INFRARED NEURAL STIMULATION MECHANISM MODELING

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2 Background

Neurostimulation is widely used to treat chronic conditions. It is usually performed by electrical stimulation of tissues. However, it suffers from several shortcomings, including stimulation artifacts, low spatial resolution, incompatibility with magnetic resonance imaging, and the order in which nerve fibers are activated is not physiological. Optical stimulation could overcome all these shortcomings.

Among the optical nerve stimulation techniques, infrared neural stimulation (INS) is very promising because it does not require any prior genetic modification. INS consists of nerve activation due to transient exposure to infrared light. Our team has developed an experimental setup capable of compound action potential (CAP) elicitation in an excised rat sciatic nerve with the help of INS [1], [2]. The setup simultaneously records the nerve electrophysiological activity and the temperature at the surface of the nerve to link the CAP triggering and temperature gradients. However, numerical modeling would be helpful to investigate further why heat accumulation results in larger CAP amplitude. Moreover, modeling the light diffusion could help us better monitor the thermal gradients induced in the nerve based on the surface temperature measurements.

In the literature, three main hypotheses are currently considered as the underlying mechanism of INS: membrane capacitance change [3]–[7], membrane nanoporation [8], [9] or thermosensitive ion channels [10], [11] could be responsible for the axon depolarization. Therefore, the precise modeling of INS is complex, but numerous axon modeling could be used to explore the impact of temperature on the nerve cell. For the sake of simplicity, this project could rely on the Hodgkin-Huxley (HH) model, extensively used in neuroscience, which has already been adapted in the context of the INS [12]–[14]. However, Forrest argues that this simplistic model does not conveniently include thermodynamics considerations in action potential triggering [15]. Therefore, another model than the one developed by Hodgkin and Huxley might be considered.

Regarding the heat diffusion in the nerve during INS, previous work already investigated how temperature evolves at different spots in the nerve [16], [17]. However, these models do not fully describe the type of thermal gradients we observed in our experiments. Based on these works, a new model could be developed to analyze the results of our ex-vivo experiments better.

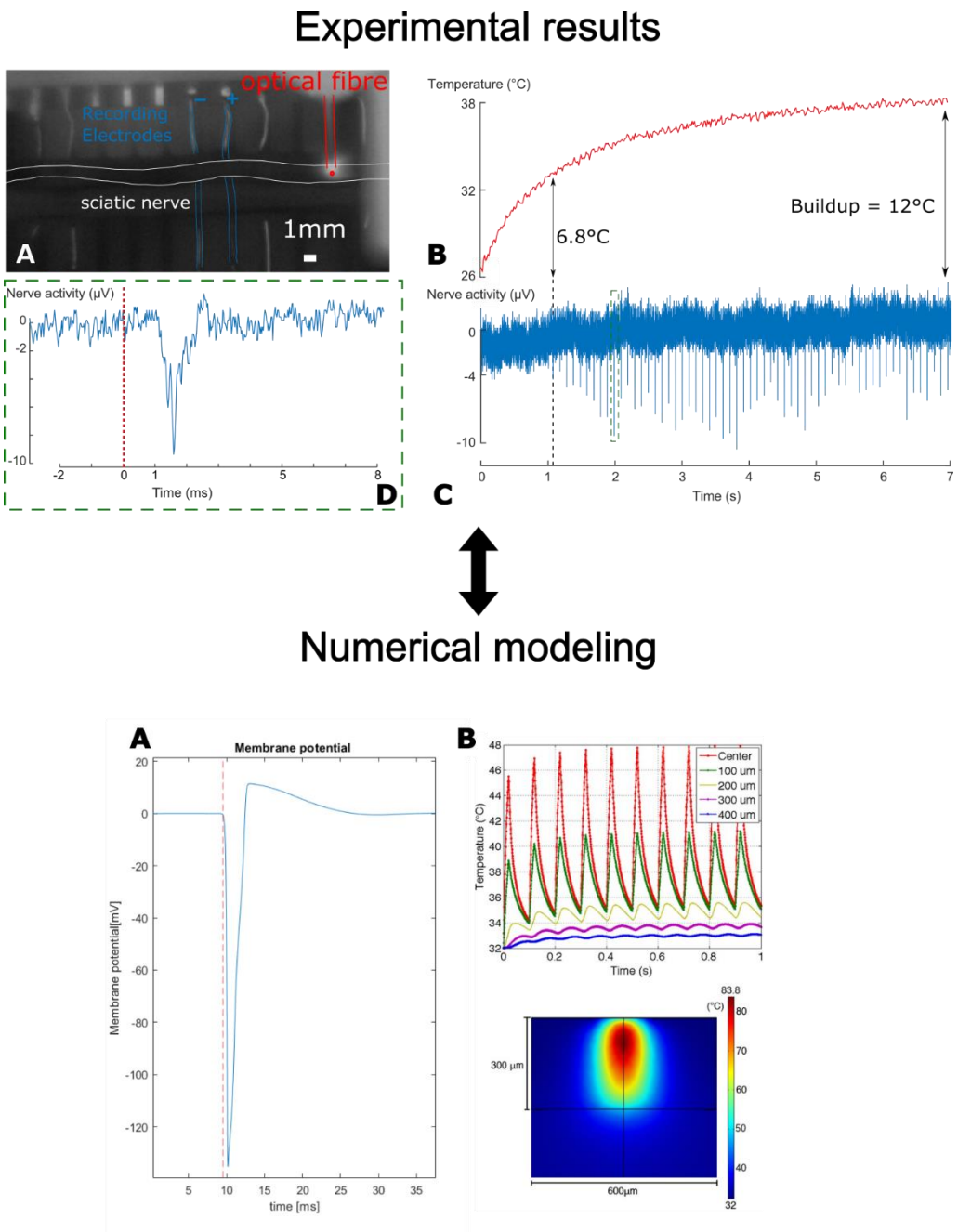

Fig. 1 **Experimental results** Infrared neural stimulation performed on a ex vivo sciatic nerve. (A) Grayscale image of the nerve obtained with IR camera. Brighter pixel is hotter. (B) Temperature of the center of the laser spot highlighted in (A) along the time. (C) Electrophysiological recording of the nerve. (D) Zoom on the 10th action potential evoked by the light pulse train after 2 seconds of stimulation (see green dashed box on C).
Numerical modeling (A) Action potential evoked with a basic Hodgkin-Huxley axon model. (B) Modeling of heating during INS (from [17]).

3 Work

The main goal of this project is to reuse the existing axon model or develop a similar model to investigate the impact of a rapid temperature increase on the membrane. The action potential (AP) elicitation will be based on a change in membrane capacitance, at least for the first model iteration. In parallel, modeling

of the heat diffusion - to better quantify the spatiotemporal temperature gradients in our experiments - could be achieved.

This work is exploratory and will require creativity and autonomy.

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