

WITHIN-SPECIES GENETIC AND ENVIRONMENTAL VARIABILITY OF ENZYMATIC KINETIC PARAMETERS AND CONCENTRATIONS

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Pioneered by the work of Heinrich and Rapoport, the silicon cell concept maintains that by specifying the properties of the enzymes in a metabolic pathway one can reconstruct in the computer the behaviour of the pathway. However, those approaches are limited by the lack of knowledge about kinetic parameters. A key issue for being able to apply those models to a range of metabolically different *Escherichia coli* strains would be to gain insight into the range of genetic variation for kinetic parameters like V_{max} (maximum velocity) and k_{cat} (catalytic constant). V_{max} is a composite parameter which depends on both k_{cat} and enzyme concentration $[E]$ through the relationship $V_{max} = k_{cat} \cdot [E]$. While cellular enzyme concentrations are known to vary considerably within a species in a broad range of organisms, much less is known about the range of variation of kinetic parameters. In this study we measured k_{cat} and $[E]$ on a variety of strains of *E. coli* and environments to assess the extent of genetic and environmental variation for enzyme concentrations and kinetic parameters. By comparing the cellular enzyme concentrations with their maximum velocity V_{max} , we produce the first large-scale analysis of the extent of within-species variation of kinetic constant k_{cat} . Altogether, the project will provide us with a unique description of the metabolism of five strains of *E. coli* at different levels of integration of the phenotype, including gene sequences, gene expression, metabolite concentrations, metabolic capabilities, and fine characterization of the carbon metabolism through enzyme kinetic parameters and concentrations.