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Fluorescent probes for dual and multi analyte detection

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1. Introduction

Small anions, cations and neutral molecules act as different biological activities and thus play various vital roles for human life. Consequently, the detection of such targets is of great interest and importance.[1] Numerous modern technologies, such as atomic absorption spectroscopy (AAS), inductively coupled plasma atomic emission spectrometry, electrochemical sensing and etc., have been developed to analyze such environmental, medical and cellular analytes concerned.[2–6]

Conventionally, the majority of analysis approaches have been restricted to measuring the concentration of one specific target. While in the practical analytical application, the complication of the physiological and/or environmental conditions embarrasses single-target analysis methods quite often. For instance, the contamination of analysis matrix resulting from the synergistic contribution of two or more infectants, often makes the single-analyte analysis platform less favorable. Thus, some methods aiming to detect multiple analytes, including sequential injection analysis (SIA), flow

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injection analysis (FIA), immunoassays and microsensor arrays, have been developed in the past decades.[7–10] Nevertheless, these methods require sample pre-treatment, extremely dilute samples and signal amplification methods.

Unlike to the aforementioned techniques, fluorescent chemosensor is widely used as a powerful tool to spy on neutral and ionic species of interest owing to its high sensitivity, selectivity, versatility, and relatively simple handling.[11–13] Usually, the spectra properties of a fluorescent probe change upon interaction with a chemical species, namely producing a detectable fluorescent signal. Conventionally, a quite large proportion of fluorescent probes on work follow the paradigm that is still dominating traditional sensor design: one receptor site for one analyte. These probes can respond to their own target with much sensitivity and selectivity, but in most cases, they failed to fulfill two or more analytes response independently. As for fluorescent probes, multi-analyte sensing can be realized by the combination of two or more probes, which each specifically respond to one particular target.[14,15] However, when taken cell imaging applications into consideration, it is hardly feasible to place two or more mono-functional probes into a cell together to detect different species. As was pointed out by Suzuki et al., the combination of several fluorescent probes produces cross-talk, a larger invasive effect, the different localization, and the different metabolisms, and photobleaching rates of individual indicators, making the scenario very complicated and unsuitable for quantitative analysis.[16] By contrast, it is supposed to realize multi-species detection in one cell with a multi-functional probe, and undoubtedly, multi-functional probes, which can sense more than one species would simplify the analysis work. Therefore, it would be beneficial to develop fluorescent probes with multi-functional capabilities that could identify two or more identities in a system.

Multi-analyte fluorescent probe is a promising tool to achieve diverse analytes sensing. In particular, dual-analyte or bifunctional probes, which refer to those based on a single host that can independently recognize two guest species with distinct spectra responses via the same or different channels, have already emerged and have gradually become a new research focus. This intriguing tool has prompted an innovative shift from selective to differential analysis. When designing a multi-analyte fluorescent sensor, the following approaches could be considered and utilized: (i) assembly of differential receptors, (ii) differential sensor–stimulus interactions, (iii) access of output via multiple channels, or (iv) access of output via differential response. Among the four approaches mentioned above, fluorescent probes that combine one or several receptors and reporter units are of particular interest, as such a constitution not only allows tuning sensitivity and selectivity by choice of the functional subunits but also allows to independently quantify the respective target analyte. Different interactions between the fluorescent probes and analytes result in multi-signaling behaviors. Based on this strategy, several groups have reported a series of bifunctional chemodosimeters or sensors based on specific chemical reactions either simultaneously or consecutively.[17–19]

Up to date, several combinations of analyte for fluorescence sensing have been reported: metal ion/metal ion, anion/metal ion, anion/anion, ion and neutral molecule and double molecules. A large number of reviews have described the performance of fluorescent probes with specific single-analyte applications, such as metal sensors,[20] anion sensors,[13] thios sensors,[21] intracellular pH indicators,[22] sensors targeting reactive oxygen and nitrogen species[23] and H_2S sensors,[24] etc. However, comprehensive summaries of small molecular fluorescent probes that target different species of analytes are not seen yet. In this article, we will review the representative examples of dual-analyte fluorescent probes, which are classified into five categories according to the different combinations of analyte: metal ion/metal ion, metal ion/anion, anion/anion, ion/molecule and molecule/molecule. Further attention will be given to the sensing mechanisms of how the molecular probe detects different analytes.

2. Dual-analyte fluorescent probe

2.1. Probes for metal ion and metal ion detection

Fluorescent sensors for metals usually contain two essential parts: a metal chelating or binding moiety and at least one fluorophore capable of absorbing and emitting light. To function as a sensor, metal binding must alter either the electronic structure or molecular conformation. Changes in the electronic structure can lead to a change in the intensity or wavelength of light absorption or emission, while changes in the molecular structure can alter the

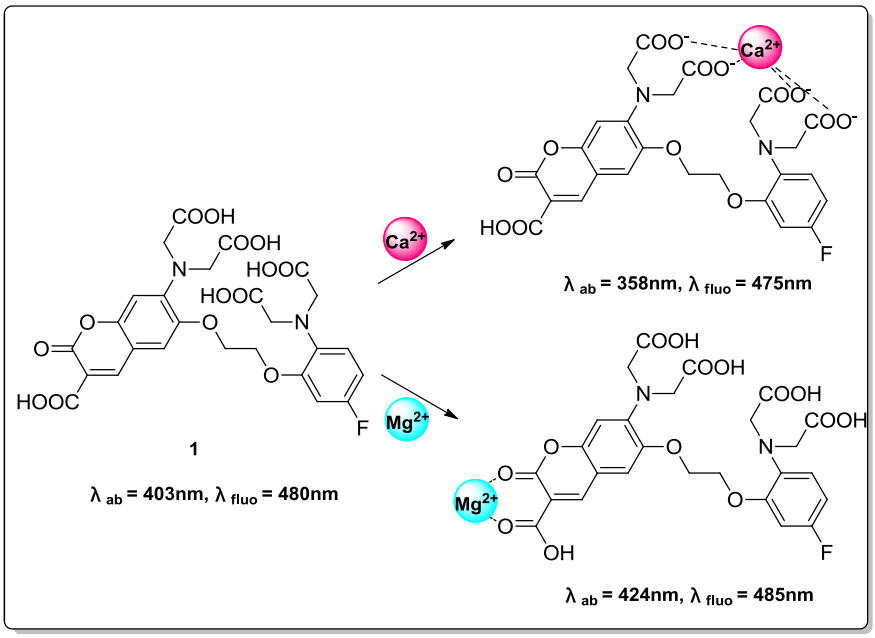

Fig. 1. Scheme of dual-analyte fluorescent probe **1** for Ca^{2+} and Mg^{2+} detection.