Statistical methods in Atomistic Computer Simulations

3. Rare events, transition state theory and committor analysis

Michele Ceriotti

MSE 639 - EPFL - EDMX

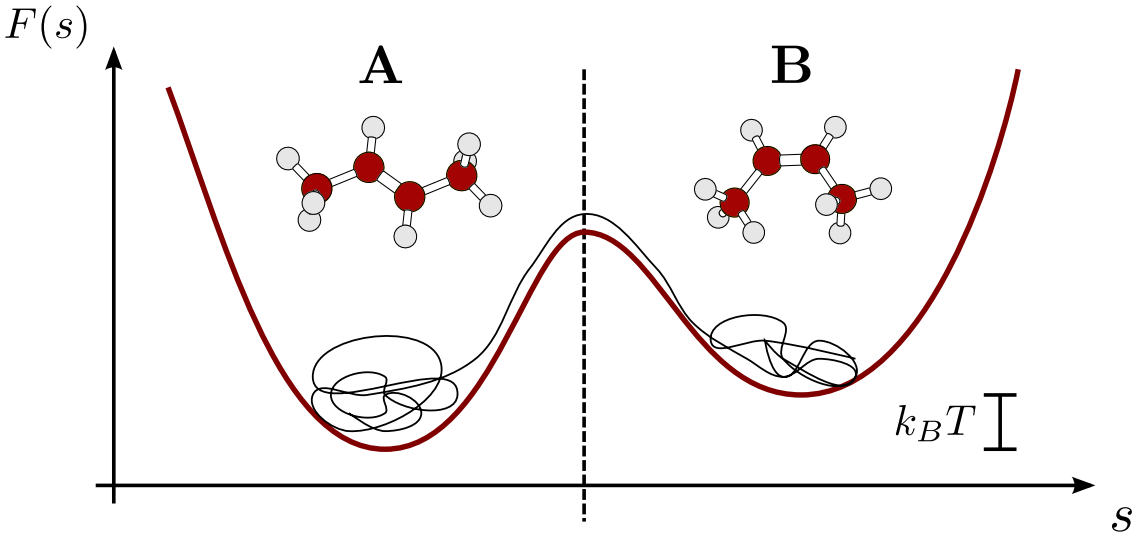
ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

Outline

1. Sampling the canonical ensemble in atomistic simulations: Monte Carlo, correlation functions, ergodicity
2. Thermostatting MD efficiently: white and colored-noise Langevin dynamics
3. Rare events: transition state theory and the transition state ensemble
4. Statistical re-weighting, biased sampling, metadynamics
5. Linear and non-linear dimensionality reduction: determining automatically order parameters

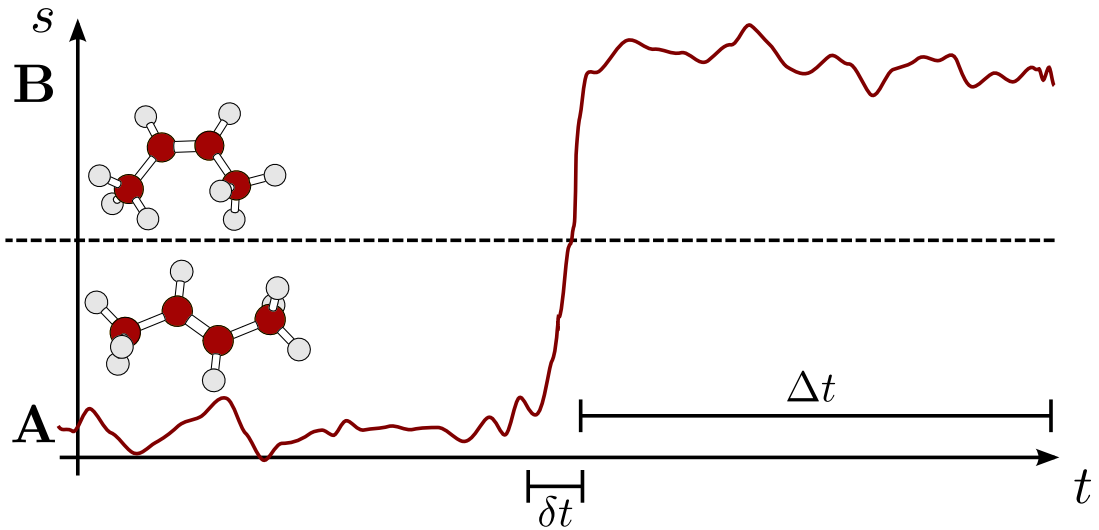
Rare events in molecular dynamics

- The time evolution of molecules and materials often involves transitions between different (meta)stable states
- These happen very infrequently (Δt) on the time scale of molecular motion, but the transition itself is very fast (δt)
- One has to simulate boring thermal fluctuations for a long time $\gg \Delta t/\delta t$ just to observe a few of the "interesting" events



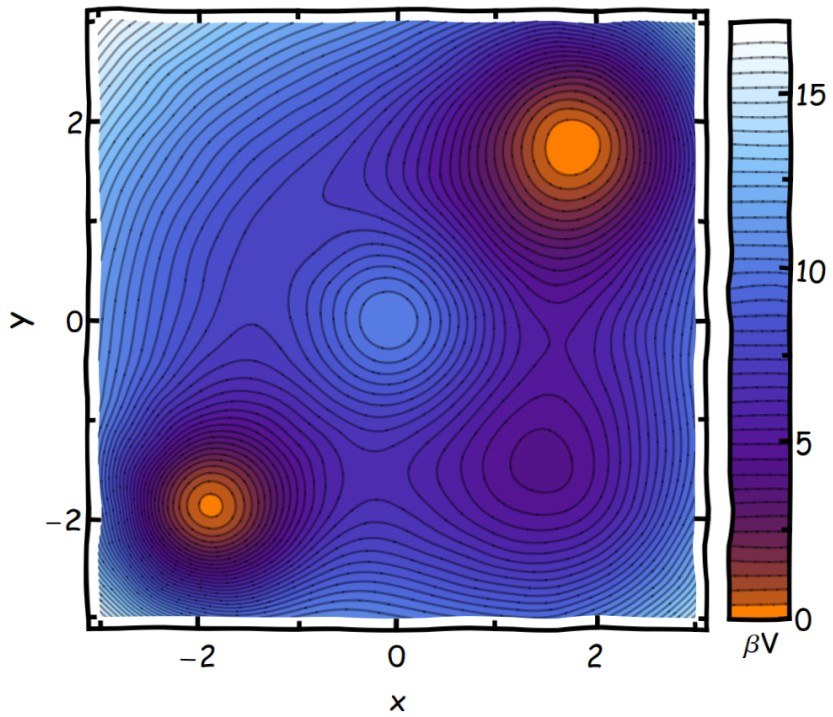
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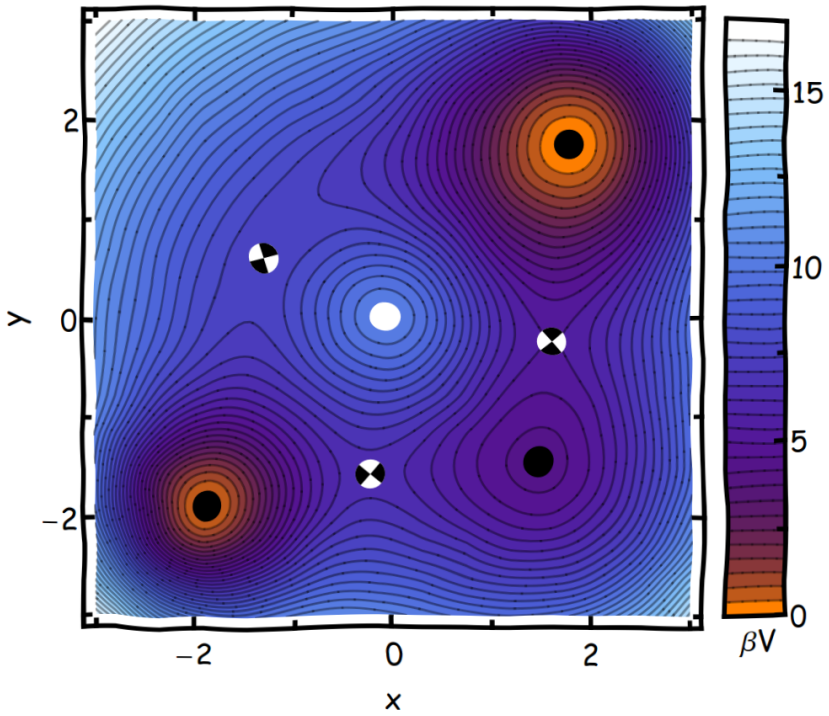
Transitions on the potential energy surface

