

Challenge Group 6

MSM with standardized protocols for
model-driven data collection

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Outline of discussion

- (1) Identification of the relevant questions
- (2) Survey of current practices across the consortium
- (3) Case studies
- (4) Discussion - how to move forward

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Questions to address as a group

- (1) Do most fields have standardized, model-driven protocols for data collection?
- (2) How can we, as a group, encourage standardization of protocols?

Question 1

(1) Do most fields have standardized, model-driven protocols for data collection?

Answer: NO

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Standardized protocols for data collection

A survey of current practices

(1) When you began your project, did your field have standardized protocols for data collection?

Mostly no. Example responses:

“Standardized protocols exist, but the data they provide is not sufficiently quantitative.”

Yankeelov, models to predict effectiveness of breast cancer neoadjuvant therapy

“Standard protocols exist for antibiotic concentrations in plasma (pharmacokinetic data)

Linderman/Kirshner, models of tuberculosis therapies

(2) Has your project led to any new protocols that have become standard or could potentially become standardized if further developed?

Most groups are moving in this direction, but success is limited

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Standardized protocols for data collection

A survey of current practices

(3) What are the barriers to standardization of protocols for model-driven data collection?

Two themes:

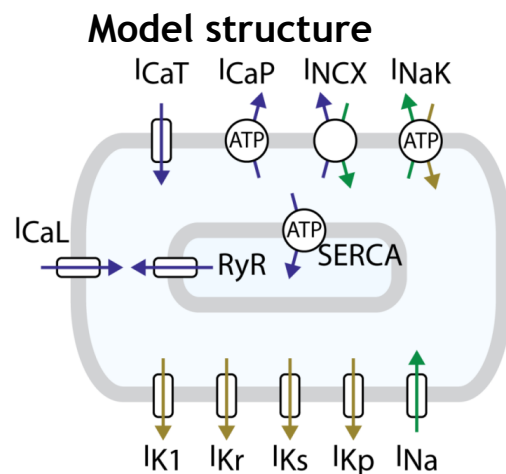
- a. The protocols are still under development and need to be validated
- b. One or more protocols have been demonstrated to be useful under particular conditions, but side-by-side comparisons between methods have not been performed.

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Quasi-standardized protocols

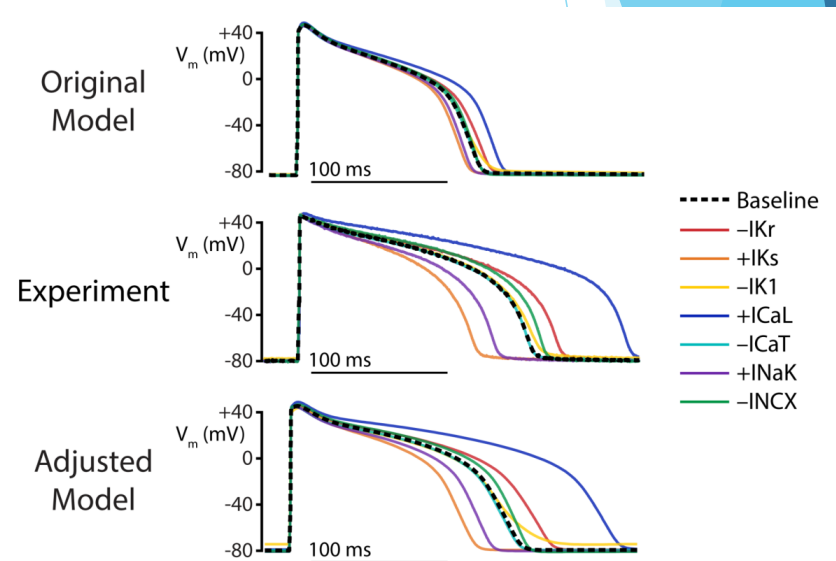
Case studies

Cardiac electrophysiology and calcium handling



Free parameters:
Expression levels of all
channels, pumps
transporters

Proposed experimental protocol



Devenyi, Ortega et al. (2017) *J Physiol.* 595:2301-17.

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Discussion questions

- (1) Are there other success stories that weren't highlighted in pre-meeting discussions?**
- (2) How do experiments and model parameterization need to be documented for protocols to become standardized more readily?**
- (3) What additional challenges are faced besides those already mentioned?**

Our project: A Multi-Scale Systems Pharmacology Approach to TB Treatment
PIs (computational) - Kirschner, Linderman
PIs (experimental) - Dartois, Flynn

(1) There are some relatively standard protocols, e.g. for tracking immune cells in blood and determining concentrations of antibiotic in plasma over time (to get pharmacokinetic data).

(2) Yes. Flynn and Dartois are the PIs developing protocols for novel forms of data collection. For example, in non-human primates the Flynn group has developed PET/CT protocols for examining lungs and tracking the time course of inflammation. Dartois has pioneered the use of MALDI-MS for examining antibiotic distribution in lung lesions. These are at present research tools that could potentially be extended/adapted/standardized for future studies. We use the data in concert with computational models, which in turn help inform what types of data and the frequency of data collection that are most useful.

(3) The protocols are at present still under development (esp. wrt interface with the computational model) and being used to answer specific research questions, here about particular antibiotics. Standardization will be useful as we look across a broad range of antibiotics.

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