

Measuring Catalytic Similarity and Exploring the Reaction Space of Enzyme Mechanisms

António Ribeiro

antonio.ribeiro@fc.up.pt

Similarity measures for protein sequence, structure, and enzyme reactions, have been essential tools for translating an abundance of experimental data about enzymes into biological insights. When it comes to reaction mechanisms, despite their importance in explaining the catalytic power of enzymes and their evolution, no similarity measures have been developed until now. We addressed this omission by creating a method to calculate mechanism similarity. We demonstrate how this method can be a helpful tool to navigate the known catalytic space and to unearth convergent and divergent evolutionary relationships.

The exploration of the reaction space has been a neglected topic when it comes to understanding the catalytic mechanism of enzymes. By analyzing the automatically generated mechanism proposals of 25 enzymes, we show how the reaction space accessible to the active site of enzymes is possibly larger than what is commonly considered. Ways to discover and characterize this large number of chemical configurations will be discussed.