From Neurons to Brains: How Holism and Reductionism are Approaching Each Other

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Sigmund Freud‘s Pioneering Approach to Mind, Brain and Behavior

Austrian Academy of Sciences, 17.10.2006

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http://www.tbi.univie.ac.at/~pks

The holism versus reductionism debate

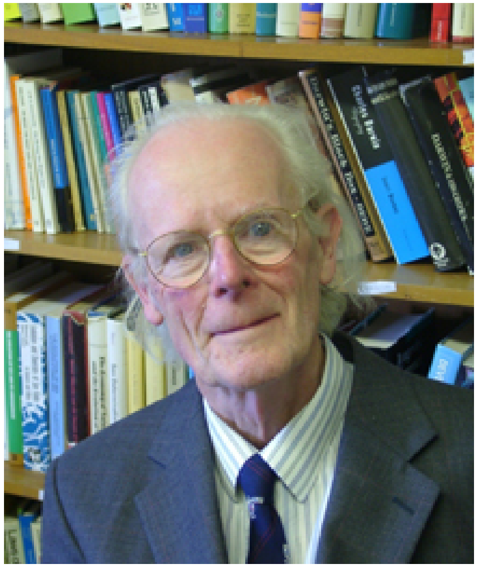
The holistic approach

Macroscopic biologists aim at a top-down approach to describe the phenomena observed in biology.

↔

The reductionists' program

Molecular biologist perform a bottom-up approach to interpret biological phenomena by the methods of chemistry and physics.



What should be the attitude of a biologist working on whole organisms to molecular biology? It is, I think, foolish to argue that we (the macroscopic biologists) are discovering things that disprove molecular biology. It would be more sensible to say to molecular biologists that **there are phenomena that they will one day have to interpret in their terms**.

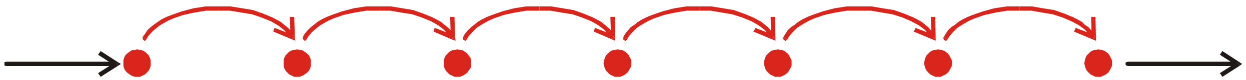
John Maynard Smith, The problems of biology. Oxford University Press, 1986.

fructose-1,6-diphosphate

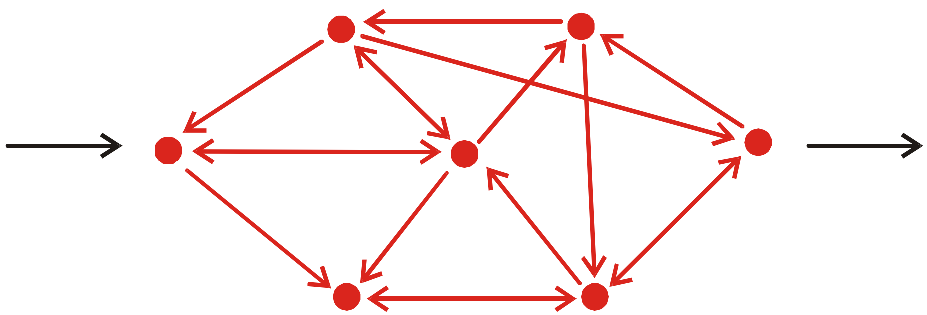
↓ aldolase

dihydroxyacetone-phosphate + glyceraldehyde-3-phosphate

A single biochemical reaction of the glycolytic chain



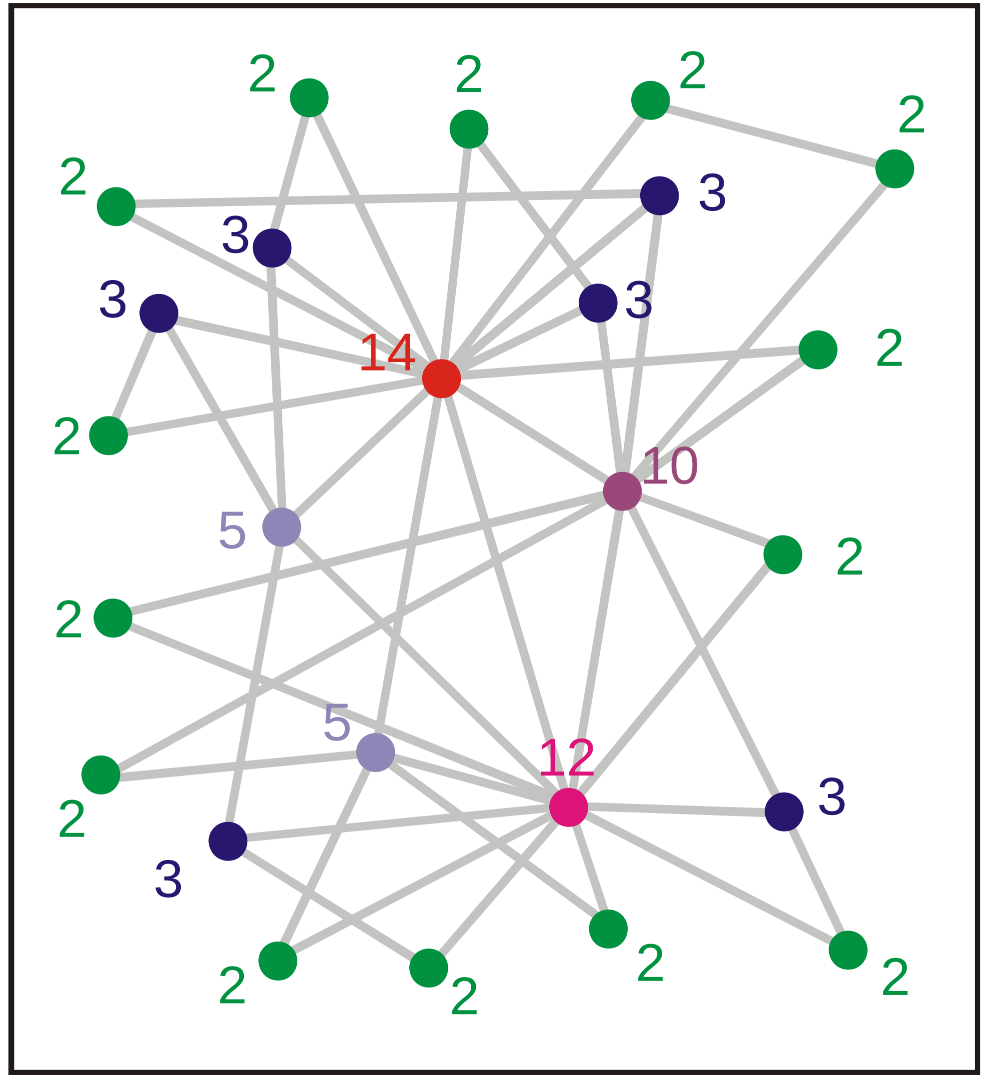
Linear chain



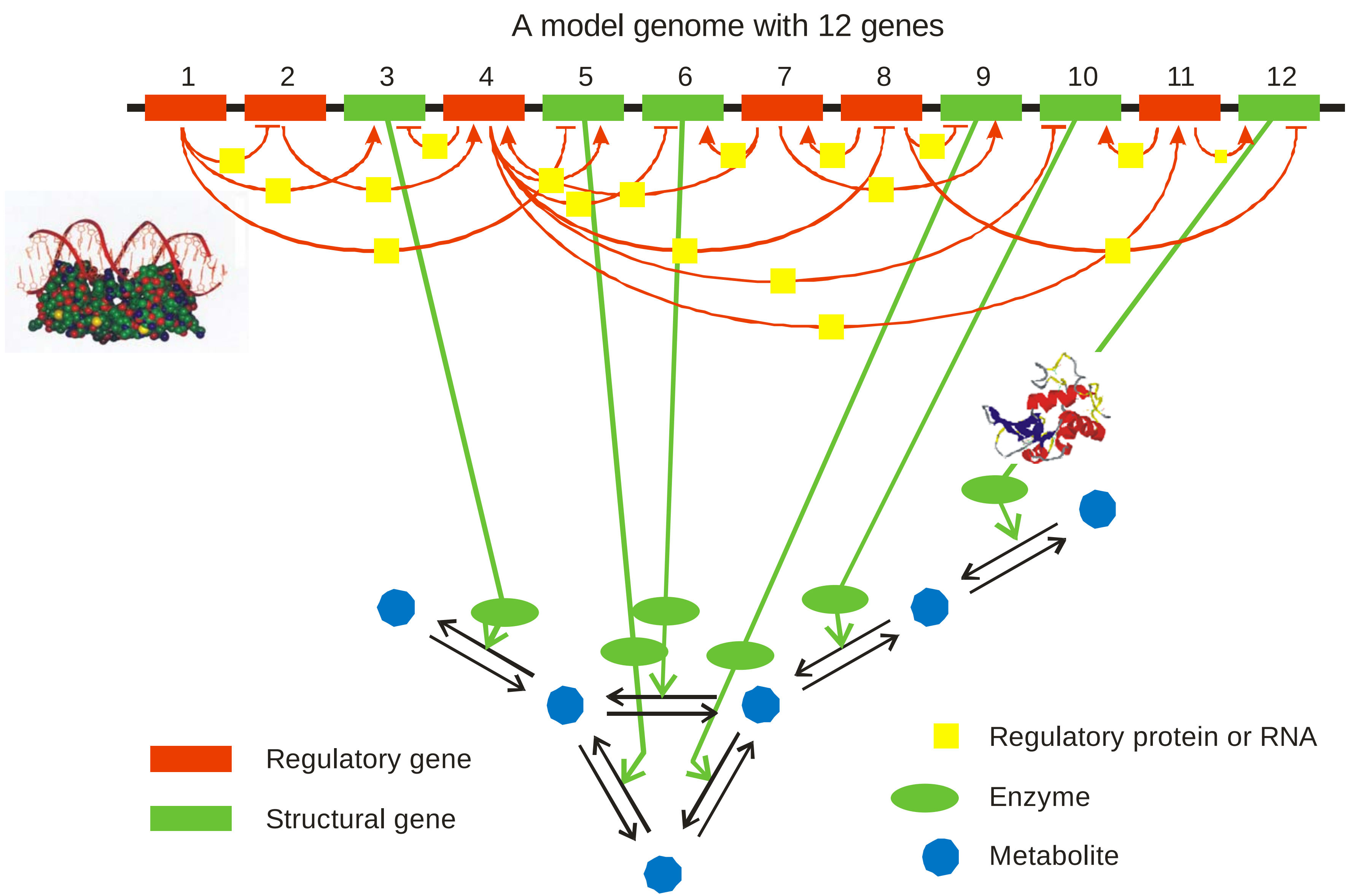
Network

Processing of information in cascades and networks

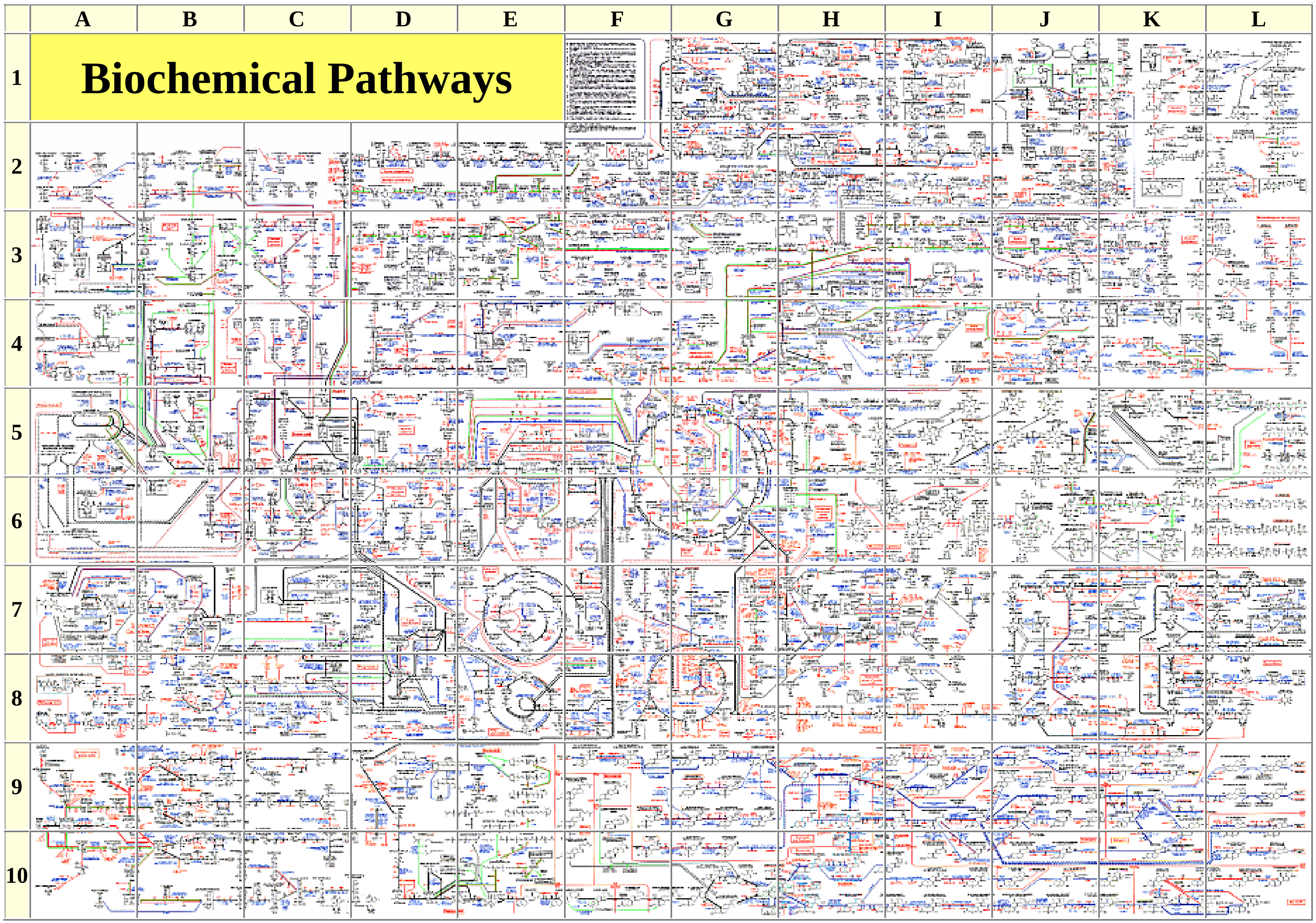
links	# nodes
2	14
3	6
5	2
10	1
12	1
14	1



