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On the electro-chemo-mechanical modelling of stomach smooth muscle contraction

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During the ingestion of a meal the activation of smooth muscle cells (SMC) in the stomach wall lead to different types of contraction and relaxation processes, enabling the stomach to perform its main functions, which are the storage, mixing and transport of food. A three-dimensional multi-field and multi-scale model of the gastric smooth muscle contraction is presented and its ability is tested in simulations performed on a tissue strip as well as on the whole organ.

1 Introduction

The gastric reservoir of the stomach, consisting of the fundus and upper corpus, stores the arriving food at low pressure by relaxing its wall, which maintains otherwise a tonic contraction. In the antral pump, featuring the lower corpus and antrum, see Figure 1 a), the food will be mixed and transported by phasic peristaltic contraction waves, moving from the corpus down to the antrum, while getting stronger in this direction. A defective reservoir function, as well as rapid or delayed gastric emptying are common diseases associated with abnormal gastric motility, the last one also referred to as gastroparesis. Thus, a three-dimensional model of gastric smooth muscle contraction, as presented here, can be useful in predicting the mechanical outcome in health and disease. For the modelling approach, the three main fields considered in the excitation-contraction process are the electrical field Φ, the chemical field $[\mathrm{Ca}^{2+}]$, and the mechanical field φ. A mechanical feedback mechanism $\Phi = \Phi(\varphi)$ is included to simulate the stretch-sensitivity of the muscle. Appropriate boundary values are applied on the numerical models of a muscle strip and of the whole stomach and the problems are solved within the finite element approach.

2 Modelling

To account for the multi-layered structure of the stomach wall, the inner layer, which only takes a passive part in the mechanical deformation, is modelled with the same approach as in [1]. The muscular layer of the stomach wall contains the smooth muscle fibres, thus an anisotropic approach is used where the strain energy function of its active part

$$\Psi_{\mathrm{a}}(\varphi) = \sum_{i=1}^{n} f_{\mathrm{s},i}\,\eta P_{\mathrm{opt}} \int \exp\left[\frac{-(\lambda_{\mathrm{s},i}-\lambda_{\mathrm{opt}})^2}{2\xi_{\mathrm{s}}^2}\right] \mathrm{d}\lambda_{\mathrm{s},i}, \tag{1}$$

is weighted in every of the n considered fibre directions with the corresponding fraction $f_{\mathrm{s},i}$. Equation (1) depends on the smooth muscle fascicle stretches λ_{s} and the parameters ξ_{s}, λ_{opt} and P_{opt}, see [1]. The level of activation $\eta \in [0,1]$ corresponds to the fraction of the cross and latch bridges of myosin and actin filaments, calculated by the extended Hai-Murphy model [2]. This model uses a calcium-transient as an input signal, which is here assumed to change in a bell-shaped manner with the SMC membrane potential Φ_{SMC} [3]

$$\dot{[\mathrm{Ca}^{2+}]} = q_0 \exp\left(\frac{-\Phi_{\mathrm{SMC}}^2}{2\xi^2}\right) - k\left([\mathrm{Ca}^{2+}] - [\mathrm{Ca}^{2+}]_{\mathrm{rest}}\right), \tag{2}$$

with the resting calcium concentration $[\mathrm{Ca}^{2+}]_{\mathrm{rest}}$ and parameters q_0, ξ and k. Specialised cells, called Interstitial cells of Cajal (ICC), generate an electrical oscillation known as slow waves, which propagate passively to neighbouring SMCs, thus generating Φ_{SMC}. They are described with a two-variable FitzHugh-Nagumo equation

$$F^{\phi}(\phi, r) = \kappa\phi(\phi-\alpha)(1-\phi) - r \quad \text{and} \quad \dot{r}(\phi, r) = \varepsilon(\gamma(\phi-\beta) - r), \tag{3}$$

where the source term F^{ϕ} is scaled and incorporated in a diffusion-reaction equation for the ICC membrane potential Φ_{ICC} to describe the movement of the slow waves in the ICC-network. Equation (3) depends on the normalised membrane potential ϕ of the ICC, the recovery variable r, the location- and stretch-dependent ε and parameters $\kappa, \alpha, \beta, \gamma$. Finally, Φ_{SMC} is calculated by scaling the normalised membrane potential with the location-dependent resting potential Φ_{SMC}^{r} and the stretch-dependent plateau potential Φ_{SMC}^{p} of the SMC slow waves. The latter one induces the mechanical feedback of the model

$$\Phi_{\mathrm{SMC}} = (\Phi_{\mathrm{SMC}}^{p} - \Phi_{\mathrm{SMC}}^{r}) \cdot \phi + \Phi_{\mathrm{SMC}}^{r}. \tag{4}$$

