Medical imaging with multi-tap CMOS image sensors

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Abstract Optical tissue imaging based on a multi-tap CMOS image sensor with lateral electric field charge modulator (LEFM) is shown. The imaging schemes are categorized into three types: 1) highly-time-resolved imaging, 2) time-division-multiplexed imaging, and 3) coded shutter imaging. In type-1, by taking advantage of sub-nano-second time resolution, fluorescence lifetime imaging, and time-resolved spectroscopy are explored. In type-2, the multi-tap CMOS image sensor is combined with synchronized illuminations to perform time division multiplexed imaging. Multi-spectral imaging and spatial frequency domain tissue imaging are studied. Type-3 is applied to blood flow imaging.

Keywords: Multi-tap CMOS image sensor, optical tissue imaging

1. Multi-tap CMOS image sensor based on lateral electric field charge modulator (LEFM)

Multi-tap image sensor pixels are equipped with a single photodiode, multiple storage diodes, and a draining path. Our group proposed a new charge modulator called lateral electric field charge modulator (LEFM) which is suitable for high-speed lossless charge transfer and multi-tap implementation[1]. The number of taps started from 1[2]. Then, it increased to 2[3-4], 4[5-7], and 8[8]. In this talk, biomedical applications of LEFM-based CMOS image sensors are explained.

2. Highly-time-resolved imaging

The main application of our time-resolving CMOS image sensors is time-of-flight depth imaging[9]. However, they are also promising for time-resolved biomedical imaging such as fluorescence lifetime imaging[2] and time-resolved spectroscopy like near-infrared spectroscopy (NIRS)[10]. LEFM is suitable for these biomedical applications because true correlated double sampling (CDS) enables to detect weak optical signal from the tissue. For these applications, low-noise time-resolving CMOS image sensors with sub-nano-second temporal resolution have been developed[3-4, 6-7].

3. Time-division-multiplexed imaging

Multi-tap CMOS image sensors are suitable for time-division-multiplexed imaging with switched illuminations or pattern projection. For example, spatial frequency domain imaging (SFDI)[11] provides two dimensional maps of tissue absorption and reduced scattering coefficients by capturing three images for three different structured illuminations. However, it suffers from motion artifact and errors by ambient light. When a 4-tap CMOS image sensor is used, three projected patterns and ambient light are assigned to each tap, respectively. Thus, motion-artifact-free SFDI with ambient light suppression is demonstrated[12].

4. Temporal coded shutter

Multi-tap pixels are also effective to bridge the gap between the bandwidths of tissue optical parameters and optical signals. For example, in multi-exposure laser speckle contrast imaging, which provides a blood flow velocity map, a high-speed image sensor operating at 1kfps is required because the speckle pattern changes at such a high frequency[13]. However, blood flow velocity itself changes at much lower frequency. For efficient lower frame rate imaging, application of temporal coded shutters to multi-tap CMOS image sensors is explored[14].

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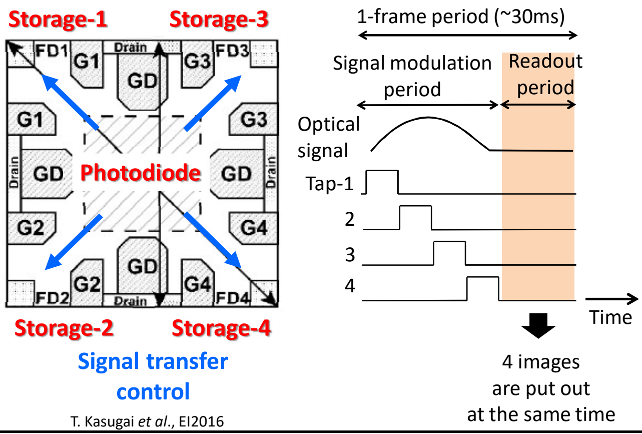
Multi-tap CMOS image sensor



