Committor guided estimates of molecular transition rates

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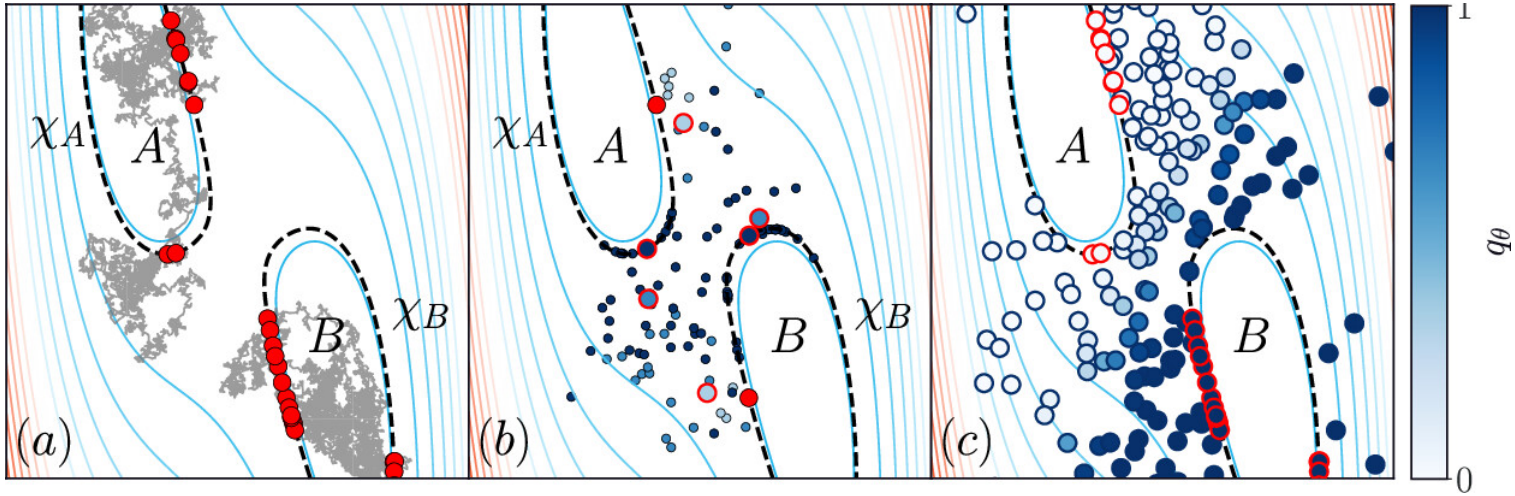
Motivation

- Committors are the "ideal reaction coordinate"
- Rare event sampling is hard, important
- ML has seen good results recently [1]



A and B basins [2]

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$$C_k \subset \Omega \quad C_k \cap C_{k'} = \emptyset \ \ \forall k, k' \in [K]$$

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$$dx_t = -\nabla U(x_t)\, dt + \sqrt{2\beta^{-1}}\, dW_t$$

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$$p_k(x_0) = E[p_k(x_\tau^{x_0})] \quad x \in \Omega^C$$

$$\approx \frac{1}{n} \sum_{i=1}^{n} p_k(x_\tau^{x_0,i})$$

Log Committor Algorithm, $A \to B$

Hill Relation: $r_{AB} = j_{A^-} \int_{\partial A} q_A(x) dx$

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$$\text{Loss:} \quad L_{nk\tau}(\theta) = \frac{1}{|[K]|} \sum_{k \in [K]} \frac{1}{2n} \sum_{i=1}^{n} \log\left(\frac{q_{\theta,k}(x_i)}{\frac{1}{M} \sum_{m=1}^{M} q_{\theta,k}(x_\tau^{x_i,m})} \right)^2$$

