# The Hodgkin-Huxley Equations and Analytical Approximations for them

Peter Schuster

Institut für Theoretische Chemie und Molekulare Strukturbiologie der Universität Wien

Seminar of the MPI for Mathematics in Science

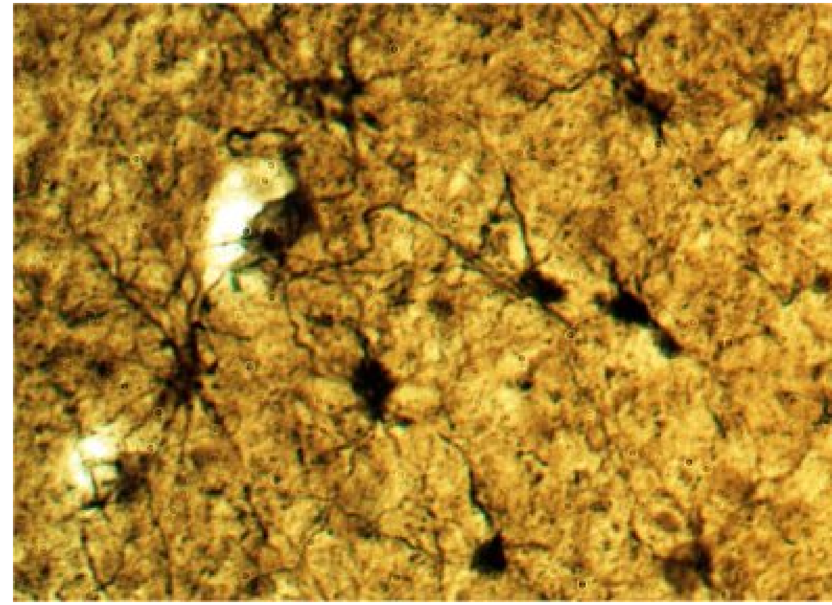
Leipzig, 22.07.2004

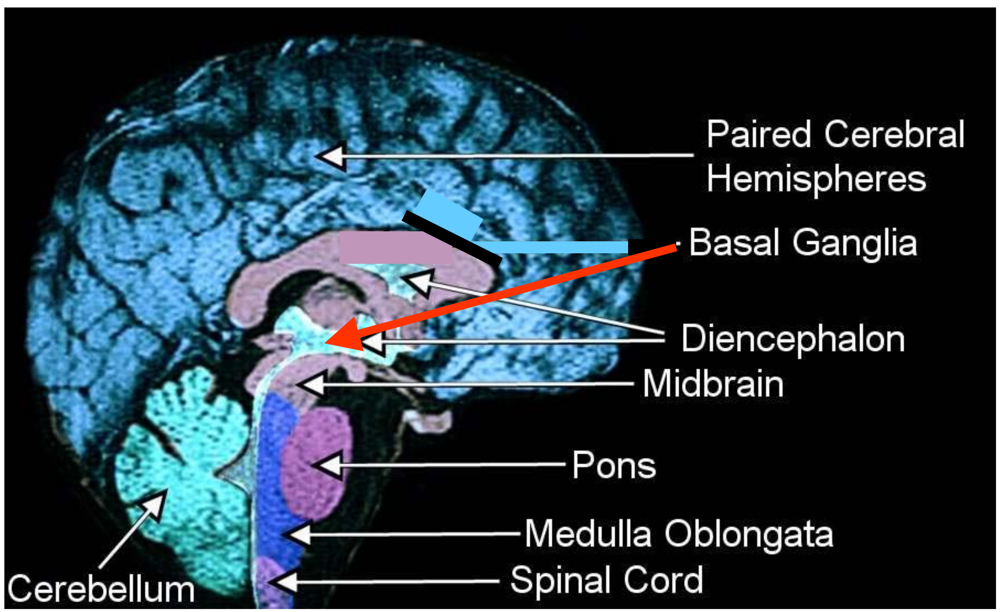
Web-Page for further information:

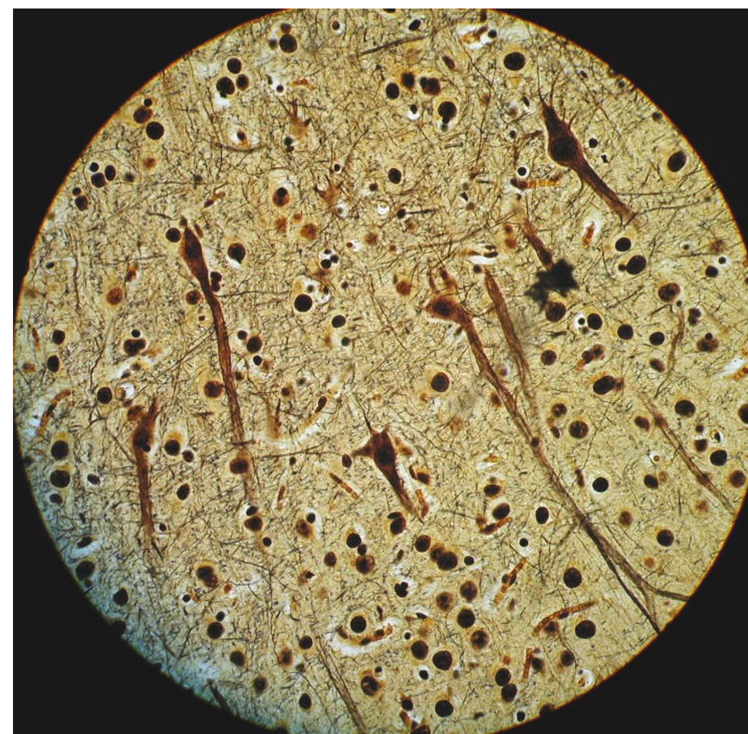
http://www.tbi.univie.ac.at/~pks

## Neurobiology

Neural networks, collective properties, nonlinear dynamics, signalling, ...





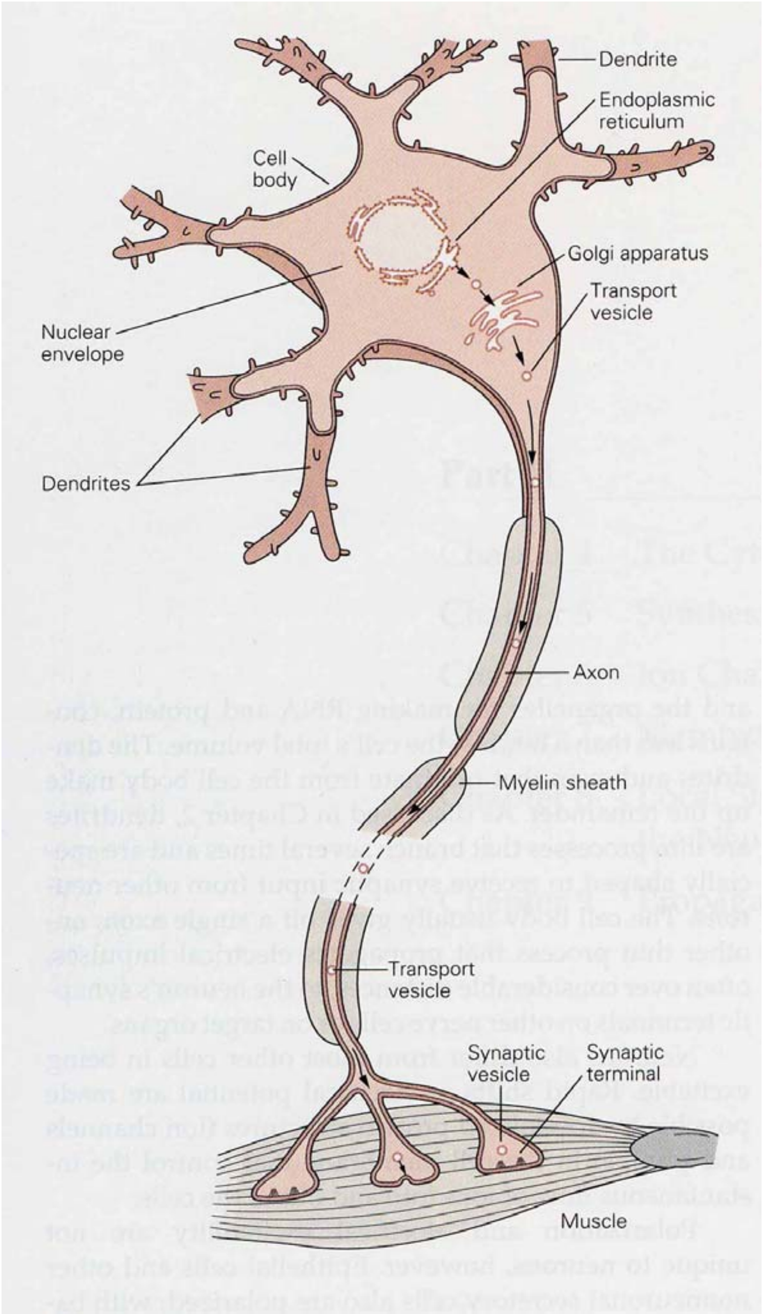



The human brain

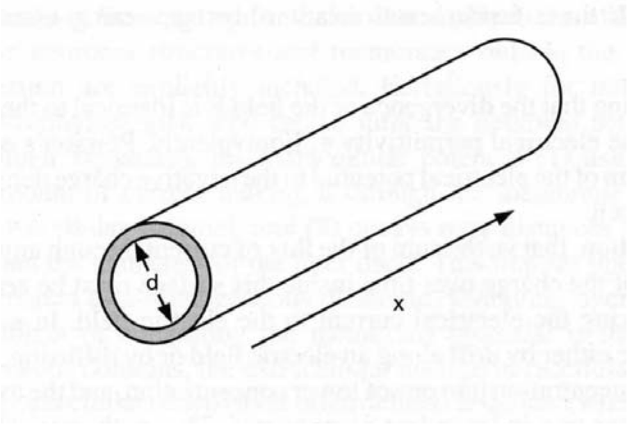
$10^{11}$ neurons connected by ≈ $10^{13}$ to $10^{14}$ synapses

# Neurobiology

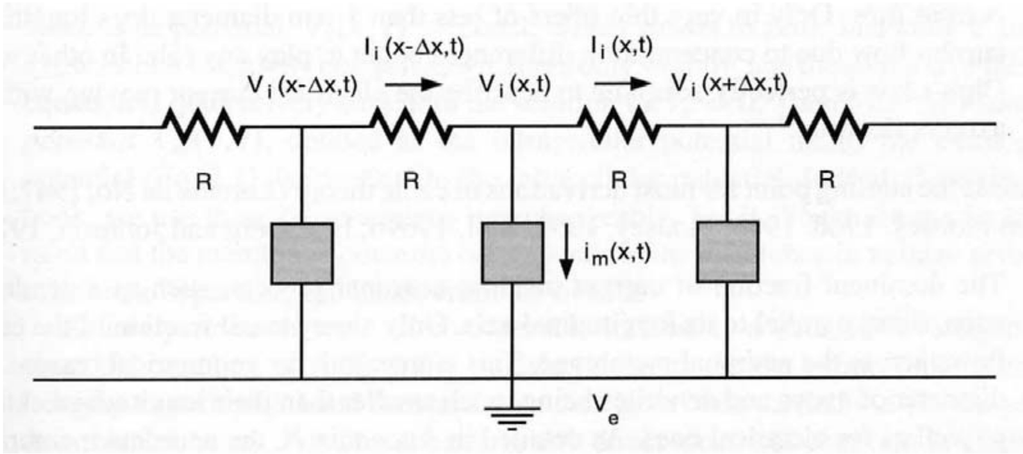
Neural networks, collective properties, nonlinear dynamics, signalling, ...




A single neuron signaling to a muscle fiber




**A**




**B**

**Fig. 2.2 Electrical Structure of a Cable** **(A)** Idealized cylindrical axon or dendrite at the heart of one-dimensional cable theory. Almost all of the current inside the cylinder is longitudional due to geometrical (the radius is much smaller than the length of the cable) and electrical factors (the membrane covering the axon or dendrite possesses a very high resistivity compared to the intracellular cytoplasm). As a consequence, the radial and angular components of the current can be neglected, and the problem of determining the potential in these structures can be reduced from three spatial dimensions to a single one. On the basis of the bidomain approximation, gradients in the extracellular potentials are neglected and the cable problem is expressed in terms of the transmembrane potential $V_m(x,t) = V_i(x,t) - V_e$. **(B)** Equivalent electrical structure of an arbitrary neuronal process. The intracellular cytoplasm is modeled by the purely ohmic resistance $R$. This tacitly assumes that movement of carriers is exclusively due to drift along the voltage gradient and not to diffusion. Here and in the following the extracellular resistance is assumed to be negligible and $V_e$ is set to zero. The current per unit length across the membrane, whether it is passive or contains voltage-dependent elements, is described by $i_m$ and the system is characterized by the second-order differential equation, Eq. 2.5.

