From molecules to organisms: the molecular level

The RNA world

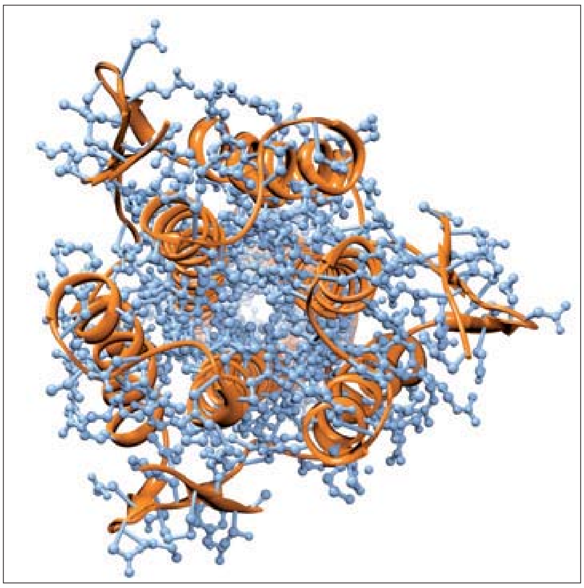
A large proportion of the genome, either in eukaryotes or prokaryotes, produces both sense and antisense transcripts. Although some recent models, such as transcriptional interference, RNA masking, RNA editing and RNA interference, have been proposed, the mechanisms underlying gene regulation by diverse sets of antisense RNA remain largely unknown. Gene regulation by endogenous small interfering RNAs (siRNAs) has been described mainly in organisms possessing RNA-dependent RNA polymerase. Although endogenous siRNAs driven from transposable elements have also been identified in mammals, the number of siRNA molecules so far identified is small. Moreover, the increasing information on the diverse biological roles of non-coding RNAs suggests that our knowledge on the information content and organisation of eukaryotic genomes is highly incomplete.

The ESF Forward Look on the RNA World – a joint activity of LESC and European Medical Research Councils (EMRC) – will be published during 2009 and will further define the most urgent research questions in the field of non-coding RNAs.

Vast research efforts are needed to refine our knowledge on how genetic information is encoded, used and transmitted. This can be performed by developing new methods of ribonucleo-proteomics on model organisms in animal, plant and marine biology. Increases in genomic data, supported by sophisticated bioinformatics approaches as well as emphasis on epigenetics and chromatin remodelling themes will also be major inputs for the future. Recent developments in DNA research, such as DNA repair, chromosome stability and related issues should not be omitted from future research efforts in life sciences. Moreover, they also have medical implications.

The protein world

In order to expand the paradigm for regulating gene transcription, protein translation, protein degradation and many other cellular processes, a better understanding of the protein world is essential. This area of research includes proteomics, structural analysis of proteins, membrane proteins, glycoproteins, protein-protein and protein-ligand complexes, as well as bioinformatics tools for the prediction of protein function. The next level of research would include detailed investigation of the identity, diversity and biological roles of metabolites in cells and organisms, employing metabolomics and metabonomics, again supported by sophisticated bioinformatics.



A model of influenza virus Hemagglutinin

The glycosylation world

If one considers DNA/RNA as the 'first language of life' and proteins as the second one, glycosylation (carbohydrate structures) can be considered as the 'third language of life'. The number of potential glycan structures is higher than the potential number of DNA, RNA or even protein structures by several orders of magnitude. Therefore, a better understanding of 'complex carbohydrates' is crucial for many fields of biology, medicine and biotechnology. Glycosylation processes or glycan structures (linked to proteins or lipids or in various free forms) are involved in a great variety of important biological processes, such as development, growth control, immune systems and host-pathogen interactions. In Europe, a strong scientific community has been developing in the various fields of glycosciences. What is needed now is a strengthening of the existing networks and better connection with other biological disciplines, including biomedical research. Within ESF, a very successful Exploratory Workshop was held on glycosciences in 2007 and a Research Networking Programme started in 2009.

