European research infrastructures for the development of nanobiotechnologies

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Research infrastructures are essential for top-level academic and industrial research activities. Throughout the successive framework programmes (FPs) of the EU, actions have been gradually developed to support researchers in accessing top-level European research infrastructures located outside their own country and also to better coordinate and integrate these infrastructures Europe-wide, enabling better research services. At the same time, research infrastructures pave the way for the development of scientific and technological advances. Under the sixth Framework Programme (FP6; 2002–2006), for example, nanobiotechnologies have benefited from these European actions through three approaches: the support of multi-disciplinary pan-European infrastructures; the support of pan-European infrastructures dedicated to biology but with usage in multiple domains of biology; and the funding of integrated centers for nanobiotechnologies. The seventh Framework Programme (FP7; 2007–2013) will reinforce these actions toward research infrastructures, with particular attention to the emergence of new ones as well as to the provision of important strategic research services in fields such as nanobiotechnologies.

Introduction

Research infrastructures are defined as major instruments, installations or facilities that provide services to support the work of researchers [1–4]. They are essential tools for the development of leading-edge research in scientific and technological fields as well as for knowledge transmission and exchanges, and knowledge preservation [3].

As a concept, European research infrastructure has developed from the physical sciences (the CERN particle physics laboratory was created some 50 years ago; http://user.web.cern.ch/User/Welcome.asp) to now encompass the environmental sciences, the biomedical sciences, the social sciences and humanities, as well as the virtual world of high-performance communication networks and high-capacity computing.

With the spread of molecular biology to almost every research laboratory, and the refinement of imaging tools at all scales, research infrastructures have become important tools for researchers in the life sciences during the past 15 years. They take various forms, and are not necessarily large-scale facilities [5], for example, they can be repositories of samples, databases, high-power computers, animal archives, large instruments (e.g. for structure determination) or integrated arrays of small research installations.

Also, nanotechnologies [6,7] have opened new fields of scientific development – for biology and health in particular [8]. Nanotechnologies, nanotechnology tools applied to the life sciences, and related research infrastructures have recently developed from production and control technologies at the nanoscale (e.g. for metallic or ceramic materials) to now encompass the biological materials and the biological domain.

Why are research infrastructures important?

Research infrastructures are at the crossroads between research, innovation and education, and they are, indeed, essential for developing first-class research activities. Because of their ability to assemble a 'critical mass' of people and investment, they contribute to the development of multidisciplinary approaches to solve increasingly complex problems, such as those occurring in biology and biomedical fields.

Research infrastructures also have an outstanding role in building the interface between science and industry; they are increasingly used by companies that are basing their development and innovation initiatives on new knowledge, new models and new discoveries (http://www.jnanobiotechnology.com/home/).

The development of new chemical or biological processes are, for example, largely based on the efficient use of new high-power computers and large scientific databases; furthermore, the development of new drugs relies on the understanding and modeling of new materials and molecules through the use of synchrotrons or neutron sources. Technologies for further improving research infrastructures often lead to spin-off products and/or start-up companies. Indeed, the landscape of Europe shows that in the places where large-scale research infrastructures are sited, often, 'technology clusters' of associated industry or so-called technology parks can be found. Such 'science parks' offer better possibilities for interdisciplinary research work as well as attracting high-tech firms, notably in the biomedical field [9,10].

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Research infrastructures are essential investments in knowledge-generating tools, which stimulate young people to embrace a scientific career, meaning the number of pupils studying science in Europe, either at school or university, grows.

Why a European approach?

It is a fact that for years research infrastructures have been funded largely by the countries themselves. European Member States have also supported the setting-up of inter-governmental organizations such as CERN, EMBL (http://www.embl-heidelberg.de/) and the European Synchrotron Radiation Facility (ESRF; http://www.esrf.eu/). Today, although some countries make substantial investments in research infrastructures, none of them can provide all of the required state-of-the-art research services on a national basis. In the less research-intensive countries, the high investment and operation costs, and the small local demand, do not permit the building and operation of needed research facilities.

Today, a European Community (EC) effort is needed to foster the building of capacities in Europe, as well as to spread their excellence. One of the key aspects of a such an approach to research infrastructures is to stimulate initiatives that benefit Europe by attracting the best scientists; by avoiding unnecessary overlaps; by enabling the development of standardized knowledge; by helping to generate economies of scale; and by generating greater efficiency of funds, critical mass, and higher visibility (Commissioner Potočnik's speech during the 3rd European Conference on Research Infrastructures: http://www.nottingham.ac.uk/ecriuk/).

