Weekly Report

Zhuoran Qiao

July 14, 2018

1 One-dimensional free energy landscape

To evaluate transiton path statistics for free energy landscapes with multi intermediate barriers, following toy landscapes were constructed(Figure 1). Free energy difference between source/sink and barrier top is $5.37kT$.

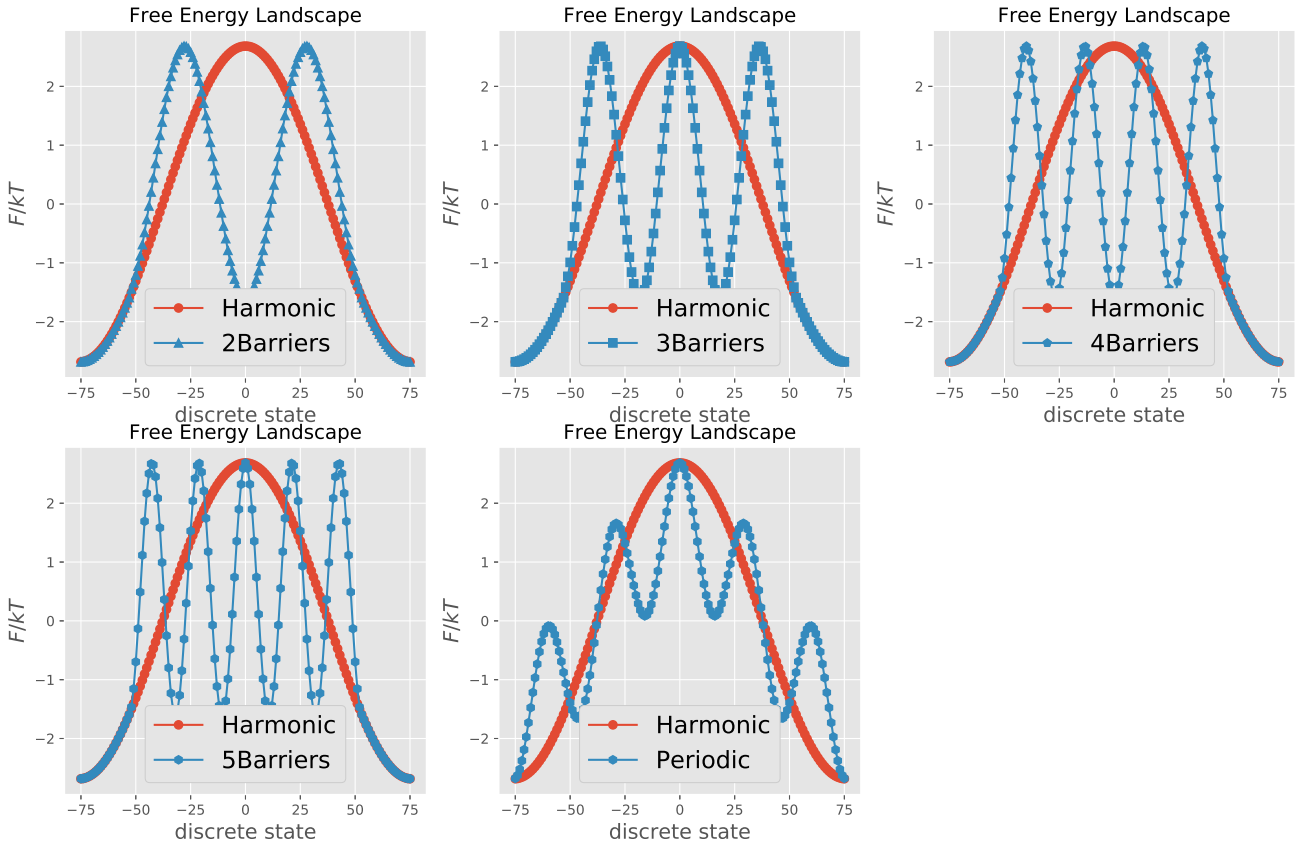

Figure 1: Model free energy landscapes.

