Dynamics of Neural Systems

Extensions of the HH Model and Simplified Neuron Models

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Overview

- Extensions of the HH model
- Simplified neuron models

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- Extensions of the HH model
- Simplified neuron models

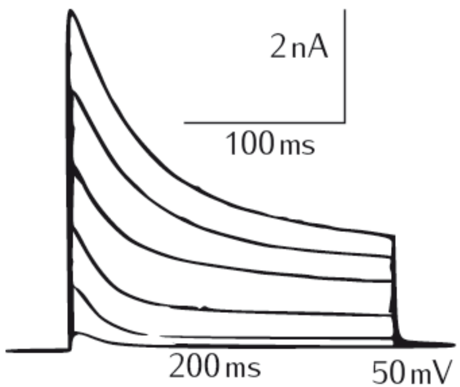
Extensions of the HH model

- While the dynamics of the classical HH model is quite rich it does not capture certain phenomena.
- Example: channels with other types of kinetics (e.g. Ca^{2+} channels).

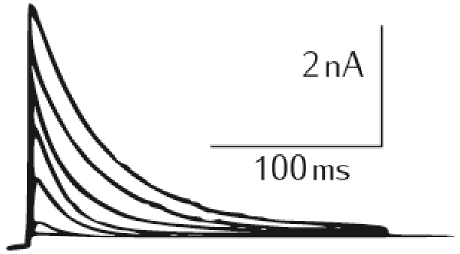
Potassium A-type current

- Different from **delayed rectifier** potassium current, as originally described by Hodgkin and Huxley.
- Type A current is inactivating and has lower activation threshold.
- Found e.g. in hippocampal CA1 and CA3 cells.
- Isolated by blocking sodium channels by Tetrodotoxin (TTX) or applying appropriate voltage step paradigms.

Delayed rectifier current



Type-A current for different clamp voltages



Model with A-type current I

- Model by Stevens and Connor (Connor et al. 1977).
- Introduction of new current: $\boxed{I_\mathrm{A} = g_\mathrm{A}(V)\left(V(t) - E_\mathrm{A}\right)}$
- Conductance defined by an activation variable a and the inactivation variable b according to the relationship: $\boxed{g_\mathrm{A} = \bar{g}_\mathrm{A} a^3 b}$
- Linear kinetic equations and form of voltage dependence as HH.
- Differential equation for membrane potential:

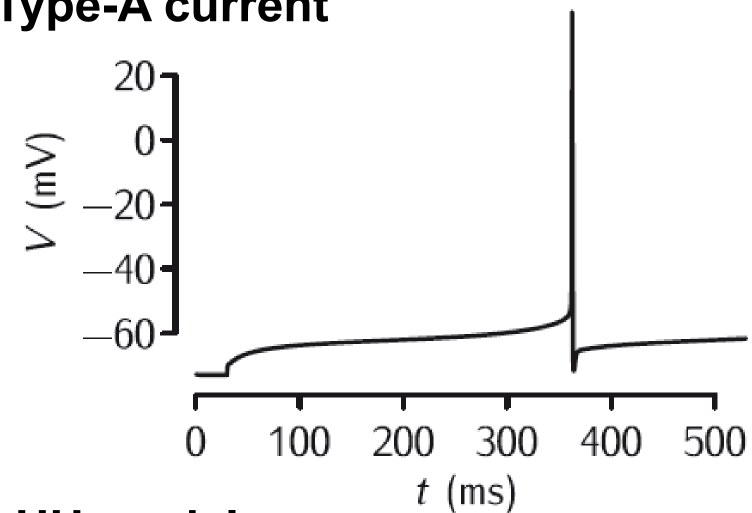
$$C\frac{\mathrm{d}V}{\mathrm{d}t} + \underbrace{\bar{g}_{\mathrm{K}^+} n^4\left(V - E_{\mathrm{K}^+}\right)}_{\text{Delayed rectifier current}} + \bar{g}_{\mathrm{Na}^+} m^3 h\left(V - E_{\mathrm{Na}^+}\right) + \underbrace{\bar{g}_\mathrm{A} a^3 b\left(V - E_\mathrm{A}\right)}_{\text{Type A current}} + \bar{g}_\mathrm{L}\left(V - E_\mathrm{L}\right) = I_\mathrm{e}(t)$$

- Other parameters of HH model need to be adapted.

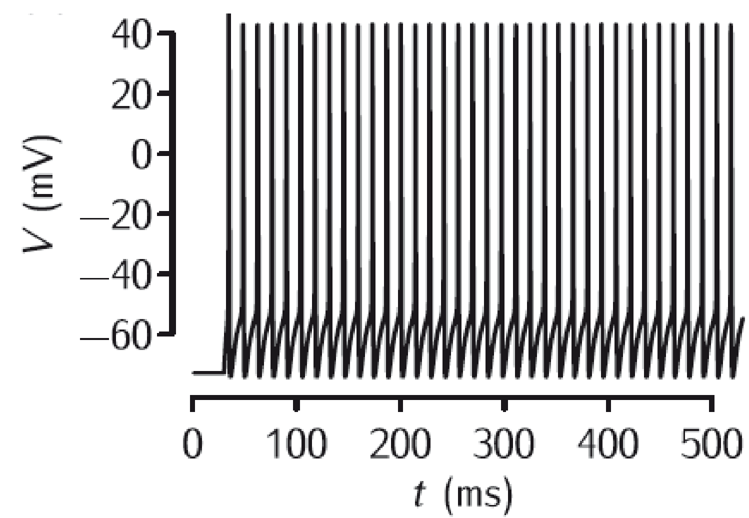
Model with A-type current II

- Model with A current and HH model behave quite differently.
- For injection of constant current strongly delayed spike emission (delay of 300 ms) for A-type model.
- Reason: A-type K^+ channel is open during the increase of the membrane potential towards the firing threshold; this delays the increase of the membrane potential substantially.

Type-A current

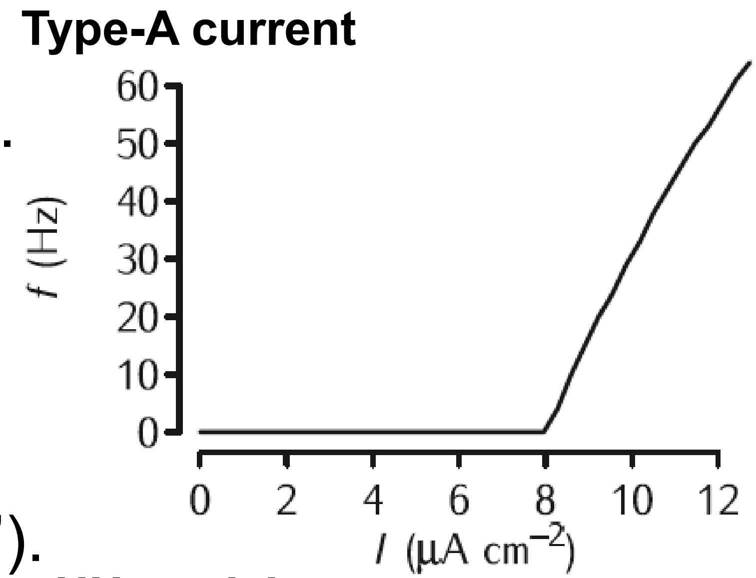


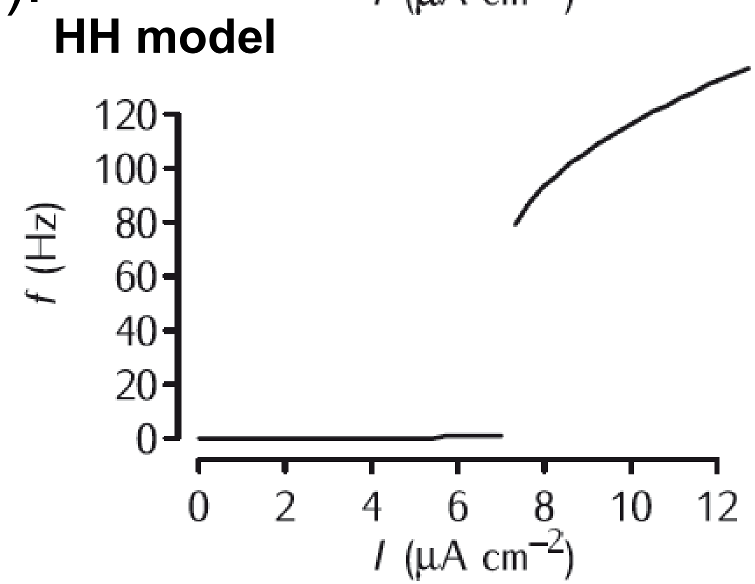
HH model



Model with A-type current III

- Very different **current–spikefrequency characteristics** from HH.
- Increase of spike rate when input current exceeds threshold.
- Model with type A current shows gradual increase of spike rate with input current (‘**type I neuron**’).
- For HH model spike rate jumps to nonzero value above threshold activation (‘**type II neuron**’).
- Difference can be understood in terms of nonlinear dynamics (see part II of this course).





