Numerical Methods for Transition Path Sampling in Chemistry

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Department of Physics

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Constraint

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$\Longrightarrow$ a dead end

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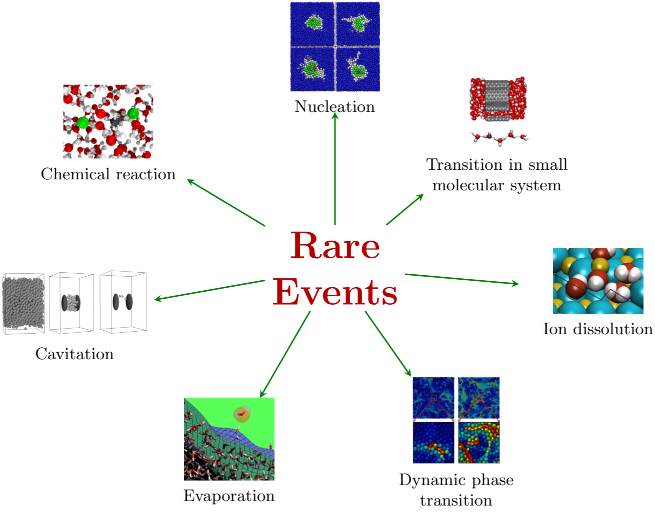
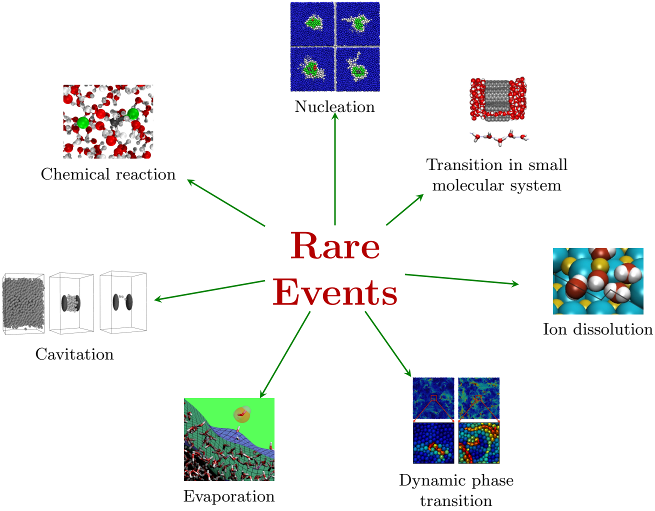
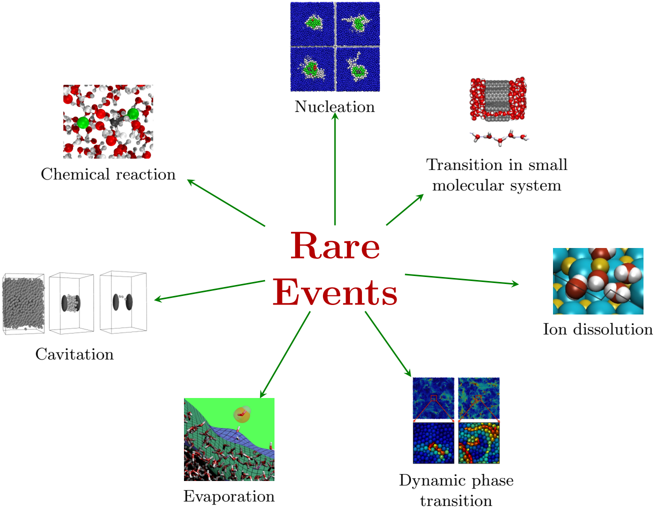
- **rare events**: biased Monte Carlo methods$\Rightarrow$Transition Path Sampling (TPS)



- event that occur over timescales far too long for standard MD
- transitions between states separated by high energy barriers



"In the fields of observation, chance favors only the prepared mind." - *Louis Pasteur*



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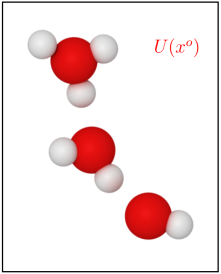
Outline

- Numerical Methods for Transition Path Sampling
  - Monte Carlo Simulation
  - Configuration vs. Trajectory Space
  - Trajectory/Path
  - Transition Path
  - Biasing the Trajectory
  - MC moves in Path Sampling
  - Shooting: Forward, Backward Simulation Step
  - Initial Trajectory
  - Acceptance Rule
- Applications in Chemistry
  - Information from the path ensemble
  - Water Chain in Nanotube
  - Other concepts

