Function, expression and evolution of insect odorant receptors

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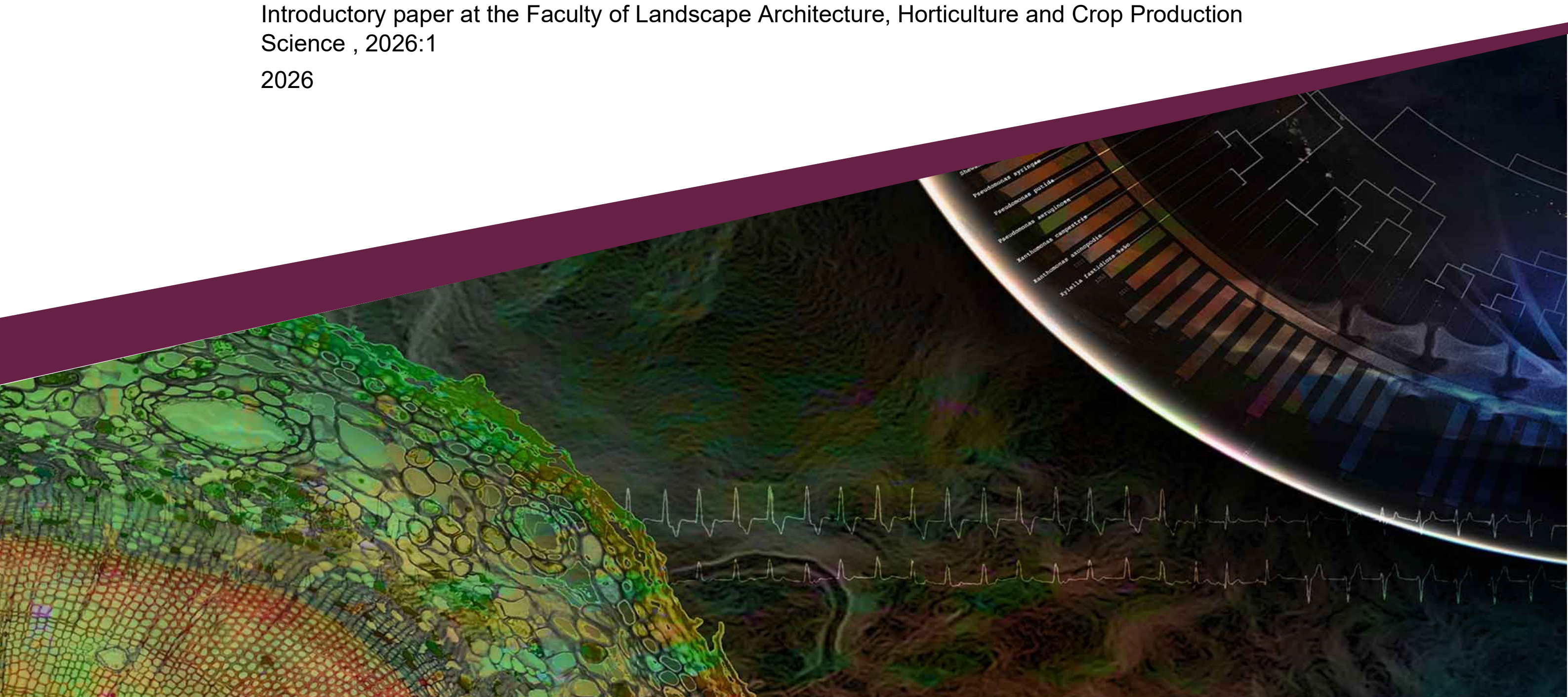
Publisher: Faculty of Architecture, Horticulture, and Crop Production Science
Introductory paper at the Faculty of Landscape Architecture, Horticulture and Crop Production Science , 2026:1
2026



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Publisher: Faculty of Architecture, Horticulture, and Crop Production Science
Year of publication: **2026**
Place of publication: **Alnarp**
Title of series: Introductory paper at the Faculty of Landscape Architecture, Horticulture and Crop Production
Part number: 2026:1
DOI: https://doi.org/10.54612/a.15k7962t3j
Keywords: odorant receptor, orco, chemosensation, insects,

Abstract

Sensing and interpreting the complex mixture of sensory input is a challenging task for all organisms. Most rely on many types of sensory inputs while specialising in one distinct form. Insects use olfaction to quickly adapt to their surroundings and this has given them the toolkit for fast evolution to occupy a wide range of ecological niches. Chemosensation is mediated through a set of receptors which bind in chemical ligands present in the insects direct surroundings mediating information about for example, presence of food resources, conspecific mates or oviposition sites. Odorant receptors (Ors) is the main family involved in olfaction and mediates a lot of the signalling for volatile organic compounds (VOC) in insects. These receptors form a heterotetrameric ion channel together with the odorant receptor co receptor (Orco) and when a VOC binds in the channel opens and there is an ion flux which generates a signal being sent to the brain, activating a behaviour. These receptors are tuned differently depending on the ecological niche of the insect and the coding of odours is not yet fully understood but new research indicates that several different members of the chemosensory receptor families can be co-expressed to improve the coding and spectrum of VOCs or ligands that an insect can sense and respond to. Ors evolved around 450 million years ago (Figure 3) most likely from terrestrial insects that developed flight where new ecological niches required new receptors with different function. Ors evolve through birth and death evolution where a gene that encodes for a receptor mutates and develops a receptor with a new function, depending on whether the new receptor increases or decreases fitness will “give birth” to a new gene and receptor or “die” and become a pseudogene without functionality.

Keywords: odorant receptor, orco, chemosensation, insects, evolution, olfaction

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Abbreviations

Or	Odorant receptor
Orco	Odorant receptor co receptor
Ir	Ionotropic receptor
Gr	Gustatory receptor
TRP	Transient receptor potential cation channel
PPK	Insect pickpocket receptor
GPCR	G-protein coupled receptor
cAMP	Cyclic adenosine mono phosphate

Infobox: The peripheral chemosensory system in insects

The peripheral chemosensory system in insects is housed in several bodily appendages, including the antennae (Vosshall et al., 1999, 2000), maxillary palps (Vosshall et al., 2000), proboscis (Dunipace et al., 2001; Wang et al., 2004), tarsi (Dunipace et al., 2001) and the ovipositor (Stocker, 1994). These appendages are equipped with cuticular hair-like structures called sensilla (Stocker, 1994) (Figure 1A). While sensilla vary in outer structure, pores or slits allow chemical ligands, i.e., odorants, to enter the sensillum lymph. In the sensillum lymph, proteins called odorant binding proteins and chemosensory proteins function to "carry" the typically hydrophobic odorant ligands through the aqueous lymph and deliver them to the target site, the olfactory receptors, by binding and thus protecting them from odour-degrading enzymes (Figure 1B) (Vogt & Riddiford, 1981). The lymph surrounds the dendrites of the olfactory sensory neurons (OSN) (Figure 1A), on which the membrane-bound olfactory receptors, e.g., odorant receptors (Ors), are expressed (Infobox A). From the somatic sensory neuron extends an axon, which allows the electrical signal that is generated by a chemical stimulus to be conveyed to the higher processing centres in the central nervous system of the insect. The OSN axons converge onto neuropil structures called glomeruli located in the antennal lobe (AL), the primary olfactory centre of the brain (Vosshall et al., 2000). The signal is integrated and processed within the AL and then sent via projection neurons (PNs) to higher olfactory centres, including the mushroom bodies and lateral horn in the protocerebrum, where the signal is integrated with other sensory inputs (Vosshall et al., 2000) (Figure 1C).

