Protein Folding & Self-Organized Criticality

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INTRODUCTION

Proteins are known to fold into tertiary structures that determine their functionality in living organisms. However, the complex dynamics of protein folding and the way they consistently fold into the same structures is unknown. Self-organized criticality (SOC) has provided a framework for understanding complex systems in various scientific disciplines through scale invariance and the associated "fractal" power law behavior. In this research, we use a simple hydrophobic-polar lattice-bound computational model to investigate self-organized criticality as a possible mechanism for generating complexity in protein folding.

SELF-ORGANIZED CRITICALITY (SOC)

SOC system is a dynamical system at a critical state that is characterized by power law behavior. It follows that these systems are both time and scale invariant.

The Sand Pile Model is the first and most well known example of a self-organizing system.

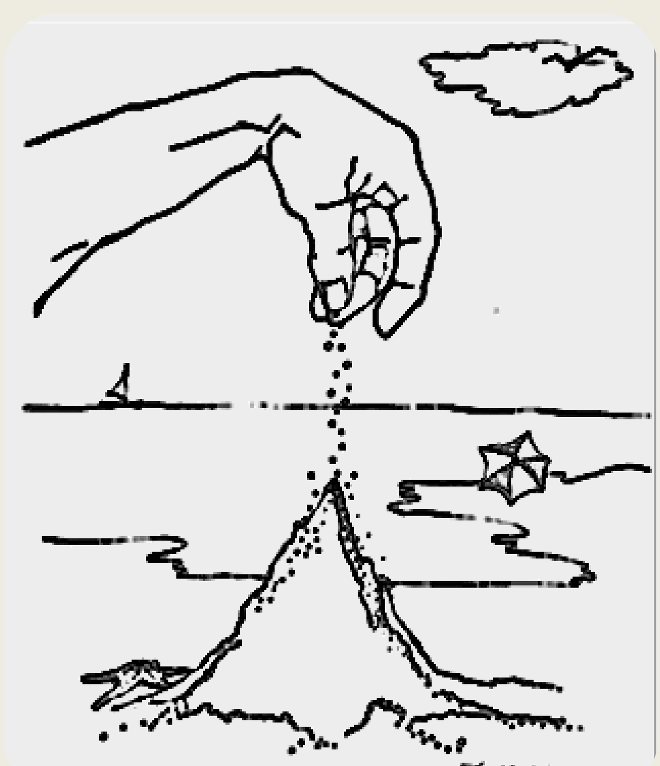

Figure 1: Representation of sand pile model

SAND PILE MODEL

Grains of sand are individually dropped onto a flat plane.

Critical Trait: steepness of slope
Critical State: slope is reached
Avalanches: grains of sand falling from steep slopes
Avalanche Size: number of grains falling

