Journal of Physiology - Paris 108 (2014) 96–111

Contents lists available at ScienceDirect

Journal of Physiology - Paris

journal homepage: www.elsevier.com/locate/jphysparis

Review Paper

Morphology and physiology of the olfactory system of blood-feeding insects

F. Guidobaldi [a,b,1], I.J. May-Concha [a,c,*,1], P.G. Guerenstein [a,b]

[a] Laboratorio de Neuroetología Ecológica, CICyTTP-CONICET, Diamante, Entre Ríos, Argentina
[b] Facultad de Ingeniería, UNER, Oro Verde, Entre Ríos, Argentina
[c] Centro Regional de Investigación en Salud Pública (CRISP), Instituto Nacional de Salud Pública (INSP), Tapachula, Chiapas, Mexico

ARTICLE INFO

Article history:
Available online 15 May 2014

Keywords:
Insect olfaction
Hematophagous insects
Disease vectors
Olfactory sensilla
Antennal lobe
Odor mixtures
Odor detection
Odor coding
Olfactory behavior

ABSTRACT

Several blood-feeding (hematophagous) insects are vectors of a number of diseases including dengue, Chagas disease and leishmaniasis which persistently affect public health throughout Latin America. The vectors of those diseases include mosquitoes, triatomine bugs and sandflies. As vector control is an efficient way to prevent these illnesses it is important to understand the sensory biology of those harmful insects. We study the physiology of the olfactory system of those insects and apply that knowledge on the development of methods to manipulate their behavior. Here we review some of the latest information on insect olfaction with emphasis on hematophagous insects. The insect olfactory sensory neurons are housed inside hair-like organs called sensilla which are mainly distributed on the antenna and mouthparts. The identity of many of the odor compounds that those neurons detect are already known in hematophagous insects. They include several constituents of host (vertebrate) odor, sex, aggregation and alarm pheromones, and compounds related to egg-deposition behavior. Recent work has contributed significant knowledge on how odor information is processed in the insect first odor-processing center in the brain, the antennal lobe. The quality, quantity, and temporal features of the odor stimuli are encoded by the neural networks of the antennal lobe. Information regarding odor mixtures is also encoded. While natural mixtures evoke strong responses, synthetic mixtures that deviate from their natural counterparts in terms of key constituents or proportions of those constituents evoke weaker responses. The processing of olfactory information is largely unexplored in hematophagous insects. However, many aspects of their olfactory behavior are known. As in other insects, responses to relevant single odor compounds are weak while natural mixtures evoke strong responses. Future challenges include studying how information about odor mixtures is processed in their brain. This could help develop highly attractive synthetic odor blends to lure them into traps.

Contents

1. Introduction . . . 97
2. The olfactory system . . . 97
   2.1. Morphology of the olfactory system . . . 98
      2.1.1. At the periphery: the insect sensilla . . . 98
      2.1.2. At the central level: the antennal lobe . . . 98
   2.2. Physiology of the olfactory system . . . 99
      2.2.1. Transport of odor molecules . . . 99
      2.2.2. Odor reception . . . 101
      2.2.3. Responses at the peripheral level . . . 102

* Corresponding author at: Laboratorio de Neuroetología Ecológica, CICyTTP-CONICET, Materi y España s/n, Diamante (CP. E3105BWA), Entre Ríos, Argentina. Tel./Fax: +54 343 498 3086/87.
E-mail address: ijmc@cicyttp.org.ar (I.J. May-Concha).
[1] F. Guidobaldi and I.J. May-Concha contributed equally to this work.

http://dx.doi.org/10.1016/j.jphysparis.2014.04.006
0928-4257/

2.2.4. Responses at the central level . . . 103
3. The olfactory behavior . . . 104
3.1. Mosquitoes . . . 104
3.2. Triatomines . . . 105
3.3. Tsetse flies . . . 105
3.4. Sandflies . . . 106
4. Conclusions . . . 106
Acknowledgments . . . 106
References . . . 106

1. Introduction

Hundreds of millions of people suffer from insect-vector borne diseases every year. These diseases mainly include malaria, yellow fever, dengue, Chagas disease, African sleeping sickness and leishmaniasis, which are spread by parasite-infected blood-feeding (hematophagous) insects such as mosquitoes, triatomine bugs, tsetse flies, sandflies (van der Goes van Naters and Carlson, 2006). Many of these diseases, including leishmaniasis, Chagas disease and dengue seriously affect public health throughout Latin America, and according to the World Health Organization vector control is the most effective way to prevent some of these illnesses (WHO, 2010). Thus, an increasing number of research projects in this region focus on methods to monitor and control the insect vectors. In particular, our group is devoted to the study of the morphology and physiology of the olfactory system of these insects (see Guerenstein and Lazzari, 2010), and to the development of odor-baited insect traps (e.g., Guidobaldi and Guerenstein, 2013). Similar traps have already successfully helped fight harmful insects (Foster and Harris, 1997; Oehlschlager et al., 2002). However, to manipulate the behavior of the vector insects efficiently, more work on their sensory biology is necessary. The aim of this manuscript is to review some of the latest information on insect olfaction with emphasis on hematophagous insects, vectors of disease, and highlight future challenges.

2. The olfactory system

Insect vectors heavily rely on their sense of smell to locate hosts, find mates, and select egg-laying ('ovipositing') sites (e.g., Zwiebel and Takken, 2004). For example, *Anopheles gambiae* mosquitoes, vectors of malaria, may detect host volatiles from up to 70 m away the odor source (Kaufmann and Briegel, 2004) while domiciliated triatomine bugs, the vectors of Chagas disease, become activated to search for blood when they sense the CO_2 exhaled by their sleeping hosts (Guerenstein and Lazzari, 2009). Sex and alarm pheromones emitted by adults also play an important role in the biology of triatomine bugs (May-Concha et al., 2013; May-Concha, 2010; Minoli et al., 2013) whereas *Culex quinquefasciatus* mosquitoes, vectors of filariasis and West Nile Virus, are attracted to oviposition sites by a pheromone released from

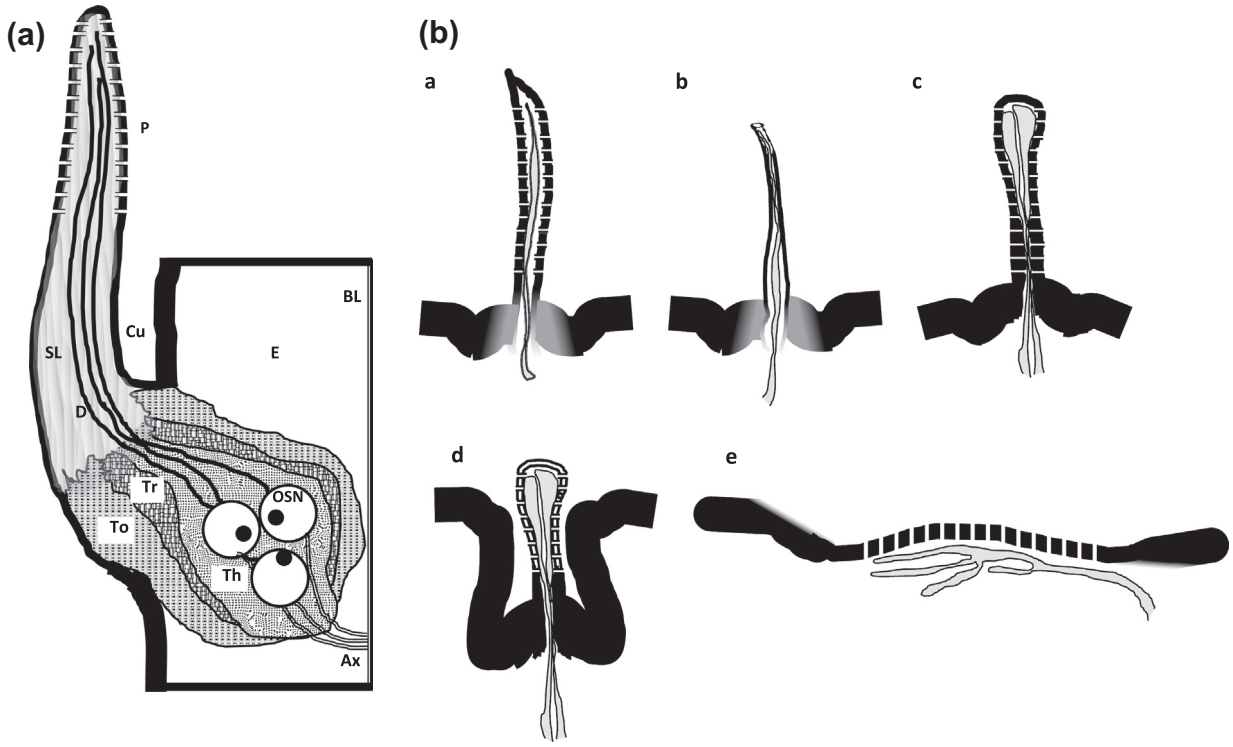

Fig. 1. (**a**) Internal structure of an olfactory sensillum. The sensillum contains one or more olfactory sensory neurons (OSNs) and three accessory cells: thechogen (Th), trichogen (Tr) and tormogen (To) cell.; P, pores; Cu, cuticule; D, dendrites; E, epidermic cell; Ax, axon; BL, basal lamine; SL, sensillum lymph. (**b**) Types of chemosensory sensilla. (a) Multiporous trichoid sensillum (olfactory), (b) uniporous trichoid sensillum (gustatory), (c) basiconical sensillum (olfactory) (d) coeloconical sensillum (olfactory) and (e) hair plate (olfactory).

maturing eggs (Mboera et al., 2000). Progress in the understanding of olfaction in flies, moths, bees and locusts helps rapidly advance the study of olfaction in vector insects, and reciprocally, advances made in mosquitoes are making important contributions to our understanding of other insect systems (Carey and Carlson, 2011).

2.1. Morphology of the olfactory system

2.1.1. At the periphery: the insect sensilla

At the peripheral level, a good part of the sensory system of insects consists of a large number of highly diverse small organs called sensilla (singular: sensillum). According to the sensory modality they sense, sensilla are classified in olfactory, gustatory, mechanosensory, while they could also house hygro- and thermoreceptors. These sensory organs are located in antennae, mouthparts (labial and maxillary palps, and proboscis, a food-sucking tubular appendage), genitalia, legs, wings (de Bruyne and Baker, 2008; Guerenstein and Hildebrand, 2008; Nichols and Vogt, 2008), but it is also possible to find them in other parts of the body (e.g., Catalá, 1995). For example, the maxillary palps of mosquitoes like *An. gambiae* and the labial palps of moths like *Manduca sexta* contain olfactory sensilla that house sensory neurons detecting CO_2 (Guerenstein et al., 2004a; Lu et al., 2007), which in both species is a crucial sensory cue for locating food resources (Guerenstein et al., 2004b; Takken and Knols, 1999; Thom et al., 2004).

Olfactory sensilla are mainly located in antennae and mouthparts and resemble hairs or plates. They have numerous pores in their walls and can house one o more bipolar olfactory sensory neurons (OSNs). The dendrites of the OSNs possess molecular receptors for particular odors. To reach the dendrite membrane, the odor molecules should pass through the sensillum wall pores, a system of channels or tubules, and finally cross the aqueous sensillum lymph that surrounds the dendrites (Steinbrecht and Stankiewicz, 1999; Steinbrecht, 1997; see Section 2.2.1, Fig. 1a). Apart from OSNs each olfactory sensillum contains three accessory cells called thecogen, trichogen and tormogen cell (Keil, 1999); the latter two provide the lymph with adequate ionic concentrations and proteins. While the dendrites of the OSNs extend to the space filled with sensillum lymph, the axon, after joining the antennal nerve, projects to the first processing center of olfactory information in the brain, the antennal lobe (AL; e.g., Anton and Homberg, 1999).

Fig. 1b shows the different morphological types of chemosensory sensilla, including trichoid (olfactory – which are multiporous- or gustatory – with a single pore at the tip), basiconic (olfactory), coeloconic (olfactory, although it may also contain hygro/thermo receptors) and hair plate (olfactory) (Altner, 1977; Altner and Prillinger, 1980). Olfactory sensilla can have a single (trichoid, basiconic and hair plates) or double (coeloconic) wall. The single wall can be thick (trichoid) or thin (basiconic and hair plates). The morphologically different types of olfactory sensilla usually correspond to different functional types. Moreover, within a morphological type functional sub-types may be found (e.g., Diehl et al., 2003). In some cases olfactory sensilla are grouped within a special structure, as in the case of the labial-palp pit organ of moths, which consists of a group of sensilla tuned to CO_2 (Guerenstein et al., 2004a; Guerenstein and Hildebrand, 2008).

The numbers of sensilla and OSNs per antenna vary dramatically among species. For example, the moth *M. sexta* contains >100,000 antennal sensilla housing >250,000 OSNs, whereas ~400 sensilla housing ~1200 OSNs are found in the *Drosophila melanogaster* antenna (Sanes and Hildebrand, 1976; Shanbhag et al., 1999). Larvae of many insect species contain olfactory systems that are simpler than their adult counterparts, perhaps reflecting the functional requirements of the two life stages. Adults often travel long distances following odor cues to find food, mates, or oviposition sites. By contrast, larvae typically hatch from eggs laid directly on or near a food source and do not navigate over long distances (Carey and Carlson, 2011). Sexual dimorphism is striking in some species. For example, female *An. gambiae* mosquitoes possess three to four times more antennal (mostly olfactory) sensilla than males (McIver, 1982). Such dimorphism correlates with the importance of olfactory cues for females to locate their vertebrate hosts (only females feed on blood; Zwiebel and Takken, 2004). The different morphological types of olfactory sensilla have been found in hematophagous insects including *C. quinquefasciatus* (Hill et al., 2009), *Aedes aegypti* mosquitoes (McIver, 1982), *Lutzomyia longipalpis* sandflies (Spegiel et al., 2005), *Cimex lectularius* bed bugs (Harraca et al., 2010) and many others (e.g., *An. gambiae*, Ghaninia et al., 2007a; Pitts et al., 2004). In the case of triatomine bugs several morphological and ultrastructural studies have been carried out (Bernard, 1974; Carbajal de la Fuente et al., 2007; Catalá, 1994; Catalá et al., 2005; Catalá and Schofield, 1994; Diehl et al., 2003; Guerenstein and Guerin, 2001; Moreno et al., 2006; Rodriguez et al., 2009). The bad news is that, unfortunately, different authors adopted different nomenclatures for these structures.

The peripheral olfactory system of insects shows a remarkable morphological diversity. The role of this diversity remains unclear but it probably reflects selection pressures for high sensitivity, phylogenetic and/or developmental constraints, and/other physical environment in which evolution took place, rather than adaptations to detect specific volatile chemicals (Hansson and Stensmyr, 2011).

2.1.2. At the central level: the antennal lobe

As mentioned above, the axons of the OSNs project into the antennal lobe (AL). The AL is a sphere-shaped region of the brain which receives sensory input from OSNs on the antennae and mouthparts (Galizia and Menzel, 2001; Guerenstein et al., 2004a; Hansson and Anton 2000; Meyer et al., 2013). The AL, analogous to the olfactory bulb of vertebrates, is typically composed of spheroid structures, called glomeruli (singular: glomerulus) surrounded by glia (Anton and Homberg, 1999; Kirschner et al., 2006). Usually all OSNs expressing the same odor receptor converge onto one of multiple glomeruli (Vosshall et al., 2000). Each glomerulus also houses neurites of local interneurons (LNs) and dendrites of uni- or multi-glomerular projection neurons (PNs). While LNs arborize in several (sometimes maybe all) glomeruli and do not have neurites outside the AL, the axons of the PNs leave the AL and transmit the partially processed information to higher brain areas (Anton and Homberg 1999; Distler and Boeckh, 1996; Tolbert and Hildebrand, 1981; Fig. 2). In some insects, information about sex pheromone is processed by a small group of relatively big glomeruli forming a single structure called macroglomerular complex (MGC; e.g., Boeckh and Boeckh, 1979; Hildebrand et al., 1980). No such macroglomerular structures have been found in hematophagous insects.

