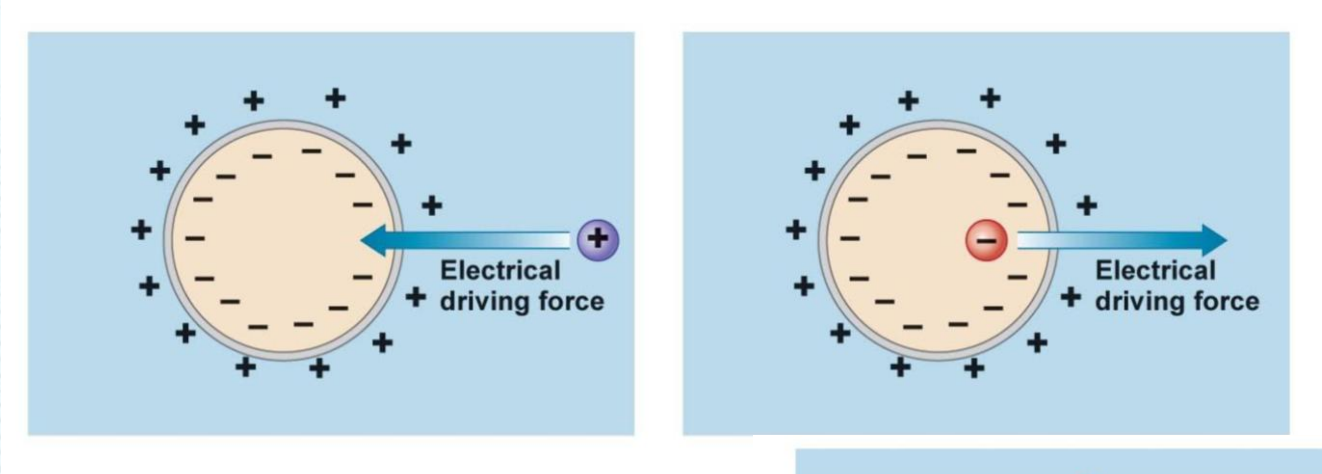
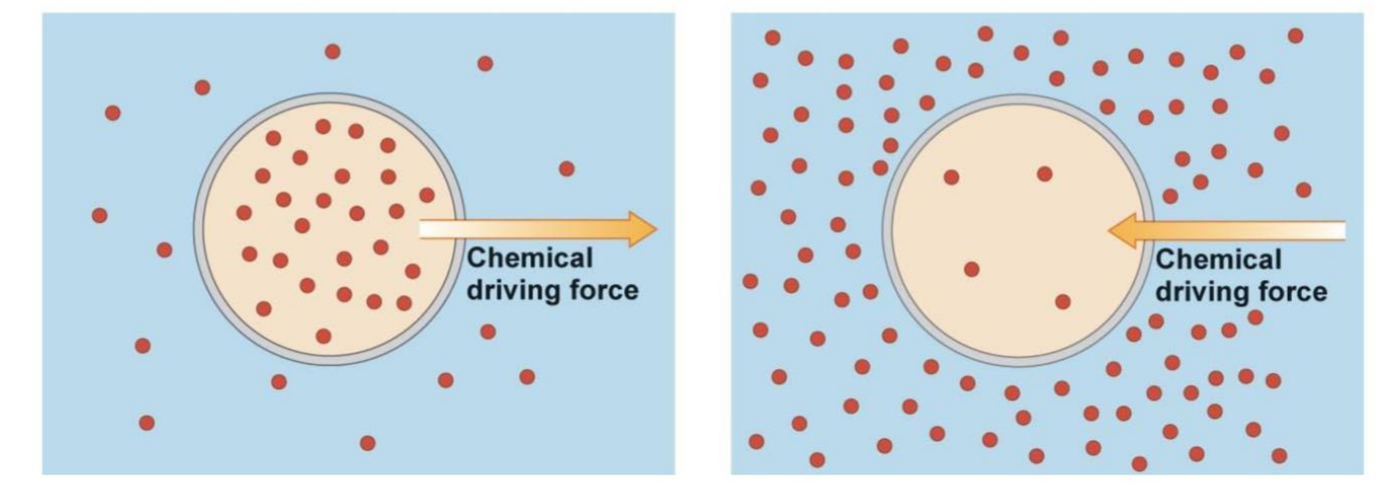
HERTIE INSTITUTE FOR
AI IN BRAIN HEALTH

# Lecture 2

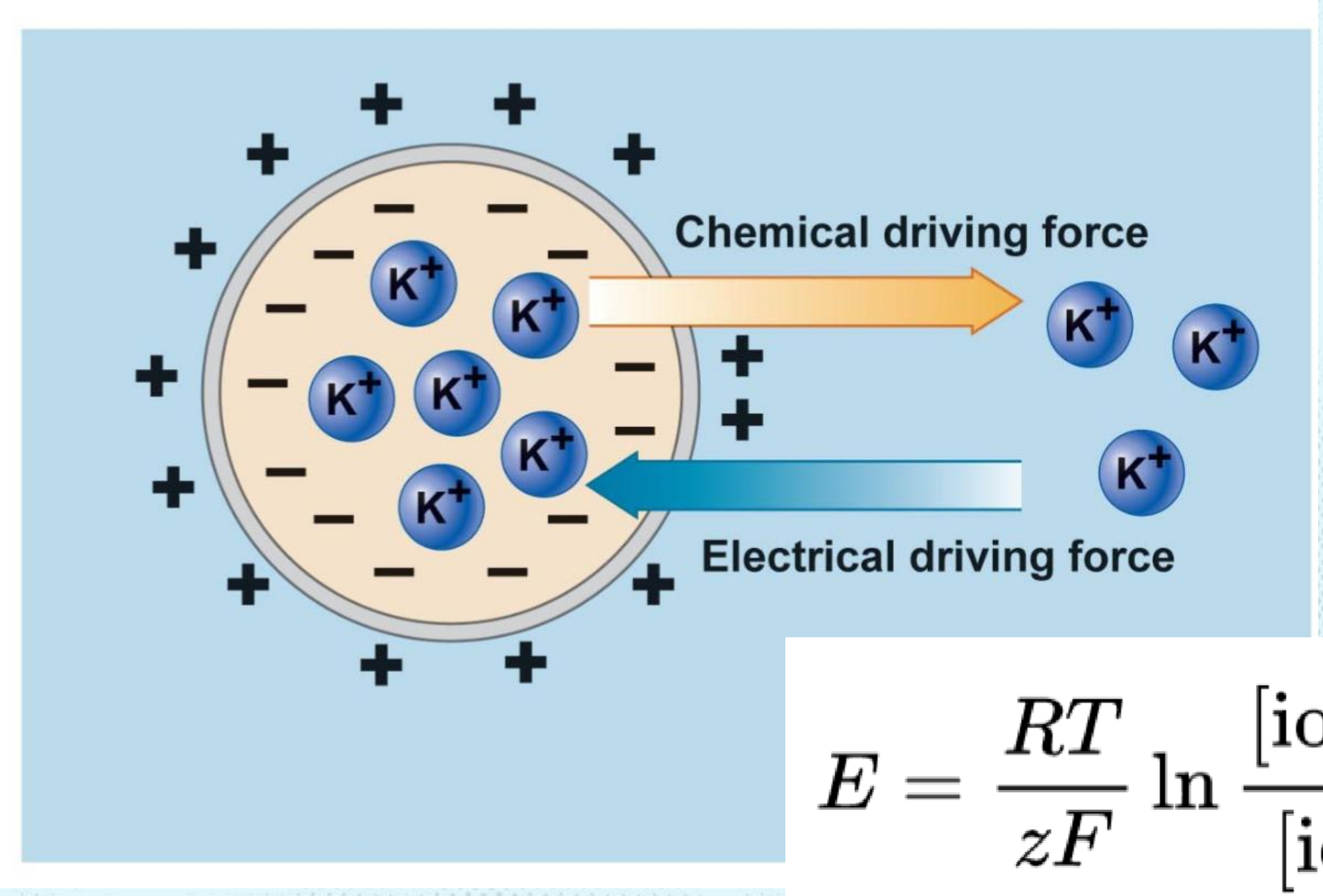
# Forces acting on ions



# Equilibrium potential

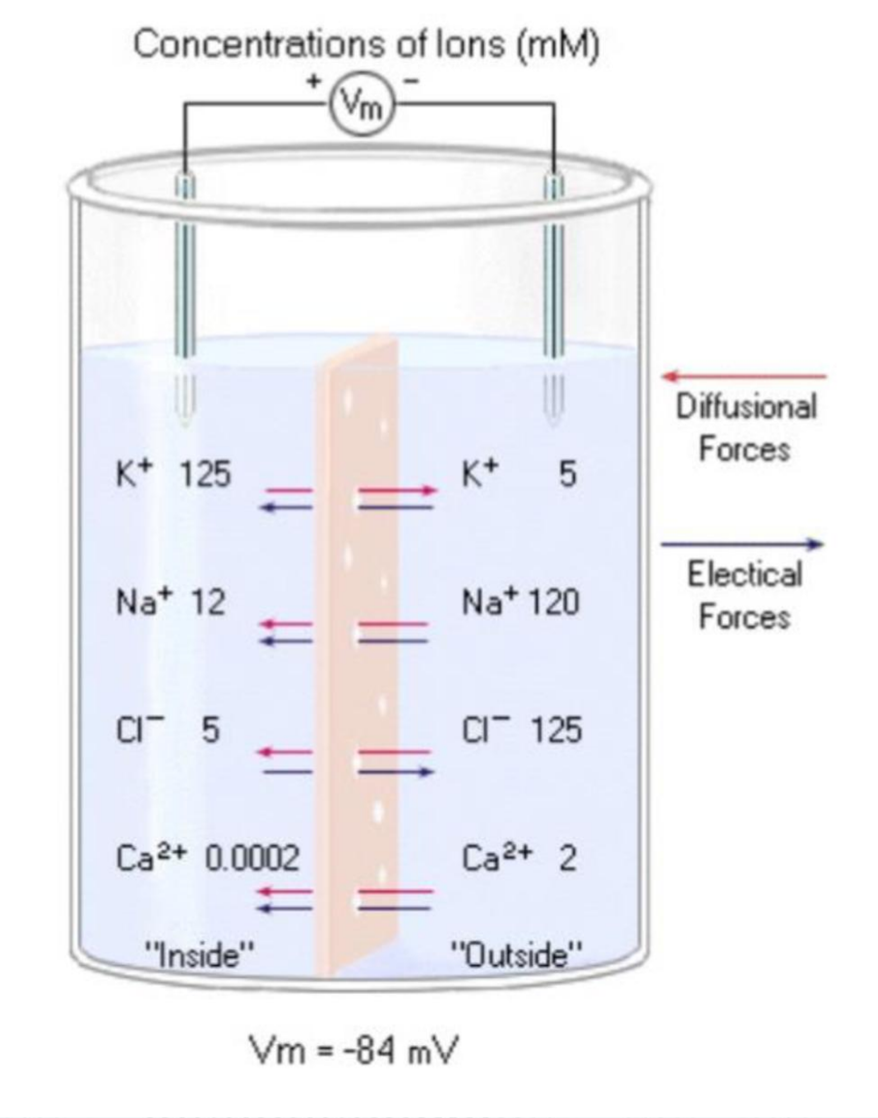
HERTIE INSTITUTE FOR AI IN BRAIN HEALTH




$$E = \frac{RT}{zF} \ln \frac{[\text{ion outside cell}]}{[\text{ion inside cell}]}$$

