# Hodgkin-Huxley Model

# Recap

# Squid Giant Axon

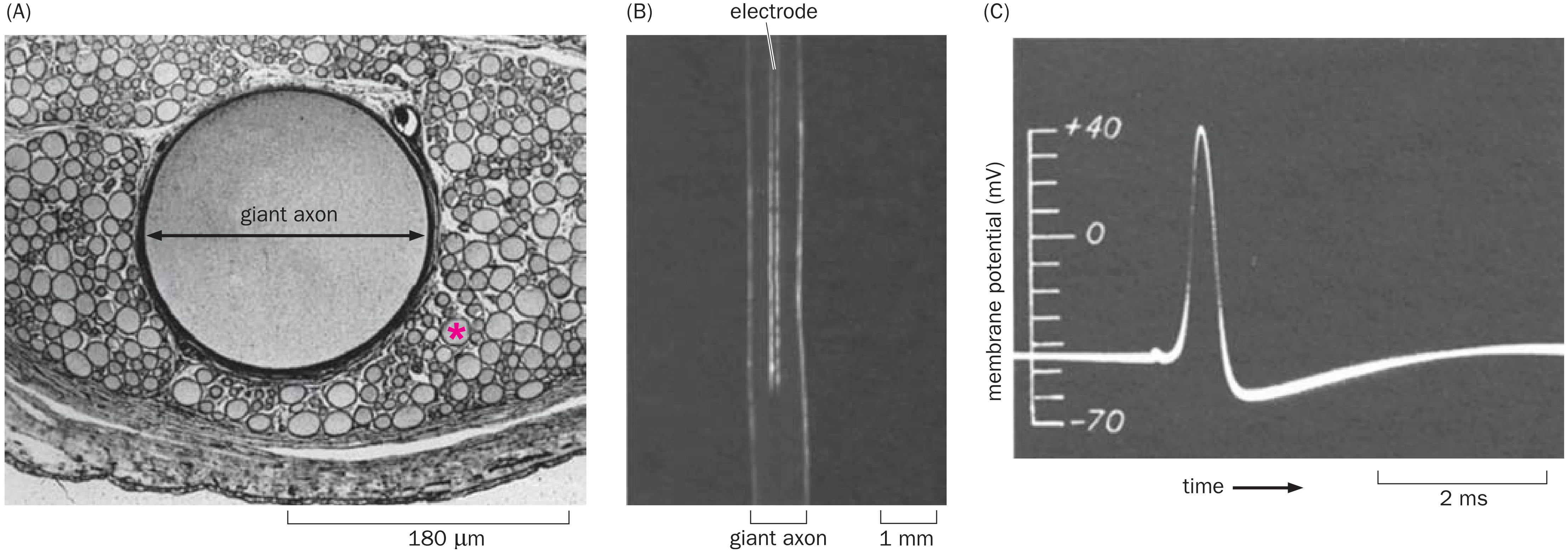
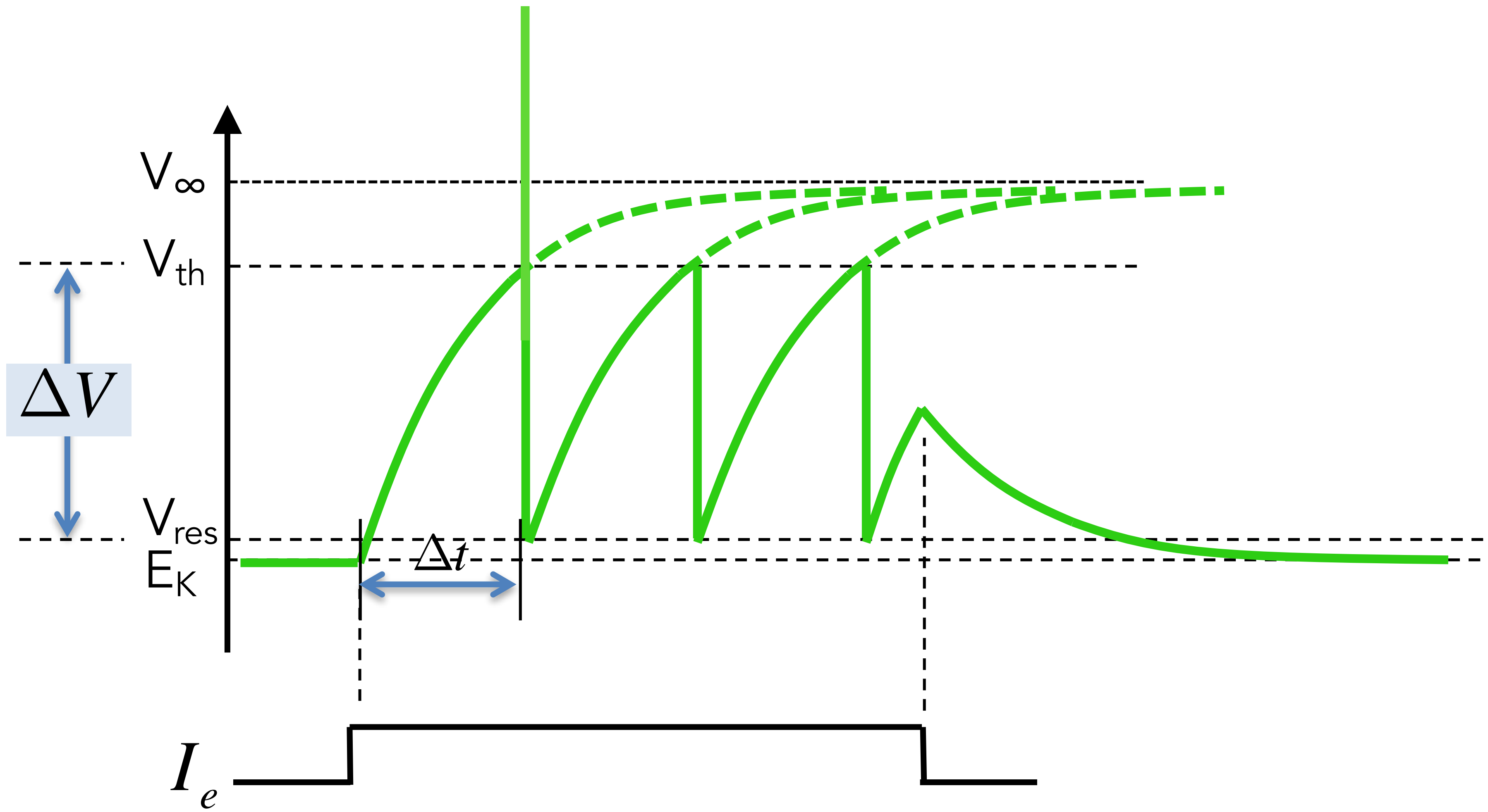



**Figure 2–19** **Studying action potentials in the squid giant axon. (A)** Electron micrograph of a cross section of a squid giant axon showing its large diameter (~180 µm for this sample) as compared to neighboring axons (for example, the axon indicated by *). **(B)** Photograph of an electrode inserted inside a squid giant axon whose diameter is close to 1 mm. **(C)** An action potential recorded from the squid giant axon. (A, courtesy of Kay Cooper and Roger Hanlon; B, from Hodgkin AL & Keyes RD [1956] *J Physiol* 131:592–616; C, from Hodgkin AL & Huxley AF [1939] *Nature* 144:710–711. With permission from Macmillan Publishers Ltd.)

