Centre of Research Excellence
British Heart Foundation Imperial College London

Simulating the electrophysiology of discretely-coupled cardiac cells in a multi-domain formulation

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ElectroCardioMaths Programme, Imperial College London

Nektar++ Workshop, 11 June 2019

Outline

- Introduction to cardiac electrophysiology
- Discrete-cell model in Nektar++
- Initial validation results
- Conclusions & Future work

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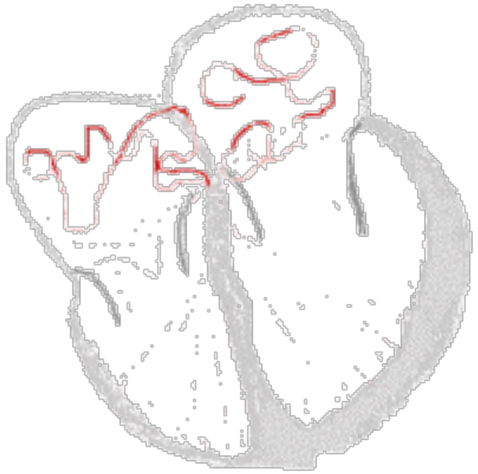
What's in a heartbeat?



JHeuser, 2005.

AC Guyton and JE Hall. Textbook of Medical Physiology. 1996.
S Rohr. Role of gap junctions in the propagation of cardiac action potential. *Cardiovasc Res.* 2004.
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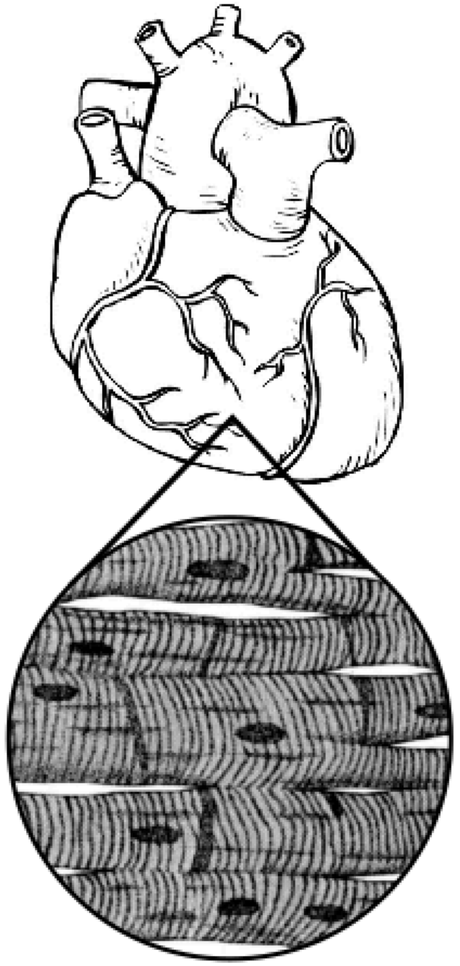

Adapted from Guyton and Hall, 1996. Fig 9-2.

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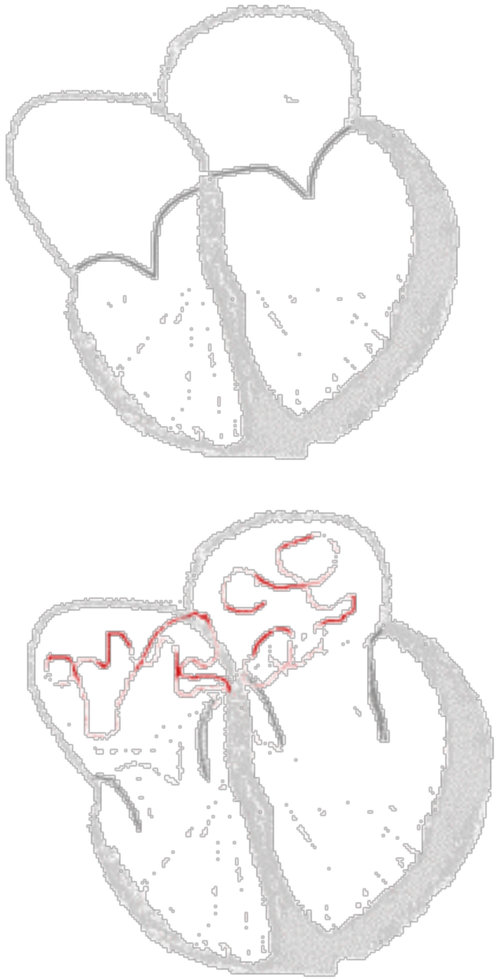

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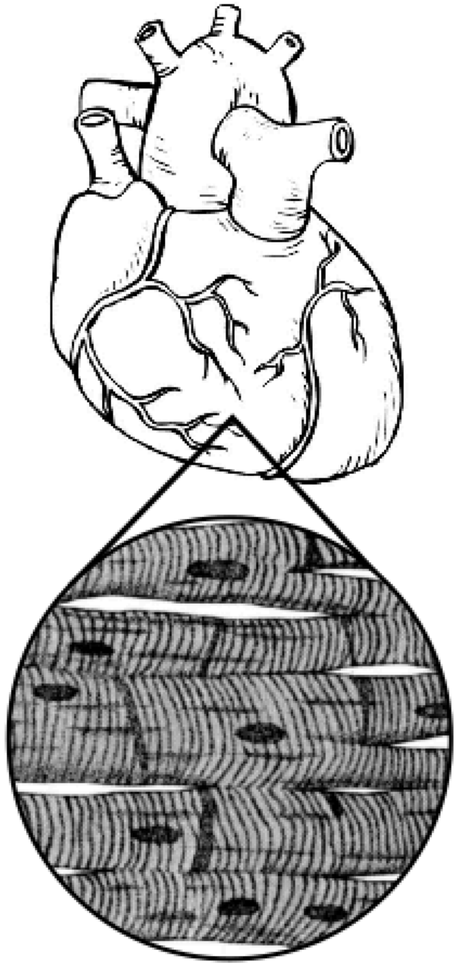

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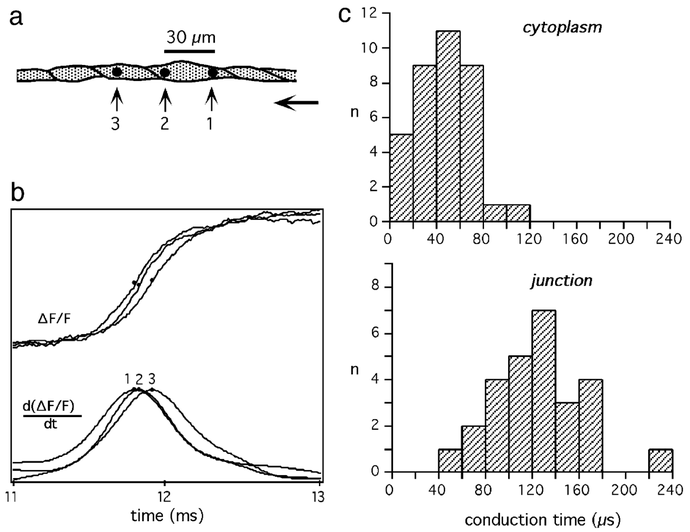
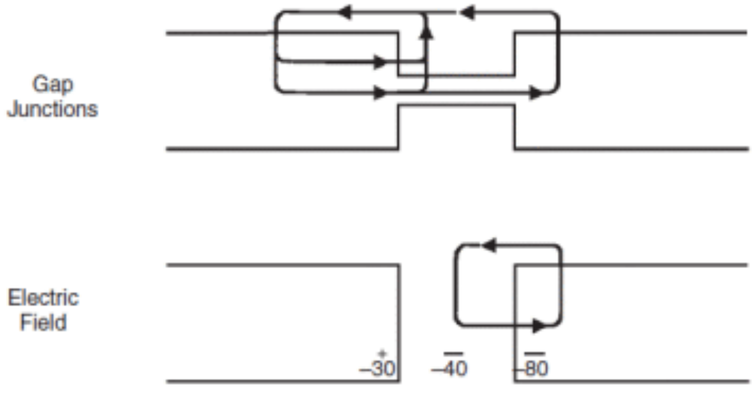


Rohr, 2004. Fig 3.



Sperelakis, 2002..

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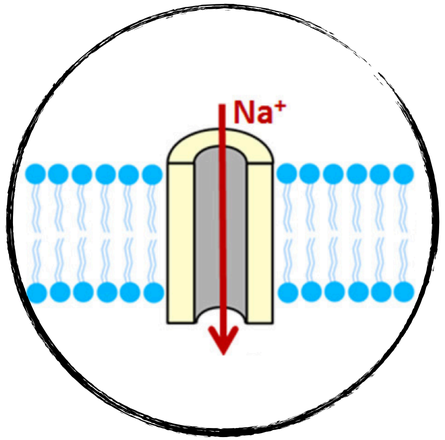
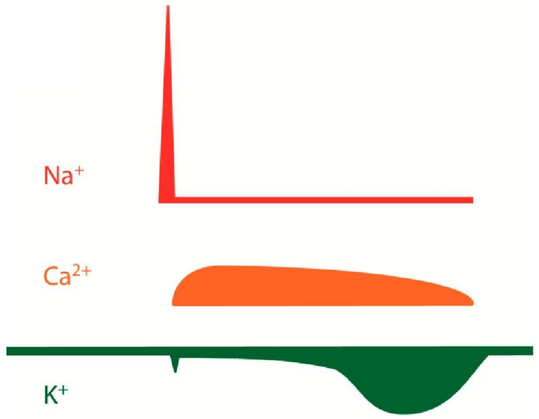
Modelling cardiac electrophysiology



Pathmanathan et al, 2018.



