Luminescent nanothermometry using short-wavelength infrared light

Ol A. Savchuk [a], J.J. Carvajal [a, *], P. Haro-Gonzalez [b], M. Aguiló [a], F. Díaz [a]

[a] Universitat Rovira i Virgili, Departament de Química Física i Inorgànica, Física i Cristal·lografia de Materials i Nanomaterials (FiCMA-FiCNA) - EMaS, Campus Sescelades, E-43007, Tarragona, Spain
[b] Fluorescence Imaging Group, Departamento de Fisica de Materiales, Facultad deCiencias, Universidad Autonoma de Madrid, 28049, Madrid, Spain

ABSTRACT

We analyzed the potentiality of the short-wavelength infrared (SWIR) emissions of different lanthanide ions (Er^{3+}, Tm^{3+} and Ho^{3+}) embedded in different hosts for luminescence thermometry. The 1.55 µm emission band generated by Er^{3+} has different Stark sub-levels that can be used in temperature sensing purposes. However, the thermal sensitivity that can be achieved with this emission is relatively low, ranging from 0.06 to 0.15% K^{-1}. In the case of Tm^{3+}, the emissions arising from the $^3F_4$ and $^3H_4$ electronically coupled energy levels are useful for luminescence thermometry, with a linear evolution for the intensity ratio in the biological range as the temperature increases, which simplifies the calibration procedure for luminescent thermometers based on this parameter. When co-doped with Ho^{3+}, an efficient energy transfer between the Tm^{3+} and Ho^{3+} ions is generated, that results in a new emission line centered at 1.96 µm that can be also used for luminescence thermometry purposes, with an enhanced thermal sensitivity when pumped at 808 nm. The thermal sensitivities achieved with these doping ions are higher than those obtained with Er^{3+} and are comparable to those reported previously for some lanthanide-doped materials operating in the visible, and in the I- and II-BWs. We demonstrated the potentiality of these emissions in the SWIR region for luminescence thermometry and imaging in *ex-vivo* experiments by monitoring the increase of temperature induced in chicken breast meat, with an experimental thermal resolution of ~0.5 K, below the theoretical value of 0.8 K predicted for particles operating in this spectral region, and a penetration depth of at least 0.5 cm.

1. Introduction

Hyperthermia in the treatment of different diseases, like cancer, requires monitoring the body temperature to ensure patient safety [1,2], and to ensure that heat has been adequately applied to the affected area, preventing damages in the surrounding health tissue. Moreover, any temperature increment in the body is usually a sign of the presence of a disease or infection [3]. Thus, temperature monitoring techniques are called to play a major role in assuring safe and effective medical treatments.

Noncontact thermometry methods, which provide fast, accurate and non invasive techniques for monitoring the temperature inside the body [4], are a real alternative to contact thermometers, especially when local temperature measurements are required. Among the different noncontact thermometry techniques, luminescence thermometry, and especially that based on lanthanide (Ln^{3+}) doped

materials, offers a high spatial and thermal resolution [5,6], as well as a reduced or non-existing toxicity, non photobleaching effect, and the possibility of excitation with low cost near IR diode lasers [7].

Ln^{3+}-based luminescence nanothermometers using upconversion mechanisms that convert efficiently near IR (NIR) radiation to visible light have been extensively studied [8–10]. However, biological tissues exhibit strong extinction coefficients in the visible, restricting their use for biomedical applications. A reduced absorption and scattering in biological tissues can be achieved by using specific wavelengths lying in the NIR, in the so called biological or therapeutic windows (BWs) [11,12]. That allowed demonstrating, for instance, in-vivo temperature controlled photothermal therapy of tumors [13]. However, still the quest for a material that maximizes the luminescence quantum efficiency in this region, allowing for high penetration depths in the body is a matter of special interest [14–21].

Despite all this work, the number of studies exploring the possibilities of longer emission wavelengths in luminescence

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thermometry are scarce. Naczynski et al. [22] reported that longer wavelengths than those considered in the BWs, lying in the so called short-wavelength IR (SWIR) that extends from 1.35 to 2.3 μm, transmit more effectively (up to three times) through specific biological tissues (oxygenated blood and melanin-containing tumors), achieving higher penetration depths due to the reduced tissue absorbance and scattering within this region. In fact, in a real scenario in which light penetrates through multiple tissue layers, and in which refractive index changes experimented by light would lead to greater scattering conditions, SWIR light would show higher signal-to-background ratios than visible or NIR light by filtering out biological tissue autofluorescence [23,24].

Here, we analyze the possibilities for temperature sensing purposes of the emissions in the SWIR region generated by Er^{3+}, Tm^{3+} and Ho^{3+} ions in different host matrices, including fluorides ($NaYF_4$), oxyfluorides (NaY_2F_5O), simple oxides (Lu_2O_3) and complex oxides ($KLu(WO_4)_2$). The reason we followed to have chosen these materials is their phonon energies, that normally increases from fluorides to complex oxides, and might play a significant role in the non-radiative relaxation processes that can happen in these materials. In fact, fluorides are in general materials with low phonon energies that tend to avoid depopulation processes of the electronic levels due to interaction with phonons [25–27]. From another side, in oxyfluorides and oxides the probabilities of non-radiative relaxations to occur increases. While being detrimental for the maximization of their emitting properties, these processes might be of interest to increase the thermal sensing efficiency or sensitivity for thermometric applications, as we have shown previously [28,29]. The thermometric responses of these particles are compared with those shown by other Ln^{3+}-doped nanoparticles operating in the visible, and in the BWs, and demonstrated the potentiality of SWIR emitting nanoparticles for temperature measurements in biological tissues by using chicken breast meat. The results indicate that SWIR emitting nanoparticles are good candidates for luminescent thermometry in biomedical applications.

