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Dynamical phase transitions of lattice protein models

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Outline

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- Why study dynamics in lattice protein model?
- The lattice Model used: variants of the Go-model
- Dynamics v Thermodynamics
- Results for the Homogeneous & Heterogeneous Go model for 48mer chain.

Introduction

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- Kinetically constrained systems show **dynamic first order transition**, but not a thermodynamic one
- If a system has a thermodynamic transition, does this automatically result in a dynamic one at T_c?
- One can use a dynamic ensemble to access such a transition
- **System considered**: a lattice protein model
- The lattice protein model is simple model with complex free energy landscapes, which can be modeled computationally
- Presence of dynamic transitions give insight into “arrested states” and metastable energy minima. → evolutionary sequence design?

J P Garrahan et al, PRL, **98**, 195702 (2007)

The Gō Model

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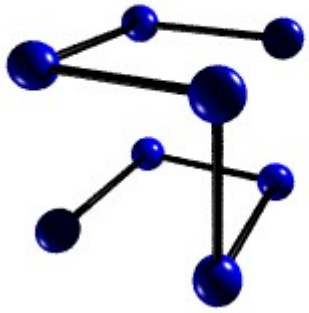
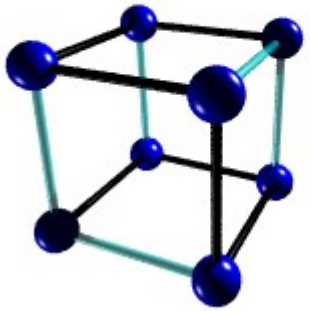
Motivation:

- Protein Folding hypothesis: contributions of native contacts are essential for folding.
- 3 simple variants are considered



Maximally compact native state



Cyan: native bonds

Beads: different amino acids

Homogeneous Model

The Hamiltonian for the lattice model takes this simple form:

$$H = \sum_{i,j} \Theta(i,j) B_{i,j}$$

$$\Theta(i,j) = \begin{cases} 0 \text{ if } i,j \text{ are not in contact} \\ 1 \text{ if } i,j \text{ are in contact} \end{cases}$$

$$B_{i,j} = contact\ energy$$

The homogeneous Gō model will assume uniform interaction energies

Bij = 0 for non-native contacts and

Bij = 1 for native contacts.

Heterogeneous Model

The Hamiltonian for the lattice model takes this simple form:

$$H = \sum_{i,j} \Theta(i,j) B_{i,j}$$

$$\Theta(i,j) = \begin{cases} 0 \text{ if } i,j \text{ are not in contact} \\ 1 \text{ if } i,j \text{ are in contact} \end{cases}$$

$$B_{i,j} = \textit{contact energy}$$

The heterogeneous Gō model: occupied lattice sites mimic amino acids, with different interaction energies associated with them.

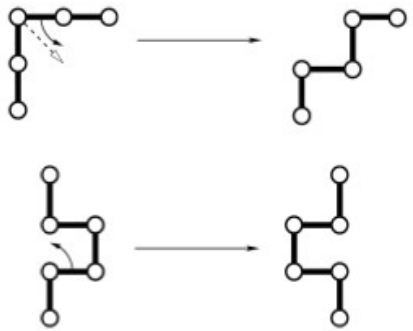
Bij = 0 for non-native contacts,

Bij = Miyazawa-Jernigan interaction matrix for native contacts.

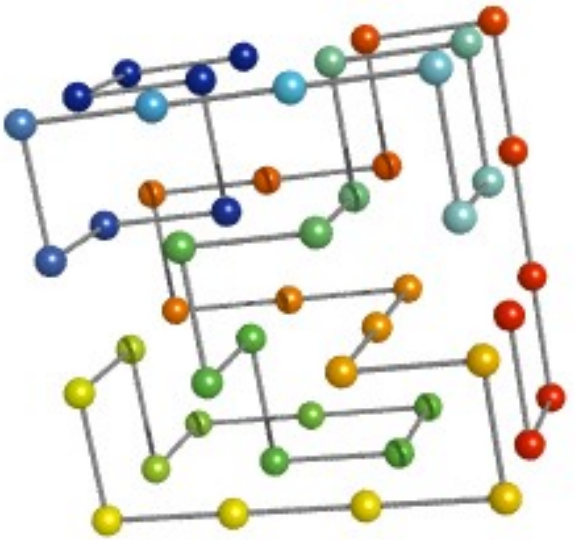
The Simulation

Simulation is based on a model by Shakhnovich et al:
• Standard Monte Carlo Metropolis dynamics are being used
• Two different types of move-sets are used in a combination to ensure ergodic sampling of conformational space.

