Spatiotemporal Pattern Formation in a Model of Electrically Coupled Smooth Muscle Cells

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Overview

Electro-mechanical coupling (EMC)

- Electro-mechanical coupling (EMC) is the contraction of muscle cell as a result of the excitability of the cell membrane in response to an external stimulation.
- In some muscle cells, for example smooth muscle cell (SMC), EMC activity is spontaneous due to ion fluxes in the cell membrane through the voltage-gated ion channels.
- This type of behaviour of the muscle cell is known as *pacemaker dynamics*.

Research goals

Motivation

- *In vivo* studies showed that pacemaker EMC activity observed in a arterial muscle cells depend on transmural pressure.
- Upon elevation of transmural pressure, spontaneous electrical firing is observed and the blood vessel constricts.

Aim

- To investigate mathematically how parameters involved in the equations governing transmural pressure influence the ionic mechanisms and EMC activity of smooth muscle cells in feline cerebral arteries.
- To study the collective behaviour of the SMCs by using a reaction-diffusion system and incorporating gap junction coupling between cells.

Schematic diagram of coupled SMCs

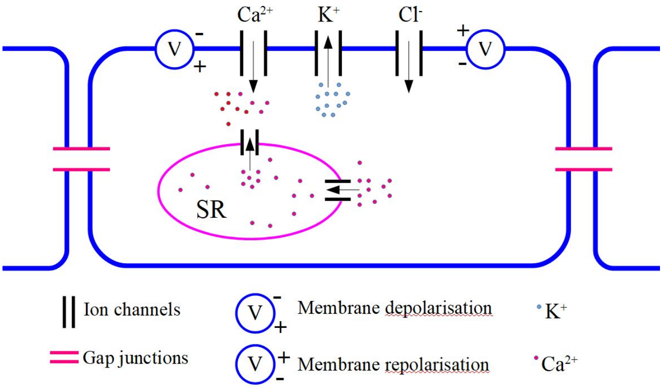

Figure 1: Schematic representation of coupled smooth muscle cells

Coupled SMCs Model

$$\frac{\partial V}{\partial \tau} = D\frac{\partial^2 V}{\partial X^2} - \overline{g}_L(V - \overline{v}_L) - \overline{g}_K N(V - \overline{v}_K) - \overline{g}_{ca} M_\infty(V)(V - 1) \tag{1a}$$

$$\frac{\partial N}{\partial \tau} = \lambda_N(V)\big(N_\infty(V) - N\big) \tag{1b}$$

where V is the membrane potential, N is the fraction of open potassium channels, and

$$M_\infty(V) = 0.5\left(1 + \tanh\left(\frac{V - \overline{v}_1}{\overline{v}_2}\right)\right)$$

$$N_\infty(V) = 0.5\left(1 + \tanh\left(\frac{V - \overline{v}_3}{\overline{v}_4}\right)\right)$$

$$\lambda_N(V) = \psi \cosh\left(\frac{V - \overline{v}_3}{2\overline{v}_4}\right)$$

with no-flux boundary conditions and initial conditions:

$$V(0, X) = V_0 + Ae^{-\left(\frac{X - X_0}{\sigma}\right)^2} \text{ and } N(0, X) = N_0, \forall\, X \in \Omega$$

Single cell dynamics

A bifurcation analysis for a single SMC [$D = 0$ in (1a)] reveals transitions between firing and resting states. We considered $\overline{v}_1$, $\overline{v}_3$ and ψ as bifurcation parameters.

