Intracellular Recording of Neural Acitivity

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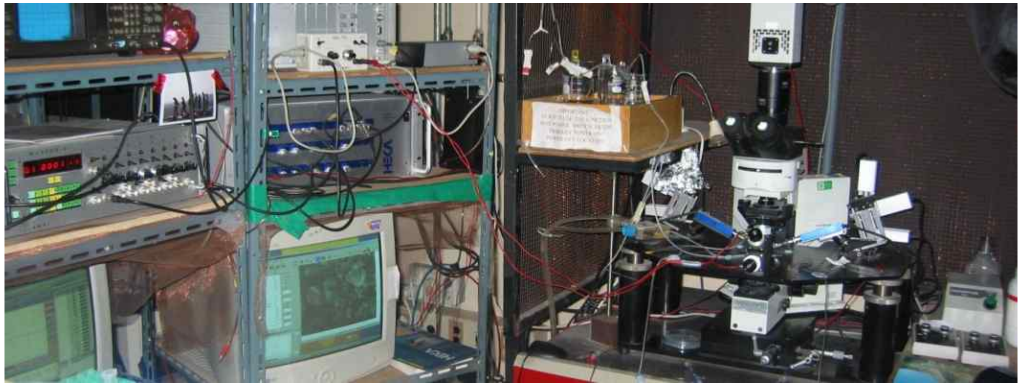
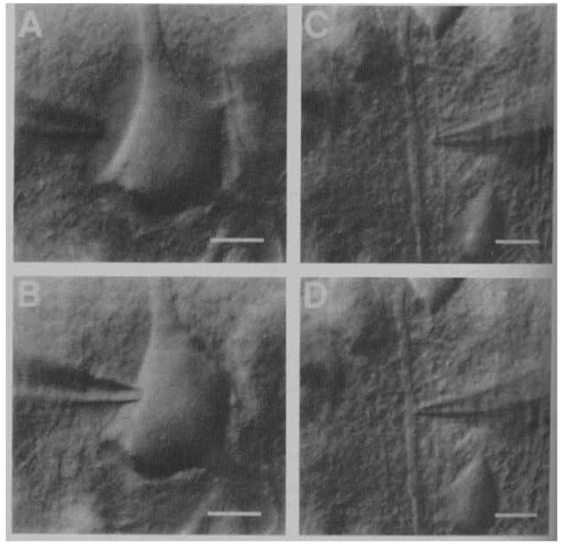
이 석 호

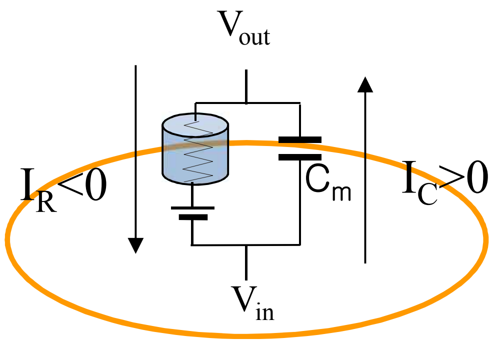
Data collection



Visualizing the neuron



이온채널을 통한 전류 (I_R)가 발생하였을 때 막전압 (V_m)의 변화



Equivalent circuit of the cell membrane

By Kirchhoff's law, $I_C + I_R = 0$

$$C_m\, dV/dt = -(I_R)$$

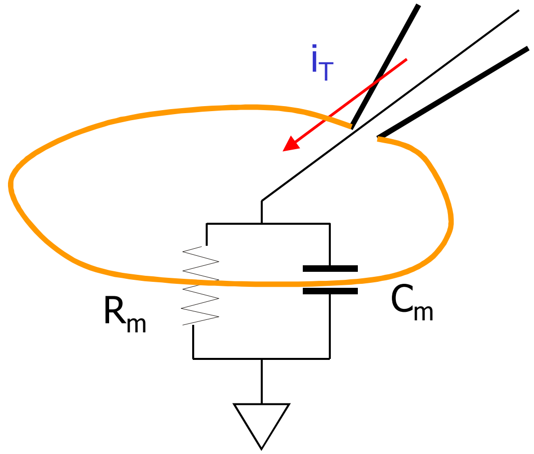
$$\Delta V_m = (-\int I_R\, dt) / C_m = \Delta Q / C_m.$$

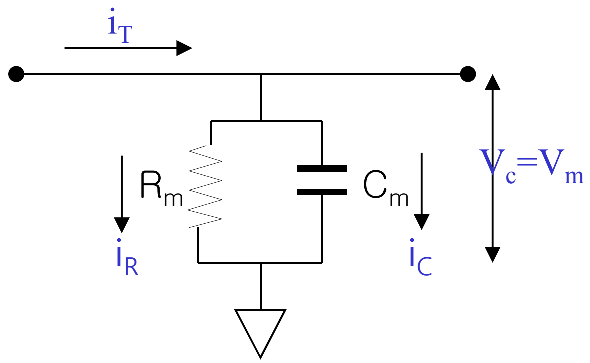
For K^+, $I_R = G_K (V_m - E_K)$

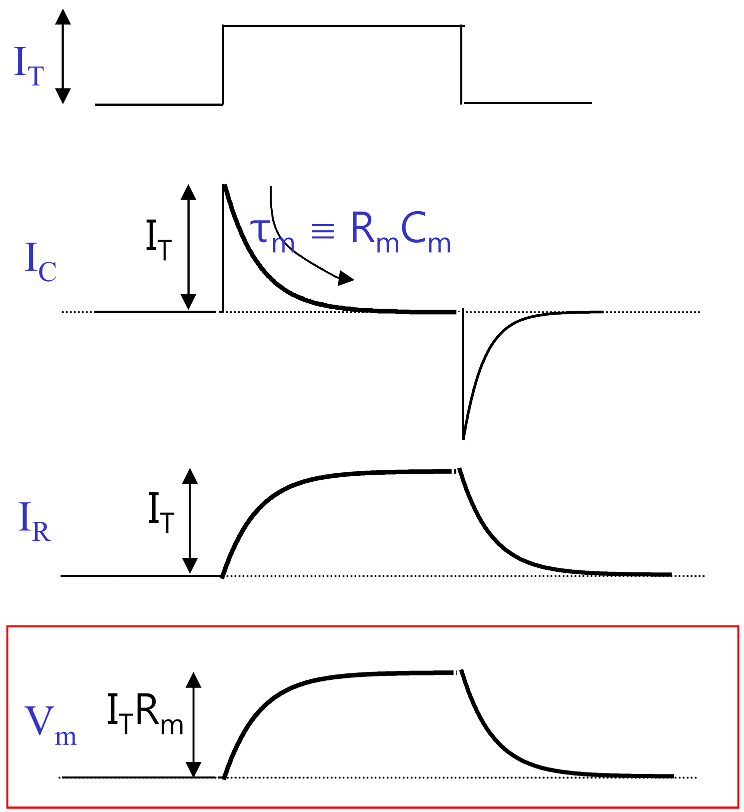
<u>Kirchhoff's law</u>

At any node in electrical circuit, current in-flow = out-flow

Passive electrical properties of the cell



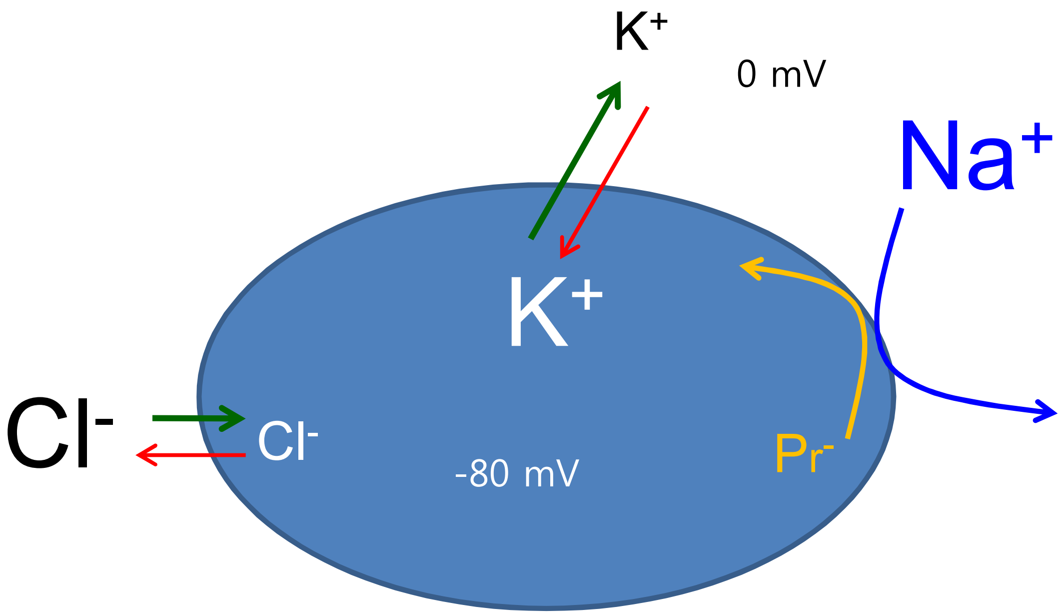




$$V_m = i_T \cdot R_m \cdot [1 - \exp(-t/\tau_m)]$$

Membrane potential is equilibrated at the point where

chemical and electrical gradients of permeant ions (K^+ & Cl^-) are balanced



Equilibrium potential

E_K = -91 mV

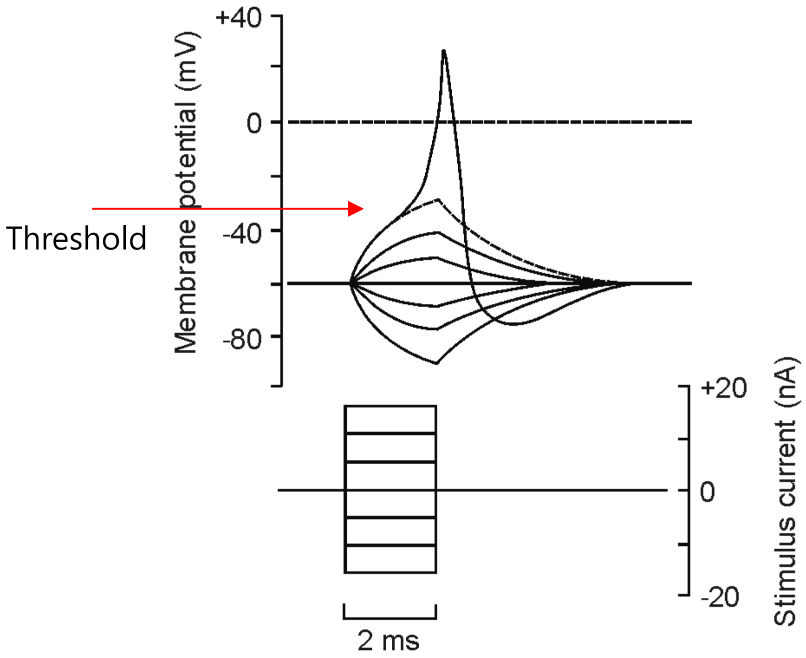
E_{Na} = +66 mV

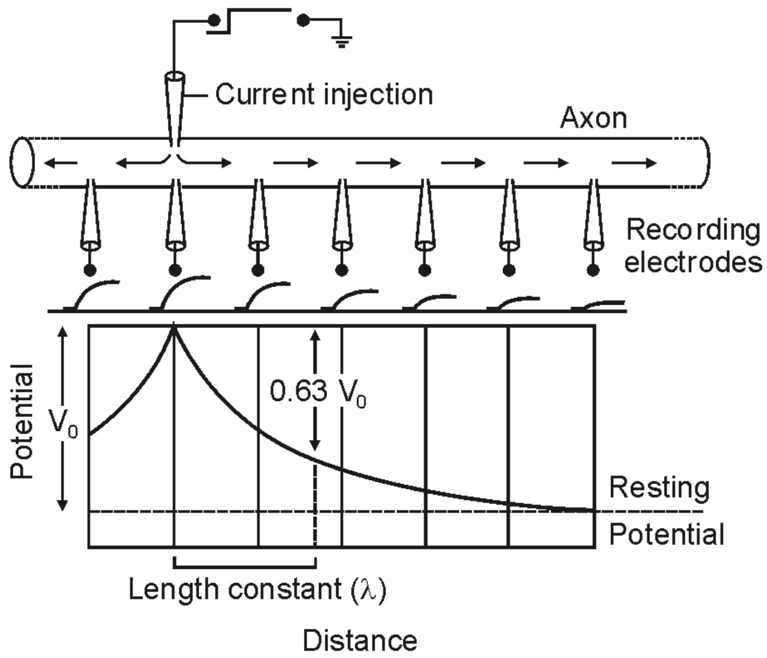
E_{Ca} = +120 mV

E_{Cl} = -70 mV

안정막전압
(resting membrane potential)
= $\Sigma G_i E_i / \Sigma G_i$
= -60 ~ -90 mV

Electrotonic and Action Potential

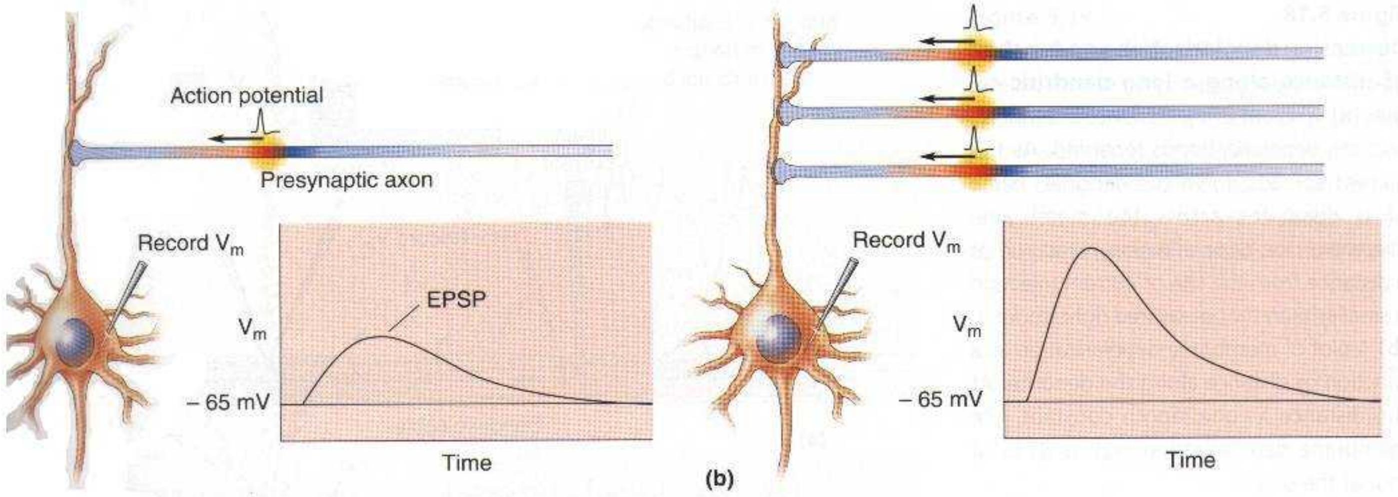




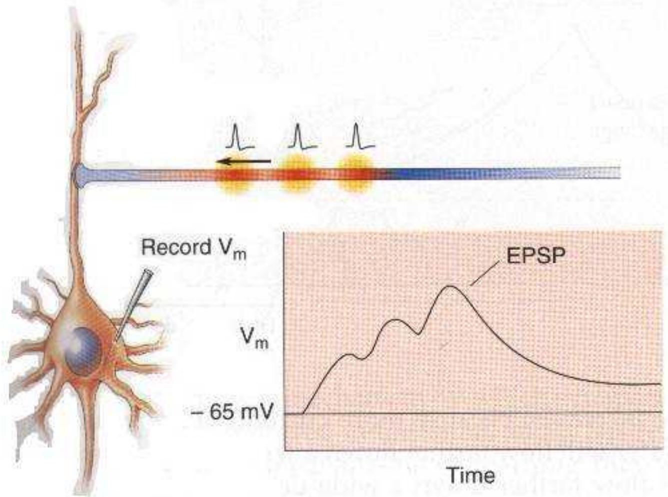
Graded response
vs
All-or-none response

Exponential decay
vs.
Regenerative rsp.