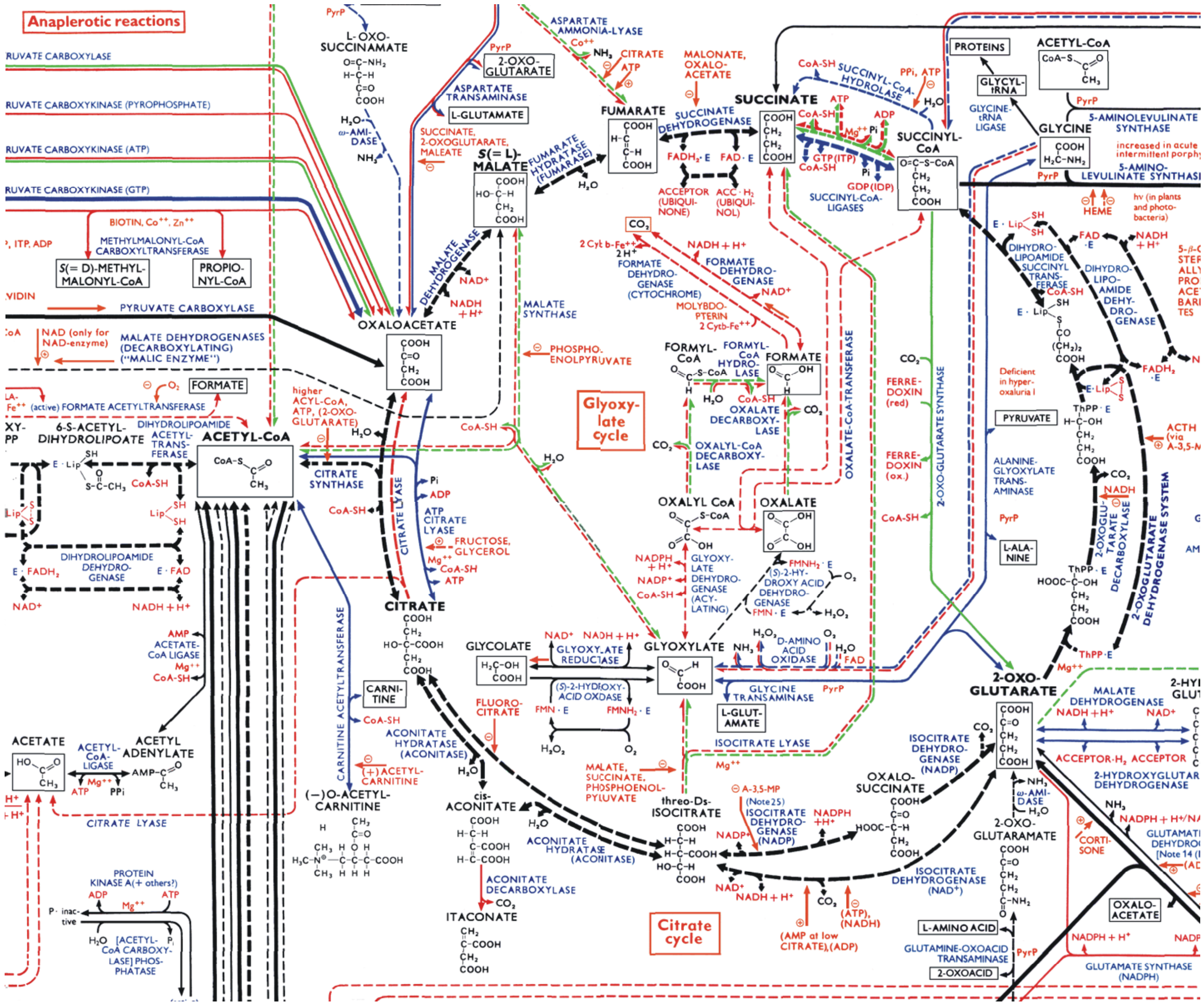
Analysis of nodes and links in a step by step evolved network



Sketch of a genetic and metabolic network

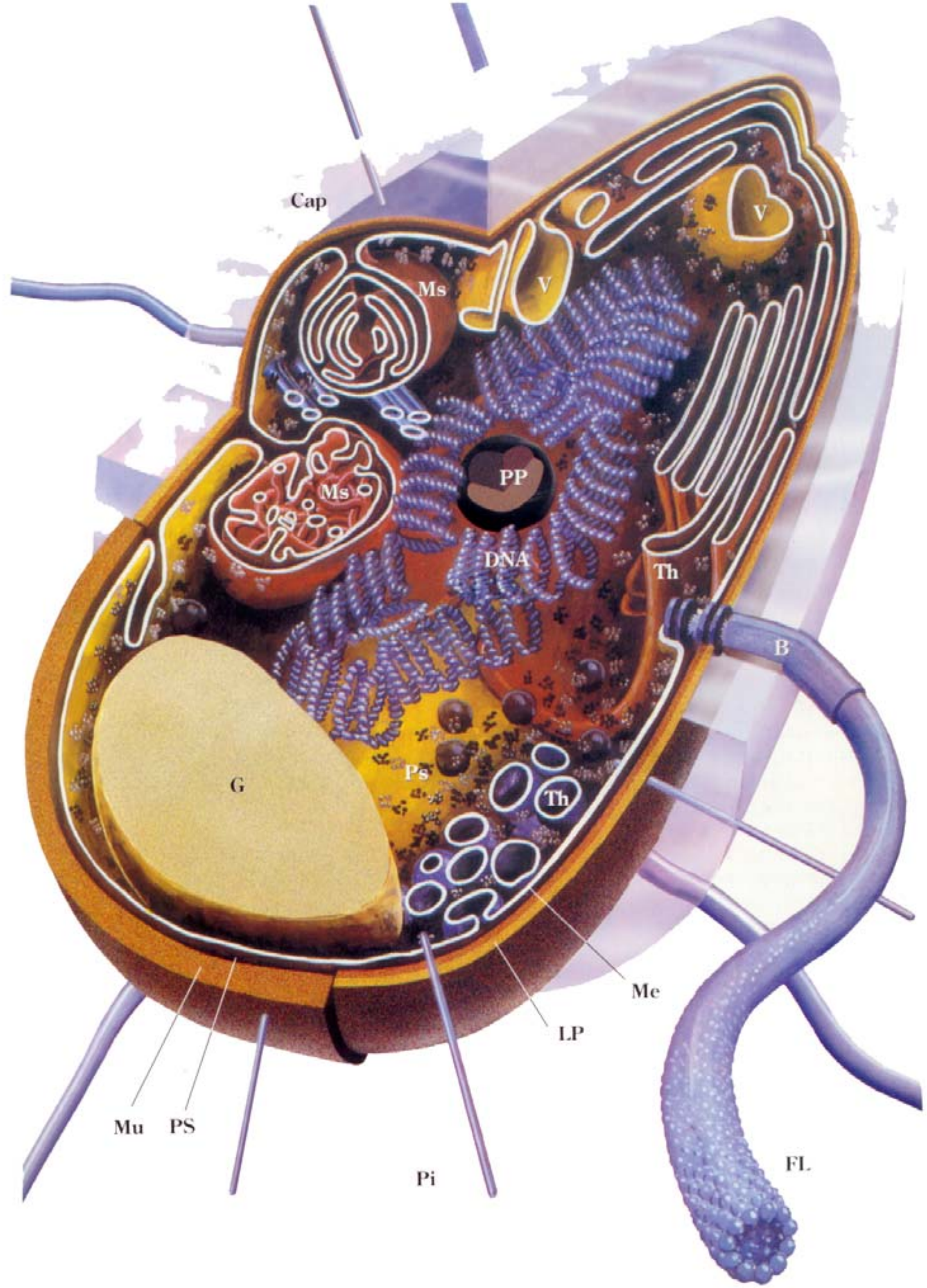


The reaction network of cellular metabolism published by Boehringer-Ingelheim.



The citric acid or Krebs cycle (enlarged from previous slide).

The bacterial cell as an example for the simplest form of autonomous life



The human body:

10^{14} cells = 10^{13} eukaryotic cells +
≈ 9×10^{13} bacterial (prokaryotic) cells,
and ≈ 200 eukaryotic cell types

The spatial structure of the bacterium *Escherichia coli*

Psychic phenomena – emotions, phantasy, dream

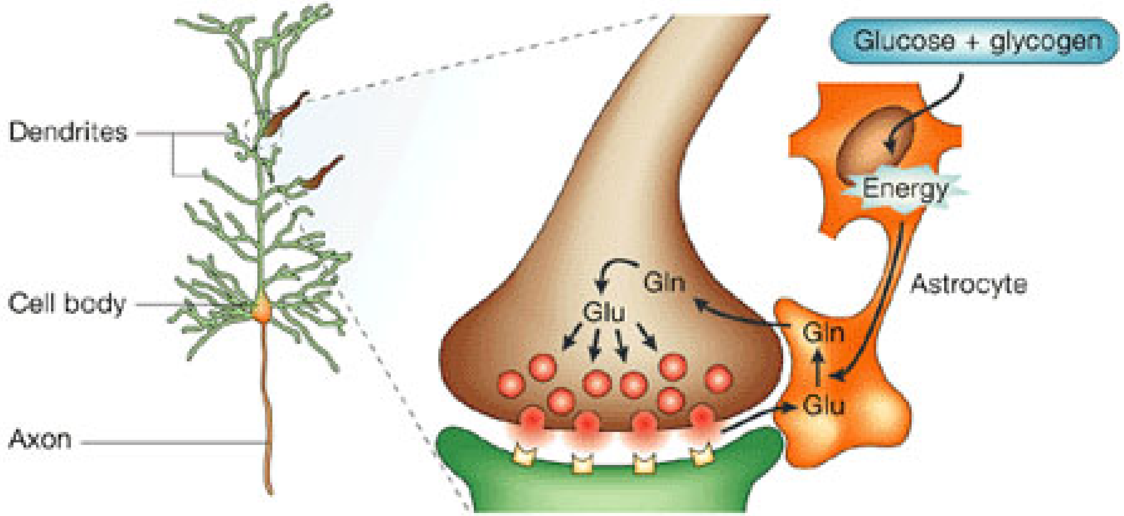
Processes in defined areas of the brain – perception, motor response, control of body homeostasis

Signal processing in networks of neurons – sensoric input of the brain and output through motor neurons,visual cortex, auditory cortex ...

Signalling cascades of neurons – control of motion, ...

