# BOLD fMRI

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# Lecture ‘series’

- Week 1: Biological basis: where’s the signal coming from?
- Week 2: Physical basis: what is the signal, how is it measured?
- Week 3: Imaging basics: imaging sequences, noise and artifacts.
- Week 4: The specific case of BOLD fMRI.
- Week 5: BOLD analysis: what’s significant and what’s not?
- Week 6: Spikes vs. BOLD: neural activity in visual areas

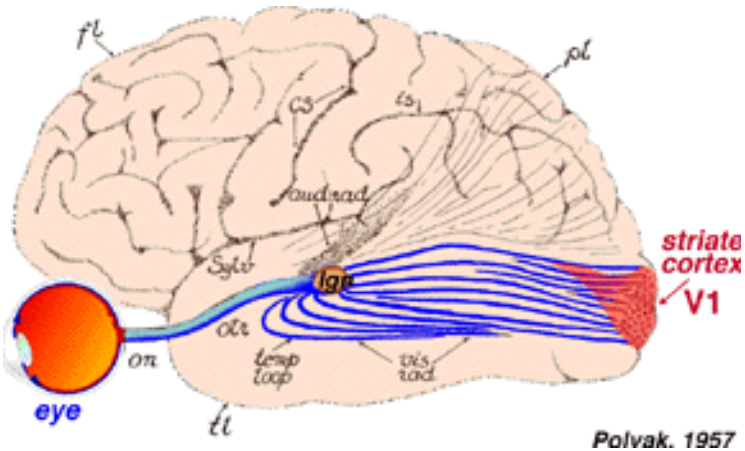
# Biological basis

- fMRI measures blood oxygenation and/or flow
- How are blood oxygenation and flow related to neural activity?
  - Oxygen consumption – Blood flow
  - Metabolism – Energy budgets
- Things to consider:
  - Spatial resolution – Spatial specificity
  - Temporal resolution – Neural specificity

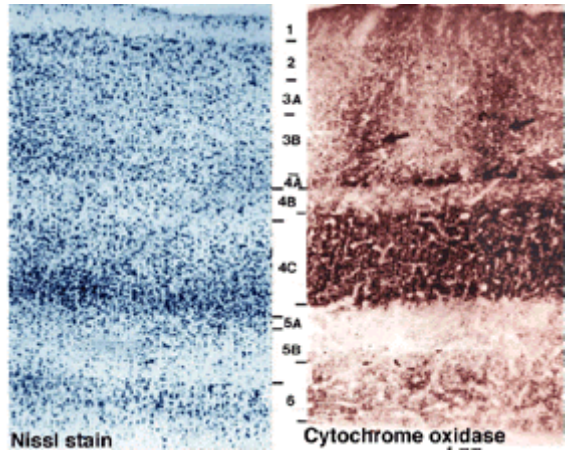
# Terms

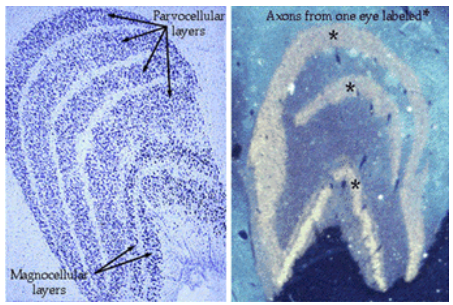
- BOLD: blood oxygenation level-dependent
- CBF: cerebral blood flow
- CBV: cerebral blood volume
- CBv: cerebral blood velocity
- $CMRO_2$: cerebral metabolic rate, oxygen
- CMRglu: cerebral metabolic rate, glucose

