Pathways and Energy Landscapes

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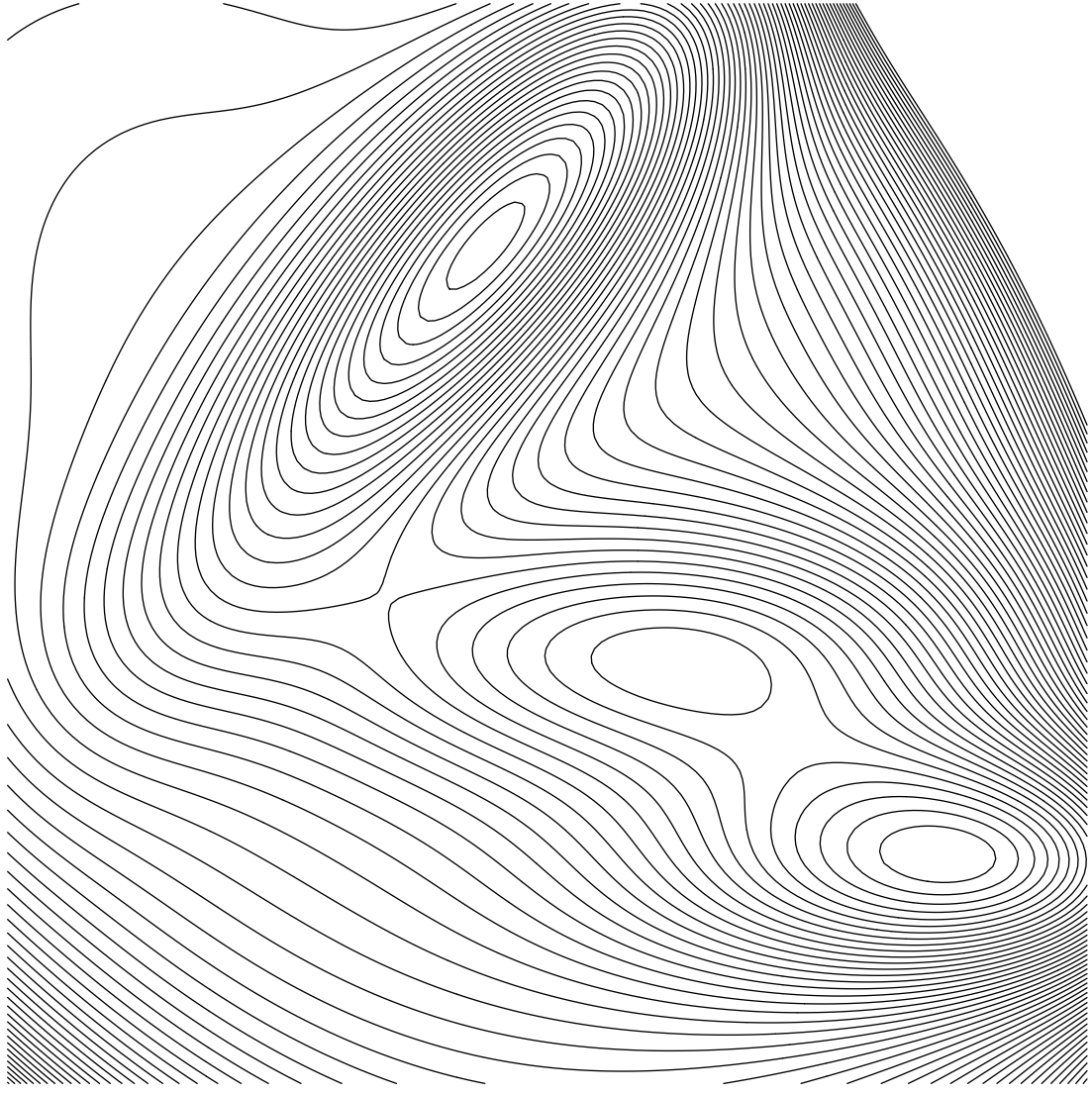
Acknowledgements

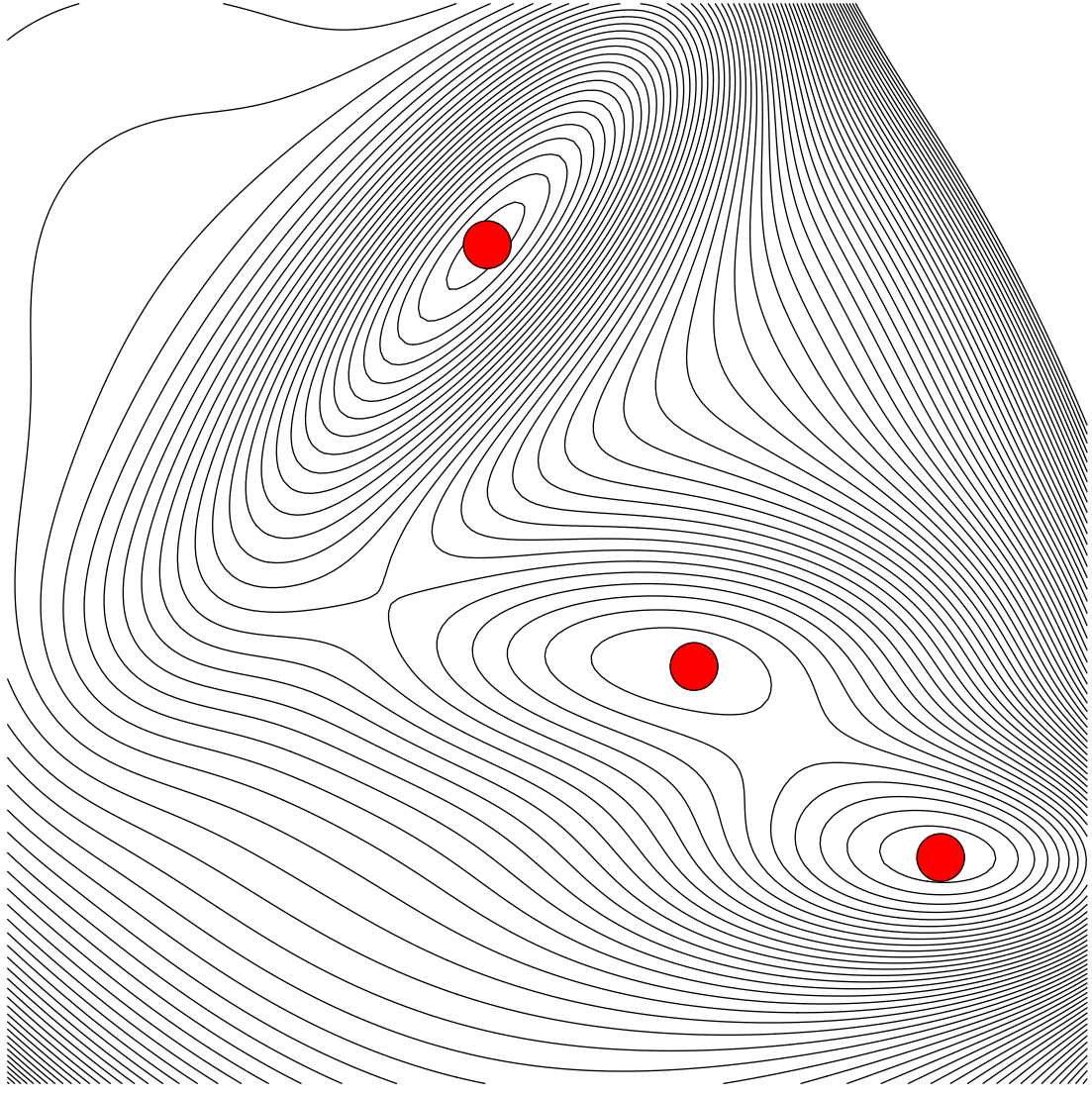
Dr David J. Wales

Darwin College
Cambridge Overseas Trust

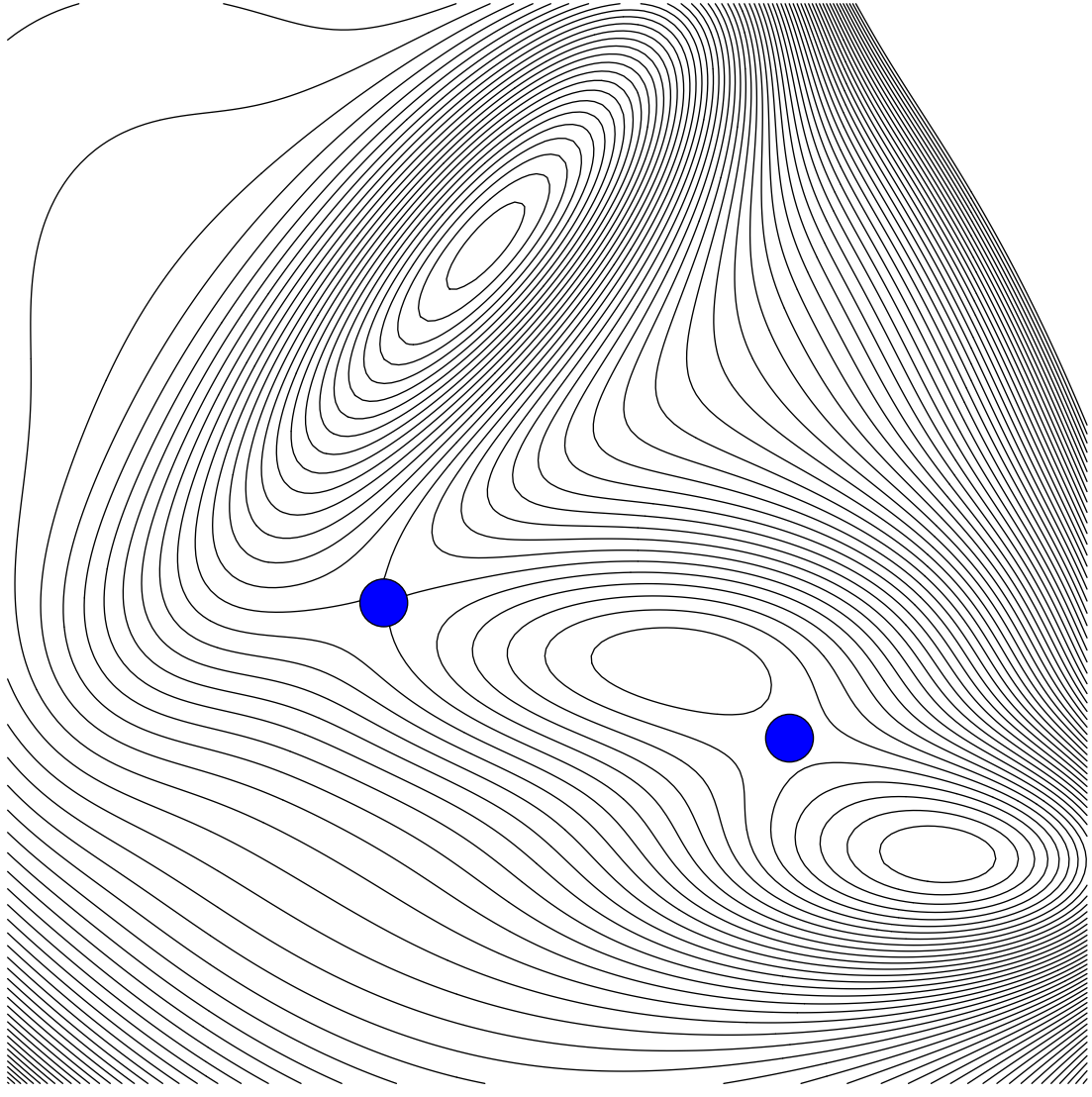
Potential energy surface (PES)



