Ag_2S nanoparticles-based thermal sensing: From photoluminescence signal to reliable temperature readings

Speaker : Lise ABIVEN, Ph.D student

lise.abiven@sorbonne-universite.fr

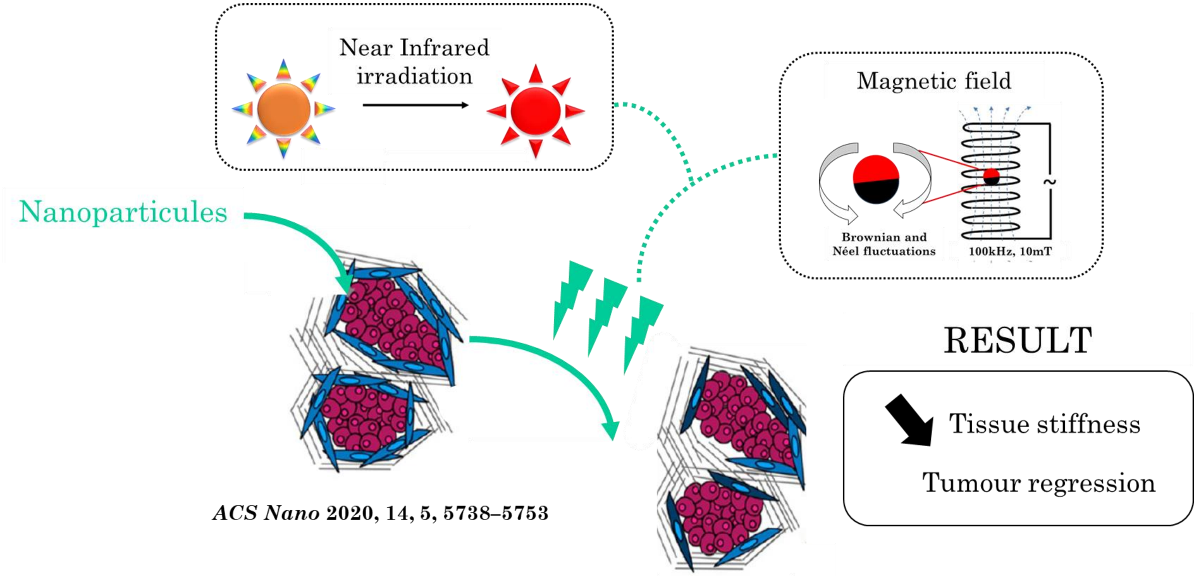
Thesis supervised by **Corinne CHANEAC, Florence GAZEAU & Bruno VIANA**

WEBINAR

Hyperthermia therapy

Tumor microenvironement modulation using nanoheaters

Theory



ACS Nano **2020, 14, 5, 5738–5753**

Impact in clinic today

Auroshell

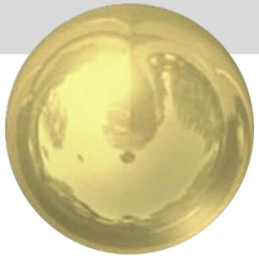
NANOSPECTRA BIOSCIENCES

AuroLase for the Ablation of Prostate Tissue

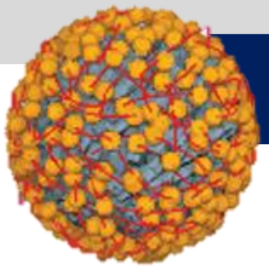
What we need tomorrow

Local temperature sensing directly at the tumour site for personalized therapy

Using light to measure temperature



Nanoparticle to heat
(Hyperthermia therapy)

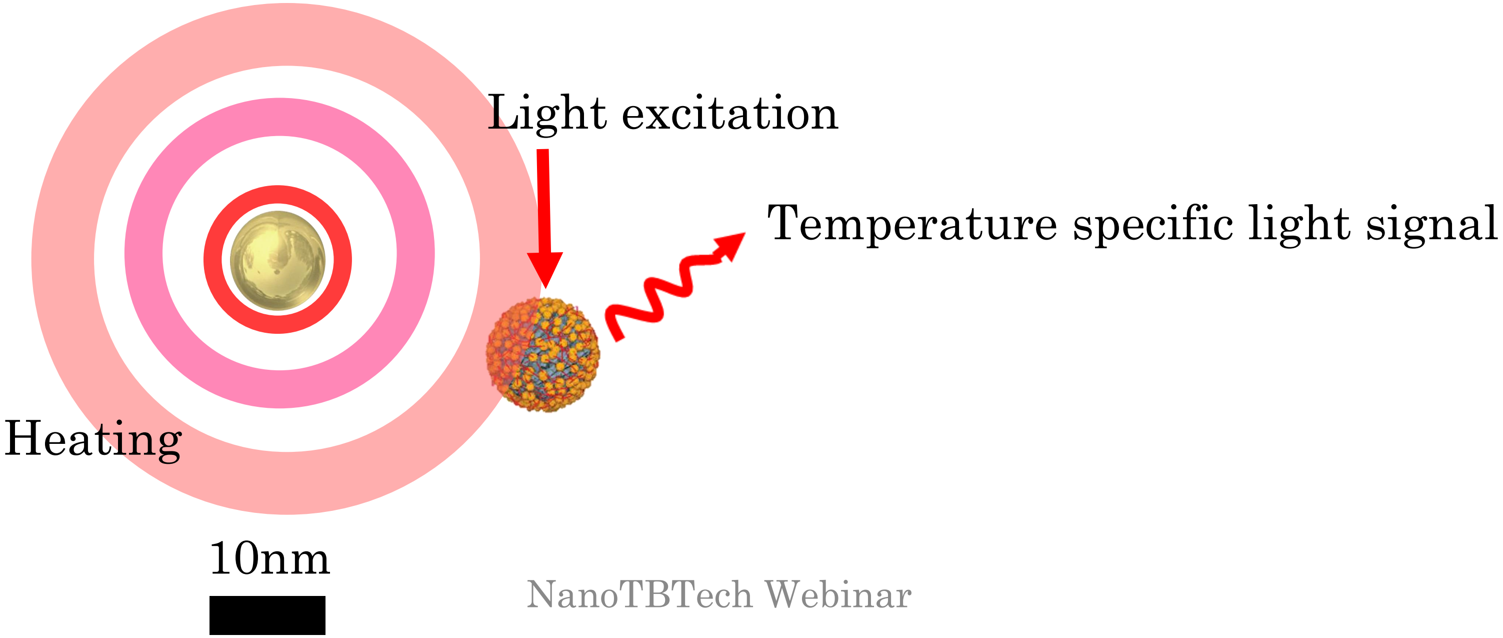


Nanoparticle to
measure temperature

Luminescence

- Real-time monitoring
- Local sensing at the tumour site
- Non-invasive and non-ionizing