One-parameter bifurcation analysis

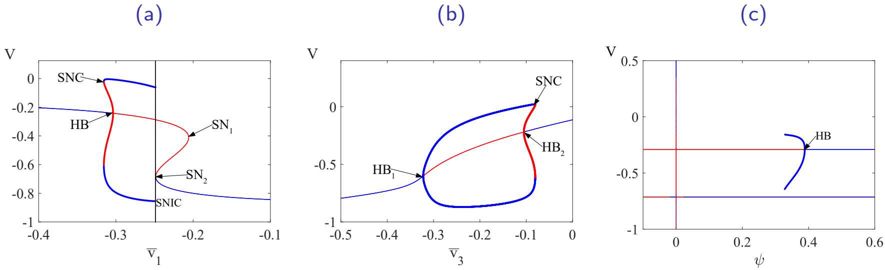

Figure 2: Bifurcation diagram of the membrane potential with $\overline{v}_1$, $\overline{v}_3$, and ψ as bifurcation parameters respectively.

Two-parameter bifurcation analysis

Modulation of model parameters induces type I and type II excitability. Simultaneous variation of $(\overline{v}_1, \overline{v}_3)$ shows the switches between the types of excitability.

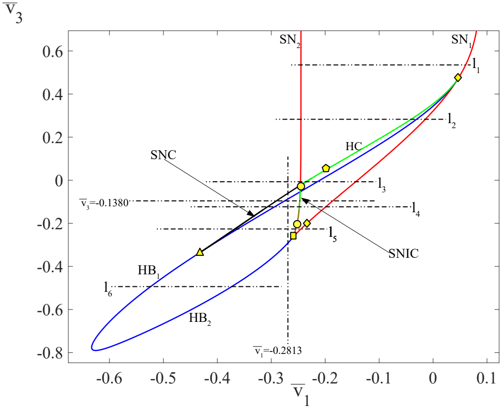

Figure 3: The filled square, diamond, triangle, pentagon and circle refers to the cuspid bifurcation point, Bodganov-Takens bifurcation and generalised Hopf bifurcation, resonant homoclinic and non-central saddle homoclinic bifurcation respectively.

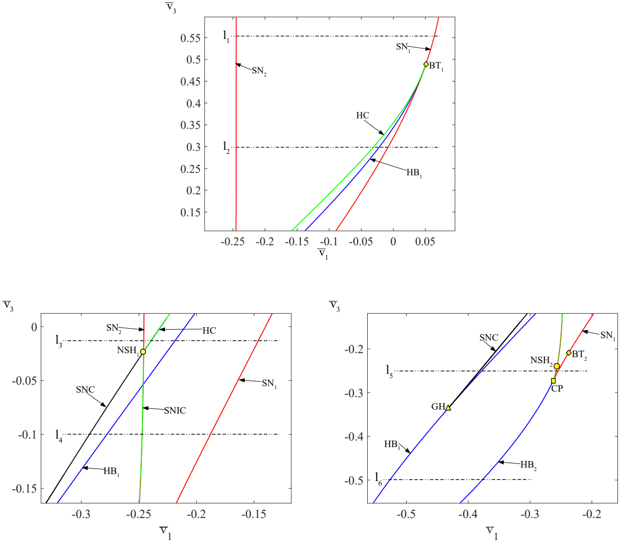

Figure 4: Enlargement of the two-parameter bifurcation diagram.

Bifurcation diagrams along lines l_1 to l_6 in Figure 9

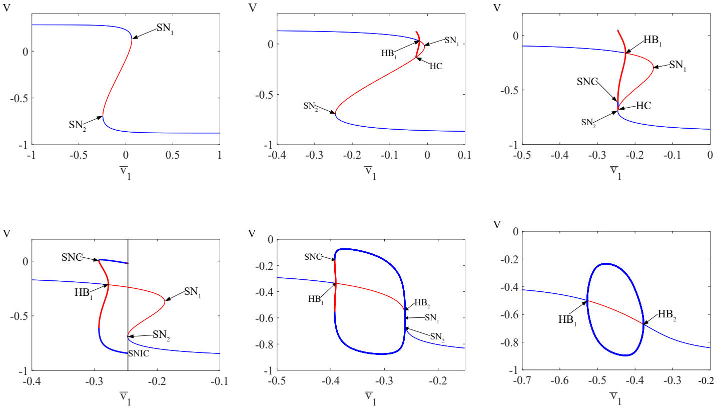

Figure 5: One-parameter bifurcation diagrams of the membrane potential V along lines l_1 to l_6 in Figure 9

