Weekly Report

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1 Introduction

a. Used kinetic Monte Carlo simulation to sample transition-path trajectories on constructed 1-d free energy landscape models;

b. Calculated distribution of transition-path transit times, 1-d finite time displacements and transition path crossing based on Transition Path Theory and simulated data;

c. Discussed asymptotic properties for free energy landscape with high frequency intermediate barriers, and possible relationship with protein folding transition path statistics.

2 Progress

2.1 One-dimensional free energy landscape

To evaluate transition path statistics for free energy landscapes with intermediate barriers, following toy free energy models were constructed (Figure 1). For all of these models, maximum barrier height $\Delta F = 5.37kT$.

2.2 Transition-path transit time distribution

Ultilizing Kinetic Monte Carlo simulation for above-mentioned 1-d discrete states models, we sampled 10000 transition-path trajectories and calculated distribution of transition-path transit times $p(t_{AB})$ for each model landscapes (Figure 2).

The apparent force constant of the barrier ω was determined by fitting the decay constant ω^{-1} of the exponential tail($p(t_{AB} > 1.5)$); barrier height ΔF was then determined by fitting theoretial expression of $p(t_{AB})$ to simulated distribution of transit times. We demonstrated that even for the harmonic landscape, deviation from theoretial expression for parabolic barrier

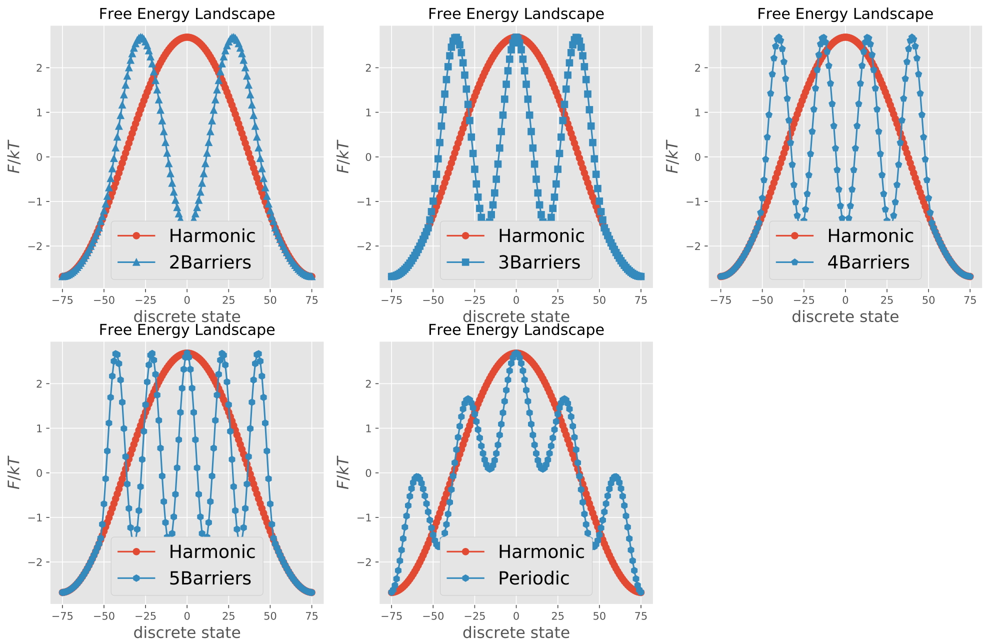

Figure 1: Model free energy landscapes.

