Modeling Nuclear and Intracellular Calcium Dynamics in Rabbit Ventricular Cardiomyocytes

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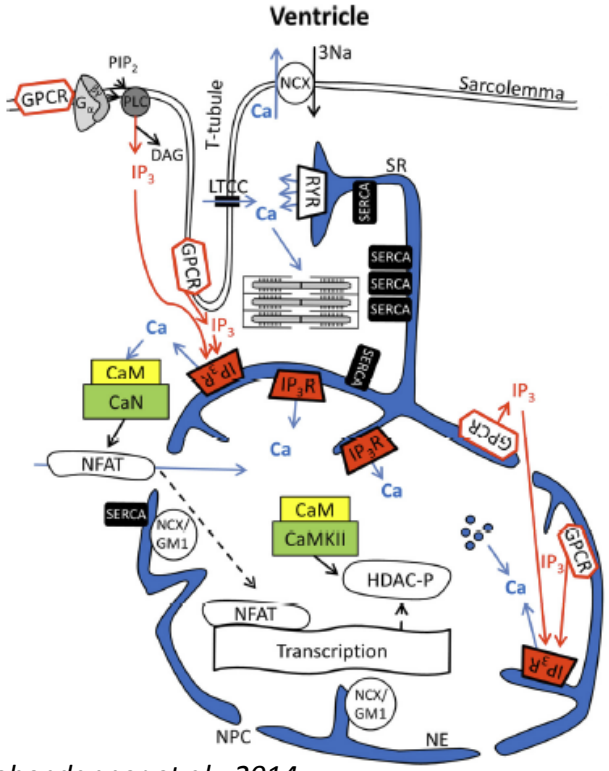
UCSD PRIME

Research Proposal



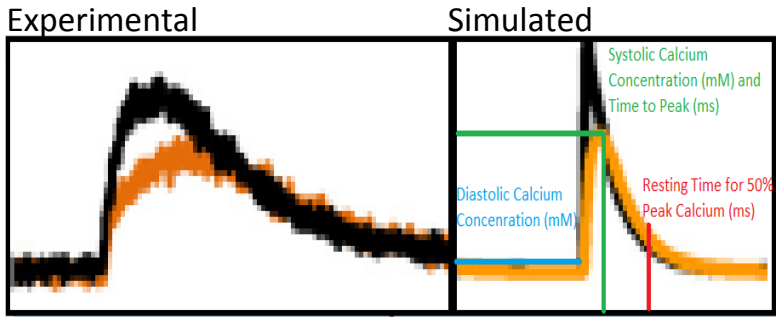
Hohendanner et al., 2014

Using the Nimrod toolkit, a set of tools that allows for investigating highly complicated parametric systems, my goal is to optimize Excitation-Contraction-Transcription-Coupling Model (Shannon-Bers-Michailova Model) for a ventricular cardiomyocyte in rabbits and run sensitivity analysis in order to elucidate how the model behaves under various stimuli.