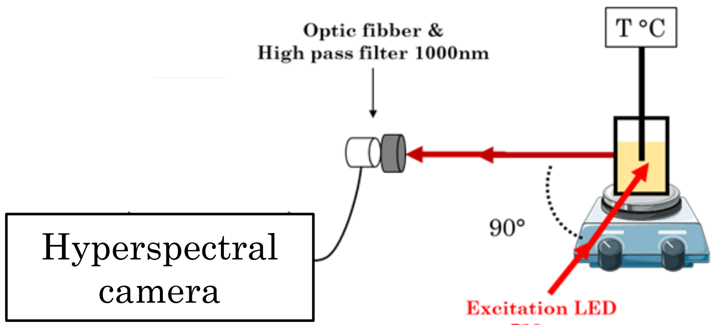
Concept



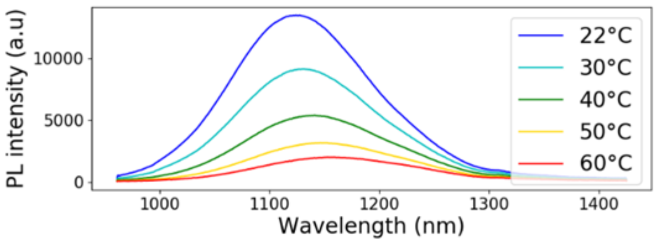
Nanothermometer calibration

- Photoluminescence = emission of light after excitation
- Spectra = fingerprint of intrinsic material temperature

1 Optical setup



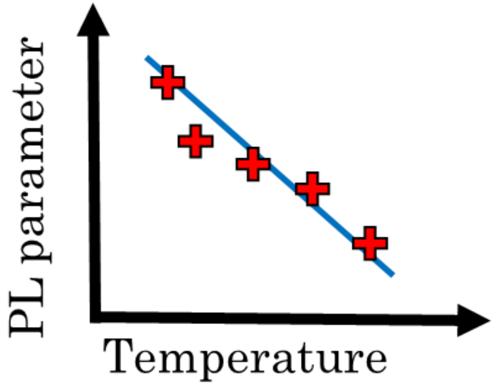
2 Spectra acquisition



Photoluminescence quenching with temperature

3 Calibration curve & modelling

- PL parameter vs. T – **P(T)**



- Relative Sensitivity vs. T – S_r (T)

$$S_r = \left| \frac{1}{P(T)} \frac{dP(T)}{dT} \right|$$

Challenge : From the source to the detector, light crosses biological tissues

nanoTBtech webinars

Aiming at reliable luminescence thermal sensing: basic strategies to overcome the problem of light attenuation in tissues

Speaker: E. Ximendes

instituto ramón y cajal de investigación sanitaria irycis

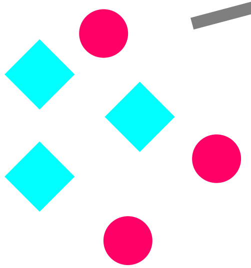
UAM

1

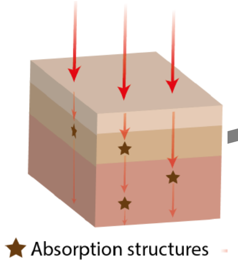
Interaction between light and matter

Light source

Incident radiation



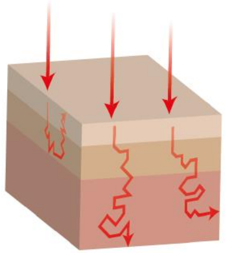
Particles with electric charges



Absorption

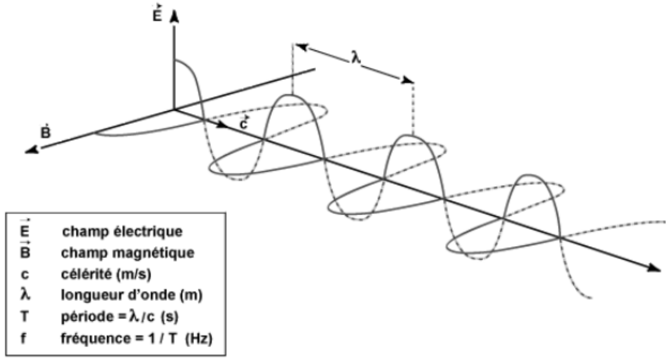
Attenuates the incident radiation, converting it into either :

- **Non-radiative processes** : vibrations of the medium (heat)
- **Radiative processes** : emission of light of different λ (fluorescence, phosphorescence)



Scattering

Incident radiation is re-emitted (same frequency) by scatterers into a certain direction. Depends on scatterers size, shape, spatial distribution



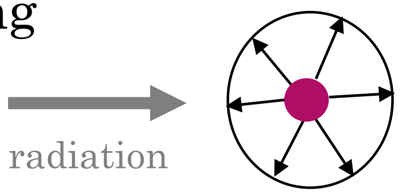
Extinction = Absorption + Scattering

Near Infrared-Emitting Nanoparticles for Biomedical Applications, Springer, 2020

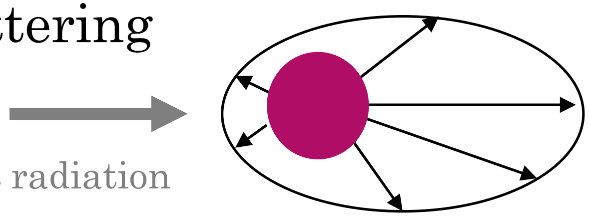
Analogy: Why the sky is blue ? … and sometimes red ?

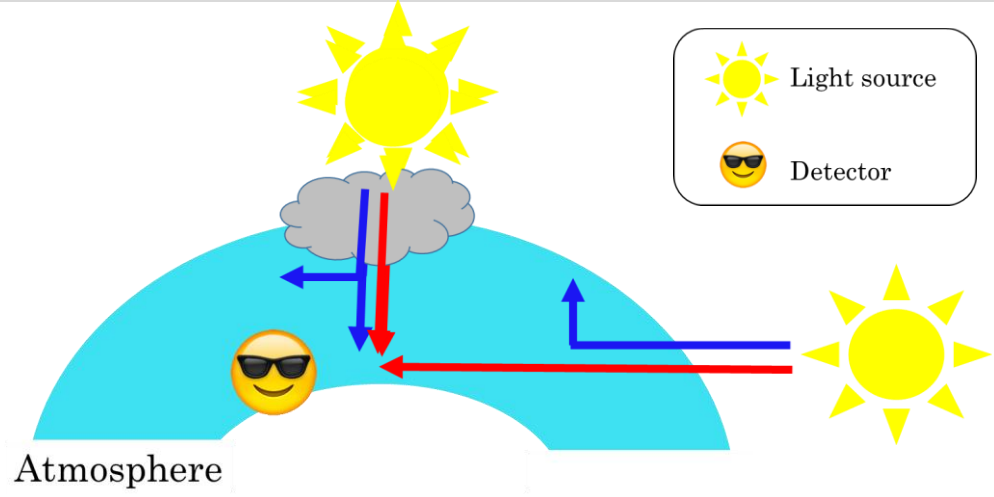
Colour results in interaction between light and matter

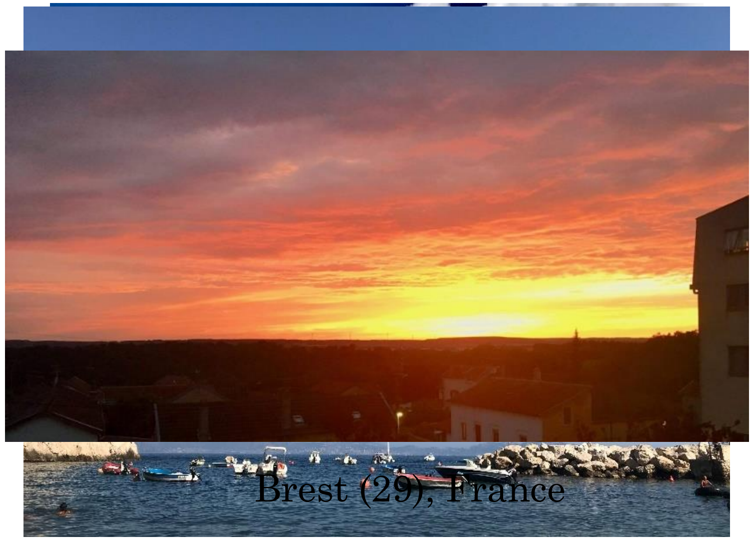
Rayleigh scattering : **λ >> scatterers size**
- High dependency on λ **(1/λ⁴)**
- Isotropic scattering



