

Recommendations of the European Alliance for Medical and Biological Engineering and Science for the 7th Framework Program of the European Commission

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Sources

The present recommendations are based on the following documents:

- European Alliance for Medical and Biological Engineering and Science “EAMBES position paper” <<http://www.eambes.org>>
- STEP Consortium “The Virtual Physiological Human in FP7” <<http://www.europysiome.org>>
- Recommendations of EAMBES member societies submitted in preparation of the Thessaloniki meeting
- Minutes of the EAMBES Division of Societies meeting, Center for Research and Technology Hellas, Thessaloniki 24-25 February 2006

Introduction

We, the European Alliance for Medical and Biological Engineering and Science (EAMBES) submit the present recommendation to the attention of the European Commission, to the European Parliament, and to the Citizen of Europe, in order to contribute to the debate over the strategic priorities that should be addressed in the Workprogramme of the 7th Framework Program for Research and Technological Development of the European Commission (FP7).

EAMBES represents 24 National Societies from 21 European Countries and 5 Transnational Societies and 26 Academic Institutions, several thousand individual researchers and professionals active in the domain of Medical and Biological Engineering and Science. The Division of Fellows will establish a forum for the discussion of future and emerging sub-disciplines within Medical and Biological Engineering and Science. Overall, through its member organisations EAMBES represents more than 8000 European experts in this field.

The present recommendation is the conclusion of a long consensus process that EAMBES started nearly three years ago and that produced firstly our position paper on European biomedical research (www.eambes.org), and now this document. In the next section we draft three long-term strategic priorities that we consider the grand challenges of biomedical engineering research, briefly describe them in a non-technical way, and highlight the impact that the achievement of these objectives will have on European economy and on the quality of life of European citizens. In the following sections we translate these global objectives into specific recommendations with respect to the priorities indicated by the European Commission proposal for a “decision of the European parliament and of the council

concerning the seventh framework programme of the European Community for research, technological development and demonstration activities (2007 to 2013)”.

Strategic priorities

EAMBES consider strategic the achievement of the following objective:

- Creation of the *Virtual Physiological Human*
- Development of a new generation of *Intelligent Medical Devices and Implants*
- *Quantitative Evidence-Based Medicine* enabled through the transfer to clinical practice of new biomedical and technological research based methods and tools

Virtual Physiological Human

The Genome project created a digital representation of the Human Genome. Using this map we can now more systematically investigate which proteins living cells express. However, in order to fully exploit the enormous potential of genomic and post-genomic research, we believe it is necessary to achieve a more ambitious objective: the *Human Physiome*. The physiome is the quantitative and integrated description of the functional behaviour of the physiological state of an individual or species. The physiome describes the physiological dynamics of the normal intact organism and is built upon information and structure (genome, proteome, and morphome). The term comes from "physio-" (life) and "-ome" (as a whole). In its broadest terms, it should define relationships from genome to organism and from functional behaviour to gene regulation. The Human Physiome is a necessary approach for the interpretation of pathological effects and symptoms, i.e. pathological deviations from the "healthy" physiological behaviour, that result from or are caused by irregular genomic sequences.

We believe the best way to pursue this objective is to develop the Virtual Physiological Human. The term Virtual Physiological Human (VPH) indicates a shared resource formed by a federation of disparate but integrated computer models of the biomechanical, biophysical, and biochemical functions of living human body able to simulate both physiological and pathological conditions. These models span multiple dimensional scales (from the whole body down to the cells and the proteins they synthesise), account for the inter-subject variability, and enable the combination of patient-specific data with population-based representations. The development, application and utilization of VPH models requires the establishment of an accreditation procedure in order to guarantee standards for high quality with special regard to validity, compatibility and modularity for integration purposes. VPH models shall be available in certified open-source configuration.

VPH models are both descriptive and predictive, comprising:

- Large collections of anatomical, physiological, and pathological data stored in digital format
- Predictive simulations developed from these collections
- Services aimed to support the researchers in the creation and maintenance of these models
- Services aimed to empower clinical, industrial and societal users in the use of the VPH resource

They are implemented as computer models and services, designed following community standards that make possible to exchange information and to realise a developmental process based on the federation of the various partial representations, each already useful by itself, into what should become one day an exhaustive and complete representation of functions of the human body. This implies the creation of brand new technologies, specifically developed to pursue this scope.