AL glomeruli can be characterized on the basis of their shape, size and position, as these parameters are conserved for a particular insect species (Sachse and Krieger, 2011). Thus, three-dimensional maps of the AL glomeruli have been established in various model species and are used as a basis to interpret data from functional AL studies. The AL of the mosquitoes *An. gambiae* and *Ae. aegypti* (Anton, 1996; Ignell et al., 2005), and the triatomine bug *Rhodnius prolixus* (Barrozo et al., 2009) have been mapped. The arrangement and number of glomeruli within the AL are largely species-specific (Kristoffersen et al., 2008). The number of glomeruli in female *Ae. aegypti* is 51 whereas in males is 49 (Ghaninia et al., 2007b; Ignell et al., 2005). Male and female *An. gambiae* have 61 and 60 glomeruli respectively. In the triatomine bug *R. prolixus*,

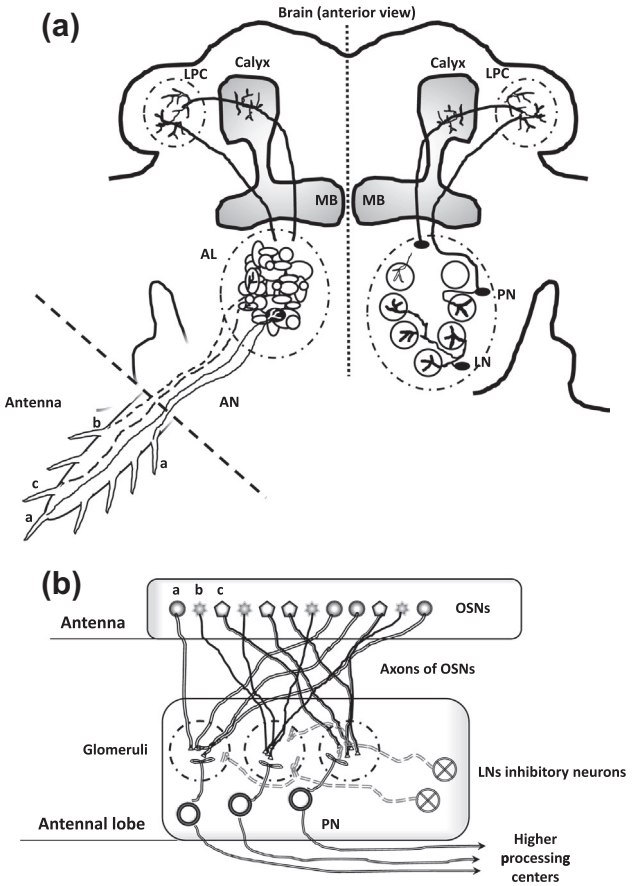

Fig. 2. (**a**) Anterior view of an adult insect brain showing olfactory pathways. Left: olfactory sensory neurons (OSNs) are located within sensilla on the antennae and mouthparts (not shown). OSN axons project, via the antennal nerve (AN), to spherical glomeruli in the antennal lobe (AL) where they synapse with local interneurons (LNs) and projection neurons (PNs). OSNs expressing the same olfactory receptor project to the same glomerulus (e.g., neurons a) while OSNs expressing other receptors project to other glomeruli (e.g., neurons b, c). Right: LNs and PNs project from cell bodies located in one of several cell clusters just outside the glomerular mass. LNs are multiglomerular and limited to the AL. PNs are uni or multi-glomerular and project outward to the lateral protocerebrum (LPC) and mushroom bodies (MB). (**b**) Schematic illustration of the glomerular organization of the AL. The axons of neurons expressing the same type of odorant receptor converge on glomeruli in the AL. The OSNs (e.g., a, b, c) denote olfactory neurons expressing a common odorant receptor. The excitatory PNs have dendrites in a single or multiple glomeruli, where it receives extensive input from a single class or a few classes of OSN, respectively. PNs send their axon to higher brain centers. The inhibitory (lateral) neurons (LNs) arborize in multiple glomeruli. A similar organization of OSNs and mitral cells (which are analogous to PNs) is found in the vertebrate olfactory bulb, the first information processing station after the olfactory epithelium. Vertebrate interneurons, however, are more numerous and complex.

only 22 glomeruli were reported whereas no obvious sexual dimorphism in the AL was observed (Barrozo et al., 2009). Thus, the number of glomeruli in hematophagous insects is rather moderate as in other insects species they range from about 50 to 60 in some Dipteran species, around 60 in moths, 160 in honeybees, and 215–460 in ants (Berg et al., 2002; Das and Fadamiro, 2013; Fishilevich and Vosshall, 2005; Galizia et al., 1999a; Ghaninia et al., 2007a; Ignell et al., 2005; Laissue et al., 1999; Nishikawa et al., 2008; Rospars, 1983; Smid et al., 2003; Zube et al., 2008). Moreover, more than 1000 'microglomeruli' constitute the AL of locusts and some social wasps (Ernst et al., 1977; Hanström, 1928; Ignell et al., 2001).These marked differences in AL architecture between species may impact the entire neural network function at the level of odor and odor mixture encoding, which seems necessary for the species-specific adaption to environmental constraints (Meyer et al., 2013).

2.2. Physiology of the olfactory system

2.2.1. Transport of odor molecules

The odor molecules that hit the antenna may reach the lymph of the olfactory sensilla through their wall pores. The aqueous sensillum lymph is rich in soluble proteins (Vogt and Riddiford, 1981). Usually some of these proteins act as carriers that transport the odor molecules through the lymph to receptors on the dendritic membrane of the OSNs where stimulus transduction will occur (Tsuchihara et al., 2005; Vogt and Riddiford, 1981). These carrier proteins transport even hydrophobic ligands. Two classes of hydrophilic soluble carrier proteins have been found in the lymph of chemosensory sensilla of insects, the odorant binding proteins (OBPs; Vogt and Riddiford, 1981) and chemosensory proteins (CSPs, Angeli et al., 1999). As vertebrate OBPs (which are lipocalins; Flower, 1996), insect OBPs and CSPs are small proteins that bind small ligands (i.e., molecules of volatile compounds). However, the two groups of proteins differ significantly in their molecular structure (e.g., OBPs: Kruse et al., 2003; Lipocalins: Bianchet et al., 1996; Wogulis et al., 2006). OBPs (ca. 14–20 kDa) and CSPs (11 kDa) have been identified in plenty of insects' genera of both hemimetabolous and holometabolous lineages (Bohbot et al., 2010).

Based on their amino acid sequence different classes of insect OBPs are recognized: PBPs (pheromone binding proteins), GOBP1 (general odorant binding proteins type 1), GOBP2 (general odorant binding proteins type 2), and ABPX (antennal binding protein X; Krieger et al., 1996; Pelosi et al., 2006). The classic OBPs have in common a pattern of 6 cystein residues in conserved positions whereas the smaller CSPs are characterized by a pattern of four cystein residues (Pelosi et al., 2006). These proteins, often originally identified in Lepidoptera (moths) were also indentified in Diptera (*Drosophila*: McKenna et al., 1994; Pikielny et al., 1994; carrion-eater blowflies: Ozaki et al., 1995; mosquitoes: Ishida et al., 2002), Hymenoptera (Danty et al., 1997); Heteroptera (Dickens et al., 1995; Dickens and Callahan, 1996), Phasmoptera (Tuccini et al., 1996) and Coleoptera (Paesen and Happ, 1995).

The ligands bind the carrier proteins with high affinity and in a reversible way (Pelosi et al., 2006). When the complex carrier protein-odor molecule (or just the odor molecule according to a different hypothesis; Hallem et al., 2004a; Krautwurst et al., 1998; Pelosi et al., 2006; Wetzel et al., 2001) reaches the OSN dendrite membrane it triggers a cascade of events that results in the transduction of the chemical signal (Leal, 2005; Pelosi et al., 2006; see Section 2.2.2; Fig. 3). After transduction was triggered the complex carrier protein-odor molecule is degraded by enzymes although an alternative model proposes that only the odor molecule is degraded (Leal et al., 2013), while the carrier protein becomes available for binding another ligand.

It has been shown that at least some OBPs have high affinity for just one or a few ligands so that these carrier proteins could be partially responsible for the response selectivity shown by some OSNs to odors (Leal, 2005). More than one type of OBP could be found in the lymph of a single sensillum (Hekmat-Scafe et al., 1997) and it is believed that they are synthesized by the accessory cells of the sensillum (Pelosi et al., 2006). Even when there is evidence of a role of the carrier proteins in olfaction (e.g., Pelletier et al., 2010), members of both OBP and CSP gene families were found to express in gustatory organs (Galindo and Smith, 2001) and even outside chemosensory tissues so that they may also have functions other than chemosensory. For example, some of these proteins may be involved in releasing chemical messages (e.g., pheromones) in the environment (e.g., Jacquin-Joly et al., 2001). Also, a classic OBP, synthesized outside a sensory organ, was found to solubilize fatty acids in the diet during feeding in the blowfly *Phormia regina* (Ishida et al., 2013) while a role in (blood) feeding was also found

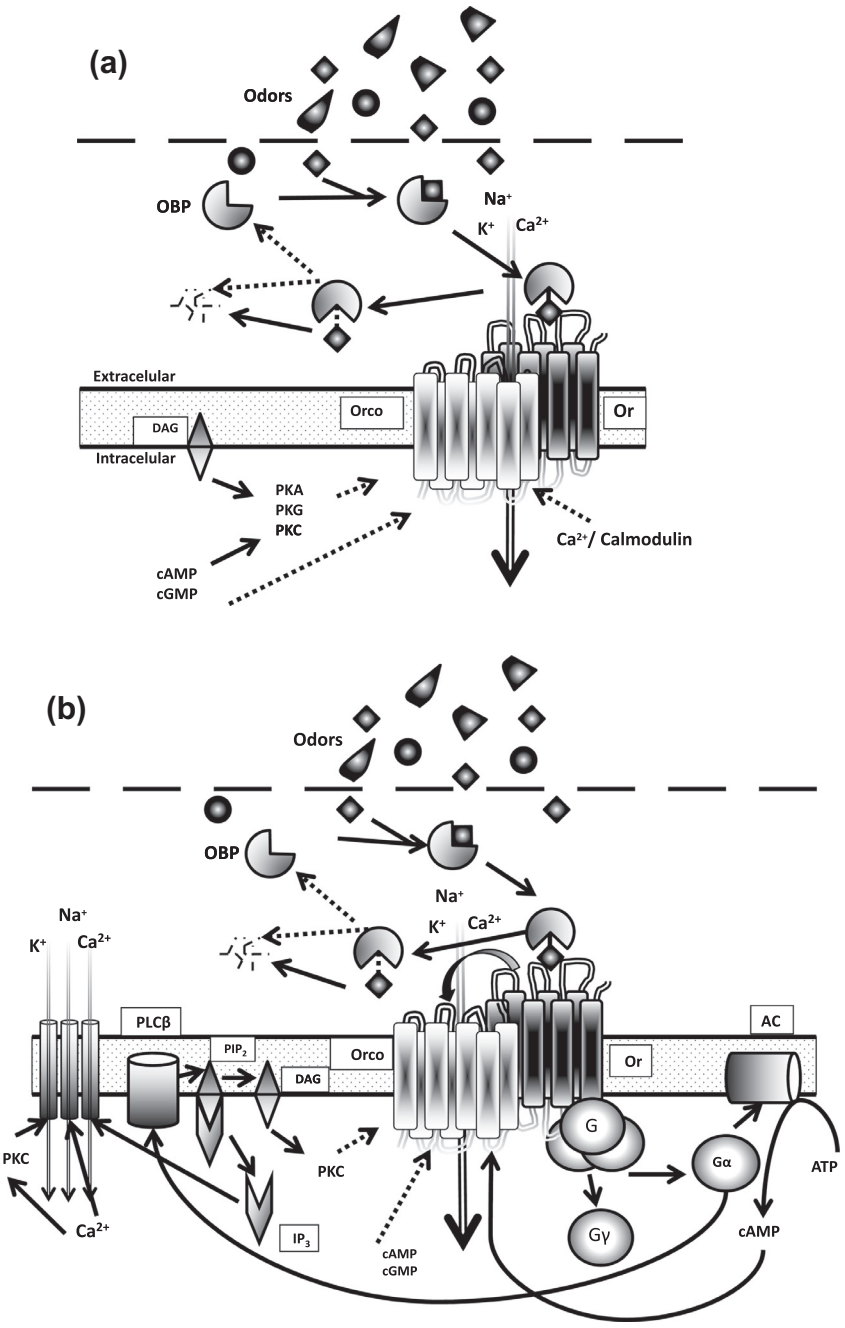

Fig. 3. Models of a typical olfactory signal transduction mechanism in trichoid and basiconic sensilla. After passing through a cuticular pore and pore channel (not shown) of the sensillum, an odor molecule is transported by an odorant binding protein (OBP) to the dendritic membrane of an olfactory sensory neuron (OSN). There it binds a particular odor receptor (OR) or, in the case of some pheromones, a sensory neuron membrane protein (SNMP) linked to an OR (not shown). Usually, OBPs and ORs bind only a specific odor compound or a specific set of odor compounds. Three hypotheses have been proposed for the following steps: (**a**) Ionotropic hypothesis. The OR-ORCO heteromer forms an odorant-gated non-specific cation channel underlying an ionotropic signal transduction process. Odorant binding to the OR triggers a current through this channel (Sato et al., 2008). The ionotropic current is assumed to be modulated via metabotropic cascades of unknown metabotropic receptors which determine sensitivity and kinetics of the ionotropic odorant response (Nakagawa and Vosshall, 2009). (**b1**) Parallel ionotropic and metabotropic cascade. According to this hypothesis the ORCO itself is the cation channel which is activated by two pathways. In the first (fast, ionotropic) pathway odor ligands activate the OR, which in turn activates the ORCO channel. In the second (slow, metabotropic) pathway activation of the OR results in activation of a trimeric G-protein and adenylyl cyclase (AC). This results in an increase of the concentration of cAMP which elicits a ionic current only after previous phosphorylation of ORCO via PKC (Wicher et al., 2008). (**b2**) Metabotropic hypothesis. The odor-OR binding activates a G-protein and phospholipase Cβ (PLCβ). This results in a rise in IP3 which increases intracellular Ca^{2+} concentrations first via rapid activation of an IP3-dependent Ca^{2+}-channel. The resulting Ca^{2+}-influx gates Ca^{2+}-dependent cation channels which underlie a combined transient transduction current. Strong or long lasting Ca^{2+} rises together with DAG activate a PKC which activates further cation channels and is assumed to phosphorylate ORCO thereby increasing its conductance (Stengl and Funk, 2013). DAG diacylglycerol, PKA protein kinase A, PKC protein kinase C, PKG protein kinase G, cAMP cyclic-AMP, cGMP cyclic-GMP, IP3 inositol 1,4,5-trisphosphate, PIP2, phosphatidylinositol 4,5-bisphosphate.

in the case of OBPs expressing in the midgut of the mosquito *Culex nigripalpus* (Smartt and Erickson, 2009).

It is known that while the *Drosophila* genome carries 49 OBP genes, *Ae. aegypti* and *An. gambiae* possess 57 and 66 putative OBP members, respectively. Among individual species, OBPs share little overall amino-acid sequence identity, ranging from 13% to 22% in these dipterans (Zhou et al., 2008). In the case of the classic 6-cysteine OBPs, the overall amino-acid identity is less than 5%.

The high diversity of OBPs would correlate with the high number of chemicals that the system needs to interact with (Mohl et al., 2002). In hematophagous insects OBPs have already been found. Thus, in the mosquito *C. quinquefasciatus* the OBP CquiOBP1 (Ishida et al., 2002; Mao et al., 2010) is known to bind an oviposition pheromone (Leal et al., 2013) while the *An. gambiae* AgamOBP1 (Wogulis et al., 2006) mediates sensing of indole, which is emitted by human sweat and water in breeding sites (Biessmann et al., 2010). In *Ae. aegypti* an OBP, AaegOBP1, has also been identified (Leite et al., 2009).

It should be mentioned that when olfactory receptors of *An. gambiae* have been expressed in sensilla on the antennae of *D. melanogaster* they responded to the same odors as in *An. gambiae* (Hallem et al., 2004b) even when the mosquito and *Drosophila* OBPs involved are structurally very different. This seems to suggest a non-essential role of OBPs in olfaction. However, other studies suggest that OBPs are necessary for an adequate electrophysiological and behavioral olfactory response in *D. melanogaster* (e.g., Xu et al., 2005).

2.2.2. Odor reception

In recent years significant advances have been made on the understanding of the events related to insect chemoreception at the dendritic membrane level. Three classes of receptors involved in olfaction have been identified: olfactory receptors (ORs), ionotropic receptors (IRs) and gustatory receptors (GRs).

2.2.2.1. ORs: olfactory receptors. ORs are part of a large family of highly divergent seven-transmembrane-domain proteins. In the membrane they are usually part of a heteromeric complex consisting on at least two subunits. While the OR subunit is a member of the diverse conventional ORs, the other, called co-receptor (ORCO), is a member of the highly conserved non-conventional ORs belonging to the DmOR83b-like sub-family of proteins (Couto et al., 2005; Hallem et al., 2006; Jones et al., 2005; Krieger et al., 2003; Larsson et al., 2004; Nakagawa et al., 2005; Pitts et al., 2004). The ligands only bind the OR subunit which confers odorant-reception specificity. The ORCO subunit does not interact with ligands and do not confer ligand specificity. Insect ORs are not homologous to the chemosensory receptors coupled to G-protein of vertebrates (Buck and Axel, 1991) and they represent a new protein family (Clyne et al., 1999a; Voshall et al., 1999). A single OSN usually expresses one type of OR although they can express up to three different types (Galizia and Sachse, 2010; Voshall et al., 1999).

Based mostly on work on *Drosophila* and moths, different hypotheses of OR-mediated insect olfactory transduction have been proposed and more than one mechanism may exist. One hypothesis suggests that the OR-ORCO heteromer forms a non-selective ligand-activated cation channel. Thus, upon odor stimulation, a Ca^{2+} influx and an increase in the non-selective cation conductance was observed. It was suggested that this ionotropic signal transduction process is independent from the pathways involving second messengers related to receptor-coupled G-protein (Sato et al., 2008; Fig. 3a). It has also been suggested that ORCO itself is the cation channel and that this channel is activated by two different pathways. In the first (fast, ionotropic) pathway odor ligands activate the OR, which in turn activates the ORCO (channel). In the second (slow, metabotropic) pathway activation of the OR results in a cascade involving a G-protein and adenylyl cyclases that activate cyclic nucleotides which elicit a ionic current only after previous phosphorylation of ORCO via PKC (Wicher et al., 2008; Fig. 3b). It has been observed that cation permeability differ among different mosquito OR complexes, thus the odorant-binding OR affects the channel pore (Pask et al., 2011). Finally, it has also been proposed that odor stimulation activates a G-protein which in turn activates a phospholipase C which leads to a rise in inositol trisphosphate (IP3). The IP3 rise activates an IP3-dependent Ca^{2+} channel so that intracellular Ca^{2+} levels increase thus, activating Ca^{2+}-dependent cation channels which leads to a transduction current. Strong or long lasting Ca^{2+} rises would lead to activation of further cation channels as well as the ORCO channel thus increasing their conductance and leading to an additional metabotropic current (Stengl et al., 1999; Stengl and Funk, 2013; Fig. 3b).

