The auxiliary region method: simulating second–order reaction systems

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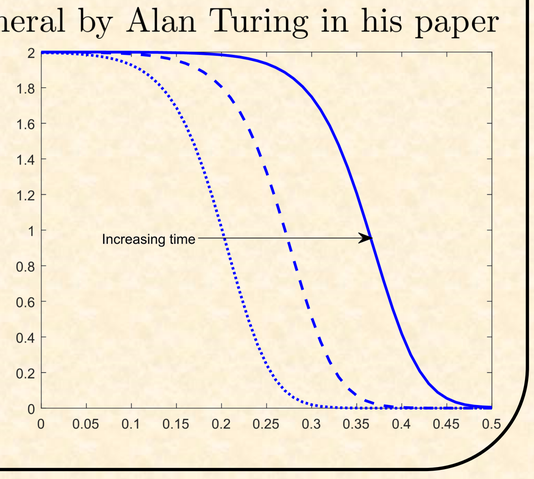
Reaction–diffusion

Reaction–diffusion systems are important tools for the modelling of many biological phenomena. Formulated in general by Alan Turing in his paper "the chemical basis of morphogenesis"[1], they are useful for modelling travelling waves (see figure on the right), cell migration and pattern formation, amongst many other systems. They combine the movement of particles down a concntration gradient (diffusion) with the interaction of particles within the system (reactions).



Spatially extended hybrid methds

Spatially extended hybrid methods split space into distinct regions, within which different modelling paradigms are used. They allow systems which comprise multiple spatial scales to be simulated both accurately and efficiently. As an example, spatially-extended hybrid methods have been used to model the release of calcium ions through gated channels[2]. For more information on such methods, see the review article by Smith and Yates (2018)[3].

The auxiliary region method (ARM) is a spatially extended hybrid method that couples the coarse PDE representation to the fine-scale individual-based paradigm.[4]

Macroscopic domain

$$\Omega_P(t) = (x_0, I(t)),$$
$$\Omega_{PA}(t) = (I(t) - h_a, I(t)).$$

The PDE is solved in one dimension, where we assume an initial condition that is translationally invariant in the y and z directions. We solve the PDE:

$$\partial_t u = D\partial_{xx} u - k_1 u^2 + k_2,$$
$$\partial_x u(x_0, t) = \partial_x u(I(t), t) = 0,$$
$$u(x, 0) = u_0(x).$$

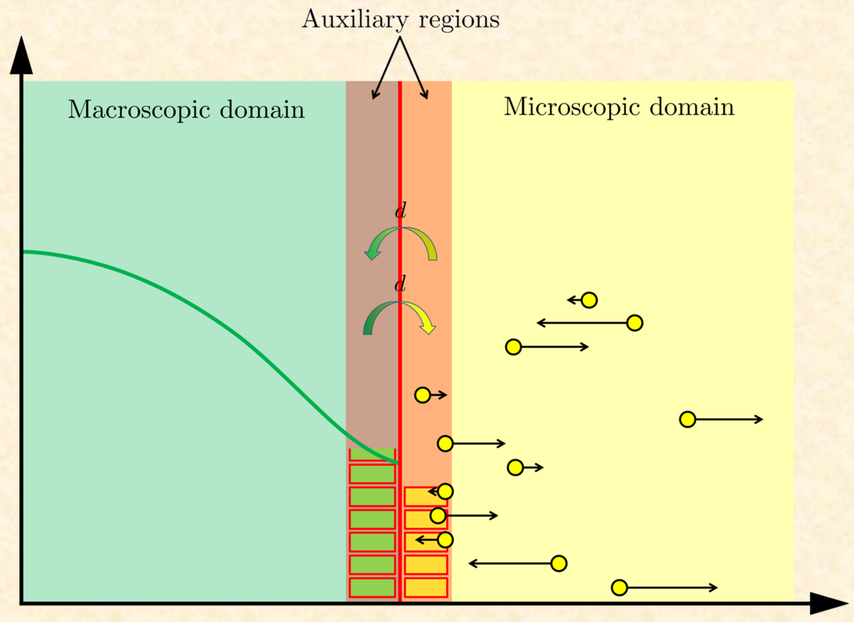
Moment closure

Used Poisson moment closure in order to form the PDE:

$$\mathbb{V}\mathrm{ar}(A) = \mathbb{E}[A] \implies \langle A^2 \rangle = \langle A \rangle + \langle A \rangle^2.$$

