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Core-Shell Nanoparticles

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History of Changes

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Abbreviations and Acronyms

ABCP	Amphiphilic block copolymer
AIBN	Azobisisobutyronitrile
AuNPs	Gold nanospheres
AuNRs	Gold nanorods
BTFA	Bis Trifluoroacetamide
BW	Biological window
CA	Citric acid
CNRS	Centre National de la Recherche Scientifique
COD	Crystallography Open Database
CSIC	Agencia Estatal Consejo Superior de Investigaciones Cientificas
CTA	Chain Transfer Agent
CTAB	Cetyl trimethylammonium bromide
DLS	Dynamic light scattering
DNPD	1,3-di(naphthalen-2-yl)propane-1,3-dione
EG	Ethylene glycol
FIBIRYCIS	Fundacion para la Investigacion Biomedica del Hospital Universitario Ramon Y Cajal
FWHMs	Full widths at half maximum
GOF	Goodness of fit
^{1}H-NMR	Proton nuclear magnetic resonance
HR-TEM	High-resolution transmission electron microscopy
ICDD	International Centre for Diffraction Data
ICP- AES	Inductively Coupled Plasma - Atomic Emission Spectrometry

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ICSD	Inorganic Crystal Structure Database
Ln^{3+}	Lanthanide ions
LPO	$LaPO_4$
LNTs	Luminescent nanothermometers
MA	Methyl acrylate
MPA	3-mercaptopropionic acid
MPEGA	Metoxy-Polyethylene glycol acid
MWCO	Molecular weight cut-off
NHs	Nanoheaters
NIR	Near Infra-Red
NPO	$NdPO_4$
NPs	Nanoparticles
OA	Oleic acid
ODE	Octadecene
PEGA	Polyethylene glycol acid
PhenA	(1,10-phenanthrolin-4-yl)methyl acrylate
PL	Photoluminescence
PTFE	Polytetrafluoroethylene
QDs	Quantum dots
RAFT	Reversible addition-fragmentation chain transfer polymerization
Re	Expected weighted profile factor (Re)
Rp	Profile factor
Rwp	Weighted profile factor
SPR	Surface Plasmon Resonance

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TEM	Transmission electron microscopy
TEOS	Tetraethoxysilan
THF	Tetrahydrofuran
TM	Transition metal
UAVR	Universidade de Aveiro
UCNPs	Upconverting nanoparticles
UU	Universiteit Utrecht
UV-VIS	Ultraviolet–visible spectroscopy
VINCA	Institut Za Nuklearne Nauke Vinca
WP	Work package(s)
WPAS	Instytut Niskich Temperatur I Badan Strukturalnych Im. Wlodzimierza Trzebiatowskiego Polskiej Akademii Nauk
XRD	X-Ray Diffraction
YAG	Yttrium aluminium garnet ($Y_3Al_5O_{12}$)
YIG	Yttrium iron garnet ($Y_3Fe_5O_{12}$)

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D2.1 Report on the synthesis conditions and on the structure and morphology of the materials to optimise the core-shell NPs architecture

The goal of the NanoTBTech project is to develop a 2-D thermal bioimaging technology featuring sub-microscale resolution, based on nanothermometers and heater-thermometer nanostructures. We will design, synthetize, and bio-functionalize nontoxic luminescent nanostructures, operating essentially beyond 1000 nm, for in vivo nanothermometry and nanoheating. Furthermore, to monitor the temperature-dependent nanostructures' luminescence we will develop a novel imaging system. The effective delivery of that major advance in 2-D thermal bioimaging will be implemented through two impactful biomedical showcases: highly spatially-modulated intracellular magnetic/optical hyperthermia and in vivo detection and tracking of cancer. Multiple conceptual breakthroughs can be further envisaged from the proposed 2D-thermal imaging system, credibly spreading its impact towards nonbiomedical technological areas.

Work package 2 (WP2) of the project is titled: "Advanced characterization of NPs & heater-thermometer nanostructures" and specifically deliverable D.2.1 (M9) is "Optimisation of the core-shell NPs architecture". The report is mainly given by a lead beneficiary of the WP2: INSTYTUT NISKICH TEMPERATUR I BADAN STRUKTURALNYCH IM. WLODZIMIERZA TRZEBIATOWSKIEGO POLSKIEJ AKADEMII NAUK (WPAS); along with other partners:

- INSTITUT ZA NUKLEARNE NAUKE VINCA (VINCA)
- UNIVERSIDADE DE AVEIRO (UAVR)
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- RAMÓN Y CAJAL HEALTH RESEARCH INSTITUTE (FIBIRYCIS)

This report describes the role of lanthanide (Ln^{3+}) and transition metal (TM) - doped core-shell nanoparticles CSNPs may have in developing advanced nanoparticle systems, with their advanced structural, morphological and luminescence features. Report consists of synthesis and basic characterization of purposeful materials examined so far (the materials are still under construction and characterisation). Some the description is the extension of work carried out in WP1, which specifically aim to improve the multifunctionality of such NPs by employing core-shell NPs, where the core and the shell be individually doped.

Four key aspects of the luminescence characteristics of NPs are engineered per the requirements of the application: i) desired excitation and emission wavelengths (BW-II and BW-III), ii) NIR electronic transitions that can be used for temperature reading, iii) quantum efficiency (q) >10% and iv) non-toxicity. These aspects are valid either for the NPs developed in WP1, or the core-shell NPs as well.

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Desired excitation and emission wavelengths (BW-II and BW-III) and NIR electronic transitions that can be used for temperature reading are controlled by the selection of the dopant: lanthanide activators (Ln^{3+}) and transition metals (TM) covering 1000-1500 nm range. Quantum efficiency and non-toxicity is considered by the host material chemistry. Host-dopant combinations are attempted using combinatorial chemistry.

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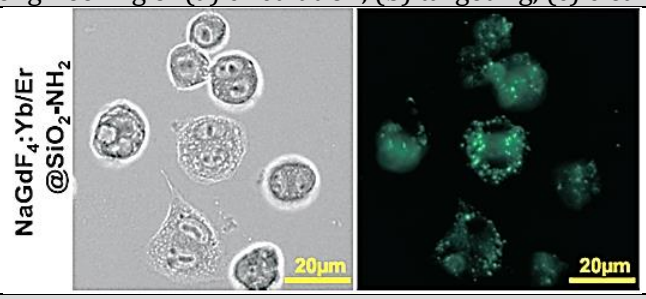
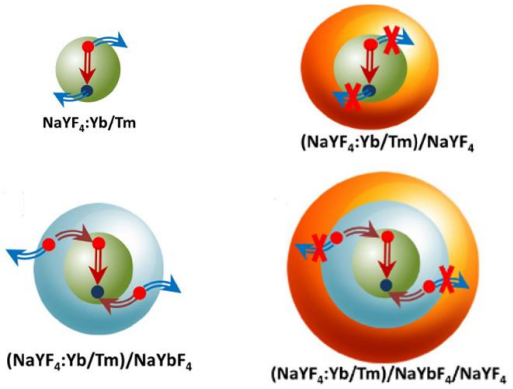
1. The purpose to make core-shell NPs

The major reason to get interest in core-shell nanoparticles (CS NPs) is the fact, that such approach enables to purposely design the photo-physical properties of such nanomaterials. This can be achieved by intentional doping of the core and the shell (or multiple shells) with different dopants. The shell may act as surface passivation (passive role aiming to protect the NPs from surface quenching), but more interesting features can be achieved when the shell is optically active, which may improve the absorption cross section as well as add additional features ,such as light-to-heat conversion.

