Lasers for skin diagnostics - chromophore mapping and photon pathlength estimation

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ALT INTERNATIONAL CONFERENCE Advanced Laser Technologies

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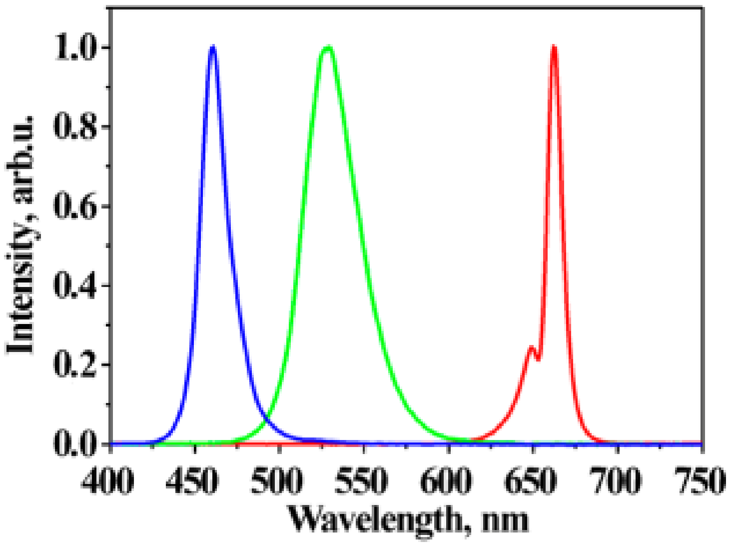
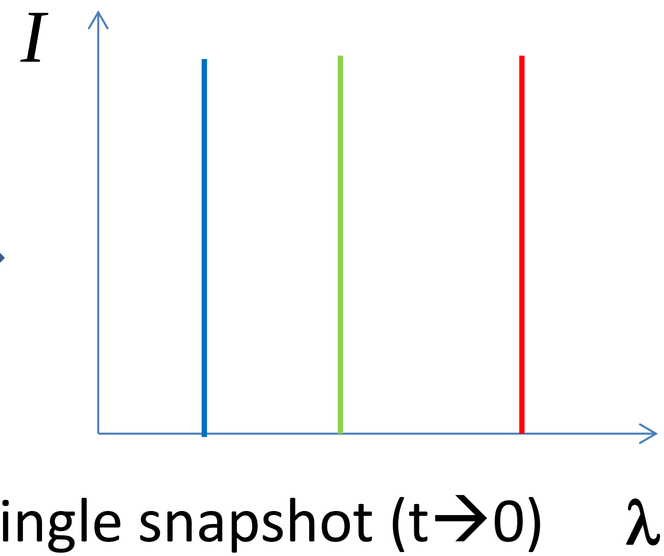
Multi-spectral-line imaging for skin chromophore mapping: the concept

Conventional:
Spectral **band** images



Sequential (t>>0)

Novel:
Spectral **line** images



Single snapshot (t→0)

n =3 → n > 3

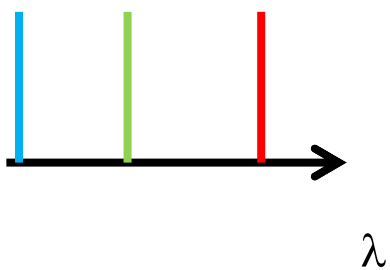
Benefits:

- Increased (ultimate) spectral selectivity, <0.01 nm
- Improved imaging quality (snapshot → avoided motion artefacts)
- Simpler/faster image processing (numbers instead of integrals over wavelength bands

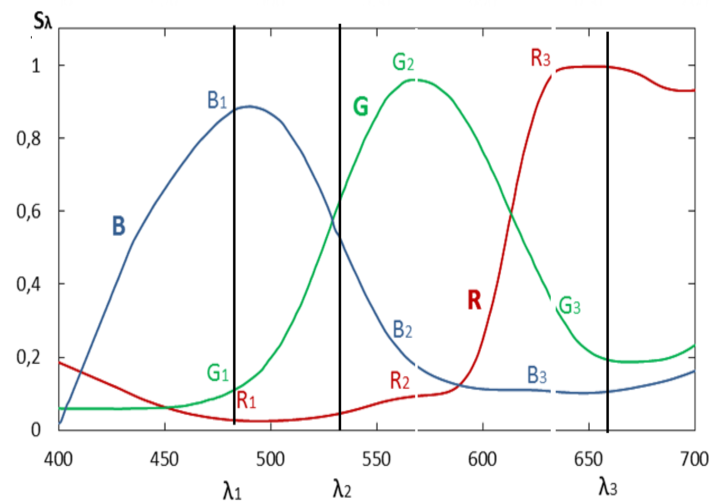
RGB snapshot triple-spectral-line imaging

3 **monochromatic spectral images** from a **single-snapshot** RGB image data can be extracted if object is <u>illuminated simultaneously at 3 laser wavelengths,</u> and the RGB-band sensitivities of the image sensor are known → corrected R-, G- and B-band images*.

<u>Illumination spectrum:</u>

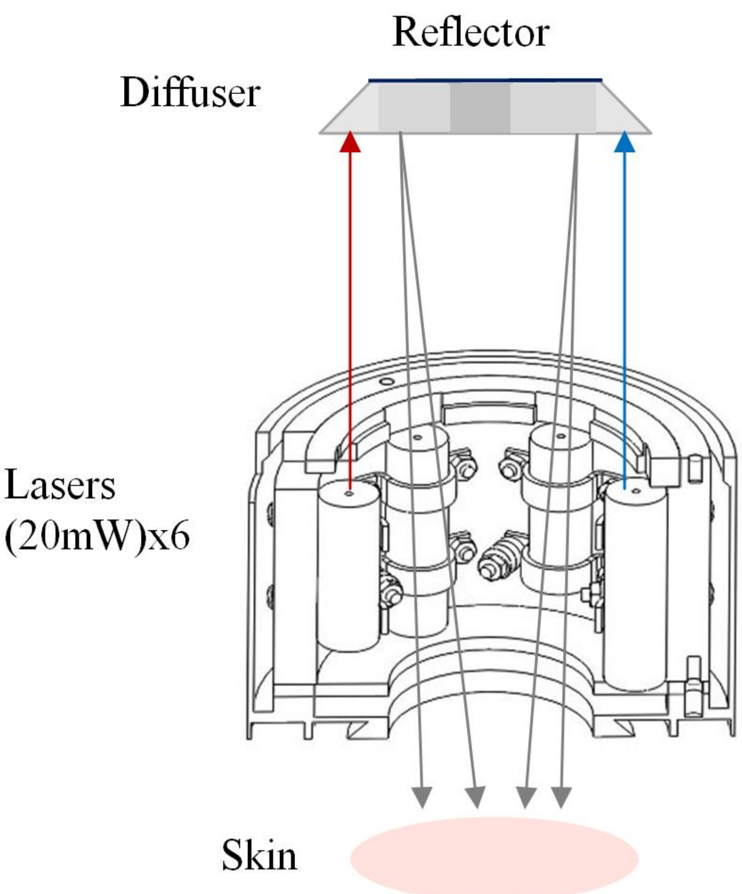


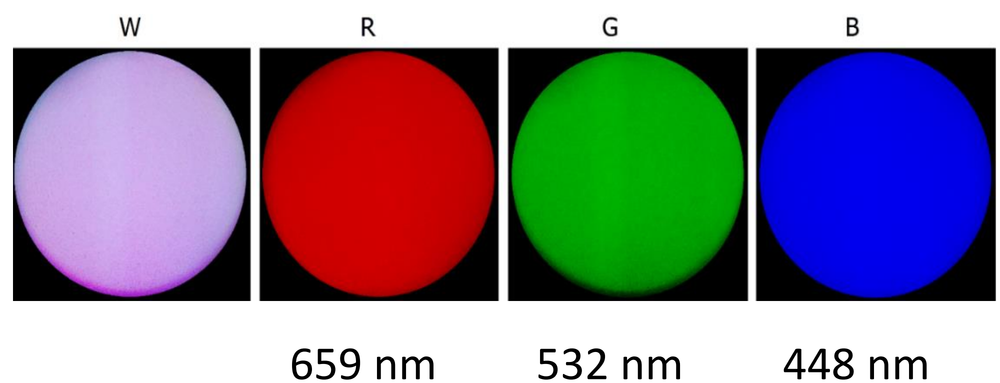
<u>RGB sensitivities of the image sensor :</u>



*) WO 2013135311 (A1). Method and device for imaging of spectral reflectance at several wavelength bands.