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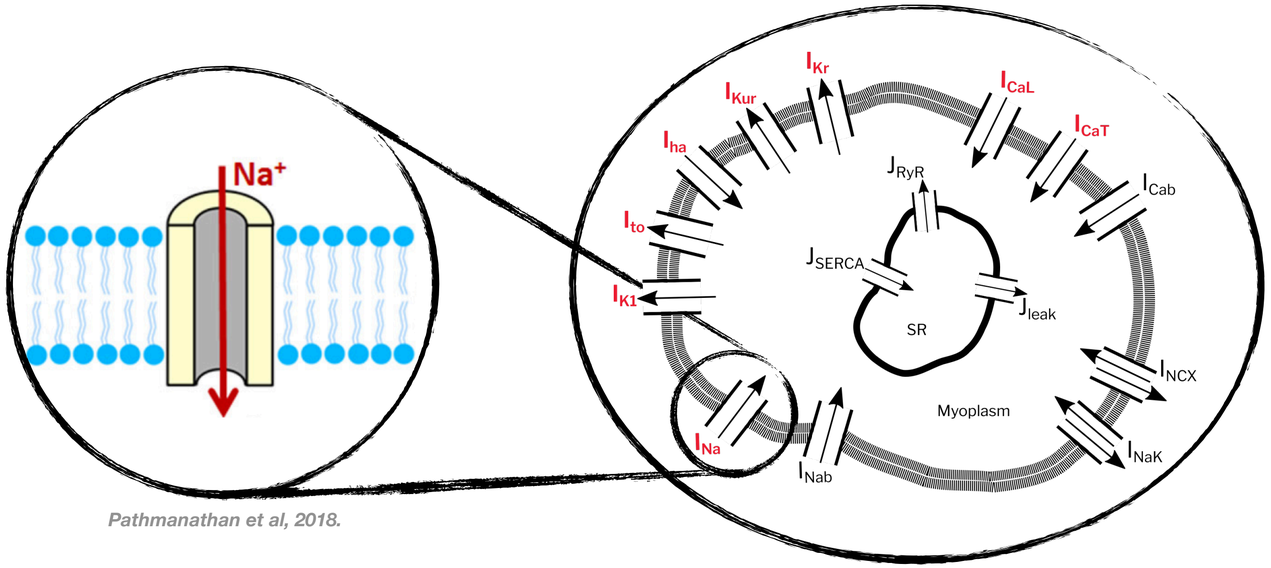

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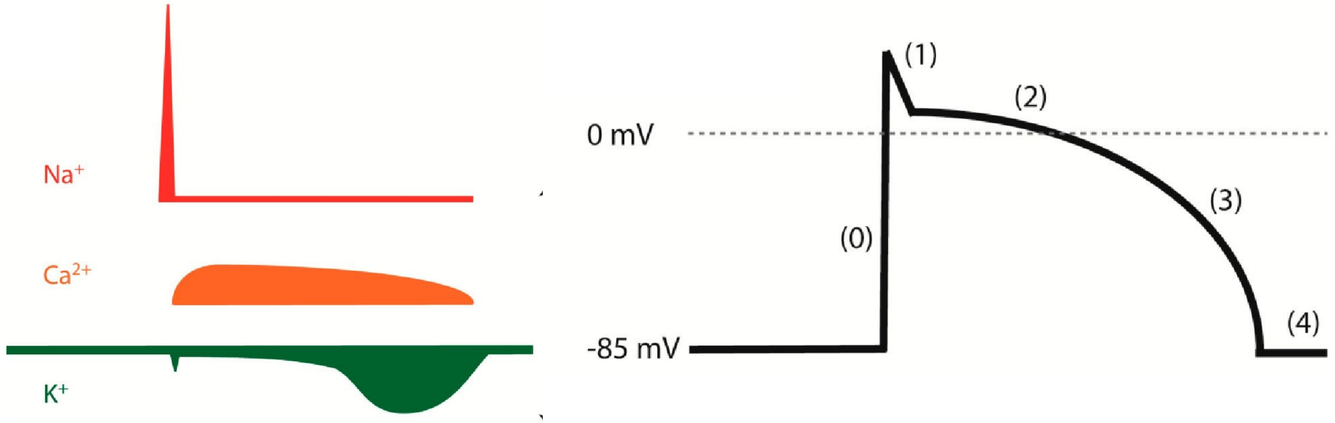

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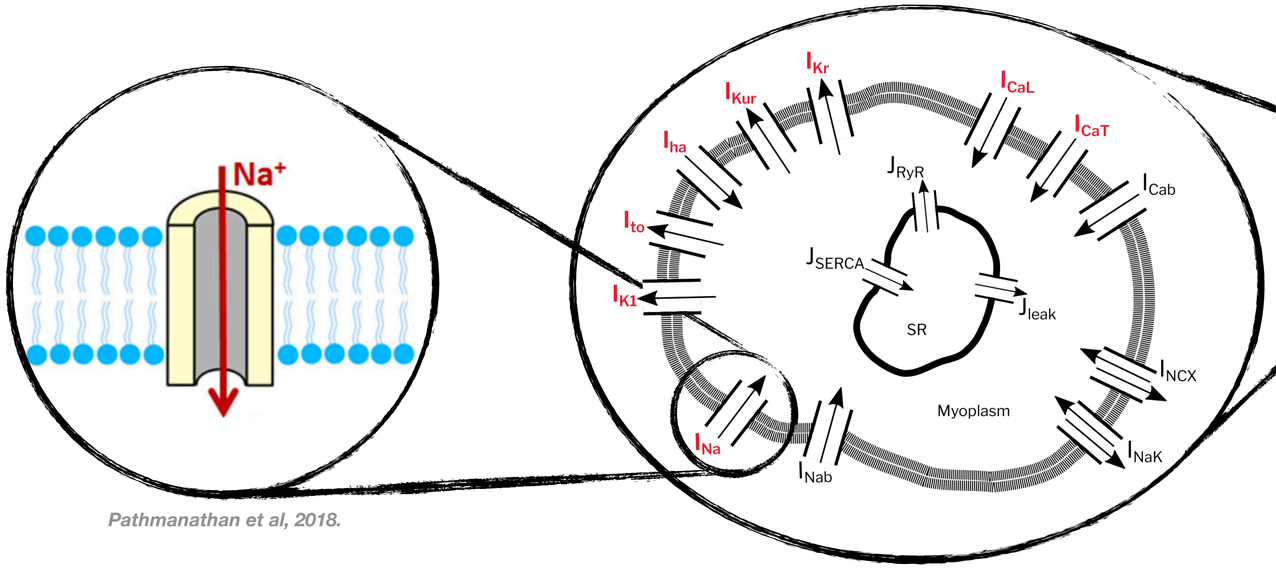

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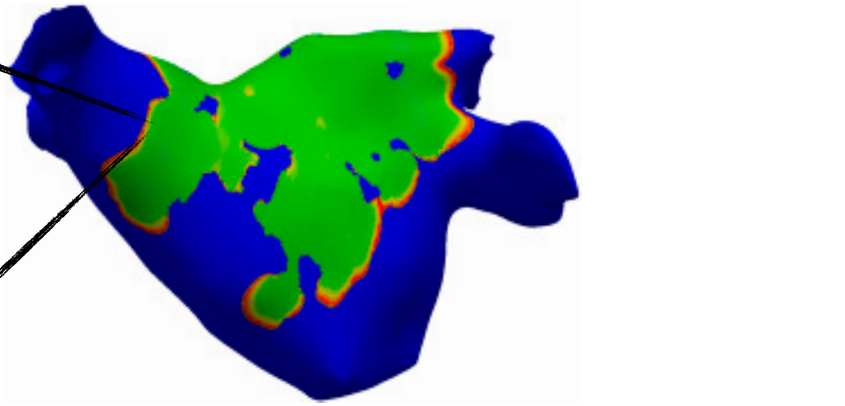

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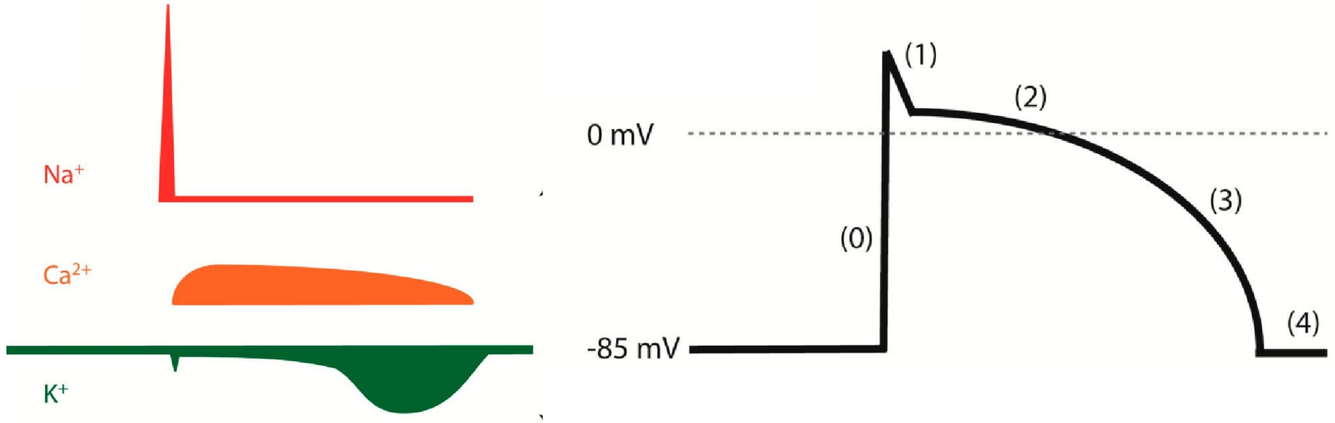

