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Supplementary Information for

Universal front-end gain control aids robust combinatorial odor coding in naturalistic environments

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Supplementary text
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Captions for Databases S1 to S2
References for SI reference citations

Other supplementary materials for this manuscript include the following:

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Supporting Information Text

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Mathematical model

Model of odor binding, Or/Orco activation, and ORN firing. We model an odor as an N-dimensional vector $\mathbf{s} = [s_1, ..., s_N]$, where $s_i > 0$ are the concentrations of individual volatile molecules (odorants) comprising the odor. The olfactory sensory system is modeled as a collection of M distinct Or/Orco complexes, each of which can be bound with any one of the odorant molecules, and can be either active (firing) inactive (quiescent). We only consider competitive binding, so a complex is bound with one odorant at most. With N possible odorants, receptor a resides in one of $2(N+1)$ possible states, $\{C_a, C_a^*, C_a\text{-}s_i, C_a^*\text{-}s_i\}$, indicating receptors that are unbound/inactive, unbound/active, inactive/bound to odorant i, and active/bound to odorant i, respectively. We set $N = 150$ and $M = 50$ throughout.

In the mean-field limit, the binding dynamics of these $2N+2$ states are described by master equations:

$$\frac{d[C_a\text{-}s_i]}{dt} = k_{ia}^{+} s_i [C_a] - k_{ia}^{-} [C_a\text{-}s_i] \quad [1]$$

$$\frac{d[C_a^*\text{-}s_i]}{dt} = k_{ia}^{*+} s_i [C_a^*] - k_{ia}^{*-} [C_a^*\text{-}s_i], \quad [2]$$

when receptor C_a is either inactive (Eq. 1) or active (Eq. 2). Further, transitions between inactive and active states are described in the mean limit via:

$$\frac{d[C_a]}{dt} = w_a^{\mathrm{u}+} [C_a] - w_a^{\mathrm{u}-} [C_a^*] \quad [3]$$

$$\frac{d[C_a^*\text{-}s_i]}{dt} = w_{ia}^{\mathrm{b}+} [C_a\text{-}s_i] - w_{ia}^{\mathrm{b}-} [C_a^*\text{-}s_i], \quad [4]$$

when receptor C_a is either unbound (Eq. 3) or bound (Eq. 4). The corresponding disassociation constants in terms of the binding transition rates are:

$$K_{ai} = \frac{k_{ai}^{-}}{k_{ai}^{+}}$$

$$K_{ai}^{*} = \frac{k_{ai}^{*-}}{k_{ai}^{+*}} \quad [5]$$

Following (**?**), we assume that in steady state, the active firing state of an Or/Orco complex is energetically suppressed from the inactive state through corresponding Boltzmann factors:

$$\frac{[C_a^*]}{[C_a]} = \frac{w_a^{\mathrm{u}+}}{w_a^{\mathrm{u}-}} \equiv e^{-\epsilon_a} \quad [6]$$

$$\frac{[C_a^*\text{-}s_i]}{[C_a\text{-}s_i]} = \frac{w_{ai}^{\mathrm{b}+}}{w_{ai}^{\mathrm{b}-}} \equiv e^{-\epsilon_{ai}}. \quad [7]$$

These energies are related through detailed balance, which we assume. Applying detailed balance to a given 4-cycle

$$C_a \to C_a^* \to C_a^*\text{-}s_i \to C_a\text{-}s_i \to C_a \quad [8]$$

gives

$$\frac{w_a^{\mathrm{u}+}}{w_a^{\mathrm{u}-}} \frac{k_{ai}^{*+}}{k_{ai}^{*-}} \frac{w_{ai}^{\mathrm{b}-}}{w_{ai}^{\mathrm{b}+}} \frac{k_{ai}^{-}}{k_{ai}^{+}} \equiv 1, \quad [9]$$

which, in conjunction with Eqs. 5, 6, and 7, gives

$$\epsilon_{ai} = \epsilon_a + \ln\left[\frac{K_{ai}^*}{K_{ai}}\right]. \quad [10]$$

