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Computational Models of Olfaction in Fruit Flies

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Introduction: Anatomy and Physiology of Olfactory System in Fruit Flies

For species survival, an organism is required to obtain energy, avoid harm, and reproduce. In all these behaviors, a neural representation of the environment, through the process of "neural encoding," is created. The main thrust of many neuroscience studies is the transformation of sensory information during initial detection, neural information processing, and generation of a percept that eventually drives specific behaviors.

Survival of many organisms, in particular insects, depends heavily on olfaction (a form of chemosensation) to obtain vivid qualitative, quantitative (Keene & Waddell, 2007) and temporal (Laurent, 1999) information about the stimulus through detection of weak and fluctuating signals with large numbers of volatile chemicals (Firestein, 2001). Thanks to the striking structural and functional similarity of olfactory systems in animals and insects (Ache & Young, 2005), researchers can generalize (Olsen & Wilson, 2008) many principles of olfactory information processing (olfactory perception, discrimination, olfactory memories, and associative learning (Laurent et al., 2001)) across species.

The small and manageable size of *Drosophila melanogaster* (briefly *Drosophila* or fruit fly), along with a comprehensive understanding of its olfactory system (including molecular description of olfactory receptor neurons), and recent advances in molecular, genetic, and neural activity recording make it a model organism to study olfactory information processing (Olsen & Wilson, 2008). Computational models provide valuable insights into information processing and transformation in terms of neural activity and plasticity for different odors/multi-odor mixtures.

In this chapter, we first summarize the structure and function of neural substrates involved in *Drosophila's* olfactory process followed by a description of information processing and associative learning. We then summarize the existing computational models of olfaction.

The Structure and Function of the *Drosophila* Olfactory System

The *Drosophila* olfactory system comprises antenna, antennal lobe (AL), mushroom body (MB), lateral horn, and output neurons as shown in Fig. 15.1 (McGuire, Deshazer, & Davis, 2005).

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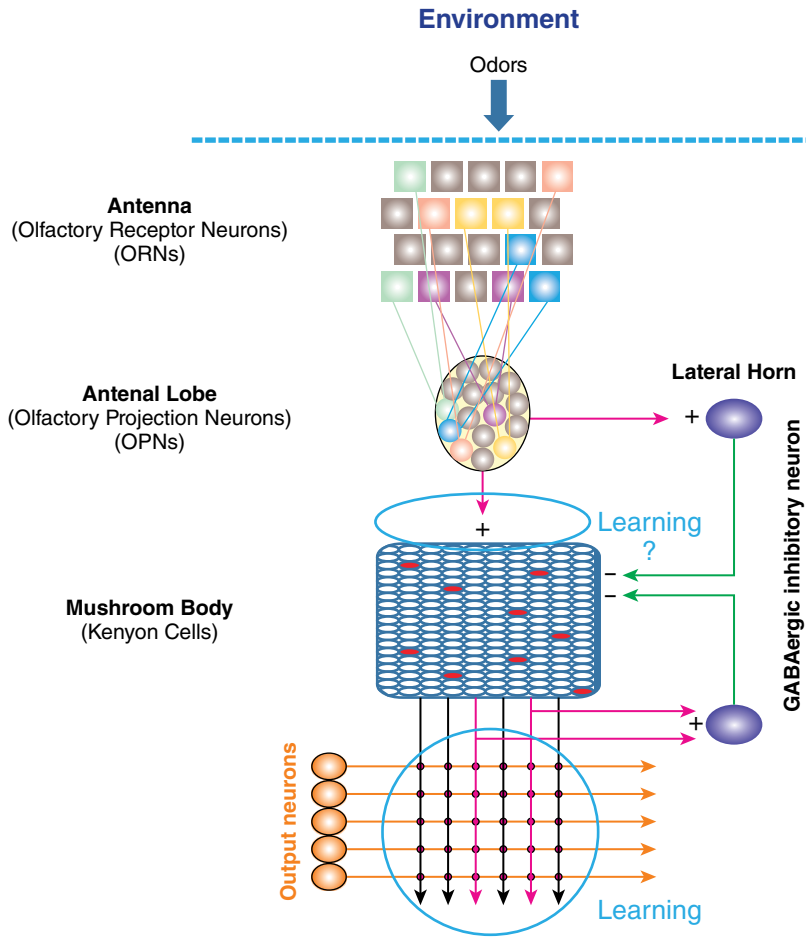

Figure 15.1 Schematic illustration of the *Drosophila* olfactory system. Odor as a stimulus in the environment binds to the receptors located on the antenna; each olfactory receptor neuron expresses one specific type of receptor (illustrated by different colors). Olfactory receptor neurons of the same class project to one glomeruli in the antennal lobe. The projection neurons in the antennal lobe, in turn, activate the Kenyon cells in the mushroom body and the lateral horn via cholinergic, excitatory synapses. GABAergic inhibitory neurons provide inhibitory effects on the activated Kenyon cells. The synapses between the output neuron and the Kenyon cells, along with the synapses between the Kenyon cells and the projection neurons, are the sites of learning.

The Antenna and Olfactory Receptor Neurons

Drosophila has two pairs of olfactory organs, the antenna and the maxillary palps. Each antenna contains about 1,200 olfactory receptor neurons (ORNs), while the maxillary palp comprises approximately 120 ORNs. ORNs, the seminal site for volatile odor reception, bear only a single odorant-specific receptor, hence the specificity. A single odorant-specific population of ORNs projects to the same glomerulus. A glomerulus in turn projects to projection neurons monosynaptically (Fishilevich & Vosshall, 2005). This leads to convergence and divergence in the neuronal information processing (Garcia-Sanchez & Huerta, 2003).