- There is not much we can do to speed up dynamics, but we can try to infer dynamical information from "static" information
- Potential energy $V(\mathbf{q})$ determines the dynamics, so can we use it without running actual trajectories?
  - Critical points, minimum energy paths, basins of attraction: it will take longer time to cross higher barriers



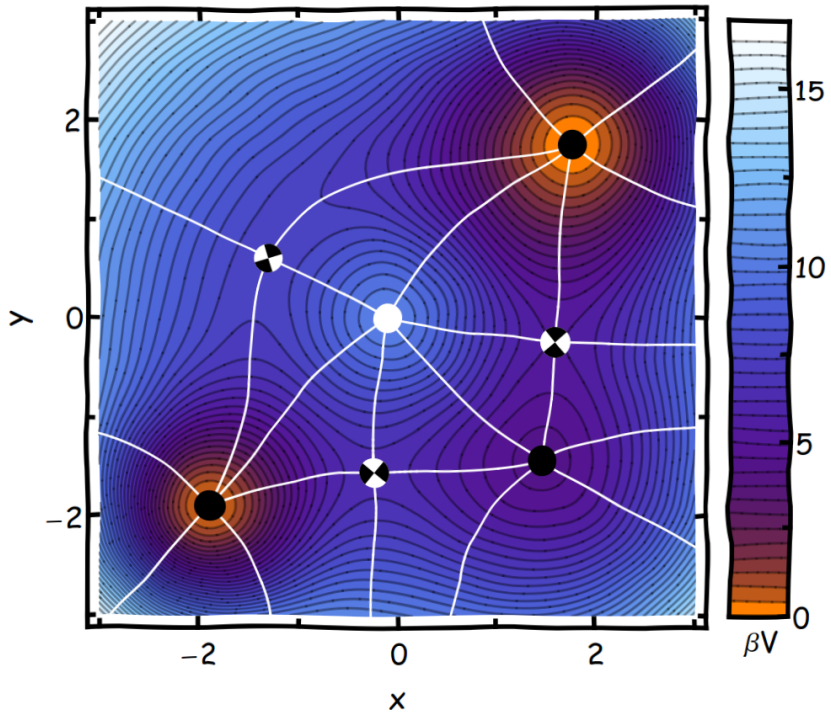
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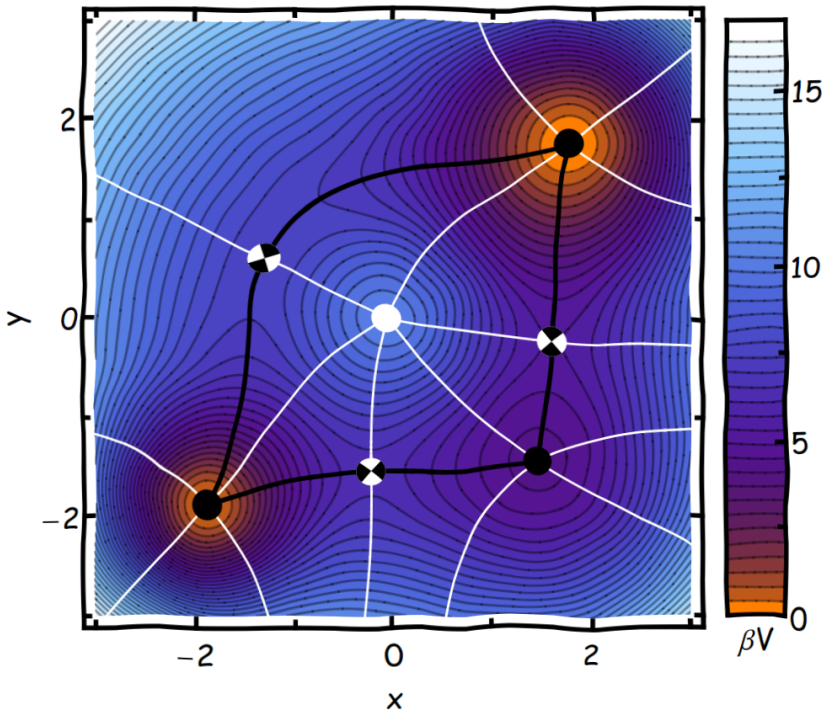
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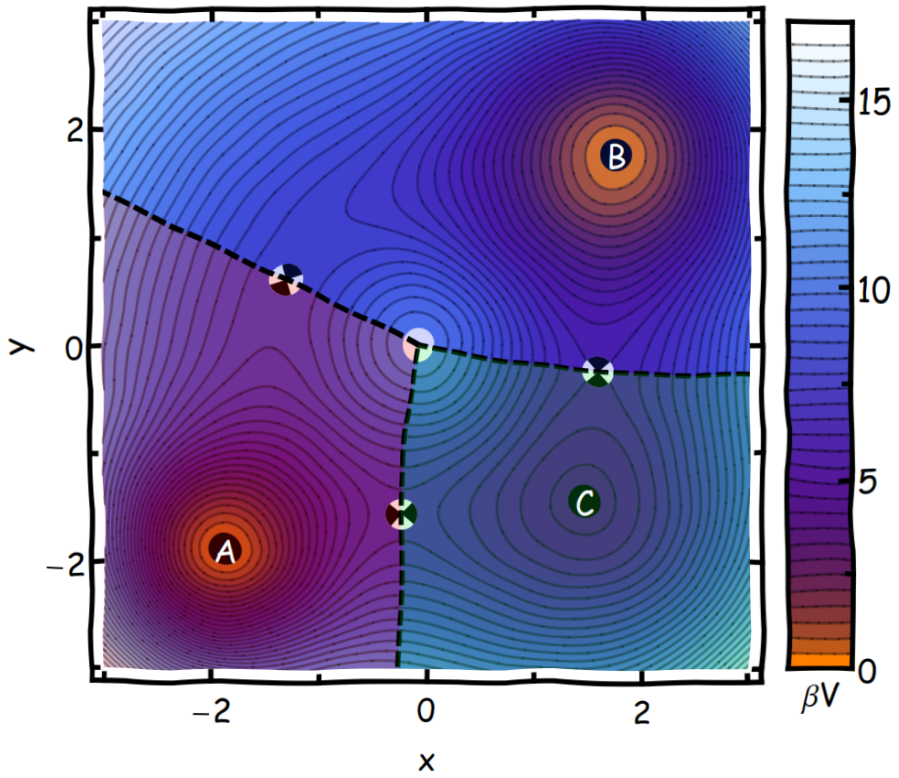
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Introducing transition state theory

