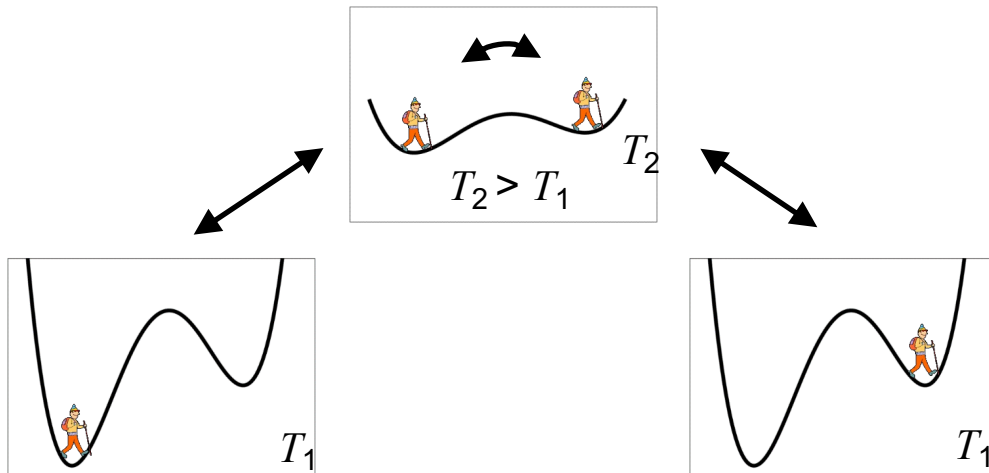# Enhanced sampling with TSS

- Times Square Sampling (TSS) is an enhanced sampling approach related to simulated (Hamiltonian) tempering
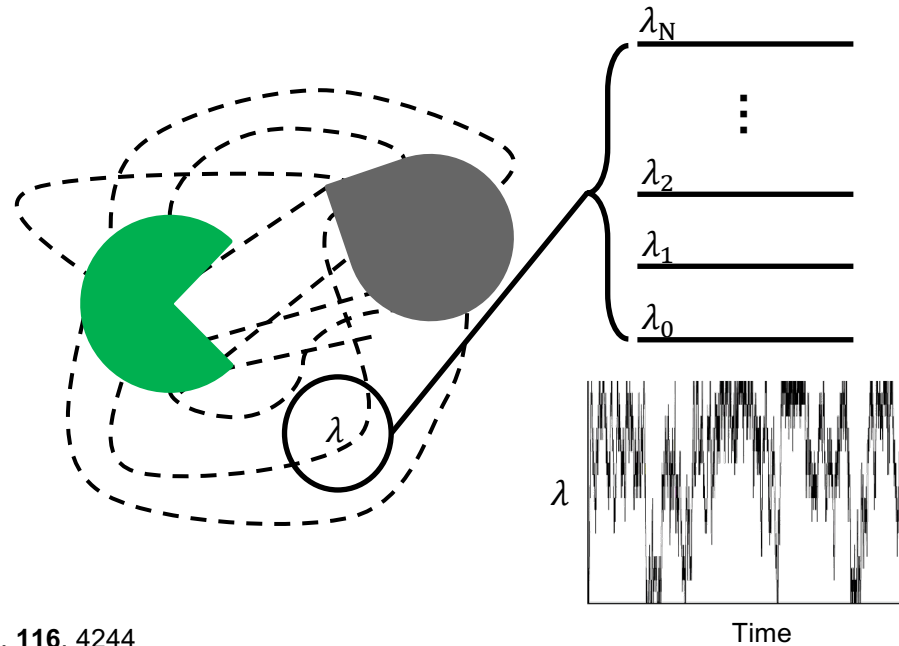- TSS has built-in online free energy estimators

Times Square Sampling: An Adaptive Algorithm for Free Energy Estimation

Cristian Predescu, Michael Snarski, Avi Robinson-Mosher, Duluxan Sritharan, Tamas Szalay & **David E. Shaw** ✉
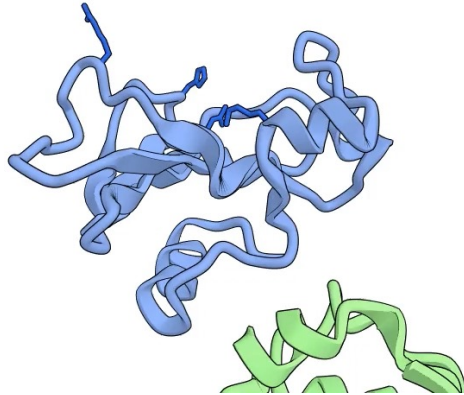
https://github.com/DEShawResearch/tss

D E Shaw Research

Tempered binding

Tempered binding speeds up escape from metastable traps
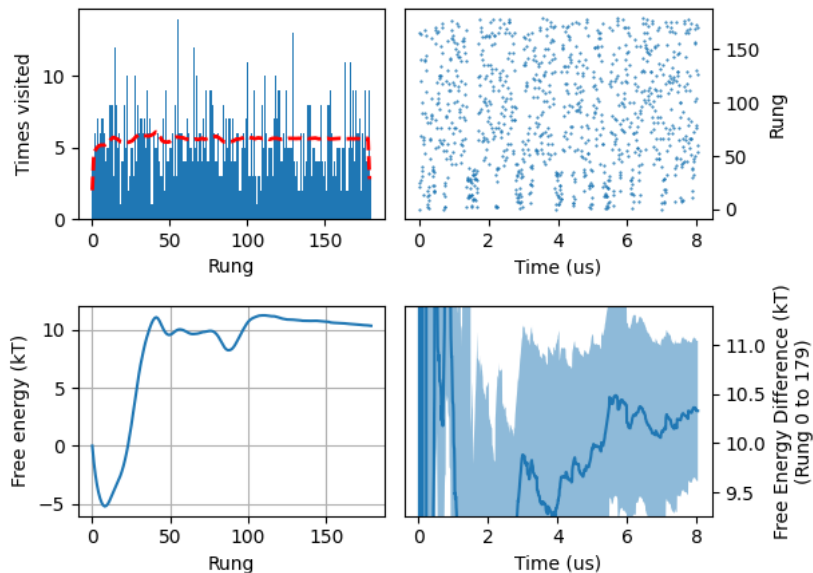
0.0 µs

Available forms of enhanced sampling

1. Simulated tempering (temperature tempering with adaptive weighting)
2. Tempered binding
3. Restraints between centers of mass of groups of atoms
4. Conformational restraints based on the calculation of the RMSD (root mean squared deviation) of a group of atoms with respect to the positions of a given reference structure

For restraints in (3) and (4), equilibria and spring constants can be varied during a simulation either according to a schedule or controlled adaptively by TSS to implement a form of umbrella sampling

Analyzing enhanced sampling runs

https://wiki.psc.edu/twiki/view/Anton/a2docs/proj/desres/doc/build/html/adaptive_enhanced_sampling.html

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Survey

https://forms.gle/ovFRm8rkLPjCe81c7