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 Goaillard notes

"average" classes vs. (VARIATION)

→ **Which parameters are relevant?**

SNPc (DANs) → CPu
PD → degen

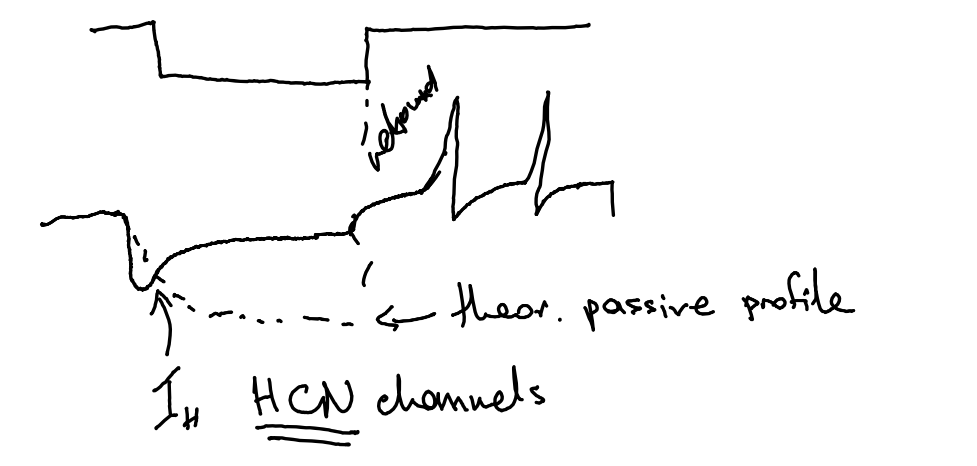
! 2-4% coverage per neuron
↳ high energy demand

→ dendr. DA release
↳ very faithful backprop. w/o attenuation

↳ also in mitral cells OB (Glut)

→ pacemaking
1-3 Hz in rat, cell-to-cell variations
hw 2-4 ms

↓
DA n
GABA n → ↑ freq, also pace (15-20 Hz)
→ smaller morpho 0.7 ms hw



(intrinsic conductances) + (morphology)

to understand firing / excitability profile

! → fairly simple dendritic structure

Cable Theory for passive propagation of signals in neurons

↳ $d_m^{3/2} = d_{D_1}^{3/2} + d_{D_2}^{3/2}$ (?)

