

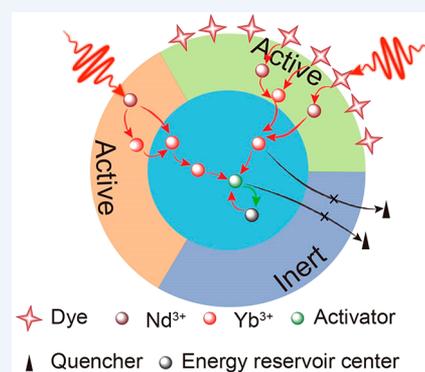
Energy Flux Manipulation in Upconversion Nanosystems

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CONSPECTUS: Lanthanide-doped upconversion nanoparticles (UCNPs) exhibit unique optical characteristics, including a large anti-Stokes shift, a long luminescence lifetime, sharp emission bands, and high photostability. These virtues make UCNPs highly useful in many emerging applications such as biolabeling, security, multicolor displays, and optogenetics. Despite the enticing prospects of UCNPs, their practical utility is greatly hindered by the low efficiency of the conversion from near-infrared (NIR) excitation to visible emission. In a typical nanosystem codoped with sensitizers and activators, upconversion processes occur through NIR light sensitization, energy transfer from sensitizers to activators, sequential energy population at the excited states of the activators, and eventually the release of higher-energy photons. In fact, in the upconversion nanosystem, each step in the energy flux, including NIR energy injection, energy transfer and migration, and energy dissipation, has a decisive effect on the resulting luminescence intensity. Important in-depth studies have been conducted in pursuit of brighter UCNPs. Specifically, lanthanide ions possessing larger absorption cross sections (Nd^{3+}) or organic dye molecules have been chosen as NIR light sensitizers to improve the light harvesting ability of upconversion nanostructures. The doping concentration and spatial distribution of lanthanide ions are strictly managed to mitigate detrimental energy cross-talk processes. The surfaces of UCNPs are passivated with epitaxially grown layers to block surface quenching. Therefore, rational design of energy flux manipulation, through control of excitation energy collection, transmission, and release in a three-dimensional nanospace of UCNPs, is crucial in constructing nanosystems with high upconversion efficiencies.

In this Account, from an energy flux manipulation perspective, we attempt to provide an overview of general and emerging strategies for the design of efficient lanthanide-mediated photon upconversion nanosystems. With the significant progress made over the past several years, we are now able to design a series of upconversion nanoplatforms with efficient NIR light harvesting ability, sufficient energy transmission channels, and low levels of luminescence quenching at the particle's surface. In addition to providing a deep understanding of the underlying mechanism of energy flux, these discoveries will guide the development of upconversion nanosystems with significantly improved performance. The key aspects of this Account of energy flux manipulation in upconversion nanosystems mainly include the management of NIR photon energy injection, the optimization of efficient energy transfer pathways, and the minimization of energy flux leakage. Future challenges and opportunities for the development of efficient upconversion nanosystems are also discussed.



1. INTRODUCTION

Lanthanide luminescence has fascinated researchers for over a century, and the topic exploded in the 1960s with the establishment of efficient separation techniques.¹ Initially, limited by conventional solid-state synthesis techniques, the study of lanthanide luminescence focused mainly on bulk materials.^{2–4} Since the 1990s, benefiting from the rapid development of nanotechnology, lanthanide nanophosphors have received considerable attention, and great strides have been made in the fundamental study and practical applications of lanthanide nanophosphors.^{5–7} In particular, lanthanide-doped upconversion nanoparticles (UCNPs) show intriguing optical properties, such as a large anti-Stokes shift, high photostability, programmable UV–visible emission, and strong resistance to background interference upon NIR light excitation.^{6,8,9} Such optical advantages enable UCNPs to rival conventional nanophosphors in many challenging applications, especially bioapplications such as long-term real-time single-particle tracking, deep-tissue imaging, and the

emerging field of remote deep-brain stimulation.^{5,10–14} However, restricted by the small absorption cross-section of lanthanide activators (such as Er^{3+} , Tm^{3+} , and Ho^{3+} of $\sim 10^{-21}$ cm^2) and an inefficient nonlinear multistep population, lanthanide-doped UCNPs often show extremely low photon conversion efficiency (<1% in absolute quantum yield) and require high NIR photon flux for excitation, which severely impedes their practical application.¹⁵

Over the past decade, the rational design of nanoscopic regimes in upconversion nanosystems for the development of efficient UCNPs has attracted tremendous interest.¹⁶ Related exploration experience has deepened our understanding of the nature of upconversion luminescence at the nanoscale level and provided valuable guidance in the construction of efficient upconversion nanoplatforms.^{17,18} Here, from an energy flux manipulation standpoint, we present an overview of recent

