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Fractional-order model of the Cajal-like interstitial cell

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1. Introduction

A simple model of the Cajal-like interstitial cells (IC-LC) based on Faville's model [3], see [9]. The comparison of this simulation with the published experimental results [5] has shown the qualitative similarity. The next step in improving this model can be the usage of the fractional-order derivative. The reason is that this derivative can take into account also the history of the whole process. A lot of papers dealing with this topic exist, e.g., [7, 10, 11]. Mainly, this approach is applied to Huxley-Hodgkin (H-H) or FitzHugh-Rinzel (FH-R) neuron model. As the main drawbacks of the models with integer-order derivatives have been stated

1. Dielectric losses in the membrane have been ignored [11].
2. The membrane capacitance has been assumed to be ideal [11].
3. The memory effect is not taken into account [7, 10].

This paper is devoted to missing software development and use it for IC-LC modelling. Here, we try to use fraction-order derivative, not on the conductance but on fluxes [7] or only on the membrane potential like in [11].

2. Short explanation of the fractional derivative

A lot of fractional derivative definitions exist. Here, we introduce the Gruenwald-Letnikov derivative [8]: The derivative of the order 1 and 2 is defined by

$$\frac{\partial}{\partial t} f(t) = \lim_{h \to 0} \frac{f(t) - f(t-h)}{h} \tag{1}$$

and

$$\frac{\partial^2}{\partial t^2} f(t) = \lim_{h \to 0} \frac{f'(t) - f'(t-h)}{h^2} = \lim_{h \to 0} \frac{f(t) - 2f(t-h) + f(t-2h)}{h^2}, \tag{2}$$

respectively.

The generalization on the n-derivative where n is an integer is then

$$\frac{\partial^n}{\partial t^n} f(t) = \lim_{h \to 0} \frac{1}{h^n} \sum_{j=0}^{n} (-1)^j \binom{n}{j} f(t - jh). \tag{3}$$

Without restriction that n be an integer we can define the Gruenwald-Letnikov derivative

$$D^q f(t) = \lim_{h \to 0} \frac{1}{h^n} \sum_{j=0}^{\infty} (-1)^j \binom{q}{j} f(t - jh). \tag{4}$$

For the binomial coefficients, it is necessary to use the Gamma function Γ:

$$\binom{q}{j} = \frac{\Gamma(q+1)}{\Gamma(j+1)\Gamma(q-j+1)}. \tag{5}$$

The meaning of the fractional derivative is not easy to define until now. Maybe, the simplest explanation can be found in [6]:

When q is non-integer then the derivative depends not only on the value of the function $f(t)$ at time t but also on previous values -– this property is called memory. In [6], the so-called Laplacean interpretation is shown. We suppose, the quantity $Y(t)$ depending on the previous values of the function $f(t)$

$$Y(t) = \int_0^t \frac{(t-\tau)^{q-1}}{\Gamma(q)} f(\tau) d\tau. \tag{6}$$

Now, we apply the Caputo derivative on both sides of this equation and the result is

$$D_C^q Y(t) = f(t). \tag{7}$$

Therefore, the memory is obtained in the fractional derivative. A general non-linear fractional system can be written as

$$D^q \mathbf{x} = \mathbf{f}(\mathbf{x}), \tag{8}$$

where $q = [q_1, q_2, \ldots, q_n]^T$for $0 < q_i < 2, (i = 1, 2, \ldots, n)$ and $x \in \mathbb{R}^n$.

We use the algorithm and code published in [4] for numerical solutions.

3. Short explanation of the stability conditions

According to theorem 4.6 in [8], system stability is given as follows: ”When we consider the incommensurate fractional-order system (FOS) $(q_1 \neq q_2 \neq \ldots \neq q_n)$ and suppose that m is the least common multiple of the denominators, u_i's of q_i's, where $q_i = v_i/(u_i;)v_i, u_i \in \mathbb{Z}^+$ for $i = 1, 2, \ldots, n$ and we set $\gamma = 1/m$. The system is asymptotically stable if

$$| \, arg(\lambda) \, | > \gamma \frac{\pi}{2} \tag{9}$$

for all roots λ of the following equation

$$\det(diag([\lambda^{mq_1} \lambda^{mq_2} \ldots \lambda^{mq_n}]) - \mathbf{J}) = 0, \tag{10}$$

where $\mathbf{J} = \frac{\partial f}{\partial x}$.” For the stability analysis, we could not find the code and therefore spatial code was developed.