Triple-wavelength laser illumination: three couples of laser modules with a flat ring-shaped diffusing reflector



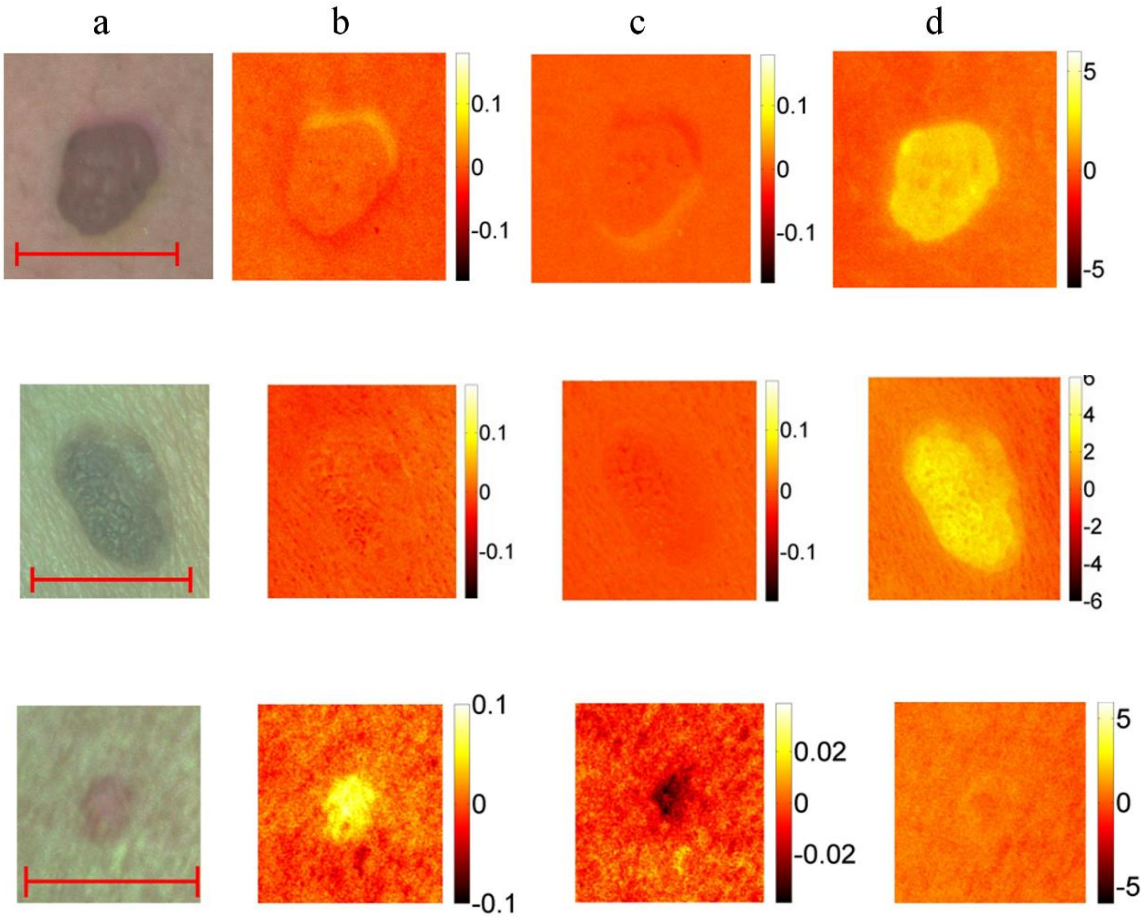


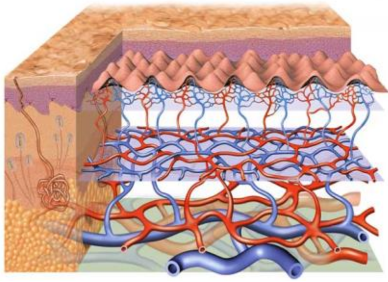
RGB images (a) and maps of chromophore content changes: b – oxy-haemoglobin, c – deoxy-haemoglobin, d – melanin.

pigmented nevus

seborrheic keratosis

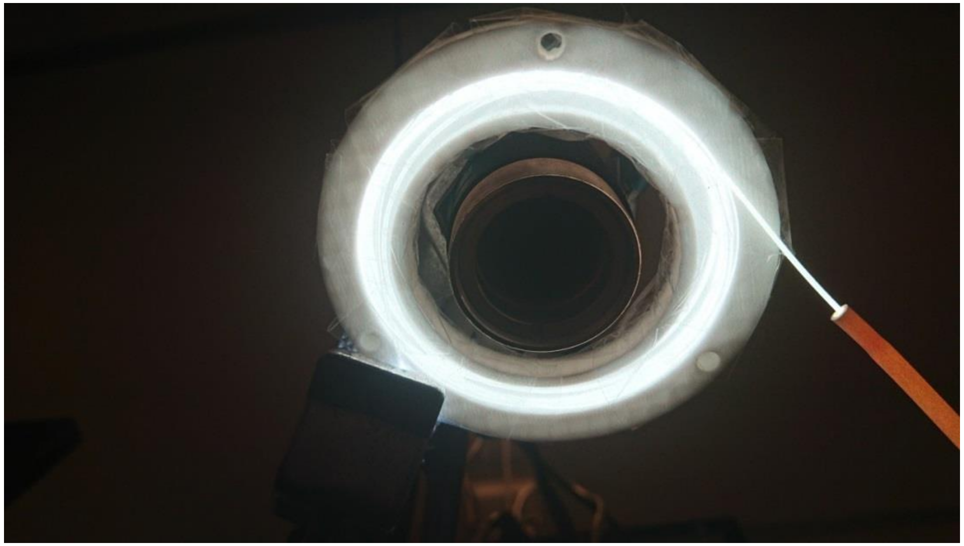
haeman-gioma



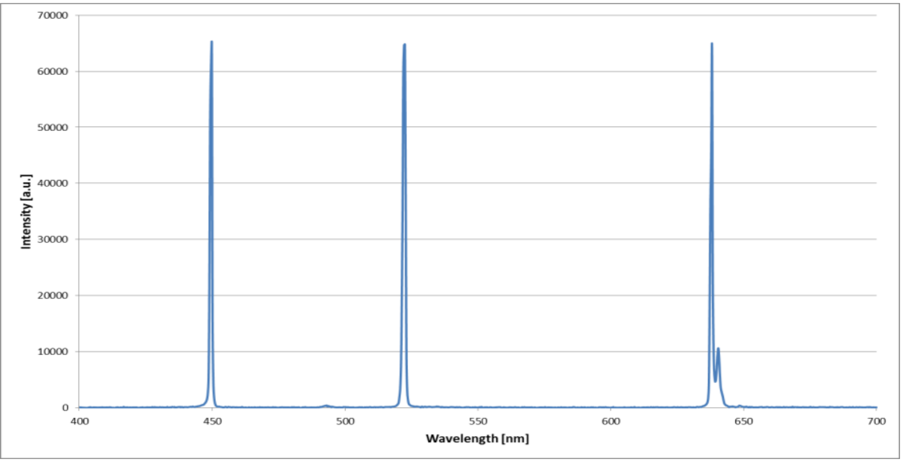


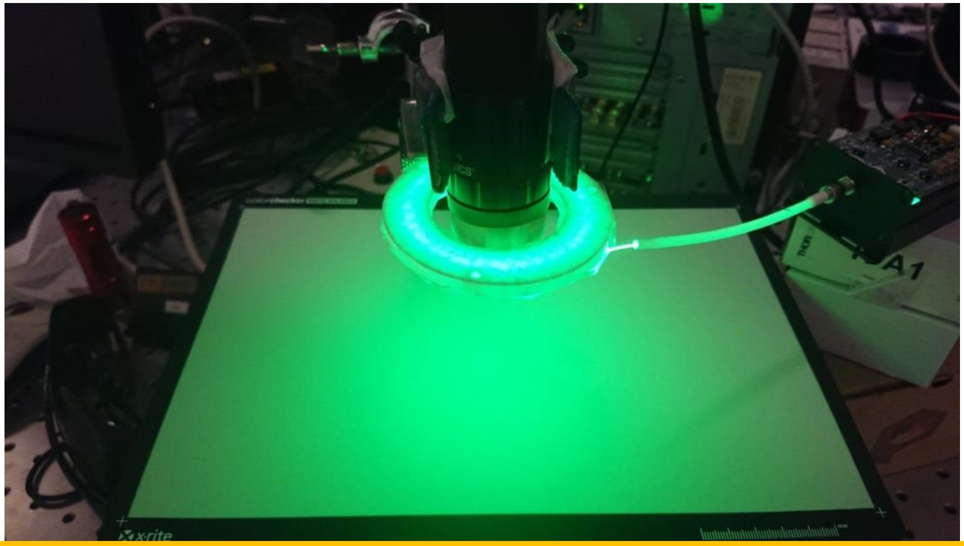
J.Spigulis, et al. Smartphone snapshot mapping of skin chromophores under triple-wavelength laser illumination. *J.Biomed.Opt.*, **2017**, 22(9): 091508.

