Refs: Ch. 16 in F+S

Bolhuis et al., Annu. Rev. Phys. Chem. 53:291:318 (2002)

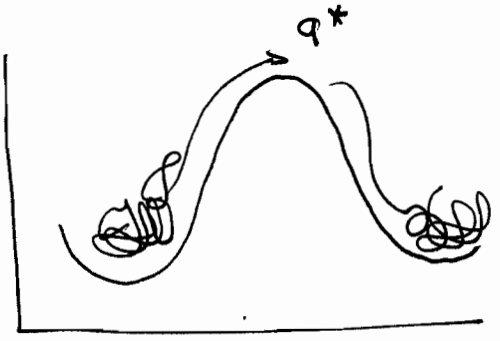
Erp + Bolhuis, J. Comp. Phys. 205:157-181 (2005)

Rare Events / Activated Processes

Maximum MD time scales for atomistic simulations

$\sim 10^{-7}$ s (100 ns)

Many processes have activated dynamics - systems spend a lot of time on one side of barrier, but once they reach it, transition to other state is quick



"reaction coordinate" q

Examples: conformational (cis/trans) transitions

diffusion in glassy matrix

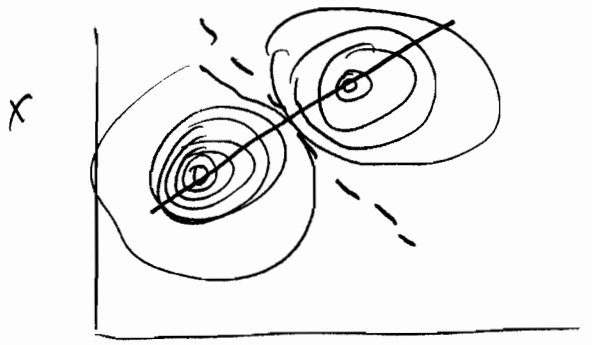
protein folding?

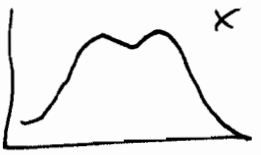
$$\text{Rate} = \left\{\begin{array}{l}\text{Probability of finding}\\ \text{system at top of}\\ \text{barrier, } q = q^*\end{array}\right\} \times \left\{\begin{array}{l}\text{Rate at which}\\ \text{Systems at}\\ q^* \text{ cross to}\\ \text{other side}\end{array}\right\}$$

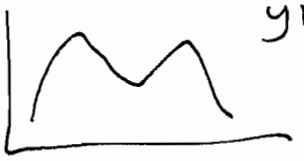
↑ Can be very low if barrier is high

↑ allows for "recrossing" - systems can slide back

Key difficulty: In realistic systems with many degrees of freedom + solvent, appropriate "reaction coordinate" is not known (and may be very complex)







true

example in 2D

Solutions: A. Parallel Replica Dynamics

B. Transition Path / Interface Sampling

Parallel Replica Dynamics

A.F. Voter, Phys. Rev. B 57:13985-88 (1998)

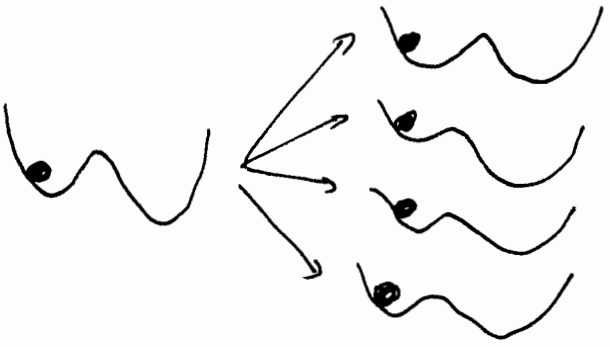
Only assumption : rare events obey exponential decay (1st order) kinetics

{Probability of system remaining in initial state after time t} $P(t) = \exp(-kt)$

e.g. protein folding $k \sim \frac{1}{ms}$ $t \to 0$ $P(t) \to 1$

$t \gg \frac{1}{k}$ $P(t) \to 0$

How do we probe ms time scales with simulations of O(10's ns) ? → Run many replicas in parallel; each has small prob. of observing transition.



