

NEURON

PROJECT

Questions (general)

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

Jean-Marc Goaillard notes

'average' classes

vs.

ⓧ VARIATION

→ Which parameters are relevant?

SNPC
(PANs)

PD → dequ

CPu

! 2-4% coverage per neuron

↳ high energy demand

→ dendr. DA release

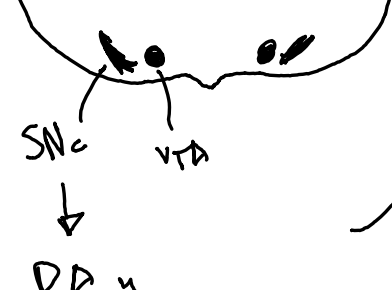
↳ very faithful backprop.
w/o attenuation

↳ also in mitral cells OB (GluT)

→ pacemaking

1-3 Hz in rat, cell-to-cell variations

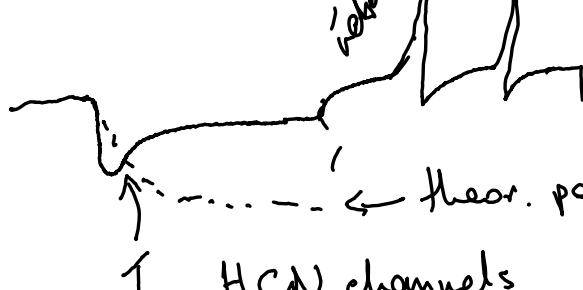
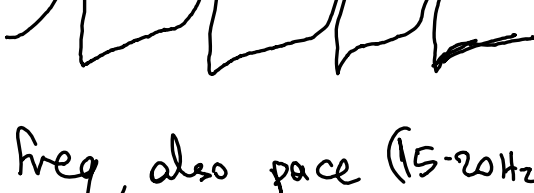
hw 2-4 ms



DA_n

GABA_n → ↑ freq, also pace (15-20 Hz)

→ smaller morpho 0.7 ms hw



I_h HCN channels

intrinsic conductances

+

morphology

to understand firing / excitability profile

! → fairly simple dendritic structure

Cable Theory for passive propagation of signals in neurons

$$d_m^{\frac{3}{2}} = d_{D_1}^{\frac{3}{2}} + d_{D_2}^{\frac{3}{2}} (?)$$

! Vetter et al. 2001

backprop.

↑

Häusser

needed

50 pS/μm²

DA

↑

CA₁

↓

punk

x

75 pS/μm²

confirmed

• ISI → f

• CV_{ISI}

!

