Stochastic Simulation of Reaction-Diffusion Systems: A Fluctuating-Hydrodynamics Approach

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Introduction

- We are interested in numerical simulation of stochastic reaction-diffusion systems
- Thermal fluctuations drive movement and collision of individual molecules

Applications include:
- Front propagation acceleration and/or directional changes
- Pattern formation – transient and steady state
- Fluctuation-induced instabilities
- Cell biology / cellular function
Introduction

• We seek a seamless approach that is efficient and accurate:
  − Our primary interest is for weak fluctuations (macroscopic scales and/or large particle count).
  − Also of concern are strong fluctuations (mesoscopic scales and/or small particle count).

• Particularly useful when populations of chemical species have different orders of magnitude, including dilute solvent-solute models.

• We use techniques developed independently for stochastic reactions and stochastic diffusion, and create new temporal integrators that combine these techniques.
Reactions

• Three classes of algorithms developed for single-cell stochastic chemistry for solving the Chemical Master Equation (CME).
  - **Stochastic Simulation Algorithm (SSA):** track each individual reaction event sequentially by repeatedly drawing from exponential random variables.
    • Exact sampling of CME, but prohibitively expensive for many zones and large particle counts
  - **Chemical Langevin Equation (CLE):** augment the reaction rates with Gaussian random noise.
    • Very efficient, but fails to produce results predicted by statistical mechanics.
  - **Tau Leaping:** track the total number of events over a time step by drawing from a Poisson random variable
    • Efficient and accurate, as long as the chemistry is not too stiff
Diffusion

- Three classes of algorithms developed for stochastic diffusion:
  - SSA: track each individual intercell “hop” sequentially by repeatedly drawing from exponential random variables.
    - Exact sampling, but prohibitively expensive for many zones and large particle counts
  - Multinomial: track the total number of hops over a time step by drawing from a Poisson random variable
    - Efficient, accurate, but limited by explicit diffusion time step
  - Fluctuating Hydrodynamics (FHD): augment diffusive fluxes with Gaussian noise using the Landau/Lifshitz formalism
    - Efficient, accurate, and allows for both explicit and implicit temporal discretization for very large time steps
“Best of Both Worlds” Approach

• Finite volume formulation.
  – Number densities expressed as averages over Cartesian grid cells

• Fluctuating Hydrodynamics diffusion approach.
  – Diffusive fluxes augmented by Gaussian White Noise, using the Landau/Lifshitz formalism
  – Implicit diffusion treatment that can greatly exceed time step for hopping and other explicit treatments

• Reactions treated as a Poisson process, 2 choices:
  – Tau-leaping (primary option)
  – SSA also an option if chemistry is stiff.

• We develop unsplit temporal integrators that are second-order in the deterministic limit, and capture the correct spectrum of equilibrium fluctuations
Spatial Discretization

- Finite volume approach
- Number densities, \( n_s \) (for species “s”) are cell-averaged.
- Diffusive and stochastic fluxes are face-averaged.
**Diffusion Model**

- We can express the stochastic diffusion-only system as a system of stochastic ODEs for the number density in each cell:

$$\frac{\partial n_s}{\partial t} = \nabla \cdot \left( D_s \nabla n_s + \sqrt{2D_s} n_s \mathbf{Z}_s^{(D)} \right)$$

- When discretized in space and time one possible scheme (forward Euler) is

$$n_{s}^{k+1} - n_{s}^{k} = \Delta t D_s \nabla_d^2 n_s^{k} + \sqrt{\frac{2D_s \Delta t}{\Delta V}} \nabla_d \cdot \left( \sqrt{n_s^{k}} \mathbf{W}_s^{k} \right)$$
Reaction Model

- Chemical Langevin equation (CLE) for stochastic reactions:

\[
\frac{dn_s}{dt} = \sum_{r=1}^{N_r} \nu_{sr} \left( a_r(n) + \sqrt{a_r(n)} \mathcal{Z}_r^{(R)} \right)
\]

- We have previously shown that describing reactions as a Markov jump process (Poisson noise) is consistent with equilibrium statistical mechanics.

