Numerical methods to overcome metastability in molecular dynamics

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Introduction

The aim of molecular dynamics simulations is to understand the relationships between the macroscopic properties of a molecular system and its atomistic features. In particular, one would like to to evaluate numerically macroscopic quantities from models at the microscopic scale.

Some examples of macroscopic quantities:

(i) Thermodynamics quantities (average of some observable wrt an equilibrium measure): stress, heat capacity, free energy,...

$$\mathbb{E}_\mu(\varphi(\boldsymbol{X})) = \int_{\mathbb{R}^d} \varphi(\boldsymbol{x})\, \mu(d\boldsymbol{x}).$$

(ii) Dynamical quantities (average over trajectories at equilibrium): diffusion coefficients, viscosity, transition rates,...

$$\mathbb{E}(\mathcal{F}((\boldsymbol{X}_t)_{t\geq 0})) = \int_{\mathcal{C}^0(\mathbb{R}_+,\mathbb{R}^d)} \mathcal{F}((\boldsymbol{x}_t)_{t\geq 0}))\, \mathcal{W}(d((\boldsymbol{x}_t)_{t\geq 0})).$$

Introduction

Many applications in various fields: biology, physics, chemistry, materials science. Molecular dynamics computations consume today a lot of CPU time.

A molecular dynamics model amounts essentially in choosing a potential V which associates to a configuration $(x_1, ..., x_N) = x \in \mathbb{R}^{3N}$ an energy $V(x_1, ..., x_N)$.

In the canonical (NVT) ensemble, configurations are distributed according to the Boltzmann-Gibbs probability measure:

$$d\mu(x) = Z^{-1} \exp(-\beta V(x))\, dx,$$

where $Z = \int \exp(-\beta V(x))\, dx$ is the partition function and $\beta = (k_B T)^{-1}$ is proportional to the inverse of the temperature.

Introduction

Typically, V is a sum of potentials modelling interaction between two particles, three particles and four particles:

$$V = \sum_{i<j} V_1(x_i, x_j) + \sum_{i<j<k} V_2(x_i, x_j, x_k) + \sum_{i<j<k<l} V_3(x_i, x_j, x_k, x_l).$$

For example, $V_1(x_i, x_j) = V_{LJ}(|x_i - x_j|)$ where $V_{LJ}(r) = 4\epsilon\left(\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right)$ is the Lennard-Jones potential.

Difficulties: (i) high-dimensional problem ($N \gg 1$) ; (ii) μ is a multimodal measure.

Introduction

To sample μ, ergodic dynamics wrt to μ are used. A typical example is the *over-damped Langevin* (or gradient) dynamics:

$$d\boldsymbol{X}_t = -\nabla V(\boldsymbol{X}_t)\, dt + \sqrt{2\beta^{-1}} d\boldsymbol{W}_t.$$

It is the limit (when the mass goes to zero or the damping parameter to infinity) of the *Langevin dynamics*:

$$\begin{cases} d\boldsymbol{X_t} = M^{-1}\boldsymbol{P_t}\, dt, \\ d\boldsymbol{P_t} = -\nabla V(\boldsymbol{X_t})\, dt - \gamma M^{-1}\boldsymbol{P_t}\, dt + \sqrt{2\gamma\beta^{-1}} d\boldsymbol{W_t}, \end{cases}$$

where M is the mass tensor and γ is the friction coefficient.

To compute dynamical quantities, these are also typically the dynamics of interest. Thus,

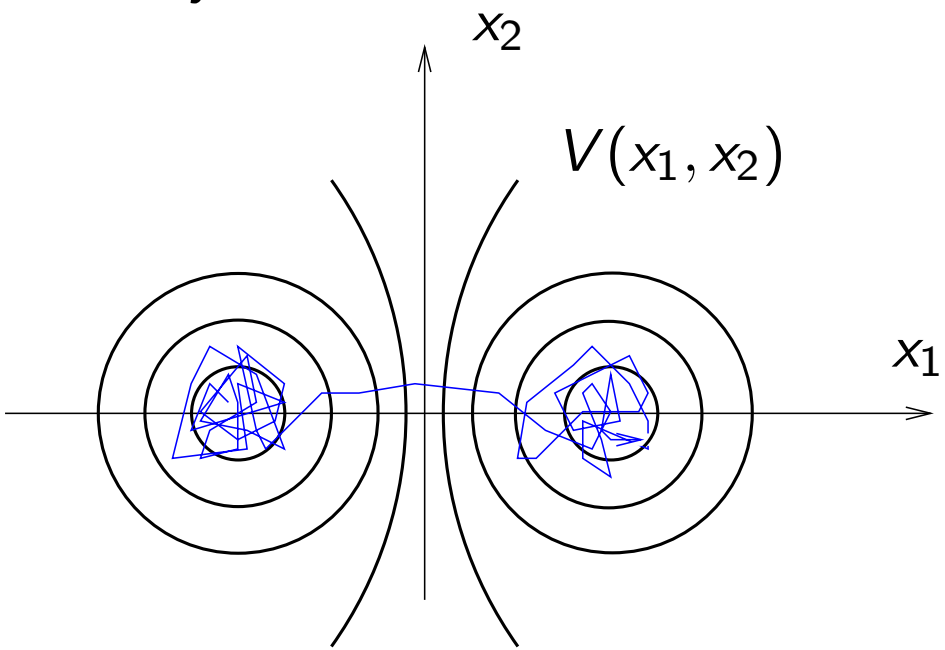
$$\mathbb{E}_\mu(\varphi(\boldsymbol{X})) \simeq \frac{1}{T}\int_0^T \varphi(\boldsymbol{X}_t)\, dt \text{ and } \mathbb{E}(\mathcal{F}((\boldsymbol{X}_t)_{t\geq 0})) \simeq \frac{1}{N}\sum_{m=1}^{N} \mathcal{F}((\boldsymbol{X}_t^m)_{t\geq 0})$$

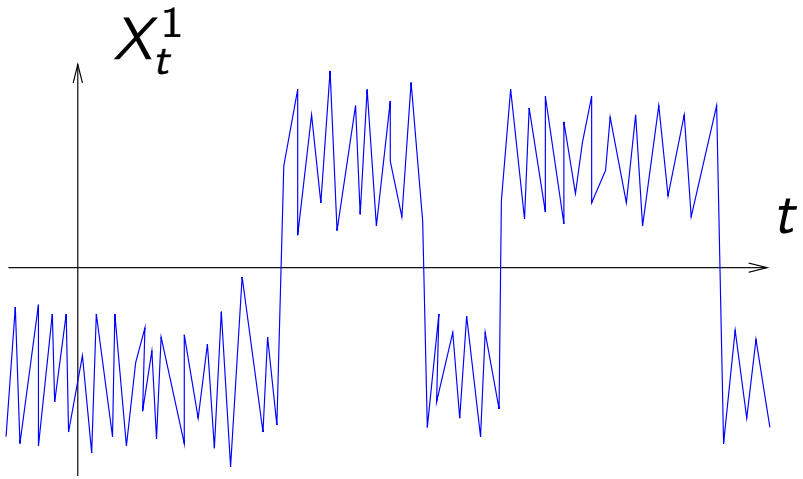
In the following, we mainly consider the over-damped Langevin dynamics.

Introduction

Difficulty: In practice, $\boldsymbol{X}_t$ is a metastable process, so that the convergence to equilibrium is very slow.

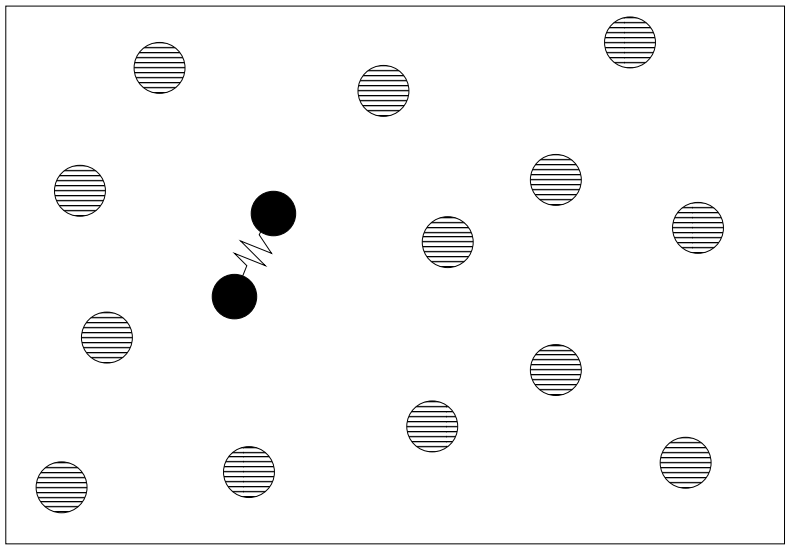
A 2d schematic picture: X_t^1 is a slow variable (a metastable dof) of the system.



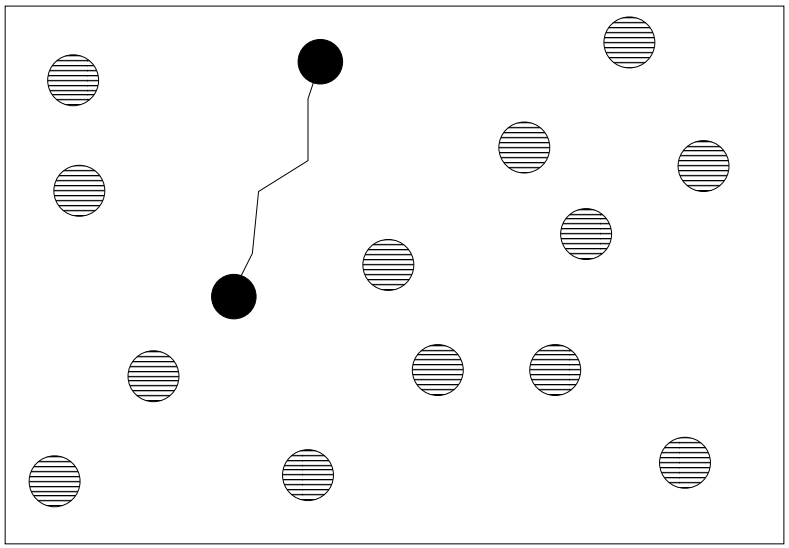


Introduction

A more realistic example (Dellago, Geissler): Influence of the solvation on a dimer conformation.



Compact state.

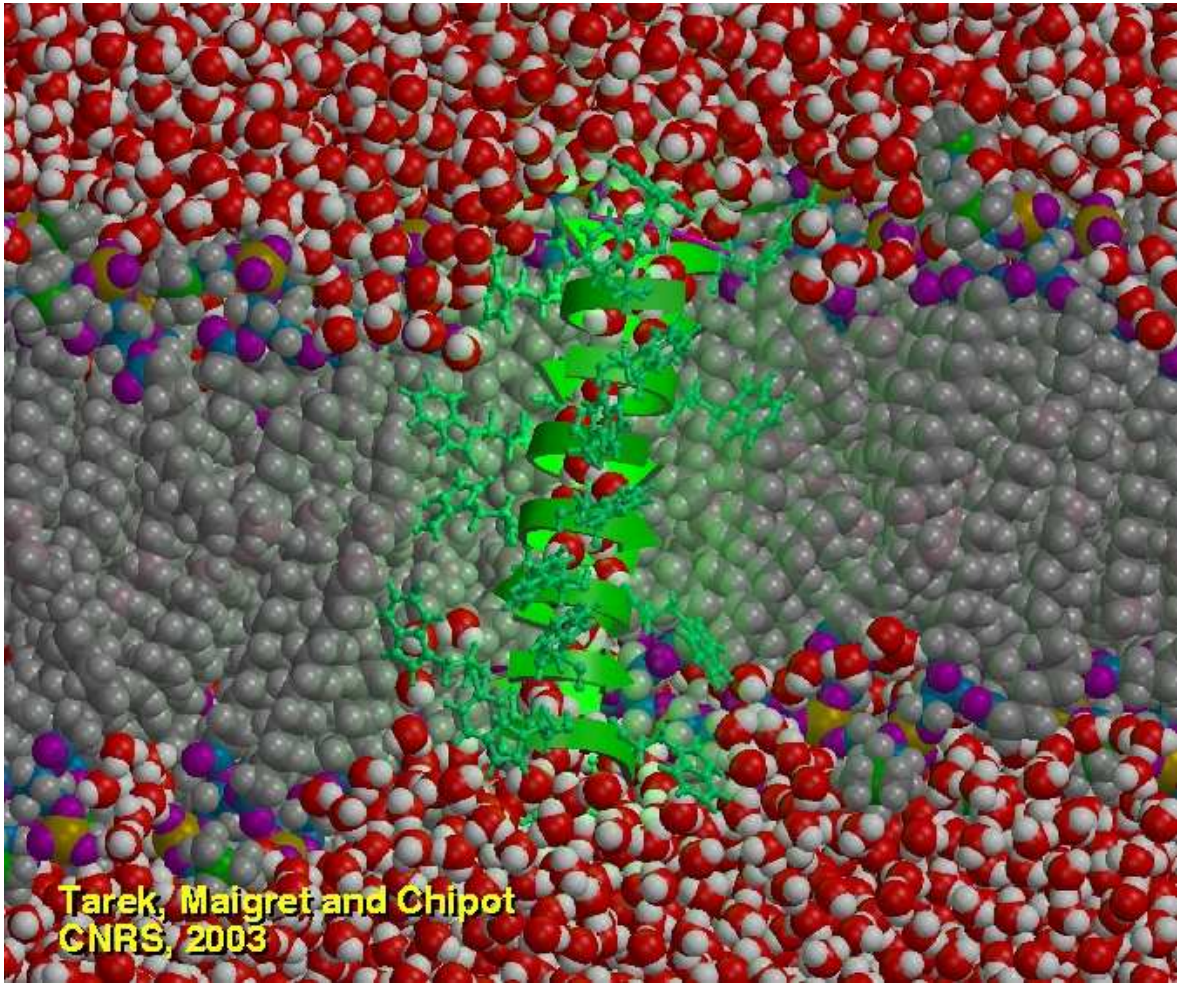


Stretched state.

The particles interact through a pair potential: truncated LJ for all particles except the two monomers (black particles) which interact through a double-well potential. A slow variable is the distance between the two monomers.

Introduction

A "real" example: ions canal in a cell membrane. *(C. Chipot)*.