Table 1. The advantages of using core-shell engineered nanoparticles

	Advantage	Demonstration	REF
1. Shell (PEG, $mSiO_2$ etc.) may increase bio-compatibility – such layer is easier for further bio-functionalization and engineering of (a) circulation, (b) targeting, (c) clearance time in vivo / in vivo			
			W.Kalas , J.Cichos, A.Bednarkiewicz et al. Toxicology in Vitro 32(2016) 16-25
2. Luminescent properties enhancement and chemical stability			
A	Shell protects NPs from (a) surface quenching and (b) etching to get bright and stable UC emission		K.Prorok et al. Nanoscale 2013
B	Doped shell increased absorption cross section		L.D.Sun et al. Chem. Eur. J. 2012, 18, 5558 F.Zhang, et. al. Nano Lett. 2012, 12, 2852 $NaGdF_4$:Er^{3+} 2%, Yb^{3+} 20% @ $NaGdF_4$:Yb^{3+} 20% J.Capobianco et al. Adv. Funct. Mater. 2009, 19, 2924 H.Qiu et al. Nanomaterials 2014, 4, 55-68

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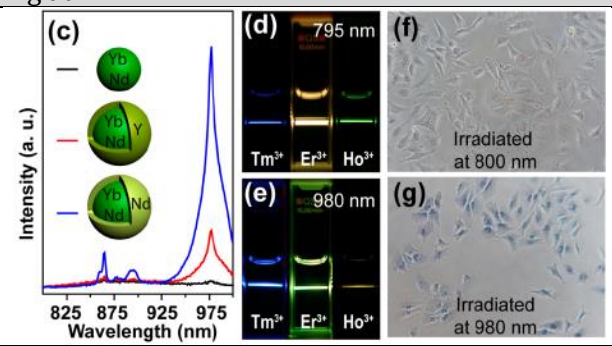
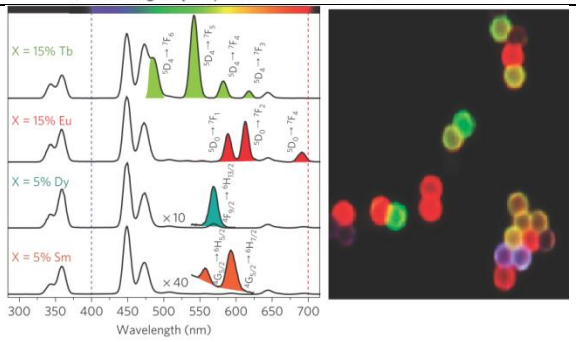
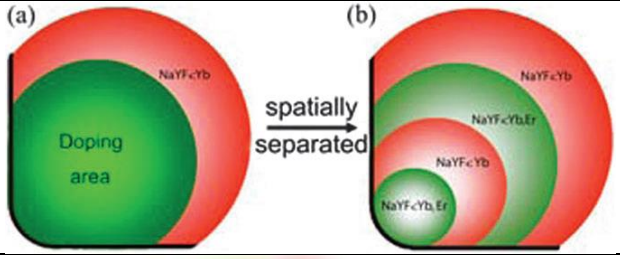
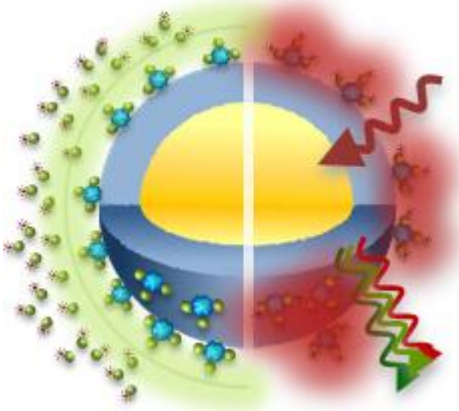
3. By separating NdYb sensitizer part from YbLn (Ln=Er/Tm/Ho/Tb/Eu) emission part to avoid parasitic $Ln^{3+} \rightarrow Nd^{3+}$ back energy transfer (BET), core-shell NPs may enable to shift of excitation wavelength from ~980 to ~808 nm aiming at:			
a	Reducing parasitic heat generation		Y. Zhong et al. Adv. Mater. 2013 X.Xie, J. Am. Chem. Soc. 2013, 135, 12608
b	Multiplexed detection		F.Wang et al. Nature Mat. 2011
4 Core-shell UCNPs may optimise			
A	Activators distribution aiming at decreased concentration quenching		Chem. Commun., 2011, 47, 11957–11959 11957
B	Energy donors distribution (in shell only) aiming at higher sensitivity of LRET sensors		unpublished
5. Core-shell UCNPs may increase functionality of materials:			

