Augmenting Low-Fidelity Electrophysiological Cardiac Cell Models with Neural Networks

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Introduction

- Cardiac alternans, a beat-to-beat variation in action potential (AP) duration or amplitude, is a precursor to life-threatening arrhythmias.
- Models such as **Mitchell–Schaeffer (MS)** and **Iyer–Mazhari–Winslow (IMW)** simulate cardiac electrophysiology at different levels of fidelity.

Action Potentials

- APs are generated by **electrical activity** on a cell membrane, such as heart muscle cells.
- They are related to ion currents flowing across the cell membrane and show a typical electrical voltage curve with rapid depolarisation, a plateau phase and repolarisation (Fig. 1).
- An electrical stimulus starts the AP, which can propagate from cell to cell across the heart. [1]

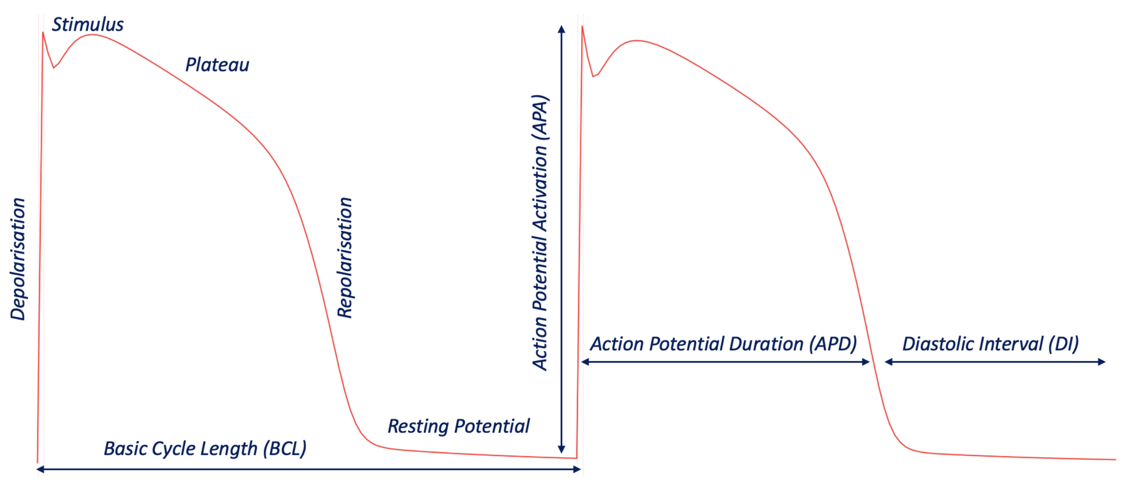

Figure 1. Action potential dynamics

Aims and Challenges

- This work explores APs and aims to augment the MS model with **neural networks (NNs)** to improve fidelity without introducing full biophysical complexity.
- Challenges arise due to:

1. Highly **non-linear** and **discontinuous** nature of the differential equations required.
2. Lack of established guidance for neural components such as the number of layers (Fig. 2), or the selection of activation functions within universal differential equations. [2]

