

Effective dynamics using conditional expectations

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Classical n -body system

Atomistic system whose position is given by $X = (X^1, \dots, X^n) \in \mathbb{R}^n$

Potential energy: $V(X)$, which contains all the physics of the system

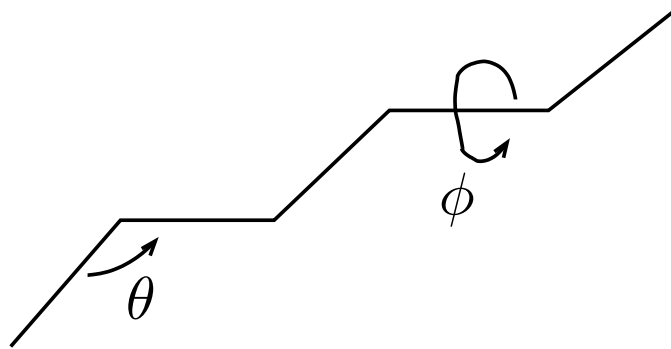
A standard task in molecular dynamics is to compute **thermodynamical averages** wrt Gibbs measure:

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

with $\beta = 1/(k_B T)$ and $Z = \int_{\mathbb{R}^n} \exp(-\beta V(X)) dX$.

A simple example

- Chain-like molecules (biological molecules, polymers, ...):



$$V(X) = \sum_i V_2 (X^{i+1} - X^i) + \sum_i V_3(\theta_i) + \sum_i V_4(\cos \phi_i)$$

with

$$V_2 (X^{i+1} - X^i) = \frac{k_2}{2} (|X^{i+1} - X^i| - d_{eq})^2, \quad V_3(\theta_i) = \frac{k_3}{2} (\theta_i - \theta_{eq})^2$$

- end-to-end distance $\langle |X^n - X^1| \rangle$

Other examples: pressure in a liquid, ...

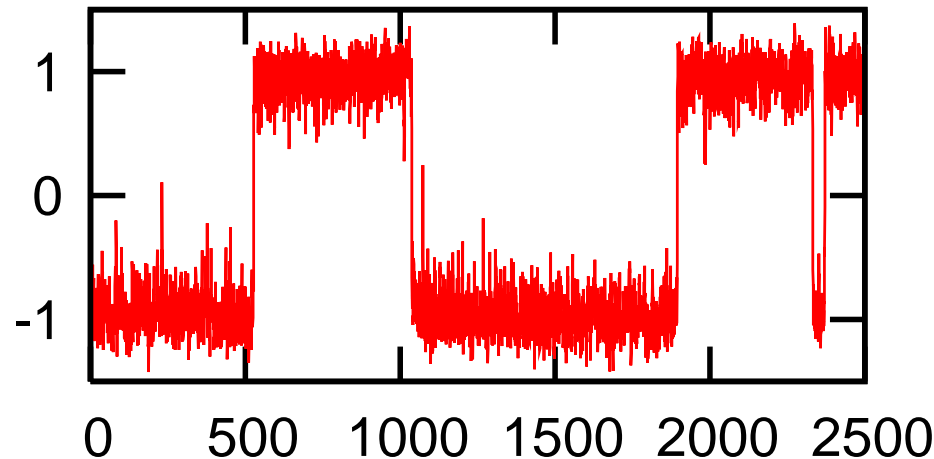
Consider the **dynamics** (overdamped Langevin equation)

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

which is ergodic for $d\mu$: for a.a. initial conditions X_0 , and a.s.,

$$\forall \text{ smooth } \phi, \quad \frac{1}{T} \int_0^T \phi(X_t) dt = \int \phi(X) d\mu + O\left(\frac{1}{\sqrt{T}}\right).$$

In practice, the constant in the $O(\cdot)$ may be big (**metastability**). Reduced description of the system, that still includes some dynamical information?



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

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

- **preservation of equilibrium properties:**

when X is distributed according to $d\mu$, then $\xi(X)$ distributed according to $\exp(-\beta A(z)) dz$:

$$\forall \text{ smooth } \phi_r, \quad \int_{\mathbb{R}^n} \phi_r(\xi(X)) d\mu = \int_{\mathbb{R}} \phi_r(z) \exp(-\beta A(z)) dz$$

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

- **estimation of the distance between z_t and $\xi(X_t)$.**

Some related works

- Mori-Zwanzig projection formalism
- Normal modes decomposition
- system reduction in the framework on SDEs (E, Vanden-Eijnden, ...):

$$\begin{aligned} dx_t &= f(x_t, y_t) dt + \sqrt{2\beta^{-1}} dB_t^1 \\ dy_t &= \frac{1}{\varepsilon} g(x_t, y_t) dt + \sqrt{\frac{2\beta^{-1}}{\varepsilon}} dB_t^2 \end{aligned}$$

If x_t is held fixed, then y_t is ergodic w.r.t. a measure independent of ε .

