Effective dynamics for the (overdamped) Langevin equation

Frédéric Legoll

ENPC and INRIA

joint work with T. Lelièvre (ENPC and INRIA)

Enumath conference, MS Numerical methods for molecular dynamics
Some quantities of interest in molecular dynamics:

- **thermodynamical averages** wrt Gibbs measure:

\[
\langle \Phi \rangle = \int_{\mathbb{R}^n} \Phi(X) \, d\mu, \quad d\mu = Z^{-1} \exp(-\beta V(X)) \, dX, \quad X \in \mathbb{R}^n
\]

- or **dynamical** quantities:
  - diffusion coefficients
  - rate constants
  - residence times in metastable basins
Molecular simulation

Some quantities of interest in molecular dynamics:

- **thermodynamical averages** wrt Gibbs measure:

  \[ \langle \Phi \rangle = \int_{\mathbb{R}^n} \Phi(X) \, d\mu, \quad d\mu = Z^{-1} \exp(-\beta V(X)) \, dX, \quad X \in \mathbb{R}^n \]

- or **dynamical quantities**:
  - diffusion coefficients
  - rate constants
  - residence times in metastable basins

In practice, quantities of interest often depend on a **few** variables.

**Reduced description** of the system, that still includes some **dynamical** information?
Example of a biological system

Courtesty of Chris Chipot, CNRS Nancy
We are interested in dynamical properties. Two possible choices for the reference dynamics of the system:

- **overdamped Langevin equation:**

  \[
  dX_t = -\nabla V(X_t) \, dt + \sqrt{2\beta^{-1}} \, dW_t, \quad X_t \in \mathbb{R}^n
  \]

- **Langevin equation** (with masses set to 1):

  \[
  \begin{align*}
  dX_t &= P_t \, dt, \\
  dP_t &= -\nabla V(X_t) \, dt - \gamma P_t \, dt + \sqrt{2\gamma\beta^{-1}} \, dW_t, \\
  X_t &\in \mathbb{R}^n, \\
  P_t &\in \mathbb{R}^n.
  \end{align*}
  \]

For both dynamics,

\[
\frac{1}{T} \int_0^T \Phi(X_t) \, dt \longrightarrow \int_{\mathbb{R}^n} \Phi(X) \, d\mu, \quad d\mu = Z^{-1} \exp(-\beta V(X)) \, dX.
\]

We will mostly argue with overdamped Langevin, and next turn to Langevin.
Metastability and reaction coordinate

\[ dX_t = -\nabla V(X_t) \, dt + \sqrt{2\beta^{-1}} \, dW_t, \quad X_t \equiv \text{position of all atoms} \]

- in practice, the dynamics is metastable: the system stays a long time in a well of \( V \) before jumping to another well:

![Diagram showing metastability with red path transitioning between wells](image)

- we assume that wells are fully described through a well-chosen reaction coordinate

\[ \xi : \mathbb{R}^n \leftrightarrow \mathbb{R} \]

\( \xi(x) \) may e.g. be a particular angle in the molecule.

Quantity of interest: path \( t \mapsto \xi(X_t) \).
Our aim

\[ dX_t = -\nabla V(X_t) \, dt + \sqrt{2\beta^{-1}} \, dW_t \quad \text{in} \quad \mathbb{R}^n \]

Given a reaction coordinate \( \xi : \mathbb{R}^n \rightarrow \mathbb{R} \), propose a dynamics \( z_t \) that approximates \( \xi(X_t) \).

- **Preservation of equilibrium properties:**
  when \( X \sim d\mu \), then \( \xi(X) \) is distributed according to \( \exp(-\beta A(z)) \, dz \), where \( A \) is the free energy.

  The dynamics \( z_t \) should be ergodic wrt \( \exp(-\beta A(z)) \, dz \).

