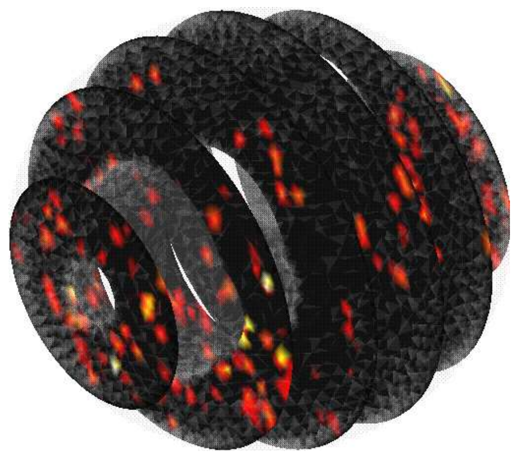
Parallel Solution of Multiscale Stochastic Chemical Kinetics



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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

System size Ω (# molecules)	Model	Name
$\gtrsim 10^6$	ODE	Macroscopic
$\sim 10^4$–10^8	SDE (Langevin)	Mesoscopic (continuous)
$\sim 10^1$–10^6	jump SDE (master equation)	Mesoscopic (discrete)
$\lesssim 10^2$	Brownian dynamics (BD)	Microscopic

Model	Assumption
BD	Brownian motion of individual molecules
jump SDE	Non-individual, (locally) well-stirred
SDE	Continuous approximation
ODE	Continuous, deterministic

The chemical master equation (*Gardiner, van Kampen*)

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

$$x \xrightarrow{w_r(x)} x - \mathbb{N}_r, \qquad \mathbb{N} \in \mathbf{Z}^{D \times R} \; (\textit{stoichiometric matrix})$$

where each propensity $w_r : \mathbf{Z}_+^D \to \mathbf{R}_+$. 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 $(\Sigma, \mathbf{F}, \mathbf{P})$.

-The *Poisson random measure*: $\mu(dt \times dz; \sigma)$, $\sigma \in \Sigma$; an increasing sequence of arrival times $\tau_i \in \mathbf{R}_+$ 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: $\bar{W}(t) = \sum_r w_r(X(t))$ (state-dependent intensity).

$$dX_t = -\sum_{r=1}^{R} \mathbb{N}_r \int_0^{\bar{W}} \hat{w}_r(X(t-);\, z)\, \mu(dt \times dz)$$

$$= -\sum_{r=1}^{R} \mathbb{N}_r w_r(X(t-))\, dt - \sum_{r=1}^{R} \mathbb{N}_r \int_0^{\bar{W}} \hat{w}_r(X(t-);\, z)(\mu - m)(dt \times dz).$$

-Where the $\hat{w}_r$ are indicator functions (a *thinning* of the measure).

The basic idea... (*Lions/Maday/Turinici '00, Staff '03, Bal '06*)

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

$$\mathcal{F}_t(y) \equiv y - \int_0^t Au(t)\, dt \text{ where } u(0) = y, \text{ and,}$$

$$\mathcal{C}_t \approx \mathcal{F}_t \text{ but faster!}$$

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 $B(\mathcal{C}_{\Delta t})^{-1}$ as an approximate inverse to $B(\mathcal{F}_{\Delta t})$:

$$v_{k+1} = v_k - B(\mathcal{C}_{\Delta t})^{-1}(B(\mathcal{F}_{\Delta t})v_k - u_0).$$

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

$$v_{k,n} = \mathcal{F}_{\Delta t} v_{k-1,n-1} - [\mathcal{C}_{\Delta t} v_{k-1,n-1} - \mathcal{C}_{\Delta t} v_{k,n-1}],$$

where the expensive evaluation of $\mathcal{F}$ 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*

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

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

-(Very) weak error:

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

Homogenization

-Ultimately, 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 $\mathcal{F}^h$;

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

-δt 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*:

$$
\left.
\begin{array}{ccccccc}
\emptyset & \xrightarrow{a/(b+y^2)} & X & \qquad & \emptyset & \xrightarrow{a/(b+x^2)} & Y \\
X & \xrightarrow{\mu x} & \emptyset & \qquad & Y & \xrightarrow{\mu y} & \emptyset
\end{array}
\right\}
$$

