Error estimates in molecular dynamics

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Outline

Some elements of statistical physics

- Microscopic description of physical systems
- Macroscopic description: average properties

Practical computation of static properties

- Ergodic averages using Langevin dynamics
- Central limit theorem and statistical error
- Bias (time step discretization, finite time sampling)

Transport coefficients

- Linear response of nonequilibrium dynamics
- Error estimates

General references (1)

- Computational Statistical Physics
  - D. Frenkel and B. Smit, *Understanding Molecular Simulation, From Algorithms to Applications* (2002)
  - M. Tuckerman, *Statistical Mechanics: Theory and Molecular Simulation* (2010)
  - M. P. Allen and D. J. Tildesley, *Computer simulation of liquids* (2017)
  - D. C. Rapaport, *The Art of Molecular Dynamics Simulations* (1995)
  - T. Schlick, *Molecular Modeling and Simulation* (2002)

- Computational Statistics [my personal references... many more out there!]
  - J. Liu, *Monte Carlo Strategies in Scientific Computing*, Springer, 2008
  - W. R. Gilks, S. Richardson and D. J. Spiegelhalter (eds), *Markov Chain Monte Carlo in Practice* (Chapman & Hall, 1996)

- Machine learning and sampling
  - C. Bishop, *Pattern Recognition and Machine Learning* (Springer, 2006)
  - K.P. Murphy, *Probabilistic Machine Learning: An Introduction* (MIT Press, 2022)

General references (2)

- Sampling the canonical measure
  - L. Rey-Bellet, Ergodic properties of Markov processes, *Lecture Notes in Mathematics*, **1881** 1–39 (2006)
  - E. Cancès, F. Legoll and G. Stoltz, Theoretical and numerical comparison of some sampling methods, *Math. Model. Numer. Anal.* **41**(2) (2007) 351-390
  - T. Lelièvre, M. Rousset and G. Stoltz, *Free Energy Computations: A Mathematical Perspective* (Imperial College Press, 2010)
  - B. Leimkuhler and C. Matthews, *Molecular Dynamics: With Deterministic and Stochastic Numerical Methods* (Springer, 2015).
  - T. Lelièvre and G. Stoltz, Partial differential equations and stochastic methods in molecular dynamics, *Acta Numerica* **25**, 681-880 (2016)

- Convergence of Markov chains
  - S. Meyn and R. Tweedie, *Markov Chains and Stochastic Stability* (Cambridge University Press, 2009)
  - R. Douc, E. Moulines, P. Priouret and P. Soulier, *Markov Chains* (Springer, 2018)

Some elements of statistical physics

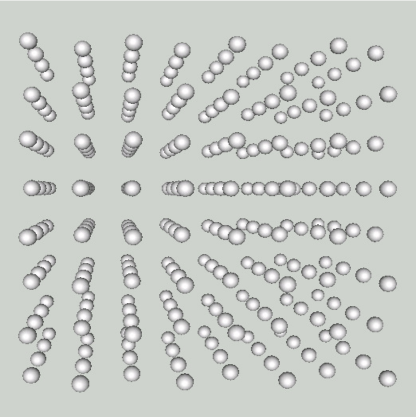
General perspective (1)

- Aims of computational statistical physics:
  - numerical microscope
  - computation of average properties, static or dynamic

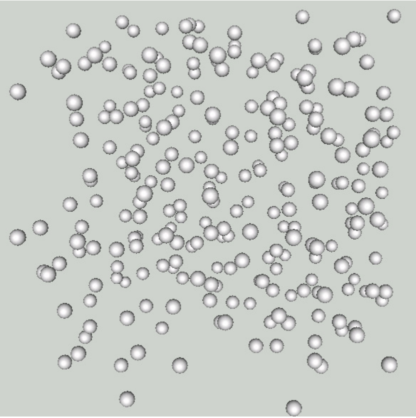
- Orders of magnitude
  - distances $\sim 1\ \mathring{A} = 10^{-10}$ m
  - energy per particle $\sim k_{\mathrm{B}}T \sim 4 \times 10^{-21}$ J at room temperature
  - atomic masses $\sim 10^{-26}$ kg
  - time $\sim 10^{-15}$ s
  - number of particles $\sim \mathcal{N}_A = 6.02 \times 10^{23}$

- "Standard" simulations
  - 10^6 particles ["world records": around 10^9 particles]
  - integration time: (fraction of) ns ["world records": (fraction of) μs]

What is the melting temperature of Argon?



