Modeling and Applications of Spatial Frequency Domain Imaging (SFDI)

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Founder and CEO – Modulated Imaging, Inc.
Outline

- Introduction – Modulated Imaging, Inc.
- Spatial Frequency Domain Imaging (SFDI)
  - Instrumentation
  - Spectral Imaging
  - Tomography
- Computational Challenges in SFDI
  - Spatial Frequency Optimization
  - Wavelength Optimization
  - Profilometry
  - Tomographic Imaging
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Virtual Photonics Technology Initiative

- Founded in 2005 by researchers at the Beckman Laser Institute, UC Irvine
- Developing SFDI and other BLI technologies for commercialization
- Interact with BLI researchers via grants and contracts
- Significant interaction on advanced computational methods
Acknowledgements

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modulated imaging
Challenges in Tissue Optics

1: Quantify Absorption, Scattering and Fluorescence

Arm planar (DC) reflectance @ 600 nm

Quantitative optical absorption map $\mu_a (\text{mm}^{-1})$
Challenges in Tissue Optics

2: Depth-resolve Signals

![Graph showing depth resolution signals with 1.9 mm and 1.1 mm depth markers.](image)
Structured Illumination Measurement and SFD Modeling in Turbid Media

Spatial Frequency Domain Modeling in Turbid Media

Spatial Frequency Domain Measurement in Diffractive Systems

Structured Illumination + Spatial Frequency Domain Analysis

Spatial Frequency Domain Measurement and Analysis
Measurement Approaches in Tissue Optics

**Spatially-resolved**

Real Domain

PSF (ρ)

Distance, ρ (mm)

Frequency Domain

MTF (ω)

Time Frequency, ω (GHz)

**Time-resolved**

PSF (t)

Time, t (ns)

FT (t)

FT⁻¹ (t)

Distance, ρ (mm)

MTF (ω)

Time Frequency, ω (GHz)
Measurement Approaches in Tissue Optics

Spatially-resolved

Real Domain

Frequency Domain

Spatial Frequency, $k \text{ (mm}^{-1}\text{)}$

Time Frequency, $\omega \text{ (GHz)}$

Distance, $\rho \text{ (mm)}$

Time, $t \text{ (ns)}$

PSF ($\rho$)

PSF ($t$)

MTF ($k$)

MTF ($\omega$)

FT($\rho$)

FT($t$)

FT$^{-1}$(k)

FT$^{-1}$(k)

FT$^{-1}$(k)
Spatial Frequency Domain Imaging (SFDI): Platform and Measurement

- Non-contact
- Scalable Field of View
- Consumer-grade electronics

Challenges in Tissue Optics

1: Quantify Absorption and Scattering

Arm planar (DC) reflectance @ 600 nm

Quantitative optical absorption map $\mu_a (\text{mm}^{-1})$

1cm
Tissue: a low-pass spatial filter

Cuccia et al., Opt Lett, 30(11), 1354-1356 (2005)

Quantify optical properties

\[ R_d(f_x) \]

Spatial Frequency, \( f_x \) (mm\(^{-1}\))

Diffuse Reflectance

Air

Turbid Medium

AC Fluence Rate
Tissue: a low-pass spatial filter

- **Diffusion Approximation**

\[
\frac{d^2}{dz^2} \varphi_0(z) - \mu'_{\text{eff}}^2 \varphi_0(z) = -3\mu tr q_0(z)
\]

\[
\mu'_{\text{eff}} = \frac{1}{\delta'_{\text{eff}}} = \left(\mu'_{\text{eff}} + k^2\right)^{1/2}
\]

\[
R_d(k) = \frac{3A \mu'_{s}/\mu tr}{\left(\mu'_{\text{eff}}/\mu tr + 1\right)\left(\mu'_{\text{eff}}/\mu tr + 3A\right)}
\]

- **Transport (Monte Carlo)**

\[
R_d(k) = 2\pi \sum_{i=1}^{n} \rho_i J_0(k\rho_i)R_d(\rho_i)\Delta\rho_i
\]

Liquid Phantom Experiments I:
Absorption and Scattering Variation

Absorption Variation Experiment

Absorption range: $0.0011 \text{ mm}^{-1} \leq \mu_a \leq 0.12 \text{ mm}^{-1}$

Scattering range: $\mu_s' \leq 0.12 \text{ mm}^{-1}$

Scattering Variation Experiment

Scattering range: $0.11 \text{ mm} \leq \mu_s' \leq 1.8 \text{ mm}^{-1}$

Absorption range: $\mu_a = 0.0049 \text{ mm}^{-1}$

$l^* \approx 0.5 \text{ mm}$

$l^* \approx 9 \text{ mm}$
SFDI Analysis - Summary
Dorsal Pedicle Skin Flap Model

Digital photograph depicts zones of necrosis, stasis, and normal tissue. The ImageJ program was used to trace the areas of necrosis and the total affected areas (necrosis + stasis). The total flap area was also traced to calculate the percent of each area.