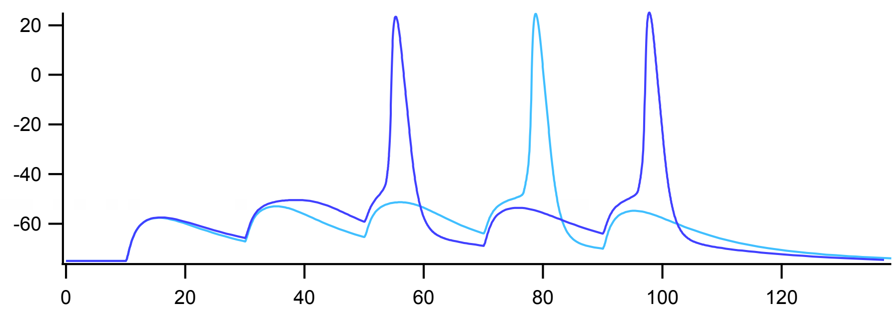
Linear summation of EPSPs



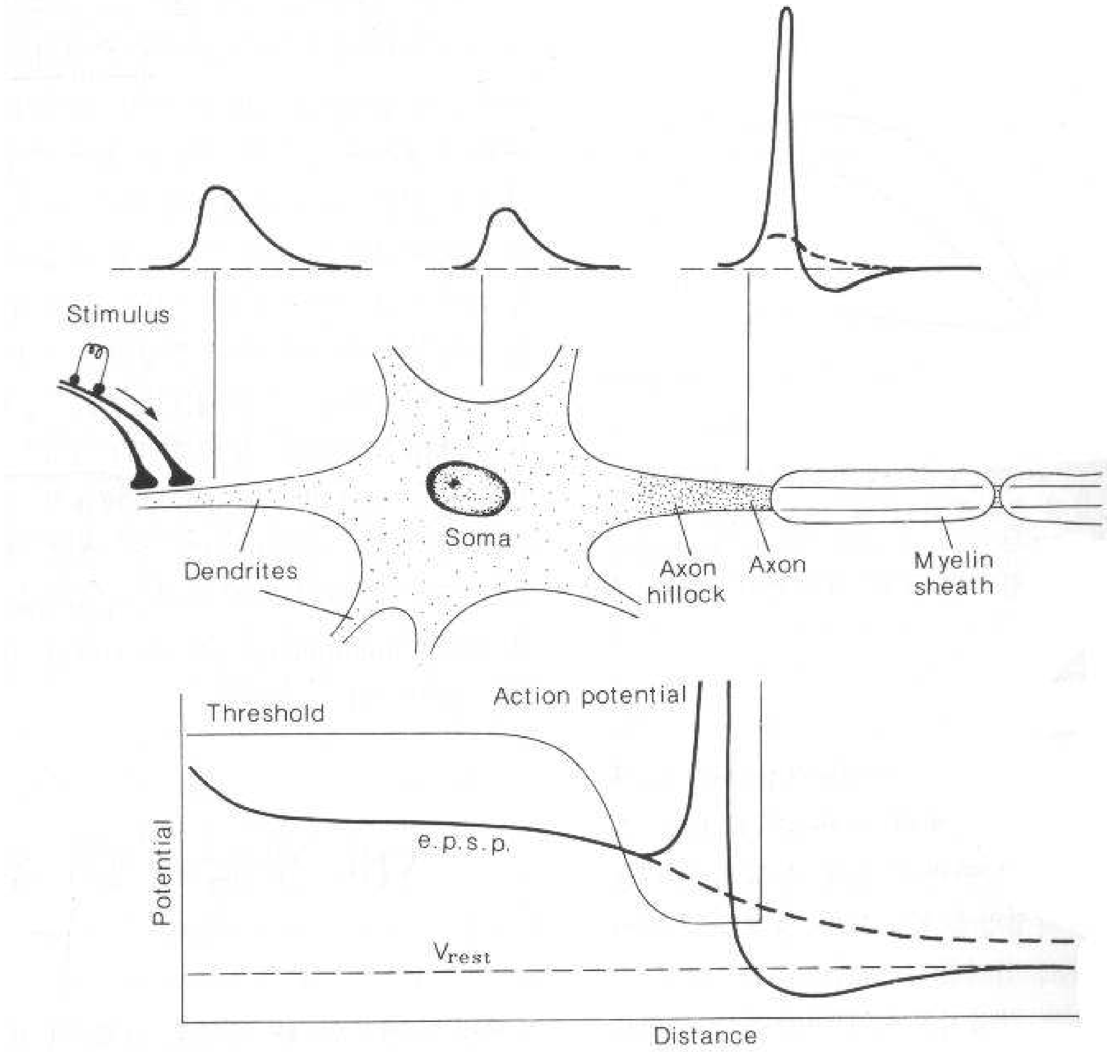
Spatial summation of EPSP



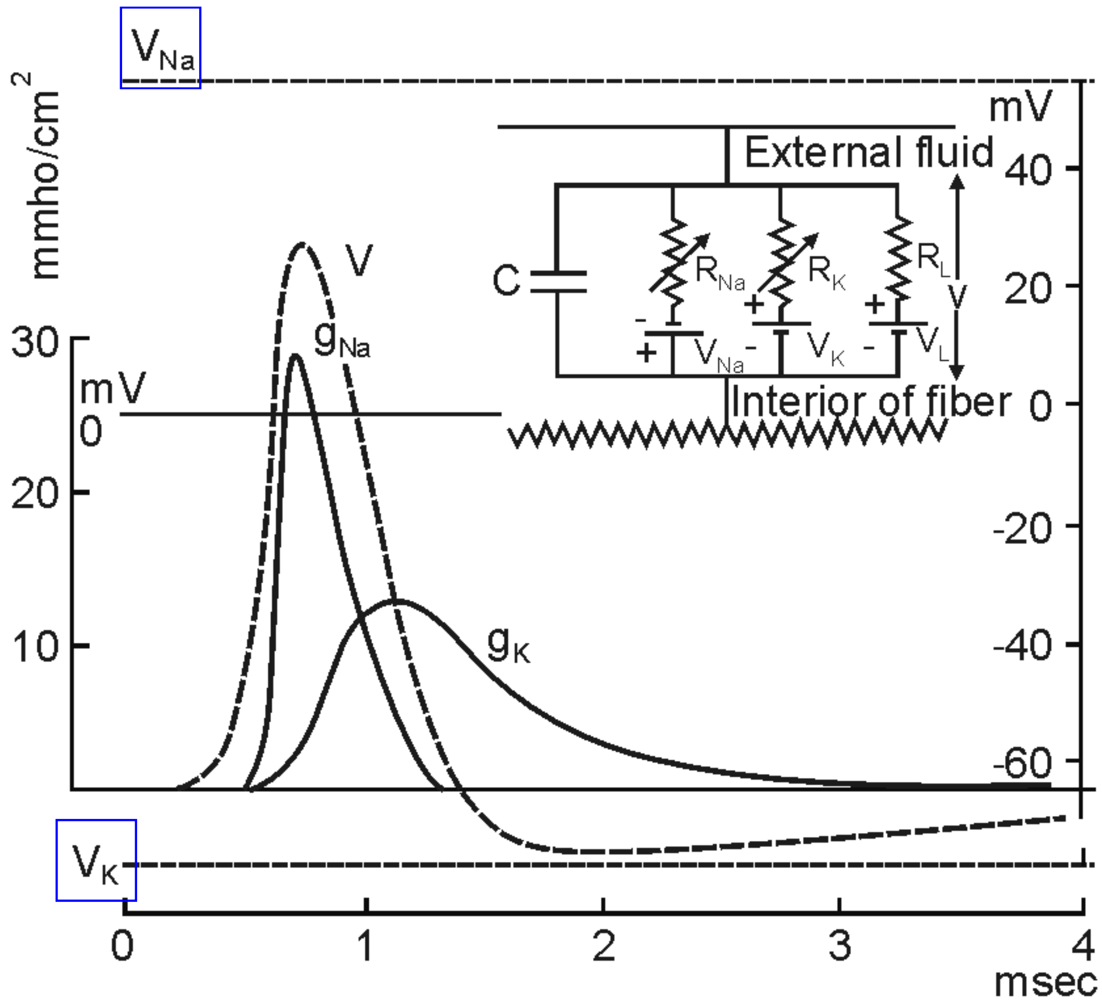
Temporal summation of EPSP



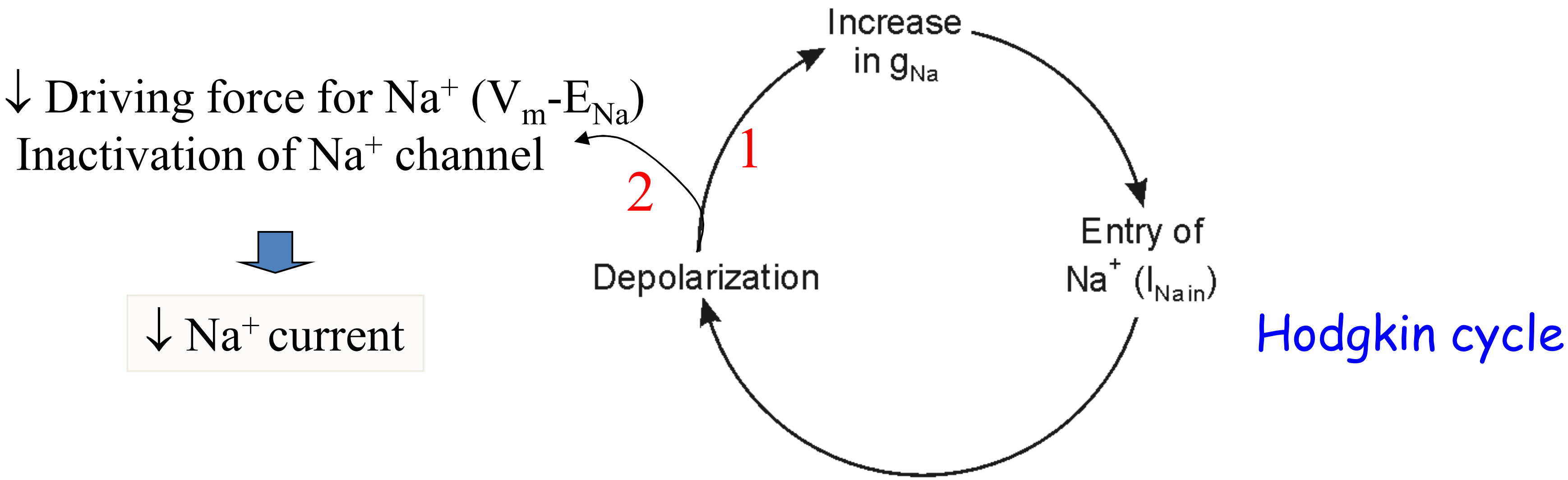
Action potential generation at an axon hillock

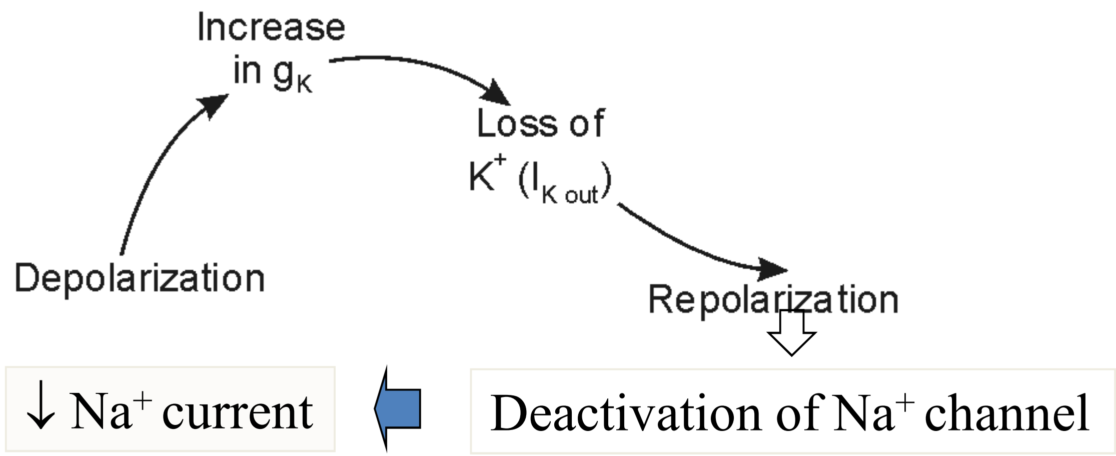


Time-dependent changes in the ionic conductance underlying AP

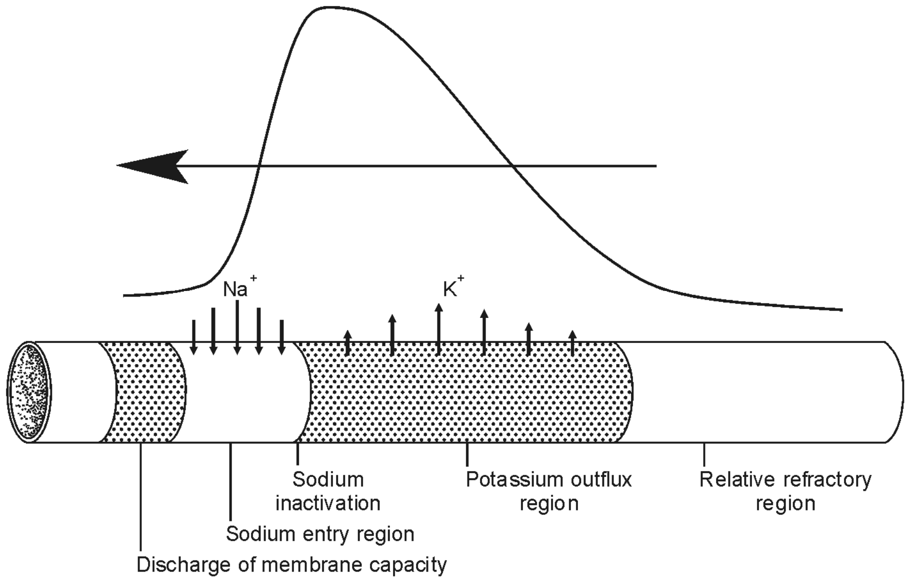


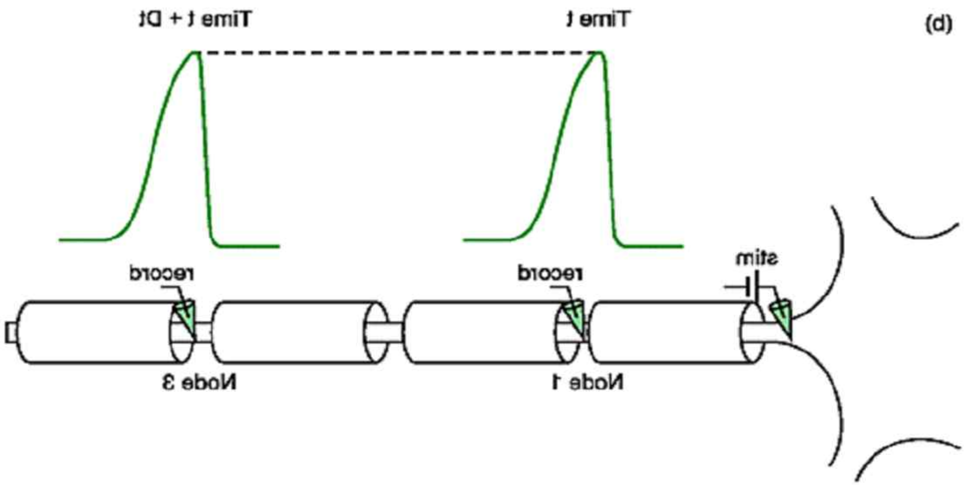
Summary for ionic mechanism of AP



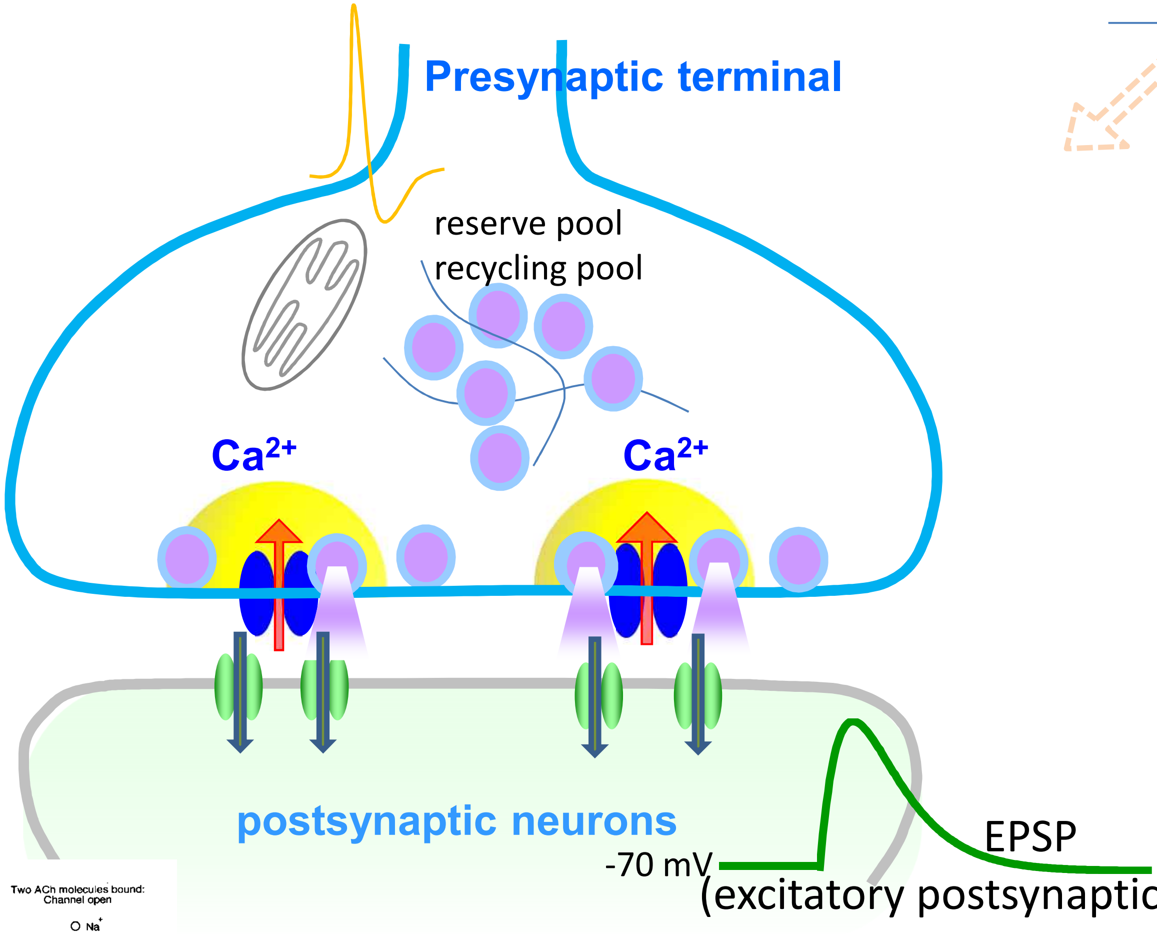


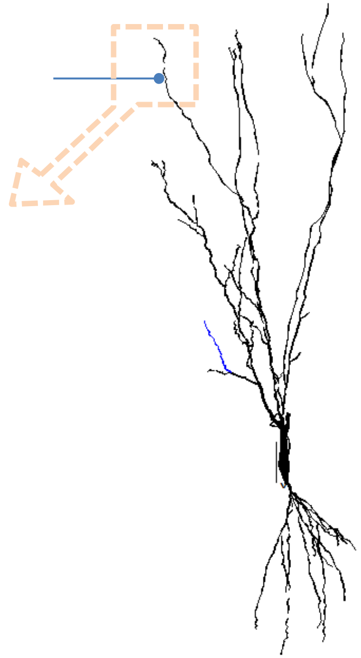
Regenerative property of Action Potential