Our framework:

- cartesian coordinates not adapted to slow/fast splitting.
- even if $\xi(x, y) = x$, the fast dynamics is different:

$$\begin{aligned} dx_t &= f(x_t, y_t) dt + \sqrt{2\beta^{-1}} dB_t^1 \\ dy_t &= \frac{1}{\varepsilon} g(x_t, y_t) dt + \sqrt{2\beta^{-1}} dB_t^2 \end{aligned}$$

Convergence to equilibrium: Fokker-Planck equation

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

The pdf $\psi(t, X)$ of X_t satisfies the **Fokker-Planck equation**:

$$\partial_t \psi = \operatorname{div} (\psi \nabla V) + \beta^{-1} \Delta \psi$$

Introduce the **equilibrium density**

$$\psi_\infty(X) = Z^{-1} \exp(-\beta V(X)), \quad d\mu = \psi_\infty(X) dX$$

We have $\nabla \psi_\infty = -\beta \psi_\infty \nabla V$. Hence the Fokker-Planck equation reads

$$\partial_t \psi = \beta^{-1} \operatorname{div} \left[\psi_\infty \nabla \left(\frac{\psi}{\psi_\infty} \right) \right]$$

We wish to prove that $\psi(t, \cdot) \rightarrow \psi_\infty(\cdot)$ as $t \rightarrow \infty$. Relative entropy argument.

Convergence to equilibrium: relative entropy

Introduce $e(t) = H(\psi|\psi_\infty) := \int_{\mathbb{R}^n} \ln \left(\frac{\psi(t, x)}{\psi_\infty(x)} \right) \psi(t, x) dx$. Then

$$\begin{aligned} \frac{de}{dt} &= \int \ln \left(\frac{\psi}{\psi_\infty} \right) \partial_t \psi + \frac{\psi_\infty}{\psi} \frac{\partial_t \psi}{\psi_\infty} \psi \\ &= \int \ln \left(\frac{\psi}{\psi_\infty} \right) \beta^{-1} \mathbf{div} \left[\psi_\infty \nabla \left(\frac{\psi}{\psi_\infty} \right) \right] \\ &= -\beta^{-1} \int \nabla \left[\ln \left(\frac{\psi}{\psi_\infty} \right) \right] \psi_\infty \nabla \left(\frac{\psi}{\psi_\infty} \right) \\ &= -\beta^{-1} \int \left| \nabla \left[\ln \left(\frac{\psi}{\psi_\infty} \right) \right] \right|^2 \psi =: -\beta^{-1} I(\psi|\psi_\infty) \end{aligned}$$

Assume that ψ_∞ satisfies a **Log-Sobolev Inequality (LSI)**: there exists $\rho > 0$ such that, for any probability measure of density ν ,

$$H(\nu|\psi_\infty) \leq (2\rho)^{-1} I(\nu|\psi_\infty)$$

Then $\frac{de}{dt} \leq -2\rho\beta^{-1}e(t)$, hence $e(t) \rightarrow 0$.

- Construction of an effective dynamics
- Assessment of its quality in terms of marginals
- Pathwise convergence in a specific case
- Numerical examples

From the dynamics on X_t , we obtain

$$\begin{aligned}d\xi(X_t) &= \nabla\xi(X_t) \cdot dX_t + \beta^{-1} \Delta\xi(X_t) dt \\ &= (-\nabla V \cdot \nabla\xi + \beta^{-1} \Delta\xi)(X_t) dt + \sqrt{2\beta^{-1}} \nabla\xi(X_t) \cdot dW_t \\ &= (-\nabla V \cdot \nabla\xi + \beta^{-1} \Delta\xi)(X_t) dt + \sqrt{2\beta^{-1}} |\nabla\xi|(X_t) dB_t\end{aligned}$$

where $dB_t = \frac{\nabla\xi(X_t) \cdot dW_t}{|\nabla\xi|(X_t)}$: B_t is a 1D standard noise.

$$\begin{aligned}\tilde{b}(t, z) &:= \mathbb{E} [(-\nabla V \cdot \nabla\xi + \beta^{-1} \Delta\xi)(X_t) \mid \xi(X_t) = z] \\ \tilde{\sigma}^2(t, z) &:= \mathbb{E} [|\nabla\xi|^2(X_t) \mid \xi(X_t) = z]\end{aligned}$$

and consider

$$d\tilde{z}_t = \tilde{b}(t, \tilde{z}_t) dt + \sqrt{2\beta^{-1}} \tilde{\sigma}(t, \tilde{z}_t) dB_t, \quad \tilde{z}_0 = \xi(X_0)$$

Then, for any t , the law of \tilde{z}_t is equal to the law of $\xi(X_t)$ (Gyongy 1986)

But $\tilde{b}(t, z)$ and $\tilde{\sigma}(t, z)$ are **extremely difficult** to compute ...