# Integrate-and-Fire model

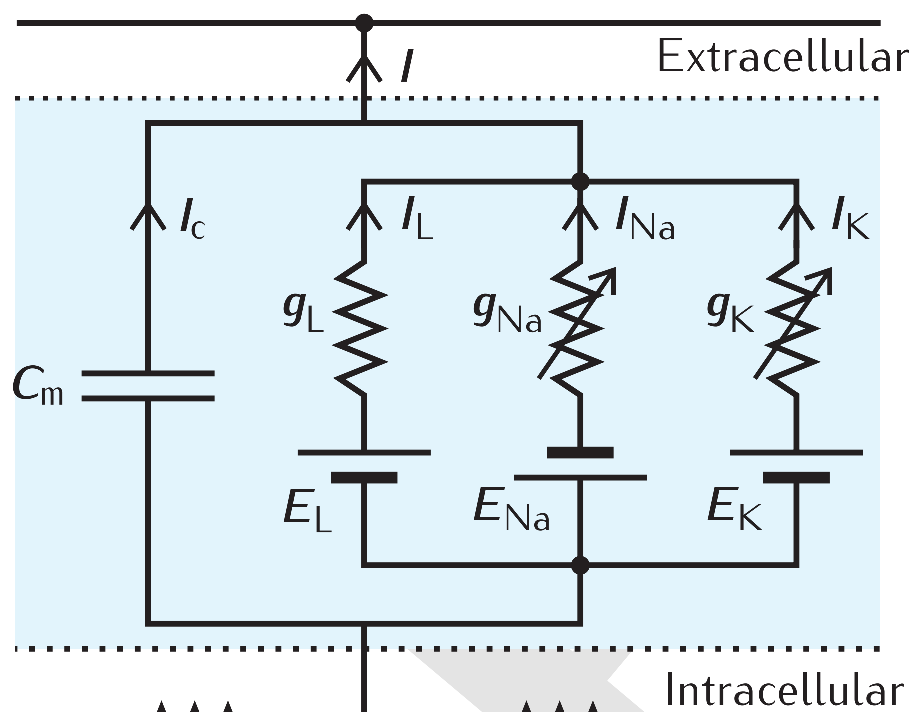



$$C\frac{dV}{dt} = -g(V - E_K) + I_e$$

$$V(t_{spike}^{-}) = V_{th}$$

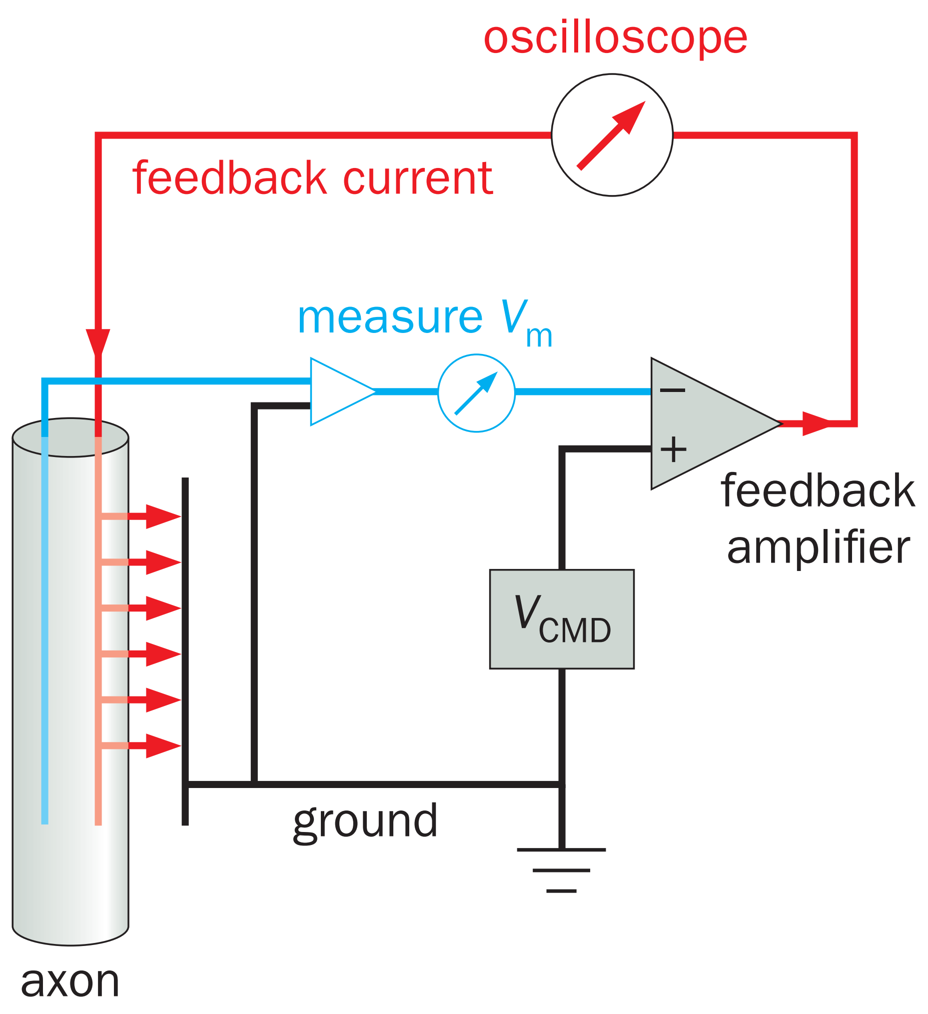
$$V(t_{spike}^{+}) = V_{res}$$

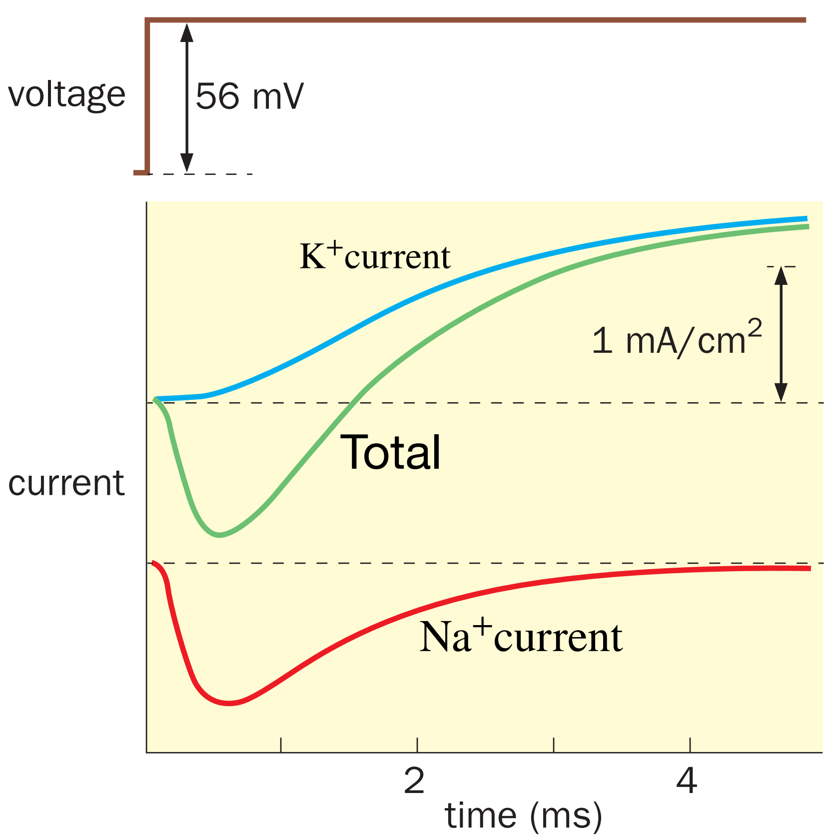
# The Equivalent Electronic Circuit of a Neuron