Move Sets:



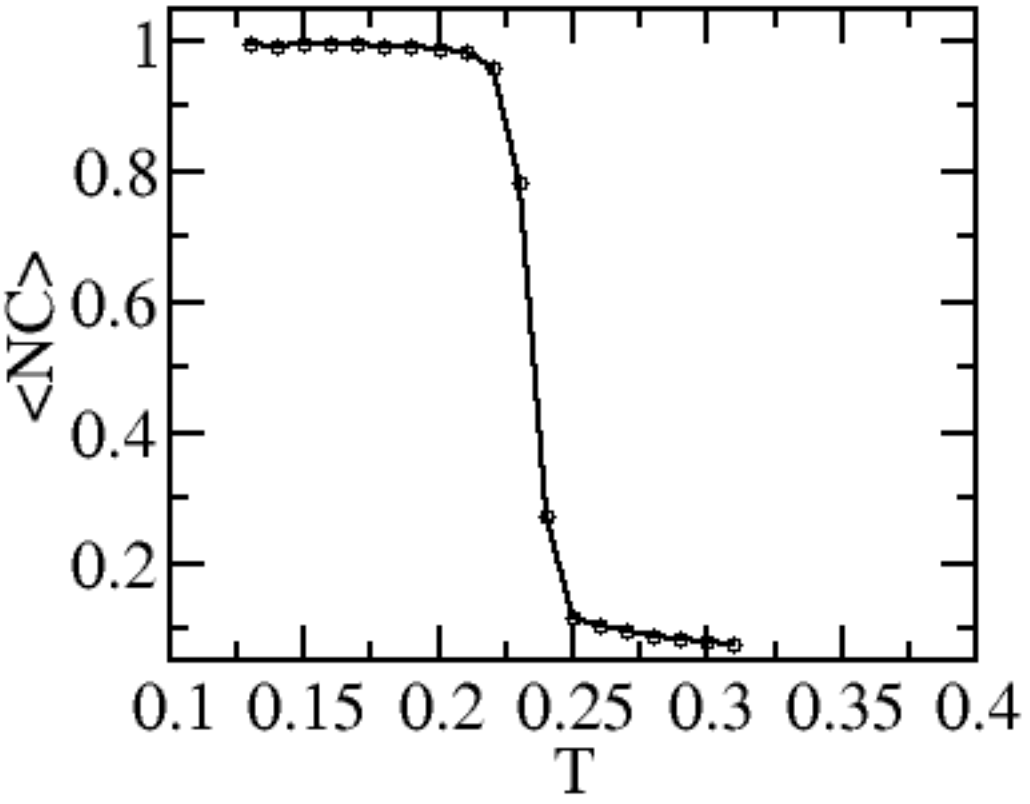
The native state of the actual 48mer which is used in simulations:



➔ Single monomer moves attempted 80% of the time
➔ Double monomer crank-shaft moves attempted 20% of the time

Sali et al. Nature (1994) vol. 369 (6477) pp. 248-251

Statics v Dynamics

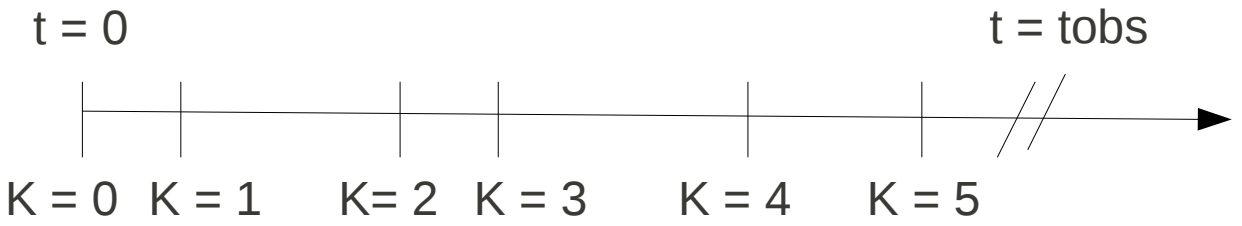


First order like thermodynamic transition

?