Mie scattering : **λ ≤ scatterers size**
- Low dependency on λ
- Anisotropic scattering







Brest (29), France

Saint-Malo (29), France

Niolon (13), France

The Radiative Transfer Equation to model light propagation

$$\nabla \cdot \mathbf{J}(\mathbf{r}) + \mu_t U(\mathbf{r}) = 0$$

Attenuation of the average intensity

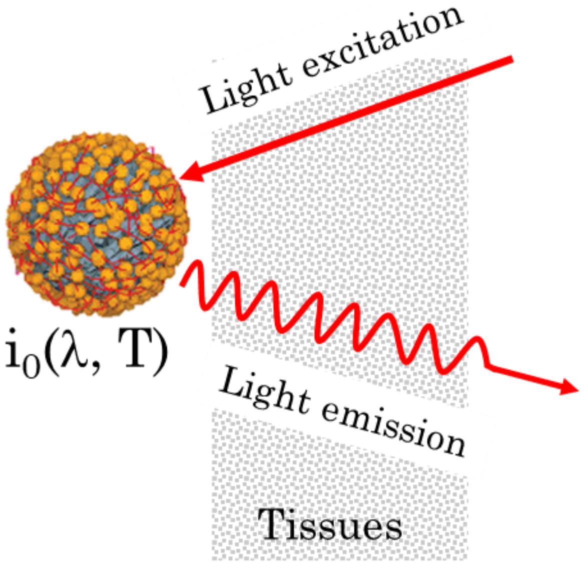
Fluctuation of energy density in a volume

Signal depth

Effective extinction coefficient

$\mu_{ext} = \mu_{abs} + \mu'_{sca}$

$$i(\lambda, T, d) = i_0(\lambda, T)e^{-h \cdot \mu_{ext}(\lambda, T)}$$



$i(\lambda, T)$

Measured PL intensity

(after light propagation in tissues)

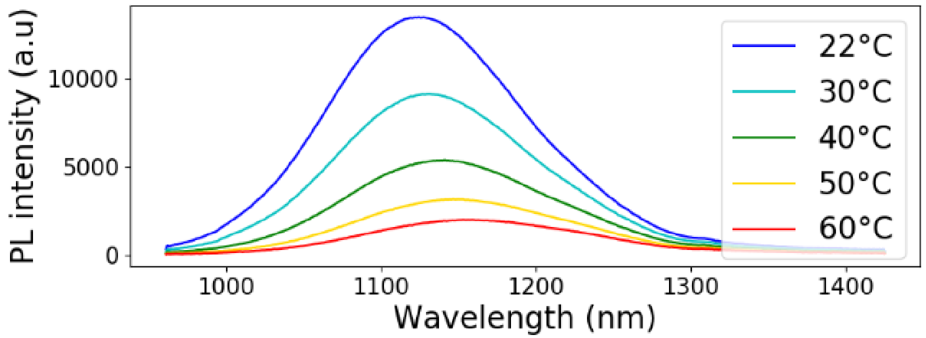
Intrinsic PL intensity

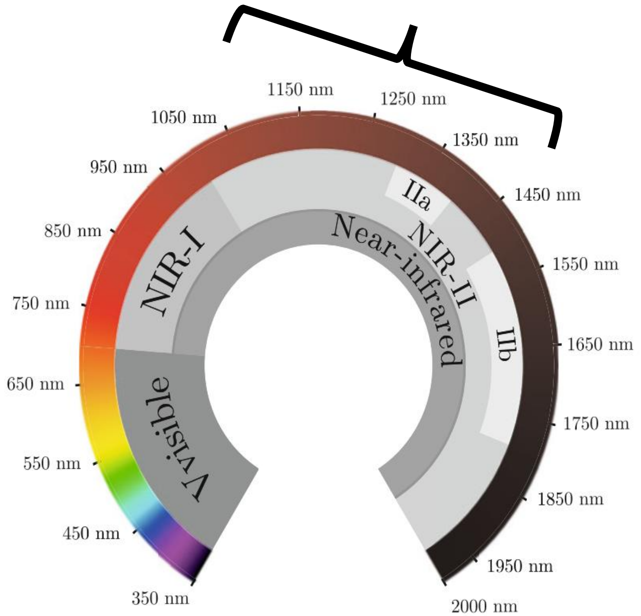
(before light propagation in tissues)

What we have learnt from theory

a. Let's choose a light source emitting in the infrared

Selected photoluminescent probe: **Ag_2S**

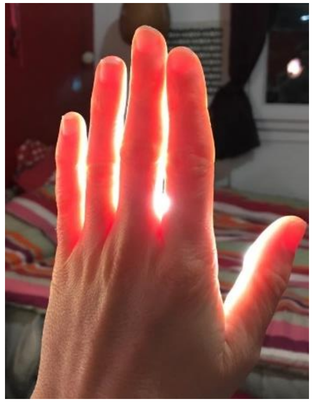




- Minimized tissue absorption
- Minimized tissue scattering

- High biocompatibility
- Long term stability in aqueous dispersion

Illustration 1



Skin behind a white light source becomes red

Illustration 2

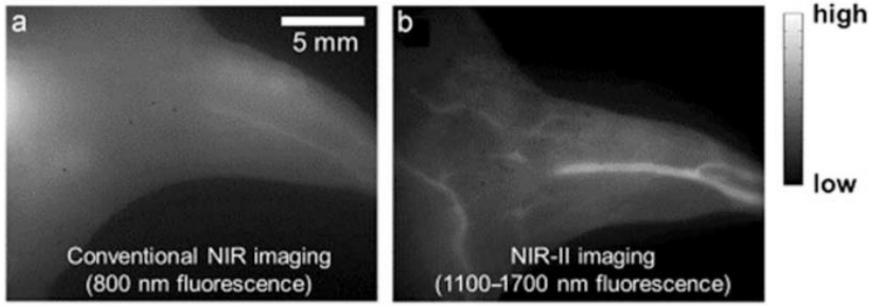


Image resolution is better using contrast agent emitting in NIR-II compare to those emitting in NIR-I

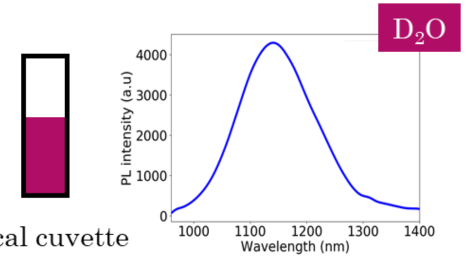
Near Infrared-Emitting Nanoparticles for Biomedical Applications, Springer, 2020

What we have learnt from theory

b. To perform **reliable temperature readings**, we must take into account the medium where light propagate

1.

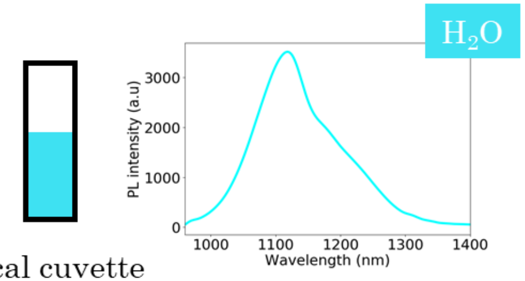
NO Absorption – NO Scattering



Optical cuvette

2.