- **Recover in \( z_t \) some dynamical information included in \( \xi(X_t) \).**

Related approaches: Mori-Zwanzig formalism, asymptotic expansion of the generator (Papanicolaou, ...), averaging principle for SDE (Pavliotis and Stuart, Hartmann, ...), effective dynamics using Markov state models (Schuette and Sarich, Lu, ...).
A super-simple case: $\xi(x, y) = x$

Consider the dynamics in two dimensions: $X = (x, y) \in \mathbb{R}^2$,

$$
\begin{align*}
\frac{dx_t}{dt} &= -\partial_x V(x_t, y_t) \, dt + \sqrt{2\beta^{-1}} \, dW^x_t, \\
\frac{dy_t}{dt} &= -\partial_y V(x_t, y_t) \, dt + \sqrt{2\beta^{-1}} \, dW^y_t,
\end{align*}
$$

and assume that $\xi(x, y) = x$. 
A super-simple case: $\xi(x, y) = x$

Consider the dynamics in two dimensions: $X = (x, y) \in \mathbb{R}^2$,

$$
\begin{align*}
    dx_t &= -\partial_x V(x_t, y_t) \, dt + \sqrt{2\beta^{-1}} \, dW_t^x, \\
    dy_t &= -\partial_y V(x_t, y_t) \, dt + \sqrt{2\beta^{-1}} \, dW_t^y,
\end{align*}
$$

and assume that $\xi(x, y) = x$. Let $\psi(t, X)$ be the density of $X$ at time $t$:

$$
\text{for any } B \subset \mathbb{R}^2, \quad \mathbb{P}(X_t \in B) = \int_B \psi(t, X) dX
$$

Introduce the mean of the drift over all configurations satisfying $\xi(X) = z$:

$$
\tilde{b}(t, z) := -\frac{\int \partial_x V(z, y) \, \psi(t, z, y) \, dy}{\int \psi(t, z, y) \, dy} = -\mathbb{E} \left[ \partial_x V(X) \mid \xi(X_t) = z \right]
$$

and consider

$$
\begin{align*}
    dz_t &= \tilde{b}(t, z_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t
\end{align*}
$$

Then, for any $t$, the law of $z_t$ is equal to the law of $x_t$ (Gyongy 1986)
Making the approach practical

\[ \tilde{b}(t, z) = -\int_{\mathbb{R}} \partial_x V(z, y) \psi(t, z, y) \, dy = - \mathbb{E} [\partial_x V(X) \mid \xi(X_t) = z] \]

\( \tilde{b}(t, z) \) is extremely difficult to compute . . . Need for approximation:
Making the approach practical

\[ \tilde{b}(t, z) = -\int_{\mathbb{R}} \partial_x V(z, y) \psi(t, z, y) \, dy = -\mathbb{E} [\partial_x V(X) \mid \xi(X_t) = z] \]

\( \tilde{b}(t, z) \) is extremely difficult to compute . . . Need for approximation:

\[ b(z) := -\int_{\mathbb{R}} \partial_x V(z, y) \psi_{\infty}(z, y) \, dy = -\mathbb{E}_\mu [\partial_x V(X) \mid \xi(X) = z] \]

with \( \psi_{\infty}(x, y) = Z^{-1} \exp(-\beta V(x, y)) \).

Effective dynamics:

\[ dz_t = b(z_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t \]

Idea: \( \tilde{b}(t, x) \approx b(x) \) if the equilibrium in each manifold

\[ \Sigma_x = \{(x, y), \quad y \in \mathbb{R}\} \]

is quickly reached: \( x_t \) is much slower than \( y_t \).
The general case: $X \in \mathbb{R}^n$ and arbitrary $\xi$

\[ dX_t = -\nabla V(X_t) \, dt + \sqrt{2\beta^{-1}} \, dW_t, \quad \xi : \mathbb{R}^n \to \mathbb{R} \]

From the dynamics on $X_t$, we obtain (chain rule)

\[ d[\xi(X_t)] = \left( -\nabla V \cdot \nabla \xi + \beta^{-1} \Delta \xi \right) (X_t) \, dt + \sqrt{2\beta^{-1}} \, |\nabla \xi|(X_t) \, dB_t \]

where $B_t$ is a 1D brownian motion.
The general case: \( X \in \mathbb{R}^n \) and arbitrary \( \xi \)

\[
dX_t = -\nabla V(X_t) \, dt + \sqrt{2\beta^{-1}} \, dW_t, \quad \xi : \mathbb{R}^n \rightarrow \mathbb{R}
\]

From the dynamics on \( X_t \), we obtain (chain rule)

\[
d[\xi(X_t)] = (-\nabla V \cdot \nabla \xi + \beta^{-1} \Delta \xi)(X_t) \, dt + \sqrt{2\beta^{-1}} \, |\nabla \xi|(X_t) \, dB_t
\]

where \( B_t \) is a 1D brownian motion.