Modeling of ligand-gated channels I

- Some channels are activated by intra- or extracellular ligands or second messengers.
- Examples: Ca^{2+} or cyclic AMP-controlled channels.
- Calcium channels responsible for a variety of interesting effects (we discuss some examples here and coarse ideas how they can be modeled; details: Sterratt book).
- Many different types of Ca^{2+} conductances with:
  - persistent characteristics (e.g. L type)
  - transient characteristics (e.g. T type)
  - Some may be involved in transmitter release at synapses (e.g. N and P type)

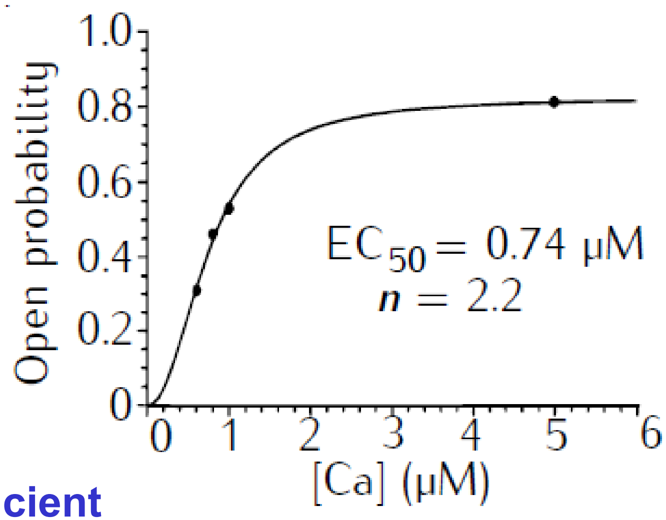
Modeling of ligand-gated channels II

- Opening probability of channel depends on Ca^{2+} concentration:

$$\boxed{P(\text{channel open}) = \frac{[\mathrm{Ca}^{2+}]^n}{K_{0.5}^n + [\mathrm{Ca}^{2+}]^n}}$$

Half maximal effective concentration **Hill coefficient**

Hill equation



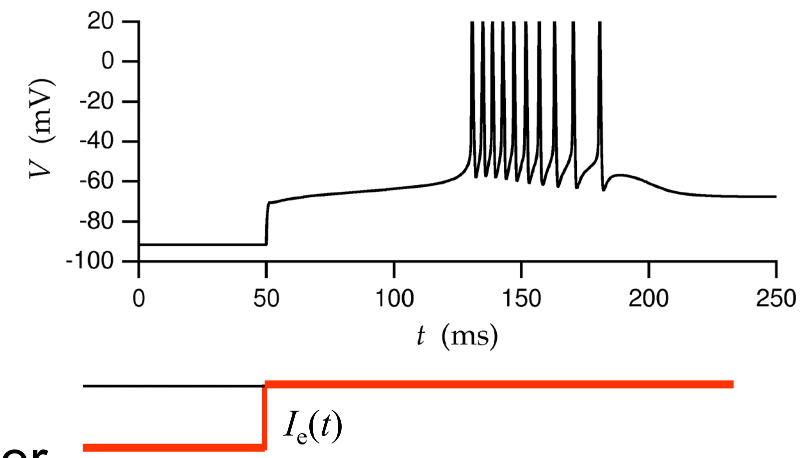
- Integration in activation dynamics by defining calcium-controlled conductivity, e.g: $\boxed{g_{\mathrm{KCa}} = \bar{g}_{\mathrm{KCa}} w}$
- The activation variable follows the kinetic equation:

$$\boxed{\frac{\mathrm{d}w}{\mathrm{d}t} = \frac{w_\infty - w}{\tau_w} \quad \text{with} \quad w_\infty = \frac{[\mathrm{Ca}^{2+}]^n}{K_{0.5}^n + [\mathrm{Ca}^{2+}]^n}}$$

Modeling of ligand-gated channels III

- In the following we discuss interesting phenomena that are induced by different types of Ca^{2+} conductances.
- Example 1: **Calcium spikes and burst activity**:
  - Slow **transient** Ca^{2+} conductance; similar to sodium conductance
  - Can generate slower transient depolarization than AP **('calcium spike'**)
  - Normal Na^{+} dynamics rides on top of this slow depolarization. $\Rightarrow$ **burst activity**.
  - Spike trains can be elicited by longer periods of hyperpolarization (**rebound activity**).
  - Model (like sodium channel): $g_{\mathrm{CaT}}(t) = \overline{g}_{\mathrm{CaT}} M^2(t) H(t)$

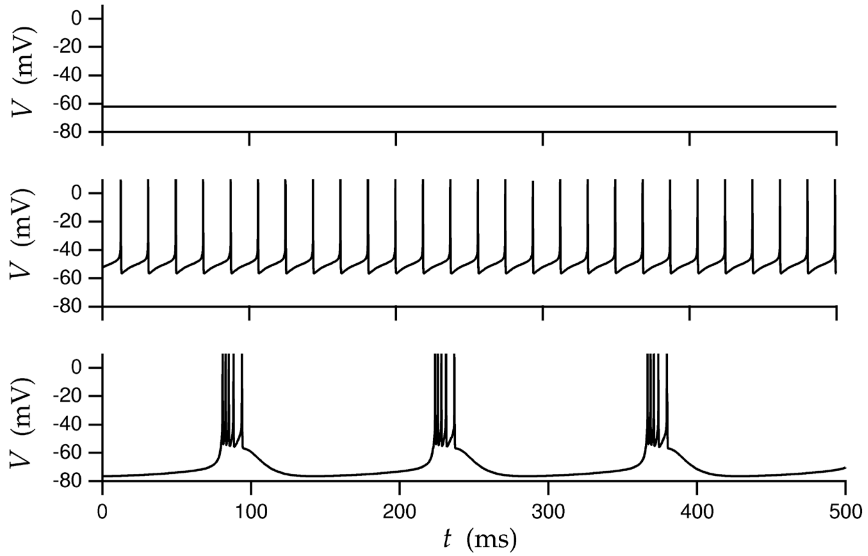
Burst elicited by hyperpolarization



Modeling of ligand-gated channels IV

- Example 2: **Firing modes of thalamic relay neurons**:
  - Different firing modes for awake state and sleep.
  - Model by Wang (1994): five conductances : (HH conductances, Ca^{2+}, persistent Na^{+} cond., mixed cation cond.)
  - Single neurons can realize multiple firing modes, dependent on injected current:
    a) no current $\Rightarrow$ neuron silent
    b) pos. current $\Rightarrow$ regular APs (wake state)
    c) small neg. current $\Rightarrow$ bursting (sleep state)
    (hyperpolarization deinactivates transient Ca^{2+} currents)

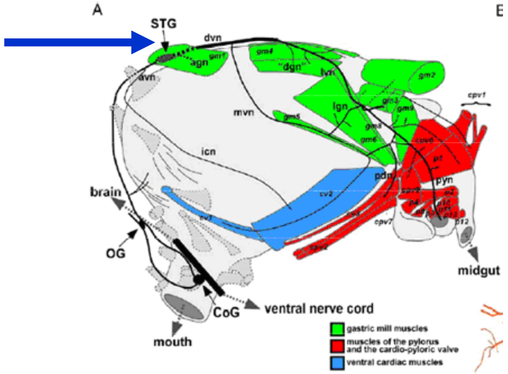
Firing modes of relay cell



Modeling of ligand-gated channels V

- Example 3: **Periodic bursting:**
  - Neurons generating periodic bursts, even without external input, very important for **central pattern generators (CPGs)** in the control of walking or chewing, or digestion.
  - Example: crustacaen somatogastric ganglion (STG) → Controls chewing and digestive rhythms in lobster and crabs.
  - Model (Turrogiano et al. 1995) contains HH currents, A current, transient Ca^{2+} conductance, and **Ca^{2+}-dependent K^+-conductance** (K(Ca); to be discussed in the following)
  - K(Ca) conductance helps repolarization of membrane after AP.

