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A minimal stochastic model of cell death signaling SUBHADIP RAYCHAUDHURI — Cell death (apoptosis) is mediated by a complex intracellular signaling network that involves a large number of components. We propose a minimal model of signaling network that can sense the strength of any extracellular stimuli such as the concentration of ligands and adapt to a fluctuating environment. Based on stochastic simulations we show that a three step slow, fast, slow pathway is enough to generate large cell to cell fluctuations under the conditions of weak stimulus. Such cell to cell stochastic fluctuations persist even in the presence of large number of molecules and cannot be captured by deterministic differential equation based models. We develop a probability distribution based approach that can characterize the stochastic fluctuations in such inherently stochastic signaling network. Interestingly, our results match with those obtained from kinetic Monte Carlo simulation of the full scale apoptotic network. Hence, our minimal signaling network can serve as a cell type independent general model of apoptosis signaling. We also discuss implications of our probability distribution based approach for diseases such as cancer that can result from disrupted apoptotic balance.

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