TMA4195 - MATHEMATICAL MODELING (FALL 2014).
PROJECT DESCRIPTIONS.

1. Project 1 : modeling of synaptic transmission

Neurons are cells which transmit and process information. Very schematically, a neuron consists of a soma (the cell body) with extensions known as dendrites and a long tail, the axon, which eventually splits into many axon terminals, see Figure 1. In the brain, neurons form a network. Two neurons are connected when an axon terminal of one neuron lies beside the termination of a dendrite, or dendrite spine, of an other neuron. The term synapse is used to denote the site where this connection occurs, see Figure 2. In a neuron, a signal received at a dendrite spine is sent through the axon by using action potentials, until it reaches the axon terminals. There, it triggers the release of neurotransmitters in the synaptic cleft, which is space contained between the presynaptic neuron (the emitter) and the postsynaptic neuron (the receiver). Neurotransmitters diffuse freely in the synaptic cleft. Located on the membrane of the postsynaptic neuron, receptor molecules, simply called receptors, have the ability to bind with the neurotransmitters. When a receptor is bound, it changes local electrical properties in the membrane. This effect is cumulative so that when enough receptors are bound, a new signal is generated in the postsynaptic neuron, which again will be transmitted along the axon and eventually excite other neurons. The goal of this project is to set up a model for the synaptic neurotransmission, that is, the sequence which covers the motion and activity of the neurotransmitters and receptors in the intercellular space. A specific motivation for setting up such quantitative model is to determine the probability of synaptic *cross-talk*, that is, the case where an axon terminal, via the neurotransmitters it releases, interacts not only with the receptors on the opposite side of the synapse but also with neighboring synapses.

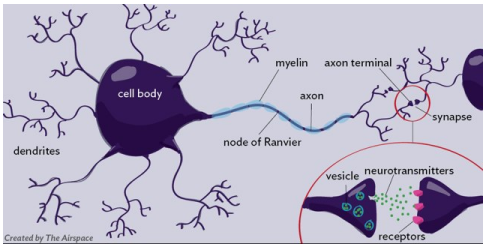

Figure 1. Schematic description of a neuron ([1]).

The neurotransmitters diffuse freely in the synaptic cleft. The diffusion of a solute in a solution results from the collisions of the solute molecules with the molecules of the solvent. Such displacement can be accurately modeled by Brownian motion. When the number of solute molecules is large enough, the concentration of the

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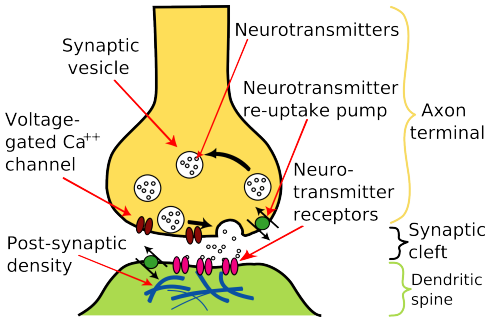

FIGURE 2. Schematic description of a synapse (from wikipedia)

solute becomes a well-defined quantity. The flux J of solvent molecules can then be approximated using the Fick law, $J = -D\nabla c$. Then, the diffusion equation

$$c_t = \kappa \Delta c, \tag{1.1}$$

expresses the conservation of the number of solute particles. The diffusion equation is strongly related to Brownian motion and we recommend [2] as an introduction to this topic.

The binding process between neurotransmitters and receptors is a reversible chemical reaction,

$$\mathrm{R} + \mathrm{N} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{R{-}N}.$$

The reaction can be modeled as a stochastic process as follows. For a given time interval, there is a probability that a bound receptor R−N releases a neurotransmitter N. Reversely, there is another probability, which now must depends on the distance between the neurotransmitter N and the free receptor R, that the neurotransmitter binds to the receptor. At the macroscopic level, chemical reaction are commonly modeled using kinetics models.

MAIN PART:

Derive the modeling equations. Propose a numerical scheme to solve the equations. Propose a geometrical model for the synapse. Implement a numerical solver.

Application: Estimate the time for a signal to be transmitted. To do so, you may consider the equilibrium state for the system in the case where the synaptic cleft is confined, that is, where we assume artificial walls which prevent neurotransmitters to leave the synaptic cleft. Such equilibrium state yields the maximum number of receptors that in practice will be bound.

FOLLOW-UP QUESTIONS:

Geometrical reduction: The intercellular space is very thin compared to the characteristic size of the cells. We want to exploit this fact and model the intercellular space as a 2-dimensional surface. By this geometrical reduction, we hope to increase the computation speed. It could be useful as the geometry of the intercellular space is typically very complex, as shown in 4.