Hart et al.: Effects of Sildenafil on Skin Flap Survival
Pig Model of Venous Occlusion

Deoxy-hemoglobin (Hb) Map During Venous Occlusion

Control

Occluded

Hb Concentration (µM)

6 min = 1 sec of video
45 minutes actual time
Cortical Spreading Depression: Chromophore Maps vs. Time

Barrel Cortex (C2) Thinned Skull Preparation

1M K+Cl-

Time Acquisition:
- 4 wavelengths (680, 730, 780, 830)
- 2 spatial frequencies (DC/AC)
- 6 sec/measurement for 35 min
Multi-Spectral Flap Data - 12 Hours Post-Op

diffuse reflectance map, 650nm

\[ \mu_a \text{ map, 650nm} \]

\[ \mu_s' \text{ map, 650nm} \]

---

**Diffuse Reflectance vs. Wavelength**

**Absorption and Fit vs. Wavelength**

**Reduced Scattering vs. Wavelength**

---

<table>
<thead>
<tr>
<th>ROI</th>
<th>( \text{HbO}_2 (\mu M) )</th>
<th>( \text{Hb} (\mu M) )</th>
<th>( \text{H}_2\text{O} ) (%)</th>
<th>( \text{HbT} (\mu M) )</th>
<th>( \text{S}_T\text{O}_2 ) (%)</th>
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<tr>
<td>ROI 1</td>
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<td>40.5</td>
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<td>136.8</td>
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<td>ROI 5</td>
<td>28.7</td>
<td>198.7</td>
<td>86.3</td>
<td>227.4</td>
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Compact Research-Grade SFDI System
Liquid Phantom Experiments II: Blood Oxygenation Phantoms

Time

Add Yeast
Liquid Phantom Experiments II: Blood Oxygenation Phantoms

(a) (b)

(c) (d)

\[ stO_2 = \frac{(pO_2)^n}{(pO_2)^n + (p_{50})^n} \]
Other Benefits of Quantitative Tissue Assessment

Fluorescence SFDI, Speckle SFDI

Reflectance SFDI

Quantitative Imaging of Absorption, Scattering, and Chromophores

Speckle SFDI

Quantitative Imaging of Blood Flow

Fluorescence SFDI

Quantitative Imaging of Extrinsic Contrast, Quantum Yield
Computational Challenges I: Optimization Of Acquisition Frequencies

Absorption Variation Experiment

\[ 0.0011 \text{ mm}^{-1} \leq \mu_a \leq 0.12 \text{ mm}^{-1} \]

\[ \mu_s' = 0.97 \text{ mm}^{-1} \]

\[ \mu_s'/\mu_a \approx 1000 \]

Scattering Variation Experiment

\[ 0.11 \text{ mm} \leq \mu_s' \leq 1.8 \text{ mm}^{-1} \]

\[ \mu_a = 0.0049 \text{ mm}^{-1} \]

\[ l^* \approx 0.5 \text{ mm} \]

\[ l^* \approx 9 \text{ mm} \]
Computational Challenges I: Optimization Of Acquisition Frequencies

Outcome: 2 frequencies (RL - 4 pictures)
Liquid Phantom Fitting Results

**Absorption Variation**

- 30 freq. fit
- 2 freq. fit
- expected

**Scattering Variation**

- 30 freq. fit
- 2 freq. fit
- expected

<table>
<thead>
<tr>
<th>Average Error (%)</th>
<th>30-freq. fit</th>
<th>2-freq fit</th>
<th>Average Error (%)</th>
<th>30-freq. fit</th>
<th>2-freq fit</th>
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<td>$\mu_a$ error</td>
<td>4.74</td>
<td>4.85</td>
<td>$\mu_a$ error</td>
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<td>$\mu_s'$ error</td>
<td>2.98</td>
<td>2.29</td>
<td>$\mu_s'$ error</td>
<td>3.05</td>
<td>10.2</td>
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Computational Challenges II: Optimization Of Acquisition Wavelengths

Outcome: 2 wavelengths x 2 frequencies (RL: 8 pictures)
Computational Challenges III: Surface Profilometry Calibration/Correction

Outcome: 5 calibration sets
Two Challenges in Tissue Optics

2: Depth-resolve Signals
Tissue: a low-pass spatial filter

Diffuse Reflectance $R_d(k)$

AC Fluence Rate

Spatial Frequency, $f_x$ (mm$^{-1}$)

Fluence rate amplitude (norm.)

Depth-resolve signals

Quantify optical properties $\mu_a, \mu_s'$
Qualitative Tomography

bottom view
absorbing and scattering
object on the surface
$\mu_a = 0.006 \text{ mm}^{-1}$ $\mu_s' = 1 \text{ mm}^{-1}$

cross-sectional view

absorbing object
2 mm below the surface
$\mu_a = \text{Inf}$

siloxane

background optical properties
$\mu_a = 0.003 \text{ mm}^{-1}$ $\mu_s' = 1 \text{ mm}^{-1}$
Qualitative Tomography

\( f_x = 0 \text{ mm}^{-1} \quad \delta h = 10.53 \text{ mm} \)

\( f_x = 0.0191 \text{ mm}^{-1} \quad \delta h = 10.32 \text{ mm} \)