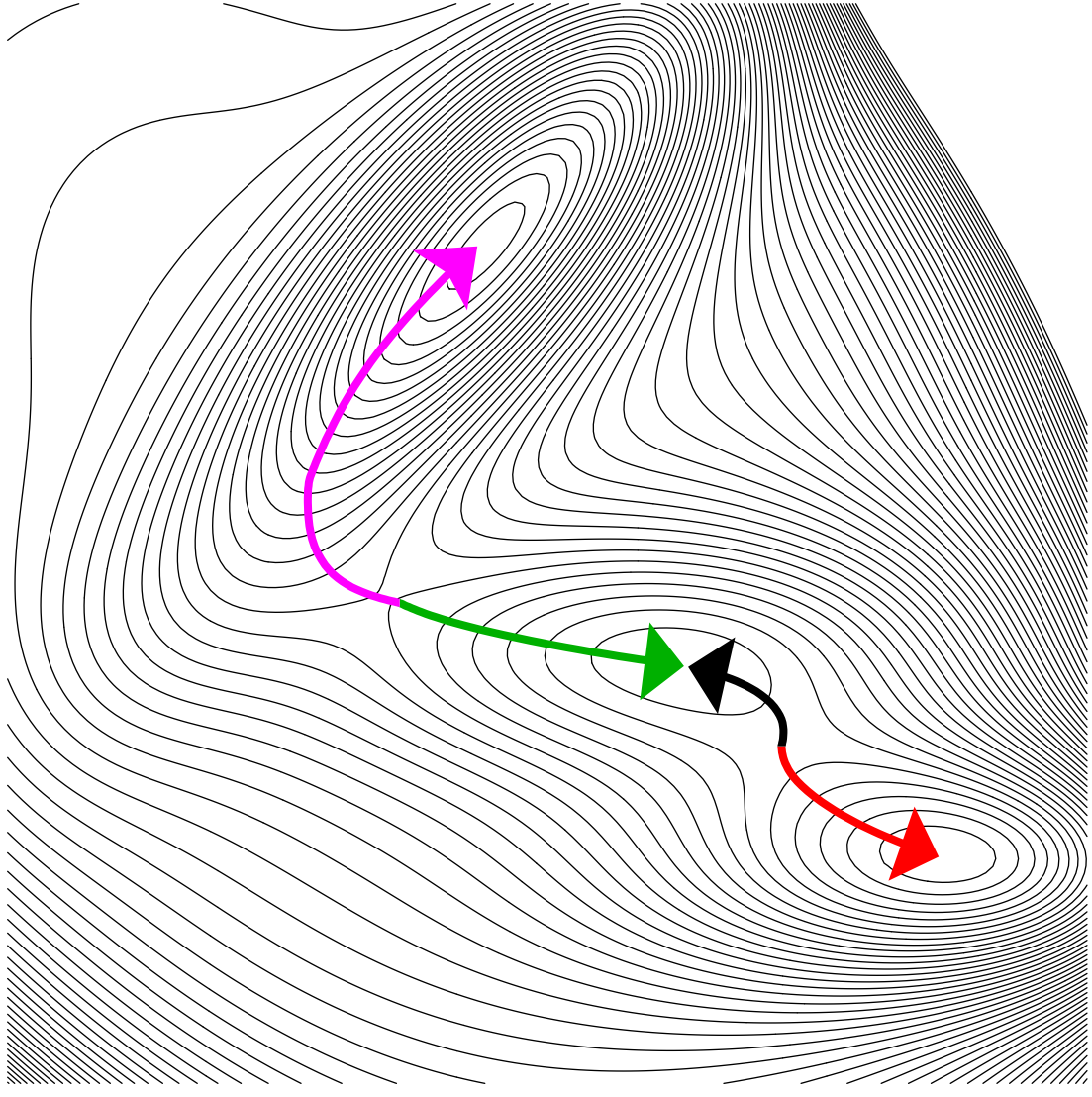
Coarse-grained PES: minima



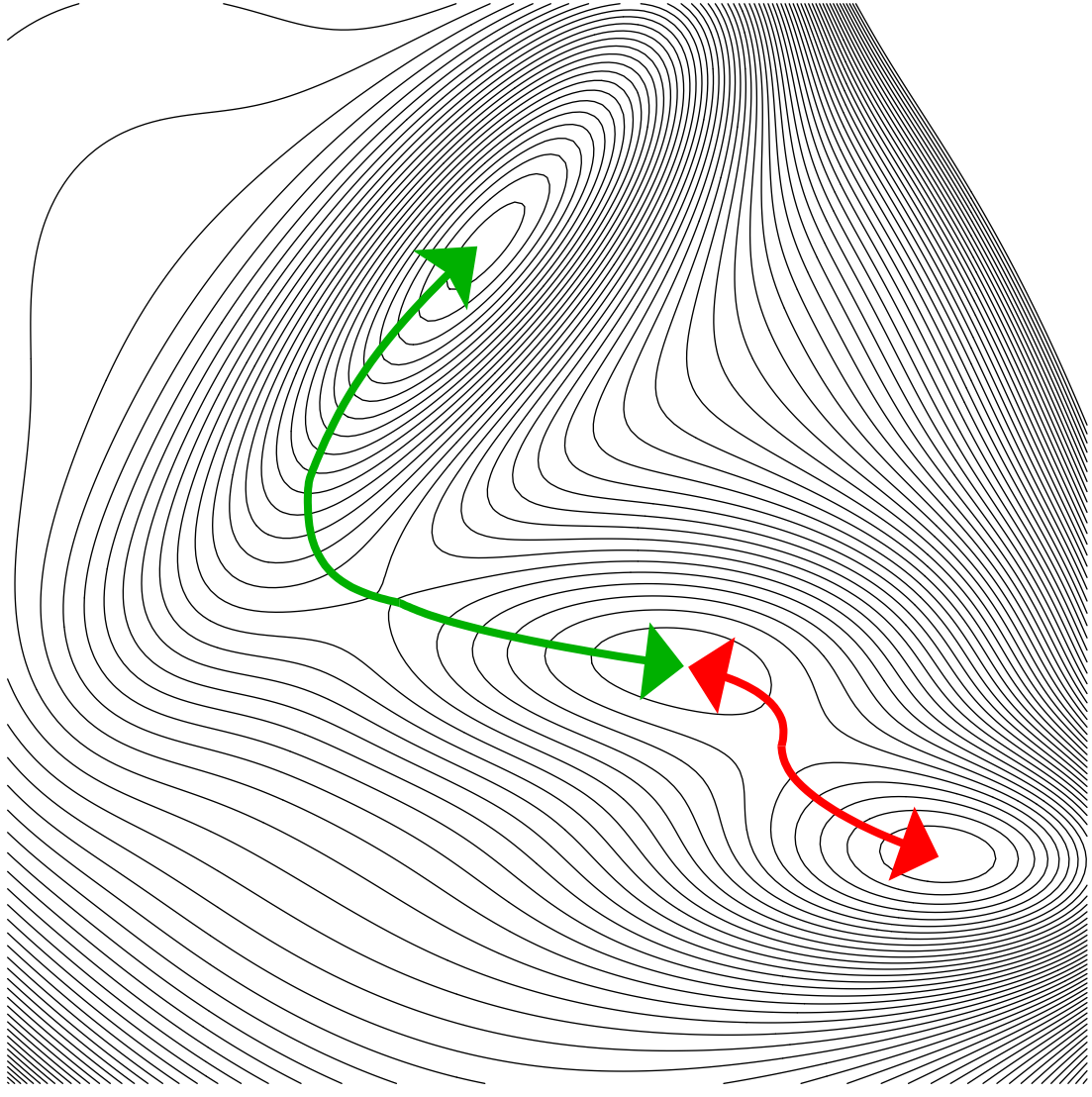
Coarse-grained PES: transition states



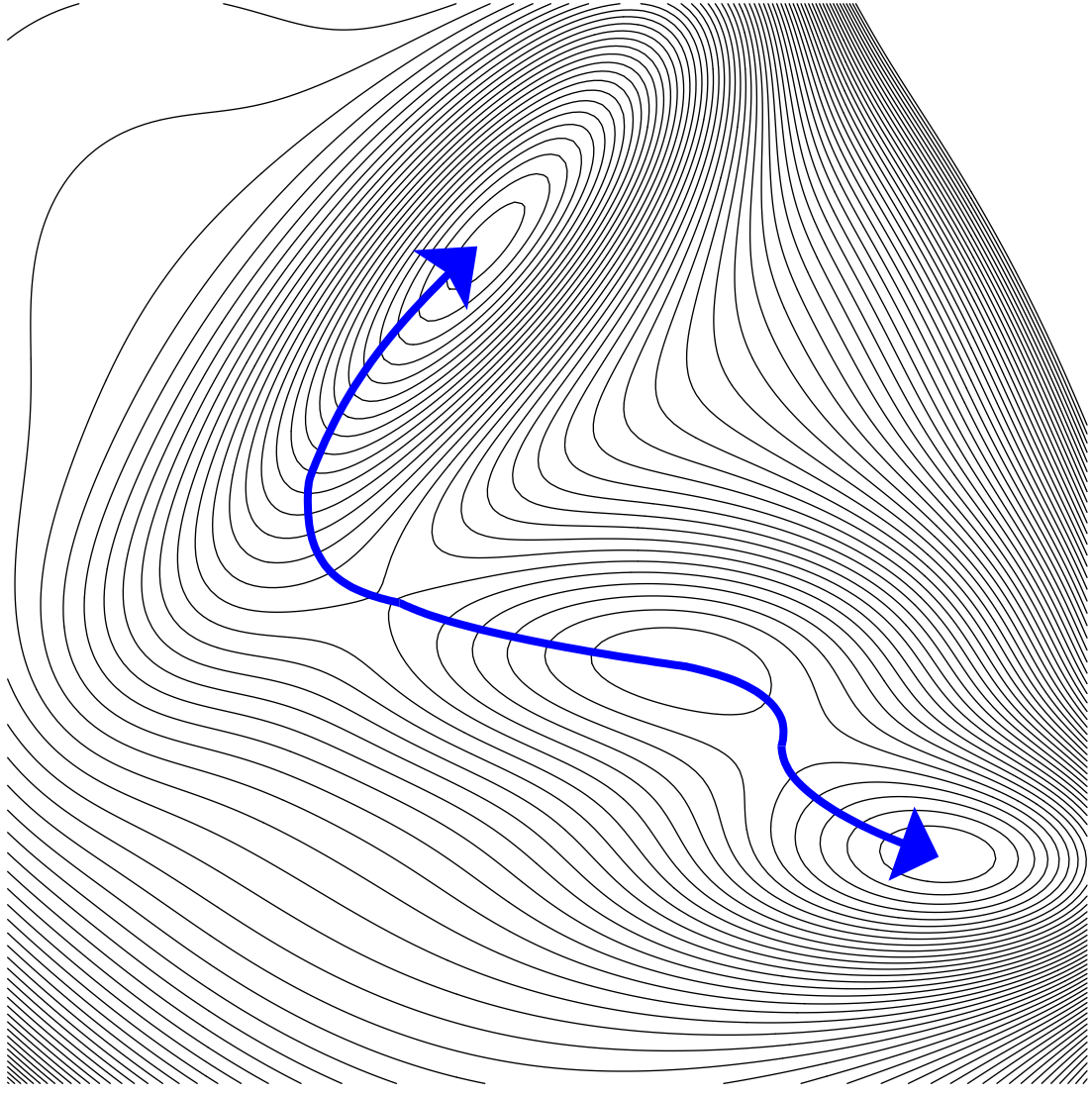
Connectivity: steepest-descent paths



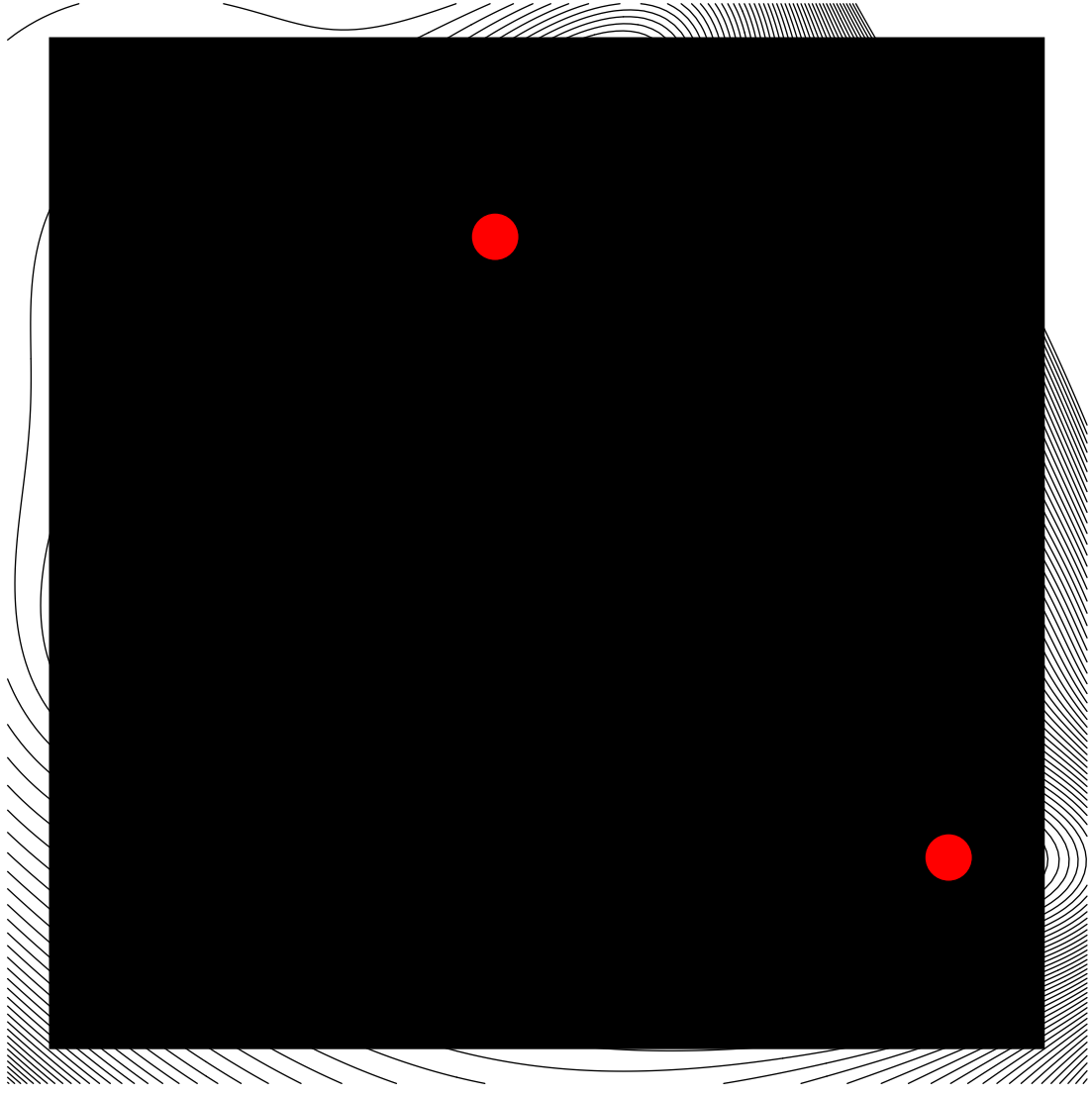
Single-step rearrangement pathways



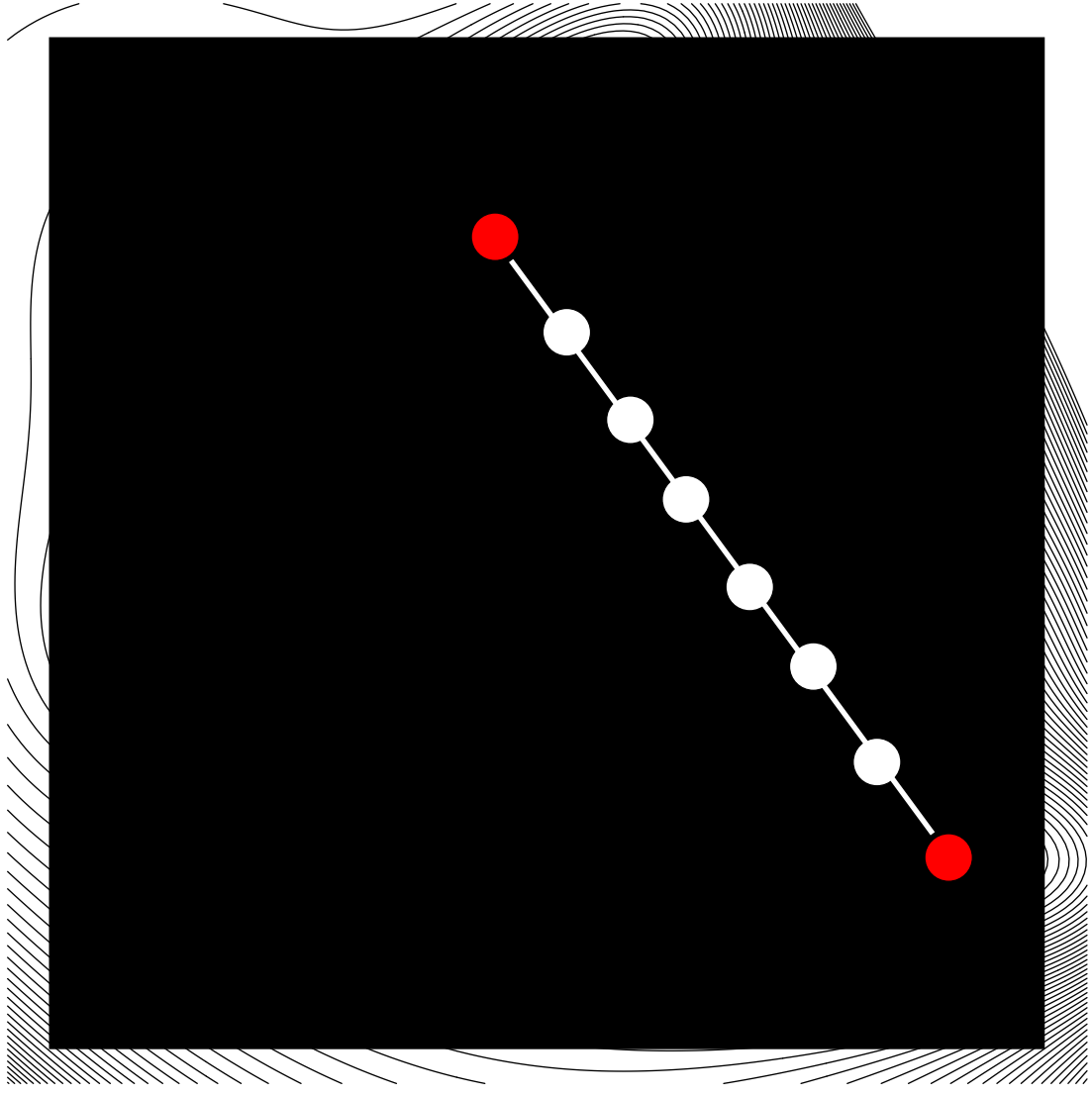
Multi-step rearrangement pathways