The binding of environmental volatile molecules (odors) to the receptor proteins on the surface of the neuronal dendrites in the antenna, ORNs (Vosshall, Wong, & Axel, 2000), triggers neuronal spikes (Benton, Vannice, Gomez-Diaz, & Vosshall, 2009). These spikes are subsequently sent to the inner parts of the insect's brain to convey the

odor's qualitative and quantitative information to ORNs (Bicker, 1999) where acetylcholine acts a primary excitatory neurotransmitter.

The Antennal Lobe (AL)

The insect AL comprises projection neurons, PNs (in *Drosophila*, n = 150–200; Stocker, Heimbeck, Gendre, & de Belle, 1997), and is analogous in structure and function to the vertebrate olfactory bulb (Strausfeld & Hildebrand, 1999). PNs receive input from the ORNs and transmit odor information to the mushroom body and the lateral horn. In *Drosophila*, PN dendrites usually innervate a single glomerulus (Stocker, Lienhard, Borst, & Fischbach, 1999) and are odor specific. Each glomerulus receives bilateral input from approximately 50 ORNs (25 per antenna) expressing identical receptors that synapse with approximately three PNs. However, each ORN is connected to all the PNs in a glomerulus (Vosshall et al., 2000).

The AL reduces the input noise by signal averaging (Laurent, 1999) and compresses the dynamic range of its projection neuron output using widespread local inhibition (Stopfer, Jayaraman, & Laurent, 2003). The PNs show sporadic activity (Wilson, Turner, & Laurent, 2004) with their responses shaped by inhibitory neurons within the AL (Wilson & Laurent, 2005). Due to the broadly tuned PNs, odor encoding at the level of the antennal lobe's output is combinatorial and thus inefficient for storage. Local neurons can be either inhibitory (gamma-aminobutyric acid (GABA)ergic, n = 100; Ng et al., 2002) or excitatory (acetylcholinergic) (Shang, Claridge-Chang, Sjulson, Pypaert, & Miesenbock, 2007), and receive input from both ORNs and the projection neurons (Wilson & Laurent, 2005). Another key chemical, nitric oxide, is known to disrupt olfactory discrimination upon blocking its production (Bicker, 2001).

The Mushroom Body (MB)

The *Drosophila* MB comprises approximately 2,500 Kenyon cells (KCs) (Stocker, 1994) that receive olfactory information from the PNs (Wong, Wang, & Axel, 2002).

KCs show high morphological, pharmacological, and peptide variation across species (Strausfeld, Sinakevitch, & Vilinsky, 2003). The invariant circuitry of the lateral horn is thought to mediate innate behaviors (Jefferis et al., 2007), whereas the MB translates olfactory sensory information into learned behavioral responses. The projection neurons' axons that innervate the MB terminate in large boutons (Wong et al., 2002) that form synapses on the KC (Butcher, Friedrich, Lu, Tanimoto, & Meinertzhagen, 2012). The KC synapses onto a relatively small number of extrinsic output neurons (Sejourne et al., 2011). The MB plays a critical role in general and associative learning (Heisenberg, 2003; Strausfeld & Hildebrand, 1999) due to the olfactory and visual inputs. Learning and memory deficits have also been reported during abnormal MB development (Heisenberg, Borst, Wagner, & Byers, 1985).

Electrophysiological and optical imaging studies show that olfactory sensory systems create representations of olfactory stimuli as KC subpopulation activity (Stopfer et al., 2003) such that each activated KC generates a few spikes. Compared to PNs (response probability = 0.64), KCs demonstrate a reduced response (response probability = 0.11) to a given odor set (Wang et al., 2004) with near zero baseline activity (Perez-Orive et al., 2004) and odor response of approximately five spikes. Another study suggested that KC synapses are updated using the Hebbian learning rule (Cassenaer & Laurent, 2007). Additionally, odor representation changes from dense (in AL) to sparse (in MB), thereby exhibiting "sparse coding" that has computational advantages for sensory representation and memory storage (Perez-Orive et al., 2004). In other words, KC sparse encoding exhibits a high level of odor selectivity (Wang et al., 2004).

Synaptic connections from the AL to the KC dendrites are sites of functional memory and ensure optimal sparse responses in the MB after sufficient odor presentations (Finelli, Haney, Bazhenov, Stopfer, & Sejnowski, 2008). The presynaptic plasticity between the KC

and the MB extrinsic neurons governs olfactory memory (Menzel & Manz, 2005). Thus, the large number of KCs allows for the computation of highly nonlinear classification schemes across projection neurons (Huerta, Nowotny, Garcia-Sanchez, Abarbanel, & Rabinovich, 2004) and increased theoretical capacity due to temporal complexity (Laurent et al., 2001). This organization of glomerular connections to the MB allows the fly to contextualize novel sensory experiences, a feature consistent with the role of this brain center in mediating learned olfactory associations and behaviors. Locust studies suggest the presence of a normalization negative feedback loop in the MB to maintain sparse output over a wide range of inputs (Papadopoulou, Cassenaer, Nowotny, & Laurent, 2011).

The GABAergic system acts as the major inhibitory neurotransmitter (Ren, Li, Wu, Ren, & Guo, 2012) in the central nervous system of *Drosophila* and was shown to be expressed in a pair of anterior paired lateral (APL) neurons that innervate the entire MB (Liu & Davis, 2009). The molecular mechanism of the GABAergic system in modulating sparse coding in the MB is not clearly understood. APL neurons provide direct feedback inhibition to the KCs (Stocker et al., 1997).

