Characterization of cardiac cellular dynamics using Physics-Informed Neural Networks

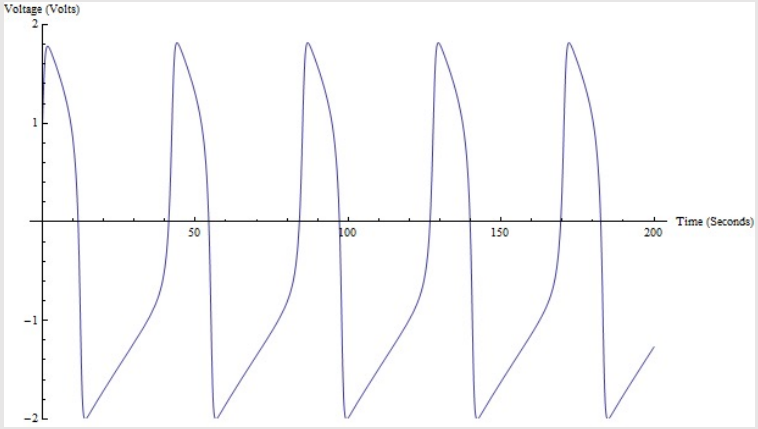
Master project

Bendik Steinsvåg Dalen

simula

There exist numerous models for heart cells

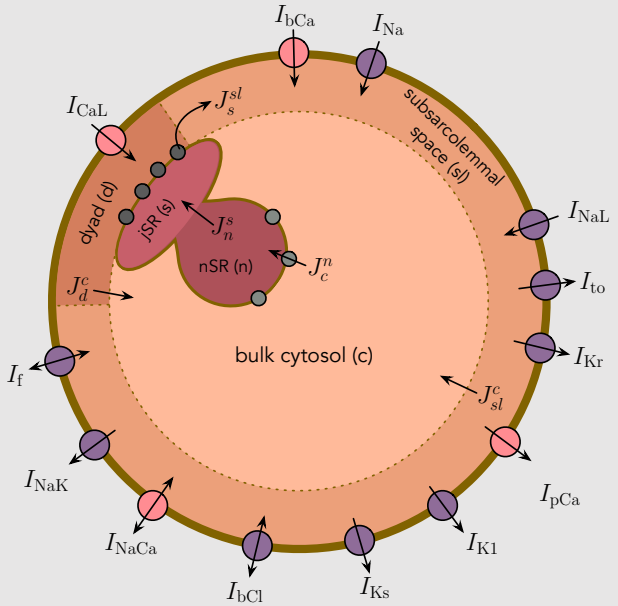
Fitzhugh-Nagumo (simple)



$$\begin{cases} \frac{dv}{dt} = v - v^3 - w + I_{\text{ext}} \\ \tau \frac{dw}{dt} = v - a - bw \end{cases}$$

https://www.normalesup.org/~doulcier/teaching/modeling/excitable_systems.html

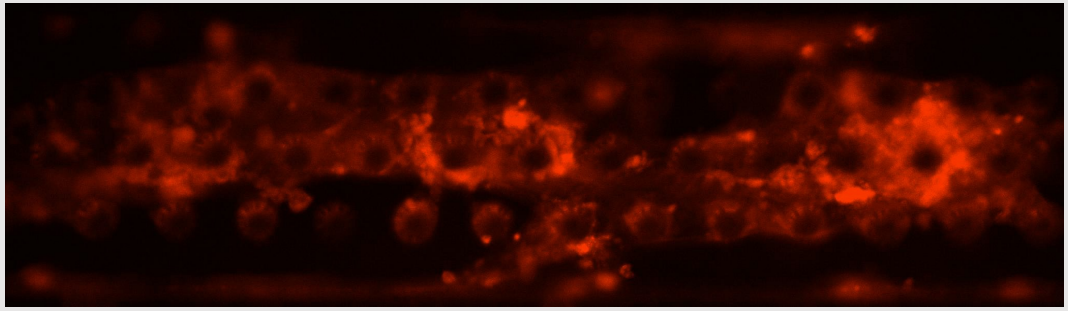
A model developed at Simula (complex)



