

Challenges in Variability and Uncertainty Quantification for Ion Channel Modelling

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Biophysical models are subject to parameter uncertainties, but also variability between measurements and uncertainty in the model structure. Such variability together with limited uncertainty quantification causes reproducibility issues in fields like biology. Here we show methods and challenges in quantifying variability and uncertainty in parameters for a cardiac potassium channel model.

Designing high information-content experiments helps us to parameterise models with short training experiments, whilst leaving time to do independent validation experiments which help with model validation and eventually model selection. We based our analysis on over 50 experimental recordings and used methods such as hierarchical Bayesian modelling to quantify the variability and uncertainty between measurements. As a bonus, we studied the correlation between model parameters.

This study raises questions about how best to account for parameter correlations, model variability, model discrepancy and uncertainty when using these models to make real world decisions, how to design the best training and validation experiments, and how to put correlated variability and uncertainty bounds on our predictions.