Finding the biophysical properties of neurons from electrophysiological recordings

ML Meeting LBL 5/9/18

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LBL
NSD

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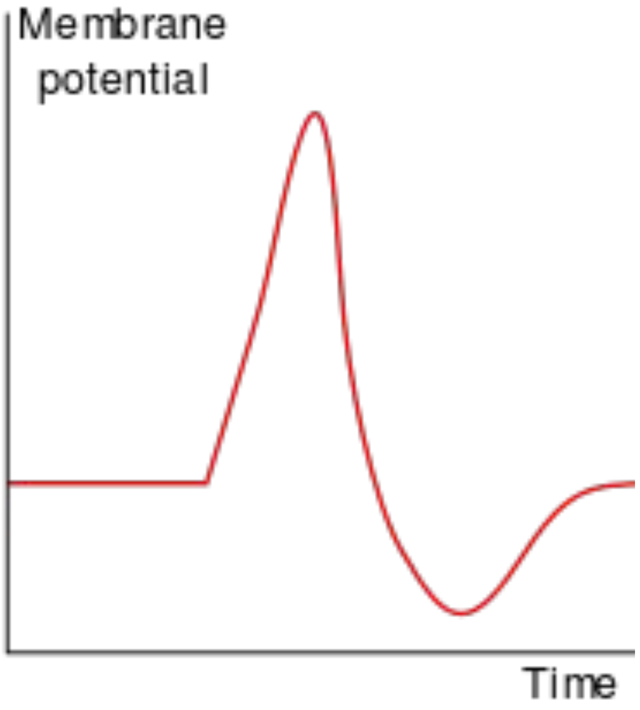
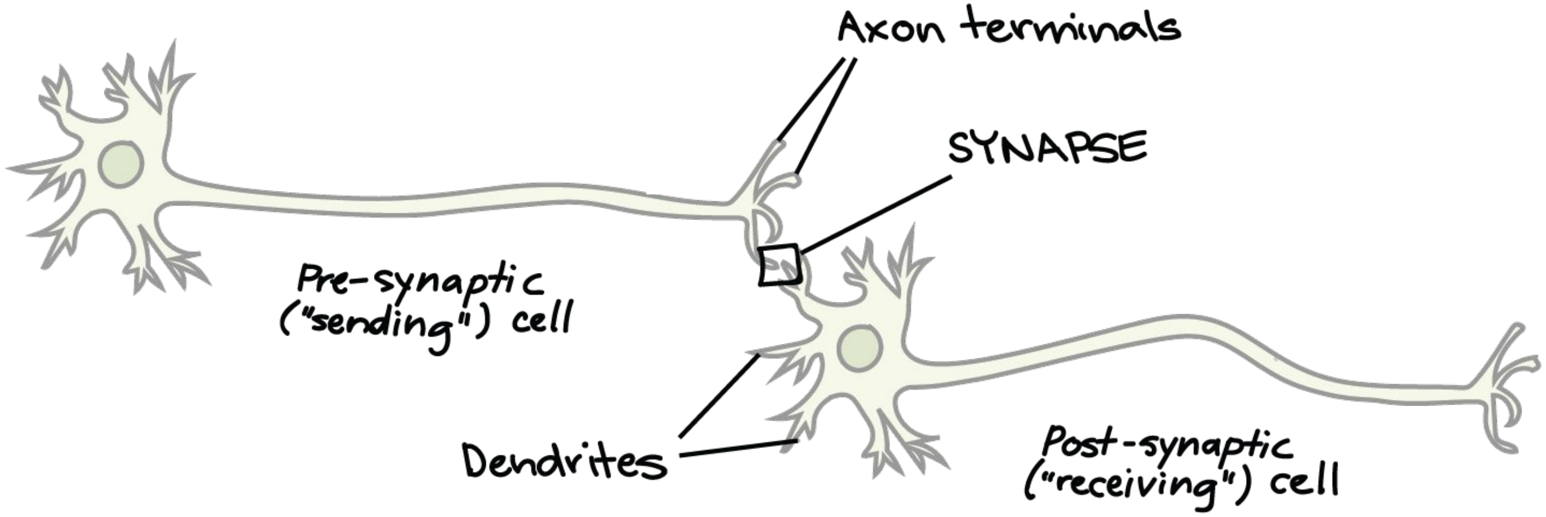
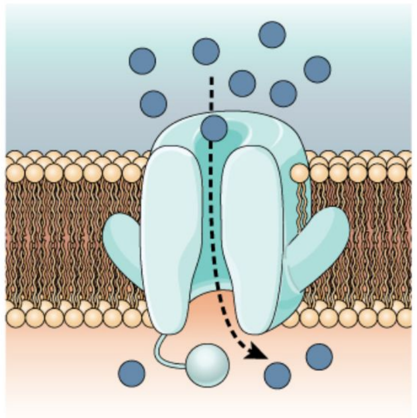
Ion channels gives neurons their electrical properties





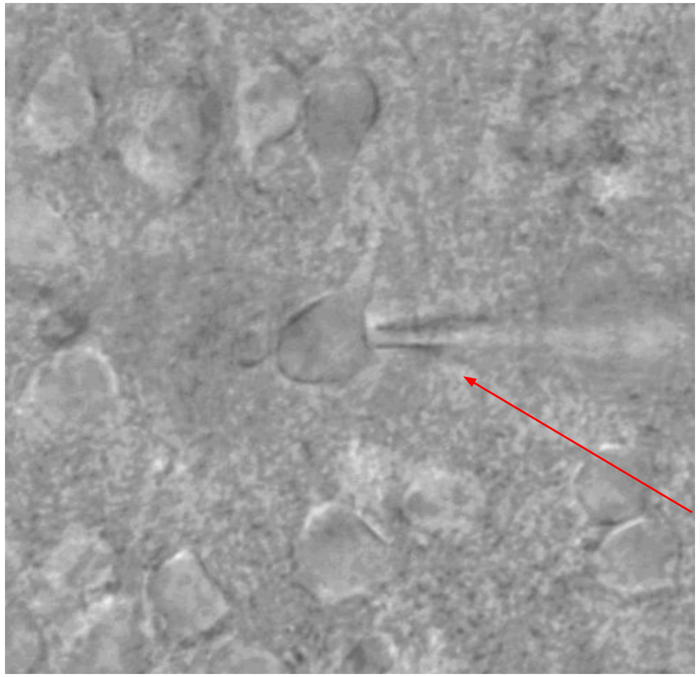


Open In response to a nerve impulse, the gate opens and Na^+ enters the cell.