Lobster and STG



Modeling of ligand-gated channels VI

- Example 3: **Periodic bursting:** (contd.)
  - Model of the K(Ca) conductance:
    Ca^{2+}-dependent K^+ current:

$$\boxed{I_{\mathrm{KCa}} = \bar{g}_{\mathrm{KCa}} c^4 (V - E_{\mathrm{K}^+})}$$

    The activation variable c follows a linear kinetic equation with:

$$\boxed{\begin{aligned} c_\infty &= \frac{[\mathrm{Ca}^{2+}]}{[\mathrm{Ca}^{2+}] + k_1} \frac{1}{1 + \exp(-(V - k_2)/k_3)} \\ \tau_c &= k_4 - \frac{1}{1 + \exp(-(V - k_5)/k_6)} \end{aligned}}$$

  - The concentration $[Ca^{2+}]$ increases though the Ca^{2+} current; in addition, an exponential decay is assumed, motivating the DEQ:

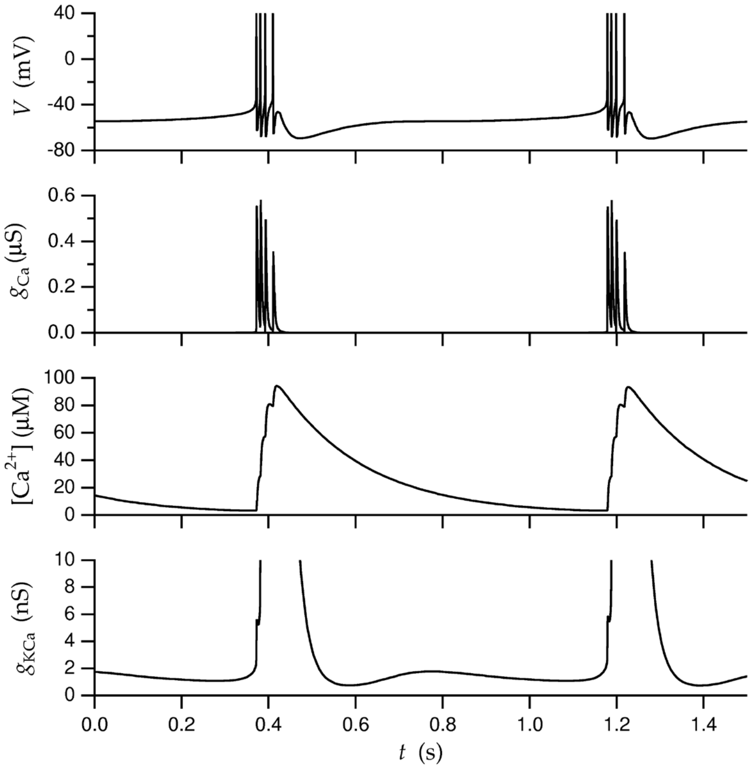
$$\boxed{\frac{\mathrm{d}[\mathrm{Ca}^{2+}]}{\mathrm{d}t} = -k_7 I_{\mathrm{Ca}^{2+}} - \frac{[\mathrm{Ca}^{2+}]}{\tau_{\mathrm{Ca}^{2+}}}}$$

Remark: calcium inflow creates neg. membrane current

Modeling of ligand-gated channels VII

- Example 3: **Periodic bursting:** (contd.)
  - Model produces **periodic bursts**.
  - Ca spikes with regular APs ‘riding’ on top.
  - Ca^{2+} current during bursts results in a dramatic increase of (intracell.) [Ca^{2+}].
  - The increase of [Ca^{2+}] activates K^+ current, which helps to stop the burst.
  - After burst the Ca^{2+} concentration decays slowly.
  - Low [Ca^{2+}] inactivates the K(Ca) current, allowing a new burst to be generated.

Model STG neurons

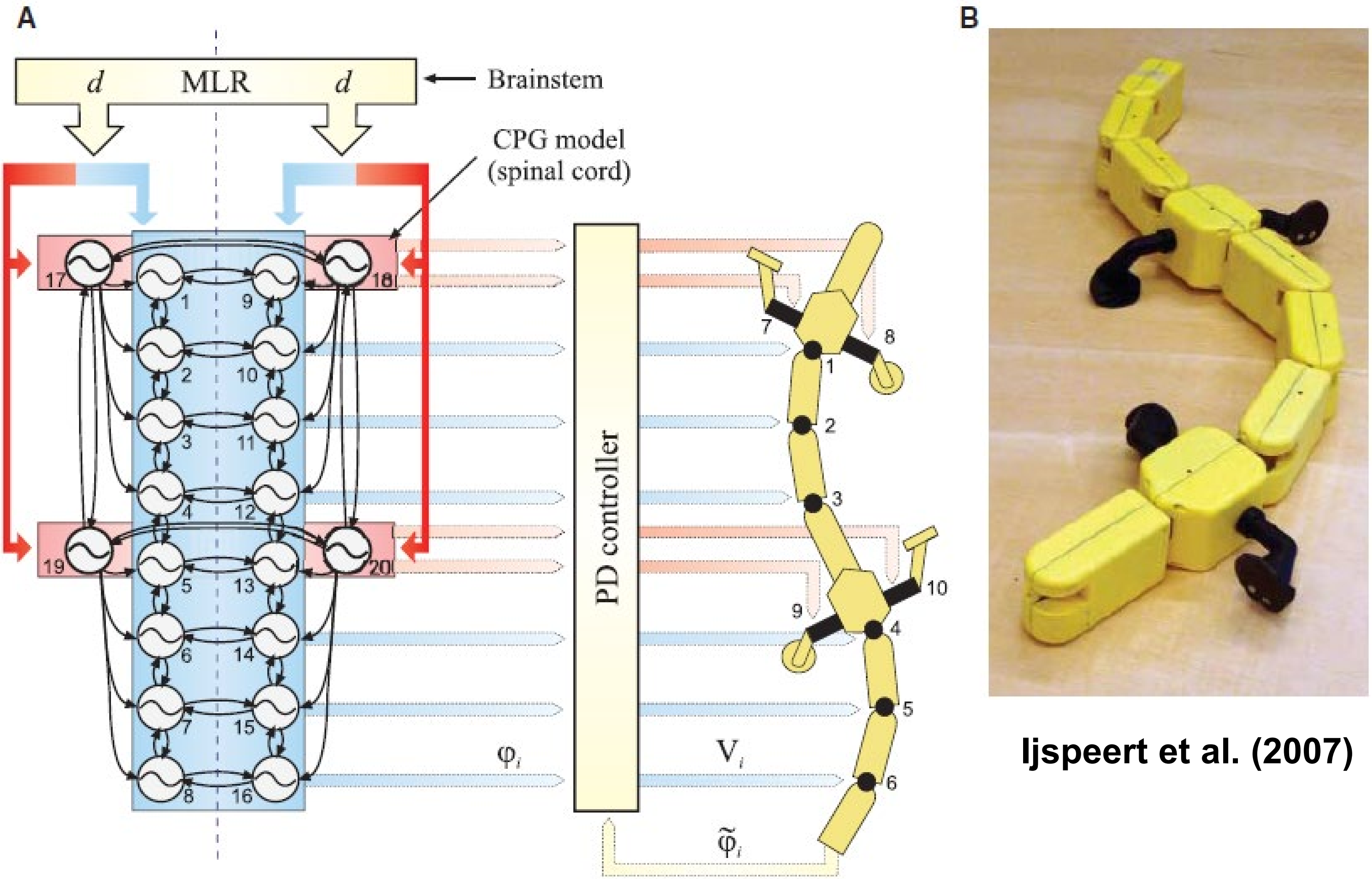


Modeling of ligand-gated channels VIII

- Example 3: **Periodic bursting:** (contd.)
  - Neural dynamics behaves similar to a **nonlinear oscillator.**
  - By coupling of such nonlinear oscillators quite complex behaviors can be generated.
  - Example: **EPFL salamander robot** (A. Ijspeert and colleagues):
    * realizes locomotion on ground and in water, and the transition between these two locomotion styles.
    * based on **dynamically coupled central pattern generators** (nonlinear oscillators).
    * works in reality (even on the lake of Geneva).

A. Ijspeert

Modeling of ligand-gated channels IX



Ijspeert et al. (2007)

− Coupled CPGs generate walking rhythms (‘dynamic movement primitives’); e.g. walking and swimming.