As many as 131 candidate AaOR genes have been identified in the *Ae. aegypti* genome (Bohbot et al., 2007). Phylogenetic analysis reveals several species-specific OR expansions in *Ae. aegypti* and, in a lesser extent, in *An. gambiae* (Bohbot et al., 2007). Thus, the *Ae. aegypti* AaOR family is significantly expanded relative to the OR families of *An. gambiae* (79 AgORs, Hill et al., 2002) and *D. melanogaster* (62 DmORs, Robertson et al., 2003), and is dominated by a large set of 40 AaORs not closely related to *An. gambiae* ORs, indicating a high evolutionary divergence in ORs that is likely to reflect their critical roles in the mosquito life cycle.

As in the case of other insects, genes encoding candidate ORs of *An. gambiae* are diverse, with the exception of the ORCO *AgOR7* (the anopheline *DmOR83b* ortholog) and other members of a highly conserved non-conventional OR subfamily that is widely expressed throughout insect olfactory organs (Hill et al., 2002; Krieger et al., 2003, 2002; Vosshall et al., 2000). AgOR7 has been reported to localize in antennae, maxillary palp and unexpectedly, the proboscis of adult *An. gambiae* (Lu et al., 2007), which has not just a gustatory but also an olfactory function (Kwon et al., 2006). Among classic ORs, AgOR28 has been found in both the maxillary palp (Lu et al., 2007) and the proboscis (Kwon et al., 2006). One of the strongest ligands for AgOR28 is acetophenone (Kwon et al., 2006; Lu et al., 2007), a plant compound that may be associated to nectar-feeding or oviposition cues. Other examples of AgORs whose ligands are now known include AgOR8 whose ligand is the vertebrate odor 1-octen-3-ol (Lu et al., 2007; an homologous was found in *Ae aegypti* as AaOR8, Bohbot and Dickens, 2009), AgOR2, narrowly tuned to a small set of aromatics including indole (a vertebrate odor also found in the mosquitoes' oviposition sites; an homologous was found in *Ae. albopictus* as AalOR2 and other species, Bohbot et al., 2011; Pelletier et al., 2010), AgOR5, narrowly tuned to 2,3-butanedione (a metabolic byproduct of human skin microflora), AgOR65 whose ligand is 2-ethylphenol (a constituent of vertebrate urine; Carey et al., 2010), AgOR1, specifically responsive to 4-methylphenol (a component of human sweat odor; Hallem et al., 2004b), AgOR48, responding to lactones (found in oviposition sites and flowers; Pask et al., 2013), AgOR40 whose natural ligand may not be known although it is known that binds the repellent DEET (N,N-diethyl-m-toluamide; Liu et al., 2010; see also Wang et al. (2010).

In the case of the southern house mosquito *C. quinquefasciatus*, as many as 177 OR genes have been identified. For this mosquito, CquiOR10 was found to be narrowly tuned to the oviposition attractant skatole (Hughes et al., 2010). In addition, CquiOR95b binds ethyl 2-phenylacteate and citronellal which are repellents for *Culex* mosquitoes (Leal et al., 2013). The ligands for other mosquito ORs have also been proposed (Rinker et al., 2012; Wang et al., 2010). It has been suggested that the expression pattern of odor receptors plays a fundamental role in the differential host preferences of even related mosquito species (Rinker et al., 2012). In the triatomine *R. prolixus*, the OR and GR genes sets consist of 115 (including 5 pseudogenes) and 28 models respectively. Additionally, a total of 18 IR gene models have been identified and it has been possible to show antenno-specific expression for several ORs and IRs (Latorre-Estivalis et al., 2012).

Although the *AaORs* have not been mapped cytologically to the *Ae. aegypti* chromosomes, *AaOR* localization on supercontigs revealed that 12 *AaORs* are paired in tandem arrays, 7 are found as triplets and many others as larger clusters of up to 11 genes

(Bohbot et al., 2007). This is similar to the organization of the *AgORs* (Hill et al., 2002) but in contrast to that of the *DmORs*, which are typically dispersed as single genes throughout the genome and at most are found in triplets (Clyne et al., 1999b; Robertson et al., 2003). Overall, 18 conserved *AaORs* share microsynteny with their *AgOR* counterparts and neighboring genes further supporting the evolutionary relationships of these receptors. Taken together, genomic clustering, conserved gene orientation, and sequence similarity provide strong evidence that these groups have arisen via gene duplication (Bohbot et al., 2007).

2.2.2.2. SNMPs: sensory neuron membrane proteins. In some OSNs a protein family known as sensory neuron membrane proteins SNMPs was implicated in chemoreception (Benton et al., 2007). SNMPs belong to a larger family of two transmembrane domain proteins known as CD36 which has a broad range of described roles including cholesterol transport by macrophage cells in humans (Febbraio and Silverstein, 2007). Among other insects they have been identified in *An. gambiae* and *Ae. aegypti*. They were found in a variety of chemosensory organs including olfactory sensilla of the antenna and palps and what appear to be chemosensory sensilla of wings and legs (Nichols and Vogt, 2008). The roles proposed in insects include transport of odors and interactions with extracellular (e.g. OBPs) and membrane (e.g. ORs) proteins. SNMPs could establish a 'molecular bridge' between pheromone molecules and some ORs (Bohbot et al., 2010). SNMPs are essential for olfactory function in pheromone-detecting OSNs in some trichoid sensilla, but are not required for functioning of basiconic sensilla suggesting that they participate in the transduction of pheromonal lipidic compounds (Benton et al., 2007).

2.2.2.3. IRs: ionotropic receptors. The OSNs of some sensilla (in particular sensilla coeloconica) do not express an OR or an ORCO (Couto et al., 2005; Scott et al., 2001; Yao et al., 2005). Those OSNs usually respond to ammonia and short chain carboxylic acids, amines and aldehydes (Benton et al., 2009; Davis and Sokolove, 1976; Diehl et al., 2003; Pappenberger et al., 1996). It has been shown that the dendritic membrane of those OSNs express a family of chemoreceptors different from the ORs and related to ionotropic glutamate receptors (iGluRs) present in neuron synapses of vertebrates and invertebrates (Benton et al., 2009). These new chemoreceptors have been called ionotropic receptors (IRs). IRs are expressed in OSNs that do not express ORs or ORCO although at least one exception exist (Benton et al., 2009). IRs are characterized by three transmembrane domains, a pore region, and venus extracellular S1 and S2 ligand-binding domains (Sachse and Krieger, 2011). Contrary to iGluRs, most IRs would not bind glutamate while the binding sites are highly divergent. For example, OSNs expressing IR64a1 have binding sites for acid compounds which are usually found in vertebrate odor (Ai et al., 2010). The IRs are also receptors for amines (Rytz et al., 2013) found in vertebrate odor. Still, there is a highly conserved region between the iGluRs and IRs corresponding to the pore of the ionic channel. The IRs would form ionic channels directly activated by ligands (Benton et al., 2009) and they would be expressed together with a co-receptor (Rytz et al., 2013). However, contrary to ORs, different co-receptors for IRs exist; IRs must express together with the co-receptors to be functional (Rytz et al., 2013). Moreover, in some OSNs possibly two different IRs are expressed and even an OR and IR expressing in the same OSN may occur (Abuin et al., 2011; Rytz et al., 2013). Recent work describes the complex physiological interaction that the IR and OR chemosensory pathways display in order to generate behavior (Silbering et al., 2011).

The ligands for *An. gambiae* IRs are being identified. Thus, it has been proposed that an important ligand for AgIR76b is butylamine (a vertebrate odor). Also, the candidate co-receptors AgIRs8a and 25a would respond to glutamate considering similarities between these two antennal IRs and iGluRs, AgIR25a seems unable to bind odors. Thus, it has been proposed that these IRs would have a role in neuromodulation of OSN function (Liu et al., 2010). The number of IRs per species show a high degree of variation ranging from 12 in the human body louse to 95 in *Ae. aegypti* (Croset et al., 2010).

2.2.2.4. GRs: gustatory receptors. CO_2, an ubiquitous volatile compound emitted by vertebrates, is a very important odor cue for hematophagous insects to find their hosts (Guerenstein and Hildebrand, 2008). The molecular chemoreceptors for CO_2 do not belong to the OR or IR families of receptors. Instead, members of the family of GRs are involved (Jones et al., 2007; Kwon et al., 2007; Suh et al., 2004). In *An. gambiae*, AgGR22, AgGR23 and AgGR24 (homologs of *Ae. aegypti* AaGR1, AaGR2 and AaGR3, respectively; Kent et al., 2008) are coexpressed in a single OSN and encode functional receptors that, when present together possibly as a heteromer, produce responses to CO_2 (Lu et al., 2007). Homologs of AgGR22 and AgGR24 were also found in the blowfly *Chrysomya megacephala* (Diptera: Calliphoridae; Wang et al., 2013). It has also been proposed that a G-protein plays a role in the responses of OSNs tuned to CO_2 (Yao and Carlson, 2010).

2.2.3. Responses at the peripheral level

The role of the peripheral olfactory system is to inform the brain, in a fraction of a second, about the quality, quantity and temporal features of the odor stimulus. That is, the system must inform about the identity and concentration of the odor constituents, if the stimulus consists of a single compound or a mixture of odors and in the latter case, the proportions of the different constituents of the mixture. Besides, it must inform if the stimulus is presented continuously or intermittently, and in the latter case at which instantaneous frequency. All this information is encoded through the spike frequency in the ensemble of OSNs upon odor stimulation (Guidobaldi and Guerenstein, 2012).

Odor stimulation could evoke excitatory (increased spike frequency) or inhibitory (spike cessation) responses in particular OSNs (de Bruyne et al., 1999; Diehl et al., 2003). Moreover, single compounds can evoke excitation in an OSN and inhibition in another (Dougherty et al., 1999), and OSNs could be excited by single compounds and inhibited by others (de Bruyne et al., 2001, 1999; Hallem et al., 2004; Kreher et al., 2005). This results in a high number of possible information codes.

'Specialist' OSNs are tuned to respond to a single compound or a few closely related compounds. Stimulation of specialist (selective) OSNs with the compound to which they are tuned results in a sensitive response with a wide dose–response curve. On the contrary, 'generalist' OSNs respond to compounds that could even be chemically rather different. Thus, many different generalist OSNs could respond to the same compound. It should be mentioned that many of the OSNs characterized do not clearly fall in any of these two categories so that a gradient that goes from specialist to generalist is found (Hallem and Carlson, 2006).

Upon stimulation with a particular odor mixture, the ensemble of OSNs would generate a response pattern that would be unique (French et al., 2011; Todd and Baker, 1999). It is the task of the CNS to decode and process this information.

Even when the integration and processing of the olfactory information occur in the CNS, in some cases interactions between the responses of OSNs have been observed at the peripheral level. Thus, reciprocal inhibition and synergism between the responses of OSNs housed in the same sensillum was found in beetles and moths (Nikonov and Leal, 2002; Ochieng et al., 2002). There is evidence that these response interactions at the peripheral level would also occur in hematophagous insects (Diehl et al., 2003).

In many cases the response of the OSNs show adaptation leading to phasic responses upon stimulation. Thus, the OSNs respond more faithfully to rapid changes in concentration than to odor presented for a prolonged time (e.g., Marion-Poll and Tobin, 1992). In natural environments odor cues are often carried by wind in an 'odor plume'. This odor plume has odor filaments that travel interspersed with clean air (similar to the smoke from a cigarette). An insect approaching the odor source would sense the odor plume as a pattern of intermittent stimulations and, up to a certain point; the phasic responses of the OSNs are able to follow the intermittency. Following the direction of the wind while receiving intermittent stimulation would ensure localization of the odor source (Todd and Baker, 1999). It has been suggested that the IRs, which have a very rapid response time, are specially adapted to follow an intermittent pattern of stimulation (Silbering and Benton, 2010).

Most if not all hematophagous insects possess OSNs that respond to CO_2 including mosquitoes (e.g., Grant et al., 1995), triatomine bugs (e.g., Barrozo and Lazzari 2004a; Guerenstein and Lazzari, 2010; Núñez, 1982; Taneja and Guerin, 1995; Wiesinger, 1956), the stable fly *Stomoxys calcitrans*, and tsetse flies (Lehane, 2005). CO_2 emanating from vertebrates is a very important cue that helps hematophagous insects detect and orientate toward a host on which they could feed (Guerenstein and Hildebrand, 2008; Lehane, 2005). The responses of the CO_2 OSNs, including those of mosquitoes show robust phasic and tonic components and this allow them to signal changes in concentration as well as the absolute ambient background CO_2 level constantly (Grant et al., 1995; Guerenstein et al., 2004a; Guerenstein and Hildebrand, 2008). Moreover, they respond not only to increases in concentration (through an increase in spike rate) but also to decreases in CO_2 levels (through spike rate decrease; Grant et al., 1995; Guerenstein et al., 2004a). A number of odor compounds have been identified that interfere with the response of the CO_2 OSNs (Guerenstein et al., 2004a; Turner et al., 2011), and this information could be used to manipulate the behavior of the insects.

Numerous papers used electrophysiological methods in olfactory sensilla to record spikes from OSNs in order to identify the odor compounds to which those sensory neurons respond to. Thus, for example, mosquito OSNs respond to the host odors lactic acid (Davis and Sokolove, 1976), nonanal (Ghaninia et al., 2008; Syed and Leal, 2009), pentylamine, butylamine, butyric and isovaleric acid (Cork and Park, 1996; Kwon et al., 2007; Pappenberger et al., 1996), 3-methyl-1-butanol, 6-methyl-5-hepten-2-one (Meijerink et al., 2001), 1-octen-3-ol, 3-methylphenol, CO_2 (Cork and Park, 1996; Lu et al., 2007; Syed and Leal, 2007), 4-methylcyclohexanol, indole, terpenes (Ghaninia et al., 2007b). Odors related to oviposition also evoked responses (e.g., Davis, 1976). Triatomines respond to the host odors nonanal, isobutyric acid (Guerenstein and Guerin, 2001), ammonia (Diehl et al., 2003; Taneja and Guerin, 1997), isobutylamine (Diehl et al., 2003) and a number of terpenes (Guerenstein, 1999). In bed bugs apart from aldehydes, sulcatone (another host odor) evoked clear responses (Harraca et al., 2012). The sandfly antenna was also studied and several electrophysiologically active host odor constituents were reported including 2-hexanone, 3-methyl butanoic acid, 4-methyl heptanone, benzaldehyde and 3-hydroxy butanone (Dougherty et al., 1999).

Regarding the insect repellent DEET, it was suggested that it acts through inhibition of the function of some ORs while it is also detected by specific ORs linked to a repellence behavior (Bohbot and Dickens, 2010; Ditzen et al., 2008; Liu et al., 2010; Syed and Leal, 2008). In a recent study (Kain et al., 2013) DEET-sensitive neurons were identified in a pit-like structure in the *D. melanogaster* antenna called the sacculus. Those neurons express a highly conserved receptor, Ir40a, and flies in which those neurons are silenced or *Ir40a* is knocked down lose avoidance to DEET. This study also tested several related natural compounds selected by a computational screening and found that most of them activate *Ir40a*+ neurons and are repellents for *Drosophila*. Those compounds are also strong repellents for mosquitoes.

It has been proposed that the events in the peri-receptor compartment of the olfactory sensilla define two different types of olfactory sensory systems (Kaissling, 1998). In the case of the 'flow detectors' the odor molecules entry the sensillum lymph in an irreversible way. Stimulus molecules can only be removed from the perireceptor compartment by enzymatic inactivation. Thus, these detectors sense the flow of molecules that hit the sensillum wall and that are irreversible adsorbed (Kaissling, 2013, 1998). Most olfactory sensilla would act as flow detectors. In the case of the 'concentration detectors' the concentration of the stimulus molecules present in the perireceptor compartment is in equilibrium with the concentration outside the sensillum. This would be due to the fact that entry in the perireceptor compartment is reversible so that the stimulus molecules could immediately leave would the outside concentration be lower than that in the sensillum lymph. In this case a system to inactivate the stimulus is not necessary. This would be the case of the CO_2 sensory system (and at least some gustatory sensory systems; Kaissling, 1998). While the response of the concentration detectors depends exclusively on the external stimulus concentration, the response of the flow detectors depends on the external concentration and the relative velocity of the air respect to the sensillum (due to wind or insect movement; Kaissling, 1998).

2.2.4. Responses at the central level

As mentioned above, the axons of the insect OSNs project into the AL where there is both convergence and integration of information. This redistribution of information help the ensemble of neurons in the AL properly encode the quality, quantity and the temporal (e.g., intermittency) and spatial (body region where the stimulus comes from) pattern of the odor stimulus (Hansson and Christensen, 1999). It should be noted that quality information not only refers to identity of single odor compounds but also of specific mixtures of compounds that activate a pattern of neurons that is particular to each of them and that cannot be predicted from the sum of the responses to their individual constituents.

OSNs with the same receptors (i.e., responding to the same odor compound/s) project to the same AL glomerulus and in most cases, each glomerulus receives afferent input of only one OSN type (Ignell et al., 2010; Vosshall et al., 2000). Thus, glomeruli represent functional units of the AL and they are part of an 'afferent map' of the AL. The number, size and position of the glomeruli are genetically determined and 3D atlas of the AL of many insect species including hematophagous, have been published (see Section 2.1.2). Moreover, a recently published atlas differentiate glomeruli with terminals of OR-expressing OSNs from glomeruli with terminals of IR-expressing OSNs (Rytz et al., 2013) while a glomerulus with terminals of CO_2 OSNs (presumably expressing a GR) has also been found (Guerenstein et al., 2004a; Suh et al., 2004). PNs could arborize in one or more glomeruli and upon odor stimulation they usually increase their spike rate and that message is sent to higher information processing centers.