Statics v Dynamics II

Looking at ensembles of trajectories
Defining a dynamic variable: native activity K (extensive in time)



$$\kappa = \frac{K}{t_{obs}}$$

The activity is incremented each time a move is proposed which induces a change in the number of native contacts of the conformation

Equilibrium distribution $P_0(\kappa)$:

→ Gaussian for a random process
→ bimodal at a critical temperature, if there is a phase transition
→ long tales indicate an abundance of rare events, hinting towards a dynamic phase transition.

Statics v Dynamics III

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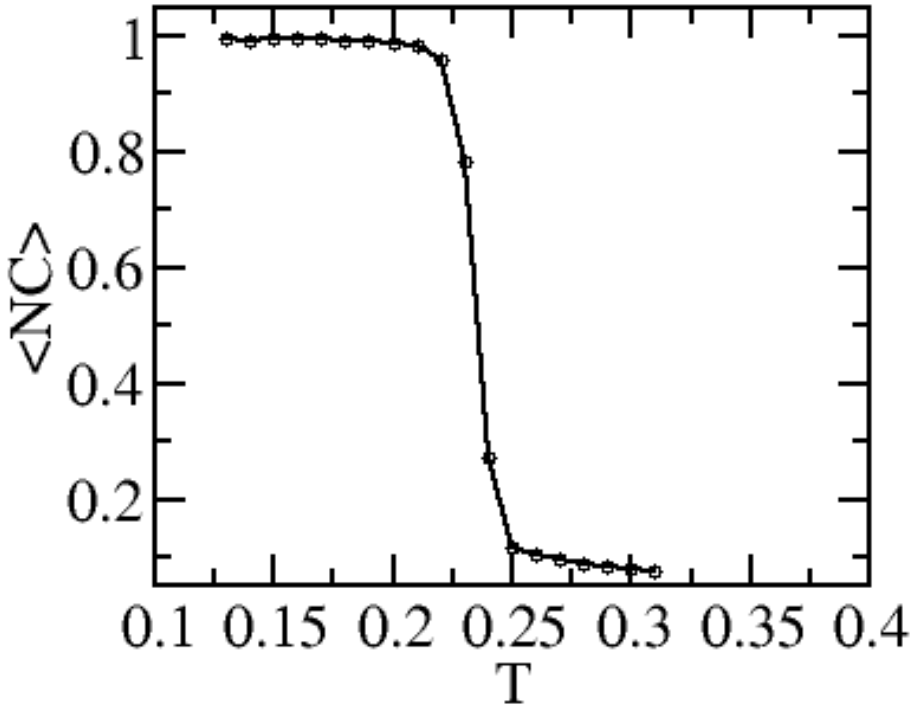
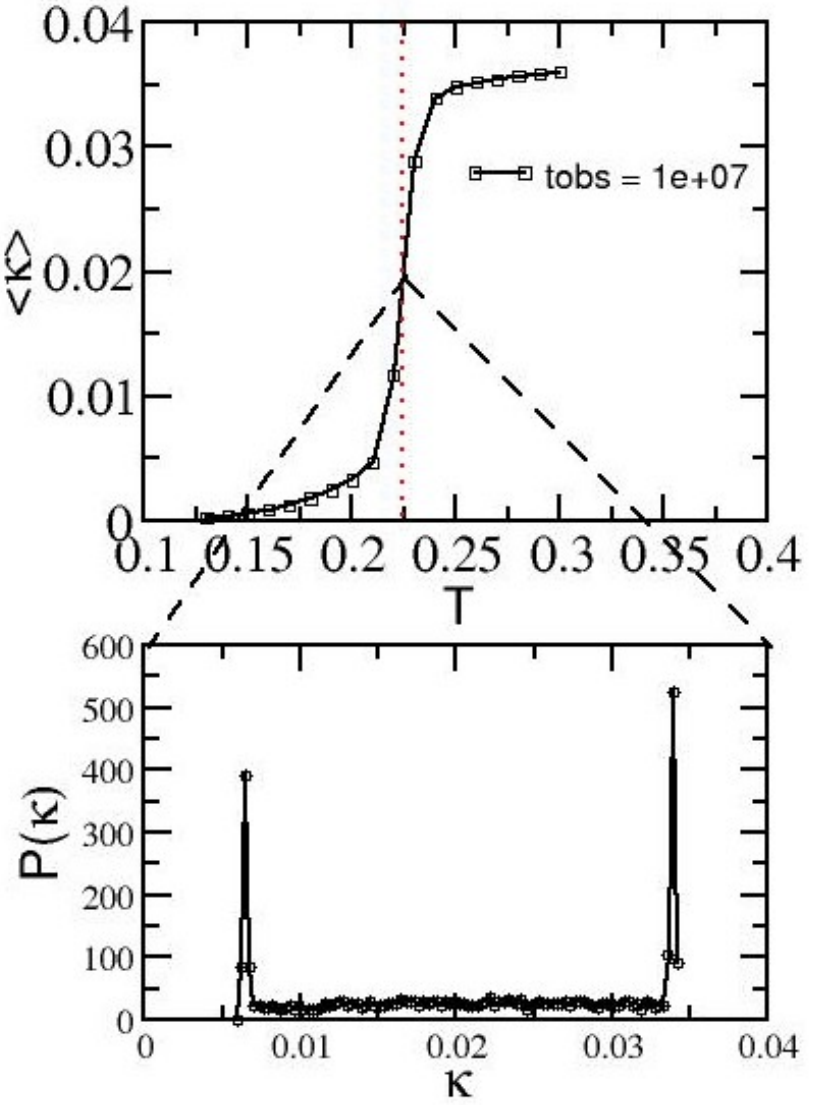
- Not a true transition, because the system is finite, finite size scaling breaks down, but the native state is very long lived.
- Correlation time > mean first passage time of the folded state





