INTEGRATIVE MODELING OF BIOLOGICAL SYSTEMS: RELATING ALTERED GENE EXPRESSION TO CELL AND TISSUE FUNCTION

Abstract

There is growing recognition that the tabulation of genetic and molecular building blocks from which biological systems are composed is not by itself sufficient for understanding the functional properties of these systems. Rather, it is becoming clear that dynamic interactions between individual system components can produce emergent, complex behaviors that are not readily predicted from knowledge of each system component alone. Experimentally-based computational models are beginning to provide powerful new tools for understanding the nature of these interactions.

This integrative “systems” approach to the understanding of structure-function issues in biology will be illustrated by our recent work on relating changes in gene expression measured in the failing heart to functional consequences at the cell and tissue level through development and application of computational models. We will describe how cDNA microarray and other technologies are used to measure changes in gene expression in the failing heart. We will describe how these data constrain computational models of the failing myocyte, and how these models are used to understand the functional importance of changes in gene expression on risk for arrhythmia, and to suggest new therapeutic targets for reducing this risk. Finally, we will discuss new emerging areas of biological modeling that may be of interest to members of the mathematical sciences community.