Imaging deep-tissue blood flow via parallelized diffuse correlation spectroscopy

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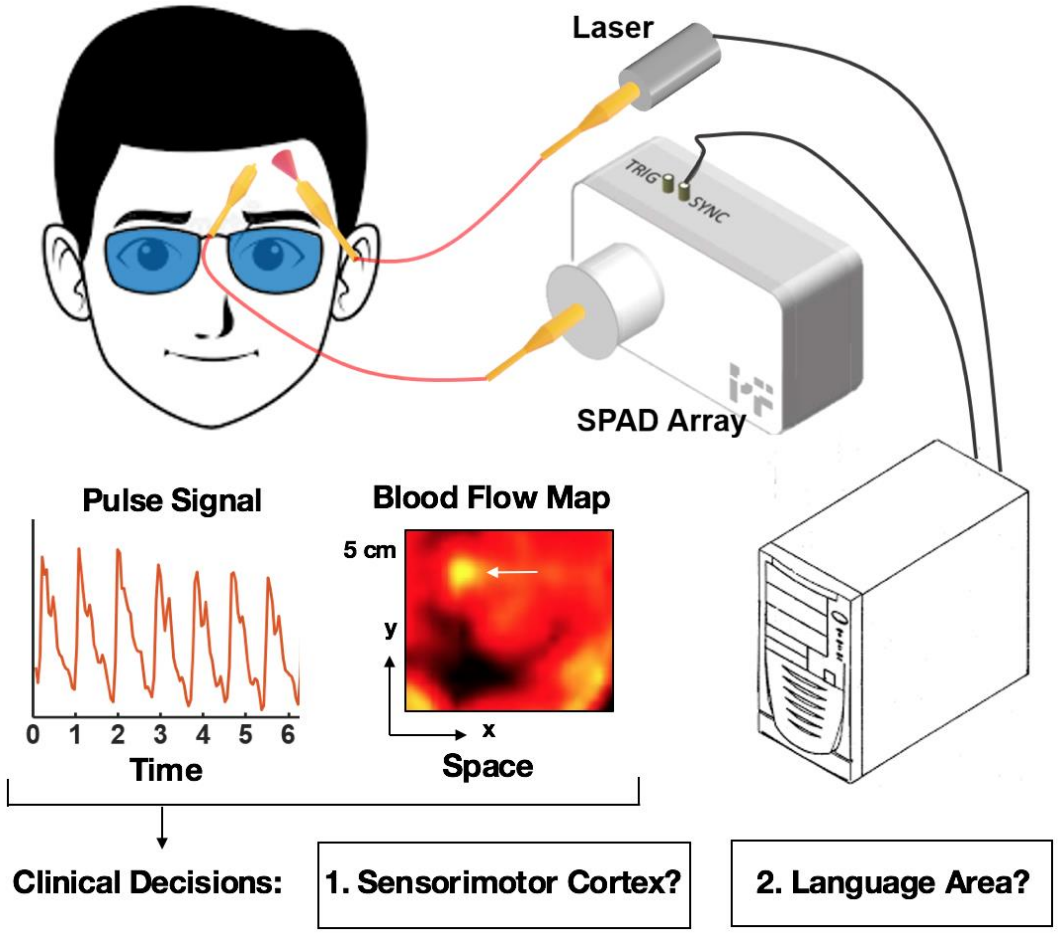
COMPUTATIONAL OPTICS LAB

Goal – optically monitor neural activity with noninvasive blood flow detection

- Measure cerebral blood flow with an inexpensive, portable optical device
- Shine visible laser light into head, rapidly detect scattered light during behavioral tasks
- Pinpoint minute blood flow fluctuations at high speed & map cortical activity
- Small, robust, requiring minimal patient cooperation

Parallelized Diffuse Correlation Spectroscopy (PDCS)

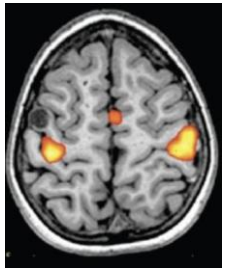


Example: eloquent cortex localization

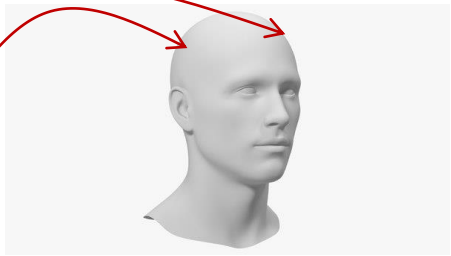
Currently workflow for adults:

1. Enter Functional Magnetic Resonance Imager

2. Execute specific tasks during neuroimaging

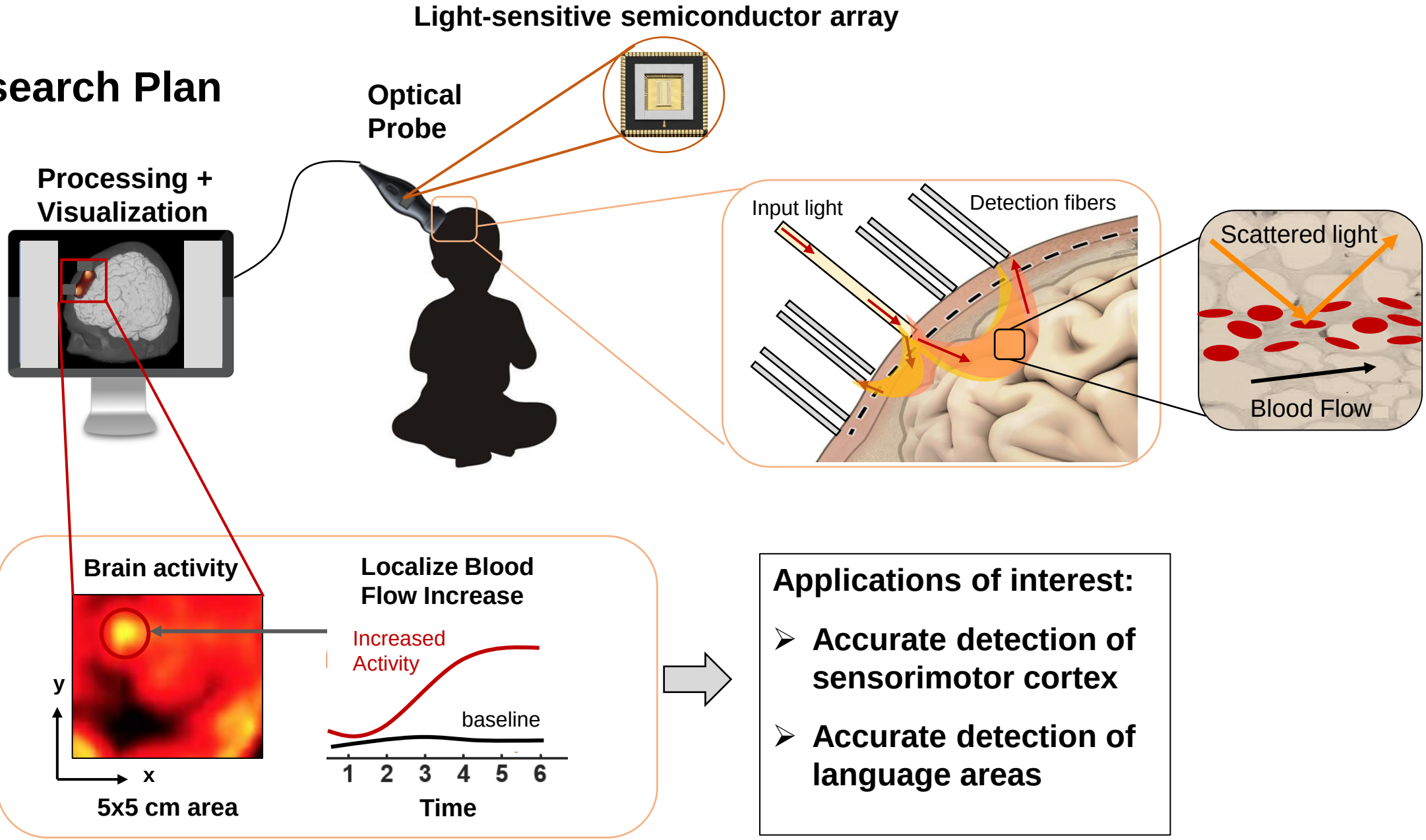




3. Map areas of heightened brain activity to anatomy

Imaging sessions last up to 45 minutes - not feasible for children under 10 years, so only option is invasive surgery

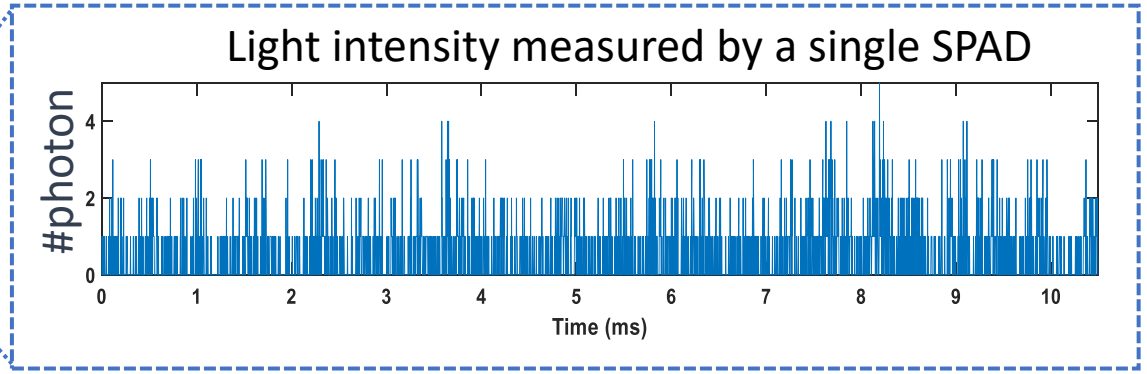
Research Plan

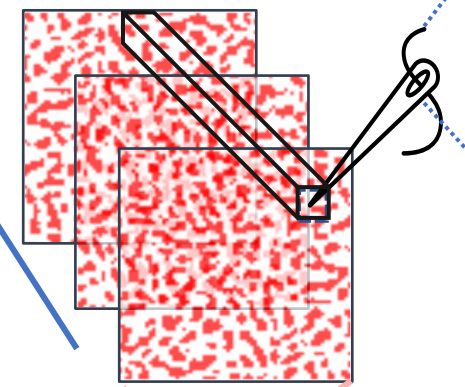


Applications of interest:

- **Accurate detection of sensorimotor cortex**
- **Accurate detection of language areas**

Diffuse Correlation Spectroscopy



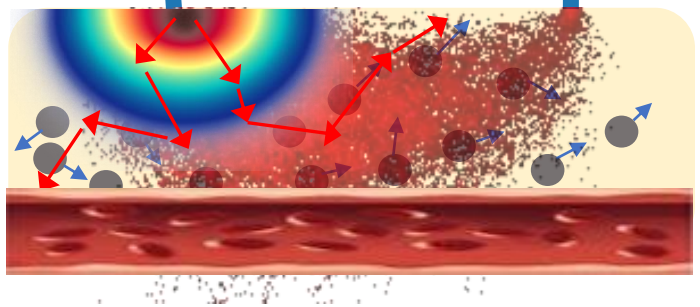


Temporal measurements

Long coherence laser

Fiber source

Fiber detector



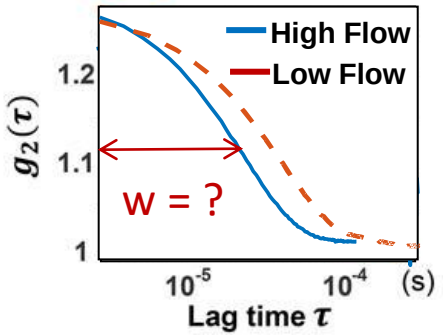
Tissue

Cortex (blood flow)

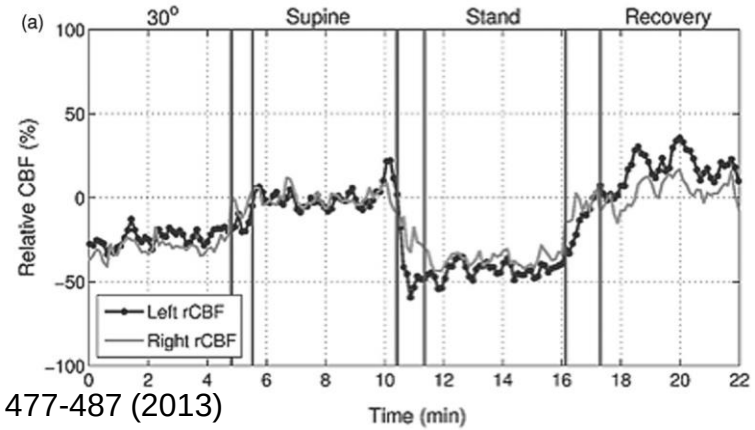
*Photon "Banana" dips down ~1/2 source-detector separation

Slow dynamics (1+ Hz)