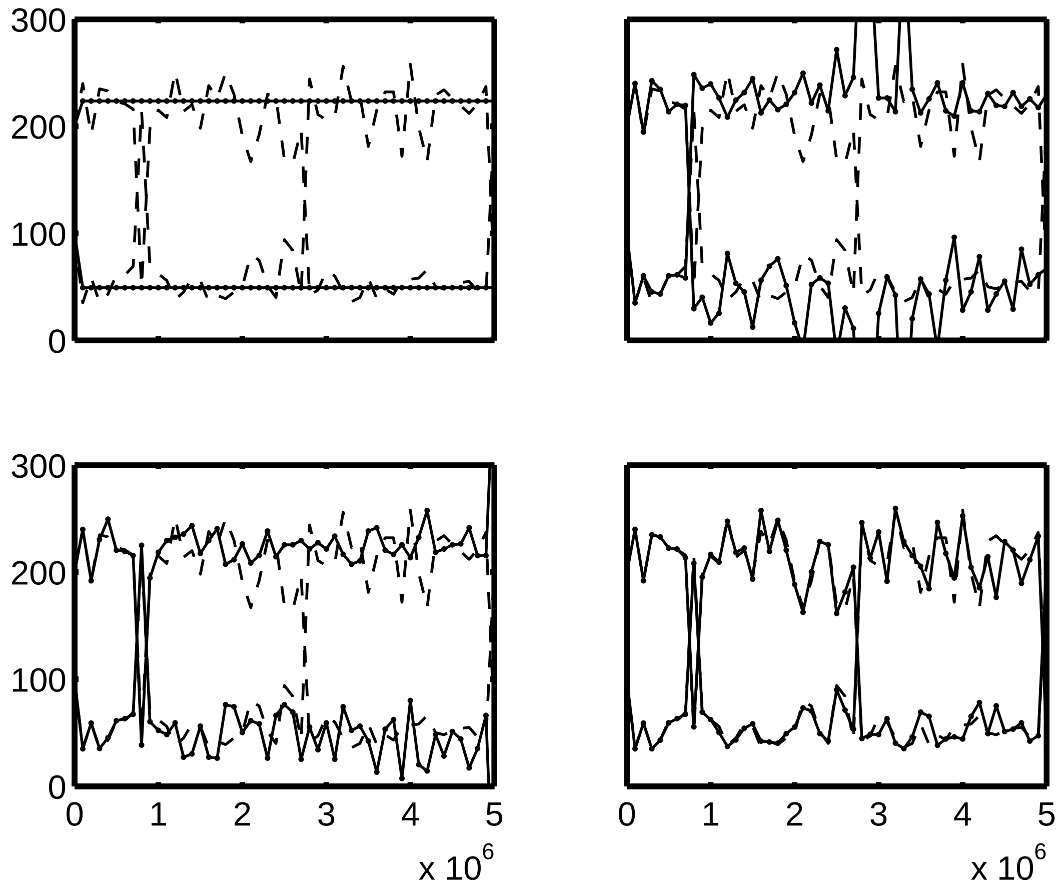


Figure 1: Solid: parallel solution after 0, 1, 2 and 4 iterations.