Sodium
Potassium
Calcium

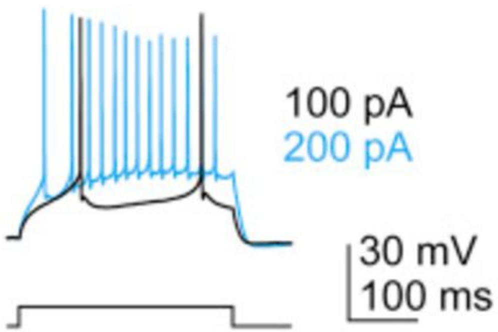
Recording from neurons only gives us gross neuronal properties

Hunt for a neuron

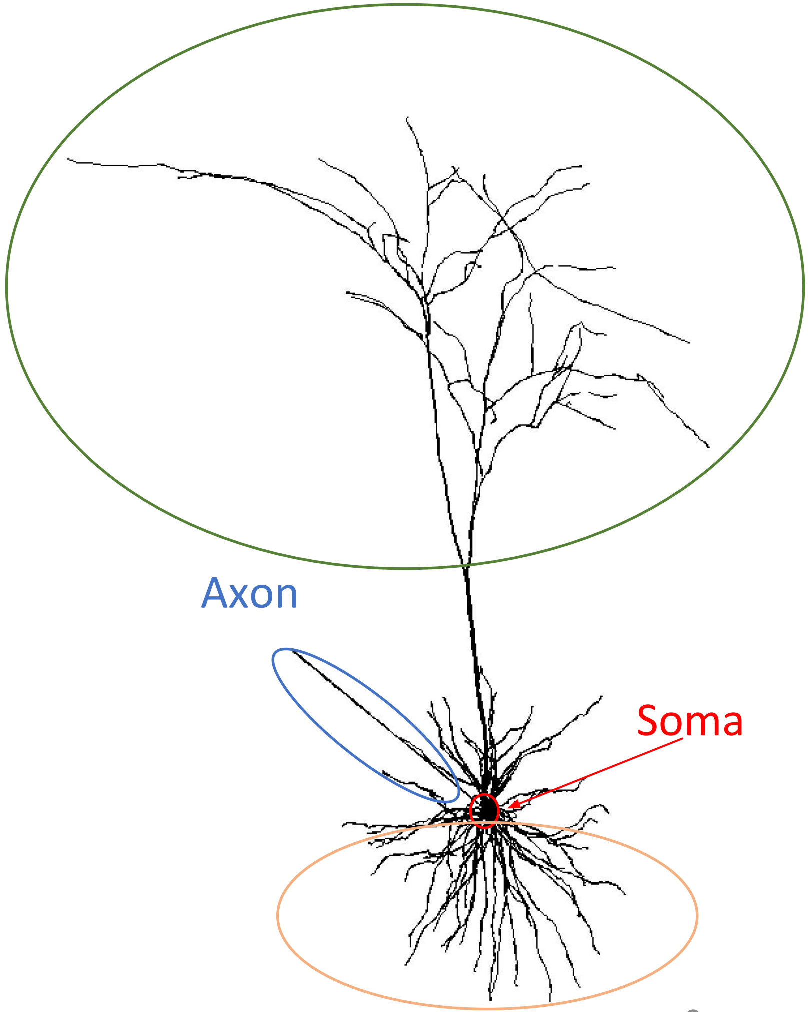


https://www.kmjacobslab.org

Stimulating the cell



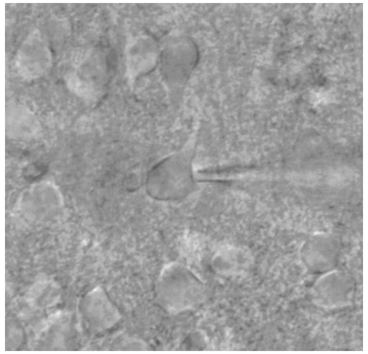
Yang & Ben-Shalom et. al. 2016

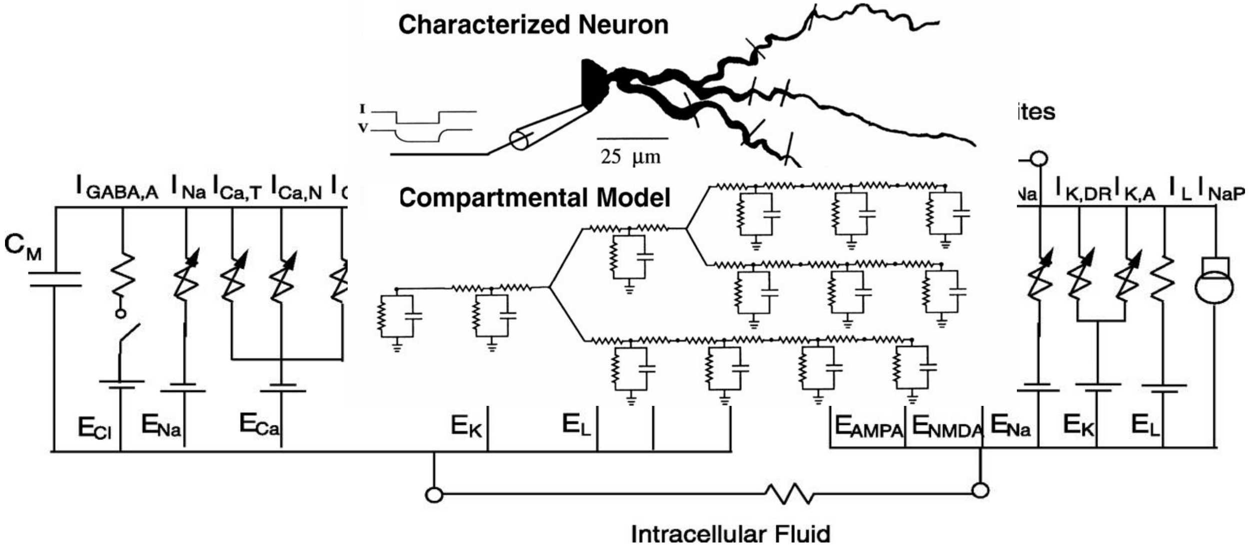


Why do we care about the ion channels distribution

- Channelopathies
  - Epilepsy
  - Autism
- Accurate models can find targets for treatments
- We do not know the distribution of ion channels, it will help us understand better how neurons work.
- Build better neuronal networks that simulate neuronal circuits

