

Monday - 25 October

10:30 am - noon

Martin Lauritzen - "So many signals - How the vasculature feeds the brain"

2:30 pm - 4:00 pm

Brian MacVicar - "Regulation of cerebral blood vessels by astrocytes and the influence of metabolism"

5:00 pm - 6:00 pm

Wine and Cheese

Tuesday - 26 October

9:30 am - 11:00 am

Frank Kirchhoff - "Two-photon imaging and genetic models to study glia function in vivo."

11:30 am - 1:00 pm

Edith Hamel - "Neuronal networks in the control of cerebral blood flow"

2:00 pm - 3:00 pm

Junior Fellows - Pablo Blinder on the angiotome / Andy Shih on single vessel microstrokes

Wednesday - 27 October

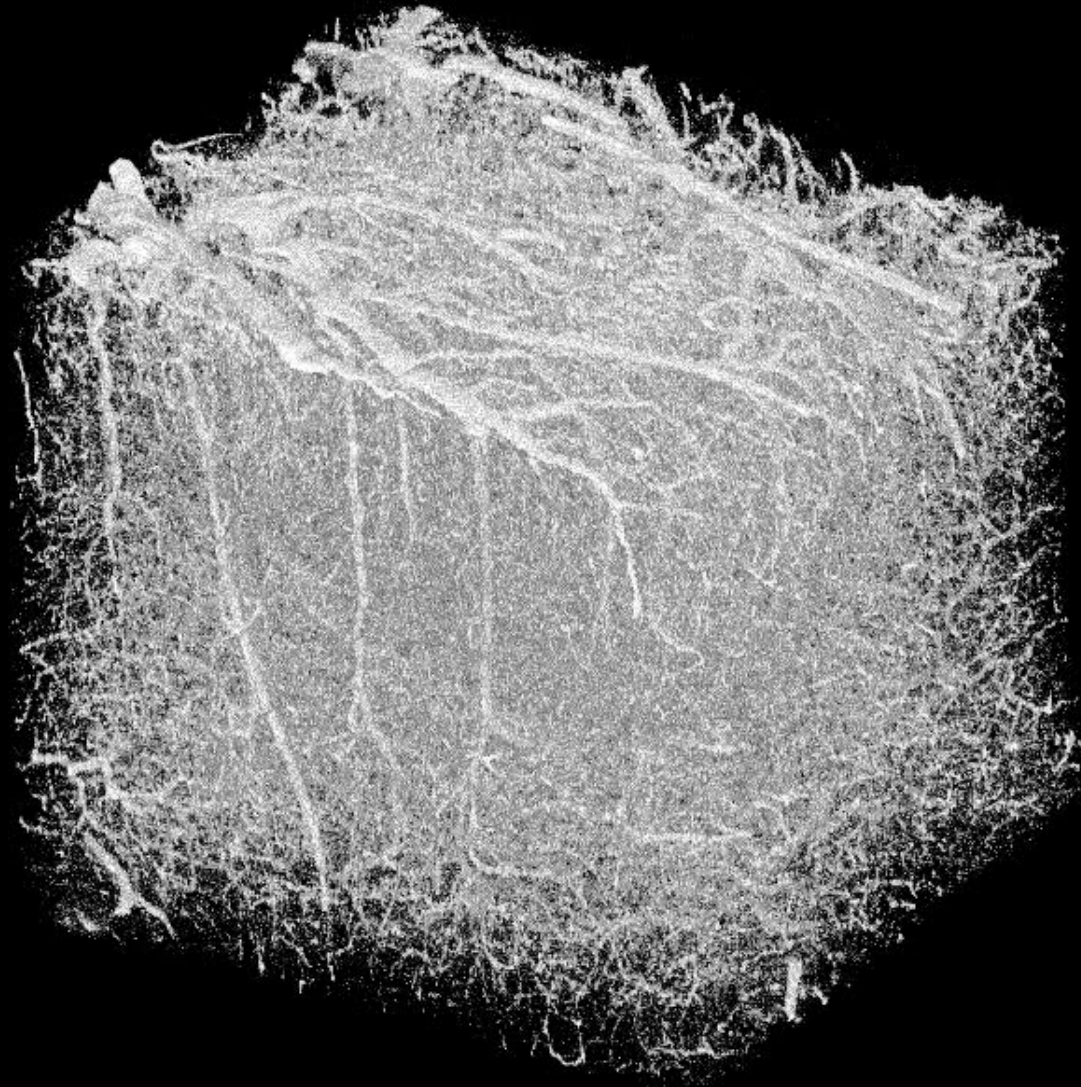
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Bruno Weber - "Cerebral blood flow and metabolism: Feeding a hungry organ"

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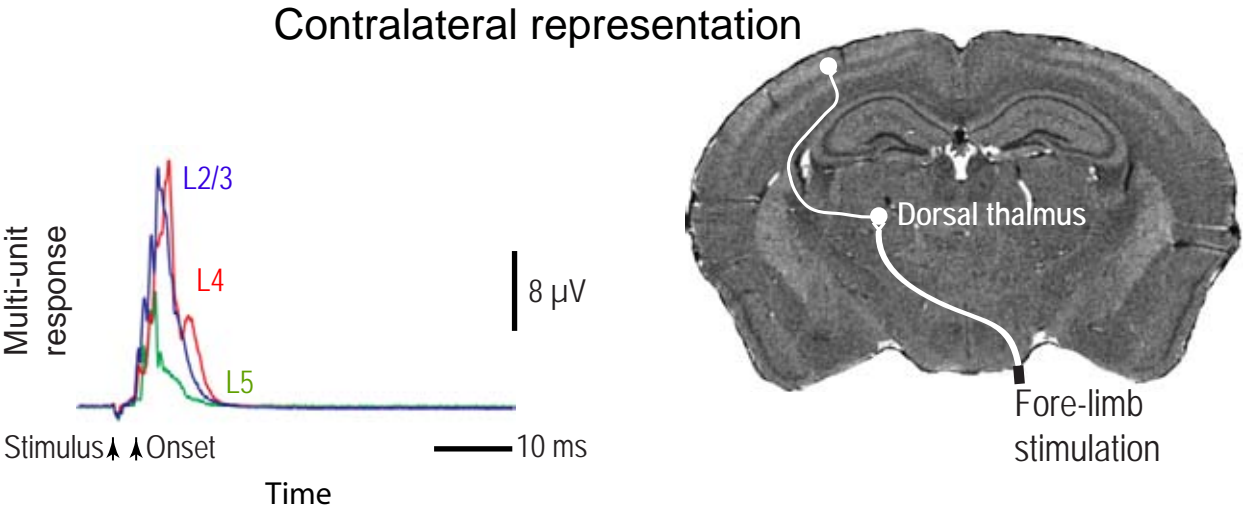
Open issues: Things we should and perhaps could do next

Highlights of the rodent angiotome: A work in progress



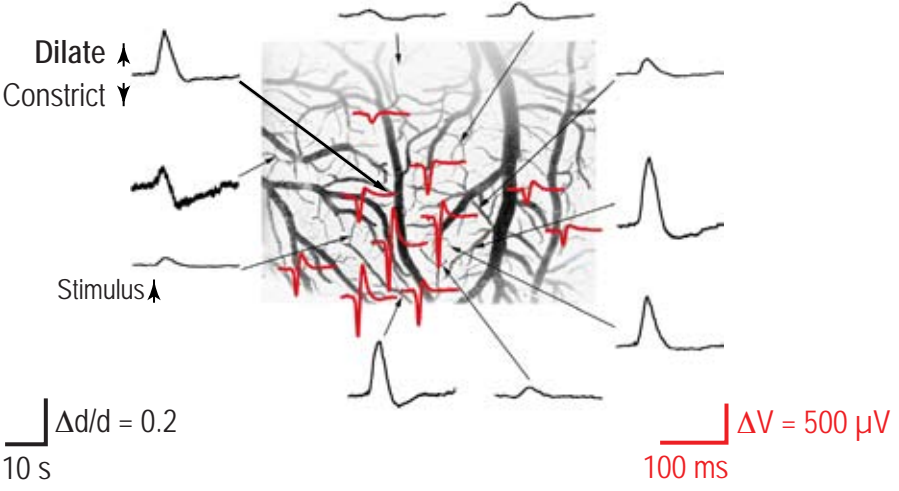
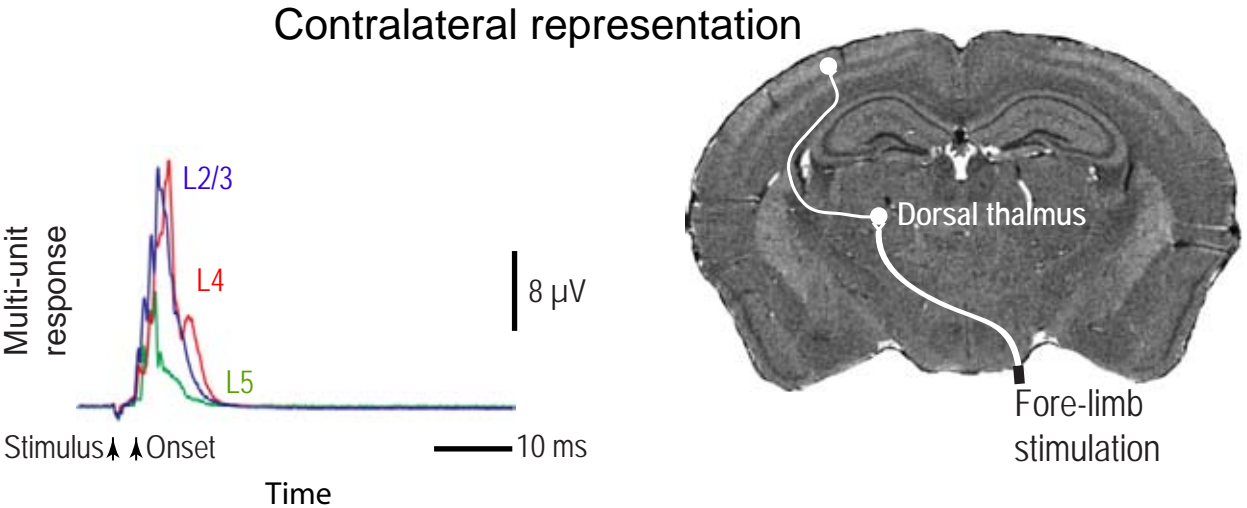
Neuronal activity changes blood flow - but logic remains to be deciphered

