

English summary

2.2 SNIPER model (continued)

Saddle-node infinite period bifurcation

$$\begin{cases} \dot{x} = x(1-x^2-y^2) + y(x-b) \\ \dot{y} = y(1-x^2-y^2) - x(x-b) \end{cases} \begin{cases} x=r\cos\varphi \\ y=r\sin\varphi \end{cases} \begin{cases} \dot{r} = r(1-r^2) \\ \dot{\varphi} = b-r\cos\varphi \end{cases}$$

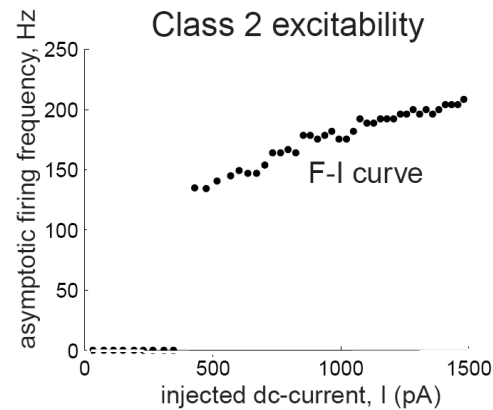
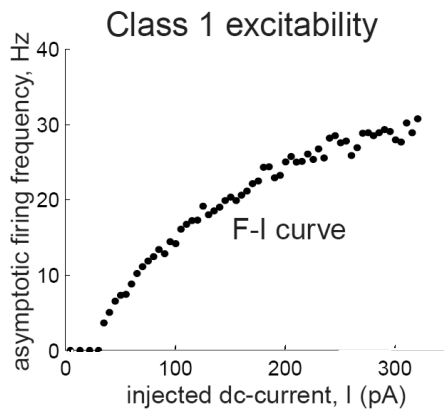
fixed points: trivial $(x_A^*, y_A^*) = (0, 0)$ with eigenvalues $\lambda_{1,2} = 1 \pm i b$ (focus)

exist only for $|b| < 1$ $\begin{cases} (x_B^*, y_B^*) = (+b, \sqrt{1-b^2}) \\ (x_C^*, y_C^*) = (+b, -\sqrt{1-b^2}) \end{cases}$ with $\lambda_1 = -2, \lambda_2 = \sqrt{1-b^2}$ (saddle)

• Emergence of limit cycle at $|b|=1$ with diverging period for $|b| \rightarrow 1$