Temporal Autocorrelation

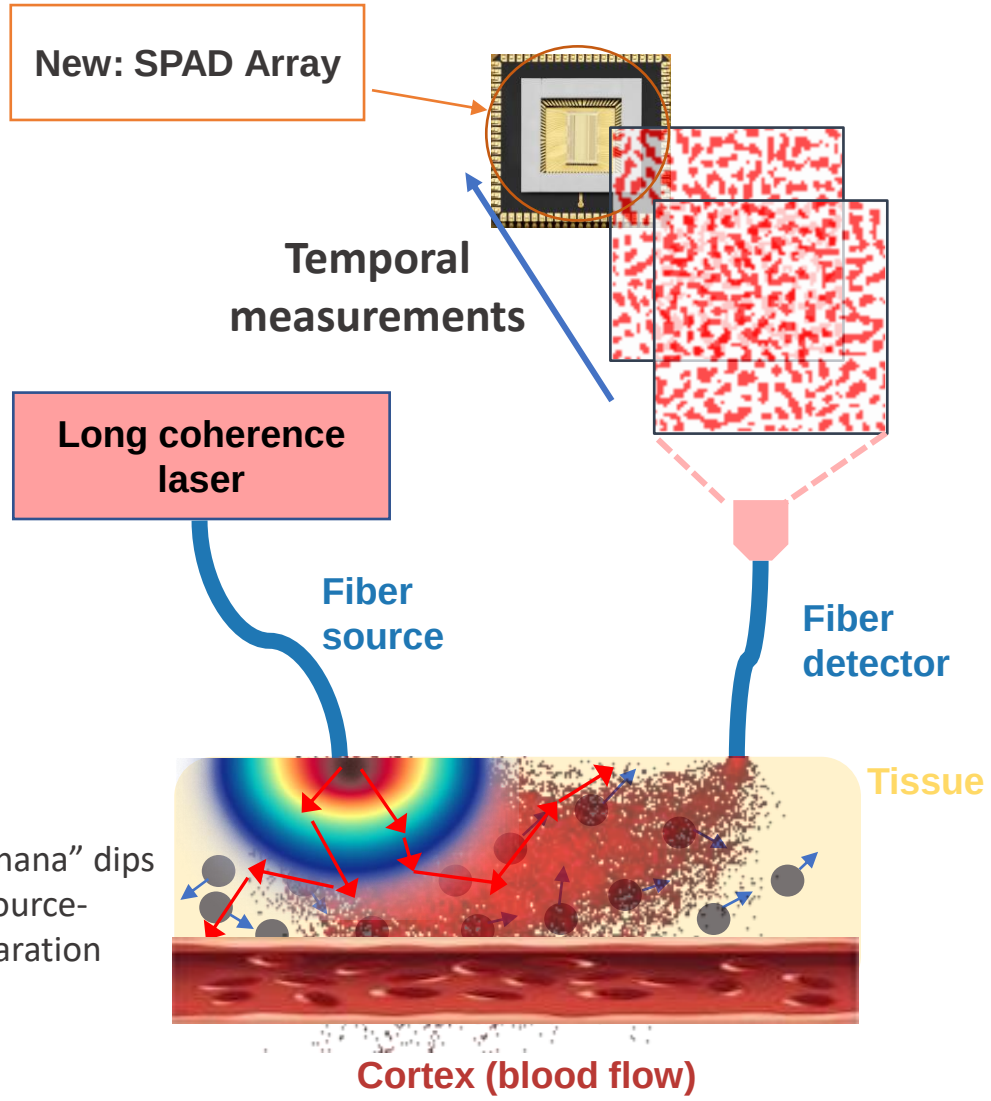


Required: average over long (1-10 sec.) window



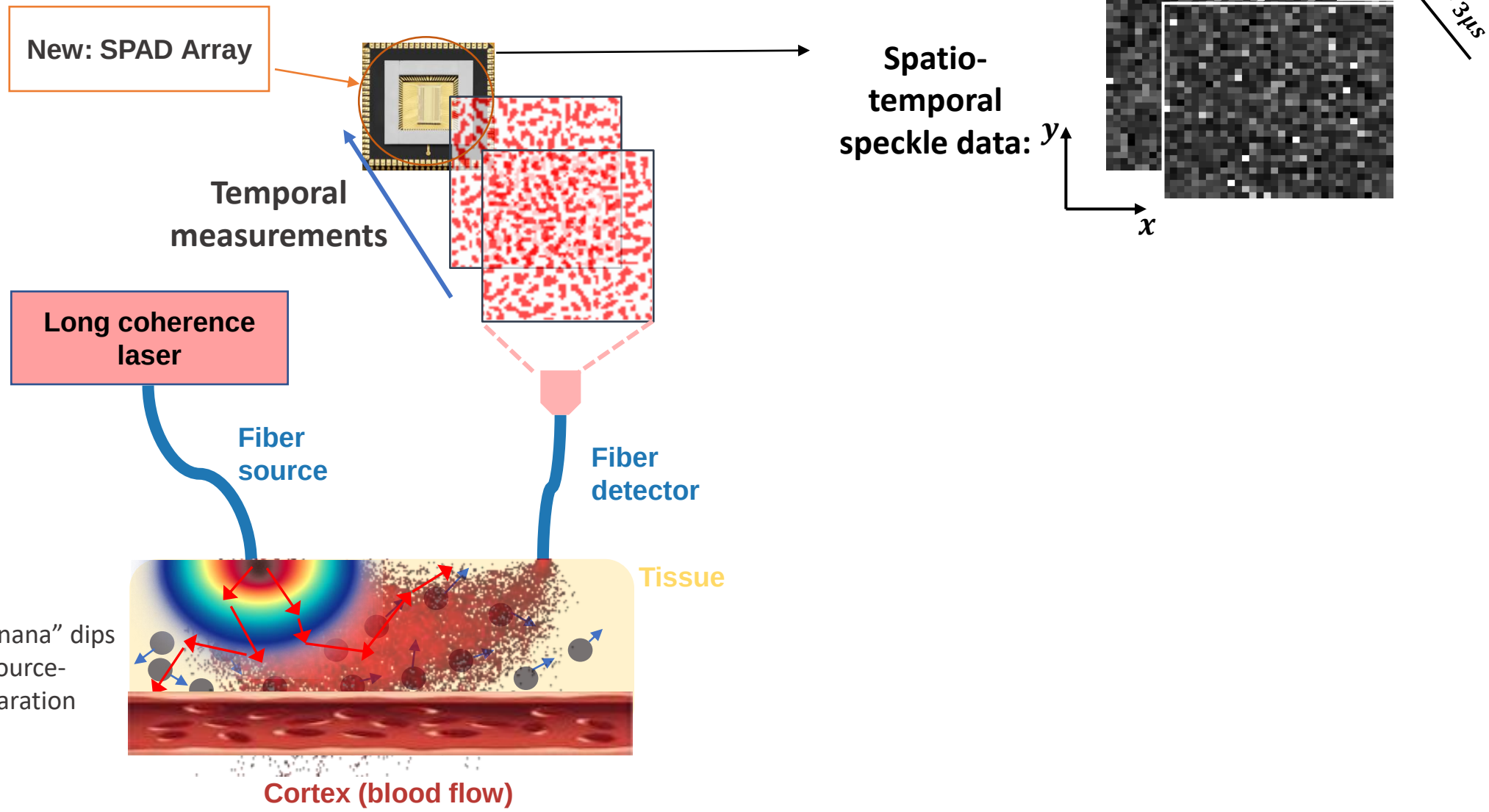
B. Edlow et al., Phys. Meas. 31 (2), 477-487 (2013)

Diffuse Correlation Spectroscopy



*Photon “Banana” dips down ~1/2 source-detector separation

Diffuse Correlation Spectroscopy



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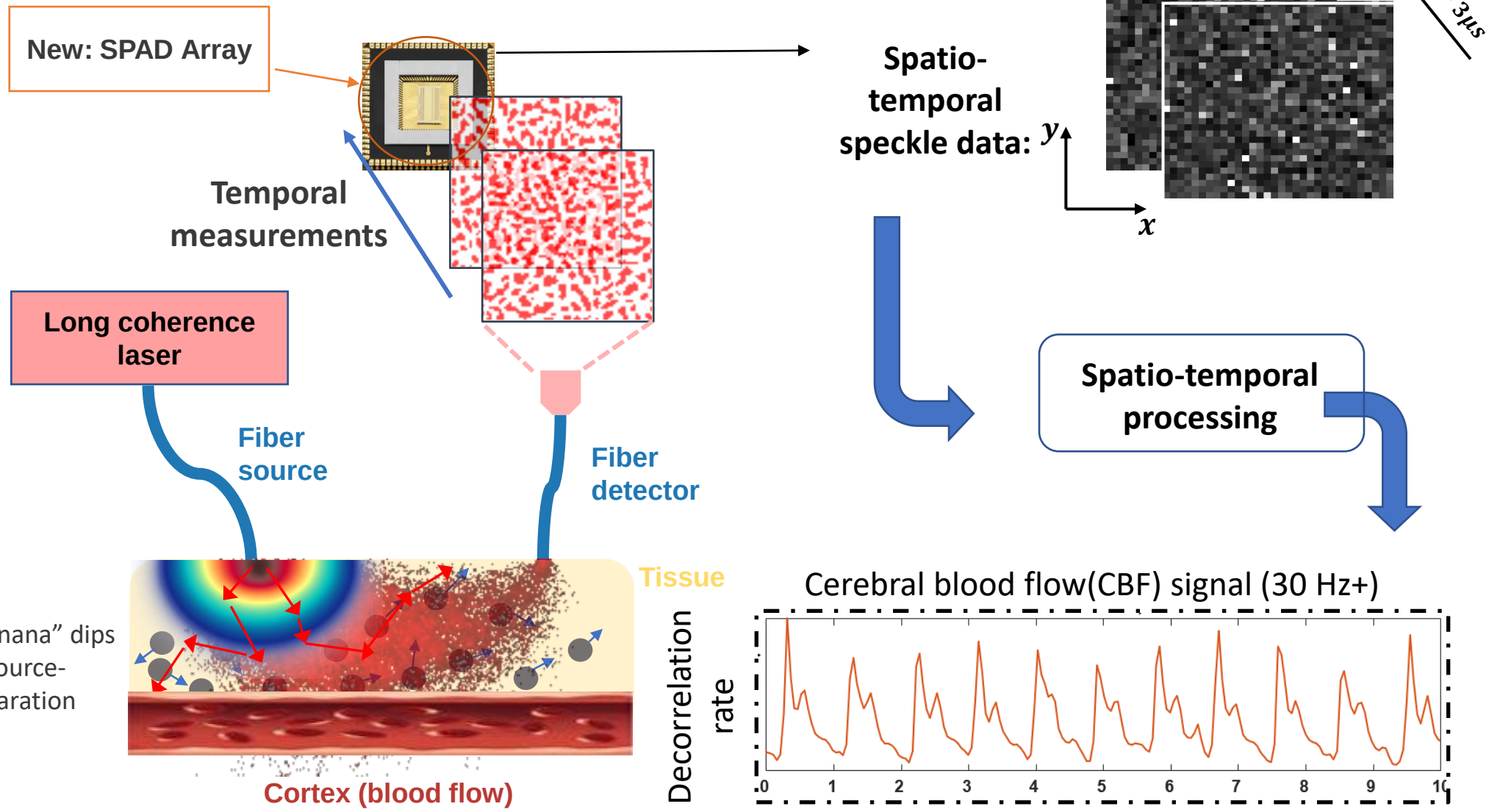
Diffuse Correlation Spectroscopy



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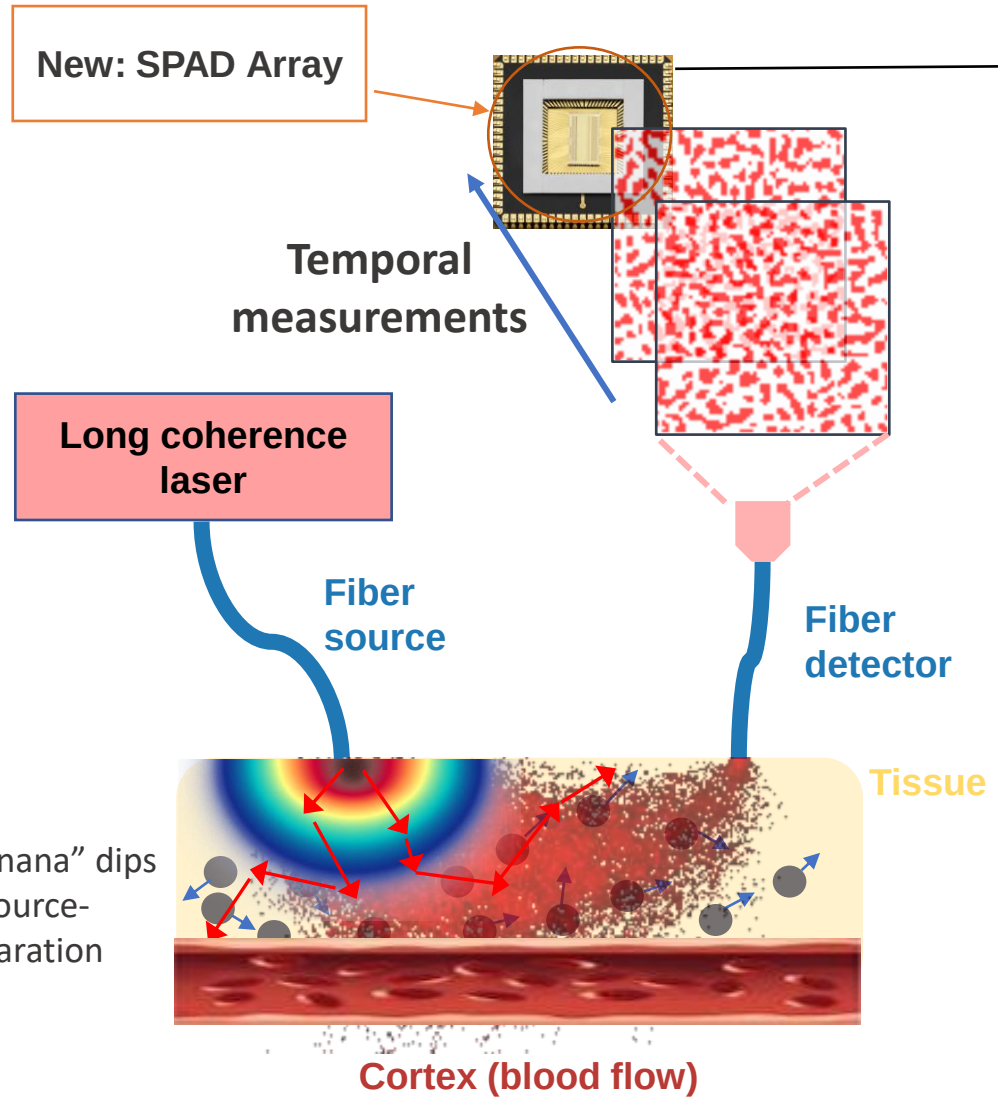
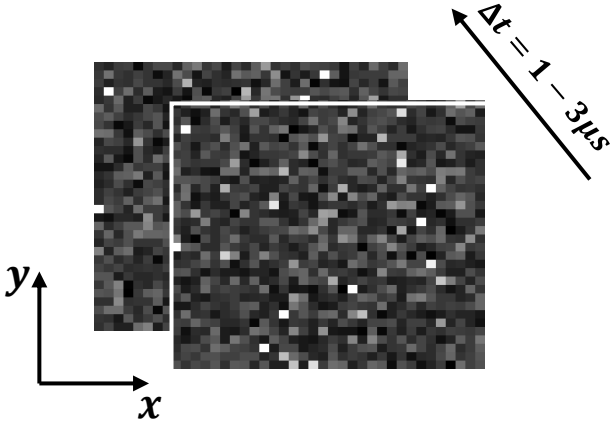
Diffuse Correlation Spectroscopy