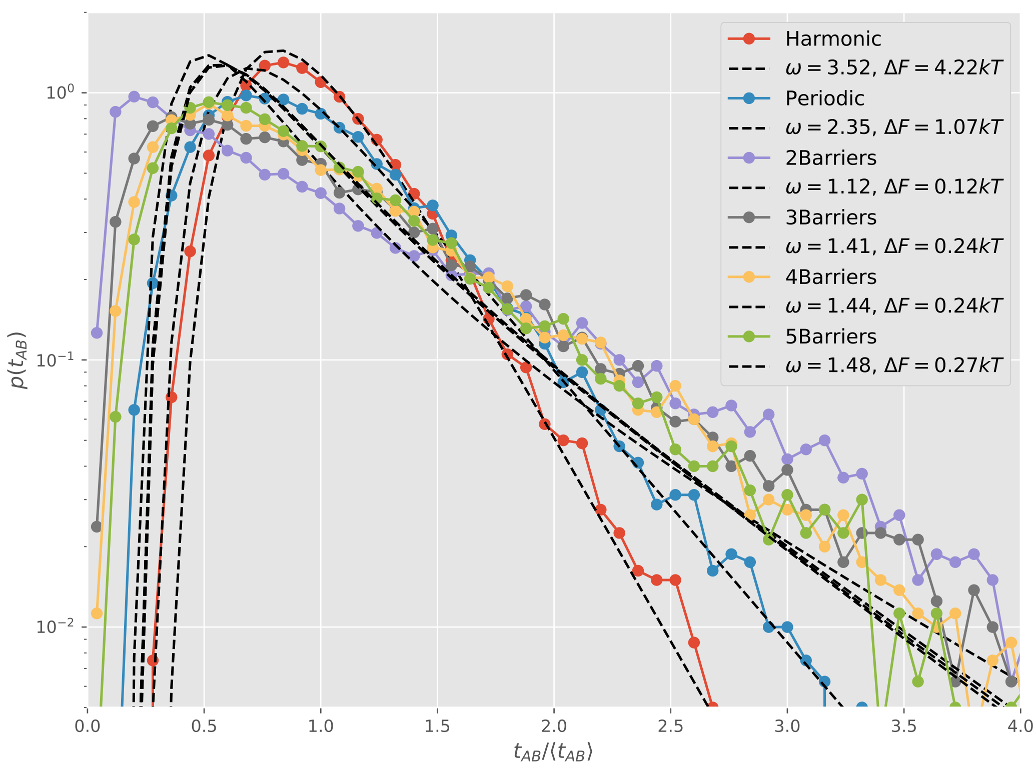

Figure 2: Transition-path transit time distribution.

crossing is non-negligible; for multi-harmonic barriers model, significant deviation from theoretical distribution was observed, resulting in much smaller and relatively unphysical fitting result for barrier height ΔF.

Interestingly, it appeared that $p(t_{AB})$ of 2Barriers model showed the most significant deviation to the harmonic model; the peak shifted to larger t_{AB} when more intermediate barriers were added.

2.3 Finite time displacement distribution

We also calculated the distribution of finite time displacement as a 1-d collective variable (Figure 3). 'Fat tail' behavior for multi-barriers models is more significant than the periodic model; when more intermidate barriers is added, a second peak emerged near the main gaussian peak, and the distance between main and the second peak is comparable to distance between intermediate barriers.