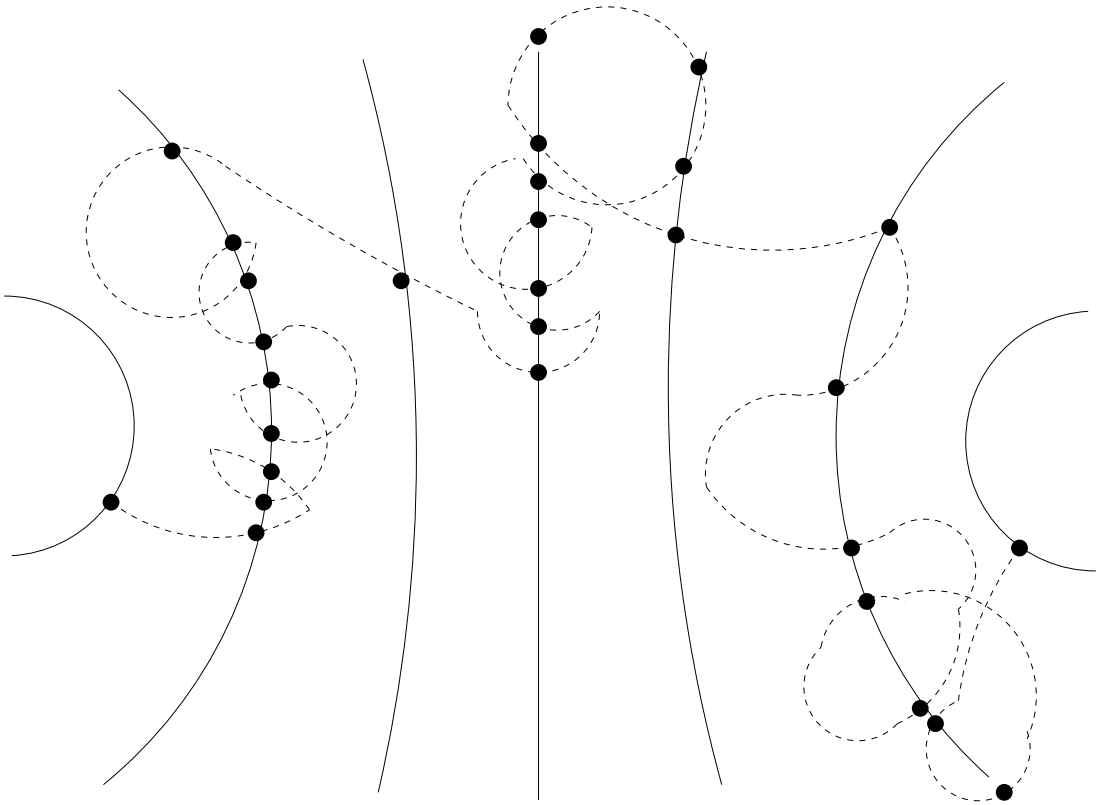
Introduction

One contral numerical difficulty is thus metastability.

Outline of the talk:

1. Adaptive biasing techniques: These belong to one class of numerical methods to compute thermodynamic quantities, and in particular free energy differences.
2. The Parallel Replica dynamics: This is one instance of an algorithm to generate efficiently metastable dynamics.

Adaptive biasing techniques

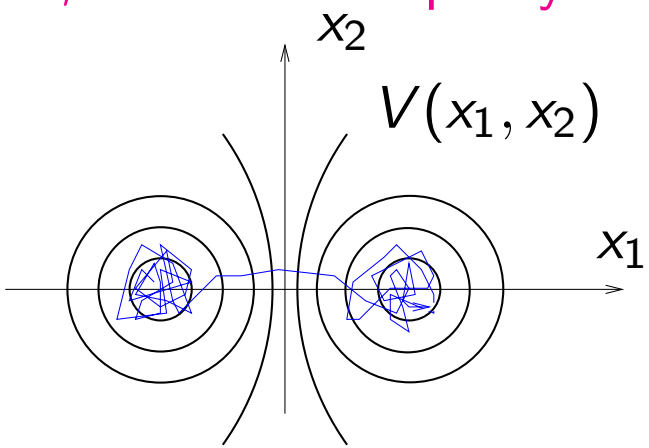


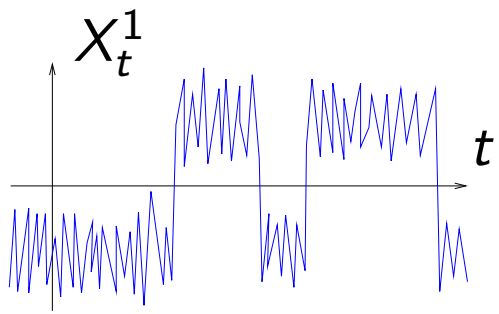
Adaptive biasing techniques

We suppose in this part that we know a slow variable of dimension 1: $\xi(\boldsymbol{X}_t)$, where $\xi : \mathbb{R}^d \longrightarrow \mathbb{T}$ is a so-called reaction coordinate.

This reaction coordinate will be used to bias the dynamics (adaptive importance sampling technique).

For example, in the 2d simple system, $\xi(x_1, x_2) = x_1$.





Adaptive biasing techniques

Let us introduce two probability measures associated to μ and ξ:

- The image of the measure μ by ξ:

$$\xi * \mu\,(dz) = \exp(-\beta A(z))\,dz$$

where the free energy A is defined by:

$$A(z) = -\beta^{-1} \ln \left(\int_{\Sigma(z)} e^{-\beta V} \delta_{\xi(x)-z}(dx) \right),$$

with $\Sigma(z) = \{x,\, \xi(x) = z\}$ is a (smooth) submanifold of $\mathbb{R}^d$, and $\delta_{\xi(x)-z}(dx)\,dz = dx$.

- The probability measure μ conditioned to $\xi(x) = z$:

$$\mu_{\Sigma(z)}(dx) = \frac{\exp(-\beta V(x))\,\delta_{\xi(x)-z}(dx)}{\exp(-\beta A(z))}.$$

Adaptive biasing techniques

In the simple case $\xi(x_1, x_2) = x_1$, we have:

- The image of the measure μ by ξ:

$$\xi * \mu\,(dx_1) = \exp(-\beta A(x_1))\,dx_1$$

where the free energy A is defined by:

$$A(x_1) = -\beta^{-1} \ln\left(\int e^{-\beta V(x_1,x_2)} dx_2\right),$$

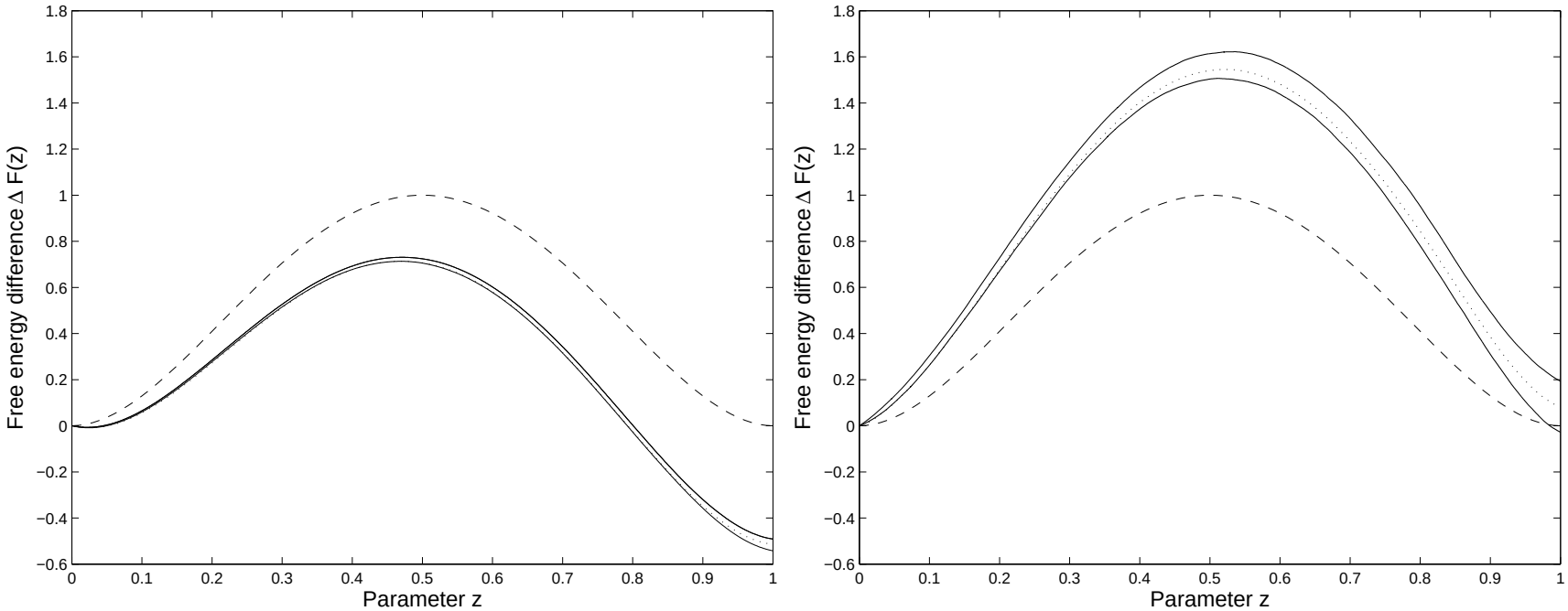
and $\Sigma(x_1) = \{(x_1, x_2),\ x_2 \in \mathbb{R}\}$.

- The probability measure μ conditioned to $\xi(x_1, x_2) = x_1$:

$$\mu_{\Sigma(x_1)}(dx_2) = \frac{\exp(-\beta V(x_1, x_2))\,dx_2}{\exp(-\beta A(x_1))}.$$

Adaptive biasing techniques

What is free energy ? The simple example of the solvation of a dimer. (Profiles computed using thermodynamic integration.)



The density of the solvent molecules is lower on the left than on the right. At high (resp. low) density, the compact state is more (resp. less) likely. The "free energy barrier" is higher at high density than at low density. Related question: interpretation of the free energy barrier in terms of dynamics ?

Adaptive biasing techniques

The bottom line of adaptive methods is the following: for "well chosen" ξ the potential $V - A \circ \xi$ is less rugged than V. Indeed, by construction $\xi * \exp(-\beta(V - A \circ \xi)) = 1_{\mathbb{T}}$.

Problem: A is unknown ! Idea: use a time dependent potential of the form

$$\mathcal{V}_t(x) = V(x) - A_t(\xi(x))$$

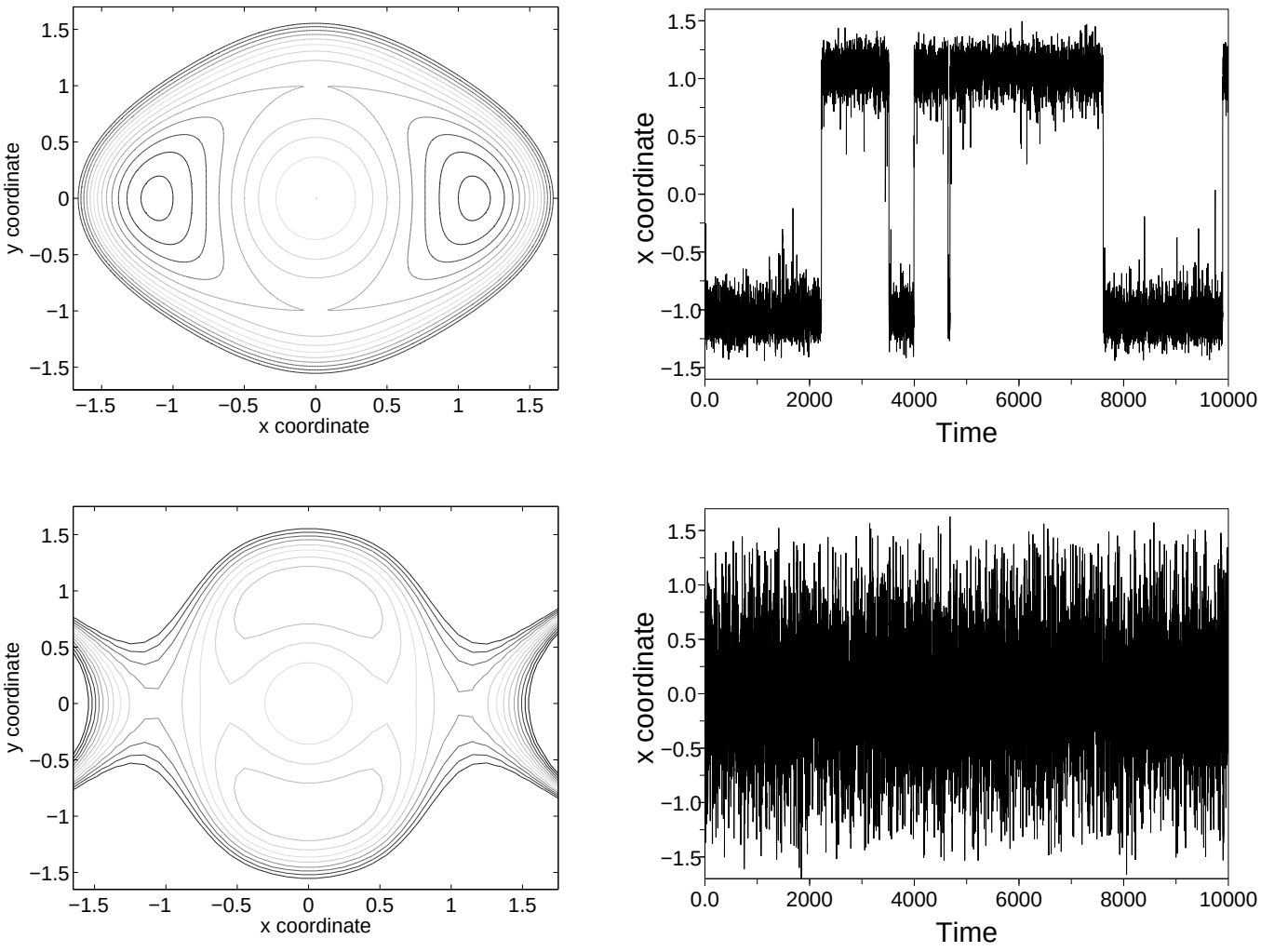
where A_t is an approximation at time t of A, given the configurations visited so far.

Hopes:

- build a dynamics which goes quickly to equilibrium,
- compute free energy profiles.

