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**Environmental statistics and optimal regulation** DAVID SIVAK, Simon Fraser University, MATT THOMSON, University of California, San Francisco — The precision with which an organism can detect its environment, and the timescale for and statistics of environmental change, will affect the suitability of different strategies for regulating protein levels in response to environmental inputs. We propose a general framework—here applied to the enzymatic regulation of metabolism in response to changing nutrient concentrations—to predict the optimal regulatory strategy given the statistics of fluctuations in the environment and measurement apparatus, and the costs associated with enzyme production. We find: (i) relative convexity of enzyme expression cost and benefit influences the fitness of thresholding or graded responses; (ii) intermediate levels of measurement uncertainty call for a sophisticated Bayesian decision rule; and (iii) in dynamic contexts, intermediate levels of uncertainty call for retaining memory of the past. Statistical properties of the environment, such as variability and correlation times, set optimal biochemical parameters, such as thresholds and decay rates in signaling pathways. Our framework provides a theoretical basis for interpreting molecular signal processing algorithms and a classification scheme that organizes known regulatory strategies and may help conceptualize heretofore unknown ones.

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