Real-time interaction with an electrophysiological cancer cell model

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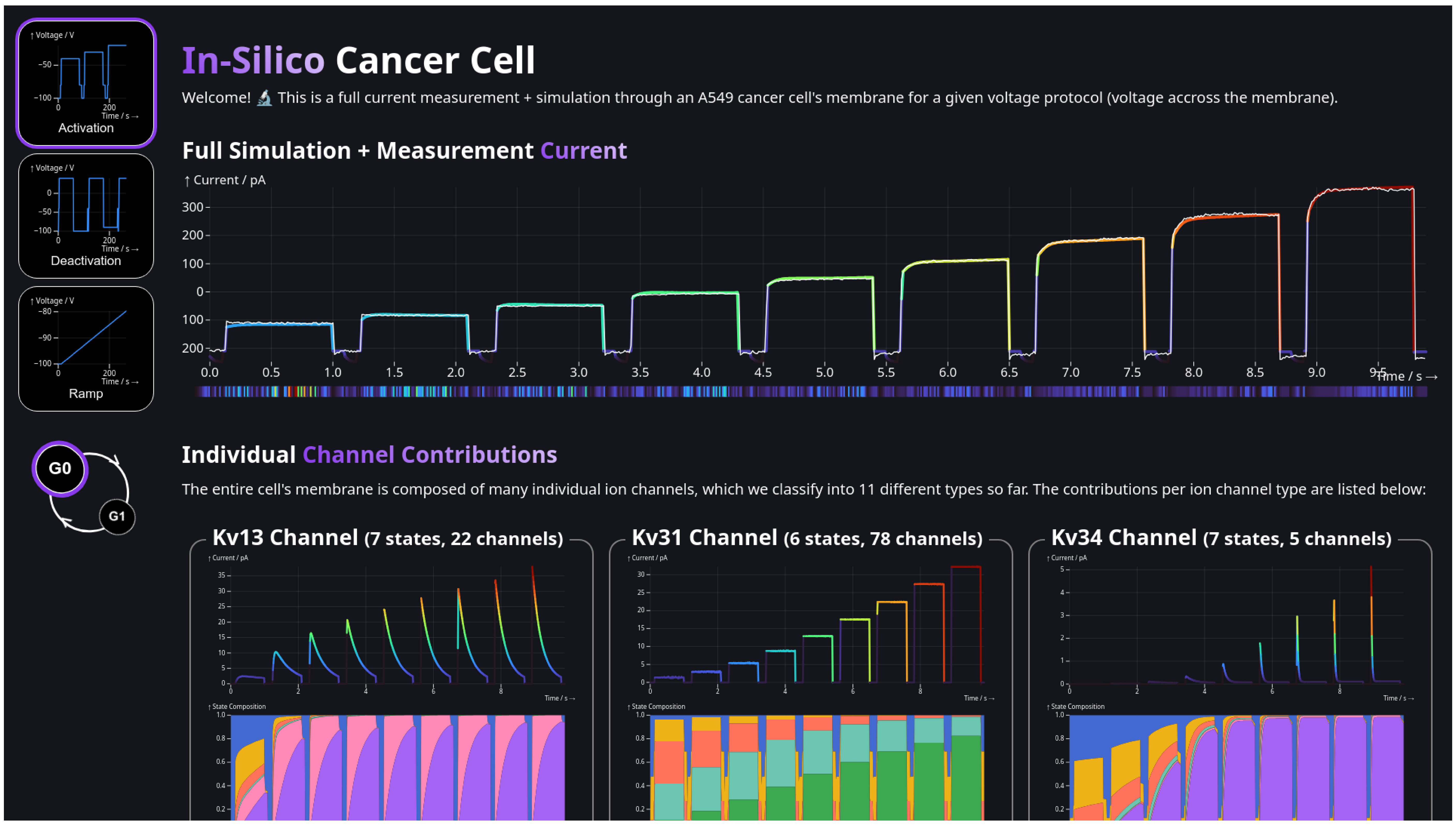
Live, In-Browser Cell Simulation Interface



Available live on in-silico.hce.tugraz.at.

Good stuff

Model

At each time step,

$$I(t) := \sum_{k=1}^{M} N_k I_k(t) = \sum_{k=1}^{M} N_k g_k p_{o,k} \left(V(t) - E_k \right) , \tag{1}$$

$$\boldsymbol{s}_{k,n+1} = H_k \left(V(t_n), \boldsymbol{C}(t_n), t_n \right) \boldsymbol{s}_{k,n} \tag{2}$$