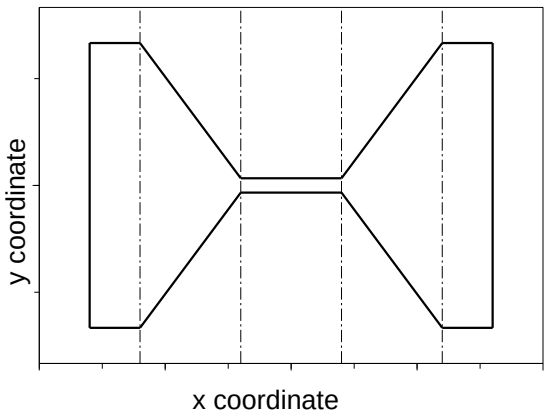
Wang-Landau, ABF, metadynamics: *Darve, Pohorille, Hénin, Chipot, Laio, Parrinello, Wang, Landau,...*

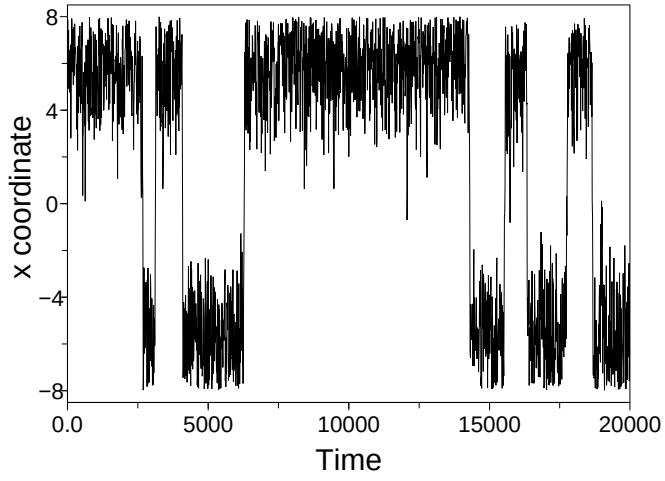
Adaptive biasing techniques

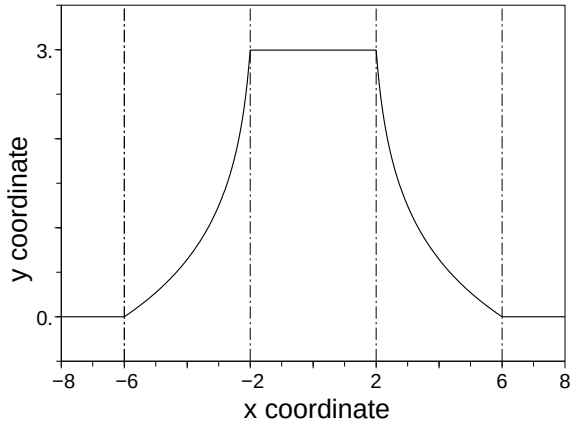


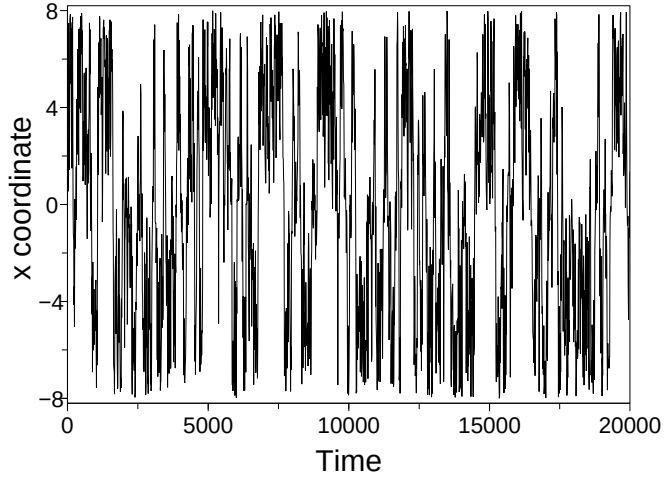
A 2d example of a free energy biased trajectory: energetic barrier.

Adaptive biasing techniques









A 2d example of a free energy biased trajectory: entropic barrier.

The ABF method

How to update A_t ? Two methods depending on wether A'_t (Adaptive Biasing Force) or A_t (Adaptive Biasing Potential) is approximated.

For the Adaptive Biasing Force (ABF) method, the idea is to use the formula

$$A'(z) = \frac{\int \left(\frac{\nabla V \cdot \nabla \xi}{|\nabla \xi|^2} - \beta^{-1} \mathrm{div} \left(\frac{\nabla \xi}{|\nabla \xi|^2} \right) \right) e^{-\beta V} \, \delta_{\xi(x)-z}(dx)}{\int e^{-\beta V} \, \delta_{\xi(x)-z}(dx)}$$

$$= \int f \, d\mu_{\Sigma(z)} = \mathbb{E}_\mu(f(\boldsymbol{X}) | \xi(\boldsymbol{X}) = z).$$

The mean force $A'(z)$ is the mean of f with respect to $\mu_{\Sigma(z)}$.

The ABF method

In the simple case $\xi(x_1, x_2) = x_1$, remember that

$$A(x_1) = -\beta^{-1} \ln \left(\int e^{-\beta V(x_1, x_2)} dx_2 \right),$$

so that

$$A'(x_1) = \frac{\int \partial_{x_1} V \, e^{-\beta V(x_1, x_2)} \, dx_2}{\int e^{-\beta V(x_1, x_2)} \, dx_2}$$

$$= \int \partial_{x_1} V \, d\mu_{\Sigma(x_1)}.$$

Notice that actually, whatever A_t is,

$$A'(z) = \frac{\int f \, e^{-\beta(V - A_t \circ \xi)} \, \delta_{\xi(x) - z}(dx)}{\int e^{-\beta(V - A_t \circ \xi)} \, \delta_{\xi(x) - z}(dx)}.$$

The ABF method

Thus, we would like to simulate:

$$\begin{cases} d\boldsymbol{X}_t = -\nabla(V - A \circ \xi)(\boldsymbol{X}_t)\, dt + \sqrt{2\beta^{-1}} d\boldsymbol{W}_t, \\ A'(z) = \mathbb{E}_\mu \left(f(\boldsymbol{X}) | \xi(\boldsymbol{X}) = z \right) \end{cases}$$

but A is unknown...

The ABF method

The ABF dynamics is then:

$$\begin{cases} d\boldsymbol{X}_t = -\nabla(V - A_t \circ \xi)(\boldsymbol{X}_t)\, dt + \sqrt{2\beta^{-1}} d\boldsymbol{W}_t, \\ A_t'(z) = \mathbb{E}\left(f(\boldsymbol{X}_t) | \xi(\boldsymbol{X}_t) = z\right). \end{cases}$$

The ABF method

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The associated (nonlinear) Fokker-Planck equation writes:

$$\begin{cases} \partial_t \psi = \operatorname{div}\left(\nabla(V - A_t \circ \xi)\psi + \beta^{-1}\nabla\psi\right), \\ A_t'(z) = \dfrac{\displaystyle\int f\, \psi\, \delta_{\xi(\boldsymbol{x})-z}(d\boldsymbol{x})}{\displaystyle\int \psi\, \delta_{\xi(\boldsymbol{x})-z}(d\boldsymbol{x})}, \end{cases}$$

where $\boldsymbol{X}_t \sim \psi(t, \boldsymbol{x})\, d\boldsymbol{x}$. A numerical illustration.

The ABF method

The ABF dynamics is then:

$$\begin{cases} d\boldsymbol{X}_t = -\nabla(V - A_t \circ \xi)(\boldsymbol{X}_t)\, dt + \sqrt{2\beta^{-1}}\, d\boldsymbol{W}_t, \\ A_t'(z) = \mathbb{E}\left(f(\boldsymbol{X}_t) | \xi(\boldsymbol{X}_t) = z\right). \end{cases}$$

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where $\boldsymbol{X}_t \sim \psi(t, \boldsymbol{x})\, d\boldsymbol{x}$. A numerical illustration.

Questions: Does A_t' converge to A' ? What did we gain compared to the original gradient dynamics ?

Longtime convergence and entropy (1)

Recall the original gradient dynamics:

$$d\boldsymbol{Q}_t = -\nabla V(\boldsymbol{Q}_t)\, dt + \sqrt{2\beta^{-1}} d\boldsymbol{W}_t.$$

The associated (linear) Fokker-Planck equation writes:

$$\partial_t \phi = \mathrm{div}\, \left(\nabla V \phi + \beta^{-1} \nabla \phi\right).$$

where $\boldsymbol{Q}_t \sim \phi(t, \boldsymbol{q})\, d\boldsymbol{q}$.

The metastable behaviour of $\boldsymbol{Q}_t$ is related to the multimodality of μ, which can be quantified through the rate of convergence of ϕ to $\phi_\infty = Z^{-1} \exp(-\beta V)$.

A classical PDE approach: use entropy techniques.

Longtime convergence and entropy (2)

Notice that the Fokker-Planck equation rewrites

$$\partial_t \phi = \beta^{-1} \mathrm{div} \left(\phi_\infty \nabla \left(\frac{\phi}{\phi_\infty} \right) \right).$$

Let us introduce the entropy:

$$E(t) = H(\phi(t,\cdot)|\phi_\infty) = \int \ln \left(\frac{\phi}{\phi_\infty} \right) \phi.$$

We have (Csiszár-Kullback inequality):

$$\|\phi(t,\cdot) - \phi_\infty\|_{L^1} \leq \sqrt{2E(t)}.$$

Longtime convergence and entropy (3)

$$\begin{aligned}\frac{dE}{dt} &= \int \ln\left(\frac{\phi}{\phi_\infty}\right)\partial_t\phi \\ &= \beta^{-1}\int \ln\left(\frac{\phi}{\phi_\infty}\right)\operatorname{div}\left(\phi_\infty\nabla\left(\frac{\phi}{\phi_\infty}\right)\right) \\ &= -\beta^{-1}\int\left|\nabla\ln\left(\frac{\phi}{\phi_\infty}\right)\right|^2\phi =: -\beta^{-1}I(\phi(t,\cdot)|\phi_\infty).\end{aligned}$$

If V is such that the following Logarithmic Sobolev inequality (LSI(R)) holds: $\forall\phi$ pdf,

$$H(\phi|\phi_\infty) \leq \frac{1}{2R}I(\phi|\phi_\infty)$$

then $E(t) \leq E(0)\exp(-2\beta^{-1}Rt)$ and thus ϕ converges to ϕ_∞ exponentially fast with rate $\beta^{-1}R$.

Metastability $\Longleftrightarrow$ small R

Convergence of ABF (1)

A convergence result [TL, M. Rousset, G. Stoltz, Nonlinearity 2008] : Recall the ABF Fokker-Planck equation:

$$\begin{cases} \partial_t \psi = \mathrm{div}\, \left(\nabla (V - A_t \circ \xi) \psi + \beta^{-1} \nabla \psi \right), \\ A_t'(z) = \dfrac{\int f\, \psi\, \delta_{\xi(x)-z}(dx)}{\int \psi\, \delta_{\xi(x)-z}(dx)}. \end{cases}$$

Suppose:

(H1) "Ergodicity" of the microscopic variables: the conditional probability measures $\mu_{\Sigma(z)}$ satisfy a LSI(ρ),

(H2) Bounded coupling: $\left\| \nabla_{\Sigma(z)} f \right\|_{L^\infty} < \infty$,

then

$$\| A_t' - A' \|_{L^2} \leq C \exp(-\beta^{-1} \min(\rho, r) t).$$

The rate of convergence is limited by:

- the rate r of convergence of $\overline{\psi} = \int \psi\, \delta_{\xi(x)-z}(dx)$ to $\overline{\psi_\infty}$,
- the LSI constant ρ (the real limitation).

Convergence of ABF (2)

In summary:

- Original gradient dynamics: $\exp(-\beta^{-1} R t)$ where R is the LSI constant for μ ;
- ABF dynamics: $\exp(-\beta^{-1} \rho t)$ where ρ is the LSI constant for the conditioned probability measures $\mu_{\Sigma(z)}$.

If ξ is well chosen, $\rho \gg R$: the free energy can be computed very efficiently. Once the free energy is known, there are classical techniques to compute averages wrt μ (unbiasing, conditioning).

Two ingredients of the proof:

(1) The marginal $\overline{\psi}(t,z) = \int \psi(t,\boldsymbol{x})\, \delta_{\xi(\boldsymbol{x})-z}(d\boldsymbol{x})$ satisfies a closed PDE:

$$\partial_t \overline{\psi} = \beta^{-1} \partial_{z,z} \overline{\psi} \text{ on } \mathbb{T},$$

and thus, $\overline{\psi}$ converges towards $\overline{\psi_\infty} \equiv 1$, with exponential speed $C \exp(-4\pi^2 \beta^{-1} t)$. (Here, $r = 4\pi^2$).

Convergence of ABF (3)

(2) The total entropy can be decomposed as [N. Grunewald, F. Otto, C. Villani, M. Westdickenberg, Ann. IHP, 2009]:

$$E = E_M + E_m$$

where

The total entropy is $E = H(\psi|\psi_\infty)$,

The macroscopic entropy is $E_M = H(\overline{\psi}|\overline{\psi_\infty})$,

The microscopic entropy is

$$E_m = \int H\Big(\psi(\cdot|\xi(x) = z)\Big|\psi_\infty(\cdot|\xi(x) = z)\Big)\,\overline{\psi}(z)\,dz.$$

We already know that E_M goes to zero: it remains only to consider E_m...

Discretization of ABF

Discretization of adaptive methods can be done using two (complementary) approaches:

- Use trajectorial averages along a single path:

$$\mathbb{E}(f(\boldsymbol{X}_t)|\xi(\boldsymbol{X}_t)=z) \simeq \frac{\int_0^t f(\boldsymbol{X}_s)\,\delta^\alpha(\xi(\boldsymbol{X}_s)-z)\,ds}{\int_0^t \delta^\alpha(\xi(\boldsymbol{X}_s)-z)\,ds}.$$

- Use empirical means over many replicas (interacting particle system):

$$\mathbb{E}(f(\boldsymbol{X}_t)|\xi(\boldsymbol{X}_t)=z) \simeq \frac{\sum_{m=1}^N f(\boldsymbol{X}_t^{m,N})\,\delta^\alpha(\xi(\boldsymbol{X}_t^{m,N})-z)}{\sum_{m=1}^N \delta^\alpha(\xi(\boldsymbol{X}_t^{m,N})-z)}.$$

This second approach is more flexible (selection mechanisms) and more efficient in cases with multiple reactive paths. [TL, M. Rousset, G. Stoltz, 2007; C. Chipot, TL, K. Minoukadeh, 2010 ; TL, K. Minoukadeh, 2010]

Adaptive biasing techniques: conclusions

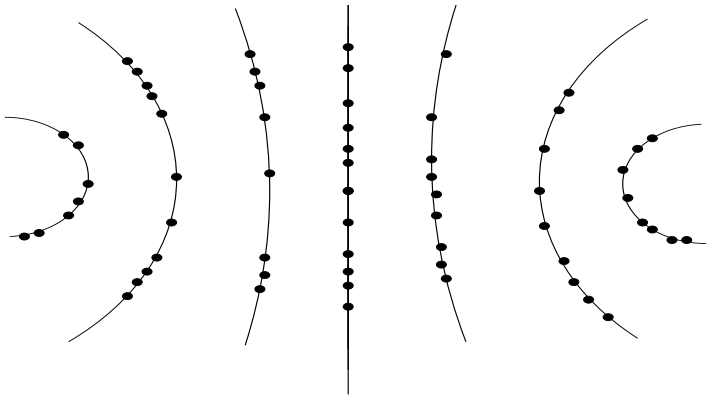
Interesting features of the algorithm: parallelization and adaptivity.

Entropy approaches are powerful techniques to investigate multimodal measures, metastable dynamics and analyze sampling algorithms.

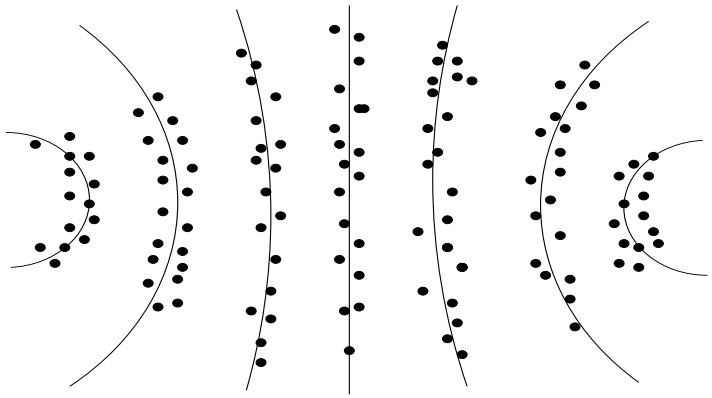
These techniques can be used whenever the sampling of a multimodal measure is involved, for example for statistical inference in Bayesian statistics [N. Chopin, TL, G. Stoltz, 2011].