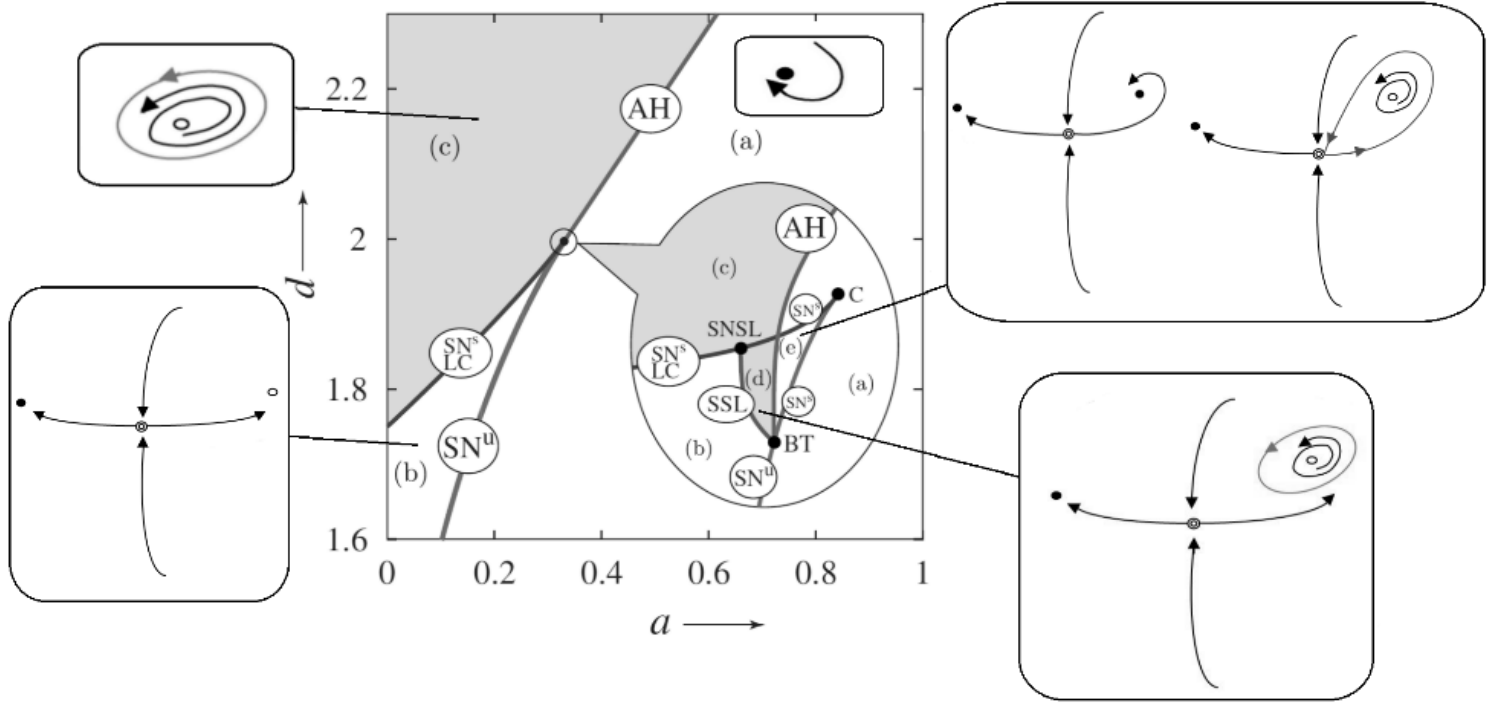
\Rightarrow excitability type I

- frequency = 0
- amplitude $\neq 0$



2.3 Hindmarsh-Rose model

$$\begin{cases} \dot{x} = c(x - \frac{x^3}{3} - y + z) \\ \dot{y} = \frac{1}{c}(x^2 + dx - by + a) \end{cases} \begin{cases} \text{cubic and quadratic nullclines} \\ \Rightarrow 1, 2, \text{ or } 3 \text{ fixed points} \end{cases}$$



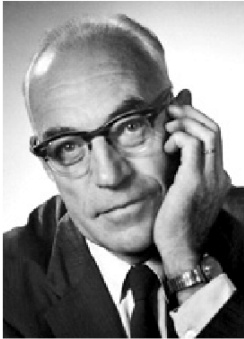
3 Physiologische Modelle

► Physiological models:

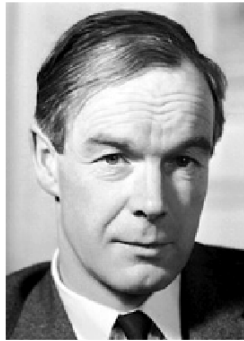
- e.g. Hodgkin-Huxley equations
- Many physiological details and processes
- Detailed description of single cell
- Many equations, many parameters
- Applicable to ensembles of many oscillators?
- Feasible for bifurcation analysis?

3.1 Hodgkin-Huxley-Modell

"for their discoveries concerning the ionic mechanisms involved in excitation and inhibition in the [...] nerve cell membrane"