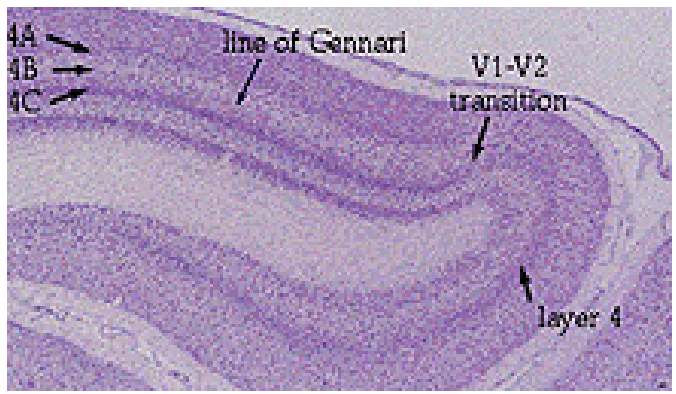
# Primary visual cortex: layers and columns

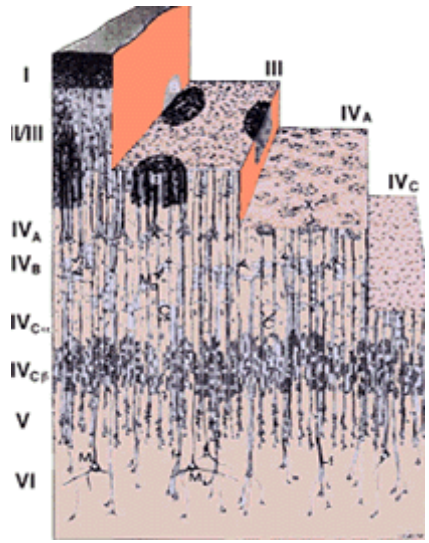






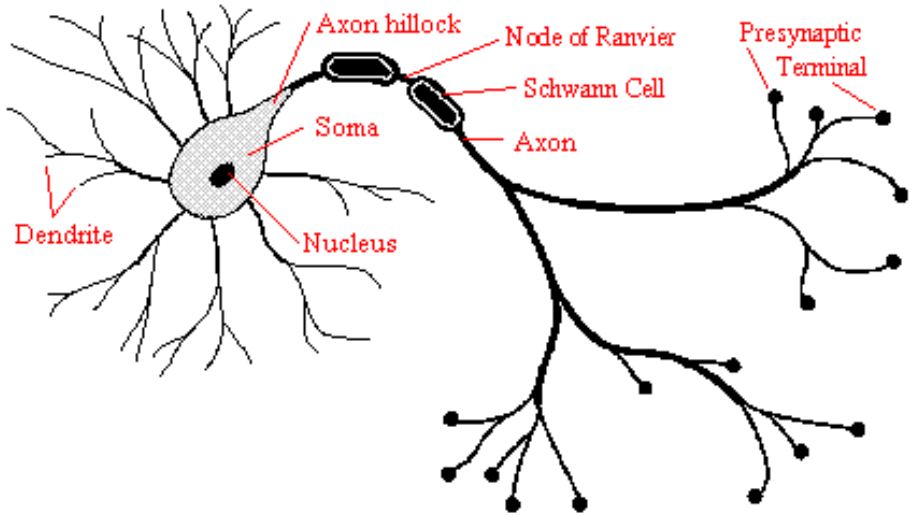



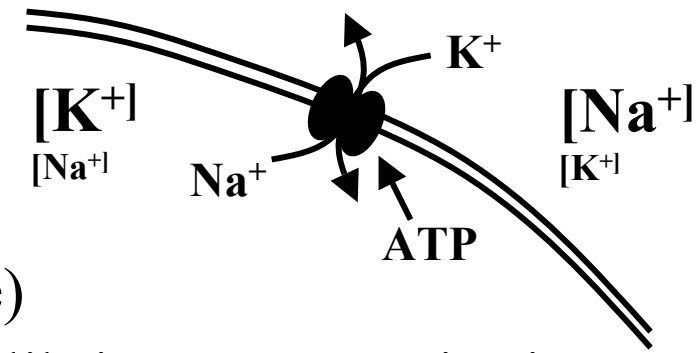

*The Primary Visual Cortex*
by Matthew Schmolesky
www.webvision.med.utah.edu/VisualCortex.html