How this reduction modify the modeling equations? Following the same steps as in the 3-dimensional case, implement a numerical solver for this case.

Clearance of neurotransmitters from the synaptic cleft: Once the neurotransmitters have been released and a signal transmitted, a new signal cannot be

resent in the same way before the synaptic cleft has been cleared from neurotransmitters. In this process, glia cells play an essential role. The membranes of the glia cells are equipped with transporters which takes up the neurotransmitters. Inside the glia cells, the neurotransmitters are transformed in a inactive variant and released again in the intercellular space to return in the axon. The overall process can be summarized in the following reaction:

$$\mathrm{T} + \mathrm{N} \rightleftharpoons \mathrm{T{-}N} \longrightarrow \mathrm{N}_{\mathrm{inactive}},$$

where T denotes the transporters and $\mathrm{N}_{\mathrm{inactive}}$ the inactive form of the neurotransmitters. Integrate the clearance of neurotransmitters in your model.

Application: Estimate the clearance time. Estimate the probability of synaptic cross-talk.

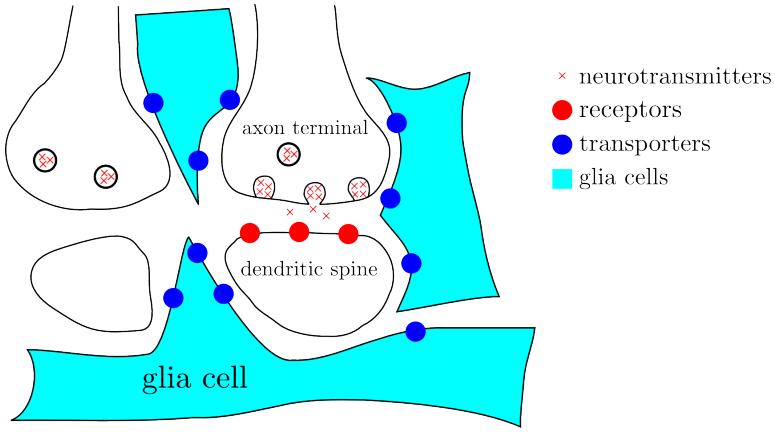

FIGURE 3. Glia cells

Coupling with flow: The intercellular space is filled with intercellular fluid. We want to study the effects of an underlying moving fluid on synaptic transmission. Derive the governing equations in this case and try to solve them.

Application: Estimate the influence of an underlying flow for synaptic cross-talk.

FIGURE 4. 3D representation of a dendrite (left) and an electron micrograph of the brain which shows a planar section of the brain where the dark lines represents the membranes of the cells (right). These documents which are taken from [3] (see also [4]) show the complicated quasi-2D structure of the intercellular space.

Height of synaptic cleft	$15\,\mathrm{nm}$
Radius of synaptic cleft	$0.22\,\mu\mathrm{m}$
Length of a dendrite	$1\,\mu\mathrm{m}$
Diffusion coefficient	$0.3\,\mu\mathrm{m}^2/\mathrm{s}$
Density of receptors on the membrane	$1000\,/\mu\mathrm{m}^2$
number of neurotransmitters released in one excitation	5000
Number of synapses in adult brain	10^{14}
Reaction constant k_1	$10^3 - 10^4\,\mathrm{mol/ms}$
Reaction constant k_{-1}	$10^{-2} - 10\,\mathrm{mol/ms}$

TABLE 1. Typical parameter values (taken from [5, 6] and Wikipedia). The dimensions of the synaptic cleft correspond to a cylindrical approximation. The reaction constants vary depending on the affinity of the receptors

2. Project 2 : Microbial Enhanced Oil Recovery

Oil recovery is split in three categories: *primary*, *secondary* and *enhanced*, which roughly characterize the level of technology and the amount of investments which is required in each case. Primary recovery uses the natural pressure drive of the reservoir and only requires the construction of production wells. For secondary recovery, water or gas is injected inside the reservoir to maintain the pressure and further push the oil. A large amount of oil remains in place due to very low permeability regions in the reservoir or significant differences in the physical properties of the injected and produced fluids (water and oil). For example, when the oil is much more viscous than the water, the water is more mobile, fingerings occur and the water fills high permeability channels, reaches quickly the production wells, letting unswept large regions of the reservoir. High surface tensions between the fluids leads to oil trapping, that is, oil which cannot be moved. Water-based enhanced oil recovery techniques aim at reducing the differences in the physical properties of the fluids by adding appropriate chemicals, as polymers or surfactants, in the injected water. Polymers increase the water viscosity while surfactants reduce the surface tension between oil and water. Microbes living at reservoir conditions naturally produce biosurfactants, biopolymers, biomass, acids, solvents, gases and enzymes, which all can have positive effect on oil recovery. In microbial enhanced oil recovery (MEOR), one tries to exploit such microbial activity by adding new microbes or stimulating those in place to produce surfactants and obtain water diverging effects towards low permeability regions due to microbial plugging.