Example of changes in the lumen of surface arterioles for the two cortical hemispheres



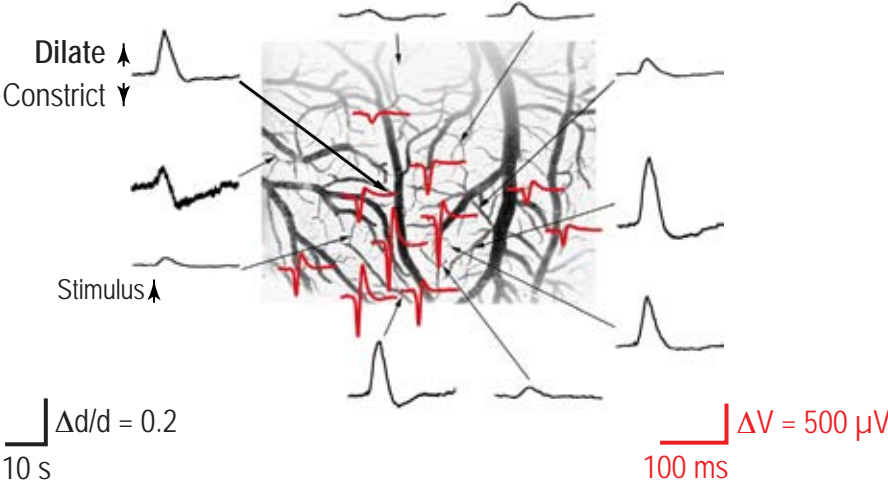
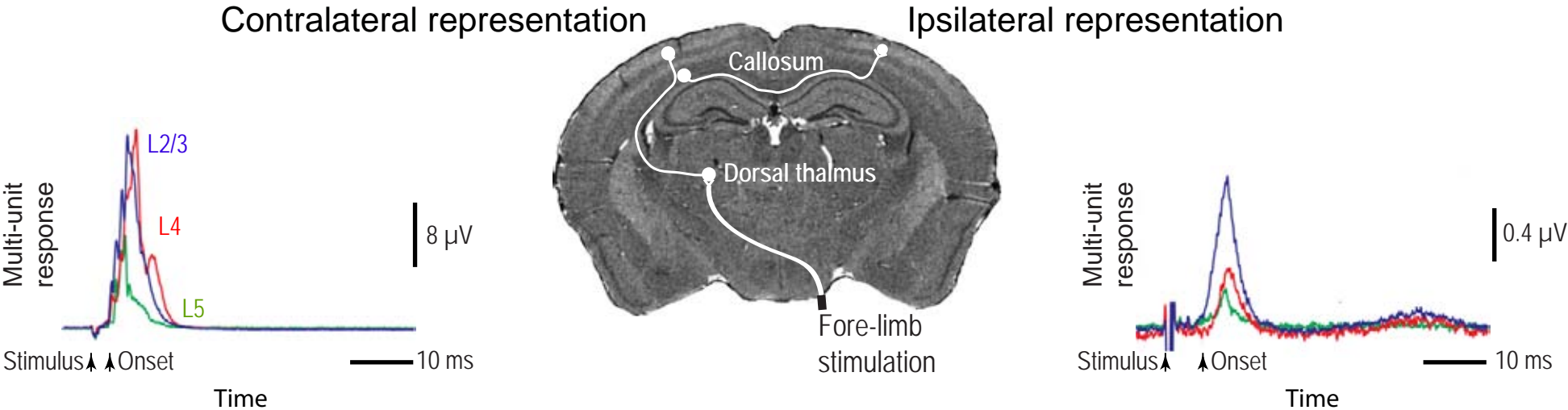
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Example of changes in the lumen of surface arterioles for the two cortical hemispheres



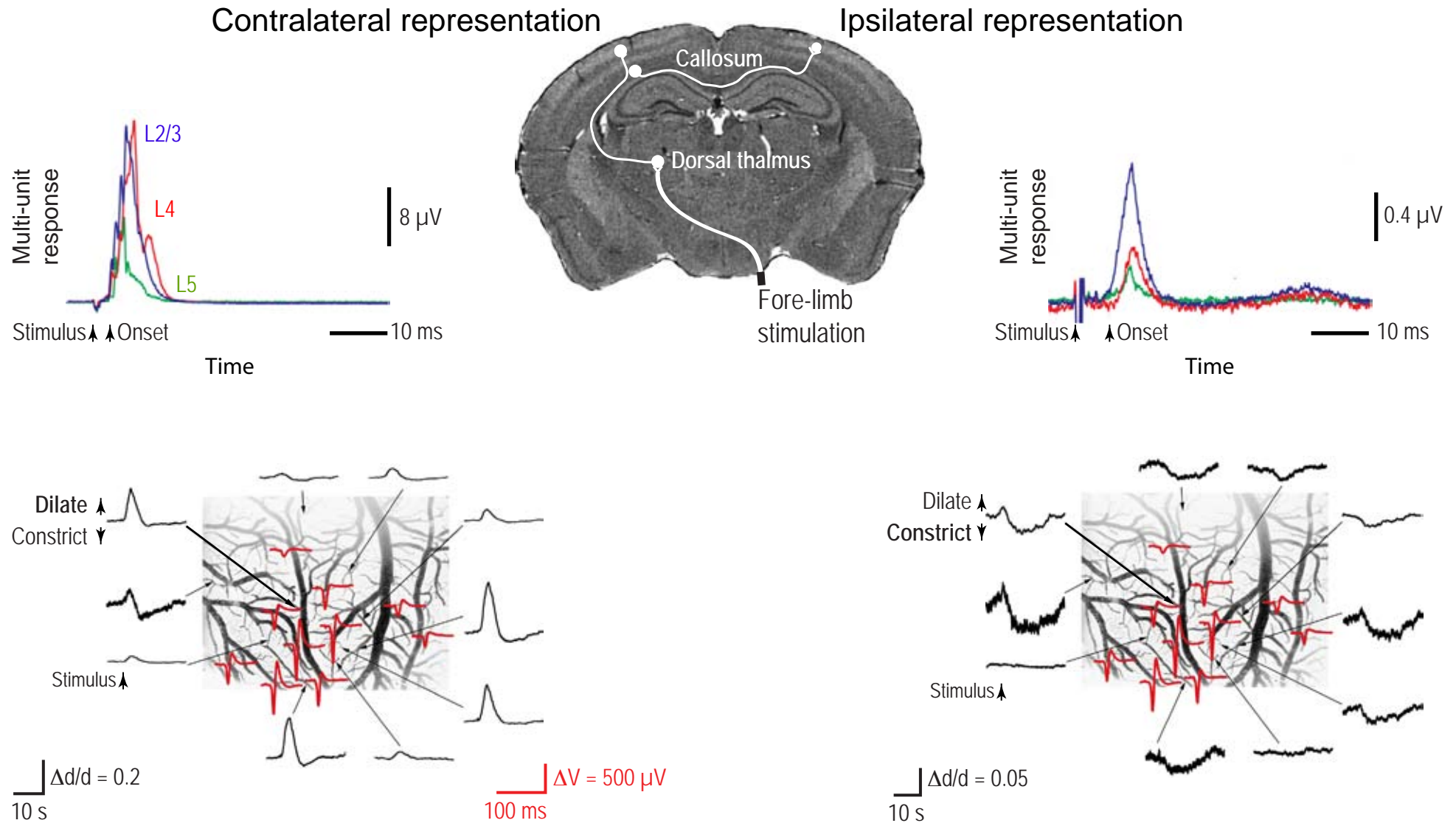
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Example of changes in the lumen of surface arterioles for the two cortical hemispheres



Neuronal activity changes blood flow - but logic remains to be deciphered

Example of changes in the lumen of surface arterioles for the two cortical hemispheres



Neurovascular coupling

Contemporary models (not independent)

Metabolic hypothesis:

Coupling mediated by vasoactive products of metabolism, such as such as H^+ or adenosine, that are released from active neurons and glia.

