Computational Modeling of Reaction-Diffusion Systems: From particle to hydrodynamic simulations

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CEA Saclay Seminar
July 2014

Outline

Reaction-Diffusion Particle Models

- Systems of diffusing particles that react with other particles upon collision are a common model in computational materials science: **reaction-diffusion models**.
- Examples include: *diffusion-limited chemical reactions, signal transduction in cells, radiation damage in metals, dopant implantation in semiconductors, epitaxial deposition and growth of thin films, population dynamics*, etc.
- Continuum models are often unable to correctly capture some key property, notably the **strong heterogeneity** in space/time (e.g., *clustering*), and intrinsic **fluctuations** (e.g., *nucleation*)
- **Continuous-Time Markov Chain** models are an attractive but *expensive* alternative:
  A collection of Brownian hard spheres that diffuse through a homogeneous continuum and react upon collision with other particles or surfaces.

Example: Chemotaxis in *E. Coli.*

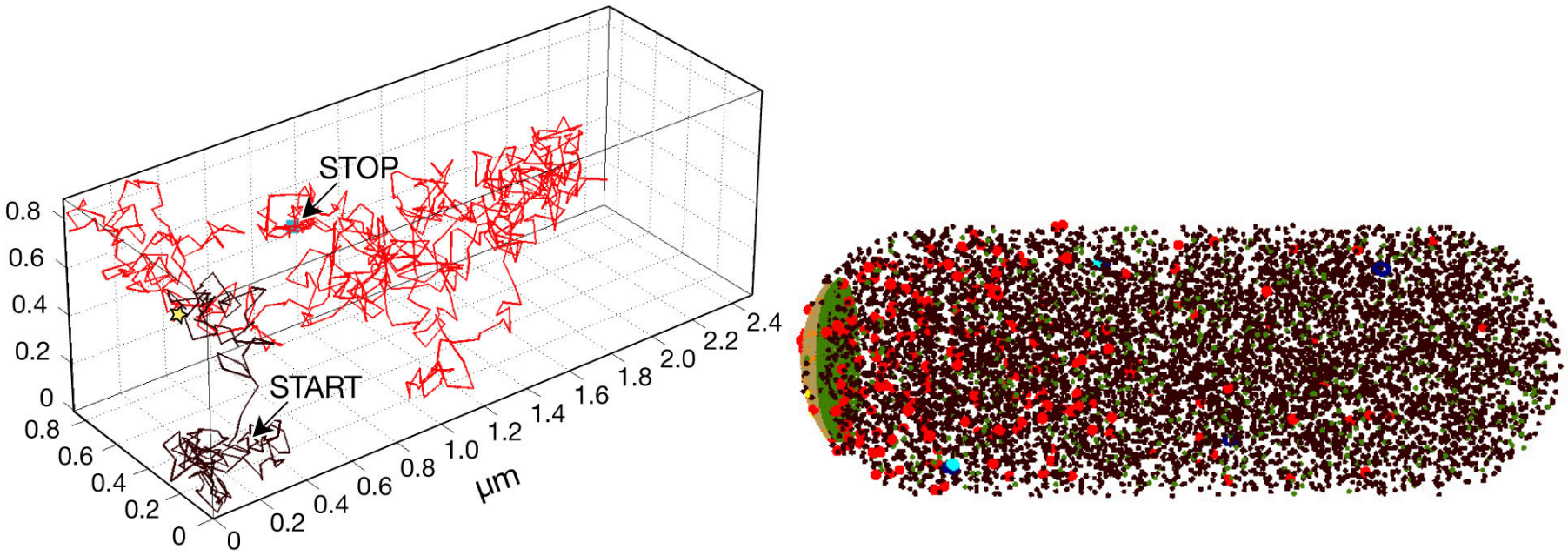


Figure: **Bacterial chemotaxis** as studied using *Smoldyn* by Karen Lipkow and Steven Andrews [*J. Bacteriol. 187(1):45-53, (2005)*]