In this project, we want to derive the governing equations for microbial enhanced oil recovery and set up a simulator to solve them numerically. By considering a simplified case, we will try to quantify the MEOR capabilities for water diverging.

Main part:

Microbial population model without flow: We first focus on the microbial activity, assuming that the substrate where the microbes live is immobile. We need a population model for the microbes. Derive such model. The model should account for the following observations: Microbes reproduce themselves and eventually die. Their reproduction rate depends on the availability of nutrients and they will usually compete for nutrients. We may consider one or several, possibly competing, species.

Modeling of microbial accumulation: The microbes can produce bio-films which enable them to stick to the rock and colonize a region. This is the origin of clogging, whose consequence is a reduction in porosity. Propose a simple model for bio-film production and its effect on porosity.

Coupling between the microbes and the flow: Let us consider a single phase model. The porous media variables are the porosity ϕ and the permeability $\mathbf{K}$. We assume that the flow is modeled by Darcy's law:

$$u = -\frac{1}{\mu}\mathbf{K}(\nabla p + \rho g \boldsymbol{e}_z). \tag{2.1}$$

Here, u is the volume flux per unit area, μ is the viscosity, g the gravity constant and $\boldsymbol{e}_z = [0, 0, 1]^t$. The permeability matrix depends on the type of the rock and, therefore, it is usually a function of the spatial coordinates, that is, $\mathbf{K} = \mathbf{K}(x, y, z)$. Mass conservation implies

$$\frac{\partial \phi}{\partial t} - \nabla \cdot \left(\frac{1}{\mu}\mathbf{K}(x, y, z)(\nabla p + \rho g \boldsymbol{e}_z) \right) = 0 \tag{2.2}$$

Derive the equations for the transport of microbes, nutrients. Include in the model the production of bio-films and accumulation of microbes which modifies the porosity and the permeability. The changes in porosity and permeability are intimately related and, to simplify, let us use an analytical expression such as the KozenyCarman equation, see [7].

Numerical simulation Derive a numerical scheme for the equations and implement it.

Application: To assess the water diverging ability of MEOR, we can consider a simple 2D case consisting of layers of different permeability, see Figure 5. If only water is injected, the water will travel very fast through the highly permeable regions and reach very quickly the production well. To prevent this scenario, we add microbes to the water. The largest amount of microbes will then be found in the region with highest water flow. Then, the microbes will start producing biofilms which will reduce the permeability, favoring the flow in the other regions of the reservoir. Check the feasibility of this scenario.

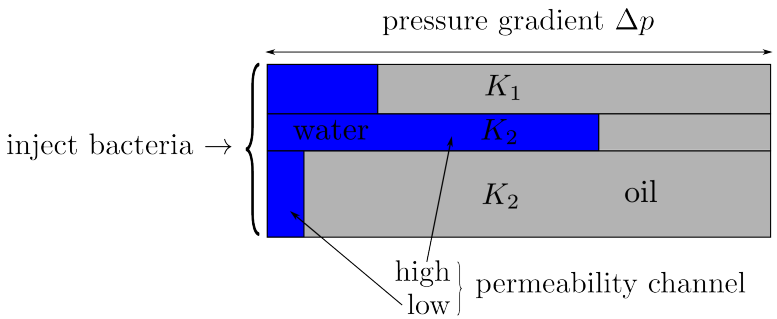

FIGURE 5. Simple 2D case with horizontal layers of different permeability.

FOLLOW-UP QUESTIONS:

Multi-phase flow and microbial surfactant

For two phases flow, the Darcy law is given by

$$u_\alpha = -\frac{k_{r\alpha}(s_\alpha)}{\mu_\alpha} k \nabla p, \tag{2.3}$$

where the function $k_{r\alpha}$, which is called the *relative permeability*, is a given function of the saturation s_α, for each phase. The residual water S_{wi} (resp. oil S_{or}) saturation denotes the amount of water (resp. oil) which is immobile. A standard analytical description of the relative permeabilities is given by the Corey model:

$$k_{rw}(S_w) = k^0_{rw} s_{wn}^{N_w} \quad \text{and} \quad k_{ro}(S_w) = (1 - S_{wn})^{N_o},$$

for some constants N_w, N_o, k^0_{rw} and where s_{wn} denotes the normalized saturation,

$$S_{wn}(S_w) = \frac{S_w - S_{wi}}{1 - S_{wi} - S_{or}}, \tag{2.4}$$

see Figure 6 for an example.