2 Transition-path transit time distribution

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

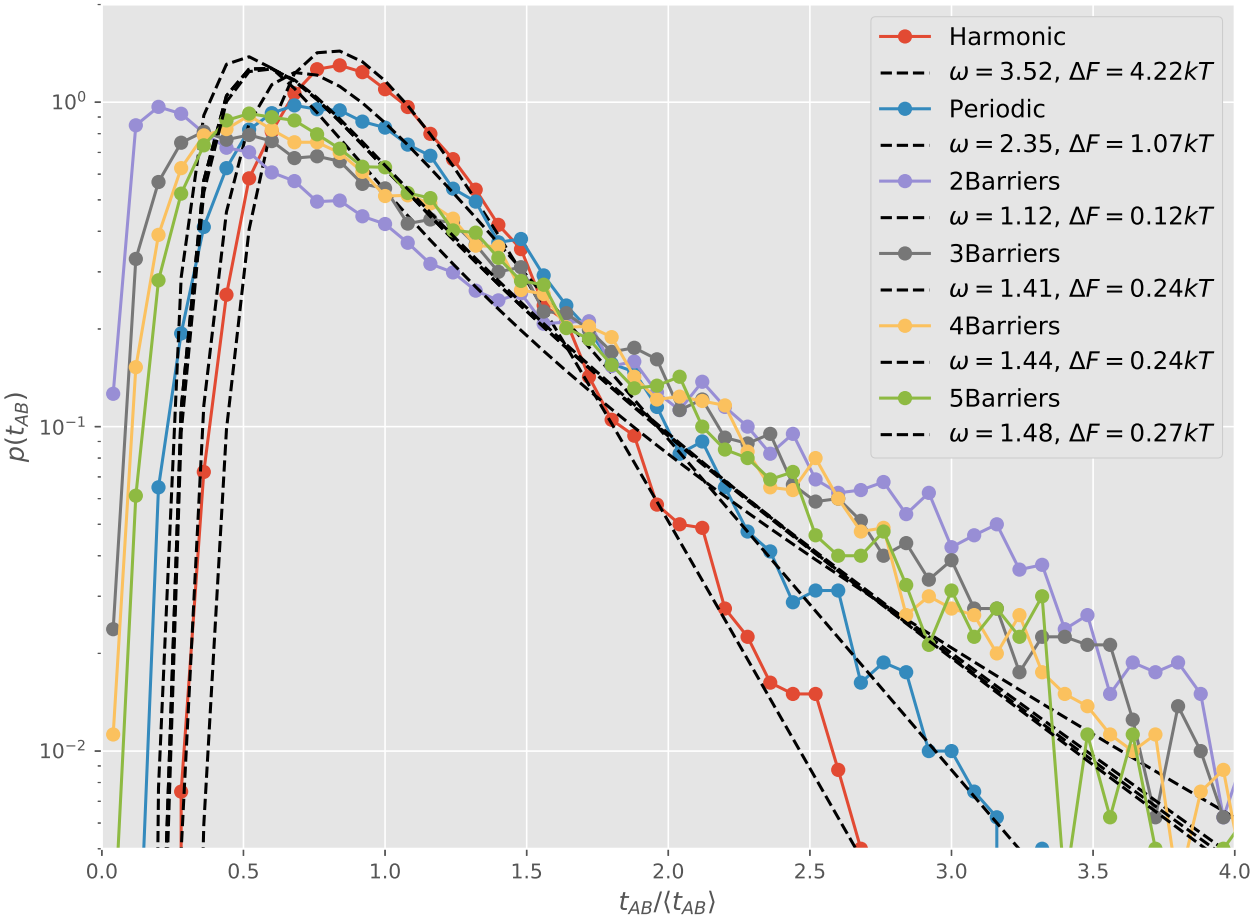

Figure 2: Transition-path transit time distribution

For each transit time distribution, the apparent force constant of the barrier ω was determined by fitting the decay constant ω^{-1} of the asymptotic 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 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 the harmonic model; the peak shifted to larger t_{AB} when more intermidiate barriers is added. As a second test, I also calculated the probability density $P(TP|x)$ that an arbitrary trajectory crossing state x is a transiton path trajectory(Figure 3); 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 intermidiate free energy well; however when more intermidate energy well was introduced, stepwise falling of $p(TP|x)$ was observed.

