Biocompatible temperature nanosensors based on Titanium dioxide

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Content summary

Nanothermometry

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- Applications
- Raman thermometry
- The method
- The material

Results and discussion

- Raman spectrum of Titanium dioxide
- Temperature determination

Conclusions

Nanothermometry

What is a nanothermometer

- temperature sensor
- micrometric and **sub-micrometric spatial resolution** required: traditional strategies can’t be applied (Quintanilla and Liz-Marzán 2018)
    - small dimensions of the probe
    - limited access to the area of interest

Nanothermometry

Applications of nanothermometers

- measurement of temperature in biological samples
  and tissues
- detection of hot-spots in microcircuits

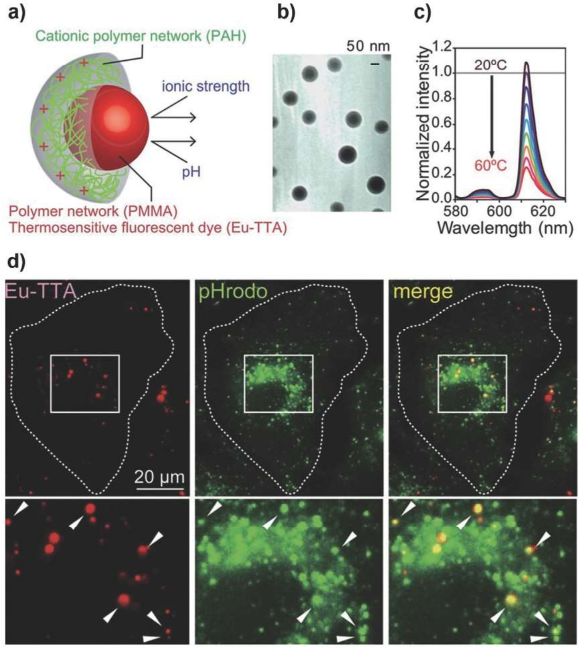

Figure: Temperature measurement of living cells using a fluorescent nanothermometer (PMMA) and a thermosensitive fluorescent dye (Eu-TTA) (Bai and Gu 2016).

Nanothermometry

Raman spectroscopy as a nanothermometry technique

- **optical** technique: advantage of contactless measurement of temperature
- non-disruptive
- **inelastic scattering of light**
- the intensity and shape of Raman signals related to temperature

Nanothermometry

Raman spectroscopy as a nanothermometry technique

Intensity, peak position and width are the parameters used to measure sample temperature (Beechem and Serrano 2011)

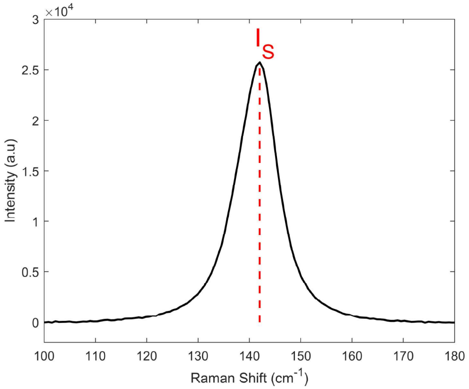

Figure: Intensity

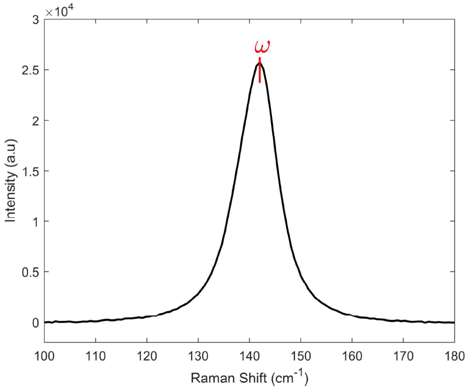

Figure: Position

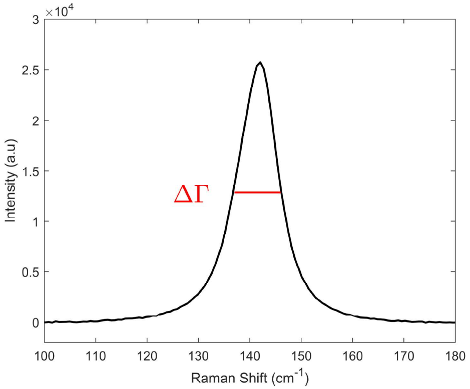

Figure: Linewidth (FWHM)