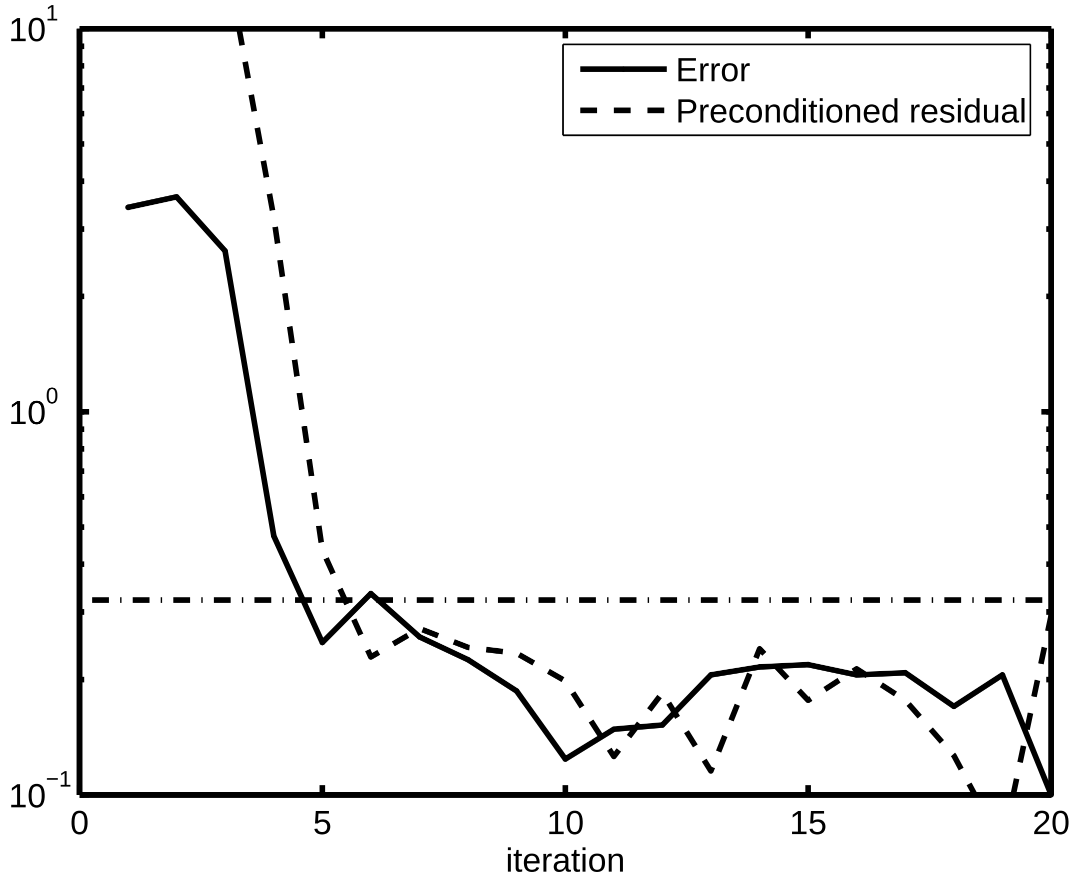


Figure 2: Dash-dot: propensities perturbed by $\pm 1\%$.

Homogenization of disparate rates

Fast dimerization/slow isomerization:

$$\left.\begin{array}{rcl} X_1 + X_1 & \overset{1/\varepsilon}{\rightleftharpoons} & X_2 + X_2 \\ X_2 & \overset{1}{\rightleftharpoons} & Y_2 \\ Y_2 + Y_2 & \overset{1/\varepsilon}{\rightleftharpoons} & Y_1 + Y_1 \end{array}\right\}$$