Free energy calculation methods

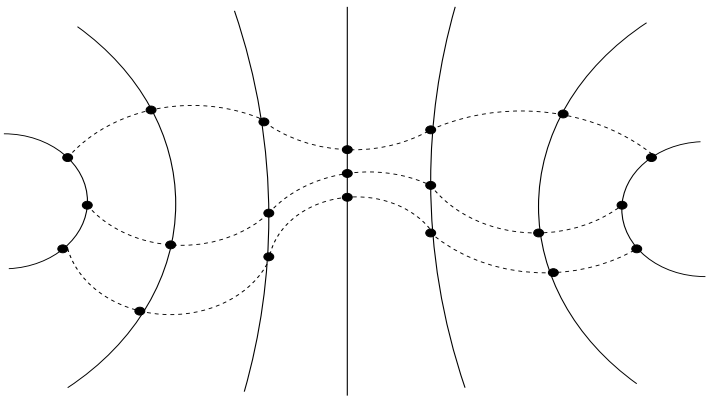
There are many other numerical methods to compute free energies.



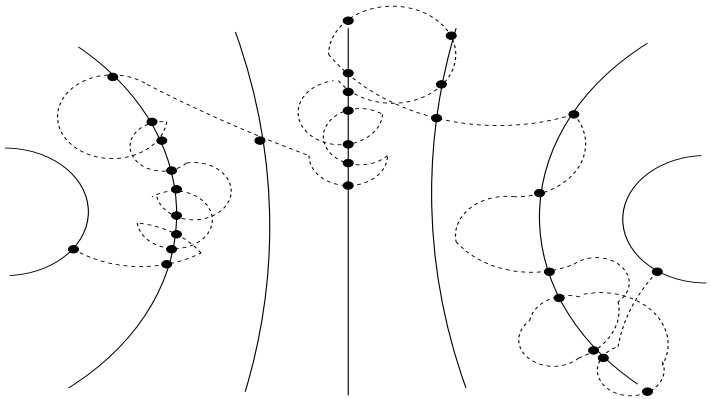
(a) Thermodynamic integration.



(b) Histogram method.

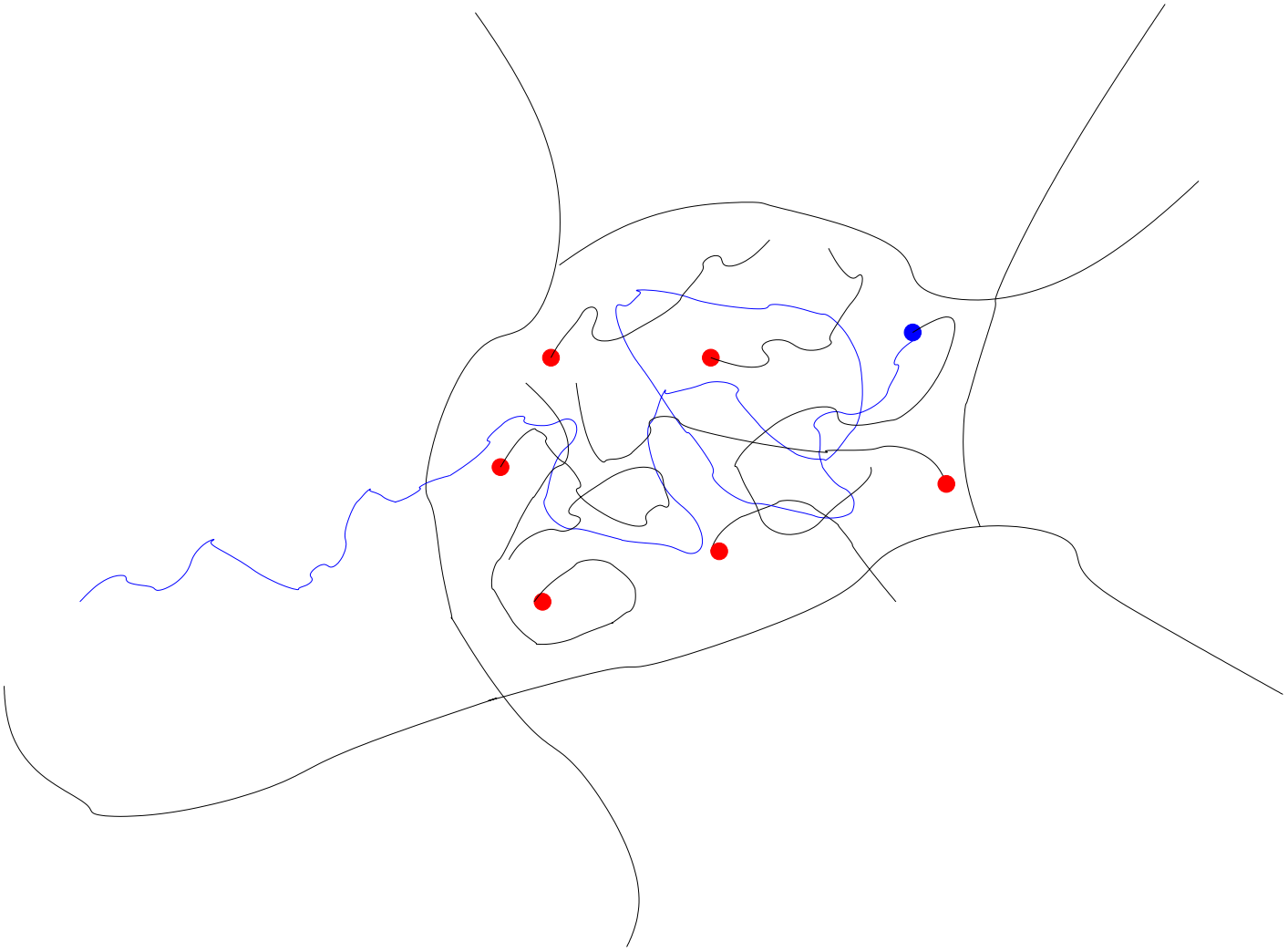


(c) Out of equilibrium dynamics.



(d) Adaptive dynamics.

The Parallel Replica Algorithm



The Parallel Replica Algorithm

The Parallel Replica Algorithm, proposed by A.F. Voter in 1998, is a method to get efficiently a "coarse-grained projection" of a dynamics.
Let us consider again the overdamped Langevin dyanmics:

$$d\boldsymbol{X}_t = -\nabla V(\boldsymbol{X}_t)\, dt + \sqrt{2\beta^{-1}} d\boldsymbol{W}_t$$

and let assume that we are given a smooth mapping

$$\mathcal{S} : \mathbb{R}^d \to \mathbb{N}$$

which to a configuration in $\mathbb{R}^d$ associates a state number. Think of a numbering of the wells of the potential V.

The aim of the parallel replica dynamics is to generate very efficiently a trajectory $(S_t)_{t\geq 0}$ which has (almost) the same law as $(\mathcal{S}(\boldsymbol{X}_t))_{t\geq 0}$.

The Parallel Replica Algorithm

Initialization: Consider an initial condition $\boldsymbol{X}_0^{ref}$ for a reference walker, the associated initial condition $S_0 = \mathcal{S}(\boldsymbol{X}_0^{ref})$, and a simulation time counter $T_{simu} = 0$.

Then, one iteration of the algorithm goes through three steps.

- The decorrelation step: Let the reference walker $(\boldsymbol{X}^{ref}_{T_{simu}+t})_{t\geq 0}$ evolve over a time interval $t \in [0, \tau_{corr}]$. Then,
  - If the process leaves the well during the time interval (*i.e.* $\exists t \leq \tau_{corr}$ such that $\mathcal{S}\left(\boldsymbol{X}^{ref}_{T_{simu}+t}\right) \neq \mathcal{S}\left(\boldsymbol{X}^{ref}_{T_{simu}}\right)$) advance the simulation clock by τ_{corr} and restart the decorrelation step ;
  - otherwise, advance the simulation clock by τ_{corr} and proceed to the dephasing step.

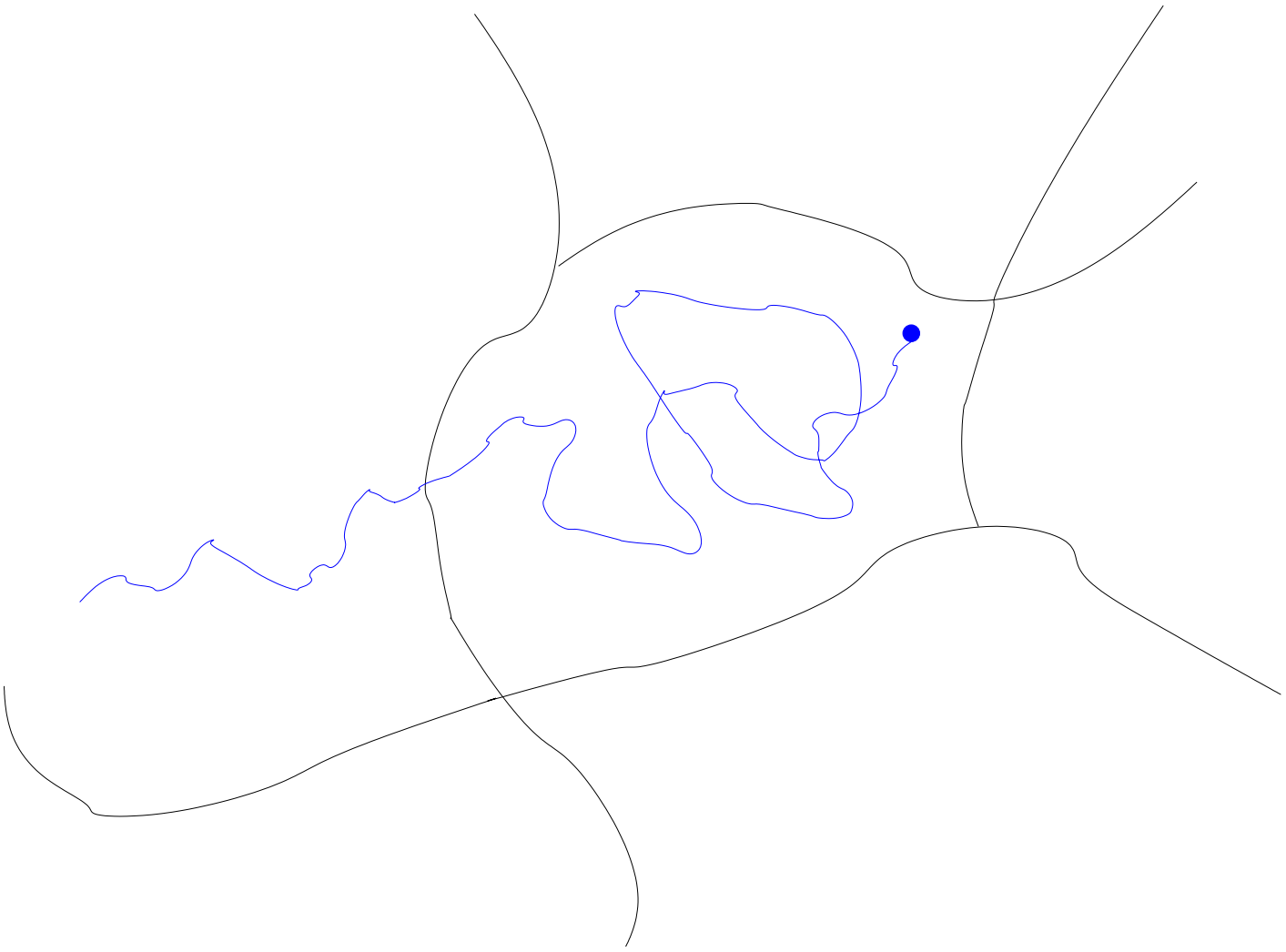
  During all this step, $S_{T_{simu}+t} := \mathcal{S}\left(\boldsymbol{X}^{ref}_{T_{simu}+t}\right)$.

The Parallel Replica Algorithm

The reference walker enters a new state

The Parallel Replica Algorithm

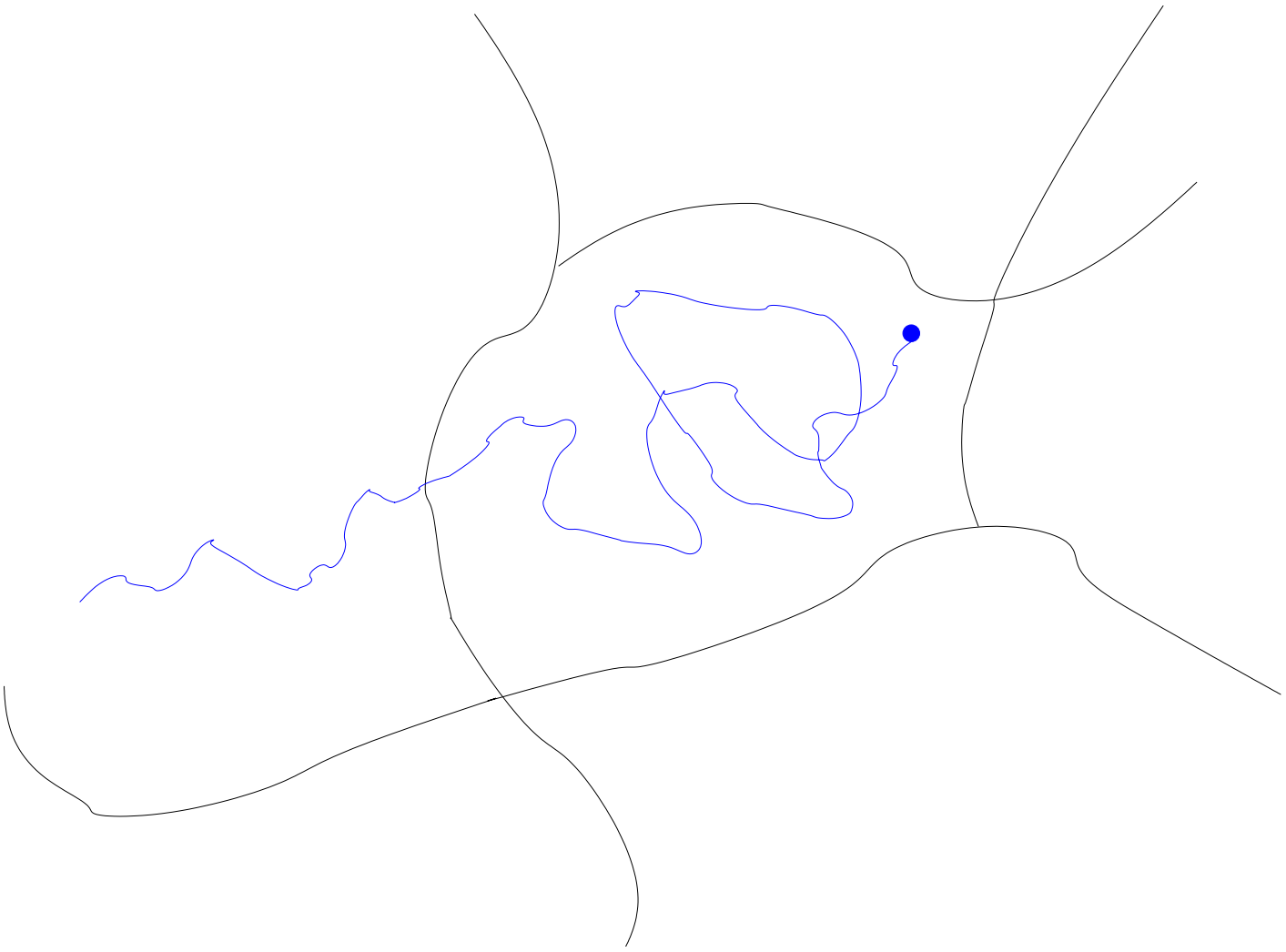
Decorrelation step: wait for a time τ_{corr}.



