S8-2

Systems Biology: Perspectives and Challenges

- Towards an Understanding of Dynamics of Life -

Kwang-Hyun Cho
School of Electrical Engineering University of Ulsan

A principal challenge for the life sciences is to understand the 'organization and dynamics' of those components that make up a living system, i.e., to investigate the spatial and temporal relationships between (macro-)molecules, cells, tissues, organs, and organisms that give rise to cause and effect in living systems. A major problem is that networks of cellular processes are regulated through complex interactions among a large number of genes, proteins, and other molecules. The fundamental goal of Systems Biology is to understand the nature of this regulation in order to gain greater insight into living systems and, ultimately, manipulate them. This is achieved not only through cataloguing and characterizing physical components, but also by the integration of this information through mathematical modeling and subsequent simulation of 'networks' or 'pathways' composed of interacting (macro-)molecules. As well as technological innovation that allow accurate, high-throughput, and spatio-temporal measurements, what is needed are theories or methodologies that explain observations. The bewildering complexity of genetic pathways, as well as the costs and effort of experiments, forces us to concentrate on models that are parts of a larger whole. It is therefore of vital importance to have methodologies that identify the key elements in a system and to estimate the error that is an inevitable consequence of necessary simplifications and assumptions in mathematical modeling. Mathematical modeling allows us to formalize and integrate existing knowledge in a precise way, providing formal methods of analysis, and therefore forms a central component in Systems Biology.

There is general agreement that a systems approach is necessary to understand the causal and functional relationships that generate the dynamics of biological networks and pathways [1]. These observations have been the basis for efforts to get the engineering and physical sciences involved in life science research. The emergence of Systems Biology is evidence for this development. A 'dynamic modeling' of a signal transduction pathway is to be used in this presentation as a guide for discussion on what the challenges are if we are to study pathways as dynamic systems [2], [3]. While acknowledging the enormous complexity of such systems, the lack of reliable, accurate and sufficiently rich data sets, and the inadequacies of our methodologies we find that even simple simulations and the modeling process itself can provide the life scientist with useful information, guiding experimental design and generating new hypotheses, and help identify which variables to measure and why [4].

Not only for experimental advances and integrated efforts to identify system dynamics, there is also a need for theoretical developments on which we can induce and speculate the embedded dynamics of life systems. Figure 1 illustrates different aspects of systems biological investigations and Figure 2 shows a typical cross-disciplinary research cycle being required in systems biology.

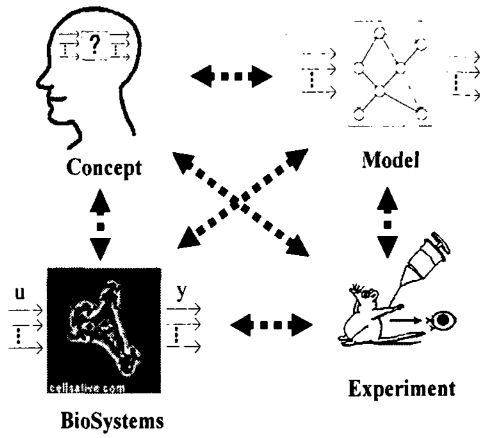

Figure 1. Elements of systems biological investigations.

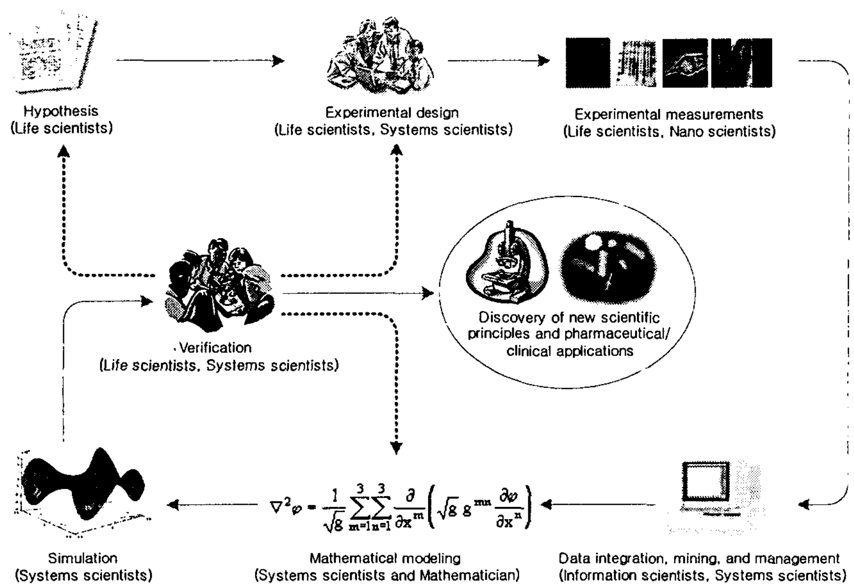

Figure 2. The dynamic research cycle in systems biology.

In the life sciences the shift of focus away from the molecular characterization of the 'nuts and bolts' of a cell to an understanding of functional activity must be paralleled with a change in the way we think about molecular systems, from 'mining genomic data' to the development of 'systems and signal-oriented methodologies'. Systems Biology is therefore as much about a new way of thinking as it is about collecting more facts. Systems Biology attracts new people, new disciplines and new ideas to the life sciences. In particular, new ideas are necessary if we are to make sense of the data and information that is being accumulated in this postgenomic era of the bio-medical sciences. Systems Biology is expected to take Genomics and Bioinformatics towards their conclusions.

References

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