

1 The monodomain model

The monodomain equations are given by

$$\frac{\partial \mathbf{s}}{\partial t} = \mathbf{F}(\mathbf{s}, v), \quad \mathbf{x} \in H, \quad (1)$$

$$\frac{\partial v}{\partial t} + I_{ion}(v, \mathbf{s}) = \nabla \cdot (\mathbf{M} \nabla v) + I_s, \quad \mathbf{x} \in H, \quad (2)$$

$$\mathbf{n} \cdot (\mathbf{M} \nabla v) = 0, \quad \mathbf{x} \in \delta H, \quad (3)$$

with $v(\mathbf{x}, t)$ the transmembrane potential (in mV), H the domain, δH the boundary of H , \mathbf{n} the outward pointing normal of the boundary, and with I_s the prescribed input current (in mV/ms) and I_{ion} the ionic current across the membrane (in mV/ms), both scaled by the cell membrane capacitance (in $\mu\text{F}/(\text{mm}^2)$). Equation (1) is a system of ODE's that models the membrane dynamics. There exist many different cell membrane dynamics models with varying degrees of complexity that can be used to specify I_{ion} , $\mathbf{F}(\mathbf{s}, v)$ and the state variables $\mathbf{s}(\mathbf{x}, t)$, see the CellML repository [9] for an overview of different types of models.

Finally, \mathbf{M} is a conductivity tensor (in mm^2/ms), that satisfies

$$\mathbf{M} = \frac{\lambda}{1 + \lambda} \mathbf{M}_i, \quad (4)$$

with $\mathbf{M}_e = \lambda \mathbf{M}_i$. Here, \mathbf{M}_e and \mathbf{M}_i are the extracellular and intracellular conductivities (in mm^2/ms), divided by the product of the membrane capacitance (in $\mu\text{F}/(\text{mm}^2)$) and the cell membrane area-to-volume ratio (in $1/\text{mm}$). By assuming that there exists a λ such that $\mathbf{M}_e = \lambda \mathbf{M}_i$ the monodomain equations can be derived from the more complicated bidomain equations [3].

2 A basic test case

For our test case, we take a square of $5 \text{ mm} \times 5 \text{ mm}$ as our domain H . We will use the Grandi cell model to model the membrane kinetics [1]. We solve our test case with the `splittingssolver` module from the `cbcbeat` Python package [10]¹ with the default parameter values and default initial conditions for v and s . The `splittingssolver` solves the monodomain PDE system and its coupled cell membrane dynamics ODE system separately, using the operator splitting scheme as described in [3]. We take typical values $\sigma_l = 0.1$

¹This electrophysiology solver package is based on the FEniCS Project software [7] and the dolfin-adjoint software [8]

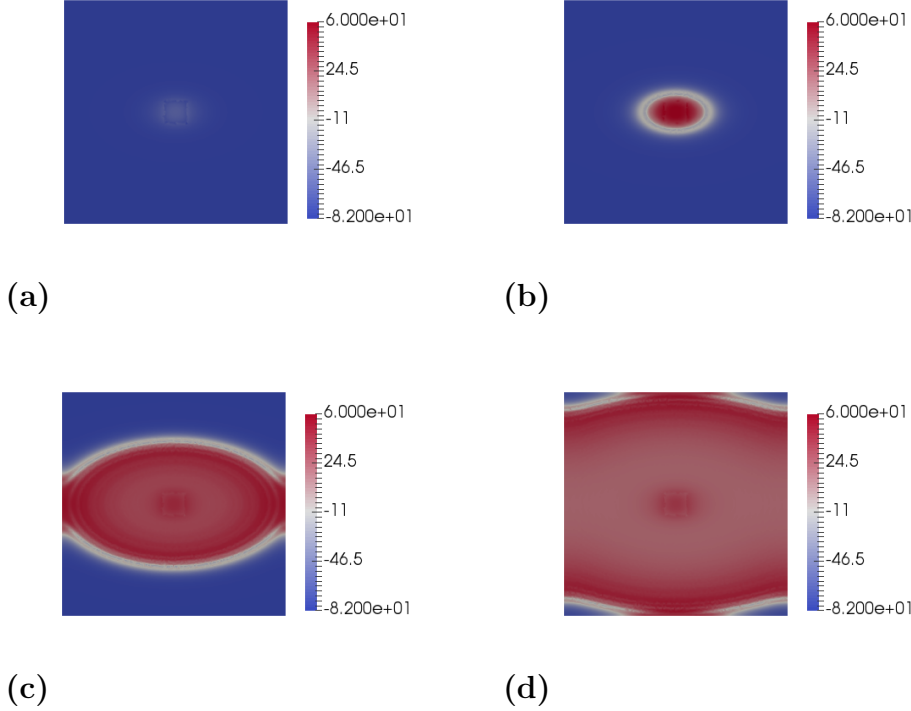


Figure 1: Heat maps of u of our basic test case at **(a)** $t = 5\text{ms}$, **(b)** $t = 15\text{ms}$, **(c)** $t = 25\text{ms}$ and **(d)** $t = 35\text{ms}$.

and $\sigma_t = 0.02$ (in mS/mm) for the longitudinal and tangential conductivity respectively and take $C_m = 0.2$ for the membrane capacitance (in $\mu\text{F}/(\text{mm}^2)$) and $\beta = 200$ for the cell membrane area-to-volume ratio (in $1/\text{mm}$) [4], data from [5, 6]. We apply a stimulus of $10 \text{ mV}/\text{ms}$ over 1 mm^2 in the centre of the square from $t = 0$ to $t = 3 \text{ ms}$. In Figure 1, we show a heat map of u at $t = 15, 20, 30$ and 40 ms . In Figure ??, we show a heat map of Ca_{sl} at the same times. This variable is one of the 37 state variables \mathbf{s} of the Grandi cell model and measures the intracellular calcium concentration [1]. In Figures ?? and ??, we plotted u and Ca_{sl} over time, both at a point at the centre of the domain (in blue) and at a point at the left lower edge (in green). We see that the ...

3 The inverse problem

It is possible to obtain measurements u_{obs} of the transmembrane potential and measurements c_{obs} of the intracellular calcium concentration Ca_{sl} over

the whole domain H at discrete points in time. With those measurements, we can estimate the value of the parameters in our model, using an adjoint-based approach.² Here, as an example, we will try to estimate the values of the σ_l parameter from the Grandi cell model. We can formulate this problem as an optimisation problem: find σ_l , such that the functional

$$\mathcal{J}(v, c, \sigma_l) = \frac{1}{N} \sum_{i=1}^N \|v - v_{\text{obs}}(t_i)\|_{L^2(H)}^2 + \|c - c_{\text{obs}}(t_i)\|_{L^2(H)}^2, \quad (5)$$

is minimized, subject to the requirements that v, c and σ_l satisfy the state system of equations (1)-(3) and initial conditions $v(\mathbf{x}, 0) = v_0(\mathbf{x})$ and $\mathbf{s}(\mathbf{x}, 0) = \mathbf{s}_0(\mathbf{x})$. Here, N are the number of measurements in time and $t_i, i = 1, \dots, N$ the respective moments in time. Using cbcbeat and the dolfin-adjoint software on which it is based, we can automatically compute the total derivative of \mathcal{J} with respect to the optimization parameter σ_l . We first generated some fake observed data for $\sigma_l = 0.15$. We then use the scipy function `minimize()` to find an optimal value for σ_l . We took $\sigma_l = 0.10$ as initial condition and found $\sigma_l = 0.149963$ after four iterations.

References

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²See, for example, [2] for an introductory text in adjoint-based optimization methods.

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