Contribution to FP7 Orientation paper on Complex Systems

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Biological Systems as Complex System

The problem: From Components Biochemistry to Systems Biology

The premise of the emergent discipline of Systems Biology is that, even if we knew the exact nature of each biochemical component in each cell of an organism, we would still know very little about how the organism works as a system, both at the cellular and super-cellular level. The complexity barrier between components and systems prevents us form predicting the behavior of biological systems, and therefore from repairing them reliably. Biological systems have obvious structure and organizational principles, but they have evolved to employ all available mechanisms, including the ones that span different scales and different modes of operation. Their behavior cannot be understood either by "reading the DNA" (even though in principle all the information is there) or by studying the biological components one by one or one level at a time.

Biological systems appear to be rather different from engineered systems, both in their use of modular organization and in their misuse of it. Still, this does not mean that they cannot be explained. A combination of "mechanistic" modeling and "phenomenological" observations will likely lead us somewhere. However, it is now evident that even when we are able to fully characterize a model from a mechanistic point of view, the model itself can express "emergent" phenomenological behavior that is not evident from the parts list. Conversely, given a known behavior and a long parts list, it is often difficult to identify the subset of the parts list that is responsible for the behavior.

These *systems complexity* problems are actually well known in computing: they are typical of information processing systems, where even small programs can be extremely subtle (and where in general predicting the behavior of a program may be undecidable). Biology is increasingly dealing with information processing mechanisms at the subcellular and intracellular level, in genomes and signalling pathways, and the same problems are becoming evident there too. The typical reaction to systems complexity in computing has been to make sure the systems are "well engineered" in the first place, so the problems do not arise as much. Unfortunately, this approach is not directly applicable to biology, where *reverse* engineering is more the issue.

Scope and Challenge

In the words of Sydney Brenner "*The problem of biology is not to stand aghast at the complexity but to conquer it*". The benefits of understanding how biological systems work will obviously be immense, especially from a medical and social point of view. The challenge then is to conquer the complexity of biological systems by all available techniques. Computing may have a direct impact on this challenge, since many principles and techniques are available there for the analysis of information systems. But, as explained above, computing has largely avoided a frontal attack on this kind of problem. Conversely, well established and sophisticated techniques from continuous mathematics have largely avoided tackling information processing systems.

Value in a Complex Systems Perspective

To overcome such a challenge, we need the help of multiple disciplines, and at the same time we need to change the perspective of each discipline. The complex systems perspective is relatively unfamiliar to many mechanistic sciences, such as computing, and a change of perspective there is needed to produce new analysis techniques. Conversely, the theory of complex systems is concerned with much simpler systems that biological systems; a change of perspective is needed there to tackle even complex engineered systems (of which information systems are a prime example), not to mention biological systems. In Biology we have non-engineered complex systems that are (in many critical ways) information processing systems. We must start from a complex systems perspective, in the broadest sense, to even appreciate the challenge; neither a mechanistic approach (build all possible models) nor a phenomenological approach (conduct all possible experiments) will work on its own.

Research Directions

Themes for Consideration in FP7 ICT

- Theory of complex information processing systems
- Modular and multi-scale organization in complex systems
- Reactive and stochastic systems: modeling, analysis and simulation
- Biological insights in the organization of complex systems / complex systems insights in the organization of biological systems

Links and references

L.Cardelli: “Abstract Machines of Systems Biology”.
<http://research.microsoft.com/Users/luca/Papers/Abstract%20Machines%20of%20Systems%20Biology%20(Draft).pdf>