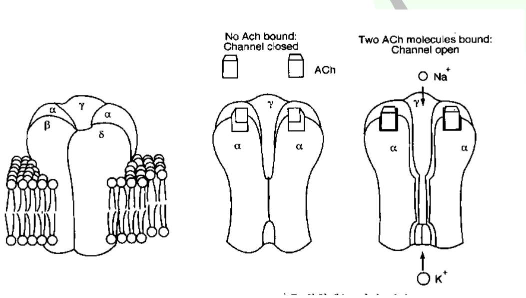




Synaptic transmission

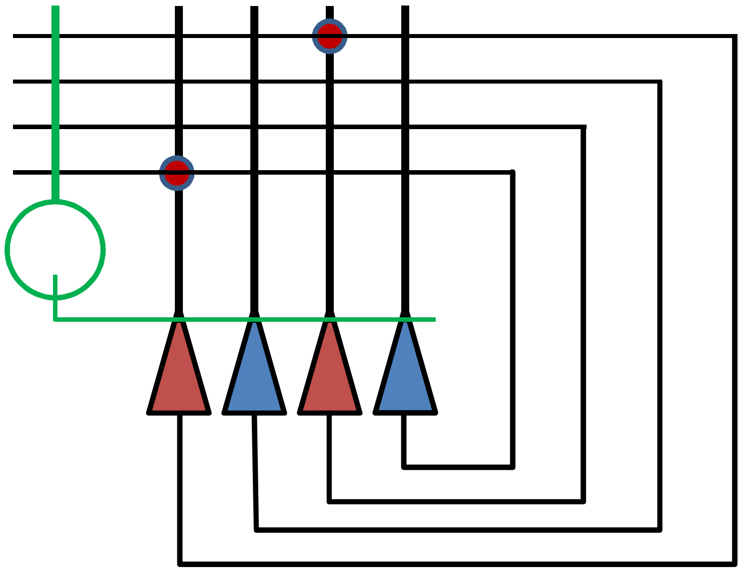


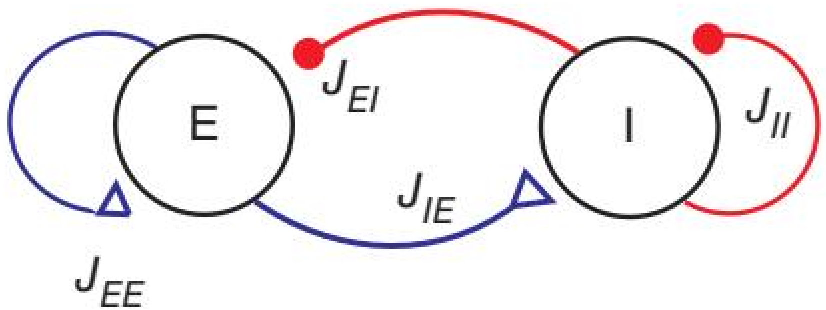




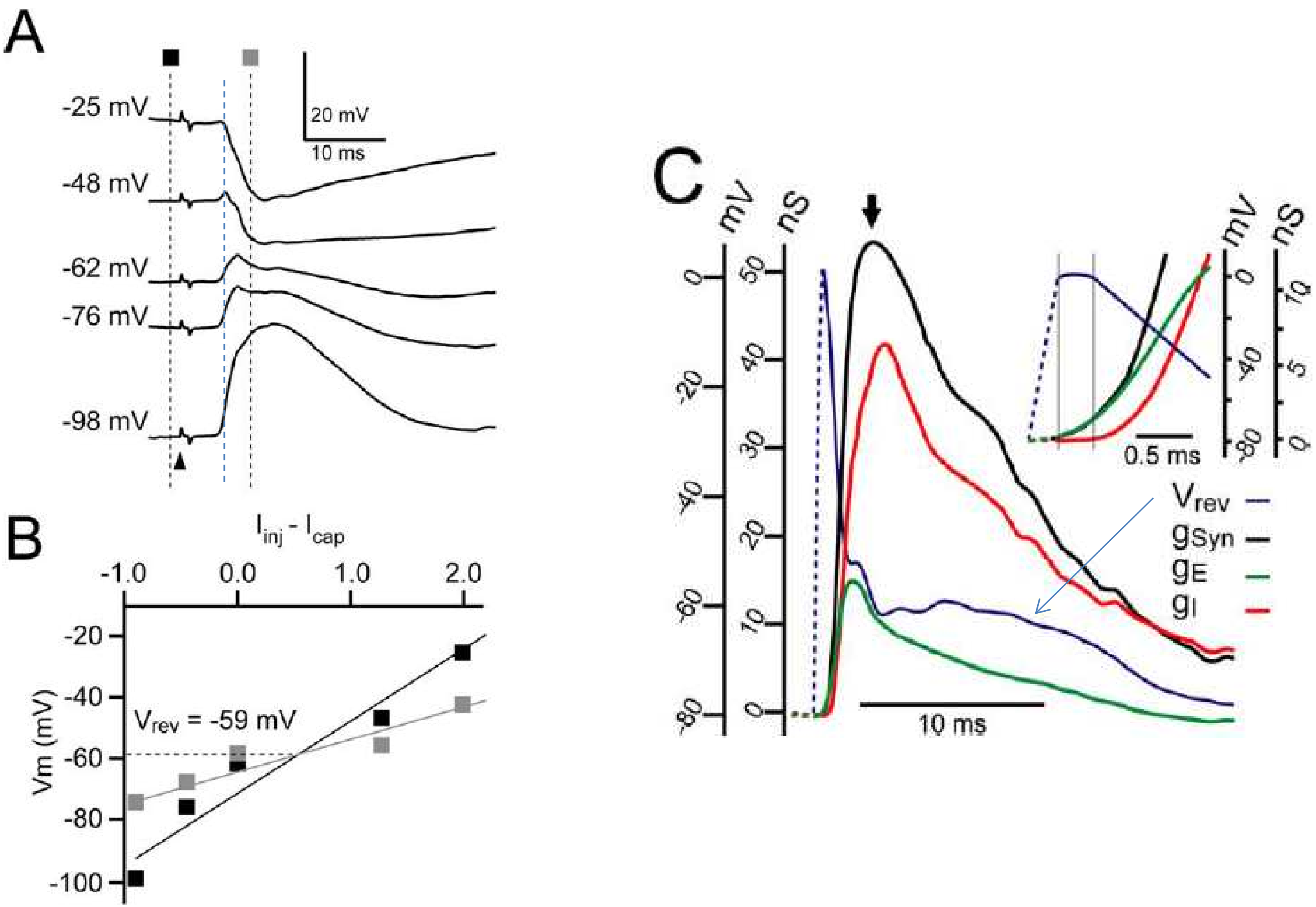
Glutamate and GABA are the most common excitatory and inhibitory NTs

NT	permeant ions	reversal potential	role
Glutamate	Na+ and K+	0 mV	excitatory
GABA	Cl-	-70 mV	inhibitory





Whisker deflection-induced syn. conductance changes in S1 PCs



Higley & Contreras, jns, 2006

Temporal structure of the input to an excitatory cell

Total exc. inputs

$\Sigma J_{ee} m_e + I_O$

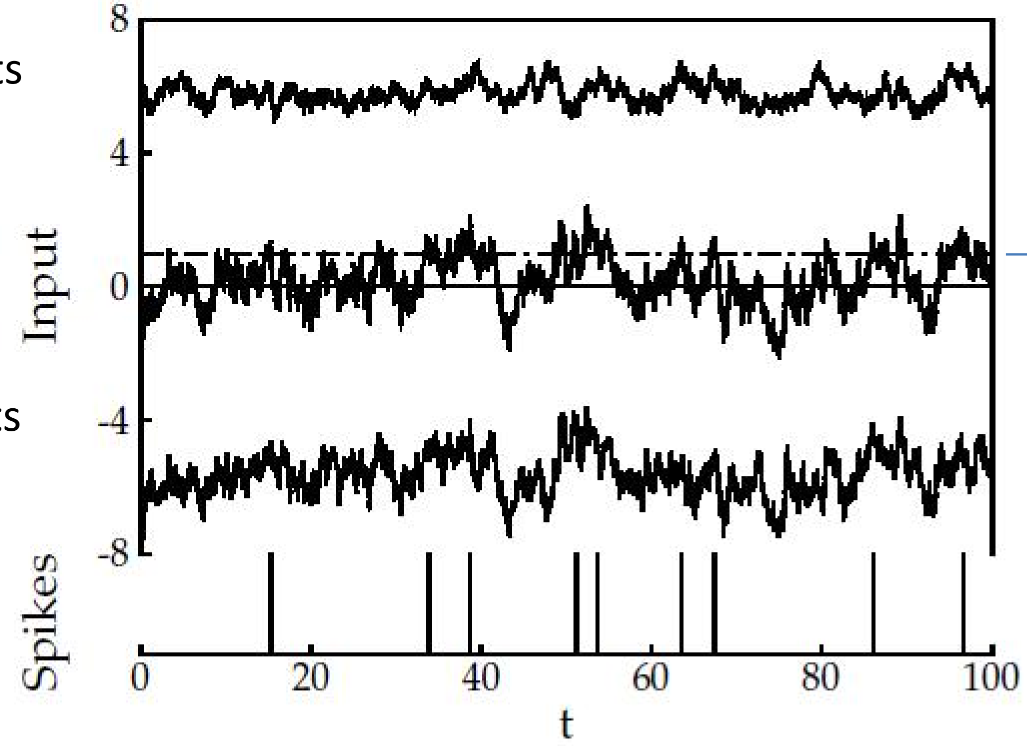
Net inputs

Total inh. inputs

$\Sigma J_{ei} m_i$

Consequent spikes

CV of ISI $\approx$ 1

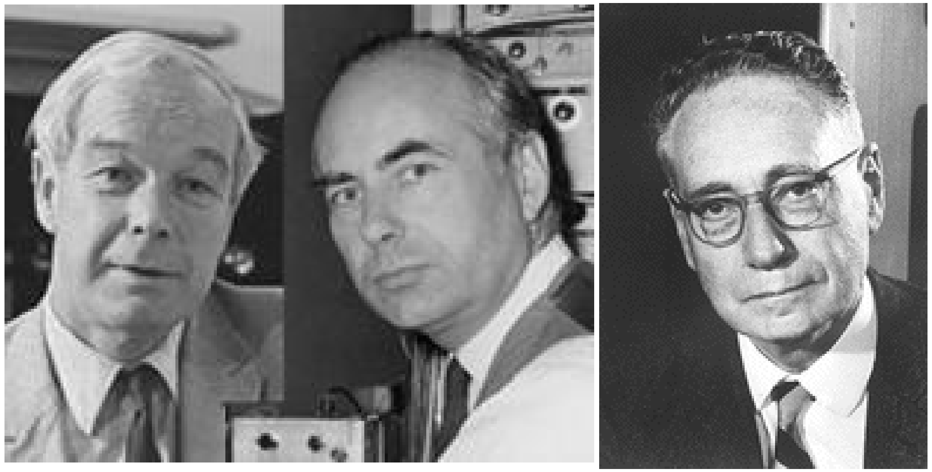


threshold (θ_e)

Neural Computation **10, 1321–1371** (1998)

Hodgkin & Huxley의 활동전압 모델

(Mathematical modeling of the channel gating kinetics)



Hodgkin, Huxley & Katz

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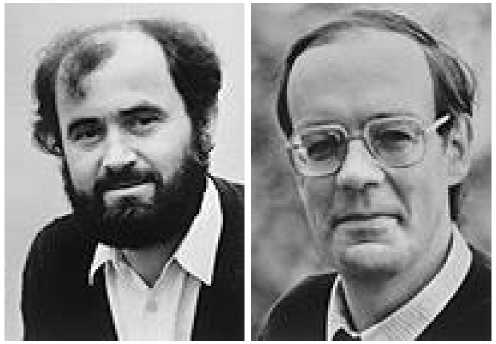
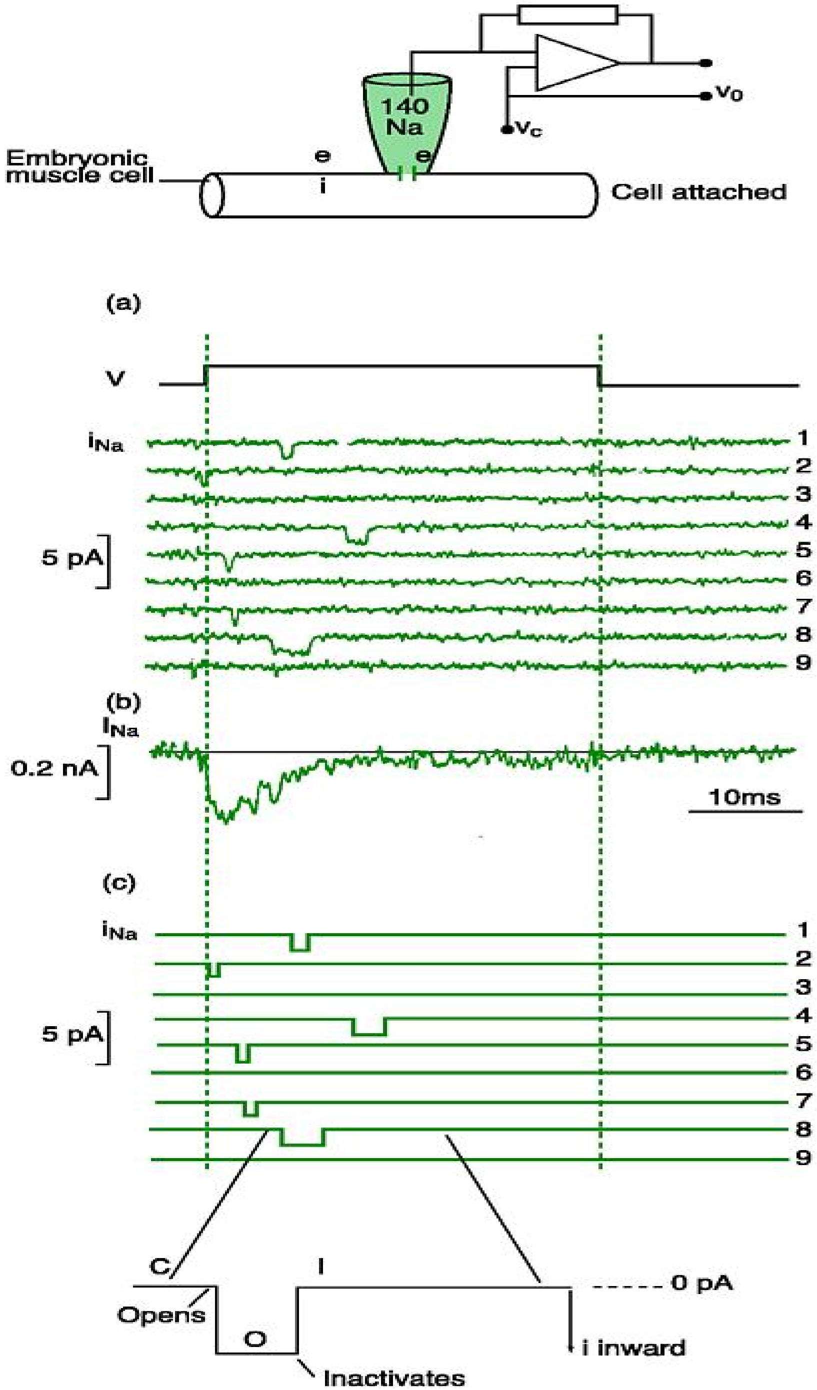
Macroscopic current is the sum of the unitary currents

Single Na^+ channel openings in response to a depolarizing step to +40 mV (muscle cell).

Cell-attached patch recordings



Neher & Sakmann



Two-state model of the K$^+$ channel gating
(when α and β are constant)

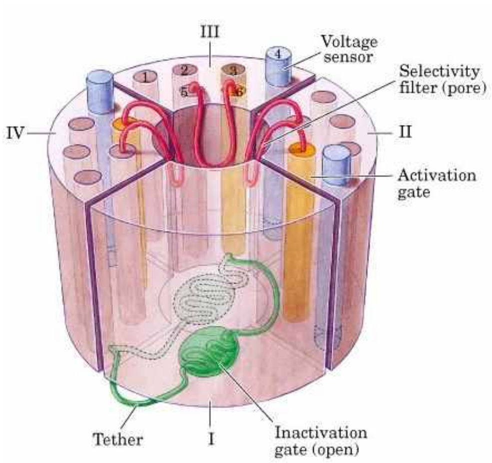
$$(1\text{-}n) \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} n$$

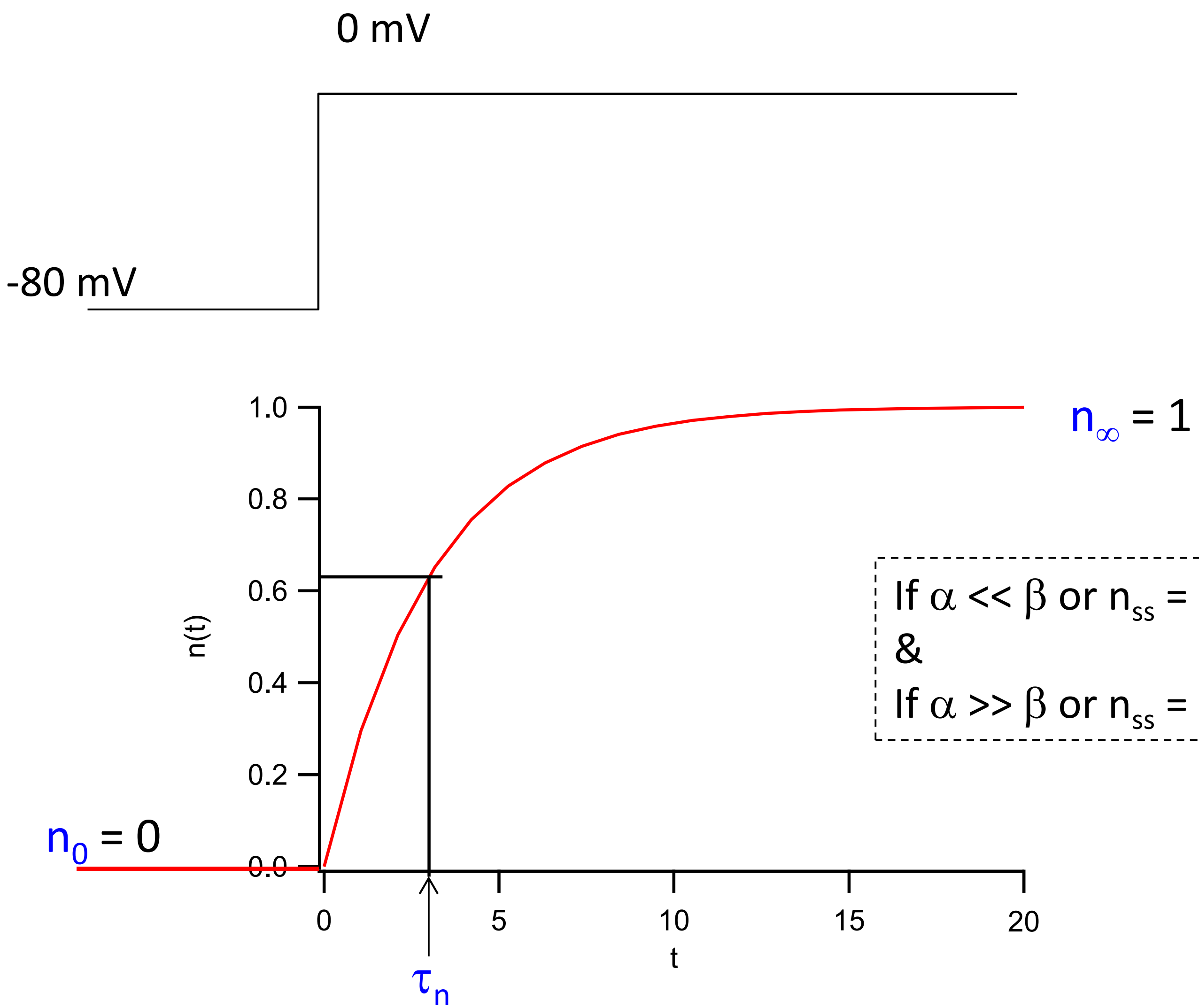
$dn/dt = \alpha \cdot (1 - n) - \beta \cdot n$

$dn/dt = 0$ when $n = n_\infty = \alpha / (\alpha + \beta)$

$dn/dt = (n_\infty - n) / \tau_n$, where $\tau_n = 1 / (\alpha + \beta)$.

$$\boxed{n(t) = n_0 + (n_\infty - n_0)\cdot[1 - \exp(-t/\tau_n)]}$$



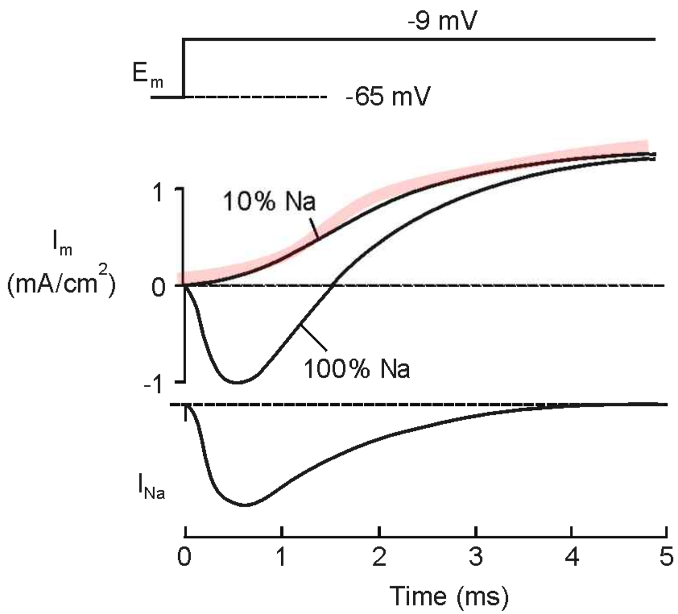


If $\alpha << \beta$ or $n_{ss} = 0$ at -80 mV
&
If $\alpha >> \beta$ or $n_{ss} = 1$ at 0 mV.