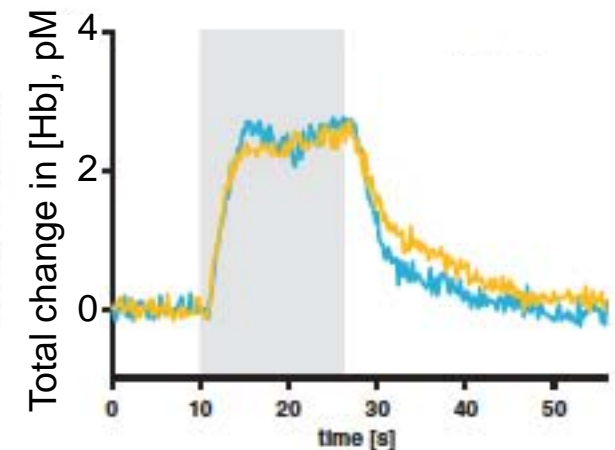
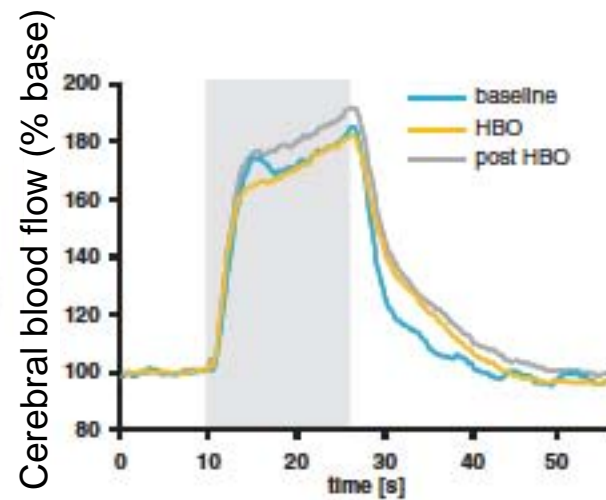
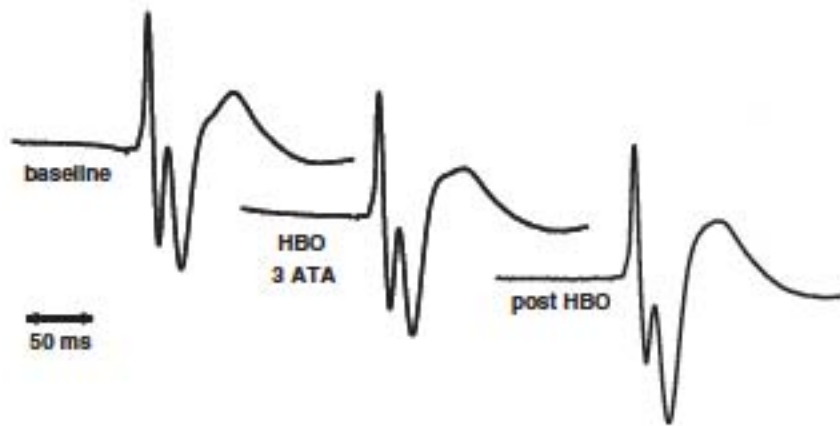
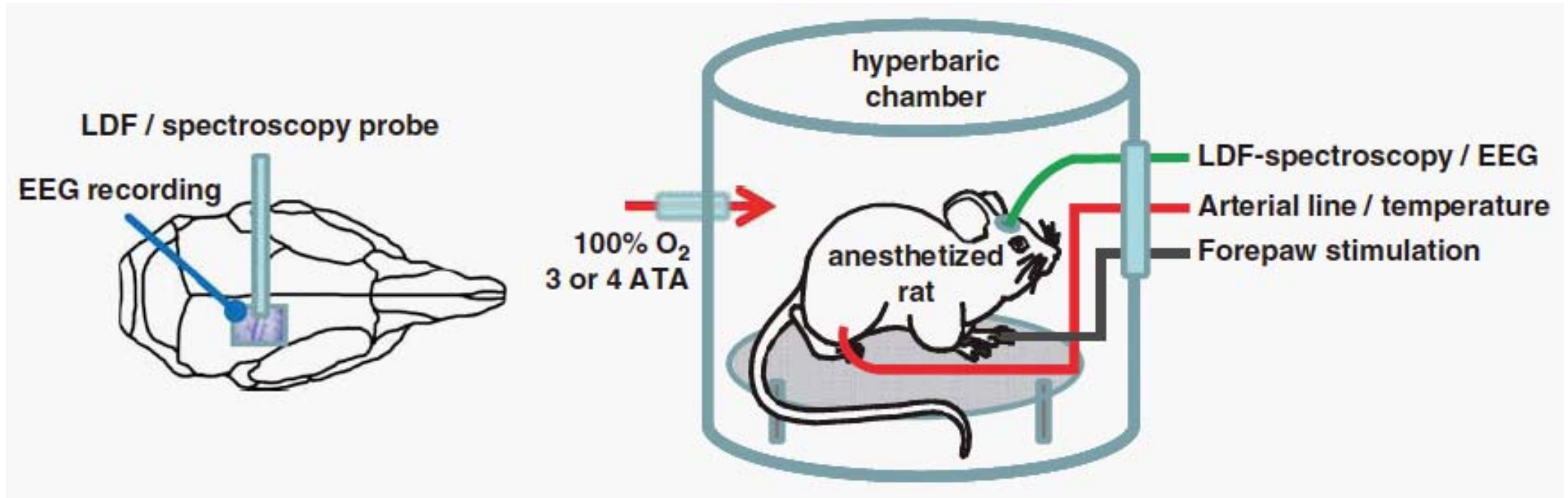
Neuronal hypothesis:

Coupling mediated by neuronal energy demand (synaptic load), either directly via interneurons or indirectly via astrocytes and NO.

Hemoglobin deoxygenation hypothesis:

Hb as master regulator of organ blood flow, such that wherever O_2 is released from Hb, the vasodilators NO or ATP is delivered.

Hyperoxygenation (3 atmospheres) does not affect cerebral blood flow



Neural activity leads to competition between dilation and constriction

- Pyramidal activation of astrocytes leads to release of vaso modulators (e.g., Harder and McVicar laboratories)
- Interneuron release of neuropeptides (e.g., Hamel and Rossier laboratories)
- Extrinsic feedback from subcortical inputs, particularly from cholinergic and serotonergic nuclei

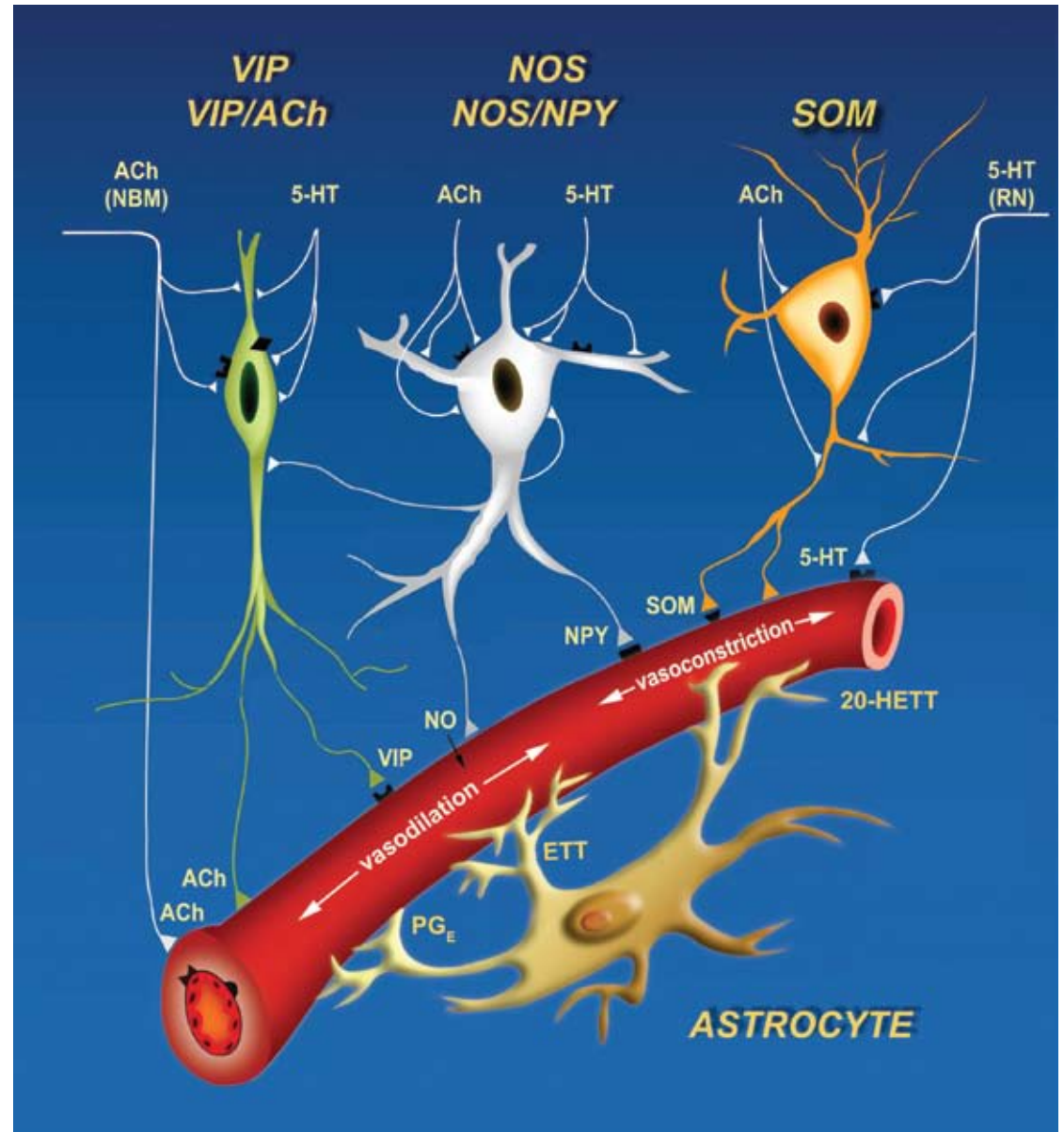


Figure adapted from Cauli, Tong, Rancillac, Serluca, Lambolez, Rossier & Hamel (J Neurosci 2004) and Iadecola & Nedergard (Nat Neurosci 2007)

