

Abstract Submitted
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Better Bet-Hedging with coupled positive and negative feedback loops JATIN NARULA, OLEG IGOSHIN, Dept. of Bioengineering, Rice University — Bacteria use the phenotypic heterogeneity associated with bistable switches to distribute the risk of activating stress response strategies like sporulation and persistence. However bistable switches offer little control over the timing of phenotype switching and first passage times (FPT) for individual cells are found to be exponentially distributed. We show that a genetic circuit consisting of interlinked positive and negative feedback loops allows cells to control the timing of phenotypic switching. Using a mathematical model we find that in this system a stable high expression state and stable low expression limit cycle coexist and the FPT distribution for stochastic transitions between them shows multiple peaks at regular intervals. A multimodal FPT distribution allows cells to detect the persistence of stress and control the rate of phenotype transition of the population. We further show that extracellular signals from cell-cell communication that change the strength of the feedback loops can modulate the FPT distribution and allow cells even greater control in a bet-hedging strategy.

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