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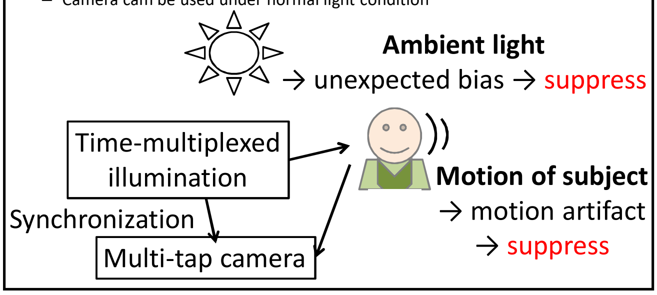
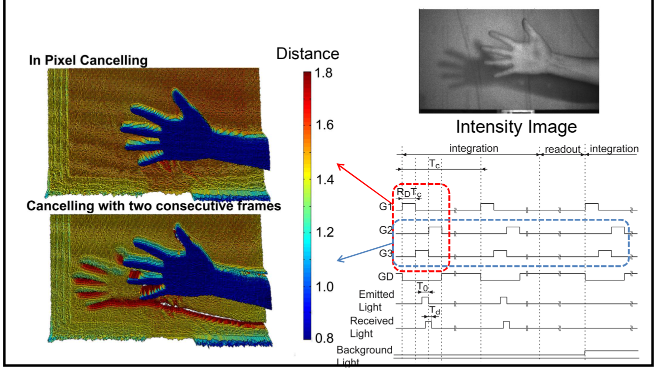
Benefits of fast lock-in detection

- High speed (high frame rate) camera is not necessary
  - Cost efficient, less processing capability required
- Suppression of motion artifact
  - Flowing liquid, moving objects are observable
    (Of course, μa and μ's maps become blurry, but no obvious artifacts appears)
- Suppression of ambient light
  - Camera cam be used under normal light condition



Motion-artifact-free backgroud-light-tolerant TOF range imaging



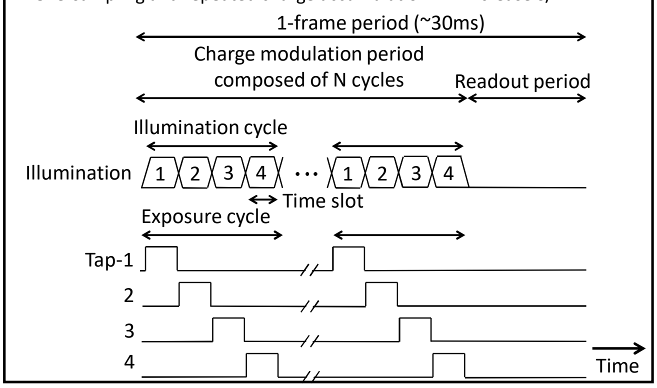
Frame rate and modulation frequency

What is the difference?

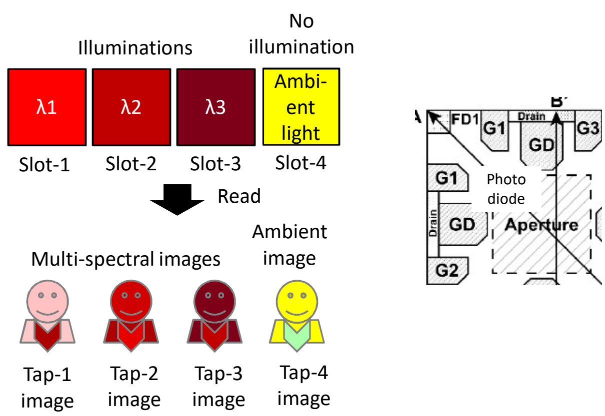
- Frame rate
  - **Change of tissue parameters**
  - E.g. Blood flow speed
- Modulation frequency of shutter speed
  - **Bandwidth of optical signal**
  - E.g. Correlation time of speckle