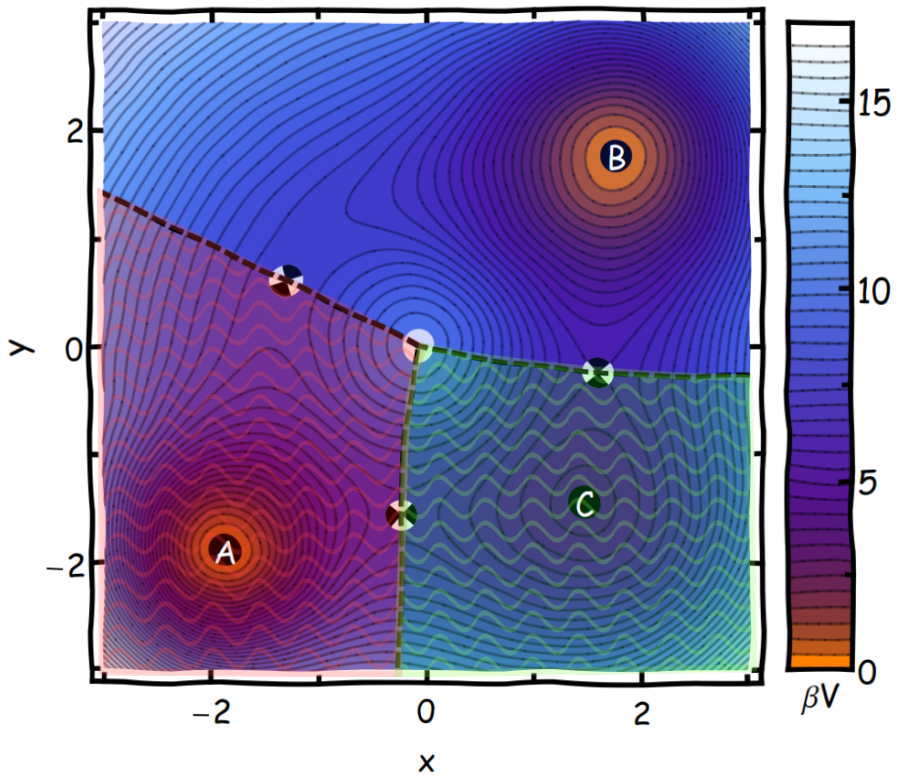
- Use the potential energy surface to associate regions of the configuration space to stable states



Subdivide the PES into the basins of attraction of the various local minima, i.e. the locus of points that converge onto each minimum upon steepest descent minimization of $V(\mathbf{q})$

Introducing transition state theory

- Transition rate between basins A and C: $k_{A\to C}(t) = \frac{d}{dt_0} P(C, t|A, t_0)$

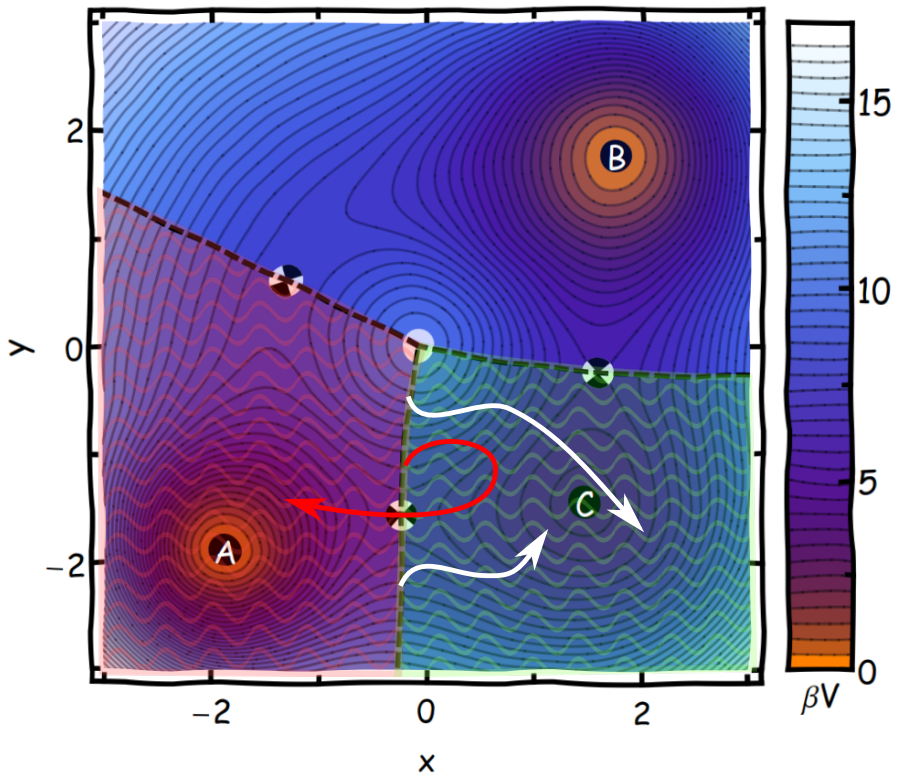


Characteristic functions $\theta_{A,C}(\mathbf{q})$ define whether a configuration belongs to the A, C basins. $\hat{\mathbf{n}}$ is the normal to the dividing surface between A and C.

$$\frac{d}{dt_0}\frac{\langle \theta_C(\mathbf{q}(t))\,\theta_A(\mathbf{q}(t_0))\rangle}{\langle \theta_A(\mathbf{q})\rangle} = \frac{\left\langle \theta_C(\mathbf{q}(t))\,\delta_{A/C}(\mathbf{q}(t_0))\,\hat{\mathbf{n}}(\mathbf{q}(t_0))\cdot\dot{\mathbf{q}}(t_0)\right\rangle}{\langle \theta_A(\mathbf{q})\rangle}$$

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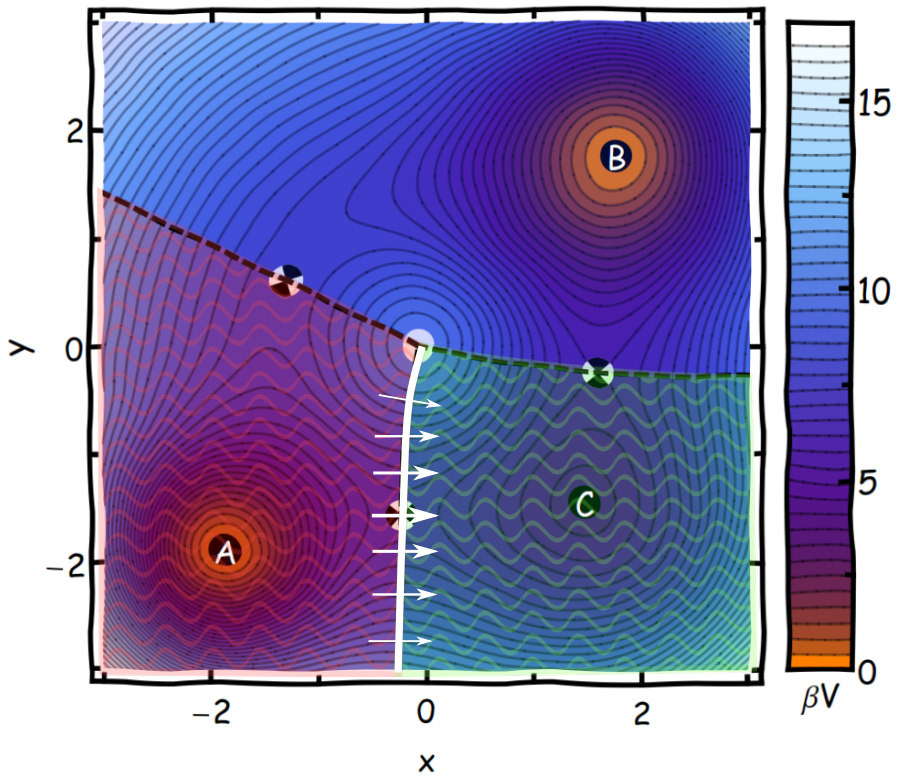