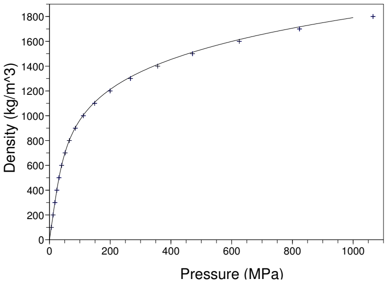
(a) Solid Argon (low temperature)

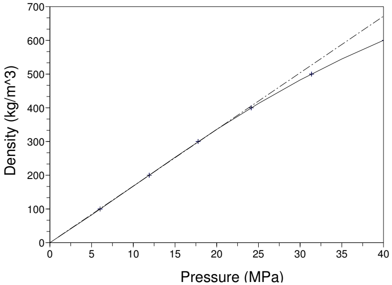


(b) Liquid Argon (high temperature)

General perspective (3)

"Given the structure and the laws of interaction of the particles, what are the macroscopic properties of the matter composed of these particles?"

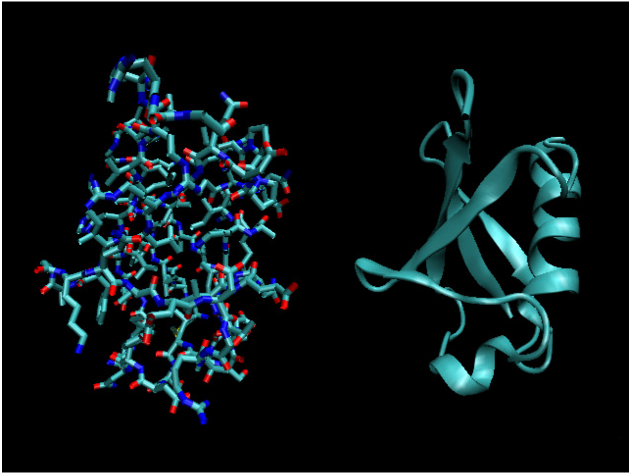




Equation of state (pressure/density diagram) for Argon at $T = 300$ K

General perspective (4)

What is the structure of the protein? What are its typical conformations, and what are the transition pathways from one conformation to another?



Microscopic description of physical systems: unknowns

• Microstate of a classical system of N particles:

$$(q,p) = (q_1,\ldots,q_N,\ p_1,\ldots,p_N) \in \mathcal{E}$$

Positions q (configuration), momenta p (to be thought of as $M\dot{q}$)

• Here, periodic boundary conditions: $\mathcal{E} = \mathcal{D} \times \mathbb{R}^{3N}$ with $\mathcal{D} = (L\mathbb{T})^{3N}$

• More complicated situations can be considered: molecular constraints defining submanifolds of the phase space

• Hamiltonian $H(q,p) = E_{\rm kin}(p) + V(q)$, where the kinetic energy is

$$E_{\rm kin}(p) = \frac{1}{2}\, p^T M^{-1} p, \qquad M = \begin{pmatrix} m_1 \, \mathrm{Id}_3 & & 0 \\ & \ddots & \\ 0 & & m_N \, \mathrm{Id}_3 \end{pmatrix}.$$

Microscopic description: interaction laws

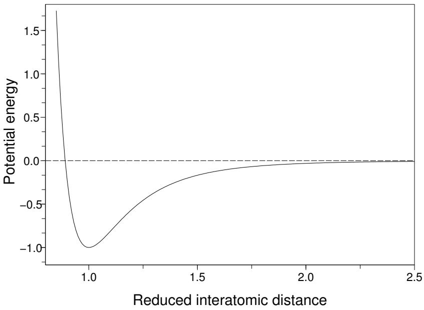
- All the physics is contained in V
  - ideally derived from quantum mechanical computations
  - in practice, empirical potentials for large scale calculations

- An example: Lennard–Jones pair interactions to describe noble gases

$$V(q_1,\dots,q_N) = \sum_{1\leqslant i<j\leqslant N} v(|q_j - q_i|)$$

$$v(r) = 4\varepsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right]$$

$$\text{Argon:}\quad \begin{cases} \sigma = 3.405\times 10^{-10}\ \text{m} \\ \varepsilon/k_{\mathrm{B}} = 119.8\ \ \text{K} \end{cases}$$



Average properties

- Macrostate of the system described by a probability measure

Equilibrium thermodynamic properties (pressure,...)

$$\mathbb{E}_\mu(\varphi) = \int_{\mathcal{E}} \varphi(q,p)\, \mu(dq\, dp)$$

- Examples of observables:
  - Pressure $\varphi(q,p) = \dfrac{1}{3|\mathcal{D}|} \displaystyle\sum_{i=1}^{N} \left(\frac{p_i^2}{m_i} - q_i \cdot \nabla_{q_i} V(q) \right)$
  - Kinetic temperature $\varphi(q,p) = \dfrac{1}{3N k_{\mathrm{B}}} \displaystyle\sum_{i=1}^{N} \frac{p_i^2}{m_i}$
- Canonical ensemble = measure on (q,p) (average energy fixed)

$$\mu_{\mathrm{NVT}}(dq\, dp) = Z_{\mathrm{NVT}}^{-1}\, \mathrm{e}^{-\beta H(q,p)}\, dq\, dp, \qquad \beta = \frac{1}{k_{\mathrm{B}} T}$$