Numerical Methods for Transition Path Sampling

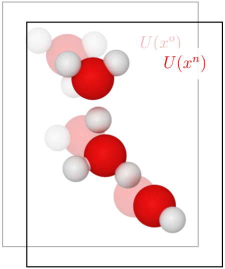
Monte Carlo Simulation



$$\{x_i^o, v_i^o\} \to \rho(x^o) \propto e^{-\beta U(x^o)}$$

- **Configuration**: a point in phase space: $\Gamma = (x_i, v_i)$

Monte Carlo Simulation



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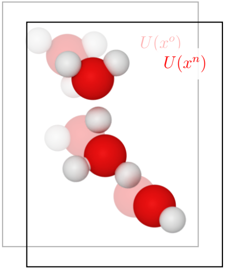

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- acceptance of the trial move:

$$p_{acc} = \min\left[1, \frac{\rho(x^n)\rho_{gen}(x^n \rightarrow x^o)}{\rho(x^o)\rho_{gen}(x^o \rightarrow x^n)}\right]$$

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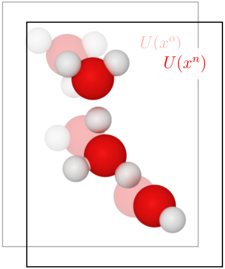

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$$\rho_{gen}(x^n \rightarrow x^o) = \rho_{gen}(x^o \rightarrow x^n)$$

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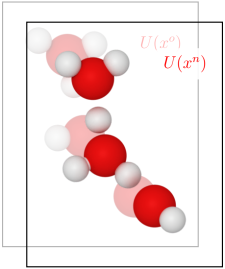

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- standard MC acceptance rule:

$$p_{acc} = \min\left[1, \frac{\rho(x^n)}{\rho(x^o)}\right]$$

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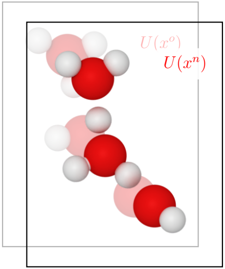

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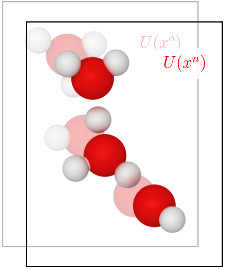

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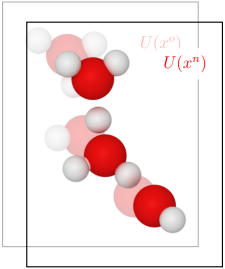

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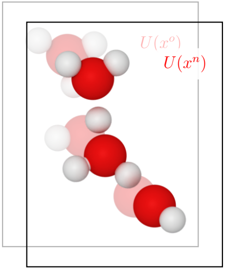

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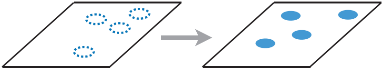
- random walk in the configuration space

Configurational Space vs Trajectory Space

Bolhuis et al., Advanced Theory and Simulations 4.4 (2021)



trial move in configurational space

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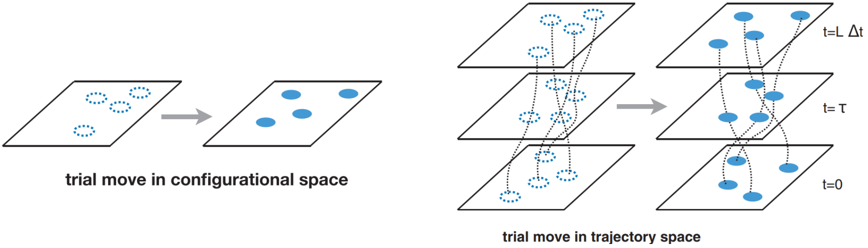

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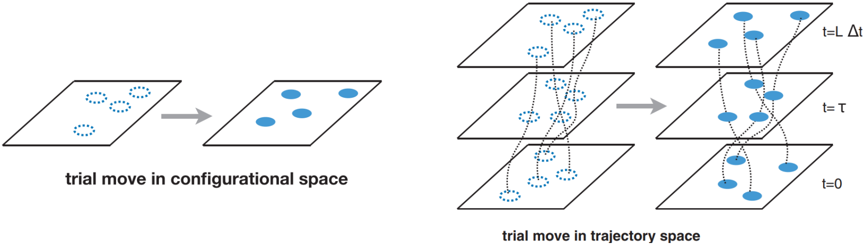

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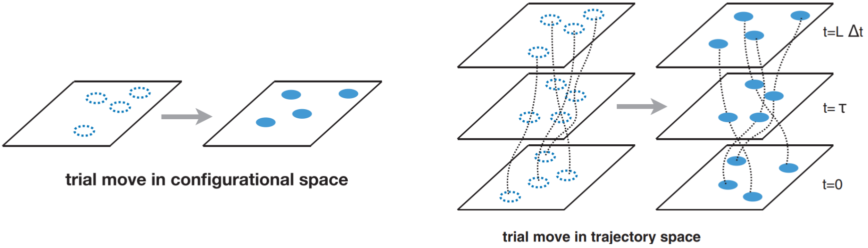