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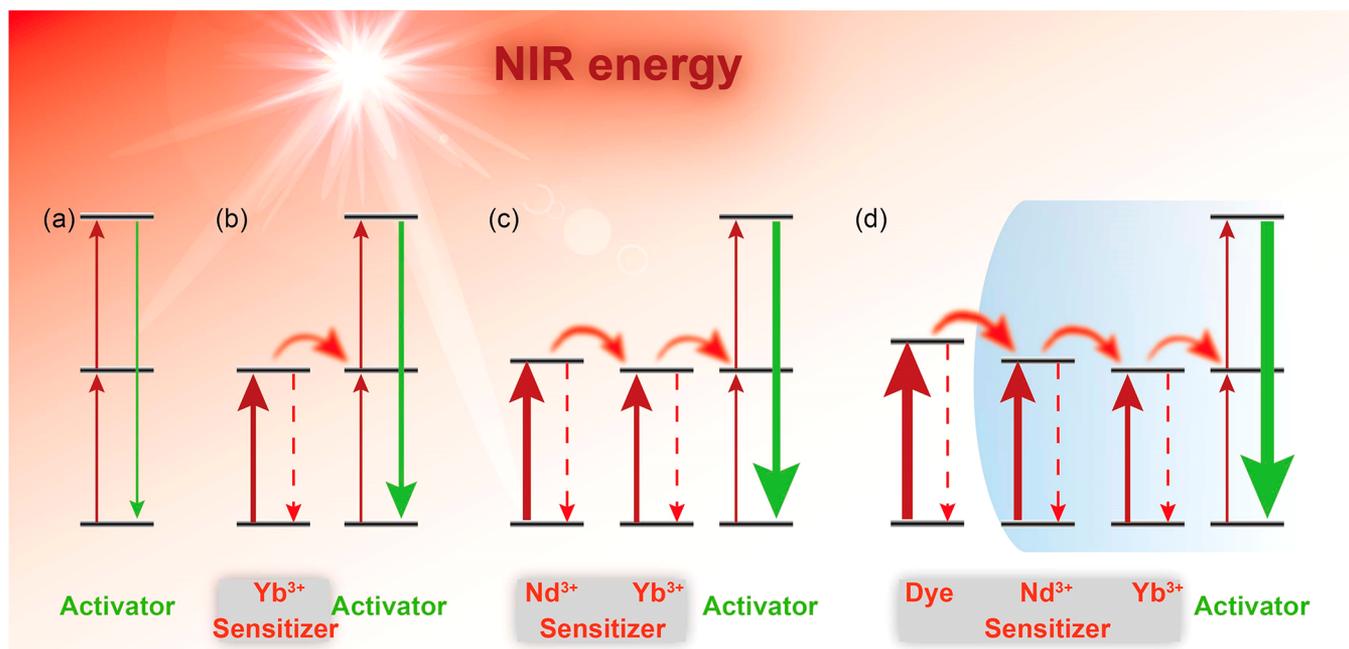


Figure 1. Schematic illustrations showing four major schemes of NIR energy injection through lanthanide-doped upconversion nanosystems: (a) sensitizer free, (b) Yb^{3+} sensitization, (c) cosensitization through Nd^{3+} - Yb^{3+} ion pair, and (d) photon upconversion through organic dye-coupled cosensitization.

advances in the art of upconversion nanosystem design. These advances include control over three pivotal steps of energy flux in the upconversion nanosystem: energy injection, transmission, and leakage.

2. INJECTION OF NIR ENERGY FLUX

Harvesting NIR photon energy is the rudimentary step in photon upconversion in a given nanosystem doped with lanthanide ions. Excellent NIR light absorption ability is a prerequisite for obtaining UCNPs with high brightness. To increase the injection of incident photons into the nanosystem, lanthanide sensitizers with larger absorption cross sections should be carefully selected. We can also employ additional sensitizers, such as organic dye antennas, to harvest more incident photons.

2.1. Lanthanide-Ion Sensitization

Upconversion luminescence originates from multistep $4f-4f$ electronic transitions within lanthanide ions, which are shielded by filled $5s^2$ and $5p^2$ orbitals. As a result, the spectral features of upconversion luminescence are hardly influenced by the coordination environment. According to the parity selection rule, the transition probabilities within the $4f^N$ configuration are extremely low, leading to insufficient NIR light absorption by lanthanide activators such as Er^{3+} , Tm^{3+} , and Ho^{3+} (Figure 1a).

To amplify the injected NIR energy flux, Yb^{3+} ions serving as NIR light sensitizers are usually codoped in a host lattice with lanthanide activators (Figure 1b). Benefiting from the large absorption cross-section of Yb^{3+} (ca. $1.3 \times 10^{-20} \text{ cm}^2$ at 980 nm) and efficient phonon-assisted resonance energy transfer from Yb^{3+} to activators, the resulting upconversion efficiency is significantly enhanced. Despite the marked enhancement, Yb^{3+} -sensitized energy transfer upconversion (ETU) nanosystems can function only in a very narrow NIR region (from 900 to 1000 nm), where excitation photons suffer severe attenuation when passing through biotissues and often cause

overheating damage.^{19,20} Therefore, new lanthanide sensitizers that can function in broader NIR regions are highly desired.

In 2013, several groups independently demonstrated efficient Nd^{3+} -sensitized nanosystems (Figure 1c).²¹⁻²⁴ Benefiting from the intrinsic multiband (740, 800, and 860 nm) sensitization of Nd^{3+} ions, Nd^{3+} -mediated UCNPs hold promise for deep-tissue imaging applications because the attenuation of excitation light caused by tissue absorption is significantly mitigated. More importantly, most of the sensitization bands of Nd^{3+} ions have absorption cross sections of $\sim 10^{-19} \text{ cm}^2$, approximately 1 order of magnitude higher than that of Yb^{3+} at 980 nm. Therefore, with the incorporation of the Nd^{3+} sensitizer, the NIR energy flux injected into the upconversion nanosystem could be greatly boosted to produce much brighter UCNPs. However, Nd^{3+} sensitizers often require the assistance of Yb^{3+} sensitizers for efficient energy transfer, which will inevitably introduce unexpected factors and complicate the design of nanostructures.^{25,26}