Prior Models of Olfaction in Fruit Flies

Most models of olfaction in fruit flies simulate associative learning. However, some models simulate olfactory memory, the role of the MB as a classifier, as well as odor discrimination. Below, we discuss these models in detail.

Models of Olfactory Associative Learning

Learning can be defined as a lasting alteration in behavior or in behavioral potential due to experience through molecular level and neuronal architecture changes in the brain (Heisenberg, 2003; Keene & Waddell, 2007). *Drosophila* exhibit the conditioned approach to or avoidance of an odor that has been paired to an appetitive or aversive stimulus, such as sugar (Tempel, Bonini, Dawson, & Quinn, 1983) or shock (Tully & Quinn, 1985). The MB is known to be a site for spatial memory and navigation without olfactory cues (Cruse & Wehner, 2011). It has also been shown that altering the MB (Heisenberg et al., 1985), blocking synaptic activity (Heisenberg, 2003; Krashes, Keene, Leung, Armstrong, & Waddell, 2007), and inhibitory silencing of the MB output/feedback neurons (Liu & Davis, 2009) cause learning, memory, and memory formation deficits, respectively. Importantly, aversive conditioning leads to changes in the antennal lobe, where the PNs change their odor responses for 3 min postconditioning (Yu, Ponomarev, & Davis, 2004).

The associative learning paradigm in *Drosophila* relies on a differential Pavlovian conditioning procedure (Tully & Quinn, 1985) where an odor (conditioned stimulus+ or CS+) is temporally paired with electric shocks (unconditioned stimulus or US) and a second odor (conditioned stimulus– or CS–) is presented without any punishment. The fly associates the odor with the punishment. As shown by numerous reports, *Drosophila* is able to establish simple forms of appetitive and aversive olfactory associations at both larval and adult stages (Pauls et al., 2010).

Second-order conditioning studies, wherein a previously conditioned stimulus (CS1) is associated with a second conditioned stimulus (CS2) to elicit a conditioned response, involves pairing of CS1 with an unconditioned stimulus (US) followed by a second-order conditioning session in which CS1 is paired subsequently with a novel stimulus, CS2. Upon successful learning, the agent demonstrates a conditioned response to CS2 similar to CS1, even though it has not been exposed to the original US during CS2 and CS1 association (Tabone & de Belle, 2011).

Information theoretic approaches have been applied to measure the *Drosophila* olfactory stimuli coding efficiency under

variable intensities (Faghihi, Kolodziejski, Fiala, Worgotter, & Tetzlaff, 2013). This study features an abstract model of the AL, the MB, and the feedback inhibitory circuitry for simulating mutual information exchange and information transmission efficiency between the olfactory environment (simulated in terms of different odor concentrations) and a subpopulation of the intrinsic MB neurons (KCs). The authors further showed the effect of different connectivity rates between olfactory projection neurons and firing thresholds of KCs. A linear relationship between the connectivity rate (linking AL and MB) and firing threshold of KCs to maximize mutual information for both low and high odor concentrations was observed. However, high odor concentrations cause a drastic, and unrealistic, decrease in mutual information for all connectivity rates compared to low concentration. Moreover, in the presence of MB feedback inhibition, mutual information transmission remains high independent of other system parameters. This finding points to a pivotal role of feedback inhibition in *Drosophila* information processing without which the systems efficiency is substantially compromised.

Memory (Brea, Urbanczik, & Senn, 2014)

One of the most important features in any behavior is the organism's ability to identify the stimulus, associate it with a reward/no reward/punitive outcome, remembering this association and its history followed by utilization of the history information in future trials to maximize the total reward obtained. In *Drosophila* and other insects, the MB (n = 2,500 neurons per hemisphere) governs olfactory memory (McGuire, Le, & Davis, 2001). The biggest challenge experienced by the MB neurons is limited storage for a very large amount of olfactory stimuli. This problem was recently addressed by Brea et al. (2014) (see Fig. 15.2), where the

