SIXTH FRAMEWORK PROGRAMME
PRIORITY 3

NANOTECHNOLOGIES AND NANO-SCIENCES, KNOWLEDGE-BASED MULTIFUNCTIONAL MATERIALS AND NEW PRODUCTION PROCESSES AND DEVICES

CONTRACT FOR:

INTEGRATED PROJECT

Annex I – "Description of work"

Project acronym: DiNAMiCS
Project full title: Diagnostic Nanotech and Microtech Sensors
Proposal /Contract no: IP 026804-2
Related to other Contract no:

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DINAMICS
Diagnostic Nanotech & Microtech Sensors

TABLE OF CONTENTS

1. PROJECT SUMMARY

DINAMICS aims to promote the uptake of nanotechnological approaches by developing an integrated cost-effective nanobiological sensor for detection of bioterrorism and environmental assays. The prime deliverable is an exploitable lab-on-a-chip device for detection of pathogens in water using on-the-spot recognition and detection based on the nanotechnological assembly of unlabelled DNA. DINAMICS will integrate DNA hybridisation sensors with microfluidics and signal conditioning/processing both on silicon and polymer substrates avoiding the use of external apparatus for fluid handling, electrical signal generation and processing, based on DNA hybridisation.

A sensory breakthrough will be achieved through two complementary technological solutions: Measurements based on electrical (capacitive) signals. If hybridisation occurs between target and probe the detected change can be functionalised. Detection through UV light absorption. Based on the recognition of different UV absorptions induced by DNA hybridisation. The development of a system where each sensing site in the microarray contains a UV microfabricated sensor is a goal of the project. After DNA hybridisation the whole array is illuminated with UV light and the absorption of each site is measured by the sensor.

The project will culminate in an integrated multi-technology product that will be high-tech, low-cost and time-efficient sensing device applicable for use in the water industry *via* the co-ordination of nano- and biotechnologies with new sensory science to deliver a product that will lead to major changes in the way the testing and diagnostics of harmful substances is done. Both methodologies will ensure an additional and reliable source of cost reduction through a drastic shortening of the sensing pipeline and without the need to transfer the samples to an analytical laboratory.

2. PROJECT OBJECTIVES

The integration and application of nanotechnologies and microelectronics to biological processes and products presents potentially enormous opportunities for a host of uses in many different markets. Companies and nations investing in research and that commercialise the results early can establish market leadership that will be difficult to match. For Europe to achieve market dominance requires a coherent integration of fragmented yet world-class skills, market pull and the means to deliver the product in a timely and cost-effective way. An IP is an appropriate mechanism for achieving this. The market pull, in the context of the NMP call text 3.4.4.7, is concern over threats to the security of water supply for human consumption. This presents a major challenge to water providers and users, and of course governments, responsible for ensuring a safe and plentiful supply of water both for personal consumption and industrial use. Detector technology based around nanotechnologies and microelectronics offers a means of developing an early warning system to alert of the presence of an attack, and of sensors that identifies its nature. Successful delivery will have a major impact on the competitiveness of SME partners in the project and the European supply chain, the security of water supply in Europe, and as a consequence the confidence of consumers.

The objective of the DINAMICS project is therefore to use these technologies to develop an integrated and cost-effective nanobiological sensor for detection of bioterrorism and environmental assays. The project's prime deliverables will be exploitable prototype mobile and continuous monitoring devices for the detection of harmful substances in the water supply network. This will radically improve upon existing technologies, as it will deliver a fast, reliable and quantifiable on-the-spot recognition and detection mechanism based on the nanotechnological assembly of "unlabelled" DNA and its subsequent hybridisation.

Current technology is limited by sensor detection sensitivity, specificity and speed of response to form the efficient identification of biological agents; whilst challenges remain in the microfabrication and integration of these sensors into reliable and cost effective devices. DINAMICS will address these issues through innovative sensor techniques, using nanotechnological and an innovative approach to device integration, all supported by novel simulation tools.

To do this requires breakthroughs in:

Improved molecule manipulation and detection requiring optimisation of formation and control of DNA nanostructures. This will lead to reliable detection mechanisms based on biomolecular recognition.

Improved integration of DNA hybridisation sensors with microfluidics and signal conditioning for processing both on silicon glass or plastic substrates.

Measurements based on electrical signals. The issue here is to develop a functionalisation procedure compatible with silicon processes as well as measurement circuits that are easy to integrate.

Detection through UV light absorption. This is completely original in the field of DNA microarrays and is based on the recognition of the different UV absorptions induced by DNA hybridisation.

Project goals:

1. Identify current and anticipated end-user requirements for DNA-based detectors for the identification of specific biohazards in the context of "first response" diagnostics and continuous monitoring
2. Develop sensor technology that will provide required sensitivity and speed of response whilst compatible with integration into a low-cost, high-volume lab-on-a-chip platform
3. Demonstrate the viability of the technology developed by producing prototype devices to meet specific end-user requirement specifications

Anticipated advances on the state of the art:

1. Optimisation and integration of electronic detection techniques into microfluidic structures for DNA detection
2. Development, optimisation and integration of UV light absorption detection techniques into microfluidic structures for DNA detection
3. Nanotechnological signal amplification for label-free DNA detection
4. Development of micro- and nanofluidic multi-physics simulation tools and multi-scale modelling strategies
5. Application of nanostructures to enhance analyte capture and enhance sensor performance
6. Integration of sample preparation operations, target detection and signal processing into a simple and reliable lab-on-a chip platform
7. Development of processes and methods for high-volume production of integrated micro-electronics and polymeric microfluidic structures

Since the Stage 2 Proposal, the DINAMICS consortium, at the request of the Commission Services, has included activities towards the development of a continuous monitoring device. Since this was not discussed at that stage, a quick review of the state of the art and an outline of the S&T approach are included in this Annex.

Breakthroughs and radical innovations expected:

1. Nanotechnologically-enhanced and novel biosensor technology
2. Integration of nano-engineered structures into microfluidics-based lab-on-a-chip platform
3. Integration of microfluidic device and biosensor technology with substrate material for low-cost, high-volume production
4. "Computational nanotechnology" toolkit

Operational objectives:

These are identified on a Work Package basis **for the full 48 months** in a format suitable for Review and Assessment, in the following tables:

WP1 INDUSTRIAL REQUIREMENTS

Project objective	Operational goal and how to achieve it	Baseline data	Success measure	Risks and assumptions
Deliver Requirements Specification documents for both a mobile and continuous monitoring device by **Month 3**	Confirm pan-European water industry development priorities within technical and cost constraints, by seeking feedback from the Advisory Board on initial briefing material identifying the views of the DINAMICS team.	Mandatory routine sampling frequency against particular pathogens Typical laboratory measurement times Emergency planning protocols (which vary between countries and distribution networks)	Endorsement of User Requirement specifications by the Advisory Board	Risk: Advisory Board does not agree that both prototypes are required
Deliver Functional Specification documents for each device by **Month 5**	Translate Requirements Specifications into stretching but attainable targets in respect of target pathogens, response time, sensitivity, reliability, functionality and ease of use. Do this by iteration between quantitative analysis, conceptual design and internal peer review (including Advisory Board). Since device sensitivity and response time are parts of a trade-off, functional specification needs to be related to a mode of use, to be identified in T1.1.	Response time after a contamination incident is currently determined by the shortest of: • Lab results from next scheduled routine sampling (days to weeks) • Appearance of symptoms in public plus identification of pathogen (1-2 days) • "Fast track" sample analysis after detection of suspicious activity (0.5-1 day) and is compounded by the need for confirmation of the nature of the threat and authorisation of appropriate action. Detector response time will be limited by preconcentration and hybridisation. We anticipate 60 – 90 minutes' total detection time. The sensitivity of a sensor type refers to concentration at the sensor itself and, depending on technology, is typically around femtomolar. Device sensitivity refers to sampled concentration. This will need to be around 1 organism per ml, requiring preconcentration and/or PCR. Target species (current thinking)[1]: *Vibrio cholerae*; *Yersinia pestis*; *Salmonella spp.*; *Shigella* species; Enteric Viruses; *Cryptosporidium parvum*	Agreement on the relevance of Functional Specifications by both DINAMICS partners and the Advisory Board	Risk: functional requirement in respect of response time not achievable in practice

[1] W. D. Burrows & S. E. Renner, "Biological Warfare Agents as Threats to Potable Water", Environmental Health Perspectives, Volume 107, Number 12, Dec 99

Deliver Test Case Specifications by **Month 6**	Set requirements for lab verification tests and field trials. Tests will be designed to be representative of the scenarios envisaged in deriving User Requirements and Functional Specifications Check attainment of specifications satisfy safety requirements	Requirements specifications from Task 1.1 Functional specifications from Task 1.2	Agreement of Test Case specifications by Advisory Board	

WP2 MICRO & NANOFLUIDICS

Project objective	Operational goal and how to achieve it	Baseline data	Success measure	Risks and assumptions
Deliver comprehensive literature review on computation of diffusion at micro- and nanoscales by **Month 8**	Establish accuracy benchmark for simulation software in tasks T2.1 and T2.2	Cranfield University past experience Results in the open literature	Timely delivery	
Deliver software shell for the integration of molecular dynamics (MD) and continuum (CFD) modelling simulations by **Month 12**	Goal: development of integration shell for the MD and CFD modules (in-house and possibly adapted commercial CFD). At the start of WP2 user requirements, functional requirements and software test specifications will be produced. We will then develop, implement and test a methodology for the timely exchange of relevant information between modules operating at the discrete and continuum scales. Shell development may proceed quasi-independently of the CFD and MD modules by careful predefinition of data interfaces and the use of dummy modules that emulate anticipated behaviour.	Integration framework: none Modules for integration: disparate stand-alone programs in Fortran 90 and C++.	Attainment of thresholds defined in Test Plan	Risk: implied one-way coupling in this project limits scope for development of more comprehensive 2-way coupling approach Risk: non-availability of suitable "hooks" from commercial CFD code
Deliver MD simulation software module for description of hybridisation events, by **Month 18**	Goal: provide one half of the multi-scale simulation software dealing with the discrete scale. This will be attained by adaptation of pre-existing potential function models. By validating the MD model against test cases at high analyte concentration, the problem will not be diffusion-limited: the MD model can be decoupled from continuum diffusion and hence tested as stand-alone.	Results of literature review, above Pre-existing potential function models	Validation against experimental data for time-evolution of % hybridisation	Risk: complexity of DNA fragments and their length distribution makes generalisation difficult Risk: probe density implies possible requirement to simulate large domain in terms of number of molecules

Deliver CFD simulation software module for description of multi-species macro-molecule diffusion at the micron- and sub-micron continuous scales, by **Month 21**	Goal: provide second half of multi-scale simulation dealing with the continuum scale. This will be attained by formulation of a new set of conservation laws and their solution procedure, based on existing experience at Cranfield. Comparative assessments will be made with commercial CFD code customised with user-defined functions. The validation requirement for a diffusion model is the attainment of a measurable steady state concentration profile. This can be provided by introducing a dilute analyte solution to a junction in a microchannel and monitoring steady-state % hybridisation at sensors arrayed along its length.	Results of literature review, above Existing methods developed by Cranfield's computational group	Validation against experimental steady state concentration data NOTE: timing of demonstration of this success metric depends on the availability of sensors in a microchannel from WP4 and 5, and hence delays delivery of the objective to Month 21.	Risk: algorithms in commercial code insufficiently accurate or robust for purpose, so that reliance is solely on in-house code: may imply more attention to front-ending: Assumption: validation data available
Deliver multi-scale modelling software suite by **Month 26**	Goal: integration of validated MD and CFD modules into a debugged integration shell. This will be attained by developing each element separately, as outlined above and validating against suitable test cases involving the dynamics of diffusion-limited hybridisation. Note: the same test cases can be used as for the CFD validation, this time concentrating on the time-evolution of % hybridisation, rather than the steady-state final values.	Integration shell, MD and CFD modules (see above)	Validation against experimental data	Assumption: validation data available
Deliver final guidelines on physical configuration of functionalised surfaces, microchannel layout and porous nanostructure to optimise diffusion and mixing, by **Month 36.**	Goal: application of multi-scale modelling software to the optimisation of microfluidics and sensor design. Whilst guidance will be provided throughout years two and three of the project from simulations using tools at their current state of development, systematic optimisation will be attainable by use of the multi-scale modelling suite from month 26 onwards. The principal approach will be sensitivity analysis and parameter variation to explore principal functional dependencies and thereby to gain early indications for performance improvement strategies	Models and software merging from WP2	Reduce sensor response time from un-optimised prototype by a factor of five.	Risk: delays in validation data or software development cause delivery too late in project for useful contribution to optimisation except by partially-validated tools.

WP3 MICROBIOLOGY & SAMPLE PREPARATION

Project objective	Operational goal and how to achieve it	Baseline data	Success measure	Risks and assumptions
Deliver a list of genes that is predicted by bioinformatics methods to be adequate for identification of each target species, by **Month 8**	Goal: gene selection adequately specific for species identification In order to design probes for target organisms (T3.2) their DNA sequence has to be available. A database search will be conducted to find all publicly available sequences.	Database Searches allow the retrieval of available sequences. Bioinformatics methods allow the assessment of the uniqueness of the sequences.	Probes can be designed that are at least 10% different from non-pathogen related species.	Risk: necessary sequence data are not publicly available and have to be sequenced. Risk: the selected genes are too similar to related non-pathogenic species causing cross-reactivity.
Deliver report on sample collection methodology by **Month 12**	Goal: identification of appropriate methodologies for collecting or preparing samples for testing. Sample collection will be in two ways: Model samples and natural water. Verification, monitoring and data acquisition will use natural sources. A sampling plan will be elaborated starting with the testing of the device. The bulk of samples will consist of untreated source water, treated water and water from points of consumption.	Sample collection plans and protocols are available for routine water monitoring.	The sample collection protocol allows for a 50% recovery of spike pathogens.	Assumption: model samples reflect natural waters.
Verify optimum preconcentration route by **Month 15**	Goal: preconcentration of extremely dilute specimen to give sufficient number of pathogens for detection in the typical microlitre quantities submitted to the device. This will be achieved by filtration, which may be the critical item in establishing detector response time.	Systems for laboratory use and for pharmaceutical production (sterile filtering) are available offering up 99% virus removal.	A preconcentration of pathogens by a factor > 1,000	Assumption: available systems can be adapted to the needs of water monitoring.
Identify and verify most appropriate lysis method by **Month 17**	Goal: to make RNA or DNA fragments of the biological material accessible for hybridisation in a manner suitable for integration with lab-on-a-chip technology. Our preferred approach to lysis is sonication, for which optimisation of power and frequency is required. Enzymatic or chemical approaches are fall-back options.	Many standard methods are available and can be adapted to DiNAMiCS needs.	Spiked amount of cells or particles reach 90% of the signal of spiked DNA.	Risk: incomplete lysis reduces availability of DNA and RNA for hybridisation. Assumption: if chemicals lysis is required, substances can be identified that are compatible with downstream processes.

Deliver probes for all target analytes by **Month 18**	Goal: design probes for all target species for incorporation into prototype devices in WP6. This will be achieved by bioinformatics methods and subsequent experimental verification.	Bioinformatics methods currently allow the prediction of useful probes with 80% success rate limiting the necessary bench work.	Probes are 95% specific	Risk: sequence data have varying degrees of quality. Risk: unspecific hybridisation or low signal
Provide on-chip PCR system by **Month 24**	Goal: provide back-up strategy in case sensitivity thresholds cannot be met. Thresholds can be met by nucleic acid amplification.	Successful designing of PCR primers is a standard procedure for the partners involved.	Sufficient amplification starting from less than 1,000 copies of target DNA	Risk: unspecific priming and low yield

WP4 SENSOR & SIGNAL DETECTION DEVELOPMENT

Project objective	Operational goal and how to achieve it	Baseline data	Success measure	Risks and assumptions
Finalise substrate surfaces and immobilisation methods for final selection of probes by **Month 27**	Goal: identify surface preparations for low cost substrate materials that are compatible with proposed immobilisation techniques. This will be achieved by characterisation of surfaces prior to and after functionalisation with probes and will involve fundamental research on test surfaces, and applied research on the surfaces of microfabricated devices. Dummy sequences will be used early in the programme to allow development to proceed independently of the final probes, available in Month 18	Many chemistries for DNA immobilisation are available.	The surface chemistry allows immobilisation of (modified) DNA. The surface are in 80% compliance with the specification needed for the detection methods	Risk: inhomogeneous surface functionalisation
Deliver working UV sensors on polymeric substrates by **Month 27**	Goal: develop novel UV sensor technology compatible with low-cost substrates This will be achieved in two stages, firstly by developing the fundamental detection science in quartz or glass, then transport it to polymeric substrates.	Current large volume UV photometers have a sensitivity of *ca*. 100 nM in 1 cm path length for DNA (from 1,000-mer down to 20-mer molecules).	Two order of magnitude improvement in sensitivity	Risk: inability to achieve sufficient sensitivity
Deliver working capacitive sensors by **Month 27**	Goal: develop capacitive detection methods Work will concentrate on testing of detection techniques, on macro-scale surfaces hard-wired to external measurement instruments through the use of custom-built macro-flow-cells. Miniaturisation will take place in Task 4.6	Current capacitive sensors have sensitivities in the nanomolar range.	Two order of magnitude improvement in sensitivity	Risk: inability to achieve sufficient sensitivity
Demonstrate significant signal enhancement by use of nanotechnological strategies by **Month 30**	Goal: reduce need for sample preconcentration by increasing sensor sensitivity by nanotechnological enhancement strategies This will be achieved by molecular recognition/self-assembly events using functionalised nanoparticles.	Currently available signal amplification methods have an amplification factor of ≤100.	Enhancement of the signal by a factor > 100	Risk: enhancement yield is too low, or kinetics too slow

Demonstrate feasibility of sensitivity/response time enhancement by use of nanoporous probe support structures by **Month 30**	Goal: improve analyte capture efficiency This will be achieved by reducing the diffusion distance from "bulk" to sensor surface, by using nanoporous structures	Open channel, sensor is a spot.	Functional nanoporous sensor with factor > 5 improved sensitivity or reduced response time	Risk: unable to functionalise nanoporous structures *in situ*. Risk: incompatibility with detection techniques
Produce signal pre-processing circuitry integrated on-chip with scaled-down sensors and defined software/hardware interface by **Month 30**	Goal: provide reliable signal processing for integration on chip with sensors and interfacing with software for prototypes in WP6 This will be accomplished in stages, initially on a board with dummy sensors emulating the appropriate signal strength and signal-to-noise characteristics.	External processing *via* cards in PC	Customised and optimised signal preprocessing on the biosensor chip operates properly with compatible dedicated microcontroller based signal reader and processor device having own user interface and data communication towards external devices and the results are displayable on a remote PC.	Risk: the size/fabrication technology/cost requirements of the envisaged biosensor chip will not allow the integration of an optimal signal preprocessing circuitry
Produce micro-scale capacitive and UV sensors integrated on chip by **Month 33**	Goal: provide core sensor technology, miniaturised for use in prototype detectors Miniaturisation will be achieved in successive steps. Nanotechnological signal enhancement strategies will be incorporated in later stages as they become available from Task 4.4.	Millimetre-scale sensors, macroscopic wiring	Micron-scale sensor dimension with integration of sensor and wiring on polymer substrate	Assumption: assembly methods are available

WP5 ENGINEERING

Project objective	Operational goal and how to achieve it	Baseline data	Success measure	Risks and assumptions
Deliver interim report on design methodology by **Month 12**	Goal: identify appropriate methods for coherent concurrent engineering science methodology for robust biosensor device design A key to achieving this demanding objective is the early education activities planned in WP7, since there is a wide variety of expert disciplines contributing to this effort. Whilst timing of this report is early in the task, it is important that the thinking process is recorder to inform other activities and communication protocols in the rest of WP5.	Functional specifications from Task 1.2 Internal progress reports on current tools and design methods from WP3 and 4	Peer review by Project Steering Committee.	Risk: gulf of comprehension between disciplines impedes development of effective concurrent engineering methodology Risk: activity regarded as of low importance
Deliver report on design methodology by **Month 21**	Goal: expand and revise interim report in the light of research results in technology and innovation work packages, incorporate nanotechnological developments from WP4 and use of simulation tools from WP2	Interim report Project progress reports	Peer review by Project Steering Committee	Risk: report identifies conflicts in proposed timings of information/hardware exchange requirements
Deliver robust microfluidics solutions to all on-chip fluid-handling operations by **Month 25**	Goal: deliver optimised manufacturable microfluidic solutions to all relevant tasks compatible with device integration considerations. Achieve by a combination of experimental and simulation work and provide validation data for CFD codes in WP2.	Successful operation of modules has been demonstrated among partners	Compliance with functional specifications	Risk: fluidics control is not compatible with sensors (voltage of electrokinetic force). Risk: bubble formation and leakage at interfaces Risk: transfer of glass-based expertise to polymeric chips

Deliver final decision on chip materials by **Month 27**	Goal: reconcile requirements of integrated sensors and electronics with manufacturing routes and cost considerations Achieve by experimental investigation of manufacturing and assembly issues for candidate materials identified WP4	Plastic microfluidic parts have already been manufactured with structure dimensions relying on process of mould making. Various methods have been described to include wiring onto microstructures Candidate materials from WP4	Parts and components delivered according to functional and reliability specifications.	Risk: ideal dimensions (as specified by simulation) cannot be manufactured in desired quality. Risk: cannot manufacture in WP4 candidate materials (driven by probe immobilisation, and integration of electronics)
Demonstrate reliable remote operation of filter-handling, sample collection, transfer and disposal operations by **Month 34**	Goal: provide reliable and robust automation solutions for the continuous monitoring device	Manual transfer of samples for bioassay Automated fluid-handling in a device for chemical toxin monitoring developed in the EC-funded AWACSS project	Compliance with functional specifications	Risk: introduction of air bubbles in the microfluidics device Risk: reliability impaired by clogging due to particles in natural waters Risk: regeneration cycles too long
Deliver hardware abstraction layer and device driver modules for embedded systems by **Month 32**	Goal: ensure maximum potential for accommodating hardware developments and new devices By introducing a hardware abstraction layer into the architecture of the embedded system, new devices can be readily accommodated by providing a device-specific driver library.	User requirements specification Commercial operating system as a development platform Data interface with detector electronics and associated protocol	"Client" testing and verification by BME	Risk: poorly-defined user requirements Risk: data interface and protocols not ready on time

Deliver documented beta release user interface software by **Month 32**	Goal: provide user-friendly interface for mobile device and integrate with remote control system for continuous monitoring device. Building on user and software requirements specifications, the software will handle "true/false" decisions on event detection and initiate communications protocols as well as responding to user commands.	User requirements specification Software requirements specification	Software demonstration Peer review of documentation by Project Steering Committee	Poor definition of user interface
Deliver report evaluating performance on Integration issues by **Month 33**	Goal: As the outcome of the "integration" task, the report will provide feedback on the implementation of the concurrent engineering approach identified in Task 5.1 The integration task stands between design methodology in Task 5.1 and prototype development in WP6. It attempts to reconcile and pull together the various pieces of technology developed in the innovation and R&D work packages. Given the strongly multidisciplinary and innovative nature of the project, it will be valuable to consolidate experience gained in design and development into a report with guidelines for similar future projects	Design methodology from Task 5.1 Research results from T4.6 and the other engineering tasks in WP5 Progress reports from WP6	Peer review report Specifications report on systems, components and integration of the overall solution.	Assumption: reconciliation of design, manufacturing and assembly issues is possible Risk: poor specifications of control algorithms and hardware/software interfacing
Deliver report on "cost engineering" by **Month 42**	Goal: identify potential for commercial production of device Approach: identify cost-saving opportunities in manufacturing and assembly methods, materials, supply chain integration plus opportunities arising from volume production. Take into account forecast cost trends.	Candidate designs and assembly methods Engineering design methodology Current capabilities of industrial technologies	Cost 30% below original costs at outset of task.	Risk: changes in specifications Risk: changes in the market situation increasing prices Risk: lack of regulatory driving force makes minimum cost exceed market value

WP6 INDUSTRIAL DEMONSTRATION & VALIDATION

Project objective	Operational goal and how to achieve it	Baseline data	Success measure	Risks and assumptions
Deliver first version of the Development Plan for the mobile and continuous prototypes, by **Month 12**	Goal: Clearly timed plan synchronised with anticipated availability of key deliverables from other Work Packages. This will require close co-operation with task leaders in WP3-5, who will convene meeting(s) dedicated to this purpose.	48-month and detailed implementation plans for WP3-5 Functional Specifications from WP1	Peer review by Project Steering Committee	Risk: plan highlights possible time scheduling clashes
Deliver first version Test Plan for both devices by **Month 12**	Goal: clear timed plan for ensuring that functional specifications are met in the laboratory environment then in the field. This will take into account practicalities such as availability of test materials, clearance for their safe usage and identification of field test sites and methods that ensure compliance with statutory safety requirements.	Functional and Demonstration Case specifications from WP1	Peer review by Project Steering Committee and Advisory Board	
Deliver second version of Development Plan for both devices by **Month 24**	Goal: revise first version in the light of progress against technical objectives in WP3-5. This will be achieved by convening special meeting(s) of WP3-5 leaders.	First version Monthly Project progress reports	Peer review by Project Steering Committee	Risk: plan highlights possible new time scheduling clashes
Deliver second version Test Plan for both prototype devices by **Month 30**	Goal: account for any changes to device specifications and/or relevant regulations	First version Updates on regulation from Knowledge Manager and Advisory Board	Peer Review by Project Steering Committee and Advisory Board	
Produce working prototype mobile device ready for field testing by **Month 40**	Goal: Produce a prototype device sufficiently developed for field testing after laboratory verification. Drawing on tools and expertise collated in WP5, and working to the Development Plan, construction of the prototype is expected to be incremental and involve separate development and testing of modular sub-assemblies. We anticipate further incremental improvements after the first round of verification testing, starting Month 30.	Version 1 Development Plan and subsequently, Version 2 Sensors and subsystems from WP3-5	Performs to Test Plan specifications Results published	Assumption: all sub-assemblies and technologies are in place on time

Produce working prototype continuous monitoring device by **Month 36**	Goal: Produce a prototype device sufficiently developed for field testing after laboratory verification. Drawing on tools and expertise collated in WP5, and working to the Development plan, construction of the prototype is expected to be incremental and involve separate development and testing of modular sub-assemblies. We anticipate further incremental improvements after the first round of verification testing, starting Month 36.	Version 1 Development Plan and subsequently, Version 2 Sensors and subsystems from WP3-5	Performs to Test Plan specifications Results published	Assumption: all sub-assemblies and technologies are in place on time
Complete field trials of automated continuous device by **Month 41**	Goal: Demonstrate feasibility and reliability of rapid DNA-based biohazard identification device, by implementation of the test Plan	Prototype performance verified in laboratory	Performs to Test and User Requirements specifications Results published	Risk: delay in availability of prototypes
Complete field trials of mobil device by **Month 45**	Goal: Demonstrate feasibility and reliability of rapid DNA-based biohazard warning device, by implementation of the test Plan	Prototype performance verified in laboratory	Performs to Test and User Requirements specifications Results published	Risk: delay in availability of prototypes

WP7 KNOWLEDGE MANAGEMENT

Project objective	Operational goal and how to achieve it	Baseline data	Success measure	Risks and assumptions
Preparation of technology route map by **month 10**	T7.2 Exploitation, using expertise in the project to define technology/infrastructure/market plan for development and exploiting the results of the project.	Survey of partners' and others' know-how Structured workshop using TRM principles	Coherent route map that will aid identification of IP and research opportunities	Risk: Incomplete skills set to prepare route map
Set up public and partner web site	T7.4 Dissemination, through a web site structured to disseminate and exchange information	Structure agreed by partners Partners' web page Links other relevant networks	Public access dissemination route Partner information exchange platform	Assumes regular input from contractors
Deliver first version of Exploitation Plan by **month 12**	T7.1 IP management and T7.2 Exploitation to develop an outline of the key exploitable technologies to be developed in or used to exploit the IP from the project	Technology route map Patent and technology survey	Acceptance by peer review of the plan	Risk: Conflict of interests from partners. Incomplete survey of competing IP.
Hold three training workshops over term of project	T7.3 Training workshops: organise and run internal training to aid cross-learning between partners	Partners will run this who is well experienced in workshop events management	Attendance from key partners and raising level of their understanding of wider technology issues	Risk: Failure to run these in time with the plan
Deliver final version of Exploitation Plan by **month 42**	Goal: T7.2 Exploitation to develop a final plan for downstream exploitation of project results	Continued input from IP surveys Results from WPs where IP can be protected	Acceptance by peer review of the plan. Clear plan for manufacture of device(s). Clear plan for further research and development	Risk: Conflict of interests from partners resulting in no agreement

WP8 CO-ORDINATION

Project objective	Operational goal and how to achieve it	Baseline data	Success measure	Risks and assumptions
Confirm technical and operational and goals and administrative procedures	T8.1.1: LAM will organise the project's kick-off meeting, with SEZ providing administrative/logistical support	Project plan	High level of interaction between partners. Minutes circulated promptly. Issues and questions resolved quickly	Participation by all partners. High level of preparation prior to the meeting.
Management of administrative activities	T8.1.2: SEZ will establish an internal DINAMICS management team at their premises	Co-ordinator experienced in framework programme activities	Efficient communication between partners. Support to the co-ordinator	Failure of partners to provide requested information on time. Good planning will minimise this risk
Effective dissemination to public and information flow between partners	T8.1.3: A DINAMICS web site will be established by SEZ, by Month 2 of the project.	The co-ordinator is very experienced in public dissemination and maintaining internal communication through project web sites.	Acceptability of design, ease of use, intensity of use, reaching an audience beyond the partners	Minimal risk, Assumes partners provides information as requested
Active management of project against measurable targets, means of monitoring, resolution of problems	T8.1.4: At Month 6 a PSC meeting will be held to review progress.	DINAMICS project plan	Evaluation of results against the project planned timescale	Failure to meet planed activities, Technical hurdles require adaptation of planed activities. DINAMICS engages with mitigation plans.
Active management of project against measurable targets, means of monitoring, resolution of problems,	T8.1.5: At Month 12 the co-ordinator will organise and direct the first annual review.	DINAMICS project plan	Evaluation of results against the project planned timescale	Failure to meet planed activities, Technical hurdles require adaptation of planed activities. DINAMICS engages with mitigation plans
Active management of project against measurable targets and Commission requirements	T8.1.6: At Month 18 a PSC meeting will be held to review progress.	DINAMICS project plan	Evaluation of results against the project planned timescale	Failure to meet planed activities, Technical hurdles require adaptation of planed activities. DINAMICS engages with mitigation plans
Secure manufacturer into project	Exploitation to develop an outline of the key exploitable technologies to be developed in or used to exploit the IP from the project	Discussion with several manufacturers during contract negotiation phase	Manufacturer secured for Board or technical involvement by Month 12	Risk: Development not aligned with manufacturer's needs

3. PARTICIPANT LIST

List of Participants

Participant Role*	Participant Number	Participant Name	Participant Short Name	Country	Date enter Project Month	Date Exit Project
CO	1	Lambda GmbH	LAM	A	1	48
CR	2	BHR Group	BHR	UK	1	48
CR	4	Idea s.r.l.	IDEA	I	1	48
CR	5	Hemosoft	HEM	TR	1	48
CR	6	MikroMikoMed Ltd.	MMM	HU	1	48
CR	8	JP Industrietechnologie und -anlagen GmbH	JP	D	1	48
CR	9	Water Research Institute Bratislava	WRI	SK	1	48
CR	10	Università di Bologna	UNIBO	I	1	48
CR	11	Budapest University of Technology and Economics	BME	HU	1	48
CR	12	Cranfield University	CRAN	UK	1	48
CR	15	Steinbeis-Europa-Zentrum	SEZ	D	1	48
CR	16	LioniX B.V.	LIONIX	NL	1	48
CR	17	Microtronics Engineering	MICRO	A	13	48
CR	18	Provenion	PRO	D	14	48

* CO=Co-ordinator
CR=Contractor

4. RELEVANCE TO THE OBJECTIVES OF THE NMP PRIORITY

RELEVANCE

The primary objective of the NMP thematic area is to promote real industrial breakthroughs, based on scientific and technological excellence. DINAMICS's research has been designed to be complementary through the creation of new knowledge and the integration and exploitation of existing and new knowledge in a nanotechnological warning systems with advanced sensor technology.

The DINAMICS project is focused directly on addressing the scientific, technical and wider societal objectives of the NMP Call text 3.4.4.7.

The nanotechnology industry will benefit from understanding and mastering on-demand manipulation of nanoparticles and the consequent exploitation of the formed nanostructures. An unprecedented integration of state-of-the art nanoscience (self-assembly and supramolecular chemistry) with the novel signal detection and microtechnologies will be reached.

This is an industrially- and SME-driven project that will culminate in an exploitable product to enable reliable testing for the safety of water supplies. The integration of sensors and fluidics into flexible cheap and disposable materials, such as glass or plastic substrates, will avoid the need for any external apparatus with fluid handling and electrical signal generation processing. Both methodologies will ensure an additional and reliable source of cost-reduction through a drastic shortening of the sensing pipeline and without the need of transferring the samples to an analytical laboratory. This will help achieve objectives of sustainable development.

The uptake in the existing microelectronic industries of the nanobiotechnologies developed by the present project will lead to a change in water safety and environmental testing. This change will drive the European leadership in a very strategic field of application that is going to have a great impact on health risks associated with water contamination and on the quality of life.

Multifunctionality: DINAMICS supports the uptake and integration of nanotechnologies into existing industrial sectors; indeed, this is one of the key innovations of the project. It aims to harmonise and improve methods for detection and measurement standards through the use of multidisciplinary technology detection platforms. The developed technologies will be amenable to simple adaptation for different kinds of tests on different families of molecules (RNA, protein, other macromolecules), by developing different sensing layers, by choosing different options for the signal enhancer molecules, and by tailoring the signal conditioning electronics, while retaining the same detection technology.

The project results will enhance future European industrial potential in the field of security research by combining multisectoral activities, thus providing new knowledge that can be used, for example, in preparation for the future European Security Research Programme.

Relevance to the aims of IPs for SMEs:
The project integrates nine high-tech SMEs, which are leaders in the domain of nanofluidics, advanced biotechnological sensors and miniaturisation as well as in the management of large international RTD projects. The SMEs active in the domain of nanotechnology and biotechnology needs to achieve a higher technological maturity of their product developments in order to achieve a commercial market breakthrough with their products and secure their market position. The European start-ups have often the best technological knowledge, but have difficulties to overcome the barriers for market entry and to transfer it in a commercial product. The DINAMICS project will help them to apply their very innovative developments in a concrete advance warning system, *i.e.* for some of them to quit the start-up phase. The nine SMEs constitute 56% of the consortium and will play the leading role in innovation, co-operation, management and exploitation. SMEs will benefit from the IP by developing novel ideas and having direct access to latest scientific research and importantly from exploitation of the project's results. The project will improve the competitiveness of the

participating SMEs by enabling each to focus on its core expertise and together to gain access to markets not available to any of them individually. The SME contribution to DINAMICS will therefore be as technology providers, scientific researchers, developers, verifiers, end-users and co-ordinator.

Target species and their detection:
At the outset we recognised that the selection of bioterrorism and environmental assays to be included into DINAMICS was of great importance, as many thousands of potential contaminants exist. The project team consulted widely to determine the most appropriate ones to focus on. It was necessary to ensure (i) EU resources are to be used effectively; (ii) consumer protection is to be enhanced; and (iii) SMEs benefit from participation.

Preliminary species targeted for detection were considered on the basis of the following considerations:

- Pathogenicity: severity of the disease, mortality rates
- Infectious dose: how many pathogens have to be ingested to cause a disease
- Incubation period: time between exposure and onset of symptoms
- Attack rate: is human-to-human transmission possible and how easily after infection?
- Difficulty to treat: are antibiotics or medication available, when does it have to be administered?
- Environmental stability: survival time in drinking water supply
- Disinfection efficiency: by chlorine or other means
- Frequency of natural outbreaks as monitored in national surveillance schemes
- No reliable screening methods are currently available
- Legislation: are pathogens currently regulated (or are expected to be in near future) in EU or national legislation?

Prokaryotes	Virus	Eukaryotes
Pseudomonas aeruginosa	Adenovirus	*Entamoeba histolytica*
Mycobacterium avium complex (MAC)	Enterovirus	*Giardia lamblia*
Escherichia coli O157:H7,	Calicivirus	*Cryptosporidium parvum*
Enterohaemorrhagic *Escherichia coli* EHEC	Hepatitis A	*Isospora belli*
Salmonella spp.,(*Salmonella typhimurium, Salmonella enterica* serotype *Typhi* strains)	Hepatitis E	*Balantidium coli*
Campylobacter spp.,	Norwalk virus	*Microsporidia spp. (Encephalitozoon intestinalis)*
C. jejuni	Norwalk-like caliciviruses (NLV)	*Acanthamoeba keratitis*
Toxoplasma gondii.	Rotavirus	*Sarcocystis hominis*
Vibrio cholerae	Echo virus	*Sarcocystis suihomini*,
Vibrio parahaemolyticus	Coxsackie virus	*Cyclospora cayetanensi*
Aeromonas hydrophila	Reovirus	
Shigella sonnei	Polio	
Legionella spp		
Helicobacter pylori		
Shigella flexneri		
Yersinia enterocolitca		
Stenotrophomonas maltophilia,		
Chryseobacterium spp.		
Brucellosis		

The first meeting of the Advisory Board representing all stakeholders will weigh all criteria above to choose the pathogens whose monitoring will have the highest impact on the safety of drinking water supplies.

Whilst the techniques will be developed against some priority assays, it is envisaged that the new bioanalytical methods will be equally applicable to

- Other kinds of water analysis, such as bottled water, drinks industry, etc.
- Different sample matrices: e.g. air , soil, etc
- A wider range of pathogens, e.g. newly emerging pathogens
- A wider range of applications: like medical diagnosis, hygienic monitoring of food processing or pharmaceutical production

This high adaptability to different purposes is on the one hand due to the inclusion of microarray technology and on the other hand the modular construction concept:

- By adapting only the first steps in the analytical procedure the device can be adapted to different matrices (changing the sampling procedure and the sample introduction method)
- Microarrays facilitate the parallel and independent detection and identification of pathogens. By adding more probes additional pathogens can be detected at marginal costs. By changing DNA probes the microarray can be easily adapted to natural mutation in the DNA sequence without affecting the remainder of the assay.
- By simplifying and adapting the sample preprocessing the technology can also be adapted to other fields of applications. This includes also a change in the probes to reflect the different pathogens of interest.

Anticipated advances on the state of the art:

1. **Optimisation and integration of electronic detection techniques into microfluidic structures for DNA detection**
2. **Development, optimisation and integration of UV light absorption detection techniques into microfluidic structures for DNA detection**
3. **Nanotechnological signal amplification for label-free DNA detection**
4. **Development of micro- and nanofluidic multi-physics simulation tools and multi-scale modelling strategies**
5. **Application of nanostructures to enhance analyte capture and enhance sensor performance**
6. **Integration of sample preparation operations, target detection and signal processing into a simple and reliable lab-on-a-chip platform**
7. **Development of processes and methods for high volume production of integrated microelectronics and polymeric microfluidic structures**
8. **Development of continuous monitoring and identification system for water-borne biological pathogens**

CURRENT STATE OF THE ART

1. Integrated electronic detection in microfluidic structures

State of the art

Electrochemistry has superior properties over many other existing measurement systems, because electrochemical biosensors can provide rapid, simple and low-cost on-field detection. Consequently, attempts have been made towards the full electronic detection of nucleic acids and proteins [1]. The sensitivity is still far from optimal: more than 10^4 analyte molecules are required for detection [2], necessitating the introduction of electroactive, enzymatic or nanoparticle labels to produce a measurable signal.

The advantages and disadvantages of various electrochemical detection methods are discussed by Drummond *et al* [3] and summarised in the table on the following page, adapted from this reference. Specific variants are discussed, for example, in references [4, 5] which review recent developments in impedimetric biosensors, and Berggren *et al.* [6] who review capacitive approaches.

Type of sensor	Advantages	Disadvantages
Direct DNA electrochemistry	Highly sensitive (femtomoles of target); requires no labelling step; amenable to a range of electrodes	High background signals; cannot be multiplexed; destroys the sample
Indirect DNA electrochemistry	Highly sensitive (attomoles of target); usually requires no labelling step; multiple target detection at same electrode	Probe substrate can be difficult to prepare; destroys the sample
DNA-specific redox indicator detection	Moderate to high sensitivity (femtomoles of target); well suited to multiple target detection; samples remain unaltered	Chemical labelling step required unless "sandwich" method used; sequence variations can be problematic
Nanoparticle-based electrochemistry amplification	Extremely sensitive (femtomole to zeptomole range, 10^{-15} to 10^{-21} moles); well suited to multiple target detection with different nanoparticles	Many development steps in assay; reliability and robustness of surface structures problematic; sample usually destroyed
DNA-mediated charge transport	Highly sensitive (femtomole range) and simple assay; requires no labelling; uniquely well suited for mismatch detection; sequence independent; amenable to multiplexing; applicable to DNA-protein sensing step	Biochemical preparation of target sample required
Detection of hybridised DNA by electrical capacitance	Requires no labelling	Interaction of biological materials with electrode can cause instabilities in measured capacitance; requires digital "embedded system" for data handling

Approach to advancing state of the art

We will pursue a biosensor for capacitive detection of biochemical reactions, where the principle is the modification of the permittivity of the space between electrode pairs by changes to their (functionalised) surfaces engendered by hybridisation events. The resulting change in capacitance can be converted into an electric signal that can easily be processed by an electronic circuit.

