1. Introduction

Olfaction, the sense of smell, is phylogenetically one of the oldest and universally used sensory perceptions in mammals. When aquatic life forms took to terrestrial environment ~200 millions year ago they evolved specific adaptations to detect airborne odors. Terrestrial vertebrates have evolved class II olfactory receptors which are sensitive to airborne odorants (Hoover, 2010). The terrestrial environment is full of volatile chemicals released by all living and nonliving things. These airborne odors could serve as cues, even over long distances, to the organisms about food sources, potential mates, nests and presence of predator. The ability to orient and successfully track various odor cues is a necessary survival skill for an organism relying on olfaction. The general features of olfactory system remains strikingly similar across the animal kingdom (Hildebrand, 1995; Eisthen, 1997, 2002; Hildebrand and Shepherd, 1997). It has been suggested that these observed commonalities could be due to adaptation for similar constraints and task requirements (Eisthen, 2002).

The olfactory bulb sends monosynaptic projections to the emotional centers of the brain such as the amygdala, suggesting a role in emotional and social attachments (Mouly and Sullivan, 2010). In humans, odors evoke various memories and emotions that are attached to a specific odorant (Chu and Downes, 2000). It has been said that these odor memories are context dependent, plastic (Freeman, 1991), long lasting and stronger compared to memories evoked by visual and verbal cues (Mouly and Sullivan, 2010).

The work described in this thesis is an attempt to understand the odor localization behavior and to investigate the physiological prerequisites in the peripheral olfactory system.

1.1. Odor guided behavior

Olfaction plays a critical role in mammalian sensory communication as the animal depends on various odors to interact with their surrounding environment for variety of purposes such as to find food and mates. In insects odors elicit strong stereotypic responses, for example, bombykol, a female silk moth odorant, attracts the male over long distances and elicits a upwind flight behavior (Brennan, 2010). On the other hand, the mammalian odor guided behaviors are context dependent and could alter with learning (Doty, 1986; Brennan, 2010).
1.2. Orientation to odors

1.2.1. The complexity of odor plumes

As air-borne odor molecules drift away from the source they form a non-uniform, patchy, fluctuating concentration gradient consisting of clouds called odor plumes. The structure of the odor plume is complex as it depends on the source size, fluid motion and odor molecule diffusion rate (Murlis et al., 1992). The plume structure is shaped by both molecular and turbulent diffusion processes. The molecular diffusion is caused by random movement of odor molecules where the rate of dispersion is determined by the molecular weight of the odor. This results in a gradual spread of odor molecules over small spatial and long temporal scales. On the other hand the turbulent diffusion caused by the air turbulence is a dominant force which separates the odor molecules over a broad spatial and temporal scale (Murlis et al., 1992).

In general, the odor plume expands with both distance from the source as well as the centerline across the plume (Willis, 2008) (Fig. 1.1). The odor concentration decreases exponentially as the distance increases from the source. In turbulent air flow conditions the effect of molecular diffusion in odor dispersion is weak. So, the ratio of different odor molecules anywhere in the plume and the source is maintained despite their disparities in their molecular weight (Vickers, 2000).

Figure 1.1. Airborne smoke plume. Top view of incense smoke plume in a wind tunnel. The air was flowing from left to right at ~ 3 cm s\(^{-1}\). The image color is inverted for better visualization.
The following key features of an odor plume might contain useful information about the odor source to animals navigating towards it (Vickers, 2000):

- Intermittency of odor
- Spatial and temporal aspects of odor distribution
- Maintenance of the odor blend ratio throughout the plume

The characteristics of odor plumes play a critical role in the strategies employed by animals to orient, track and locate the odor source (Vickers, 2000; Weissburg, 2000).

### 1.2.2. Orientation strategies

The chemical or odor source localization behaviors are classified into three broad categories (Vickers, 2000; Dusenbery, 2001; Gomez-Marin and Louis, 2012).

1) **Klinokinesis**: Initiation of non-directed orientation based on temporal comparison of the gradient concentration as the organism moves in the gradient. Here, the rate of turning or new orientation depends on odor intensity.

2) **Klinotaxis**: Initiation of directed orientation based on sequential comparison of the gradient concentration as the organism moves in the gradient. The organism samples intensity using a single-point sensor(s) moving sideways.

3) **Tropotaxis**: Simultaneous spatial comparison of odor intensity using bilateral sensors.

**Klinokinesis**

The ‘biased random walks’ of bacterium *Escherichia coli* and nematodes *Caenorhabditis elegans* are the examples of klinokinesis mechanism. Bacterial chemotaxis consists of two swimming behaviors, ‘run’ and ‘tumble’ (Berg and Brown, 1972) (*Fig. 1.2 A*).

a) **Run**: smooth swimming in a straight line in a particular direction

b) **Tumble**: stop and turn to head in random direction

Increasing attractant or decreasing repellent intensity results in decreased frequency of tumbling and vice-versa (Adler, 1975). It is unlikely that the bacteria senses the concentration along its length, as the concentration difference would be too small for
**Klinotaxis**

An organism reorients itself based on sequential sampling of odor or chemical intensity to either side of its body. This typically takes a sinuous path with frequent sampling of intensity by turning the head side to side (Fig. 1.2B).