! • Vetter et al. 2001

Häusser ↑ — needed 50 pS/µm² → 75 pS/µm² confirmed

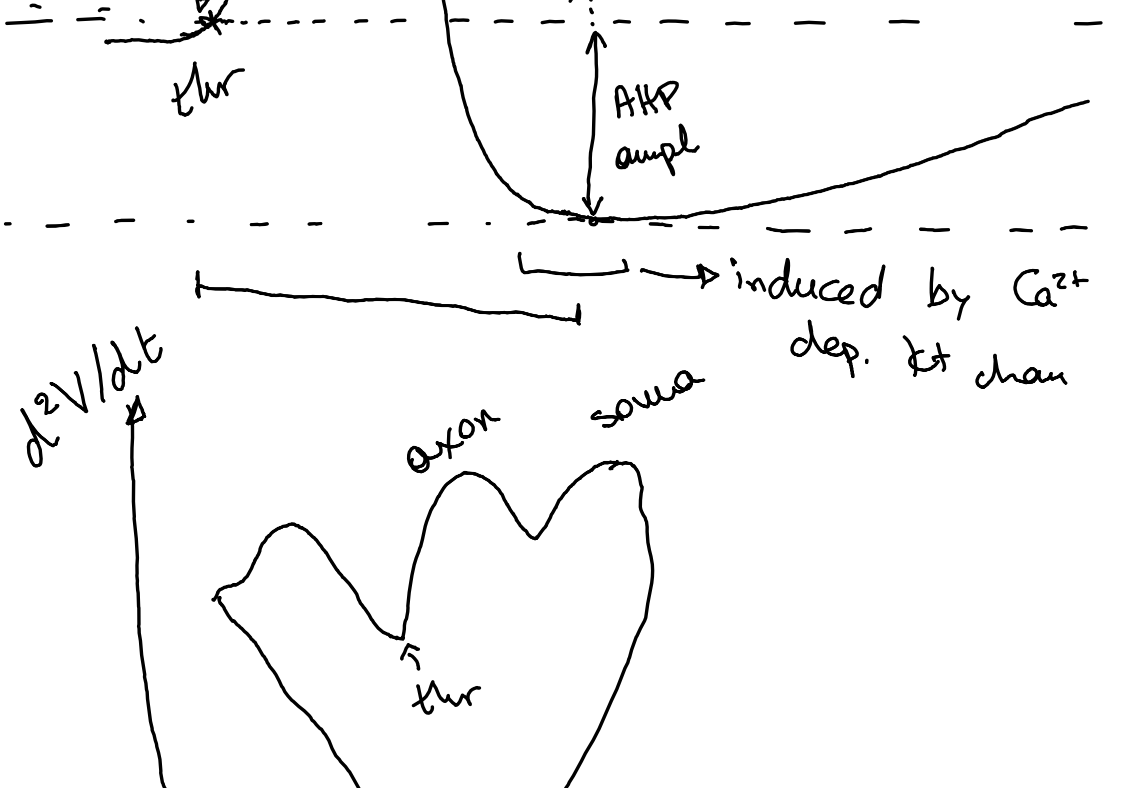
backprop.
DA ↑
CA1 ↓
purk ×

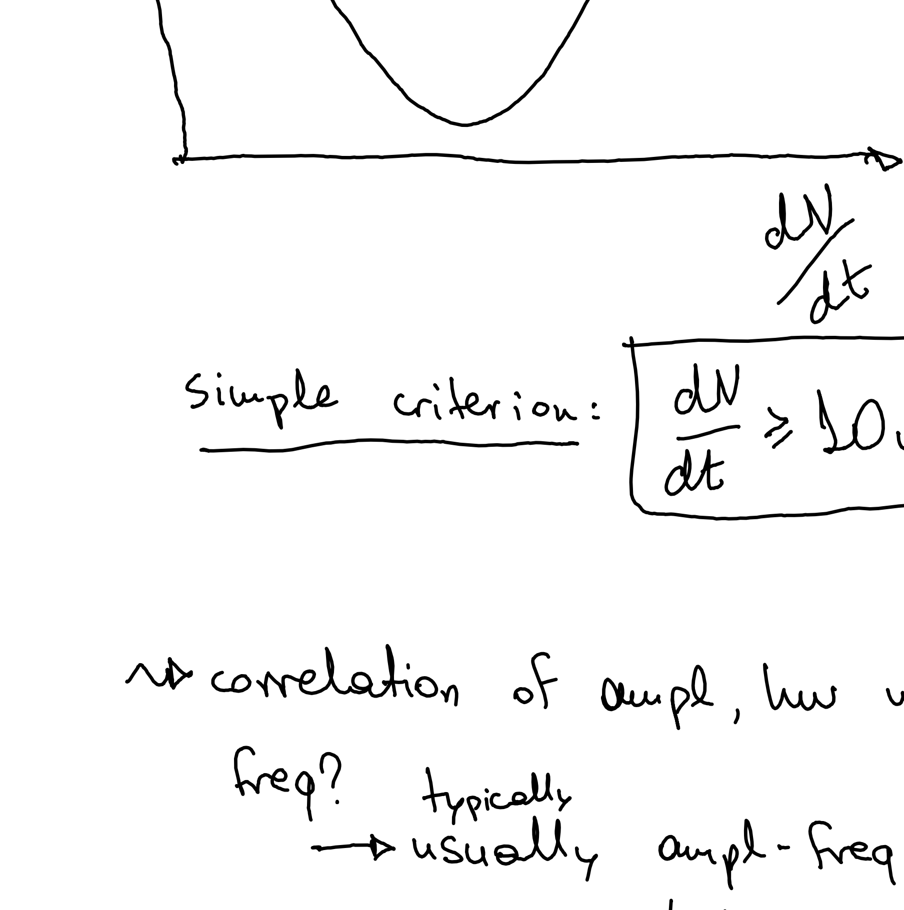
• ISI → f
• CV_{ISI}

! | First version of model is purely deterministic ↓ completely regular |
|---|

↳ 1) look at all values, figure out which change

2) figure out which are important

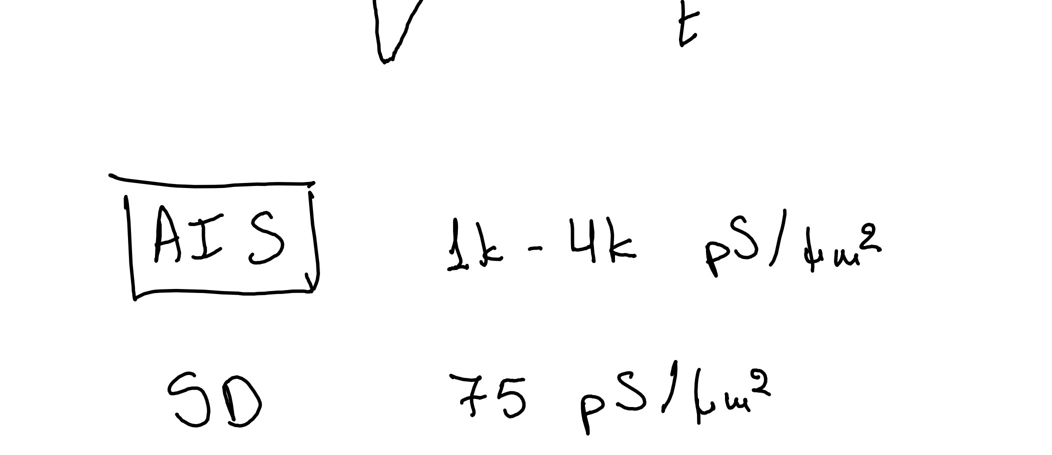




Simple criterion: $\frac{dV}{dt} \geq 10\,mV/ms$

→ correlation of ampl, hw w/ freq?
→ usually (typically) ampl - freq. → NEG
hw as well? (because of slope changes)

! Erlanger Gaser
↳ refractory period → INACTIVATED Na^+ channels

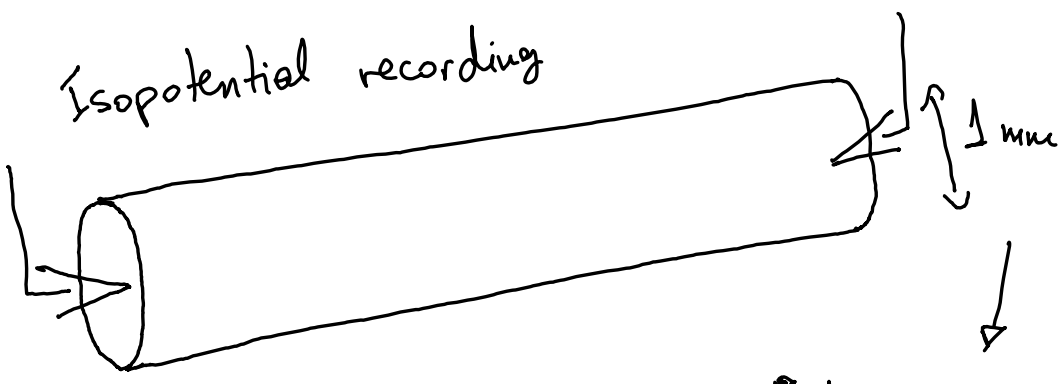


AIS	1k - 4k pS/µm²
SD	75 pS/µm²

Ion channels

Jean-Marc Goaillard notes

Hodgkin-Huxley

