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Exercise 9

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Question 1: Reaction-Diffusion in the QS model

In this exercise, we will implement a simplified version of the Quorum Sensing model introduced earlier in the exercises. In order to familiarize yourself again with the model, re-read the JMB paper given on the course web page. The QS model comprises three components: (i) diffusion and exponential decay of signaling molecules outside bacteria, (ii) an ODE model for the production of molecules inside bacteria and (iii) handling of the influx and outflux of molecules across the cell membrane. The key simplification we apply to the QS model is the fact that we do not resolve the spatial extension of a single bacterium. This means that our computational particles completely enclose a model bacterium. Hence, we can greatly simplify the third component. A computational particle p at position x_p will hence contain either free space or free space **and** a bacterium.

a) Implement first the source term f of the ODE inside a cell. You can find the formula in the JMB paper. The code template reads like this:

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% Code for Exercise 8 - Source term in the QS model
%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%
% Input
% u_c:      (numParticles x 1)-Vector of concentration
%           of AHL species inside a bacterium
% alpha:    Standard production rate alpha
% beta:     Increased production rate beta
% gamma:    Decay rate
% x_tresh:  Threshold concentration
% n:        Order of polymerization
%
% Output
% f:       (numParticles x 1)-vector of concentration
%          change of AHL species
%
% function f = fQS(u_c,alpha,beta,u_tresh,n)
```

For all following simulations, we use the parameters $\alpha = 1$ for the standard production rate, $\beta = 100$ for the increased production rate, $u_{\text{thresh}} = 2$, and polymerization degree $n = 10$.

Test your implementation by plotting u_c vs. f. f should have a sigmoidal shape with offset α, limit value $\alpha + \beta$ and the inflection point at u_{thresh}. This function should be called by the next routine.

For a particle at x_p that contains both a bacterium and free space the following pair of ODEs has to be integrated:

$$\begin{aligned} \frac{d}{dt} u_c(x_p) &= f(u_c) + d_1\, u_e(x_p, t) - d_2\, u_c(x_p, t) \\ \frac{d}{dt} u_e(x_p) &= -d_1\, u_e(x_p, t) + d_2\, u_c(x_p, t) - \gamma u_e(x_q, t), \end{aligned} \tag{1}$$

where $u_e(x_p)$ is the "extracellular" and $u_c(x_p)$ the "intracelluar" concentration of AHL. Assuming all bacteria are of equal size and shape, the surface area of the bacterium has been included into the parameters d_1, d_2 already. Similar to the routine `applyBrusselator` from the previous exercise the following code template can be used to model the ODE:

```
%%%%%%%%%%%%%%%%%%%%%%%%%%%%
% Code for Exercise 8 - Reaction inside and outside the bacteria
%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%
% Input
% u_c:      (numParticles x 1)-Vector of concentration
%           of AHL species inside bacteria
% u_e:      (numParticles x 1)-Vector of concentration
%           of AHL species outside bacteria
% QScellIndex: Indices where bacteria are located
% QSParams: Parameters used for modeling the source f
% Output
% du_c:      (numParticles x 1)-vector of concentration
%            change of AHL species inside
% du_e:      (numParticles x 1)-vector of concentration
%            change of AHL species outside
%
% function [du_e,du_c] = applyQS(u_e,u_c,QScellIndex,QSParams)
```

Note that this routine computes the derivatives according to eq. (1) only for particles that contain a bacterium. The list of these particles indices should be given in the argument `QScellIndex`. For those particles that contain "extracellular" space only, the reaction part for $u_e(x_q, t)$ consists only of $-\gamma u_e(x_q, t)$ because the evolution of the concentration of AHL u_e is governed by diffusion and decay:

$$\frac{\partial}{\partial t} u_e(x_q, t) = D\, \Delta u_e(x_q, t) - \gamma u_e(x_q, t) \tag{2}$$

As usual, diffusion is solved using the PSE operator (with the same parametrization as in the previous exercises) which is applied to **all** particles x_q in the computational domain. As in the previous exercises use an explicit Euler scheme for the time stepping. We use $d_1 = 0.25$ and $d_2 = 2.5$, i.e. the outflux out of bacterial cells is ten times higher than the influx.

b) We will now validate the code. For this purpose create a 2D computational domain in [0,50] and place 51 particles per dimension on a grid with equidistant spacing (i.e. $h = 1$). For all upcoming simulations set the diffusion constant $D = 1$ and use the time step $dt = h^2/(4\,D)$. We consider periodic boundary conditions.

For the first validation case, place one bacterium cell in the center of the domain and set $u_c(t = 0) = u_{\text{thresh}}$. Use $\gamma = 0.5$, $\gamma_e = 0.5$ and simulate until time $T = 20$. Monitor the evolution of the total amount of u_e in the whole domain. Plot this total amount versus time. The total extracellular amount u_e should converge to ≈ 165, the total amount including the cellular AHL ($u_e + u_c$) should converge to ≈ 202. How does this change when you set $\gamma = 0$ and re-run the simulation?

The second benchmark case checks the ability of activating the luminescence of a nearby bacterium. Place again one bacterium in the center of the domain with the same initial conditions as before. Place now a second bacterium at a distance of around 4 away from the central one and set $u_c(t = 0) = 0$. Choose a lower degradation rate, for example $\gamma = \gamma_e = 0.05$. Run the simulation. When do you activate the second bacterium? It should be below $T = 50$. Can you see the time of activation from plotting total amount versus time?

In the final test case, we consider a small population of bacteria. For this purpose download the file bacterialPos.dat from the course website. It contains the location of 15 bacteria in the domain. Set again $\gamma = \gamma_e = 0.5$ and the initial u_c of the first 7 bacteria to u_{thresh} and the rest to 0. Plot the concentration field after short time ($t = 1$, $t = 10$). Are the bacteria able to activate their population members? Simulate at least until time 200. If yes, at what point in time? What happens if you decrease γ? How does the concentration field change qualitatively?

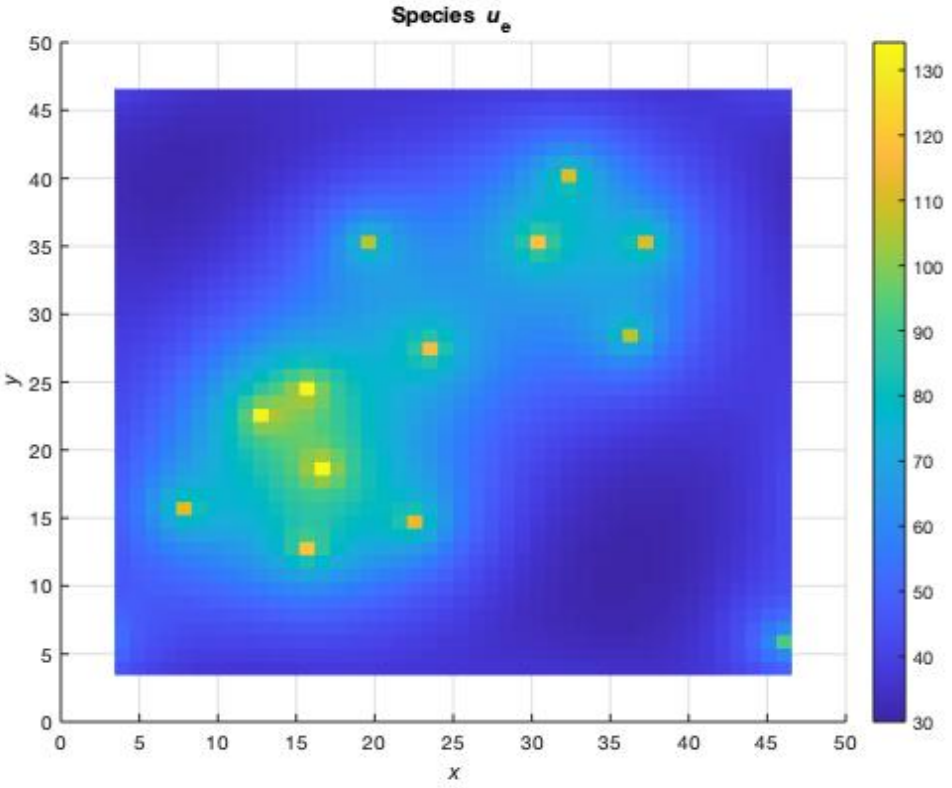

Figure 1: Final concentration field for $\gamma = 0.01$ at $T = 200$.