Time-division-multiplexed imaging

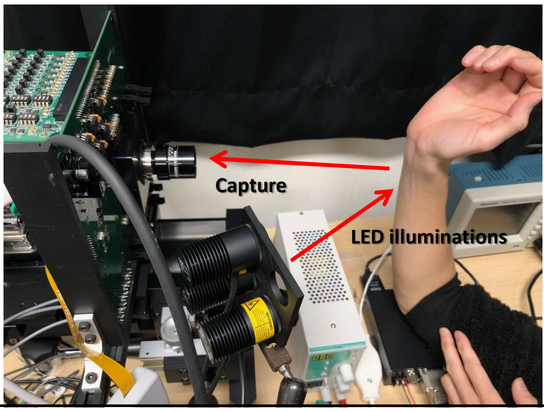
- Shorter exposure/illumination cycle will enhance isochronism between the taps, or the same motion blur will appear among the taps
- Oversampling and repeated charge accumulation will increase S/N



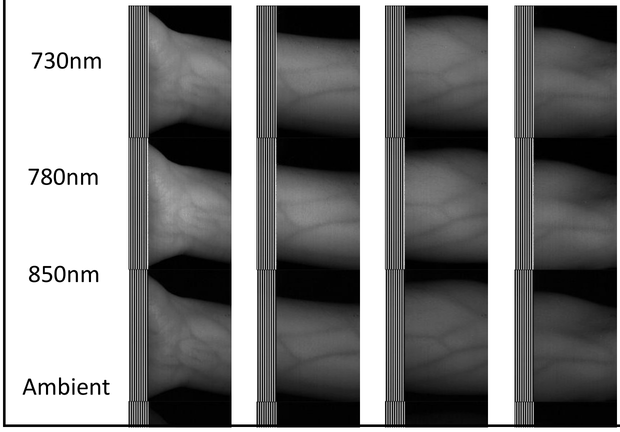
Multi-spectral imaging



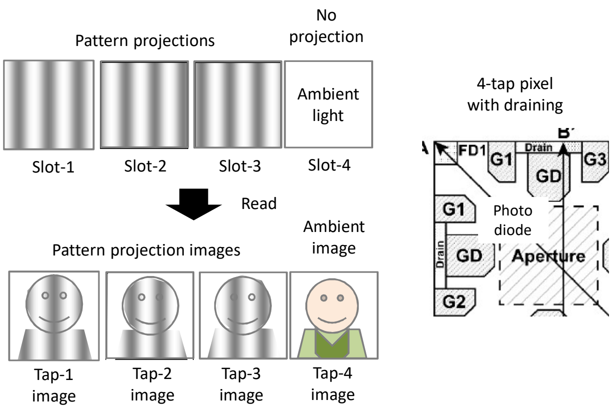
Experimental setup



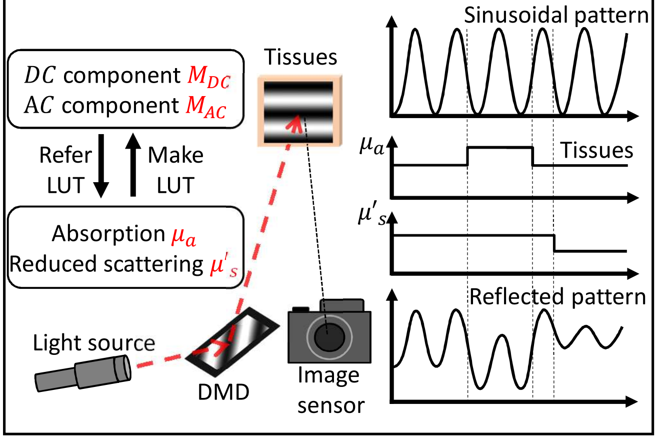
Examples of multi-spectral imaging



Functional assignment to the taps in this work

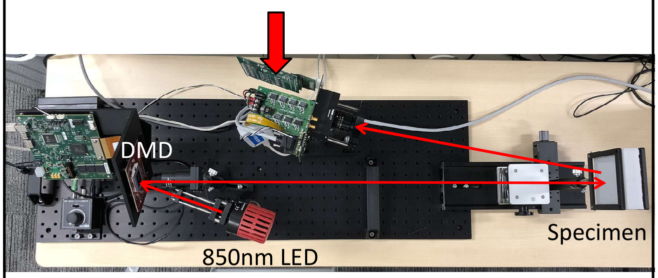


Spatial frequency domain imaging (SFDI)



