Text S1 includes:

- Segmentation of the *On* phase in firing response patterns
- Receiver operating characteristic (ROC) analysis
- *On/Off* neuron model equations
- Casting and search game theory
- References

Segmentation of the *On* phase in firing response patterns. Following pheromone stimulation, the discharge pattern changed from spontaneous activity to the *On* phase. Interspike interval (ISI) distributions were well described by gamma densities (mean and coefficient of variation ± s.d.): f_0 ($\overline{ISI}$ = 85 ± 33 ms and CV = 0.8 ± 0.1) for the spontaneous activity versus f_1 ($\overline{ISI}$ = 10 ± 3 ms and CV = 0.34 ± 0.07) for the *On* (n = 11 neurons, >6 trials per neuron). For every spike train, the change from f_0 to f_1 was detected using a CUSUM algorithm *(1-2)*. The log-likelihood of f_1 relative to f_0, based on a single observation (the i-th ISI), is

$$\mathrm{s}(ISI_i) = \log\left(\frac{f_1(ISI_i)}{f_0(ISI_i)}\right)$$

The CUSUM algorithm allows processing consecutive ISIs by computing iteratively a cumulative sum of log-likelihood ratios

$$g_i = \max(g_{i-1} + s(ISI_i), 0) \qquad \text{(S1)}$$

with initial condition $g_0 = 0$. A change is detected as soon as $g_i \geq \theta$ (decision threshold = θ, *On* latency = time of detection). The end of the *On* was determined by the inhibitory period (ISI ≥ 100ms).

Receiver operating characteristic (ROC) analysis. According to signal detection theory, faster detection can be achieved at the expense of a higher false alarm rate and, vice versa, the more accurate the detection the higher the detection delay. Speed and accuracy can be traded by adjusting the decision threshold θ in the CUSUM detector (see above). A low θ will favour speed whereas a high θ results in a late but more accurate detection. We show that the speed-accuracy trade-off improves when considering the simultaneous activity of several neurons (n = 3 *On/Off* neurons recorded simultaneously). The pheromone was detected as soon as the average cumulative sum $\frac{1}{N}\sum_{k=1}^{N} g_i^k$ for N neurons exceeds the decision threshold θ (g_i^k for the k-th neuron computed as in Eq. S1). The ROC curve *(3)* was estimated by computing detection and false alarm rates for different thresholds (see in Fig. S2A the ROC curves obtained at 0.01 ng). Figure S2A shows that the area under the ROC curve increases with the dose and the number of neurons. The improvement in speed-accuracy trade-off resulting from using multiple neurons is probably due to correlated *On* activity. To assess the level of synchronization, we simultaneously recorded from 5 pairs of neurons (five pheromone pulses of 200ms, air gap of 300, 500 or 700ms). As shown in Fig. S2B, pulsed stimulations lead to rapid synchronization. The spikes emitted by different neurons were as precise and reliable as those produced by a single cell across repetitions (σ =3.6 ms and ρ =0.1, Fig. 2B in manuscript). Precision and reliability differed neither between successive pheromone pulses, nor between the different stimulation conditions (not significant, Kruskal-Wallis).

***On/Off* neuron model equations**. Our *On/Off* neuron model was a conductance-based model, with the membrane potential V governed by (Eq. S2)

$$C\frac{dV}{dt} = -g_L(V - E_L) - I_{Na} - I_{Kd} - I_{Ca} - I_{SK} + I_{ORN} \tag{S2}$$

The membrane capacitance C = 22.9 pF, leak conductance g_L = 0.011161 µS and reversal potential E_L = -61.4 mV were taken from *(4).* Intrinsic sodium (I_{Na}) and delayed rectifier potassium (I_{Kd}) were described by (Eqs. S3-S5)

$$I = \overline{g} m^M h^N (V - E) \tag{S3}$$

$$\frac{dm}{dt} = (m_\infty - m)/\tau_m \tag{S4}$$

$$\frac{dh}{dt} = (h_\infty - h)/\tau_h \tag{S5}$$

where m_∞ , h_∞ , τ_m and τ_h are nonlinear functions of V. The I_{Na} current was derived from data in *(5)*. It has M=3, N=1, E_{Na} = 48.2 mV, $\overline{g}_{Na}$=9 µS, $m_{Na\infty} = 1/(1 + \exp((-15.8\text{-}V)/9.32))$, $h_{Na\infty} = 1/(1 + \exp((V+31.1)/9.75))$, $\tau_{mNa} = 0.19 + 2.17 \exp(-(-23.33 - V)^2/(13.71)^2)$, $\tau_{hNa} = 1.57 + 8.83 \exp(-(-29.15 - V)^2/(9.65)^2)$. The I_{Kd} current was derived from data in (6-7). It has M=4, N=0, E_K = -91.6 mV, $\overline{g}_{Kd}$=2.5 µS, $m_{Kd\infty} = 1/(1 + \exp((-18.5\text{-}V)/22.5))$ and $\tau_{mKd} = 1.62 + 6.93 \exp(-(-33.65 - V)^2/(66.88)^2)$. The current I_{Ca} was derived from data in *(4).*

