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PERPETUAL POINTS IN THE CAJAL-LIKE INTERSTICIAL CELL MODEL

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Abstract: *Cajal-like interstitial cells (IC-LC) play important role in both physiological and pathological function of the bladder. The authors developed relative simple mathematical model consisting of five nonlinear ODEs. The model accuracy was verified using published experimental results. Deeper analysis of this model has shown existence of the multi-stable and hidden attractors which can have important influence on the behavior of the whole bladder. As the most effective way to obtain these attractors seems to be to use the method based on the calculation of the perpetual point. In the contribution is shortly introduced the definition of these points. Although this method is till now not fully proved it allows to calculate some multi-stable or hidden attractors. The goal is to show the application of this method on the more complex 5D system. This is presented on suitably chosen example.*

Keywords: Cajal-like interstitial cells, bladder, nonlinear dynamical system, hidden attractors, perpetual points.

1. Introduction

The simple model based on the current knowledge about these cells was introduced in Rosenberg & all (2016) where also the basic dynamical analysis was done. For this purpose was used the free software package MATCONT. The basic result is shown on Fig. 1. The area between the both curves starting from the Bautin bifurcation correspond to the oscillation.

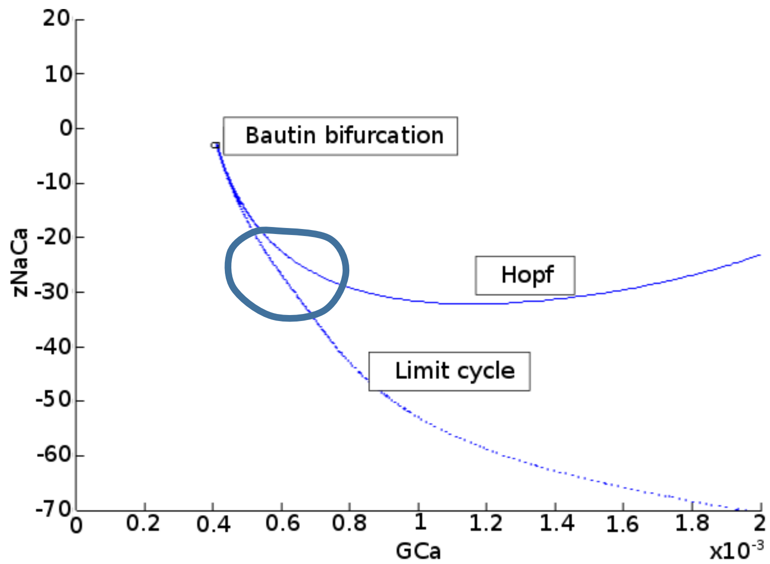

Fig. 1: Bifurcation diagram of the IC-LC model.

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While deeply studying the system in the area marked with circle in Fig.1, it can be seen very complicated behavior. There exist two stable attractors with the non-intersecting basins of attraction-one stable fix point and one self-excited attractor in the marked area. Multistability in dynamical system is a common feature. Uncovering all co-existing attractors and their basins of attraction are very important for understanding the systems. One of the major difficulties in understanding such systems is to locate the co-existing attractors.

The definition of the hidden attractors presented in Prasad (2015) is the following: An attractor is called a hidden attractor if its basin of attraction does not intersect with small neighborhoods of non-stable equilibria, otherwise it is called a self-excited attractor. It's important to mention that in the definition in Prasad (2015), the attractors are either oscillating or chaotic. In this contribution the usual definition of attractors including also the stable fixed points is used. Because of place shortage in here, the deeper explanation will be introduced during the conference presentation.

The examples and different methods for obtaining such attractor can be found e.g. in Kuznetsov (2015) or Kuznetsov & all (2014), where 1-3 dimensional systems are investigated. The following system is 5-dimensional and relatively very complex due to the interconnection of all the dimensions.

2. Description of the dynamical cell model

The schema of the simplified model of IC-LC is shown on the Fig. 2.