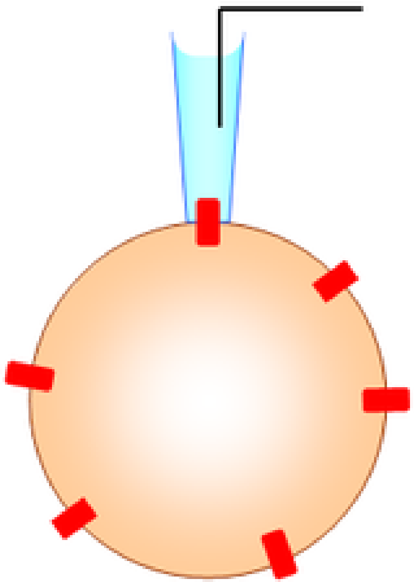
Single neuron – refractory, oscillatory, and spike emitting behavior

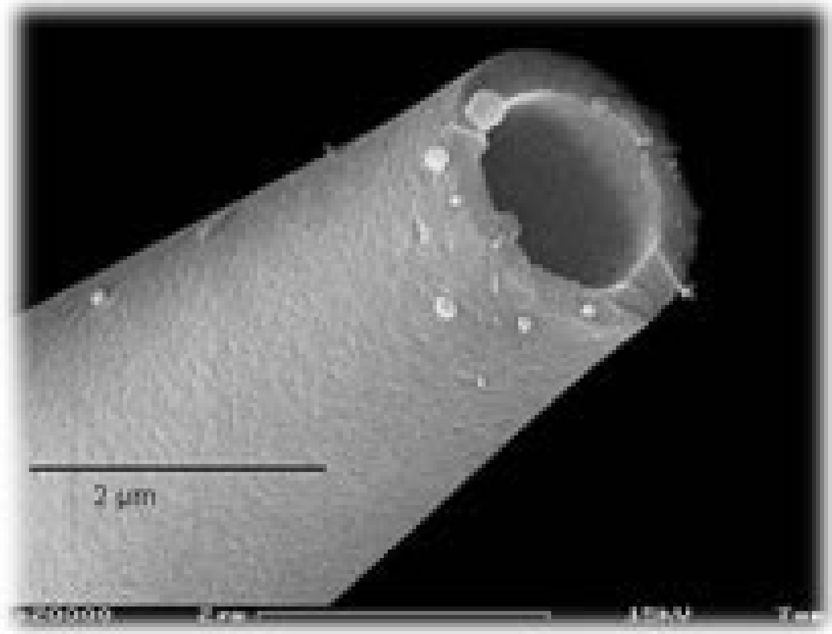
Single synapse – signal transmission chemistry



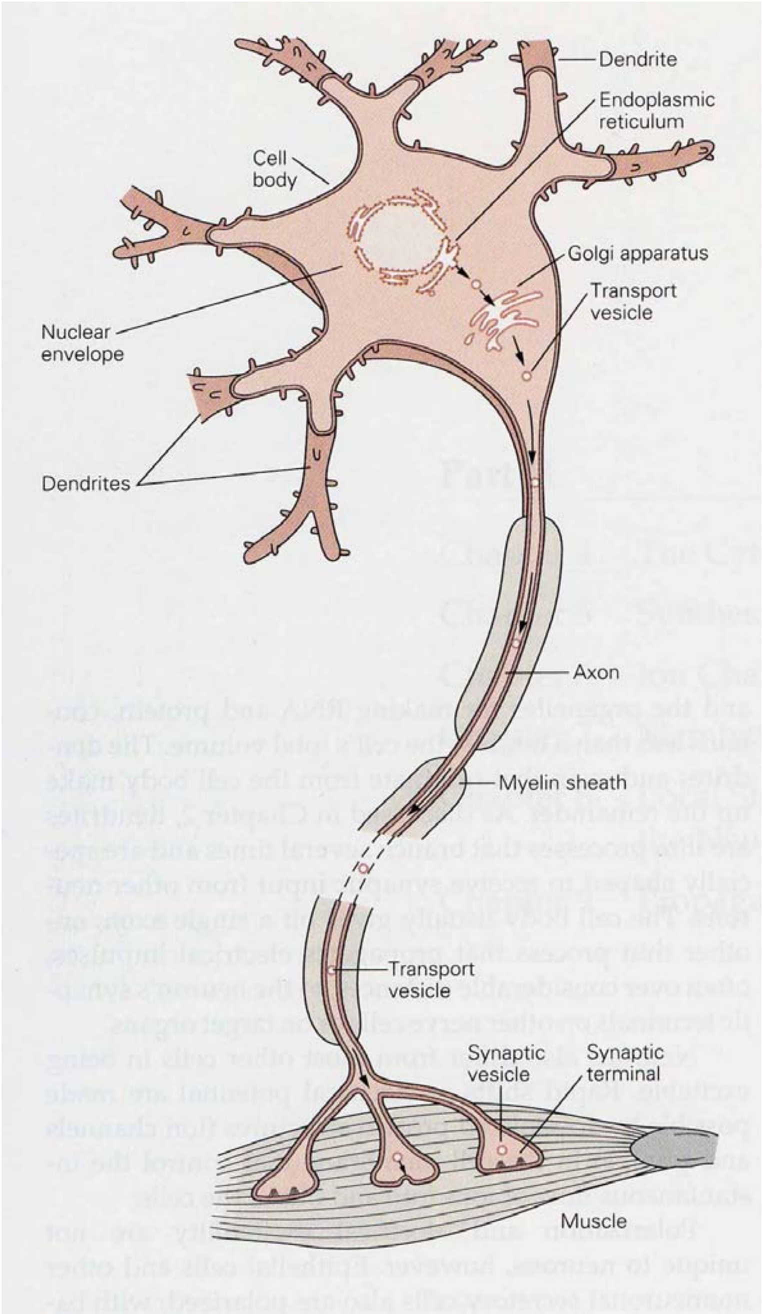
Chemistry of synapses and metabolism of neurons

Drawing from *Nature Reviews Neuroscience* **2**, 685-694 (2001)

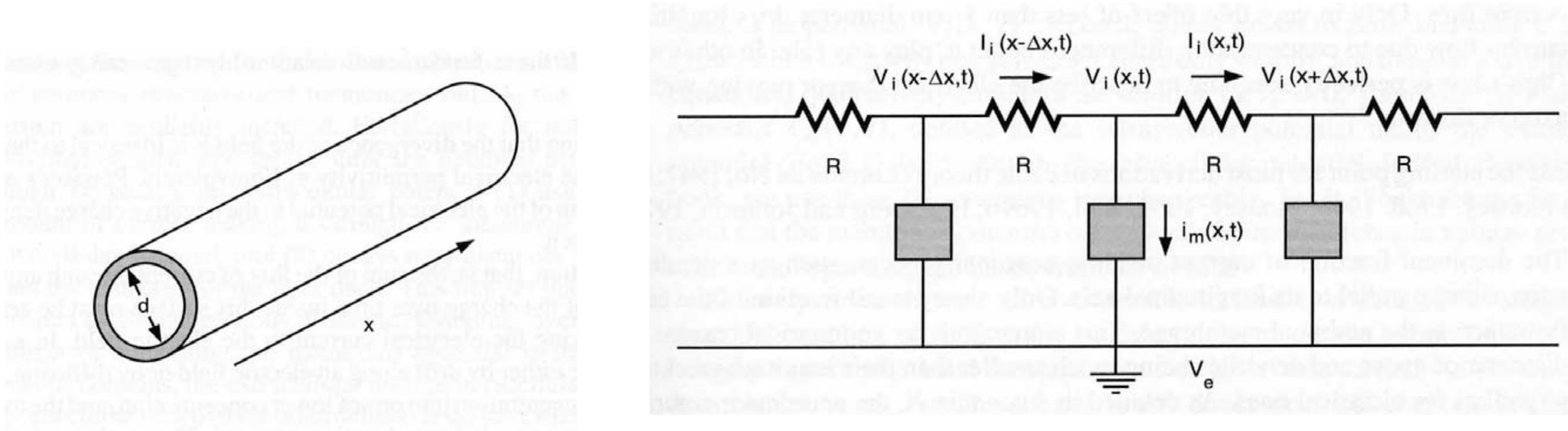




The patch clamp technique



A single neuron signaling to a muscle fiber



A

B

Fig. 2.2 ELECTRICAL STRUCTURE OF A CABLE **(A)** Idealized cylindrical axon or dendrite at the heart of one-dimensional cable theory. Almost all of the current inside the cylinder is longitudional due to geometrical (the radius is much smaller than the length of the cable) and electrical factors (the membrane covering the axon or dendrite possesses a very high resistivity compared to the intracellular cytoplasm). As a consequence, the radial and angular components of the current can be neglected, and the problem of determining the potential in these structures can be reduced from three spatial dimensions to a single one. On the basis of the bidomain approximation, gradients in the extracellular potentials are neglected and the cable problem is expressed in terms of the transmembrane potential $V_m(x,t) = V_i(x,t) - V_e$. **(B)** Equivalent electrical structure of an arbitrary neuronal process. The intracellular cytoplasm is modeled by the purely ohmic resistance R. This tacitly assumes that movement of carriers is exclusively due to drift along the voltage gradient and not to diffusion. Here and in the following the extracellular resistance is assumed to be negligible and V_e is set to zero. The current per unit length across the membrane, whether it is passive or contains voltage-dependent elements, is described by i_m and the system is characterized by the second-order differential equation, Eq. 2.5.

Christof Koch, Biophysics of Computation. Information Processing in single neurons.
Oxford University Press, New York 1999.

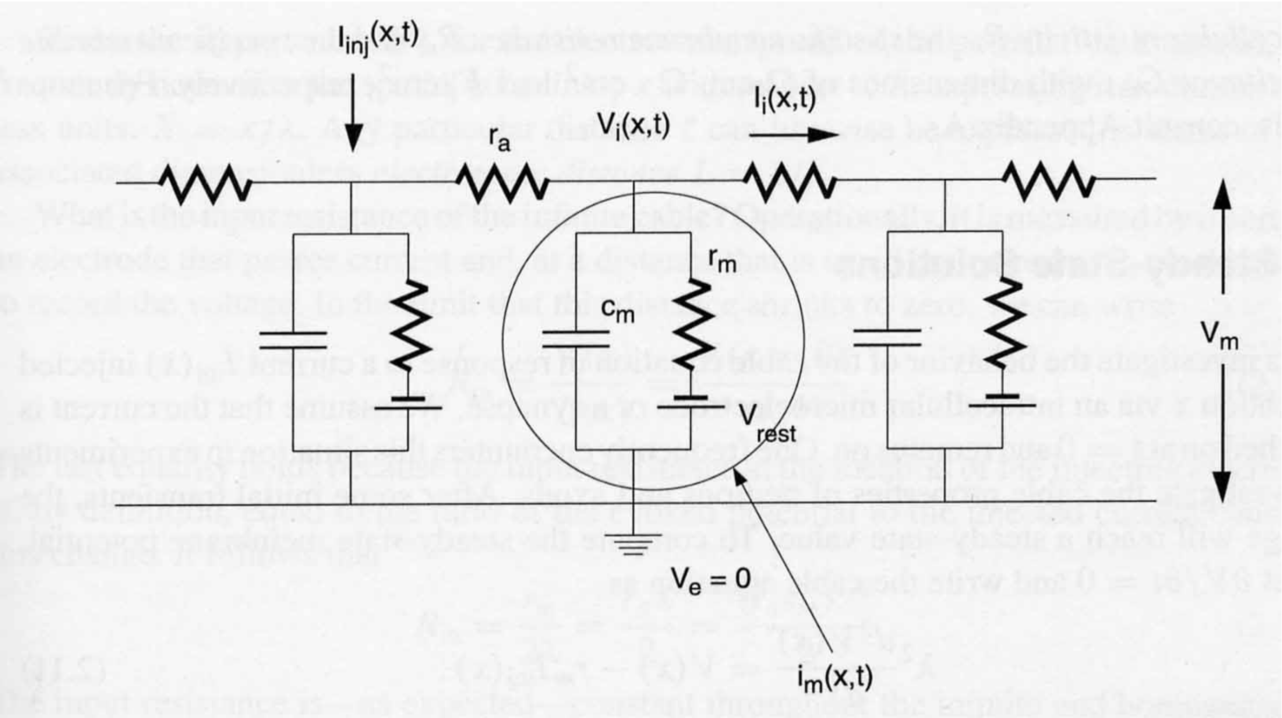


Fig. 2.3 A SINGLE PASSIVE CABLE Equivalent lumped electrical circuit of an elongated neuronal fiber with passive membrane. The intracellular cytoplasm is described by an ohmic resistance per unit length r_a and the membrane by a capacitance c_m in parallel with a passive membrane resistance r_m and a battery V_{rest}. The latter two components are frequently referred to as *leak resistance* and *leak battery*. An external current $I_{inj}(x, t)$ is injected into the cable. The associated linear cable equation (Eq. 2.7) describes the dynamics of the electrical potential $V_m = V_i - V_e$ along the cable.

Christof Koch, Biophysics of Computation. Information Processing in single neurons.
Oxford University Press, New York 1999.

