Towards a systemic prediction of all cell component concentrations: the Resource Balance Analysis (RBA)

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Constraint-based approaches such as Flux Balance Analysis permit quantitative predictions for the metabolic function during the exponential growth by integrating the stoichiometry of the metabolic network and assuming some "optimization" principle on cell flux distribution. However, the bacterium is also confronted with other structural constraints implied by the general problem of resource management between the different components of the cell. Enzymes and ribosomes are indeed composed of metabolic precursors such as amino acids. The bacterium must decide to use the metabolic precursors either to increase the metabolic network capacity, or to increase the capacity of the translation apparatus.

Through the mathematical formalisation of the problem of resource repartition as an optimization problem, we demonstrated the existence of a trade-off for the protein repartition between the translation apparatus and the metabolic network. The resolution of this optimization problem allows the estimation for a given medium composition of (*i*) the maximal growth rate reachable; (*ii*) the concentrations of ribosomes, the concentration of proteins involved in the metabolic network and more generally the resource repartition between cell components; (*iii*) the flux distribution.

Beyond the interest of predict the repartition of the resources between cell components, this optimization problem allows us to recover the functional modules recently identified for *Bacillus subtilis*, which paves the way towards predict the genetic regulatory network.

The proposed method, named ``Resource Balance Analysis'' (RBA), predicts the concentration of the main cellular components and defines the formal background to investigate, in the future, many biological aspects such as the amino acid composition of enzymes, the codon usage, the emergence of structured genetic regulations. RBA sounds also promising to study the evolution of the organism regulatory networks with respect to their ecological niche.