Example: Radiation Damage

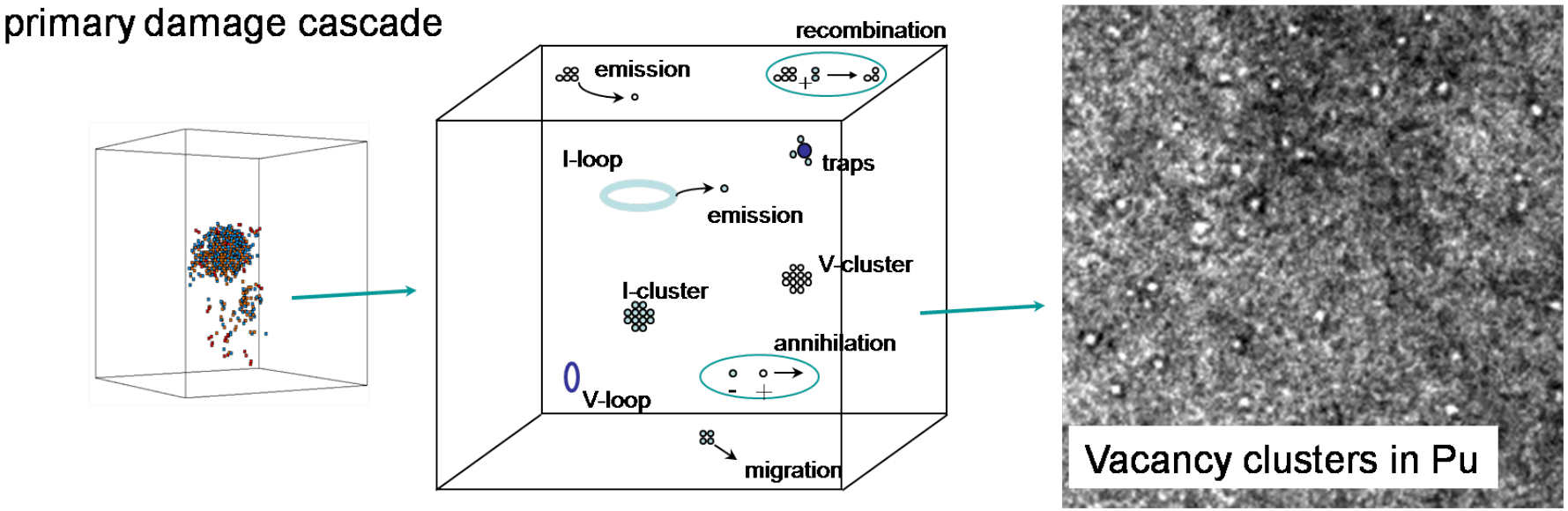
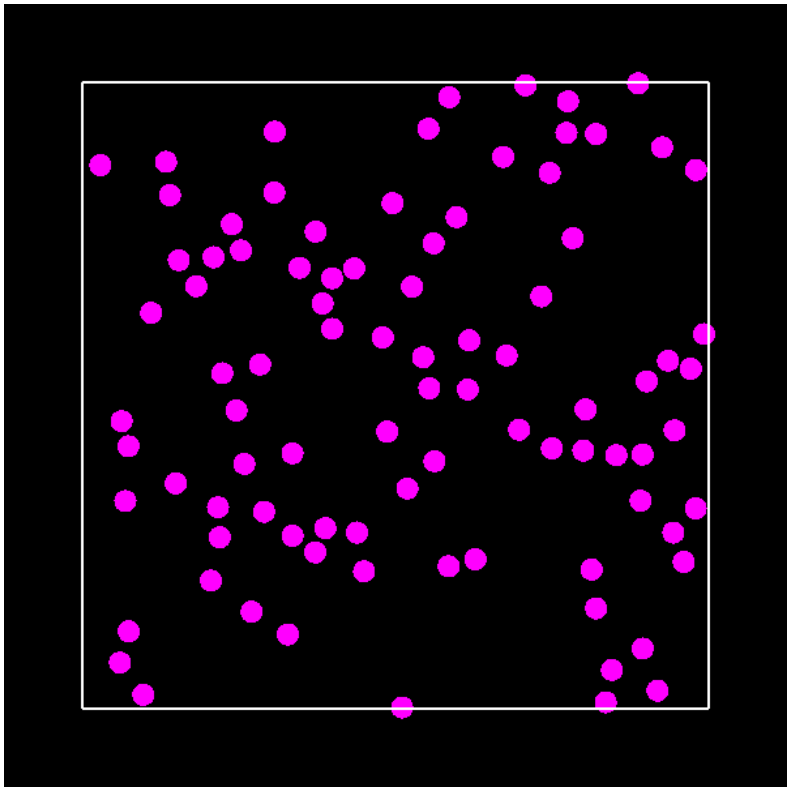


Figure: Defect creation and clustering in metals during irradiation.

Diffusion Kinetic Monte Carlo

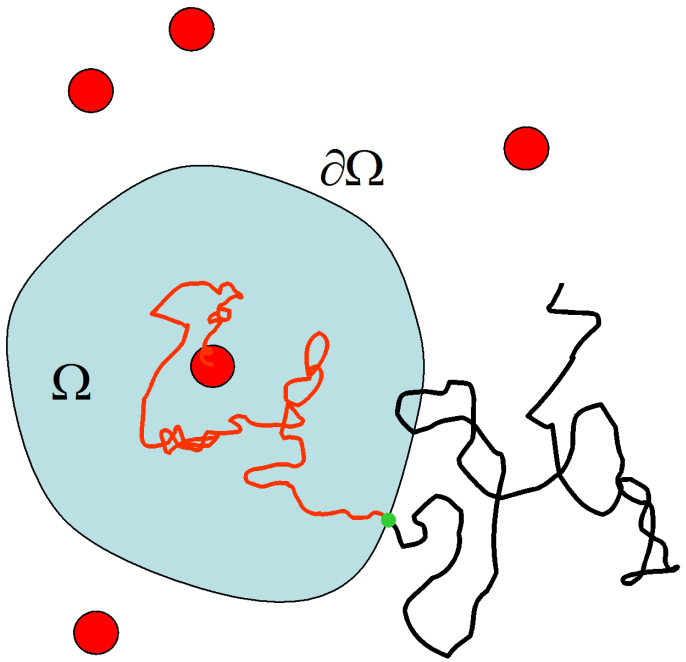


(MNG)

- Some or all unit events are diffusion hops: a set of N hard objects walking randomly on a lattice or in continuum space.
- Upon collision particles *react* (**collision events**).
- Example: Diffusion-controlled annihilation $A + A \to 0$.
- Great many diffusion hops necessary to bring particles to collisions at low density.

Traditional *synchronous* $n-$fold event-driven algorithm (BKL). Other types of Poisson events (birth, decay, boundary, etc.) are easy to handle.