Another goal of EC actions is to stimulate the emergence of new management approaches towards infrastructures. Too many of them have difficulties in opening themselves to the competition that is growing in the research business. Indeed, if an industrial company can be defined as an organization creating wealth, then research infrastructures are part of the knowledge industry of tomorrow. Consequently, organizational structures have to develop, possibly growing from national- and public-based bodies to international and public–private-based organizations.

The research community, particularly in the life sciences, recognizes the need to organize itself to generate the political support required for the needed European-scale research infrastructures to become a reality (ELSF: http://www.elsf.org/research_infrastructures.html).

What form do the European actions take?

An EC policy to support research infrastructures has, therefore, been successfully developed throughout consecutive framework programmes (FPs; Box 1) by financing the access of researchers to key facilities and the networking of infrastructures, including joint research projects to improve their performance. Although these were mainly based on national efforts, the emergence of new research infrastructures has also begun to be supported under the latest program, FP6, and will be continued under FP7.

Despite starting with humble beginnings in FP2, the framework programs of the EC have gradually increased their support to research infrastructures, up to some €730 million under FP6. Today, 300 or so existing research infrastructures of pan-European interest are being virtually integrated, to boost their capacity and performance (http://cordis.europa.eu/fp7/infrastructures/). Through this support, >4000 European researchers benefit annually by gaining direct access to facilities located outside their own country, and several millions by gaining internet access to pan-European scientific databases.

Box 1. The framework programme

Since the early 1980s, the European Union has developed a community, multi-annual framework programme for research and technological development, according to the Article 166 of the Treaty of European Union, and six framework programmes have been run since 1984 (http://cordis.europa.eu/infrastructures/). The seventh started in January 2007 and will last up to 2013, with approximately €50 billion of financial resources.

What research infrastructures exist for nanobiotechnologies?

The first EC approach is to support large and unique pan-European infrastructures as essential tools for a large spectrum of scientists, including biologists. Today, in laser facilities, synchrotrons, or neutron source facilities, for example, mathematicians, physicists, chemists, biologists, computing experts, engineers and material scientists work together and offer the highest quality of services to research teams working in all scientific fields. Under FP6, the European Commission is providing financial support (>€60 million for the past four years) to a series of such key analytical and multi-disciplinary research infrastructures, for offering access to researchers and for coordinating their current activities and future technological developments. Neutron sources, synchrotron radiation sources and lasers will soon be able to picture phenomena such as chemical reactions occurring at the picosecond. An essential asset of these infrastructures is that they enable scientists, particularly nanobiotechnologies, to undertake and resolve complex problems as part of inter-disciplinary teams and through personal interactions with researchers coming from different countries.

The second approach is to support pan-European research infrastructures dedicated to biology, but with usage in multiple domains of biology. An important boost to this was given under FP6, to develop instrumentation for resolving protein structure; these infrastructures efficiently complemented the genomics and proteomics projects funded under the FP6 health theme. Besides support to the above-mentioned, large multi-disciplinary installations, seven FP6 contracts, with a total EC contribution of €20 million, are providing access to major European instruments dedicated to the resolution of protein structure on the basis of NMR, X-ray crystallography, small-angle X-ray scattering, neutron crystallography and electron microscopy technologies. An interesting example is the Centre for Integrated Structural Biology project, in Grenoble (CISB; http://www.ibs.fr/content/ibs/presentation/psb); this combines the resources of the European Molecular Biology Laboratory (EMBL; http://www.embl-heidelberg.de/), the European Synchrotron Radiation Facility (http://www.esrf.eu/), the Institut Laue-Langevin (http://www.ill.fr/) and Grenoble

University (http://www.grenoble-universites.fr/90633135/1/fiche___pagelibre/). A new laboratory complex was built, with new technical platforms for high-throughput protein expression and crystallization, protein sample quality control, *in vivo* isotope labeling, high-throughput X-ray crystallographic data collection, neutron crystallography and electron microscopy. A crucial asset of this new infrastructure is that the combination of the various technologies should stimulate research across the domains of structural biology, with a special focus on virology.