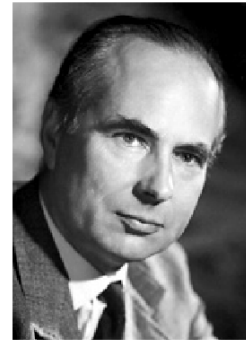


Sir John Carew Eccles



Alan Lloyd Hodgkin

* 5. 2. 1914
† 20. 12. 1988



Andrew Fielding Huxley

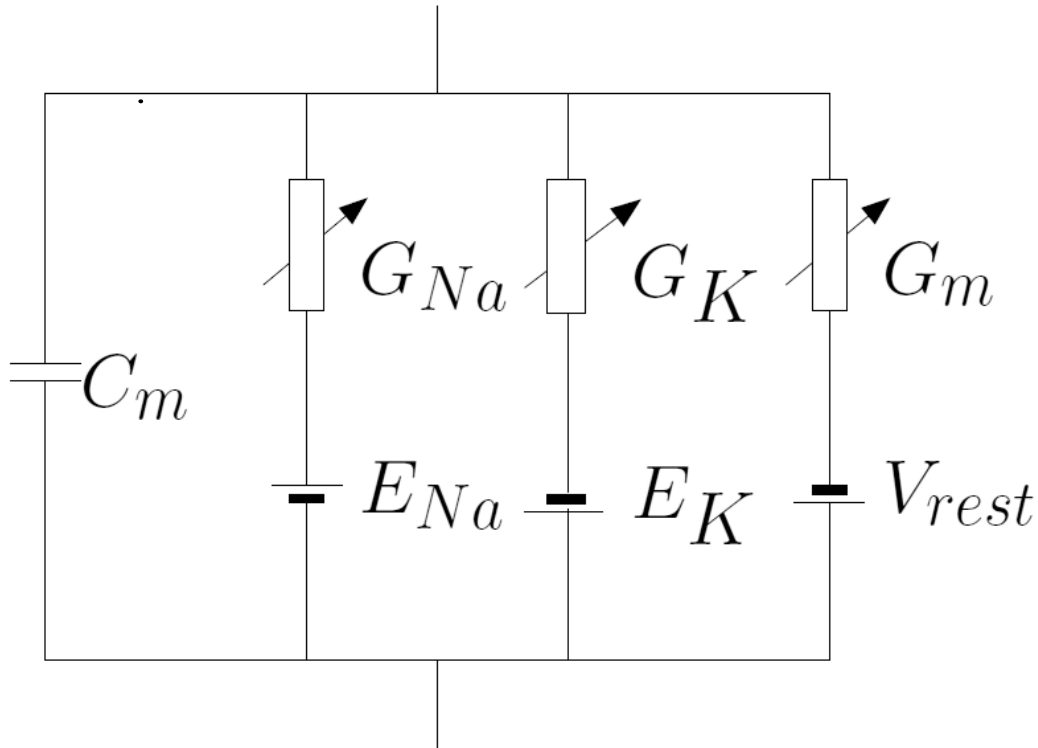
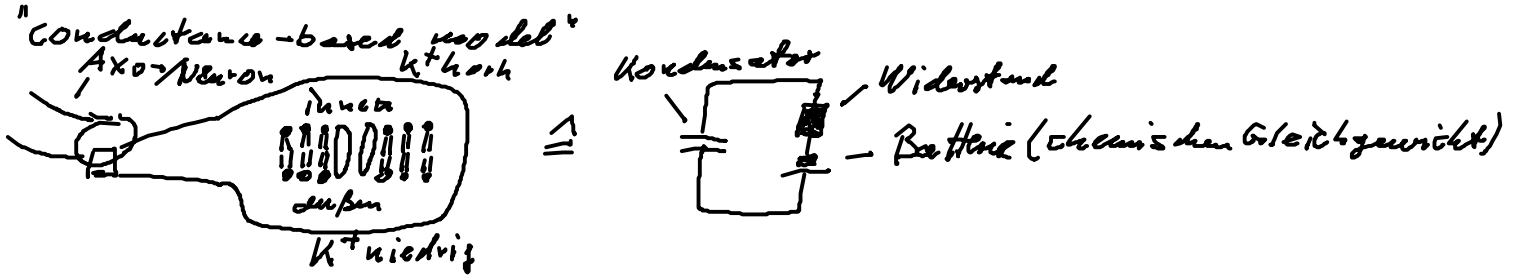
* 22. 11. 1917
† 30. 5. 2012