Developing a functionalisation layer is a key step for sensitive and satisfactory sensor performance. Chemistries must be selected that simultaneously: 1) allow immobilisation of biological species, 2) partly define the electronic properties of the sensor and 3) avoid degeneration of biological layers.

Circuit design should consider achieve required accuracy, minimise cost, handle noise, and permit integration (electronics preferably on a silicon chip). An aspect of great importance is the determination and elimination of parasitic parameters.

The influences of temperature and humidity on the biosensor have to be quantified and handled and mechanical and environmental factors controlled.

References

[1] Eugenii Katz, Itamar Willner, "Probing Biomolecular Interactions at Conductive and Semiconductive Surfaces by Impedance Spectroscopy: Routes to Impedimetric Immunosensors, DNA-Sensors, and Enzyme Biosensors", *Electroanalysis*, 2003, **15, No. 11**

[2] C. Guiducci *et al.*, "DNA detection by integrable electronics," *Biosensors and Bioelectronics*, 2004, **19 (8)**, 781–787

[3] Drummond *et al.*, *Nature Biotechnology*, 2003, **21 (3)**, 1192 – 1199
[4] Kerman *et al.*, *Meas. Sci. Technol.*, 2004, **15**, R1 – R11
[5] Guan *et al.*, *J. Biosci. & Bioeng.*, 2004, **97 (4)**, 219 – 226
[6] Berggren *et al.*, *Electroanalysis*, 2001, **13**, 173 – 180

2. UV light absorption detection technique

State of the art

Whilst fluorescence labelling of hybridised target molecules [1], is sensitive and accurate, confocal fluorescence scanners remain costly and cumbersome, preventing the use of DNA chips as a decentralised testing tool. Miniaturisation of laser fluorescence is not straightforward, since it involves the design of ultra-sensitive, low-noise photodiodes with on-chip filters. Therefore researchers often combine capillary electrophoresis with end column detection [2]. Recently several attempts have been made to integrate hydrogenated amorphous silicon photodiode detectors for fluorescence detection on the chip [3]. Optoelectronic DNA chips using CMOS photodetectors have been used on a chip in combination with enzyme-catalysed chemiluminescence [4].

Light absorption detectors using quartz as a substrate have seen improved signal-to-noise ratio by using an optical slit on the microchip to cut off stray light [5]. Monolithic integration of silicon substrate has been accomplished using an optical fibre to enable alignment-free operation [6]. Other optical detection principles used for detection on microfluidic structures are optical interferometry [7]; changes in the apparent colour of thin film of porous silicon [8] due to changes in the refractive index; surface plasmon resonance techniques of biomodified gold thin films [9]. First attempts have been made to enhance the detection by monolithic silicon optoelectronic transducer with gold nanoparticles [10].

Extended standard CMOS technology has been used to integrate light source and photodetector with a microfluidic device for absorption measurements [11]. Integrated semiconductor fluorescence sensors usually suffer from high excitation laser background that only can be overcome by improvements of the excitation filters [12, 13]. Further improvements can be obtained with different doping for the photodetector [14]. Even integration of laser sources on the chip using vertical cavity surface emitting lasers has been demonstrated [13].

Approach to advancing state of the art

The measurement of absorption of ultraviolet by species in solution provides one of the most widely used and cost effective methods of quantitative analysis available in analytical laboratories. The optical absorption properties of a transparent substrate with a functionalised surface are changed on hybridisation. The aim is to develop label-free molecular detection on low-cost high-parallel optoelectronic devices using nucleic acids to absorb 260 nm ultraviolet light strongly. The absorption of UV light passing through a layer of DNA molecules, immobilised on a substrate, would be characterized by an extremely high concentration and a very short optical path. In particular, for a layer density of 10^{13} molecules/cm^2 (which corresponds to the density of oligonucleotides immobilised on quartz substrates), concentration can be evaluated as 0.03 M and optical path as 5 nm. Therefore, absorbance is expected to be around 10^{-3}. Previous results on measurement of DNA layer absorbance of non-covalently bound molecules are reported in [15, 16], but exhaustive quantitative analysis has not been performed. This direct-detection approach, which relies only on DNA molecular absorption, will be developed in parallel with the nanotechnological signal amplification approach described below (see next subsection). The nanotechnological signal amplification will be tailored specifically to bring a high number of UV-absorbent molecules onto the sensing device.

Amorphous silicon photodetectors are planned because:

- Low-cost material, low-temperature deposition process: PECVD (Plasma-enhanced Chemical Vapour Deposition)
- Deposition compatible with low-cost substrates with predeposited conductor film
- Fabrication on substrates of any size
- Device implementation can be tuned to improve resolution or selectivity in UV range.

Hydrogenated amorphous silicon (a-Si:H) has been widely investigated as a material for large area applications. In particular, due to the high absorption coefficient of the active layer, amorphous silicon photodetectors have been very successful in photo-sensing arrays [17, 18, 19]. UV photosensors made from thin films of a-Si:H and a-SiC:H can be deposited on an electrode of conducting material by PECVD. A key research issue is the trade-off between the electronic and optical requirements, regulated by the thickness and impurity concentrations of the p-doped layer.

References

[1] M. Schena, & R.W. Davies, "Technology Standards for Microarray Research", in *Microarray Biochip Technology*, M. Schena (Ed.), 2000, Eaton Publishing, Natick, USA

[2] Y.W. Lin, T.C. Chiu & H.T. Chang, "Laser-induced fluorescence technique for DNA and proteins separated by capillary electrophoresis", *J. Chromatogr. B. Analyt. Technol. Biomed. Life Sci.*, 2003, **793(1)**, 37 – 48

[3] T. Kamei *et al.*, "Integrated hydrogenated amorphous Si photodiode detector for microfluidic bioanalytical devices", *Anal. Chem.*, 2003, **75 (20)**, 5300 – 5305

[4] F. Mallard *et al.*, "Optoelectronic DNA chip: high performance chip reading with an all-electric interface", *Biosens. Bioelectron.*, 2005, **20 (9)**, 1813 – 20

[5] H. Nakanishi *et al.*, *Electrophoresis*, 2001, **22 (2)**, 230 – 4. Related Articles, Links Fabrication of quartz microchips with optical slit and development of a linear imaging UV detector for microchip electrophoresis systems.

[6] K.B. Mogensen *et al.*, *Electrophoresis*, 2001, **22 (18)**, 3930 – 3938. Related Articles, Links Monolithic integration of optical waveguides for absorbance detection in microfabricated electrophoresis devices.

[7] V.S. Lin *et al.*, *Science*, 1997, **278 (5339)**, 840 – 843. Related Articles, Links A porous silicon-based optical interferometric biosensor.

[8] R. Jenison, M. Rihanek & B. Polisky, "Use of a thin film biosensor for rapid visual detection of PCR products in a multiplex format", *Biosens. Bioelectron.*, 2001, **16 (9-12)**, 757 – 763

[9] R.J. Heaton, A.W. Peterson & R.M. Georgiadis, "Electrostatic surface plasmon resonance: Direct electric field-induced hybridisation and denaturation in monolayer nucleic acid films and label-free discrimination of base mismatches", *PNASm*, 2001, **98 (7)**, 3701

[10] K. Misiakos *et al.*, *Anal. Chem.*, 2004, **76 (5)**,1366 – 1373. Related Articles, Links A monolithic silicon optoelectronic transducer as a real-time affinity biosensor.

[11] P. LeMinh *et al.*, "Monolithic integration of a novel microfluidic device with silicon light emitting diode-Antifuse and photodector", ESSDERC, 2002

[12] F. Fixe *et al.*, "An on-chip thin film photodetector for the quantification of DNA probes and targets in microarrays", *Nuc. Acid Res.*, 2004, **32**, e70

[13] E. Thrush *et al.*, "Monolithically integrated semiconductor fluorescence sensor for microfluidic applications", *Sensors and Actuators B*, 2005, **105**, 393 – 399

[14] V. Namasivayam *et al.*, "Advances in on-chip photodetection for applications in miniaturised genetic analysis systems", *J. Micromech. Microeng.*, 2004, **14**, 81 – 90

[15] L. Jie & M. Liu, "Layer-by-layer assembly of DNA films and their interactions with dyes", *J. Phys. Chem. B*, 1999, **103**, 11393 – 11397

[16] X. Shi, R.J. Sanedrin & F. Zhou, "Structural Characterisation of Multilayered DNA and Polylysine Composite Films: Influence of Ionic Strength of DNA Solutions on the Extent of DNA Incorporation", *J. Phys. Chem. B*, 2002, **106**, 1173 – 1180

[17] M.F. Bohm *et al.*, *Mater. Res. Soc. Symp. Proc.*, 1998, **507**, 327

[18] R.A. Street *et al.*, *Mater. Res. Soc. Symp. Proc.*, 1995, **377**, 757

[19] G. De Cesare *et al.*, "Amorphous silicon-silicon carbide photodiodes with excellent sensitivity and selectivity in the vacuum ultraviolet spectrum", *APL*, 1995, **67**, 335

3. Nanotechnological signal amplification for label-free DNA detection

State of the art

Very few techniques (radioactivity or fluorescence) offer required sensor sensitivity, but radioactive and fluorescent labelling of DNA raise concerns over safety and cost, respectively. The latter is also true for the rather sensitive fluorescent quantum dots [1].

Other standard methods use PCR for amplification and labelling for downstream signal generation. PCR or similar techniques are limited to a few hundred copies of the target in the sample volume. More sensitive variations of PCR, like nested PCR, are not usually compatible with highly multiplexed PCRs necessary for screening applications in bioterrorism. Low detection limits for PCR usually require good DNA purification otherwise unspecific fragments will be amplified.

Alternatively, through various nanotechnological strategies, some molecular recognition signals can become so evident to be seen by the naked eye [2, 3, 4]. Briefly, the target molecule is labelled by a metallic nanoparticle (*e.g.* gold) and subsequently, the nanoparticles are grown by a chemical "blind" development (silver). First attempts have been made to combine this nanotechnological strategy with microelectronics [5]. Even though highly sensitive, nanotechnological approaches usually work by increasing the effect of an already established DNA-DNA recognition event. To be detectable, a number of these events are necessary, requiring more traditional amplification techniques like PCR to detect the presence of a few analyte molecules. To date, the few cases of nanotechnological analyte amplification reported [6] are not designed to run in a disposable microarray device with a cheap detection system, and are not thought to be employed in a device expecting negative specimens most the time.

Approach to advancing state of the art

In our approach, the hybridisation of the analyte "target" molecule with a suitable oligonucleotide probe will trigger, like catalysts, the breakdown and/or the formation of a high number of detectable nanostructures. The amplification of these detectable entities, in a second step, will be a much simpler process. This two-step double amplification has two advantages: it provides a multiplicative signal enhancement and it can be used to reduce spurious signals leading to false positives, similar to an ELISA sandwich assay.

Signal amplification development will start from existing methods that will be expanded and adapted to the sensing technologies employed for the signal detection.

A number of possible approaches will be considered.

- Template-assisted DNA cleavage can be used to disrupt DNA nanostructures and produce multiple instances of a structure in response to only one target molecule [7].
- DNA-mediated controlled aggregation of colloidal nanoparticles can be used to either produce disruptable nanostructures or to make a structure grow after a hybridisation signal.
- Streptavidin can be used as a branching point for 4 biotin-labelled DNA strands to obtain dendrimer-like DNA structures [8] to further enhance the detection. The DNA nanostructures can be labelled with gold nanoparticles [9].
- Antibodies directed towards double-stranded DNA could be used to grow protein-DNA nanostructures at the site of recognition. The recognition will be triggered by the formation of a double helix during hybridisation. At low target concentrations the second binding site of the antibody will be unoccupied so (functionalised) dsDNA can be used to grow a nanostructure.
- Electroless metal deposition on the recognition spot can be simply implemented either by growing metal nanoparticles bound on the site as a result of the recognition process, or by starting the metal reduction with some chemical that will bind only to double-stranded DNA (such as intercalators).

References

[1] W.C. Chan & S. Nie, "Quantum dot bioconjugates for ultra-sensitive nonisotopic detection", *Science*, 1998, **281 (5385)**, 2016 – 2018
[2] C.A. Mirkin *et al.*, "A DNA-based method for rationally assembling nanoparticles into macroscopic materials", *Nature*, 1996, **382,** 607 – 609
[3] Remacle Patent
[4] T.A Taton, *et al.*, "Scanometric DNA array detection with nanoparticle probes", *Science*, 2000, **289**, 1757 – 1760
[5] Remacle, Silver microelectronics
[6] Achenbach *et al.*, *Curr. Pharm. Biotech.*, 2004, **5**, 321 – 336
[7] Sando *et al.*, *J. Am. Chem. Soc.*, 2003, **125**, 15720 – 15721

[8] C.M. Niemeyer, "Semi-synthetic nucleic acid-protein conjugates: applications in life sciences and nanobiotechnology", *J. Biotechnol.*, 2001, **82**, 47 – 66
[9] C.M. Niemeyer *et al*., "Oligofunctional DNA-gold nanoparticle conjugates", *Angew. Chem. Int. Ed. Engl.*, 2003, **42**, 5766 – 5770

4. Micro- and nanofluidic multi-physics multi-scale modelling

State of the art

Microfluidics has been a research subject of increasing interest because of the wide range of practical applications such as genetic research drug discovery and proteomics. The field lies at the interfaces between engineering, chemistry, and biology; and aims to develop lab-on-a-chip systems as an enabling technology. Engineering challenges include understanding of the flow and mass transfer phenomena, development of accurate computational models, as well as the realisation of optimised processes in mixing, reaction, separation, preconcentration, and detection of chemical species.

Two-fluid laminar flow at low Reynolds numbers are extensively used in chemical separation, extraction and detection [1-4] as well as in microreactors [5], micromixing devices [6] and biotechnology [7]. An extensive review of microfluidic devices applications in biotechnology and organic chemistry can be found in [8]. Another important application of microfluidics is in microfabrication [9], where liquid interfaces are created by laminar flow in microfluidic channels. In all the above applications, the characteristic microchannel dimensions are of the order 100 μm, which is still in the domain of continuum mechanics simulations. The Reynolds numbers occurring in these applications range from $Re < 1$ in flow sensors, heat sink channels, capillary tubes, *e.g.* in diffusion broadening dominated problems [11, 12], to $Re > 10^3$ in microvalves, micronozzles, or pump applications.

In addition to microfluidics, it has also been demonstrated that nanofluidic channels can be used for single cell analysis. In [13] the electrophoretic behaviour of single, fluorescently labelled DNA molecules in rectangular silicon nanochannels with a cross-sectional area down to 150 × 180 nm was studied. The active control of single molecules of DNA in such small channels was achieved through electrokinetic transport. Long DNA molecules have also been separated by electrokinetically pumping the molecules through a nanofluidic device consisting of alternating thin and thick regions with different depths [14]. This alternative change in depth caused size-dependent trapping of DNA, which created an electrophoretic mobility difference enabling separation without the use of a gel matrix or pulsed electric field. Although a nanofluidic channel has great potential in single molecule analysis and the development of drug delivery systems, application of such devices in diagnostics is not yet practical. The bottleneck is the lack of fundamental understanding of transport phenomena in nanoscale devices, which has largely hindered the systematic design and precise control of such devices. To date, there are limited reports regarding fluid flow in nanofluidic channels, where electrical double layer is overlapped in most applications. Computational modelling of flow and mass transport phenomena in micro- and nanochannels involves a variety of physical scales in space and time. Both continuum and molecular effects can become important and their study requires different computational modelling strategies to be employed.

Approach to advancing state of the art

DINAMICS will advance the state of the art by:

- Developing quantitative understanding of nanoscale transport involving a description of the all relevant phenomena and their interactions
- Developing computational strategies for the coupling of simulations at the continuum and discrete molecular scales

References

[1] H. Hisamoto *et al.*, "On-Chip Integration of Neutral Ionophore-Based Ion Pair Extraction Reaction", *Anal. Chem.*, 2001, **73**, 1382
[2] W.E. TeGrotenhuis *et al.*, "Microchannel devices for efficient contacting of liquids in solvent extraction", *Separation Science and Technology*, 1999, **34 (6)**, 951

[3] W.E. TeGrotenhuis *et al.*, "Solvent Extraction and Gas Absorption Using Microchannel Contactors", in *Microreaction Technology: Industrial Prospects*, W. Ehrfeld, (Ed.) 2000, Springer-Verlag, 541 – 550
[4] B.H. Weigl & P. Yager, "Microfluidic diffusion-based separation and detection", *Science*, 1999, **15**, 346
[5] C.N. Baroud *et al.*, "Reaction-diffusion dynamics: confrontation between theory and experiment in a microfluidic reactor", *Phys. Rev. E*, 2003, **63**, 060104(R)
[6] Deshmukh, A.D. Liepmann & A.P. Pisano, "Characterisation of a Micro-Mixing, Pumping, and Valving System", Proceedings of the 11th International Conference on Solid State Sensors and Actuators (Transducers '01), München, Germany, June 10-14, 2001, 950 – 953
[7] P.K. Wong Y.-K. Lee, & C.M. Ho, "Deformation of DNA molecules by hydrodynamic focusing", *J. Fluid Mech.*, 2003, **497**, 55
[8] H. Andersson, "Microfluidic Devices for Biotechnology and Organic Chemical Applications", Ph.D. thesis, Royal Institute of Technology, Stockholm, Sweden, 2001
[9] P.J. Kenis, R.F. Ismagilov & G.M. Whitesides, "Microfabrication inside capillaries using multiphase laminar flow patterning", *Science*, 1999, **285**, 83
[10] D. Drikakis & M. Kalweit, "Computational Modelling of Flow and Mass Transport Processes in Nanotechology", in *Handbook of Theoretical and Computational Nanotechnology*, M. Rieth & W. Schommers (Eds.), 2004, American Scientific Publishers
[11] P. Gravesen, J.O. Branebjerg, O.S. Jensen, "Microfluidics – A Review", *J. Micromech. Microeng.*, 1993, **3**, 168
[12] E. Shapiro & D. Drikakis, "Artificial Compressibility, Characteristics-based Schemes for Variable Density, Incompressible, Multi-Species Flows. Part II. Multigrid Implementation and Numerical Tests", *Journal of Computational Physics*, in print, 2005
[13] L.C. Campbell *et al.*, "Electrophoretic manipulation of single DNA molecules in nanofabricated capillaries", *Lab. Chip*, 2004, **4**, 225 – 229
[14] J. Han & H.G Craighead, "Separation of long DNA molecules in a microfabricated entropic trap array", *Science*, 2000, **288**, 1026 – 1029

5. Application of nanostructures to enhance analyte capture and enhance sensor performance

State of the art

Biosensors, like DNA microarrays, typically involve a sensor "spot" in a chamber or at a channel wall. Analytes reach the sensor surface from the bulk liquid by diffusion, since there is no turbulent transport at these dimensions. Thus, the time taken for the analyte to accumulate on the sensor in sufficient numbers to trigger a detection event is dependent upon the diffusivity of the DNA fragments in the solution, their concentration in the bulk and the typical diffusion distance. Thus, for a given response time, diffusion can limit the threshold detection concentration in the sample [1] or for a given concentration, diffusion can limit response time. Long analysis times (*e.g.* 12-24h) have been tackled by the introduction of so-called hybridisation stations using different kinds of agitation systems, like pumps [2] or acoustic waves [3] to induce turbulent transport.

Since response also depends on available sensor surface area, analyte capture can be further improved using 3D structures, like gel pads [4] or porous materials [5] aimed at increasing the surface area on which probes are anchored or combinations thereof with agitation [6]. Other approaches to increase the active surface area are to tentatively build up a pseudo-three-dimensional structure using the so-called 'dendrimeric' linker system [7]. Nanotechnological approaches have been attempted either by incorporating multi-walled nanotubes in the sensor surface [8, 9] or by using nanoengineered porous structures made of polyelectrolyte multilayer [10].

Approach to advancing state of the art

DINAMICS will advance the state of the art by using engineered nanoporous structures to effect both approaches simultaneously, in a manner that is consistent with manufacturing constraints and detection principles.

First attempts have been made to use macroporous structure for electrical detection using a silicon electrode [11]. We will reduce the pore size as much as possible, since linear reduction of pore sizes reduces the diffusion time in a quadratic manner [6]. Introducing flow through this structure could offer further improvement by eliminating diffusion as the major means of mass transport. To address flow resistance concerns and improve analyte capture, DINAMICS will use monolith technology. Silica and polymer monoliths have so far mainly been used in chromatography and solid phase extraction applications [12].

The major research issues will be

- Compatible material selection (conductance and UV-transparency required for capacitive and optical sensors, respectively)
- Obtaining optimal pore size and morphology
- DNA immobilisation on surface of porosity
- *In-situ* fabrication or packaging
- Prevention of clogging

References

[1] P.E. Sheehan & L.J. Whitman, "Detection Limits for Nanoscale Biosensors", *Nano. Lett.*, 2005, **5**, 803 – 807
[2] HS400 Hybridisation Station, Tecan Schweiz AG, Männedorf, Switzerland
[3] ArrayBooster™ , Advalytix AG, Brunnthal, Germany, http://www.advalytix.de
[4] E. Timofeev *et al.*, "Regioselective immobilization of short oligonucleotides to acrylic copolymer gels" *Nucl. Acids Res.* 1996, **24 (16)**, 3142 – 3148
[5] V. Benoît *et al.*, "Evaluation of Three-dimensional Microchannel Glass biochips for multiplexed nucleic acid fluorescence hybridisation assays", *Anal. Chem.*, 2001, **73**, 2412 – 2420
[6] Y. Wu *et al.*, "Quantitative assessment of a novel flow-through porous microarray for the rapid analysis of gene expression profiles", *Nucl. Acids Res.*, 2004, **32 (15)**, e123
[7] M. Beier & J.D Hoheisel, "Versatile derivatisation of solid support media for covalent bonding on DNA-microchips", *Nucleic Acids Res.*, 1999, **27**, 1970 – 1977
[8] Li *et al.*, *Nano. Lett.*, 2003, **3**, 597 – 602
[9] Cai *et al.*, Anal. Bioanal. Chem., 2003, **375** , 287 – 293
[10] X. Zhou, L. Wu L & J. Zhou, "Fabrication of DNA microarrays on nanoengineered polymeric ultra-thin film prepared by self-assembly of polyelectrolyte multi-layers", *Langmuir*, 2004, **20 (20)**, 8877 – 8885
[11] Archer *et al.*, "Macroporous Silicon Electrical Sensor for DNA Hybridisation Detection", *Biomed. Microdev.*, 2004, **6 (3)**, 203 – 211
[12] F. Svec, "Preparation and HPLC applications of rigid macroporous organic polymer monoliths", *J Sep. Sci.*, 2004, **27 (10-11)**, 747 – 766

6. Integration of sample preparation operations, target detection and signal processing into a simple and reliable lab-on-a-chip platform

State of the art

Miniaturised "Total Analysis System" analysis systems offer improved efficiency with respect to: sample size, response time, analytical performance, process control and throughput. The first analysis systems for molecular biology in the early and mid nineties focused on a single step in the analysis procedure like PCR [1] or CE [2]. Meanwhile, increasingly complex microfluidic analyis systems are under investigation. A highly integrated device was presented by Affymetrix [3], which comprised: DNA extraction, preconcentration, DNA amplification and hybridisation. A series of papers by Y. Liu [4-6] from Motorola shows slower progress to full integration. Starting with a simple concept they arrive at a device that tries to integrate: sample preparation, PCR amplification, and DNA micro-array detection over a period of three years. Recently systems [7,8] were presented that try to identify pathogen micro-organisms. But these systems are yet not fully integrated. In particular, they lack sample preparation steps, like cell lysis and DNA preconcentration [9, 10].

Very recently, an autonomous pathogen detection system has been described [11] for the monitoring the environment for airborne biological threat agents.

Approach to advancing state of the art
Major challenges for the total integration of microfluidic chips are:

- Sensitivity limited by sample volume
- Integrated ultra-sensitive detection
- Heterogeneous material integration
- Integrated microvalves and micropumps
- Packaging (Interconnects, filling, bubbles, dead volume, leakage)
- Microflow measurement and control
- Reagent storage and reconstitution
- Control algorithms, data processing and communications

DINAMICS proposes a modular system whereby each module will communicate with its neighbouring module(s) *via* a defined interface. The major modules will be 1) sample and DNA preconcentration 2) all reactions within the microfluidic structure comprising a cartridge and 3) the durable parts. This "Cartridge Concept" separates the system components into disposable and durable parts for the mobile device. The disposable cartridge is usually in contact with the sample and does the liquid handling, minimising cross-contamination. The measuring device contains the electronics, signal processor, power source and interactive display. Modularisation will reduce costs, avoid unnecessary waste, facilitates production and packaging/assembly. The modules ideally interconnect by self alignment or by electronic contacts.

Principal research challenges are:

- The interface between the macroscopic world and the microfluidics device
- Reconciliation of sensor material requirements with manufacturing and cost contraints
- Control of microfluidics and compatibility of active control with sensors

References
[1] M.A. Northrup *et al.*, "DNA amplification with a microfabricated reaction chamber", *Proc. Transducers*, 1993, 924 – 926
[2] C.S. Effenhauser, G.J.M. Bruin & A. Paulus, "Integrated chip-based capillary electrophoresis", *Electrophoresis*, 1997, **18**, 2203 – 2213
[3] R.C. Anderson *et al.*, *Nucl. Acids Res.*, 2000, **28**, e60
[4] Y. Liu *et al.*, *Anal. Chem.*, 2001, **73**, 4196 – 4201
[5] Y. Liu *et al.*, "DNA amplification and hybridisation assays in integrated plastic monolithic devices", *Anal. Chem.*, 2002, **74**, 3063 – 3070
[6] R.H. Liu *et al.*, "Self-contained, fully integrated biochip for sample preparation, polymerase chain reaction amplification, and DNA microarray detection", *Anal. Chem.*, 2004, **76 (7)**, 1824 – 1831
[7] E.T. Lagally *et al.*, "Integrated portable genetic analysis microsystem for pathogen/infectious disease detection", *Anal. Chem.*, 2004, **76**, 3162 – 3170
[8] C.S. Liao *et al.*, "Micromachined PCR system for multiple DNA amplification of upper respiratory tract infectious diseases". *Biosens. Bioelectron.*, 2005, **20**, 1341 – 1348
[9] B.S. Broyles S.C. Jacobson & J.M Ramsey, "Sample filtration, concentration and separation integrated on microfluidic devices", *Anal. Chem.*, 2003, **75**, 2761 – 2767
[10] C.-Y. Lee *et al.*, "Integrated microfluidic systems for cell lysis, mixing/pumping and DNA amplification", *Micromech. Microeng.*, 2005, **15 (6)**, 1215 – 1223
[11] B.J. Hindson *et al.*, "APDS: the autonomous pathogen detection system", *Biosens Bioelectron.*, 2005, **20 (10)**, 1925 – 1931

7. Development of processes and methods for high volume production of integrated micro-electronics and polymeric microfluidic structures

State of the art

Integration of microfluidics with electronics would appear to favour silicon, but for CE-applications, conductivity has proved problematic due to the high voltages required to drive of electro-osmotic flow (EOF), whilst amplification in an untreated native silicon PCR chip had a high failure [1]. Consequently most early microfluidic systems were sculptured from glassy materials. However machining these materials presents a number of problems. Fabrication of planar glass devices is a serial operation, so fabrication is often time-consuming and expensive. The isotropic nature of wet-etching processes generally yield channels with sloping walls and relatively low aspect ratios. Furthermore, bonding is necessary to create useful fluidic structures from etched substrates. Normally thermal bonding is used to add a cover plate. A temperature in excess of 400 °C is necessary, which might be incompatible with the integration of some elements. Bonding is also serial in nature and often time-consuming. Glass and silicon have high costs, especially for disposable devices that should be used in order to minimise cross-contamination. So, if microfluidic devices are to be mass produced, alternative materials and fabrication methods must be adopted, which should:

- Have low cost
- Possess appropriate chemical, thermal, electrical and optical properties
- Be compatible to chemical and biological reagents
- Be easily machinable and applicable to mass replication technologies
- Allow facile bonding and encapsulation of the structured substrate
- Provide a variety of surface properties and surface chemistries

Polymers and plastics represent a broad class of materials that best qualify this wish list.

Research issues are:

- Selection of suitable materials
- Fabrication (direct, indirect or lamination)
- Bonding

Approach to advancing state of the art

Effort will be directed to find the optimal material(s) that is compatible with the requirements of the detection methods (optical and electrical), the transport mechanism (control of electro-osmotic flow and passive elements), chemical reactions and the manufacturing process.

A process for the automated large-scale integration of metal wiring or optical detectors (amorphous silicon) will have to be developed/optimised. It will be determined whether the amorphous silicon can directly deposited on a pre-made polymer structure without causing too much thermal stress or whether it has to be produced by silicon processing and consecutively integrated into a polymer device (*e.g.* by RMPD). Candidate methods for applying/integrating conductive wires on a polymer substrate include: vapour deposition, filling carbon ink into microchannels, laminating foils with flat wiring, printing of conducive ink, site directed *in-situ* chemical deposition of metals or integration of pre-made wires

Two different fabrication methods (mould injection and direct generation of 3D structure using RMPD) will be used to explore the full range of possible polymers. Each of the fabrication methods is optimal for certain polymers exhibiting different physical properties.

References

[1] A. de Mello, “Plastic fantastic”, *Lab Chip*, 2002, **2**, 31N - 36N
[2] A. Reinhardt & R. Gotzen (MicroTEC, Duisburg, Germany), “Microstructure and systems production with Rapid Micro Product Development (RMPD) for medical and other applications” at Conference on Laser Optics for Young Scientists – LO’2000 St. Petersburg, Russia
[3] A. Reinhardt & R. Gotzen, “Growing up, Additive Processes in MEMS Fabrication and Packing” at RadTech Conference July 2004, Berlin, Germany

8. On-line Measurement of Viruses/Bacteria in Water

State of the art

Continuous and on-line systems to detect pathogens in water have become highly desirable since bioterrorist attacks on the water supply have become a more realistic threat scenario [1]. Yet currently there is no single method to collect, process and analyse a water sample for all pathogens of interest [2]. The earliest systems for continuous monitoring were designed to monitor physical parameters, like pH, turbidity, *etc*., as proxies for water quality. Next, attempts were made to develop systems for chemical analysis, often originating from regulatory requirements to monitor pesticides or other chemicals brought into the water supply system via agriculture or environmental pollution [3, 4].

An immunological on-line detection system for pesticides [3, 4] had detection limits of about 1ng l^{-1} using a fluorescence based detection system. Assuming an average molecular weight of MW 250 g mol^{-1} this is equivalent to about 5×10^{10} molecules per litre of water. Systems to detect pathogens in water require a much lower detection limit 10 – 100 molecules per litre, assuming a daily consumption of 1 litre of drinking water and a range of 10 – 100 viruses as an infectious dose. Infectious doses of bacteria are higher but still in the range of 1×10^5.

Recent research in detection systems for pathogens focused on airborne infections, *e.g.* Automated Biological Agent Testing System (ABATS) [5], autonomous pathogen detection system (APDS) [6]. The BEADS (Biodetection Enabling Analyte Delivery System) platform [7] only recently focused on the analysis on water. The key features of these systems are automation using modified equipment from medical analysis and on-line/autonomous processing. Rapid analysis is often obtained by sequential injection analysis (SIA) [8]. Operation times for autonomous monitoring have been demonstrated for 24 hours [8] or 7 days [6]. Pathogens are either detected by immunological methods [8] or PCR based detection [7] or a combination of the two [6].

All systems for the detection of pathogens use some form of concentration of bacteria to reach the necessary limit of detection. Compared to systems for the detection of toxic chemicals, a preconcentration by a factor of at least 1×10^5 is necessary when using immunological systems. When using systems that include sample amplification (PCR), which typically have an amplification factor of 1×10^9, the problem is only partly solved since a PCR reaction can be conducted only in small volumes, usually up to 50 µl, which also represents a need for volume reduction of 1×10^5. A problem associated with the concentration of the organisms, is the co-concentration of inhibitors for nucleic acid methods [7].

Approach to advancing state of the art

Recovering viruses from environmental water samples was the objective of some recent publications [9-15]. Various ultrafiltration methods (hollow fibre and tangential flow) used in the pharmaceutical industry for sterile filtration have proven useful and recovery rates varying from 50 – 90% were obtained. The concentration factors up to 1×10^4 [11] were demonstrated. The filtration time is dependent on the filter size and the flow rates determined by the molecular mass cut off. A practical approach will assemble a cascade of filters in order to prevent clogging through sediments and will increase the concentration factor by having a two-step enrichment. Putting several filters in parallel can speed up the concentration process with reasonable cost. Tangential flow filtration also offers the possibility to sample or continuously withdraw from the retention volume by an automated system. Ultrafiltration methods also offer the possibility of regeneration of the filters, reducing the costs. An automated system could use two filter systems facility monitoring while one filter is regenerated.

References

[1] J.A. Foran & T.M. Brosnan, “Early warning systems for hazardous biological agents in potable water”, *Environ. Health Perspect.*, 2000, **108 (10)**, 993 – 995

[2] T.M. Straub & D.P. Chandler, “Towards a unified system for detecting waterborne pathogens”, *J. Microbiological Methods*, 2003, **53**, 4185 – 4197

[3] J. Tschmelak *et al.*, “Automated Water Analyser Computer Supported System (AWACSS) Part I: Project objectives, basic technology, immunoassay development, software design and networking”, *Biosens Bioelectron.*, 2005, **20**, 1499 – 1508

[4] J. Tschmelak *et al.*, "Automated Water Analyser Computer Supported System (AWACSS) Part II: Intelligent, remote-controlled, cost-effective, on-line, water monitoring measurement system", *Biosens Bioelectron.*, 2005, **20**, 1499 – 1508

[5] P.A. Emanuel, I.R. Fruchey, A.M. Bailey, J.L. Dang, K. Niyogi, J.W. Roos, D. Cullin & D.C. Emanuel, "Automated screening for biological weapons in homeland defence", *Biosecur. Bioterror.*, 2005 **3 (1)**, 39 – 50

[6] B.J. Hindson, A.J. Makarewicz, U.S. Setlur, B.D. Henderer, M.T. McBride & J.M. Dzenitis, "APDS: the autonomous pathogen detection system", *Biosens Bioelectron.*, 2005, **20 (10)**, 1925 – 1931

[7] T.M. Straub, B.P. Dockendorff, M.D. Quinonez-Diaz, C.O. Valdez, J.I. Shutthanandan, B.J. Tarasevich, J.W. Grate JW & C.J. Bruckner-Lea, "Automated methods for multiplexed pathogen detection", *J. Microbiol. Methods*, 2005, **62 (3),** 303 – 316

[8] B.J. Hindson, S.B. Brown, G.D. Marshall, M.T. McBride, A.J. Makarewicz, D.M. Gutierrez, D.K. Wolcott, T.R. Metz, R.S. Madabhushi, J.M. Dzenitis & B.W. Colston, Jr., "Development of an automated sample preparation module for environmental monitoring of biowarfare agents", *Anal. Chem.*, 2004, **76 (13)**, 3492 -3497

[9] J. Olszewski, L. Winona & K.H. Oshima, "Comparison of 2 ultra-filtration systems for the concentration of seeded viruses from environmental waters", *Can. J. Microbiol.*, 2005, **51 (4)**, 295 – 303

[10] V.R. Hill, A.L. Polaczyk, D. Hahn, J. Narayanan, T.L Cromeans, J.M. Roberts& E. Amburgey, "Development of a rapid method for simultaneous recovery of diverse microbes in drinking water by ultra-filtration with sodium polyphosphate and surfactants", *Appl. Environ. Microbiol.*, 2005, **71 (11)**, 6878 – 6884

[11] S.A. Rutjes, R. Italiaander, H.H. van den Berg, W.J. Lodder & A.M. de Roda Husman, "Isolation and detection of enterovirus RNA from large-volume water samples by using the NucliSens miniMAG system and real-time nucleic acid sequence-based amplification", *Appl. Environ. Microbiol.*, 2005, **71 (7)**, 3734 – 3740

[12] V.N. Morozov, M. Evanskey, Y.K. Tan, D. Shaffer, T.Y. Morozova & C. Bailey, "Ultra-filtration Membrane for Electrophoretic Capturing of Pathogens for AFM Imaging", *Langmuir*, 2006, **22 (4)**, 1742 – 1748

[13] M.M. Ehlers, W.O. Grabow & D.N. Pavlov, "Detection of enteroviruses in untreated and treated drinking water supplies in South Africa", *Water Res.*, 2005, **39 (11)**, 2253 – 2258

[14] B.H. Lapizco-Encinas, R.V. Davalos, B.A. Simmons, E.B. Cummings & Y. Fintschenko, "An insulator-based (electrodeless) dielectrophoretic concentrator for microbes in water", *J. Microbiol. Methods*, 2005, **62 (3)**, 317 – 326

[15] L. Kittigul, S. Ekchaloemkiet, F. Utrarachkij, K. Siripanichgon, D. Sujirarat, S. Pungchitton & A. Boonthum, "An efficient virus concentration method and RT-nested PCR for detection of rotaviruses in environmental water samples", *J. Virol. Methods*, 2005, **124 (1-2)**, 117 – 122

[16] C.R. Cabrera & P. Yager, "Continuous concentration of bacteria in a microfluidic flow cell using electrokinetic techniques", *Electrophoresis*, 2001, **22 (2)**, 355 – 362

BREAKTHROUGHS AND RADICAL INNOVATIONS EXPECTED

- Full nanotechnological approach to formation of DNA sensor structures/surfaces, with advanced single-molecule nanoscience and nanotechnology for the tailoring, characterisation and development of the sensing surfaces. This will allow radical reduction of the threshold of detection of nucleic acids on microfabricated sensors
- Nanotechnological signal amplification strategies integrated with the most advanced electrical and UV absorption detection methodologies in order to reach single-molecule per sensing spot sensitivity in a microarray
- Radically new approaches to integration of sensor with signal conditioning and processing circuits both in Silicon and plastic or glass substrates (polysilicon TFT), underpinning potential for lower cost higher volume production
- Development of fundamental understanding, through multi-scale and multi-physics modelling, of transport phenomena in nanoscale devices, to facilitate their systematic design, optimisation and control

- Microfabrication of nanostructures in microfluidic devices
- Integration of sample preparation operations, molecular interaction sensing, electrical signal generation and processing into the same device, with great potential for the production of small, sensitive, cheap and simple to use detection devices. This breakthrough will generate the birth of a new generation of sensors for safety, health and security where cost, portability, easiness of use are major concerns
- Fully computerised hazardous substance identification mechanism.

5. POTENTIAL IMPACT

In Europe many SMEs are active in the field of advanced sensors, microfabrication and biotechnology. They are in a transition phase due to the appearance of nanotechnological scientific breakthroughs. Many SMEs are facing the challenge to integrate these scientific concepts in their commercial vision for future products in order to remain competitive. The DINAMICS project will support SMEs to achieve this integration process of nanofluidics and nanostructure manipulation in DNA sensors.

Economic impact:
The project will enable the SMEs that are operating in the specific areas to work together, and through integration and transfer of knowledge, develop a product that has a unique application within the market. Present on-the-spot detection mechanisms available are the Water test kits that test for bacteria and four other major contaminants frequently found in water supplies in 10 minutes. However, they can be unreliable since they are only valuable as a preliminary screening of the drinking water and require the full laboratory analysis if the pre-screening indicates a serious contamination. With the new method, full laboratory analysis will be unnecessary. Although the SME participants will naturally be the immediate beneficiaries of the work, the impact on the wider business community in Europe and globally could be significant. This is because the SMEs do not have the facilities to mass produce, service or support the products and processes that the work may eventually deliver. It is therefore most likely that the consortium or individual partners will seek to license the technology for wider and quicker uptake.

Direct and indirect economic benefits:
The project activities will develop a technological platform for a new generation of DNA and protein sensors that will lead to improvements in the way water testing is done. The present technology will gain access to smaller, cheaper and faster devices that will make the identification of many harmful substances within minutes and directly at the point-of-care, thus doing away with the conventional techniques, where samples are sent to a laboratory and put through labour-intensive processes that may take several hours to achieve a result. A reliable on-site detection method for hazardous substances/biological pathogens would have a direct impact on the large-scale screening of potential biological weapon attacks. Recent developments in pathogenic detection technology allows for the integration of even the most complicated biomolecular system into a microchip. The conventional methods of analysis are incapable of dealing with large-scale biological weapon attacks due to the complicated analysers and analytical centres that require transportation of samples from the origin and results usually take several hours to materialise. The application of biochips will reduce the analysis time to mere minutes and will be highly reliable. SMEs will benefit from this project by having access to and applying the latest research to their industrial needs which will make them more competitive on the European market. Their revenue will increase as will their employment (leading to regional unemployment decreases).

The project will allow SMEs to take advantage of novel technologies and improve their trade barriers. SMEs will internationalise their activities by co-operation with other SMEs in Europe, establish better communication with the EC, and use the project contacts as means for obtaining future public contracts.