Practical computation of average properties

Computing average properties

Main issue

Computation of high-dimensional integrals... Ergodic averages

$$\mathbb{E}_\mu(\varphi) = \lim_{t \to +\infty} \widehat{\varphi}_t, \qquad \widehat{\varphi}_t = \frac{1}{t}\int_0^t \varphi(q_s, p_s)\, ds$$

- One possible choice: Langevin dynamics with friction parameter $\gamma > 0$

= Stochastic perturbation of the Hamiltonian dynamics

$$\begin{cases} dq_t = M^{-1} p_t \, dt \\ dp_t = -\nabla V(q_t)\, dt - \gamma M^{-1} p_t \, dt + \sqrt{\frac{2\gamma}{\beta}}\, dW_t \end{cases}$$

Almost-sure convergence of ergodic averages[1]

[1] Kliemann, *Ann. Probab.* **15**(2), 690-707 (1987)

Langevin dynamics (2)

Evolution semigroup $\left(\mathrm{e}^{t\mathcal{L}}\varphi\right)(q,p) = \mathbb{E}\left[\varphi(q_t,p_t)\,\middle|(q_0,p_0)=(q,p)\right]$

Generator of the dynamics $\mathcal{L}$

$$\frac{d}{dt}\left(\mathbb{E}\left[\varphi(q_t,p_t)\,\middle|(q_0,p_0)=(q,p)\right]\right) = \mathbb{E}\left[(\mathcal{L}\varphi)(q_t,p_t)\,\middle|(q_0,p_0)=(q,p)\right]$$

Generator of the Langevin dynamics $\mathcal{L} = \mathcal{L}_{\mathrm{ham}} + \gamma\mathcal{L}_{\mathrm{FD}}$

$$\mathcal{L}_{\mathrm{ham}} = p^T M^{-1}\nabla_q - \nabla V^T \nabla_p, \qquad \mathcal{L}_{\mathrm{FD}} = -p^T M^{-1}\nabla_p + \frac{1}{\beta}\Delta_p$$

Existence/uniqueness of invariant probability measure, characterized by

$$\forall \varphi \in C_{\mathrm{c}}^{\infty}(\mathcal{E}), \qquad \int_{\mathcal{E}} \mathcal{L}\varphi\, d\mu = 0$$

Here, canonical measure $\mu(dq\,dp) = Z^{-1}\mathrm{e}^{-\beta H(q,p)}\,dq\,dp = \nu(dq)\,\kappa(dp)$

Fokker–Planck equations

Convenient to work in $L^2(\mu)$ with $f(t) = \psi(t)/\mu$

Evolution of the law $\psi(t)$ of the process at time $t \geqslant 0$

$$\frac{d}{dt}\left(\int_{\mathcal{E}} \varphi\, \psi(t)\right) = \int_{\mathcal{E}} (\mathcal{L}\varphi)\, \psi(t) = \int_{\mathcal{E}} (\mathcal{L}\varphi)\, f(t)\, d\mu = \int_{\mathcal{E}} \varphi (\mathcal{L}^* f)(t)\, d\mu$$

Fokker–Planck equations ($\mathcal{L}^\dagger$ adjoint on $L^2(\mathcal{E})$, $\mathcal{L}^*$ adjoint on $L^2(\mu)$)

$$\partial_t \psi = \mathcal{L}^\dagger \psi, \qquad \partial_t f = \mathcal{L}^* f$$

Simple computations show that $\mathcal{L}^* = -\mathcal{L}_{\mathrm{ham}} + \gamma \mathcal{L}_{\mathrm{FD}}$

$$\mathcal{L}_{\mathrm{FD}} = -\frac{1}{\beta} \sum_{i=1}^d \partial_{p_i}^* \partial_{p_i}, \qquad \mathcal{L}_{\mathrm{ham}} = \frac{1}{\beta} \sum_{i=1}^d \partial_{p_i}^* \partial_{q_i} - \partial_{q_i}^* \partial_{p_i}$$

so that convergence results for $\mathrm{e}^{t\mathcal{L}}$ and $\mathrm{e}^{t\mathcal{L}^*}$ are very similar

Hamiltonian and overdamped limits

- As $\gamma \to 0$, the Hamiltonian dynamics is recovered

$$\frac{d}{dt}\mathbb{E}\left[H(q_t,p_t)\right] = -\gamma\left(\mathbb{E}\left[p_t^T M^{-2} p_t\right] - \frac{1}{\beta}\mathrm{Tr}(M^{-1})\right)dt$$

Time $\sim \gamma^{-1}$ to change energy levels in this limit[2]

