

Paper reference

Uetz, Peter and Finley, Jr, Russell L. From protein networks to biological systems. FEBS Letters 579 (2005) 1821-1827.

Cites: Sharan, et. al. Conserved patterns or protein interaction in multiple species. PNAS, 102(6): 1974-1979, 2005.

Abstract

Uetz and Finley describe the role of protein interaction networks in the creation of systems-level biological models. The authors posit that a true system model would need: the molecules involved; the concentrations of those molecules; how those molecules fit together; the effect of each individual part on its neighbors; and a description of how concentrations, interactions, and mechanics change over time. The authors identify limitations with existing protein interaction maps, particularly those generated by high-throughput screens.

Uetz and Finley suggest that, to help model biological processes, and better visualize and manipulate those models, researchers need more dynamic and realistic representations of the underlying processes. They sketch an “interactive cell TV” (iCell-TV) system that would allow users to navigate a biological process, zoom in and out on particular proteins of interest, and vary the underlying time scale.

Discussion

Uetz and Finley present the role of protein interaction networks in a systems-level understanding of biology. They note that protein interaction networks are a critical component of any such understanding. However, key limitations exist with existing protein interaction maps. In particular, interactions generated by high-throughput screens are subject to a high-degree of false negatives. The authors cite studies in which the false negative rates for yeast two-hybrid screens are ~85% and 50% in co-affinity purify / Mass Spectrometry (co-AP/MS). However, Sharan et. al take advantage of these same experimentally measured interactions in yeast and *Drosophila* to predict interactions in other organisms. Given the high-rate of false negatives in these assays, their use in predicting novel interactions with Sharan et. al’s approach comes into question. Still, Uetz and Finley consider this kind of predicted interaction as a “draft”—that is, there a nonzero signal to noise ratio.

Moreover, the authors find the display of protein interaction maps online to be hamstrung. They note that in many interaction maps on the web, each node represents a generic version of a protein, without regard to how isoforms (variants of that same protein), could interact in that network. The authors suggest that protein interaction maps could be improved by the addition of structural protein information, as well as experimental .

Rather than an advance over Sharan et. al’s work, the paper presents an overview of the state of protein interaction networks and their use as an input into systems-biology models. The authors suggest that the state of protein interaction networks needs to improve before it can be fully integrated into systems-biology models. Specifically, Uetz and Finley note that the prediction of pairwise protein interactions is improved by the general principle that, if an interaction is found across multiple different assays, it has a higher likelihood of being a true positive. Indeed, Srinivasan et. al. found this result by combining four different types of functional genomic data (coexpression, coevolution, coinheritance, and colocation) in a subsequent paper.¹

Finally, the authors suggest that our understanding of systems biology could be improved through the development of an iCell-TV system, which could be used to visualize and model cell behavior. Note the similarities to E-Cell, a Japan-based research project aimed at developing “the necessary theoretical supports, technologies and software platforms to allow whole cell simulation.”²

¹ Srinivasan, et. al. Integrated protein interaction networks for 11 microbes. 2006, NUMB 3909, pages 1-14

² <http://www.e-cell.org/>