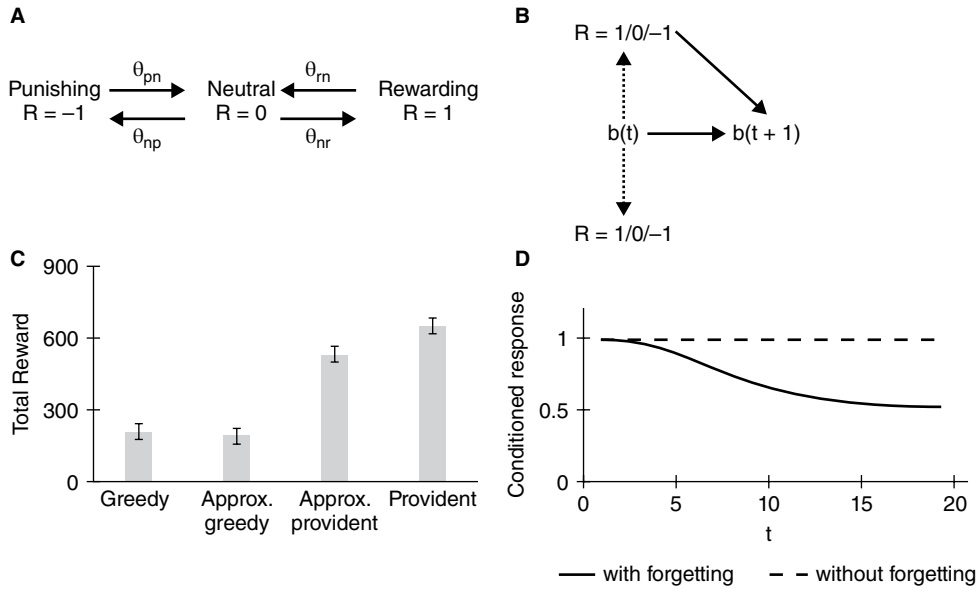

Figure 15.2 (A) Stochastic changes in the environmental state from punishing (p), neutral (n), and rewarding (r). The rate of changes of the environmental state are denoted by θ_{pn}, θ_{np}, θ_{m}, and θ_{nr}. (B) The belief (b) and policy changes in the environment. Belief influences the appetitive or aversive reaction, with appetitive action only updating the agent's information about the environmental state. (C) Total reward obtained ± SEM for greedy and provident policy. Note that provident policy yields higher total reward than the greedy policy. (D) Conditioned response changes under two policies: with forgetting and without forgetting. Redrawn from Brea et al. (2014).

authors presented a computational model of de-learning (forgetting) the association. The study was based on molecular studies from Shuai and colleagues (2010) and Berry, Cervantes-Sandoval, Nicholas, and Davis (2012), which assigned the de-learning phenomena to G-protein Rac and dopamine. In this study, Brea et al. (2014) presented *Drosophila* with an odor, the approaching of which led to reward or appetitive (R = 1)/punishment (R = −1)/no reinforcement (R = 0). The total reward received is the difference between the reinforcement obtained and the cost of response. The model also includes a belief module that represents the environmental state and comprises the belief probabilities for reward (b_r), no reinforcement (b_n), and punishment (b_p) with $b_n + b_r + b_p = 1$.

Upon receiving a punishment the subsequent b_p increases, with the fruit fly anticipating a higher punitive outcome. However, if the fly chose an aversive strategy, the belief drifts toward a stationary value. Thus, the agent obtains knowledge of the environmental transitional rate through experience. The experimental paradigm did not allow for the estimation of future rewards, hence the discount factor (γ) = 0. Various choices of the environmental state transition probability ($\theta_{pn} = \theta_{rn} = 4/15$, $\theta_{nr} = \theta_{np} = 1/30$, $\theta_{pr} = \theta_{rp} = 0$) were re-parameterized using $\rho_r = Z^{-1}\theta_{nr}\theta_{pn} = \rho_p = Z^{-1}\theta_{rn}\theta_{np} = \frac{1}{10}$ and $\rho_n = Z^{-1}\theta_{rn}\theta_{pn} = \frac{8}{10}$, where $Z = \theta_{nr}\theta_{pn} + \theta_{rn}\theta_{np} + \theta_{rn}\theta_{pn}$. It was proposed that alteration in the transition rates θ_{rn} and θ_{pn} is sufficient for implementing the greedy policy; however, to incorporate the future rewards, a provident policy was employed, which leads to reward rate maximization with higher total rewards. The study also computationally showed that spaced trials elicit a slower forgetting rate (a response informative of slow transitions); reversal learning showed a high forgetting rate (a response informative about fast transition).

Insects navigate (identify the target, perform path integration, and determine the velocity/distance/direction information in a complex environment) to obtain food and avoid obstacles (Wehner, 2009). Together with the visual scene the directional information is intimately associated (and remembered) to obtain complete information of the visual surroundings. *Drosophila melanogaster*, similar to its insect counterparts is able to determine size, color, and contour orientation. However, a close inspection of the neural substrates attributed the olfactory processing only to the MB and not to the central complex that is known to play a crucial role in orientation behavior and multisensory integration (Ofstad, Zuker, & Reiser, 2011). It was also shown that MB silencing leads to impaired odor learning. However, silencing the ellipsoid body did not affect the olfactory learning but had a significant effect on impairment of visual place learning.

Decorrelation and Integration Dynamics of the Antennal Lobe (AL) (Muezzinoglu, Huerta, Abarbanel, Ryan, & Rabinovich, 2009)

ORNs provide extensive information about the odors presented. However, large time constants and highly variable signals make quick and accurate information processing difficult. AL perform quick and accurate information processing due to their ability to perform filtering and serve as a memory unit, attributed to an excitatory (PN) and inhibitory (LN) pool. AL output when passed onto the MB leads to the identification and discrimination of the signal. In their study Muezzinoglu et al. (2009a) present a model of antennal lobe dynamics that, using the raw data from the sensors, is able to encode the odor-specific information for the classifier to classify (see Fig. 15.3).

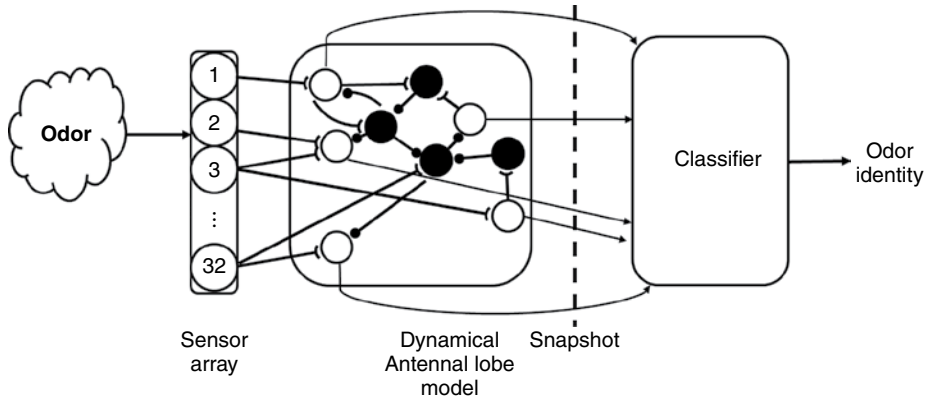

Figure 15.3 Overall schema of the model. The odor is detected by sensory array, which passes on the information to the antennal lobe model. In the antennal lobe the slow and noisy signals are refined by the excitatory and inhibitory neurons. The classifier then receives this information and discriminates the signals to respective odors. Redrawn from Muezzinoglu et al. (2009a).

