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Noise-Induced Symmetry-Breaking Underlies Reliable and Flexible Cellular Decision-Making

All-or-none decision-making by a cell such as differentiation and apoptosis is tightly linked to symmetry-breaking in intracellular networks. The underlying mechanism of such symmetry-breaking has been considered to be the deterministic bifurcation generated by positive feedback loops. By controlling the onset of the bifurcation and the stability of the bifurcated attractors by external inputs, it can also implement various cellular functions such as hysteresis, irreversibility, and history-dependent memory. Waddington expressed its importance for development in a metaphor of the famous epigenetic landscape, in which the fate of each cell is gradually determined in the the landscape of potential whose complexity increases during development. While the deterministic bifurcation has already been accepted as the primary mechanism of the experimentally observed symmetry-breaking, it has rarely been proven experimentally because the bistability is the deterministic concept and we cannot completely eliminate noise from biological systems. Furthermore, the bistable attractor lacks the property to flexibly produce the distinctive outputs according to the subtle external guidance signal. This indicates that the bistable attractor is not the best dynamical behavior to implement the flexible decision-making while it is better to reinforce and memorize the determined decision.

In this work, I reveal that a noise-induced symmetry-breaking, another mechanism of symmetry-breaking in a noisy system, can also produce the distinctive outputs required for cellular decision-making. Such noise-induced property is shown to have the function to flexibly respond to the external guidance signal even with substantial noise in the signal. The underlying logic of this flexibility is revealed to be the Bayesian information decoding that optimally extracts the information from the noisy signal. The biological validity of the noise-induced symmetry-breaking and Bayesian information decoding will be demonstrated by using various cellular phenomena such as signal transduction, immune-response and polarity formation. Furthermore, I propose an experimental procedure to discriminate the noise-induced symmetry-breaking from the deterministic bifurcation by using single-cell time-lapse measurement. This result will serve to experimentally investigate the noise-induced symmetry-breaking and the related Bayesian information processing by a cell.

References

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