Methods

The model network consisted of 90 PNs and 30 LNs, in accordance with the experimentally observed ratio of approximately three PNs to one LN in the locust AL (Leitch and Laurent, 1996). The membrane potential of each PN and LN was governed by a single-compartment equation obeying Hodgkin-Huxley type kinetics. The PN and LN currents were taken from those used by Bazhenov *et al.* (2001) in their locust AL model.

Intrinsic Currents

Each PN was equipped with Hodgkin-Huxley sodium and potassium spiking currents as well as a transient potassium current. LNs in the locust AL, however, do not generate traditional action potentials; rather, LNs exhibit slow 20-30 ms calcium spikes that decrease in frequency after 100-200 ms of steady stimulation (Laurent *et al.*, 1993). Thus, LNs in our model network were equipped with a calcium current, a calcium-dependent potassium current, and a traditional potassium current. Details are given in the appendix.

Synaptic Currents

PN cholinergic synapses and LN GABAergic synapses were modeled by fast-activating synaptic currents. While cholinergic transmission was modeled via stereotyped neurotransmitter release in response to a presynaptic PN action potential, a continuous coupling model was used to simulate GABAergic transmission - neurotransmitter release was dependent upon the level of presynaptic LN depolarization (Laurent *et al.*, 1993). Additionally, a slow inhibitory synaptic current from LNs to PNs was introduced in order to reproduce the slow temporal patterns observed experimentally in PN odor responses (Laurent *et al.*, 1996). The current was modeled as acting through slowly-activating inhibitory receptors and required a series of approximately three LN calcium spikes to become active. A slow synaptic inhibitory current is consistent with the experimental results of Barbara *et al.* (2005) in the honeybee AL (see Discussion for further justification). Details are given in the appendix.

Network Properties

The network consisted of randomly interconnected PNs and LNs with cell-type specific connection probabilities. The PN-PN and PN-LN connection probability was 0.1, while the LN-LN connection probability was 0.25 and the LN-PN connection probability was 0.15. The lack of anatomical or functional glomerular units containing more than one PN within the locust AL suggests that spatially uniform connectivity statistics are a reasonable assumption (Leitch and Laurent, 1996; Laurent, 1996; Wilson and Mainen, 2006). We experimented with a wide range of connection probabilities and determined that sparse network connectivity (specifically sparse PN-PN connectivity) was required in order to reproduce the known features of locust AL physiology. Each PN received background current input in the form of a Poisson spike train with a mean rate of 3500 spikes/second and a spike strength of 0.0654 μA. In agreement with experiment, this resulted in a background PN firing rate of approximately 2-4 spikes/second (Perez-Orive *et al.*, 2002). All simulations were performed using the explicit Euler method with a time step of 0.01 ms.

Odor Simulation

An odor was simulated by stimulating a set of 36 PNs and 12 LNs. Each stimulated cell received stimulus current in the form of 200 independent Poisson spike trains, each with a mean rate of 35 spikes/second and a spike strength of 0.01743 μA (PNs) or 0.01667 μA (LNs). Due to the large convergence ratio of ORN inputs onto PNs in the locust (Hildebrand *et al.*, 1997; Homberg *et al.*, 1989; Mazor and Laurent, 2005) and their mean-driven log-linear response properties (Rubin and Katz, 1999; Duchamp-Viret *et al.*, 2000; Wachowiak and Cohen, 2001; Meister and Bonhoeffer, 2001; Reisenman *et al.*, 2004; Hallem and Carlson, 2006), we modeled ORN input to each AL neuron as a stochastic process (with Poisson statistics) rather than simulating individual ORNs explicitly. Consistent with experiment, PNs which were active during stimulus presentation exhibited firing rates of 10-40 spikes/second (Perez-Orive *et al.*, 2002). Twenty trials were performed for each stimulus with a 10 second total duration for each