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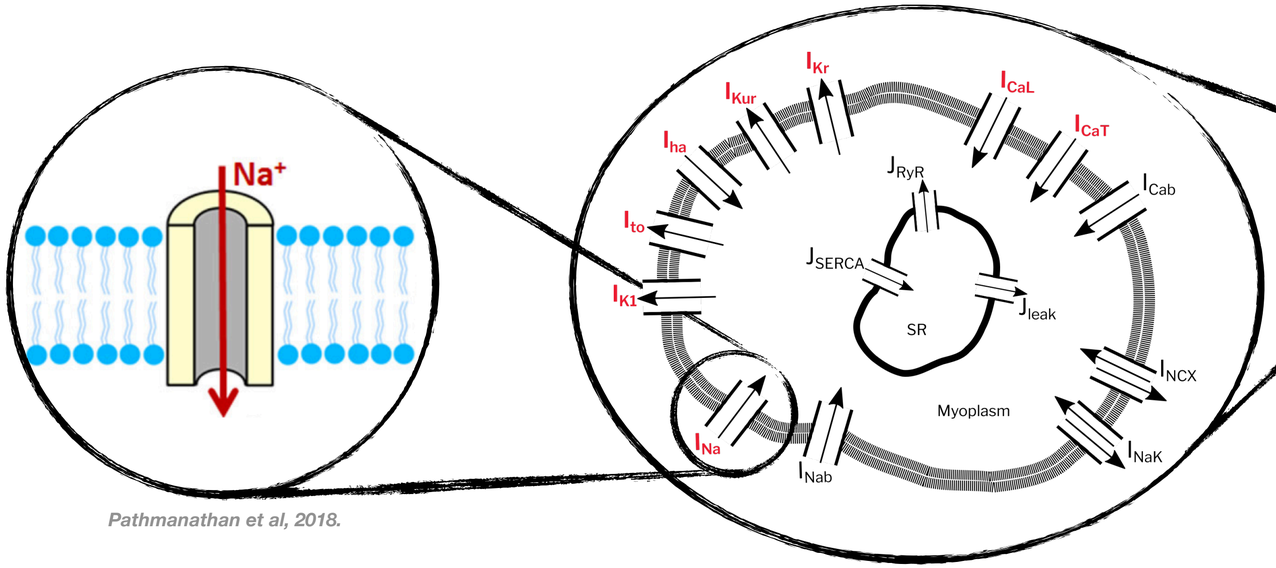

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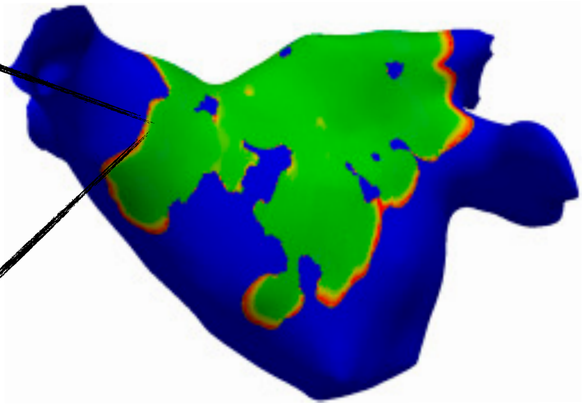

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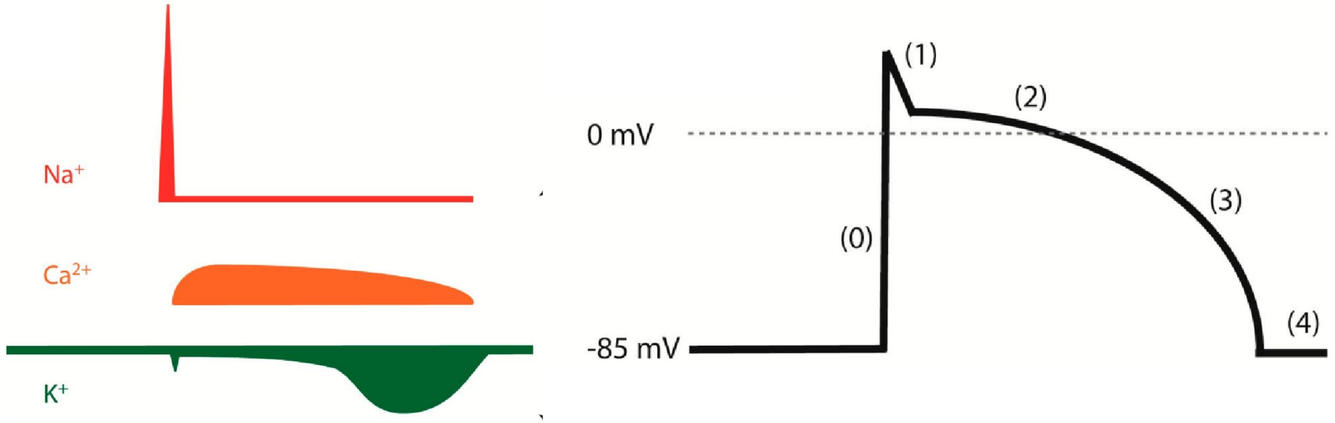

- Steep spatial gradient at wavefront.
- Stiffness of ODE cell model.
- Geometric complexity.

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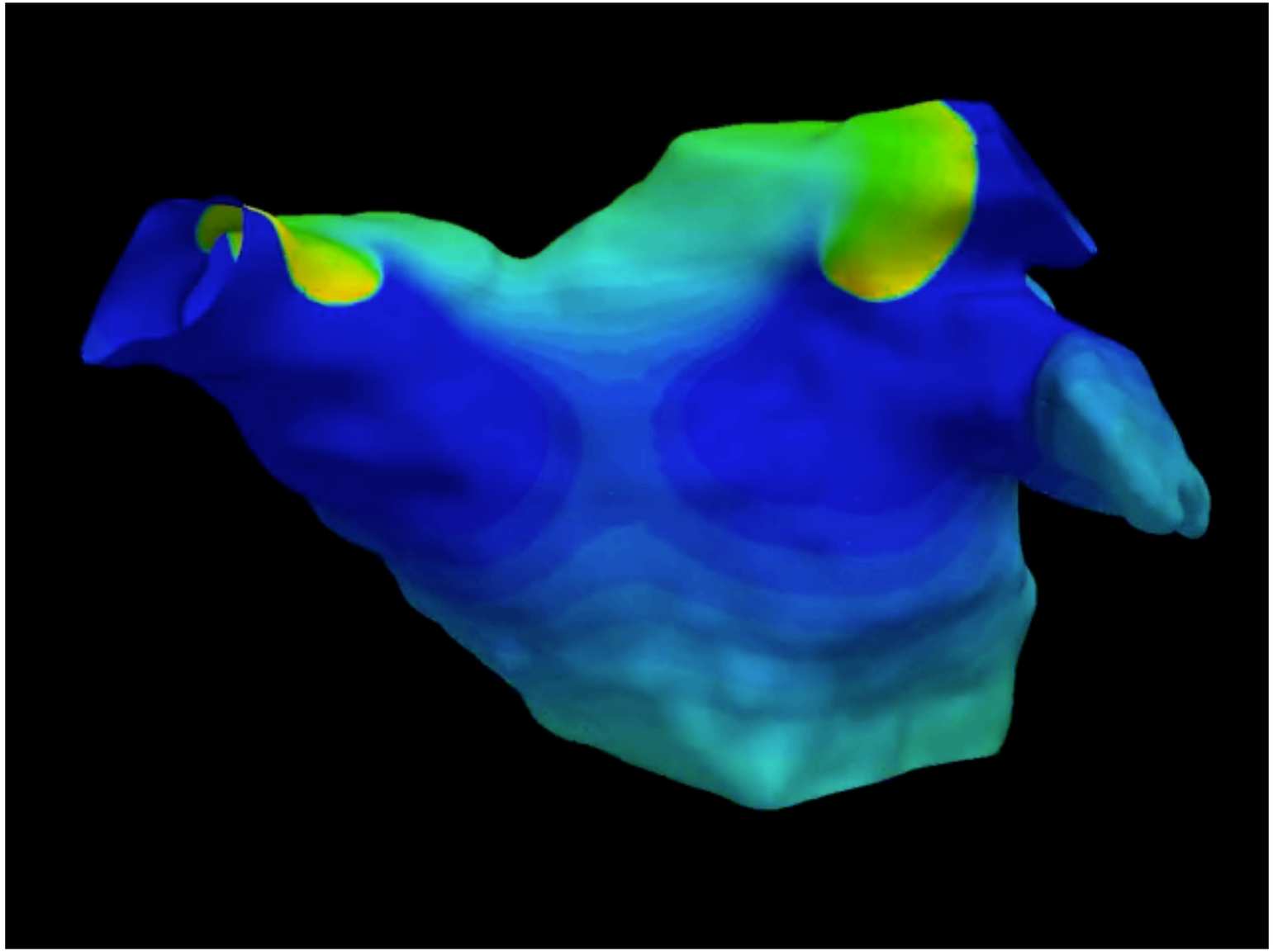
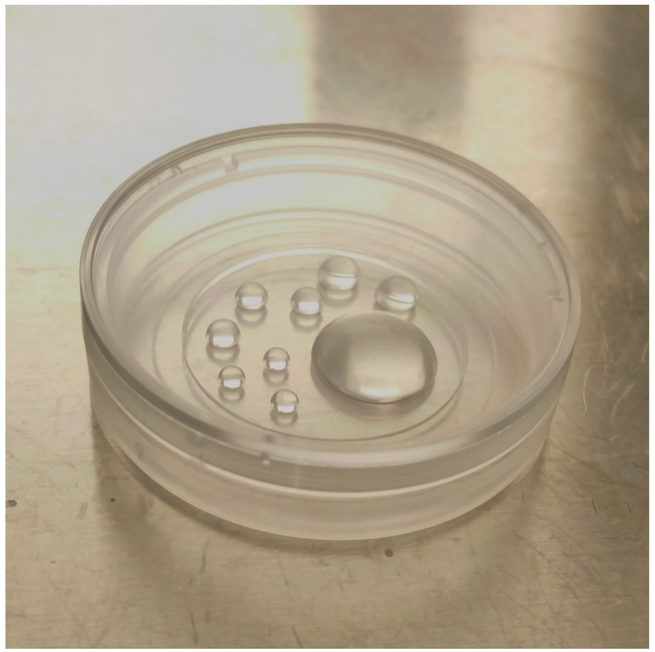
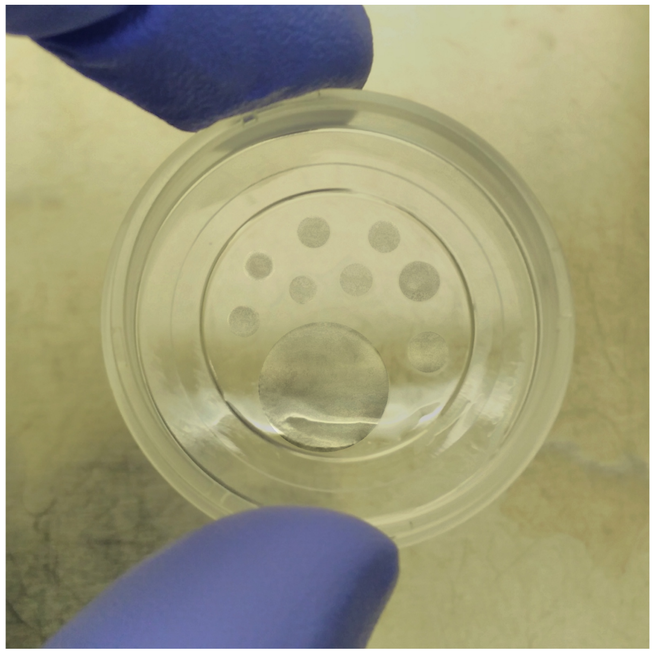
Organ-scale rotational activity