J. Physiol. (1952) 117, 500–544

A QUANTITATIVE DESCRIPTION OF MEMBRANE CURRENT AND ITS APPLICATION TO CONDUCTION AND EXCITATION IN NERVE

BY A. L. HODGKIN AND A. F. HUXLEY

From the Physiological Laboratory, University of Cambridge



Kirchhoff-Gesetz ($\sum_{k=1}^n I_k = 0$ an einem Knoten)

$$I_m = - \underbrace{(I_{Na} + I_K + I_{leak})}_{I_{ionic}}$$

Membran

Spannung am Kondensator (Membran): $Q = CU$

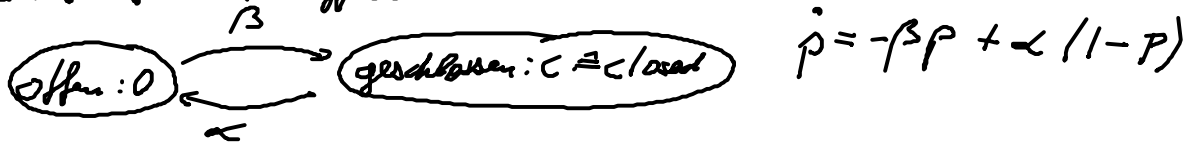
$$\dot{Q} = C\dot{U} \Rightarrow C\dot{U} = I_m = -I_{ionic}$$

Ohm'sches Gesetz: $U = RI \Rightarrow g_{ion}(V - E_{ion}) = I_{ion}$ mit $ion \in \{K, Na, leak\}$
 $R = \frac{1}{g}$ - Leitfähigkeit

E_{ion} (Batterie) ergibt sich aus dem sog. Nernst-Potenzial bei unterschiedlichen Ionenkonzentrationen: $E_{ion} \sim \ln \frac{[ion]_{in}}{[ion]_{out}}$ Ionenkonzentration

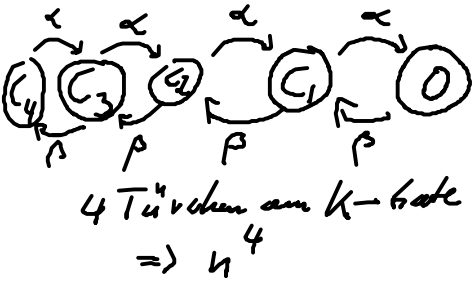
Ableitung: Leitfähigkeit g_{ion} hängt nicht linear von V ab!

$\Rightarrow g_{ion}(V) = \bar{g} p(V)$ "gating variable" (spannungsabhängig)
 maximale Leitfähigkeit \bar{g} Wahrscheinlichkeit für offenes Gate β



angewendet auf K^+ -Ionen:

$I_K = g_K(V) (V - E_K) = \bar{g}_K n^4 (V - E_K)$ mit $\dot{n} = \alpha_n(V)(1-n) - \beta_n(V)n$



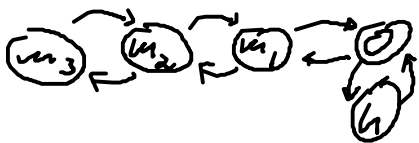
$\alpha_n(V) = 0.01 \frac{10 - V}{e^{(10-V)/10} - 1}$

$\beta_n(V) = 0.125e^{-V/80}$

angewendet auf Na^+ -Ionen:

$I_{Na} = g_{Na}(V) (V - E_{Na}) = \bar{g}_{Na} m^3 h (V - E_{Na})$ mit $\dot{m} = \alpha_m(V)(1-m) - \beta_m(V)m$
 $\dot{h} = \alpha_h(V)(1-h) - \beta_h(V)h$