The model comprises a sensory layer (analogous to the ORN), dynamical layer (analogous to the antennal lobe), and a classifier (analogous to the MB). The dynamical unit comprises excitatory and inhibitory neurons.

The neural activity for N_E neurons in the PN pool is given by $x_i(t)$, where $i = 1, 2, \ldots, N_E$. Similarly, the activity for N_I neurons in the LN neuron pool is given by $y_i(t)$, where $i = 1, 2, \ldots, N_I$. The $S_i^E(t)$ and $S_i^I(t)$ from receptors along with their weighted sum serve as inputs to the dynamical layer. The time constant (β) is determined using Wilson–Cowan dynamics in Eq. 15.1 and Eq. 15.2.

$$\beta \frac{dx_i(t)}{dt} = \Theta\left(\begin{array}{l}\sum_{j=1}^{N_E} w_{ij}^{EE} x_j(t) - \sum_{j=1}^{N_I} w_{ij}^{EI} y_j(t) \\ + g_{inp}^E S_i^E(t) - x_i(t) + \mu_i^E(t)\end{array}\right)\cdots$$
$$for, i \in 1, 2, \ldots, N_E$$

(Eq. 15.1)

$$\beta \frac{dy_i(t)}{dt} = \Theta\left(\begin{array}{l}\sum_{j=1}^{N_E} w_{ij}^{IE} x_j(t) - \sum_{j=1}^{N_I} w_{ij}^{II} y_j(t) \\ + g_{inp}^I S_i^I(t) - y_i(t) + \mu_i^I(t)\end{array}\right)\cdots$$
$$for, i \in 1, 2, \ldots, N_I$$

(Eq. 15.2)

where, E and I are excitatory and inhibitory neurons, w_{ij}^{XY}; $X, Y \in [E, I]$ are weights from Y to X, $S_i^X(t)$ is the input from the odor sensors, g_{inp}^X is the weight for the $S_i^X(t)$, μ_i^Y is the noise, and Θ is a unit ramp activation function that is given in Eq. 15.3.

$$\Theta(u) = \begin{cases} 0, & u < 0 \\ u, & u \geq 0 \end{cases}\cdots$$

(Eq. 15.3)

The weights (Eq. 15.4) are chosen as follows:

$$w_{ij}^{XY} = g^Y \cdot \begin{cases} 1, & with\ probability\ p^{XY} \\ 0, & with\ probability\ 1 - p^{XY} \end{cases}\cdots$$

(Eq. 15.4)

where g^0 is the coupling strength and p^{XY} is a model parameter. The neurons are not self-excitatory or self-inhibitory $\left(w_{ii}^{XX} = 0\right)$.

Outputs from the dynamic layer are sent to a support vector machine classifier with a linear kernel to classify the odors.

The model reduces within-class variance and increases between-class variance. The temporal nature of the model imparts the model a short-term working memory, thus allowing efficient odor discrimination during the early odor period. One of the limitations of the model is the nonbiologically realistic classifier.

Mushroom Body as Classifier (Muezzinoglu et al., 2009b)

As discussed earlier in "Decorrelation and Integration Dynamics of the Antennal Lobe," the employed classifier is not biologically relevant. In the follow-up study, Muezzinoglu and colleagues (2009b) present a biologically relevant model of MB for AL output identification (see Fig. 15.4). Muezzinoglu et al. (2009a) and Muezzinoglu et al. (2009b) share identical model design as described in Fig. 15.3. The main focus of this study was to classify the previously obtained AL outputs. In this model the authors used a nonlinear expansion of the AL output to MB, with the addition of a gain term to have uniform KC activity, a Hebbian learning rule to update the KC to output neuron connections, and a learning signal to update the output neuron's synapses.

The activity patterns in the locust showed that the AL output is discretized through feedforward inhibition onto MB calyces (Perez-Orive et al., 2002). Therefore, KC neurons were designed as McCulloch–Pitts neurons (with neural outputs as 0 for no spike and 1 for a spike) given in Eq. 15.5.

$$\mu_j = \Phi\left(\sum_{i=1}^{N_E} c_{ji} x_i - \theta^{\mathrm{KC}}\right), \quad j = 1, 2, \ldots, N_{KC} \ \ldots \tag{Eq. 15.5}$$

where, x is the output from PN of AL and $\boldsymbol{x} = (x_1, x_2, \ldots x_{\mathrm{NE}})$; $c_{ij} \in [0 \ \ 1]$, which is the connectivity matrix of $N_E \times N_{KC}$ *size*; θ^{KC} is the firing threshold, and $\Phi(\cdot)$ is a Heaviside function. To reduce the instability only 20% of the top $n_{KC} = N_{KC}/5$ neurons that receive the most excitation in the $\boldsymbol{x}$ are admitted.