Current project: 4-line laser illumination by a side-emitting optical fiber ring



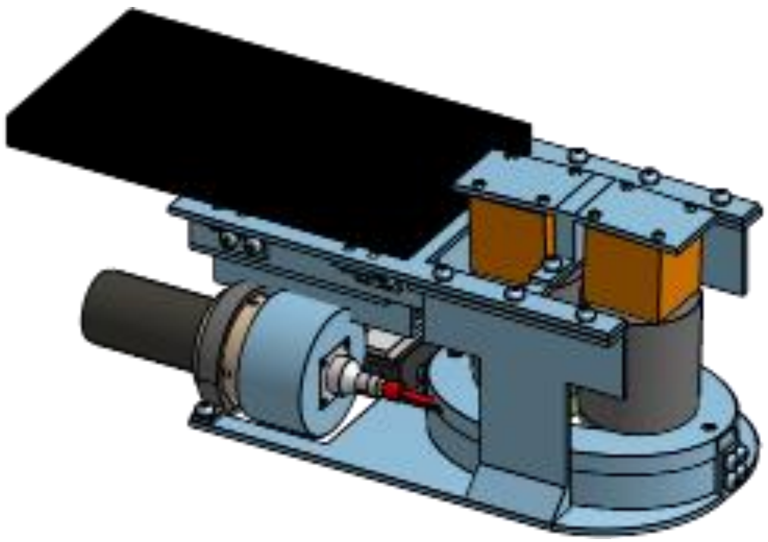
450/523/638 nm + 850 nm





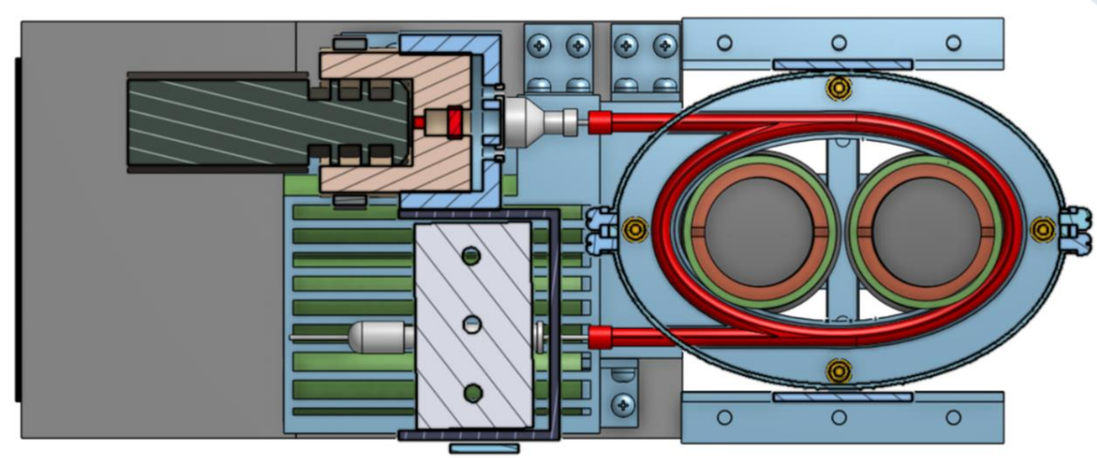
LV 11644 B, 1995. Side-emitting optical fiber (D. Pfafrods, M. Stafeckis, J. Spigulis, D. Boucher);
LV patent application # P-19-45, 21.08.2019.

The new (4+1) wavelength prototype: design concept



Step 1 - 450/523/638/850 nm illumination for snapshot mapping of 4 skin chromophores (HbO, Hb, Mel, Blr) and calculation of the MM criterion;

Step 2 – 405nm excitation for skin fluorescence imaging (MM – SK differentiation)



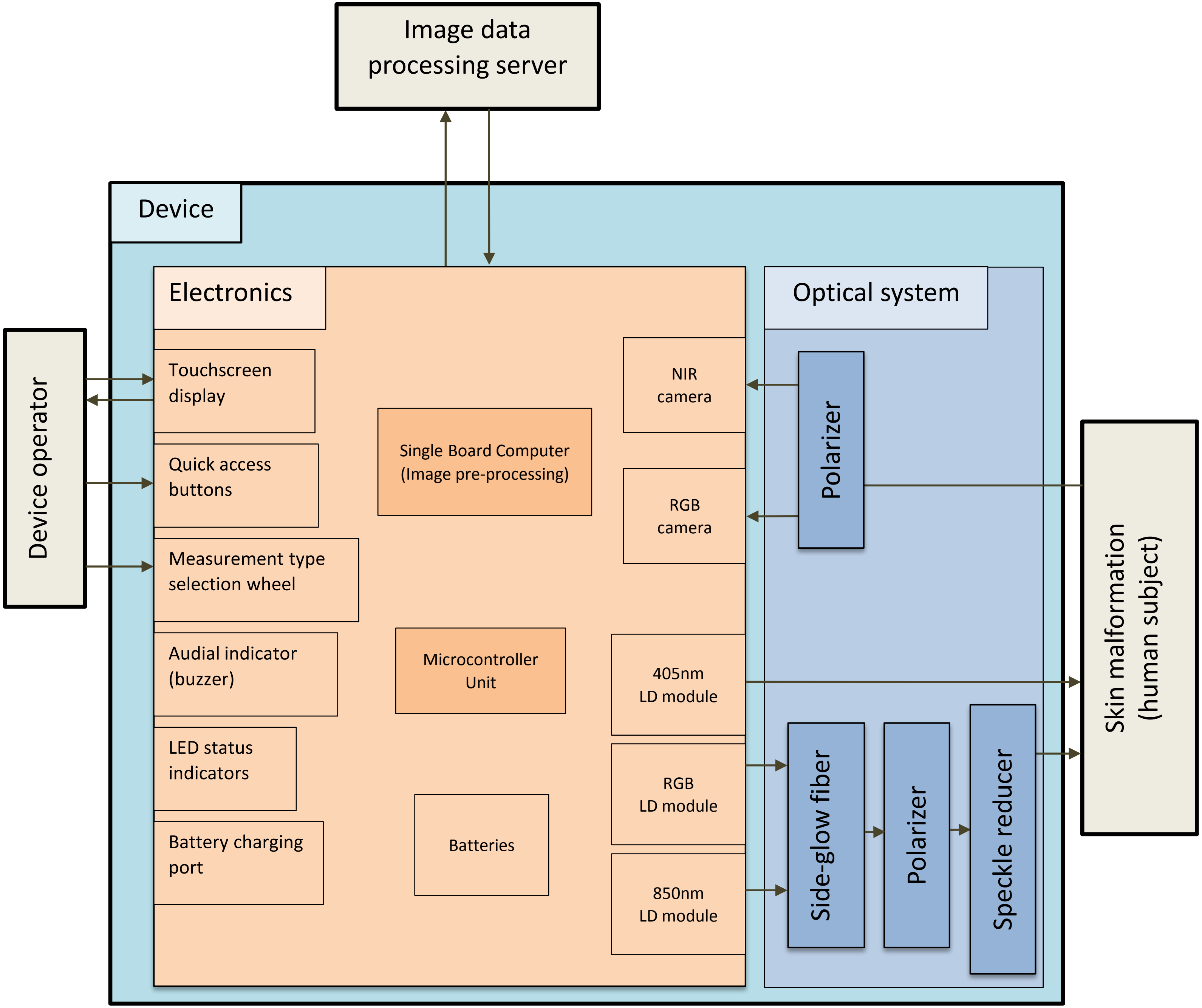


Image data processing server
Device
Electronics
Optical system
Device operator
Touchscreen display
Quick access buttons
Measurement type selection wheel
Audial indicator (buzzer)
LED status indicators
Battery charging port
Single Board Computer (Image pre-processing)
Microcontroller Unit
Batteries
NIR camera
RGB camera
405nm LD module
RGB LD module
850nm LD module
Polarizer
Side-glow fiber
Polarizer
Speckle reducer
Skin malformation (human subject)