2.2. Organic Dye Sensitization

Although lanthanide sensitizers, especially Nd^{3+} ions, can help harvest additional incident photons, their absorption cross sections are still several orders of magnitude smaller than those of commonly used dye molecules. Inspired by a pioneering work published in 2012, dye-sensitized upconversion has drawn substantial research interest.²⁷ In a typical dye-mediated upconversion nanosystem, energy harvested via surface-bounded dye antennas could be transferred to lanthanide sensitizers (Nd^{3+} or Yb^{3+}) doped into UCNPs, providing significantly elevated NIR energy flux injection in the upconversion nanosystem and thus enhanced upconversion luminescence output (Figure 1d).²⁸ Moreover, the broadband sensitization (full width at half-maximum > 50 nm) provided by dye antennas allows efficient photon upconversion upon excitation by an incoherent light source.²⁹ More importantly, in addition to the tailorable sensitization of dye sensitizers through rational design of their molecular structures, the

sensitization region could be further expanded through cosensitization with multiple dyes, whose interlaced sensitization regions are simultaneously used for NIR light harvesting.^{30,31}

Despite the greatly improved energy flux injection in UCNPs, dye-sensitized upconversion nanosystems should be rationally designed to make maximum use of the energy harvested by NIR dye antennas. In addition, the low photostability of dye antennas is a challenge to practical applications of dye-sensitized upconversion nanosystems. Another problem is that such dye-modified nanosystems often make further surface functionalization or bioconjugation difficult.

3. OPTIMIZATION OF ENERGY TRANSFER PATHWAYS

Upon photon injection, the efficient delivery of harvested NIR energy from sensitizers to activators is also crucial for ensuring

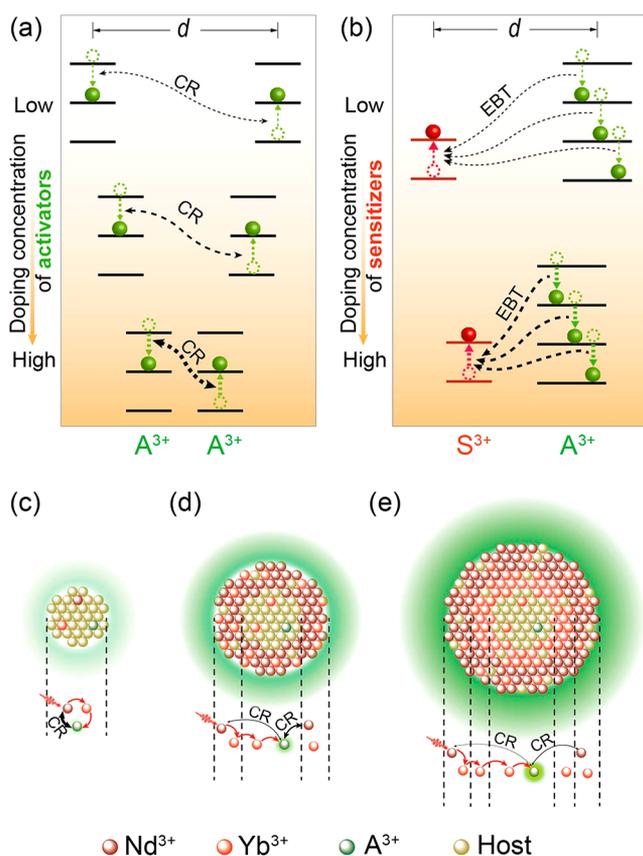


Figure 2. Schematic illustrations of energy cross-talk (a) between activators and (b) between sensitizers and activators in lanthanide-doped upconversion nanosystems. (c–e) Rational design of upconversion nanosystems based on Nd^{3+} sensitization. (c) Nd^{3+} sensitizers codoped with activators within the same spatial region. (d) Core–shell strategy for the spatial isolation of Nd^{3+} sensitizers and activators. (e) Multilayer core–shell design with Yb^{3+} doping in the intermediate layer for the maximum elimination of energy cross-talk.

efficient photon upconversion.³² However, during the process of energy transfer, different types of obstacles, such as unwanted energy cross-talk between the activators themselves or with sensitizers, small spectral overlap between different sensitizers, and sizable energy gaps between sensitizers and specific activators, can lead to inefficient energy delivery from

sensitizers to activators, diminishing the luminous efficiency. Therefore, strategies should be adopted to promote efficient energy transfer pathways to ensure the smooth and efficient delivery of harvested NIR energy to the activators.

3.1. Mitigating Energy Cross-Talk

Ideally, upon accepting energy from the sensitizers, the activators are populated stepwise to their higher excited states without any energy cross-talk with adjacent activators or sensitizers. However, given the copious energy levels of the activators, zero energy cross-talk is impossible, and the energy cross-talk can dominate in heavily doped systems.^{33,34}

The energy cross-talk between activators is usually more severe than that between an activator and a sensitizer. For commonly used activators, especially blue-emitting Tm^{3+} ions, the optimal doping amount is generally less than 2 mol %.²¹ Although a higher doping concentration could enable the acceptance of more energy from sensitizers, the exacerbated cross-relaxation (CR) among Tm^{3+} ions drastically depopulates their higher emitting levels and quenches their upconversion emission (Figure 2a). Upon high power excitation ($>1 \text{ MW/cm}^2$), however, the energy cross-talk would be suppressed to some extent by the efficient excited state population, and the optimized doping amount could reach a much higher level.^{35,36}

Considering that the typical sensitizer Yb^{3+} possesses a single excited state, energy cross-talk between Yb^{3+} ions would not reduce the total excited state population, allowing a high doping concentration to ensure the enhanced injection of NIR energy flux.³⁷ Unfortunately, the energy cross-talk between activators and sensitizers would still occur via energy back-transfer (EBT) upon heavier doping of sensitizer ions (Figure 2b).³⁸

Compared to the Yb^{3+} sensitizer, the energy cross-talk between sensitizers and activators is much more severe in Nd^{3+} -sensitized upconversion nanosystems due to the multi-excited state nature of the Nd^{3+} ion. Our group found that almost 90% of the upconversion fluorescence can be quenched with only 1 mol % Nd^{3+} codoping.¹⁹ However, other researchers did not expect such concentration quenching, and Nd^{3+} sensitizers were usually codoped with activators in the same spatial region of UCNPs according to several early reports (Figure 2c).^{22,23} To overcome the problem of energy cross-talk, core–shell strategies have been developed to spatially separate Nd^{3+} sensitizers and activators. In core–shell upconversion nanosystems, Yb^{3+} sensitizers are generally codoped with Nd^{3+} sensitizers in the same spatial layer to bridge the interfacial energy transfer from Nd^{3+} to the activators (Figure 2d).

