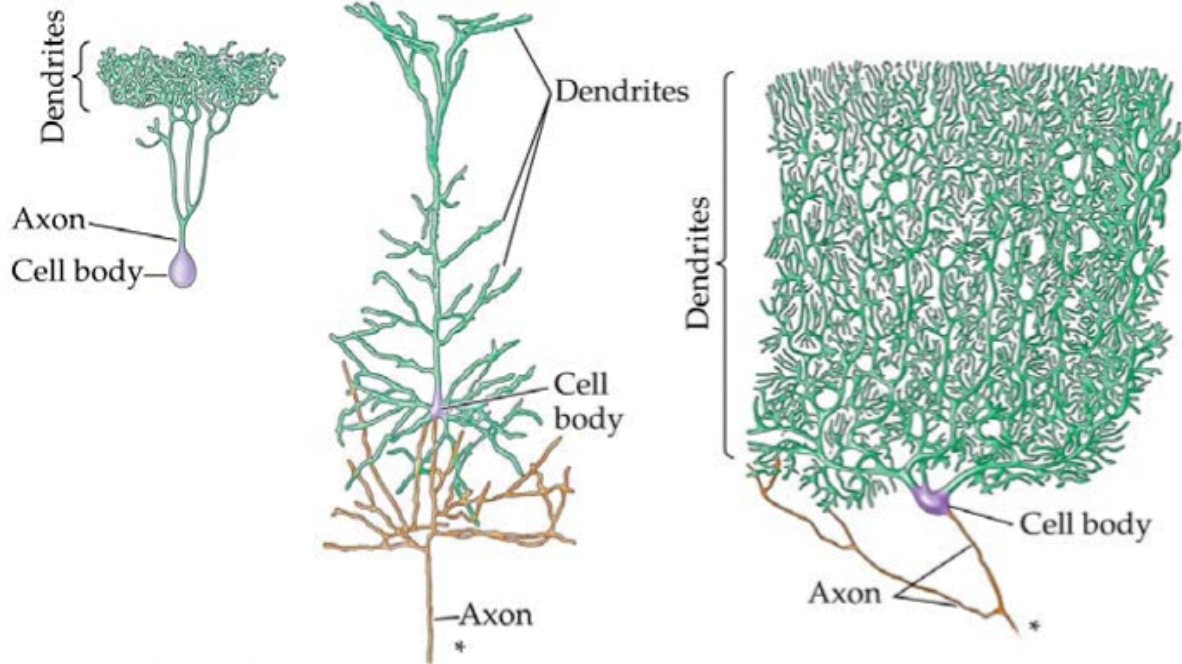
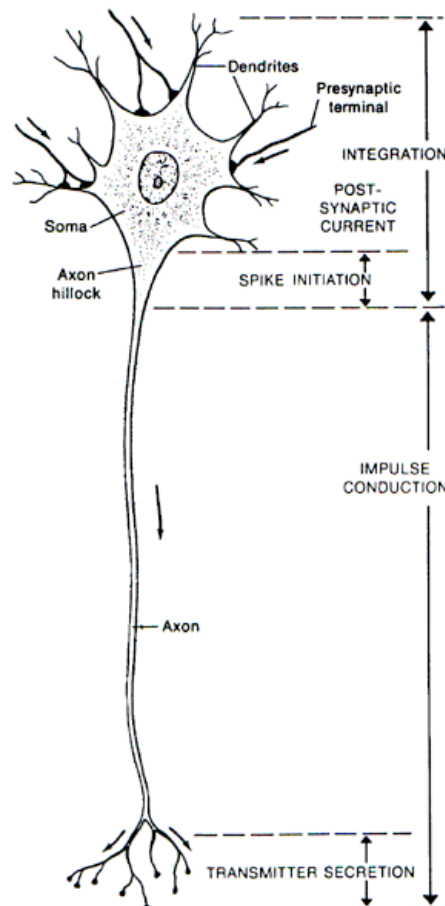


(D) Retinal amacrine cell (E) Cortical pyramidal cell (F) Cerebellar Purkinje cells