Region of tristability

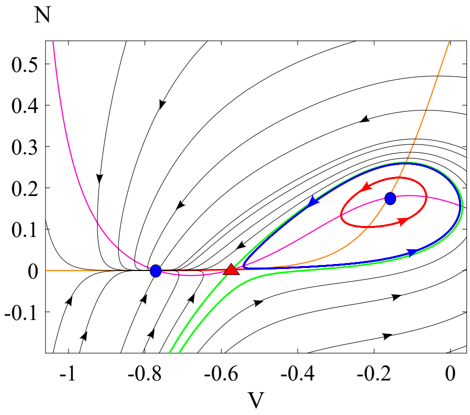

Figure 6: A phase plane diagram along slice l_3 showing the tristability phenomenon. The red and blue curves are the unstable and stable periodic orbits. The magenta and orange curves are the nullclines for N and V. The black curves are the solution tractories. The filled blue circle and red triangle refers to the stable and unstable equilibria, respectively.

Computational results of the coupled SMCs model

Variation of model parameters results in wide range of spatiotemporal patterns including stationary inhomogeneous patterns, travelling pulses and fronts with spatiotempoaral chaos.

Effect of varying $\overline{v}_1$

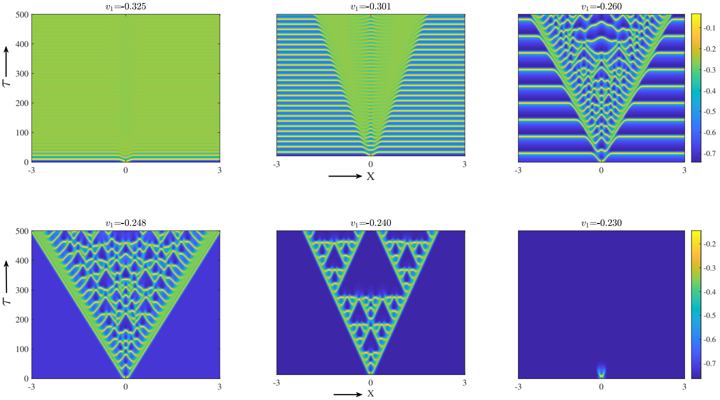

Figure 7: Space-time plot of the membrane potential V for selected values of parameter v_1

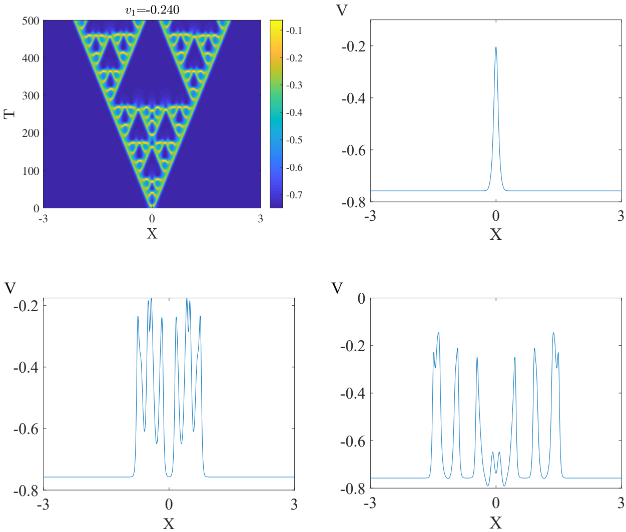

Figure 8: Solution profile are shown for times $\tau = 20; 200; 400$. The solution starts as a pulse, which then destabilizes to create secondary waves moving in opposite direction of the pulse that collide into one another.