Introduce the average of the drift and diffusion terms:

\[
b(z) := \int (-\nabla V \cdot \nabla \xi + \beta^{-1} \Delta \xi)(X) \, \psi_\infty(X) \, \delta_{\xi(X) = z} \, dX
\]

\[
\sigma^2(z) := \int |\nabla \xi(X)|^2 \, \psi_\infty(X) \, \delta_{\xi(X) = z} \, dX
\]

Eff. dyn.: \[
dz_t = b(z_t) \, dt + \sqrt{2\beta^{-1}} \, \sigma(z_t) \, dB_t
\]

The approximation makes sense if, in the manifold

\[
\Sigma_z = \{X \in \mathbb{R}^n, \quad \xi(X) = z\},
\]

\( X_t \) quickly reaches equilibrium. \( \xi(X_t) \) much slower than evolution of \( X_t \) in \( \Sigma_z \).
Some remarks

Effective dynamics:

\[ dz_t = b(z_t) \, dt + \sqrt{2\beta^{-1}} \, \sigma(z_t) \, dB_t \]

- OK from the statistical viewpoint: the dynamics is ergodic wrt \( \exp(-\beta A(z))dz \).

- Using different arguments, this dynamics has been obtained by [E and Vanden-Eijnden 2004], and [Maragliano, Fischer, Vanden-Eijnden and Ciccotti, 2006].

- In the following, we will
  - numerically assess its accuracy
  - derive error bounds

In practice, we pre-compute \( b(z) \) and \( \sigma(z) \) for values on a grid (remember \( z \) is scalar), and next linearly interpolate between these values.
Dimer in solution: comparison of residence times

- solvent-solvent, solvent-monomer: truncated LJ on $r = ||x_i - x_j||$:

$$V_{WCA}(r) = 4\varepsilon \left( \frac{\sigma^{12}}{r^{12}} - 2 \frac{\sigma^6}{r^6} \right) \text{ if } r \leq \sigma, \ 0 \text{ otherwise (repulsive potential)}$$

- monomer-monomer: double well on $r = ||x_1 - x_2||$

Reaction coordinate: the distance between the two monomers
Dimer in solution: comparison of residence times

- solvent-solvent, solvent-monomer: truncated LJ on $r = ||x_i - x_j||$:
  \[ V_{WCA}(r) = 4\varepsilon \left( \frac{\sigma^{12}}{r^{12}} - 2 \frac{\sigma^6}{r^6} \right) \quad \text{if } r \leq \sigma, \ 0 \text{ otherwise (repulsive potential)} \]

- monomer-monomer: double well on $r = ||x_1 - x_2||$

Reaction coordinate: the distance between the two monomers

<table>
<thead>
<tr>
<th>$\beta$</th>
<th>Reference dyn.</th>
<th>Effective dyn.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>262 ± 6</td>
<td>245 ± 5</td>
</tr>
<tr>
<td>0.25</td>
<td>1.81 ± 0.04</td>
<td>1.68 ± 0.04</td>
</tr>
</tbody>
</table>
Accuracy assessment: some background materials
Accuracy assessment: some background materials

\[ dX_t = -\nabla V(X_t) \, dt + \sqrt{2\beta^{-1}} \, dW_t \]

Let \( \psi(t, X) \) be the probability distribution function of \( X_t \):

\[ \mathbb{P}(X_t \in B) = \int_B \psi(t, X) \, dX \]

Under mild assumptions, \( \psi(t, X) \) converges to \( \psi_\infty(X) = Z^{-1} \exp(-\beta V(X)) \) exponentially fast:

\[ H(\psi(t, \cdot) | \psi_\infty) := \int \psi(t, \cdot) \ln \frac{\psi(t, \cdot)}{\psi_\infty} \leq C \exp(-2\rho t) \]

Relative entropy is interesting because \( \|\psi(t, \cdot) - \psi_\infty\|_{L^1}^2 \leq 2 H(\psi(t, \cdot) | \psi_\infty) \).

The larger \( \rho \) is, the faster the convergence to equilibrium.

Remark: \( \rho \) is the Logarithmic Sobolev inequality constant of \( \psi_\infty \).
A convergence result

\[ dX_t = -\nabla V(X_t) \, dt + \sqrt{2\beta^{-1}} \, dW_t, \quad \text{consider } \xi(X_t) \]

Let \( \psi_{\text{exact}}(t, z) \) be the probability distribution function of \( \xi(X_t) \):

\[ \mathbb{P}(\xi(X_t) \in I) = \int_I \psi_{\text{exact}}(t, z) \, dz \]

On the other hand, we have introduced the effective dynamics

\[ dz_t = b(z_t) \, dt + \sqrt{2\beta^{-1}} \sigma(z_t) \, dB_t \]

Let \( \phi_{\text{eff}}(t, z) \) be the probability distribution function of \( z_t \).

