COMPUTATIONAL BIOLOGY

Predicting enzyme turnover rates

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Prediction of kinetic parameters is important in understanding biochemical networks. The activity of enzymes is a regulator for the metabolic flux and the proteome of an organism. Thus, the growth rate, physiology and fitness of an organism depend upon it. Such properties are very important in the design of high-performance synthetic cells for the production of target chemicals in high yields.

Now, David Heckmann, Bernhard O. Palsson and co-workers applied machine learning to the in silico prediction of enzyme turnover numbers based upon different parameters including network context, enzyme biochemistry, protein structure and assay conditions. The machine learning models then provide turnover numbers as outputs and give insights into which features influence the kinetic properties the most. Eventually, this might allow more precise modelling of metabolic processes, proteomes, growth rates and so on.

For example, features such as high flux and water access to the active site of the enzyme led to the prediction of higher turnover numbers. In contrast, a deep active site contributed to the prediction of a lower turnover rate. Interestingly, the Michaelis

constant was a strong contributor to modelling the in vitro turnover number, but not the in vivo turnover number. Enzymes that catalyse multiple reactions had a lower predicted value for the turnover number compared to enzymes that are optimized for a single reaction. Interestingly, prediction accuracy of the machine learning models was found to be higher for the turnover number in vivo than in vitro.

Understanding how different features can be used to increase the predictive accuracy of models for in vivo and in vitro turnover rates opens the way to better decipher complex metabolic and biochemical processes. This is likely to be helpful in the engineering of cellular factories for improved chemicals production and to set-up optimized in vitro enzyme reaction cascades. Certainly, it will be exciting to see what impact this approach can make in the future in diverse fields such as enzyme catalysis, medicine and fundamental biochemistry.

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