# What happens when *one* neuron is active?

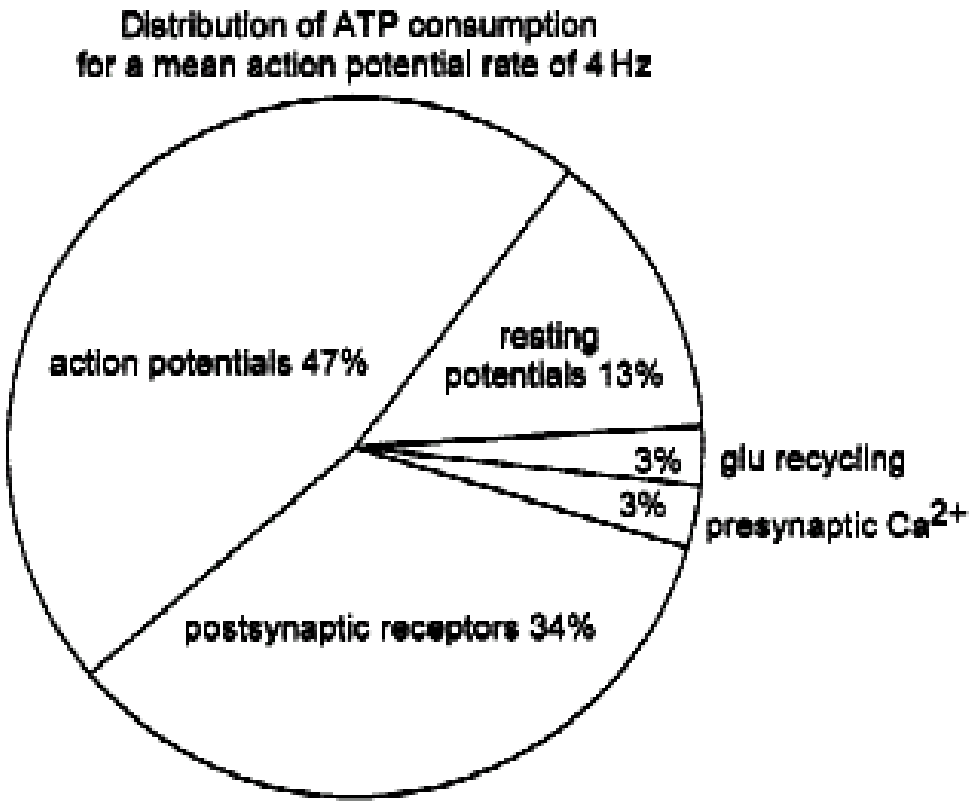


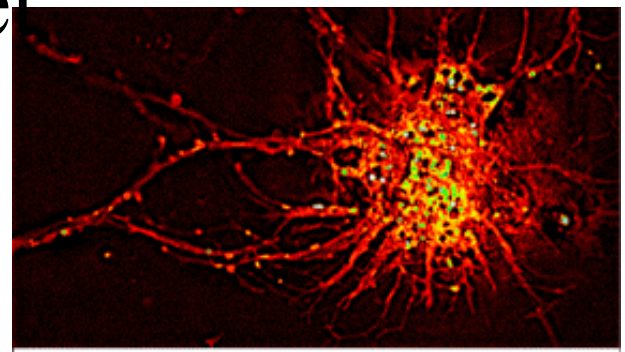

http://www.bae.ncsu.edu/bae/research/blanchard/…/neuron.gif

- Activity ≡ increased firing rate
- Increased firing rates run down membrane potential
- Membrane potential results from high [K+] in the cell and high [Na+] outside the cell
- ATP is consumed to restore membrane potential (Na/K-ATPase)
- ATP is also required to restore equilibrium at synaptic sites