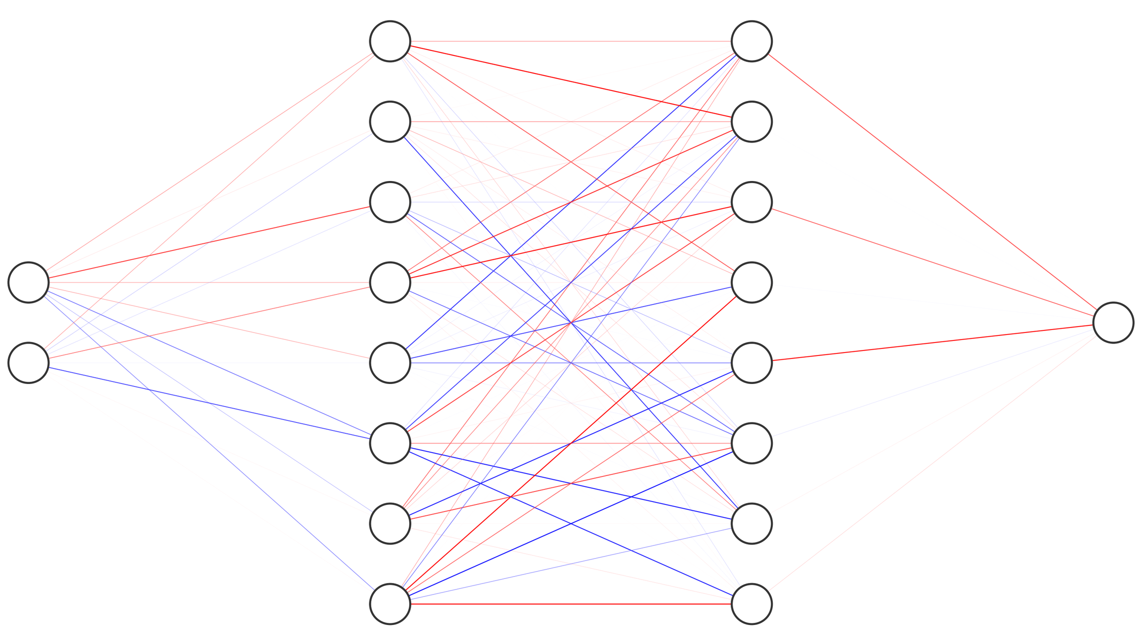

Figure 2. Graphical representation of a neural network

Methodology

1. **Model exploration -** Implement and analyse the MS and IMW cardiac action models in Julia.
2. **Model tuning -** Adjust MS parameters to approximate IMW dynamics.
3. **Model Comparison -** Generate AP data, and analyse AP characteristics by creating morphology plots.
4. **Parameter Predictions -** Train NNs to predict the next AP parameter directly from short histories.

$$APD_{n+1},\ APA_{n+1} = NN(APD_n,\ APA_n,\ DI_n)$$

5. **Neural network integration -** Augment the MS model with an additional NN-driven current to approximate the IMW model.

Model Exploration

- Both models reproduced **alternans** in AP duration (APD) and amplitude (APA) under appropriate stimulus forcing (Fig. 3).
- IMW model generated physiologically realistic AP morphologies with **phase-1 notch** and prolonged plateau.
- Parameter tuning brought the MS model closer to IMW behaviour.