Although spatially separated doping can effectively minimize the energy cross-talk between Nd^{3+} sensitizers and activators,¹⁹ interfacial energy cross-talk between them still occurs. To further suppress the interfacial energy cross-talk, as shown in Figure 2e, a sandwich configuration is usually constructed in which a bifunctional Yb^{3+} -doped interlayer blocks the interfacial energy cross-talk but links the energy transfer between the Nd^{3+} sensitizers and the activators.²⁵ However, to achieve a balance of high-efficiency energy transfer with minimal cross-talk, the thickness of this interlayer must be carefully tuned to maximize the resulting upconversion emission. In addition to the energy cross-talk between Nd^{3+} and the activators, we found that the energy cross-talk between the Nd^{3+} sensitizers themselves is quite severe.^{19,39} Although

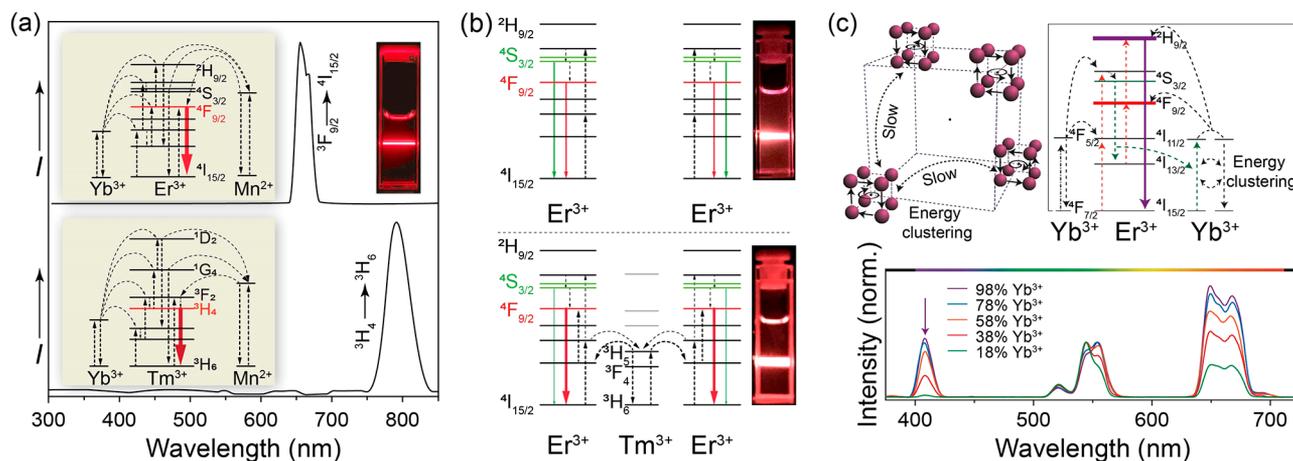


Figure 3. (a) Proposed working mechanism of upconversion nanosystems with Mn^{2+} reservoir centers and upconversion emission spectra of KMnF_3 :Yb/Er (top) and KMnF_3 :Yb/Tm (bottom) nanocrystals. The inset shows a photograph of KMnF_3 :Yb/Er solution upon 980 nm laser excitation. (b) Comparison of upconversion mechanisms of NaErF_4 nanocrystals without and with Tm^{3+} reservoir centers. Insets: Corresponding photographs of the colloidal solutions irradiated with a 980 nm diode laser. (c) Schematic representation showing the topological energy clustering crystal sublattice and the upconversion population processes of UCNPs with Yb^{3+} energy clusters. The bottom shows the emission spectra of KYb_2F_7 :Er/Lu (2/0–80 mol %) nanocrystals. Adapted with permission from ref 42, Copyright 2011 WILEY-VCH Verlag GmbH & Co. KGaA; ref 44, Copyright 2017 WILEY-VCH Verlag GmbH & Co. KGaA; and ref 45, Copyright 2014 Macmillan Publishers Limited, respectively.