Christof Koch, Biophysics of Computation. Information Processing in single neurons.
Oxford University Press, New York 1999.

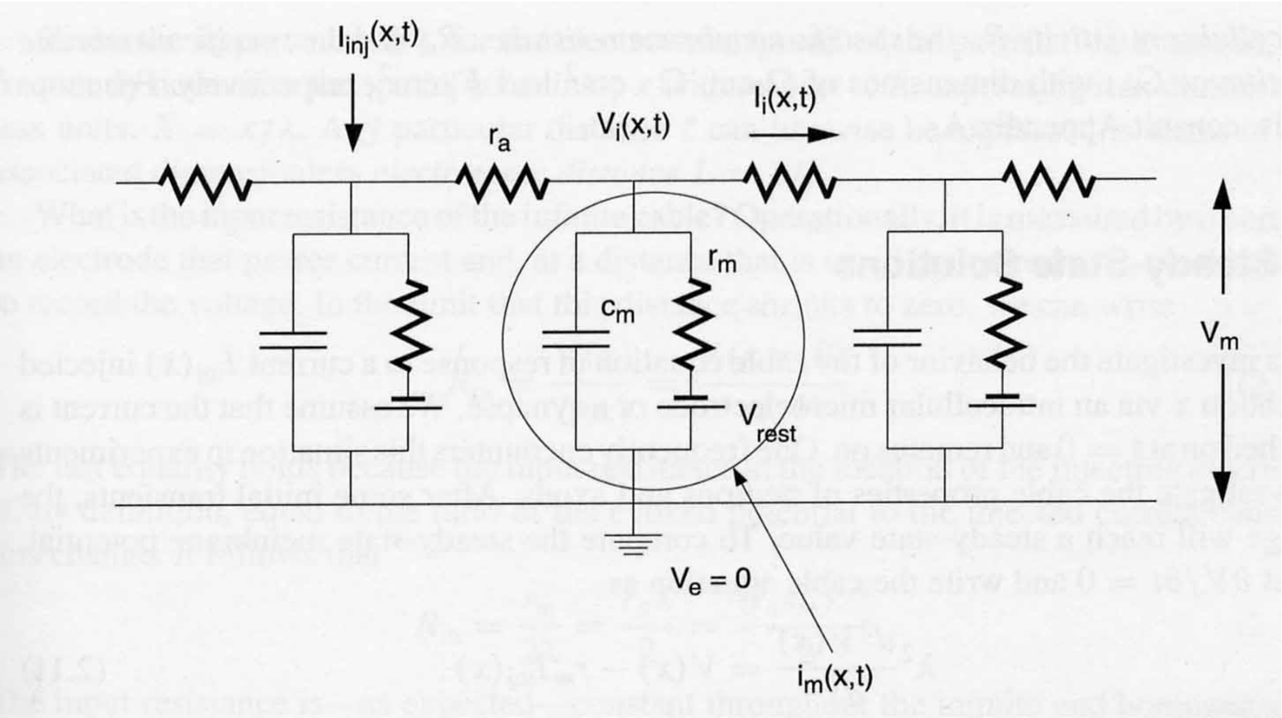



**Fig. 2.3 A Single Passive Cable** Equivalent lumped electrical circuit of an elongated neuronal fiber with passive membrane. The intracellular cytoplasm is described by an ohmic resistance per unit length $r_a$ and the membrane by a capacitance $c_m$ in parallel with a passive membrane resistance $r_m$ and a battery $V_{\text{rest}}$. The latter two components are frequently referred to as *leak resistance* and *leak battery*. An external current $I_{\text{inj}}(x,t)$ is injected into the cable. The associated linear cable equation (Eq. 2.7) describes the dynamics of the electrical potential $V_m = V_i - V_e$ along the cable.

Christof Koch, Biophysics of Computation. Information Processing in single neurons. Oxford University Press, New York 1999.

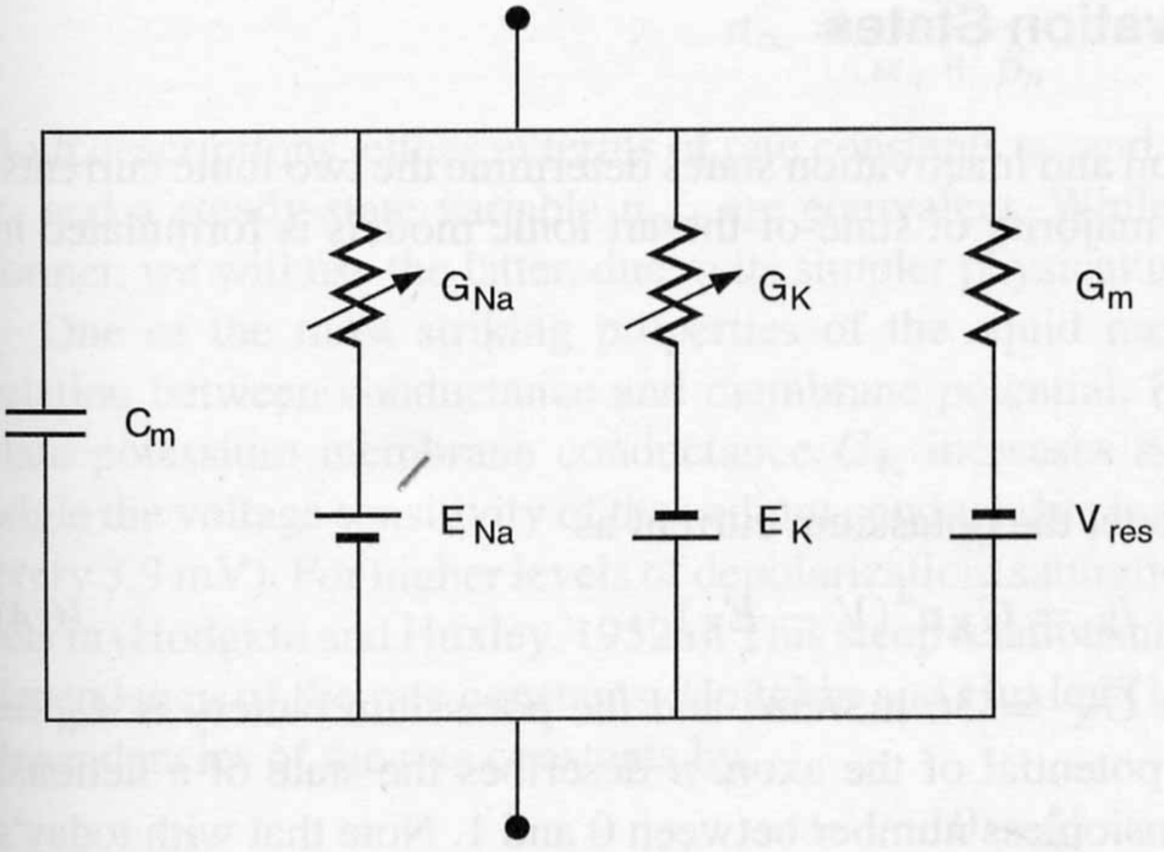
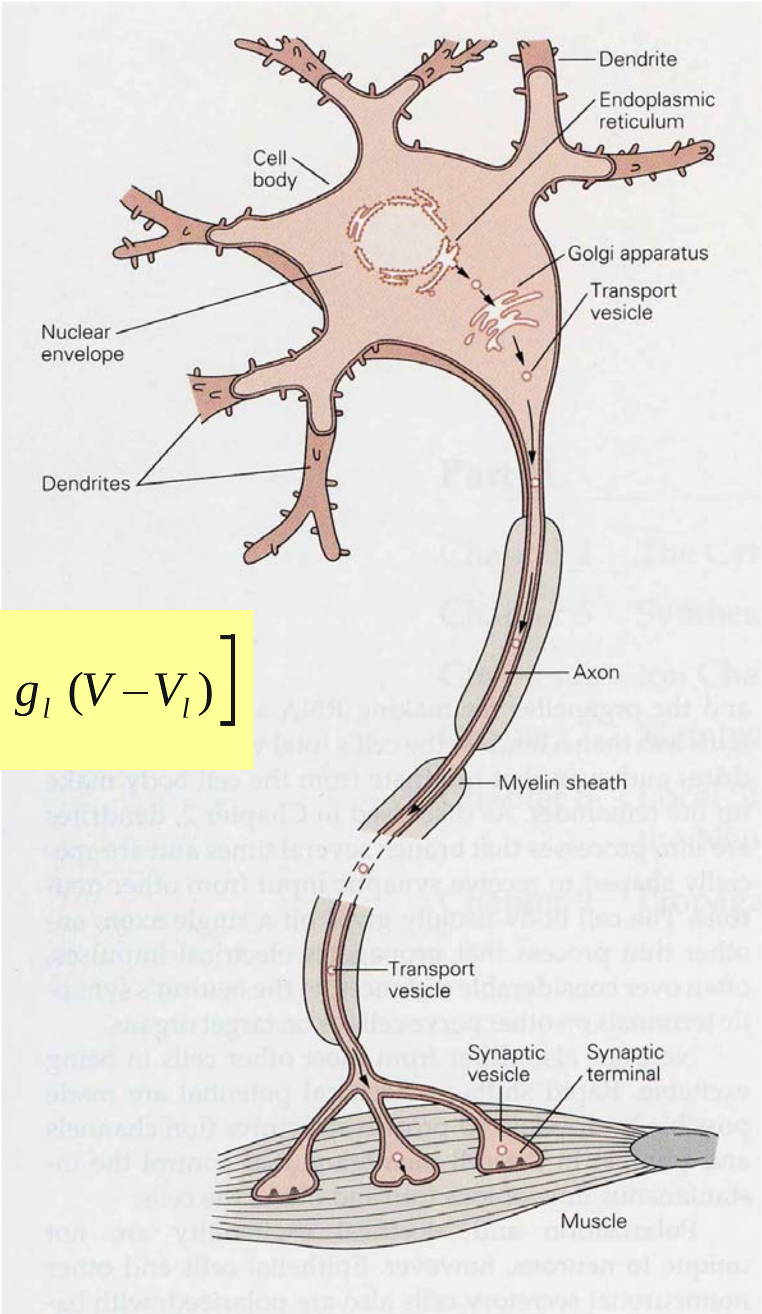



**Fig. 6.2 Electrical Circuit for a Patch of Squid Axon** Hodgkin and Huxley modeled the membrane of the squid axon using four parallel branches: two passive ones (membrane capacitance $C_m$ and the leak conductance $G_m = 1/R_m$) and two time- and voltage-dependent ones representing the sodium and potassium conductances.

Christof Koch, Biophysics of Computation. Information Processing in single neurons.
Oxford University Press, New York 1999.

