Abstract Submitted
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Combinatorial control of heterogeneous cell populations[1] C. PIERMAROCCHI, P. DUXBURY, Physics and Astronomy, Michigan State University, G. PATERNOSTRO, J. FEALA, S. TIZIANI, J. AXELROD, A. CHAUDHURY, J. CHOI, The Burnham Institute, La Jolla, A. MCCULLOCH, J. CORTES, Department of Engineering, UC San Diego — In medicine, a recent pharmacological approach involves systematic discovery of combinatorial therapies, in which different drugs are simultaneously used to control different pathways associated with a cellular function. This control must occur with minimal response in other non-target cells exposed to treatment, i.e. it has to be selective. We have investigated the statistics of selective control of the human apoptosis (cell death) signaling network. We have built a model for a heterogeneous population of cells, characterized by a signaling network with identical topology, but having different link strengths. The control of the life/death signal is realized by acting with external perturbations, modeling the effect of drugs, on the nodes and on the signaling flow. Concepts from statistical physics and information theory, including entropy, frustration, and nonlinearity have been used to characterize the general properties of selective control. This knowledge was used as a guide in designing algorithms for identifying selective perturbations. Some of these algorithms have been implemented *in vitro* in high throughput experiments on real cell lines where a large number of combinations of different drugs can be tested.

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