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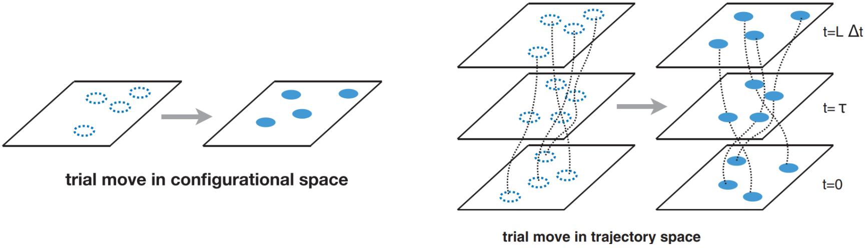

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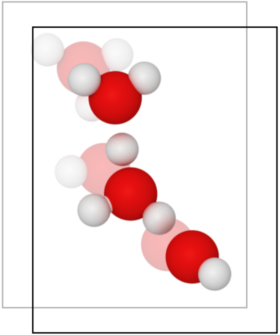
- a conceptual shift

$$\left\{ \begin{array}{c} \text{static analysis} \\ \text{of configuration} \\ \rho(x) \end{array} \right\} \Rightarrow \left\{ \begin{array}{c} \text{a statistical analysis of} \\ \text{entire dynamical pathways} \\ \rho[\mathbf{x}] \end{array} \right\}$$

Trajectory/Path

- Trajectory/path: a sequence of points in the phase space, $\mathbf{x} \equiv \{(x_0, v_0), (x_1, v_1)\}$



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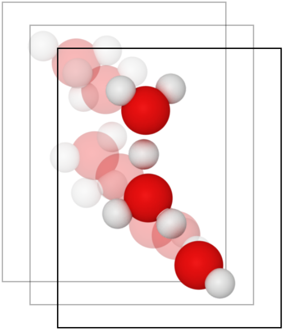

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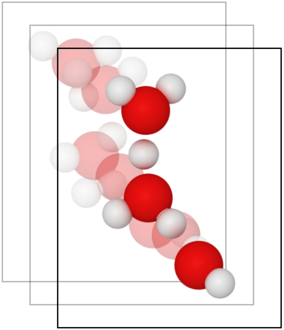

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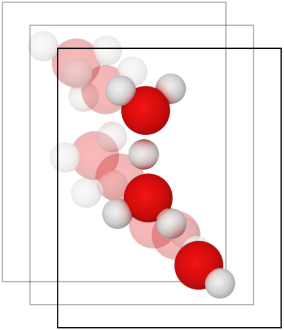
$$\rho[\mathbf{x}] \propto \rho(x_0) p(x_0 \to x_1) p(x_1 \to x_2)$$



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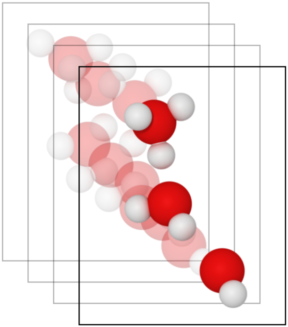
$$\rho[\mathbf{x}] \propto \rho(x_0) \prod_{i=0}^{2} p(x_i \to x_{i+1})$$



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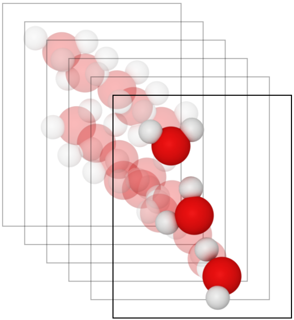
$$\rho[\mathbf{x}] \propto \rho(x_0) \prod_{i=0}^{4} p(x_i \rightarrow x_{i+1})$$



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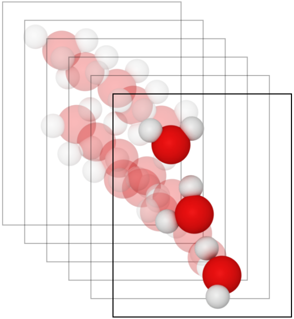

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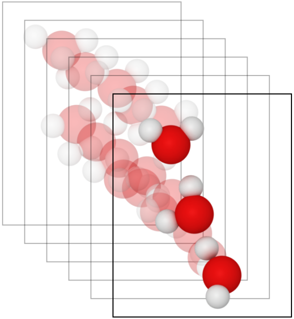
- Key Question: "What are the most likely ways for a system to get from point A to point B?"