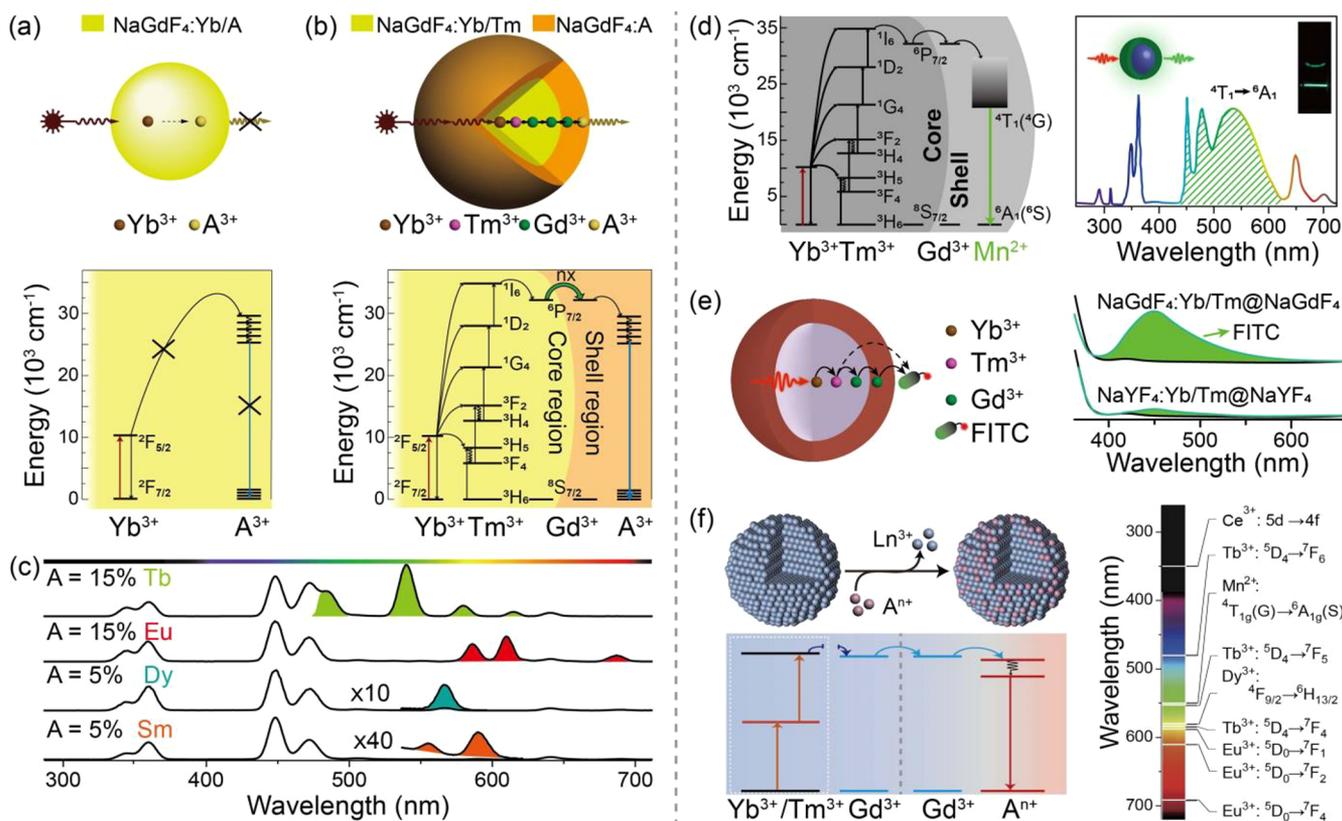


Figure 4. Schematic design and proposed energy transfer mechanisms for (a) energy transfer upconversion and (b) energy migration-mediated upconversion with activators without long-lived intermediary energy states. (c) Emission spectra recorded from energy migrating UCNPs doped with different activators. (d) Proposed energy migration upconversion mechanism (left) of Mn^{2+} -activated core-shell UCNPs and the corresponding upconversion emission profiles (right). (Inset: the corresponding luminescence photo taken from a cyclohexane solution of the nanoparticles.) (e) Illustration of mechanism (left) of energy migration upconversion-coupled energy transfer and upconversion emission spectra (right) for FITC-coupled UCNPs with and without the energy migration configuration. (f) Schematic representation of a typical cation exchange process and proposed energy migration upconversion process for cation exchange-mediated luminescence. Typical luminescent ions used for cation exchange-mediated luminescence tuning and their main emitting transitions are listed at the right column. Adapted with permission from ref 47, Copyright 2011 Macmillan Publishers Limited; ref 49, Copyright 2015 WILEY-VCH Verlag GmbH & Co. KGaA; ref 50, Copyright 2016 American Chemical Society; and ref 51, Copyright 2016 Macmillan Publishers Limited, respectively.

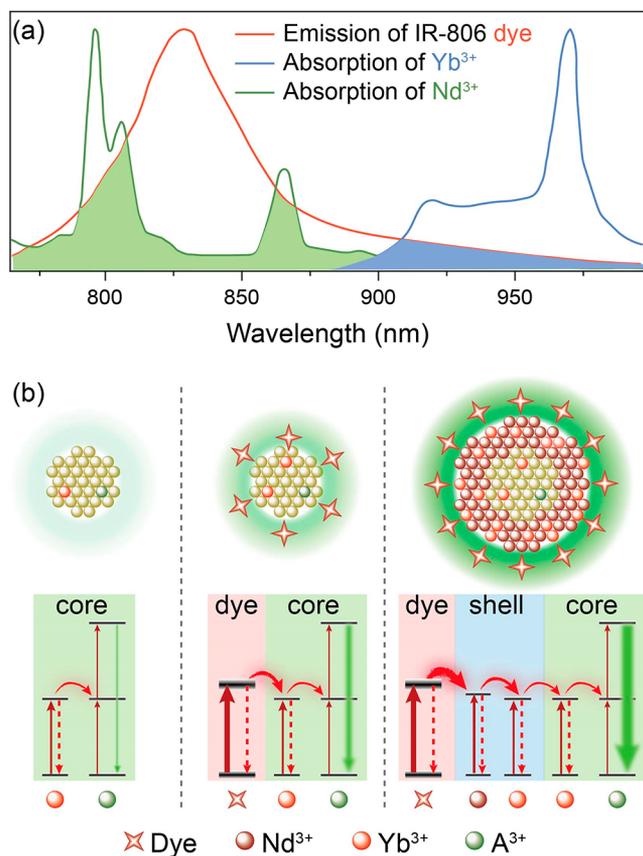


Figure 5. (a) Spectral overlap of the emission spectrum of IR-806 dye antenna with the absorption spectra of Yb^{3+} and Nd^{3+} sensitizers. (b) Schematic illustrations of the working mechanisms of conventional upconversion nanosystems (left) and dye-sensitized upconversion occurring in the core (middle) and the core-shell structure (right).