trial. Stimulus onset occurred at $t_o = 1$ second and stimulus offset occurred at $t_d = 3.5$ seconds. In order to capture the experimentally observed time course of ORN input to the locust antennal lobe (Wehr and Laurent, 1999), we modeled stimulus rise as exponential with a rise time of 400 ms, while stimulus decay was modeled as root exponential with a decay time of approximately 1000 ms. The odor-evoked input rate of ORN spikes to a stimulated cell in the network was given by $R(t) = r_m exp(-(t - (t_o + s))^2/c_1)$ for $t = t_o$ to $t = t_o + s$, by $R(t) = r_m$ for $t = t_o + s$ to $t = t_d$, and $R(t) = r_m exp(-sqrt(t - t_d)/c_2)$ for $t > t_d$, where $s = 400$ ms was the rise time, $c_1 = 100,000$, $c_2 = sqrt(1000)$ were the scaling constants, and r_m was the maximal stimulus-evoked ORN input rate (described above).

It is generally thought that the olfactory system initially encodes odors in a combinatorial manner - different odors are represented by differing (but potentially overlapping) subsets of active ORNs (Joerges *et al.*, 1997; Vickers and Christensen, 1998; Vickers *et al.*, 1998; Malnic *et al.*, 1999; Ache and Young, 2005; Wang *et al.*, 2003; Ng *et al.*, 2002). We therefore explored one paradigm of odor simulation, referred to as the combinatorial paradigm, in which different odors were simulated by stimulating varying subsets of 36 PNs and 12 LNs, with the statistics of current input (described above) uniform across stimulated cells. In addition to coding stimuli in the combinatorial paradigm, we also examined network behavior when differing stimuli were represented via an intensity paradigm. In this case, odors were represented as intensity distributions, and the set of 36 PNs and 12 LNs receiving stimulus current was fixed across stimuli. This fixed subset of cells was divided into six groups of 6 PNs and 2 LNs, and each group was assigned a factor of 1.0, 0.9, 0.8, 0.7, 0.6, or 0.5 (with each group being assigned a distinct factor). The mean stimulus input rate to each group was multiplied by its assigned factor (with otherwise unaltered current input statistics), and different odors were simulated by rearranging the group-factor assignments. The intensity paradigm of odor encoding was motivated by the observation that varying the concentration of a given odor tends to modulate the firing rates of responding ORNs in vivo (de Bruyne *et al.*, 2001; Wang *et al.*, 2003; Friedrich and Korsching, 1997; Meister and Bonhoeffer, 2001), and hence stimuli coded in the intensity paradigm can be thought of as representing differing concentrations of the same odor.

Local Field Potential

In the locust, the local field potential (LFP) is measured from the mushroom body, and oscillations in the LFP are taken as an indicator of PN synchrony (Laurent *et al.*, 1996). In order to assess PN synchrony in our model, we computed the LFP of the network as the average membrane potential of all 90 PNs. The power spectrum of the LFP of the PN odor response was computed during the period of stimulus presentation (1-3.5 sec) using a single trial. Additionally, we computed the total integrated power of the LFP in the 15-25 Hz range as a function of time; the integrated power was computed in 200 ms sliding windows with a 50 ms step size and was averaged over the 20 trials performed for a given stimulus.

Principal Component Analysis

Principal component analysis (PCA) was performed on the stimulus-response data of the network. For a given stimulus, we computed the 90×2000 matrix of PN firing rates in 50 ms time bins over the entire 10 second trial duration; the matrix entries were then averaged over the 20 trials performed for the given stimulus. We performed PCA on the matrix of trial-averaged PN firing rates, projected the data onto the first three principal components, and plotted the resulting three dimensional stimulus-response trajectories. By dividing the sum of the magnitudes of the eigenvalues of the first three principal components by the sum of the magnitudes of all eigenvalues, we computed the fraction of the data variance captured by the first three principal components. In all cases, the first three principal components captured more than 90% of the total data variance. Stimulus-response trajectories resulting from single trial data matrices were similar to trial-averaged trajectories; however, trial-averaged trajectories were more well-defined and thus these are shown in plots. Qualitatively, the general features exhibited by the dynamics of the response trajectory were independent of the stimulus used.