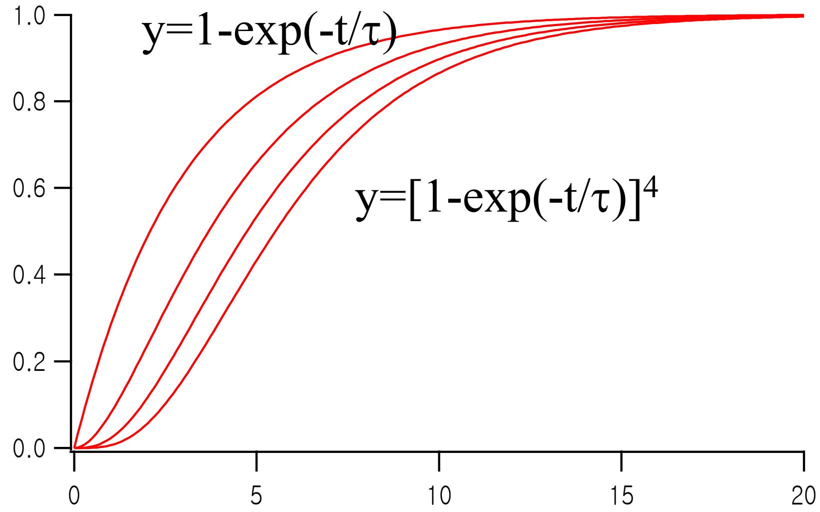
$$dn/dt = (n_\infty - n) / \tau_n$$

$$n(t) = n_0 + (n_\infty - n_0)\cdot[1 - \exp(-t/\tau_n)]$$

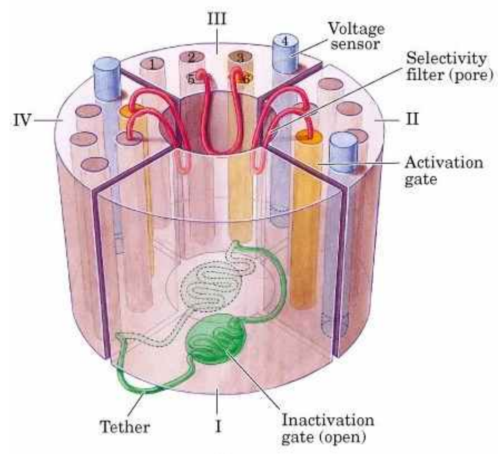
Modeling of the K⁺ current activation time course



$$n(t) = n_{ss}\,[1 - \exp(-t/\tau_n)]$$



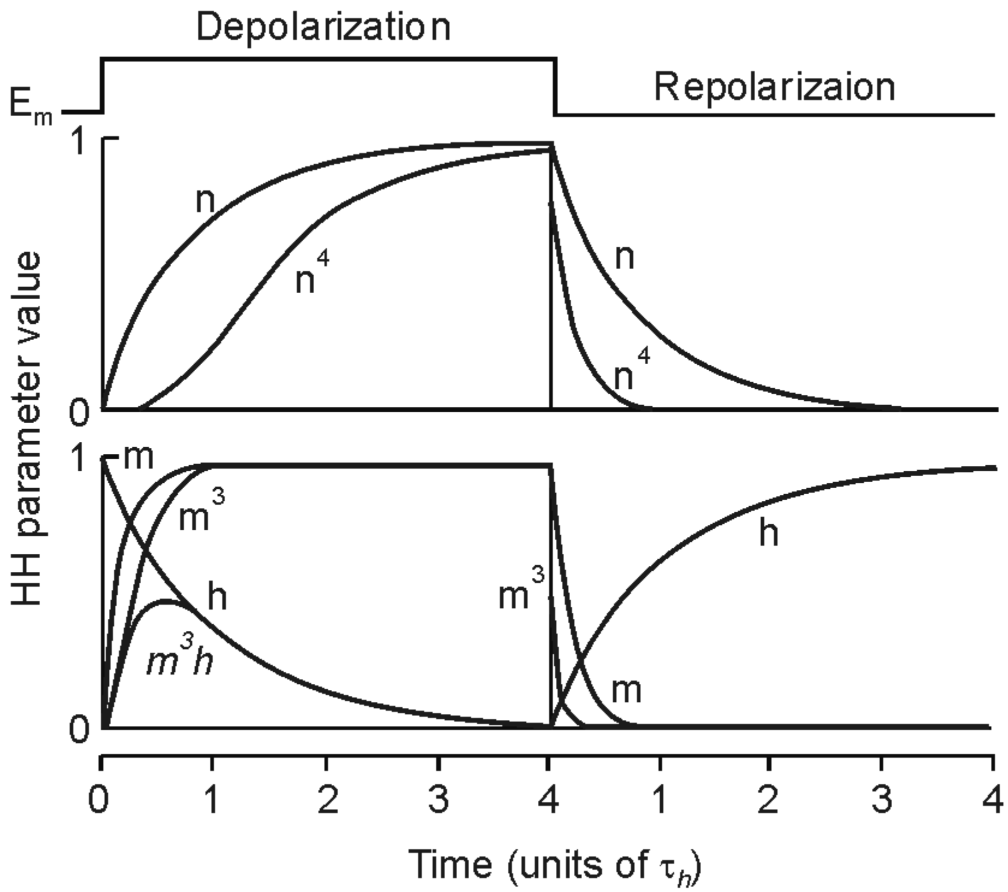
$$\boxed{I_K = G_{K,max} \cdot n^4 \cdot (V_m - E_K)}$$



Modeling the activation time course of Na^+ and K^+ current

$I_{Na} = G_{Na} \cdot (V_m - E_{Na})$

$I_K = G_K \cdot (V_m - E_K)$



$G_K = G_{K,max} \cdot n^4$

If $n_{ss} = 1$ and $n_0 = 0$

$n(t) = 1 - e^{-t/\tau n}$

$G_{Na} = G_{Na,max} \cdot m^3 \cdot h$

If $m_{ss} = 1$ and $m_0 = 0$

$m(t) = 1 - e^{-t/\tau m}$

If $h_{ss} = 0$ and $h_0 = 1$

$h(t) = e^{-t/\tau h}$

$m(t) = m_0 + (m_\infty - m_0) \cdot [1 - \exp(-t/\tau_m)]$

$h(t) = h_0 + (h_\infty - h_0) \cdot [1 - \exp(-t/\tau_h)]$

α and β are V_m-dependent variables

$$(1\text{-}n) \underset{\beta(v)}{\overset{\alpha(v)}{\rightleftharpoons}} n$$

$$I_K = G_{K,max} \cdot n_{v,t}^{\ 4} \cdot (V_m - E_K)$$

At a given voltage v,

$dn_v/dt = \alpha_v \cdot (1 - n_v) - \beta_v \cdot n_v = (n_{v,\infty} - n_v) / \tau_{n,v}$

$n_v(t) = [n_{v,\infty} - n_{v,0}] \cdot [1 - \exp(-t/\tau_{n,v})]$, where $n_{v,0} \equiv n_v(0)$

$\tau_{n,v} = 1 / (\alpha_v + \beta_v)$

$n_{v,\infty} = \alpha_v / (\alpha_v + \beta_v)$

Determining rate constants from experimental data

$$\alpha(v) = n_{\infty}(v) / \tau(v)$$

$$\beta(v) = 1/\tau(v) - \alpha(v)$$

$\alpha_n(v) = 0.01[10-(v-v_r)]/\{\exp[10-(v-v_r)]/10\}-1$

$\beta_n(v) = 0.125 \exp[-(v-v_r)/80]$

$V_r = -65$ mV

<u>Numerical integration</u>

using

Euler method or

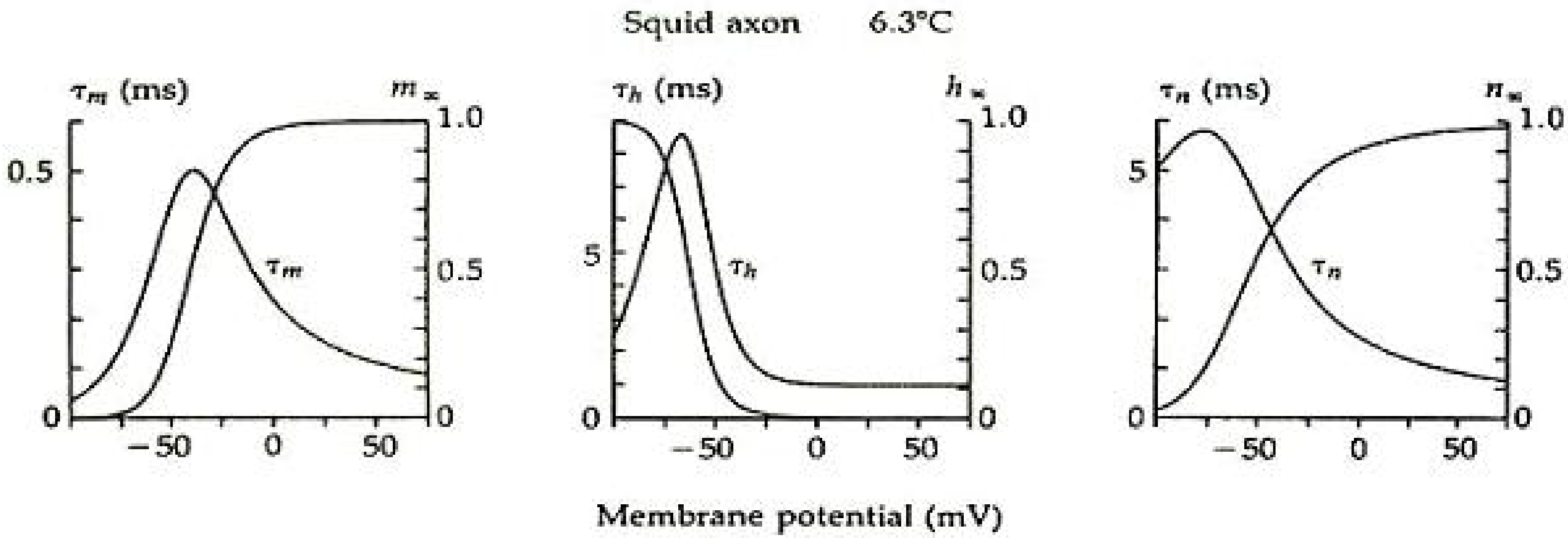
Runge-Kutta method

Since $\Delta V_m = -\int I_R \, dt / C_m$

$\Sigma I_m = I_{Na} + I_K + I_{leak}$

$dV/dt = -\Sigma I_m / C_m$,

$V_{i+1} = V_i + dV/dt \cdot \Delta t$



Reconstruction of the action potential from rate constants data

$V_i = V_{i-1} + dV/dt \cdot \Delta t$

$\downarrow$

$\alpha_n(V_i)$ & $\beta_n(V_i)$

: empirically determined

$\downarrow$

$dn/dt = \alpha_n \cdot (1 - n) - \beta_n \cdot n$

$\downarrow$

$n_i = n_{i-1} + dn/dt \cdot \Delta t$

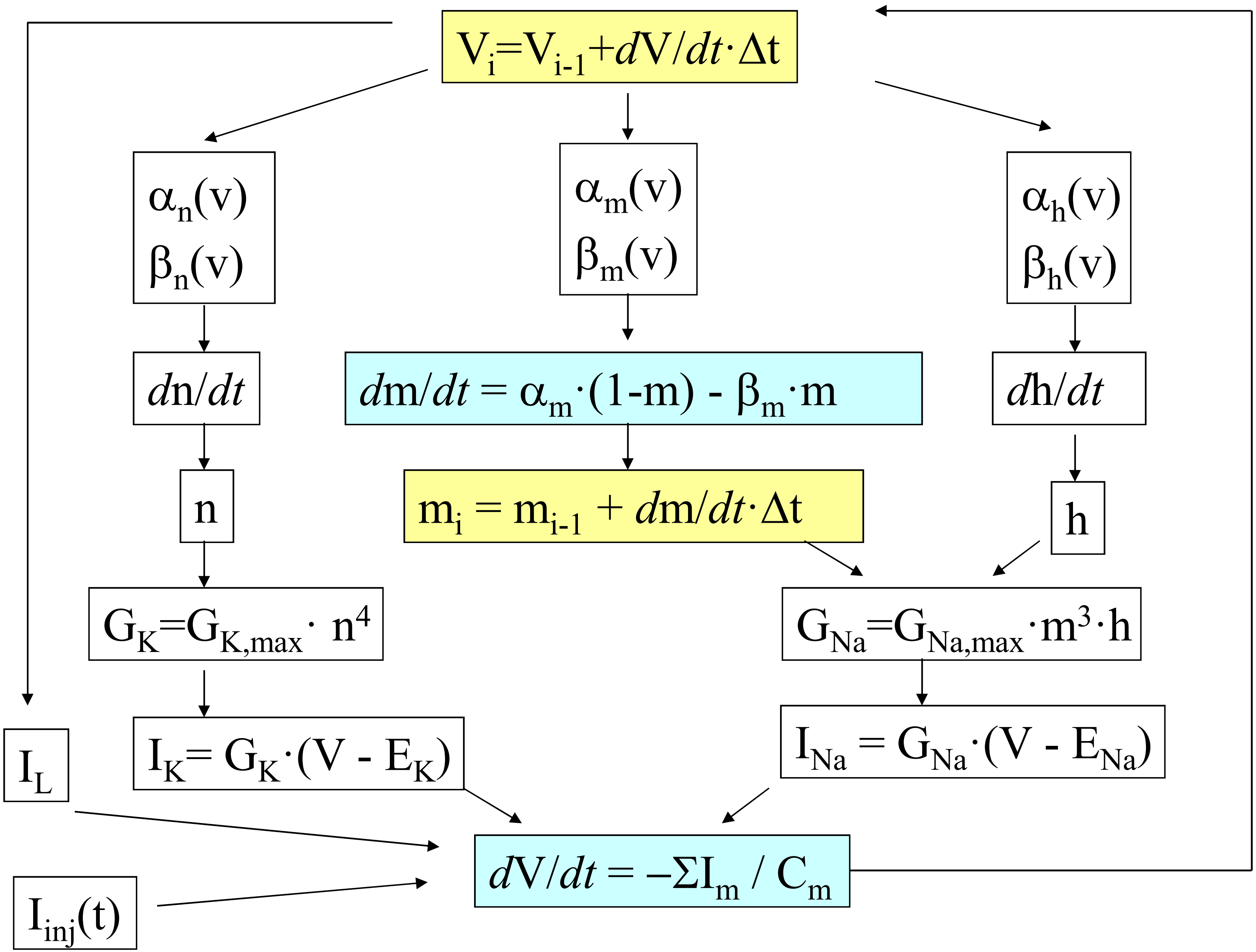
$\downarrow$

$G_K = G_{K,max} \cdot n^4$

$\downarrow$

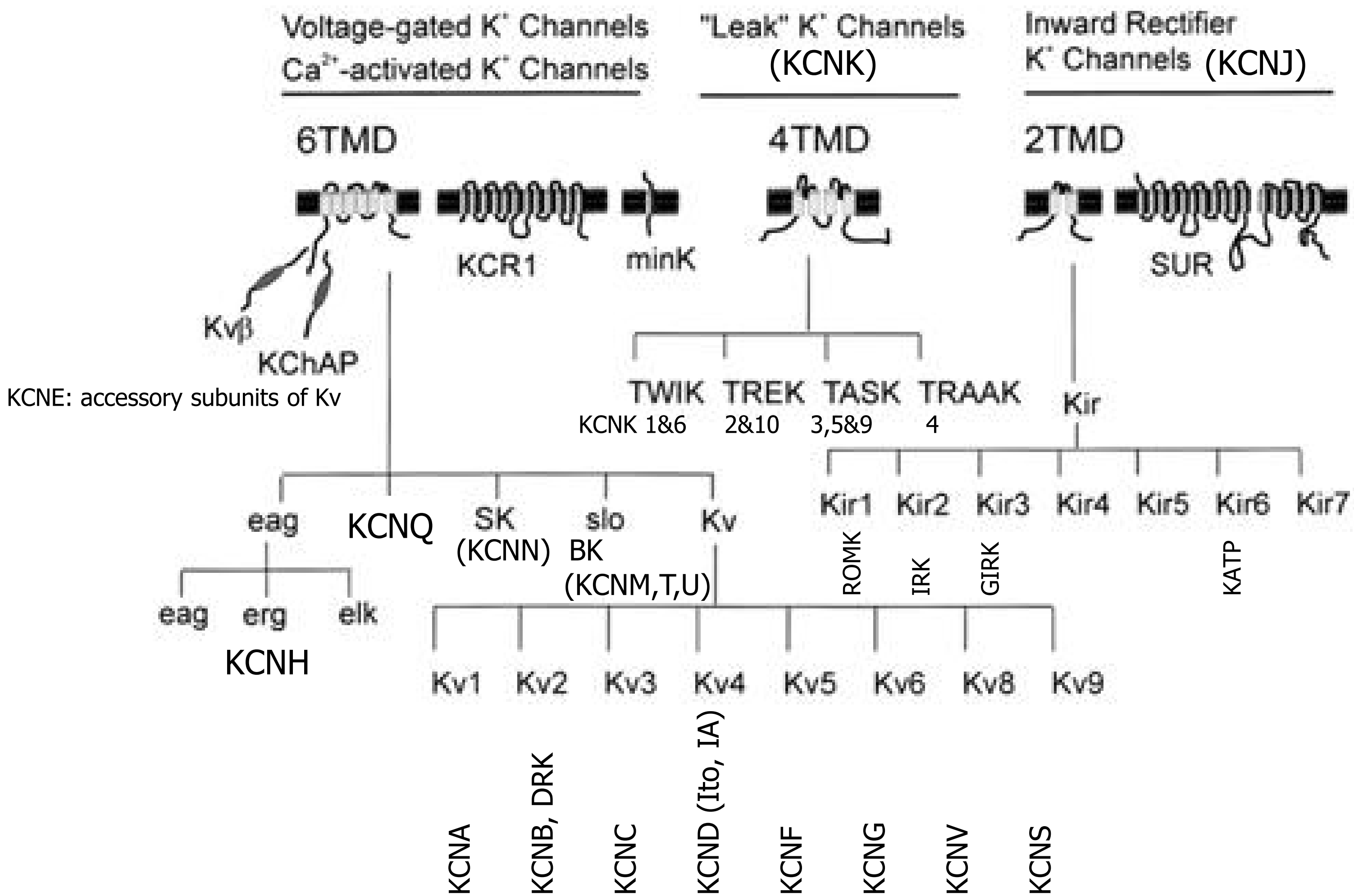
$I_K = G_K \cdot (V_i - E_K)$

$dV/dt = \Sigma I_m / C_m$



$V_i = V_{i-1} + dV/dt \cdot \Delta t$
$\alpha_n(v)$
$\beta_n(v)$
$\alpha_m(v)$
$\beta_m(v)$
$\alpha_h(v)$
$\beta_h(v)$
dn/dt
$dm/dt = \alpha_m \cdot (1-m) - \beta_m \cdot m$
dh/dt
n
$m_i = m_{i-1} + dm/dt \cdot \Delta t$
h
$G_K = G_{K,max} \cdot n^4$
$G_{Na} = G_{Na,max} \cdot m^3 \cdot h$
I_L
$I_K = G_K \cdot (V - E_K)$
$I_{Na} = G_{Na} \cdot (V - E_{Na})$
$dV/dt = -\Sigma I_m / C_m$
$I_{inj}(t)$