Base Algorithm Results

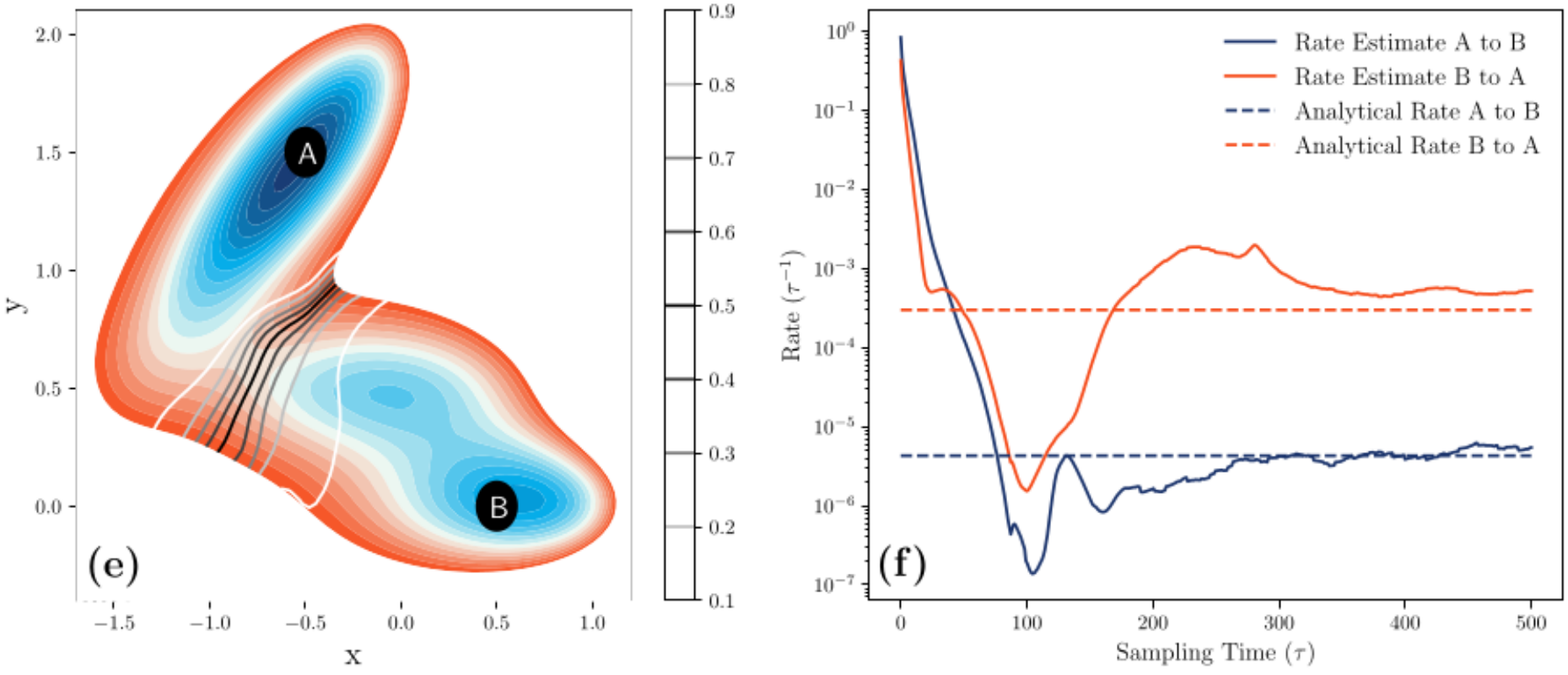


Figure: Muller-Brown Potential e) MLSE Committor f) Rate estimates [2]

Base Algorithm Results (cont.)

