Effective dynamics for the (overdamped) Langevin equation

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ACMAC workshop Coarse-graining of many-body systems
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
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- 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?
We are interested in dynamical properties. Two possible choices for the reference dynamics of the system:

- **overdamped Langevin equation**:

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

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

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

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:

- 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), . . .
A natural candidate

Residence times in wells are often associated with free energy barriers. This comes from TST if \( u_t := \xi(X_t) \) follows the dynamics

\[
du_t = -A'(u_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t. \tag{1}
\]

- this dynamics is indeed ergodic \( \text{wrt} \) \( \exp(-\beta A(z)) \, dz \).

- however, it is not invariant by a reparametrization: consider a one-to-one function \( h \), and consider \( \zeta(X) := h(\xi(X)) \):

  level sets associated to \( \xi = \) level sets associated to \( \zeta \)

Dynamics \( (1) \) for RC \( \xi \) and next one-to-one change of coordinate \( \xi \to \zeta \)

\( \neq \)

Dynamics \( (1) \) for RC \( \zeta \).

Dynamical content of the free energy \( A \)?
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

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Outline of the talk

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

- **Construction** of an effective dynamics. When do we recover
  \[ du_t = -A'(u_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t \]

- **Numerical examples**: residence times in metastable regions
- **Assessment** of the accuracy of the proposed dynamics

- Extend the procedure to the Langevin equation:
  \[ dX_t = P_t \, dt, \quad dP_t = -\nabla V(X_t) \, dt - \gamma P_t \, dt + \sqrt{2\gamma\beta^{-1}} \, dW_t \]
A super-simple case: $\xi(x, y) = x$

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

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

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 $t$:

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

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

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

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

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

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

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

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

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

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

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 \( \xi \)

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

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 brownianian 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.:

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

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 \( \Sigma_z \).
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
Effective dynamics and free energy

Is this effective dynamics the same as

\[ du_t = -A'(u_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t, \quad A \text{ free energy associated with } \xi(X) \]

- The effective dynamics is

\[ dz_t = b(z_t) \, dt + \sqrt{2\beta^{-1}} \, \sigma(z_t) \, dB_t, \quad \sigma^2(z) = \langle |\nabla \xi|^2 \rangle_{\Sigma z}. \]

- If \(|\nabla \xi(X)| = 1\), then \(\sigma(z) = 1\) and \(b(z) = -A'(z)\). We recover the free energy. An example:

\[ \xi(X) = X^j.\]

- In general, \(\sigma(z)\) is not a constant, and \(b(z) \neq -A'(z)\). Dynamics are different, and yield very different numerical results.

- Our dynamics is invariant through reparametrization \(\zeta(X) = h(\xi(X))\), in contrast to the dynamics associated with \(A'\).
Accuracy assessment: residence times

In practice:

- we consider a finite interval for $z$
- we pre-compute $b(z)$ and $\sigma(z)$ for values on a grid (remember $z$ is scalar)
- we linearly interpolate between these values

Residence times computations: for a given reaction coordinate $\xi$,

- we define the starting well as $\{x \in \mathbb{R}^n; \xi(x) > \xi_{th}\}$
- generate a set of initial conditions in the well distributed according to the Gibbs measure
- run the full dynamics from each $x_i$ until the other well has been reached → reference residence time
- run the effective dynamics

$$dz_t = b(z_t) \, dt + \sqrt{2\beta^{-1}} \, \sigma(z_t) \, dB_t, \quad z_{t=0} = \xi(x_i).$$
Residence times for the butane molecule

\[ V(X) = \sum_i V_2 \left( \|X^{i+1} - X^i\| \right) + V_3(\theta_1) + V_3(\theta_2) + V_4(\phi) \]

\[ V_2(\ell) = \frac{k_2}{2}(\ell - \ell_{eq})^2, \quad V_3(\theta) = \frac{k_3}{2}(\theta - \theta_{eq})^2 \]

Reaction coordinate: \( \xi(X) = \phi \), the dihedral angle.

Residence time in primary well before going to one of the two secondary wells:

- complete model (reference): \( 31.937 \pm 0.561 \)
- effective dynamics prediction: \( 32.037 \pm 0.558 \)
- free energy dynamics prediction: \( 37.122 \pm 0.644 \)
**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

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Accuracy of the effective dynamics

- We have numerically compared residence times in metastable regions.

- It is possible to derive an analytical estimate ensuring that

\[
P(z_t \in I) \approx P(\xi(X_t) \in I)
\]

at any time \( t \), for any interval \( I \subset \mathbb{R} \), where \( z_t \) follows our effective dynamics.

