Probing human brain function with (time-resolved) diffusing-wave spectroscopy

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1. Optical imaging of brain function
2. Diffusing-wave spectroscopy
3. Slow functional signals
4. Transient signals
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Why brain imaging?

cognitive processes
  feeling
  thinking
  acting

representations in the brain
  spatio-temporal activation patterns

current issues:
  - how does the brain process cognitive tasks?
  - physiological origins of psychological disorders
  - post-trauma rehabilitation
  - intensive care (stroke, ...)

● in-vivo-, non-invasive methods

sensoric homunculus:
Optical methods for measuring functional brain activity

- low cost (relative to MRI, ...)
- portable
- non-ionizing radiation
- non-invasive
- functional contrast
- extrinsic markers: fluorophores
- intrinsic markers:
  - hemoglobin, cytochrome, water, ...
- continuous measurements

- laser Doppler
- fluorescence imaging
- reflectance imaging
  ...
Optical imaging through the skull?

challenges:

multiple light scattering

absorption

- scalp, skull
- cell membranes
- vesicles
- mitochondria
- blood vessels
- hemoglobin
- melanin

near infrared (NIR): “optical window”

● reduced penetration depth, spatial resolution
Putting multiple scattering to work

illumination with coherent light:

\[ \text{Laser} \]

autocorrelation function of scattered field:

\[ g_1(\tau) = \int_{L_o}^{\infty} ds \ P(s) \left[ g_1^{(1)}(\tau) \right]^{\frac{s}{L}} \approx \exp \left( -2 \left( \frac{L}{l_s} \right)^2 k_0 D\tau \right) \]

\[ \text{sample thickness} \]
\[ \text{transport mean free path length} \]

→ DWS is sensitive to nanometer displacements

G. Maret, P. E. Wolf, Z. Phys. B 65, 409 (1987);
DWS from motor cortex activation

motor cortex stimulation:

finger opposition exercise:
100s activation, 90s rest

C3 response:

contralateral (right hand):
stimulation vs. baseline

enhanced dynamics during activation

Motor cortex activation: group study

11 right-handed subjects:

- **cortical diffusion coefficients**
- **scalp diffusion coefficients**

![Graph showing relative cortical and scalp diffusion coefficients]

- *hemispheric asymmetry*
- *40% functional acceleration of cortical dynamics*

Enhancing the sensitivity: Multispeckle correlation

average DWS signals from equivalent, but independent, speckles:

- Multimode fiber
- Few-mode fibers
- Laser
- Avalanche photodiodes
- PC
- Autocorrelators
- 32-channel autocorrelator
- Multifiber bundle
- Avalanche photodiodes
DWS signals from deeper cortical areas: visual cortex

stimulation:
50s full-field flickering
at 8Hz

occipital cortex
response:

visual cortex signals are small: 
~2% in $g^{(1)}(\tau)$


Steady-state flickering: discriminate signal from cortex?

9 right-handed subjects:

data analysis:

average decay time

\[ \tau_d = \int_{\tau_1}^{\tau_2} g_b^{(1)}(\tau) \, d\tau \]

\( p = 0.028 \)
\( p = 0.021 \)
\( p = 0.075 \)
\( p = 0.064 \)
\( p = 0.419 \)

long-distance probe discriminates signal from cortex

Visual stimulation: origin of functional DWS signal?

**functional signals:**

long distance probe:

-\( \Delta \) decay time: -3.8% / -3.0%
-\( \Delta \) transmission: -2.49% / -2.26%

PET:

-\( \Delta \) rCBF ~ +68%
-\( \Delta \) CBV ~ +21%

heart rate:

+1%  
not significant

\* functional acceleration of DWS decay is consistent with regional cerebral blood flow increase

F. Jaillon et al.,  
*Opt. Express* 15, 6643 (2007)
Transient functional signals

Experiment design:
- 30 s baseline (black screen)
- 60 s full-field 7.5 Hz flickering
10 blocks

Group average of large-distance data (n=5):

- Increased $\tau_d$ (+6%)
- Decreased $\tau_d$ (-3%)

biphasic dynamics

transient slowing-down of dynamics for short stimulation

Transient signals: averaged response

experiment design:
- 8.2 s checkerboard flickering, 7.5 Hz
- 8-12 s randomized interblock intervals
- 90 blocks

group average of large srd data (n=10):

![Graph showing relative value over decay time and count rate with short stimulation blocks reducing dynamics](image)

\[ \Delta = 1.2 \% \quad p = 0.04 \]
\[ \Delta = 0.15 \% \quad p = 0.21 \]

Mapping of transient hemodynamic signal

experiment design:
- 8.2s checkerboard flickering, 7.5 Hz
- 8-12s randomized interblock intervals
- 90 blocks

single subject data

transient blood flow change is localized

Conclusions

Diffusing-wave spectroscopy:
- intrinsic contrast
- fast (26 ms resolution)
- highly sensitive to function
- 1 cm resolution
- continuous
- insensitive to motion artefacts
- insensitive to magnetic and electric fields
- portable

method for measuring functional brain activity

Outlook:
- quantitative understanding of DWS signals
- size and shape of volume probed
- improved spatial resolution, tomography
- functional signals in single subjects
- optimization of probe placement
- fast signals ↔ electrical activation