- Overdamped limit $\gamma \to +\infty$ with $M = \mathrm{Id}$: rescaling of time γt

$$\begin{aligned} q_{\gamma t} - q_0 &= -\frac{1}{\gamma}\int_0^{\gamma t} \nabla V(q_s)\,ds + \sqrt{\frac{2}{\gamma\beta}}W_{\gamma t} - \frac{1}{\gamma}\left(p_{\gamma t} - p_0\right) \\ &= -\int_0^t \nabla V(q_{\gamma s})\,ds + \sqrt{2\beta^{-1}}B_t - \frac{1}{\gamma}\left(p_{\gamma t} - p_0\right) \end{aligned}$$

which converges to the solution of $dQ_t = -\nabla V(Q_t)\,dt + \sqrt{2\beta^{-1}}\,dB_t$

- Alternatively, $\mathrm{e}^{\gamma t(\mathcal{L}_{\mathrm{ham}} + \gamma\mathcal{L}_{\mathrm{FD}})} \approx \mathrm{e}^{t\mathcal{L}_{\mathrm{ovd}}}$ with $\mathcal{L}_{\mathrm{ovd}} = -\nabla V^T\nabla_q + \beta^{-1}\Delta_q$

- In both cases, slow convergence, with rate scaling as $\min\left(\gamma, \gamma^{-1}\right)$

[2] Hairer and Pavliotis, *J. Stat. Phys.*, **131**(1), 175-202 (2008)

Statistical error (1)

- **Asymptotic variance** $\sigma_\varphi^2 = \lim_{t\to+\infty} t \, \mathrm{Var}_\mu(\widehat{\varphi}_t)$: with $\Pi\varphi = \varphi - \int_\mathcal{E} \varphi \, d\mu$,

$$\sigma_\varphi^2 = \lim_{t\to+\infty} \int_0^t \left(1 - \frac{s}{t}\right) \mathbb{E}_\mu \left[\Pi\varphi(q_t,p_t)\Pi\varphi(q_0,p_0)\right] ds$$
$$= 2\int_0^{+\infty} \int_\mathcal{E} (\mathrm{e}^{s\mathcal{L}}\Pi\varphi)\Pi\varphi \, d\mu \, ds = 2\int_\mathcal{E} (-\mathcal{L}^{-1}\Pi\varphi)\Pi\varphi \, d\mu$$

Well-defined provided $-\mathcal{L}\Phi = \Pi\varphi$ has a solution in $L_0^2(\mu) = \Pi L^2(\mu)$

A Central Limit Theorem holds in this case[3]: $\boxed{\widehat{\varphi}_t - \mathbb{E}_\mu(\varphi) \simeq \frac{\sigma_\varphi}{\sqrt{t}}\mathcal{G}}$

- Sufficient condition: integrability of the semigroup, *e.g.*

$$\left\|\mathrm{e}^{t\mathcal{L}}\right\|_{\mathcal{B}(L_0^2(\mu))} \leqslant C\mathrm{e}^{-\lambda t}$$

so that $-\mathcal{L}^{-1} = \int_0^{+\infty} \mathrm{e}^{s\mathcal{L}} \, ds$

[3] R. N. Bhattacharya, *Z. Wahrsch. Verw. Gebiete* (1982)

Statistical error (2)

Prove exponential convergence of the semigroup $\mathrm{e}^{t\mathcal{L}}$ on $E \subset L_0^2(\mu)$

- Lyapunov techniques[4] $L^\infty_{\mathscr{K}}(\mathcal{E}) = \left\{ \varphi \, \text{measurable}, \, \sup \left| \frac{\varphi}{\mathscr{K}} \right| < +\infty \right\}$
- standard hypocoercive[5] setup $H^1(\mu)$
- $L^2(\mu)$ after hypoelliptic regularization[6] from $H^1(\mu)$
- direct transfer from $H^1(\mu)$ to $L^2(\mu)$ by spectral argument[7]
- directly[8] $L^2(\mu)$ (recently[9] Poincaré using $\partial_t - \mathcal{L}_{\mathrm{ham}}$)
- coupling arguments[10]
- direct estimates on the resolvent using Schur complements[11]

Rate of convergence $\min\left(\gamma, \gamma^{-1}\right)$ so variance $\sim \max\left(\gamma, \gamma^{-1}\right)$

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[4] Wu ('01); Mattingly/Stuart/Higham ('02); Rey-Bellet ('06); Hairer/Mattingly ('11)
[5] Villani (2009) and before Talay (2002), Eckmann/Hairer (2003), Hérau/Nier (2004),...
[6] Hérau, *J. Funct. Anal.* (2007)
[7] Deligiannidis/Paulin/Doucet, *Ann. Appl. Probab.* (2020)
[8] Hérau (2006), Dolbeaut/Mouhot/Schmeiser (2009, 2015)
[9] Armstrong/Mourrat (2019), Cao/Lu/Wang (2019), Brigatti (2021), Brigati/Stoltz (2023)
[10] Eberle/Guillin/Zimmer, *Ann. Probab.* (2019)
[11] Bernard/Fathi/Levitt/Stoltz, *Annales Henri Lebesgue* (2022)

