Wrocław, 25.07.2022

Abstract of doctoral dissertation

Evaluating the impact of chemical composition and architecture of lanthanide doped colloidal core-shell $NaYF_4$ nanoparticles on their luminescence properties: from fundamental material science to bio-nano-technological applications

Author: Agata Kotulska, MSc
Supervisor: Prof. Artur Bednarkiewicz, PhD, DSc

Institute of Low Temperature and Structure Research
Polish Academy of Sciences

Scope of the thesis

This work presents the experimental and theoretical characterization of optical properties of lanthanide ion (Ln^{3+}) doped inorganic nanomaterials (LnNPs). The studies are aiming to understand the relationship between the composition and compositional architecture with the functionality of such nanoparticles for modern applications of luminescent labels. The scope of interest included Förster resonant energy transfer (FRET), and super-resolution imaging. The latter was achieved either by the application of nonlinearity of emission (in the photon avalanche process, PA), or could be possible via double beam photoexcitation. This scope of work required optical characterization of nanomaterials, designing and developing optical measurement setups as well as developing software to analyse and *in silico* simulate photophysical processes. The results achieved by the theoretical analysis and experiments were compared to understand whatever LnNPs can be applied as alternative luminescent labels to the well-known fluorescent compounds. The impact of numerous experimental parameters, such as the compositional architecture of lanthanide doped nanoparticles, were analysed to enhance the efficiency of the energy transfer. Moreover, the impact of selected parameters (such as wavelength, pump power, and duration time of photoexcitation laser beam) for emission spectra or luminescence lifetimes was studied. The results allowed us to understand whether LnNPs can be alternative biosensing or super-resolution imaging labels.

Abstract
Rare earth elements (lanthanide ions, Ln^{3+}) have been studied for several decades as a research subject in material science, and have been applied as optically active elements in lasers, TV screen phosphors, lighting, anti-counterfeiting protection, etc. [7]–[9]. Moreover, the developments of reliable and reproducible colloidal nanoparticle synthesis and biofunctionalization protocols enabled numerous biomedical applications of these luminescent labels as nano reporters in biosensing [10]. The development of such luminescent materials has triggered also other, new possibilities, especially in the super-resolution imaging of biological processes [11]. The features of the lanthanide ion doped nanoparticles (LnNPs), are narrowband absorption and emission bandwidths, relatively high anti-Stokes emission intensity, long living excited states, and good photostability [12]. These properties enabled to develop new materials and inspired new possibilities. In this work optical properties of lanthanide doped nanoparticles, and possible applications in super-resolution imaging of biological samples and resonance energy transfer (FRET) sensing are presented. In particular, theoretical analysis of highly non-linear photon avalanching (PA) nanoparticles for super-resolution imaging was performed, and compared with an experimentally observed enhancement of optical resolution. This dissertation contains a set of modelling results and spectroscopic characterization of lanthanide ions (Ln^{3+}).

Nanocrystals doped with Ln^{3+} ions can be applied as alternative to other labels (organic dyes, quantum dots, or lanthanide ion doped nanoparticles etc.), and have shown a high potential in fluorescence microscopy for imaging structures of sizes below the diffraction resolution limit (so-called super-resolution imaging) [3]. However, despite recent progress, further development of an experimental optical setup allows us to characterize and improve the properties of new designed material compositions. Additionally, the computational models, such as the proposed Virtual Nanoparticle model (VNP) was proposed and used to understand how the Ln^{3+} ions distribution impact the performance of sensors and resonance energy transfer (FRET) efficiency [3].

The focus of this thesis is the fundamental characterisation of optically active nanomaterial properties, toward implementation of such newly developed Ln^{3+} doped labels for sub-diffraction limit and bio-sensing. For the former, two different approaches and methods were developed and compared: (1) double wavelength photoexcitation optical setup for materials characterisation, and (2) the study of highly nonlinear photon avalanche emission (PA based single beam super-resolution imaging PASSI) [2]. Moreover, new labels (e.g. for STED) were sought, such as lanthanide ions doped nanomaterials. For the latter, LnNPs have shown suitability for observation and quantified description of biomolecules interaction at the nanometer scale [11]. Additionally, the VNP has been shown and compared with experimental results. This computational model enabled us to select parameters with an essential influence on the energy transfer efficiency values from lanthanide ions to an organic dye attached to the surface [5]. It was shown that measurement methodology itself, by considering the duration, energy, and wavelength of the photoexcitation pulse delivered to the upconverting donor nanoparticle, affects the efficiency and kinetics of energy transfer to the multiple-molecular acceptors [6]. The characterisation of fundamental optical properties of newly synthesized NPs and the capability to control and enhance FRET efficiency, can enable further improvements in the design of fluorescent labels with stable, optically active materials [13].

