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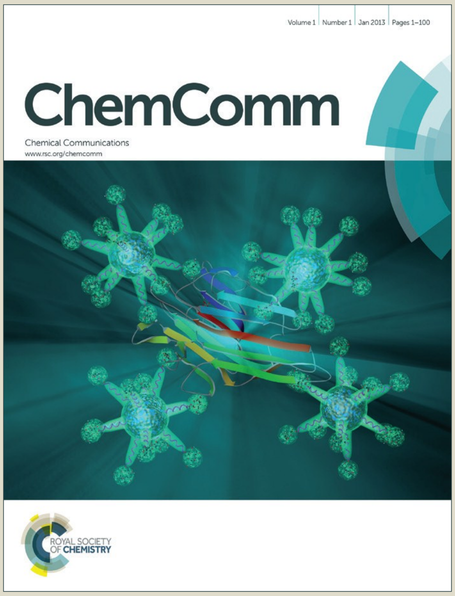

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FEATURE ARTICLE

Using low-energy near infrared light and upconverting nanoparticles to trigger photoreactions within supramolecular assemblies

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This overview highlights how the high-energy ultraviolet or visible light required to drive photochemical reactions can be overcome by integrating the chromophores into supramolecular structures containing upconverting nanoparticles with trivalent lanthanide dopants (such as Tm^{3+} and Er^{3+}). These nanoparticles are particularly interesting systems because they absorb multiple photons of near infrared light and convert them into higher-energy light which is emitted in the ultraviolet and visible regions of the electromagnetic spectrum. The upconverting nanoparticles effectively act as nanoscopic 'light bulbs', and in this way, less damaging near infrared light can be used to trigger photochemical reactions for use in imaging and small molecule release. Several examples of how this phenomenon is being used in photochemistry will be presented with the focus being on self-assembled supramolecular systems, some of which are being used in cells and small animals.

Introduction

Light is one of the most useful stimuli to control chemical processes and is ubiquitous in a wide range of uses, from lithography to biomedicine.[1] This versatility is due in part to the ability of the user to precisely control when and where the light induces photochemical reactions. This multipurpose stimulus is not without its limitations, however, and the fact that organic chromophores typically absorb light in the visible or ultraviolet region of the electromagnetic spectrum is one of the major ones. Both of these types of light are not always practical when applied to sensitive environments such as live cells and tissue because they are prone to cause damage to the surroundings.[2] They also do not penetrate as deeply into heterogeneous materials as do longer wavelengths of light such as those in the near infrared (NIR) region of the spectrum.[3]

The use of upconverting materials helps overcome the need for exposing delicate systems to the damaging UV or high-energy visible light required to initiate photochemistry. Upconversion is the process in which multiple photons are absorbed and combined to produce a photon of higher energy than those absorbed, which is emitted from the molecule or material.[4] Many organic systems undergo this process (the reader is surely aware of two-photon imaging[5] and two-photon polymerization[1b]), however, because they often have low two-photon-absorbing cross sections, high intensity light is needed to ensure both photons are absorbed simultaneously by the molecules or materials.[1b,6]

Using upconverting inorganic materials doped with lanthanide ions overcomes many of the problems associated with organic materials. As early as the 1960s, Auzel and co-workers discovered that by exciting the Yb^{3+} ions doped into a glass matrix with 980 nm light, the emission from the co-doped Er^{3+} ions could be observed.[7] However, it has only been recently that analogous upconverting nanoparticles (UCNPs) having controlled size, structure, morphology and surface ligands have been developed.[8]

In order to achieve the sequential absorption, UCNPs typically contain trivalent ions of the *d*-block and *f*-block elements, which absorb several near-infrared (NIR) photons and emit UV and/or visible photons throughout the electromagnetic spectrum.[9] The absorption-emission process in UCNPs involves more than one photon of NIR light and electronic excitations that occur in real energy levels, which results in the need for significantly lower intensities of light than for conventional two-photon absorbing dyes.[10] Other advantages UCNPs have over conventional fluorophores are their (1) excellent photostability and lack of photobleaching, (2) non-blinking and continuous emission, (3) long fluorescent lifetimes, (4) and sharp emission bands.[9b] It is also notable that the NIR light used as the excitation source lies in the 'therapeutic window' where this light has its maximum depth of penetration in tissue.[11] Also, UCNPs can be conveniently decorated with biocompatible polymers and antibodies to decrease toxicity, prolong circulation time, and increase tissue selectivity. Because of these beneficial optical properties, decorated UCNPs are being developed for a wide range of biomedical end-uses including imaging and photodynamic therapy.[4] Non-biomedical uses where

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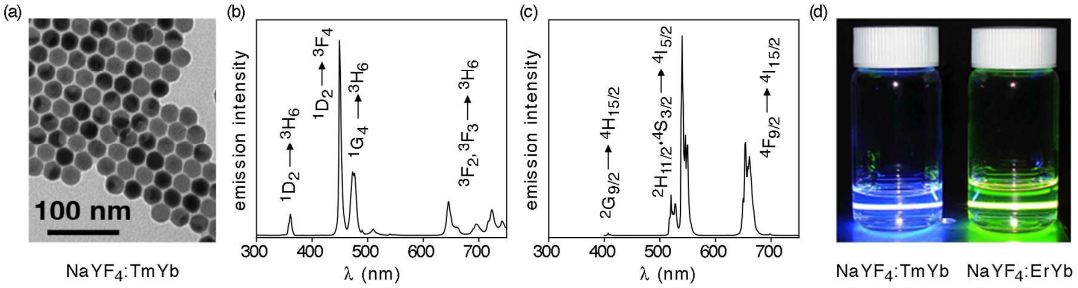