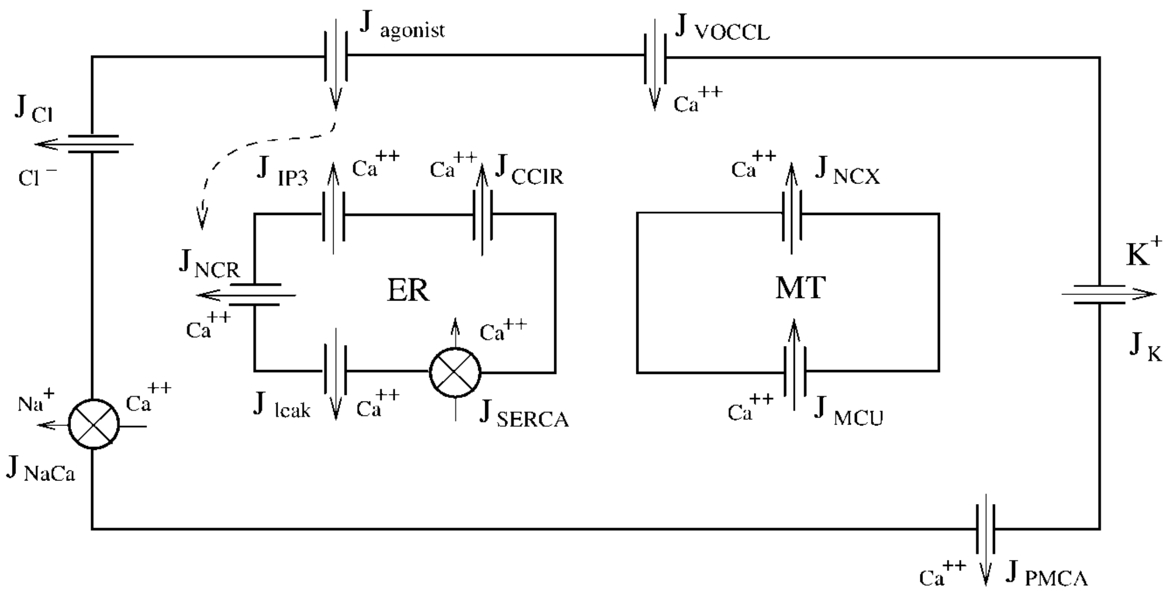

*Fig. 2: The schema of the IC-LC. **J** represent the fluxes of the ionts through the channels and pumps. For its meaning see Rosenberg & all (2016).*

The corresponding basic equations for Ca^{2+} concentration in cytoplasm (*c* ev. *cc*), in endoplasmic reticulum (cer), in mitochondria (cmt), for membrane potential (*v*) and for the membrane auxiliary variable *w* have the following form

$$\frac{dc}{dt} = \boldsymbol{G_{Ca}} \frac{v - z_{Ca1}}{1 + e^{-\frac{v - z_{Ca2}}{R_{Ca}}}} + G_{NaCa} \frac{c}{c + x_{NaCa}} (v - \boldsymbol{z_{NaCa}}) + g_c(c, cER, cMT, v, w) \ , \tag{1}$$

$$\frac{dc_{ER}}{dt} = g_{cER}(c, cER, cMT, v, w) \ , \tag{2}$$

$$\frac{dv}{dt} = \gamma \cdot \left[-2 \cdot \boldsymbol{G_{Ca}} \frac{v - z_{Ca1}}{1 + e^{-\frac{v - z_{Ca2}}{R_{Ca}}}} - G_{NaCa} \frac{c}{c + x_{NaCa}} (v - \boldsymbol{z_{NaCa}}) \right] + g_v(c, cER, cMT, v, w) \ , \tag{3}$$

$$\frac{dw}{dt} = g_w(c, cER, cMT, v, w), \tag{4}$$

$$\frac{dc_{MT}}{dt} = g_{cMT}(c, cER, cMT, v, w) \tag{5}$$

Functions $g_x(x = c, cER, cMT, v, w)$ are defined in Rosenberg & all (2016).