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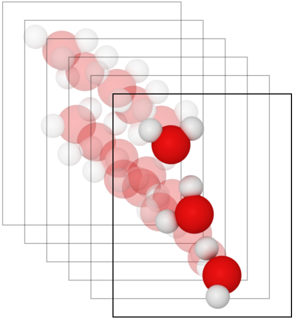
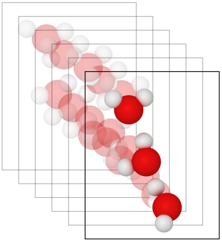
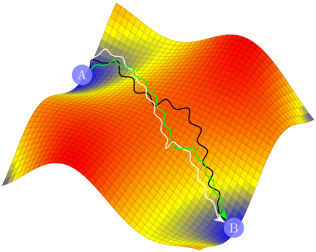


- Key Question: "What are the most likely ways for a system to get from point A to point B?"
  - reactive trajectory $\Rightarrow$ valid transition paths

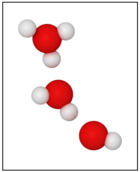
Transition Path

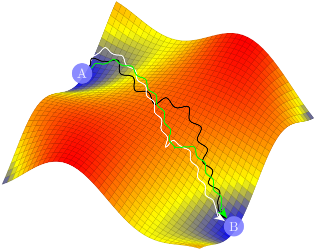




- transition path: a trajectory of a system that connects two stable basins (A,B) separated by a high energy barrier

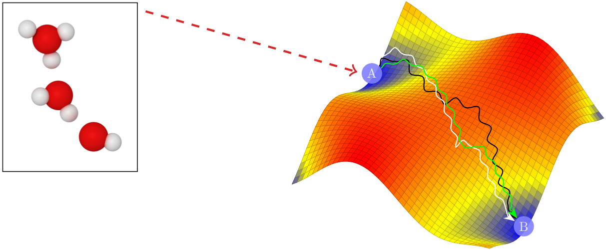
Transition Path





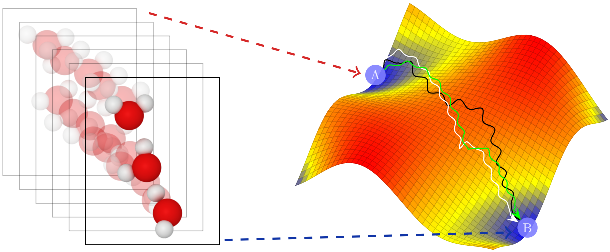
- chemical reaction:

Transition Path



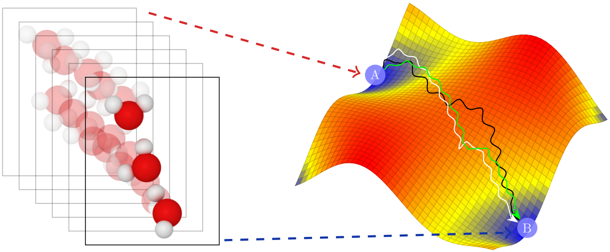
- chemical reaction: reactant (basin A)
  - hydrogen detaching from a H_3O^+ (basin A)

Transition Path



- chemical reaction: reactant (basin A) $\rightarrow$ product (basin B)
  - hydrogen detaching from a H_3O^+ (basin A) and bonding with a neighboring H_2O (basin B)

Transition Path



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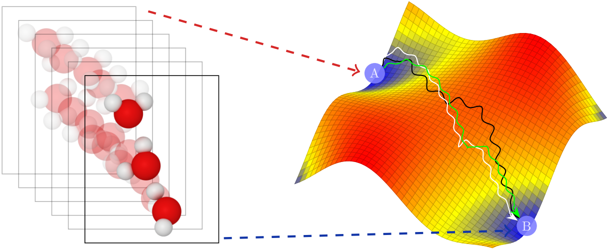

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  - Na^+/Cl^- detaching from a kink site on a salt crystal (basin A) and entering the surrounding water (basin B)

Biasing the Trajectory

- Biasing in Monte Carlo Simulation

$$\rho_{bias} \propto w_{bias}\rho(x)$$

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- Biasing the path ensemble:

$$\rho_{AB}[\mathbf{x}] \propto w_{bias}[\mathbf{x}]\rho[\mathbf{x}]$$

where $w_{\text{bias}}\left[\mathbf{x}\right] \equiv h_A\left(x_0\right) h_B\left(x_L\right)$,

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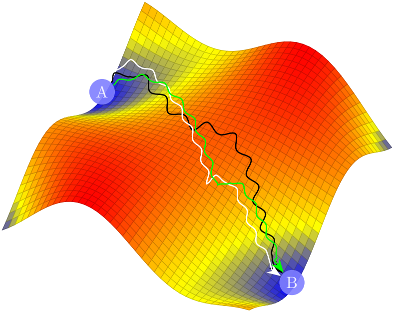
where $w_{\text{bias}}[\mathbf{x}] \equiv h_A(x_0)\, h_B(x_L)$,



