A Macroscopically Consistent Reactive Langevin Dynamics Model

Samuel A. Isaacson Qianhan Liu Konstantinos Spiliopoulos Chen Yao

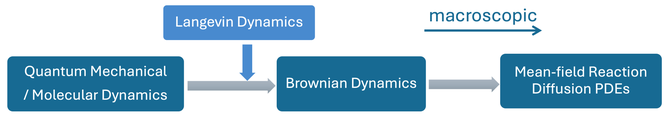
Department of Mathematics and Statistics, Boston University

Introduction

An Introductive Example

Consider two substrates A and B, which move freely in a cell and can combine to form a complex C. How can we model such a system?

- Model the particle movements: $\dot{X}_t = \sqrt{2D}\dot{W}_t$ (Brownian Dynamics / Diffusion).
- Model the binding process $\mathrm{A} + \mathrm{B} \to \mathrm{C}$:
  rate function $K(x_1, x_2)$: probability per time the binding happens.
  placement density $m(x_3|x_1, x_2)$: placing C at x_3 given A, B are at x_1, x_2.



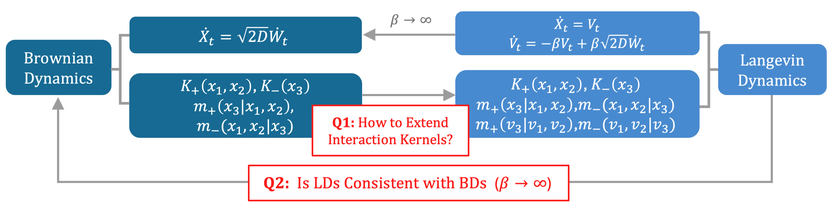
From Brownian Dynamics to Langevin Dynamics

Incorporating inertial forces $(m\dot{V}_t)$ is essential for accurately modeling a variety of physical systems of interacting particles. To account for inertial forces, we use Langevin Dynamics (LDs) to describe random movements of particles, i.e.

$$\dot{X}_t = V_t, \quad \dot{V}_t = -\beta V_t + \beta\sqrt{2D}\dot{W}_t,$$

where β is the friction constant and D is the diffusion constant.

Our Targets - Answer Two Key Questions



Main Contributions

1. Deriving novel reactive interaction kernels for Langevin Dynamics models which are consistent with detailed balance, and with commonly used kernels in the over-damped (high-friction/small-mass) limit.
2. Showing the resulting Langevin Dynamics limit to the Brownian Dynamics in the over-damped limit.

Reactive Interaction Kernels

In Brownian and Langevin Dynamics, interactions between different particle species are characterized by reaction rate functions and placement densities of positions x_i and velocities v_i. To illustrate these models, let's consider the reaction $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C}$.

Reaction Rate Function

- $K_+(x_1, x_2)$: probability density per time that an A at x_1 binds with a B at x_2.
- $K_-(x_3)$: probability density per time that a C particle will unbind at x_3.

$$K_+(x_1, x_2) = \lambda_+ \mathbb{1}_{[0,\varepsilon]}(|x_1 - x_2|), \qquad K_-(x_3) = \lambda_-.$$

Placement density of Positions

- $m_+(x_3|x_1, x_2)$: the probability density for placing a product particle C at x_3 given the reactants A and B are located at x_1 and x_2 respectively.

$$m_+(x_3|x_1, x_2) = \delta(x_3 - (\alpha x_1 + (1-\alpha)x_2)).$$

- $m_-(x_1, x_2|x_3)$: the probability density for placing unbound particles A and B at x_1 and x_2 respectively given the reactant particle C at x_3.

$$m_-(x_1, x_2|x_3) = \frac{1}{|B_\varepsilon|}\mathbb{1}_{[0,\varepsilon]}(|x_1 - x_2|)\delta(x_3 - (\alpha x_1 + (1-\alpha)x_2)).$$

Placement density of Velocities

- $m_+(v_3|v_1, v_2)$: the probability density of assigning velocity v_3 to the product C, given that reactants A and B have velocities v_1 and v_2 respectively.

$$m_+(v_3|v_1, v_2) = \delta\left(v_3 - \frac{m_1 v_1 + m_2 v_2}{m_3}\right).$$

- $m_-(v_1, v_2|v_3)$: the probability density of assigning velocities v_1 and v_2 to particles A and B respectively, given the reactant C has the velocity v_3.

$$m_-(v_1, v_2|v_3) = \delta\left(v_3 - \tfrac{(m_1 v_1 + m_2 v_2)}{m_3}\right) \times \mathcal{G}_d(v_1 - v_2; (D_1\beta_1 + D_2\beta_2)\mathrm{I}_d).$$

Remark: Other reaction rate functions and displacement densities for $\mathrm{A} \rightleftharpoons \mathrm{B}$ and $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C} + \mathrm{D}$ are given in the paper [1].

Langevin Dynamics Converge to Brownian Dynamics in the Overdampled Limit

For simplicity, here we consider a system with either a particle pair (A, B) or a single C, undergoing the reversible reaction $\mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{C}$. A general derivation for multi-particle systems with generic reversible reactions yielding the same conclusion is available in the paper for interested readers.