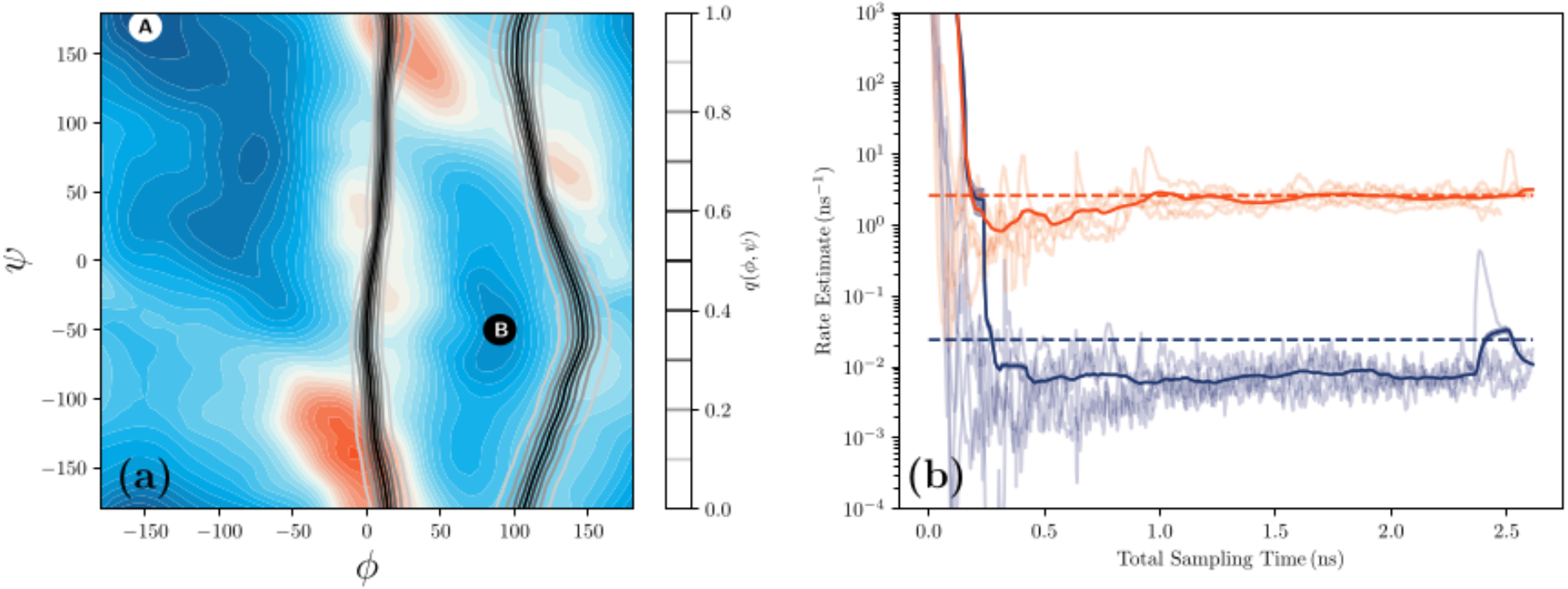


Figure: Dialanine peptide a) MLSE Committor on ϕ, ψ b) Rate estimates [2]

