TMA4195 Mathematical Modelling Project

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Deriving the modelling equations

Diffusion equation

Flux J:

$$J = -D\nabla c$$

$$c_t = \kappa \Delta c$$
$$\frac{dc}{dt} = \kappa \nabla^2 c$$

Neumann BC:

$$\nabla c \cdot n = g(t, c)$$

The binding process

First we look at the reversible chemical reaction

$$\mathrm{R} + \mathrm{N} \rightleftharpoons \mathrm{RN}$$

with reaction rate k_1^* to the right and k_2^* to the left, being respectively the probability for the reactions to occur in their direction. We get 3 ODE's from this chemical reaction:

$$\frac{d[\mathrm{R}]}{dt} = -k_1^*[\mathrm{R}][\mathrm{N}] + k_2^*[\mathrm{RN}],$$
$$\frac{d[\mathrm{N}]}{dt} = -k_1^*[\mathrm{R}][\mathrm{N}] + k_2^*[\mathrm{RN}],$$
$$\frac{d[\mathrm{RN}]}{dt} = k_1^*[\mathrm{R}][\mathrm{N}] - k_2^*[\mathrm{RN}],$$

where [R], [N] and [RN] are the concentratinos of the receptors, neurotransmitters and the bound product of them. We may consider [N][R] the probability of a neurotransmitter meeting an unoccupied receptor, and $\bar{k}_1^*$ the probability of the binding reaction happening. Likewise for $\bar{k}_2^*$. P^R is the probability of a receptor being unoccupied, $(1-P^R)$ the probability that the neurotransmitter is attatched to the receptor, leeds to the following simplification of the above ODE's:

$$\begin{aligned}\frac{d[\mathrm{N}]}{dt} &= -\bar{k}_1^*[\mathrm{N}]P^R + \bar{k}_2^*(1-P^R),\\ \frac{dP^R}{dt} &= -\bar{k}_1^*[\mathrm{N}]P^R + \bar{k}_2^*(1-P^R).\end{aligned}$$

If we assume that the receptors are not uniformly distributed, we need to introduce a $\gamma(x)$ to describe the density of receptors. At the boundary:

$$\begin{aligned}\frac{d[\mathrm{N}]}{dt} &= -\bar{k}_1^*[\mathrm{N}]\gamma P^R + \bar{k}_2^*\gamma(1-P^R),\\ \frac{dP^R}{dt} &= -\bar{k}_1^*[\mathrm{N}]\gamma P^R + \bar{k}_2^*\gamma(1-P^R),\end{aligned}$$

which are Neumann boundary conditions (inserting c for [N])

$$\begin{aligned}\kappa\nabla c\cdot n &= -\bar{k}_1^* c\gamma P^R + \bar{k}_2^*\gamma(1-P^R),\\ \frac{dP^R}{dt} &= -\bar{k}_1^* cP^R + \bar{k}_2^*(1-P^R),\end{aligned}$$

Glia cells

$$\mathrm{T} + \mathrm{N} \rightleftharpoons \mathrm{TN} \rightarrow \mathrm{N}_{\mathrm{inactive}} + \mathrm{T}$$

Define k_3, k_4, k_5 as the reaction rates of first rightward, first leftward, second rightward equation.

Similarly to the binding process, we get the following sets of equations:

$$\begin{aligned}\kappa\nabla c\cdot n &= -\bar{k}_3 c\gamma^T P^T + \bar{k}_4\gamma^T(1-P^T),\\ \frac{dP^T}{dt} &= -\bar{k}_3 cP^T + (1-P^T)(\bar{k}_4+\bar{k}_5),\end{aligned}$$

Combining these equations, we get

$$\kappa \nabla c \cdot n = -c(\bar{k}_1^* \gamma^R P^R + \bar{k}_3 \gamma^T P^T) + \bar{k}_2^* \gamma^R (1 - P^R) + \bar{k}_4 \gamma^T (1 - P^T),$$
$$\frac{dP^R}{dt} = -c\bar{k}_1^* P^R + \bar{k}_2^* (1 - P^R),$$
$$\frac{dP^T}{dt} = -c\bar{k}_3 P^T + (\bar{k}_4 + \bar{k}_5)(1 - P^T),$$

1D solution using solver

Modelling the equation in one dimension is done by considering the points a and b, and the line between them. In this case, a is on one side of the synaptic cleft, and b is on the other side. Due to this, the boundary conditions for a and b differ. For a, we have

$$\kappa \nabla c = -k_3 c P^T + k_4 (1 - P^T),$$

and for b we have

$$\kappa \nabla c = -k_1 c P^R + k_2 (1 - P^R).$$

The next step is to combine these boundary conditions with the modelling equation to form a matrix equation.

