

Outside the box: imaging quantum leap 'sees' deeper into live organs



Using a unique approach, scientists have created a new biomedical imaging contrast agent to help in "seeing" deeper into live tissue, opening the way for exponential advancements in optical imaging technology.

The research is the result of an international collaboration between [Fudan University in China](#) and the [University of Technology Sydney \(UTS\)](#). The results of this new study demonstrate the potential to enhance bio-imaging resolution beyond the current possibilities of **CT** and **PET** imaging technology. This breakthrough in imaging technology was achieved using a unique approach to overcome a major obstacle in **"seeing" deeper and clearer into live organs** say the scientists in the study published in [Nature Photonics](#).

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"This outcome is a great example that shows how we transform advances in photonics and material sciences into revolutionary biotechnologies at IBMD," said senior author of the study and Director of the [UTS Institute for Biomedical Materials & Devices \(IBMD\)](#), Professor [Dayong Jin](#).

Optical contrast agents are used primarily to improve the visualisation and differentiation in tissue and blood vessels in both clinical and research settings.

To optimise the brightness of a contrast agent, and to efficiently illuminate single cells and **biomolecules**, the challenge lies in **overcoming a limitation in physics**, called **"concentration quenching"**. This is caused by the cross relaxation of energy between emitters when they are too close to each other, so that having too many emitters leads to a quenching of the overall brightness.

"The new approach in this research was to unlock the concentration quenching effect by using the **pure rare earth element ytterbium** that only has a single excited state to avoid inter-system cross relaxation", explained Professor Jin, "so that a network of over 5,000 pure ytterbium emitters can be tightly condensed within a space of 10 nm in diameter, a thousand times smaller than a cell".

At this emitter density all possible atomic doping sites are occupied by ytterbium within the **crystal lattice structure**, and once properly passivated (made unreactive), by a thin layer of **biocompatible calcium fluoride**, the material is free of concentration quenching.

"This enables the efficiency of photonics conversion to approach the theoretical limit of 100%. This not only benchmarks a new record in photonics and material sciences, but also opens up a lot of potential applications", stated Professor Jin.

Lead author on the paper, [Yuyang Gu](#), PhD student at Fudan University, said that **"using this new contrast agent in a mouse model allowed us to see through whole mice"**.

The fundamental physics of the fluorescent probes used in optical imaging means there is only a **narrowly defined near infrared (NIR)** "window" (optical transparency window) beyond which visible light cannot penetrate tissue. **To design a contrast agent that both absorbs and emits in the NIR without losing the energy is difficult.**

"Although **ytterbium has a 'pure energy'** level that helps protect **photons** absorbed in the NIR band before being emitted, with negligible loss of energy, the simple excited state only permits emissions in the very similar band of NIR, which makes it impractical to use the conventional colour filters to discriminate the emissions from the highly scattering environment of laser excitation", explained Professor Jin.

"The research needed 'new physics'. We really had to think outside the box."

Instead of spectrally "filtering" the signal emissions, the researchers further employed a time-resolved technique that paused the excitation light, and took advantage of the "photon storage" property of ytterbium emitters, slowing down the emission of light, long enough to allow a clearer separation between the excitation and emission of light in the time domain. **Professor Jin likens this phenomena to the scenario when, after powering off a TV, the long-lived fluorescence of a "ghost" image is seen as an afterglow in the darkness.**

For the past five years, Jin and his team have developed a library of Super Dots, π -Dots, Hyper Dots and Thermal Dots as multiphoton luminescent probes for sensing and imaging applications.

"This outcome is another quantum leap, bringing us a new set of research capacities towards the development of more efficient and functional nanoscale sensors and biomolecular probes" said Jin.

Fudan University Chief Investigator, Professor [Fuyou Li](#) said "This is a 'new' luminescent process with high efficiency. We hope to find more suitable applications based on the fine tuning of the decay process of such kind of probes."

The combined use of high density of ytterbium emitters and time-resolved approach meant it was possible to maximise the number of emitters, the light conversion efficiency and the overall brightness of the contrast agent, and thereby significantly improving detection sensitivity, resolution and depth.

Jin said that this is another example of how breakthroughs in physics can lead to the development of new and improved medical technologies citing the evolution, and revolution, in diagnostic methods such as **X-rays**, **CT** and **PET** imaging.

Source: [UNIVERSITY OF TECHNOLOGY SYDNEY](#)

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