As we mentioned above, many OSNs are specialized in detecting a single odor compound. Thus, if the OSNs of the olfactory system were all specialists each glomerulus would represent a particular odor compound and the glomerular pattern in the AL would constitute a simple, unequivocal 'functional (chemotopic) map' (e.g., Hildebrand, 1996). However, because some generalist OSNs occur and a single odor could stimulate more than one type of OSN (see Section 2.2.3), the functional AL map is somewhat more complex (Hansson and Christensen, 1999). This complexity could be reflected by more than one glomerulus responding to the same

odor compound (so that overlapped responses may occur) although this type of response could also originate in the neural interactions within the AL (see below). In any case, the AL functional map is stereotyped as a particular odor at a certain concentration always evokes a similar glomerular activation pattern even in different individuals of the same species (Galizia et al., 1999b; Lei et al., 2004; Sachse et al., 1999). The AL functional map consists on a combinational activation of glomeruli. As natural odors usually consist on mixtures of several odor compounds, these are represented in an even more complex combinatorial way.

The LNs are in a good part responsible for the interactions between neurons arborizing in different glomeruli (Reisenman et al., 2011). These interactions are frequently inhibitory (involving GABAergic LNs) although excitatory interactions (involving cholinergic LNs) have been found in *Drosophila* (Huang et al., 2010; Yaksi and Wilson, 2010). Thus, AL neurons (largely the LNs) modulate the afferent glomerular map. Often the neural interactions in the AL consist on lateral inhibition and could serve to enhance the contrast between two patterns of glomerular stimulation (Christensen et al., 1998).

It has been proposed that apart from the spatial glomerular representation of odor quality within the AL the temporal pattern of stimulation of the AL glomeruli also encodes odor information. The most important parameters of this temporal pattern would involve duration of glomerular activation, temporal sequence of global glomerular activation and synchrony of activation of the PNs involved in the response (Christensen et al., 2003; Dacks et al., 2009b; Ignell et al., 2010; Stopfer et al., 1999). Dissimilar odors could be discriminated through just the spatial representation whereas to discriminate similar odors both the spatial and temporal representation would be at play. It should be mentioned that the representation of odors in the AL is modified by olfactory learning (Daly et al., 2004).

Odor concentration is in part encoded by the frequency of the spikes in the individual OSNs and AL neurons involved. However, due to convergence of information, sensitivity at the level of AL is higher (Hansson and Christensen, 1999; Ignell et al., 2010). Moreover, because individual OSNs responding to a particular odor could respond to a different although overlapping range of concentrations (Guerenstein et al., 2004a), the range of concentrations to which the average AL neuron respond should be broader. PNs responding independently of the odor concentration have also been found (Ignell et al., 2010). Odor concentration could also be represented by the pattern of glomerular activation.

The neuronal circuits within the AL are complex. It is known that OSNs are cholinergic and synapse with LNs and PNs while LNs synapse with other LNs, with PNs and could establish presynaptic contact with OSNs (Sachse and Krieger, 2011). The neuronal interactions already observed in the insect AL include lateral inhibition, lateral excitation, feed-forward excitation, feed-forward and feed-back inhibition, and disinhibition (Christensen et al., 1993; Sachse and Krieger, 2011).

As mentioned above odor stimuli travel in an 'odor plume' that consists on filaments of odor interspersed with clean air. An insect flying toward the source of the odor plume would sense an intermittent pattern of odor stimulation. Some AL PNs are able to follow that pattern of intermittent odor stimulation up to at least 10 Hz (Christensen and Hildebrand, 1988; Guerenstein et al., 2004a). This ability would be related to the fact that those PNs display a particular response pattern when stimulated with an odor pulse. Their response consists not just on an excitation but in a triphasic (−/+/−) or biphasic (−/+) pattern of response (Christensen and Hildebrand, 1997; Lei and Hansson, 1999; Lei et al., 2009). Thus, the inhibitory phases of the response (involving GABAergic LNs) would allow those PNs shunt their response between stimulations so that the neuron is ready to encode a new odor pulse by a new train of impulses. That is, only the phasic part of the response would be displayed and this would roughly correspond to the moment when the odor hits the antenna. Even when some single odor compounds can evoke a triphasic response pattern (e.g., Dacks et al., 2009b; Guerenstein et al., 2004a), other odor compounds are not able to evoke this response pattern *per se*.

In the case of the sex pheromone of a moth it has been shown that a synthetic version of the pheromone blend was able to evoke a triphasic pattern of response and orientation in an odor plume only when it has the correct (natural) proportion of the two key odor constituents (Christensen and Hildebrand, 1997). This emphasizes the importance of the identity and proportions of compounds when developing a synthetic odor mixture that simulates a natural blend.

The inhibitory LNs would also play a role in the synchronization of the response of intra and interglomerulus PNs that participate of a particular behavioral response (Lei et al., 2002). This synchronization would accentuate the representation of the olfactory stimulus in the AL and is also important for odor mixture coding (Clifford and Riffell, 2013). Moreover, it has been proposed that the coding of odor mixtures is a highly combinatorial process and an array of mixture-constituents interactions were reported including suppression, hypoadditivity, and synergism (Chaffiol et al., 2012; Guerenstein et al., 2005; Kuebler et al., 2011). It is known that the activity of the AL is modulated by the biogenic amines serotonin and octopamin. (Dacks et al., 2012, 2009a; Homberg and Müller; 1999).

Most information on AL function comes mainly from moths, locusts, flies and honeybees. In hematophagous insects the processing of olfactory information at the central level is largely unexplored. Using silicon multielectrode recording arrays we currently aim at studying the neural networks in the AL of triatomine bugs as there is already an important amount of information on triatomine olfaction at the peripheral level (Bernard, 1974; Diehl et al., 2003; Guerenstein, 1999; Guerenstein and Guerin, 2001; Mayer, 1968; Taneja and Guerin 1997) and olfactory behavior (Barrozo and Lazzari 2004a,b; Bodin et al., 2008; Guerenstein and Guerin 2001; Guerenstein and Lazzari, 2010; Taneja and Guerin 1997, 1995) available. Work at the AL level could help us build highly attractive synthetic odor mixtures as, for example, behavioral synergistic interactions occur when stimulating hematophagous insects with those stimuli (mosquitoes: e.g., Bosch et al., 2000; Smallegange et al., 2005; triatomine bugs: e.g., Barrozo and Lazzari 2004b; Guidobaldi and Guerenstein, 2013).

3. The olfactory behavior

The hematophagous lifestyle is associated with major morphological, physiological as well as behavioral adaptations (Lazzari et al., 2013). The behavioral adaptations are already under study and include refuge and host finding which largely involve chemical cues (e.g., Guerenstein and Lazzari, 2010; Takken and Knols, 1999). Other olfactory behaviors under study include mate finding, as well as alarm and aggregation behavior. As many blood-feeding insects are medically important species, a significant amount of work on their behavior has been carried out. Here we succinctly summarize some aspects of that work.

3.1. Mosquitoes

Mosquitoes transmit potentially fatal human diseases such as malaria, yellow fever, dengue and West Nile virus (Qiu and van Loon, 2010). Olfaction has a major role in the life cycle of mosquitoes to ensure survival and reproduction (Dethier, 1957).

Several studies have aimed at understanding how mosquitoes locate and choose their vertebrate hosts using their odors (e.g., *Anopheles*: Meijerink et al., 2000; Takken and Knols, 1999; and *Aedes*: Dekker et al., 2005; Logan et al., 2008). More than 400 compounds have already been isolated and identified from human skin extracts (Dormont et al., 2013a, 2013b). However only a fraction of them are detected by the mosquitoes. For example, human skin emits high amounts of lactic acid, and this compound proved to be a mosquito attractant (Dekker et al., 2002; Geier and Boeckh, 1999). CO_2 is also a known general mosquito attractant (Guerenstein and Hildebrand, 2008) whereas ammonia (produced by microbial activity in sweat) attracts *An. gambiae* and *Ae.* aegypti (Braks and Takken, 1999; Geier et al., 1999a). A synergistic attractive effect was found between lactic acid and CO_2 (Geier and Boeckh, 1999), and between lactic acid, ammonia and a mixture of aliphatic carboxylic acids (Smallegange et al., 2005, 2002; Bosch et al., 2000). Addition of CO_2 and 3-methyl-1-butanol to the latter mixture resulted in very high attraction in field conditions (Mukabana et al., 2012). Interestingly, *Ae. aegypti* females are able to orient upwind to certain odors even under continuous odor stimulation, without stimulus intermittency (Geier et al. 1999b).

Oviposition site selection is influenced by visual, tactile, and olfactory factors, the latter being considered of primary importance (Ponnusamy et al., 2008). Some odor attractants involved in this behavior have been identified from plants (Olagbemiro et al., 2004), feces (Millar et al., 1992), and secretions from mosquito larvae, pupae and eggs (Blackwell and Johnson, 2000; Chadee, 1993; Zahiri et al., 1997). Gravid female *Ae. aegypti* respond to a synthetic oviposition attractant blend consisting of skatole, n-heneicosene, p-cresol and phenol (Baak-Baak et al., 2013). P-cresol alone also served as oviposition attractant for *Ae. triseriatus* (Bentley and Day, 1989; Bentley et al., 1981, 1979) and *Ae. albopictus* (Allan and Kline, 1995) whereas skatole has been reported as an oviposition attractant for *C. quinquefasciatus* (Millar et al., 1992; Olagbemiro et al., 2004), *Ae. albopictus* (Allan and Kline, 1995), *An. gambiae* (Blackwell and Johnson, 2000), *Toxorhynchites moctezuma* and *T. amboinensis* (Collins and Blackwell, 2002).

3.2. Triatomines

Currently, there is consensus that chemical cues play an important role in the host- and refuge-finding, and in sexual, alarm and aggregation behaviors of triatomine bugs (Guerenstein and Lazzari, 2009; Cruz-López et al., 2001).

Adults and nymphs of triatomines spend daylight hours aggregated in crevasses and in caves. It has therefore been suggested that they may produce aggregation pheromones. Experiments on the aggregation behavior of several species of *Triatoma* suggested that their feces are a source of an aggregation pheromone that attracts and aggregates bugs in its proximity (Alzogaray et al., 2005; Lorenzo-Figueiras et al., 2009, 1994; Lorenzo-Figueiras and Lazzari, 1998; Lorenzo and Lazzari, 1996; Schofield and Patterson, 1977). The pheromone present in the feces are not species specific and are capable of attracting bugs of other species (Lorenzo-Figueiras and Lazzari, 1998; Pires et al., 2002). The active constituents of feces can be extracted using polar solvents and chemical analyses have revealed multiple compounds whose biological roles are not yet clear (Alzogaray et al., 2005; Cruz-López et al., 2001, 1995).

Food source detection is achieved via the sensing of air currents carrying odors, water vapor and heat from vertebrates (Barrozo et al., 2003; Bodin et al., 2009; Fresquet and Lazzari, 2011; Guerenstein and Lazzari, 2009; Guerenstein and Guerin, 2001; Ortiz and Molina, 2010). The stimulation of the triatomine OSNs by host odors in an air current evokes upwind orientation (Guerenstein and Lazzari, 2010). In human dwellings triatomine usually search for food while walking on the ceiling. In this case, host odors are transported by convection currents and reach the bugs from below triggering a characteristic behavior: the bugs let themselves fall onto the host (Guerenstein et al., 1995; Guidobaldi and Guerenstein, 2013; Pimenta et al., 2007). It is known that the host odors that attract triatomines include CO_2, carboxylic acids, aldehydes, octenol and ammonia (Barrozo and Lazzari, 2004a,b; Guerenstein and Guerin, 2001; Guidobaldi and Guerenstein, 2013; Núñez, 1982; Otálora-Luna et al., 2004; Taneja and Guerin, 1997, 1995). However, high levels of attraction are reached only when the odor compounds are presented together in a particular odor mixture that, up to a certain point, represents a simplified version of the natural host odor. Thus, synergistic interactions in the responses to odor blends have been observed (Barrozo and Lazzari, 2004b; Guidobaldi and Guerenstein, 2013).

The mating behavior of various triatomine species has been studied under laboratory conditions (Cruz-López et al., 2001). Thus, it was found that mating couples release volatile compounds that are attractive to males (Manrique and Lazzari, 1995). Further work revealed that a particular gland of adult females is the source of this sexual pheromone (Crespo and Manrique, 2007; Manrique and Lorenzo, 2012; May-Concha et al., 2013). The pheromone consists of a complex mixture of ketones, alcohols, dioxolanes and aldehydes (Manrique et al., 2006; May-Concha et al., 2013; Pontes et al., 2008; Vitta and Lorenzo, 2009). In contrast to mosquitoes intermittency of the CO_2 odor-plume seems not to play a relevant role for orientation (Barrozo and Lazzari, 2006).

When disturbed, triatomines release a pungent odor that repels conspecifics (Schofield, 1994). This alarm pheromone is composed of isobutyric acid and a complex mixture of other volatiles including short-chain esters and acids (Cruz-López et al., 1995; González-Audino et al., 2007; Guerenstein and Guerin, 2004; Manrique et al., 2006; May-Concha, 2010) produced by a gland present in both male and female adults. (Manrique et al., 2006; May-Concha et al., unpublished data on *Triatoma dimidiata*; Minoli et al., 2013).

3.3. Tsetse flies

The role of olfaction in the host-oriented behavior of tsetse flies has been studied. Odors play a role in host location although the relative importance of olfactory stimuli varies between species. For the Morsitans-group (*Glossina pallidipes* and *G. m. morsitans*), host odors elicit long range (~100 m) orientation whereas the *Palpalis* group (*G. palpalis* spp. and *G. fuscipes* spp.) are much less responsive (Torr and Solano, 2010). Several field studies on the *Morsitans*-group suggested three main phases in their orientated responses to a host: 1. odor-induced activation, which marks the initiation of host-orientated responses and search for directional cues (Brady and Crump, 1978; Hargrove and Brady, 1992; Torr and Hargrove 1999; Torr, 1988a); 2. long-range odor responses that induce tsetse to fly upwind (Gibson and Brady, 1988, 1985; Griffiths et al., 1995; Torr, 1988b); and 3. short range responses which lead to landing and feeding on the host (Gibson and Torr, 1999; Sutcliffe 1987). It has been observed that the short range location is largely a response to visual cues. Indeed, tsetse are unable to locate an odor source precisely without a visual target (Vale, 1974) and flies approaching an odor source can be diverted towards an odorless visual target (Torr, 1989). However, although host odors appear to have no effect on close-range orientation they do increase landing responses (Hargrove, 1980; Vale, 1974; Warnes, 1995).

Various field and laboratory studies have assessed whether the components of host odor have specific behavioral effects (Willemse and Takken, 1994). Laboratory and field studies both

suggest that CO_2 has an important activating effect whereas other components such as acetone or octenol do not (Bursell, 1984; Torr, 1988a). In addition, tsetse exhibit long range anemotaxis (Kennedy, 1977) in response to CO_2 (Colvin et al., 1989), acetone and octenol (Bursell, 1984; Paynter and Brady, 1993). Field studies have also shown strong synergistic attraction effects between CO_2 and both octenol and acetone (Torr, 1990; Vale and Hall, 1985).

3.4. Sandflies

A number of studies highlighted the importance of odors in sandfly (phlebotome) host-seeking by demonstrating attraction to odors produced by animal baits in the field (e.g., Campbell-Lendrum et al., 1999). Moreover, attraction of sandflies to CO_2 has been recorded in the field in different species (*L. longipalpis*; Quinnell et al., 1992; *L. evansi*; Montoya-Lerma and Lane, 1996; *L. whitmani*; Campbell-Lendrum et al., 1999). However, although many species of sandflies respond to CO_2 to some extent, it is unlikely to be the sole mediator of attraction. In field experiments CO_2 attracted less than half the number of sandflies caught using whole human odor (Pinto et al., 2001). Thus, laboratory studies have demonstrated that other odor constituents that female *L. longipalpis* use to locate a suitable host include carboxylic acids (e.g., 2-methyl propanoic acid), ketones (e.g., 4-methyl-2-pentanone) and aldehydes (e.g., benzaldehyde) (Dougherty et al., 1999).

It is known that chemical signals have a key role in both courtship and sexual behavior in general (Lane and Ward, 1984). The sex pheromone of male *L. longipalpis* and *L. cruciata* is produced by glandular tissue underlying cuticular papules (Mangabeira, 1969; Serrano, 2013). Live males and extracts from the gland were found to be attractive on their own and in combination with host odor to unfed virgin females (Hamilton et al., 1999, 1994; Lane et al., 1985; Lane and Ward, 1984; Morton and Ward, 1989; Serrano, 2013). The active compounds of the gland are terpenes (Krishnakumari et al., 2004; *L. longipalpis*: Hamilton et al., 1999; *L. cruciata*: Serrano, 2013).

Chemical cues from eggs are attractive to conespecific gravid females (Dougherty and Hamilton, 1997; Dougherty et al., 1995, 1992; El Naiem and Ward, 1992). The origin of the oviposition pheromone was traced to the accessory glands of the post blood-fed female and the chemical was identified as n-dodecanoic acid (Dougherty and Hamilton, 1997).

4. Conclusions

Knowledge about insect communication through odors could lead to the development of efficient and practical attractants and repellents to manipulate the behavior of harmful insects. Inhibition of their olfactory function is also conceivable (Turner et al., 2011; Logan et al., 2008; Guerenstein et al., 2004a). It should be emphasized that in order to efficiently manipulate olfactory behavior the natural context associated with each particular odor signal must be understood and taken into account. Knowledge on hematophagous insect olfaction has already helped improve strategies for surveillance and control of these important vectors of disease (Carey and Carlson, 2011) and much progress should be expected in the near future driven by the high amount of information that is now being generated on the molecular bases of the olfactory system. Future challenges include studying how information about odor mixtures is processed in the brain of blood-feeding insects. This could accelerate the development of highly attractive synthetic odor blends to lure them into traps.