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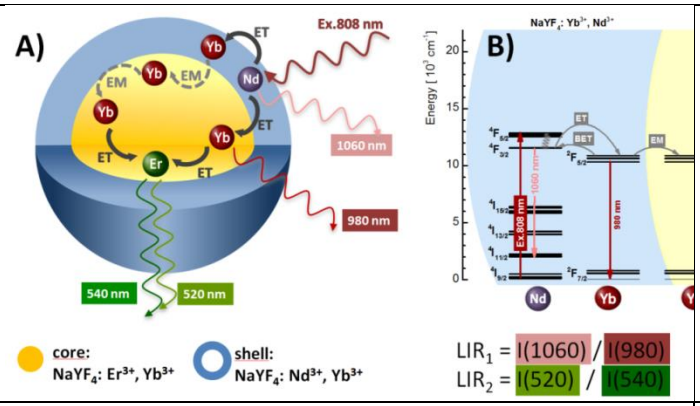
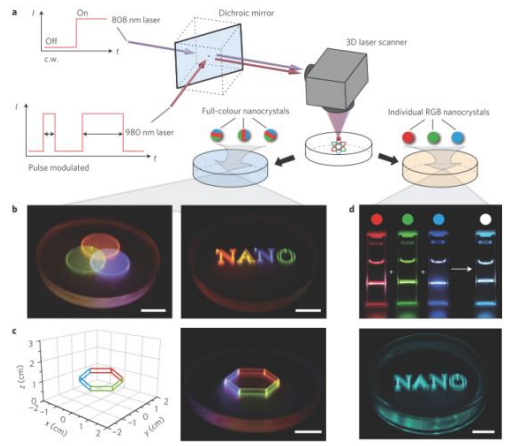
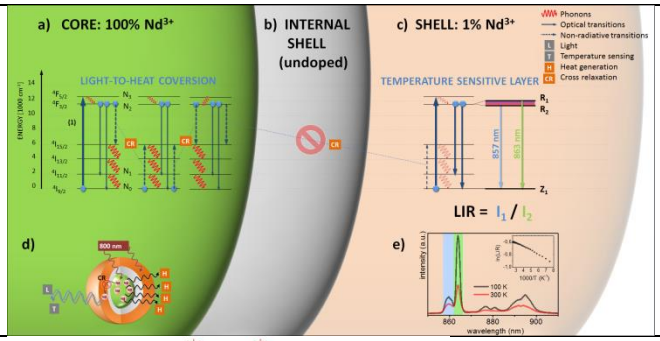
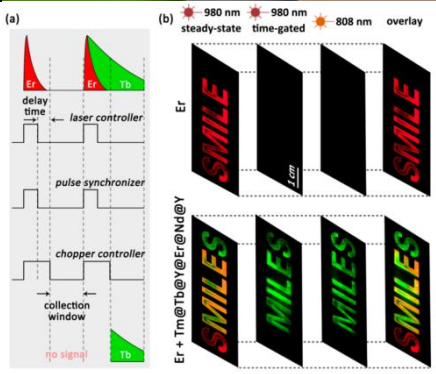
A	By increased temperature range of highly sensitive responsiveness		L.Marciniak , A.Bednarkiewicz*, et al. Nanoscale 2016
B	Volumetric RGB display		R.Deng, X.Liu et al., Nature Nano DOI: 10.1038/NNANO.2014.317
C	Combined heating & T sensing NPs		L.Marciniak, A.Pilch, S.Arabasz, D.Jin, A. Bednarkiewicz*, Nanoscale 2017
D	Anti-forgery protection		H.Dong, L.D.Sun,C.H.Yan, et al., ACS Nano 2017, 11, 3289−3297

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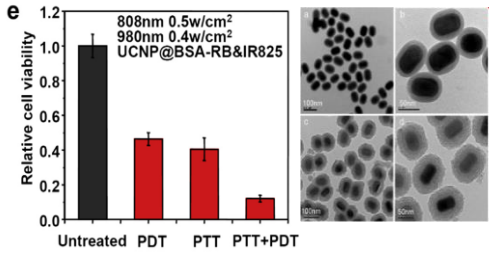
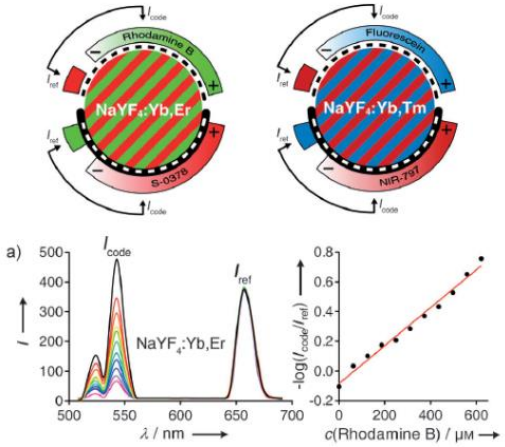
E	Drug delivery - light/pH triggered drug delivery / UC PDT		Q. Chen et al. / Biomaterials 35 (2014) 2915
F	Ratiometric sensors (NIR excitation!) with bioresponsive molecules through "inner-filter" effect		H.H. Gorris et al., Angew. Chem. Int. Ed. 2013, 52, 3584 – 3600

2. Short state-of-the-art in core-shell NPs for thermometric and light-to-heat conversion

Numerous requirements are made for thermometer – heater NPs: firstly heaters must be effective enough to entail temperature higher than 42°C – suitable for hyperthermia treatment, because cancer cells are more susceptible to temperatures in the range of 42-45°C as compared to the healthy ones [1]. Temperature growth must be assured within possibly minimum laser power density, because high power density may cause cell damage. Also it is important to choose NPs concentration wisely: although increasing concentration is providing higher temperature growth, higher concentration could decrease cell viability [2]. Because of that, it is required to select NPs that are effective also in small concentration. The excitation wavelength both for luminescence and heating should be located in one of the BW to enable deep tissue penetration. For luminescent material excitation wavelength should be matched with excited energy level to start luminescence process. Excitation wavelength for NHs must be located in absorption spectrum and the most desirable path of relaxation are non-radiative transitions. The most effective light-to heat conversion is when the absorption value is the highest.

It is recommended for NPs dedicated for photothermal therapy (PTT) to have low particle size, to enable NPs migration between tissues. It is claimed that for systemic administration optimal particle

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size is in range of 2-200nm, although some studies have shown that size under 50nm provides fewer side effects [3]. The synthesis of core-shell NPs with particle size lower than 50nm is still a challenge. Although there are many NPs suitable for PTT applications and many materials were investigated, core-shell structure in PTT is still novel and further studies on architecture of core-shells is still needed. Core shells for different imaging and therapy techniques are widely described in [4]. Although there are various nanomaterials for PTT applications such as gold nanorods, UCNPs, carbon dots, and TMDCs, metal oxides, black phosphorus and polymeric nanomaterials, UCPNs have advantages such as improved penetration depth, low radiation damage, minimized autofluorescence, high stability and low cytotoxity [5],[6].

One of the first use of core-shell NPs for simultaneous luminescent thermometry and heating is the research done by Marciniak et al. (Table 1.5c [7], where single particle thermometer – heater was proposed and optimized towards bright NIR emission of thermometer and efficient light-to-heat conversion also in NIR spectral region. For this purpose, stoichiometric $NaNdF_4$ core was covered with undoped – separation $NaYF_4$ shell and covered with 1%Nd^{3+} doped second shell. These studies revealed important data and conclusions. For example, it seems reasonable to separate photoexcitation dedicated for light-to-heat conversion from the one dedicated for luminescent thermometry. This is important for addressability – temperature readout should now induce heating by itself. Another important issue noticed was the necessity to develop primary thermometers, i.e. thermometers, whose readout does not depend on local environment and photoexcitation intensity.

Another promising application of UCNPs for PTT was made by Shao at al [6]. Core-shell $NaGdF_4$:Yb^{3+} core and shell highly doped with Yb^{3+}/Nd^{3+} ions in a size lower than 10nm was successfully synthesized. The PTT was realized in 808nm excitation (Nd^{3+}) and 980nm (Yb^{3+}) but Nd^{3+} has 10 times higher cross-section than Yb^{3+} and on 980 nm there is strong absorption of water. Core provides the temperature reading with 0.0012°C^{-1} sensitivity at 30 °C. NPs with shell with the higher (0.7) Nd^{3+} concentration provides temperature increase (ΔT) 10.3°C with the density power density 7.6W/cm^2.