2 unabhängige Kanäle



$\alpha_m(V) = 0.1 \frac{25 - V}{e^{(25-V)/10} - 1}$

$\beta_m(V) = 4e^{-V/18}$

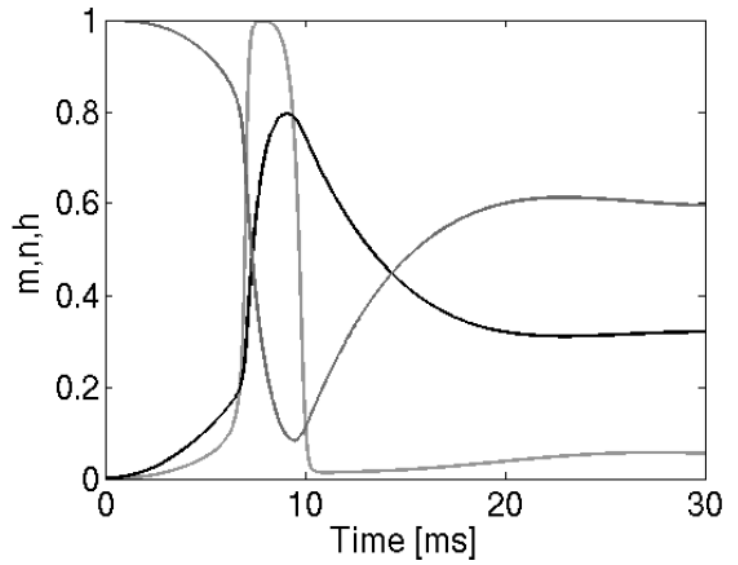
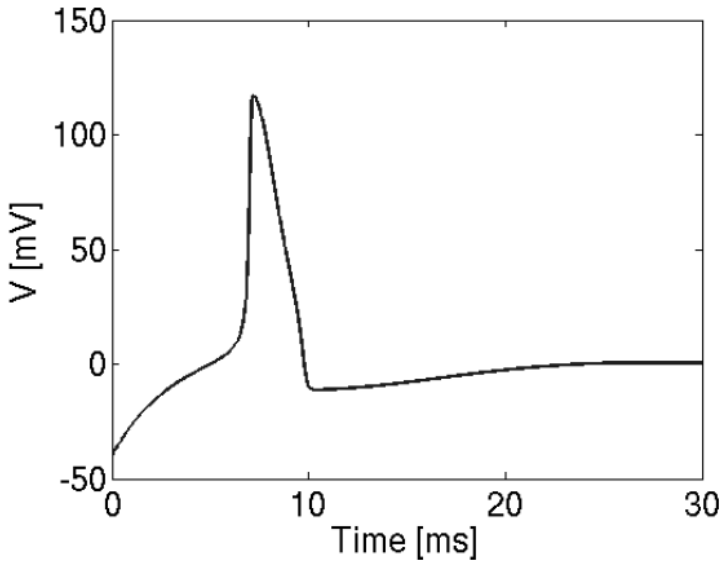
$\alpha_h(V) = 0.07e^{-V/20}$

$\beta_h(V) = \frac{1}{e^{(30-V)/10} + 1}$

Gleichung für das Membranpotential:

$$C_m \dot{V} = -\bar{g}_K n(V)^4 (V - E_K) - \bar{g}_{Na} m(V)^3 h(V) (V - E_{Na}) - \bar{g}_{leak} (V - E_{leak})$$

\uparrow K-Aktivierung \uparrow Na-Aktivierung \uparrow Na-Inaktivierung



Left panel: Membrane voltage. Right panel: Activation potential, for sodium activation m (green) and inactivation h (pink) and potassium activation n (black).

Gleichungen für n , m und h : $\tau_n = \frac{1}{\alpha_n + \beta_n}$

$n_\infty = \frac{\alpha_n}{\alpha_n + \beta_n}$ analog für m und h

$$\tau_m(V) \frac{dm}{dt} = -m + m_\infty(V)$$

$$\tau_h(V) \frac{dh}{dt} = -h + h_\infty(V)$$

$$\tau_n(V) \frac{dn}{dt} = -n + n_\infty(V)$$

Lösung für konstantes V ("Voltage clamp")