Yb^{3+} sensitizers could efficiently extract energy from excited Nd^{3+} sensitizers, excessive Nd^{3+} doping would still lead to severe CR and reduce energy output to the Yb^{3+} sensitizers.

3.2. Introduction of Energy Reservoir Centers

The inhibition of energy cross-talk between lanthanide ions can considerably enhance the overall efficiency of upconversion luminescence. However, in some special cases, UCNPs with specific strong emission bands or even a single emission band are highly desired. To satisfy this criterion, energy reservoir centers, such as transition-metal ions and lanthanide ions, are usually introduced into upconversion nanosystems to reserve energy for subsequent transfer to activators.

Among transition-metal ions, Mn^{2+} has been found to be the most efficient energy reservoir center in lanthanide-doped UCNPs.^{40,41} In 2011, using Mn^{2+} as the energy reservoir center, our group developed single-band emitting UCNPs that display intense red or NIR emission (Figure 3a).⁴² In Mn^{2+} -based upconversion nanosystems, instead of emitting high-energy photons, activators at higher energy levels depopulate by transferring their energy to adjacent Mn^{2+} reservoir centers. Subsequently, the energy stored in these energy reservoirs is delivered back to the activators to generate intense single-band upconversion fluorescence at a longer wavelength. Thus, through this exchange-energy transfer process, the use of Mn^{2+} energy reservoir centers could enable the redistribution of the total energy in the upconversion nanosystem and allow the concentrated energy in lower-excited states to be

depopulated in support of intense single-band emission at a longer wavelength.

Similar to Mn^{2+} , lanthanide ions,⁴³ such as Tm^{3+} ,⁴⁴ could also serve as energy reservoirs that can transfer the stored energy back to the activators and shift the corresponding population to lower excited states (Figure 3b). With Tm^{3+} codoping, the red upconversion emission from Er^{3+} -activated UCNPs was further boosted.

Apart from the aforementioned energy reservoir centers, in some particular lattice environments, lanthanide sensitizers are able to function as excitation energy reservoir centers. In 2014, we described a new class of upconversion nanocrystals adopting an orthorhombic crystallographic structure in which the lanthanide sensitizers (Yb^{3+}) and activators are distributed in arrays of tetrad clusters (Figure 3c).⁴⁵ Because of the short distance between lanthanide ions in each cluster, the excitation energy was well confined within the sublattice domain, leading to elevated excitation energy density in the subnanospace. Therefore, the nonlinear upconversion emission, especially the short wavelength emission, could be significantly enhanced.

3.3. Mediating Sublattice Energy Migration

Activators such as Er^{3+} , Ho^{3+} , and Tm^{3+} are commonly used to realize efficient upconversion emission due to the small energy gaps (less than 2000 cm^{-1}) from Yb^{3+} sensitizers to their long-lived intermediary energy states. However, activators such as Tb^{3+} , Eu^{3+} , Dy^{3+} , and Sm^{3+} , which feature extremely large energy transfer gaps ($>7000\text{ cm}^{-1}$) with Yb^{3+} sensitizers, perform quite poorly in conventional ETU (Figure 4a).⁴⁶

In 2011 and 2012, our group solved this problem by controlling gadolinium (Gd) sublattice-mediated energy migration in a well-defined core-shell nanosystem (Figure 4b).^{47,48} The $\text{Yb}^{3+}/\text{Tm}^{3+}$ ion pair doped in the core could harvest NIR pump photons to accumulate energy at higher excited states of Tm^{3+} activators. The accumulated energy could be extracted by Gd^{3+} ions for subsequent random energy hopping through the Gd^{3+} sublattice and finally reach the activators doped in the shell layer. This energy migration strategy enabled the incident NIR energy to overcome the large energy gaps between Yb^{3+} sensitizers and these particular activators, giving rise to efficient upconversion luminescence. Therefore, through this strategy, upconversion emission could be fine-tuned for a wide range of lanthanide activators without long-lived intermediate energy states (Figure 4c). Furthermore, in 2015, based on energy migration upconversion, we successfully obtained UCNPs with strong green upconversion emission from transition-metal ions (Mn^{2+}) at room temperature (Figure 4d).⁴⁹ Later, in 2016, as shown in Figure 4e, through coupling Förster resonance energy transfer (FRET) with energy migration upconversion, we successfully enhanced the acceptor emission for large UCNPs (30 nm) by over 600-fold with surface-anchored molecular acceptors.⁵⁰ This work suggests the potential application of energy migration-coupled energy transfer for ultrasensitive biological sensing. Recently, our group demonstrated a cation exchange strategy for expeditiously accessing large classes of UCNPs in the energy migration upconversion regime (Figure 4f).⁵¹ By combining cation exchange with energy migration, the group of upconversion activators was further expanded, and the luminescence properties of the nanocrystals could be easily tuned while preserving the size and crystal phase of the initial UCNPs.