SMEs will also gain direct benefits such as: medium and long-term activities (*i.e.* patents for new lab-on-a-chip systems), reductions in energy and resources expenditures, cost reductions and modernisation.

European dimension:

Contribution to the ERA: The project contributes to the implementation of the European Research Area for the following reasons: the European dimension of the project is ensured by the number of the participating countries (ten) as well as by the scientific recognition and experience of the partners that generate an appropriate critical mass, where the scientific excellence, the research facilities and the application possibilities are well balanced. By pooling core innovators, scientific expertise and necessary support in specialist areas, critical masses of knowledge and experience will be generated to provide advice and research capability as well as to spread excellence, disseminate knowledge and exploit results throughout Europe and elsewhere. This will also release resources to expand expertise, to provide opportunities for training and allow

flexibility to respond to specific situations in a dynamic way, giving both national and Europe-wide benefits. Additional benefits would be accrued from alleviating the workloads of some key scientists in Europe, who are under constant demand for their expertise. Electronic publication of information from DINAMICS will be useful and can be used throughout Europe, and potentially further afield. This innovative platform technology, merging genomic and combinatorial technologies and implementation of nanotechnological approaches, could benefit enormously to further accelerating novel bio-marker discovery and development of bio-chips for efficient protein/DNA profiling for various applications.

Results deriving from the this IP will allow the development of next generation diagnostic devices in the sector of public health/safety, leading to faster market penetration and company growth. All of that can be made possible only by integrating at a European level a critical mass like that in DINAMICS.

The development of the new value-added families of devices requires a multidisciplinary and interdisciplinary environment (chemistry, physics, microelectronics, biochemical engineering); a strong integration of skills; and, at the same time, it will create new knowledge-based and multidisciplinary career profiles. The multidisciplinary partnership of this project includes scientists, managers, university/research institutions' staff, industries and SMEs. The transfer of know-how between the partners will contribute to the development of skills in the Community and to a pre-competitive environment where European industries overcome national boundaries to develop fundamental and applied research with the collaboration of non-industrial institutions and companies. Several partners of the consortium have already collaborated in the context of other European programmes and research activities and will constitute a core around which the others will gather to ensure balance in terms of scientific excellence, research facilities and application possibilities. The DINAMICS activities will promote and strengthen collaboration and networking among the different actors involved, not only in research activities but also in training, dissemination of results, and potential creation of new technology-based companies across Europe.

Contribution to community objectives:
Quality of life and health will be enhanced through the implementation of DINAMICS. On-the-spot monitoring and identification will reduce the risk of hazards spreading through quick identification of pathogens within the water supply. This will help to minimise threats and prevent wider population contamination and ensure eater quality for production processes dependent on water, *e.g.* food production. Security of the water supply will be aided, as DINAMICS will provide a deterrent to possible terrorists. The project will increase the S*afety* of personnel involved in containing any incident as the sensors will provide timely and accurate identification of the hazard so that suitable agents can be quickly deployed.

Employment, through strengthening established SMEs and creating new employment opportunities in the relevant areas. More generally, consumer confidence will be more easily recovered in the event of an attack by swift and accurate containment and redemption of a hazard. DINAMICS will be part of this capability.

Environment, through developing small portable testing labs that will reduce the need for sending for laboratory testing and reduce testing time, human power and energy associated with it. The World Health Organisation estimates that around 6% of the global burden of disease is related to water. The substances are mainly pollutants (chemicals, biocides, plant protection products, metals, *etc*.) found in water which represent a risk for the aquatic environment but also for human health (human toxicity *via* aquatic exposure routes). Better safety and management of water and sanitation would therefore prevent over 30 million cases of water-related disease per year in the European Region.

The gender dimension:
The consortium is acutely aware of the gender equality issues within the project, and of the under-representation of female scientists in this area. A plan has been proposed for addressing this imbalance, which is shown in Section 6 of this document.

IPR:
A legal consortium agreement will be drawn up and signed by all partners to protect individual partners' existing intellectual property and ensure that any subsequent generic information obtained during the project will be available to all partners. This document has been written in close consultation with the partners and therefore, it corresponds closely to the needs of the industry. A kick-off meeting will be used to launch the project and to ensure that the project develops to benefit the industrial and particularly SME partners. The ownership of any intellectual property rights gained from this research will remain within the consortium, to be decided within the group on the basis of input of each partner to the specific issue. The consortium members will benefit from early royalty-free access to any patentable ideas produced by the project. All partners accept that prior to submission of papers, permission from the PSC should be issued, thereby securing patents or granting licences for the developed technology (if applicable). Furthermore, this permission will ensure that no conflicts of interests will arise between the partners in DINAMICS.

Impact of training and education:
The impact of this project will extend beyond the partners, by collaborations, identifying and engaging with appropriate resources to expand expertise and provide opportunities for training and personal development. Training and education activities will provide the opportunity to spread excellence, disseminate knowledge and exploit results throughout Europe and beyond. This includes the participation in at least twenty conferences, the organisation of eight training workshops and six scientific seminars, establishing agreed procedures for the development and use of common resources and equipment, and establishing programmes of training and for the staff exchange between partners.

5.1 CONTRIBUTION TO STANDARDS

The development of DINAMICS will contribute to the standardisation of the quality of water for human consumption such as those set up by the World Health Organisation, especially the substances that have not yet been specified. DINAMICS aims to harmonise and unify the means of detecting hazardous substances in water systems and processes. Developing a standardised library of substances found in water will be one of the outcomes that will be made available to the European Communities. The implementation of such a library would reduce the risks of these hazards spreading through the water system by quick identification of pathogens within the water supply. The library will also build on methodologies agreed by the partners which will naturally be based around recognised standards. In particular:

DINAMICS aims to provide more realistic and useful test procedures to measure the effects and dynamic performance of specific hazards in different pipeline systems and over a range of operating conditions

The applicability or otherwise of the standards used in the project will be reported to the partners and disseminated more generally. The DINAMICS partners will proactively engage standards organisations, through technical and standards committees at both national and international bodies that they are already in contact with. This will be done by promoting the impact of the scientific and technical results arising from the project. For example, WRI represents Slovakia in harmonising measurement and analytical practices with European Union standards, and so will represent the project to standards organisations. Equally, for instance, BHR, through its membership of British Water, will communicate the results to the Drinking Water Inspectorate and their representatives on relevant national and international standards bodies.

Integration of the biosensor with lab-on-a-chip technology will facilitate the development of a portable mobile device capable of reducing pathogen identification time from days to hours or even minutes.

The enabling technologies developed in DINAMICS will underpin future development of remote detectors for early-warning systems, and will offer potential for wider industrial application.

5.2 CONTRIBUTION TO POLICY DEVELOPMENTS

The events of September 11th 2001 and the subsequent 'anthrax' scare brought to the world's attention the threat of deliberate attacks through the use of biological, chemical or nuclear agents. These terrorist acts had a significant impact in Europe and highlighted the need to take a proactive stance within the European Union, which has since reviewed existing systems of protection, to minimise the health threats to its citizens. The project will therefore be organised to complement and adhere to EU policy objectives including the following:

- Water Framework Directive 2000/60/EC of the European Parliament and of the Council of 23rd October 2000, introduces in Article 16(2) a scientifically based methodology for selecting priority substances on the basis of their significant risk to or *via* the aquatic environment.
- "Life sciences and biotechnology – A Strategy for Europe" COM(2002) 27. To help the Union to harness the life sciences and biotechnology in many areas, such as health care, agriculture, food, industrial uses and the environment in order to create a sustainable, knowledge-based economy.
- The European Union drew up the Council Directive 98/83/EC on the quality of water intended for human consumption, adopted by the Council on 3rd November 1998 (World Health Organisation guidelines and Scientific Committee on Toxicology and Ecotoxicology). This new Directive provides a sound basis for both the consumers throughout the EU and the suppliers of drinking water.
- Programme on preventing and limiting the consequences of chemical, biological, radiological or nuclear terrorist threats (Doc.15861/02, Presse 413)
- Protection of civilian populations against CBRN terrorist attacks (Doc. 12159/02, ST 9787/1/03)
- Decision of EU Council 2001/C 82/1
- On co-operation in the European union on preparedness and response to biological and chemical agent attacks (health security) (COM(2003) 320 Final

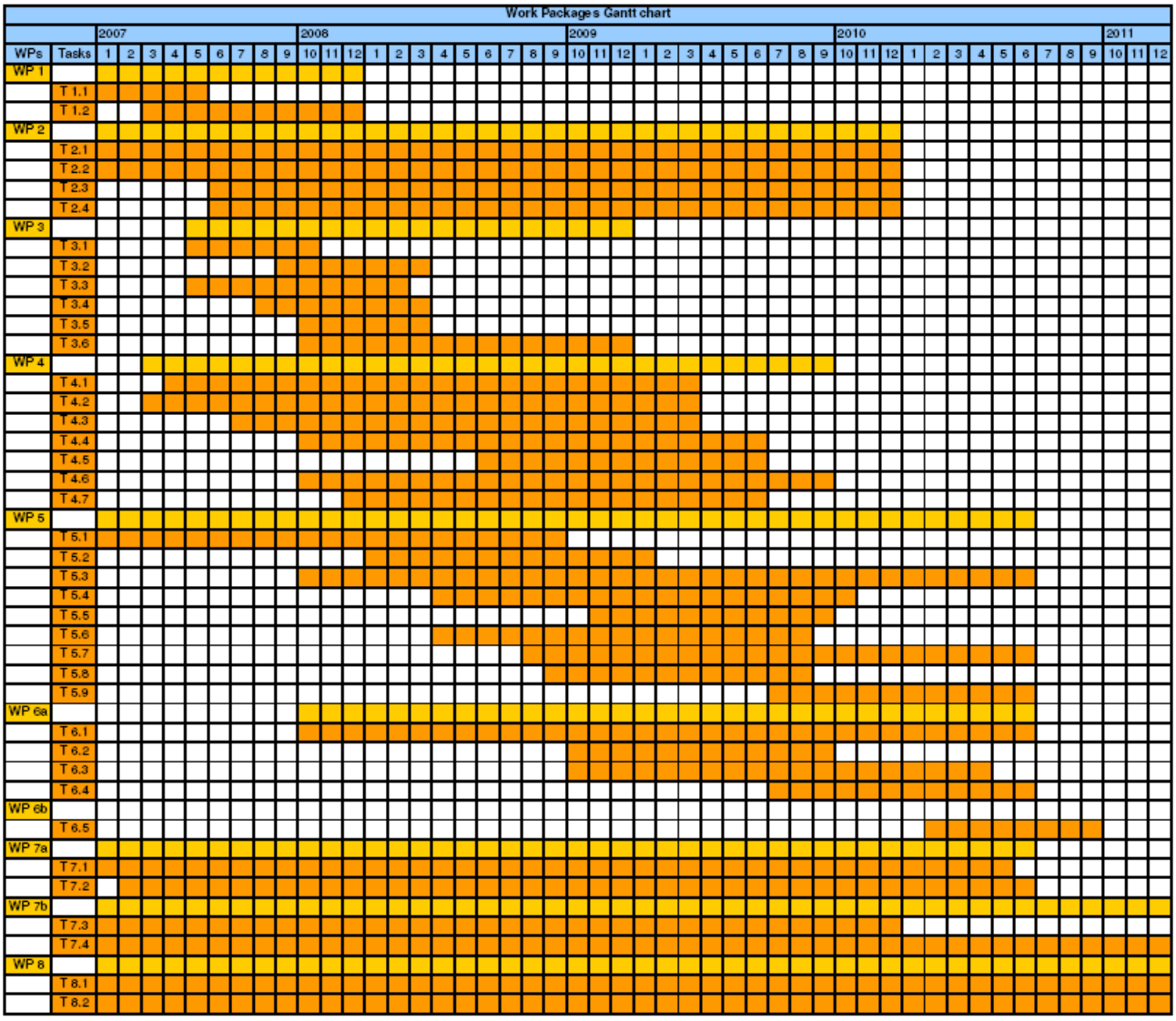
5.3 RISK ASSESSMENT AND RELATED COMMUNICATION STRATEGY

This area has been comprehensively reviewed in the Review and Assessment tables in Section 2 of this document. Each operational goal has an associated risk, with an appropriate mitigation strategy in place.

6. OUTLINE IMPLEMENTATION PLAN FOR THE FULL DURATION OF THE PROJECT

The overall forty-eight -month implementation plan is summarised in Fig. 1, on the following page, which identifies Work Packages and major tasks within them. It indicates which are innovation, RTD, demonstration, training or management activities; shows linkages between tasks; and locates them approximately on a timeline. This diagram does not intend to locate tasks and interactions precisely in time. Rather, task durations and start dates are indicative. Arrows feeding into the start of a task signify that it depends on a predecessor, whilst arrows feeding in to the side of a task suggest ongoing interaction or input part-way through.

Fig. 1 The overall 48-month implementation plan



6.A. ACTIVITIES

6.1 RESEARCH, TECHNOLOGICAL DEVELOPMENT AND INNOVATION ACTIVITIES

Work Package 1: Industrial Requirements
Work Package leader: LAM (IND, A) , Dr. Christian Mittermayr
Deputy leader: , Mag. Florian Winner
Partners: LAM, WRI, BHR, IDEA, HEM, LIONIX

Objectives: See Section 2

Description:
Preliminary consultation with a range of experts and water industry professionals across Europe reveals the lack of a consistent and coherent pan-European view on appropriate responses to a perceived bioterrorist threat. This is compounded by a diversity of commercial arrangements for the secure delivery of safe drinking water and the lack of appropriate regulatory instruments, the emphasis having previously been on routine sampling to ensure pathogens remain below safe limits.

The consortium understands the desirability, from a homeland security perspective, of a continuous monitoring system, but also recognises that this represents the greatest challenge in terms of automation, systems integration and reliability. It also has to be recognised that installation of a continuous monitoring system implies widespread installation of automatic devices at many hundreds of points across a network to protect the supply where it is most vulnerable, downstream of potable water treatment works and service reservoirs. It is not clear how many water companies would shoulder this cost voluntarily, and indeed attitudes are likely to differ between member states, influenced by commercial arrangements and cultural norms. However, in the current climate, it is expected that regulation will be forthcoming, so DINAMICS will develop the technology to cater for the anticipated demand. In addition, particular safety requirements already pertain to certain industrial users who are potential terrorist targets, particularly in the food and drink sector. These companies may be expected to represent early adopters of continuous monitoring technology.

Consultation has also highlighted the interim need for a “first response” device that would provide rapid identification of the nature of a biohazard, for example if there were physical or CCTV evidence of intrusion or tampering. By cutting out the pathology lab, a mobile device could provide point-of-sampling diagnostics and raise an alarm within an hour of an incident, representing a dramatic improvement on current practice.

The strategy in the project, therefore, is to develop two prototype devices (in WP6), one for a mobile device and the other for a continuous monitoring device, drawing on common DNA extraction and detection technologies, but with significantly different product engineering. The first would cater for the current “first response” demand, with an additional potential market for routine monitoring. The second will address a current market in security of supply to key industrial users and future wider demand following anticipated regulation in the domestic supply market.

WP1 will provide the common view necessary to reconcile technology push with market pull in terms of current and future user requirements and device functional specifications. It will also reconcile, for each prototype, what we believe to be technologically feasible with the practical requirements of public protection in terms of sensitivity and response speed.

Response speed (from contamination to identification of a “positive”) is governed by four elements:

1. Sampling frequency
2. Sample preparation time
3. Sensor response time
4. System reaction time

In either a mobile or a continuous system, items 2 and 3 are a function of the technology, and target figures may be measured in tens of minutes.

In either system, item 4 is a combination of machine and human protocols and the reaction time depends to a large extent on how we define the "system", *e.g.* does it include the authorities' decision time? Assuming the machine element only is considered, the key issue is the definition of the requirement for repeat diagnoses to eliminate false positives.

It is anticipated that a "continuous" device would comprise repeat sample extraction and processing from a continuous stream. With each sample subjected to a sequence of operations, item 1 (sampling frequency) would be selected to match the longest operation. Hence item 4 would be the sum of items 2 and 3 plus the required number of repeats × the time of the longest operation. For a continuous device, with, say, 3 readings to validate a "positive", one might realistically target a total response time (excluding the authorities' reaction time) of around one hour. This needs to be balanced against the residence time to the consumer's tap from points upstream, in order to identify an appropriate device installation strategy.

For a mobile device, detection time is likely to be limited by time lag between an incident and time of arrival of personnel at an appropriate sampling location. This could be affected by many variables, mostly related to geography and procedures.

The sensitivity of a sensor type refers to concentration at the sensor itself and, depending on technology, is typically around femtomolar. DiNAMiCS aims to improve on this with nanotechnological enhancement strategies. Device sensitivity refers to sampled concentration. This will need to be around 1 organism per ml, requiring preconcentration and/or PCR.

In detecting biological pathogens, two broad approaches are possible: detect the presence of a wide range of toxins and/or pathogens by virtue of their effect on an intermediate organism (the "dead fish" paradigm) or detect specific target species. The first is possibly more reliable in detecting the presence of a threat, but says nothing about its nature. Being DNA-based, DiNAMiCS is inherently specific. However, by employing multiple sensor sites, it can simultaneously target multiple species, listed in Section 2.

Tasks:

Task 1.1 Requirements specifications
(LAM , WRI, BHR)

Prepare briefing material for inaugural Advisory Board meeting, to include:

1. Proposed target organisms
2. Proposed likely threat scenarios with associated time lag from contamination site to tap
3. Tolerable contamination levels
4. Summary of known relevant emergency planning across Europe together with the project team's best estimates on:
    - Response time
    - Detection limits
    - Target costs for engineered devices produced in volume
    - Development timescales for "first response" and "continuous monitoring" systems.

The Advisory Board will convene to establish a common view on the requirements of an early warning system, taking into account the foregoing factors plus differences between European nations in terms of:

1. Supply infrastructure
2. Legislative framework
3. Asset ownership and management arrangements
4. Investment regimes
5. Tolerable system price

From conversations already held with Water Industry figures, the consortium believes that requirements will be identified both for a mobile device and for a continuous monitoring device, each use in particular circumstances. Therefore a Requirements Specification document will be compiled for each device, against a defined typical application.

Task 1.2 Functional Specification and Demonstrator Case specifications
(LAM, WRI, BHR, IDEA, HEM, LIONIX)

Using the results of Task 1.1, and in consultation with the Advisory Board, a functional specifications document will be produced and validated for both a mobile and a continuous monitoring device and a staged development plan, working towards a continuous monitoring prototype. This will be based on sample preparation and sensor technology developed for the initial mobile prototype, but will also identify required developments specific to a continuous monitoring second prototype. Progress towards an automated device for remote continuous monitoring might need to be prioritised over considerations of its integration into an early warning system within the budgetary constraints of the project. If so, this will be identified early and addressed in the Exploitation Plan, for post-project development.

Exploitation:
By defining the problem and the scope of solutions within and beyond the project, these activities form the framework in which the exploitation plan (T7.2) will be developed.

Work Package 2: Micro- and nanofluidics
Work package leader: BHR Group (SME, UK) Dr. David Brown
Deputy leader: Cranfield University (RES, UK) Dr. Dimitris Dikakis
Partners: BHR, CRAN

Objectives: See Section 2

Description:
At micron- and sub-micron-scales, mass transport is dominated by laminar diffusion and surface charge behaviour rather than turbulence. Sensor detection limits and response time are typically proscribed by species diffusion, so nanotechnological strategies will be investigated to reduce diffusion distances to help address this issue. In order to evaluate potential strategies and to optimise sensor design, it is necessary to develop an integrated quantitative understanding of the physicochemical behaviour of micro- and nanofluidic systems and the tools to describe it. At the micron (channel dimension) scale, conventional computational fluid dynamics (CFD) is prone to inaccuracy in the prediction of mixing and diffusion, especially of macromolecules in aqueous systems. The nanometre scale (typical of porous structures that might be used for the enhancement of analyte capture), is at the limit of continuum mechanics. Here we need to develop simulation tools and computational methodologies that describe the interactions of all relevant physical phenomena at both the discrete and the continuum scales and across the relevant range of time scales (multi-scale, multi-physics modelling).

Tasks:

T2.1 Diffusion and mixing in micro-and nanofluidics
(BHR, CRAN)

Cranfield's group will contribute to the evaluation of the fluidics diffusion through analytical and numerical investigations. This will also include a comprehensive literature survey. This will inform preliminary design decisions in WP3 and 5, prior to the development of more sophisticated modelling and simulation strategies in T2.1 and 2.2, for which it will also form a benchmark.

T2.2 Multi-scale modelling methodologies
(BHR, CRAN)

CRAN will employ both computational fluid dynamics (CFD) and molecular dynamics (MD) techniques to model flow and mass transport. The CFD modelling will include an investigation of the suitable set of conservation laws for the problem in question; modelling source terms associated with diffusion; formulation of the numerical procedure for the conservation laws (this will be based on existing computational methods developed by CRAN which will be extended for the new set of conservation laws). In addition to the continuum mechanics approaches, the group will also employ MD techniques. Within this task, the suitability of existing potential function models in the context of MD will be investigated and their implementation in MD codes carried out. BHR will contribute to the development of computational strategies for the coupling of these models.

T2.3 Development of simulation toolkit
(BHR, CRAN)

This task will encompass extensive CFD and MD simulations on representative and relevant test cases. Where possible, results of simulations will be validated against data emerging from the sensor development activities in WP4. Additional activity will comprise development and refinement of computational algorithms for the efficient coupling of models across length- and timescales, *i.e.* implementation of the strategies identified in T2.2. CRAN will concentrate on molecular dynamics aspects; BHR will concentrate on CFD approaches. There will be close collaboration on the issue of coupling and methodology.

T2.4 Design support and optimisation
(BHR, CRAN)

CRAN will carry out parametric simulations for different sizes of the device. Note that even small changes in the design may require re-visiting the mathematical/numerical foundation of the computational physics models (CFD & MD). This task will therefore overlap with T2.3, reflecting the necessity of iteration between models and simulations in these work packages. CRAN will investigate by means of CFD and MD potential mixing concepts for enhancing the performance of the microfluidics and nanofluidics devices. The micro- and nanofluidics studies will be performed in parallel. CRAN will work closely with BHR to provide possible solutions for optimising the micro- and nanofluidics for mixing.

Knowledge and IP management:
CRAN brings background IP in respect of molecular dynamics models and high resolution CFD techniques. Exploitable IP is expected in respect of multi-scale modelling methodologies, requiring liaison with T7.1.

BHR intends to register a member of staff for a Ph.D. at CRAN, with research concentrating on the CFD and multi-scale modelling methodology aspects of the work. Thus, references above to the CRAN's modelling group will include BHR staff.

Dissemination:
The Fluid Mechanics & Computational Science group at CRAN will contribute to the dissemination of the work through publications to scientific journals and conference proceedings. Moreover, the group will contribute to the dissemination by organising workshops jointly with other partners. Finally, CRAN will contribute throughout the project to the technology transfer of computational modelling practices to the interested SME partners.

Work Package 3: Microbiology and sample preparation
Work Package leader: MMM (SME, HU) Robert Deak
Deputy leader: Dr. Metzinger
Partners: LAM, WRI, MMM, LIONIX, BME

Objectives: See Section 2

Description:
This work package is concerned with selection of target organisms, finding the appropriate genes (DNA stretches) for their detection, design of the highly specific probes, and, if necessary, optimal primers for pre-amplification. Various steps will be checked for getting appropriate DNA fragments of the target organisms to the detector module in sufficient concentration, with sufficient purity for their reliable detection.

Tasks:

T3.1 Gene selection
(LAM, MMM)

In order to design probes for target organisms (T3.2) their DNA sequence has to be available. A database search will be conducted to find all publicly available sequences. Attempts will be made to contact research groups to access sequence information outside the public domain. Also, the sequences of closely related non-pathogenic organisms will be searched, since they are necessary to avoid a probable cross-reactivity causing false alarms.

T3.2 Probe design
(LAM, MMM)

The strategy for designing probes is dependent on the type of organism and the gene used. Bacteria have a much high number of genes and their sequence has usually a lower within species variability then that of viruses. The most important property of a good probe is high specificity (no cross-reactivity and hence no false positives) and high sensitivity (no false negatives, low limit of detection). Computer algorithms will be used to pre-screen potential probe candidates according to the criteria above. Experiments will narrow down the candidates and allow fine-tuning of the probe sequence.

If pre-amplification of DNA/RNA proves to be necessary, it would be highly advantageous to have as few as possible different primers (*e.g.* for PCR). Therefore it is desirable to use conservative gene (region) for the probe design. This should be a rather difficult task in viruses, but for bacteria a high likelihood for finding such a region exists.

Probes designed here will be incorporated into prototype devices in WP6.

T3.3 Sample collection
(WRI)

Sample collection will be done in two ways: model samples and natural water. Verification, monitoring and data acquisition will use natural sources. A sampling plan will be elaborated starting with the testing of the device. The bulk of samples will consist of untreated source water, treated water and water from points of consumption.

T3.4 Sample preconcentration
(MMM, WRI, LAMBDA, LIONIX)

Since the infectious dose of some bacteria or viruses is very small, threshold concentration at the point of sampling may be low. The volume that can be processed in a microfluidic device is, by definition, tiny. This means that the number of target organisms in the volume of water required to fill the microfluidic detector could be negligible. A preconcentration step is therefore necessary: we estimate that a factor of about 10^3 –10^4 should be required. We propose to do this by filtration. Special consideration will be given to the selection of filter type and pore size required to handle a broad range of target organisms of differing size, without excessive compromise of filtration time. The effect of waste organic material has also to be considered when estimating the efficiency of the filtering methods. Techniques considered will include ultra-filtration (hollow fibre and tangential flow), reverse osmosis, cation-coated filter method. The properties of the filter material, charge, elution buffer, pore size, filtration time and filtration conditions have to be optimised.

This task may overlap to some extent with T3.5, since combined lysis/filtration operations will be investigated. It will also involve close discussion on manufacturing and integration issues with partners in T5.3 and 5.7

T3.5 Cell lysis
(MMM, LAM, BME, WRI)

To make RNA or DNA fragments of the biological material accessible for hybridisation, cells and viruses must be lysed. This can be accomplished by enzymatic, chemical or mechanical means. Sonication is a mechanical method that involves no reagent addition and can be easily controlled electronically, and hence is the proposed method. Two approaches to integration with the microfluidic device will be compared: 1) outside the cartridge, hence reusable; 2) inside, hence disposable. Ultrasound is known to disrupt RNA and DNA, which is beneficial because it both enhances the mobility of the analytes and can destroy secondary structures in the nucleic acid that often hinder hybridisation. However when the nucleic acid pieces become too short, a decrease in signal results. Optimisation of the power input and frequency will therefore be performed. Strategies for combined lysis and filtration will be investigated by MMM.

This Task will involve close discussion of microfluidics, manufacturing and integration issues with partners in T5.2, 5.3 and 5.7.

T3.6 Amplification and on-chip PCR
(LAM, MMM, LIONIX)

Whilst it is hoped that sensitivity thresholds will be met without recourse to nucleic acid amplification, this might prove necessary. During the development and testing phase amplifications systems are necessary to validate individual modules. The most common method is PCR (polymerase chain reaction) for all DNA organisms and RT-PCR for RNA viruses. Both procedures need extensive optimisation in the case of multiplex application, when largely varying genes and organisms have to be amplified simultaneously. Various methods of thermal cycling described in the literature will be evaluated for effectiveness and feasibility of integration into the device. These will include passive cycling by convection (reducing the need for cooling) and possible new approaches that involve performing reverse transcription and subsequent PCR in the same chamber.

It is anticipated that there will need to be a trade-off between the advantages of isothermal amplification techniques (heating and cooling cycles add complexity and cost and could stress the chip material) and its disadvantages (speed and enzyme inventory). These issues will be researched in this Task in close contact with partners in T5.2, 5.3 and 5.7 dealing with microfluidics, manufacturing and integration issues.

Knowledge and IP management:
T3.2: IP issues have to be considered since many useful genes (regions) have been subject to patent protection.

Work Package 4: Sensor and signal detection development
Work Package leader: University Bologna (RES, I) Dr. Carlotta Guiducci
Deputy leader: Idea (SME, I) Augusto Pieracci
Partners: IDEA, UNIBO, LAM, BME, BHR, CRAN, FP

Objectives: See Section 2
Description:
This work package concerns two main problems to be solved.

1. Development and optimisation of sensors for capacitive as well as optical detection techniques
2. Development of appropriate electronics.

Both of these innovative activities are new ‘transferrable’ specific enabling pieces of work.

Tasks:

T4.1 Surface science
(UNIBO, BME, LAM)

This work package is concerned with the characterisation of surfaces prior to and after functionalisation with probes. This will involve fundamental research on test surfaces, and applied research on the surfaces of microfabricated devices. Test surfaces can be chemically derivatised for oligonucleotide attachment at UNIBO. Synthetic functionalised oligonucleotide probes will be obtained from commercial suppliers and anchored on the test surfaces. Whilst the specific sequences to be employed in prototype devices (WP6) are being identified in T3.2, it will be possible to work with "dummy" sequences. This is a central activity, with strong links to sensor development in T4.2 and 4.3; to sensor nanotechnological enhancement strategies in T4.5 and 4.6; and also to activities associated with the production of prototype demonstrators in WP6. Early liaison between T4.7 and both T4.2 and 4.3 is required to define interfacing between sensor and electronics.

T4.2 UV sensor development
(UNIBO, LAM)

This work package will undertake the research necessary to develop this novel detection method. Macro-sized test surfaces for UV-detection measurements can be purchased from commercial suppliers and chemically derivatised in the UNIBO laboratories as described in T4.1. Initial development work will concentrate on quartz or glass.

A core issue is the difficulty in derivatising the surface of transparent polymeric materials that may be compatible with the UV technique and offer potential for low-cost large-scale production. Recently methods have become available to bind DNA to polymers. This method will be made available to the consortium through a partner (LAM). Simple geometries should prove useful in validating the molecular dynamics, CFD and coupled multi-scale models in WP2.

T4.3 Electronic (capacitive) sensor development
(UNIBO, LAM)

UNIBO will be able to prepare macro-sized clean and flat metal surfaces for testing of electrical detection techniques, through its high-vacuum metal evaporation system. These can be simply hand-wired to external measurement instruments through the use of custom-built macro-flow-cells. This task may also provide validation for WP2.

T4.4 Nanotechnological signal enhancement
(UNIBO, LAM)

Several possible strategies towards the amplification of the signal due to recognition between nucleic acids will be attempted, with the goal of applying it towards the integrated surface-bound detection of a low number of nucleic acids. Candidate strategies were outlined in the discussion of "approach and state of the art", above. Signal amplification will be obtained by molecular recognition/self-assembly events of functionalised nanoparticles. The advantage of molecular self-assembly is that it does not increase the complexity of the device, in manufacturing terms. The materials used for the nanoparticles depend on the detection system. For UV-detection, high absorption or emission will be required; while, for impedance measurements, the dielectric constant has to be optimised. The performance of the proposed strategies will be tested first with conventional "high-price, high-effort" research laboratory techniques, and then put to the test of the detection methods used for the integration in the microfluidics device. If successful, sensors employing these strategies will be miniaturised in T4.6 and incorporated into prototypes in WP6.

T4.5 Nanotechnological approaches to detection enhancement
(BHR, , LIONIX)

The specialist literature on chaotic advection will be reviewed, to investigate the practicality of initiating it within the DINAMICS biosensor and to estimate the increase in diffusion coefficient that may be achieved. Literature covering both theoretical aspects and practical implementations will be included.
The combination of geometrical features or time-varying inlet velocities likely to lead to chaotic advection will be specified. This will be undertaken within the framework of the design process for the system as a whole and for the loc device as a component. Hence they will be specified with regard to manufacturing feasibility and to other design requirements for the system and component.
The effect of the specified design parameters will be confirmed experimentally, in either a physical or numerical model. The design parameters may be amended as necessary to improve performance, within the constraints of the overall design of the system and component.

T4.6 Detection scale-down and integration
(IDEA, LAM, BME, FP)

Electronic and UV measurements of DNA hybridisation on the surface will be performed with and without techniques for nanotechnological signal enhancement (T4.5). Test surfaces of progressively smaller size will be employed in order to study the behaviour of the system when it approaches the millimetre/micrometre scale employed in microfluidics. This will enable validation of computations (T2.3) aimed establishing the relationship between diffusion distance and size (see discussion of T4.5, above).

T4.7 Signal processing
(IDEA, UNIBO, BME)

Detection of DNA with the capacitive or UV technique is based on measurements of electrical characteristics coming from biosensor devices. The first electronics prototype will be realised as a system-on-board including:

- Signal acquisition interface (conditioning, A/D conversion);
- Control unit (microprocessor-based);
- Control interface (graphical unit and/or standard communication interface)
- Power system (battery)

The signal acquisition interface is the critical part of the system, due to low levels of electrical sensor signal. The acquisition technique will be implemented exploiting a differential measurement between the signal of sensor under test and that of a dummy sensor to reduce the signal-to-noise ratio (SNR) and enhance system sensibility. Costs, dimension and flexibility (software reprogramming) will be considered during the development of the prototype to match the project's requirements.

T 4.8 Validation of hydrodynamic strategies
(LIONIX, UNIBO, CRAN)
Fabrication of microfluidic structures with which the simulation results on hydrodynamic focussing can be verified. This includes the interface between the microfluidic chips and the optical setup at Bologna as well as the fluidic handling system. CRAN will develop the numerical tools and perform numerical simulations and parameter calculations to support and aid the designs of the microfluidic channels and the focussing device. CRAN will discuss the experimental results obtained by UNIBO and refine the numerical models, if necessary. UNIBO will perform optical observations on the suitability of the implemented microfluidic structures.

Knowledge and IP management:
UNIBO brings important background IPR to the project in respect of: electrical read-out of the site(s) using a suitable sensor for each site in the arrays; optical (UV) detection by means of optical-electric transduction; specific (original) sensors: UV and optical sensors (particularly those realised in amorphous silicon), spads, and non-volatile memory cells. Further innovations are expected in respect of both these areas and nanotechnological enhancement strategies. Close liaison with T7.1 is therefore planned.

Exploitation plan:
For IDEA, the ambition is ultimately to gain competitive advantage, both by making better products for measurement systems and by acquiring new know-how.

Dissemination:
The research results obtained by the DINAMICS project will be published at international conferences, EU-workshops and in journals. It is also hoped that they might be used for forming new start-up companies. The results will also be used in educational activities such as courses and M.Sc. graduation projects, and also in Ph.D. projects.

Work Package 5: Engineering
Work Package leader: Microtronics Engineering (SME, A) Dr. Andreas Aigelsreiter
Deputy leader: Hans-Peter Buber
Partners:, MICRO, PRO, HEM, BME, BHR, CRAN, LAM, LIONIX, FP*

Objectives:
See Section 2

Description:
This work package draws on the various multidisciplinary research activities in microfluidics (WP2), probe and sensor development (WP3 and 4), to address generic issues of device design and integration. This will inform the design of specific prototype devices in the demonstration activities of WP6.

Tasks:

T5.1 Design Methodology and toolkit
(BME, MICRO, PRO, CRAN)

The detector devices will draw on technologies based in a range of disciplines (microbiology, molecular biology, nanotechnology, materials science, fluid dynamics, electronics, software, production engineering), each with its own design methods, simulation and computer-aided engineering tools. This work package will review current design methods, existing and new simulation tools (from T2.4) and identify interface issues. It will provide a coherent concurrent engineering methodology for the design and manufacture of robust biosensor devices, produced in significant volumes to performance criteria identified in T1.5. This design methodology will inform activities elsewhere in WP5.

T5.2 Microfluidics operations
(BHR, LAM, LIONIX, PRO)

Microfluidic solutions to a range of tasks must be selected and optimised within the constraints of an integrated device that is capable of being manufactured. These include mixing, heating, fluid transfer, metering and flow control. A combination of experimental work and simulation will be employed to evaluate alternative strategies and optimise solutions. Development work on sonication as a cell lysis method and, if required, on-chip PCR will build on research work in T3.5 and 3.6, respectively. Experimental testing will provide valuable early feedback to the computational modelling arm of the project in WP2, to improve subsequent simulations for optimisation activities. The design methodology of T5.1 should ensure close collaboration between these activities and considerations of manufacturing in T5.4.

T5.3 Automation
(MICRO, PRO, FP)

A reduction of sample volume from around 10 – 100 litres to a volume amenable to processing in microfluidics devices (typically less than 500 μl) needs several stages of preconcentration, such as ultra-filtration. In an automatic remote-monitoring device, the final volume has to be reliably transferred to the microfluidics devices, whilst the filters have to be automatically regenerated or replaced at appropriate intervals.

T5.4 Manufacturing Issues
(MICRO, PRO, LAM)

Having identified substrate material(s) that are compatible with the requirements of the detection methods, transport mechanism, and chemical reactions, compatibility with desirable manufacturing routes may determine final material selection, and will inform ongoing research in WP4. Issues to be addressed include surface activation methods; heterogeneous material integration (wiring, optical detectors); fabrication methods; channel formation: dimensional control, bonding, jointing between disposable and reusable elements. Options were outlined in item 7 of the "Approach and state of the art" section of the Stage 2 Proposal. JP will identify engineering issues arising from alternative fabrication routes. Manufacturing issues arising from sonication and, if required, on-chip PCR, will be undertaken in this task.

T5.5 System Architecture
(MICRO)

In a complex system the overall architecture and the interplay of various modules and parts has to be carefully designed to ensure a fully operational device. A concept of the overall system architecture has to be established and transferred into a complete design in an iterative process. All units and interfaces have to be identification and clearly defined. A central repository of all interphase specification has to be created, maintained and regularly updated. This is of particular importance in a geographically dispersed collaborative project, where many partners provide only part or modules for the whole system.

T5.6 Embedded systems
(HEM, BME, PRO)

A mobile computer system will be selected among the products of various vendors in the market. The embedded operating system of the mobile device will be decided. All the embedded software will be developed on this operating system.

In order to have flexible software, a hardware abstraction layer is introduced in the architecture of the embedded software. In this way, the software can drive not only the first LoC prototype developed within the project, but also new versions of the hardware and other devices to be developed in the future (including the continuous monitoring device). In order to integrate with a new hardware device, only a device driver library will be developed for each device and installed to the system. The specifications of the device driver libraries will be defined in the package and its result will guide Task 5.7. According to these specifications, device driver library or libraries for the LoC modules will be written within this task.

BME will behave as a contractor (acquirer) of the developed software and define the software requirement specifications of the software modules to be produced in each task. BME will also test and verify modules delivered.

T5.7 User interfacing, software validation and support
(HEM, BME)

The embedded software of the proposed devices will be implemented in this task. It will communicate with the integrated LoC chips using the device drivers implemented in Task 5.6. The detailed user requirements will be determined using the results of Task 1.2, but basically software will have the following features:

- User management policy: functionality for different user authorisations.
- When a detection event occurs, a set of actions are performed (sending e-mail or SMS messages, web service call, transmitting data)
- Data monitoring and statistical analysis features to help avoid false decisions. This is about storing data coming from the devices and converting it into information.
- Ease of integration with remote systems using standard methods, protocols and formats.
- The device should be remote controllable.

A user's guide of the system and a context-sensitive help will be prepared. After the release of the software for each new prototype, verification and validation of the system will be performed. New requirements will appear during the development of new prototypes and demonstration phases. Validation is different from the verification actions performed at the end of each task: verification ensures that the specified software requirements are met; validation determines fitness for purpose. HEM and BME will identify criteria for validation of all required work products. BME will perform required validation activities.

T5.8 Integration
(MICRO, PRO, BME, LAM, FP,)

This task is strongly linked to Task 5.1 and is essentially the development test bed for the concurrent engineering design methods developed there. It also draws heavily on the research activities on scale-down in T4.6 and the other engineering tasks in WP5. It will develop the modular concept for the mobile device with reusable and disposable parts, integrate the automation strategies into the remote continuous monitoring device, and manage the reconciliation of design, manufacturing and assembly issues. On the mechanical side, particular attention will be paid to module interconnects, leakage elimination and fluidics control. On the operational side, overcoming challenges of filling, reagent storage and reconstitution will be priorities. Control algorithms and hardware/software interfacing will be specified here in close collaboration with T5.6.

T5.9 Cost engineering
(MICRO, PRO, LAM, FP)

Since one of the primary aims of the project is to develop technology for low-cost high-volume biosensor devices, this important task is central both to the engineering design methodology and to the exploitation plan. Candidate designs and assembly methods will be subjected to close scrutiny for their current and forecast cost implications with reference to projected trends in relevant technologies, security of supply of critical materials and items, and potential for unit cost reduction at higher volumes of production.

Knowledge and IP management:
Innovation is expected in T5.5 (incorporation of nanostructures) and T5.8 (integration). In particular, close attention will be paid, in T7.1, to emerging patents in respect of integration in the closely-related point-of-care medical diagnostics market, which is fast-moving, competitive and litigious.

Exploitation plan:
This work package will incrementally lay the groundwork for the production of demonstration prototypes, whose exploitation is discussed in the description of WP6, below. However, by addressing the underlying engineering issues associated with volume production of low cost devices, it presents the opportunity to exploit these developments in other markets such as point-of-care medical diagnostics.