Introduce the error

\[ E(t) := \int_{\mathbb{R}} \psi_{\text{exact}}(t, \cdot) \ln \frac{\psi_{\text{exact}}(t, \cdot)}{\phi_{\text{eff}}(t, \cdot)} \]

We would like \( \psi_{\text{exact}} \approx \phi_{\text{eff}} \), e.g. \( E \) small . . .
Decoupling assumptions

\[ \Sigma_z = \{ X \in \mathbb{R}^n, \xi(X) = z \}, \quad d\mu_z \propto \exp(-\beta V(X)) \delta_{\xi(X) = z} \]

assume that the Gibbs measure restricted to \( \Sigma_z \) satisfy a Logarithmic Sobolev inequality with a large constant \( \rho \), uniform in \( z \) (no metastability in \( \Sigma_z \)).
Decoupling assumptions

\[ \Sigma_z = \{ X \in \mathbb{R}^n, \, \xi(X) = z \}, \quad d\mu_z \propto \exp(-\beta V(X)) \delta_{\xi(X) = z} \]

- Assume that the Gibbs measure restricted to \( \Sigma_z \) satisfy a Logarithmic Sobolev inequality with a large constant \( \rho \), uniform in \( z \) (no metastability in \( \Sigma_z \)).

- Assume that the coupling between the dynamics of \( \xi(X_t) \) and the dynamics in \( \Sigma_z \) is weak:
  If \( \xi(x, y) = x \), we request \( \partial_{xy} V \) to be small.

In the general case, recall that the free energy derivative reads

\[ A'(z) = \int_{\Sigma_z} F(X) d\mu_z \]

We assume that \( \max |\nabla_{\Sigma_z} F| \leq \kappa \).
Decoupling assumptions

\[ \Sigma_z = \{ X \in \mathbb{R}^n, \xi(X) = z \}, \quad d\mu_z \propto \exp(-\beta V(X)) \delta_{\xi(X)-z} \]

- Assume that the Gibbs measure restricted to \( \Sigma_z \) satisfy a Logarithmic Sobolev inequality with a large constant \( \rho \), uniform in \( z \) (no metastability in \( \Sigma_z \)).

- Assume that the coupling between the dynamics of \( \xi(X_t) \) and the dynamics in \( \Sigma_z \) is weak:
  
  If \( \xi(x, y) = x \), we request \( \partial_{xy} V \) to be small.

  In the general case, recall that the free energy derivative reads

  \[ A'(z) = \int_{\Sigma_z} F(X) d\mu_z \]

  We assume that \( \max |\nabla_{\Sigma_z} F| \leq \kappa \).

- Assume that \( |\nabla\xi| \) is close to a constant on each \( \Sigma_z \), e.g.

  \[ \lambda = \max_X \left| \frac{|\nabla\xi|^2(X) - \sigma^2(\xi(X))}{\sigma^2(\xi(X))} \right| \text{ is small} \]
**Error estimate**

\[
E(t) = \text{error} = \int_{\mathbb{R}} \psi_{\text{exact}}(t, \cdot) \ln \frac{\psi_{\text{exact}}(t, \cdot)}{\phi_{\text{eff}}(t, \cdot)}
\]

Under the above assumptions, for all \( t \geq 0 \),

\[
E(t) \leq C(\xi, \text{Initial Cond.}) \left( \lambda + \frac{\beta^2 \kappa^2}{\rho^2} \right)
\]

Hence, if the coarse variable \( \xi \) is such that

- \( \rho \) is large (fast ergodicity in \( \Sigma_z \)),
- \( \kappa \) is small (small coupling between dynamics in \( \Sigma_z \) and on \( z_t \)),
- \( \lambda \) is small (\( |\nabla \xi| \) is close to a constant on each \( \Sigma_z \)),

then the effective dynamics is accurate:

at any time, law of \( \xi(X_t) \approx \text{law of } z_t \).

