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*Challenges in Computational Medicine and Biology.*

Modern biology involves analyzing very large networks of interacting molecular parts. In contrast to the "gene-centric" era, this seems to call for large-scale mathematical modeling. Even assuming biological systems exhibit general properties and are amenable to modeling, the challenges are still overwhelming, at least for having a major impact in medicine and biology. One high barrier is technical: measured against the complexity of the processes (e.g., gene regulation), and the dimension ( $d$ ) of the data (e.g., DNA microarrays), the number of available samples ( $n$ ) is minuscule; indeed, this "small  $n$ , large  $d$ " dilemma reaches extremes in computational biology. Another barrier is cultural: the "black box" decision rules generated by computational learning inhibit biological understanding and clinical applications. I will talk about several cases studies in attempted generalization. One is estimating the topology and statistics of signaling networks, where grand goals have overrun good sense. Another is an approach to cancer biomarker discovery based solely on orderings of mRNA concentrations and sufficiently accurate and transparent for practical diagnosis and prognosis, and for modeling pathway deregulation. (Received September 19, 2009)