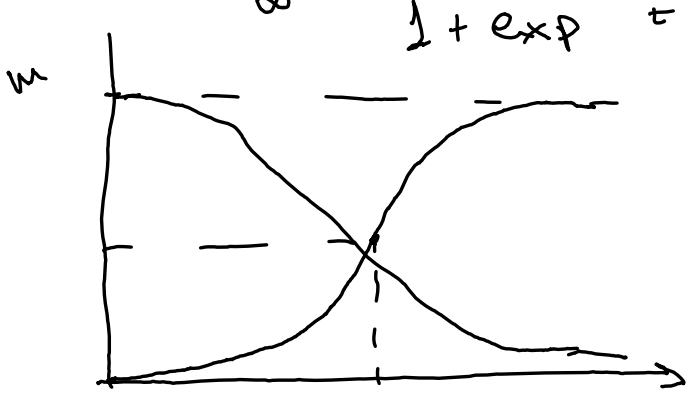


! 100 m/s conduction

→ ion replacements

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

$$m_\infty = \frac{1}{1 + exp\frac{(V - V_{\infty})}{\tau}}$$



$Na^+ \rightarrow m_\infty$

h_∞

$$I_{ion} = g_{max} \cdot m^a \cdot h^b (V_{m(t)} - E_{ion})$$

K^+ (KDR) $\rightarrow n_\infty$

Na^+	50 mV
K^+	-90 mV
Ca^{2+}	+50mV +120 mV
Cl^-	-60mV -70 mV

REVERSAL POTENTIALS

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

---

in the model

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

g_{KDR} 1 gating var.

g_A → 2 gating var!

g_H

$g_{Ca\,L}$ ↓ g_{SK}

! dif. g_{max} per compartment

↳ we can monitor V_m in any part of the neuron

---

axon fixed à 800µm length

↳ Educated, simplified guesses

NEURON

1) build compartments geom.