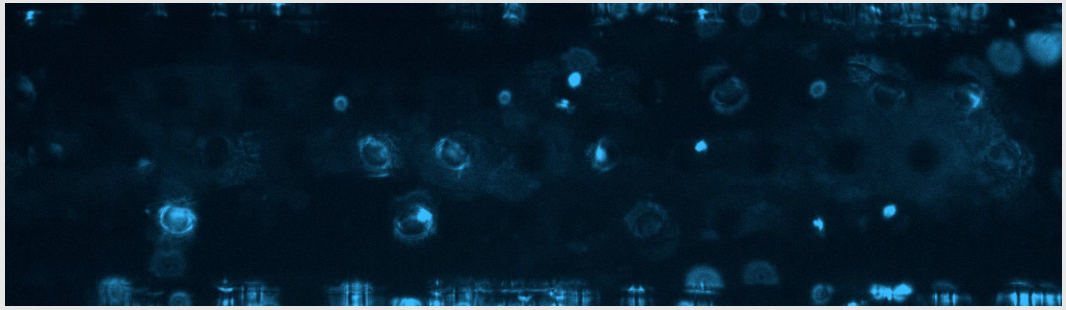
Jæger, K. H., Charwat, V., Charrez, B., Finsberg, H., Maleckar, M. M., Wall, S., ... & Tveito, A. (2020). Improved computational identification of drug response using optical measurements of human stem cell derived cardiomyocytes in microphysiological systems. *Frontiers in pharmacology*, *10*, 1648.