From molecules to organisms: the cellular and organismal levels

Understanding evolutionary questions

More advanced genomic techniques can provide a deeper appreciation and understanding of evolutionary questions across a range of taxa. New technological developments such as association mapping are enhancing the potential of quantitative genetics, molecular paleontology and evolutionary genetics. Important research questions in the biomedical, agricultural and environmental disciplines include: What is the genetic basis for specific phenotypic traits? How can we interpret genotype-phenotype interrelationships? What is the basis for genetic diversity amongst individuals and populations? Answering these questions might now become possible due to the fast development of sequencing methods. Within ESF, a new EUROCORES Programme, *Ecological and Evolutionary Functional Genomics (EuroEEFG)*, has recently been initiated (spring 2009) and will tackle some of these questions.

Analyses of Phylogenetics and Evolution (APE)

Over the last few years, the freeware package APE for evolutionary studies, written in the R language, has become a primary tool in taxonomy. R is widely used for statistical analysis and is of interest to any biologist. APE is specifically dedicated to phylogeny, population genetics and evolution. Phylogenetic analysis covers a wide range of methods from reconstructing gene trees and estimating divergence dates, to analysing diversification. APE provides functions for reading, writing, plotting and manipulating phylogenetic trees, analysing comparative data in a phylogenetic framework, analysing diversification, computing distances from allelic and nucleotide data and reading nucleotide sequences. It includes several other advanced tools, such as the computation of minimum spanning trees or the estimation of population genetics parameters. All these diverse tasks rely heavily on computational statistics.

Until recently, most of these methods were only available in specialized software. APE provides them all in a single, free package. In taxonomy, it is important to have access to this broad range of analyses from macroevolutionary processes to population genetics, because we are looking at the genetic effects of environmental change over very long periods of time.

APE is under constant development. New methods are gradually implemented in the package and can be adapted to the need of the users. It provides a flexible framework for developing and implementing new statistical methods for the analysis of evolutionary processes and its ongoing maintenance is expected to be fruitful.

Analysing integrated reponses from molecules to behaviour

The neurosciences have developed very rapidly over the past decades. Conceptual and technological progress have occurred in neurogenetics, microscopy of living neurons, neurophysiology, neuroimmunology, *in vivo* networking analysis, brain (molecular and cellular) imaging and the study of animal behaviour (ethology). A once descriptive science has evolved fast into a quantitative biology of causal links, where dynamic processes take centre stage. The availability of neurogenomics, transgenesis in rodents, improved imaging and neurophysiological techniques have made it possible to study the neuronal system from molecules to behaviour in an integrative way. This brings new opportunities for the biological and psychological description of the brain. It improves insight into brain processes and enables, for example, medical treatments of brain-disorders to be developed. The range and amount of information that is needed to get better insight into complex neuronal processes demand an integrated international approach, and further integration of traditionally separated areas such as genetics, neurobiology, informatics, ethology, psychology, and medical sciences will be indispensible.

The contribution of systems biology

The concept of systems biology remains a challenging framework for research in various life science disciplines. Questions that need to be answered in the next decade(s) include: What can realistically be expected from systems biology, in terms of input to: basic biomolecular research; environmental research (stress responses or host-pathogen interactions, for example)? How can systems biology approaches be efficiently organised?

Applying new tools to help understand the environment

Using the new tools and techniques mentioned above to develop comprehensive and integrated studies in the traditional 'black boxes' would be a major stepping stone. Detailed studies of oceanic phyto- and zooplankton populations have, for example, been difficult so far. By combining new genomics tools – which can identify suites of genes with key functions – with cellular imaging, the diversity and function of planktonic populations can be established. This is also true for the soil ecosystem, where an integrated analysis is desperately needed. These developments provide substantial opportunities to identify organisms in previously unexplored habitats (such as the soil) and to enhance our understanding of functions, processes and conservation, at the ecosystem level.

Microbial diversity

Research using metagenomic approaches is urgently needed to explore the evolution and functional diversity of microbial communities in the soil and marine environment, and in the mammalian body.