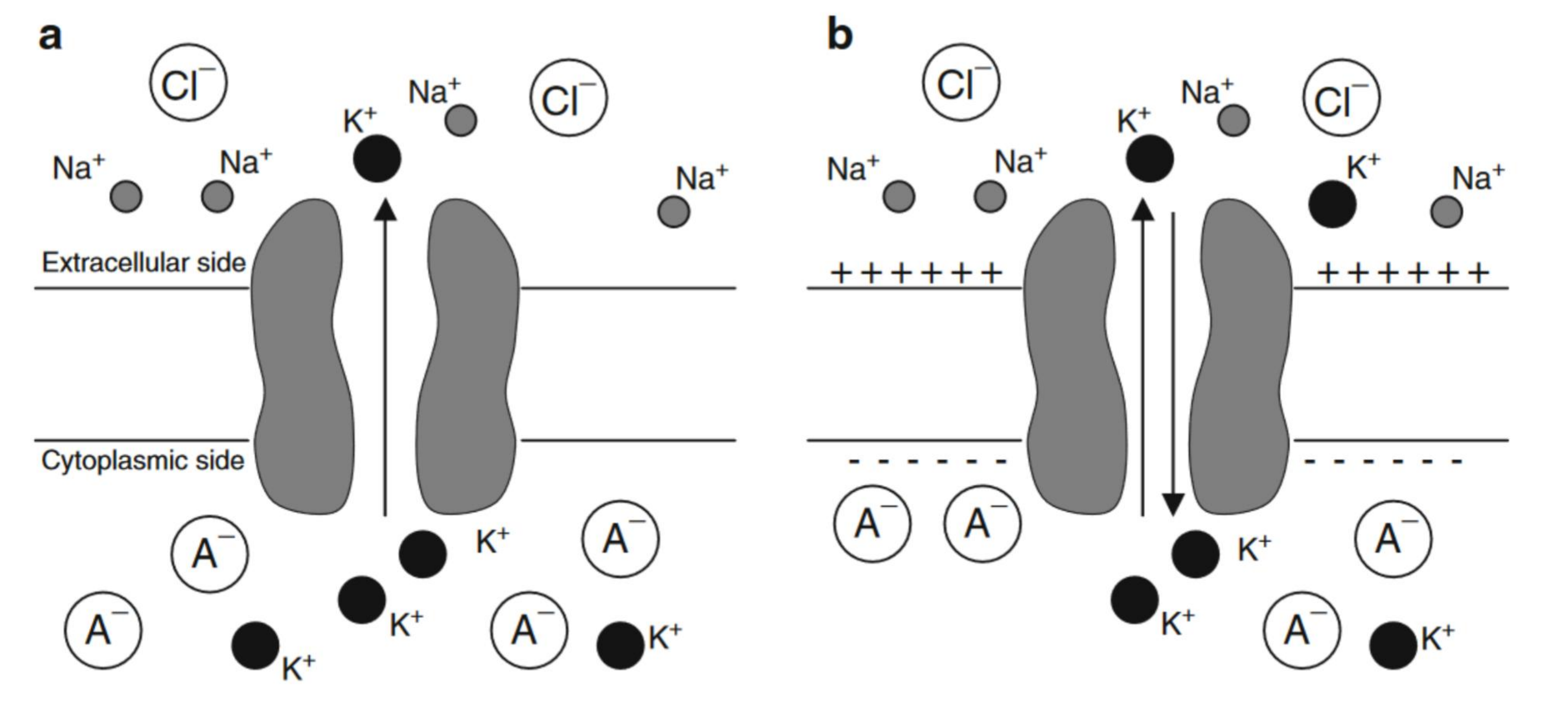
# Typical ion concentrations

HERTIE INSTITUTE FOR AI IN BRAIN HEALTH



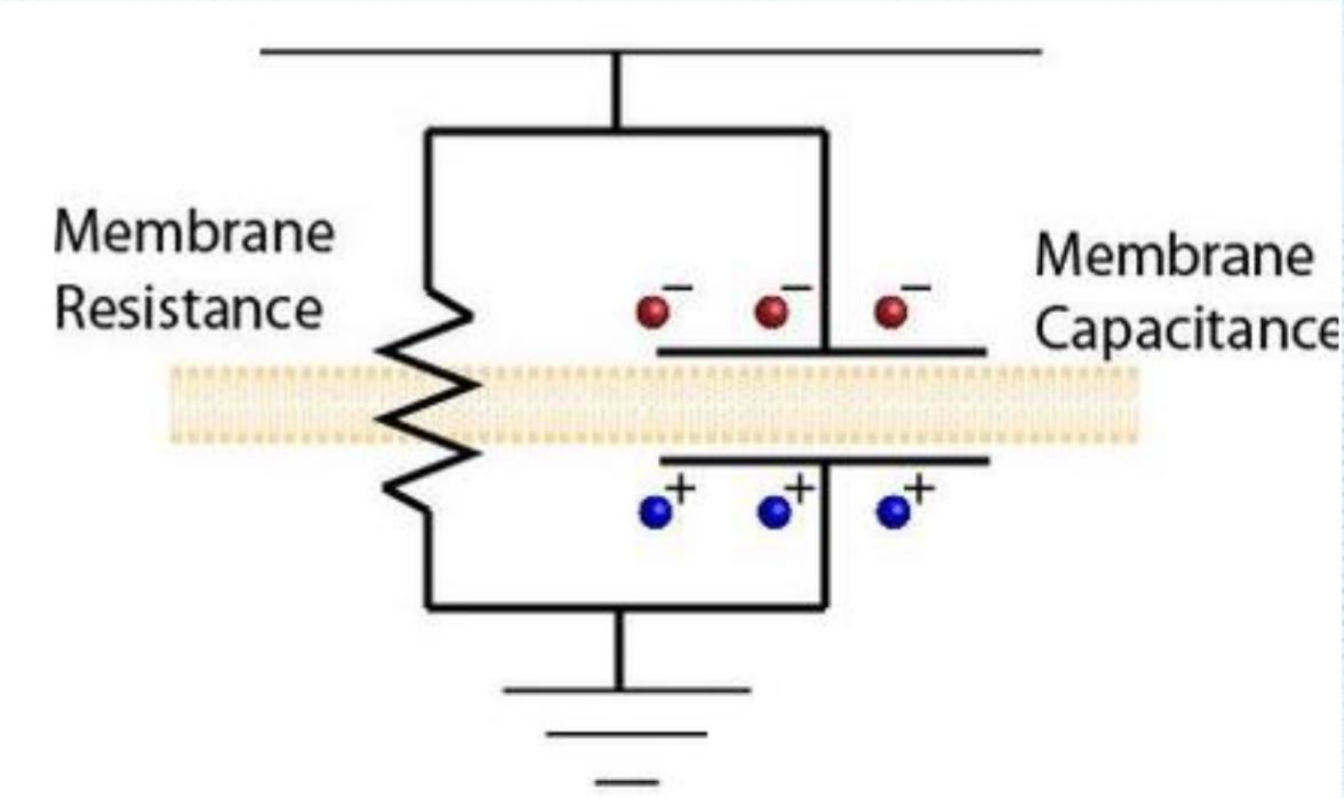
# Resting state potential

HERTIE INSTITUTE FOR AI IN BRAIN HEALTH



# Equvivalent circuit model





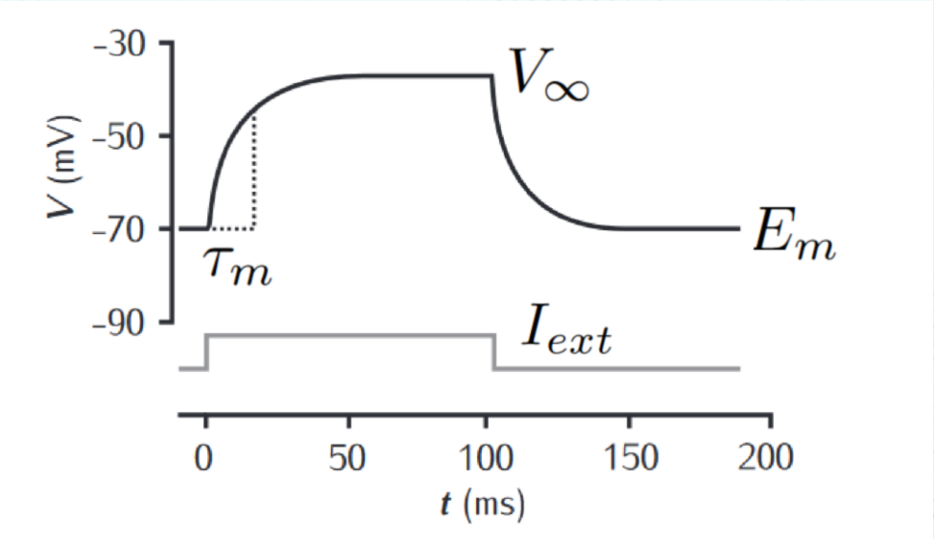

$$c_m \frac{dV}{dt} = -i_m + \frac{I_e}{A} .$$

$$i_m = \sum_i g_i (V - E_i) .$$

# Passive neuron model

HERTIE INSTITUTE FOR AI IN BRAIN HEALTH

$$c_m \frac{dV}{dt} = -i_m + \frac{I_e}{A} .$$

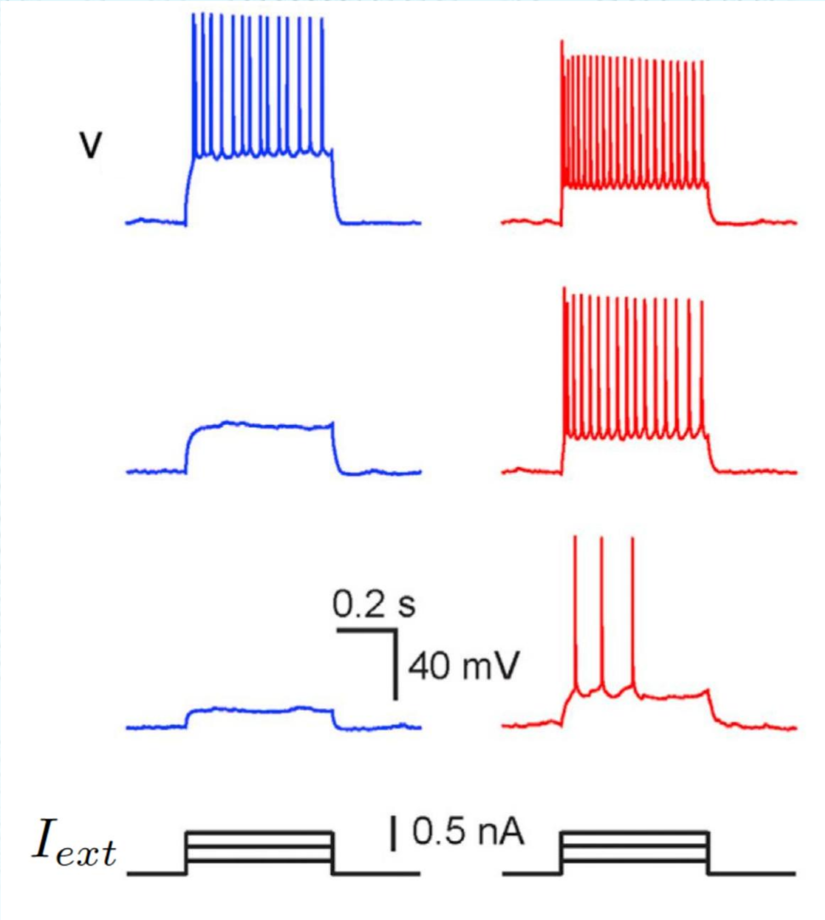



Angus Chadwick

$$V(t) - E_m = \boxed{e^{-t/\tau_m}(V(0) - E_m)} + \boxed{\frac{1}{g_m \tau_m} \int_0^t e^{-(t-t')/\tau_m} I_{ext}(t')dt'}$$

