Criticality of Biochemical Feedback

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Biochemical feedback leads to dynamical transitions between cellular states, reminiscent of phase transitions in equilibrium systems. Yet cells are far from equilibrium. Here we show using a generic birth-death model that despite being far from equilibrium, biochemical feedback near a bifurcation point exhibits the scaling exponents of the equilibrium mean-field universality class. The theory allows us to calculate an effective order parameter, temperature, external field, and heat capacity from T cell fluorescence data without fitting. Experiments agree with the scaling predictions, suggesting that this type of nonequilibrium criticality may play an important role in immunology.

MANY biological systems have been observed to transition between monostable and bistable states. Such transitions are reminiscent of phase transitions in equilibrium physics [1], but biological systems are inherently nonequilibrium systems. Equilibrium critical points have rigorously-defined properties, such as scaling exponents, but analogous properties for nonequilibrium systems are poorly understood. In this work, we examine the scaling properties of a nonequilibrium biochemical feedback model near a dynamic transition point, and establish the model's relationship to equilibrium models.

Our model consists of a biochemical birth-death process with feedback. We are interested in one molecular species within the cell, which can be created and degraded, while other molecular species within the cell form a chemical bath. By varying biochemical parameters, the probability distribution of the molecule of interest can transition from unimodal to bimodal.

By studying the scaling properties of the probability distribution, we find that this system can be mathematically mapped to a mean field equilibrium system. This mapping allows one to define an effective reduced temperature, dimensionless field, order parameter, and effective heat capacity for the nonequilibrium system. Near the transition point, the scaling exponents α, β, γ, and δ match those of the equilibrium system, thus implying that the nonequilibrium system is in the equilibrium mean-field universality class.

Our theory provides a framework for extracting statistical physics properties from experimental data without the use of fitting. We test the theory against experiments using measurements of doubly phosphorylated ERK (ppERK) in T cells [2]. Figure 1 shows experimental data and theoretical curves for various effective feedback functions. The data agree well with predictions, showing that the complicated feedback of the experimental system is well described by a simple birth-death model with an effective biochemical feedback. Additionally, the effective heat capacity calculated from the experimental system agrees with our prediction (Fig. 1 inset). Interestingly, the effective heat capacity also allows one to map fluorescence intensity to molecule number.

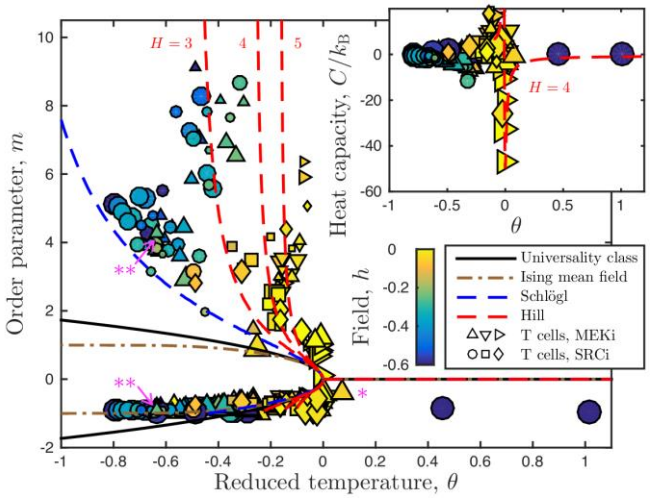

Fig. 1 Experimental data compared with theoretical predictions of the model.

Our results show that a generic model of biochemical feedback near its dynamic transition point exhibits the scaling properties of the equilibrium mean-field universality class, despite being far from equilibrium. By discovering the effective order parameter, temperature, external field, and heat capacity of the system, we have quantitatively translated both the model and T cell fluorescence data into the language of statistical physics. Doing so has revealed agreement between the data and predictions of the theory, with no fitting.

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REFERENCES

[1] Mora T, and Bialek W (2011) *J. Stat. Phys.* 144: 268-302.

[2] Vogel RM, Erez A, Altan-Bonnet G (2016) *Nature Communications* 7, 12428.