Goal: Spatiotemporal equations for cortical blood flow dynamics

$$\text{Vascular output} \equiv f \left(\begin{array}{c} \text{Smooth muscle tension} \\ \vdots \\ \text{Vascular architecture} \end{array} \right)$$

$$\text{Smooth muscle tension} \equiv f \left(\begin{array}{c} \text{SOM+ inhibitory interneuron activation} \\ \text{VIP+ inhibitory interneuron activation} \\ \vdots \\ \text{Astrocyte activation} = f(\text{excitatory cell activation}) \\ \text{Extracortical and endothelial contributions} \\ [\text{O}_2]_{\text{tissue}} \end{array} \right)$$

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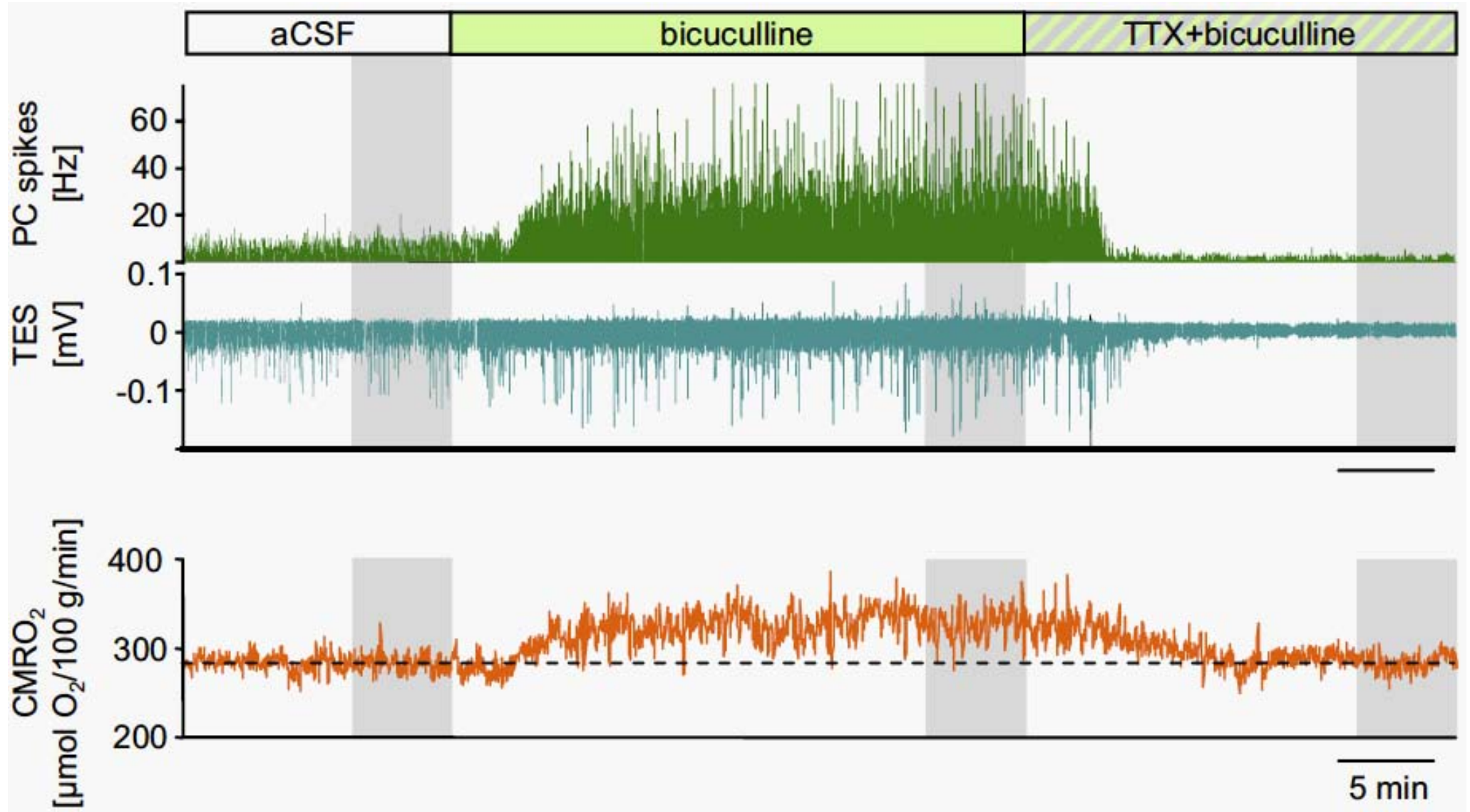
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Open issues: Things we should and perhaps could do next

Cerebral oxygen metabolism versus components of neuronal activation



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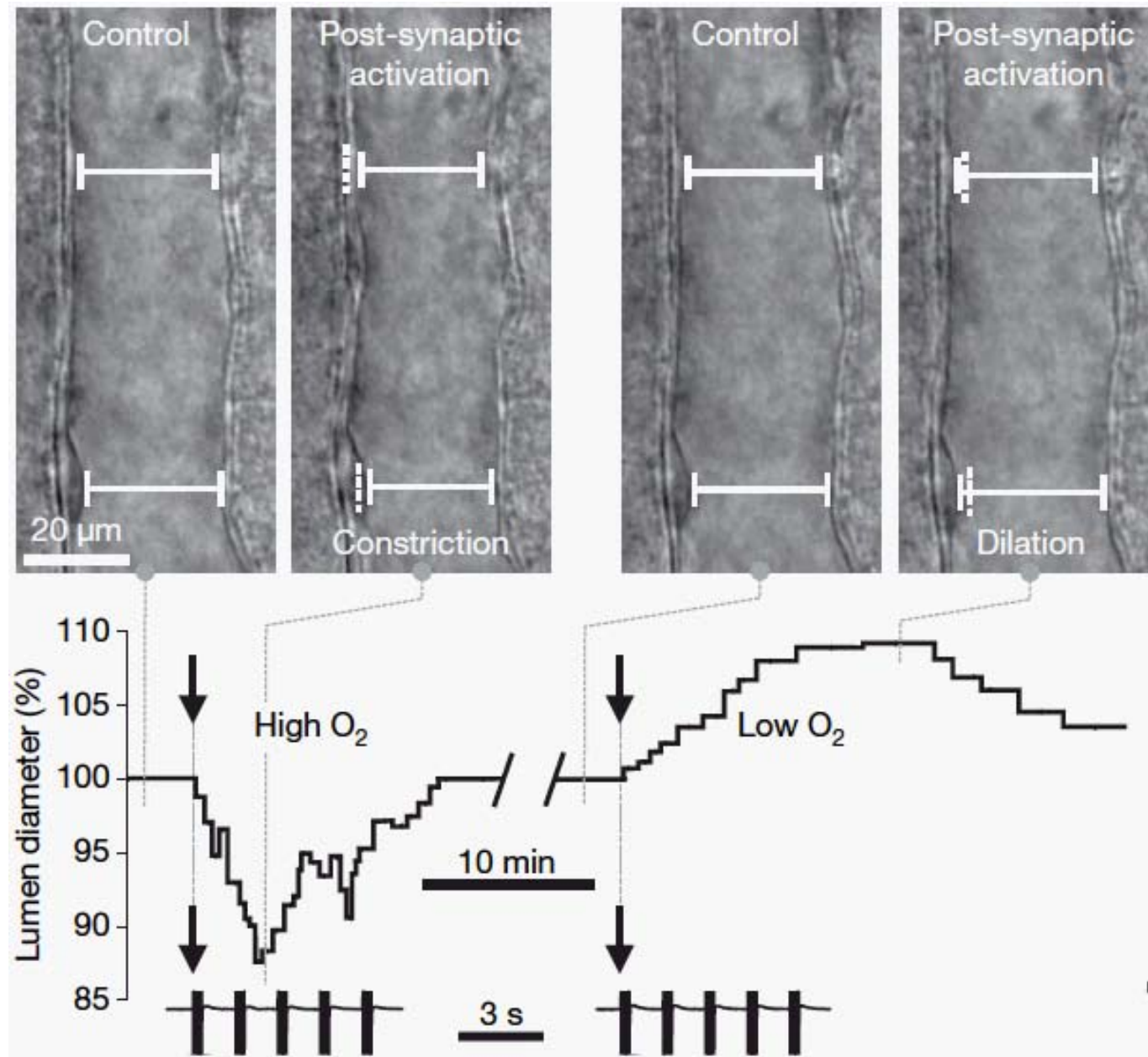
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Open issues: Things we should and perhaps could do next