This is the fraction of dynamical trajectories starting on the boundary between A and C at time t_0, and staying in C until time t

$$\frac{d}{dt_0}\frac{\langle \theta_C(\mathbf{q}(t))\,\theta_A(\mathbf{q}(t_0))\rangle}{\langle \theta_A(\mathbf{q})\rangle} = \frac{\left\langle \theta_C(\mathbf{q}(t))\,\delta_{A/C}(\mathbf{q}(t_0))\,\hat{\mathbf{n}}(\mathbf{q}(t_0))\cdot\dot{\mathbf{q}}(t_0)\right\rangle}{\langle \theta_A(\mathbf{q})\rangle}$$

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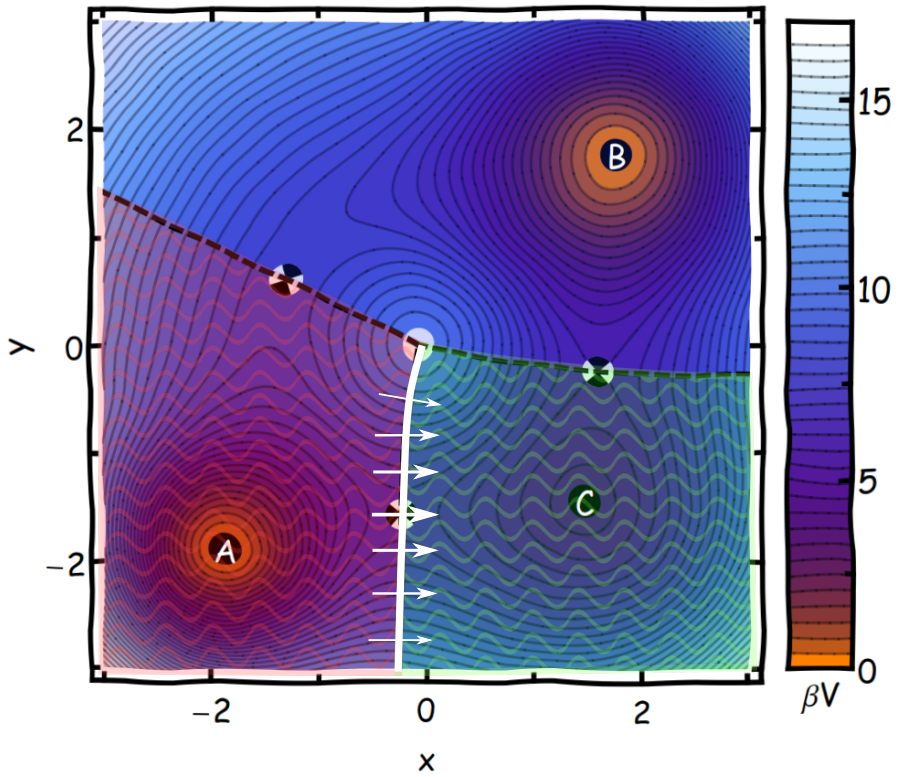


Transition state theory: limit for $t \to 0^+$ – assume all trajectories headed towards C stay there forever. No *recrossing*

$$k_{A\to C}(t \to 0^+) = k^{TST}_{A\to C} = \frac{\left\langle \theta_C(\mathbf{q}(t \to 0^+))\, \delta_{A/C}(\mathbf{q}(0))\, \hat{\mathbf{n}}(\mathbf{q}(0)) \cdot \dot{\mathbf{q}}(0) \right\rangle}{\langle \theta_A(\mathbf{q}) \rangle}$$

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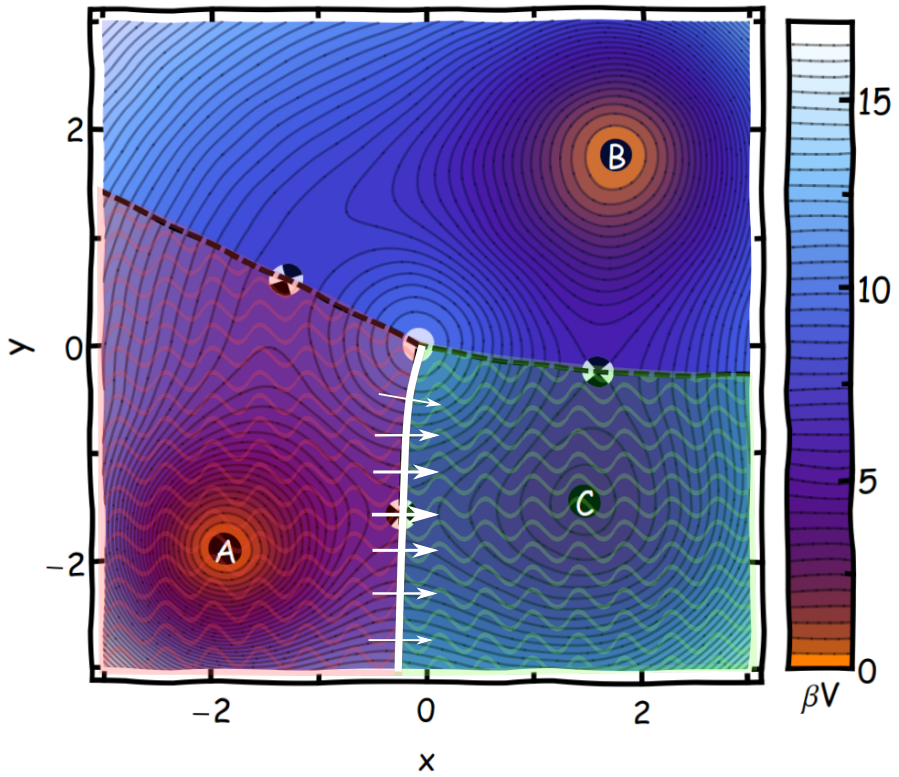


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$$\lim_{t\to 0^+} \theta_C(\mathbf{q}(t)) = \delta_{A/C}(\mathbf{q}(0))\,\theta(\dot{\mathbf{q}}(0)\cdot\hat{\mathbf{n}}(\mathbf{q}(0)))$$

Introducing transition state theory

- Assuming for simplicity one single mass m, the flux average can be factored, and $\hat{\mathbf{n}}$ selects one single component of the momentum. $\theta_C(\mathbf{q}(dt))$ picks the positive component

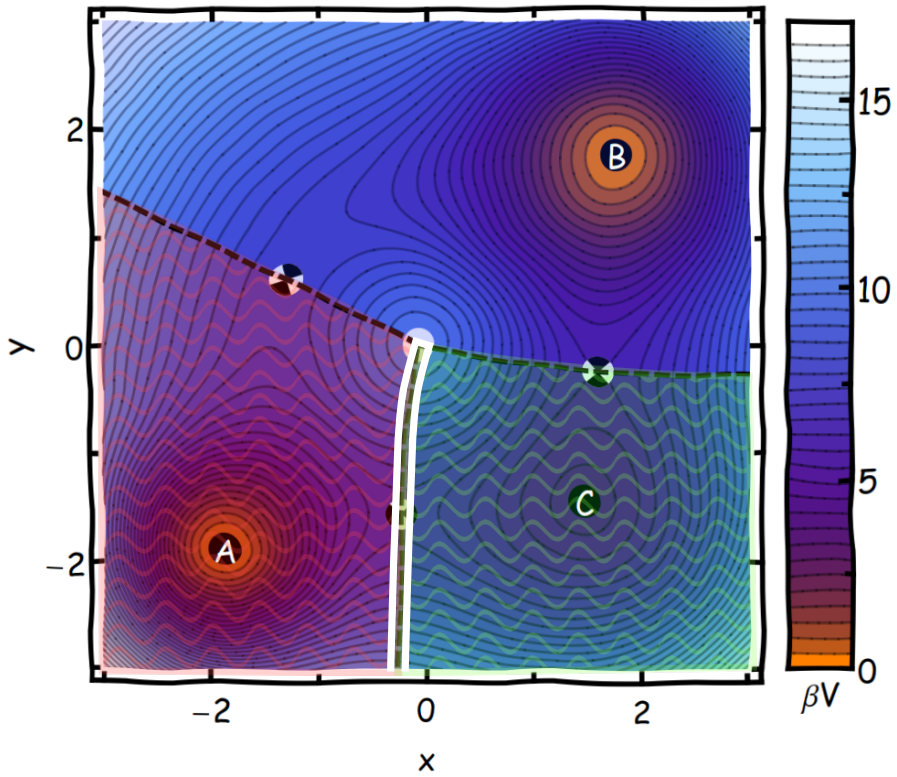


If all masses are the same, the dot product with the normal $\hat{\mathbf{n}}$ just selects one "random" component

$$\langle \theta(\mathbf{p}(t)\cdot\hat{\mathbf{n}}(\mathbf{q}(0)))\,\hat{\mathbf{n}}(\mathbf{q}(0))\cdot\mathbf{p}(0)\rangle = \langle p\,\theta(p)\rangle = \frac{1}{2}\langle|p|\rangle = \sqrt{\frac{m}{2\pi\beta}}$$