•

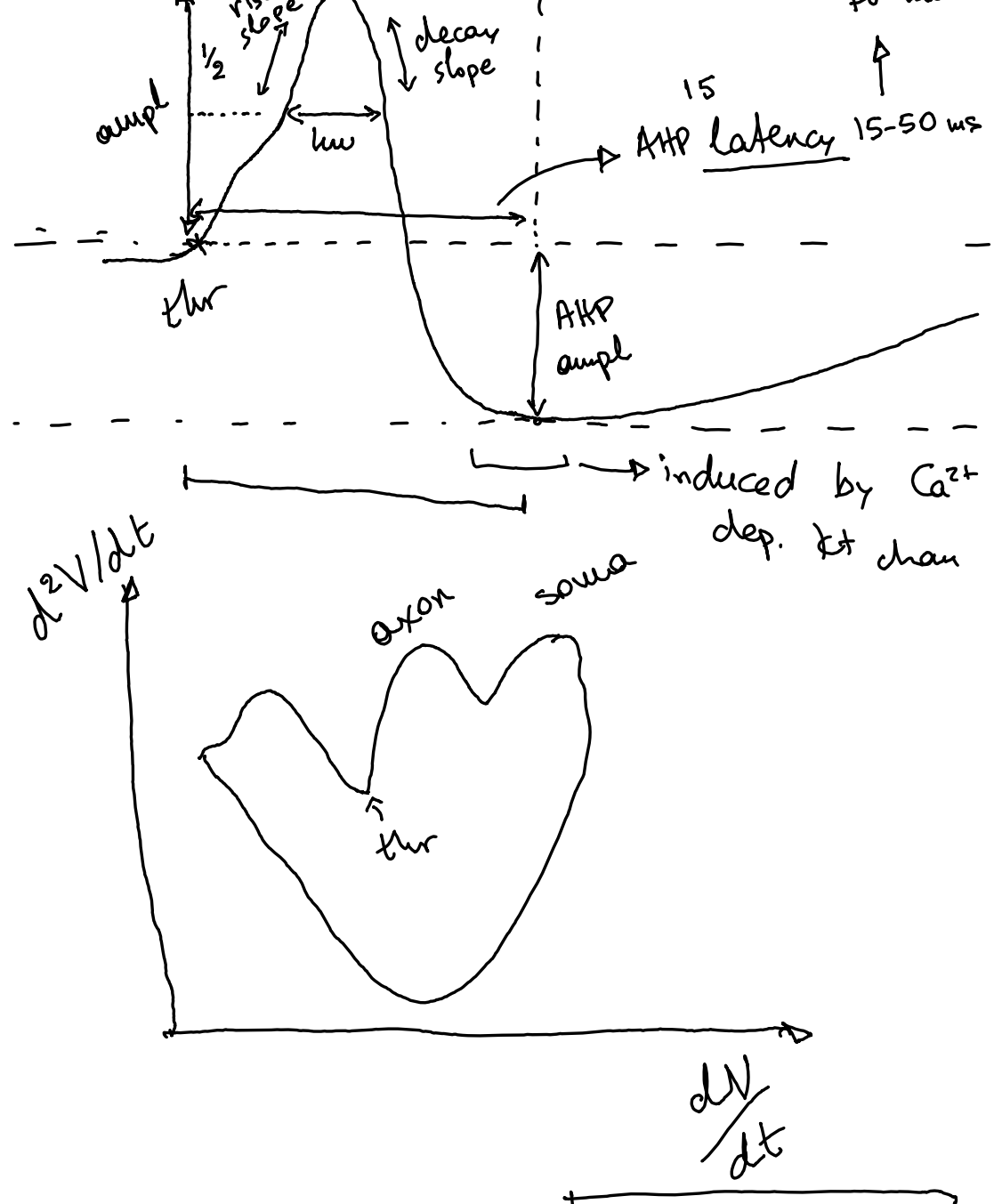
First version of model is purely deterministic

↓

completely regular

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

2) figure out which are important



Simple criterion:

$$\frac{dV}{dt} \geq 10 \text{ mV/ms}$$

→ correlation of ampl, hw w/

freq?

typically

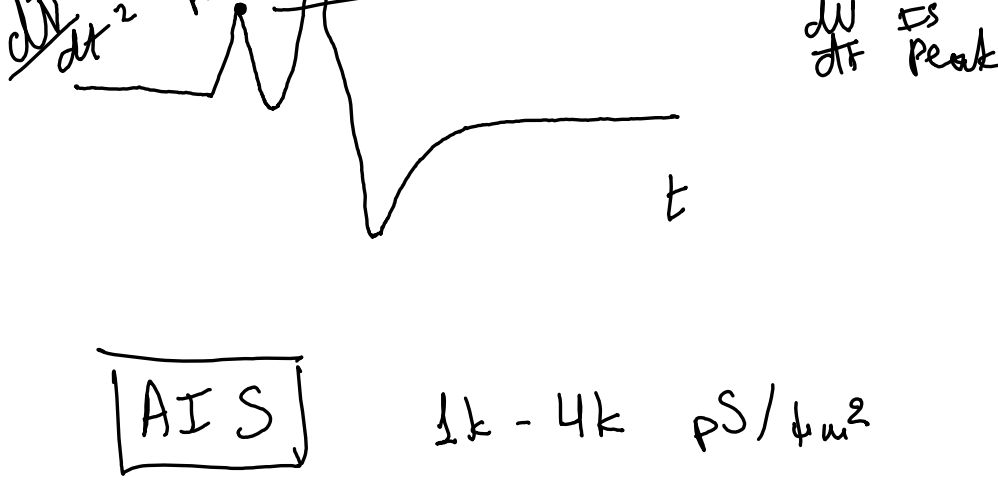
→ usually ampl-freq. → NEG

hw as well?