Modeling of ligand-gated channels X

EPFL salamander robot **Ijspeert et al. (2007)**

Overview

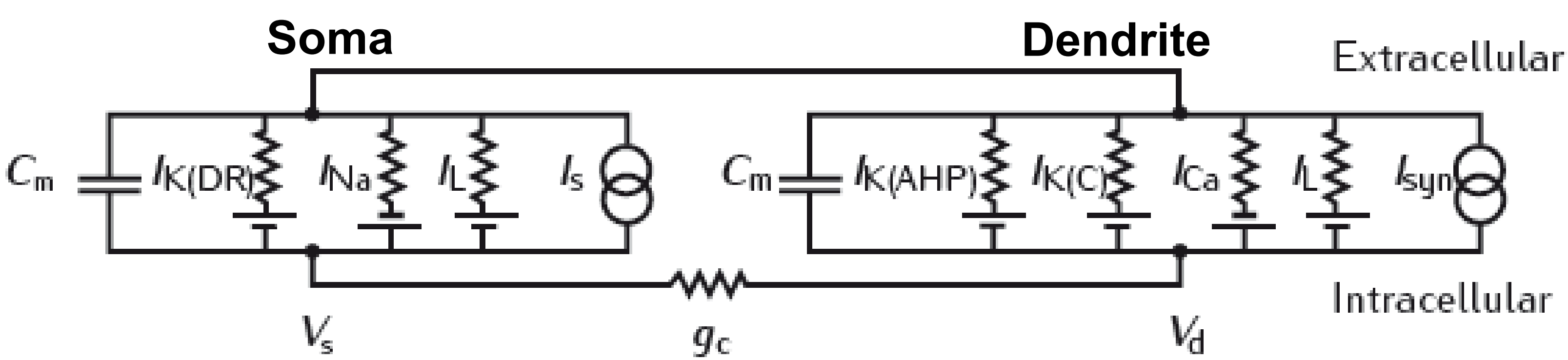
- Extensions of the HH model
- Simplified neuron models

Simplified neuron models

- So far we have mainly extended the HH model by integration of more / different components.
- Resulting models very difficult to analyze mathematically.
- For many applications it is useful to reduce the complexity of such models, retaining essential dynamical properties.
- Main reasons:
  1) understanding what the necessary essential components are
  2) building and analysis of models with many neurons
- Different approaches for the reduction of model complexity.

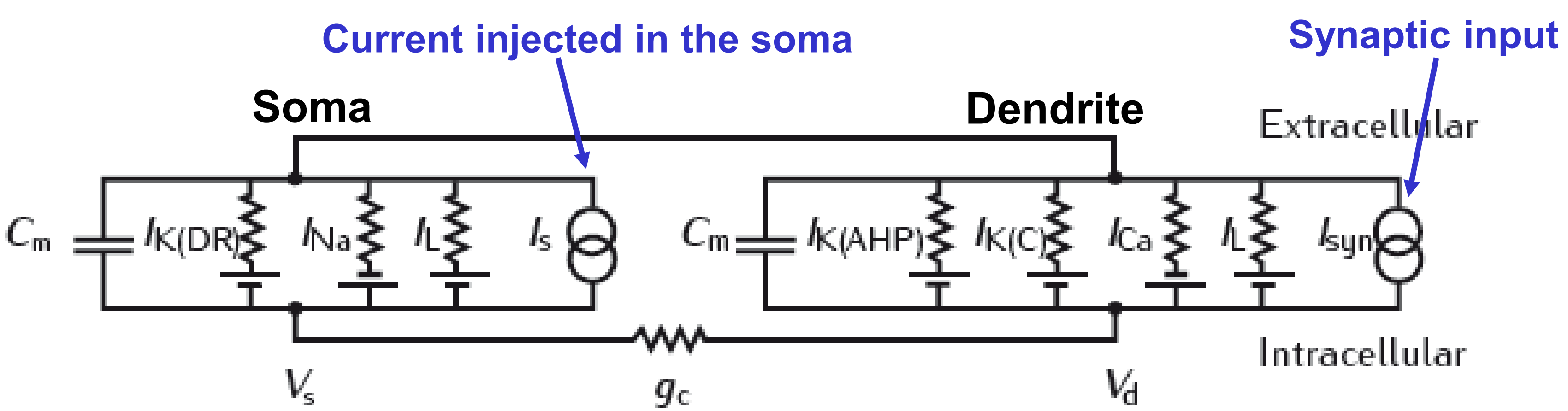
Reduction of number of compartments

- Lumping up **compartments**, similar to the Rall model discussed before; not always justified!
- Example: **Pinsky-Rinzel model** of CA3 neurons in the hippocampus:
  - **Two compartments** modeling soma and dendrite.
  - Derived from 19 compartment model by Traub et al. (1991).
  - Soma compartment: sodium (Na) and potassium delayed-rectifier (K(DR)) current + leak current (L).



Reduction of number of compartments

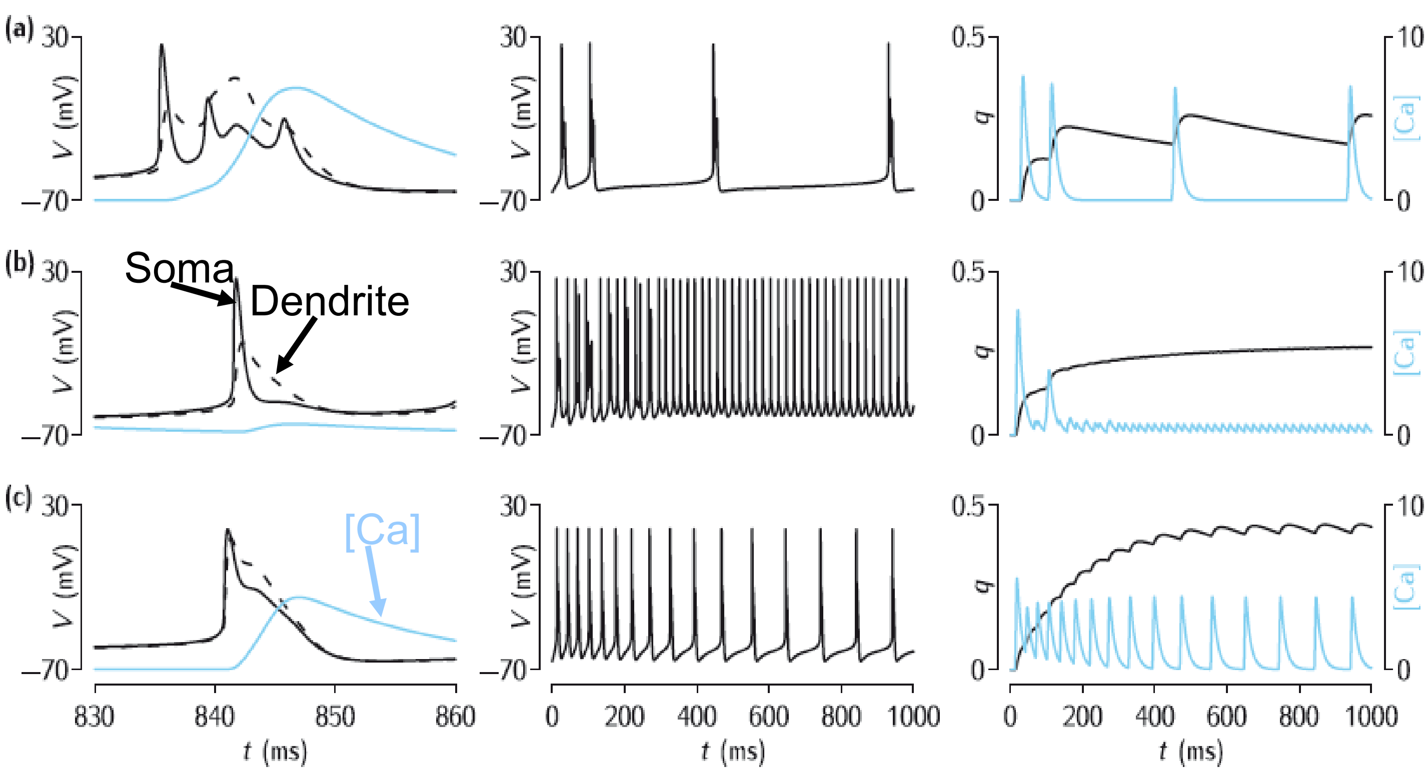
- Example: **Pinsky-Rinzel model** (cont.)
  - Dendrite compartment: voltage-dependent calcium current (Ca), voltage-independent Ca-dep. potassium AHP current (AHP: after hyperpolarization), calcium-dependent potassium current (K(C))
  - coupling conductance between compartments g_c
  - In addition, variation of proportion of membrane surface that is belonging to the soma vs. dendrite (details: Sterratt book)
  - Model reproduces variety of realistic activity patterns.