Need for **approximation**:

$$\begin{aligned}\tilde{b}(t, z) &= \mathbb{E} [(-\nabla V \cdot \nabla \xi + \beta^{-1} \Delta \xi) (X_t) \mid \xi(X_t) = z] \\ b(z) &:= \mathbb{E}_\mu [(-\nabla V \cdot \nabla \xi + \beta^{-1} \Delta \xi) (X) \mid \xi(X) = z]\end{aligned}$$

Idea: $\tilde{b}(t, z) \approx b(z)$ 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 Σ_z .

Consider the **effective dynamics**

$$dz_t = b(z_t) dt + \sqrt{2\beta^{-1}} \sigma(z_t) dB_t, \quad z_0 = \xi(X_0)$$

with $\sigma^2(z) := \mathbb{E}_\mu [|\nabla \xi|^2(X) \mid \xi(X) = z]$.

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

- In the general case, obtain estimates between the law of z_t and the law of $\xi(X_t)$, for any t , in terms of relative entropy.
- the potential V is frequently of the form

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

- rough dependence of the above estimate in ε ?
- exploit this structure to properly define $\xi(X)$?
- consider a more restrictive case to obtain stronger results (pathwise convergence):

$$\mathbb{E} \left[\sup_{t \in (0, T)} |\xi(X_t) - z_t|^2 \right].$$

An entropy convergence result

$$dX_t = -\nabla V(X_t) dt + \sqrt{2\beta^{-1}} dW_t, \quad \text{pdf } \psi(t, X)$$

The pdf of $\xi(X_t)$ is

$$\bar{\psi}(t, z) = \int_{\mathbb{R}^n} \psi(t, X) \delta(\xi(X) - z)$$

On the other hand, we have introduced the effective dynamics

$$dz_t = b(z_t) dt + \sqrt{2\beta^{-1}} \sigma(z_t) dB_t, \quad z_0 = \xi(X_0)$$

Let $\phi(t, z)$ be the pdf of z_t . Introduce the relative entropy:

$$E(t) := H(\bar{\psi}|\phi) = \int_{\mathbb{R}} \ln \left(\frac{\bar{\psi}(t, z)}{\phi(t, z)} \right) \bar{\psi}(t, z) dz.$$

We would like $\bar{\psi} \approx \phi$, 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 conditioned probability measures $d\mu_z$ satisfy a log-Sobolev inequality with a large constant ρ (uniform in z). They can be **quickly sampled**.
- assume that the coupling between the dynamics of $\xi(X_t)$ and the dynamics in Σ_z is **weak**:

$$\text{At equilibrium, } \xi \sim \exp(-\beta A(z)) dz \text{ with } A'(z) = \int_{\Sigma_z} F(X) d\mu_z$$

We assume that $\|\nabla_{\Sigma_z} F\|_{L^\infty} \leq \kappa$.

When $\xi(x, y) = x$, $\nabla_{\Sigma_z} F = \partial_{xy} V$: weak-coupling between x and y .

- assume that $|\nabla \xi|$ is **close to a constant** on each Σ_z , e.g.

$$\lambda = \left\| \frac{|\nabla \xi|^2(X) - \sigma^2(\xi(X))}{\sigma^2(\xi(X))} \right\|_{L^\infty} < +\infty$$

A bounded entropy result

$$E(t) := H(\bar{\psi}|\phi) = \int_{\mathbb{R}} \ln \left(\frac{\bar{\psi}(t, z)}{\phi(t, z)} \right) \bar{\psi}(t, z) dz.$$

Under the above assumptions, for all $t \geq 0$,

$$E(t) \leq \frac{\|\nabla \xi\|_{L^\infty}^2}{4} \left(\lambda + \frac{\beta^2 \kappa^2}{\rho^2} \right) H(\psi(0, \cdot) | \psi_\infty)$$

Hence, if ξ is such that

- ρ is large (**strong mixing** in Σ_z),
- κ is small (**small coupling** between dynamics in Σ_z and on z_t),
- λ is small ($|\nabla \xi|$ is **close to a constant** on each Σ_z),

then the effective dynamics z_t obtained by conditional expectations is close to the real dynamics $\xi(X_t)$ in the sense of relative entropy.