Brain slice as a test bed for assessing the direct role of O₂



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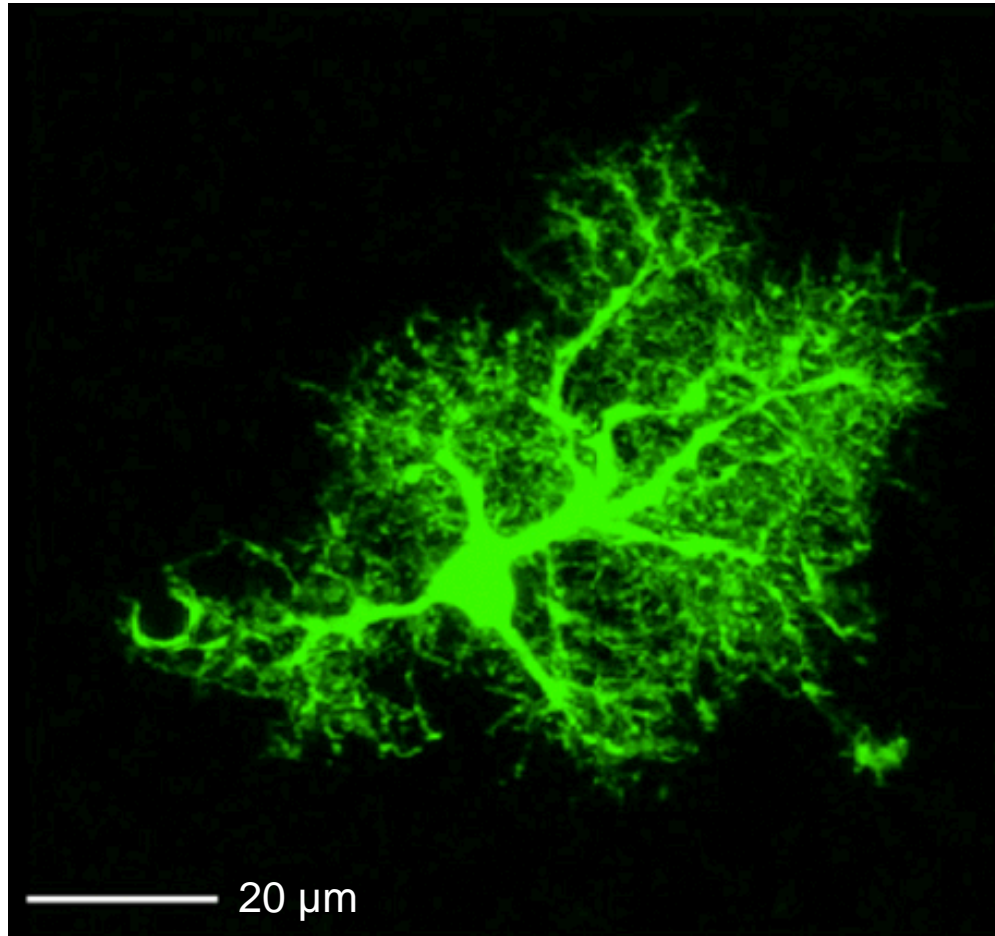
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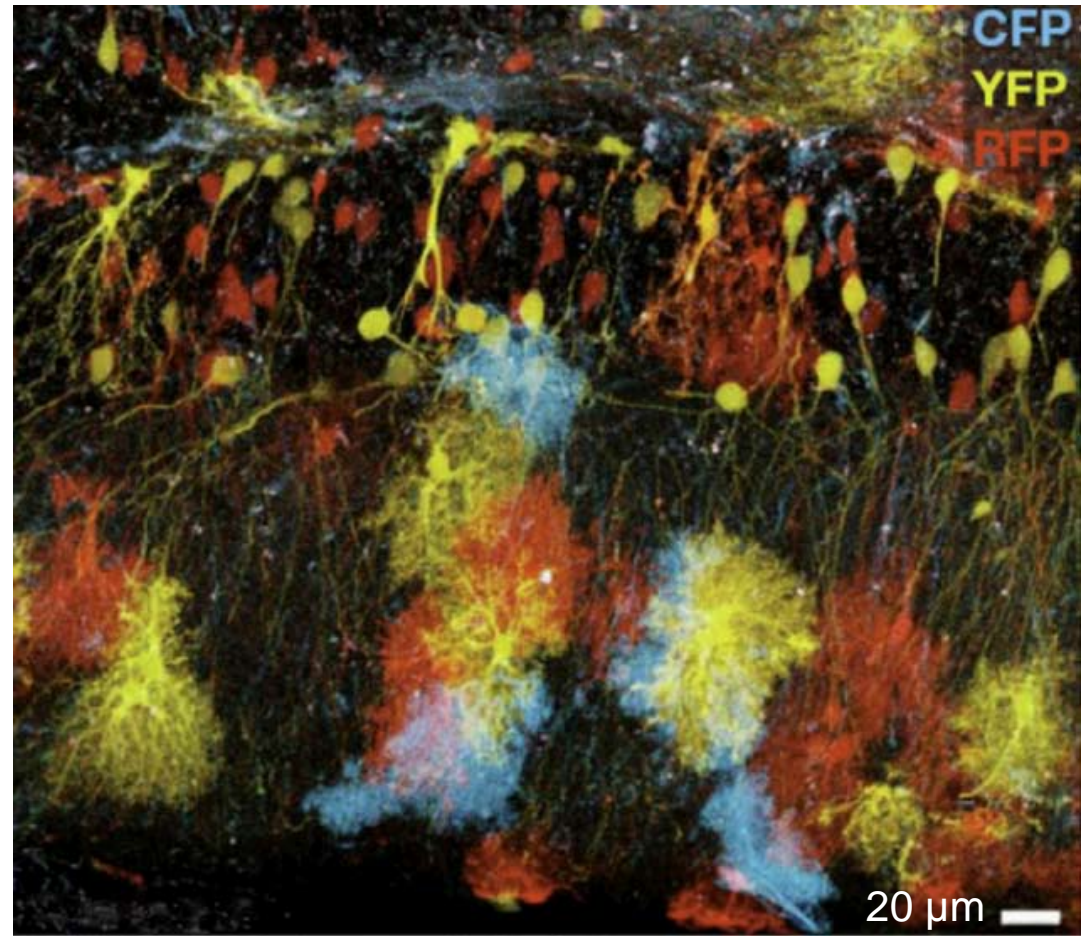
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Open issues: Things we should and perhaps could do next

Astrocytes: The other brain cell

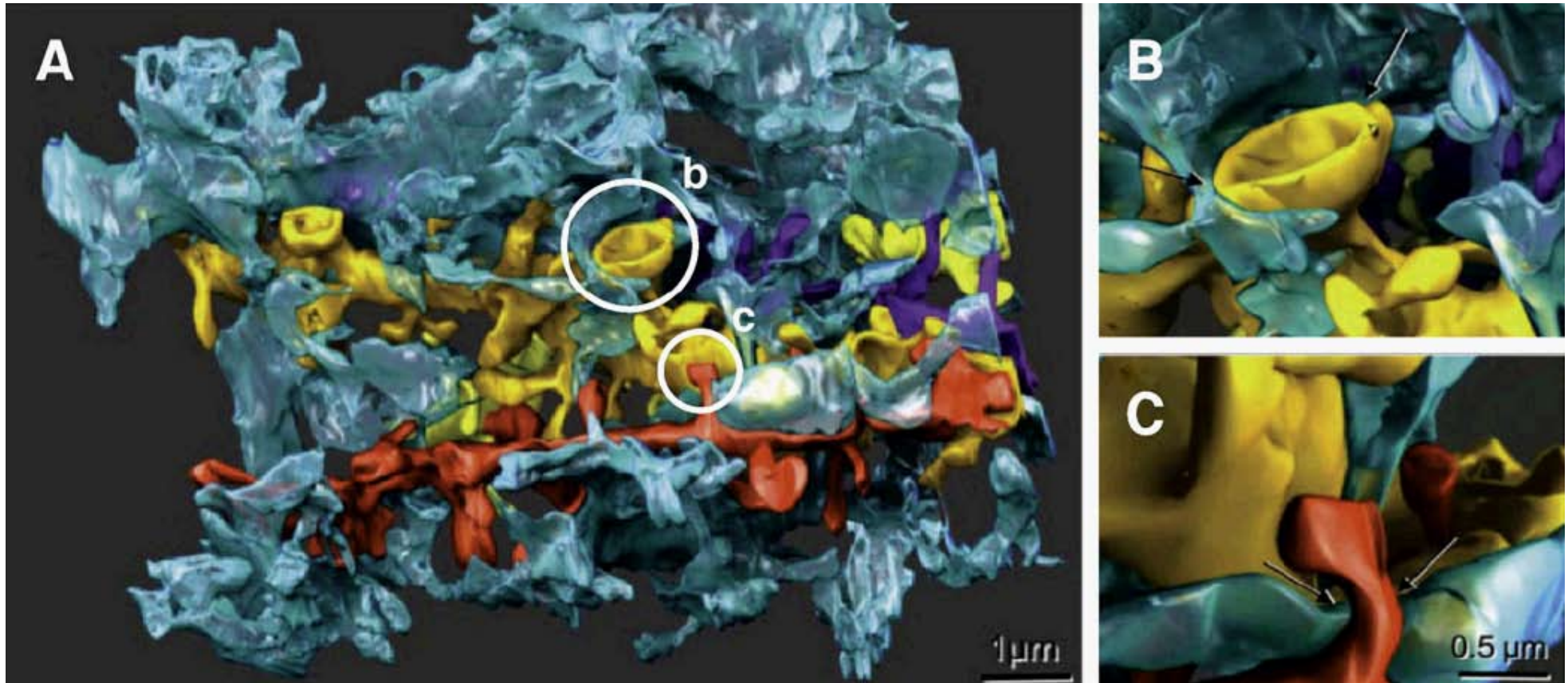


Reichenbach, Derouiche & Kirchhoff
(Brain Research Reviews 2010)