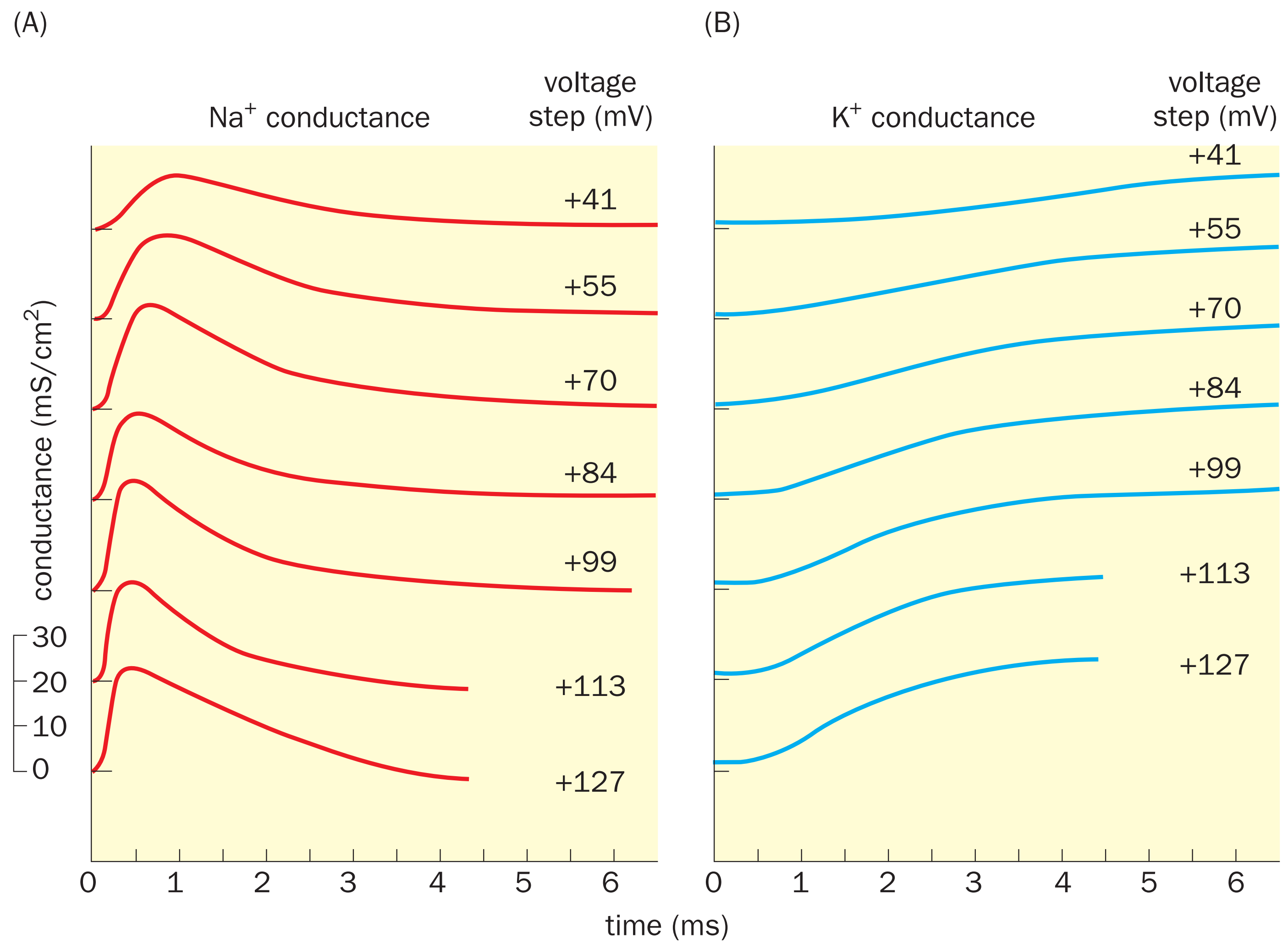

$$C_m \frac{dV}{dt} = -\sum_i g_i(V)(V - E_i) - \bar{g}_L(V - E_L) + I_e$$

# Voltage Clamp Recording



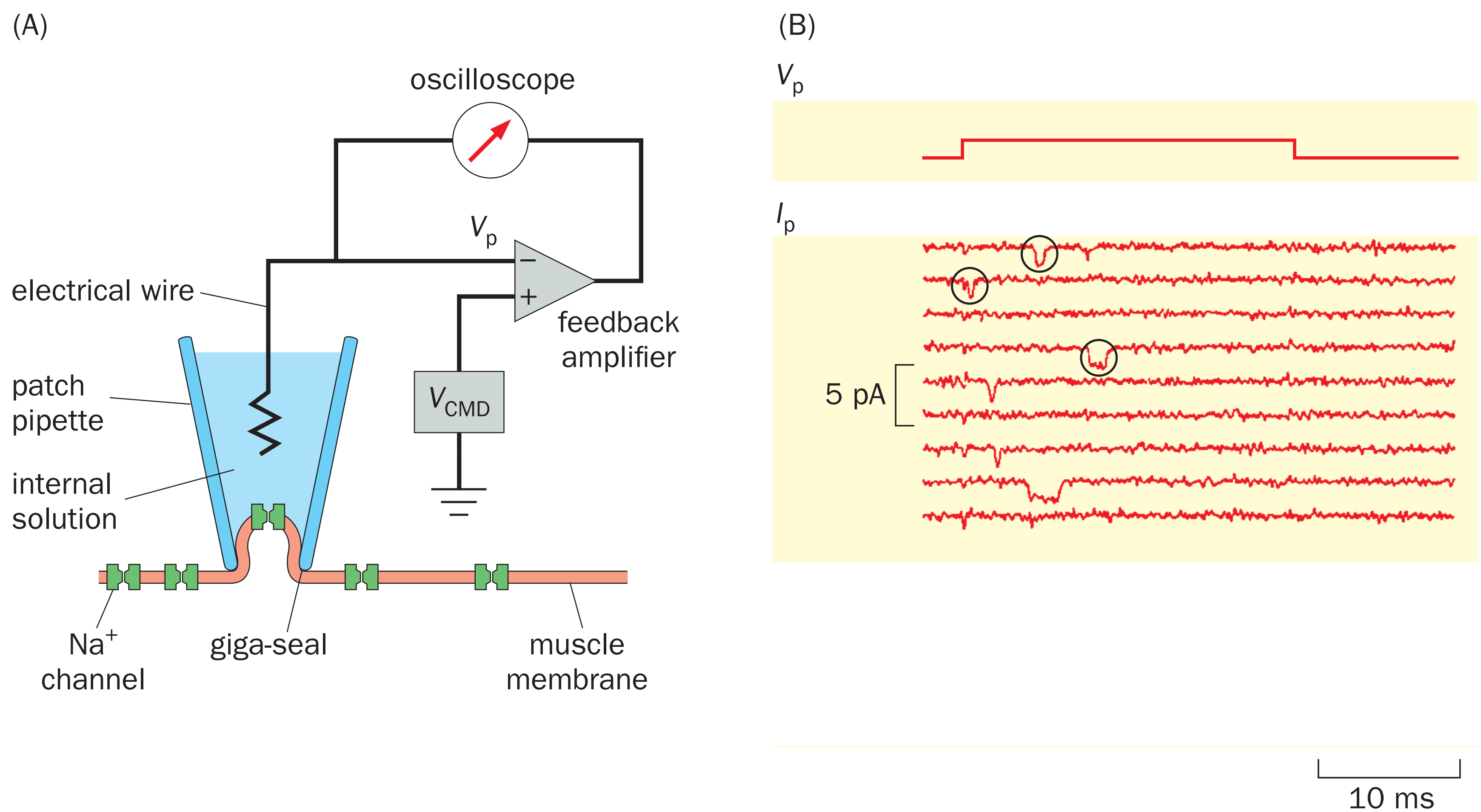



# Voltage-gated Conductance

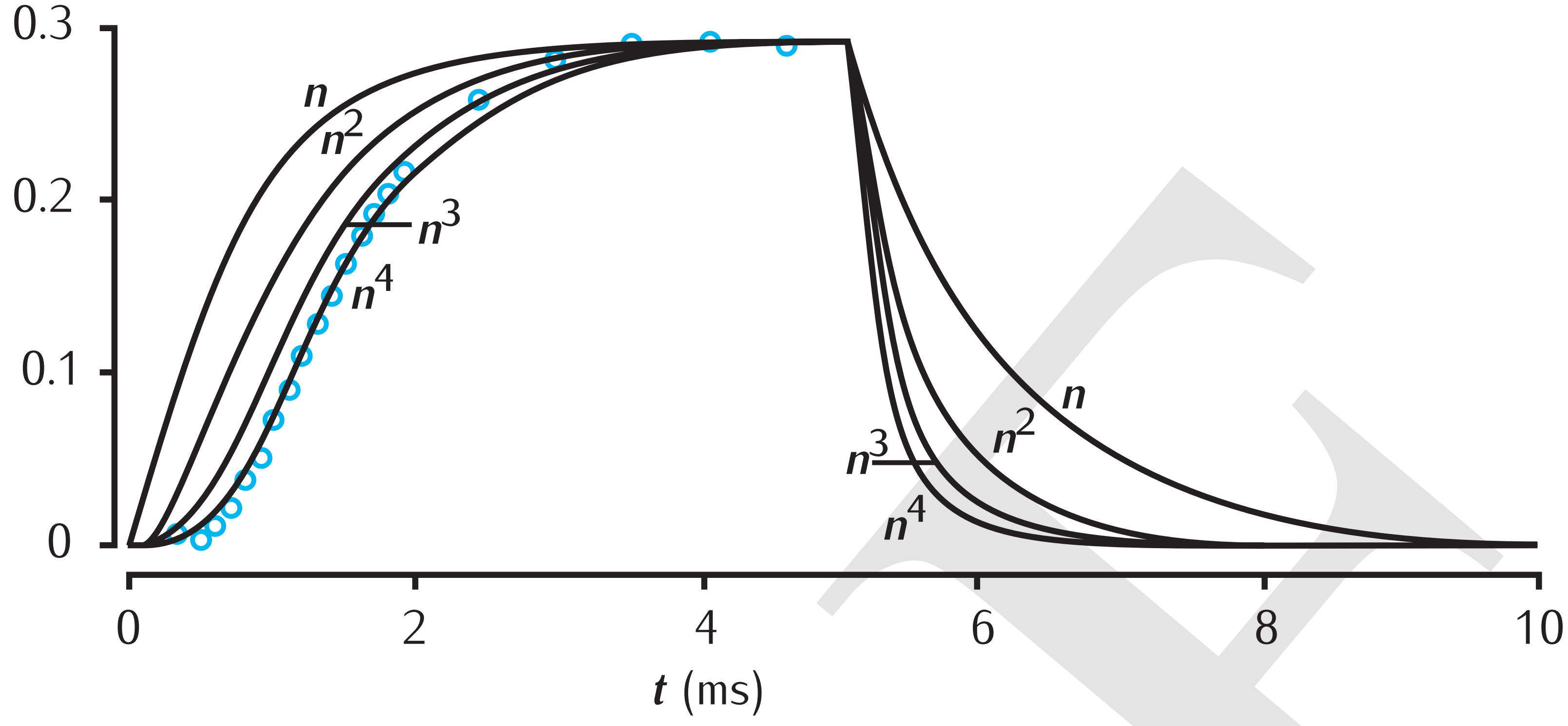


# Patch-clamp recording allows the measurement of single channel conductance

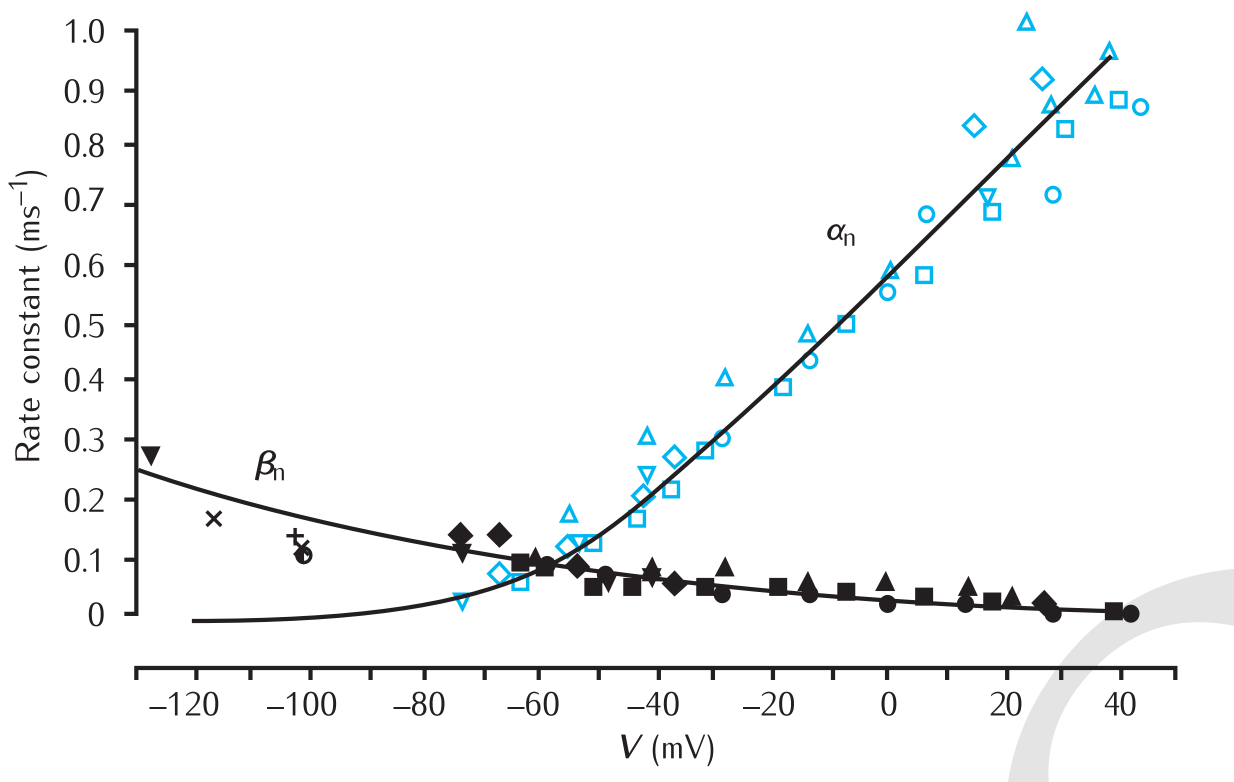
$$g_i = \bar{g}_i P_i(V)$$

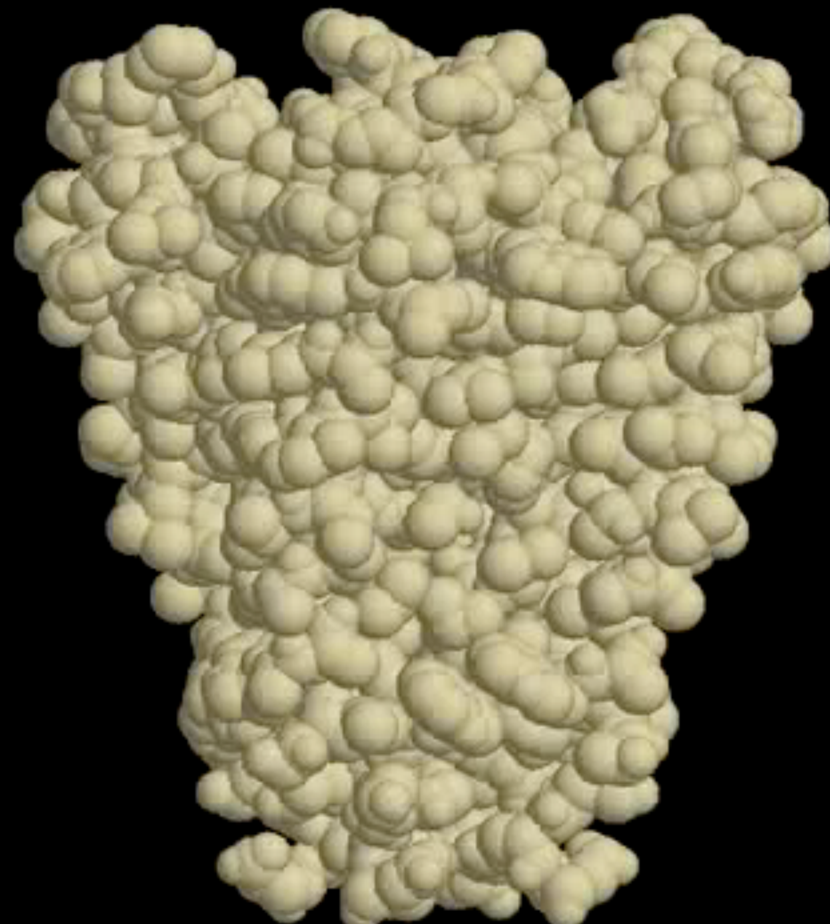


# Voltage-gated Conductance of $K^+$

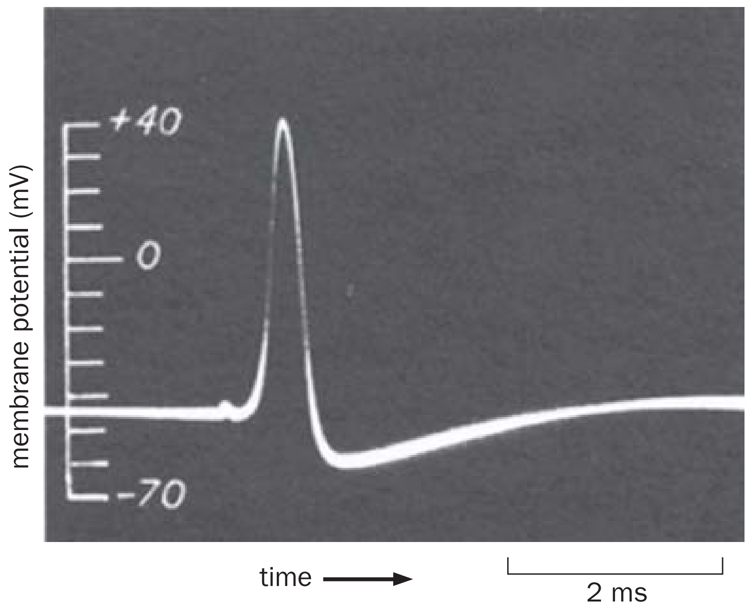


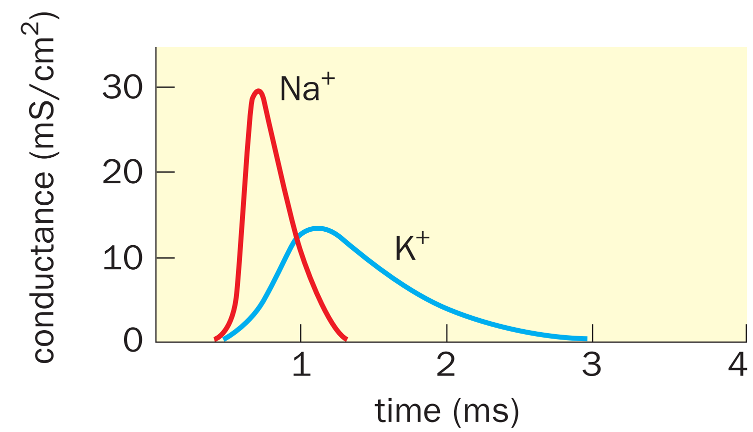