Standard expression in MD: $V_\varepsilon(X) = V_0(X) + \frac{1}{\varepsilon}q^2(X)$

- LSI estimate for the measure μ restricted on $\{X; \xi(X) = z\}$:
This measure essentially looks like a gaussian measure of variance $O(\varepsilon)$.
Such gaussian measures satisfy a LSI with $\rho_\varepsilon = O(1/\varepsilon)$.

- Mean-force $F(X)$ estimation: $A'(z) = \int_{\Sigma_z} F(X) d\mu_z$, $\kappa_\varepsilon = \|\nabla_{\Sigma_z} F\|_{L^\infty}$?

$$\begin{aligned} F(X) &= \frac{\nabla V \cdot \nabla \xi}{|\nabla \xi|^2} - \beta^{-1} \operatorname{div} \left(\frac{\nabla \xi}{|\nabla \xi|^2} \right) \\ &= \frac{2q(X)}{\varepsilon} \frac{\nabla q \cdot \nabla \xi}{|\nabla \xi|^2} + O(1), \quad \text{assuming that } \nabla \xi = O(1). \end{aligned}$$

If $\nabla \xi \cdot \nabla q = 0$, then $\kappa_\varepsilon = O(1)$, otherwise $\kappa_\varepsilon = O(1/\varepsilon)$.

$$E(t) \leq \frac{\|\nabla\xi\|_{L^\infty}^2}{4} \left(\lambda + \frac{\beta^2 \kappa^2}{\rho^2} \right) H(\psi(0, \cdot) | \psi_\infty)$$

where λ measures how much $|\nabla\xi|$ deviates from a constant on Σ_z .

$$\rho_\varepsilon = O(1/\varepsilon).$$

- If $\nabla\xi \cdot \nabla q = 0$, then $\kappa_\varepsilon = O(1)$, hence $\kappa_\varepsilon/\rho_\varepsilon = O(\varepsilon)$, and “good” estimate. In the absence of λ ,

$$E(t) = O(\varepsilon^2).$$

- If $\nabla\xi \cdot \nabla q \neq 0$, then $\kappa_\varepsilon = O(1/\varepsilon)$, hence $\kappa_\varepsilon/\rho_\varepsilon = O(1)$, and

$$E(t) = O(1),$$

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

Can we get stronger results?

A commutative diagram?

$$V_\varepsilon(X) = V_0(X) + \frac{1}{\varepsilon} q^2(X), \quad X \in \mathbb{R}^2$$

2D dynamics on X_t^ε

$\xrightarrow[\varepsilon \rightarrow 0]{\text{[pathwise cv]}}$

1D limit dynamics on \bar{X}_t



Itô computation



Nonclosed dynamics on $\xi(X_t^\varepsilon)$

One-to-one change of variable



$$\xi_t = \xi(\bar{X}_t)$$



Conditional expectations



Dynamics on $z_t^\varepsilon \approx \xi(X_t^\varepsilon)$

$\xrightarrow[\varepsilon \rightarrow 0]{?}$

Dynamics on ξ_t

$$dz_t^\varepsilon = b_\varepsilon(z_t^\varepsilon) dt + \sigma_\varepsilon(z_t^\varepsilon) dB_t$$

Sufficient conditions for the two dynamics to be identical:

$$\nabla\xi(X) \cdot \nabla q(X) = 0 \text{ for all } X \in \mathbb{R}^2$$

Recall $V_\varepsilon(X) = V_0(X) + \frac{1}{\varepsilon}q^2(X)$, hence the limit dynamics lives on

$$\mathcal{M} = \{X \in \mathbb{R}^2; q(X) = 0\}.$$

We ask that the parametrization ξ of \mathcal{M} is orthogonal to the direction ∇q where sampling is fast.

