Incorporation of spatially extended bodies in MCell (TR&D1 and TR&D2)

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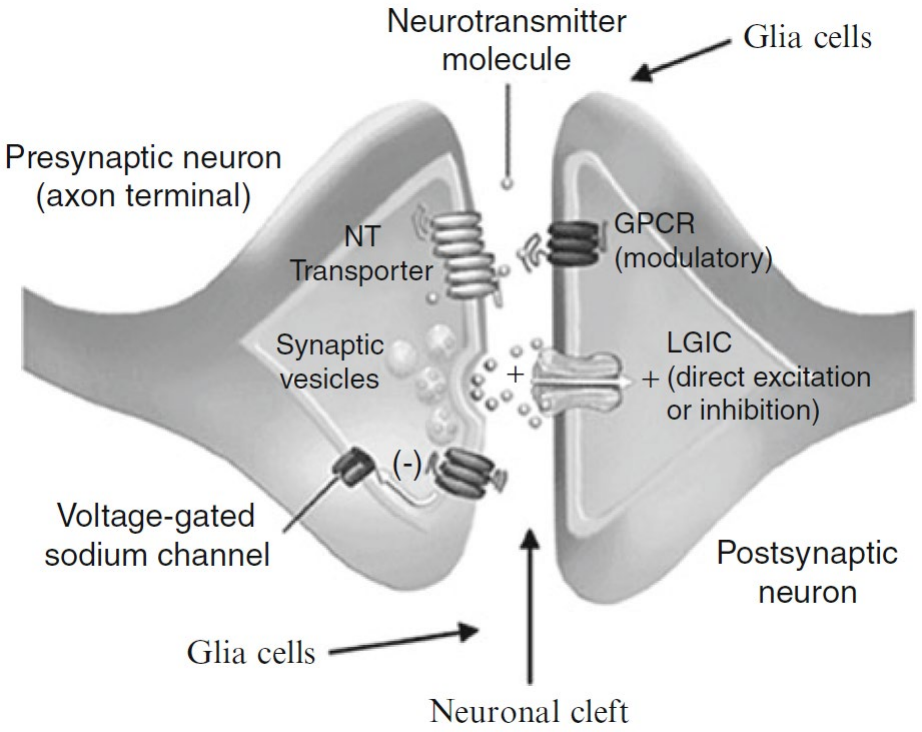
Current state of MCell:

In MCell[†], reaction-diffusion problems of a set of molecules are modelled as stochastic processes based on Monte-Carlo methods within a region, which can be either a surface of a (pre/post)-synaptic neuron, or the space bounded by those surfaces, the so-called neuronal cleft.

- Each molecule is modelled as a point-particle.
- Diffusion of each particle is governed by an overdamped stochastic dynamics.
- The orientation of the possible binding sites does not play a role (structural information).
- Non-binding particles passes through each other.
- Codes governing the motion of particles in $\mathbb{R}^2$ and $\mathbb{R}^3$ are separate.



[†] Kerr et al., SIAM J. Sci. Comput. 30 (6) (2009) 3126

Fig. Schuss Z. Brownian Dynamics at Boudaries and Interfaces, Springer, 2013.

- Definition of the problem:

  To capture the behavior of particles **with spatial extent** based on their rigid body features, dynamics, diffusion and hydrodynamic interactions.

  - Coarse-graining the structure of molecules: Representing them as rigid bodies. Depending upon their symmetries,
    - Spherical and (a)symmetric tops In $\mathbb{R}^3$.
    - Elliptic or circular thin discs in $\mathbb{R}^2$.

- How can we accomplish our goals (without a major change in the code base)?
  - Choice of integrators for 2d and 3d cases: Efficient, low relative error regarding the deterministic part.
  - Choice of the overlap algorithm for the collision detection: Efficient, reusable in 2d and 3d cases with less effort (not require to implement separate analytical geometric methods).
  - Computationally inexpensive way to do the scattering calculations during collision without effecting the concurrent stochastic events.

The geometric integrator for Langevin systems

- The Langevin type equations in the form of Ito of rigid bodies under the influence of conservative forces, hydrodynamic interactions, and thermal noise†:
  - Linear motion

$$dR^i = \frac{P^i}{m^i} dt$$

$$dP^i = f^i(R,Q)dt - \sum_{j=1}^{n} \xi_{tt}^{ij}(R,Q)\frac{P^i}{m^j} dt - \frac{1}{2}\sum_{j\bar{=}1}^{n} \xi_{tr}^{ij}(R,Q)A^T\left(Q^j\right)D^j\hat{S}^T\left(Q^j\right)\Pi^j dt - \frac{1}{2}\sum_{j=1}^{n} b_{tt}^{ij}(R,Q)dW^j + \sum_{j=1}^{n} b_{tr}^{ij}(R,Q)dW^j$$

where n is the number of rigid bodies, $R^i(0) = r^i$ and $P^i(0) = p^i$ are the center of mass coordinates and corresponding conjugate momenta for rigid body *i*, respectively.

$$b(r,q)b^T(r,q) = 2k_BT\xi(r,q)$$

†Davidchack et al. J. Chem. Phys. 2017.