**Neurobiology**

Neural networks, collective properties, nonlinear dynamics, signalling, ...




$$\frac{dV}{dt} = \frac{1}{C_M}\left[I - g_{Na} m^3 h (V - V_{Na}) - g_K n^4 (V - V_K) - g_l (V - V_l)\right]$$

$$\frac{dm}{dt} = \alpha_m (1-m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h (1-h) - \beta_h h$$

$$\frac{dn}{dt} = \alpha_n (1-n) - \beta_n n$$

Hogdkin-Huxley OD equations

A single neuron signaling to a muscle fiber

$$\alpha_m = \frac{x}{e^x - 1}, \quad x = \frac{25 - V}{10} \ ; \quad \beta_m = 4 \exp\left[-\frac{V}{18}\right]$$

$$\alpha_h = 0.07 \exp\left[-\frac{V}{20}\right] \ ; \quad \beta_h = \frac{1}{e^x - 1}, \quad x = \frac{30 - V}{10}$$

$$\alpha_n = \frac{x}{10(e^x - 1)}, \quad x = \frac{10 - V}{10} \ ; \quad \beta_n = 0.125 \exp\left[-\frac{V}{80}\right]$$

Gating functions of the Hodgkin-Huxley equations

$$\frac{\partial m}{\partial t} = \Theta(T)\left[\alpha_m(1-m) - \beta_m m\right]$$

$$\frac{\partial h}{\partial t} = \Theta(T)\left[\alpha_h(1-h) - \beta_h h\right]$$

$$\frac{\partial n}{\partial t} = \Theta(T)\left[\alpha_n(1-n) - \beta_n n\right] ,$$

$$\text{where } \Theta(T) = 3^{(T-6.3)/10}$$

Temperature dependence of the Hodgkin-Huxley equations

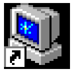
$$\frac{dV}{dt} = \frac{1}{C_M}\left[ I - \bar{g}_{Na}\, m^3 h\,(V - V_{Na}) - \bar{g}_K\, n^4\,(V - V_K) - \bar{g}_l\,(V - V_l) \right]$$

$$\frac{dm}{dt} = \alpha_m (1-m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h (1-h) - \beta_h h$$

$$\frac{dn}{dt} = \alpha_n (1-n) - \beta_n n$$

Hogdkin-Huxley OD equations



Hhsim.lnk

Simulation of space independent Hodgkin-Huxley equations:

Voltage clamp and constant current

$$\frac{1}{R}\frac{\partial^2 V}{\partial x^2} = C\frac{\partial V}{\partial t} + \left[g_{Na}\, m^3\, h(V - V_{Na}) + g_K\, n^4\,(V - V_K) + g_l\,(V - V_l)\right] 2\pi\, r\, L$$

$$\frac{\partial m}{\partial t} = \alpha_m\,(1 - m) - \beta_m\, m$$

$$\frac{\partial h}{\partial t} = \alpha_h\,(1 - h) - \beta_h\, h$$

$$\frac{\partial n}{\partial t} = \alpha_n\,(1 - n) - \beta_n\, n$$

Hodgkin-Huxley PDEquations

Travelling pulse solution: $V(x,t) = V(\xi)$ with

$$\xi = x + \theta\, t$$

Hodgkin-Huxley equations describing pulse propagation along nerve fibers

$$\frac{1}{R}\frac{d^2V}{d\xi^2} = C_M\,\theta\frac{dV}{d\xi} + \left[\,\bar{g}_{Na}\,m^3\,h(V-V_{Na}) + \bar{g}_K\,n^4\,(V-V_K) + \bar{g}_l\,(V-V_l)\right] 2\pi r L$$

$$\theta\,\frac{dm}{d\xi} = \alpha_m\,(1-m) - \beta_m\,m$$

$$\theta\,\frac{dh}{d\xi} = \alpha_h\,(1-h) - \beta_h\,h$$

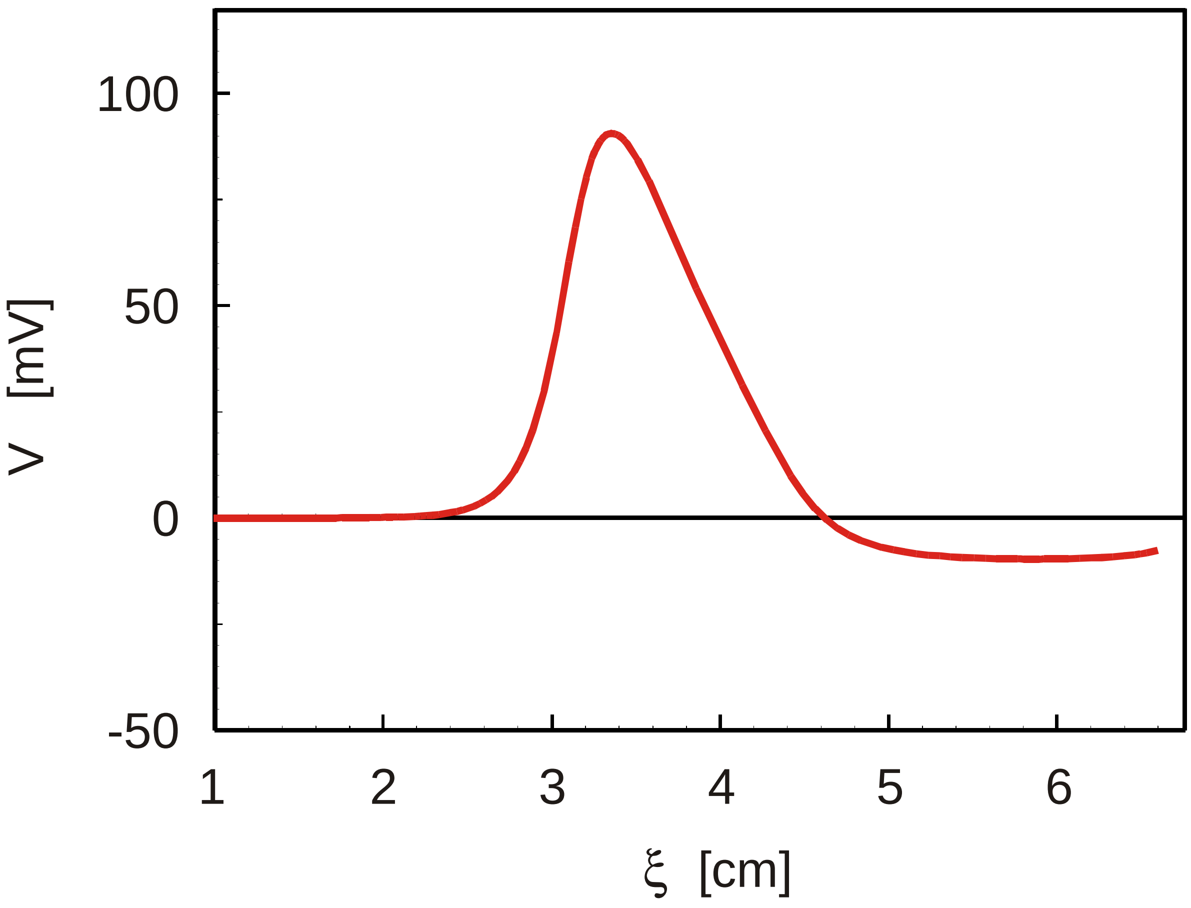
$$\theta\,\frac{dn}{d\xi} = \alpha_n\,(1-n) - \beta_n\,n$$

Hodgkin-Huxley PDEquations

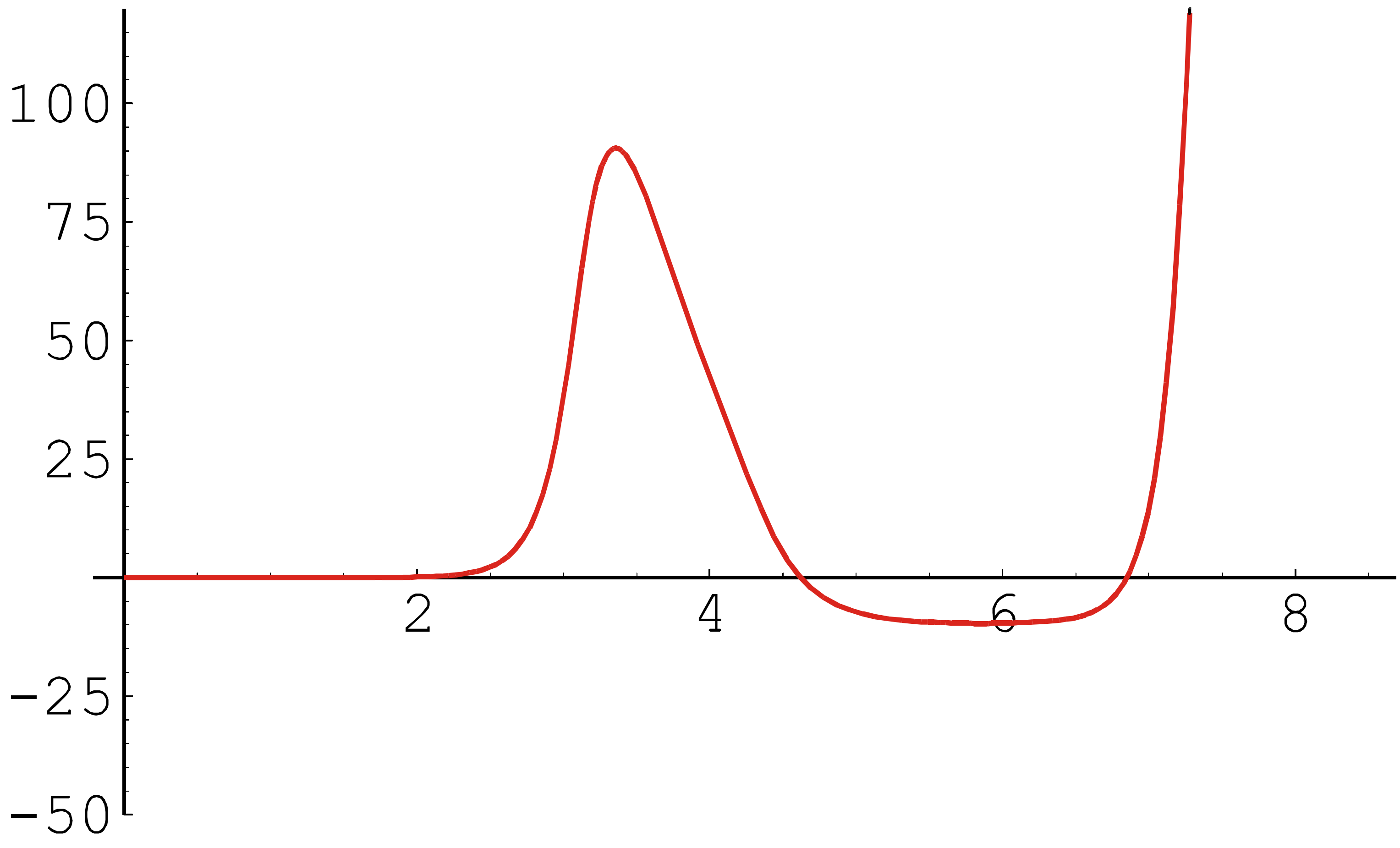
Travelling pulse solution: $V(x,t) = V(\xi)$ with

$$\xi = x + \theta\,t$$

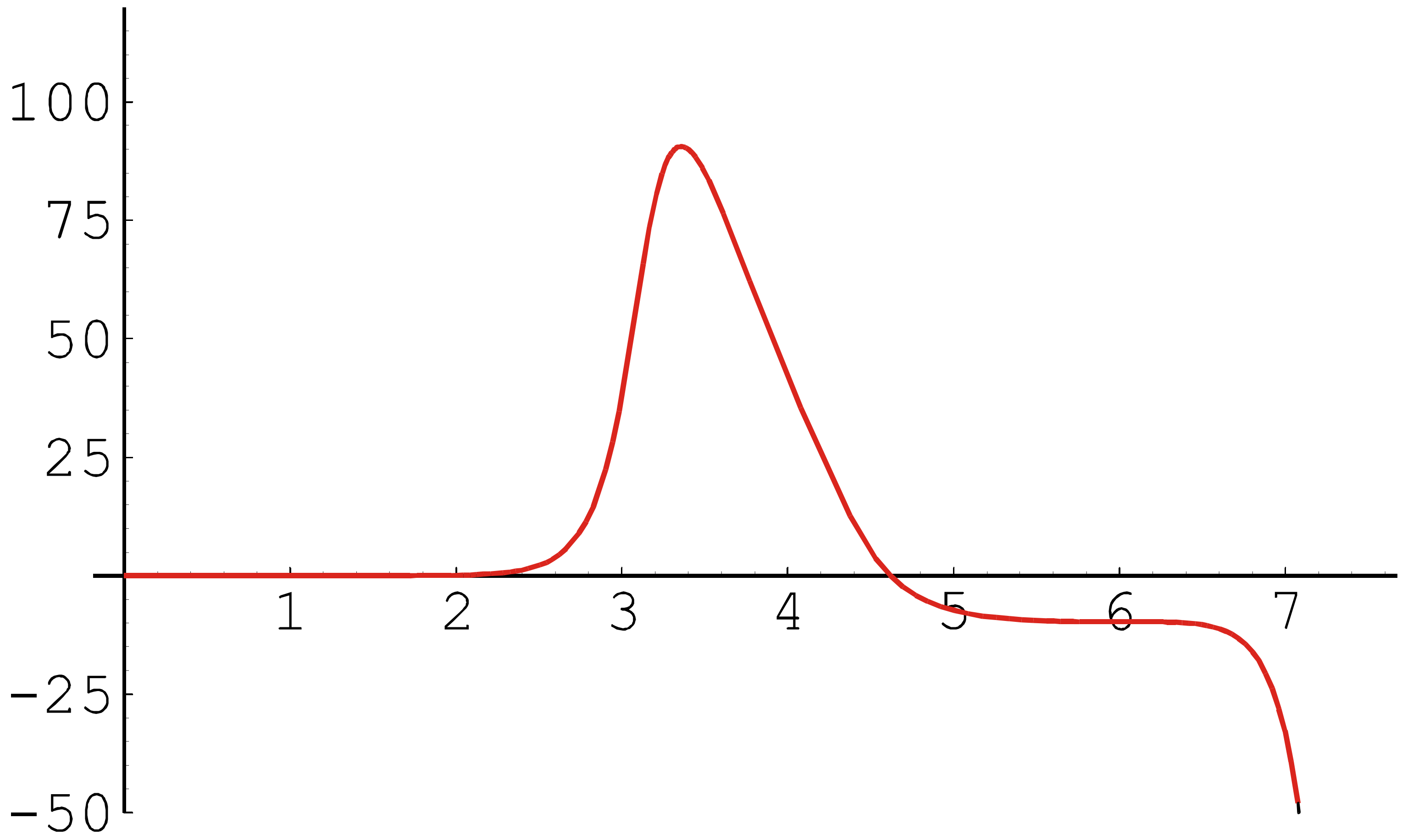
Hodgkin-Huxley equations describing pulse propagation along nerve fibers