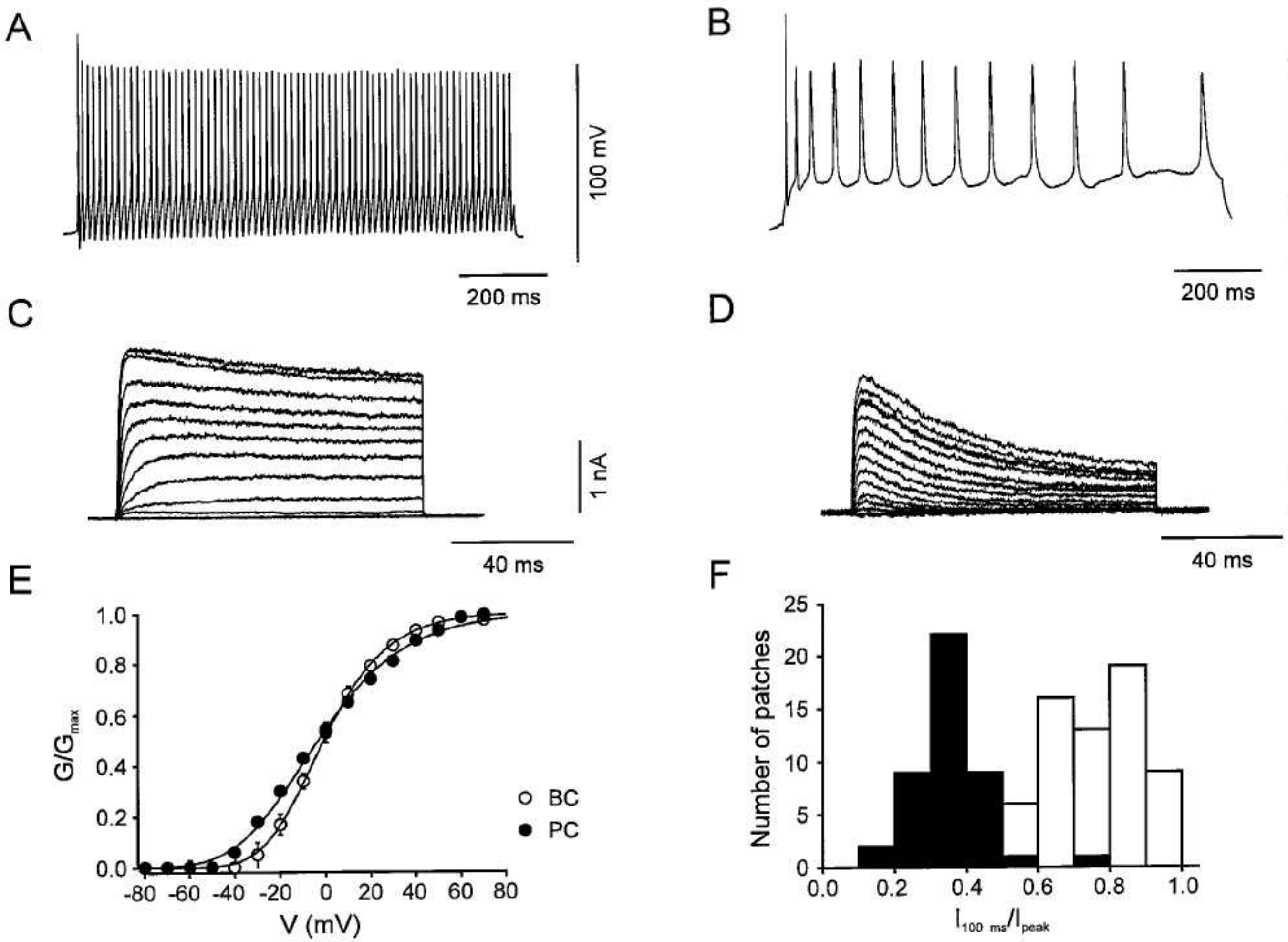
Three groups of K+ channel principal subunits



High voltage-activated K+ current

Kv3.1 or Kv3.2
(Basket cell)

Kv4.2 or Kv4.3
(Pyramidal cell)



MartinaJonas (1998) 18: 8111-25

Extracellular Recording of Neural Acitivity

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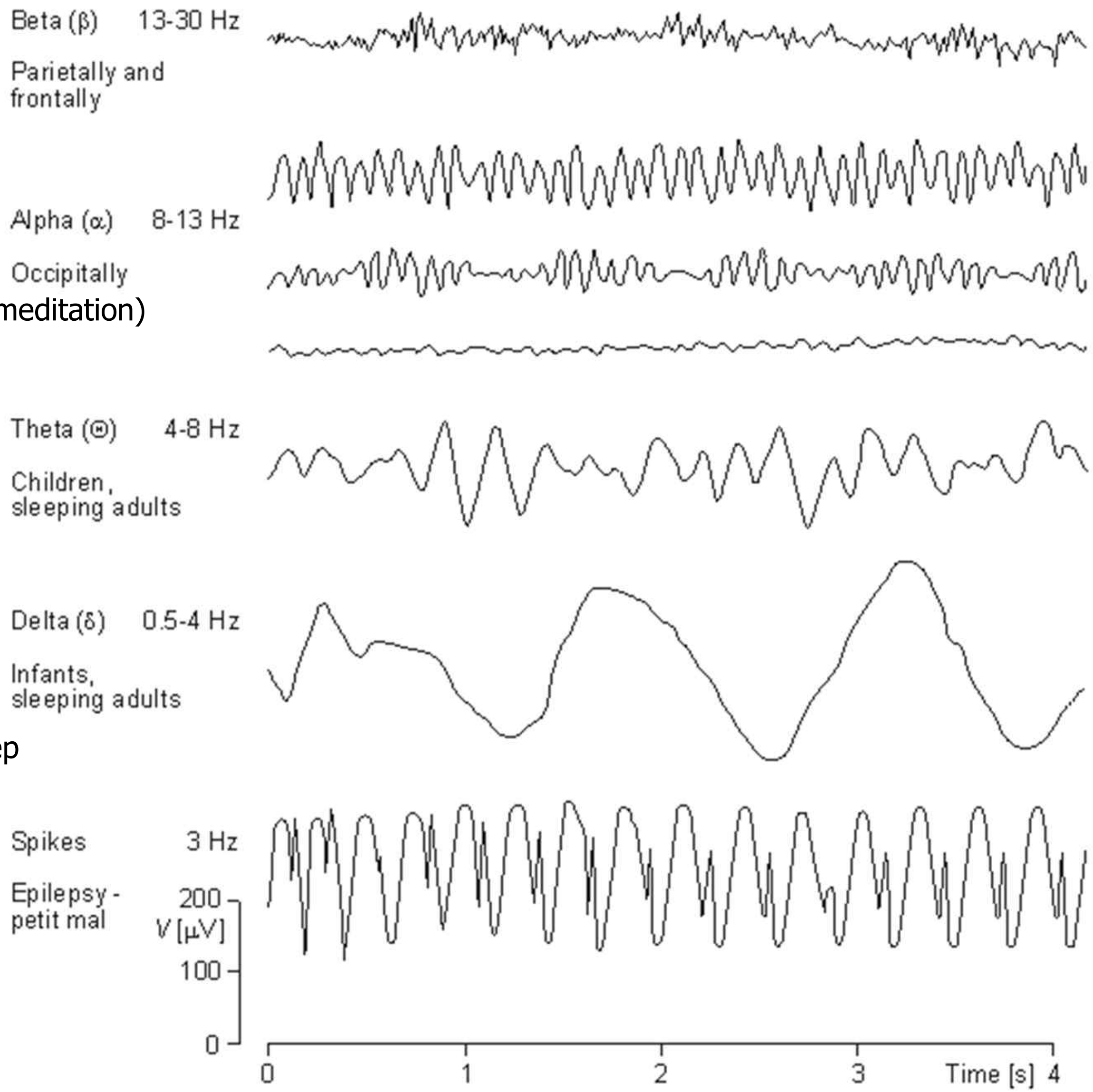
Electroencephalogram (EEG)

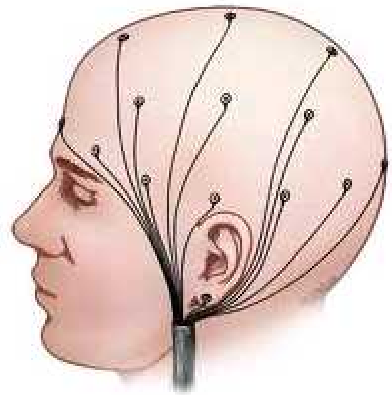
arousal

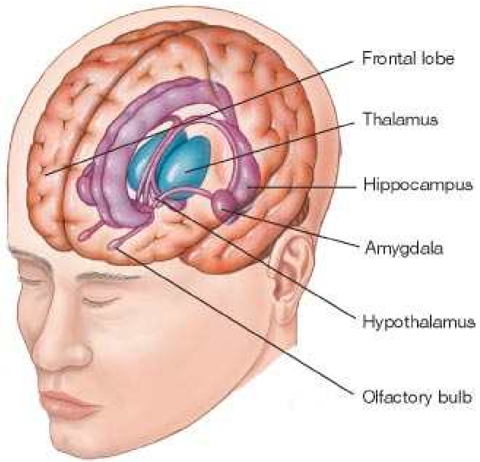
relaxed (meditation)

sleep

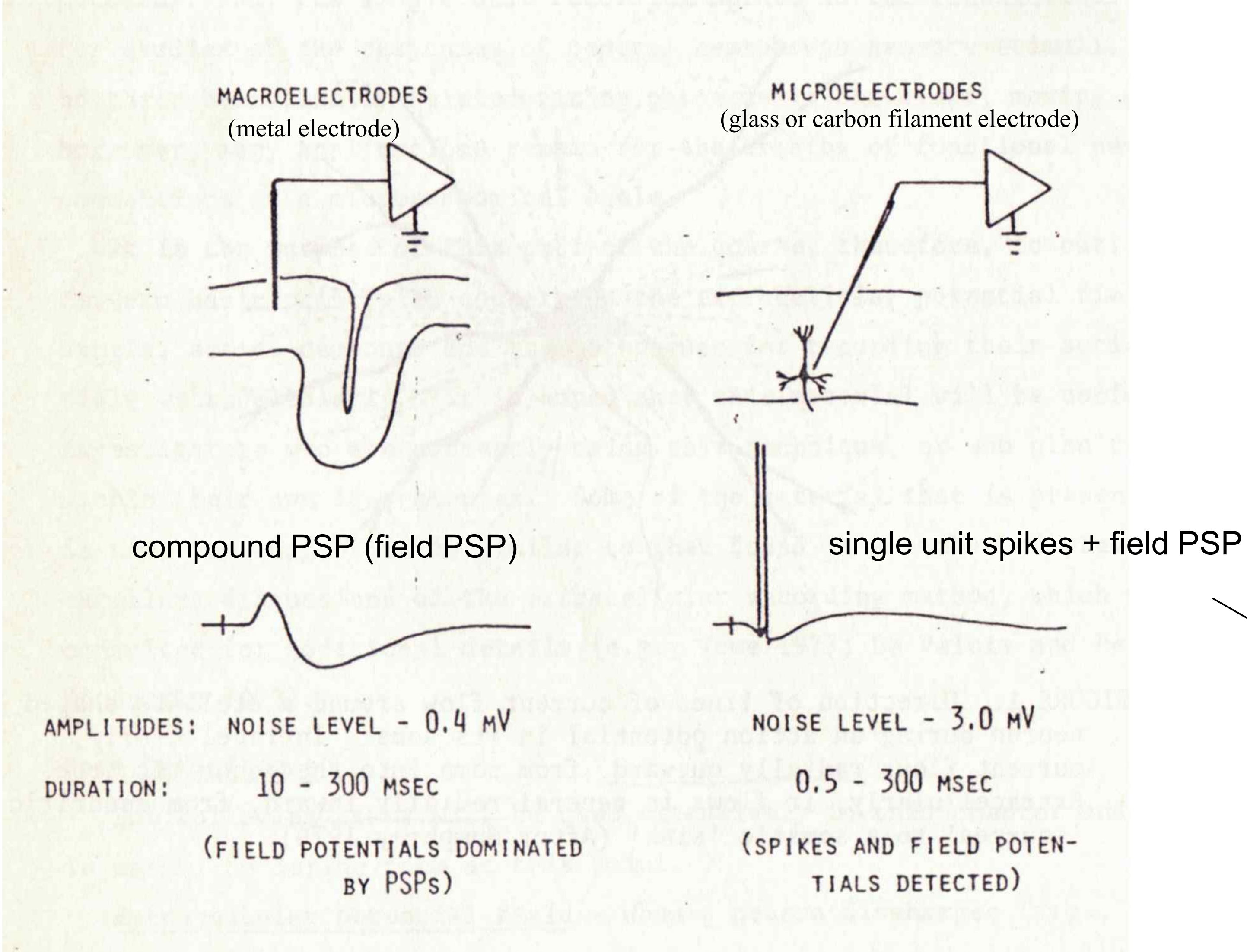
deep sleep

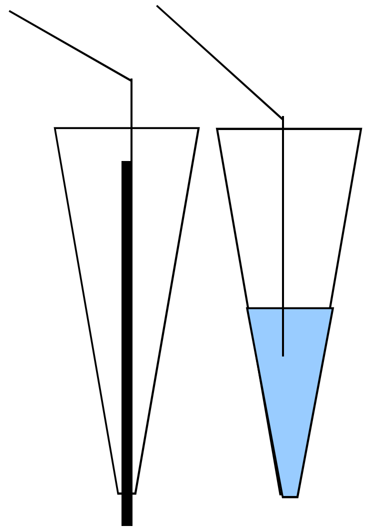






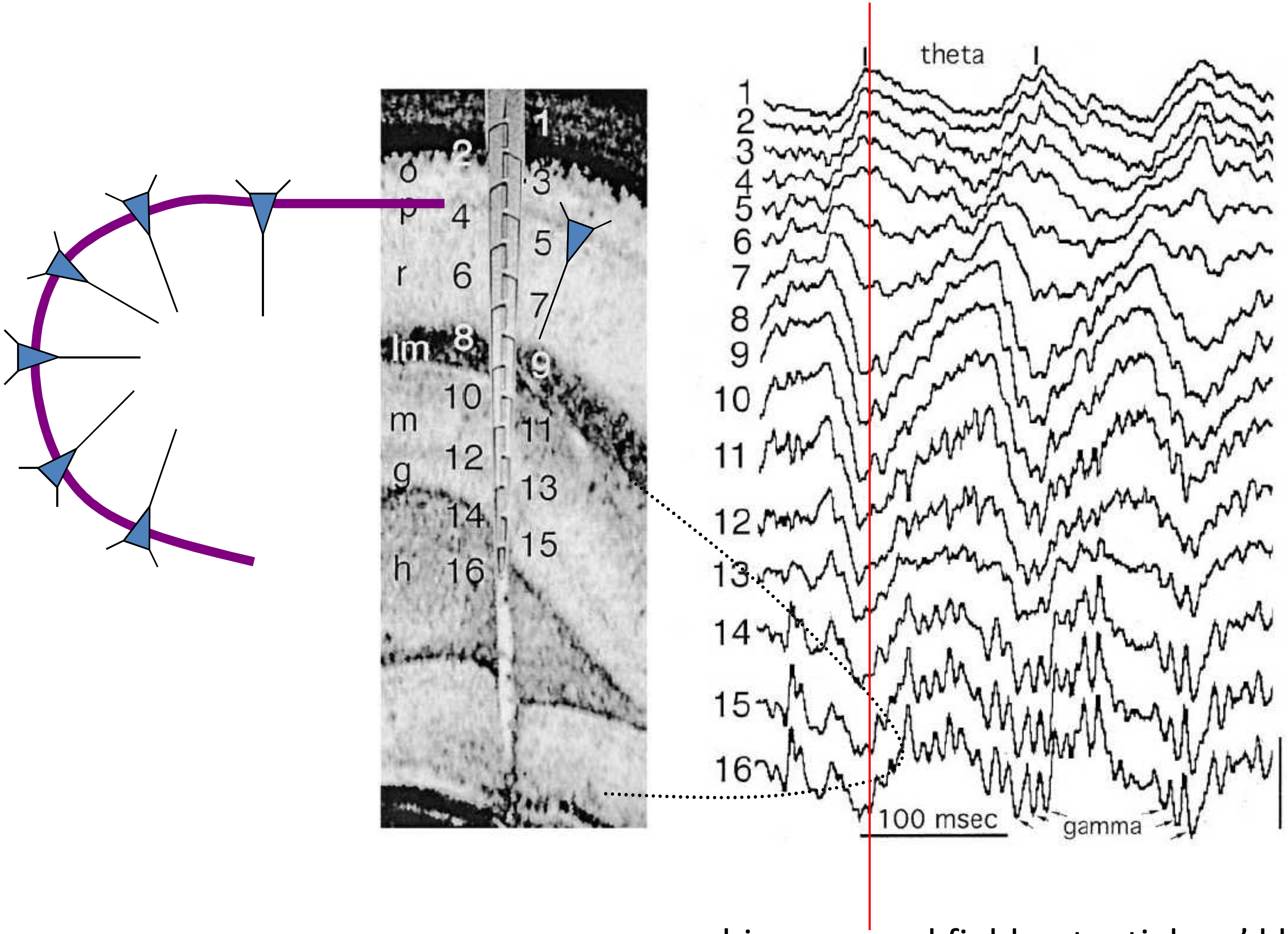
Macro- vs Micro-electrode





dimension of the exposed tip of a microelelctrode:
< 5 μm in diameter and < 20 μm in length

