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Using dynamics to identify network topology SAHAND JAMAL RAHI, The Rockefeller University, KRASIMIRA TSANEVA-ATANASOVA, University of Bristol — To elucidate the topology of a signaling pathway, generally, experimentalists manipulate a cell's molecular architecture, for example, by knocking out genes. Molecular biology techniques, though, are not only invasive and labor-intensive, they have also often been eluded by the complexity of biological networks, e.g., in the case of the gonadotropin-releasing hormone (GnRH) system. Inspired by the rapidly accumulating examples of oscillatory signaling in biology, we explored whether such dynamical stimuli can be used to discriminate different topologies of adaptive pathways, which are ubiquitous in biology. Responses to static inputs are nearly indistinguishable given strong measurement noise. Sine function stimuli, widely used in physics, are difficult to implement in standard microfluidics or optogenetics set-ups and do not simplify the mathematical analysis because of the nonlinearities in these systems. With periodic on-off pulses, which can be easily produced, however, simple adaptive circuit motifs and detailed models from the literature robustly reveal distinct output characteristics, which manifest in how the period of maximal output varies with pulse width. Our calculations provide a framework for using existing methods to discover difficult to reveal mechanisms. Furthermore, our results constrain the possible design principles of the presumed frequency decoders in biological systems where pulsatile signaling has recently been discovered.

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