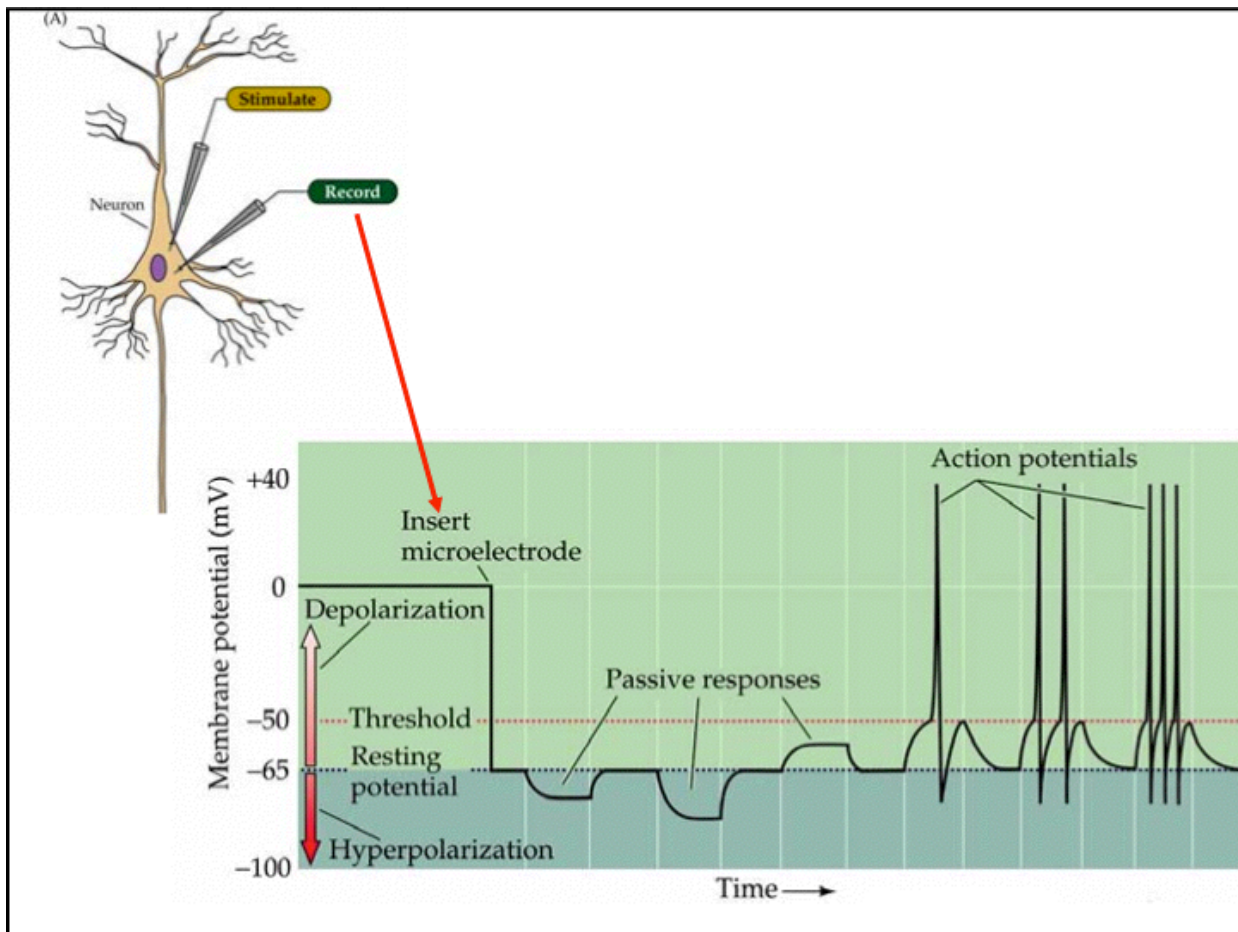


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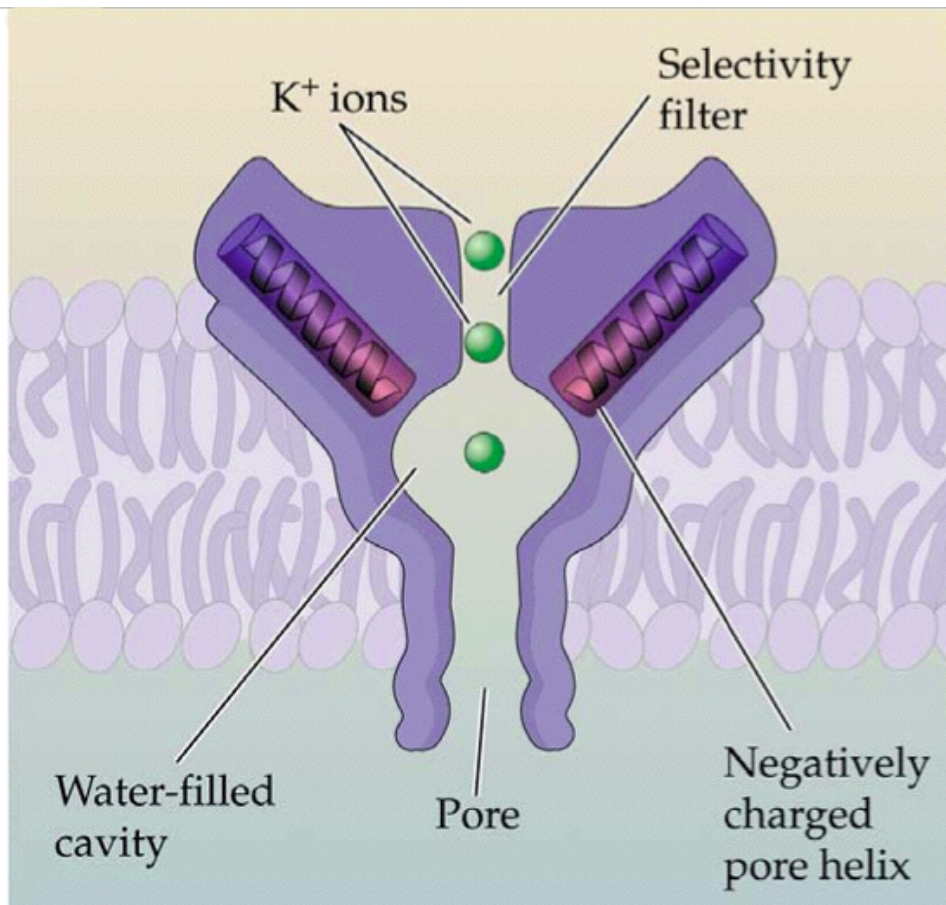
01\_neurons.pdf



