

Considering identifiability, model selection, experimental artefacts and model discrepancy in design of experiments to build ion channel models

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Abstract: Today our field continues to use the same approach to voltage-clamp protocol design that Hodgkin & Huxley used, in terms of designs that enable model parameter values to be estimated manually from graph paper. We have been developing short, high-information voltage clamp protocols to characterise ion currents. I will discuss various rationales for designs that consider parameter identifiability, model selection and minimising experimental artefacts. We then use computational optimisation to fit simple mathematical models for hERG/IKr to the resulting currents, and use it to predict the results of conventional voltage clamp protocols and physiological action potential clamps. There are also opportunities to use mathematical models to account for patch clamp artefacts to consolidate information from different patch clamp recordings more reliably, as well as a new ensemble approach to get a bound on the effects of model discrepancy.