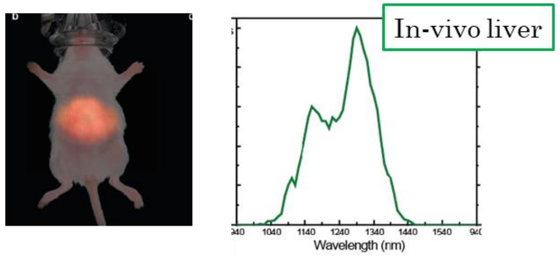
Absorption – NO Scattering



Optical cuvette

3.

Absorption – Scattering



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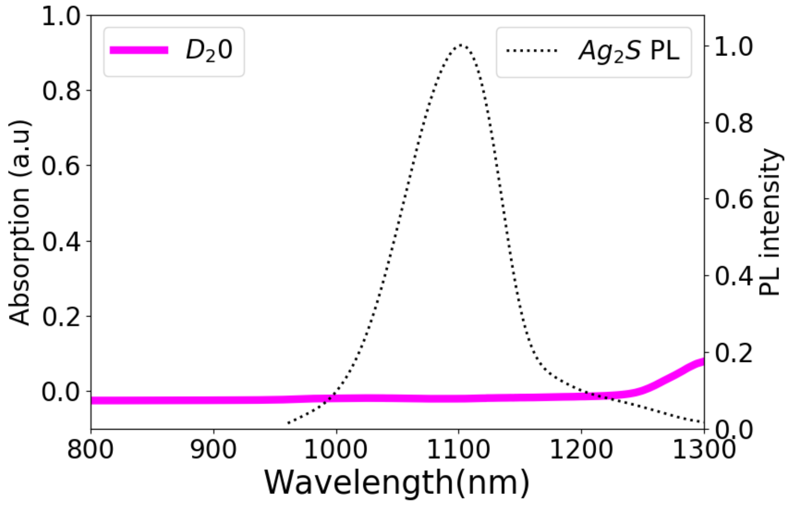
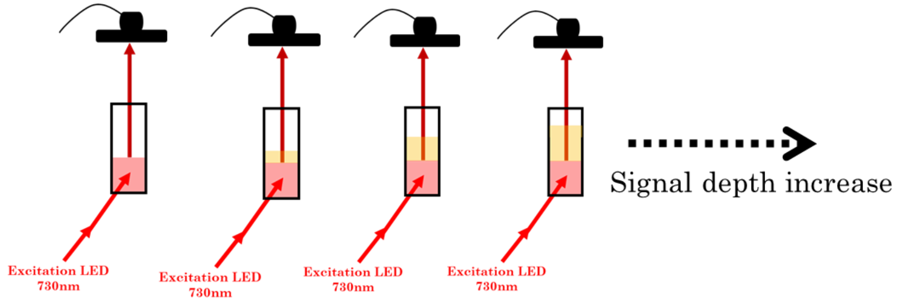
Proof of concept

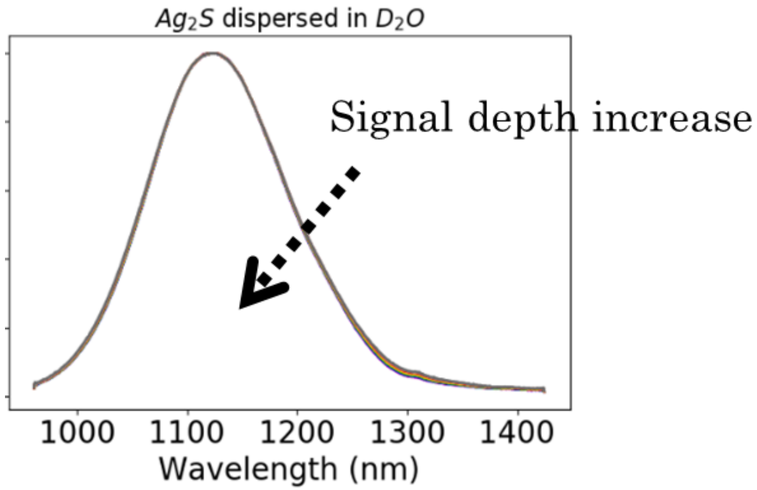
Data treatment suggestion

Perspective

1. NO Absorption – NO Scattering: D_2O







$$i(\lambda,T,d) = i_0(\lambda,T)e^{-h\,.\,\mu_{ext}(\lambda,T)}$$

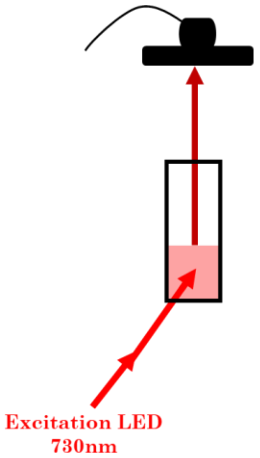
$$\boxed{i(\lambda,T,d) = i_0(\lambda,T)}$$

