
Metastability in the Modified Ising Model of Gene Regulatory Networks

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Abstract: Over the last couple of decades, phase transitions that involve an abrupt, coherent change in order parameter caused by symmetry breaking have been shown to also emerge as a fundamental mechanism in cellular organization. Models constructed based on statistical mechanics of biological systems directly from real data are capable of simulating dynamics in large scales and are capable of predicting similarities between apparently unrelated complex systems. Using an adaptation of a well-established model to study cooperative phenomena, I show the existence of metastable states in phase transitions occurring in a gene regulation network. The network exhibits a cascade of multiple states with different energy levels thereby indicating clusters in the network that work coherently. This phenomenon was previously known to be occurring only in magnetic mixtures.

Keywords: Metastability, Magnetization Plateaus, Ising Model, Gene Regulatory Networks, Phase Transitions

1. Introduction

Dynamics in life sciences can be investigated through the interaction of genes that control a specific cell function wherein certain coherent states of genes or collections of genes correspond to the healthy or functional states of a biological system. Over the last couple of decades, such dynamical phase transitions that involve an abrupt, coherent change in order parameter caused by symmetry breaking have been shown to also emerge as a fundamental mechanism in the cellular organization [4], [6], [7]. Models constructed based on statistical mechanics of biological systems directly from real data are capable of simulating dynamics in large scales and are capable of predicting similarities between apparently unrelated complex systems [2]. An adaptation of the Ising model to capture phase transitions occurring in gene regulation networks (that exhibit asymmetric states of activity i.e. 0 and 1), called the modified Ising model was proposed in a previous work [5]. With simulated networks to show the proof-of-concept, a first-order phase transition was observed in the presence of a finite external field. Here I would like to show that this model can capture phase transitions in gene regulation networks obtained from public databases. Specifically, these networks exhibit metastability in the presence of a magnetic field wherein a cascade of multiple states with different energy levels appear to coexist. Such a hysteretic behavior wherein the system shows the dependence of the state of the system on its history emerges as a property of this model. This unique phenomenon has been shown to exist in classical Ising models of certain specific mixtures of magnetic materials and is often referred to as “magnetization plateaus”, “devil’s staircase” and the like [1], [3]. I show here the existence of these metastable states in a real-world gene-regulatory network and discuss its implications.

2. Results and Discussion

The modified Ising model is an adaptation of the classical Ising model with binary states

$$H = -J \sum_{ij} A_{ij} s_i s_j - B \sum_i s_i$$

where H is the system Hamiltonian, J is the coupling constant, A_{ij} is the network adjacency matrix, s_i is the state variable, $[0, 1]$ (illustrated in Fig. 1. (A)) and B is the magnetic field. The *Escherichia coli* K-12 transcriptional regulatory network is a standardized dataset wherein new models has been conventionally tested owing to its simplicity and thorough knowledge of its connectivity structure and hence we choose this network here to demonstrate metastability [8]. *E.Coli* gene regulatory network has 1550 nodes and 3244 links and therefore a sparse connectivity structure, not unlike, most other scale-free networks (as shown in Fig. 1(B)). Monte Carlo simulations of a ferromagnetically coupled modified-Ising model of a *E.Coli* network under the influence of magnetic field reveals a phase transition from very low values of order parameter (wherein only few nodes are active) to a fully active state. In this we observe that the network exhibits a cascade of multiple states with different energy levels that indicates clusters in the network that work coherently and exhibit the same magnitude of order parameter. Such magnetization plateaus are observed only for positive coupling constants of this network.

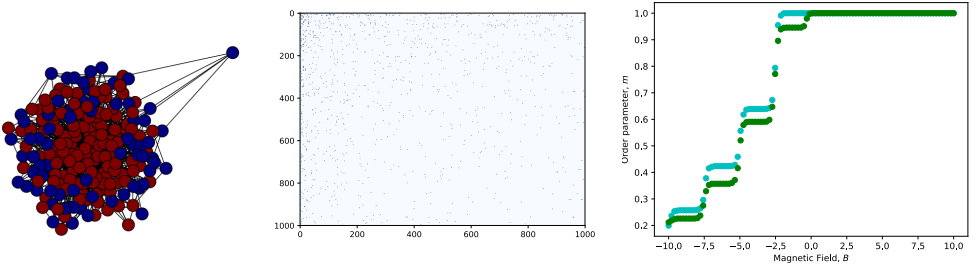


Fig. 1. Metastability in the Modified Ising Model of *E. Coli* Gene Regulatory Network: (A) Left subfigure indicates the functional states of nodes in the network (active or inactive) indicated by red and blue color respectively (B) Center subfigure shows the adjacency matrix of this network which is undirected, sparse with a connection probability of 0.001 to 0.1 (C) Right subfigure shows the magnetization plateaus in the Modified Ising Model of the *E. Coli* network for coupling constant, $J = 5$. The green curve shows the forward hysteric curve (when the system is driven from low magnetic field to high) while the cyan curve shows the reverse hysteric curve.

3. Concluding Remarks

The phenomena of hysteresis have been investigated in biological networks largely with dedicated models, such as that of gene switches before. Such models are usually characterized by few genes that interact with each other whose interaction dynamics are elucidated in high resolution. In this work, I show the existence of hysteresis using an adaptation of a well-established statistical mechanical model for a gene regulation network of large size, however with a coarser description of the gene interaction. We can observe the hysteric phenomena at this scale coming out as an emergent property of the system. This phenomenon was previously known to be occurring only in magnetic mixtures.

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