Some other report by Shao [8] presented another core-shell structure dye-sensitized $NaYF_4$: Yb^{3+}/Er^{3+} @ $NaYF_4$: Yb^{3+}/Nd^{3+}. The role of IR-806 dye was to increase the light absorptivity of NPs at 808nm excitation wavelength. The thermal sensitivity of Er@10Yb/30Nd UCNPs was S_R=1.2 x 10^{-2} /°C at 30 °C. Temperature increase after irradiation of 808nm, power density 3.6 W/cm^2 was ~10°C in concentration of the UCNPs 10 mg/mL, dye/nanoparticle weight ratio: 1:300 and power density: 3.6 W/cm^2.

One of the reports by Zhang at al [9] was about core-shell $NaYF_4$:Er^{3+}/Yb^{3+}@$NaYF_4$:Tm^{3+}/Yb^{3+} for nanothermometry and PTT application. Core - Er^{3+}/Yb^{3+} enables temperature sensing, and also effect generate heat because of accompanying nonradiative transitions. Shell - Tm^{3+}/Yb^{3+} is the main area where heating energy from light energy is obtained. The NPs size with shell is ~23nm. For temperature sensing resulting sensitivity for temperature detection was 0,0035/K measured in 980nm excitation wavelength and 24W/cm^2 density power. Irradiation with 980nm with density power 129W/cm^2 resulted in 7°C temperature increase after 30min of irradiation.

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In a subsequent publication Zhang at al [10] proposed another core-shell NPs - $NaYF_4:Er^{3+},Yb^{3+}@NaYF_4$, but the lanthanide core-shell NPs was conjugated with gold nanorods for more effective light-to heat conversion. As in previous report, excitation wavelength for temperature sensing was 980 nm, but for addititional heat generation on gold nanorods, NPs were simultaneously irradiated by 808nm. The nanothermometer sensitivity was ~0.004/K around 301-337K at density power 16.1W/cm^2. Averaged core-shell size was ~25nm. Simultaneously using two excitation wavelengths provides more effective light-to-heat conversion. Also, there was a considerable observation that eigen temperature differ significantly from solution temperature – when the 55°C temperature increase of eigen temperature was measured under ~16W/cm^2 of irradiation by 808 and 980nm, the solution temperature growth was only 25°C It was proven that NPs enable repeatable and controllable eigen temperature increase.

Different other NPs suitable for hyperthermia, doses, power densities, irradiation times and efficiency of therapies were compared in a broad review by Chien et al [5].

There are multiple examples of nanomaterials which provide multiple applications, can act as temperature luminescent sensors, imaging particle (MRI, CT, upconversion luminescence) and agent for chemotherapy, photodynamic and photothermal therapy. It is important to combine that methods because it enable to diagnose and therapy of cancer more precisely. Thermal sensing and photothermal therapy, when used simultaneously, provides controlled heat generation, which minimize the risk of overheating of healthy cells.

The example of multifunctional NPs for imaging and therapy of cancer: core-shell $NaYF_4$:Yb,Er@$NaGdF_4$, UCNPs for upconversion luminescence (Er^{3+}) and MRI (Gd^{3+}). This core-shell was improved by additional Au nanocrystal layer for PTT and attached –DOX ligand for chemotherapy. The upconversion luminescence requires 980nm photoexcitation and three characteristic bands (521, 540, 654nm) proper for Er^{3+} ion are observed. Photothermal therapy was proposed under 808nm, although the maximum of absorption peak is near 515nm. The efficiency of 12% was reached with 1.5W/cm power density [2].

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3. Results

3.1. $NaYF_4$ core-shell nanoparticles

3.1.1. Synthesis of core-shell $NaYF_4$ @ $NaYF_4$ nanoparticles

Preparation of Lanthanide Acetate: Stoichiometric amounts of lanthanide oxides were mixed with 50% aqueous acetic acid. The mixture was stirred and heated to obtain a clear and transparent solution. The final precursor was obtained by evaporation of solvents at prevacuum and further drying at 130 °C for 24 h.

Synthesis of Core Nanoparticles: Lanthanide acetates were added to the flask with oleic acid and octadecene. The solution was stirred and heated to 140 °C under vacuum for 30 min to form a Ln(oleate)3 complex and to remove total oxygen and remaining water. Next, the temperature was lowered to 50 °C, and ammonium fluoride (NH_4F) and sodium hydroxide (NaOH) dissolved in methanol were added to the reaction flask. The resulting cloudy mixture was stirred for 30 min at 70 °C. Next, the reaction temperature was increased, and the methanol was evaporated. After removing methanol, the solution was heated up to 300 °C under nitrogen atmosphere and kept in such conditions for 1 h. Next, the nanoparticles were precipitated using ethanol and n-hexane, centrifuged at 10000 rpm for 10 min, and washed with ethanol. Finally, the prepared core NPs were dispersed in chloroform.

Synthesis of Core/Shell Nanoparticles: Lanthanide acetates were added to the flask with oleic acid and octadecene. The solution was stirred and heated to 140 °C under vacuum for 30 min to form the $Ln(oleate)_3$ complex and to remove the total oxygen and remaining water. The temperature was lowered to 60 °C, and the reaction flask was placed under a flow of nitrogen. A solution of core nanoparticles in $CHCl_3$ was added to the solution. The solution was maintained at 80 °C until all of the chloroform was removed. Next, the temperature was lowered to 50 °C and ammonium fluoride (NH_4F) and sodium hydroxide (NaOH) dissolved in methanol were added to the reaction flask. The resulting cloudy mixture was stirred for 30 min at 70 °C. Next, the reaction temperature was increased, and the methanol was evaporated. After removing methanol, the solution was heated to 300 °C under nitrogen atmosphere and kept in such conditions for 1 h. Next, the nanoparticles were precipitated using ethanol and n-hexane, centrifuged at 10000 rpm for 10 min, and washed with ethanol. Finally, the prepared nanoparticles were dispersed in chloroform.

