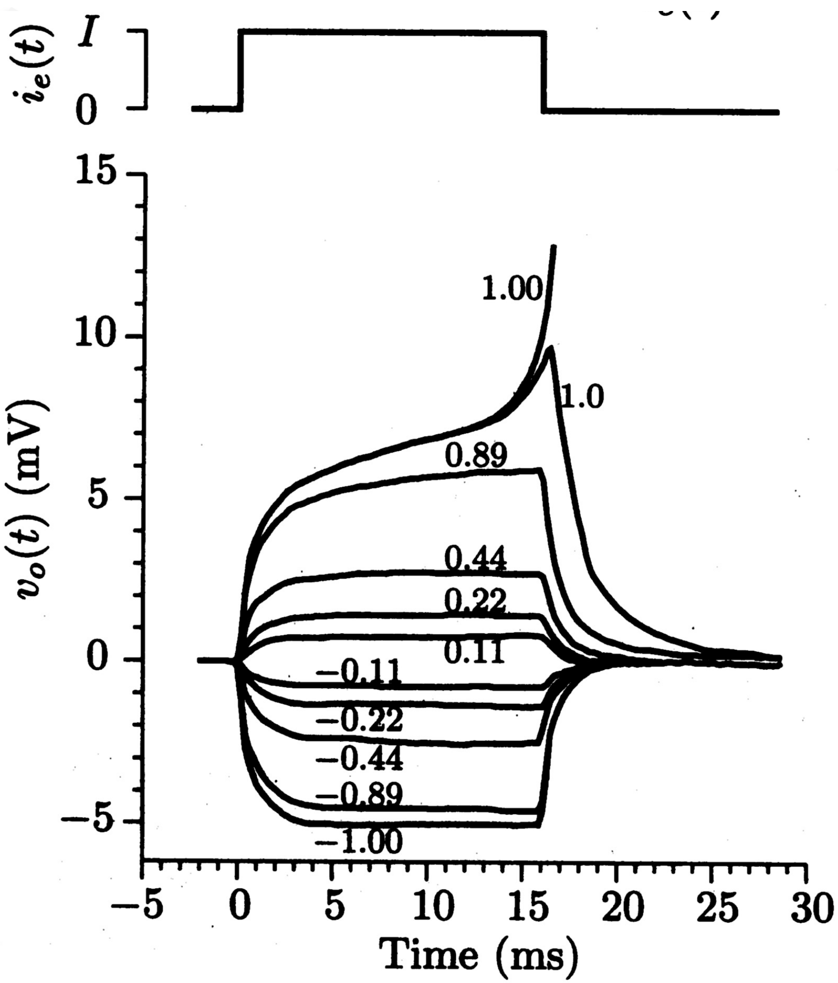
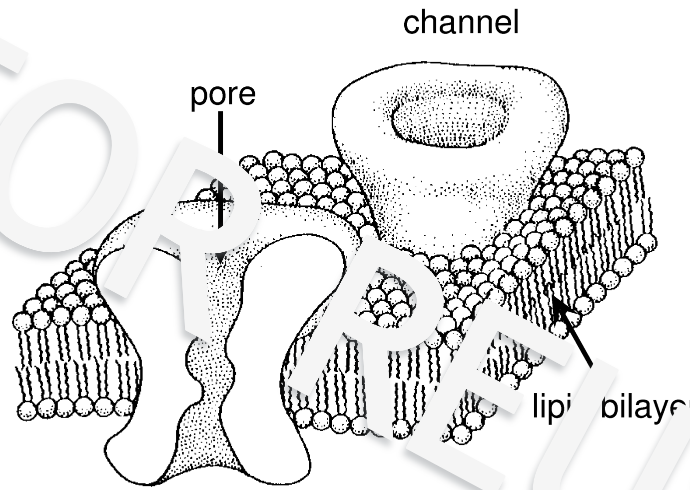
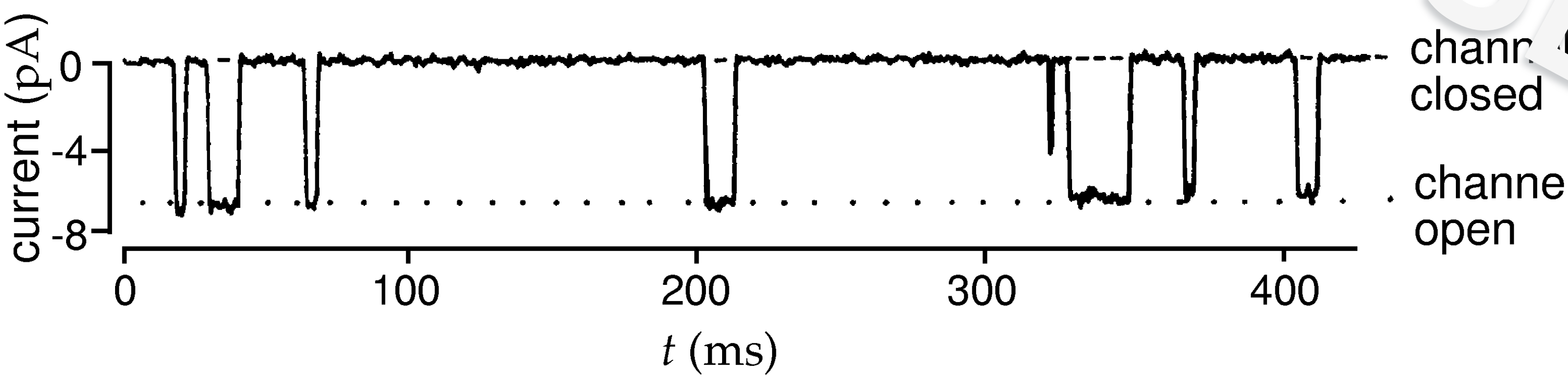
But what makes a neuron *compute*?