Residual saturations correspond to the amount of liquid which is trapped in the pore due to the effects of capillary forces, see Figure 7. Surfactants lower the surface tension between the two phases and the consequence is that some of the trapped oil is released. The detailed mechanisms are complex but we may consider a synthetic model where we parametrize the relative permeability curves by the interfacial

surface tension, see [8]. In such approach, large residual saturation and Corey coefficients would correspond to large interfacial surface tension. The dependence of the interfacial surface tension is depicted in 8.

Extend the single flow model with microbes from the previous question to handle multi-phase flow. Propose a simple model for the production of surfactants, where it is directly correlated with the microbial activity. After choosing a simple parametrization of the interfacial surface tension curve in Figure 8, propose a simple analytical expression of the relative permeability as a function of surfactant concentration. This expression will depend on a set of few parameters that you will introduced, which we call the surfactant parameters, and which quantify the quality of the surfactant produced by the microbes. Finally, incorporate the effect of microbial surfactant production in the multi-phase flow solver.

Application: We consider a simple reservoir model with

- a simple geometry, say a box,
- a constant permeability and porosity,
- a constant initial microbial concentration,
- one injection and one production well.

Quantify the effect of the following parameters,

- concentration of nutrient injection,
- surfactant production rate of the microbes,
- surfactant parameters,

on the increase in oil recovery.

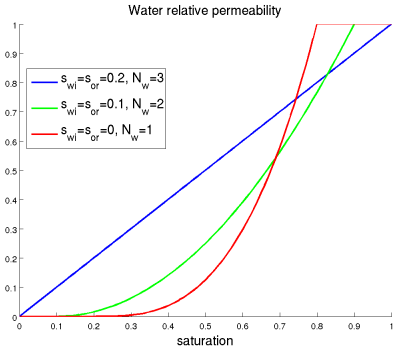

FIGURE 6. Examples of Corey relative permeability with different parameter values.

Competing microbes

The laboratory experiments of water flooding with surfactant producing microbes are in many cases very promising in term of increased oil recovery. However, field experiments do not confirm these predictions. An explanation can be that laboratory experiments do not take into account the microbial activity of the specie which originally populate the reservoir. The proliferation of the beneficial microbes, that is, those which produce surfactant, can be severely limited by parasite species. Still the microbes have different needs, which can be exploited to give a selective advantage to the beneficial specie.

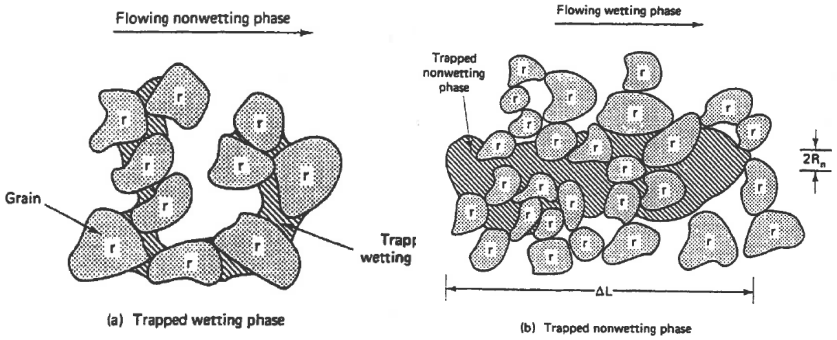

FIGURE 7. Schematic illustration from trapped wetting and non-wetting phases.

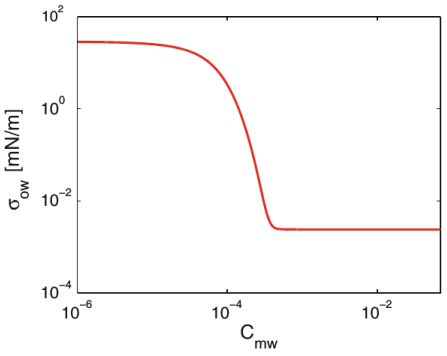

FIGURE 8. Interfacial surface tension versus surfactant concentration. from [9]

Introduce in your model a parasite microbe which does not produce surfactant and compete with the beneficial specie of microbe.

Application: Introduce two types of nutrients, type A and type B. The nutrient A is used by both species and they compete for it. The nutrient B is only used by the beneficial specie. By injecting nutrient B, we favor the beneficial microbe. Consider the same reservoir setting as in the previous question and quantify the benefit in increased oil recovery compared to the cost of the injection of nutrient.

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