Prediction of Allosteric Sites by Failure-Induced Flow Redistribution in Complex Networks

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Abstract

Allostery is an important phenomenon that drives regulation of activity in many cellular processes. When a ligand binds to a protein, the protein transmits signals from the site at which the ligand binds to another, often remote, site. The site where the ligand binds is called the regulation site, and the remote site is called the active site. These signals, propagated across the entire molecule, influence how receptive the active site is to binding with more ligands. A positive signal enhances the ability of the active site to bind with more ligands, and a negative signal inhibits the ability of the active site to bind with more ligands. The original ligand that binds at the allosteric site is called the effector. As a classic example, an oxygen effector binding to a hemoglobin molecule increases the likelihood of the hemoglobin molecule to bind with more oxygens.

Despite how important this phenomenon is to cellular processes, the underlying reasons behind how the signals propagate from the regulation site to the active site are not yet fully understood. Towards the natural sciences side of the spectrum, explanations have been put forward that usually entail a thermodynamic or free energy view of allostery. We will examine an approach on the mathematical and computer science side of the spectrum, which puts forward a structural approach. Using concepts from graph theory, such as network flow, in combination with ideas from mathematics and electrical engineering, we will examine a method that can be used to help identify allosteric sites and the key bonds involved in the process of signal propagation.