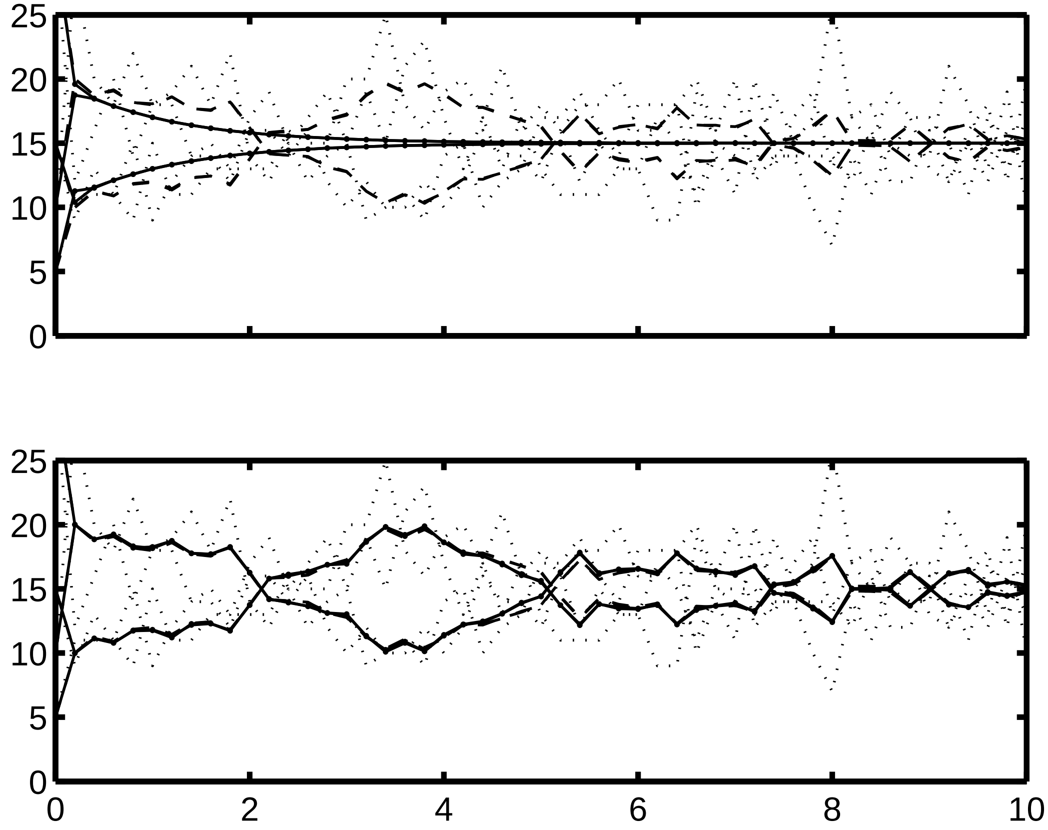
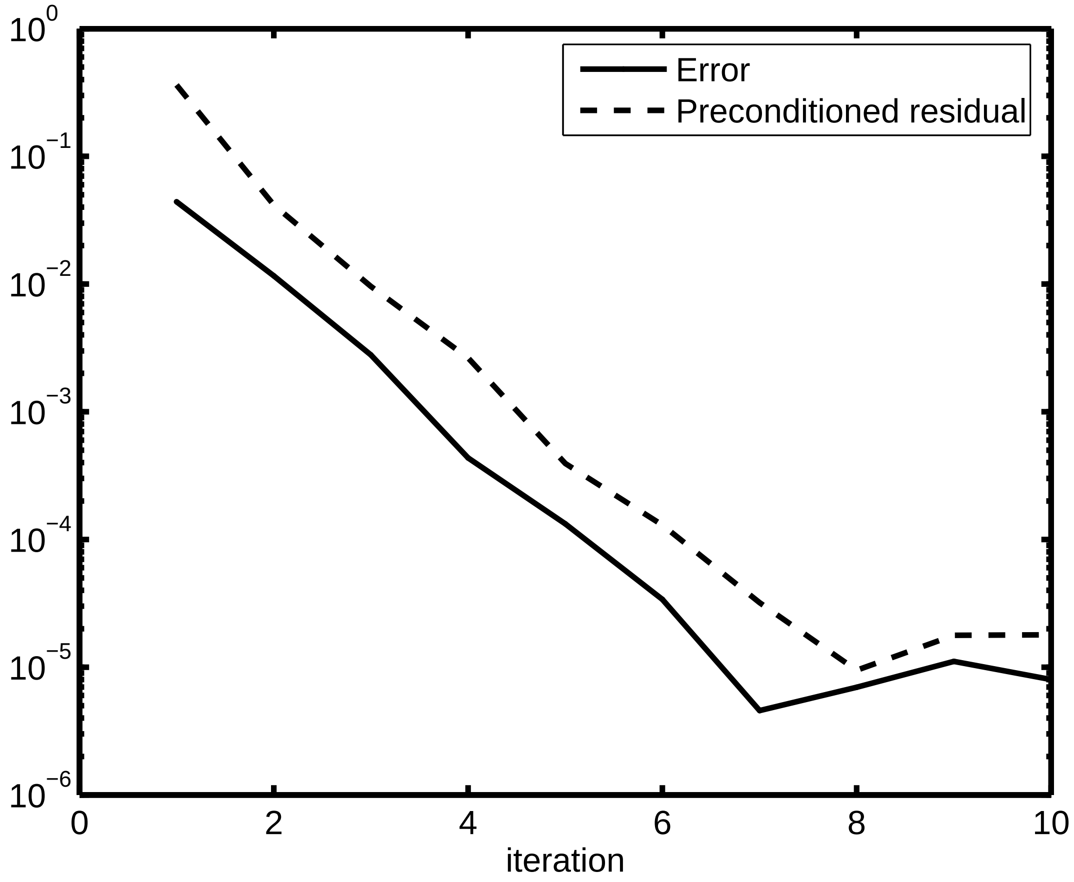


Figure 3: Original (dot) and homogenized (dash) trajectories. In solid: parallel solution (0 and 1 iteration).

Disparate rates



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 *solution* rather than a homogenized *equation* — generalizes to other types of SDEs
  -parareal applied to stiff stochastic equations (previously unclear)
- A *fix* number of parareal iterations can be thought of as a stochastic/deterministic *hybrid* with very few parameters
- Yet to do: better efficiency through multilevel parallelism, analysis of open system