# Energy budget



Mitochondria of neuron revealed by staining with a rhodamine 123 derivative

Expert Reviews in Molecular Medicine
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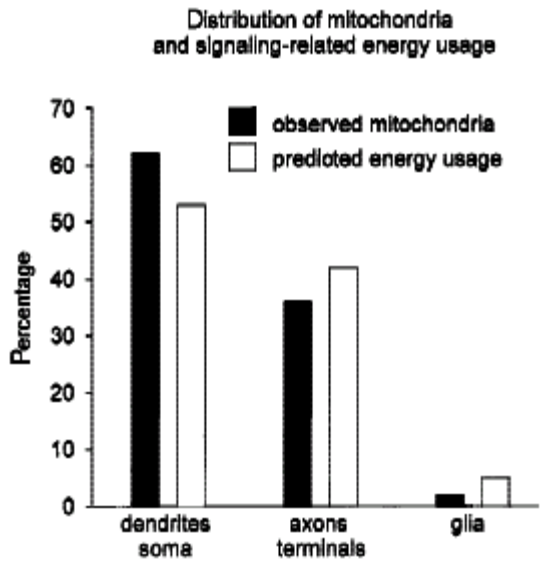
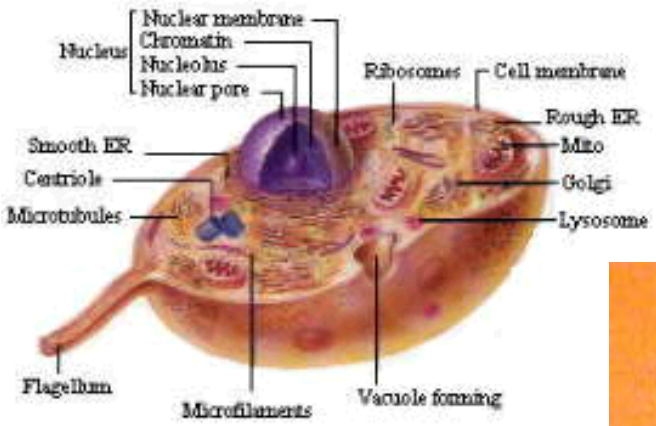