Assuming the binding dynamics are fast, then the probability that receptor a is bound by ligand i when inactive and active can be derived from Eqs. 1 and 2 as

$$p_{ai}^{\mathrm{b}} = \frac{s_i/K_{ai}}{1 + \sum_j^N s_j/K_{aj}} \quad [11]$$

$$p_{ai}^{\mathrm{b},*} = \frac{s_i/K_{ai}^*}{1 + \sum_j^N s_j/K_{aj}^*}. \quad [12]$$

The average activity A_a of complex a is the likelihood that the complex is active, unbound or unbound (equivalantly, the proportion of Or/Orco complexes in a given ORN that are active):

$$A_a = \frac{[C_a^*] + \sum_i^N [C_a^*\text{-}s_i]}{[C_a^*] + \sum_i^N [C_a^*\text{-}s_i] + [C_a] + \sum_i^N [C_a\text{-}s_i]}. \quad [13]$$

Using the master equations between active and inactive states Eq. 3 and 4, A_a obeys the master equation

$$\frac{dA_a}{dt} = w_a^+(1 - A_a) + w_a^- A_a \quad [14]$$

with effective transition rates

$$w_a^+ = \sum_i^N p_{ai}^{\text{b}} w_{ai}^{\text{u}+} + p_a w_a^{\text{u}} \quad [15]$$

and analogously for w_a^-. Setting Eq. 14 to zero gives the steady state average activity level of Or/Orco complex a and ORN firing rates:

$$A_a = \left(1 + e^{\epsilon_a} \frac{1 + \sum_i^N s_i/K_{ai}}{1 + \sum_i^N s_i/K_{ai}^*}\right)^{-1} \quad [16]$$

$$r_a(t) = f(\int^t h(t-\tau)A(\tau)d\tau), \quad [17]$$

$$[18]$$

where $h(t)$ and f are a temporal filter and rectifying linear unit (with threshold $\theta = 5$ Hz) as noted in the main text.

Compressed sensing decoding of ORN response. CS addresses the problem of determining a sparse signal from a set of linear measurements, when the number of measurements is less than the signal dimension. Specifically, it is a solution to

$$\mathbf{y} = \mathbf{R}\mathbf{x}, \quad [19]$$

where $\mathbf{x} \in \mathbb{R}^N$ and $\mathbf{y} \in \mathbb{R}^M$ are vectors of signals and responses, respectively, and $\mathbf{R}$ is the measurement matrix. Since measurements are fewer than signal components, then $M < N$, whereby $\mathbf{R}$ is wide rectangular and so Eq. 19 cannot be simply inverted to produce $\mathbf{x}$. The idea of CS is to utilize the knowledge that $\mathbf{x}$ is sparse, i.e.g only K of its components, $K \ll N$ are nonzero. Both the measurements and sparsity are thus combined into a single constrained optimization routine:

$$\hat{x}_i = \text{argmin} \sum_i^N |x_i| \quad \text{such that } \mathbf{y} = \mathbf{R}\mathbf{s} \quad [20]$$

where $\hat{x}_i$ are the optimal estimates of the signal components and the sum, which is known as the L_1 norm of $\mathbf{x}$, is a natural metric of sparsity.

The L_1 norm is a convex operation and the constraints are linear, so the optimization has a unique global minimum. To incorporate the nonlinear response of our encoding model into this linear framework, we assume that the responses are generated through the full nonlinear steady state response, Eq. 16- 17, but that the measurement matrix $\mathbf{R}$ needed for decoding uses a linear approximation of this transformation. Expanding Eq. 17 around $\mathbf{s}_0 = \mathbf{s} - \Delta\mathbf{s}$ gives

$$\Delta r_a(t) = r_a(\mathbf{s}(t)) - r_a(\mathbf{s}_0(t)) \quad [21]$$

$$\Delta r_a(t) = \int^t d\tau h(t-\tau) \sum_i^N A'_{ai}\Big|_{\mathbf{s}_0} \Delta s_i \quad [22]$$

