Integration of biomass functions of genome-scale metabolic models with experimental data reveals universally essential cofactors in prokaryotes

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Knowledge of the core biochemical composition of the cell is critical for genome-scale metabolic modelling. In order to identify the universal core organic cofactors for prokaryotes, we performed a detailed analysis of biomass objective functions (BOFs) of 71 manually curated genome-scale prokaryotic models. These were then compared and integrated with the ModelSEED framework for biomass composition, experimental data on gene essentiality, curated enzyme-cofactor association data and a comprehensive survey of the literature. Surprisingly, no cofactor was present in all the BOFs analysed, including the important redox cofactor nicotinamide adenine dinucleotide (NAD) or its derivatives. Our results indicate not only the redox cofactors but also others such as coenzyme A, flavins and thiamin as universally essential for prokaryotes and therefore as important to include in the BOFs of future genome-scale models of prokaryotic organisms.

Virtual mitochondrion : a modular and multi level whole-mitochondrion model

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Virtual Mitochondrion is a project of a multilevel modelling of mitochondrial bioenergy metabolism. It involves: - A molecular/atomic level with stochastic modelling (Gillespie) of electrons and protons transfers in respiratory chain complexes and super complexes of respiratory chain. It allowed us to predict a natural bifurcation of electrons in complex III, to clarify the antimycin inhibition constraints and to simulate the ROS production in complex I and III. It also permits to jump to the upper level of enzyme kinetics. - A mitochondrial level with the global modelling of the respiratory chain using simple but thermodynamical correct kinetics equations developed for the respiratory chain complexes (Henri-Michaelis-Menten like equations with the introduction of the proton gradient). The aim is to understand how local changes (pathological mutations for instance, drug effect, competition between respiratory substrates) in respiratory complexes influence the global behaviour of the oxidative phosphorylation. (In collaboration with Edda Klipp, Berlin). - A cell level with the description of simple(s) model(s) of central energy metabolism easy to manipulate and to understand. The aim is to coherently integrate various types of data, metabolomics, fluxomics, transcriptomics and to follow the reroutings of metabolism, their regulations and controlling steps/targets (Metabolic Control Analysis). In this work, our purpose is not only to fit the experimental results but also to evidence inconsistencies that will lead to unveil mechanisms which were not taken into account.