Excitability arises from ion channel nonlinearity

- voltage dependent
- transmitter dependent (synaptic)
- Ca dependent
- mechanosensitive

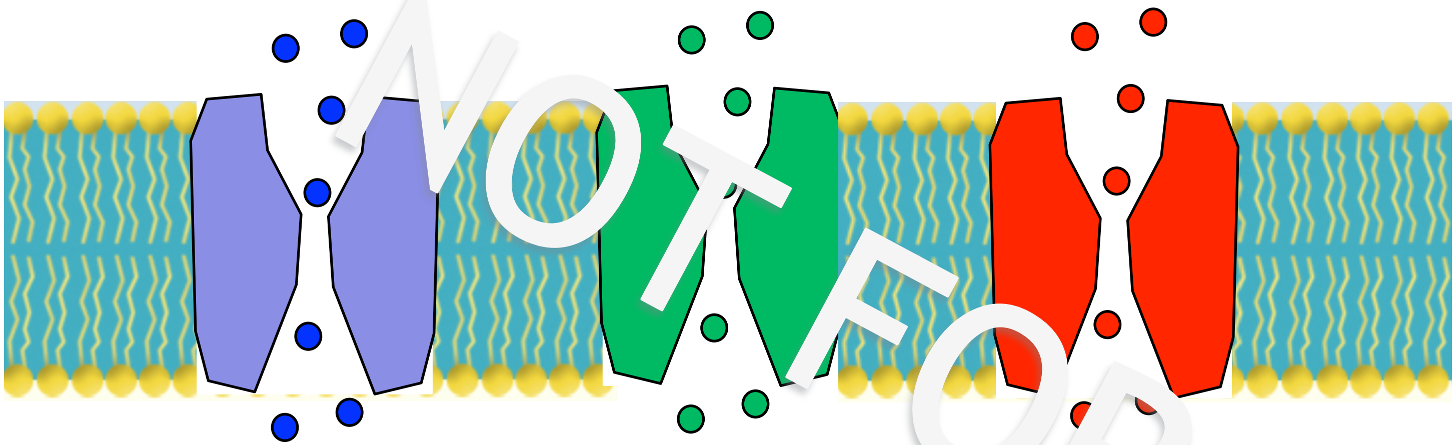


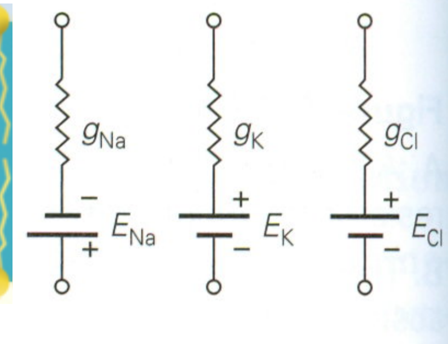


Best pics are all from Dayan and Abbott, *Theoretical Neuroscience*

Parallel paths for different ions to cross membrane

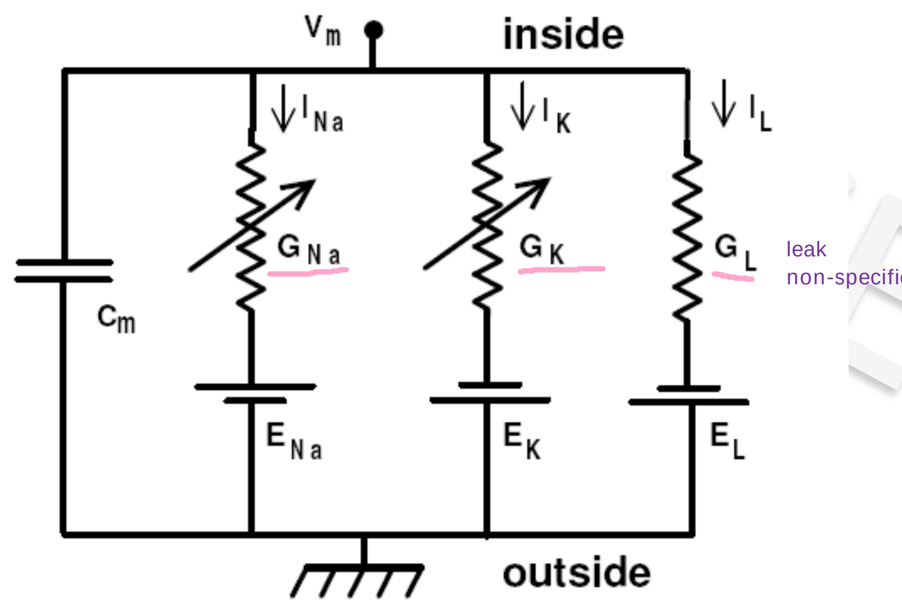
$I_i = g_i\,(V\text{-}E_i)$





New equivalent circuit:

Variable conductance

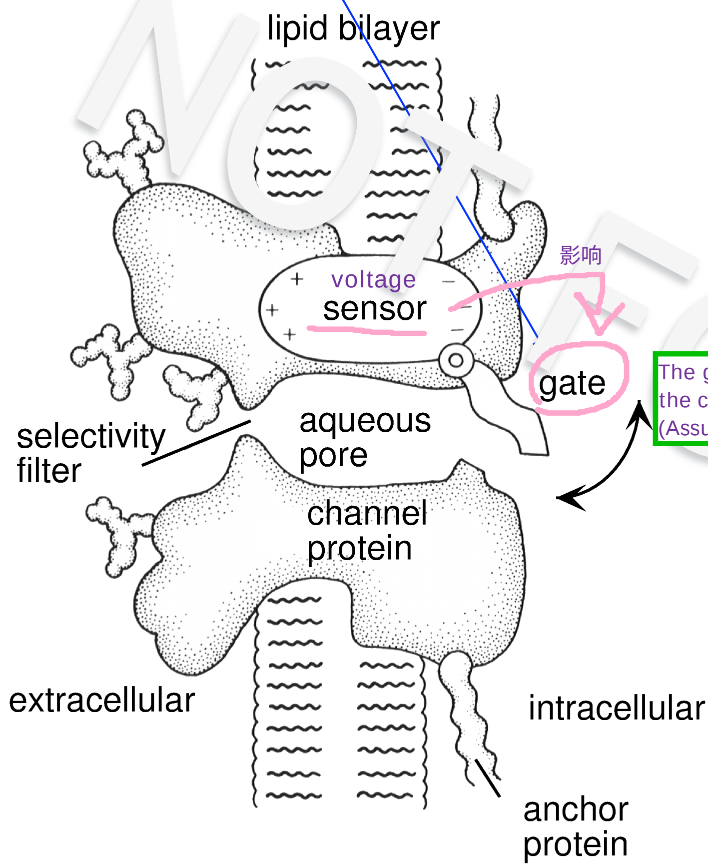


The ion channel is a cool molecular machine

K channel: open probability increases when depolarized

Gating depends on subunit state

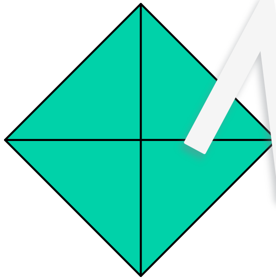
$$P_K \sim n^4$$



The gate here consists of four sub-units that need to be in the correct configuration in order for ions to flow through (Assume independent)

Persistent conductance

The ion channel is a cool molecular machine

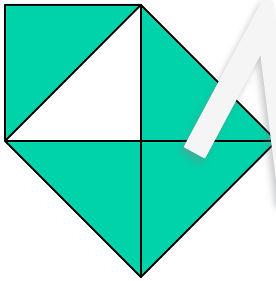


n describes a subunit

n	is open probability
$1 - n$	is closed probability

This picture is not from Dayan and Abbott, for instance

The ion channel is a cool molecular machine



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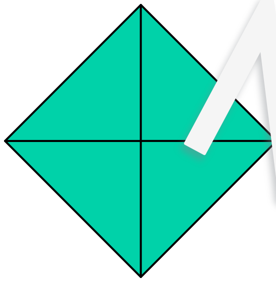
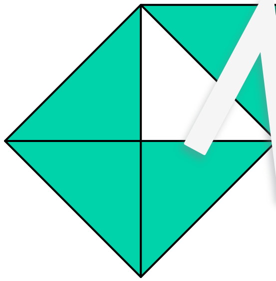
The ion channel is a cool molecular machine



n describes a subunit

n	is open probability
$1 - n$	is closed probability

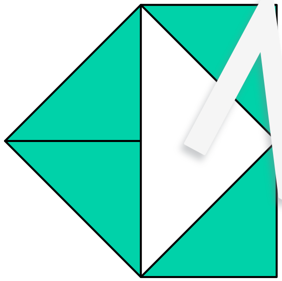
The ion channel is a cool molecular machine



n describes a subunit

n	is open probability
$1 - n$	is closed probability

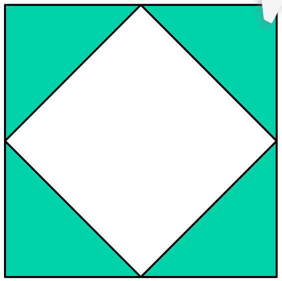
The ion channel is a cool molecular machine