$$r_a(\mathbf{s}_0) = \int^t d\tau h(t-\tau) \sum_i^N A_a(\mathbf{s}_0) \quad [23]$$

$$A_a(\mathbf{s}_0) = \frac{\sum_1^N s_{0,i}/K_{ai}^*}{\sum_1^N s_{0,i}/K_{ai}^* + e^{\epsilon_a}} \quad [24]$$

$$A'_{ai}\Big|_{\mathbf{s}_0} = \frac{e^{\epsilon_a}/K_{ai}^*}{(\sum_i^N s_{0,i}/K_{ai}^* + e^{\epsilon_a})^2}, \quad [25]$$

where we have assumed $K_{ai} \gg s_i$, and where Eqs. 22 and 23 hold only for integrands above 5 Hz (and are zero below), as per the linear rectifier f. We assume that the neural system has access to background $\mathbf{s}_0$, presumed learned, and to the linearized response matrix, Eq. 25, but must infer the excess signals Δs_i from excess ORN firing rates $\Delta r_a(t)$. Thus, this corresponding to the CS framework (Eq. 20) via $\Delta\mathbf{r} \to \mathbf{y}$, $\Delta\mathbf{s} \to \mathbf{x}$, and $A'_{ai}\big|_{\mathbf{s}_0} \to \mathbf{R}$. We optimize the cost function in Eq. 20 using sequential least squares programming, implemented in Python through using the scientific package SciPy.

Figure	N	M	K	$\mu_{a,\mathrm{L}}$	$\mu_{a,\mathrm{H}}$	$\nu_{a,\mathrm{L}}$	$\nu_{a,\mathrm{H}}$	$\epsilon_{a,0}$	ϵ_{L}	ϵ_{H}	$s_{0,\mathrm{L}}$	s_k	$s_{k,\mathrm{F}}$
??	200	40	6	$2 \cdot 10^{-4}$	10^{-3}	10^{-2}	1.0	5.4	5.4	10	-	$\mathcal{N}\left(\frac{s_0}{5}, \frac{s_0}{15}\right)$	–
??	100	50	7	0.5	0.5	0.8	0.8	5.4	3.1	10	10^{-1}	$\mathcal{N}\left(\frac{s_0}{3}, \frac{s_0}{15}\right)$	–
??	100	50	7	0.5	0.6	0.6	0.9	5.4	3.1	10	10^{-1}	$\mathcal{N}\left(\frac{s_0}{3}, \frac{s_0}{15}\right)$	—
??	100	50	7	0.5	0.6	0.6	0.9	5.4	3.1	10	10^{-1}	$\mathcal{N}\left(\frac{s_0}{3}, \frac{s_0}{15}\right)$	–
??-??	100	50	7	0.5	0.6	0.6	0.9	5.4	3.1	10	10^{-1}	$\mathcal{N}\left(\frac{s_0}{3}, \frac{s_0}{15}\right)$	$\mathcal{N}(1, \frac{1}{5})$
??	100	50	7	0.5	0.6	0.6	0.9	–	–	–	10^{-2}	$\mathcal{N}\left(\frac{s_0}{3}, \frac{s_0}{9}\right)$	–
??	100	50	7	0.5	0.6	0.6	0.9	–	–	–	10^{-2}	$\mathcal{N}\left(\frac{s_0}{3}, \frac{s_0}{9}\right)$	–

Table S1. Parameters for simulations in all of the figures.

