Exercise 7

During development, a large number of symmetry breaks occur, and most of these are precise, reliable, and wired in the DNA of the organism. One mechanism that can lead to deterministic symmetry breaks is the Turing patterning mechanism. In this exercise, we will focus on the impact of additional feedbacks and solve the Turing mechanism on growing domains. As in Exercise 5, we will use the ligand-receptor based Turing mechanism

$$\begin{aligned} \partial u/\partial t &= \Delta u + \gamma f(u,v) \\ \partial v/\partial t &= d\Delta v + \gamma g(u,v) \end{aligned} \tag{1}$$

with

$$\begin{aligned} f(u,v) &= a - uv^2 \\ g(u,v) &= b + uv^2 - v \end{aligned} \tag{2}$$

Here, u and v are variables that describe the interaction between a receptor, u, and a ligand v. f, and g are functions that describe the reactions kinetics of u, and v, and $d = D_v/D_u$ is the relative diffusion coefficient. The Laplace operator Δ specifies the spatial derivative. The parameters are all positive constants.

Problems 2-4 are for students with more advanced numerical training. By doing these problems you will learn how to simulate models where signalling (Turing mechanism) and domain deformation / outgrowth are coupled. It requires a more advanced command of FEM; we recommend the use of the FEM software COMSOL.

1. **Effect of feedbacks on the Ligand-receptor based Turing Pattern**. In exercise 5, you visualised the Turing space dependence of Eq. 1, 2 on a and b for $\gamma = 10$ and $d = 50$ by checking for each parameter pair a,b if the real parts of all eigenvalues are negative in the absence of diffusion and become positive in the presence of diffusion.

   Now consider an additional negative feedback of the complex u^2v on the production of v. Therefore the equation for v changes to:

$$\partial v/\partial t = d\Delta v + \gamma\left(\frac{b}{1+\frac{u^2v}{p}} - u^2v\right) \tag{3}$$

   where p is large in case of a weak feedback and low in case of a strong feedback. Plot the Turing space dependence on a and b for $p = 0.1$. What do you observe? Why is this biological relevant?

2. **Turing Patterns on a growing domain.** You will now solve Eq. 1, 2 on a growing domain. This exercise is best carried out using a FEM software package for numerical simulations such as COMSOL Multiphysics.

   i) Create a one by one square as domain. Set up the two reaction-diffusion equations with zero flux boundary conditions in a way that you have full control over diffusion, dilution and transport terms. Choose initial values which will let you observe the effects of these terms.

   ii) Add growth via ALE (i.e. the deforming geometry or moving mesh node in COMSOL). Check how dilution and transport change your solution when you let the domain grow with constant or linear growing speed. What are the conserved quantities in each case? Think about possible uses.

   iii) Add the reaction terms to your model. To observe Turing patterns, you can use $a = 2$, $b = 0.25$, $\gamma = 1$, and $d = 0.01$. Observe how the generated patterns change if you let the domain grow with transport and dilution either turned on or off.

3. **Reaction-diffusion models on a deforming 2D domain** Here you will solve a Turing model on a 2D domain (square) that deforms according to the local concentration profile. We will now use an equation system with explicit representation of both diffusion coefficients,

$$\begin{aligned} \partial u/\partial t &= D_u \Delta u + \gamma f(u,v) \\ \partial v/\partial t &= D_v \Delta v + \gamma g(u,v) \end{aligned} \tag{4}$$

   i) Implement the model in Comsol following the guidelines given below.

   ii) Explore the model with different growth rates. What do you observe?

   iii) Use different functions for how the growth speed depends on your variables and study the impact on pattern formation.

   Guidelines:

   1. Create a one by one square as domain; make the corner slightly rounded with the Fillet tool.
   2. Mesh the domain with a free quadrangular mesh.
   3. Define the following parameters: $\gamma = 100$, $a = 0.1$, $b = 0.9$, $D_\mathrm{v} = 40$, $D_\mathrm{u} = 1$
   4. Create a random function of two variables.
   5. Define the reaction-diffusion kinetics in your model using the PDE coefficient form interface.
   6. To model domain deformation add the deformed geometry interface. Define free deformation of the mesh on the entire computational domain. Further define the prescribed mesh velocity at all domain boundaries proportional to u^2. *Hint: use variable normal to the surface nx and ny.*

7. Create a two step solver: first use a time-dependent solver which solves the equations on a constant domain, then use a time-dependent solver which solves the equations on a deforming domain; use the solutions form the first solver as the initial conditions. *Hint: the interface can be added/removed from the solver in Physics Interfaces menu.* For fast and accurate solutions choose the PARDISO solver and update the Jacobian at every time step.

4. **Reaction-diffusion models on a deforming 3D domain** Here you will solve the previous Turing model on a 3D domain (sphere) that deforms according to the local concentration profile.

   i) Implement the model in Comsol following the guidelines given below.

   ii) Explore the model with different growth rates. What do you observe?

   iii) Use different functions for how the growth speed depends on your variables and study the impact on pattern formation.

   iv) Vary the thickness of the sphere and make sure that it's thickness is significantly less than the length scal eof the pattern. What happens if this is not the case?

   Guidelines:

   1. Create a unit sphere with radius $r = 1$ and thickness $0.05 \times r$. *Hint: use surface type in the type submenu; thickness can be defined in the layer submenu.*
   2. Mesh the domain with a free tetrahedral mesh.
   3. Define the following parameters $\gamma = 30$, $a = 0.05$, $b = 2$, $D_{\mathrm{v}} = 50$, $D_{\mathrm{u}} = 1$

   4.-7. Proceed as in the 2D problem.