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Dynamics signatures generated by regulatory networks

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The results presented in this talk are strongly motivated by attempts to characterize the dynamics of regulatory networks in biological systems. There are three fundamental questions that we attempt to address are: (1) given a time series of gene expression, e.g. RNA-Seq, can one determine regulatory networks that can generate such a time series, (2) given a regulatory network can one determine the types of dynamics that it is capable of generating in a robust manner, and (3) how robust are these networks with respect to expression of particular 'dynamic phenotypes? There are obvious challenges to answering these questions: (1) biological data tends to be extremely noisy and typically imprecisely measured, (2) the associated mathematical models are derived using heuristic arguments as opposed to first principles, (3) the associated parameter spaces are high dimensional and most parameters are either poorly measured or unknown, and (4) answers to many relevant questions require characterizing global dynamics. We will discuss the mathematical ideas and software associate with the Dynamics Signatures Generated by Regulatory Networks (DSGRN) project. This is based on a combinatorial approximation of dynamics that leads to a natural decomposition of parameter space into semi-algebraic sets. We will discuss how this approach leads to efficient computations and mathematically rigorous results that address the four challenges. We will show how these techniques can be applied to questions related to Malaria and Cancer networks. Finally, if time remains we will discuss related open mathematical questions.