

NEURON
PROJECT

Questions (general)

- ~> How do neurons deal with morphological and biophysical variation?
- ~> What is the connection between the two?

20.11.2025

Jean-Marc Goosillard notes

"average" classes vs. **VARIATION**

→ Which parameters are relevant?

SNP_c → CP_c
 DA → degeneracy
 ↓
 2-4% coverage per neuron
 → high energy demand

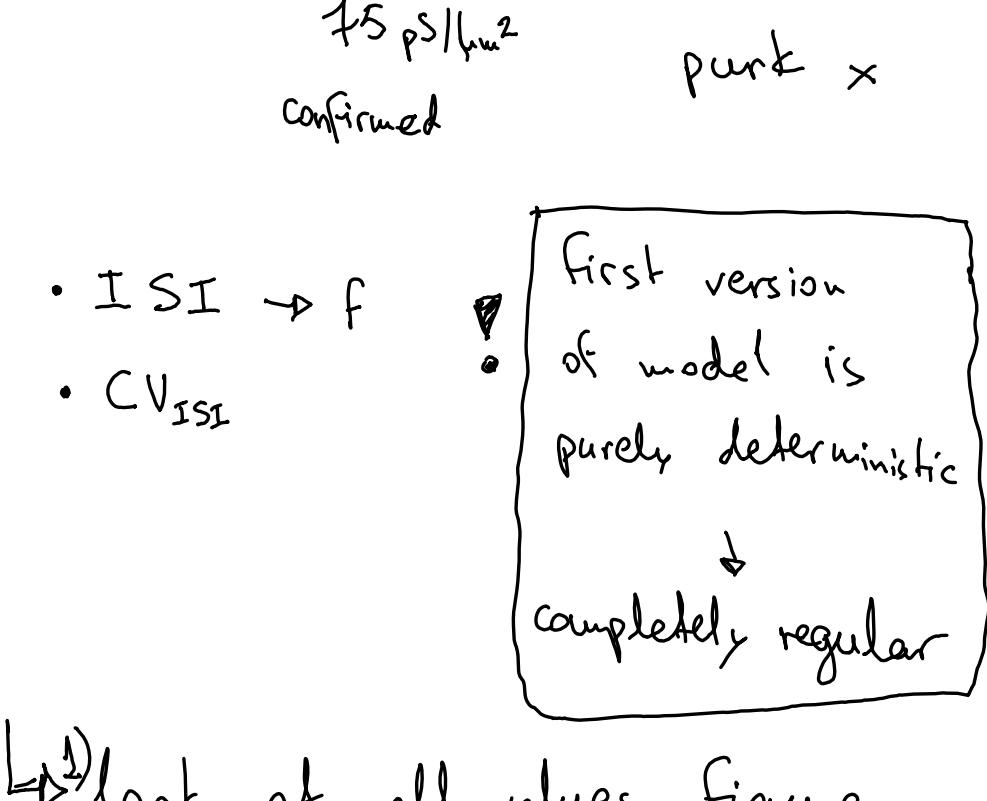
→ dendr. DA release

→ very faithful backprop.
 w/o attenuation

→ also in mitral cells OB (Glu)

→ pacemaking

1-3 Hz in rat, cell-to-cell variations
 hz 2-4 ms



intrinsic conductances + morphology
 to understand firing/excitability profile

? → fairly simple dendritic structure

Cable Theory for passive propagation of signals in neurons

$$d_{\text{out}}^{3/2} = d_{D_1}^{3/2} + d_{D_2}^{3/2} \quad (?)$$

! Vetter et al. 2001 backprop.

Hausser DA

75 pS/μm² CA1

confirmed purk x

- ISI → f
- CV_{ISI}

! first version of model is purely deterministic

completely regular

! look at all values, figure out which change

2) figure out which are important

Simple criterion: $\frac{dV}{dt} > 50 \mu V/\mu s$

! correlation of ampl, hbar w/ freq? typically

→ usually ampl-freq. → NEG

hbar as well? (because of slope changes)