Work Package 6: Industrial Demonstration and Validation
Work Package leader: WRI (RES, SK) Dr. Livia Tothova
Deputy leader: Dr. Miloslava Proksova
Partners: WRI, BHR LAM, MMM, HEM, BME, MICRO, FP

Note: For convenience, software development and test planning activities (HEM, BME) are described in T5.6 and 5.7, but budget is allocated in Tasks 6.2 and 6.3.

Objectives: See Section 2

Description:
This Work Package is concerned with the systematic development of pre-industrial prototypes of a mobile instrument and a remote automatic device. The targeted application for the mobile device is "first response" threat identification in the water supply, but the device offers the prospect of reducing reliance on laboratory services for routine quality monitoring. The continuous monitoring device is targeted for installation as part of an early warning system.

Obviously prototype development involves a very close relationship with WP5, in which design, manufacturing and integration issues will be resolved. The importance of the planning stage, T6.1, cannot be overemphasised, since this forms the link between device requirements definition from T1.2, the practical realisation of design solutions in T6.2 and T6.3 and their laboratory verification, field trials and demonstration in T6.4 and T6.5.

The planning, prototyping and laboratory verification (T6.1-6.4) are RTD activities: field trials and demonstration of the prototypes are Demonstration activities. They are grouped into the same Work Package because all are concerned with the manufacture of actual working devices.

Tasks:

T6.1 Development and Test Plan
(WRI , BHR, LAM, HEM, BME, MICRO, FP,MMM)

Development Plan: (WRI, BHR, LAM, HEM, BME, MICRO, FP,)
Starting from defined device requirements from T1.2, partners will liaise with Work Package leaders of WP1-5 to scope out realistic engineering specifications for each prototype in T6.2, taking into account the likely availability of RTD results on the timeline. (Detailed planning for the development of each prototype will take place within T6.2.) Contingency plans will be developed to cover possible critical path delays. This information will be fed to WP7 to assist in the forward planning of dissemination activities.

The development of the continuous montintoring and the mobile device will be sequential. First reseources will be focused on the continuous montintoring device. When the specifications of the continuous monitoring device are fulfilled RTD resources will focus on the mobile detection device. This approach ensures that at least one functional prototype is accomplished at the end of the project rather than having the risk that none of the devices reaches specification through the split of resources.

Test Plan: (WRI , FP LAM, HEM, BME)
Testing will be both in the laboratory and in the field (T6.4 and T6.5, respectively). Laboratory tests (T6.4) will first be conducted in distilled water then by samples collected in the field. Both will be spiked by surrogate DNA of bacteria and viruses or non-pathogen relatives of the pathogen organisms. Preliminary tests can also be conducted using model organisms. Optimal procedures for each stage (lysis, hybridisation, *etc*.) will be established for all pathogen organisms; at first, individually, then working towards simultaneous detection of all target organisms in a single device. This will also inform the Development Plan. Field trials will involve samples from treated water, consumption point and other relevant sources. Protocols will need to reconcile the need for testing realistic threat scenarios with safety requirements. The Test Plan will cover schedules and protocols for laboratory and field tests taking into account the foregoing.

T6.2 Prototype Development
(MICRO, PRO, LAM, HEM, BME, MMM)

The detailed scope and timeline for prototype development and testing will be defined in T6.1. However, the tasks involved in the production of the prototype comprise the following: develop engineering design specification from user requirements and development plan; identify quality control requirements; follow design methodology developed in T5.1 to address concurrent engineering issues; manufacture; test components and assemblies. Particular attention will be paid to ease-of-use and cost issues, compatibility and reliability of interconnects. Appropriate QC criteria will be developed for component and assembly testing to meet relevant performance criteria such as speed, ease of use by non technical personnel, specificity to the target analyte, sensitivity, accuracy, resolution, repeatability, dynamic range, robustness, reasonable lifetime, safety and integrity. Devices will be verification-tested in the lab in T6.3 and the final device field tested and demonstrated in T6.4.

Over the course of the project, advances will be made permitting increasing functional integration of preconcentration, cell lysis, PCR and detection stages, microfluidics elements, control systems, electronics, software, data and user interface. As the R&D for these subsystems develops, engineering issues over fabrication and integration will be progressed in WP5.

The first prototype will be designed such that it will server as starting point for both the (trans)portable system (e.g. mounted on a truck) and the stationary, automated, continuous system. See Figure 2 below.
Engineering specifications will detail the requirements in common for both the device and those which are specific for each.

The "continuous monitoring" device envisaged by DINAMICS is not truly continuous: it will not involve a continuous steady stream over the sensor spots. Due to the fact that the most sensitive molecular biological detection processes are batch processes, making a continuous measurement is theoretically not possible. Yet, the ideal concept of continuous measurement can be approximated in practice by reducing the measurement interval. When starting from a simple stationary device the most obvious but still challenging engineering approaches are automatization and paralellization. Automatization can be realized by adding a modul for sample preprocessing. Parallelization is done by duplicating processing units. To get further improvements reducing the time necessary for each process step is necessary. (See Figure 2 below).

Through remote automatic operation the device will repeatedly withdraw samples from a continuous stream of water at a sampling interval determined by the longest timescale of each subsequent operation on this sample (see the description of WP1 for a discussion on this point). The automated stationary system has to be able to be controlled remotely. Other concerns for the continuous device are maintaining filter condition, automation of sampling, flushing, probe regeneration and long-term reliability.

Approaches to make a device mobile are trying to shrink the size of parts, decrease the energy consumption, reducing modules if possible, allowing manual operation and sample introduction and increasing ruggedness.
To make a device more mobile requires several cycles of miniturization and reduction of complexity. The stages cold be defined as stationary -> transportable -> portable -> handheld device.For a mobile device a physical user interface has to be foreseen.

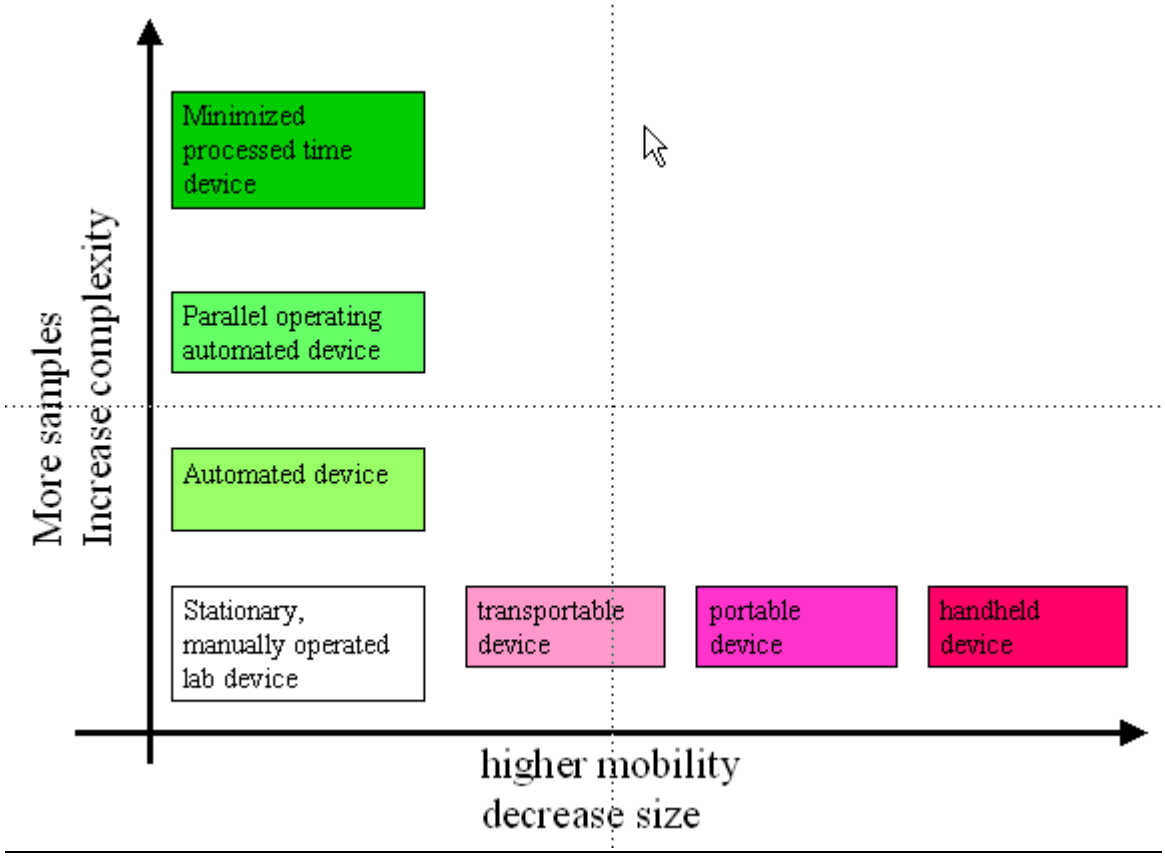


Fig. 2: Development Axis for prototype development.

T6.3 Lab Verification
(WRI, MMM)

Prototype verification will be done in laboratory conditions by comparing results with those obtained by standard cultivation methods applicable under EU regulations (*Legionella sp.* ISO 11731, *E. coli* EN ISO 9308-1, intestinal *enterococci* EN ISO 7899-2). Results of comparative tests will be summarised according to the verification protocol and will contain statistical analysis of results. The report will also consider the suitability of the entire analytical system for specific environments.

T6.4 Field Testing and Demonstration
(WRI, MMM)

See Section 6.2, below

Exploitation:
See Section 6.2, below.

WP7: Knowledge Management (Tasks T7.1 and T7.2)

Tasks within WP7 specifically concerned with innovation activities can be divided IP Management and Exploitation Management. There is a task for each, described below.

Work Package leader: SEZ (Type: Other; D) Dr. Jonathan Loeffler
Deputy leader: Dr. Ulrich Sutter
Partners: SEZ, BHR, LAM

Objectives: See Section 2

Description:
The Knowledge Management activities deal with ownership and exploitation rights within the consortium as well as policy on relevant rival Intellectual Property (IP) outside the consortium. It is therefore important to distinguish clearly between:

- IP ownership *vs*. IP exploitation rights
- IP exploitation rights during the project *vs*. IP exploitation rights after the project

The knowledge generated in DINAMICS will consist of both tangible and intangible **results** that will be either kept confidential, legally protected (intellectual property), used as a basis for exploitation or future research projects, disseminated *via* scientific meetings, journals, EU channels or transferred to third parties. The management of this knowledge will need to be regularly **identified, monitored** and **judged** and mechanisms prepared for this process.

IP management activities are undertaken in Task 7.1, exploitation in Task 7.2. Details of the relevant plans are given in Sections 6.5 and an outline of Planning and Management with respect to Knowledge issues in Section 7.

The exploitation strategy and the IPR issues will be regularly reviewed by the Knowledge Management Team during the project and discussed during the meeting of the Steering Committee.

Tasks:

T7.1 IP Management
(SEZ)

Activities primarily surround the maintenance and implementation of the Knowledge Management Plan, detailed in Section 6.5, below and include the following:

- Maintenance of IP aspects of Consortium Agreement:
- Compile register of relevant background IP
- Maintain record of foreground IP developed
- Police access to foreground and background IP within the project under the terms of the consortium Agreement

For the IP monitoring and policy the following tasks are planned:

- Monthly patent survey to identify and analyse the influence of new patents on the project
- Proactively advise partners of relevant existing and new patents
- Advise Project Management Board on policy with respect to rival third party patents and IP

T7.2 Exploitation Management
(SEZ, BHR, LAM, MICRO)

One of the activities in this task is the construction, maintenance and implementation of the Exploitation Plan, detailed in Section 6.5. This describes the activities and, in broad terms, ground rules for commercial arrangements surrounding the use of DINAMICS's results, technology and know-how outside and beyond the project, considering the benefit for each partner especially for the SMEs. Primary responsibility will reside with SEZ
Another important task is the creation of a Technology Roadmap. BHR will be primarily responsible for this, supported by SEZ, LAM, CRAN and LIONIX.

6.2 DEMONSTRATION ACTIVITIES

Work Package 6: Industrial Demonstration and Validation
Work Package leader: WRI (RES, SK) Dr. Livia Tothova
Deputy leader: Dr. Miloslava Proksova
Partners: WRI, BHR, LAM, HEM, BME, MICRO, FP, MMM

T6.5 Field Testing and Demonstration
(WRI)

The prototype devices (TP6.2 and T6.3) will be tested and demonstrated in the field, in line with protocols developed in the Test Plan (T6.1). Field tests and demonstrations will address two questions:

a) Ease and speed of use in the field
b) Fitness for purpose

Item b) raises problems reconciling the need to demonstrate the ability to detect dangerous pathogens at significant levels with the health and safety requirements of testing the device under realistic operating conditions. These issues will be carefully considered in T6.1 in which test protocols will be developed. There is also an inherent challenge in respect of the continuous device: it will not be possible, at the end of a finite-duration project, to demonstrate long-term reliability of a device designed for continuous, remote online operation.

Exploitation:
Demonstrator prototypes will be targeted at current water industry requirements, so demonstration activities should help to make estimates of current market demand. Any exploiable technology should be market as early as possible. Industrial demonstrations present an opportunity to leverage dialogue with end-users on future requirements and hence enable the identification of specifications and industrialisation needs of a commercial system, which should be implemented as a continuation of the project.

6.3 TRAINING ACTIVITIES

Work Package WP7 deals with knowledge management in a broader sense and also includes IP Management and Exploitation Planning (T7.1 and T7.2, respectively), which are described under Management Activities in Section 6.4, below.

Work Package 7
Work Package leader: SEZ (Type: *Other*; D) Dr. Jonathan Loeffler
Deputy leader: Dr. Ulrich Sutter
Partners: All

WP7: Training (Tasks T7.3 and T7.4)

Tasks within WP7 specifically concerned with training can be divided into Internal and External Training (dissemination) activities. There is a task for each, described below.

Objectives: See Section 2
Tasks:

T7.3 Internal Training and Technology Transfer
(SEZ to co-ordinate, all partners to participate)

DINAMICS is an extremely interdisciplinary project, encompassing a very diverse range of expertise, many of them highly specialised and leading-edge. Both nanotechnology and DNA manipulation are key strategic technologies for a future European knowledge-based economy in which entrepreneurial SMEs are expected to play a driving role in innovation. Microfluidics is a critical enabling technology in emerging markets such as point-of-care diagnostics, whilst multi-scale modelling and simulation is important not just for optimisation of microfluidics, but also increasingly to steer materials design, investigate and develop biological and bio-engineered systems *in silico*. Electronics and software remain central to the development of products incorporating developments in these areas. Knowledge in each of these areas is increasingly specialised and time-consuming to acquire.

As an absolute minimum, this suggests that partners need a "crash course" in each other's core disciplines, simply in order to appreciate the implications and interdependence of their technical decisions. However, and more significantly, innovation is born of cross-fertilisation. Thus, in order to equip partners better to exploit emerging market opportunities, it is highly beneficial to foster understanding of how knowledge and technologies from other sectors, can be incorporated into one's own products, or how one's own expertise can create synergies with others'. In SMEs in particular, short-term pressures and small staff numbers often mean that training budgets can be non-existent, tight or highly focused, and so opportunities to think outside one's customary domain are limited.

DINAMICS offers an opportunity to address these issues. Training activities between partners are regarded as vital to:

- Secure "buy-in" to common project objectives
- Reduce the risk of misunderstanding between partners with its attendant consequences for technology and product development and hence to facilitate the smooth development of prototype devices
- Foster creative innovation within and beyond the project
- Help partners understand future opportunities
- Inform and guide the Exploitation Plan

To these ends Task 7.3 will organise:

- Eight internal training workshops (the first 3 in Months 1 – 12)
- Ten exchanges of personnel (the first 5 in Months 1 – 12)

This will reinforce the knowledge of SMEs inside the core consortium and the exchange of scientific know-how between the academic partners early in the project and ensure that partners remain up to date on relevant developments in each others' fields.

T7.4 Dissemination
(SEZ, UNIBO, BME, CRAN; all other partners invited to participate)

Since the consortium has identified the potentially wide application of biosensor technologies in various markets, maximisation of the exploitation potential requires a well-planned dissemination exercise outside the consortium.

The objective is to disseminate the DINAMICS results to potential users and a wider public of stakeholders (like water supply organisations, policymakers, authorities with responsibility for security measures). Therefore it is of great interest and importance to keep the stakeholders as well as the potential users informed about actual developments of the DINAMICS project. This will be done on the one hand by participating in conferences and workshops and on the other hand by publishing articles in relevant high ranked scientific and industrial journals. Furthermore, information will also be regularly published *via* a dedicated web site. (The domain name, "www.dinamics.org" has already been registered.)

The DINAMICS consortium will also make extensive use of existing European Networks (CORDIS and Innovation Relay Centers) and Technology Platforms covering nanotechnology, the environment and technology transfer (like NanoForum, Water Supply and Sanitation Technology Platform, Nanomedicine, *etc*.). The consortium will issue information *e.g.* through professional magazines, fairs, conferences and seminars as dissemination paths. In this manner, twenty articles and newsletters are foreseen as well two seminars (organised by the three university partners) in order to disseminate new scientific knowledge to lab technicians, students and young professionals. Participation at five technological fairs for take-up measures is planned.

6.4 MANAGEMENT ACTIVITIES

Project Management activities take place within WP8 under two Tasks, dealing with technical and administrative affairs. WP8 is outlined here, for completeness, and detailed in Section 7.

Work Package 8: Project Management
Work Package leader: LAM (IND, A), Dr. Christian Mittermayr
Deputy leader: Mag. Florian Winner
Partners: LAM, BHR, SEZ, Work Package Leaders

Description:
Work Package 8 comprises project-level management activities relating to:

- Administration and finance co-ordination (Task 8.1 SEZ)
- Project co-ordination and technical management, (Task 8.2: LAM, BHR,)

Tasks:

T8.1 Administration and Finance Co-ordination
(SEZ)

SEZ will handle all of the project's routine administration and financial functions. SEZ will establish an internal group responsible for this work. SEZ will act as an administrative link between the co-ordinator and the project's participants: The composition and activities of partners in this WP are described in detail in Section 7.

This task will consist of the following activities:

- Ensure an effective communication strategy is put in place within the consortium.
- Support to the Project Management Board and Project Steering Committee and project co-ordinator
- Project administration and logistics for organising meetings, reports, agendas, minutes, venues, brochures *etc*.
- Promotion of continual partner communication *via* scheduled teleconferences
- Preparing and checking financial statements and assembly of annual reports based upon partner information and activities
- Responsibility for development and maintenance of the project web site
- Public Relations

T8.2 Project co-ordination and technical management
(LAM , BHR, Work Package Leaders)

Project and technical co-ordination are complementary roles. The former is primarily outward-facing towards the Commission and focuses on the make-up and operation of the consortium. Technical co-ordination, by contrast, is inward-facing towards the Project Steering Committee (PSC), and focuses on technical issues.

The project co-ordinator, LAM, will be responsible for the overall management of the project and liaison with the Commission. LAM will be responsible for ensuring that the project runs smoothly and meets all its objectives.

This task will consist of the following activities:

- At the launch of the project, elect representatives to take on any key roles not already identified and established at the kick-off meeting.
- Ensure an effective communication strategy is put in place with the Commission and any related EC projects
- Initiating reviews of the resource distribution, if necessary
- Promotion of continual partner communication *via* scheduled teleconferences

All issues related to research management will be managed by the PSC and supported by the Project Management Panel. Given the wide diversity of disciplines involved in this project – often requiring a significant level of background knowledge – it is important that a technical overview is maintained. Whilst this does not require detailed understanding of each discipline, it does require sufficient grasp of the science and technology to understand the implications of options and decisions in one part of the project for the others.

The primary roles of technical management in DINAMICS, as in all Integrated Projects, are:

- To ensure that a cluster of activities, many of which could stand alone as projects in their own right, are convergent on common objectives
- To take overall responsibility for the delivery of the technical objective
- To do so in full cognisance of commercial opportunities and constraints

As described in section 7, the PSC is formed from Work Package leaders and is the key body at all three management levels: strategic, executive and implementation. Its role is to integrate the Work Packages and produce deliverables and milestones to time, budget and quality. The task of the Technical Co-ordinator is to enable the PSC to fulfil its stated role. BHR will undertake this task by

- holding monthly Interwise meetings of the PSC, and 6-monthly physical meetings. Agendas will be agreed beforehand, meetings minuted and decisions recorded.
- advising the PSC on key technical issues affecting the fulfillment of its role. This may be done pro-actively, identifying issues for PSC decision; or reactively, responding to requests from the PSC.
- monitoring progress against plan and recording PSC decisions to maintain or modify the plan

This involves:

- Responsibility for producing and maintaining a credible project plan
- Advising the Project Management Board on the appropriate balance between time, budget and quality of deliverables

- Understanding the implications of changes or delays within or between Work Packages and devising (at Project level) and supporting (at Work Package level) contingency strategies and plans
- Advising the Project Management Board on technical implications of budgetary decisions
- Advising the Project Management Board on IP policy from a technical perspective and on implications of third party IP
- Liaising closely with Work Package leaders and ensuring that effective technical communication is occurring between Work Packages
- Ensuring that all partners understand and support technical objectives
- Helping to resolve conflict of a technical nature

6.B. PLANS

6.5 PLAN FOR USING AND DISSEMINATING KNOWLEDGE

Knowledge management falls under three categories:

- IP Management
- Exploitation Management
- Dissemination Management

each with its own **Plan** under the responsibility of a **Manager** reporting to the **Knowledge Manager** on the Project Management Board (see Section 7). Each Plan is explained below.

IP Management Plan

Knowledge required for the execution of the project (background IP) and knowledge generated by the project (foreground IP) will be managed in accordance with the principles and articles of a Consortium Agreement (CA). The IP Manager will provide support and assistance to partners wishing to apply for patent cover for their inventions, under terms defined in the CA. *Consortium Agreement*
Because the IP issues are very crucial for such a complex and integrated project the maintenance of IP aspects within the project will be managed by applying a Consortium Agreement which considers the following points:

- **Confidentiality, secrecy and patenting**
- **Publication**
- **IP ownership**:
  - *Background IPR*: list of relevant background IP from each partner which is needed to carry out the project
  - *Foreground IPR*: maintain record of foreground IP developed
- **IP Utilisation and Access Rights:** police the Access Rights to foreground and background IP within the project under the terms of the Consortium Agreements and the General Conditions (Annex II) of the EC contract.

Innovation generated during the project by partner who wish to apply for patent protection, will be treated under the appropriate level of secrecy until such time as its disclosure will not adversely affect patent applications (confidentiality agreement). Such circumstances are most likely to arise during the development of 'new processes' and not with results generated using these processes. The intention to apply for a patent will be communicated to the IP Manager, who will provide support, guidance and assistance. The inventor will have ownership of IP generated by the project's work, but royalty-free licences will be granted to partners in order to perform work within the project. Use outside and beyond the project will be subject to separate agreements negotiated between the partners concerned.

Because of the size of the project and the different levels of integration, there will be **joint inventions** in which the contributions of each project partner cannot be protected individually. Concerned parties should negotiate, on a case-by-case basis, ownership and rights to exploit the relevant IPR: joint ownership, or one owner with favourable licences for the other parties, *etc*. Negotiations will be facilitated by the Knowledge Manager. If amicable resolution cannot be attained, Section 7.3 describes the arbitration rules that will apply.

Whilst publication is under the remit of the Dissemination Manager, any intention to publish will be referred to both the IP Manager, who could exercise a veto if, in his or her judgement, this could seriously affect the interests of a partner. The rules for vetoing or accepting publication will be given in the Exploitation Plan.

The IPR necessary to exploit the results of DINAMICS will be clarified in terms such as:
- Background and foreground that partners bring to, or will develop during the project
- Ownership of this knowledge and access right to it during and after the project

The table below is an illustrative draft of the **knowledge base** that will be an essential input into the **Exploitation Plan**. All partners will populate this **before** the Consortium Agreement is signed.

Background / Foreground IPR

Workpackage	Background IPR	Owners	Access rights	Foreground IPR	Owners
WP2: Micro- and nano-fluidics *(Leader: BHR)*	▪Molecular dynamics models ▪High resolution CFD	Cranfiel Uni Cranfiel Uni	▪Free for DINAMICS	▪Multi-scale modelling technologies	BHR, Cranfield
WP3: Microbiology and sample preparation *(Leader: IFCOR)*	▪Patent protection of useful genes (regions) ▪Trade secrets	Third party Lambda	▪Research exemption ▪Free for DINAMICS	▪New genes for identification ▪Probe sequence ▪Sample pre-processing procedure	Lambda, IFCOR, MMM
WP4: Sensor and signal detection development *(Leader: IDEA)*	▪Electrical read-out of the sites ▪Optical (UV) detection by optical electric transduction ▪UV and optical sensor (amourphous silicon) ▪Method to bind DNA to polymer	Uni Bologna Uni Bologna Uni Bologna Lambda	▪Free for DINAMICS	▪Capacitive detection technique ▪UV detection technique ▪Probe immobilisation chemistry ▪Signal amplification system ▪Capture of the DNA sample	Idea, UniBol Lambda Idea, UniBo, BME BHR, JP
WP5: Engineering *(Leader: JP)*				▪Microfluidics operation ▪Embedded software	BHR, Lambda, JP Hemosoft

The **Access Rights** of the DINAMICS project are based on the General Conditions (Annex II) of the EC contract and deal with the following topics:

- Access Rights to pre-existing know-how
- Access Rights to knowledge resulting from the project
- Access Rights for third parties

The consortium agreement makes a difference between access rights "needed" for carrying out the project and access rights for "commercial" purposes after the end of the project.

The general principles for **Access rights** to **Pre-Existing Know-How** (and PEKH to be excluded) is that this will be granted on a **royalty-free basis** for the project's duration. Conditions for use after the end of project of these underlying patents will be detailed further in the **Exploitation Plan** as well as other access rights *e.g.* for affiliates and for parties joining or leaving the project. For **software development**, a **quid pro quo** arrangement will be put into the **Exploitation Plan**. Partners who develop data and models grant the code developers post-project exploitation rights to their data and models free of charge, whilst the code developers grant other partners post-project exploitation rights to at least core components of their software (sufficient to run the "foreground IP modules") free of charge. Assuming that agreement is reached on this central quid pro quo, there should be no need to make source code available, or to consider any requirement for sublicensing.

IP monitoring and policy

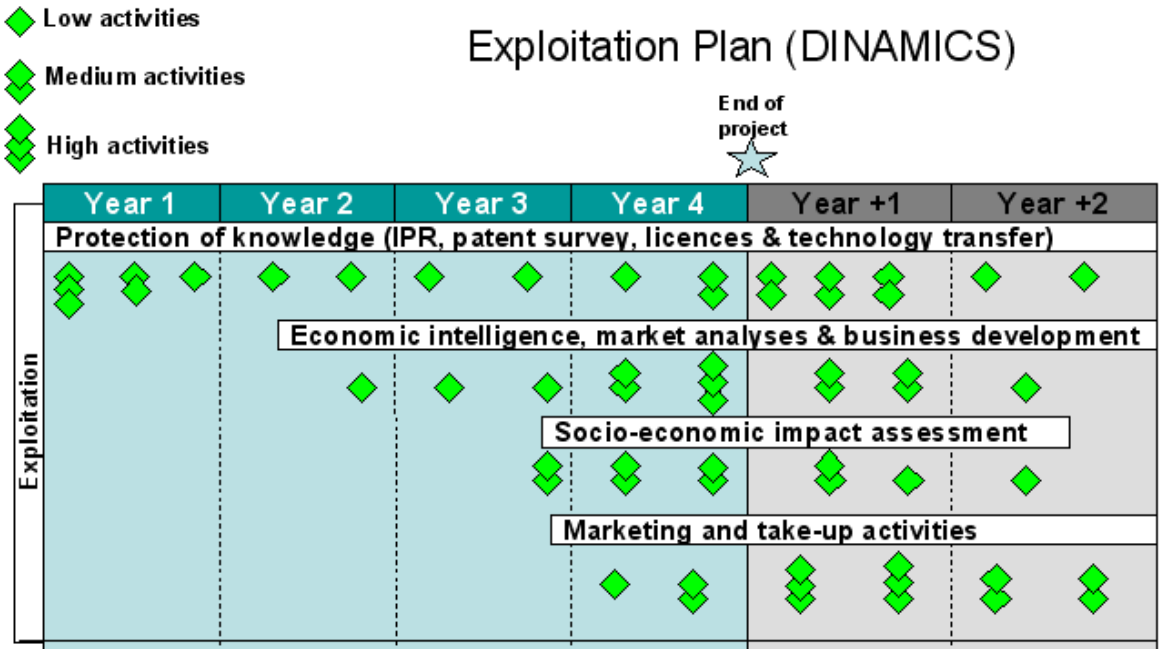
The IP Manager will conduct monthly reviews of third party patents relevant to DINAMICS partners, who, along with the Project Management Board will be advised of their existence and potential significance. In particular, the technical co-ordinator and his assistant will form a view as to its potential to impede exploitation and if technical work-arounds are feasible. In these circumstances, the Knowledge Management

team will advise the Project Management Board on policy, for example, whether to seek an alliance or a licensing agreement.

Exploitation plan

Co-operation between the partners during and after the end of the project plays an essential role in the successful exploitation of the technology innovations. It is necessary to show for each partner and especially for the SMEs, how they will benefit from the innovative results of the DINAMICS project and how they can integrate these results in their future commercial products.

The diagram on the following page presents an overview of the exploitation and activities during the project but also after the end:



In a first step, the rules for the distribution of the Industrial Property Rights (IPR) are elaborated in a consortium agreement in order to define a first **Exploitation Strategy** for the consortium, which will be the basis for the development of an **Exploitation Plan**.

A **knowledge database** will be established and updated with the knowledge generated, used and disseminated in the course of the project. This will form an essential input into the Exploitation Plan. Examples of the activities that the Exploitation Manager will be responsible for is given in the table below:

Research & innovation	IPR and knowledge management activity
Perform the research	• Protect knowledge during research process or publish or put into public domain following project strategy and consortium agreement protocols
Protect and disseminate research results	• Use IPR to control downstream use, even in public domain: open source licences, copyright, database rights, software related IPR • Publish research results with/without IPR
Exploit research results, convert results to a public or a commercial product	• Create knowledge databases, software • Use IPR to secure product development and/or R&D investment • Use licensing for revenue • Use IPR for enforcement against misuse • Updates of standards • Mechanisms for these to be defined in Exploitation Plan

Define new RTD project topics based on knowledge generated in project	• Review prior knowledge • Identify existing IPR protection • Identify IP that can be generated through new RTD projects

The exploitation plan will consider access rights to knowledge for use outside the project; these will be conditional on separate agreements between the relevant partners defining the terms and conditions of this use. However, when inventors are unable themselves to exploit knowledge they have generated in the project, they will be encouraged to license the knowledge more widely to ensure maximum exploitation of the project's results. The consortium is very aware of the need that the maximum amount of information generated during the project will be disseminated to the appropriate stakeholders in as rapid a fashion as possible, provided that this does not damage partners' industrial competitiveness or harm any patent applications.

The **exploitation plan** will give the steps for the exploitation of the results in future commercial products considering the following aspects:

1. Advantages of the developed results/technologies: The technological advantages as well as the respective commercial advantages of the DINAMICS results will be analysed and benchmarked.
2. Identification of threats and competitors (including regulatory constraints): Possible exploitation barriers (standards, ethical and regulatory aspects) will be identified and their impact assessed to optimise the market entry strategy. The emergence of new competing technologies will be analysed.
3. Market analysis: The partners will examine the main areas of business, the market structure in the main industrial sectors of application including its customers, end users and competitors. It will give precise information on market size and accessibility.
4. Market strategy and financial forecast: Using all the former gathered information, a suitable market entry strategy will be worked out including a financial forecast.
5. Action plan and marketing activities: On the basis of the market strategy a precise action plan will be developed and the corresponding marketing materials will be prepared.
6. Recommendation for future R&D development: The need for future R&D activities will be described and take-up measures (especially for SMEs) planned.

Another important issue is the **exploitation mechanism** of the IP and knowledge generated in the DINAMICS project. The final product will be further refined, manufactured and taken to the market by the manufacturer partner, to be recruited. This product will be sold, which will raise income for that company. It will consist of several building blocks employing technology generated during the project, or indeed provided by project partners. Therefore, the manufacturer will require licences for the technology. It is proposed that such licences be exclusive to the manufacturer in return for royalties or exclusive supply agreements with the partners. This will generate a **win-win-situation** for both the manufacturer and the other DINAMICS partners and provide an income stream for the SMEs and a powerful distribution route for their technology

Dissemination plan

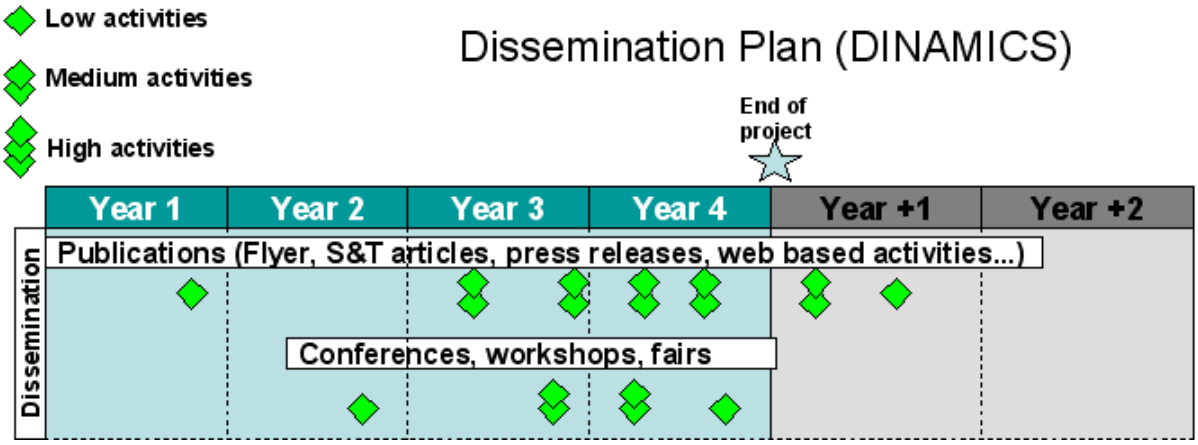
The dissemination activities will be co-ordinated by the Dissemination Manager using the reports and other deliverables generated by the project. His or her role will be both proactive and reactive: he or she will handle requests for publication by partners (likely to be more technical in nature) to ensure that the policy of the Consortium Agreement is followed, and will seek to publicise the project and its significance to the wider public.

Non-confidential findings will typically include literature reviews, experimental techniques and protocols, general trends. Partners' requests for publication will be submitted to the Dissemination Manager, who will check with the IP Manager that publication does not infringe another partner's interests.

Dissemination will be through various routes such as:

- Publications in high-quality technical, business and scientific journals
- Presentations at conferences, symposia and seminars, and the associated diffusion of this information to peers
- Liaisons with other framework programme projects: it will be a priority of the project to liaise with other relevant projects
- Existing European Networks (CORDIS and Innovation Relay Centres)
- Technology Platforms covering nanotechnology, environment and technology transfer (*e.g.* NanoForum, Water Supply and Sanitation Technology Platform, Nanomedicine)
- Specific user groups
- Standards and regulatory committees
- Educational courses
- Dedicated web site

The dissemination activities foreseen are displayed in the figure below:



The project web site will be designed and implemented within the first three months of the project. It is planned to have the following features:

- Distinctive domain name
- Summary, description of project objectives, methods and expected benefits
- NMP logo and acknowledgement of EC financial contribution
- Description of the partners, contact details and links to their web sites
- Public news area for dissemination of project results
- Hyperlinks to useful web sites, including CORDIS, WWW Virtual Library and related projects
- Private area for project members, including bulletin board for news items and events
- Counter for total "hits" (useful for assessing effectiveness of the web site dissemination of results), Bibliography, Technical Annex I, an on-line reporting mechanism for progress monitoring

A biannual summary will be posted by SEZ, in addition to items posted by individual members. The project's newsletters will also be available online. Members will be notified by e-mail of new items.

6.6 GENDER ACTION PLAN

Background

The consortium respects the European Union's objectives in Articles 2 and 3 of the Amsterdam Treaty with respect to the balanced participation of women and men in the decision-making process.

The consortium acknowledges that gender differences are the result of learned roles that vary widely within and across European regions, and therefore special attention within the project will be dedicated to understanding and addressing these issues resulting in the elimination of inequalities and the promotion of equality. Through focused efforts to ensure that gender policy is translated into positive targeted actions, the resource and skill base within all aspects of the project will be strengthened, thereby helping to maintain and further develop the critical mass of expertise and resources achieved within the project.

Management Board

Gender Action Plan

A special gender action programme is set up to attempt to involve more women in the monitoring of water security and safety. The issue of involvement of women is not specific to this field, but rather a more general issue for science as a whole, and the physical sciences in particular. At the same time, it is not a problem that can be "fixed" at the research level. There is limited interest from women in science and engineering in general and there is consequently a need to consider how awareness of the discipline can be raised, beginning at secondary school level. Without an adequate number of female students entering into university programmes, the situation in research in general will not improve.

To ensure that the commitment to gender issues is kept as an important topic during the life of DINAMICS, a number of action points have been agreed by the consortium and some recommendations have also been formulated for gender mainstreaming within the project. These are:

1. Gender statistics
Gender statistics on the workforce employed by the project will be collated annually in order to monitor the status of women in the project and the progress made in terms of gender balance as the project moves forward.

2. Mainstreaming gender equality
Mainstreaming gender equality is a commitment to ensure that women's, as well as men's, concerns and experiences are integral to activities such as research, policy development, programme delivery or technical assistance activities, so that women and men can benefit equally. The issue needs to be treated in the same way as any other organisational function, such as staffing, budgeting or annual reporting. DINAMICS's partners have given a strong commitment that in employing any new staff or students for the project's work, they will take into account the need to encourage more women to work in science. In advertising for and selecting candidates for training, it will ensure men and women having equal access to these opportunities and encourage equal numbers of men and women to take part.

3. Recommendations for redressing work-life balance
DINAMICS recognises the need to treat the employee as a whole person. Partners are asked to verify that their employment contracts allow for parental leave and part-time working/job sharing for women with young children. If this is not the case, the consortium management will request measures be taken to rectify the situation.

4. Raising scientific awareness: (Network of women scientists):
The project partners will create a website in the public domain outlining the role of women in the project ("Women in DINAMICS") which aims to give relevant information to female participants for all gender-specific aspects. It will suitable to promote the awareness of gender issues among interested website readers. It will also include profiles of all the women scientists working in the project and links to relevant websites

(*e.g.* the EC's women in science site, http://europa.eu.int/comm/research/science-society/women-science/women-science_en.html).The

5. Other activities

Wherever possible, 'outreach' events will be organised by individual organisations to address the under-representation of women in science. These will include annual visits to schools by all scientific organisations in the project to encourage female science pupils to take an interest in this area.

The project steering committee has been charged with ensuring a rigorous policy for enforcing gender equality. The consortium is keen to see more female scientists involved in this important area, and contribution from female representatives at meetings will be particularly encouraged. The PSC will ensure that discrimination within the project on grounds of gender (or any other factor) is strictly prohibited. Any transgressions will be severely dealt with, if necessary, by requesting the replacement of a contractor.

Partners have given an undertaking that in employing any new staff or students for the project's work they will take into account the need to encourage more women to work in science. In advertising for and selecting candidates for training, a quota, agreed on by the PMP, will be set for the fraction of women to take part. These undertakings are given as a commitment to the acknowledgment that the role of women in science is an important topic.

6. Other issues

Although gender differences do not come within the scope of the results of work completed by DINAMICS, the development of new means of testing for contaminants in water will have a positive impact on women's and men's health and address the special concerns of younger consumers.

6.7 RAISING PUBLIC PARTICIPATION AND AWARENESS

Raising public participation and awareness falls under the responsibility of the project steering committee

The project web site will include information about the research work undertaken, the objectives of the project and their likely societal implications. This means of dissemination creates broader awareness of the project and the inclusion of contact details for the relevant people allows any representatives of special interest groups to make contact, and share views and even develop broader means of public awareness. Many other dissemination activities will be undertaken by the consortium (newsletters, brochures, presentations etc).

Some of the partners in DINAMICS are also involved in undergraduate teaching. These partners are encouraged to include a short discussion of the project's work in relevant lecture courses to help promote even wider awareness.

