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Anticipating scientific and technological needs

NEST

New and Emerging Science and Technology

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Synthetic Biology

2003/4-NEST-PATHFINDER INITIATIVES

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This document complements the NEST 2003 work programme, by providing more detailed guidance to those who may wish to submit proposals on the above PATHFINDER initiative.

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Please note that there is a National Contact Point (NCP) for NEST in your country who can offer personalized services. The mission of NEST NCPs is to inform, advice and support potential applicants in the preparation, submission and follow-up of NEST proposals.
For contact details: http://www.cordis.lu/nest/ncp.htm

1. RATIONALE FOR THE INITIATIVE

"Synthetic biology" is a recently-coined term that is gaining currency within the scientific community. At present, it represents a vision, rather than a reality, but a vision that seems increasingly attainable in the coming decades, on the basis of rapid advances that are being made in cell and molecular biology, genetics and associated fields, as well as in computational sciences.

The core of this vision is that, by drawing on knowledge developed in biology, and adapting engineering design and production principles that have been developed in the Information and Communication Technology (ICT) arena, it is possible now to set off the creation of essentially artificial (i.e. "synthetic") systems using biological engineering design principles with unprecedented power and efficiency. These systems will be intended for diverse uses throughout the economy, in areas such as health, energy, environment or materials.

The vision is attractive from the scientific and technological perspective. Today, it is impossible to predict precisely what kind of systems will be ultimately developed. However, it is possible to imagine that they could combine levels of complexity, versatility, efficiency and "intelligence" which will go far beyond those of existing technological capabilities, with design and fabrication practices integrating the principles of existing technological systems, as in the ICT field (design and building of systems "to order", based on standard components and interfaces, with continually upgraded device technologies, using programmable "bio-fab" plants). These new technological advances will in addition help to achieve new scientific understanding.

Synthetic biology is a very recent field of research. Only a small number of research centres, mainly outside Europe, explicitly use the term "synthetic biology" to describe their work. However, this area is also of enormous strategic and economic significance, representing an arena in which open and public scientific knowledge will be progressively embedded in technological and engineering "solutions", with vast implications for the ownership and control of intellectual property, and for economic development more broadly.

The objective of this PATHFINDER initiative is to encourage across Europe a comparable sense of engagement with the possibilities of synthetic biology. Europe has a vital and dynamic tradition of research in molecular biology, genetics, mathematics, and other disciplines which form the foundations for synthetic biology. This initiative intends to promote the translation of these capabilities into technological and engineering opportunities and achievements, which are as exciting in terms of their contribution to future science as they are important from the strategic and commercial perspective.

2. THE TECHNOLOGY VISION AND ITS RELATION TO CURRENT SCIENCE

The concept of synthetic biology as a *"technological system"* follows a closely similar logic to the scientific agenda for "***systems*** biology". Indeed, the parallels are so close that synthetic biology can be considered as the technological counterpart to the emerging science of systems biology.

The key idea is that of a **"hierarchical module-based" approach**, which views sub-cellular biology as a system of interacting modules with particular functions (protein or protein-DNA clusters, signalling pathways, transport mechanisms, energy production modules and components, organelles, cell metabolism). Evidence to date suggests that these basic modules are relatively small in number and broadly similar in basic characteristics across different organisms, although with substantial variation in their specifics.

- From the ***scientific*** (systems biology) perspective, this approach is attractive because it provides tools for a level of analysis enabling us to understand cells as systems in a way that is not possible at the molecular level. It implies a scientific agenda of identifying and cataloguing the various module types within and across organisms, investigating the workings of individual modules and their interactions, and building a global picture in terms of a hierarchical structure of processes and interactions at different levels.

- From the ***technological*** (synthetic biology) perspective, the module-based approach holds out the promise of using these sub-cellular modules in different combinations and for different purposes than those of "natural" systems. It suggests the long-term vision of developing a new area in which engineered modules will be used as versatile "building blocks", with standardised functionality and interfaces, in the form of a technological system not unlike that of electronics/ICT today.

Thus, synthetic biology is envisaged as a technological endeavour that, for its success, will imply the creation of fully interdisciplinary networks of expertise in Europe, interfacing science and engineering.

