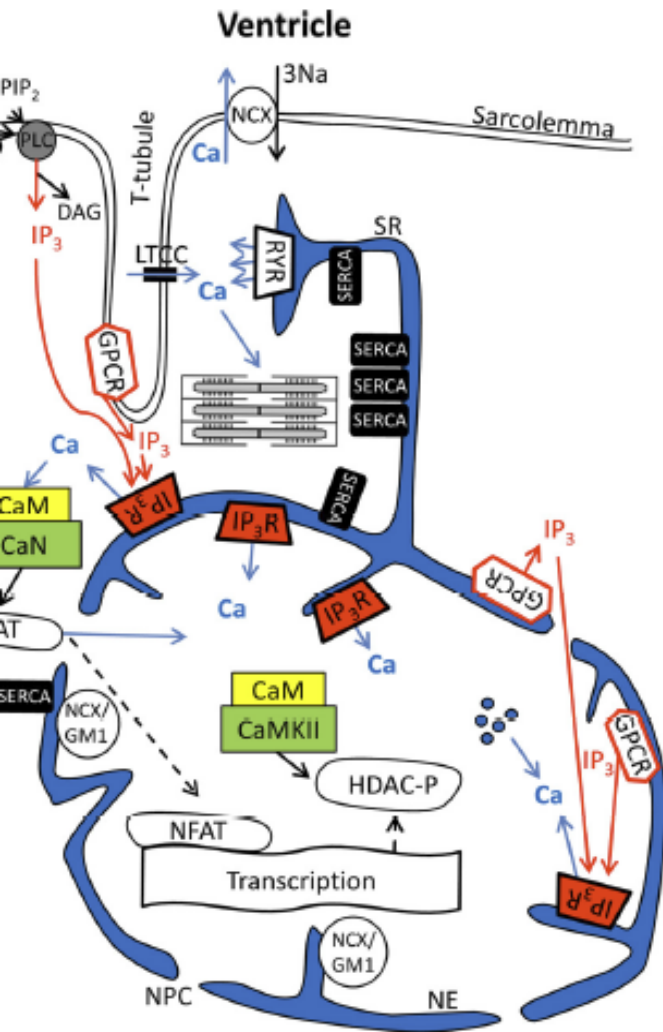


Modeling Nuclear and Intracellular Calcium Dynamics in Rabbit Ventricular Cardiomyocytes

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UCSD PRIME



Research Proposal



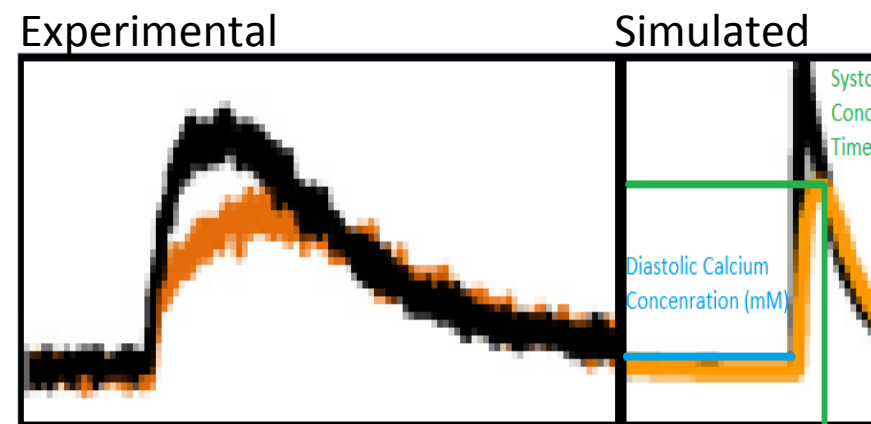
ner et al., 2014

Using the Nimrod toolkit, a set of tools that allows for investigating high 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.

