Multimodal optical neural imaging with VCSEL light sources

Techniques in Biophotonic Imaging Photonics Media Webinar
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Dr. Ofer Levi
Institute of Biomaterials and Biomedical Engineering
The Edward S. Rogers Sr. Department of Electrical and Computer Engineering,
University of Toronto, Toronto, Ontario, M5S 3G9
Biophotonics.utoronto.ca

Our research areas

We develop bio-sensors and biomedical imaging systems

- Miniature bio-sensors for optical sensing inside Lab-on-a-Chip micro-fluidics chips
- Bio-sensors and optical imaging systems for portable in vivo imaging of neural activity and disease progression applications
Optical imaging and stimulation

Optical brain imaging and stimulation is minimally invasive. It avoids artifacts in electrical recording or stimulation.

Near IR optical imaging

We like to use near IR light for live tissue imaging. Relatively cheap, high resolution, safe.

Favorable optical tissue properties:
\[ \mu_{\text{abs}} \sim 0.04 \text{ cm}^{-1} \quad \mu_{\text{scattering}} \sim 10 \text{ cm}^{-1} \]

Other benefits:
- Low tissue auto-fluorescence
- Increased availability of near IR molecular markers (Cy5.5, IR800, NIR-664, etc.)
- Emerging near IR fluorescent proteins
- Spectroscopy of tissue chromophores (concentration of lipids, water, oxygenation level)

blood flow: Laser speckle contrast imaging

Speckle is an interference phenomenon: Constructive/destructive interference of diffusely reflected light

- SPECKLE PATTERN results: Dark and light spots seen at detector
- What if there is movement in the sample? SPECKLE CONTRAST


blood oxygenation: Intrinsic optical signal imaging

Tissue Oxygen metabolism is studied by multi-wavelength reflectance imaging, called Intrinsic Optical Signal imaging

We use 3 wavelengths: 670, 795, 850 nm

Apply Beer-Lambert law for concentration changes (< mM)

Coherence Modulation: Current Sweeping in a VCSEL

VCSEL: Vertical Cavity Surface Emitting Laser

- Near lasing threshold, emits as a single transverse mode
- Higher currents excite multiple transverse modes
- By rapidly sweeping the operating current, one can superimpose the laser modes, broadening spectrum

Result: tuneable coherence

VCSEL illumination (spot shape) in the far field regime

Current sweeping allows a fast sweep between all spatial modes, a reduction of the coherence effects and creation of a high brightness “LED like” source

Coherence length evaluation

670 nm

795 nm

850 nm

- Current sweep can broaden VCSEL laser emission spectra, integrated over ~ few msec. of a camera frame
- Interferograms of sweep mode show corresponding reduced coherence, similar for each of 3 wavelengths

Coherence length: $L_c = \frac{2c\ln(2)}{\pi} \cdot \frac{1}{\Delta \nu} \approx 0.44 \frac{\lambda_0^2}{\Delta \lambda}$

Simultaneous IOSI and LSCI

Fast frame by frame switching between different lasers and single / multi-transverse modes allow imaging flexibility

680 nm - single mode  795 nm - multimode

680 nm - multimode  850 nm - multimode

Single mode - imaging blood flow (high coherence)
Multi-mode - imaging tissue oxygenation (low coherence)
Results: LSCI and IOSI

Grey – Induced ischemia period
Knot to create a transient ischemia

Vessel Clustering

Simultaneous imaging of blood flow and oxygenation during Ischemia allows automated clustering of veins and arteries

Multi-exposure LCS1-vessel depth discrimination

Applying multi-exposure technique with VCSELs:
- improved flow velocity evaluation
- Estimating the contribution of static and dynamic speckle patterns from skull and tissue - depth discrimination (~ 200 μm)


Blood Brain Barrier Disruption Imaging

A leak in the barrier results in flow reduction in veins

Vein/Artery Blood flow ratio

Fluorescence (d)
**Blood Brain Barrier Disruption Imaging**

Comparison of blood flow to fluorescence changes

Application of BBB disrupting drug (DOC) results in fluorescent marker leakage and flow velocity changes

S. Dufour et al. “Laser speckle contrast imaging as an intrinsic method to monitor blood brain barrier integrity” in preparation

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**Multimodal imaging and electrophysiology: Epilepsy**

Multimodal imaging of blood flow, oxygenation and fluorescence is compared to electrophysiology recording

S. Dufour et al. “Multimodal optical brain imaging for in vivo epilepsy studies”, in preparation
Forward looking: Our Multi-modality high sensitivity imaging system can be easily modified to incorporate brain stimulation.

Summary

• Developed a multi-modality optical neural imaging system, using a fast camera and miniature VCSELs.
• This imaging system is a fast, versatile, miniature, low cost imaging solution for optical brain imaging.
• Study the progression and treatment of neurological disorders including Ischemic stroke and Epilepsy.
• Discussed the path to a portable imaging system, for brain imaging in freely-behaving animals.
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