Odor Discrimination

We used a simple algorithm based on distances of individual trial firing rate vectors to template firing rate vectors for each odor to assess stimulus classification by the model network. To test the ability of the network to discriminate among N simulated odors in a given 50 ms time bin, we computed the 90 dimensional vector of trial-averaged PN firing rates for each of the N odors in the 50 ms bin; these vectors were used as the templates for each of the N odors. For each of the 20N trials, we computed the Euclidean distance between the vector of PN firing rates for the trial and each of the odor templates. If the Euclidean distance from the trial to each of the odor templates was minimized for odor j, we designated that the network classified the trial as a presentation of odor j. If the trial was indeed a presentation of odor j, then the trial was deemed correctly classified by the network, and the discriminability of the network in the given 50 ms time bin was determined as the fraction of the 20N trials correctly classified by the network. The overall ability of the network to discriminate among the N simulated odors was determined as the time-averaged discriminability of the network during the period of stimulus presentation (1-3.5 seconds).

We chose this particular linear discriminator to match that utilized by Mazor and Laurent (2005) in their analysis of odor discrimination using stimulus-evoked recordings from locust PNs. The choice of 50 ms time bins was motivated by the physiology of Kenyon cells (KCs), the neurons of the mushroom body that read PN activity (Kenyon, 1896; Laurent and Naraghi, 1994). PNs send barrages of spikes to both KCs and LHIs, which are GABAergic interneurons located in a structure called the lateral horn (Hansson and Anton, 2000). Additionally, 20 Hz oscillations seen in the LFP of the mushroom body indicate that PN input to KCs and LHIs is globally synchronized on a 50 ms time scale (Laurent and Davidowitz, 1994; Laurent et al., 1996). Since KC dendrites are known to receive GABAergic input (Leitch and Laurent, 1996) and LHI axon collaterals have been shown to diffusely overlap KC dendrites, LHIs are the likely source of the strong, periodic, phase-delayed inhibition seen in recordings from KCs (Perez-Orive et al., 2002). Thus, KCs receive globally synchronized PN input in 50 ms epochs, and towards the end of each epoch the membrane potential of every KC is effectively reset by inhibition arriving from the lateral horn. This suggests that KCs integrate PN activity over a time scale no greater than 50 ms, and hence it is probable that odor discrimination in the locust brain occurs over similar temporal windows.

Appendix

The membrane potential of each PN and each LN was governed by equations of the following form:

$$C_m \frac{dV_{PN}}{dt} = -g_L(V_{PN} - E_L) - I_{Na} - I_K - I_A$$

$$-I_{GABA} - I_{slow} - I_{nACH} - I_{stim}$$

$$C_m \frac{dV_{LN}}{dt} = -g_L(V_{LN} - E_L) - I_{Ca} - I_{CaK} - I_K$$

$$-I_{GABA} - I_{nACH} - I_{stim}.$$

The parameters for the passive leak current were $C_m = 1.0 \ \mu F$, $g_L = 0.3 \ \mu S$, $E_L = -64 \ mV$ for PNs and $C_m = 1.0 \ \mu F$, $g_L = 0.3 \ \mu S$, $E_L = -50 \ mV$ for LNs.

Intrinsic Currents

The intrinsic currents consisted of fast sodium and potassium currents I_{Na} and I_K, a transient calcium current I_{Ca}, a calcium-dependent potassium current I_{CaK}, and a transient potassium current I_A. All such currents obeyed equations of the following form:

$$I_j = g_j m^M h^N (V - E_j).$$

The maximal conductances were $g_{Na} = 120 \ \mu S$, $g_K = 3.6 \ \mu S$, $g_A = 1.43 \ \mu S$ for PNs and $g_{Ca} = 5.0 \ \mu S$, $g_{CaK} = 0.045 \ \mu S$, $g_K = 36 \ \mu S$ for LNs. The reversal potentials were $E_{Na} = 40 \ mV$, $E_K = -87 \ mV$ for PNs and $E_{Ca} = 140 \ mV$, $E_K = -95 \ mV$ for LNs.

The gating variables $m(t)$ and $h(t)$ take values between 0 and 1 and obey the following equations:

$$\frac{dm}{dt} = \frac{m_\infty(V) - m}{\tau_m(V)}$$

$$\frac{dh}{dt} = \frac{h_\infty(V) - h}{\tau_h(V)}.$$

I_{Na} and I_K are described in Hodgkin and Huxley (1952).