02\_neuronParts.tif

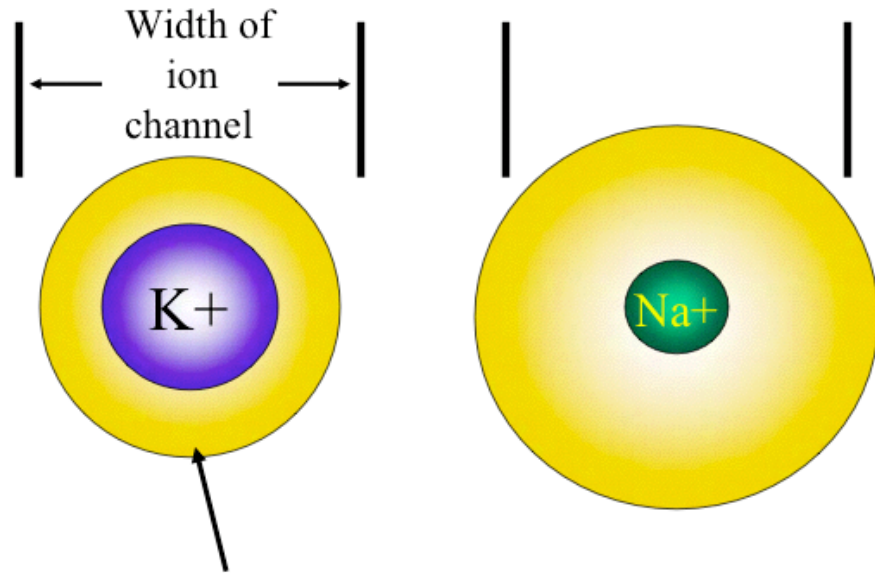


03\_memPot.pdf



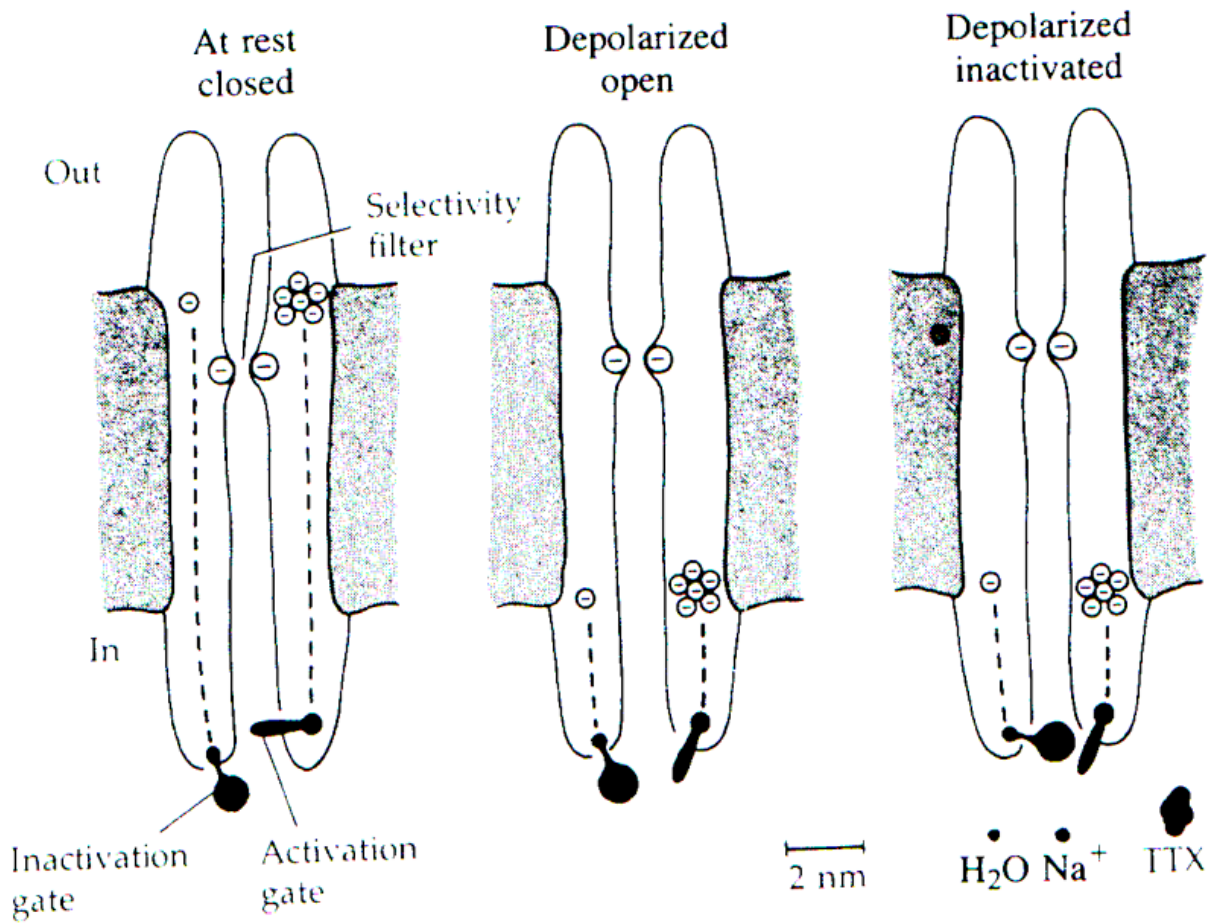
04\_channel.pdf

# Ion Selectivity



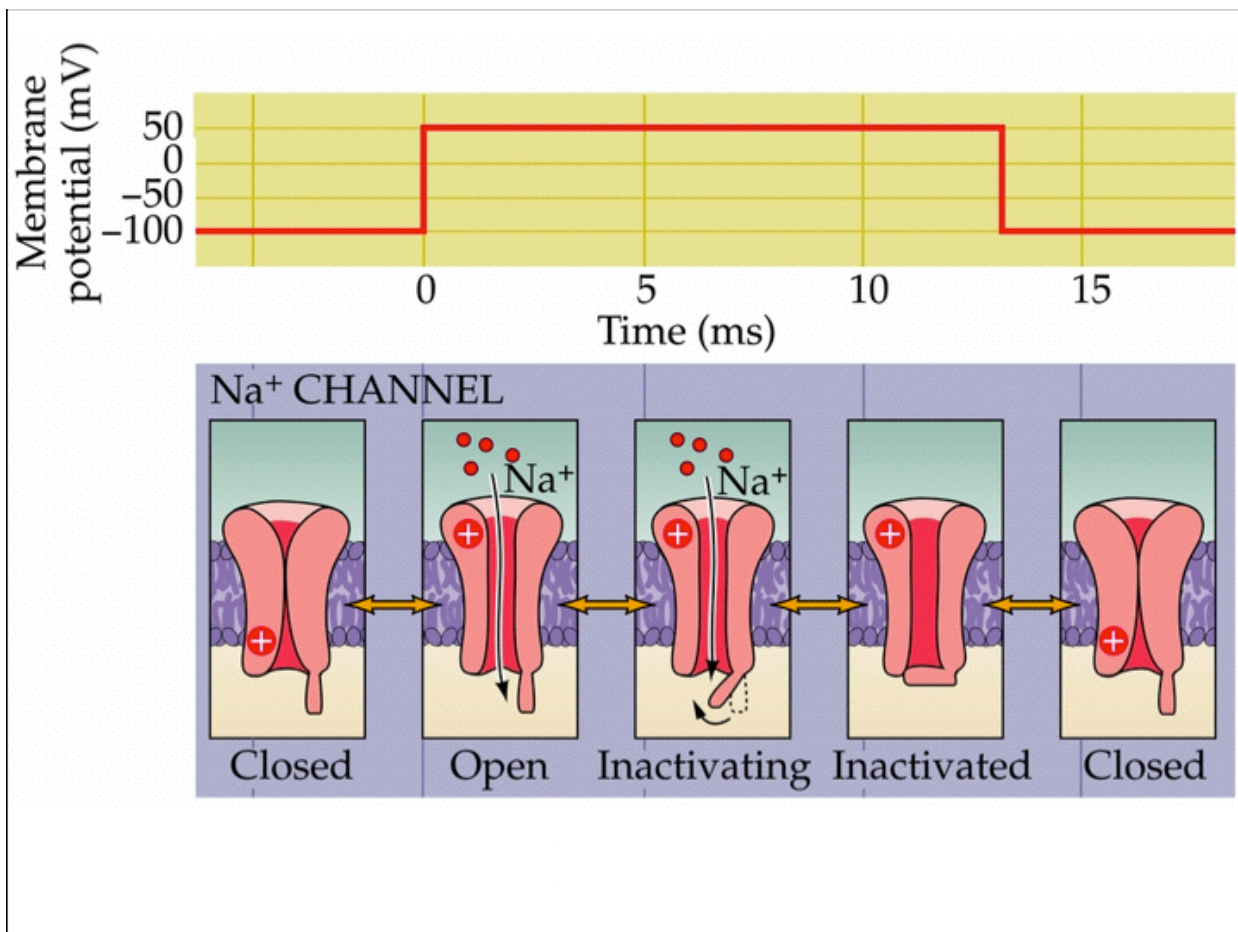
Cloud of waters of hydration surrounding K<sup>+</sup> ion is smaller due to weaker electrostatic pull of K<sup>+</sup> (even though K<sup>+</sup> nucleus is larger than Na<sup>+</sup>)

05\_ions.pdf

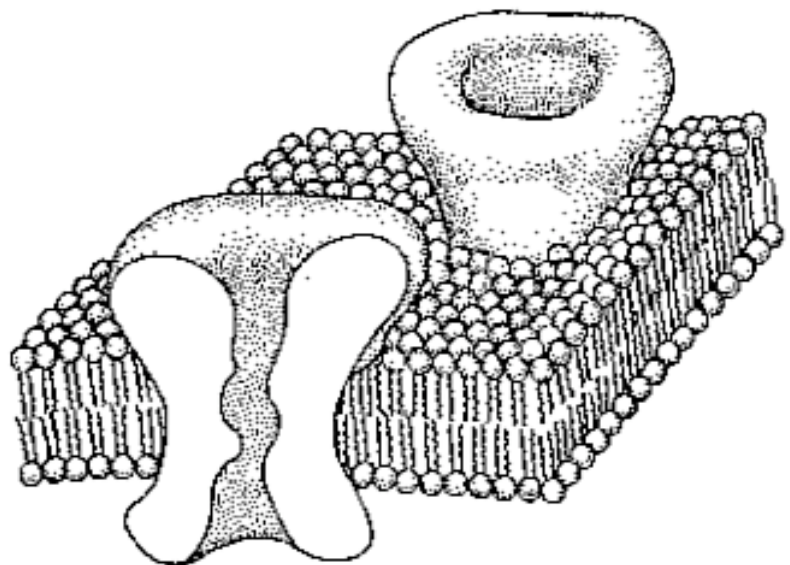
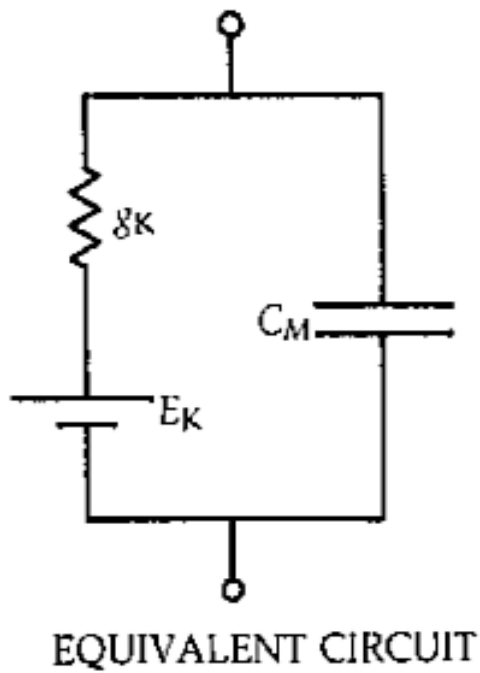