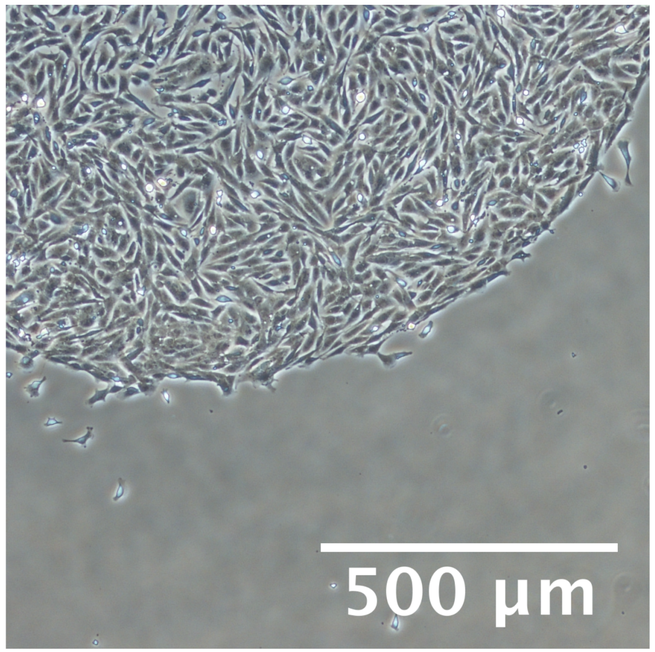


Cantwell CD et al. High-order spectral/hp element discretisation for reaction–diffusion problems on surfaces: Application to cardiac electrophysiology. Journal of computational physics. 2014 Jan 15;257:813-29.

Biological preparation

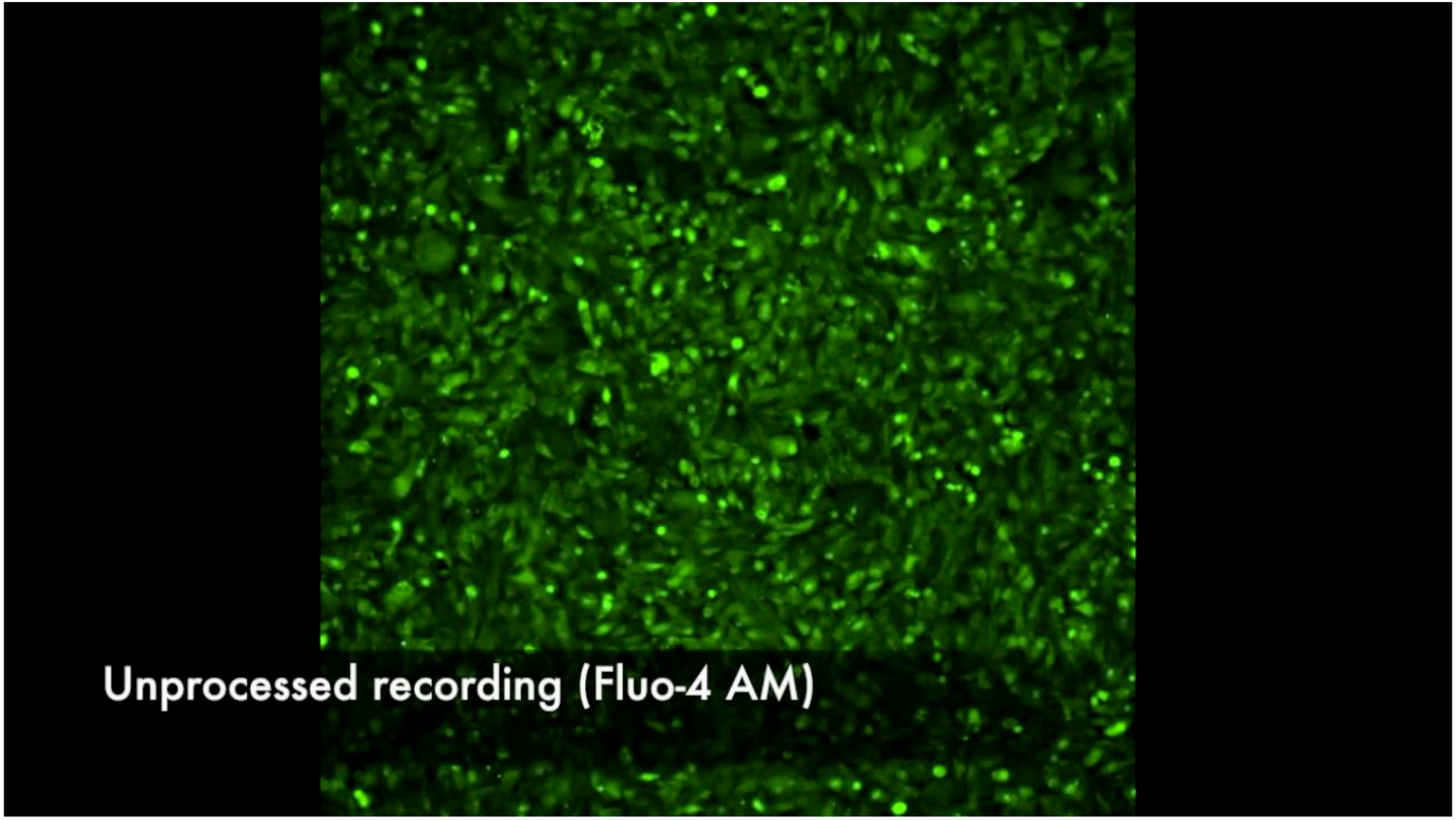






Houston C et al. Characterisation of re-entrant circuit (or rotational activity) in vitro using the HL1-6 myocyte cell line. Journal of molecular and cellular cardiology. 2018 Jun 1;119:155-64.

Cell-scale rotational activity



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Hypothesis & Aims

We hypothesise that conduction features at a cellular level are a key factor in the initiation and perpetuation of re-entrant arrhythmias and fibrillation *in vivo*.

We aim to develop the first biophysically-validated and morphologically-accurate discrete cell model for action potential propagation in cardiac cell monolayers.