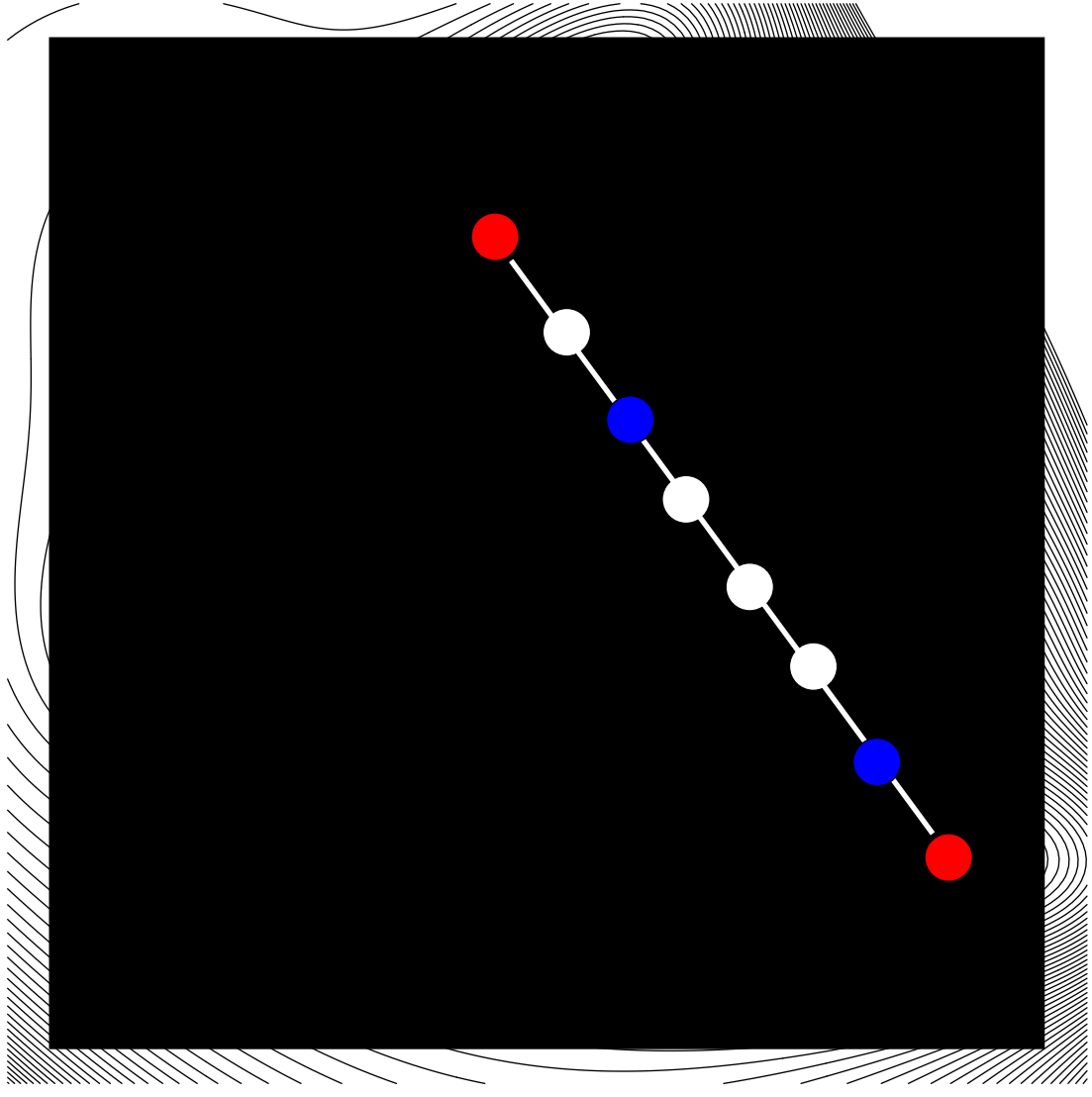
Double-ended methods for finding RP's



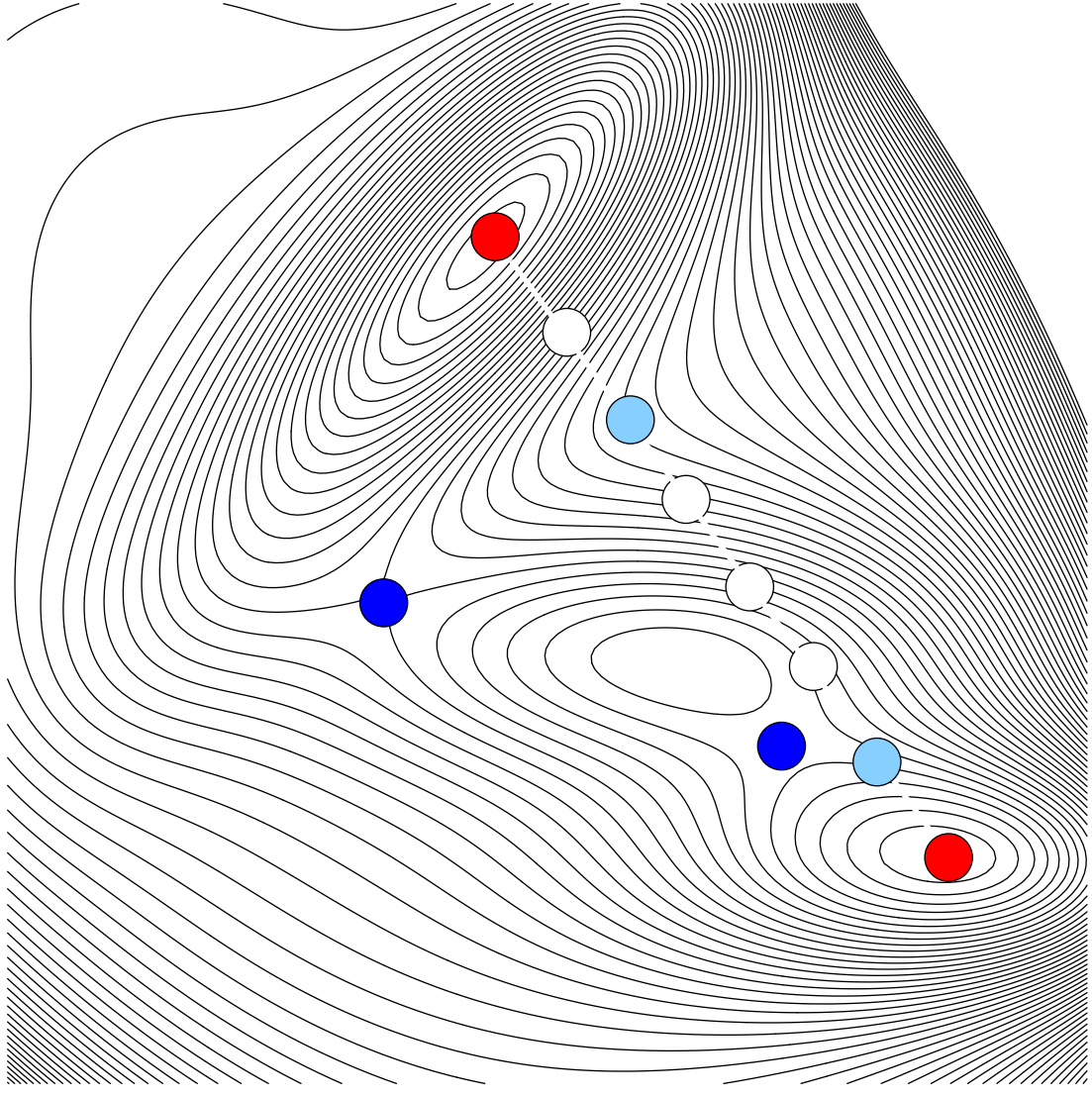
Linear synchronous transit



Linear synchronous transit



Linear synchronous transit



$$\mathbf{g} + \widetilde{\mathbf{g}}$$

Nudged elastic band method

$$\mathbf{g}_i = \mathbf{g}_i^{\perp} + \widetilde{\mathbf{g}}_i^{\parallel} \qquad \mathbf{g}_i^{\perp} = \nabla_i V_i - \mathbf{g}_i^{\parallel}$$