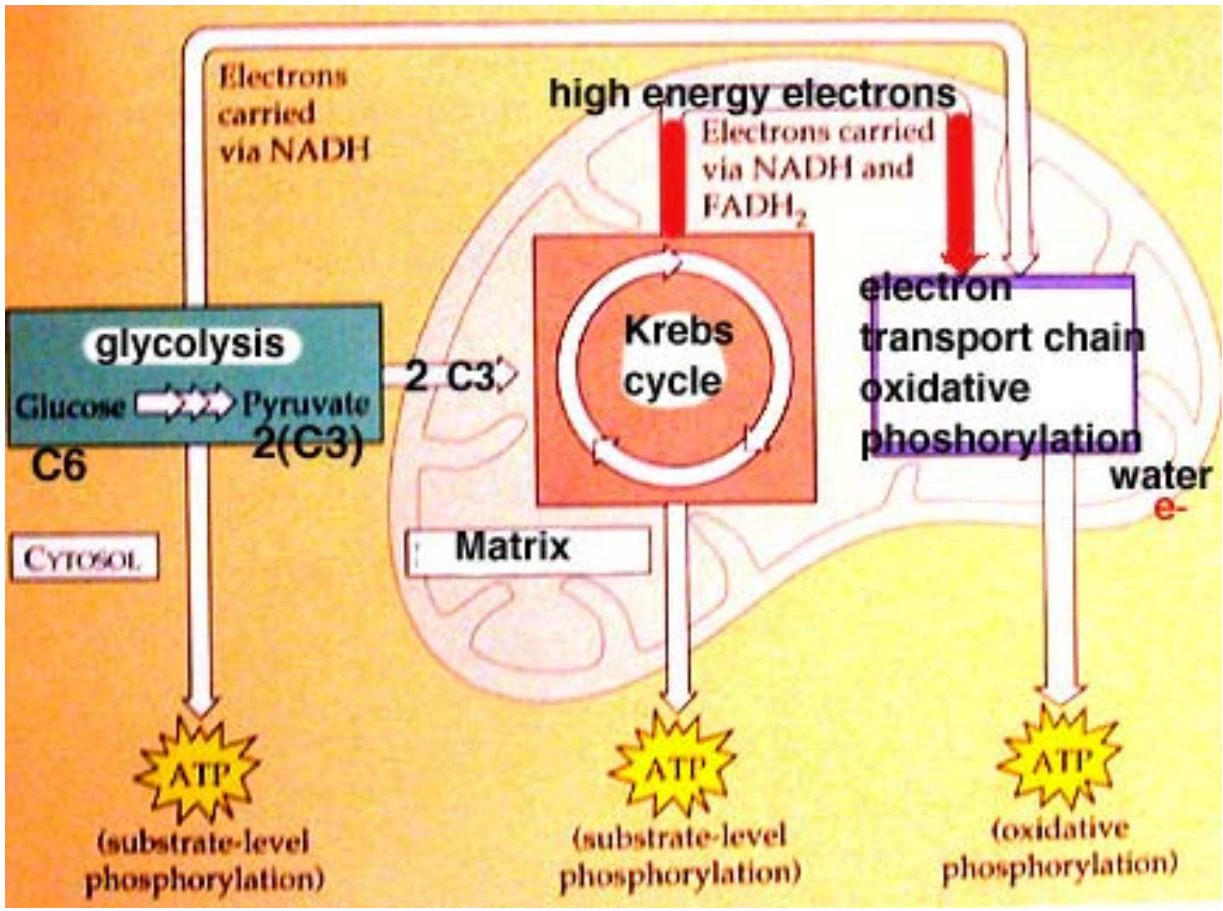

**Attwell, D. and S. B. Laughlin** (2001). "An energy budget for signaling in the grey matter of the brain." J Cerebral Blood Flow Metabolism **21**: 1133-1145.

# A brief digression into cell biology




http://personal.nbnet.nb.ca/trevgall/biology/

ATP is generated by aerobic glycolysis and anaerobic TCA cycle

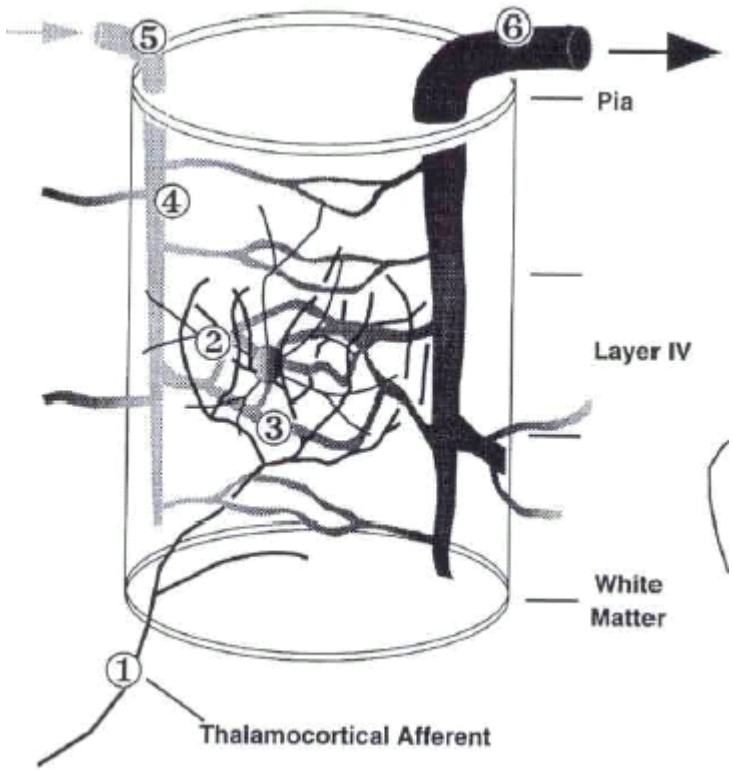



http://academic.brooklyn.cuny.edu/biology/bio4fv/page/metab_overview1424.JPG

# What happens when many neurons are active?

- The population needs increased CBF to provide glucose and oxygen
  - Excitatory vs. inhibitory activity
    - 90% of neurons are glutamatergic/excitatory
    - 10% GABAergic/inhibitory
  - It's not just neurons doing the signaling (neurons and glia exist in ~1:1 ratio)
- Possible signals for increased blood flow:
  - Increased extracellular potassium (direct or indirect effect)
  - NO: range and timing match well
  - Other signals transmitted along capillaries or glia?