6.C. MILESTONES

6.8 MAJOR MILESTONES OVER FULL PROJECT DURATION

Milestone: Expected result and achievements	Delivery Date (Month)	To be delivered
M8.1: Project kick-off meeting	1	Minutes
M1.1: Device requirements specifications	3	Report
M1.2: Device functional specifications	5	Report
M1.3 Test Case definition	6	Report
M8.2: Identification of potential manufacturing partner	6	Selection of one or more candidates for the consortium's approval
M3.1: List of genes	8	Report
M2.1: Demonstration of integration shell	12	Software
M3.2: Selection of probes	15	Report
M3.3: Decision about the sample collection	12	Report
M6.1: Delivery of first version of Development and Test Plans	12	Report
M7.1: Exploitation plan	12	Report
M8.3: First annual meeting	12	Minutes
M8.4: Annual review: decision on project continuation	14	Report
M2.2: Validation of MD software against data for hybridisation dynamics	24	Report and software
M3.4: Decision on need for DNA sequencing	15	Report
M3.5: Decision on on-chip PCR requirement	16	Report
M3.6: Sample preparation protocol – filtration and lysis system	16	Report
M4.1: First system-on-board for lab characterisation and validation	18	Hardware & report
M5.1: Selection of substrate material for prototype devices	18	Report
M8.5: Manufacturer signed up as contractor	18	Contract amendment
M3.7 Achievement of on-chip PCR	24	Demonstration or report of functioning module
M2.3 Simulation software	30	Beta release of multi-scale modelling software suite
M4.2 Achievement of nanotechnological signal enhancement method(s)	24	Demonstration or report of functioning nanotechnology-enhanced biosensor
Functioning scaled-down biosensor integrated with electronics on substrate identified in WP5 18-month interim report	24	Demonstration or report of functioning module
First draft Integration Plan	24	Report
M6.3 Second Revision Test plan including lab and field test protocols	24	Report
Second Interim Report from WP5	24	Report updating progress on all Engineering issues and identifying planned approach to integration

Software User Requirements specifications for continuous prototype	30	Report
Second Revision Prototype Development plan	30	Report, peer-reviewed by Advisory Board
M2.4 Optimised microfluidics	36	Demonstration or report of superior performance
Final device-scale biosensors integrated with electronics on-chip	36	Demonstration or report of superior performance
Biosensor incorporating engineered nanostructure	36	Demonstration or report of (a) functionality and (b) reduced response time
Prototype for mobile device	36	Device ready for laboratory verification
Design for continuous device	36	Report
Third Revision Exploitation Plan	36	Report
Lab verification of both prototypes	42	Demonstration to partners
Field demonstration of both prototypes	48	Demonstration to industry
Final Exploitation plan	48	Report Agreements for post-project collaboration
Final reports	48	Reports

7. PROJECT MANAGEMENT

The project management activities in DINAMICS will provide an effective and efficient structure and mechanisms for:

- Communicating and interfacing at executive and implementation levels both within and outside (*e.g.* with the Commission) the consortium
- Decision-making to direct the project's outcome, manage IP, resolve problems, etc
- Providing administrative and technical co-ordination and management.
-

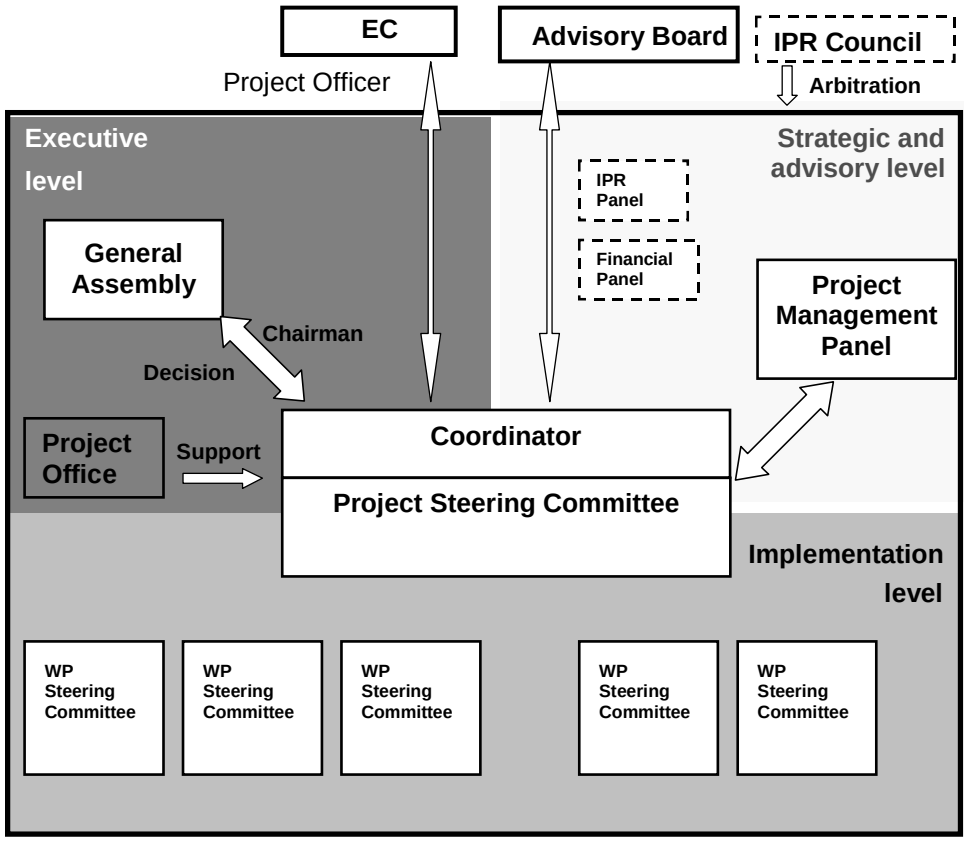
7.1 PROJECT STRUCTURE

Management principles and organisation

The DINAMICS project management will be performed applying the tools and experience of the Co-ordinator and Project Office to carry out international development projects, but adapted to the specific environment related to an Integrated Project under the FP6. This management implies a multidisciplinary activity to be performed by a wide team of partners including end users, suppliers, university and research centres, from different fields.

The organisational structure is defined according to the EC Model Contract and the Consortium Agreement.

The organisation, management and governance structure as well as the decision-making process is shown in the following chart:



The structure of the management organisation is defined in Section 3 of the CA. The responsibilities and authority of the different involved Committees and Boards are described in the Section 5 of the same document.

Project Decision Bodies and Organisation Breakdown Structure

The management structure comprises three management levels:

- *Strategic and advisory level*, consisting of the Project Management Panel (PMP), the Advisory Board (AB), the IPR and Financial panels. The PMP is established by the Project Steering committee and charged with the development of the general project strategy and the identification of possible needs of consortium modification or budget redistribution following the evolution of project results and goals. The AB provides business advice on all aspects of the project necessary to maximise exploitation and uptake of the results.
- *Executive Level*, includes the Project Steering Committee together with the General Assembly, the latter being the voting body for proposals coming from the first. The Project Steering Committee is also in charge of the executive decisions associated with the day-by-day management of the project.
- *Implementation Level*, integrating the Project Steering Committee with the Work Package Steering Committees.

The Project Co-ordination Committee is the key body in the management of the project, linking the strategic and executive levels, therefore ensuring that the day-to-day actions are always carried out in line with global project goals and responding to changes with flexibility and agility.

7.2 ROLES

The following table shows in summary the roles, authorities & responsibilities each Committee/Board has, the members in which they consist of, & the frequency of their meetings:

The Consortium Agreement properly describes these Committees/Boards & their functions.

Committee / Panel	Authority / Decision on	Members	Functions	Meetings
General Assembly (GA)	Implementation Plan Budget New & exclusion of parties Work Package modifications CA & modifications	All partners	Ultimate decision-making body of the Consortium	At least yearly
Project Steering Committee (PSC)	Technical day-to-day planning and management of deliverables, budgets, financial. EstablishPMP	Chairman of WPSC (= WP leaders)	Organisational arrangements & integration of all WP, ensuring smooth interaction. Assurance of timely milestones achievement & deliverables availability with the proper scientific & technical quality.	At least half-yearly
WP Steering committees	Detailed day-to-day planning of deliverables, budgets, finances	All members of a particular WP	Organisational arrangements, work procedures & time schedule of each WP.	As needed
Project Co-ordinator	Without decision power	Project Co-ordinator	Single contact point between DINAMICS & the EC. Chairman of the PCC & GA. Contact point for interactions among the management boards.	
Project Management Panel (PMP)	Without decision power	LAM, BHR, SEZ, UNIBO, Manufacturer	Development of strategic plans to be submitted to the GA Preparation of Annual Implementation Plan	At least half-yearly

Project Office	Without decision power	To be arranged by the Project Co-ordinator: will be assigned to SEZ	Support parties & outside communications through the web site. Support the Project Co-ordinator on the organisation of meetings, consolidation of progress reports & financial statements & maintenance of project documentation	On demand by Project Co-ordinator
IPR Panel (optional)	Without decision power	set up by PSC	Consulting & advisory body to the PCC for issues related to IPR (confidentiality, patents, Publications & exploitation issues), integrating the parties interests.	On demand by PSC
Financial Panel (Optional)	Without decision power	set up by PSC	Consulting & advisory body to the PCC for issues related to budget & finances (cost scheduling, payments, liability & reserve & audits).	On demand by PSC
IPR Council (optional)	Arbitration	3 independent members from European patents, standardisation & publication bodies.	Arbitration of potential discussions & conflicts among parties on IPR & exploitation issues.	

Advisory Board

The Advisory Board, comprising a number of experts from acknowledged organisations completes, at executive level, the business, user and supplier interests of the project. The Board members will act as an advisory committee for the project and will be responsible for judging (based on their own experiences and business sectors) the developments and deliverables from the project against industrial requirements, best practices and quality standards. They will be regularly informed about progress, will meet periodically, and may in addition be asked to advise on issues that affect the success of the project (on a "management by exception" basis).

The AB will advise the project, as necessary, on issues such as European policy, legislation, water safety, monitoring, detection systems, biological threats and emergency planning.

Work Package Leaders

This table indicates WP leaders and deputies and the level of interaction between different WPs.

Work Package No.	Work Package Leader	WP Deputy Leader	Major WP Interactions
1	Dr. Christian Mittermayr	Mag. Florian Winner	2,3,5,6,7
2	Dr. David Brown (BHR)	Dr. Dimitris Ditrakis (CRAN)	4,5,6
3	Robert Deak	Krisztina Metzinger	5,6
4	Dr. Carlotta Guiducci (UniBo)	Dr. Augusto Pieracci (IDEA)	2,5,6
5	Ing. Andreas Aigelsreiter	Martin Buber	1,2,3,4,6,7
6	Dr. Livia Tothova	Dr. Miloslava Proksova	1,2,4,7
7	Dr. Jonathan Loeffler (SEZ)	Dr. Ulrich Sutter (SEZ)	1,2,4,5,6
8	Dr. Christian Mittermayr(LAM)	Mag. Florian Winner (LAM)	all WPs

The DINAMICS structure aims to establish effective communication and collaboration within and between the project work packages. The following text will give information about the duties of key managers.

Members of the WPs will meet every six months to discuss progress, alongside the plenary meetings. It is considered particularly important to have small group meetings, as those participants who are not fluent in English (the working language of the project) will be able better to contribute than in large plenary sessions. The WP leaders will be responsible for their individual WPs, and will co-ordinate the contributions of each partner involved. This will assist with the management of the project. They are responsible for identifying risks and for proposing solutions if problems arise in their WPs.

Meeting schedule summary
All partners will be expected to attend the annual meetings. The formal meeting schedule is summarised in the table below:

Management Unit	Frequency of meeting	Quantity during project	Notes
PSC	Every 6 months	9	
PMP	Every 6 months	9	Linked to PSC meetings
WPSC	as needed	as needed	WPs differ in length
GA	Every 12 months	5	Annual Meetings
AB	Every 12 months	4	Linked to PSC meetings

7.3 DECISION-MAKING MECHANISMS

Methods for monitoring and reporting progress and documenting results

The project's progress will be monitored against the defined milestones and deliverables. Reports required by the Commission must be submitted within four weeks at the request of the co-ordinator. All partners will report to the co-ordinator as and when required. Frequent and meaningful communication between partners is essential to the success of this project. Partners will be expected to use e-mail, telephone and fax to keep in regular contact with each other. Conference calls will also be arranged between partners. Aside from the meetings, reports and newsletters, the communication strategy will revolve around the project web site .

Decision making rules and Conflict resolution measures

The initial organisation structure of the DINAMICS project shall comprise the following:

a. **General Assembly** (GA) as the ultimate decision-making body of the Consortium,
b. **Project Steering Committee** (PSC) as the supervisory body for the project execution, which shall report and be accountable to the GA
c. **Project Co-ordinator** (PC) as the intermediary to the Commission is authorised to carry out the project management and administration, shall report and be accountable to the PSC.
d. **Workpackage Steering Committees (WPSC),** as the technical management group for each Work package.
e. **Project Office (PO)** as support for day-by-day project management for the PSC, established if necessary by the Coordinator**.**

Decision-making rules:

The responsibility and decision-making rules of the management entities are described in detail in the consortium agreement
An Outline of the decision making of the various management bodies is given below:

Committee/ Panel	Quorum	Necessary majority	Voting rule
GA	≥ 66% of parties	≥ 75 %	One vote/ party
GA: 5.2.2 Decisions (double majority)	≥ 66% of parties AND ≥ 66% of shares	≥ 75 % AND ≥ 75 %	One vote/ party AND Project Share in %
PSC	≥ 50% of members	≥ 50% votes	One vote / Member
WPSC	≥ 50% of members	≥ 50% votes	One vote / Member
Other panels	≥ 50% of members	≥ 50% votes	One vote / Member

Conflict resolution
All disputes or differences arising in connection with the project DINAMICS which cannot be settled amicably shall be first resolved by mediation and finally settled by arbitration in Brussels under the rules of arbitration of the International Chamber of Commerce by one or more arbitrators to be appointed under the terms of those rules.

All disputes or differences concerning IPR issues are to be settled amicably by an IPR Council.

The IPR Council can be appealed to by each contractor for clarification of controversies or disputes. The IPR Council shall comprise three representatives who are not involved in the project and who are neither interconnected nor economically related in any manner with any of the contractors. It is envisaged that its members should consist of one representative of each of the European Patent Office, UNICE and the IPR Helpdesk. The decisions of the IPR Council need a simple majority only. The members of the IPR Council will be appointed by the Project Management Board.

7.4 INCORPORATION OF A NEW PARTNERS

At the recommendation of the project evaluators, a manufacturer (Partner 17) is to be incorporated to the consortium by Month 18, at the latest. The project co-ordinator will assume responsibility for organising a search for and selection of the suitable candidate and propose the candidate (accepted by the consortium) to the Project Officer for acceptance and preparation of the corresponding contract amendment. Fulfilment of this condition will be checked at the second review. Failure to comply with this recommendation may result in the discontinuation of the project.

A future partner (FP) (Partner 18) for system integration will be incorporated into the consortium in order to replace a partner that has to leave the consortium due to economic reasons. The project co-ordinator will assume responsibility for organising a search for and selection of the suitable candidate and propose the candidate (accepted by the consortium) to the Project Officer for acceptance and preparation of the corresponding contract amendment.

8. DETAILED IMPLEMENTATION PLAN –MONTHS 13 -30

8.1 INTRODUCTION – GENERAL DESCRIPTION AND MILESTONES

The implementation plan for the first eighteen months is key to ensuring the project meets its longer term goals. A series of milestones have been carefully and deliberately timed to ensure individual contributions link together sequentially providing a controlled route to delivering each of the project's elements. These milestones will be used as a co-ordination tool to measure project accomplishments. The entire consortium is critically aware that delays in achieving milestones, even at an early stage of the project, could result in their removal from future activities. The project is intended to run for four years. This is realistically the minimum timeframe for a project of this scope. The implementation plan has been designed so that work can begin immediately, but some of the tasks require input from other work packages (WPs) before they can begin their activities.

DINAMICS is focused on the development of DNA-based biosensor enabling technology targeted at the water industry with broad applicability to other industrial areas. Every effort has been made during the planning process to provide robust and focused mechanisms that will enable the project to meet its stated objectives in a controlled way and with control of risks. A structure has been proposed that contains comprehensive planning, management and control elements. These embrace measurable and quantitative characteristics, to allow progress to be monitored and managed. These factors are endorsed by the SME management team, (technical and managerial) who rely upon very similar systems for the efficient operation of their own businesses. Integrating organisational control tools into the project are most useful when they provide a means to evaluate potential problems effectively. DINAMICS deals with this by maximising opportunities to mitigate risks by removing or modifying barriers. The success of this implementation plan depends upon two key elements.

1. Careful initial planning
2. The care and skill applied to the management of risk

DINAMICS's detailed approach provides a means to monitor and to influence the project's progress for the benefit of both individual participants, and for the coherent operation of the project. In terms of project planning, the contractors have endeavoured to plan work and to specify project activities so that clarity will reveal any misunderstandings. Comprehensiveness will remove contradictory assumptions, and the rigour placed on planning details will have exposed technical and practical detail.

Each work package includes its own Gantt chart showing the timing of activities and a table indicating risks and mitigation activities.

A degree of flexibility is also necessary. As knowledge, circumstances, and other external influences occur, it is possible that parts of the original plan may have to be modified accordingly. This is why partners will have a comprehensible and ongoing view of the project. The management team, and its organisation, provides the framework to plan activities, to communicate with everybody on a regular basis, and to implement appropriate risk response strategies.

Milestones months 13-30

Milestone ref.	Milestone: Expected result and achievements	Delivery Date (Month)	To be delivered
M8.4	Annual review: decision on project continuation	14	Report
M2.2	Validation of MD software against data for hybridisation dynamics	15	Report and software
M3.4	Decision on need for DNA sequencing	15	Report
M3.5	Decision on on-chip PCR requirement	16	Report
M3.6	Sample preparation protocol – filtration and lysis system	16	Report
M4.1	First system-on-board for lab characterisation and validation	18	Hardware & report
M5.1	Selection of substrate material for prototype devices	18	Report
M8.5	Manufacturer signed up as contractor	18	Contract amendment
M4.1	First system-on-board for laboratory characterization and validation	18	Hardware & report
M8.6	Future Partner signed up as contractor	19	Contract amendment
M5.3	Draft System Architecture Description	20	Report
M2.2	Validation of MD software against data for optimized ion dynamics	24	Report
M3.7	Achievement of on-chip PCR	24	Report
M4.2	Achievement of nanotechnological signal enhancement method(s): Demonstration or report of functioning nanotechnology-enhanced biosensor	24	Report
M6.2	Delivery of second version of Development Plan	24	Report
M5.4	Prototyp of sample lysis system	25	Hardware & report
M5.5	Prototyp of microfluidic DNA Preconcentration System	25	Hardware & report
M5.6	Prototyp of PCR-on-Chip System	25	Hardware & report
M8.7	Annual review: decision on project continuation	26	Contract amendment
M4.3	Design Parameters for Development Prototype	27	Report
M5.2	Selection of substrate material for prototype devices	27	Report
M2.3	Demonstration of beta release of multi-scale modelling software suiteDemonstration of beta release of multi-scale ptimize software suite	30	Report
M5.1	Robust microfluidics solutions	30	Report
M5.7	Prototyp of Automated Filtration System	30	Hardware & report
M6.3	Delivery of second version of Test Plan	30	Report

8.2 PLANNING AND TIMETABLE

		Project month	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Gantt chart																				
			2008									2009								
Activities	WPs	Tasks	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9
DEMO																				
	WP 6b																			
		T 6.4																		
MANAGE																				
	WP 8																			
		T 8.1	D8.6	D8.7, D8.8, D8.9, M8.4					M8.6						D8.10	D8.11 D8.14 M8.7				D8.12 D8.13
			D8.15																	
		T 8.2		D8.18						D8.19						D8.20				
RTD																				
	WP 1																			
		T 1.1																		
		T 1.2																		
	WP 2																			
		T 2.1																		
		T 2.2				D2.2		D2.9, D2.4, D2.5 M2.1						M2.2						
		T 2.3												D2.6						M2.3
		T 2.4						D2.5 D2.6						D2.7 D2.8						
	WP 3																			
		T 3.1																		
		T 3.2			M3.4			D3.5												
		T 3.3		D3.3																
		T 3.4			D3.4															
		T 3.5		D3.2		D3.6, M3.6														

		T 3.6				M3.5				D3.7				M3.7							

Gantt chart

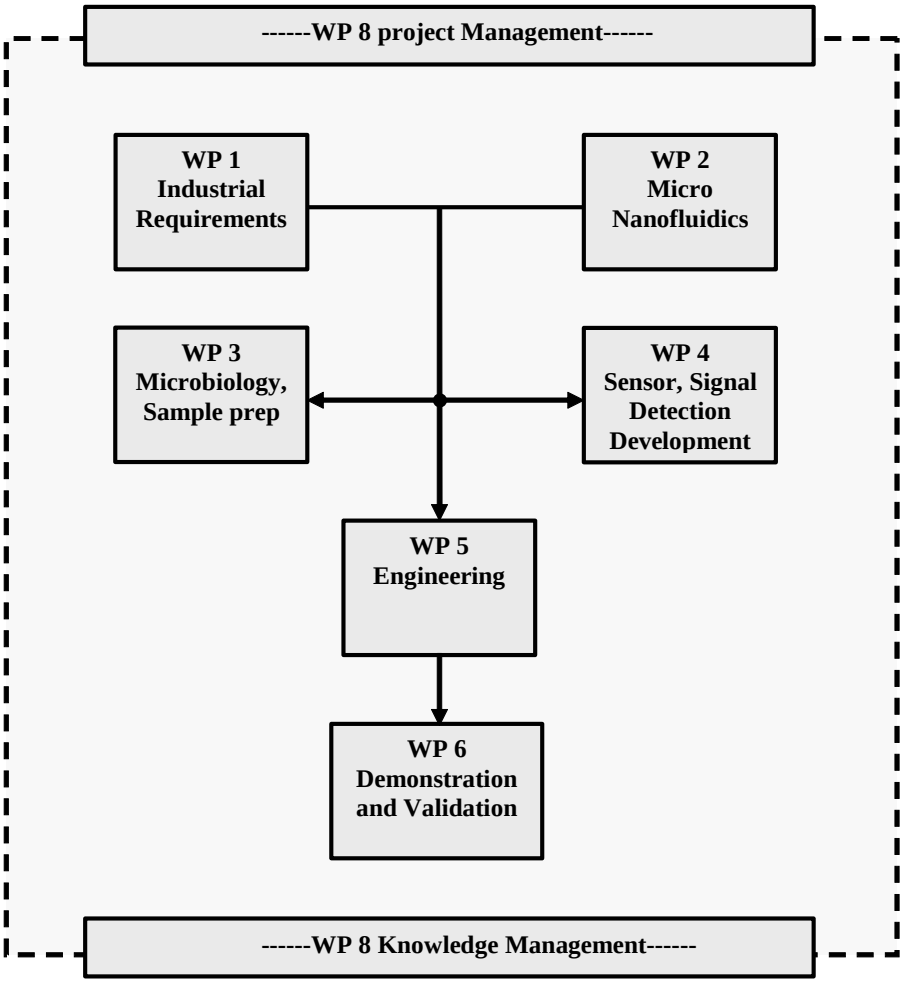
			2008										2009								
Activities	WPs	Tasks	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	
	WP 4																				
		T 4.1						D4.6									D4.8				
		T 4.2						D4.3									D4.9				
		T 4.3						D4.4									D4.10				D4.14
		T 4.4												M4.2							D4.13
		T 4.5													D4.7		M4.3				D4.11
		T 4.6																			
		T 4.7						D4.5, M4.1													
		T4.8																			D4.12
	WP 5																				
								D5.20													
		T 5.2												D5.2	M5.5						M5.1 D5.3
		T 5.3						D5.4, D5.5			D5.6			D5.7, D5.9, D5.10	M5.4, M5.6						D5.8, M5.7
		T 5.4						D5.11									D5.12 M5.2				D5.13
		T 5.5						D5.14,		M5.3				D5.15							D5.16
		T 5.6												D5.17							
		T 5.7																			D5.18 D5.19
		T 5.8																			
	WP 6a																				
		T 6.1												D6.4							D6.5
		T 6.2																			D6.5
		T 6.3																			
	WP 7a																				
		T 7.1						D7.11						D7.13							D7.15

		T 7.2		D7.10														D7.14		
TRAIN																				
	WP 7b																			
		T 7.3																		
		T 7.4	D7.9					D7.12												D7.16

8.3 GRAPHICAL PRESENTATION OF WORK PACKAGES (18 MONTH PLAN)

Work package interaction:
WP1 provides linkages both with the other RTD work packages by defining limits on response time and threshold concentration; and with the demonstration activities in WP6 by providing user specifications for prototype devices. WP2 will deliver simulation tools for optimising the design of sensors in WP4 and microfluidic elements in WP3, 5 and 6. Data from WP4 may be useful in validating these simulation tools (see Section 2). Whilst WP3 will provide the definition of oligonucleotides for immobilisation on sensor surfaces, and therefore will ultimately inform WP4, the core innovation activities in WP4 can proceed on the basis of readily available "dummy" systems such as *E-coli*, and are therefore not directly dependent on WP3. On the other hand there is a strong interdependence between sensor development and miniaturisation activities in WP4 and Engineering issues in WP5. The demonstrator Work Package, WP6, obviously requires decisions about pre-treatment from WP3, integrated sensor and detection technology from WP4 and due consideration of device design, engineering and manufacturing in WP5. Whilst not shown explicitly, there is constant interaction of all work packages with both management and education training and dissemination issues in WP7 and 8.

Interrelationship between work packages



8.4 WORK PACKAGE LIST/OVERVIEW

Work Package List (18 month period Month 13 -30)

Work-package no.	Work package title	Lead contractor no.	Person-months	Start month	End month	Deliverables
2	Micro and Nanofluidics	2	44	1	30 (36)	D2.24- D2.78
3	Microbiology and sample preparation	6	70	5	24 (24)	D3.2-D3.7
4	Sensor and signal detection development	4	103	4	30 (33)	D4.3-D4.15
5	Engineering	17	142,5	10	30 (42)	D5.2-D5.19
6	Industrial demonstration and validation	13	53,5	10	30 (48)	D6.4-D6.6
7	Knowledge management	15	33,66	1	30 (48)	D7.9-D7.16
8	Project Co-ordination	1	10,85	1	30 (48)	D8.6 - D8.20
		Total	**469,51**			

8.5 DELIVERABLES LIST

DELIVERABLES LIST (18 MONTH PERIOD MONTHS 13-30)

Deliverable no.	Deliverable name	WP No.	Lead participant	*Estimated indicative person months*	Nature	Dissemination Level	Delivery Date (month)
D7.9	First scientific seminar	7	UNIBO	1	O	PU	Month 13
D8.6	First annual meeting minutes	8	SEZ	0.5	R	CO	Month 13
D3.2	DNA preconcentration method	3	LIONIX	10	R	CO	Month 14
D3.3	Sample collection protocol	3	WRI	11	R	CO	Month 14
D7.10	Exploitation Workshop	7	LAM	1	O	Co	Month 14
D8.7	First annual report	8	SEZ	3	R	CO	Month 14
D8.8	Annual review meeting with external evaluators	8	LAM	2	O	CO	Month 14
D8.9	Annual report on advancement of gender issues (Gender manager, Month 14)	8	SEZ	0.1	R	PU	Month 14
D3.4	Sample filtration and preconcentration	2	WIR& MMM	11	R	CO	Month 15
D3.6	Cell lysis methods	3	BME	22	R	CO	Month 16
D2.9	Description of MD modules for nanofluidic devices	2	CRAN	23	O	CO	Month 18
D2.4	Description of MD modules for microfluidic devices	2	CRAN	23	O	CO	Month 18
D2.5	Pre-calculations to support decisions on sensor design and sale-down in T4.4-T4.6	2	CRAN & BHR	5	R	Co	Month 18
D3.5	Final probe set	3	LAM& MMM	13	R	CO	Month 18
D4.3	First prototype of UV sensor	4	UNIBO	15	P	CO	Month 18

D4.4	First prototype of capacitive sensor	4	UNIBO	14	P	CO	Month 18
D4.5	First prototypes of electronics for interface with deliverables D4.3 and D4.4	4	IDEA	20	P	CO	Month 18
D4.6	Report of the surface characteristics of prototype sensors	4	UNIBO	6	R	Co	Month 18
D5.11	Manufacturing considerations for substrate material selection	5	LAM	3	R	Co	Month 18
D5.14	Draft System Architecture Description and Engineering Specifications	5	MICRO	2	R	Co	Month 18
D5.4	Report on Macro-Micro-Fluidic-Interfaces	5	PRO	3	R	Co	Month 18
D5.5	Design for Automated Filtration System	5	MICRO	5	R	Co	Month 18
D7.11	Patent and technology watch update	7	SEZ	1	R	Co	Month 18
D7.12	Second scientific seminar	7	UNIBO	1	O	Pu	Month 18
D5.20	Final Version of the Design Methodology	5	MICRO	2	R	Co	Month 18
D3.7	PCR-protocol for Validation	3	MMM& LAM	6	R	Co	Month 20
D8. 12	PSC Meeting	8	SEZSEZ	0,50,5	R	Co	Month 20
D5.6	Design of sample lysis system	5	BME	7	R	Co	Month 21
D2.6	Description of first prototype multi-scale, multi-physics software	2	CRAN & BHR	12	R	Co	Month 24
D2.7	Post-calculation report to support decisions on design amendments	2	CRAN & BHR	2	R	Co	Month 24
D5.10	Prototyp of PCR-on-Chip System	5	LIONIX	4	P	Co	Month 24
D5.15	1st revision of System Architecture Description and Engineering Specifications	5	MICRO	1	R	Co	Month 24
D5.17	Deliver hardware abstraction layer and device driver modules for embedded systems	5	HEM	6	R	Co	Month 24
D5.2	First Design of Microfluidic System	5	PRO	2	R	Co	Month 24
D5.7	Prototyp of sample lysis system	5	BME	2	R	Co	Month 24
D5.9	Prototyp of microfluidic DNA Preconcentration System	5	LIONIX	2	P	Co	Month 24
D6.4	Second version Development Plan	6	MICRO	3	R	Co	Month 24

D7.13	Patent and technology watch update	7	SEZ	1	R	Co	Month 24
D4.7	Literature review on chaotic advection	4	BHR	3	R	Co	Month 25
D8. 10	2nd annual meeting minutes	8	SEZ	0,1	R	Co	Month 25
D8. 11	2nd annual report	8	LAM& SEZ& BHR	1	R	Co	Month 26
D8. 14	Annual report on advancement of gender issues	8	SEZ	0,2	R	Co	Month 26
D8.15	Agendas, Papers and Minutes for monthly Project Steering Committee meetings (Web-mounted Reports, monthly)	8	BHR	1	R	Co	monthly
D4.10	Second prototype of capacitive sensor	4	UNIBO & BME	3	P	Co	Month 27
D4.11	Quantified design parameters for nanotechnological detection enhancement	4	BHR & LIONIX	4	R	Co	Month 27
D4.12	Report on initial results with various microfluidic structures	4	UNIBO& LIONIX	5	R	Co	Month 27
D4.8	Report on surface modification protocols and the use of sequences identified in T3.2	4	UNIBO	4	R	Co	Month 27
D5.12	Deliver final decision on chip materials	5	LAM	2	R	Co	Month 27
D4.9	Prototype of UV sensor based on polymeric material	4	LAMBDA & UNIBO	5	P	Co	Month 27.
D7.14	Final TRM report	7	BHR	1,5	R	Co	Month 29
D4.13	Report on an agreed upon protocols and reagents for nanotechnological signal enhancement	4	UNIBO	6	R	Co	Month 30
D4.15	Second prototypes of electronics for UV sensor and capacitive sensor	4	IDEA & BME	2	P	Co	Month 30
D5.13	Report on manufacturing issues	5	MICRO	6	R	Co	Month 30
D5.16	2nd revision of System Architecture Description and Engineering Specifications	5	MICRO	2	R	Co	Month 30
D5.18	Deliver documented beta release user interface software	5	HEM	10	R	Co	Month 30
D5.19	Concept for data processing and statistical analysis	5	HEM	5	R	Co	Month 30
D5.8	Prototyp of Automated Filtration System	5	MICRO	6	P	Co	Month 30

D6.5	Second version Test Plan	6	WRI	3	R	Co	Month 30
D6.6	1st technical drawing of device prototype	6	MICRO	3	R	Co	Month 30
D7.15	Patent and technology watch update	7	SEZ	1	R	Co	Month 30
D7.16	Report on conference participation and scientific articles	7	UniBo	0,2	R	Co	Month 30
D8.13	PSC Meeting	8	SEZ	1	O	Co	Month 30
D8.13	PSC Meeting	8	SEZ	1	O	Co	Month 30
D5.3	Deliver robust microfluidics solutions to all on-chip fluid-handling operations	5	PRO	5	R	Co	Month 30

8.6 WORK PACKAGE DESCRIPTIONS

Work Package Number	**WP2**	**Start date**	Month 1	**Duration**	36 Months
Title: Micro- and nanofluidics (Months 13 – 30)		**Work package Leader:** BHR			
Participant	**Person Months:**	**Role of partner:**			
BHR	13	T2.1 – T2.4: CFD approaches and simulations, scale coupling algorithms, industrial supervision of employee PhD, sensor and subsystem simulation., software comparison and validation studies.			
CRAN	31	T2.1 – T2.4: Development and testing of CFD and MD approaches. CFD and MD simulations using higher order methods, Coupling of physics across scales.			
Total Person Months	44				

Objectives (Months 13-30):

- To develop a quantitative understanding of the physiochemical behaviour of micro- and nano-fluidic systems
- To develop and validate prototype state-of-the-art simulation tools
- To use these tools to simulate the relevant continuum and molecular level phenomena in the sensor and other areas of the proposed LOC device.
- To support sensor and micro-fluidic design and optimisation efforts

Description of work to be undertaken (Months 13-30):

During the second stage of DINAMICS, WP2 plans further implementation of the methodology and code modules already developed, with initial and continuing validation and exploitation of the prototype software tools being developed.

Simulations (coupled and uncoupled) will be undertaken to support the design and development work performed within WP4, WP5 & WP6. The performance of these tools will be compared (where possible) to commercial non-coupled tools.

Task 2.1 Diffusion and Mixing at micro- and nanoscales
Month 1 – Month 15

T2.1 has initially focused on a critical review of mechanisms, models and data describing the relevant diffusion and flow phenomena in nano- and micro-scale devices. Numerical and analytical simulation procedures for these phenomena have also been reviewed.

Task 2.2 Multi-scale modelling methodology
Month 1 - Month M18

T2.2 is primarily concerned with the development of optimum methodologies, models, and numerical procedures for the simulation of relevant continuum and molecular scale behaviour (convection, diffusion, hybridisation and binding). Both Molecular Dynamics and CFD techniques are being developed. A number of techniques are being applied to effectively couple these molecular and continuum level simulations:

- A Lagrangian "meta-model"
- Selective grid refinement

Task 2.3 Development of Simulation Toolkit
Month 8 to Month 36

T2.3 is concerned with the development and testing of a suite of software tools based on the methodologies and models selected and described in T2.2. This task will encompass extensive CFD and MD simulations on representative and relevant test cases. Initial validation and testing will be on de-coupled or partly coupled

tools, with later simulations testing the fully coupled code. Where possible, results of simulations will be validated against data emerging from the sensor development activities in WP4. Additional activity will comprise development and refinement of computational algorithms for the efficient coupling of models across length- and timescales, i.e. implementation of the strategies identified in T2.2.

Task 2.4 Design Support: simulation and optimisation
Month 8 – Month 36

T2.4 focuses on the application of those tools developed in T2.3 to perform simulations of potential or prototype devices developed within DINAMICS. Initial simulations will be performed using the relevant codes (CFD or MD) in stand-alone (un-coupled) mode, to support design decisions in other work packages. These, and later coupled simulations, should not necessarily be limited to only the sensor component/section of the whole LOC device.

Efforts will be focused on the identification of concepts and strategies to optimise the performance and efficiency of the relevant section of the device. In the sensor section this includes the reduction of response time, increasing the detection limits, and maximising gain. This task will therefore overlap with T2.3, reflecting the necessity of iteration between models and simulations in these work packages.

The performance of the software tools developed will be compared (where possible) to "industry standard" stand-alone software packages.

Completed Deliverables:

D2.1 "A Comprehensive Review on the Computation of Diffusion at Micro- and Nano- Scales", (Report, T2.1, CRAN, Delivered M8)

D2.2 "Methodology for scale-coupling" (Report/Software description, T2.2, CRAN & BHR, Delivered Month 12)

D2.3 "Integration shell for multi-scale modelling" (Report/Software Description, T2.2, CRAN, Delivered Month12)

Deliverables Planned for Month 13 – Month 36

D2.4 Description of CFD models of microfluidic devices (Report/Software description, T2.2, CRAN, Month 18)

D2.5 Pre-calculations to support decisions on sensor design and sale-down in T4.4-T4.6 (Report, T2.4, CRAN & BHR, Month 18)

D2.6 Description of first prototype multi-scale, multi-physics software (Report/Software description, T2.3, CRAN & BHR, Month 24)

D2.7 Post-calculation report to support decisions on design amendments (Report, T2.4, CRAN & BHR, Month 24)

D2.8 Report on application of multi-scale modelling toolkit to optimisation of microfluidics and sensor design (Report, T2.4, CRAN & BHR, Month 36)

D2.9 Description of MD modules for nanofluidic devices (Report/Software description, T2.2, CRAN, Month 18)

Expected results and corresponding milestones:

M2.1 Demonstration of integration shell (Deliverable D2.3, Completed Month 12, Responsibility:

BHR/CRAN, "software description")

Milestones Planned for Month 13 – Month 36

M2.2 Validation of MD software against data for hybridisation dynamics (Month 24, responsibility: CRAN, "Report/Software description")

M2.3 Demonstration of beta release of multi-scale modelling software suite (Month 30, responsibility: CRAN, Report/Software description)

M2.4 Demonstration of optimised fluid dynamics (Month 36, responsibility: BHR, Report)

Work Package Number	**WP2**	**Start date**	Month 1	**Duration**	36 Months
Title: Micro- and nanofluidics (Months 13 – 30)		**Work package Leader:** BHR			
Participant	**Person Months:**	**Role of partner:**			
BHR	17	T2.1 – T2.4: CFD approaches and simulations, scale coupling algorithms, industrial supervision of employee PhD, sensor and subsystem simulation., software comparison and validation studies.			
CRAN	31	T2.1 – T2.4: Development and testing of CFD and MD approaches. CFD and MD simulations using higher order methods, Coupling of physics across scales.			
Total Person Months	48				

Objectives (Months 13-30):

- To develop a quantitative understanding of the physiochemical behaviour of micro- and nano-fluidic systems
- To develop and validate prototype state-of-the-art simulation tools
- To use these tools to simulate the relevant continuum and molecular level phenomena in the sensor and other areas of the proposed LOC device.
- To support sensor and micro-fluidic design and optimisation efforts

Description of work to be undertaken (Months 13-30):

During the second stage of DINAMICS, WP2 plans further implementation of the methodology and code modules already developed, with initial and continuing validation and exploitation of the prototype software tools being developed.

Simulations (coupled and uncoupled) will be undertaken to support the design and development work performed within WP4, WP5 & WP6. The performance of these tools will be compared (where possible) to commercial non-coupled tools.

Task 2.1 Diffusion and Mixing at micro- and nanoscales
Month 1 – Month 15

T2.1 has initially focused on a critical review of mechanisms, models and data describing the relevant diffusion and flow phenomena in nano- and micro-scale devices. Numerical and analytical simulation procedures for these phenomena have also been reviewed.

Task 2.2 Multi-scale modelling methodology
Month 1 - Month M18

T2.2 is primarily concerned with the development of optimum methodologies, models, and numerical procedures for the simulation of relevant continuum and molecular scale behaviour (convection, diffusion, hybridisation and binding). Both

Molecular Dynamics and CFD techniques are being developed. A number of techniques are being applied to effectively couple these molecular and continuum level simulations:

- A Lagrangian "meta-model"
- Selective grid refinement

Task 2.3 Development of Simulation Toolkit
Month 8 to Month 36

T2.3 is concerned with the development and testing of a suite of software tools based on the methodologies and models selected and described in T2.2. This task will encompass extensive CFD and MD simulations on representative and relevant test cases. Initial validation and testing will be on de-coupled or partly coupled tools, with later simulations testing the fully coupled code. Where possible, results of simulations will be validated against data emerging from the sensor development activities in WP4. Additional activity will comprise development and refinement of computational algorithms for the efficient coupling of models across length- and timescales, i.e. implementation of the strategies identified in T2.2.

Task 2.4 Design Support: simulation and optimisation
Month 8 – Month 36

T2.4 focuses on the application of those tools developed in T2.3 to perform simulations of potential or prototype devices developed within DINAMICS. Initial simulations will be performed using the relevant codes (CFD or MD) in stand-alone (un-coupled) mode, to support design decisions in other work packages. These, and later coupled simulations, should not necessarily be limited to only the sensor component/section of the whole LOC device.

Efforts will be focused on the identification of concepts and strategies to optimise the performance and efficiency of the relevant section of the device. In the sensor section this includes the reduction of response time, increasing the detection limits, and maximising gain. This task will therefore overlap with T2.3, reflecting the necessity of iteration between models and simulations in these work packages.

The performance of the software tools developed will be compared (where possible) to "industry standard" stand-alone software packages.