Figure 1. (a) TEM images of Tm^{3+} doped NaYF$_4$ upconverting nanoparticles (NaYF$_4$:TmYb). Emission spectra of CHCl$_3$ dispersions of (b) NaYF$_4$:TmYb and (c) NaYF$_4$:ErYb nanoparticles when exposed to 980 nm light. (d) Photographs of CHCl$_3$ dispersions of NaYF$_4$:TmYb (left) and NaYF$_4$:ErYb nanoparticles (right) when exposed to 980 nm light.

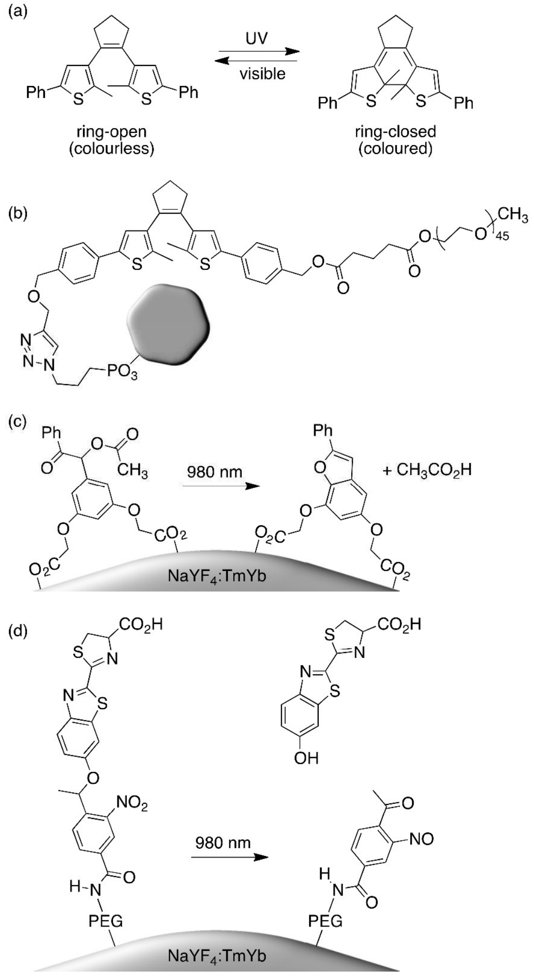
UCNPs can have an impact include molecular sensing,[12] photovoltaic light harvesting,[13] optical bar-coding[14] and in 3D display technologies.[15] The scope of technologies that take advantage of UCNPs is expected to expand.

Some of the most common examples of UCNPs are based on hexagonal NaYF$_4$ nanocrystals doped with Tm^{3+} or Er^{3+} ions, which depending on their composition emit ultraviolet, violet, blue, green, and red light upon absorbing NIR light (typically 980 nm). Two such systems are shown in Figure 1, which illustrates the spectral emission bands and visible colours emitted from the NaYF$_4$ doped with Yb^{3+} and either Tm^{3+} (NaYF$_4$:TmYb – UV and blue light is emitted) or Er^{3+} (NaYF$_4$:ErYb – green and red light is emitted). Many of these UV and visible emission bands overlap with the absorption bands of photoresponsive chromophores including photocages[16] and photoswitches,[17] which provides a means to trigger photochemical processes that require potentially damaging high-energy light with near infrared light.

Several examples of photochemical processes that have been triggered with UCNPs and NIR light are shown in Scheme 1. One of the first examples came from our group where we demonstrated that the UV-light-induced ring-closing reaction of a diarylethene derivative (Scheme 1a) can be driven using the UV light generated by the NaYF$_4$:TmYb nanoparticles, and the reverse visible-light-induced ring-opening reaction can be achieved using visible light generated by the NaYF$_4$:ErYb nanoparticles (the ring-closed isomers are coloured). We first demonstrated this photochemistry in two separate polymer films,[18] followed by a single solution system using UCNPs having both Tm^{3+} and Er^{3+} dopants (within core-shell-shell nanoparticles), and using different intensities of NIR light to control which reaction was being activated.[19] The next generation of systems had the photoswitches anchored to the surface of the UCNPs in order to enhance the energy-transfer process and increase the efficiency of photoswitching (Scheme 1b).

More complex supramolecular systems involve multiple components that all play essential roles in the function of the final assembly. In this short review, we aim to present illustrative examples that show the recent advances in the use of UCNPs and NIR light to trigger photochemical processes in supramolecular assemblies.

The UV light generated when the NaYF$_4$:TmYb nanoparticles are irradiated with NIR light has also been utilized to cleave bonds within photoactive chromophores and liberate initially 'caged' compounds. One of the early examples takes advantage of the dialkoxybenzoin chromophore (Figure 1c).[20] Another uses an *ortho*-nitrobenzyl alcohol derivative (Figure 1d).[21] Both of these chromophores have been used extensively in photorelease applications.



