494d A Network Decomposition Framework for Integration of Knowledge on Regulatory Networks in Biological Systems

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Regulatory networks in biological systems are quite complex because of the high degree of interactions between associated genes, proteins, and metabolites. With this as motivation, we developed a novel tool to help elucidate the network topology of regulatory systems. A network is first broken down into its smallest elements (e.g., genes, proteins, metabolites, phosphorylated/unphosphorylated species, allosteric effectors, transcriptional repressors/activators), and rebuilt again from the ground-up. Through systematic enumeration of highest-level mechanistic interactions, lower-level interactions can be inferred in a self-consistent manner, and hence a framework into which all existing knowledge about the regulatory networks can be integrated. The method has some interesting features: (1) all knowledge about regulatory interactions in the network can be integrated/summarized within a compact representation, (2) no aesthetic intelligence is required in spatial arrangement of network elements, (3) new elements and knowledge can be easily appended, and conversely, smaller subsets of the network can be easily extracted, (4) correlations between elements are self-consistent and explicitly presented, (5) exertion of regulatory control can be shown to propagate through lower-level interactions, and (6) everything follows simple arithmetic operations. The method is potentially useful as discovery tool in unearthing novel regulatory structures. Application of the method to regulatory networks governing carbon catabolite repression in Escherichia coli will be presented.