Towards bladder function modeling: FES induced detrusor activity modelling

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Abstract

We present a smooth muscle model which enables the simulation of its contraction under functional electrical stimulation (FES). The model takes into account chemical and microscopic mechanics of the contraction. In order to illustrate the model performances, we simulate a well known example: the behaviour of the bladder under electrical stimulation using a Finetech / Brindley implant. This approach allows to compare our qualitative results with experimental data available in the literature. Simulated output (pressure, volume and urine flux) show good consistency both in shape and time course. With the objective to obtain quantitative simulations, we propose a setup for animal in-vivo experiments which should allow us to perform the identification of the model parameters. Preliminary experimental data is presented.

1. Introduction

Muscle modeling is necessary to understand how a contraction is performed, in order to characterize it quantitatively for diagnosis purpose and control strategies design in the framework of functional electrical stimulation (FES). In this paper, we focus on the modeling of one specific smooth muscle: the detrusor. Detrusor constitutes the wall of the bladder, when it contracts, it induces bladder voiding. When bladder control is deficient, one possible solution is to control the contraction through FES [1]. Classically, stimulation is applied on sacral roots, one main drawback of this approach is that both the detrusor and the striated sphincter are stimulated. Sphincter contraction mechanically occludes the urethra. Nevertheless, voiding is possible due to the fact that detrusor has very slow dynamics compared to sphincter. It is important to note that, if electrical stimulation is not correctly managed, intravesical pressure may increase and provoke urine feedback in the kidneys [2]. Individual modeling and estimation of the parameters for each patient may help to tune accurately the stimulators to avoid such problems. In the following, a description of the smooth muscle model is given, as well as the experimental protocol we propose in order to identify model parameters. In the results section we simulate Brindley implant and present preliminary data recorded in vivo.

2. Materials and methods

2.1. Smooth muscle modeling

This section describes the bladder model we developed. The model has a chain structure: the output of one stage is the input of the next stage. The input of the model is the FES signal and the output is the pressure and volume of the bladder. In the following we describe the main characteristics of the model, for more details see [3].

The first stage of the model computes the calcium dynamics induced by the FES signal. The evolution of calcium concentration in the cell is expressed as the sum of all calcium currents through the membrane and with the sarcoplasmic reticulum. We base our work on the contribution of Königsberg et al. [4] for the expression of the currents. We concentrate on the mechanisms directly influenced by neural stimulation and thus consider the currents driven by membrane potential $v_i$:

$$J_{vocc} = G_{Ca} \frac{v_i - v_{Ca}}{1 + e^{(v_i - v_{Ca2})/R_{Ca}}}$$

$$J_{extrusion} = D_{Ca} \left(1 + \frac{v_i - v_d}{R_d}\right)$$

Once the calcium concentration is computed it can be used as the input command of our modified Hai & Murphy model (Fig. 1). The rate constants $k_1$ and $k_6$ are then calcium dependent through a sigmoidal relationship. Also, $k_4$ and $k_7$ depend on contraction speed. This takes into accounts the...
higher probability for a bridge to break if the actin and myosin filaments are moving relatively to each other. The next part of the model links the kinetic equations from Hai & Murphy to Huxley’s cross-bridge model. Considering the introduction of force/length relationship \( f(l_{\epsilon_c}) \) and our definition of \( f \) and \( g \) the derivative of the first and second order moments of \( n \), portion of attached bridges, can be obtained. They are equivalent to the stiffness and force of the contractile element \( E_c \):

\[
\dot{k}_c = f(\epsilon_c) f(\xi, t) - (f + g)(\xi, t) k_c \tag{3}
\]

\[
\dot{F}_c = \frac{f(\epsilon_c) f(\xi, t)}{2} - (f + g)(\xi, t) F_c + \epsilon_c k_c \tag{4}
\]

Due to the relatively slow contraction speed and the distributed character of the mass, the contribution of the inertial terms is very small. We thus use a simple three compartment model: \( E_c \), the contractile element; \( E_s \), the serial linear elasticity element; and \( E_p \) the parallel damping and exponential elasticity elements.