! Erlanger Gasser

refractory period → INACTIVATED Na⁺ channels

AIS 1k - 4k pS/μm²

SD 75 pS/μm²

! Na⁺/Ca²⁺ oscill. → spikes generated

! spikes back-propagated

! Nav_{1.2}

Ion channels

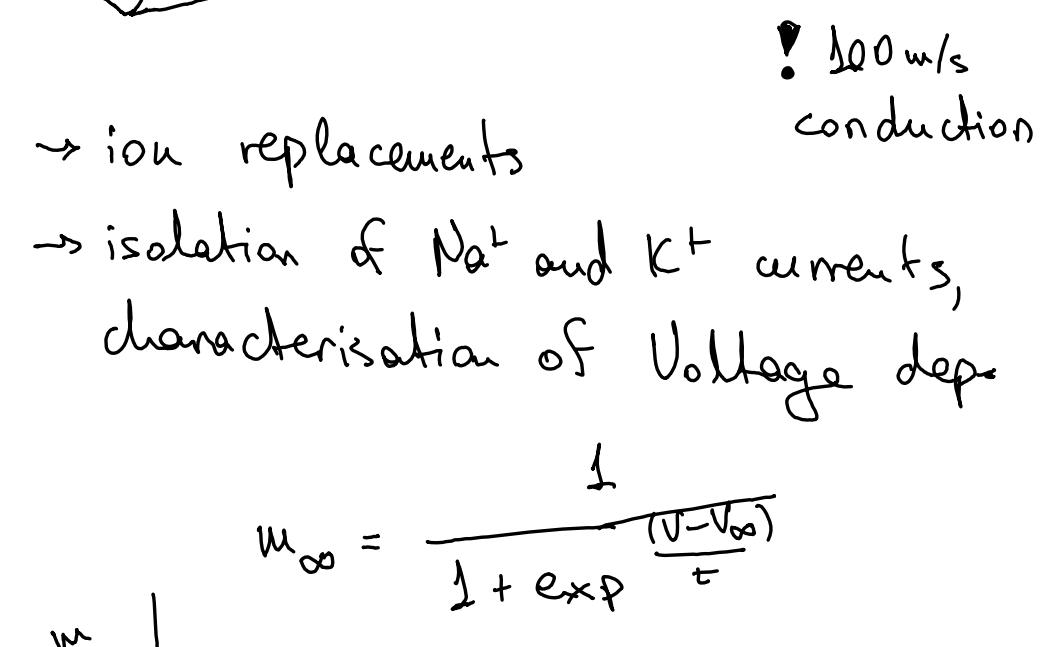
Jean-Marc

Gaillard

notes

Hodgkin-Huxley

Isopotential recording

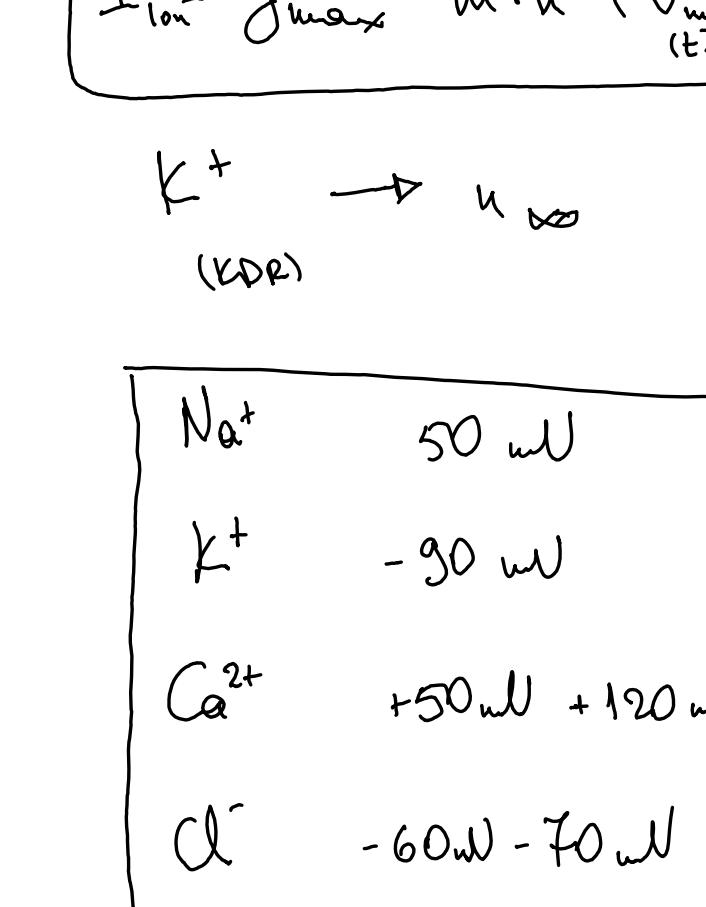


! 100 m/s

conduction

→ ion replacements

→ isolation of Na^+ and K^+ currents,
characterisation of Voltage dep.