*Photon "Banana" dips down ~1/2 source-detector separation

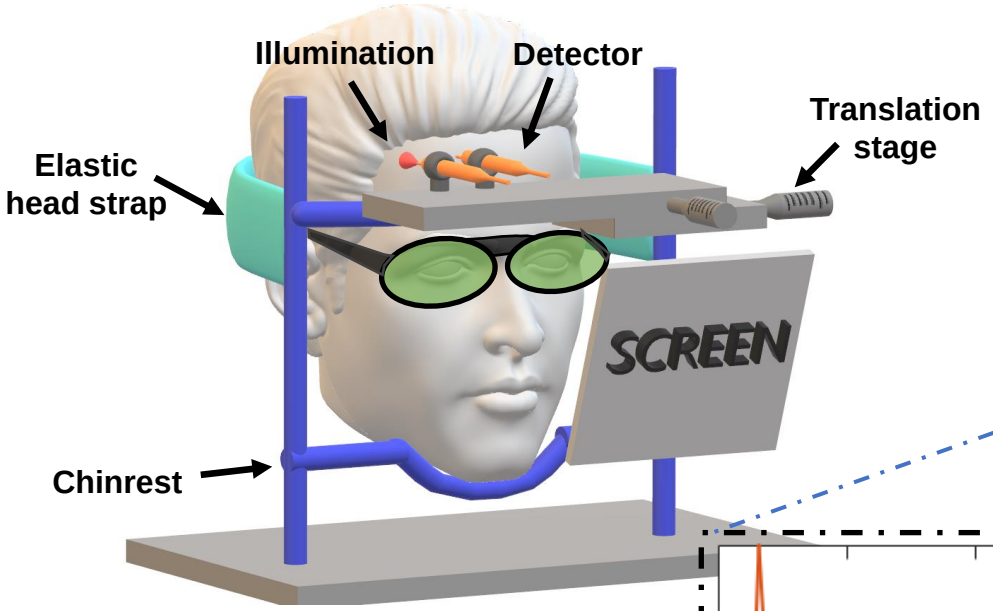
Spatio-temporal speckle data:

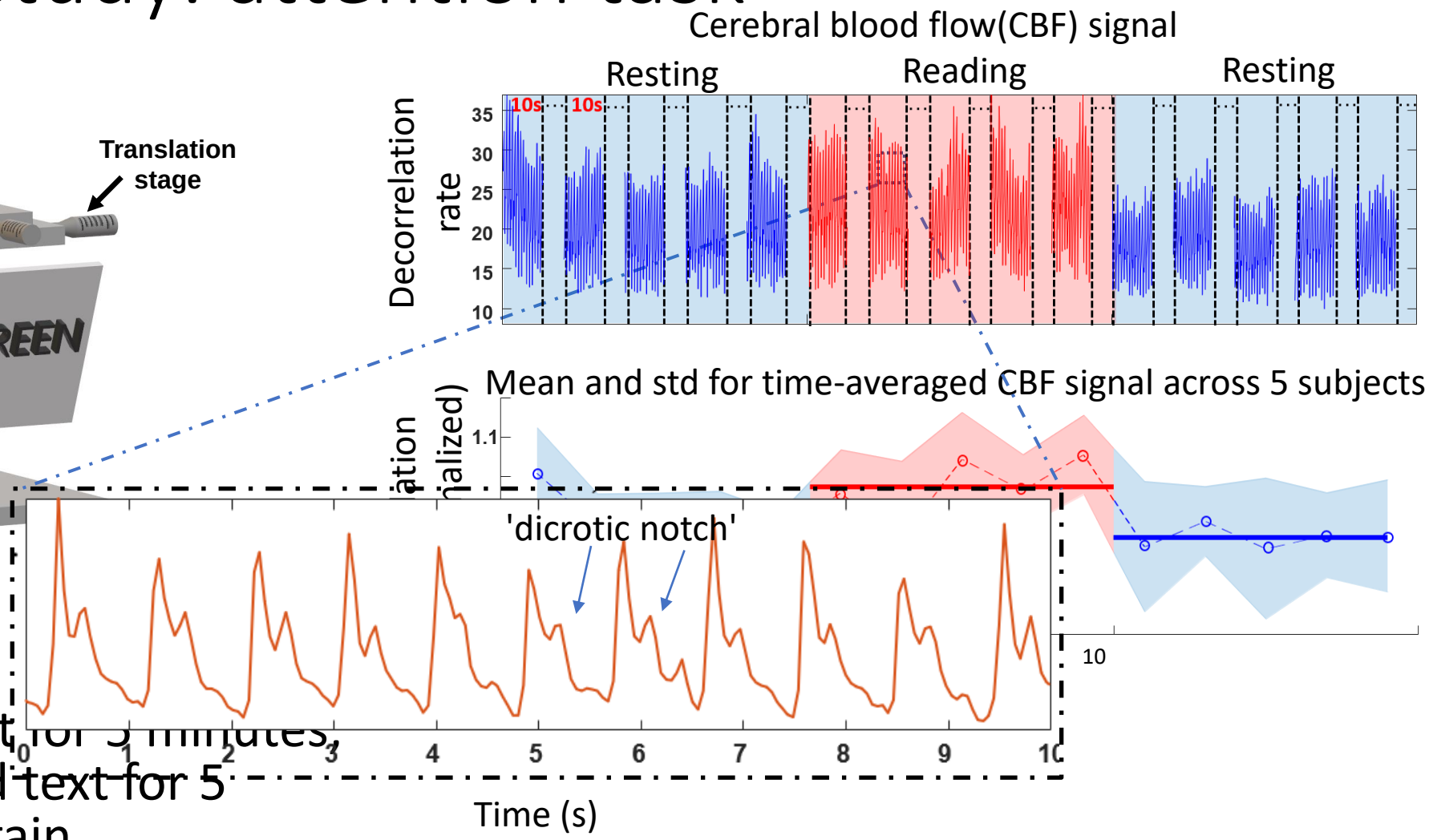


Requirements of SPAD array:

- **Single-photon sensitivity with high QE**
- **No TC-SPC required**
- **300 kHz – 1 MHz frame rate (now relaxed)**
- **As many pixels as possible**
- **Current setups use Photon Force PF32**

Preliminary study: attention task

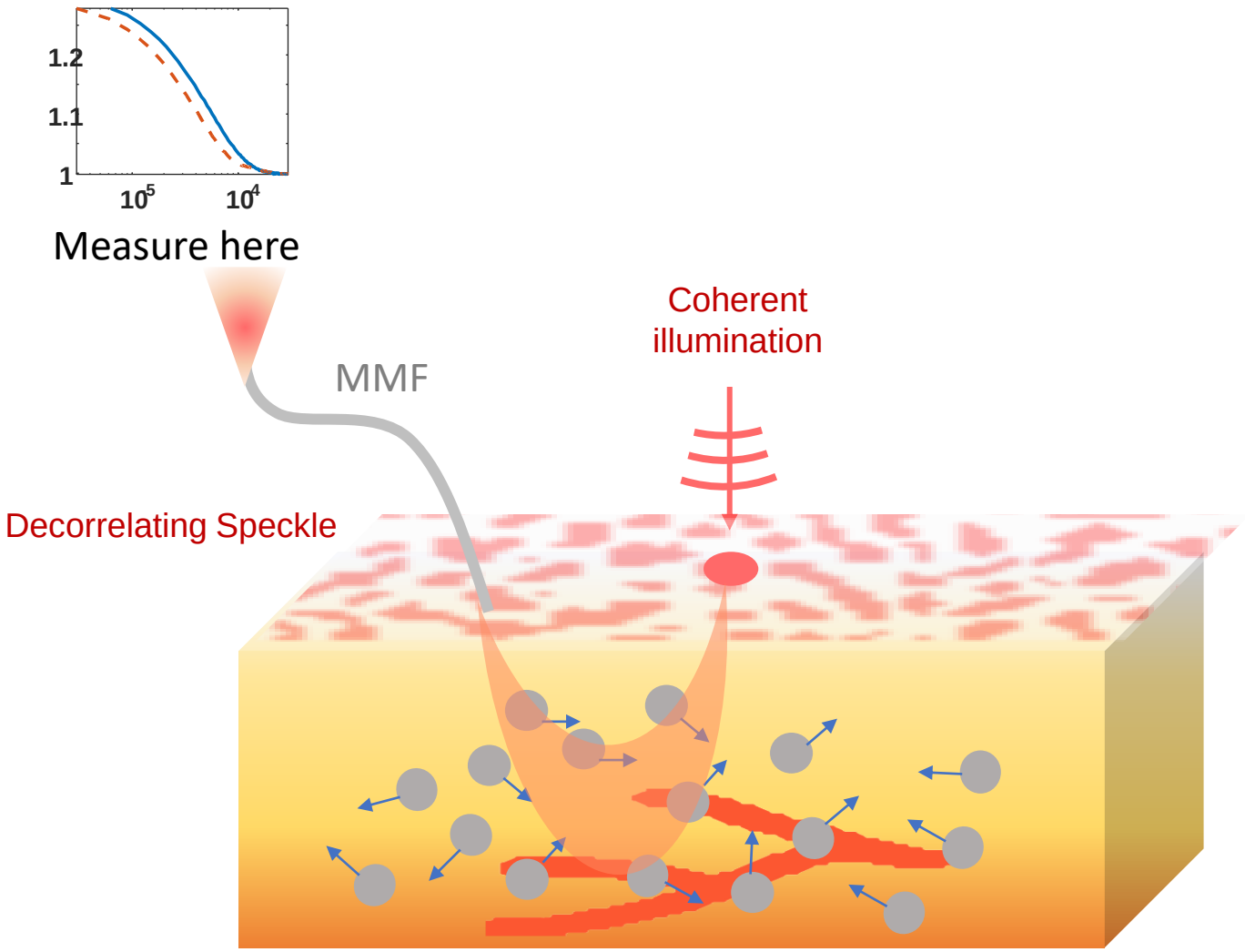




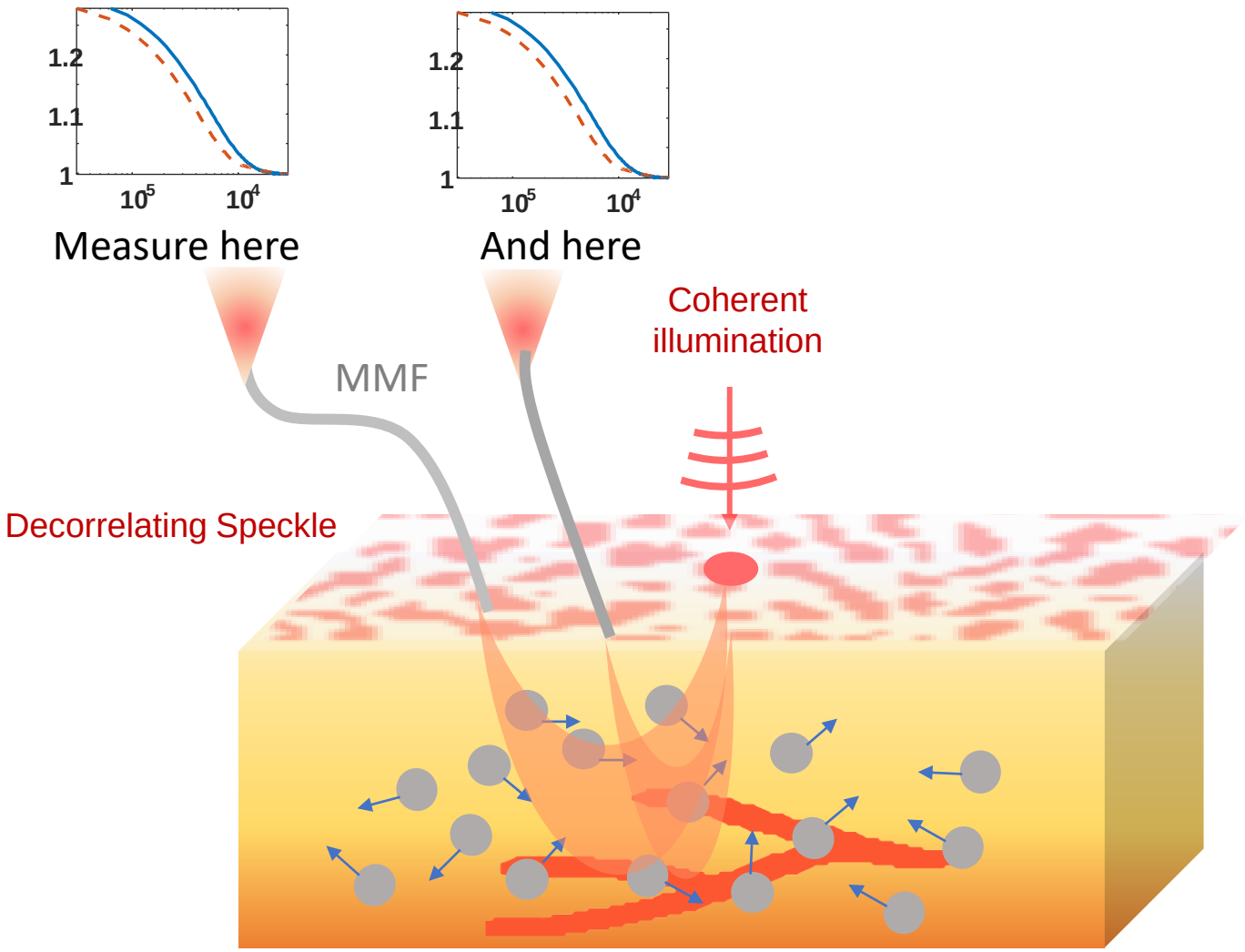
- Subjects asked to rest for 5 minutes, concentrate and read text for 5 minutes, then rest again.

