Phosphoinositide Cycles as Biological Triggers

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ABSTRACT

Phosphoinositide signaling has been implicated in many cellular phenomena, including cytoskeletal dynamics, gradient sensing in motile cells, endocytosis and vesicle trafficking, and mitogenic signaling. Its membrane localization allows for spatial regulation, and the possibility of coupling biochemistry to mechanical deformation. The cyclic nature of the regulatory loops, which control the interconversion between different phosphorylated states of phosphatidylinositol, suggests that phosphoinositide cycles could act as triggers for the phenomena in which they are implicated. We describe a mathematical model for a generic phosphoinositide cycle coupled to membrane deformation, and thereby interpret receptor-mediated endocytosis as a triggerable event. We analyze the parameter space for bistability and study the effect of "noise" on the triggering event. The details of the triggering event are particularly important in cases where a single signaling pathway is responsible for relaying a signal to the cell and for receptor internalization. By treating species diffusion explicitly we also treat gradient sensing in chemotaxis in the context of this model. Here, bistability and noise play crucial roles in setting the limits of robustness in gradient detection.

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