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Limits on energy dissipation qualitatively change kinetic proofreading in single cells[1] JAYAJIT DAS, The Research Institute at the Nationwide Children's Hospital and the Ohio State University — Cell signaling events, composed of biochemical reactions, usually occur in the absence of the detailed balance condition and continuously dissipate energy. Consequently, when energy supply is limited, specific chemical modification steps might not occur due to the lack of energy to support those reactions. How does the absence of such modification steps, that are intrinsically stochastic in nature, affect single cell signaling kinetics? I address this question in the context of a kinetic proofreading scheme used in a simple model of early time T cell signaling. I show, using exact analytical calculations and numerical simulations, that the amount of energy dissipation needed to execute a desired discrimination scheme depends on whether the decision is made at the transient state or in the steady state of the kinetics. Using a modified Gillespie algorithm for simulating biochemical reactions in energy limited conditions, I show that restricting energy dissipation leads to poorer discrimination in single cells for weak and low affinity ligands. Furthermore, restricting energy dissipation produced substantially larger intrinsic cell-to-cell variations of proteins with qualitatively different distributions than the system with unlimited supply of energy.

[1]NIH

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