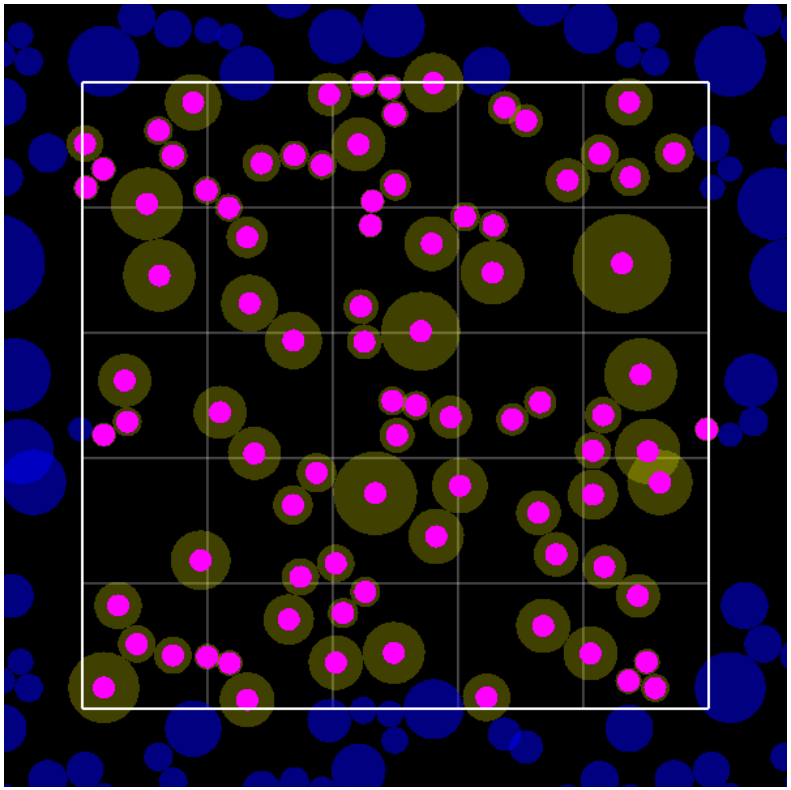
Green's Function Diffusion Theory



- Given a region of space Ω, one can determine the probability distributions for when and where (on $\partial\Omega$) a particle will first leave that region (*first-event prediction*).
- Given that a particle has not yet left that region, one can determine the probability of finding the particle at some point inside the region at a given time (*no-event propagation*).

For pairs of particles, reduce to two *independent* **center-of-mass** and **difference walkers**.

First Passage Kinetic Monte Carlo (FPKMC)



(MNG)

- Construct disjoint protective regions (cubes, spheres) at $t = 0$.
- Main events are **(super)hops** to $\partial\Omega$. For each walker (particle or pair) **randomly** draw first passage time from the appropriate PDF.
- Find the earliest time in the queue, propagate the particle/pair to boundary/collision, construct a new protective region, insert back into queue with a new event time, repeat [1, 2]!

Advantages of the Algorithm

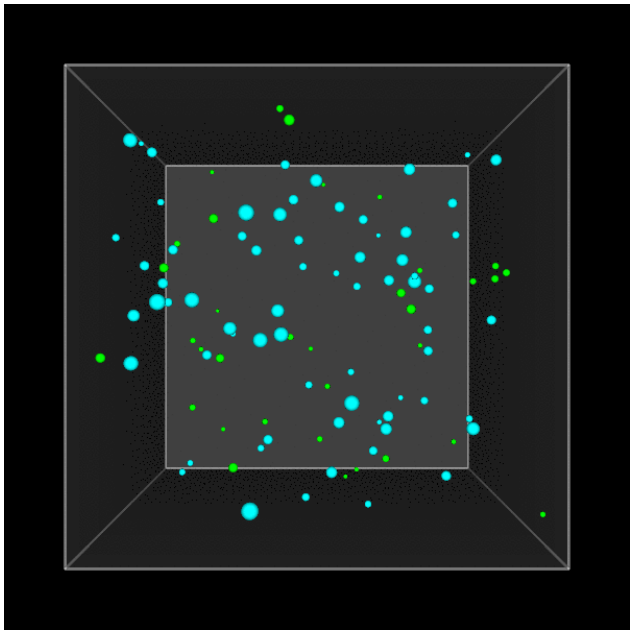
- The FPKMC algorithm is **exact** for continuous diffusion problems because it breaks the hard N-body problem into tractable one- and two-body problems.
- It is the first use we know of of **time-dependent Green's functions**.
- The algorithm automatically adjusts to variable timescales: **multiscale**.
- We have a code that implements different types of reactions (annihilation, coalescence, chemical reactions, decay/emission, hard-sphere repulsion).

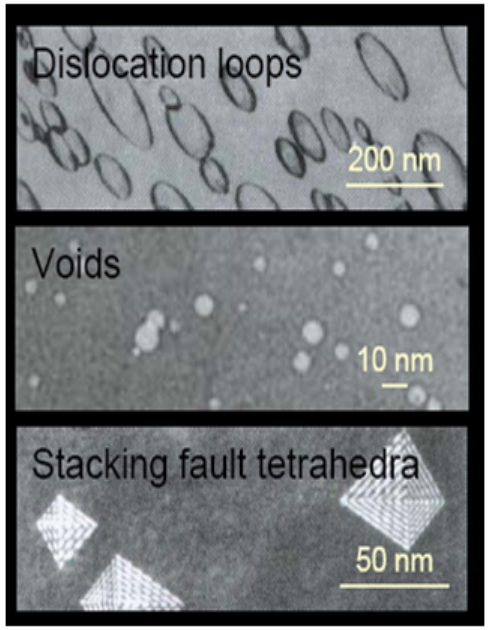
Disadvantages of the Algorithm

- The method is significantly more **complicated** to implement than BKL KMC and it requires analytical solutions (1-body and 2-body problems).
- Multi-particle reactions cause complications or slowdown (ex., nearly triple collisions).
- One can combine the asynchronous super-hops with local synchronous small hops in a **mixed time-driven/event-driven approach** [3].
- FPKMC can be viewed as a **general-purpose accelerator** that brings particle within interaction range quickly, after which application-specific handling should take over.

FPKMC for Radiation Damage

- Diffusion-reaction model for **radiation damage in metals**: diffusing and reacting *vacancies* and *interstitials* and their clusters





- A Kinetic Monte Carlo (KMC) simulation faithfully follows every **atomistic event**: *cascade insertion*, *diffusion hop*, *annihilation*, *recombination*, *clustering*, *dissociation*, *trapping*, *escape*, etc [4].

Radiation Damage KMC Model

- Very simple additive hard-sphere model for **testing** purposes, based on work by Barbu *et al*.
- **Species**:
  - *monomers*, including highly-mobile interstitials (I) and less-mobile vacancies (V), with diffusion coefficient
$$D_1 = D_0 e^{-E_m/kT}$$
  - mobile *cluster species*, including dimers (I_2 and V_2) and trimers (I_3 and V_3), with radius
$$R_c \sim R_0 + (R_1 - R_0)c^{1/3}$$
  - *immobile* species representing clusters larger than any of the mobile species (I_c and V_c)
  - *Frenkel pairs* (IV), inserted randomly with some rate

Model contd.

