87. Conditions For Duality Between Fluxes and Concentrations in Biochemical Networks

Ronan M.T. Fleming1(ronan.mt.fleming@gmail.com), Nikos Vlassis2, Ines Thiele1, Michael A. Saunders3

1Luxembourg Centre for Systems Biomedicine, University of Luxembourg, 7 avenue des Hauts-Fourneaux, Esch- sur-Alzette, Luxembourg. 2Adobe Research, 345 Park ave, San Jose, CA, USA. 3Dept of Management Science and Engineering, Stanford University, Stanford, CA, USA.

http://www.en.uni.lu/lcsb/research/systems_biochemistry

Project Goals: In experimental systems biology, the majority of high throughput experimental data is of molecular abundance and the minority is of reaction rates. We seek a modeling framework flexible enough to integrate experimental data on both rates and abundance. With explicit rep- resentation of molecular abundance it becomes possible to mechanistically model regulation, e.g., genetic regulation, where the abundance of an active transcription factor modulates the rate of transcription by binding to a sequence motif in competition with other genomic structural proteins. Phenomenological kinetic models (e.g., Michaelis-Menten kinetics) are potentially more biochemi- cally realistic than flux balance models as they simultaneously represent concentration and flux, but their solution for a steady state concentration quickly becomes intractable for networks with over ˜100 reactions. Our goal is to develop the first algorithms for tractable modeling of steady state flux and concentration at genome-scale.

Mathematical and computational modeling of biochemical networks is often done in terms of either the concen- trations of molecular species or the fluxes of biochemical reactions. When is mathematical modeling from either perspective equivalent to the other? Mathematical duality translates concepts, theorems or mathematical structures into other concepts, theorems or structures, in a one-to-one manner. We present a novel stoichiometric condition that is necessary and sufficient for duality between unidirectional fluxes and concentrations. Our numerical ex- periments, with computational models derived from a range of genome-scale biochemical networks, suggest that this flux-concentration duality is a pervasive property of biochemical networks. We also provide a combinatorial characterisation that is sufficient to ensure flux-concentration duality. That is, for every two disjoint sets of molec- ular species, there is at least one reaction complex that involves species from only one of the two sets. When unidirectional fluxes and molecular species concentrations are dual vectors, this implies that the behaviour of the corresponding biochemical network can either be described entirely in terms of concentrations or unidirectional fluxes.