2. Experimental section

2.1. Nanoparticles used

Hexagonal 1% Er, 20% Yb:$NaYF_4$, 1% Tm, 20% Yb:$NaYF_4$ and 1% Er, 20% Yb:NaY_2F_5O particles were purchased to Boston Applied Technology. As received particles were mixed with water and centrifugated at 8000 rpm to separate microparticles from nanoparticles. Only particles with nanometer sizes were used in this work.

4% Er, 20% Yb doped Lu_2O_3 nanoparticles were synthesized by the modified Pechini sol-gel method [30]. Lu_2O_3 (99.9999%), Er_2O_3 (99.9%) and Yb_2O_3 (99.9%) were dissolved in hot nitric acid to form the nitrate salts. The nitrate salts were dissolved in an aqueous solution, and ethylenediaminetetraacetic acid (EDTA), used as complexation agent, was added with a molar ratio to metal cations CM = [EDTA]/[METAL] = 1. After that, ethylene glycol (EG), used as esterification agent, was added to the mixture in a molar ratio CE = [EDTA]/[EG] = 2, and the solution was heated to 323 K under constant stirring to form a transparent solution. Then, the solution was dehydrated at 363 K to form a polymeric viscous white gel, before it was calcined at 573 K to eliminate the organic compounds and form the precursor powders. Finally, the samples were calcined at 1073 K for 2 h to obtained the nanocrystalline powder.

Monoclinic $KLu(WO_4)_2$ singly doped with 1% Tm; co-doped with 1% Tm, 10% Yb; 1% Tm, 1.5% Ho or 3% Er, 10% Yb, and triply doped with 1% Tm, 10% Yb, 1.5% Ho were synthesized also by the modified Pechini sol-gel method [21]. Monoclinic double tungstate nanoparticles were chosen as an example of a complex oxide because of

the excellent results obtained in luminescence thermometry when using these materials in other spectral ranges [21,31,32]. For that, stoichiometric proportions of Ho_2O_3 (99.9999%), Tm_2O_3 (99.9%), Yb_2O_3, and Lu_2O_3 were dissolved in hot nitric acid to form the nitrate precursors. In this case we used citric acid (CA) as the chelating agent, with the same molar ratio, together with ammonium tungstate ($NH_4)_2WO_4$ (99.99%) and potassium carbonate K_2CO_3 (99.99%). The aqueous solution was heated at 353 K under magnetic stirring during 24 h until complete dissolution. After adding EG, the solution was heated at 373 K to generate the polymeric gel that was calcined at 1023 K for 2 h to form the desired nanoparticles.

2.2. Structural and morphological characterization

The crystalline structure of all nanoparticles was investigated by means of X-ray powder diffraction analysis using a Bruker-AXS D8-Discover diffractometer using Cu Kα radiation, getting in all cases the crystalline phase desired. Results are summarized in Figs. S1–S3 in the Supporting Information.

The size and morphology of all the samples were investigated by using a transmission electron microscope (TEM) JEOL 1011 operating with an accelerating voltage of 100 kV. The results are also summarized in the Supporting Information (see Figs. S1–S3).

2.3. Comparative intensity photoluminescence measurements

Nanoparticles were placed in a borosilicate bottom flat vial and compacted to ensure that they fully fill the bottom of the vial. The vial was inserted in a sample holder that was placed inside an integrating sphere (Labsphere 4GPS-020-SL). Samples were excited with a 200 μm core diameter fiber-coupled laser diode from Apollo Instruments, Inc. emitting at 808 or 980 nm. The laser beam was collimated to a spot size of 3 mm on the sample, and a power of 100 mW. The emission arising from the nanoparticles was collected using a Yokogawa AQ6375 optical spectrum analyzer (OSA) under the same operating conditions to ensure that intensity comparison from the different samples is reliable.

2.4. Temperature dependent photoluminescence measurements

For the temperature-dependent photoluminescence experiments, the nanoparticles powders (not compressed) were introduced into a customized Linkam THMS 600 heating stage, with a boron nitride disk that homogenizes the temperature distribution inside the chamber and along the sample. The heating stage was placed in a homemade microscope setup in which the same diode lasers described before, with emissions at 808 and 980 nm were used to excite the sample, using a 40× microscope objective and a N.A. of 0.6, that produced a laser spot of ~10 μm on the sample. The emission was collected by the same microscope objective, and after passing a dichroic filter for elimination of the excitation wavelength, was sent to the Yokogawa AQ6375 OSA.

3. Results and disscusion

3.1. Er^{3+} emissions in the SWIR

Er^{3+}, Tm^{3+} and Ho^{3+} ions show several SWIR emission lines that can be used in nanothermometry. Spectra of Er^{3+}, Yb^{3+} co-doped nanoparticles excited at 980 nm and collected inside the integrating sphere are shown in Fig. 1(a). The emission spectra consist of a broad band located at around 1.55 μm with an internal structure due to the emission lines arising from the different Stark sublevels. The mechanism of production of this emission band is