Scheme 1. Some illustrative examples of using UCNPs and NIR light to trigger organic photochemistry.

Upconverting nanoparticles and near infrared light in macroscopic assemblies

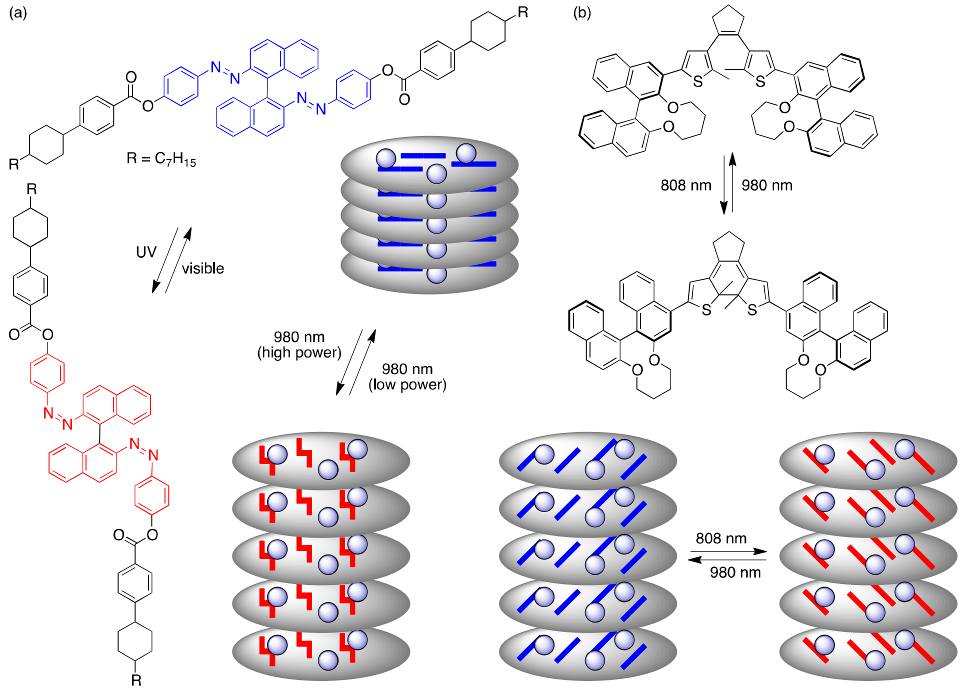
The use of the light generated by UCNPs to trigger photochemical processes of small molecules in macroscopic assemblies is best illustrated by using examples where the components are influential in the structure and function of liquid crystals and hydrogels, although some elegant examples of polymer photo-actuators have been reported.[22]

In liquid crystals

When small photoresponsive molecules such as azobenzene[23] or diarylethene[24] derivatives are doped into host-guest liquid crystal systems, exposing them to specific colours of light changes them into isomeric forms that consequently effect the orientation of the molecules within the liquid crystal. The result is the modulation of the refractive index or chirality of the bulk material. Different colours of light can change them back again. Unfortunately, prolonged exposure to the high-energy light needed to achieve these transformations increases the chance of photodegradation compared to using NIR light.

An elegant example that uses this approach is one where Li and co-workers took advantage of low-energy NIR light to reversibly change the pitch of a photoresponsive, self-assembled liquid crystal containing upconverting β–$NaGdF_4$:TmYb nanoparticles. The net result was the controllable and reversible change in the refractive index of the liquid crystal phase due to the isomerization of the azobenzene mesogens from their *trans*-isomers to their *cis*-isomers (Scheme 2).[25]

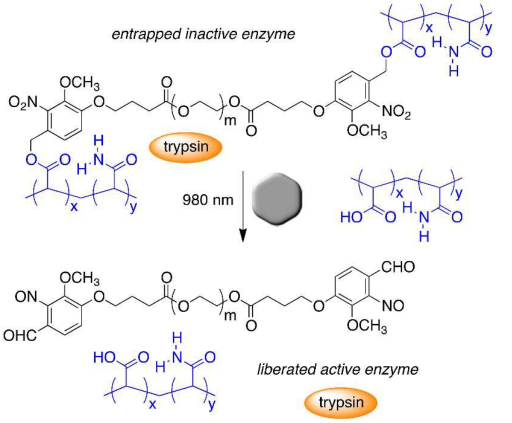
The appeal of this system is that much like the core-shell-shell UCNPs we reported,[19] controlling the intensity of the NIR light allows the user to decide whether UV light or visible light is generated in the upconverting process. One limitation of this self-assembled liquid crystal system is the spontaneous isomerization of the azobenzenes from their *cis*-isomers back to their *trans*-isomers in the dark. The same researchers[26] overcame this problem by using the diarylethene derivatives as the photoresponsive systems because chromophores containing this backbone are typically stable in both isomeric states and spontaneous reversion is not common. In this case, it was the change in chirality and not the pitch of the liquid crystal phase that was reversibly modulated using a combination of diarylethene derivatives, UCNPs co-doped with several ions (Nd^{3+}, Yb^{3+}, Er^{3+} and Tm^{3+}) and different colours of light. When excited by 808 nm light, the energy transfer process from Nd^{3+} to Yb^{3+} to Er^{3+} within the lattice of the nanoparticle produced UV light that triggered ring closing of the diarylethene derivatives. Visible light generated from the UCNPs when they are irradiated with 980 nm light regenerated the ring-open isomers. The differences in the chirality between the ring-opened and ring-closed isomers resulted in right- or left-handed nematic phases, causing different light polarizability of the liquid crystal system.