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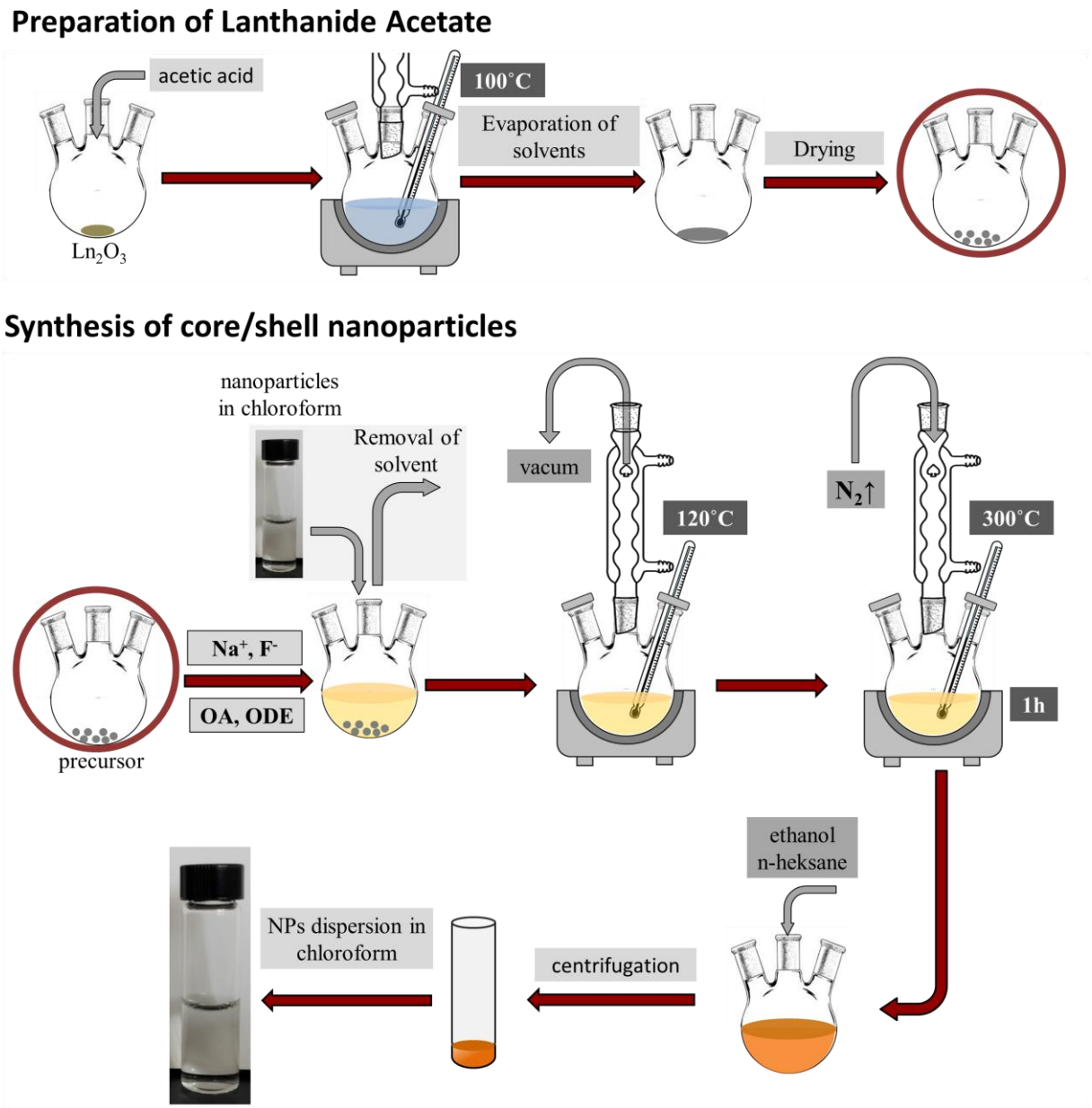

Figure 1. Synthesis of core-shell NaYF4 @ NaYF4 nanoparticles

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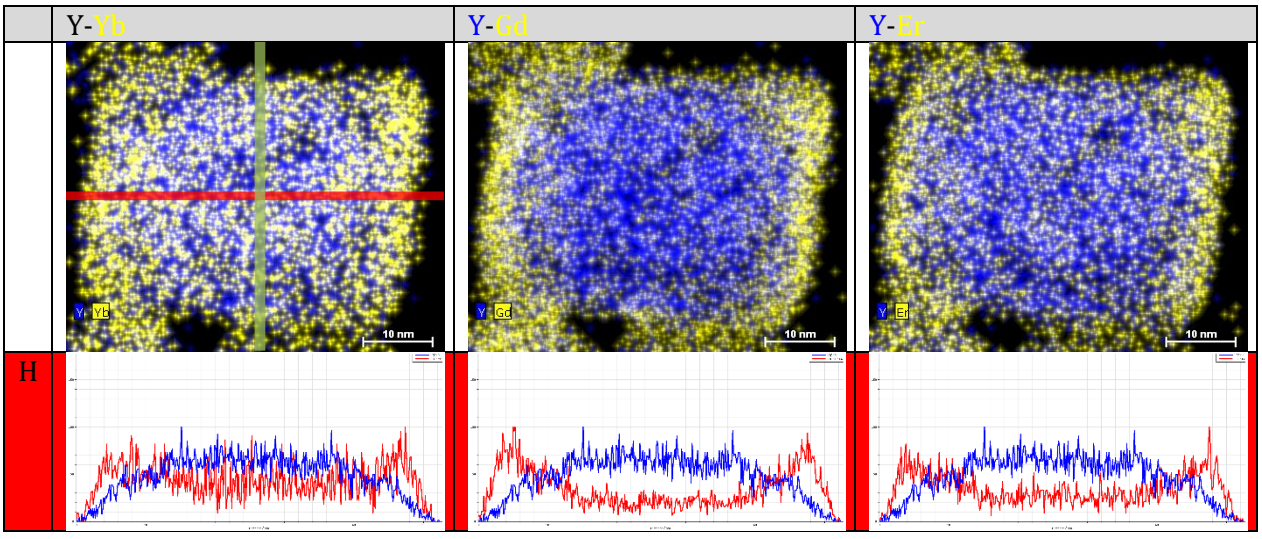
Table 1. The core-shell samples which have been synthesized so far, under characterisation

Sample	Core	Shell	Shell
FET_37	$NaYF_4$:20%Yb, 5%Nd	$NaYF_4$:20%Yb, 20%Dy	X
FET_40	$NaYF_4$:20%Yb, 2%Er,5%Mn	$NaYF_4$	X
FET_41	$NaYF_4$:20%Yb, 0,2%Tm,5%Mn	$NaYF_4$	X
FET_45	$NaYF_4$:20%Yb, 20%Sm,4%Nd	$NaYF_4$	$NaYF_4$:5%Yb, 2%Nd
FET_11	$NaYF_4$:20%Yb	$NaGdF_4$:20%Yb2%Er	

3.1.2. Characterisation of structure (XRD), morphology (TEM), composition architecture (TEM-EDS) of core-shell NaYF4@NaYF4 NPs

So far only one core-shell nanoparticle has been examined towards the composition of single nanoparticle (Fig.2) The sample (FET_11) was made to understand how precisely we can dope core and the shell in an individual way. Using Y or Gd should provide sufficient contrast in TEM and TEM-EDX, while Yb and Er, should be doped into core (Yb) and shell (Er). This will be the first try to understand the formation of core-shell NPs, in order to address the functions of such complex NPs. From Fig.2, one may note Yb rich core and shell, Gd and Er rich shell, which all indicate the nanoparticle of intentional composition NaYF4:Yb @ NaGdF4:YbEr has been actually synthesized. Currently we are working on the modelling to verify how sharp the edge between core and the shell is. These results shell help us optimize the composition and intentional design of future heater-thermometer nanoparticles.