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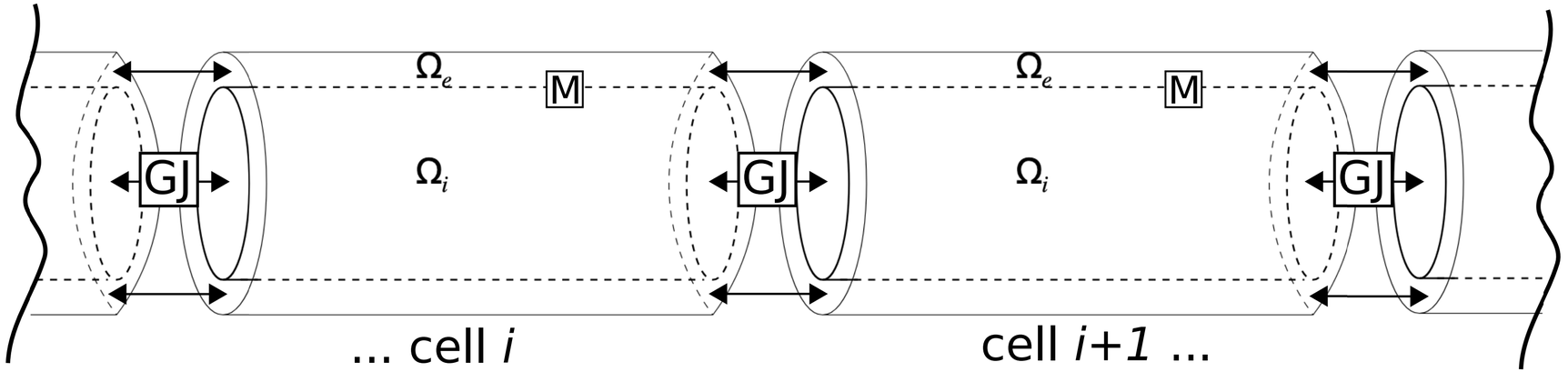
Idealised model for cable of cells



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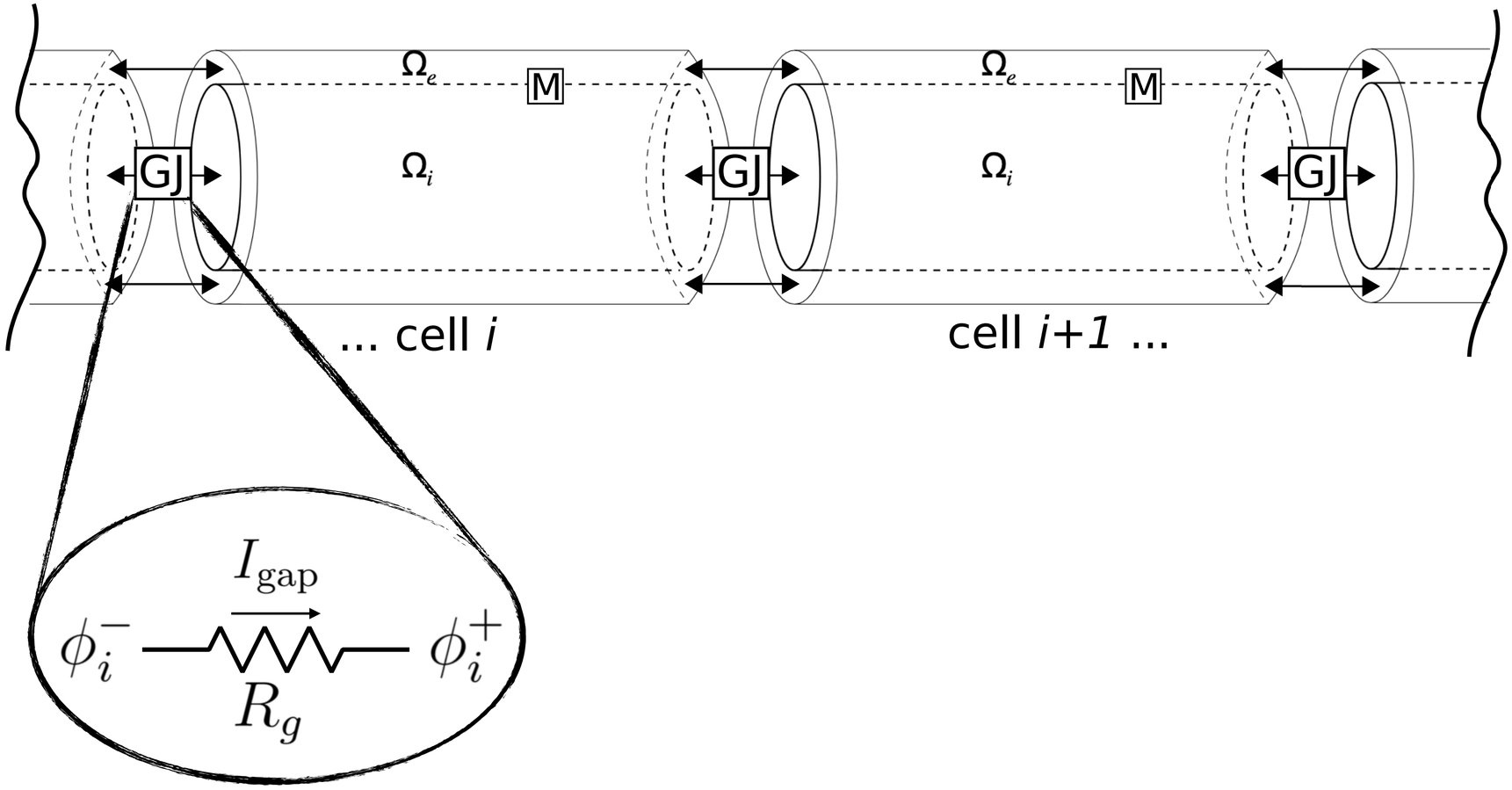

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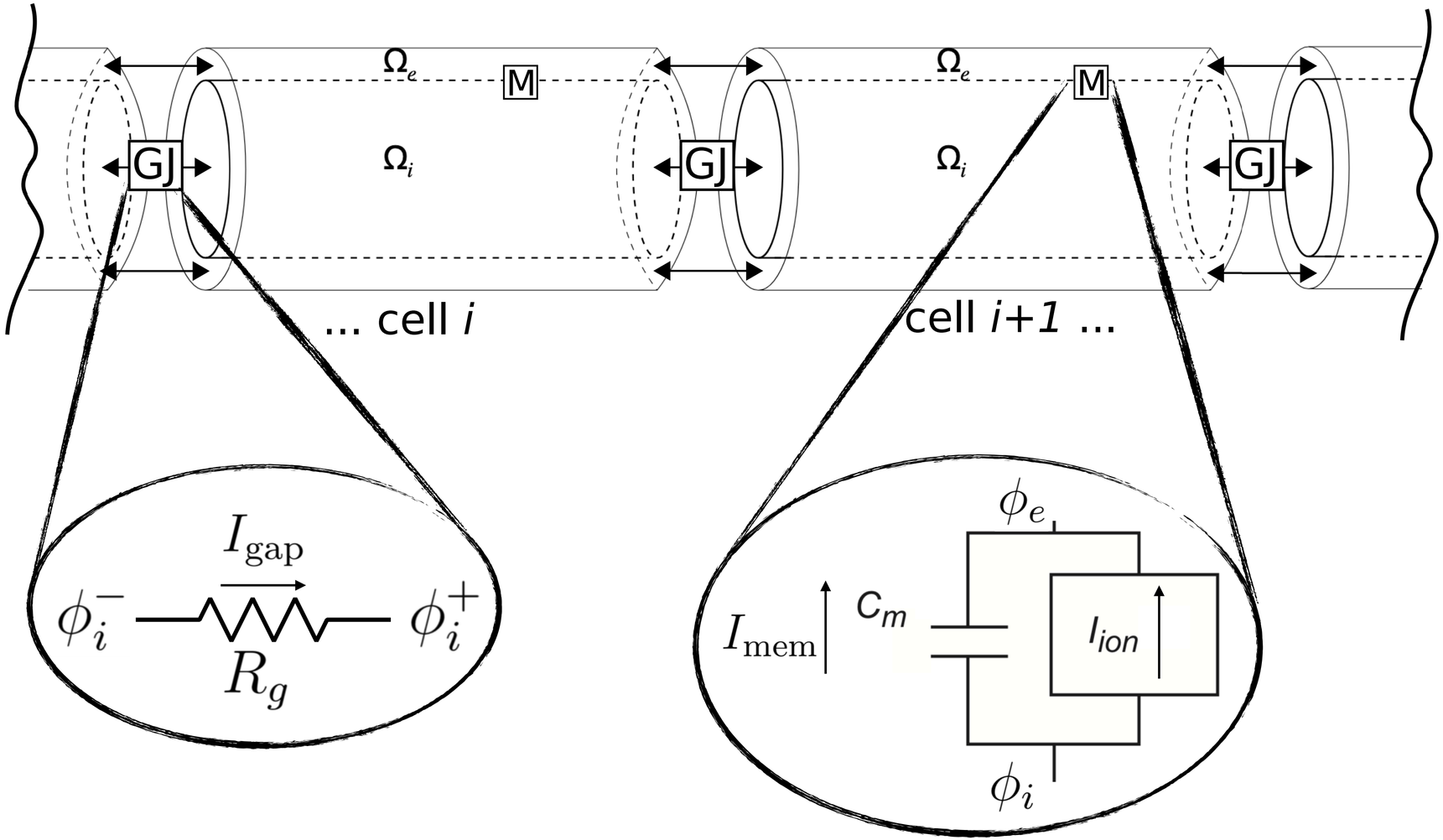