Intelligent Medical Devices and Implants

Medical devices are becoming more and more important in the daily life of many European citizens. Implantable and wearable devices help to compensate the limitations that diseases or simply the aging process would otherwise impose to our daily life. They help our children with congenital cardiovascular defects to survive until the age when it is possible to surgically correct the malformation, or our children that faced the surgical removal of a portion of their skeleton because of bone tumours, to return to their normal daily life. They help many of us to compensate for auditory or visual sensorial limitations. They help us to train our bodies, to keep them healthy to recover from the effects of a disease or of an accident. They help our elders to return to normal and active life after heart attacks, osteoporotic fractures, or after a stroke.

Basic technological research in these years has produced dramatic advancements in sectors such as micro and nanosensors, microelectronics, wireless communication, material sciences. Thanks to biomechanics, bioelectronics and bioengineering we have now a much better understanding on how these medical devices interact with the human body, and what are the ideal condition under which they operate. This makes possible the creation of an entirely new generation of medical devices, called *Intelligent Medical Devices*.

Under this term we include medical devices able to adapt to changes under pathophysiological conditions or the changes occurring in other medical devices; expose monitoring functions that allow collecting non-invasively information about the device itself, its efficacy, or the conditions of the host; self-predict its failure before it produces any adverse effect of the host; simplify remote care by continuously communicating with personal digital devices, local (e.g. body) or wide-area networks, private and public communication networks enabling totally new seamless and effective ways to monitor and improve the health and continuity of care of European citizens; integrate with environmental controls such as those provided by ambient intelligence, protected residences, and healthcare centres, in ways that allow the medical device to monitor the health conditions of the host, and adjust the environmental conditions accordingly.

Quantitative Evidence-Based Medicine

Medicine is still considered by a considerable number of practitioners as an art rather than a science. While the personal skills of the single medical professional play an undeniable role in the success of any clinical procedure, in the last few years there has been a constant trend of the clinical practice toward the so called evidence-based medicine, suggesting that medical professionals should take decision based on hard facts rather than opinions whenever possible. This has been translated so far in systematic revision of the documented clinical experience by means of accurate statistical analysis, and by formalisations of the personal experience of multiple practitioners by means of formalised consensus processes.

We advocate that in many cases the best evidence we can provide to support any clinical decision is a quantitative indicator. It is surprising how many important decisions are taken in the daily practice without any reliable quantitative information on the functional effects of a disease, on the outcomes of a treatment, or on the efficacy of a rehabilitation program. We propose to develop and validate new technology, new methods and new clinical protocols enabling a medicine based first and most on quantitative evidences.

This translates into:

- a) the development of new technology generating reliable quantitative information during diagnosis, planning, treatment, monitoring and rehabilitation;
- b) in protocols, algorithms and models that analyse, combine, and manage biomedical data from the molecular all the way up to the phenotype, recorded via medical imaging and biomedical instrumentation in order to generate reliable quantitative information;
- c) in laboratory and clinical studies that demonstrate the efficacy of quantitative information in the clinical decision-making process including issues related with pharmacovigilance, adverse effects of drugs and adherence in relation with clinical outcomes and patient safety.

Specific recommendations relative to FP7 activities

EAMBES NOTE

The proposed topics for the work programme are materialised by bullet points, under the relevant rubrics of the current Commission proposal for the Cooperation Specific Programme of the 7th Framework programme

Biotechnology, generic tools and technologies for human health

- High-throughput research. To catalyse experimental progress in biomedical research by enhancing data generation, standardisation, acquisition and analysis.
 - New tools for Physiomics : new protocols, standards, technologies and analysis procedures to develop parts of the human physiome, and its relation with morphome, proteome, and genome (e.g. modelling the electrophysiology of human hart from proteins to the whole hart function; development of a model of the structural competence of the skeleton that accounts for all relevant factors from whole body motion to the metabolism of related hormones)
- Detection, diagnosis and monitoring. With emphasis on non-invasive or minimally invasive approaches.
 - Optimisation of new diagnostics tools based on biomedical technologies through novel interpretation schemas (e.g. indirect assessment of microcirculation, quantitative functional assessment of the musculoskeletal system by combination of imaging, measurements and modelling)
 - Microvascular circulation based diagnosis linked for example with diabetes, monitoring regenerative medicine, injury / trauma
 - Fracture risk in osteoporosis and other skeletal diseases