Also of great relevance is the development of and access to protein ligands. These can, indeed, pave the way to *in vivo* imaging, *in vivo* diagnostics and drug development and therapeutics, with huge benefits for healthcare. The European Commission is funding a promising FP6 project, ProteomeBinders (http://www.proteomebinders.org/), which aims to coordinate the existing repositories. The project will, indeed, equip the bases for a comprehensive, characterized and standardized collection of specific ligand-binding reagents, including antibodies, as well as novel protein scaffolds and nucleic acid aptamers. Such a project should lead, within a few years, to the establishment of a unique but distributed EU resource infrastructure that is accessible to all European biologists.

Last, but not least, is the strong support given to bioinformatics through five FP6 contracts, with a total EC contribution of €22 million. Life sciences generate a vast array of data, from molecules to systems, for example, nucleotide sequences, gene expression profiles, protein sequences, structural data, protein interactions and brain images. It is essential to collect, archive and curate these data because a few hours of computer work, comparing sequences, expression and other profiles, can cut years of laboratory work. The funded databases will have an extremely broad range of users, from academic scientists to industry, in all domains of biology (e.g. FP6 Felics project; http://www.felics.org/page.php?page=home).

A third Community approach is to support the development of integrated centers specifically for nanobiotechnologies. Nanobiotechnologies require equipment and installations that are not only unique and costly but also complementary and medium-size. An example of this approach is the Bio-Nanotechnology European Infrastructure under construction in AREA Science Park (BINASP), near Trieste, Italy (http://www.binasp.net/). With a EC contribution of €1.9 million, the pan-European goal of the BINASP project is to set a platform that is open to users with a special interest in cardiovascular medicine, molecular oncology and neuroscience. The infrastructure will consist of a coherent set of instrumentation for micro- and nanobiology: a microscopy and nanoscopy unit, atomic force microscopy, scanning near-field optical microscopy and Raman microscopy facilities, a unit for molecular imaging of live experimental animals, a system for the fabrication of nanovectors and nanostructures, and an animal house.

The vision and strategic research agenda recently published by the Nanomedicine European Technology Platform [8,11] outlines the need for such infrastructures to be integrated poles of excellence for nanobiotechnology, with complementary expertise that is open to a large number of scientists, from public and private partners, to support their experiments and also to train them on these new technologies. The strategic agenda published after an extensive and broad consultation within the scientific community stresses the need for each centre to be, in some way specialized, to prevent duplications and fragmentation and to constitute nodes of a European network [11]. Besides their European objectives, and in coherence with the ongoing preparation of the European Institute of Nanobiotechnologies (EIN; http://www.nano2life.de/), these infrastructures should also have a regional policy for supporting the regional development of nanobiotechnology clusters.

The future of European actions

The future looks positive for the research infrastructures in Europe. Today, research infrastructures are considered a key element for capacity building in most European Member States and at the Union level. They have been recognized by the European Council as important milestones in the discovery of new knowledge as well as in the transfer of this knowledge towards industry and society. For this reason, the EC [2] will continue to support existing infrastructures and will also increase support for the emergence of new research infrastructures, which the scientific community needs in the next 20 years. To attain the objective of developing new pan-European research infrastructures (or major upgrades), two stages are clearly required: the identification of the needs of the scientific community, for which the role of a forum such as ESFRI is essential (Box 2); and clear public support for the implementation of these projects.

ESFRI has begun its work in developing the first European roadmap for new research infrastructures (or major upgrade) for the next 10 to 20 years. The first version of the roadmap was published on 19 October 2006 [3], with updates to follow: this is an ongoing process. The different projects have been reviewed according to two main criteria: the scientific case (scientific impact and pan-European character); and the concept case (technical feasibility and political support). Biology projects related to nanobiotechnologies that are recommended by ESFRI are the further development of bioinformatics facilities, biobanks and bio-molecular resources, and facilities for structural biology. Emerging needs have also been identified, in particular, for chemical biology and synthetic biology infrastructures.

FP7 [2] will support the development of new infrastructures on the basis of the ESFRI roadmap. To

Box 2. What is ESFRI?

A European strategy forum on research infrastructures (ESFRI; http://cordis.europa.eu/esfri/home.html) was launched in April 2002. This brings together representatives of the 25 EU Member and 7 Associated States, appointed by research ministers, and one representative of the European Commission. Its role is to jointly reflect on the development of strategic policies for pan-European research infrastructures, including the preparation of a European Roadmap (first version published in October 2006, with regular updates to come as different areas mature) and to act as an incubator for concrete projects with pan-European interest; however, it is not a decision-making body.

do this, the EC action will focus on the preparatory phase, to support the decision-making process leading to the actual construction (or major up-grade), together with all stakeholders. The preparatory phase, during which the European Commission will act as a facilitator, should help to reach a final agreement between the different funding bodies. Building on the achieved technical, legal, administrative and financial agreements, using the complementarity between national and EC instruments (such as the Structural Funds [http://www.eugrants.org/] or the European Investment Bank [EIB; http://www.eib.org/]), the construction plans will then be implemented, with possible EC financial support, whenever it is essential for the success of the project.