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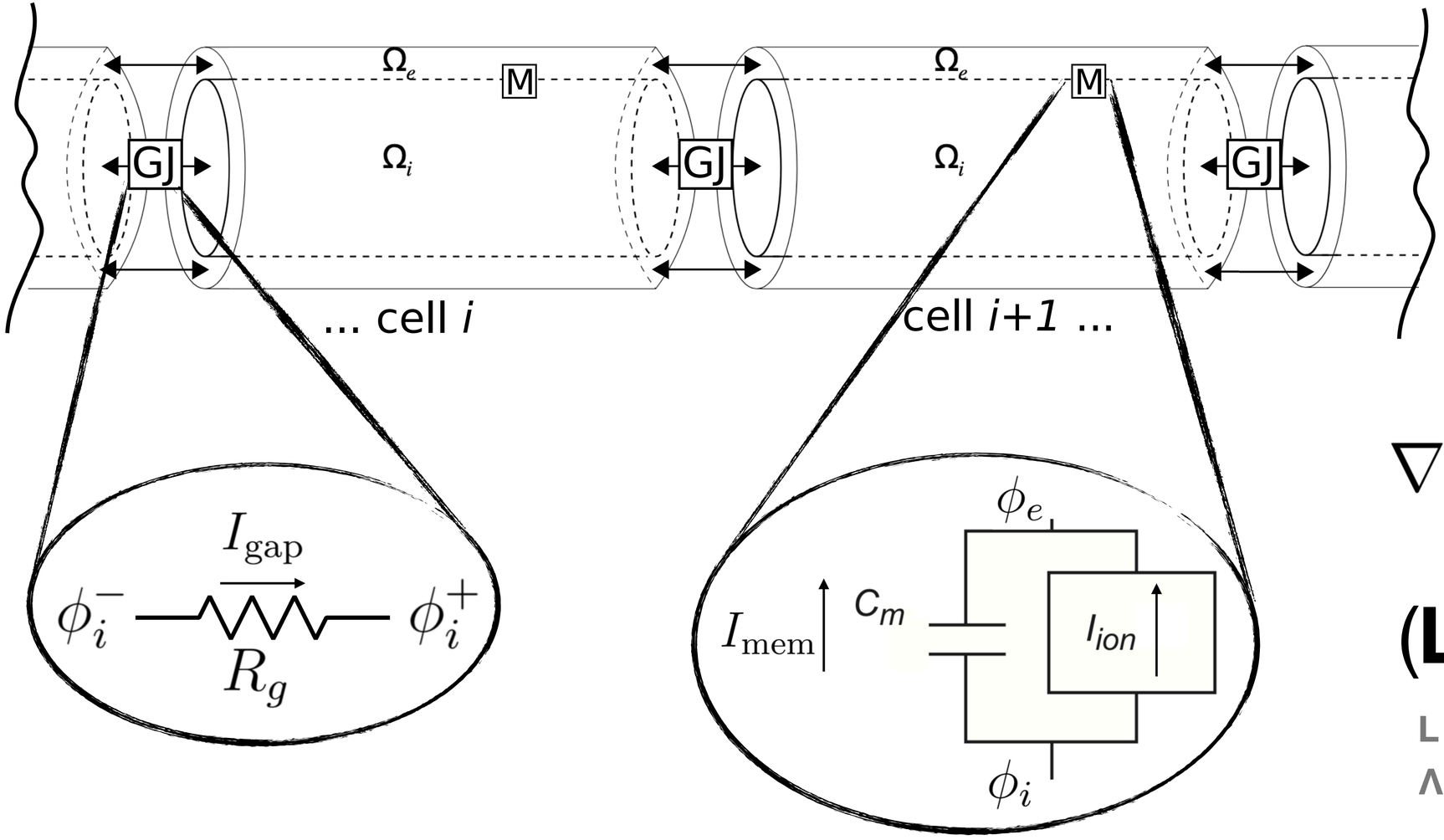


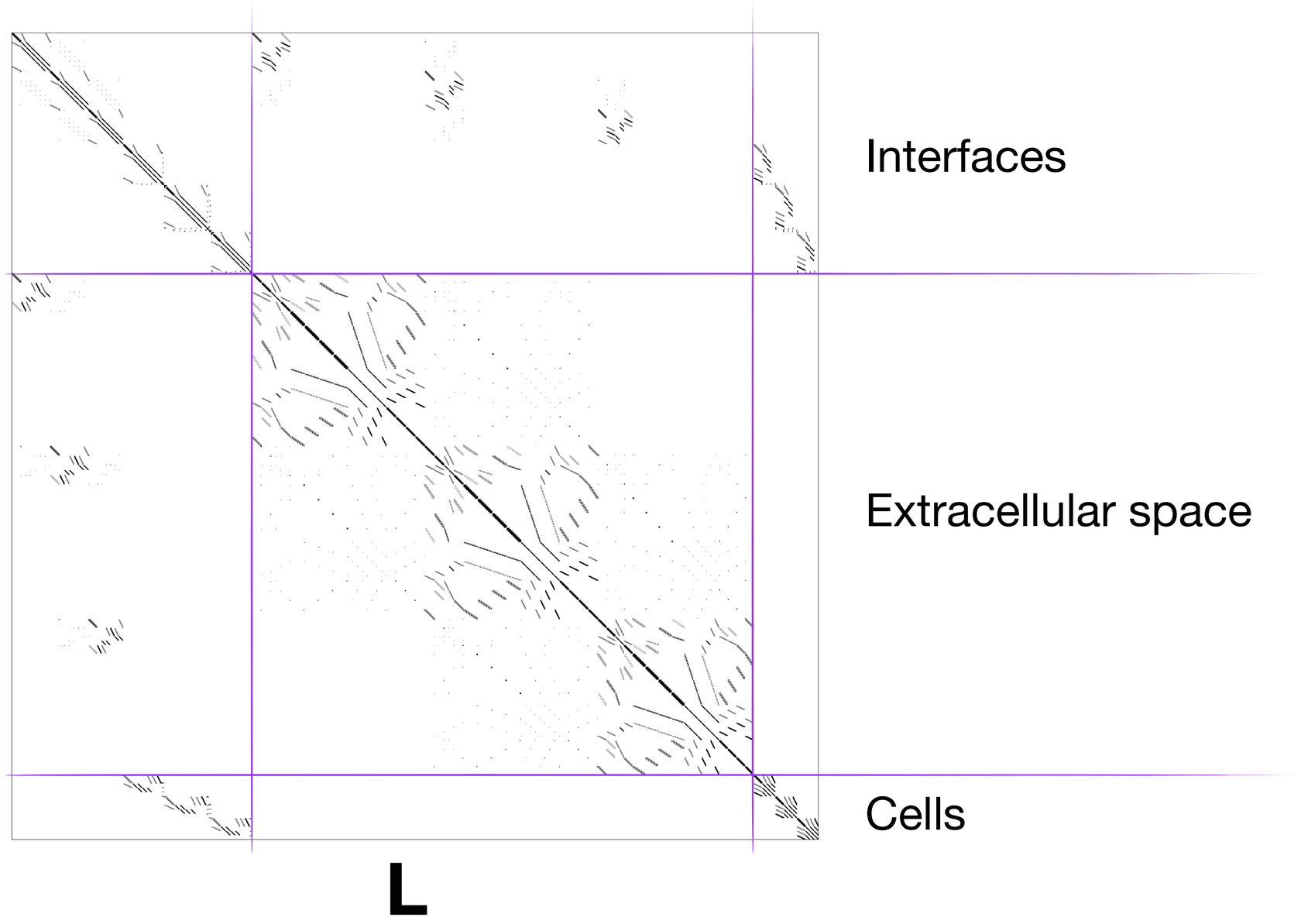
$$\nabla \sigma_{(i,e)} \nabla \phi = 0$$

$$\mathbf{(L + \Lambda)\hat{u} = f}$$

L = discrete Laplacian

Λ = interface coupling

Multi-domain global matrix system



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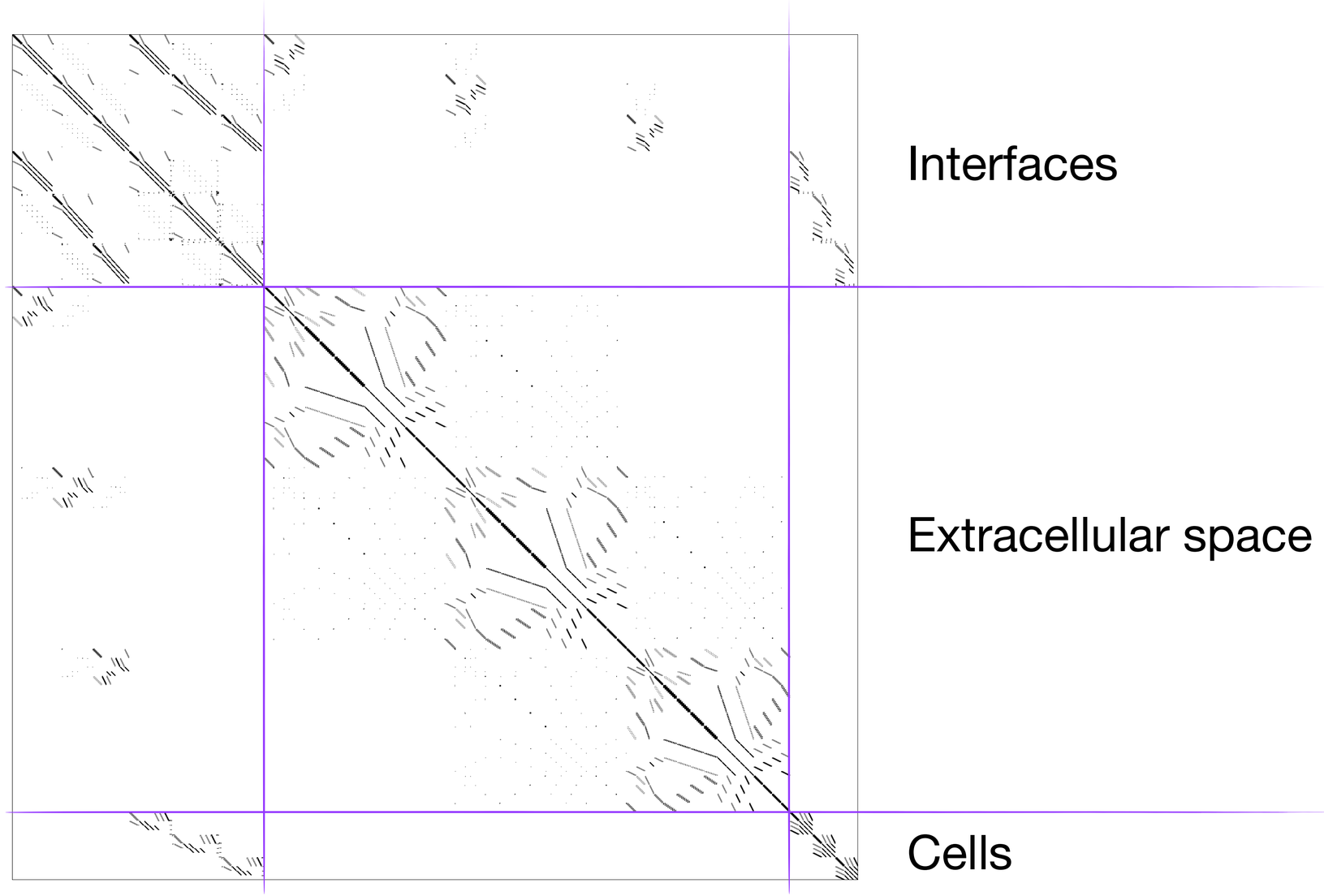