$$\mathbf{g}_i^{\parallel} = \left(\nabla_i V_i \cdot \hat{\boldsymbol{\tau}}_i\right) \hat{\boldsymbol{\tau}}_i \qquad \hat{\boldsymbol{\tau}}_i = \frac{(j-i)(\mathbf{X}_j - \mathbf{X}_i)}{|\mathbf{X}_j - \mathbf{X}_i|}$$

$$\widetilde{\mathbf{g}}_i^{\parallel} = k_{spr}\left(|\mathbf{X}_i - \mathbf{X}_{i-1}| - |\mathbf{X}_{i+1} - \mathbf{X}_i|\right) \hat{\boldsymbol{\tau}}_i$$

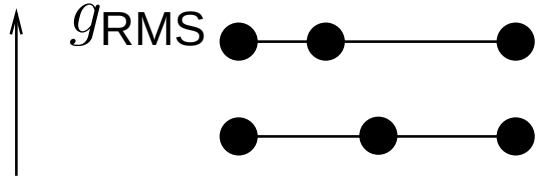
- Band is a discrete representation of the path;
- corner cutting and sliding down problems are dealt with via projections;
- objective function is unknown;
- quenched velocity Verlet algorithm is used for minimisation.

G. Henkelman and H. Jónsson, J. Chem. Phys., 113, 9978 (2000)

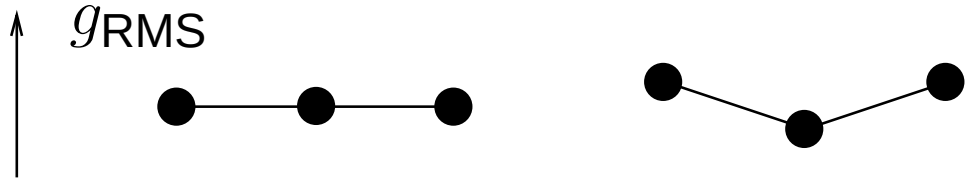
$\widetilde{\mathbf{g}}^{\parallel} + \mathbf{g}^{\perp}$ ($\mathbf{g}^{\parallel}$ and $\widetilde{\mathbf{g}}^{\perp}$ are projected out)

Elastic vs. ‘nudged elastic’

- Spring gradient is minimised when the images are equispaced along the path;



- short paths are NOT favoured over the long ones, however;



$\Rightarrow$ Overall rotation and translation must be removed for the solution to be unique.

NEB highlights

- Band is a discrete representation of a pathway;
- Initial guess is required;
- Two parameters must be provided:
  - number of images;
  - spring force constant;
- Minimisation can easily become ill-conditioned;
- Object function is unknown;
- Problems with convergence and termination criteria;
- ORT removal affects:
  - stability;
  - efficiency.

Doubly nudged elastic bands

Only the component of $\widetilde{\mathbf{g}}$ that interferes with $\mathbf{g}^{\perp}$ is projected out:

$$\mathbf{g}_{\mathrm{DNEB}} = \mathbf{g}^{\perp} + \widetilde{\mathbf{g}} - (\widetilde{\mathbf{g}} \cdot \hat{\mathbf{g}}^{\perp})\hat{\mathbf{g}}^{\perp}.$$

NEB properties such as the absence of corner-cutting and sliding down are preserved. In addition:

- overall rotation and translation need NOT be removed;
- minimisers with superlinear/quadratic convergence can be used.

S. A. Trygubenko and D. J. Wales, J. Chem. Phys., 120, 2082 (2004)

S. A. Trygubenko and D. J. Wales, J. Chem. Phys., 121, 6689 (2004)

NEB and DNEB comparison

TABLE II. The minimal number of iterations needed to produce connected pathways for four degenerate rearrangements of LJ_7 using a 50-image NEB. The strategy of this calculation is identical to the one described in the caption to Table I, except that the number of images was fixed.

Method	1–2	2–3	3–4	4–5
DNEB/L-BFGS	131[a]	493	171	326
DNEB/SQVV	1130	15 178	2777	23 405[b]
NEB/SQVV	11 088[b]	—[c]	30 627	—[c]

[a]The number of iterations is the sum of the SQVV preoptimization steps (100 on average) and the actual number of iterations needed by L-BFGS minimizer.

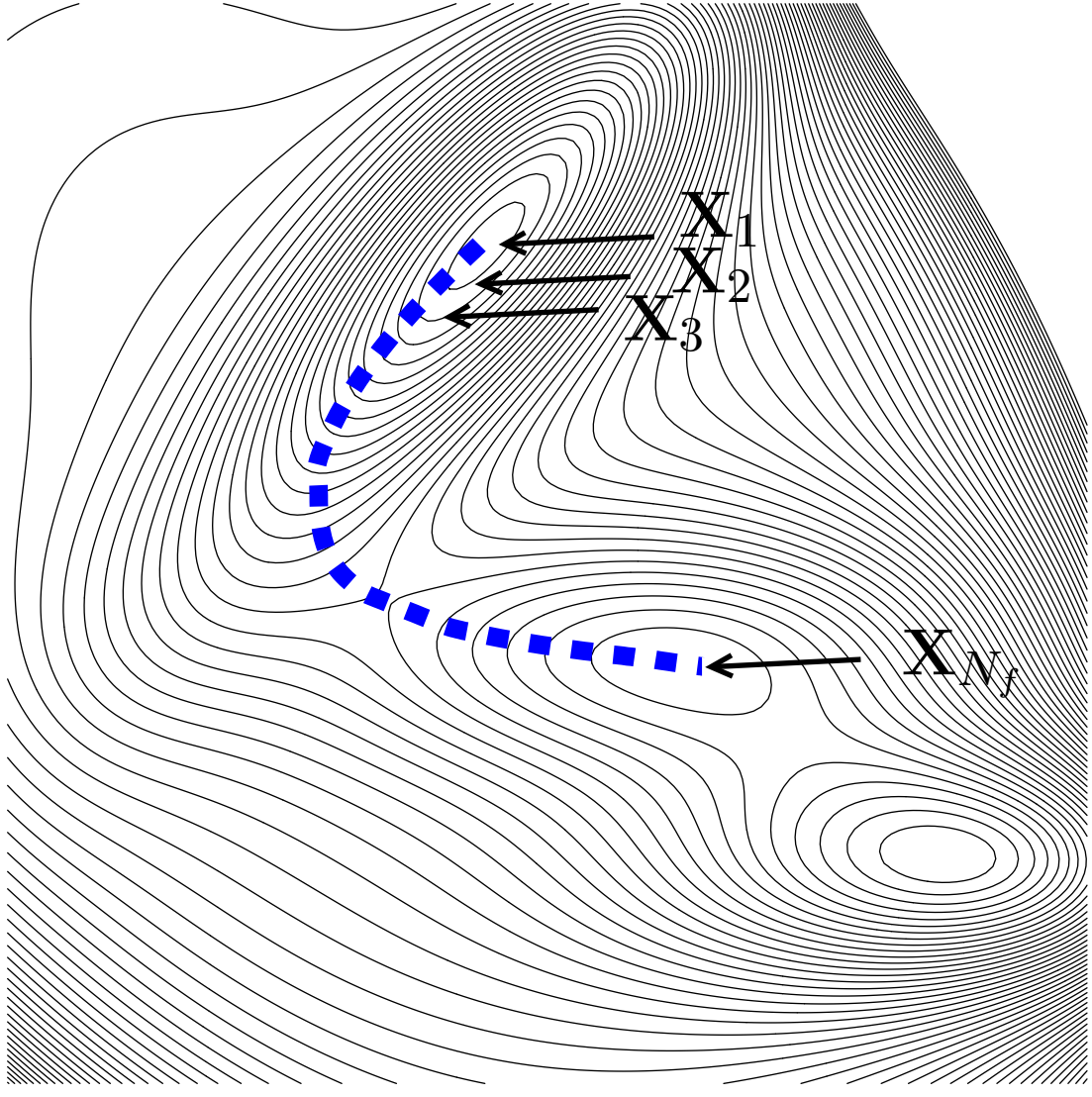
[b]This value is not directly comparable since DNEB converged to a different path that contains more intermediate minima.

[c]Cases where we were unable to obtain a connected pathway.

Summary 1

- What is a RP?
  - single-step and multi-step paths;
  - a discrete representation.
- How to find a RP?
  - double-ended methods;
  - nudged elastic bands;
  - doubly nudged elastic bands.
- Why pathways are important?
  - Mechanism;
  - Kinetics.
- Properties of RP.
- Why some RP are difficult to find?

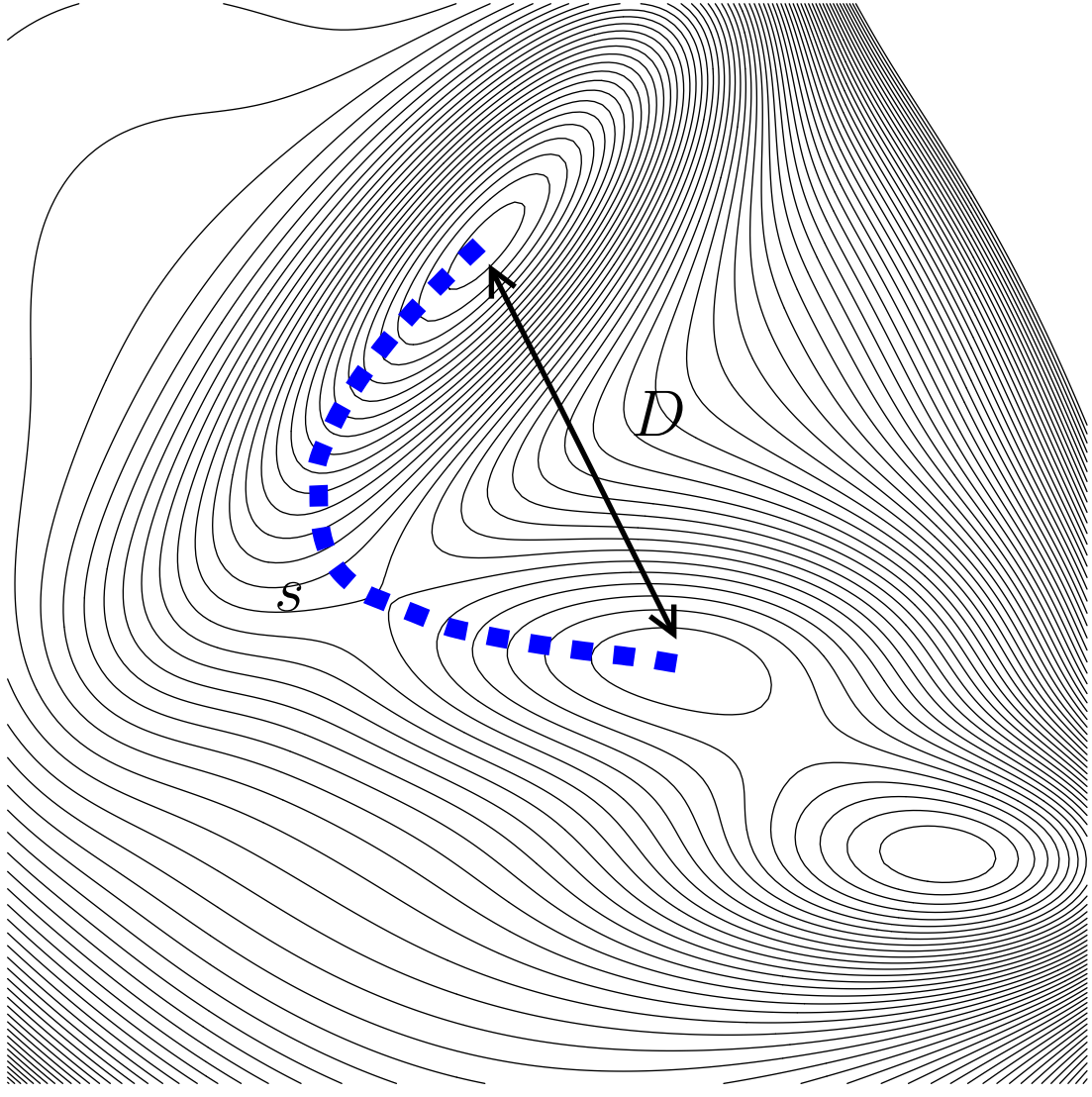
Points along the path: $\mathbf{X}_0, \mathbf{X}_1, \mathbf{X}_2, \ldots$