We want to be able to fit models to experimental data

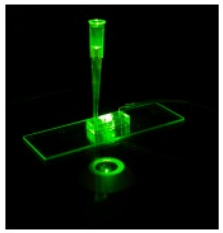
Voltage

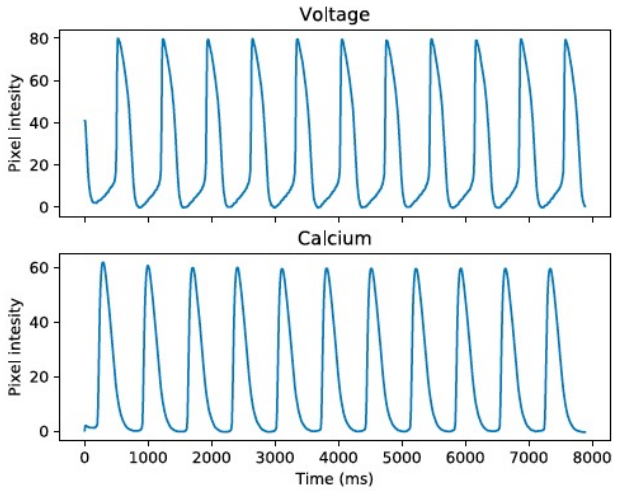


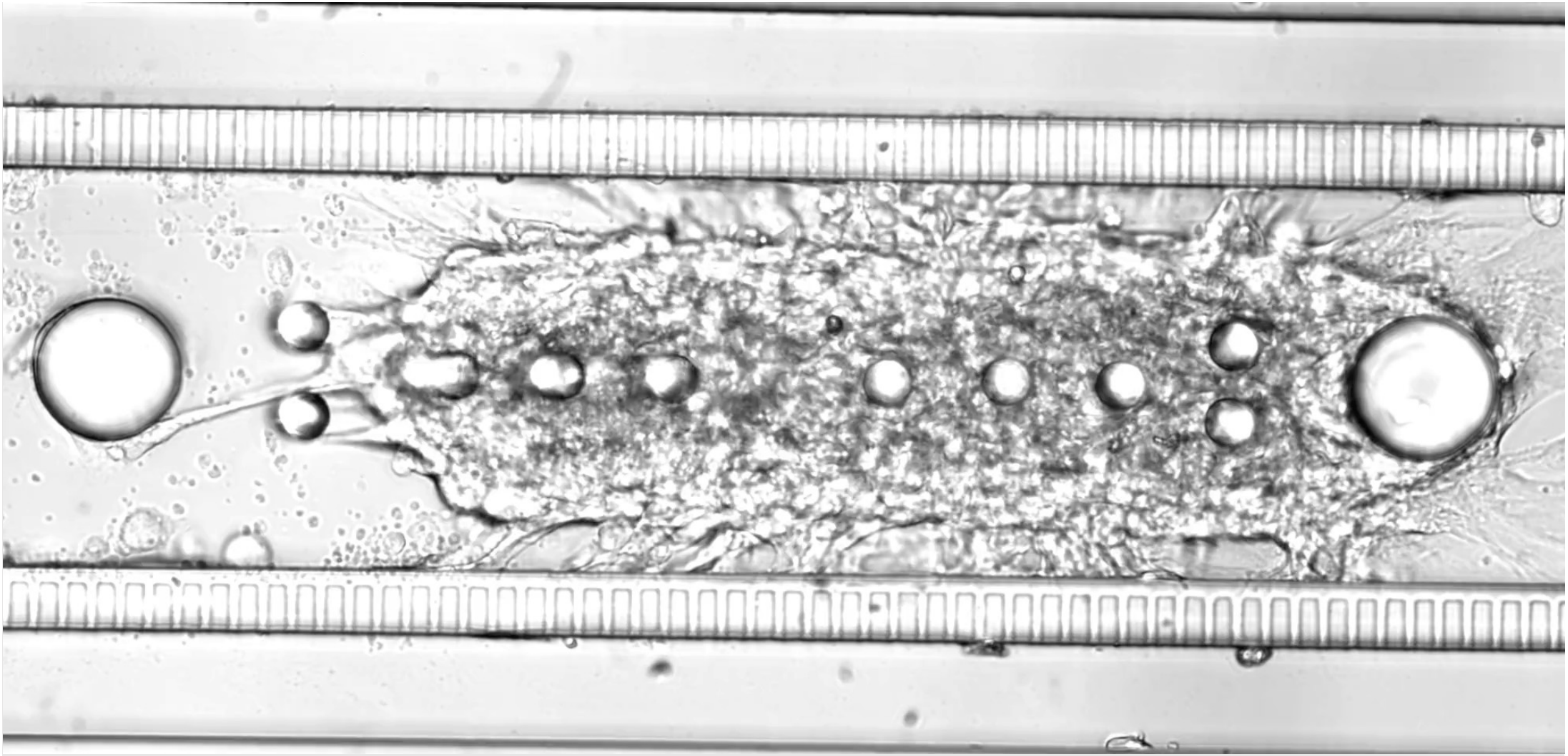
Calcium



Optical Action Potential Measurements







We fit data to models using standard optimization techniques

- Select some parameters in the model that you want to adjust to fit the data
- Form a cost/loss function that represents the error between model and data
- Use an optimization method to minimize the cost function with respect to the chosen parameters

Aim of thesis – compare deep learning approach with standard approach

PLOS COMPUTATIONAL BIOLOGY

RESEARCH ARTICLE

Systems biology informed deep learning for inferring parameters and hidden dynamics