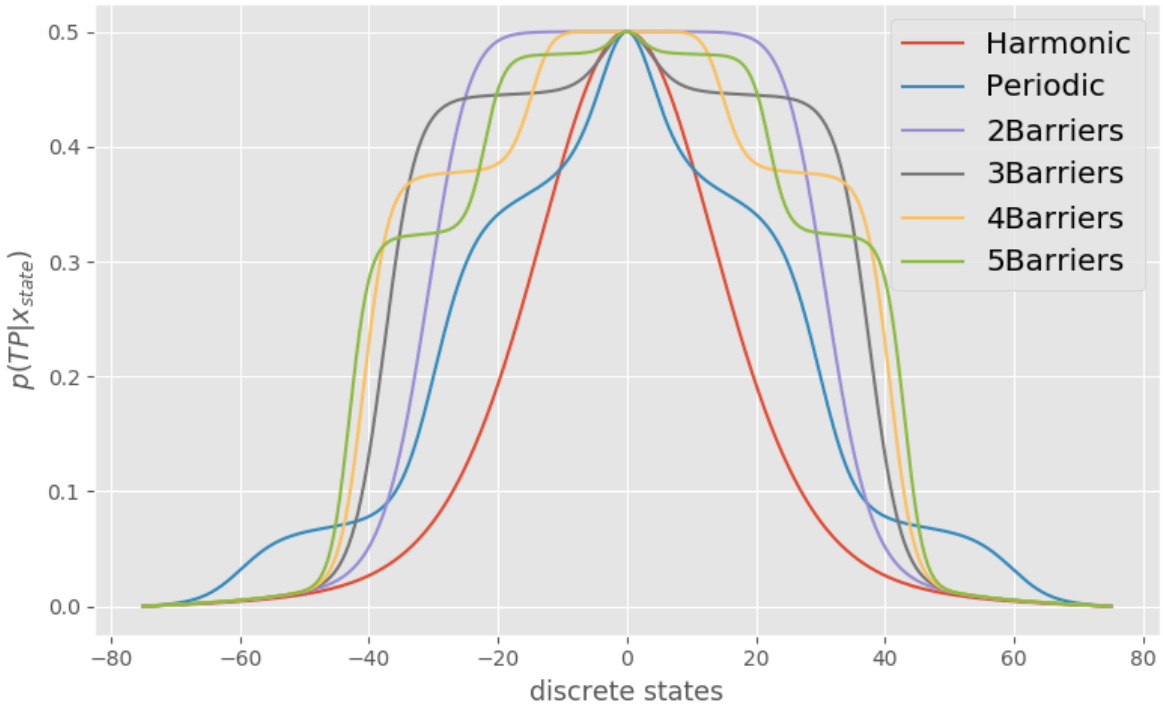

Figure 3: Probability distribution for transion-path crossing.

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 barriers is introduced, the whole free energy landscape could be reduced to 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 100 intermidiate barriers('Highfreq'), as well as a 'flatted' harmonic model in which $\Delta F = 1.34kT$(Figure 4). I repeated $p(TP|x)$ calulation for these models(Figure 5), and the result showed that the distribution of $p(TP|x)$ of high frequency model strongly resembled to the