Compartmental models

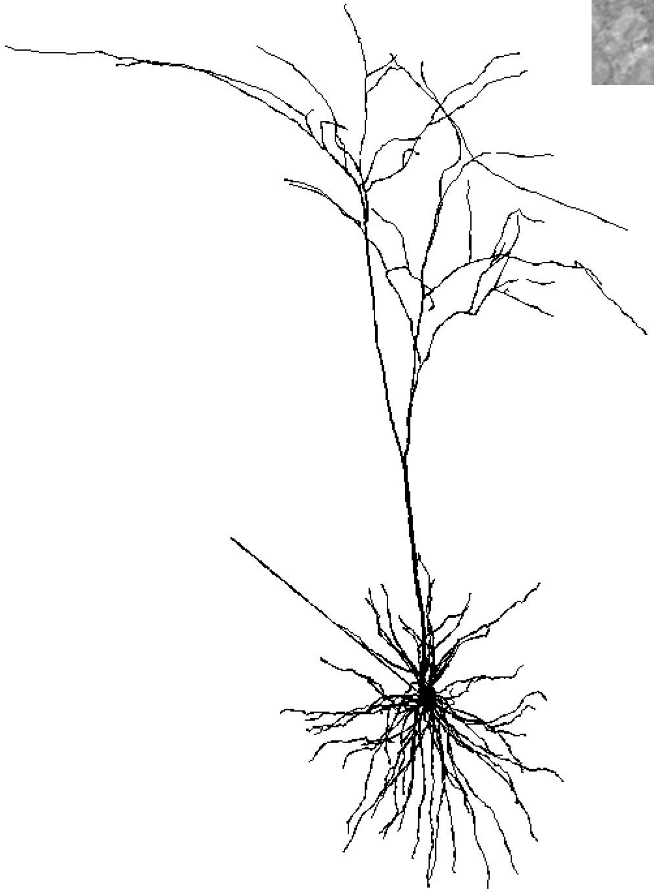




Canavier & Landry. 2006.

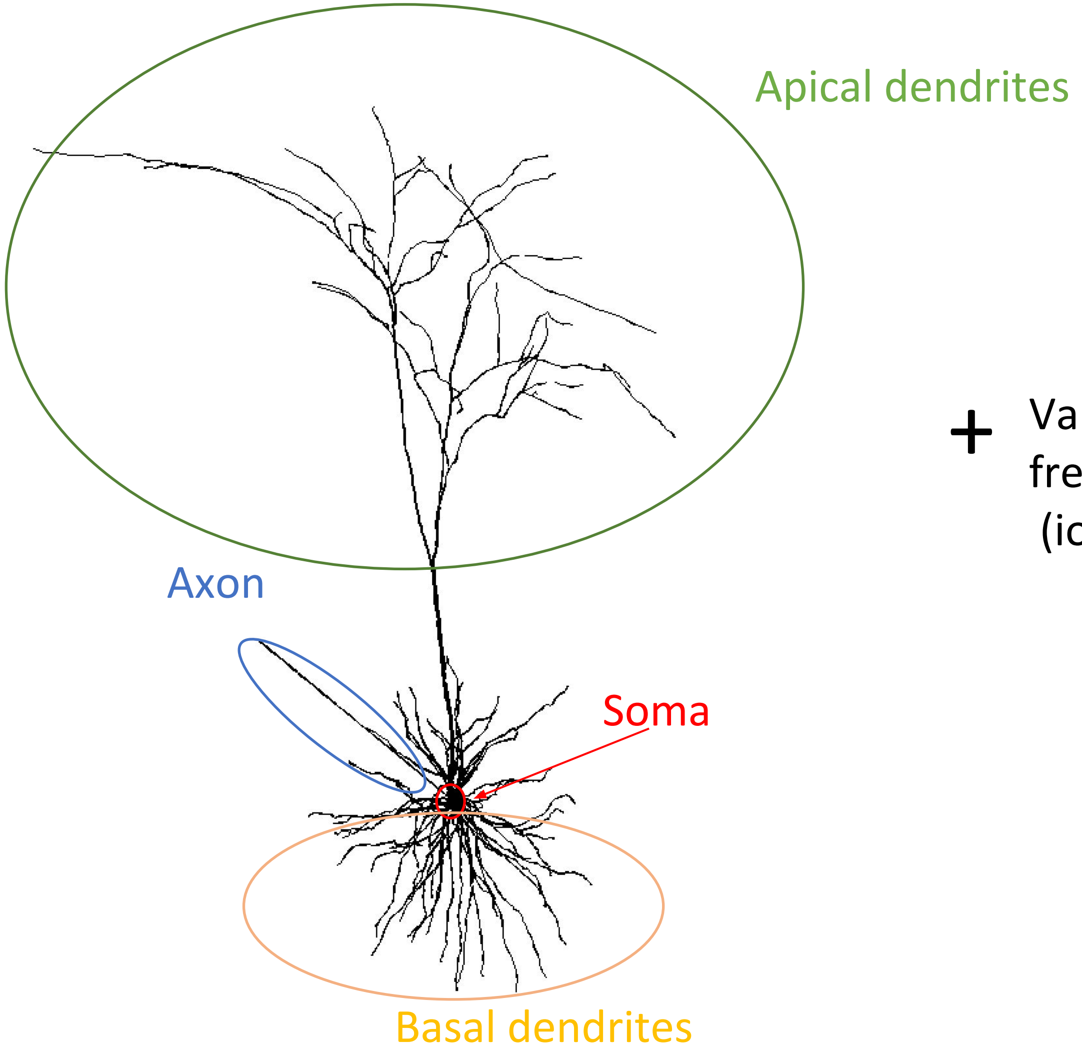
NEURON

for empirically-based simulations of neurons and networks of neurons

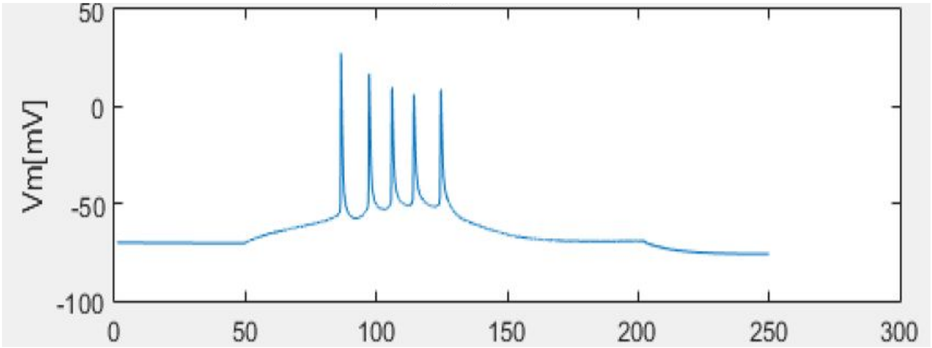


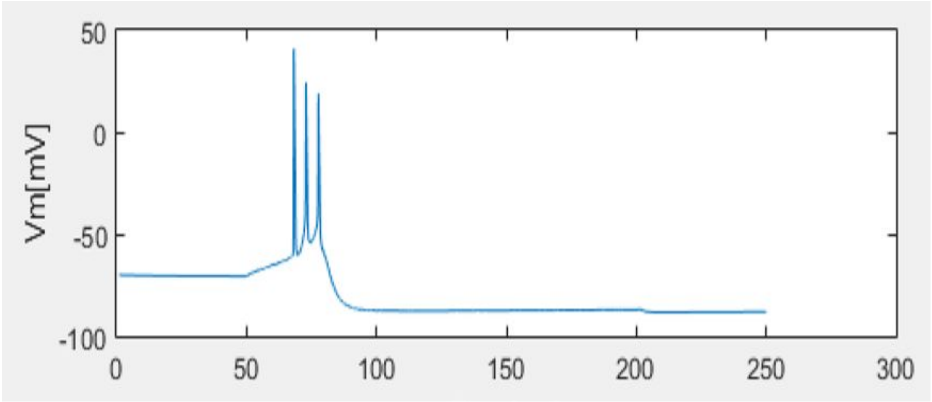
Mainen & Sejnowski. 1996.