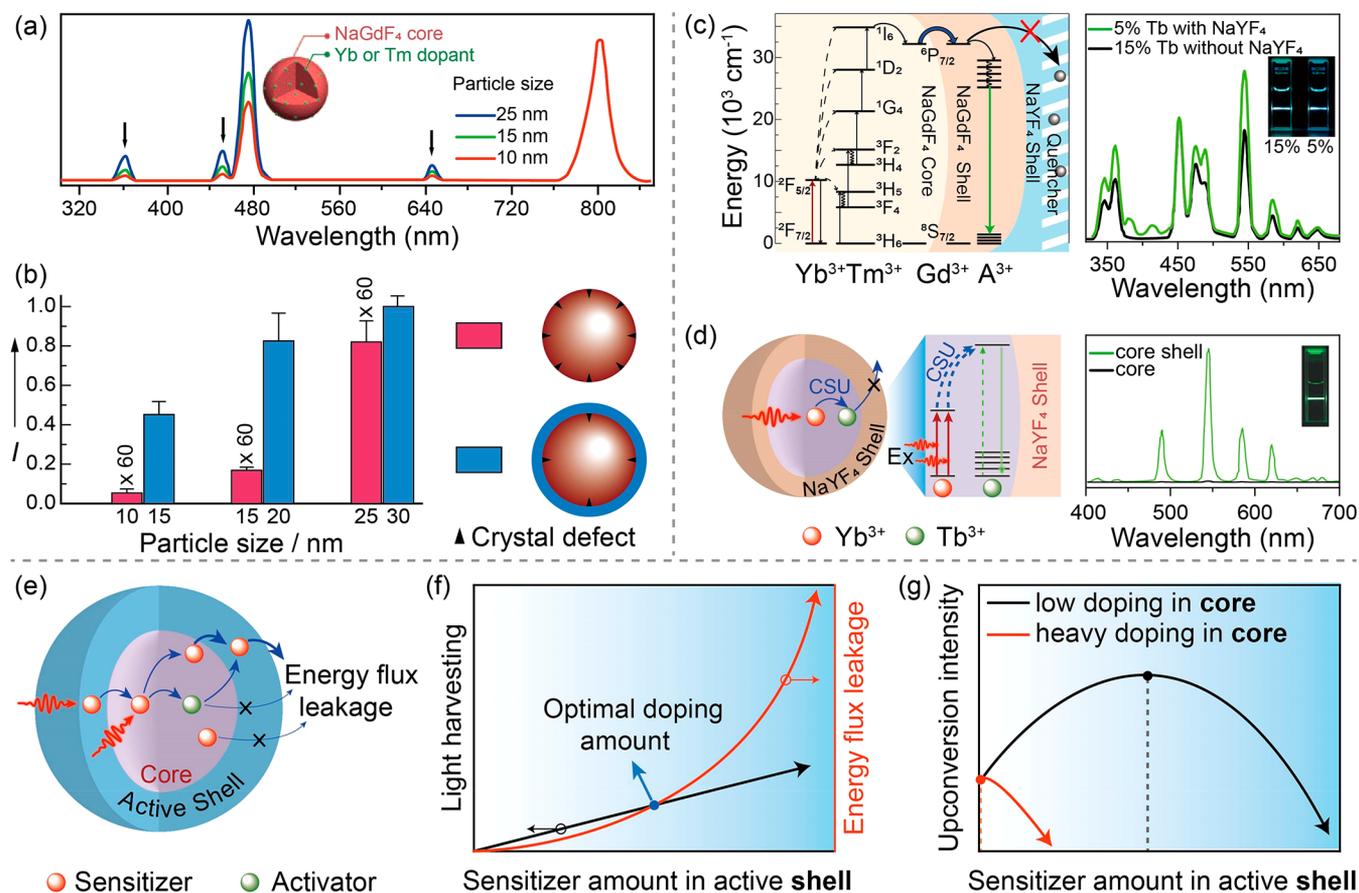


Figure 6. (a) Upconversion emission spectra of NaGdF₄:Yb/Tm UCNPs of various diameters. (b) Upconversion emission intensity comparison of NaGdF₄:Yb/Tm nanoparticles of different sizes, without and with a passivation layer. (c) Left panel: Proposed energy transfer mechanisms in core-shell-shell UCNPs, mediated by energy migration. Right panel: comparative spectroscopic studies of NaGdF₄:Yb/Tm@NaGdF₄:Tb (15%) and NaYF₄-coated NaGdF₄:Yb/Tm@NaGdF₄:Tb (5%) nanoparticles. (d) Energy transfer mechanism of cooperative sensitization upconversion (left) and upconversion emission of UCNPs with and without inert shell passivation. The inserted image shows a photographic image of UCNPs with NaYF₄ layer protection. (e) Energy flux in a core-active shell upconversion nanosystem. (f) Relationship between NIR light harvesting ability and energy flux leakage for sensitizers doped at different concentrations. (g) Effects of the active shell strategy on upconversion luminescence, recorded with low or high levels of dopants in the core region. Adapted with permission from ref 56, Copyright 2010 American Chemical Society; ref 48, Copyright 2012 American Chemical Society; and ref 46, Copyright 2015 WILEY-VCH Verlag GmbH & Co. KGaA, respectively.

3.4. Elevating the Efficiency of Energy Transfer from Dye to Lanthanide Sensitizers

For dye-sensitized photon upconversion nanosystems, the most straightforward strategy to ensure efficient upconversion emission is to elevate the efficiency of energy transfer from dye antennas to lanthanide sensitizers upon NIR irradiation.²⁸ In a number of early reports, conventionally used Yb³⁺ sensitizers were selected to collect the excitation energy from the dye antennas and transfer it to adjacent activators.²⁷ However, the efficiency of energy transfer from dye to Yb³⁺ sensitizers is inefficient owing to the limited spectral overlap between the singlet emission spectrum of the dye and the absorption spectrum of the Yb³⁺ ions (Figure 5a).⁵² Although the spectral overlap can be increased by enhancing the triplet emission of the dye antennas, the stringent requirement of an oxygen-poor environment severely limits the practical feasibility of this approach.⁵³ To solve this problem, the core-shell strategy involving Nd³⁺/Yb³⁺ cosensitization was again applied to the dye-sensitized upconversion nanosystem (Figure 5b). With multiple large-cross-section absorption bands covered by the NIR emission spectra of dye antennas, Nd³⁺ sensitizers could accumulate the energy from dye sensitizers more efficiently.²⁹