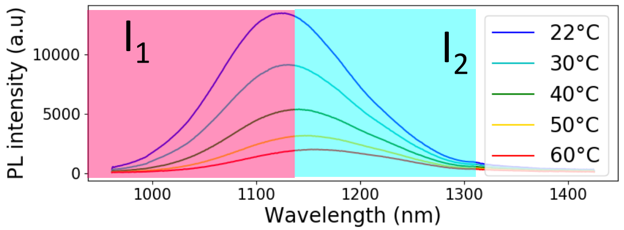
$\mu_{ext}\,(\lambda,T)$=0

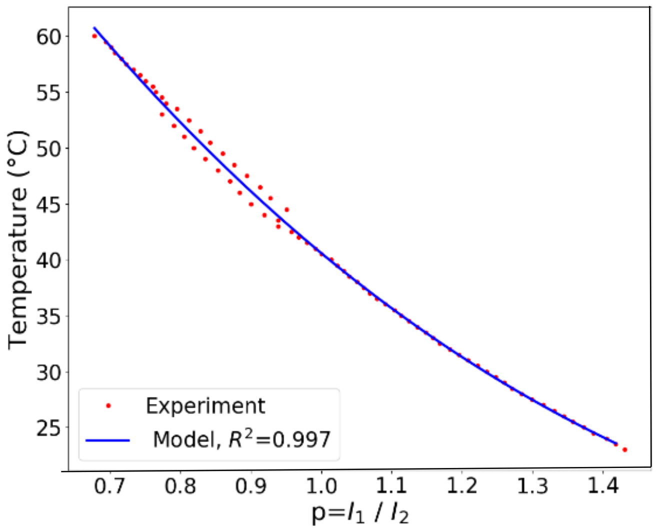
Measured PL intensity through D_2O

Temperature sensing

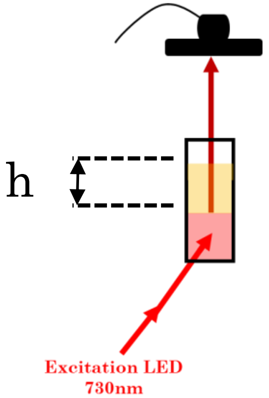
Calibration

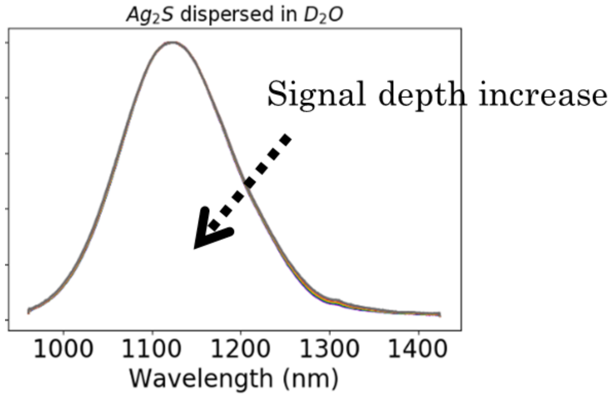


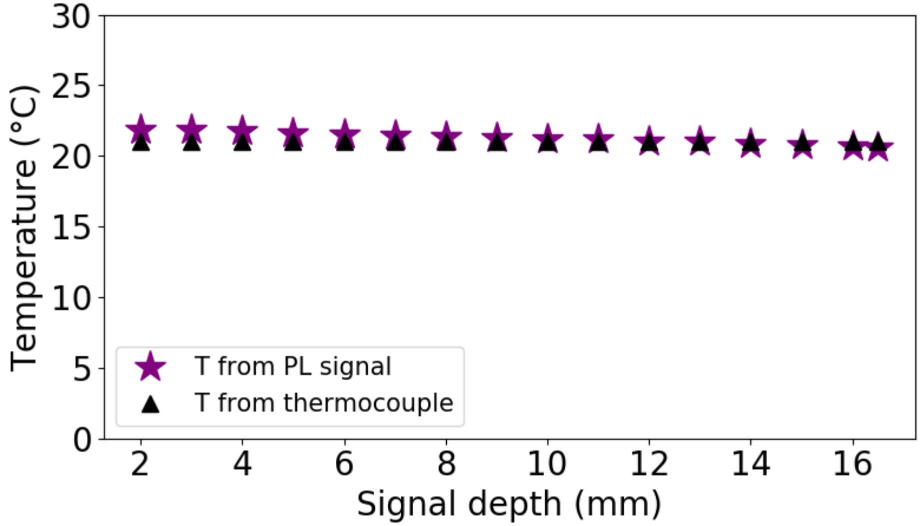




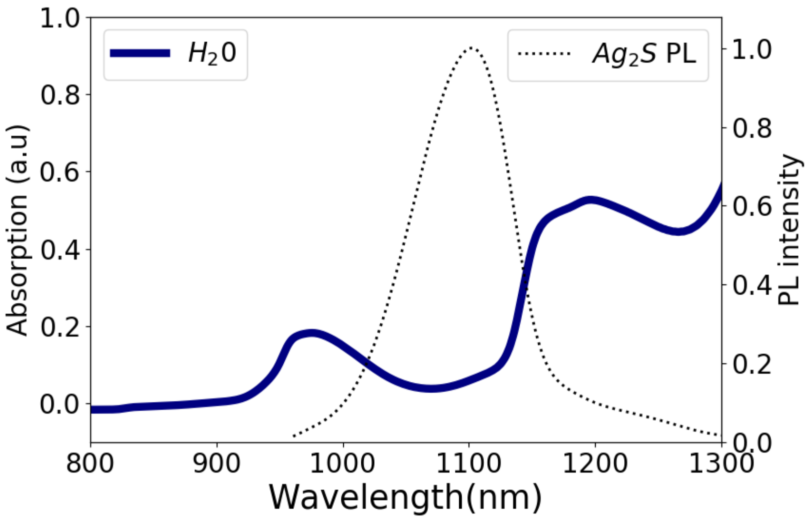
Measure

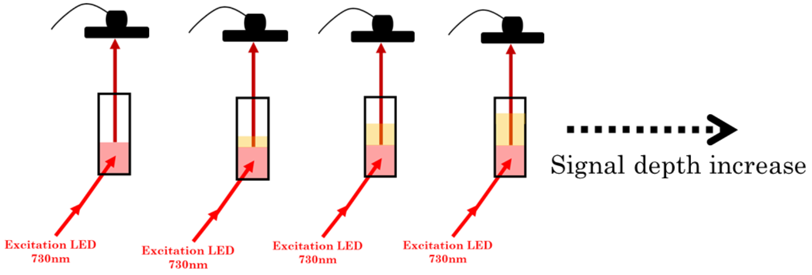


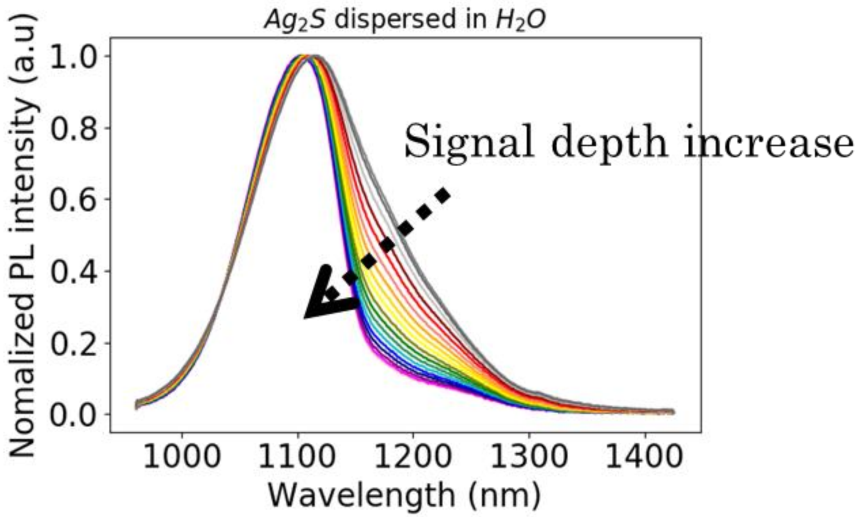




2. Absorption – NO Scattering: H_2O







$$i(\lambda, T, d) = i_0(\lambda, T)e^{-h \cdot \mu_{ext}(\lambda,T)}$$

$$\boxed{i(\lambda, T, d) = i_0(\lambda, T)e^{-h \cdot \mu_{abs}(\lambda,T)}}$$

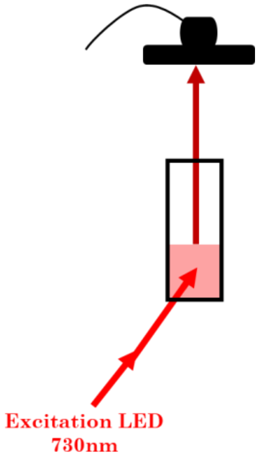
$$\mu_{ext}(\lambda, T) \sim \mu_{abs}(\lambda, T)$$