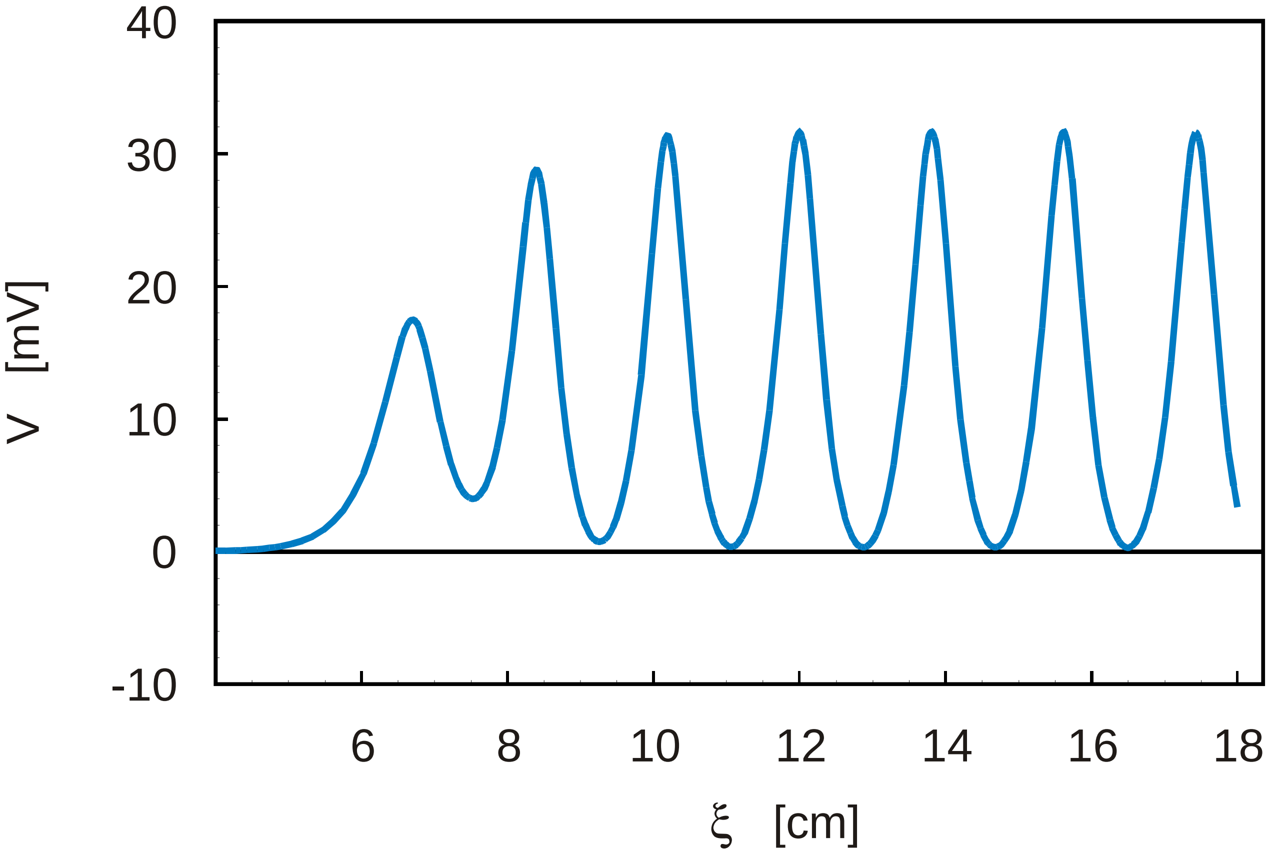

T = 18.5 C; θ = 1873.33 cm / sec



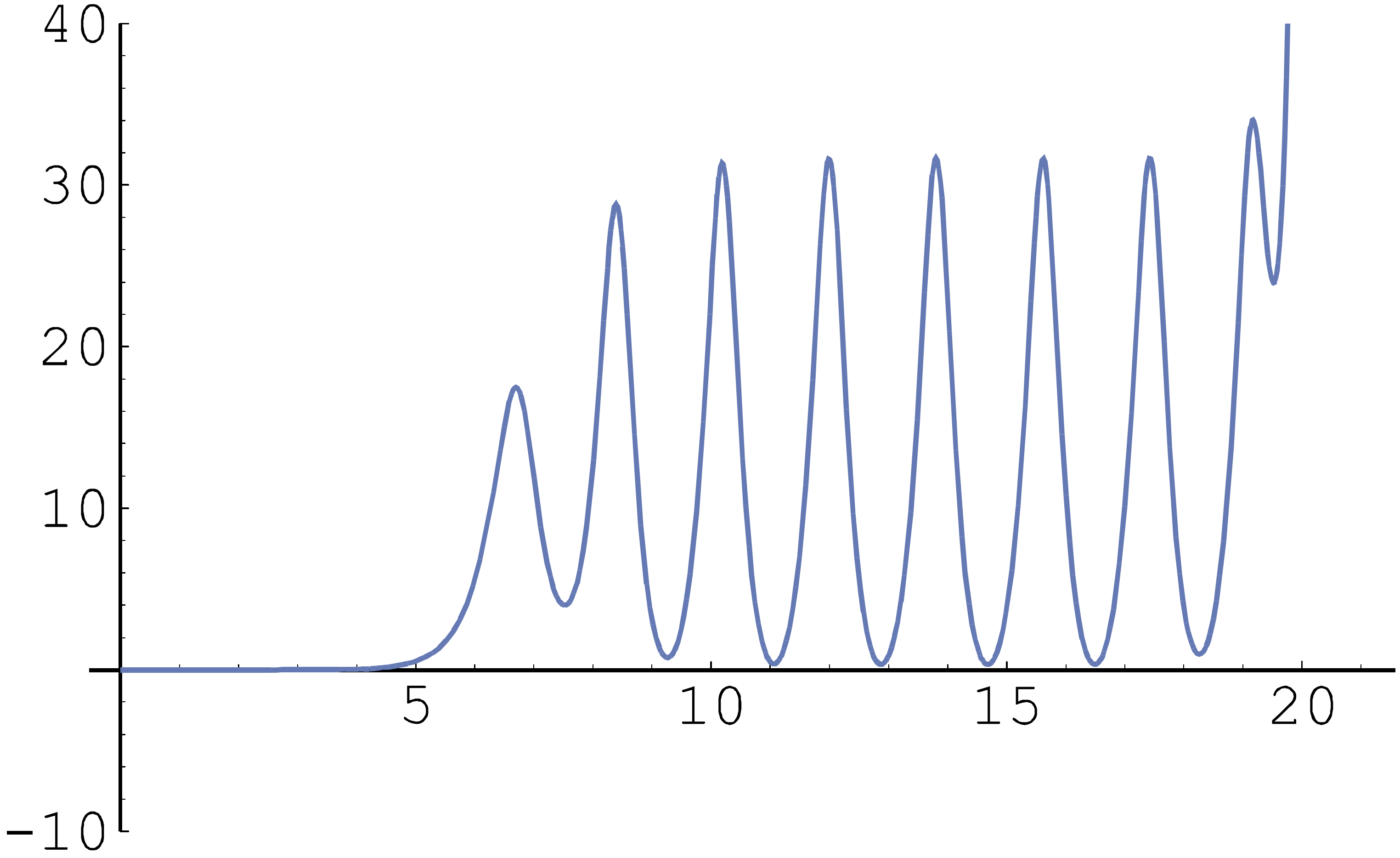

T = 18.5 C; θ = 1873.3324514717698 cm / sec



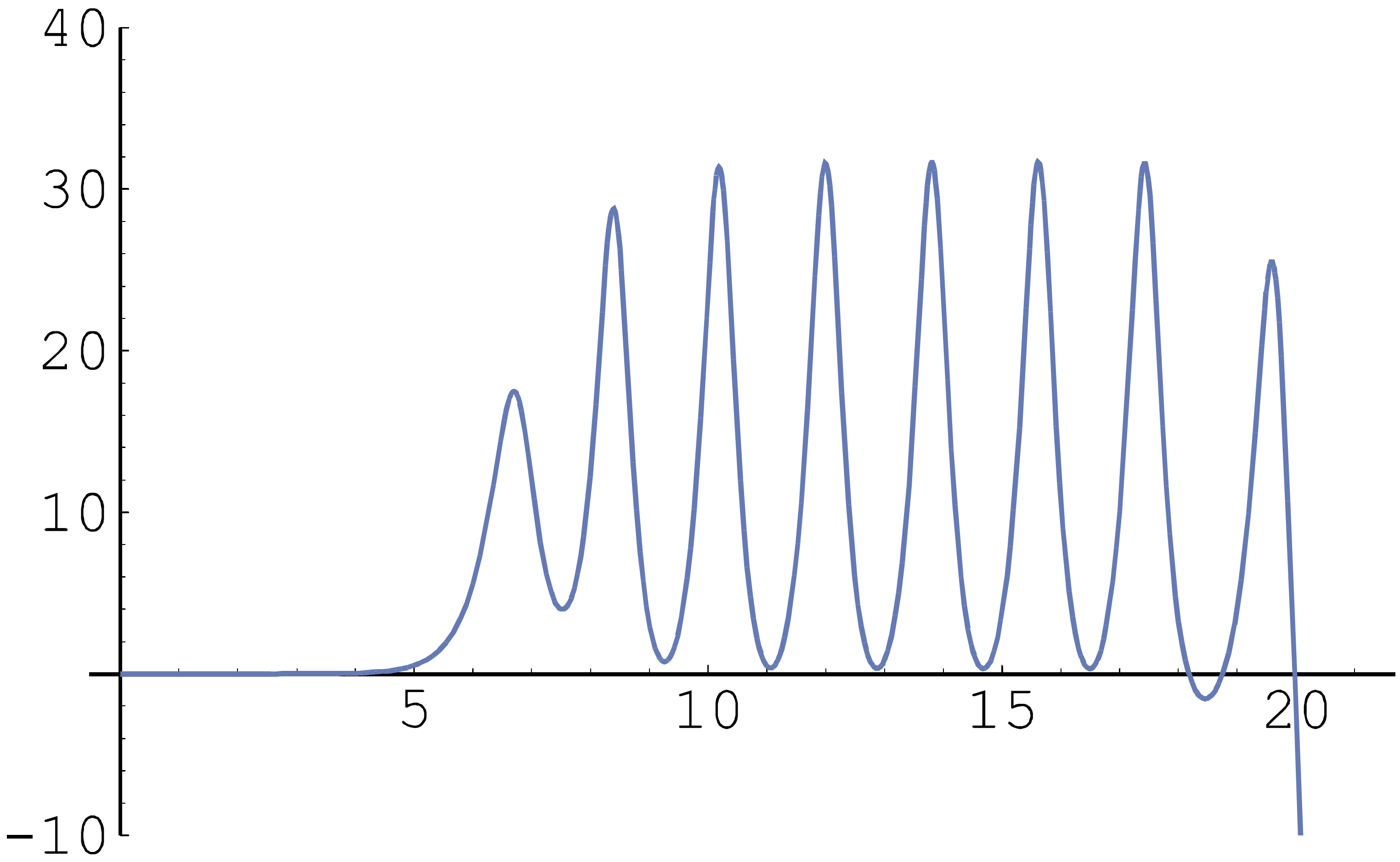

T = 18.5 C; θ = 1873.3324514717697 cm / sec



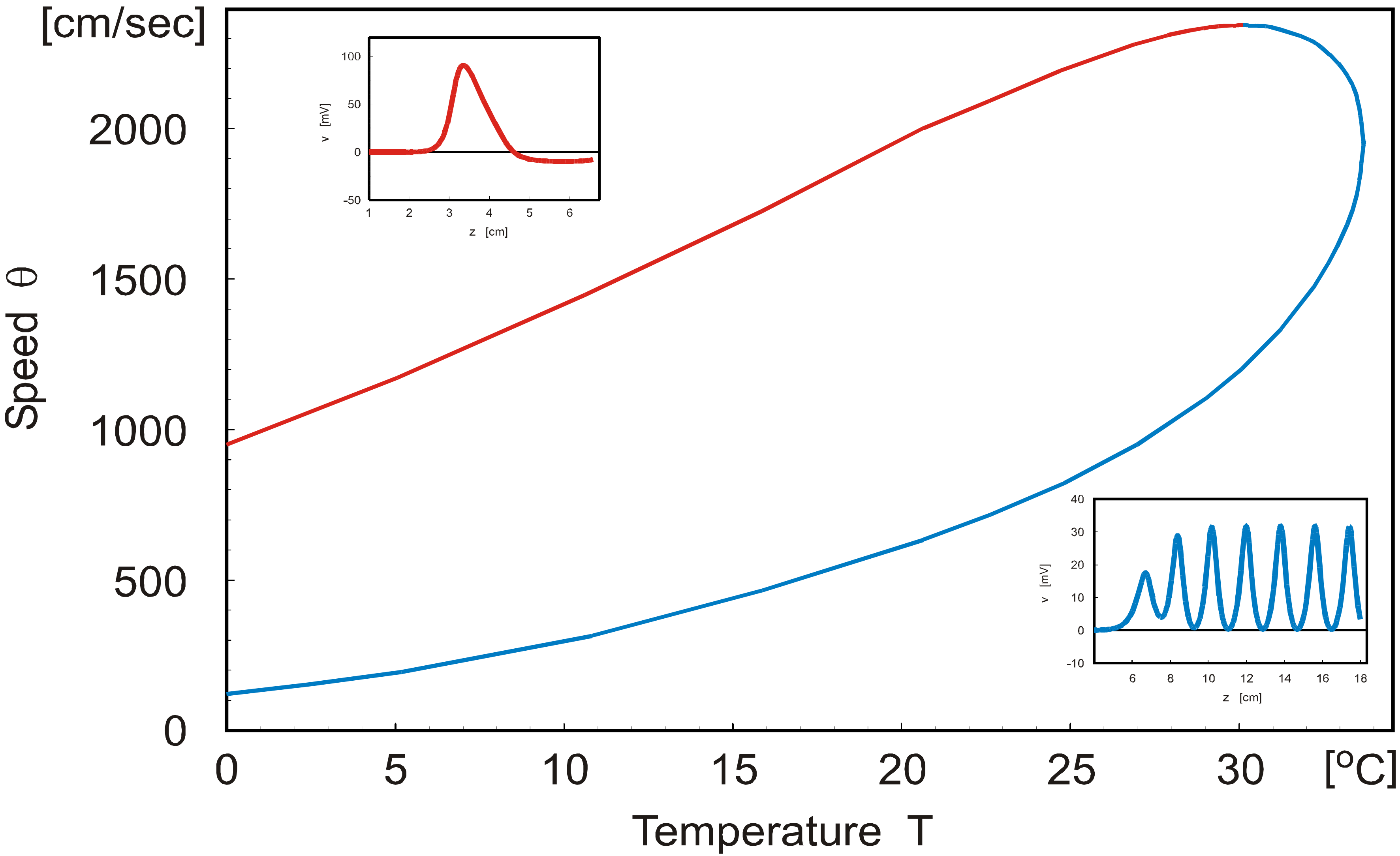

T = 18.5 C; θ = 544.070 cm / sec




T = 18.5 C; θ = 554.070286919319 cm/sec




T = 18.5 C; θ = 554.070286919320 cm/sec




Propagating wave solutions of the Hodgkin-Huxley equations

## FitzHugh-Nagumo Equations

$$\frac{\partial V'}{\partial t'} = -V'(V'-a)(V'-1) - Y - \frac{\partial^2 V'}{\partial x'^2}$$
$$\frac{\partial Y'}{\partial t'} = bV' \text{ all quantities dimensionaless}$$
$$\frac{d}{d\zeta}\left[\frac{d^2V'}{d\zeta^2} - c\frac{dV'}{d\zeta} - V'(V'-a)(V'-1)\right] - \frac{b}{c}V' = 0, \text{ with } \zeta = x' + ct'$$
$$c(a, b=0) = \frac{1}{\sqrt{2}}(1-2a) - \text{Propagation of the Pulse Front}$$
$$c(a,b) < c(a,0) \text{ Front slows down to shape the back of the pulse}$$

The good news: The pulse, stationary in the frame of $\zeta$, is now described by an ordinary third order differential equation. The bad news is that the result is a structurally unstable homoclinic orbit, which is why calculations take a bit of care. We have found an analytic expression for $c(a,b)$.

Connection to Hodgkin-Huxley: $[h,n]$ are relatively slow variables, so keep them at resting values. This results in a contracted two-dimensional Hodgkin-Huxley $[V,m]$ system which describes the pulse front at the full speed $\theta$ to very close approximation. The two descriptions are now equivalent under the transformations

