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Network theory and prediction of regulatory switches

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While the influence of the high intracellular concentration of macromolecules on cell physiology is increasingly appreciated, its impact on the function of intracellular molecular interaction networks remains poorly understood. To test the effect of molecular crowding on the function of metabolic networks, we introduce a modified form of flux balance analysis that takes into account the constraint imposed by the limit on the attainable concentration of enzymes in the crowded cytoplasm. We demonstrate and experimentally confirm that the method can successfully predict the existence of regulatory points that allow switching from high to low biomass yield pathways when changing cellular growth rate. These results demonstrate that molecular crowding represents a bound on the achievable functional states of metabolic networks, and provide a systematic approach to uncover potential regulatory points in cellular metabolism.