

Simultaneous Imaging of Cerebral Blood Flow and Partial Pressure of Oxygen During Functional Activation



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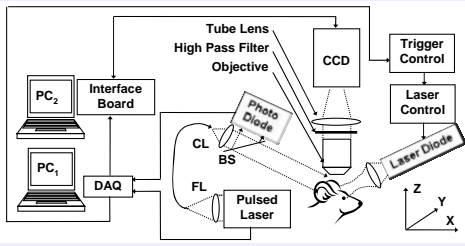
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Introduction

- Monitoring the spatio-temporal characteristics of partial pressure of oxygen (pO₂) and cerebral blood flow (CBF) is crucial for studying normal and pathophysiological brain conditions.
- We present the development of a novel simple imaging technique that provides high-resolution real-time two-dimensional images of pO₂ and CBF in the brain vasculature by combining phosphorescence lifetime imaging with laser speckle contrast imaging.
- The oxygen-dependent quenching of phosphorescence provides a more direct way for pO₂ measurement [2] than previously used spectral imaging [1].
- We demonstrate the potential of the system as a novel tool for quantitative analysis of the dynamic delivery of oxygen by imaging the pO₂ and CBF during cortical spreading depression in rats. The results from this system will guide a better understanding of neurovascular coupling in normal and diseased brains.

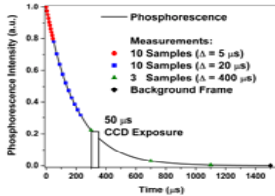
Methods



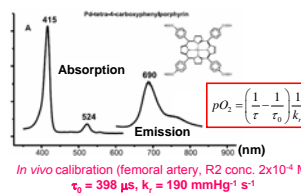
Experimental setup. Two personal computers (PC1 and PC2) are controlling triggering signals and image acquisition. CCD – charge coupled device, BS – beam splitter, CL – collimating lens, FL – focusing lens, DAQ – data acquisition board.

- The imaging was performed through the sealed cranial window (4x4 mm opening; dura mater removed).
- The camera (Imager QE, La Vision) frame rate was synchronized with the triggering rate of the pulsed laser (10 Hz) used for excitation of phosphorescence (Brilliant, 532 nm wavelength, 4.5 ns pulse duration).
- pO₂ in blood was obtained by measuring the phosphorescence lifetime of Oxypor R2 [3].
- CBF was estimated based on speckle contrast imaging at $\lambda = 808 \text{ nm}$ [4].
- The whole imaging cycle of obtaining frames of both pO₂ and CBF takes $\approx 4 \text{ s}$.

Sampling of the Phosphorescence Intensity Decay

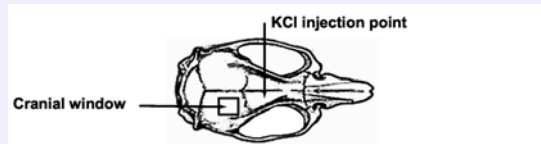


Oxypor R2: Gen 2 polyglutamic Pd porphyrin dendrimer

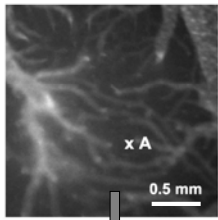


Imaging of Cortical Spreading Depression

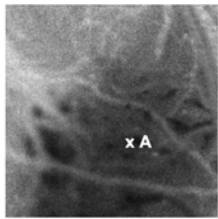
- CSD is a self-propagating wave of cellular depolarization that has been implicated in migraine and in progressive neuronal injury after stroke and head trauma [5]. The mechanism of CSD wave propagation remains poorly understood [6], and it is the subject of intense research [7].
- 1x1 mm opening on frontal bone was used to induce the CSD by injection of KCl solution.
- The course of the induced CSD waves was monitored with our setup during 10 minutes.



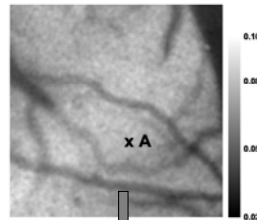
Phosphorescence Intensity



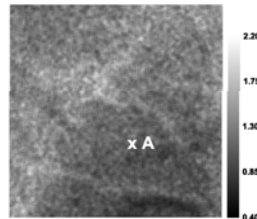
pO₂ (mmHg) at t = 107 s



Speckle Contrast

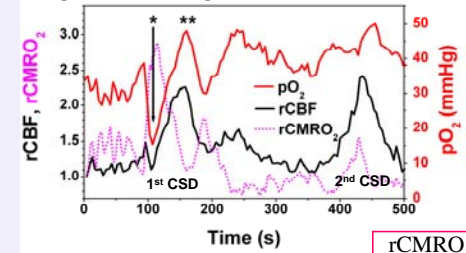


Blood Flow (a.u.) at t = 105 s



Imaging of Cortical Spreading Depression

rCBF, rCMRO₂ and rCMRO₂ Temporal Evolutions at Point A



- The large simultaneous drops in both pO₂ and CBF upon arrival of the 1st CSD can be clearly seen (*). They are followed by the significant increase (**) of pO₂ and CBF [8].
- The decrease in CBF at 107 s (*) is particularly interesting, since it was likely caused by CSD-induced vasoconstriction.
- The absence of a similar CBF decrease at the 2nd CSD (= 430 s) and absence of the pO₂ drop at the same time may suggest that CSD-induced vasoconstrictions play a dominant role in creating the large pO₂ decay at the 1st CSD.

Conclusions

- We developed a simple novel imaging technique that provides 2D maps of pO₂ in the brain vasculature and CBF by combining phosphorescence lifetime imaging with laser speckle contrast imaging.
- The excitation of dye with the laser pulses instead of with flash lamp pulses and usage of high light-collection efficiency optics allowed us to obtain high speed and high SNR images of pO₂ without image intensifier. In addition, phosphorescence lifetime measurements are not sensitive to the changes in absorbance of other tissue chromophores.
- The capability of our system was demonstrated by imaging CSD in rats.
- The instrument has the potential to be a novel tool for quantitative analysis of the dynamic delivery of oxygen that will lead to a better understanding of neurovascular coupling in normal and diseased brain.

References

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