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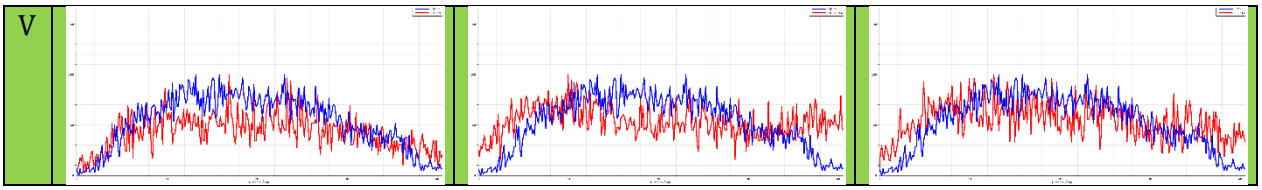

Figure 2 . TEM-EDX composition map.

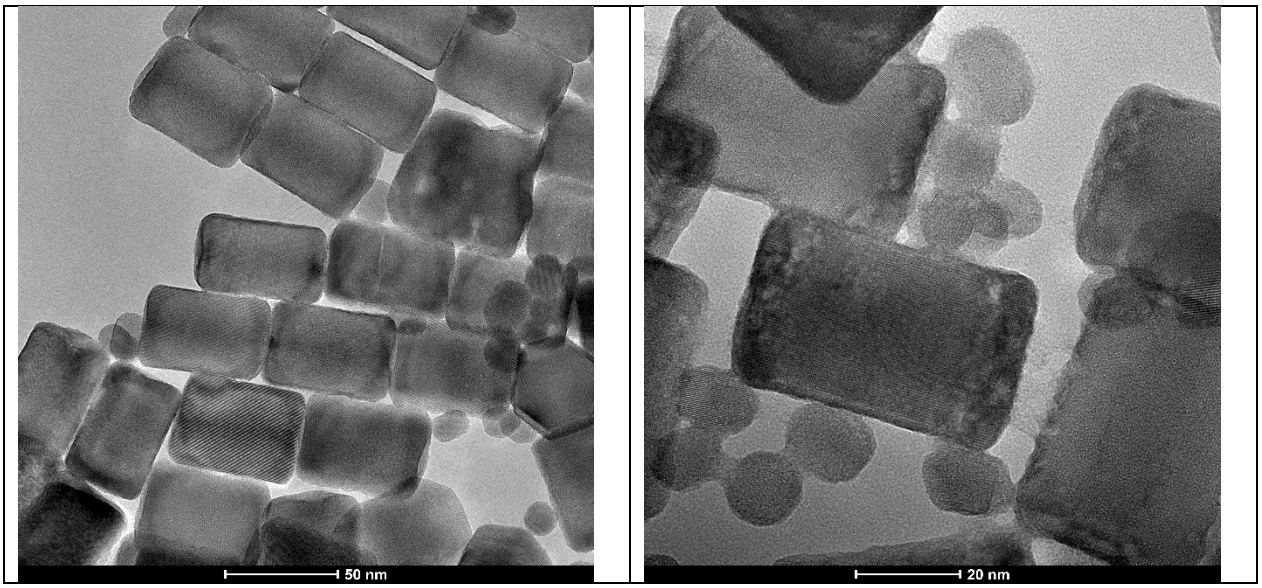

Figure 3. Morphologies of FET_11 sample. The synthesis protocol is under optimisation.

3.1.3. Conclusions

- $NaYF_4$@$NaGdF_4$ core-shell NPs have been successfully synthesized, but two morphologies were achieved, which requires further optimisation.
- Y and Gd ions provide sufficient contrast for TEM imaging to visualize the edge between core and shell
- Distribution of active dopants was confirmed by TEM-EDS maps, which enables to draw qualitative conclusions about accuracy we can engineer core-shell nanoparticle of designed composition

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3.1.4. Future work

Table 2. Samples which are to be synthesized and studied in near future.

Sample	Core	Shell	Shell
FET_38	$NaYF_4$:15%Yb, 5%Tb, 10%Mn	$NaYF_4$	$NaYF_4$:5%Yb, 2%Nd
FET_39	$NaYF_4$:15%Yb, 5%Tb, 5%Mn	$NaYF_4$	x
FET_42	$NaYF_4$:15%Yb, 5%Tb,10%Mn	$NaYF_4$	x
FET_43	$NaYF_4$:15%Yb, 5%Tb,10%Mn	$NaYF_4$	$NaYF_4$:20%Nd, 20%Dy
FET_44	$NaYF_4$:15%Yb, 5%Tb,10%Mn	$NaYF_4$	$NaYF_4$:20%Nd, 20%Sm
FET_50	$NaYF_4$:50%Yb, 50%Sm	$NaYF_4$	$NaYF_4$:5%Yb, 2%Nd
FET_51	$NaYF_4$:50%Yb, 50%Dy	$NaYF_4$	$NaYF_4$:5%Yb, 2%Nd

Some of these nanoparticles have been synthesized already, and are under evaluation. These nanoparticles are meant to help to understand the energy transfer for enhanced light-to-heat conversion as well as enhanced upconversion emission.

3.2. Nanometer size polistyrene NPs co-doped with UCNps and AuNPs

3.2.1. Nanometer size polistyrene NPs co-doped with UCNps and AuNPs

Liquid styrene was mixed with 1ml of cyclohexane and the nanoparticles (UCNP's or AuNP's). The as prepared mixture was added to water solution of sodium dodecyl sulfate (SDS). After that the obtained solution was treated using ultrasound for 15 minutes to obtain a miniemulsion. Subsequently the solution was transferred to 250ml three neck reaction flask and stirred. The potassium peroxydisulfate was added to reaction flask and the obtained mixture was stirred under nitrogen atmosphere for 10 minutes. After that the temperature of reaction was increased to 80oC. The solution was maintained at this temperature for 24 hours. After that the polystyrene nanospheres were collected by centrifugation (14 000rpm, 10min) and dispersed in 10 ml of water.