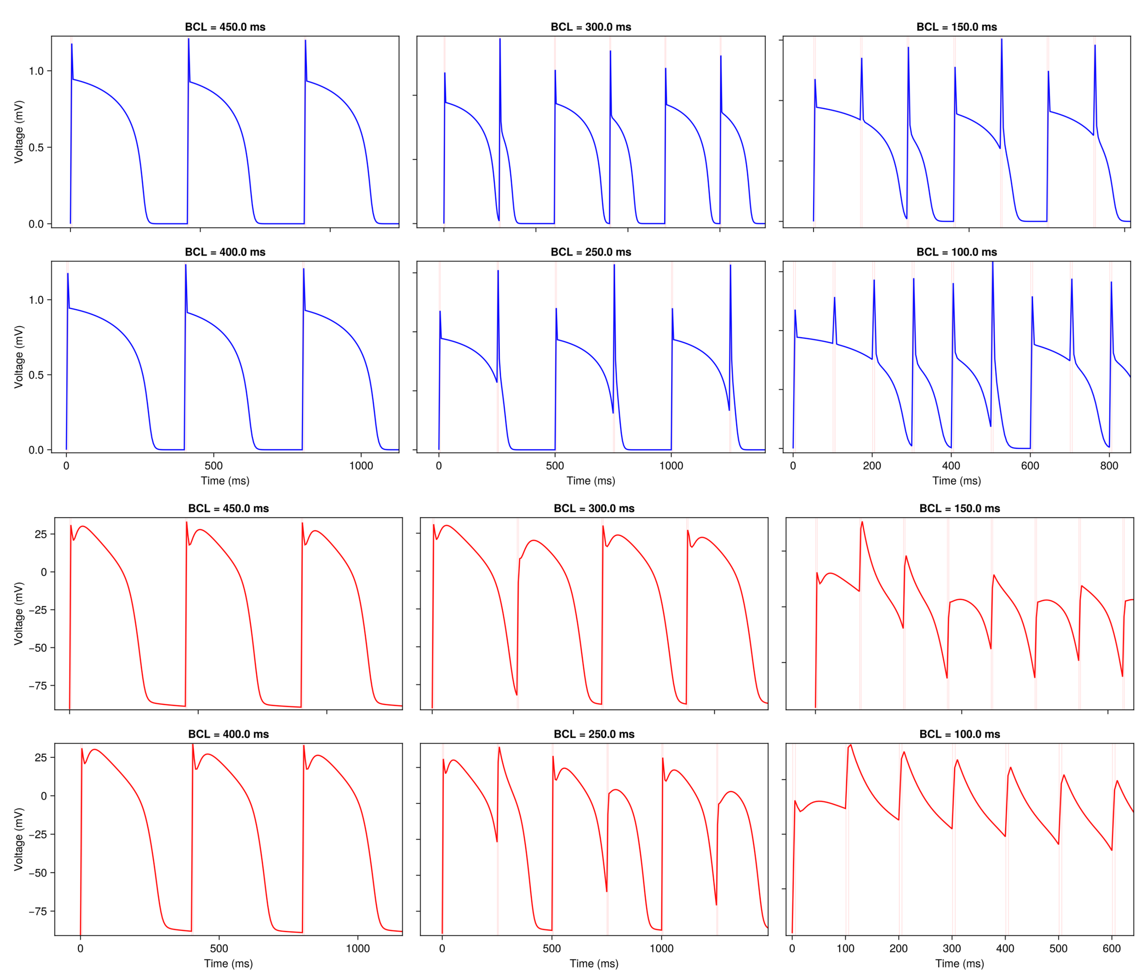

Figure 3. MS (blue) and IMW (red) voltage traces

Comparison of the models

- APD, APA, and DI maps offered insights into **discrepancies** between the different models (Fig.4).
- Maps show bifurcations when alternans occurs.
- **Tuning** the MS model to better resemble the IMW model led to **anomalous poor matching** of the **statistical properties** of the maps.

