Condensed representations of synergistic behavior in biological regulatory networks

Armindo Salvador*and Michael A. Savageau
Department of Microbiology and Immunology – The University of Michigan
5641 Medical Sciences II, Ann Arbor, MI 48109-0620, USA
(armindo@umich.edu)

Part of the difficulty in understanding biological regulatory networks, even when mathematical models are available, lies in our limited ability to apprehend complex relationships between large sets of variables. To overcome this difficulty, one must often distill the essential information into numerical indexes with clear and intuitive physical meaning and translate the results into effective visual representations. When addressing system responses, first-order differential coefficients (variously known as "sensitivities", "log gains", "control coefficients") are usually the indexes of choice [1, 2, 3, 4]. An important limitation of the first-order coefficients is that they overlook synergistic interactions between system components. A new formalism for synergism analysis [5, 6], however, addresses this shortcoming while sharing the advantages of first-order analysis. The new formalism quantifies the synergistic nature of the responses through second-order differential coefficients ("synergism coefficients"). When applied to a mathematical model, synergism analysis pinpoints responses that deviate from linear/additive behaviour (synergisms) or from power-law/multiplicative behaviour (logsynergisms). For small perturbations, the analytical approach yields good approximations of the numerically calculated synergisms and logsynergisms. In this work, we apply synergism analysis to a large-scale model of a biological regulatory network and show that it provides for an effective visualization of synergistic interactions at the systemic level.

References

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