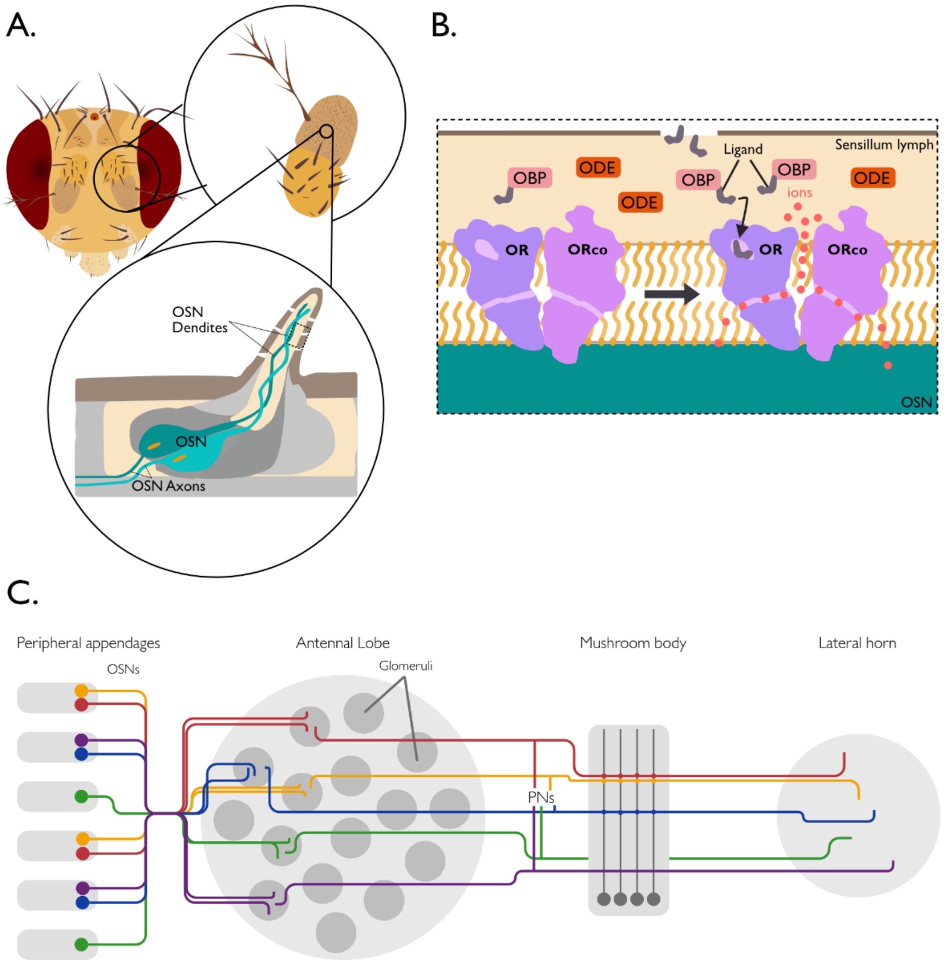

Figure 1. Infobox figure. Representation of the peripheral and central chemosensory system and higher processing

1. Introduction

Interpreting the world is a complex task for an organism, due to the countless stimuli influencing its behaviour in relation to the environment. These stimuli are generally made up of visual, tactile (mechanosensory), heat, humidity, auditory and chemosensory cues (Dethier, 1976; Roskies et al., 1995; Shamma, 2004; Su & Wang, 2014). To make sense of these stimuli, the sensory systems hosted in an organism must detect, process and sort the information into an internal representation. Whether it is for finding nutrients by seeking flowers or blood (Dethier, 1976), e.g., in the case of mosquitoes, and oviposition sites (Dougherty et al., 1995; Städler, 1978), or avoiding noxious chemicals (Newland, 1998) or predators (Heads, 1985), these senses work in conjunction to allow an individual organism to detect stimuli in its immediate habitat (Dall et al., 2005). Due to evolutionary adaptation and the habitual needs of an organism, there is often a larger reliance on one sensory system, which is why certain animals may have immaculate hearing, vision or sense of smell. For example, in insects, the rapid evolution of the chemosensory system has, in large part, proved crucial to their success, and is the common denominator that mediates behavioural expression across this diverse group of organisms (Suh et al., 2014). Insects represent one of the most abundant and diverse groups of organisms, occupying a wide range of ecological niches. Their evolutionary success is closely linked to the adaptations they are able to make, among which the development of sophisticated chemosensory systems has played a key role. This essay explores the function, molecular structure, expression and evolution of chemosensory receptors that are involved in the chemosensory systems with a focus on odorant receptors.

2. The chemosensory receptors of insects

Chemosensation in insects includes the detection of ecologically- and behaviourally-relevant chemical stimuli in the environment and subsequent processing of this information, and is an ancient way for these animals to obtain information from their surrounding world (Hansson & Stensmyr, 2011; Suh et al., 2014). The peripheral chemosensory system of insects involves different bodily appendages, which differ morphologically depending on the taxa, but generally include the antennae, the maxillary palps, the proboscis, tarsi and the ovipositor (Fowler & Montell, 2013; Stocker, 1994). The OSNs housed in these organs express members of five families of receptors on the dendritic membrane (Infobox A), of which two specialise fully in chemosensation, one partially in chemosensation and partially in other sensory modalities, and two that are also involved in various types of other sensory modalities. First, the odorant receptors (Ors) are, along with the other receptor families, responsible for the transduction of olfactory information from chemically diverse volatile organic compounds to the central nervous system (Benton et al., 2006; Clyne et al., 1999; Gao & Chess, 1999; Keller & Vosshall, 2016; Levy et al., 1991), and are the focus of this essay. Second, the gustatory receptors (Grs) (Clyne et al., 2000) are involved in taste sensation of sugar compounds (Dahanukar et al., 2007; Jiao et al., 2007), bitter compounds (Moon et al., 2006) as well as in the detection of carbon dioxide (Yao & Carlson, 2010). Third are the ionotropic receptors (Irs), the most ancient of the chemosensory receptors in most animals (Croset et al., 2010), and is the second receptor family involved, to a large extent, in olfaction, but they also have a different function compared to Ors. These receptors respond to different volatile organic compounds compared to Ors, usually carboxylic acids and amines, but are also involved in temperature and humidity sensation (Abuin et al., 2011; Benton et al., 2009; Wicher & Miazzi, 2021).

The two remaining families expressed in the olfactory organs mediate more diverse functions in insects: the transient receptor potential (TRP) cation channels and the insect pickpocket (PPK) receptors are both involved in multiple modalities of sensation. The transient receptor potential cation channels are divided into seven subfamilies of receptors based on their amino acid sequence (Montell, 2005), and are involved in chemosensation, such as olfaction and taste, seemingly tuned to contact irritants and repellents, such as citronellal in mosquitoes and N,N-diethyl-m-toluamide (DEET) in *Drosophila melanogaster* (Dennis et al., 2019; Kwon et al., 2010), as well as in thermotaxis, nocireception, light sensation and mechanosensation in *D. melanogaster*, *Bombyx mori*, *Apis mellifera* and *Tribolium castaneum* (Fowler & Montell, 2013; Matsuura et al., 2009). The PPKs are part of the DEG/ENaC family, and these ion channels mediate, e.g., mechano- and chemosensation (Kellenberger & Schild, 2002). Specific members, e.g., ppk28, are responsible for water taste, while ppk11 and ppk19 are responsible for salt taste sensation, in *D. melanogaster*. Other members of the PPK family are also involved in olfaction, e.g., *D. melanogaster* ppk25, which is necessary in males for sensing female pheromones and *D. melanogaster* ppk23, which is involved in courtship behaviour (Cameron et al., 2010; Chen et al., 2010; Lin et al., 2005; Liu et al., 2003; Lu et al., 2012).

3. Function of divergent odorant receptors and the conserved co-receptor

Insect Ors are seven-transmembrane receptors, which are expressed in the lipid membrane of OSNs, and was first identified in *D. melanogaster* (Clyne et al., 1999; Gao & Chess, 1999). Compared to its vertebrate G-protein coupled receptor (GPCR) counterparts, insect Ors have an inverted topology, where the N-terminus is intracellular and the C-terminus extracellular (Benton et al., 2006). Odorant receptors are ligand-gated non-selective cation channels that pass Na+, K+, and Ca2+ ions when activated. Insect Ors have been elusive to identify due to the differences in sequence and topology compared to their vertebrate or nematode Caenorhabditis elegans counterparts. The breakthrough came in the late 1990s when the first insect genome, that of *D. melanogaster*, was sequenced (Adams et al., 2000). This made it possible to identify the large Or family in the genome, demonstrating that *D. melanogaster* had 48 Ors involved in olfactory signal transduction; following improvements in the annotation of the genome we know today that the total number of Ors in *D. melanogaster* is closer to ~60. In other insect species, the number of genes encoding Ors varies from single digits to several hundreds (Montagné et al., 2015), with a high diversity amongst the receptors, reflected in 17-26% amino acid sequence identity between Ors (Vosshall, 2000; Vosshall et al., 1999). This potentially reflects the ecological adaptation of various insect species to their ecological needs (Hansson & Stensmyr, 2011).