An optimal approach for nanobiotechnologies

Under FP6 and FP7, the actions for research infrastructures are clearly multidisciplinary and, thus, a good place to cover some of the needs for analytical facilities and for nanobiotechnologies. However, an obvious challenge will be to ensure a good and improved coherence with the other diverse actions and themes of FP7. A second challenge for the EC will be to offer a more favorable and reactive environment for emerging scientific fields. The new development of targeted topics under the FP7 Research Infrastructures action (one of the FP7 topics to be published is dedicated to nanobiotechnology infrastructures, in particular for simulation, design and control of biomaterial structure and reactions at nano level) should hopefully help in achieving this. Finally, the ESFRI-based process is new in the European landscape and, as such, there clearly exists some room for improvements, with the challenge of ensuring strong support from the scientific community [5] (http://www.elsf.org/research_infrastructures.html).

Today, research in nanobiotechnology is emerging, research teams are gathering their resources and ideas, and the current knowledge development necessitates laboratory work based on the efficient coordination at a broad scale and on multidisciplinary or biology (at large) research infrastructures. However, the emergence of integrated centers for nanobiotechnologies seems to now also be required; soon, the time might come for developing dedicated research infrastructures for nanobiotechnologies spanning the entire European research area.

References

1 Decision No 1513/2002/EC of the European Parliament and of the Council of 27 June 2002 concerning the Sixth Framework Programme of the European Community for research, technological development and demonstration activities, contributing to the creation of the European Research Area and to innovation (2002 to 2006), *Official Journal of the European Union* L 232/1–33 (http://eur-lex.europa.eu/LexUriServ/site/en/oj/2002/l_232/l_23220020829en00010033.pdf)

2 Decision No 1982/2006/EC of the European Parliament and of the Council of 18 December 2006 concerning the Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007–2013), *Official Journal of the European Union* L 412/1–41 (http://eur-lex.europa.eu/LexUriServ/site/en/oj/2006/l_412/l_41220061230en00010041.pdf)

3 European Strategy Forum on Research Infrastructures. *European Roadmap for Research Infrastructures Report 2006*, EU Publications Unit (ftp://ftp.cordis.europa.eu/pub/esfri/docs/esfri-roadmap-report-26092006_en.pdf)

4 Danish Council for Strategic Research (2005) *Future Research Infrastructures – Needs Survey and Strategy Proposal,* Danish Research Agency In: http://www.forskningsinfrastruktur.dk/FUTURE%20RESEARCH.pdf)

5 Gannon, F. (2006) Life science infrastructures are different. *EMBO Rep.* 7, 347

6 Nanotechnology Communication (2004) Communication from the Commission – towards a European strategy for nanotechnology. *COM* 338, EU Publications Office (ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/nano_com_en_new.pdf)

7 Communication from the Commission to the Council, the European Parliament and the Economic and Social Committee (2005). Nanosciences and nanotechnologies: An action plan for Europe 2005–2009. *COM* 243, EU Publications Office (ftp://ftp.cordis.europa.eu/ pub/nanotechnology/docs/action_plan_brochure.pdf)

8 European Technology Platform on NanoMedicine. Nanotechnology for Health (2005). *Vision Paper and Strategic Research Agenda for NanoMedicine*, EU Publications Office (ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/nanomedicine_visionpaper.pdf)

9 Federal Ministry of Education and Research (2006) *BioRegions in Germany. Strong impulses for the national technological development* (2006). Federal Ministry of Education and Research (BMBF) Publications and Website Division (http://www.bmbf.de/pub/bioregions_in_germany_en.pdf)

10 Report of a team led by Lord Sainsbury, Minister for Science (1999) *Biotechnology Clusters*, Department of Trade and Industry (http://www.dti.gov.uk/files/file28706.pdf)

11 European Technology Platform on NanoMedicine. Nanotechnology for Health (2006) *Strategic Research Agenda for Nanomedicine,* EU Publications Office (ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/nanomedicine_bat_en.pdf)