Different parameters values leads to different model's output



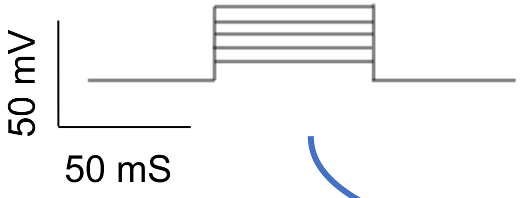
+ Values for
free parameters
(ion channels dist.)





Fitting models to electrophysiological data

Stimuli



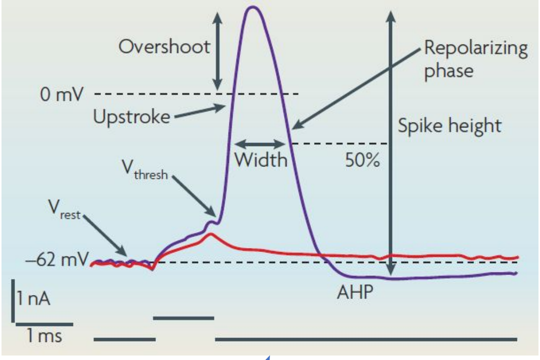
Values for free parameters

Free Parameters:
gna_dend
gna_soma
gna_node
gkv_soma
gkv_axon
gkm_soma
gkm_dend
Passive parameters:
Cm
Rm
g_leak
g_Ih

Neuronal Model

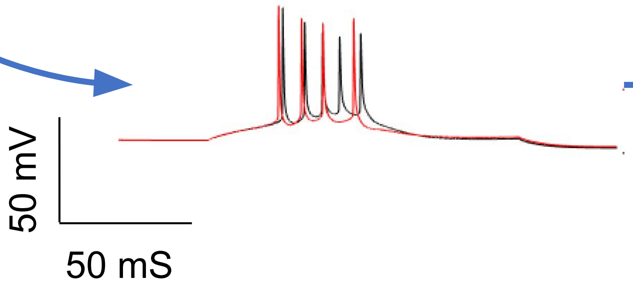
Genetic Algorithm

Score functions



Score functions:
RMS
KL Divergence
Feature based:
AP height
AP width
Resting potential
etc...

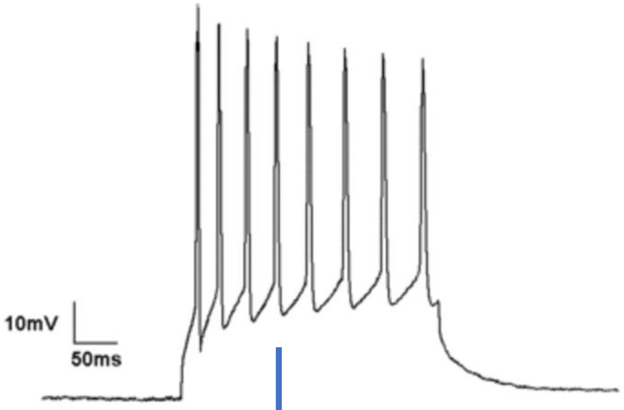
Simulated waveform



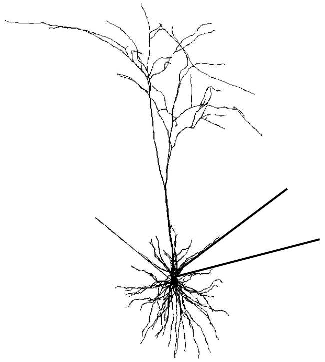
Target data
Model's output

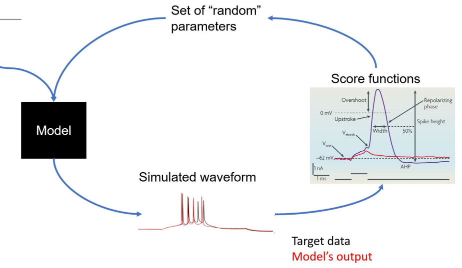
Real vs Surrogate Data: Using voltages created by the model

Target data



Recorded neuron





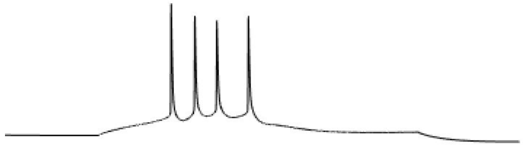
Neuron's properties
Na Conductance at the axon
K Conductance at the soma
…

