Microchimica Acta (2023) 190:23
https://doi.org/10.1007/s00604-022-05606-w

EDITORIAL

# Topical Collection "Upconversion fluorescent nanomaterials for biodetection and bioimaging"

**Yong Zhang**[1]

Published online: 14 December 2022


Traditional fluorescent materials such as organic dyes and proteins are often excited by high-energy ultraviolet (UV) light to emit low energy visible light. Fluorescence is generated based on a down-conversion process that converts high-energy photons to low-energy photons. Most fluorescent materials are down-converting materials. Fluorescent dyes and proteins are not photochemically stable. A common problem when using these materials for fluorescence based detection or imaging is fluorescence quenching. Furthermore, they have different excitation wavelengths and therefore require different lasers for excitation. Inorganic fluorescent nanocrystals have much better photochemical stability. Semiconductor quantum dots are a good example. They have broad excitation bands and size-tuneable emission colors, so multiple quantum dots can be excited with a single laser to produce multi-colour emissions. They are photochemically stable and do not photobleach. Quantum dots have been widely used for fluorescence-based detection and imaging in vitro and in vivo. However, quantum dots are photoblinking and consist of toxic heavy metals, which limit their application in molecular detection and in vivo studies.

Lanthanide doped nanocrystals exhibit narrow emission bands, strong fluorescence emission, and good photostability. The rich energy level structure of lanthanide ions allows different designs to be proposed to control the energy transfer pathway so their excitation and emissions can be tuned. Upconversion fluorescence is based on the anti-Stokes process. After two or more low-energy photons are absorbed in sequence, the low-energy photons are converted into high-energy photons, thereby generating upconversion fluorescence, which is very unique and different from traditional down-conversion fluorescence. The excitation light is typically in the near-infrared (NIR) wavelength range while the emission can be upconverted to shorter NIR, visible, or UV wavelength ranges. When upconversion materials are used in biodetection and bioimaging, autofluorescence is low, and the sensitivity and signal-to-noise ratio are high because most biomolecules do not possess this unique upconversion property.

The Topical Collection "Upconversion fluorescent nanomaterials for biodetection and bioimaging" focuses on the use of upconversion nanocrystals (UCNPs) with novel compositions/structures, tunable fluorescence emission, and improved fluorescence intensity for biodetection and bioimaging. All the articles can be accessed via this link:

https://link.springer.com/collections/bdijejdfaa

A review article by Liu and co-workers discusses the different emission mechanisms of lanthanide doped UCNPs and technical approaches for the synthesis and surface functionalization of these nanocrystals. Hydrophobic surfactants are often used to control the growth of the nanocrystals and their shape and size, and surface modification must be performed to convert the hydrophobic surface to a hydrophilic surface so that the nanocrystals can be well dispersed in water based biological solutions. It also reviews the various biological applications of UCNPs, especially bioimaging and biosensing, as well as future challenges such as low quantum yield and potential toxicity.

Liu et al. developed a novel dual-flux immunochromatographic assay (dICA) method based on specially designed UCNPs with orthogonal red and green emission upon excitation at 980 nm and 808 nm, respectively. The red emission is used for self-calibration and quality control while the green emission is used to detect the target antigen based on specific antigen–antibody binding. The test strip was used for the simultaneous quantitative detection of ochratoxin A (OTA) and deoxynivalenol (DON), indicating that the developed dICA can rapidly, sensitively, and reliably detect a variety of

✉ Yong Zhang
biezy@nus.edu.sg

[1] Department of Biomedical Engineering, College of Design and Engineering, National University of Singapore, Singapore 117583, Singapore

mycotoxins, fungal metabolites, naturally occurring toxins in contaminating grains, and other products.

UCNP-based nanosensors were designed to detect small molecules such as thyroid-stimulating hormone (TSH) and pH changes in food spoilage. Lan et al. developed an aptamer sensor based on luminescence resonance energy transfer (LRET) between UCNPs and tetramethylrhodamine (TAMRA) for high sensitivity detection of TSH. UCNPs and TAMRA were conjugated to aptamers that specifically bind TSH. In the presence of TSH, both UCNPs and TAMRA bind to TSH to form a hairpin-like structure, and the distance between UCNPS and TAMRA is greatly reduced, resulting in a change in the luminescence intensity of UCNPs, thus allowing quantitative detection of TSH. In another study reported by Mei et al., nanosensors were designed by encapsulating UCNPs into a metal–organic framework (ZIF-8) in which doxorubicin (DOX) was absorbed into the pores of ZIF-8. The blue emission of UCNPs was quenched by DOX via fluorescence resonance energy transfer (FRET). When the nanosensors were exposed to food samples with different pH values, ZIF-8 collapsed to release DOX molecules, resulting in fluorescence recovery of UCNPs with a good linear relationship with pH changes.

UCNPs have also been used as fluorescent nanoprobes for cell imaging due to their resistance to photobleaching and less background autofluorescence. Neoh et al. reported that glycosylated phospholipid-coated UCNPs exhibited highly selective accumulation in cancer cells compared to normal cells. When irradiated by a 980-nm laser, bladder cancer cells showed much stronger upconversion fluorescence emission at 540 nm and 660 nm due to the accumulation of UCNPs in these cells. UCNPs were also used to study intracellular pathways of photosensitizers and cell-particle interactions which were largely unexplored. Zhu et al. used the dual emission of photo-switchable UCNPs with orthogonal red and green fluorescence emission to trigger reactive oxygen species (ROS) production and simultaneously track the intracellular pathways of photosensitizers, including their endosomal escape via photochemical internalization (PCI).

UCNPs were not only used as fluorescent probes for detection and imaging but also as delivery vehicles for therapeutic agents. Zhang et al. designed a UCNP-based nanoplatform for cell nucleus-targeted photodynamic therapy (PDT) by loading the photosensitizer rose bengal (RB) into mesoporous silica coated on the surface of the UCNPs and incorporate amine groups to the particle surface which can target the cell nucleus. ROS generated by RB upon light irradiation as part of the PDT process can also help particles escape from acidic lysosomes. In another study reported by Cruz and co-workers, UCNPs were used as nanocarriers for the delivery of OVA 254–267 (OVA24) peptide antigen and Pam3CysSerLys4 (Pam3CSK4) adjuvant into dendritic cells (DCs), and in vitro cell studies were performed. These particles were found to induce robust immune responses including DC maturation, T cell activation and proliferation, and interferon gamma (IFN-γ) production, suggesting that these particles could be used for DC-based immunotherapy. UCNPs were also used for in vivo imaging and tracking of particles in lymph nodes.

Overall, the eight articles compiled in this Topical Collection provide an overview of recent developments in UCNP technology in bioanalytics, bioimaging, and PDT. UCNPs can be used as fluorescent nanoprobes for biodetection and bioimaging and as nanocarriers for delivery of therapeutic agents for disease treatment.

Yong Zhang,
Senior Associate Editor, *Microchimica Acta*

## Declarations

**Conflict of interest** The authors declare no competing interests.