Scheme 2. (a) Using the UV and visible light generated by β–$NaGdF_4$:TmYb UCNPs when they are exposed to different power densities of NIR light to alter the pitch in photoresponsive azobenzene liquid crystal phases. The grey discs in the cartoons represent the liquid crystal layers, the blue spheres represent the UCNPs, and the blue and red shapes represent the *trans-trans*-isomer and *cis-cis*-isomer of the azobenzene mesogen, respectively. (b) Using the UV and visible light generated by UCNPs co-doped with a chiral dithienylethene, Nd^{3+}, Yb^{3+}, Er^{3+} and Tm^{3+} when they are exposed to 808 nm and 980 nm light to toggle the organic chromophore between its ring-open and ring-closed isomers, which alters the liquid crystal phase between left-handed (left cartoon) and right-handed helixes (right cartoon). The grey discs in the cartoons represent the liquid crystal layers, the blue spheres represent the UCNPs, and the blue and red shapes represent the ring-open and ring-closed isomers of the dithienylethene, respectively.

In hydrogels

Hydrogels consist of a network of polymer chains that are hydrophilic and swell in water to trap water-soluble guest molecules. Several examples of photoresponsive hydrogels have been developed to release large entrapped biomolecules by exposing them to UV light,[27] a technology that has great potential for treating diseases and studying biological events, except for the fact that high energy UV light will potentially harm live cells and shows poor tissue penetration. We combined research efforts with Yue Zhao to demonstrate that trypsin (an enzyme that cleaves peptide bonds in proteins) entrapped along with $NaYF_4$:TmYb UCNPs within a photoresponsive hydrogel shows no activity on its fluorogenic substrate, (CBZ-Arg)2-R110 until the system is exposed to NIR light (Scheme 3).[28] The UV light generated through the upconverting process cleaved the *ortho*-nitrobenzilic linker holding the hydrogel chains together and released the enzyme where its bioactivity was recovered. A similar approach was used in our collaboration to dissociate micelles as will be discussed next.

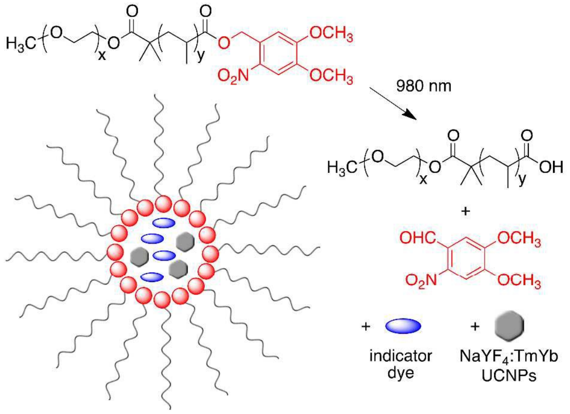


Scheme 3. Using the UV light generated by $NaYF_4$:TmYb UCNPs when they are exposed to NIR light to break apart the polymers in a hydrogel and release trypsin. The grey shape represents the UCNPs trapped within the hydrogel.

Upconverting nanoparticles and near infrared light in self-assembled micelles

When amphiphilic polymers[29] (those having both hydrophobic and hydrophilic sections) self-assemble into spherical micelles in aqueous medium, hydrophobic molecules become entrapped within the core of the spheres. Micelles that are photoresponsive and disassemble when exposed to light have been developed for controlled release of therapeutics.[30] Once again, the use of these systems is hampered by the delivery of the UV light needed to trigger the photochemistry. The marriage of upconverting processes and well-known photochemistry can provide a potential solution.

This solution was demonstrated by our collaborator Yue Zhao using micelles self-assembled from poly(ethylene oxide)-block-poly(4,5-dimethoxy-2-nitro-benzyl methacrylate) that had entrapped an indicator dye and $NaYF_4$:TmYb upconverting nanoparticles within their core (Scheme 4).[31] The UV light generated by the UCNPs when exposed to NIR light was suitable to cleave the hydrophobic *ortho*-nitrobenzilic sections off the amphiphilic polymers resulting in the disassembly of micelles and release of the indicator dye.



Scheme 4. Using the UV light generated by $NaYF_4$:TmYb UCNPs when they are exposed to NIR light to break apart the polymers in a hydrogel and release indicator dye.

Almutari and co-workers improved on our system using more complex micelles, which underwent a series of sequential bond breaking reactions initially triggered by the photocleavage of an *ortho*-nitrobenzyl chromophore, and subsequently released the encapsulated payload.[32] The appeal of their designer micelles lies in the fact that only a minimum amount of NIR light was needed to initiate the micelle decomposition, which will potentially further reduce any photodamage to the surroundings. A more recent example was reported by Dong and co-workers in which they describe how similar systems can target cancer cells and release the therapeutic, doxorubicin using NIR light and UCNPs.[33] Their micelles had entrapped both the UCNPs and doxorubicin, and also possessed lactose components to enable cellular endocytosis through the binding of lactose to the asialoglycoprotein receptors located on the surface of cells. Irradiating the cells with NIR light triggered the decomposition of the micelles and released doxorubicin, which resulted in cellular cytotoxicity.

