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
9:30 am - 11:00 am
Bruno Weber - "Cerebral blood flow and metabolism: Feeding a hungry organ"

11:00 pm - ∞
Open issues: Things we should and perhaps could do next
Highlights of the rodent angiotome: A work in progress

Adapted from Tsai, Kaufhold, Blinder, Friedman, Dew, Karten, Lyden & Kleinfeld (2009) and Blinder*, Tsai*, Kaufhold & Kleinfeld (in preparation)
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

Contralateral representation

Multi-unit response

L2/3

L4

L5

Stimulus Onset

Time

8 µV

10 ms

Dorsal thalamus

Fore-limb stimulation

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
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

Contra\-lateral representation

Ipsi\-lateral representation

\[ \Delta \frac{d}{d} = 0.2 \]

\[ \Delta V = 500 \mu V \]

\[ 100 \text{ ms} \]

\[ 10 \text{ s} \]
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 O₂ is released from Hb, the vasodilators NO or ATP is delivered.
Hyperoxygenation (3 atmospheres) does not affect cerebral blood flow

Lindauer, Leithner, Kaasch, Rohrer, Foddis, Fuchtemeier, Offenhauser, Steinbrink, Royl, Kohl-Bareis & Dirnagl (JCBFM 2010)
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 & Needergard (Nat Neurosci 2007)
Goal: Spatiotemporal equations for cortical blood flow dynamics

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

Smooth muscle tension \( \equiv f \left( \begin{array}{c}
\text{SOM+ inhibitory interneuron activation} \\
\text{VIP+ inhibitory interneuron activation} \\
\vdots \\
\text{Astrocyte activation} = f(\text{excitatory cell activation}) \\
\text{Extracortical and endothelial contributions} \\
\left[ O_2 \right]_{\text{tissue}}
\end{array} \right) \)
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Open issues: Things we should and perhaps could do next
Cerebral oxygen metabolism versus components of neuronal activation

Thomsen, Piilgaard, Gjedde, Bonvento & Lauritzen (Journal of Neurophysiology 2009)
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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

Gordon, Choi, Rungta, Ellis-Davies & MacVicar (Nature 2009)
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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)

Astrocytes: The tripartite (two neurons and one astrocyte) synapse
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Open issues: Things we should and perhaps could do next
Brain slice as a test bed for assessing neurovascular signaling

Rancillac, Rossier, Guille, Tong, Geoffroy, Amatore, Arbault, Hamel & Cauili (Journal of Neuroscience 2006)
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Open issues: Things we should and perhaps could do next
3-D anatomy of cortical vasculature

Reichold, Stampanoni, Keller, Buck, Jenny & Weber (JCBFM 2009)
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*

Shih, Driscoll & Kleinfeld (unpublished)
Simultaneous *in vivo* recordings relate blood flow to intracellular [Ca\textsuperscript{2+}]

OGB1-AM and vessels

Astrocytes

Neuronal Ca\textsuperscript{2+}

Astrocyte Ca\textsuperscript{2+}

Capillary RBC speed

Shih, Driscoll & Kleinfeld (unpublished)
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)
Shih, Driscoll & Kleinfeld (unpublished)
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**Open issues: Things we should and perhaps could do next**

Thursday – 28 October
9:30 am - 11:00 am
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”