$$D = \frac{r}{2R_2C_m} \ [336 \ \frac{\text{cm}^2}{\text{sec}}] \quad \Gamma = \sqrt{\frac{G_{\text{Na}}h(0)}{C_mD}} \ [14.5876 \ \text{cm}^-1]$$
$$V' = \frac{V}{E_{\text{Na}}}, E_{\text{Na}} = 115 \ \text{mv}, \ \zeta = \Gamma z, \ c = \frac{\theta}{\Gamma D} \ [\Gamma D = 4903 \ \frac{cm}{sec}$$

Advantage: Provides a bridge between between detailed Hodgkin-Huxley based conductance models and formal spiking models which dispense with such details [a pulse is regarded as a delta-function-like spike].

$$\frac{\partial V}{\partial t} = -V(V-a)(V-1) - Y + \frac{\partial^2 V}{\partial x^2}$$

$$\frac{\partial Y}{\partial t} = bV - \epsilon Y \quad \text{where } 0 \le a \le \frac{1}{2}$$

$$\epsilon = 0: \quad \frac{d}{d\xi}\left(\frac{d^2V}{d\xi^2} - \theta\frac{dV}{d\xi} - V(V-a)(V-1)\right) - \frac{b}{\theta}V = 0$$

FitzHugh-Nagumo model of the Hodgkin-Huxley equations

V ...... potential ; Y ...... refractory variable

$$\frac{d^2V}{d\tau^2} = -k(V-q_1)(V-q_2)\frac{dV}{d\tau} + \Big[I' - V\Big] - \frac{\epsilon}{b}\Big[V(V-a)(V-1)\Big]$$

$$\text{with } q_{1,2} \equiv \frac{1}{3}\Big[(a+1) \mp \sqrt{(a+1)^2 - 3(a+\epsilon)}\Big],\ \ k \equiv \frac{3}{\sqrt{b}},\ \ I' \equiv \frac{\epsilon}{b}I,\ \ \tau = \sqrt{b}\,t$$

FitzHugh – Nagumo Equation

$$\longrightarrow \qquad \frac{d^2V}{d\tau^2} = -k(V-q_1)(V-q_2)\frac{dV}{d\tau} + I' - V$$

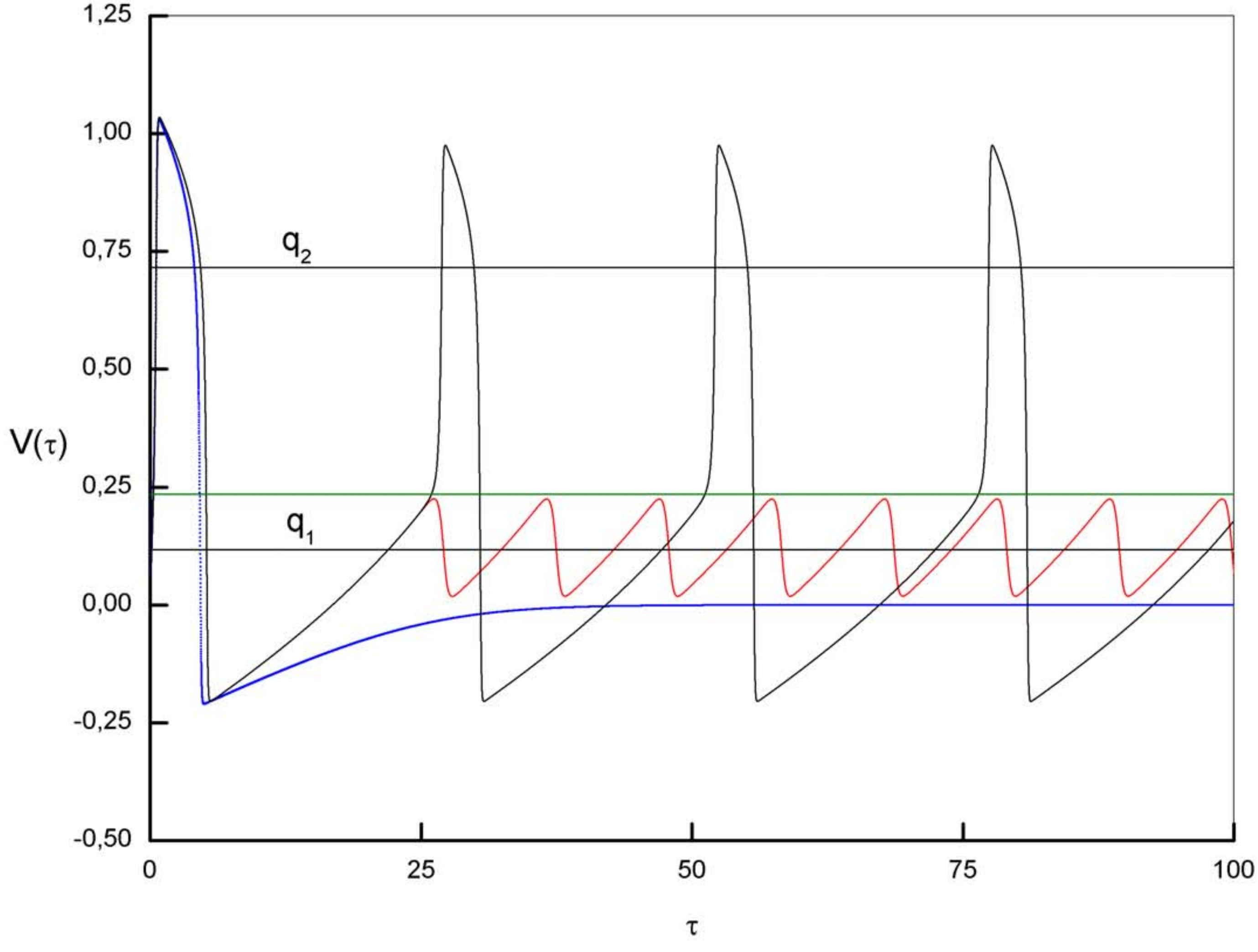
Reduced Model

$$\longrightarrow \qquad \frac{d^2V}{d\tau^2} + \sigma k'\frac{dV}{d\tau} + V = I' \ \text{ with } \Big[k' = kf(V_{\min}) = \frac{k}{4}(q_1 - q_2)^2\Big]$$