While these are all elegant demonstrations, the appeal of using smaller nano-assemblies for *in vivo* imaging and photorelease lies in the ease at which they will be circulated in body and endocytosed by cells.[34] The next section will discuss how NIR light and UCNPs can be used to release small molecules entrapped within the shell of the nanoparticle itself.

Upconverting nanoparticles and near infrared light in nanoparticle assemblies

Several examples of upconverting nanoparticles coated with amphiphilic polymer shells or mesoporous silica shells have been developed for NIR-light-induced imaging and release of molecules.[35] The appropriate coating material renders the entire nano-assembly water dispersible and provides host cavities where small guest molecules can be entrapped. These systems have the appeal that a single UCNP host can be loaded with multiple guest molecules and act as a more effective delivery vehicle or imaging agent. By appropriate stimulation, such as irradiation with light, encapsulated guest molecules can be released from the host or undergo photochemical reactions important for imaging applications.

In polymer self-assemblies coated onto UCNPs

The upconverting nanoparticles discussed in this review typically have hydrophobic ligands coating their surface (oleate ligands, for example) because of the way they are synthesized. In order to convert them into versions capable of triggering photochemistry in aqueous environments, ligand exchange with photoresponsive chromophores bearing water-compatible groups must be done. While we have shown this to be effective using polyethylene glycol decorated dithienylethene derivatives for imaging in live organisms,[36] a more effective method is to use self-assembly and amphiphilic polymers. Two approaches to make these supramolecular systems are shown schematically in Figure 2.

In the first approach (Figure 2a), an amphiphilic polymer spontaneously self-assembles around oleate coated UCNPs with its hydrophobic alkyl or aryl groups interdigitating into the hydrophobic shell around the nanoparticle. The result is the water-compatible polyethylene glycol chains of the polymer projecting away from the UCNP and into the bulk aqueous environment. When hydrophobic, photoresponsive chromophores are present, they are trapped inside the inner layer due to the hydrophobic effect. The self-assembled systems are remarkably stable and leaching of the chromophore does not readily occur.

This approach has many advantages. It is relatively ‘universal’ and the choice of hydrophobic molecule that can be trapped is almost limitless. Because it takes advantage of spontaneous self-assembly, it can be thought of as a ‘plug-and-play’ method to make complex water soluble nanosystems. Most importantly, even though the whole nano-assembly is water soluble, the local environment around the hydrophobic chromophores resembles those in organic solvents, which provides a better setting for the photochemistry to take place. It is well known that the presence of water molecules limits or completely terminates many photochemical events.[37] Water can also play a role in the photochemical pathway, and produce unexpected and unwanted products.[38] The amphiphilic polymer approach illustrated in Figure 2 minimizes these detrimental effects.

Several examples of hydrophobic, photoresponsive chromophores we have encapsulated in self-assembling supramolecular structures are shown below. In our original example that uses this approach, photoresponsive dithienylethenes (**DTE-1** and **DTE-2**) and a dibenzofuran analogue (**DBFE**) were used to demonstrate that the photochemical ring-closing and ring-opening reactions (see Scheme 1a for analogous reactions) are the same whether the chromophores are trapped in the nano-assembly or dissolved in organic solvents.[39] We also encapsulated a ‘turn-on’ fluorescent dibenzothiophene version (**DBTE**) that toggles between a ‘dark’ ring-open state and a ‘bright’ ring-closed state for multi-colour imaging applications in organisms.[40] The self-assembly procedure was also used to trap porphyrin chromophores (**TPP**) and show effective energy-transfer between the UCNPs and macrocycles when exposed to NIR light.[41]

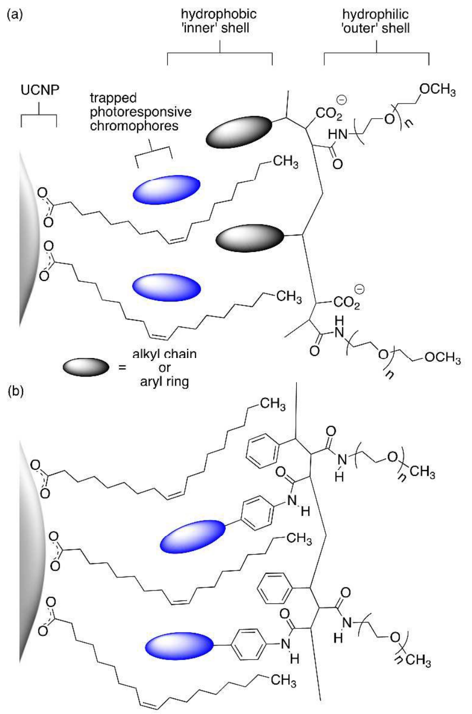
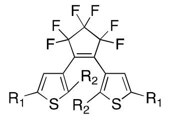
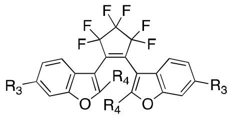


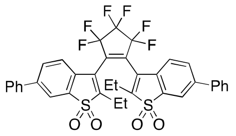
Figure 2. Illustrations showing the general structures of water-dispersible, self-assembled supramolecular nanosystems made from oleate-decorated UCNPs wrapped with an amphiphilic polymer. (a) The hydrophobic inner layer close to the nanoparticle traps guest molecules through the hydrophobic effect and shields them from the bulk water. (b) The chromophores can also be covalently attached to the backbone of the amphiphilic polymer where they can interdigitate into the oleate coating.



