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Cell fate reprogramming by control of intracellular network dynamics[1] JORGE G. T. ZANUDO, REKA ALBERT, The Pennsylvania State University — Identifying control strategies for biological networks is paramount for practical applications that involve reprogramming a cell's fate, such as disease therapeutics and stem cell reprogramming. Although the topic of controlling the dynamics of a system has a long history in control theory, most of this work is not directly applicable to intracellular networks. Here we present a network control method that integrates the structural and functional information available for intracellular networks to predict control targets. Formulated in a logical dynamic scheme, our control method takes advantage of certain function-dependent network components and their relation to steady states in order to identify control targets, which are guaranteed to drive any initial state to the target state with 100% effectiveness and need to be applied only transiently for the system to reach and stay in the desired state. We illustrate our method's potential to find intervention targets for cancer treatment and cell differentiation by applying it to a leukemia signaling network and to the network controlling the differentiation of T cells. We find that the predicted control targets are effective in a broad dynamic framework. Moreover, several of the predicted interventions are supported by experiments.

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