- **Reactions**:
  - *Coalescence*: $I + I \to I_2$ or $V + V_3 \to V_{c=4}$
  - Partial *annihilation*: $I_2 + V_{c=4} \to V_2$
  - Decay or *emission*: $V_{c=5} \to V_{c=4} + V$, or $I_2 \to I + I$, with rate

$$\Gamma_c = \Gamma_0 D_1 a^{-2} c^{2/3} e^{-E_b(c)/kT},$$

$$E_b(c) = E_f + [E_b(2) - E_f] \frac{c^{2/3} - (c-1)^{2/3}}{2^{2/3} - 1}.$$

Validation

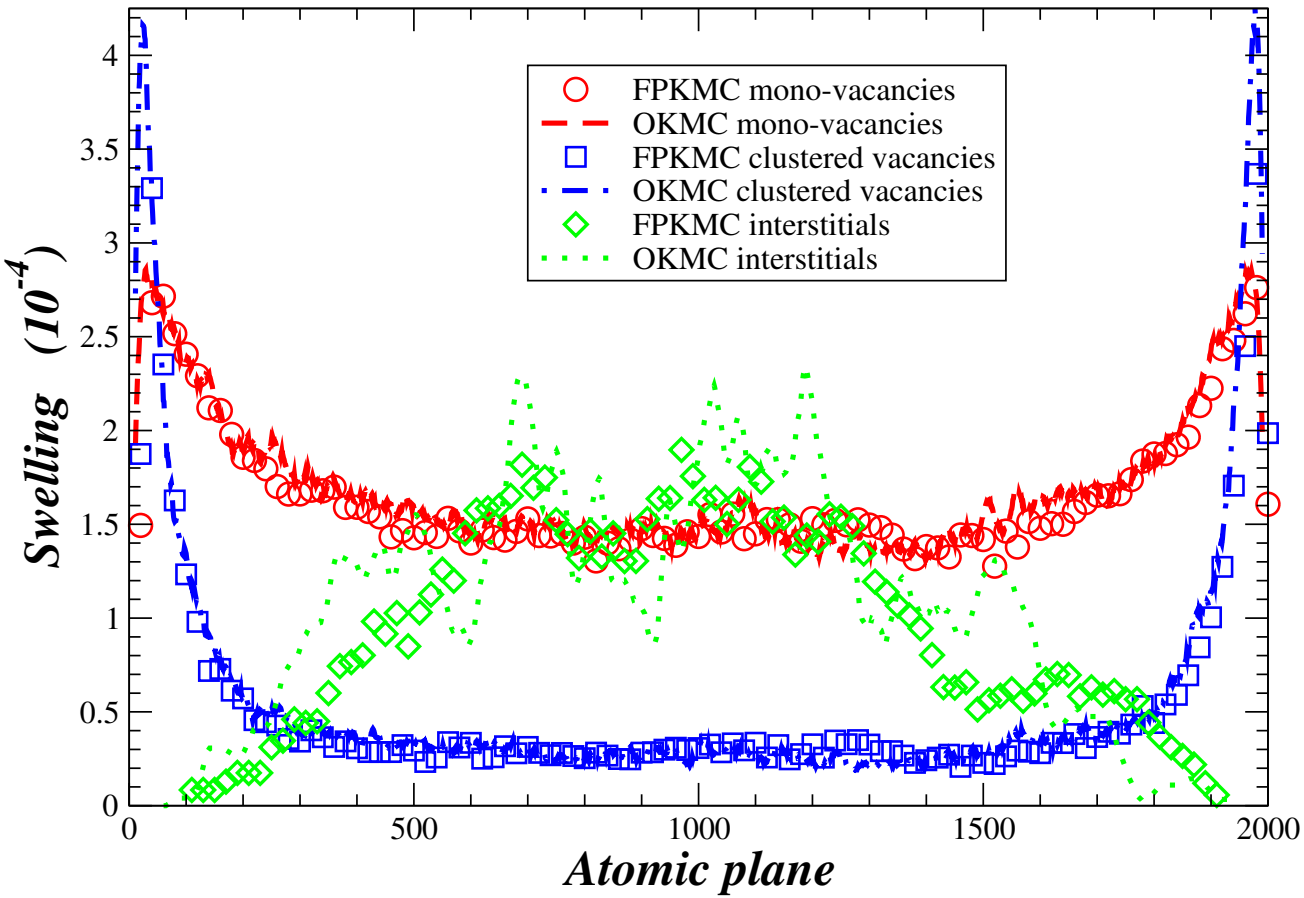


Figure: Comparison of the density profile between FPKMC (symbols) and CEA OKMC code from LAKIMOCA (lines) simulations of a $0.287\mu m$-thick film of α-iron subjected to 120 seconds of electron radiation at a temperature $T = 200^{o}C$.

Extensions of FPKMC

- Recently the group of Linda Petzold has extended first-passage to **lattice models** (discrete space), notably, surface growth [5].
- The groups of Paul Atzberger and Samuel Isaacson have recently extended FPKMC to handle **external biasing potentials** [6].
- First-passage problem out of the protective domain U [6]:

$$\partial_t \rho = D\boldsymbol{\nabla} \cdot \left(\frac{\rho}{k_B T} \boldsymbol{\nabla} V + \boldsymbol{\nabla} \rho \right) \text{ and}$$

$$\rho\left(\mathbf{r}, 0\right) = \delta\left(\mathbf{r} - \mathbf{r}_0\right) \text{ and } \rho\left(\partial U, t\right) = 0,$$

is hard to solve analytically so in [6] a lattice discretization is used.