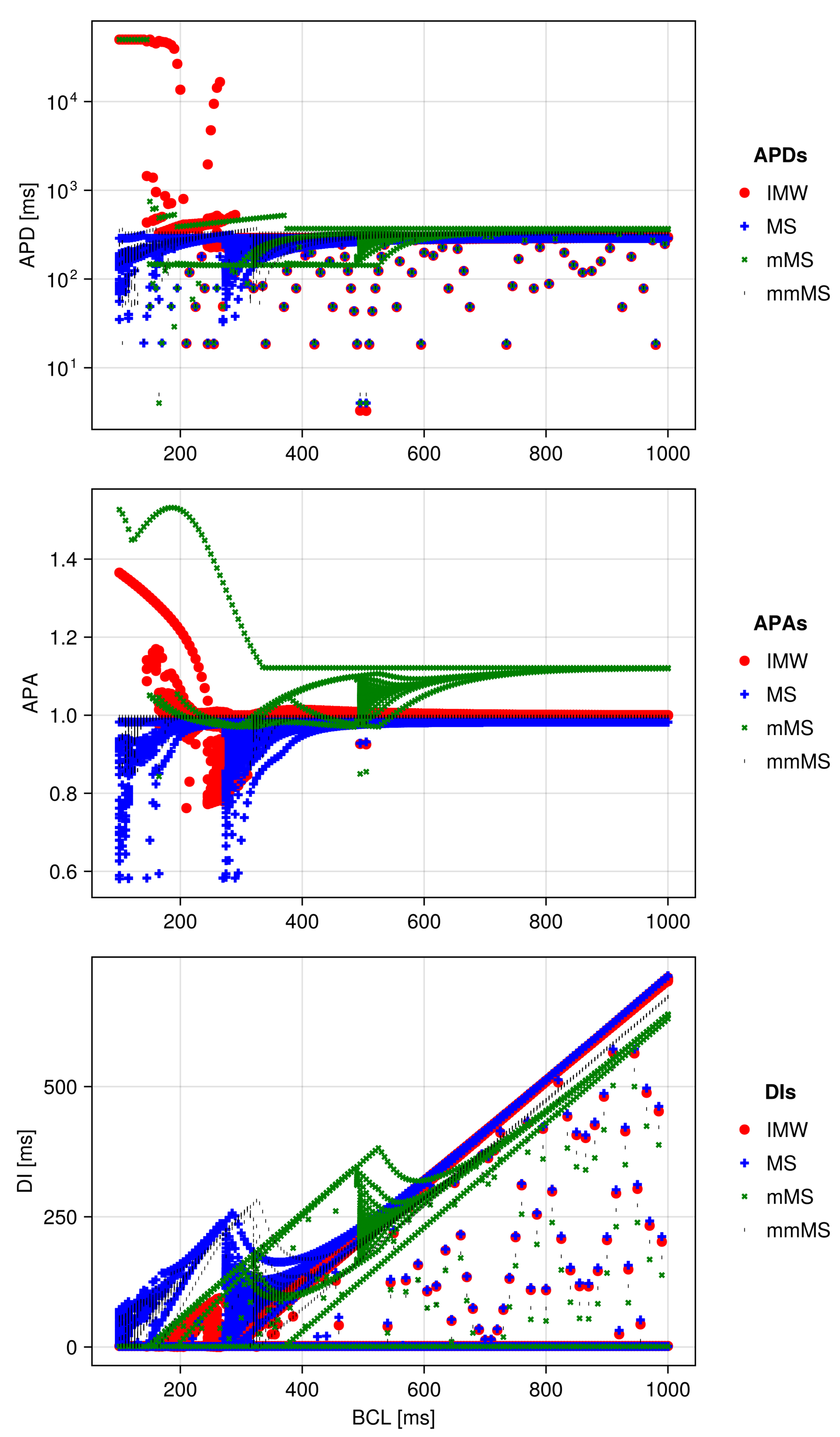

Figure 4. Plots of the APD, APA, and DI of the IMW model, MS model and modified MS model for a range of BCLs

Parameter Predictions

- Training NNs enabled **robust prediction** of AP characteristics across BCLs (Fig. 5).