(because of slope changes)

! Erlanger Caser

↳ refractory period → INACTIVATED Na⁺ channels



[AIS]

1k - 4k pS/μm²

SD

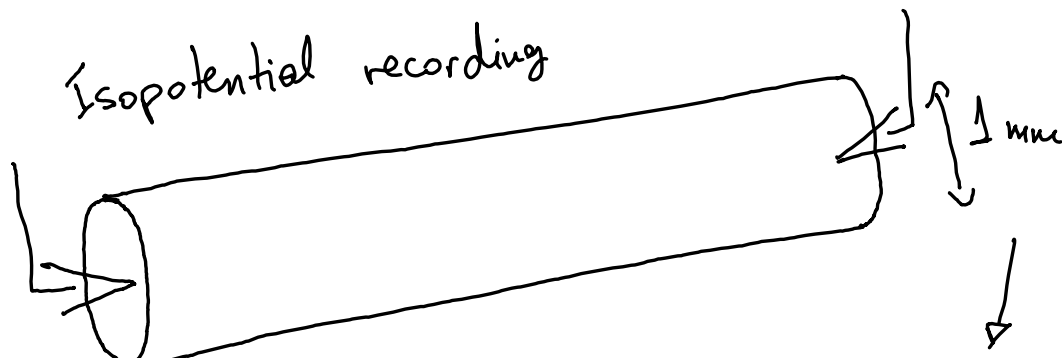
75 pS/μm²



Ion channels

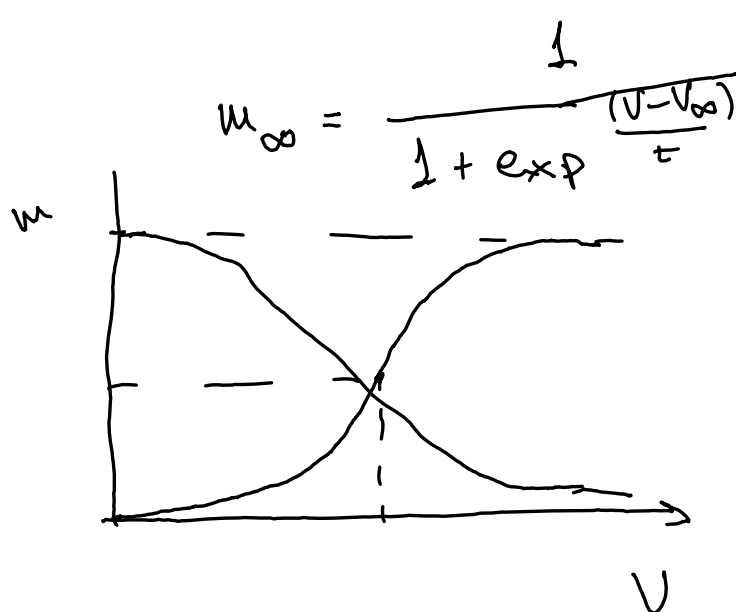
Jean-Marc
Goaillard
notes

Hodgkin-Huxley



→ ion replacements

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



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

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

$\text{K}^+ \rightarrow n_{\infty}$
(KDR)

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

REVERSAL
POTENTIALS

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

g_{Na}

g_{L}

in the
model
 $\rightarrow E_{\text{rev}} = -50 \text{ mV}$

g_{KDR}

1 gating var.

g_{A}

→ 2 gating var!

g_{H}

g_{CaL}

↓
 g_{SK}

! dif. g_{max} per compartment

→ we can monitor V_m in any part of the neuron

axon fixed @ 800 μm length

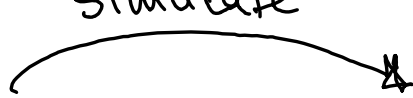
→ Educated, simplified guesses

NEURON

- 1) build compartments, geom.
 - 2) define biophysics of compartm.
-

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

simulate



infer
parameters
from recordings

↳ clone github repository
locally

21.11.2025

- ✓ 1) Literature
- ✓ 2) Data → stats
- 3) model → running → play w/ param.
- 4) model → implement KO morpho

Currents

I_{Na} } \rightarrow + Pacemaking freq.
AP shape
 I_{KDR} }

I_A \rightarrow \uparrow rebound delay

I_{H} \rightarrow sag, \downarrow rebound delay

I_{CaL} } pacemaking freq,
regularity

I_{SK} } AHP (peak, latency)

Features altered in KO

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

• frequency $\downarrow 65\%$

• regularity $- C_{ISI} \uparrow 172\%$

• AP ampl $\downarrow 10\%$ (Na^+)?