# Link to blood flow



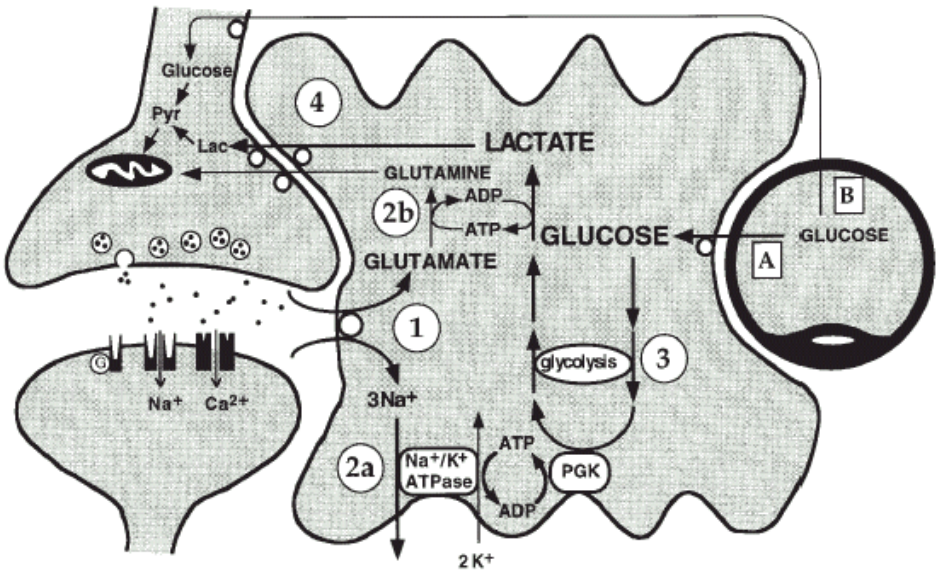

1. Incoming signal
2. Synaptic activity
3. Accumulated ions, neurotransmitters, signaling molecules
4. Artereolar relaxation
5. Flow changes at a larger scale and
6. Increased blood volume in venuole

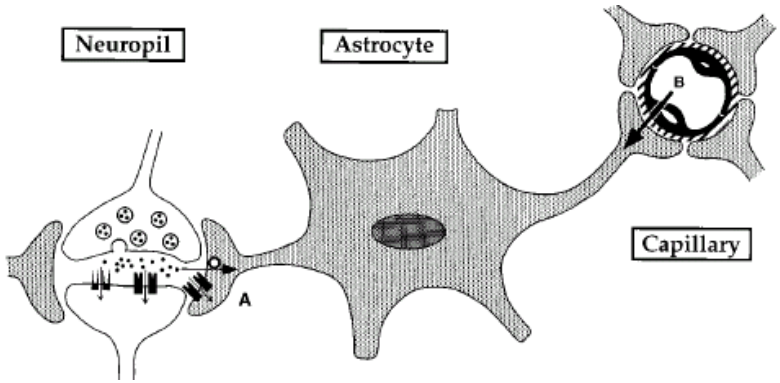
**Figure 12**, from Woolsey, T. A *et al.* (1996). "Neuronal units linked to microvascular modules in cerebral cortex: response elements for imaging the brain." Cerebral Cortex **6**: 647-660.

