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Simple Model of the Cajal-Like Interstitial Cell and Its Analysis

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Abstract: Cajal-like interstitial cells (IC-LC) can be detected e.g. in the bladder wall tissue. The current research proves their important role in both physiological and pathological function of this organ. The authors developed relative simple mathematical model consisting of five nonlinear ODEs. The model accuracy was verified using published experimental results. Presented nonlinear dynamical system was then analyzed using software Matcont. This analysis allowed to simulate the influence of different drugs on the function of the bladder. The drug influence was again compared with the experimental results.

Introduction

To model the pathological events in the lower part of urinary tract (LPUT) like the over-active bladder (OAB) and detrusor over-activity (DO), it seems to be necessary to take into account all cellular types present in the detrusor tissue. Besides the smooth muscle cells (SMC) there are the Cajal-like interstitial cells (ICCLC) and urothelium cells. According to the last investigations (see e.g. the survey [1] and [2]), the ICCLC are involved in the spontaneous contractile activity during bladder filling. For this purpose it's useful to develop relatively simple model based on the current knowledge about these cells ([3], [4], [5]). Such a model allows to study the influence of different drugs using free software packages like MATCONT or XPPAUT. This is the goal of this contribution.

Description of the model

According the above mentioned papers the scheme of ICCLC presented in Fig. 1 was used.

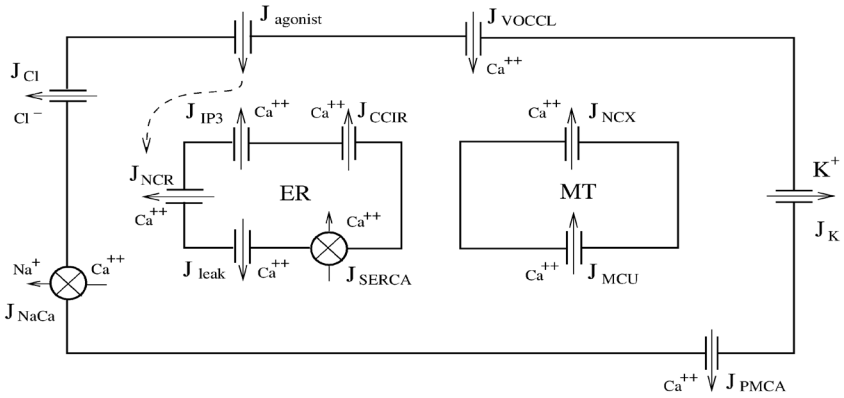

Fig 1: Schema of ICCLC with all fluxes. ER is the endoplasmatic reticulum and MT is the mitochondria.

The basic equations for Ca2++ concentration in cytoplasm (c ev. cc), in ER (c_{ER}), in MT (c_{MT}), for the membrane potential (v) and the variable w are following

$$\frac{dc}{dt} = J_{IP3} - J_{VOCCL} + J_{CICR} + J_{IICR} + J_{Leak} - J_{SERCA} - J_{PMCA} + J_{NaCa} - J_{MCU} + J_{NCX}; \qquad (1)$$

$$\frac{dc_{ER}}{dt} = J_{SERCA} - J_{CICR} - J_{IICR} - J_{Leak}; \tag{2}$$

$$\frac{dv}{dt} = \gamma \cdot [J_{Cl} - J_{VOCCL} - J_{NaCa} - J_K]; \tag{3}$$

$$\frac{dw}{dt} = \lambda \cdot \left[S \cdot \frac{(c+x_w)^2}{(c+x_w)^2 + beta \cdot e^{-\frac{v - z_{Ca3}}{R_K}}} - w \right]; \tag{4}$$

$$\frac{dc_{MT}}{dt} = J_{MCU} - J_{NCX}. \tag{5}$$

On the right hand sides there are the ion fluxes. The corresponding formulas and basic values of parameters was taken from literature, mainly from [5] and [6]. The parameters were then fitted in accordance with published experimental results.

Some results

As an example, in Fig. 2 there is shown the influence of the equilibrium potential of the Na-Ca exchanger zNaCa, which can be advantageously influenced by drug.

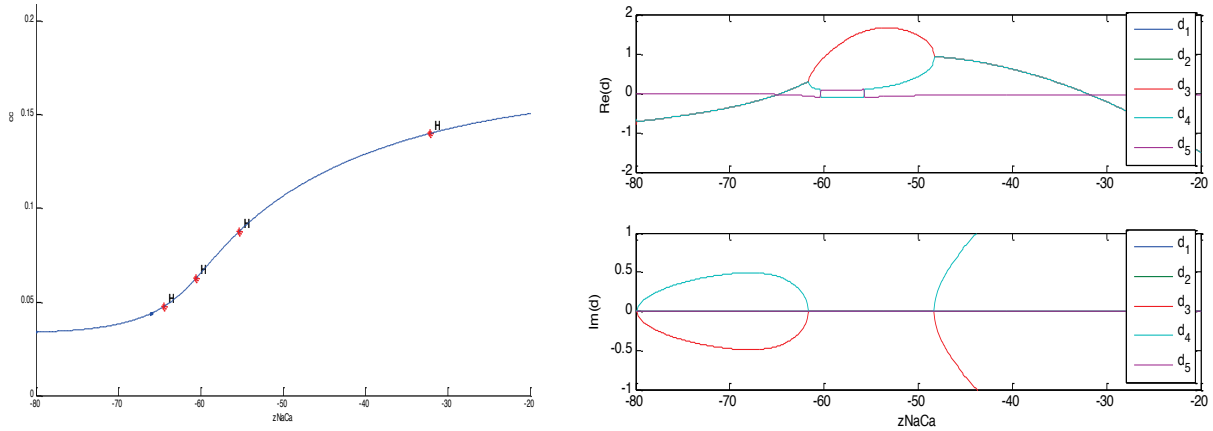

Fig. 2: left: Influence of zNaCa on Ca2++ concentration; right: change of eigenvalues. H are the bifurcation points – comparing with the eigenvalues change, the stability can be determined.

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