

Multi-Physics Computational Models for Neuro-Chip Simulation

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1. Introduction

Neuro-chips are bio-hybrid devices in which living brain cells and silicon circuits are coupled together. Neuro-chips are presently being used as a non-invasive technique to *record cellular response to drugs*. A long-term objective is to employ them as an instrument to cure *neurological disorders* or to develop organic computers.

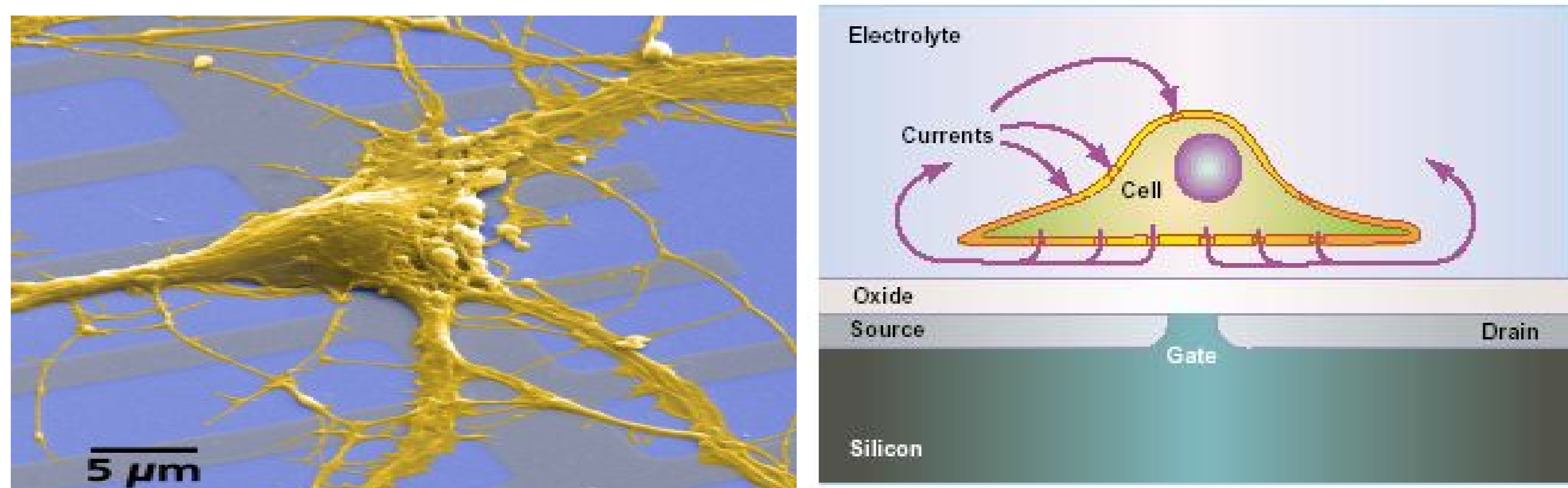


Figure 1: (Left) neuron from rat brain on a linear array of transistors: the ionic current in the cell interacts with the electronic current in the silicon substrate. [2]. (Right) schematics of a neuro-chip [5].

- The basic principle of neuro-chip functioning consists of transducing the input biological signal coming from the neuron (ionic current) into an electrical signal (electric current) that can be measured at the output terminals of the electronic substrate.
- The quality of this measure *strongly depends* on the voltage variation $\Delta V_G = \mathcal{O}(mV)$, which drives the open Gate of the silicon device, due to the membrane ion current $I_M = \mathcal{O}(nA)$.
- This voltage variation depends on the cell-to-substrate distance $\delta \in [50 \div 100] nm$ and on the ionic concentration in the electrolyte cleft, which modulates the electrical resistance of the interstitial cleft.

2. Materials and Methods

All of the above mentioned electro-chemical effects should be properly accounted for by an accurate and robust *numerical simulation tool*, to be used as a predictive instrument for a sound technological design of a bio-hybrid device.

With this aim, we propose a multi-physics computational model of a neuro-chip subject to an applied external stimulation, consisting of [6]:

- the Poisson-Nernst-Planck (PNP) system of non-linearly coupled partial differential equations to account for ionic electrodiffusion processes in the intra- and extra-cellular sites;
- nonlinear interface transmission conditions to account for ion transport across membrane channels and cell-to-chip capacitive coupling;
- the Hodgkin-Huxley ordinary differential system to consistently update at each time level the ionic channel conductance.