Model's parameters
Na Conductance at the axon
K Conductance at the soma
…

=

Neuronal model

Target Data/Surrogate Data



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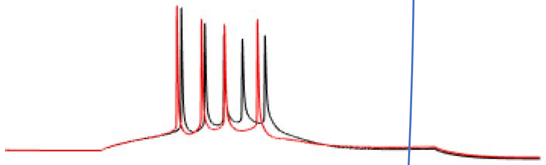
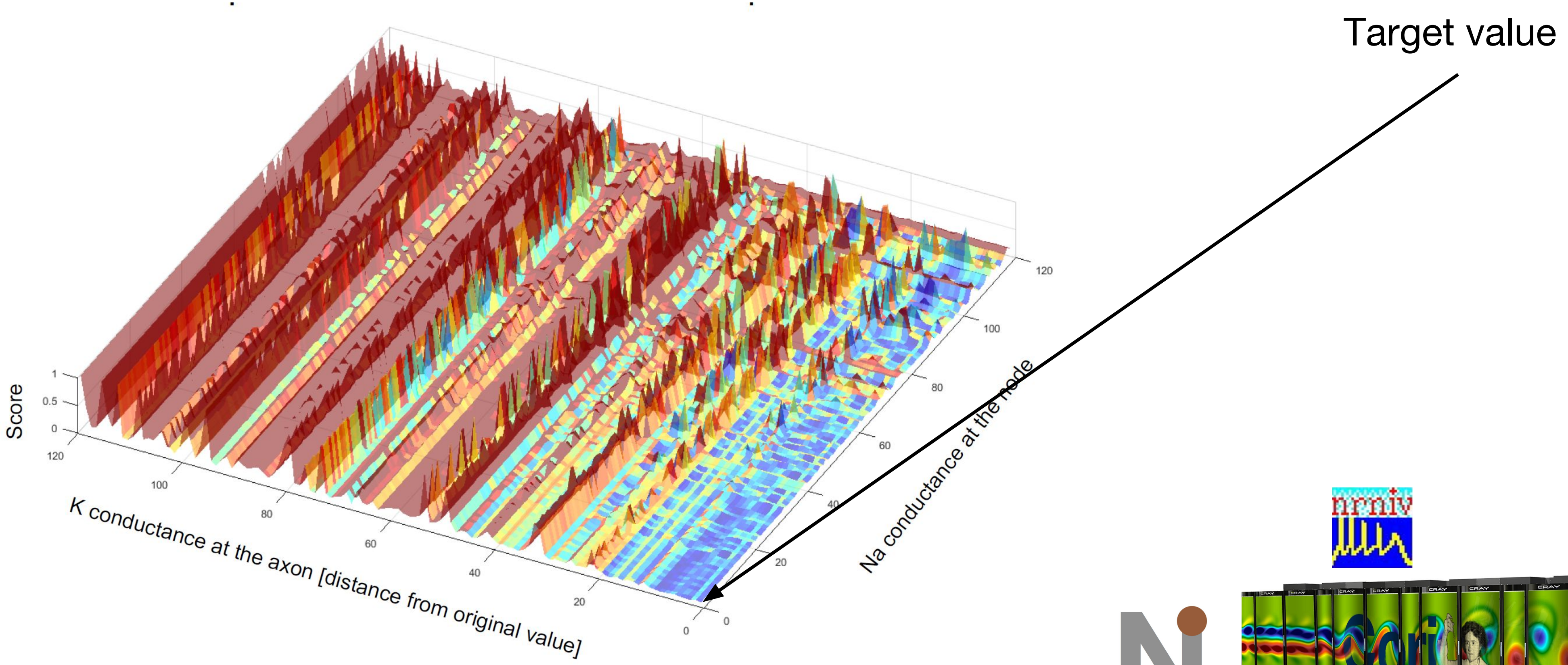
Model's parameters
Na Conductance at the axon
K Conductance at the soma
…