Introducing transition state theory

- Finally: an expression for the rate that **only involves ensemble averages** and no dynamical information



$$k^{TST}_{A\to C} = \frac{1}{m}\frac{\left\langle \delta_{A/C}(\mathbf{q})\right\rangle}{\langle \theta_A(\mathbf{q})\rangle}\frac{1}{2}\langle |p|\rangle = \frac{1}{\sqrt{2\pi m\beta}}\frac{\left\langle \delta_{A/C}(\mathbf{q})\right\rangle}{\langle \theta_A(\mathbf{q})\rangle}$$

Harmonic TST

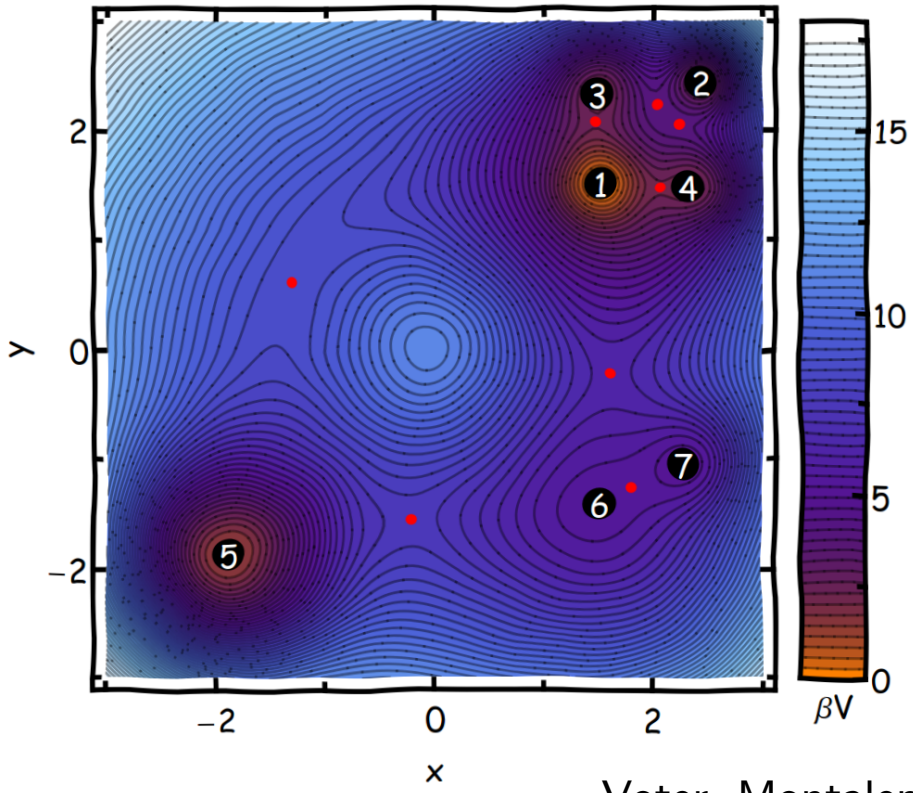
- One can simplify the rate calculation even further by expanding the potential around the minimum (potential energy: V_A) and transition state (potential energy: $V^\ddagger$)
- Let ω_i^A be the harmonic frequencies at the minimum, and $\omega_i^\ddagger$ the **positive** frequencies at the transition state: the negative mode is orthogonal to the dividing surface.
- The integrals in the TST rate expression can be worked out analytically, and give the undergraduate TST rate expression

$$k_{A\to C}^{hTST} = \frac{1}{2\pi}\frac{\prod_i \omega_i^A}{\prod_i \omega_i^\ddagger} e^{-\beta\left(V^\ddagger - V_A\right)} = \nu^\star e^{-\beta\left(V^\ddagger - V_A\right)}$$

  - This is easily adapted to include nuclear quantum effects
  - This assumes that that $\beta\left(V^\ddagger - V_A\right) \gg 1$, and that there is a single transition path

Markov chains and disconnectivity graphs

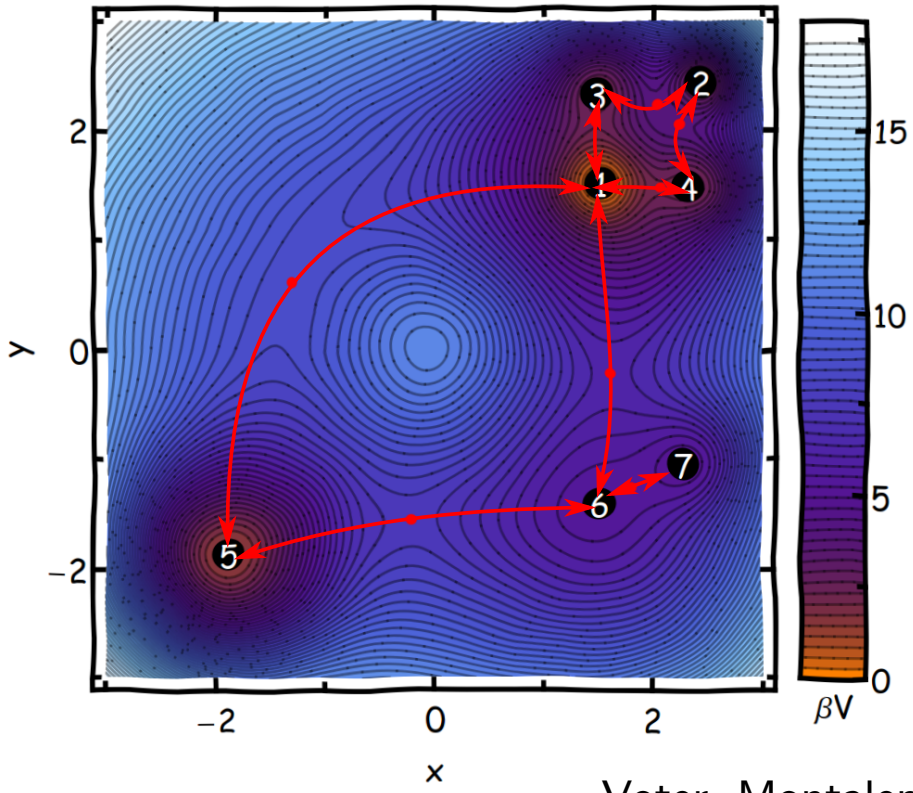
- Let's try to figure out a picture of dynamics based on these rates: a network of discrete states and reaction rates
  - Several methods available to search for minima and transition states (basin hopping, nudged elastic band, dimer method...)
  - "Markov state models" or "Kinetic Monte Carlo" – depending on communities – to make sense of the reaction network



Becker & Karplus, J. Chem. Phys. 1997
Voter, Montalenti, Germann, Ann. Rev. Mater. Res. 2002