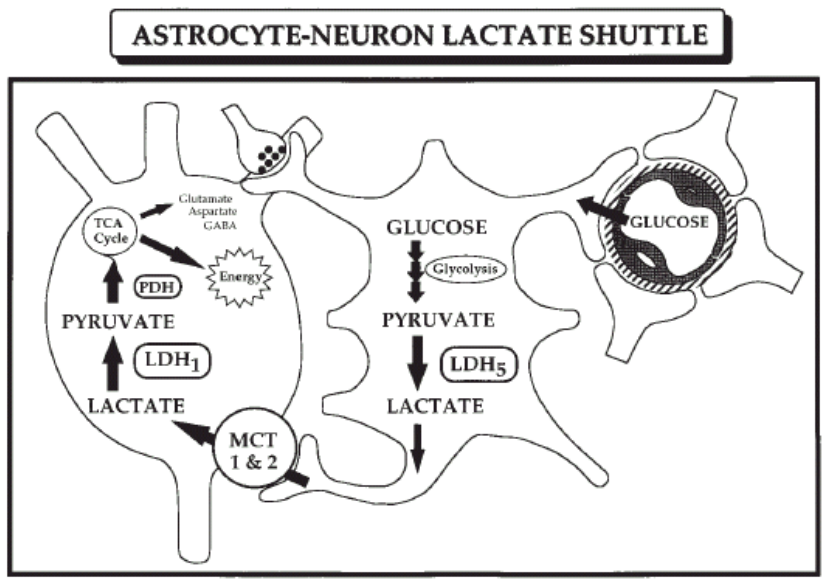
# Decoupling of CBF, CMRglu and $CMRO_2$

- PET studies by Fox and Raichle demonstrated 40% increase in CBF and CMRglu, but only 5% increase in $CMRO_2$
  - Fox, P. T. and M. E. Raichle (1986). "Focal physiological uncoupling of cerebral blood flow and oxidative metabolism during somatosensory stimulation in human subjects." Proc Natl Acad Sci USA 83: 1140-1144.
  - Fox, P. T., M. E. Raichle, M. A. Mintun and C. Dence (1988). "Nonoxidative glucose consumption during focal physiologic neural activity." Science 241: 462-464.
- Positive BOLD signal confirms this!
- Is neural activity anaerobic? Is oxygen consumption delayed? Is CBF much more widespread than $CMRO_2$?

# Magistretti hypothesis

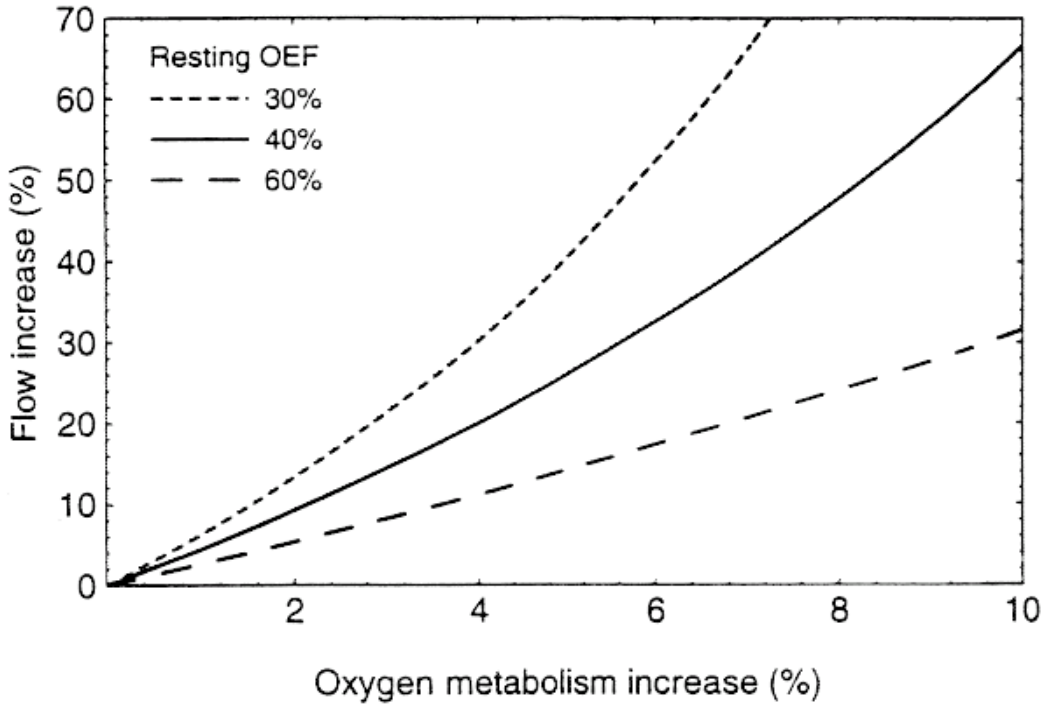



**Magistretti, P. J. and L. Pellerin** (1999). "Astrocytes couple synaptic activity to glucose utilization in the brain." News in Physiological Sciences **14**: 177-182.