3. Results and Discussion

We test the mathematical formulation on two cases of physiological interest, namely, the Hodgkin-Huxley axon [3] and a neuro-chip similar to that of [1].

3.1 Action Potential Simulation

We consider the propagation of an action potential in an unmyelinated neuronal axon, as a consequence of an increase at time $t = 0 s$ of the Cl^- conductance at the center of the axon [4]. The simulated axon length is equal to $4000 \mu m$, while the diameter is equal to $1 \mu m$. Time snapshots of the electric potential spatial distribution along the axon, at $t = 3 ms$ and $t = 5 ms$, shown in Fig. 2 clearly demonstrate the spreading of the action potential towards the two ends of the axon. A similar trend can be observed in Figs. 3 and 4, where the variation of Cl^- concentration and the gating variable spatial distribution are reported.

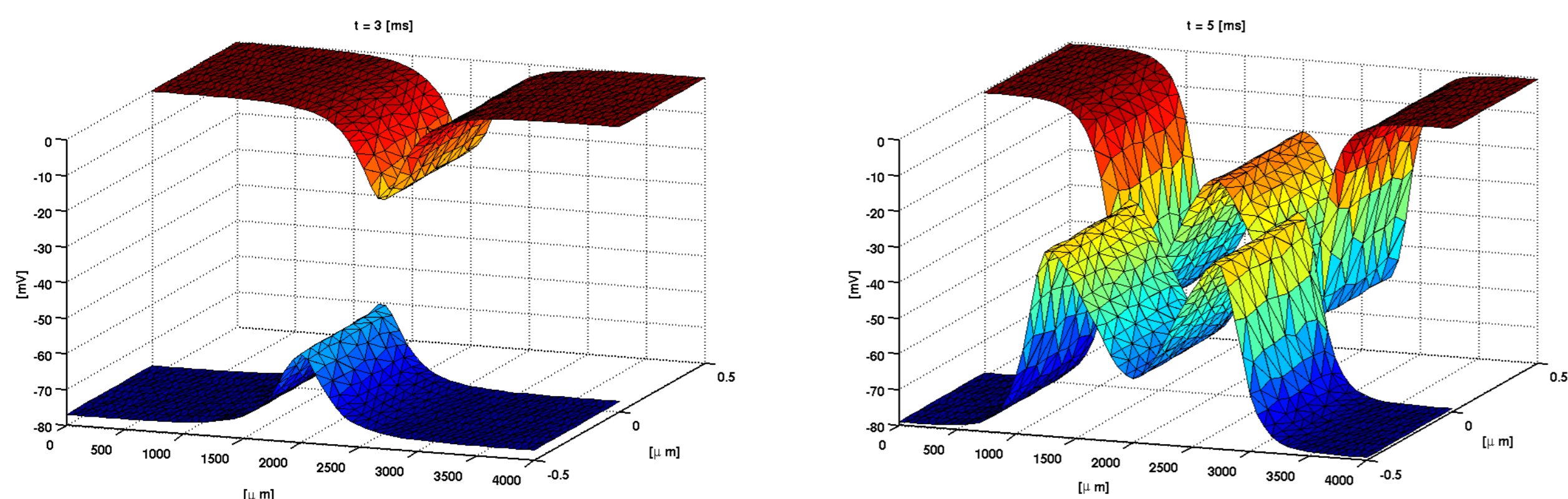


Figure 2: Computed action potential at two different time levels.