Biasing the Trajectory

- Biasing in Monte Carlo Simulation

$$\rho_{bias} \propto w_{bias}\rho(x)$$

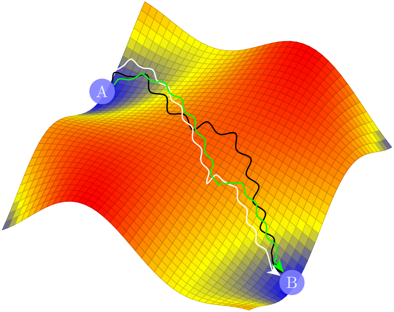
- Biasing the path ensemble:

$$\rho_{AB}[\mathbf{x}] \propto w_{bias}[\mathbf{x}]\rho[\mathbf{x}]$$

where $w_{\text{bias}}\,[\mathbf{x}] \equiv h_A\,(x_0)\,h_B\,(x_L)$,

- indicator function/population operator

$$h_{A,B}(x) = \begin{cases} 1 & x \in A, B \\ 0 & x \notin A, B \end{cases}$$



Moves for Trajectory Sampling

What moves are used to sample the biased path distribution?

Moves for Trajectory Sampling

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Shooting move

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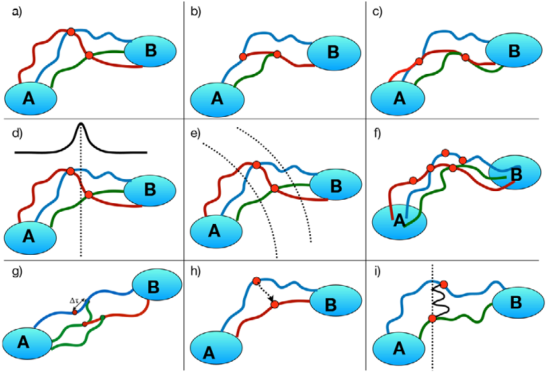
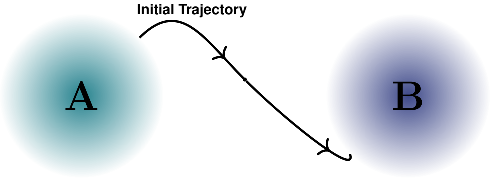


Bolhuis et al., Advanced Theory and Simulations 4.4 (2021)

Initial Trajectory



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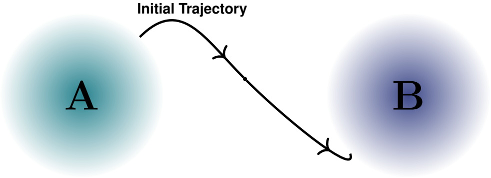
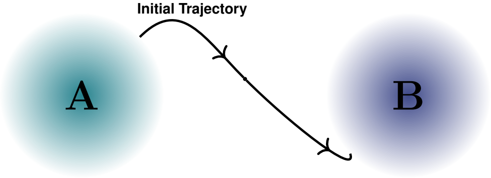


- *In practice*: initial paths are obtained from a high-temperature simulation

Initial Trajectory



- *In practice*: initial paths are obtained from a high-temperature simulation
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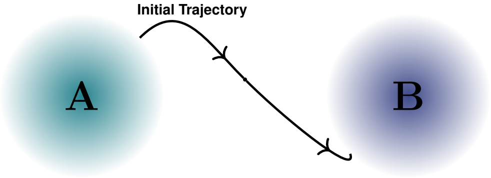
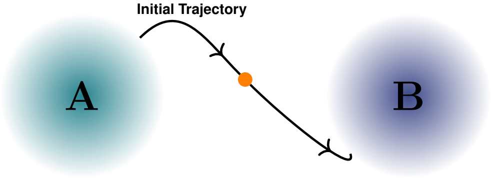


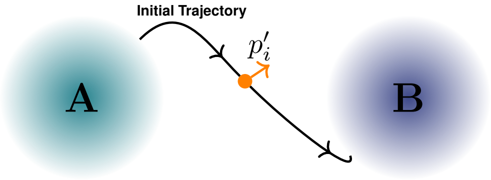
- *In practice*: initial paths are obtained from a high-temperature simulation
- run a long simulation using distributed computing or a massively parallel supercomputer (Folding@Home, Anton)
- biased/steered simulation (umbrella, metadynamics)

Shooting Method



- select a point on a transition path, (x, v) (shooting point ●)