n describes a subunit

n	is open probability
$1 - n$	is closed probability

The ion channel is a cool molecular machine

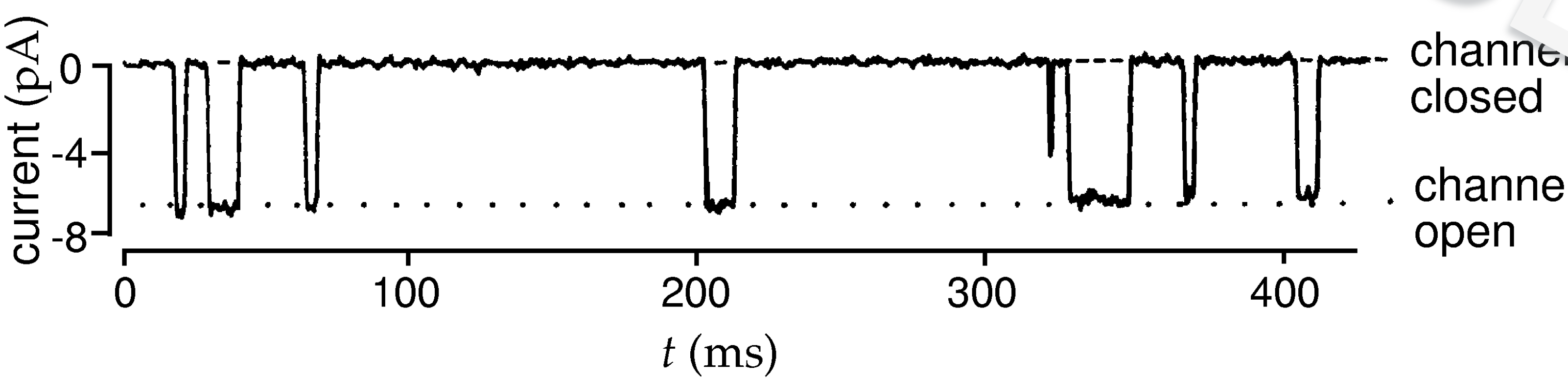


n describes a subunit

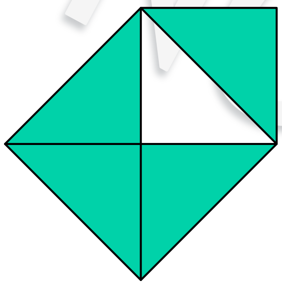
n	is open probability
$1 - n$	is closed probability

$$\boxed{P_K \sim n^4}$$

4个同时打开的时候，离子通道允许电流通过。



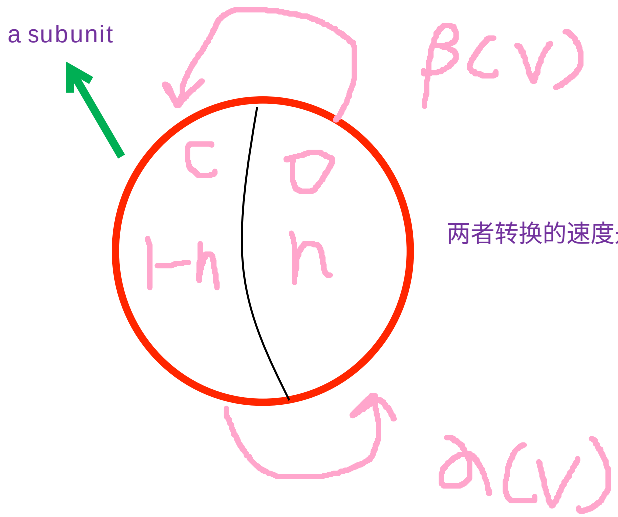
The ion channel is a cool molecular machine



也就是n其实是电压的函数
电压决定了转换的概率，和概率平衡的点
n不光可以理解成概率，还可以理解成在某个状态的量（总量是1然后sample）

n describes a subunit

n	is open probability
$1 - n$	is closed probability



两者转换的速度是电压的函数

Transitions between states occur at voltage dependent rates

Transitions rate

$\alpha_n(V)$ C → O

$\beta_n(V)$ O → C

从关到开的速率 × 关着的概率（可以理解成总体是1，有1-n个是关着的）

$$\frac{dn}{dt} = \underbrace{\alpha_n(V)(1-n)}_{\text{how much add}} - \underbrace{\beta_n(V)n}_{\text{how much lose}}$$

Dynamics of activation: persistent conductance

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

代

We can rewrite:

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

一个常数而已，和上面的式
子没关系，另一种表达方式

得

代

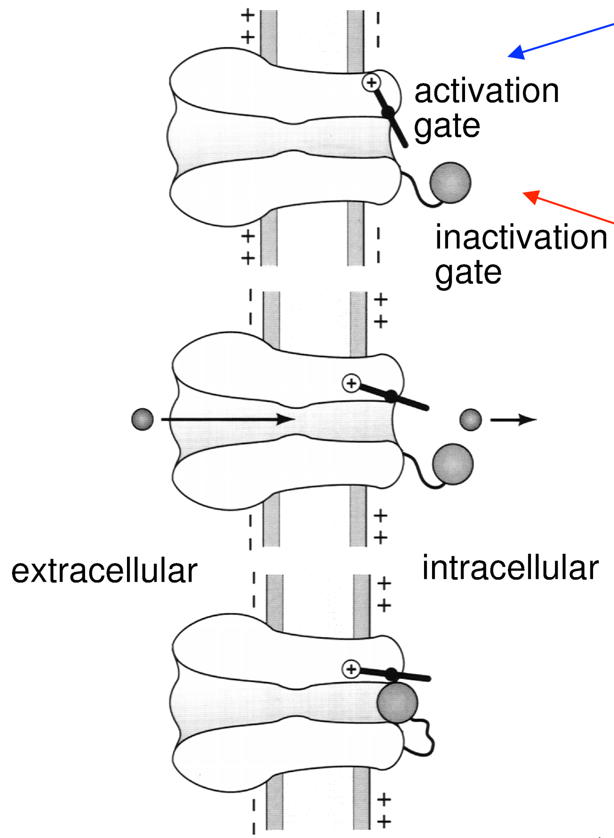
where

$$\tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)}$$

$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)}$$

n_inf表达的是平衡态，把导数等于0就可轻松得到。

Transient conductances



Gate acts as in previous case

3个子成分
P = m（打开的概率）

Additional gate can block channel when open

还有一个gate会阻止激活，所以它要关了才能激活
P = h（关闭这个阻止激活门的概率）

$P_{Na} \sim m^3h$

电压增强，m增加（激活离子通道），h减少（关闭离子通道）

m is activation variable
h is inactivation variable

m and *h* have opposite voltage dependences:
depolarization increases *m*, activation
v+
hyperpolarization increases *h*, deinactivation
v-
关闭抑制激活

Dynamics of activation and inactivation

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

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

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

So will get equivalent forms as for *n*…

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

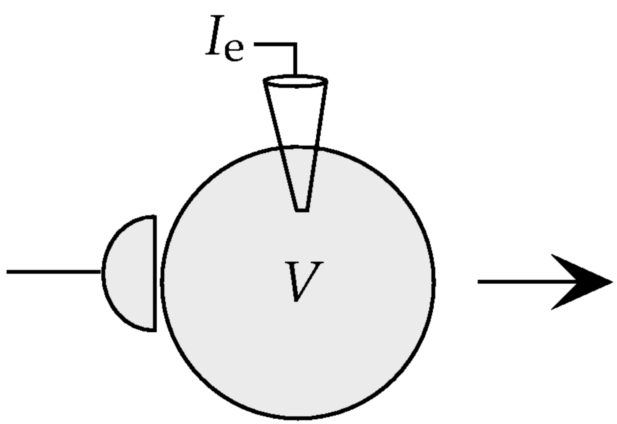
导电率根据电压变化：n越大，打开的门越多，导电率越好

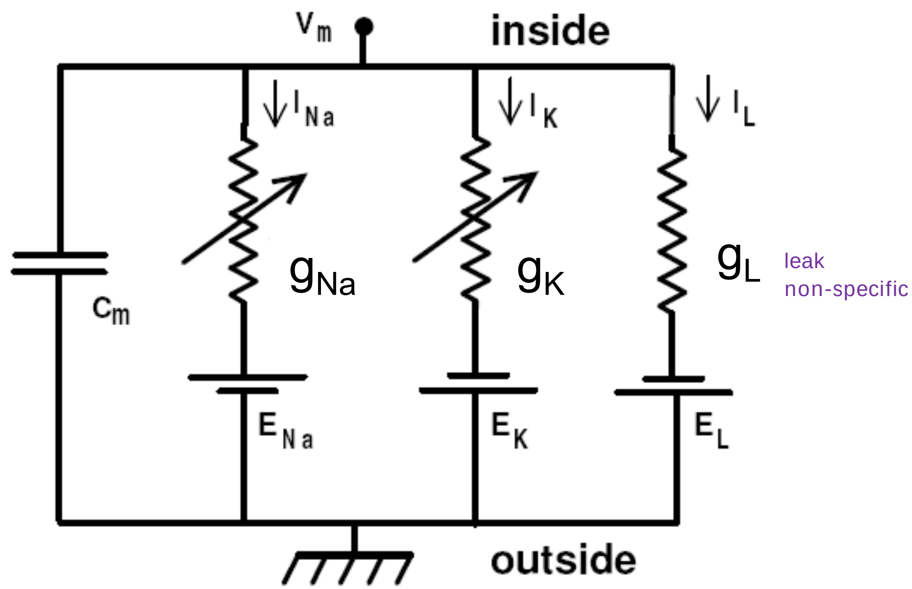
V-dependent conductances

$$g_K(V) = \bar{g}_K \, n^4$$

$$g_{Na}(V) = \bar{g}_{Na} \, m^3 h$$

Putting it together





Ohm's law: $V = IR$ and Kirchhoff's law

$$\boxed{C_m \frac{dV}{dt}} = \boxed{-\sum_i g_i (V - E_i)} + \boxed{I_e}$$

Capacitative current

Ionic currents

Externally applied current

Hodgkin and Huxley's Nobel equation

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

$$-C_m \frac{dV}{dt} = g_L(V - E_L) + \bar{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}}) + \bar{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}}) - I_e$$