- Connecting molecular with functional information (e.g. metabolic level)
- Technologies for multiscale integration (e.g. combining tissue biopsy with organ imaging info)
- Predicting suitability, safety and efficacy of therapies. To develop and validate biological markers, in vivo and in vitro methods and models, including simulation, pharmacogenomics, targeting approaches and alternatives to animal testing.
 - Model based therapy management (e.g. subject-specific modelling as tool to monitor the efficacy of a therapy such as modelling of renal replacement therapies)
 - Assessment of patient specific drug response (e.g. hypertension treatment)
 - Bioreactors as disease models
- Innovative therapeutic approaches and intervention. To consolidate and ensure further developments in advanced therapies and technologies with potential application in many diseases and disorders.
 - Biomedical Technology inducing remodelling / adaptation / functional recovery (e.g. temporary organ assist, minimally invasive tissue augmentation/destruction)
 - Minimally invasive therapies enabled by multifunctional devices and smart tools (e.g. minimally invasive surgery, interventional cardiology, in-utero, radiology, gynaecology and neurosurgery)
 - Intelligent implants, drug delivery systems and prosthetics (e.g. artificial pancreas)
 - Hybrid organs (Bioartificial pancreas)

Translating research for human health

- Integrating biological data and processes: large-scale data gathering, systems biology. To generate and analyse the vast amount of data needed to understand better the complex regulatory networks of thousands of genes and gene-products controlling important biological processes.
 - Use of virtual physiological human models to investigate biological processes on a systemic level under pathophysiological conditions (e.g. chronic and rare diseases)
 - Virtual physiological human enabled annotation procedures to support integration and interpretation of a wide variety of biological data (e.g. sleep staging data)
- Research on the brain and related diseases, human development and ageing. To explore the process of healthy ageing and the way genes and environment interact with brain activity, under normal conditions as well as in brain diseases.
- Translational research in infectious diseases. To address anti-microbial drug resistance, the global threats of HIV/AIDS, malaria and tuberculosis as well as emerging epidemics (e.g. SARS and highly pathogenic influenza).

- Translational research in major diseases: cancer, cardiovascular disease, diabetes/obesity; rare diseases; and other chronic diseases (e.g. osteoarthritis). To develop patient-oriented strategies from prevention to diagnosis and treatment including clinical research.

Optimising the delivery of health care to European citizens

- Translating clinical outcome into clinical practice. To understand clinical decision-making and how to translate outcomes of clinical research into clinical practice and especially addressing the specificities of children, women and elderly population.
 - Optimisation of translation of information from new types of data gathered from new technology into medical knowledge (e.g. use of inference and semantic technologies for interpretation of data related to cervical cancer coming from various inhomogeneous data sources)
- Quality, efficiency and solidarity of health systems including transitional health systems. To translate effective interventions into management decisions, to ensure an adequate supply of human resources, to analyse factors influencing equity of access to high quality health care, including analyses of changes in population (e.g. ageing, mobility and migration, and the changing workplace).
- Enhanced disease prevention and better use of medicines. To develop efficient public health interventions addressing wider determinants of health (such as stress, diet or environmental factors). To identify successful interventions in different health care settings for improving the prescription of medicines and improving their use by patients (including pharmacovigilance aspects).
- Appropriate use of new health therapies and technologies. Long term safety aspects and monitoring of large scale use of new medical technologies (including devices) and advanced therapies ensuring a high level of protection for public health.
 - Guidelines and best practices on using medical technologies
 - Health technology assessment of new technology solutions
 - Long term safety aspects, cost effectiveness, quality of life and monitoring of large scale use of new medical technologies (including devices) and advanced therapies (e.g. patient registries)

ICT Technology Pillars

- Nano-electronics, photonics and integrated micro/nano-systems. pushing the limits of miniaturisation, integration, variety and density; increasing performance and manufacturability at lower cost; facilitating incorporation of ICT in range of applications; interfaces; upstream research requiring exploration of new concepts.
 - magnetic nanostructures for molecular diagnostic and therapy.
 - magnetic nano-markers
 - magnetic based drug delivery technologies
- Ubiquitous and unlimited capacity communication networks: ubiquitous access over heterogeneous networks - fixed, mobile, wireless and broadcasting networks spanning from the personal area to the regional and global area - allowing the seamless delivery of ever higher volumes of data and services anywhere, anytime.

