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Manipulating pH using near-infrared light assisted by upconverting nanoparticles

Upconverting nanoparticles convert near-infrared (NIR) light to UV or visible light, which can activate photoresponsive Ru complexes. Because NIR light can penetrate deeply into tissue, the NIR photoactivation approach shows deep-tissue biomedical applications.

As featured in:
See Si Wu et al., Chem. Commun., 2016, 52, 13959.
Manipulating pH using near-infrared light assisted by upconverting nanoparticles†

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Near-infrared light can be used to manipulate the pH of aqueous solutions by using upconverting nanoparticle-assisted photocleavage of a ruthenium complex photobase. Upconverting nanoparticles and the photobase were also introduced into a pH-responsive hydrogel, in which near-infrared irradiation induced swelling of the hydrogel.

pH is an important parameter in many chemical, physical and biological processes.1,2 Photoacids/bases, which can decrease/increase pH upon light irradiation, enable remote control of pH with high spatiotemporal resolution.3 Light-induced pH change can further control deformation of hydrogels,4 conductivity,5 polymerization,6 and host–guest interactions.7 pH manipulation has been proposed as a powerful technique to achieve control over relevant paths related to several diseases such as cancer, cardiovascular disease, Alzheimer’s disease, etc.8 However, most photoacids/bases are sensitive to only UV light which can damage biological systems.9–11 Recently, Liao et al. reported visible-light-responsive photoacids.4,8,12,13 Further, one of their photoacids can be used in PBS buffer,8 which is desirable for biomedical applications. Nevertheless, visible light is still not able to deeply penetrate into tissue.14 Compared to UV and visible light, near-infrared (NIR) light is better suited for biomedical applications because NIR light causes less photodamage to biological systems and can penetrate much deeper into tissue.15 Therefore, developing NIR light-induced pH manipulation represents significant progress for the biomedical field.

A promising approach to NIR light-induced pH manipulation is based on photochemistry assisted by lanthanide-doped upconverting nanoparticles (UCNPs). UCNPs can convert NIR light into UV/visible light.16,17 The upconverted UV/visible light can then induce photo-reactions of conventional UV/visible-light-sensitive compounds. This process is called UCNP-assisted photochemistry.18–21 UCNP-assisted photoisomerization,22,23 photocleavage,24–26 photopolymerization,27,28 and photocoupling reaction29 have already been studied in the context of various applications.30–37 Additionally, a new type of UCNP-assisted photochemical process, “UCNP-assisted photoinduced protonation/deprotonation”, was proposed in the outlook of a recent review.33 These previous works inspired us to use NIR light to control pH assisted by UCNPs.

Here, we experimentally demonstrate that the combination of UCNPs and a photobase enables the control of pH by NIR light (Fig. 1a). We refer to this new combination as a photon upconversion pH manipulation. The complex \([\text{Ru(bpy)}_2(\text{PPh}_3)(\text{BuNH}_2)]^{2+}\) was used as the photobase, which can be cleaved by the blue light emitted from the UCNPs. The butylamine released from the photobase can then protonate poly(acrylic acid) to induce swelling of the hydrogel.

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† Electronic supplementary information (ESI) available. See DOI: 10.1039/c6cc05287h

\[\text{Ru(bpy)}_2(\text{PPh}_3)(\text{BuNH}_2)\]

(a)

(b)

(c)

Fig. 1 Schematic illustration of photon upconversion pH manipulation and NIR light-induced swelling of the nanocomposite hydrogel. (a) The blue emission from UCNPs triggers the cleavage of the Ru photobase (Ru-A) and induces pH change. (b) The butylamine released from Ru-A results in the deprotonation of poly(acrylic acid) (PAA). (c) NIR light-induced swelling of the nanocomposite hydrogel, which was prepared by introducing UCNPs and Ru-A into crosslinked PAA. All the symbols are shown in (a) and (b).
UCNP emission. Further, we have recently demonstrated because of spectral overlap of Ru complex absorption and UCNP emission. Further, we have recently demonstrated the true sectioning power of the upconversion excitation, allowing precise z-axis manipulation of the downstream effects of NIR light irradiation. On these bases, Ru-A was combined with UCNP emission, which would convert NIR light into blue light to enable the release of n-butylamine from Ru-A (Fig. 1a). The released butylamine would then increase the pH of an aqueous solution. When NIR light-induced release of n-butylamine occurs in the presence of poly(acrylic acid) (PAA), PAA can become more hydrophilic via deprotonation and thus swell due to electrostatic repulsion (Fig. 1b). Thus, to demonstrate the potential application of NIR light-manipulated pH, we introduced UCNP emissions and Ru-A into a PAA hydrogel (Fig. 1c).