The output neurons of MB are modeled as McCulloch–Pitts neurons. $z_l = \Phi\left(\sum_{j=1}^{N_{KC}} w_{lj} \cdot \mu_j - \theta^{\mathrm{LB}}\right)$, $l = 1, 2, \ldots, N_{LB}$. The LB denotes the MB lobes. Similar gain control (the neuron that receives the highest input fires) is employed. The synaptic weights are updated using the Hebbian rule, $w_{lj}(n+1) = H\left(z_l, \mu_j, w_{lj}(n)\right)$, where $H(z, \mu, w) = w + 1$ when $z = 1$, $\mu = 1$ and 0 otherwise. Synaptic strength is strengthened with probability p_+ if the presynaptic and postsynaptic neurons fire together. Learning is terminated when optimal performance is reached.

Self-organization in the Olfactory System (Nowotny, Huerta, Abarbanel, & Rabinovich, 2005)

In this model the insect olfactory system was modeled using random connectivity and self-organization (see Fig. 15.5). The model features a robust learning algorithm with local learning and competition and without the need to hard code special connectivity patterns or process the input information. The map model comprises spiking neurons with a discrete time dynamical map. The membrane voltage (V) of the neuron is given in Eq. 15.6.

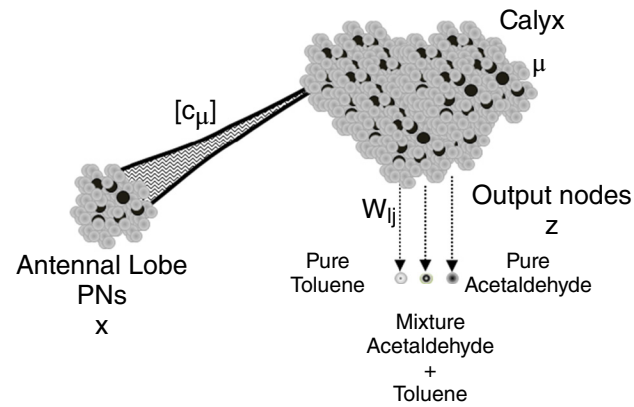

Figure 15.4 Model for classifying the antennal lobe outputs by mushroom body neurons. The weights between the antennal lobe neurons to calyx are initially randomly set, and are updated based on the binary reward signal. Redrawn from Muezzinoglu et al. (2009b).

$$V(t+\Delta t)=\begin{cases} V_{spike}\left(\dfrac{\alpha V_{spike}}{V_{spike}-V(t)-\beta I_{syn}}+\gamma\right), & for\ \mathrm{V}(\mathrm{t})\le 0 V_{spike}(\alpha+\gamma), \\ \mathrm{V}(\mathrm{t})\le \mathrm{V}_{\mathrm{spike}}(\alpha+\gamma) V(t-\Delta t)<0-V_{spike}, & otherwise \end{cases} \ldots \quad \text{(Eq. 15.6)}$$

where $V_{spike}=60\,\mathrm{mV}$, $\alpha=3$, $\beta=2.64\ \mathrm{M\Omega}$ (input resistance of the cell), and $\gamma=-2.468$. These map model neurons had a response similar to the Hodgkin–Huxley model. All neurons except PN (which are modeled as input pattern-based, short, square voltage pulses at spike times) were modeled as map neurons. The synapses are modeled as:

$$I_{syn}(t+\Delta t)=g_{syn}S(t)(V_{rev}-V_{post}(t)\ldots \quad \text{(Eq. 15.7)}$$

where, V_{rev} is reversal potential with $V_{rev}=0\,\mathrm{mV}$ for excitatory and $V_{rev}=-92\,\mathrm{mV}$ for inhibitory synapses, V_{post} is the postsynaptic neuron membrane potential.

$$S(t+\Delta t)=\begin{cases} S(t)e^{-\Delta t/\tau_{syn}}+\delta & presynaptic\ spike\ at\ t \\ S(t)e^{-\Delta t/\tau_{syn}} & otherwise \end{cases} \ldots \quad \text{(Eq. 15.8)}$$

In Eq. 15.8, $S(t)$ is the amount of neurotransmitter at postsynaptic receptors. A small amount of neurotransmitter, δ, is released within Δt and is exponentially decreased at the rate of $\Delta t/\tau_{syn}$ when the presynaptic neuron is firing.

The external KC (eKC) neurons are all-to-all mutually inhibitory. The iKCs-eKC synapses are updated as Eq. 15.9 and Eq. 15.10.

$$g_{raw}(t+\Delta t)=\begin{cases} g_0+(g_{raw}(t)-g_0)\exp(-\Delta t/\tau_{decay}) & no\ spikes\ at\ t \\ g_0+g_{raw}(t)-(g_0)\exp(-\Delta t/\tau_{decay}) & \ldots \\ \quad +A(t_{post}-t_{pre}-\tau_{shift}) & \\ & pre\ or\ post\ synaptic\ spike\ at\ t \end{cases} \quad \text{(Eq. 15.9)}$$

$$A(\tau)=\begin{cases} y_- & \tau<\tau_- \\ a_-\tau+y_0\tau_- & <\tau\le 0 \\ a_+\tau+y_0 & 0<\tau\le\tau_+ \\ y_+\tau_+ & <\tau \end{cases} \ldots \quad \text{(Eq. 15.10)}$$

where, g_0, g_{raw}, a_-, a_+, τ, τ_{decay}, τ_{shift}, τ_-, τ_+, y_0, y_+, and y_- are constants, g_{max} is maximal synaptic strength, and

$$g_{syn}=g_{max}\left(\frac{\tanh\left(\dfrac{g_{raw}(t)-g_{mid}}{g_{slope}}\right)+1}{2}\right).$$

The model is able to successfully classify the input odor patterns through a self-organizing model design. iKC and eKC connectivity did not affect the performance, iKC is versatile for a range of gains and gain control improves performance for significantly overlapping classes.