Properties of elementary rearrangements

- Uphill barrier $E_u = E_{\mathrm{ts}} - \max\left(E_{\mathrm{m1}}, E_{\mathrm{m2}}\right)$
- Downhill barrier $E_d = E_{\mathrm{ts}} - \min\left(E_{\mathrm{m1}}, E_{\mathrm{m2}}\right)$
- Barrier asymmetry $\beta = \left(E_u - E_d\right)/E_u$
- Endpoint separation $D = \sqrt{\sum_{i=1}^{N}\left(\mathbf{r}_i(N_f) - \mathbf{r}_i(1)\right)^2}$
- Path length $s = \sum_{j=2}^{N_f}\sqrt{\sum_{i=1}^{N}\left(\mathbf{r}_i(j) - \mathbf{r}_i(j-1)\right)^2}$
- Pathway nonlinearity $\alpha = (s - D)/s$
- Path length asymmetry $\pi = |s_u - s_d|/\max(s_u, s_d)$
- Localisation $N_p = N/\gamma'(d)$
- Cooperativity $N_c = \sum_{k=1}^{N} k\Theta_k$

Path length and endpoint separation



Localisation

Integrated path length for atom i:

$$d_i = \sum_{j=2}^{N_f} \left| \mathbf{r}_i(j) - \mathbf{r}_i(j-1) \right|.$$

Curtosis of the distribution of displacements $\{d\} = \{d_1, d_2, \ldots, d_N\}$:

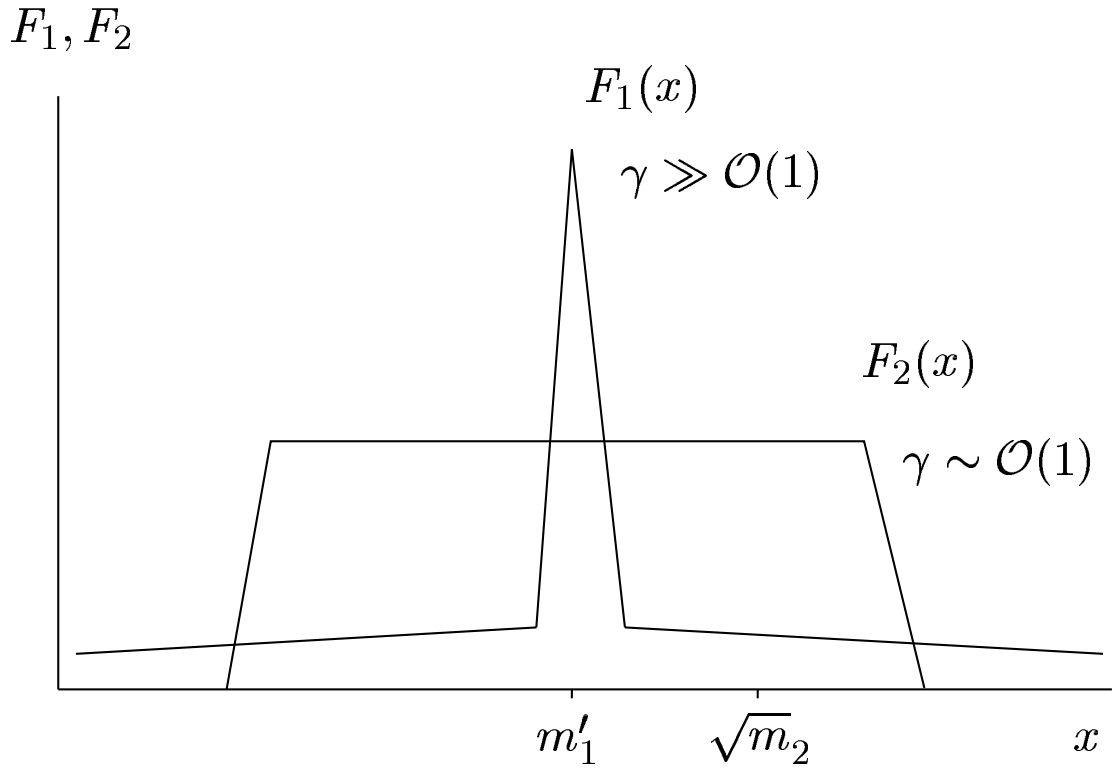
$$\gamma'(d) = m'_4 / \left(m'_2\right)^2,$$

where m'_n is the nth moment about the origin for data set $\{d\}$:

$$m'_n = \sum_{i=1}^{N} \left(d_i\right)^n / N.$$

Participation index N_p

$$N_p = \frac{N}{\gamma'(d)}$$



F. H. Stillinger and T. A. Weber, Phys. Rev. A, 28, 2408 (1983)

S. A. Trygubenko and D. J. Wales, J. Chem. Phys., 121, 6689 (2004)

Cooperativity index N_c

$$N_c = \sum_{k=1}^{N} k\Theta_k,$$

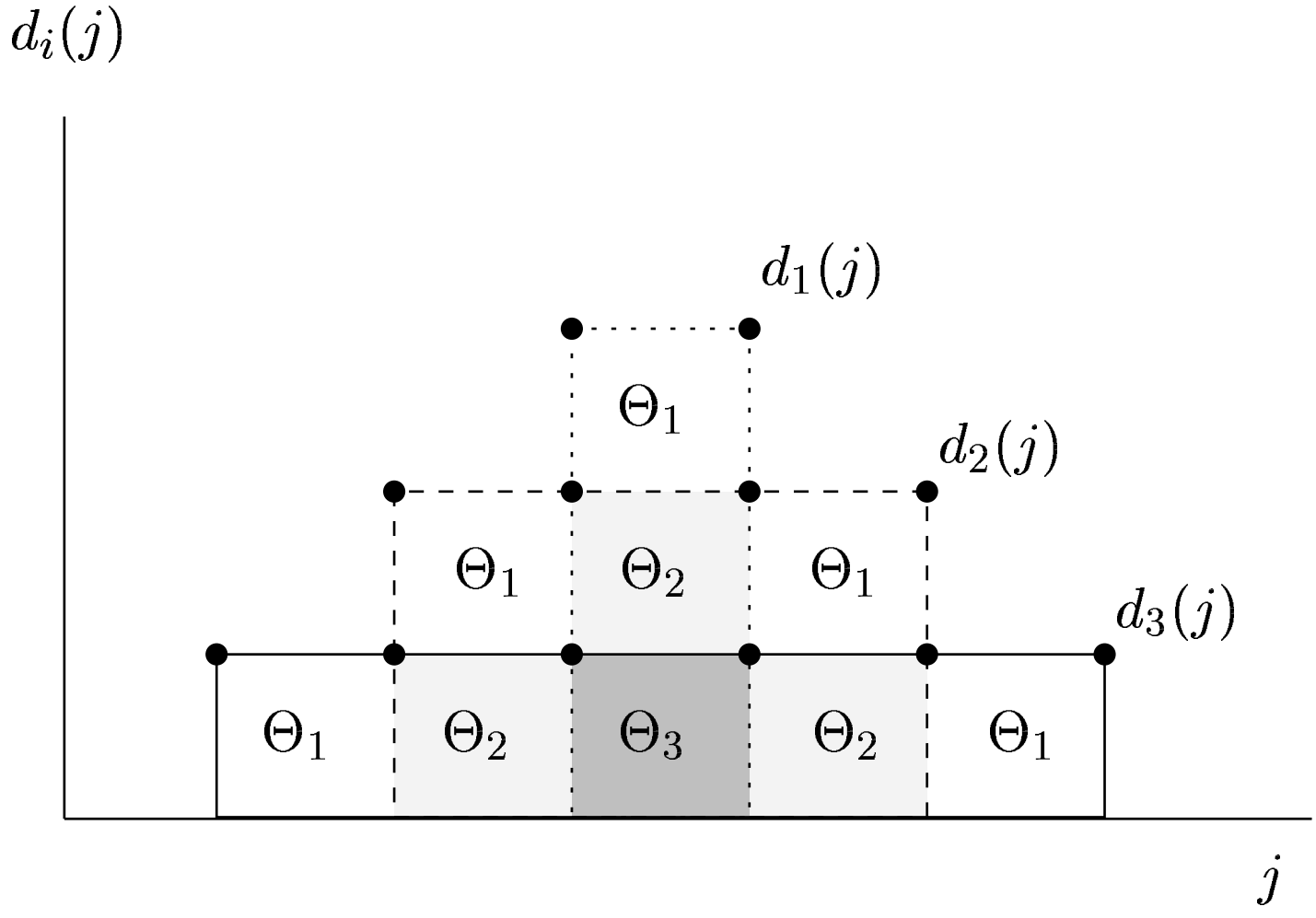
where

$$\Theta_k = \frac{1}{\Delta_{tot}} \sum_{j=2}^{N_f} \Big[\Delta_k(j) - \Delta_{k+1}(j) \Big],$$

where $\Delta_i(j)$ is the displacement of atom i in frame j with index i numbering the atoms in frame j in descending order according to the magnitude of $d_i(j)$, k ranges from 1 to N, $\Delta_{tot} = \sum_{j=2}^{N_f} \Delta_1(j)$ and $\Delta_{N+1}(j)$ is defined to be zero for all j.