Continuum Reaction-Diffusion Models

- If we have **many small diffusing particles** that react with (nearly) **stationary large sinks and sources** we can spatially coarse-grain the particle description and use a continuum concentration field $c(\mathbf{r}, t)$ for each species.
- It is important to note that this "continuum" description can also account for spatial fluctuations (fluctuating hydrodynamics, discussed later).
- Consider a diffusing species that reacts upon touching the surface of a sphere $\mathcal{S}$ (**Smoluchowski model**), henceforth called a particle.
- Diffusion equation for the concentration of the species $c(\mathbf{r}, t)$,

$$\partial_t c = \chi \boldsymbol{\nabla}^2 c + s(\mathbf{r}, t) \text{ in } \Omega \setminus \mathcal{S}, \tag{1}$$

$$\chi (\mathbf{n} \cdot \boldsymbol{\nabla} c) = k\, c \text{ on } \partial\mathcal{S}, \tag{2}$$

where k is the *surface* reaction rate.

Minimally-Resolved Model

- Often KMC similar to FPKMC ("walk on spheres") is used to solve this equation by simulating explicit trajectories of the diffusing particles: expensive.
- We have developed a **minimimally-resolved** continuum modeling approach that solves the diffusion PDE using **standard grid methods**.
- We do not care about the fine details of the concentration around a particle, and only account for an effective source-sink.
  We will call our particles "**blobs**" since they can be thought of as a sort of diffuse sphere.
- Take an **Immersed Boundary** (IB) method approach and describe the interaction using a localized smooth **kernel** $\delta_a(\Delta\mathbf{r})$ with compact support of size a (integrates to unity).

Local Averaging and Spreading Operators

- The reactant concentration field $c(\mathbf{r}, t)$ is extended over the whole domain, *including* the particle interior. Let the position of the spherical particle be $\mathbf{q}$.
- The **local averaging operator** $\mathbf{J}(\mathbf{q})$ averages the concentration inside the particle to estimate the local concentration

$$c_{\mathbf{q}}(t) = \int \delta_a(\mathbf{q} - \mathbf{r})\, c(\mathbf{r}, t)\, d\mathbf{r} \equiv [\mathbf{J}(\mathbf{q})]\, c.$$

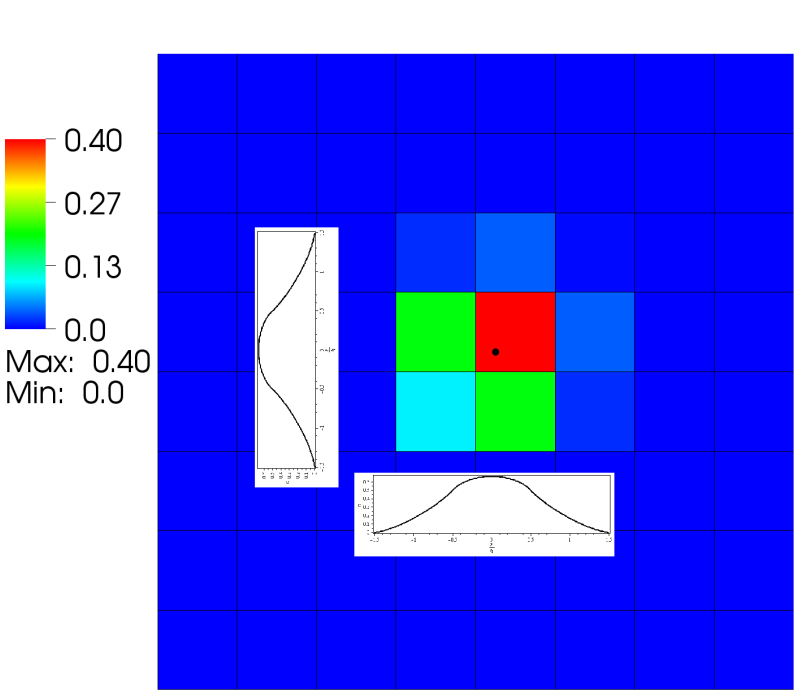
- The reverse of local averaging is accomplished using the **local spreading operator** $\mathbf{S}(\mathbf{q})$,

$$\lambda_{\mathbf{q}}(\mathbf{r}, t) = \lambda(t)\, \delta_a(\mathbf{q} - \mathbf{r}) \equiv [\mathbf{S}(\mathbf{q})]\, \lambda.$$

- For multi-particle problems, define **composite** local averaging and spreading **operators**,

$$(\mathcal{J} c)_i \equiv [\mathbf{J}(\mathbf{q}_i)]\, c \quad \text{and} \quad \mathcal{S}\boldsymbol{\lambda} = \sum_{i=1}^{N} [\mathbf{S}(\mathbf{q}_i)]\, \lambda_i.$$

