Modeling Nuclear and Intracellular Calcium Dynamics in Rabbit Ventricular Cardiomyocytes

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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).
Results from Nimrod/O after fitting model to parameter values within a 50% difference of suggested default values.

Systolic nuclear calcium concentration is quite large, above 30% threshold criteria for optimizing the model.

May have to refine optimization methods. This is likely due to large standard deviation taken into account when performing optimization.

Before continuing onto further sensitivity analysis more optimization must be done.
Future Plans

- Investigate other optimization methods and build a workflow to test 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 regulate nuclear Ca2+
Byron Bay, New South Wales

Left: Cape Byron Bay Lighthouse.
Middle left: View from a lookout of Byron Bay.
Middle right: Tour bus of eager internationals going into the countryside.
Bottom left: View of a majestic lake in the country.
Bottom right: First kangaroo burger! Don’t worry it’s eco-friendly to eat these guys!
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