Micro-nano-bio convergence systems for biomedical applications: State of the art and Future perspectives under the EC-ICT Program

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Introduction

A key goal of modern medicine is to identify diseases at the earliest possible stage, intervene before symptomatic disease becomes apparent and monitor both the progress of the diseases and the effect of intervention and therapeutic procedures. This requires technologies capable of detecting pre-disposition to disease conditions or earliest possible signatures of emerging disease and supporting immediate, specific and highly targeted intervention. Research and development at the interface of micro-nanosystems and biology combining information and communication technologies, has the potential to provide the necessary technological platforms and enhanced ability to sense, detect, analyse, communicate, respond and monitor. This currently leads to the development of new medical technology fields and applications e.g. molecular imaging, point of care testing, gene therapy and bionics (including on and inside the body sensors and other miniaturised smart systems) which are expected to revolutionise the healthcare provision and quality of life.

Micro-Nano-Bio convergence systems under EU–Research and Development Program: Rational and Current activities

Under the research and technology development framework programme (FP) 6 of the European Union [2002-2006], the Information Society Technologies program (IST), micro-nano systems sector[2], strongly supported through academic and industrial cooperative projects the area of "micro-nano-bio convergence" systems, striving to reach a balance between technological innovation (discovery) and integration into functional systems that can be plugged into real-life environment (applied research) [1]. The cluster of EC-funded projects on Micro-Nano-Bio Convergence Systems**,** "so-called" MNBS**,** regroup projects developing systems that use a vast array of technologies to integrate across traditional boundaries between the micro-nano- bio, and info worlds, enabling a wide range of applications from health care to food quality monitoring (fig. 1). The group is currently divided, in two main categories:

- *Biosensors, DNA & protein arrays, biochips, lab on chip, and other miniaturised systems enabling point of care, in vitro molecular diagnosis, and biological/biochemical analysis.* Such projects develop and integrate components and modules e.g. microfluidics, biosamples preparation, sensing, detection, signal processing and data management. Applications in biomedicine and healthcare include e.g. early cancer diagnostics, prognosis and disease recurrence (e.g. breast, prostate, lung and colorectal), malaria detection, diabetes monitoring and deep vein thrombosis early detection. Another promising research activity is on wearable biochemical sensing though sweat analysis, targeting applications such as sports and human performance, obesity and wound healing.
- *Body sensors, implantable systems, endoscopic probes, active electrodes and other miniaturised systems interacting with the human body to enable several applications* e.g. drug delivery, repairing of vital functions, diagnosis, monitoring and well being. These projects develop and integrate components and systems e.g. sensors, actuators, micro/nano electrodes, power supply, signal & data processing, and wireless telecommunication modules to fulfil predefined applications requirements. Such example is smart implant sensors and systems e.g. glaucoma & retina sensor, intra-cranial pressure sensor, cochlear implant, functional electrical stimulation for limp motion, activity monitor, sphincter sensor and biosensor for blood glucose monitoring. Other examples include endoscopic probes for gastrointestinal tumour recognition and therapy, active neural electrode system for

[1] The views developed in this article are that of the authors and do not reflect necessarily the position of the European Commission
[2] Micro & Nano Systems FP6 project portfolio: http://cordis.europa.eu/ist/mnd/publications.htm.

stimulation and recording of brain activity and disorders; drug delivery through intraoral microsystem; non invasive sensors systems for attention, stress, vigilance and sleep on the go.