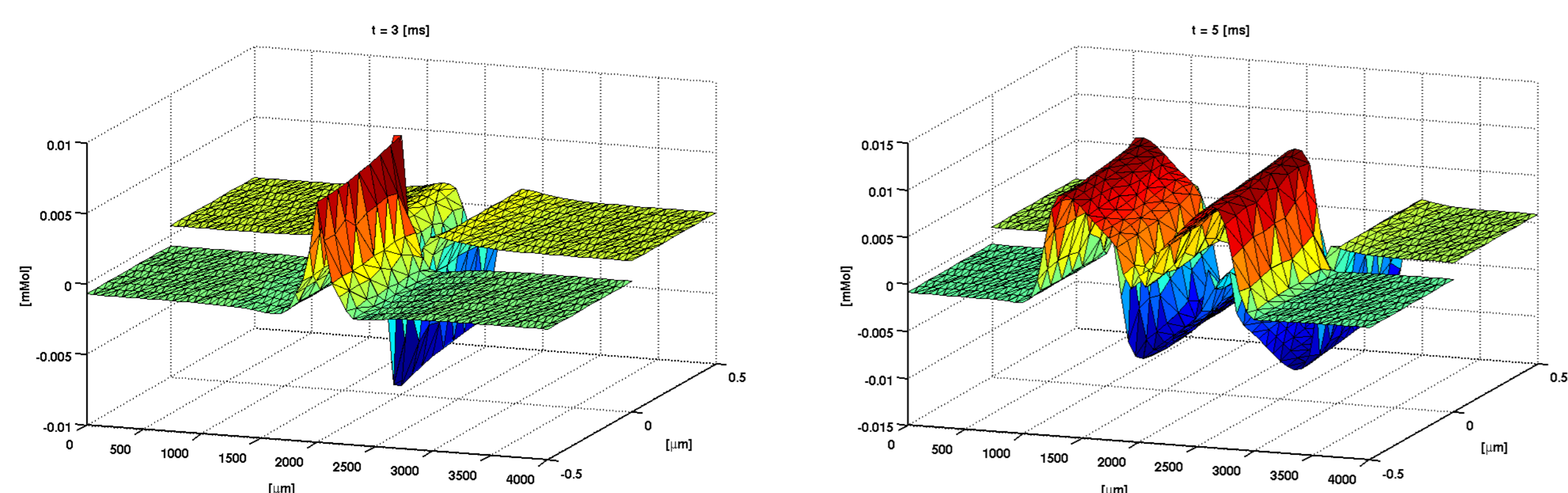


Figure 3: Computed chlorine concentration variation at two different time levels.

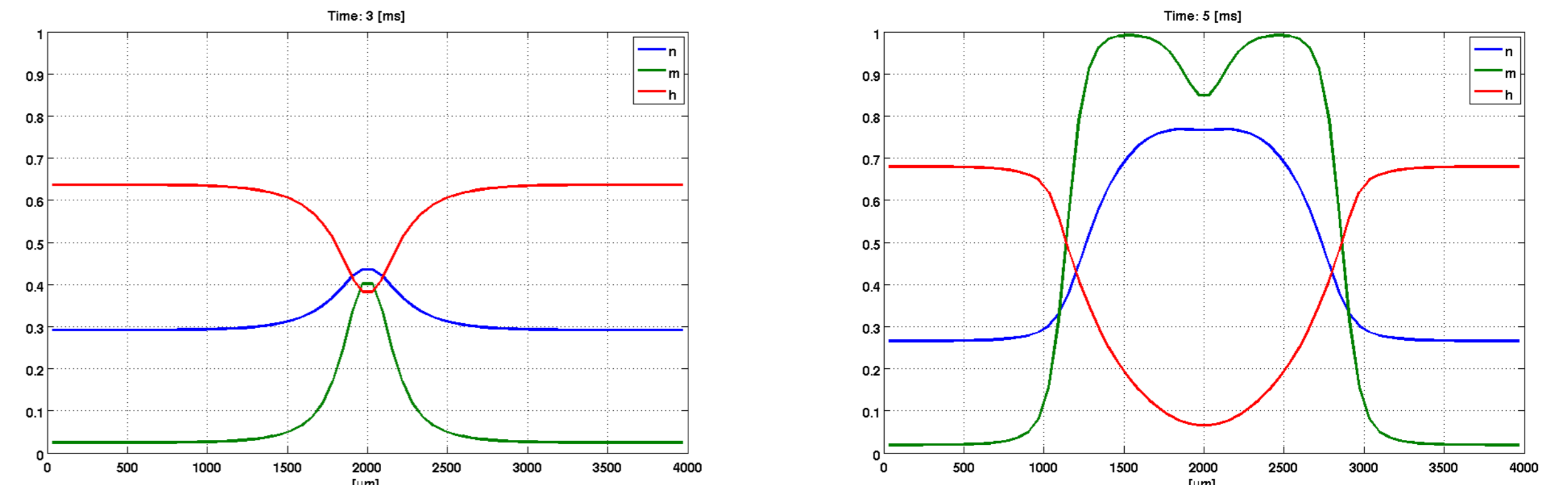


Figure 4: Computed gating variables at two different time levels.