The I_{Ca} current has $M = 2$, $N = 1$, $m_\infty = 1/(1 + exp(-(V + 20)/6.5))$, $\tau_m = 1 + (V + 30)0.014$, $h_\infty = 1/(1 + exp((V + 25)/12))$, $\tau_h = 0.3exp((V - 40)/13) + 0.002exp(-(V - 60)/29)$ (Laurent et al., 1993).

The I_{CaK} current has $M = 1$, $N = 0$, $m_\infty = [Ca]/([Ca] + 2)$, $\tau_m = 100/([Ca] + 2)$ (Sloper and Powell, 1978).

The I_A current has $M = 4$, $N = 1$, $m_\infty = 1/(1 + exp(-(V + 60)/8.5))$, $\tau_m = (0.27/(exp((V + 35.8)/19.7) + exp(-(V + 79.7)/12.7)) + 0.1)$, $h_\infty = 1/(1 + exp((V + 78)/6))$, $\tau_h = 0.27/(exp((V + 46)/5) + exp(-(V + 238)/37.5))$ for $V < -63\ mV$ and $\tau_h = 5.1$ for $V > -63\ mV$ (Huguenard *et al.*, 1991).

The dynamics of intracellular calcium concentration [Ca] were governed by the following equation:

$$\frac{d[Ca]}{dt} = -AI_T - \frac{[Ca] - [Ca]_\infty}{\tau},$$

where $[Ca]_\infty = 0.00024\ mM$, $A = 0.0002\ mM \cdot cm^2/(ms \cdot \mu A)$, and $\tau = 150\ ms$.

Synaptic Currents

The GABA and nicotinic acetylcholine currents were governed by equations of the following form:

$$I_j = g_j[O](V - E_j).$$

The reversal potentials were $E_{nACH} = 0\ mV$ and $E_{GABA} = -70\ mV$. The fraction of open channels [O] obeyed the equation

$$\frac{d[O]}{dt} = \alpha(1 - [O])[T] - \beta[O].$$

For nicotinic acetylcholine synapses [T] was governed by the equation

$$[T] = A\theta(t_0 + t_{max} - t)\theta(t - t_0).$$

For GABAergic synapses [T] was governed by the equation

$$[T] = \frac{1}{1 + exp(-(V(t) - V_0)/\sigma)}.$$

$\theta(x)$ is the Heaviside step function, t_0 is the time of receptor activation, $A = 0.5$, $t_{max} = 0.3\ ms$, $V_0 = -20\ mV$, and $\sigma = 1.5$. For GABAergic synapses the rate constants were $\alpha = 10\ ms^{-1}$ and $\beta = 0.16\ ms^{-1}$, while for nicotinic acetylcholine synapses the rate constants were $\alpha = 10\ ms^{-1}$ and $\beta = 0.2\ ms^{-1}$ (Bazhenov *et al.*, 2001).

The slow inhibitory current from LNs to PNs was governed by the following scheme:

$$I_{slow} = g_{slow}\frac{[G]^4}{[G]^4 + K}(V - E_K)$$

$$\frac{d[R]}{dt} = r_1(1 - [R])[T] - r_2[R]$$

$$\frac{d[G]}{dt} = r_3[R] - r_4[G],$$

where the reversal potential was $E_K = -95\ mV$ and the rate constants were $r_1 = 0.5\ mM^{-1}ms^{-1}$, $r_2 =$ 0.0013 ms^{-1}, $r_3 = 0.1\ ms^{-1}$, $r_4 = 0.033\ ms^{-1}$, and $K = 100\ \mu M^4$ (Destexhe *et al.*, 1996; Bazhenov *et al.*, 1998).

Maximal synaptic conductances were $g_{GABA} = 0.3\ \mu S$ from LNs to LNs, $g_{GABA} = 0.36\ \mu S$ and $g_{slow} = 0.36\ \mu S$ from LNs to PNs, $g_{nACH} = 0.045\ \mu S$ from PNs to LNs, and $g_{nACH} = 0.009\ \mu S$ from PNs to PNs.