The final equation was

$$\hat{M}\dot{X}(t) = -\kappa \hat{K} X(t) - k_3 \hat{Q}^a (X(t)) X(t) + k_4 (1 - X_{N+1}(t)) \hat{d}^a$$
$$+ (k_4 + k_5)(1 - X_{N+1}(t)) \hat{e}^a - k_1 \hat{Q}^b (X(t)) X(t) + k_2 (1 - X_{N-2}(t)) \hat{d}^b,$$

and was found by Jorg Henrik Holstad [1] Here, X is a vector of length N + 2, consisting of the concentrations at the nodes, as well as the probabilities P_a^T and P_b^R: $X = \begin{bmatrix} C \\ P_a^T \\ P_b^R \end{bmatrix}$.

A plot using N = 9 internal nodes is shown below:

[1] Jorg Henrik Holstad. (2011). Modellering av Diffusjon av Nevrotransmittere i den Ekstracellelaere Vaesken. Retrieved from https://www.duo.uio.no/bitstream/handle/10852/10871/MasteroppgaveHenrikHolstad.pdf

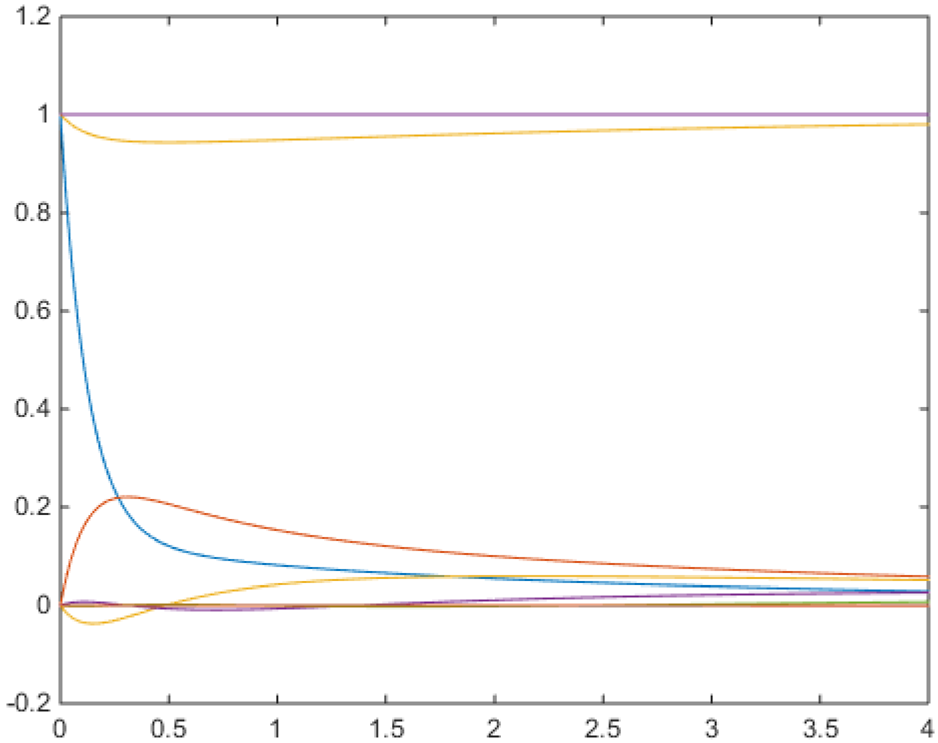

Figure 1: a = 0, b = 8, N = 9, $k_1 = k_2 = k_3 = k_4 = k_5 = 0.5, P_a^T(0) = P_b^R(0) = 1$