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Mathematical and numerical modeling of presynaptic phase of fast transport

Neurotransmitters in the terminal bouton of a presynaptic neuron are stored in vesicles, which diffuse in the cytoplasm and, after a stimulation signal is received, fuse with the membrane and release its contents into the synaptic cleft. It is commonly assumed that vesicles belong to three pools whose content is gradually exploited during the stimulation.
The physiological assumptions that lead to the proposed model are the following:

1. Terminal bouton occupies a fixed domain, a fixed part of the domain boundary are the vesicle release sites.
2. The unknown of the model is the concentration of vesicles in the cytoplasm. The unit in which this value is expressed can either be the mass or the quantity of the vesicles or the fraction of cytoplasm volume they occupy.
3. Vesicles diffuse inside the terminal bouton and they are synthesized in some subdomain of the bouton.
4. The efficiency of the vesicle synthesis is proportional to the difference between the equilibrium concentration (above which the synthesis does not take place) and current concentration.
5. Vesicles do not leave the domain unless the action potential arrives. The arrival of the action potential triggers the possibility of the vesicles release through some fixed period of time. The number of vesicles that can be released in a unit time through the unit area is proportional to the vesicle concentration in the vicinity of the release site.
6. Neither re-uptake nor recycling of released vesicles is considered.
7. The availability of vesicles for release depends only on their location. The docking sites are modeled implicitly as the areas in the vicinity of the release sites specified on the bouton boundary.

The following variables and parameters which express various physiological quantities are introduced:

(i) $\Omega \subset \mathbb{R}^N,\ N \in \{2, 3\}$ - the domain of the terminal bouton,
(ii) $\Omega_1 \subset \Omega$ - the domain of neurotransmitter production,
(iii) $\partial\Omega_d \subset \partial\Omega$ - neurotransmitter release sites on the cell membrane,
(iv) $f : \Omega \to \mathbb{R}$ - neurotransmitter source density defined, for example, by $f(x) = 0$ outside Ω_1 and $f(x) = f_z$ on Ω_1,
(v) $\bar{\rho}$ - the balance concentration of neurotransmitter in the bouton,
(vi) α - the coefficient denoting the rate of neurotransmitter exocytosis, α is the number of vesicles (or molecules) which are released through the unit area of the membrane in unit time by the unit difference of the concentration in

the cell and outside the cell (1 action potential activates 300 vesicles and 1 vesicle contains $10^3 - 10^4$ molecules of neurotransmitter),

(vii) $a_{ij} : \Omega \to \mathbb{R}$ - the diffusion tensor for the vesicles with a neurotransmitter,

(viii) τ - the time period through which the neurotransmitter is released from the docked vesicles to the cleft (0.2 - 0.5 ms),

(ix) t_0 - the arrival moment of the potential (it is possible that there are many such moments during the simulation).

The unknown in the model is the function $\rho : \Omega \times [0, T] \to \mathbb{R}$ denoting the concentration of the vesicles with neurotransmitter.
The function is the solution of the equation

$$\frac{\partial \rho(x,t)}{\partial t} = \sum_{i,j=1}^{N} \frac{\partial}{\partial x_i} \left(a_{ij}(x) \frac{\partial \rho(x,t)}{\partial x_j} \right) + f(x)(\bar{\rho} - \rho(x,t))^+. \tag{1}$$

The equation is accompanied by boundary and initial conditions implied directly by physiology of vesicle release as well as their initial distribution (see [1,2]):

$$\sum_{i,j=1}^{N} a_{ij} \frac{\partial \rho(x,t)}{\partial x_j} n_i = 0 \quad \text{for} \quad (x,t) \in (\partial\Omega - \partial\Omega_d) \times [0,T], \tag{2}$$

$$\sum_{i,j=1}^{N} a_{ij} \frac{\partial \rho(x,t)}{\partial x_j} n_i = 0 \quad \text{for} \quad (x,t) \in \partial\Omega_d \times ([0,t_0) \cup (t_0+\tau, T]), \tag{3}$$

$$\sum_{i,j=1}^{N} a_{ij} \frac{\partial \rho(x,t)}{\partial x_j} n_i = \alpha \rho(x,t) \quad \text{for} \quad (x,t) \in \partial\Omega_d \times [t_0, t_0+\tau], \tag{4}$$

$$\rho(x,0) = \rho_0(x) \quad \text{on} \quad \Omega, \tag{5}$$

where $(n_i)_{i=1}^N$ is the unit normal vector directed outside Ω.
The model is analyzed and simulations of the vesicular kinetics using Finite Element Method are done.

References

[1] A. Bielecki, P. Kalita, *Model of neurotransmitter fast transport in axon terminal of presynaptic neuron*, J. Math. Biol. **26** (2008) 559–576.

[2] A. Bielecki, P. Kalita, M. Lewandowski, B. Siwek, *Numerical simulation for a neurotransmitter transport model in the axon terminal of a presynaptic neuron*, Biol. Cybern. **102** (2010) 489–502.