- the potential \( V \) is frequently of the form

\[
V_\varepsilon(X) = V_0(X) + \frac{1}{\varepsilon}q^2(X)
\]

Bond length potentials are much stiffer than bond angle potentials, . . .

Exploit this structure to go further.
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

\[ \| \psi(t, \cdot) - \psi_\infty \|_{L^1}^2 \leq 2H(\psi(t, \cdot) | \psi_\infty) . \]

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 (uniform in \( z \)) constant \( \rho \) (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 (uniform in $z$) constant $\rho$ (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

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

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

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

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

- 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 \( \xi \).
Rough estimation in a particular case

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

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

- 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.

Two possible reaction coordinates:

- the angle \( \xi_1(X) = \theta_{ABC} \)
- the distance \( \xi_2(X) = r_{AC}^2 \)

\( \xi_1(X) = \theta_{ABC} \) satisfies the orthogonality condition, whereas \( \xi_2(X) = r_{AC}^2 \) does not.
Residence times as a function of $\beta$

$\xi_1 = \theta_{ABC}$

$\xi_2 = r_{AC}^2$

$\ln(\text{residence time})$ as a function of $\beta$
Consider the simple case $\xi(x, y) = x$. Can we get pathwise accuracy, e.g.

$$
\mathbb{E} \left[ \sup_{0 \leq t \leq T} |x_t - z_t|^2 \right] \leq \frac{C(T)}{\rho}
$$
Consider the simple case $\xi(x, y) = x$. 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:

$$
\begin{align*}
 dx_t &= -\partial_x V(x_t, y_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t \\
 &= -b(x_t) \, dt + e(x_t, y_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t
\end{align*}
$$

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

$$
\forall x, \quad \mathbb{E}_\mu [e(X)|\xi(X) = x] = 0.
$$
Introduce the marginal $\psi_x^\infty(y) = \frac{\psi_\infty(x, y)}{\int \psi_\infty(x, y) \, dy}$. For a well chosen operator $L^x$, we have

$$\int e(x, y) \psi_x^\infty(y) \, dy = 0 \quad \text{and} \quad (L^x)^* \psi_x^\infty = 0.$$  

We thus can solve the Poisson equation $L^x u(x, \cdot) = e(x, \cdot)$.

We have

\[
\begin{align*}
  dz_t &= -b(z_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t \\
  dx_t &= -b(x_t) \, dt + e(x_t, y_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t \\
  &= -b(x_t) \, dt + (L^x_t u)(x_t, y_t) \, dt + \sqrt{2\beta^{-1}} \, dB_t
\end{align*}
\]

Assuming spectral gap $\rho$ on $-L^x$ (ind. of $x$) $\rightarrow$ estimates on $u$, which give

$$\mathbb{E} \left[ \sup_{0 \leq t \leq T} |x_t - z_t|^2 \right] \leq \frac{C(T)}{\rho}$$
Numerical illustration: the tri-atomic molecule

\[ V(X) = \frac{1}{2} k_2 (r_{AB} - \ell_{eq})^2 + \frac{1}{2} k_2 (r_{BC} - \ell_{eq})^2 + k_3 W(\theta_{ABC}), \quad k_2 \gg k_3 \]
We have considered until now the overdamped Langevin equation:

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

Consider now the Langevin equation:

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

Aim:

- build a (tractable) effective dynamics
- show equilibrium consistency
- numerical results

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 \( D(X, P) = P^T \nabla^2 \xi(X) P - \nabla \xi(X)^T \nabla V(X) \).
Building the effective dynamics - 2

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:

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

The equilibrium measure on \((\xi(X), v(X, P))\) is

\[
\exp \left[ -\beta A(\xi_0, v_0) \right] = \int \exp \left[ -\beta \left( V(X) + P^T P/2 \right) \right] \delta_{\xi(X) - \xi_0, v(X, P) = v_0}
\]

which is such that, for any smooth test function \(\Phi\), we have

\[
\int_{\mathbb{R}^n \times \mathbb{R}^n} \Phi(\xi(X), v(X, P)) \, d\mu(X, P) = \int_{\mathbb{R} \times \mathbb{R}} \Phi(\xi_0, v_0) \exp(-\beta A(\xi_0, v_0)) \, d\xi_0 \, dv_0
\]

**Proposition:** The measure \(\exp \left[ -\beta A(\xi_0, v_0) \right] \, d\xi_0 \, dv_0\) is an invariant measure of the effective dynamics.