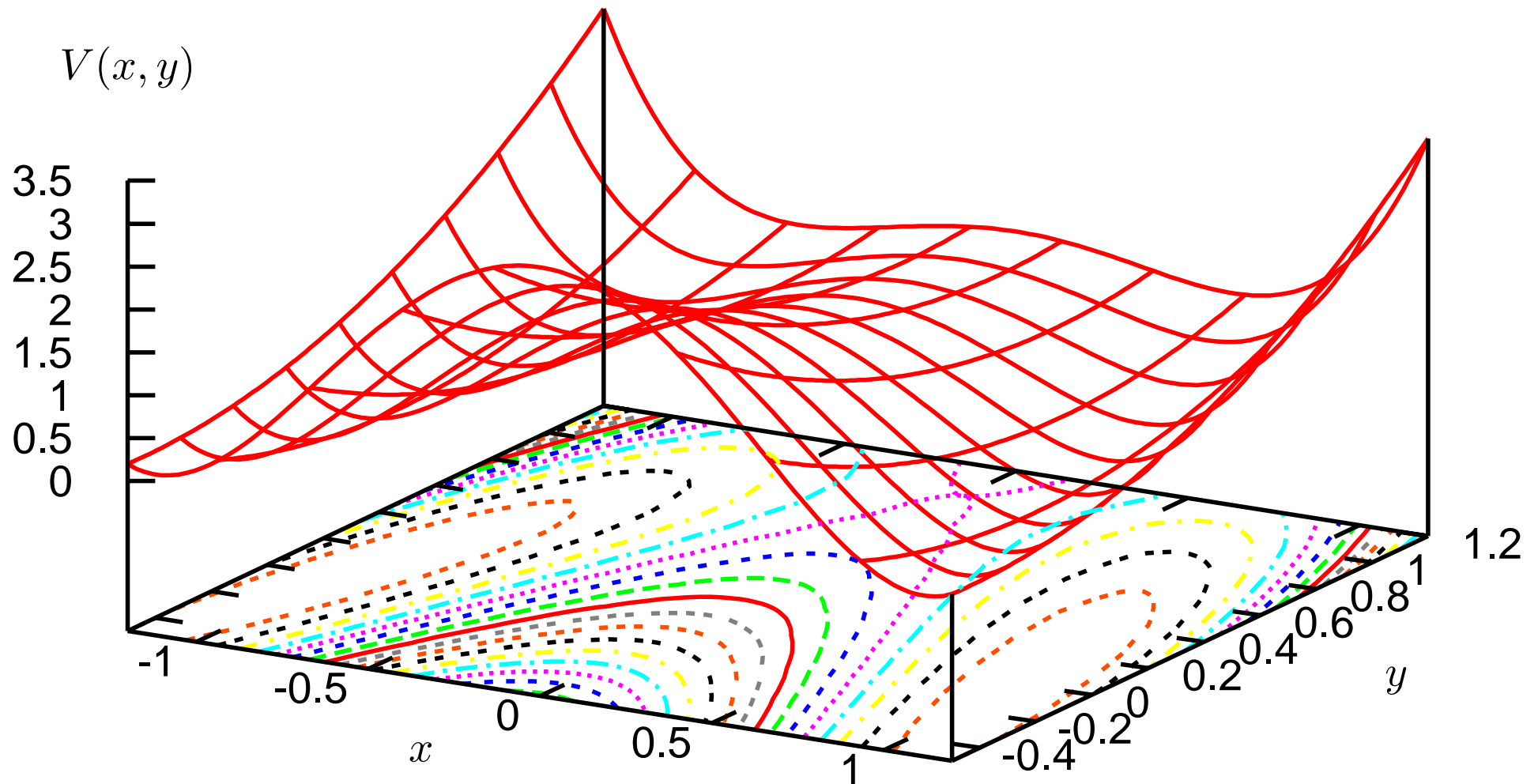
Hence, if the orthogonality condition holds:

- our effective dynamics is a good approximation of the true dynamics $\xi(X_t)$, on finite time intervals ($X \in \mathbb{R}^2$).
- good entropy estimate ($X \in \mathbb{R}^n$).