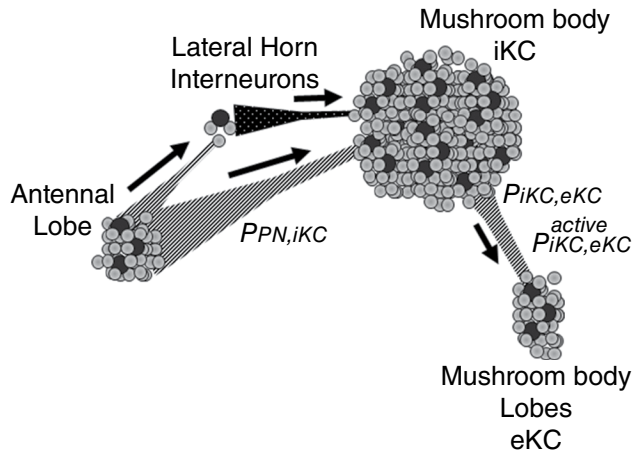

Figure 15.5 Overall model design: the antennal lobe is connected to lateral horn interneurons and the mushroom body by all-to-all excitatory connections containing inhibitory Kenyon cells (iKC). Lateral horn neurons connect to iKC by all-to-all excitatory connections. iKC is connected to the excitatory Keynon cells (eKC). Within the eKC all the connections are all-to-all inhibitory. Redrawn from Nowotny et al. (2005).

Compound Odor Discrimination (Wessnitzer, Young, Armstrong, & Webb, 2012)

Insects are able to distinguish a mixture of complex odors. To our knowledge, the Wessnitzer et al. (2012) model is the only one presented that is able to distinguish multiple odors. In this model, a single odor activates only one set of glomeruli, but a multiple odor combination activates a combined glomeruli set (see Fig. 15.6). One of the striking features of this modeling approach is that the KC synaptic strength (and not its number) plays a crucial role in multi-odor detection. The model implements a spike timing-dependent plasticity (STDP) with neurotransmitter-based signaling in the unconditioned stimulus. Similar to other models this model comprises ORN that project to the MB (comprising PN and LN), the outputs from PN are projected to the KC, which in turn project to the extrinsic neurons (EN). DA modulates plasticity in the KC–EN synapse. In this model the neurons are modeled as Izhikevich neurons with change in membrane potential (v) as follows:

$$C\dot{v} = k(v - v_r)(v - v_t) - u + I + \left[\xi \sim N(0,\sigma)\right] \ldots \quad \text{(Eq. 15.11)}$$

$$\dot{u} - a\left(b(v - v_r) - u\right) \ldots \quad \text{(Eq. 15.12)}$$

$$v = \begin{cases} c & v > v_t \\ v & otherwise \end{cases} \ldots \quad \text{(Eq. 15.13)}$$

$$u = \begin{cases} u + d & v > v_t \\ u & otherwise \end{cases} \ldots \quad \text{(Eq. 15.14)}$$

where, u is the recovery current (Eq. 15.12), a, b, c, d, and k are model parameters, $C(=4)$ is the capacitance, $v_r(=-85)$ is the resting membrane potential, $v_t(=-25)$ the instantaneous threshold potential, and ξ is the Gaussian noise term. The synaptic inputs (I) are modeled as Eq. 15.15.

$$I = gS(v_{rev} - v) \ldots \quad \text{(Eq. 15.15)}$$

$$v_{rev} = \begin{cases} 0\,mV & excitatory\ synapse \\ -92\,mV & inhibitory\ synapse \end{cases} \ldots \quad \text{(Eq. 15.16)}$$

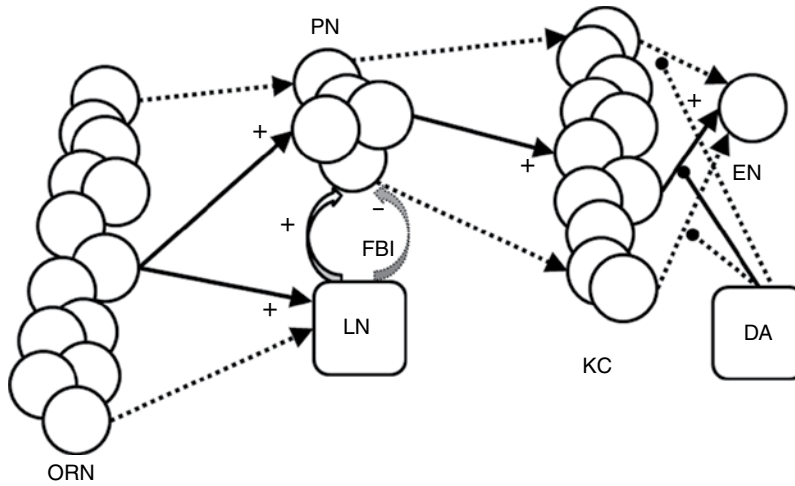

Figure 15.6 The model overview containing the connections from olfactory receptor neurons' (ORN) convergence to antennal lobe projection neurons (PN) and projection neurons' divergence to the Kenyon cells (KC). The model employs a global reinforcement signal using dopamine (DA) to enforce spike timing-dependent plasticity (STDP). The output of the Kenyon cell is sent to the extrinsic neurons (EN). Redrawn from Wessnitzer et al. (2012).

