POLICY FORUM: EUROPEAN POLICY

Interesting Times—Biology, European Science, and EMBL

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These are exciting times for biological research; they are also challenging for European science. Access to the total genome sequences of several organisms will lead biology to previously unimaginable insights, as these sequences are analyzed using bioinformatics and both established and novel experimental methods. In Europe, scientists and policy-makers now perceive significant problems: a serious gap in resources for critical areas of biology relative to other industrialized countries, and a lack of coherent policies that are needed to maximize the total impact of our diverse national and international efforts. This is the dual context within which the European Molecular Biology Laboratory (EMBL) has developed recently its scientific program for the next 5 years (*1*), and is preparing the associated budget.

In summary, the laboratory will be addressing the challenge of the times by focusing on functional genomics as its central theme, based on our combined strength in experimental biology, bioinformatics and technology development. Despite its strong reputation, EMBL is an institution of modest size, and has been underfunded in the last decade. The scientific plans will require budgetary increases that will be reasonable in absolute figures, given the present core budget of approximately 45 million euros (US$44 million). Our existing Units (the Research Programs in the main laboratory in Heidelberg and in Monterotondo) and the Outstations in Grenoble, Hamburg, and Hinxton (European Bioinformatics Institute, EBI) are the essential foundations for these plans, and must be reinforced. A major part of the planned growth is to build up the EBI as a world center in bioinformatics. To bolster our strength in mouse biology, Monterotondo will need to double in size to six research groups to achieve critical mass. Thematic initiatives across the Units will capitalize on our interdisciplinarity, for which adequate resources in Heidelberg are vital. At the structural biology Outstations, we will need to invest in equipment upgrades and staff for the x-ray beam lines that are very much in demand. Finally, we intend to build on our extensive collaborations across Europe, offering new opportunities for institutional partnerships.

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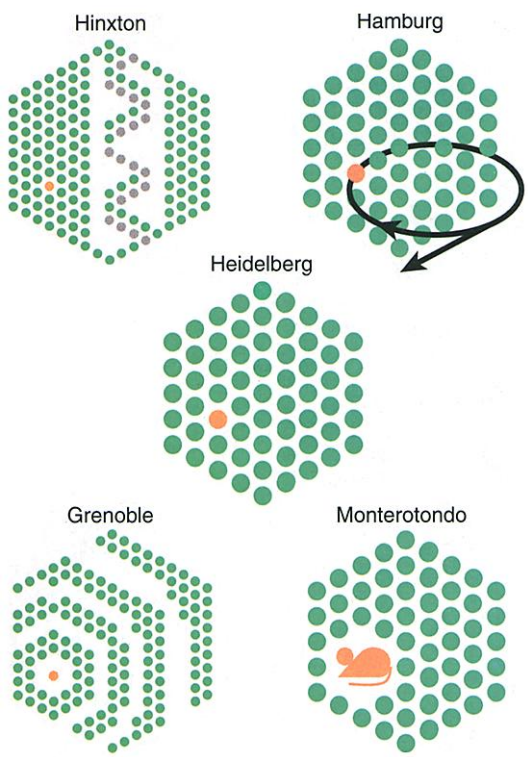
The EMBL Profile

Our central mission is to promote the development of molecular biology throughout Europe: to foster leading-edge research that opens up new fields, to develop new techniques and instrumentation, and to provide advanced training and services to the scientific community. This complex mission is supported by activities and policies that give EMBL a unique profile. Appointments are made strictly on merit, not by national quotas. Yet, by inclusive recruitment, EMBL is the most international institution in biology worldwide, with no single nationality predominating. Our scientists come from engineering, informatics, and diverse physical and biomedical sciences, permitting interdisciplinary innovation. Staff contracts are for fixed terms, up to 9 years, with rare exceptions for continuity. As a result of high turnover, the laboratory is extremely youthful and flexible, evolves rapidly, stays current, and avoids rigid borders between its Units.



Logos of EMBL Units

Our research landmarks include systematic genetic analysis of embryonic development in *Drosophila*; molecular cell biology of membrane traffic; elucidation of RNA maturation, transport, and translational control; introduction of biocomputing and bioinformatics in Europe; and development of enabling technologies such as the use of synchrotron radiation in biology, cryoelectron microscopy, advanced light microscopy, and mass spectrometry for protein identification. Often, collaboration between instrumentation developers and experimental biologists has proved crucial to success. Major, widely appreciated services are offered at synchrotron beam lines for structural biology in Hamburg and Grenoble, and through global bioinformatic resources at the EBI. Smaller, but valuable, infrastructures also serve visitors in Heidelberg.

The EMBL has an unparalleled record of advanced training and research networking in Europe. When our scientific alumni leave EMBL, they carry with them its standards, contacts, and international collaborative outlook. Out of more than 1500 to date, three-quarters work in and benefit the member states, often in leading positions. In addition, nearly 2000 visitors participate in research projects annually; establish collaborations; are trained in specific methods; or attend up to 25 practical courses, workshops, and conferences. EMBL is the European equivalent of the Cold Spring Harbor Laboratory in the United States.

In the last decade, the EMBL international Ph.D. program has grown to a steady state of 170 students, selected from a large and diverse pool of applicants. Their studies begin with an intensive core course program in Heidelberg, followed by supervised research at any EMBL site. This leads to a degree that is granted by national Universities, EMBL itself, or, jointly, under agreements negotiated between EMBL and national institutions.