06\_channelGate.tif



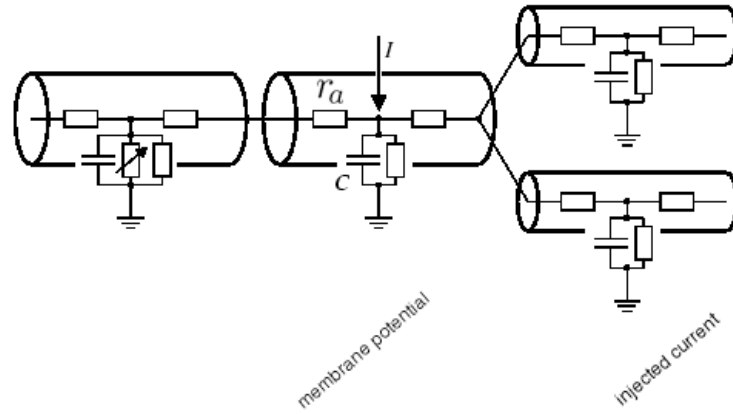


07\_channelStates.pdf



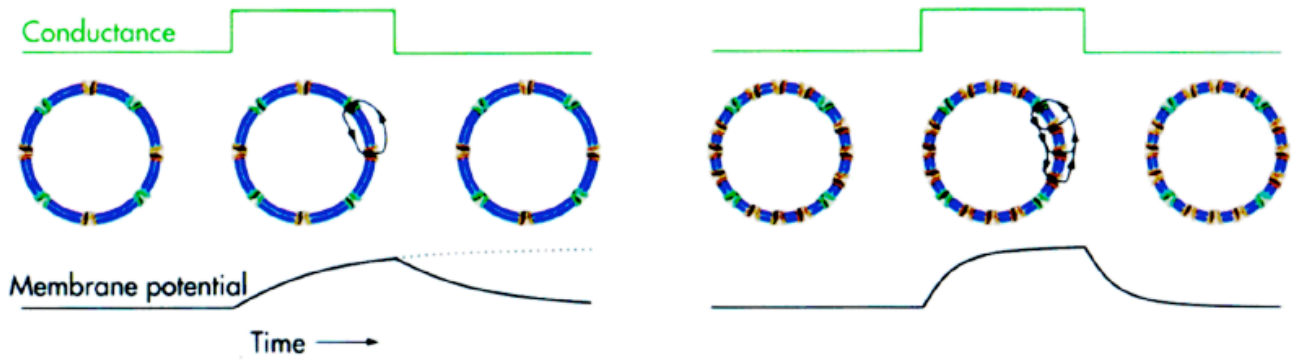
08\_equivCircuit.psd

Current-Voltage Equation



$$\frac{1}{r_a} \frac{\partial^2 V}{\partial x^2} + C \frac{dV}{dt} = I$$

09\_IV\_eq.psd

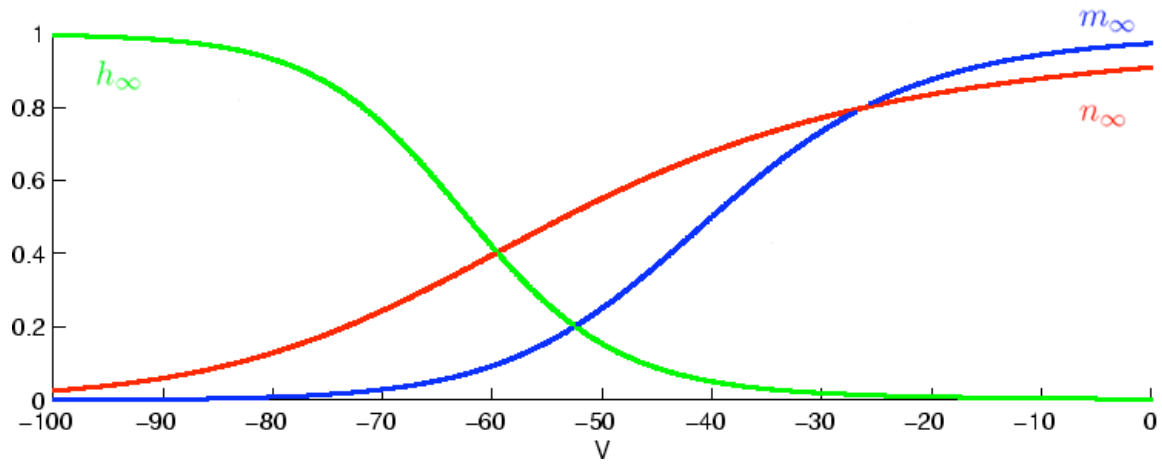


$$C \frac{dV}{dt} = I_{stim} - g_L(V - V_L)$$

### Hodgkin-Huxley Equation

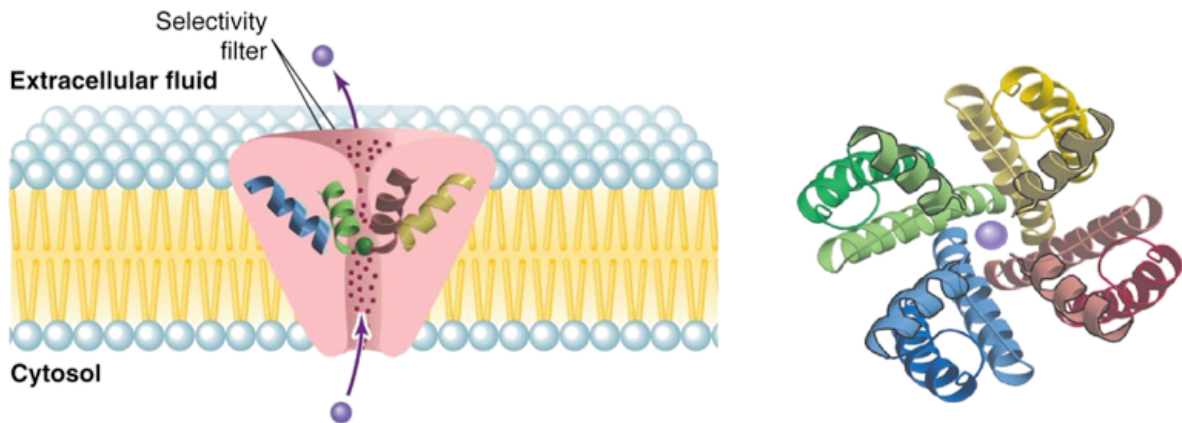
$$C \frac{dV}{dt} = I_{stim} - g_L(V - V_L) - \bar{g}_{Na} m^3 h (V - V_{Na}) - \bar{g}_K n^4 (V - V_K)$$

$$\frac{dm}{dt} = \frac{1}{\tau_m} (m_{\infty}(V) - m) \quad \frac{dh}{dt} = \frac{1}{\tau_h} (h_{\infty}(V) - h) \quad \frac{dn}{dt} = \frac{1}{\tau_n} (n_{\infty}(V) - n)$$