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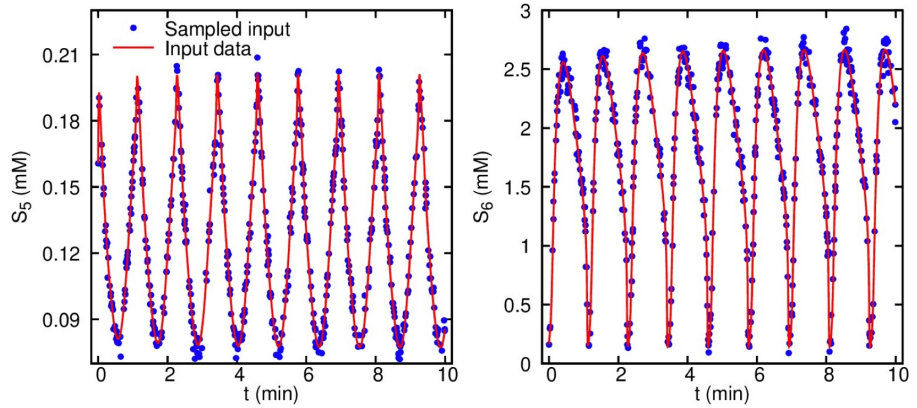
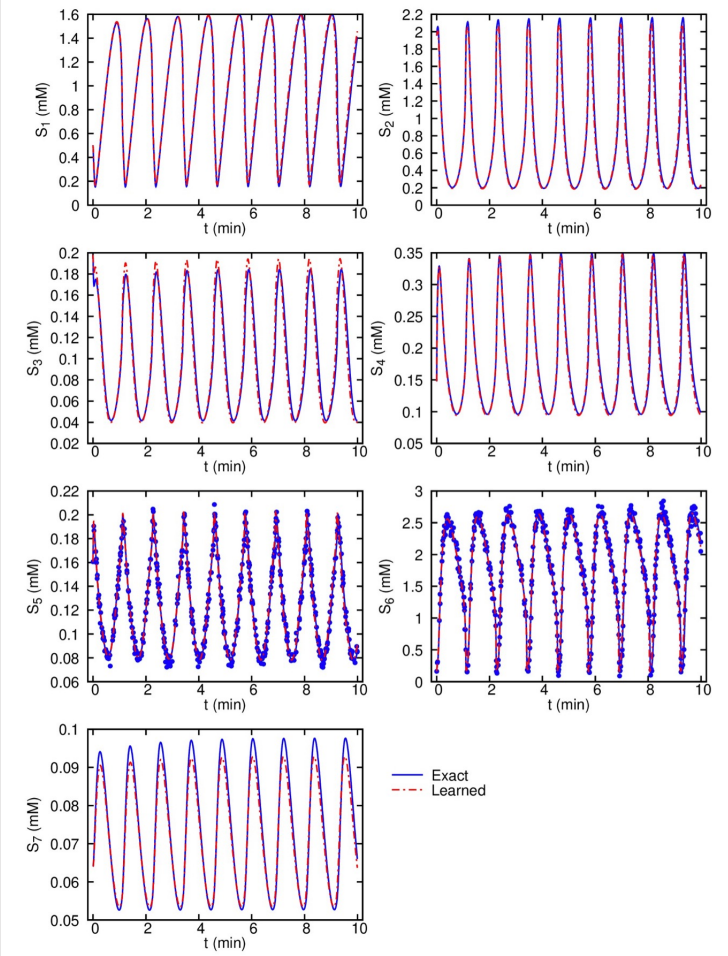


Fig 2. Glycolysis oscillator noisy observation data given to the algorithm for parameter inference. 500 measurements are corrupted by a zero-mean Gaussian noise and standard deviation of $\sigma = 0.1\mu$. Only two observables S_5 and S_6 are considered and the data are randomly sampled in the time window of $0 - 10$ minutes.



Look at parameter identifiability

How confident can we be that we will get the correct value

Table 3. Parameter values for yeast glycolysis model and each corresponding inferred values. The standard deviations are estimated using Eq. (S3) in S1 Text as practical non-identifiability analysis based on the FIM.

Parameter	Target value	Inferred value (Noiseless observations)	Inferred value (Noisy observations)	Standard deviation
J_0	2.5	2.50	2.49	0.18
k_1	100	99.9	86.1	62.0
k_2	6	6.01	4.55	21.3
k_3	16	15.9	14.0	21.9
k_4	100	100.1	97.1	103.6
k_5	1.28	1.28	1.24	0.25
k_6	12	12.0	12.7	5.1
k	1.8	1.79	1.55	4.34
κ	13	13.0	13.4	25.9
q	4	4.00	4.07	0.27
K_1	0.52	0.520	0.550	0.091
ψ	0.1	0.0994	0.0823	0.317
N	1	0.999	1.29	2.94
A	4	4.01	4.25	2.28

https://doi.org/10.1371/journal.pcbi.1007575.t003

Suggested approach

- Start reading the paper and understand the method
- Try to run the code – make sure you can reproduce the results
- Create a repo on GitHub for the master project – give nick and me read access.
- Try to implement the Fithugh-Nagumo model and use the deep learning approach to estimate parameters
  - Could also use a more advanced model with similar complexity as the one described in the paper
- Test out more traditional approaches to estimate parameters and compare with deep learning based approach
  - should agree on a few methods here
- Investigate how the results depends on different settings. Number of layers, what type of layers, noise in data, amount of data etc.
- Try with a more complicated model and repeat.

http://www.scholarpedia.org/article/Models_of_cardiac_cell

Resources

- https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1007575
- https://github.com/alirezayazdani1/SBINNs
- Material from summer school
- Mathematical Physiology book
  - https://link-springer-com.ezproxy.uio.no/book/10.1007/978-0-387-75847-3
  - Chapter 5 (Should read 1.1 and 2.6 first)