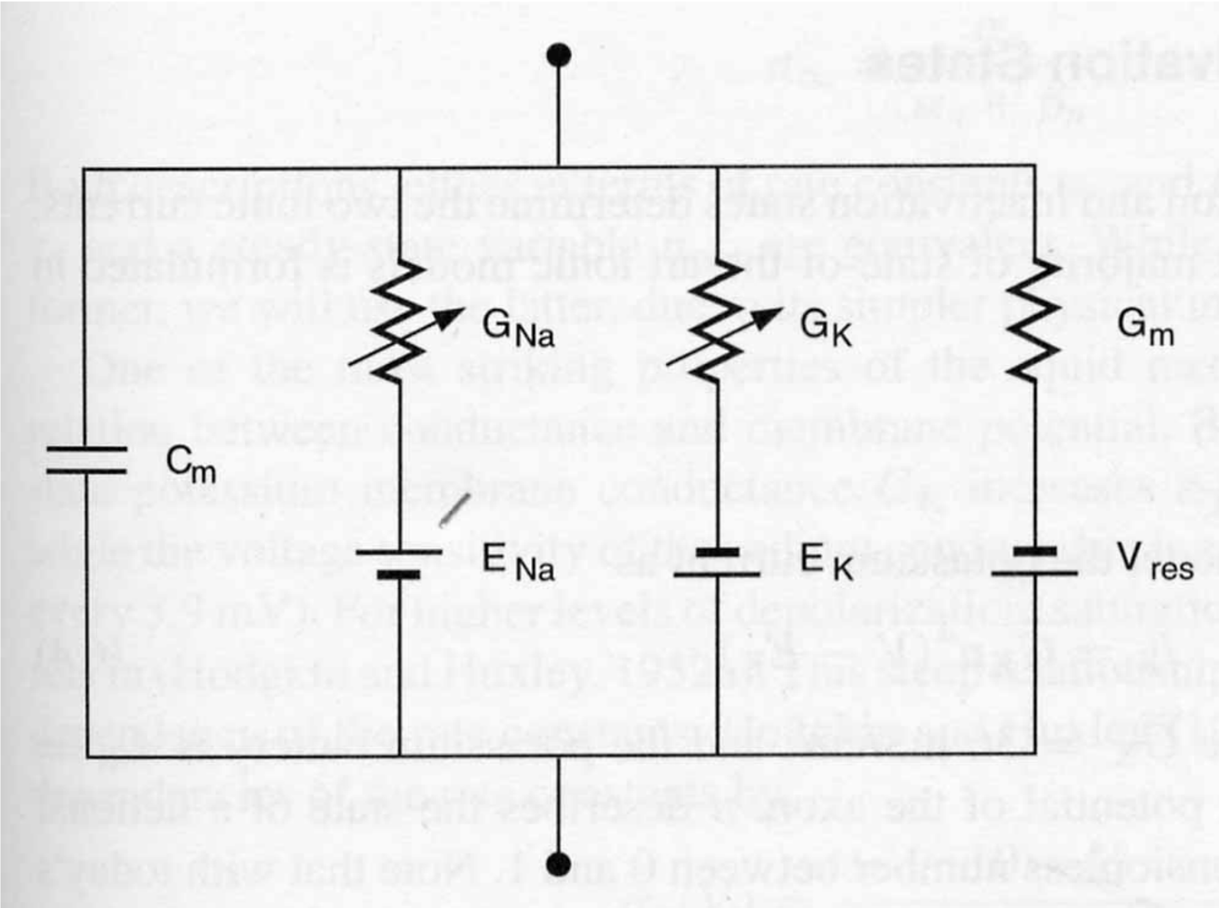
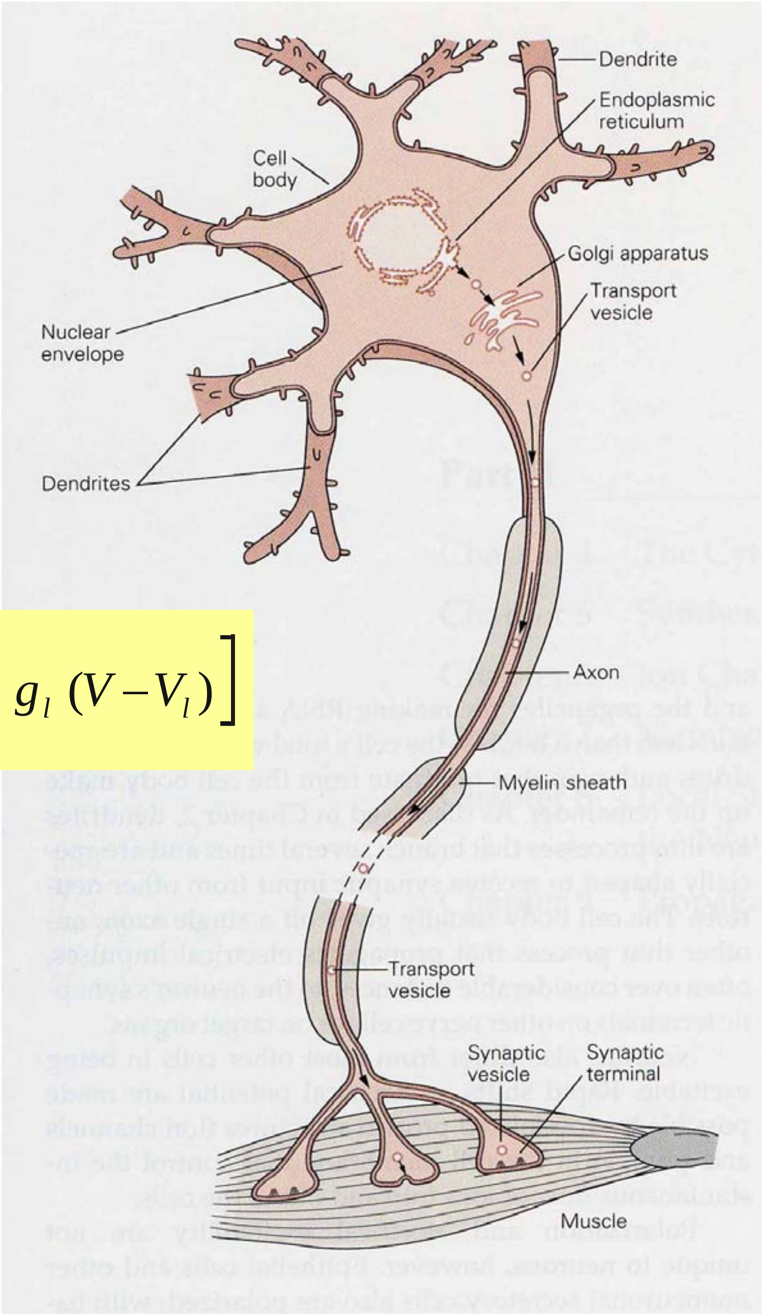


Fig. 6.2 Electrical Circuit for a Patch of Squid Axon Hodgkin and Huxley modeled the membrane of the squid axon using four parallel branches: two passive ones (membrane capacitance C_m and the leak conductance $G_m = 1/R_m$) and two time- and voltage-dependent ones representing the sodium and potassium conductances.

Christof Koch, Biophysics of Computation. Information Processing in single neurons.
Oxford University Press, New York 1999.

Hodgkin, A. L. and Huxley, A. F.: ***A Quantitative Description of Membrane Current and its Application to Conduction and Excitation in Nerve***. *Journal of Physiology* **117**: 500-544 (1952)



$$\frac{dV}{dt} = \frac{1}{C_M}\left[I - g_{Na}\, m^3 h\,(V - V_{Na}) - g_K\, n^4\,(V - V_K) - g_l\,(V - V_l)\right]$$

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

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

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

Hogdkin-Huxley OD equations

A single neuron signaling to a muscle fiber

$$\alpha_m = \frac{x}{e^x - 1}, \quad x = \frac{25 - V}{10} \quad ; \quad \beta_m = 4 \exp\left[-\frac{V}{18}\right]$$

$$\alpha_h = 0.07 \exp\left[-\frac{V}{20}\right] \quad ; \quad \beta_h = \frac{1}{e^x - 1}, \quad x = \frac{30 - V}{10}$$

$$\alpha_n = \frac{x}{10(e^x - 1)}, \quad x = \frac{10 - V}{10} \quad ; \quad \beta_n = 0.125 \exp\left[-\frac{V}{80}\right]$$

Gating functions of the Hodgkin-Huxley equations

$$\frac{\partial m}{\partial t} = \Theta(T)\left[\alpha_m(1-m) - \beta_m m\right]$$

$$\frac{\partial h}{\partial t} = \Theta(T)\left[\alpha_h(1-h) - \beta_h h\right]$$

$$\frac{\partial n}{\partial t} = \Theta(T)\left[\alpha_n(1-n) - \beta_n n\right] ,$$

$$\text{where } \Theta(T) = 3^{(T-6.3)/10}$$

Temperature dependence of the Hodgkin-Huxley equations

$$\frac{1}{R}\frac{\partial^2 V}{\partial x^2} = C\frac{\partial V}{\partial t} + \left[g_{Na} m^3 h (V - V_{Na}) + g_K n^4 (V - V_K) + g_l (V - V_l) \right] 2\pi r L$$

$$\frac{\partial m}{\partial t} = \alpha_m (1 - m) - \beta_m m$$

$$\frac{\partial h}{\partial t} = \alpha_h (1 - h) - \beta_h h$$

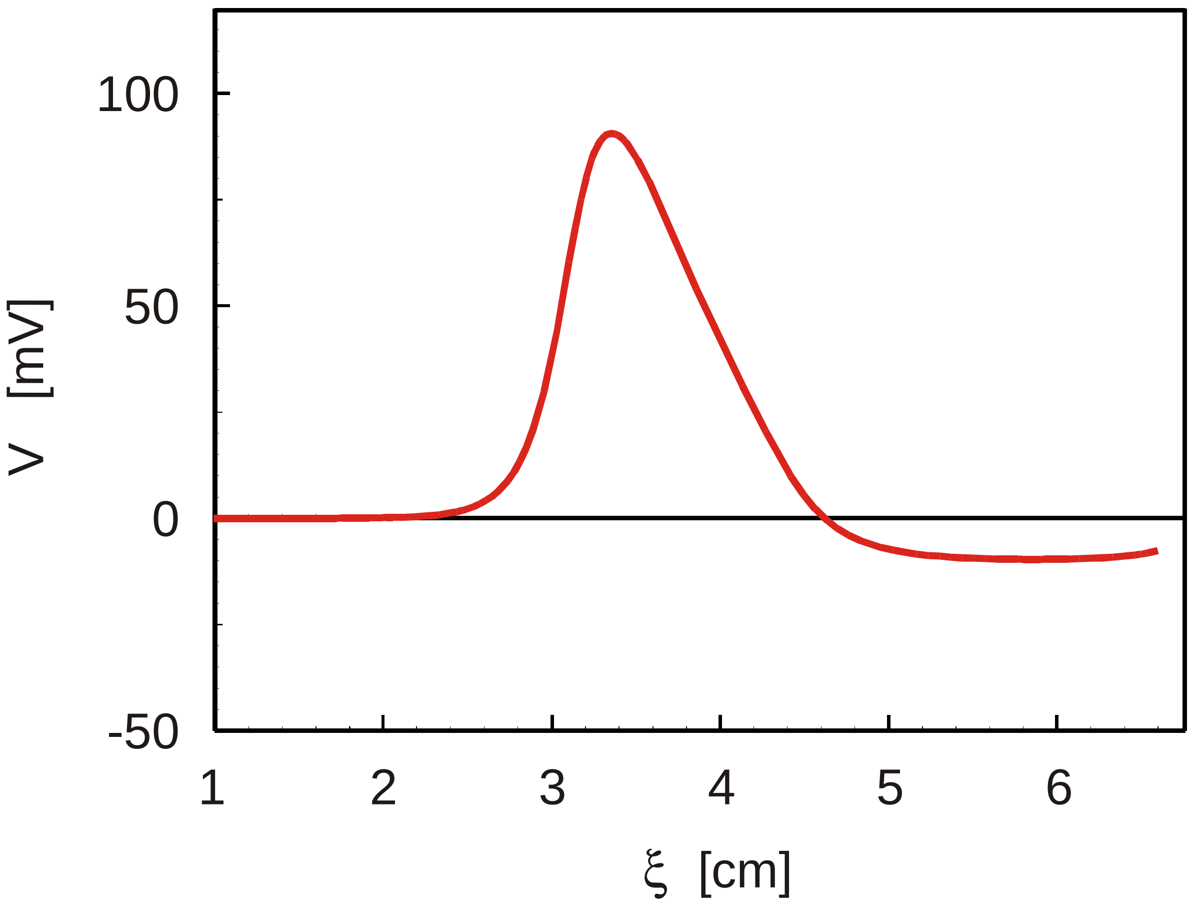
$$\frac{\partial n}{\partial t} = \alpha_n (1 - n) - \beta_n n$$

Hodgkin-Huxley PDEquations

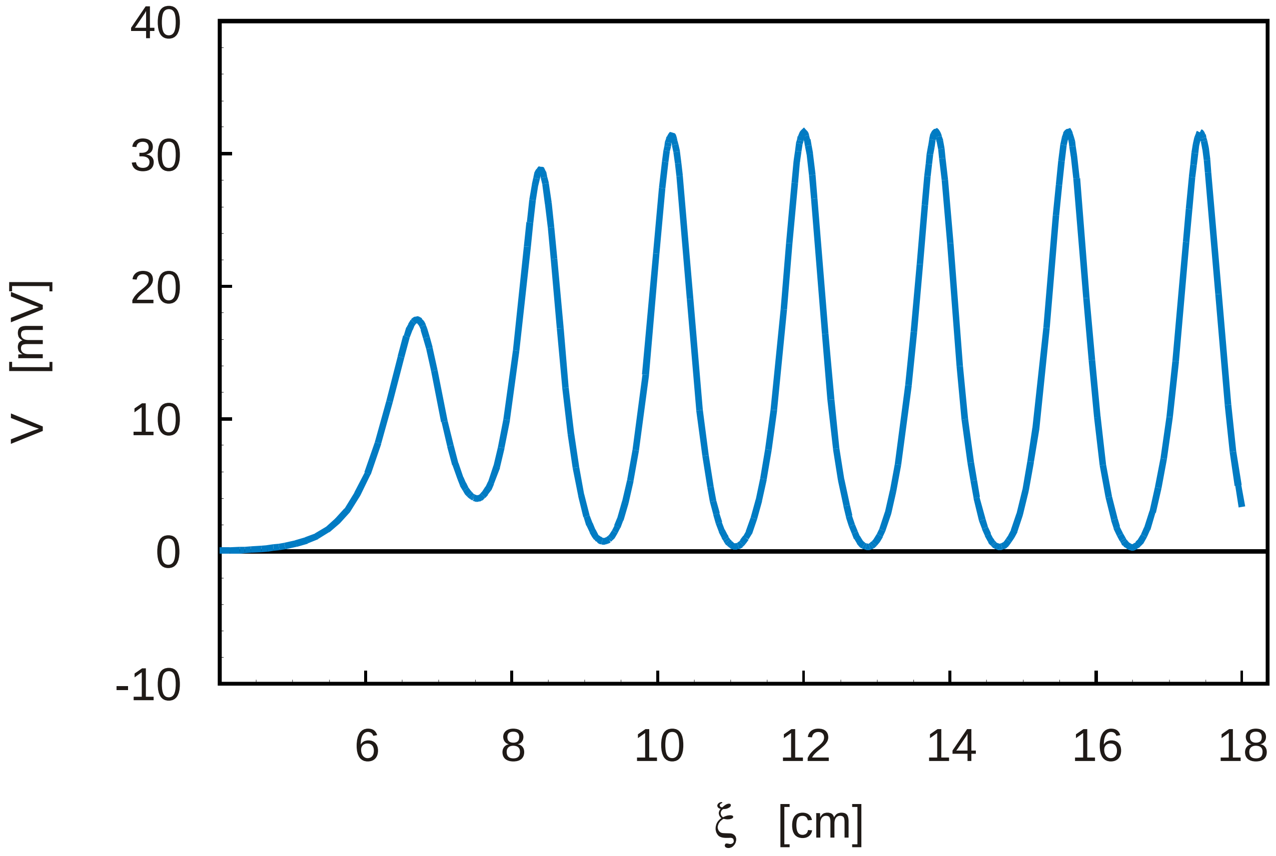
Travelling pulse solution: $V(x,t) = V(\xi)$ with