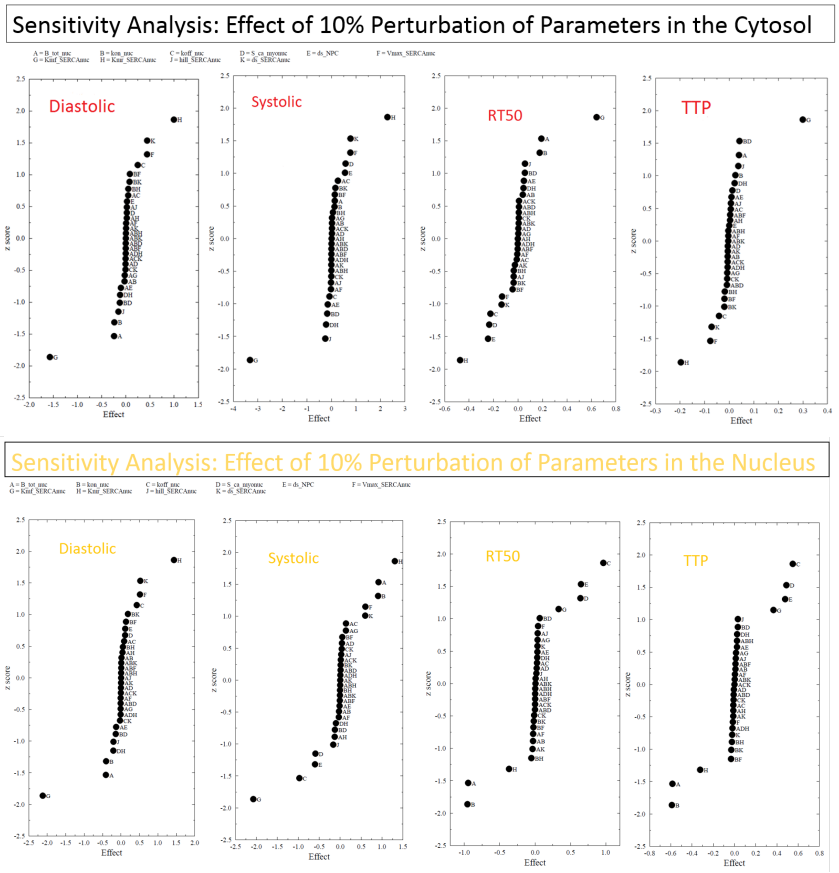
The model will be optimized and fitted for 4 kinetic measurements of calcium:

- Systolic (mM)
- Diastolic (mM)
- Time-to-peak (ms)
- Resting time to 50% peak calcium concentration (ms)

Left: Schematic for a ventricular cardiomyocyte.
Right: Experimental calcium vs. simulated data from MATLAB, Both plots show calcium vs. time (non-dimensionalized).



Progress: Conducted Sensitivity Analysis after Perturbing Parameters 10%



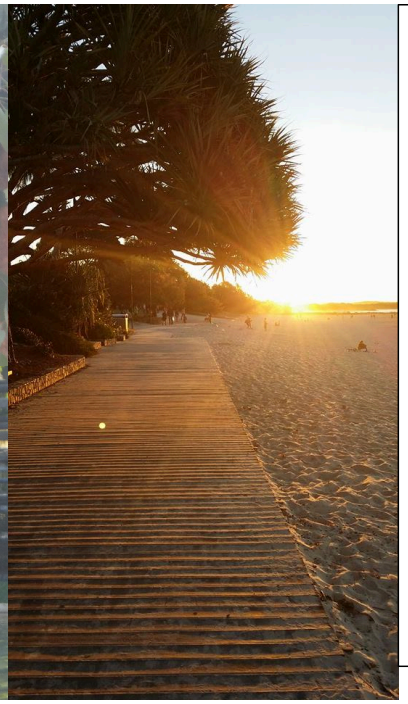
- Ran sensitivity analysis and determined effects of perturbation on kinetic parameters:
  - Those parameters were selected for optimization based off which produced a significantly negative effect (those to the left of 0.0 and below a z-score of -1.5)
  - These parameters selected will be fed into Nimrod/O to find optimal parameter values.

Future Plans

- Consider the addition of a sodium buffering equation in the nucleus in order to correct drift within the model.
- Will continue fitting various ranges of parameter values after investigating a feasible range of parameters.
  - Conduct sensitivity analysis by perturbing parameters in the nucleus by ±10, 30, 50, and 100%.
- Run additional sensitivity analysis in order to identify mechanisms that regulates nuclear Ca2+

Australia Zoo & Sunshine Coast





Top left: PRIME Students posing with the Irwin family at the Australia Zoo.
Bottom left: Me riding a merciless croc eating a small child.
Top right: A baby koala just waking up for afternoon lunch.
Bottom right: Lunch time for Casper the croc!
Right: Barely catching the sunset at Noosa Main Beach.

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In memory of Dr. Michailova…
a mother, mentor, and scientist.