4. Fractional-order model of IC-LC

The whole model of IC-LC was described in detail in [9]. It has the form

$$d^q \mathbf{x} = \mathbf{f}(\mathbf{x}; \mu), \tag{11}$$

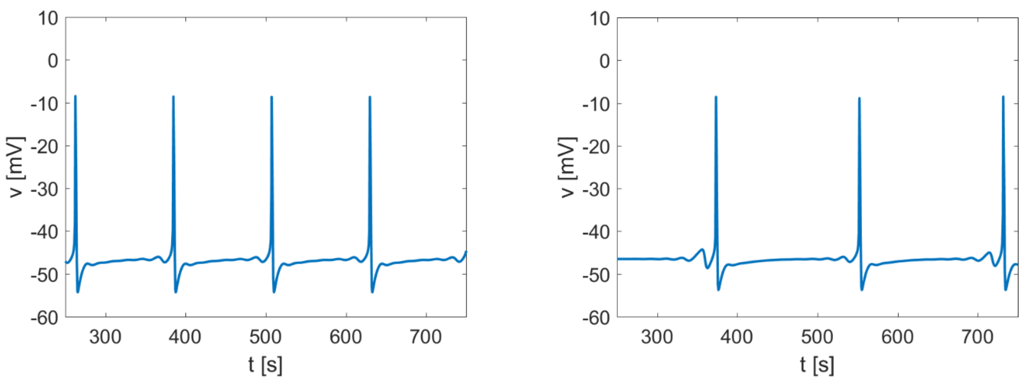
where $\mathbf{x} = [c, cer, v, w, cmt]$. Parameters c, cer, and cmt are Ca2+ concentrations (M) in the cytoplasm, in ER, and in MT, respectively. Variable v is the membrane potential (mV) and w is the dimensionless help variable. Function $f(x)$ is a vector of the right-side, see [9]. Whereas μ is the vector of control parameters. Like in [9], we use as control parameters the conductance of the voltage-operated calcium channel GCa $\mu\text{M}/(\text{mV} \cdot \text{s})$ and the reverse potential of the sodium/calcium exchanger zNaCa (mV). This is given with the Goldman-Hodgkin-Katz equation and the Nernst equations [1]

$$zNaCa = \frac{RT}{F}\left(4\ln\frac{\mid Na\mid_e}{\mid Na\mid_i} - \ln\frac{\mid Ca\mid_e}{\mid Ca\mid_i}\right), \tag{12}$$

where R is the gas constant, T absolute temperature, and F Faraday constant. They can be influenced by either nimodipine or change of external Na concentration, respectively. Experiments published in [2] show the decrease of $[\mathrm{Na}]_\mathrm{e}$ from 130 to 13 mM doubles the frequency of spontaneous Ca2+ oscillations.

To analyze this model, we have used the developed code which allows us to solve commensurate and incommensurate FOS, find its equilibrium points and solve their properties.

As an example, we show the influence of q on the period of the spontaneous oscillation of IC-LC which can be compared with the experiments [5]. In Fig. 1, the situation is set for $GCa = 0.001$ and $zNaCa = -60$. All other data are the same as in [9]. In Fig. 1a, integer-order derivatives are used. In Fig. 1b, there is set $\mathbf{q} = [1\ 1\ 0.95\ 1\ 1]$. The decrease of $\mathbf{q}$ lowers the frequency of the spontaneous oscillations.



(a) $\mathbf{q} = [1\ 1\ 1\ 1\ 1]$

(b) $\mathbf{q} = [1\ 1\ 0.95\ 1\ 1]$

Fig. 1. Influence of fractional derivate order $\mathbf{q}$ for $GCa = 0.001$ and $zNaCa = -60$

Another example is the modelling of the influence of zNaCa change. In Fig. 2, we can see the situation for $zNaCa = -59$ with the integer-order derivative (Fig. 2a) and with $\mathbf{q} = [1\ 1\ 0.8\ 1\ 1]$ (Fig. 2b). Again, we can see that it is possible to obtain the result comparable with the experiments by changing $\mathbf{q}$.

In all cases, the calculation starts from the equilibrium point. The stability condition in Eq. (8) is not fulfilled. It means, the situation is $\mid \arg(\lambda) \mid_{min}= 0.7129$ and $\gamma\frac{\pi}{2} = 1.579$ in Fig. 2a.

5. Conclusion

The developed software allows the simulation of the spontaneous oscillation of IC-LC using the fractional-order derivative and the stability on the incommensurate systems. The comparison with the experimental results shows the positive influence of this derivative. In further work, we will focus our attention on further parameters tuning and finding the chaotic regions which can correspond with some pathological effects.

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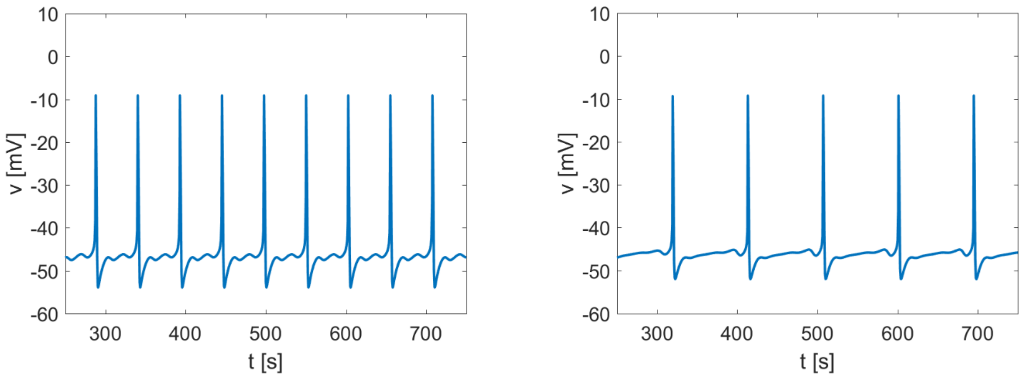

(a) $\mathbf{q} = [1\ 1\ 1\ 1\ 1]$

(b) $\mathbf{q} = [1\ 1\ 0.8\ 1\ 1]$

Fig. 2. Influence of fractional derivate order $\mathbf{q}$ for $GCa = 0.001$ and $zNaCa = -59$

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