Shooting Method



- select a point on a transition path, (x, v) (shooting point ●)
- perturb the momenta of the system at that point (x, v')

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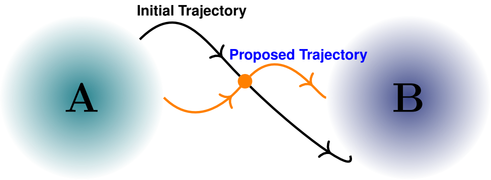
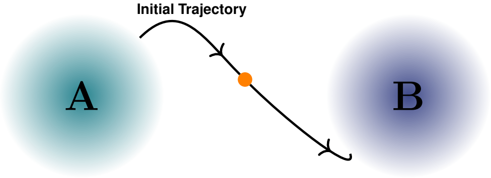


- select a point on a transition path, (x, v) (shooting point ●)
- perturb the momenta of the system at that point (x, v')
- simulate forward and backward in time from this single, perturbed point, (trial trajectory)

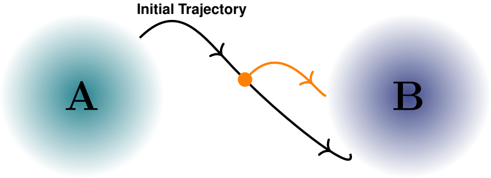
Forward Simulation Step



Forward Trajectory:

- start at the perturbed point (x_τ, v'_τ) (frame τ)

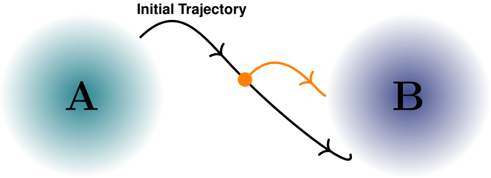
Forward Simulation Step



Forward Trajectory:

- start at the perturbed point (x_τ, v'_τ) (frame τ)
- use the new, randomly perturbed momenta to integrate the equations of motion forward in time, $(x'_i, v'_i)\ \forall i \in \{\tau + 1, \ldots, L\}$

Forward Simulation Step



Forward Trajectory:

- start at the perturbed point (x_τ, v'_τ) (frame τ)
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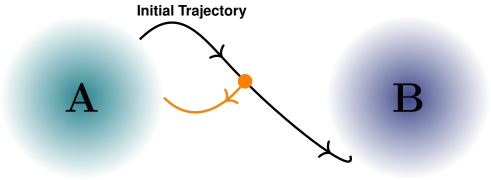
- stop when a stable state (B) is reached

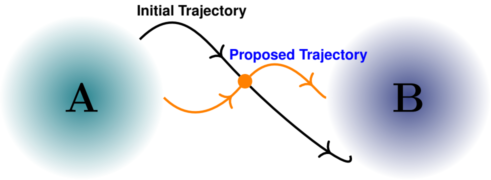
Backward Simulation Steps



Reverse Trajectory:

- reverse the momenta: $p_\tau \to -p_\tau$ (frame τ)
- integrate the equation of motion forward in time, $(x'_j, v'_j)\ \forall j \in \{\tau - 1, \ldots, 0\}$
- stop when a stable state (A) is reached

Proposed Trajectory



Concatenate the segments; this will be the proposed trajectory

$$\mathbf{x}_{trial} \sim \rho_{AB}[\mathbf{x}]$$

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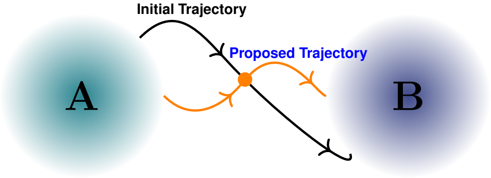

Concatenate the segments; this will be the proposed trajectory

$$\mathbf{x}_{trial} \sim \rho_{AB}[\mathbf{x}]$$

- Accept or Reject?

Final Step

- Acceptance probability:

$$P_{acc}[\mathbf{x}^o \to \mathbf{x}^n] = \min\left(1, \frac{\rho_{AB}[\mathbf{x}^n]\rho_{gen}[\mathbf{x}^n \to \mathbf{x}^o]}{\rho_{AB}[\mathbf{x}^o]\rho_{gen}[\mathbf{x}^o \to \mathbf{x}^n]}\right)$$

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- this acceptance is reduced to:

$$P_{acc} = \begin{cases} h_A\left(x_0\right) h_B\left(x_L\right) & \text{fix length L} \\ h_A\left(x_0\right) h_B\left(x_L\right) \min(1, L_n/L_o) & \text{flexible length L} \end{cases}$$

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! if accepted: new starting point