# Voltage-gated Conductance of $K^+$





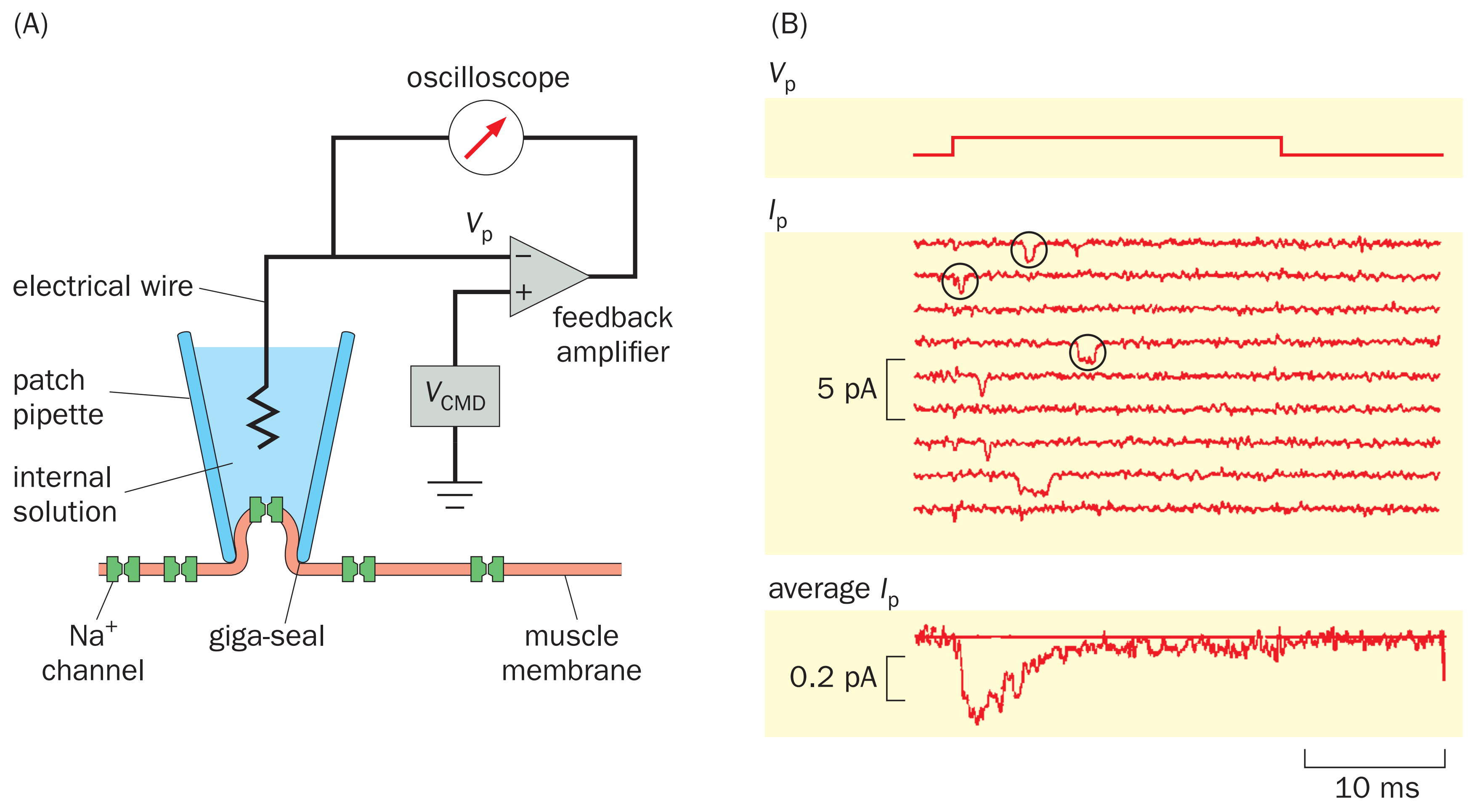
(C)



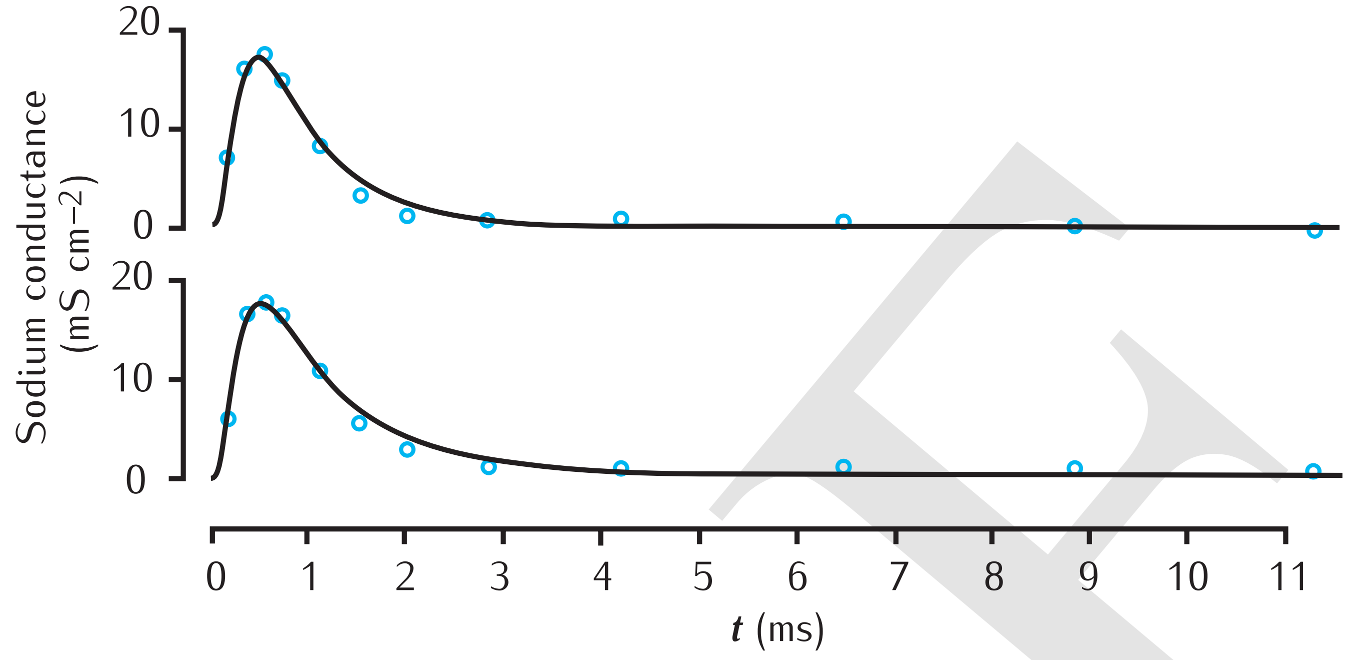




$$C\frac{dV}{dt} = -g_K n^4 (V - E_K) - g_{Na} m^3 h (V - E_{Na}) - g_L (V - E_L) - I_e$$

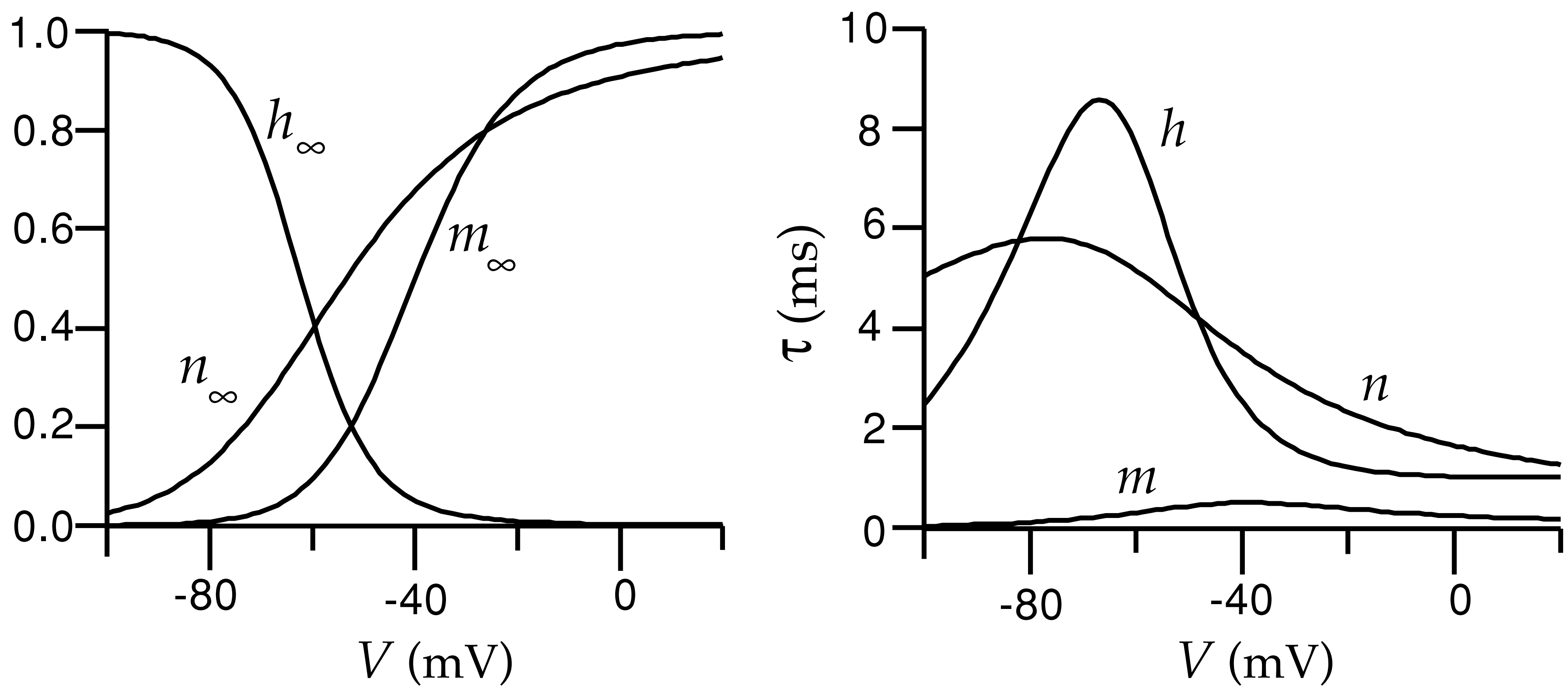
# Transient $Na^+$ channel conductance



# Transient $Na^+$ channel conductance



# Transient $Na^+$ channel conductance



# A simplified two-dimensional model

$$C_m \frac{dV}{dt} = -\bar{g}_K n(V - E_K) - \bar{g}_{Na} m_\infty(V)(V - E_{Na}) - \bar{g}_L(V - E_L) + I_e$$