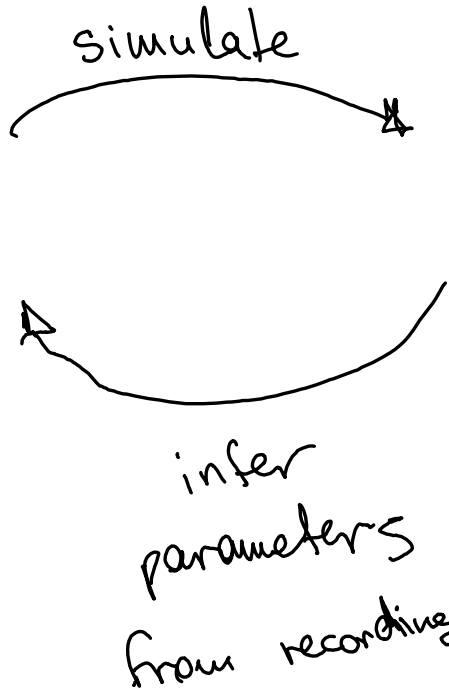
2) define biophysics of compartm.

---

2) ↳ play first w/ avg wt model

2) ↳ explore conductance changes
(to match KO pheno)
↳ (grid)(?) search ranges
in an efficient way

3) plug conductances in KO morpho



↳ clone github repository
locally

21.11.2025

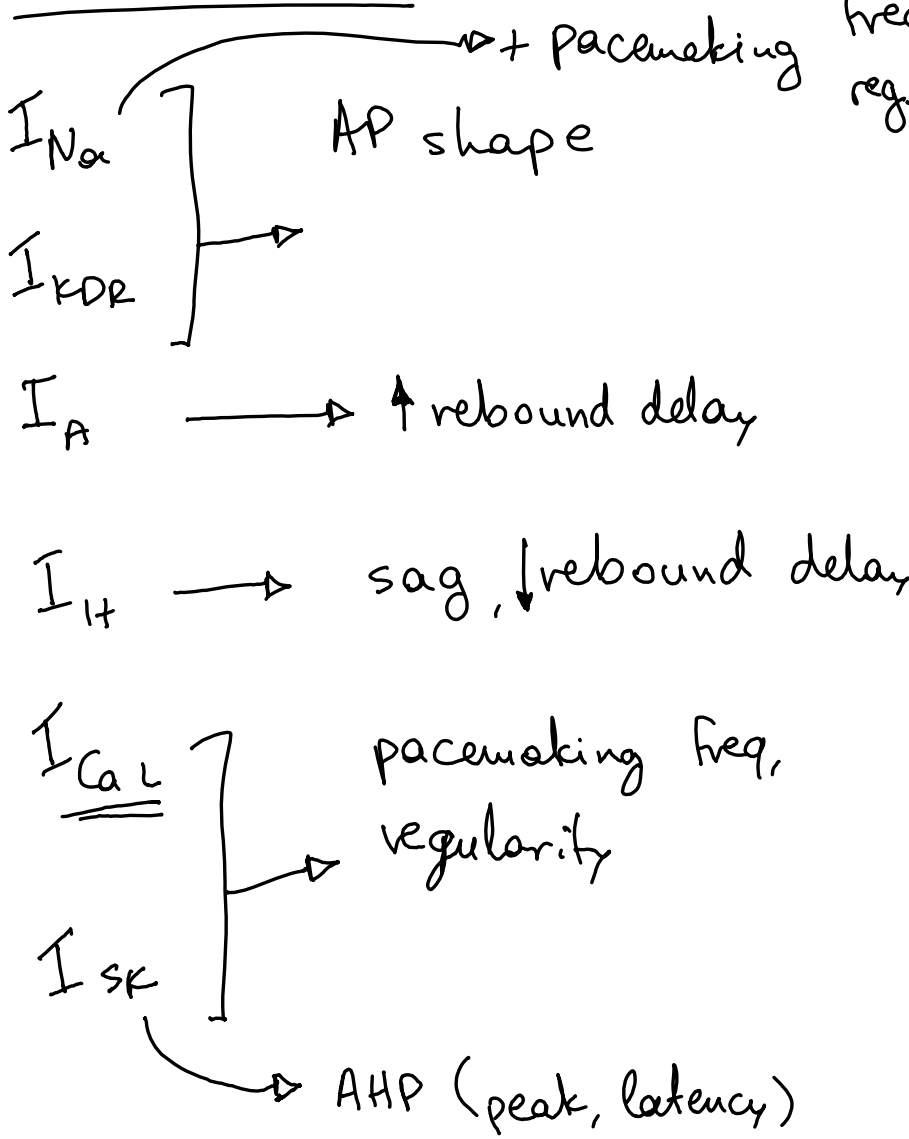
✓1) Literature

✓2) Data → stats

3) model → running → plan w/ param.

4) model → implement KO morpho

Currents


+ pacemaking
freq. reg.?
I_{Na}
I_{KDR}
AP shape
I_A
↑ rebound delay
I_{ht}
sag, ↓ rebound delay
I_{CaL}
I_{SK}
pacemaking freq, regularity
AHP (peak, latency)

Features altered in KO

→ g_{Na}, g_{CaL} (g_{SK})

- frequency ↓ 65%
- regularity — CV_{ISI} ↑ 172%

- AP ampl ↓ 10% (Na^+)?

rise ↖ ↕ related ↙ decay

- AP hw ↑ 11%

↳ in our case: decay contr. more than rise → Kv3 → g_{KDR}

- AHP latency ↑ 74%

→ ~~g_{KDR}~~ Kv3, g_{sK} SK

✓ check thr, slope ↑, slope ↓

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

Goals

✓ 1) features to target

✓ 2) parameters to target

3) models to work on

→ search algorithms?

