



IVC 16 (16th International Vacuum Congress)
ICSS - 12 (12th International Conference on Solid Surfaces)
NANO - 8 (8th International Conference on Nanometer-Scale Science and Technology)
AIV - 17 (17th Vacuum National Symposium)

NanoSystems Biology

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Systems biology analyzes biological systems by measuring the steady-state and dynamic relationships of the elements in the system in response to genetic or environmental perturbations across their developmental or physiological time dimensions.ⁱ Systems biology is concerned with defining the protein biomodules (e.g., groups of proteins that execute a particular phenotypic function such as galactose and glucose metabolism or protein synthesis) and the protein networks of life (e.g., the skeletal framework of cells and their signal transduction pathways). Systems biology is also concerned with delineating the gene regulatory networks that govern the expression patterns of proteins across developmental or physiological time spans. It is also concerned with delineating the cells effective integration of the protein and gene regulatory networks.

The goal of systems biology is to capture global sets of biological information from as many hierarchical levels of information as possible (DNA → RNA → protein → protein interactions, biomodules, protein and gene regulatory networks → cells → organs → individuals → populations → ecologies) and integrate them.ⁱⁱ This is the start point for the formulation of detailed graphical or mathematical models of biological systems, which are then refined by hypothesis-driven, iterative systems perturbations and data integration. The key is that phenotypic features of the system must be tied directly to the behavior of the protein and gene regulatory networks. Ultimately, these models will explain the systems or emergent properties of the biological system of interest. Once the model is sufficiently accurate and detailed, it will allow biologists to accomplish two tasks never before possible: 1) predict the behavior of the system given any perturbation, and 2) redesign or perturb (e.g., with drugs) the gene regulatory networks to create completely new emergent systems properties. This latter possibility lies at the heart of predictive medicine. Thus, systems biology is hypothesis-driven, global, quantitative, iterative, integrative, and dynamic.

Over the past few years, certain methods of systems biology (large scale genomics and proteomics measurements) have been applied to the investigation of human diseases, with the result that many diseases which are characterized by a single clinical presentation (i.e. an unexpected mass in the breast) actually stratify into multiple disease types, each with its own pattern of gene and protein expression, and each with different molecular errors as the root causes of the disease. As systems biology approaches expand toward capturing and integrating many of the hierarchical levels of information associated with disease and health, it will be possible to, for the first time, develop a detailed molecular picture of many diseases. Out of this molecular picture can arise information related to the identity and progression of the disease, as well as the response of the disease to therapies. Unfortunately, such analysis are currently constitute a large scale research project, and, if applied to humans, are most often carried out in the autopsy stage.

In this talk I will discuss a cross-disciplinary project that is being headed by three institutions: Caltech, the Institute for Systems Biology in Seattle, and the UCLA Geffen School of Medicine.ⁱⁱⁱ The goal is to develop a suite of nanotechnology tools – ranging from integrated microfluidics to nanoelectronics to nanomechanical devices – that will enable a large-scale, systems-biology driven, multiparameter analysis within a clinical setting – i.e. every patient, every visit. Such an analysis constitutes an ‘informative diagnosis’ of disease. I will discuss the current state-of-the-art in terms of the development of this tool set, and I will present this development of a tool set within the larger context of a fundamental biology problem, and the specific context of cancer as a model disease.



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ⁱ Ideker, T., Galitski, T. and Hood, L. "A new approach to decoding life: systems biology," *Annual Review of Genomics and Human Genetics* **2**:343-372, 2001.

ⁱⁱ Ideker, T.; Thorsson, V.; Ranish, J.A.; et al. Integrated genomic and proteomic analyses of a systematically perturbed metabolic network. *Science* 292:929-934, 2001.

ⁱⁱⁱ James R. Heath, Michael E. Phelps, and Leroy Hood, "NanoSystems Biology," *Molecular Imaging and Biology*, **5**, 312 (2003).