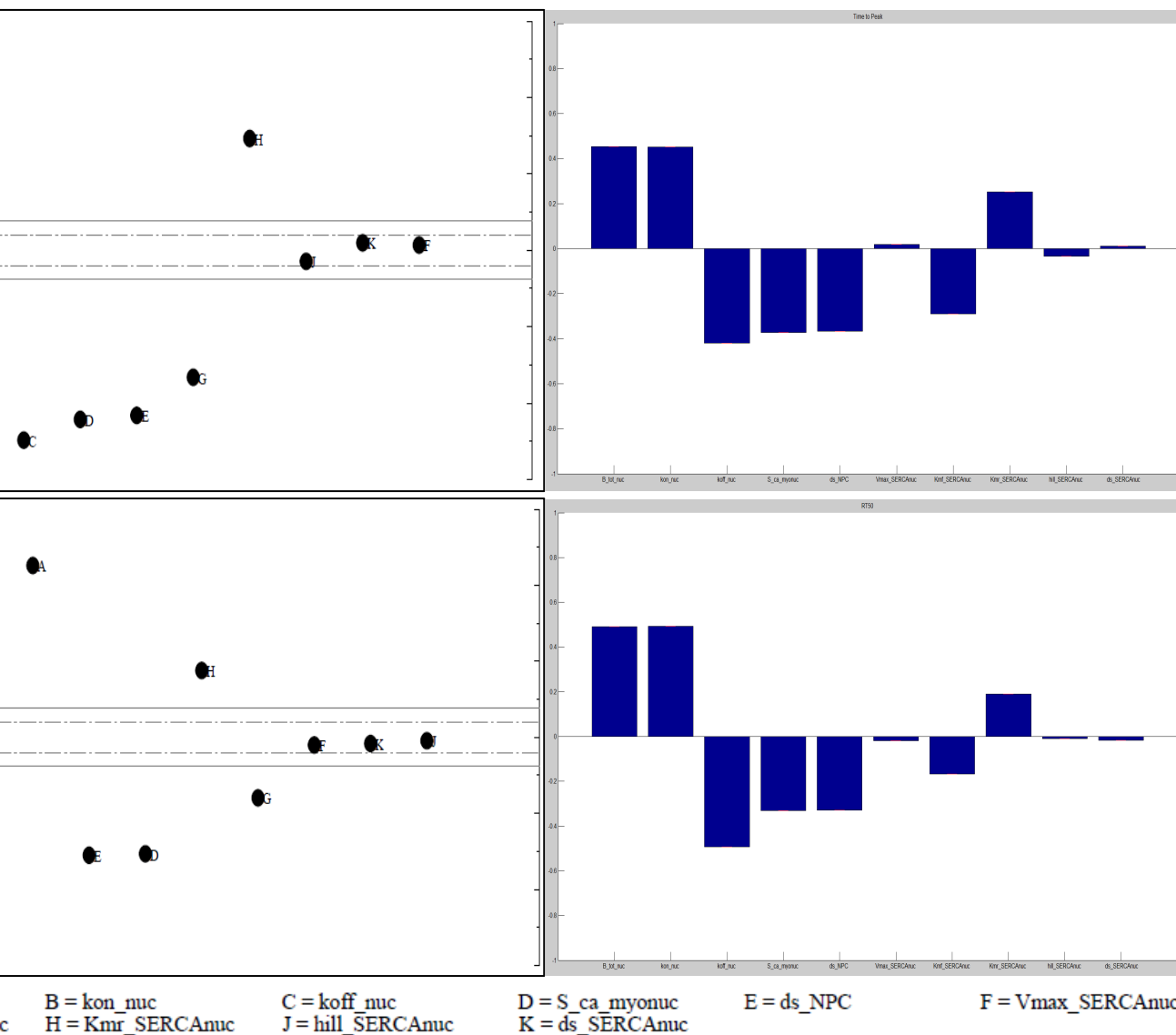
The model will be optimized and fitted for 4 kinetic measurements of calcium:

- 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).