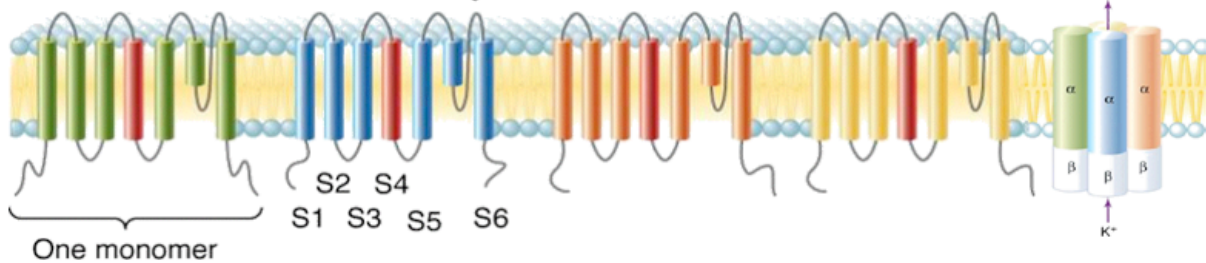


11\_hh\_eq.psd

### Molecular Structure of Ion Channels



### Eukaryotic K<sup>+</sup> channel



12\_moleChannel.psd

A. Properties of Voltage-Activated K <sup>+</sup> Channels										Inward-rectifier K <sup>+</sup> Channels														
Accession	Gene	Species	Channel	Subunit	Properties	Accession	Gene	Species	Channel	Subunit	Properties	Accession	Gene	Species	Channel	Subunit	Properties	Accession	Gene	Species	Channel	Subunit	Properties	
K011	KCNK1	Human	IRK1	IRK1	IRK1	K012	KCNK2	Human	IRK2	IRK2	IRK2	K013	KCNK3	Human	IRK3	IRK3	IRK3	K014	KCNK4	Human	IRK4	IRK4	IRK4	IRK4
K015	KCNK5	Human	IRK5	IRK5	IRK5	K016	KCNK6	Human	IRK6	IRK6	IRK6	K017	KCNK7	Human	IRK7	IRK7	IRK7	K018	KCNK8	Human	IRK8	IRK8	IRK8	IRK8
K019	KCNK9	Human	IRK9	IRK9	IRK9	K020	KCNK10	Human	IRK10	IRK10	IRK10	K021	KCNK11	Human	IRK11	IRK11	IRK11	K022	KCNK12	Human	IRK12	IRK12	IRK12	IRK12
K023	KCNK13	Human	IRK13	IRK13	IRK13	K024	KCNK14	Human	IRK14	IRK14	IRK14	K025	KCNK15	Human	IRK15	IRK15	IRK15	K026	KCNK16	Human	IRK16	IRK16	IRK16	IRK16
K027	KCNK17	Human	IRK17	IRK17	IRK17	K028	KCNK18	Human	IRK18	IRK18	IRK18	K029	KCNK19	Human	IRK19	IRK19	IRK19	K030	KCNK20	Human	IRK20	IRK20	IRK20	IRK20
K031	KCNK21	Human	IRK21	IRK21	IRK21	K032	KCNK22	Human	IRK22	IRK22	IRK22	K033	KCNK23	Human	IRK23	IRK23	IRK23	K034	KCNK24	Human	IRK24	IRK24	IRK24	IRK24
K035	KCNK25	Human	IRK25	IRK25	IRK25	K036	KCNK26	Human	IRK26	IRK26	IRK26	K037	KCNK27	Human	IRK27	IRK27	IRK27	K038	KCNK28	Human	IRK28	IRK28	IRK28	IRK28
K039	KCNK29	Human	IRK29	IRK29	IRK29	K040	KCNK30	Human	IRK30	IRK30	IRK30	K041	KCNK31	Human	IRK31	IRK31	IRK31	K042	KCNK32	Human	IRK32	IRK32	IRK32	IRK32
K043	KCNK33	Human	IRK33	IRK33	IRK33	K044	KCNK34	Human	IRK34	IRK34	IRK34	K045	KCNK35	Human	IRK35	IRK35	IRK35	K046	KCNK36	Human	IRK36	IRK36	IRK36	IRK36
K047	KCNK37	Human	IRK37	IRK37	IRK37	K048	KCNK38	Human	IRK38	IRK38	IRK38	K049	KCNK39	Human	IRK39	IRK39	IRK39	K050	KCNK40	Human	IRK40	IRK40	IRK40	IRK40
K051	KCNK41	Human	IRK41	IRK41	IRK41	K052	KCNK42	Human	IRK42	IRK42	IRK42	K053	KCNK43	Human	IRK43	IRK43	IRK43	K054	KCNK44	Human	IRK44	IRK44	IRK44	IRK44
K055	KCNK45	Human	IRK45	IRK45	IRK45	K056	KCNK46	Human	IRK46	IRK46	IRK46	K057	KCNK47	Human	IRK47	IRK47	IRK47	K058	KCNK48	Human	IRK48	IRK48	IRK48	IRK48
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K063	KCNK53	Human	IRK53	IRK53	IRK53	K064	KCNK54	Human	IRK54	IRK54	IRK54	K065	KCNK55	Human	IRK55	IRK55	IRK55	K066	KCNK56	Human	IRK56	IRK56	IRK56	IRK56
K067	KCNK57	Human	IRK57	IRK57	IRK57	K068	KCNK58	Human	IRK58	IRK58	IRK58	K069	KCNK59	Human	IRK59	IRK59	IRK59	K070	KCNK60	Human	IRK60	IRK60	IRK60	IRK60
K071	KCNK61	Human	IRK61	IRK61	IRK61	K072	KCNK62	Human	IRK62	IRK62	IRK62	K073	KCNK63	Human	IRK63	IRK63	IRK63	K074	KCNK64	Human	IRK64	IRK64	IRK64	IRK64
K075	KCNK65	Human	IRK65	IRK65	IRK65	K076	KCNK66	Human	IRK66	IRK66	IRK66	K077	KCNK67	Human	IRK67	IRK67	IRK67	K078	KCNK68	Human	IRK68	IRK68	IRK68	IRK68
K079	KCNK69	Human	IRK69	IRK69	IRK69	K080	KCNK70	Human	IRK70	IRK70	IRK70	K081	KCNK71	Human	IRK71	IRK71	IRK71	K082	KCNK72	Human	IRK72	IRK72	IRK72	IRK72
K083	KCNK73	Human	IRK73	IRK73	IRK73	K084	KCNK74	Human	IRK74	IRK74	IRK74	K085	KCNK75	Human	IRK75	IRK75	IRK75	K086	KCNK76	Human	IRK76	IRK76	IRK76	IRK76
K087	KCNK77	Human	IRK77	IRK77	IRK77	K088	KCNK78	Human	IRK78	IRK78	IRK78	K089	KCNK79	Human	IRK79	IRK79	IRK79	K090	KCNK80	Human	IRK80	IRK80	IRK80	IRK80
K091	KCNK81	Human	IRK81	IRK81	IRK81	K092	KCNK82	Human	IRK82	IRK82	IRK82	K093	KCNK83	Human	IRK83	IRK83	IRK83	K094	KCNK84	Human	IRK84	IRK84	IRK84	IRK84
K095	KCNK85	Human	IRK85	IRK85	IRK85	K096	KCNK86	Human	IRK86	IRK86	IRK86	K097	KCNK87	Human	IRK87	IRK87	IRK87	K098	KCNK88	Human	IRK88	IRK88	IRK88	IRK88
K099	KCNK89	Human	IRK89	IRK89	IRK89	K100	KCNK90	Human	IRK90	IRK90	IRK90	K101	KCNK91	Human	IRK91	IRK91	IRK91	K102	KCNK92	Human	IRK92	IRK92	IRK92	IRK92
K103	KCNK93	Human	IRK93	IRK93	IRK93	K104	KCNK94	Human	IRK94	IRK94	IRK94	K105	KCNK95	Human	IRK95	IRK95	IRK95	K106	KCNK96	Human	IRK96	IRK96	IRK96	IRK96
K107	KCNK97	Human	IRK97	IRK97	IRK97	K108	KCNK98	Human	IRK98	IRK98	IRK98	K109	KCNK99	Human	IRK99	IRK99	IRK99	K110	KCNK100	Human	IRK100	IRK100	IRK100	IRK100

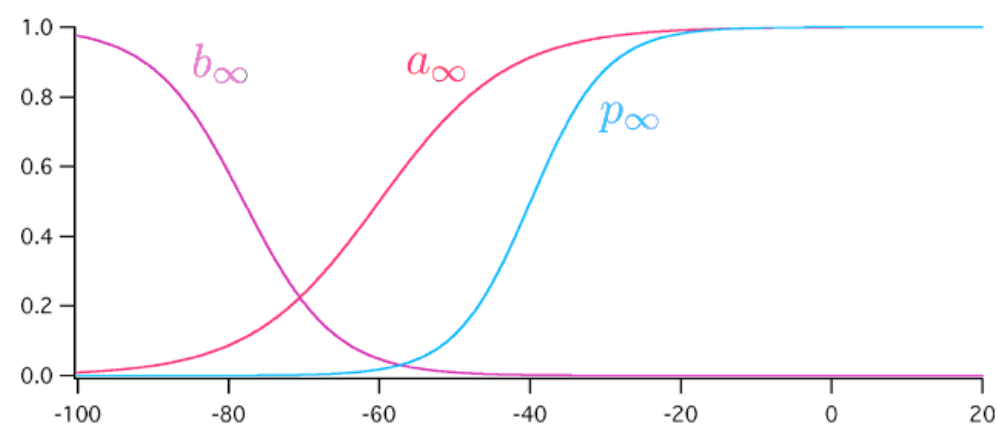
W. A. Coetzee, Y. Amarillo, J. Chiu, A. Chow, D. Lau, T. McCormick, H. Moreno, M. S. Nadal, A. Ozols, D. Pournazeri, M. S. Shapiro, E. Vega-Quintero de Mera, and B. Rudy. Molecular diversity of K<sup>+</sup> channels. *Ann NY Acad Sci.* 1998;233-295, 1999.

14\_K\_channels.psd

### Hodgkin-Huxley Equation + a Zoo of Channels

$$C \frac{dV}{dt} = I_{stim} - g_L(V - V_L) - \bar{g}_{Na} m^3 h (V - V_{Na}) - \bar{g}_K n^4 (V - V_K) - \bar{g}_{NaP} p^4 (V - V_{NaP}) - \bar{g}_A a^4 b (V - V_A)$$

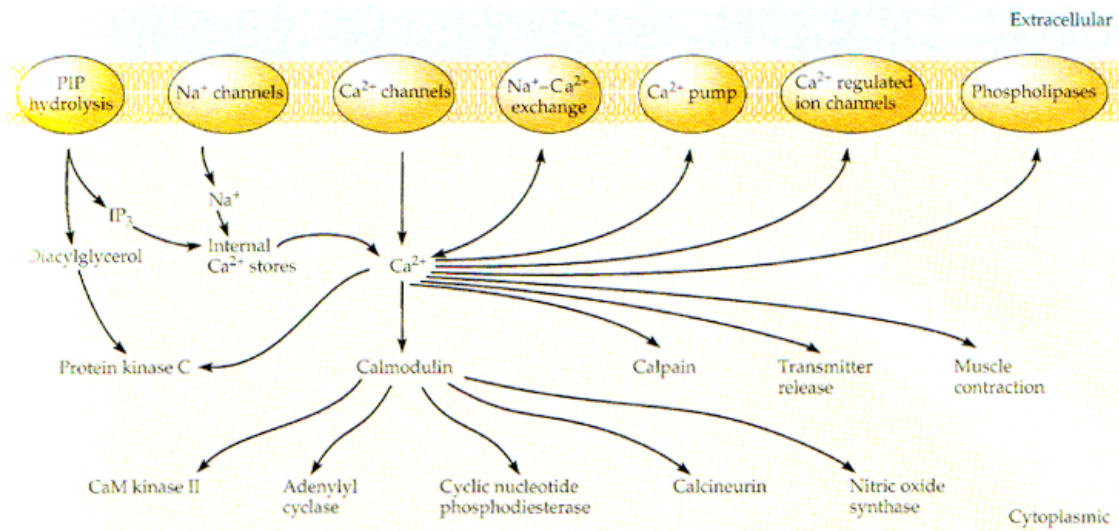
persistent sodium current      transient potassium current (A-current)