Or/Orco energies of activation ϵ_a and enforcement of Weber's Law. To enforce Weber's Law, we assume the receptor activities feed back onto ϵ_a through the free energies. For the static case, adaptation is perfect, whereby Or/Orco activities are pegged to perfectly adapted values $\bar{A}_a$. Incorporating this into Eq. 16, and assuming $K^*_{ia} \ll s \ll K_{ia}$, gives

$$\bar{\epsilon}_a = \ln\left(\frac{1-\bar{A}_a}{\bar{A}_a}\right) + \ln\left(\sum_i^N \frac{s_i}{K^*_{ia}}\right). \qquad [26]$$

Assuming that the excess signals are small, $\Delta s_i < s_0$, this gives

$$\epsilon_a \approx \ln(s_0) + \epsilon_{a,0}, \qquad [27]$$

where $\epsilon_{a,0}$ are receptor-dependent constants. In the static case, we choose these constants such that ϵ_a in both adaptive and non-adaptive systems are equivalent, equal to ϵ_{L}, at a given low concentration, $s_{0,\mathrm{L}}$. Below this concentration, we assume adaptation is not in effect, so $\epsilon_a = \epsilon_{\mathrm{L}}$.

It is important to note that while the linearized gain Eq. 25 utilized by the decoding algorithm appears to rely on ϵ_a, by the above argument ϵ_a can in principle be determined by firing rates alone. That is, ϵ_a is inferred in time through integration of Eq. **??**, which relies only on the current ORN activity.

Odor signals. Odor signals $\mathbf{s}$ are N-dimensional vectors presumed sparse whereby only K components, s_k are nonzero, $K \ll N$. The magnitudes of the nonzero components s_k are denoted $s_0 + \Delta s_k$. Here, Δs_k is a random vector, while s_0 is both the center of linearization and, in the case of the adaptive system, the value dictating the strength of adaptive feedback $\epsilon_a \sim \ln\langle s_0 \rangle$.

All the signal intensities are in arbitrary units, as they can be scaled to any range by a corresponding shift in the scales of K_{ia} and K^*_{ia}.

Dynamic adaptation. Dynamic adaptation is enforced through

$$\frac{d\epsilon_a(t)}{dt} = \frac{1}{\tau_a}\left[A_a - \bar{A}_a\right]. \qquad [\mathbf{??}]$$

The perfectly adapted activity levels $\bar{A}_a$ are determined by evaluating Eq. 16 at a given odor intensity, $s_{0,\mathrm{L}}$, corresponding to a minimum stimulus at which adaptation takes effect. The decoding step is assumed instantaneous, so decoded odor identity $\hat{\mathbf{s}}$ is determined by the current value of ϵ_a (which, by virtue of Eq. **??**, is determined by ORN activity a short time prior).

For the simulations with two fluctuating odors (Figs. **??**), the traces shown correspond to the values of s_0 (in blue) and $s_{0,\mathrm{b}}$ (orange), where $s_{0,\mathrm{b}}$ is the baseline concentration of the background odor components, to which the excess signals $\Delta s_{k,\mathrm{b}}$ are added to set the individual odorant concentrations. We choose $\Delta s_{k,\mathrm{b}} \sim \mathcal{N}(s_{k,\mathrm{b}}/3, s_{k,\mathrm{b}}/9)$.

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Materials. Add a Materials subsection if you need to.

Methods. Add a Methods subsection if you need to.