$$\xi = x + \theta t$$

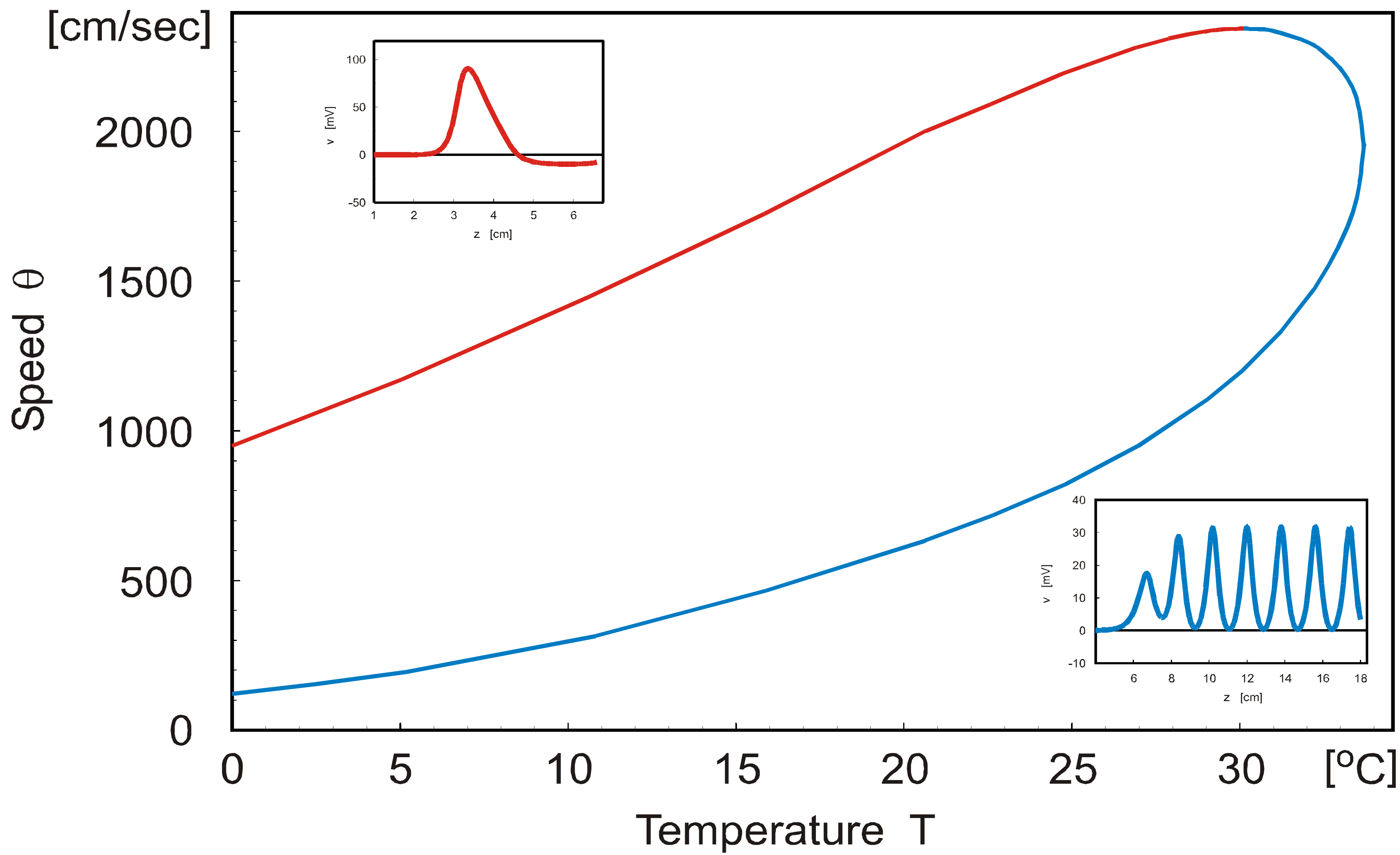
Hodgkin-Huxley equations describing pulse propagation along nerve fibers