$$\Rightarrow \tau_n \dot{n} = -n + n_\infty \text{ Aufg. 10.10.18}$$

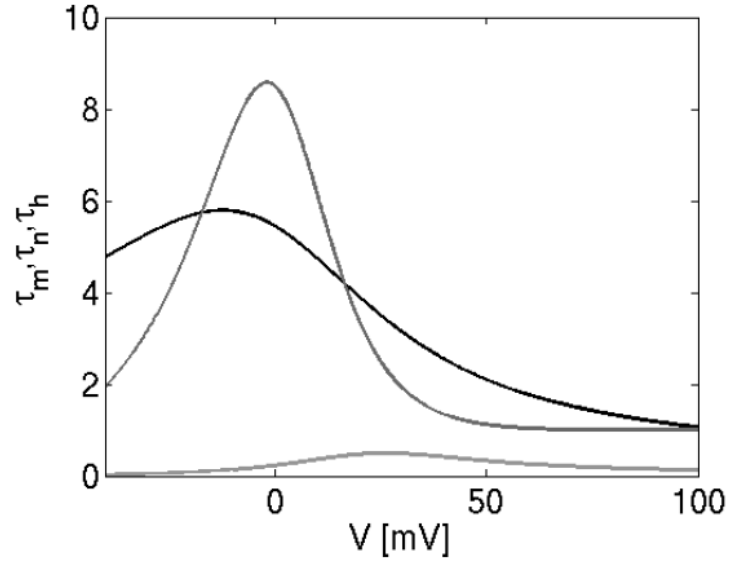
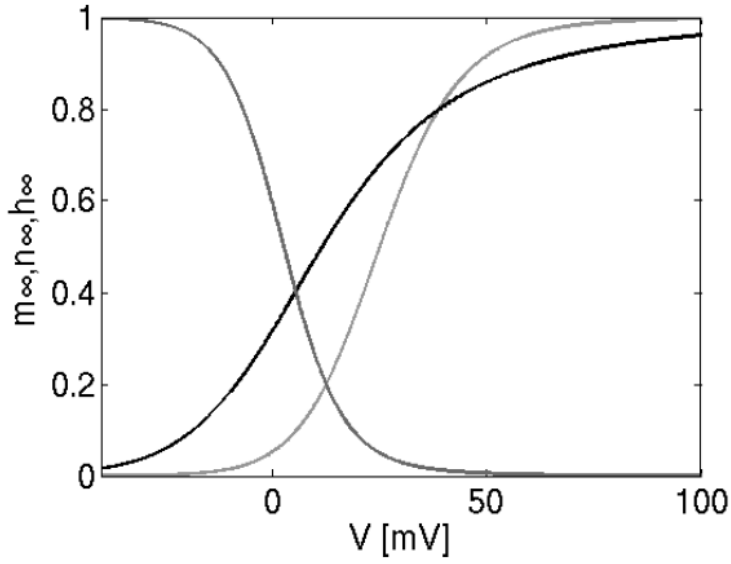
$$\Rightarrow n(t) = n_\infty + (n_0 - n_\infty) e^{-t/\tau_n}$$