- The dephasing step: Duplicate the walker $\boldsymbol{X}_{T_{simu}}^{ref}$ into N replicas. Let these replicas evolve independently and in parallel over a time interval of length $\tau_{dephase}$. If a replica leaves the well during this time interval, restart the dephasing step for this replica. Throughout this step, the simulation counter is stopped.

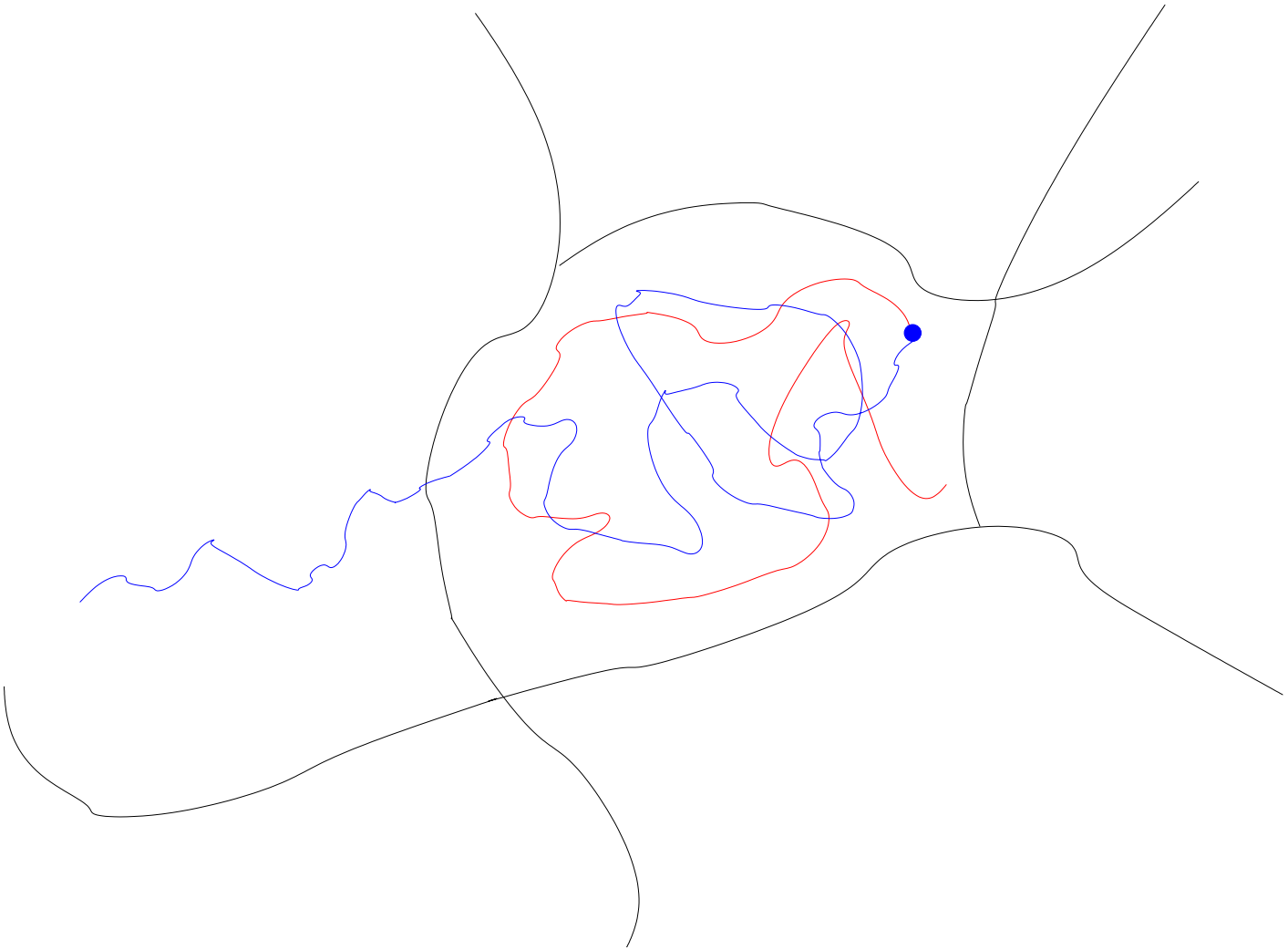
The Parallel Replica Algorithm

Dephasing step.



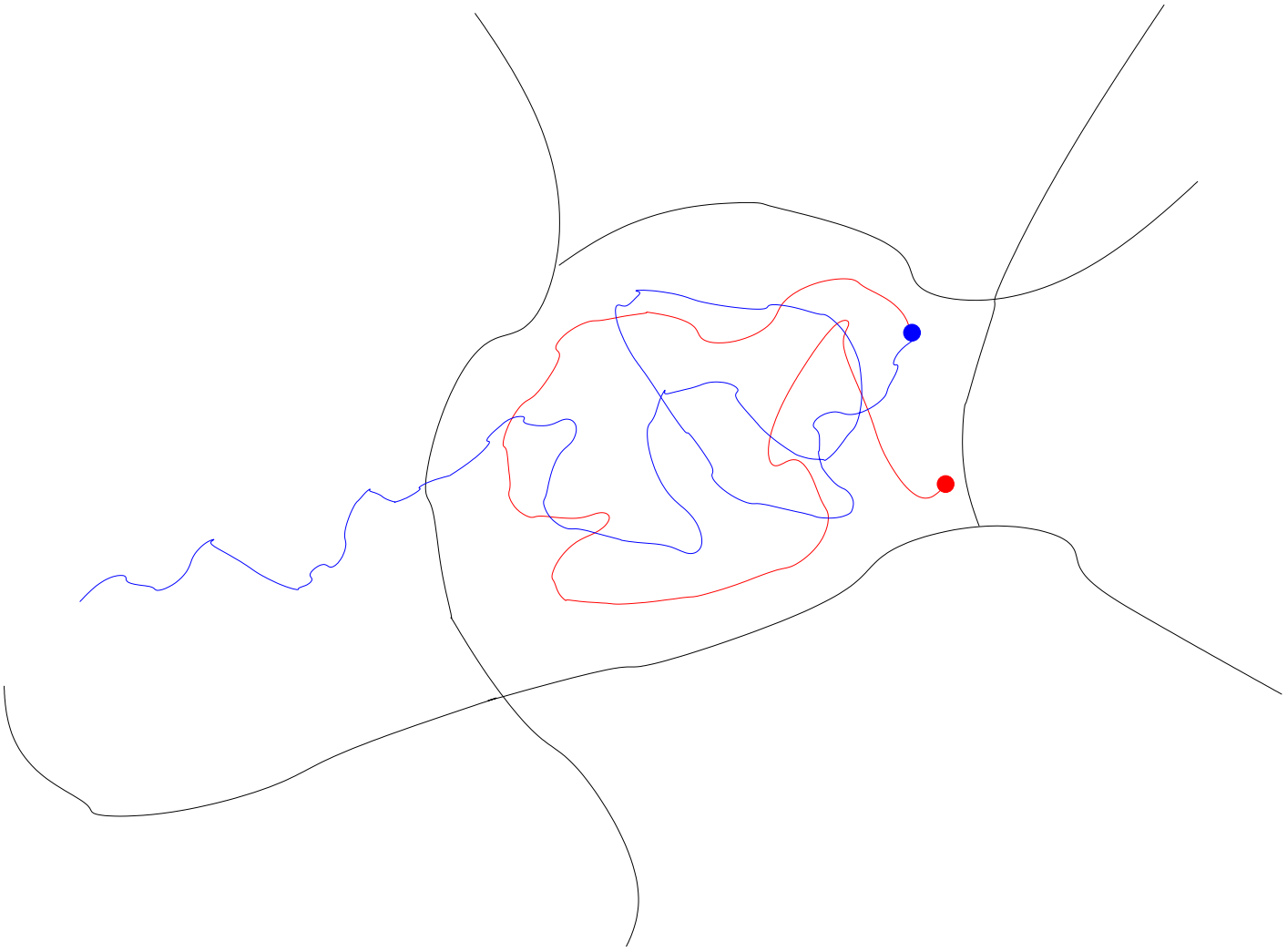
The Parallel Replica Algorithm

Dephasing step: generate new initial conditions in the state.



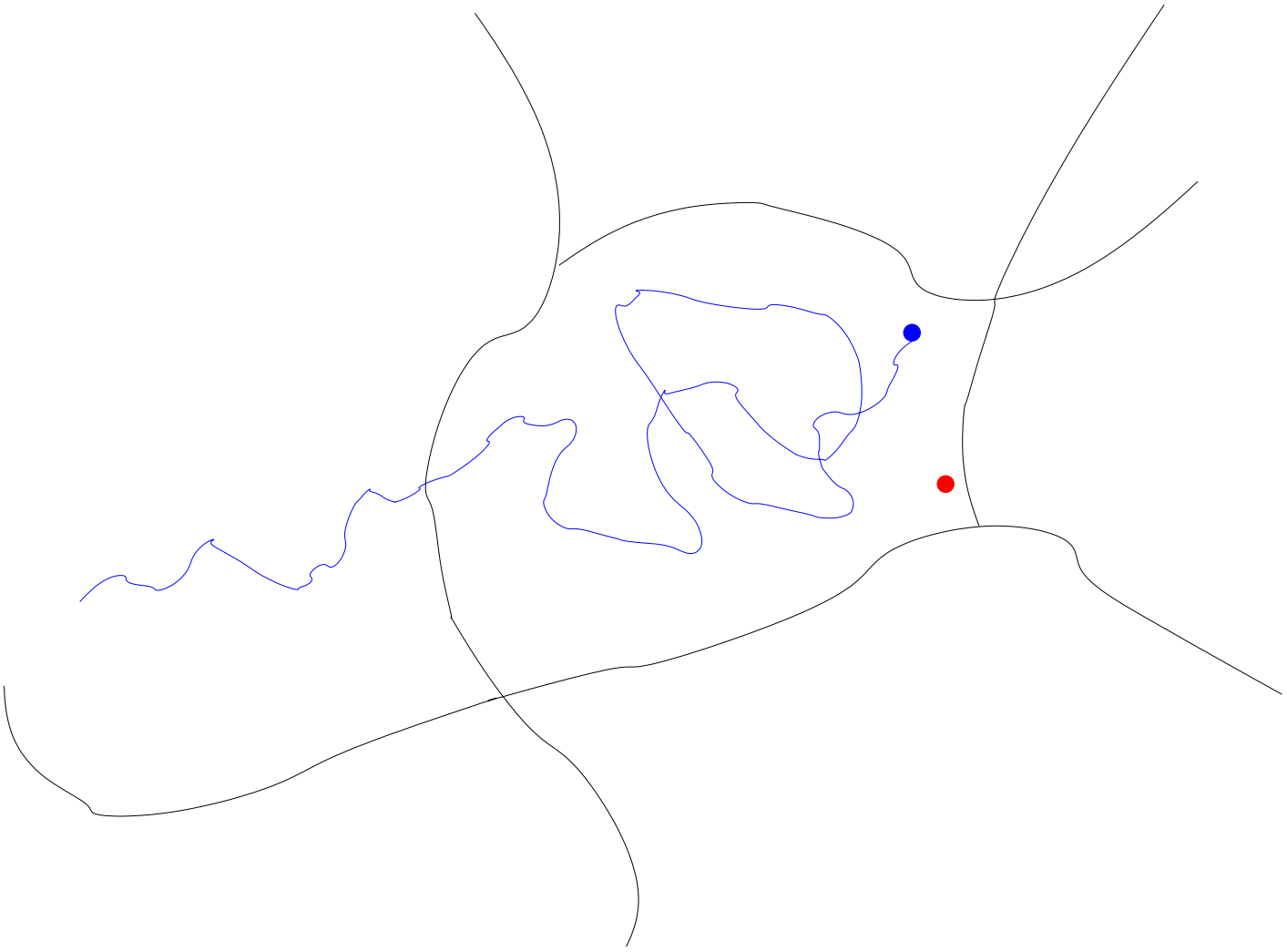
The Parallel Replica Algorithm

Dephasing step: generate new initial conditions in the state.