! if rejected: stays on the old path

Unpacking the acceptance rule

Lets focus on the acceptance ratio:

$$\implies \frac{\rho_{AB}[\mathbf{x}^n]\rho_{gen}[\mathbf{x}^n \rightarrow \mathbf{x}^o]}{\rho_{AB}[\mathbf{x}^o]\rho_{gen}[\mathbf{x}^o \rightarrow \mathbf{x}^n]}$$

$$\rho_{gen}[\mathbf{x}^o \rightarrow x^n] = p_{sel}(x^o_\tau) \prod_{i=\tau}^{L-1} p(x^n_i \rightarrow x^n_{i+1}) \prod_{i=1}^{\tau} \bar{p}(x^n_i \rightarrow x^n_{i-1})$$

$$\bar{p}(x_i \rightarrow x_{i-1}) \implies (x_i, -v_i)$$

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Lets focus on the acceptance ratio:

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$$p_{sel}(x_\tau^n) = 1/(L-1)$$

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$$\frac{p_{sel}(x_\tau^o)}{p_{sel}(x_\tau^n)} = \frac{L-1}{L-1} = 1$$

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- microscopic reversibility

$$\rho(x_i) p(x_i \to x_{i+1}) = \rho(x_{i+1}) \bar{p}(x_{i+1} \to x_i)$$

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- let's introduce the following definitions:

$$P_{\text{forward}}(x_{\tau\ldots L}) \equiv \prod_{i=\tau}^{L-1} p(x_i \to x_{i+1})$$

$$P_{\text{backward}}(x_{0\ldots\tau}) \equiv \prod_{i=1}^{\tau-1} \bar{p}(x_i \to x_{i-1})$$

Unpacking the acceptance rule

$$\frac{\rho_{gen}[\mathbf{x}^n \to \mathbf{x}^o]}{\rho_{gen}[\mathbf{x}^o \to \mathbf{x}^n]} = \frac{P_{\text{forward}}(x^o_{\tau\ldots L}) P_{\text{backward}}(x^o_{0\ldots L})}{P_{\text{forward}}(x^n_{\tau\ldots L}) P_{\text{backward}}(x^n_{0\ldots L})}$$

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- acceptance ratio: flexible length

$$\frac{\rho_{AB}[\mathbf{x}^n]\rho_{gen}[\mathbf{x}^n \to \mathbf{x}^o]}{\rho_{AB}[\mathbf{x}^o]\rho_{gen}[\mathbf{x}^o \to \mathbf{x}^n]} = h_A(x_0^n)h_B(x_L^n)\frac{p_{sel}(x_\tau^o)}{p_{sel}(x_\tau^n)}$$

- if only the momenta are perturb:

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- the initial trajectory is always a transition path:

$$h_A(x_0^o)h_B(x_L^o) = 1$$

- if the length of the trajectory is not fixed:

$$\frac{p_{sel}(x_\tau^o)}{p_{sel}(x_\tau^n)} = \frac{L_n}{L_o}$$

Summary

- trajectory/path: $\mathbf{x} \equiv \{(x_0, v_0), (x_1, v_1) \ldots, (x_L, v_L)\}$

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$$P_{acc}[\mathbf{x}^o \to \mathbf{x}^n] = h_A(x_0^n) h_B(x_L^n) \min\left(1, \frac{p_{sel}(x_\tau^o)}{p_{sel}(x_\tau^n)}\right)$$

Application in Chemistry

  $\rho_{AB}[\mathbf{x}]$

Information from the Path Ensembles

$\rho_{AB}[\mathbf{x}] \implies$ a large ensemble of valid transitions paths can be used to analyze the following:

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PNAS

Check for updates

Reaction coordinates and rates from transition paths

Robert B. Best and Gerhard Hummer*

Laboratory of Chemical Physics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Building 5, Room 132, Bethesda, MD 20892-0520

Edited by Bruce J. Berne, Columbia University, New York, NY, and approved February 28, 2005 (received for review October 31, 2004)

The molecular mechanism of a reaction in solution is reflected in its transition-state ensemble and transition paths. We use a Bayesian formula relating the equilibrium and transition-path ensembles to identify transition states, rank reaction coordinates, and estimate

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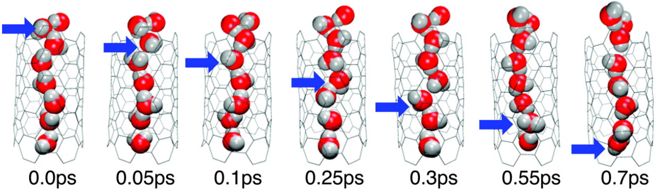
transition path of water inside a carbon nanotube



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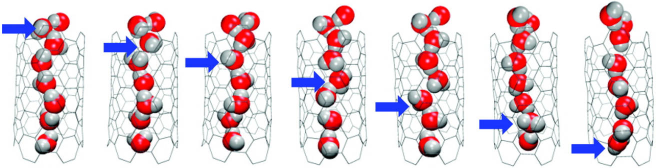