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

# Fix Point on one dimension

$$\frac{dV}{dt} = F(V)$$

$$F(V^*) = 0$$

# Fix Point in high dimensions

$$\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x})$$

$$\mathbf{f}(\mathbf{x}_\infty) = 0$$

$$\mathbf{f}(\mathbf{x}(t)) = \mathbf{f}(\mathbf{x}_\infty) + \mathbf{J}\epsilon(t),$$

$$J_{ij} = \frac{\partial f_i(x_1, \ldots, x_j, \ldots, x_N)}{\partial x_j}$$

$$\frac{d\epsilon}{dt} = \mathbf{J}\epsilon$$

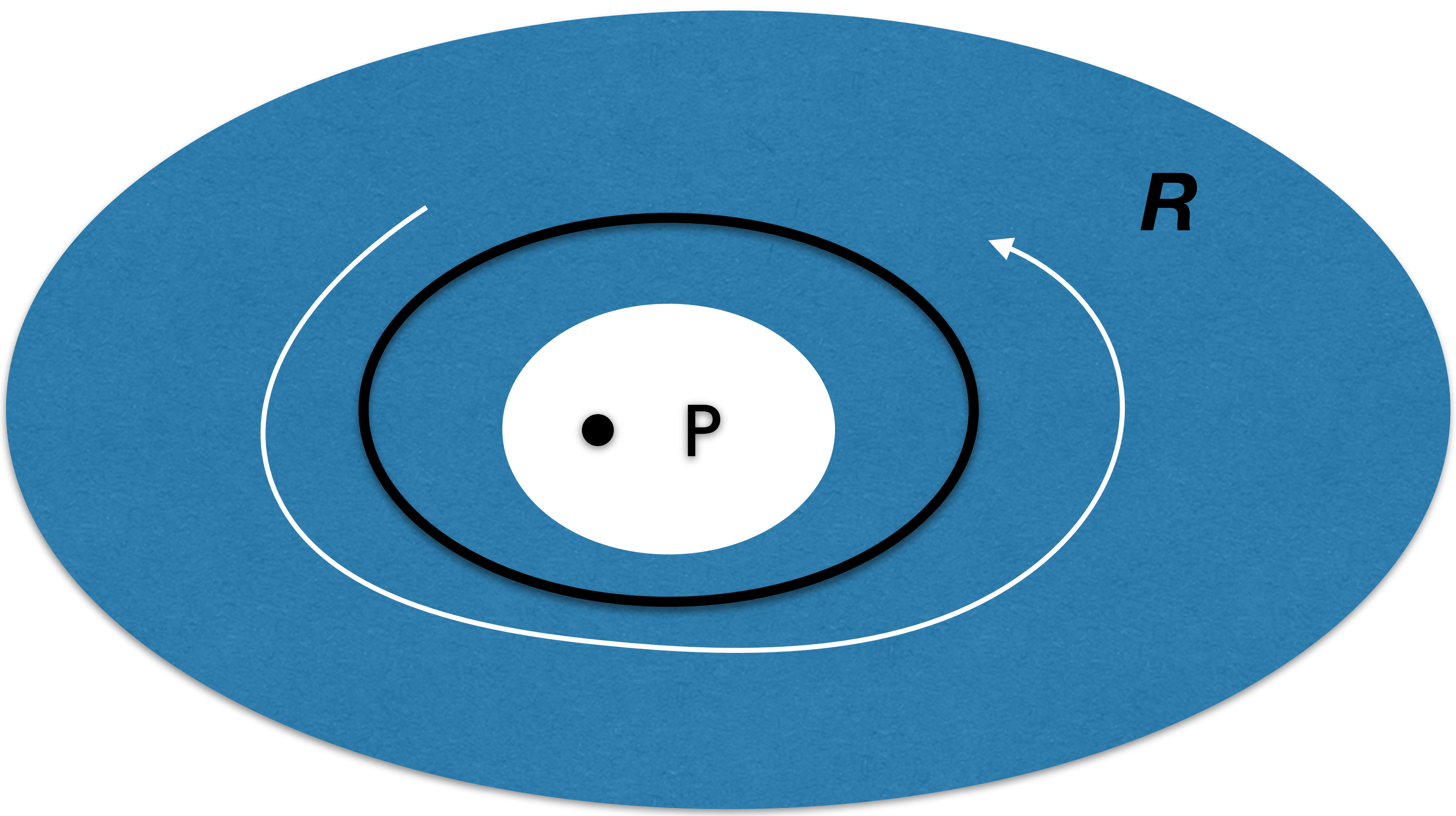
An example, fix point in two dimensions…

# Poincare-Bendixson Theorem (2D)

- *R* is a closed, bounded subset of the plane;
- $\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x})$ is a continuously differentiable vector field on an open set containing *R*;
- *R* does not contain any fixed points; and
- There exists a trajectory *C* that is "confined" in *R*, in the sense that it starts in *R* and stays in *R* for all future time

Then either *C* is a closed orbit, or it spirals toward a closed orbit at $t \to \infty$. In either case, *R* contains a closed orbit.

# Poincare-Bendixson Theorem (2D)



# Fixed points and stability

Global stability: starting from **any** initial condition

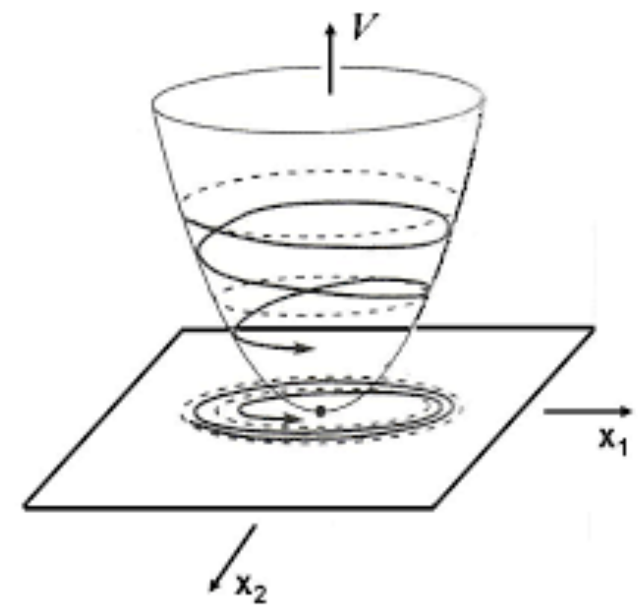
$$\frac{d\mathbf{u}}{dt} = \mathbf{f}(\mathbf{u})$$

Lyapunov function $V(u)$

$V(u) \geq \mathrm{V}_0,$ has a lower bound

$$\frac{d}{dt}V(u(t)) \leq 0$$

$$\frac{d}{dt}V\big(u(t)\big) = 0 \Rightarrow \nabla V(u) = 0$$




**Theorem**: If there exists a Lyapunov function, the system is (globally) stable where the trajectory will converge to one of the extrema of $V(u)$.