Practical computation of average properties

- Numerical scheme = Markov chain characterized by evolution operator

$$P_{\Delta t}\varphi(q,p) = \mathbb{E}\Big(\varphi\left(q^{n+1},p^{n+1}\right)\Big|(q^n,p^n)=(q,p)\Big)$$

- Discretization of the Langevin dynamics: splitting strategy

$$A = M^{-1}p\cdot\nabla_q, \qquad B = -\nabla V(q)\cdot\nabla_p, \qquad C = -M^{-1}p\cdot\nabla_p + \frac{1}{\beta}\Delta_p$$

- First order splitting schemes: $P_{\Delta t}^{ZYX} = \mathrm{e}^{\Delta t Z}\mathrm{e}^{\Delta t Y}\mathrm{e}^{\Delta t X} \simeq \mathrm{e}^{\Delta t\mathcal{L}}$
- Example: $P_{\Delta t}^{B,A,\gamma C}$ corresponds to (with $\alpha_{\Delta t} = \exp(-\gamma M^{-1}\Delta t)$)

$$\begin{cases} \widetilde{p}^{n+1} = p^n - \Delta t\,\nabla V(q^n), \\ q^{n+1} = q^n + \Delta t\, M^{-1}\widetilde{p}^{n+1}, \\ p^{n+1} = \alpha_{\Delta t}\widetilde{p}^{n+1} + \sqrt{\dfrac{1-\alpha_{\Delta t}^2}{\beta}M}\,G^n, \end{cases} \tag{1}$$

where G^n are i.i.d. standard Gaussian random variables

Practical computation of average properties (2)

- Second order splitting $P_{\Delta t}^{ZYXYZ} = \mathrm{e}^{\Delta t Z/2}\mathrm{e}^{\Delta t Y/2}\mathrm{e}^{\Delta t X}\mathrm{e}^{\Delta t Y/2}\mathrm{e}^{\Delta t Z/2}$

- Example: $P_{\Delta t}^{\gamma C,B,A,B,\gamma C}$ (Verlet in the middle)

$$\begin{cases} \widetilde{p}^{n+1/2} = \alpha_{\Delta t/2} p^n + \sqrt{\dfrac{1-\alpha_{\Delta t}}{\beta} M}\, G^n, \\ p^{n+1/2} = \widetilde{p}^{n+1/2} - \dfrac{\Delta t}{2}\, \nabla V(q^n), \\ q^{n+1} = q^n + \Delta t\, M^{-1} p^{n+1/2}, \\ \widetilde{p}^{n+1} = p^{n+1/2} - \dfrac{\Delta t}{2}\, \nabla V(q^{n+1}), \\ p^{n+1} = \alpha_{\Delta t/2} \widetilde{p}^{n+1} + \sqrt{\dfrac{1-\alpha_{\Delta t}}{\beta} M}\, G^{n+1/2}, \end{cases}$$

- Other category: Geometric Langevin algorithms, *e.g.* $P_{\Delta t}^{\gamma C,A,B,A}$

Error estimates on the computation of average properties

Types of errors

Estimators of $\mathbb{E}_\mu(\varphi)$

$$\widehat{\varphi}_t = \frac{1}{t}\int_0^t \varphi(q_s,p_s)\,ds, \qquad \widehat{\varphi}_{\Delta t}^N = \frac{1}{N}\sum_{n=1}^N \varphi(q^n,p^n)$$

Statistical error (variance of the estimator)

- dictated by the central limit theorem for continuous dynamics
- discrete dynamics: asymptotic variance coincides at order Δt^α

Bias (expectation of the estimator)

- finite time integration time $\to$ bias $\mathrm{O}\left(\frac{1}{t}\right)$
- discretization of the dynamics $\to$ bias $\mathrm{O}(\Delta t^\alpha)$

Finite time integration bias

Bias $\mathrm{O}(1/t)$, typically smaller than statistical error $\mathrm{O}(1/\sqrt{t})$

$$\left|\mathbb{E}\left(\widehat{\varphi}_t\right) - \mathbb{E}_\mu(\varphi)\right| \leqslant \frac{K}{t}$$

Key equality for the proofs: introduce $-\mathcal{L}\Phi = \Pi\varphi$ and write

$$\begin{aligned} \widehat{\varphi}_t - \mathbb{E}_\mu(\varphi) &= \frac{1}{t}\int_0^t \Pi\varphi(q_s,p_s)\,ds \\ &= \frac{\Phi(q_0,p_0) - \Phi(q_t,p_t)}{t} + \sqrt{\frac{2\gamma}{\beta}}\,\frac{1}{t}\int_0^t \nabla_p\Phi(q_s,p_s)^\top dW_s \end{aligned}$$

with Ito calculus $d\Phi(q_s,p_s) = \mathcal{L}\Phi(q_s,p_s) + \sqrt{2\gamma\beta^{-1}}\nabla_p\Phi(q_s,p_s)^\top dW_s$