3.2 Neuro-Chip Response to a Depolarizing Pulse of $+80 mV$

We consider a preliminary simulation of a neuro-chip by the numerical study of the response of a field-effect transistor with metal-free gate oxide under an intracellular voltage depolarization stimulating impulse similar to that discussed in [1].

The geometry of the simulated device is similar to what schematically depicted in Fig. 1 (right). The cell-to-chip distance δ is taken equal to $100 nm$, while cell diameter is taken equal to $20 \mu m$.

Fig. 5 illustrates the time behavior of the computed differential gate voltage ΔV_G and of the membrane current I_M . The predicted maximum value of $\Delta V_G = 10 mV$ and the value of the membrane current at the end of the time response ($t = 20 ms$) $I_M = 250 \mu A m^{-1} \cdot 20 \mu m = 5 nA$ are *in good agreement* with the experimental data of [1]. Fig. 6 illustrates the spatial distribution of the electrostatic potential in the electrolyte cleft separating cell and substrate. The steep layers are due to *charge screening effects*, while the non-linear behavior of potential is due to the *full PNP* charge transport modeling in the cleft.

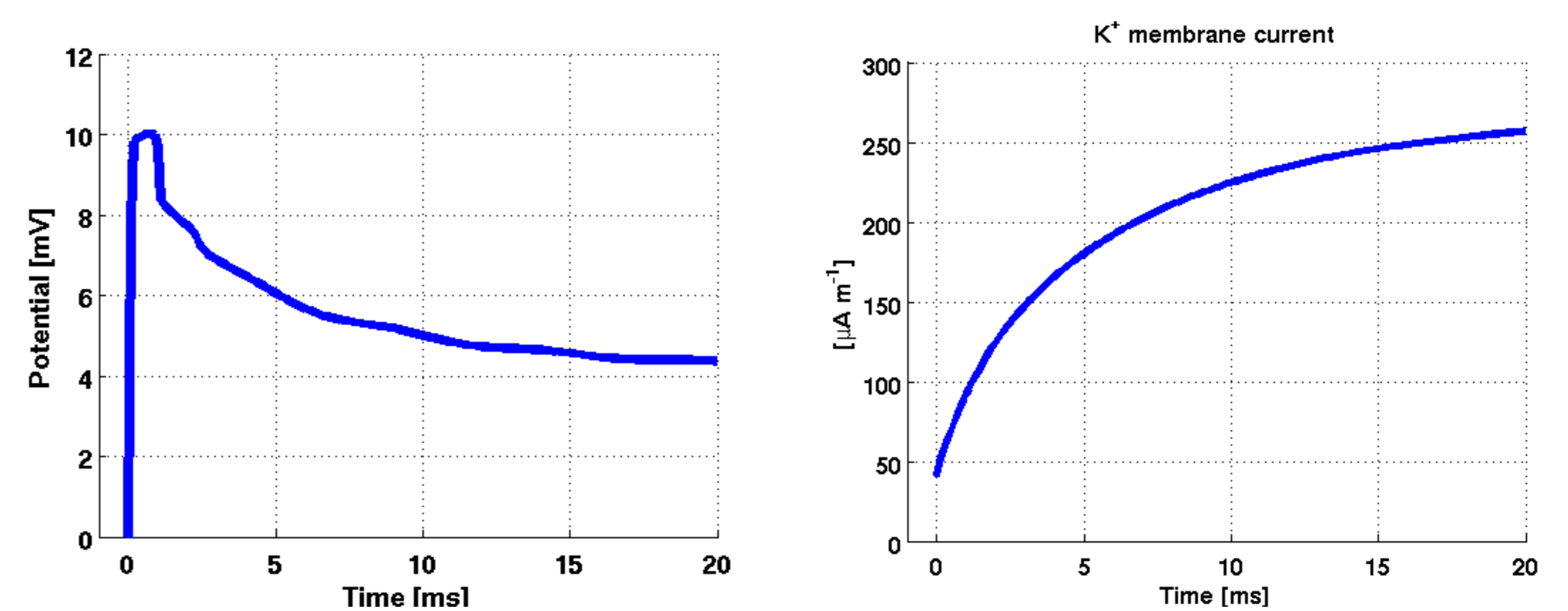


Figure 5: (Left) computed variation of Gate voltage; (right) computed membrane current.