Base Algorithm Problems

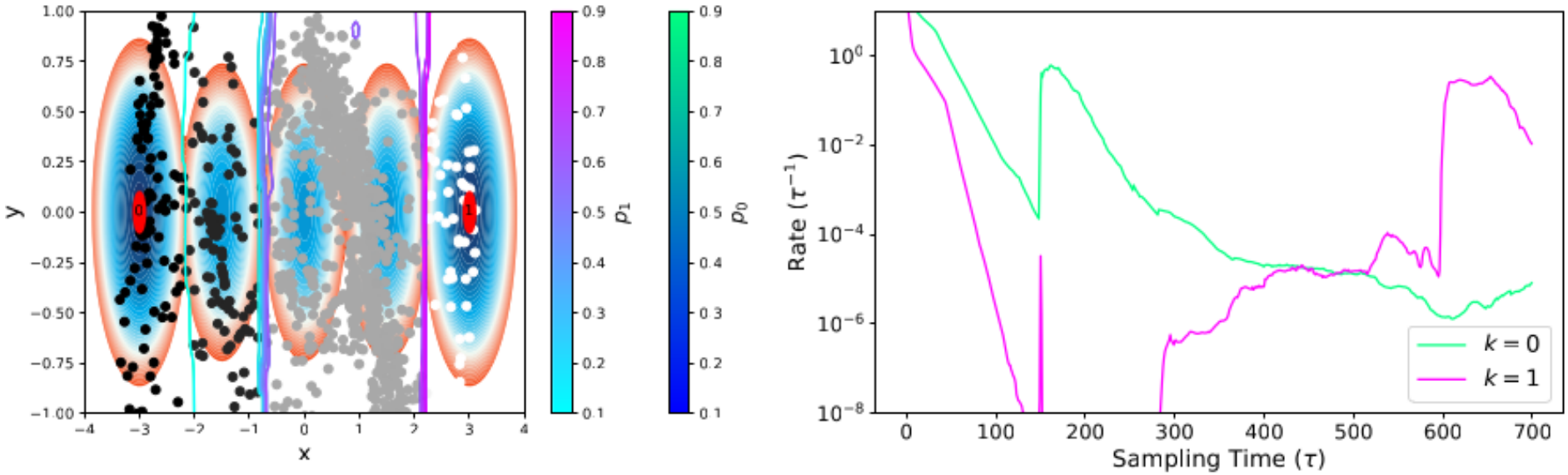
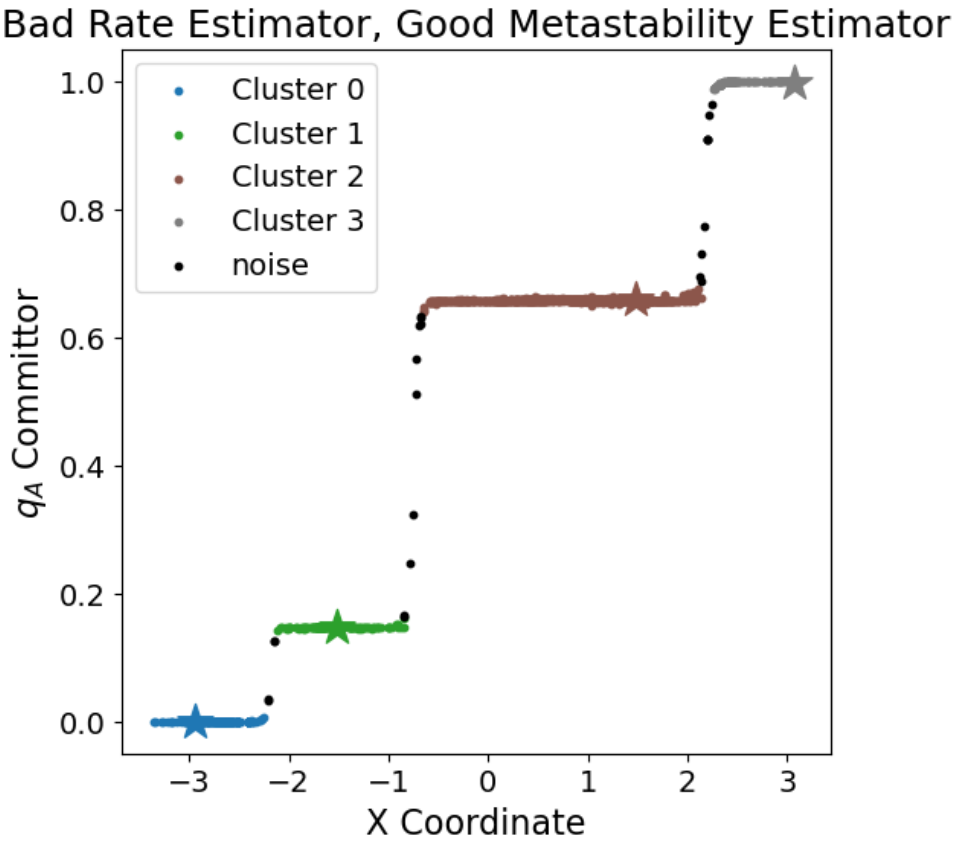