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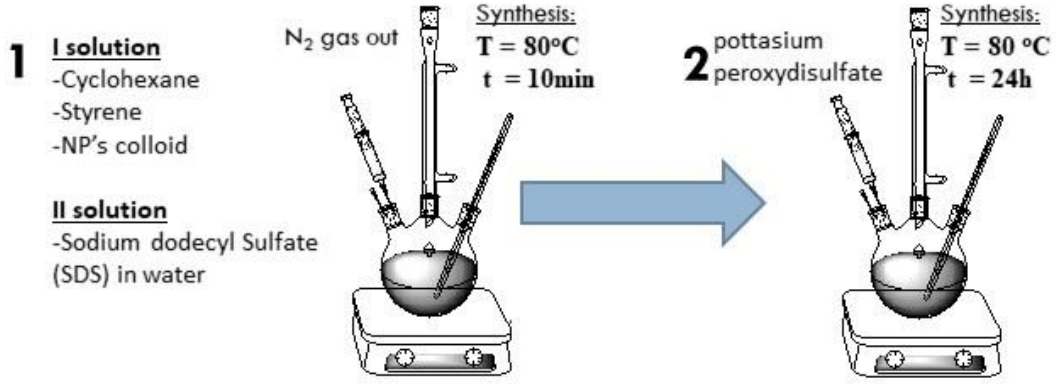

Figure 4. The scheme of synthesis PS coated nanoparticles

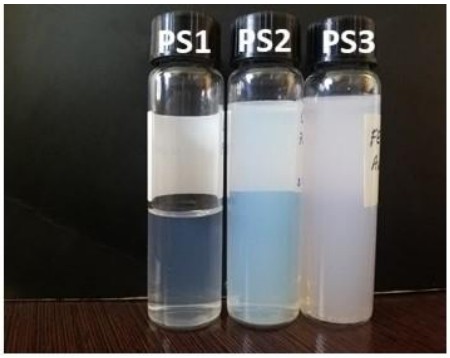

Figure 5. Pictures of the obtained colloidal nanoparticles.

Table 3. Nanometer size polystyrene NPs co-doped with UCNps and AuNPs

Sample	Core	Information
PS_1	PS coated UCNP's	1ml of UCNP's colloid was added, reaction time 24h
PS_2	PS coated AuNP's	0,5ml of AuNP's colloid was added, reaction time 24h
PS_3	PS coated AUNP's	1ml of AuNP's colloid was added, reaction time 18h

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3.2.2. Characterisation of morphology (SEM) of $NaYF_4$@PS nanoparticles

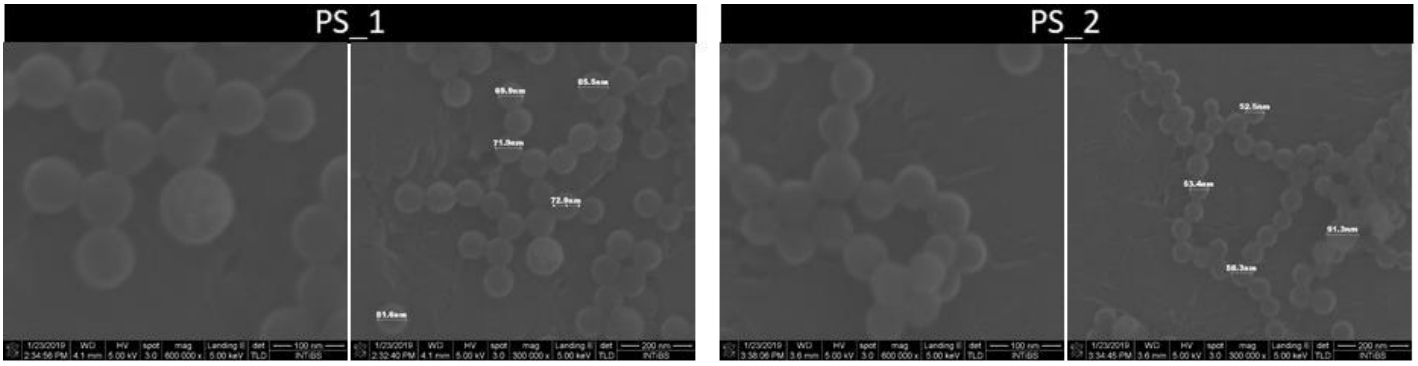

Figure 6. TEM images of synthesized PS coated nanoparticles.

3.2.3. Conclusions

- The challenge is to encapsulate NPs in polystyrene
- The obtained colloids are slightly cloudy, only colloids with AuNp's has little red color because of Au NP's color
- The nanoparticles are dispersed in water, and the colloids are very stable

3.2.4. Future work

- Optimisation of synthesis procedure to reproducibly "dope" UCNPs or AuNPs within such PS nanobeads
- Verification of spectroscopic properties (luminescence spectra, FTIR spectra and luminescence lifetimes) of the obtained nanomaterials as compared to bare nanomaterials

3.3. Gold nanospheres (AuNPs) and AuNPs@SiO2 core-shell nanostructures

Introduction: In the previous deliverable (D1.1_Del1_First Generation of Nanoparticles) colloidal synthesis of gold nanospheres and AuNPs@SiO_2 core-shell nanostructures with detail synthesis procedure and UV-VIS characterization is reported. Further plan was to preform transmission electron microscopy (TEM-EDS) in order to determine AuNPs size and silica shell thickness.

3.4. Gold nanorods (AuNR) and AuNRs@SiO2 core-shell nanostructures

Introduction: In the previous deliverable (D1.1_Del1_First Generation of Nanoparticles) colloidal synthesis of gold nanorods and AuNRs@SiO_2 core-shell nanostructures with detail synthesis

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procedure and UV-VIS characterization is reported. Further plan was to preform transmission electron microscopy (TEM-EDS) in order to determine AuNRs aspect ratio and silica shell thickness.

3.5. Ag_2S colloidal dispersions

In the previous deliverable (D1.1_Del1_First Generation of Nanoparticles) microwave-hydrothermal synthesis of Ag_2S QDs with detail synthesis procedure and UV-VIS characterization is reported. Detailed precursor quantities and reaction parameters are given again in Table 4 for clarification. Further plan was to preform photoluminescent measurements and according to the obtained results efforts toward developing improved QDs synthesis methodology (size distribution and q) to make them operational for bio-applications in the NIR spectral region will be continued.

Table 4 Precursor quantities and reaction parameters used for Ag_2S colloids synthesis.

Sample	$AgNO_3$ (g)	MPA (ml)	EG (ml)	Temperature (°C)	Time (min.)
1	0.0255	0.305	4.5	160	30
2	0.0255	0.305	4.5	145	60
3*	0.0255	0.305	4.5	145	50
				120	70
4**	0.0255	0.305	4.5	145	10
				145	15
				145	35
5	0.051	0.71	4.5	145	60
6	0.051	0.71	4.5	160	60

3.6. Photoluminescent (PL)characterization and quantum yield (QY)

Photoluminescent spectra of Ag_2S colloid samples (λ_{ex}=808 nm) presented in the Figure 1 show broad, complex emission (1000-1400 nm) in the BW-II. Emission peak placed at 1000 – 1200 nm can be attributed to the band edge/near band emission while complex shoulder placed at 1200 – 1400 nm can be attributed to the defect level/surface state emissions. Absolute quantum yields are calculated and presented in Tables 2 and 3 for all synthesized samples as well as commercially available Ag_2S-PEG sample.