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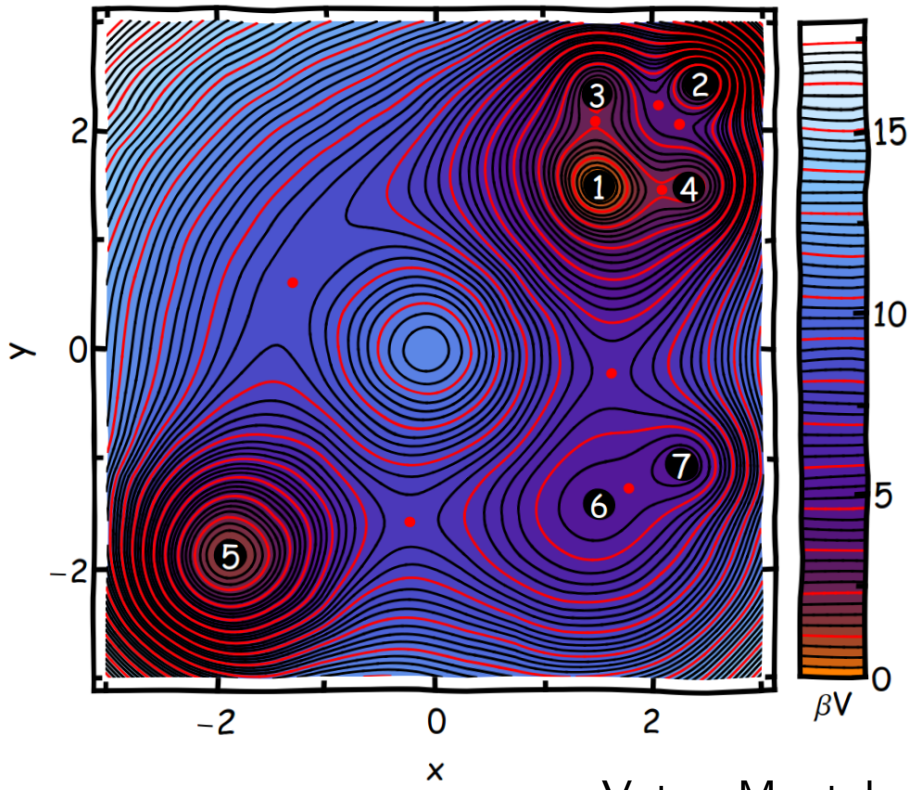
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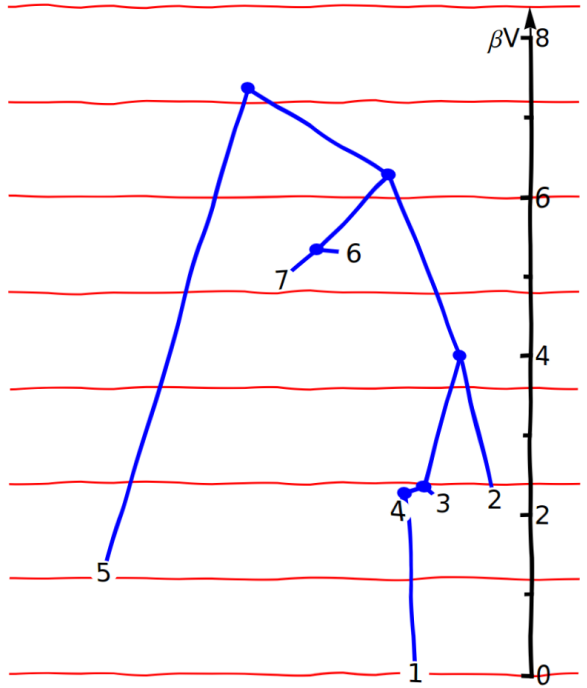


Becker & Karplus, J. Chem. Phys. 1997
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Markov chains and disconnectivity graphs

- Represent PES information with disconnectivity graphs
- Tree structure, local minima are leaves and saddle points are nodes
  - Visualize how stable states and transition pathways become populated with growing temperature
  - Can be coarse-grained in energy if desired





Becker & Karplus, J. Chem. Phys. 1997

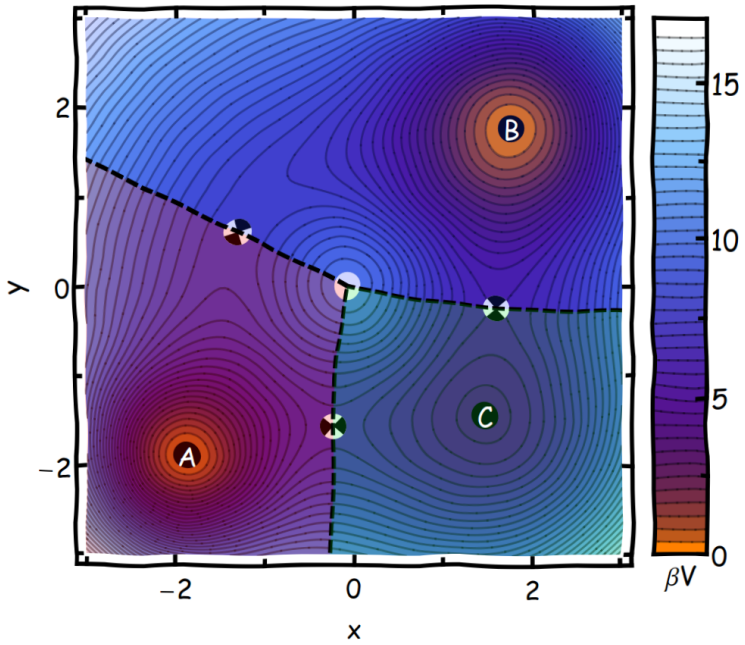
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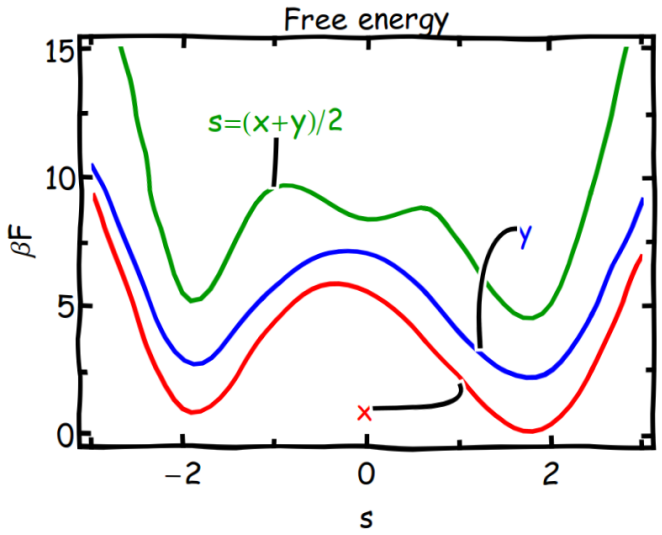
Collective coordinates and free energy

- Problem: how to characterize basins in complex systems? Too many (shallow) minima, hard to define basin boundaries.
- Define collective variable $s(\mathbf{q})$ to follow the system across transitions. Free energy relative to $s(\mathbf{q})$

$$F(s) = -\frac{1}{\beta} \ln \langle \delta(s - s(\mathbf{q})) \rangle = -\frac{1}{\beta} \ln \int d\mathbf{q} e^{-\beta V(\mathbf{q})} \delta(s - s(\mathbf{q})) + C$$

- Transition state ensemble: the set of $\mathbf{q}$ with the $s(\mathbf{q}) = s^{\ddagger}$, the maximum of $F(s)$. Two basins: $s < s^{\ddagger}$ and $s > s^{\ddagger}$