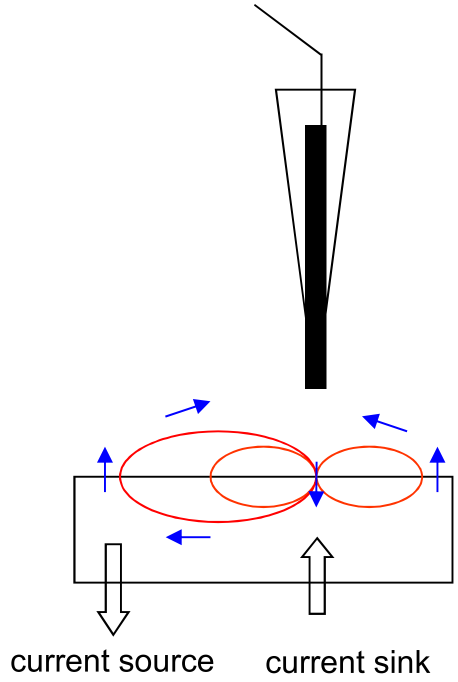
Pyramidal neuron as a current dipole

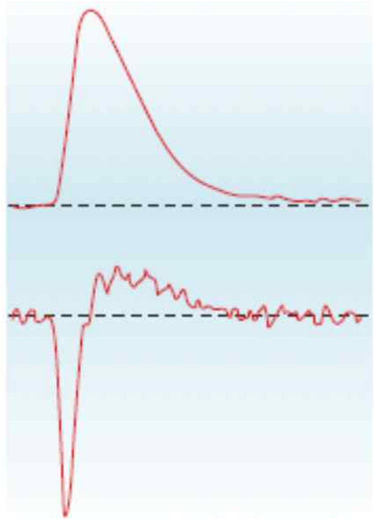


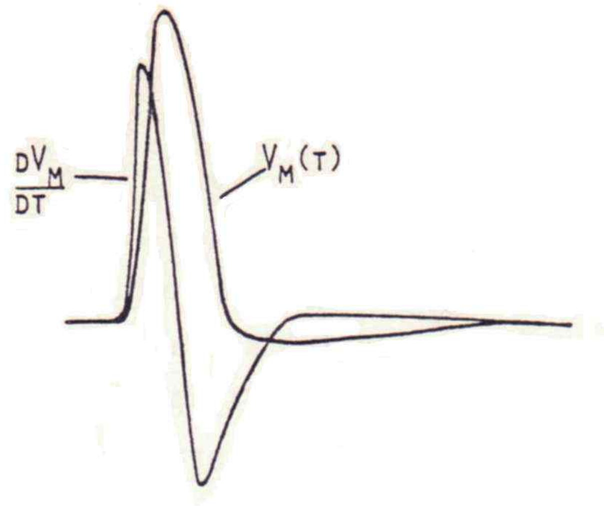
The gradual phase reversal: supports the theory of a pyr cell as a dipole

hippocampal field potential rec'd by macroelectode

Extracellular recording of single unit action potential







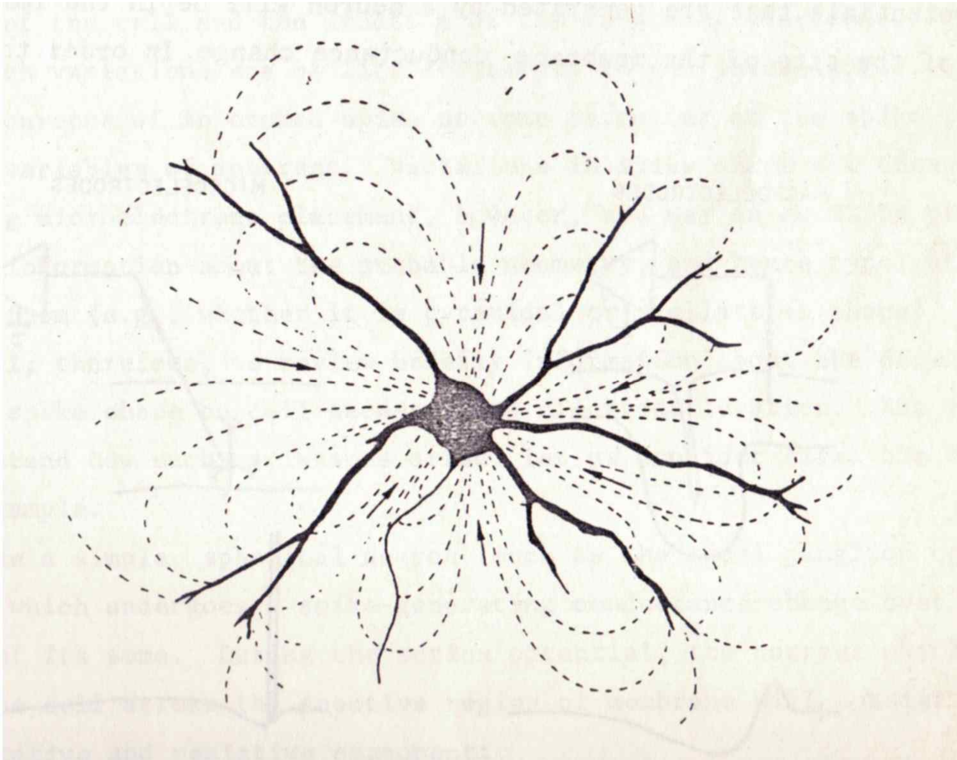
*Good extracellular recording electrode

- small: unit spike activity
- low impedance: high S/N ratio

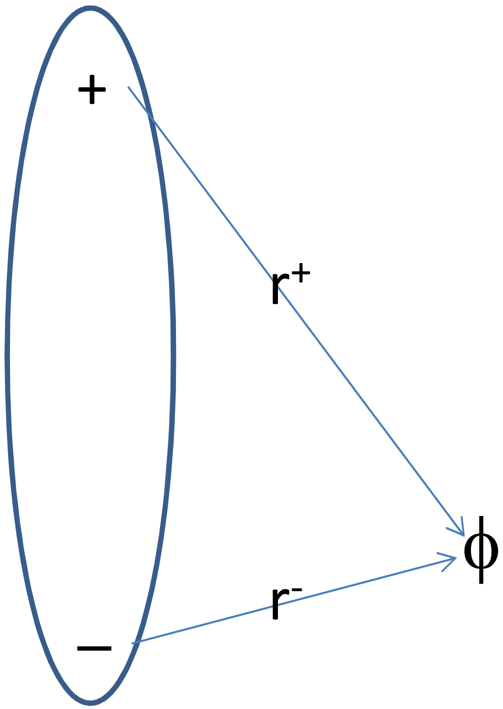
carbon filament and platinum black

Field potential

a potential difference generated by a flow of current thr. finite extracelluar (EC) medium



Direction lines of EC current flow around a stellate cell during somtic action potential



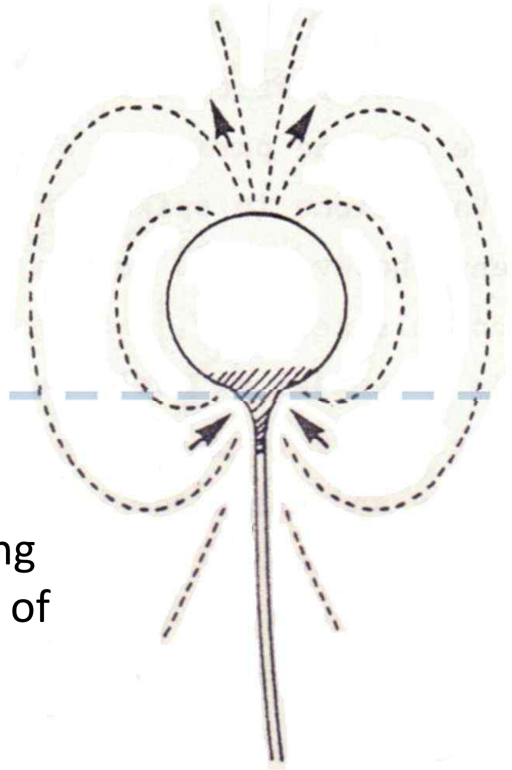
$$\varphi = \frac{1}{4\pi\sigma}\left(\frac{J^+}{r^+} - \frac{J^-}{r^-}\right)$$

When $J^+ = J^-$.

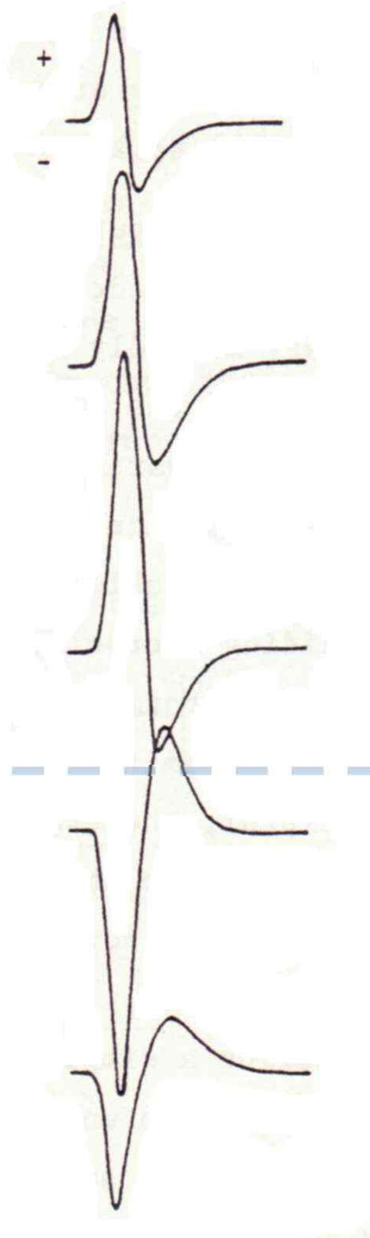
$$\varphi = \frac{J}{4\pi\sigma}\left(\frac{1}{r^+} - \frac{1}{r^-}\right)$$

φ, electric potential
J, charge
r, distance

The shape of EC spikes depends on
1) the location of the recording electrode
2) the geometry of the cell

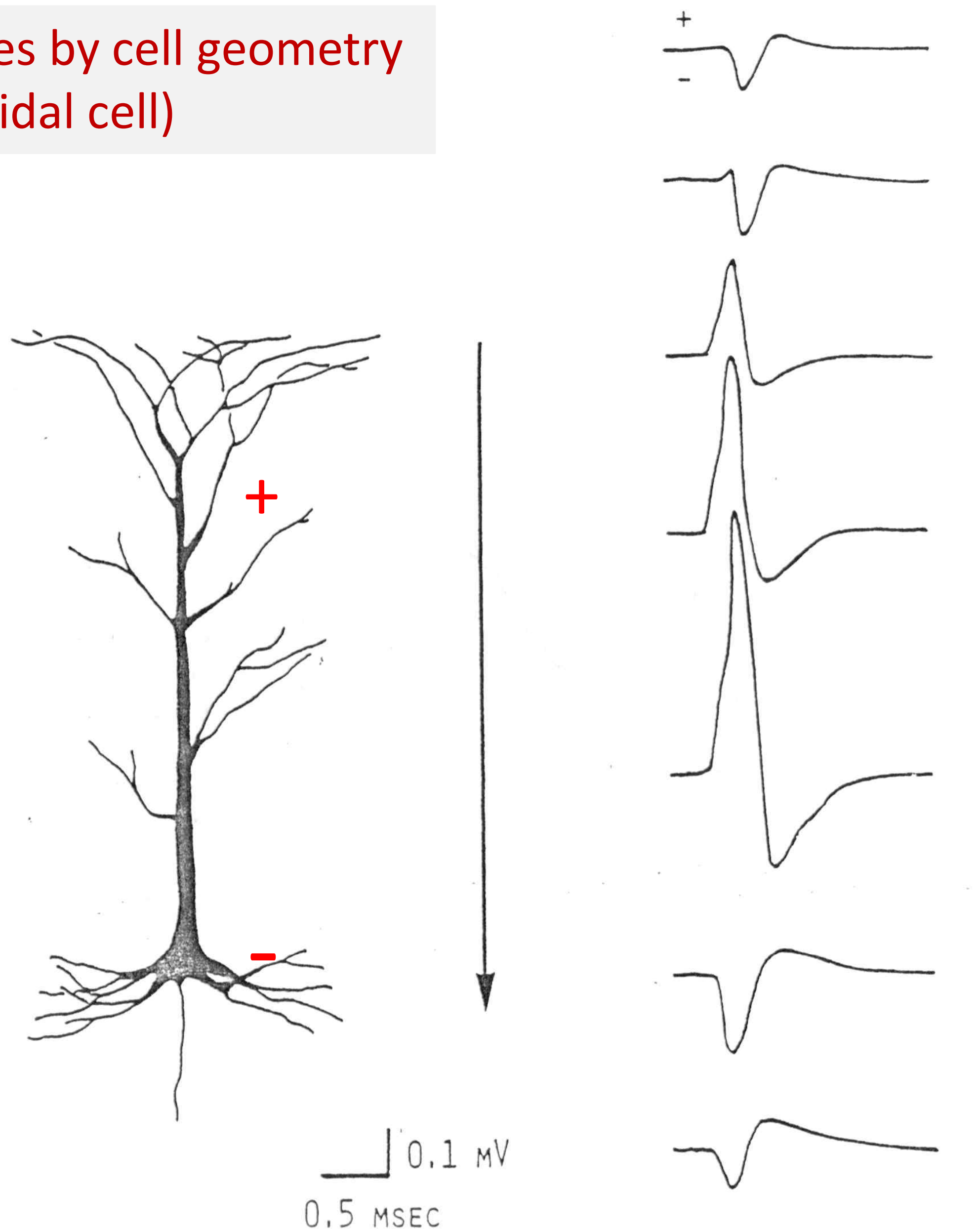


EC current flow during an AP at axon hillock of a spherical cell



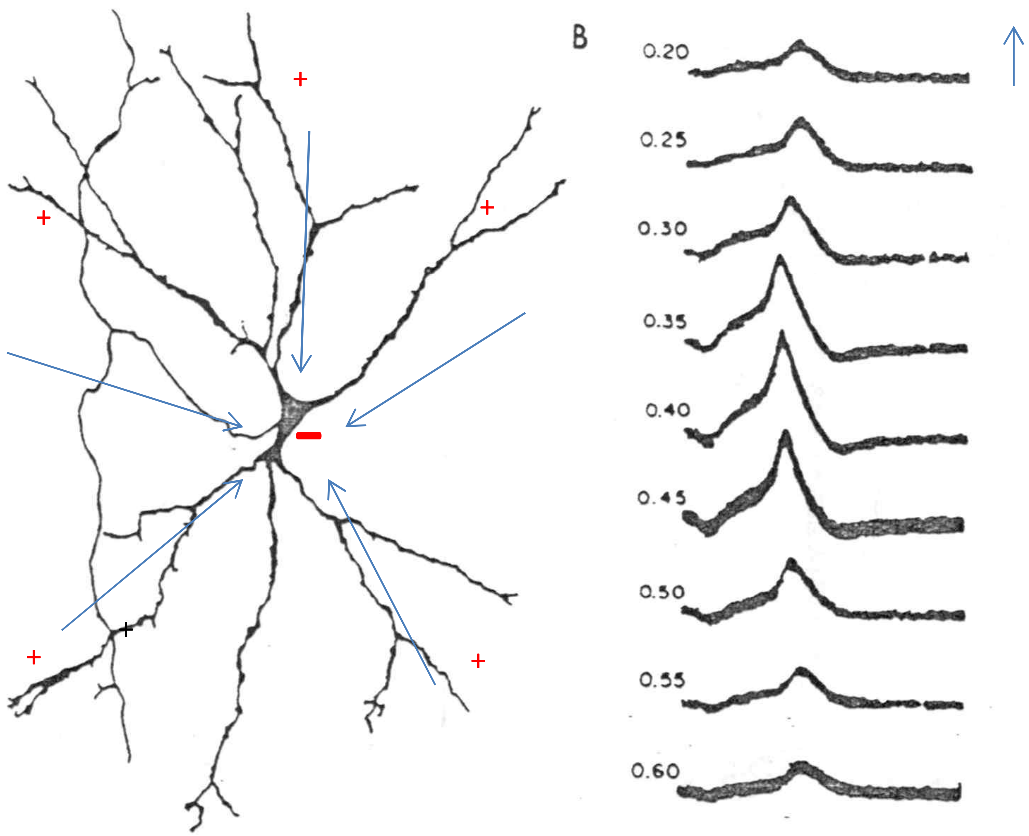
EC spikes recorded from electrodes at different depth

Shaping of EC spikes by cell geometry (pryamidal cell)



EC spikes at different electrode locations during an somatic APdu

Shaping of EC spikes by cell geometry (stellate cell)



negativity is shown as upward deflection

Dendtric current sources (J^{+}) are more distributed in SC than in PC
⇒ Concentrated sink at the soma dominates the EC spike everywhere.