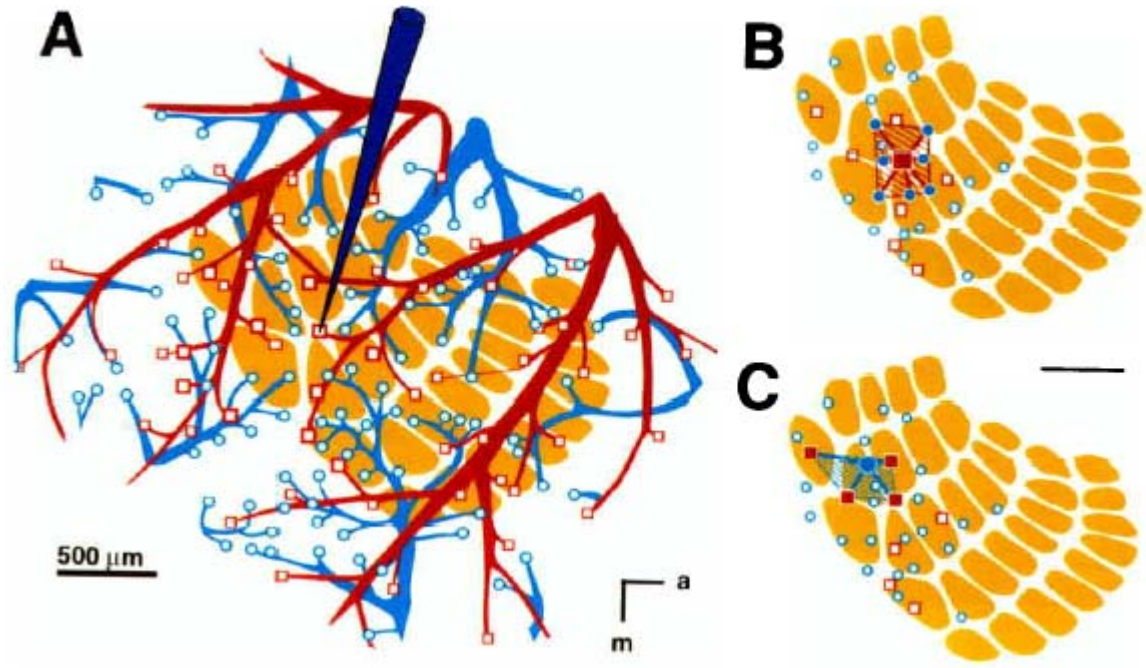
# The Balloon model (Buxton)




- Two main features
  - CBF and $CMRO_2$ are coupled
  - Limitation is rate at which $O_2$ is extracted from capillaries
- Also
  - Undershoot after stimulus is increased CBV, not delayed oxygen consumption
  - Not 'watering the garden for the sake of one thirsty flower' (in original context, Malonek and Grinvald, 1996)

**FIG. 3**. Fractional change in cerebral blood flow required to produce a given fractional change in the rate of delivery of $O_2$ to the tissue, calculated from Eq. 5 for three values of the resting oxygen extraction fraction. Tight coupling of flow and metabolism requires a large change in flow in order to produce a much smaller change in oxygen metabolism, but the exact relationship depends strongly on the resting OEF.
*From:* Buxton: J Cereb Blood Flow Metab, Volume 17(1).January 1997.64-72

# Spatial specificity




Cortical territory for a *large venuole* is about the size of a barrel, but …
… not in register with barrels
… not in register with feeding arterioles, where CBF is regulated

**Figure 10**, from Woolsey, T. A *et al.* (1996). "Neuronal units linked to microvascular modules in cerebral cortex: response elements for imaging the brain." Cerebral Cortex **6**: 647-660.