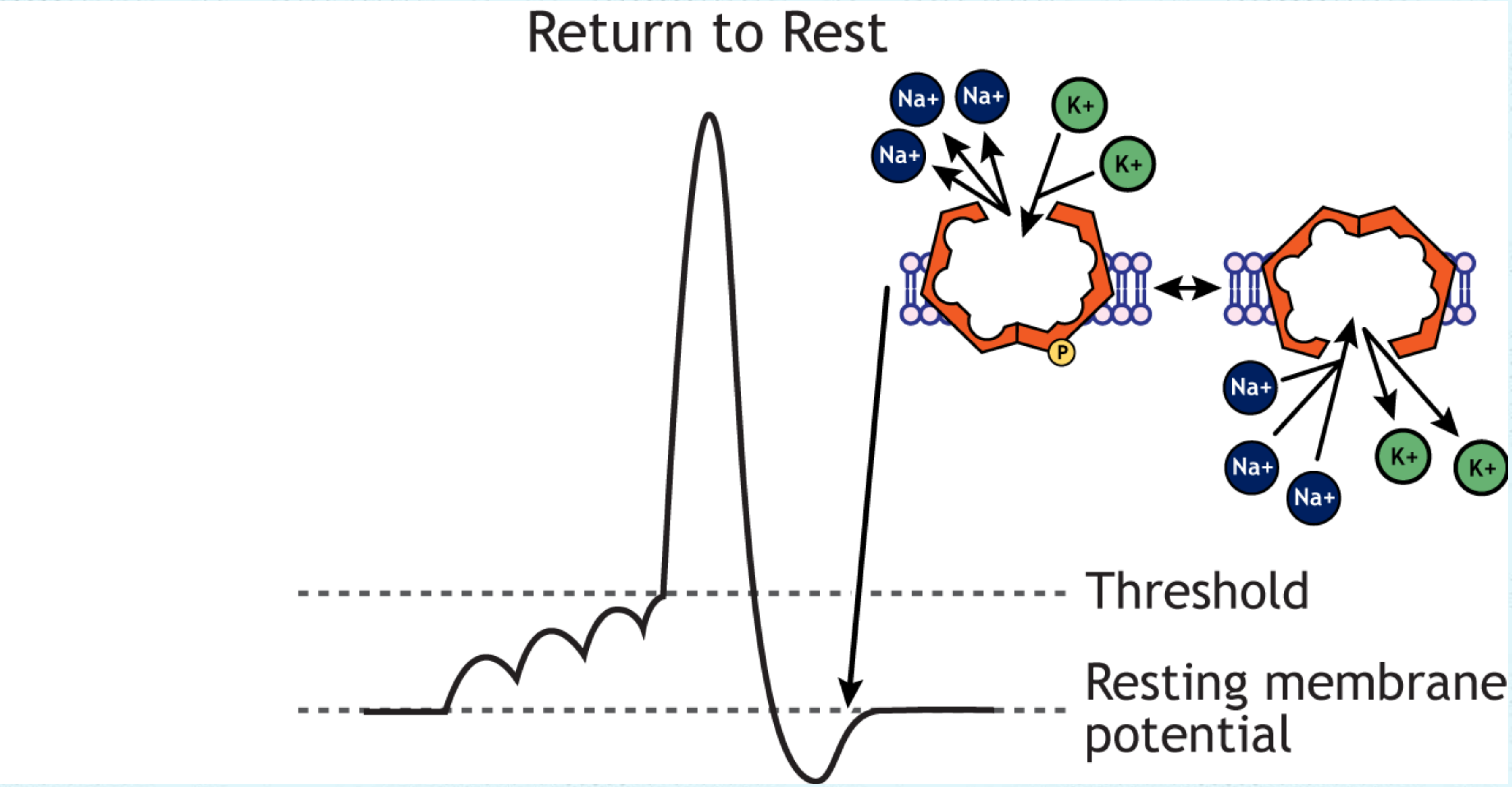
Decay of initial membrane potential towards resting potential

Low-pass filter of external current input (also called a “leaky integrator”)




Angus Chadwick

# Action potentials

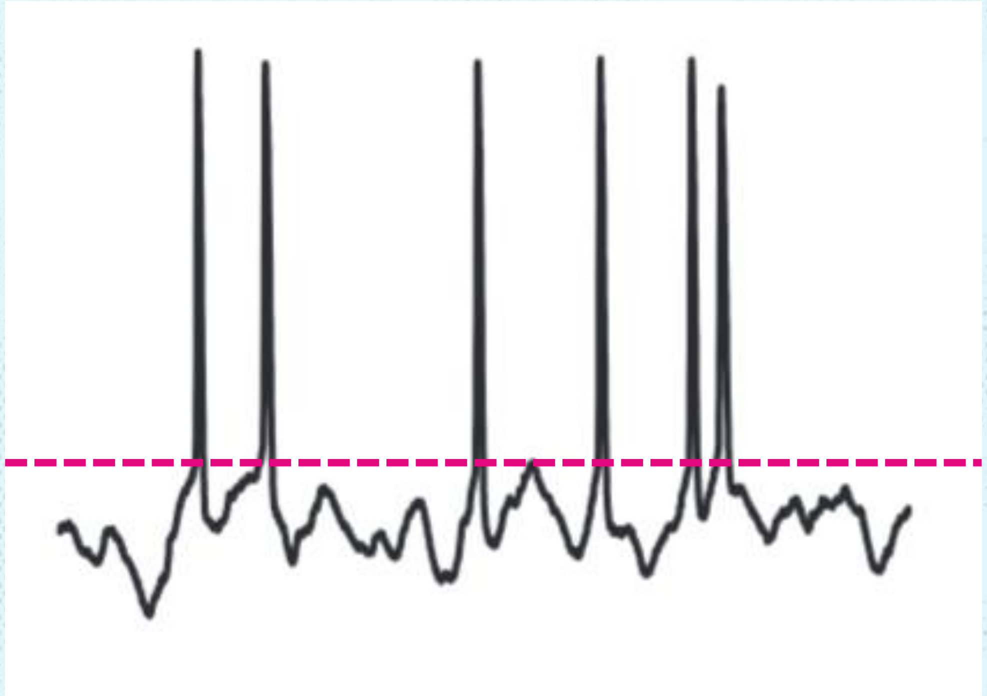



Casey Henley, CC-by-NC-SA

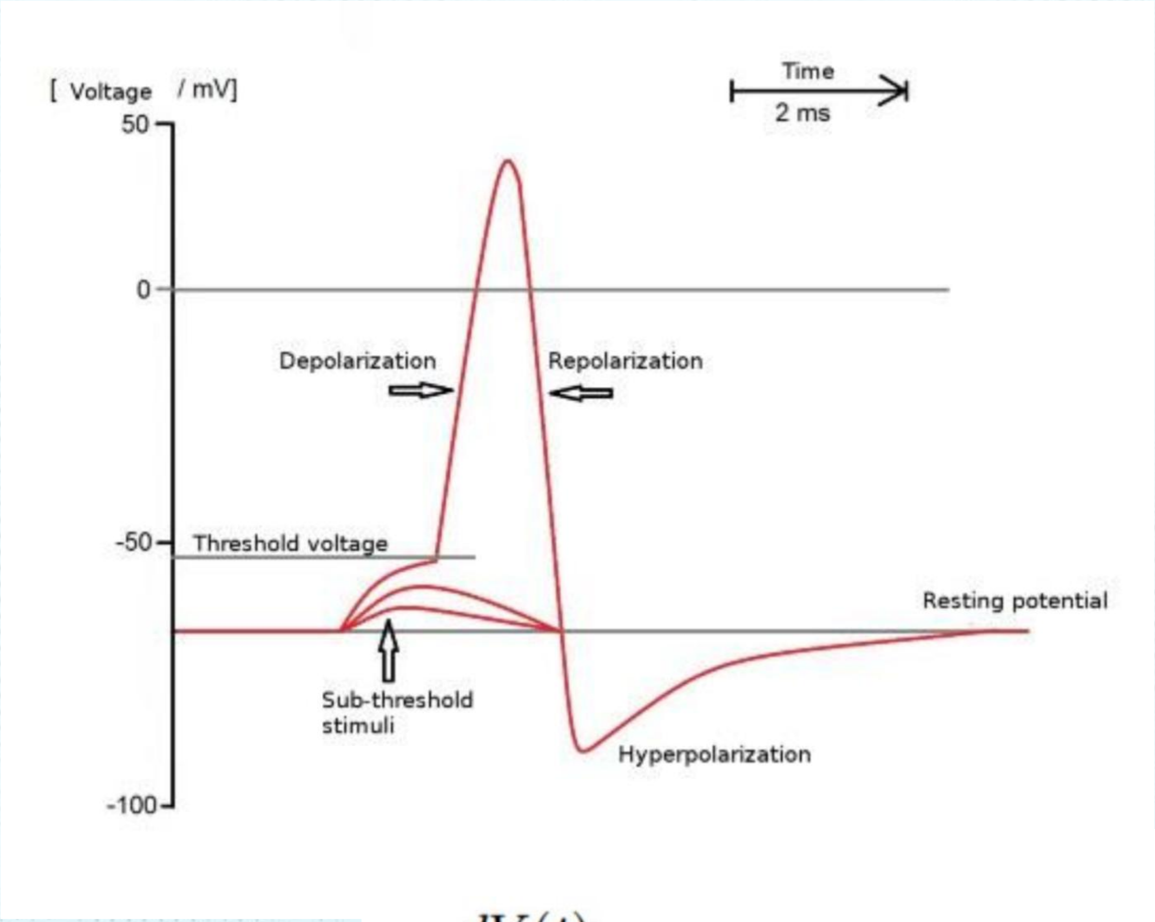
# Action potentials are the "unit of communication"

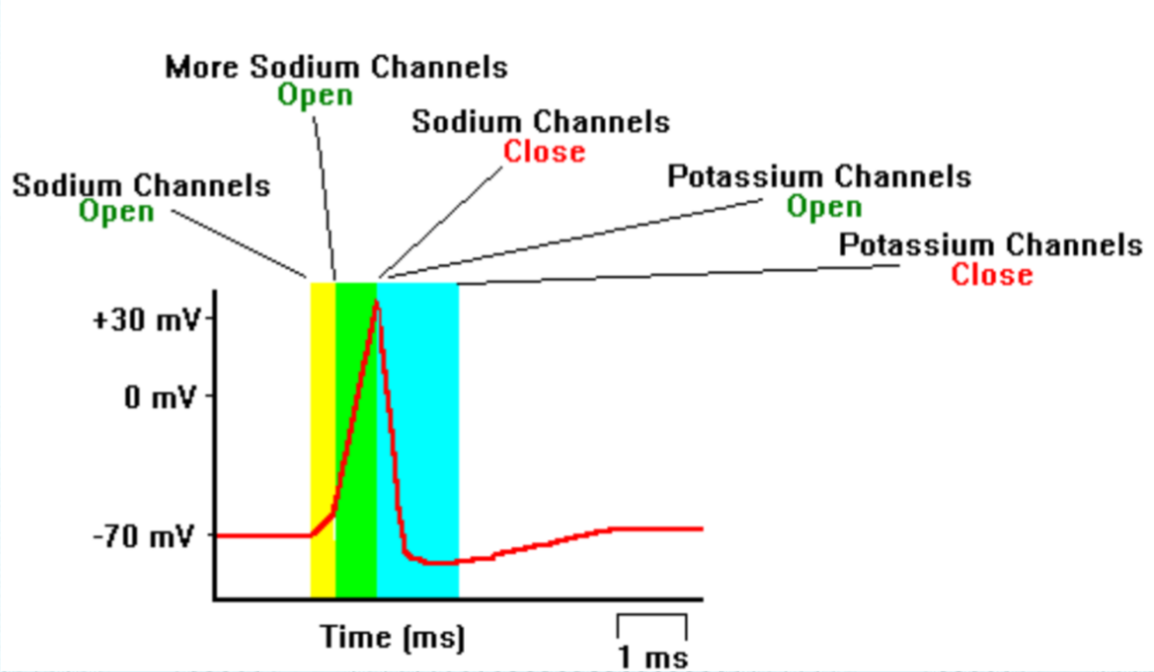
HERTIE INSTITUTE FOR AI IN BRAIN HEALTH

- Action potentials are discrete events
- "All or none"-dynamics at approx. -50 mV
- Due to non-linearities and voltage dependence of conductances $g_i$