Liu, Wenhui, et al. "Fast and sensitive diffuse correlation spectroscopy with highly parallelized single photon detection." APL Photonics. APL Photonics 6 (2021): 026106

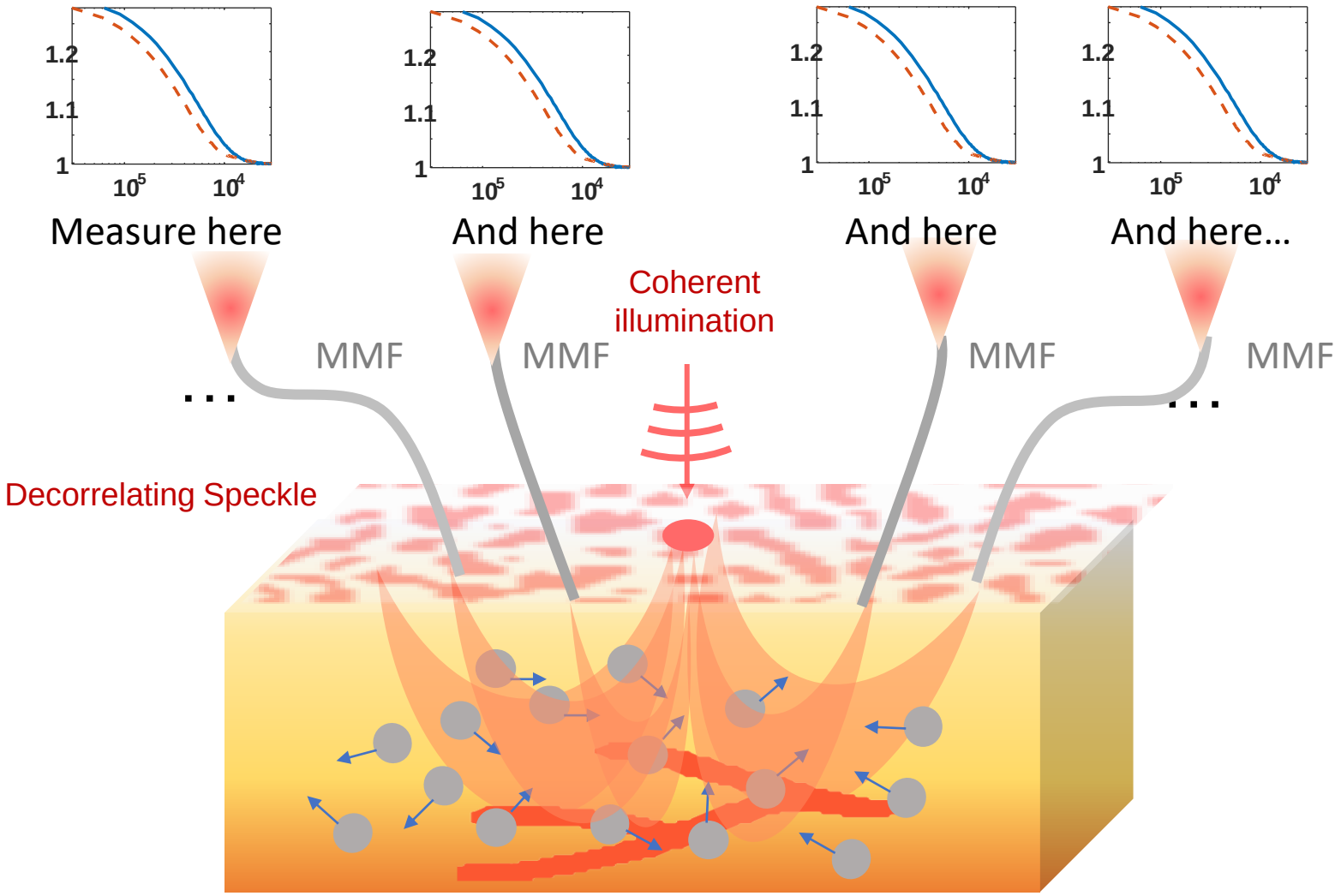
From detection to image formation



From detection to image formation



From detection to image formation



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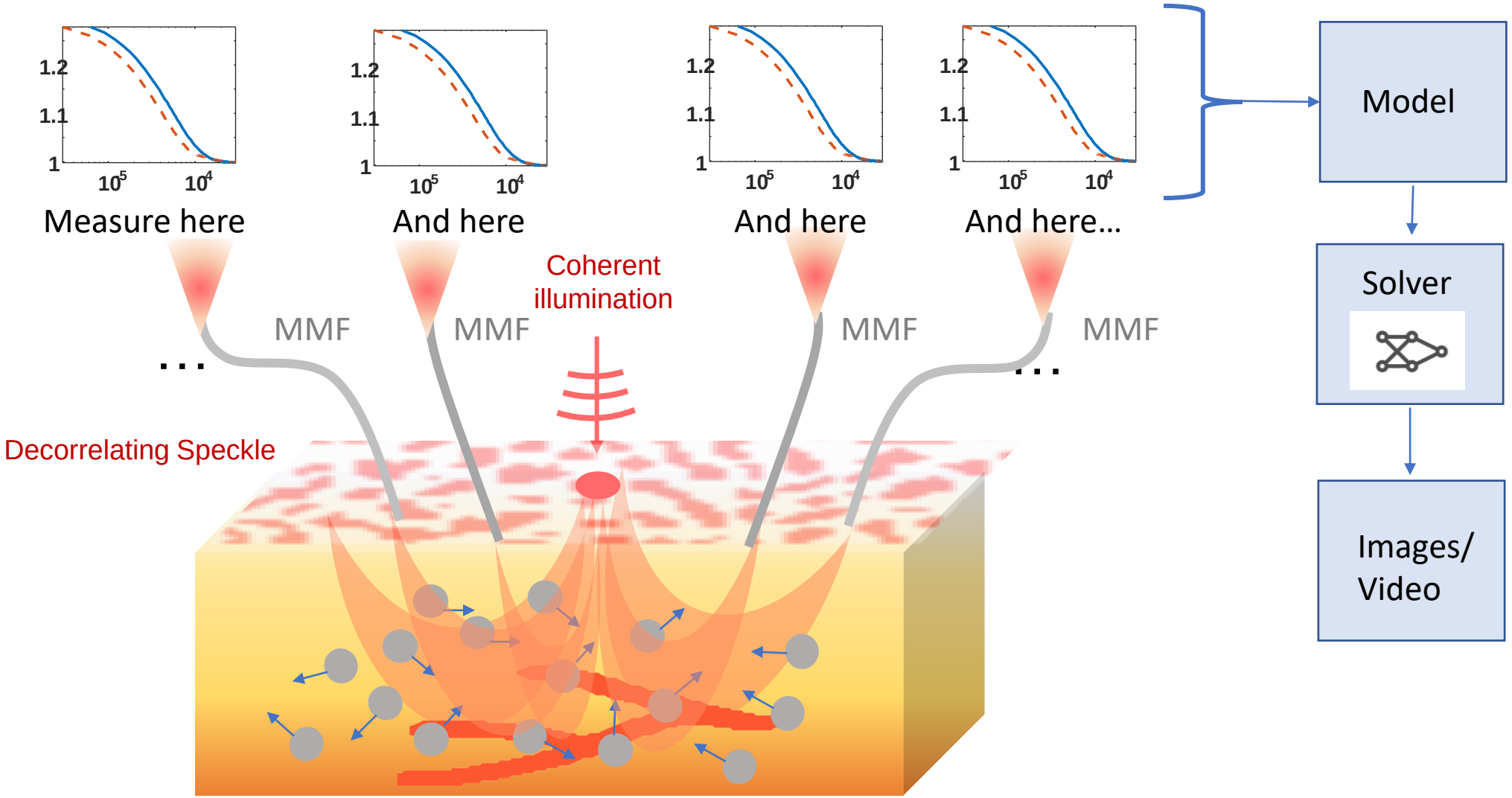

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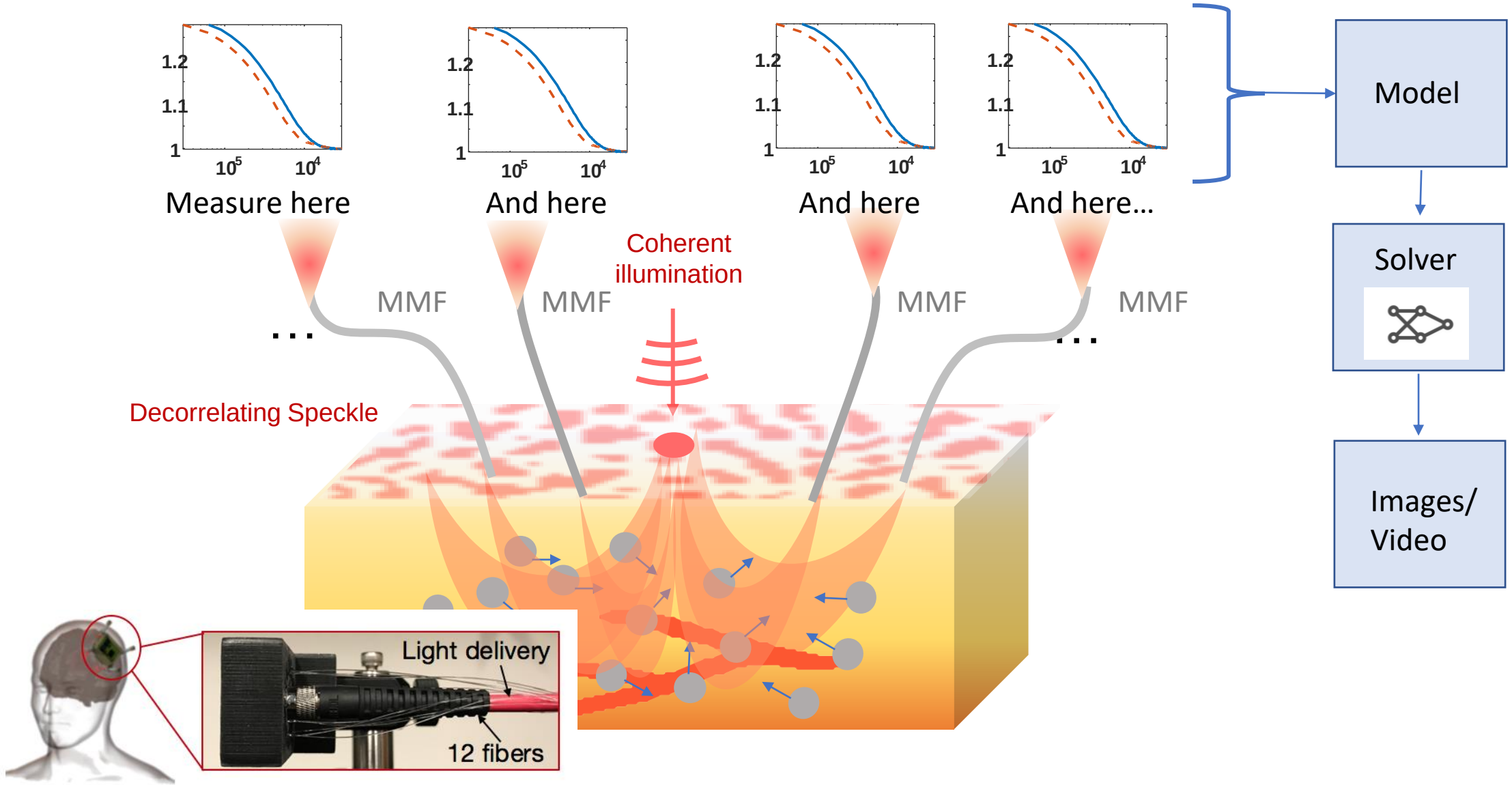
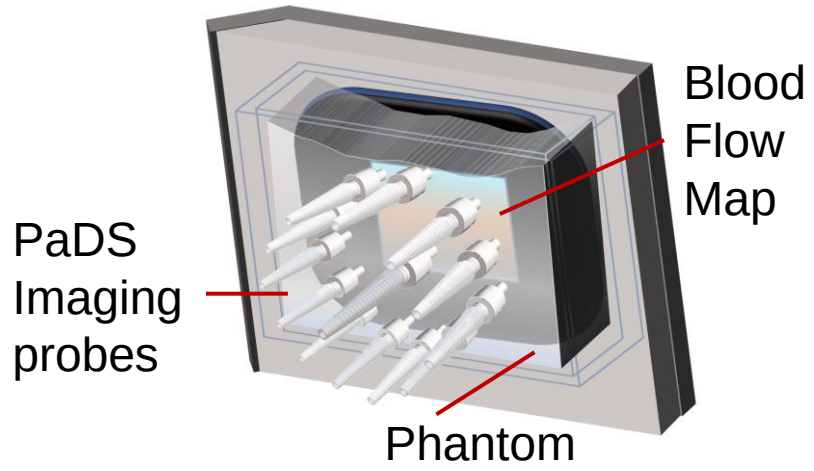


Preliminary Experimental results

Phantom tissue setup (8-10 mm thick)



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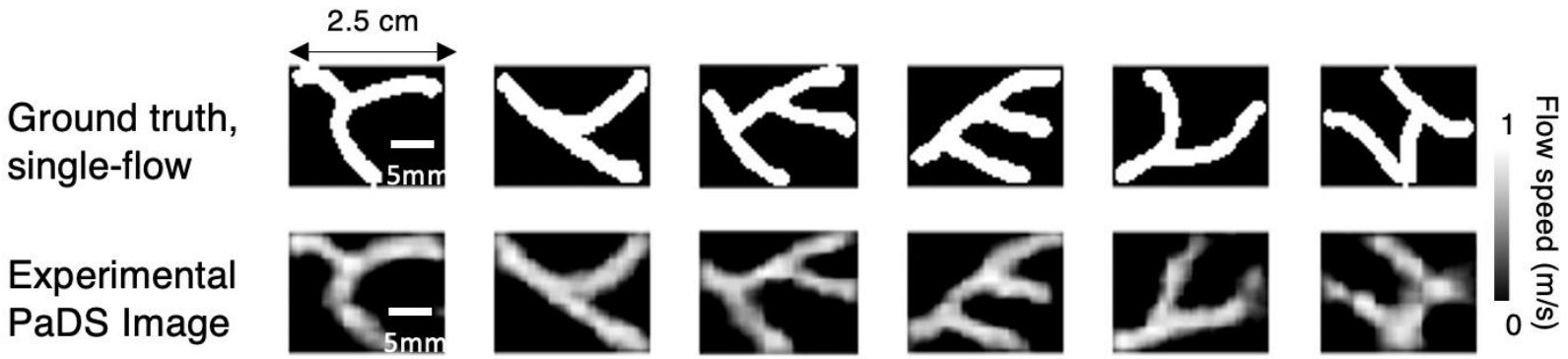

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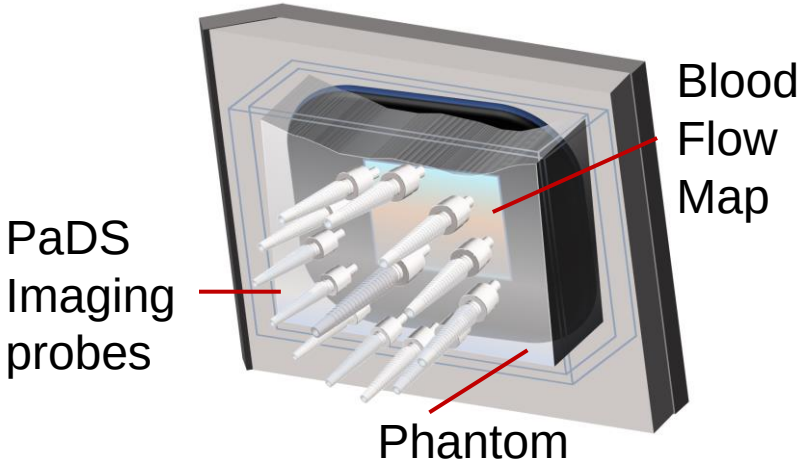