\( f_x = 0.0763 \text{ mm}^{-1} \quad \delta h = 8.21 \text{ mm} \)

\( f_x = 0.5724 \text{ mm}^{-1} \quad \delta h = 1.72 \text{ mm} \)

raw image data (AC+DC)
Quantitative optical tomography of sub-surface heterogeneities using spatially modulated structured light

Soren D. Konecky, Amaan Mazhar, David Cuccia, Anthony J. Durkin, John C. Schotland, Bruce J. Tromberg

Abstract: We present a wide-field method for obtaining three-dimensional images of turbid media. By projecting patterns of light of varying spatial frequencies on a sample, we reconstruct quantitative, depth resolved images of absorption contrast. Images are reconstructed using a fast analytic inversion formula and a novel correction to the diffusion approximation for increased accuracy near boundaries. The method provides a more accurate quantification of optical absorption and higher resolution than standard diffuse reflectance measurements.

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OCIS codes: (110.0113) Imaging through turbid media; (170.3880) Medical and biological imaging; (170.6510) Spectroscopy, tissue diagnostics

Fig. 2:
Example of a reconstructed image of a single absorbing tube located 3 mm below the surface of a tissue simulating phantom. (a) Schematic of the tissue simulating phantom. (b) Volume rendering of the three-dimensional reconstructed image. (c) Slices through the reconstructed image at depths of d = 1-5 mm.

Quantitative Optical Tomography


Green’s Functions in the SFD

• Diffusion Approximation

\[ \frac{d^2}{dz^2} \varphi_0(z) - \mu'_{\text{eff}} \varphi_0(z) = -3\mu_{tr} q_0(z) \]

\[ \mu'_{\text{eff}} = \frac{1}{\delta'_{\text{eff}}} = \left( 3\mu_a \mu_{tr} + k_x^2 + k_y^2 \right)^{1/2} \]

\[ \varphi_0(k_x, k_y, z) = C_1 \exp(-\mu_{tr} z) + C_2 \exp(-\mu'_{\text{eff}} z) \]

\[ \varphi_{\text{pert}}(k_x, k_y, z) = C_3 \frac{\exp(-\mu'_{\text{eff},\text{pert}} |z - z_{\text{pert}}|)}{\mu'_{\text{eff},\text{pert}} z_e + 1} \]

• Transport (Monte Carlo)

\[ \varphi(k_x, k_y, z) = \sum_{m=1}^{M} \sum_{n=1}^{N} \varphi(x_m, y_n, z) e^{ik_x x_m + ik_y y_n} \Delta x_m \Delta y_n \]

Object Spatial Frequency Space

Forward Modeling (Simulation)

Perturbation @ 4mm Depth (1.5mm dia.)
- Object Fourier Spectrum
- Diffusion Kernel
- Diffuse Reflectance Spectrum At Surface
- Diffuse Reflectance Image At Surface

30mm

Reconstructed Object Image @ 4mm depth
- Reconstructed Object Spectrum
- Diffusion Kernel (from measured avg. optical properties)
- Diffuse Reflectance Spectrum
- Diffuse Reflectance Measurement (1.5mm absorber, 4mm deep)

Inverse Problem (Real Data)
Reconstruction: Single Depth

Reconstructed Object

Spatial Profile

FWHM = 1.7 mm

Intensity

x (mm)

30 mm

d = 4 mm
Multiple “Views”
Frequency-dependent depth sensitivity

illumination frequency, $f_{x, \text{ill}}$

$f_x = 0.1 \text{ mm}^{-1}$, $0.2 \text{ mm}^{-1}$, ...

0°, 120°, 240°

(demod)

$R_d (x,y)$ @ $f_{x, \text{ill}}$

absorbing object

fluence rate amplitude (norm)
Tomographic Inversion

Forward Model (@ each $p_i$, $q_i$)

$$R_d(x,y)$$

$$f_{x,\text{ill}}$$

$$\text{Diff} (f_{x,\text{ill}}, z)$$

$$\mu_a(p_i, q_i)$$

$$R_d(p_i, q_i)$$

Inverse Model (@ each $p_i$, $q_i$)

$$D^{-1}(z, f_{x,\text{ill}})$$

$$R_d(f_{x,\text{ill}})$$

$$\mu_a(p_i, q_i)$$

2D FFT

$$2 \sigma$$

Modulated Imaging
Multi-Frequency Reflectance

Perturbation @ 0/mm Frequency Illumination

Perturbation Profiles@ Each Illumination Frequency

Normalized Profiles@ Each Illumination Frequency

30 mm
Tomographic Reconstruction

Depth (mm)

0.2mm 1.0mm 1.8mm 2.4mm 3.2mm 4.0mm 4.8mm 5.6mm 6.4mm 7.2mm 8.0mm 8.8mm 9.6mm
Ongoing Work

- Clinical Deployment
- Multi-modality imaging (laser speckle, fluorescence)
- Advanced modeling (acceleration, layers, tomography)
Optical Property Resolution with MI

Gelatin phantoms with 3x optical property step at 0mm and 2mm beneath the surface

(a)

Optical property edge response function for $\mu_a$ (top) and $\mu_s'$ (bottom) expts

(b)