*Remark: this is not an asymptotic result, and this holds for any \( \xi \).*

This bound may be helpful, in some cases, to discriminate between various reaction coordinates.
Rough estimation in a particular case

Standard expression in MD: \( V_{\varepsilon}(X) = V_0(X) + \frac{1}{\varepsilon}q^2(X) : \quad \nabla q \equiv \text{fast direction} \)

\[
E(t) = \text{error} = \int_{\mathbb{R}} \psi_{\text{exact}}(t, \cdot) \ln \frac{\psi_{\text{exact}}(t, \cdot)}{\phi_{\text{eff}}(t, \cdot)}
\]

- If \( \nabla \xi \cdot \nabla q = 0 \), then the direction \( \nabla \xi \) is decoupled from the fast direction \( \nabla q \), hence \( \xi \) is indeed a slow variable, and it turns out that

\[
E(t) = O(\varepsilon).
\]

- If \( \nabla \xi \cdot \nabla q \neq 0 \), then the variable \( \xi \) does not contain all the slow motion, and bad scale separation:

\[
E(t) = O(1),
\]

hence the laws of \( \xi(X_t) \) and of \( z_t \) are not close one to each other.

The condition \( \nabla \xi \cdot \nabla q = 0 \) seems important to obtain good accuracy.
Tri-atomic molecule

\[ V(X) = \frac{1}{2} k_2 (r_{AB} - \ell_{eq})^2 + \frac{1}{2} k_2 (r_{BC} - \ell_{eq})^2 + k_3 W_{DW}(\theta_{ABC}), \quad k_2 \gg k_3, \]

where \( W_{DW} \) is a double well potential.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>( \xi_1(X) = \theta_{ABC} )</td>
<td>yes</td>
<td>0.700 ± 0.011</td>
<td>0.704 ± 0.011</td>
</tr>
<tr>
<td>( \xi_2(X) = r_{AC}^2 )</td>
<td>no</td>
<td>0.709 ± 0.015</td>
<td>0.219 ± 0.004</td>
</tr>
</tbody>
</table>
We have considered until now the overdamped Langevin equation:

\[ dX_t = -\nabla V(X_t) \, dt + \sqrt{2\beta^{-1}} \, dW_t \]

Consider now the Langevin equation:

\[
\begin{align*}
    dX_t &= P_t \, dt \\
    dP_t &= -\nabla V(X_t) \, dt - \gamma P_t \, dt + \sqrt{2\gamma\beta^{-1}} \, dW_t
\end{align*}
\]

Can we extend the numerical strategy?

Joint work with F. Galante and T. Lelièvre.
Building the effective dynamics - 1

\[ dX_t = P_t \, dt, \quad dP_t = -\nabla V(X_t) \, dt - \gamma P_t \, dt + \sqrt{2\gamma\beta^{-1}} \, dW_t \]

We compute

\[ d[\xi(X_t)] = \nabla \xi(X_t) \cdot P_t \, dt \]

We introduce the coarse-grained velocity

\[ v(X, P) = \nabla \xi(X) \cdot P \in \mathbb{R} \]

and have (chain rule)

\[ d[v(X_t, P_t)] = \left[ P_t^T \nabla^2 \xi(X_t) P_t - \nabla \xi(X_t)^T \nabla V(X_t) \right] \, dt \]

\[ -\gamma v(X_t, P_t) \, dt + \sqrt{2\gamma\beta^{-1}} \left| \nabla \xi(X_t) \right| \, dB_t \]

where \( B_t \) is a 1D Brownian motion.

We wish to write a closed equation on \( \xi_t = \xi(X_t) \) and \( v_t = v(X_t, P_t) \).

Introduce \( D(X, P) = P^T \nabla^2 \xi(X) P - \nabla \xi(X)^T \nabla V(X) \).
Without any approximation, we have obtained

\[ d\xi_t = v_t \, dt, \]
\[ dv_t = D(X_t, P_t) \, dt - \gamma v_t \, dt + \sqrt{2\gamma\beta^{-1}} |\nabla \xi(X_t)| \, dB_t \]

To close the system, we introduce the conditional expectations with respect to the equilibrium measure \( \mu(X, P) = Z^{-1} \exp[-\beta (V(X) + P^T P/2)] \):

\[ D_{\text{eff}}(\xi_0, v_0) = \mathbb{E}_\mu(D(X, P) \mid \xi(X) = \xi_0, v(X, P) = v_0) \]
\[ \sigma^2(\xi_0, v_0) = \mathbb{E}_\mu(|\nabla \xi|^2(X) \mid \xi(X) = \xi_0, v(X, P) = v_0) \]