Also allows to prove CLT: martingale part dominant, with variance

$$\frac{2\gamma}{\beta t^2}\int_0^t \mathbb{E}\left[\left|\nabla_p\Phi(q_s,p_s)\right|^2\right] ds \sim \frac{2\gamma}{\beta t}\int \left|\nabla_p\Phi\right|^2\,d\mu = \frac{2\gamma}{\beta t}\int \Phi(-\mathcal{L}\Phi)\,d\mu$$

Timestep discretization bias

The ergodicity of numerical schemes can be proved ($\mathcal{D}$ bounded):

$$\frac{1}{N_{\rm iter}} \sum_{n=1}^{N_{\rm iter}} \varphi(q^n, p^n) \xrightarrow[N_{\rm iter}\to+\infty]{} \int \varphi(q,p)\, d\mu_{\gamma,\Delta t}(q,p)$$

Systematic error estimates: α order of the splitting scheme

$$\int_{\mathcal{E}} \varphi(q,p)\, \mu_{\gamma,\Delta t}(dq\, dp) = \int_{\mathcal{E}} \varphi(q,p)\, \mu(dq\, dp) + \Delta t^{\alpha} \int_{\mathcal{E}} \varphi(q,p) f_{\alpha,\gamma}(q,p)\, \mu(dq\, dp) + \mathrm{O}(\Delta t^{\alpha+1})$$

Correction function $f_{\alpha,\gamma}$ solution of an appropriate Poisson equation

$$\mathcal{L}^* f_{\alpha,\gamma} = g_\gamma$$

where g_γ depends on the numerical scheme (adjoints taken on $L^2(\mu)$)

Proof for the first-order scheme $P_{\Delta t}^{\gamma C,B,A}$ (1)

- By definition of the invariant measure, $\displaystyle\int_{\mathcal{E}} P_{\Delta t}\phi \, d\mu_{\gamma,\Delta t} = \int_{\mathcal{E}} \phi \, d\mu_{\gamma,\Delta t}$, so

$$\int_{\mathcal{E}} \left[\left(\frac{\mathrm{Id} - P_{\Delta t}}{\Delta t}\right)\phi\right] d\mu_{\gamma,\Delta t} = 0$$

- In view of the BCH formula $\mathrm{e}^{\Delta t A_3}\mathrm{e}^{\Delta t A_2}\mathrm{e}^{\Delta t A_1} = \mathrm{e}^{\Delta t \mathcal{A}}$ with

$$\mathcal{A} = A_1 + A_2 + A_3 + \frac{\Delta t}{2}\Big([A_3, A_1 + A_2] + [A_2, A_1]\Big) + \dots,$$

it holds $P_{\Delta t}^{\gamma C,B,A} = \mathrm{Id} + \Delta t \mathcal{L} + \dfrac{\Delta t^2}{2}\left(\mathcal{L}^2 + S_1\right) + \Delta t^3 R_{1,\Delta t}$ with

$$S_1 = [C, A + B] + [B, A], \qquad R_{1,\Delta t} = \frac{1}{2}\int_0^1 (1-\theta)^2 \mathcal{R}_{\theta\Delta t} \, d\theta,$$

Proof for the first-order scheme $P_{\Delta t}^{\gamma C,B,A}$ (2)

- The correction function $f_{1,\gamma}$ is chosen so that

$$\int_{\mathcal{E}} \left[\left(\frac{\mathrm{Id} - P_{\Delta t}^{\gamma C,B,A}}{\Delta t} \right) \phi \right] (1 + \Delta t f_{1,\gamma})\, d\mu = \mathrm{O}(\Delta t^2)$$

This requirement can be rewritten as

$$0 = \int_{\mathcal{E}} \left(\frac{1}{2} S_1 \phi + (\mathcal{L}\phi) f_{1,\gamma} \right) d\mu = \int_{\mathcal{E}} \varphi \left[\frac{1}{2} S_1^* \mathbf{1} + \mathcal{L}^* f_{1,\gamma} \right] d\mu,$$

which suggests to choose $\mathcal{L}^* f_{1,\gamma} = -\dfrac{1}{2} S_1^* \mathbf{1}$ (well posed equation)

- Replace ϕ by $\left(\dfrac{\mathrm{Id} - P_{\Delta t}^{\gamma C,B,A}}{\Delta t} \right)^{-1} \varphi$? No control on the derivatives...