Livet, Weissman, Kang, Draft, Lu, Bennis,
Sanes & Lichtman (Nature 2007)

Astrocytes: The tripartite (two neurons and one astrocyte) synapse



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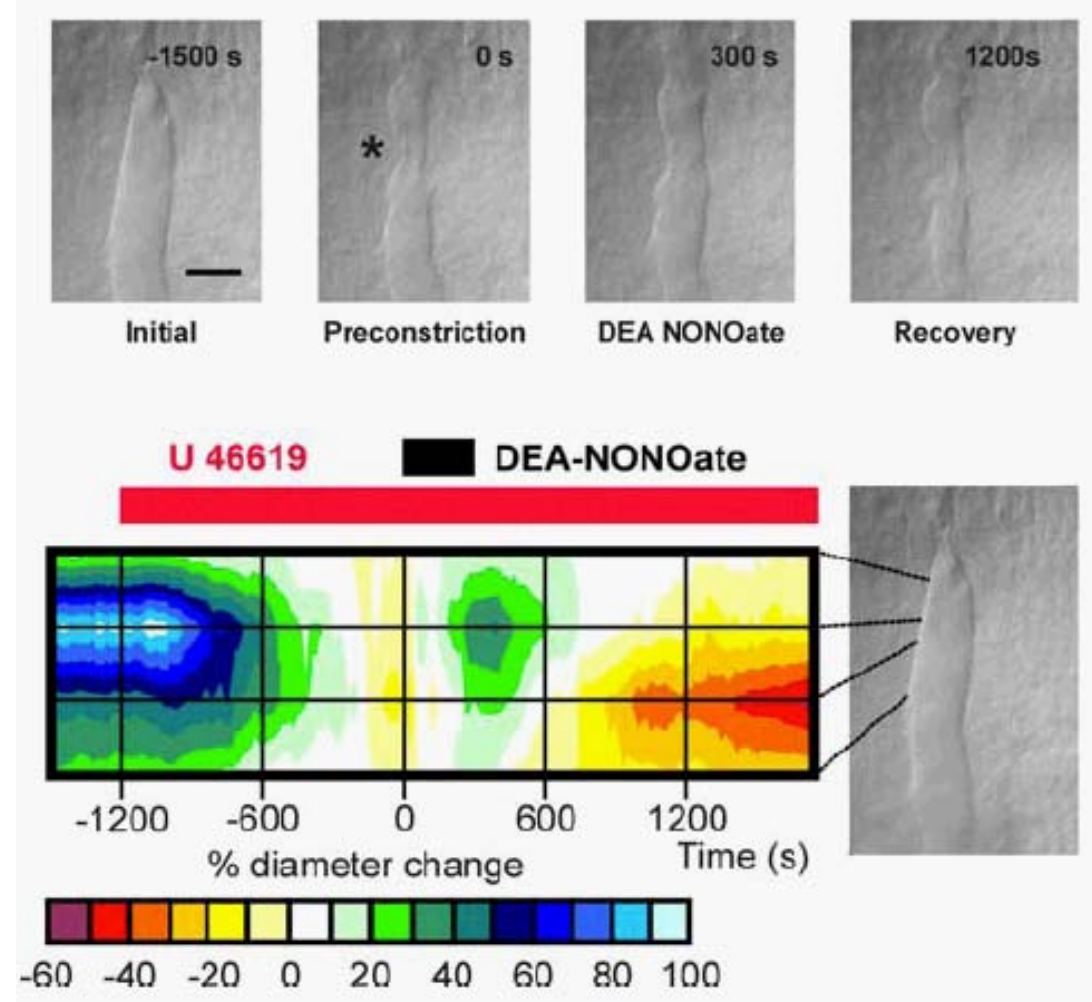
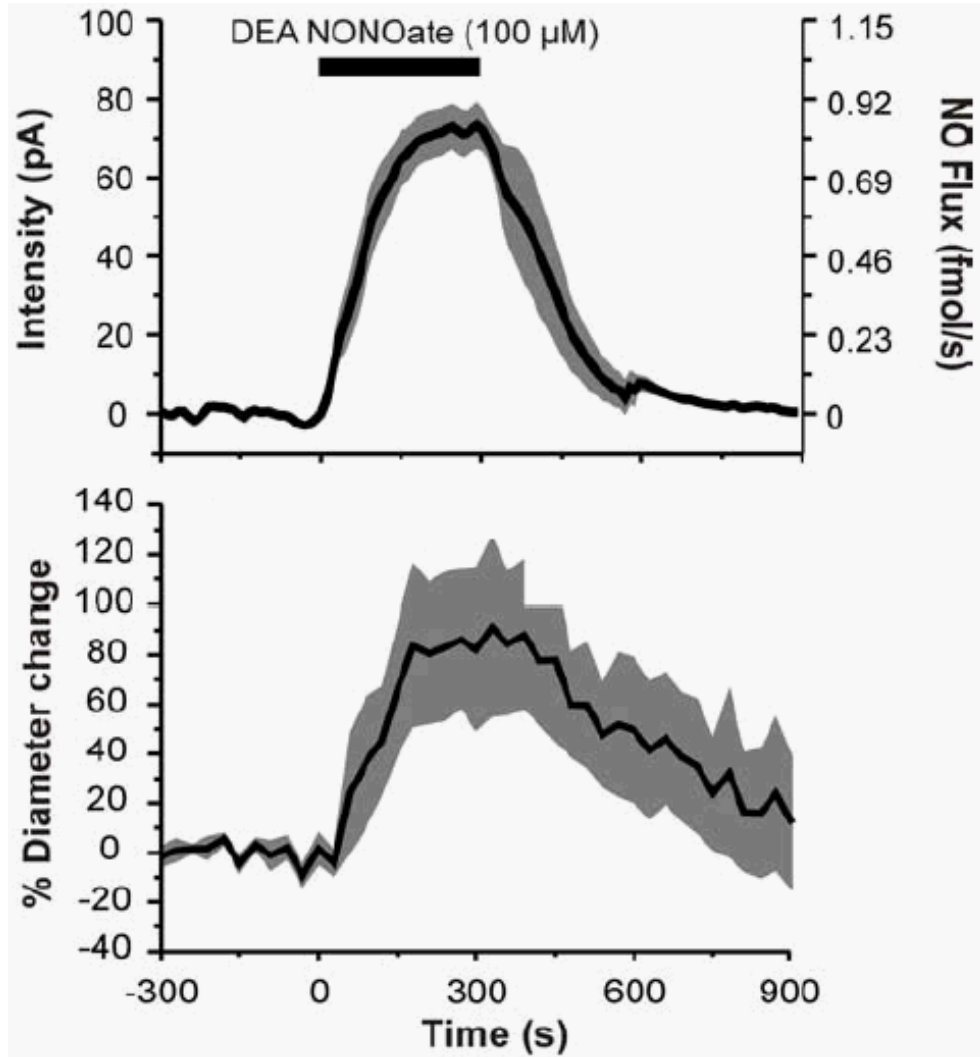
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Brain slice as a test bed for assessing neurovascular signaling