Discrete Averaging and Spreading



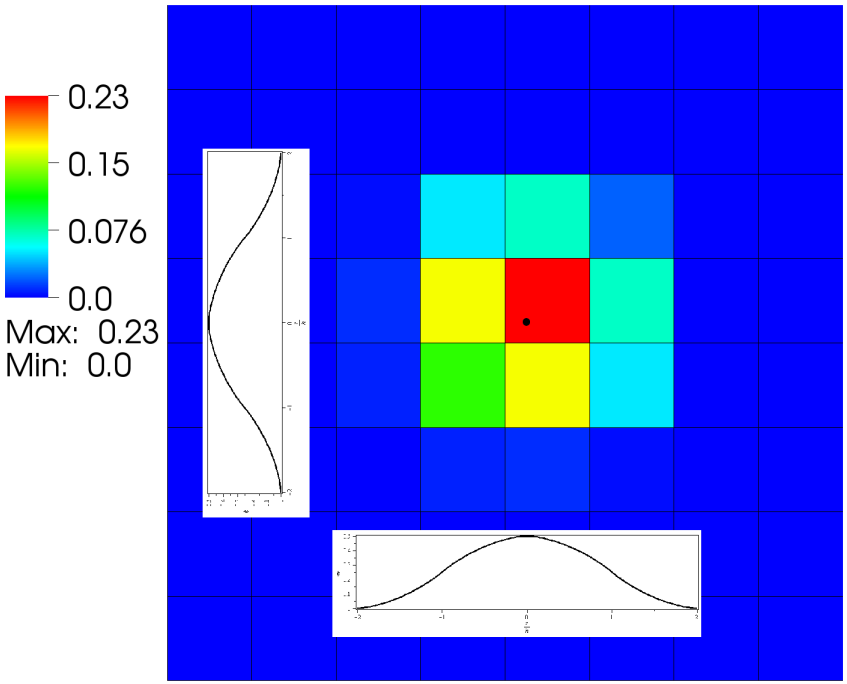


Figure: Illustration of discrete kernel functions used to represent the interaction between the particles and the grid used to solve the concentration equation. (*Left panel*) The three-point ($w = 3$) Peskin kernel φ_3. (*Right panel*) The four-point ($w = 4$) Peskin kernel φ_4.

Reactive Blobs

- **Smoluchowski** model:

$$\partial_t c = \chi \boldsymbol{\nabla}^2 c + s(\mathbf{r}, t) \text{ in } \Omega \setminus \mathcal{S}, \tag{3}$$

$$\chi (\mathbf{n} \cdot \boldsymbol{\nabla} c) = k\, c \text{ on } \partial\mathcal{S}, \tag{4}$$

- **Reactive-blob** model [7]:

$$\partial_t c = \chi \boldsymbol{\nabla}^2 c - \kappa \left[\int \delta_a (\mathbf{q} - \mathbf{r})\, c(\mathbf{r}, t)\, d\mathbf{r} \right] \delta_a (\mathbf{q} - \mathbf{r}) + s,$$

or compactly, continuum or discrete,

$$\partial_t c = \chi \boldsymbol{\nabla}^2 c - (\boldsymbol{\mathcal{S}} \boldsymbol{\kappa} \boldsymbol{\mathcal{J}})\, c + s, \tag{5}$$

where $\kappa = 4\pi k a^2$ is the overall reaction rate.

Spatio-Temporal Discretization

- After temporal discretization using a backward Euler step for $\mathbf{c}$,

$$\frac{\mathbf{c}^{n+1}-\mathbf{c}^{n}}{\Delta t}=\chi\mathbf{L}\mathbf{c}^{n+1}-\boldsymbol{\mathcal{S}}^{n}\boldsymbol{\kappa}\boldsymbol{\mathcal{J}}^{n}\mathbf{c}^{n+1}+\mathbf{s}^{n}, \tag{6}$$

  which requires solving a linear system of the form

$$\left(\Delta t^{-1}\mathbf{I}-\chi\mathbf{L}+\boldsymbol{\mathcal{S}}\boldsymbol{\kappa}\boldsymbol{\mathcal{J}}\right)\mathbf{c}=\mathbf{B}\mathbf{c}=\mathbf{g}. \tag{7}$$

- If $\Delta t\to\infty$ the backward Euler method approaches a **steady-state solver**.
- We have developed **multigrid-based iterative solvers** to solve the reaction-diffusion equation (7) [7].

Diffusion-Limited Regime

- In the diffusion-limited case, $\kappa_i \to \infty$ and the boundary condition becomes absorbing,

$$c = 0 \text{ on } \partial\mathcal{S}.$$

- The reactive blob equations approach a **saddle-point** (constrained) **problem**:

$$\begin{aligned} \partial_t c &= \chi \boldsymbol{\nabla}^2 c - \boldsymbol{\mathcal{S}}\boldsymbol{\lambda} + s, \\ \text{s.t. } \boldsymbol{\mathcal{J}} c &= 0, \end{aligned} \tag{8}$$

  where the sink strengths $\boldsymbol{\lambda} \leftarrow \boldsymbol{\kappa}\boldsymbol{\mathcal{J}} c$ are a Lagrange multiplier corresponding to the constraint.

- Numerically solving the saddle-point system is hard but recently we have developed efficient preconditioners that can handle up to $10K$ blobs (particles, sinks or sources) in three dimensions.

Smoluchowski problem

- For an isolated sphere of radius a immersed in a reservoir of the reactant with concentration c_∞,

$$c(r) = c_\infty \left(1 - \frac{1}{1+P}\frac{a}{r}\right). \tag{9}$$

- The speed of diffusion vs reaction is measured by the dimensionless number $P = \chi/(ka) = \mathrm{Da}^{-1}$:
  The reaction is diffusion-limited if $P \ll 1$, and reaction-limited if $P \gg 1$.
- The total rate of consumption of the reactant is