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

$g_K(V) = \bar{g}_K\, n^4$

$g_{Na}(V) = \bar{g}_{Na}\, m^3 h$

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

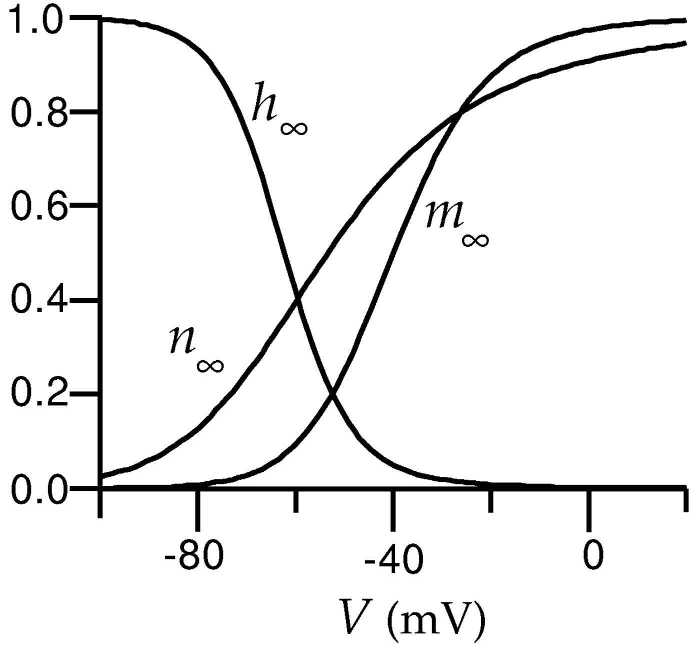
$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h$$

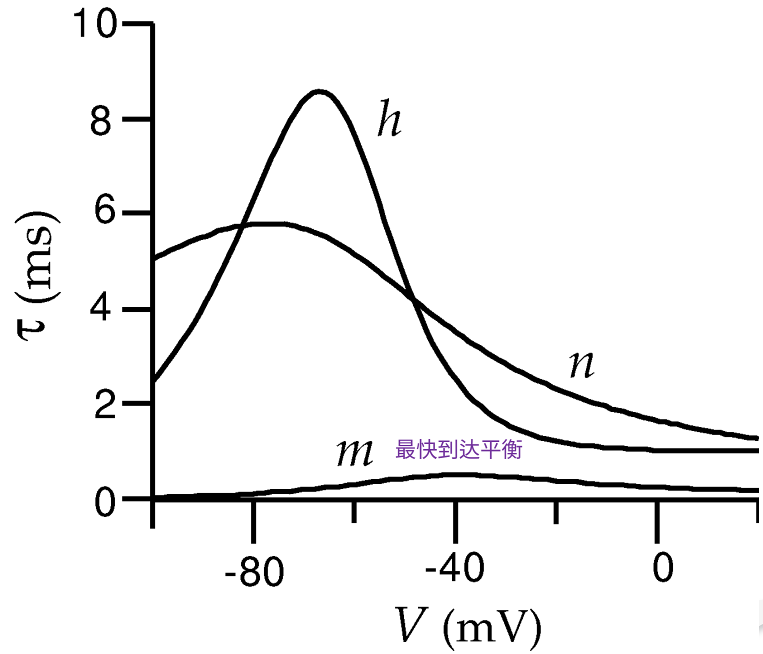
Dynamics of activation and inactivation

τ：到平衡点的速率

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

n governs the opening of the potassium channel, and both n and h must be large for the sodium channel to be open