Acknowledgments

We thank Fundación Bunge y Born and Agencia Nacional de Promoción Científica y Tecnológica, Argentina, for funding this project through grants FBB28/10 and PICT-PRH-2009-43, respectively. We also thank the Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina for funding our work and for fellowships to FG and IJMC. We are grateful to the two anonymous reviewers for comments and suggestions that greatly improved this manuscript. This paper originated from the meeting "Neuroethology and Neurobiology of Memory in the South Cone: A Tribute to Professor Hector Maldonado". We are grateful to the organizers of the meeting: Ana Silva, Lidia Szczupak and Daniel Tomsic. This paper is dedicated to the memory of the late Professor Héctor Maldonado.

The following figures were inspired from previously published material:

Figure 1b: Modified from Fig.3 in Hartenstein V. 2005. Development of Insect Sensilla. Lawrence, I.G., Kostas, L., Sarjeet S.G. (Eds.), Comprehensive Molecular Insect Science. Elsevier B.V. 3.15, pp. 379–419.

Figure 2a: Modified from Fig.1 in Vogt, R.G., 2005. Molecular Basis of pheromone detection in insects. Lawrence, I.G., Kostas, L., Sarjeet S.G.(Eds.), Comprehensive Molecular Insect Science. Elsevier B.V. 3.15, pp.753–786.

Figure 2b: Modified from Fig. 3b in Bargmann (2006). Comparative chemosensation from receptors to ecology. Nature 444, 295–301.

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, 44–60.

Ai, M., Min, S., Grosjean, Y., Leblanc, C., Bell, R., Benton, R., Suh, G.S.B., 2010. Acid sensing by the *Drosophila* olfactory system. Nature 468, 691–696.

Allan, S.A., Kline, D.L., 1995. Evaluation of organic infusions and synthetic compounds mediating oviposition in *Aedes albopictus* and *Aedes aegypti* (Diptera: Culicidae). J. Chem. Ecol. 21, 1847–1860.

Altner, H., 1977. Insektensensillen: bau und funktionsprinzipien. Verh Dtsch Zool Ges. 70, 139–153.

Altner, H., Prillinger, L., 1980. Ultrastructure of invertebrate chemo-, thermo- and hygroreceptors and its functional significance. Int. Rev. Cytol. 67, 69–139.

Alzogaray, R.A., Fontan, A., Camps, F., Masuh, H., Santo, O.P., Fernandez, D., Cork, A., Zerba, E., 2005. Behavioural response of *Triatoma infestans* (Klug) (Hemiptera: Reduviidae) to quinazolines. Molecules 10 (9), 1190–1196.

Angeli, S., Ceron, F., Scaloni, A., Monti, M., Monteforti, G., Minnocci, A., Petacchi, R., Pelosi, P., 1999. Purification, structural characterization, cloning and immunocytochemical localization of chemoreception proteins from *Schistocerca gregaria*. Euro. J. Biochem. 262 (3), 745–754.

Anton, S., 1996. Central olfactory pathways in mosquitoes and other insects. Ciba. Found. Symp. 200, 184–192, discussion 192–196, 226–232.

Anton, S., Homberg, U., 1999. Antennal lobe structures. In: Hansson, B.S. (Ed.), Insect Olfaction. Springer, Heidelberg, New York, pp. 97–124.

Baak-Baak, C.M., Rodriguez-Ramirez, A.D., Garcia-Rejón, J.E., Rios-Delgado, S., Torres-Estrada, J.L., 2013. Development and laboratory evaluation of chemically-based baited ovitrap for the monitoring of *Aedes aegypti*. J. Vect. Ecol. 38 (1), 175–181.

Barrozo, R.B., Lazzari, C.R., 2004a. Orientation behaviour of the blood-sucking bug *Triatoma infestans* to short-chain fatty acids: synergistic effect of L-lactic acid and carbon dioxide. Chem. Senses. 29, 833–841.

Barrozo, R.B., Lazzari, C.R., 2004b. The response of the blood-sucking bug *Triatoma infestans* to carbon dioxide and other host odours. Chem. Senses 29, 319–329.

Barrozo, R.B., Lazzari, C.R., 2006. Orientation response of haematopha gous bugs to CO_2: the effect of the temporal structure of the stimulus. J. Comp. Physiol. A 192, 827–831.

Barrozo, R.B., Manrique, G., Lazzari, C.R., 2003. The role of water vapour in the orientation behaviour of the blood-sucking bug *Triatoma infestans* (Hemiptera, Reduviidae). J. Insect Physiol. 48, 315–321.

Barrozo, R.B., Couton, L., Lazzari, C.R., Insausti, T.C., Minoli, S.A., Fresquet, N., Rospars, J.P., Anton, S., 2009. Antennal pathways in the central nervous system of a blood-sucking bug, *Rhodnius prolixus*. Arthrop. Struct. Dev. 38, 101–110.

Bentley, M.D., Day, J.F., 1989. Chemical ecology and behavior aspects of mosquito oviposition. Ann. Rev. Entomol. 34, 401–421.

Bentley, M.D., McDaniel, I.N., Yatagai, M., Lee, H.P., Maynard, R., 1979. *P*-Cresol: an oviposition attractant of *Aedes triseriatus*. Environ. Entomol. 8, 206–209.

Bentley, M.D., McDaniel, I.N., Yatagai, M., Lee, H.P., Maynard, R., 1981. Oviposition attractant and stimulants of *Aedes triseriatus* Say (Diptera: Culicidae). Environ. Entomol. 10, 186–189.
Benton, R., Vannice, K.S., Vosshal, L.B., 2007. An essential role for a CD36-related receptor in pheromone detection in *Drosophila*. Nature 450, 289–293.
Benton, R., Vannice, K.S., Gomez-Diaz, C., Vosshall, L.B., 2009. Variant ionotropic glutamate receptors as chemosensory receptors in *Drosophila*. Cell 136, 149–162.
Berg, B.G., Galizia, C.G., Brandt, R., Mustaparta, H., 2002. Digital atlases of the antennal lobe in two species of tobacco budworm moths, the oriental *Helicoverpa assulta* (male) and the American *Heliothis virescens* (male and female). J. Comp. Neurol. 446, 123–134.
Bernard, J., 1974. Etude électrophysiologique de récepteurs impliqués dans l'orientation vers l'hôte et dans l'acte hématophage chez un Hémiptère: *Triatoma infestans*. Ph.D. Thesis, University of Rennes, Rennes. p. 285.
Bianchet, M.A., Bains, G., Pelosi, P., Pevsner, J., Snyder, S.H., Monaco, H.L., Amzel, L.M., 1996. The three-dimensional structure of bovine odorant binding protein and its mechanism of odor recognition [see comments]. Nat. Struct. Biol. 3, 934–939.
Biessmann, H., Andronopoulou, E., Biessmann, M.R., Douris, V., Dimitratos, S.D., Eliopoulos, E., Guerin, P.M., Iatrou, K., Justice, R.W., Krober, T., Marinotti, O., Tsitoura, P., Woods, D.F., Walter, M.F., 2010. The *Anopheles gambiae* odorant binding protein 1 (AgamOBP1) mediates indole recognition in the antennae of female mosquitoes. PLoS ONE 5 (3), e9471.
Blackwell, A., Johnson, S.N., 2000. Electrophysiological investigation of larval water and potential oviposition chemoattractants for *Anopheles gambiae* s.s. Ann. Trop. Med. Parasitol. 94, 389–398.
Bodin, A., Barrozo, R.B., Couton, L., Lazzari, C.R., 2008. Temporal modulation and adaptive control of the behavioural response to odours in *Rhodnius prolixus*. J. Insect Physiol. 54, 1343–1348.
Bodin, A., Vinauger, C., Lazzari, C.R., 2009. Behavioural and physiolo gical state dependency of host seeking in the bloodsucking insect *Rhodnius prolixus*. J. Exp. Biol. 212, 2386–2393.
Boeckh, J., Boeckh, V., 1979. Threshold and odor specificity of pheromone-sensitive neurons in the deutocerebrum of *Antheraea pernyi* and *A. polyphemus* (Saturniidae). J. Comp. Physiol. A. 132, 235–242.
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.D., Dickens, J.C., 2010. Insect repellents: modulators of mosquito odorant receptor activity. PLoS ONE 5 (8), e12138.
Bohbot, J., Pitts, R.J., Kwon, H.W., Rützler, Robertson, H.M., Zwiebel, L.J., 2007. Molecular characterization of the *Aedes aegypti* odorant receptor gene family. Insect Mol. Biol. 16, 535–537.
Bohbot, J., Lu, T., Zwiebel, L.J., 2010. Molecular regulation of olfaction in mosquitoes. In: Takken, W., Knols, B.G.J. (Eds.), Olfaction in Vector-Host Interactions. Wageningen Academic Publishers, Wageningen, pp. 17–38.
Bohbot, J.D., Jones, P.L., Wang, G., Pitts, R.J., Pask, G.M., Zwiebel, L.J., 2011. Conservation of indole responsive odorant receptors in mosquitoes reveals an ancient olfactory trait. Chem. Senses 36, 149–160.
Bosch, O.J., Geier, M., Boeckh, J., 2000. Contribution of fatty acids to olfactory host finding of female *Aedes aegypti*. Chem. Senses 25, 323–330.
Brady, J., Crump, A.J., 1978. Control of circadian activity rhythms in tsetse flies – environment of physiological clock? Physiol. Entomol. 3, 177–190.
Braks, M.A.H., Takken, W., 1999. Incubated human sweat but not fresh sweat attracts the malaria mosquito *Anopheles gambiae* sensu stricto. J. Chem. Ecol. 25, 663–672.
Buck, L., Axel, R., 1991. A novel multigene family may encode odorant receptors: a molecular basis for odor recognition. Cell 65, 175–187.
Bursell, E., 1984. Effects of host odour on the behaviour of tsetse. Insect Sci. Appl. 5, 345–349.
Campbell-Lendrum, D.H., Pinto, M.C., Brandao-Filho, S.P., de Souza, A.A., Ready, P.D., Davies, C.R., 1999. Experimental comparison of anthropophily between geographically dispersed populations of *Lutzomyia whitmani* (Diptera: Psychodidae). Med. Vet. Entomol. 13, 299–309.
Carbajal de la Fuente, A.L., Minoli, S.A., Lopes, C.M., Noireau, F., Lazzari, C.R., Lorenzo, M.G., 2007. Flight dispersal of the Chagas disease vectors *Triatoma brasiliensis* and *Triatoma pseudomaculata* in northeastern Brazil. Acta Trop. 101, 115–119.
Carey, A.F., Carlson, J.R., 2011. Insect olfaction from model system to disease control. Proc. Natl. Acad. Sci. USA 108 (32), 12987–12995.
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, 66–71.
Catalá, S., 1994. The cave organ of Triatominae (Hemiptera, Reduviidae) under scanning electron-microscopy. Mem. Inst. O. Cruz. 89, 275–277.
Catalá, S., 1995. Los patrones de las sensilla. In: Proceedings of the International Wopkshop on Population Genetics and Control of *Triatoma*. Santo Domingo de los Colorados, Ecuador, pp. 59–62.
Catalá, S., Schofield, C., 1994. Antennal sensilla of *Rhodnius*. J. Morphol. 219, 193–203.
Catalá, S., Sachetto, C., Moreno, M., Rosales, R., Salazar-Schettino, P.M., Gorla, D., 2005. Antennal phenotype of *Triatoma dimidiata* populations and its relationship with species of phyllosoma and protracta complexes. J. Med. Entomol. 42, 719–725.
Chadee, D.D., 1993. Oviposition response of *Aedes aegypti* (L.) to the presence of conspecific eggs in the field in Trinidad. WI. J. Florida Mosq. Contr. Ass. 64, 63–66.
Chaffiol, A., Kropf, J., Barrozo, R.B., Gadenne, C., Rospars, J.P., Anton, S., 2012. Plant odour stimuli reshape pheromonal representation in neurons of the antennal lobe macroglomerular complex of a male moth. J. Exp. Biol. 215, 1670–1680.
Christensen, T.A., Hildebrand, J.G., 1988. Frequency coding by central olfactory neurons in the sphinx moth *Manduca sexta*. Chem. Senses 13, 123–130.
Christensen, T.A., Hildebrand, J.G., 1997. Coincident stimulation with pheromone components improves temporal pattern resolution in central olfactory neurons. J. Neurophysiol. 77, 775–781.
Christensen, T.A., Waldrop, B.R., Harrow, I.D., Hildebrand, J.G., 1993. Local interneurons and information processing in the olfactory glomeruli on the moth *Manduca sexta*. J. Comp. Physiol. A 173, 385–399.
Christensen, T.A., Waldrop, B.R., Hildebrand, J.G., 1998. Multitasking in the olfactory system: context-dependent responses to odors reveal dual GABA-regulated coding mechanisms in single olfactory proyection reurons. J. Neurosc. 18, 5999–6008.
Christensen, T.A., Lei, H., Hildebrand, J.G., 2003. Coordination of central odor representations through transient, non-oscillatory synchronization of glomerular output neurons. Proc. Natl. Acad. Sci. USA 100, 11076–11081.
Clifford, M.R., Riffell, J.A., 2013. Mixture and odorant processing in the olfactory systems of insects: a comparative perspective. J. Comp. Physiol. 199, 911–928.
Clyne, P.J., Warr, C.G., Freeman, M.R., Lessing, D., Kim, J., Carlson, J.R., 1999a. A novel family of divergent seven transmembrane proteins: candidate odorant receptors in *Drosophila*. Neuron 22, 327–338.
Clyne, P.J., Certel, S.J., de Bruyne, M., Zaslavsky, L., Johnson, W.A., Carlson, J.R., 1999b. The odor specificities of a subset of olfactory receptor neurons are governed by Acj6, a POU-domain transcription factor. Neuron 22, 339–347.
Collins, I.E., Blackwell, A., 2002. Olfatory cues for oviposition behavior in *Toxorhynchites moctezuma* and *Toxorhynchites amboinensis* (Diptera: Culicidae). J. Med. Entomol. 39, 121–126.
Colvin, J., Brady, J., Gibson, G., 1989. Visually-guided, upwind turning behaviour of free-flying tsetse flies in odourladen wind: a wind-tunnel study. Physiol. Entomol. 14, 31–39.
Cork, A., Park, C., 1996. Identification of electrophysiologically-active compounds for the malaria mosquito, *Anopheles gambiae*, in human sweat extracts. Med. Vet. Entomol. 10, 269–276.
Couto, A., Alenius, M., Dickson, B.J., 2005. Molecular, anatomical, and functional organization of the *Drosophila* olfactory system. Curr. Biol. 15, 1535–1547.
Crespo, J.G., Manrique, G., 2007. Mating behavior of the hematophagous bug *Triatoma infestans*: role of Brindley's and metasternal glan ds. J. Insect Physiol. 53, 708–714.
Croset, V., Ryts, 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 Genet. 6 (8), e1001064.
Cruz-Lopez, L., Morgan, E.D., Ondarza, R.N., 1995. Brindley's gland exocri ne products of *Triatoma infestans*. Med. Vet. Entomol. 9, 403–406.
Cruz-López, L., Malo, E.A., Rojas, J.C., Morgan, E.D., 2001. Chemical ecology of triatomine bugs: vectors of Chagas disease. Med. Vet. Entomol. 15, 351–357.
Dacks, A.M., Green, D.S., Root, C.M., Nighorn, A.J., Wang, J.W., 2009a. Serotonin modulates olfactory processing in the antennal lobe of *Drosophila*. J. Neurogenet. 23, 366–377.
Dacks, A., Guerenstein, P., Reisenman, C., Martin, J., Lei, H., Hildebrand, J., 2009b. Olfaction in invertebrates: *Manduca*. In: Squire, L.R. (Ed.), Encyclopedia of Neuroscience, vol. 7. Academic Press, Oxford, pp. 49–57.
Dacks, A.M., Riffel, J.A., Martin, J.P., Gage, S.L., Nighorm, A.J., 2012. Olfactory modulation by dopamine in the context of aversive learning. J. Neurophysiol. 108 (2), 539–550.
Daly, K., Christensen, T.A., Lei, H., Smith, B., Hildebrand, J.G., 2004. Learning modulates the ensemble representations for odors in primary olfactory networks. Proc. Natl. Acad. Sci. USA 101, 10476–10481.
Danty, E., Michard-Vanhée, C., Huet, J.C., Genecque, E., Pernollet, J.C., Masson, C., 1997. Biochemical characterization, molecular cloning and localization of a putative odorant-binding protein in the honey bee *Apis mellifera* L. (Hymenoptera: Apidea). FEBS Lett. 414 (3), 595–598 (15).
Das, P., Fadamiro, H.Y., 2013. Species and sexual differences in antennal lobe architecture and glomerular organization in two parasitoids with different degree of host specificity, *Microplitis croceipes* and *Cotesia marginiventris*. Cell Tiss. Res. 352, 227–235.
Davis, E.E., 1976. A receptor sensitive to oviposition site attractants on the antennae of the mosquito, *Aedes aegypti*. J. Insect Physiol. 22, 1371–1376.
Davis, E.E., Sokolove, P.G., 1976. Lactic acid-sensitive receptors on the antennae of the mosquito, *Aedes aegypti*. J. Comp. Physiol. 105, 43–54.
de Bruyne, M., Baker, T.C., 2008. Odor detection in insects: volatile codes. J. Chem. Ecol. 34, 882–897.
de Bruyne, M., Clyne, P.J., Carlson, J.R., 1999. Odor coding in a model olfactory organ: the *Drosophila* maxillary palp. J. Neurosc. 19, 4520–4532.
de Bruyne, M., Foster, K., Carlson, J.R., 2001. Odor coding in the *Drosophila* antenna. Neuron 30, 537–552.
Dekker, T., Steib, B., Carde, R.T., Geier, M., 2002. L-Lactic acid: a human-signifying host cue for the anthropophilic mosquito *Anopheles gambiae*. Med. Vet. Entomol. 16, 91–98.
Dekker, T., Geier, M., Carde, R.T., 2005. Carbon dioxide instantly sensitizes female yellow fever mosquitoes to human skin odours. J. Exp. Biol. 208, 2963–2972.
Dethier, V.G., 1957. The sensory physiology of blood-sucking arthropods. Exp. Parasitol. 6, 68–122.