The last stage of the model is specific to the bladder. It computes the pressure and outflow from the force generated by smooth muscles cells. For the geometry of the bladder we propose the most simple model, which is an hollow sphere with a circular opening standing for the urethra. To get pressure from a one dimension tangential force, we used the same formulae that link the stress in the heart wall and blood pressure [6].

Finally, to get the outflow condition when emptying the bladder we will use the law of Bernouilli assuming a perfect fluid and an irrotational outflow. Considering all pressures in respect to abdominal pressure, we can write the outflow as a function of bladder pressure [8].

2.2. Experimental setup

![Fig. 2: 1 Stimulator; 2 Realtime control box; 3 Acquisition electronics.](image)

We have designed an experimental setup in order to elicit artificial contractions of the detrusor and record intravesical pressure, the goal being to compare recorded data with the model output. Acute experiments were conducted on 2 anaesthetized New Zealand white rabbits. Bladder was exposed via abdominal incision. Current pulses were delivered to the parasympathetic nerve at the bladder wall (Fig 3). They are generated by the stimulator developed in our team [7] (Fig 2) and applied using a bipolar hook electrode. This stimulation site has two advantages: a simple surgical approach and the stimulation is applied only to nerve fibres leading to the detrusor. The first quantity we measure is intravesical pressure. We use Deltran I transducer (Utah Med.) connected to a trans-urethral catheter. It gives us an image of the pressure and its evolution in isovolumic conditions. We also record EMG signals from the bladder wall ([8] [9]). They are collected with wire electrodes inserted tangentially in the bladder using hypodermic needles. The EMG signals are amplified 4000 times and filtered (highpass \( f_h=10\)Hz and lowpass \( f_l=4kHz \)) before recording. To limit noise from the power line, all equipments are battery powered.

3. Results

3.1. Simulation results

In order to compare the output of our model to experimental data available in the literature, we simulated the behaviour of the human bladder undergoing the stimulation of a FineTech / Brindley implant [1]. Our simulation works in two phase: 1) closed sphincter and contracting detrusor induce an isometric contraction. 2) opened sphincter while stimulation is off. As the sphincters have much higher dynamics than the detrusor, we consider the sphincters either opened or closed synchronously with the FES signal off or on, without any dynamics. Our results are presented on figure [1]. They are summarized by the applied stimulus, bladder pressure and volume, and urine flux. They show a good consistency with the experimental results published by Brindley et al. [11], both in their time scale and shape. The pressure curve shows the same small oscillations due to the intermittent stimulation. The outflow has the same round envelope as
Fig. 4: Qualitative simulation results of the behaviour of an artificially stimulated bladder. Quantities are shown normalised to their maximum.

seen in Brindley’s data. The outflow itself falls to zero while the sphincters are closed, leading to voiding in bursts.

3.2. Experimental results

Fig. 5: First experimental results on animal model.

The experimental data gathered are compared to the predictions of the model. In Figure 5 we present preliminary experimental results. Stimulation parameters were: frequency=5Hz, amplitude=5mA and Pulse-width=500µs. We can see a quick rise of intravesical pressure on the onset of stimulation and its much slower return to baseline when stimulation is over. The rapid change around 40 seconds was due to bowel movements. They also could be used to identify its parameters using extended Kalman filtering methods.

4. Conclusion

We developed a model of smooth muscle in order to simulate the bladder function when it is artificially activated through FES. This paper presents the main aspects of our model: it takes into account calcium dynamics and the microscopic mechanics of contractions, and uses a refined mechanical model, in order to produce simulations of realistic behaviours reported in literature. To obtain quantitative simulation, we need to perform the identification of the model’s parameters. A simpler mechanical model helps here, leading to fewer parameters to identify. We now try to identify our bladder model on rabbits before carrying out experiments on humans. Then, FES implant may be optimised and accurately tuned to perform micturition with the best low pressure / high outflow ratio. First results will be presented on in-vivo experiments we are carrying out.

References