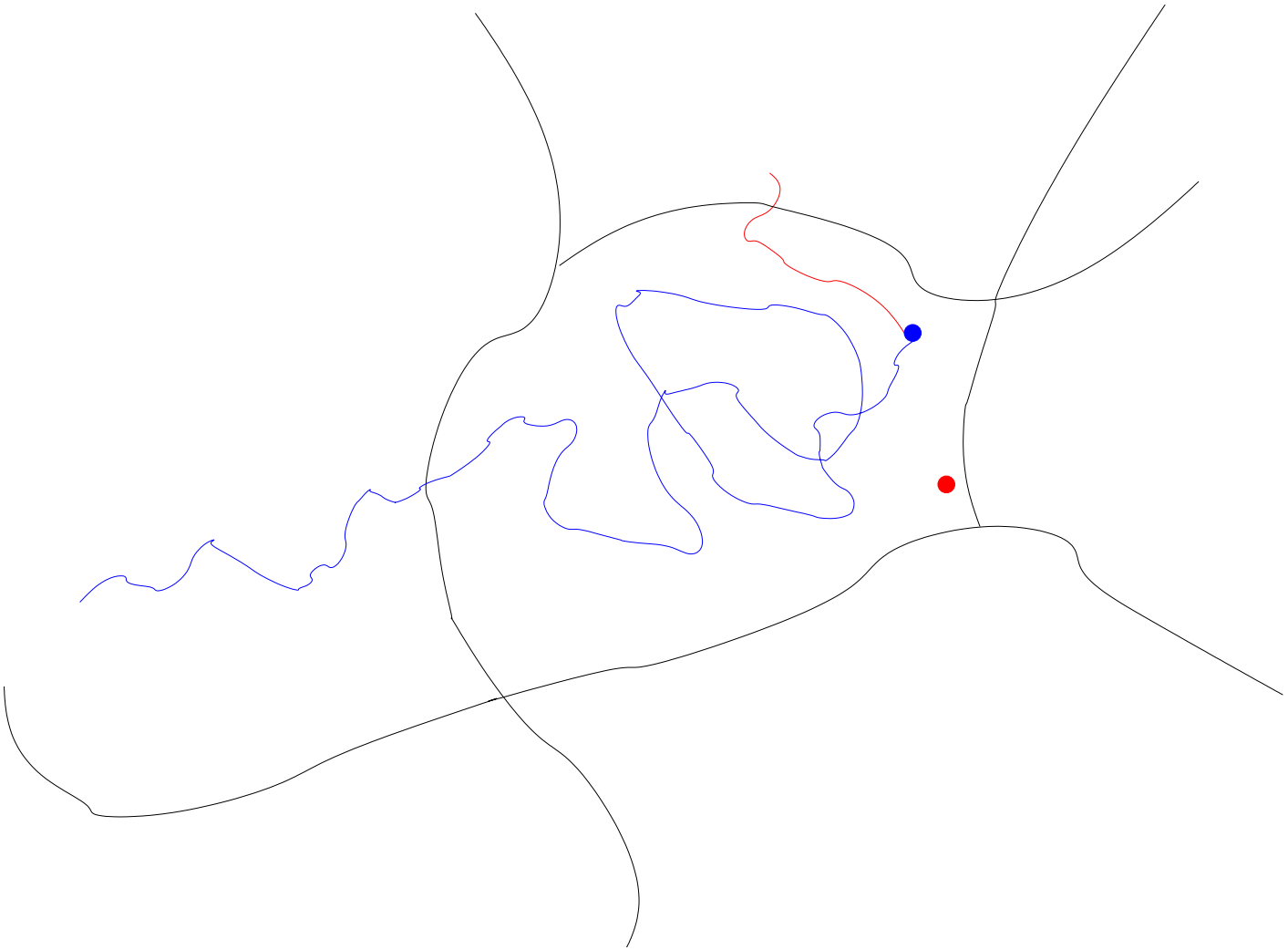
The Parallel Replica Algorithm

Dephasing step: generate new initial conditions in the state.



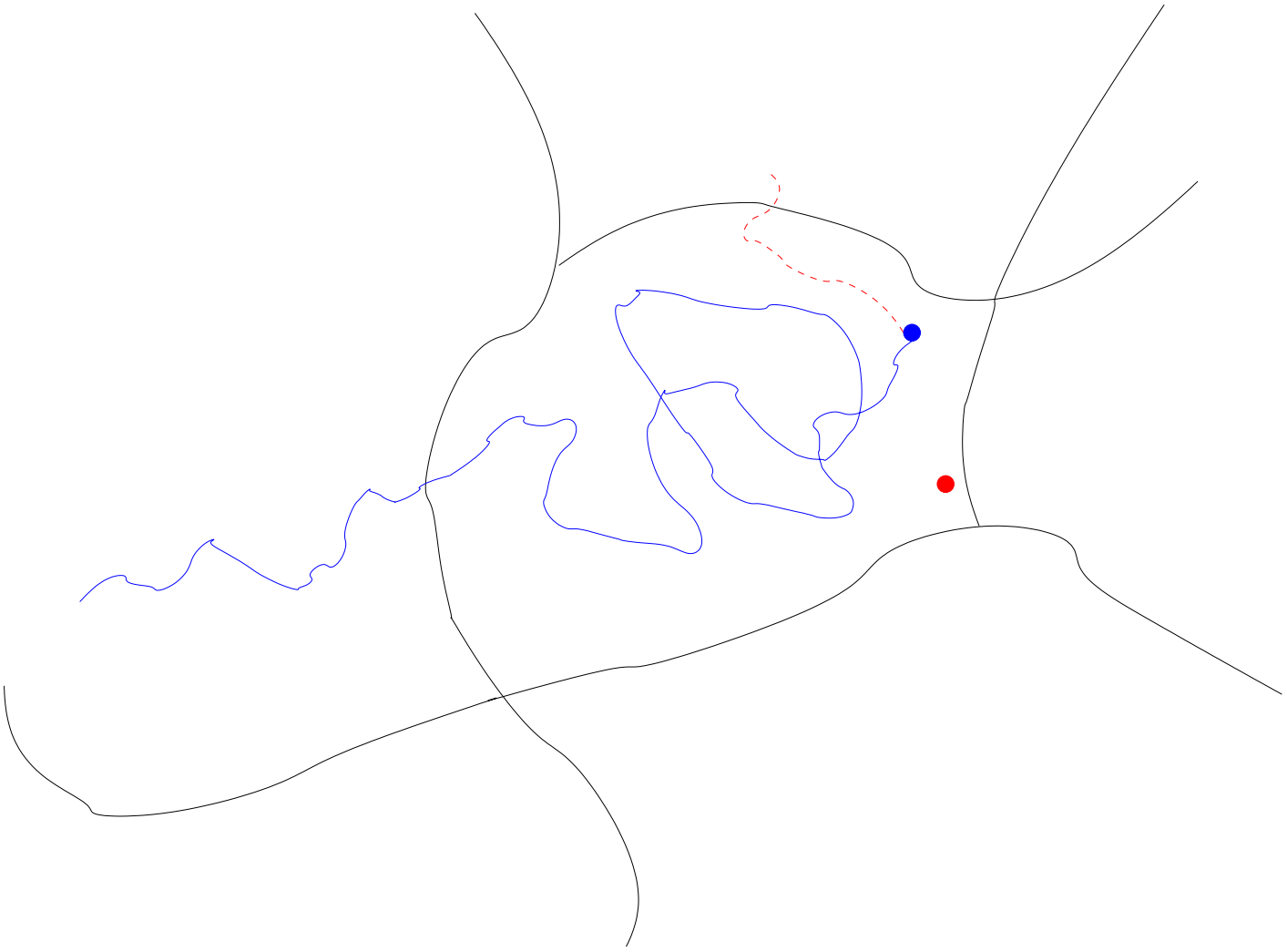
The Parallel Replica Algorithm

Dephasing step: generate new initial conditions in the state.



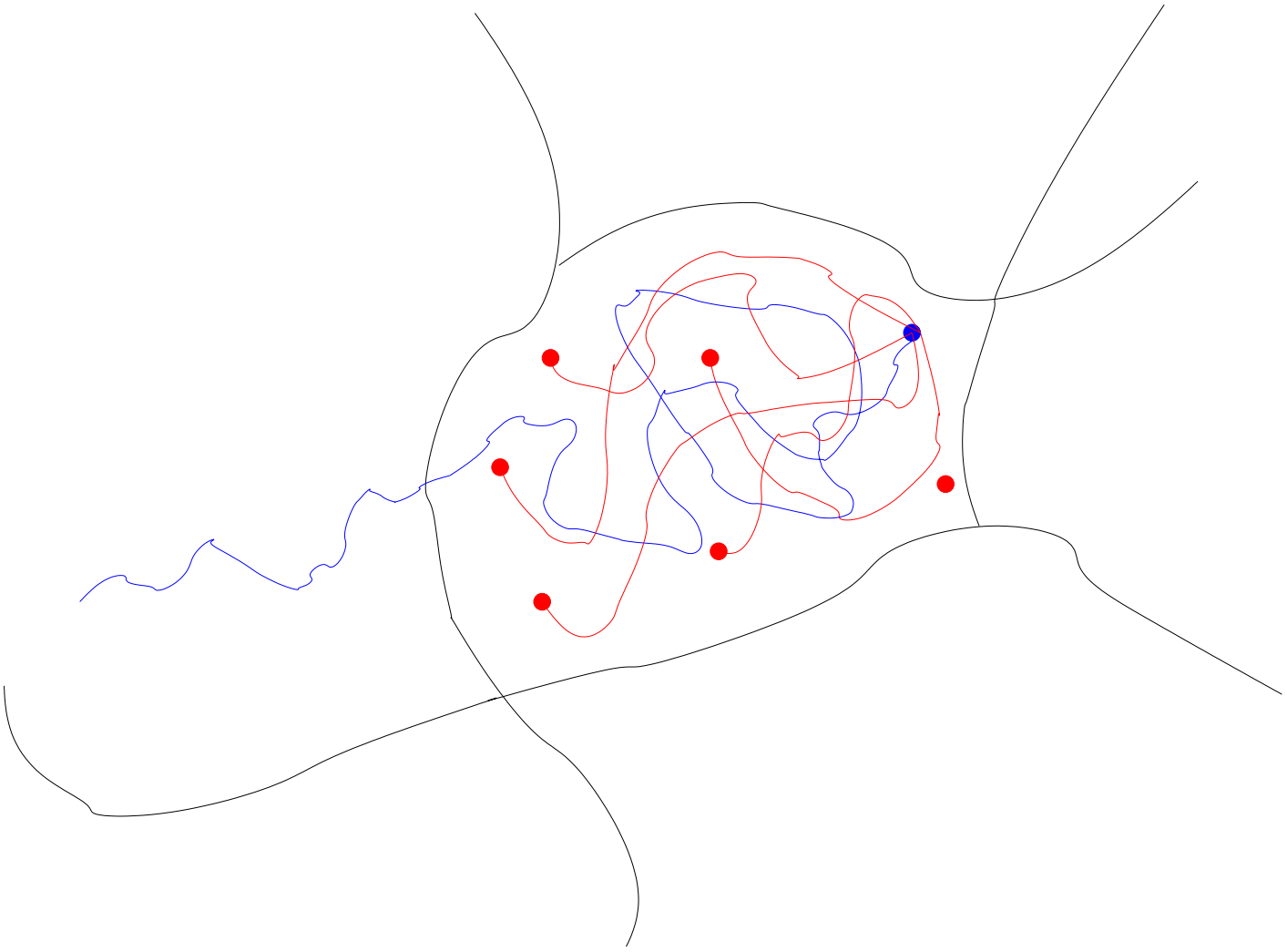
The Parallel Replica Algorithm

Dephasing step: generate new initial conditions in the state.



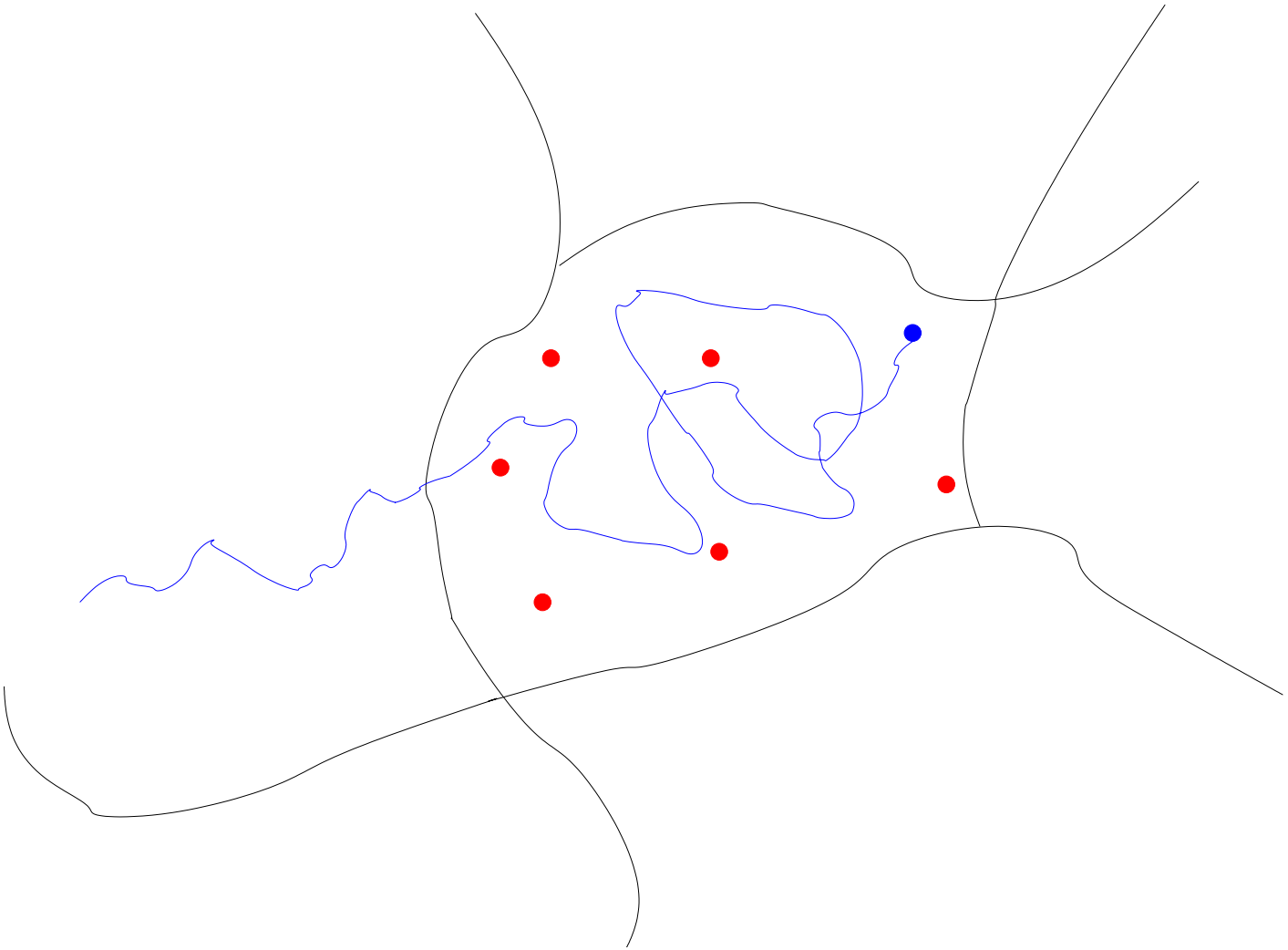
The Parallel Replica Algorithm

Dephasing step: generate new initial conditions in the state.



The Parallel Replica Algorithm

Dephasing step: generate new initial conditions in the state.