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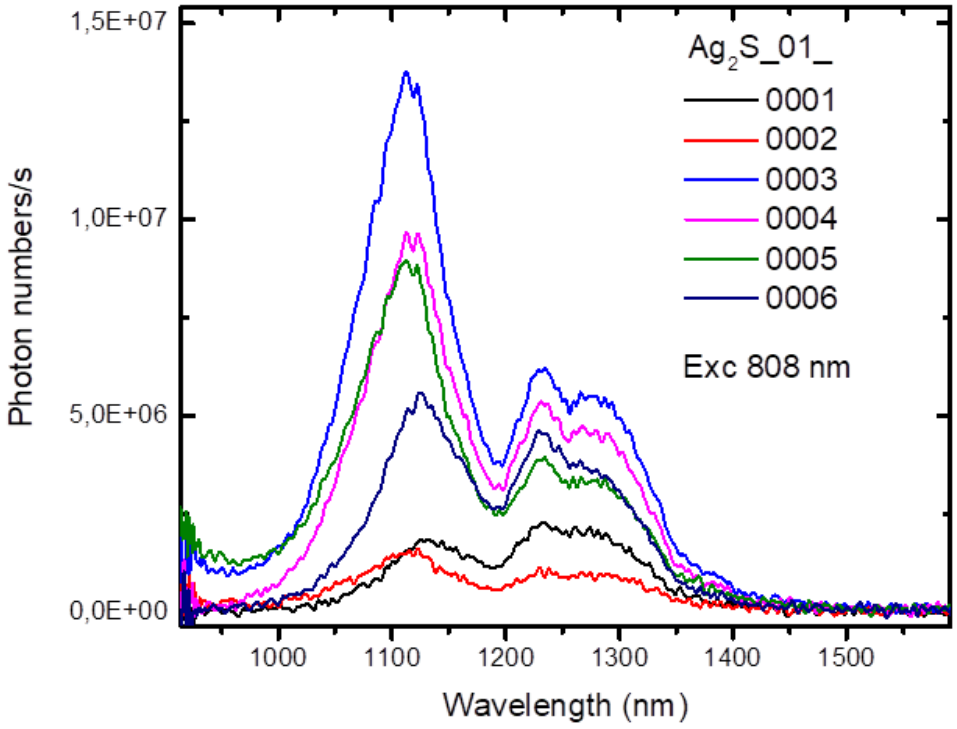

Figure 7 Photoluminescent spectra of Ag2S colloid samples (λex=808 nm).

Table 5 Absolute quantum yield (QY) of the synthesized samples (LPD 576.77 W/cm² and λ_{ex}=808 nm) in methanol.

Sample	Ag_2S_01_0001	Ag_2S_01_0002	Ag_2S_01_0003	Ag_2S_01_0004	Ag_2S_01_0005	Ag_2S_01_0006
Absolute QY	(5.0±0.5)x10^{-4}	(5.0±0.5)x10^{-4}	(2.3±0.2)x10^{-3}	(2.4±0.2)x10^{-3}	(3.3±0.3)x10^{-3}	(1.5±0.2)x10^{-3}

Table 6 Absolute quantum yield (QY) of the commercial Ag2S-PEG nanoparticles (λ_{ex}=808 nm) in water.

P. Density (W/cm^2)	20	64	102	145
Absolute QY	$(8.0 \pm 0.8) \times 10^{-4}$	$(7.8 \pm 0.8) \times 10^{-4}$	$(7.1 \pm 0.7) \times 10^{-4}$	$(7.1 \pm 0.7) \times 10^{-4}$

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4. Conclusions and further work

We should search for single nanoparticle based heather/thermometer, which is important for several reasons, such as:

(i) simplicity to synthesize such NPs in opposite to hybrid multi-particle combined constructs

(ii) the possibility to address a given function (heating or temperature readout) with photoexcitation wavelength (e.g. 1064 for thermometry with Nd^{3+} and 808 for light-to-heat conversion) or similar.

To achieve these goals, precise knowledge is important how to design and synthesise such NPs, prevent interaction of dopants of the core and the shell, design how to make primary thermometers etc.

WPAS is going to synthesize and characterize numerous core-shell nanoparticles to understand how precisely we are in synthesizing intentional compositions. This will require continuous feedback from TEM-EDX maps as well as involvement of spectroscopic characterisation to light induce specific functions of the NPs. We will continue the work towards coving the UCNPs or AuNPs with polymeric shell, as this may enable to combine different types of NPs (e.g. UCNPs, Ln:NPs, TM:NPs, AuNPs etc.) within single nano PS bead. The PS shall also enable to simplify biofunctionalization step, i.e. attaching bio-recognition molecules, such as antibodies by other partners of the consortium. Preliminary TEM-EDS maps of $NaYF_4$@$NaGdF_4$ provide promising initial studies, which will be continued. For example, new samples have been made (e.g. 5Nd20Yb@20Yb20Dy, 15Yb5Tb10Mn@...@2Nd5Yb, 4Nd20Yb20Sm@...@2Nd5Yb) and are under TEM-EDS evaluation. These studies shall help us understand hot to precisely doped core-and shell, what are ther interactions between ions in the core and in the shell and how to specifically address core or shell, for either thermometry or light-to-heat conversion. For example 5Nd20Yb@20Yb20Dy sample may be used as NIR nanothermometer under 800 nm (to excite Nd^{3+} ions, which transfer their energy to Yb^{3+}), while 980 nm photoexcitation is dedicated for YbDy heater.

VINCA is going to work on next steps of PEGylation of Ag_2S QDs, in order to:

- increase QY by decreasing defect level/surface state emission losses

- decrease QDs toxicity, increase blood circulation time, suppress the non-specific binding of charged molecules to the modified surfaces and to increase solubility and stability of hydrophobic QDs in aqueous medium.

- According to TEM results sample/s for measuring light-to-heat conversion will be chosen.

- According to TEM and light-to-heat results sample/s for fabrication of AuNPs-hybride structures will be chosen.

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The TEM characterisation of VINCA samples will be performed. Moreover, as soon as the newly developed setup for light to heat conversion efficiency is ready, these nanoparticles will also undergo this advanced characterisation.

For ***PEGylation*** polyethylene glycols with different functional groups (e.g. Hydrazide functionalized PEG, Thiol functionalized methoxyl PEG, Thiol functionalized carboxyl PEG…..) will be used [1–3].

Another challenge is to develop standardized and reliable system to quantitatively characterize thermometers and light-to-heat converters (NanoTBTech deliverables of 2020, in progress). This shall enable to compare the behaviour and properties of different nanoparticles (NTMs and NHs) coming from different groups, different batches and different materials (AuNPs, Ln^{3+} doped NPs, TM doped NPs etc.).

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