Reduction of number of compartments

- Example: **Pinsky-Rinzel model** (cont.)

Membrane potentials and Ca^{2+} concentration for one AP | **Membrane potential** | **Ca^{2+} concentration and AHP activation variable q**

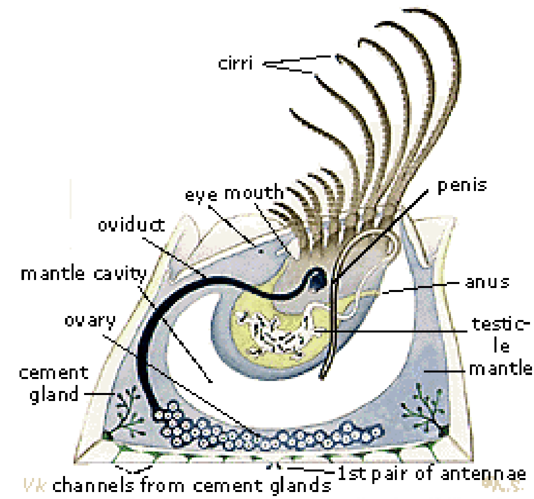


I_s $\frac{\mathrm{mA}}{\mathrm{cm}^2}$	g_c $\frac{\mathrm{mS}}{\mathrm{cm}^2}$	
0.15	2.1	Short bursts; initiated form soma
0.5	2.1	Mainly regular APs; [Ca] remains small
0.5	10.5	Single spikes with long after-depolarizing shoulder

Reduction of number of state variables

- Example: **Morris-Lecar model**
  - **Single compartment** $\Rightarrow$ mathematically much simpler; allows application of dynamical systems theory (see later).
  - Originally model for barnacle giant muscle fibre.
  - Potassium and calcium conductance; both **not inactivating**. $\Rightarrow$ Both represented by a single state variable.
  - Additional leak conductance; Na can be neglected.
  - Further assumption: **Ca^{2+} dynamics** responds **instantaneously** to voltage changes. $\Rightarrow$ Dynamic equation for $[Ca^{2+}]$ can be neglected, and concentration is defied by the stationary value $[Ca^{2+}]_\infty$; this trick removes another dynamical state variable.
  - Only two state variables: V and w (potassium state).

Barnacles



Reduction of number of compartments

- Example 2: **Morris-Lecar model** (contd.)
  - **Model equations:**

$$C\frac{\mathrm{d}V}{\mathrm{d}t}+\bar{g}_{\mathrm{K}^+}w\left(V-E_{\mathrm{K}^+}\right)+\bar{g}_{\mathrm{Ca}^{2+}}m_\infty(V)\left(V-E_{\mathrm{Ca}^{2+}}\right)+\bar{g}_{\mathrm{L}}\left(V-E_{\mathrm{L}}\right)=I_{\mathrm{e}}(t)$$

$$\frac{\mathrm{d}w}{\mathrm{d}t}=\frac{w_\infty(V)-w}{\tau_w(V)}$$

with

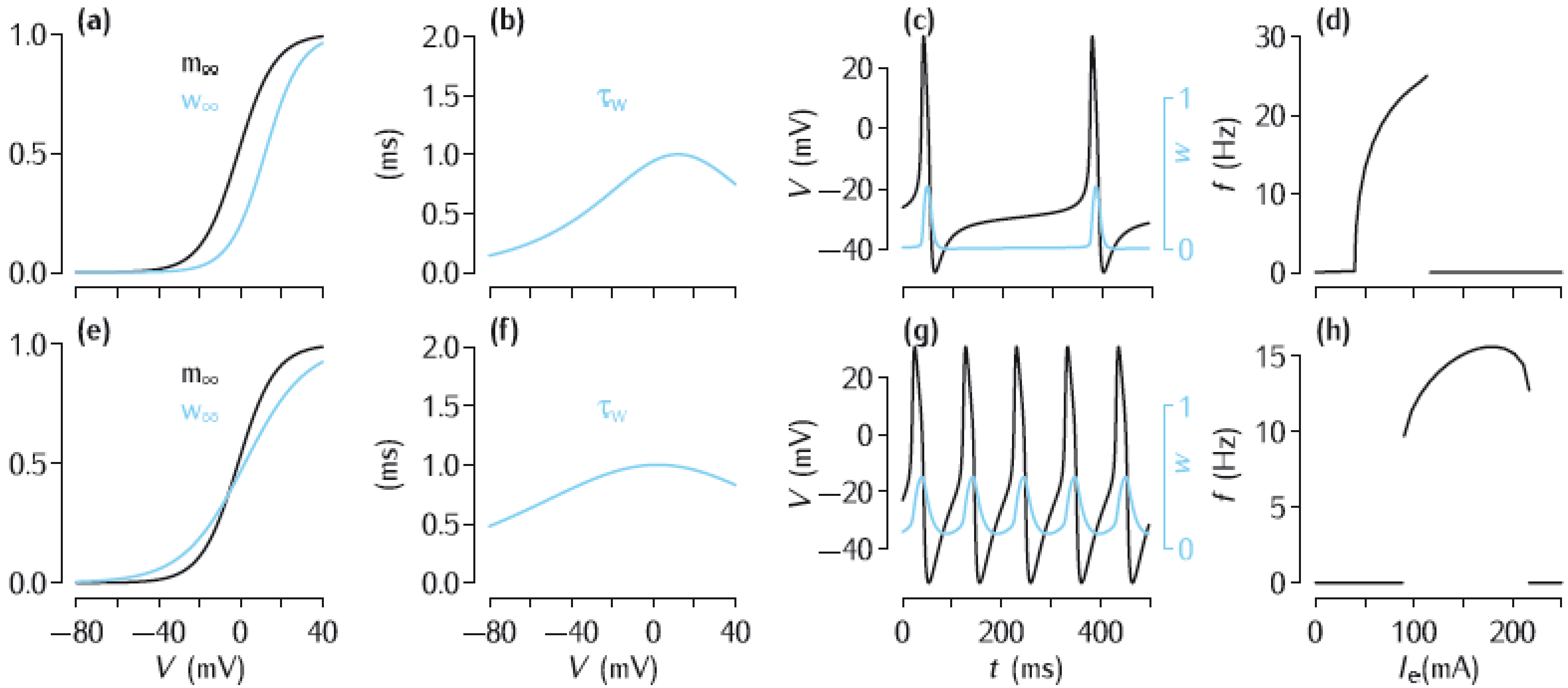
$$m_\infty(V)=0.5\,(1+\tanh(V-V_1)/V_2)$$

$$w_\infty(V)=0.5\,(1+\tanh(V-V_3)/V_4) \qquad \text{Constants}: \quad \bar{g}_i, E_i, V_i, \phi$$

$$\tau_w(V)=\phi/\cosh\frac{V-V_3}{2V_4}$$

Reduction of number of compartments

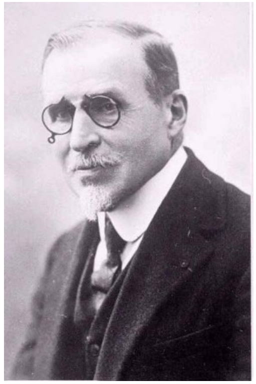
- Example 2: **Morris-Lecar model** (contd.)
  - Dependent on parameters, **type I** and **type II behavior** can be generated:



Type I behavior

Type II behavior

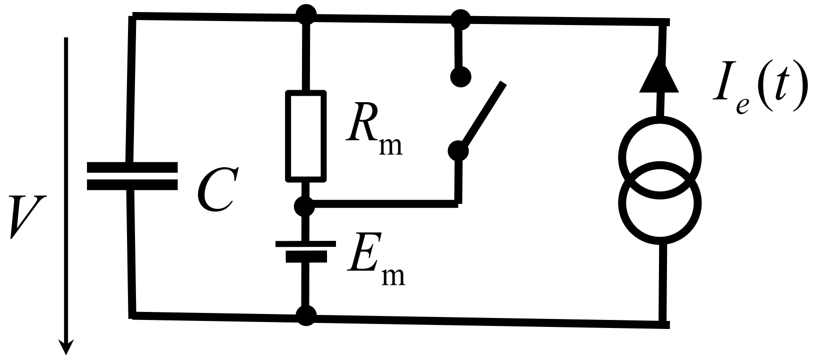
Integrate and fire (IF) models I

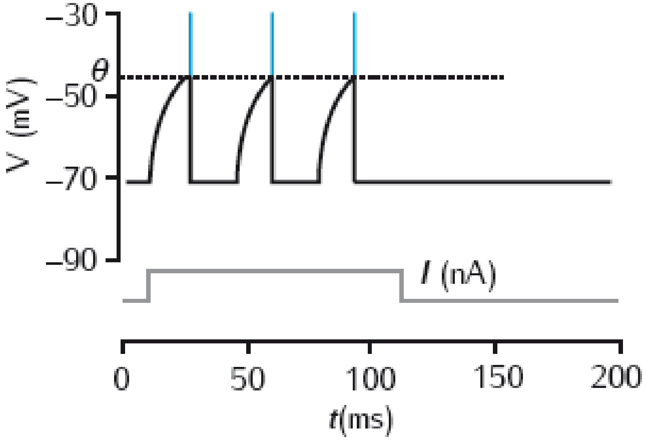


L. Lapicque

- Direct modeling of spikes by delta peaks; neglecting details of underlying dynamics.
- First used by Lapicque (1907); analyzed in detail much later.
- Simple IF model: Passive membrane dynamics integrates current until potential reaches threshold θ, then spike is initiated and potential is reset to E_m.

Simple IF model





Integrate and fire (IF) models II

- Until V reaches threshold θ the potential follows the passive membrane dynamics:

$$\boxed{C\frac{\mathrm{d}V}{\mathrm{d}t}+\frac{V(t)-E_\mathrm{m}}{R_m}=I_\mathrm{e}(t) \quad\Leftrightarrow\quad \tau_m\frac{\mathrm{d}V}{\mathrm{d}t}=E_\mathrm{m}-V(t)+R_m I_\mathrm{e}(t)}$$

- We have derived the solution of this equation for $V(0) = E_\mathrm{m}$ and constant input current I_0:

$$V(t)=E_\mathrm{m}+R_m I_0(1-e^{-t/\tau_\mathrm{m}}) \quad \text{with} \quad \tau_\mathrm{m}=R_\mathrm{m}C$$

- From this we obtain with $\tilde{\theta}=\theta-E_\mathrm{m}$ the time between two spikes:

$$T_s=-\tau_m\ln\left(1-\frac{\tilde{\theta}}{R_\mathrm{m}I_0}\right)$$

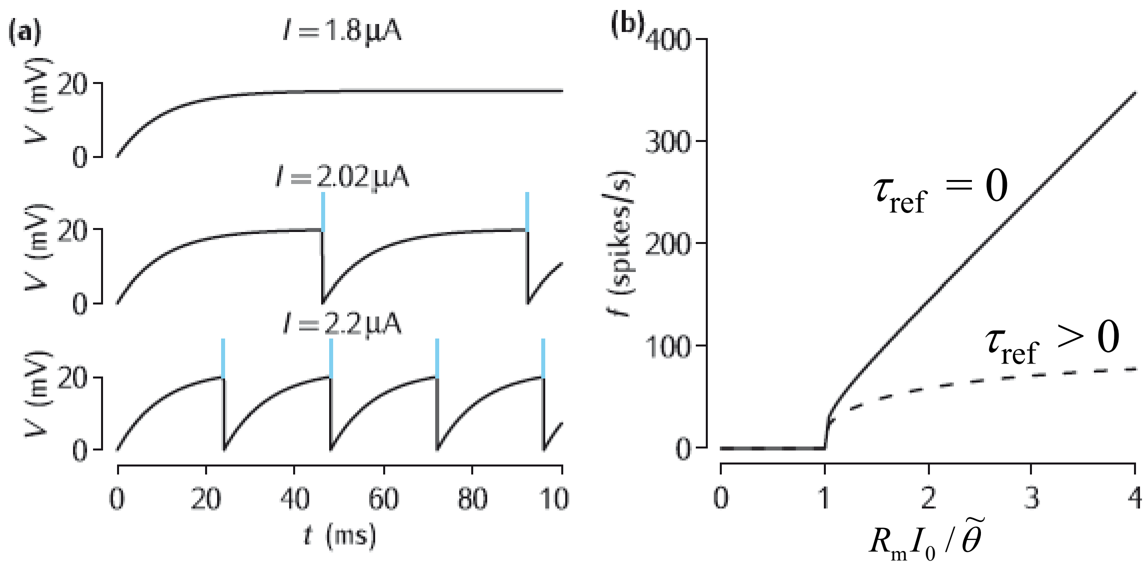
Integrate and fire (IF) models III

- With an additional absolute refractory period τ_{ref} this implies for the firing frequency:

$$\boxed{f(I_0) = \frac{1}{T_s + \tau_{\text{ref}}} = \frac{1}{\tau_{\text{ref}} - \tau_{\text{m}} \ln\left(1 - \tilde{\theta} / R_{\text{m}} I_0\right)}}$$

- Remark: for $\tau_{\text{ref}} = 0$ and large I_0 because of $\ln(1\text{-}x) = \text{-}x + O(x^2)$ approximately linear transfer function:

$$f(I_0) \approx \frac{R_{\text{m}}}{\tau_{\text{m}} \tilde{\theta}} I_0$$

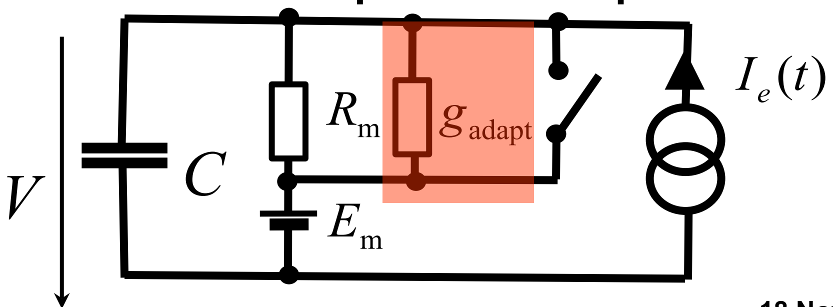


Extensions of IF models I

- Basic IF model too simple to reproduce several typical properties of neurons; extensions have been proposed that make the behavior more similar to real neurons.
- Often neurons show **spike rate adaptation**: Firing rate for sustained constant input current decreases throughout spike train.
- Integration in model: Add repolarizing **adaptation conductance** in the model that increases by $\Delta g_{\mathrm{adapt}}$ after each spike, and which decays exponentially between spikes according to the equation:

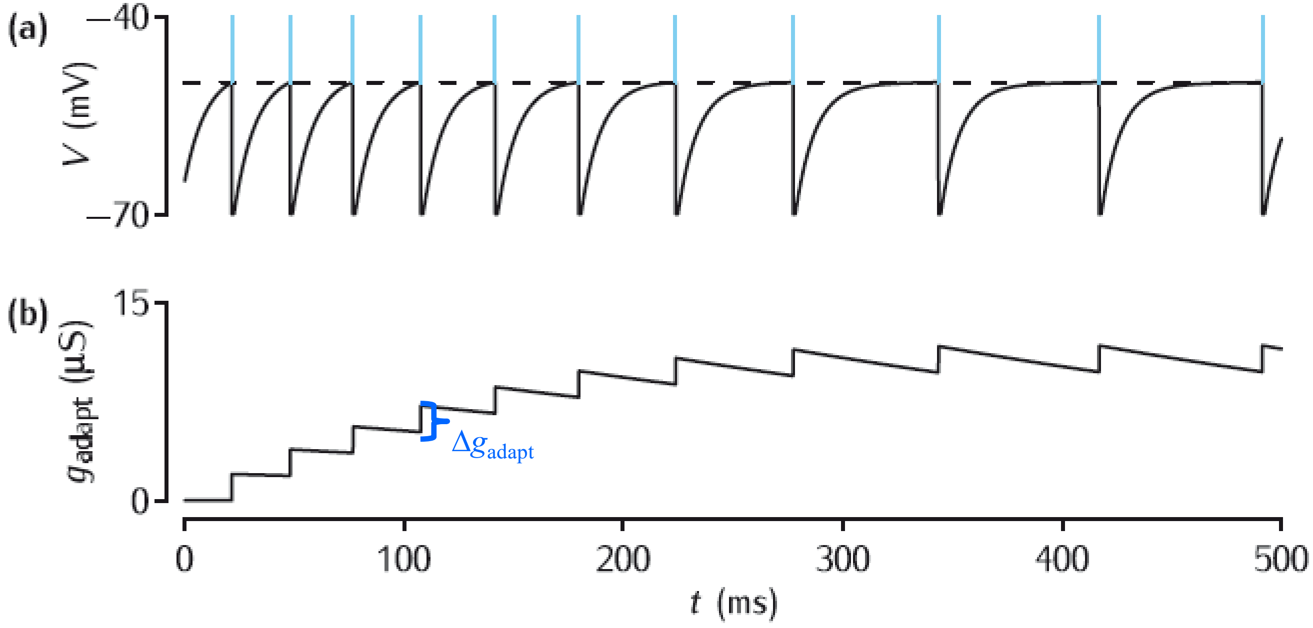
$$\boxed{\frac{\mathrm{d}g_{\mathrm{adapt}}}{\mathrm{d}t} = -\frac{g_{\mathrm{adapt}}}{\tau_{\mathrm{adapt}}}}$$