Kolmogorov Forward Equation

Let's define a *state* of a particle as $\xi_i = (x_i, v_i)$. Denote $p_{12}(\xi_1, \xi_2, t)$ as the probability that A and B are at states ξ_1 and ξ_2 at time t. $p_3(\xi_3, t)$ represents the probability that C is at ξ_3 at t. The evolution of p_{12} and p_3 satisfy the following *Kolmogorov forward equation*

$$\begin{aligned}\frac{\partial p_{12}}{\partial t} &= \sum_{i=1}^{2}\mathcal{L}_i p_{12} - K_+(x_1, x_2)p_{12}(\xi_1, \xi_2, t) + \int_{\Omega\times\mathbb{R}^d} p_3(\xi_3, t)K_-(x_3)m_-^\beta(\xi_1, \xi_2|\xi_3)\,d\xi_3,\\ \frac{\partial p_3}{\partial t} &= \mathcal{L}_3 p_3 - K_-(x_3)p_3(\xi_3, t) + \int_{(\Omega\times\mathbb{R}^d)^2} p_{12}(\xi_1, \xi_2, t)K_+(x_1, x_2)m_+^\beta(\xi_3|\xi_1, \xi_2)\,d\xi_1\,d\xi_2,\end{aligned} \tag{1}$$

where $m_+^\beta(\xi_3|\xi_1, \xi_2) = m_+^\beta(x_3|x_1, x_2)m_+^\beta(v_3|v_1, v_2)$ and the transport operator $\mathcal{L}$ is

$$\mathcal{L}_i = \beta_i\nabla_{v_i}\cdot[v_i + \beta_i D_i\nabla_{v_i}] - v_i\cdot\nabla_{x_i}.$$

Detailed Balance Relation

We assume designed interaction functions satisfy the detailed balance relation

$$K_+(x_1, x_2)m_+^\beta(\xi_3|\xi_1, \xi_2)\bar{p}_{12}(\xi_1, \xi_2) = K_-(x_3)m_-^\beta(\xi_1, \xi_2|\xi_3)\bar{p}_3(\xi_3), \tag{2}$$

where $\bar{p}_{12}(\xi_1, \xi_2)$ and $\bar{p}_3(\xi_3)$ are equilibrium solutions.

Asymptotic Expansion and Term Balance

Substitute the following asymptotic expansions of p_{12} and p_3 as $\beta \uparrow \infty$ into the Kolmogorov forward equations

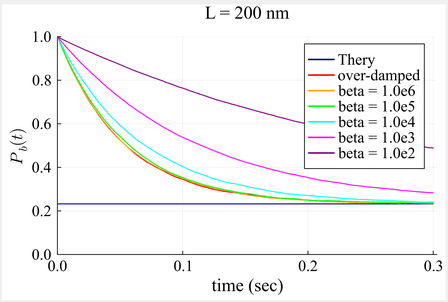
$$\begin{aligned}p_{12}(\xi_1, \xi_2, t) &\sim p_{12}^{(0)}(\xi_1, \xi_2, t) + \tfrac{1}{\sqrt{\beta}}p_{12}^{(1)}(\xi_1, \xi_2, t) + \tfrac{1}{\beta}p_{12}^{(2)}(\xi_1, \xi_2, t) + \ldots,\\ p_3(\xi_3, t) &\sim p_3^{(0)}(\xi_3, t) + \tfrac{1}{\sqrt{\beta}}p_3^{(1)}(\xi_3, t) + \tfrac{1}{\beta}p_3^{(2)}(\xi_3, t) + \ldots.\end{aligned}$$

Balancing terms with order $O(\beta)$, $O(\sqrt{\beta})$, and $O(1)$, and solve equations, we get

$$\begin{aligned}\frac{\partial g_{12}}{\partial t} &= (D_1\Delta_{x_1} + D_2\Delta_{x_2})g_{12} - K_+(x_1, x_2)g_{12} + \int_{\mathbb{R}^d} K_-(x_3)m_-(x_1, x_2|x_3)g_3(x_3, t)\,dx_3,\\ \frac{\partial g_3}{\partial t} &= D_3\Delta_{x_3}g_3 - K_-(x_3)g_3 + \int_{\Omega^2} K_+(x_1, x_2)m_+(x_3|x_1, x_2)g_{12}(x_1, x_2, t)\,dx_1\,dx_2,\end{aligned}$$

where $g(x, t) = \int p^{(0)}(x, v, t)dv$. **This implies the overdamped limits of Langevin Dynamics models are consistent with the corresponding Brownian Dynamics models.**

Numerical Simulation



(1) Convergence of Langevin to Browian Dynamics as $\beta \uparrow \infty$ ("overdamped").
(2) Convergence of reactive Langevin and Brownian Dynamics to the stable-state of well-mixed CME model ("Theory") which is equal to 0.2323 in this example.

[1] Isaacson, S. A., Liu, Q., Spiliopoulos, K., & Yao, C. A Macroscopically Consistent Reactive Langevin Dynamics Model. Preprint submitted to arXiv (2025)