$$\text{Na}^+ \rightarrow m_\infty$$

$$h_\infty$$

$$I_{\text{ion}} = g_{\text{max}} \cdot m \cdot h \cdot (V_m - E_{\text{ion}})$$

$$g_{\text{max}} = g_{\text{unit}} \cdot N$$

$$g_{\text{Na}} \quad g_L \quad \rightarrow E_{\text{rev}} = -50 \text{ mV}$$

$$g_{\text{KDR}} \quad 1 \text{ gating var.}$$

$$g_A \rightarrow 2 \text{ gating var.}$$

$$g_H$$

$$g_{\text{CaL}}$$

$$g_{\text{SK}}$$

! dif. g_{max} per compartment

→ we can monitor V_m in any part of the neuron

axon fixed & 800 μm length

→ Educated, simplified guesses

NEURON

- 1) build compartments geom.
 - 2) define biophysics of compartment.
-

- 1) ↳ play first w/ avg wt model
- 2) ↳ explore conductance changes
(to match to phys)
↳ (grid) (?) search ranges
in an efficient way
- 3) plug conductances in to morphs



infer
parameters
from recordings

→ clone github repository
locally

21.11.2025

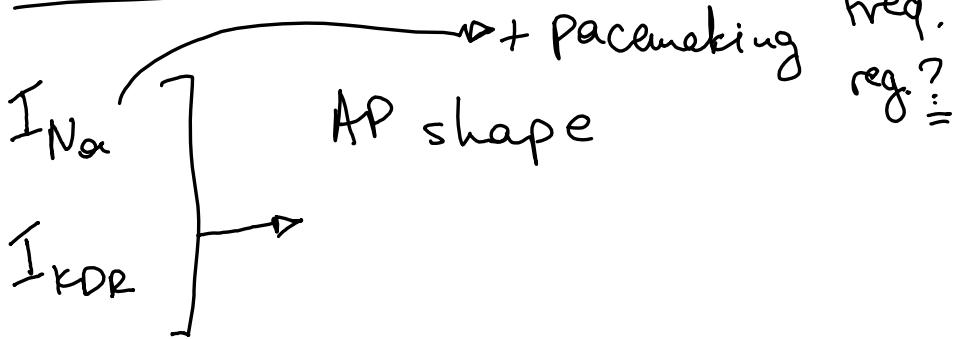
✓ 1) Literature

✓ 2) Data → sets

3) model → running → play w/ pattern.

4) model → implement KO morphs

Currents



I_A \longrightarrow \uparrow rebound delay

I_{I+} \longrightarrow sag, \downarrow rebound delay

I_{CaL} \longrightarrow pacemaking freq., regularity

I_{SK} \longrightarrow AHP (peak, latency)

Features altered in KO

g_{Na}, g_{CaL} (g_{SK})

- frequency $\downarrow 65\%$.
- regularity $\rightarrow CV_{ISI} \uparrow 172\%$

- AP ampl $\uparrow 10\% \text{ (Na}^+?)$
- rise \searrow
decay \nwarrow AP h_w $\uparrow 11\%$.
in our case:
decay contr. more than rise $\rightarrow k_w 3$

g_{KDR}

- AHP latency $\uparrow 74\%$.

~~g_{KDR}, g_{SK}~~
 $k_w 3$ SK

✓ check thr, slope \uparrow , slope \downarrow

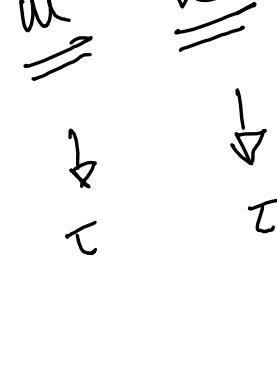
dV/dt peaks, d^2V/dt^2 peaks

Goals

- ✓ 1) features to target
 - ✓ 2) parameters to target
 - 3) models to work on
- search algorithms?

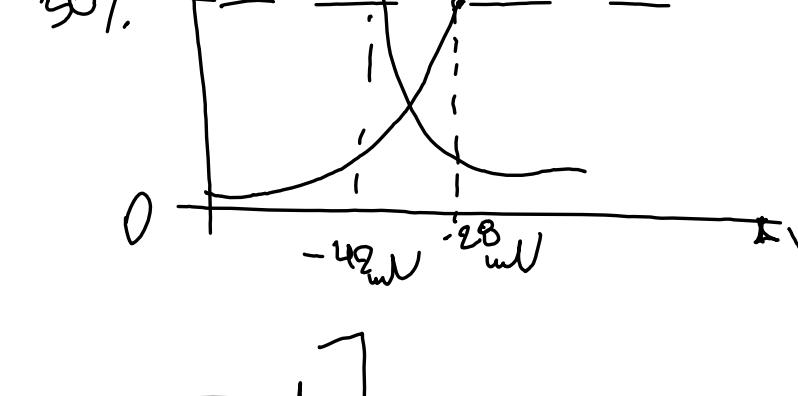
24.11.2025

$g_{Ca^{2+}}$ g_{Sk} g_{Na}

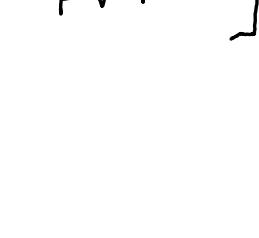


ACTIVATION AND INACTIVATION

VARIABLES OF g_{Na}



contributes to
sub-threshold
DEPOLARISATION



contributes to
REPOLARISATION

! HOWEVER, overall minor
contribution + major contr.
in features that we do
not see any change in
(sag ampl., rebound delay)