15\_hh\_plus.psd

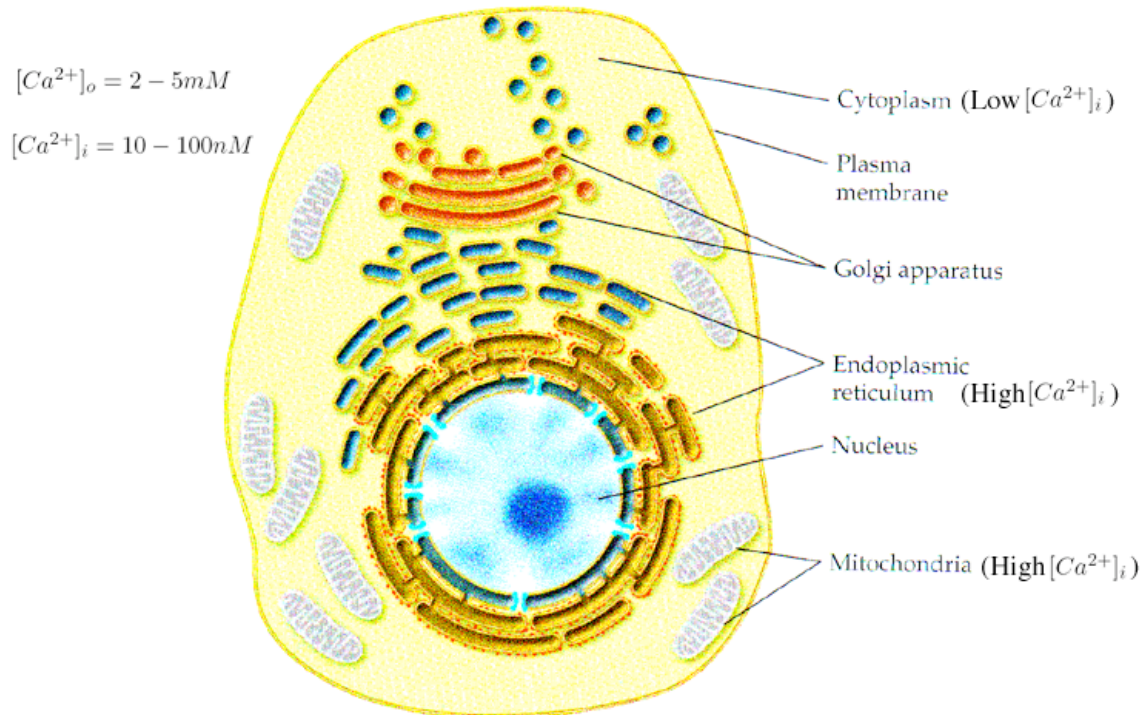


## Calcium is a Primary Intracellular Messenger



21\_CaCells.psd

## Calcium is Highly Buffered in the Cytoplasm



Linear model of removal and buffering: 
$$\frac{[Ca^{2+}]_i}{dt} = \frac{1}{\tau_{Ca}} ([Ca^{2+}]_{\infty} - [Ca^{2+}]_i)$$

22\_buffered.psd



## Goldman-Hodgkin-Katz Current Equation

$$I_{Ca} = P_{Ca} 2vF \frac{[Ca^{2+}]_i - [Ca^{2+}]_o e^{-v}}{1 - e^{-v}}$$

$$v = \frac{2VF}{RT}$$

Faraday's const.  
gas const.

$$P_{Ca} = \frac{\text{(flux density across unit area of membrane)}}{\Delta[Ca^{2+}]}$$

Permeability

Nernst Potential for  $Ca^{2+}$  (~140 mV)

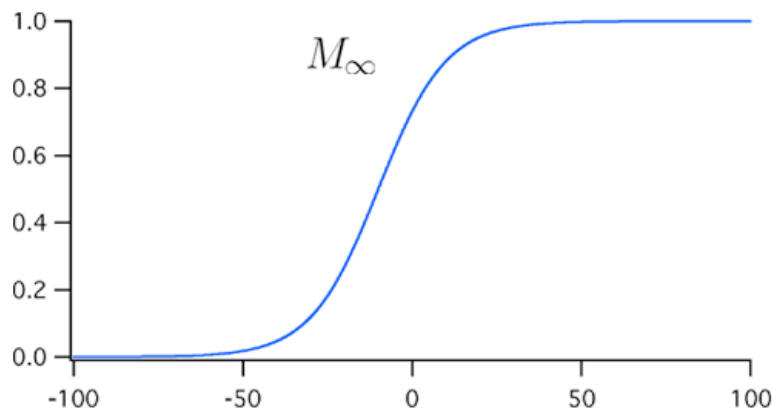
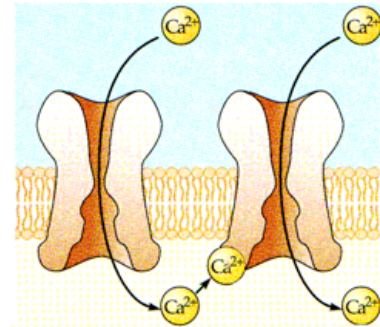
$$E_{Ca} = 12.5 \cdot \log \frac{[Ca^{2+}]_o}{[Ca^{2+}]_i} \Rightarrow I_{Ca} \propto (V - E_{Ca})$$

23\_Nernst.psd

## High-threshold (long-lasting) Calcium Current

$$I_L = \bar{g}_L M^3 (V - E_{Ca})$$

High threshold  $Ca^{2+}$  current  
-> allows calcium entry during action potential.



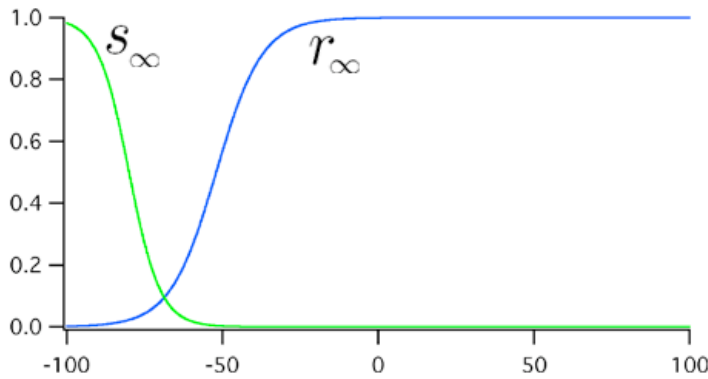
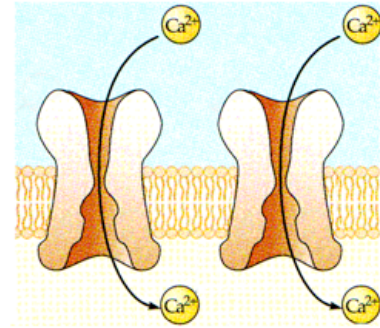
$I_L$  is only activated at very depolarized levels.  
Inactivation may depend on the intracellular Ca concentration.

24\_iL.psd

## Low-threshold (transient) Calcium Current

$$I_T = \bar{g}_T r^3 s (V - E_{Ca})$$

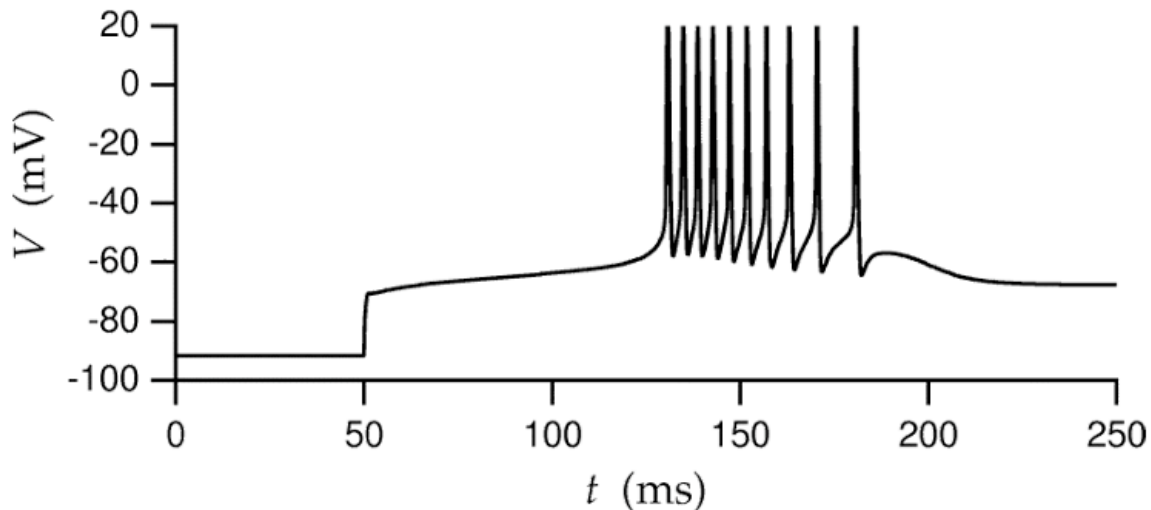
Transient low threshold Ca<sup>2+</sup> current  
 -> generates a burst of action potentials.