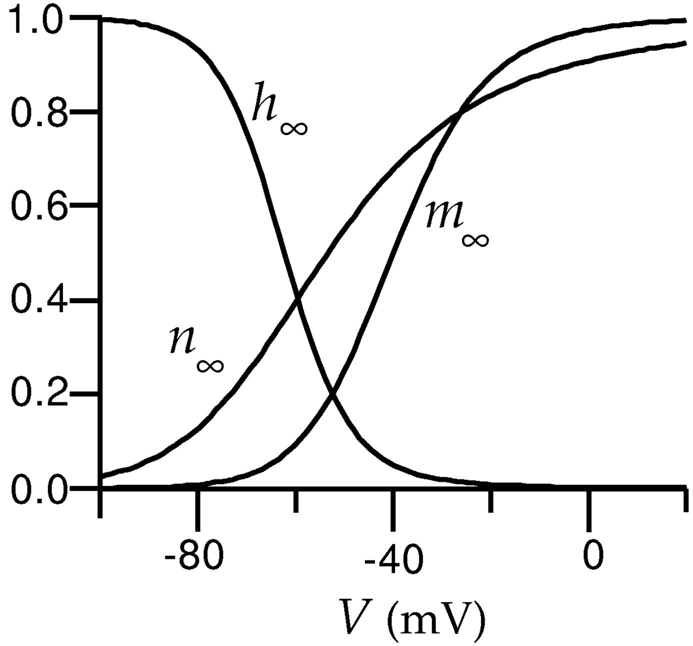


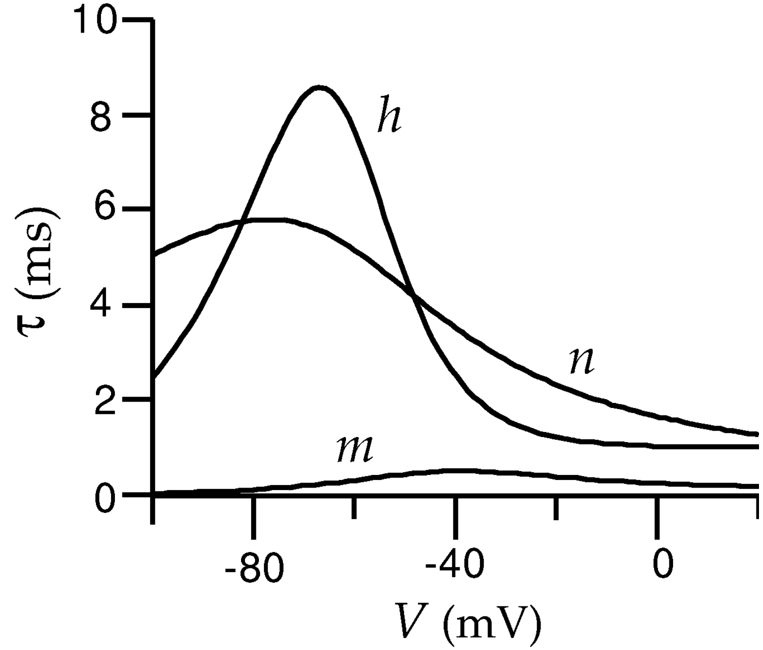
This is where each variable is going

This is how fast it gets there

Dynamics of activation and inactivation

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



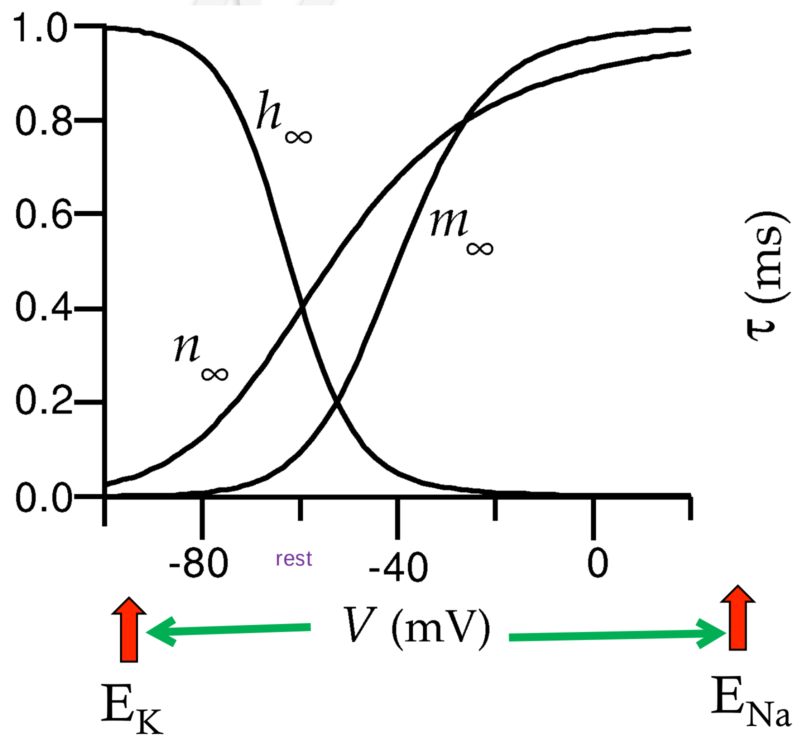


This is where each variable is going

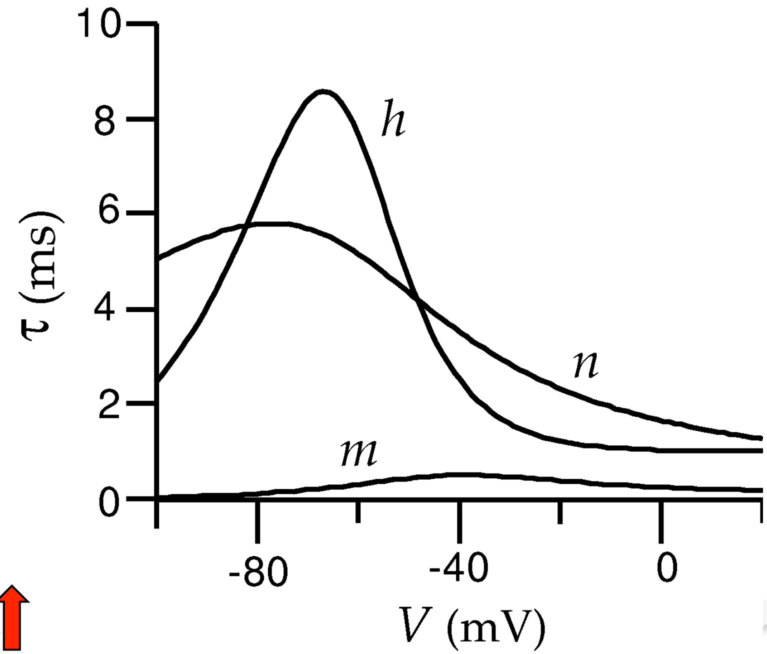
This is how fast it gets there

Anatomy of a spike

Steady state



Time constant

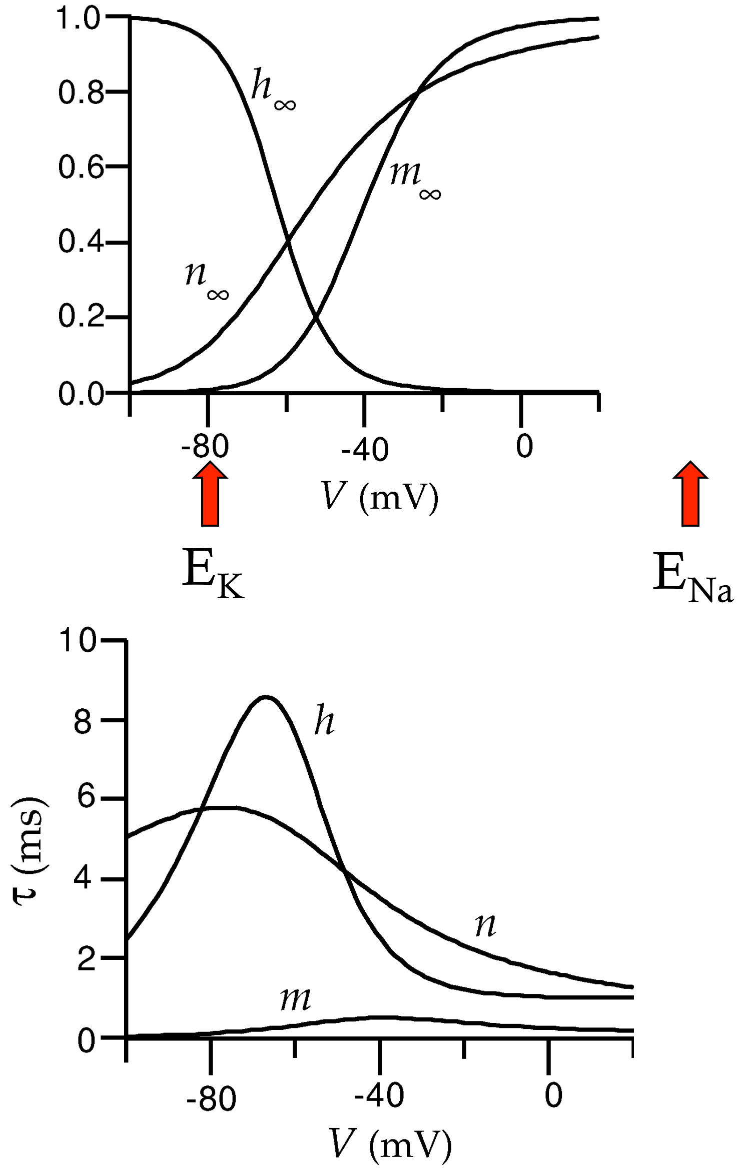