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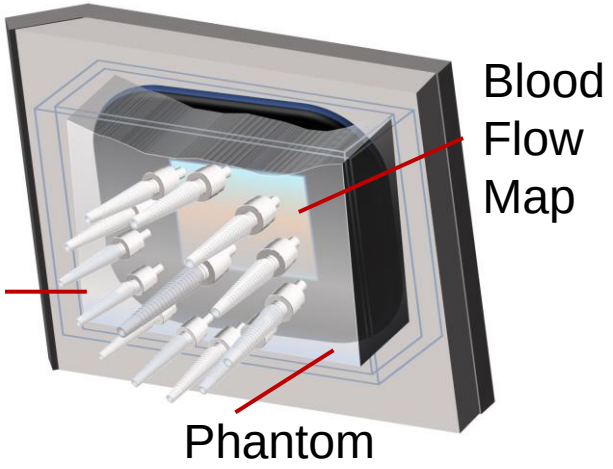
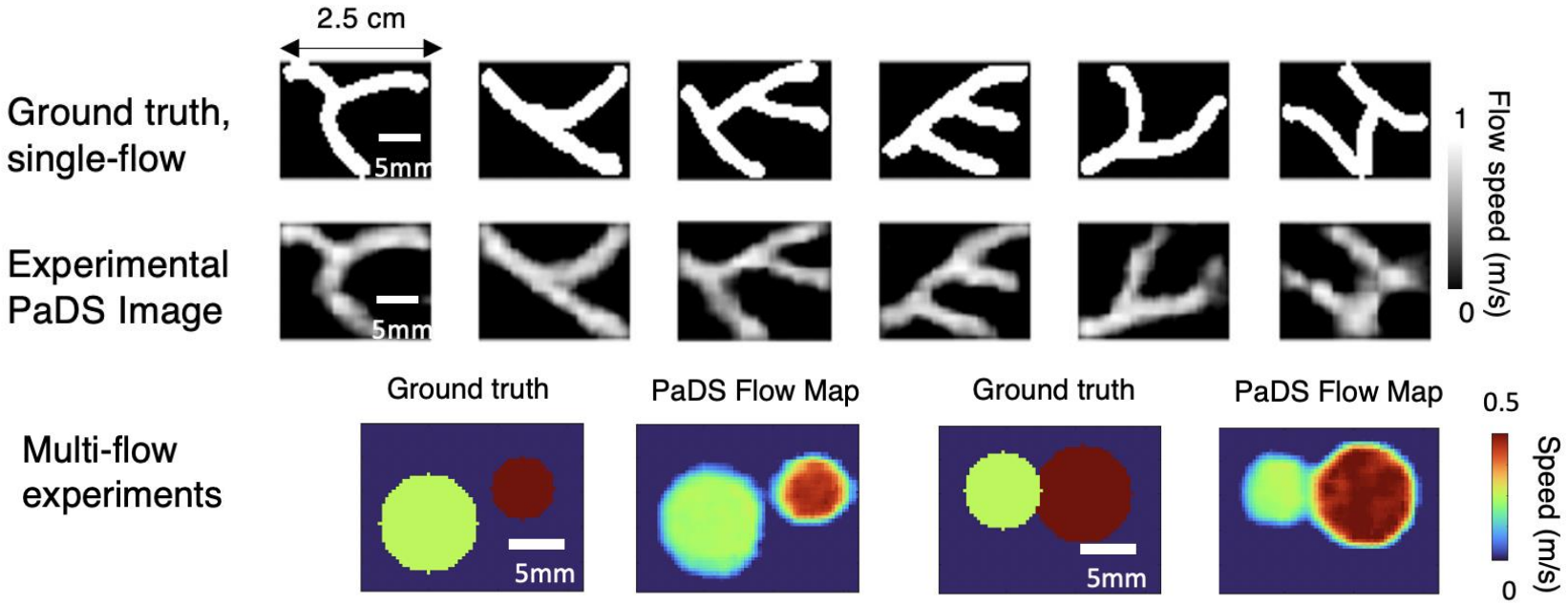


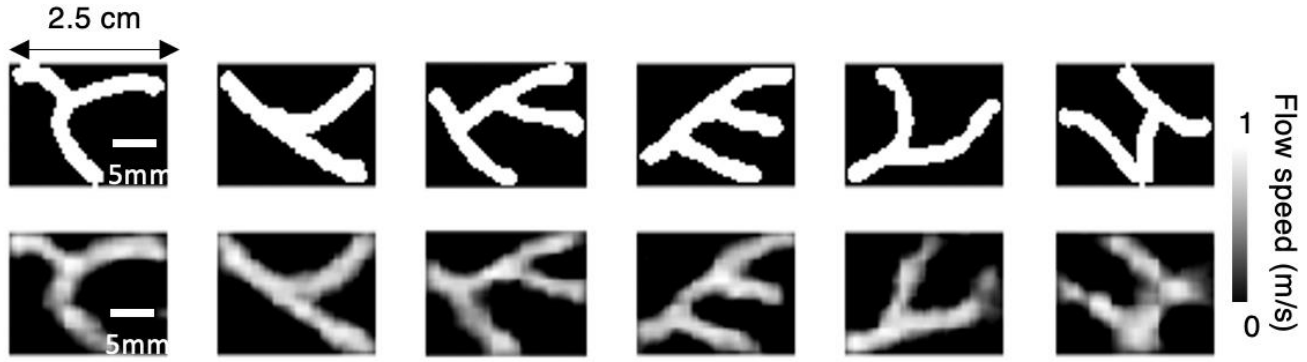


Preliminary Experimental results

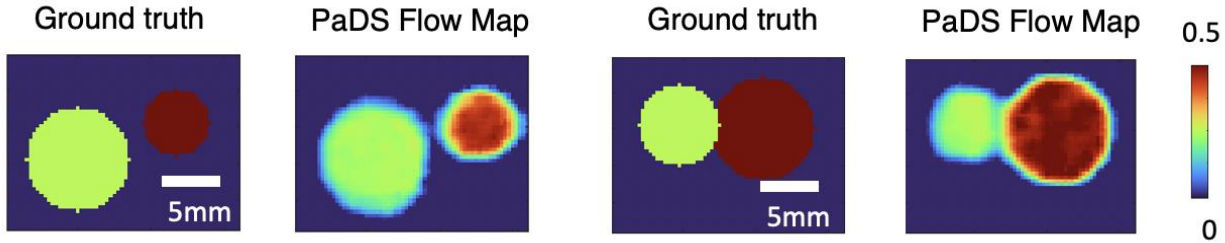
S. Xu et al., "Imaging dynamics beneath turbid media via parallelized single-photon detection," Advanced Science (accepted 2022)

Ground truth, single-flow

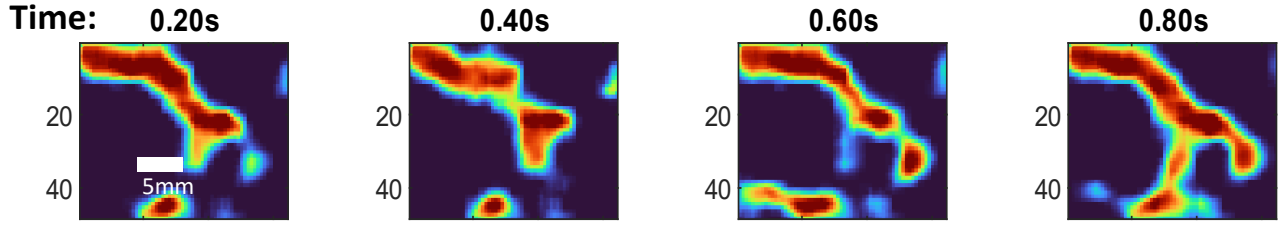
Experimental PaDS Image



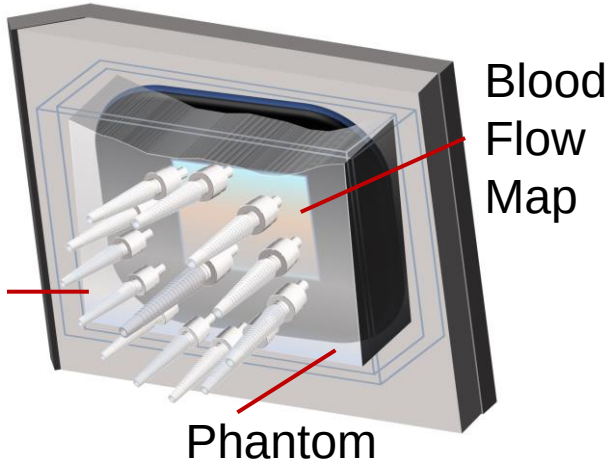
Multi-flow experiments

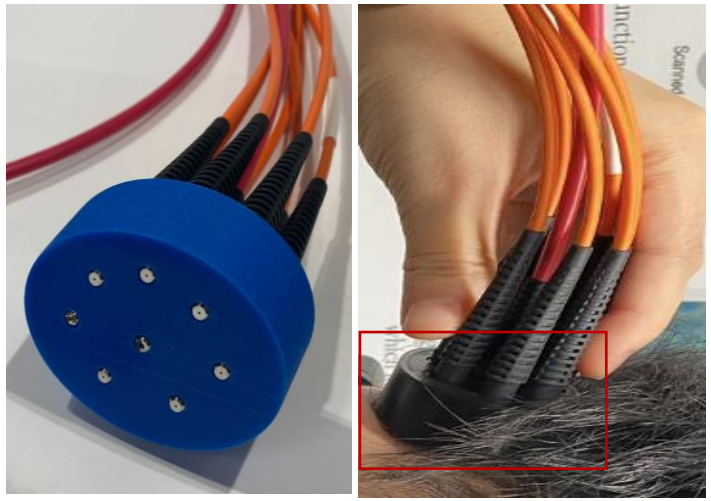


In Vivo PaDS Video, human subject



Phantom tissue setup (8-10 mm thick)





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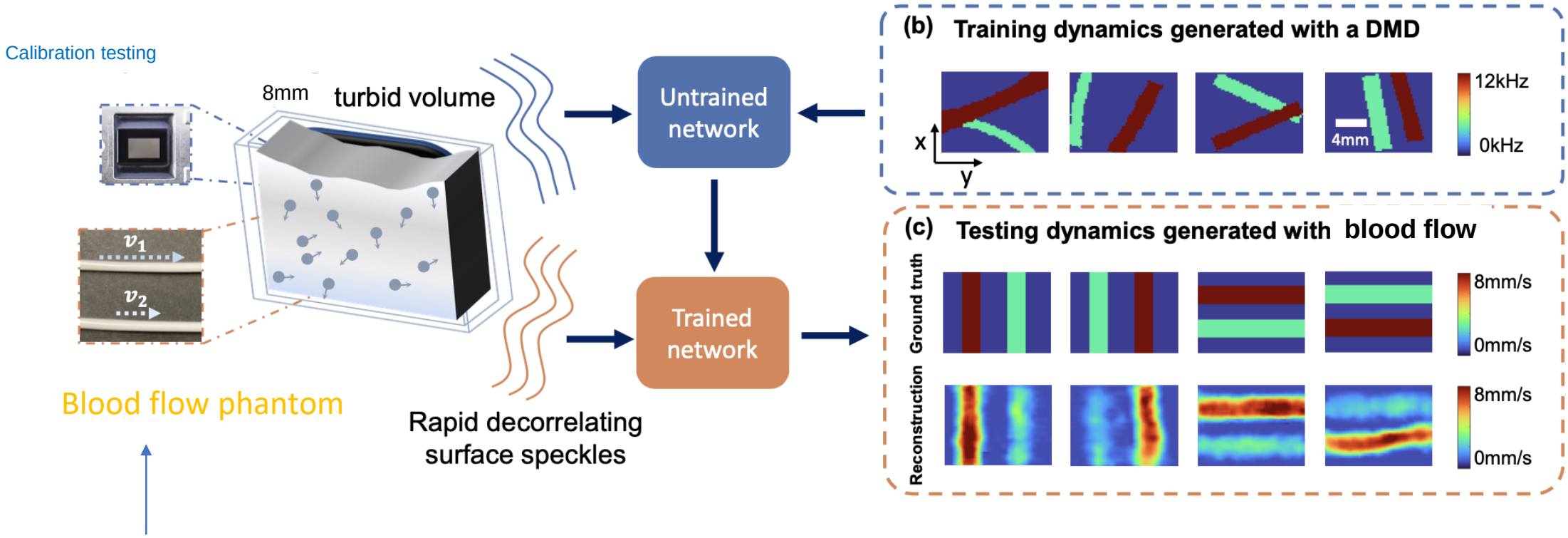


Tubes with liquid blood phantom with 5 µm spheres

Example Specs:
- **8 mm deep**
- **5x5 cm area**
- **10 Hz sampling rate**

Siegert's relation for spatial and temporal variance

- $\kappa^2(T) = \frac{2}{T}\int_0^T \left(1 - \frac{\tau}{T}\right) c_t(\tau) d\tau$

  - *spatial variance / speckle contrast:* $\kappa^2(T) = \frac{\sigma_s^2(T)}{\langle I \rangle^2}$, $\sigma_s^2(T)$, at exposure T

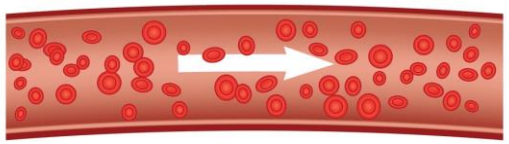
  - *temporal variance / autocorrelation:* $c_t(\tau) = \frac{\langle (I(t) - \langle I \rangle)(I(t+\tau) - \langle I \rangle) \rangle}{\langle I \rangle^2}$
    $= g_2(\tau) - 1$