Extendin the transition

The statistical weight of each trajectory will be weighted according to s (a field introduced to the dynamical ensemble).

$$P[trajectory] \rightarrow P[trajectory]e^{-s\kappa}$$

S = 0 represents the original ensemble and is the only physically accessible ensemble.

Analogue to umbrella sampling:

$$P(x) = P_0(x)e^{-\beta H}$$

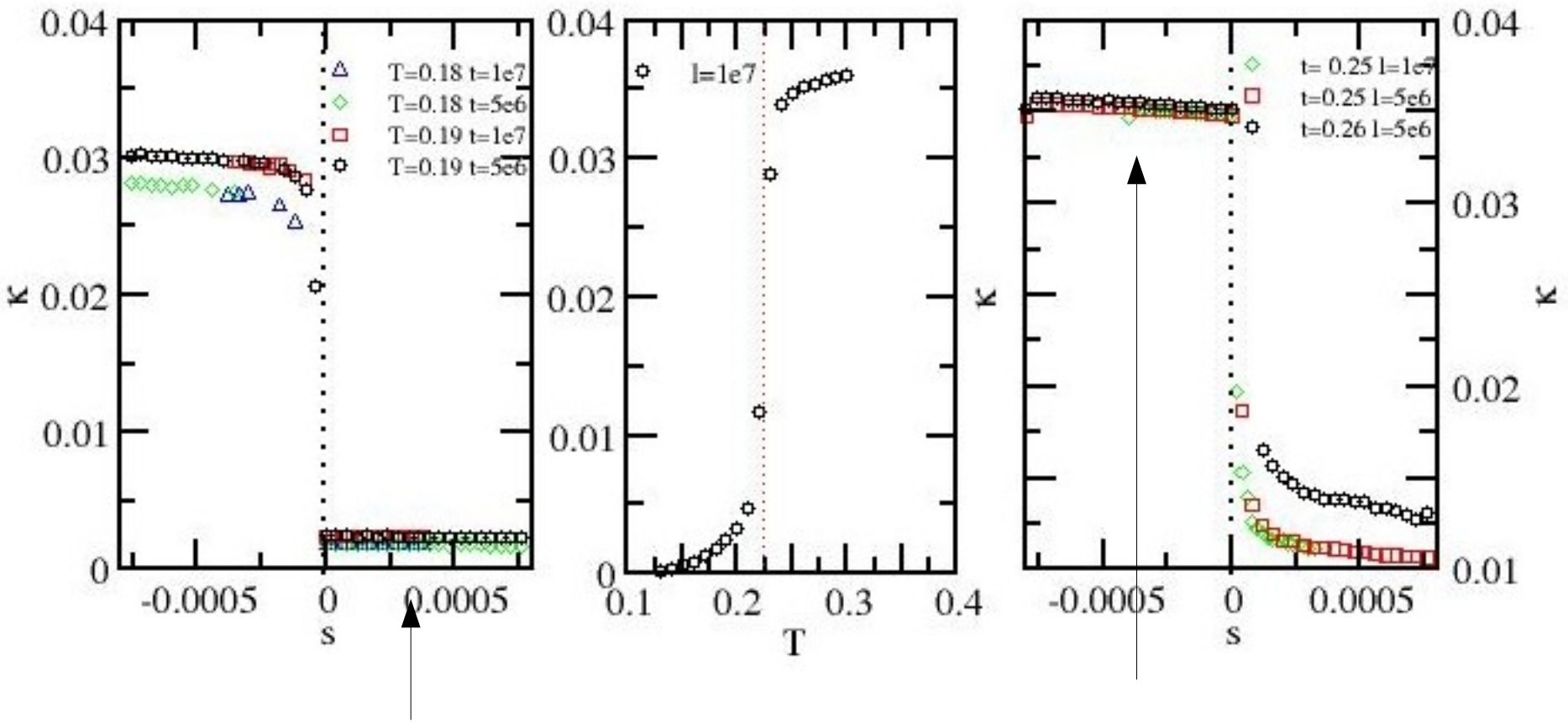
H is an external biasing potential.