Deliverables:

D2.2 Methodology for scale-coupling (Report/Software description, T2.2, CRAN & BHR, Month 16)
D2.3 Description of MD modules for nanofluidic devices (Report/Software description, T2.2, CRAN, Month 18)
D2.4 Description of CFD models of microfluidic devices (Report/Software description, T2.2, CRAN, Month 18)
D2.5 Pre-calculations to support decisions on sensor design and sale-down in T4.4-T4.6 (Report, T2.4, CRAN & BHR, Month 18)
D2.6 Description of first prototype multi-scale, multi-physics software (Report/Software description, T2.3, CRAN & BHR, Month 24)
D2.7 Post-calculation report to support decisions on design amendments (Report, T2.4, CRAN & BHR, Month 24)
D2.8 Report on application of multi-scale modelling toolkit to optimisation of microfluidics and sensor design (Report, T2.4, CRAN & BHR, Month 36)

Expected results and corresponding milestones:

M2.1 Demonstration of integration shell (Deliverables D2.2, Month 18, responsibility: BHR/CRAN, "software description")

M2.2 Validation of MD software against data for hybridisation dynamics (Deliverable D2.3, Month 24,

responsibility: CRAN, “Report/Software description”)

M2.3 Demonstration of beta release of multi-scale modelling software suite (Deliverables D2.6, Month 30, responsibility: CRAN, Report/Software description)

M2.4 Demonstration of optimised fluid dynamics (Deliverables D2.8, Month 36, responsibility: BHR, Report)

Work Package Number	**WP3**	**Start date**	Month **5**	**Duration**	**20** Months
Title: Microbiology and sample preparation		**Work package Leader: MMM**			
Participant	**Person Months:**	**Role of partner:**			
MMM	14	T3.2, T3.4-T3.6: Work package leader; Database search, target gene (region) selection, probe design; sample concentration (filtration models, strategies); cell lysis methods, PCR			
LAM	22	T3.2, T3.4-T3.6: Database search, target gene (region) selection, probe design; DNA preconcentration; PCR system development			
WRI	10	T3.3, T3.4, T3.5: Sample collection methods and handling protocols, sample preconcentration by filtration; cell lysis			
LIONIX	6	T3.4, T3.6 DNA preconcentration: interface with microfluidics; PCR on chip development			
BME	18	Task 3.5 Cell lysis			
Total Person Months	**77**				

Objectives (month 13-30):

- To design probes for the target analytes
- To define sample collection and pre-concentration protocols
- To define cell lysis protocol for Nucleis Acid
- To develop on chip PCR

Description of work to be undertaken (month 13-30):

Task 3.2 Probe design

According to the results of "T3.1 Gene selection" the sequences of the probes will be designed.
The strategy for designing probes is dependent on the type of organism and the gene used. The most important property of a good probe is high specificity and high sensitivity. Computer algorithms will be used to meet these criteria. Experiments will narrow down the candidates and allow fine-tuning of the probe sequence. The same gene (region) for the probe design will be selected for bacteria and eukaryotes, if possible.

Task 3.3 Sample collection

A sampling plan will be detailed. Water samples will be necessary to use for "T3.4 Sample preconcentration" and "T3.5 Cell lysis and DNA preconcentration methods", Verification, monitoring.

Task 3.4 Sample preconcentration

Since the infectious dose of some bacteria or viruses is very small, a pre-concentration step is necessary: it is estimated that a factor of about 10^3 –10^4 will be required. Special consideration will be given to the selection of filter type and pore size required to handle a range of target organisms of differing size. The interference of organic material has to be taken into account. Techniques considered will include ultra-filtration (hollow fibre and tangential flow), reverse osmosis and cation-coated filter methods.
Pre-filtration step will be examined by WRI and MMM in order to separate the bigger particles which may cause difficulties in the real filtration step.

Task 3.5 Cell lysis and DNA preconcentration methods

To make DNA or RNA fragments of the biological material accessible for hybridisation, cells and viruses must be lysed. Strategies for combined lysis and filtration will be investigated by BME, MMM and WRI. Two approaches to integration with the microfluidic device will be compared: 1)
outside the cartridge, hence reusable; 2) inside, hence disposable. A pre-concentration step for DNA investigated by LIONIX) will further improve the detection limit.

Task 3.6 Amplification and on-chip PCR

Validation of probe specificity is best done by PCR-products, since no live organisms are necessary and sample material can be made available in almost unlimited amounts. For this reason PCR methods have to be developed no matter if PCR is absolutely necessary for reaching the detection limit or not.

The most common method is PCR for DNA and RT-PCR for RNA targets. Both procedures need extensive optimisation in the case of multiplex application. Amplification of Nucleic Acid (NA) will be used to check the sensitivity, specificity of the system. Real-Time PCR method will be used to test the effectiveness of the step of filtration&lysis. For this test standard NA isolation and amplification protocols will be applied. The on-chip PCR possibilities will be examined by LIONIX.

Deliverables:

D3.2 DNA preconcentration method (Report, T3.5, LIONIX, Month 14)
D3.3 Sample collection protocol (Report, T3.3, WRI, Month 14)
D3.4 Sample filtration and preconcentration (Report, WRI, MMM, T3.4, Month 15)
D3.5 Final probe set (Report, T3.2, LAM, MMM, Month 18)
D3.6 Cell lysis methods (Report, BME, T3.5, Month 16)
D3.7 PCR-protocol for Validation (Report, LAM, MMM, T3.6, Month 20)

Expected results and corresponding milestones:

M3.4 Decision on need of DNA sequencing (Month 15, Responsibility: LAM, MMM)
M3.5 Decision on whether on-chip PCR is required (Month 16, Responsibility: LAM, MMM)
M3.6 Sample preparation protocol – filtration and lysis system (Month 16, Responsibility: MMM, WRI, BME)
M3.7 Achievement of on-chip PCR (Month 24, Responsibility: LIONIX)

Work Package Number	**WP4**	**Start date**	Month **4**	**Duration**	**30** Months
Title: Sensor and Signal Detection Development (MONTH 13-30)		**Work package Leader: UNIBO**			
Participant	**Person Months:**	**Role of partner:**			
UNIBO	50	Co-ordination of the whole development; Work package leader. T4.1-4.4, T4.7: Development of detection techniques; evaluation of nanotechnological signal enhancement.			
IDEA	12	T4.6, T4.7: Development of the systems electronics up to prototyping level			
LAM	21	T4.1-4.4, T4.6: Development and testing of sensors. (Starting from the third year of the project, in charge of industrialisation of sensors.)			
BME	9	T4.1, T4.6-4.7: Implementation of patterned thin metallic film for substrates preparation; probe immobilisation with copolymerisation technique. Share development of the systems electronics with IDEA			
BHR	4	T4.5 Critical review of literature, both from theoretical and practical standpoints. Specification of design parameters.			
LIONIX	7	T4.5, T4.8 Consultant on manufacturing constraints on the design parameters Manufacturing chips for validation of the hydrodynamic focussing (including fluidics setup)			
Total Person Months					

Objectives:

Develop integrated capacitive detection technique

Develop integrated UV-detection technique

Investigate the potential of chaotic advection to reduce diffusional length and time scales in a microchannel. Specify design parameters likely to initiate chaotic advection, within the framework and constraints of a system-wide design process. Confirm that the specified design parameters do lead to chaotic advection within the final prototype design, using either a physical or numerical model.

To validate SNR improvement by use of hydrodynamic focussing strategies. Validation will be done by means of optical measurements on microfluidic structures.

Enhance signal amplification system using nanotechnology

Identify the optimal probe immobilisation chemistry

Description of work to be undertaken:

T 4.1 Surface Science (UNIBO, BME, LAM) This work package is concerned with the characterisation of surfaces prior to and after functionalisation with probes. This will involve fundamental research on test surfaces, and applied research on the surfaces of microfabricated devices. Test surfaces can be chemically derivatised for oligonucleotide attachment at UNIBO. Synthetic functionalised oligonucleotide probes will be obtained from commercial suppliers and anchored on the test surfaces. Whilst the specific sequences to be employed in prototype devices (WP6) are being identified in T3.2, it will be possible to work with "dummy" sequences. This activity should interact with sensor development in T4.2 and 4.3, with sensor nanotechnological enhancement strategies in T4.5 and 4.6 and also with activities associated with the production of prototype demonstrators in WP6.

T 4.2 UV Sensor development (UNIBO, LAM) Whilst initial development work will concentrate on quartz or glass, a core issue is the difficulty in derivatising the surface of transparent polymeric materials that may be compatible with the UV technique and offer potential for low cost large-scale production. The derivatisation technique will be made available to the consortium through a partner (LAM).

T 4.3 Capacitive Sensor Development (UNIBO, LAM, BME) UNIBO will be able to prepare macro-sized clean and flat metal surfaces for testing of electrical detection techniques, through its high-vacuum metal evaporation system. BME will develop micro-sized electrodes on glass substrates. These can be simply hand-wired to external measurement instruments through the use of custom-built macro-flow-cells.

T 4.4 Nanotechnological Signal Enhancement (UNIBO, LAM) Possible strategies towards the amplification of the signal due to recognition between nucleic acids will be attempted, with the goal of applying it towards the integrated surface-bound detection of a low number of nucleic acids. The performance of these strategies will be tested.

T4.5 Nanotechnological Detection Enhancement (BHR, LIONIX) The specialist literature on chaotic advection will be reviewed, to investigate the practicality of initiating it within the DINAMICS biosensor and to estimate the increase in diffusion coefficient that may be achieved. Literature covering both theoretical aspects and practical implementations will be included.
The combination of geometrical features or time-varying inlet velocities likely to lead to chaotic advection will be specified. This will be undertaken within the framework of the design process for the system as a whole and for the loc device as a component. Hence they will be specified with regard to manufacturing feasibility and to other design requirements for the system and component.

T 4.6 Detection Scale-Down and Integration (IDEA, LAM, BME, MMM) Electronic and UV measurements of DNA hybridisation on the surface will be performed with and without techniques for nanotechnological signal enhancement (T4.4). Test surfaces of progressively smaller size will be employed in order to study the behaviour of the system when it approaches the millimetre/micrometre scale.

T 4.7 Signal Processing (IDEA, UNIBO, BME) Signal processing will be realised as embedded systems on a separate board. A data acquisition technique will be implemented exploiting a differential measurement between the signal of sensor under test and that of a dummy sensor to reduce Signal-to-Noise Ratio (SNR) and enhance system sensibility. As IDEA is a small company, the considerable effort will be shared with BME.

T 4.8 Validation of hydrodynamic strategies (LIONIX, UNIBO) Fabrication of microfluidic structures with which the simulation results on hydrodynamic focussing can be verified. This includes the interface between the microfluidic chips and the optical setup at Bologna as well as the fluidic handling system. In WP2 numerical tools will be developed and numerical simulations and parameter calculations will be performed to support and aid the designs of the microfluidic channels and the focussing device. WP2 will also be able to discuss the experimental results obtained by UNIBO and refine the numerical models, if necessary. UNIBO will perform optical observations on the suitability of the implemented microfluidic structures.

Deliverables:

D4.3 First prototype of UV sensor (Hardware, T4.2, UNIBO, Month 18)

D4.4 First prototype of capacitive sensor (Hardware, T4.3, UNIBO, Month 18)
D4.5 First prototypes of electronics for interface with deliverables D4.3 and D4.4 (Hardware, T4.7, IDEA, Month 18)
D4.6 Report of the surface characteristics of prototype sensors (Internal report, T4.1, UNIBO, Month 18)
D4.7 Literature review on chaotic advection (Report, T4.5, BHR, Month 25)
D4.8 Report on surface modification protocols and the use of sequences identified in T3.2 (Report, T4.1, UNIBO, Month 27)
D4.9 Prototype of UV sensor based on polymeric material (Hardware, T4.2, LAMBDA and UNIBO, Month 27).
D4.10 Second prototype of capacitive sensor (Hardware, UNIBO and BME, Month 27)
D4.11 Quantified design parameters for nanotechnological detection enhancement (Report, T4.5, BHR and LIONIX, Month 27)
D4.12 Report on initial results with various microfluidic structures (Report, T4.8 UNIBO, LIONIX, Month 27)
D4.13 Report on an agreed upon protocols and reagents for nanotechnological signal enhancement (Report, T4.4, UNIBO, Month 30)
D4.15 Second prototypes of electronics for UV sensor and capacitive sensor (Hardware, T4.7, IDEA and BME, Month 30)
D4.16 Report on capacitive and UV measurement on DNA hybridization on surface of micro-sized dimensions and with and without nanotechnological enhancement (Report, T4.6, UNIBO, Month 33).

Expected results and corresponding milestones:

M4.1 First system-on-board for laboratory characterisation and validation (Month18, responsibility: IDEA, UNIBO)

M4.2 Achievement of nanotechnological signal enhancement method(s) Demonstration or report of functioning nanotechnology-enhanced biosensor (Month 24 responsibility: UNIBO).

M4.3 Design Parameters for Development Prototype (Deliverables D4.7, D4.11, Month 27, responsibility: BHR)

M4.4 Identification of the most suitable channel-sensor architecture to increase detection efficiency by means of hydraulic channel design (Month 33, responsibility: LIONIX, UNIBO)

Work Package Number	**WP5**	**Start date**	Month 10	**Duration**	45 Months
Title: Engineering (months 13-30)		**Work package Leader**: Micro			
Participant	**Person Months:**	**Role of partner:**			
MICROTRONICS	**34**	Manufacturer, System integration, Coordination of system architecture , T5.1			
PROVENION	18	T5.2: Microfluidics operations: integration with engineered device T5.3: Automation of Microfluidics			
BME	12	T5.1, T5.6:			
HEM	42	T5.6: Software engineering: embedded systems T5.7: User interfacing, software validation and support			
LAM	25	T5.2, T5.4: Industrialisation of microfluidic devices, manufacturing of DNA microarrays in MF systems			
LIONIX	6	T5.2: Microfluidics operations: integration with engineered device			
BHR	3	T5.2: Microfluidics simulations			
CRAN	2,5	T5.2: Microfluidics simulations			
FP	10	T5.4 Manufacturing, T5.8 Integration			
Total Person Months	155,5				

Objectives (months 13-30):

- Demonstrate reliable operation of filter-handling, sample collection, transfer and disposal operations
- Deliver robust microfluidics solutions to all on-chip fluid-handling operations
- Deliver final decision on chip materials
- Integrate DNA microarrays with functionalised surfaces into microchannels
- Deliver hardware abstraction layer and device driver modules for embedded systems
- Use results of experimental work packages, simulation and prior experience to identify candidate design solutions
- Define System Architecture

Description of work to be undertaken (months 13-30):

This work package draws on the various multidisciplinary research activities in microfluidics (WP2), probe and sensor development (WP3 and 4), to address generic issues of device design and integration. This will inform the design of specific prototype devices in the demonstration activities of WP6.

T5.1 Design Methodology and toolkit
(MICRO)
Deliver a coherent concurrent engineering methodology for the design and manufacture of robust biosensor devices, produced in significant volumes to performance criteria identified in T1.2.
The design methodology will define: tasks and responsibilities, identify interface issues, communication means, time scale etc.).

T5.2 Microfluidics operations
(BHR, CRAN, LIONIX, PRO, LAM)

A combination of experimental work and simulation will be employed to evaluate alternative strategies and optimise solutions. [BHR, CRAN, Lionix, LAM]

Select microfluidic solutions for mixing, heating, fluid transfer, metering and flow control tasks within the constraints of an integrated device that is capable of being manufactured. [PRO, Lionix]
Evaluate alternative Dosing approaches: input from an outside storage container vs on-chip-storage.
Evaluation of alternative Valve-on-the-Chip-solutions
Develop a concept for a spatially integrated, multichannel dosing system for minute volumnes and a control mechanism. [PRO, LAM]

T5.3 Automation
(MICRO , BME, PRO, LIONIX)

A reduction of sample volume from around 10 – 100 litres to a volume amenable to processing in microfluidics devices (typically less than 500 µl) needs several stages of preconcentration, such as ultra-filtration. In an automatic remote-monitoring device, the final volume has to be reliably transferred to the microfluidics devices, whilst the filters have to be automatically regenerated or replaced at appropriate intervals.

Develop reliable approaches to the transfer of samples to microfluidics devices, Evaluate various approaches for Macro-Micro-Fluidic-Interface [(PRO])
Automation of filtration to optimize it for machine integration (based on module-prototypes supplied by task partners) [(MICRO, BME, WRI]..)
A redesign of the sample treatment (lysis, pre-concentration) to optimize it for machine integration (based on module-prototypes supplied by task partners) ([BME, LIONIX, MICRO].).
Design and Manufacture On-Chip-PCR-System (LIONIX, PRO)

T5.4 Manufacturing Issues
(LAM, MICRO, PRO)

Initiate research to evaluate candidate substrate material(s) for final material selection, with regard to surface activation methods; heterogeneous material integration (wiring, optical detectors); fabrication methods; dimensional control of channel formation, bonding, jointing between disposable and reusable elements. [LAM, MICRO, PRO]

Identify engineering issues arising from alternative fabrication routes. Avoid any conflicting requirements that might affect assembly and manufacturing. Various process steps might be to harsh for some materials. Certain dimensional requirtements might need special equipment for assemebly.
[MICRO, PRO]

T5.5 System Architecure
(MICRO)

Establishing a concept for and design of the overall system architecture, identification and clear definition of units and interfaces required to manufacture a prototype; coordination of all involved project partners.

T5.6 Embedded systems
(HEM, BME, MICRO, PRO)

The embedded operating system and the microcontroller programming standards will be decided. All the embedded software will be developed on this operating system.

In order to have flexible software, a hardware abstraction layer is introduced in the architecture of the embedded software. In this way, the software can drive not only the first LoC prototype developed within the project, but also new versions of the hardware and other devices to be developed in the future (including the

continuous monitoring device). In order to integrate with a new hardware device, only a device driver library will be developed for each device and installed to the system. The specifications of the device driver libraries will be defined in the package and its result will guide Task 5.7. According to these specifications, device driver library or libraries for the LoC modules will be written within this task.

T5.7 User interfacing, software validation and support
(HEM, BME)

The embedded software of the proposed devices will be implemented in this task. It will communicate with the integrated LoC chips using the device drivers implemented in Task 5.6. The detailed user requirements will be determined using the results of Task 1.2, but basically software will have the following features:

- User management policy: functionality for different user authorisations.
- When a detection event occurs, a set of actions are performed (sending e-mail or SMS messages, web service call, transmitting data)
- Data monitoring and statistical analysis features to help avoid false decisions. This is about storing data coming from the devices and converting it into information.
- Ease of integration with remote systems using standard methods, protocols and formats.
- The device should be remote controllable.

A user's guide of the system and a context-sensitive help will be prepared. After the release of the software for each new prototype, verification and validation of the system will be performed. New requirements will appear during the development of new prototypes and demonstration phases. Validation is different from the verification actions performed at the end of each task: verification ensures that the specified software requirements are met; validation determines fitness for purpose. HEM and BME will identify criteria for validation of all required work products. BME will perform required validation activities.

T5.8 Integration
(MICRO, MANUFACTURER, FP)

This task is implements the design of T5.5. It also draws heavily on the research activities on scale-down in T4.6 and the other engineering tasks in WP5. It will develop the modular concept with reusable and disposable parts, integrate the automation strategies, and manage the reconciliation of design, manufacturing and assembly issues. On the mechanical side, particular attention will be paid to module interconnects, leakage elimination and fluidics control. On the operational side, overcoming challenges of filling, reagent storage and reconstitution will be priorities. Control algorithms and hardware/software interfacing will be specified here in close collaboration with T5.6.
- integration of units supplied by project partners,
- run technical integration tests to verify proper function of integrated electronics, mechanics and software from the mechatronics point of view only;
- tests from the application's point of view (e.g. biological, usability,…) are not subject to the integration tests [MICRO]

T5.9 Cost engineering
(MICRO, PRO, LAM)

Since one of the primary aims of the project is to develop technology for low-cost high-volume biosensor devices, this important task is central both to the engineering design methodology and to the exploitation plan. Candidate designs and assembly methods will be subjected to close scrutiny for their current and forecast cost implications with reference to projected trends in relevant technologies, security of supply of critical materials and items, and potential for unit cost reduction at higher volumes of production.

Deliverables:

D5.2 First Design of Microfluidic System (Report, T5.2, PRO, Month 24)
D5.3 Deliver robust microfluidics solutions to all on-chip fluid-handling operations (Report, T5.2, PRO, Month 30)

D5.4 Report on Macro-Micro-Fluidic-Interfaces (Report, T5.3, PRO. Month 18)
D5.5 Design for Automated Filtration System (Report- Construction Plan, T5.3, MICRO, Month 18)
D5.6 Design of sample lysis system (Report, T5.3, BME, Month 21)
D5.7 Prototyp of sample lysis system (Report, T5.3, BME, Month 24)
D5.8 Prototyp of Automated Filtration System (Prototyp, T5.3, MICRO, Month 30)
D5.9 Prototyp of microfluidic DNA Preconcentration System (Prototyp, T5.3, LIONIX, Month 24)
D5.10 Prototyp of PCR-on-Chip System (Prototyp, T5.3, LIONIX, Month 24)

D5.11 Manufacturing considerations for substrate material selection (Report, T5.4, LAM, Month 18)
D5.12 Deliver final decision on chip materials (Report, T5.4, LAM, Month 27**)**
D5.13 Report on manufacturing issues (Report, T5.4, MICRO, Month 30**)**

D5.14 Draft System Architecture Description and Engineering Specifications(Report, T5.5, MICRO, Month 18)
D5.15 1st revision of System Architecture Description and Engineering Specifications (Report, T5.5, MICRO, Month 24)
D5.16 2nd revision of System Architecture Description and Engineering Specifications (Report, T5.5, MICRO, Month 30)

D5.17 Deliver hardware abstraction layer and device driver modules for embedded systems (Report, T5.6, HEM, Month 24)

D5.18 Deliver documented beta release user interface software (Report, T5.7, HEM, Month 30)
D5.19 Concept for data processing and statistical analysis (Report, T5.7, HEM, Month 30)

D5.20 Final Version of the Design Methodology (Report, T5.1, MICRO, Month 18)

Expected results and corresponding milestones:

M5.1 Robust microfluidics solutions (Month 30, PRO)
M5.2 Selection of substrate material for prototype devices (Month 27, LAM)
M5.3 Draft System Architecture Description (Month 20, MICRO)
M5.4 Prototyp of sample lysis system (BME, Month 25)
M5.5 Prototyp of microfluidic DNA Preconcentration System (LIONIX, Month 25)
M5.6 Prototyp of PCR-on-Chip System (LIONIX, Month 25)
M5.7 Prototyp of Automated Filtration System (MICRO, Month 30)

Work Package Number	**WP6**	**Start date**	Month **10**	**Duration**	**39** Months
Title: Industrial requirements		**Work package Leader: WRI**			
Participant	**Person Months:**	**Role of partner:**			
WRI	**13**	T6.1, T6.4,: Work package leader, Development and test plan, laboratory and field verification			
BHR	**2**	T6.1: Development plan: input on microfluidics optimisation			
LAM	5,5	T6.1: Development plan: input on DNA preconcentration issues and lab protocols.			
HEM	10	T6.1: Development plan: input on software/IT issues			
MICRO	4	T6.1, T6.2, T6.3, T6.4 Basic support for partners when creating the development plan; establish 1pc of prototype (on-site) support for WRI, analyse/review of test results			
BME	8,5	T6.1: Development plan: input on manufacturing, QA issues and input on biosensors			
MMM	4,5	T6.1, T6.4, Development plan: input on concentration sample, DNA preconcentration issues and lab protocols.			
Total Person Months	**45,5**				

Objectives: (month 13-30)

- revise first version development plan in the light of progress against technical objectives
- account for any changes to device specifications and/or relevant regulations

Description of work to be undertaken:

T6.1 Development and test plan

This work package is focused to revise first version of Development plan in the light of the project progress, particularly with respect to technical objectives in WP 3 - 5. Meetings of these WP leaders will be organized when necessary either in person or on-line through interwise. Revision of the first version of Development plan will be transformed to second version of Test plan for prototype.

T6.2 Prototype Development

This work package will begin in Month 22. The prototype construction will be based on tools and expertise collatedin WP 5 and the Development Plan, as well as the System Archtecture Description and Engineering Specifications (D5.14-16). These documents will detail the different specifications of the automated and the mobile device.
The first prototype will focus on the continuous monitoring device. As soon as sufficient progress is made resources can be directed to the trans(portable) device.

T6.3 Lab Verification

This work package begin in Month 24 and during second period (13 - 30 month) will be verified or validated those processes and methods which will be prepare as prototype (e.g. efficiency of filtration)

T6.4 Field Testing and Demonstration

This work package begin in Month 31 and during second period (13 - 30 month) other work within this work package is prepared

Deliverables:

D6.4 Second version Development Plan (Report, T6.1, MICRO, Month 24)
D6.5 Second version Test Plan (Report, T6.1, WRI, Month 30)
D6.6 1st technical drawing of device prototype (Report, T6.2, MICRO, Month 30)

Expected results and corresponding milestones:

M6.2 Delivery of second version of Development Plan (Deliverables D6.4, Month 24, responsibility: MICRO)
M6.3 Delivery of second version of Test Plan (Deliverables D6.5, Month 30, responsibility: WRI)

Work Package Number	**WP7**	**Start date**	Month 1	**Duration**	**48 Months**
Title: Knowledge Management (months 13-30)		**Work package Leader: SEZ**			
Participant	**Person Months:**	**Role of partner:**			
SEZ	**13,2**	T7.1 Intellectual Property Management; T7.2 Exploitation Management ; T7.3 Internal Training and Technology Transfer ; T7.4 Dissemination ;			
LAM	2,5	T7.2 + T7.3 ;			
BHR	4,86	T7.2			
UNIBO	2,7	T7.2 + T7.3 + T7.4			
BME	2,7	T7.2 + T7.3 + T7.4			
CRAN	2,7	T7.2 + T7.3 + T7.4			
OTHER PARTNERS	4,2 (total)	T7.3: Delivery of and attendance at internal training events			
Total Person Months	**32,86**				

Objectives:

- To show each partner and especially the SMEs, how they will benefit from the innovative results of the DINAMICS project and how they can integrate these results in their future commercial products.
- To ensure the consortium's foreground IP is managed and protected
- To avoid patent infringement
- To assure a successful technology and knowledge transfer between the academic partners and the SMEs
- To disseminate the scientific knowledge and the results achieved with the new technologies developed outside the core consortium in order to achieve a broad pan-European impact

Description of work to be undertaken:

Task 7.1 Intellectual property management

- Conduct a report about the patent and technology watch update every six months.

Task 7.2 Exploitation

- Produce a technology roadmap.
- An exploitation strategy as well as an exploitation plan have been defined during the exploitation seminar in June 2008 for the consortium, which will be the basis for the development of the final exploitation plan.The exploitation plan will give the steps for the exploitation of the results in future commercial products, including the following aspects:
  - Analysis and benchmarking of technological and commercial advantages of the DINAMICS results
  - Identification of threats and competitors, including standards, ethical and regulatory constraints
  - Market segmentation, research and analysis
  - Marketing strategy and financial forecast
  - Marketing action plan and marketing activities
  - Recommendations for future R&D development, with particular emphasis on take-up measures for SMEs

  It is intended to update the tables of this exploitation plan (see revised deliverable D7.3+D7.7) on an annually basis. The exploitation plan will differentiate in the application of components as well as of mobile man operated and stationary continuous-monitoring devices.

Task 7.3 Internal training and technology transfer

It is foreseen to organise 3 exchange of personal in the second project period and 2 in the third period to reinforce the knowledge of SMEs inside the core consortium and the exchange of scientific know-how between the academic partners. The explanation for this devision into two years and for the delay is due to the fact that during the first year of the project specifications had to be defined. These specifications resulted in modules which have to be combined in the second and third year where it makes sense now to do these staff exchanges. The following staff exchanges during the second project period are foreseen:

- CRAN -> LAM (M16)
- BME -> UniBo (M19)
- UniBo -> LAM (M20)

Task 7.4 Dissemination

As described on p. 72, the main dissemination activities are foreseen in year 3 and 4, when concrete project results can be presented outside the consoritum. The partners will participate to several conferences and produce articles and newsletters. Information about DINAMICS will be disseminated through European Networks and Technology Platforms covering nanotechnology, environment and technology transfer (*e.g*. NanoForum, Water Supply and Sanitation Technology Platform (WSSTP), Innovation Relay Centres and CORDIS). New scientific knowledge will be also disseminated to students, lab technicians and young professionals through two seminars organised by the three universities participating in the project. Although UNIBO has overall responsibility for the organisation of these workshops, they will be hosted at different locations by the universities in the project. This will allow for maximum impact. Although the project will have its own web site for publication of material, DINAMICS will also make use of the well-established NanoForum site to ensure maximum impact for its results. SEZ will be responsible for these liaisons.

Deliverables:

D7.10 Exploitation Workshop (Workshop, T7.2, LAM, M14)
D7.9 First scientific seminar (T7.4, UNIBO, Month 18)
D7.11 Patent and technology watch update (Report, T7.1, SEZ, Month 18)
D7.12 Second scientific seminar (T7.4, UNIBO, Month 24)
D7.14 Final TRM report (Report, T7.2, BHR, Month 29)
D7.13 Patent and technology watch update (Report, T7.1, SEZ, Month 29)
D7.15 Patent and technology watch update (Report, T7.1, SEZ, Month 30)
D7.16 Report on conference participation and scientific articles (Report, T7.4, UniBo, Month 30)

Expected results and corresponding milestones:

Work Package Number	**WP8**	**Start date**	Month **1**	**Duration**	**48** Months
Title: Project Management (months 13-30)		**Work package Leader: LAM**			
Participant	**Person Months:**	**Role of partner:**			
LAM	**4,75**	T8.2 Project co-ordination and technical management			
BHR	2	T8.2 Project co-ordination and technical management			
SEZ	4,1	T8.1 Administration and finance co-ordination			
Total Person Months	**10,85**				

Objectives:

- To co-ordinate and manage the project's resources, including holding four PMB/PSC meetings
- To establish and update coherent programme of technical activities and manage contingencies
- To monitor the progress of the project, and to achieve its deliverables and milestones on time
- To establish effective communications media including the project web site

Description of work to be undertaken:

Task 8.1 Co-ordination and administrative management

Interaction (minutes of meetings and summary of email exchanges) with the advisory board will be documented in a dedicated area on the DINAMICS fileserver. To reduce the burden on the advisory board members remote review will be used as the main form of interaction. Yet at least one meeting per year is planned to facilitate personal contact.

The tasks of the Advisory board are decribed in the section 7.2 Roles (Project Decision Bodies) and in the individual tables of the section "Operational Objectives" in Chapter 2.

Attempts will be made to include four nerw members to the AB in oder to increase

- the geographic scope of the advisory board as well as
- the diversity of the background of the AB members (e.g. decision makers, regulative bodies, standardzing committees and end-users, like water works and drinking water companies).

T8.1.3: Maintance and update of the DINAMICS webpage.

This web site will be used as the main means of communication between partners, for promoting the project externally, and to advertise project meetings, workshops, and training events.

Relevant project news which inform partners of the overall progress will be published quarterly on the internal project website.

T8.1.4: Till Month 20, a PSC meeting will be held to review progress. Till month 30 a PSC meeting will be planned. The results will be published on the project's web site, including any decisions made. All project members' opinions will be sought on these decisions.

T8.1.5:

A review meeting with external evaluators will be organised by the Commission to assess both the new Annex I and the annual report at the end of year 1 and year 2. *A report on the the advancement of gender issues will be part of the activity report.*

At Month 24, the co-ordinator LAM will organise and direct the second annual review. Attendance is mandatory all members. This meeting will look at all aspects of the project it will make recommendations for the workplan for the period from Months 19 25 to 4848. A detailed year-end report will also be produced, with an in-depth nonconfidential summary to ensure that the project's results can be disseminated as widely as possible. Annex I to the contract will be updated for the period from Month 25 to Month 42.

Task 8.2 Technical management

T8.2.1: The Work Package leaders will carry out the technical management against the targets set out in this Annex. Simple standards for the management of each WP will be used. Co-ordination of the work packages will be carried out both by monthly web-based (Interwise) meetings of the Project Steering Committee. Where appropriate, there will be intermittent WP and inter-WP meetings to help achieve successful integration and

progress in and between work packages. The technical co-ordinator will provide minutes of the web-based meeting.
T8.2.2: The monthly meetings also will judge progress against technical milestones, deliverables and targets Achievement of target or any remedial action will be formally recorded and monitored.

T8.2.3 Interaction with other Framework projects will be attempted. D7.2 and D7.5 provided a list of projects (section 3.3) of interest for DINAMICS. It is planned to contact the five most relevant projects for DINAMICS, which are:
SMART-BIOMEMS, Micro^{2}DNA, microBUILDER, INFLUS, NEUROTAS.
The coordinators of the these projects will be contacted to evaluate if there is any overlapping research interest or synergies with DINAMICS. The possibility of joint dissimenation activities will be discussed, and accordingly implemented.

Deliverables:

D8.6 First annual meeting minutes (Minutes, T8.1.5, SEZ, Month 13)
D8.7 First annual report (Report, T8.1.5, LAM/SEZ/BHR, Month 14)
D8.8 Annual review meeting with external evaluators (Meeting, T8.1.5, LAM, Month 14)
D8.9 Annual report on advancement of gender issues (Report, T8.1.5, SEZ, Month 14)
D8.10 10 2nd annual meeting minutes (Minutes, T8.1.5, SEZ, Month 25)
D8.11 11 2nd annual report (Report, T8.1.5, LAM/SEZ/BHR, Month 26)
D8.12 PSC Meeting (Minutes, T8.1.4, SEZ, Month 20)
D8.13 PSC Meeting (Invitation, T8.1.4, SEZ, Month 30)
D8.14 Annual report on advancement of gender issues (Report, T8.1.5, SEZ, Month 26)
D8.15 Agendas, Papers and Minutes for monthly Project Steering Committee meetings (Web-mounted Reports, BHR, monthly)

Expected results and corresponding milestones:
M8.4 Annual Review: decision on project continuation (Responsibility: LAM, Month 14)
M8.5 Manufacturer signed up as contractor (Responsibility: LAM, Month 18)
M8.6 Future Partner signed up as contractor (Responsibility: LAM, Month 19)
M8.7 Annual review: decision on project continuation (Responsibility: LAM, Month 26)

9. PROJECT RESOURCES AND BUDGET OVERVIEW

The following pages detail the project's resource and distribution for both the eighteen-month period from Month 13 to Month 30, and the full duration of the project. It also includes a breakdown of major cost items: both consumables and capital purchases needed and identified by the partners. Details about the participants and their involvement are summarised. This section also gives detailed information about the project advisory board.

9.1 EFFORTS FOR THE FULL DURATION OF THE PROJECT

IP Effort Form – Indicative efforts for full duration of project

Project: 026804 – DINAMICS

IP Activity Type	RTD/Innovation activities	Demonstration activities	Training activities	Consortium management activities	TOTAL per PARTICIPANT
LAM	127	0	2	11	140
BHR	45	0	0	5	50
IDEA	37	0	0	0	37
HEM	75	0	2	0	77
MMM	28	0	2	0	30
WRI	52	14	2	0	68
UNIBO	97	0	2	0	99
BME	91	0	2	0	93
CRAN	78	0	2	0	80
SEZ	30	0	3	11	44
LIONIX	11	0	2	0	13
Micro	68	0	0	0	68
Pro	30	0	0	0	30
TOTAL per ACTIVITY Type	769	14	19	27	
Overall TOTAL efforts					829

9.2 EFFORTS FOR 18 MONTHS PERIOD MONTH 13 – MONTH 30 (IP EFFORTS FORM 2)

IP Effort Form – Indicative efforts for 18 months period covering detailed implementation plan (project Month 13 to 30)

	Lam	BHR	Idea	Hem	MMM	JP	WRI	UniBo	BME	Cran	SEZ	LioniX	Micro	Pro	TOTAL (ALL PARTNERS)
RTD/ Innovation Activities															
WP1															0
WP2	0	13	0	0	0	0	0	0	0	31	0	0	0	0	44
WP3	22	0	0	0	14	0	10	0	18	0	0	6	0	0	70
WP4	21	4	12	0	0	0	0	50	9	0	0	7	0	0	103
WP5	25	3	0	42	0	0	0	0	12	2,5	0	6	34	18	142,5
WP6	5,5	2	0	10	4,5	0	13	0	8,5	0	0	0	4	6	53,5
WP7	1,5	4,86	0	0	0	0	0	1,7	1,7	1,7	12	0	1	0	24,46
Total RTD/ Innovation activities	75	26,86	12	52	18,5	0	23	51,7	49,2	35,2	12	19	39	24	437,46
Demonstration activities															
WP6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
WP7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total demo activities	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Training activities															
WP7	1	0	0	1	1	0	1	1	1	1	1,2	1	0	0	9,2
Total training activities	1	0	0	1	1	0	1	1	1	1	1,2	1	0	0	9,2
Management activities															
WP8	4,75	2	0	0	0	0	0	0	0	0	4,1	0	0	0	10,85
Total management activities	4,75	2	0	0	0	0	0	0	0	0	4,1	0	0	0	10,85
TOTAL (ALL ACTIVITIES)	80,75	28,86	12	53	19,5	0	24	52,7	50,2	36,2	17,3	20	39	24	457,51

9.3 OVERALL BUDGET FOR THE FULL DURATION OF THE PROJECT

Participant n°	Organisation short name[41]	Cost model used	Estimated eligible costs and requested EC contribution (whole duration of the project)		Costs and EC contribution per type of activities[42] RTD[43] or Innovation-related[45] activities -1	Demonstration activities[44] -2	Training activities[46] - 3	Consortium Management activities[47] -4	Total (5)=(1)+(2)+(3)+(4)	Total Receipts[42]
1	Lam	FC		*Direct costs (a)*	1294672	0	8800	56400	1359872	
				of which subcontracting	25000	0	0	8000	33000	
				Indirect costs (b)	111760	0	1760	9680	123200	
			Eligible costs	*Total eligible costs (a)+(b)*	1406432	0	10560	66080	1483072	
			Requested EC contribution		703216	0	10560	66080	779856	0
2	BHR	FC		*Direct costs (a)*	297752	0	0	30751	328503	
				of which subcontracting	0	0	0	4000	4000	
				Indirect costs (b)	546508	0	0	60726	607234	
			Eligible costs	*Total eligible costs (a)+(b)*	844260	0	0	91477	935737	
			Requested EC contribution		422130	0	0	91477	513607	0
4	Idea	FCF		*Direct costs (a)*	145000	0	0	4000	149000	0
				of which subcontracting	0	0	0	4000	4000	
				Indirect costs (b)	29000	0	0	0	29000	
			Eligible costs	*Total eligible costs (a)+(b)*	174000	0	0	4000	178000	

Participant n°	Organisation short name[41]	Cost model used	Estimated eligible costs and requested EC contribution (whole duration of the project)		Costs and EC contribution per type of activities[42] RTD[43] or Innovation-related[45] activities -1	Demonstration activities[44] -2	Training activities[46] - 3	Consortium Management activities[47] -4	Total (5)=(1)+(2)+(3)+(4)	Total Receipts[42]
			Requested EC contribution		87000	0	0	4000	91000	
				Direct costs (a)	288500	0	7000	4000	299500	
				of which subcontracting	0	0	0	4000	4000	
				Indirect costs (b)	57700	0	1400	0	59100	
			Eligible costs	*Total eligible costs (a)+(b)*	346200	0	8400	4000	358600	
5	Hem	FCF	Requested EC contribution		173100	0	8400	4000	185500	0
				Direct costs (a)	326688	0	7000	4000	337688	
				of which subcontracting	0	0	0	4000	4000	
				Indirect costs (b)	65336	0	1400	0	66736	
			Eligible costs	*Total eligible costs (a)+(b)*	392024	0	8400	4000	404424	
6	MMM	FCF	Requested EC contribution		196012	0	8400	4000	208412	0

Participant n°	Organisation short name[41]	Cost model used	Estimated eligible costs and requested EC contribution (whole duration of the project)		Costs and EC contribution per type of activities[42] RTD[43] or Innovation-related[45] activities -1	Demonstration activities[44] -2	Training activities[46] - 3	Consortium Management activities[47] -4	Total (5)=(1)+(2)+(3)+(4)	Total Receipts[42]
9	WRI	FCF		*Direct costs (a)*	322400	44800	6400	4000	377600	
				of which subcontracting	0	0	0	4000	4000	
				Indirect costs (b)	64480	8960	1280	0	74720	
			Eligible costs	*Total eligible costs (a)+(b)*	386880	53760	7680	4000	452320	
			Requested EC contribution		193440	18816	7680	4000	223936	0
10	UniBo	FC		*Direct costs (a)*	504975	0	9551	4000	518526	
				of which subcontracting	0	0	0	4000	4000	
				Indirect costs (b)	236255	0	4871	0	241126	
			Eligible costs	*Total eligible costs (a)+(b)*	741230	0	14422	4000	759652	
			Requested EC contribution		370615	0	14422	4000	389037	0
11	BME	AC		*Direct costs (a)*	375200	0	6400	4000	385600	
				of which subcontracting	16000	0	0	4000	20000	
				Indirect costs (b)	71840	0	1280	0	73120	
			Eligible costs	*Total eligible costs (a)+(b)*	447040	0	7680	4000	458720	
			Requested EC contribution		447040	0	7680	4000	458720	0