gress: Nimrod/E & PLS Tool Results



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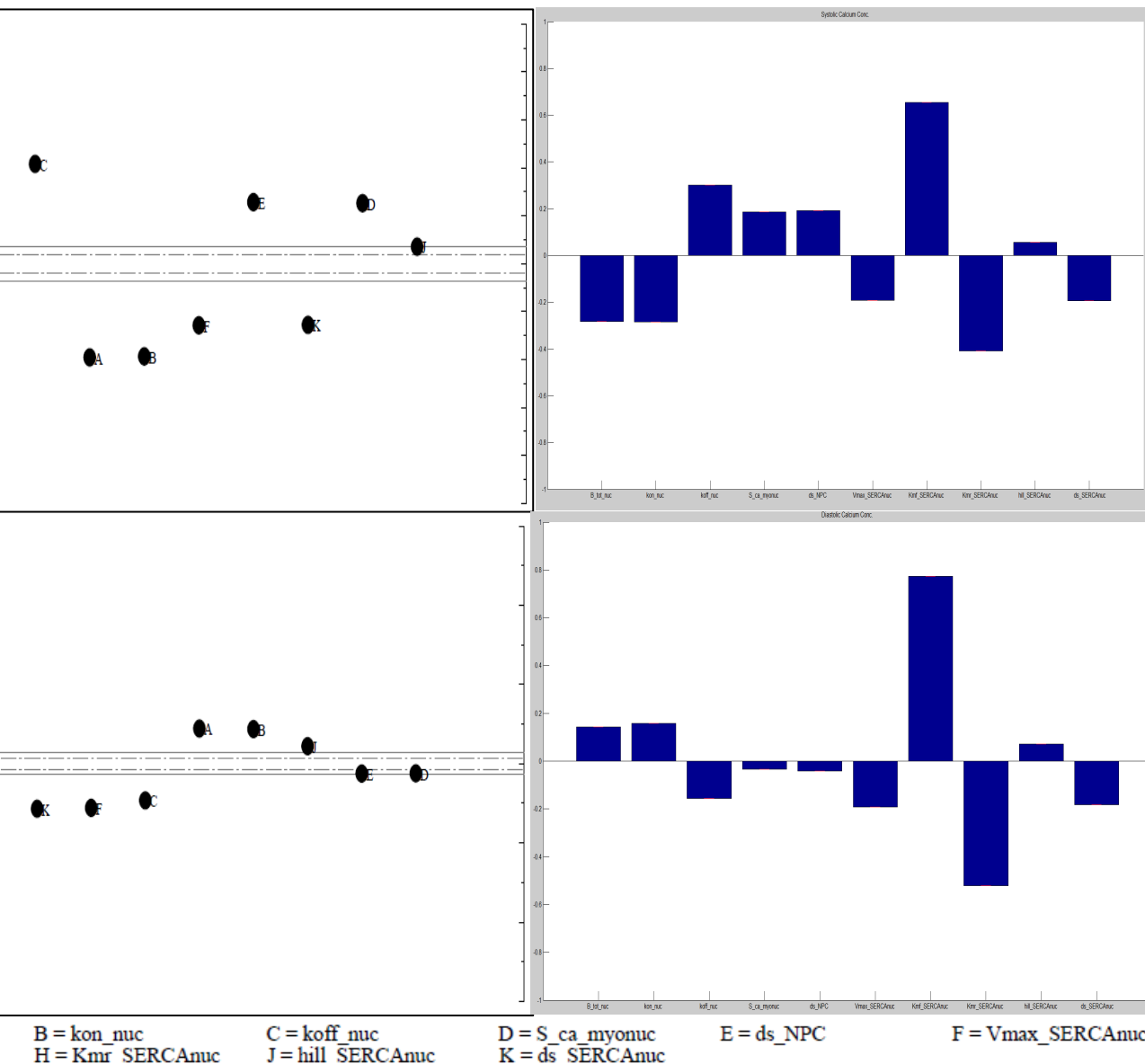


Figure: Results from a $\pm 10\%$ perturbation in nuclear parameter values. The left column of plots are the Lenth plots from Nimrod /E and to the right are the corresponding PLS regression plots explaining the correlation.

Left: Nimrod/E's Lenth Plot. Top plot corresponds to systolic calcium and the bottom corresponds to diastolic calcium measurement.

Right: Results from the PLS Tool. Variables going to right correspond to (A-K). Note there is no variable for parameter G.

Parameter G has a relatively strong correlation with both systolic and diastolic calcium measurements.

Parameter H has an relatively strong indirect correlation with both systolic and diastolic calcium measurements.

ection Slide

oad blocks:

experienced problems quantifying relationship
and the degree of correlation between key
parameters.

ncountered issues with fitting experimental
ata.

ssues estimating parameter values.

Successes:

Learned how to use PLS regression tool and
make corresponding plots to Nimrod/E data.

Cleaned up data analysis methods - reducing
variation across samples allowing for accurate
fits.

Refined optimization script, creating 4 additional
versions serving different purposes.

e Plans

Extract more kinetic parameter data from experimental data and calculate population statistics.

Carry out parameter estimation using experimental data.

Conduct sensitivity analysis by perturbing parameters in the nucleus by ± 10 , 30, 50, and 100%.

Identify mechanisms that contribute to nuclear Ca^{2+} transport.

Surfer's Paradise, Gold Coast

Relaxing with some
at SkyPoint's

Welcoming sign to

View of the Gold
the SkyPoint
the 77th floor!

t: Group selfie!

ht: Beautiful night
the Skypoint tower.



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.I.P. Dr. Anushka Michailova



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