- Rely on the "nice" properties of the continuous dynamics, *i.e.* functional estimates[12] on $\mathcal{L}^{-1}$ to use pseudo-inverses

$$Q_{1,\Delta t} = -\mathcal{L}^{-1} + \frac{\Delta t}{2} (\mathrm{Id} + \mathcal{L}^{-1} S_1 \mathcal{L}^{-1})$$

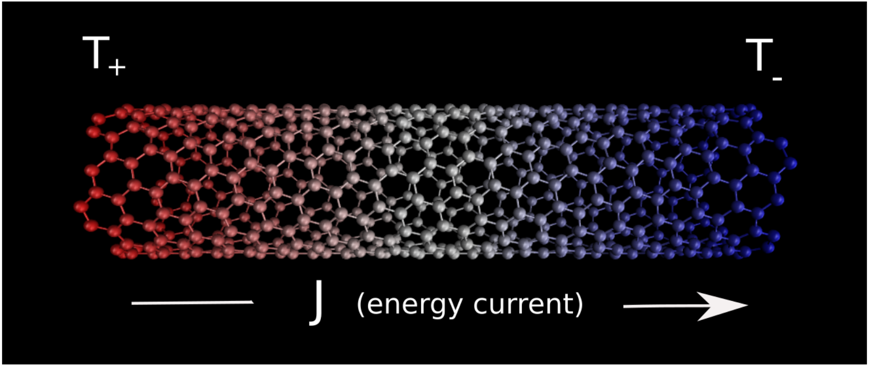
[12] D. Talay, Stoch. Proc. Appl. (2002); M. Kopec (2015)

Transport coefficients

Physical context and motivations

Transport coefficients (*e.g.* thermal conductivity): quantitative estimates

$$J = -\kappa \nabla T \qquad \text{(Fourier's law)}$$

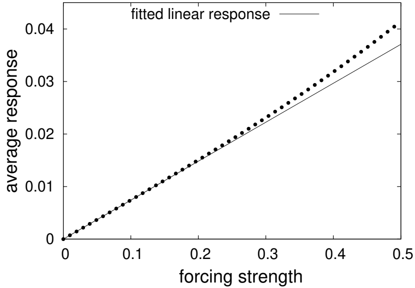


Slow convergence due to large noise to signal ratio
Long computational times to estimate κ (up to several weeks/months)

Example: $\mathcal{D} = (L\mathbb{T})^d$, non-gradient force $F \in \mathbb{R}^d$

$$\begin{cases} dq_t = M^{-1}p_t\,dt \\ dp_t = \Big(- \nabla V(q_t) + \eta F \Big) dt - \gamma M^{-1} p_t\,dt + \sqrt{\dfrac{2\gamma}{\beta}}\,dW_t \end{cases}$$

Response function $R(q,p) = F^T M^{-1} p$ = velocity in direction F



Existence/uniqueness of invariant probability measure (Lyapunov)

Generator $\mathcal{L} + \eta\widetilde{\mathcal{L}}$ with $\widetilde{\mathcal{L}} = F^T\nabla_p$

$$\mathbb{E}_\eta(R) = \int_{\mathcal{E}} R\,\psi_\eta \approx \alpha\eta$$

α = transport coefficient

Definition of transport coefficients (1)

Perturbative regime: invariant measure $\psi_\eta = f_\eta \mu$ with $f_\eta = 1 + \mathrm{O}(\eta)$

$$\forall \varphi, \qquad 0 = \int_{\mathcal{E}} \left[\left(\mathcal{L} + \eta \widetilde{\mathcal{L}} \right) \varphi \right] f_\eta \, d\mu = \int_{\mathcal{E}} \varphi \left[\left(\mathcal{L} + \eta \widetilde{\mathcal{L}} \right)^* f_\eta \right] d\mu$$

* = adjoints on $L^2(\mu)$ $\qquad (\partial_{q_i}^* = -\partial_{q_i} + \beta \partial_{q_i} V$ and $\partial_{p_i}^* = -\partial_{p_i} + \beta (M^{-1} p)_i)$

Fokker–Planck equation

$$\left(\mathcal{L} + \eta \widetilde{\mathcal{L}} \right)^* f_\eta = 0$$

By identifying powers of η (recalling $\Pi \varphi = \varphi - \mu(\varphi)$)

$$f_\eta = 1 + \eta \mathfrak{f}_1 + \eta^2 \mathfrak{f}_2 + \dots, \qquad -\mathcal{L}^* \mathfrak{f}_1 = \widetilde{\mathcal{L}}^* \mathbf{1} = \Pi \widetilde{\mathcal{L}}^* \mathbf{1} = S$$

Running example: $\mathcal{L}^* = -\mathcal{L}_{\mathrm{ham}} + \gamma \mathcal{L}_{\mathrm{FD}}$ and $\widetilde{\mathcal{L}}^* = -\widetilde{\mathcal{L}} + \beta F^T M^{-1} p$

$$S(q,p) = \beta F^T M^{-1} p$$

Definition of transport coefficients (2)

Response property $R \in L_0^2(\mu) = \Pi L^2(\mu)$, conjugated response $S = \widetilde{\mathcal{L}}^* \mathbf{1}$:

$$\alpha = \lim_{\eta \to 0} \frac{\mathbb{E}_\eta(R)}{\eta} = \int_{\mathcal{E}} R \mathfrak{f}_1 \, d\mu = \int_{\mathcal{E}} R \left[(-\mathcal{L}^*)^{-1} S \right] d\mu = \int_{\mathcal{E}} \left(-\mathcal{L}^{-1} R \right) S \, d\mu$$

$$= \int_0^{+\infty} \left[\int_{\mathcal{E}} \left(\mathrm{e}^{t\mathcal{L}} R \right) S \, d\mu \right] dt = \int_0^{+\infty} \mathbb{E}_0 \Big(R(q_t, p_t) S(q_0, p_0) \Big) dt$$

In practice:

- Identify the response function and the reference dynamics
- Construct a physically meaningful perturbation (bulk or boundary driven)
- Obtain the transport coefficient α (thermal cond., shear viscosity,...)