«Bottleneck» in chromophore mapping: remitted **photon path length** in skin

Beer–Lambert–Bouguer law[27]

$$\begin{cases} \ln\left(\frac{I_1}{I_{01}}\right) = -l_1[\Delta c_a \cdot \varepsilon_a(\lambda_1) + \Delta c_b \cdot \varepsilon_b(\lambda_1) + \Delta c_c \cdot \varepsilon_c(\lambda_1)] \\ \ln\left(\frac{I_2}{I_{02}}\right) = -l_2[\Delta c_a \cdot \varepsilon_a(\lambda_2) + \Delta c_b \cdot \varepsilon_b(\lambda_2) + \Delta c_c \cdot \varepsilon_c(\lambda_2)] , \\ \ln\left(\frac{I_3}{I_{03}}\right) = -l_3[\Delta c_a \cdot \varepsilon_a(\lambda_3) + \Delta c_b \cdot \varepsilon_b(\lambda_3) + \Delta c_c \cdot \varepsilon_c(\lambda_3)] \end{cases} \tag{1}$$

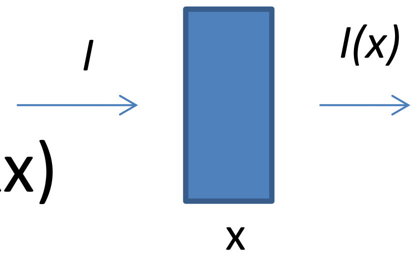
where $\varepsilon_i(\lambda_j)$ is extinction coefficients of three regarded chromophores at three exploited wavelengths and l_j is absorption path length in skin at a particular wavelength. Chromophore concentration increase or decrease at each image pixel (or selected group of pixels) is found by solving the linear equation system (Eq. 1) with abbreviated measured quantities $k_j = \ln(I_j/I_{0j})$:

$$\begin{aligned} \Delta c_a &= A_1 \cdot k_1 + A_2 \cdot k_2 + A_3 \cdot k_3 \\ \Delta c_b &= B_1 \cdot k_1 + B_2 \cdot k_2 + B_3 \cdot k_3 . \\ \Delta c_c &= C_1 \cdot k_1 + C_2 \cdot k_2 + C_3 \cdot k_3 \end{aligned} \tag{2}$$

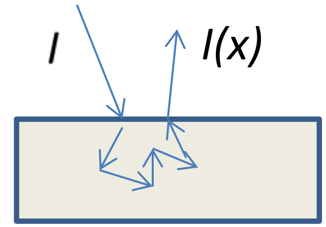
Skin-remitted photon path length estimation by Monte-Carlo simulations (A.Bykov, Oulu)

Slab absorption,

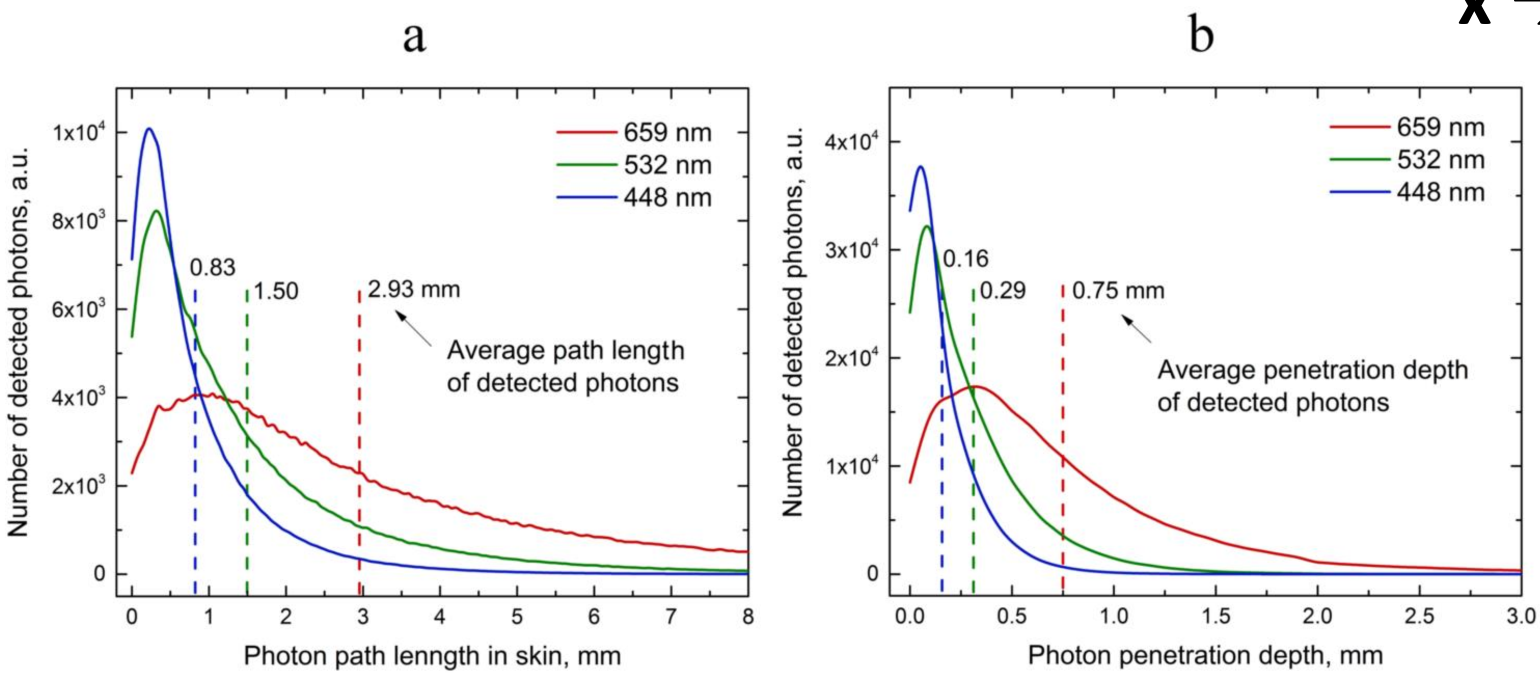
$I(x) = I \exp(-kx)$



Diffuse reflectance absorption:



x → f(x) !



J.Spigulis, I.Oshina, A.Berzina, A.Bykov, "Smartphone snapshot mapping of skin chromophores under triple-wavelength laser illumination", *J.Biomed.Opt.*, **22**(9), 091508 (2017).

Can the distribution of photon path lengths in skin be measured directly?