S. A. Trygubenko and D. J. Wales, J. Chem. Phys., 121, 6689 (2004)

Θ_k overlaps

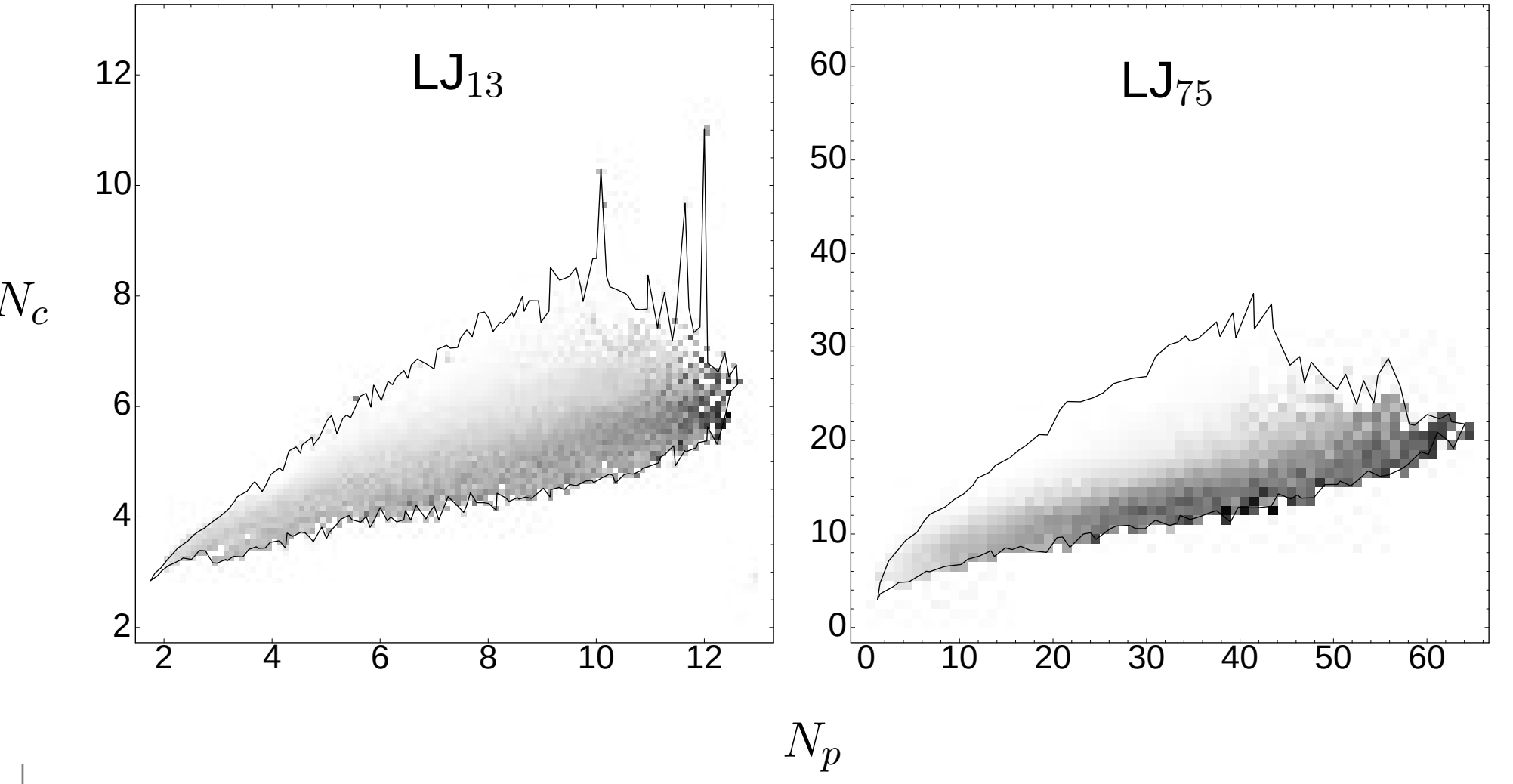


$\Theta_1 = 5/9$, $\Theta_2 = 3/9$, and $\Theta_3 = 1/9$.

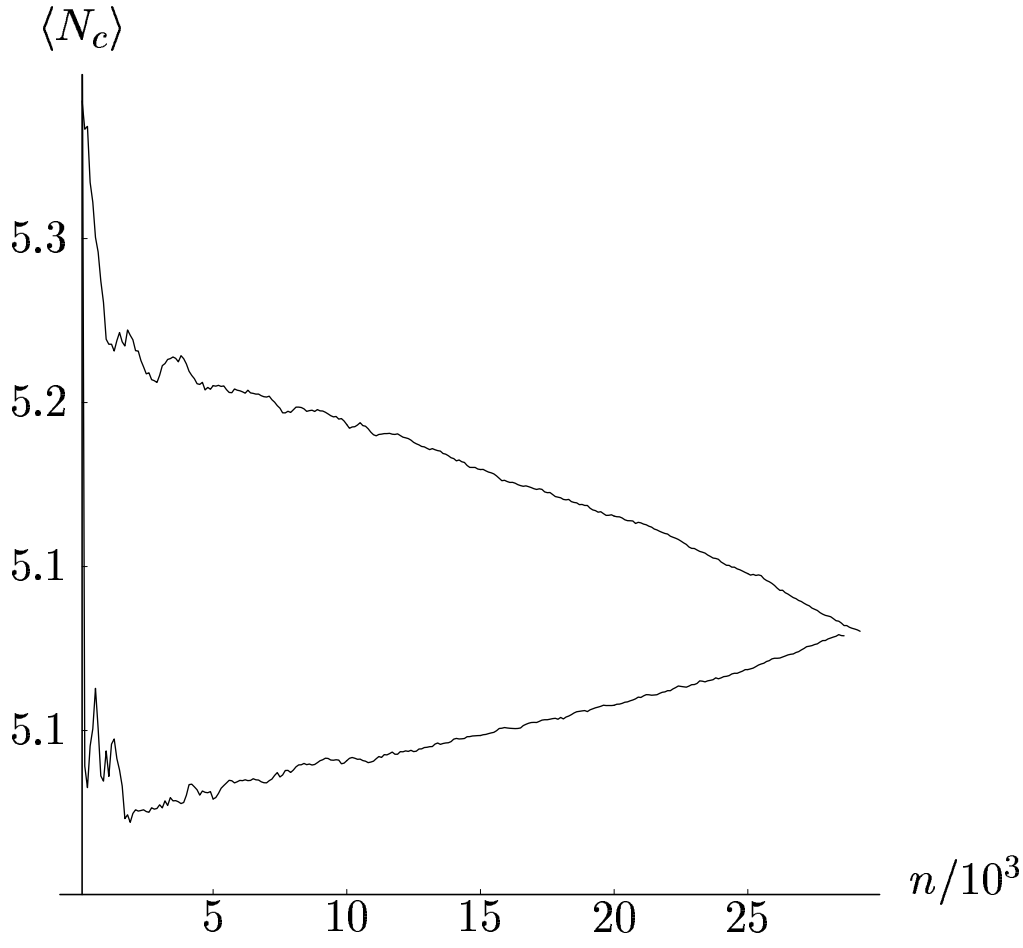
Examples of usage

$N_p \in [1, N]$ (usually)
$N_c \in [1, N]$
$N_c \leqslant N_p$.

Average barrier as a function of N_p and N_c



Sampling for cooperative paths



The average value of N_c for two LJ_{13} pathway databases as new paths are added.

Summary 2

- s can be used as a reaction coordinate;
- Energy barrier determines the speed of a reaction;
- End point separation D is an upper bound for s;
- Pathways can be non-linear and asymmetric;
- Uncooperative rearrangements are hard to find;
- N_p and N_c indices;
- Correlation between barrier height and cooperativity;
- Sampling for cooperative paths.
- How to find a pathway if the endpoints are far apart?

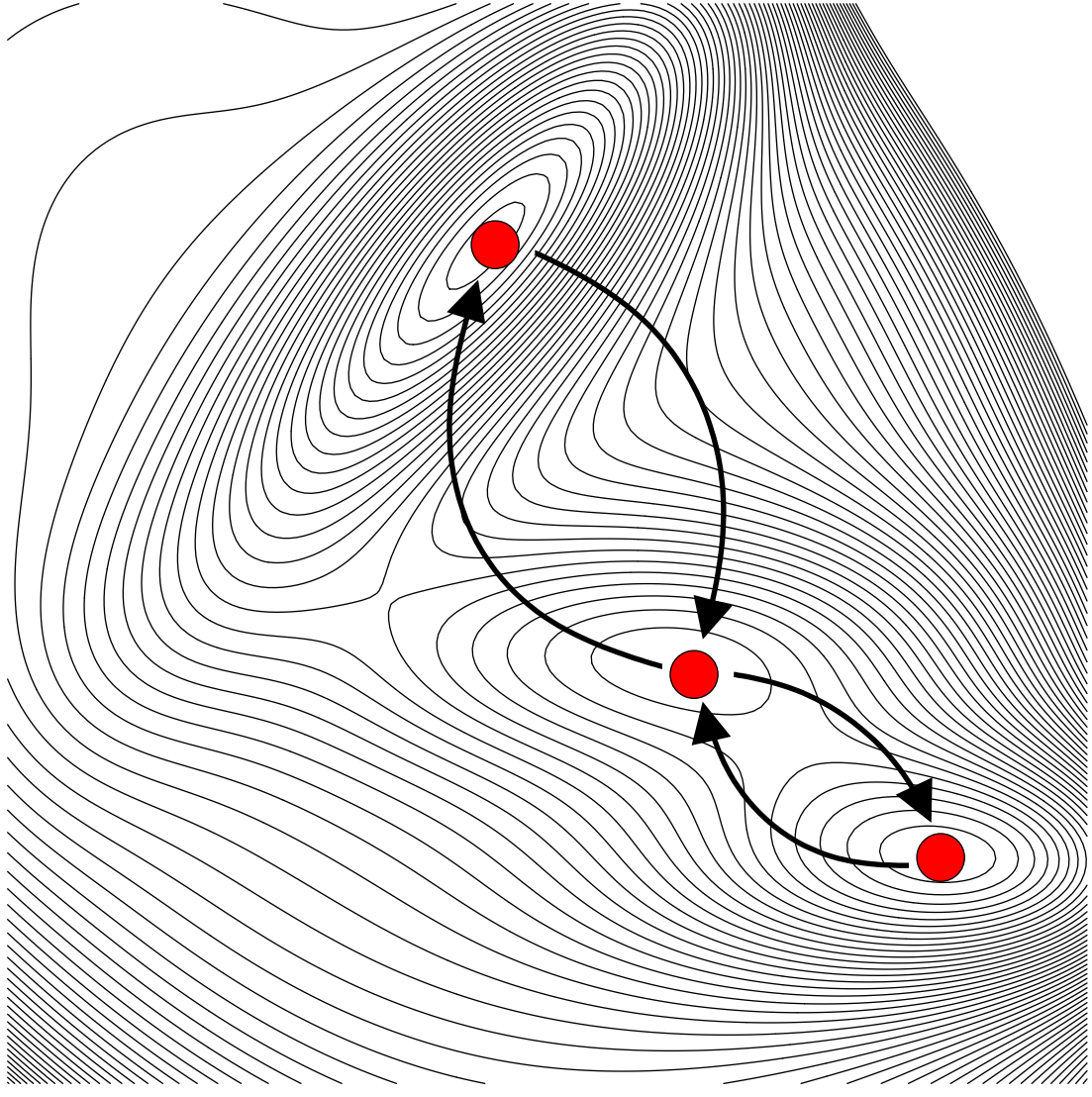
Distant endpoints

It is unlikely that a connected pathway will be found after one DNEB search because

- multiple barrier and path length scales exist on a complex PES (e.g. for one of our LJ_{75} samples: $s \in [10^{-4}, 20.0]$, $\Delta V \in [10^{-7}, 17.0]$);
- linear interpolation guessing becomes poorer as the endpoint separation increases;
- we don't know the answer before we start! (number of images)

However, it is likely that some relevant stationary points will be found. Therefore, we require an incremental algorithm for constructing the pathway that is based on consecutive DNEB searches.

Graph theory representation



Dijkstra algorithm

- Solves single-source/single-destination shortest paths problem;
- directed or undirected graph;
- edge weight must be non-negative;
- greedy strategy;
- for sparse graphs a good implementation scales as $|V| \log |E|$, a bad one — as $|V||E|$.

E. W. Dijkstra, Numerische Math., 1, 269 (1959)

Dijkstra-based connection algorithm

- stationary points database is treated as a complete graph;
- one of the endpoints is chosen to be the source;
- cost function is defined as