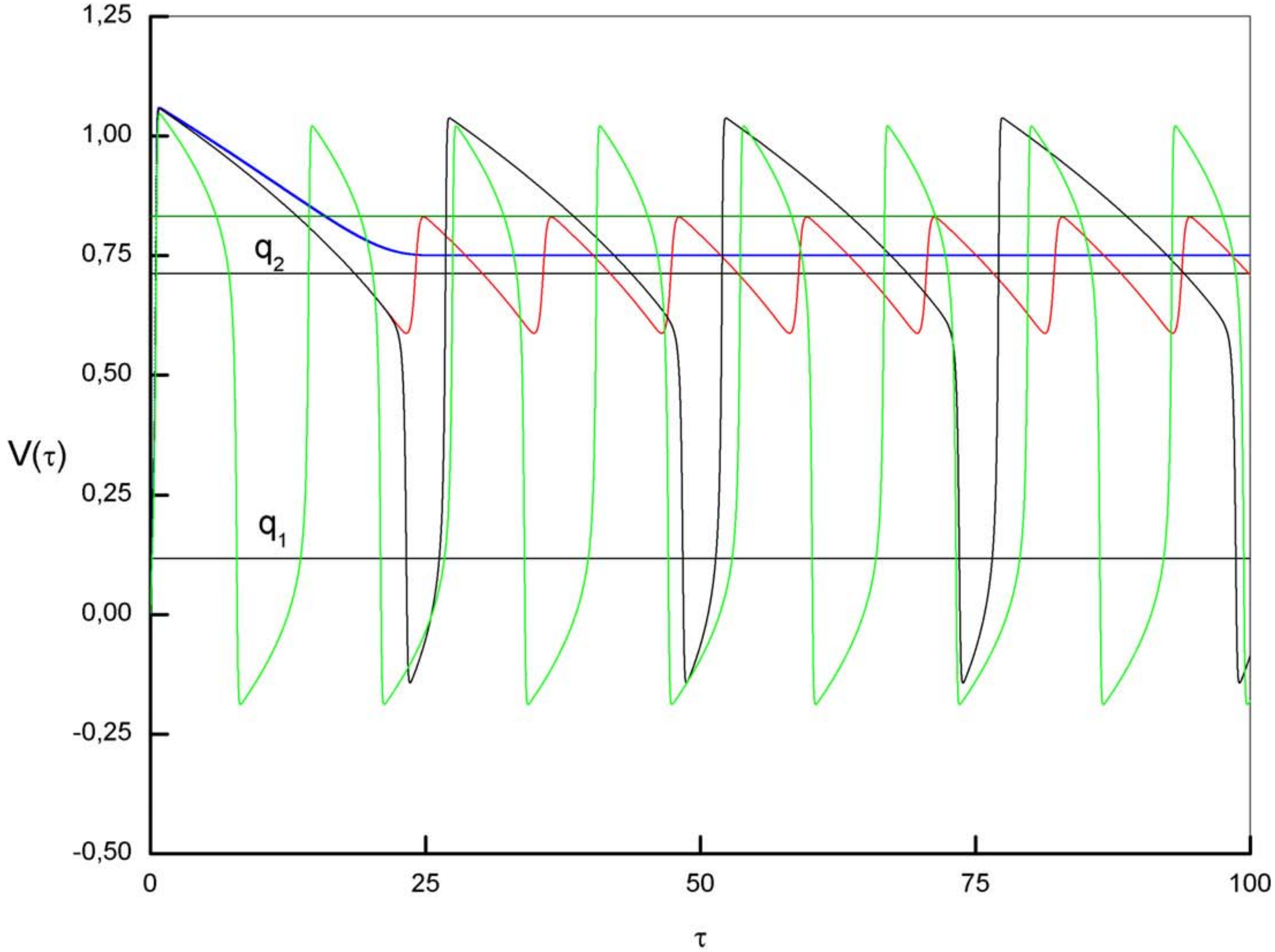
$$\text{and } \Big[\sigma = -1 \text{ for } q_1 < V < q_2,\ \ \sigma = +1 \text{ otherwise}\Big]$$

Reduced Broken – Linear Model

FitzHugh-Nagumo model and ist approximations




FitzHugh-Nagumo equation: reduced model




FitzHugh-Nagumo equation: reduced model

$$\frac{d^2V}{d\tau^2} = -k(V-q_1)(V-q_2)\frac{dV}{d\tau} + \Big[I' - V\Big] - \frac{\epsilon}{b}\Big[V(V-a)(V-1)\Big]$$

$$\text{with } q_{1,2} \equiv \frac{1}{3}\Big[(a+1) \mp \sqrt{(a+1)^2 - 3(a+\epsilon)}\Big], \;\; k \equiv \frac{3}{\sqrt{b}}, \;\; I' \equiv \frac{\epsilon}{b}I, \;\; \tau = \sqrt{b}\,t$$

$$\text{FitzHugh} - \text{Nagumo Equation}$$

$$\longrightarrow \qquad \frac{d^2V}{d\tau^2} = -k(V-q_1)(V-q_2)\frac{dV}{d\tau} + I' - V$$

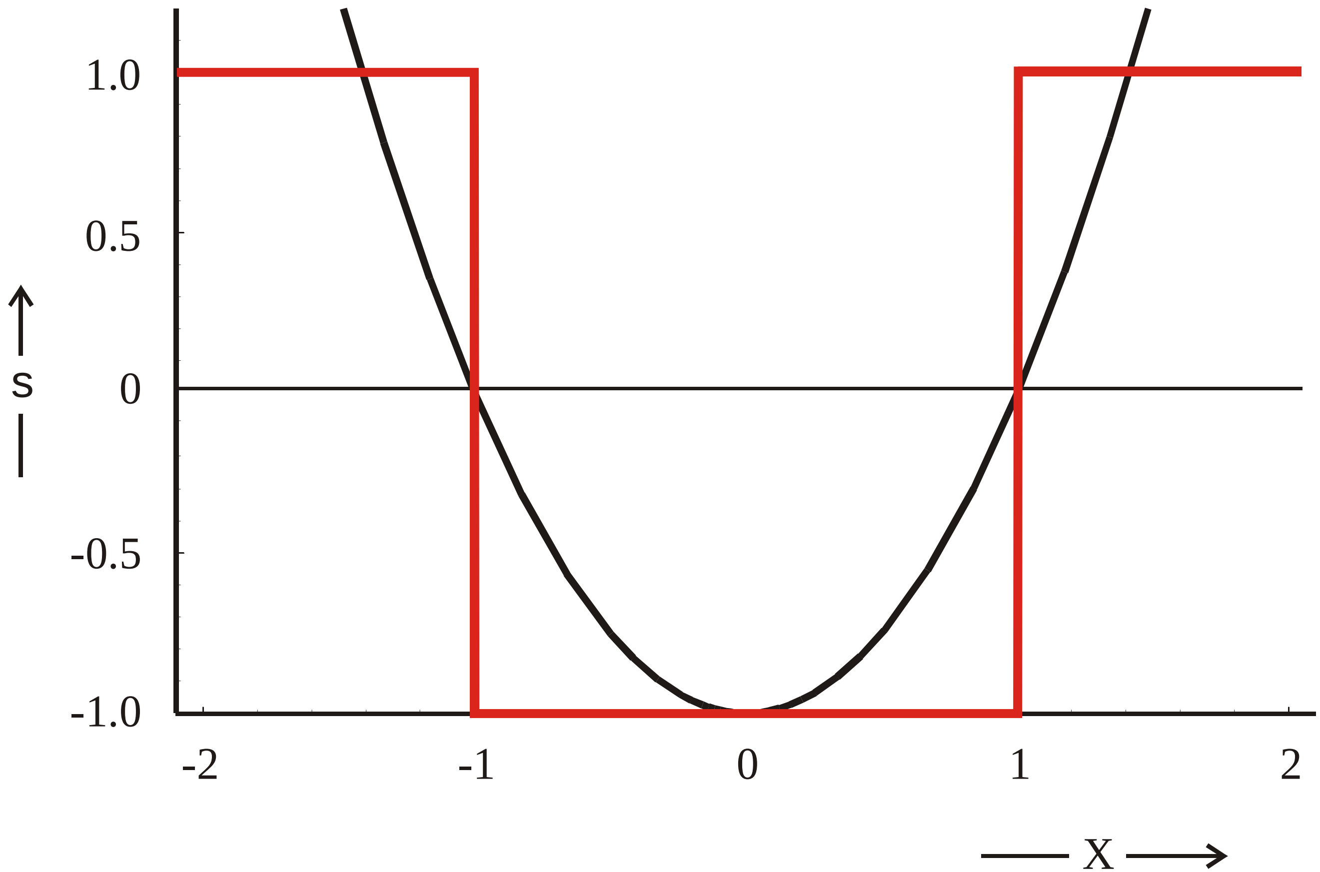
$$\text{Reduced Model}$$

$$\longrightarrow \qquad \frac{d^2V}{d\tau^2} + \sigma k'\frac{dV}{d\tau} + V = I' \text{ with } \Big[k' = kf(V_{\min}) = \frac{k}{4}(q_1 - q_2)^2\Big]$$

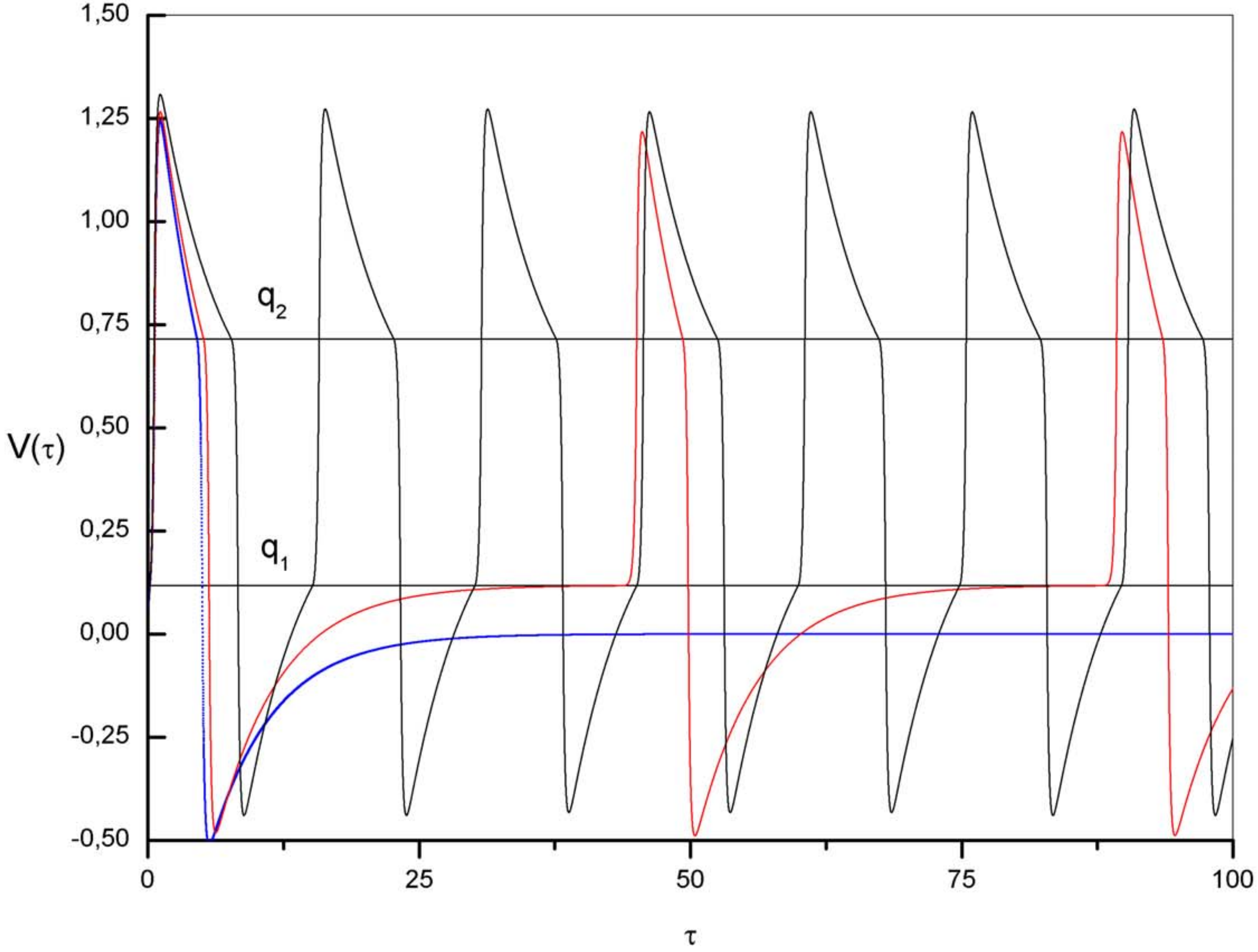
$$\text{and } \Big[\sigma = -1 \text{ for } q_1 < V < q_2, \;\; \sigma = +1 \text{ otherwise}\Big]$$