- We also have an option to use SSA:

\[
\frac{dn_s}{dt} = \sum_{r=1}^{N_r} \nu_{sr} \frac{P(a_r(n) \Delta V dt)}{\Delta V dt}
\]

\[
\frac{dn_s}{dt} = \mathcal{R}_s(n, dt)
\]
Temporal Discretization

• Putting diffusion and reactions together, we have developed a 2-stage, implicit, tau-leaping scheme that is second-order deterministically, and produces third-order structure factors. (ImMidTau)

\[
\begin{align*}
\tilde{n}_s^k & = n_s^k + \frac{D_s \Delta t}{2} \nabla_d^2 n_s^k + \sqrt{\frac{D_s \Delta t}{\Delta V}} \nabla_d \left( \sqrt{\tilde{n}_s^k} W_s^{(1)} \right) + \sum_{r=1}^{N_r} \frac{\nu_{sr} \mathcal{P}^{(1)}(a_r^k \Delta V \Delta t/2)}{\Delta V}, \\
n_s^{k+1} & = n_s^k + D_s \Delta t \nabla_d^2 \left( \frac{n_s^k + n_s^{k+1}}{2} \right) \\
& + \sqrt{\frac{D_s \Delta t}{\Delta V}} \nabla_d \left( \sqrt{\tilde{n}_s^k} W_s^{(1)} \right) + \sqrt{\frac{D_s \Delta t}{\Delta V}} \nabla_d \left( \sqrt{n}((2n_s^k - n_s^k)^+ W_s^{(2)} \right) \\
& + \sum_{r=1}^{N_r} \frac{\nu_{sr} \mathcal{P}^{(1)}(a_r^k \Delta V \Delta t/2)}{\Delta V} + \sum_{r=1}^{N_r} \frac{\nu_{sr} \mathcal{P}^{(2)}((2a_r^k - a_r^k)^+ \Delta V \Delta t/2)}{\Delta V}
\end{align*}
\]

• We also have a stiff chemistry integrator that uses SSA (ImMidSSA)
Structure Factor for Model Equations

- The static structure factor quantifies the spectrum of fluctuations at equilibrium. For a single-species model:

  \[ S(k) = \langle (\delta \hat{n}_k)(\delta \hat{n}_k^*) \rangle, \quad \delta \hat{n}_k = \mathcal{F}(n - \bar{n}) \]

- We take the Fourier transform of the linearized reaction-diffusion equations:

  \[
  \frac{d}{dt} \delta \hat{n}_k = -Dk^2 \delta \hat{n}_k + \sqrt{2D\bar{n}} i k \cdot \hat{Z}_{k}^{(D)} - r \delta \hat{n}_k + \sqrt{2\bar{n}} \hat{Z}_{k}^{(R)}
  \]

  \[ r = -a'(\bar{n}), \quad \bar{\Gamma} = \frac{1}{2} \sum_{r=1}^{N_r} \nu_r^2 a_r(n) \]

- Use the Ornstein-Uhlenbeck equation to obtain

  \[
  S(k) = \frac{D\bar{n}k^2 + \bar{\Gamma}}{Dk^2 + r}
  \]
Schlögl Model

- Single-species Schlögl model: $\frac{k_1}{k_2} 2X \rightleftharpoons 3X \quad \frac{k_3}{k_4} \emptyset \rightleftharpoons X$

- Consider an out-of-equilibrium monostable case.