$I_T$  is activated at lower voltages than the L current. Under physiological conditions the T current can be triggered by hyperpolarizing the membrane potential, which completely removes inactivation. A subsequent synaptic input activates a broad action potential, on top of which sodium spikes can ride.

25\_iT.psd

## Postinhibitory Rebound and Bursting



The model neuron was held hyperpolarized for an extended period (until the conductances came to equilibrium) by injection of constant negative electrode current. At  $t = 50$  ms, the electrode current was set to zero, and a burst of Na spikes was generated due to an underlying Ca<sup>2+</sup> spike caused by a transient Ca<sup>2+</sup> conductance. The delay in the firing is caused by the presence of the A-current in the model.

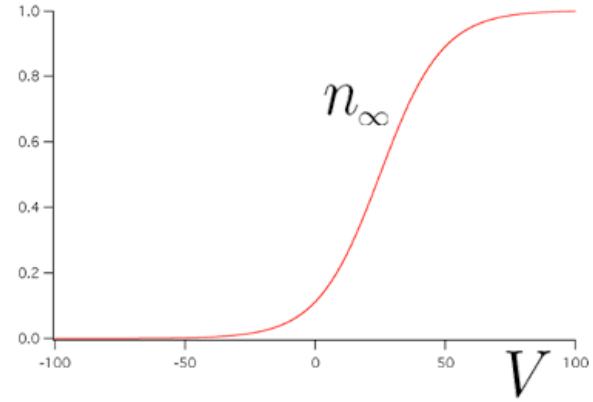
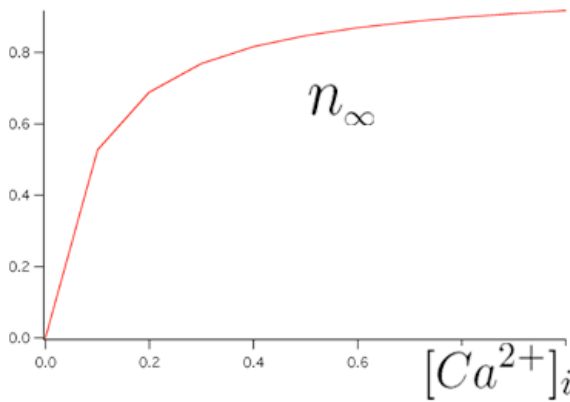
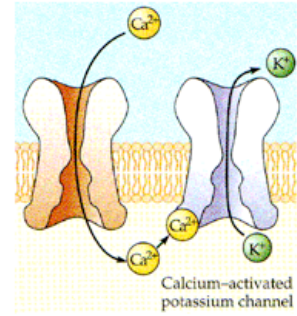
26\_PIR.psd

## Calcium-activated Potassium Current

$$I_C = \bar{g}_C n(V, [Ca^{2+}]_i)(V - E_K)$$

Ca<sup>2+</sup> activated K<sup>+</sup> current

- > calcium and voltage dependent
- > involved in repolarization of action potential.



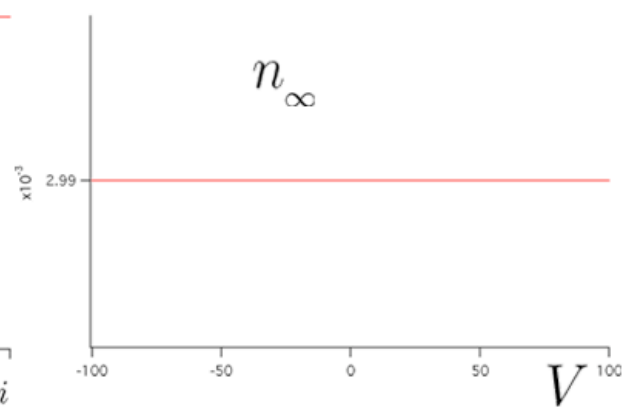
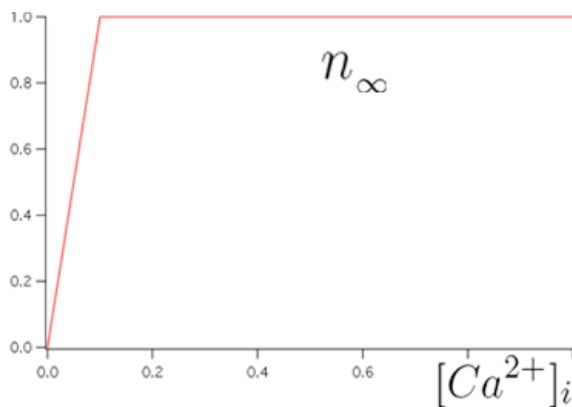
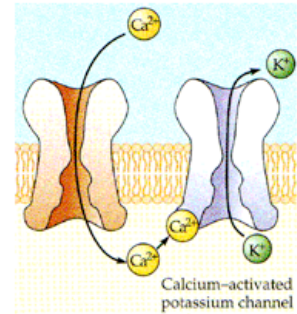
27\_iC.psd

## After-hyperpolarization Potassium Current

$$I_{AHP} = \bar{g}_{AHP} n([Ca^{2+}]_i)(V - E_K)$$

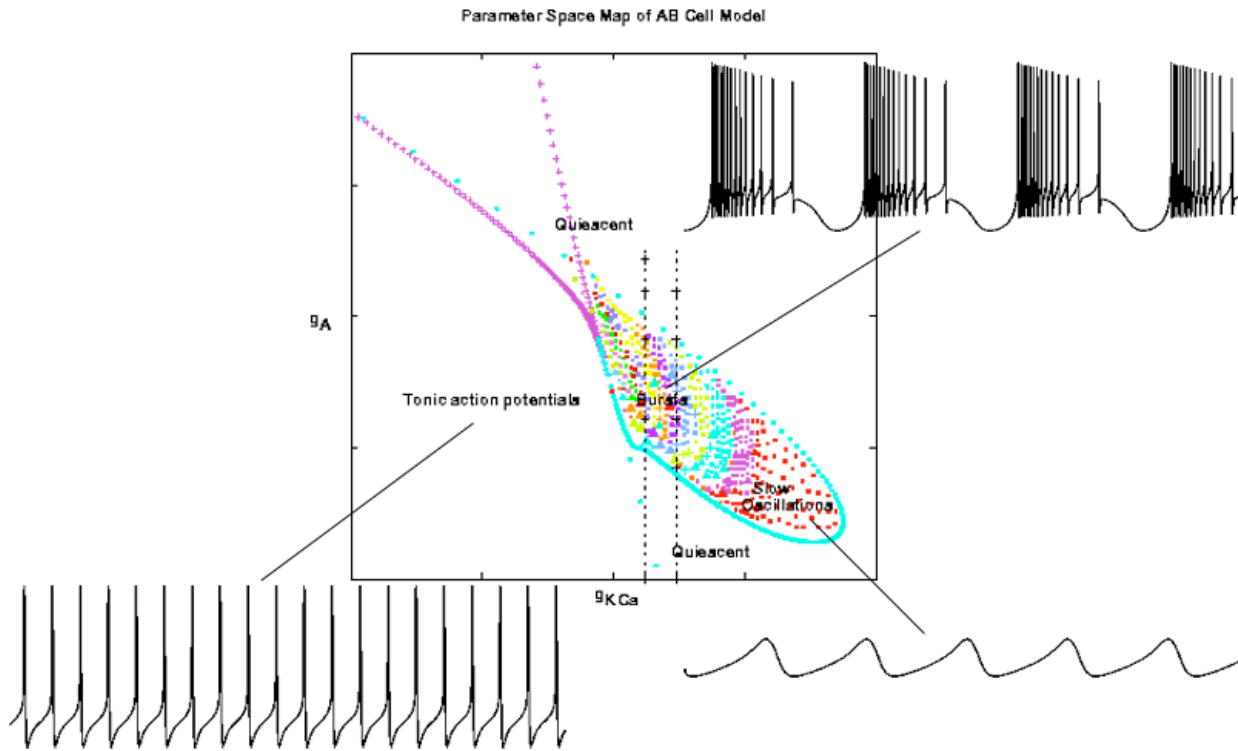
Slow, Ca<sup>2+</sup> activated K<sup>+</sup> current

- > calcium dependent, voltage independent
- > hyperpolarizes the cell after a spike train
- > slows down rate of action potential generation.



