PREFACE

> *Smell is a potent wizard that transports you across thousands of miles and all the years you have lived.*
>
> ***Helen Keller***

This poignant quotation by Helen Keller speaks to the evocative nature of olfaction for humans. Beyond being simply an important diagnostic mechanism for interpreting the environment, olfaction can often recall old memories or stir complex emotions. In my home country of Australia, there are stories of soldiers returning from battle in World War II by ship and realizing that they were nearing their homeland prior to sighting it, simply from the characteristic smell of the oil-laden *Eucalyptus* trees that dominate much of the Australian landscape. These weary combatants were not just detecting trees but imbibing their loved ones, their childhoods, their hopes, and their loss.

Coming from Helen Keller, this quote also subtly hints at the key role olfaction plays when sight is not the primary sense used for navigation. This is actually the case for most of the animals on earth; huge numbers of species of invertebrates use olfaction as their key method of assessing their environment and detecting food, mates, hosts, predators, etc. In creatures such as insects, olfaction-related cognition is much simpler than for humans; however, it is known to be important in individual learning, in parasitic wasps for example. Olfaction is so important to insects that they have evolved extremely sensitive olfactory receptors (ORs) to detect low concentrations (sometimes nanomolar and below) of volatile compounds; these receptors largely reside in their antennae but do occur elsewhere. The olfactory sensitivity of insects helps make them formidable evolutionary competitors but is also exploited by humans to disrupt insect behavior (e.g., pheromone disruption of moth pests and pheromone trapping).

Olfaction has attracted significant scientific interest for many years. In 1937, Japanese researchers utilized electrodes to measure the negative electrical potential generated across olfactory epithelium of dogs, caused by olfactory stimulation. This technique was adapted for study of frogs and rabbits in 1956 and given the name electro-olfactography; it has since been widely utilized for study of olfaction in mammals. In 1957, the technique was adapted to insects and named electroantennography, and in 1959 the first insect pheromones were characterized from the silk moth, *Bombyx mori*.

While electrophysiological techniques such as these were used successfully for decades and could be used to detect the presence and degree of olfactory stimulation by various compounds, they were unable to decipher the molecular basis of olfaction.

However, around the same time in 1953, Watson and Crick published the structure of DNA. This was a seminal moment in science and was built on by others to produce great advances in our understanding of molecular biology and in the power of the techniques available to study it. Then in 1991, Richard Axel and Linda Buck discovered that vertebrate ORs were a subclass of the well-known G protein-coupled receptor (GPCR) family of proteins. This discovery (which was subsequently recognized with a Nobel Prize in 2004) combined with advances in DNA/RNA sequencing technologies and bioinformatics led to the elucidation of OR repertoires of a range of vertebrate species and of associated molecular signaling processes. The first vertebrate receptor to be deorphaned (have its cognate ligands characterized) was OR17 from the rat in 1998, which was shown to react to C_7–C_{10} saturated aldehydes.

Because insects also express many GPCRs including homologs of human proteins (e.g., serotonin and histamine receptors), it was expected that invertebrate ORs would be readily isolated through homology searches. While this was true for the nematode *Caenorhabditis elegans*, it took until 1999 for the first insect OR to be identified from the vinegar fly (*Drosophila melanogaster*) using unbiased approaches. This is because insect ORs are not GPCRs but an unrelated group of receptor proteins with a similar tertiary structure. Being different to classic GPCRs, the signaling mechanisms have also proven to be different in insects, such as the existence of a highly conserved universal chaperone protein and the activation of both metabotropic and ionotropic signaling cascades (first reported in 2008).

The purpose of this volume is to summarize the latest understanding of molecular mechanisms of olfaction in vertebrates and insects. I have chosen to focus most chapters on insects for several reasons. First, molecular biology of insect olfaction is still an evolving paradigm compared to that of vertebrate olfaction which is relatively well characterized. Second, insects are a megadiverse group that interact with varying levels of specificity, with virtually all other land organisms and therefore as a group have a huge array of ORs that detect countless volatile compounds, many important to humans. This is of great interest in terms of studying general biology but insect ORs also show huge promise in many applications such as pest/disease management and biosensing. Lastly, a lean toward insects gives a point of differentiation with other works on olfaction that have traditionally focused on mammals, of which there are relatively few species.

This first edition of *Molecular Basis of Olfaction* is designed to provide insight into key areas of olfaction research and is intended for use by researchers, teachers, students, molecular biologists, and biologists in general. Leading researchers from China, United States, France, Germany, Sweden, and New Zealand have contributed the chapters presented here, and I take this opportunity to sincerely thank all authors for their effort and expertise.

The chapter "Mammalian Olfactory Receptors: Molecular Mechanisms of Odorant Detection, 3D-Modeling, and Structure–Activity Relationships" by Persuy and coworkers from France summarizes our knowledge of molecular mechanisms of odorant detection in mammals and includes 3D modeling of mammalian ORs, and relationships between receptor structure and activity. In chapter "Olfactory Signaling in Insects," Dieter Wicher (Max Planck Institute for Chemical Ecology) discusses cellular signaling in various types of olfactory neurons in insects. The chapter "Advances in the Identification and Characterization of Olfactory Receptors in Insects" by Montagné *et al.* provides an insight into the latest advances in isolating and characterizing insect ORs, including the use of transcriptomics. The final two chapters focus on specific areas of insect olfaction research of importance to humans. The chapter "Olfactory Disruption: Toward Controlling Important Insect Vectors of Disease" by Sparks *et al.* (U.S. Department of Agriculture) discusses disruption of olfaction in insect vectors of human disease such as mosquitoes and tsetse flies. The last chapter ("Pheromone Reception in Moths: From Molecules to Behaviors" by Zhang and colleagues) summarizes knowledge of one of the great olfactory phenomena in biology, pheromone detection by moths, and the events leading from antennal detection of a pheromone to neural processing and resultant behaviors.

I anticipate that future editions of this volume will update these summaries as well as expanding the focus of the current edition.

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