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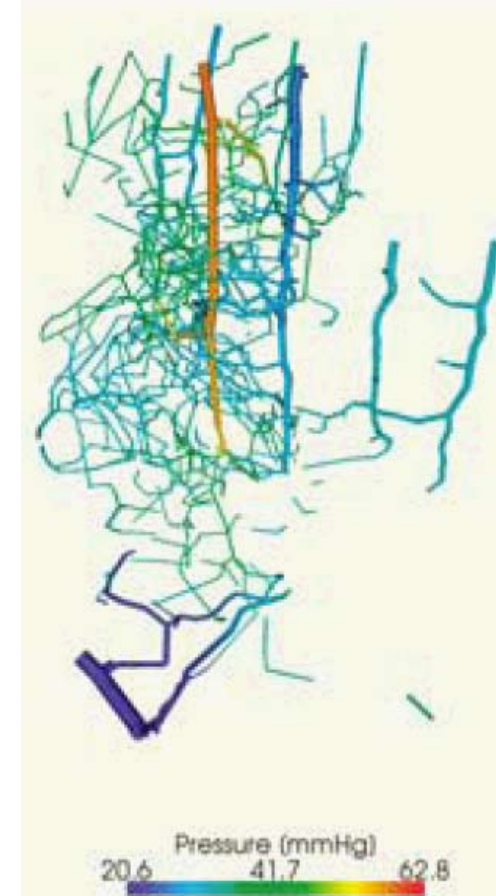
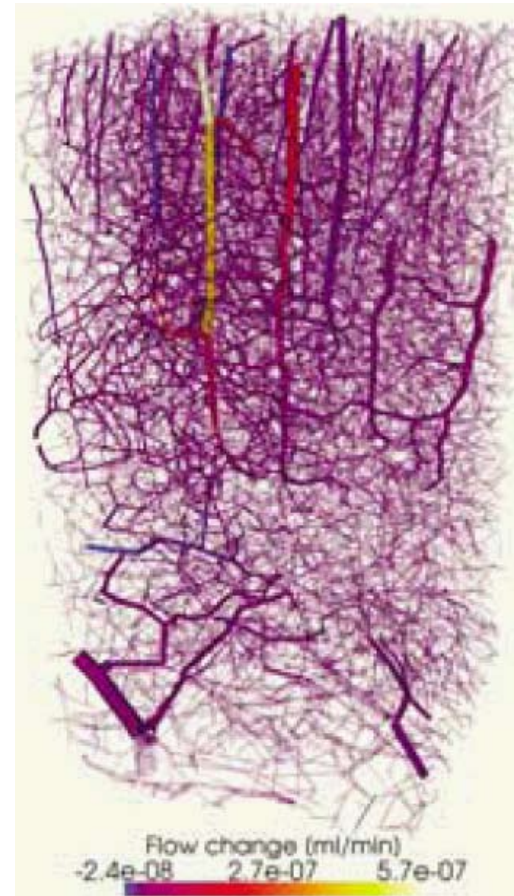
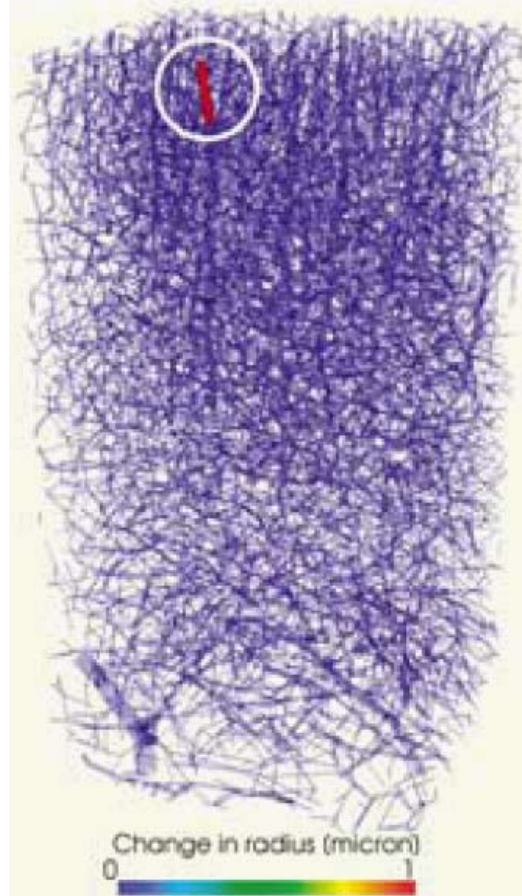
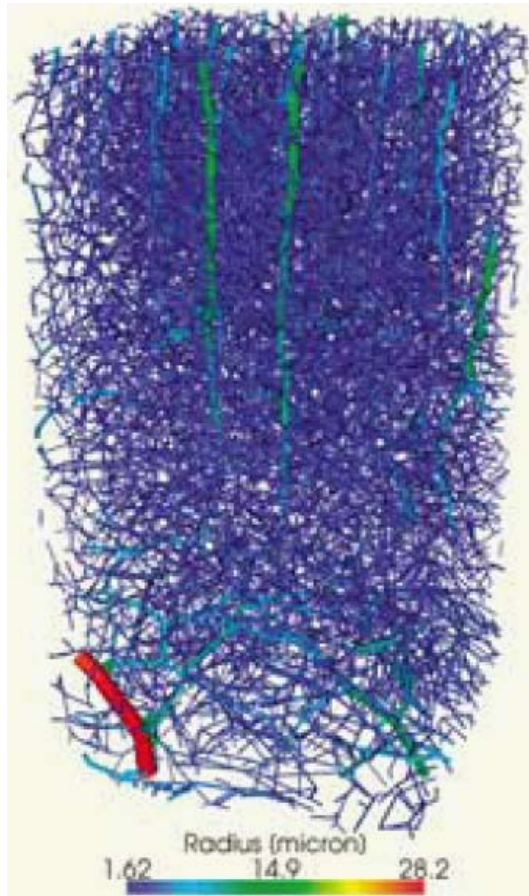
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Open issues: Things we should and perhaps could do next

3-D anatomy of cortical vasculature

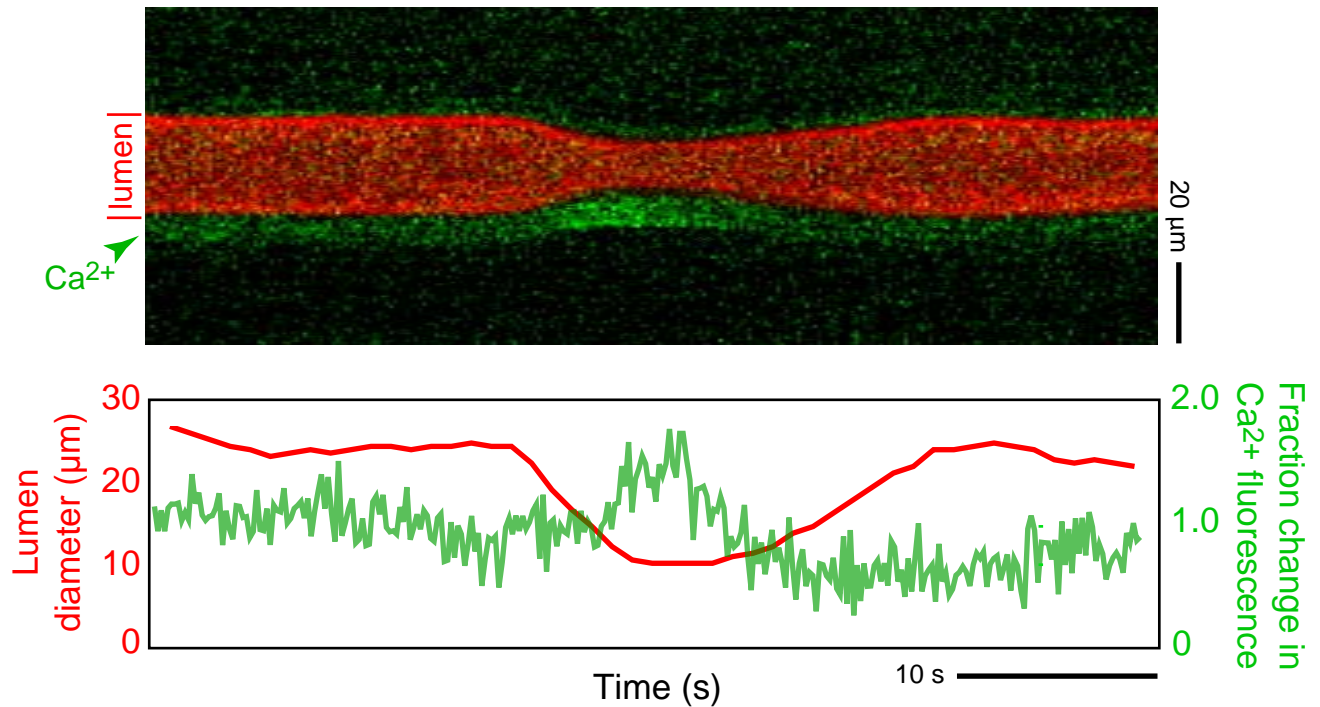
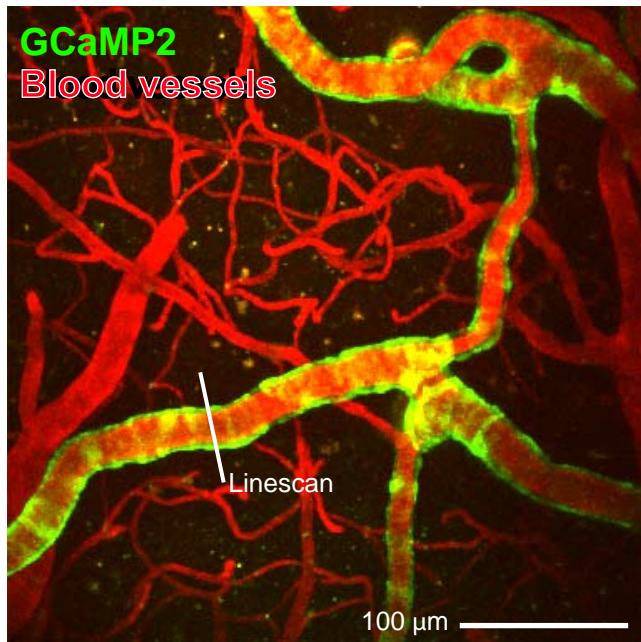