The geometric integrator for Langevin systems

- Rotational motion

$$dQ^i = \frac{1}{4}\hat{S}(Q^i)D^i\hat{S}^T(Q^i)\Pi^i dt$$

$$d\Pi^i = F^i(R,Q)dt + \frac{1}{4}\hat{S}(\Pi^i)D^i\hat{S}^T(Q^i)\Pi^i dt$$

$$-\sum_{j=1}^{n}\check{S}(Q\hat{}i)\xi_{rr}^{ij}(R,Q)A^T(Q^j)D^j\hat{S}(Q^j)\Pi^j dt$$

$$-2\sum_{j=1}^{n}\check{S}(Q^i)\xi_{rt}^{ij}(R,Q)\frac{P^j}{m^j}dt$$

$$+2\sum_{j=1}^{n}\check{S}(Q^i)b_{rr}^{ij}(R,Q)dW^j + 2\sum_{j=1}^{n}\check{S}(Q)b_{tr}^{ij}(R,Q)dW^j$$

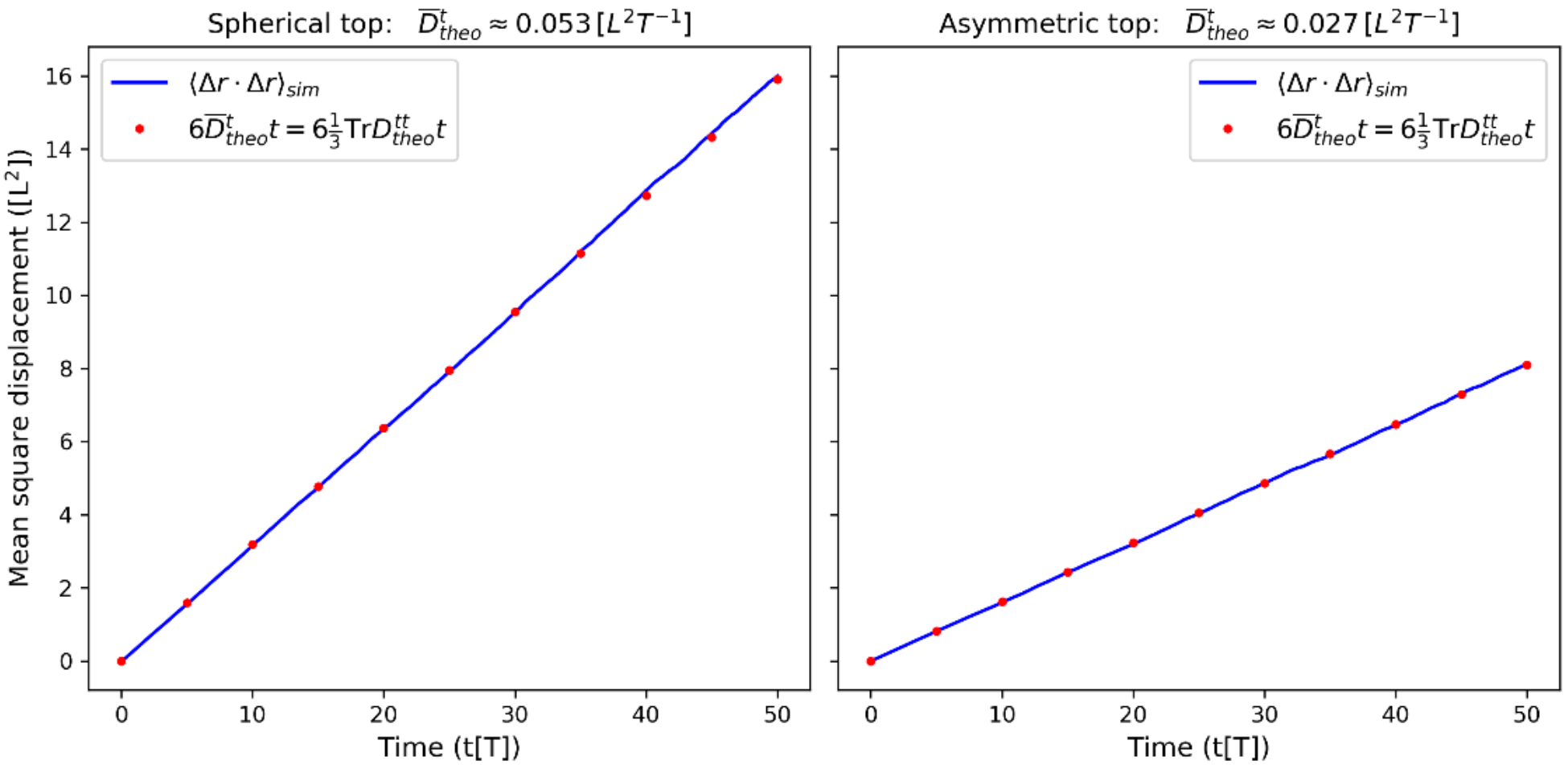
where $Q^i(0) = q^i$ and $\Pi^i(0) = \pi^i$ are the quaternions and the corresponding conjugate momenta, respectively.

$$q^{iT}\pi^i = 0, \qquad |q^i| = 1$$

†Davidchack et al. J. Chem. Phys. 2017.