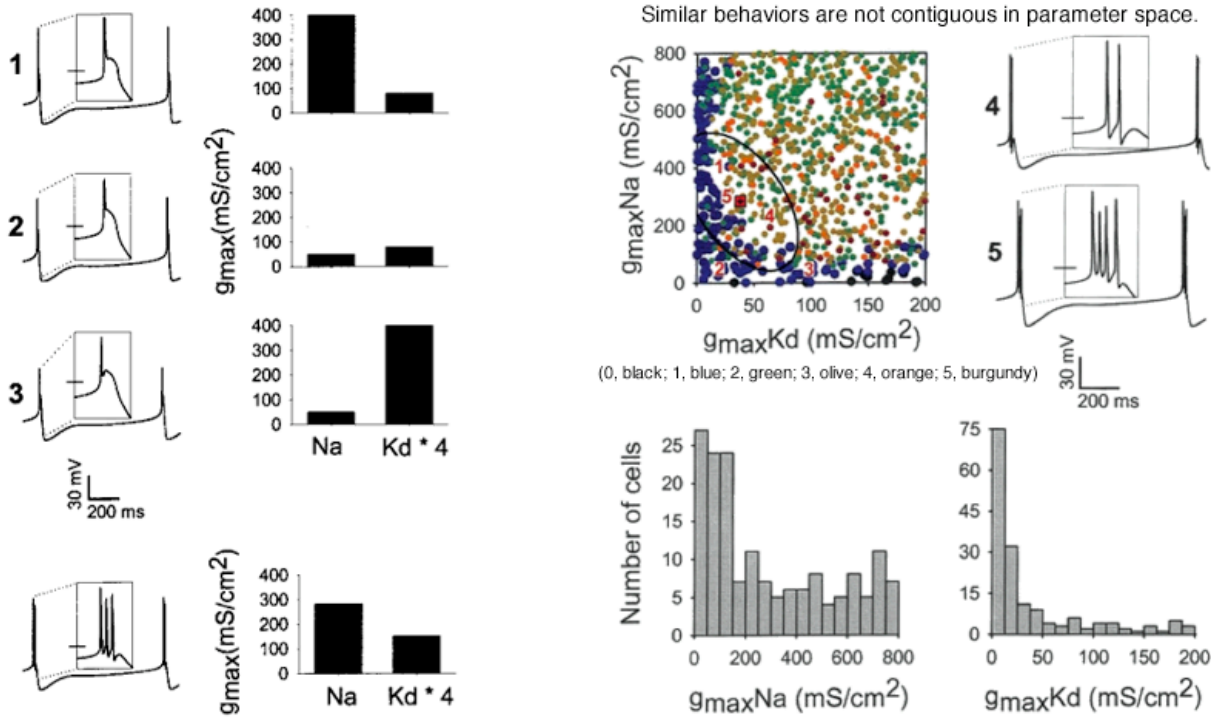
28\_iAHP.psd

# Interactions of Currents Generate Many Spike Patterns



29\_Guckenheimer.psd

## The Same Spike Pattern may be Generated by Different Combinations of Current Densities

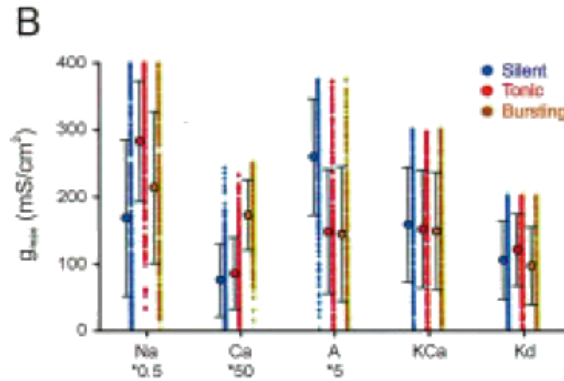
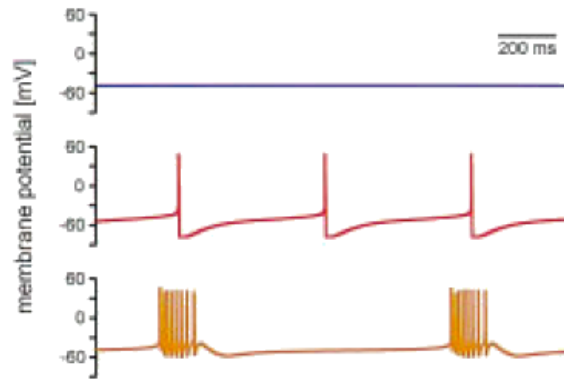


Golowasch, Goldman, Abbott and Marder (2002)

30\_Golowasch02.psd



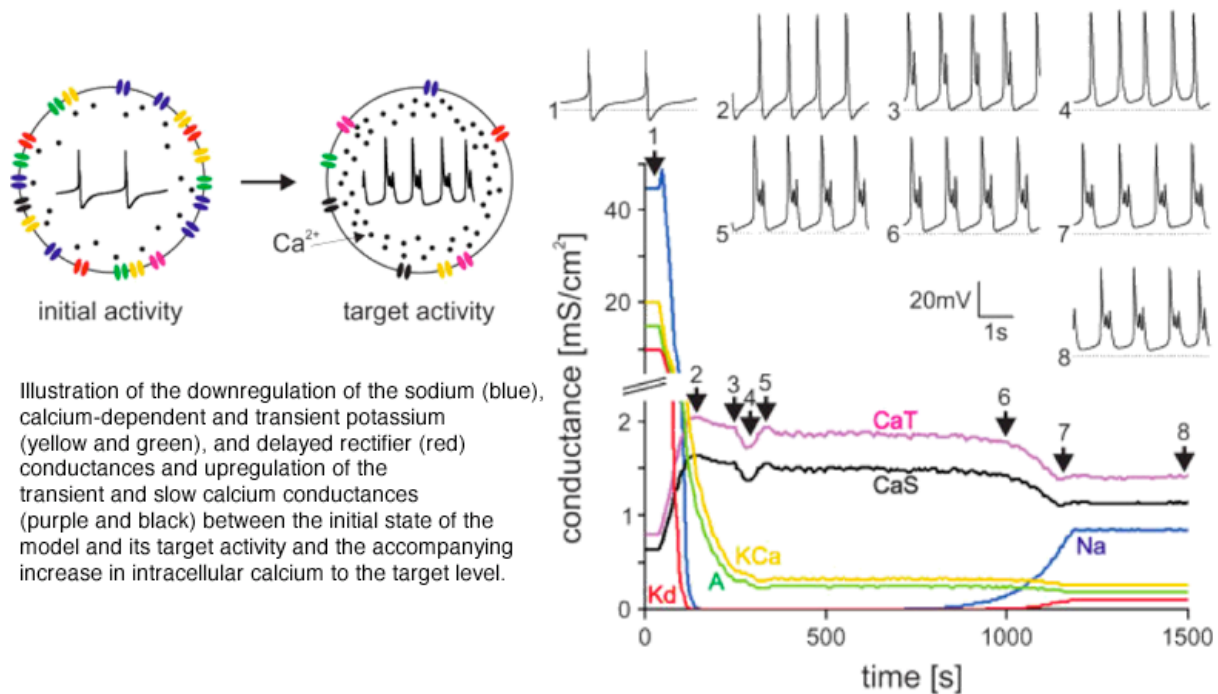
## The Same Spike Pattern may be Generated by Different Combinations of Current Densities



Marder and Prinz (2002)

31\_Marder02b.psd

## Combinations of Current Densities are Selected by Adaptive Processes in each Neuron Type



Marder and Prinz (2002)

32\_Marder02b.psd