rise \nwarrow
decay \swarrow • AP h_w \uparrow related

$\uparrow 11\%$

in our case:
decay contr. more than rise $\rightarrow K_{v3}$

g_{KDR}

• AHP latency $\uparrow 74\%$

~~g_{KDR}~~
 ~~K_{v3}~~ g_{SK}
 SK

✓ check thr, slope \uparrow , slope \downarrow

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

Goals

✓ 1) features to target

✓ 2) parameters to target

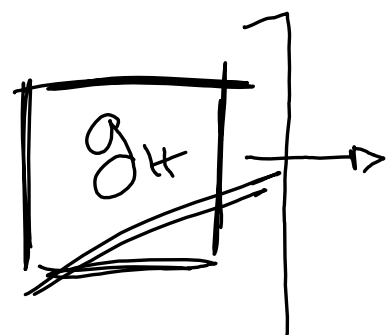
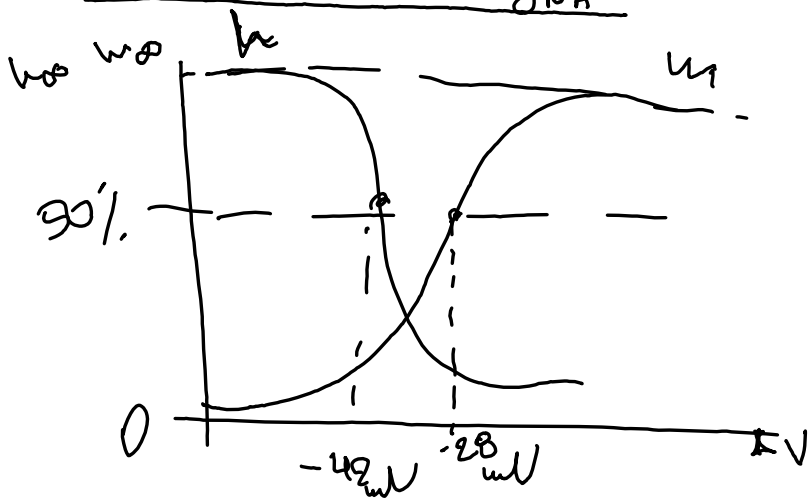
3) models to work on

→ search algorithms?