Formulation as a Quadratic Program

Relaxing the integer condition on the solution, and letting $\boldsymbol{d} := \boldsymbol{I}_{\text{meas}}$ for brevity, we can reformulate **??**,

$$\boldsymbol{N}_{\text{opt}} \approx \underset{\boldsymbol{x} \in \mathbb{R}_+^M}{\arg\min}\, f(\boldsymbol{x}) = \underset{\boldsymbol{x} \in \mathbb{R}_+^M}{\arg\min}\, {}^1\!/\!_2 \left\| R\boldsymbol{x} - \boldsymbol{d} \right\|_2^2 ,$$

with cost function $f : \mathbb{R}^M \to \mathbb{R}^+$, which we manipulate to

$$\begin{aligned} f(\boldsymbol{x}) &= {}^1\!/\!_2 (R\boldsymbol{x} - \boldsymbol{d})^T (R\boldsymbol{x} - \boldsymbol{d}) \\ &= {}^1\!/\!_2 \left(\boldsymbol{x}^T R^T R \boldsymbol{x} - \boldsymbol{x}^T R^T \boldsymbol{d} - \boldsymbol{d}^T R \boldsymbol{x} + \boldsymbol{d}^T \boldsymbol{d} \right) \\ &= {}^1\!/\!_2 \left(\boldsymbol{x}^T P \boldsymbol{x} + \boldsymbol{x}^T \boldsymbol{q} + \boldsymbol{q}^T \boldsymbol{x} \right) + \mathcal{O}(1) \\ &= {}^1\!/\!_2 \boldsymbol{x}^T P \boldsymbol{x} + \boldsymbol{q}^T \boldsymbol{x} + \mathcal{O}(1) \end{aligned}$$

where we let $P := R^T R \in \mathbb{R}^{M \times M}$ and $\boldsymbol{q} := -R^T \boldsymbol{d} \in \mathbb{R}^M$ and leave out the constant $\boldsymbol{d}^T \boldsymbol{d}$ as $\mathcal{O}(1)$. We can express the nonnegativity constraint $\boldsymbol{x} \geq \boldsymbol{0}$ as an equality constraint using a slack variable $\boldsymbol{s} \in \mathbb{R}_+^M$,

$$-\boldsymbol{x} + \boldsymbol{s} = \boldsymbol{0} \quad \Leftrightarrow \quad A\boldsymbol{x} + \boldsymbol{s} = \boldsymbol{b} ,$$

where we set $A := -\mathbb{1} \in \mathbb{R}^{M \times M}$ and $\boldsymbol{b} := \boldsymbol{0} \in \mathbb{R}^M$. This leaves us with a constrained *quadratic program*,

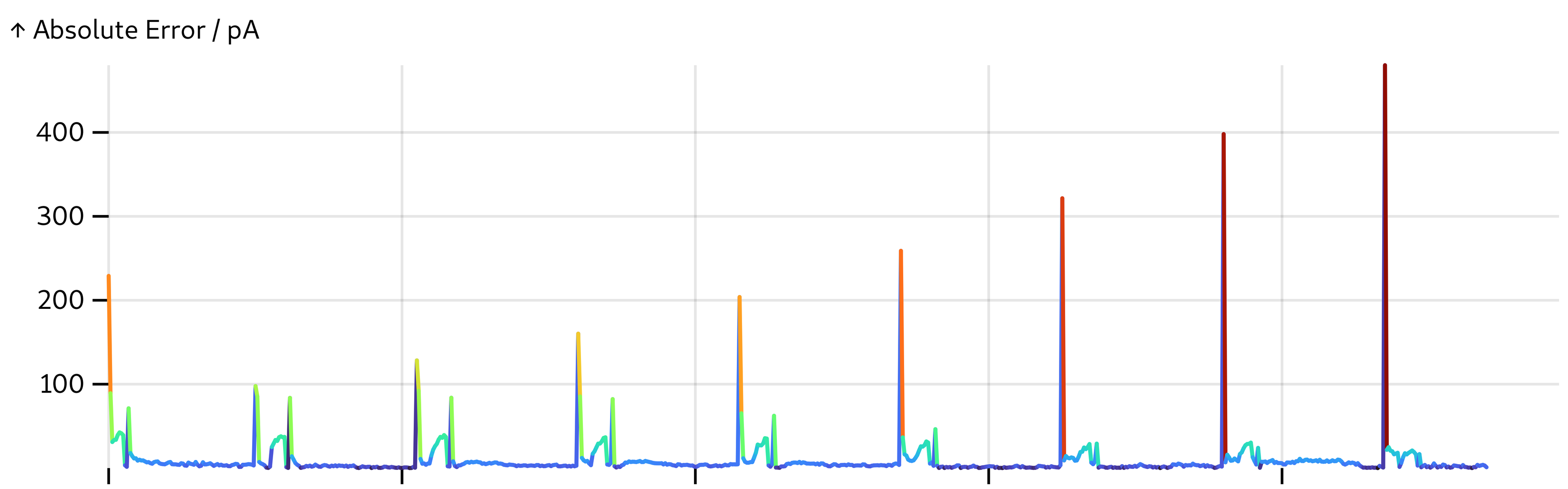
$$\min_{\boldsymbol{x} \in \mathbb{R}^M} \frac{1}{2} \boldsymbol{x}^T P \boldsymbol{x} + \boldsymbol{q}^T \boldsymbol{x}, \tag{3}$$

$$\text{s.t. } A\boldsymbol{x} + \boldsymbol{s} = \boldsymbol{b} , \ \boldsymbol{s} \in \mathbb{R}_+^M . \tag{4}$$