The Scientific Context and the Plans

In the second half of the 20th century, the biological research community embarked on one of the greatest scientific revolutions of all times. For the first time in history, we are beginning to understand the fundamental nature of life itself—a subject

at least as interesting as the nature of the cosmos or the ultimate composition of matter. This revolution continues to accelerate, underpinning a technological revolution in medicine, agriculture, and the biotechnology industry. Biology is becoming less reductionist and more integrative, as it seeks to understand the logic of complex living systems in molecular terms. The evolutionary unity of life at the molecular level has become evident, greatly facilitating the transfer of knowledge from tractable model organisms to complex species including humans. Novel methods, equipment, and large-scale facilities, both physical (for example, synchrotrons) and electronic (interconnected global databases), are now crucial, as biology becomes "big science."

Adjusting to these changes, the blueprint for EMBL in 2001–2005 envisages a judicious combination of organizational stability and programmatic ferment. It grows out of current strengths while setting new directions, with functional genomics as a central theme.

By next year, numerous microbial and several multicellular genomes, including the human, will have been deciphered. Biology will be faced with an enormous challenge: understanding how the information of the entire genome affects the biology of the organism. Molecular analysis is clearly required to understand higher levels of biological organization, but the converse is also true: the biology of the molecules of life can only be understood in the context of functioning cells and organisms. EMBL is in a favorable position in this new era, precisely because of its strength in basic research at interconnected levels (molecular structures, gene expression, cell and developmental biology), coupled with bioinformatics and instrumentation development. In the next 5 years it will be vital to safeguard this strength in our evolving Units, while using our flexibility from turnover and relying on our unique collaborative culture, to build interunit initiatives that cut across traditional disciplines.

Initiatives targeted on bioinformatics, genomics, and proteomics aim to integrate technology development for global analysis with challenging fundamental problems of experimental biology. An initiative on molecular interactions, based on the emerging realization that multimolecular machines are the key mediators of biological function, will develop methods for isolation and characterization of functional macromolecular complexes in cells and developing organisms. An initiative on the intracellular RNA world will focus on post-transcriptional gene expression as a mechanistically integrated process of RNA remodeling. Another initiative seeks to combine quantitative experimental analysis with new inputs from chemistry and physics, as well as modeling, to elucidate the systems properties of complex biological phenomena such as morphogenesis. Finally, by cultivating interactions with medical research institutions, we aim to alert both medical researchers and our scientists to the potential medical applications of the discoveries at EMBL.

Service, advanced training, and support for visitors are well-established activities, only limited by the available resources. For the next 5 years we propose a new thrust in outreach activities: the development of locally funded bilateral partnerships with institutions in the member states. We envisage collaborations whereby EMBL would help update or set up facilities in the partner institution; temporary external sponsorship of groups at EMBL followed by relocation to the sponsoring partner institution; transient establishment of local EMBL units, which then devolve to the national system; and broader institutional affiliations, for example, for facilitating international recruitment and advisory structures or reciprocal access to facilities and sustained collaborations. The rationale is to contribute toward overcoming the fragmentation of science efforts in Europe, by promoting a cooperative network of centers of excellence.

Toward a Robust European Science Policy

Like CERN and other intergovernmental research institutions, EMBL is the legacy of the postwar vision of science on a European scale. Currently, there are three science systems in Europe: national, intergovernmental, and European Union (EU). A major challenge is how to articulate these systems properly, to create synergies, and to amplify the dynamism of the whole. The challenge is especially important for the life sciences and "e-science" because of their expected pivotal role in the 21st century. A recent experience gives cause for concern.

The EU has funded the EBI generously since its inception, through competitive grants. In November 1999, the EBI's applications under the new multiannual EU Framework V Programme were turned down for being "out of scope." The same happened to other previously EU-supported infrastructures in the life sciences, including the European Mouse Mutant Archive (EMMA). Apparently, the rules under the EU "Support for Research Infrastructures" program had changed to exclude support for the actual operation of infrastructures. The wisdom of such a decision, when biology depends ever more on robust infrastructures, was challenged vigorously (*2*, *3*). The failure to inform infrastructure operators directly, transparently, and well in advance to allow arrangements for alternative support was especially regrettable. Because of the rapid growth and strategic importance of bioinformatics, we had committed to the EBI more than half of the requested growth for all EMBL in 2001–2005. Now we have also asked our member states to fill the gap left by the EU.

Nevertheless, there is some ground for optimism. A recent European Commission document (*4*) "Towards a European research area" proposed by the new EU Commissioner for Research, P. Busquin begins: "Even more so than the century that has just finished[,] the XXI century we are now entering will be the century of science and technology....In Europe, however, the situation concerning research is worrying." Referring to an expanding gap of tens of billion euros between the research expenditures of the United States and Europe, the document moves away from the misguided orthodoxy that all is well with the European science base and that the EU should concentrate on applied research directed toward industry and "socioeconomic" objectives. It calls for a "European approach to research facilities" and seems to signal a renewed favorable attitude toward the European intergovernmental organizations. It promises that "In form as in content the Sixth Framework Programme will have to be thoroughly rethought out in the light of the project to develop the European research area."

The other powerful bodies of the EU are the Council of Ministers and the European Parliament. The successive presidents of the Council this year will be J. M. Gago (Portugal) and C. Allègre (France), influential ministers who are scientists with a European vision. The new parliament is also likely to favor European cooperation. Finally, the life sciences research community is beginning to formulate and project its views in an effective manner (*5*). This may be the year for a common effort toward a more robust European science policy. In the long run, our institutions—EMBL included—will prosper, not in isolation, but in the context of an improved climate for stronger, consistent, and coordinated support for science in Europe.

References and Notes

1. www.embl-heidelberg.de/ExternalInfo/scipro
2. *Nature* **402**, 1 (1999).
3. M. Ashburner *et al.*, *Nature* **402**, 12 (1999).
4. http://europa.eu.int/comm/research/area.html
5. http://www.elsf.org