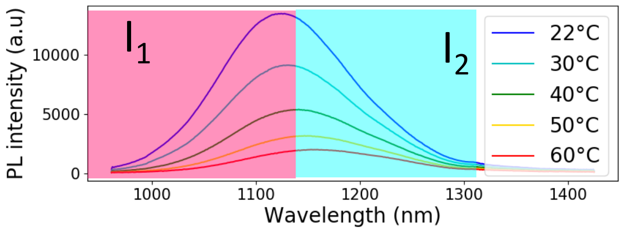
Measured PL intensity through H_2O

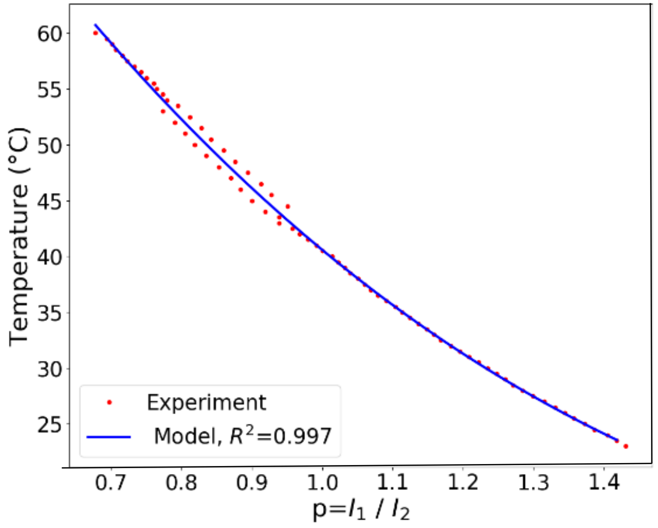
Temperature sensing

Calibration

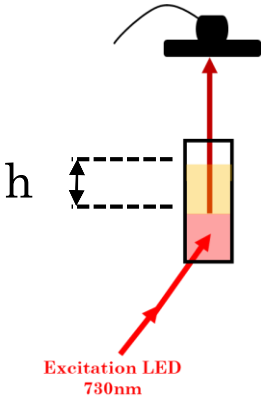
Signal depth = 0

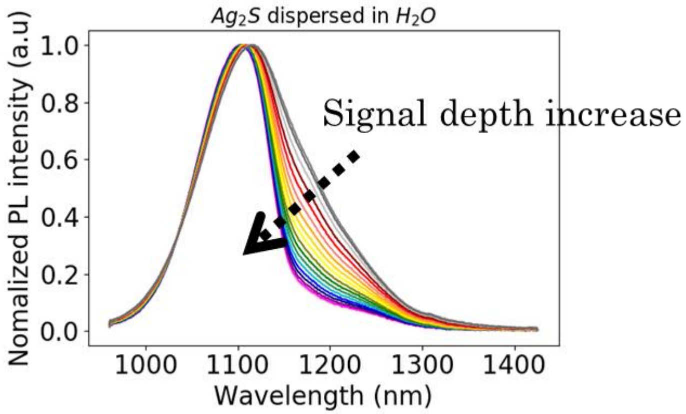


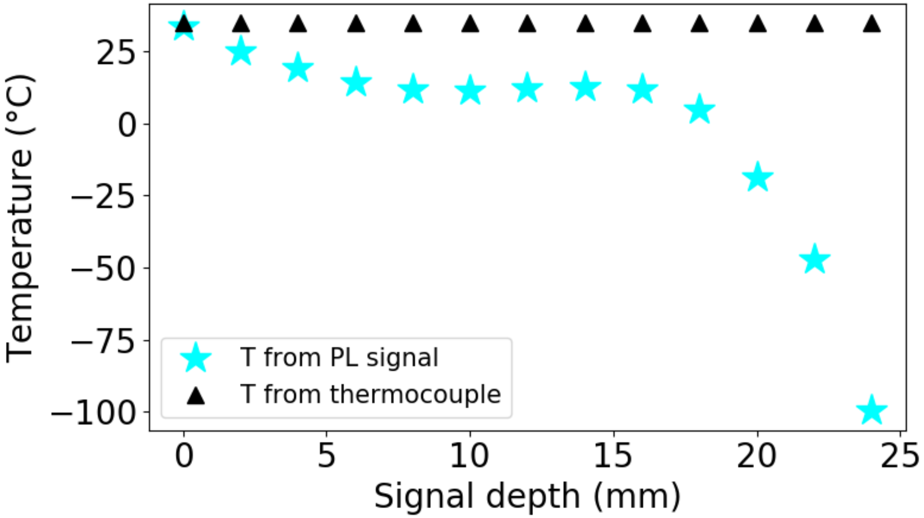




Measure





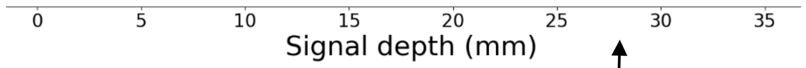


Can we use predictive learning to extract features from the signal ?

Our strategy

How to quantify similarities between two spectra ?

Signal depth data set (h_i)

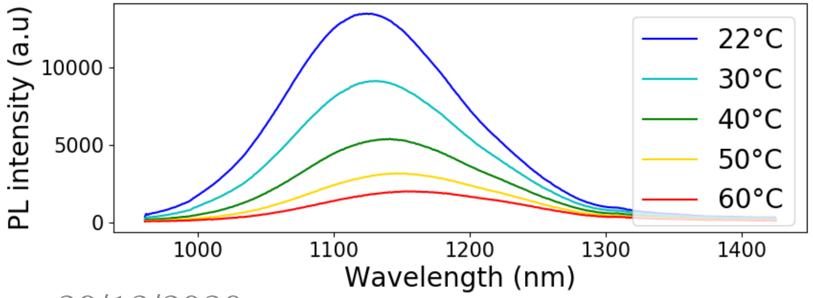


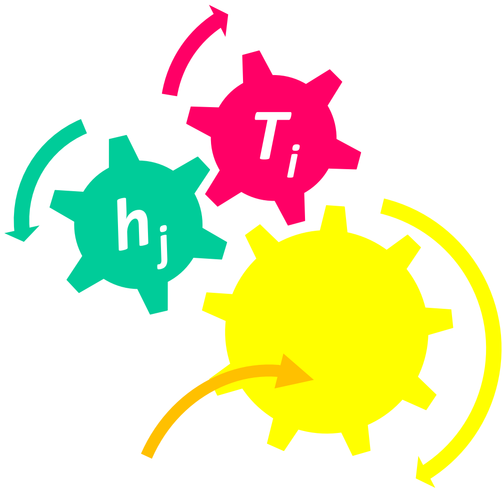
$$i_0^{calculated}(\lambda, T) = i(\lambda, T, h)\, e^{h_i \cdot \mu_{eff}(\lambda, T)}$$

input — *from experiment*

Temperature-labelled data set

$$i_0^{standard}(\lambda, T_i)$$



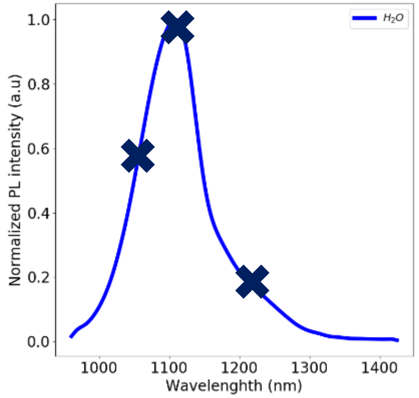


We search for simiarities maximisation between spectra

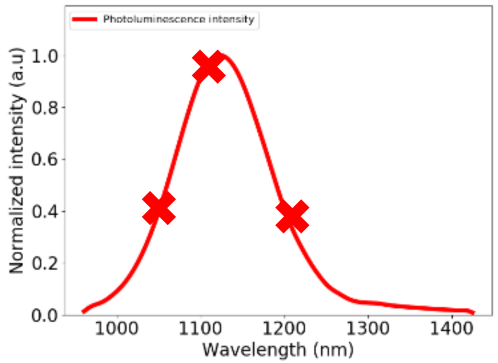
Similarity indicator between two spectra