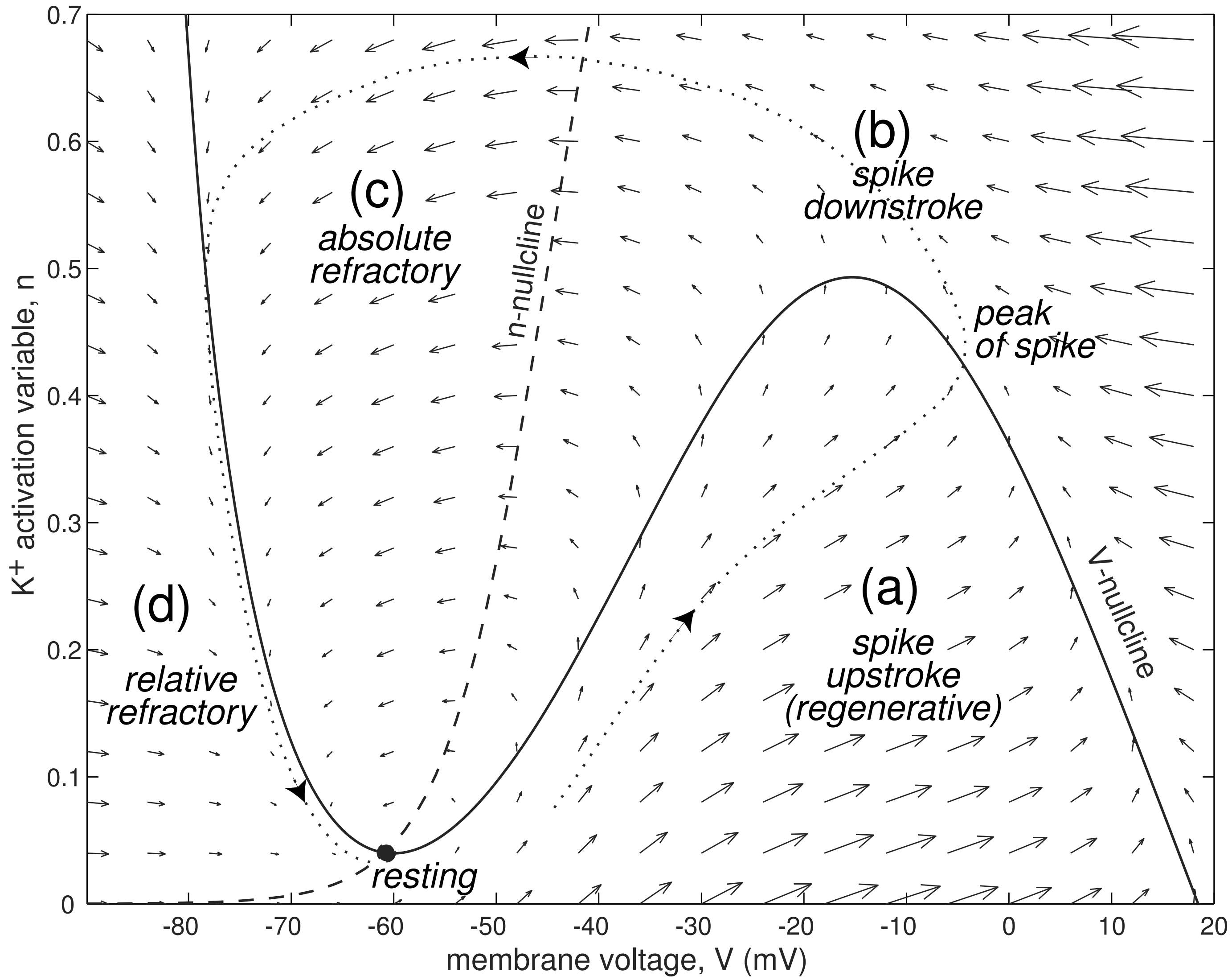
# An example

$$\frac{dx}{dt} = -x + 4y$$

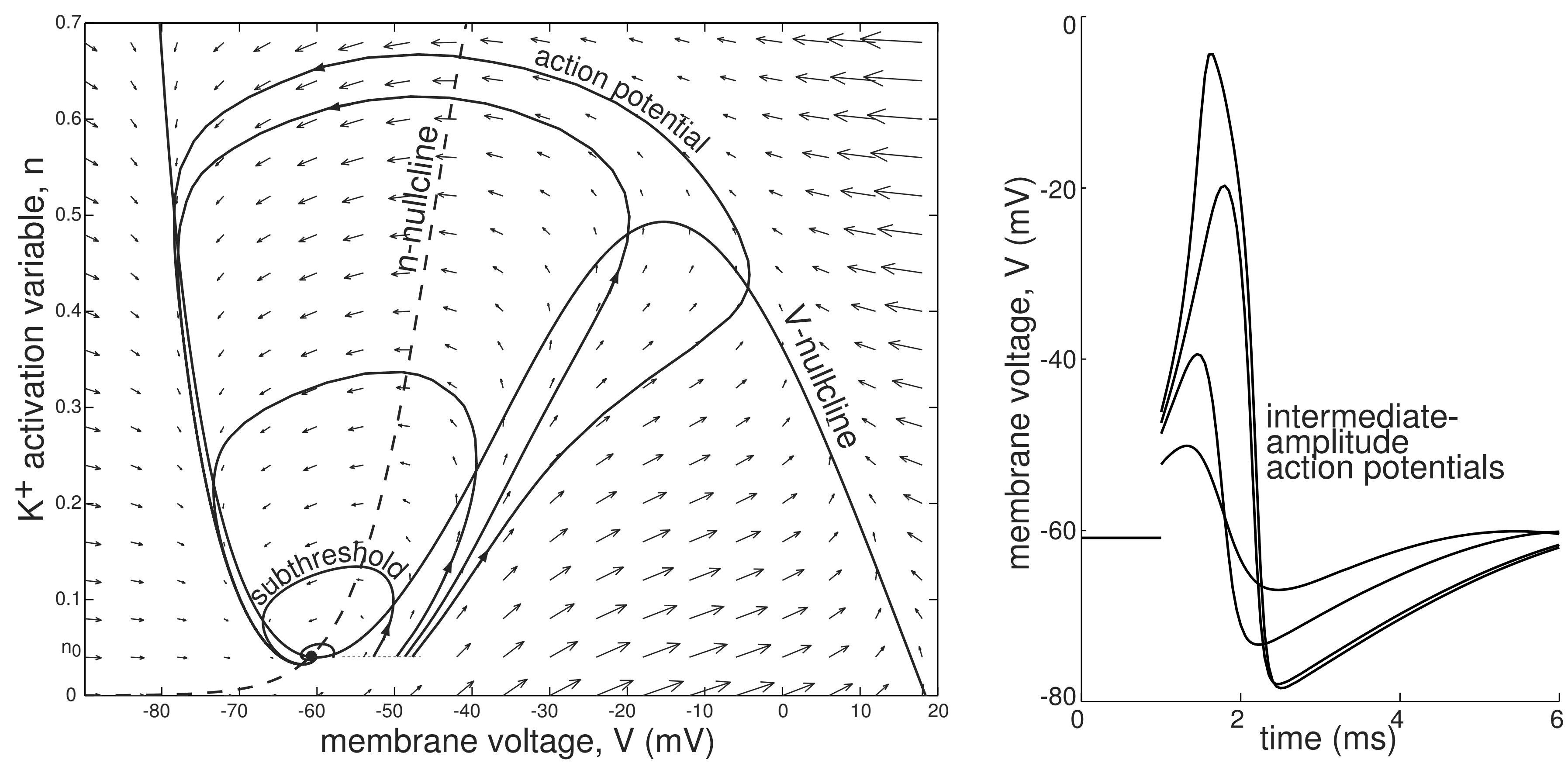
$$\frac{dy}{dt} = -x - y^3$$

Consider $\quad V(x, y) = x^2 + \alpha y^2$

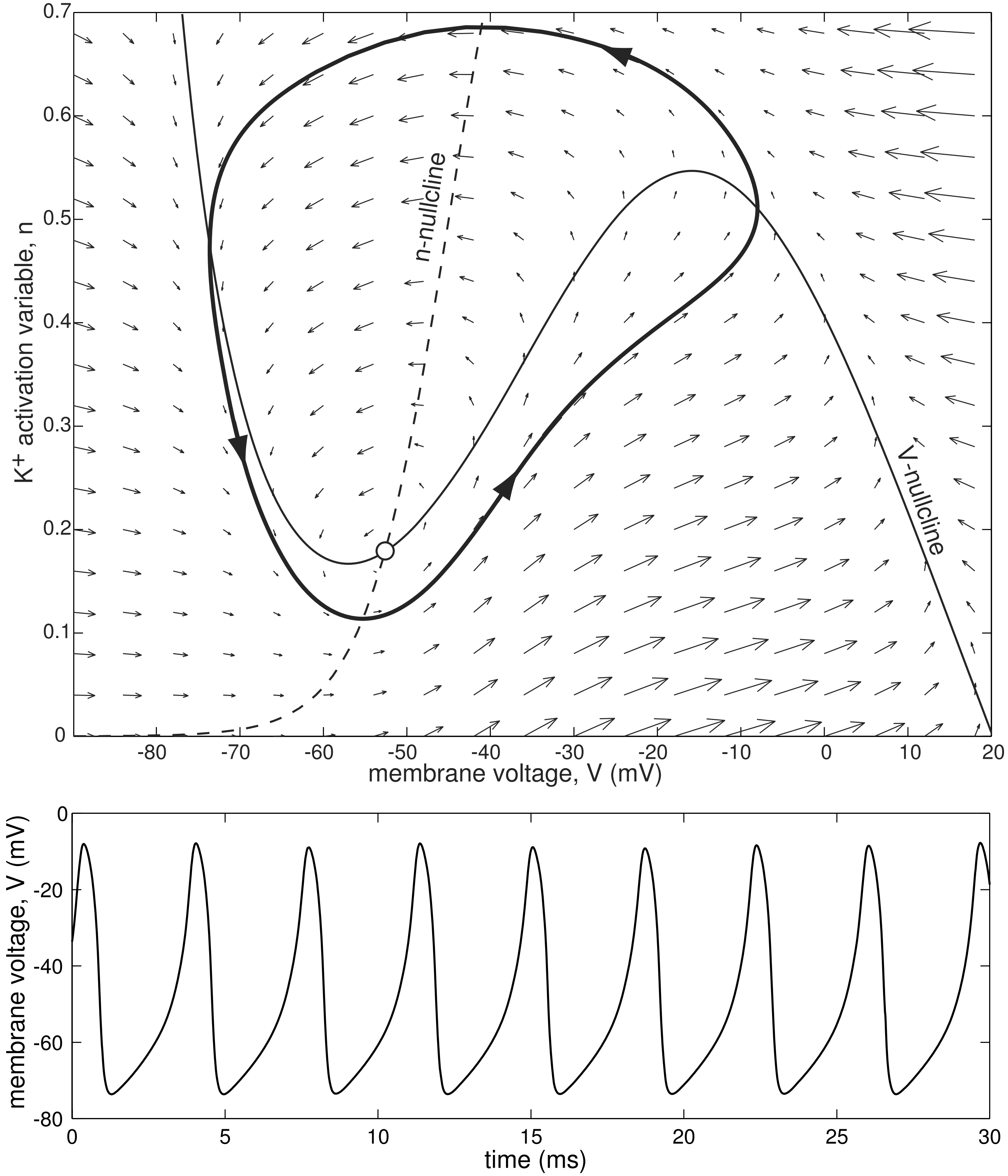
$$\dot{V} = 2x\dot{x} + 2\alpha y\dot{y} = 2x(-x + 4y) + 2\alpha y(-x - y^3)$$



(a)
spike
upstroke
(regenerative)
(b)
spike
downstroke
peak
of spike
(c)
absolute
refractory
(d)
relative
refractory
resting
n-nullcline
V-nullcline
K+ activation variable, n
membrane voltage, V (mV)
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
-80
-70
-60
-50
-40
-30
-20
-10
0
10
20



action potential
n-nullcline
V-nullcline
subthreshold
$n_0$
K+ activation variable, n
membrane voltage, V (mV)
intermediate-
amplitude
action potentials
membrane voltage, V (mV)
time (ms)