Simple spike models

1) LIF model
2) Izhikevich model

Leaky Integrate and Fire model

$\Sigma\, I_m = -G_{in}(V - E_L) + I_o.$

$dv/dt = \Sigma\, I_m \,/\, C_m$ ....(Eq1)

$v(i+1) = v(i) + dt\,(\Sigma\, I_m \,/\, C_m)$

If $(v > V_{thr})$ && $(t_{postAP} > T_{rfr})$

$\quad v \leftarrow V_{peak}$

elseif $v == V_{peak}$

$\quad v \leftarrow V_{reset}$

endif

$G_{in}/C_m = 1/(R_m C_m) = 1/\tau_m$

$I_o / C_m = I_o R_m / \tau_m$

$C_m \, dv/dt = -G_{in}(V - E_L) + I_o$ ....(Eq1)

$\tau_m \, dv/dt = V - E_L + R_m I_o$ . ...(Eq2)

If $E_L = 0$, $V_{inf} = R_m I_o$.

$v(t) = v_0 + (V_{inf} - v_0)[\ 1 - \exp(-t/\tau_m)\ ]$ ....(Eq3)

Firing freq. vs I_O

$v(t) = v_0 + (V_{inf} - v_0)[\ 1 - \exp(-t/T_m)\ ]$ ....(Eq3)

If $V_{inf} > V_{thr}$, and $v_0 = V_{reset}$

$V_{thr} = V_{reset} + (V_{inf} - V_{reset})\ [\ 1 - \exp(-T_{isi}/T_m)\ ]$

$T_{isi} = T_m \ln[(V_r - V_{inf}) / (V_{th} - V_{inf})]$ ....(Eq4)

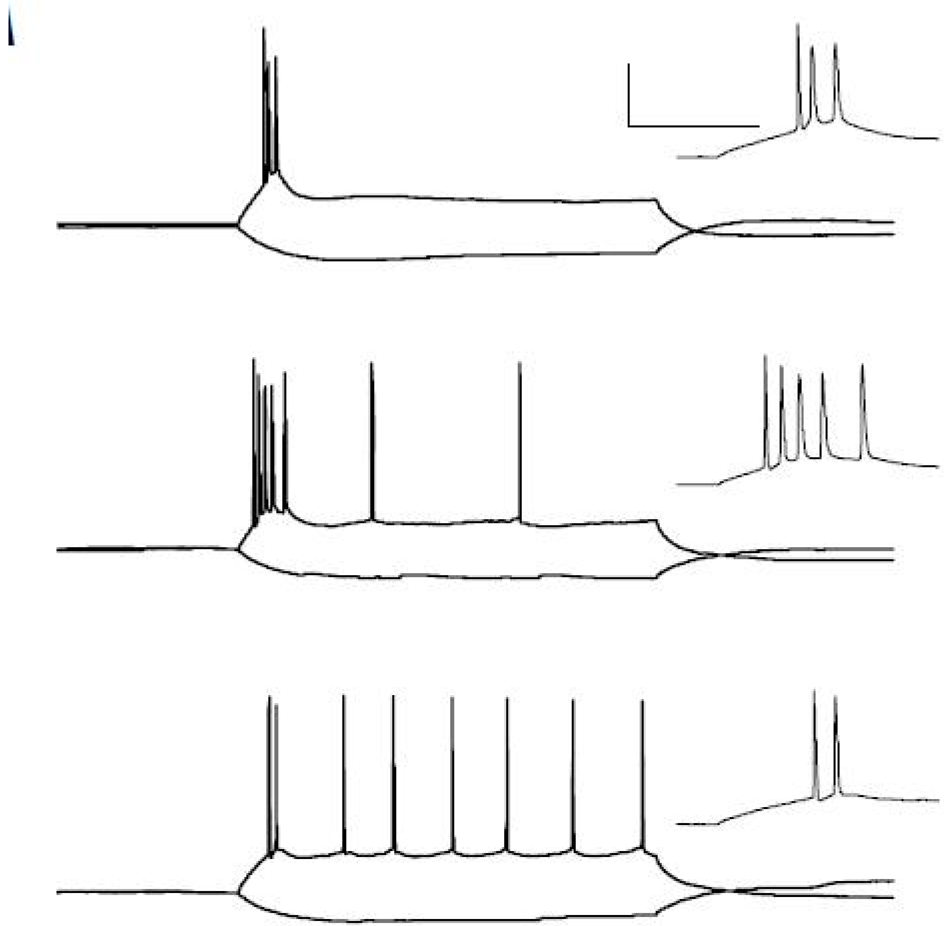
Homework

Make LIF model using given parameters:

V_{thr} = -55 mV
V_{reset} = -70 mV
V_{peak} = 20 mV
R_m = 100 MOhm
T_m = 10ms

Verify Eq. 4 from simulated spike frequencies

Neurons display a varity of spiking patterns



Izhikevich Spike Model

v ↔ m
u ↔ n
c ↔ Vpeak

$$\boxed{\begin{aligned} v' &= 0.04v^2 + 5v + 140 - u + I \qquad (1)\\ u' &= a(bv - u) \qquad (2)\end{aligned}}$$

with the auxiliary after-spike resetting

$$\text{if } v \geq +30 \text{ mV}, \qquad \text{then } \begin{cases} v \leftarrow c \\ u \leftarrow u + d. \end{cases} \qquad (3)$$

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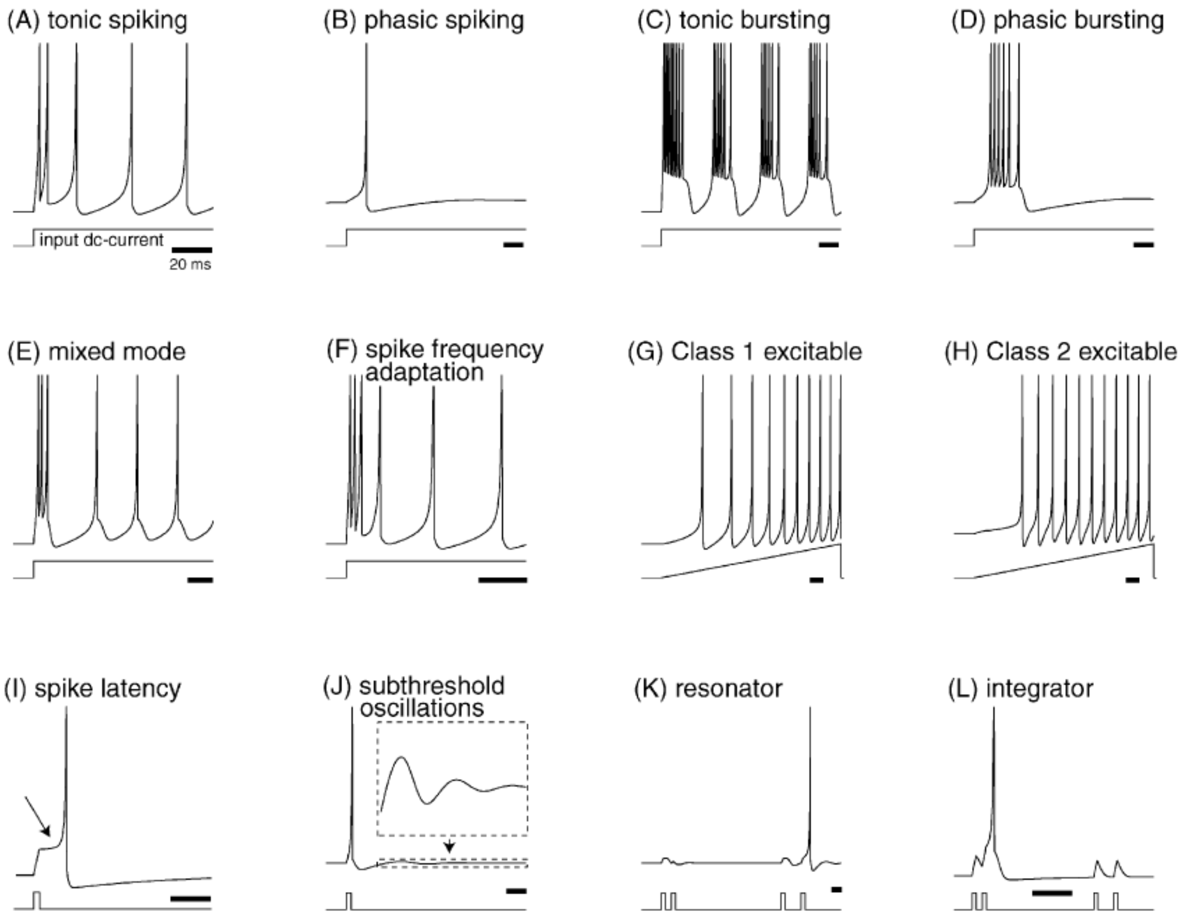
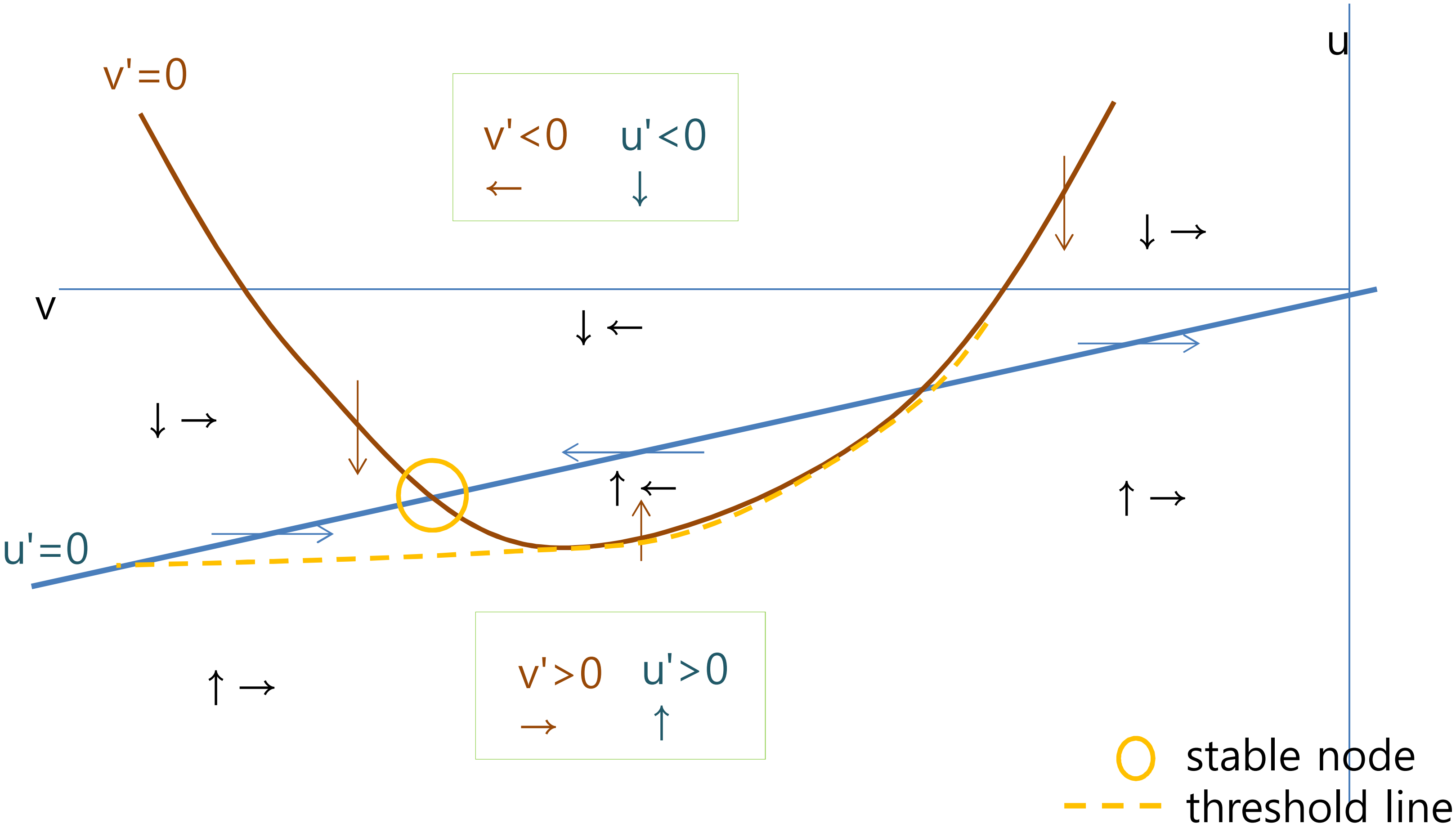
Which Model to Use for Cortical Spiking Neurons?

Eugene M. Izhikevich




```
pars = [a,        b,        vret,     d,         I].
pars=[0.02       0.2      -65       6         14 ;...  % tonic spiking
      0.02       0.25     -65       6         0.5 ;... % phasic spiking
      0.02       0.2      -50       2         15 ;...  % tonic bursting
      0.02       0.25     -55       0.05      0.6 ;... % phasic bursting
      0.02       0.2      -55       4         10 ;...  % mixed mode
      0.01       0.2      -65       8         30 ;...  % spike frequency adaptation
      0.02       -0.1     -55       6         0  ;...  % Class 1
      0.2        0.26     -65       0         0  ;...  % Class 2
      0.02       0.2      -65       6         7  ;...  % spike latency
      0.05       0.26     -60       0         0  ;...  % subthreshold oscillations
      0.1        0.26     -60       -1        0  ;...  % resonator
      0.02       -0.1     -55       6         0  ;...  % integrator
```