Experimental setup

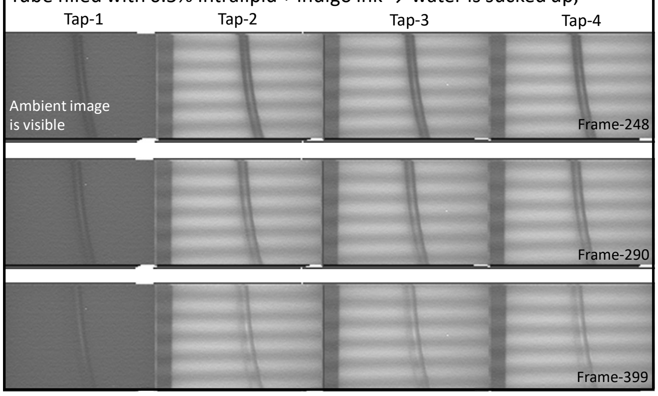
4-tap
TOF camera

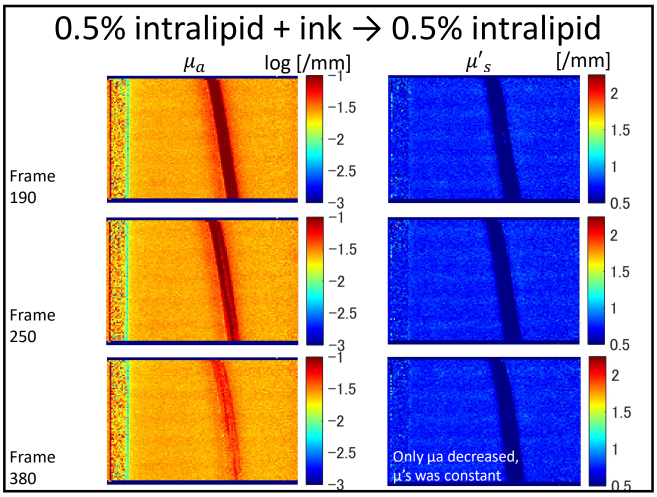


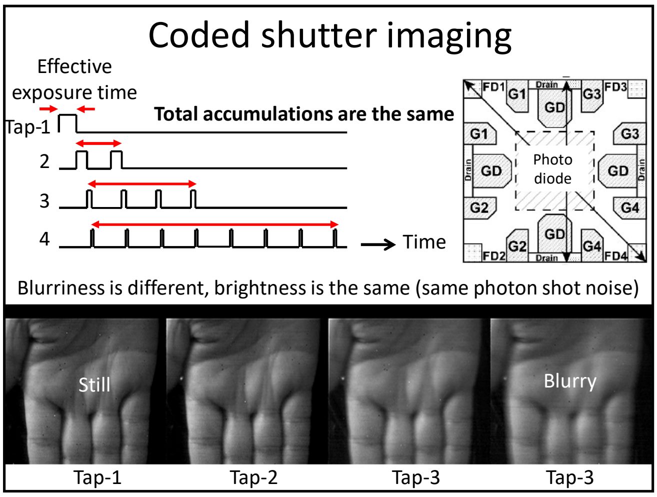
Example of captured image@23fps, f= 0.1mm^{-1}

1ms/time slot (limited by DMD), 4-times oversampling

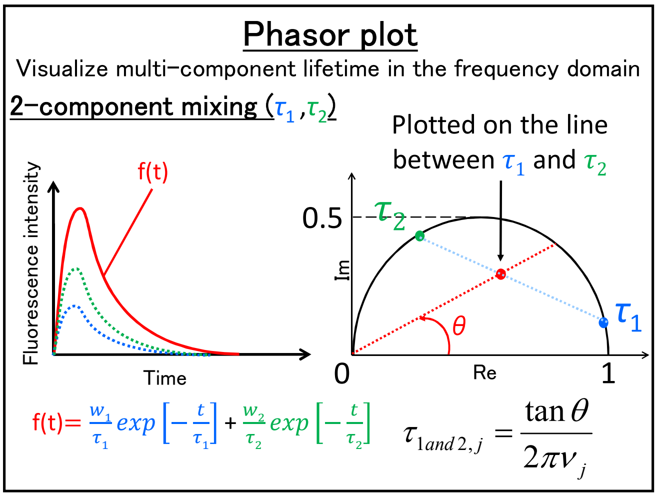
Tube filled with 0.5% intralipid + indigo ink → water is sucked up,