Under classical assumptions, our effective dynamics is hence ergodic for the correct equilibrium measure.
Practical implementation

We need to compute conditionned averages, such as

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

One possibility is to use the constrained dynamics

\[
\begin{align*}
\frac{dX_t}{dt} &= P_t \, dt, \\
\frac{dP_t}{dt} &= -\nabla V(X_t) \, dt - \gamma P_t \, dt + \sqrt{2\gamma/\beta^{-1}} \, dW_t + \nabla \xi(X_t) \, d\lambda_t, \\
\xi(X_t) &= \xi_0,
\end{align*}
\]

as proposed by [Lelièvre, Rouset and Stoltz 2011], to sample the Gibbs measure conditionned at \( \xi(X) = \xi_0, v(X, P) = 0 \).
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.
Sketch of the proof in the case $X = (x, y)$, $\xi(X) = x$

Fokker-Planck (reference dynamics): $\partial_t \psi = \text{div} \ [\psi \nabla V] + \beta^{-1} \Delta \psi$

Let $\psi_{\text{exact}}(t, x)$ be the law of $\xi(X_t) = x_t$, that is $\psi_{\text{exact}}(t, x) = \int \psi(t, x, y) \, dy$:

$$
\partial_t \psi_{\text{exact}} = \partial_x \left[ \int \psi \partial_x V \, dy \right] + \beta^{-1} \partial_{xx} [\psi_{\text{exact}}] \\
= \partial_x [\tau(t, x) \psi_{\text{exact}}(x)] + \beta^{-1} \partial_{xx} [\psi_{\text{exact}}]
$$

where $\tau$ is the ideal/exact drift: $\tau(t, x) = \int \psi(t, x, y) \partial_x V(x, y) \, dy$. 
Sketch of the proof in the case $X = (x, y)$, $\xi(X) = x$

Fokker-Planck (reference dynamics): $\partial_t \psi = \text{div} \ [\psi \nabla V] + \beta^{-1} \Delta \psi$

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\partial_t \psi_{\text{exact}} = \partial_x \left[ \int \psi \partial_x V \, dy \right] + \beta^{-1} \partial_{xx} [\psi_{\text{exact}}]
= \partial_x [\tau(t, x) \psi_{\text{exact}}(x)] + \beta^{-1} \partial_{xx} [\psi_{\text{exact}}]
$$

where $\tau$ is the ideal/exact drift: $\tau(t, x) = \int \psi(t, x, y) \partial_x V(x, y) \, dy$.

The effective dynamics reads $dz_t = -W'(z_t) \, dt + \sqrt{2/\beta} \, dB_t$, with

$$
W'(z) = \mathbb{E}_\mu [\partial_x V(X) \mid \xi(X) = z] = \int \psi_\infty(x, y) \partial_x V(x, y) \, dy.
$$

The law $\phi_{\text{eff}}$ of $z_t$ satisfies $\partial_t \phi_{\text{eff}} = [W' \phi_{\text{eff}}]' + \beta^{-1} \phi''_{\text{eff}}$. 
Sketch of the proof - 2

\[ E(t) = H(\psi_{\text{exact}}|\phi_{\text{eff}}) = \int_{\mathbb{R}} \ln \left( \frac{\psi_{\text{exact}}(t,x)}{\phi_{\text{eff}}(t,x)} \right) \psi_{\text{exact}}(t,x) \, dx \]

Time derivative of the error:

\[
\frac{dE}{dt} = -\beta^{-1} I(\psi_{\text{exact}}|\phi_{\text{eff}}) + \int_{\mathbb{R}} \psi_{\text{exact}} \partial_x \left( \ln \frac{\psi_{\text{exact}}}{\phi_{\text{eff}}} \right) (W'(x) - \tau(t,x))
\]

\[
\leq -\beta^{-1} I(\psi_{\text{exact}}|\phi_{\text{eff}}) + \frac{1}{2\alpha} \int \psi_{\text{exact}} \left( \partial_x \left( \ln \frac{\psi_{\text{exact}}}{\phi_{\text{eff}}} \right) \right)^2 
\]

\[
\quad + \frac{\alpha}{2} \int \psi_{\text{exact}} (W'(x) - \tau(t,x))^2
\]

\[
= \left( \frac{1}{2\alpha} - \beta^{-1} \right) I(\psi_{\text{exact}}|\phi_{\text{eff}}) + \frac{\alpha}{2} (*) \quad \text{(arbitrary } \alpha)\]