There are more different organisms per unit of soil than in any other environment on Earth, with major differences in species composition in different places. Soils are exceptionally complex, highly dynamic systems, a result of biotic and abiotic interaction processes. Microbial populations in the soil play key roles in carbon fluxes in soils. Different functional groups, such as bacteria, degrader fungi and mycorrhizal fungi, co-exist and interact with each other. One challenge not yet resolved experimentally is to reveal the molecular mechanisms by which the physiological activities of algae, fungi, bacteria and archaea determine the nutrient stream to and from different nutrient pools, under ever changing nutrient, temperature, moisture and oxygen conditions.

Similarly, the microorganisms living in close association with the human body outnumber its own cells by about one order of magnitude. It is well known that microbial populations living in the gut and other epithelial surfaces of the mammalian body have important biological functions, such as in immunology and the digestion of food. But there is ample scope to explore our co-evolution with these organisms.

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Bacteria

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Anemone nemorosa

From populations and communities to ecosystems

While the study of ecosystem processes has been the focus of much attention over the past decade, exploration of extreme events and environments has been limited.

Studies on the possible effects of climate change on fauna and flora have increased in recent years. But one aspect that has been largely ignored is that small climate shifts result in a disproportionate increase in the number and probability of extreme climatic events, such as extreme heat, drought, storms and intense precipitation. An exceptionally hot and dry summer, such as 2003 in Europe, statistically only occurs every 9000 years, but General Circulation Models predict that by 2100 one in two summers will be comparable, or even hotter and drier. Less extreme events will obviously become more frequent too. Studies of the impact of such extremes on, for example, plant communities, are scarce. Drought tends to affect plant growth negatively, mostly because of stomatal closure and the associated reduced gas exchange. It is, however, unclear whether the same precipitation deficit has comparable effects in different seasons. Moreover, knowledge on the interaction of drought and heat waves is scarce, and responses to each of these extremes are not necessarily additive.

The study of invasive species is of high importance, because it links extreme events with climate change, ecosystem science, global trade and ecology. A number of Exploratory Workshops have already been funded by ESF in this area. Changes in community composition caused by extreme events may create opportunities for invasive alien species to establish. Climate change will also shift species' relative abilities to compete and may result in new possibilities for invasive species. Invasive species are themselves a contributing factor to global ecosystem change, additional to climate change, with international travel and trade playing a major role. Using advanced modelling techniques to assess invasibility and invasiveness, it may become possible to predict which species may threaten native and managed ecosystems, in both terrestrial and aquatic environments. Such modelling also offers potential for planning restoration and remediation.

The role of nitrogen is important in the interaction between extreme events, climate change and the rate at which ecosystems are affected. The natural abundance of useable nitrogen is low, and considerable human input is already required to produce food for the world's population. This will almost certainly increase, as will the release of nitrogen oxides into the atmosphere from fossil fuel combustion. Changes in the nitrogen cycle have already exacerbated aquatic, coastal and terrestrial eutrophication, acidification, climate change, photochemical smog, poor urban air quality and stratospheric ozone depletion, all of which have impacts on

Infrared heating systems to study the effects of climate warming on tundra ecosystems

humans and ecosystems on regional and global scales. Understanding the cascade of nitrogen in an ecological context, its effects and its interaction with other environmental concerns must be at the vanguard of the next decade's environmental research strategy.

Finally, although much attention has been given to the consequences of climate change for ecosystems, there is a dearth of information on how to manage ecosystems to mitigate global change effects and provide sustainable delivery of environmental services. There are many possibilities: using terrestrial ecosystems to sequester carbon in the soil, or to produce bioenergy, and using wetlands for water-cleaning are examples. This area of study deserves urgent and robust investigation. To understand the effects of anthropogenic pollutants on ecosystems, attention must be directed towards the rate of pollutant uptake, rather than pollutant concentration in the air, water or soil. This flux-based approach will eventually provide a deeper understanding, and permit us to assess the effects of pollution on organisms, communities and ecosystems.