If the distribution of remitted photon propagation times in skin *f(t)* is measured, the corresponding distribution of photon path lengths can be found as

$$f(s) = f(t) \cdot c/n \qquad (1),$$

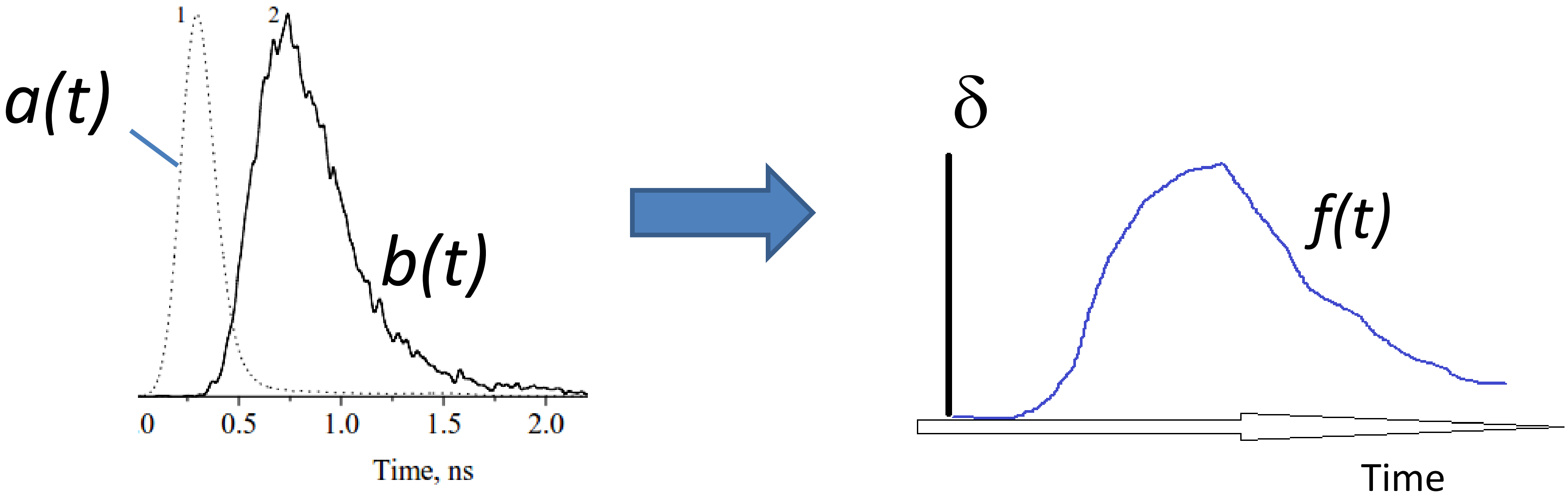
where *c* is the speed of light in vacuum and *n* is the mean refraction index of superficial skin tissues (n ~ 1.36).

The function *f(t)* – response to delta-pulse - is «hidden», it can be found by de-convolution of the integral

$$b(t) = \int_0^t a(t-\tau) f(\tau) d\tau \qquad (2),$$

where *a(t)* is the temporal shape of input laser pulse and *b(t)* – the shape of skin output pulse at the same wavelength.

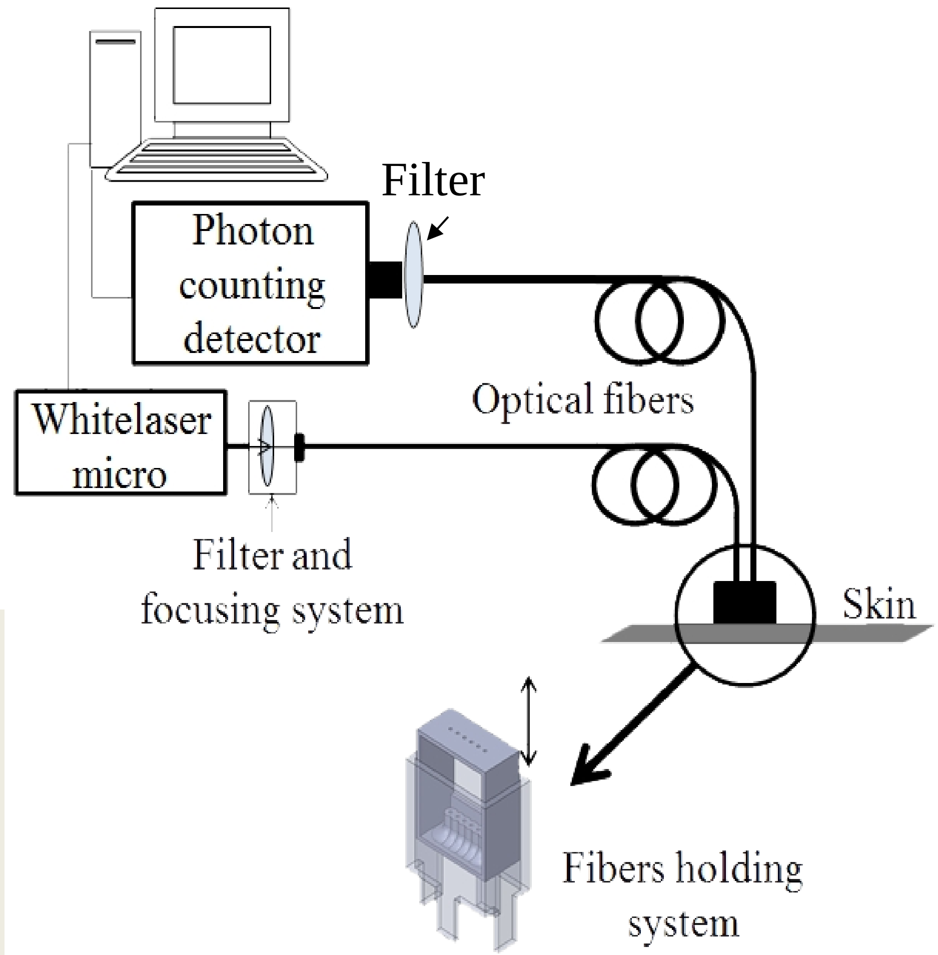
The main idea



$$b(t) = \int_0^t a(t-\tau) f(\tau) d\tau$$

$f(s) = f(t) \cdot c/n$

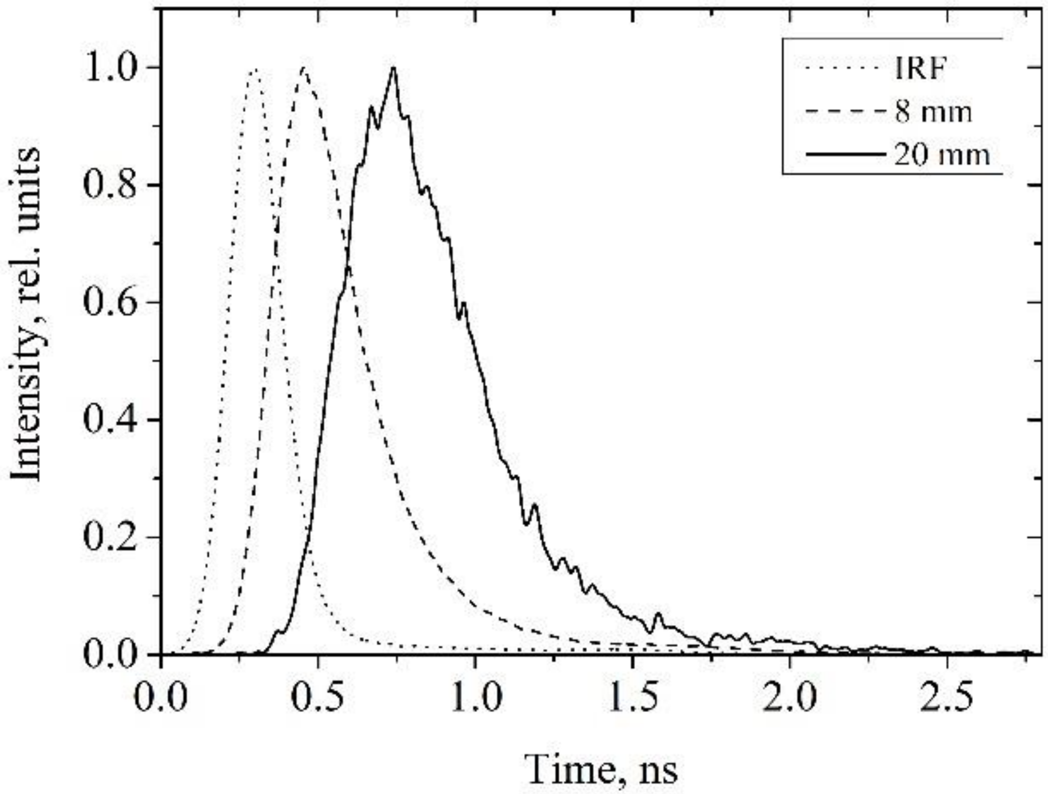
Setup for skin diffuse reflectance kinetics



Difference from the fluorescence setup:

- «white» broadband ps laser used;
- spectral bands selected by couples of equal interference filters, 520...800 nm;
- special fibre holder designed; inter-fiber distances 8, 12, 16, 20 mm

