

Predicting the effects of changes on living systems

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Can scientists predict what happens when they introduce a change into a living system—for example, if they change the structure of a gene or administer a drug? Just as changing one letter can completely change the meaning of a word, the change of a single letter of the genetic code (referred to as a single nucleotide polymorphism, or SNP) can subtly affect the meaning of a gene's instructions or alter them completely, making the effect of any change extremely hard to predict. Such changes are thought to be responsible for much of the variation between members of a single species—for example, in susceptibility to different diseases. The ability to successfully predict the effect of such changes would accelerate drug discovery and provide a deeper understanding of the processes of life.



In collaboration with Jasmin Fisher at Microsoft Research Cambridge, professor Yanay Ofran and his colleagues at Bar Ilan University have embarked on a program of scientific research that aims to resolve some of the questions underlying this overall goal, and some of their early results have now been published.

One of the researchers' first tasks was to determine whether it is possible to predict how a complex network of biochemical interactions will change when a SNP (pronounced "snip") alters the function of one of the network's components. In an August 2012 paper entitled, "Static Network Structure Can Be Used to Model the Phenotypic Effects of Perturbations in <u>Regulatory Networks</u>" (available at <u>Bioinformatics</u> with paid subscription), the authors describe their success in analyzing static models of biological networks and correctly predicting the response to changes more than 80 percent of the time. This enables the functions of the network to be deduced, the foundation for building a more expressive <u>dynamic model</u>.

Building static networks is a challenge in itself; before beginning this work, the researchers needed to understand which genes are active in a particular cell and what they do. In their latest publication entitled, "Assessing the Relationship between Conservation of Function and Conservation of Sequence Using Photosynthetic Proteins" (available at *Bioinformatics* with paid subscription), the Ofran lab has shown that, while sets of related genes with similar structure diverge in function more quickly than previously thought, selected smaller pieces of each gene may still be useful in predicting function.

There are many unresolved challenges along the way to the eventual goal of predicting the effect of a SNP—understanding which genes are switched on in which cells and how drugs interact with proteins are just two active areas of investigation—but once the goal is reached, an understanding of the functions of all genes and how changes affect



biological systems could lead to the development of computational models to predict and cure many diseases.

Provided by Microsoft

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