From the above, it seems clear that the pursuit of this technological vision should make a vital contribution to scientific quantitative and qualitative understanding, by developing and testing the "laws" of biological design through "forward engineering". More crucially, it is also of significant interest to Europe from the perspective of future economic and social benefit.

3. ORGANISATION OF THE INITIATIVE

NEST has limited resources dedicated to early stage funding of emerging research areas. The organization of this initiative reflects these parameters. It will involve:

- A series of research projects (using the STREP instrument – specific targeted research projects), aiming to develop and demonstrate the technologies for synthetic biology.

- A networking action (using the CA instrument - co-ordination action), with the function of developing a wider European "community of knowledge" in the area of synthetic biology, exchanging knowledge and experience and promoting a wider understanding of the prospects for synthetic biology, within the perspective of the strategic, technological and economic importance of this discipline for Europe.

In its management role, the Commission, for its part, will work towards the development of institutional co-ordination between this initiative and other areas of research and support, within the context of the European Research Area.

4. WHAT KIND OF RESEARCH WILL BE PURSUED?

As specified in the work programme, the research projects will be oriented towards design and engineering of new biology-based systems and processes with substantially different characteristics and performance from natural systems, and with real applications in mind.

The research will draw from ongoing theoretical and experimental work in systems biology and other relevant fields, such as computational biology, genetics, protein engineering, bio-mimetic chemistry, structural biology, biophysics and biochemistry.
Although the field is at a very early stage of development, projects should address a variety of different challenges and opportunities for technology development. The projects selected will be ambitious "beacon projects" which, by seeking to develop technological opportunities at the limits of scientific understanding, expand the knowledge base in significant ways.

These projects should be clearly directed towards ***technological*** objectives, and should share a common strategic perspective on what constitutes the "technology system" of synthetic biology, as described above. Despite their different specific orientations, the projects funded are expected to contribute to achieving the vision of synthetic biology in a coherent way.

Within these parameters, and bearing in mind the current state of knowledge, it is expected that projects will work on a variety of existing model systems, and that they will focus on different aspects of the technology system, while following the "module-based" philosophy.

Projects should, as a general rule, aim to arrive at practical demonstrations of "generic functionality" of components and systems, by integrating design and engineering methods. This may involve scientific work to infer broadly-applicable design principles for biology-based systems, to validate them in a general way, as well as work aimed at developing engineering methods to apply them. Projects should preferably address at least one of, among other, the following aspects:

- Engineered functional building blocks: (sub-cellular "modules", biosynthetic pathways, molecular machinery, signalling pathways, transport mechanisms etc.) using biological processes to achieve substantially new functionality.
- Interfaces and components: These could include modifications of input-output processes and hierarchical interactions between different subcellular building blocks or engineered subcellular elements (eg synthetic chromosomes, engineered signalling pathways, transport modules…) that should make possible the development of procedures enabling specific modules to be added or subtracted from cellular systems.
- Working platforms: These could include "optimized" organisms for synthetic biology applications (i.e. to maximise efficiency of the engineered system, minimize "maintenance and housekeeping" requirements, or provide particular characteristics of robustness or environmental compatibility, etc.) or non-living carrier systems for biology-based engineering.

- Control, regulatory, and communication systems: These could include genetic regulatory circuits, enabling particular sub-cellular processes to be brought on or off-stream, feedback mechanisms within individual components and modules to regulate their behaviour or communication methods.

Safety and security technologies (including containment technologies) and production methods might also be considered as project objectives. However, although design tools (computational analysis, methods for functional protein design, systems modelling…) are expected to be an intrinsic element and an important outcome of projects, they are not expected to be the central objective of specific research under this initiative.

The real-life applicability of technologies for synthetic biology is an important dimension of projects to be funded. For this reason, it is expected that projects will have novel and specific applications in mind. These could include, but are not limited to:

- Energy production (photosynthesis, hydrogen production).
- Biochemical synthesis, eg production of materials such as natural polymers, engineering materials, bioactive substances…).
- Communication systems.
- Sensing processes (eg "biological sentinels").
- Intelligent therapeutic agents.

For these reasons, projects should also be concerned with "practical engineering issues" such as quality, efficiency, sensitivity and robustness factors, and "usability" more broadly.

Partnerships must gather all the relevant disciplines necessary to carry out the research.