- The parallel step: Let all the replicas evolve independently and track the first escape event:

$$T = \inf_k T_W^k = T_W^{K_0}$$

where $K_0 = \arg\inf_k T_W^k$ and

$$T_W^k = \inf\{t \geq 0,\ \mathcal{S}(\boldsymbol{X}^k_{T_{simu}+t}) \neq \mathcal{S}(\boldsymbol{X}^k_{T_{simu}})\}$$

is the first time the k-th replica leaves the well. Then:

$$T_{simu} = T_{simu} + NT \text{ and } \boldsymbol{X}^{ref}_{T_{simu}+NT} = \boldsymbol{X}^{K_0}_{T_{simu}+T}.$$

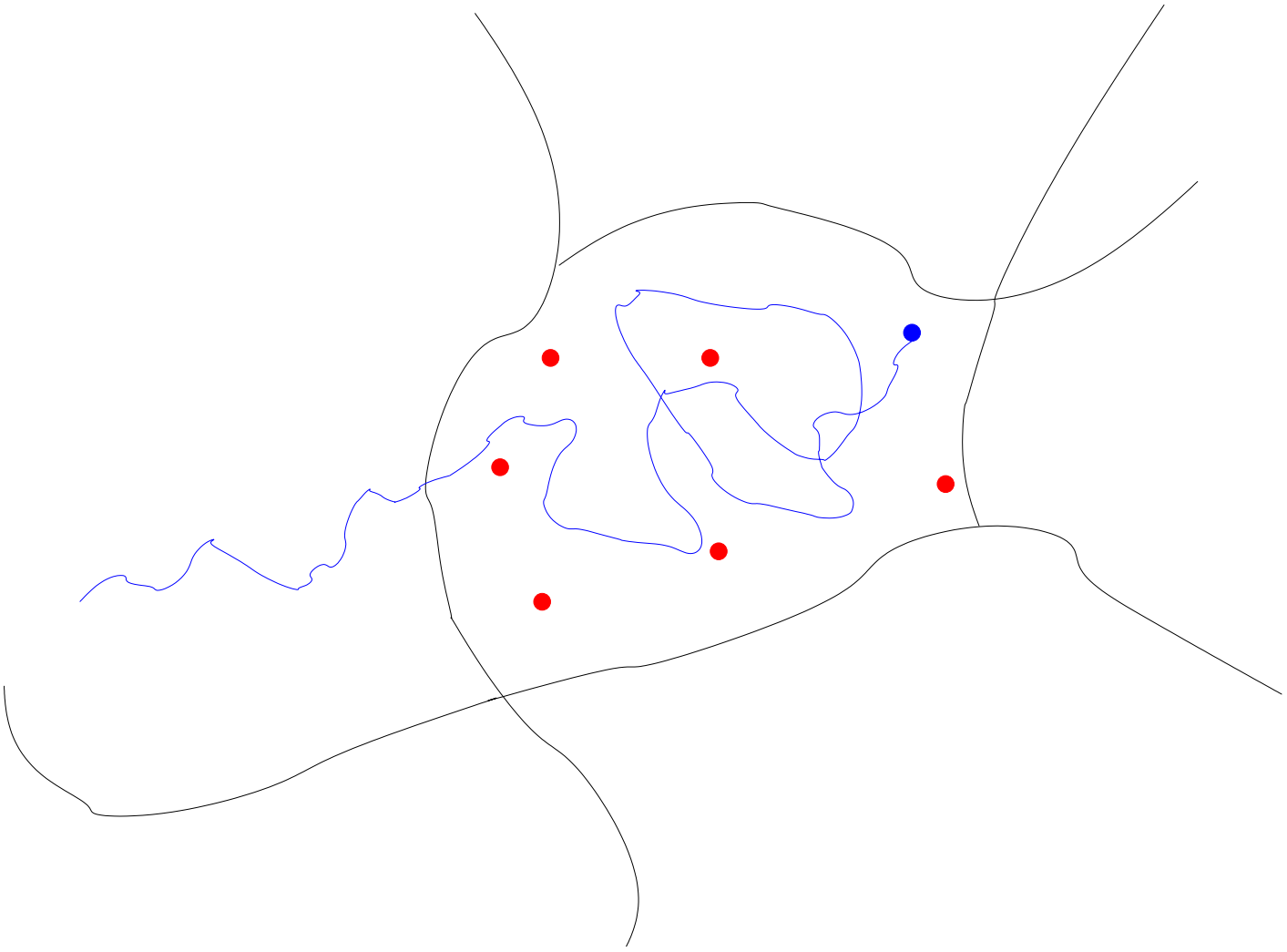
Moreover, over $[T_{simu}, T_{simu} + NT]$, the state dynamics S_t is constant and defined as:

$$S_t = \mathcal{S}(\boldsymbol{X}^1_{T_{simu}}).$$

Then, go back to the decorrelation step...

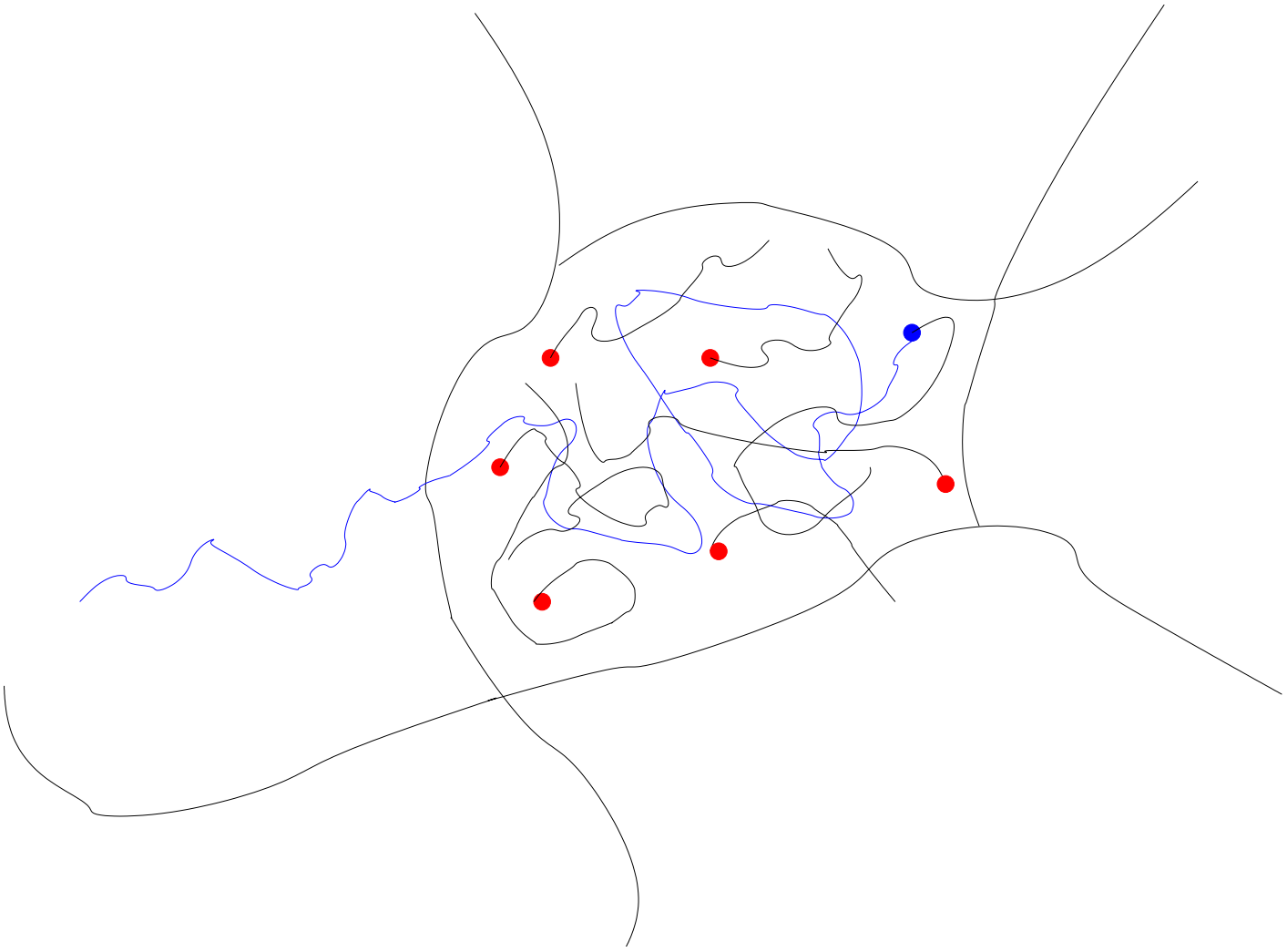
The Parallel Replica Algorithm

Parallel step.



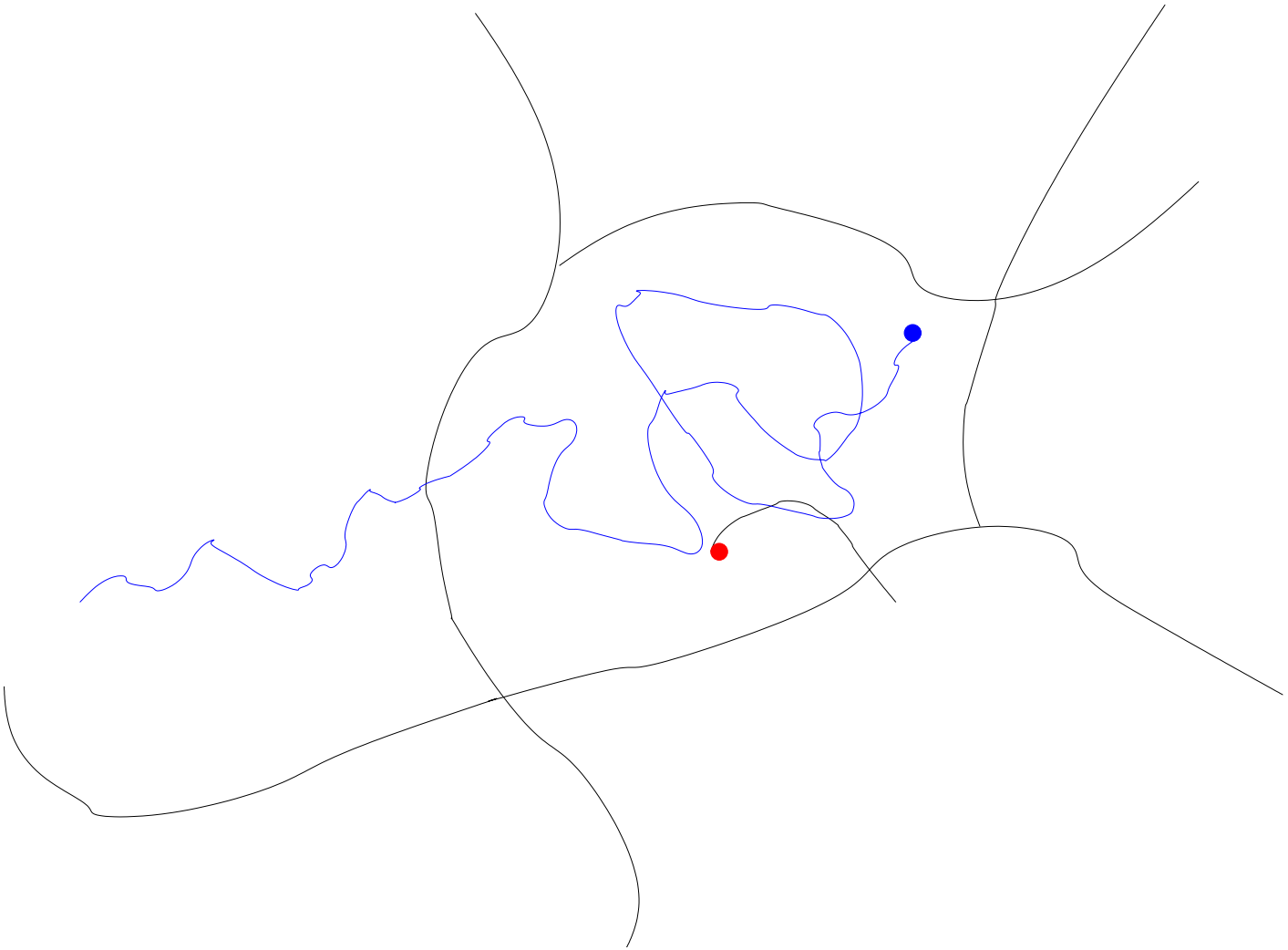
The Parallel Replica Algorithm

Parallel step: run independent trajectories in parallel...



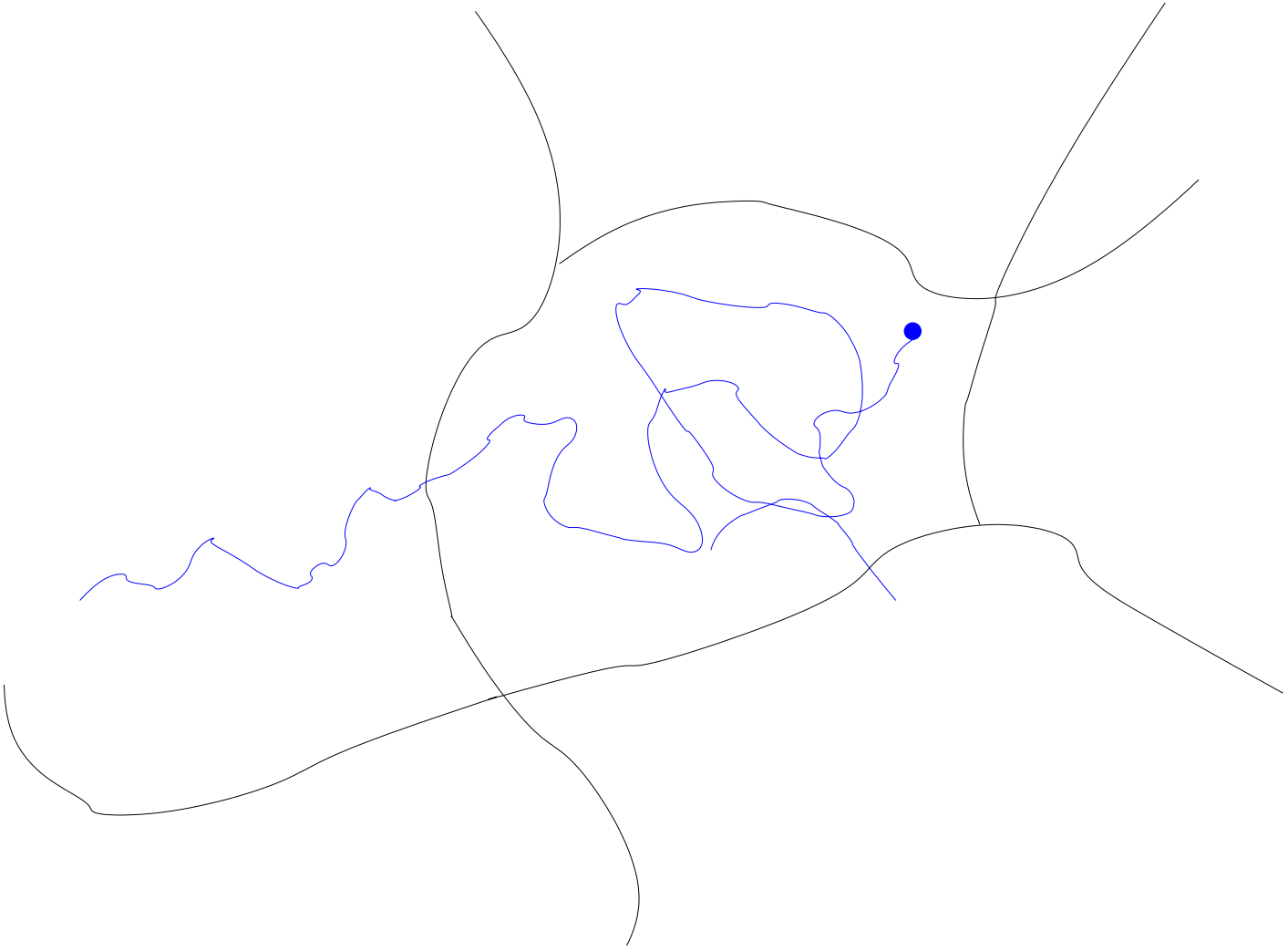
The Parallel Replica Algorithm

Parallel step: ... and detect the first transition event.