# Action potentials

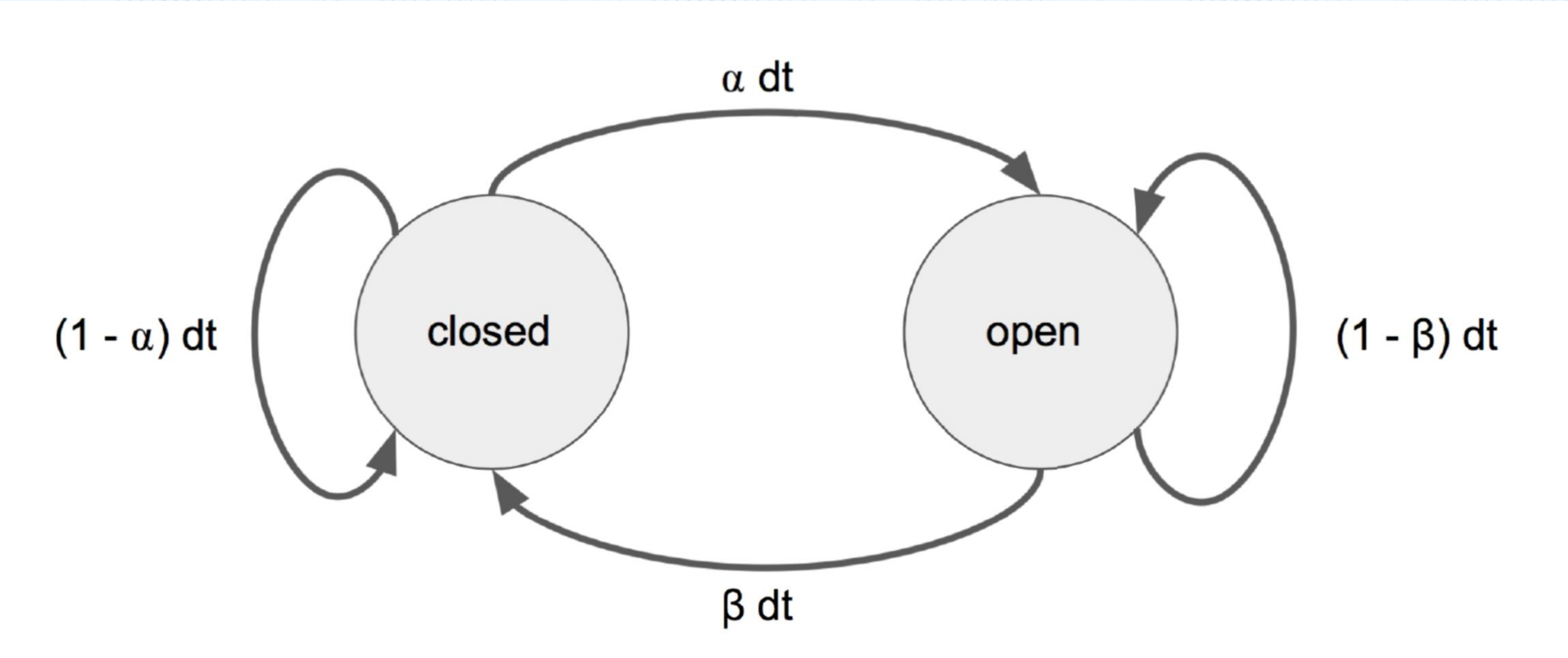



$$c_m \frac{dV(t)}{dt} = -g_{leak}[V(t) - E_{leak}] - g_{Na}(V,t)[V(t) - E_{Na}] - g_K(V,t)[V(t) - E_K] + I_{ext}$$

# Ion channels opening and closing

HERTIE INSTITUTE FOR AI IN BRAIN HEALTH

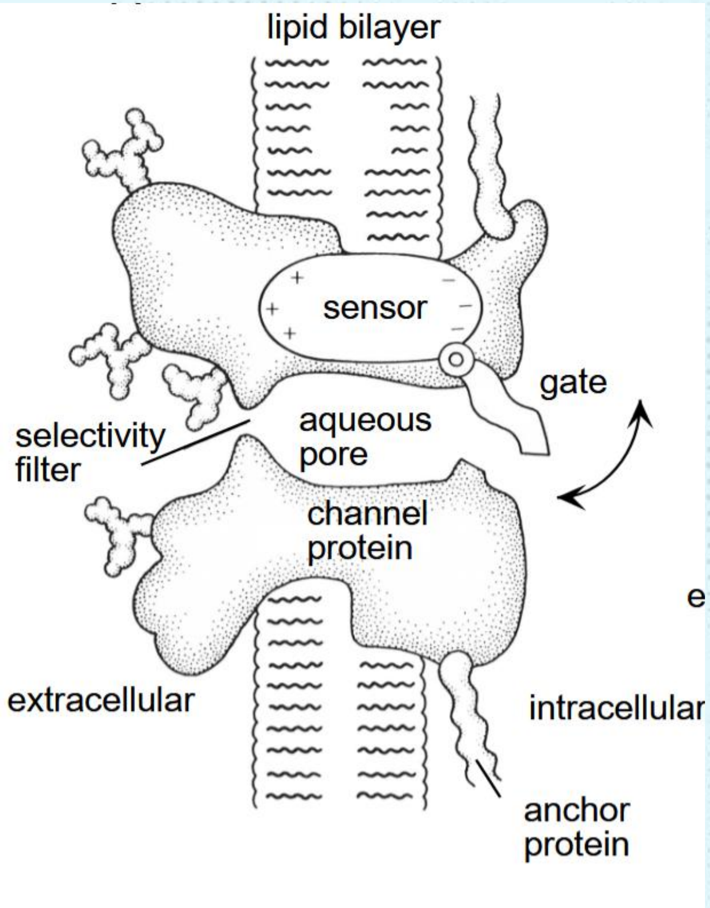


# Voltage gated ion channels

HERTIE INSTITUTE FOR AI IN BRAIN HEALTH

- Opening of $K^+$-channel $P_K = n^k$
- $n \in [0,1]$ is a gating variable modelling probability of being open
- Voltage dependence:

$$\frac{dn}{dt} = \underbrace{\alpha_n(V)(1-n)}_{\text{opening}} - \underbrace{\beta_n(V)n}_{\text{closing}}$$



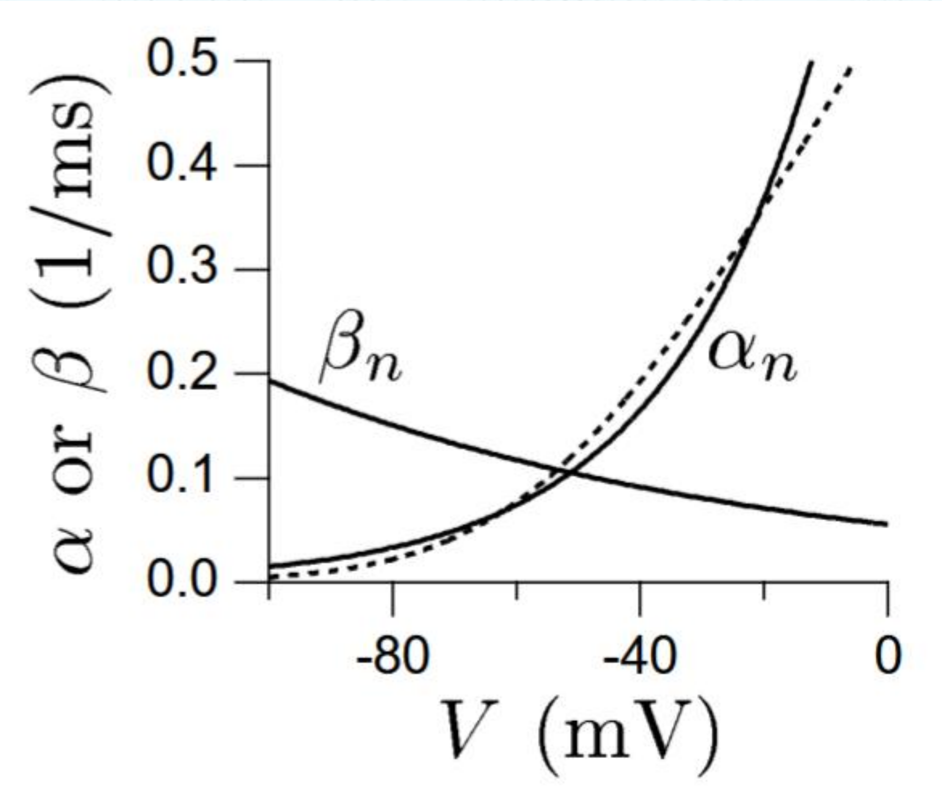

Dayan & Abbott, 2001

# Opening and closing functions

- Determine channel kinetics
- Fit to experimental data

$$\alpha_n = \frac{.01(V+55)}{1-\exp(-.1(V+55))}$$

$$\beta_n = 0.125\exp(-0.0125(V+65))$$




Dayan & Abbott, 2001

# Modelling transient channel kinetics

HERTIE INSTITUTE FOR AI IN BRAIN HEALTH

- Two voltage-dependent processes:
  - Opening $m$
  - Inactivating $h$

$$P_{\mathrm{Na}} = m^k h\,.$$

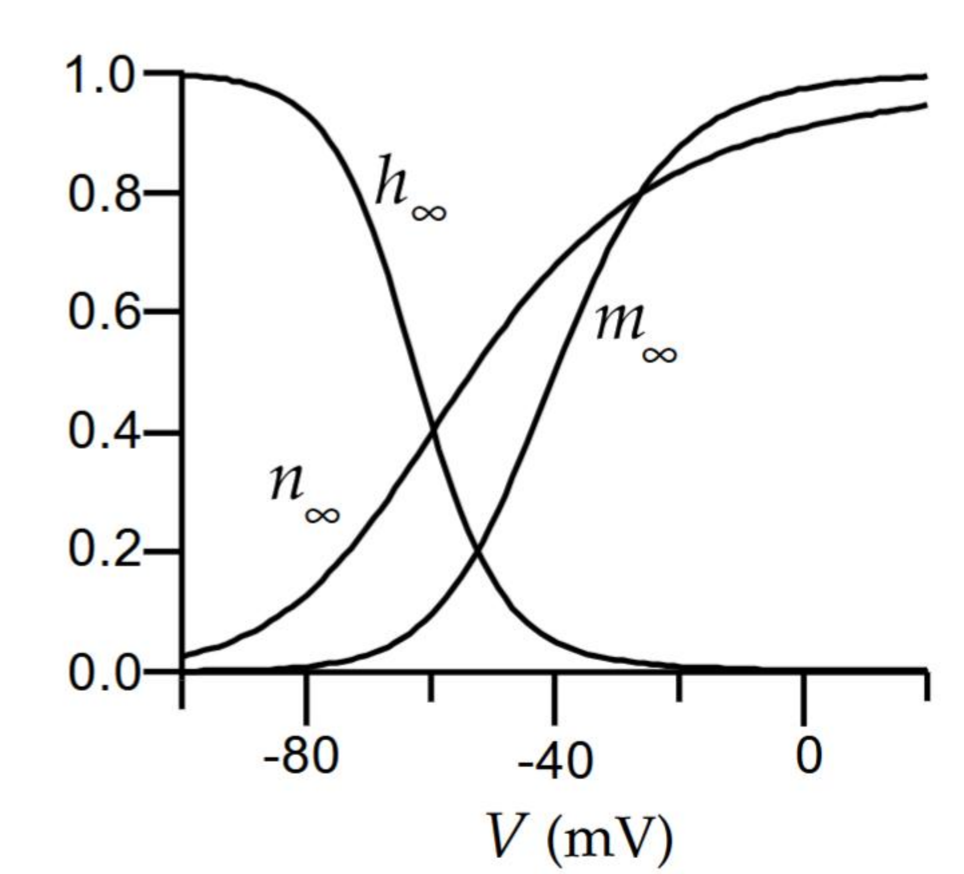
- Rate functions:

$$\alpha_m = \frac{.1(V+40)}{1-\exp(-.1(V+40))}$$

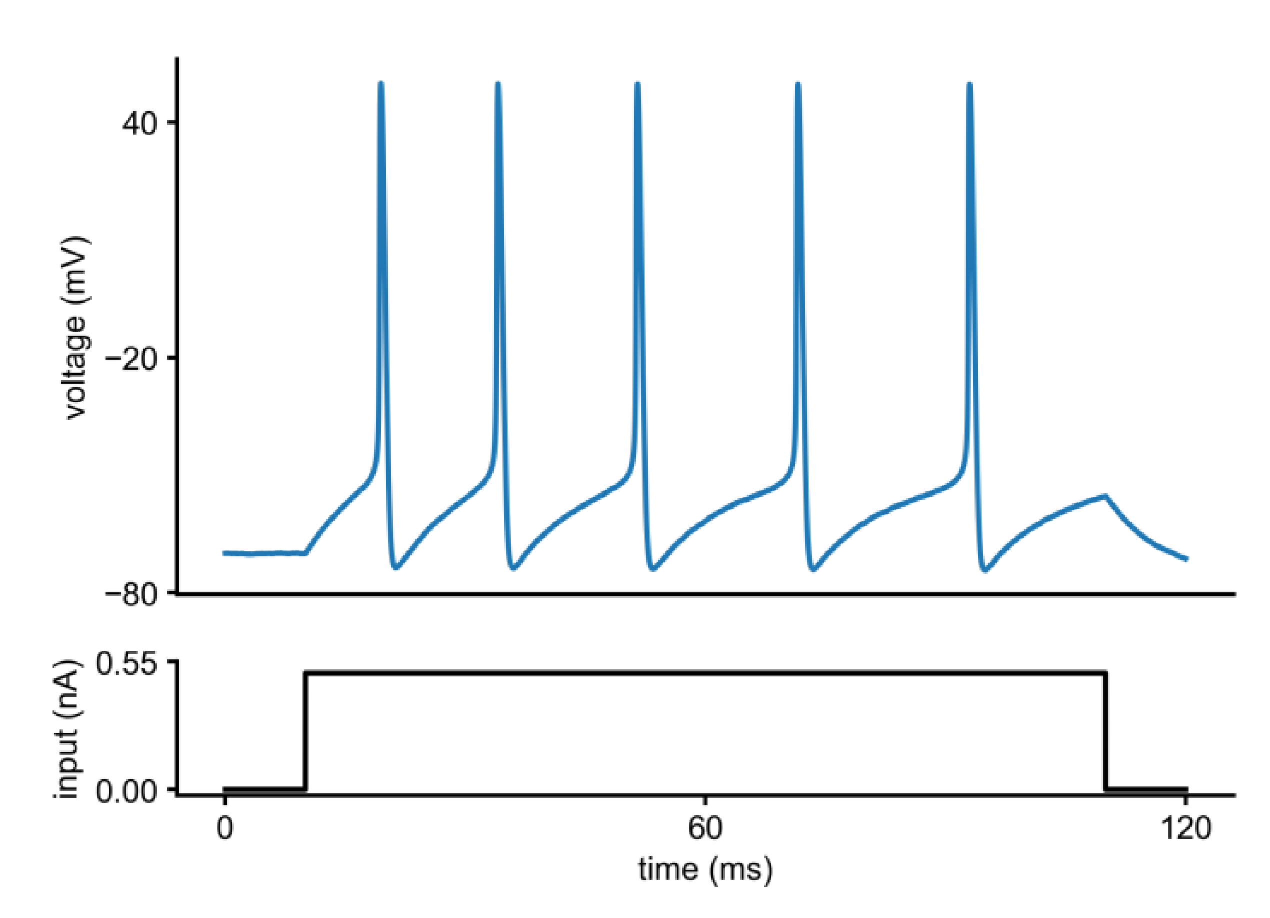
$$\alpha_h = .07\exp(-.05(V+65))$$

$$\beta_m = 4\exp(-.0556(V+65))$$

$$\beta_h = 1/(1+\exp(-.1(V+35)))$$




Dayan & Abbott, 2001



40
−20
−80
voltage (mV)
0.55
0.00
input (nA)
0
60
120
time (ms)

# The Hodgkin-Huxley model

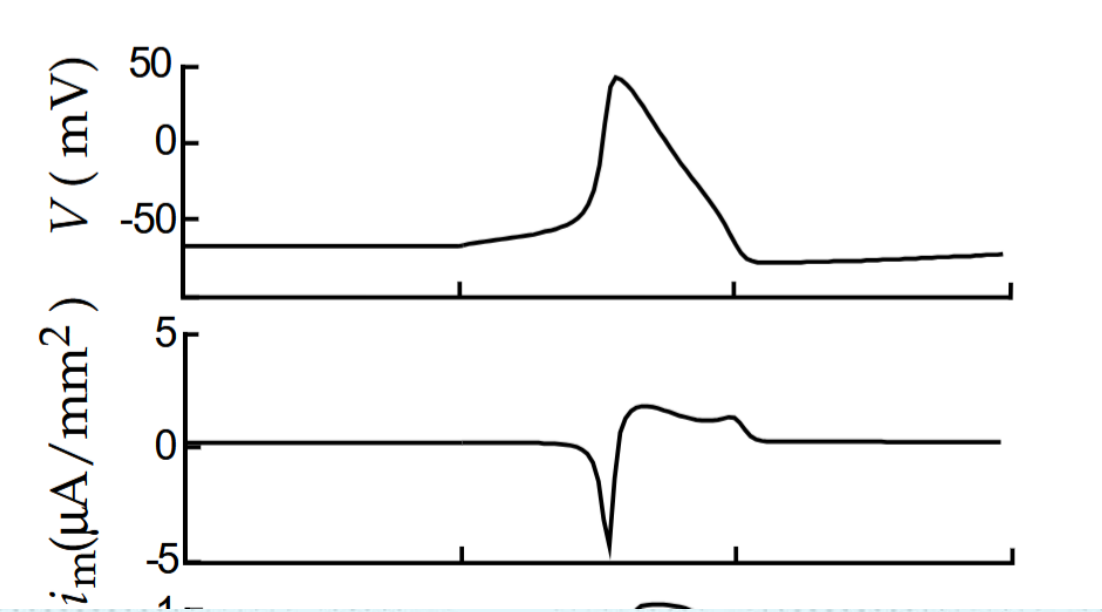
HERTIE INSTITUTE FOR AI IN BRAIN HEALTH

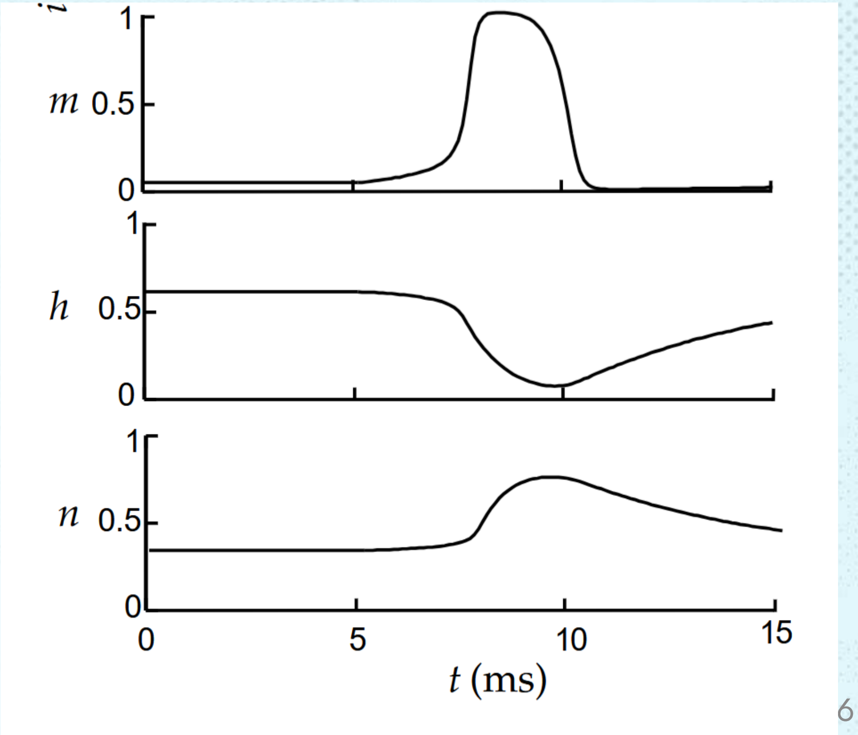
Dayan & Abbott, 2001

- Model of action potential generation

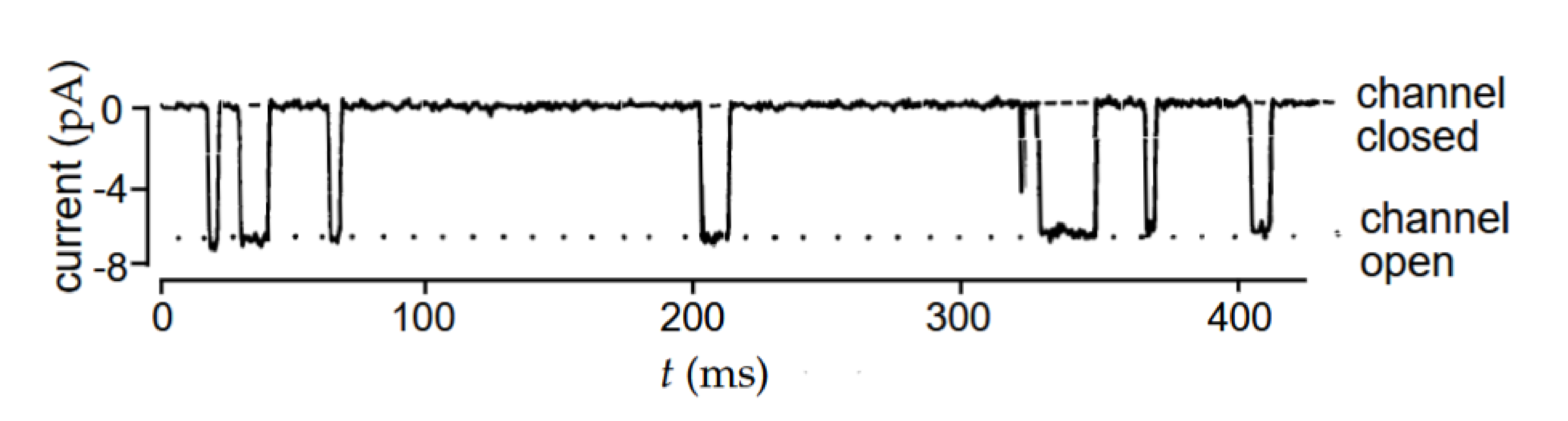
$$c_m \frac{dV}{dt} = -i_m + \frac{I_e}{A}\,.$$

$$i_m = \overline{g}_L(V - E_L) + \overline{g}_K n^4 (V - E_K) + \overline{g}_{Na} m^3 h (V - E_{Na})$$



