Trends in Analytical Chemistry 62 (2014) 123–134

Contents lists available at ScienceDirect

Trends in Analytical Chemistry

journal homepage: www.elsevier.com/locate/trac

Lanthanide-doped nanomaterials for luminescence detection and imaging

Shiguo Wang, Leyu Wang *

State Key Laboratory of Chemical Resource Engineering, Beijing Key Laboratory of Environmentally Harmful Chemical Analysis, Beijing University of Chemical Technology, Beijing 100029, China

ARTICLE INFO

Keywords:
Downconversion
Dual-mode luminescence
Functionalization
Lanthanide-doped nanomaterial
Luminescence
Multicolor emission
Nanocomposite
Optical imaging
Theranostics
Upconversion

ABSTRACT

Lanthanide-doped inorganic nanomaterials are a prominent class of nanocrystals with multicolor emissions that are an essential tool for optical imaging in analytical chemistry. Based on the excellent luminescence of lanthanide-doped nanomaterials, novel nanocomposites with diverse sizes (sub-10 nm) and properties, such as luminescence-plasmon, magnetism-luminescence, and upconversion (UC) and downconversion (DC) dual-mode luminescence, have been designed and prepared. These functional nanocomposites have been achieved by functionalization of lanthanide-doped nanomaterials with various types of polymers, responsive moieties, and targeting molecules. Here, we summarize the recent advancements in application of lanthanide-doped luminescence nanocomposites in analytical chemistry and highlight the challenges for future research. Precisely regulated and multicolor-emission lanthanide-doped nanocomposites will be a next thrust for applications in theranostics. Future applications of lanthanide-doped nanocomposites will benefit from such research.

Contents

* Corresponding author. Tel.: +86 10 64427869; fax: +86 10 64427869.
E-mail address: lywang@mail.buct.edu.cn (L. Wang).

http://dx.doi.org/10.1016/j.trac.2014.07.011

1. Introduction

One goal of analytical chemistry is to probe the chemical constituents, interactions and distributions in complex systems (such as environmental, biological, medical and therapeutic systems) by means of sensitive, selective and specific sensors. Luminescence imaging represents an essential tool to visualize analytes and subcellular structures in real time. To achieve the goal, many luminescent detectors have been explored and developed using conventional organic fluorescent scaffolds and emerging nanomaterials [1]. Among them, lanthanide-doped inorganic nanomaterials are a prominent class of nanocrystals with multicolor emission. Due to the unique $4f^n$ inner shell configurations of Ln^{3+} ions, lanthanide-doped nanomaterials, rich in magnetic and optical properties, can perform ultrasensitive *in vitro* and *in vivo* bioassays with excellent photostability, narrow emission bands, and high chemical stability.

Generally, lanthanide-doped nanomaterials are categorized into lanthanide-doped nanorods (NRs), nanospheres (NSs), nanoparticles (NPs) and quantum dots (QDs) according to different sizes and morphologies. Especially, lanthanide-doped NPs (the majority of lanthanide-doped nanomaterials) are categorized into upconversion NPs (UCNPs) and downconversion NPs (DCNPs) based on the mechanism of luminescence. DCNPs in DC luminescence (DCL) are involved in the process that obeys Stokes' law: absorbing a short-wavelength light and releasing long-wavelength emission through lanthanide doping. UC is the process that absorbs two or more low-energy photons, such as near-infrared (NIR) photons, and releases a high-energy luminescence photon [2].

Different from conventional organic dyes (single- or two-photon dyes), dye-contained fluorescent NPs (e.g., dye-doped silica NPs) and luminescent lanthanide complexes used as probes for optical imaging, both DCNPs and UCNPs possess unique tunable optical properties through variation of lanthanide dopants and host matrices, such as multicolor and multifunctional imaging [3]. Furthermore, UCNP-based UC luminescence (UCL) imaging shows excellent optical features, such as narrow anti-Stokes shifted light and low autofluorescence background. Especially, after the surface modification with various types of polymers, antennas, and targeting molecules, such as folic acid, antibodies, DNA and RNA, the functionalized lanthanide-doped nanocomposites with low toxicity and excellent tissue-penetration depth because of long-wavelength irradiation have been excellent candidates for further application in analytical chemistry, and biochemical, medical and materials fields [3]. Lanthanide-doped nanocomposites have found wide applications from solid laser and display devices to quantitative and qualitative analysis and *in-vivo* detection, cell imaging, animal imaging, and other advanced applications [3–7].

