Parallel Solution of
Multiscale Stochastic Chemical Kinetics

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Overview

- Stochastic chemical kinetics: the *what* and the *why*
- Multiple scales: a hierarchy of models/solution methods
- The mesoscopic model; master equation/jump SDE
  - Poisson random measure and nonlinear noise
- The parareal algorithm
- Combined scales in parallel
  - Convergence and homogenization
- Example: stochastic toggle switch
- Example: homogenization of disparate rates
- Conclusions
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<th>System size $\Omega$ (# molecules)</th>
<th>Model</th>
<th>Name</th>
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<td>$\geq 10^6$</td>
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<td>Macroscopic</td>
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<td>SDE (Langevin)</td>
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<tr>
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The chemical master equation (Gardiner, van Kampen)

State vector \( x \in \mathbb{Z}_+^D \) counting the number of molecules of each of \( D \) species; \( R \) specified reactions defined as transitions between the states,

\[
x \xrightarrow{w_r(x)} x - \mathbb{N}_r, \quad \mathbb{N} \in \mathbb{Z}^{D \times R} \text{ (stoichiometric matrix)}
\]

where each propensity \( w_r: \mathbb{Z}_+^D \rightarrow \mathbb{R}_+ \). The master equation is

\[
\frac{\partial p(x,t)}{\partial t} = \sum_{r=1}^{R} w_r(x + \mathbb{N}_r)p(x + \mathbb{N}_r,t) - \sum_{r=1}^{R} w_r(x)p(x,t).
\]

-Discrete PDE in \( D \) dimensions for the probability density \( p \).
-Several simulation algorithms exist (SSA, NRM, ...).
The jump SDE \((Plyasunov '05, Li '07, Ikeda/Watanabe, Gihman/Skorohod)\)

- Probability space \((\Sigma, F, P)\).
- The Poisson random measure: \(\mu(dt \times dz; \sigma), \sigma \in \Sigma\); an increasing sequence of arrival times \(\tau_i \in \mathbb{R}_+\) with random “marks” \(z_i\) uniformly distributed in \([0, \bar{W}]\). Deterministic intensity is \(m(dt \times dz) = dt \times dz\).
- Closed system: \(\bar{W} := \sum_r \max_x w_r(x)\).
- Open system: \(\hat{W}(t) = \sum_r w_r(X(t))\) (state-dependent intensity).

\[
\begin{align*}
\text{d}X_t &= -\sum_{r=1}^{R} N_r \int_0^{\bar{W}} \hat{w}_r(X(t-); z) \mu(dt \times dz) \\
&= -\sum_{r=1}^{R} N_r w_r(X(t-)) dt - \sum_{r=1}^{R} N_r \int_0^{\bar{W}} \hat{w}_r(X(t-); z)(\mu - m)(dt \times dz).
\end{align*}
\]

- Where the \(\hat{w}_r\) are indicator functions (a thinning of the measure).
The basic idea... (Lions/Maday/Turinici '00, Staff '03, Bal '06)

\[ \dot{u} = -Au, \quad t \in [0, T] \text{ with some } u(0) = u_0. \]

\[ F_t(y) \equiv y - \int_0^t Au(t) \, dt \text{ where } u(0) = y, \text{ and,} \]

\[ C_t \approx F_t \text{ but faster!} \]

Discretize time in \( N = T/\Delta t \) chunks. Any solver \( S \in \{ \mathcal{F}_\Delta t, \mathcal{C}_\Delta t \} \) can be used to compute a numerical solution:

\[
B(S)v = \begin{bmatrix}
  I & 0 & 0 & 0 \\
  -S & I & 0 & 0 \\
  0 & -S & I & 0 \\
  0 & 0 & -S & I
\end{bmatrix}
\begin{bmatrix}
  v_0 \\
  v_1 \\
  v_2 \\
  v_3
\end{bmatrix}
= \begin{bmatrix}
  u_0 \\
  0 \\
  0 \\
  0
\end{bmatrix}
= u_0.
\]
Parareal is the fix-point iteration obtained by using $B(C_{\Delta t})^{-1}$ as an approximate inverse to $B(F_{\Delta t})$:

$$v_{k+1} = v_k - B(C_{\Delta t})^{-1}(B(F_{\Delta t})v_k - u_0).$$

Let $v_{0,0} = u_0$ and $v_{0,n} = C_{\Delta t}v_{0,n-1}$ to start up the algorithm. Then

$$v_{k,n} = F_{\Delta t}v_{k-1,n-1} - [C_{\Delta t}v_{k-1,n-1} - C_{\Delta t}v_{k,n-1}],$$

where the expensive evaluation of $F$ is trivially parallel.

- In fact, the algorithm is strictly parallel (serial version is pointless).
Convergence results

- Setup: use for $\mathcal{C}$ the macroscopic ODE (rate equations), and use a stochastic simulation technique for $\mathcal{F}$.
- The RMS-error

$$\left( E[\tilde{X}_{k,n} - X_n]^2 \right)^{1/2} \leq C_{1,T} S_{\mathcal{F}}^k \leq C_{2,T} M^{2-k} \quad \text{(nonlinear transient)},$$

where $S_{\mathcal{F}} \propto \sqrt{L}$ (total Lipschitz constant) and where $M$ is the initial RMS-error.
- (Very) weak error:

$$|E[\tilde{X}_{k,n} - X_n]| \leq C_{3,T} \Delta t^{k/2}.$$
Homogenization

-Utimately, the convergence depends rather strongly on the Lipschitz constant! The reason is the lack of sufficiently high order (strong) consistency of $\mathcal{C}$ w.r.t. $\mathcal{F}$.

-For stiff models one is often interested in seeking an effective slow dynamics. A way to achieve this is to replace $\mathcal{F}$ with a homogenized version $\mathcal{F}^h$:

$$\mathcal{F}^h X_0 := \frac{1}{\delta t} \int_{\Delta t - \delta t}^{\Delta t} Y(t) \, dt, \quad \text{where } Y(t) = \mathcal{F}_t X_0,$$

-\(\delta t\) large enough to contain several fast reactions but short enough to be essentially independent on the slow scales.

-Again, this homogenization is strictly parallel.
**Stochastic toggle switch**

Biological 'transistor' in the regulatory network of *E. coli*:

\[
\emptyset \xrightarrow{a/(b+y^2)} X \quad \emptyset \xrightarrow{a/(b+x^2)} Y \\
X \xrightarrow{\mu x} \emptyset \quad Y \xrightarrow{\mu y} \emptyset
\]
Figure 1: Solid: parallel solution after 0, 1, 2 and 4 iterations.
Figure 2: Dash-dot: propensities perturbed by ±1%.
Homogenization of disparate rates

Fast dimerization/slow isomerization:

\[
\begin{align*}
X_1 + X_1 & \xrightleftharpoons{1/\varepsilon} X_2 + X_2 \\
X_2 & \xrightleftharpoons{1} Y_2 \\
Y_2 + Y_2 & \xrightleftharpoons{1/\varepsilon} Y_1 + Y_1
\end{align*}
\]
Figure 3: Original (dot) and homogenized (dash) trajectories. In solid: parallel solution (0 and 1 iteration).
Conclusions

- Mesoscopic stochastic kinetics (jump SDE/master equation): (locally) well stirred chemical reactions
  - macroscopic limit: nonlinear ODE/(reaction-diffusion PDE)
- Parareal combination jump SDE/ODE
  - RMS-convergence depends on the Lipschitz constant
  - convergence of the first moment as $\Delta t \to 0$
- Homogenization in parallel: homogenized \textit{solution} rather than a homogenized \textit{equation} — generalizes to other types of SDEs
  - parareal applied to stiff stochastic equations (previously unclear)
- A \textit{fix} number of parareal iterations can be thought of as a stochastic/deterministic \textit{hybrid} with very few parameters
- Yet to do: better efficiency through multilevel parallelism, analysis of open system