Transition state theory on the FES

- One can repeat the TST reasoning and obtain

$$k_{A\to C}^{TST} = \phi\left(s^{\ddagger}\right)\frac{e^{-\beta F\left(s^{\ddagger}\right)}}{\int_{-\infty}^{s^{\ddagger}} e^{-\beta F(s)}\mathrm{d}s}, \quad \phi\left(s^{\ddagger}\right) = \frac{\left\langle \delta\left(s\left(\mathbf{q}\right)-s^{\ddagger}\right)\left|\mathbf{M}^{-1/2}\nabla s\left(\mathbf{q}\right)\right|\right\rangle}{\sqrt{2\pi\beta}\left\langle \delta\left(s\left(\mathbf{q}\right)-s^{\ddagger}\right)\right\rangle}$$

$$k_{A\to C}\left(t\right) = \frac{\left\langle \delta\left(s\left(\mathbf{q}\left(0\right)\right)-s^{\ddagger}\right)\left(\nabla s\left(\mathbf{q}\left(0\right)\right)^{T}\mathbf{M}^{-1}\mathbf{p}\right)\theta\left(s\left(\mathbf{q}\left(t\right)\right)-s^{\ddagger}\right)\right\rangle}{\left\langle \theta\left(s^{\ddagger}-s\left(\mathbf{q}\right)\right)\right\rangle}$$

$$\lim_{t\to 0^{+}}\theta\left(s\left(\mathbf{q}\left(t\right)\right)-s^{\ddagger}\right) = \delta\left(s\left(\mathbf{q}\left(0\right)\right)-s^{\ddagger}\right)\theta\left(\nabla s\left(\mathbf{q}\left(0\right)\right)^{T}\mathbf{M}^{-1}\mathbf{p}\right)$$

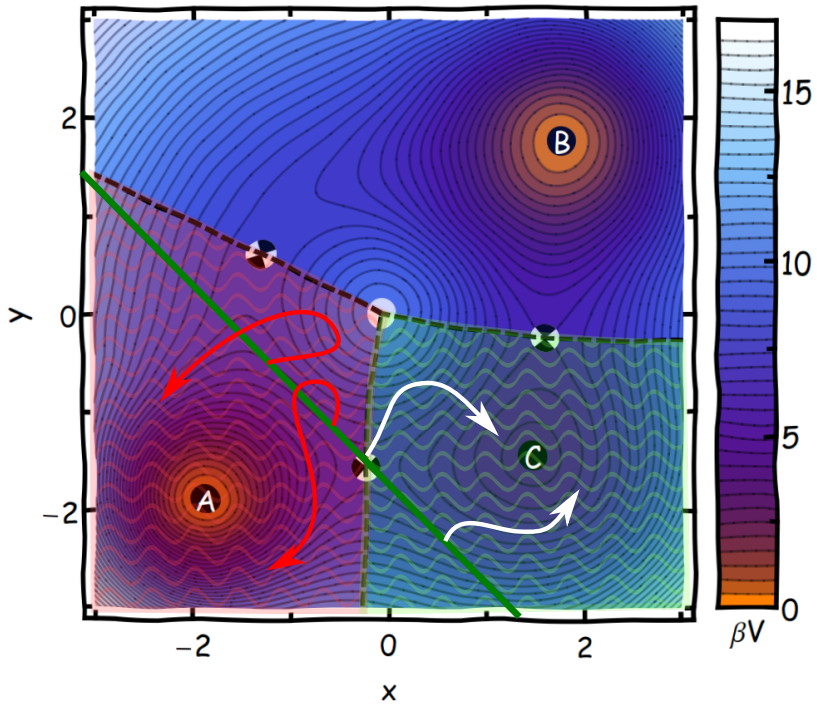
$$\frac{\int \mathrm{d}\mathbf{p}\left(\nabla s\left(\mathbf{q}\left(0\right)\right)^{T}\mathbf{M}^{-1}\mathbf{p}\right)e^{-\frac{\beta}{2}\mathbf{p}\mathbf{M}^{-1}\mathbf{p}^{T}}\theta\left(\nabla s\left(\mathbf{q}\left(0\right)\right)^{T}\mathbf{M}^{-1}\mathbf{p}\right)}{\int \mathrm{d}\mathbf{p}e^{-\frac{\beta}{2}\mathbf{p}\mathbf{M}^{-1}\mathbf{p}^{T}}} = \frac{\left|\mathbf{M}^{-1/2}\nabla s\left(\mathbf{q}\right)\right|}{\sqrt{2\pi\beta}}$$

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Cool: this is all written in terms of configurational integrals - no dynamics needed!
Problems: 1. there is a geometric flux factor ϕ; 2. often re-crossings are not negligible



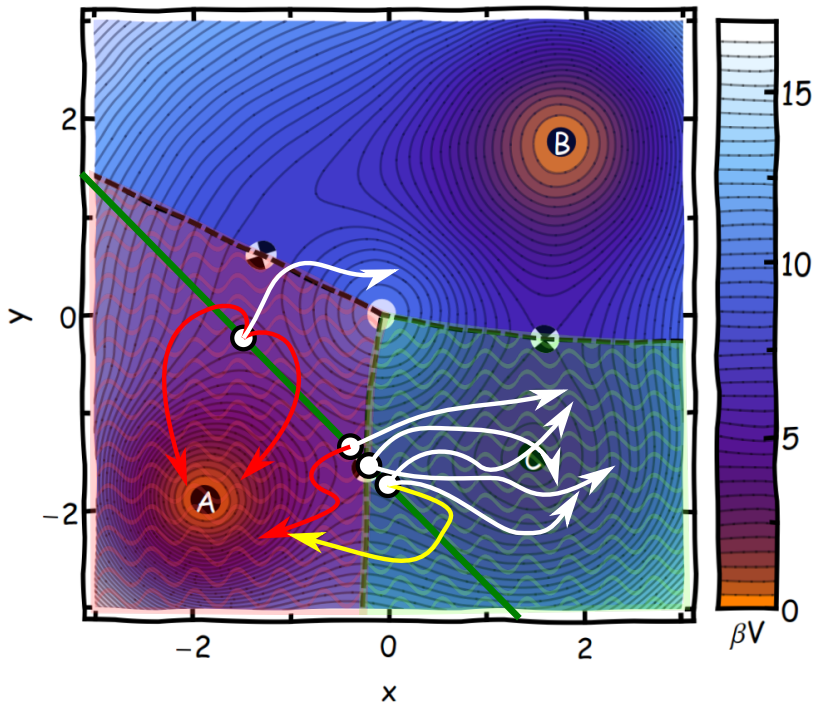
Beyond transition state theory

- Let's step back from the approximation behind TST, and write out $k_{A\to C}(\tau) = k^{TST}_{A\to C}\kappa(\tau)$, with the transmission coefficient

$$\kappa(\tau) = \frac{\left\langle \delta\left(s(\mathbf{q}(0)) - s^{\ddagger}\right)\left(\nabla s(\mathbf{q}(0))^{T}\mathbf{M}^{-1}\mathbf{p}\right)\theta\left(s(\mathbf{q}(\tau)) - s^{\ddagger}\right)\right\rangle}{\left\langle \delta\left(s(\mathbf{q}) - s^{\ddagger}\right)\left|\mathbf{M}^{-1/2}\nabla s(\mathbf{q})\right|\right\rangle / \sqrt{2\pi\beta}}$$

- For large τ, $\kappa(\tau)$ should reach a plateau. If re-crossing is low, $\kappa(\tau) \approx 1$

The two integrals are both constrained to the dividing surface. If we can generate configurations having $s(\mathbf{q}(0)) = s^{\ddagger}$, we can compute $\kappa(\tau)$ with short dynamical trajectories of length $\approx \delta t$