3. Dynamical analysis of the system

The equations (1) – (5) describe the nonlinear autonomous dynamical system

$$\dot{\boldsymbol{x}} = \boldsymbol{F}(\boldsymbol{x}; G_{Ca}, z_{NaCa}) \tag{6}$$

where the state space vector is $\boldsymbol{x} = [c, cer, v, w, cmt]^{\boldsymbol{T}}$.

The properties of this system can be studied using methods of the corresponding theory of dynamical systems. As the control parameters will be used as an example the conductance of the voltage operated calcium channel GCa and the reverse potential of the sodium/calcium exchanger zNaCa. The reason for this choice is the possibility to change their values using different drugs like nimodipin or the external calcium concentration. For this can be found the published experimental results allowing the verification. The meaning and values of the other parameters can be found in Rosenberg & all (2016).

According to Prasad (2015) the coexisting and hidden attractors can be approached starting from the perpetual points instead from nonstable fixed points. In the perpetual points the acceleration

$$\ddot{\boldsymbol{x}} = {}^{d\boldsymbol{F}}\!/_{d\boldsymbol{x}}\, \boldsymbol{F} = \boldsymbol{G}(\boldsymbol{x}) = \boldsymbol{0} \tag{7}$$

is equal zero but the velocities are non-zero, see Prasad (2015). Among the solutions of (7) there are both - the fixed points (**FP**) and perpetual point (**PP**). Let the eigenvalues of F are λ and of G are μ. In the **PP**, it is fulfilled

$$\mu = \lambda^2. \tag{8}$$

To demonstrate that, a point in the oscillating area was chosen. The coordinates of the fix and perpetual points were searched using special developed program starting from the different points in the domain $x_1 \in (-0.2; 0.2); x_2 = 0.2; x_3 \in (-70; 20); x_4 = 0.1; x_5 = 0.00001$.

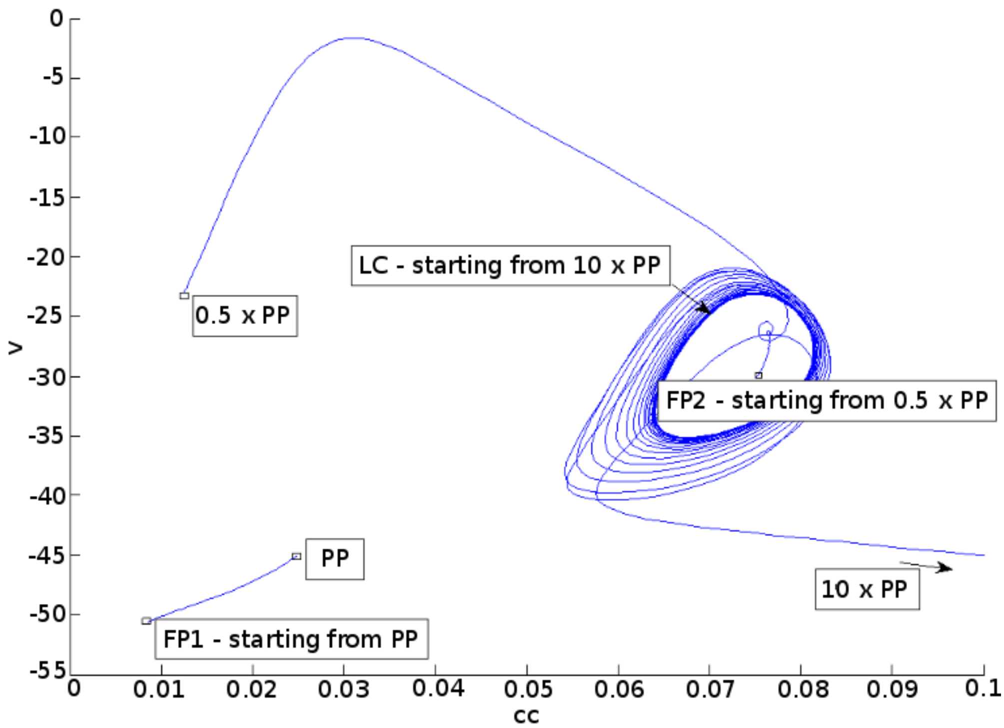

Fig. 3: Self-excited and coexisting attractors for GCa=0.0006 and zNaCa=-24.