Drosophila larva has been shown to use klinotaxis to navigate chemical and temperature gradients (Garrity et al., 2010; Gomez-Marín et al., 2010, 2011; Luo et al., 2010; Gomez-Marín and Louis, 2012). The larvae sequentially sample the gradient concentration by lateral head movements and make directed turns (Gomez-Marín et al., 2011). The larva has two bilaterally symmetric olfactory organs yet it does not require both the organs for gradient navigation (Louis et al., 2008).

**Tropotaxis**

In tropotaxis, orientation to odors depends on comparison of simultaneously sampled intensity by spatially separated sensors (Fig. 1.2C). This method does not require any ‘memory’ and the mean direction of heading is decided based on instantaneous comparison of intensity.

Tropotaxis using bilateral sensor has been shown to be used by honey bees (Martin, 1965), *Drosophila* (Borst and Heisenberg, 1982; Duistermars et al., 2009; Gomez-Marín et al., 2010, 2011), desert ants (Steck et al., 2010), sharks (Gardiner and Atema, 2010), rats (Rajan et al., 2006; Khan et al., 2012), and humans (von Bekesy, 1964; Porter et al., 2006). Table 1.1 summarizes studies investigated role of bilateral odor sampling in odor source localization.

### 1.2.3. Odor tracking

As discussed above, the odor spread direction is determined by the fluid flow direction and it is filamentous and patchy. Detecting both the fluid flow direction and odor is necessary for an animal to track that odor. Since odor plume is discontinuous, the animal will face intermittency in odor information as it moves upstream or upwind. It has been said that the intermittency is a key feature in determining the odor tracking behavior structure (Willis, 2008).
1.3. Bilateral comparison

As discussed earlier animals use both sequential and simultaneous sampling strategies to track odors to its source. The sequential strategy involves sampling of two different spaces one after the other and compare odor intensity to determine the direction of heading. On the other hand simultaneous strategy involves sampling of two different spaces simultaneously and compares the intensity to determine directions of heading. The later strategy uses bilateral sampling using antennae in crustacean and insects and nostrils in mammals.

Bilateral odor sampling contributes significantly to odor localization in many species. This has been shown in crayfish (Kraus-Epley and Moore, 2002), fruit flies (Borst and Heisenberg, 1982; Louis et al., 2008; Duistermars et al., 2009), bees (Martin, 1965), moths (Takasaki et al., 2012), ants (Steck, 2012), moles (Catania, 2013), rats (Rajan et al., 2006) and humans (von Bekesy, 1964; Porter et al., 2006). See Table 1.1 for more details. The loss of one of the sensors reduces the animals’ ability to localize odors and tracking behavior.

Odor source direction or localization information can be extracted from the timing and intensity difference between the two sensors. This is analogous to the auditory system which extracts the sound direction information using the time and the loudness differences of the sound waves reaching the two ears. The ability to use inter- antenna or nostril intensity and timing differences to localize odor has been demonstrated in several animals such as silk moths (Takasaki et al., 2012), rats (Rajan et al., 2006) and humans (von Bekesy, 1964). For rats, an inter-nostril time difference as small as 50ms is sufficient to determine the odor direction (Rajan et al., 2006). The sharks has been shown to use inter-nostril time differences rather than inter-nostril intensity differences (Gardiner and Atema, 2010). Whether the animals use both intensity and timing cues to localize odor or either one of them needs to be investigated. It is often assumed that animals use inter-antenna or nostril concentration difference to detect the odor gradient (Koehl, 2001; Porter et al., 2006).

The bilateral comparison of odor intensity provides instantaneous information about the odor gradient (Webster et al., 2001). Most of the studies discussed above observed that the simultaneous sampling by bilateral sensors improves the odor tracking efficiency of organisms (Vickers, 2000; Kraus-Epley and Moore, 2002; Porter et al., 2006; Rajan et al., 2006; Louis et al., 2008; Steck et al., 2010; Khan et al., 2012; Catania, 2013). Human
Subjects were slower and less efficient when tracking odor trail with ‘non-spatial’ prism, in which both the nostrils were made to sample the same point in the environment (Porter et al., 2005).

1.4. Questions addressed in this thesis

As discussed in the previous sections, animals use bilateral sampling to track odors efficiently by using inter-nasal/antennal odor intensity and timings as cues. The key assumptions for bilateral comparison are **Symmetry**: bilateral equivalence at all levels of the olfactory processing and **Laterality**: bilateral distinction of the information. Absence of any one of these prerequisites might upset the efficiency of odor localization behavior. The role of bilateral odor sampling in localizing odor sources has been demonstrated in many species, including rats (see Table 1.1), but the prerequisites for bilateral comparisons have not been verified rigorously.

**Symmetry**: The olfactory bulb (OB) receives input from the receptor neurons located in the olfactory epithelium which lines the posterior nasal cavity (Fig. 1.3A). Axons of neurons expressing a specific receptor type converge onto two bilaterally symmetric glomeruli in the olfactory bulb (Ressler et al., 1994; Mombaerts et al., 1996). The odor evoked activity patterns of glomeruli are bilaterally symmetric as predicted by the anatomical organization.
1.5. References