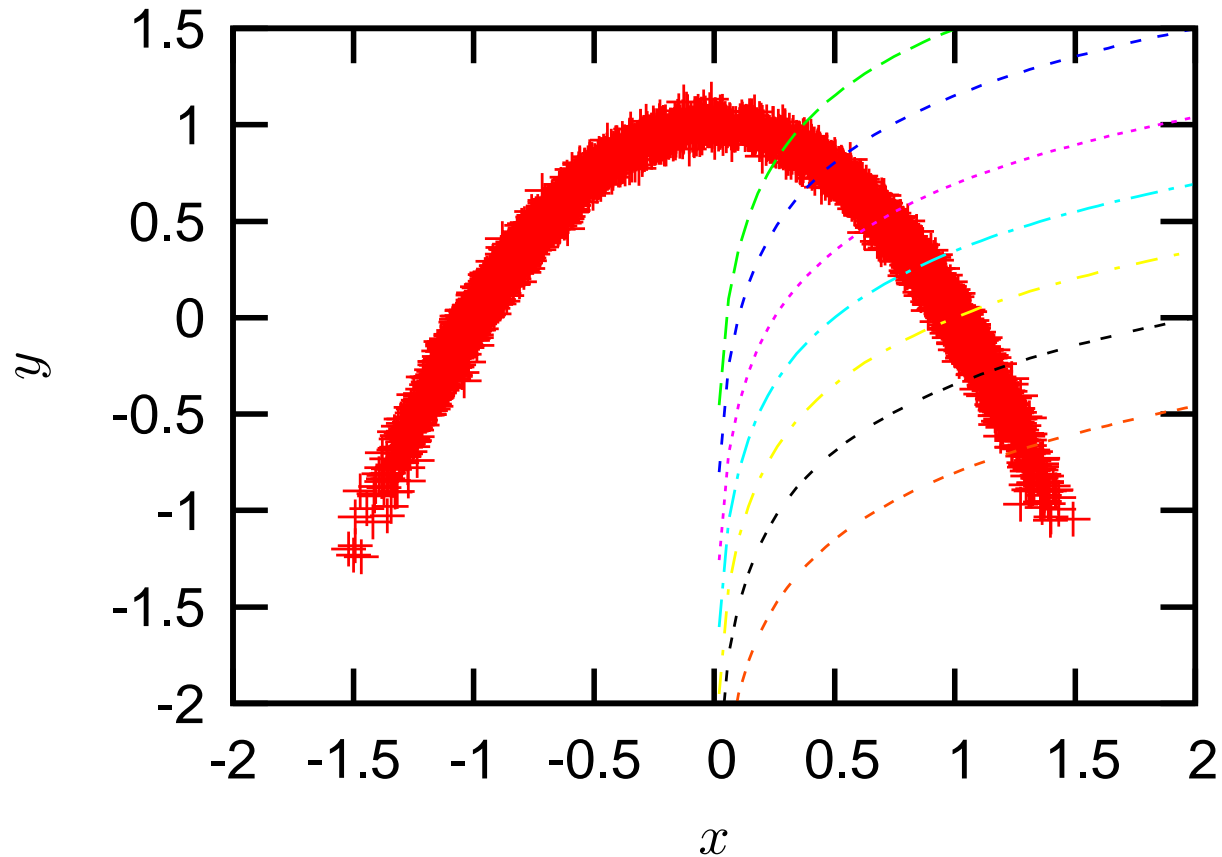
A toy example

$$V(x, y) = (x^2 - 1)^2 + (y + x^2 - 1)^2$$

Two wells $V(\pm 1, 0) = 0$, one saddle point $V(0, 1) = 1$.



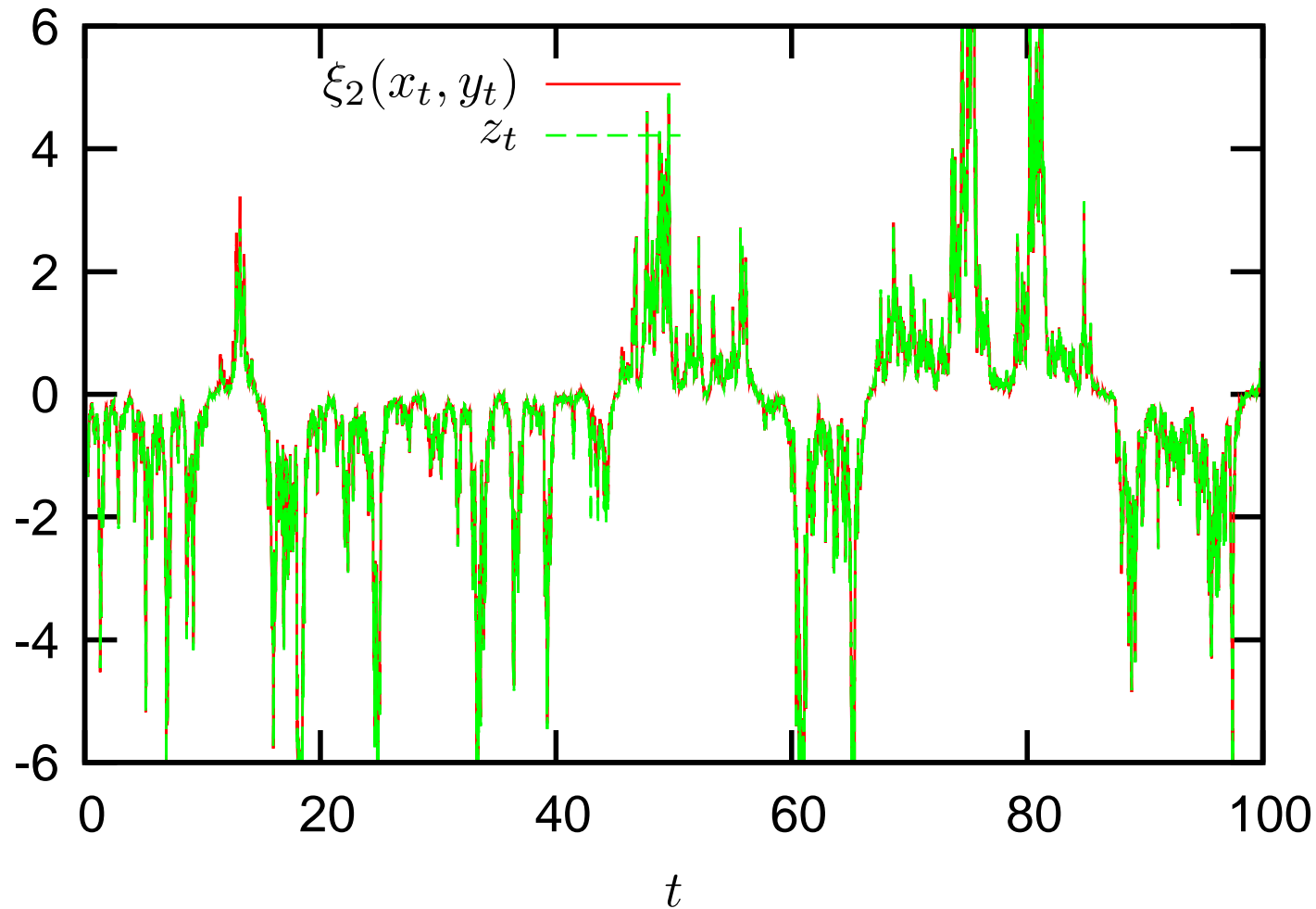
A numerical 2D example: $\varepsilon = 0.01$, $\beta = 3$



