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HAS MOLAR YIELD IN METABOLIC NETWORKS BEEN MAXIMIZED DURING EVOLUTION?

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It is often been assumed that, during evolution, the network structure and kinetic properties of metabolic systems have changed so as to maximize the molar yield of biotransformations, that is, the conversion ratio between product (e.g. ATP or biomass) and substrate. This assumption underlies an approach to computing unknown fluxes, frequently called Flux Balance Analysis. Here, the relevance and applicability of that assumption are critically examined, and it is compared with the principle of maximizing pathway flux. We discuss diverse experimental evidence showing that, often, those biochemical pathways are operative that allow fast but low-yield synthesis of important products. Examples are provided by fermentation in *S. cerevisiae* and several other yeast species, as well as homolactic fermentation in *Lactobacillus plantarum*. Moreover, evolutionary game theory shows that organisms can be trapped in a Tragedy of the Commons, in which resources are not utilized economically. All this this leads us to the conclusion that maximization of molar yield is by no means a universal principle.