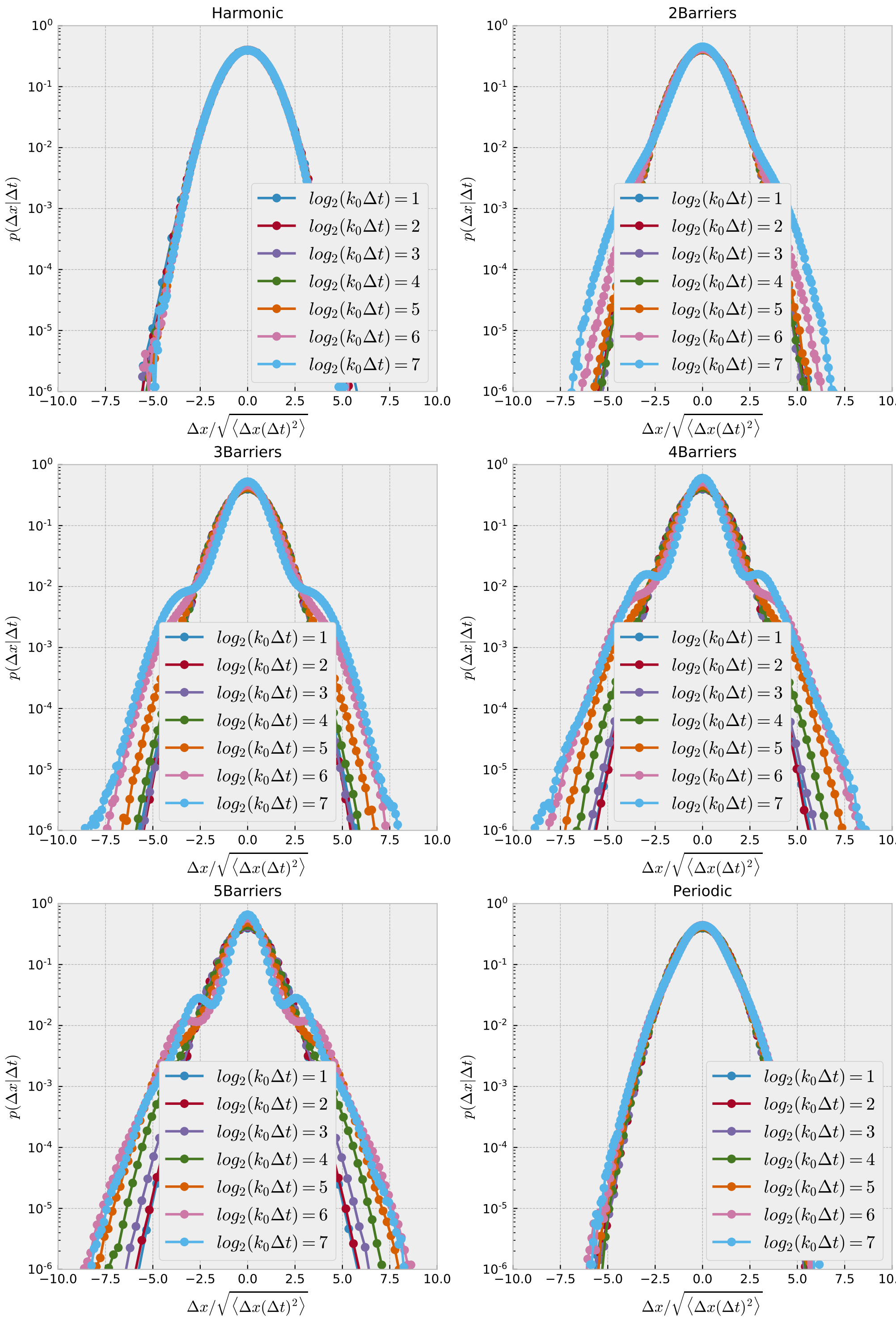

Figure 3: Distribution of finite-time displacements.

2.4 Transition path trajectory crossing probability distribution

As a second test, I also calculated the probability density $P(TP|x)$ that an arbitrary trajectory crossing state x is a transition path trajectory(Figure 4) based on distribution of steady state probability and committor distribution; for two barriers model, a constant plateau emerged near the barriers region, which could be attributed to barrier recrossing due to stabilizing effect of the intermediate free energy well; however when more intermidate energy well was introduced, stepwise falling of $p(TP|x)$ was observed.