$$P_s(x) = P_0(x)e^{-s\kappa}$$

κ is native activity

- Using transition path sampling techniques, the tails of the equilibrium native activity distribution can be sampled efficiently.
- s=0 reconstructs the equilibrium distribution
- The active inactive transition can be moved away from T_c using s.

Transition in s-ensemble



Equilibrium behaviour
Transition possible
with negative s

Transition to low
“activity” with positive s

Heterogeneous Results I

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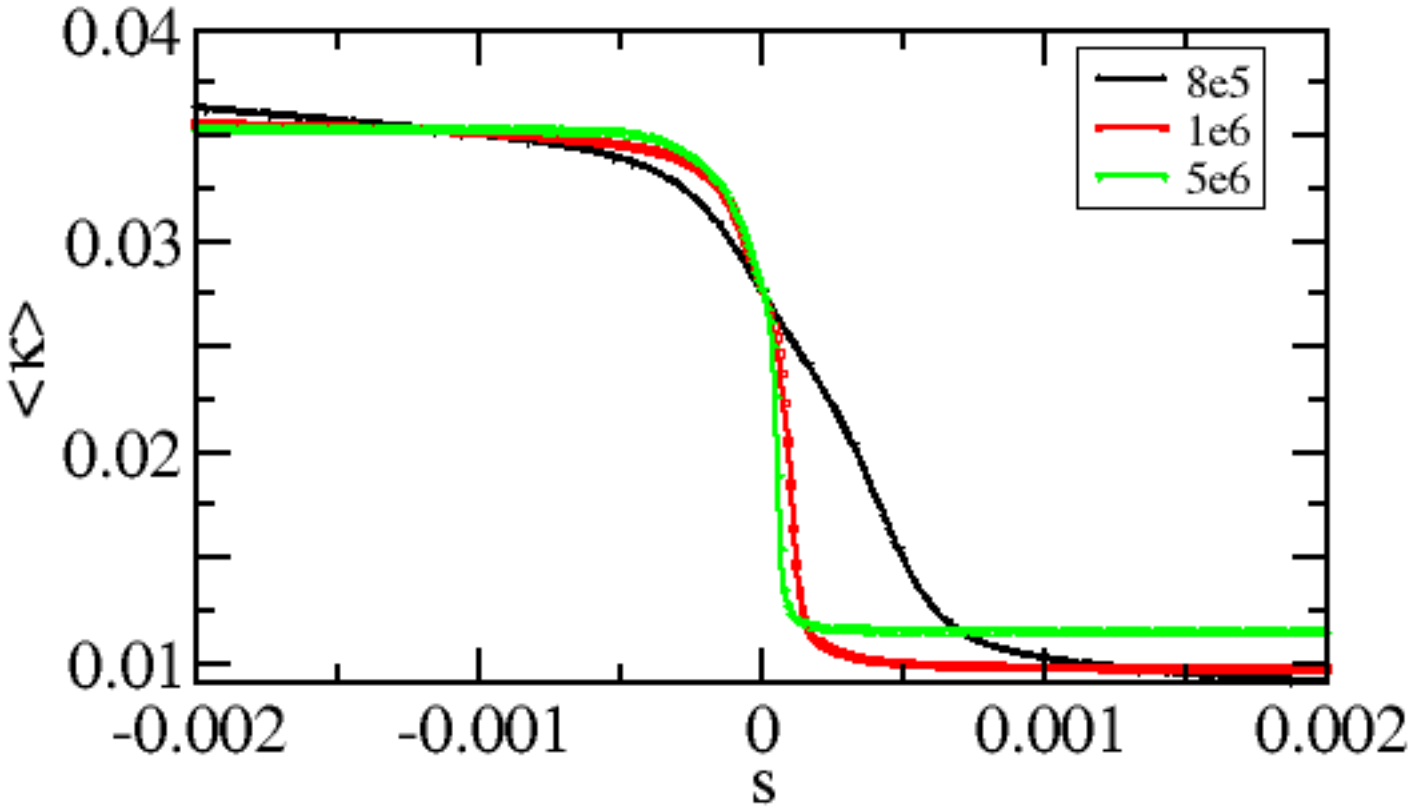
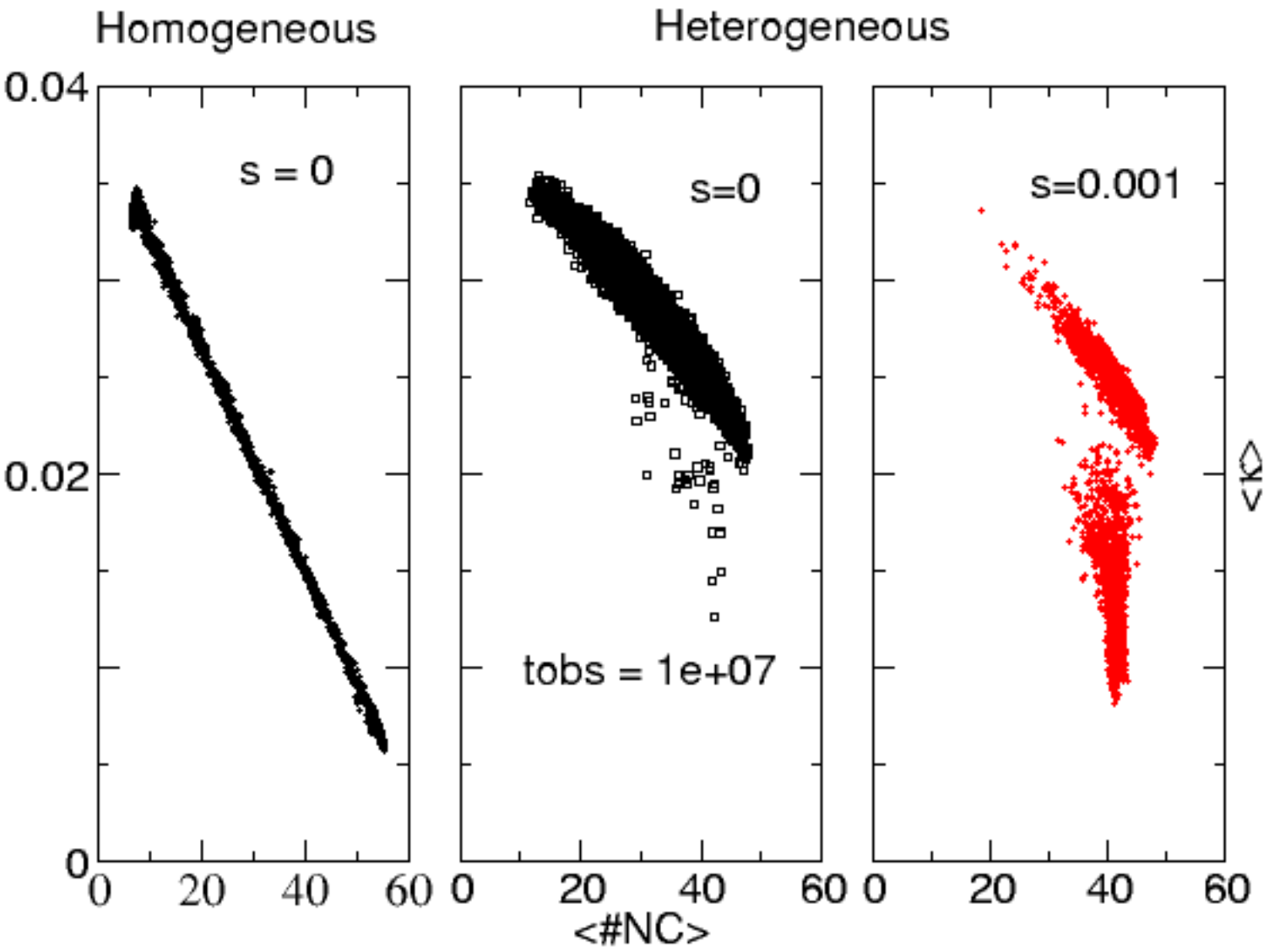