1) Kotulska AM, Prorok K, Bednarkiewicz A, *Spectral properties of Tm^{3+} doped $NaYF_4$ up-converting nanoparticles under single and double photoexcitation wavelengths*. Methods and Applications in Fluorescence **7**, 1–8 (2019). DOI: 10.1088/2050-6120/ab11a4
2) Bednarkiewicz A, Chan E, Kotulska AM, Marciniak L, Prorok K, *Photon avalanche in lanthanide doped nanoparticles for biomedical applications: Super-resolution imaging*. Nanoscale Horizons **4**, 881–889 (2019). DOI: 10.1039/c9nh00089e
3) Lee C, Xu EZ, Liu Y, Teitelboim A, Yao K, Fernandez-Bravo A, *et al., Giant nonlinear optical responses from photon-avalanching nanoparticles*. Nature **589**, 230–235 (2021). DOI: 10.1038/s41586-020-03092-9
4) Kotulska A.M, *Försterowski rezonansowy transfer energii (FRET) — podstawy fizyczne i zastosowania*. Postępy Fizyki **72**, 8–15 (2021).
Available at: https://www.ptf.net.pl/media/cms_page_media/993/PF_1_2021.pdf
5) Pilch-Wrobel A, Kotulska AM, Lahtinen S, Soukka T, Bednarkiewicz A, *Engineering the Compositional Architecture of Core-Shell Upconverting Lanthanide-Doped Nanoparticles for Optimal Luminescent Donor in Resonance Energy Transfer: The Effects of Energy Migration and Storage*. Small **18**, 2200464 (2022). DOI: 10.1002/smll.202200464
6) Kotulska AM, Pilch-Wróbel A, Lahtinen S, Soukka T, Bednarkiewicz A, *Upconversion FRET quantitation: the role of donor photoexcitation mode and compositional architecture on the decay and intensity based responses*. Light: Science & Applications **11**, 256 (2022). DOI: 10.1038/s41377-022-00946-x
7) Fernandez-Bravo A, Yao K, Barnard ES, Borys NJ, Levy ES, Tian B, *et al., Continuous-wave upconverting nanoparticle microlasers*. Nature Nanotechnology **13**, 572 – 577 (2018). DOI: 10.1038/s41565-018-0161-8
8) Eliseeva S, Bünzli J-CG., *Rare earths: jewels for functional materials of the future*. New Journal of Chemistry **35**: 1165-1176 (2011). DOI: 10.1039/C0NJ00969E
9) Zheng B, Fan J, Chen B, Qin X, Wang J, Wang F, *et al., Rare-Earth Doping in Nanostructured Inorganic Materials*. Chemical Reviews, **6**, 5519 – 5603 (2022). DOI: 10.1021/ACS.CHEMREV.1C00644
10) Prorok K., Wawrzyńczyk D., Misiak M., Bednarkiewicz A., *Active-Core-Active-Shell Upconverting Nanoparticles: novel mechanisms, features and perspectives for bio-labeling*, [in:] *Upconverting Nanomaterials: Perspectives, Synthesis, and Applications*, Altavilla C. (ed.), Taylor & Francis Group, Boca Raton, 196-254 (2016). DOI: 10.1201/9781315371535
11) Francés-Soriano L, Ferrera-González J, María González-Béjar, Pérez-Prieto J., *Near-infrared excitation/emission microscopy with lanthanide-based nanoparticles.* Analytical and Bioanalytical Chemistry **414**: 4231-4310 (2022). DOI: 10.1007/s00216-022-03999-4
12) Misiak M., Prorok K., Bednarkiewicz A., *Biologiczne zastosowania nanoluminoforów domieszkowanych lantanowcami (Biological applications of lanthanide doped nanomarkers).* Wiadomości Chemiczne **66**, 393–443 (2012).
Available at: https://www.dbc.wroc.pl/Content/19021/PDF/WCh_5_6_2012.pdf
13) Prorok K, Olk M, Skowicki M, Kowalczyk A, Kotulska A, Lipiński T, *et al., Near-infrared excited luminescence and in vitro imaging of HeLa cells by using Mn^{2+} enhanced Tb^{3+} and Yb^{3+} cooperative upconversion in $NaYF_4$ nanocrystals*. Nanoscale Advances **1**, 2463-3473 (2019). DOI: 10.1039/C9NA00336C