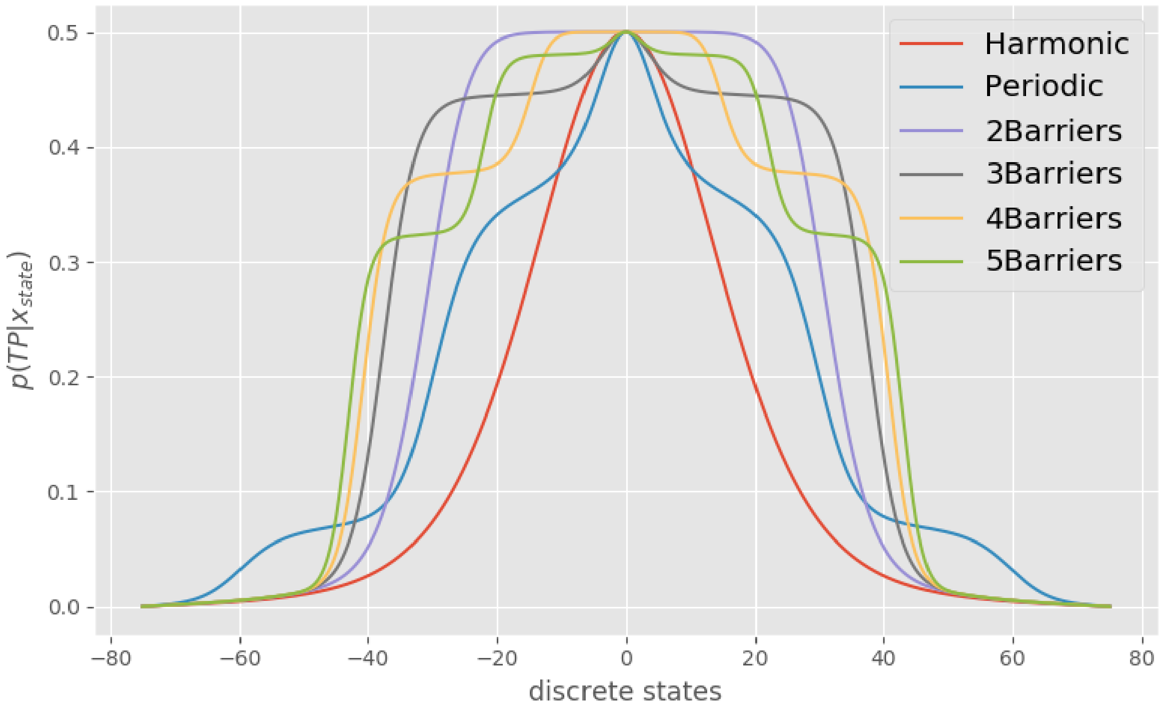

Figure 4: Probability distribution for transition-path trajectory crossing.

To find a physical explanation for the shapes of $p(TP|x)$ and $p(t_{AB})$, we assume that intermediate free energy wells could be treated as coarse-grained states, and when infinite number of barriers is introduced, the whole free energy landscape could be reduced to asymptotic landscape of discrete CG states, meaning that time scale of high frequency oscillation and intermidate barrier crossing is well separated. For the cases of finite intermidate free energy wells, it's possible that the 'coupling' between oscillation at local free energy minimums and global barrier crossing is non-negligible, causing large deviation of $p(t_{AB})$ to theoretical distribution.

To preliminarily test this assumption, we constructed a model free energy landscape with 50 intermediate barriers('Highfreq'), as well as a 'flatted' harmonic model in which $\Delta F = 1.34kT$

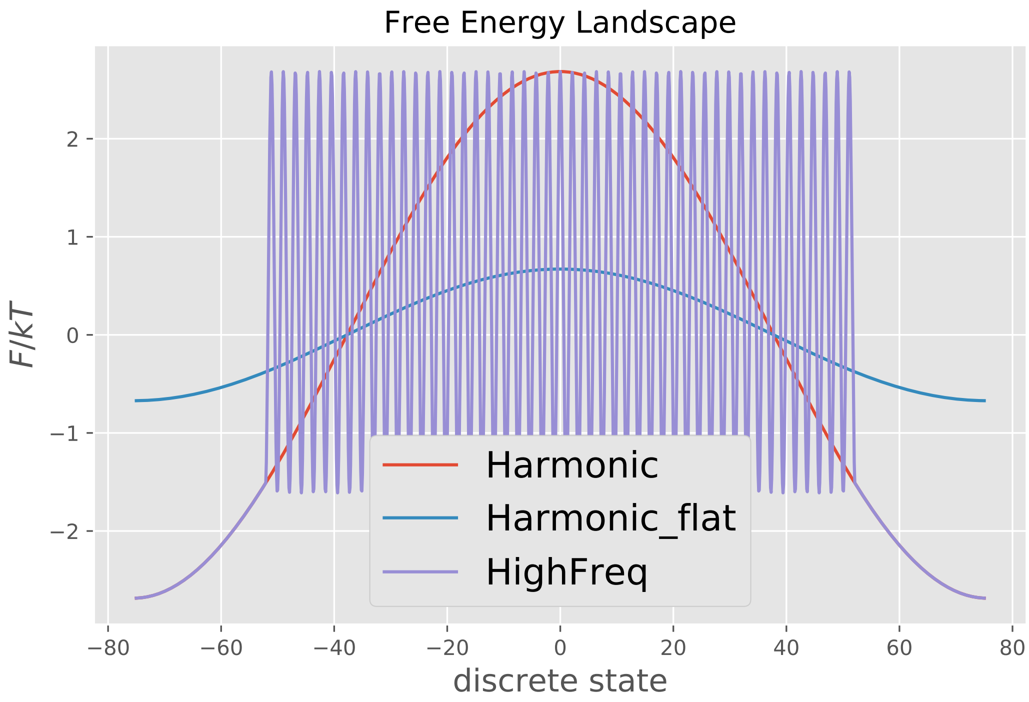

Figure 5: Toy free energy landscapes for harmonic model, high frequency model, and flatted harmonic model.