NaYF₄:Yb,Tm@NaYF₄ UCNP (core = NaYF₄: 0.5 mol% Tm³⁺; shell = NaYF₄) with a diameter of 50 nm were synthesized as the upconverters (Fig. 2a). These UCNP emissions were induced by the photon upconversion process. When irradiating a dispersion of UCNP emissions and Ru-A with NIR light, the absorption band of Ru-A in the blue light region overlapped with the blue emission of the UCNP emissions (Fig. 2a). To demonstrate absorption of upconverted blue light by Ru-A, we compared the upconversion luminescence spectra of UCNP emissions in the presence and absence of Ru-A. The intensity of upconversion luminescence of UCNP emissions at 440 nm and 470 nm decreased significantly in the presence of Ru-A (Fig. 2b). Additionally, Ru-A with higher concentration absorbed more upconverted blue light and resulted in lower emission intensity. In contrast, the emission at 800 nm, a spectral region where Ru-A has no absorption, still remained (Fig. 2b). This result proved efficient absorption of the upconverted blue light by Ru-A. When irradiating a dispersion of UCNP emissions and Ru-A with NIR light, the absorption band of Ru-A decreased and red shifted (Fig. 2c). This spectral change was identical to that observed for Ru-A which was directly photocleaved using blue light (Fig. S1, ESIF). Thus, Ru-A was photocleaved through NIR light irradiation. The exposure of Ru-A to NIR light in the absence of UCNP emissions did not change the absorption spectrum (Fig. S2, ESIF), proving that the photocleavage of Ru-A was induced by the photon upconversion process.

To demonstrate a NIR light-induced pH increase, an aqueous dispersion of UCNP emissions was prepared by ultrasonic treatment of UCNP emissions in water (Fig. S3 and Video 1, ESIF). Afterwards, Ru-A was introduced into the UCNP dispersion. The UCNP/Ru-A dispersion was placed into an ice bath and irradiated with NIR light. The NIR light-induced pH change of the UCNP/Ru-A dispersion was measured (Fig. 3a). The initial pH of the UCNP/Ru-A dispersion was 5.2, which did not change in the dark. However, exposure to NIR light (5.5 W cm⁻²) changed the pH from 5.23 to 6.80 (Fig. 3a). NIR light irradiation can induce the release of n-butylamine from Ru-A (Fig. 2). The coordinated n-butylamine in Ru-A does not act as a base because its electron pair is strongly coordinated to Ru³⁺. However, the released free n-butylamine is a relatively strong base with pKₐ 10.77. Thus, the NIR light-induced pH change was attributed to the released n-butylamine from Ru-A. As a control experiment, exposure of Ru-A in the absence of UCNP emissions to NIR light in an ice bath showed no pH change (Fig. S4, ESIF), which further confirmed that the pH change was due to the photon upconversion process. In addition, NIR light irradiation also changed the color of the dispersion because the absorption spectra of Ru-A and the Ru-aqua photoproduction (Ru–H₂O, Fig. 1a) are different. Moreover, the ratio of UCNP emissions to Ru-A was tuned to investigate its influence on the pH change of the solution. The concentration of UCNP emissions was fixed. As the concentration of Ru-A increased, the pH change was larger (Fig. 3b). The larger pH change was because more
n-butylamine could be released from Ru-A with a higher concentration. Thus, the ratio of UCNPs to Ru-A can be used to adjust the range of pH change.

Subsequently, the NIR light-manipulated pH increase was used to control deformation of a pH-sensitive hydrogel. A nanocomposite hydrogel was prepared by cross-linking PAA in the presence of Ru-A and UCNPs. Upconverted luminescence was observed from the nanocomposite hydrogel upon irradiation with NIR light (Fig. 4a), which further confirmed that UCNPs were incorporated inside the hydrogel. A nanocomposite hydrogel with a volume of 0.28 cm$^3$ was immersed in an aqueous solution (pH 3.5) and irradiated with NIR light for 15 min in an ice bath. NIR light irradiation was conducted in an ice bath because an ice bath can prevent overheating problems of NIR light irradiation and heat-induced side effects (Fig. S5 and S6, ESI†). After irradiation, the volume of the hydrogel increased to 0.37 cm$^3$, which was 32% greater than the hydrogel before irradiation (Fig. 4b, left). In addition, the color of the hydrogel changed from orange to brown upon NIR light irradiation, which is identical to the color change observed in the dispersion of UCNPs and Ru-A upon NIR light irradiation (Fig. 3a). Thus, the swelling was attributed to the deprotonation of PAA by the n-butylamine released from Ru-A.

In a control experiment, the hydrogel without irradiation did not change in size or color (Fig. 4b, right). In another two control experiments, hydrogels with only Ru-A or UCNPs were prepared. The hydrogel with Ru-A and without UCNPs did not show any color or volume change upon NIR light irradiation in an ice bath (Fig. S7, ESI†). The hydrogel incorporating only UCNPs was also unresponsive to NIR light irradiation (Fig. S8, ESI†). These results further confirmed that the swelling of the hydrogel was due to the released n-butylamine upon NIR light irradiation.

In conclusion, we demonstrated that NIR light could increase the pH with the assistance of UCNPs and the photobase Ru-A. UCNPs converted NIR light into blue light, which triggered the release of n-butylamine from Ru-A. The released n-butylamine could further deprotonate PAA. The strategy of photon upconversion pH manipulation was further developed to control the swelling of pH-sensitive PAA hydrogels. Not only Ru-A but many other photoacids/photobases can also alter solution pH after light irradiation. Thus, the concept “photon upconversion pH manipulation” reported in this work is a general approach to controlling pH by NIR light. Also, photon upconversion
pH manipulation can not only induce swelling of pH-sensitive hydrogels but can also stimulate other pH-responsive materials, such as micelles, capsules, and supramolecules. Thus, photon upconversion pH manipulation is a new and general way to control pH-responsive materials with high spatiotemporal resolution for various applications.

Z. C. and Y. X. were supported by the CSC program. R. E. is a member of CONICET. We thank H. Menges for measuring the upconverting luminescence spectra. This work was partly supported by the Deutsche Forschungsgemeinschaft (DFG, WU 787/2-1).

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