$$= n_0 - (n_0 - n_\infty) (1 - e^{-t/\tau_n})$$

$$m(t) = m_0 - (m_0 - m_\infty) (1 - e^{-t/\tau_m})$$

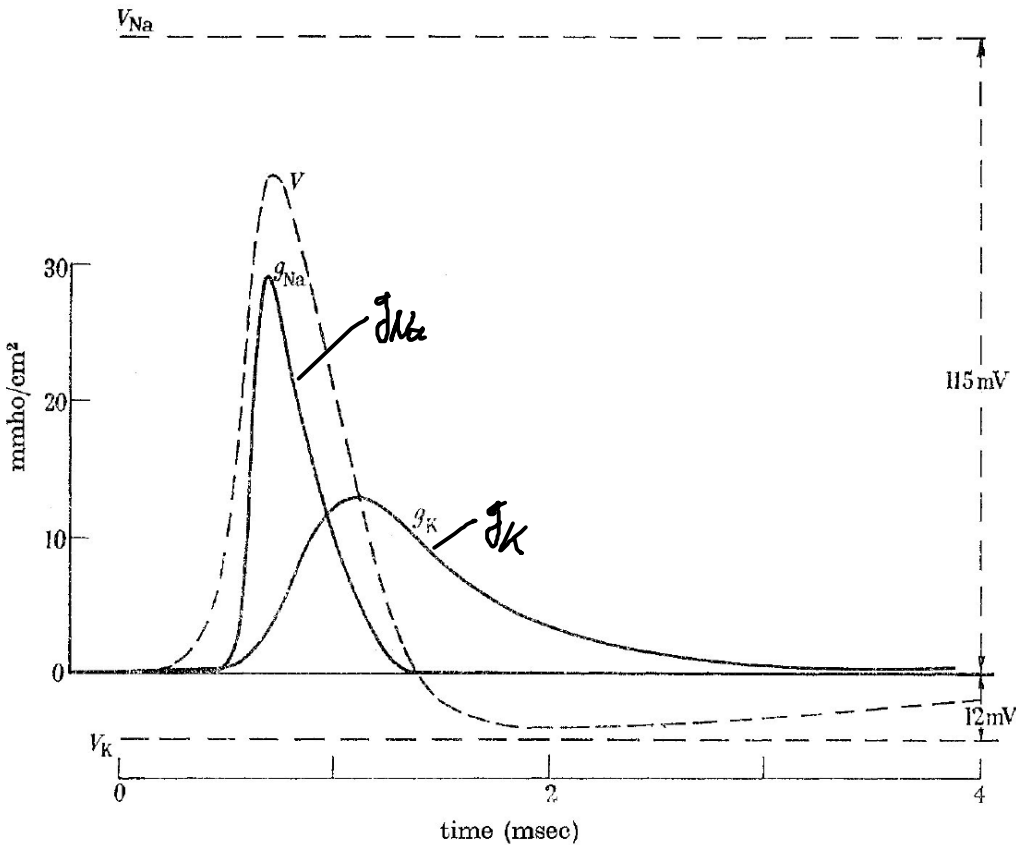
$$h(t) = h_0 - (h_0 - h_\infty) (1 - e^{-t/\tau_h})$$

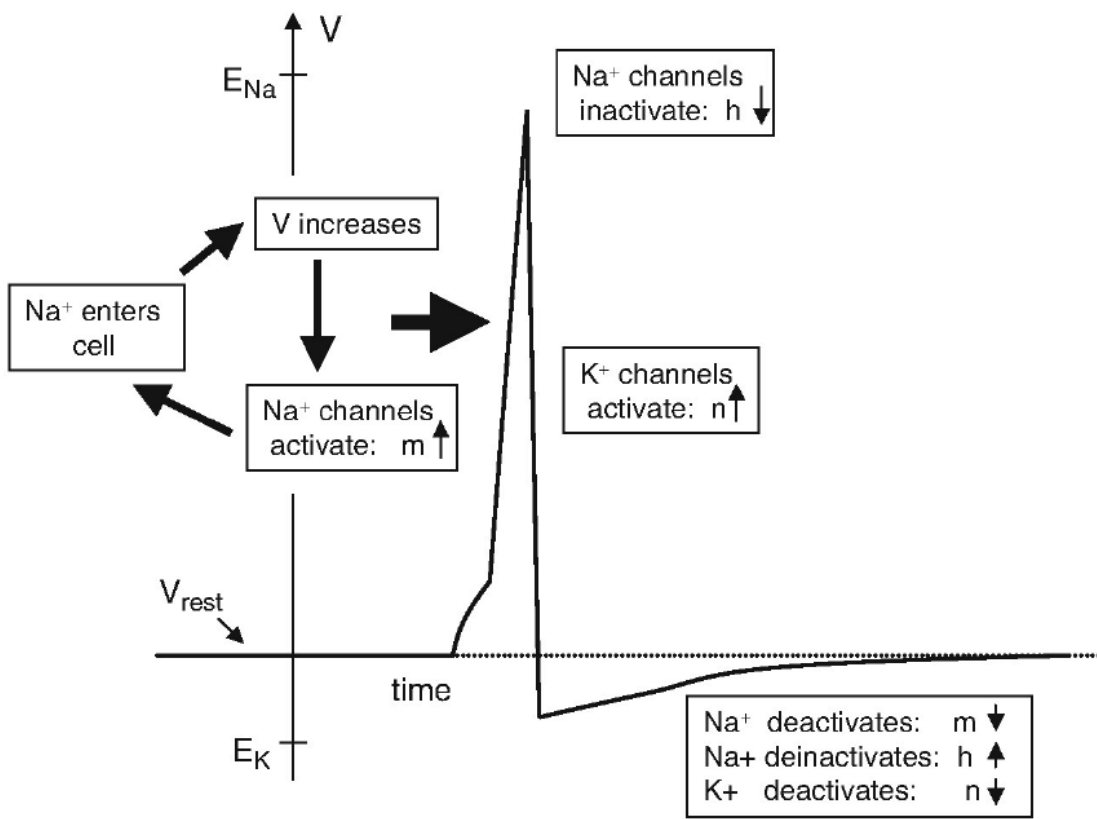
V variable $\Rightarrow \tau_n(V), n_\infty(V) \dots$