Description of the method for temperature determination

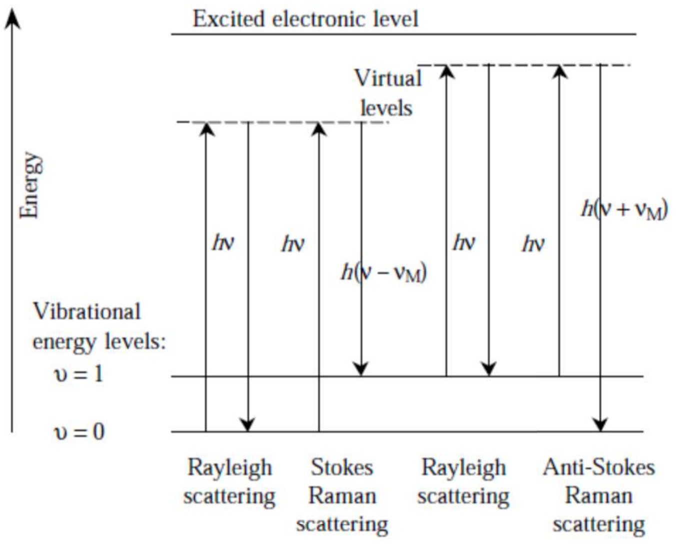

Figure: Origin of Stokes (left) and anti-Stokes scattering (right).

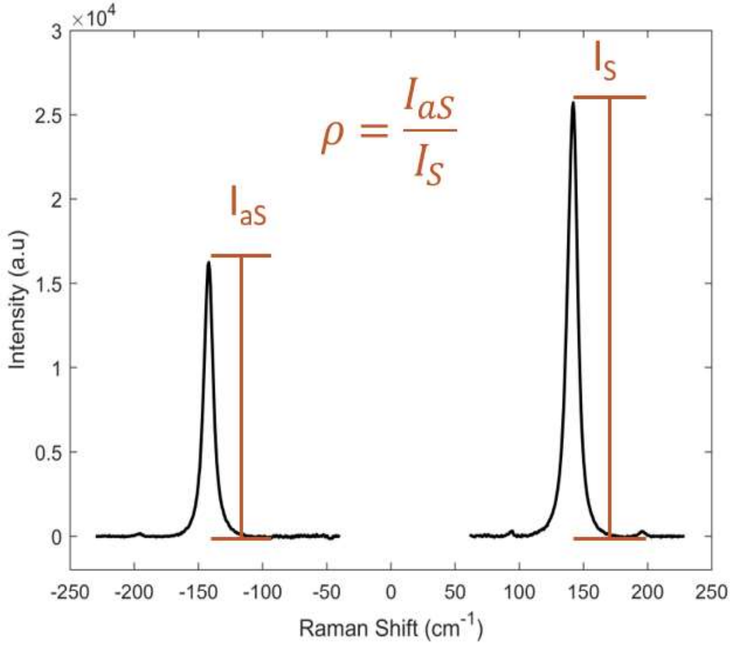

Figure: Ratio of anti-Stokes and Stokes intensities in the Raman spectrum.

Nanothermometry

Requirements for a Raman nanothermometer

- a large Raman scattering **cross-section** (to reach high signal-to-noise ratios)
- **high intensity** Raman peaks at **low Raman shifts** (the upper limit depends on the working temperature, in general near room temperature it's 600 cm^{-1}); indeed the lower the Raman shift the more sensitive is the peak intensity to temperature (Tuschel 2019),
- well-defined and distinguishable Raman peaks,
- low absorbance at the excitation wavelength, to avoid heating mechanisms

Nanothermometry

Literature

Studies of Raman temperature measurement can be found in literature for **Silicon, Gallium Arsenide, Gallium Nitride and graphene**.

Also **Titanium dioxide** (TiO_2) has been tested in few works as a Raman temperature thermometer for Titanium dioxide microparticles and for thin films of Titania used in solar cells.

Nanothermometry

Titanium dioxide

- anatase, rutile and brookite
- wide band gap **insulator** (3.0 eV)
- chemical stability and **nontoxicity**
- photocatalysis, optical coatings, optoelectronic devices and biomedicine

