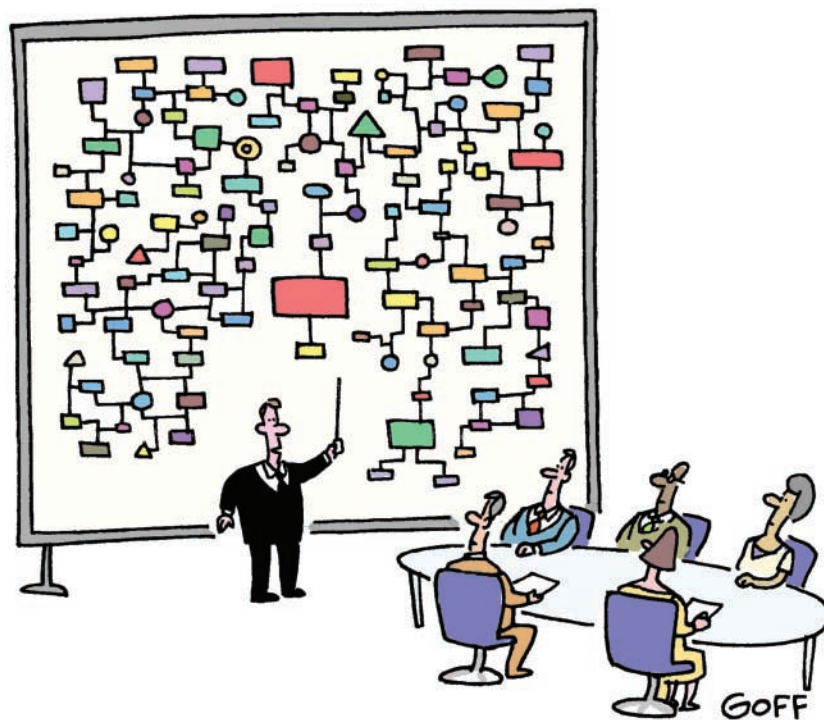


Computational cell biology

Ira Mellman¹ and Tom Misteli²

¹Editor-in-Chief and ²Editorial Board Member, The Journal of Cell Biology

All of us who do experiments and think about biology on a daily basis know that biological systems are exceedingly complex. Biologists have long avoided facing up to the interconnected nature of cellular processes by using reductionist approaches. This strategy has been spectacularly successful in identifying key factors for many fundamentally important biological processes. However, the traditional methods of cell and molecular biology are not very well suited to illuminating the big picture of how the manifold cellular events we have discovered are interconnected. As we explore in increasing detail the molecular nature of cells and organisms, it is becoming unavoidably clear that our simple, reductionist models can be incomplete, inaccurate, or entirely incorrect. Pathways are rarely linear, but are usually branched and interconnected; proteins rarely interact with just a few partners, but generally form extensive interaction networks; and cellular components rarely just reside and act in one place, but dynamically shuttle between cellular locals where they may participate in various functions. The recent wave of genomic, proteomic, and other “-omic” strategies has made us acutely aware of the convoluted nature of biological systems. Clearly, the level of complexity that is emerging in biological systems is beyond what we can comprehend using conventional, often qualitative, cell and molecular-biological methods. To gain a global picture of biological systems, we need help in acquiring, processing, analyzing, and interpreting the multitude of interactions and dynamic events that occur



“And that’s why we need a computer.”

in a cell at any given time. Computational methods are now coming to our rescue. Computational methods have permeated the field of cell biology over the last decades. Most of us now use image analysis software, structural modeling programs, and sequence alignment tools on a daily basis without appreciating that they are computational applications. Up to now, these methods have largely been the supporting cast to the established major experimental tools of cell biologists. In addition, the limited mathematical training of most cell biologists has slowed the wide acceptance of computation analysis in cell biology. Perhaps the time has come, however,

to acknowledge the dawn of a new age in cell biology, where computation is an equal to the more conventional molecular tools. This new era in cell biology promises to reveal entirely novel concepts of cellular organization and function that cannot be extracted using traditional cell biological approaches.

This issue of the *Journal of Cell Biology* contains three reviews on computational cell biology. Further reviews on related topics will follow. The present reviews cover fields in which computation is already having a major influence. **Computational image** analysis is providing the means to analyze the dynamics of cellular factors in space

©The New Yorker Collection from cartoonbank.com. All rights reserved.

and time in many dimensions, allowing the capture of events in living cells and organisms with unprecedented precision. **Computational modeling** allows the dynamic interactions of cellular structures, components, and pathways to be probed not only in a quantitative manner, but also with the ability to make quantitative predictions. **Systems biology** approaches are taking advantage of computational methods to acquire and analyze interaction networks with the goal of mapping networks and finding patterns of regulation within them. In addition to these reviews, the paper by Jacquet et al. in this issue exemplifies an interdisciplinary computational–cell biological approach. The authors describe the oscillatory shuttling between the nucleus and the cytoplasm of a yeast stress response factor, and they provide a predictive

computational modeling framework for the study of this phenomenon.

The purpose of the reviews is twofold: first, to introduce these novel, and to many still unfamiliar, techniques to the cell biology community; and second, to signal to cell biologists and, maybe more importantly, to computational biologists, that the *JCB* is realizing the influence computation is having on how we do cell biology. Like so many times before when new methodologies appeared on the scene, the *JCB* seeks to be at the forefront of these trends and to contribute to defining the directions of an exciting, emerging field. Computational cell biology will very much be an interdisciplinary effort between cell and computational biologists and much of the success of these powerful new approaches will depend on the willingness to communicate across discipline

barriers. The *JCB* is eager to make a contribution to building the necessary bridges between the communities by encouraging submission of computational papers and ensuring competent, fair review of manuscripts incorporating computational cell biology.

Computation is changing the way we do biology. Computational cell biology is widening our horizon and permitting us to address issues globally without having to sacrifice molecular details. The cell biology community and the *JCB* can undoubtedly look forward to many computational cell biology papers and the novel, exciting concepts that will emerge from them.

We would especially like to thank Karen Dell, *JCB* Reviews Editor, Sati Motieram, Editorial Assistant, and Mike Rossner, Managing Editor, for their help in producing this series of reviews.