The Or complex is made up of two units: first, the divergent odorant receptor unit of the complex, which functions as a ligand-gated ionotropic receptor where the bound ligand acts like a key in a lock, opening the gated ion channel, generating a flux of ions (Sato et al., 2008; Wicher et al., 2008). Second, is the highly conserved Or co-receptor (Orco). Orco is believed to be generally insensitive to natural odorants and is instead activated by cyclic nucleotides, such as cyclic adenosine monophosphate (cAMP), during the signalling cascade when information is being translated from chemical signals to electrical signals in the OSN (Wicher et al., 2008). It is, however, possible for certain synthetic agonists, such as N-(4-Ethylphenyl)-2-{[4-ethyl-5-(pyridin-3-yl)-4H-1,2,4-triazol-3-yl]sulfanyl}acetamide (VUAA1) to bind in and activate the co-receptor (Jones et al., 2011; Pacalon et al., 2023). The mode for activation is thus two-sided; the divergent Ors are ionotropic, generating a fast transient signal when binding to an odorant, while Orco is metabotropic, i.e., activated by a cyclic-nucleotide (cAMP), generated from the binding of a ligand (Miazzi et al., 2016), resulting in a slower signal with larger amplification (Wicher et al., 2008). Orco also serves other functions besides being a metabotropic ion channel, e.g., playing a crucial role in regulating the transportation to the OSN membrane and the dendritic localisation of the Or-Orco complex (Benton et al., 2006; Larsson et al., 2004),(Benton et al., 2006; Larsson et al., 2004),(Benton et al., 2006; Larsson et al., 2004). Another function of Orco is that of regulating the spontaneous activity of the OSN by acting as a pacemaker (Stengl & Funk, 2013). This is important, as the ability to provide temporal encoding carries both quantitative and qualitative information about an odorant, which, when generating neuronal spiking, is sent to the brain and carries meaningful information triggering a certain behaviour (Deng et al., 2011; Stengl & Funk, 2013).

Several ancestral basal insect species, such as the jumping bristle tail Machilis hrabei, which diverged early in the main evolutionary lineage of insects, lack Orco and instead form a homotetrameric ion channel composed of only divergent Ors, which, in the presence of a ligand, opens the pore to elicit an ion flux (Del Mármol et al., 2021; Thoma et al., 2019). Many insects, mainly winged, however, do not form Or homotetramers but instead a heterotetrameric ion channel between divergent Ors and the conserved Orco in a 1:3 stoichiometric configuration (Butterwick et al., 2018; J. Zhao et al., 2024). As this ion channel is ligand-gated, when a ligand binds to the Or, a conformational change is induced in the structure of the complex, resulting in the opening of the ion channel (J. Zhao et al., 2024).

Structurally, the amino acid sequence dictates the folding of a protein, which is more diverse for Ors than that of Orco, theoretically leading to more diverse tuning receptors. It is thought that a cognate ligand binds to the tuning Or via a binding pocket that changes morphology after the molecular structure of the ligand (Del Mármol et al., 2021). However, it was found that M. hrabei Or5 binds both the natural ligand eugenol, as well as the synthetic ligand DEET (diethyltoluamide), in the same site, with the same amino acids interacting with the ligand despite these compounds having different properties and size (Del Mármol et al., 2021). This implies that an Or that has evolved to bind a natural ligand can also be activated by a manmade synthetic agonist that is very different in size and chemical properties. Changing the amino acid sequence predictably changes how the protein interacts with these ligands as well. It was observed that substituting a certain amino acid, M209, from methionine to valine or alanine, increased the binding affinity for DEET and reduced it for eugenol (Del Mármol et al., 2021). This may suggest that the layout of the binding pocket dictates the affinity of the ligand, as methionine is a larger amino acid compared to valine or alanine, while eugenol is a smaller molecule than DEET, together suggesting that the space in the binding pocket is suboptimal for the smaller molecule. This kind of substitution is not unique to MhrOr5 but has been demonstrated in other insect Ors as well (Franco et al., 2022; Hill et al., 2015; Leary et al., 2012; Yang et al., 2017).

Selection pressure affects binding affinity of Ors, ultimately affecting the coding by Ors and dictates how and what an insect can sense in terms of odours (Hansson & Stensmyr, 2011). The first functional characterisation of an Or repertoire, in *D. melanogaster*, revealed that at high dilutions many receptors have a tendency to respond to a variety of chemical compounds of different size, electric charge or inductive properties potentially showing widely tuned receptors (Hallem & Carlson, 2006). Later a large part of the *Anopheles gambiae* Or repertoire was characterised also showing that a single receptor responds to several ligands, including esters, alcohols, aldehydes or aromatic compounds (Carey et al., 2010). These studies, however, have a couple of unfavourable traits for the functional characterisation of Or genes to ecologically relevant ligands. Among these is the use of quite high concentrations, which are unlikely to be the ecologically relevant amounts that the insects are exposed to in their everyday lives. More recently, there have been two additional studies that have functionally characterised Or repertoires, in *Locusta migratoria* (Chang et al., 2023) and *Spodoptera littoralis* (de Fouchier et al., 2017). The Or repertoire of *L. migratoria* shows low redundancy, compared to other species tested, when exposed to ecologically relevant compounds at relevant concentration levels with receptors usually responding to only one or a few compounds that are of similar size, charge or have same characteristics (Chang et al., 2023). For the moth *S. littoralis*, a similar trend can be seen with a few exceptions (de Fouchier et al., 2017). Lastly, two studies in *Anopheles coluzzii*, in which Omondi et al exposed a set of Ors to headspace collections of human and floral odours showing high specificity in certain receptors to some compounds, usually with only one or two compounds eliciting a response, while a few receptors are more promiscuous in their response patterns (A. B. Omondi et al., 2019; B. A. Omondi et al., 2026).

Not only did the studies in *L. migratoria* and *A. coluzzii* expose the insects to ecologically-relevant compounds, but also at physiologically relevant levels. A potential explanation for why the cognate ligands have been missed in previous studies could be that most receptors are specialists (narrowly tuned), but that there are generalists which respond to the compounds of similar size, electric charge or inductive properties, such as esters, acids, indoles, aldehydes, and hydrocarbons. (Ignell & Hansson, 2004). The studies in *L. migratoria* and *A. coluzzii* showed that at ecologically relevant levels, there seems to be more specificity, in which receptors are more narrowly tuned compared to the older studies (Chang et al., 2023; A. B. Omondi et al., 2019; B. A. Omondi et al., 2026). While the understanding of the determinants of receptor tuning remains incomplete, it may reflect a variation of the canonical concept of combinatorial coding, where an odour is represented by patterns of activity across multiple receptors rather than by a single dedicated receptor (Andersson et al., 2015). Alternatively, information may be conveyed by narrowly tuned Ors through labelled-line coding, in which specific receptor-neuron pathways are specialised for detecting single biologically relevant cues (Stensmyr et al., 2012). Whether this concept is valid for mosquitoes is currently debated, as there is accumulating evidence suggesting co-expression of chemosensory receptors in single OSNs.

4. Co-expression and redundancy of chemosensory receptors in dipterans

There has long been a canonical view regarding odour coding in insects, in that each OSN expresses a single receptor class, and these in turn innervate the same glomerulus in the AL (Infobox C) (Couto et al., 2005; Gao et al., 2000; Laissue et al., 1999). Historically, this leads to two modes of odour coding in the insect. In the first mode, named labelled lines, a single narrowly tuned chemosensory receptor is expressed in a single class of OSN, which innervates a single glomerulus (Figure 2a). Some chemical signals, such as pheromones, attract only conspecifics of the opposite sex and so is a unique signalling cue for the conspecific to detect (Christensen & Hildebrand, 1987). However, since these compounds are so distinct they can also be detected by an individual that wants to avoid the individual (Kempraj et al., 2020) or its offspring, such is the case for a genus of parasitoid wasp, which oviposit and kill *Drosophila* larvae (Ebrahim et al., 2015). This, however, has a considerable downside due to the narrow specificity of the receptor: the insect is only able to sense as many ligands as it has receptors for. For the insect to get around this, insects can use combinatorial coding. In this kind of encoding, a ligand activates a unique complement of more broadly tuned receptors and thus activates a unique combination of glomeruli (Kreher et al., 2008). While combinatorial coding most likely is utilised by most insects, it is well suited for polyphagous insects for example, moths, such as *S. littoralis*, that feed on a large number of different plants (Salama et al., 1971) or mosquitoes that feed on different types of resources (Hill & Ignell, 2021) due to the diverse odour landscape necessary to be navigated. An organisation like this has traditionally held true for certain species, such as *A. mellifera* (Flanagan & Mercer, 1989), *Manduca sexta* (Grosse-Wilde et al., 2011) and *D. melanogaster* (Benton et al., 2009; Laissue et al., 1999). However, as described below, more recent research hypothesises variation among species in regards to how odour coding works.