The distribution of avalanches follow a power law behavior

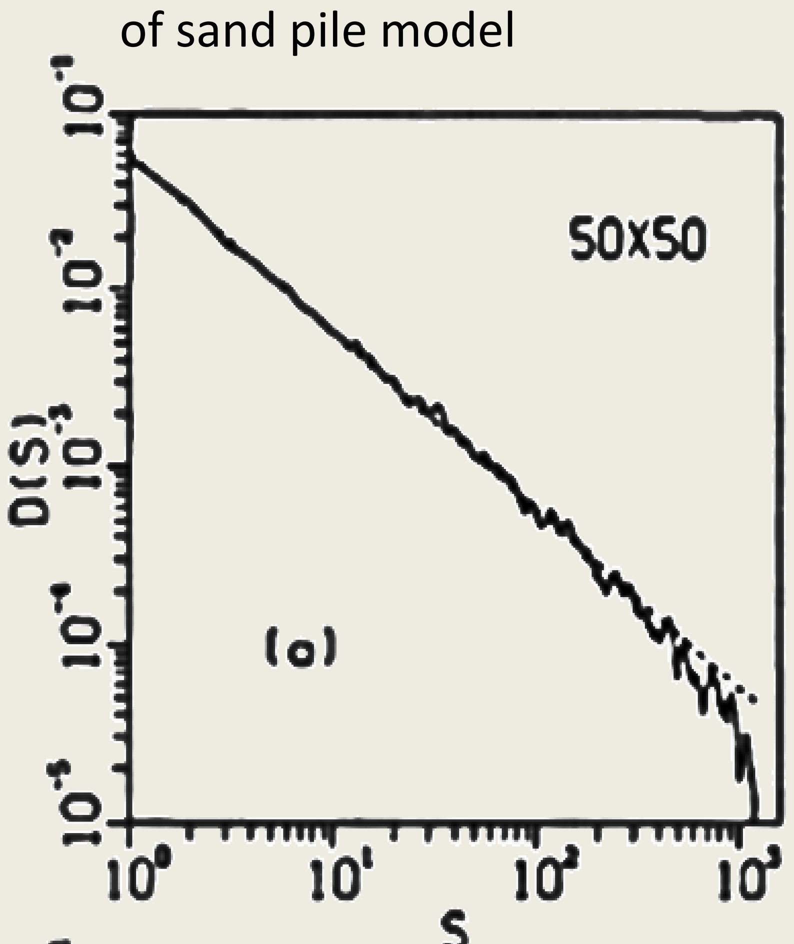

Figure 2: Avalanche size distribution for the sand pile model

PROTEIN FOLDING MODEL

Critical Trait: minimizing energy
Critical State: non-native structure
Avalanches: rapid changes in structure (due to overcoming energy barriers)
Avalanche Size: consecutive folds

HYDROPHOBIC-POLAR (HP) MODEL

Simplified model for understanding how a protein folds in space.

- 3D lattice: 1 bond length, no stretching
- HP model: 2 types of amino acids- hydrophobic (H) and polar (P)
- One amino acid moves at a time