Skin input and remitted pulse shapes, 650 nm

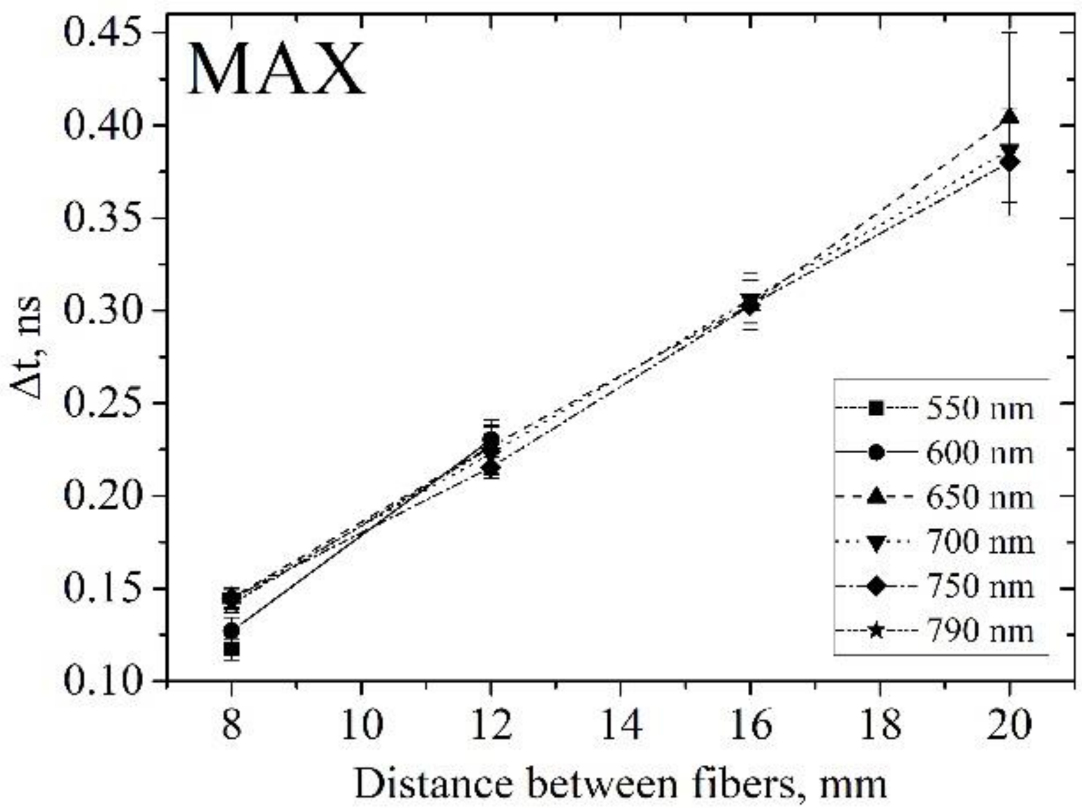


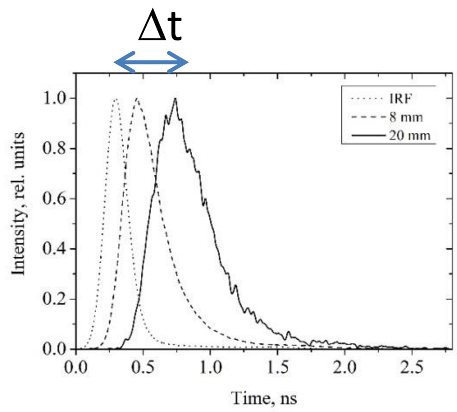
Measured:

- time-shift of pulse peaks
- Increase of FWHM
- Propagation time of the «first» photons

Left volar forearm of a single volunteer

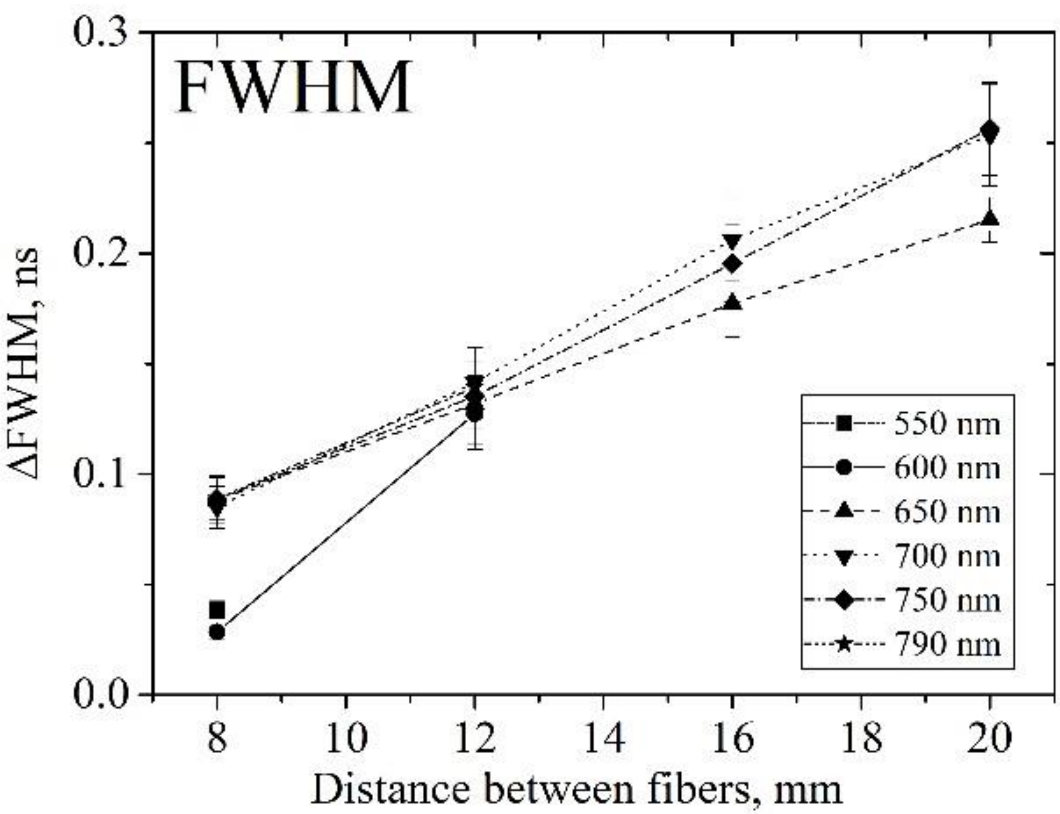
Input-output pulse peak delay

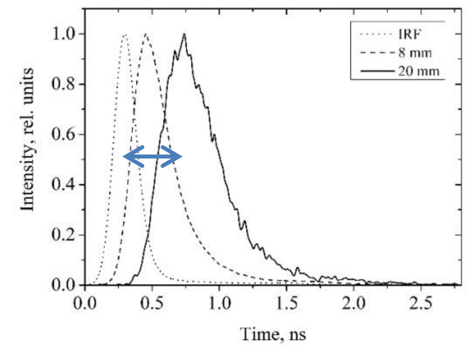




Left forearms of 8 volunteers, averaged values

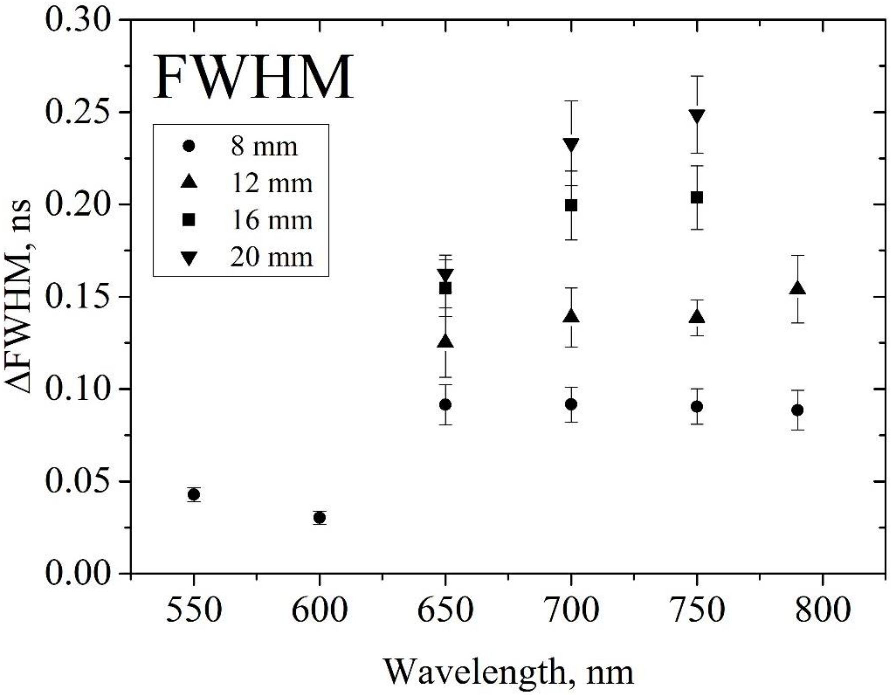
Output-input pulse half-width difference