Chosen the point (0;0.2;-45;0.1;0.00001) as an initial one, the perpetual point **PP** = $0.0249; 0.1669; -44.9989; 0.0011; 0.0005$ has been found. Starting the numerical solution from this point, one obtains the stable fixed point **FP**1- see Fig.3. Since we are in the oscillating area, this fixed point is one of the set of coexisting stable attractors.

Running along the line in the 5D configurational space (see Fig. 4 where the 3D subspace c – cer –v is shown only) what is performed by changing the length of the vector **PP**, one intersects the basins of attraction of the other attractors. As an example, the fix point **FP**2 corresponding with the starting point 0.5x**PP** – the non-stable attractor is shown.

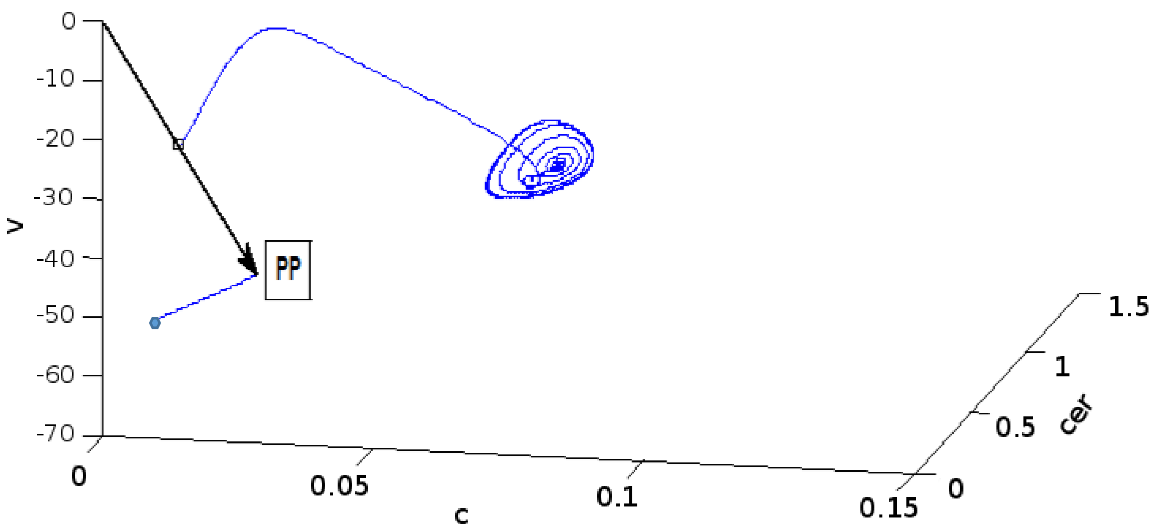

Fig. 4: Configurational 3D subspace with both coexisting attractors and the perpetual point.

Going further (10x**PP**), the self-excited attractor is obtained (its basin of attraction contains the neighborhoods of the non-stable equilibrium point FP2) and it corresponds with the Fig. 3.

4. Conclusions

The simple model (1)-(5) allows to simulate not only the basic properties of the ICCLC but also find the coexisting and hidden attractors. As an effective method for searching these attractors seems to be to use the perpetual points with their properties. In this contribution the application of the method to relatively complex 5D nonlinear model of the Cajal-like interstitial cell was shown.

The whole algorithm consisting from the finding of all perpetual points, corresponding attractors and their basins of attraction will be discussed in the in more detail during the conference presentation.

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