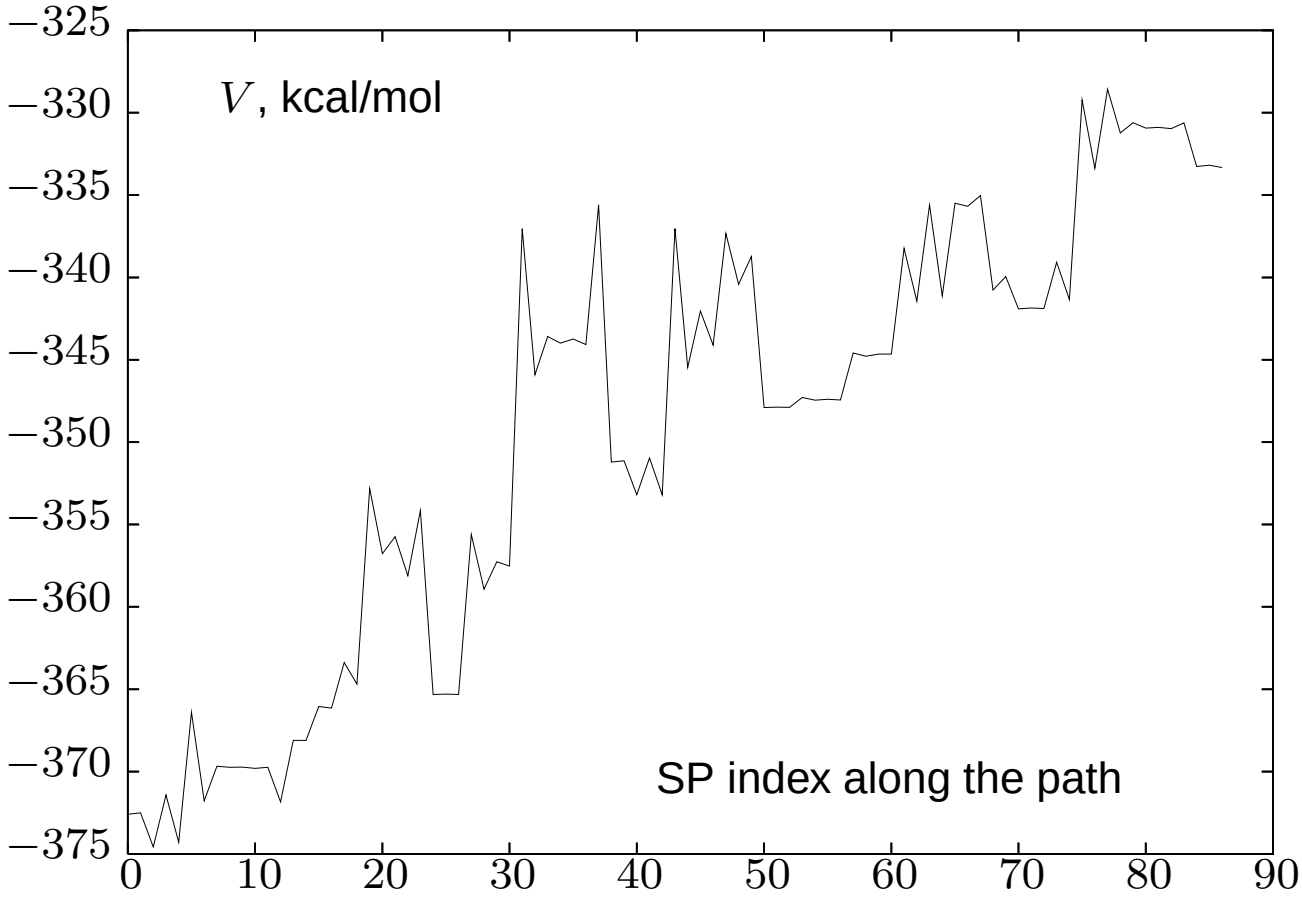
$$w(u,v) = \begin{cases} 0, & \text{if } u \text{ and } v \text{ are connected via a single ts,} \\ \infty, & \text{if } n(u,v) = n_{max}, \\ f(D(u,v)), & \text{otherwise;} \end{cases}$$

- DNEB searches are initiated for every gap in the shortest path.

J. M. Carr, S. A. Trygubenko and D. J. Wales, J. Chem. Phys., 122, 234903 (2005)

A 2D example

Application to tryptophan zipper



Approximately 200 DNEB searches and 50 Dijkstra runs.

Final database size is 200 minima and 150 transition states.

Summary 3

- Graph representation of PES;
- Nodes represent minima;
- Edges represent transition states;
- Dijkstra-based connection algorithm;
- Discrete path sampling (DPS) theory;
- How to find the fastest pathway?
- How to optimise pathway ensemble?

A set of linear master equations

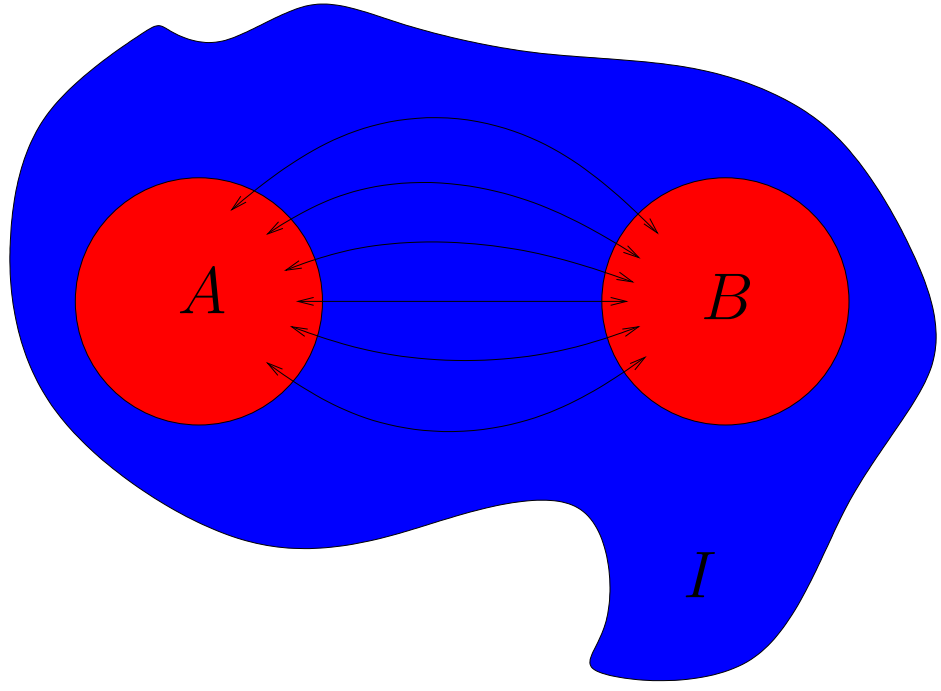
governs the evolution of the occupation probabilities towards equilibrium

$$\frac{dP_\alpha(t)}{dt} = \sum_{\beta \in AdjIn[\alpha]} k_{\alpha,\beta} P_\beta(t) - P_\alpha(t) \sum_{\beta \in AdjOut[\alpha]} k_{\beta,\alpha},$$

where $P_\alpha(t)$ is the occupation probability of state α at time t.

N. G. van Kampen, Stochastic Processes in Physics and Chemistry, Elsevier (1981)

A two-state model



All the states are classified into A, B and I, and local mutual equilibrium is assumed within the A and B sets

$$P_a(t) = \frac{P_a^{eq} P_A(t)}{P_A^{eq}} \quad \text{and} \quad P_b(t) = \frac{P_b^{eq} P_B(t)}{P_B^{eq}}.$$

Steady-state approximation

When the steady-state approximation is applied to all the intervening states $i \in I$

$$\frac{dP_i(t)}{dt} = 0,$$

the system of linear master equations can be written as

$$\begin{aligned} \frac{dP_A(t)}{dt} &= k_{A,B}P_B(t) - k_{B,A}P_A(t), \\ \frac{dP_B(t)}{dt} &= k_{B,A}P_A(t) - k_{A,B}P_B(t), \end{aligned}$$

where the rate constants $k_{A,B}$ and $k_{B,A}$ ...

D. J. Wales, Mol. Phys., 100, 3285 (2002)

Rate constants $k_{A,B}$ and $k_{B,A}$

are the sums over all possible paths within set I of the products of the branching probabilities corresponding to the elementary transitions for each path:

$$k_{A,B} = \sum_{a \leftarrow b} \frac{k_{a,i_1}}{\sum_{\alpha_1} k_{\alpha_1,i_1}} \frac{k_{i_1,i_2}}{\sum_{\alpha_2} k_{\alpha_2,i_2}} \cdots \frac{k_{i_{n-1},i_n}}{\sum_{\alpha_n} k_{\alpha_n,i_n}} \frac{k_{i_n,b}\, p_b^{\mathrm{eq}}}{P_B^{\mathrm{eq}}}$$

$$= \sum_{a \leftarrow b} P_{a,i_1} P_{i_1,i_2} \cdots P_{i_{n-1},i_n} \frac{k_{i_n,b}\, p_b^{\mathrm{eq}}}{P_B^{\mathrm{eq}}},$$

and similarly for $k_{B,A}$. The sum is over all possible paths that begin from a state $b \in B$ and end at state $a \in A$.

D. J. Wales, Mol. Phys., 100, 3285 (2002)

Finding the fastest path

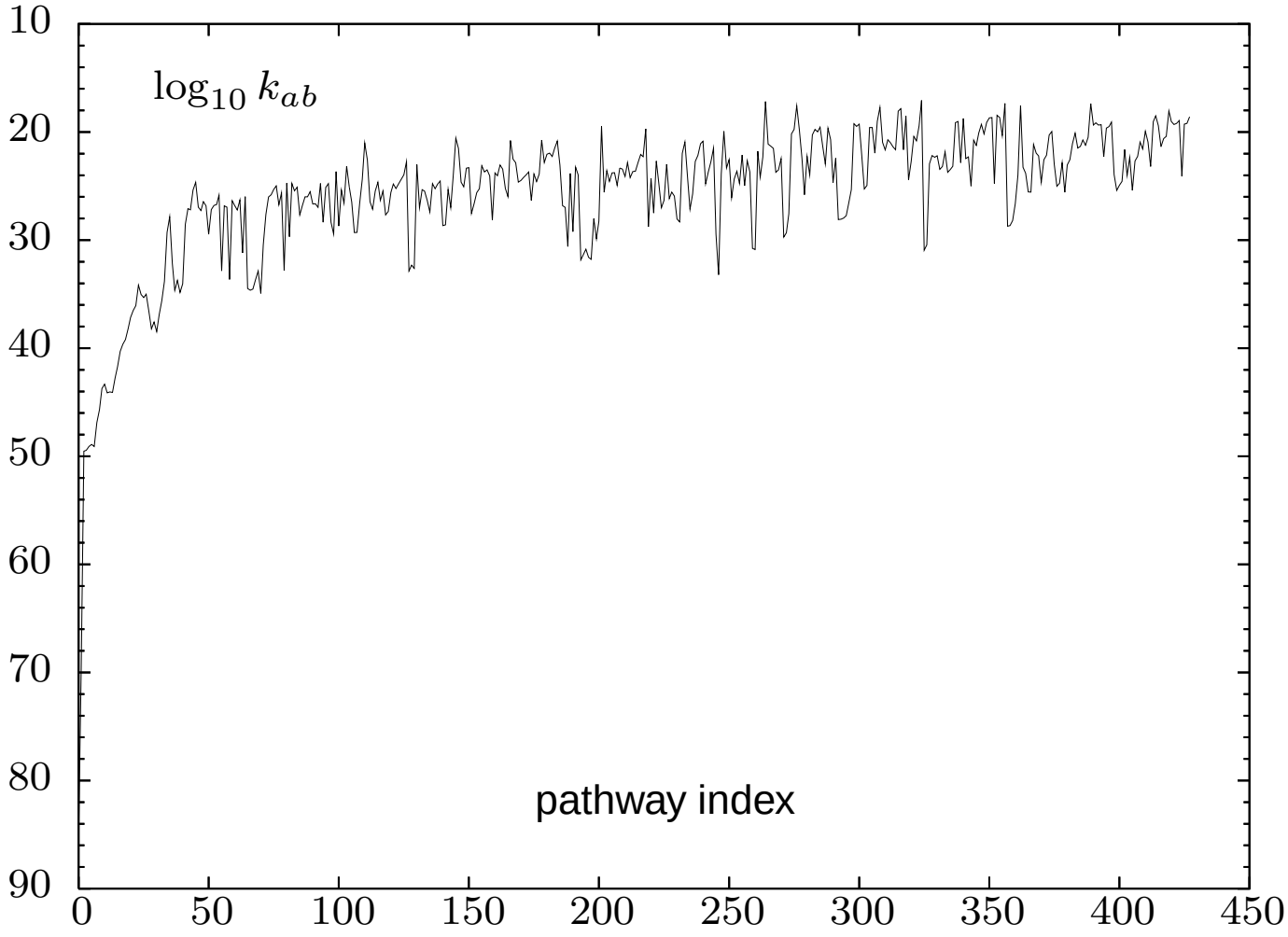
Using DPS non-recrossing rate definition it is possible to find the pathway with the largest k_{ab} by solving a single-source shortest paths problem as follows:

- database of stationary points is treated as a symmetric digraph;
- the weight of each directed edge $\alpha \rightarrow \beta$ is defined as