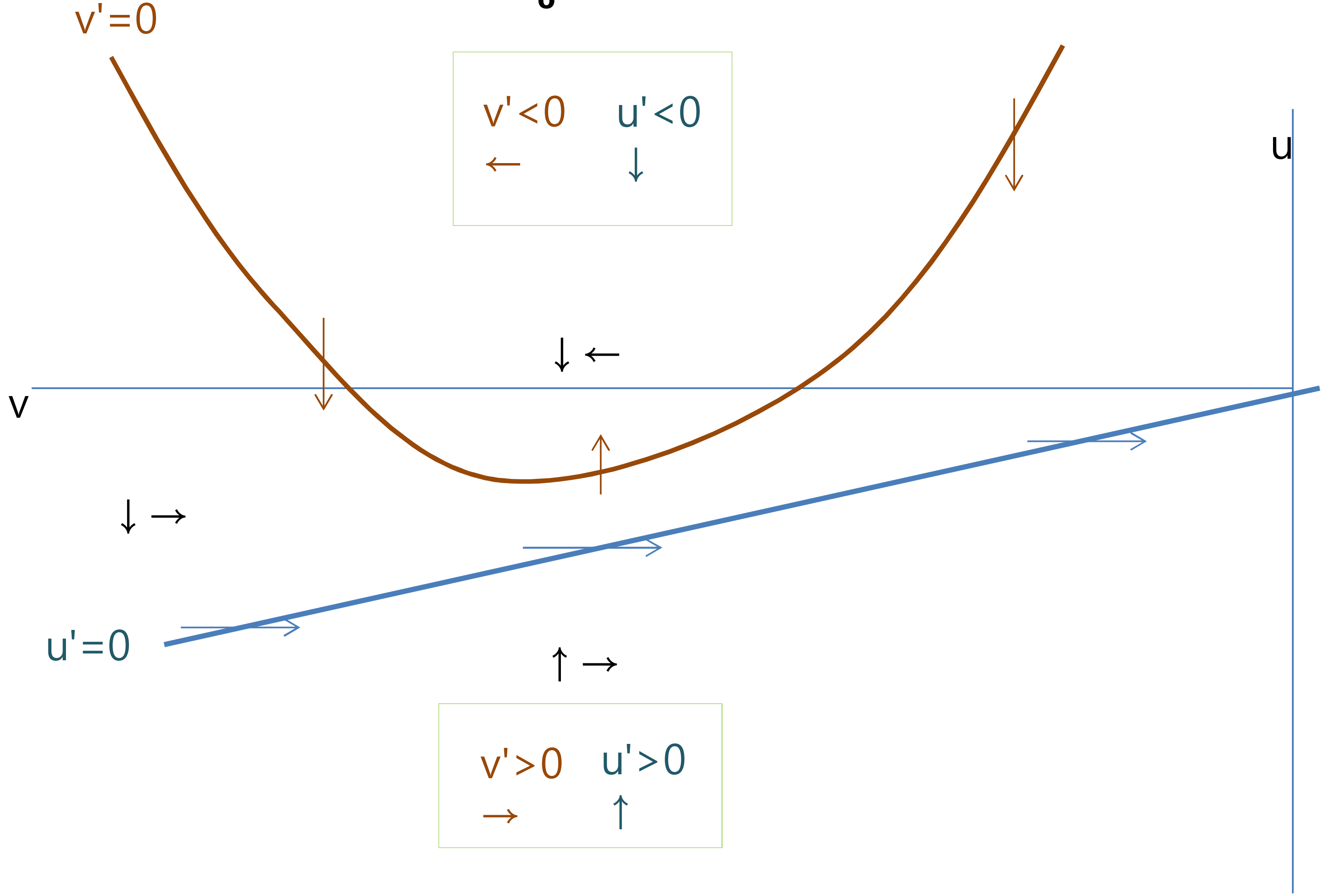
$I_o = 0$



$$v' = 0.04\,v^2 + 5\,v + 140 - u + I_o$$
$$u' = a\,(b\,v - u)$$

$$u = 0.04\,v^2 + 5\,v + 140 + I_o$$
$$u = b\,v$$

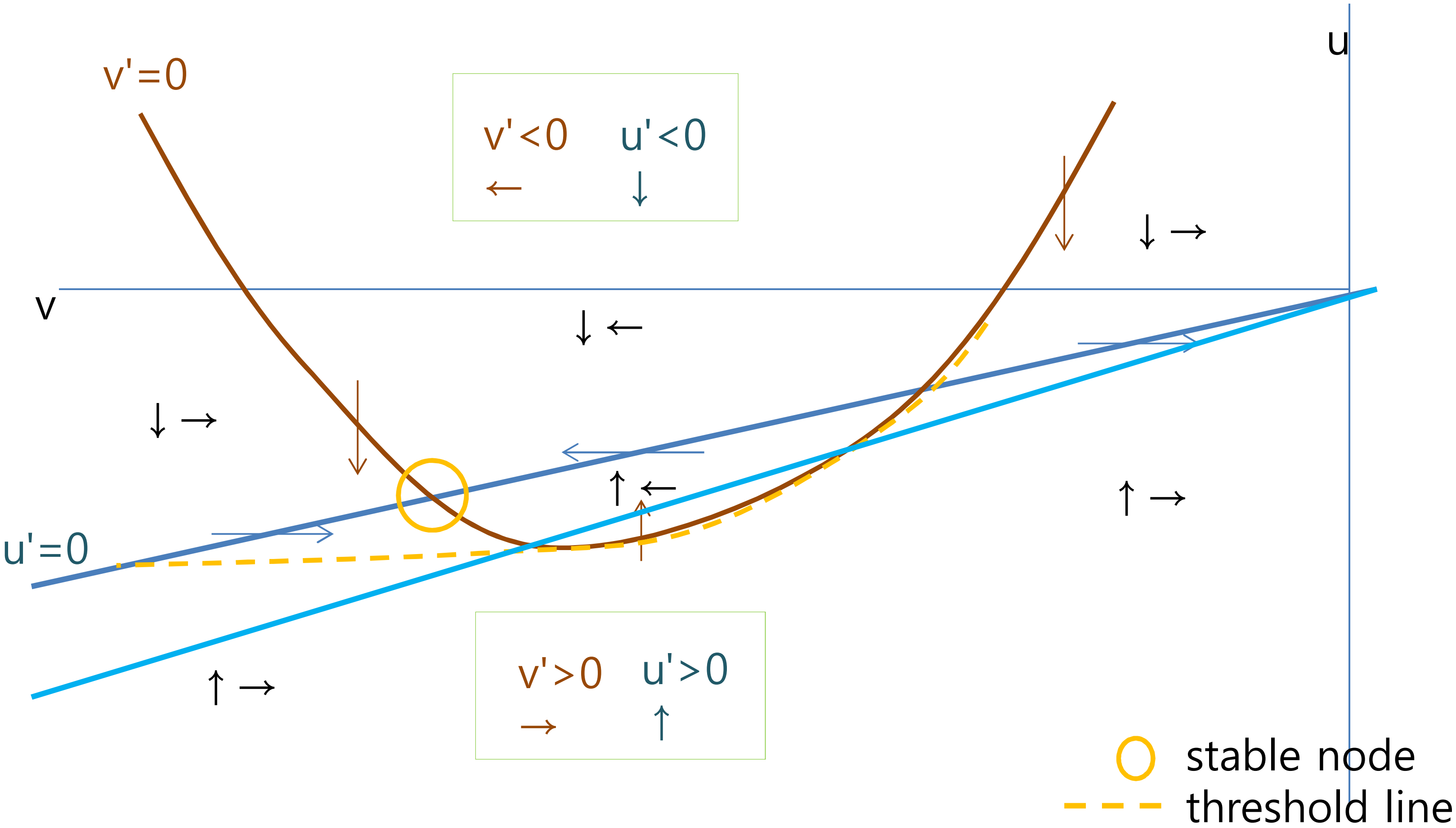
$I_o > 0$



$$v' = 0.04\,v^2 + 5\,v + 140 - u + I_o$$
$$u' = a\,(b\,v - u)$$

$$u = 0.04\,v^2 + 5\,v + 140 + I_o$$
$$u = b\,v$$

The higher b, the lower I_o req'd for evoke AP

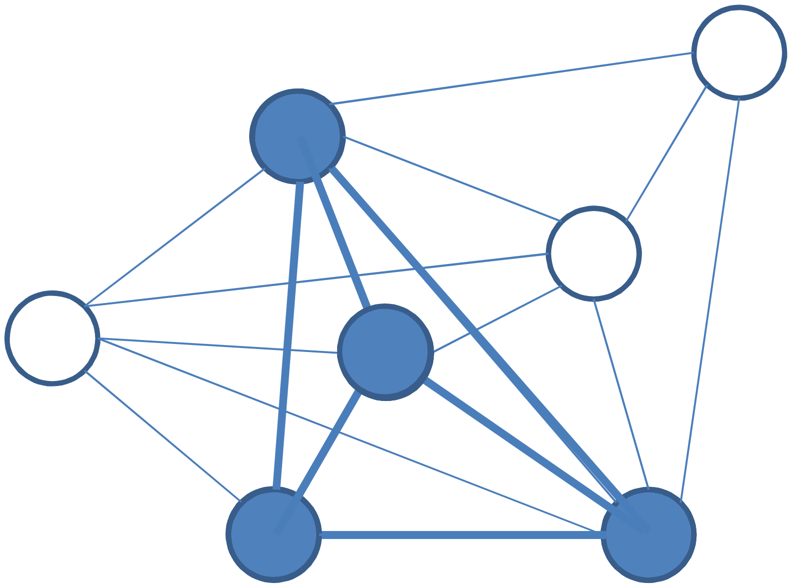


$$u = 0.04\, v^2 + 5\, v + 140 + I_o$$
$$u = b\, v$$

Simulation for
pattern completion from partial cue
by
auto-associational network

Pattern completion by auto-associative network

pattern completion



Random recurrent network

connected with Hebbian synapses

(Hopfield network)

Pattern completion: X' -> X

Training pattern (Z)

Z = [1,0,1,0]

Hebbian connectivity (J_H)

J_H = Z' * Z

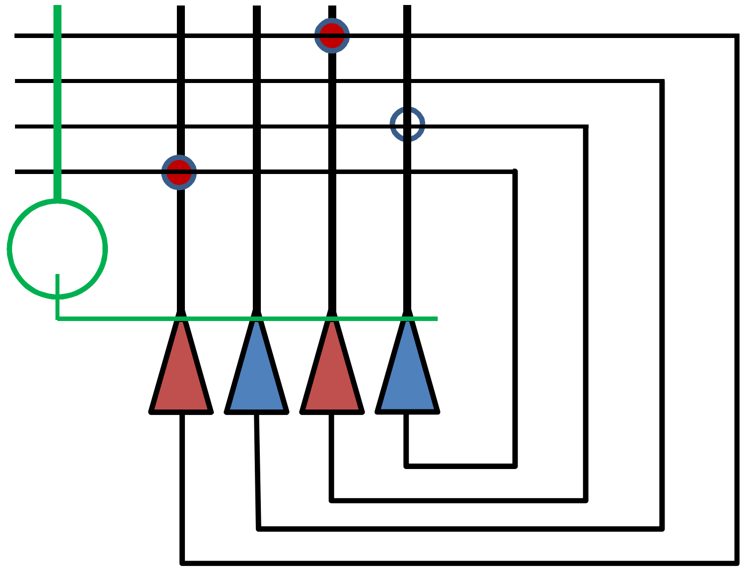
Structural connectivity (c)

W = rand(Npc,Npc);

W = ceil(W + (c-1));

Syn Wt matrix (WJ)

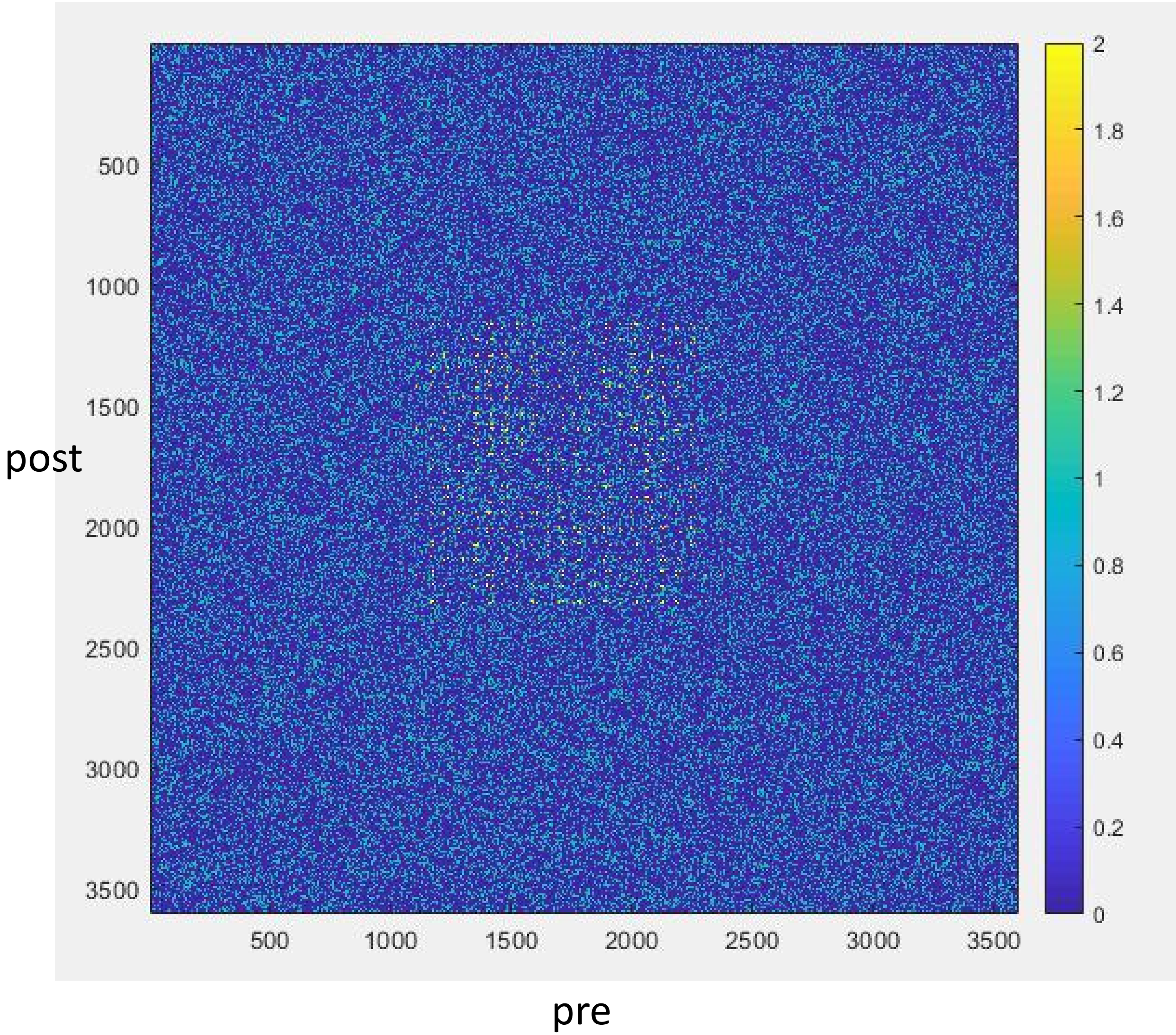
WJ = w * J_H .*W



c = 0.25

w = 2.0

Syn Wt Matrix (WJ)



% Initial cue, X_0 = random firing 10% of trained pattern

X_0 = double(img(:)).*rand(Npc, 1);
X_0 = max(0,ceil(X_0-0.9));

X = zeros(Npc, time)

time step →

$$
\begin{array}{c|ccccc}
 & 1 & 0 & 0 & 0 & 1 \\
\text{cell ID} & 0 & 0 & 1 & 0 & 0 \\
 & 1 & 1 & 0 & 0 & 0 \\
 & 0 & 0 & 0 & 1 & 0 \\
 & X_0 & & & &
\end{array}
$$

Loop

% I_{syn}(i,t): synaptic inputs to i-th PC at t

I_{syn}(:,t) = WJ *X(:,t);

% threshold

T(t) = g1*sum(X(:,t));

% net input current

I_{net}(:,t) = Isyn(:,t) - T(t);

% Izhikevich spike model

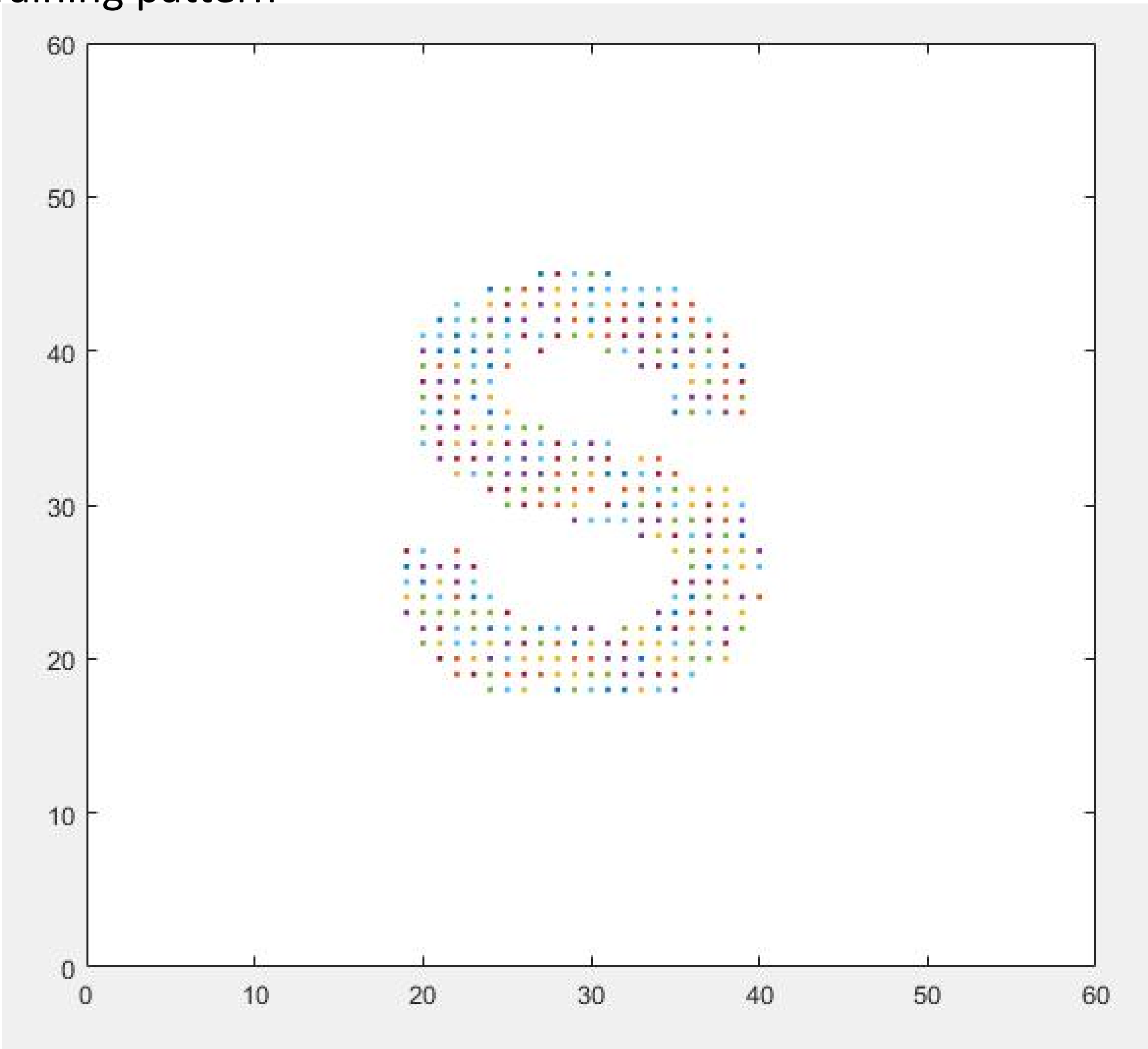
v = v + [0.04*v^2 + 5*v + 140 -uiz+ I_{net}];
uiz=uiz+aiz.*(biz.*v-uiz);
fired=find(v>=30);   v(fired)=vret; uiz(fired)=uiz(fired)+ud;
X(fired, t+1) = 1;

g1 = 0.5

vrest = -65
vret = -58

aiz = 0.02
biz = 0.25
ud = 4

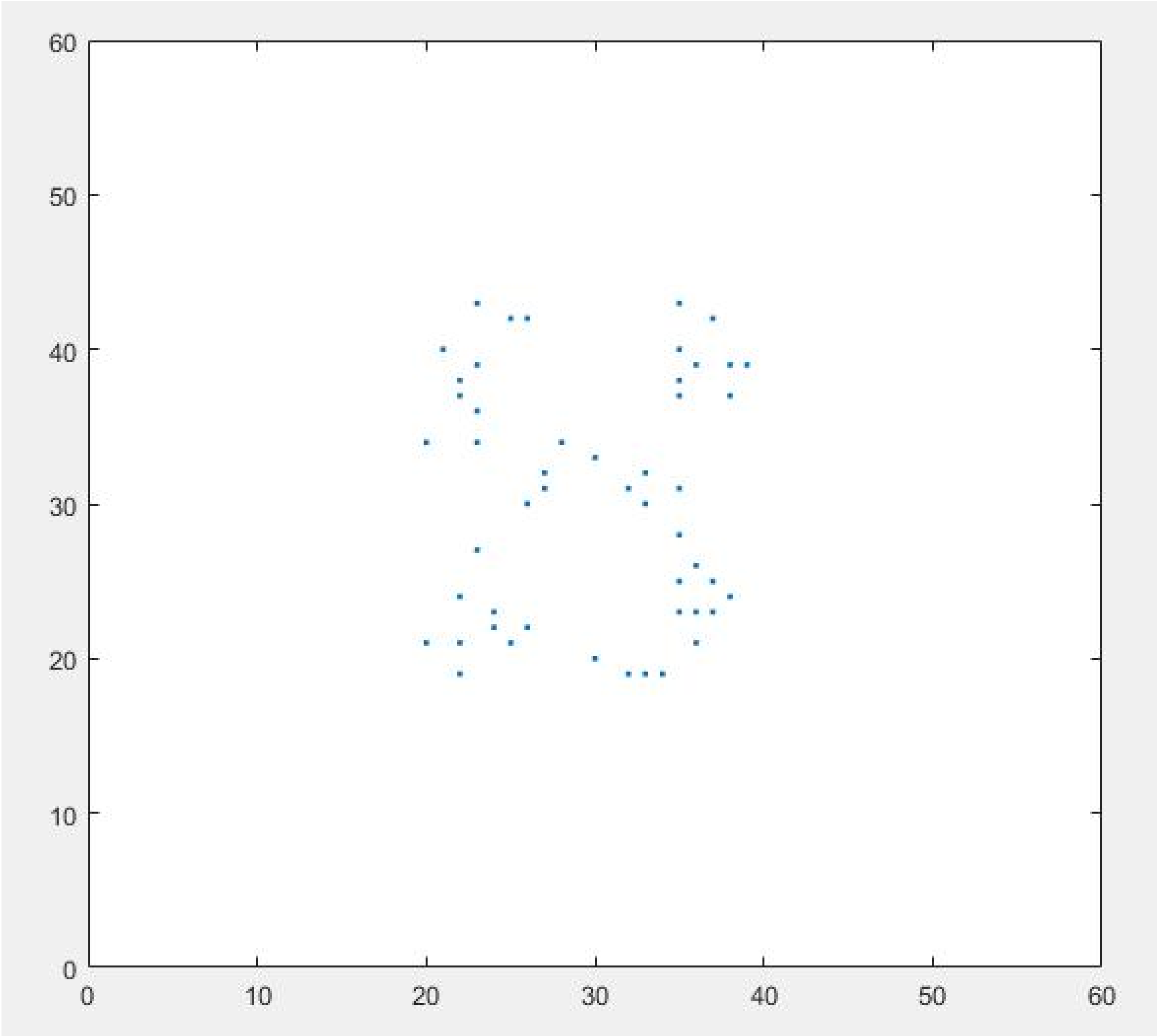
Training pattern



N_{pc} = 60 x 60 = 3600

Each pixel represents spike activity of a neuron

Partial cue



Homework

1. Train the network with another pattern, and retrieve one of two patterns using a partial cue.

2. Discuss what mechanisms are implemented in the brain to retrieve a single pattern from a recurrent network in which multiple patterns are embedded.