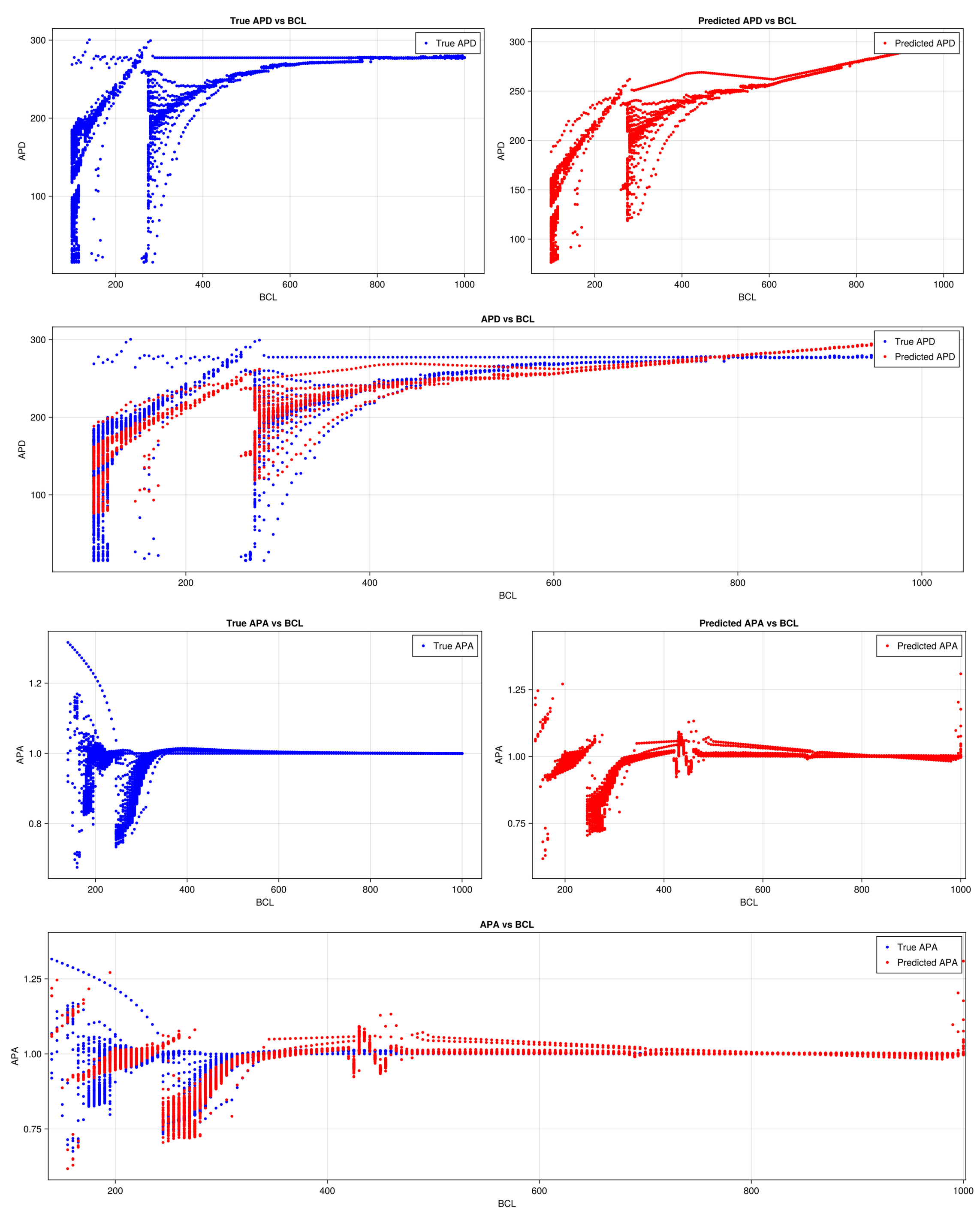

Figure 5. MS APD and IMW APA predictions with NNs

Augmenting MS Model with NNs

- Relative decrease in loss did not fully translate into accurate repolarisation dynamics.
- Strong agreement with IMW depolarisation and early plateau phases (Fig. 6).
- This outcome may deviate from expectations due to a lack of expressivity in the NN and the accumulation of gradients over time.

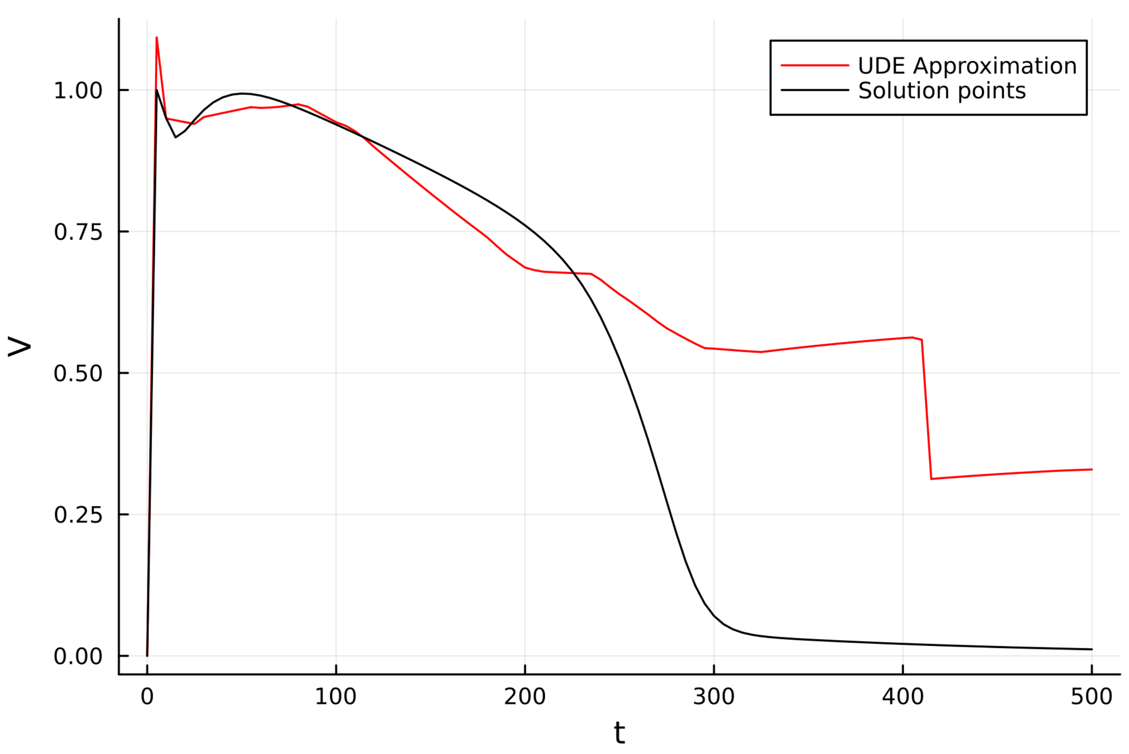

Figure 6. Simulated NN predicted AP based on the MS model (shown in red) compared to the IMW model AP (shown in black)

Conclusion

- Results suggest NN-augmented low-fidelity models may provide **surrogates** for complex biophysical simulations.
- May **support future studies** of cardiac restitution and arrhythmogenesis.

References

1. Asghari-Targhi, A. (2017) Action potential duration alternans in mathematical models of excitable cells. https://theses.gla.ac.uk/8460/
2. Rackauckas, C. et al. (2020) Universal differential equations for scientific machine learning. doi:10.21203/rs.3.rs-55125/v1.