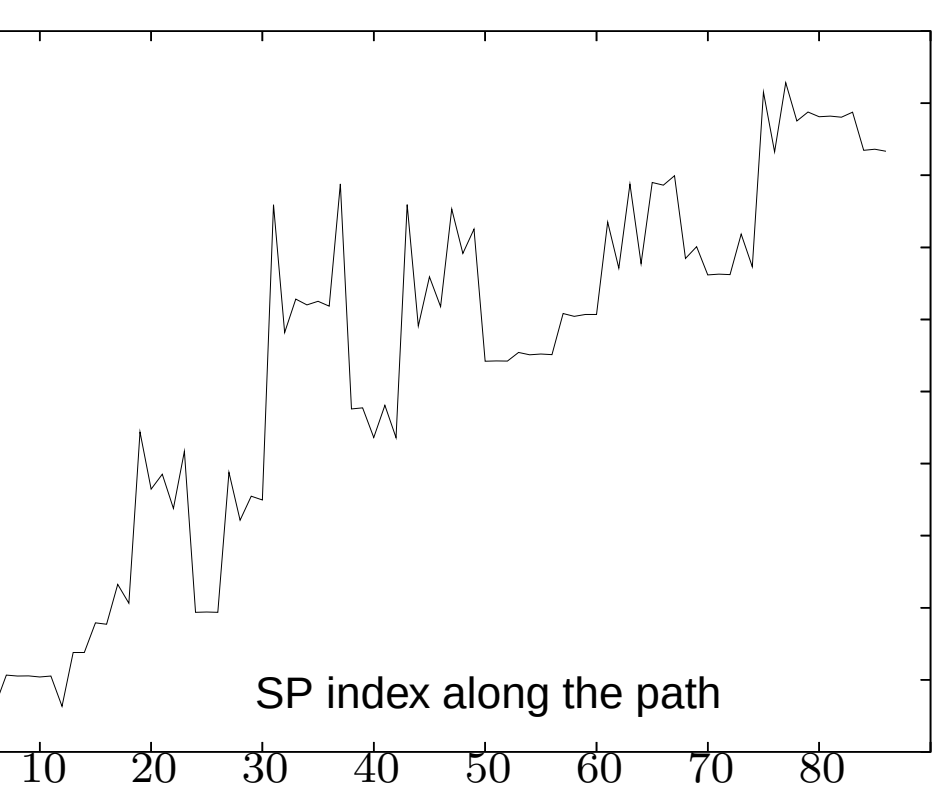
$$w(\beta, \alpha) = \ln\left(\frac{\sum_\gamma k_{\gamma\alpha}}{k_{\beta\alpha}}\right);$$

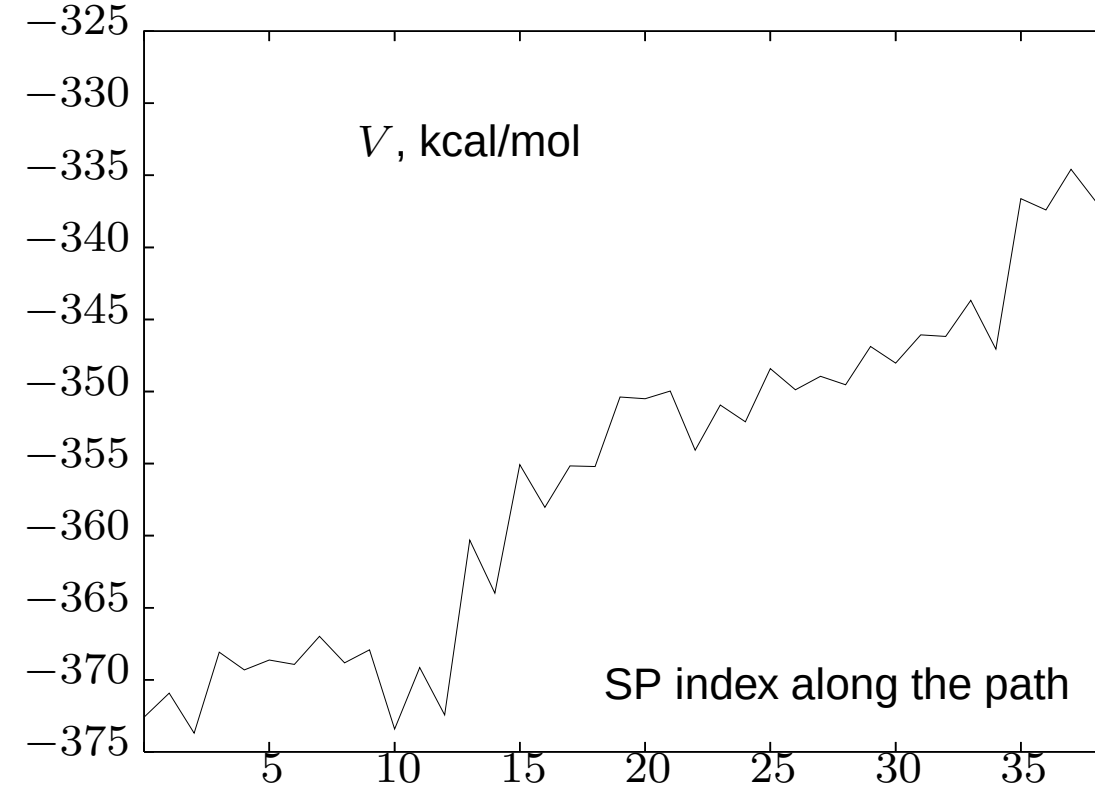
Since edge weight is non-negative Dijkstra algorithm can be applied. If the graph is sparse and evolves, e.g., as the sampling goes, it is advantageous to use dynamic graph algorithms such as dynamic Dijkstra.

Optimising pathway ensemble



Trpzip: initial path vs. fastest path





Number of steps:	86	40
DPS rate k_{ab}:	$7.7 \cdot 10^{-86}$	$2.6 \cdot 10^{-19}$
DPS rate k_{ba}:	$4.5 \cdot 10^{-107}$	$1.5 \cdot 10^{-40}$

Summary 4

- Graph theory tools are very useful in studing PES;
- Breadth-first search can be used to find the shortest pathway in linear time;
- Discrete path sampling allows to associate a rate constant with discrete pathway;
- Adopting DPS non-recrossing rates and our definition of the cost function the fastest path can be identified with Dijkstra algorithm in $|V| \log |E|$ time. Previously in our group we were using Bellman-Ford algorithm for this purpose;
- Pathway ensemble can be optimised utilising this information.
- How to augment DPS rate with recrossings?

Chapman-Kolmogorov equations

The matrix form of the system of Chapman-Kolmogorov equations for homogeneous discrete-time Markov chains allows us to obtain the n-step transition probability matrix $\mathbf{P}^{(n)}$ recursively as

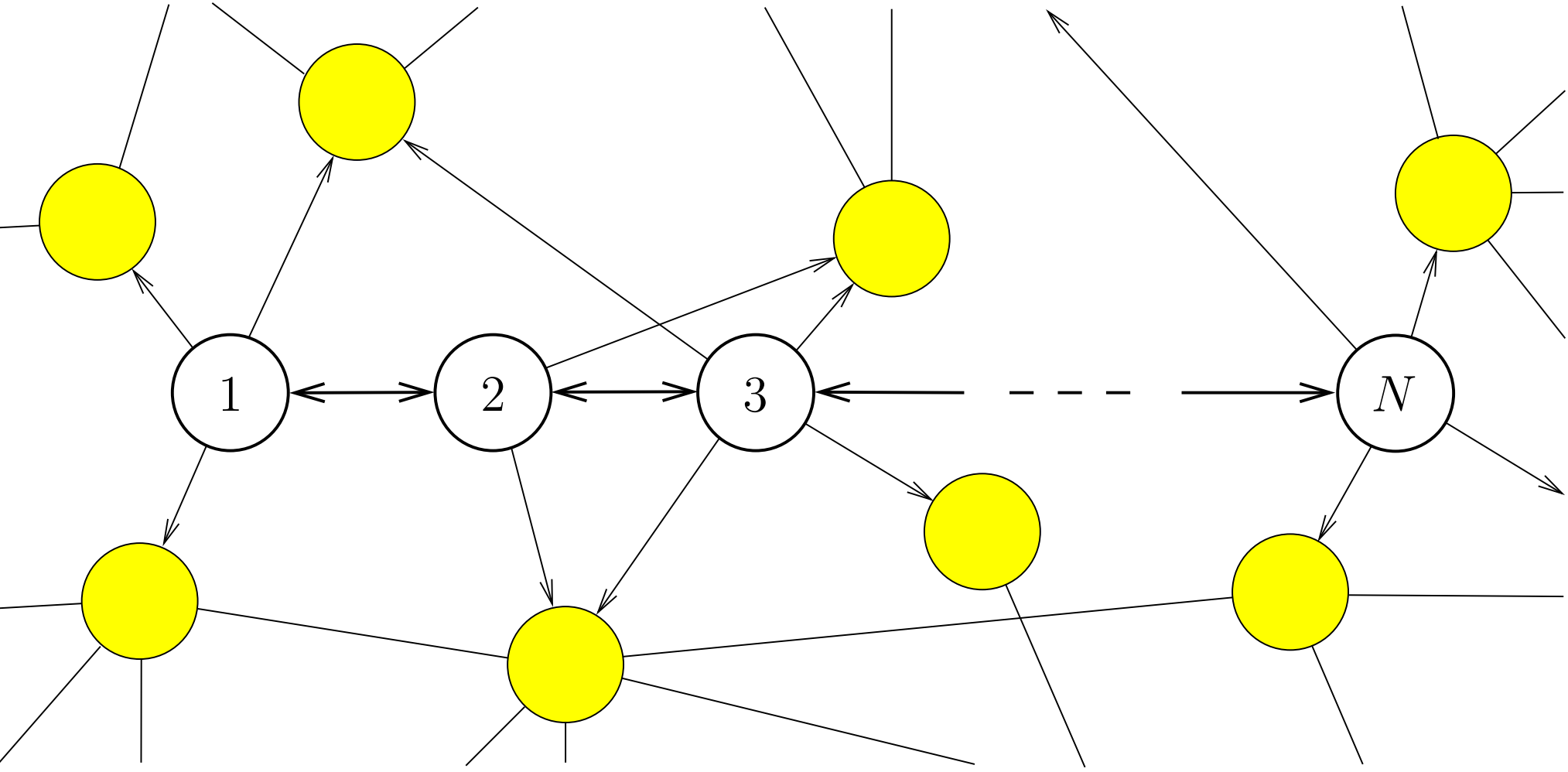
$$\mathbf{P}^{(n)} = \mathbf{P}\mathbf{P}^{(n-1)} = \mathbf{P}^{n}.$$

The total transition probability $\mathcal{P}_{\alpha,\beta}^{C_N}$ can then be computed as

$$\mathcal{P}_{\alpha,\beta}^{C_N} = \sum_{n=1}^{\infty} \left[\mathbf{P}^{n}\right]_{\alpha,\beta},$$

where we approximate the sum using a finite number of terms, M, according to some given convergence criterion.

Chain graph C_N



Total transition probabilities for C_N

We showed that $\mathcal{P}_{\beta,\beta}^{C_N}$ can be calculated exactly as

$$\begin{aligned}
\mathcal{P}_{\beta,\beta}^{C_N} &= \sum_{m=0}^{\infty} (P_{\beta-1,\beta}P_{\beta,\beta-1}L_{\beta-1} + P_{\beta,\beta+1}P_{\beta+1,\beta}R_{\beta+1})^m \\
&= (1 - P_{\beta-1,\beta}P_{\beta,\beta-1}L_{\beta-1} - P_{\beta,\beta+1}P_{\beta+1,\beta}R_{\beta+1})^{-1} \\
&= \left(1 - \frac{L_\beta - 1}{L_\beta} - \frac{R_\beta - 1}{R_\beta}\right)^{-1} = \frac{L_\beta R_\beta}{L_\beta - L_\beta R_\beta + R_\beta},
\end{aligned}$$

where ...

L_j and R_j

L_j and R_j are:

$$L_j = \begin{cases} 1, & j = 1, \\ \dfrac{1}{1 - P_{j-1,j} P_{j,j-1} L_{j-1}}, & j > 1, \end{cases}$$

$$\text{and} \quad R_j = \begin{cases} 1, & j = N, \\ \dfrac{1}{1 - P_{j+1,j} P_{j,j+1} R_{j+1}}, & j < N. \end{cases}$$

Total transition probabilities for C_N

$$\mathcal{P}^{C_N}_{\alpha,\beta} = \begin{cases} \mathcal{P}^{C_N}_{\beta,\beta} \prod_{i=\alpha}^{\beta-1} P_{i,i+1} L_i, & \alpha < \beta, \\ \mathcal{P}^{C_N}_{\beta,\beta} \prod_{i=\beta+1}^{\alpha} P_{i,i-1} R_i, & \alpha > \beta. \end{cases}$$

Summary 5

- Exact total transition probabilities for C_N in linear time;
- Mean escape times from C_N in linear time;
- Exact total transition probabilities for complete graph K_N in N^3 time;
- Mean escape times from K_N in N^3 time;
- Exact total transition probabilities and mean escape times for sparse arbitrary digraphs in $\langle d \rangle^3 N$ time.
- This method is particularly suitable for studing rare events as, unlike with matrix multiplication and kinetic Monte Carlo methods, the complexity does not depend on the rarity of an event.

This is an ongoing project to be finished later on this year.

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