Effective dynamics:

\[ d\xi_t = v_t \, dt, \quad dv_t = D_{\text{eff}}(\xi_t, v_t) \, dt - \gamma v_t \, dt + \sqrt{2\gamma\beta^{-1}} \sigma(\xi_t, v_t) \, dB_t \]

Again, this dynamics is consistent with the equilibrium properties: it preserves the equilibrium measure \( \exp[-\beta A(\xi_0, v_0)] \, d\xi_0 \, dv_0 \).
Numerical results: the tri-atomic molecule

\[ V(X) = \frac{1}{2} k_2 (r_{AB} - \ell_{eq})^2 + \frac{1}{2} k_2 (r_{BC} - \ell_{eq})^2 + k_3 W_{DW}(\theta_{ABC}), \quad k_2 \gg k_3, \]

where \( W_{DW} \) is a double well potential.

Reaction coordinate: \( \xi(X) = \theta_{ABC} \).

<table>
<thead>
<tr>
<th>Inverse temp.</th>
<th>Reference</th>
<th>Eff. dyn.</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \beta = 1 )</td>
<td>9.808 ± 0.166</td>
<td>9.905 ± 0.164</td>
</tr>
<tr>
<td>( \beta = 2 )</td>
<td>77.37 ± 1.23</td>
<td>79.1 ± 1.25</td>
</tr>
</tbody>
</table>

Excellent agreement on the residence times in the well.
Going back to the overdamped case, with $\xi(x, y) = x$, can we get **pathwise accuracy**, e.g.

$$
\mathbb{E} \left[ \sup_{0 \leq t \leq T} |x_t - z_t|^2 \right] \leq \frac{C(T)}{\rho} \quad ?
$$
Pathwise accuracy (ongoing work with T. Lelièvre and S. Olla)

Going back to the overdamped case, with $\xi(x, y) = x$, can we get pathwise accuracy, e.g.

$$\mathbb{E} \left[ \sup_{0 \leq t \leq T} |x_t - z_t|^2 \right] \leq \frac{C(T)}{\rho}$$

$z_t$ is the effective dynamics trajectory:

$$dz_t = -b(z_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t$$

$(x_t, y_t)$ is the exact trajectory:

$$dx_t = -\partial_x V(x_t, y_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t$$

$$= -b(x_t) \, dt + e(x_t, y_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t$$

By construction, $b(x) = \mathbb{E}_\mu [\partial_x V(X)|\xi(X) = x]$, hence

$$\forall x, \quad \mathbb{E}_\mu [e(X)|\xi(X) = x] = 0.$$
Let $L^x$ be the Fokker-Planck operator corresponding to a simple diffusion in $y$, at fixed $x$:

$$L^x \phi = \text{div}_y (\phi \nabla_y V) + \beta^{-1} \Delta_y \phi$$

For any $x$,

$$\mathbb{E}_\mu [e(X) | \xi(X) = x] = 0 \implies \exists u(x, \cdot) \text{ s.t. } (L^x)^* u(x, \cdot) = e(x, \cdot)$$

Assume that $L^x$ satisfies a (large) spectral gap $\rho \gg 1$. Then, $\|u\| \leq C/\rho \ll 1$.

We have not been able to show a bound on $\mathbb{E} \left[ \sup_{0 \leq t \leq T} |x_t - z_t|^2 \right]$, but we have shown that

$$\mathbb{P} \left( \sup_{0 \leq t \leq T} |x_t - z_t| \geq c \rho^{-\alpha} \right) \leq \frac{C}{\ln(\rho)}$$

for any $0 \leq \alpha < 1/2$. This somewhat explains the good results we observe on the residence times.
Numerical illustration: the tri-atomic molecule

\[ V(X) = \frac{1}{2} k_2 (r_{AB} - \ell_{eq})^2 + \frac{1}{2} k_2 (r_{BC} - \ell_{eq})^2 + k_3 W(\theta_{ABC}), \quad k_2 \gg k_3 \]
Conclusions

- We have proposed a “natural” way to obtain a closed equation on $\xi(X_t)$.
- Encouraging numerical results and rigorous error bounds (marginals at time $t$ and in probability on the paths).

Once a reaction coordinate $\xi$ has been chosen, computing the drift and diffusion functions $b(z)$ and $\sigma(z)$ is as easy/difficult as computing the free energy derivative $A'(z)$.

The approach can be extended to the Langevin equation.

FL, T. Lelièvre, S. Olla, in preparation
F. Galante, FL, T. Lelièvre, in preparation