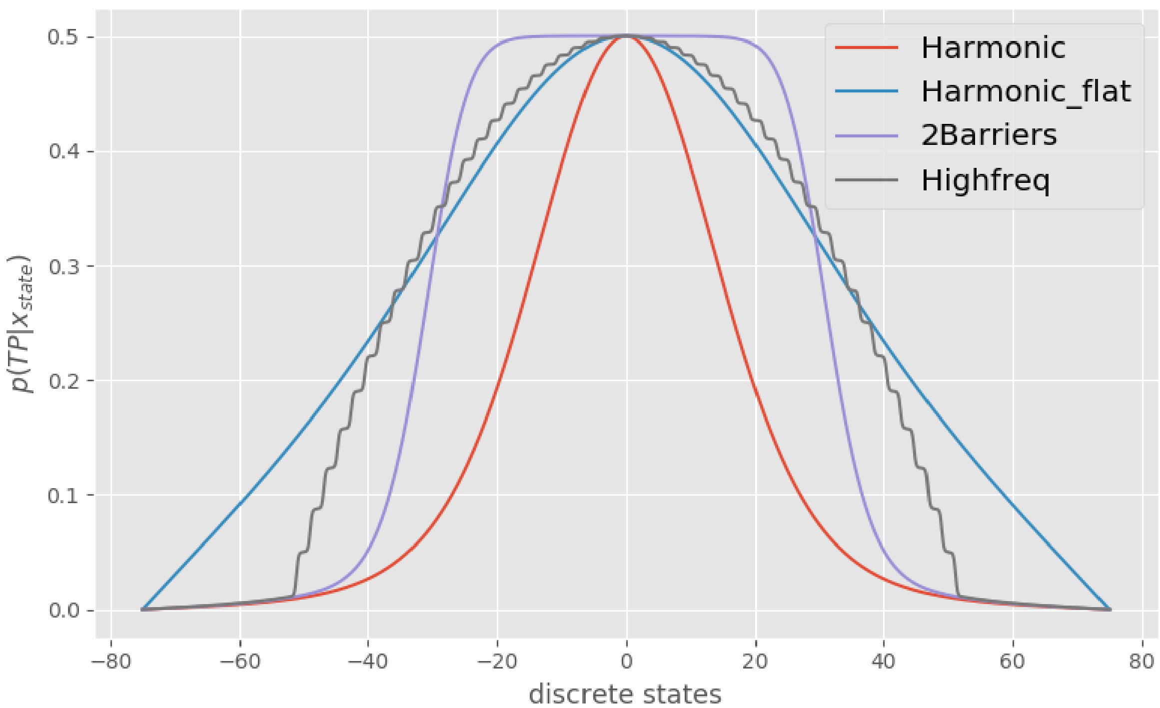

Figure 6: Comparision of $p(TP|x)$ for harmonic, flattened harmonic, 2 barriers and high frequency barriers free energy models.

(Figure 5). I repeated $p(TP|x)$ calulation for these models (Figure 6), and the result showed that the distribution of $p(TP|x)$ of high frequency model strongly resembled the flatted harmonic model near the barrier region, indicating well separation of time scale for the high frequency free energy landscape model.

That result is probably important for giving explanation to the fact that protein folding transition-path statistics can be described by one-dimentional coordinate, but the empirical ΔF is much lower than real barrier height.

3 Future plan

a. KMC sampling for transition paths on high frequency model and flattened harmonic model is required to further test the assumption in 2.4, which can be finished on next week; larger scale simulation is also needed to refine transit time distribution data.

b. Deciding future proposal for synonymous codon usage project.

References