- We have analyzed the discrete structure factors for our 2-stage implicit diffusion schemes (and other 2-stage explicit-diffusion schemes) and compared to the continuum result:
Schlögl Model - Structure Factor

\[ \ell \sim \sqrt{D/r} \]  
\[ \beta = D \Delta t / \Delta x^2 \]

(penetration depth)  
(explicit diffusion Courant number)
Small Number of Molecules

- Diffusion – pure arithmetic averaging of number densities to faces used to multiply stochastic fluxes is problematic.

\[ \frac{dn_s}{dt} = D_s \nabla_d^2 n_s + \sqrt{\frac{2D_s}{\Delta V}} \nabla_d \cdot \left( \sqrt{n_s} \nabla s \right) \]

- We need stochastic fluxes to “shut off” as the number density in either face approaches zero (in order to avoid driving the number densities negative)

\[ \tilde{n}(n_1, n_2) = \left( \frac{n_1 + n_2}{2} \right) H_0(n_1 \Delta V)H_0(n_2 \Delta V) \]

- Smoothed Heaviside function allows for more gradual transition to zero number densities on face
Small Number of Molecules

- Using $H_0$, vs. $H$ (discontinuous Heaviside), here is the distribution of number densities in a diffusion-only test with an average $N = 5$.

- Reactions – use continuous-range number densities with law of mass action correction, ensuring each rate is non-negative; e.g.,

$$2X \xrightleftharpoons[k_2]{k_1} 3X$$

$$a(n) = k_1 n^+ (n - \frac{1}{\Delta V})^+ - k_2 n^+ (n - \frac{1}{\Delta V})^+ (n - \frac{2}{\Delta V})^+$$

$$n^+ = \max(n, 0)$$
Schlögl Model – Thermodynamic Equilibrium

- Single-species Schlögl model \( \frac{k_1}{k_2} 2X \rightleftharpoons \frac{k_3}{k_4} 3X \) \( \rightleftharpoons \) \( \emptyset \)

- We have performed detailed analysis demonstrating we match the structure factor and equilibrium distribution for \(~10\) molecules per cell.
Turing-like Pattern Formation

- We compare our new approach with an RDME Scheme (Strang splitting; multinomial diffusion + SSA)
  - The movie shows the time evolution of $n_U$

FHD, $\Delta t = 0.1$  
RDME, $\Delta t = 0.01$
Turing-like Pattern Formation

• Baras-Pearson-Mansour (BPM) Model
  – 3 Species, 7 Reactions
  – Diffusion coefficient and reaction rates correspond to a limit cycle

\[
\begin{align*}
U + W & \xrightarrow{k_1} V + W, & 2V & \xrightleftharpoons[k_2][k_3] W, \\
U & \xrightleftharpoons[k_4][k_5] \emptyset, & V & \xrightleftharpoons[k_6][k_7] \emptyset.
\end{align*}
\]

• We initialize the system by choosing a point on the limit cycle and perturbing the data with a Poisson distribution
Turing-like Pattern Formation

- Analysis of pattern formation time scales, comparing strong fluctuations ($A=1$), weak fluctuations ($A=10$), and deterministic
  - All simulations use the same random initial perturbation
Front Propagation

- 2 species, 4 reaction model (Lemarchand)

\[ A \xrightarrow{k_1} \emptyset, \quad 2A + B \xrightarrow{k_2} 3A, \quad B \xrightleftharpoons[k_3]{k_4} \emptyset. \]

- 3D simulation comparing deterministic vs. stochastic evolution
  - Parallel implementation using BoxLib allows for scalability on leadership class computing facilities.

- We initialize a spherical bubble with interior/exterior equilibrium states and perturb with Poisson noise.
Front Propagation

Deterministic

Stochastic
Conclusions / Future Work

• Our implicit diffusion, two-stage, tau-leaping scheme compares favorable to RDME for large fluctuations, and can seamlessly handle the deterministic limit.
  – SSA can be used for rapid reactions

• Implementation of reactions into existing FHD models containing more physics (advection, multicomponent diffusion, thermal gradients, barodiffusion, charged particles).
  – See the next talk by J. Peraud, Low Mach Number Fluctuating Hydrodynamics for Electrolytes