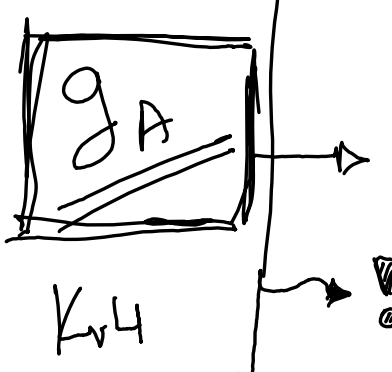
$g_{Ca^{2+}}$ g_{SK} g_{Na}

\underline{u} \underline{h}
 \downarrow \downarrow
 τ τ

ACTIVATION AND INACTIVATION VARIABLES OF g_{Na}

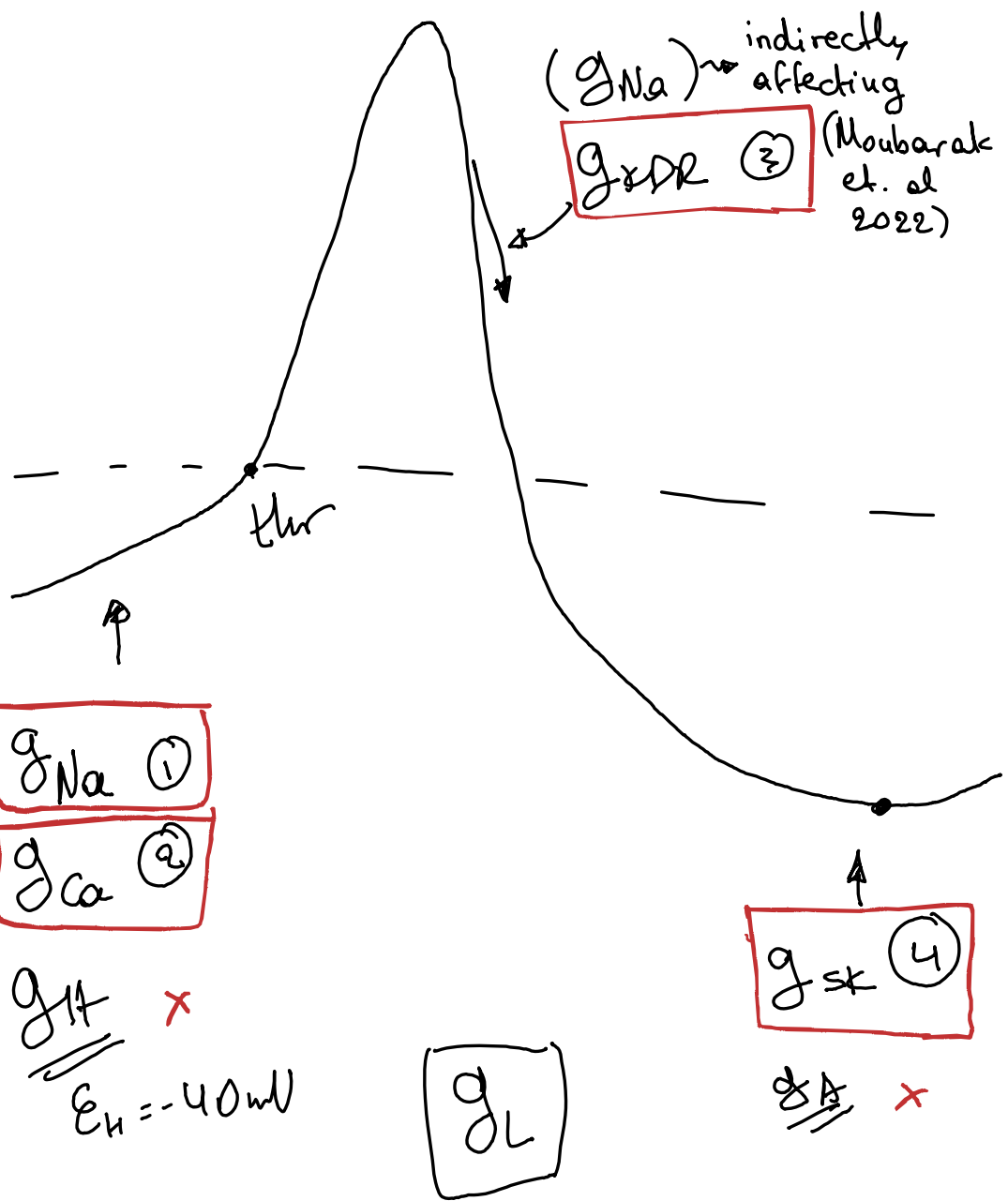


contributes to sub-threshold DEPOLARISATION



contributes to REPOLARISATION

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



ADDITIONAL INFO

24.11.2025

2007 paper

g_A

→ higher density @
the soma, uniform
in dendrites

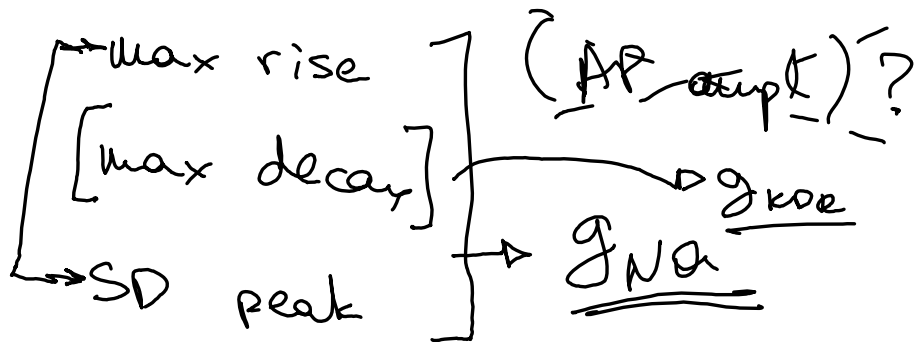
Also dif. parameters

Moubarak

2022

↳ indirect correlation
of decay w/ g_{Na}

! \uparrow freq. \rightarrow \uparrow regularity



AP latency \parallel $\underline{ISI_{avg}}$

! 30-50 ms

$\rightarrow g_{Na}, g_{CaL}$

! 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

→ $25-165 \text{ pS}/\mu\text{m}^2$ g_{Na}

range used in Moulouk
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

↓

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

Parameters

g_{Na}

g_{Ca}

g_{KDR}

g_K