Additionally, due to their larger sizes, core-shell UCNPs have a larger surface area to bind more dye antennas. Moreover, with Nd³⁺ sensitizers doped into the shell layer (with a thickness usually less than 3 nm), the average distance between the dye donors and lanthanide acceptors (Nd³⁺) could be significantly shortened, further improving the energy transfer efficiency. Despite the efficient energy transfer from the dye antennas to the Nd³⁺ sensitizers, the upconversion system would also inevitably suffer energy losses during the transmission from Nd³⁺ to Yb³⁺ sensitizers. Therefore, the doping strategy in dye-Nd³⁺-Yb³⁺-trisensitized upconversion nanosystems should be carefully optimized.

4. MINIMIZATION OF ENERGY FLUX LEAKAGE

Surface quenching poses a great threat to nanophosphors: the excited states of phosphors can be depopulated nonradiatively via detrimental interaction with surface quenchers such as crystal defects, surface ligands, and surrounding solvent molecules.^{54,55} Therefore, for lanthanide-doped UCNPs, especially those with sizes of approximately 10 nm, the energy flux leakage through surface quenching should be minimized as much as possible.

In 2010, our group demonstrated direct evidence of surface quenching in UCNPs.⁵⁶ According to a systematic investigation of the emission intensities of core and core–shell UCNPs of various sizes, we found that when lanthanide activators and sensitizers were exposed on the surface, the effect of surface quenching on upconversion luminescence, especially at shorter wavelengths, dominates in small UCNPs (Figure 6a). With the protection of an epitaxially grown inert layer (ca. 2.5 nm in thickness), surface-induced luminescence quenching could be significantly mitigated, especially for small UCNPs (Figure 6b). In addition, we demonstrated that the thin passivation layer would not prevent the practical use of UCNPs in lanthanide resonance energy transfer studies. Two years later, we applied the passivation layer strategy to the energy migration upconversion system (Figure 6c).⁴⁸ We were surprised to find that with the inert layer protection, less than one-third of the original doping level is required to achieve the original luminous intensity. Furthermore, in 2015, our group, for the first time, unexpectedly observed strong green upconversion emission from Yb³⁺/Tb³⁺-codoped UCNPs with surface passivation layer protection (Figure 6d).⁴⁶ Although the luminescence intensity was still much weaker than that of commonly prepared Yb³⁺/A³⁺ (A = Er, Ho, or Tm)-codoped UCNPs, the inert shell effectively minimized the energy flux leakage to ensure efficient cooperative sensitization upconversion (CSU) from Yb³⁺ sensitizers to Tb³⁺ activators.

To further enhance the upconversion emission, a core-active shell strategy was proposed by Fiorenzo et al.,⁵⁷ where instead of using an inert shell, lanthanide sensitizers (Yb³⁺) are doped into the passivation layer to further improve the light harvesting ability (Figure 6e). Although the upconversion emission could be enhanced to some extent through such a core-active shell strategy, the doping concentration of lanthanide sensitizers in the shell layer should be carefully tuned. Despite the enhanced light harvesting ability, the sensitizers in the active shell bridge the energy leakage from the core to the surface quenchers, and this deleterious effect overshadows the enhancement in light harvesting when sensitizer doping in the active shell is excessive (Figure 6f).³⁷ Especially when the core is heavily doped, even slight sensitizer doping into the active layer could result in severe energy leakage, and in this case, a thick inert layer is usually used to suppress the concentration quenching arising from energy flux leakage (Figure 6g).⁵⁸ For the construction of biocompatible UCNPs, the core-active shell strategy should be used with caution since the sensitizer-mediated energy leakage, especially through Yb³⁺ ions, could dominate in aqueous solutions.

5. CONCLUSIONS

Rational manipulation of the energy flux in lanthanide-doped UCNPs through control of NIR energy injection, the energy transfer pathway, and energy leakage allows the construction of efficient upconversion nanosystems with high designability and tunability for a broad range of applications. Despite some empirical findings, further efforts are needed to determine the detailed mechanisms of energy transfer within three-dimensional nanospace.⁵⁹ The key challenges for the future development of UCNPs for practical applications involve enhancing the luminescence efficiency, decoupling the dependency on laser excitation, and exploring NIR dye antennas with high resistance to photobleaching. More importantly, the development of UCNPs with host materials that are highly

responsive to physical or chemical variables would greatly enrich their application prospects.

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Notes

The authors declare no competing financial interest.

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Kezhi Zheng earned his B.S. degree in physics from Harbin Normal University. He received his Ph.D. degree in Physical Electronics from Jilin University. He then joined the faculty at College of Electronic Science and Engineering, Jilin University as an assistant professor, and was promoted to associate professor in 2015. He is currently a postdoctoral fellow in the group of Prof. Xiaogang Liu. His current research interests focus on the design of upconversion materials for emerging applications.

Xiaogang Liu received his B.E. degree in Chemical Engineering from Beijing Technology and Business University, China. He received his M.S. degree in Chemistry from East Carolina University and completed his Ph.D. at Northwestern University. He then carried out postdoctoral work at MIT for two years before joining the National University of Singapore in 2006. Currently, he sits as an Associate Editor for *Nanoscale* and serves on the editorial boards of *Chemistry—An Asian Journal*, *Advanced Optical Materials*, *Journal of Luminescence*, and *Journal of Physical Chemistry Letters*. His research encompasses areas including nanostructured catalysis, optical nanomaterials, optogenetic neuronal stimulation, and X-ray imaging.

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