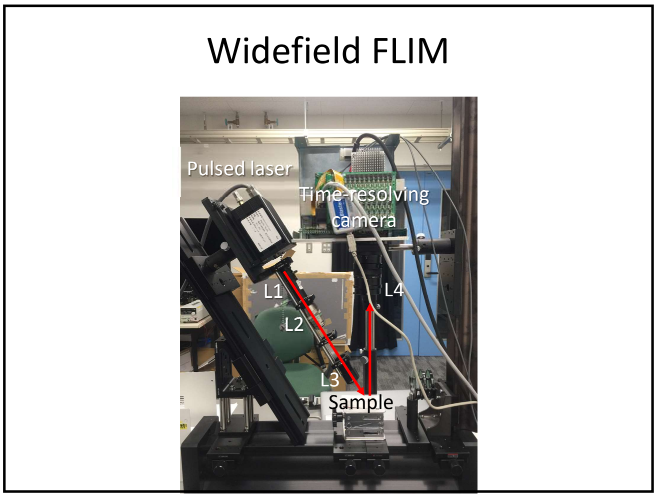


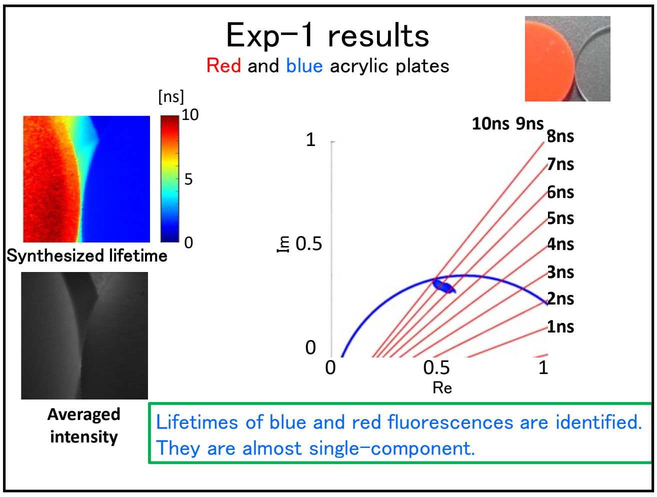




Fluorescence lifetime imaging with phasor plot

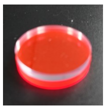


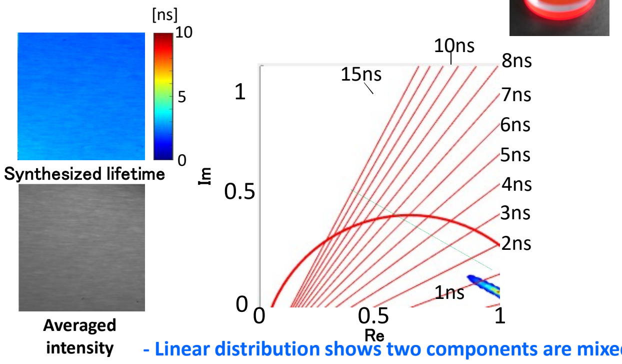




Exp-2 results

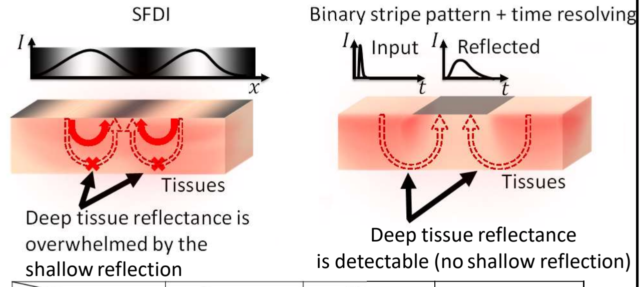
Stacked red and blue acrylic plates





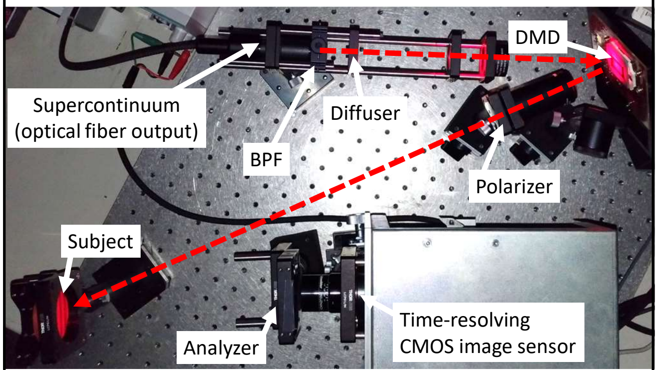
- Linear distribution shows two components are mixed
- But their fundamental components are not obvious (should be on the line)

Limitation of SFDI and proposal



	Pattern	Light	Depth
SFDI	Sinusoidal	CW	~mm
Time-resolving	Binary stripe	Impulse	~10mm

Experimental setup



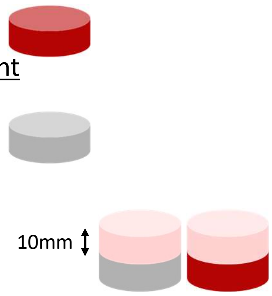
Experiments

SFDI

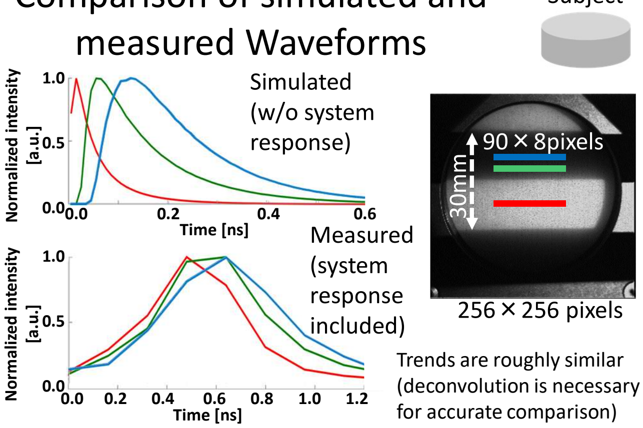