Note that

\[
\tau(t,x) = \int_{\mathbb{R}} \partial_x V(x,y) \psi(t,x,y) \, dy
\]

\[
W'(x) = \int_{\mathbb{R}} \partial_x V(x,y) \psi_\infty(x,y) \, dy
\]
Sketch of the proof - 3

\[ W'(x) - \tau(t, x) = \int \partial_x V(x, y) \nu_1^x(y) \, dy - \int \partial_x V(x, y) \nu_2^{t,x}(y) \, dy \]

\[ = \int (\partial_x V(x, y_1) - \partial_x V(x, y_2)) k^{t,x}(y_1, y_2) \, dy_1 \, dy_2 \]

\[ |W'(x) - \tau(t, x)| \leq \|\partial_{xy} V\|_{L^\infty} \int |y_1 - y_2| k^{t,x}(y_1, y_2) \, dy_1 \, dy_2 \]

with \( \int k^{t,x}(y_1, y_2) \, dy_2 = \nu_1^x(y_1) \) and \( \int k^{t,x}(y_1, y_2) \, dy_1 = \nu_2^{t,x}(y_2) \).
Sketch of the proof - 3

\[ W'(x) - \tau(t, x) = \int \partial_x V(x, y) \nu_1^x(y) \, dy - \int \partial_x V(x, y) \nu_2^{t,x}(y) \, dy \]

\[ = \int (\partial_x V(x, y_1) - \partial_x V(x, y_2)) k^{t,x}(y_1, y_2) \, dy_1 \, dy_2 \]

\[ |W'(x) - \tau(t, x)| \leq \|\partial_{xy} V\|_{L^\infty} \int |y_1 - y_2| k^{t,x}(y_1, y_2) \, dy_1 \, dy_2 \]

with \[ \int k^{t,x}(y_1, y_2) \, dy_2 = \nu_1^x(y_1) \] and \[ \int k^{t,x}(y_1, y_2) \, dy_1 = \nu_2^{t,x}(y_2) \]. Optimize on \[ k^{t,x} \] :

\[ |W'(x) - \tau(t, x)| \leq \|\partial_{xy} V\|_{L^\infty} W_1(\nu_1^x, \nu_2^{t,x}) \quad \text{[Wasserstein distance]} \]

\[ \leq \frac{\|\partial_{xy} V\|_{L^\infty}}{\rho} \sqrt{I(\nu_2^{t,x} | \nu_1^x)} \quad \text{[Talagrand + ISL on } \nu_1^x \text{]} \]

Hence,

\[ (*) = \int \psi_{\text{exact}} (W'(x) - \tau(t, x))^2 \leq \frac{\|\partial_{xy} V\|_{L^\infty}^2}{\rho^2} \int \psi_{\text{exact}} I(\nu_2^{t,x} | \nu_1^x) \leq \frac{\|\partial_{xy} V\|_{L^\infty}^2}{\rho^2} I(\psi | \psi_{\infty}) \]
\[ \frac{dE}{dt} \leq \left( \frac{1}{2\alpha} - \beta^{-1} \right) I(\psi_{\text{exact}}|\phi_{\text{eff}}) + \frac{\alpha}{2} \frac{\|\partial_{xy}V\|_{L^\infty}^2}{\rho^2} I(\psi|\psi_{\infty}) \]

\[ = \left( \frac{1}{2\alpha} - \beta^{-1} \right) I(\psi_{\text{exact}}|\phi_{\text{eff}}) - \frac{\alpha\beta\|\partial_{xy}V\|_{L^\infty}^2}{2\rho^2} \partial_t H(\psi|\psi_{\infty}) \]

Take \(2\alpha = \beta\) to cancel the first term:

\[ \frac{dE}{dt} \leq -\frac{\beta^2\|\partial_{xy}V\|_{L^\infty}^2}{4\rho^2} \partial_t H(\psi|\psi_{\infty}) \]

Integrate in time, with \(E(0) = 0\), and \(H(\psi(t)|\psi_{\infty}) \geq 0\):

\[ E(t) \leq \frac{\beta^2\|\partial_{xy}V\|_{L^\infty}^2}{4\rho^2} H(\psi(t = 0)|\psi_{\infty}) \]

We hence need \(\|\partial_{xy}V\|_{L^\infty} = \|\nabla_{\Sigma_z} F\|_{L^\infty} < +\infty\) and ISL on \(\nu_{1}^{x}(dy) = \psi_{\infty}(x, y) \, dy\), e.g. marginals of \(d\mu\) at fixed \(\xi(X)\).
Conclusions

- We have proposed a “natural” way to obtain a closed equation on $\xi(X_t)$.
- Encouraging numerical results and rigorous error bounds.

If possible, better to choose $\xi$ orthogonal to fast directions.

More generally, once the 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 $A'(z)$.
- once $A'(z)$, $b(z)$ and $\sigma(z)$ have been computed, safer to compute dynamical quantities using $b(z)$ and $\sigma(z)$ than using $A'(z)$.

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