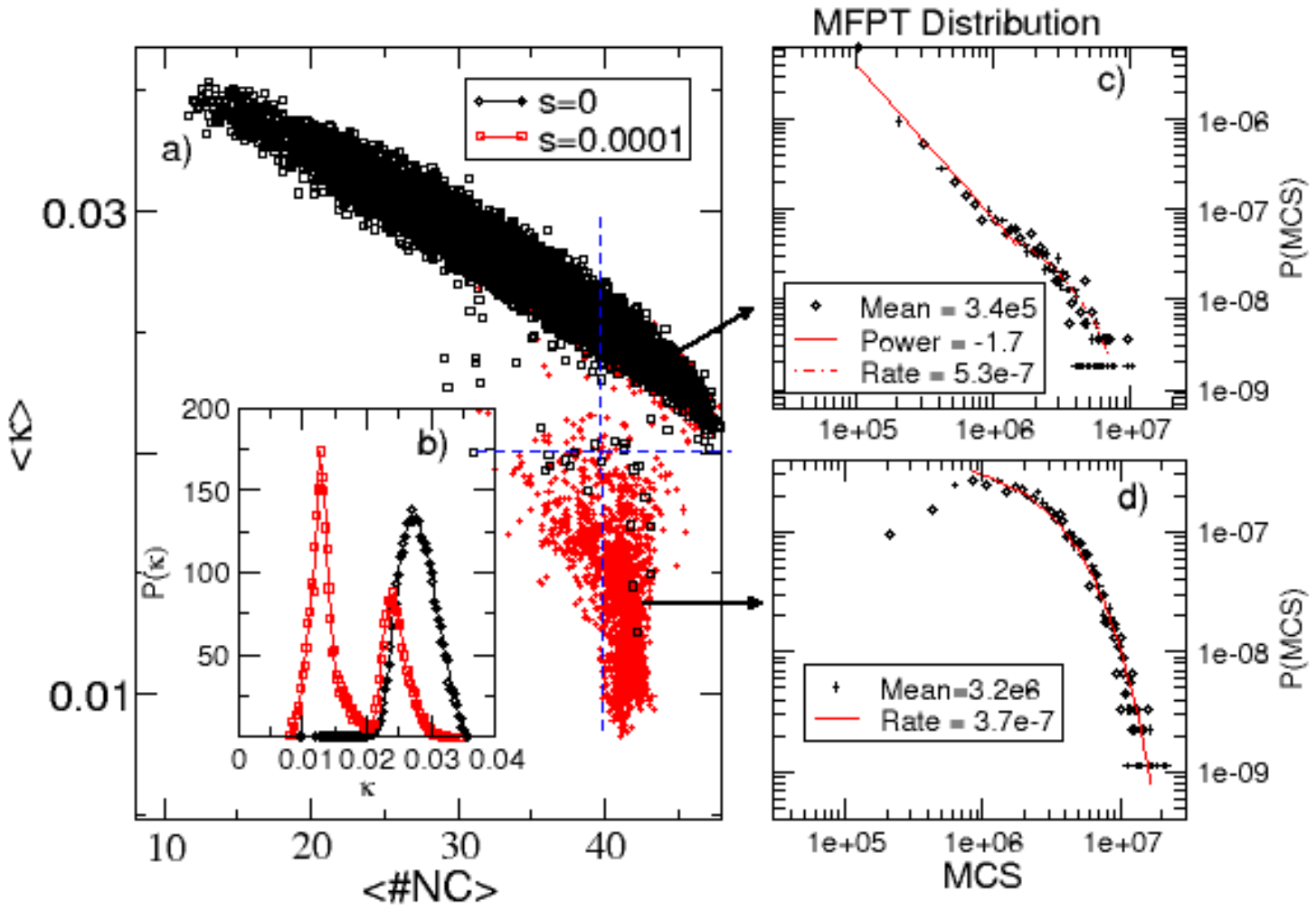
Finite size scaling with the observation time measured in Monte Carlo Steps larger than the first passage time of the system. First order like transition between active and inactive trajectories, consisting of representative conformations.