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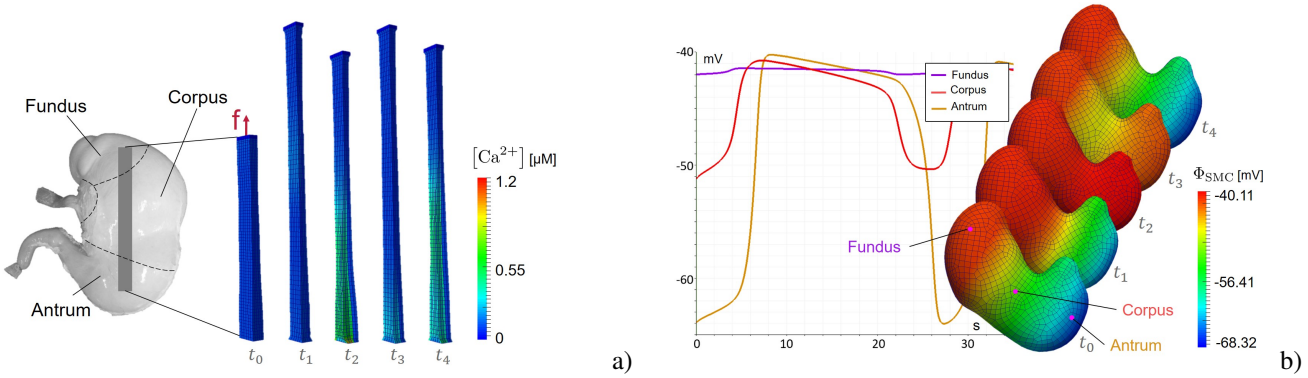

Fig. 1: a) Simulation of the traction of a gastric tissue strip and evolution of the intracellular calcium ion concentration $\left[\mathrm{Ca}^{2+}\right]$. b) Simulation of the whole stomach with the evolution of the SMC membrane potential Φ_{SMC} and illustration of the slow wave behaviour in the fundus, corpus, and antrum.

3 Numerical examples

In a first example the mechanical feedback mechanism of our model is investigated. Therefore we simulate the traction of a longitudinal tissue strip of the stomach wall, which includes the three anatomical regions. The strips thickness and the thicknesses of the two layers are based on histological investigations. The strip is fixed on one side and pulled at the other side with a tensile load f, increasing at first linearly until a maximum value and then being constant over the simulation time. In Figure 1 a) the deformation and the corresponding calcium ion concentration at different time steps $t_i, i = 1, ..., 4$, is illustrated. When the tensile load reaches its stationary value and the strip elongates to a maximum at t_1, the $\left[\mathrm{Ca}^{2+}\right]$ in the fundus stays in the region of $\left[\mathrm{Ca}^{2+}\right]_{\mathrm{rest}} = 0.15\ \mu$M, while it slightly starts to increase in the upper corpus. In the next time step this increase propagates from the corpus down to the antrum, leading to values up to $\left[\mathrm{Ca}^{2+}\right] = 0.6\ \mu$M and stronger, now visible contractions in the muscular layer, resulting in a shortening of the tissue strip. Hereafter, $\left[\mathrm{Ca}^{2+}\right]$ decreases at first in the corpus and then in the antrum, followed by a relaxation in the whole strip, which elongates again due to the tensile load. In the last time step the previously described process starts to repeat again. The contraction in the distal half of the strip is due to the increased, stretch-dependent plateau potential of the SMC membrane potential. Everytime a slow wave signal moves along the strip, the $\left[\mathrm{Ca}^{2+}\right]$ increases, leading to the typical phasic contractions. To better understand the region-dependent slow wave behaviour, in a second example we investigate the dynamics of the SMC membrane potential Φ_{SMC} on the whole undeformed stomach, see Figure 1 b), also tracked at three different locations denoting the fundus, corpus, and antrum. The stomach is fixed with finite springs at the greater and smaller curvature, representing the fixation via ligaments. During the simulation the fundus does not show electrical oscillation but a constant membrane potential of -40 mV at every time step t_i. In the whole stomach wall a gradient of the resting membrane potential Φ^r_{SMC} of the slow waves at time step t_0 is observed, decreasing in aboral direction from -40 mV to -70 mV. During the simulation the slow waves reach their peaks first in the corpus and then in the antrum, depolarising the stomach everywhere to -40 mV. Hereafter, in time steps t_3 and t_4, the membrane potential decreases at first in the corpus, followed by the antrum, until the resting membrane potential is reached.

4 Conclusion

Several cell and tissue models are available describing parts of the gastric contraction process, see [2] and [5]. However, little has been documented on stomach smooth muscle contraction regarding three-dimensional boundary problems and the whole mechano-electrochemical process. Our model is able to replicate several events observed in the in vivo stomach, for instance the electrical tone in the fundus, the underlying slow wave activity, which organizes the gastric motor pattern, or the stretch-sensitivity, see [4]. The latter one regulates the activation of gastric peristalsis when food is present. For future work our model should be able to replicate the whole digestive process in terms of smooth muscle contraction.

References

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