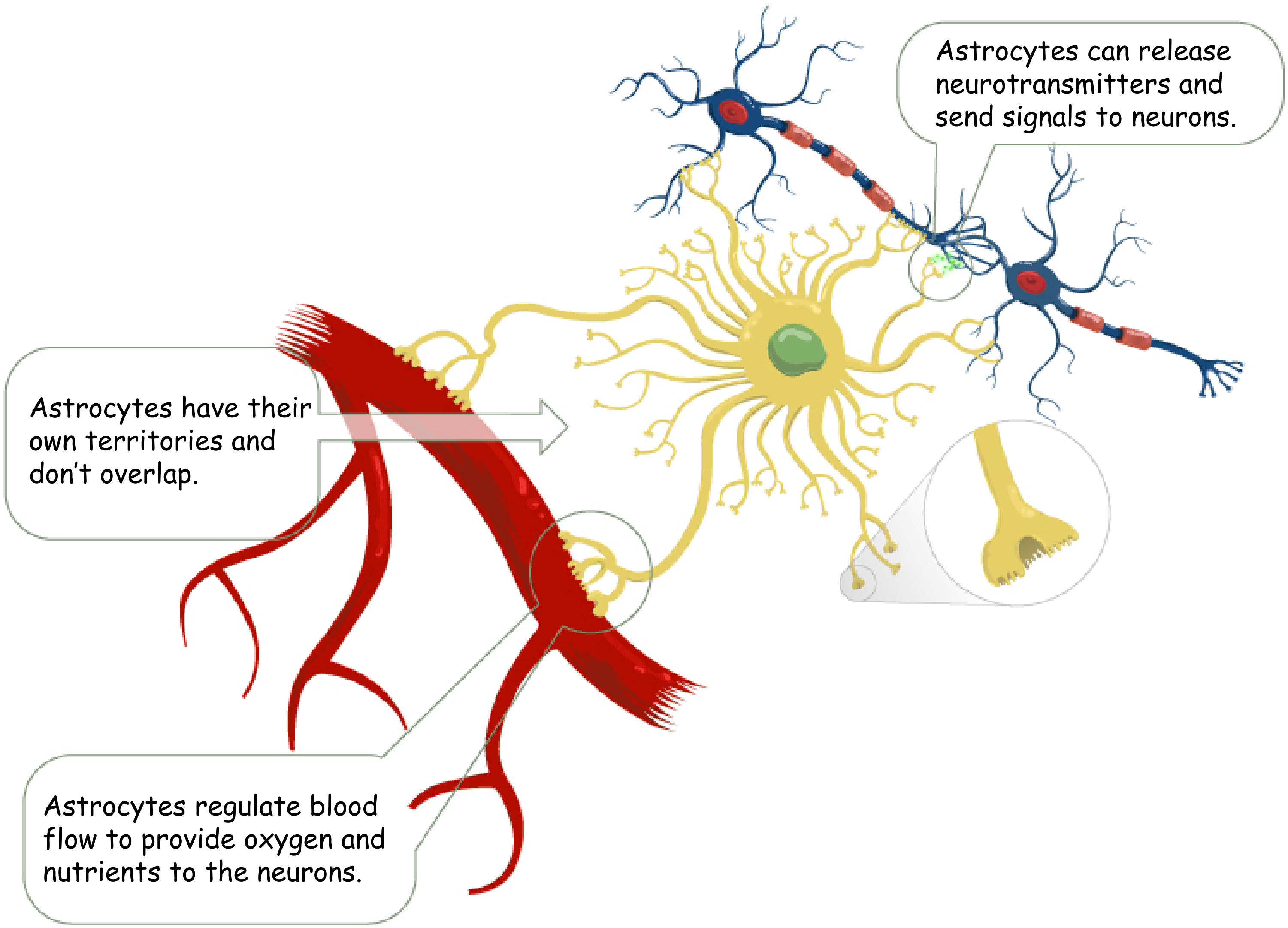
T = 18.5 C; θ = 1873.33 cm / sec



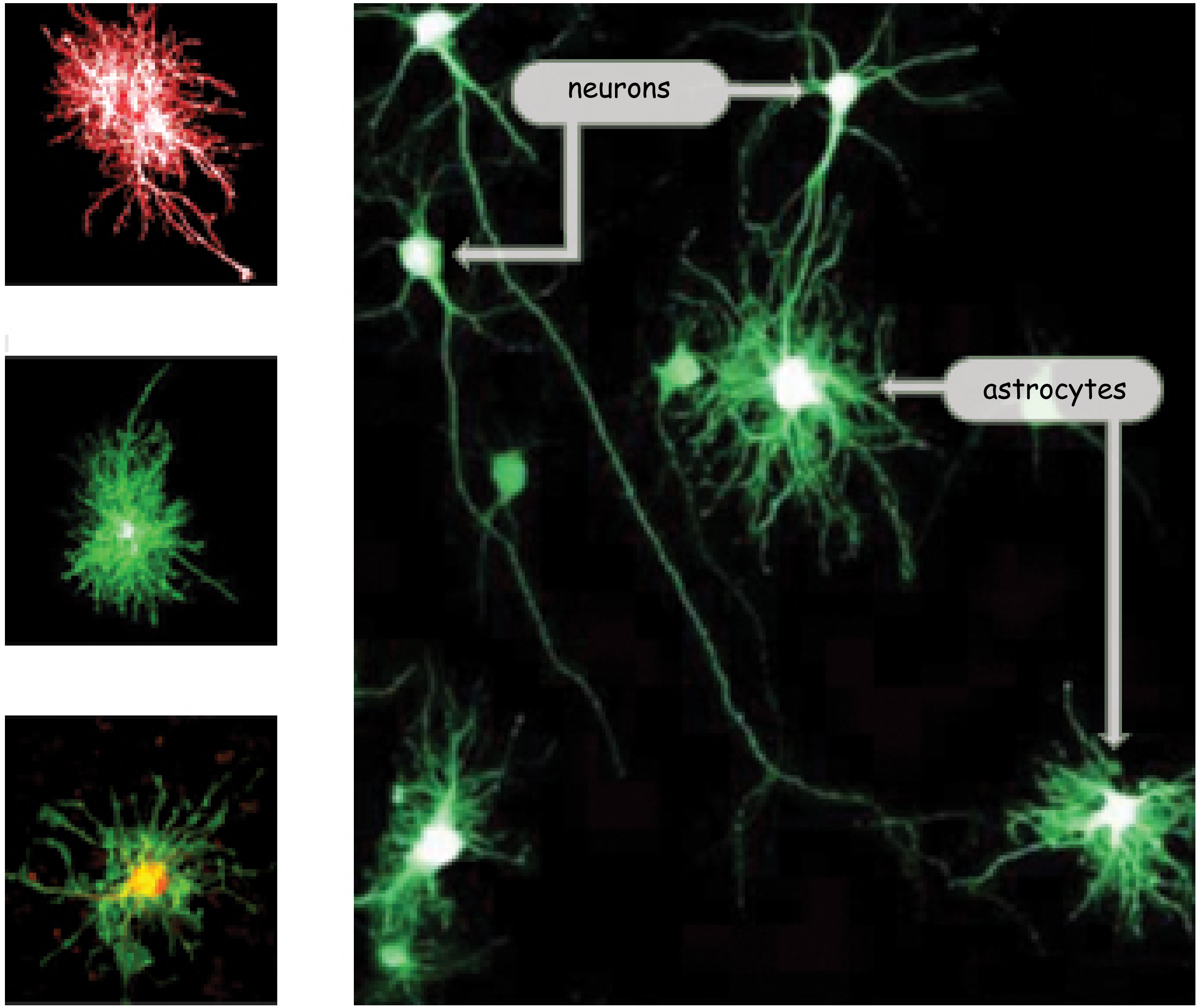
T = 18.5 C; θ = 544.070 cm / sec



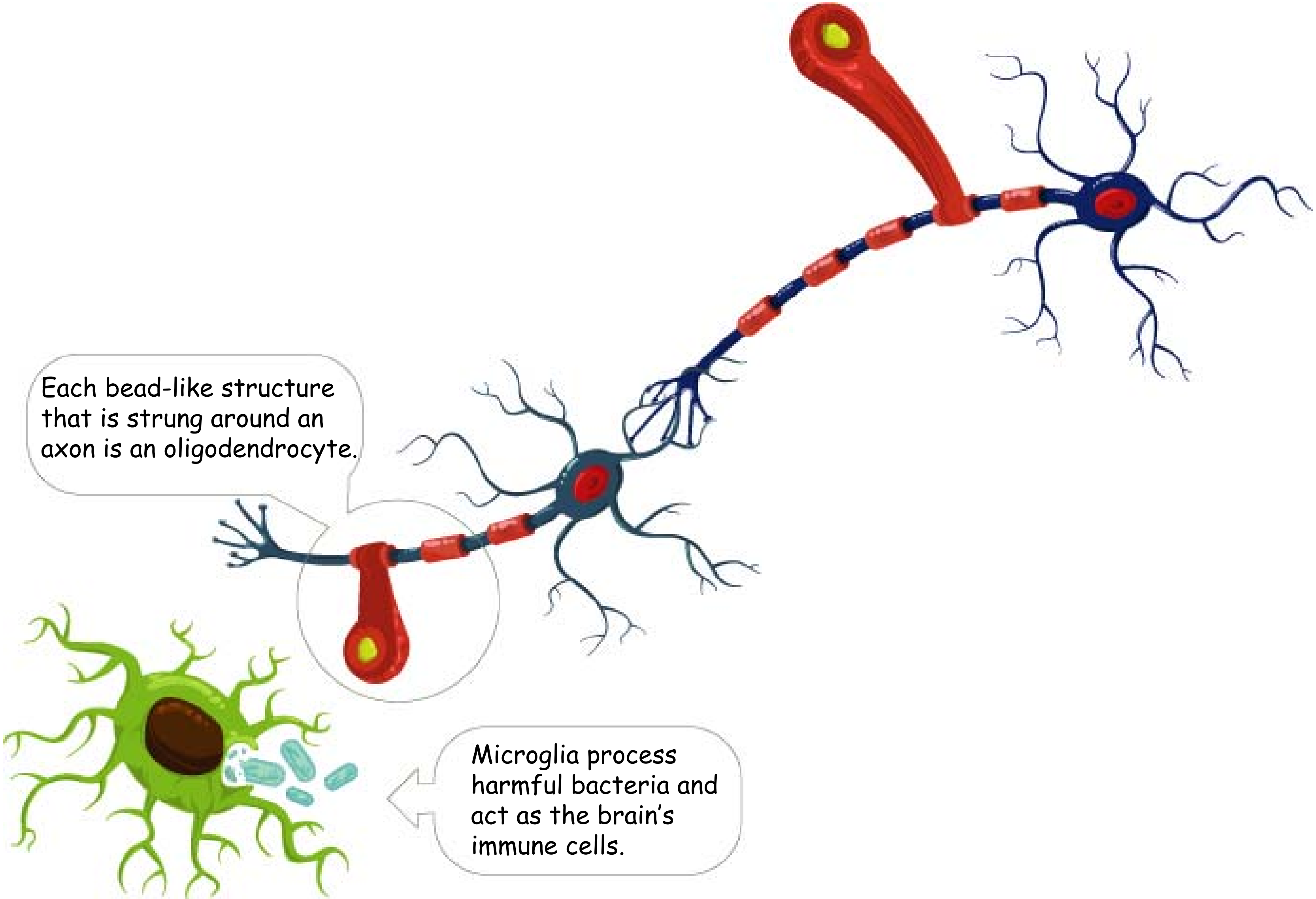
Propagating wave solutions of the Hodgkin-Huxley equations


Astrocytes can release neurotransmitters and send signals to neurons.
Astrocytes have their own territories and don't overlap.
Astrocytes regulate blood flow to provide oxygen and nutrients to the neurons.