It has been known for over a decade that *Aedes aegypti* expresses almost twice as many Ors (~130) (J. Bohbot et al., 2007; Matthews et al., 2016) in olfactory tissues as there are olfactory glomeruli in their brain (~60-80) (Ignell et al., 2005; Shankar & McMeniman, 2020; Z. Zhao et al., 2022). This clear mismatch of Ors to glomeruli leads to the hypothesis of co-expression and co-option of receptors in single OSNs, thereby challenging the canonical view (Adavi et al., 2024). Co-expression and co-option of receptors is not limited to Ors, as Ors co-express with Irs, and moreover, Irs co-express with each other and with Grs (Figure 2). More specifically, OSNs were previously thought to express a single receptor type. However, emerging evidence is pointing towards the expression of multiple Or +

Orco classes together with Irs and potentially Grs in the maxillary palps of *Ae. aegypti* (Adavi et al., 2024; Herre et al., 2022) as well as for co-reception of Or + Orco classes in *A. gambiae* (Karner et al., 2015). Similar expression patterns have been observed in the model organism *D. melanogaster*, *Drosophila sechellia* and *A. coluzzii*, where it was shown that Ors and Orco co-express with the Ir co-receptors Ir8a, Ir25a and Ir76b, for example, Ir25a is co-expressed in ~88% and Orco in ~82% of all olfactory sensory neurons and that they innervate at the same glomeruli in the antennal lobe (Task et al., 2022).

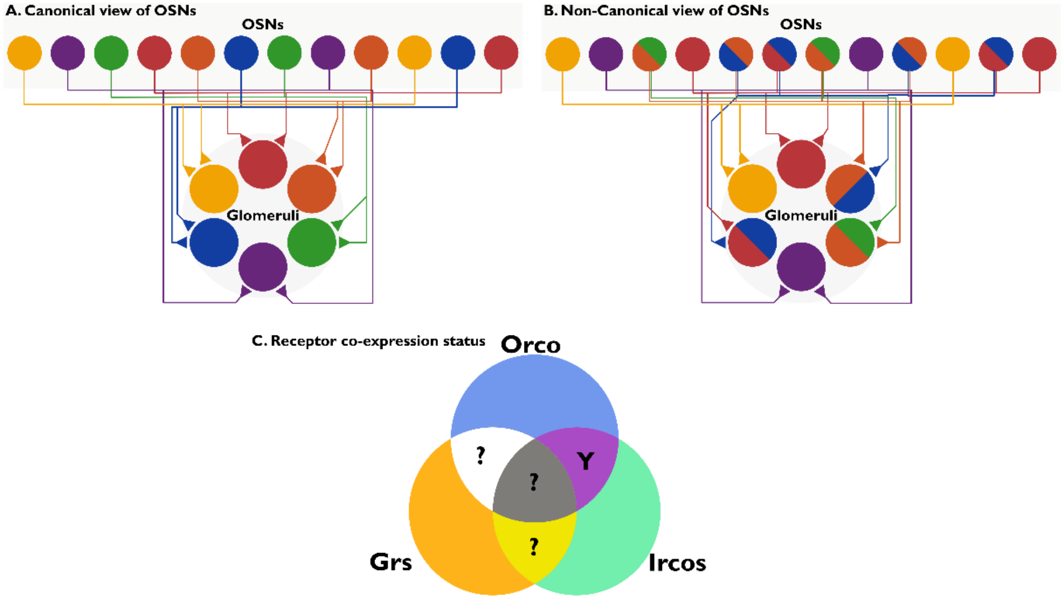

Figure 2. Odor coding schematic of insect olfactory sensory neurons

For insects filling ecological niches with complex chemosensory landscapes, there may be many reasons for the co-expression of members of different chemosensory gene families in a single OSN instead of the expression of a single receptor type. Receptor co-expression could allow robust mosquito attraction to humans by detection of redundant cues that are present in human odour, which is made up of a blend of compounds sometimes in the hundreds (Bernier et al., 1999). Furthermore, redundancy could be used for the rapid detection of specific odour blends or ratios of individual components in a blend, as the processing of this information would no longer rely on subsequent layers of processing in the higher processing centres (Rauscher & Wolff, 2023). An example of this is the host-seeking behaviour of *Ae. aegypti*, which is highly anthropophilic, and where attraction is mediated by two appendages, the antennae for which the odor coding has not been functionally characterised but if similar to another highly anthropophilic species *A. gambiae* sense a wide spectrum of odorants (Carey et al., 2010; Chen et al., 2019) and the maxillary palp which respond to fewer odorants and is also highly sensitive to CO2 (J. D. Bohbot & Dickens, 2009; Gillies, 1980; Grant et al., 1995). Studies demonstrating that knockout mutants of either Orco or certain Grs sensitive to CO2 specifically retain attraction towards human hosts indicates a robust system for host seeking in this mosquito species (McMeniman et al., 2014; Z. Zhao et al., 2022). There is evidence pointing towards the co-expression of several chemosensory receptors in *Ae. aegypti*, for example, Ir co-receptors being expressed in all Orco- and AaegGr3-positive sensory neurons, which is believed to expand the functional responses of the OSNs in which these receptors are expressed (Herre et al., 2022). It is possible that this co-expression of receptors allows for a redundant function to strengthen the attraction towards human hosts for the different volatile cues they emanate (Herre et al., 2022). Furthermore, it is hypothesised that co-expressed receptors, tuned to similar ligands at different concentration ranges, could extend the dynamic range of an OSN (Rauscher & Wolff, 2023).

5. Evolution of odorant receptors in insects

Contemporary and ancient insect Ors are theorised to have evolved from Grs, with Orco as a basal lineage (Robertson et al., 2003). Insect Grs have been described as distant relatives and linked to homologs in other animals, as well as in protists, fungi and plants, which links the ancient receptor family to many more organisms than previously thought (Robertson, 2015). The common ancestor linking insect Ors and Grs are referred to as gustatory receptor-like (GRL), and have through phylogenetic relationships been identified in vastly taxonomically different taxa (Benton et al., 2020).

Terrestrialisation of insects is regarded as the origin of the evolution of insect Ors, over 400 million years ago (Brand et al., 2018; Engel & Grimaldi, 2004). This historical event diverged the hexapods, which later evolved into insects from crustaceans (Robertson et al., 2003). A study by Brand et al. (2018), partially built on (Missbach et al., 2014), concluded that Ors have been present in most ancestors of insects since this divergence event. These studies demonstrate the evolution of insect Ors from the ancient Collembola (springtails), Diplura (two-pronged bristletails) and Archaeognatha (jumping bristletails), with the prior two not being part of Insecta, to the more contemporary neopteran insects. When looking at these findings, there seems to be a clear evolutionary point in time at which Ors evolved, around 400 million years ago (Figure 3). Annotated genomes of ancient hexapods, e.g., Collembola and Diplura, lack genes encoding for Ors, but do contain genes encoding for Irs (Figure 3). Ors and Orco seem to have evolved in Archeognatha and Zygentoma (silverfish), respectively, as they are missing in the genomes of more ancient hexapods; both orders are within the wingless insects (Apterygota), dismissing Missbach's initial claim that only winged insects have evolved Ors.