$$\text{Reduced Broken} - \text{Linear Model}$$

FitzHugh-Nagumo model and ist approximations



1.0
0.5
0
-0.5
-1.0
s
-2
-1
0
1
2
X




FitzHugh-Nagumo equation: broken linear model

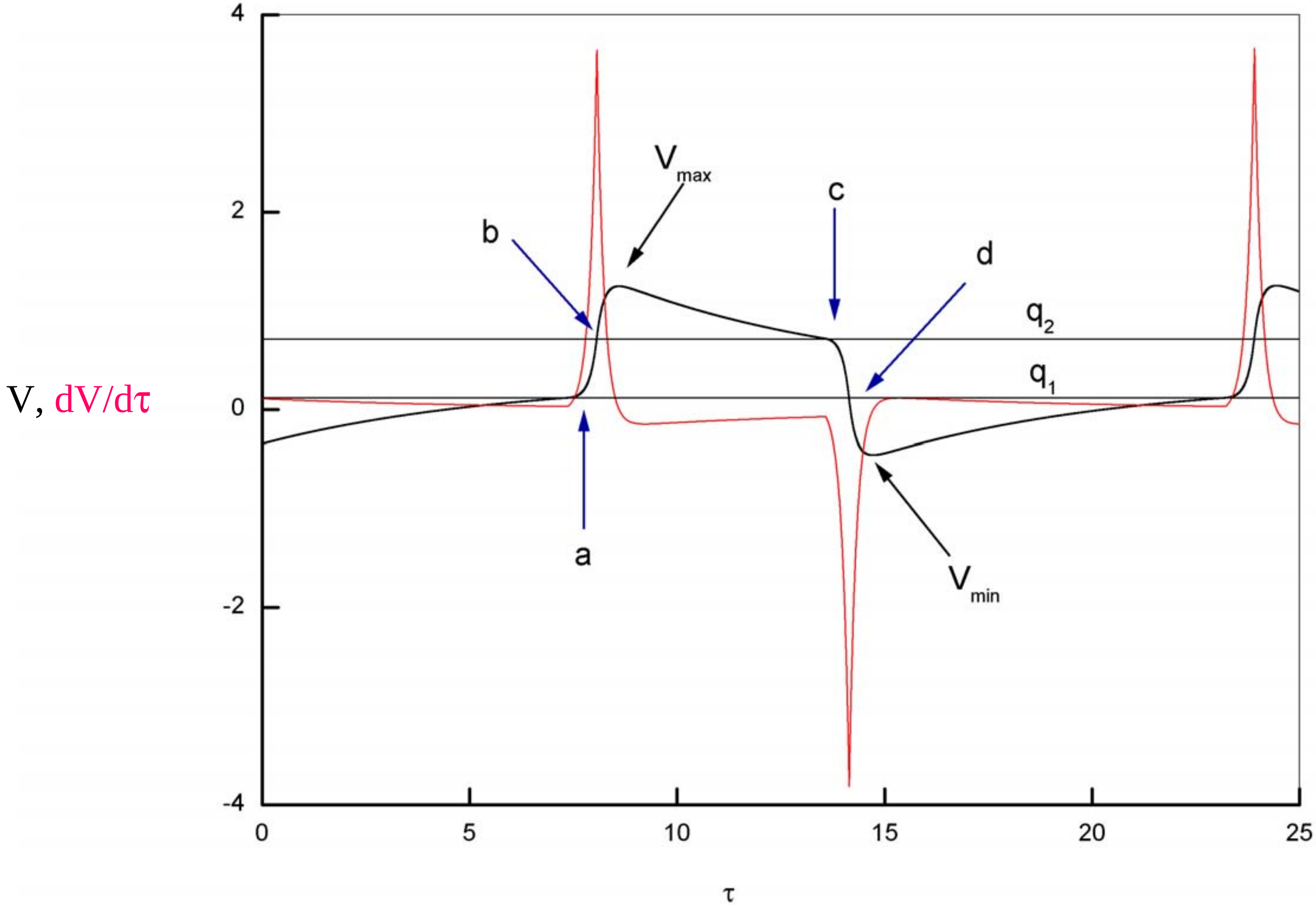
$$x(\tau) = \frac{v(0) - s_2(\sigma)x(0)}{s_1(\sigma) - s_2(\sigma)} \exp(s_1(\sigma)\tau) + \frac{s_1(\sigma)x(0) - v(0)}{s_1(\sigma) - s_2(\sigma)} \exp(s_2(\sigma)\tau)$$

$$s_1(-1) = p_1, s_2(-1) = p_2 \;\; [q_1 < V < q_2],$$

$$s_1(1) = -p_2, s_2(1) = -p_1 \;\; [\text{otherwise}]$$

$$p_1 = \frac{1}{2}[k' + \sqrt{(k')^2 - 4}], \;\; p_2 = \frac{1}{2}[k' - \sqrt{(k')^2 - 4}],$$

$$\text{with} \;\; p_1 + p_2 = k', \;\; p_1 p_2 = 1$$




Close-up of the relaxation oscillation as used in the calculations of period and pulse amplitude in the Reduced Broken-Linear Model

$$T(I') \to k' \ln\left[\frac{(2q_2 - q_1 - I')(I' + q_2 - 2q_1)}{(q_2 - I')(I' - q_1)}\right],$$

$$\text{where } k' = \frac{3}{4\sqrt{b}}(q_1 - q_2)^2$$

$$V_{\max} = 2q_2 - q_1, \; V_{\min} = 2q_1 - q_2 \text{ if } q_1 < I' < q_2$$

$$\frac{d}{d\xi}\left(\frac{d^2V}{d\xi^2} - \theta\frac{dV}{d\xi} - V(V-a)(V-1)\right) - \frac{b}{\theta}V = 0$$

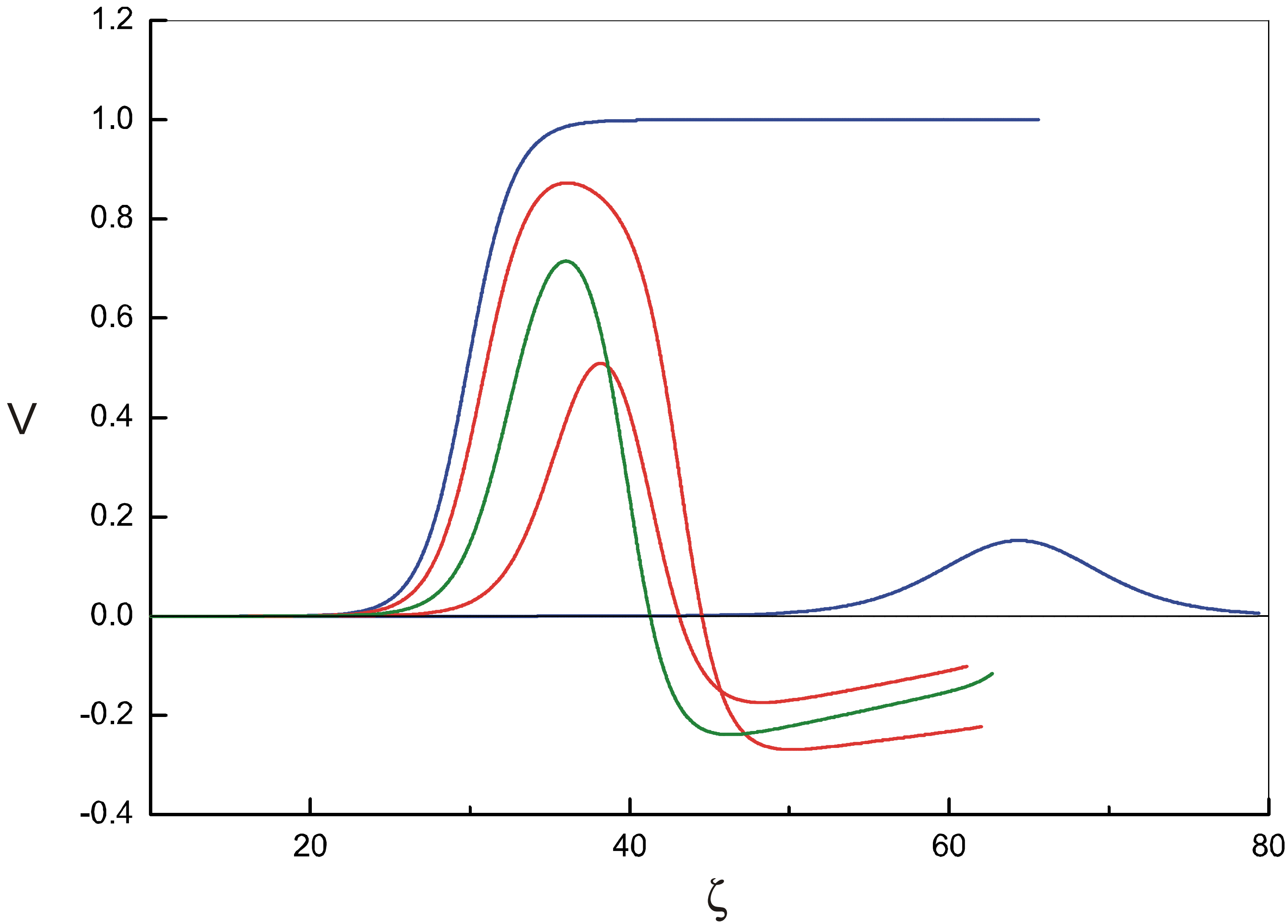
FitzHugh-Nagumo pulse propagation

$$D\frac{d^2V}{d\xi^2} - \theta\frac{dV}{d\xi} - \frac{g_{\mathrm{Na}}}{C_m}\,h(0)\,m^3(V - E_{\mathrm{Na}}) = 0, \quad D = \frac{r}{2R_2C_m}\ ,$$

$$\theta\frac{dm}{d\xi} = \Theta(T)\left\{\left[\alpha_m(V) - \alpha_m(0)\right] - \left[\alpha_m(V) + \beta_m(V)\right]m\right\},\ m(0) = 0\ .$$

Reduced Hodgkin-Huxley equations

*V* , *m* ...... fast variables, *n* , *h* ...... *slow variables*



1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
V
20
40
60
80
ζ

$$\theta = \frac{(\lambda_o^2 - a) + \sqrt{(\lambda_o^2 - a)^2 - 4b}}{2\lambda_o} \quad \text{where}$$

$$\lambda_o = \left\{ \frac{\left[11\Gamma + 2(4 + 3\Gamma a)\right] + (4 + 3\Gamma)(1 - 2a)\sqrt{1 - \frac{8(2+7\Gamma)b}{(2\Gamma-1)(1-2a)^2}}}{4(2 + 7\Gamma)} \right\}^{\frac{1}{2}}$$