Our approach

Spectrum i

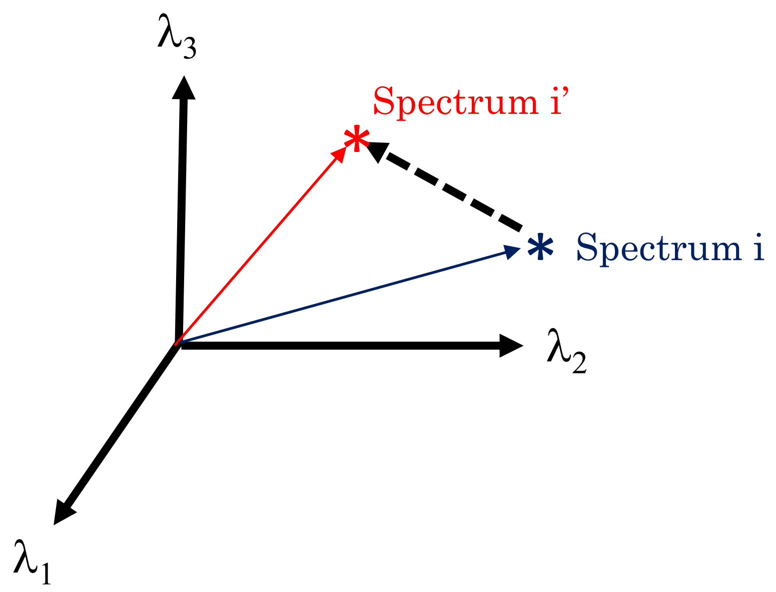


Spectrum i’



3 couples (PL intensity, Wavelength)

Spectra are vector in dimension 3



We can calculate distance between two points = similarity indicator

The lower distance, the higher similarity indicator

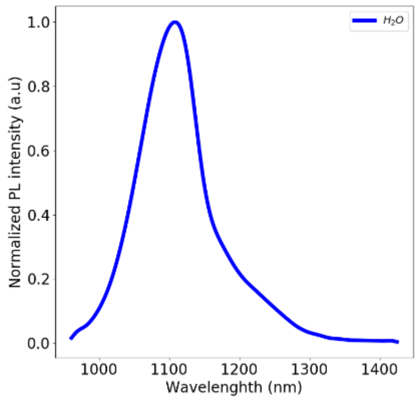
d=0 => spectra are the same => same feature (T, signal depth, tissue type)

$$d^2(i,i') = \sum_{k=1}^{3}(x_{ik} - x_{i'k})^2$$

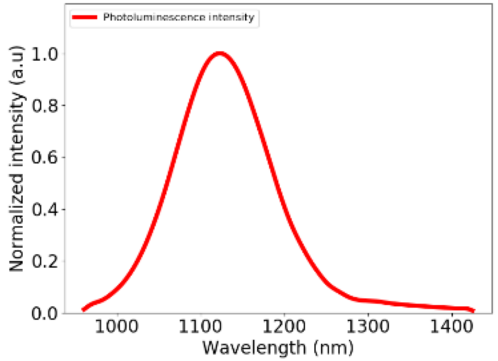
Similarity indicator between two spectra

Our approach

Spectrum i



Spectrum i'



1024 couples (PL intensity, Wavelength)

Spectra are vector in dimension 1024

We cannot vizualize it but it is exactly the same than in dimension 3

We can calculate distance between two points = similarity indicator

The lower distance, the higher similarity indicator

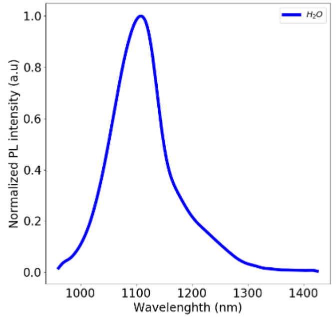
d=0 => spectra are the same => same feature (T, signal depth, tissue type)

$$d^2(i,i') = \sum_{k=1}^{1024} (x_{ik} - x_{i'k})^2$$

Algorithm content – Proof of concept

input

$i(\lambda, T, h)$

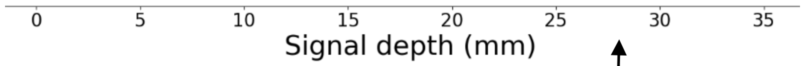


output

$T = 40°C$

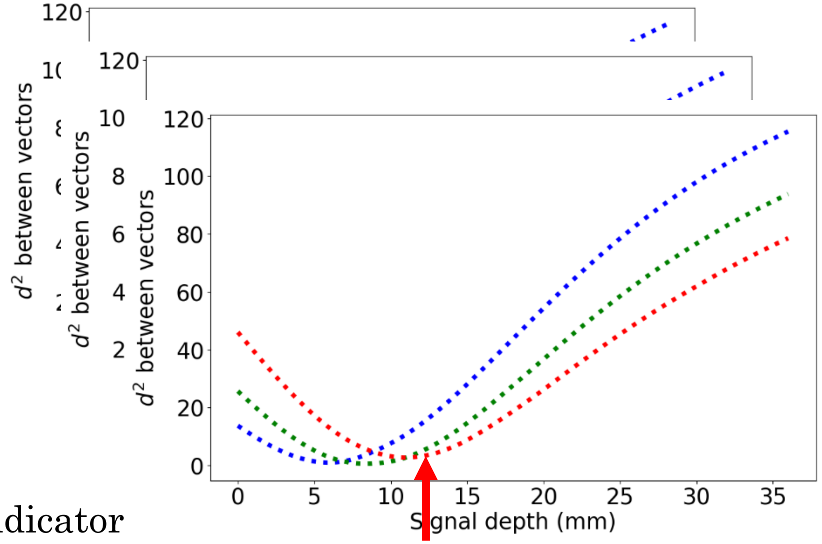
$h = 7.2mm$

Signal depth data set (h_i)



$$i_0^{calculated}(\lambda, T) = i(\lambda, T, d)\, e^{h_i \cdot \mu_{eff}(\lambda, T)}$$