$$\lambda = \frac{4\pi a \chi c_\infty}{(1+P)}. \tag{10}$$

Example: Numerics

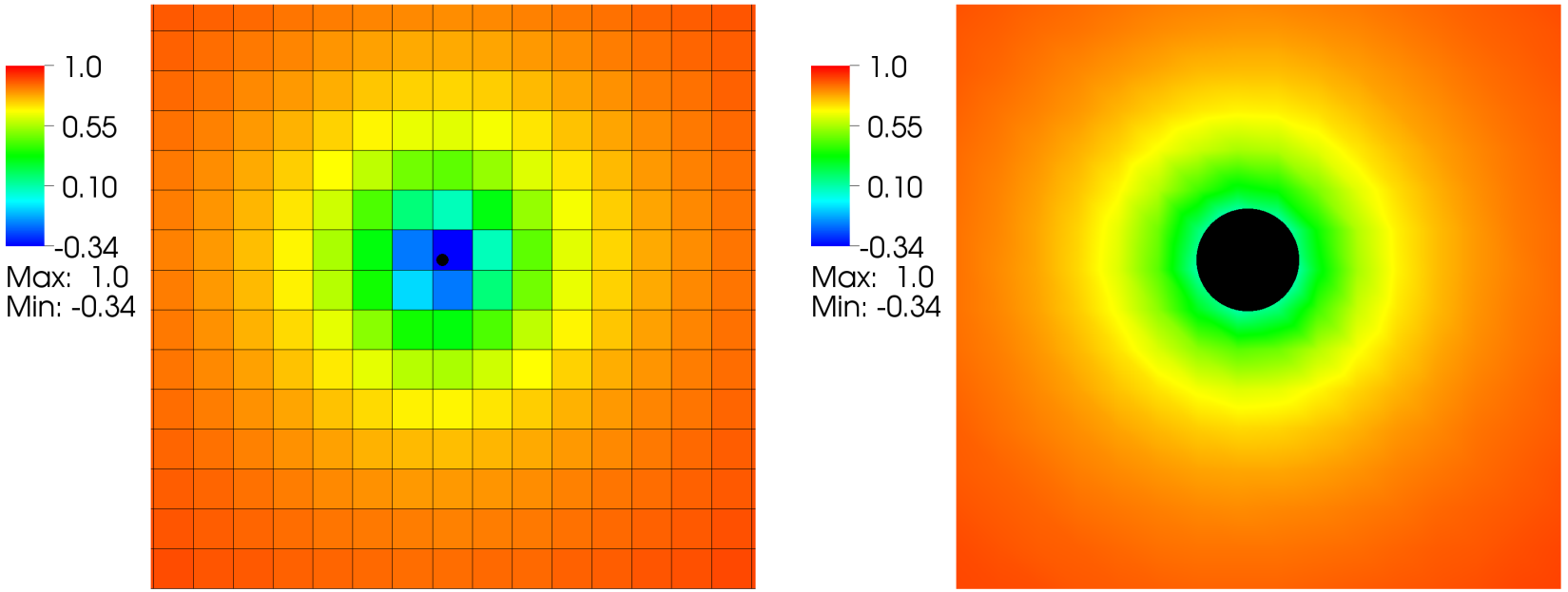


Figure: Ratio $c(\mathbf{r})/c_\infty$ for a single blob placed at the center a large cubic box with the concentration at the boundaries fixed to c_∞.

Example contd.

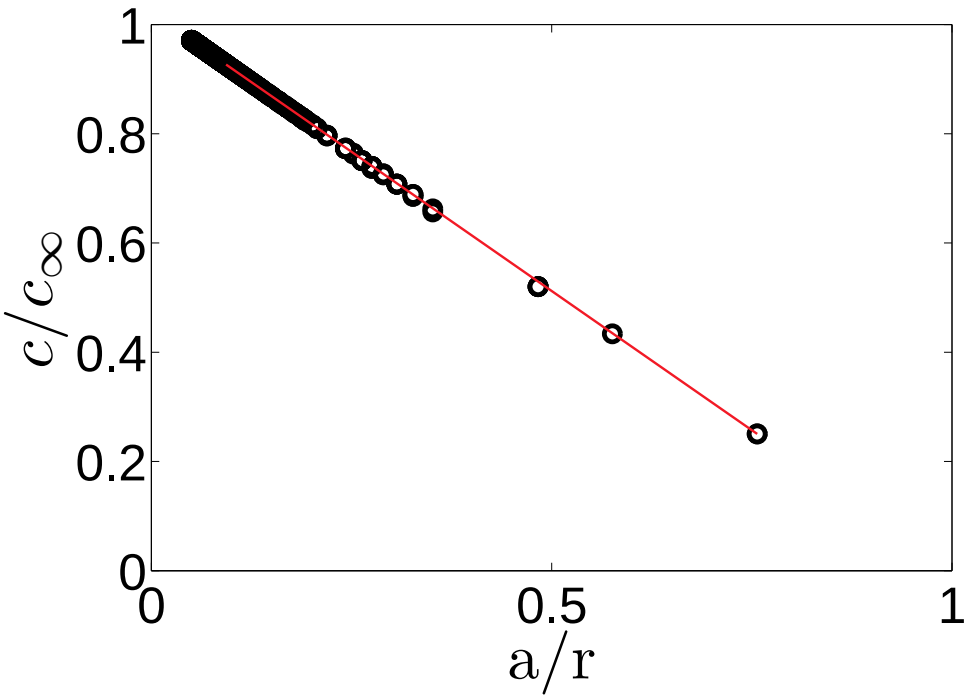


Figure: Decay of the concentration around a blob in a cubic domain of 100^3 grid cells with Dirichlet boundary conditions.

Reaction-Diffusion Processes

- Let us now consider the case when the small diffusing particles react with each other, but there is enough particles to allow for a description in terms of concentration fields.
- There will be a number of **species** and **reaction channels** converting species:

$$\left(\vartheta_1^+, \ldots, \vartheta_n^+\right) \leftrightarrow \left(\vartheta_1^-, \ldots, \vartheta_n^-\right).$$

  The standard **stochiometric coefficients** are $\boldsymbol{\nu} = \boldsymbol{\vartheta}^- - \boldsymbol{\vartheta}^+$ (negative for reactants), and mass conservation requires that $\sum_k \nu_k m_k = 0$, where **m** are the molecular masses.
- **Cluster dynamics** modeling of radiation damage falls in this category (each species is a given cluster size), as do **chemical reactions**.
- We can also account for **fluctuations** by writing a **Master Equation** (ME) description of the reactions.
- One can use (asynchronous or synchronous) **KMC algorithms** to generate trajectories according to the ME (Gillespie SSA, first reaction, next reaction, etc.).

Rate Equations

- For large concentrations we expect deterministic **law of mass action** (LMA) kinetics with rate $r(\mathbf{n})$,

$$\partial_t \mathbf{n} = \left(k^+ \prod_k^{\text{reac}} n_k^{\vartheta_k^+} - k^- \prod_k^{\text{prod}} n_k^{\vartheta_k^-} \right) \boldsymbol{\nu} = \left(r^+(\mathbf{n}) - r^-(\mathbf{n}) \right) \boldsymbol{\nu} = r(\mathbf{n}) \boldsymbol{\nu},$$

  where $\mathbf{n}(t) = \mathbf{N}(t)/V$ is the number density and V is the volume of the "**well-stirred vessel**" containing $\mathbf{N}(t)$ molecules.