Auxiliary region method (ARM)

Reaction system: $2A \xrightarrow{k_1} \emptyset, \quad \emptyset \xrightarrow{k_2} A.$



Microscopic domain

$$\Omega_B(t) = (I(t), x_0) \times (y_0, y_1) \times (z_0, z_1),$$
$$\Omega_{BA}(t) = (I(t), I(t) + h_a) \times (y_0, y_1) \times (z_0, z_1).$$

We track the positions of each individual particle, allowing them to diffuse and react with one another.

Diffusion

Update particle i at position $\boldsymbol{X}_i(t)$ at time t according to the computational SDE:

$$\boldsymbol{X}_i(t + \Delta t) = \boldsymbol{X}_i(t) + \sqrt{2D\Delta t}\ \boldsymbol{\xi}_i,\ \boldsymbol{\xi}_i \sim N(\boldsymbol{0}, I),$$

where I is the 3×3 identity matrix.

Reactions

We use the λ-ρ method[7] in order to complete second-order reaction pathway. This converts k_1 and Δt into P_λ and ρ:

- ρ: The reaction radius.
- P_λ: The probability of reacting in a time-interval of length Δt if two particles are within a distance ρ.

Animation of the λ-ρ method

Adaptive interface

We move the interface based on local density conditions.[5] If the number of particles in $\Omega_{PA}(t)$ drops below a value β_ℓ we move the interface towards the PDE subdomain. If the number of particles in $\Omega_{BA}(t)$ increases above a second value, $\beta_u > \beta_\ell$, we move the interface towards the individual-based subdomain.

Animation of the interace conditions

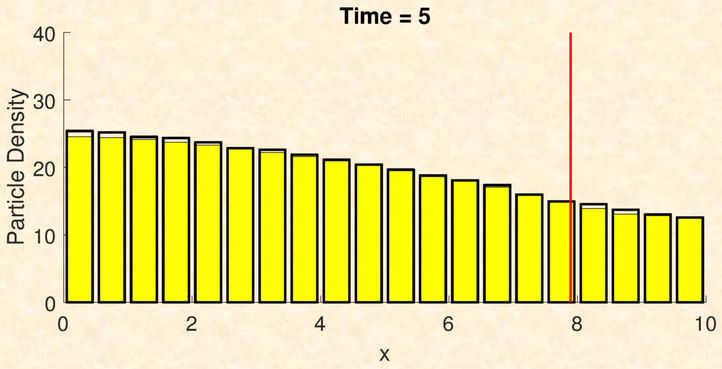
Animated 1D-to-3D auxiliary region method

Auxiliary regions

Diffusion and reaction events that occur in $\Omega_{BA}(t)$ exclusively are completed using the Gillespie algorithm.[6] Diffusive events occur with rate D/h_a^2 and the reaction pathways are completed using the usual kinetic reaction propensity functions.

Results

We have simulated the reaction–diffusion system using the ARM, with the results to the right (scan the QR code for a time varying plot). The yellow bars are the average of the ARM solution, the black bars the individual-based simulation across the entire domain, and the red line is the average interface position.



Animated results and error plot

Future work

We will now look at adding the following:

- Replacing the PDE with an **SPDE**: This corrects variance damping that occurs in the microscopic subdomain.
- Implement a **growing domain**: Adds biological realism to the method — allows for the simulation of more complicated behaviour.

Get in touch*

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