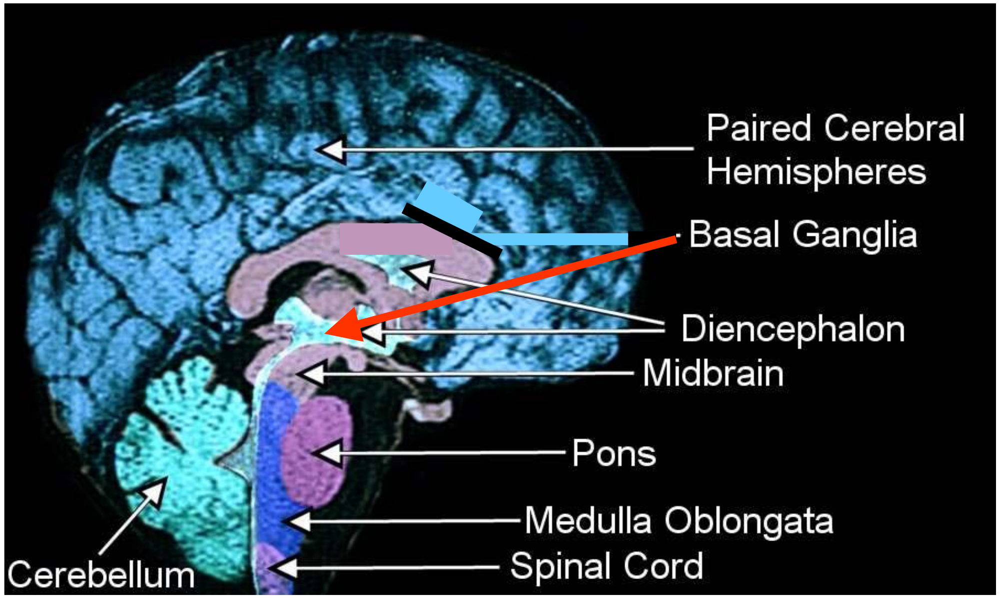
Astrocytes

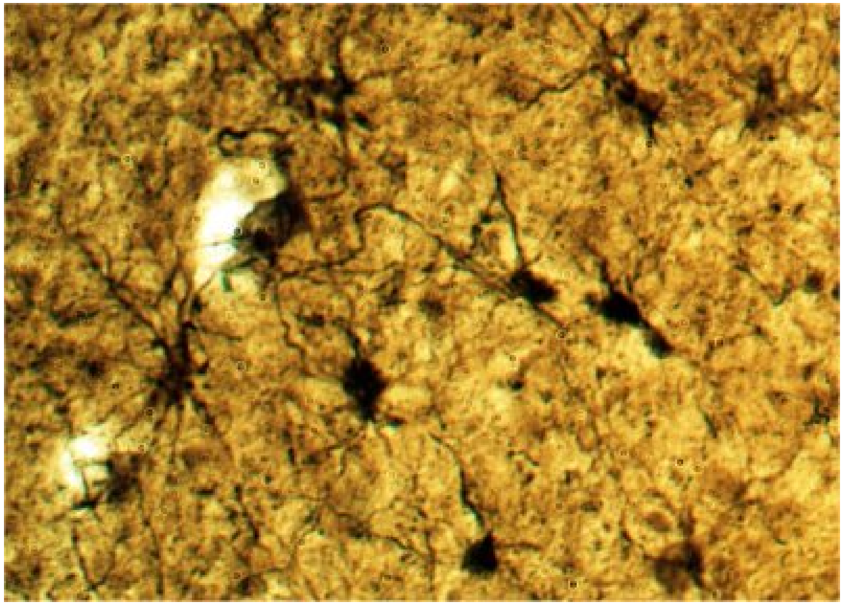


Photos of neurons and astrocytes



Oligodendrocyte





The human brain

10^{11} neurons connected by $\approx 10^{13}$ to 10^{14} synapses

Computer axial tomography – CAT

Magnetic resonance imaging – MRI

Functional magnetic resonance imaging – fMRI

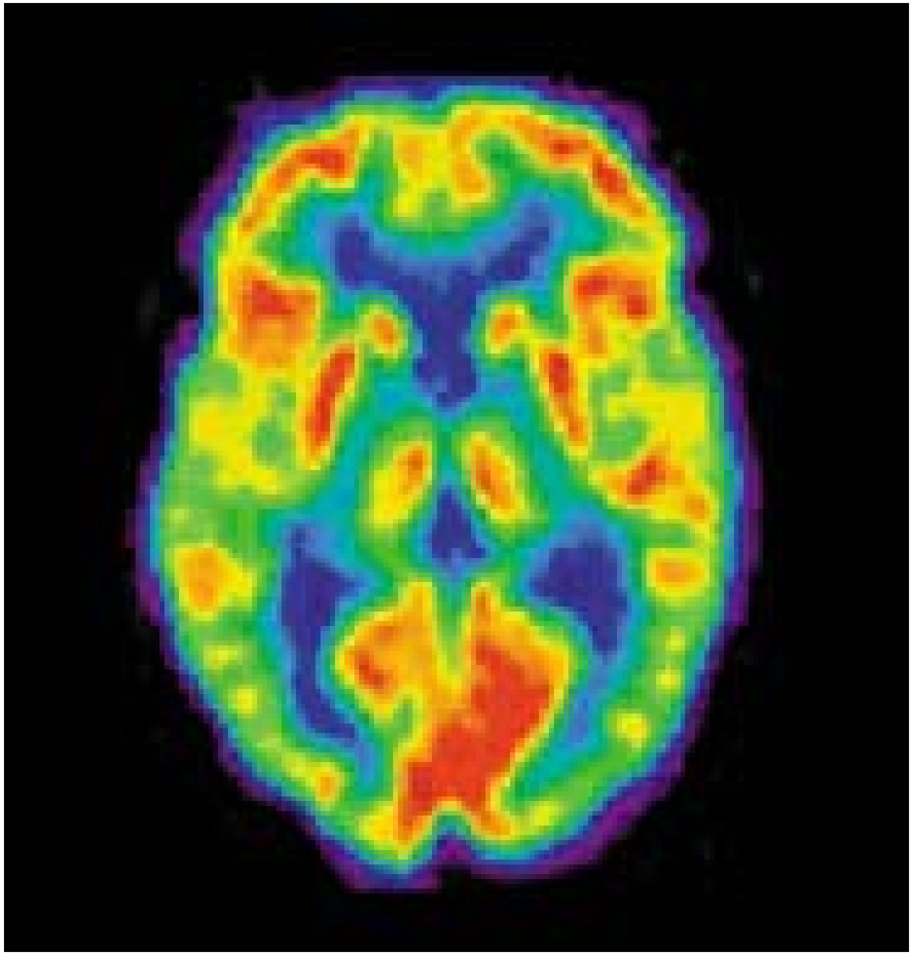
Positron emission tomography – PET

Single photon emission computed tomography - SPECT

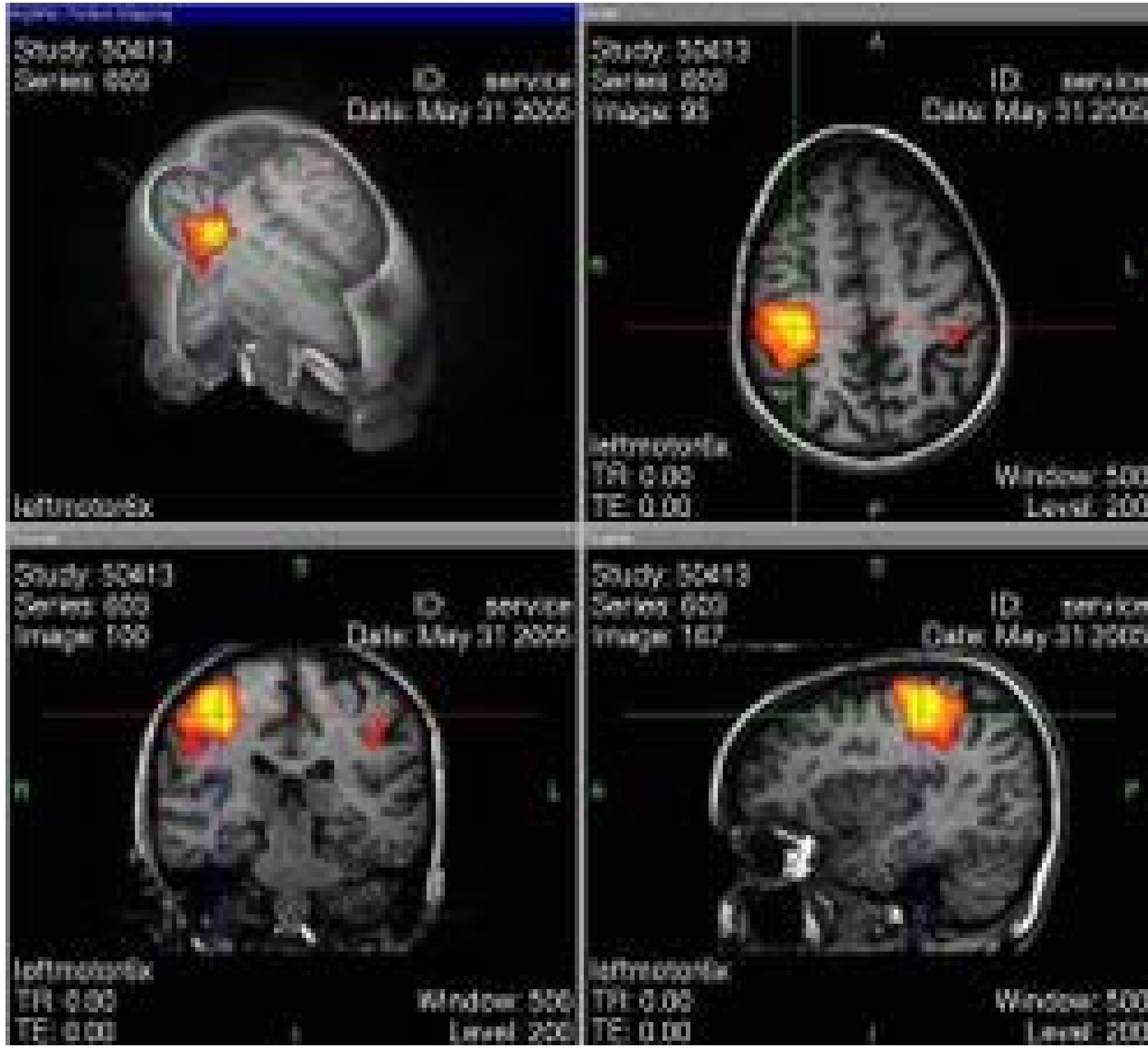
Diffuse Optical Tomography - DOT

Neuroimaging techniques

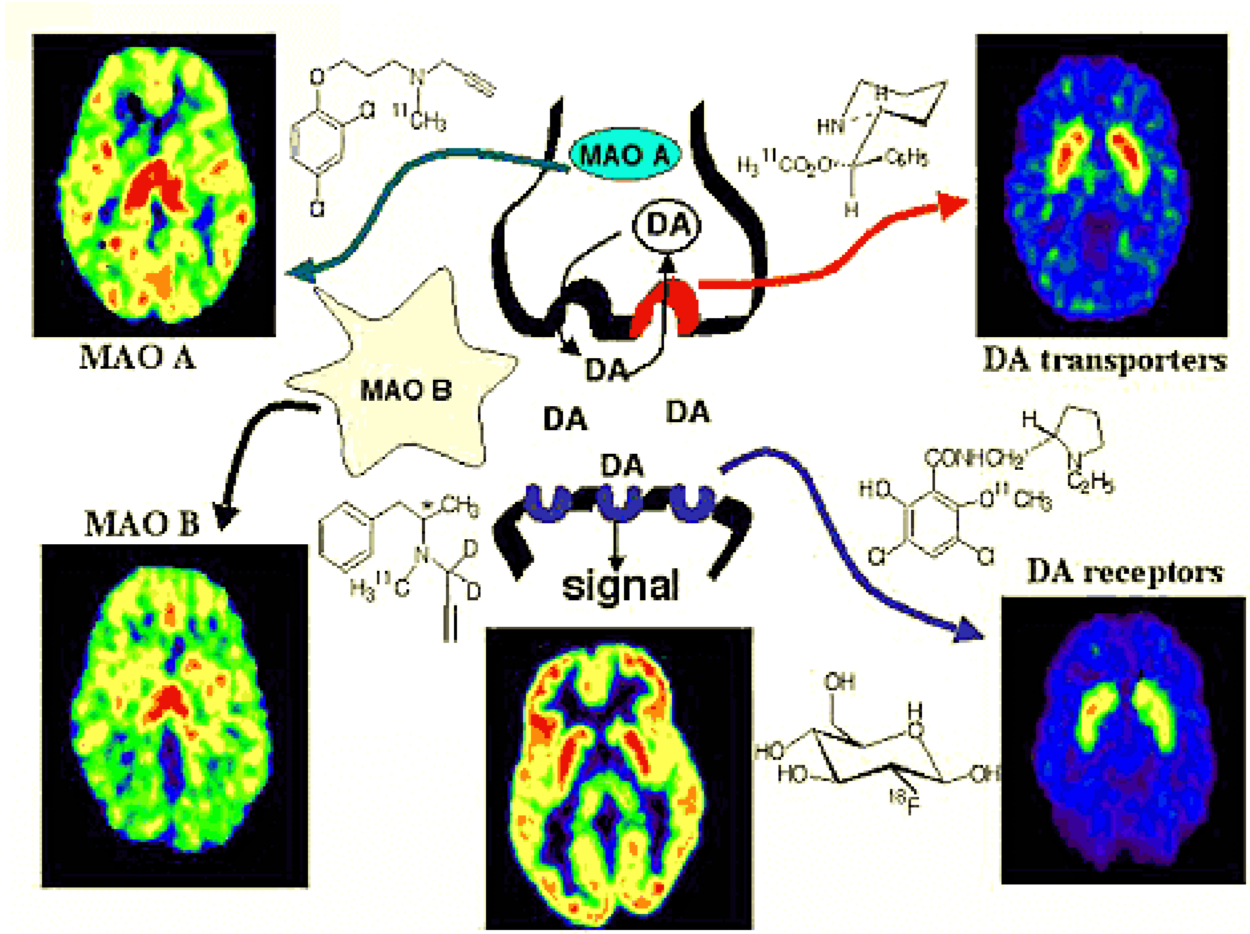
Magnetic resonance imaging - MRI



Positron emission tomography - PET



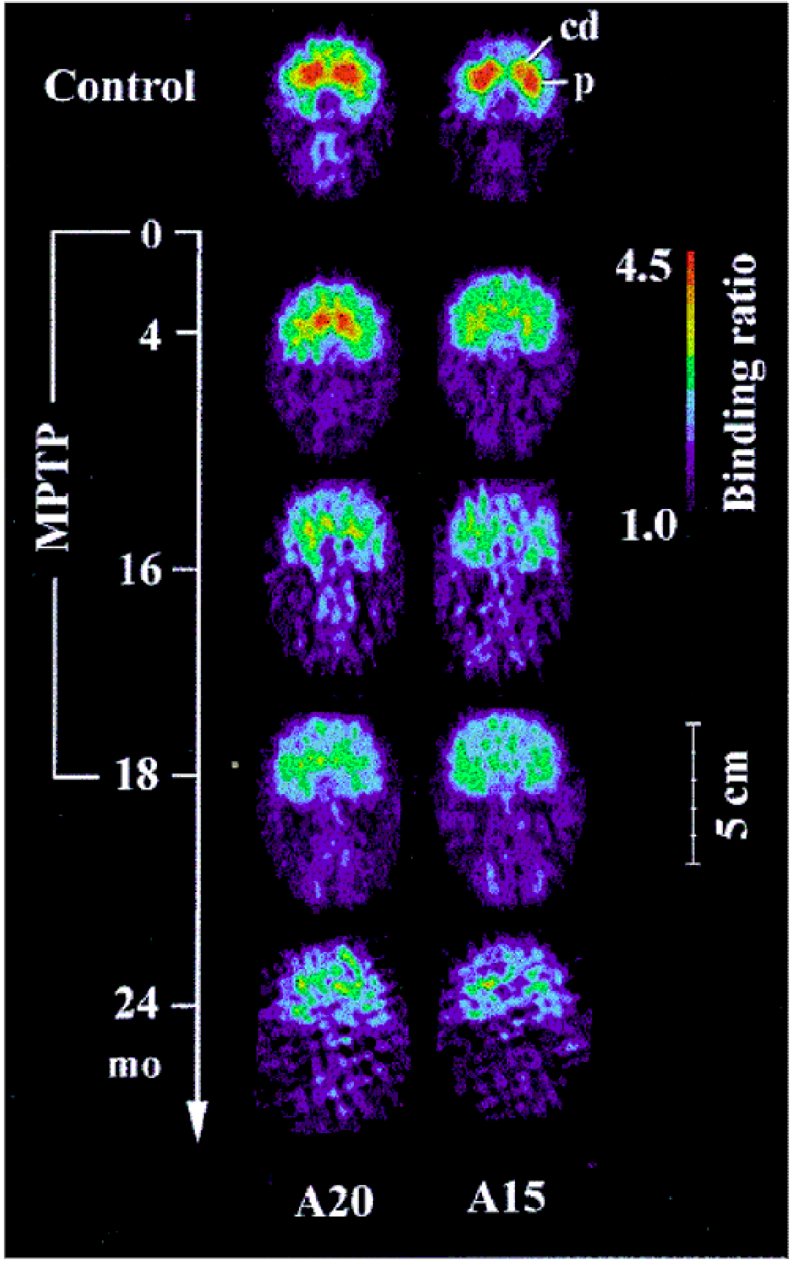
Functional magnetic resonance imaging - fMRI