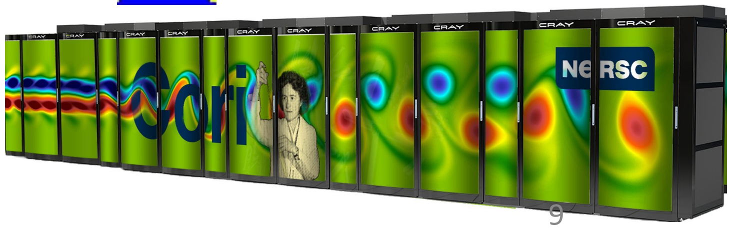


Fitting

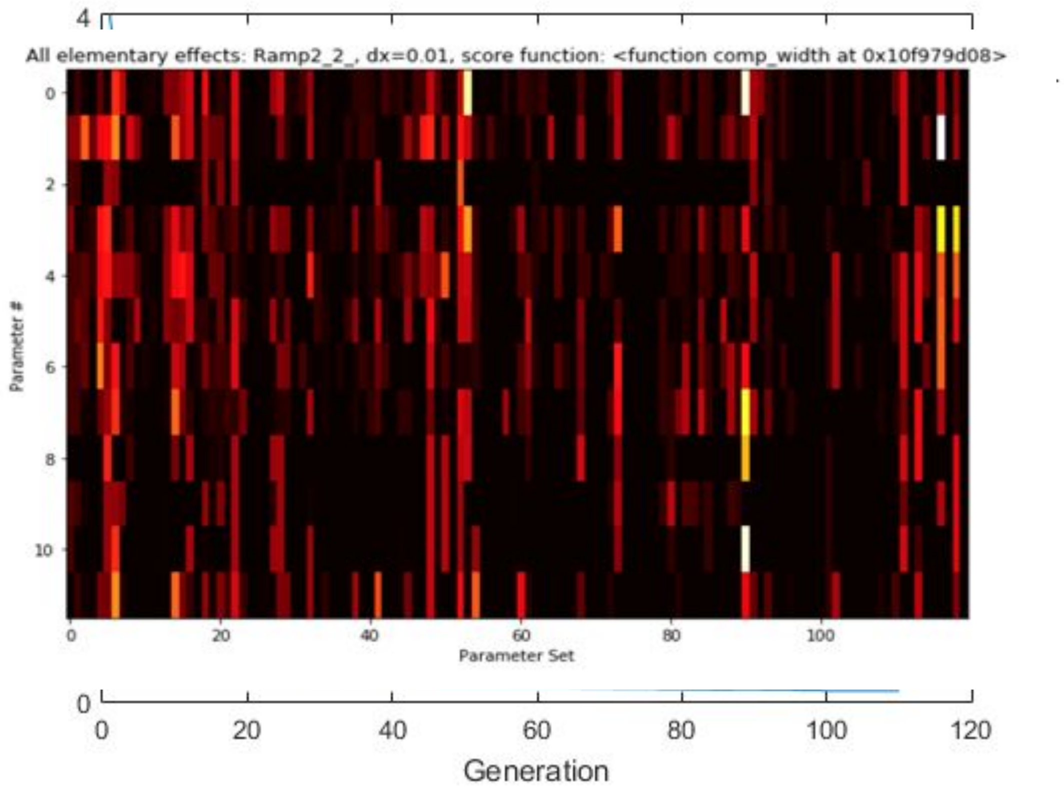
Neuronal model

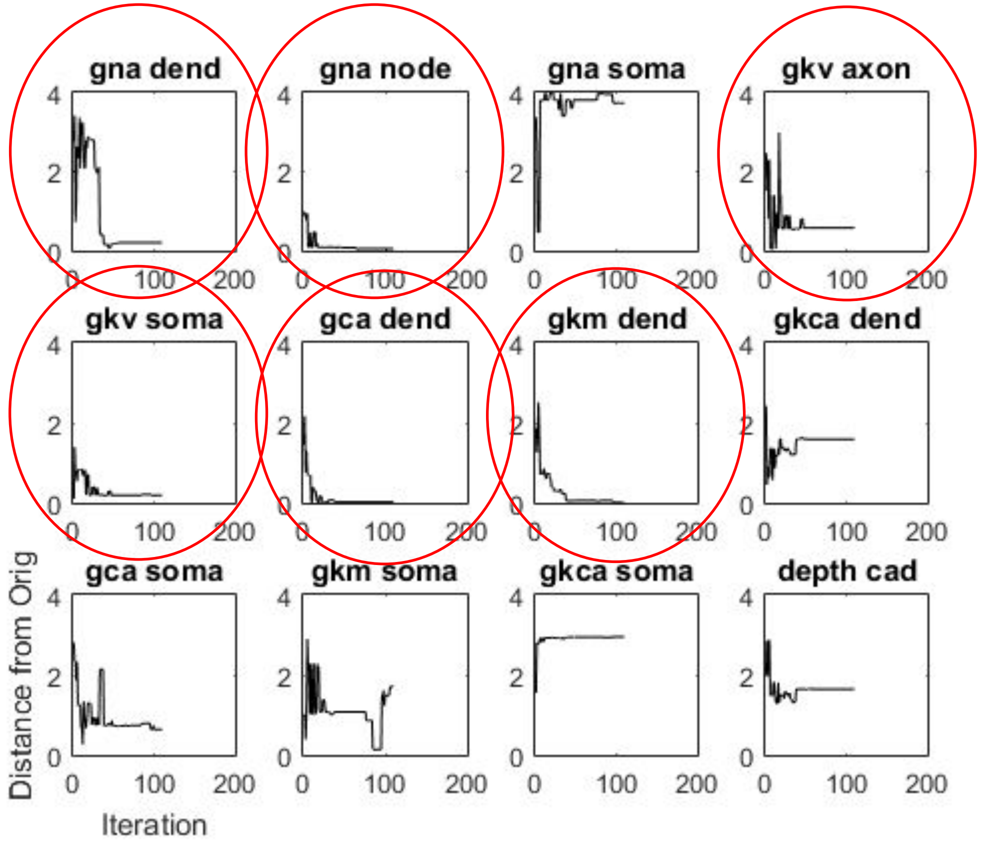
The actual parameters space has many local minima



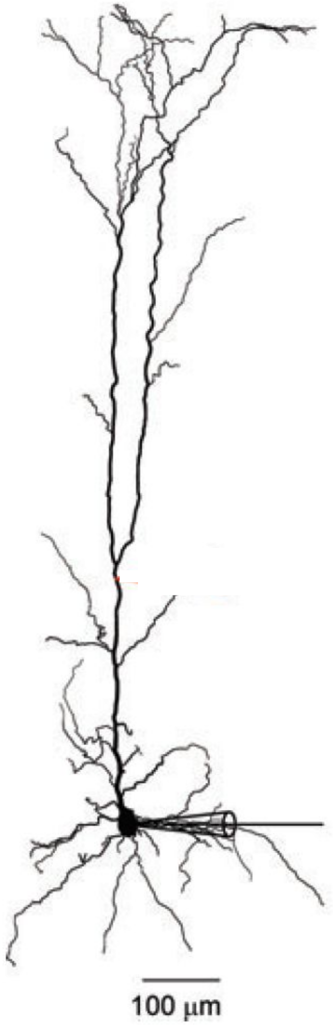


Combined score function constrains some but not all parameters





Alternatively we can separate parameters experimentally

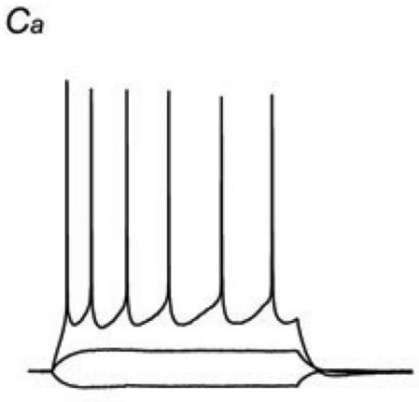


Step 3
(K-blockers)

Step 2(TTX)

Step 1

Reduction of degeneracy



Experimentally guided modelling of dendritic excitability in rat neocortical pyramidal neurones

Naomi Keren[1,2], Dan Bar-Yehuda[1] and Alon Korngreen[1,2]

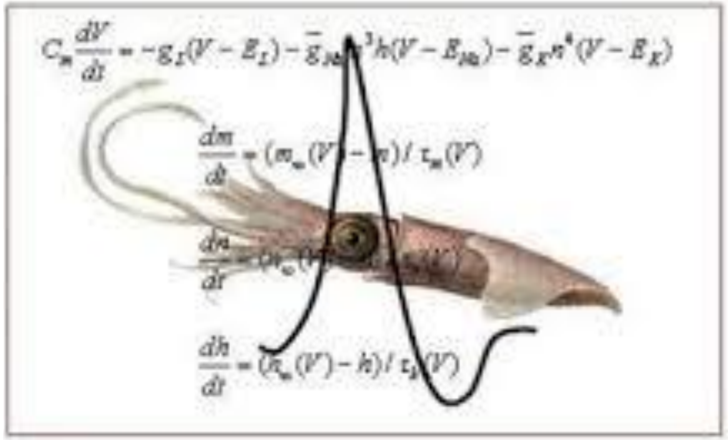
[1] *The Leslie and Susan Gonda Interdisciplinary Brain Research Center, Bar-Ilan University, Ramat Gan 52900, Israel*
[2] *The Mina and Everard Goodman Faculty of Life Sciences, Bar-Ilan University, Ramat Gan 52900, Israel*

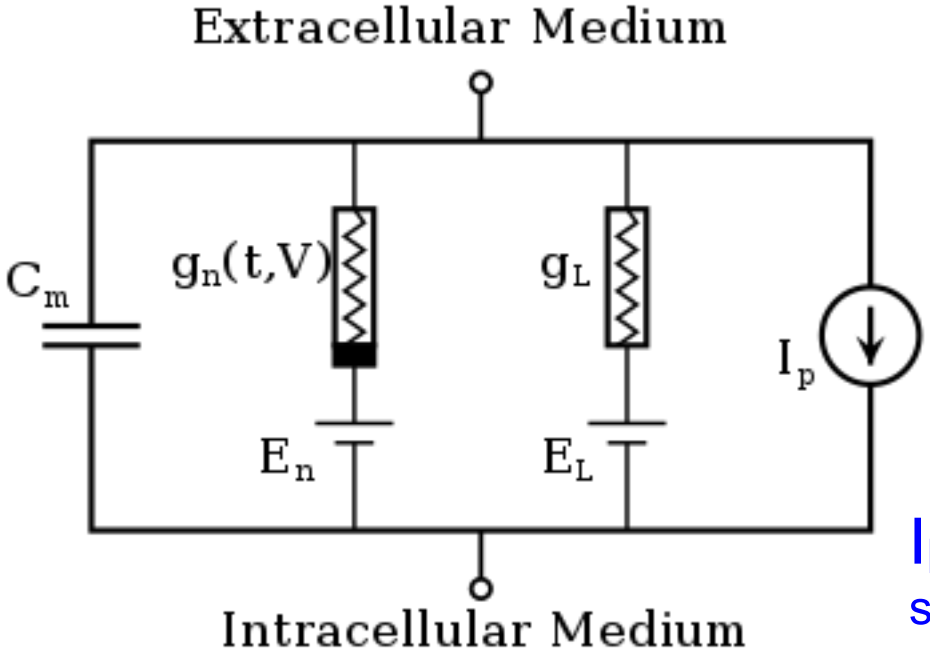
Parameters:

gna_dend
g[illegible]ma
g[illegible]de
gkv_soma
gk[illegible]n
gk[illegible]ma
gkm_dend
Passive parameters:
Cm
Rm
g_leak
g_Ih

spherical cell with 2 ion channels

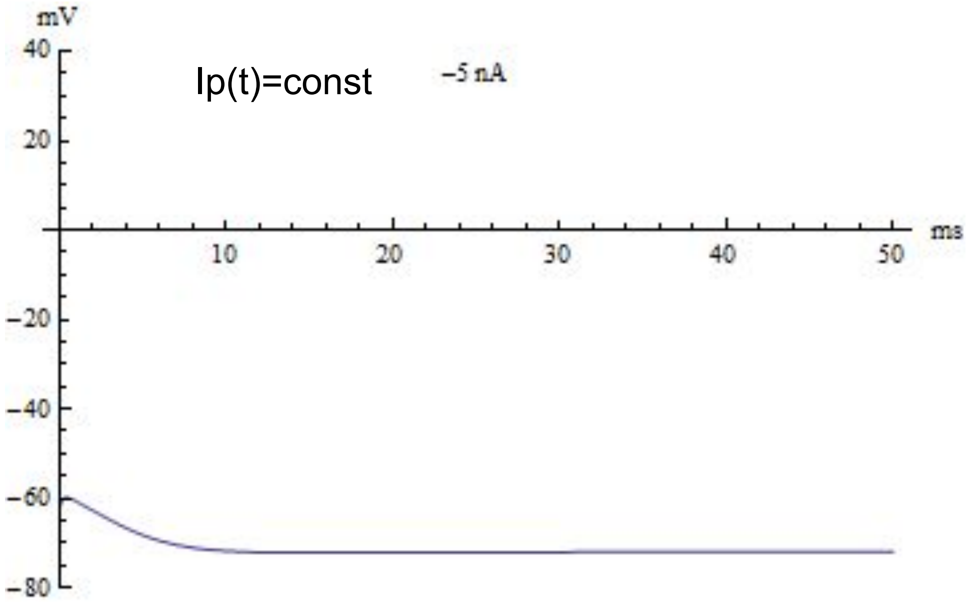
Hodgkin–Huxley 1953 model, Nobel Prize in 1963





$I_p(t)$
stimulus

$$I = C_m \frac{dV_m}{dt} + g_K(V_m - V_K) + g_{Na}(V_m - V_{Na}) + g_l(V_m - V_l)$$

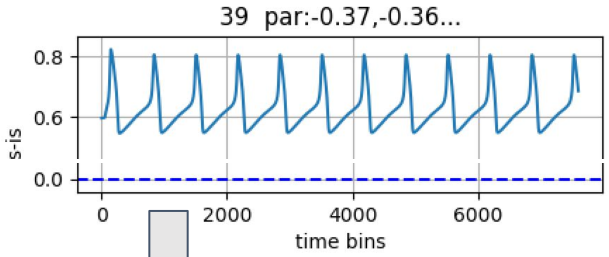


g_N - potassium conductivity
non-linear, hyperpolarization

g_L - sodium conductivity
linear ~leak, depolarization

https://en.wikipedia.org/wiki/Hodgkin-Huxley_model

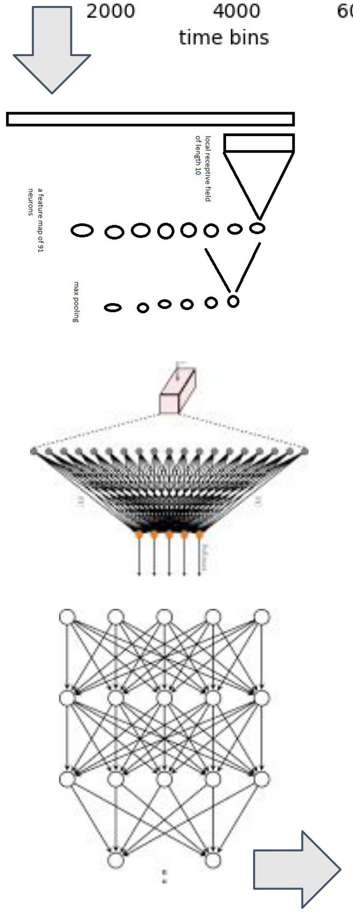
2D regression of modern HH model (leak is also nonlinear)



Input: 3k trace

each: 7600 floats,
amplitude normalized

5 CNN blocks
K= [4,6,8,10,12]



input 1D vector, K features

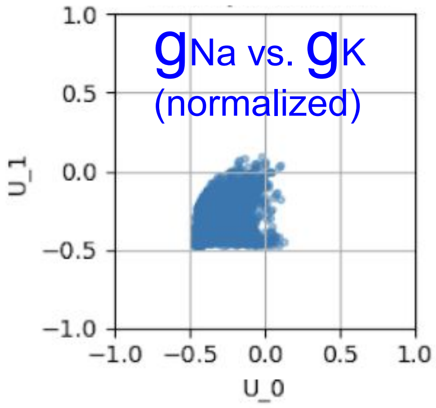
5 CNN blocks
* local reception filed , kernel=7
* activation=LeakyReLU
* maxPool, len=3

n=31 x K=12 **Flatten** → 372

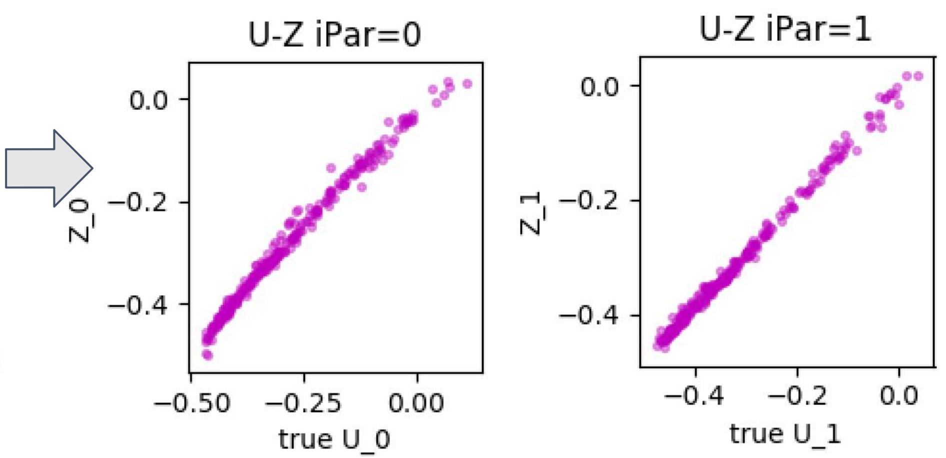
2 FC blocks
* Dense(10,act=LeakyReLU)
* Dropout(0.1)