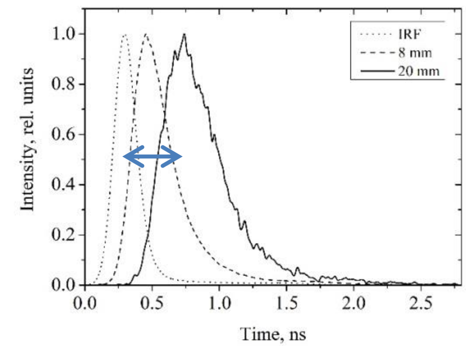


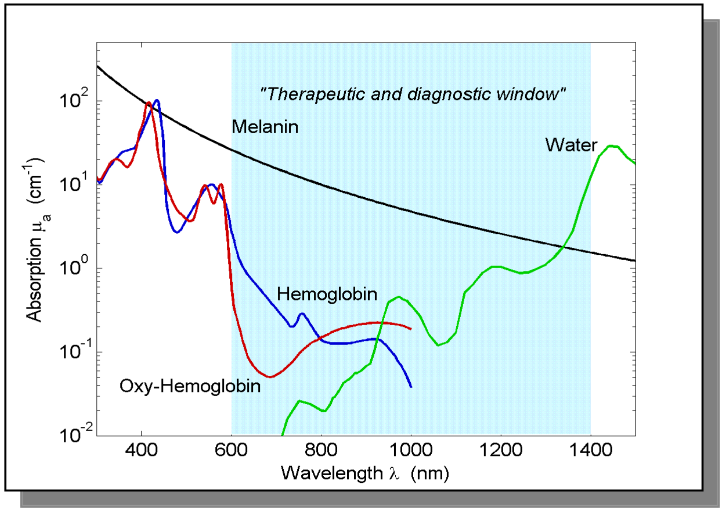


Left forearms of 8 volunteers, averaged values

Differences of pulse half-widths: spectral dependences

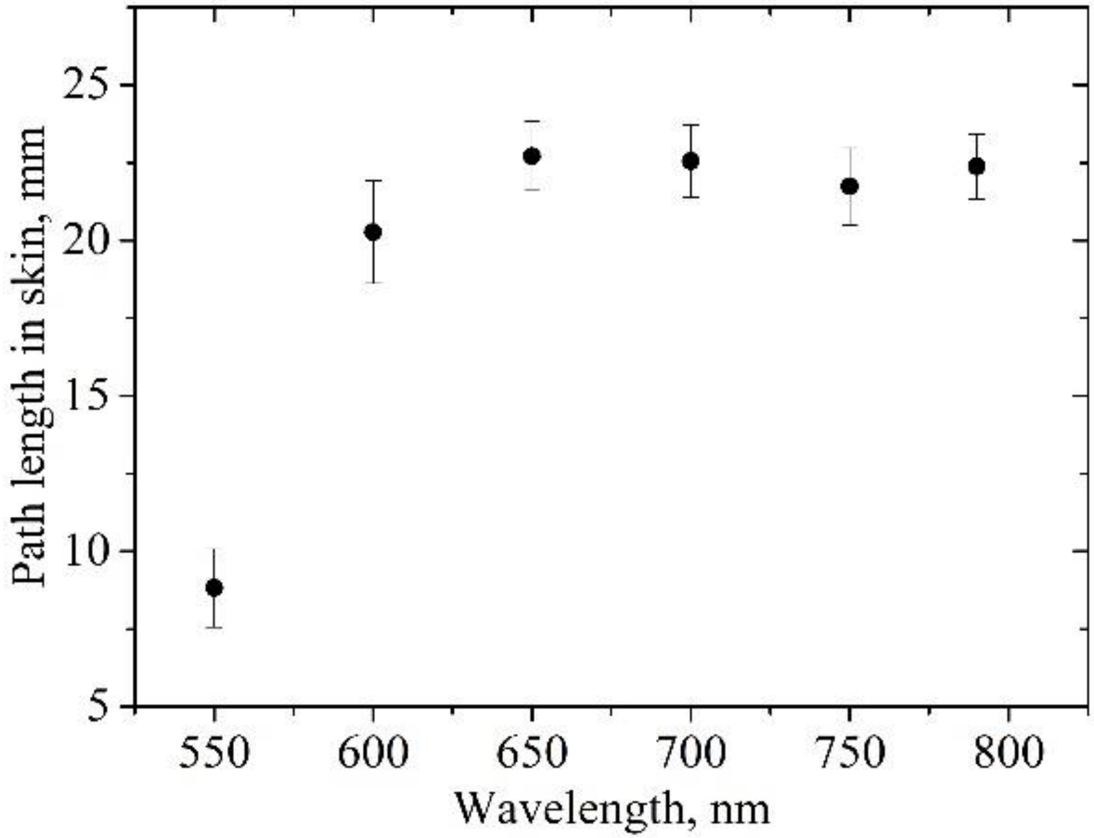


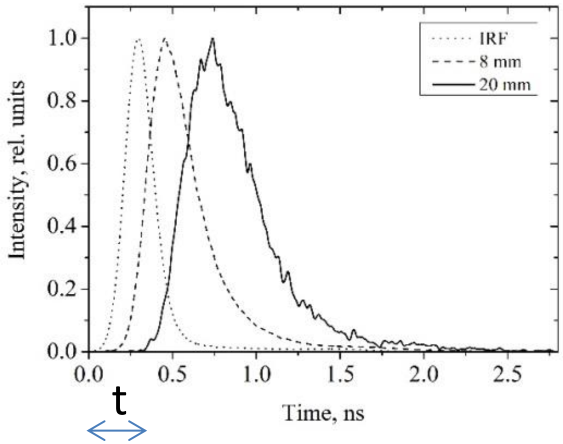




Left forearms of 8 volunteers, averaged values; «jump» around 600nm observed only at 8 mm Inter-fibre distance, unsufficient S/N at longer distances for 550nm and 600nm

Measured path length of the "first" skin-remitted photons as a function of wavelength at inter-fiber distance 8mm (single volunteer)

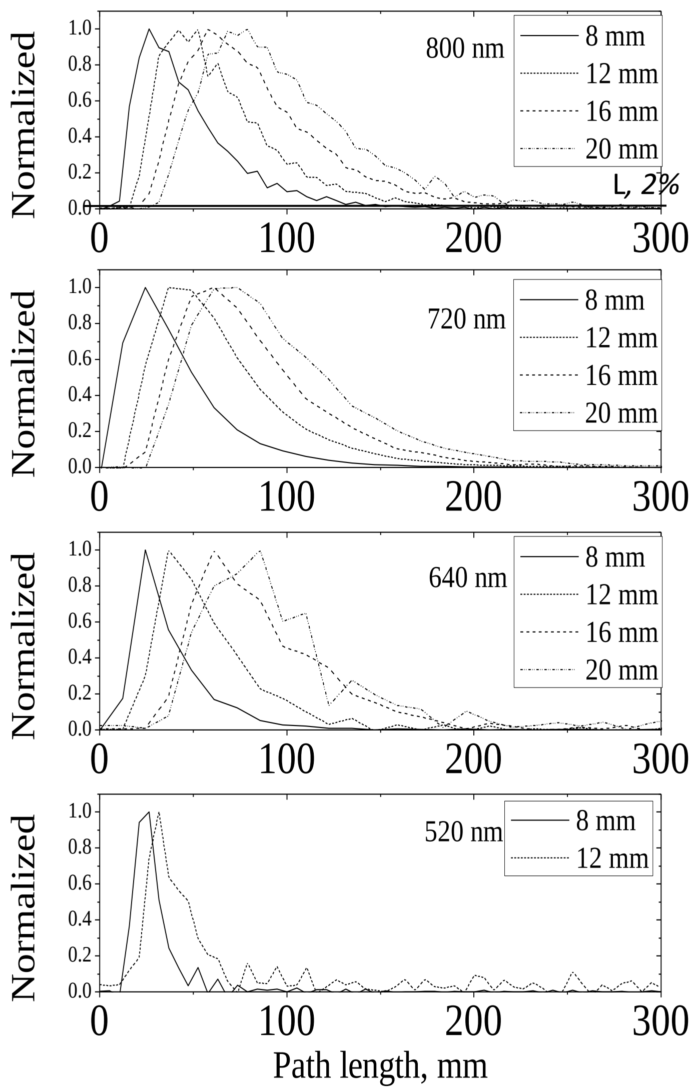




$s = t \cdot c/n$

M.Osis, et al. "Skin remittance kinetics at the spectral range 550-790 nm", *Quant.Electr.*, **49**(1), 2–5 (2019).