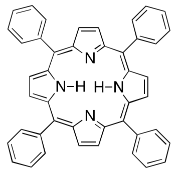
DTE–1: R_1 = phenyl, R_2 = methyl
DTE–2: R_1 & R_2 = thiophene



DBFE: R_3 = PEG, R_4 = phenyl

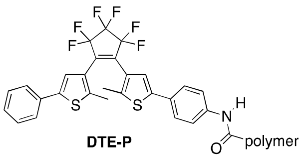


DBTE

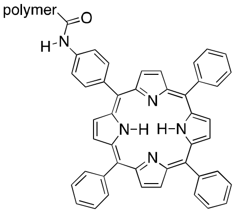


TPP

A major drawback of this procedure is the low number of chromophores encapsulated into the nano-assembly. In our cases, less than 100 chromophores are captured by each supramolecular system.[39,41] This limitation can be easily overcome by attaching the chromphores to the amphiphilic polymer backbone prior to self-assembly. The result is a water soluble nano-assembly where the hydrophobic chromophores interdigitate into the oleate ligands on the UCNP’s surface and the polyethylene glycol chains remain projecting into the aqueous solvent as shown in Figure 2b. The method still relies on spontaneous self-assembly and any chromophore bearing an amine can be easily incorporated. For example, we have increased the loading of dithienylethene chromophores three times higher using polymer **DTE-P** (shown below) compared to the original system.[42] The photochemistry of the diarylethenes in the new nano-assemblies was retained. The merit and versatility of the modified approach was strengthened by repeating the procedure using amino-porphyrin derivatives.[41] Again, the number of macrocycles increased (seven times, in this case) using the polymer **TPP-P**, which resulted in an enhancement in the energy-transfer process.



DTE-P



TPP-P

A similar approach was used by Zheng, Ford and co-workers to trap manganese coordination compounds using different amphiphilic polymers from those we used (Figure 3).[43] The blue light generated when UCNPs doped with Tm^{3+} ions were irradiated with NIR light resulted in the breakdown of the coordination compound and release of carbon monoxide (CO) into the bulk environment. Nitric oxide (NO) ligands were displaced from iron complexes by taking advantage of the green light emitted from UCNPs doped with Er^{3+},[44] however in this example the coordination compound was not trapped in a hydrophobic polymer layer but in mesoporous silica, which is the subject of the next section in this article.

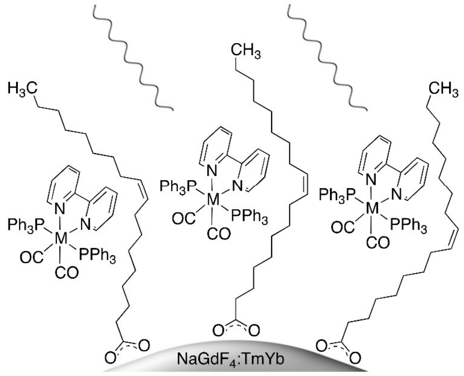
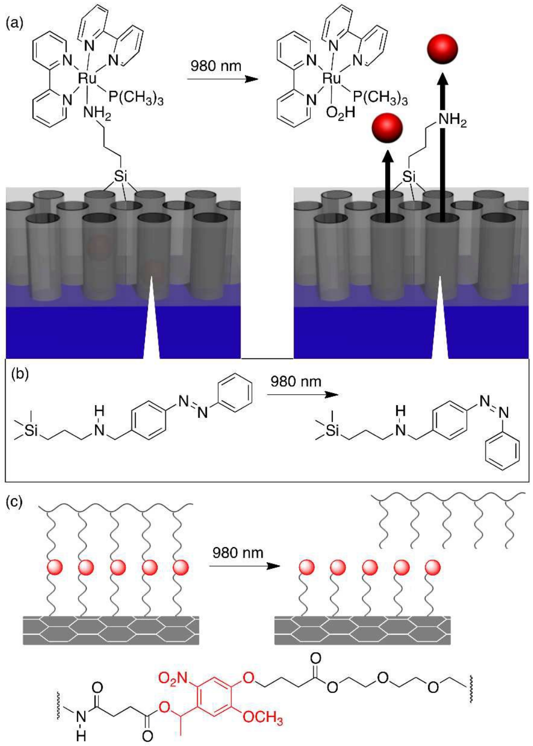


Figure 3. Carbon monoxide is produced when trapped manganese coordination compounds breakdown due to the blue light generated when the UCNPs are irradiated with NIR light. The wavy lines in the figure represent the hydrophobic chains in the amphiphilic phospholipid-functionalized poly(ethylene glycol) used.

