

## **A systematic investigation into the quantitative effect of pH changes on the upper glycolytic enzymes of *Escherichia coli* and *Saccharomyces cerevisiae***

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Kinetic modelling of biological phenomena in an attempt to understand the underlying dynamics and complexity of life is becoming an indispensable tool to systems biology. A new paradigm of mathematical and computational integration of experimental data has shifted the focus in biological sciences from mere characterisation and cataloguing of the components of life, to a more holistic view. The functioning of these components in dynamic interactions in non-linear biochemical networks is now a major field of interest for many biologists. Classically, enzyme kinetic assays are optimised for yielding the maximal activity of the enzyme of interest. This raises the question of how applicable the obtained kinetic parameters are for systems biology, especially when considering how the intracellular reality (in terms of pH and ionic strength and composition) affects the catalytic activity of enzymes *in vivo*. Another concern is how accurate and predictive the kinetic models, constructed from such obtained data, can be. Much effort has been directed towards the standardisation of enzyme kinetics for systems biology and *in vivo*-like assay media have been developed for the determination of enzyme kinetic parameters in both *Escherichia coli* and *Saccharomyces cerevisiae*. However, the effect of pH changes on kinetic parameters of enzymes, has been somewhat neglected in systems biology studies. With this in mind we investigated the quantitative effects elicited by pH changes on the upper glycolytic enzymes in *Escherichia coli* and *Saccharomyces cerevisiae* using NMR spectroscopy. This is especially important as recent studies have shown that intracellular pH, while remaining a tightly homeostatically controlled parameter, is not as constant as once thought and has been shown to vary in response to environmental perturbation. The investigation focused on parameter estimation and the unique identifiability of the estimated parameters. The main aim of this project is the development of a robust, reliable technique for parameter identification from experimental data using mathematical and computational approaches.