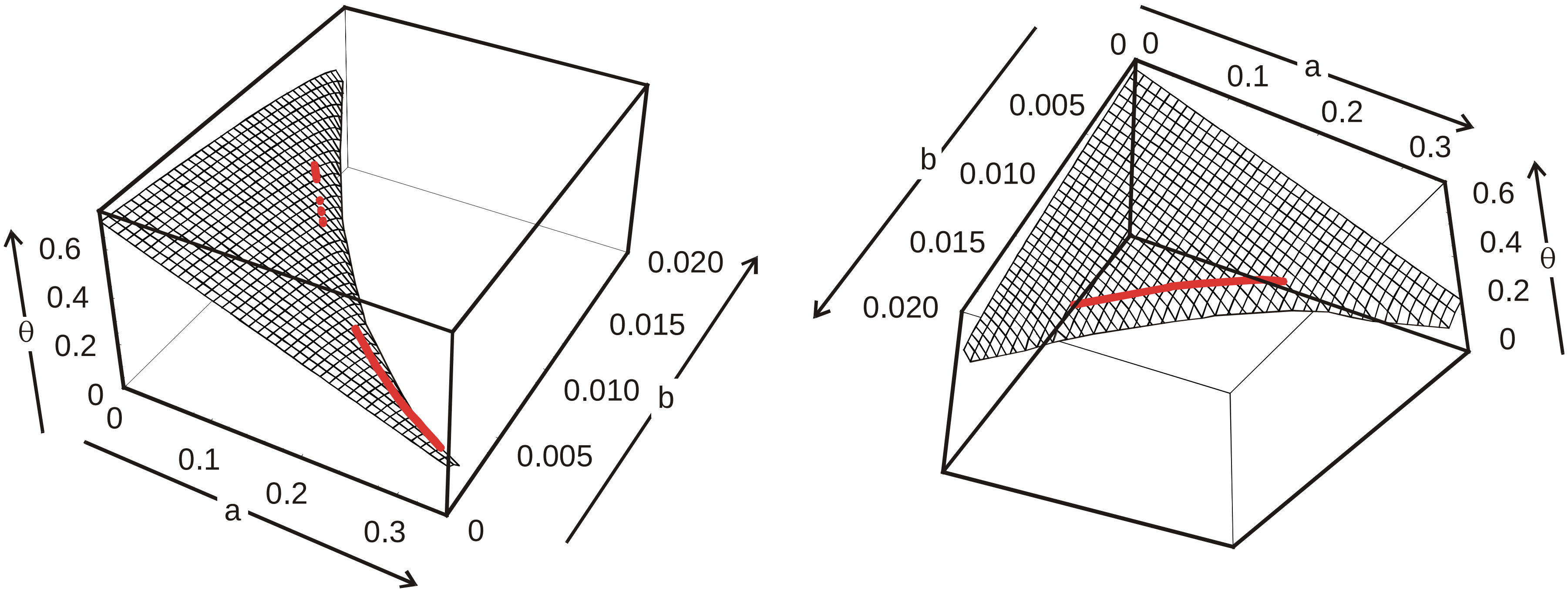
$$\Gamma(u_o) = \frac{\left[1 + \frac{u_o^2}{11}\right] + \left[\frac{(4-2a)u_o - 2(1+a)}{3(1+2a)}\right] \ln\left[1 + \frac{3(1+2a)u_o}{2(1+a)}\right]}{u_o + \frac{2u_o^2}{11}}$$

$$\approx 1.5177 - 2.1590a + 1.4419a^2 \quad \text{with the parameter restrictions}$$

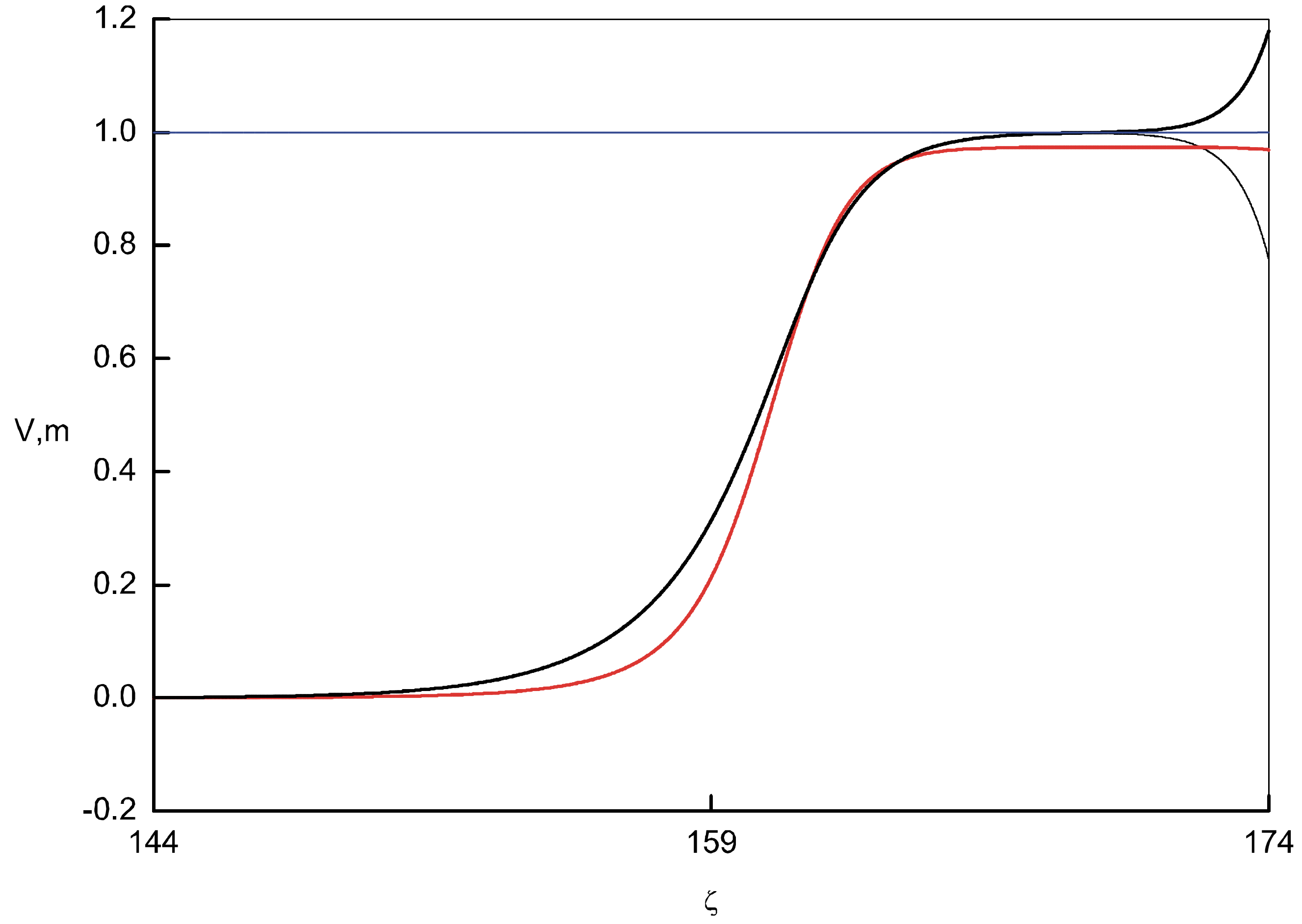
$$0 \le a < \frac{1}{2} \qquad \text{and} \qquad 0 \le b \le b^* = \frac{(2\Gamma - 1)(1 - 2a)^2}{8(2 + 7\Gamma)} \; ,$$

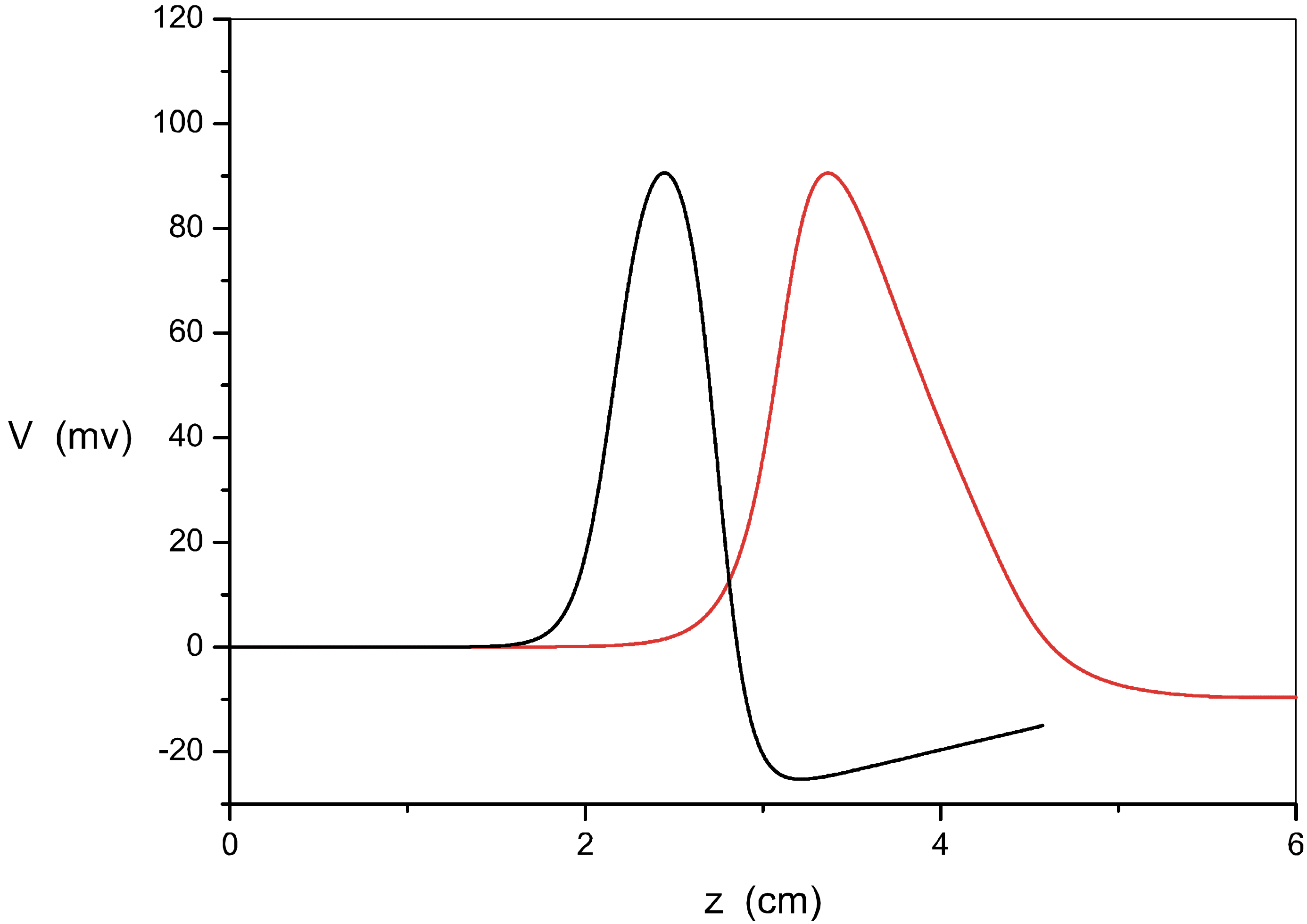
and $u_o$ is the real root of the cubic equation

$$18(1 - a)(1 + 2a)^2 u_o^3 + 9(1 + 2a)(3 - 4a - 8a^2)u_o^2 -$$
$$- (10 + 80a + 88a^2)(1 + a)u_o - 16(1 + a)^3 = 0 \; .$$



0.6
0.4
θ
0.2
0
0
0.1
0.2
a
0.3
0
0.005
0.010
b
0.015
0.020
0
0
a
0.1
0.2
0.3
0.005
b
0.010
0.015
0.020
0.6
0.4
θ
0.2
0


1.2
1.0
0.8
0.6
0.4
0.2
0.0
-0.2
V,m
144
159
174
ζ



120
100
80
60
40
20
0
-20
V (mv)
0
2
4
6
z (cm)

**References**

Paul E. Phillipson, Peter Schuster, ***Dynamics of relaxation oscillations***, *Int.J.Bifurcation and Chaos* **11**:1471-1481, 2001

Paul E. Phillipson, Peter Schuster, ***Bistability of harmonically forced relaxation oscillations***, *Int.J.Bifurcation and Chaos* **12**:1295-1307, 2002

Paul E. Phillipson, Peter Schuster, ***An analytic picture of neuron oscillations***, *Int.J.Bifurcation and Chaos* **14**:1539-1548, 2004

Paul E. Phillipson, Peter Schuster, ***A comparative study of the Hodgkin-Huxley and FitzHugh-Nagumo models of neuron pulse propagation***, *Int.J.Bifurcation and Chaos,* submitted 2004

# Coworker

**Paul Phillipson**, Department of Physics,
University of Colorado, Boulder, CO

**Universität Wien**

**Österreichische Akademie der Wissenschaften**



# Acknowledgement of support

Österreichische Akademie der Wissenschaften,

Universität Wien and University of Colorado

Web-Page for further information:

http://www.tbi.univie.ac.at/~pks