Positron emission tomography - PET

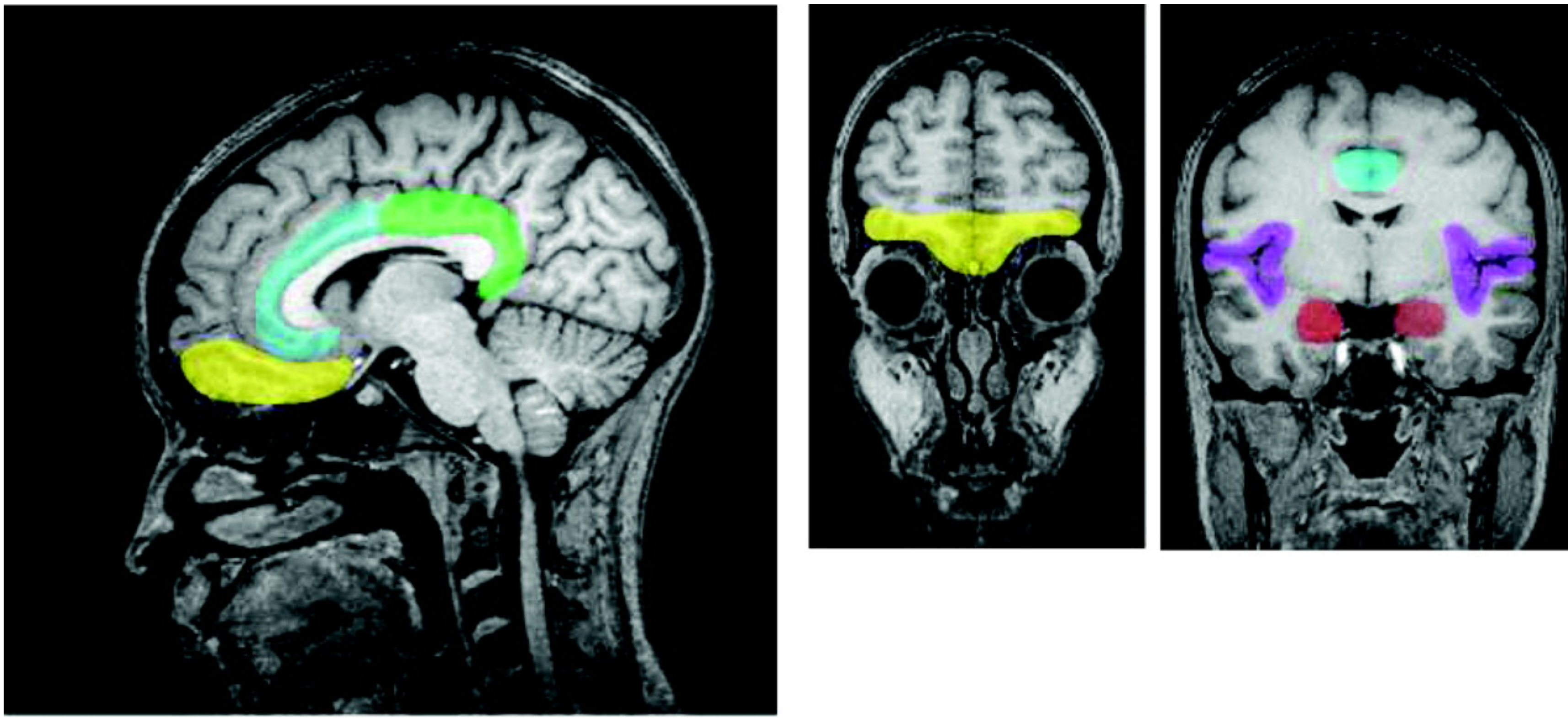
Monoamineoxidase – MAO
Dopamine -DA

Different activities monitored by PET



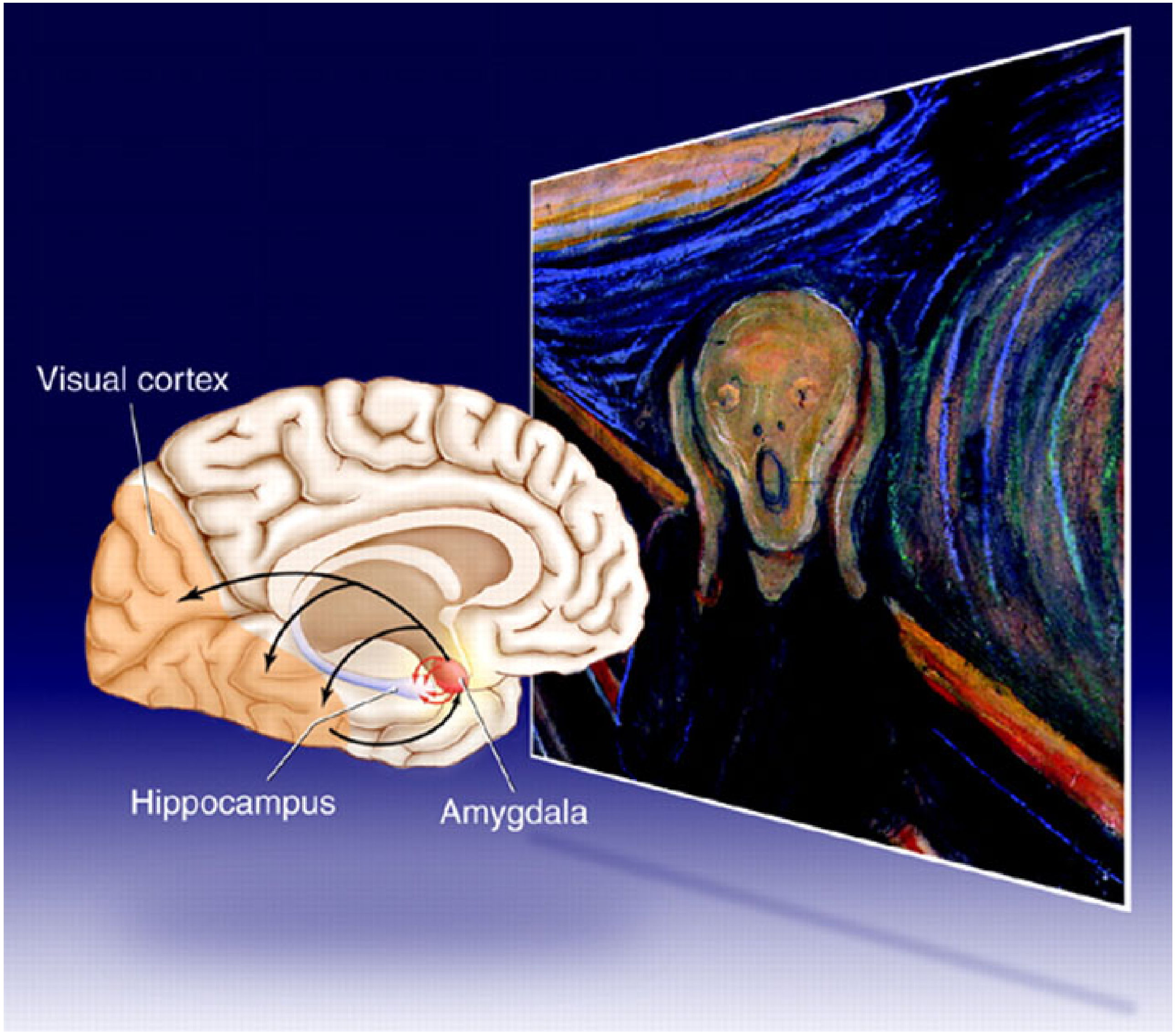
An ^{11}C positron emission study of the progression of Parkinson‘s disease in a primate model

Figure taken from *Nature Medicine* **4**, 1308-1312 (2002)



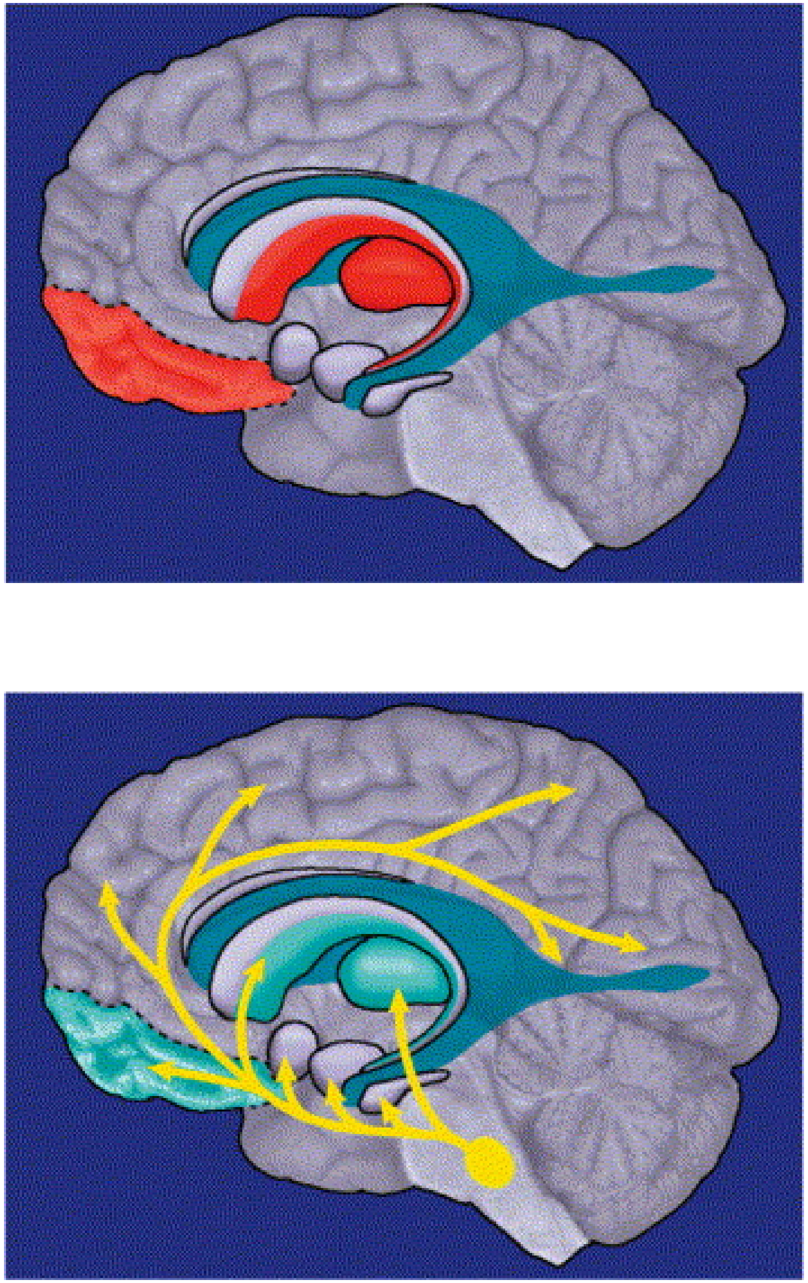
Brain regions involved in emotional experience: Amygdala (linking perception, automatic emotional response and memory), orbitofrontal cortex, insular cortex, anterior and posterior cingulate cortices.

Picture taken from *Science* **298**, 1191-1194 (2002)



Emotional-perceptual-memory circuit in the human brain

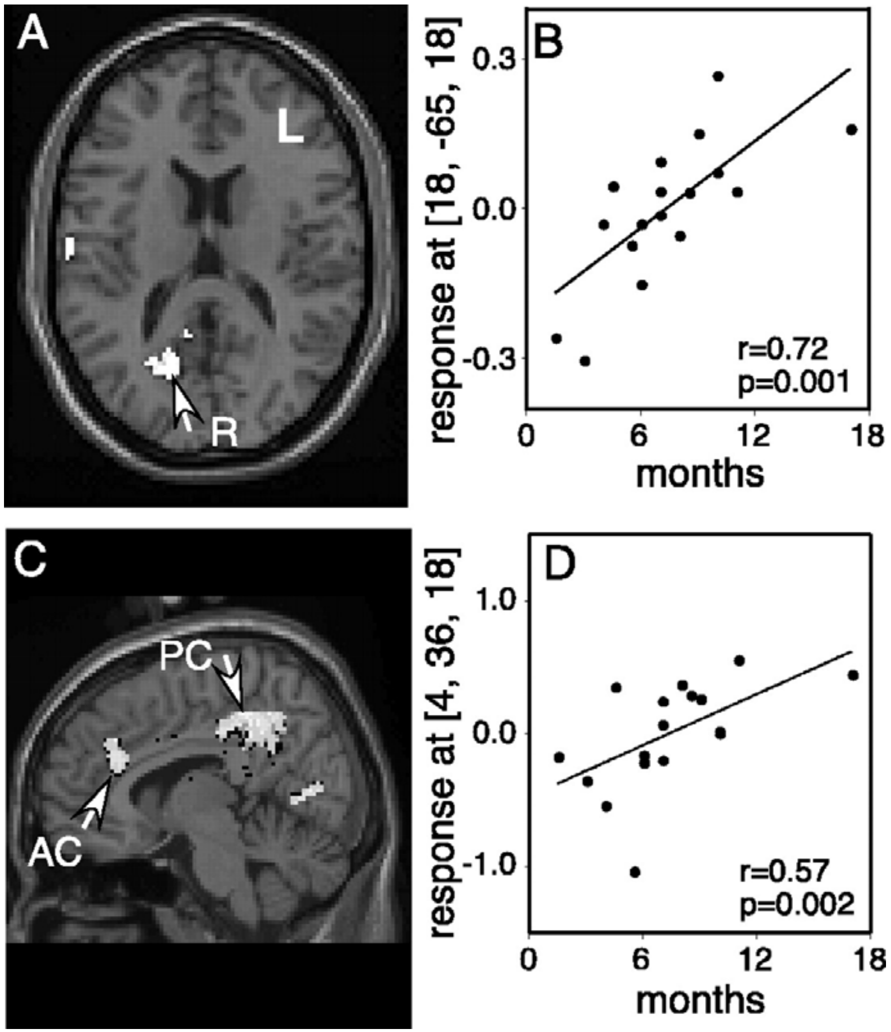
Picture taken from *Science* **298**, 1191-1194 (2002)



Dan J. Stein. Obsessive-compulsive disorder.
Lancet **360**:397-405, **2002**.

FIG. 5. Length of time in love correlated with activation in specific regions

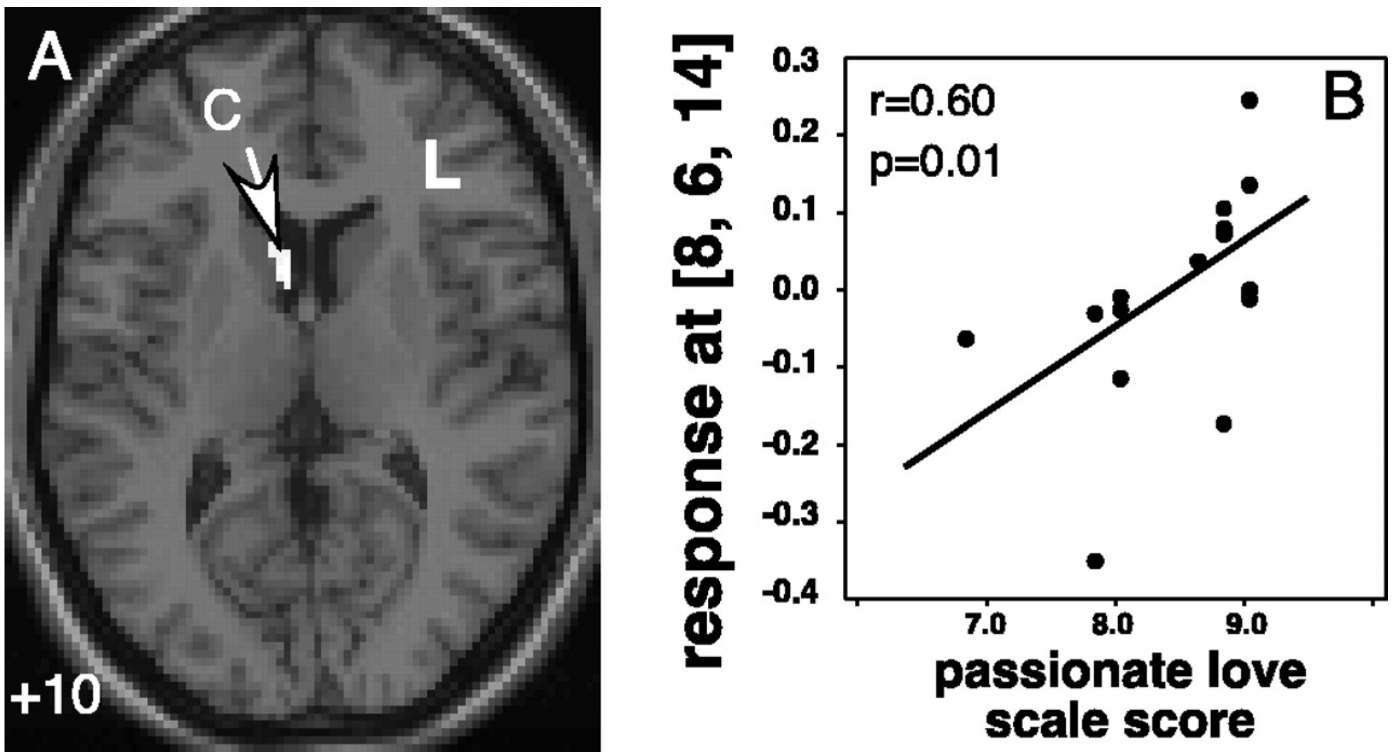
Regions are indicated on axial (*A*) and sagittal (*C*) sections



Aron, A. et al. J Neurophysiol 94: 327-337 2005;
doi:10.1152/jn.00838.2004

Journal of Neurophysiology

FIG. 3. Activation in the anteromedial caudate body was correlated with the passionate love scale (PLS) scores of participants



Aron, A. et al. J Neurophysiol 94: 327-337 2005;
doi:10.1152/jn.00838.2004

Jean-Martin Charcot

The New York Times, 26.09.2006: ***Is hysteria real? Brain images say yes***.

Coworkers

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Universität Wien

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