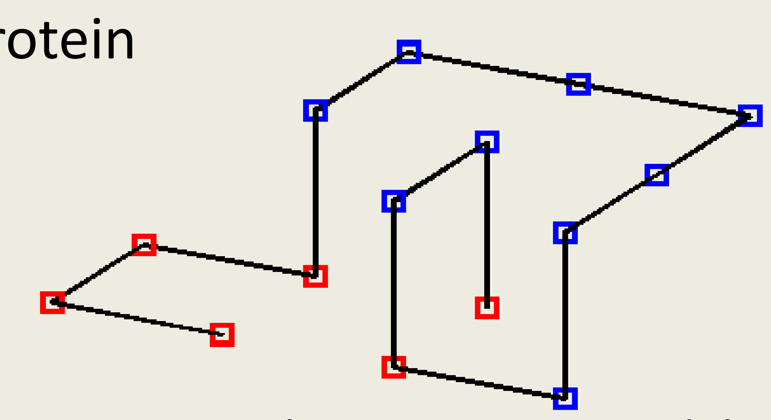

Figure 3: 3D lattice protein model in its native (folded) state

ALGORITHM

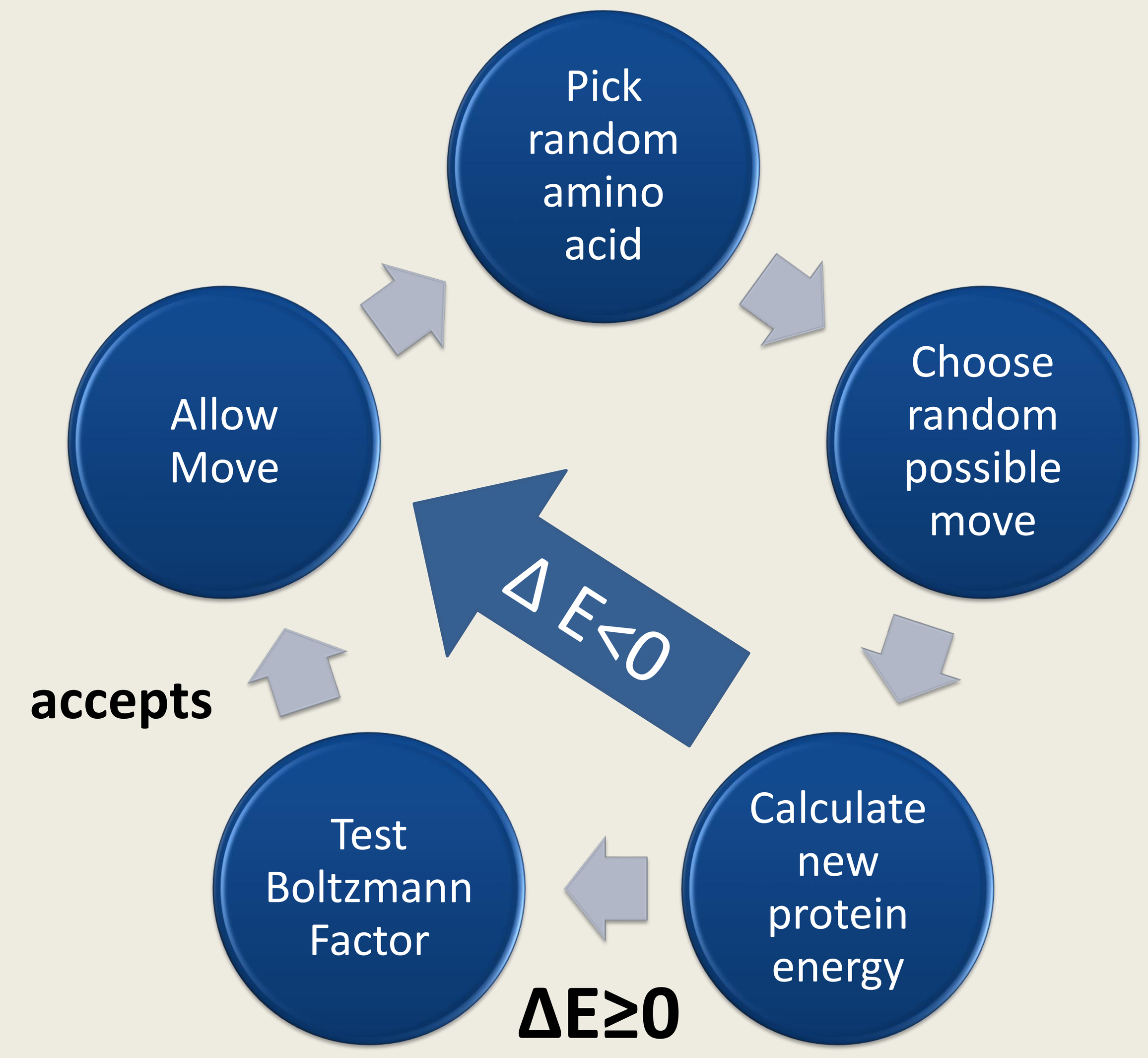

Figure 4: Flow diagram representing the computation sequence of the folding process