The remitted photon path length distributions in normal skin, 520-800 nm



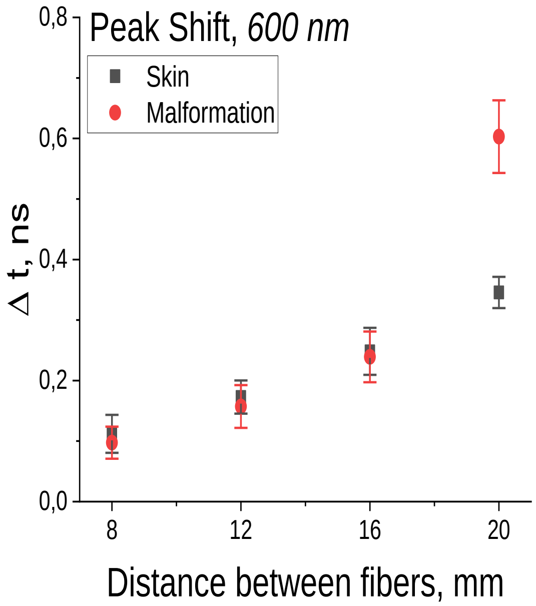
De-convoluted from measurement data using the **Tichonov's regularization** method

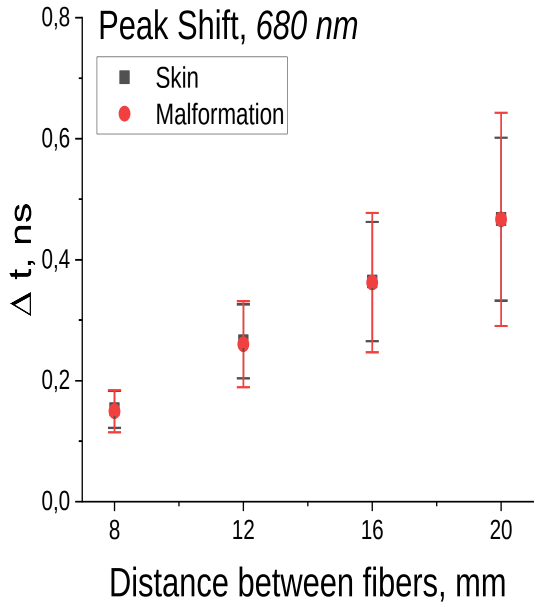
The «longest» path lengths (tail, 2% level)

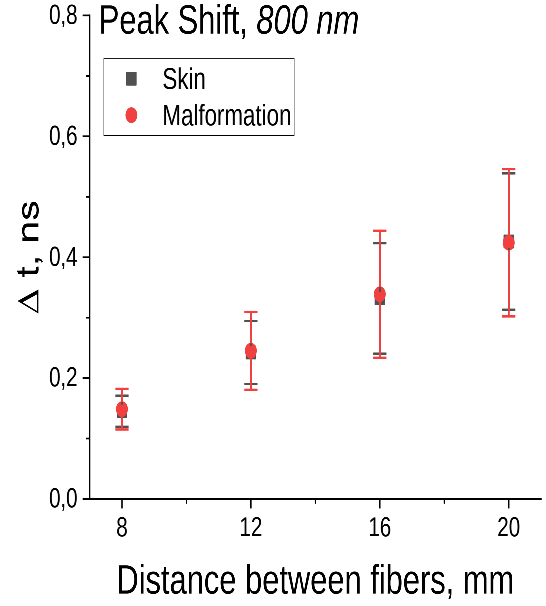
λ, nm	**L, mm (±12)**			
	8 mm	12 mm	16 mm	20 mm
520	117	105	-	-
640	162	204	268	276
720	273	266	267	308
800	251	300	319	304

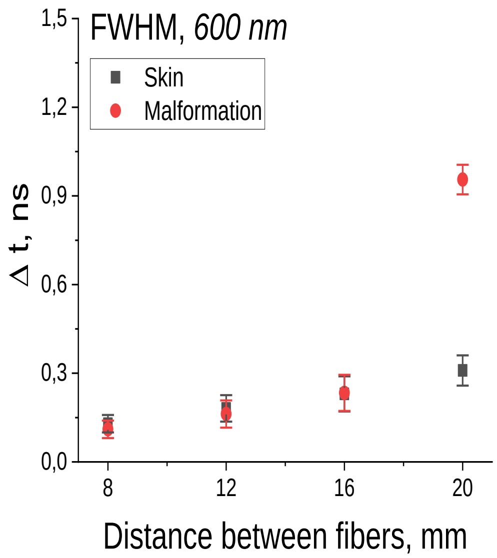
V.Lukinsone, et al. "Towards direct measurements of remitted photon path lengths in skin: kinetic studies in the spectr al range 520-800 nm", Proc. SPIE 11075 – 4, (2019)

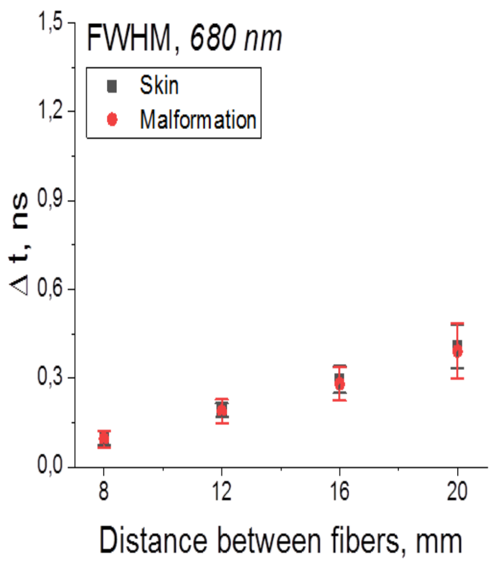
Healthy skin vs 8 pigmented lesions: pulse peak shifts

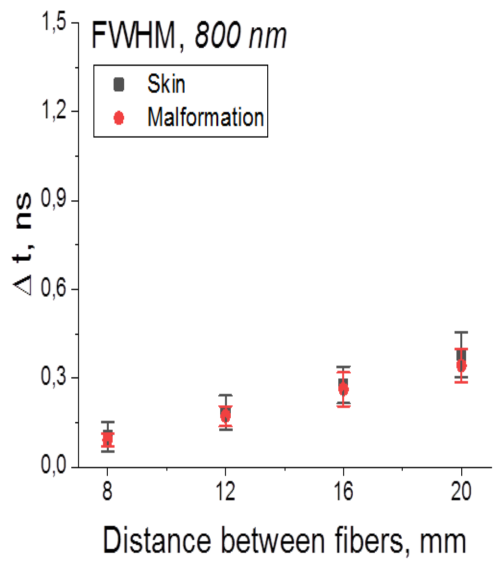












SUMMARY

- Two laser-based techniques for optical skin assessment under development:
  - multi-laser illumination for skin chromophore mapping,
  - sub-ns laser pulse diffuse reflectance from skin for determination of remitted photon path length distributions
- Both techniques show potential for improved quantitative non-invasive skin diagnostics
- Further experimental and clinical studies are in progress

Acknowedgements

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<u>The main topics:</u>

- **Biomedical tissue imaging**
- **Optical clinical diagnostics and monitoring**
- **Skin optics and spectroscopy**

Thank You!

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