Simulation results without any external forces

Parallelly generated ensemble of 10,000 independent trajectories for both a spherical and an asymmetric top. The simulation times and number of steps are chosen as 50 [T] and 10^4 respectively. Since the integrator has a natural over-damped limit, both bodies translationally diffuse with the overall average translational self-diffusion constants along their principal axes.



Collision Detection

- We should be careful when dealing with collision of bodies in stochastic processes.
- Stochastic kicks instantaneously change both the center of mass positions and the orientations of the bodies about to collide.
- We need two phases regarding the numerical integration:
  - Stochastic phase
  - Deterministic phase: Stochastic variables within the time interval Δt are assumed to be frozen, hence deterministic collision could be applicable.
- Continuously turning-on and -off the stochastic part of the integrator depending on the numerical integration scheme with the correct placement of the overlap algorithm!
- Possible issues:
  - Retroactive collision detection could be expensive (time bisection).
  - In 2d case, estimates of instantaneous translational and rotational pre-velocities while using overdamped equations could result in erroneous net impulse transfer, thereby effecting post-velocities and related coordinates.
  - Careless implementation of collision can result in increasing errors during long simulations, thus leading to a poor thermodynamic limit. In MCell, long simulation time is a sought-after feature.

Toy model in $\mathbb{R}^2$ - a rough collision detection

- 3 equivalent point-particles represented as circular discs to visualize a roughly estimated collision.
- Numerical integration scheme: First order point-particle overdamped integrator.
- Directions of their instantaneous velocities are estimated in terms of the changes in their coordinate vectors.
- Their speeds are assigned as the same and equal to the most probable speed w.r.t. 2d Maxwell-Boltzmann velocity distribution.
- Whenever an overlap is approximately detected within a predetermined threshold in the next frame, we calculate the impulse transferred during the collision to obtain the post-velocities. Then new coordinates are determined by those.
- Detected collisions are displayed with a “!!! BAM !!!” effect in the following video. Number of time steps are also shown during the animation.

Efficient overlap algorithm for ellipsoids

- An efficient overlap algorithm for rigid bodies should be implemented in two phases:
  - Broad-phase: No need to run an overlap check if the c.o.m. distances between a pair of bodies are larger than a spatial cutoff, i.e. they do not sense each other.
  - Narrow-phase: They are close enough to have a possible collision, therefore an overlap algorithm should be triggered for all such pairs.

- Perram-Wertheim overlap algorithm† is the ideal one for hard ellipsoids/ellipses. It is efficient and precise. It can be applied to determine possible overlaps in 2d and 3d cases. It can potentially provide
  - Contact points on the ellipsoids.
  - An upper bound to estimate the shortest directional distance between two ellipsoids' possible contact points measured along the direction of interbody vector connecting their c.o.m.'s.

†Perram et al. J. Comp. Phys. 58 (1985) 409.

Perram-Wertheim† Overlap Algorithm

Let's define two ellipsoids by their quadratic forms:

$$A(x) = (x - r)A(x - r), \qquad B(x) = (x - s)B(x - s),$$

$$A = \sum_i a_i^{-2} u_i \otimes u_i, \qquad B = \sum_i b_i^{-2} v_i \otimes v_i,$$

where u_i, v_i are the semi-axis vectors and a_i, b_i are their lengths. Let's define the following affine combination

$$S(\lambda, x) = \lambda A(x) + (1 - \lambda)B(x),$$

where $\lambda \in [0,1]$. The solution of the following optimization problem

$$F(A, B) = \max_{\lambda} \min_{x} S(\lambda, x)$$

allows us to determine three possible mutual configurations of the ellipsoids:

$$F(A,B) \begin{cases} < 1 \\ = 1 \text{ for A and B} \\ > 1 \end{cases} \begin{cases} \text{overlapping,} \\ \text{externally tangential,} \\ \text{nonoverlapping.} \end{cases}$$

†Perram et al. J. Comp. Phys. 58 (1985) 409.

Application to diffusing rigid bodies represented by elliptic thin discs in $\mathbb{R}^2$

- 3 equivalent 2d rigid bodies represented by elliptic discs.
- Diffusions are governed by the overdamped Langevin equations in the lab frame.
- Random directions on the discs stand for possible binding sites.
- The outliers ":", "--" and "being filled" represent broad-phase (long-distance), non-overlapping in narrow-phase (intermediate distance) and overlapping cases (when we need to implement the retroactive collision detection), respectively.
- Time steps are shown in the animation.

Thank you for your patience!

Collaborators:

Tom Bartol, Ivet Bahar, Terrence Sejnowski