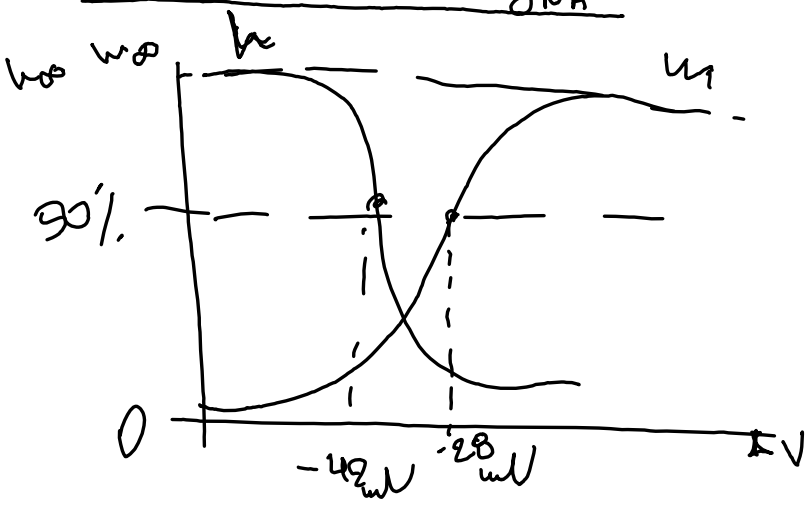
24.11.2025

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

m h

↓ τ ↓ τ

ACTIVATION AND INACTIVATION VARIABLES OF g_{NA}

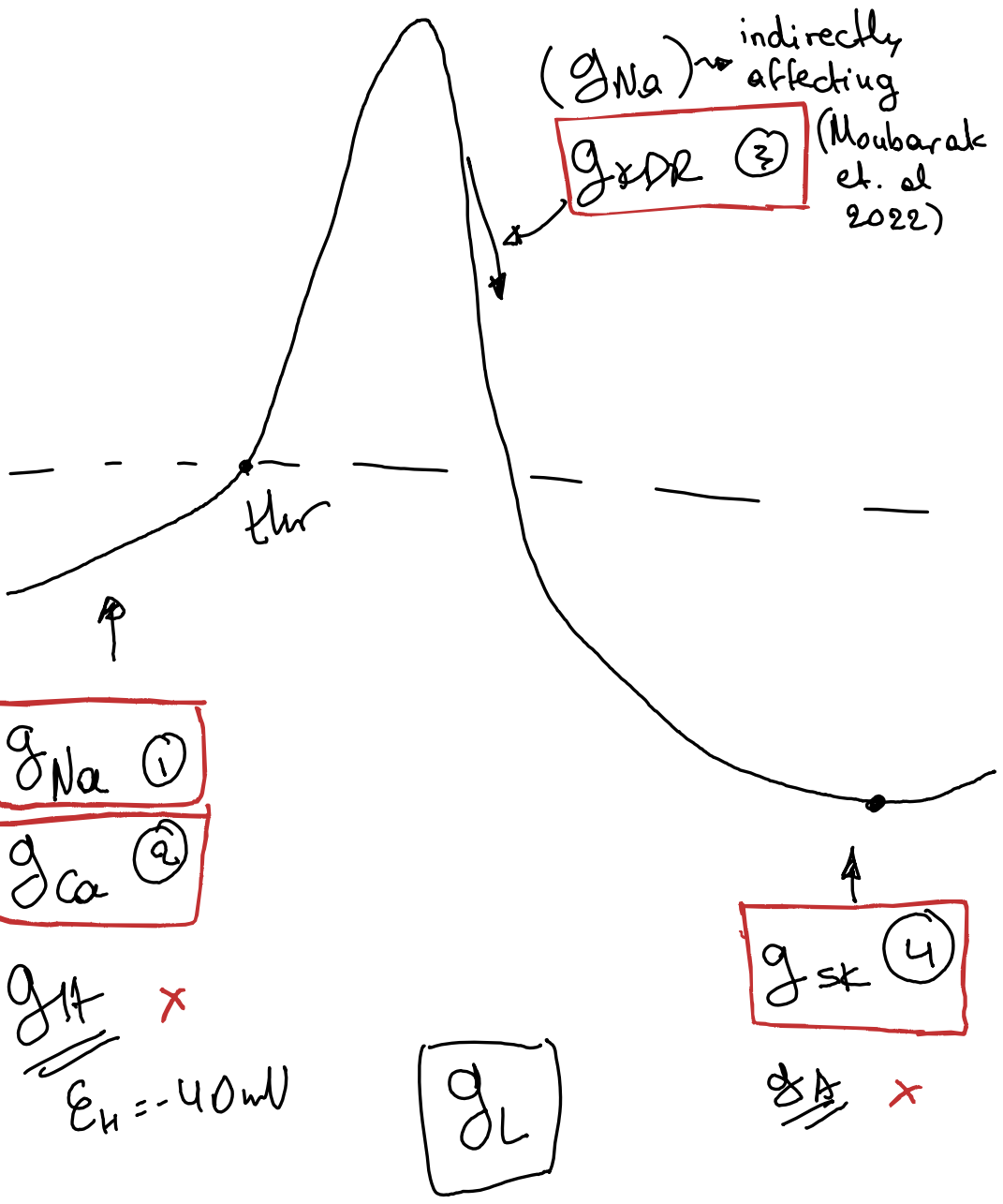


g_H → contributes to sub-threshold DEPOLARISATION

g_A → contributes to REPOLARISATION

K_v4

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



ADDITIONAL INFO

24.11.2025

2007 paper

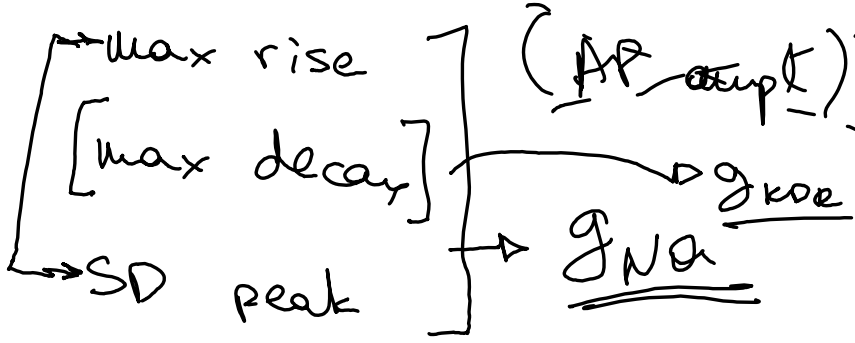
g_A → higher density @ the soma, uniform in dendrites

↳ Also dif. parameters

Moubarak 2022

↳ indirect correlation of decay w/ g_{Na}

! ↑ freq. → ↓ regularity



AHP latency // ISI avg → g_{KCa} (g_{Ca})

↓

! 30-50 ms → g_{Na}, g_{CaL}

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 $pS/\mu m^2$ g_{Na}

range used in Moubarak papers

to look up:

↳ ! CONDUCTANCE ~~RANGES~~

in HH 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_{KCa}

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

Presentation

- 30-40 mins
- all students present
- single project line