IF model with spike rate adaptation



Extensions of IF models II

- Example simulation:



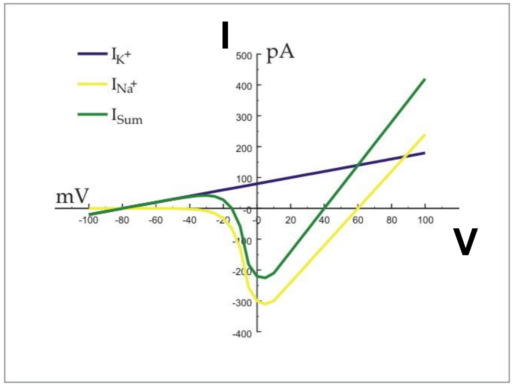
Extensions of IF models III

- For model with active conductances total ionic current changes its sign from outward to inward if potential increases beyond threshold.
- For linear IF model outward current keeps increasing close to threshold.
- Better approximation by **quadratic integrate and fire neuron**; membrane potential between spikes follows DEQ:

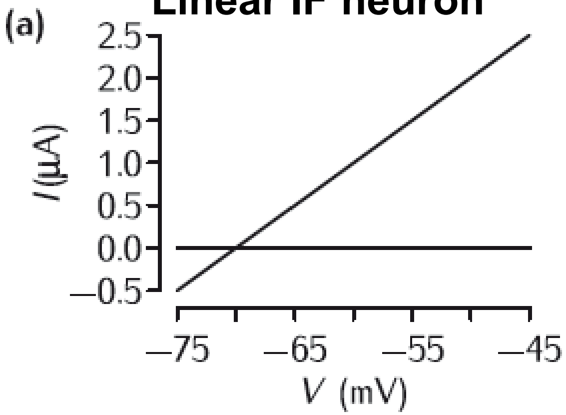
$$\boxed{C\frac{\mathrm{d}V(t)}{\mathrm{d}t}+\frac{(V(t)-E_{\mathrm{m}})(V_{\mathrm{thr}}-V(t))}{R_m(V_{\mathrm{thr}}-E_{\mathrm{m}})}=I_{\mathrm{e}}(t)}$$

- Other similar nonlinear models have been tested.

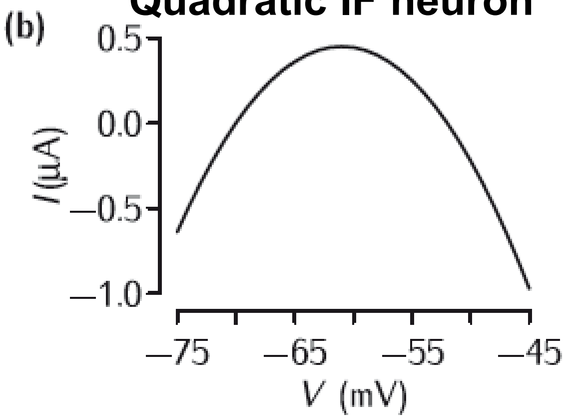
Real I-V characteristics



Linear IF neuron



Quadratic IF neuron



Extensions of IF models IV

- Adding a recovery variable, modeling difference between inward and outward current, one obtains **Izhikevitch model**:

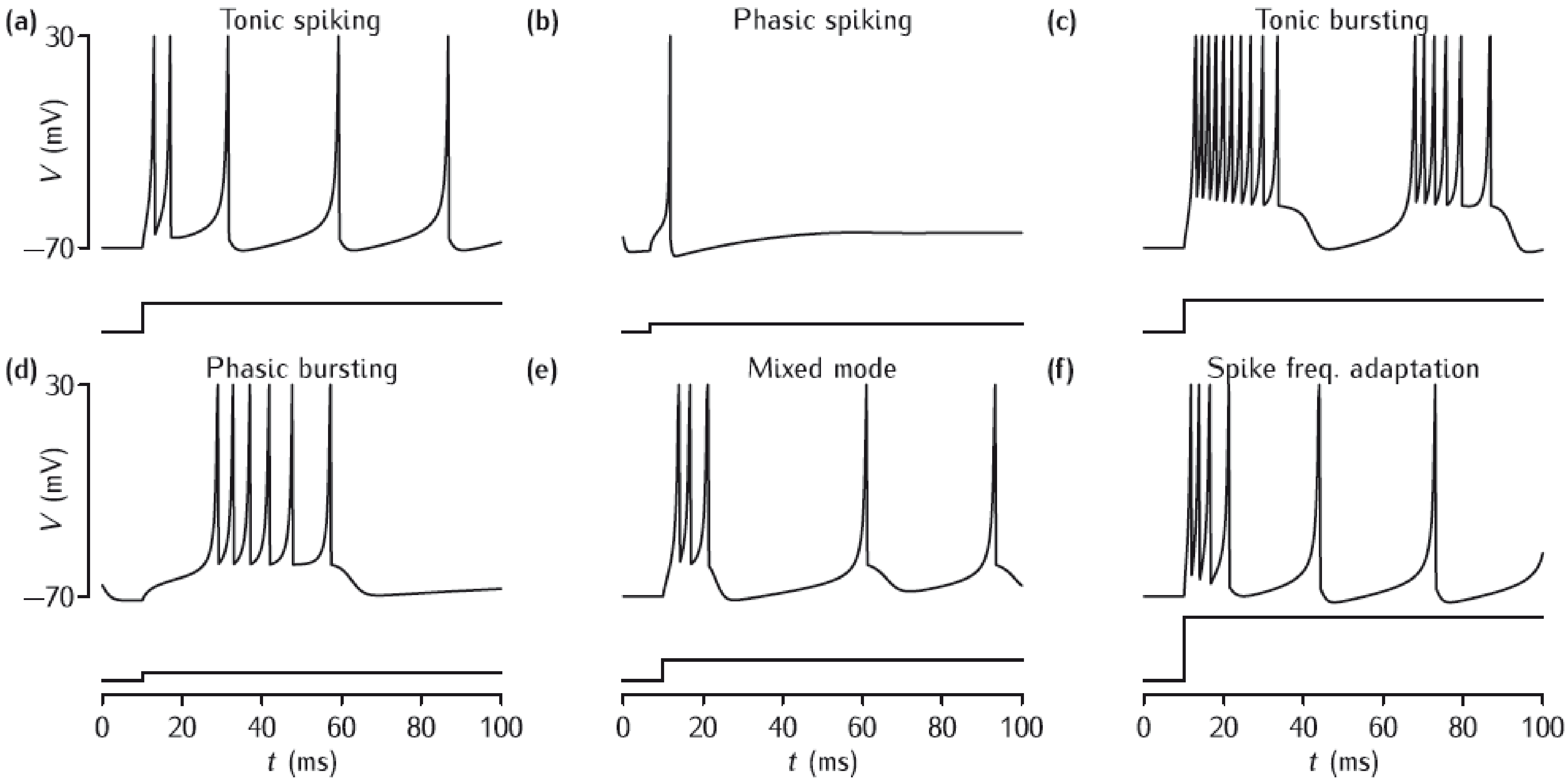
$$\boxed{\begin{array}{l} \dfrac{\mathrm{d}V}{\mathrm{d}t} = k(V(t)-E_{\mathrm{m}})(V(t)-V_{\mathrm{thr}}) - u + I_{\mathrm{e}}(t) \\ \dfrac{\mathrm{d}u}{\mathrm{d}t} = a(b(V(t)-E_{\mathrm{m}})-u) \\ \text{where for } V > \theta \text{ the dyanamic variables are reset to:} \\ \mathrm{V} \rightarrow \mathrm{c}, \mathrm{u} \rightarrow \mathrm{u}+\mathrm{d} \end{array}}$$

- This model can reproduce many interesting behaviors of real neurons.