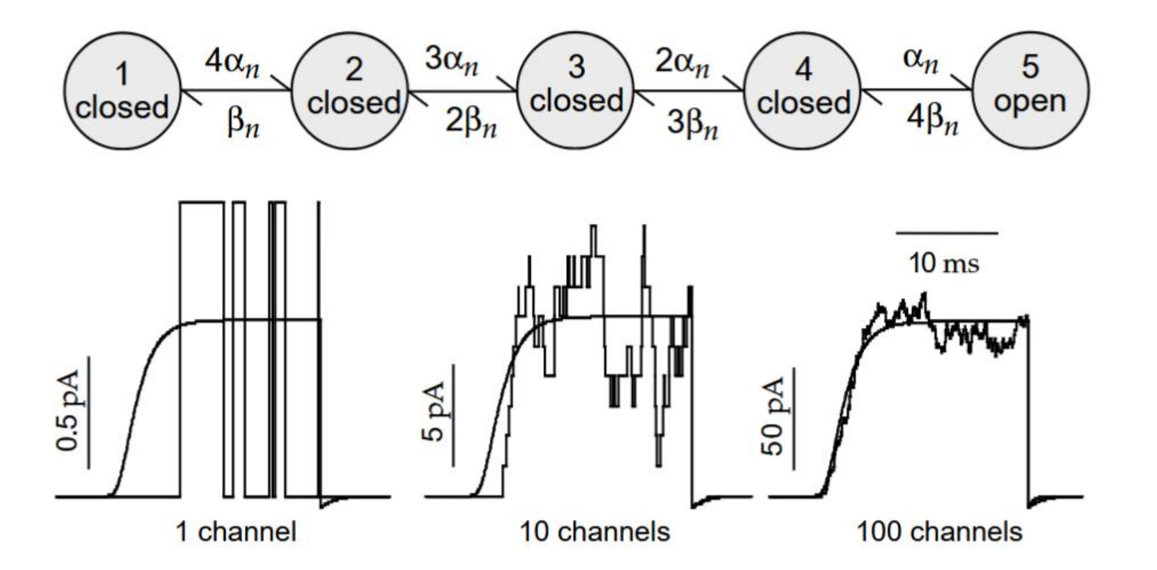



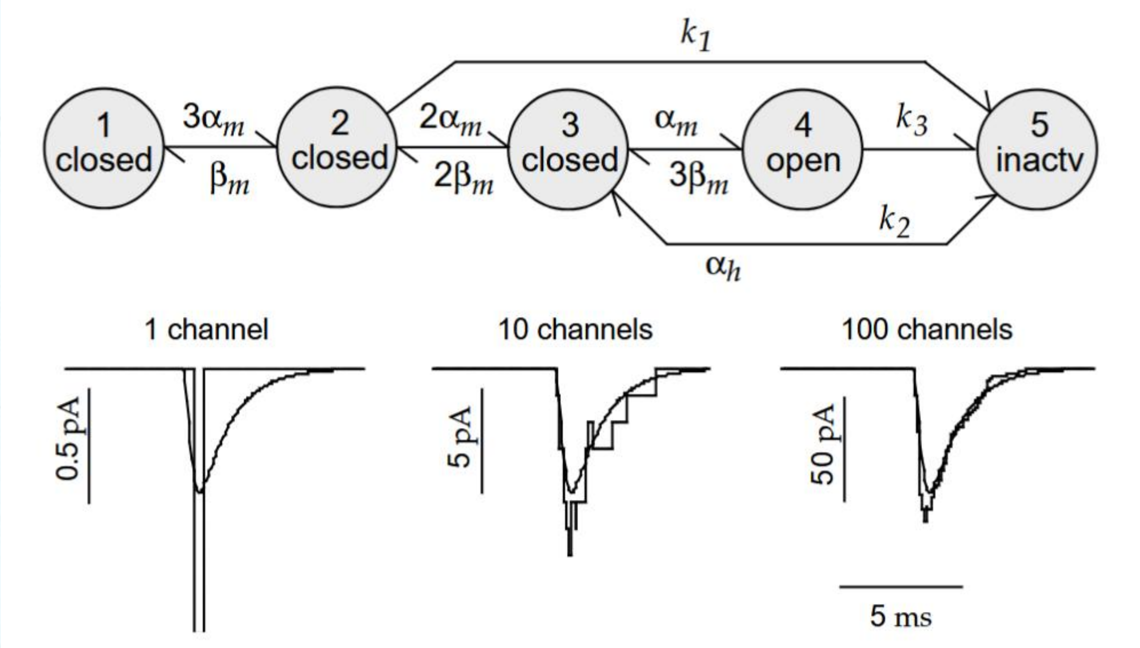
# Actual data



current (pA)
0
-4
-8
0
100
200
300
400
t (ms)
channel closed
channel open

# Stochastic ion channel models



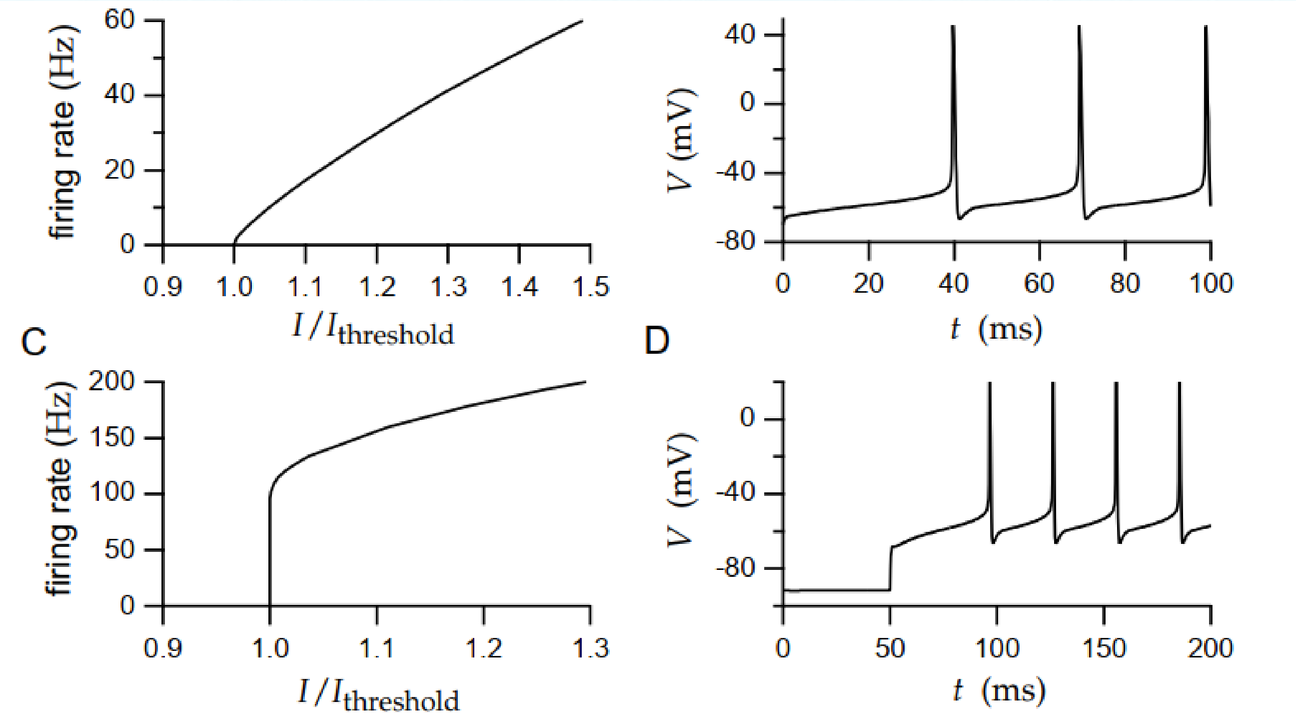



# Why is the HH model a good model?

HERTIE INSTITUTE FOR AI IN BRAIN HEALTH

- Explained measured data
- Led to predictions:
  - Kinetics of ion channels
  - Changes with temperature
  - Effect of toxins like TTX
- Can be extended

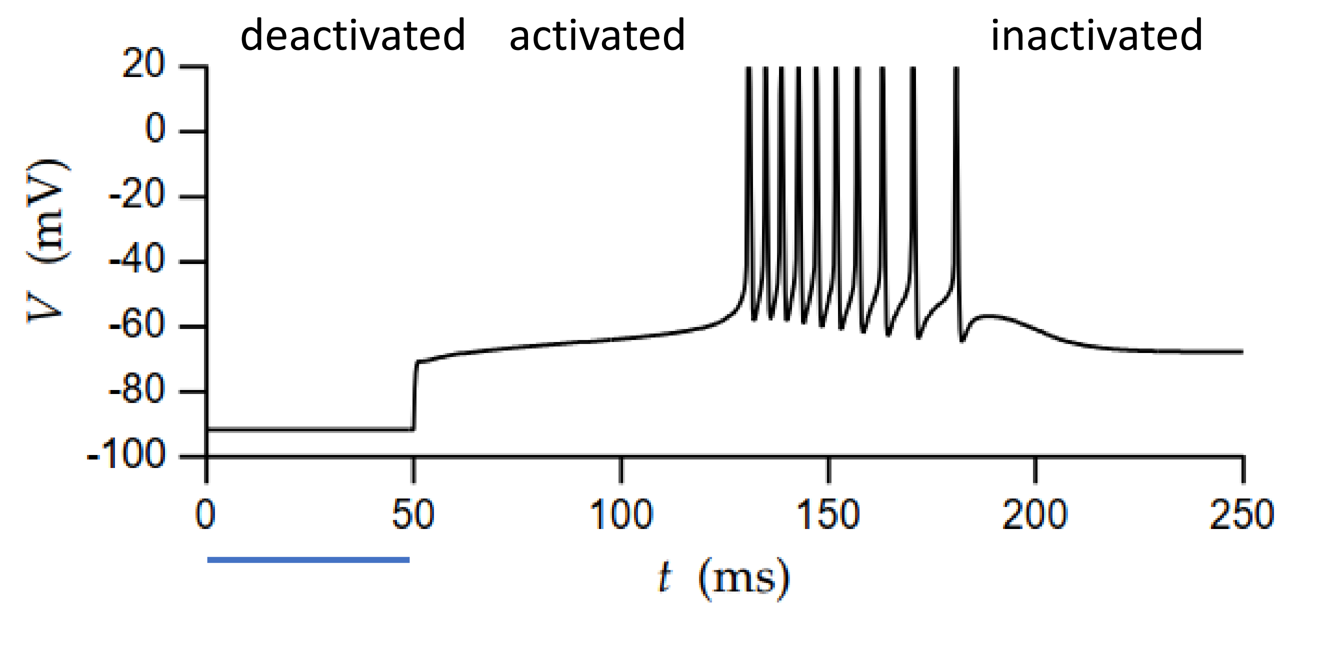
# General conductance-based models




- Transient $K^+$-channel
- Rapidly inactivating
- Linearizes firing over threshold

$$i_m = \overline{g}_L(V - E_L) + \overline{g}_{Na} m^3 h (V - E_{Na}) + \overline{g}_K n^4 (V - E_K) + \overline{g}_A a^3 b (V - E_A)$$