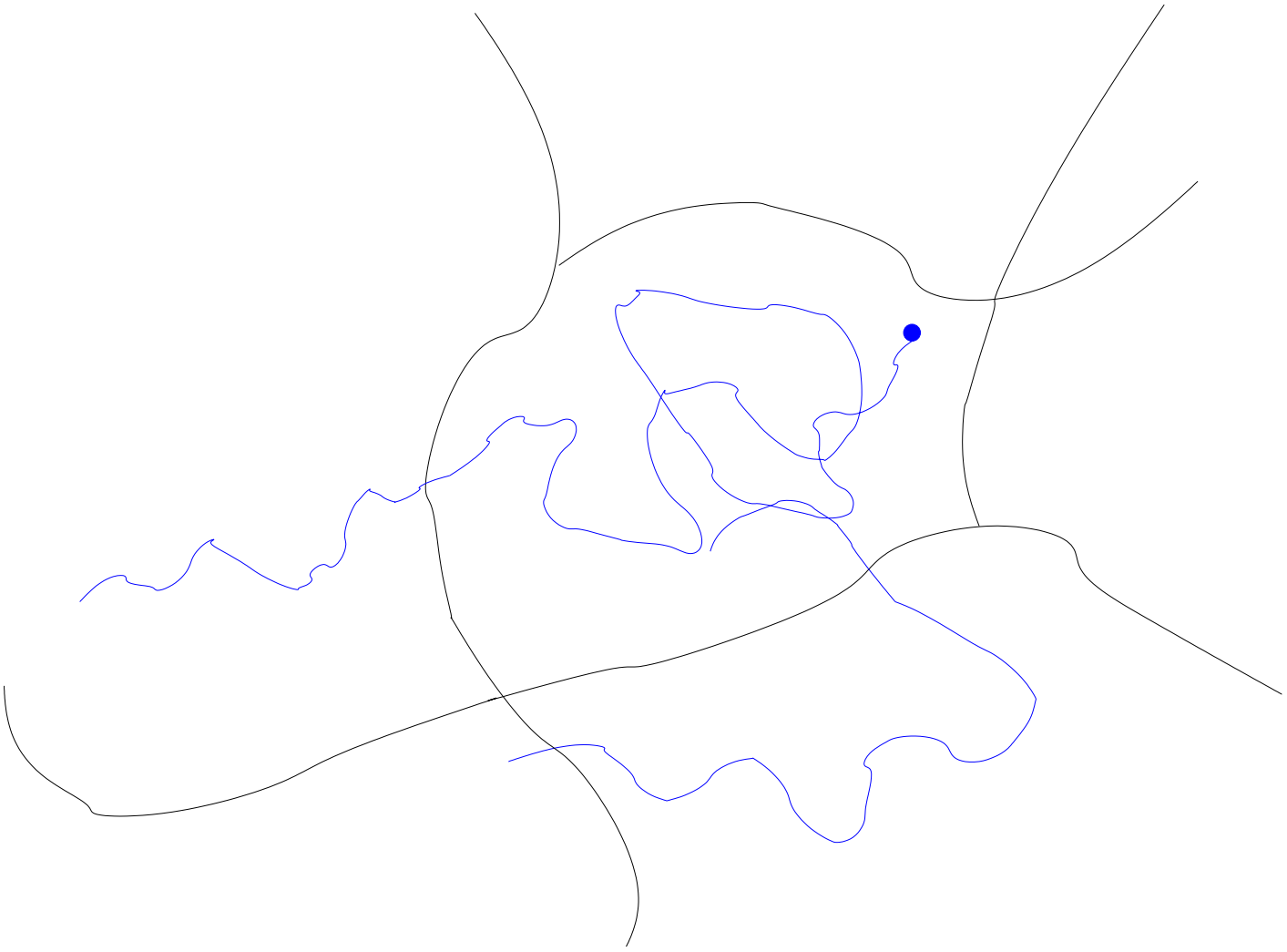
The Parallel Replica Algorithm

Parallel step: update the time clock: $T_{simu} = T_{simu} + NT$.



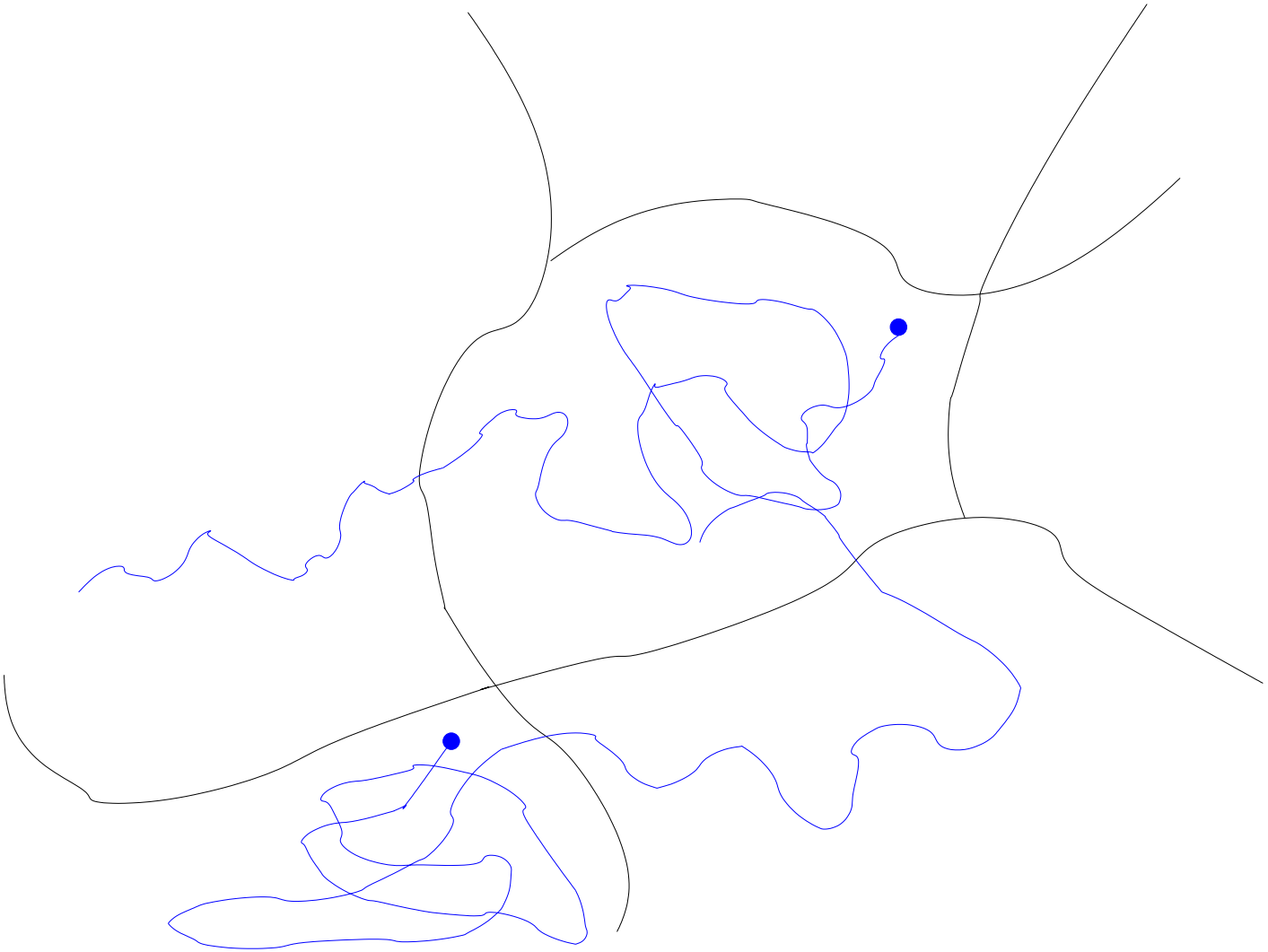
The Parallel Replica Algorithm

A new decorrelation step starts...



The Parallel Replica Algorithm

New decorrelation step



The Parallel Replica Algorithm

Analysis of the algorithm: the parallel step would introduce no error if

- the escape time T_W^1 was exponentially distributed
- and independent of the next visited state.

This essentially amounts to assuming that $\mathcal{S}(\boldsymbol{X}_t)$ is a Markov chain...

How to analyze the error introduced by the algorithm ?

This is related to the general question: how to relate a continuous state space Markov dynamics to a discrete state space Markov dynamics ? Pitfalls: (i) the temperature is not necessarily small (ii) the partition of the state space may be anything (iii) no thermodynamic limit in general (non-homogeneous systems).

The quasi-stationary distribution

The quasi-stationary distribution (QSD) ν for $\boldsymbol{X}_t$ and associated to the actual well W is a probability measure which is (i) supported by W and such that (ii): $\forall t > 0$, $\forall A \subset W$,

$$\nu(A) = \frac{\displaystyle\int_W \mathbb{P}(\boldsymbol{X}_t^{\boldsymbol{x}} \in A,\, t < T_W^{\boldsymbol{x}})\, \nu(d\boldsymbol{x})}{\displaystyle\int_W \mathbb{P}(t < T_W^{\boldsymbol{x}})\, \nu(d\boldsymbol{x})}.$$

If $\boldsymbol{X}_0 \sim \nu$ and if $(\boldsymbol{X}_s)_{0 \leq s \leq t}$ has not left the well, then $\boldsymbol{X}_t \sim \nu$.

Let $L = -\nabla V \cdot \nabla + \beta^{-1}\Delta$ be the infinitesimal generator of $(\boldsymbol{X}_t)$. Then the density u of ν ($d\nu = u(\boldsymbol{x})d\boldsymbol{x}$) is the first eigenfunction of $L^* = \operatorname{div}(\nabla V + \beta^{-1}\nabla)$ with absorbing boundary conditions:

$$\begin{cases} L^* u = -\lambda_1 u \text{ on } W, \\ \quad u = 0 \text{ on } \partial W. \end{cases}$$

The quasi-stationary distribution and the dephasing step

Property of the QSD: If $\boldsymbol{X}_0 \sim \nu$ then, the first exit time T_W from W is exponentially distributed with parameter λ_1 and is a random variable independent of the first hitting point $\boldsymbol{X}_{T_W}$ on ∂W.

The dephasing step is very much related to the so-called Fleming-Viot process and may be seen as a way to get N i.i.d. random variables distributed according to the QSD.

Remark: In general, T_W exponentially distribtued is *not* sufficient for $\boldsymbol{X}_0$ to be distributed according to ν.

The parallel step

As announced above, starting from the QSD, the parallel step is exact. This is stated precisely here.

Let us start from N initial conditions $\boldsymbol{X}_0^k$ i.i.d. in the well W and let the processes evolve independently. Let us denote

$$T_W^k = \inf\{t > 0, \boldsymbol{X}_t^k \notin W\}$$

the escape time for the k-th replica, and

$$T = T_W^{K_0} \text{ where } K_0 = \arg \min_{k \in \{1,\dots,N\}} T_W^k$$

the *first* escape time over all processes.

- Assume that T_W^1 is exponentially distributed [OK starting from QSD.] Then NT has the same law as T_W^1.
- Assume that T_W^1 is independent of $\boldsymbol{X}_{T_W^1}^1$ [OK starting from QSD.] Then $\boldsymbol{X}_{T_W^{K_0}}^{K_0}$ has the same distribution as $\boldsymbol{X}_{T_W^1}^1$ and is independent of $T_W^{K_0}$.

The decorrelation step

We would like to quantify the error introduced by the dephasing and parallel steps, when the decorrelation step is successful.

As shown above, when the decorrelation step is successful, it is assumed that the reference walker is distributed according to the QSD. If it was indeed the case, the algorithm would be exact. The decorrelation step can be seen as a way to probe this assumption. What is the error introduced there ?

The decorrelation step

We have the following error estimate in total variation norm: for $t \geq \frac{C}{\lambda_2 - \lambda_1}$,

$$\sup_{f, \|f\|_{L^\infty} \leq 1} \left| \mathbb{E}(f(T_W - t, \boldsymbol{X}_{T_W}) | T_W \geq t) - \mathbb{E}^\nu(f(T_W, \boldsymbol{X}_{T_W})) \right| \leq C \exp(-(\lambda_2 - \lambda_1)t),$$

where $-\lambda_2 < -\lambda_1 < 0$ are the two first eigenvalues of L^* with absorbing boundary conditions on ∂W.

This shows that τ_{corr} should be chosen such that:

$$\tau_{corr} \geq \frac{\overline{C}}{\lambda_2 - \lambda_1}.$$

On the other hand, it should be smaller than the typical time to leave the well, $\mathbb{E}(T_W)$. Since $\mathbb{E}^\nu(T_W) = 1/\lambda_1$, this typically implies the spectral gap requirement,

$$\frac{\overline{C}}{\lambda_2 - \lambda_1} \leq \frac{1}{\lambda_1}.$$

The Parallel Replica Algorithm: conclusions

This can be generalized to other dynamics (coarse-graining of kMC).

Main results:

- The QSD is a good intermediate between continuous state dynamics and kMC-like approximations.
- The error analysis holds whatever the partition. But the method requires metastability between the states to be computationally efficient.
- The parameter τ_{corr} should be adjusted in terms of the two first eigenvalues of the Fokker-Planck operator with absorbing boundary conditions.

Conclusion

Notice that the numerical methods we have presented are based on some dimension reduction and coarse-graining techniques (through the functions ξ or $\mathcal{S}$). They are easy to parallelize.

Main open problems in MD:

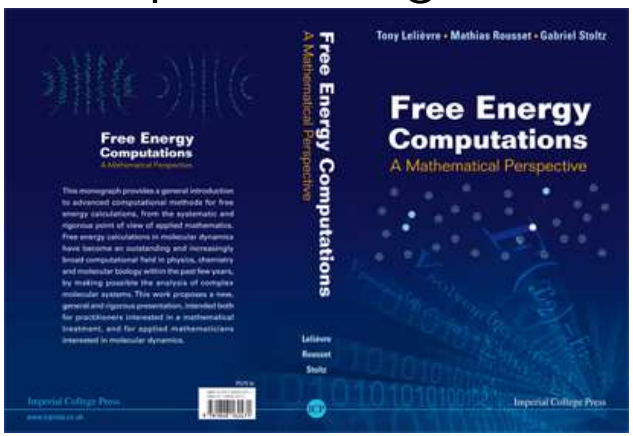
- How to generate efficiently metastable dynamics ?
- Out-of-equilibrium systems: models, analysis, sampling methods ?

If you want to know more about these, come to the minisymposia !

Conclusion

A few references:

- T. Lelièvre, M. Rousset and G. Stoltz, *Long-time convergence of an Adaptive Biasing Force method*, Nonlinearity, 21, 1155-1181, 2008.
- T. Lelièvre, M. Rousset and G. Stoltz, *Free energy computations, a mathematical perspective*, Imperial College Press, 2010.



- C. Le Bris, T. Lelièvre, M. Luskin and D. Perez, *A mathematical formalization of the parallel replica dynamics*, `http://arxiv.org/abs/1105.4636`.