$$V_\varepsilon(x, y) = (x^2 - 1)^2 + \frac{1}{\varepsilon}(x^2 + y - 1)^2$$

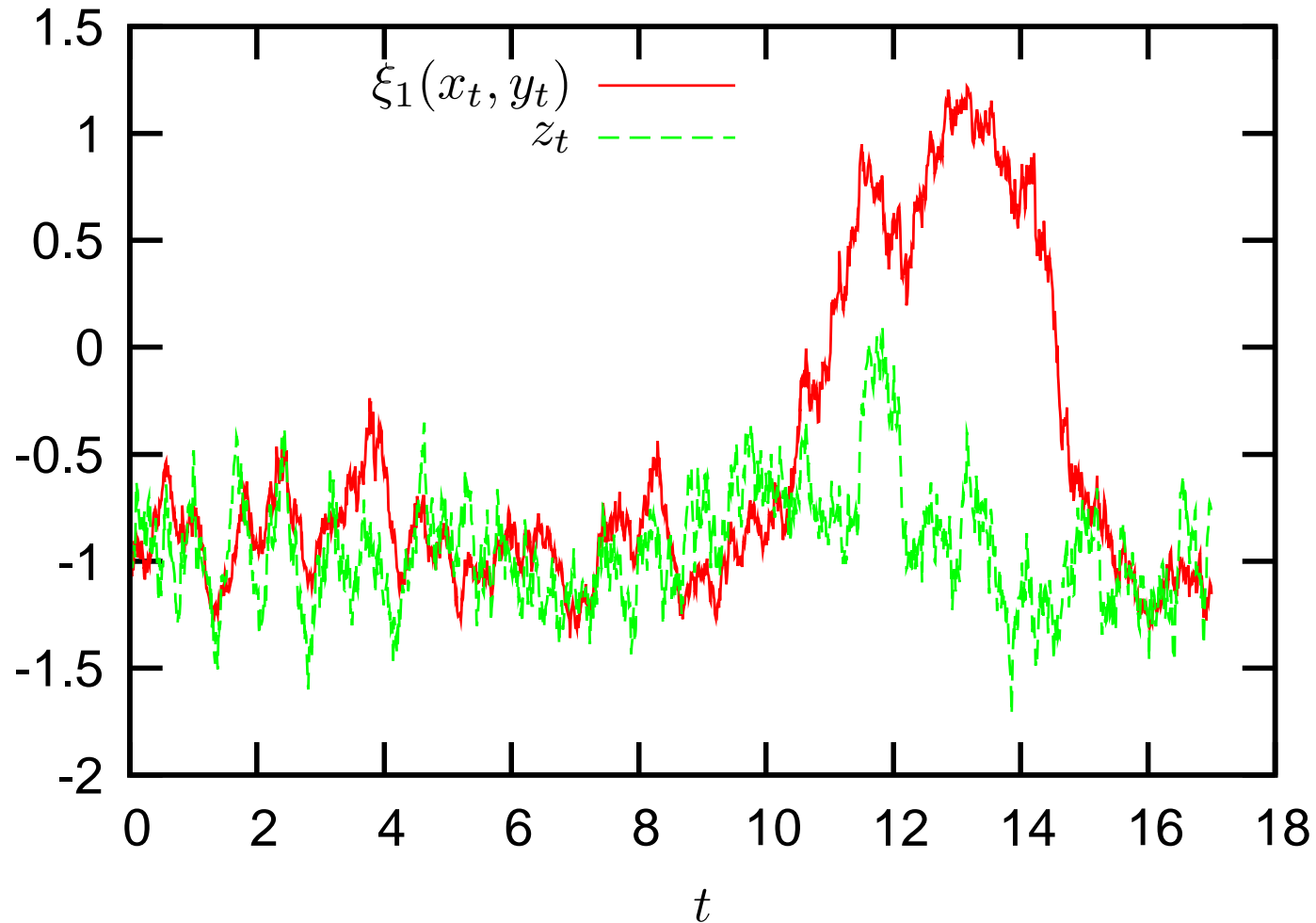
Two possible reaction coordinates: $\xi_1(x, y) = x$, $\xi_2(x, y) = x \exp(-2y)$