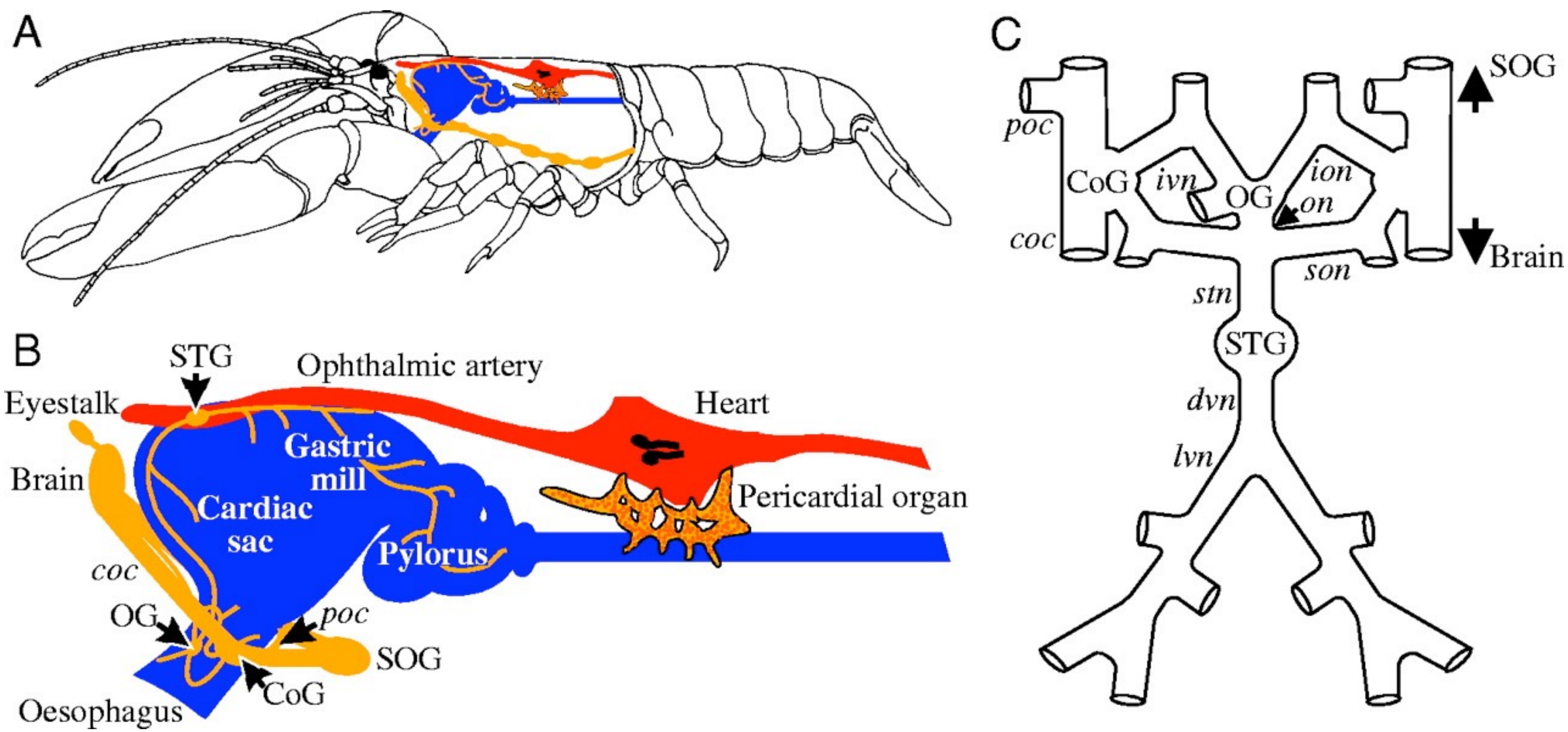


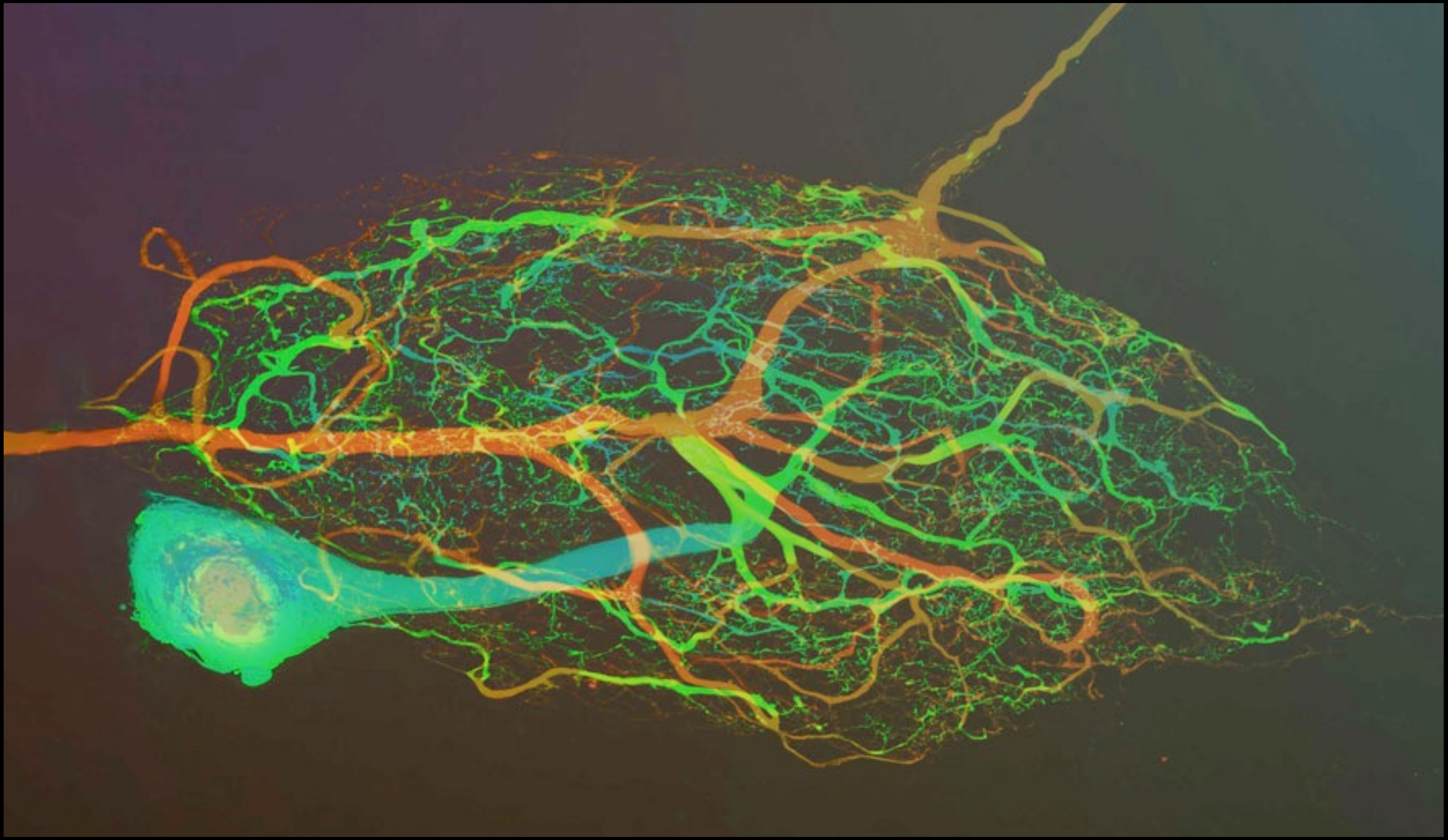
n-nullcline
V-nullcline
K+ activation variable, n
membrane voltage, V (mV)
membrane voltage, V (mV)
time (ms)

“With four parameters I can fit an elephant, and with five I can make him wiggle his trunk.”