In porous silica host shells around UCNPs

Through solution chemistry a shell of mesoporous silica can be deposited around upconverting nanoparticles. These shells provide channels that act as host sites for entrapment of guest molecules. Because the size of the channels and cavities within the mesoporous silica coating is tunable,[45] they can be designed to act as hosts for a wide range of guests including small molecules such as the cancer therapeutic, doxorubincin,[46] and large DNA macromolecules.[47] Three approaches that have been successfully used to release these and other biologically important payloads are shown in Scheme 6.



Scheme 6. Three methods to harness NIR light and UCNPs to release guest molecules from within the channels in mesoporous silica shells 'on-command'. (a) Photoresponsive "caps" are cleaved from the entrance of the channels, (b) isomerization of azobenzene chromophores acts as "mixers" within the channels, and (c) large sections of wrapped polymers are cleaved of the surface of the nano-systems.

The first method involves a photoresponsive coordination compound installed near the openings of the channels in the mesoporous silica shell around the UCNPs (Scheme 6a).[46a] These bulky complexes effectively act as channel caps and prevent leaking of the entrapped drug (in this case doxorubincin). The UV light generated when the $NaYF_4$:TmYb nanoparticles are irradiated with NIR light is used to break off the ruthenium complex from the amine ligand, which clears the path for the release of the entrapped anticancer drug. In this case the actual release is 'passive' by nature and diffusion controlled after the channel caps are removed. Macromolecules such as caged DNA and RNA can also be loaded into the channels of the mesoporous silica shell surrouding the UCNPs, and they can be activated using the UV photons generated by the upconversion process to uncage them.[47]

The second approach uses an 'active' release mechanism, according to the authors.[48] They attached photoresponsive azobenzene chromophores onto the internal walls of the channels in the mesoporous silica shell, which prevent leaking of entrapped doxorubicin by blocking the path through the channels. When the $NaYF_4$:TmYb nanoparticles are exposed to NIR light, the UV light generated by the nanoparticles triggers an isomerization reaction (Scheme 6b) of the chromophore and produces the *cis*-isomer. The authors suggest that this photoreaction results in the chromophores acting as molecular “stirrers” that actively force the doxorubicin out of the channels. Their elegant follow-up paper describes how they can use the energy transfer quenching of the nanoparticle’s fluorescence by the entrapped doxorubicin in combination with magnetic resonance imaging (MRI) as a multimodal tracking tool for the release of the drug.[49] A recent study suggested that a Janus-type mesoporous silica upconverting nanoparticle is capable of releasing molecular payloads in both a ‘passive’ and ‘active’ manner by heating or by irradiation with NIR light.[50] However, others pointed out that the all the ‘active’ release examples are likely due to the heating of the medium surrounding the nano-assembly instead of the rotational motion of the azobenzene chromophores on the channel walls.[51] In either case, the photorelease using NIR light and UCNPs was successfully achieved.

In the third and last example that will be discussed in this section, a polymer is synthesized from alkene monomers (using metathesis chemistry) that were attached to the surface of the mesoporous shell surrounding the upconverting nanoparticles (Scheme 6c). The resulting polymer seals the openings of the channels and prevents leaking of entrapped molecules. The monomers contain photoresponsive *ortho*-nitrobenzyl linkers, which can be cleaved using the UV light generated when $NaYF_4$:TmYb UCNPs are irradiated with NIR light. The net result is that large fragments of the encapsulating polymer “peel off” the nano-assumbly and allow the guest molecules to escape. This approach has been utilized to release doxorubicin[52] or platinum complexes[53] for anti-cancer applications.

Challenges and their solutions when using NIR triggered photochemistry and UCNPs

Despite the appeal of using upconverting nanoparticles and low-energy near infrared light to trigger photoreactions that typically require higher energy UV or visible light, some challenges should be addressed. Two of the major ones are discussed in the following sections.

Photodamage and upconversion efficiency enhancement

One problem is the low efficiency of the upconverting process. In the UCNPs, the transient states that result in the upconverted emission lie on the *4f* orbital energy levels of the lanthanide ions. However, these *4f* orbitals are electronically shielded by the outer-lying *6s* and *6p* orbitals, which results in the non-participation in bonding of the *4f* orbitals and their maintaining atomic character. Also, the electric dipole transitions between the *f* orbitals that generate the necessary intermediate excited states remain parity-forbidden.[54] These are the reasons that the intensity of the excitation laser must exceed a certain threshold to effectively produce the upconverted light, especially UV light, which is the result of a multi-photon upconvertion process.[55] The consequence is the potential damage to the surrounding medium by the laser light, an issue particularly relevant if the end-use involves *in vivo* therapy or diagnosis where high-intensity NIR light produces heat and can damage biological matter.[56] According to the “American National Standard for Safe Use of Lasers”, the maximum permissible exposure for skin is on the order of several hundred $mWcm^{-2}$.[57] Due to the intrinsic natural of *4f* orbitals responsible for upconversion, and given the fact that biological tissues significantly absorb and scatter NIR light,[55] low-intensity of NIR light may not be able to activate UCNPs for upconversion when the particles are buried within tissue. This issue is being addressed by researchers who have found several approaches to enhance UCNP upconversion efficiencies including lattice manipulation, surface passivation and surface plasmon enhancement.