Left panel: Steady state activation and inactivation functions. Right panel: Voltage dependent time constants, for sodium activation m (green) and inactivation h (pink) and potassium activation n (black).

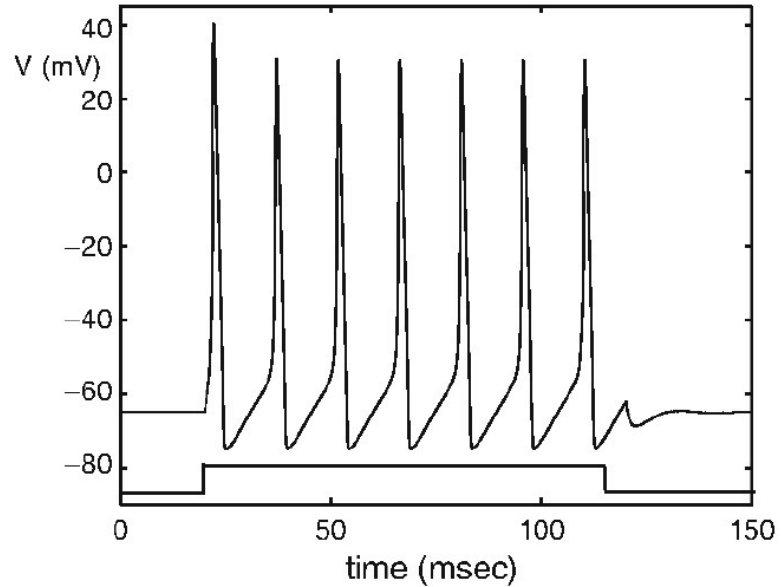
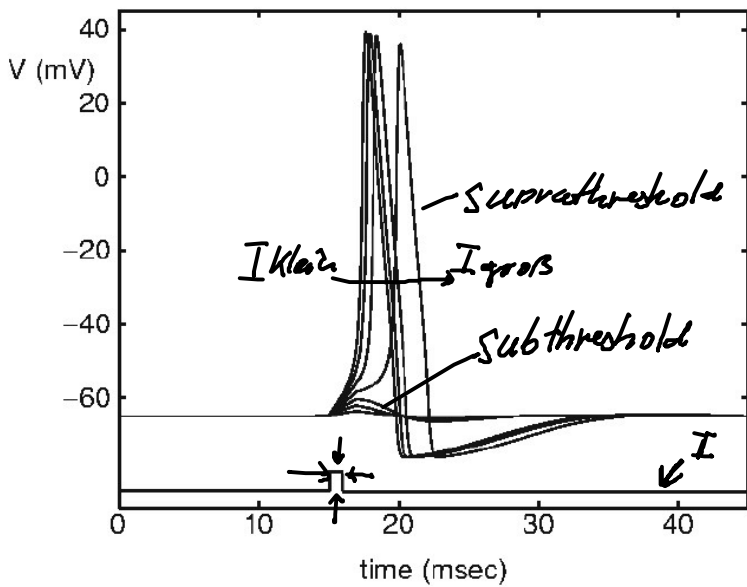
Spannungsabhängige Leitfähigkeiten $g_K, g_{Na} \Rightarrow$ zeitabhängige Leitfähigkeiten während eines Pulses





dynamisches Verhalten: zusätzlicher Strom als Bifurkationsparameter I

$$C_m \dot{V} = I - I_{ion}$$



Erhöhung/längere Dauer von $I \Rightarrow$ Fixpunkt (Ruhezustand) wird instabil in einer Hopf-Bifurkation (\Rightarrow Anregbarkeit Typ II)