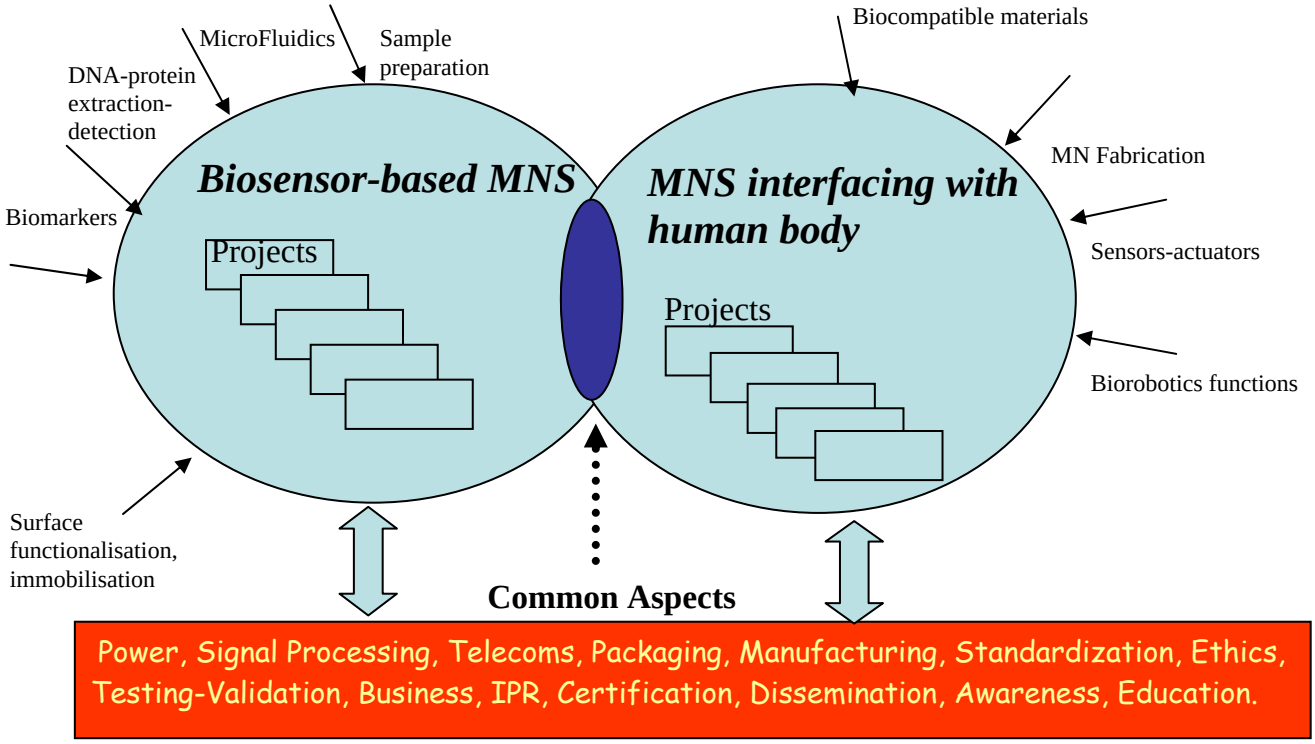

Figure 1: MNBS Cluster of EC-Funded activities

In addition to the individual project activities, cluster (concertation) workshops are organised at yearly basis in order to evaluate the technological coverage of the field and identify gaps, to build critical mass of activities with clear visibility and societal impact, to identify possible synergies and interesting topics for further collaboration and identify structural constrains in the exploitations of the results and share best practices [2].

The conclusion from the last concertation workshop in March 2008 stress major issues to be tackled by the group. For example in the area of in-vitro biosamples analysis, where the projects strive to improve the current health care through the early detection and diagnosis of diseases at the point of care the technological challenges e.g. on sample preparation, microfluidics, label-free detection, optical detectors, immobilization techniques and system integration, represent common interest topics for collaboration. For projects working on MNBS interacting with the human body, implantable sensors, neuroelectrodes, biocompatible materials, power solutions for wearable microsystems and flexible substrates are, among other, major challenges and topics for collaboration. In addition, standards, clinical validation and strong involvement of end-users were brought up as essential elements in the process of commercialization the technologies

Future Challenges

Research and innovation on converging Micro-Nano-Bio-ICT systems is essential to achieve better quality and cost-effectiveness of pHealth. A well known example of MNBS is the biochip: it allows the integration of all stages required for a complete biological analysis on one single device, providing enormous advantages over conventional techniques requiring time-consuming and labour-intensive analysis, as well as the need to use costly, bulky and slow laboratory equipment.

The main challenges for the development of the new generation of medical devices and pHealth systems are directly linked to three major "dimensions of progress" i.e. *computerisation* (employment of ICT), miniaturisation

(decreasing size of devices, systems and components) and molecularisation (integration of molecular and cell biology) [3].

Computerisation will enable e.g. integrated bioinformatics medical data management, increasing data rates and storage power for personal healthcare devices, tele-transmission of patient data, etc. The impact of miniaturisation is on the application or the delivery of a given function. Future micro-nano systems will consist of integrated smart systems which will: sense and diagnose a situation qualitatively and quantitatively, address and identify each other, have predictive capacity, be able to interface, interact and communicate with the environment and with other systems, and be able to act, perform multiple tasks and activities. Integration into the whole fabrication sequence ready for industrialization and especially, integration with other devices to make a system is, also, a critical and very challenging task. Major challenges of "molecularisation" include: the development of new marker molecules; the immobilization of active molecules on surfaces and in exact positions; new surface chemistry; biocompatibility and multiplexing techniques to ensure powerful and accurate signal output. A further key issue is to develop reliable and reproducible engineering, chemistries and bioprocesses at the molecular level that can be manufactured, in bulk, in mass production systems to take nanotechnologies from a laboratory tool to being commercial products in the full range of markets.

In the medical setting the future demand micro-nano systems (MNS) should be able to operate at a small but not necessarily nano scale. For example they need to be small enough to sit in hollow organs, such as blood vessels, the digestive tract or various parts of the body cavity and within organs, such as the heart. Such devices may well be constructed from nano components including sensors, power systems, processors and communications components. The key technological requirements to fulfil are e.g. [3]:

- Miniaturised, intelligent, extra corporal, intracorporal, endoscopic or implanted sensor components and systems for deriving biochemical parameters (e.g. proteins), performing blood pressure & glucose monitoring, electrical tissue or nerve stimulation or microsurgical procedures and tissue interaction
- Flexible substrates, energy harvesting technologies and manufacturing of miniaturized modules.
- Methods and approaches for handling miniaturized components and systems (e.g. micro fluidics, DNA arrays and lab on chip).
- Kinaesthetic and cutaneous-like sensors and display: expected to immerse the surgeon in a new world of tactile and stereognostic sensations making operation more accurate, safe and fast. As an example, haptics surgical gloves can today be conceived integrating soft and hard materials and technology incorporating new sensors, actuators, processors and haptic displays.

One of the main purposes of MNBS cluster is to reach a common understanding of R&D and market challenges in the field. With a clear visibility and critical mass of activities it aims at leading to a broader EU sustainable and competitive initiative such as a European body, a forum or joint venture with public and private stake holders. Their role is to increase and improve the investment in R&D, to promote innovation and uptake of the MNBS, to facilitate the sustainable use of resources, identify strategic drivers and contribute to a strong European industrial base. Collaboration with other initiatives like CIP (Competitiveness and Innovation Program), National Programs, Regional Policies, EUREKA, etc, would be required to implement such initiative.

References

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