Considering the rapid development of lanthanide-doped nanocomposites in most areas of analytical chemistry, we review the advancements of functionalized lanthanide-doped nanocomposites, discuss their representative applications in analytical chemistry, and highlight the challenges for future research and development. Precisely regulated and multicolor-emission lanthanide-doped nanocomposites will be a next thrust for future applications.

2. General requirements for lanthanide-doped nanocomposites

2.1. Host materials, activators and sensitizers

Conventionally, the host matrices, sensitizer, and activator are the major components influencing the optical properties of DCNPs and UCNPs. Up to now, in the UC luminescent system, hexagonal-phase (β-phase) $NaYF_4$ is one of the most efficient host materials emitting strong UCL via co-doping with Yb^{3+}-Er^{3+} or Yb^{3+}-Tm^{3+} ion pairs. Meanwhile, $LaVO_4$ and LaF_3 DCNPs with special photochemical properties remain efficient hosts for DC luminescence emitting strong green or red DC luminescence via doping with Ce^{3+}-Tb^{3+} ion pairs or Eu^{3+} ions, which have found wide application in analytical chemistry. Much attention has been paid to the following research:

(i) doping UCNPs and DCNPs with new rare-earth (RE) ion couples; and,
(ii) exploration of new host materials;

To date, fluorides and metal oxides, such as $NaYbF_4$, $NaGdF_4$, $NaLuF_4$, $LiLuF_4$, Y_2O_3, Gd_2O_3, Y_2O_2S, CaF_2 and YF_3, have been employed as novel host materials for the doping of Ln^{3+} to achieve the desirable DC or UCL due to their low phonon energies. With recent research on lanthanide co-doping of Yb^{3+}-Er^{3+}, Yb^{3+}-Tm^{3+}, Gd^{3+}, and Nd^{3+}, the typical DC and UC luminescent systems have found more and more applications in analytical chemistry.

2.2. General requirements

With NPs being introduced into analytical chemistry, the range and the limit of detection (LOD) of analytical chemistry have been greatly broadened due to the enhanced permeability and retention (EPR) effect of nanomaterials. The ideal nanocomposites for analytical application should have several basic features, such as relatively small average particle size (sub-50 nm) with low toxicity, good dispersibility and biocompatibility and high chemical stability as well as excellent optical features. Furthermore, to uncover the secrets of the biology via analytical chemistry, it is essential to understand many functions of analytes in living systems by means of luminescent imaging. However, due to the complexity of the microenvironment of living cells and animals, this task remains challenging. UCNP nanosensors absorbing in the NIR region and nanosensors emitting in the NIR region are expected to be superior to conventional fluorescent probes due to the following advantages:

(i) low phototoxicity;
(ii) high chemical stability and excellent photostability;
(iii) enhanced tissue-penetration depth: NIR photons travel through tissue much more efficiently than those in the visible range; and, finally,
(iv) low autofluorescence, narrow absorption bands, and tunable colors with a broad choice and high extinction coefficients.

These prominent properties make UCNP nanosensors ideal imaging candidates that are particularly suitable for detection at deeper sites to afford deep tissue and live animal imaging with high spatial resolution and high extinction coefficients against conventional methods.

2.3. Surface functionalization

Lanthanide-doped nanocomposites for detection and bioimaging should be water-soluble but their applications are often greatly limited due to the hydrophobic surface of nanomaterials, such as surfaces with oleic acid (OA) or oleylamine (OAm). Thus, surface functionalization of lanthanide-doped nanomaterials from