Looking at the evolutionary timeline, a widening of Or repertoires in more evolved insects compared to their predecessors can be observed (Figure 3). In terrestrial insects, for example, jumping bristletails, such as M. hrabei, five genes encode Ors, but not Orco (Figure 3), while the genome of another ancient but more evolved insect, the firebrat, Thermobia domestica, contains a much larger repertoire of 43 Ors and a gene encoding for Orco (Figure 3), and which also have an amino acid sequence similar to contemporary neopteran insects (Brand et al., 2018; Missbach et al., 2014). The same kind of evolutionary pattern with presence and absence can be seen when looking at ancient flying insects and comparing them to their more evolved counterparts. Ladona fulva is a dragonfly that has three genes encoding for Ors and one for Orco, and, in contrast, the slightly more evolved mayfly Ephemera danica encodes 46 Ors and has one gene encoding for Orco (Ioannidis et al., 2017), pointing towards the absence of ancient Ors in the ancestral dragonflies and potentially a dependence on other sensory inputs, such as vision, rather than olfaction. This lack of ancestral Ors could be due to the reduction or loss of Ors that were independent of Orco, as in basal insects, such as *M. hrabei*. This species appears to lack an Orco ortholog yet subsequently evolved Orco-dependent Ors following the emergence of Orco (Brand et al., 2018; Thoma et al., 2019). These studies provide an overview of the evolution of Ors from the terrestrialisation of insects. In summary, when the insects were solely terrestrial, only a handful of Ors and Irs appear to have been necessary, but as time passed, more complex or different niches might have needed to be filled, and so more advanced olfactory systems evolved due to the selective pressure of the new niche. Moreover, when insects became capable of flight, they possibly came into contact with more volatile compounds going through the air instead of being close to the ground, with some exceptions like *L. fulva*.

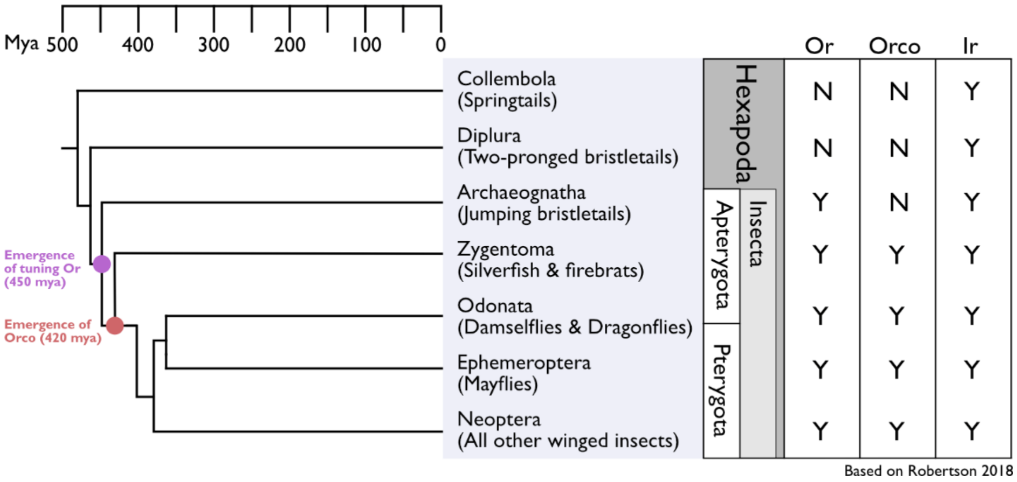

Figure 3. Phylogeny of the emergence of tuning Ors, Orco as well as Irs across the last 500 million years (mya).

6. Birth and death of odorant receptors

Genes encoding the diverse Ors are believed to evolve through something called the birth-and-death evolutionary model (Nei et al., 2008). This model implies that if a gene coding for an Or mutates and the new receptor has a different function than the predecessor, and fitness is increased in the individual, then this increases the selective pressure positively for this change, and so a new gene is “born”. In contrast, if the new gene, and therefore receptor, has a detrimental impact on the fitness of an individual, it will not be selected for and so become a non-functional pseudogene. Pseudogenes are genetic sequences that resemble functional genes, but due to degeneration, exhibit features that render them non-functional. Pseudogenes are considered “junk DNA”, and although rare in insects, such as *D. melanogaster*, when compared to vertebrates (Harrison et al., 2003), pseudogenes are still bloating the genome and are not subject to natural selection, which is not necessarily detrimental but non-beneficial to the animal (Balakirev & Ayala, 2003). This kind of process, when repeated many times over a long stretch of time, contributes to the large variety of Or genes. This evolution of new Or genes enables insects to fill niches and adapt quickly to new environments, speaking in relative terms.

In *Drosophila*, estimates of birth-and-death rates of genes have been conducted by calculating the number of birth-and-death changes per gene and million years. Across *Drosophila* as a whole, an estimated ~17 new gene gains or ~17 losses occur every one million years during the evolution of a certain species in the family (Hahn et al., 2007). What is interesting is that the rates for chemosensory genes are considerably higher when compared to other gene families and to the entire genome (Hahn et al., 2007). For example, for Ors, there is a gain or loss every 3 million years, which at first glance does not seem to be high, but as the family of Ors in *D. melanogaster* is ~60 genes compared to the entire genome of 14.000 genes, the rate is very high (Eirín-López et al., 2012; Hahn et al., 2007; McBride et al., 2007). This leads to many rapid changes in the gene family, making it possible for insects to adapt relatively easily, but this also means that the genome runs the risk of generating non-functional pseudogenes.

The effects of birth and death evolution can have a slight but important impact on Ors, changing the function and structure of the protein structure as well as affecting the tuning. As birth and death evolution changes genes that encode proteins, such as Ors, there is a change in their amino acid sequence either by deletion, addition or substitution of amino acids (Hill et al., 2015). This change in sequence has the possibility to alter the function of the receptor and therefore changing the affinity towards or against ligands. *Culex quinquefasciatus* is known as the southern house mosquito and is a vector of various mosquito-borne diseases, e.g., Zika and Western

Equine encephalitis virus. *C. quinquefasciatus* expresses two specific receptors, CqOr113 and Cq118, that are tuned towards 1-octen-3-ol and that are homologous to *A. gambiae* and *Ae. aegypti* Or8 (Grant et al., 1995). The *C. quinquefasciatus* CqOr113 and Cq118 receptors have high shared identity except at the C-terminus, where they differ with a seven amino acid insertion, four amino acid substitutions, as well as a deletion of the entire predicted extracellular C-terminus of CqOr113 (Hill et al., 2015). This slight difference in receptor structure due to birth and death evolution enhances the receptor's tuning towards the S enantiomer of 1-octen-3-ol instead of the R enantiomer, both when tested in vivo and in vitro (Hill et al., 2015). This highlights and merges the importance of stereochemistry with receptor function and birth and death evolution, and it is this kind of evolution that gives rise to rapid ligand specificity change and, in turn, diversity of Ors due to the adaptations to the ecological niches of insects.

7. Conclusions

Odorant receptors are part of a complex machinery that makes up the chemosensory system of an insect. From the molecular interactions between the receptor itself and its ligand to the signalling of these interactions to the brain, to the evolution of the various components involved in this machinery. There are a lot of truths regarding Ors remaining to be found and explored so that the research community can develop a better understanding of them and develop tools against insects that are detrimental to us as humans, as well as benefit the ones who do us good through the utilisation of their olfactory systems. While we have a general understanding of the structure and function of Ors, there is a need to delve deeper into these topics, as well as the expression and co-expression of these receptors in conjunction with other chemosensory receptors, as well as mapping the functional genomics of Ors in more species than the few that have been done.

8. References

Abuin, L., Bargeton, B., Ulbrich, M. H., Isacoff, E. Y., Kellenberger, S., & Benton, R. (2011). Functional architecture of olfactory ionotropic glutamate receptors. Neuron, 69(1), 44–60.

Adams, M. D., Celniker, S. E., Holt, R. A., Evans, C. A., Gocayne, J. D., Amanatides, P. G., Scherer, S. E., Li, P. W., Hoskins, R. A., Galle, R. F., George, R. A., Lewis, S. E., Richards, S., Ashburner, M., Henderson, S. N., Sutton, G. G., Wortman, J. R., Yandell, M. D., Zhang, Q., … Venter, J. C. (2000). The genome sequence of Drosophila melanogaster. Science (New York, N.Y.), 287(5461), 2185–2195.

Adavi, E. D., Dos Anjos, V. L., Kotb, S., Metz, H. C., Tian, D., Zhao, Z., Zung, J. L., Rose, N. H., & McBride, C. S. (2024). Olfactory receptor coexpression and co-option in the dengue mosquito. In bioRxivorg (p. 2024.08.21.608847). https://doi.org/10.1101/2024.08.21.608847

Andersson, M. N., LÃ¶fstedt, C., & Newcomb, R. D. (2015). Insect olfaction and the evolution of receptor tuning. Frontiers in Ecology and Evolution, 3, 145054.