Blood flow leads to faster decorrelation

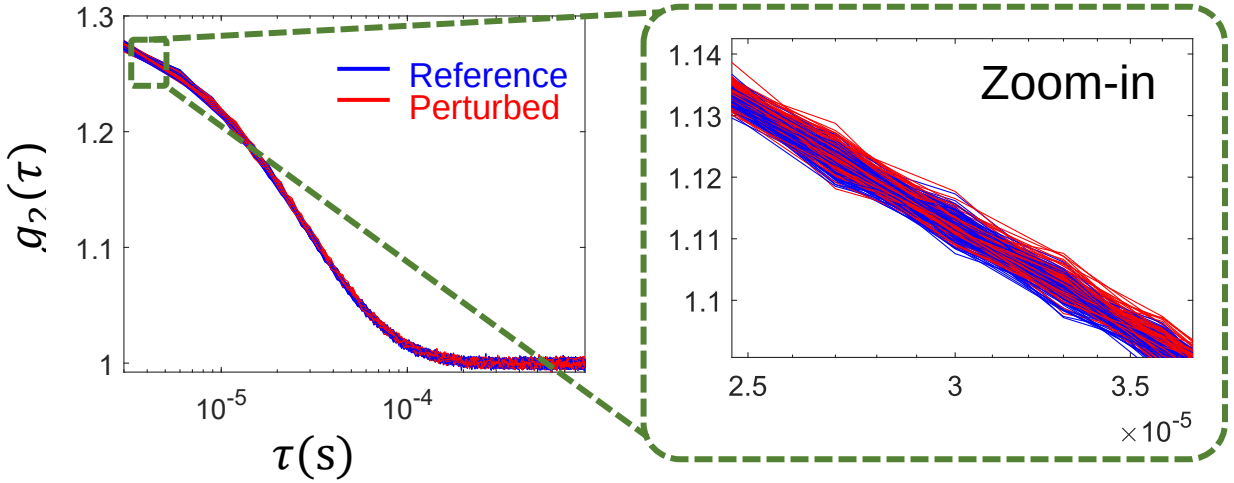
5 mm phantom tissue depth

Reference: $v = 0\text{mm/s}$

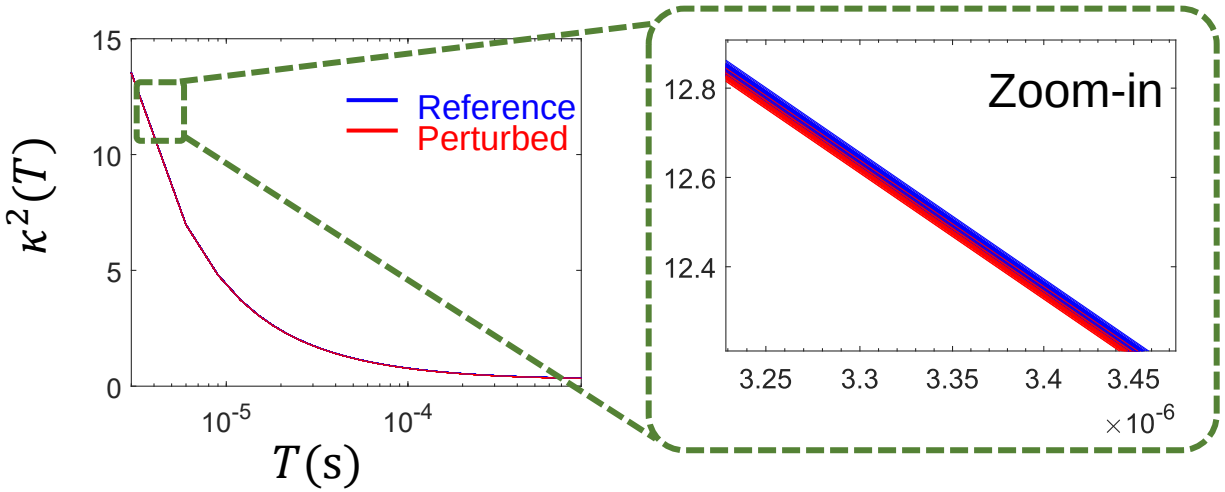
Perturbed: $v = 0.5\text{mm/s}$



temporal variance / autocorrelation $g_2(\tau)$



spatial variance / speckle contrast: $\kappa^2(T)$

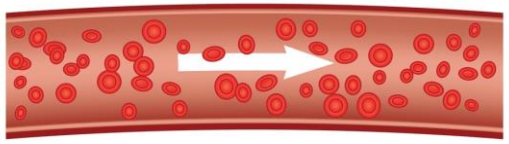


Decorrelation depends on flow rate

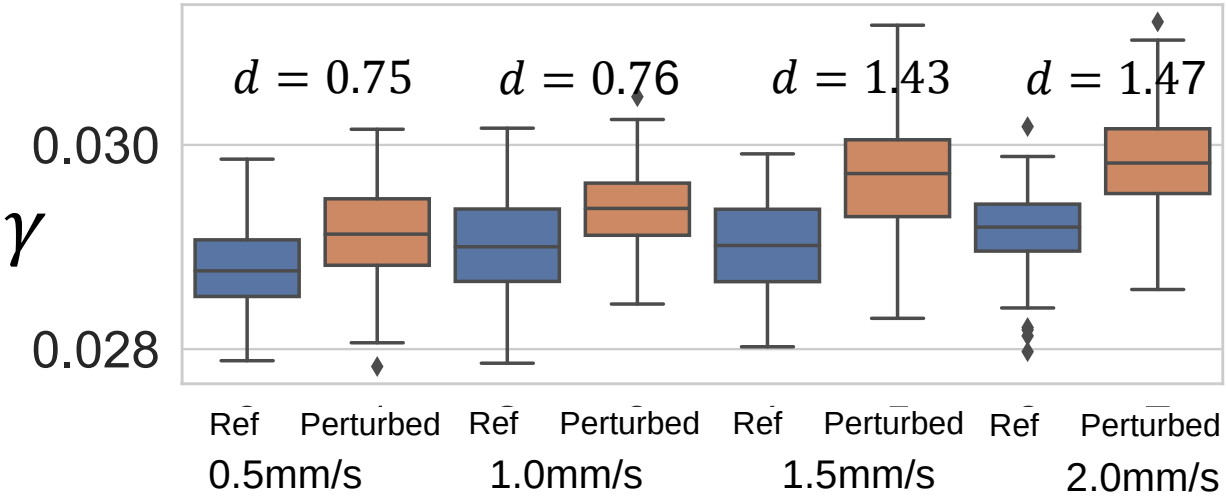
5 mm phantom tissue depth

Reference: $v = 0\text{mm/s}$

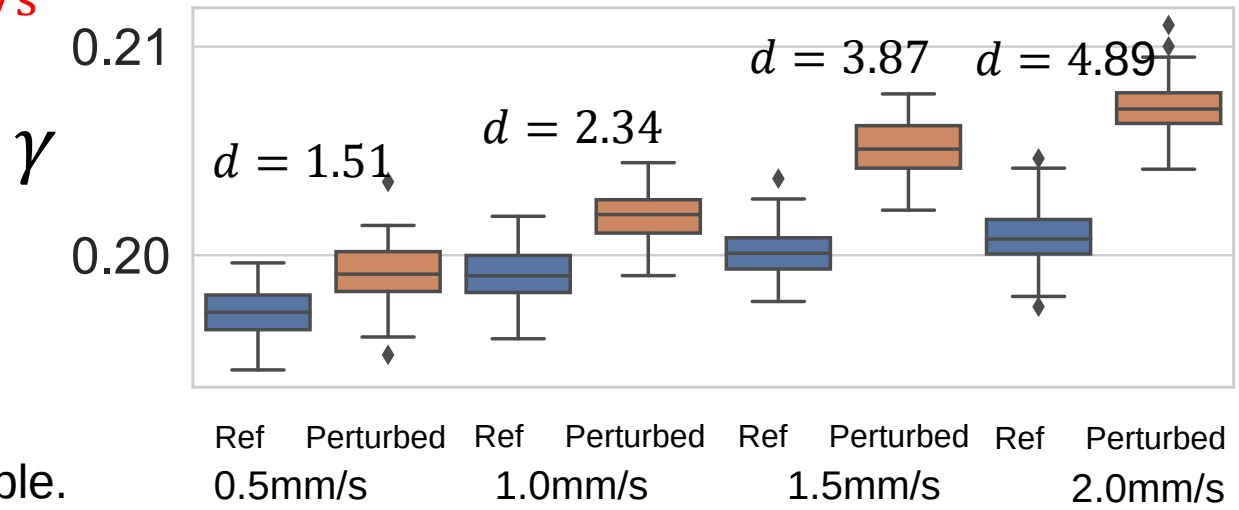
Perturbed: $v = 0.5 - 2\text{mm/s}$



temporal variance / autocorrelation $g_2(\tau)$

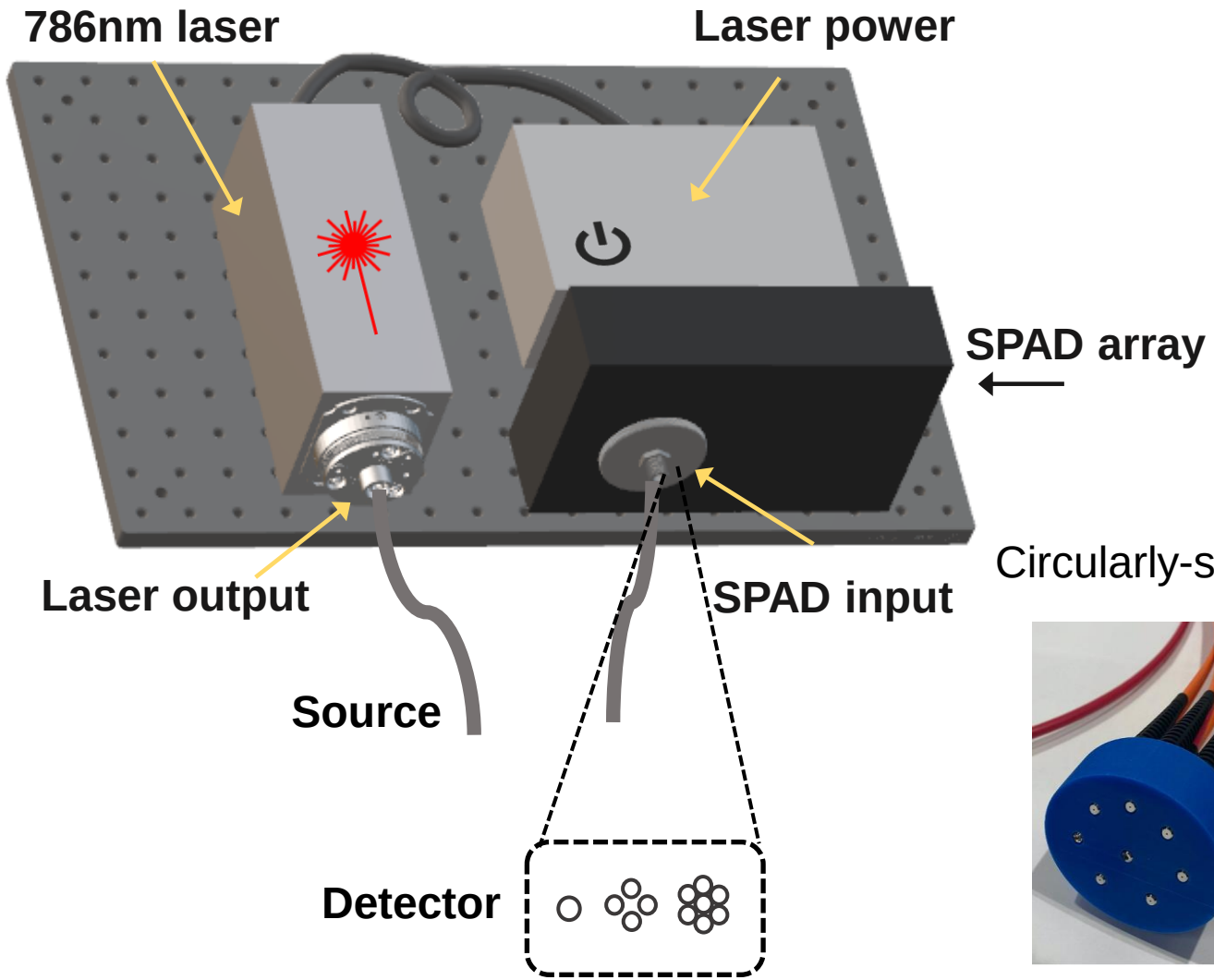


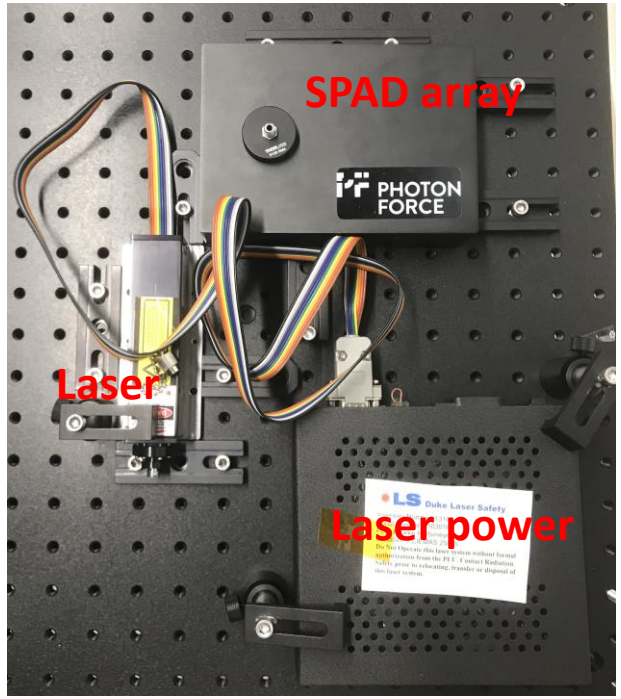
spatial variance / speckle contrast: $\kappa^2(T)$



γ = Retrieved decorrelation rate
d = Cohen's d
d > 0.8 is considered as largely separable.