Figure: 5 Linear Wells a) MLSE Committor b) "Rate estimates"

Fixing the Base Algorithm

1. Run a short sample from base algorithm
2. Run DBSCAN on q_A committor values into K clusters (including originals 2)
3. $$x_{k,c} = \arg\min_{x_{k,i}} \{U(x_{k,i})\}$$
4. Rerun simulation with K basins to sample from starting from $x_{k,c}$ to train

$$q_{\theta,k} : \Omega \to \mathbb{R}^K \xrightarrow{\text{softargmax}} [0,1]^K$$



DBSCAN on q_A committor

Improved Algorithm Results

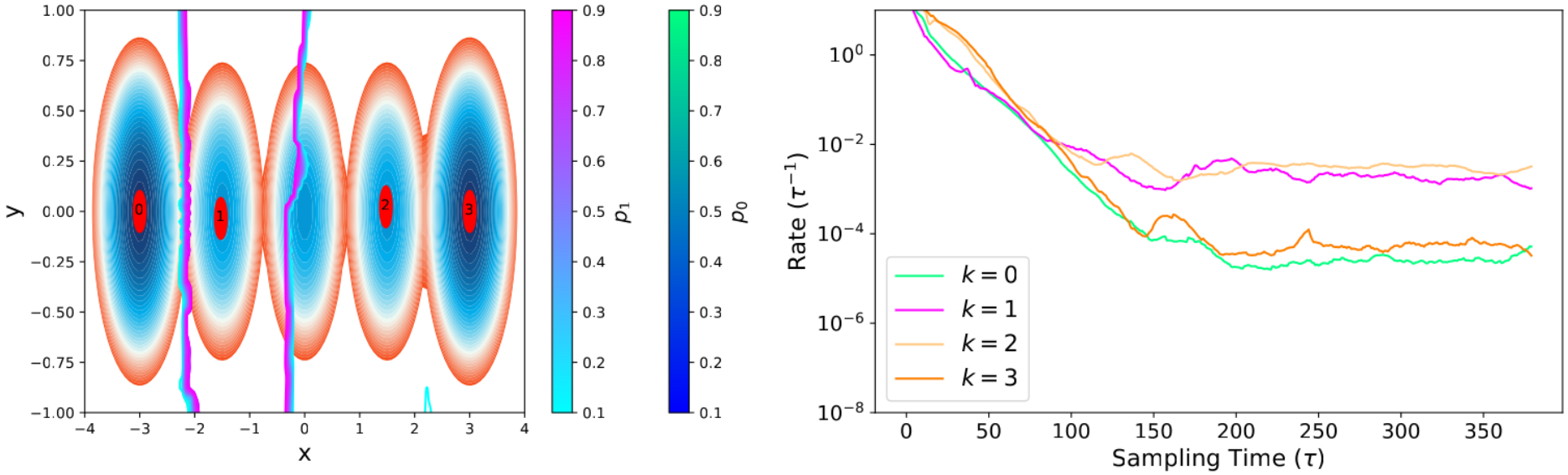


Figure: 5 Linear Wells a) MLSE Committor b) Rate estimates

Composite Rates from Continuous Time Markov Chains

$$Q_{ij} = k_{i\to j}, \quad Q_{ii} = -\sum_{j\neq i} k_{i\to j} = -j_k - \int_{\partial C_k} q_k(x)dx \quad \text{(Hill Relation)}$$

$$\sum_k Q_{ik}\, m_{kj} = -1, \quad i \neq j; \quad m_{jj} = 0$$

$$T_{ij} \sim \mathrm{Exp}(k_{ij}) \implies \mathbb{E}[T_{ij}] = \frac{1}{k_{ij}} \implies k_{ij} = \frac{1}{m_{ij}}$$

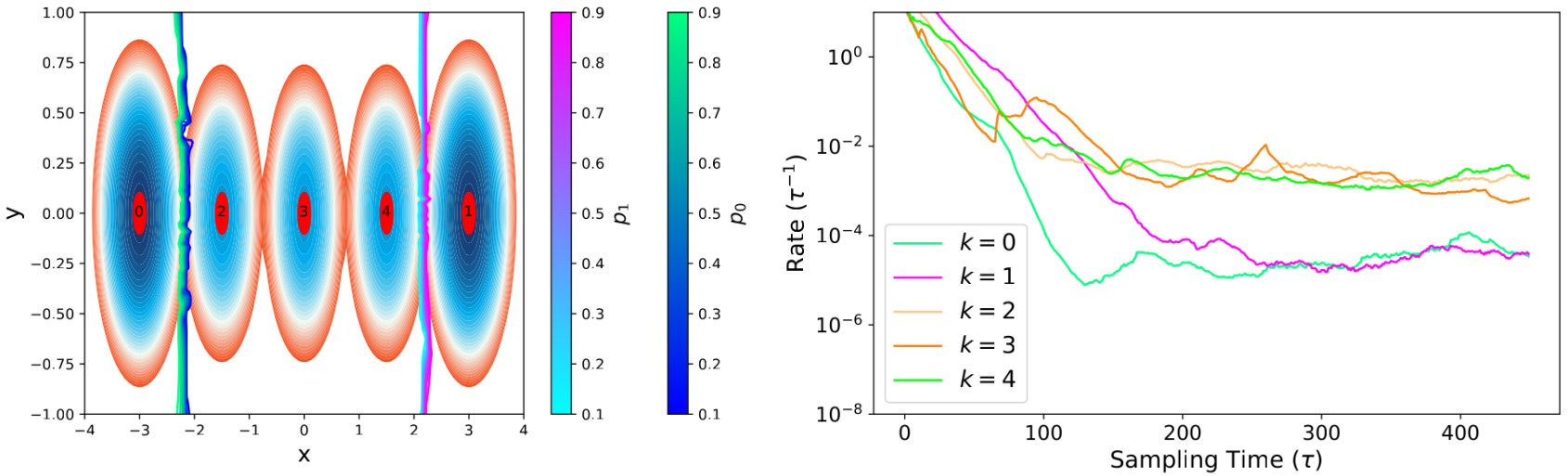


Figure: Rates from 0 to 1 can now be computed with a CTMC

References I

John Strahan, Chatipat Lorpaiboon, Jonathan Weare, and Aaron R. Dinner.
Bad-neus: Rapidly converging trajectory stratification, 2024.

Andrew R. Mitchell and Grant M. Rotskoff.
Committor guided estimates of molecular transition rates.
arXiv preprint arXiv:2408.05879, 2024.