Balakirev, E. S., & Ayala, F. J. (2003). Pseudogenes: are they “junk” or functional DNA? Annual Review of Genetics, 37(1), 123–151.

Benton, R., Dessimoz, C., & Moi, D. (2020). A putative origin of the insect chemosensory receptor superfamily in the last common eukaryotic ancestor. eLife, 9. https://doi.org/10.7554/eLife.62507

Benton, R., Sachse, S., Michnick, S. W., & Vosshall, L. B. (2006). Atypical membrane topology and heteromeric function of Drosophila odorant receptors in vivo. PLoS Biology, 4(2), e20.

Benton, R., Vannice, K. S., Gomez-Diaz, C., & Vosshall, L. B. (2009). Variant ionotropic glutamate receptors as chemosensory receptors in Drosophila. Cell, 136(1), 149–162.

Bernier, U. R., Booth, M. M., & Yost, R. A. (1999). Analysis of human skin emanations by gas chromatography/mass spectrometry. 1. Thermal desorption of attractants for the yellow fever mosquito (Aedes aegypti) from handled glass beads. Analytical Chemistry, 71(1), 1–7.

Bohbot, J. D., & Dickens, J. C. (2009). Characterization of an enantioselective odorant receptor in the yellow fever mosquito Aedes aegypti. PloS One, 4(9), e7032.

Bohbot, J., Pitts, R. J., Kwon, H.-W., Rützler, M., Robertson, H. M., & Zwiebel, L. J. (2007). Molecular characterization of the Aedes aegypti odorant receptor gene family. Insect Molecular Biology, 16(5), 525–537.

Brand, P., Robertson, H. M., Lin, W., Pothula, R., Klingeman, W. E., Jurat-Fuentes, J. L., & Johnson, B. R. (2018). The origin of the odorant receptor gene family in insects. eLife, 7. https://doi.org/10.7554/eLife.38340

Butterwick, J. A., Del Mármol, J., Kim, K. H., Kahlson, M. A., Rogow, J. A., Walz, T., & Ruta, V. (2018). Cryo-EM structure of the insect olfactory receptor Orco. Nature, 560(7719), 447–452.

Cameron, P., Hiroi, M., Ngai, J., & Scott, K. (2010). The molecular basis for water taste in Drosophila. Nature, 465(7294), 91–95.

Carey, A. F., Wang, G., Su, C.-Y., Zwiebel, L. J., & Carlson, J. R. (2010). Odorant reception in the malaria mosquito Anopheles gambiae. Nature, 464(7285), 66–71.

Chang, H., Unni, A. P., Tom, M. T., Cao, Q., Liu, Y., Wang, G., Llorca, L. C., Brase, S., Bucks, S., Weniger, K., Bisch-Knaden, S., Hansson, B. S., & Knaden, M. (2023). Odorant detection in a locust exhibits unusually low redundancy. Current Biology, 33(24), 5427–5438.e5.

Chen, Z., Liu, F., & Liu, N. (2019). Human odour coding in the yellow fever mosquito, Aedes aegypti. Scientific Reports, 9(1), 13336.

Chen, Z., Wang, Q., & Wang, Z. (2010). The amiloride-sensitive epithelial Na+ channel PPK28 is essential for drosophila gustatory water reception. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 30(18), 6247–6252.

Christensen, T. A., & Hildebrand, J. G. (1987). Male-specific, sex pheromone-selective projection neurons in the antennal lobes of the moth Manduca sexta. Journal of Comparative Physiology. A, Sensory, Neural, and Behavioral Physiology, 160(5), 553–569.

Clyne, P. J., Warr, C. G., & Carlson, J. R. (2000). Candidate taste receptors in Drosophila. Science (New York, N.Y.), 287(5459), 1830–1834.

Clyne, P. J., Warr, C. G., Freeman, M. R., Lessing, D., Kim, J., & Carlson, J. R. (1999). A novel family of divergent seven-transmembrane proteins: candidate odorant receptors in Drosophila. Neuron, 22(2), 327–338.

Couto, A., Alenius, M., & Dickson, B. J. (2005). Molecular, anatomical, and functional organization of the Drosophila olfactory system. Current Biology: CB, 15(17), 1535–1547.

Croset, V., Rytz, R., Cummins, S. F., Budd, A., Brawand, D., Kaessmann, H., Gibson, T. J., & Benton, R. (2010). Ancient protostome origin of chemosensory ionotropic glutamate receptors and the evolution of insect taste and olfaction. PLoS Genetics, 6(8), e1001064.

Dahanukar, A., Lei, Y.-T., Kwon, J. Y., & Carlson, J. R. (2007). Two Gr genes underlie sugar reception in Drosophila. Neuron, 56(3), 503–516.

Dall, S. R. X., Giraldeau, L.-A., Olsson, O., McNamara, J. M., & Stephens, D. W. (2005). Information and its use by animals in evolutionary ecology. Trends in Ecology & Evolution, 20(4), 187–193.

de Fouchier, A., Walker, W. B., 3rd, Montagné, N., Steiner, C., Binyameen, M., Schlyter, F., Chertemps, T., Maria, A., François, M.-C., Monsempes, C., Anderson, P., Hansson, B. S., Larsson, M. C., & Jacquin-Joly, E. (2017). Functional evolution of Lepidoptera olfactory receptors revealed by deorphanization of a moth repertoire. Nature Communications, 8(1), 15709.

Del Mármol, J., Yedlin, M. A., & Ruta, V. (2021). The structural basis of odorant recognition in insect olfactory receptors. Nature, 597(7874), 126–131.

Deng, Y., Zhang, W., Farhat, K., Oberland, S., Gisselmann, G., & Neuhaus, E. M. (2011). The stimulatory Gα(s) protein is involved in olfactory signal transduction in Drosophila. PloS One, 6(4), e18605.

Dennis, E. J., Goldman, O. V., & Vosshall, L. B. (2019). Aedes aegypti mosquitoes use their legs to sense DEET on contact. Current Biology: CB, 29(9), 1551–1556.e5.

Dethier, V. G. (1976). The hungry fly: A physiological study of the behavior associated with feeding. The Hungry Fly: A Physiological Study of the Behavior Associated with Feeding. https://psycnet.apa.org/record/1976-27370-000

Dougherty, M. J., Guerin, P. M., & Ward, R. D. (1995). Identification of oviposition attractants for the sandfly Lutzomyia longipalpis (Diptera: Psychodidae) in volatiles of faeces from vertebrates. Physiological Entomology, 20(1), 23–32.

Dunipace, L., Meister, S., McNealy, C., & Amrein, H. (2001). Spatially restricted expression of candidate taste receptors in the Drosophila gustatory system. Current Biology, 11(11), 822–835.

Ebrahim, S. A. M., Dweck, H. K. M., Stökl, J., Hofferberth, J. E., Trona, F., Weniger, K., Rybak, J., Seki, Y., Stensmyr, M. C., Sachse, S., Hansson, B. S., & Knaden, M. (2015). Drosophila avoids parasitoids by sensing their semiochemicals via a dedicated olfactory circuit. PLoS Biology, 13(12), e1002318.

Eirín-López, J. M., Rebordinos, L., Rooney, A. P., & Rozas, J. (2012). The birth-and-death evolution of multigene families revisited. Genome Dynamics, 7, 170–196.

Engel, M. S., & Grimaldi, D. A. (2004). New light shed on the oldest insect. Nature, 427(6975), 627–630.

Flanagan, D., & Mercer, A. R. (1989). An atlas and 3-D reconstruction of the antennal lobes in the worker honey bee, Apis mellifera L. (Hymenoptera : Apidae). International Journal of Insect Morphology and Embryology, 18(2-3), 145–159.

Fowler, M. A., & Montell, C. (2013). Drosophila TRP channels and animal behavior. Life Sciences, 92(8-9), 394–403.

Franco, F. P., Xu, P., Harris, B. J., Yarov-Yarovoy, V., & Leal, W. S. (2022). Single amino acid residue mediates reciprocal specificity in two mosquito odorant receptors. eLife, 11(e82922). https://doi.org/10.7554/eLife.82922

Gao, Q., & Chess, A. (1999). Identification of candidate Drosophila olfactory receptors from genomic DNA sequence. Genomics, 60(1), 31–39.