$I_{Ca} = \overline{g}_{Ca} m_{Ca} h_{Ca\infty}(V - E_{Ca})$ and $dm_{Ca}/dt = (m_{Ca\infty} - m_{Ca})/\tau_{mCa}$ with E_{Ca} = 160 mV, $\overline{g}_{Ca}$=0.4 µS, $m_{Ca\infty} = 1/(1 + \exp((-10.6\text{-}V)/8.5))$, $h_{Ca\infty} = 1/(1 + \exp((V+29.6)/8.4))$ and $\tau_{mCa} = 1/(0.19\ ((19.88 - V)/\exp(-1 + 0.1(19.88 - V)) + 0.046 \exp(-V/20.73))$.

The current I_{SK} was modified from *(8).* $I_{SK} = \overline{g}_{SK} m_{SK\infty}(V - E_K)$ with SK conductance $\overline{g}_{SK}$=0.1 µS and $m_{SK\infty} = 1/(1 + \exp(\text{-}1.12\text{-}2.508 \log((\mathrm{Ca}\text{-}Ca_{\infty})/1000)))$. The calcium concentration evolved as $dCa/dt = 0.9\, I_{Ca} - (Ca - Ca_{\infty})/\tau_{Ca}$ with the calcium time constant $\tau_{Ca} = 900$ ms.

The current I_{ORN} mimicked the total input received from a population of 100 ORNs. It was modelled as a sum of exponential decays $I_{ORN} = 0.02\text{pA} \times \sum_{i,f} e^{-(t-t_i^f)/\tau}$ where t_i^f is firing time *f* of the *i*-th pre-synaptic ORN and τ =10 ms. The ORNs were considered to be non-homogeneous Poisson processes with the rate parameter λ(t) derived by fitting real ORN responses (Fig. S3A). The ordinary differential equations (S2-S5) were numerically integrated with a classical fourth-order Runge-Kutta method (time step = 10 µs). Simulations of the *On/Off* neuron model are shown in Fig. S3B.

Casting and search game theory. Tracking the pheromone source can be seen as a race with a single winner, that is, the fastest moth to reach the female. Casting should therefore be optimized so as to keep the search time, *i.e.* distance, as small as possible. We aimed at minimizing the maximum search distance (minimax strategy) and analyzed casting using search game theory *(9)*. Given that the searcher detects at plume centerline and nowhere else (deterministic search problem), the search can be decomposed into the following steps (Fig. S4): a casting path Π_s^p, starting from *s* and hitting the plume centerline in *p*, and a surge path $|pt|$, *i.e.* the straight line from *p* to target *t*. As *t* can be anywhere, the so-called competitive ratio *r* calculates the worst-case search distance in comparison to the shortest distance between *s* and *t* (Eq. S6).

$$r = \max_t \frac{\Pi_s^p + |pt|}{|st|} \qquad \text{(S6)}$$

If no direction information is available, *e.g.* before initial contact with the pheromone (Fig. S4A), the situation is similar to searching for the origin of a ray in the plane. There, spiral-surge achieves a competitive ratio of 22.51306… *(10)*. If prior information is provided by the average wind direction, *e.g.* after having lost contact with the pheromone (Fig. S4B), there is a more efficient strategy: relocate the plume centerline by casting in a line perpendicular to the wind. Crosswind casting can be formulated as a linear search problem for which the optimal solution is to zigzag alternatively to the left and to the right, doubling the path length in every step *(11)*. In the worst case, zigzag casting yields a search trajectory that is 9 times longer than the shortest distance between *s* and *p (11)*. The competitive ratio can thus be written as (Eqs. S7-S8)

$$r = \max_{t} \frac{9|sp| + |pt|}{|st|} \tag{S7}$$

$$= \max_{\beta} \cos\beta \left(9 + \sqrt{\frac{1}{(\cos\beta)^2} - 1} \right) \tag{S8}$$

where the angle $\beta := \angle tsp$ depends on the position of *t* on the plume centerline (see Fig. S4B). The maximum is obtained for $\beta = 0.11065$ ... rads, leading to a competitive ratio *r* = 9.05538… Note that the minimum value of 9 is obtained for $\beta = 0$ rads, *i.e.* when *t* is in *p* so that the target is located with casting only.

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