# Conductance-based models

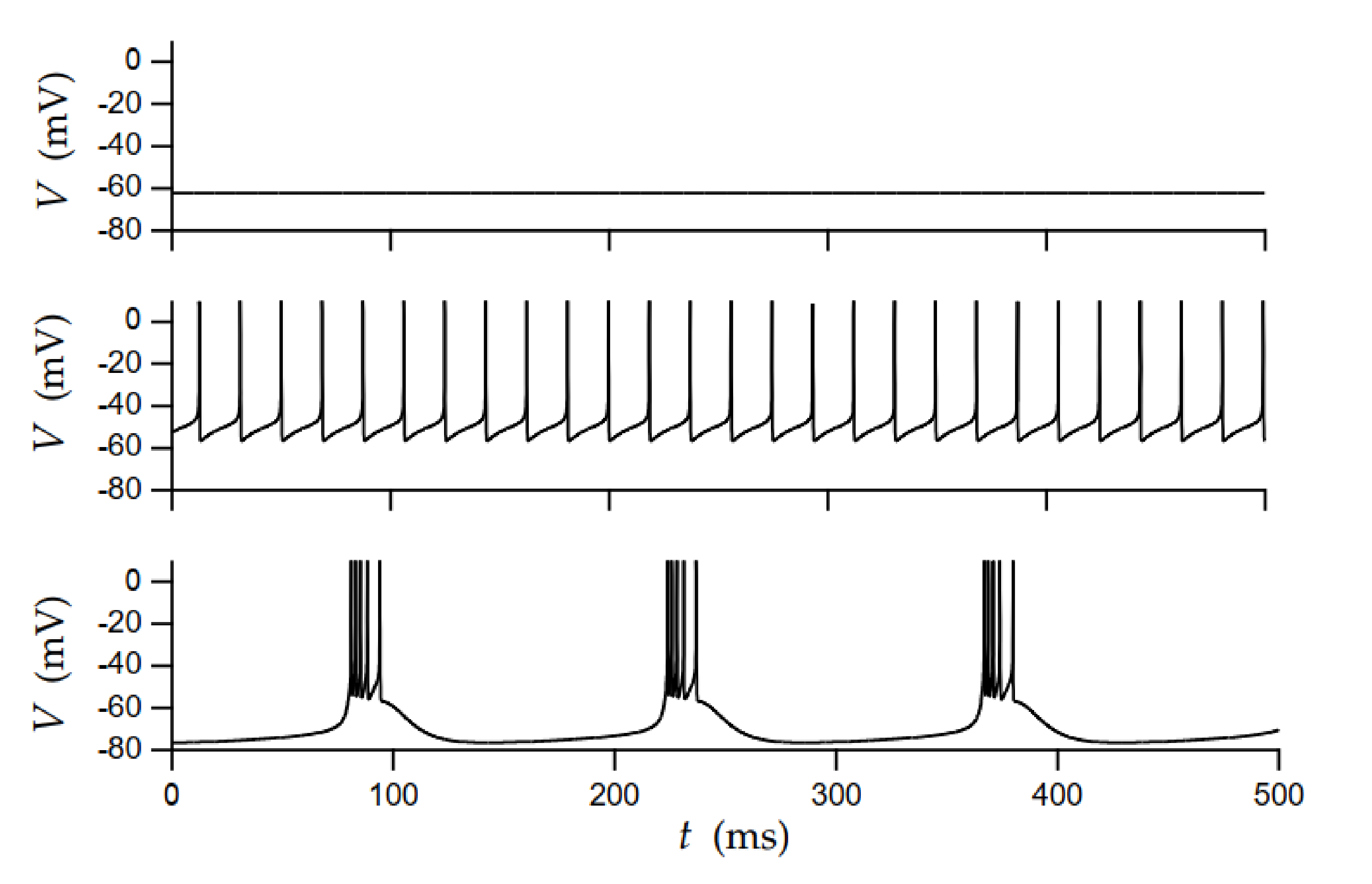



$$i_{\mathrm{CaT}} = \overline{g}_{\mathrm{CaT}} M^2 H (V - E_{\mathrm{Ca}})$$

- Transient $Ca^{2+}$-channel
- Multiple types of $Ca^{2+}$ channels, including persistent/transient
- Slower $Na^{+}$ conductance, depolarization can be called "Ca spike"

# Conductance-based models

- $Ca^{2+}$-conductance is important for modelling state dependency
- Positive current: regular firing
- Negative current: oscillatory bursty firing



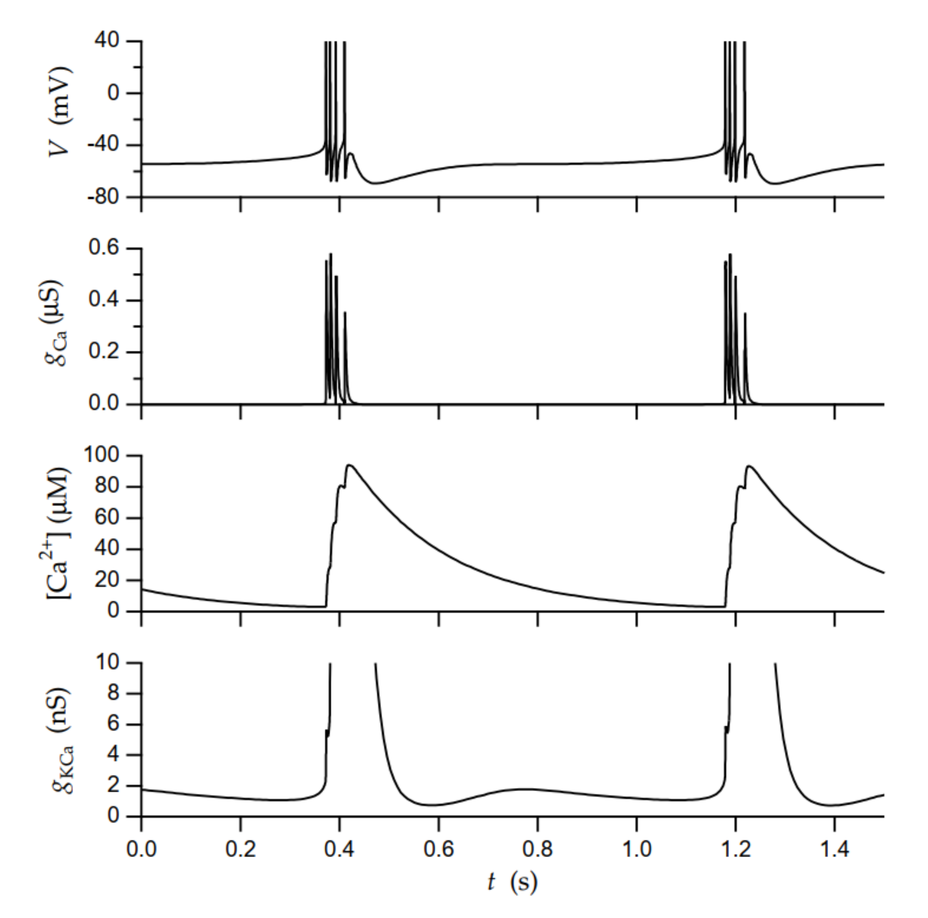
# Conductance-based models

HERTIE INSTITUTE FOR AI IN BRAIN HEALTH

- Not only voltage dependence: $Ca^{2+}$-dependent $K^+$-channel
- Important for modelling adaptation
- Requires $Ca^{2+}$-model

$$i_{\mathrm{KCa}} = \overline{g}_{\mathrm{KCa}} c^4 (V - E_{\mathrm{K}})$$

$$\frac{d[\mathrm{Ca}^{2+}]}{dt} = -\gamma i_{\mathrm{Ca}} - \frac{[\mathrm{Ca}^{2+}]}{\tau_{\mathrm{Ca}}}$$



# Neurons are cables

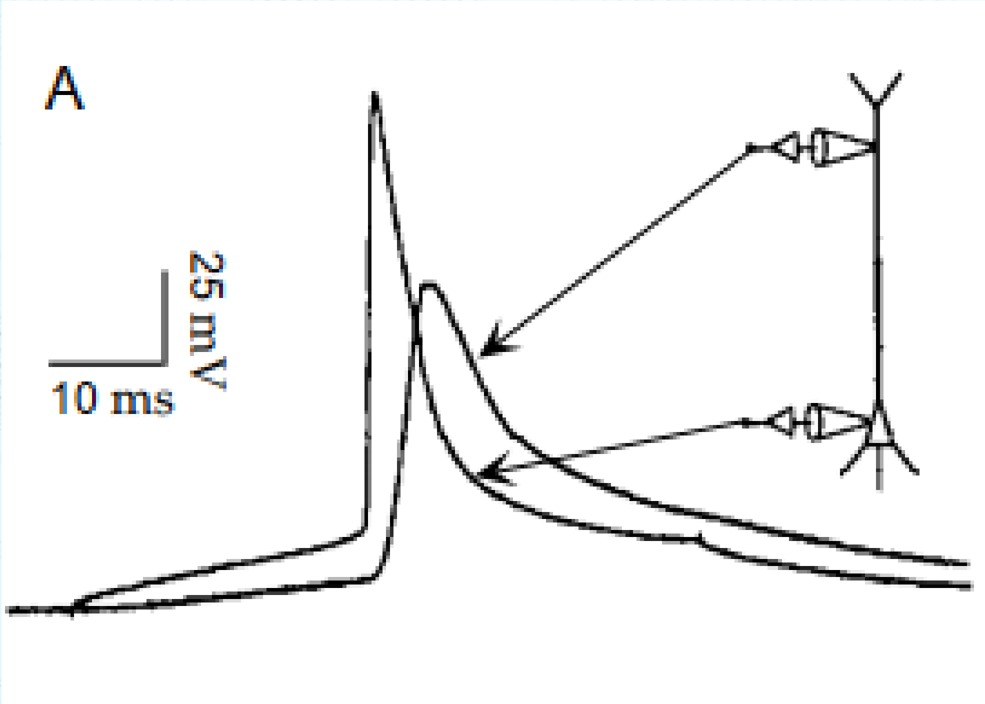


- Until now: membrane potential across entire neuron as one variable

- Neurons have long and narrow processes -> delay, attenuation

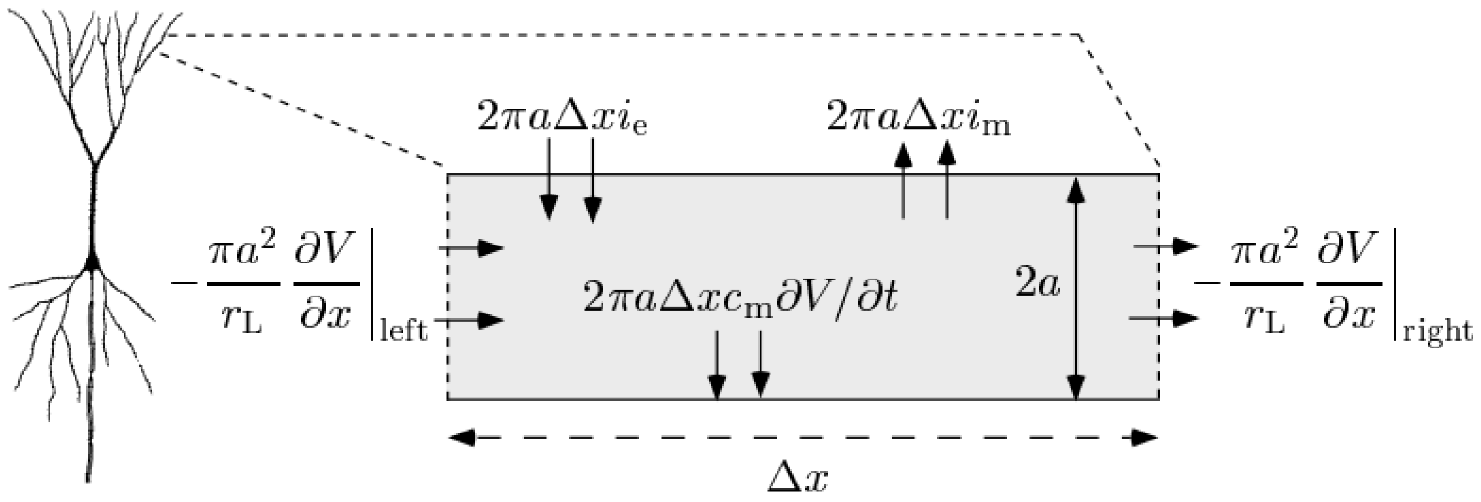
- Longitudinal current:

$$I_L = -\frac{\pi a^2}{r_L}\frac{\partial V}{\partial x}$$



# The cable equation

- Short segment with radius $a$ and length $\Delta x$
- Currents:
  - Capacitative membrane
  - Neighboring segments
  - Conductances
  - Electrodes / Input




$$2\pi a \Delta x c_m \frac{\partial V}{\partial t} = -\left(\frac{\pi a^2}{r_L}\frac{\partial V}{\partial x}\right)\Big|_{left} + \left(\frac{\pi a^2}{r_L}\frac{\partial V}{\partial x}\right)\Big|_{right} - 2\pi a \Delta x (i_m - i_e)\,.$$

$$c_m \frac{\partial V}{\partial t} = \frac{1}{2 a r_L}\frac{\partial}{\partial x}\left(a^2 \frac{\partial V}{\partial x}\right) - i_m + i_e\,.$$