AVALANCHE DISTRIBUTION

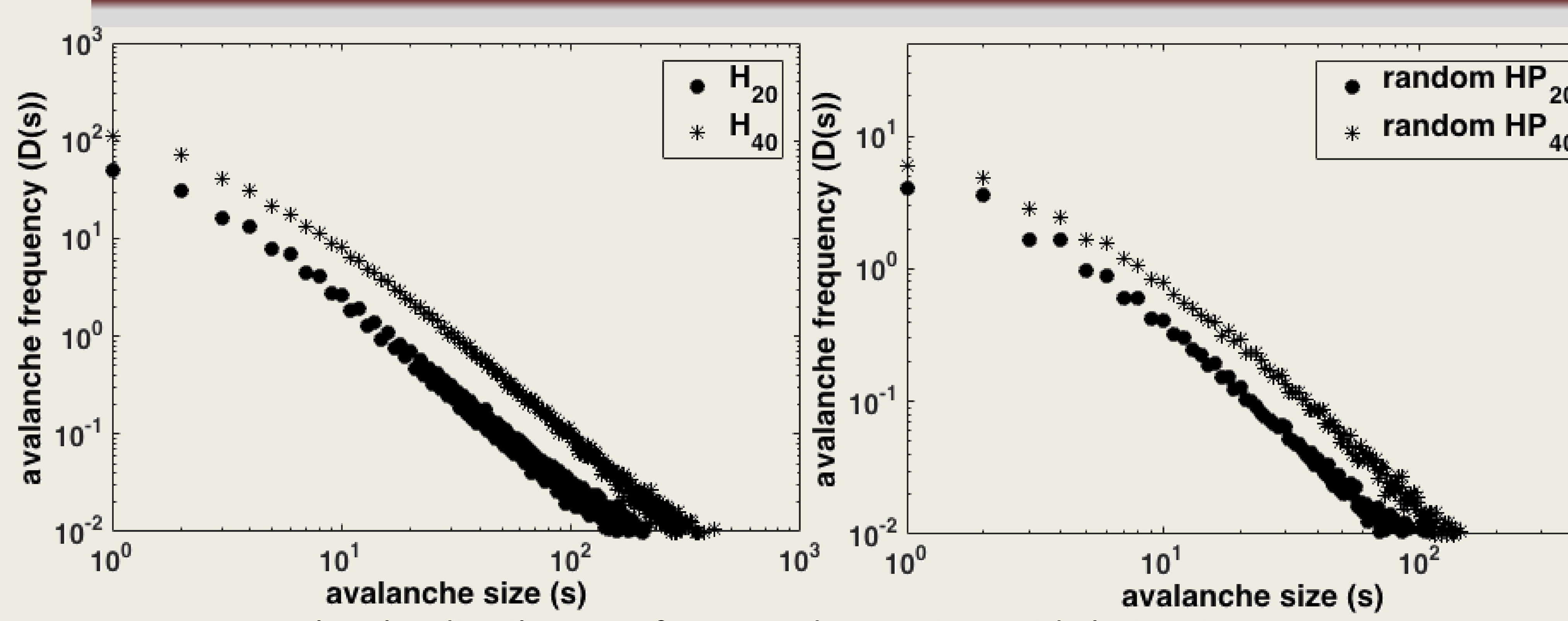

Figure 5: Avalanche distributions for 20 and 40 amino acid chain. Since SOC systems follow a power law, an avalanche distribution on a log plot should show a straight line

AVALANCHE STOPPING

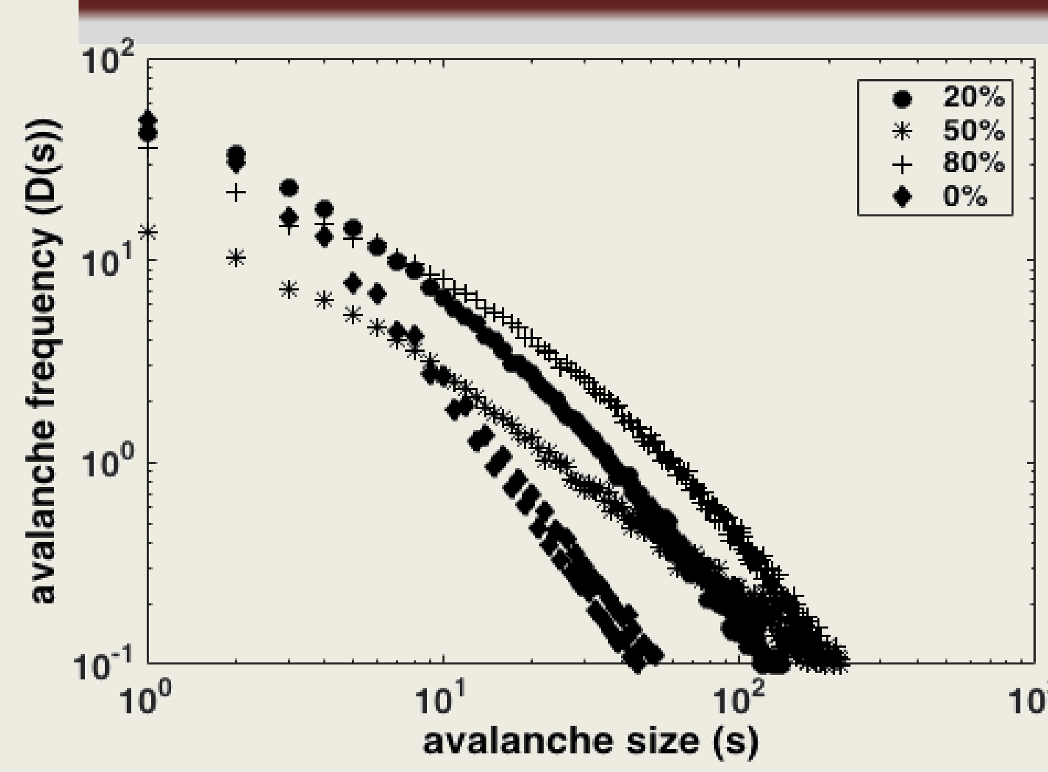

Figure 6: Stopping avalanches to inspect SOC resilience

- Individual folds are randomly prevented throughout the folding process
- What impact does random stopping have on the avalanche distribution?

DISCUSSION

- Avalanche distributions in figure 5 exhibits power law, although this feature alone doesn't support the presence of SOC
- Avalanche stopping alters SOC characteristics

FUTURE RESEARCH

- Does the model exhibit other SOC features? For longer protein chains?
- Do more sophisticated models exhibit SOC?
- Is tertiary structure connected to SOC?

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H. Frauenfelder, Proc. Natl. Acad. Sci. U. S. A. **99 Suppl 1**, 2479 (2635 (1995002)