For the running example, definition of mobility with $R(q,p) = F^T M^{-1} p$

$$\lim_{\eta \to 0} \frac{\mathbb{E}_\eta \left(F^T M^{-1} p \right)}{\eta} = \beta \, F^T D F, \quad D = \int_0^{+\infty} \mathbb{E}_0 \Big((M^{-1} p_t) \otimes (M^{-1} p_0) \Big) \, dt$$

Error estimates for nonequilibrium molecular dynamics

Example: $\mathcal{D} = (L\mathbb{T})^d$, non-gradient force $F \in \mathbb{R}^{3N}$

$$\begin{cases} dq_t^\eta = M^{-1} p_t^\eta \, dt \\ dp_t^\eta = \Big(-\nabla V(q_t^\eta) + \eta F \Big) dt - \gamma M^{-1} p_t^\eta \, dt + \sqrt{\dfrac{2\gamma}{\beta}} \, dW_t \end{cases}$$

Estimator of linear response (observable R with equilibrium average 0)

$$\widehat{A}_{\eta,t} = \frac{1}{\eta t} \int_0^t R(q_s^\eta, p_s^\eta) \, ds \xrightarrow[t \to +\infty]{\text{a.s.}} \alpha_\eta := \frac{1}{\eta} \int_{\mathcal{E}} R \, f_\eta \, d\mu = \alpha + \mathrm{O}(\eta)$$

Issues with linear response methods:

- Statistical error with asymptotic variance $\mathrm{O}(\eta^{-2})$
- Bias $\mathrm{O}(\eta)$ due to $\eta \neq 0$
- Bias from finite integration time
- Timestep discretization bias

Error estimates on the Green–Kubo formula

- Aim: approximate $\alpha = \displaystyle\int_0^{+\infty} \mathbb{E}_0\Big(R(q_t,p_t)S(q_0,p_0)\Big)\,dt$
- **Issues with Green–Kubo formula:**
  - Truncature of time (exponential convergence of $\mathrm{e}^{t\mathcal{L}}$)
  - The statistical error for correlations increases a lot with time lag[13]
  - Timestep bias and quadrature formula

Possible benefits from...

- Fourier approaches and time series analysis[14]
- importance sampling on trajectory space[15]

[13] de Sousa Oliveira/Greaney, *Phys. Rev. E* **95** (2017)
[14] Ercole/Marcolongo/Baroni, *Sci. Rep.* **7** (2017)
[15] Donati/Hartmann/Keller, *J. Chem. Phys.* **146** (2017)

Study of alternative approaches: several year workplan!

Alternatives to direct NEMD/GK, possibly with some blending

- Alternative fluctuation formulas[16]
- Control variate approaches[17] (better solutions to Poisson equation needed...)
- Use coupling methods between X_t^η and X_t^0, *e.g.* sticky coupling[18]
- Rely on tangent dynamics[19] for $T_t = \lim_{\eta \to 0}(X_t^\eta - X_t^0)/\eta$
- Optimize synthetic forcings[20]
- Large deviation techniques to estimate second order cumulants[21]
- Norton dynamics[22] (dual approach where the flux is fixed)
- Transient methods[23]

Quantify variance and bias and apply to physical systems

[16] Plechac/Stoltz/Wang (2021, 2023)

[17] Mangaud/Rotenberg (2020); Roussel/Stoltz (2019), Pavliotis/Stoltz/Vaes (2022), currently Pavliotis/Spacek/Stoltz/Vaes

[18] Eberle/Zimmer (2019); Durmus/Eberle/Enfroy/Guillin/Monmarché (2021); currently Darshan/Eberle/Stoltz

[19] Assaraf/Jourdain/Lelièvre/Roux, *Stoch. Partial Differ. Equ. Anal. Comput.* (2018)

[20] Evans/Morriss (2008); Spacek/Stoltz (2023)

[21] Limmer/Gao/Poggioli (2021); currently Guyader/Gastaldello/Stoltz/Vaes

[22] Evans/Morriss (2008); Blassel/Stoltz (2023) and now Darshan/Iacobucci/Olla/Stoltz

[23] Ciccotti/Jacucci (1975); currently Monmarché/Spacek/Stoltz