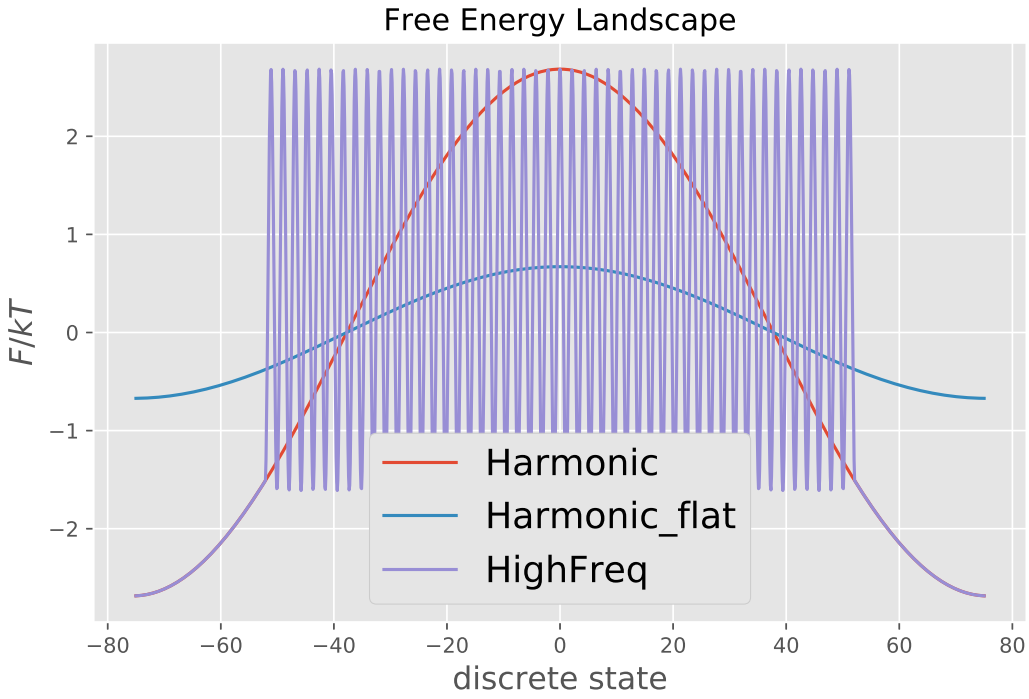

Figure 4: Toy free energy landscapes for harmonic model, high frequency model, and flatted harmonic model.

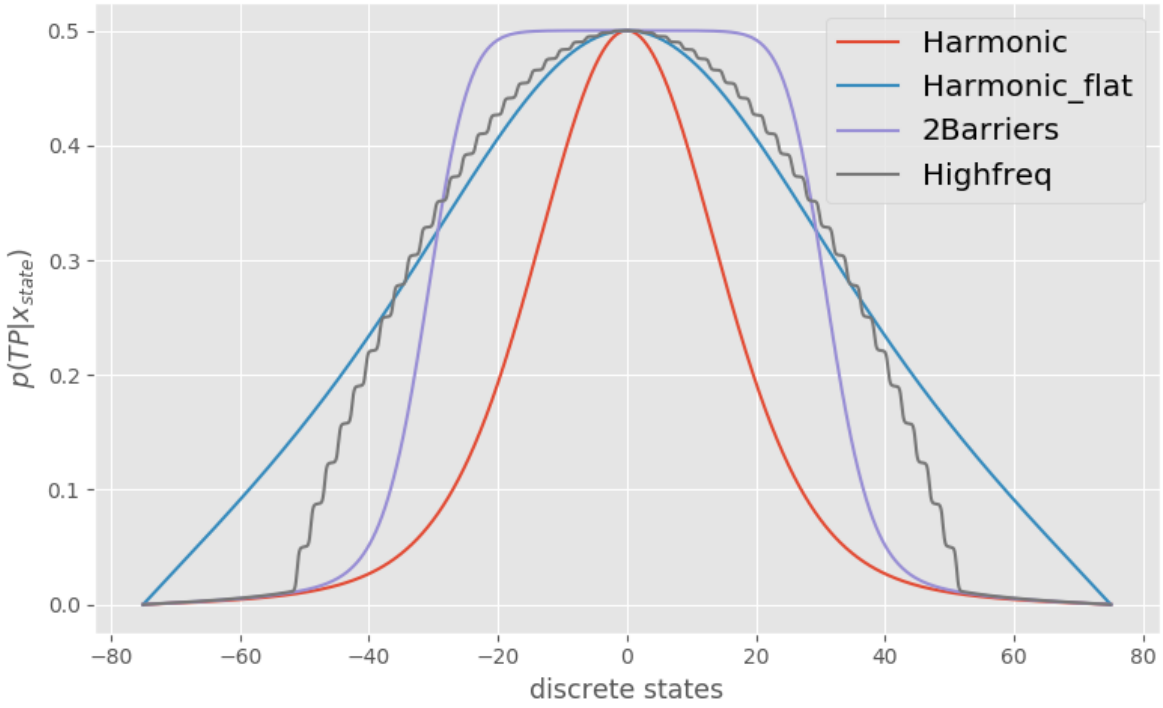

Figure 5: Comparision of $p(TP|x)$ for harmonic, flattened harmonic, 2 barriers and high frequency barriers free energy models.

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. We also need KMC sampling of transition paths on these models to further test this assumption, which can be finished on next week.