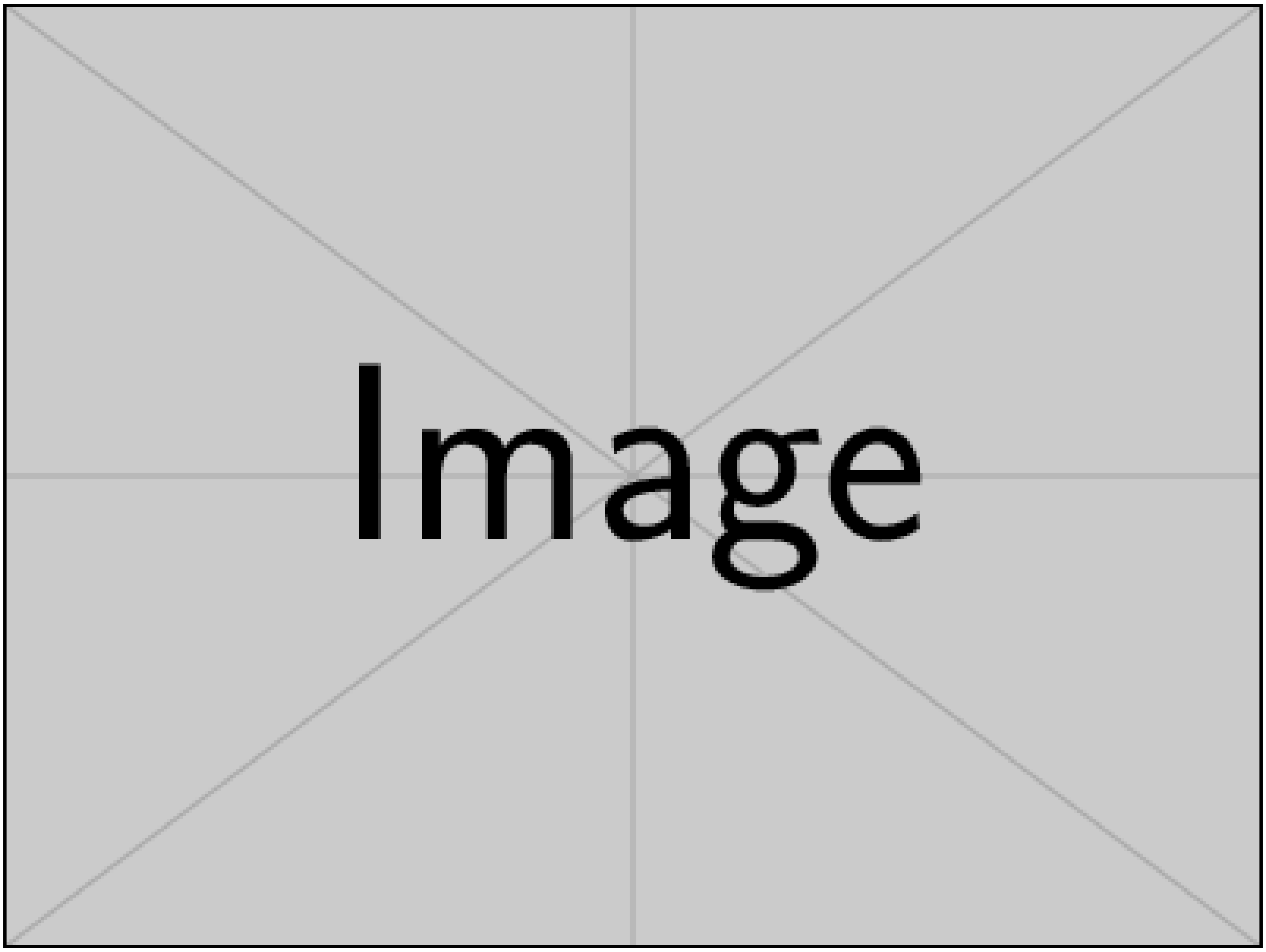

Fig. S1. First figure

Fig. S2. Second figure

Table S2. This is a table

Species	CBS	CV	G3
1. Acetaldehyde	0.0	0.0	0.0
2. Vinyl alcohol	9.1	9.6	13.5
3. Hydroxyethylidene	50.8	51.2	54.0

Movie S1. Type caption for the movie here.

Movie S2. Type caption for the other movie here. Adding longer text to show what happens, to decide on alignment and/or indentations.

Movie S3. A third movie, just for kicks.

Additional data table S1 (dataset_one.txt)

Type or paste caption here.

Additional data table S2 (dataset_two.txt)

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References

1. Varga A, Edmonds AN (2016) Multilingual extraction and editing of concept strings for the legal domain. *Advances in Computer Science: an International Journal* 5(4):18–23.
2. Olsen TE, Stensland G (1992) On optimal timing of investment when cost components are additive and follow geometric diffusions. *Journal of economic dynamics and control* 16(1):39–51.