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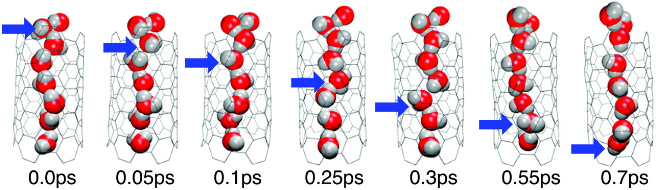

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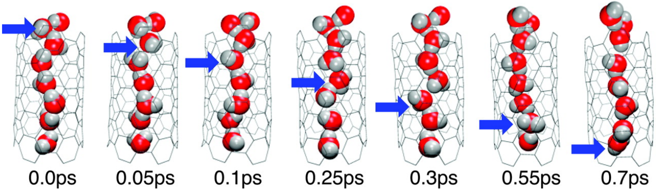

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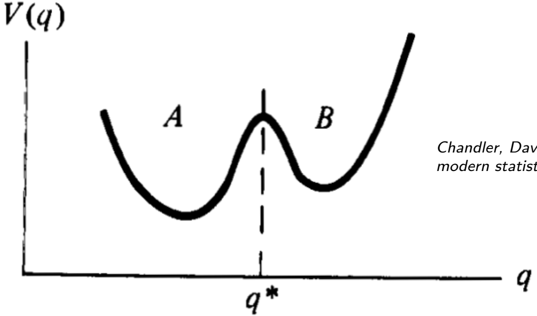
- reaction coordinate analysis
  - dipole moment M_z was determined to be a good reaction coordinate

Other concepts

- Reaction coordinate
- Committor
- Separatrix
- Other variations of TPS
- Existing tools

Reaction Coordinate

- TPS doesn't use a reaction coordinate!
  reaction coordinate →TPS postprocessing analysis tool
- **reaction coordinate** (q) is a variable that captures the progress of transition, one where the energy of a system has a well-defined maximum q^* (**transition state**) along the path



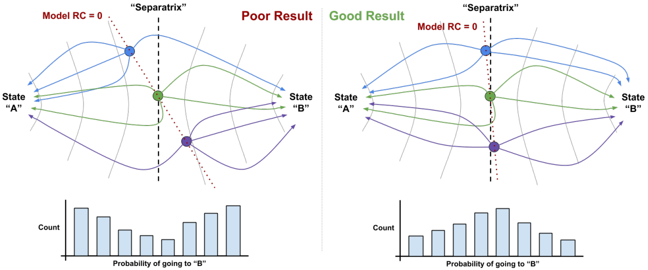
Chandler, David, "Introduction to modern statistical mechanics" (1987)

Committors and Separatrix

- **committor**, $p_A(x, t_s)$: the probability that a trajectory, initiated from a configuration x, will end in state A a short time t_s later

$$p_B(x, t_s) = 1 - p_A(x, t_s)$$

- **separatrix**: the surface in configuration space where the committor value is approximately $p_A \simeq p_B \simeq 1/2$



https://atesa.readthedocs.io/

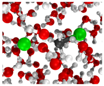
Other Variations and Existing Tools

- Transition Interface Sampling (TIS): an extension of TPS designed to improve the rate constant calculations
- Multiple State TPS (MSTPS): allows for the sampling of transitions between more than two stable states in a single calculation
- Replica Exchange TIS (RETIS): improves sampling efficiency by exchanging paths between different interfaces, similar to replica exchange in standard MC simulations
- Machine Learning-based TPS: the use of ML to classify stable states or identify reaction coordinates

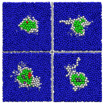
OpenPathSampling   ATESA   PyRETIS — rare events in Python

Applications of TPS in Chemistry

- reactions coordinate
- free energy barrier

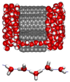


Chemical reaction



Nucleation

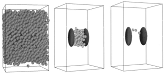
- uses Replica Exchange Transition Interface Sampling (RETIS)



Transition in small molecular system

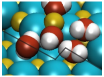
- proton transport: 1 proton/hr at neutral pH events

TPS



Cavitation

- reaction coordinate
- mechanism of the rare events

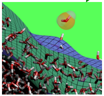


Ion dissolution

- detachment rate constant:

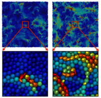
$$k_{\mathrm{Cl}^-} = 6300\,\mathrm{ms}$$

$$k_{\mathrm{Na}^-} = 160\,000\,\mathrm{ms}$$



Evaporation

- 4696 evaporation trajectories



Dynamic phase transition

- could define and track "excitations" as they occurred