Heterogeneous Results II



Heterogeneous Results III



≠ Homogeneous

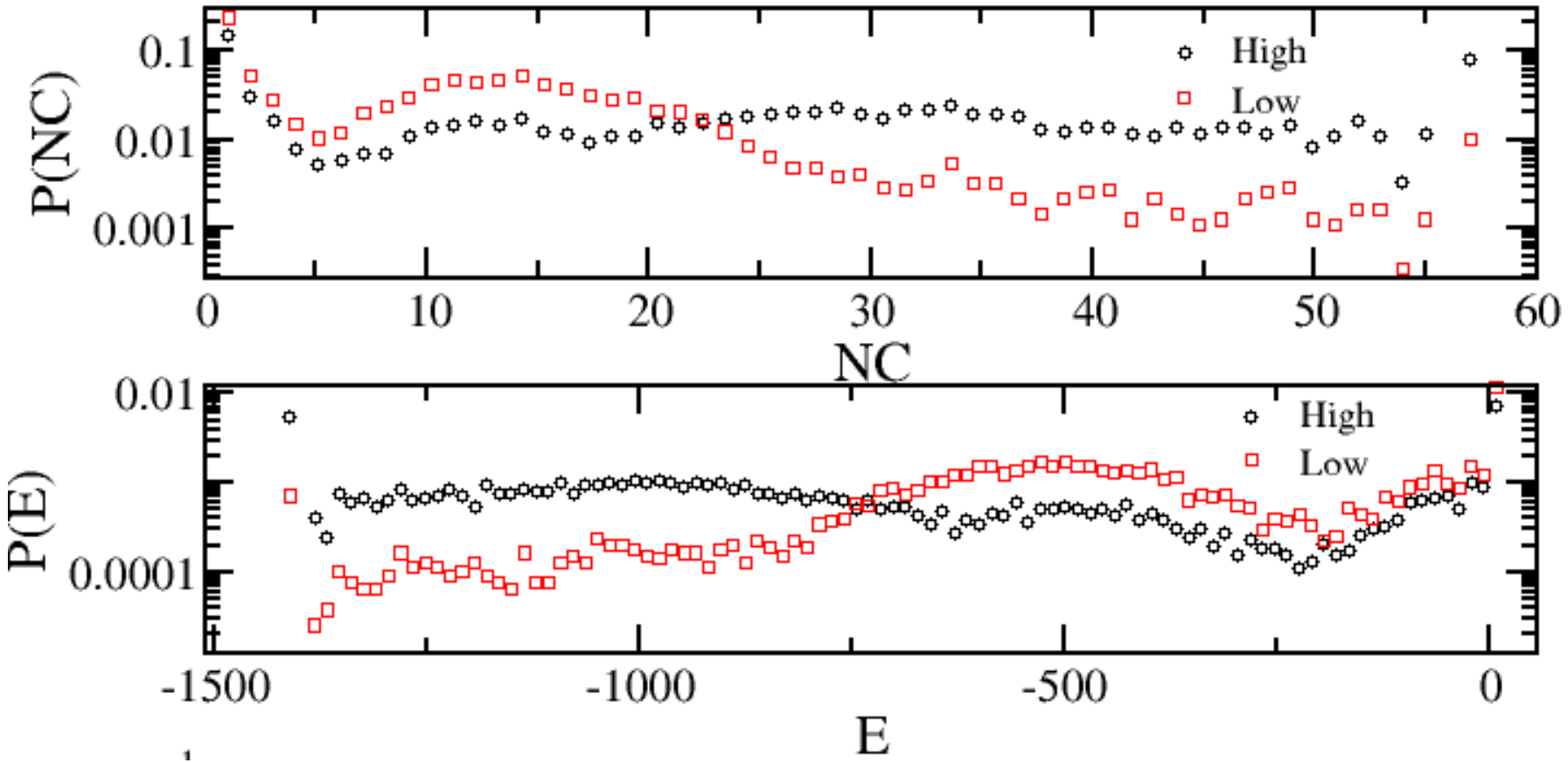
Transition is not between native and unfolded state

Nativeness and activity are no longer correlated.

Mean first passage times from each “phase” behave differently.

Low activity: trapping state

Heterogeneous Results III



Summary & Outlook

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- Dynamic first order like transition in lattice proteins found, **between active and inactive phases**
- Homogeneous models behave very differently from heterogeneous models:
- **Homogeneous:** native state very long lived, dynamic transition between native state and unfolded states
- **Heterogeneous:** native state much shorter lived, but reached more easily.

  Dynamic transition between **trapped states** and on folding pathway stats. Separation of time scales of trapped state & native state

- Extend the analysis to non-native interactions
- Choose different dynamic order parameter like the general activity of the system

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