$$\mathbf{L} + \mathbf{\Lambda}$$

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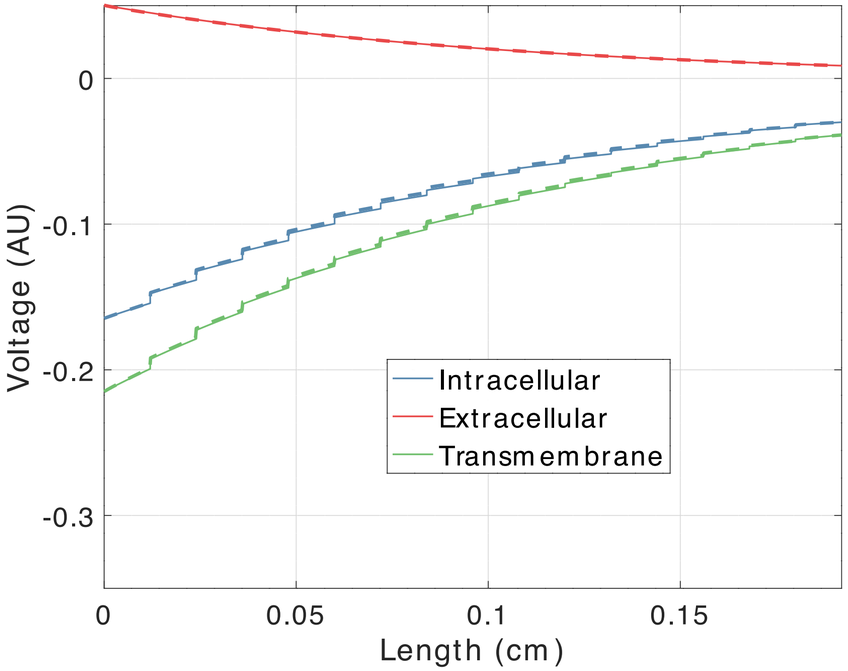
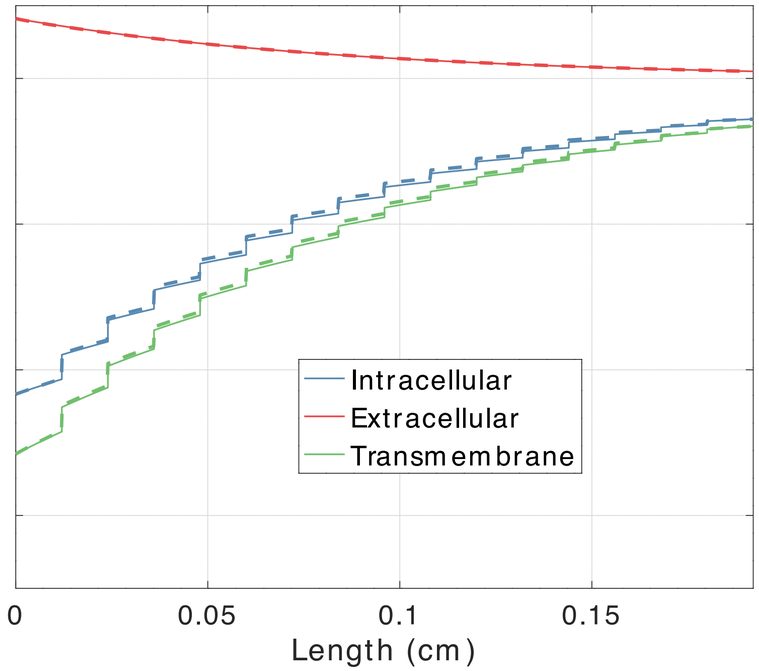
Steady-state solution for fixed potential at cable end

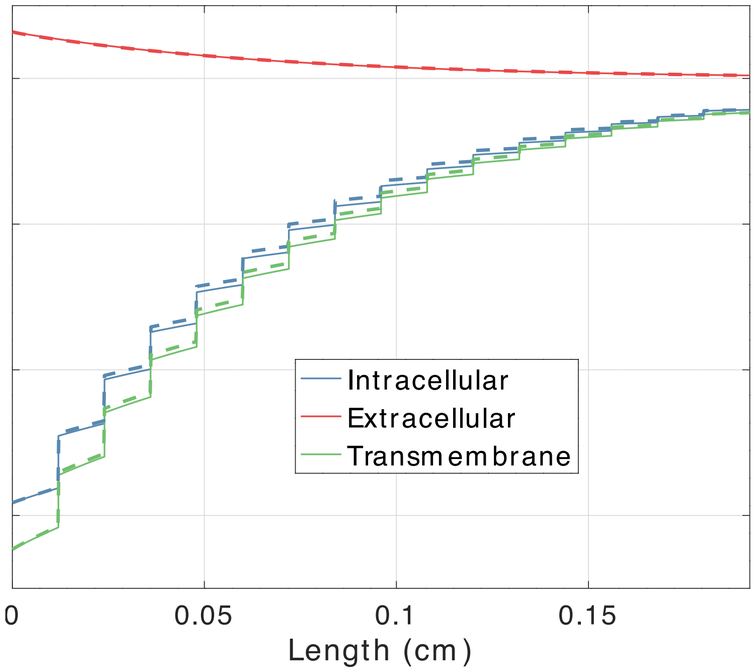
λ_g=0.11cm



λ_g=0.09cm



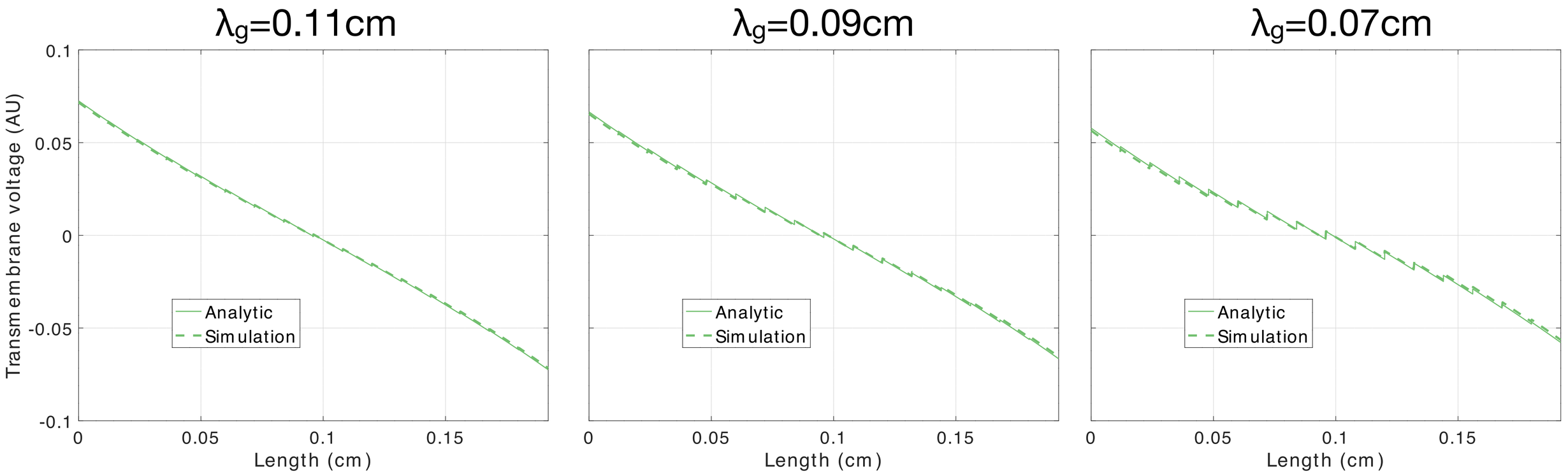
λ_g=0.07cm



$\lambda_g \downarrow$ $R_g \uparrow$

Increased gap junction resistance leads to greater proportion of decay across gap junctions.

Steady-state solution for current injected into cable



$\lambda_g \downarrow$ $R_g \uparrow$

‘Speed bumps’ at gap junctions as current redistributes for path of least resistance.

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Conclusions

We have constructed a multi-domain formulation within the Nektar++ framework to solve steady-state solutions for cell-level conduction in cardiac electrophysiology.