International co-operation (partners outside the EU and associated states) are welcomed. However, it should be noted that partners from countries with highly developed Science/Technology capabilities (US, Japan, Canada, Australia…) will normally not be able to receive funds from NEST.

5. WHAT KIND OF RESEARCH WILL NOT BE PURSUED?

In accordance with NEST mandate and the work programme, this initiative will not support research of limited interdisciplinary nature, or of limited long-term scientific impact. Furthermore, the project objectives should lie outside the existing Thematic Priorities of the Framework Programme.
Specific examples of areas excluded are:

- Research related to Artificial Life.
- Research whose main focus is computational or biomimetic chemistry or other areas of basic science.
- Research on functional genomics and proteomics, single-component genetic engineering and classical biotechnology.
- Research on structural biology and systems biology mainly aimed at the generation of basic knowledge.
- Research on tissue engineering.
- Research on artificial organs and bionics implants.

6. WHAT IS THE FUNCTION OF THE CO-ORDINATION ACTION?

The role of the co-ordination action (CA)[1] is to provide broader networking of the research community in Europe in relevant fields around the theme of synthetic biology, in order to create a "community of knowledge" with a common perspective on the development and goals of the discipline.

Creating a forum for the development and exchange of ideas, on a cross-disciplinary basis, is core to the networking approach. The work programme specifies that the CA should also address issues such as the intellectual and material infrastructure requirements of synthetic biology, perspectives and strategies for innovation and industrial translation, including intellectual property, and analysis of the issues related to societal acceptance, including ethical, safety and regulatory aspects, giving the enormous potential of this new technology.

The CA instrument may involve various different types of activity, including meetings, seminars, studies, exchanges of personnel, among others. Thus, depending on the proposals submitted, the strategy adopted and the specific work it carries out could be configured in a number of different ways. It could have a role in the co-ordination of research projects funded under this PATHFINDER initiative. It could organise think tanks, feasibility studies, interdisciplinary dialogue and interchange, seminar series on key topics etc.

The CA also provides the research community with a means to generate ideas for further development of synthetic biology within the institutional environment of the European Research Area, including European and other programmes for training, mobility, infrastructure development, etc.

7. PRESENTATION OF PROPOSALS

Proposals will be presented as individual FULL PROPOSALS for research projects (STREPs) or co-ordination actions (CAs), to meet the deadline 14 April 2004. They will be evaluated individually, according to the standard FP6 evaluation criteria for these instruments. A guide for proposers, and guidance notes for proposal evaluation will be published on the NEST web-site.

A pre-proposal check service will be provided up to three weeks before the deadline. This will enable brief feedback to be given to proposers, in order to help them judge the relevance of their proposals. This service is to assist proposers; it does not contribute to the official independent evaluation (peer review) of proposals, once they are submitted. It is left at the discretion of the proposers at what point during the assembly of the proposal they judge it convenient to make use of this service.

[1] The possibility of more than one co-ordination action might be considered if there are compelling reasons for this.

Proposers are encouraged to be concise and address the specific evaluation criteria in their proposals:

- **Relevance:** it should be shown how the proposal meets the requirements set out above, including ambitious goals and the broader spirit of the PATHFINDER initiative on synthetic biology.

- **Excellence:** the rationale (design principles) should be clearly set out, and the feasibility of the methodology, including genetic manipulations, clearly explained. The research should be presented in the context of an assessment of the current state of the art, demonstrating the specific advances that are to be sought and the extent to which these extend the state of the art.

- **Impact:** the shot-time outcome and generic applicability of the work, as well as its broader scientific impact, should be justified in relation to an ultimate "technological system" for synthetic biology.

- **Consortium:** The required full range of competences necessary to perform and integrate the proposed research should be demonstrated.

- **Financial aspects:** the requirements for, and the use of, funds should be sufficiently detailed for the independent evaluators to assess the feasibility and cost-effectiveness of the use of resources (personnel and equipment). Project lifespan should not exceed 3-4 years, and a community grant of €2 million.

- **Management:** A clear plan for the conduct of the work, including an assessment of risks and a risk management plan, is required. In addition, any relevant safety concerns (i.e. possible risks to human health or environment in the case of accidental release of organisms) and ethical considerations should be stated, as well as the ways these will be addressed in the course of the project.