Gao, Q., Yuan, B., & Chess, A. (2000). Convergent projections of Drosophila olfactory neurons to specific glomeruli in the antennal lobe. Nature Neuroscience, 3(8), 780–785.

Gillies, M. T. (1980). The role of carbon dioxide in host-finding by mosquitoes (Diptera: Culicidae): a review. Bulletin of Entomological Research, 70(4), 525–532.

Grant, A. J., Wigton, B. E., Aghajanian, J. G., & O’Connell, R. J. (1995). Electrophysiological responses of receptor neurons in mosquito maxillary palp sensilla to carbon dioxide. Journal of Comparative Physiology. A, Sensory, Neural, and Behavioral Physiology, 177(4), 389–396.

Grosse-Wilde, E., Kuebler, L. S., Bucks, S., Vogel, H., Wicher, D., & Hansson, B. S. (2011). Antennal transcriptome of Manduca sexta. Proceedings of the National Academy of Sciences of the United States of America, 108(18), 7449–7454.

Hahn, M. W., Han, M. V., & Han, S.-G. (2007). Gene family evolution across 12 Drosophila genomes. PLoS Genetics, 3(11), e197.

Hallem, E. A., & Carlson, J. R. (2006). Coding of Odors by a Receptor Repertoire. Cell, 125(1), 143–160.

Hansson, B. S., & Stensmyr, M. C. (2011). Evolution of insect olfaction. Neuron, 72(5), 698–711.

Harrison, P. M., Milburn, D., Zhang, Z., Bertone, P., & Gerstein, M. (2003). Identification of pseudogenes in the Drosophila melanogaster genome. Nucleic Acids Research, 31(3), 1033–1037.

Heads, P. A. (1985). The effect of invertebrate and vertebrate predators on the foraging movements of Ischnura elegans larvae (Odonata: Zygoptera). Freshwater Biology, 15(5), 559–571.

Herre, M., Goldman, O. V., Lu, T.-C., Caballero-Vidal, G., Qi, Y., Gilbert, Z. N., Gong, Z., Morita, T., Rahiel, S., Ghaninia, M., Ignell, R., Matthews, B. J., Li, H., Vosshall, L. B., & Younger, M. A. (2022). Non-canonical odor coding in the mosquito. Cell, 185(17), 3104–3123.e28.

Hill, S. R., & Ignell, R. (2021). Modulation of odour-guided behaviour in mosquitoes. Cell and Tissue Research, 383(1), 195–206.

Hill, S. R., Majeed, S., & Ignell, R. (2015). Molecular basis for odorant receptor tuning: a short C-terminal sequence is necessary and sufficient for selectivity of mosquito Or8: Basis of odorant receptor ligand selection in Or8. Insect Molecular Biology, 24(4), 491–501.

Ignell, R., Dekker, T., Ghaninia, M., & Hansson, B. S. (2005). Neuronal architecture of the mosquito deutocerebrum. The Journal of Comparative Neurology, 493(2), 207–240.

Ignell, R., & Hansson, B. (2004). Insect olfactory neuroethology – An electrophysiological perspective. In T. A. Christensen (Ed.), Methods in Insect Sensory Neuroscience (pp. 319–347). CRC Press.

Ioannidis, P., Simao, F. A., Waterhouse, R. M., Manni, M., Seppey, M., Robertson, H. M., Misof, B., Niehuis, O., & Zdobnov, E. M. (2017). Genomic features of the damselfly Calopteryx splendens representing a sister clade to most insect orders. Genome Biology and Evolution, 9(2), 415–430.

Jiao, Y., Moon, S. J., & Montell, C. (2007). A Drosophila gustatory receptor required for the responses to sucrose, glucose, and maltose identified by mRNA tagging. Proceedings of the National Academy of Sciences of the United States of America, 104(35), 14110–14115.

Jones, P. L., Pask, G. M., Rinker, D. C., & Zwiebel, L. J. (2011). Functional agonism of insect odorant receptor ion channels. Proceedings of the National Academy of Sciences of the United States of America, 108(21), 8821–8825.

Karner, T., Kellner, I., Schultze, A., Breer, H., & Krieger, J. (2015). Co-expression of six tightly clustered odorant receptor genes in the antenna of the malaria mosquito Anopheles gambiae. Frontiers in Ecology and Evolution, 3, 134855.

Kellenberger, S., & Schild, L. (2002). Epithelial sodium channel/degenerin family of ion channels: a variety of functions for a shared structure. Physiological Reviews, 82(3), 735–767.

Keller, A., & Vosshall, L. B. (2016). Olfactory perception of chemically diverse molecules. BMC Neuroscience, 17(1), 55.

Kempraj, V., Park, S. J., & Taylor, P. W. (2020). Forewarned is forearmed: Queensland fruit flies detect olfactory cues from predators and respond with predator-specific behaviour. Scientific Reports, 10(1), 7297.

Kreher, S. A., Mathew, D., Kim, J., & Carlson, J. R. (2008). Translation of sensory input into behavioral output via an olfactory system. Neuron, 59(1), 110–124.

Kwon, Y., Kim, S. H., Ronderos, D. S., Lee, Y., Akitake, B., Woodward, O. M., Guggino, W. B., Smith, D. P., & Montell, C. (2010). Drosophila TRPA1 channel is required to avoid the naturally occurring insect repellent citronellal. Current Biology: CB, 20(18), 1672–1678.

Laissue, P. P., Reiter, C., Hiesinger, P. R., Halter, S., Fischbach, K. F., & Stocker, R. F. (1999). Three-dimensional reconstruction of the antennal lobe in Drosophila melanogaster. The Journal of Comparative Neurology, 405(4), 543–552.

Larsson, M. C., Domingos, A. I., Jones, W. D., Chiappe, M. E., Amrein, H., & Vosshall, L. B. (2004). Or83b encodes a broadly expressed odorant receptor essential for Drosophila olfaction. Neuron, 43(5), 703–714.

Leary, G. P., Allen, J. E., Bunger, P. L., Luginbill, J. B., Linn, C. E., Jr, Macallister, I. E., Kavanaugh, M. P., & Wanner, K. W. (2012). Single mutation to a sex pheromone receptor provides adaptive specificity between closely related moth species. Proceedings of the National Academy of Sciences of the United States of America, 109(35), 14081–14086.

Levy, N. S., Bakalyar, H. A., & Reed, R. R. (1991). Signal transduction in olfactory neurons. The Journal of Steroid Biochemistry and Molecular Biology, 39(4B), 633–637.

Lin, H., Mann, K. J., Starostina, E., Kinser, R. D., & Pikielny, C. W. (2005). A Drosophila DEG/ENaC channel subunit is required for male response to female pheromones. Proceedings of the National Academy of Sciences of the United States of America, 102(36), 12831–12836.

Liu, L., Leonard, A. S., Motto, D. G., Feller, M. A., Price, M. P., Johnson, W. A., & Welsh, M. J. (2003). Contribution of Drosophila DEG/ENaC genes to salt taste. Neuron, 39(1), 133–146.

Lu, B., LaMora, A., Sun, Y., Welsh, M. J., & Ben-Shahar, Y. (2012). ppk23-Dependent chemosensory functions contribute to courtship behavior in Drosophila melanogaster. PLoS Genetics, 8(3), e1002587.

Matsuura, H., Sokabe, T., Kohno, K., Tominaga, M., & Kadowaki, T. (2009). Evolutionary conservation and changes in insect TRP channels. BMC Evolutionary Biology, 9(1), 228.

Matthews, B. J., McBride, C. S., DeGennaro, M., Despo, O., & Vosshall, L. B. (2016). The neurotranscriptome of the Aedes aegypti mosquito. BMC Genomics, 17(1), 32.

McBride, C. S., Arguello, J. R., & O'Meara, B. C. (2007). Five Drosophila genomes reveal nonneutral evolution and the signature of host specialization in the chemoreceptor superfamily. Genetics, 177(3), 1395–1416.

McMeniman, C. J., Corfas, R. A., Matthews, B. J., Ritchie, S. A., & Vosshall, L. B. (2014). Multimodal integration of carbon dioxide and other sensory cues drives mosquito attraction to humans. Cell, 156(5), 1060–1071.