E. Izhikevitch 

Extensions of IF models V

- Example behaviors of Izhikevitch model for different parameter settings:



Rate-based models I

- For some applications approximation if detailed spike-timing is highly relevant (e.g. for synchronization, representation of timing, etc.); for others not.
- Form the basis of what is called '**deep neural networks**'.
- Dynamics of rate-based models much easier to analyze than the one of spiking networks.
- Adrian (1928): firing frequency of cutaneous sensors of the frog varies linearly with the stimulus intensity.
- Assumption of a **transfer function** f that maps input current directly to a spike rate.
- This approximation forms the basis of classical **artificial neural networks** (ANNs); often combined with learning rules for synaptic weights.

Rate-based models II

- Typical transfer functions:

  Linear threshold function:
  (e.g. Hartline & Ratliff, 1958; since 2008: 'ReLU nonlinearity')

Threshold parameter

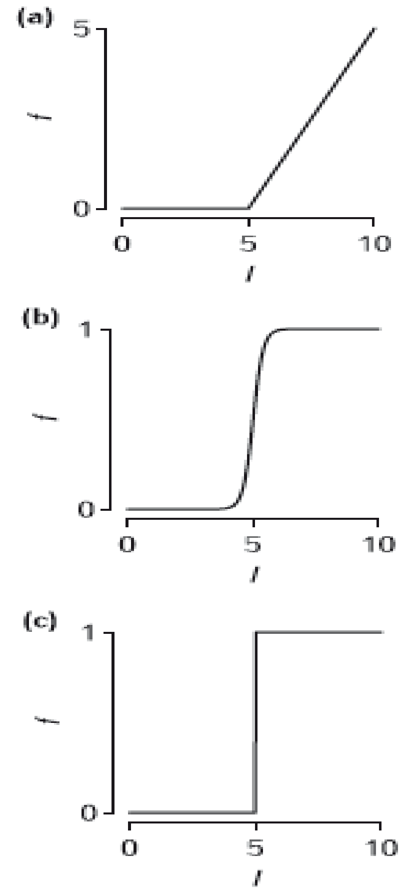
$$f(I) = \begin{cases} 0 & \text{for} \quad I < \theta \\ k(I-\theta) & \text{for} \quad I \geq \theta \end{cases}$$

  Sigmoid function:

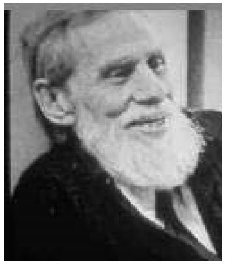
$$f(I) = \frac{\bar{f}}{1+\exp(-k(I-\theta))}$$

  Step function:
  ('McCulloch-Pitts neuron', 1943)

$$f(I) = \begin{cases} 0 & \text{for} \quad I < \theta \\ 1 & \text{for} \quad I \geq \theta \end{cases}$$



W. Pitts



W. McCullogh

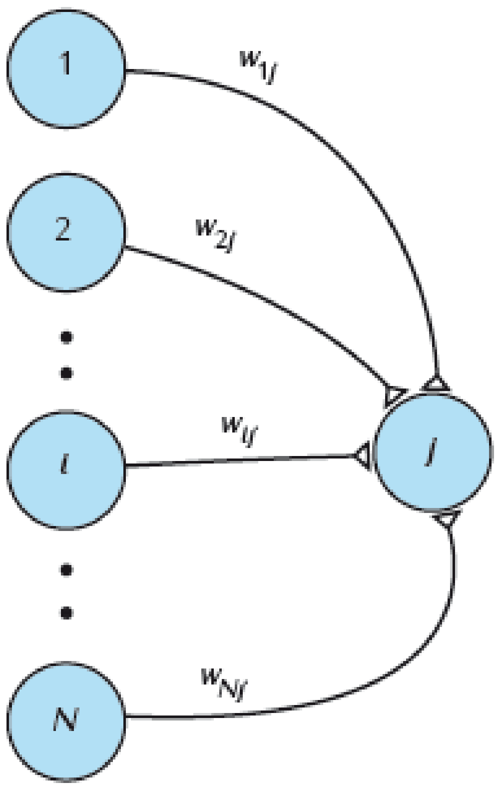
Rate-based models II

- Example 1: **Feed-forward neural network**:

$$\boxed{I_{\text{out,n}} = \sum_m w_{nm} f(I_m)}$$

(Used, for example, to model visual filters or object re-cognition.)

- Input currents: I_m;
Thresholded inputs / firing rates: $f(I_m)$
Output currents: $I_{\text{out},n}$



Rate-based models III

- Example 2: **Dynamic feed-forward neural network I**: (ctd.)

  One can interpret $I_{\text{out},n}$ as function of the total synaptic input current of the neuron that is generated by the input firing rates $f(I_m)$:

$$\boxed{I_{\text{out},n}(t) = \sum_m \int_{-\infty}^{t} \kappa(t-t')\, w_{nm} f(I_m(t'))\, \mathrm{d}t'}$$

Synaptic kernel: determines shape of postsynaptic response for a spike

  Choosing $\kappa(t) = \frac{1}{\tau}\exp(-t/\tau)$ gives exactly the solution of the differential equation above for $I_{\text{out},n}$ since then $\kappa(t)$ is the corresponding Green's function (impulse response).

Rate-based models IV

- Example 3: **Dynamic feed-forward neural network II**:

$$\tau \frac{\mathrm{d}v_n}{\mathrm{d}t} = -v_n(t) + f\left(\sum_m w_{nm} \underbrace{f\big(I_m(t)\big)}_{}\right)$$
$$= -v_n(t) + f\left(\sum_m w_{nm} v_m(t)\right)$$

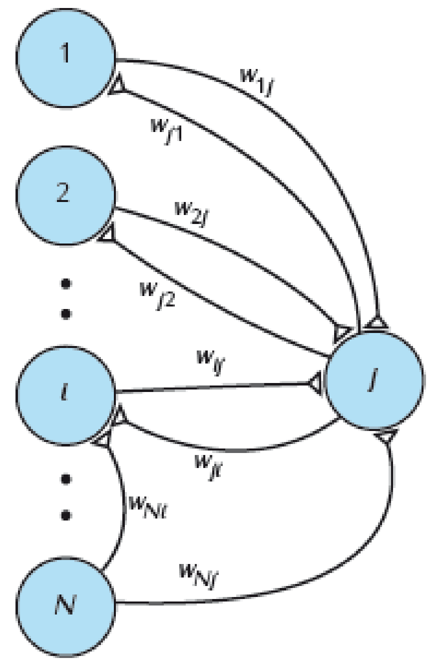
(frequency as state variable)

Interpretation: Output firing rate $v_n(t)$ reaches its stationary value with some delay since membrane acts as a low-pass filter. Remark: ‘Threshold outside summation.’

Rate-based models IV

- Example 4: **Recurrent neural network (RNN):**

$$\boxed{\tau \frac{\mathrm{d}I_n}{\mathrm{d}t} = -I_n(t) + \sum_m w_{nm} f(I_m(t)) + \underbrace{I_{n,\mathrm{ext}}(t)}_{\text{Additional external input}}}$$



(All neurons connected to all neurons with feed-forward and feedback connections.)

- Suitable for modeling memory and active pattern formation.
- Similar network can be formulated using firing rate as state variable (‘summation inside the threshold function’).
- More detailed examples follow in the ‘dynamics block’ of this lecture.

Things to remember

- A-type current → 1), 3), 4)
- Type I / II neurons → 1), 3), 4)
- Roles of calcium and coarse idea how these influences can be modeled → 4)
- Strategies to simplify models → 1), 3), 4)
- IF model and extensions → 1), 2), 3), 4)
- Rate-based models → 1), 4)

Literature (for this lecture)

1) Dayan P. & Abbott, L.F. (2001 / 2005) *Theoretical Neuroscience: Computational and Mathematical Modeling of Neural Systems.* MIT Press, Cambridge MA, USA. Chapters 5 and 6.

2) Gerstner, W. & Kistler, W. (2002) *Spiking Neuron Models - Single Neurons, Populations, Plasticity.* Cambridge University Press, UK. Chapters 1, and 4.

3) Izhikevich, E.M. (2007) *Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting.* Cambridge MA, USA.

4) Sterratt, D., Graham, B, Gillies, A., Willshaw, D. (2011) *Principles of Computational Modelling in Neuroscience.* Cambridge University Press, UK. Chapters 6, and 8.