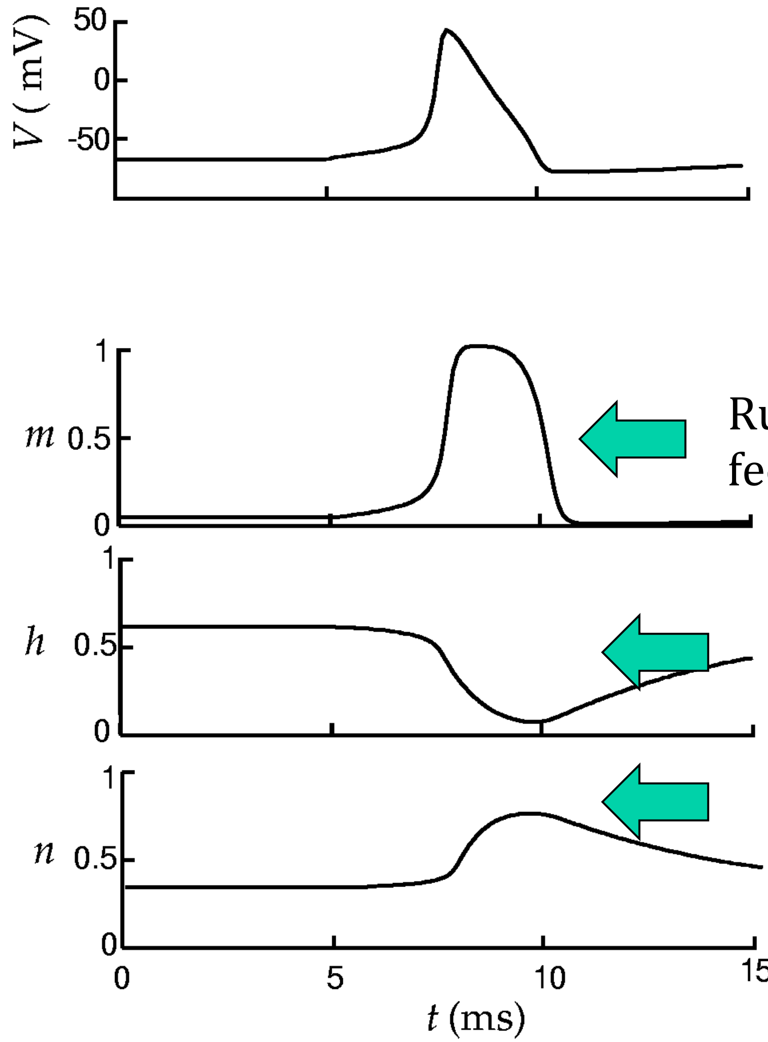
m速度最快，然后是n，最后是h

$$g_K(V) = \bar{g}_K n^4$$

$$g_{Na}(V) = \bar{g}_{Na} m^3 h$$

Anatomy of a spike





Runaway +ve feedback

Double whammy

All the dynamics here are explained by simple linear equation by a linear circuit, or a simple rate equation, except for two things: the multiplicative factors that relate the subunit behavior to the channel conductance's and the voltage dependence of the subunit dynamics.

Where to from here?