Neurovascular coupling

**What are some of the ties with emerging techniques
in neuroscience?**

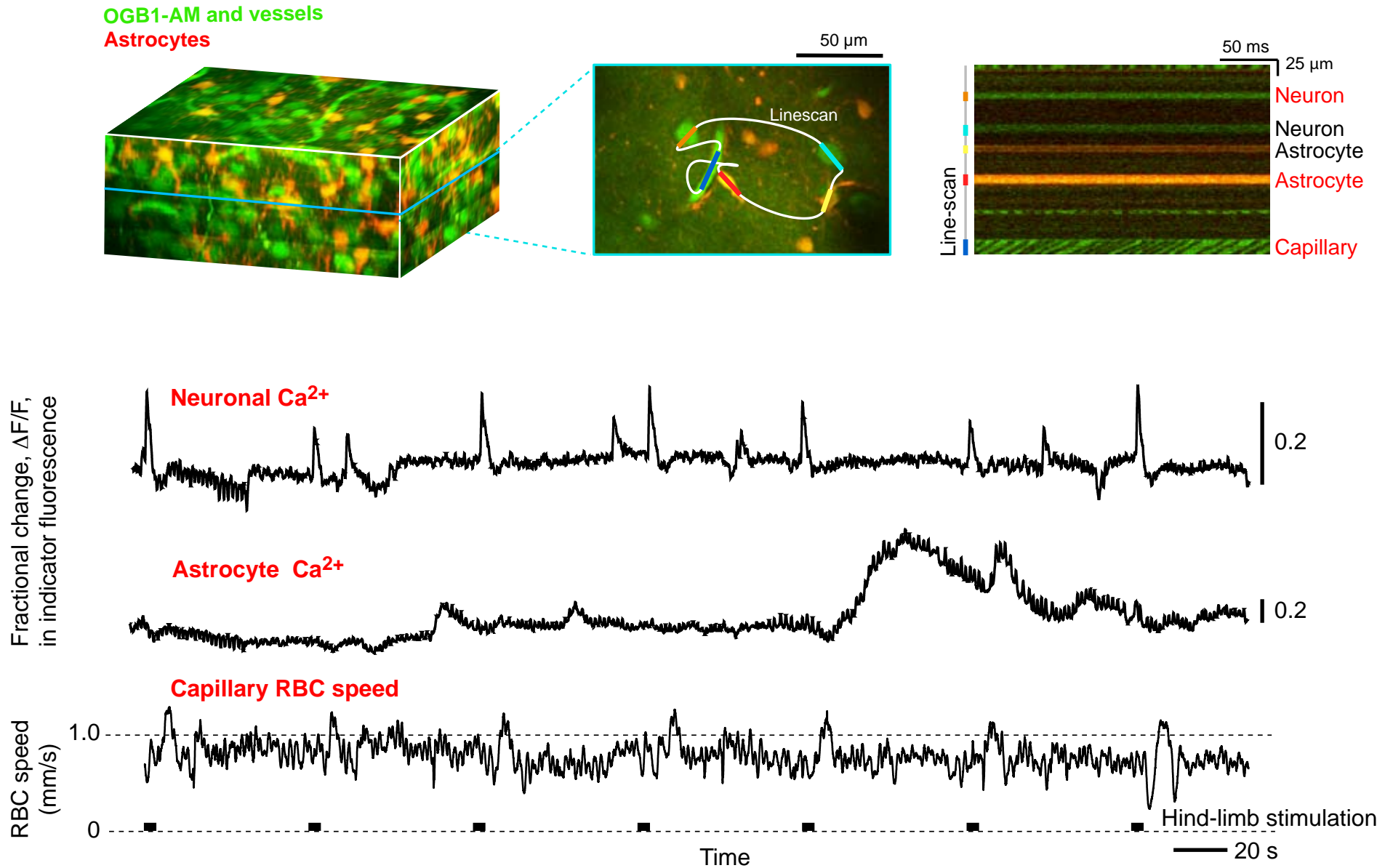
Smooth muscle activation may be imaged concurrent with blood flow

Example of measurements of muscle $[Ca^{2+}]$ and lumen diameter in α -actin-BAC-GCaMP2 mice*



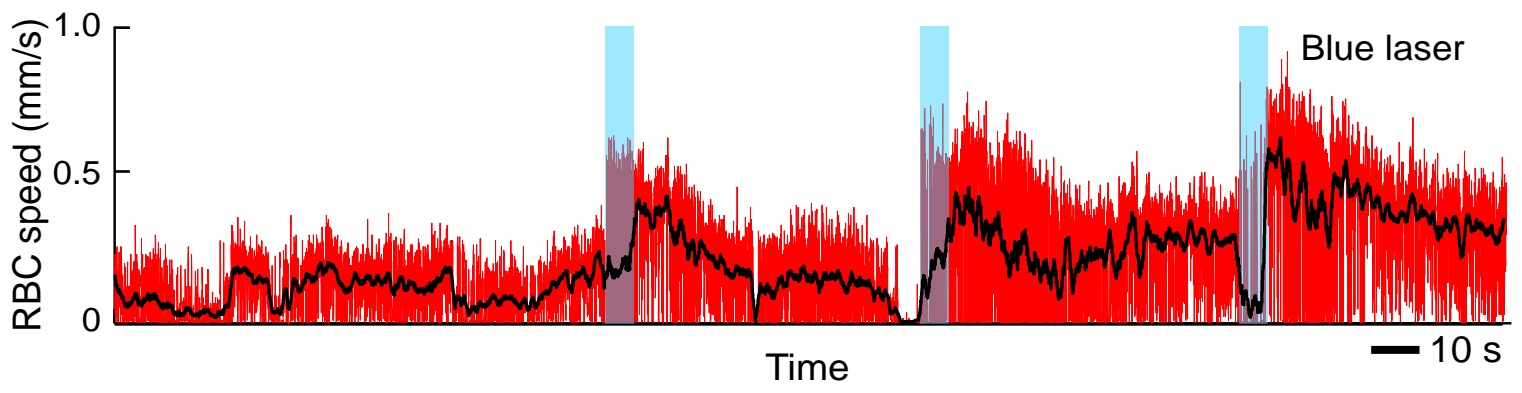
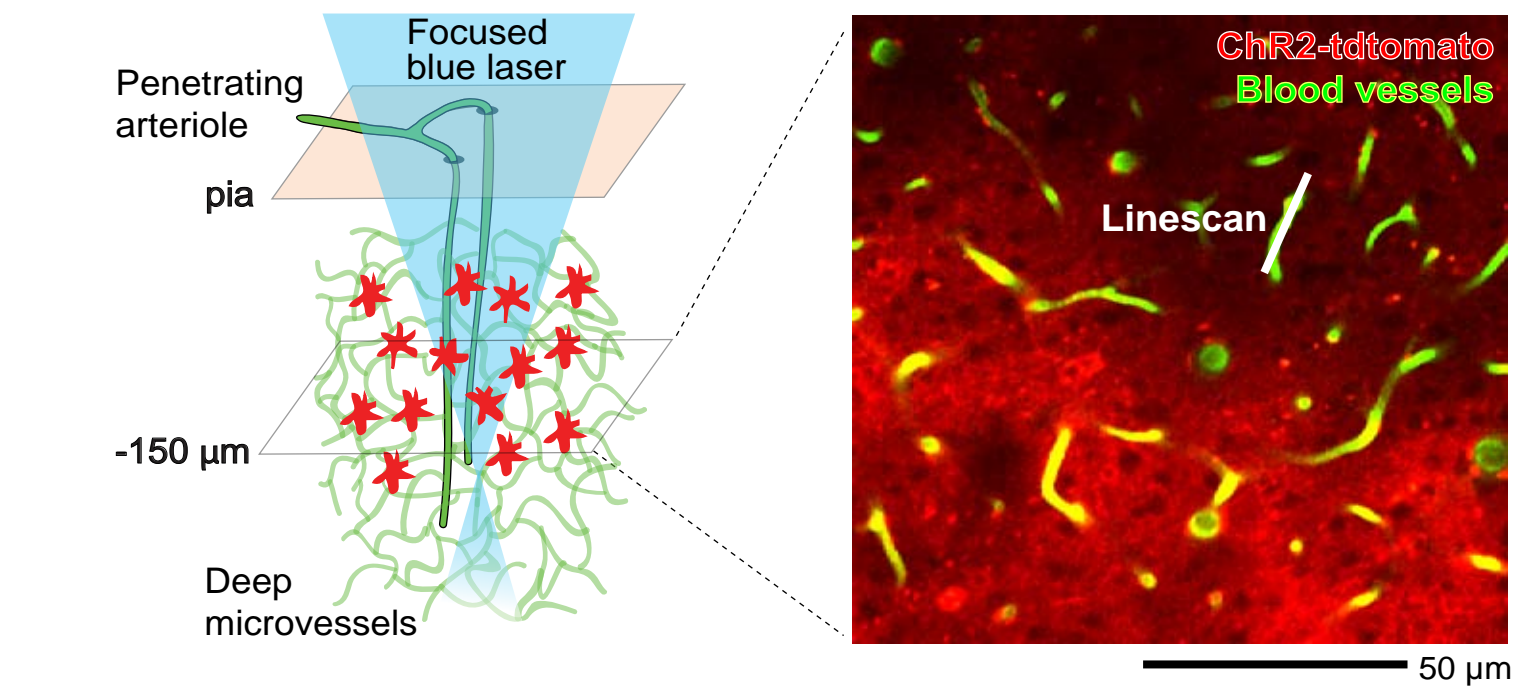
*Ji, Feldman, Deng, Greene, Wilson, Lee, Johnston, Rishniw, Tallini, Zhang, Wier, Blaustein, Xin, Nakai & Kotlikoff (JBC 2004)
Shih, Driscoll & Kleinfeld (unpublished)

Simultaneous *in vivo* recordings relate blood flow to intracellular $[Ca^{2+}]$



Targeted optogenetic molecules to selectively activate specific cell types*

Example of astrocytes (GFAP-Cre +/- mice and FLEX-ChR2-tdtomato construct in AAV2/5)



*Boyden, Zhang, Bamberg, Nagel, Deisseroth (Nat Neurosci 2005)
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David Hansel – “Selective persistent states in balanced networks”

11:30 am - 1:00 pm

Carl von Vreeswijk - “Emerging techniques for the analysis of network dynamics”

Friday – 29 October

9:30 am - 11:00 am

Ila Fiete – “Path integration and position encoding in grid cells”