Output 2 floats: Z1, Z2
Dense(2, act=linear)

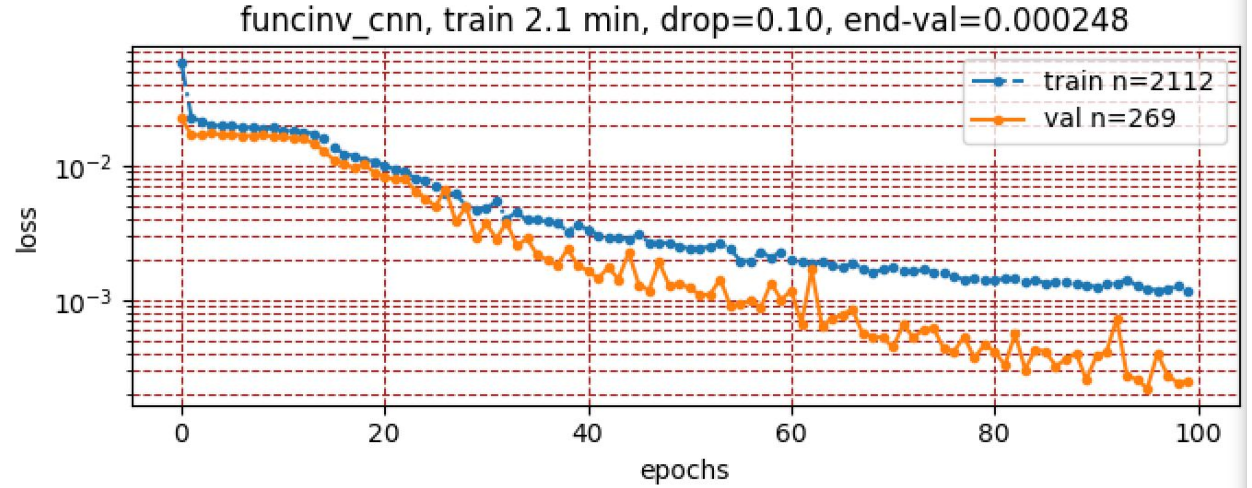
Truth



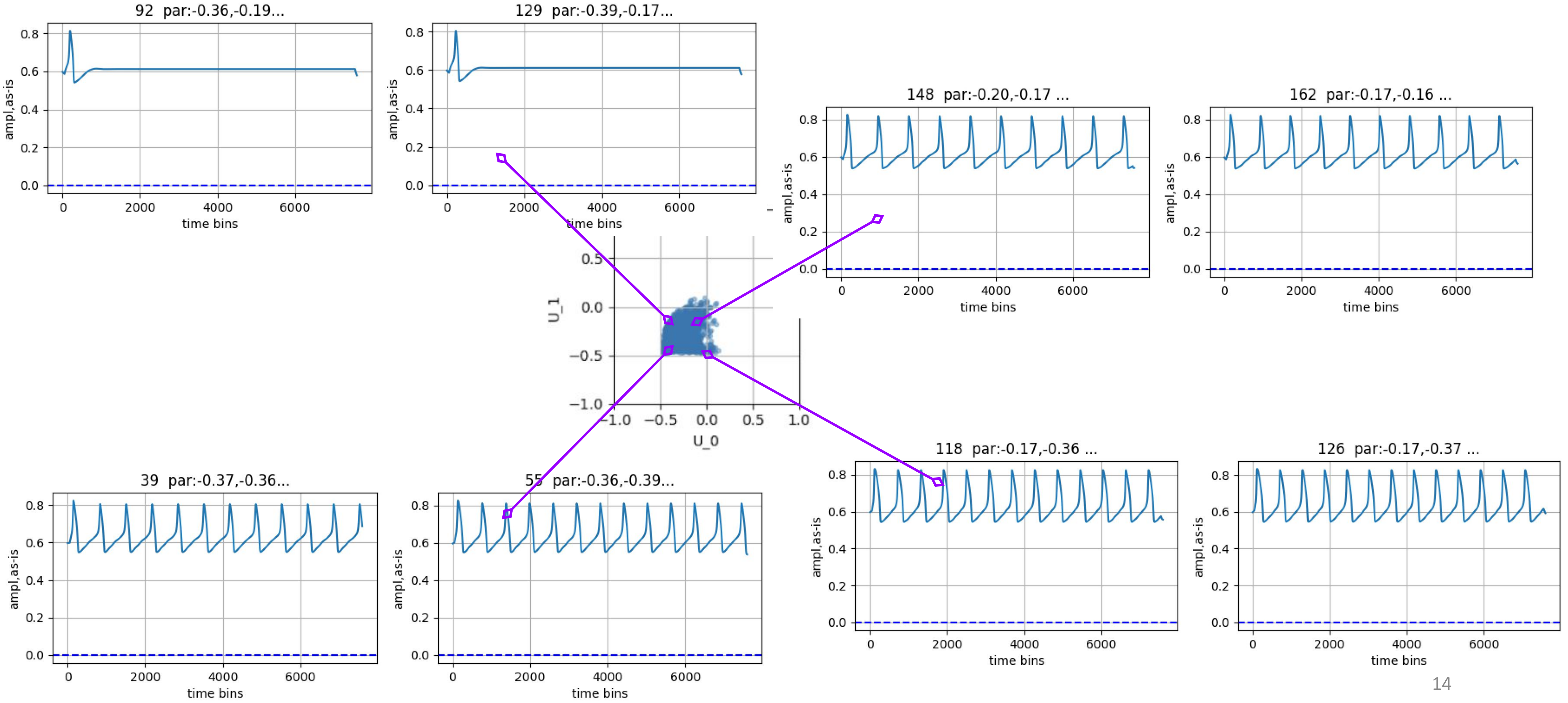
Correlation with Truth



Training: 5.8k params, adam, MSE



Examples of traces for different param choice



Outlook

- Test ML-based regression on HH-cell model with higher dimension of parameter space
- Apply ML model to modern cell model w/ ~30 params
    - reduction of dimensionality to avoid degeneration
    - feature engineering
    - pre-training on HH cell-model
    - include stimulus in the training
- Extract cell params from empirical recordings from neurons