A small amount of neurotransmitter $(\phi = 0.5)$ is released post presynaptic spike as described in Eq. 15.17.

$$\dot{S} = -\frac{s}{\tau_{syn}} + \phi\delta\left(t - t_{pre}\right)\ldots \qquad \text{(Eq. 15.17)}$$

where, τ_{syn} is synaptic timescale.

An odorant (O) comprises various ligands $\left[L_1, L_2, \ldots L_{20}\right]$. In this model the authors chose two to six ligands for discrimination. The instantaneous firing rate R for ligand L is given in Eq. 15.18.

$$R_i^{Lj} = \left[1 + \left(\frac{K_i^{Lj}}{\left[L_j\right]}\right)^{-m}\right]^{-1} \ldots \qquad \text{(Eq. 15.18)}$$

where K_i^{Lj} is the ith receptor binding affinity to L_j. $\left[L_j\right]$ is ligand concentration, and molecular Hill equivalent $(m) = 1$.

For antennal lobe dynamics the authors used a standard self-organizing map algorithm (Kohonen, 1990). The KC, which act as coincidence detectors, connect randomly to the calyx.

$$\underset{\left(KC\ is\ active\right)}{\Pr} = \left(\frac{A_{PN}}{T_{PN}}\right)^{C} \ldots \qquad \text{(Eq. 15.19)}$$

Pr is the probability of KC activity, A_{PN} is the number of active projection neurons, T_{PN} is the total number of projection neurons, and C is KC's coincidence threshold. KC only fires when three to six coincident inputs out of 10 PN fire together. A low $g_{PN\text{-}KC}$ threshold is insufficient for KC excitation. The output is obtained through a single EN.

Learning is governed by the neurotransmitter released as in Eq. 15.20.

$$\dot{g} = cd\ldots \qquad \text{(Eq. 15.20)}$$

$$\dot{c} = -\frac{c}{\tau_c} + STDP\left(t_{pre} - t_{post}\right)\delta\left(t - t_{pre/post}\right)\ldots \qquad \text{(Eq. 15.21)}$$

where g is synaptic conductance, c is the synaptic tag is modified using STDP, $\delta(t)$ is *Dirac* delta function, τ_c is the time constant, and STDP is as follows:

$$STDP\left(t_{pre} - t_{post}\right) = \begin{cases} A_+ e^{\frac{t_{pre} - t_{post}}{\tau_+}} & for\ t_{pre} - t_{post} < 0 \\ A_- e^{\frac{-\left(t_{pre} - t_{post}\right)}{\tau_-}} & for\ t_{pre} - t_{post} \geq 0 \end{cases} \ldots \qquad \text{(Eq. 15.22)}$$

where, t_{pre} and t_{post} are spiking timings of pre- and postneurons, respectively.

The model also had a measure of performance through learning index (LI) given in Eq. 15.23.

$$LI = spikes_X - spikes_Y \ldots \qquad \text{(Eq. 15.23)}$$

Functionally the antennal lobe integrates multiple ORN inputs and normalizes the PN response.

Conclusions and Future Work

The *Drosophila* olfactory system has been studied by neurobiologists for more than 13 years. These intensive studies have enriched human knowledge on neuroanatomy, electrophysiology, and information processing principles of olfaction in *Drosophila*. *Drosophila*'s ability to learn, memorize, and recall stimulus, and associate it with reward, along with small manageable organism size with fewer neurons and simple odor circuitry make it a model organism in odor studies. The large structural homology between insect and vertebrate olfactory systems enables researchers to apply mechanistic and behavioral principles observed in the "mini-brains" of insects to humans.

Additionally, sparse coding in the MB and dentate gyrus is another feature that the memory centers of vertebrates and invertebrates have in common. Sparse coding and sparse spiking are involved in efficient input pattern separation and encoding. Sparse coding and sparse spiking have received due attention from computational and theoretical

researchers to explore and propose novel hypotheses that cannot currently be studied with experiments.

Computational models of the olfactory system provide valuable insights into the interaction between various neural substrates involved in processing and discriminating various odors. All the models discussed above show high performance due to the limited number of neural structures involved but are unable to distinguish a large number of unique odors, and are unable to learn, forget, and adapt to the stimulus as quickly as the real fruit fly. This inability is partly due to the fact that connections between various neural substrates are developed over numerous exposures to different stimuli over the course of the fruit fly development. Recent findings suggest that *Drosophila* individuals are able to identify odor intensities (de Bruyne, Foster, & Carlson, 2001; Stopter et al., 2003) and the temporal profile of an odor (de Bruyne et al., 2001). The temporal intensity variation helps the organism identify not merely the presence or absence of reward but also the reward location and influences chemotaxis (Gomez-Marin, Stephens, & Louis, 2011). Future research efforts might be directed toward a comprehensive model of the olfactory system that is able to distinguish a large number of odors along with their intensities to present a more realistic picture of ongoing computations in odor processing. This could lead to new theories and hypotheses about the computations performed by the neural system. To achieve these goals, the main challenge is to explore neural circuits underlying input–output processed (even simplistic models) in flies. Some efforts have been successful in showing the possibility of developing such bio-inspired artificial systems in robotic control systems (Hart, Kreinar, Chrzanowski, Daltorio, & Quinn, 2015).

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