Dickens, J.C., Callahan, F.E., 1996. Antennal-specific protein in tarnished plant bug, *Lygus lineolaris*: production and reactivity of antisera. Entomol. Exp. Appl. 80, 19–22.
Dickens, J.C., Callahan, F.E., Wergin, W.P., Erbe, E.F., 1995. Olfaction in a hemimetabolous insect: antennal-specific protein in adult *Lygus lineolaris* (Heteroptera: Miridae). J. Insect Physiol. 41, 857–867.
Diehl, P.A., Vlimant, M., Guerenstein, P.G., Guerin, P.M., 2003. Ultrastructure and receptor cell responses of the antennal grooved peg sensilla of *Triatoma infestans* (Hemiptera: Reduviidae). Arthrop. Struct. Dev. 31, 271–285.
Distler, P.G., Boeckh, J., 1996. Synaptic connection between olfactory receptor cells and uniglomerular projection neurons in the antennal lobe of the American cockroach, *Periplaneta americana*. J. Comp. Neurol. 370, 35–46.
Ditzen, M., Pellegrino, M., Vosshall, L.B., 2008. Insect odorant receptors are molecular targets of the insect repellent DEET. Science 319, 1838–1842.
Dormont, L., Bessiére, J.M., Cohuet, A., 2013a. Human skin volatiles: a review. J. Chem. Ecol. 39, 569–578.
Dormont, L., Bessiére, J.-M., Mc Key, D., Cohuet, A., 2013b. New methods for field collection of human skin volatiles and perspectives for their application in the chemical ecology of human/pathogen/vector interactions. J. Exp. Biol. 216 (Pt 15), 2783–2788.
Dougherty, M.J., Hamilton, J.G.C., 1997. Dodecanoic acid is the oviposition pheromone of *Lutzomyia longipalpis*. J. Chem. Ecol. 23, 2657–2671.
Dougherty, M.J., Ward, R.D., Hamilton, J.G.C., 1992. Evidence for the accessory glands as the site of production of the oviposition pheromone of *Lutzomyia longipalpis* (Diptera: Psychodidae). J. Chem. Ecol. 18, 1165–1175.
Dougherty, M.J., Guerin, P., Ward, R.D., 1995. Identification of oviposition attractants for the sandfly *Lutzomyia longipalpis* (Diptera: Psychodidae) present in volatiles of faeces from vertebrates. Physiol. Entomol. 20, 23–32.
Dougherty, M.J., Guerin, P.M., Ward, R.D., Hamilton, J.G.C., 1999. Behavioural and electrophysiological responses of the phlebotomine sandfly *Lutzomyia longipalpis* (Diptera: Psychodidae) when exposed to canid host odour kairomones. Physiol. Entomol. 24 (3), 251–262.
El Naiem, D., Ward, R.D., 1992. Oviposition attractants and stimulants for the sandfly *Lutzomyia longipalpis* (Diptera: Psychodidae). J. Med. Entomol. 29, 5–12.
Ernst, K.D., Boeckh, J., Boeckh, V., 1977. A neuroanatomical study on the organization of the central antennal pathways in insects. Cell Tiss. Res. 176, 285–306.
Febbraio, M., Silverstein, R.L., 2007. CD36: implications in cardiovascular disease. Int. J. Biochem. Cell Biol. 39, 2012–2030.
Fishilevich, E., Vosshall, L.B., 2005. Genetic and functional subdivision of the *Drosophila* antennal lobe. Curr. Biol. 15, 1548–1553.
Flower, D.R., 1996. The lipocalin protein family: structure and function. Biochem. J. 318, 1–14.
Foster, S.P., Harris, M.O., 1997. Behavioural manipulation methods for insect pest management. Ann. Rev. Entomol. 42, 123–146.
French, A.S., Torkkeli, P.H., Schuckel, J., 2011. Dynamic characterization of *Drosophila* antennal olfactory neurons indicates multiple opponent signaling pathways in odor discrimination. J. Neurosc. 31, 861–869.
Fresquet, N., Lazzari, C.R., 2011. Response to heat in *Rhodnius prolixus*: the role of the thermal background. J. Insect Physiol. 57, 1446–1449.
Galindo, K., Smith, D.P., 2001. A large family of divergent *Drosophila* odorant-binding proteins expressed in gustatory and olfactory sensilla. Genetics 159, 1059–1072.
Galizia, C.G., Menzel, R., 2001. The role of glomeruli in the neural representation of odours: results from optical recording studies. J. Insect Physiol. 47, 115–130.
Galizia, C.G., Sachse, S., 2010. Odor coding in insects. In: Menini, A. (Ed.), The Neurobiology of Olfaction. CRC Press, Boca Raton, pp. 35–70.
Galizia, C.G., McIlwrath, S.L., Menzel, R., 1999a. A digital three-dimensional atlas of the honeybee antennal lobe based on optical sections acquired by confocal microscopy. Cell Tiss. Res. 295, 383–394.
Galizia, C.G., Sachse, S., Rappert, A., Menzel, R., 1999b. The glomerular code for odor representation is species specific in the honeybee *Apis mellifera*. Nat. Neurosci. 2, 473–478.
Geier, M., Boeckh, J., 1999. A new Y-tube olfactometer for mosquitoes to measure the attractiveness of host odours. Entomol. Exp. Appl. 92, 9–19.
Geier, M., Bosch, O.J., Boeckh, J., 1999a. Ammonia as an attractive component of host odour for the yellow fever mosquito, *Aedes aegypti*. Chem. Senses 24, 647–653.
Geier, M., Bosh, O.J., Boeckh, J., 1999b. Influence of odour plume structure on upwind flight of mosquitoes towards hosts. J. Exp. Biol. 202, 1639–1648.
Ghaninia, M., Hansson, B.S., Ignell, R., 2007a. The antennal lobe of the African malaria mosquito, *Anopheles gambiae*-innervation and three-dimensional reconstruction. Arth. Struct. Dev. 36 (1), 23–39.
Ghaninia, M., Ignell, R., Hansson, B.S., 2007b. Functional classification and central nervous projections of olfactory receptor neurons housed in antennal trichoid sensilla of female yellow fever mosquitoes, *Aedes aegypti*. Euro. J. Neurosci. 26 (6), 1611–1623.
Ghaninia, M., Larsson, M., Hansson, B.S., Ignell, R., 2008. Natural odor ligands for olfactory receptor neurons of the female mosquito *Aedes aegypti*: use of gas chromatography-linked single sensillum recordings. J. Exp. Biol. 211, 3020–3027.
Gibson, G., Brady, J., 1985. Anemotactic' flight paths of tsetse flies in relation to host odour: a preliminary video study in nature of the response to loss of odour. Physiol. Entomol. 10, 375–406.
Gibson, G., Brady, J., 1988. Flight behaviour of tsetse flies in host odour plumes – the initial response to leaving or entering odour. Physiol. Entomol. 13, 29–42.
Gibson, G., Torr, S.J., 1999. Visual and olfactory responses of haematophagous Diptera to host stimuli. Med. Vet. Entomol. 13, 2–23.
González-Audino, G.P., Alzogaray, R.A., Vannesa, C., Masuh, H., Fontán, A., Gatti, P., Martínez, A., Camps, F., Cork, A., Zerba, E., 2007. Volatile compounds secreted by Brindleýs glands of adult *Triatoma infestans*: identification and biological activity of previously unidentified compounds. J. Vector Ecol. 32, 75–82.
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. J. Comp. Physiol. A 177, 389–396.
Griffiths, N., Paynter, Q., Brady, J., 1995. Rates of progress up odour plumes by tsetse flies: a mark-release video study of the timing of odour source location by Glossina pallidipes. Physiol. Entomol. 20, 100–108.
Guerenstein, P.G., 1999. Sensory and behavioural responses of Triatoma infestans to host and conspecific odours. Ph.D. Thesis, University of Neuchâtel, Switzerland, p. 137.
Guerenstein, P.G., Guerin, P.M., 2001. Olfactory and behavioural responses of the blood-sucking bug *Triatoma infestans* to odours of vertebrate hosts. J. Exp. Biol. 204, 585–597.
Guerenstein, P.G., Guerin, P.M., 2004. A comparison of volatiles emit ted by adults of three triatomine species. Entomol. Exp. Appl. 111, 151–155.
Guerenstein, P.G., Hildebrand, J.G., 2008. Roles and effects of environmen tal carbon dioxide in insect life. Ann. Rev. Entomol. 53, 161–178.
Guerenstein, P.G., Lazzari, C.R., 2009. Host-seeking: How triatomines acquire and make use of information to find blood. Acta Trop. 110, 148–158.
Guerenstein, P.G., Lazzari, C.R., 2010. The role of olfaction in host seeking of Triatominae bugs. In: Takken, W., Knols, B. (Eds.), Ecology and Control of Vector-Borne Diseases, Olfaction in Vector-Host Interactions, vol. II. Wageningen University Press, Wageningen, pp. 309–325.
Guerenstein, P.G., Lorenzo, M.G., Núñez, J.A., Lazzari, C.R., 1995. Bakers-yeast, an attractant for baiting traps for Chagas-disease vectors. Experientia. 51, 834–837.
Guerenstein, P.G., Christensen, T.A., Hildebrand, J.G., 2004a. Sensory processing of ambient CO_2 information in the brain of the moth *Manduca sexta*. J. Comp. Physiol. A 190, 707–725.
Guerenstein, P.G., Yepez, E.A., van Haren, J., Williams, D.G., Hildebrand, J.G., 2004b. Floral CO_2 emission may indicate food abundance to nectar-feeding moths. Naturwissenschaften 91, 329–333.
Guerenstein, P.G., Thom, C., Pawlowski, V., Paulk, A., Christensen, T.A., Hildebrand, J.G., 2005. Is there a functional rationale for the glomerular spatial map in an insect's olfactory lobe? Society for Neuroscience Abstracts, 614–620.
Guidobaldi, F., Guerenstein, P.G., 2012. El Sistema Olfativo de los Insectos. In: Rojas, J.C., Malo, E.A. (Eds.), Temas selectos de Ecología químicas de insectos. Ecosur, Chiapas, pp. 46–71.
Guidobaldi, F., Guerenstein, P.G., 2013. Evaluation of a CO_2-free commercial mosquito attractant to capture triatomines in the laboratory. J. Vector Ecol. 38, 245–250.
Hallem, E.A., Carlson, J.R., 2006. Coding of odors by a receptor repertoire. Cell 125, 143–160.
Hallem, E.A., Fox, A.N., Zwiebel, L.J., Carlson, J.R., 2004a. Mosquito receptor for human-sweat odorant. Nature 427, 212–213.
Hallem, E.A., Ho, M.G., Carlson, J.R., 2004b. The molecular basis of odor coding in the *Drosophila* antenna. Cell 117, 965–979.
Hallem, E.A., Dahanukar, A., Carlson, J.R., 2006. Insect odor and taste receptors. Ann. Rev. Entomol. 51, 113–135.
Hamilton, J.G.C., Dougherty, M.J., Ward, R.D., 1994. Sex pheromone activity in a single component of tergal gland extract of *Lutzomyia longipalpis* (Diptera: Psychodidae) from Jacobina, Northeastern Brazil. J. Chem. Ecol. 20, 141–151.
Hamilton, J.G.C., Hooper, A.M., Mori, K., Pickett, J.A., Sano, S., 1999. 3-Methyl-α-himachalene confirmed, and the relative stereochemistry defined, by synthesis as the sex pheromone of the sandfly *Lutzomyia longipalpis* from Jacobina. Brazil. Chem. Comms., 355–356.
Hansson, B.S., Anton, S., 2000. Function and morphology of the antennal lobe: new developments. Ann. Rev. Entomol. 45, 203–231.
Hansson, B.S., Christensen, T.A., 1999. Functional characteristics of the antennal lobe. In: Hansson, B.S. (Ed.), Insect Olfaction. Springer, Berlin, pp. 126–157.
Hansson, B.S., Stensmyr, M.C., 2011. Evolution of insect olfaction. Neuron 72 (5), 698–711.
Hanström, B., 1928. Vergleichende Anatomie des Nervensystems der wirbellosen Tiere. Springer, Berlin, Heidelberg, New York, p. 628.
Hargrove, J.W., 1980. The effect of model size and ox odour on the alighting response of *Glossina morsitans* Westwood and *Glossina pallidipes* Austen (Diptera: Glossinidae). Bull. Entomol. Res. 70, 229–234.
Hargrove, J.W., Brady, J., 1992. Activity rhythms of tsetse flies (*Glossina* spp) (Diptera: Glossinidae) at low and high temperatures in nature. Bull. Entomol. Res. 82, 321–326.
Harraca, V., Ignell, R., Christer, L., Ryne, C., 2010. Characterization of the antennal olfactory system of the bug (*Cimex lectularius*). Chem. Senses 35, 195–204.
Harraca, V., Ryne, R., Birgersson, G., Ignell, R., 2012. Smelling your way to food: can bed bugs use our odour? J. Exp. Biol. 215, 623–629.
Hekmat-Scafe, D.S., Steinbrecht, R.A., Carlson, J.R., 1997. Coexpression of two odorant-binding protein homologs in *Drosophila*: implications for olfactory coding. J. Neurosci. 17, 1616–1624.
Hildebrand, J.G., 1996. Olfactory control of behaviour in moths: central processing of odor information and the functional significance of olfactory glomeruli. J. Comp. Physiol. A 178, 5–19.

Hildebrand, J.G., Matsumoto, S.G., Camazine, S.M., Tolbert, L.P., Blank, S., Ferguson, H., Ecker, V., 1980. Organisation and physiology of antennal centres in the brain of the moth *Manduca sexta*. In: Insect Neurobiology and Pesticide Action (Neurotox 79). Society of Chemical Industry, London, pp. 375–382.

Hill, C.A., Fox, A.N., Pitts, R.J., Kent, L.B., Tan, P.L., Chrystal, M.A., Cravchik, A., Collin, F.H., Robertson, H.M., Zwiebel, L.J., 2002. G protein-coupled receptors in *Anopheles gambiae*. Science 298, 176–178.

Hill, S.R., Hansson, B.S., Ignell, R., 2009. Characterization of antennal trichoid sensilla from female southern house mosquito, *Culex quinquefasciatus* Say. Chem. Senses 34, 231–252.

Homberg, U., Müller, U., 1999. Neuroactive substances in the antennal lobe. In: Hansson, B.S. (Ed.), Insect Olfaction. Springer, Berlin, pp. 182–204.

Huang, J., Zhang, W., Qiao, W., Hu, A., Wang, Z., 2010. Functional connectivity and selective odor re sponses of excitatory local interneurons in *Dro sophila* antennal lobe. Neuron 67, 1021–1033.

Hughes, D.T., Pelletier, J., Luetje, C.W., Leal, W.S., 2010. Odorant receptor from the southern house mosquito narrowly tuned to the oviposition attractant skatole. J. Chem. Ecol. 36, 797–800.

Ignell, R., Anton, S., Hansson, B., 2001. The antennal lobe of orthoptera: anatomy and evolution. Brain, Behav. Evol. 57, 1–17.

Ignell, R., Dekker, T., Ghaninia, M., Hansson, B.S., 2005. Neuronal architecture of the mosquito deutocerebrum. J. Comp. Neurol. 493, 207–240.

Ignell, R., Sengul, M., Hill, S., Hansson, B., 2010. Odour coding and neural connections. In: Takken, W., Knols, B.G.J. (Eds.), Olfaction in Vector-Host Interactions. Wageningen Academic Publishers, Wageningen, pp. 63–90.

Ishida, Y., Cornel, A.J., Leal, W.S., 2002. Identification and cloning of a female antenna-specific odorant-binding protein in the mosquito *Culex quinquefasciatus*. J. Chem. Ecol. 28, 867–871.

Ishida, Y., Ishibashi, J., Leal, W.S., 2013. Fatty acid solubilizer from the oral disk of the blowfly. PLoS One 8 (1), e51779.

Jacquin-Joly, E., Vogt, R.G., Francois, M.C., Nagnan-Le Meillour, P., 2001. Functional and expression pattern analysis of chemosensory proteins expressed in antennae and pheromonal gland of *Mamestra brassicae*. Chem. Senses 26, 833–844.

Jones, W.D., Nguyen, T.A., Kloss, B., Lee, K.J., Vosshall, L.B., 2005. Functional conservation of an insect odorant receptor gene across 250 million years of evolution. Curr. Biol. 15, 119–121.

Jones, W.D., Cayirlioglu, P., Kadow, I.G., Vosshall, L.B., 2007. Two chemosensory receptors together mediate carbon dioxide detection in *Drosophila*. Nature 445, 86–90.

Kain, P., Boyle, S.M., Tharadra, S.K., Guda, T., Pham, C., Dahanukar, A., Ray, A., 2013. Odour receptors and neurons for DEET and new insect repellents. Nature 502, 507–512.

Kaissling, K., 1998. Flux detectors versus concentration detectors: two types of chemoreceptors. Chem. Senses 23, 99–111.

Kaissling, K.E., 2013. Kinetics of olfactory responses might largely depend on the odorant–receptor interaction and the odorant deactivation postulated for flux detectors. J. Comp. Physiol. A. Neuroethol. Sens. Neural. Behav. Physiol. 199 (11), 879–896.

Kaufmann, C., Briegel, H., 2004. Flight performance of the malaria vectors *Anopheles gambiae* and *Anopheles atroparvus*. J. Vector Ecol. 29, 140–153.

