CHAPTER 1

Welcome to Fluorescent Chemosensors

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> A fluorescent chemosensor is a compound of abiotic origin that complexes to an analyte reversibly with concomitant fluorescence signal transduction.
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> A. W. Czarnik (1993)

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1.1 Introduction

This book, entitled *Fluorescent Chemosensors*, is part of the Monographs in Supramolecular Chemistry series edited by Philip Gale and Jonathan Steed and follows in the footsteps of the seminal book on *Fluorescent Chemosensors for Ion and Molecule Recognition* published as part of the ACS Symposium Series and edited by Anthony W. Czarnik in 1993. That book provided access to a collection of groundbreaking chapters on fluorescent chemosensors by pioneers of the field, including Bernard Valeur, A. Prasanna de Silva, Roger Y. Tsien and Joseph R. Lakowicz.

With this book on fluorescent chemosensors, the editorial team of Wu, Sedgwick, He and James have assembled a diverse collection of chapters from world-leading experts involved in fluorescent chemosensors, including Anthony Czarnik; Christopher Chang; Meng Li; Young Tae Chang; Hwan Myung Kim; Jong Seung Kim; Eric Anslyn; Silvia Giordani; Kate Jolliffe; Bo Tang; Shin Mizukami; Fabiao Yu; Tasuku Hirayama; Safacan Kölemen, Elizabeth New and Thorfinnur Gunnlaugsson.

Together the chapters take us on a journey from receptor-based to reaction-based sensing systems using traditional synthetic design and diversity-oriented synthesis for detecting chirality, phosphates, reactive oxygen, zinc ions (Zn^{2+}), sulfane sulfur/selenium species and other transition metals. The systems described are both molecular-based and nanoparticle-based and have uses in disparate fields, including medical diagnostics, theranostics and environmental sensing. Specific techniques discussed include two-photon fluorescence, ratiometric and aggregation-induced emission (AIE) (Figure 1.1).

Whether you are visiting for the first time or as a regular visitor, we are delighted to welcome you to the fluorescent chemosensor realm, we hope you enjoy your stay.

1.2 Summary of Contents

Chapter 2 (Anthony W. Czarnik)

Tony Czarnik presents his original introductory chapter for the ACS Symposium Series book on *Fluorescent Chemosensors for Ion and Molecule Recognition*. While the chapter was written to coincide with the original chemosensors collection, the content remains pertinent and as fresh today as it did almost 30 years ago.

Chapter 3 (Christopher J. Chang)

Chris Chang provides an excellent overview and introduction to activity-based sensing (ABS) for biological applications. As an emerging area of sensor research, ABS leverages the unique chemical reactivity of a given analyte of interest, rather than traditional binding-based approaches, which rely on

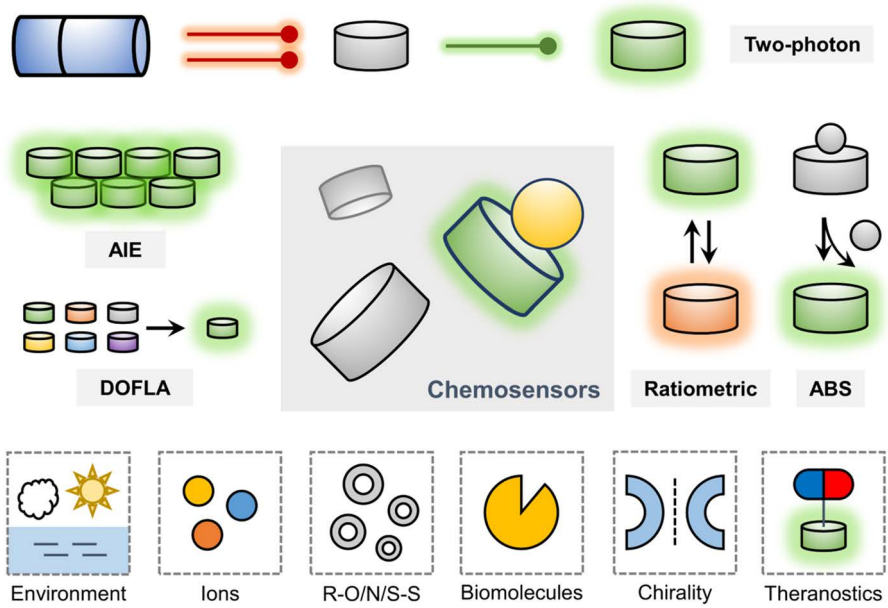

Figure 1.1 Schematic describing the chemosensor systems covered in this book. AIE, aggregation-induced emission; ABS, activity-based sensing; DOFLA, diversity-oriented fluorescent library approach, R-O/N/S-S, reactive oxygen, nitrogen, and sulfur species.

lock-and-key molecular recognition, to achieve selectivity in complex biological environments. The chapter covers design principles for ABS and provides examples of activity-based imaging probes, highlighting the applicability of the ABS approach to identify and characterize new biology.

Chapter 4 (Meng Li)

The chapter by Meng Li provides the latest research achievements on AIE-based fluorescent systems. AIE is a relatively recently discovered approach towards the development of fluorescent chemosensors, where molecules in an aggregated state exhibit enhanced fluorescence emission. The chapter covers the developments of AIE over the past decade, including organic luminescent molecules and clusteroluminogens.

Chapter 5 (Animesh Samanta and Young-Tae Chang)

The chapter by Animesh Samanta and Young-Tae Chang summarizes the recent developments of chemical probes/sensors and chemosensors using a diversity-oriented fluorescent library approach (DOFLA) and their biological and environmental applications. Consisting of six sections, including

the concept of diversity-oriented fluorescent library, mechanism of signal transduction, screening strategies and reviews of recent examples from *in vitro* spectra-based screening, cell-based screening and *in vivo* whole organelle-based screening.