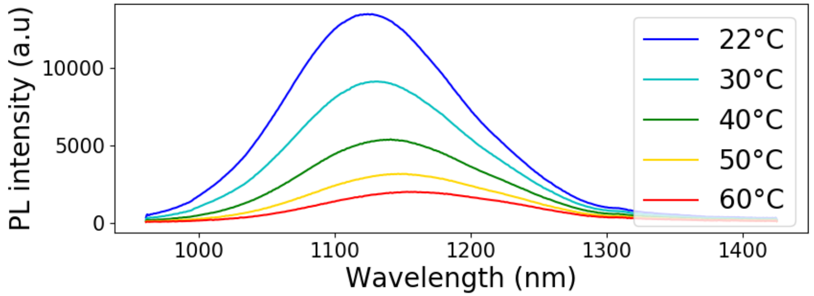
input *from experiment*

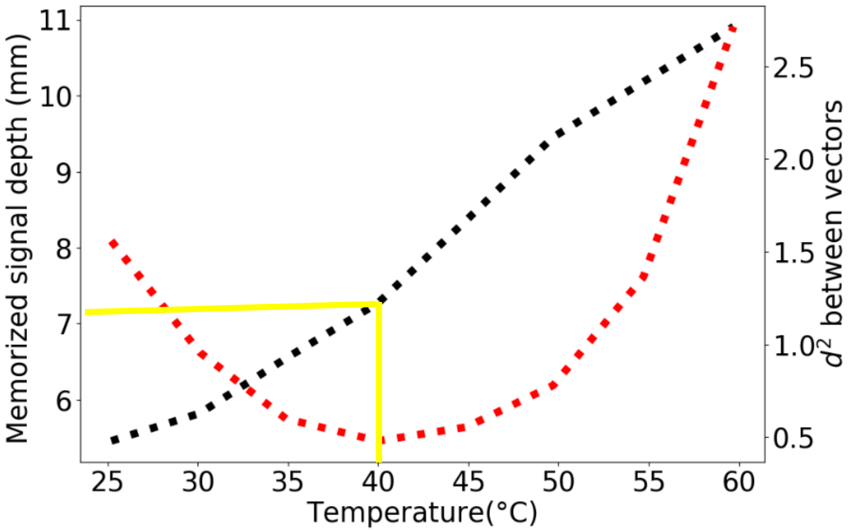


Similarity indicator increase

Temperature-labelled data set

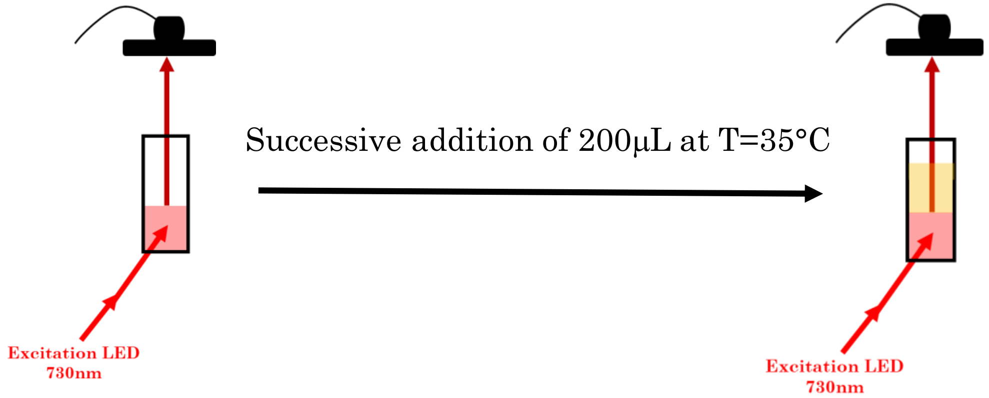
$i_0^{standard}(\lambda, T_i)$

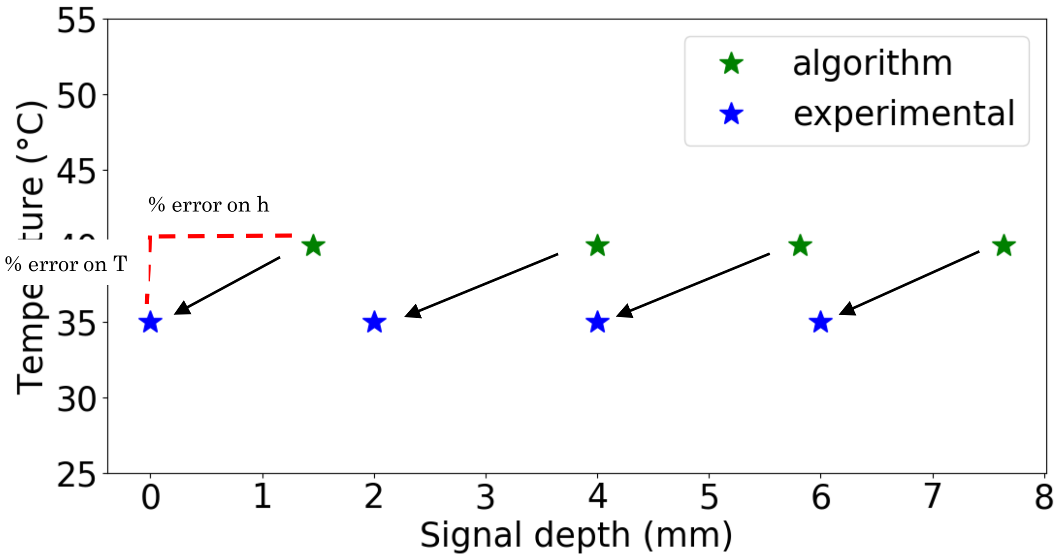




$T = 40°C$

Results – Proof of concept





Relative error for temperature 14%

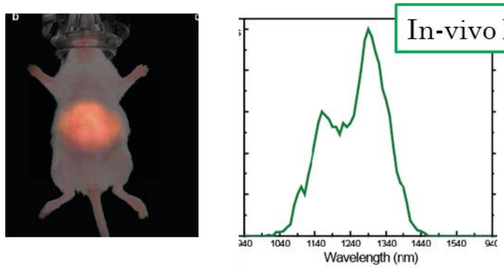
Relative error for signal depth 40%

Work is going on ☺

3. Absorption – Scattering: Biological tissues

Challenge

To perform reliable T reading deep into tissues, we need to model light propagation in tissues



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The example of healthy human skin

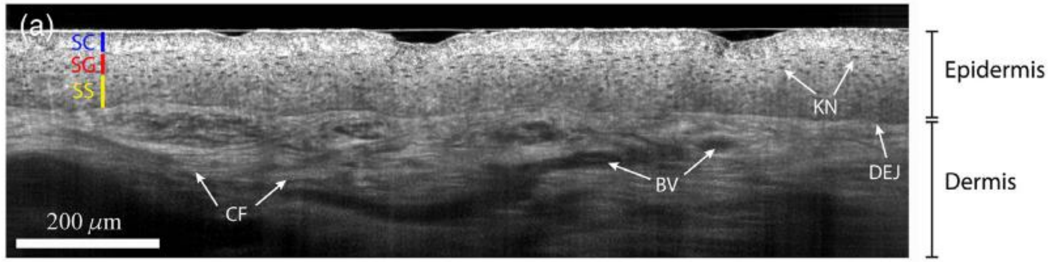
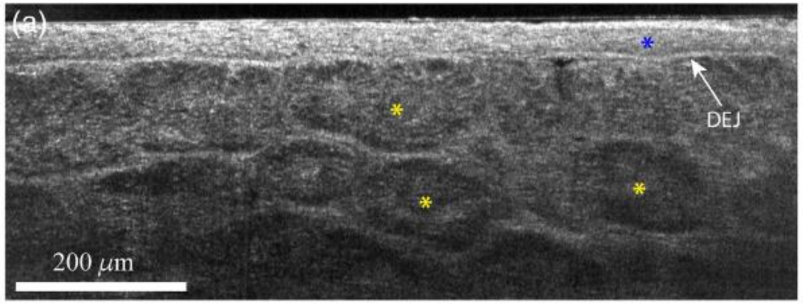


Fig. 5 LC-OCT images of healthy human skin on the back of the hand from (a) a 25-year-old man, phototype 2 and (b) a 23-year-old woman, phototype 5. SC, stratum corneum layer; SG, stratum granulosum layer with stretch nuclei; SS, stratum spinosum layer with roundish nuclei; SB, stratum basale rich in melanin in darker phototypes; CF, collagen fibers; BV, blood vessel; KN, nuclei of keratinocytes; DEJ, dermal–epidermal junction.

Opportunity

► Can we perform early stage tumor detection by studying PL signal ?

* Tumor island



From healthy to pathologic tissues : Optical parameter evolution

- ↗ μ_{abs} due to higher angiogenesis activity
- ↗ μ_{sca} due to nucleus size increase for epithelium cells

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THANK YOU !

lise.abiven@sorbonne-universite.fr

Corinne Chanéac
Estelle Glais

Florence Gazeau
Alba Nicolas-Boluda
Alice Balfourier

Bruno Viana
Victor Castaing

Cyrille Richard
Johanne Seguin
Thomas Lécuyer