Synthetic Biology: challenges ahead

This expanding scientific discipline is proving extremely popular and is attracting engineering and system design experts to the field of Biology.

As Bioinformatics and Computational Biology will be essential components of new technical and scientific developments, it is vital to follow the discussion generated by the recent ESF Exploratory Workshop (October 13–16, 2005, Constructing and de-constructing Life, Magalia, Spain) and the 2005 report of the NEST High-Level Expert Group on Synthetic Biology: Applying Engineering to Biology (http://www.eurosfaire.prd.fr/nest/documents/pdf/NEST_syntheticbiology_b5_eur21796_en.pdf).

Synthetic Biology stands at the meeting-point of two cultures. The first, represented by those interested in ‘deconstructing life’, dissects biological systems in the search for simplified and minimal forms that will help us understand the adaptation and evolution of natural processes. This approach includes experiments to obtain information on isolated parts of biological systems, the simulation of these systems and then the prediction of associated properties followed by further experimental verification. Well-known examples include work on metabolic pathways such as glycolysis (Hans Westerhoff, Free University of Amsterdam) and the simulation of cell systems using stochastic approaches (Luis Serrano, EMBL, Heidelberg). Simplified systems, based on phospholipids (Doron Lancet, Weizmann Institute, Rehovot) or polymers (Steen Rasmussen, Los Alamos National Laboratory), are used to explore possible prebiotic systems. Directly related to this activity is research into minimal forms of life and minimal genomes (Tom Knight, MIT Artificial Intelligence Laboratory). An essential part of this approach is the definition of biological systems that make modeling and simulation feasible: biodegradation networks (Alfonso Valencia, National Center of Biotechnology, Madrid), minimal genomes (Andres Moya, Instituto Cavanilles, Valencia), etc.). The development of computer viruses (Chris Adami, Santa Fe Institute) to study properties of biological evolution can also be included in this kind of research. In short, this approach focuses on the definition of material or virtual systems that help investigate the properties of complex biological problems.

The second, complementary and symmetrical culture is the ‘Construction of life’ approach. In this case, the goal is to build systems inspired by biological principles, use biological or chemical components to reproduce the behavior of live systems. Highlights of this kind of approach are the designs of Drew Endy (MIT Department of Biology) and Ron Weiss (Department Electrical Engineering Princeton University) who have started to address biological phenomena with the conceptual weaponry of electrical engineering. The general underlying notion is to combine autonomous, modular, robust and reusable components. Characteristic specimens of this sort are the input components that sense a given environment, such as interfacing with biological signals, internal components, processing of biological input information inside a synthetic system to minimize side-effects, and output components, which send the signal processed by the synthetic setup back to the endogenous biological system.

A very attractive and on-going by-product of this research is the development of a registry of Standard Biological Parts (http://parts.mit.edu), which includes lists of formed components, which, as they comply with international standards, can be easily distributed and shared. The second step will involve the combination of these components into working devices: associated research is seeking to define containers for these machines, which could range from simple lipid vesicles (Peter Walde, ETH; Albert Libchaber, the Rockefeller University) to minimal genomes (Hamilton Smith, Venter Institute).

There is a clear difference between the intellectual goals of these two fields. The ‘deconstruction’ community seeks to understand biological systems and their evolution, whereas the ‘construction’ community searches for general design principles regardless of their relationship to actual Biology. Both communities, however, hope that the exploration and/or construction of these (biological) systems will expand our understanding of the organizational principles of living molecular systems, and both are linked by their dependence on very similar theoretical, experimental and computational techniques.

This new drive towards ‘construction’ and ‘deconstruction’ of biological phenomena gives a new dimension and adds a new value to traditional research into the origin of life on Earth. Such research, now under the umbrella of Synthetic Biology, was for decades restricted to the field of the Chemistry of prebiotic systems. The body of theories and simulations on primitive, pre-cellular metabolism (Eric Smith, Santa Fe Institute) and on the transitions between living and non-living systems (Steen Rasmussen, Los Alamos National Laboratory; Norman Packard, Protolife Srl) provides a wealth of conceptual and material assets that the new field will be able to build on.

Both the ‘deconstruction’ and the ‘construction’ approach generate extremely interesting scientific and technical challenges, among which there are at least two that are likely to influence the future of Computational Biology and Bioinformatics. The first issue is how to synthesize chromosomes containing well-defined functional regions (genes) under clear controllable replication, transcription and translation conditions. This fascinating prospect will require all our skills in analyzing, predicting and designing genome elements, with many implications for genome analysis, comparative genomics and transcription regulation. The second key issue is the modulation of functional specificity. Both newly designed components and those extracted from biological systems require a clear understanding of how they adapt to specific working conditions and how the interactions that determine the properties of stability and adaptation of molecular systems could be engineered. A clear example is the design of Transcription factors able to trigger the activation of specific genes, whether these are designed rationally (Homme Hellinga, Duke University) or obtained by directed evolution (Víctor de Lorenzo, National Center of Biotechnology). Computational analysis of protein families and of protein/DNA
structures is, of course, essential for the development of these components.

Apart of the instrumental role of Bioinformatics in Synthetic Biology in the design of synthetic chromosomes and components of a desired specificity, there are interesting additional opportunities as well for the development of computational models to analyze, simulate and predict the behavior of artificial and synthetic systems, in what is a new growing field.