$(g_{Na}) \rightsquigarrow$ indirectly
affecting
 $g_{IPR} \text{ (?)}$ (Moubarak
et. al
2022)



$g_{Na} \text{ (1)}$

$g_{Ca} \text{ (2)}$

$g_{IPR} \times$

$$E_h = -40 \text{ mV}$$

$g_{Sk} \text{ (4)}$

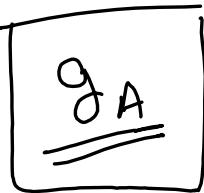
$g_A \times$

g_L

ADDITIONAL INFO

24.11.2025||

2007 paper



→ higher density @
the same, uniform
in dendrites

? Also dif. parameters

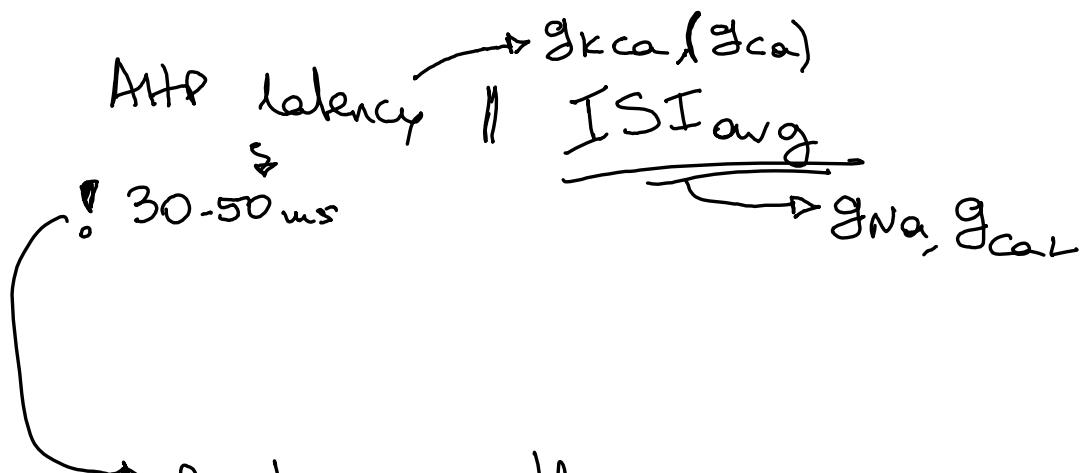
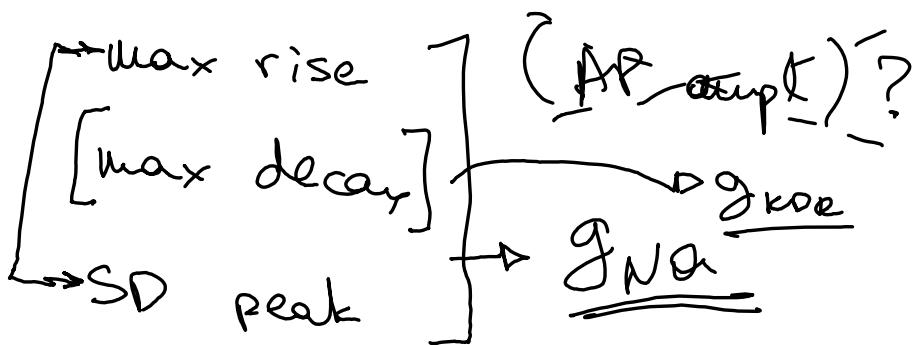
Moubarak

2022

↳ indirect correlation

of decay w/ g_{Na}

! \uparrow freq. \rightarrow \uparrow regularity



If it was the main determinant of fir. freq., we would have a way higher rate (10-20 Hz)

Conductances ranges to test

→ 5-10 fold change

→ $25-165 \text{ } \mu\text{S}/\text{cm}^2$

g_{Na}

range used in Moubarek
papers

↳ ! to look up:

CONDUCTANCE RANGES

in HT models

↳ specifically in DA neurons?

24.11.2025

Features

- (AP ampl?)
- AP rise
 - AP decay
 - SD peak
 - AHP latency
 - ISI avg

Parameters

- g_{Na}
- g_{Ca}
- g_{KDR}
- g_K

↓

possible addition
(later, no priority): thr

As a feature that
does not change
among the 2 genotypes.

for starters

- explore SD only
- keep ABD and nABD homogeneous