

# Notes on sampling discussion

- Can we make sure we are tied to statistics? Optimal methods
- Standard methodological challenges?
- Standardize input formats
- Type of X depends on type of problem.
- Different toy sets?
- Need metric of success for given problems. Benchmark runs ones had confidence in?
- Standardized methods of efficiency. Consensus calculation result. 2015 haswell. Force evaluations vs potential evaluations as measure of efficiency.
- How much more is an accurate sample worth than less accurate sample?
- Really good sampling could escape from metastable states that are actually important.
- Important to define what you need to sample.
- Problem with toys: something that can be enumerated, but good methods for that size problem might not scale.
- Pathological cases:  $K_{on}$  and  $K_{off}$ .
- Some work on reconstructing kinetics, but MUCH further behind than reconstructing thermodynamics.
- Host-guest: good enough?
- What do we need for them?
- What are the toy systems for sampling?
  - List of prioritized toy systems.
- System where you can get a gold standard result. How well can you reproduce that ensemble. How close can you get to the converged result. Should have the same "features" but what are they?

# Notes on sampling discussion

- Question that comes up again and again?
  - Do I do repeated simulations?
  - Do I do one long one?
- Test systems for sampling methods: need them to be simpler.
- Ask separately: how quickly can the faster methods converge
- Now lets take what we learned and apply it to the appropriate method.
- Model test systems have to be simple enough that we KNOW THE RIGHT ANSWER.
- Sampling challenge: a while before a protein represents a gold standard system (because we can't compute the right answer).
- Distribution of barrier heights. Series the same height. Free energies of minima the same. How fast to homogeneous distribution.
- Torsional barrier system, independent torsions. All minima have same free energy?
  - Cyclic polymer?
- Can we explicitly put in entropic bottlenecks?
- Lots of parameters in most methods, makes comparisons hard.
- Better to have analytical potentials (have to do a separate implementation) or molecular examples (ala dipeptide)?
- 1 ms BPTI: still finding new things to do!

# Todos

- Decide on set of toy systems to test sampling.
  - Bernie Brooks tried to start something like this 4-5 years ago, nobody participated.
- Default parameters: common release of parameter stating how do we know what will work?
- Something like D3R? Omnia MD with all methods implemented for comparison?