- Conventional SFDI method is confirmed
- M_{DC} and M_{AC} are measured
- 2D maps of μ_a and μ'_s are made by referring LUT

Time-resolved measurement

- Waveforms for simulation and experiment are compared
- Influence of the 2[nd] layer phantom to the waveform is measured

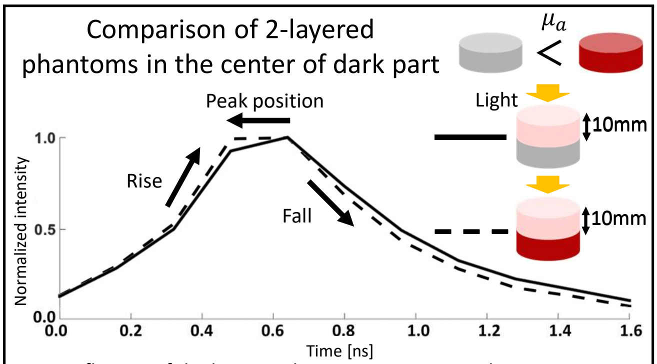


Comparison of simulated and measured Waveforms



Trends are roughly similar (deconvolution is necessary for accurate comparison)

Comparison of 2-layered phantoms in the center of dark part



- Influence of the bottom phantom was measured (shorter delay, steeper rise and fall due to larger absorption)
- Inverse problem solving is necessary to decompose the optical properties of each layer