- Merging mobile networks and static telecommunication infrastructure for use in welfare and health delivery
 - Develop location-based and location dependent biomedical services
 - Deploy personalised quality control techniques for patient safety and effective self-care
- Embedded systems, computing and control: powerful, secure and distributed computing and communication systems that are embedded in objects and physical infrastructures and that can control and adapt to their environment.
- Incorporate ambient intelligence techniques in a wider scale and embed proactive monitoring processes
- Software, Grids, security and dependability: dynamic, adaptive, dependable and trusted software and services, and new processing architectures, including their provision as a utility.
- Develop new association and inference models on diverse biomedical data repositories
 - Enable dynamic formulation and execution of combinatorial analysis via resource orchestrations (workflow modelling)
 - Utilise the existing ICT infrastructure (e.g., Grids and emerging technologies) as a true source of value for the biomedical community, enabling:
 - large-scale epidemiological studies
 - drug discovery and testing
 - disease modelling
 - presymptomatic testing through modelling and predicting diseases
 - delineation of metabolic pathways
 - Assistive living and self-care
 - Interconnect biosensors in a GRID enabled environment (ambient biosensor networks)
 - Toward a unified European Grid infrastructure for the Virtual Physiological Human
- Knowledge, cognitive and learning systems: capturing and exploiting knowledge embedded in web and multimedia content; bio-inspired artificial systems that perceive, understand, learn and evolve, and act autonomously; learning by machines and humans based on a better understanding of human cognition.
- Construction of semantically enriched biomedical sources based on commonly accepted open standards
 - Simplify access to complex and specialised bio - information/systems (virtualisation of sources)
 - Encode biomedical knowledge in reusable and interchangeable formats

- Address the issue of data and information overflow through ‘tagging’ processes of the data acquired usable for medical decision support
 - Data mining of HIV/AIDS Electronic Health Records for improving chronic HIV therapy
 - Knowledge management infrastructures and models for the Virtual Physiological Human
- Simulation, visualisation, interaction and mixed realities: tools for innovative design and creativity in products, services and digital media, and for natural, language-enabled and context-rich interaction and communication.
 - Virtual reality based surgical trainers linked to Virtual Physiological Human tools
 - Development and efficacy assessment of innovative interfaces to data and simulation services to be used by medical professionals (e.g. navigation and interactive visualisation of the Virtual Physiological Human repositories)
 - Integration of nanorobotics within advanced surgical tools
 - New perspectives in ICT drawing on other science and technology disciplines, including insights from physics, biotechnologies, materials- and life-sciences, for miniaturisation of ICT devices to sizes compatible and interacting with living organisms, to increase performance of systems engineering and information processing, and for modelling and simulation of the living world.
 - Link biological with medical information and identify more effective and measurable markers for disease monitoring through the deployment of micro-nano sensors
 - Modelling bone self-healing process and bone adaptation to the environmental conditions as a theoretical paradigm toward self-adaptive and self-repairing structural materials

Integration of Technologies

- Personal environments: personal communication and computing devices, accessories, wearables, implants; their interfaces and interconnections to services and resources.
 - Personal health environments, including the integration and communication between intelligent medical devices, biomedical instrumentation, environmental controls, etc.
- Home environments: communication, monitoring, control, assistance; seamless interoperability and use of all devices; interactive digital content and services.
 - Aids for independent living for elderly and handicapped
- Robotic systems: advanced autonomous systems; cognition, control, action skills, natural interaction; miniaturisation.

- Surgical robotics with semi-autonomous operation and ergonomic interfacing
- Intelligent infrastructures: tools making infrastructures that are critical to everyday life more efficient, easier to adapt and maintain, more robust to usage and resistant to failures.

