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Towards a New Evolutionary Paradigm for Biology, Solving Genotype-Phenotype, and Personalizing Treatments

Abstract:

A persistent biomedical challenge is to turn data into knowledge and therapy. The sheer complexity, heterogeneity, and mass of information are daunting, however. Here, we describe various steps to integrate structured and unstructured data, that is, data in databases or text form. One step is illustrated by a network spanning hundreds of species that predicts the function of a malarial gene, revealing it to be a likely target of the best known antimalarial drug. Another step is text-mining to predict new protein-protein interactions by machine reasoning over PubMed. Finally, a third step is to measure fitness perturbations unique to individuals with a differential equation for the *Evolutionary Action (EA)* of sequence variations in the fitness landscape. Mutational, clinical, and population data show that EA agrees with the impact of point mutations in proteins; with the morbidity and mortality of clinical mutations; and with the human population frequencies of coding polymorphism. Strikingly, we can now integrate Evolutionary Action to recover genes that drive complex phenotypes, for example cancer or autism, and drug resistance in bacteria. Beyond expanding mechanistic insights, Evolutionary Action introduces a new and general differential calculus to measure topology and dynamics in the fitness landscape. Combined with AI and network techniques, it personalizes an integrative and large-scale hypotheses generation framework to each individual patient's relevant mutational fluctuations. Hopefully, diverse applications from biological engineering to precision medicine should benefit.

Keck Seminar

Friday, October 13, 4pm

BioScience Research Collaborative

Room 280 (2nd Floor)



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