Keil, T.A., 1999. Morphology and development of the peripheral olfactory organs. In: Hansson, B.S. (Ed.), Insect Olfaction. Springer, Berlin, pp. 5–47.

Kennedy, J.S., 1977. Olfactory responses to distant plants and odor sources, in: Shorey, H.H., Mc Kelvey, J.J. (Eds.), Chemical Control of Insect Behavior: Theory and Application. John Wiley & Sons, New York, pp. 67–91.

Kent, L.B., Walden, K.K.O., Robertson, H.M., 2008. The Gr family of candidate gustatory and olfactory receptors in the yellow fever mosquito *Aedes aegypti*. Chem. Senses 33, 79–93.

Kirschner, S., Kleineidam, C.J., Zube, C., Rybak, J., Grünewald, B., Rössler, W., 2006. J. Comp. Physiol. 499 (6), 933–952.

Krautwurst, D., Yau, K.W., Reed, R.R., 1998. Identification of ligands for olfactory receptors by functional expression of a receptor library. Cell 95 (7), 917–926.

Kreher, S.A., Kwon, J.Y., Carlson, J., 2005. The molecular basis of odor coding in the *Drosophila* larva. Neuron 46, 445–456.

Krieger, J., Von Nickisch, E., Mameli, M., Pelosi, P., Breer, H., 1996. Binding proteins from the antennae of *Bombyx mori*. Insect Biochem. Mol. Biol. 26, 297–307.

Krieger, J., Raming, K., Dewer, Y.M., Bette, S., Conzelmann, S., Breer, H., 2002. A divergent gene family encoding candidate olfactory receptors of the moth *Heliothis virescens*. Euro. J. Neurosci. 16, 619–628.

Krieger, J., Klink, O., Mohl, C., Raming, K., Breer, H., 2003. A candidate olfactory receptor subtype highly conserved across different insect orders. J. Comp. Physiol. A 189, 519–526.

Krishnakumari, B., Sarita-Raj, K., Hamilton, J.G.C., 2004. Synthesis of 9-methylgermacrene from germacrone, an active analogue of (S)-9-methylgermacrene-B, sex pheromone of the Phlebotomine sandfly, *Lutzomyia longipalpis*, from Lapinha Brazil. In: P-183, IUPAC International Conference on Biodiversity and Natural Products: Chemistry and Medical Applications, 26–31 January 2004. New Delhi, India.

Kristoffersen, L., Hansson, B.S., Anderbrant, O., Larsson, M.C., 2008. Aglomerular hemipteran antennal lobes-basic neuroanatomy of a small Nose. Chem. Senses 33, 771–778.

Kruse, S.W., Zhao, R., Smith, D.P., Jones, D.N., 2003. Structure of a specific alcohol-binding site defined by the odorant binding protein LUSH from *Drosophila melanogaster*. Nat. Struct. Biol. 10, 694–700.

Kuebler, L.S., Olsson, S.B., Weniger, R., Hansson, B.S., 2011. Neuronal processing of complex mixtures establishes a unique odor representation in the moth antennal lobe. Front. Neural Circuits 5, 7.

Kwon, H.W., Lu, T., Rutzler, M., Zwiebel, L.J., 2006. Olfactory responses in a gustatory organ of the malaria vector mosquito *Anopheles gambiae*. Proc. Natl. Acad. Sci. USA 103, 13526–13531.

Kwon, J.Y., Dahanukar, A., Weiss, L.A., Carlson, J.R., 2007. The molecular basis of CO_2 reception in *Drosophila*. Proc. Natl. Acad. Sci. USA 104, 3574–3578.

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*. J. Comp. Neurol. 405, 543–552.

Lane, R., Ward, R.D., 1984. The morphology and possible function of abdominal patches in males of two forms of *Lutzomyia longipalpis* (Diptera: Phlebotominae). Cahiers dOffice de la Recherche Scientifique et Technique Outre-Mer. Entomol. Med. Parasitol. 22, 245–249.

Lane, R., Phillips, A., Molyneux, D.H., Procter, G., Ward, R.D., 1985. Chemical-analysis of the abdominal glands of two forms of *Lutzomyia longipalpis* – site of a possible sex-pheromone. Ann. Trop. Med. Parasitol. 79, 225–229.

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, 703–714.

Latorre-Estivalis, J.M., Robertson, H.M., Omondis, A.B., Lorenzo, M.G., 2012. Molecular bases of chemoreception in *Rhodnius prolixus*. Abstracts of the 2° ALAEQ Meeting, Argentina.

Lazzari, R.C., Pereira, M.H., Lorenzo, M.G., 2013. Behavioural biology of Chagas disease vectors. Mem. Inst. O. Cruz. 108, 34–47.

Leal, W.S., 2005. Pheromone reception. Top. Curr. Chem. 240, 1–36.

Leal, W.S., Choo, Y.M., Xu, P., da Silva, C.S.B., Ueira-Vieira, C., 2013. Differential expression of olfactory genes in the southern house mosquito and insights into unique odorant receptor gene isoforms. Proc. Natl. Acad. Sci. USA 110, 18704–18709.

Lehane, M.J., 2005. The Biology of Blood-sucking Insects. Cambridge University Press, New York.

Lei, H., Hansson, B.S., 1999. Central processing of pulsed pheromone signals by antennal lobe neurons in the male moth *Agrotis segetum*. J. Neurophysiol. 81, 1113–1122.

Lei, H., Christensen, T.A., Hildebrand, J.G., 2002. Local inhibition modulates odor-evoked synchronization of glomerulus-specific output neurons. Nat. Neurosc. 5, 557–565.

Lei, H., Christensen, T.A., Hildebrand, J.G., 2004. Spatial and temporal organization of ensemble representations for different odor classes in the moth antennal lobe. J. Neurosci. 24, 11108–11119.

Lei, H., Riffell, J.A., Gage, S.L., Hildebrand, J.G., 2009. Contrast enhancement of stimulus intermittency in a primary olfactory network and its behavioral significance. J. Biol. 8, 21.

Leite, N.R., Krogh, R., Xu, W., Ishida, Y., Iulek, J., Leal, S., 2009. Structure of an odorant-binding protein from the mosquito *Aedes aegypti* suggests a binding pocket covered by a pH-sensitive "Lid". PLoS ONE 4, e8006.

Liu, C., Pitts, R.J., Bohbot, J.D., Jones, P.L., Wang, G., Zwiebel, L.J., 2010. Distinct olfactory signaling mechanisms in the malaria vector mosquito *Anopheles gambiae*. PLoS Biol. 8 (8), e1000467.

Logan, J.G., Birkett, M.A., Clark, S.J., Powers, S., Seal, N.J., Wadhams, L.J., Mordue Luntz, A.J., Pickett, J.A., 2008. Identification of human-derived volatile chemicals that interfere with attraction of *Aedes aegypti* mosquitoes. J. Chem. Ecol. 34, 308–322.

Lorenzo, M.G., Lazzari, C.R., 1996. The spatial pattern of defecation in *Triatoma infestans* and the role of faeces as a chemical mark of the refuge. J. Insect Physiol. 42, 903–907.

Lorenzo-Figueiras, A.N., Lazzari, C.R., 1998. Aggregation in the haematophagous bug *Triatoma infestans*: a novel assembling factor. Physiol. Entomol. 23, 33–37.

Lorenzo-Figueiras, A.N., Kenigsten, A., Lazzari, C.R., 1994. Aggregation in the haematophagous bug *Triatoma infestans*: chemical signals and temporal pattern. J. Insect Physiol. 40, 311–316.

Lorenzo-Figueiras, A.N., Girotti, J.R., Mijailovsky, S.J., Juarez, M.P., 2009. Epicuticular lipids induce aggregation in Chagas disease vectors. Parasit. Vect. 2 (8), 1–7.

Lu, T., Qiu, Y.T., Wang, G., Kwon, J.Y., Rützler, M., Kwon, H., Pitts, R.J., van Loon, J.J.A., Takken, W., Carlson, J.R., Zwiebel, L.J., 2007. Odor coding in the maxillary palp of the malaria vector mosquito *Anopheles gambiae*. Curr. Biol. 17, 1533–1544.

Mangabeira, O.F., 1969. Sobre a sistematica e biologia dos *Phlebotomus* do Ceara. Ver. Brás. Malariol. Doen. Trop. 12, 3–26.

Manrique, G., Lazzari, C.R., 1995. Existence of a sex pheromone in *Tria toma infestans* (Hemiptera: Reduviidae): I. Behavioural evidence. Mem. Inst. O. Cruz. 90, 645–648.

Manrique, G., Lorenzo, M., 2012. The sexual beahaviour of Chagas' disease vectors: chemical signals mediating communication between male and female triatomine bugs. Psyche 2012, 1–8, ID. 862891.

Manrique, G., Vitta, A.C., Ferreira, R.A., Zani, C.L., Unelius, C.R., Lazzari, C.R., Diotaiuti, L., Lorenzo, M.G., 2006. Chemical communication in Chagas disease vectors. Source, identity and potential function of volatiles released by the metasternal and Brindley's glands of *Triatoma infestans* adults. J. Chem. Ecol. 32, 2035–2052.

Mao, Y., Xu, X., Xu, W., Ishida, Y., Leal, W.S., Ames, J.B., Clardy, J., 2010. Crystal and solution structures of an odorant-binding protein from the southern house mosquito complexed with an oviposition pheromone. Proc. Natl. Acad. Sci. USA 107, 19102–19107.

Marion-Poll, F., Tobin, T.R., 1992. Temporal coding of pheromone pulses and trains in *Manduca sexta*. J. Comp. Physiol. A 171, 505–512.
May-Concha, I.J., 2010. Compuestos volatiles emitidos por adultos en disturbio y copula de Triatoma dimidiata (Hemiptera: Reduviidae), vector de la enfermedad de Chagas. M.Sc. Thesis. Instituto Nacional de Salud Pública, Tapachula. pp. 1–26.
May-Concha, I., Rojas, J.C., Cruz-Lopez, L., Millar, J.G., Ramsey, J.M., 2013. Volatile compounds emitted by *Triatoma dimidiata*, a vector of Chagas disease: chemical analysis and behavioural evaluation. Med. Vet. Entomol. 27, 165–174.
Mayer, M.S., 1968. Response of single olfactory cell of *Triatoma infestans* to human breath. Nature 220, 924–925.
Mboera, L.E.G., Takken, W., Mdira, K.Y., Chuwa, G.J., Pickett, J.A., 2000. Oviposition and behavioral responses of *Culex quinquefasciatus* to skatole and synthetic oviposition pheromone in Tanzania. J. Chem. Ecol. 26 (5), 1193–1203.
McIver, S.B., 1982. Sensilla of mosquitoes (Diptera: Culicidae). J. Med. Entomol. 19, 489–535.
McKenna, M.P., Hekmat-Scafe, D.S., Gaines, P., Carlson, J.R., 1994. Putative *Drosophila* pheromone-binding proteins expressed in a subregion of the olfactory system. J. Biol. Chem. 269, 16340–16347.
Meijerink, J., Braks, M.A.H., Brack, A.A., Adam, W., Dekker, T., Posthumus, M.A., van Beek, T.A., van Loon, J.J.A., 2000. Identification of olfactory stimulants for *Anopheles gambiae* from human sweat samples. J. Chem. Ecol. 26, 1367–1382.
Meijerink, J., Braks, M.A.H., Van Loon, J.J.A., 2001. Olfactory receptors on the antennae of the malaria mosquito *Anopheles gambiae* are sensitive to ammonia and other sweat-borne components. J. Insect Physiol. 47, 455–464.
Meyer, A., Galizia, C.G., Nawrot, M.P., 2013. Local interneurons and projection neurons in the antennal lobe from a spiking point of view. J. Neurophysiol. 110, 2465–2474.
Millar, J.G., Chaney, J.D., Mulla, M.S., 1992. Identification of oviposition attractants for *Culex quinquefasciatus* from fermented Bermuda grass infusions. J. Am. Mosq. Control Assoc. 8, 11–17.
Minoli, S., Palottini, F., Manrique, G., 2013. The main component of an alarm pheromone of kissing bugs plays multiple roles in the cognitive modulation of the escape response. Front. Behav. Neurosci. 7 (77), 1–10.
Mohl, C., Breer, H., Krieger, J., 2002. Species-specif ic pheromonal compounds induce distinct con formational changes of pheromone binding protein subtypes from *Antheraea polyphemus*. Invert Neurosci. 4, 165–174.
Montoya-Lerma, J., Lane, R.P., 1996. Factors affecting host preference of *Lutzomyia evansi* (Diptera: Psychodidae), a vector of visceral leishmaniasis in Columbia. Bull. Entomol. Res. 86, 43–50.
Moreno, M.L., Gorla, D., Catalá, S.S., 2006. Association between antennal phenotype, wing polymorphism and sex in the genus *Mepraia* (Reduviidae: Triatominae). Infec. Genet. Evol. 6 (3), 228–234.
Morton, I.E., Ward, R.D., 1989. Laboratory response of female *Lutzomyia longipalpis* sandflies to a host and male pheromone source over distance. Med. Vet. Entomol. 3, 219–223.
Mukabana, W.R., Mweresa, C.K., Otieno, B., Omusula, P., Smallegange, R.C., van Loon, J.J., Takken, W., 2012. A novel synthetic odorant blend for trapping of malaria and other African mosquito species. J. Chem. Ecol. 38 (3), 235–244.
Nakagawa, T., Vosshall, L.B., 2009. Controversy and consensus: noncanonical signaling mechanisms in the insect olfactory system. Curr. Opin. Neurobiol. 19 (3), 284–292.
Nakagawa, T., Sakurai, T., Nishioka, T., Touhara, K., 2005. Insect sex-pheromone signals mediated by specific combinations of olfactory receptors. Science 307, 1638–1642.
Nichols, Z., Vogt, R.G., 2008. The SNMP/CD36 gene family in Diptera, Hymenoptera and Coleoptera: *Drosophila melanogaster*, *D. pseudoobscura*, *Anopheles gambiae*, *Aedes aegypti*, *Apis mellifera*, and *Tribolium castaneum*. Insect Biochem. Mol. Biol. 38, 398–415.
Nikonov, A.A., Leal, W.S., 2002. Peripheral coding of sex pheromone and behavioral antagonist in the Japanese beetle, *Popillia japonica*. J. Chem. Ecol. 28, 1075–1089.
Nishikawa, M., Nishino, H., Misaka, Y., Kubota, M., Tsuji, E., Satoji, Y., Ozaki, M., Yokohari, F., 2008. Sexual dimorphism in the antennal lobe of the and *Camponotus japonicus*. Zool. Sci. 25, 195–204.
Núñez, J.A., 1982. Food source orientation and activity in *Rhodnius prolixus*. Bull. Entomol. Res. 72, 253–262.
Ochieng, S.A., Park, K.C., Baker, T.C., 2002. Host plant volatiles synergize responses of sex pheromone-specific olfactory receptor neurons in male *Helicoverpa zea*. J. Comp. Physiol. A. 188, 325–333.
Oehlschlager, A.C., Chinchilla, C., Castillo, D., Goncalez, L., 2002. Control of red ring disease by mass trapping of *Rhynchophorus palmarum* (Coleoptera: Curculionidae). Flor. Entomol. 85, 507–513.
Olagbemiro, T.O., Birkett, M.A., Mordue Luntz, A.J., Pickett, J.A., 2004. Laboratory and field responses of the mosquito, *Culex quinquefasciatus*, to plantderived *Culex* spp. oviposition pheromone and the oviposition cue skatole. J. Chem. Ecol. 30, 965–976.
Ortiz, M.I., Molina, J., 2010. Preliminary evidence of *Rhodnius prolixus* (Hemiptera: Triatominae) attraction to human skin odour ex tracts. Acta Trop. 113, 174–179.
Otálora-Luna, F., Perret, J.L., Guerin, P.M., 2004. Appetence behaviours of the triatominebug *Rhodnius prolixus* on a servosphere in response to the host metabolites carbon dioxide and ammonia. J. Comp. Physiol. A. 190, 847–854.
Ozaki, M., Morisaki, K., Idei, W., Ozaki, K., Tokunaga, F., 1995. A putative lipophilic stimolant carrier protein commonly found in the taste and olfactory systems. Euro. J. Biochem. 230, 298–308.
Paesen, G.C., Happ, G.M., 1995. The B proteins secreted by the tubular accessory sex glands of the male mealworm beetle, *Tenebrio molitor*, have sequence similarity to moth pheromone-binding proteins. Insect Biochem. Mol. Biol. 25, 401–408.
Pappenberger, B., Geier, M., Boeckh, J., 1996. Responses of antennal olfactory receptors in the yellow fever mosquito *Aedes aegypti* to human body odours. In: Bock, G.R., Cardew, G. (Eds.), Olfaction in Mosquito-Host Interactions, Ciba Foundation Symposium 2000. Wiley, Chicester, New York, pp. 254–266.
Pask, G.M., Jones, P.L., Rützler, M., Rinker, D.C., Zwiebel, L.J., 2011. Heteromeric Anopheline odorant receptors exhibit distinct channel properties. PLoS ONE 6 (12), e28774.
Pask, G.M., Romaine, I.M., Zwiebel, L.J., 2013. The molecular receptive range of a lactone receptor in *Anopheles gambiae*. Chem. Senses 38, 19–25.
Paynter, Q., Brady, J., 1993. Flight responses of tsetse flies (*Glossina*) to octenol and acetone vapour in a wind tunnel. Physiol. Entomol. 18, 102–108.
Pelletier, J., Hughes, D.T., Luetje, C.W., Leal, W.S., 2010. An odorant receptor from the southern house mosquito *Culex pipiens quinquefasciatus* sensitive to oviposition attractants. PLoS ONE 5 (4), e10090.
Pelosi, P., Zhou, J.J., Ban, L.P., Calvello, M., 2006. Soluble proteins in insect chemical communication. Cell Mol. Life Sci. 63, 1658–1676.
Pikielny, C.W., Hasan, G., Rouyer, F., Rosbach, M., 1994. Members of a family of *Drosophila* putative odorant-binding proteins are expressed in different subsets of olfactory hairs. Neuron 12, 35–49.
Pimenta, F.E., Diotaiuti, L., Lima, A.C., Lorenzo, M.G., 2007. Evaluation of cultures of *Saccharomyces cerevisae* as baits for *Triatoma dimidiata* and *Triatoma pallidipennis*. Mem. Inst. O. Cruz 102 (2), 229–231.
Pinto, M.C., Campbell-Lendrum, D.H., Lozovei, A.L., Teodoro, U., Davies, C.R., 2001. Phlebotomine sandfly responses to carbon dioxide and human odour in the field. Med. Vet. Entomol. 15, 132–139.
Pires, H.H., Lorenzo, M.G., Diotaiuti, L., Lazzari, C.R., Lorenzo-Figueiras, A.N., 2002. Aggregation behaviour in *Panstrongylus megistus* and *Triatoma infestans*: inter and intraspecific responses. Acta Trop. 81, 47–52.
Pitts, R.J., Fox, A.N., Zwiebel, L.J., 2004. A highly conserved candidate chemoreceptor expressed in both olfactory and gustatory tissues in the malaria vector *Anopheles gambiae*. Proc. Natl. Acad. Sci. USA 101, 5058–5063.
Ponnusamy, L., Xu, N., Nojima, S., Wesson, D.M., Schal, C., Apperson, C.A., 2008. Identification of bacteria and bacteriaassociated chemical cues that mediate oviposition site preferences by *Aedes aegypti*. Proc. Natl. Acad. Sci. USA 105, 9262–9267.
Pontes, G.B., Bohman, B., Unelius, C.R., Lorenzo, M.G., 2008. Metasternal gland volatiles and sexual communication in the triatomine bug, *Rhodnius prolixus*. J. Chem. Ecol. 34, 450–457.
Qiu, Y.T., van Loon, J.J.A., 2010. Olfactory physiology of blood-feeding vector mosquitoes. In: Takken, W., Knols, B.G.J. (Eds.), Olfaction in Vector-Host Interactions. Wageningen Academic Publishers, Wageningen, pp. 39–62.
Quinnell, R.J., Dye, C., Shaw, J.J., 1992. Host preferences of the phlebotomine sandfly *Lutzomyia longipalpis* in Amazonian Brazil. Med. Vet. Entomol. 6, 195–200.
Reisenman, C., Dacks, A., Hildebrand, J., 2011. Local interneuron diversity in the primary olfactory center of the moth *Manduca sexta*. J. Comp. Physiol. A 197, 653–665.
Rinker, D.C., Jones, P.L., Pitts, R.J., Rutzler, M., Camp, G., Sun, L., Xu, P., Dorset, D.C., Weaver, D., Zwiebel, L.J., 2012. Novel high-throughput screens of *Anopheles gambiae* odorant receptors reveal candidate behaviour-modifying chemicals for mosquitoes. Physiol. Entomol. 37, 33–41.
Robertson, H.M., Warr, C.G., Carlson, J.R., 2003. Molecular evolution of the insect chemoreceptor gene superfamily in *Drosophila melanogaster*. Proc. Natl. Acad. Sci. USA 100 (Suppl. 2), 14537–14542.
Rodriguez, R.J., Catalá, S.S., Fuentes-Gonzalez, O., Nodarse, J.F., 2009. Fenotipo antenal de dos tipos de especies cubanas del complejo *flavida*: *Triatoma flavida* y *Triatoma Brunei* (Reduviidae: Triatominae). Rev. Cubana Med. Trop. 61 (3), 226–231.
Rospars, J.P., 1983. Invariance and sex-specific variations of the glomerular organization in the antennal lobes of a moth, *Mamestra brassicae*, and a butterfly, *Pieris brassicae*. J. Comp. Neurol. 220, 80–96.
Rytz, R., Croset, V., Benton, R., 2013. Ionotropic Receptors (IRs): chemosensory ionotropic glutamate receptors in *Drosophila* and beyond. Insect Biochem. Mol. Biol. 43, 888–897.
Sachse, S., Krieger, J., 2011. Olfaction in insects: the primary processes of odor recognition and coding. e-Neuroforum 2, 49–60.
Sachse, S., Rappert, A., Galizia, C.G., 1999. The spatial representation of chemical structures in the antennal lobe of honeybees: steps towards the olfactory code. Euro. J. Neurosci. 11, 3970–3982.
Sanes, J.R., Hildebrand, J.G., 1976. Structure and development of antennae in a moth, *Manduca sexta*. Dev. Biol. 51, 280–299.
Sato, K., Pellegrino, M., Nakagawa, T., Nakagawa, T., Voshall, L.B., Touhara, K., 2008. Insect olfactory receptors are heteromeric ligand-gated ion channels. Nature 452, 1002–1007.
Schofield, C.J., 1994. Triatominae Biology & Control. ZENECA Public Health Fernhurst Haslemere, Surrey, UK, p. 71.
Schofield, C.J., Patterson, J.W., 1977. Assembly pheromone of *Triatoma infestans* and *Rhodnius prolixus* nymphs (Hemiptera: Reduviidae). J. Med. Entomol. 13, 727–734.
Scott, K., Brady, R.J.R., Cravchik, A., Morozov, P., Rzhetsky, A., Zuker, C., Axel, R., 2001. A chemosensory gene family encoding candidate gustatory and olfactory receptors in *Drosophila*. Cell 104, 661–673.
Serrano, D.A.K., 2013. Búsqueda de la feromona sexual de *Lutzomyia cruciata* (Diptera: Psychodidae). Tesis Licenciatura IBT. Universidad Autónoma de Chiapas, Centro de Biociencias Campus IV, Tapachula, Chiapas, México, p. 30.