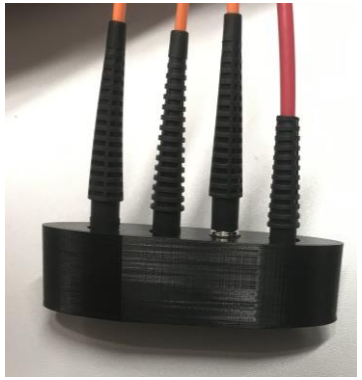
Current efforts – Next-gen PDCS



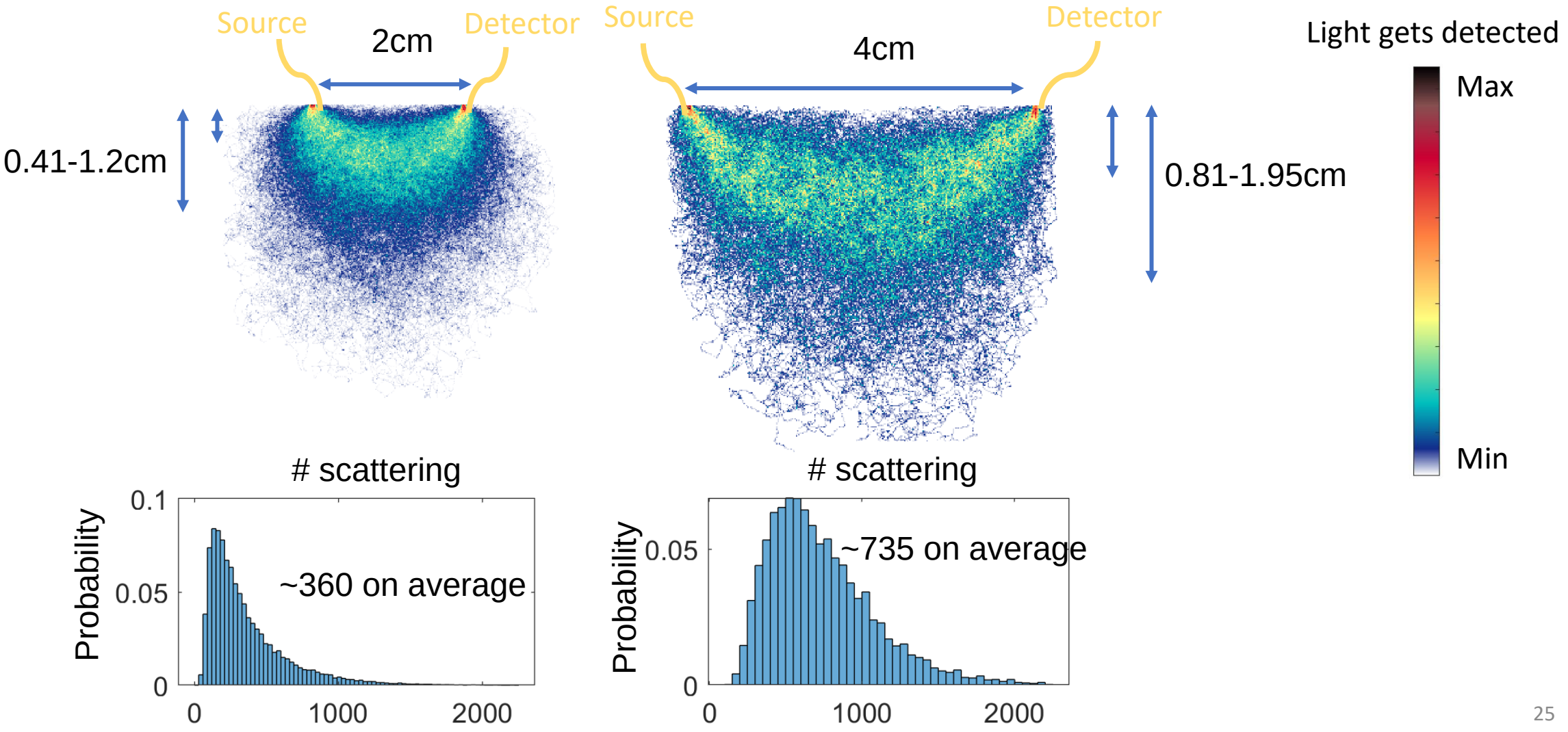


Circularly-shaped

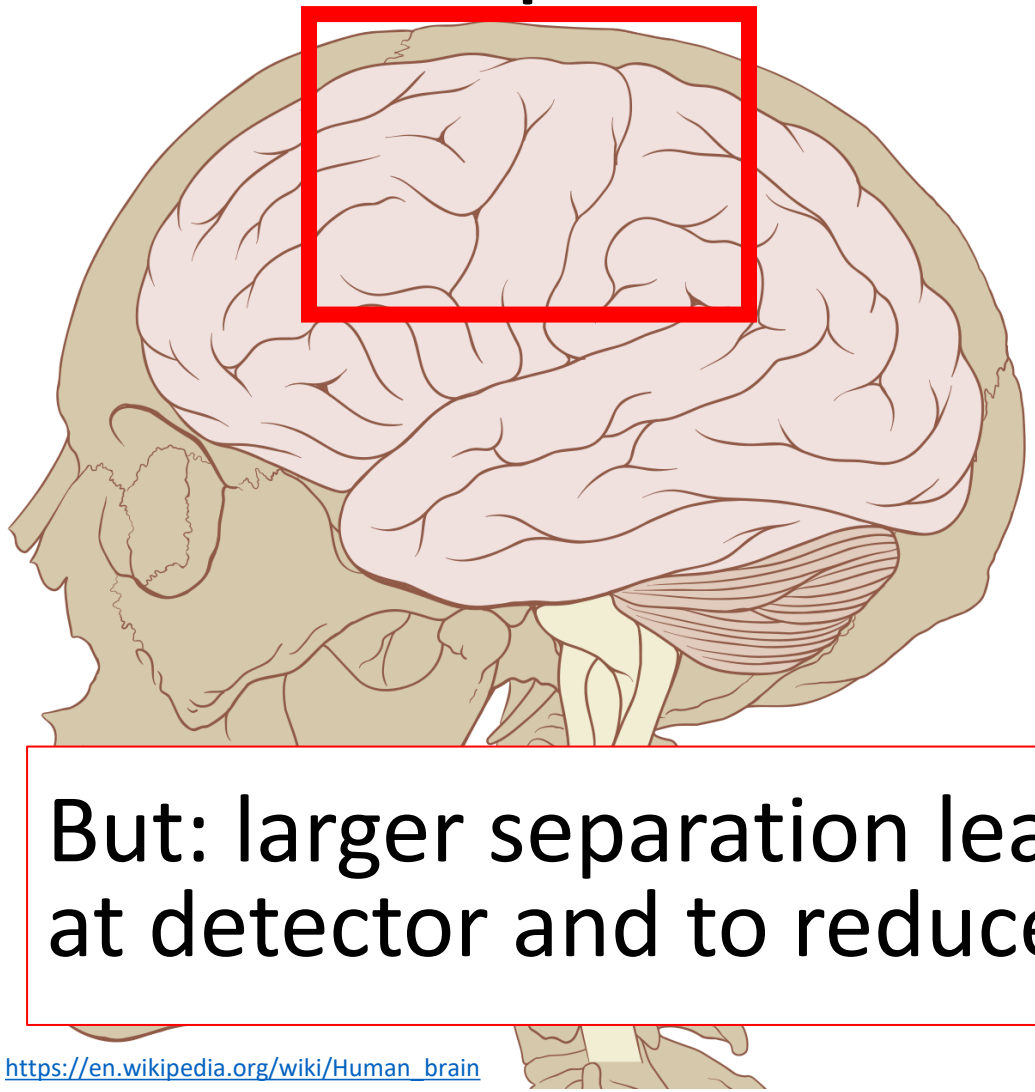
Multi-distance

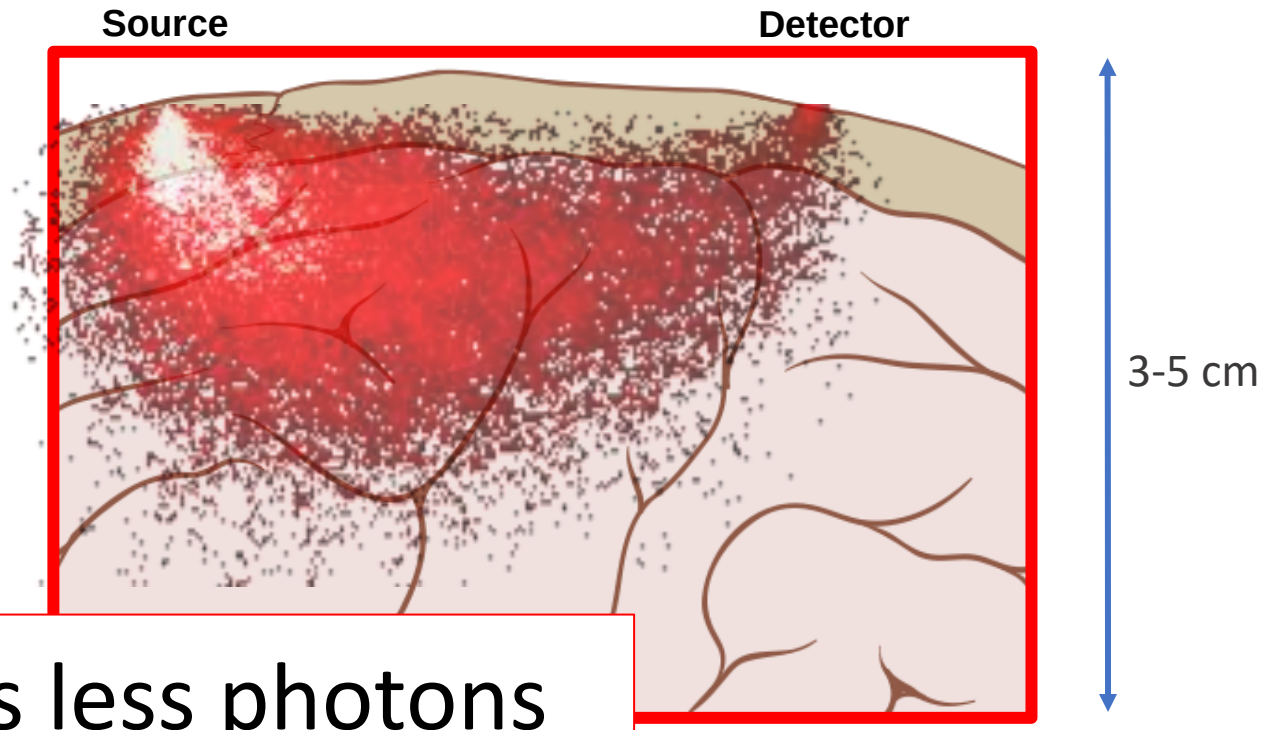


Going deeper with larger source-detector separation



Goal: increase source-detector separation to look deeper into the brain





But: larger separation leads less photons at detector and to reduced SNR

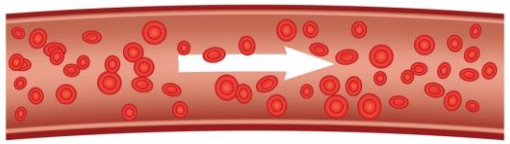
https://en.wikipedia.org/wiki/Human_brain