- For a single uni-directional reaction channel, KMC solves the non-Gaussian SDE,

$$d\mathbf{n} = V^{-1} \mathcal{P}(V r(\mathbf{n}) dt) \boldsymbol{\nu},$$

  where $\mathcal{P}(X)$ is a Poisson random variable with mean X.
  Note that the random increments are most of the time zero and occasionally one or so (inefficient – use KMC/SSA instead!)

Chemical Langevin Equation

- If the populations are large, $\mathbf{N} \gg 1$ and $V \to \infty$, we can replace the Poisson variable by a Gaussian random variable (Kurtz theorem) and write

$$d\mathbf{n} = \mathcal{N}\left(r\left(\mathbf{n}\right) dt,\ V^{-1}\, r\left(\mathbf{n}\right) dt\right) \boldsymbol{\nu}$$

  where $\mathcal{N}\left(\mu,\, \sigma^2\right)$ denotes a normal variable of mean μ and variance σ^2.

- This is the **Chemical Langevin Equation** (CLE) of Gillespie

$$d\mathbf{n} = \left[r\left(\mathbf{n}\right) dt + \sqrt{V^{-1} r\left(\mathbf{n}\right) dt}\, \mathcal{N}\left(0,\, 1\right)\right] \boldsymbol{\nu},$$

  which is consistent with a standard SODE driven by Brownian motion.

- Unfortunately, the CLE has limitied utility: It **only** describes **short time** dynamics. The CLE **fails** to correctly describe **long-time** dynamics, including reproducing the correct steady-state (equilibrium) distribution or rare events (transitions among metastable states).

Langevin Approximation

- For a reversible reaction we get the **Ito SODE** driven by the white-noise process $\mathcal{W}(t)$,

$$\frac{d\mathbf{n}}{dt} = \left[\left(r^+(\mathbf{n}) - r^-(\mathbf{n}) \right) + (2V)^{-\frac{1}{2}} \left(\frac{r^+(\mathbf{n}) + r^-(\mathbf{n})}{2} \right)^{\frac{1}{2}} \mathcal{W}(t) \right] \boldsymbol{\nu}.$$

- It can be shown that if the original ME obeys detailed balance with respect to a suitable distribution, there is **only one** Gaussian SODE that is also in detailed balance with the right distribution, and correctly reproduces very long-time dynamics (including rare events).
- This SODE was first proposed by Hanggi/Grabert/Talkner [8] and relies on the **kinetic** stochastic interpretation:

$$\frac{d\mathbf{n}}{dt} = \left[\cdots + (2V)^{-\frac{1}{2}} \left(\frac{r^+(\mathbf{n}) - r^-(\mathbf{n})}{\ln r^+(\mathbf{n}) - \ln r^-(\mathbf{n})} \right)^{\frac{1}{2}} \diamond \mathcal{W}(t) \right] \boldsymbol{\nu}.$$

Langevin Approximation

- The key differences between the two Langevin approximations is that the CLE uses an **arithmetic mean** of $r^+(\mathbf{n})$ and $r^-(\mathbf{n})$ and is **Ito**, while the Hanggi equation uses the **logarithmic mean** and is **kinetic**.
  This makes a big difference in terms of long-time dynamics!
- Note that for the Hanggi equation to apply the reaction has to be **reversible** (otherwise there cannot be detailed balance and thermodynamic equilibrium).
- But both Langevin equations seem to have **serious deficiencies** and in general it is not clear a Langevin approximation is suitable.
- The idea of τ-**leaping** is to generate Poisson $V^{-1}\mathcal{P}(V\,r(\mathbf{n})\,\tau)$ instead of Gaussian increments, and otherwise pretend one is solving a standard SODE.
- Perhaps one can replace Poisson (integer) variables with something easier to generate efficiently (e.g., continuous approximation)?

Fluctuating Hydrodynamics

- One can include diffusion, and more generally full hydrodynamics in the description: **fluctuating hydrodynamics**.
- As an example consider the simple **dimerization** reaction

$$2A \underset{k}{\overset{k'}{\rightleftharpoons}} A_2$$

call c_1 the concentration of A and c_2 of A_2 (not independent!).

- For a spatially-extended system, with diffusion, the dynamics can (perhaps) be described by the **spatial CLE**

$$\begin{aligned}\partial_t c_2(\mathbf{r},t) = \left(kc_1^2 - k'c_2\right) + \left(kc_1^2 + k'c_2\right)^{\frac{1}{2}} \mathcal{W}(\mathbf{r},t) \quad \text{reaction} \\ + \chi \boldsymbol{\nabla}^2 c_2 + \boldsymbol{\nabla}\cdot\left(\left(2\chi c_2\right)^{\frac{1}{2}} \mathcal{Z}(\mathbf{r},t)\right) \quad \text{diffusion}\end{aligned}$$

or the related Hanggi-type equation (work in progress).

Conclusions

- **Asynchronous event-driven algorithms** like FPKMC are powerful tools to deal with systems with vastly disparate time scales, but they require lots of precomputed analytical solutions.
- Future: Account for **long-ranged interactions** (e.g., electrostatic or elastic) *approximately* to model radiation damage modeling without bias factors.
- Future: When very fast species (e.g., interstitials) are present they slow down even event-driven algorithms: multiscale methods to utilize this **separation of time-scales**.

contd.

- After **spatial coarse-graining** over a reference volume V one can obtain reaction-diffusion (S)PDEs from the microscopic dynamics.
- When the reaction can be treated as a boundary condition on surfaces we can use **immersed boundary methods** to solve the diffusion equation.
- When the reactions are among diffusing particles themselves a combined ME/SPDE/CLE description applies: **reactive fluctuating hydrodynamics.**
- In general real-world problems such as radiation damage require **combining all approaches**.

References/Questions?

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