We solve the quadratic problem in this exact form using Clarabel [1]. Note that in Clarabel notation, the slack variable is to be taken as an element of the nonnegativity cone.
The integer solution can then be obtained from rounding,

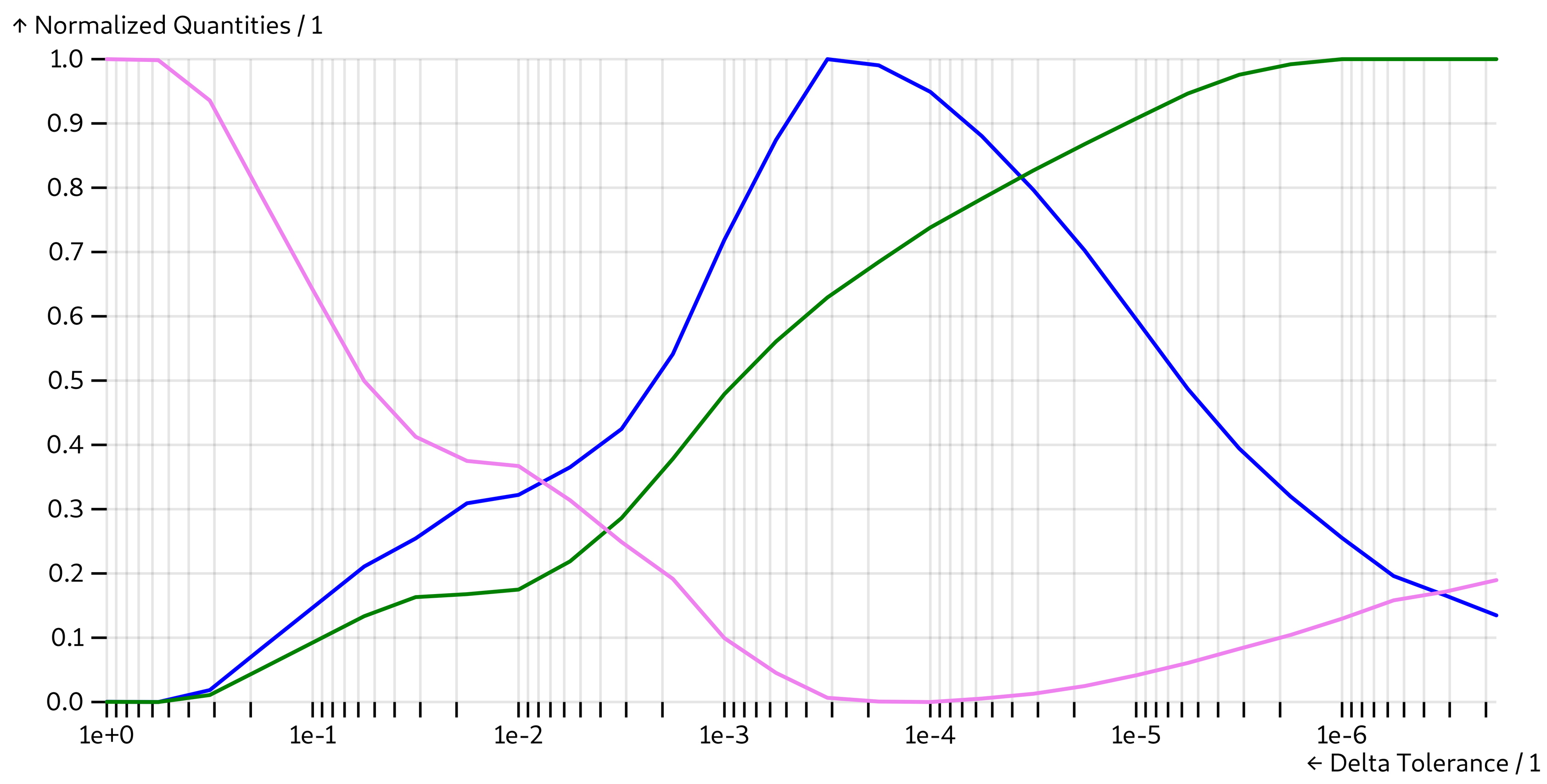
$$\boldsymbol{N}_{\text{opt}} = \lfloor \boldsymbol{x} \rceil \in \mathbb{N}_0^M .$$

Pointwise Error between Simulation and Measurements



Adaptive Timestepping

$$(\Delta t)_{n+1} = (\Delta t)_n \left(\frac{\Delta^{\text{tol}}}{\sum_{k=1}^{M} N_k \left\| \boldsymbol{s}_{k,n+1} - \boldsymbol{s}_{k,n} \right\|_2} \right)^{1/2} , \tag{5}$$



Comparison of Optimization Methods

Algorithm	Abbreviation	Runtime / ms	RMSE / pA
Particle Swarm Optimization	PSO	22571	27.69
Gradient Descent + More Thuente	GD	18924	32.34
Limited-Memory BFGS + Hager Zhang	LBFGS	4845	32.20
Non-Negative Least Squares [2]	NNLS	318	28.00
Quadratic Program	QP	18	28.13