Public Abstract
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Title:STABILITY, STATES, AND INTERACTIONS OF THE ENZYME PMM/PGM BY NMR AND MULTIVARIATE ANALYSIS

Phosphomannomutase/phosphoglucomutase (PMM/PGM) contributes to the infectivity of an opportunistic human pathogen *Pseudomonas aeruginosa* by participating carbohydrate biosynthesis. As a phospho-transfer enzyme, PMM/PGM catalyzes reversible conversion between 1- and 6- phosphosugars via a bisphosphorylated hexose intermediate rotating 180° in the catalytic cleft. Although PMM/PGM is well studied both structurally and kinetically, the mechanisms of its intramolecular and intermolecular communication are less well understood, especially in solution. Multiple solution NMR techniques are used in this dissertation's work to reveal information on PMM/PGM interactions at the atomic level. NMR-detected hydrogen exchange in combination with molecular dynamics and electrostatic calculations found phosphorylation of active Ser108 residue stabilizes PMM/PGM by attracting domains together. Responses of PMM/PGM to various phosphosugars were characterized by NMR-detected titrations. The large set of assigned peaks were analyzed by various types of principal component analysis (PCA) to derive binding isotherms, over-arching relationships among phosphosugar ligand binding reactions, and equilibrium shifts of PMM/PGM during its catalytic cycle. PCA was also found to be able to extract binding isotherms directly from non-interpreted 2D NMR spectra of complexes forming in solution. Procedures were identified that are reliable for obtaining the binding isotherms, regardless of the spectral peaks being in the fast, slow, or intermediate exchange regimes, or mixtures thereof. Applying PCA to time-domain NMR data also yields binding isotherms from titrations in fast or slow exchange. The algorithm readily extracts from an MRI movie its time courses, such as breathing and heart rate in chest imaging. To enable the community to exploit these new capabilities, we have developed the multi-platform software named TREND to track equilibrium and non-equilibrium population shifts among 2D data frames. The principal components obtained represent the main changes among the data frames. Besides binding isotherms and time courses, the main changes extracted by TREND can be any variety of population shifts. TREND can reconstruct the series of measurements from selected principal components. TREND supports multiple data formats, including raw NMR data, images, movies, lists, and spreadsheet files. The software can also be used for data clustering or noise filtering.