Chapter 6 (Hwan Myung Kim)

The chapter by Hwan Myung Kim describes the development of two-photon (TP) probes with improved sensitivities for measuring target analytes in biological specimens. Coverage includes photo-physiological properties, basic TP probe design strategies and representative TP sensors for biological systems.

Chapter 7 (Paramesh Jangili and Jong Seung Kim)

The chapter by Paramesh Jangili and Jong Seung Kim discusses how ratiometric chemosensors can be developed to detect biological/environmentally important analytes. Highlighting the basic principles and design strategies of ratiometric fluorescent chemosensors, including photophysical/chemical sensing mechanisms based on different molecular types (*i.e.*, small molecule and nanoparticle), with appropriate examples.

Chapter 8 (Eric V. Anslyn)

The chapter by Eric Anslyn covers both historical and modern examples of chirality sensing *via* UV-visible, fluorescence and circular dichroism spectroscopy. Each technique possesses unique advantages, which are leveraged to tailor sensing schemes to a particular application. These optical signaling methods are well suited for high-throughput screening platforms as they can be performed in parallel with multiwell plates. This allows for rapid detection at low cost, which is advantageous compared to intrinsically serial conventional chromatographic methods.

Chapter 9 (Silvia Giordani)

The chapter by Silvia Giordani provides an overview of fluorescent carbon nanoparticles, supported by selected literature examples, namely on carbon nano-onions, fluorescent carbon dots and detonation nanodiamonds. Significantly, the fluorescent and sensing properties of these types of nanoparticles can be easily modulated, affording chemical tools with wide applicability in imaging and sensing.

Chapter 10 (Katrina Jolliffe)

The chapter by Kate Jolliffe outlines the development of small-molecule fluorescent chemosensors for phosphate species. Phosphate species are ubiquitous in nature, play diverse roles in biological systems and display extensive

variation of types of functionalized phosphate species (*e.g.*, ATP, DNA). Key examples of interaction types, varied approaches to chemosensor design and fluorescence response mechanisms are highlighted.

Chapter 11 (Ping Li and Bo Tang)

The chapter by Ping Li and Bo Tang covers sensors for reactive oxygen species (ROS) that are widely involved in signal transduction of physiological processes. Non-invasive fluorescence imaging techniques have gradually matured enabling the tracking of active molecules such as ROS. This chapter summarizes the development of fluorescent sensors for ROS in living cells and *in vivo*.

Chapter 12 (Shin Mizukami)

The chapter by Shin Mizukami introduces the fluorescence-based imaging of zinc, which is important since disruption of zinc homeostasis is associated with various diseases, such as Alzheimer's disease and diabetes. Therefore, investigating its functions and physiological roles is important. The chapter highlights organelle-targeting small-molecule probes and protein tag–small-molecule hybrid probes, which are expected to have a higher potential for accurately visualizing and quantifying labile Zn^{2+} ions at the organelle level.

Chapter 13 (Linlu Zhao and Fabiao Yu)

The chapter by Linlu Zhao and Fabiao Yu covers the development of selective sensors for sulfane sulfur and reactive selenium species. These species are important antioxidant biomarkers for aging and disease development. Since the intracellular levels and distribution of sulfane sulfur and reactive selenium species can directly evidence the dynamic state of oxidative stress, they may reveal the difference between physiological and pathological processes. Fluorescence bioimaging has the advantages of high temporal and spatial resolution, low invasiveness and fast response, and has become a powerful tool for intracellular detection. This chapter outlines the design strategy and development of fluorescent probes for the detection of sulfane sulfur and reactive selenium species.

Chapter 14 (Tasuku Hirayama)

The chapter by Tasuku Hirayama covers examples of activity-based probes for transition metal ion detection. Such metal ions are involved in various biological processes, and their essential roles and pathological involvement have provided a motive for the development of new synthetic chemical tools for the detection and monitoring of metal ions in cells and in

living organisms. Activity-based probes provide new possibilities for the detection of biological metals and avoid many disadvantages associated with chelation-based probes (*e.g.*, fluorescence quenching effect of *d* unsaturated metal ions).

Chapter 15 (Safacan Kolemen)

The chapter by Safacan Kolemen introduces photodynamic therapy, which is a clinically approved treatment modality for a wide range of medical conditions, including malignant cancers. The technique employs cytotoxic reactive oxygen species (ROS), particularly singlet oxygen ($^1O_2$), to kill diseased cells. Spatiotemporal control of ROS generation and consequent cancer cell selectivity is one of the most important characteristics of photosensitizers to minimize severe adverse effects, as well as to enhance therapeutic outcomes. As such, activatable photosensitizers that are OFF prior to activation with various tumor-associated intracellular stimuli are essential.

Chapter 16 (Elizabeth J. New)

The chapter by Liz New covers fluorescent sensors developed for environmental monitoring of chemical pollutants and other substances that can cause harm to society and the natural world. Fluorescent-sensing platforms provide high sensitivity using much cheaper and smaller instrumentation than traditional analytical techniques. The chapter highlights fluorescent platforms developed for environmental sensing, with a particular focus on examples that have been successfully applied in the field.

Chapter 17 (Thorfinnur Gunnlaugsson)

The chapter by Thori Gunnlaugsson discusses the construction of lanthanide-based sensors/probes and their use in sensing and imaging. Lanthanides (*e.g.*, Eu(III) and Tb(III)) exhibit many advantageous optical properties, including long excited-state lifetimes, improved signal-to-noise ratios and long emission wavelengths. Design strategies towards lanthanide-based luminescence systems have been discussed and representative examples provided which illustrate the versatility and wide-ranging applications of these systems.