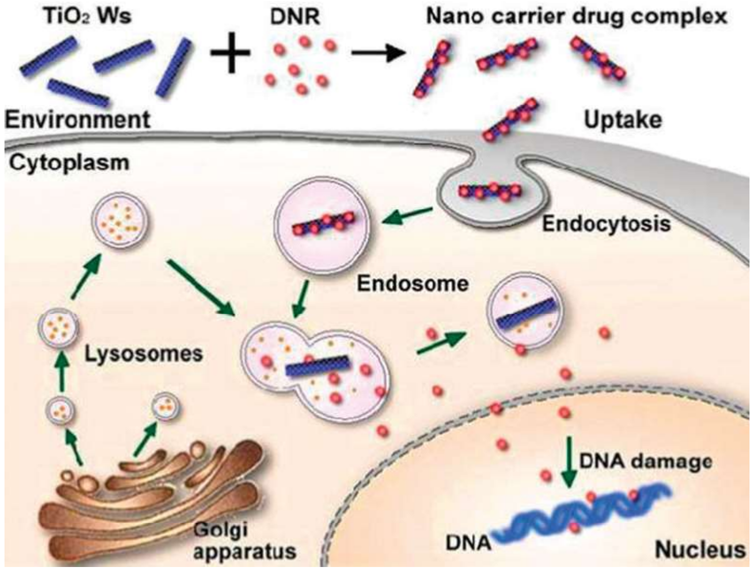

Figure: TiO_2 whiskers (Ws) drug delivery mechanism (Yin et al. 2013).

Characterization of Titanium dioxide

through Raman spectroscopy

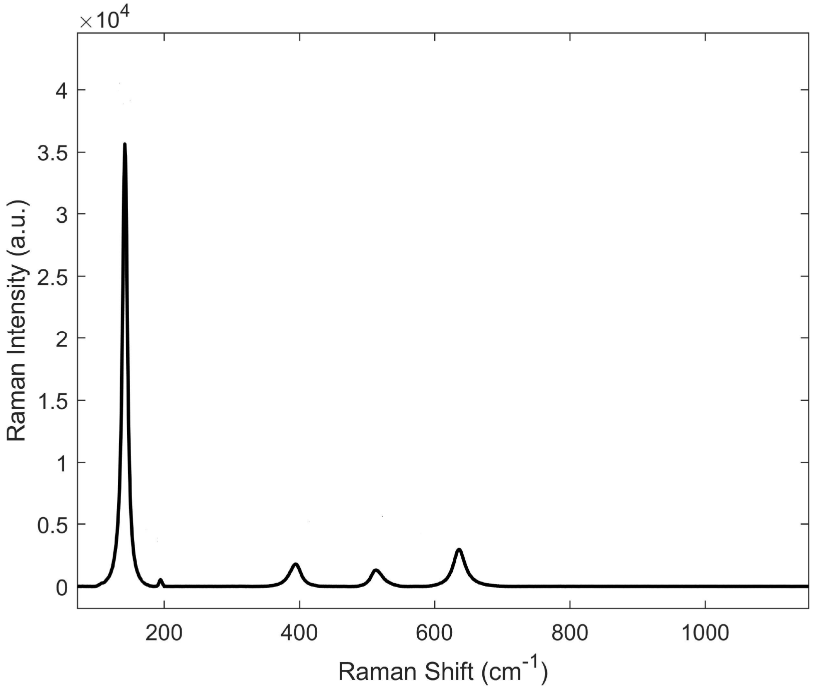

Figure: Anatase Stokes Raman spectrum

We choose **Titanium dioxide anatase** for our research as it seems to suite perfectly all the requirements for a good Raman thermometer.

Characterization of Titanium dioxide

through Raman spectroscopy

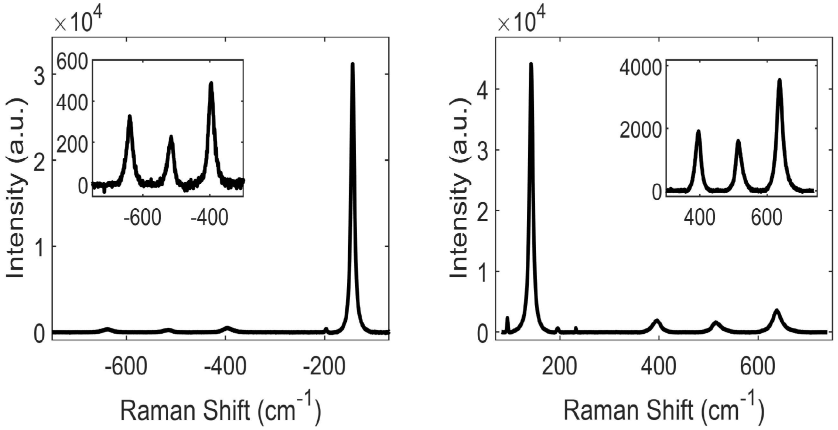

Figure: Anatase Stokes and anti-Stokes spectra recorded at 647.1 nm and 298 K.

By observing Stokes and anti-Stokes spectra, it turned out that **the best peak for temperature monitoring is the one at 143 cm^{-1}**. It's well defined, very intense even at low laser powers, and highly sensitive to temperature, thanks to its low Raman shift.