Participant n°	Organisation short name[41]	Cost model used	Estimated eligible costs and requested EC contribution (whole duration of the project)		Costs and EC contribution per type of activities[42] RTD[43] or Innovation-related[45] activities -1	Demonstration activities[44] -2	Training activities[46] - 3	Consortium Management activities[47] -4	Total (5)=(1)+(2)+(3)+(4)	Total Receipts[42]
12	Cran	AC		*Direct costs (a)*	526640	0	11600	4000	542240	
				of which subcontracting	0	0	0	4000	4000	
				Indirect costs (b)	105328	0	2320	0	107648	
			Eligible costs	*Total eligible costs (a)+(b)*	631968	0	13920	4000	649888	
			Requested EC contribution		631968	0	13920	4000	649888	0
15	SEZ	AC		*Direct costs (a)*	191954	0	16800	95600	304354	
				of which subcontracting	0	0	0	34000	34000	
				Indirect costs (b)	38391	0	3360	12320	54071	
			Eligible costs	*Total eligible costs (a)+(b)*	230345	0	20160	107920	358425	
			Requested EC contribution		230345	0	20160	107920	358425	0
16	LioniX	FC		*Direct costs (a)*	88000	0	10000	4000	102000	
				of which subcontracting	0	0	0	4000	4000	
				Indirect costs (b)	44000	0	8000	0	52000	
			Eligible costs	*Total eligible costs (a)+(b)*	132000	0	18000	4000	154000	
			Requested EC contribution		66000	0	18000	4000	88000	0

Participant n°	Organisation short name[41]	Cost model used	Estimated eligible costs and requested EC contribution (whole duration of the project)		Costs and EC contribution per type of activities[42] RTD[43] or Innovation-related[45] activities -1	Demonstration activities[44] -2	Training activities[46] - 3	Consortium Management activities[47] -4	Total (5)=(1)+(2)+(3)+(4)	Total Receipts[42]
17	Micro	FC		*Direct costs (a)*	589400	0	0	3000	592400	
				of which subcontracting	0	0	0	3000	3000	
				Indirect costs (b)	105816	0	0	0	105816	
			Eligible costs	*Total eligible costs (a)+(b)*	695216	0	0	3000	698216	
			Requested EC contribution		347608	0	0	3000	350608	0
18	Pro	FC		*Direct costs (a)*	281800	0	0	3000	284800	
				of which subcontracting	0	0	0	3000	3000	
				Indirect costs (b)	117306	0	0	0	117306	
			Eligible costs	*Total eligible costs (a)+(b)*	399106	0	0	3000	402106	
			Requested EC contribution		199553	0	0	3000	202553	0
TOTAL[48]			Eligible costs		6826701	53760	109222	303477	7293160	
			Requested EC contribution		4068027	18816	109222	303477	4499542	0

Estimated breakdown of the EC contribution per reporting period			
Reporting Periods	**Month x – Month y**	**Estimated Grant to the Budget**	
		Total	**In which first six months**
Reporting Period 1	M1 – M12	1205020	
Reporting Period 2	M13 – M24	1668819	765653
Reporting Period 3	M25 – M36	1097839	606229
Reporting Period 4	M37 – M48	527864	327647
Reporting Period 5	M49 – M60	-	-
Reporting Period 6	M61 – M72	-	-
Reporting Period 7	M73 – M84	-	-

9.4 BUDGET FOR THE MONTHS 13- 30

Participant n°	Organisation short name[41]	Cost model used	Estimated eligible costs and requested EC contribution (whole duration of the project)		Costs and EC contribution per type of activities[42]				Total (5)=(1)+(2)+(3)+(4)	Total Receipts[42]
					RTD[43] or Innovation- related[45] activities -1	Demonstration activities[44] -2	Training activities[46] -3	Consortium Management activities[47] -4		
					Month 13-30	Month 13-30	Month 13-30	Month 13-30	Month 13-30	Month 13-30
1	Lam	FC	Eligible costs	*Direct costs (a)*	717500	0	4400	22900	744800	
				of which subcontracting	25000	0	0	2000	27000	
				Indirect costs (b)	66000	0	880	4180	71060	
				Total eligible costs (a)+(b)	783500	0	5280	27080	815860	
			Requested EC contribution		391750	0	5280	27080	424110	0
2	BHR	FC	Eligible costs	*Direct costs (a)*	148701	0	0	11700	160401	
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	326201	0	0	24289	350490	
				Total eligible costs (a)+(b)	474902	0	0	35989	510891	
			Requested EC contribution		237451	0	0	35989	273440	0
4	Idea	FCF	Eligible costs	*Direct costs (a)*	51000	0	0	1000	52000	
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	10200	0	0	0	10200	
				Total eligible costs (a)+(b)	61200	0	0	1000	62200	
			Requested EC contribution		30600	0	0	1000	31600	0
5	Hem	FCF	Eligible costs	*Direct costs (a)*	204000	0	3500	1000	208500	0

Participant n°	Organisation short name[41]	Cost model used	Estimated eligible costs and requested EC contribution (whole duration of the project)		Costs and EC contribution per type of activities[42]				Total (5)=(1)+(2)+(3)+(4)	Total Receipts[42]
					RTD[43] or Innovation- related[45] activities -1	Demonstration activities[44] -2	Training activities[46] -3	Consortium Management activities[47] -4		
					Month 13-30	Month 13-30	Month 13-30	Month 13-30	Month 13-30	Month 13-30
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	40800	0	700	0	41500	
				Total eligible costs (a)+(b)	244800	0	4200	1000	250000	
			Requested EC contribution		122400	0	4200	1000	127600	
			Eligible costs	*Direct costs (a)*	117750	0	3500	1000	122250	
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	23550	0	700	0	24250	
				Total eligible costs (a)+(b)	141300	0	4200	1000	146500	
6	MMM	FCF	Requested EC contribution		70650	0	4200	1000	75850	0
			Eligible costs	*Direct costs (a)*	0	0	0	0	0	
				of which subcontracting	0	0	0	0	0	
				Indirect costs (b)	0	0	0	0	0	
				Total eligible costs (a)+(b)	0	0	0	0	0	
8	JP	FCF	Requested EC contribution		0	0	0	0	0	0
9	WRI	FCF	Eligible costs	*Direct costs (a)*	122600	0	3200	1000	126800	0
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	24520	0	640	0	25160	

Participant n°	Organisation short name[41]	Cost model used	Estimated eligible costs and requested EC contribution (whole duration of the project)		Costs and EC contribution per type of activities[42]				Total (5)=(1)+(2)+(3)+(4)	Total Receipts[42]
					RTD[43] or Innovation- related[45] activities -1	Demonstration activities[44] -2	Training activities[46] -3	Consortium Management activities[47] -4		
					Month 13-30	Month 13-30	Month 13-30	Month 13-30	Month 13-30	Month 13-30
				Total eligible costs (a)+(b)	147120	0	3840	1000	151960	
			Requested EC contribution		73560	0	3840	1000	78400	
			Eligible costs	*Direct costs (a)*	257919	0	4776	1000	263695	
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	125929	0	2436	0	128365	
				Total eligible costs (a)+(b)	383848	0	7212	1000	392060	
10	UniBo	FC	Requested EC contribution		191924	0	7212	1000	200136	0
			Eligible costs	*Direct costs (a)*	167940	0	3200	1000	172140	
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	33588	0	640	0	34228	
				Total eligible costs (a)+(b)	201528	0	3840	1000	206368	
11	BME	AC	Requested EC contribution		201528	0	3840	1000	206368	0
			Eligible costs	*Direct costs (a)*	209660	0	5800	1000	216460	
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	41932	0	1160		43092	
				Total eligible costs (a)+(b)	251592	0	6960	1000	259552	
12	Cran	AC	Requested EC contribution		251592	0	6960	1000	259552	0

Participant n°	Organisation short name[41]	Cost model used	Estimated eligible costs and requested EC contribution (whole duration of the project)		Costs and EC contribution per type of activities[42]				Total (5)=(1)+(2)+(3)+(4)	Total Receipts[42]
					RTD[43] or Innovation- related[45] activities -1	Demonstration activities[44] -2	Training activities[46] -3	Consortium Management activities[47] -4		
					Month 13-30	Month 13-30	Month 13-30	Month 13-30	Month 13-30	Month 13-30
15	SEZ	AC	Eligible costs	*Direct costs (a)*	76200	0	6720	31960	114880	
				of which subcontracting	0	0	0	9000	9000	
				Indirect costs (b)	15240	0	1344	4592	21176	
				Total eligible costs (a)+(b)	91440	0	8064	36552	136056	
			Requested EC contribution		91440	0	8064	36552	136056	0
16	LioniX	FC	Eligible costs	*Direct costs (a)*	103000	0	5000	1000	109000	
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	76000	0	4000	0	80000	
				Total eligible costs (a)+(b)	179000	0	9000	1000	189000	
			Requested EC contribution		89500	0	9000	1000	99500	0
17	Micro	FC	Eligible costs	*Direct costs (a)*	358700	0	0	1000	359700	
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	60688	0	0	0	60688	
				Total eligible costs (a)+(b)	419388	0	0	1000	420388	
			Requested EC contribution		209694	0	0	1000	210694	0
18	Pro	FC	Eligible costs	*Direct costs (a)*	207640	0	0	1000	208640	0

Participant n°	Organisation short name[41]	Cost model used	Estimated eligible costs and requested EC contribution (whole duration of the project)		Costs and EC contribution per type of activities[42]				Total (5)=(1)+(2)+(3)+(4)	Total Receipts[42]
					RTD[43] or Innovation- related[45] activities -1	Demonstration activities[44] -2	Training activities[46] -3	Consortium Management activities[47] -4		
					Month 13-30	Month 13-30	Month 13-30	Month 13-30	Month 13-30	Month 13-30
				of which subcontracting	0	0	0	1000	1000	
				Indirect costs (b)	93844	0	0	0	93844	
				Total eligible costs (a)+(b)	301484	0	0	1000	302484	
			Requested EC contribution		150742	0	0	1000	151742	
TOTAL[48]			Eligible costs		3681102	0	52596	109621	3843319	
			Requested EC contribution		2112831	0	52596	109621	2275048	0

9.5 MANAGEMENT LEVEL DESCRIPTION OF RESOURCES AND BUDGET

Financial information – whole duration of the project

No	Acronym	Nation	Cost model	Person month	Labour	Travel	Other costs	Sub-contract	Overheads	Total Costs	EC contrib.
1	Lam	A	FC	140	616000	48000	662872	33000	123200	1483072	779856
2	BHR	UK	FC	50	267503	12000	45000	4000	607234	935737	513607
4	Idea	I	FCF	37	111000	12000	22000	4000	29000	178000	91000
5	Hem	TR	FCF	77	269500	8000	18000	4000	59100	358600	185500
6	MMM	HU	FCF	30	105000	8000	220688	4000	66736	404424	208412
8	JP	D	FCF	0	0	0	0	0	0	0	0
9	WRI	SK	FCF	68	217600	14000	142000	4000	74720	452320	223936
10	UniBo	I	FC	99	472796	8000	33730	4000	241126	759652	389037
11	BME	HU	AC	93	297600	8000	60000	20000	73120	458720	458720
12	Cran	UK	AC	80	464000	8000	66240	4000	107648	649888	649888
15	SEZ	D	AC	44	246354	14000	10000	34000	54071	358425	358425
16	LioniX	NL	FC	13	65000	8000	25000	4000	52000	154000	88000
17	Micro	A	FC	68	428400	6000	155000	3000	105816	698216	350608
18	Pro	D	FC	30	205800	6000	70000	3000	117306	402106	202553
Total				829	3766553	160000	1530530	125000	1711077	7293160	4499542

Breakdown of other costs full duration of project

Nr.	Partner	Reason for purchase	Consumables Budget	Equipment Specification	Equipment Budget	Total Costs
1	Lam	Consumables: primer, probes, isolation of RNA/DNA, cell culture, gene synthesis, dyes, chemicals, enzymes, reagents, For the production of polymeric microstructures, extraction of DNA and RNA,	120000			120,000
		data processing , automated dispensing and mixing A dust free and contamination free working environment , DNA amplification, the optimisation of DNA microarray hybridisation For the transport of samples in the lab-on-chip, for the replacement of wear-and-tear parts of the DNA sequencer (Laser). If the microfluidic devices are to be mass produced, appropriate fabrication methods such as injection moulding have to be adopted and a specific mould insert has to be designed. In order to test several designs, specific mould inserts for the prototypes have to be designed. Additional surface coatings may be required. Several (e.g. photosensitive materials) will be tested.		Computer, software Automatised extraction Automated liquid handling Laminar Flow, PCR-Hood Thermocycler Small instruments: Water bath, thermo-block, pipettes, vortex, gel-electrophoreses Hybridisation oven Microfluidics pumps Sequencer wear replacement part	179,000	179,000
		SUM	120,000		179,000	**299,000**

2	BHR	Network hardware and storage for a dedicated computational cluster is required throughout the project to perform large scale computations using CFD and multi-scale techniques with common protocols of other partners modelling activities. Purchase M0 used to M48.		Local computer network consisting of two nodes dedicated to the project. Associated data storage, handling and transfer hardware and power supplies for managing large volumes of processing information.	20,000	20,000
		Workstations to support the development of the computational codes as well as post-processing of the computational results. These will be used throughout the project.		2 Sun workstations with dual processors	10,000	10,000
		Code development software licences for the development of CFD, molecular dynamics and multi-scale modelling simulations.		Intel Fortran 9.0 for Linux, Microsoft Visual Studio .NET 2003 for Windows including Visual C++, Tecplot for CFD graphics	15,000	15,000
		SUM	0		45,000	**45,000**
4	Idea	Project and simulation of electronic systems, Testing and debugging of electronic systems, Testing and debugging of electronic systems	10,000			10,000
				Personal computer, Oscilloscope, Signal Generation	12,000	12,000
		SUM	10,000		12,000	**22,000**
5	HEM	Two mobile devices and accessories to develop software on them. Vendor of the device will be decided during Months 15-18. Therefore, this cost is an approximate value.	0	Development Devices	5000	5,000
		Operating System(s), database server, compilers, device driver and software development kits, emulators, chip programmers. All development software will be purchased for four developer licence. Vendor again depends on the selection of the mobile device.	0	Development software, hardware and Licences	8000	8,000
		In addition to the compilers and software development kits, communication protocols (such as TCP/IP stack), encryption, reporting libraries are generally available separately in the market.	0	Software libraries	5000	5,000
		SUM	0		18000	**18,000**
6	MMM					
		For modelling the preconcentration method before miniaturising. As it is not clarified which kind of filtration solution is applied or could be applied, the cost cannot be calculated exactly. (This cost and additional consumables for filtration have been reduced)		Filtration system; Millipore	8000	8,000
		To develop the filtration (preconcentration) and lysis (on filter lysis) we need to check the yield of sample material and the recovery		Robotic Nucleic Acid (NA) isolation instrument; MagNA Pure LC Instrument, Roche	70,000	70,000
		For storage of viruses		-80 °C freezer	12,000	12,000
		Consumables	130688			130,688
		SUM	130688		90000	**220,688**

9	WRI	Various consumable items, including: chemicals, PCR kits, bacteria, membrane filters biohazard bags.	34,000		0	34,000
		Consumables requested are needed for cultivation of micro-organisms (culture medium, Petri dishes, membrane filters). For modelling the preconcentration method before miniaturising. Exact costs will depend on the filtration choosen,	50,000			50,000
		Consumables for the execution of tests in WP 6. e.g.: Membrane filters and sample flasks are needed for collection of samples, concentrating the sample and transporting them. Bacteriological strains are needed for laboratory tests of the device, if the device is able to recognise the target micro-organisms. Bacteriological validation (petris dishes, media)	58,000			**58,000**
		SUM	142,000		0	**142,000**
10	UniBo	Instrument for accurate solvent-free surface cleaning and preparation, Instrument for the quantitative determination of surface functionalisation with oligonucleotides; Accurate impedance characterisation for biosensor electrodes		Plasma processor type "femto" from Diener electronic GmbH, Nikon inverted optical microscope TE2000U with epifluorescence device and digital camera. Low frequency impedance analyser	14730	14,730
		Consumables	19,000			19,000
		SUM	19000		14730	**33,730**
11	BME	A part of the envisaged experiments requires potentiostatic monitoring of two channels, but with the currently available electrochemical workstation, only quasi-bipotentiostatic measurements can be taken. This means that control electronic circuitry switches the measuring circuitry between the two monitored working electrodes with a frequency of 3 Hz. It means that some phenomena occurring with a faster time constant cannot be characterised.		Programmable electrochemical potentiostat workstation, Manufacturer and model: Voltalab-80 with optical fibre microprobes and a Multiplexer	40,000	40,000
		Consumables	20,000			20,000
		SUM	20,000		40,000	**60,000**
12	Cran	A small computational cluster (from a highly-reliable vendor) is required for performing large scale computations using CFD, molecular dynamics and multi-scale techniques. The central computational facilities at Cran are overloaded by several existing users and queuing times can vary from a few days to weeks. In order to perform the computational tasks and deliver the work on time, a dedicated facility is required. Note that the Fluid Mechanics group will also invest internal resources to extend the six nodes facility with additional nodes.	6,240	Sun Fire X4100 Server, 2 * AMD Opteron Model 275 processors, 6 nodes	34,500	40,740
		Workstations to support the development and debugging of the computational codes as well as post-processing of the computational results.		3 Sun Java Workstation W2100z, 2 Opteron 252 (2.6 GHz) Processors	13,000	13,000
		A fast-response, highly-reliable network attached storage (NAS) array is required for continuous access of large blocks of data throughout the project.		Sun StorEdge 3511 SATA Array, Sun StorEdge 3511 Rack Ready, 3TB and 2 AC power supplies.	12,500	12,500
		SUM	6,240		60,000	**66,240**
15	SEZ	Brochures, Publicity, Website	10,000		0	**10,000**
16	LioniX	Consumables:Substrates and chemical for manufacturing microfluidic modules, valves, tubing, etc.	10,000	Clean room, for manufacturing microfluidic devices, photolithographic methods need a dust-free environment. Control and generation of high voltage, pumps, actuators.	15000	**25,000**
17	Micro	Parts for the prototype	155,000		0	**155,000**
18/	Pro	Parts for the prototype	70,000	-	0	**70,000**

The co-ordinator, LAM, has a budget for other costs. This fund will cover the following:

Other costs	Amount (€)
Costs for new members (manufacturer, future partner)	363872
Consumable + Equipment for Lambdas R&I	299,000
Total	662872

The co-ordinator, LAM, has a budget for travel costs. This fund will cover the following:

Travel Costs	Amount (€)
Travel costs for the Advisory Board	24,000
Travel costs for Lamda	24,000
Total	48,000

Breakdown of the allocation of budget between activities

Key Activity Split	% Allocation of Budget
RTD and Innovation-related	93.37%
Demonstration	0.74%
Training	1.70%
Consortium management activities	4.20%

Cost Breakdown	% Allocation of Budget
Labour	51,6%
Travel	2,2%
Other costs	21%
Sub-contracting	1,7%
Overheads	23,5%

Contractors using the additional cost reporting model have indicated the other own resources that they intend to contribute to the project

Partners using AC Cost Model	Other own resources contributed to the project	Approximation of the value of these resources
BME	Additional own resources of BME-ETT available to support the RTD activities in DINAMICS:	€660,110
CRAN	(i) Staff time for Prof. Drikakis over the 48-month period (ii) HPC cluster (60 – 70 nodes) including maintenance and management (computer officer) (iii) Software developed (pre-existing know-how)	€65,000 €135,000 Not applicable Total: €200,000
SEZ	SEZ will finance the difference in overhead costs through the internal budget of the Steinbeis Foundation.	*ca*. €16,000

Financial information –months 13-30 of the project

No	Acronym	Nation	Cost model	Person month	Labour	Travel	Other costs	Sub-contract	Overheads	Total Costs	EC contrib.
1	Lam	A	FC	80,75	355300	20000	342500	27000	71060	815860	424110
2	BHR	UK	FC	28,86	154401	5000	0	1000	350490	510891	273440
4	Idea	I	FCF	12	36000	4000	11000	1000	10200	62200	31600
5	Hem	TR	FCF	53	185500	4000	18000	1000	41500	250000	127600
6	MMM	HU	FCF	19,5	68250	3000	50000	1000	13650	135900	75850
8	JP	D	FCF	0	0	0	0	0	0	0	0
9	WRI	SK	FCF	24	76800	5000	44000	1000	25160	151960	78400
10	UniBo	I	FC	52,7	251695	4000	7000	1000	128364	392059	200136
11	BME	HU	AC	50,2	160640	3000	7500	1000	34228	206368	206368
12	Cran	UK	AC	36,2	209960	3000	2500	1000	43092	259552	259552
15	SEZ	D	AC	17,3	96880	5000	4000	9000	21176	136056	136056
16	LioniX	NL	FC	20	100000	3000	5000	1000	80000	189000	99500
17	Micro	A	FC	39	245700	3000	110000	1000	60688	420388	210694
18	Pro	D	FC	24	164640	3000	40000	1000	93845	302485	151742
Total				457,51	2105766	65000	641500	47000	973453	3832719	2275048

Breakdown of other costs, months 13-30

	Partner	Cost of consumables	Cost of equipment	Total other Costs
1	LAM	45000	97500	142500
2	BHR	0	0	0
4	IDEA	11000	0	11000
5	HEM	0	18000	18000
6	MMM	20000	30000	50000
8	JP	0	0	0
9	WRI	44000	0	44000
10	UNIBO	7000	0	7000
11	BME	7500	0	7500
12	CRAN	2500	0	2500
15	SEZ	4000	0	4000
16	LIONIX	5000	0	5000
17	Micro	110000	0	110000
18	Pro	40000	0	40000

The co-ordinator, LAM, has a budget for other costs. This fund will cover the following:

Other costs	**Amount (€)**
Costs for new members (manufacturer, Future partner)	200000
Consumable + Equipment for Lambdas R&I	142500
Total	342500

The co-ordinator, LAM, has a budget for travel costs. This fund will cover the following:

Travel Costs	**Amount (€)**
Travel costs for the Advisory Board	8000
Travel costs for Lam	12000
Total	20000

Cost Breakdown	% Allocation of Budget
Labour	54,9%
Travel	1,7%
Other costs	16,7%
Sub-contracting	1,2%
Overheads	25,4%

10. ETHICAL ISSUES

This document has been written with an awareness of the ethical and gender aims of the Treaty on European Union. This project raises no ethical concerns.

The research does not involve any:

1. Research activity aiming at human cloning for reproductive purposes.
2. Research activity intended to modify the genetic heritage of human beings, which could make such changes heritable.
3. Research activities intended to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer.

11. OTHER ISSUES

No other issues are relevant to this project.

APPENDIX A – CONSORTIUM DESCRIPTION

A.1 PARTICIPANTS AND CONSORTIUM

Summary of Partner roles

Partner no.	Organisation	Short name	Type	Country	Employees	Key personnel	Summary of Partners' Role
1	Lambda GmbH	LAM	IND	A	11	Dr. C. Mitterrmayr	Project Co-ordination, Leader WP8: technical management, DNA preconcentration, cell lysis: sonication, PCR system development. Application of project results to the development of low-cost DNA microarrays.. Active in WP1, 3, 4, 5, 6, 7 and 8.
2	BHR Group	BHR	(SME) RES	UK	65	Dr. M Dawson, Dr. G. Pollard	Leader WP2: Micro- and nanofluidics. WP8: Technical co-ordination. Will model the transportation and fate of organisms and model for the design of the microfluidic devices. Where possible, results of simulations will be validated against data emerging from the sensor development activities in WP4. Active in WP1, 2, 4, 5, 6 and 7.
4	Idea s.r.l.	IDEA	(SME) OTH	I	3	Dr. A. Pieracci	Leader WP4: Sensor and signal detection development. Apply expertise in embedded systems, in particular the front-end electronics for the sensors. Electronic and UV measurements of DNA hybridisation on the surface will be performed with and without techniques for nanotechnological signal enhancement For IDEA, one ambition is ultimately to gain competitive advantage, both by making better products for measurement systems and by acquiring new know-how. Active in WP1, 4,7 and 8.
5	Hemosoft	HEM	(SME) OTH	TR	20	Dr. Serkan Kaygun Gunes Tavmen	Development of mobile computer system that manages the data of a multitude of novel LoC type multi-biosensors. Integration of new software. A user guide to the system and context-sensitive help will be prepared. After the release of the software for each new prototype, verification and validation of the system will be performed, Active in WP1, 5, 6 and 7.
6	MikroMikoMed Ltd.	MMM	(SME) IND	HU	6	Dr. R. Deák	Leader WP3: Probe and Primer development. Making RNA and DNA fragments accessible for hybridisation and applying real-time methods to the detection and identification of biohazards. Strategies for combined lysis and filtration will be investigated by MMM. Active in WP3 and 7.

9	Water Research Institute Bratislava	WRI	RES	SK	204	Dr. L. Tóthová Dr. M. Prokšová	ZsVS will confirm candidate organisms, identify optimum distribution of detectors, work towards and derive specification of detectors. Verification, monitoring and data acquisition from prototypes. Verification of and training in the analytical methods used, based on national and international standards. Contribution to standards using outputs from practices and methods developed. T3.3: Sample collection, starting from defined device requirements from T1.2, Key contributor to sample preconcentration by filtration activities (T3.4). WRI will liaise with Work Package leaders of WP1-5 to scope out realistic engineering specifications. Active in WP1, 3, 5, 6 and 7. Leader WP6: Co-ordination, responsibility for Development and Test Plans.
10	Università di Bologna	UNIBO	HE	I	220	Dr. C. Guiducci, Dr. Zuccheri,	Development of micro- and nanodevices for DNA detection using UV and capacitance techniques. Application of nanotechnology to enhance DNA sensor signals. Key contributor to the first electronics prototype T4.7 will be realised as a system-on-board including: signal acquisition interface (conditioning, A/D conversion); control unit (microprocessor based); control interface (graphical unit and/or standard communication interface); power system (battery). Training and education of future engineers and scientists. UNIBO brings important background IPR to the project. Active in WP4, 7 and 8.
11	Budapest University of Technology and Economics	BME	HE	HU		Dr. Santha	Design, material selection and fabrication of high density microelectronic prototype devices/sensors. Signal acquisition interface is the critical part of the system, due to low levels of electrical sensor signal. Acquisition technique will be investigated/ implemented exploiting a differential measurement between the signal of sensor under test and that of a dummy sensor to reduce Signal-to-Noise ratio (SNR) and enhance system sensibility. Training and education of future engineers and scientists. Active in WP4, 5, 6 and 7.

12	Cranfield University	CRAN	HE	UK	1000	Prof. D. Drikakis	Evaluation of fluidics diffusion, analytical and numerical investigations, Transport modelling in nanochannels, experimental testing and dissemination activities. This will also include a comprehensive literature survey. This will inform preliminary design decisions in WP3 and 5, prior to the development of more sophisticated modelling and simulation strategies in T2.1 and 2.2, for which it will also form a benchmark. Active in WP2, 4 and 7.
15	Steinbeis-Europa-Zentrum	SEZ	OTH	D	60	Dr. J. Loeffler. Dr. U. Sutter	Leader WP7: Knowledge management. Responsible for IP and exploitation. Management and co-ordination of technology translation and dissemination events. Active in WP7 and 8. Project administration and finance. Responsible for development and maintenance of project web site. Dissemination to non-technical audiences outside of project.
16	LioniX BV	LIONIX	(SME) OTH	NL	20	Dr. H. Leeuwis Dr. T. Veenstra	preconcentration, Task 3.: Task 5.2: Development work on sonication as a cell lysis method and, if required, on-chip PCR will build on research work in T3.and 3.6. Active in WP1, 3, 5 and 7.
17	Microtronics Engineering	MICRO	SME	A	20	Dr. Aigelsreiter	Manufacturing Partner, Responsible for System Architecture, Automation of Filtration and Sample Pretreatment, Leader WP5
18	Provenion	PRO	SME	D	20	DI B. Sander	Automated Microfluidic Operation, Prototyp Development, System Engineering

Partner descriptions

1. Lambda GmbH (LAM, A)

Overview: LAM is a biotech company that has eleven employees, eight of whom work in R&D. It was founded in 1999 in Austria. It is a wholly-owned subsidiary of Greiner Bio-One BioScience (Frickenhausen, Germany). In 2001, LAM and Greiner Bio-One started a strategic co-operation and in April 2003 LAM was fully acquired by Greiner Bio-One. It is a research oriented company: 50% of the employees have at least a master's degree. The background of the research personal is diverse covering chemistry, biology, genetics and bioinformatics. A production facility for IVD approved DNA-microarrays has been established. ISO 9001:2000 and ISO 13485:2003 certification was achieved in 2005. The company develops and produces DNA microarrays for the detection of pathogens (viruses and bacteria) for medical diagnostics and pharmaceutical quality control. Two medical products have been IVD approved. LAM has extensive expertise in primer and DNA-probe design using bioinformatics and experimental approaches. Research activities aim at integrating DNA microarrays onto microfluidic point-of-care systems for medical applications. PCR-free detection techniques are studied using chemical and nanoparticle signal amplification methods in order to reduce the complexity of microfluidic platforms. LAM is a partner in the consortium "ultra-sensitive genomics and proteomics" founded by the Austrian Genome Project (GEN-AU). LAM's mother company Greiner Bio-One BioScience has a proven track record in the production of polymer laboratory equipment and prototype microfluidic devices are available, including devices that incorporate metal conductors for electrical measurements on polymer surfaces. These technologies are readily available to LAM.

Key Personnel: Dr. Christian Mittermayr

Expertise: LAM's expertise lies in probe design, bioinformatics (RNA/DNA-extraction), DNA/RNA labelling (fluorescent dyes, biotion and quantum dots), bacterial or viral gene handling, high throughput DNA-arrays and microfluidics.

Relevance: Involvement in the Austrian Genome Project "Ultra-sensitive Genomics and Proteomics". The major research focus of LAM is the detection of human pathogens (bacteria and viruses). The mid-term goal is to establish a high-throughput microfluidics platform for the screening analysis of human pathogens. The company was invited to the Round Table by the Austrian representative to ERA-NET Pathogenomics to define key research areas. COST 853 – Agricultural Biomarkers for Array Technology

Competence: Possibly the first European company that has two CE-IVD accredited DNA-microarray kits for pathogen detection. Five DNA microarray kits have been brought to the market. Validation of DNA microarrays according the Pharmacopœia standard. ISO Certified R&D and production of DNA microarrays. As a part of a globally acting German/Austrian holding (GBO International), is has links to a strong distribution structure, particularly in France, Holland and the UK. LAM's parent company is a market leader in MTPs and has extensive know-how in the mass production of microfluidic devices by flow-injection moulding and the functionalisation of polymers. LAM has access to GBO's know-how, including:

- Mould injection production of microfluidics arts
- Surface chemistry for functionalisation of polymers
- Integration of metal wires with polymers
- Optical properties of polymers

Needs/Benefits to Partner: The developed detection techniques will not only be useful for bioterrorism, but also for civil use in medical diagnostics. Strategically, low-cost detection techniques will allow the development of "side-chair tests" or make DNA microarrays accessible to less developed countries, increasing the market size. Techniques developed for the safe validation of the detection device will be generally useful in the development of civil applications. (Very few viruses can be grown in culture. Pathogenic viruses rarely can be handled outside of S3/4 labs, which are not readily affordable to industry.) DNA chip Technology in diagnostic laboratories for microbiological tests is LAM's top priority research interest; as well as automatisation of DNA chip handling (microfluidics); development of sensitive and cheap detection systems (as a substitute for fluorescence labels); and integration of the detection systems into microfluidics.

2. BHR Group Ltd. (BHR, UK)

Overview: Formed as the British Hydromechanics Research Association in 1947, BHR Group Ltd. is now a privately-owned SME specialising in research, development and application of innovative solutions to fluid engineering problems. Its core competence is in fluid dynamics and process technology. BHR works in partnership with industry, developing new fluid engineering technologies, processes and products; and translates academic research into applied industrial solutions and design guidelines. For example, it has created a world-leading body of expertise on mixing through its Fluid Mixing Processes (FMP) consortium, which provides its members with design and scale-up rules for stirred tanks, jet mixed systems and in-line mixing devices. The Engineering Analysis and Simulation (EASI) section provides mathematical modelling and computational simulation skills across BHR's businesses. This includes customising commercial code for specialist applications, such as embedding mass transfer and reaction models into CFD (*e.g.* Leefe *et al.* "Modelling reaction plumes in stirred vessels", presented at ISMIP5 Conference, Seville, June 2004). EASI has relevant experience in multi-scale simulation, developing methodologies for passing information between models operating at different length- and time-scales (see, for example, contractor reports for European Space Agency projects 8124/89/NL/PH(SC) and 10006/92/NL/PP(SC)). The Strategic Technologies section monitors long-term developments in technologies and markets relevant to BHR's businesses (technology road mapping), and initiates research projects to develop technologies that will underpin future growth. This is exemplified by BHR's Technology Translator role in the ProBio Faraday partnership, which facilitates the exploitation of biocatalysis within the UK (see http://www.pro-bio-faraday.com).

Key personnel: Simon Leefe, B.A. (Oxon.), Ph.D., C.Eng., M.I.Mech.E., A.M.I.Chem.E.

Employed by BHR Group for 17 years, initially as an expert in fluid sealing technology, and subsequently as manager of the engineering analysis and simulation group. Responsible for company-wide development and implementation of CFD and mathematical modelling tools. Wide experience across the engineering disciplines. Particular expertise includes mathematical modelling of physical systems and use of analysis in engineering design; development of "embedded models" for third party CFD codes; development of software for specialist applications; design and supervision of theoretical and experimental projects.

Geoff Pollard, B.Sc., Ph.D.

Technology Translator and member of the Steering Committee of the Pro-Bio Faraday Partnership, which facilitates the explotation of biocatalysis within the UK. Member of the Marine Biotechnology Group of the Foresight Marine Panel. Prior to this, he was engaged in inventing, developing and commercialising non-intrusive mixing technology. He was a member of the Advisory Group of the Technology Transfer Programme of the UK Basic Technologies Initiative and has experience of facilitating four technology roadmaps. These include the Pro-Bio roadmap (in collaboration with others), a roadmap on urology, one on immobilisation in catalysis (www.bhrgroup.com/extras/immocat.htm) and one currently under development on the role of catalysis in renewable feedstocks.

David A R Brown, BEng (Hons)

Employed at BHR for over 10 years, working on a variety of mixing related projects largely for the process industries. He has led BHR Group's world leading "Fluid Mixing Processes" industrial consortium project for the last 7 years, which has involved projects covering both homogeneous and heterogeneous mixing in the laminar, transitional, and turbulent regimes - and in batch and continuous systems. He has extensive experience of both physical and computational modelling of fluid flow systems. He also leads BHR Group's Mathematical Modelling section, which focuses on the application of Computational Fluid Dynamics techniques to solve problems for a wide variety of industries, including the Chemical Process, Water, Power, and Manufacturing industries.

Mick Dawson PhD, BSc (Eng)

March 2000 to present: BHR*Solutions* Research Director. Profit and loss responsibility for a team of 15 staff. Research services encompass consortium projects for the chemical process industries and the water industry. Continues to be involved in technical consultancy for the water industry. Mick Dawson graduated in

Biochemical Engineering from University College London. He completed Chemical Engineering PhD at Birmingham University studying oxygen mass transfer and mixing in pilot scale fermenters. Mr. Dawson joined BHR Group in 1992 as a Project Engineer in the Fluid Mixing Processes consortium. He is involved in water industry project work from 1992 onwards joining BHR Group Utilities section in 1993. He has expertise in Process Mixing (e.g. inline mixing, gas-liquid mixing), Mass Transfer, fermentation and water treatment process engineering

Expertise: BHR specialises in software development/application (modelling and simulation); testing components and systems; and manufacture and supply (prototypes, test rigs, specialist equipment). It is an independent contract research, development and consultancy company dealing in all aspects of fluid engineering and its impact on processes and products. It is the world's leading authority on mixing processes, sealing technology and fluid hydraulics and is highly industry focused, enabling clients to optimise plant performance and maximise revenue. It is also involved in the strategic technologies *i.e.* it identifies relevant long-term markets and relevant emerging technologies, develop tools and technologies to support future needs of business. It hasexperience in previous Framework programmes as partner and as co-ordinator and is involved in technology translation from academia to industry and between disciplines.
Relevance: Proposed contributions by BHR are modelling of transport processes at different scales; coupling of transport models between scales; optimisation of microfluidics; technology transfer; delivering the technology exploitation plan and technology demonstration.

Competence: BHR will bring experience in engineering of fluid-handling devices; expertise in computational modelling of fluid flows and species transport; partnership with Cranfield University in Computational Nanotechnology and Multi-scale Modelling; experience of Technology Transfer and Technology Translation; and close relationships with UK water companies.

Needs/Benefits to Partner: BHR hopes to gain a toolkit for modelling small-scale fluid dynamics, improved multi-scale modelling methodologies, accurate numerical methods for species transport, better links with European sensor and diagnostics communities and exploitable technology

4. IDEA SrL (IDEA, I)
Overview: IDEA is the first spin-off created by a university in Italy. It works in the field of electronic systems with the aim to develop prototypes to be industrialised elsewhere. So far, it has developed three proprietary products (a system for automatic inventorisation of books in libraries, a system of audio-guides for museums and a system for distributing messages through displays in large public buildings). Because of its excellent relationship with the academic environment, IDEA has long experience in participating in research projects. IDEA is working in the development of embedded systems for different applications, from industrial control to aerospace research. It has participated in two European Projects (E-TOUR and FRAFEM, dedicated to electronic tools for tourism and software for image processing in the medical field. IDEA is an SME with highly relevant expertise in the field of electronic design.

Key personnel: Ing Augusto Pieracci

Expertise: IDEA's electronics design centre offers a wide range of services, from writing the specifications to studying the feasibility; from the development of the PCB to the realisation of prototypes. IDEA has extensive experience in embedded systems programming and firmware for all types of devices, from simple protocol translators to microcontrollers and programmable devices (FPGA, DSP I.). IDEA's main aim is to become a technological pole for small and medium enterprises, as well as for international companies, providing technological and scientific transfer from the academic environment to industrial markets.

Relevance: Experienced in embedded systems development, it had worked on front-end electronics for sensors similar to those proposed by DINAMICS. It is closely associated with the University of Bologna.

Competence: Five years' experience in embedded systems design at prototype level. Strong collaboration with the university research environment.

Needs/Benefits to Partner: IDEA will benefit from being in the project as it will find complementary expertise and know-how, particularly regarding industrialisation of prototypes. The relationships established in the project with other partners represents an important opportunity to grow and operate in the international context.

5. Hemosoft Bilişim ve Eğitim Hiz. Ltd. Şti. (HEM, TR)

Overview: HEM is a research and technology development company that is supported by several governmental organisations and institutions such as the Small and Medium Enterprises Development Organisation Technology Development Centre, Middle East Technical University (METU); the Software Development Centre, TUBITAK (The Scientific and Technical Research Council of Turkey); and METU Technopolis. HEM produces software and electronic systems, turn-key solutions and project development; and provides educational support and consultancy.

Competence: HEM is mainly involved in medical applications and e-government projects. It is experienced in distributed internet applications (DNA), database development, object-oriented programming, hardware integration and automation. The Nationwide Blood Bank Information Management System (BBIMS) developed for the Turkish Red Crescent is currently being implemented. The Azerbaijani version of BBIMS has been qualified by UNDP, which is an example of HEM's internationally competitive applications. One of the company's earlier projects, IMAD, was one of the first e-government applications that was developed for the Ministry of Foreign Affairs to automate its Administration and Finance Department. This software is operational in one hundred and sixty-three missions in ninety countries.

Relevance: Estimating requirements of the customers and developing user-friendly software to complement hardware. Increasing the dimension of the targeted market by designing modular and expandable applications. Maximising success by obeying software engineering standards.

Needs/Benefits to Partner: HEM will increase its competitiveness among competing Turkish companies by being part of an FP6 project. It will gain vital experience in a multinational, multidisciplinary project. It hopes to develop the following expertise during the project:

- Data acquisition and logging
- Approximate string matching for the extracted DNA strings
- COTS available devices from various vendors: Smart devices (Pocket PC, Palm), PC100 boards and Single Board Computers
- SOAP Client Applications for SBC's
- Nanotechnological approaches
- Multi-national and multi-contractor project management.

6. MikroMikoMed Ltd. (MMM, HU)

Overview: MMM was founded in 2002. The company's profile includes classical culturing and PCR microbiological laboratories. Quality management systems are implemented in both the traditional and PCR laboratories. The activities are managed and performed by a medical doctor, a biologist, two food engineers (biotechnologists) and two technicians. The following techniques are available in the MMM laboratories:

- Real-time PCR technology
- Traditional PCR technologies
- Automated sample preparation system
- Robotic DNA amplification and detection system
- Traditional industrial microbiology (plating, filtration, homogenisation *etc*.)
- Human microbiological diagnostics (*e.g.* STDs, HPV)

Research and development focuses on new applications of real-time PCR-based microbiological methods. MMM has developed more than fifty real-time PCR applications for microbiological approaches (for the detection and identification of viruses, bacteria, yeasts and moulds). The applications are designed to be

comparable with traditional culturing microbiology. It aims to fit these methods to the needs and demands of food industry. MMM is also active in food microbiology and hygiene, including culturing and PCR-based diagnostic methods; detection and identification of foodborne pathogens and food spoilage micro-organisms. It aims to provide complex solutions (from sampling to feedback to the production line) to its industrial partners. Other areas of activity are in human health microbiological diagnostics, applying both culturing and PCR-based techniques; and microbiological training for industrial partners, highlighting the use of real-time PCR techniques. MMM has a co-operation agreement with Roche Hungary Ltd. in the field of PCR-based developments. It also collaborates with the National Collection of Agricultural and Industrial Micro-organisms (NCAIM), Hungary.