3 Finite time displacement distribution

In order to examine when the one-dimensional coordinate projection could be recognized as effective reaction coordinate, we then examine the probability distribution of committors for transition path trajectories $p(q|TP)$, for which a single peak of probability $p(q|TP)$ have been ultilized as a indicator for 'good' reaction coordinates. Firstly, We found that for harmonic toy model, the shape of $p(q|TP)$ is very sensitive to the definition of source/sink region. For illustration, $p(q|TP)$ for two different selection of source/sink regions was compared: in the first case, only two free energy minimum was indentified as source or sink**(S1)**; in the second case, only the barrier top was defined as the transition path, while other two region of the free energy landscape was calssified as source/sink**(S2)**.

local linked

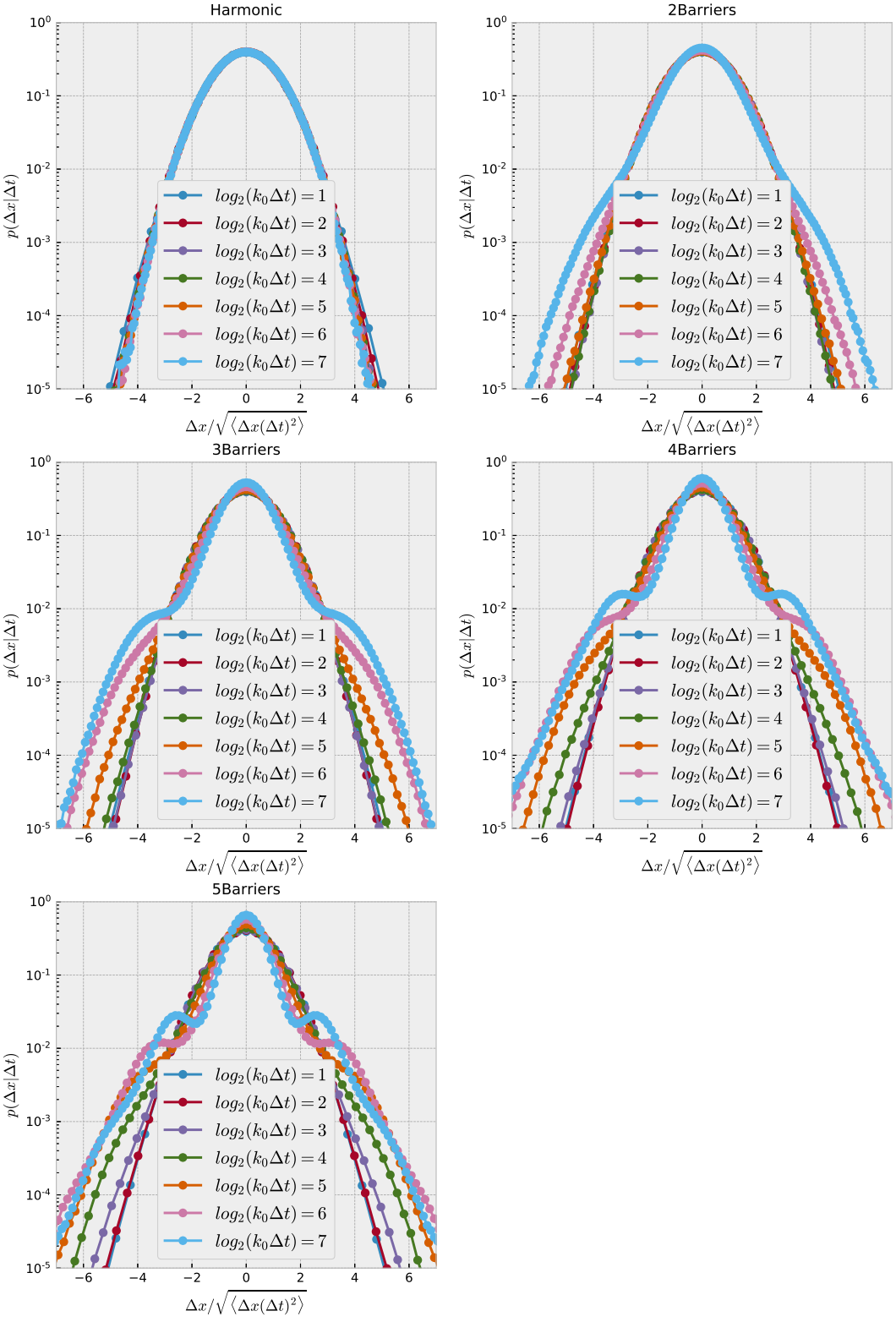

Figure 6: Distribution of finite time displacements.