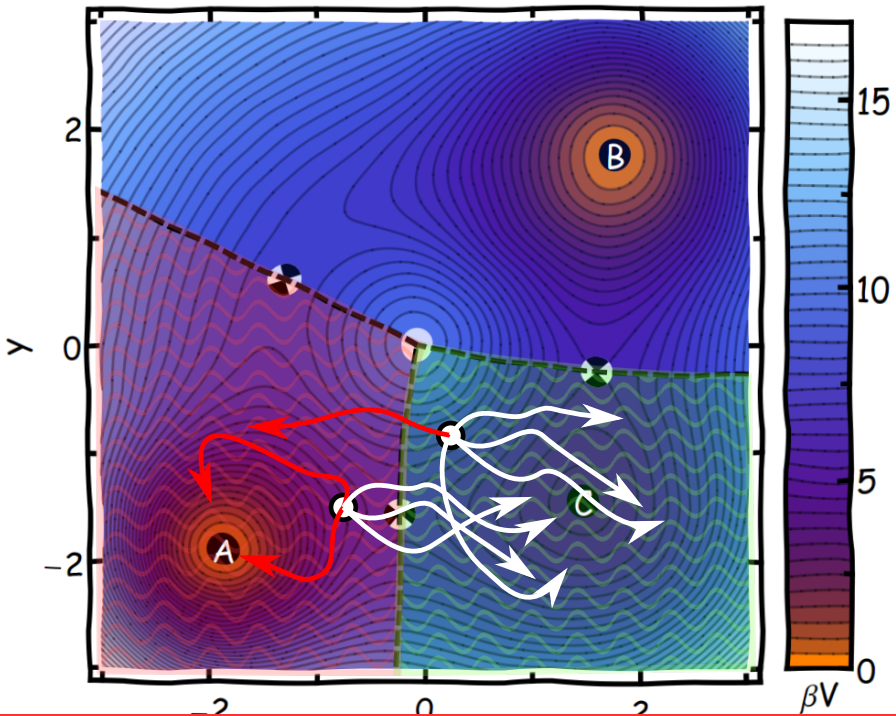


CH Bennet, Algorithms for Chemical Computations 1977; D.Chandler J.Chem.Phys 1978

Committor analysis

- Systematic way to analyze the quality of a collective variable
  - Compute the committor: "shoot" trajectories from a point $\bar{\mathbf{q}}$, and see how many end up in the products
  - Look at the transition state ensemble $s(\mathbf{q}) = s^{\ddagger}$, and compute the distribution of committor

$$p_C(\bar{\mathbf{q}}, \tau) = \frac{\langle \delta(\mathbf{q} - \bar{\mathbf{q}}) \theta_C(\mathbf{q}(\tau)) \rangle}{\langle \delta(\mathbf{q} - \bar{\mathbf{q}}) \rangle}$$

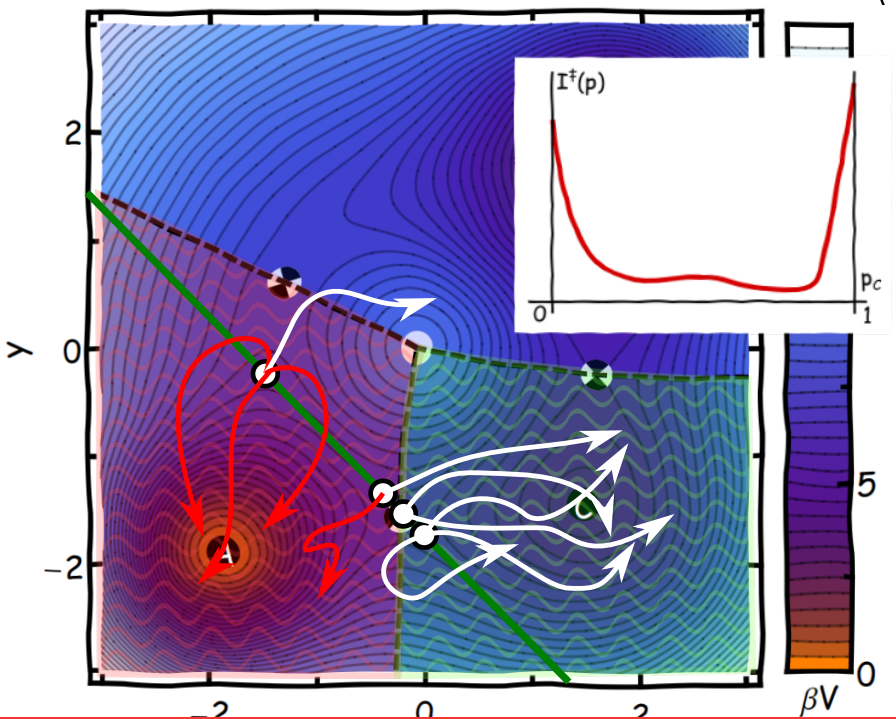


Bolhuis et al., Ann. Rev. Phys. Chem. 2002

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$$I^{\ddagger}(p) = \frac{\left\langle \delta\left[p - p_C(\mathbf{q}, \tau)\right] \delta\left(s^{\ddagger} - s(\mathbf{q})\right)\right\rangle}{\left\langle \delta\left(s^{\ddagger} - s(\mathbf{q})\right)\right\rangle}$$



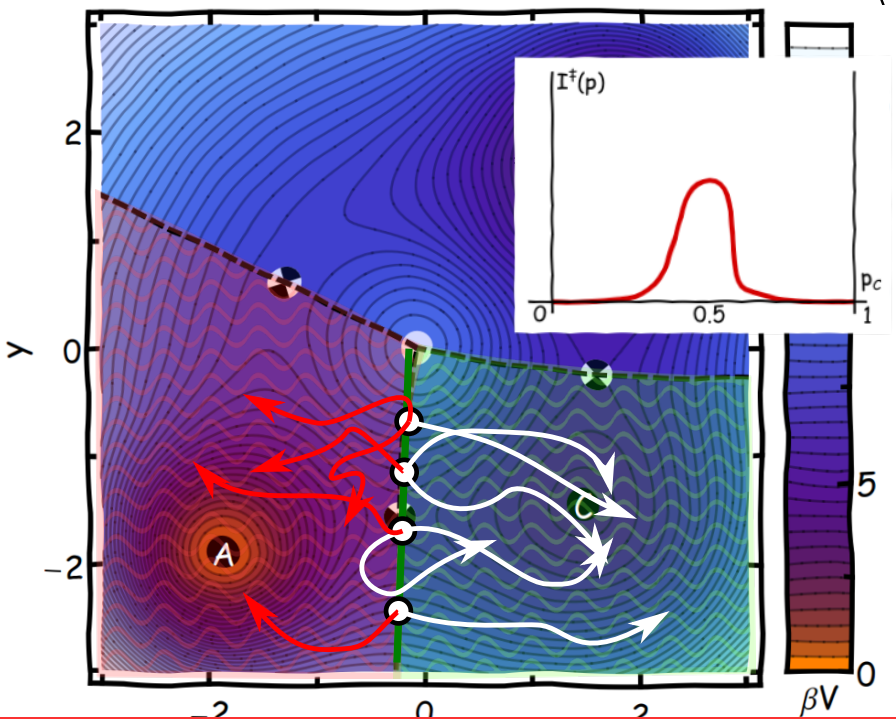
Bad CVs give committor histogram that is constant or peaked at 1 and 0. Good CVs have committor histogram peaked at p_C =0.5

Bolhuis et al., Ann. Rev. Phys. Chem. 2002

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Wrap up and take home

- Complex systems with many meta-stable states exhibit multiple time scales. **Rare events** happen infrequently, but are fast - a very large number of steps is needed for molecular dynamics
- Construct approximate dynamical models based on **static** information:
  - mapping critical points on the potential energy surface
  - in complex systems, one has to coarse grain the system and use **collective variables** to introduce a **free energy** surface
  - it is possible to correct for dynamical effects by combining static information and (short) dynamical trajectories
- Still we have to discuss how to compute efficiently the free energy profile in presence of rare events (next talk)

Bibliography

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