Effective dynamics with the second reaction coordinate



$$q(x, y) = x^2 + y - 1, \quad \xi_2(x, y) = x \exp(-2y) : \quad \nabla \xi_2 \cdot \nabla q = 0$$

Effective dynamics with the first reaction coordinate



$$q(x, y) = x^2 + y - 1, \quad \xi_1(x, y) = x : \quad \nabla \xi_1 \cdot \nabla q \neq 0$$

Free energy barriers are often associated with residence times in the wells.

Is our effective dynamics the same as

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

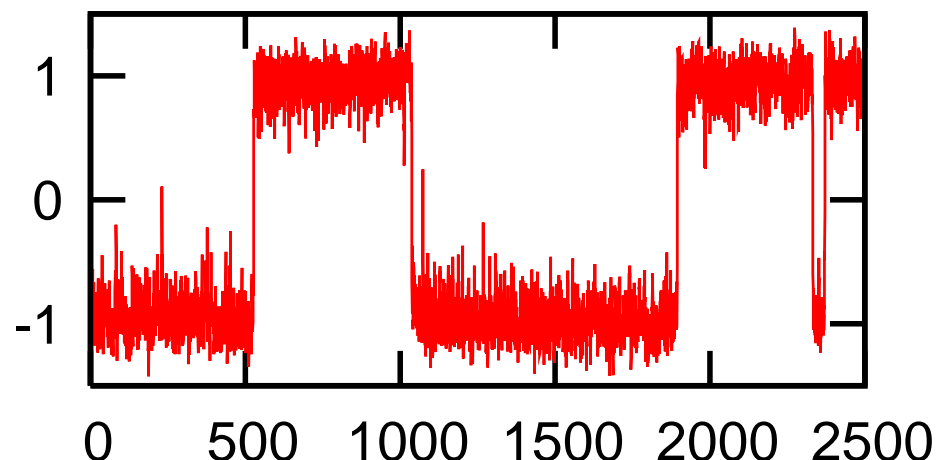
e.g. the dynamics driven by the free energy A associated with the reaction coordinate $\xi(X)$?

$$\text{Recall } \sigma^2(z) = \mathbb{E}_\mu [|\nabla\xi|^2(X) \mid \xi(X) = z]$$

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

- 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 $b(z) \neq -A'(z)$, even up to a multiplicative constant.

Approximation of residence times ($\varepsilon = 0.01, \beta = 3$)



Reac. Coord.	Full dyn.	Reduced dynamics
$\xi_2(x, y) = x \exp(-2y)$	32.5 ± 0.5	32.7 ± 0.5 (Eff. dyn.)
$\xi_2(x, y) = x \exp(-2y)$	32.5 ± 0.5	6.4 ± 0.3 (based on $A(\xi_2)$)
$\xi_1(x, y) = x$	31.6 ± 0.5	24.4 ± 0.4

If $\xi_1(x, y) = x$, effective dynamics \equiv dynamics driven by free energy.

It seems that residence times are well approximated by the reduced dynamics when the “good” reaction coordinate and the “good” dynamics are used.

- We have proposed a “natural” way to obtain a closed equation on $\xi(X_t)$, by **conditional expectations** (natural extension of the Gyongy result).
- In some cases, we are able to estimate the **accuracy** of this effective equation.
- Encouraging **numerical results** on some simple cases.

F. Legoll, T. Lelièvre, *Effective dynamics using conditional expectations*,
Arxiv preprint 0906.4865