有機分子、電気化学、分子生物学の融合
CREATION AND APPLICATION OF CHEMICAL SENSING PROBES

Koji Suzuki*, **, Keitato Umezawa*, Hiroki Hifumi*, Hiroaki Komatsu*, Aki Honda*, **, Naoko Iwasawa* and Daniel Citterio*

* Department of Applied Chemistry, Faculty of Science and Technology, Keio University,
(Center for Science and Technology for Designing Functions)
** Core Research for Evolution Science and Technology (CREST)

Chemical sensing probes are functional molecules and unique sensing devices which are designed to detect many chemical substances. Our developed probes can realize new chemical sensors that are useful for environmental, biological, medical and clinical measurements.

1. Optical Imaging probes

Fluorescence imaging in the near-infrared (NIR) region of 650-900 nm has several advantages, and because of the low excitation energy and deep penetration depth of NIR light, it is highly useful as a sensitive, noninvasive, and simple imaging strategy for deeper tissues or living organisms. Cyanine dyes are commercially available NIR dyes, but their optical properties (quantum yields or photostabilities) are often insufficient for practical applications. Therefore, new NIR fluorescent dyes as alternatives to cyanine dyes are required.

Boron-dipyrromethene (BDP) dyes have excellent optical properties such as high absorption coefficients, high quantum yields, sharp spectral bands, high photostabilities and an insensitivity to solvent polarity. Nevertheless, the development of NIR fluorescent BDPs with retained optical characteristics is challenging and only slightly investigated. Therefore, we designed and synthesized novel BDP dyes (KBDP-X series) based on two concepts, *i.e.*, the fusion of the BDP core with heteroaryl moieties such as furan or thiophene, and introduction of electron-donating moieties.

Some of the newly developed dyes exhibited excellent optical properties including an intense absorption band at 673 nm with high absorption coefficient (～ 200,000 $M^{-1}cm^{-1}$), narrow half maximum width (～28nm), intense fluorescent band at 685 nm with an extremely high quantum yield (～ 0.68), and quantum yield insensitivity toward solvent polarity. These characteristics are superior to the presently available NIR dyes.

To maintain proper functions within living cells, intracellular ions and proteins cooperatively work in a chain reaction. One example is the competitive relation between magnesium and calcium ions. Not only does magnesium replace calcium ions in a cell, it is also known to be involved in the sclerosis of arteries caused by the accumulation of calcium. To clarify the relation and function of these two ions, we have designed and synthesized a multi-fluorescent molecular probe called KCM-1. With the addition of calcium ions, the spectral maximum of the formed ion complex peak of KCM-1 is blue-shifted, while the complexation with magnesium ion produces a red-shift. To realize the simultaneous imaging of the two ions, we used artificial neural networks, an information processing technology, which can realize an unusual multichemical sensing.

2. MRI probes

Magnetic resonance imaging (MRI) is a useful diagnostic tool, which is applied for preoperative as well as postoperative diagnoses without exposing the patient to harmful radiation, which cannot be avoided in case of using X-rays and γ-radiation in connection with computer tomography (CT) and PET. The MRI signals origin from the protons of in vivo water molecules based on the NMR principle and positional information is obtained by using gradient magnetic fields. Since the sensitivity of the NMR technique is relatively low, direct in vivo imaging of substances is difficult, except for water molecules that are present in a high concentration. If the physiological phenomena are visualized by using MRI, MRI can become a more useful diagnostic technique in hospitals.

To achieve this purpose, we have designed and synthesized novel MRI probes (KMR series) which can respond to a concentration of potassium ions, calcium ions and glucose. These MRI probes are composed of a gadolinium complex that has a high relaxivity and recognition sites which can selectively combine with intravital molecules. The recognition sites are composed of two 15-crown-5 ethers for the potassium ion (KMR-K series), a BAPTA-like structure for the calcium ion (KMR-Ca series) and two phenylboronic acid groups for glucose (KMR-Glu series).

Ion and glucose detection that is considered to be impossible, in principle, by using MRI can be made possible using the newly designed MRI probes. With further development of this novel concept of MRI probes, the possibilities of MRI diagnosing, which is non-invasive using non-radiating rays, is expected to expand and become a breakthrough for future diagnostic imaging.

As shown in Fig. 1, the combined technologies for the imaging of organs and the imaging of cells using chemical sensing probes will open the way to the new direction of imaging world for humans.

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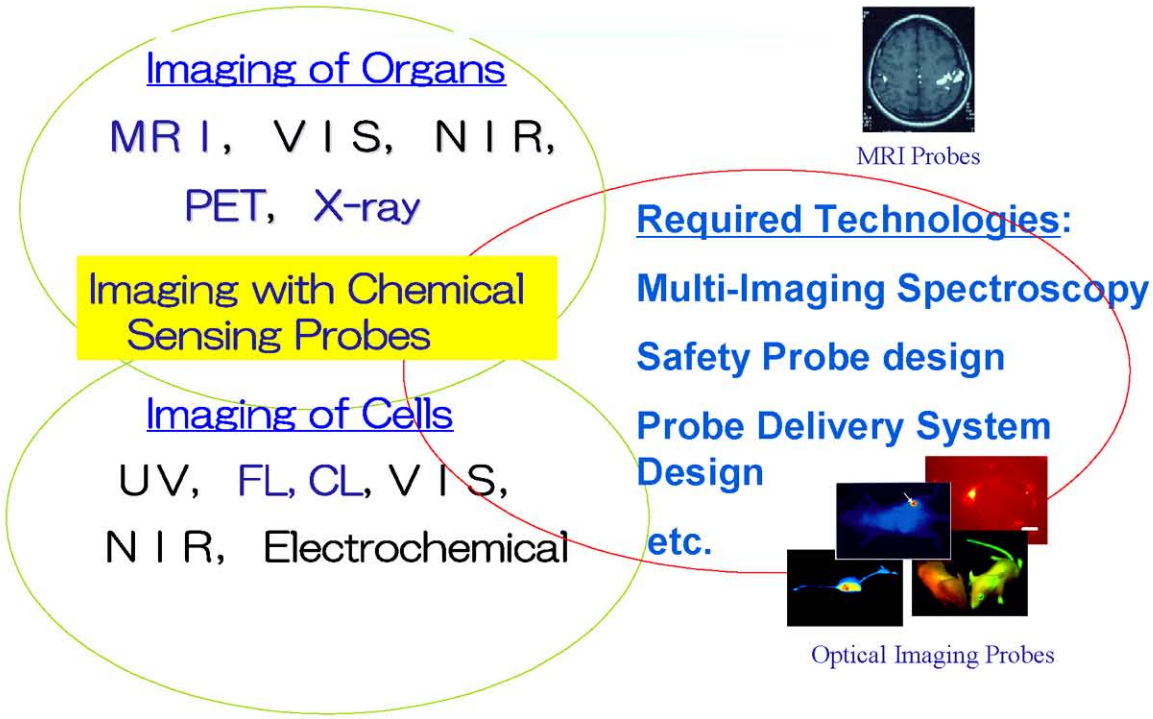

Fig. 1 Imaging World with Chemical Sensing Probes and related technologies

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