Dionne and co-workers reported a two-fold enhancement in the upconversion efficiency of Er^{3+} doped UCNPs by applying appropriate pressure onto the crystal lattice.[58] Their work revealed the intricate relationship between the upconversion efficiency and the distance separating the ions within the crystal lattice. Another effect was shown by Liu and co-workers who describe how the direct contact of solvent molecules with the lanthanide ions significantly quenches the upconverted emission intensity.[59] This problem can be minimized by adding a coating layer around the UCNP to passivate its surface and improve the upconversion efficiency, and many of the examples if systems described in this review take advantage of this approach.

In the examples where plasmon enhanced upconversion is used,[60] a metal such as gold or silver is coated onto the UCNP (the UCNPs can also be placed near an array of gold pillar-like plasmonic structures).[61] The metal will effect the surrounding electromagnetic field, help concentrate the incident field at the UCNPs and enhance radiative decay of the upconversion process. This effect depends on the type of metal, the shell thickness and whether the metal is coated onto the UCNP or is in close proximity to it, and using it has increased the upconversion efficiency from a small amount to more than 100 fold.[60]

Unwanted photochemical processes

Another issue with upconversion processes that should not be downplayed is the presence of unwanted photochemical processes. Just because NIR light can be used to convert NIR light into UV and visible light to trigger photochemical reactions, does not mean that the direct, one-photon absorption reactions are absent. This is why patients who undergo photodynamic therapy (a commercialized method to treat some cancers) can encounter skin sensitivity to ambient light after receiving the therapy due to the photo-toxicity of the photo-sensitizers.[62] Although we[41] and others[63] have demonstrated the use of NIR light and UCNPs to successfully activate photo-sensitizers for potential photodynamic therapy, the absorption of the UV and visible light by the chromophores remains. Our answer to this problem was to utilize self-assembly and wrap a UV-absorbing amphiliphic polymer around $NaYF_4$:TmYb UCNPs decorated with photoresponsive diethienylethene ligands following the approach described in Figure 2 of this review. We tethered UV-blocking molecules to the ends of the hydrophilic chains of the amphiphilic polymer to act as “sunscreen” and prevent the external UV light from reaching the inner layers of the self-assembled nanostructure where the photoresponsive chromophores lie (Figure 4).

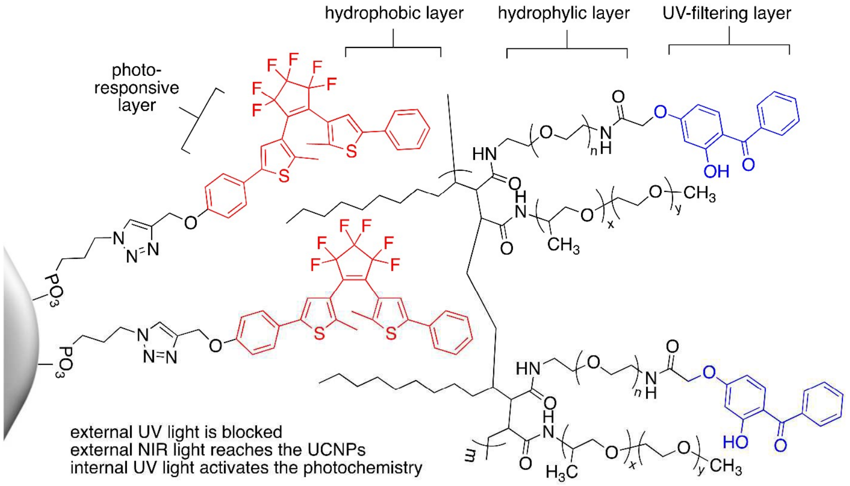


Figure 4. A nano-assembly that has UV-blocking chromophores prevents UV light from activating the one-photon photochemistry of dithienylethenes near the surface of the NaYF$_4$:TmYb UCNPs. NIR light can reach the UCNPs where it is converted to UV light in a multi-photon to activate the dithienylethenes from inside the nano-assembly.

When our nano-assembly was exposed to ambient sunlight, the UV-blocking chromopores on the periphery prevent the UV component in the light reaching the dithienylethene molecules and little photochemistry occurs. But when the nano-assemblies are irradiated with NIR light, these photons penetrate through all the layers, reach the UCNP core, and generate UV light that is emitted out to the inner layer containing the organic chromophores. A large extent of UV-triggered ring-closing of the dithienylethene molecules was observed. This approach has another distinction. It also prevents any UV light generated from the UCNPs leaking out into the surrounding environment and minimizes damage caused by the upconverting process itself.

Conclusions and perspectives

While there was a large gap in the time between when Auzel and co-workers first discovered the lanthanide-based upconversion phenomenon in bulk materials to the development of designer upconverting nanoparticles, this phenomenon has become one of the most promising current ways to carry out photochemistry while avoiding direct exposure of sensitive environments to damaging UV and visible light. Since the demonstration of our first example,[20] numerous elegant and complex systems have been created to control optical imaging in living cells and small animals, bio- and chemosensors, and small molecule delivery.[64]

As highlighted in this article, the use of hybrid, self-assembled, supramolecular structures offers more advanced properties and functions. We anticipate that similar systems will be integrated into dynamic materials such as photoresponsive self-healing polymer[65] and dry adhesives,[66] and controlling the structures of extracellular matrices.[67] We have just broken the surface in the range of technologies based on upconverting nanoparticles.

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