Miazzi, F., Hansson, B. S., & Wicher, D. (2016). Odor-induced cAMP production in Drosophila melanogaster olfactory sensory neurons. The Journal of Experimental Biology, 219(Pt 12), 1798–1803.

Missbach, C., Dweck, H. K., Vogel, H., Vilcinskas, A., Stensmyr, M. C., Hansson, B. S., & Grosse-Wilde, E. (2014). Evolution of insect olfactory receptors. eLife, 3, e02115.

Montagné, N., de Fouchier, A., Newcomb, R. D., & Jacquin-Joly, E. (2015). Advances in the identification and characterization of olfactory receptors in insects. Progress in Molecular Biology and Translational Science, 130, 55–80.

Montell, C. (2005). The TRP superfamily of cation channels. Science's STKE: Signal Transduction Knowledge Environment, 2005(272), re3.

Moon, S. J., Köttgen, M., Jiao, Y., Xu, H., & Montell, C. (2006). A taste receptor required for the caffeine response in vivo. Current Biology, 16(18), 1812–1817.

Nei, M., Niimura, Y., & Nozawa, M. (2008). The evolution of animal chemosensory receptor gene repertoires: roles of chance and necessity. Nature Reviews. Genetics, 9(12), 951–963.

Newland, P. L. (1998). Avoidance reflexes mediated by contact chemoreceptors on the legs of locusts. Journal of Comparative Physiology. A, Neuroethology, Sensory, Neural, and Behavioral Physiology, 183(3), 313–324.

Omondi, A. B., Ghaninia, M., Dawit, M., Svensson, T., & Ignell, R. (2019). Age-dependent regulation of host seeking in Anopheles coluzzii. Scientific Reports, 9(1), 9699.

Omondi, B. A., Wondwosen, B., Dawit, M., Hill, S. R., & Ignell, R. (2026). Age-dependent perception of floral emissions and the role of CO2 in regulating nectar-seeking in mosquitoes. Scientific Reports, 16(1), 8484.

Pacalon, J., Audic, G., Magnat, J., Philip, M., Golebiowski, J., Moreau, C. J., & Topin, J. (2023). Elucidation of the structural basis for ligand binding and translocation in conserved insect odorant receptor co-receptors. Nature Communications, 14(1), 8182.

Rauscher, M. J., & Wolff, G. H. (2023). Non-canonical odor representation and learning in Dipteran brains. Molecular Psychology: Brain, Behavior, and Society, 2, 6.

Robertson, H. M. (2015). The insect chemoreceptor superfamily is ancient in animals. Chemical Senses, 40(9), 609–614.

Robertson, H. M., Warr, C. G., & Carlson, J. R. (2003). Molecular evolution of the insect chemoreceptor gene superfamily in Drosophila melanogaster. Proceedings of the National Academy of Sciences of the United States of America, 100 Suppl 2(suppl_2), 14537–14542.

Roskies, A., Friedman, G. C., & O'Leary, D. D. (1995). Mechanisms and molecules controlling the development of retinal maps. Perspectives on Developmental Neurobiology, 3(1), 63–75.

Salama, H. S., Dimetry, N. Z., & Salem, S. A. (1971). On the host preference and biology of the cotton leaf worm Spodoptera littoralis Bois. Zeitschrift Für Angewandte Entomologie, 67(1-4), 261–266.

Sato, K., Pellegrino, M., Nakagawa, T., Nakagawa, T., Vosshall, L. B., & Touhara, K. (2008). Insect olfactory receptors are heteromeric ligand-gated ion channels. Nature, 452(7190), 1002–1006.

Shamma, S. A. (2004). Topographic organization is essential for pitch perception. Proceedings of the National Academy of Sciences of the United States of America, 101(5), 1114–1115.

Shankar, S., & McMeniman, C. J. (2020). An updated antennal lobe atlas for the yellow fever mosquito Aedes aegypti. PLoS Neglected Tropical Diseases, 14(10), e0008729.

Städler, E. (1978). CHEMORECEPTION OF HOST PLANT CHEMICALS BY OVIPOSITING FEMALES OF DELIA (HYLEMYA) BRASSICAE. Entomologia Experimentalis et Applicata, 24(3), 711–720.

Stengl, M., & Funk, N. W. (2013). The role of the coreceptor Orco in insect olfactory transduction. Journal of Comparative Physiology. A, Neuroethology, Sensory, Neural, and Behavioral Physiology, 199(11), 897–909.

Stensmyr, M. C., Dweck, H. K. M., Farhan, A., Ibba, I., Strutz, A., Mukunda, L., Linz, J., Grabe, V., Steck, K., Lavista-Llanos, S., Wicher, D., Sachse, S., Knaden, M., Becher, P. G., Seki, Y., & Hansson, B. S. (2012). A conserved dedicated olfactory circuit for detecting harmful microbes in Drosophila. Cell, 151(6), 1345–1357.

Stocker, R. F. (1994). The organization of the chemosensory system in Drosophila melanogaster: a review. Cell and Tissue Research, 275(1), 3–26.

Su, C.-Y., & Wang, J. W. (2014). Modulation of neural circuits: how stimulus context shapes innate behavior in Drosophila. Current Opinion in Neurobiology, 29, 9–16.

Suh, E., Bohbot, J., & Zwiebel, L. J. (2014). Peripheral olfactory signaling in insects. Current Opinion in Insect Science, 6, 86–92.

Task, D., Lin, C.-C., Vulpe, A., Afify, A., Ballou, S., Brbic, M., Schlegel, P., Raji, J., Jefferis, G. S. X. E., Li, H., Menuz, K., & Potter, C. J. (2022). Chemoreceptor co-expression in Drosophila melanogaster olfactory neurons. eLife, 11. https://doi.org/10.7554/eLife.72599

Thoma, M., Missbach, C., Jordan, M. D., Grosse-Wilde, E., Newcomb, R. D., & Hansson, B. S. (2019). Transcriptome surveys in silverfish suggest a multistep origin of the insect odorant receptor gene family. Frontiers in Ecology and Evolution, 7(281), 475054.

Vogt, R. G., & Riddiford, L. M. (1981). Pheromone binding and inactivation by moth antennae. Nature, 293(5828), 161–163.

Vosshall, L. B. (2000). Olfaction in Drosophila. Current Opinion in Neurobiology, 10(4), 498–503.

Vosshall, L. B., Amrein, H., Morozov, P. S., Rzhetsky, A., & Axel, R. (1999). A spatial map of olfactory receptor expression in the Drosophila antenna. Cell, 96(5), 725–736.

Vosshall, L. B., Wong, A. M., & Axel, R. (2000). An olfactory sensory map in the fly brain. Cell, 102(2), 147–159.

Wang, Z., Singhvi, A., Kong, P., & Scott, K. (2004). Taste representations in the Drosophila brain. Cell, 117(7), 981–991.

Wicher, D., & Miazzi, F. (2021). Functional properties of insect olfactory receptors: ionotropic receptors and odorant receptors. Cell and Tissue Research, 383(1), 7–19.

Wicher, D., Schäfer, R., Bauernfeind, R., Stensmyr, M. C., Heller, R., Heinemann, S. H., & Hansson, B. S. (2008). Drosophila odorant receptors are both ligand-gated and cyclic-nucleotide-activated cation channels. Nature, 452(7190), 1007–1011.

Yang, K., Huang, L.-Q., Ning, C., & Wang, C.-Z. (2017). Two single-point mutations shift the ligand selectivity of a pheromone receptor between two closely related moth species. eLife, 6. https://doi.org/10.7554/eLife.29100

Yao, C. A., & Carlson, J. R. (2010). Role of G-proteins in odor-sensing and CO2-sensing neurons in Drosophila. The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 30(13), 4562–4572.

Zhao, J., Chen, A. Q., Ryu, J., & Del Mármol, J. (2024). Structural basis of odor sensing by insect heteromeric odorant receptors. Science (New York, N.Y.), 384(6703), 1460–1467.

Zhao, Z., Zung, J. L., Hinze, A., Kriete, A. L., Iqbal, A., Younger, M. A., Matthews, B. J., Merhof, D., Thiberge, S., Ignell, R., Strauch, M., & McBride, C. S. (2022). Mosquito brains encode unique features of human odour to drive host seeking. Nature, 605(7911), 706–712.