Shanbhag, S.R., Müller, B., Steinbrecht, R.A., 1999. Atlas of olfactory organs of *Drosophila melanogaster*-1. Types, external organization, innervation and distribution of olfactory sensilla. Int. J. Insect Morphol. Embryol. 28, 377–397.
Silbering, A., Benton, R., 2010. Ionotropic and metabotropic mechanisms in chemoreception: 'chance or design'? EMBO Rep. 11 (3), 173–179.
Silbering, A., Ryts, R., Grosjean, Y., Abuin, L., Ramdya, P., Jefferis, G.S., Benton, R., 2011. Complementary function and integrated wiring of the evolutionarily distinct *Drosophila* olfactory subsystems. J. Neurosci. 31, 13357–13375.
Smallegange, R.C., Geier, M., Takken, W., 2002. Behavioural responses of *Anopheles gambiae* to ammonia, lactic acid and a fatty acid in a y-tube olfactometer. In: Proceedings of the Section Experimental and Applied Entomology, vol. 13. N.E.V., Amsterdam, pp. 147–152.
Smallegange, R.C., Qiu, Y.T., Van Loon, J.J.A., Takken, W., 2005. Synergism between ammonia, lactic acid and carboxylic acids as kairomones in the host-seeking behaviour of the malaria mosquito *Anopheles gambiae* sensu stricto (Diptera: Culicidae). Chem. Senses 30, 145–152.
Smartt, C.T., Erickson, J.S., 2009. Expression of a novel member of the odorant-binding protein gene family in *Culex nigripalpus* (Diptera: Culicidae). J. Med. Entomol. 46 (6), 1376–1381.
Smid, H.M., van Bleeker, M.A., Loon, J.J., Vet, L.E., 2003. Three-dimensional organization of the glomeruli in the antennal lobe of the parasitoid wasps *Cotesia glomerata* and *C. rubecula*. Cell Tiss. Res. 312, 237–248.
Spegiel, C.N., Oliverira, S.M.P., Brazil, R.P., Soares, M.J., 2005. Structure and distribution of sensilla on maxillary palps and labella of *Lutzomyia longipalpis* (Diptera: Psychodidae) sand flies. Microsc. Res. Tech. 66, 321–330.
Steinbrecht, R.A., 1997. Pore structures in insect olfactory sensilla: a review of data and concepts. Int. J. Insect Morphol. Embryol. 26, 229–245.
Steinbrecht, R.A., Stankiewicz, B.A., 1999. Molecular composition of the wall of insect olfactory sensilla: the chitin question. J. Insect Physiol. 45, 785–790.
Stengl, M., Funk, N.W., 2013. The role of the coreceptor Orco in insect olfactory transduction. J. Comp. Physiol. A. 199, 897–909.
Stengl, M., Ziegelberger, G., Boekhoff, I., Krieger, J., 1999. Perireceptor events and transduction mechanisms in insect olfaction. In: Hansson, B.S. (Ed.), Insect Olfaction. Springer-Verlag, Berlin, pp. 49–66.
Stopfer, M., Wehr, M., Macleod, K., Laurent, G., 1999. Neural dynamics, oscillatory synchronisation, and odour codes. In: Hansson, B.S. (Ed.), Insect Olfaction. Springer-Verlag, Berlin, pp. 163–180.
Suh, G.S., Wong, A.M., Hergarden, A.C., Wang, J.W., Simon, A.F., Benzer, S., Axel, R., Anderson, D.J., 2004. A single population of olfactory sensory neurons mediates an innate avoidance behaviour in *Drosophila*. Nature 431, 854–859.
Sutcliffe, J.F., 1987. Distance orientation of biting flies to their hosts. Insect Sci. Appl. 8, 611–616.
Syed, Z., Leal, W.A., 2007. Maxillary palps are broad spectrum odorant detectors in *Culex quinquefasciatus*. Chem. Senses 32, 727–738.
Syed, Z., Leal, W.S., 2008. Mosquitoes smell and avoid the insect repellent DEET. Proc. Natl. Acad. Sci. USA 105, 13598–13603.
Syed, Z., Leal, W.S., 2009. Acute olfactory response of *Culex* mosquitoes to a human- and bird-derived attractant. Proc. Natl. Acad. Sci. USA 106, 18803–18808.
Takken, W., Knols, B.G.J., 1999. Odor-mediated behavior of Afrotropical malaria mosquitoes. Ann. Rev. Entomol. 44, 131–157.
Taneja, J., Guerin, P.M., 1995. Oriented responses of triatomines bugs *Rhodnius prolixus* and *Triatoma infestans* to vertebrate odours on a servosphere. J. Comp. Physiol. A 176, 455–464.
Taneja, J., Guerin, P.M., 1997. Ammonia attracts the haematophagous bug *Triatoma infestans*: behavioural and neurophysiological data on nymphs. J. Comp. Physiol. A 181, 21–34.
Thom, C., Guerenstein, P.G., Mechaber, W.L., Hildebrand, J.G., 2004. Floral CO_2 reveals flower profitability to moths. J. Chem. Ecol. 30 (6), 1285–1288.
Todd, J.L., Baker, T.C., 1999. Function of peripheral olfactory organs. In: Hansson, B.S. (Ed.), Insect Olfaction. Springer-Verlag, Berlin, pp. 67–96.
Tolbert, L.P., Hildebrand, J.G., 1981. Organization and synaptic ultrastructure of glomeruli in the antennal lobes of the moth *Manduca sexta*: A study using thin sections and freeze-fracture. Proc. R. Soc. Lond. B 213, 279–301.
Torr, S.J., 1988a. The activation of resting tsetse flies (*Glossina*) in response to visual and olfactory stimuli in the field. Physiol. Entomol. 13, 315–325.
Torr, S.J., 1988b. The flight and landing of tsetse (*Glossina*) in response to components of host odour in the field. Physiol. Entomol. 13, 453–465.
Torr, S.J., 1989. The host-orientated behaviour of tsetse flies (*Glossina*): the interaction of visual and olfactory stimuli. Physiol. Entomol. 14, 325–340.
Torr, S.J., 1990. Dose responses of tsetse flies (*Glossina*) to carbon dioxide, acetone and octenol in the field. Physiol. Entomol. 15, 93–103.
Torr, S.J., Hargrove, J.W., 1999. Behaviour of tsetse (Diptera: Glossinidae) during the hot season in Zimbabwe: the interaction of micro-climate and reproductive status. Bull. Entomol. Res. 89, 365–379.
Torr, J.S., Solano, P., 2010. Olfaction in Glossina-Host interactions: a tale of two tsetse Olfaction in vector-host interactions. In: Takken, W., Knols, B.G.J. (Eds.), Ecology and Control of Vector-Borne Diseases, vol. 2. Wageningen Academic Publishers, pp. 265–289.
Tsuchihara, K., Fujikawa, K., Ishiguro, M., Yamada, T., Tada, C., Ozaki, K., Ozaki, M., 2005. An odorant-binding protein facilitates odorant transfer from air to hydrophilic surroundings in the blowfly. Chem. Senses 30, 559–564.
Tuccini, A., Maida, R., Rovero, P., Mazza, M., Pelosi, P., 1996. Putative odorant-binding proteins in antennae and legs of *Carausius morosus* (Insecta, Phasmatodea). Insect Biochem. Mol. Biol. 26, 19–24.
Turner, S.T., Li, N., Guda, T., Githure, J., Carde, R.T., Ray, A., 2011. Ultra-prolonged activation of CO_2-sensing neurons disorients mosquitoes. Nature 474, 87.
Vale, G.A., 1974. Responses of tsetse flies (Diptera, Glossinidae) to mobile and stationary baits. Bull. Entomol. Res. 64, 545–588.
Vale, G.A., Hall, D.R., 1985. The role of 1-octen-3-ol, acetone and carbon dioxide in the attraction of tsetse flies, *Glossina* spp. (Diptera: Glossinidae), to ox odour. Bull. Entomol. Res. 75, 209–217.
van der Goes van Naters, W., Carlson, R.J., 2006. Insect as chemosensors of human and crops. Nature 444, 302–307.
Vitta, A.C.R., Lorenzo, M.G., 2009. Copulation and mate guarding behav iour in *Triatoma brasiliensis*. J. Med. Entomol. 46, 789–795.
Vogt, R.G., Riddiford, L.M., 1981. Pheromone binding and inactivation by moth antennae. Nature 293, 161–163.
Voshall, L., Amrein, H., Morozov, P., Rzhetsky, A., Axel, R., 1999. A spatial map of olfactory receptor expression in the *Drosophila* antenna. Cell 96, 725–736.
Vosshall, L.B., Wong, A.M., Axel, R., 2000. An olfactory sensory map in the fly brain. Cell 102, 147–159.
Wang, G., Carey, A.F., Carlson, J.R., Zwiebel, L.J., 2010. Molecular basis of odor coding in the malaria vector mosquito Anopheles gambiae. Proc. Natl. Acad. Sci. USA 107, 4418–4423.
Wang, X., Zhong, M., Liu, Q., 2013. Molecular characterization of the carbon dioxide receptor in the oriental latrine fly, *Chrysomya megacephala* (Diptera: Calliphoridae). Parasitol. Res. 112 (7), 2763–2771.
Warnes, M.L., 1995. Field studies on the effect of cattle skin secretion on the behaviour of tsetse. Med. Vet. Entomol. 9, 284–288.
Wetzel, C.H., Behrendt, H.-J., Gisselmann, G., Stortkuhl, K.F., Hovemann, B., Hatt, H., 2001. Proc. Natl. Acad. Sci. USA 98, 9377.
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 cyclicnucleotide- activated cation channels. Nature 452, 1007–1012.
Wiesinger, D., 1956. Die Bedeutung der Umweltfaktoren für den Saugakt von *Triatoma infestans*. Acta Trop. 13, 97–141.
Willemse, L.P.M., Takken, W., 1994. Odor-induced host location in tsetse flies. J. Med. Entomol. 31 (6), 775–794.
Wogulis, M., Morgan, T., Ishida, Y., Leal, W.S., Wilson, D.K., 2006. The crystal structure of an odorant binding protein from *Anopheles gambiae*: evidence for a common ligand release mechanism. Biochem. Biophys. Res. Commun. 339, 157–164.
World Health Organization, 2010. Chagas disease (American trypanosomiasis). Fact sheet N°340 <http://www.who.int/mediacentre/factsheets/fs340/en/index.html>.
Xu, P., Atkinson, R., Jones, D.N., Smith, D.P., 2005. *Drosophila* OBP LUSH is required for activity of pheromone-sensitive neurons. Neuron 45, 193–200.
Yaksi, E., Wilson, R.I., 2010. Electrical coupling be tween olfactory glomeruli. Neuron 67, 1034–1047.
Yao, C.A., Carlson, J.R., 2010. Role of G-proteins in odor-sensing and CO_2-sensing neurons in *Drosophila*. J. Neurosci. 30, 4562–4572.
Yao, C.A., Ignell, R., Carlson, J.R., 2005. Chemosensory coding by neurons in the coeloconic sensilla of the *Drosophila* antenna. J. Neurosci. 25, 8359–8367.
Zahiri, N., Rau, M.E., Lewis, D.J., 1997. Oviposition responses of *Aedes aegypti* and *Ae. atropalpus* (Diptera: Culicidae) females to waters from conspecific and heterospecific normal larvae and from larvae with *Plagiochis elegans* (Trematoda: Plagiorchiidae). J. Med. Entomol. 35, 565–568.
Zhou, J.J., He, X.L., Pickett, J.A., Field, L.M., 2008. Identification of odorant-binding proteins of the yellow fever mosquito *Aedes aegypti*: Genome annotation and comparative analyses. Insect Mol. Biol. 17 (2), 147–163.
Zube, C., Kleineidam, C.J., Kirschner, S., Neef, J., Rossler, W., 2008. Organization of the olfactory pathway and odor processing in the antennal lobe of the ant *Camponotus floridanus*. J. Comp. Neurol. 506, 425–441.
Zwiebel, L.J., Takken, W., 2004. Olfactory regulation of mosquito-host interactions. Insect Biochem. Mol. Biol. 34, 645–652.