MMM has well-developed strategies for sample preparation from industrial materials such as filtrable and non-filtrable fluids (beverages, water, milk *etc*.), viscid materials (*e.g.* syrups), solid matrices (cheese, meat *etc*.). Due to the long-standing and wide-ranging experience MMM, it has personal contacts with and access to governmental microbiological laboratories, including virus laboratories. MMM's laboratory personnel have three years' experience in the field of research and development, as well as in the routine traditional and DNA-based microbiology. It has access to numerous strains of bacteria and fungi.

Relevance: MMM's microbiological laboratories have been in DNA-based microbiological approaches and applications since 2002. The current team includes a skilled medical doctor (clinical microbiologist); a biologist (human clinical mycologist); food engineers (biotechnologists); and an analytical professional. Additionally, MMM's collaborators can contribute additional expertise to the project consortium.

Competence: MMM has proved to be a valuable partner for R&D activities, and several applications it has developed have been implemented for food and environmental use. The available equipment and highly skilled personnel provide a strong and reliable background for microbiological developments.

Needs/Benefits to Partner: The project enables MMM to contribute to a highly important issue. The company would be proud to turn its theoretical knowledge and experiences from clinical and industrial practice to the benefit of this project. The practical application of the outputs of the project will complete the present range of its services for industrial purposes. Participating in this project consortium will help MMM to advance its research activities and to be involved in other national and/or European-scale R&D.

9. Water Research Institute (WRI, SK)

Overview: WRI is a governmental organisation dealing with practically all water management issues. It has been appointed the National Water Reference Laboratory for Slovakia (NRL) by the government. The main objective was to harmonise the standard practice of the European Union and the rules of the OECD with the hydroanalytical practice in Slovakia. The main activities were agreed by the three responsible ministries (Agriculture, Environment and Health). The NRL activities are focused on the development, verification, validation and implementation of the analytical methods, quality control and quality assurance for the Slovak hydroanalytical laboratories; training for the system of quality control analysis; co-operation on preparation and distribution of certified reference materials (CRMs) for the water sector; bilateral and multilateral international projects; and consultancy and auditing for the water sector in Slovakia.

Key Personnel: Dr. Livia Tóthová, Dr. Miloslava Prokšová

Expertise: The NRL at WRI is able to cover the fields of basic physical/chemical methods, organic and inorganic trace analysis, radiochemistry, hydrobiology, microbiology, eco-toxicology, analytical quality control, quality assurance and data management. It is accredited by the Slovak National Accreditation Service according to the standards set by STN EN ISO/IEC 17025 "General requirements for competence of testing and calibration laboratories" for one hundred and fifty-four tests.

Competence: The NRL at WRI has co-operated in many projects and other activities on an international, bilateral and regional level. Some of them are from PHARE (*e.g.* Quality of sediments and biomonitoring, Biodiversity of the River Danube); the TACIS programme (*e.g.* Analyses of water and sediment samples of the River Prut); EU projects (*e.g.* Development of automated monitoring systems for determination of pesticides and their degradation products at trace levels in aquatic environment, Analysis of priority pollutants from agriculture and industry as a basis for the improvement of water quality in Slovakia, DRINKNET, EQUATE); other international Projects (*e.g.* Sampling and analytical survey for the UN/ECE, FITA 4 (Water quality toxicity testing and the public health); the Fifth Framework Programme (DANUBS, AWACSS, TISA River); the Sixth Framework Programme (AQUATERRA, NORMAN). WRI also participated in international activities under the umbrella of the International Commission for the Protection of the Danube River (Joint Danube Survey, Investigation of the Tisza River).

Relevance: WRI has considerable experience in water analysis and is familiar with the water supply system and the demand for safety water delivery.

Needs/Benefits to Partner: Classic analytical services in water supply have delayed responses. New sensors speed the process of obtaining results and therefore reduce the risk of delivery of contaminated water to the water supply system. The proposed system could be used for many different types of contaminants or pollutants in water according demands that are specific to this area of world. The risk of bio-terrorism, currently very high, is delivering ever stronger rules for water supply. The paramount need for safe water delivery is making the development of such analytical methods (very quick response) crucial. No such technology is currently available on the market, which is why WRI is so keen to assist the DINAMICS project.

10. University of Bologna (UNIBO, I)

Overview: The staff involved in the project belong to the Department of Biochemistry "G. Moruzzi" and the Department of Electronics and Informatics. The laboratory on nanoscience and nanobiotechnology, headed by Prof. Bruno Samorì, has long-standing experience in the chemistry, biology and biophysics of DNA, in particular in its superstructures and recognition processes. The group is equipped with state-of-the-art instrumentation for the Atomic Force Microscopy-based manipulation and imaging of single molecules (Veeco's Nanoscope IIIa, Veeco's Picoforce, Asylum Reseach's MFP-1D). The group also owns a high-vacuum surface-coating apparatus (Edwards).

The Microelectronics Laboratory, which is directed by Prof. Bruno Riccò, has traditionally focused on modelling experimental characterisation of solid-state devices and on the design and design automation of circuits and systems. In the last few years, the two groups have actively co-operated in the development of label-free DNA sensors with direct electronic transduction. The group is equipped with standard electrical measurements instrumentation (Semiconductor Parameter Analyzer, LCZ meter, precision generators and

multimeters), virtual instrumentation (National Instrument hardware and Labview software), a probe station for electrical measurements of integrated circuits and systems. Basic equipment for UV measurements has also been purchased.

Key Personnel: Bruno Samorì is Professor of Organic Chemistry at the School of Biotechnology of UNIBO. He carried out research with polarised spectroscopy techniques on liquid crystalline materials until 1990, at UNIBO; at King's College London with S. F. Mason; at the University of California (Berkeley) with I. Tinoco; and at the University of New Mexico with C. Bustamante. The focus of his research then moved to studies of DNA superstructures using AFM. His research activities are presently focused on DNA-based nanobiotechnologies and on single-molecule mechanochemistry in recognition and adhesion events in molecular and cell biology. Prof. Samorì is a member of the Editorial Board of ChemBioChem (Wiley-VCH), and of the Scientific Advisory Committee of the International Society for Nanoscale Science, Computation and Engineering (ISNSCE). He has been President of the Division of the Chemistry of Biological Systems of the Italian Chemical Society and also of the Italian Society of Microscopic Sciences.

Giampaolo Zuccheri is a full-time Staff Researcher at the Department of Biochemistry of UNIBO (since 2002). He holds a degree in Industrial Chemistry (UNIBO) and a Ph.D. in Chemistry (University of Calabria). He has worked at the Lawrence Berkeley National Labs (Berkeley, California) and at the University of Oregon. He is currently working with Bruno Samorì and teaching nanobiotechnology for the degree in biotechnology of UNIBO. His interests focus on the chemistry and biophysics of nucleic acids and proteins and on their nanobiotechnological applications. In 1994, Dr. Zuccheri was one of the recipients of the annual prize of the Italian Federation of the Chemical Industry (Federchimica) and in 1998 he was awarded the Borsellino prize of the Italian Society for Pure and Applied Biophysics (SIBPA). He is currently a member of the National Institute for the Physics of Matter (INFM), of the Italian Chemical Society (SCI), of the National Consortium of Materials Science and Technology (INSTM).

Bruno Riccò is a Professor of Electronics at School of Engineering of UNIBO. He holds a Ph.D. in Physics from Cambridge University. He has been Visiting Scholar at the University of Stanford, the IBM Thomas J. Watson Research Centre, the University of Washington. Prof. Riccò has worked in the field of microelectronics, where has made significant contributions in many areas, including the physics and modelling of electron transport in polycrystalline silicon, tunnelling in heterostructures, silicon dioxide physics; Monte Carlo device simulation; non-volatile memories; IC testing and design for testability; and low power design. On these subjects, Prof. Riccò has (co-)authored several patents and over two hundred and ninety publications. In 1995 he received the G. Marconi Award of AEI (Italian Association of Electrical and Electronics Engineers) for his research activity. In 1999 he founded the first university spin-off (Micro-idea) in Italy. He has been the President of the Technical Board of the National Consortium for Research in Microelectronics (ULISSE); Italian Representative in the (European) JESSI Committee for Basic Long-term Research; and President of the Microelectronics Group of AEI. He has been European Editor of IEEE Transaction on Electron Devices. He is a Fellow of the IEEE.

Expertise: The main scientific role of UNIBO's laboratory of nanosciences and nanobiotechnology within DiNAMiCS is to experiment on the use of nanotechnological approaches towards the enhancement of the sensors signals elicited by DNA recognition. The present project will make it possible to Prof. Samorì's group to extend its fundamental research on surface functionalisation with biomolecules and on DNA superstructures to more applicative aspects based on the triggered formation or breakdown of novel DNA-based superstructures. The main scientific role of UNIBO's microelectronics Laboratory is (i) to develop methods and design circuits for direct on-chip measurement and read-out, as required by the targeted bio-sensors; (ii) to assess and characterise the accuracy and sensibility of the bio-sensors; and (iii) to develop circuits and techniques to enhance them, as required by the system specifications.

Relevance: Large research institution including all scientific expertise relevant to the project. Significant effort and know-how in the field of micro-fabricated devices for DNA detection/recognition. Had the main role in putting together an IP that was "conceptually" a predecessor of DiNAMiCS.

Competence: Twenty years' experience of participation in European Projects (starting from "Microelectronic Regulation", predecessor of the first Esprit Programme). Co-ordinated several European projects and participated to several networks of excellence, particularly in the field of microelectronics. Know-how covering a number of different areas, including IT, as well as biology and medicine.

Needs/Benefits to Partner: UNIBO will benefit from DINAMICS, particularly in that it will learn from other partners' industrial know-how and specifications from real applications (for development of devices and systems aimed at the market). It will also gain from general contacts with other organisations at international level with complementary expertise (in particular regarding fabrication and industrialisation).

Recent publications of interest for DINAMICS:

- B. Samorì and G. Zuccheri, "DNA Codes for Nanoscience", *Angew. Chem. Int. Ed. Engl.* 2005, **44 (8)**, 1166-1181
- M. Brucale, G. Zuccheri and B. Samorì, "The dynamic properties of an intramolecular transition from DNA duplex to cytosine-thymine motif triplex", *Org. Biomol. Chem* , 2005, **3**, 575
- B Samorì, G. Zuccheri, P. Baschieri, "Protein unfolding and refolding under force: methodologies for nanomechanics", *Chem. Phys. Chem.*, 2005, **6(1)**, 29-34.
- C. Guiducci, C. Stagni, G. Zuccheri, A. Bogliolo, L. Benini, B. Samorì, B. Riccò, "DNA detection by integrable electronics", *Biosensors and Bioelectronics*, 2004, **19 (8)**, 781.
- B. Sampaolese, A. Bergia, A. Scipioni, G. Zuccheri, M. Savino, B. Samorì and P. De Santis, "Recognition of the DNA sequence by an inorganic crystal surface", *Proc. Natl. Acad. Sci. USA*, 2002, **99**, 13566.
- Y. Bustanji, C. R. Arciola, M. Conti, E. Mandello, L. Montanaro, B. Samorì, "Dynamics of the Interaction between a Fibronectin Molecule and a Living Bacterium under Mechanical Force", *Proc. Natl. Acad. Sci. USA*, 2003, **100**, 13292-13297
- L. Benini, M. Poncino, "Ambient Intelligence: A Computational Perspective," in *Ambient Intelligence: Impact on Embedded-system Design*, Kluwer Academic Publishers, 2003
- C. Stagni, C. Guiducci, M. Lanzoni, L. Benini, B. Riccò, "Hardware-Software Design of a Smart Sensor for Fully-Electronic DNA Hybridisation Detection", in *Proceedings of the Design, Automation and Test Conference*, 2005, in press
- C. Guiducci, C. Stagni, G. Zuccheri, A. Bogliolo, L. Benini, B. Samorì. B. Riccò, "A Biosensor for Direct Detection of DNA Sequences", *Proceedings of European Solid-State Device Research Conference ESSDERC2002*, 2002, 479-482
- C. Guiducci, V. Stambouli, L. Benini, B. Riccò, "Conductive Oxides as New Materials for Electrical DNA Detection", *Proceedings of the Eighth world congress on Biosensors*, Granada (Spain), Elsevier, 2004

11. Budapest University of Technology and Economics, Dept. of Electronics Technology (BME, HU)
Overview: The Department at BME was founded forty years ago to teach and research the topics of materials science, physical design and manufacturing technology in the field of electronics. The concept of electronics technology refers to the area of technology associated with or applied to the realisation of electronic circuits, modules and systems. In accordance with this, among others, BME focuses on the following areas of microelectronics technology:

- Printed circuit technology, including the fabrication of high density interconnect, multilayer, microvia boards, and computer aided design
- High density assemblies with fine pitch components (CoB, BGA, CSP, flip chip), multi-chip modules
- Sensors, actuators and displays, enzyme-based biosensors, electrically-operated DNA sensors, non-invasive and minimally invasive biomedical applications of sensors and microsystems
- Deposition of electron-conductive polymers, organically functionalised and nanostructured films
- Laser technology (applying 5 wavelengths from UV to IR), microvia drilling, pattern generation, trimming, *etc*.
- Quality control and reliability, performance analyses, accelerated lifetime test, life cycle modelling;

The department has twelve full-time professors and sufficient technical assistance (webmaster, technicians, *etc*.) to fulfil the planned activity. The main activity of BME is the education of undergraduate and Ph.D. students, but the department has a wide range of multinational industrial connections for RTD and training purposes, assisted by close collaborative links with companies such as Flextronics Hungary Ltd., ELCOTEQ Hungary Ltd., Bosch Hungary Ltd., SANMINA-SCI Ltd., Samsung SDI Hungary Ltd., JABIL Ltd., *etc*. The wide range of professional connections in the new member states and associated candidate countries made BME a valuable project partner. The department is constantly active in disseminating the latest RTD results in several international and Hungarian organisations and events, like IMAPS, IEEE-CPMT, ISSE (International Spring Seminar on Electronics Technology), SIITME (International Symposium for Design and Technology of Electronic Packages), OPAKFI (Scientific Society for Optics, Acoustics, Motion Pictures and Theatre Technology), HTE (Scientific Association of Infocommunications), MEISZ (Hungarian Federation for the Electronics and Infocommunication), *etc*.

Examples of EC-funded projects include:

- SIGMA: FP4 INCO-Copernicus, 1997 - 2000.
- CHEAP-MULTICHIP-MODULES: FP4 INCO-Copernicus, 1997 - 2000.
- FLEXIL: FP5 RTD, April 1. 2002 – March 31. 2003
- LIDCAT: FP5 RTD, June 1. 2002 – April 30. 2003
- NETPACK, FP5, December 1. 2002 – March 31. 2004
- EUROTRAINING, FP5, August 1. 2002 – December 31. 2004
- CCMESYS: FP5, June 1. 2002 – November 30. 2004
- LEADOUT: FP6 CRAFT, September 15. 2004 for 3 years
- FLEXNOLEAD: FP6 CRAFT, for 2 years
- EMCI: FP6 STREP, for 2 years

The existing BME infrastructure includes:

- Laboratory complex for the printed wiring boards, with an everyday running prototyping facility
- Thin-film laboratory and laboratory for photolithography and chemical processes
- Laser processing laboratory, with advanced surface profiling, test and microscopy facility
- Circuit Modules laboratory, including the assembly of chips and fine-pitch components
- Sensors and Actuators Centre, including the facility for electrodeposition and characterisation of polymer films, solid and liquid material tests with UV/VIS/NIR spectroscopic microprobes
- Laboratory for Computer Aided Design and Manufacturing (CAD/CAM) of circuit modules
- Laboratory for electronics and measuring techniques, including performance and signal integrity facility

- Laboratories for Quality Control and lifetime test of electronic modules and systems equipped with highly accelerated stress test equipment, climatic test chamber, X-ray microscope

Key Personnel: Dr. Hunor Santha, Prof. Gábor Harsányi,

Expertise: Research, development, design and prototyping of high density electronic modules and sensors; laser patterning; and, *via* generation of laminated and flexible substrates for MCM prototypes, sensor technology and applications. BME also has expertise in biomedical sensor applications; the development of high quality Internet-based materials to support education and networking to disseminate knowledge; promoting information exchange and training. It has considerable EC project experience, as listed above, and experience of industrial projects (with GE, Samsung, Flextronics, Elcoteq, *etc*.)

Relevance: The Sensor Laboratory of BME has conducted research since 1997 on biosensors and sensors in biomedical applications. The current team covers a very broad and interdisciplinary background, including a medical doctor, bioengineer, electrical engineer and biomedical engineer. Additionally, the whole Department of Electronics Technology is committed to support the research topics of the Sensor Laboratory, which will ensure easy access to a broad and thorough expertise in materials science and a vast experience in electronics for the project consortium.

Competence: BME has proven to be a good partner for European-scale RTD activities, co-operating in research projects and networks, *e.g.* the department has co-ordinated the NETPACK Club of the NETPACK Project, organised workshops for the EuroTraining Project, *etc*. Since 1997, five projects supported by the EC have been completed successfully, two projects are in progress and a further three are approved. The technical tasks assigned to BME in the workplan fit very effectively with the expertise of the researchers involved and the available equipment.

Needs/Benefits to Partner: RTD activities of BME can move towards nanobiotechnology and life science applications, with the help of DINAMICS, which serves the strategic objectives of BME. It has an obvious interest to give tasks to its researchers in topics of high societal importance and requiring skills in cutting edge technologies, as this helps to maintain its staff's high professional quality. The possibility of establishing spin-off companies after the project is also an attractive point.

12. Cranfield University (CRAN, UK)

Overview: The Fluid Mechanics and Computational Science Group at CRAN is the largest academic centre for postgraduate studies in science and technology in Western Europe. Its research, teaching and technology development functions are closely linked to industry, public and defence sectors across the UK, Europe and internationally. CRAN has established activity in the broad areas of mechanical, manufacturing and aerospace engineering, management, applied science and medical science. The Fluid Mechanics and Computational Science Group (FmaCS), directed by Prof. Drikakis, is currently engaged in several research topics and new initiatives in relation to computational fluid dynamics; microfluidics; physiological modelling; computational nanotechnology; and modelling of flow, mass, diffusion and chemical reaction transport process at macro-, micro- and nanoscales. Several of the current and past projects carried out by the group are closely related to those to be addressed herein and there is a high degree of commonality in terms of challenges arising from complex unsteady simulations and transport process modelling. Further, the present project requires the use of high-resolution/high-order computational methods for flows featuring unsteadiness in which the group has extensive experience. Therefore, the project will draw upon a substantial body of existing capabilities and expertise. The computational activity at CRAN is supported by the Cambridge-Cranfield High Performance Computing Facility (CCHPCF) which was funded under an SRIF initiative by Cambridge University and CRAN. CRAN will primarily contribute to the computational modelling (computational fluid dynamics and multiscale modelling) in connection with the objective of optimisation of the formation of nanotechnological probes within the microfluidic flow using computational fluid dynamics. Furthermore, the FMCS group will contribute to the optimisation design studies.

Key Personnel: Prof. Dimitris Drikakis

Expertise: Development and application of computational methods and models. Computational Fluid Dynamics (CFD) and Computational Nanoscience (CNS) and Nanotechnology (CNT) models. Some examples include CFD: flow and mass transport, heat transfer, diffusion processes, multi-material flows, mixing and turbulence, and shockwave physics; and CNT: microfluidics, nanofluidics, membranes modelling, molecular dynamics, and multiscale modelling.

Relevance: The FMCS group has been involved several national and international (EC-funded) projects, as well as industrially-supported projects in the field of computational fluid dynamics, fluid mechanics and transport phenomena and computational nanotechnology. Prof. Drikakis is currently involved in projects related to micro- and nanofluidics.

Competence: Prof. Drikakis has eighteen years of research experience in CFD and more recently in computational nanotechnology. Furthermore, he has managed several EU, industrial and EPSRC research projects. He has developed computational methods and models pertinent to micro- and nanofluidics (and transport phenomena in general) and is currently supervising a group of fifteen research assistants in the above fields. Many of these developments are suitable both for serial and HPC parallel computers.

Needs/Benefits to Partner: CRAN will benefit from this project because the FMCS group's main activity is the development of advanced computational strategies in the context of continuum and molecular mechanics for a broad area of fluid flow and mass transport problems. The project will also provide the opportunity to the group to collaborate with a number of SMEs and other academic institutions thus enhancing its scientific and technical competence.

15. Steinbeis-Europa-Zentrum (SEZ, D)

Overview: The Steinbeis Foundation for Economic Promotion was founded by the government of Baden-Württemberg in 1971 with a foundation capital of €15 million. The Foundation runs approximately 500 so-called "Technology Transfer Centres", mainly in Baden-Württemberg, but also in other regions in Germany and beyond – in Austria, Switzerland, Norway, Chile and Malaysia. The Technology Transfer Centres are mostly attached to research organisations in order to guarantee close connection between R&D and industry. More than three thousand researchers, consultants and engineers carry out more than twenty thousand contracts per year to improve the strategy, products and process development of companies. The Steinbeis Foundation undertakes:

- Research and development for companies, with special competence in the economically important fields of technology and growth
- Technology transfer, providing commercial solutions for public sector assignments
- Consultancy services along the whole value chain: technology and innovation watch; audit; assessment; foresight; developing new technologies, processes, methods and systems; management; marketing; sales; financing and shareholding; and regional economic development;
- Policy advice, evaluation and expert opinions for public and private organisations, companies, banks, *etc*.
- Training and further education for companies

SEZ is an entity of twenty people within the Steinbeis Foundation, responsible for the support of European research projects and transnational co-operation in Europe. It was founded in March 1990 and has been a member of the European network of Innovation Relay Centres (IRC) since 1995 and head of the IRC consortium responsible for Baden-Württemberg, Thuringia and northern Switzerland. SEZ is also the official National Contact Point (NCP) for SMEs in the Baden Württemberg region. In Germany, a national agreement created a network of regional contact points for SMEs, in order to allow an easier access to this service in their region. It aims to promote technology transfer from universities and polytechnics to local industrial firms.

SEZ is a non-profit organisation with an annual budget of in excess of €1 million, 85% of which is raised through external funding. Its core activities are:

- To assist organisations to participate in European R&D projects
- To support the management of international research projects
- To provide assistance with the exploitation of the research results
- To promote transnational technology transfer
- To stimulate and support the innovation process in industrial companies

Key Personnel: Dr. Ulrich Sutter and Dr. Jonathan Loeffler

Expertise: SEZ has vast experience of organising workshops, conferences and brokerage events for technology transfer; as well as finding partners for RTD proposals. It has been involved in more than twenty-five European projects in the last years such as:

- NANOROADSME – Development of advanced technology roadmaps in nanomaterial sciences and industrial adaptation to small and medium sized enterprises – Specific Support Action – DG Research (2004 – 2006)
- NANOMAT – Targeted action to encourage the participation of SMEs in the 6th Framework Programme in the nanotechnologies and nanomaterials fields – ETI Specific Support Action - DG Research (2004 – 2006)
- Innovation Relay Centre – Co-ordinator of one of fifty-two IRCs in charge of DG Innovation with the mission to support transnational technology transfer. (1993 – 2006)

The foundation has participated in some fifty EC projects, fifteen as co-ordinator and has acted as project manager for SMEs in a further seven. SEZ also has extensive experience in organising workshops, conferences and brokerage events for technology transfer, as well as finding partners for RTD proposals.

Relevance: Work package leader for dissemination activities. Involvement in transnational technology transfer methods and implementation of best practices, especially for SMEs. Dissemination of project results in European networks and national nanotechnology clusters.

Competence: Fifteen years' experience in transnational technology transfer and support of EC research projects for SMEs. NCP for SMEs in Baden-Wuerttemberg and Innovation Relay Centre since 1995. SEZ employs qualified chemists, materials scientists and biologists. It is involved in a network of more than six hundred technology transfer centres implemented in universities and research institutes, bringing together more than eight hundred professors.

Needs/Benefits to Partner: SEZ will benefit from the project by having the possibility to transfer and disseminate new research results to relevant industrial partners in its SME networks. Expand its network of contacts in the domain of nanomaterials.

16. LioniX BV (LIONIX, NL)

Overview: LIONIX is a private company based in Enschede, the Netherlands, with about twenty people. It is a leading provider in the development and small to high volume production of innovative products based on microsystems technology, MEMS and nanotechnology. The core technologies are integrated optics and micro- and nanofluidics. LIONIX works on a customer-specified basis and has started its own product designs on an OEM base. It aims at an open and sustained relationship with its customers, and strives for an early involvement and a leading role in the whole trajectory, from concept development to supply during the lifecycle of the micro-product or -system. In order to minimise risks, projects are executed in a phased set-up. LIONIX guarantees the application of leading-edge technologies. Its employees have in-depth knowledge and years of hands-on experience in micro- and nanofabrication technologies in general, and the application of integrated optics and micro- and nan fluidics in particular. LIONIX's team is creative and innovative, and is contributing to advancing the front lines of technology. The combination of micro- and nanofluidics and integrated optics gives LIONIX an unrivalled expertise in the emerging area of lab-on-a-chip, while the combination of integrated optics with the micromechanics expertise assures a strong position in the area of MOEMS (Micro-Electro-Optical Mechanical Systems). Shareholders of LIONIX include the University of Twente and the Dutch Innovation Stimulation fund "Innofonds".

Key personnel: Mr. Henk Leeuwis

Active in the MST for over twenty years, he has carried out research as well as development work resulting in several products such as chemical (CHEMFETs), magnetic and micromachined sensors, microfluidic components and systems. He has been project manager and department head, with responsibility for marketing and sales (Dutch Centre for Micro-Electronics, 3T BV) with a focus on custom-specific development of leading edge microsystems for large industrial companies. He was active in European programmes as project leader for RTD projects and as a proposal evaluator. He is Honorary Founder and Board Member of the Dutch Micro- and Nanotechnology Association (MinacNed) and is involved in numerous governmental task forces and committees.

Dr. R.G. Heideman

René Heideman, Chief Technology Officer, obtained his M.Sc. and his Ph.D. degrees in applied physics at the University of Twente (subject: "Optical waveguide based evanescent field immunosensors"). The work was focused on researching the possibilities of commercial application of the sensors developed during the Ph.D. period. His postdoctoral positions concerned the development of a fully packaged integrated optical (bio) chemical sensor, resulting in the patented Mach-Zehnder interferometer, and of the development of integrated optical components for the telecom field, with a focus on an integrated acousto-optical isolator. Furthermore, a TE/TM polarisation splitter, an electro-optical modulator and an acousto-optical mode splitter have been developed. After his postdoctoral positions, he applied his extensive know-how in industry for TMP and Mierij Meteo. In this latter company, he was manager of the integrated optics R&D group. He has written over fifty papers and holds about ten patents in the integrated optics field.

17. Microtronics Engineering GmbH (MICRO, A)

Overview: Microtronics is an innovative producer of wireless and optical measuring systems. The total staff of 20 persons is assigned to the divisions R&D (50%), production, service and support (35%), administration and sales (15%). MT was founded in 2006 as spin-off after a 5 years history as electronics department of INAUT Automatisierungs GmbH. The company is owned by it's three persons management board (51%: Hans-Peter Buber, Stefan Pfeffer, Andreas Aigelsreiter) as well as financial and strategic investors (49%). With our Know How in the areas of electronics, mechanics, optics and software we can realize all solutions in our EN ISO 9001:2000 and EN ISO 13980:2002 certified production- and development facilities in Austria.

Key Personnel: Andreas Aigelsreiter, Hans-Peter Buber, Stefan Pfeffer

Expertise: MT's expertise lies in design, development and production of mechatronic systems.

Relevance: Proven experience in design, development and construction of complex mechatronic machines especially from DNA analysis device "hybOrg" and feasibility study "fluorescent online measurement of microbiological parameters in water"

Competence: 3D-CAD mechanics design, electronics design, software design and development, assembling of mechanics and electronics, system integration, production of low volume series (<10.000 units per year), second level support for complex machines, ISO and ATEX certified development and production facility

Needs/Benefits to Partner: MT brings experience in successful development of DNA analysis systems and all of its associated parts into the project. Designing practicable system architecture, settlement of such a project and integration of scientific results as well as complete units supplied by third parties are well known activities. On the other hand MT relies on the biological and biochemical input of the scientific project partners.

18 . Provenion GmbH (PRO, D)

Overview: Provenion engineering is a practice oriented development enterprise, translating new procedures into industrial products. One focus is the holistic development of software controlled electro-mechanical precision devices in the range of biological- and medical technology, as well as for quality assurance in production processes.
Provenion‘s performance is characterized by multidisciplinary knowledge. The team embodies four mechanical engineers, three electronic engineers, one software architect and two software engineers as well as three precision mechanics. Provenion`s business network extends that team by physicists doctors and a close relationship to several faculties of the Munich University.

Reference Projects:

- The development of a fully automized in-vitro analyzer for DNA/RNA, running the gen-i® procedure.
- Programming of software packages for assay development.
- Development of an equipment for percutane transluminal angioplasty with radioactive fluids (itm Rhenium-PTA©)
- Development of endodontic treatment devices for S.E.T. GmbH.
- System integration of microdosing technology in a bio-analytical device.
- System integration of opto-electronics and vision technology in a micro fluidic device for bio-medical production.
- Advancement of an x-ray examination device.
- Development of magneto – hydraulic fuel direct injection systems.

Provenion is certified DIN ISO 9001:2000 and familiar with FDA and EN/ISO compliant development documentation.

Key Personnel: Dipl.Ing Bernhard Sander,

Expertise: Micro fluidic; micro dosage; fluid atomisation; opto-electronics; design of complex precision mechanical devices; software engineering; electronic engineering; development of measure and control software for lab & analysis; prototyping; manufacture of special purpose devices and machines.

Relevance: World leading in electronic controlled fuel direct injection systems for two-cycle engines - complying with 2006EPA / 2008CARB "Three star ultra low emission standards"

Competence: Automated measuring technology for quality management and product testing machines; micro hydraulic measuring technology for development of fluidic components; software for lab measurement technology; micro mechanic fluid control devices; vision technology based manufacturing and testing processes; efficient pressure- and spray generators.

Needs/Benefits to Partners: manufacture and prototyping of mechanic / electronic test setups; measure- control- and analysing software; fluidic and micro fluidic components and setups; know how of serial production needs in a development process; coordination and definition of interfacial needs between the developed modules.

Management team: Key Personnel

Dr. Christian Mittermayr
A project and innovation manager at Lambda GmbH. He is a chemist by training, with a specialisation in biotechnology and analytical chemistry and he has more than ten years' experience in research at various positions. His early research focused on statistical data analysis and signal processing. Because of this wide expertise he now heads multidisciplinary projects at Lambda, like lab-on-a-chip-based microarrays or nanotechnological signal enhancement. During the last three years he was also sub-project leader of a consortium within the Austrian Genome Project GEN-AU

Geoff Pollard, B.Sc., Ph.D.
Technology Translator and member of the Steering Committee of the Pro-Bio Faraday Partnership, which facilitates the explotation of biocatalysis within the UK. Member of the Marine Biotechnology Group of the Foresight Marine Panel. Prior to this, he was engaged in inventing, developing and commercialising non-intrusive mixing technology. He was a member of the Advisory Group of the Technology Transfer Programme of the UK Basic Technologies Initiative and has experience of facilitating four technology roadmaps. These include the Pro-Bio roadmap (in collaboration with others), a roadmap on urology, one on immobilisation in catalysis (www.bhrgroup.com/extras/immocat.htm) and one currently under development on the role of catalysis in renewable feedstocks.

Dr. Ulrich Sutter
Dr. Sutter holds a degree in physics and a doctorate in engineering sciences from the University of Karlsruhe. He was working for over three years at the Institute of Ceramics in Mechanical Engineering (IKM) at the University of Karlsruhe in the field of material science (piezoceramics) and nanotechnology. At the moment, he is working as a consultant for the Steinbeis-Europa-Zentrum in the field of nanotechnologies, new materials and production technology (NMP). He has good experience in addressing the difficulties and demands of research organisations and SMEs working on a European level as well as funding mechanisms for SMEs, technology profiling and innovation auditing. He has also knowledge in the field of IPR, as well as in patent analysis.

Dr. Jonathan Loeffler
Director of the Steinbeis-Europa-Zentrum Karlsruhe, he holds a degree in chemistry and a doctorate in materials science from the University of Stuttgart. He has over four years' experience in thin-film and microstructure technologies. He has been working for the Steinbeis Foundation since 1996 and has specialised in the support of SMEs, in the management of European Projects and in the international technology transfer, in particular between German and French companies. He has been leading various European research projects with SMEs and has been participating in many different support activities from the European Commission in the domain of technology roadmaps, Innovation Management Techniques, Best Practice of Innovation and European management. He has good experience in addressing the difficulties and demands of SMEs working on a European level. He became director of the Steinbeis-Europa-Zentrum Karlsruhe in March 2000.

Advisory Board member profiles

Dr. Beate Hambsch
Technologie Zentrum Wasser (Water Technology Center)

The Water Technology Center (TZW) is the center of applied water research of the DVGW, the German Gas- and Waterworks Association. The DVGW is political and economical independent. The association follows non-profit goals only. The TZW co-operates with water works by doing joint research projects. The TZW is contact point for authorities, ministries and associations in all questions concerning surface and ground water, drinking water and water technology. The TZW provides a link between the DVGW, the basic research at the universities and the water treatment companies. The TZW is involved in all questions concerning water chemistry, water technology, microbiology, site management, groundwater and soil, material testing, corrosion and distribution systems. The TZW is initiator and member of several national and international joint research projects with subsidy from the DVGW, the German Ministry of Research and Education, the European Union and others.

Beate Hambsch is the Head of the Microbiology Department. Her main working areas are:

- Microbiological analysis of drinking water and raw water
- Practical microbiological problems in drinking water treatment and supply
- Measures in case of emergency
- Legionella-Monitoring

Dr. Hambsch is regularly pusblishing in scientific journals and working on technical reports. She partipated in several European funded projects. Recently she worked on Coliform bacteria in drinking water, Enteropathogen Viruses in surface water as well as on the automated detecton of Cryptosporidia and Giardia in water samples.

Dr. Steve Pedley
The Robens Centre for Public and Environmental Health (RCPEH), University of Surrey, UK
The RCPEH is a department of the European Institute of Health and Medical Sciences (EIHMS), University of Surrey. The RCPEH is a World Health Organisation Collaborating Centre for the Protection of Water Quality and Human Health. In this capacity, the RCPEH provides support to the WHO for the production and dissemination of health-based guidelines for the quality of drinking water and recreational waters. Dr. Pedley is a microbiologist with over twenty-five years' experience of research and consultancy work. For the past thirteen years he has specialised in water quality, pollution control and public health. He has extensive experience in bacteriological and virological techniques, and public health microbiology related to water quality. Dr. Pedley has carried out research and consultancy projects on behalf of NERC, EPSRC, UK Environment Agency, USEPA, WHO, UNEP, DFID, British Council, DANIDA, FAO, Save the Children Federation, World Bank and the International Atomic Energy Agency. He has worked on a number of water quality monitoring and assessment projects, including assessments of national and local capacity in Kenya, Ethiopia, Zimbabwe and Qatar, and infrastructure development in The Gambia, Ghana, Uganda, Costa Rica, Turkmenistan and Mauritius.

Prof. Dr. Franz Allerberger
Austrian Agency for Health and Food Safety (AGES)
AGES combines five federal public health laboratories, three agricultural research centres, five food control institutes and four veterinary institutes. Their mandate is to protect the health of humans, animals and plants, by effective and efficient evaluation of food safety, and by the epidemiological surveillance of communicable and non-communicable infectious diseases. About fifteen national reference labs for infectious diseases are located at AGES. Prof. Dr. Allerberger is head of Business and Human Medicine.

Prof. Dr. Allerberger studied medicine at the University in Innsbruck, Austria and has a Master of Public Health from Johns Hopkins University in Baltimore (Maryland, USA). He is a consultant for hygiene and clinical microbiology. In 1989-90, he undertook a residency at the Mayo Clinic in Rochester (Minnesota, USA) and during 1993-4 he was a faculty member at Johns Hopkins University. Starting from 1992 he worked in various roles for the Austrian Federal Ministry of Health and as a professor at the University of Innsbruck (Institute for Hygiene and Social Medicine) until he became Head of Business Area Human Medicine at the Austrian Agency for Health and Food Safety in 2003. Prof. Dr. Allerberger has published about one hundred and fifty scientific papers, co-authored two books for clinical microbiology and was contributor to a video course on bio-warfare for medical personal. He has received seven awards, is editor of the European Journal of Clinical Microbiology & Infectious Diseases and is on the advisory board or peer reviewer for five scientific journals. In Austria, Prof. Dr. Allerberger was responsible for establishing the diagnostic laboratory facilities for anthrax and smallpox within the national alarm plans and organised – on behalf of the Federal Ministry for Health – hands-on courses for medical laboratory staff on the detection of dangerous pathogens.

Paul Horton
Chartered Institution of Water and Environmental Management (CIWEM)

CIWEM is an independent professional body and a registered charity, advancing the science and practice of water and environmental management for a clean, green and sustainable world. The present day Institution was formed in 1987 when the Institution of Public Health Engineers merged with the Institution of Water Engineers and Scientists and the Institute of Water Pollution Control to form the Institution of Water and Environmental Management.The Institution was granted a Royal Charter in 1995 and was proud to celebrate its centenary in the same year.

Paul Horton is Director for International Development and responsible for International matters within the Institution and the further development of CIWEM worldwide. This involves working with CIWEM international branches, UK and overseas members; the European Water Association and other professional bodies; relevant trade organizations, who have an international dimension; building links with appropriate governmental and intergovernmental bodies; and influencing the development of EU policy.

A.2 SUBCONTRACTING

Subcontracting is required by three partners, LAM (partner 1),BME (partner 11) and SEZ (partner 15). The selection of all subcontractors will be done in compliance with the Art. II.6 of Annex II.

LAM needs to subcontract the manufacturing of moulds, which are used to develop microfluidic structures in polymers *via* a mould injection process. While R&D work is involved in designing the microfluidic structures, the manufacturing of moulds is a well-established process that is offered by specialised companies at competitive prices. It is common practice for plastic manufacturers using injection moulding to outsource the mould making to these specialist companies. This is expected to cost €25,000.

BME's Department of Electronics Technology is mainly focused on electrical engineering and some aspects of microtechnology and biosensors. Some specific tasks require the use of equipment and services that are not available in-house, and fall outside BME's everyday activities. This service is only required for limited periods during the project, and it is uneconomical to purchase these resources.

1. Test units and prototypes of microfluidic structures will demand drilling of glass sheets, most probably with an excimer laser, which is not available with the appropriate wavelength within the department at BME. Therefore, such tasks will be outsourced.
2. Some specialised mechanical engineering and manufacturing tasks, *e.g.* CNC machining of thermoplastic polymers or hard alloys will be outsourced to a company having the necessary equipment and know-how.
3. Some mechanical testing tasks for prototypes and their components in the latter phase of the project will need a subcontractor with suitable testing facilities.
4. Certain unpredictable problems requiring expertise in organic chemistry and chemistry might not be solved by BME, since its background in this regard is mainly some biofunctionalisation strategies and electrode testing.
5. To support the activities towards industrialisation, one or two independent experts will be contracted in the issue of manufacturability in order to obtain independent opinion and personal consultation for refinements directly from the industry.
6. When some intellectual property would be generated during the project, external patent attorneys will be contracted to support the scientific staff, because this is the usual practice at the university and no patent attorneys are available as full-time employees.

The estimated cost of this is a total of €16,000 for the full duration of the project.

SEZ will subcontract standard project-accompanying tasks to subcontractors, like readily available IT resources and services for project management, the development and maintenance of the DINAMICS online corporate communication platform, including an online document management system, a discussion forum and a public website. In the domain of financial project management, software products equivalent to the software tool "VITAMIB", which was especially developed for financial controlling in an european research project supported by the EC, will be considered for the project management."

Depending on the skills of potential subcontractors, the subcontracting tasks will be divided into one or two subcontracts. If possible, there will be only one subcontract. If none subcontractor can be found whom is able to carry out all tasks, two subcontracts will be concluded: one for the website design, programming and maintenance and one for the installation, adaptation and maintenance of the content management system. SEZ will issue the subcontract."

The estimated cost of this is a total of €30,000 for the full duration of the project.

Audit certificates for all partners will usually be subcontracted to an external auditor. An allowance of €1,000 per partner per year has been assigned for this.

A.3 THIRD PARTIES

LAM has access to resources at Greiner BioOne (Frickenhausen, Germany). LAM is a wholly-owned subsidiary of GBO and, through a contract, it has access to resources at cost. Since company policy aims at increasing efficiency and reducing cost by exploiting synergies and reducing overhead by avoiding redundancy of key personnel and equipment, research resources are split between the locations and sited where most appropriate.

The resources relevant to the DINAMICS project comprise personnel and usage of instruments and machinery in the R&D department, construction office and the production facility. Usage of these resources is anticipated in WP4 and WP5. The value of these resources is approximately €160,000 for the whole duration of the project.

A.4 COMPETITIVE CALLS

No competitive call is planned for including a new partner to the consortium. The consortium and the project co-ordinator will identify the appropriate candidate.

A.5 THIRD COUNTRY PARTICIPANTS

No third country participants are involved in DINAMICS.