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Illuminating Biology with Visible-Light-induced Biocompatible Reactions

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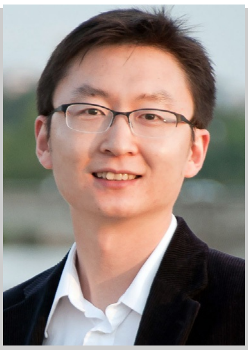

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What is your current research focus and why is it important?

We develop new biocompatible visible-light-induced chemical methods to study biology, including the discovery of new visible-light-induced chemical reactions and the development of new optochemical biology tools. Traditionally, biological applications of photochemical reactions used direct irradiation on substrates with UV light, which required the use of biologically harmful UV light and light-absorbing substrates. We use visible-light-absorbing photocatalysts/photosensitizers to induce electron/energy transfer with non-visible-light-absorbing substrates, or form visible-light-absorbing donor–acceptor complexes from non-visible-light-absorbing substrates (Figure 1a).[1] These new light-induced reaction modes enable additional desirable characteristics for biocompatible reactions: i) Stable substrates with fast reaction kinetics; ii) Versatile bond formation and cleavage reactions; and iii) External modulation with high temporal and spatial precision. To date, we have developed the first dual photoredox/benziodoxole (BI) system for carboxylate and alcohol activation, in which the "inert" cyclic iodine(III) reagents BIOH/BIOAc enable biomolecule-compatible photooxidative reactions.[2] We have demonstrated the first visible-light-induced alkoxyl radical generations from alcohol derivatives or alcohols, and that the selective functionalization of inert C(sp^3)–H and C(sp^3)–C(sp^3) bonds can be achieved under mild and biomolecule-compatible conditions.[3] We have also reported Hantzsch ester (a synthetic analogue of NADH), or boronic acids, that formed donor–acceptor complexes for metal-free visible-light-induced reactions without photocatalysts.[4]

Recently, optogenetics centered on photosensitive proteins have been widely accepted and applied in the biological community.[5] The complementary optochemical biology methods centered on light-induced chemical reactions may provide molecule-level precision with light modulation.[1,6] We have shown the first photocatalytic reaction in live cells for bioactive molecules release with visible light (Figure 1b).[7] The deboronative hydroxylation is enabled by photocatalytic generation of hydrogen peroxides with organic dyes, which performs in bacteria and mammalian cells including neurons. The subcellular-specific photorelease of bioactive molecules in live cells can be realized by mitochondria-localized photocatalysts, which cannot be realized by traditional UV light irradiation. We are currently developing versatile bond-cleavage and bond-formation reactions in live cells, which will enable optochemical manipulation of biological functions with high temporal and spatial precision.

What are the critical issues and what are the future perspectives that need to be addressed for the field to progress?

The complexity of requirements grows exponentially from small molecule-compatible reactions to living organism-compatible reactions (Figure 2).[8] Organic chemists are good at inventing new chemical reactions, and they pay attention to ambient reaction conditions, excellent chemoselectivity, and functional group compatibility. However, they are less concerned with air compatibility, room temperature, and neutral aqueous conditions criteria, not to mention the biomolecule functional group compatibility, as these requirements are not needed for small molecules. In contrast, while biologists work with biomolecules, live cells, or living organisms, they do not have the expertise to invent the new chemical transformations needed, and they generally only turn to literature within their own research discipline. There is a huge gap here, which calls for the development of new biocompatible reactions to fulfil the demands. Visible-light-induced reactions provide great opportunity with the excellent biomolecule-compatibility, and the live-cell compatibility has also come to the fore recently.[7] In this newly burgeoning and booming field, scientists may use visible light to achieve the selective modification of biomolecules, and the photo-manipulation of live cells and living organisms. It is expected that the superior biocompatibility of visible light, and especially near-infrared light, combined with their high

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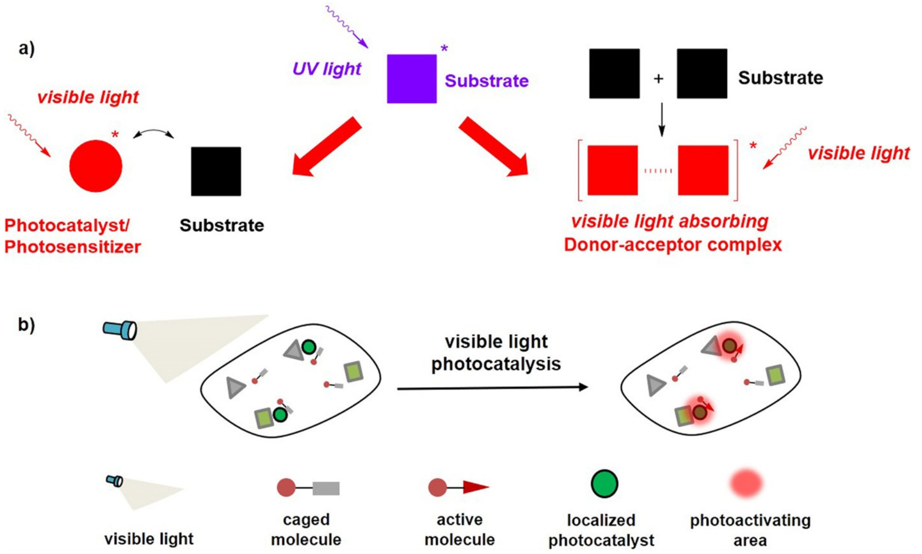

Figure 1. The visible-light-induced reactions and their applications in live cells.

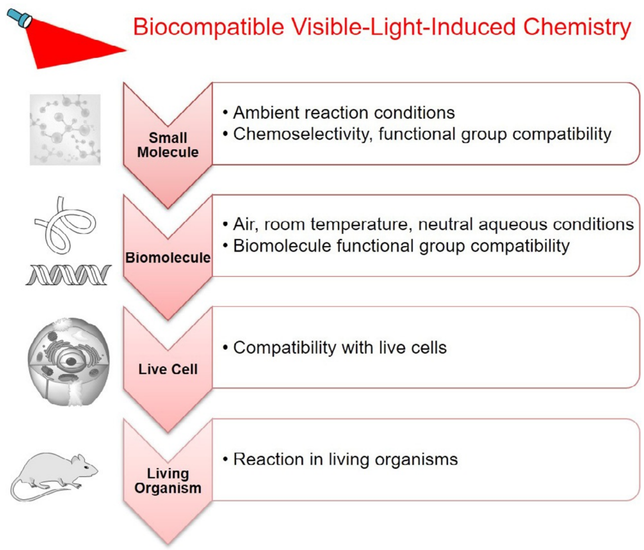

Figure 2. The development of biocompatible visible-light-induced reactions.

temporal and spatial precision, will have an unimaginable future for diagnostic and therapeutic applications.

What is, in your personal opinion, most critical to teach students in university chemistry courses?

I was trained at undergraduate and graduate level as an organic chemist, and at postdoctoral level as a chemical biologist. Photochemistry is the new discipline I am learning, and I am enthusiastic about it. In today's scientific research, multidisciplinary and interdisciplinary are the key words. My suggestion to university chemistry students is to make every effort to reach out to new disciplines and never stop learning.

Acknowledgements

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