Applications Research

- ICT meeting societal challenges: New systems and services in areas of public interest improving quality, efficiency, access and inclusiveness; user friendly applications, integration of new technologies and initiatives such as ambient assisted living.
 - for health, improving disease prevention, early diagnosis and personalisation; autonomy, safety and mobility of patients; health information space for knowledge discovery.
 - Toward the Virtual Physiological Human: technology, standardisation, infrastructure, and establishment of relevant collections for the creation of European VPH resource.
 - Subject-specific computer modelling as a tool for personalised risk analysis, treatment planning and monitoring
 - The assessment of behavioural long term profiles based on pervasive and intelligent networks of sensors.
 - Electronic patient diaries in PDAs used for increasing patient adherence in phase I, II, III, IV clinical trials
 - Continuous monitoring of drug effects / adverse drug effects
 - Develop artefact rejection / data quality control techniques due to the involvement of non-experts in measurements
 - Point of care systems for in vitro diagnostics
 - to improve inclusion and equal participation and prevent digital divides; assistive technology; design-for-all.
 - for mobility; intelligent ICT-based transportation systems and vehicles enabling people and goods to move safely, comfortably and efficiently.
 - in support of the environment and sustainable development, to reduce vulnerability and to mitigate the consequences of natural disasters and industrial accidents.
 - for governments; efficiency, openness and accountability, for a world-class public administration and links to citizens and businesses, supporting democracy.
- ICT for content, creativity and personal development:
 - new media paradigms and new forms of content; creation of interactive digital content; enriched user experiences; cost-effective content delivery.
 - Integrate clinical, biological and research data sources into reference knowledge databases
 - Dissemination of the ‘trans-cultural mobile European patient model’

- Technology-enhanced learning; adaptive and contextualised learning solutions; active learning.
- ICT-based systems to support accessibility and use over time of digital cultural resources and assets, in a multilingual environment
- ICT supporting businesses and industry:
 - new forms of dynamic networked co-operative business processes, digital ecosystems; optimised work organisation and collaborative work environments.
 - Manufacturing: rapid and adaptive design, production and delivery of highly customised goods; digital and virtual production; modelling, simulation and presentation tools; miniature and integrated ICT products;
 - Innovative methods for the design and the risk analysis of medical devices
- ICT for trust and confidence: identity management; authentication and authorization; privacy enhancing technologies; rights and asset management; protection against cyber threats.

Future and Emerging Technologies: to support research at the frontier of knowledge in core ICTs and in their combination with other relevant areas and disciplines; to nurture novel ideas and radically new uses and to explore new options in ICT research roadmaps.

- Measure human emotions and affection
- The grand challenges toward the Virtual Physiological Human
- Predicting tissue adaptation and healing

Nanosciences, nanotechnologies, materials and new production technologies

Nanosciences, nanotechnologies

- Generating new knowledge on interface and size-dependent phenomena; nano-scale control of material properties for new applications; integration of technologies at the nano-scale; self-assembling properties; nano-motors; nano-machines and nano-systems; impact on human safety; health and the environment; metrology, nomenclature and standards; exploration of new concepts and approaches for sectoral applications.
 - Food safety technology (e.g. packaging, sensing)
 - Connecting nano to macro: predicting macroscopic effects of molecular and tissue-level modifications on the biomechanical properties of living tissues

Materials

- Generating new knowledge on high performance materials for new products and processes; knowledge-based materials with tailored properties; integration of nano-molecular-micro levels in the chemical technology and materials processing industries; new nano-materials, bio-materials and hybrid materials, including design and control of their processing.

- Tools and methods to design micro-manufactured biomaterials (e.g. morphology optimisation of micro-manufactured synthetic materials mimicking the microstructure of bone tissue, vessels and skin)
- Biomimetics: Biocompatibility of magnetic nanostructures for molecular diagnostic and therapy
- Nano-bio: development of neuronal interfaces
- Smart textiles for wound care

New Production

- Creating conditions and assets for knowledge-intensive production; development of new engineering concepts exploiting the convergence of technologies (e.g. nano,bio,info,cognitive and their engineering requirements) for the next generation of high value-added products and services, and adaptation to the changing needs.

Integration of technologies for industrial applications

- Integrating new knowledge and technologies an nano, materials and production in sectoral and cross sectoral applications such as : health, construction, transport, energy, chemistry, environment, textiles, and clothing, pulp and paper, mechanical engineering.
 - Medical device design and production
 - Intelligent medical devices that collect environmental information using nano-sensors, adapt through nano-actuators, and communicate with the patient information system.