

**P030** Structure-Based Estimation of Enzyme Kinetic Parameters for Systems Biology

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Molecular interaction fields, such as the electrostatic potential, are key determinants of enzyme activity and the rates at which enzyme reactions occur.

The qPIPSA method for quantitative comparison of 3D molecular interaction fields can be applied to enzymes from different species or to mutants of a single enzyme. When a correlation between computed similarity indices or total differences in electrostatic potentials and enzymatic kinetic parameters, such as  $K_m$  and  $k_{cat}/K_m$  can be established, it yields insight into the species-to-species or mutational variations in enzyme kinetic parameters. The approach can be used to assess the consistency of experimentally measured data, detect experimental outliers and estimate kinetic parameters for missing species.

The qPIPSA approach can also be employed to investigate individual enzymes in an entire metabolic pathway. As an example, we compare the enzymes of glycolysis for a set of chosen model organisms with sufficient similarity in sequence and secondary structure. The conservation of electrostatic potentials at or near the active site points to optimized and conserved enzymatic mechanisms across a set of diverse species. Along the pathway, the enzymatic steps with the most conserved electrostatic potentials are in the middle of the glycolytic pathway.