Effect of varying ψ

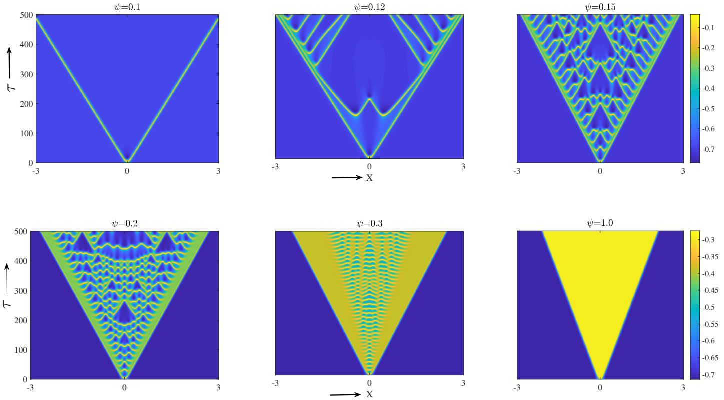

Figure 9: Space-time plot of the membrane potential V for selected values of parameter ψ

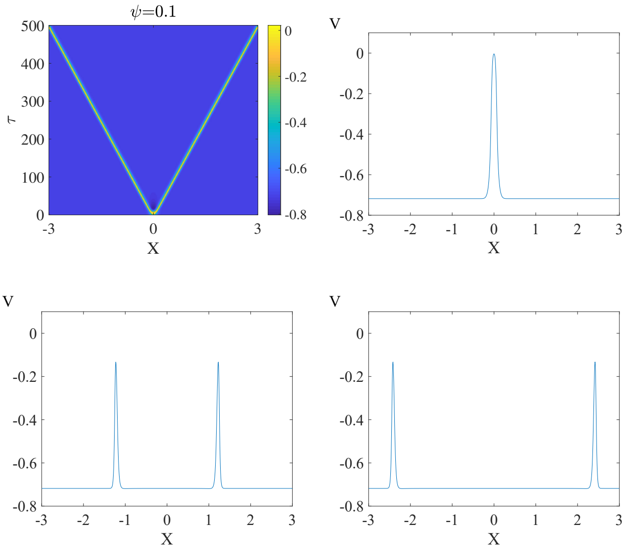

Figure 10: Solution profile are shown for times τ = 20; 200; 400. The solution starts as a pulse, which then turn into two stable pulses propagating in opposite direction.

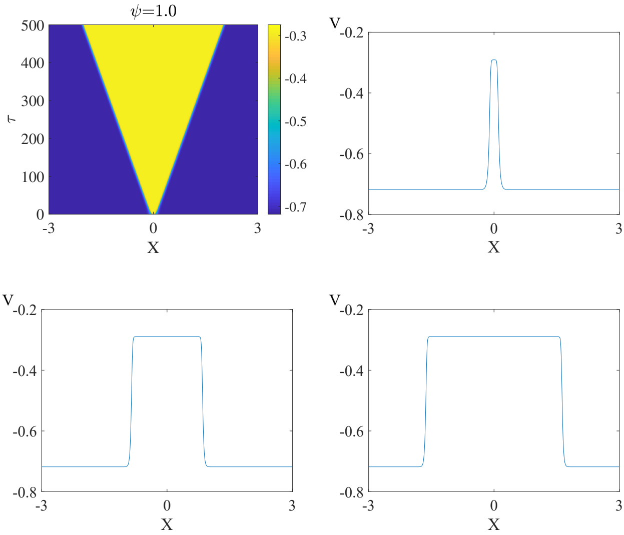

Figure 11: Solution profile are shown for times $\tau = 20; 200; 400$. The solution starts as a pulse with a plateau, which then turn into glued fronts propagating in opposite direction.

Summary

- We investigated the role of physiological parameters on EMC activity of SMCs in feline cerebral arteries.
- We found that the EMC is regulated by model parameters not external sources.
- Our results indicate that in some parameter regimes the coupled cells exhibit spatiotemporal chaos.
- These results could be useful in improving the understanding of physiological responses and disorders in smooth muscles.

Future outlook

- It remains to analyse the spectral stability of the travelling wave solutions observed in the model.
- Modify the model by incorporating the Na^+ inward current.