Calibration curve

Relation between the anti-Stokes/Stokes ratio and temperature, used as the calibration curve:

$$\rho = C \cdot \frac{(v + v_0)^3}{(v - v_0)^3} exp\left(-\frac{hv}{kT}\right) \tag{1}$$

ρ = anti-Stokes/Stokes ratio
C = calibration constant
v = frequency of the Raman mode
v_0 = frequency of the laser
h = Planck's constant
k = Boltzmann's constant
T = temperature of the sample

Calibration procedure

Example: $\lambda_{exc} = 647.1nm$

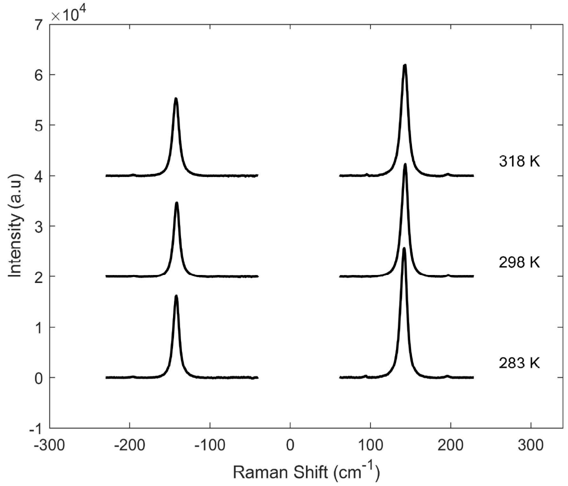

Figure: Raman spectra of the lower-frequency E_g mode at 283, 298 and 318 K

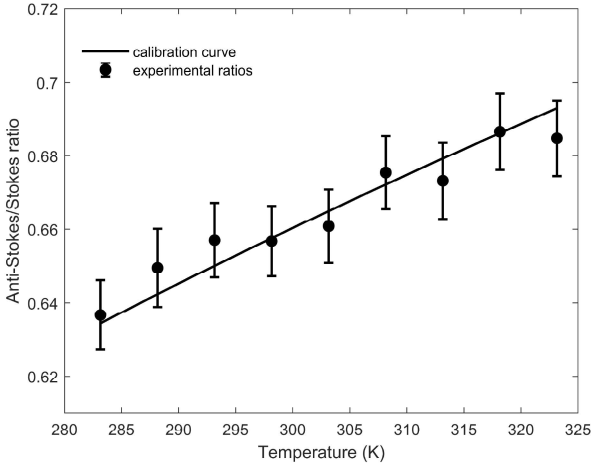

Figure: anti-Stokes/Stokes experimental ratios (circles); calibration curve (solid line).

Temperature determination

Calibration of row data

$$\rho_{ex} = \frac{I_{aS}}{I_S} \qquad T_{ex} = \frac{hv/k}{ln\left(\frac{\frac{(v+v_0)^3}{(v-v_0)^3}}{\rho_{ex}}\right)} \tag{2}$$

$$\rho_c = \rho_{ex}/C \qquad T_c = \frac{hv/k}{ln\left(\frac{\frac{(v+v_0)^3}{(v-v_0)^3}}{\rho_c}\right)} \tag{3}$$

Table

λ_{exc} [nm]	aS/S ratio	Row Temp. [K]	Calibration const.	Sample Temp. [K]
514.5	0.5231	292	0.979 ± 0.006	301
568.2	0.5120	281	0.964 ± 0.007	296
647.1	0.6569	425	1.22 ± 0.01	298

Table: Experimental anti-Stokes/Stokes ratios (column II) and row temperatures (column III) determined at 298 K as function of the excitation wavelength. Values of the calibration constant (column IV); Sample temperature obtained from experimental anti-Stokes/Stokes ratios (column V).

Temperature determination

Calibration of row data

- calibration procedure at 514.5, 568.2 and 647.1 nm
- calibration constants determined with a precision of approximately 0.6-0.8 (less than 1%)
- considering that the area of the peak can be determined by means of a Voigt fit with a precision of 1%, **the total uncertainty on the temperature measurement can be as good as 5 K**
- the goodness of the calibration was evaluated on the base of room temperature measurements on the same sample of Titanium dioxide powder

Conclusions

- **Titanium dioxide** is proposed as a Raman thermometer for **biological applications**, in a wide optical range. It has been tested at three different wavelengths, 514.5, 568.2 and 647.1 nm.
- the calibration constant is mainly due to an instrumental factor, as the correction for the anti-Stokes/Stokes ratio shows a good correlation with the correction derived from the **instrumental response function**
- future perspectives: study of more complex systems; Raman thermometry in the IR region of the spectrum, close to the biological window

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