Step 1 : replicate initial state into M copies ($M \gg 1$)

Step 2 : Run each copy separately -

- until a transition is observed on one processor i :

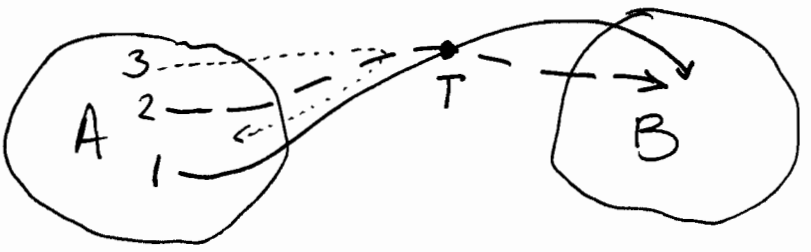
Increment time by $t_{sum} = \sum_{j=1}^{M} t_j$;

Step 3: Replace all replicas by configuration i, continue simulation (for multi-step transitions).

Transition Path Sampling:

"Throwing Ropes over Rough Mountain passes, In the Dark"

key Idea: Importance Sampling in Trajectory Space



* Stable, long-lived, well characterized ensembles of states A and B (not always easy)
* Start from arbitrary trajectory 1 that connects states A and B (may need to initialize near barrier and integrate forward/backwards in time)
* Perturb trajectory 1 at random time slice (e.g. by changing momenta). Generate trajectory 2 by integrating backwards/forward in time

{We cannot perturb just the initial conditions of trajectory 1 because most likely the resulting trajectory will not end up in B}

Accept/reject new trajectory as part of the ensemble if it starts at A and ends at B, with probability

$$\mathcal{P} = \min\left\{1, \frac{N(n)}{N(o)}\right\} \left[= \min\left\{1, \exp(-\beta \Delta u)\right\}\right.$$

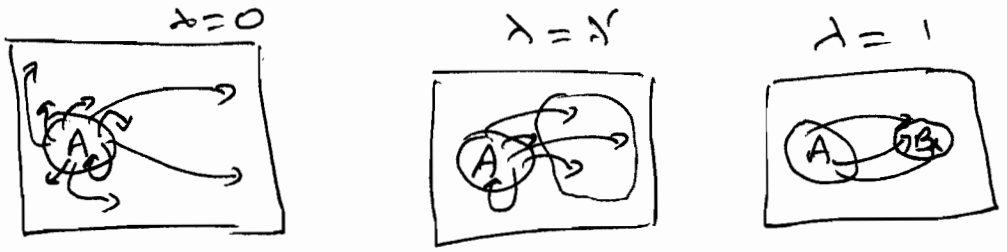
(Δu is for momentum change)

The "densities of states" $N(n)$, $N(o)$ for the new and old trajectories depend on the dynamical evolution rule and the initial and final configurations (see Bolhuis review)

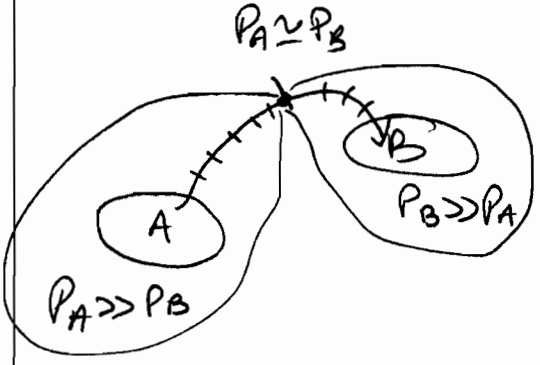
Trajectory 3 (generated from perturbation of trajectory 2) is rejected because it starts + ends in A.

Initial Trajectory

The generation of a plausible initial configuration can be done by use of a step-wise process to narrow down the area in configuration space:



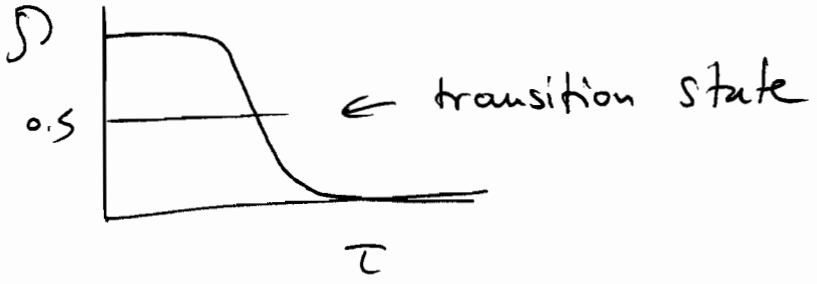
Constructing transition States Surface



Along trajectory from A → B

"Commitor" function

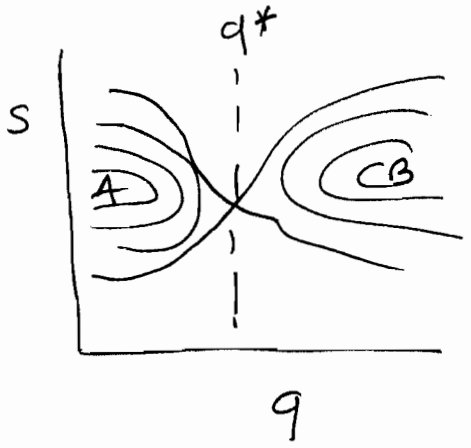
$\wp$ gives probability of perturbed trajectories to return to A

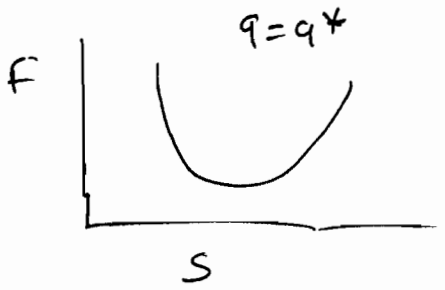


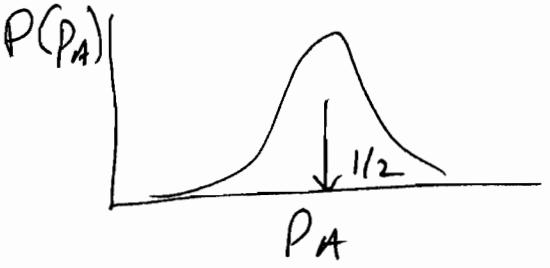
Order parameters vs reaction Coordinates

Even with transition path sampling, it is not easy to identify "good" reaction coordinates — but at least one can diagnose situations with "bad" choices / a mismatch between the chosen order parameter to split states into A and B and the true (relevant)

reaction coordinates.

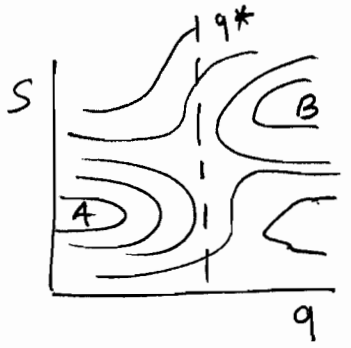


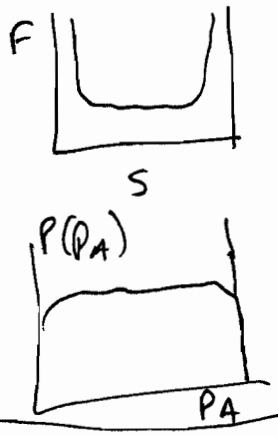




Ideal case - single free energy minimum

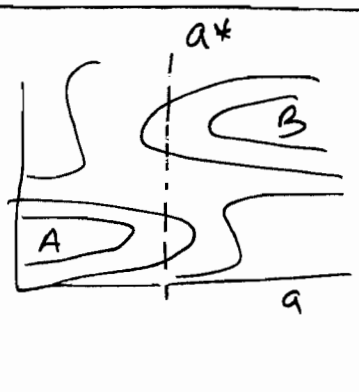
q good rxn coordinate - P(P_A) histogram peaks at 1/2

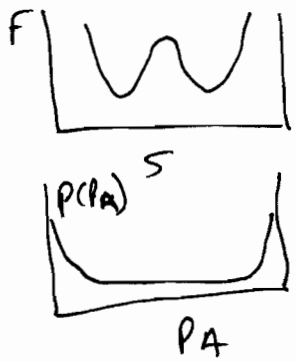




S also important,

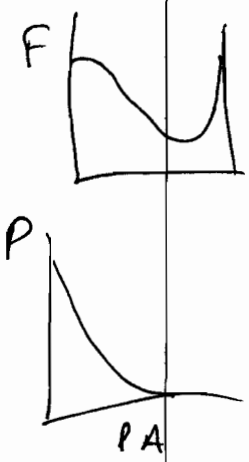
q dominant





barrier in F(S)

Bimodal in P_A



q not a good coordinate