

Research Highlights

Article

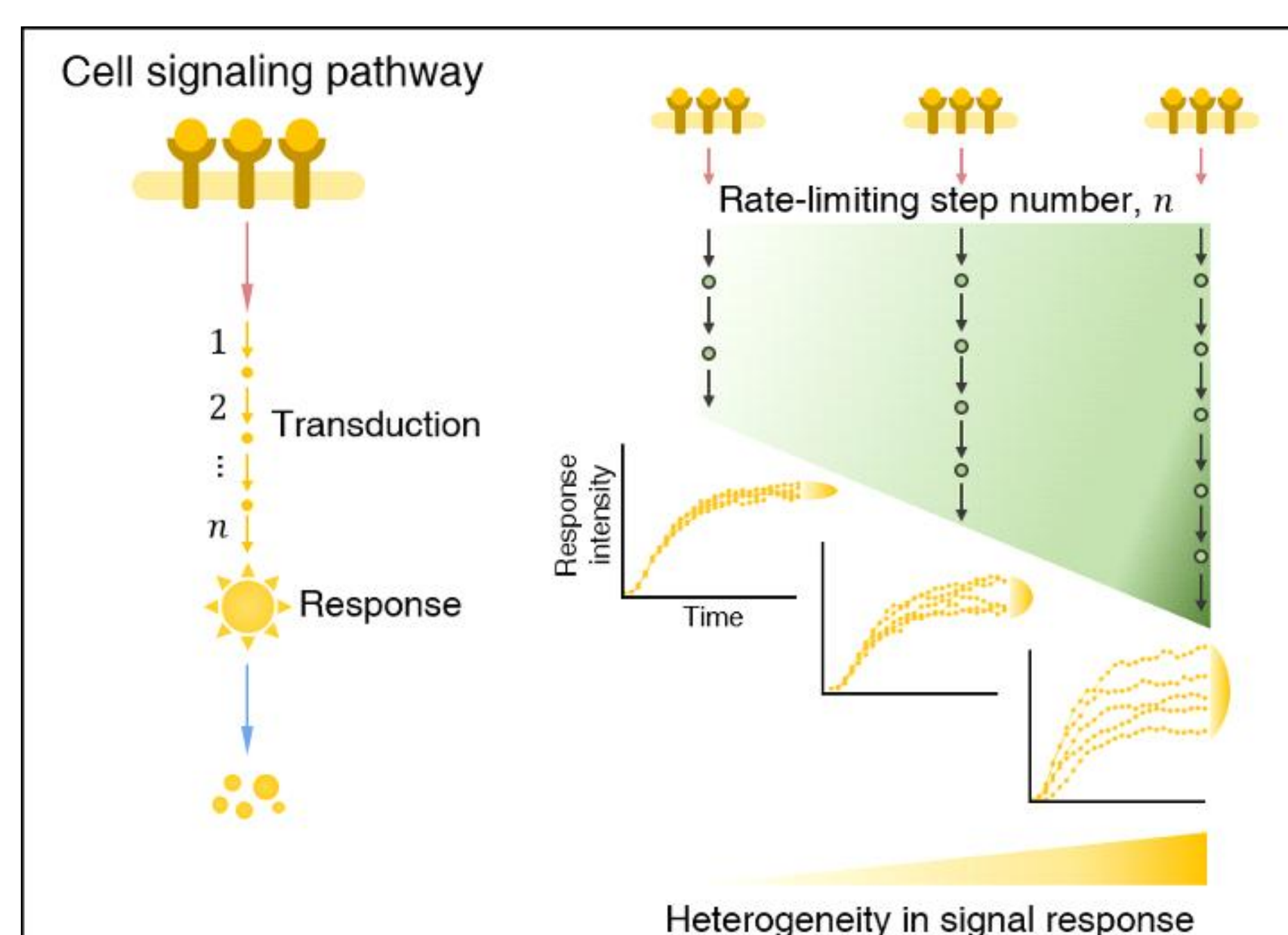
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Systematic inference identifies a major source of heterogeneity in cell signaling dynamics: The rate-limiting step number

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Cells in the human body contain signal transduction systems that respond to various external stimuli. Interestingly, even the same external stimuli are given, response of individual cells are greatly heterogeneous. This leads to emergence of persister cells that are highly resistant to drugs. However, it has been still a closed book because most of intermediate signal transduction reactions are unobservable. In this work, by means of queueing theory, we derived a mean formula of the stochastic process representing cell signalling pathway and developed a Bayesian inference method to estimate associated parameters. We found that the cell-to-cell variability increases as the effective length of cell signaling pathway (i.e., the number of rate-limiting step) increases. This finding could identify more effective chemotherapies that overcome fractional killing of cancer cells caused by the cell-to-cell variability.



Summary figure