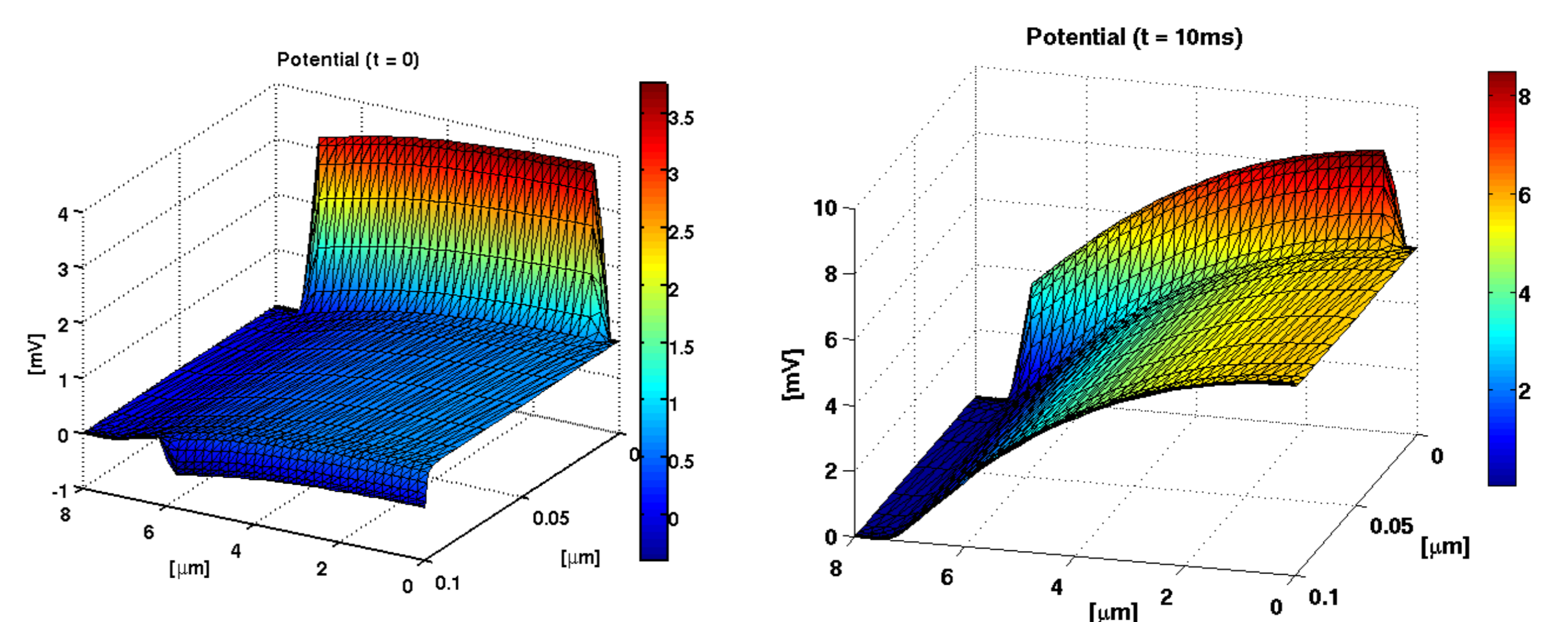


Figure 6: Computed potential distribution in the interstitial cleft between cell and substrate. (Left) $t = 0 ms$; (right) $t = 10 ms$.

4. Acknowledgements

The author gratefully acknowledges the contribution to the presented research provided by Marco Brera, Degree Student; Yoichiro Mori, PhD., M.D.; Prof. Joseph W. Jerome; Bice Chini, PhD., M.D.; Paola Causin, PhD.; Paolo Zunino, PhD; and Carlo de Falco, PhD..

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