The framework reproduces known analytical solutions for a cable of connected cardiac cells.

What's next?

Incorporate time-dependent features at interfaces (i.e. cell model ODEs).

Direct biophysical validation of our model with one-to-one matching biological preparations.

Prediction of effects of changes to intercellular coupling on cell-scale conduction patterns.

- Generalise multi-domain support in the library.
- Parallelise solving in separate domains.

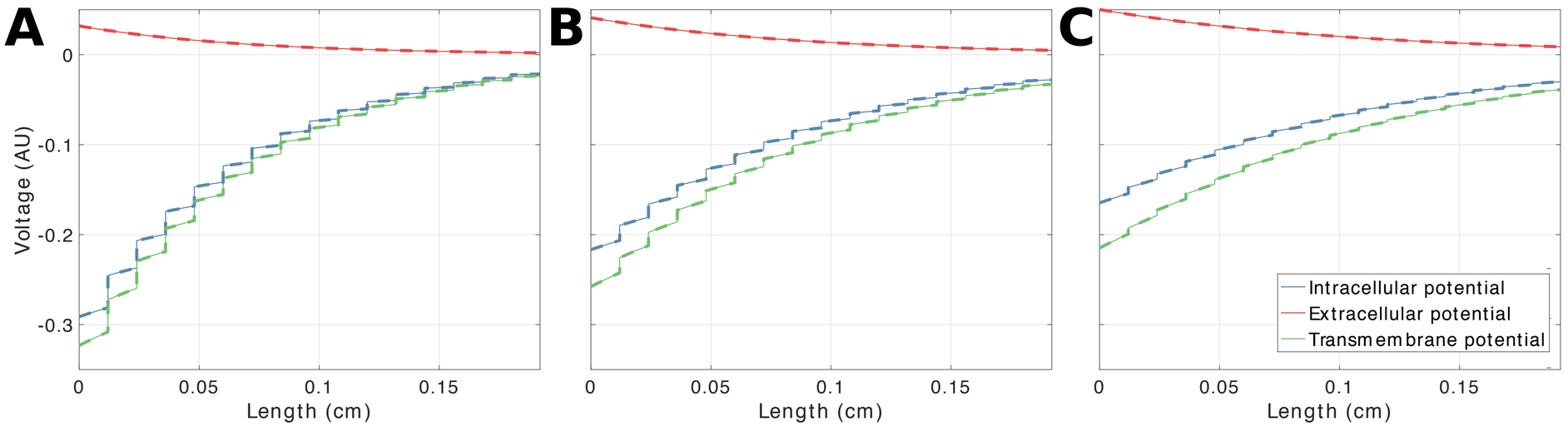
Acknowledgements

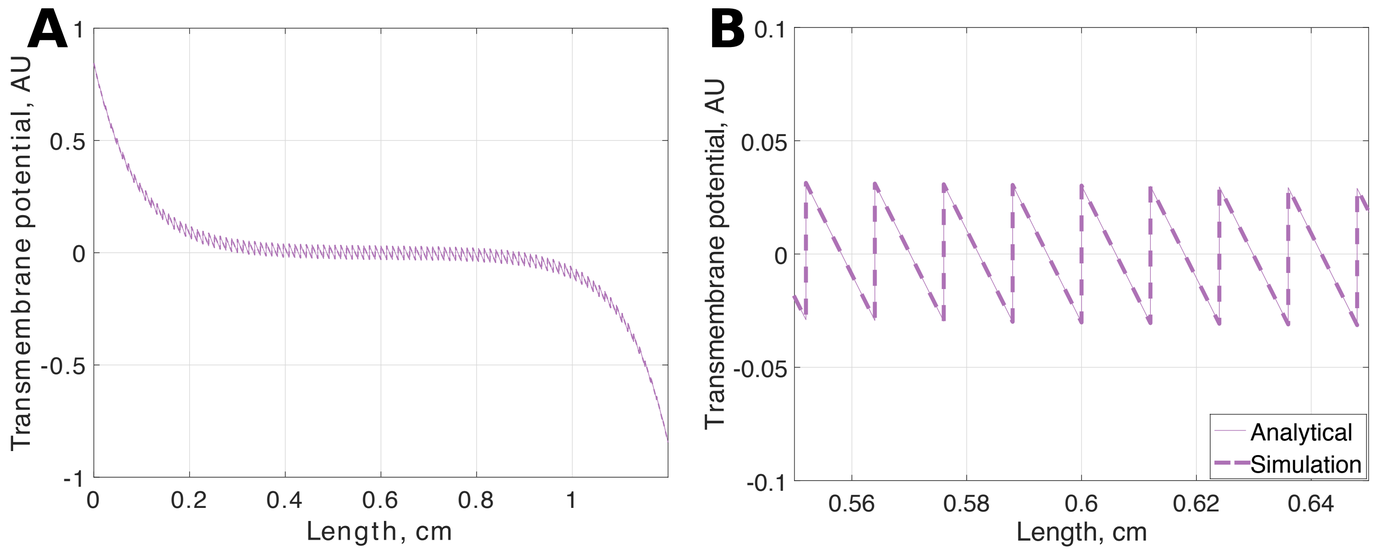
Supervisors
Dr Chris Cantwell
Dr Rasheda A Chowdhury
Prof Spencer Sherwin
Prof Nicholas S Peters
Dr Emmanuel Dupont (past)

ElectroCardioMaths Group
Dr David Pitcher
Dr Fu Siong Ng

PhD Assessors
Prof Denis Doorly
Prof Cesare Terraciano

1D steady-state solutions





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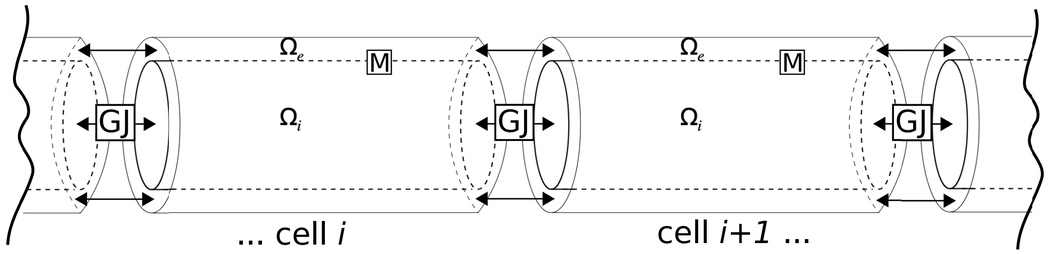

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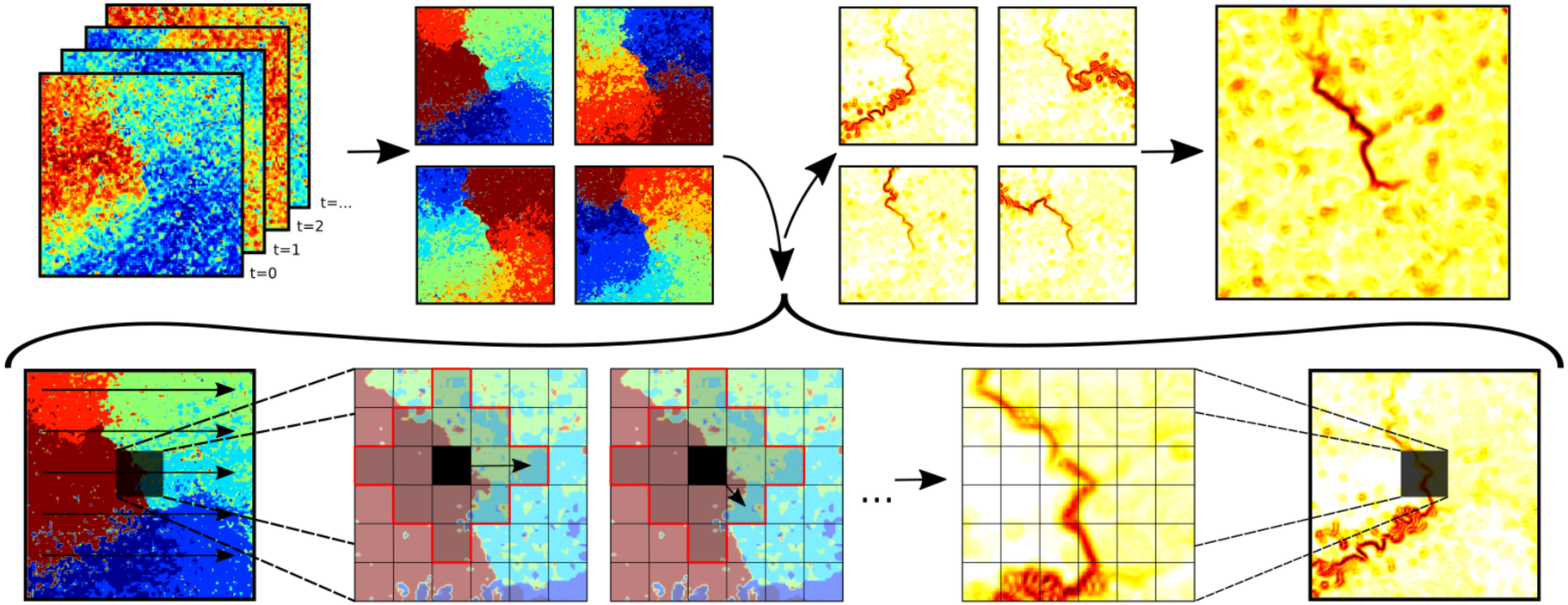
Conduction block/slowing algorithm



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