3cm s-d separation, 1.5cm thick tissue phantom

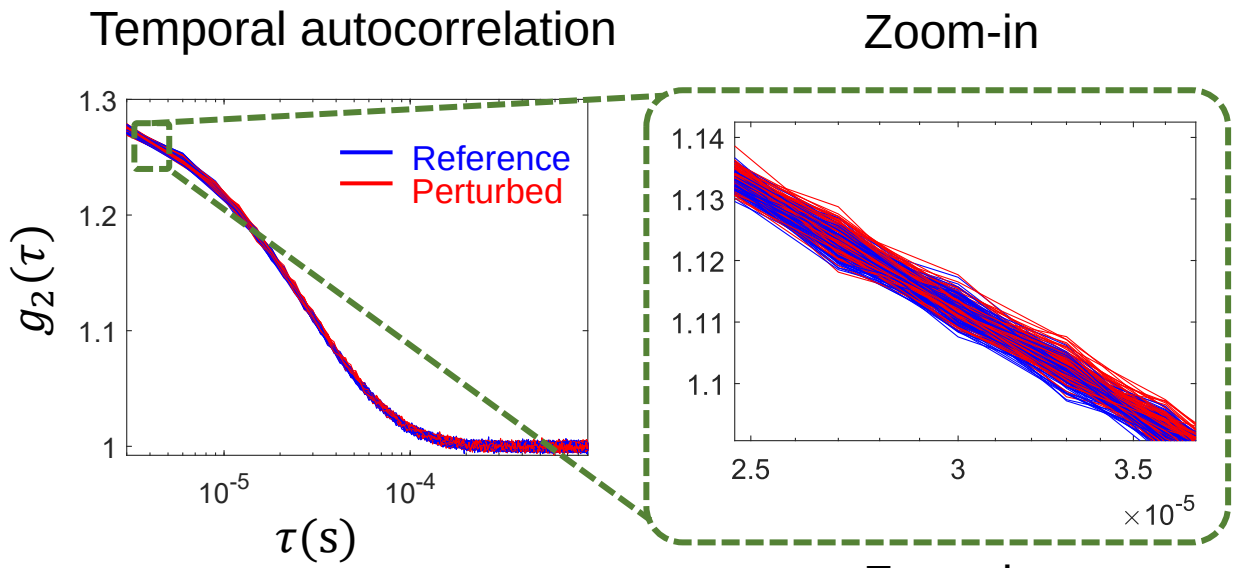
Reference: $v = 0\text{mm/s}$

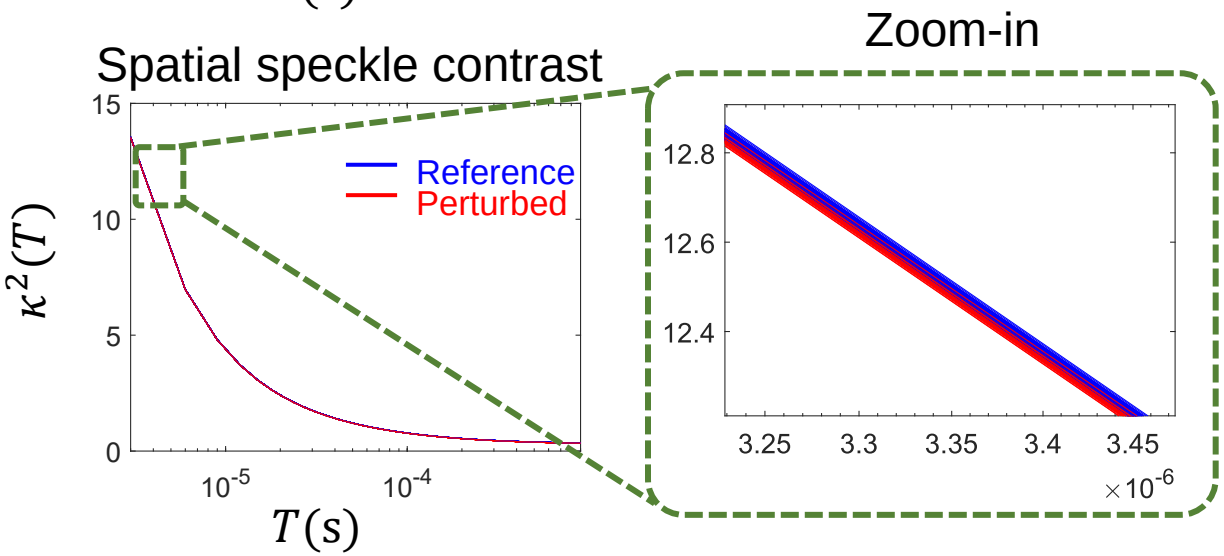
x100

Perturbed: $v = 0.5\text{mm/s}$



x100



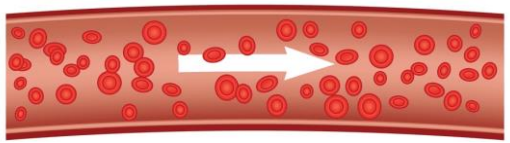


4cm s-d separation, 2.0cm thick tissue phantom

Reference: $v = 0\text{mm/s}$

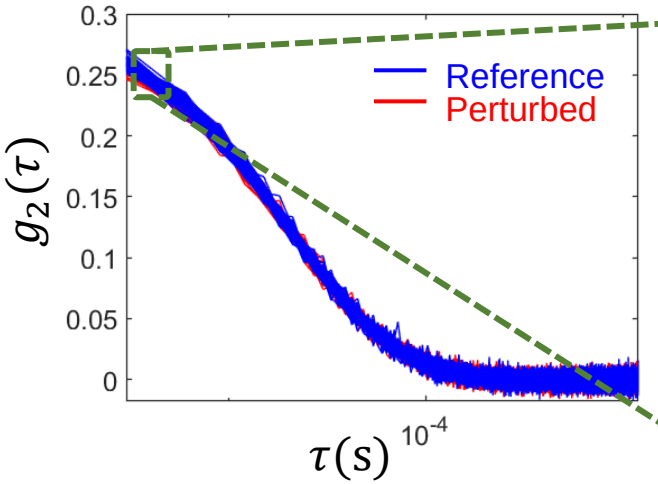
x75

Perturbed: $v = 1\text{mm/s}$

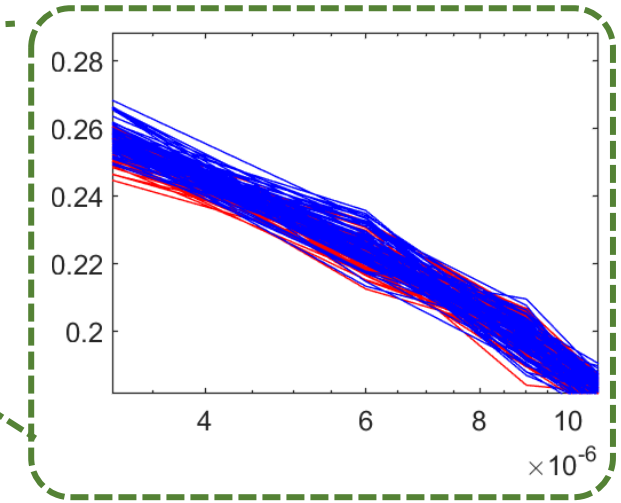


x75

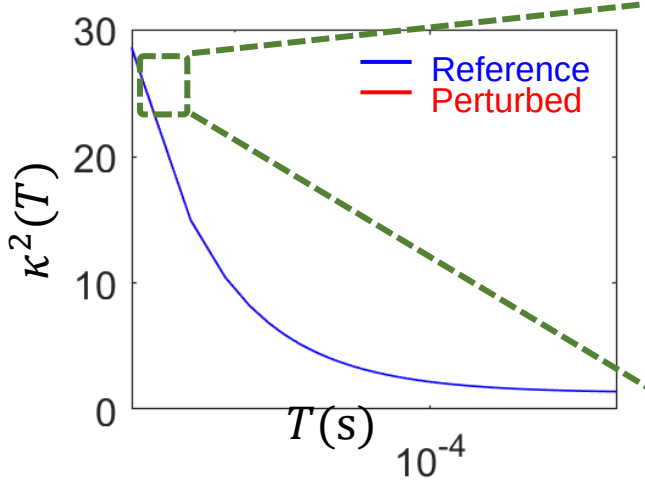
Temporal autocorrelation



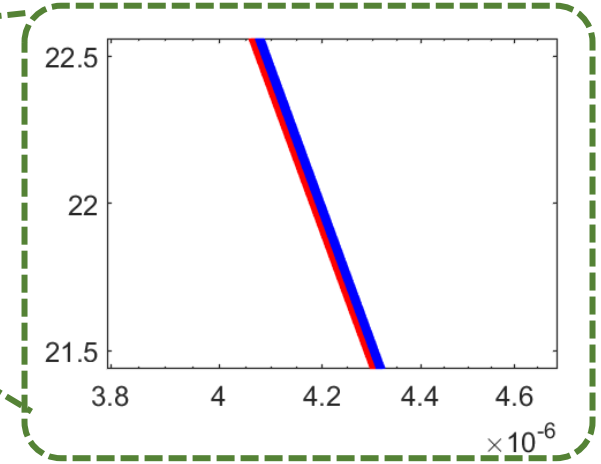
Zoom-in



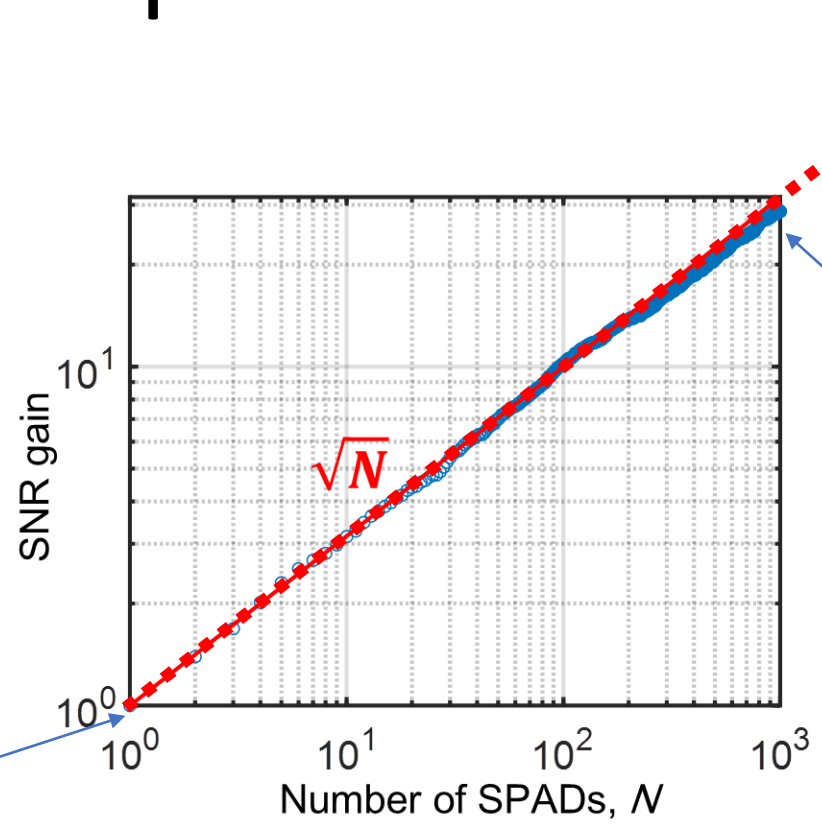
Spatial speckle contrast



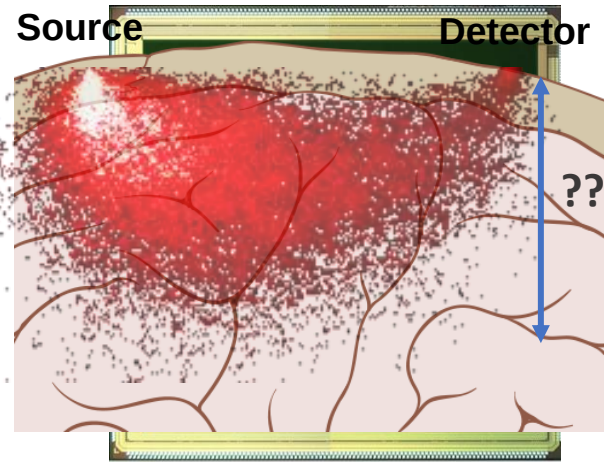
Zoom-in



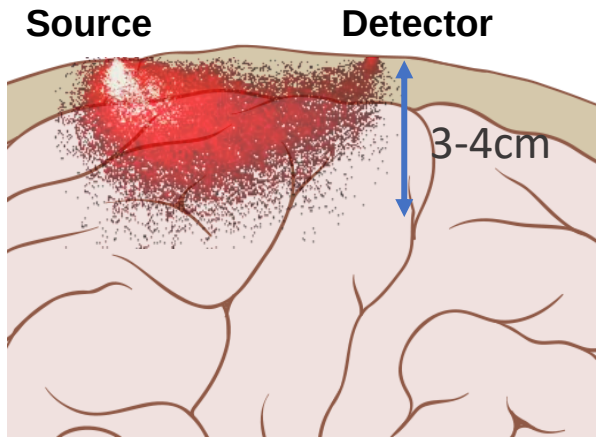
Larger SPAD arrays increase PDCS SNR and allow us to look deeper into tissue



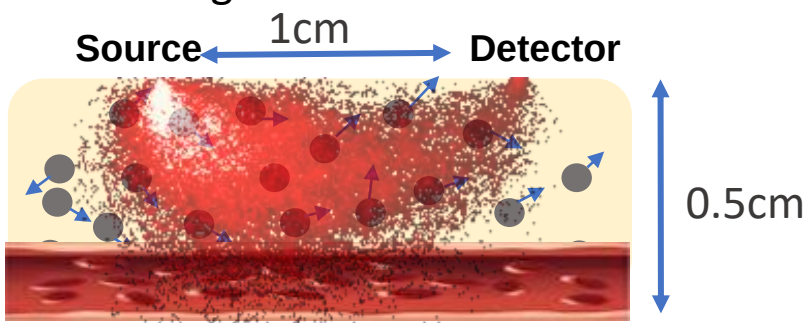
Goal : we need more SPADs!



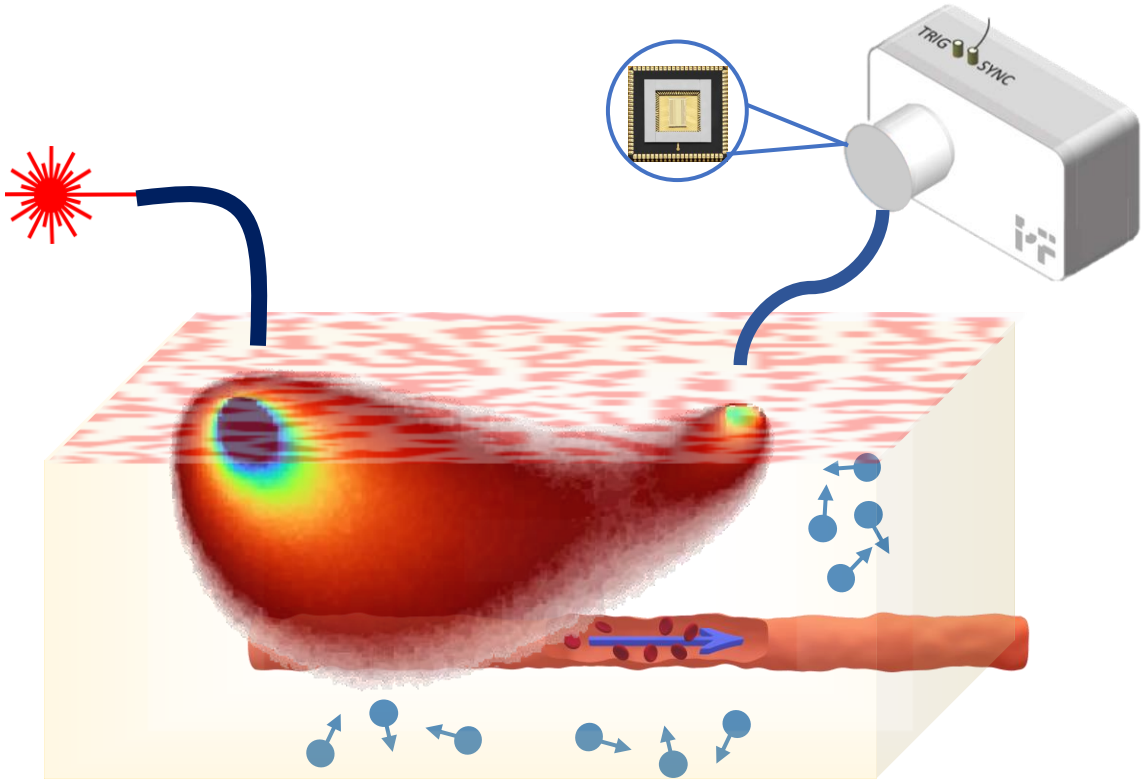
32x32 SPAD array N = 1064



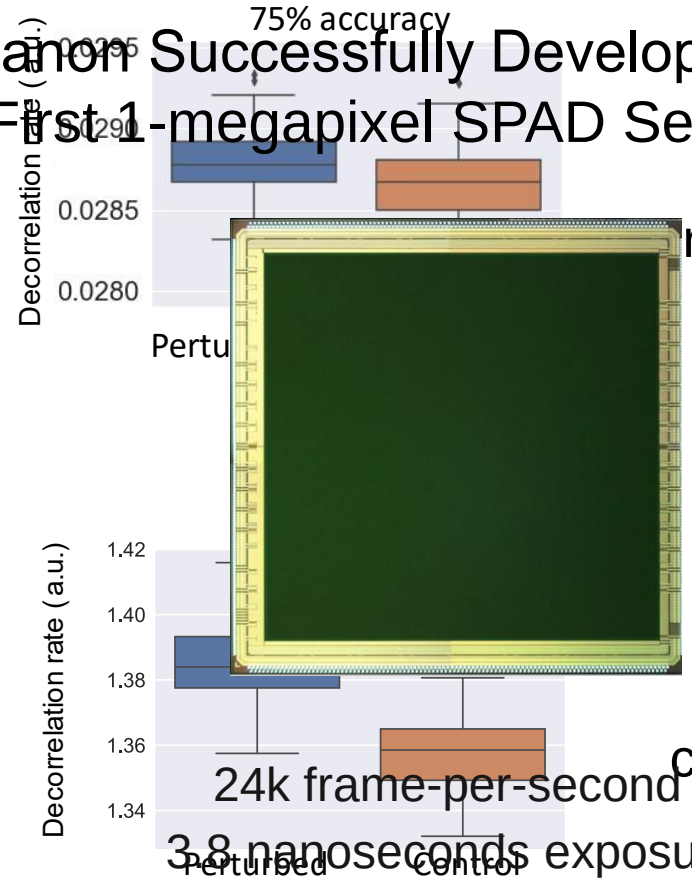
Single SPAD N = 1



Summary: SPAD arrays are great for measuring deep-tissue blood flow



Canon Successfully Develops the World's First 1-megapixel SPAD Sensor in 2021



Temporal relation-based

Spatial contrast-based

24k frame-per-second

3.8 nanoseconds exposure

Thanks for your attention

Questions? Please email
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our funding sources!

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