*John von Neumann*

# Stomatogastric nervous system (STG)





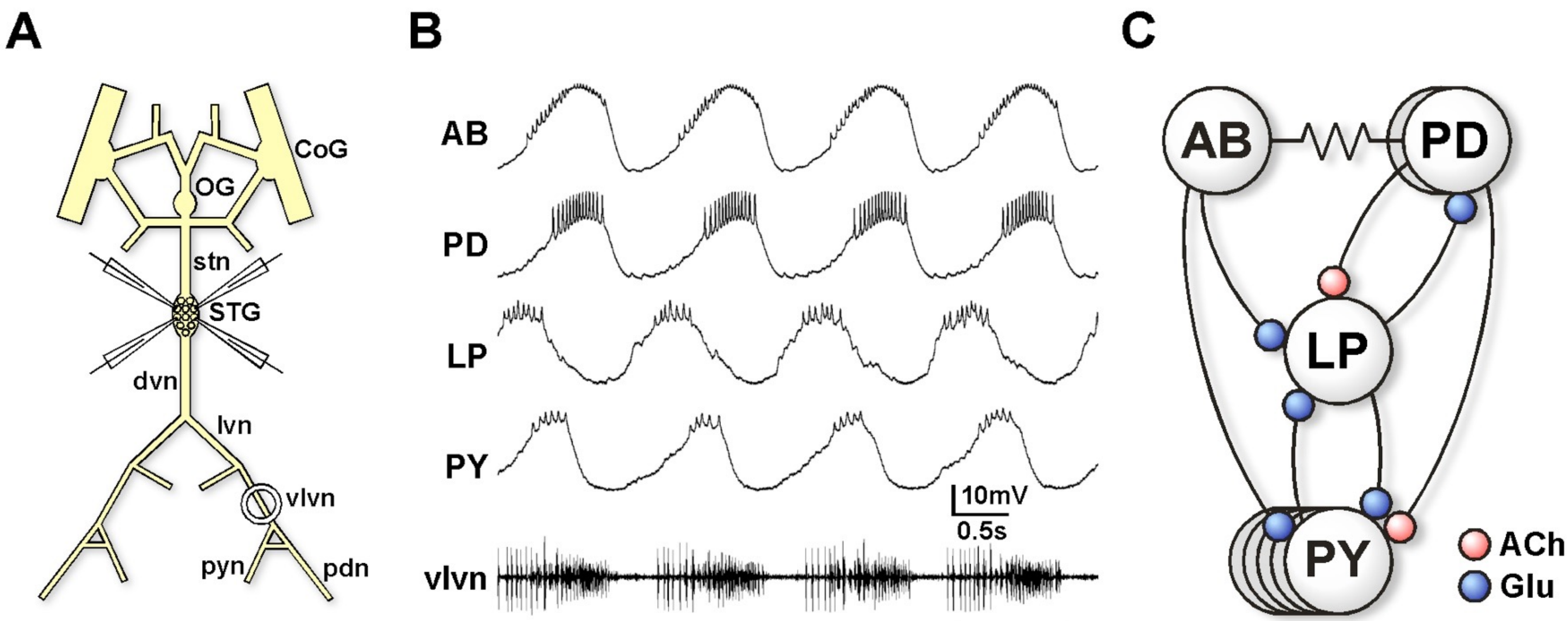
*Eve Marder*

# The voltage dependent conductances play a major role in determining the neural activity patterns

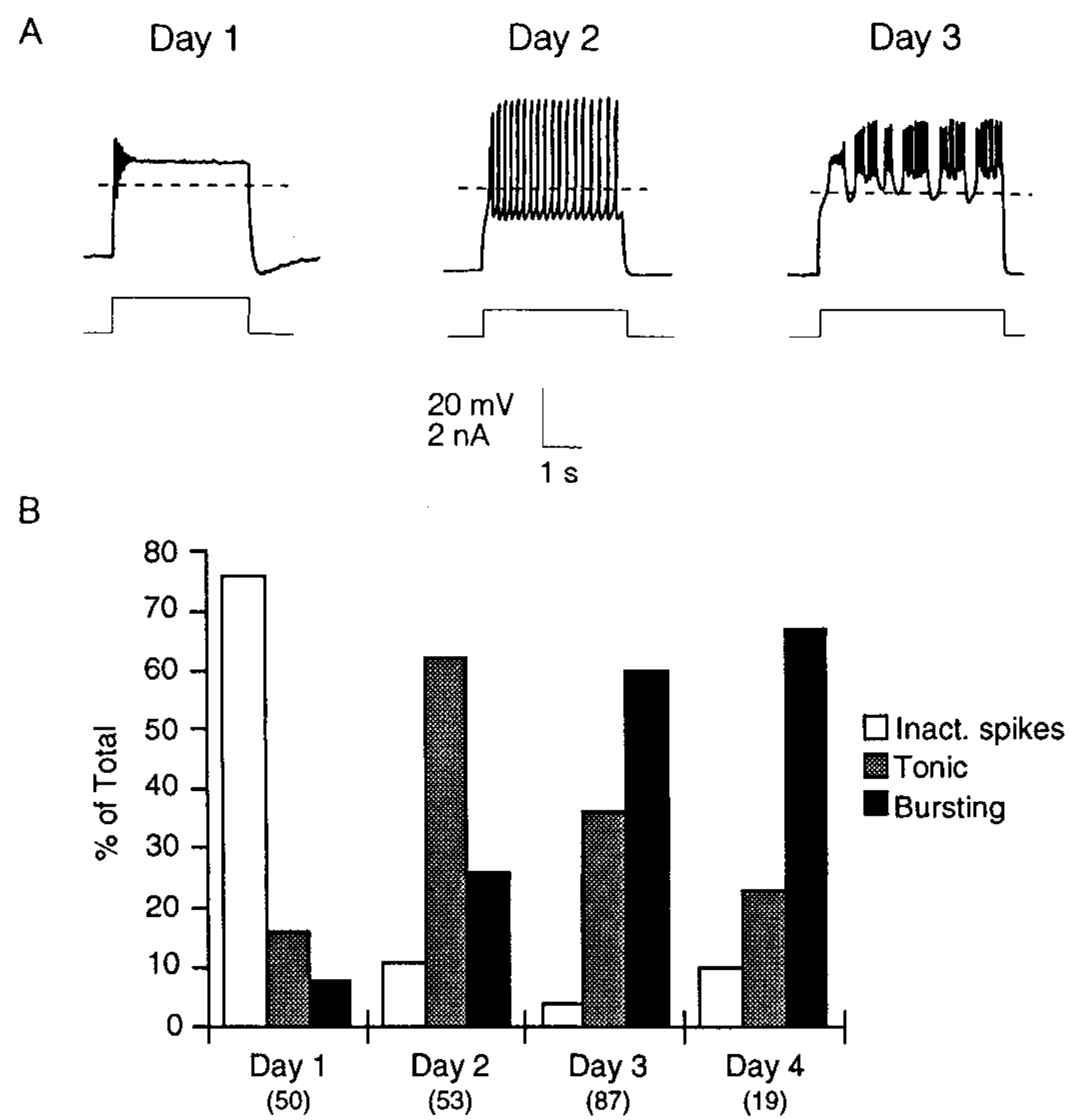
- **$I_{Na}$**: depolarization-activated transient sodium current that produces the rising phase of an action potential
- **$I_K$** : delayed rectifier potassium current that is responsible for the falling phase of the action potential
- **$I_{NaP}$** : a persistent sodium current that can initiate and maintain tonic or burst firing
- **$I_h$** : a hyperpolarization-activated inward current that can initiate bursting
- **$I_{CAN}$** : a calcium activated non-selective cation current that maintains a depolarized plateau
- **$I_{K(Ca)}$** : a calcium activated potassium current that could be responsible for burst termination
- **$I_A$** : a transient potassium current that is activated by depolarization and acts to delay spike and burst initiation

*From Scholarpedia.org*

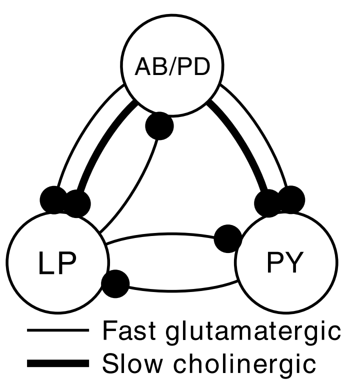
# STG has identified neurons with stereotypical activity patterns

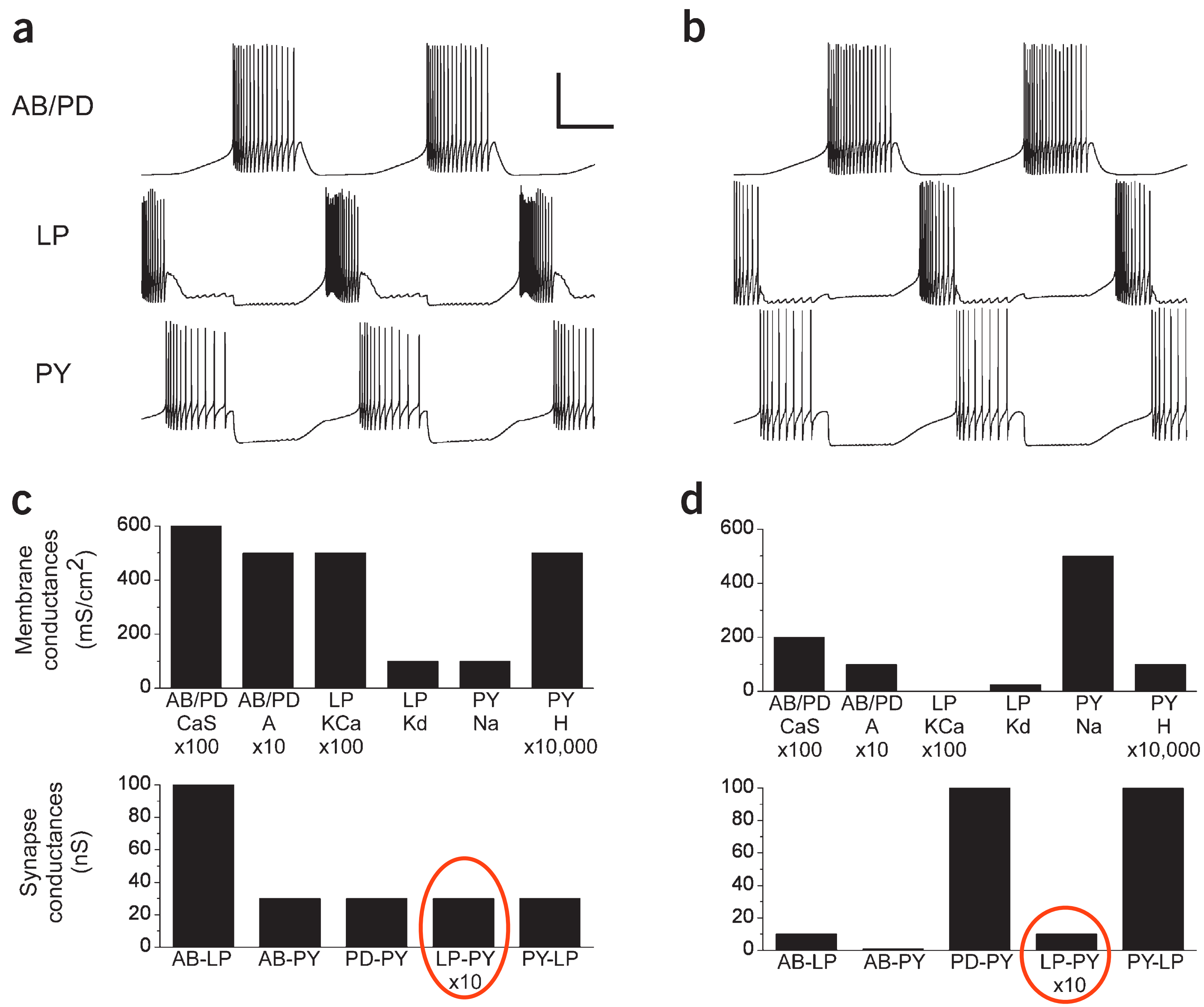


# Change of activity pattern over time



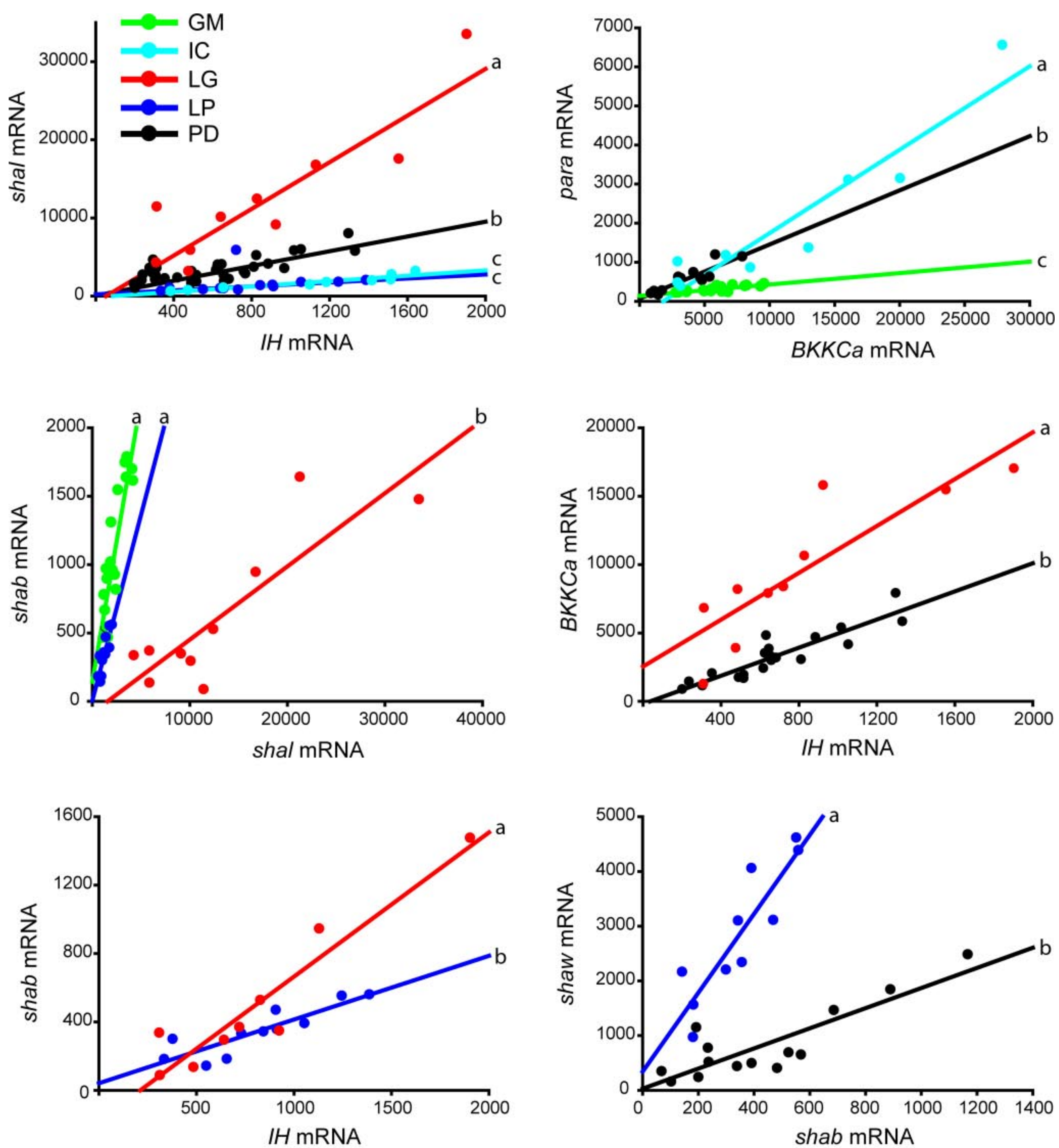
# Similar neural activities with widely different model-network properties




*Prinz, Bucher and Marder*
*Nature Neuroscience Dec 2004*

# Pair-wise correlation of ion channel expression levels in different cells




- $I_{Na}$: para mRNA
- $I_A$: shal mRNA
- $I_{CaK}$: BKKCa mRNA
- $I_H$: IH mRNA
- $I_K$: shab, shaw mRNA

Schultz, Goaillard, Marder
PNAS 2006