# The cable equation – analytic solution by linear approximation

HERTIE INSTITUTE FOR AI IN BRAIN HEALTH

- Linear approximation of membrane currents

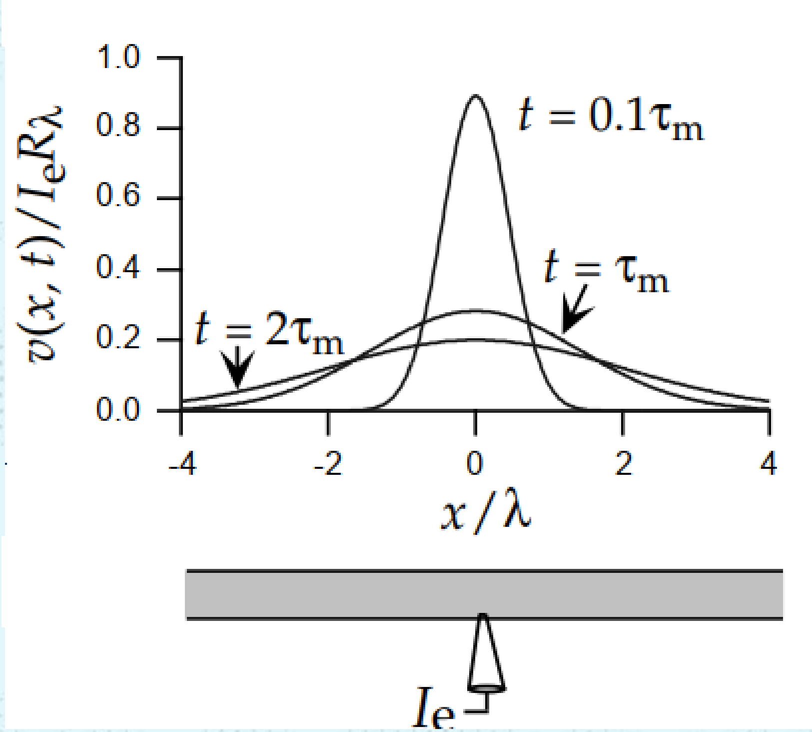
$$i_m = (V - V_{rest})/r_m$$

- Electrotonic length

$$\lambda = \sqrt{\frac{a r_m}{2 r_L}}$$

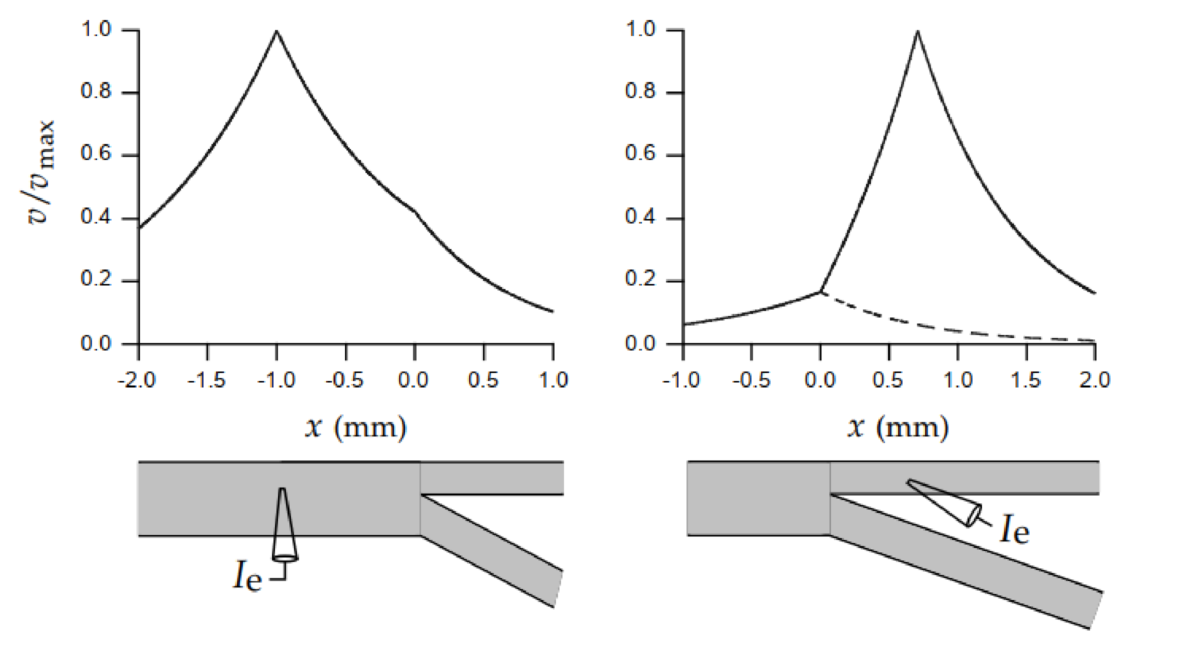
- Simplified:

$$\tau_m \frac{\partial v}{\partial t} = \lambda^2 \frac{\partial^2 v}{\partial x^2} - v + r_m i_e$$



# Branching cables

HERTIE INSTITUTE FOR AI IN BRAIN HEALTH



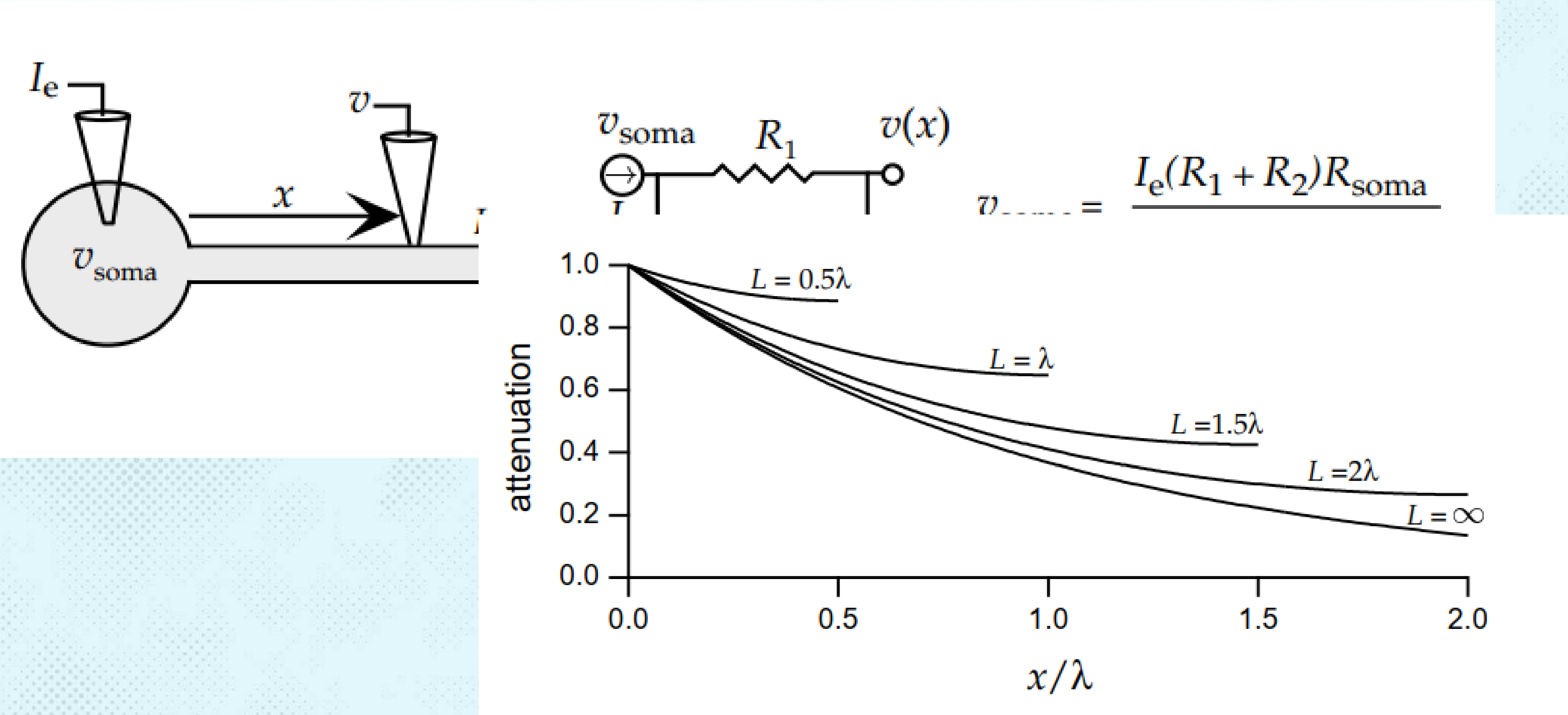

$$p_i = \frac{a_i^{3/2}}{a_1^{3/2} + a_2^{3/2} + a_3^{3/2}}$$

$$\lambda_i = \sqrt{\frac{a_i r_m}{2 r_L}} \, ,$$

$$R_{\lambda_i} = \frac{r_L \lambda_i}{\pi a_i^2}$$

$$v_1(x) = p_1 I_e R_{\lambda_1} \exp(-x/\lambda_1 - y/\lambda_2)$$
$$v_2(x) = \frac{I_e R_{\lambda_2}}{2} \left[\exp(-|y-x|/\lambda_2) + (2p_2 - 1)\exp(-(y+x)/\lambda_2)\right]$$
$$v_3(x) = p_3 I_e R_{\lambda_3} \exp(-x/\lambda_3 - y/\lambda_2)\,, \qquad (6.2$$

# Rall modell



$I_e$
$v$
$x$
$v_{soma}$
$v_{soma}$
$R_1$
$v(x)$
$I_e(R_1 + R_2)R_{soma}$
attenuation
1.0
0.8
0.6
0.4
0.2
0.0
0.0
0.5
1.0
1.5
2.0
$x/\lambda$
$L = 0.5\lambda$
$L = \lambda$
$L = 1.5\lambda$
$L = 2\lambda$
$L = \infty$

# Multicompartment models