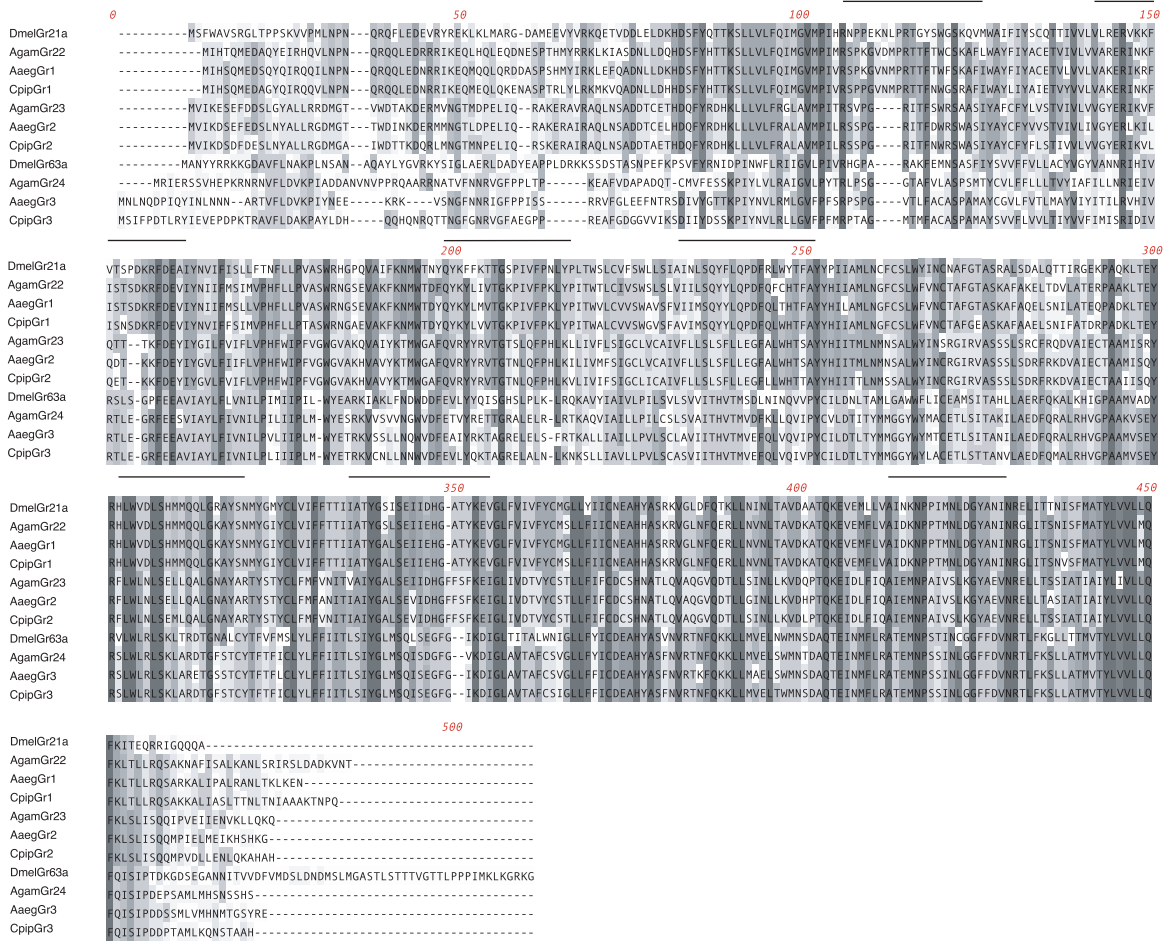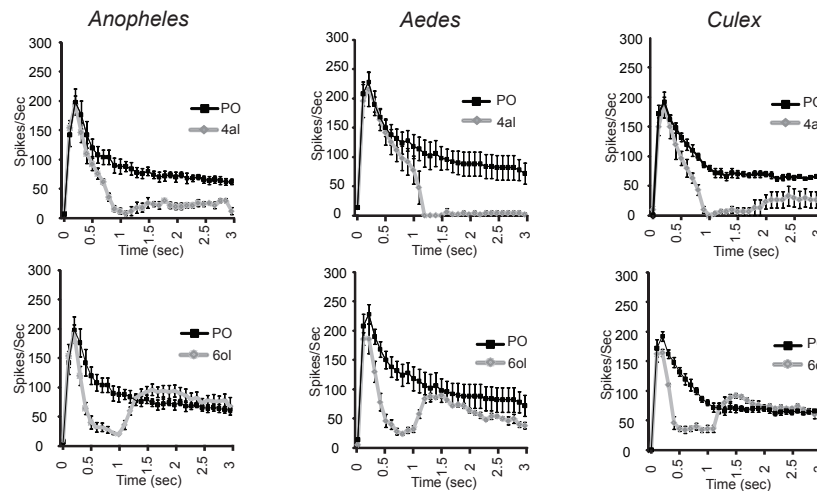**Supplemental figure 1: CO$_2$ receptors are highly conserved in insects.**
**a,** Alignment of the amino acid sequences of CO$_2$ receptor orthologs using ClustalW from *D. melanogaster* (Dmel), *A. gambiae* (Agam), *A.aegypti* (Aaeg) and *C. quinquefasciatus* (Cpip). Recreated using sequences from Robertson et. al. 2009. **b,** Mean spikes per second of cpA neuron for 3-sec stimulus of 0.15% CO$_2$ overlayed with 0.5-sec odour, counted in 100-msec bins, n=5, error bars=s.e.m.
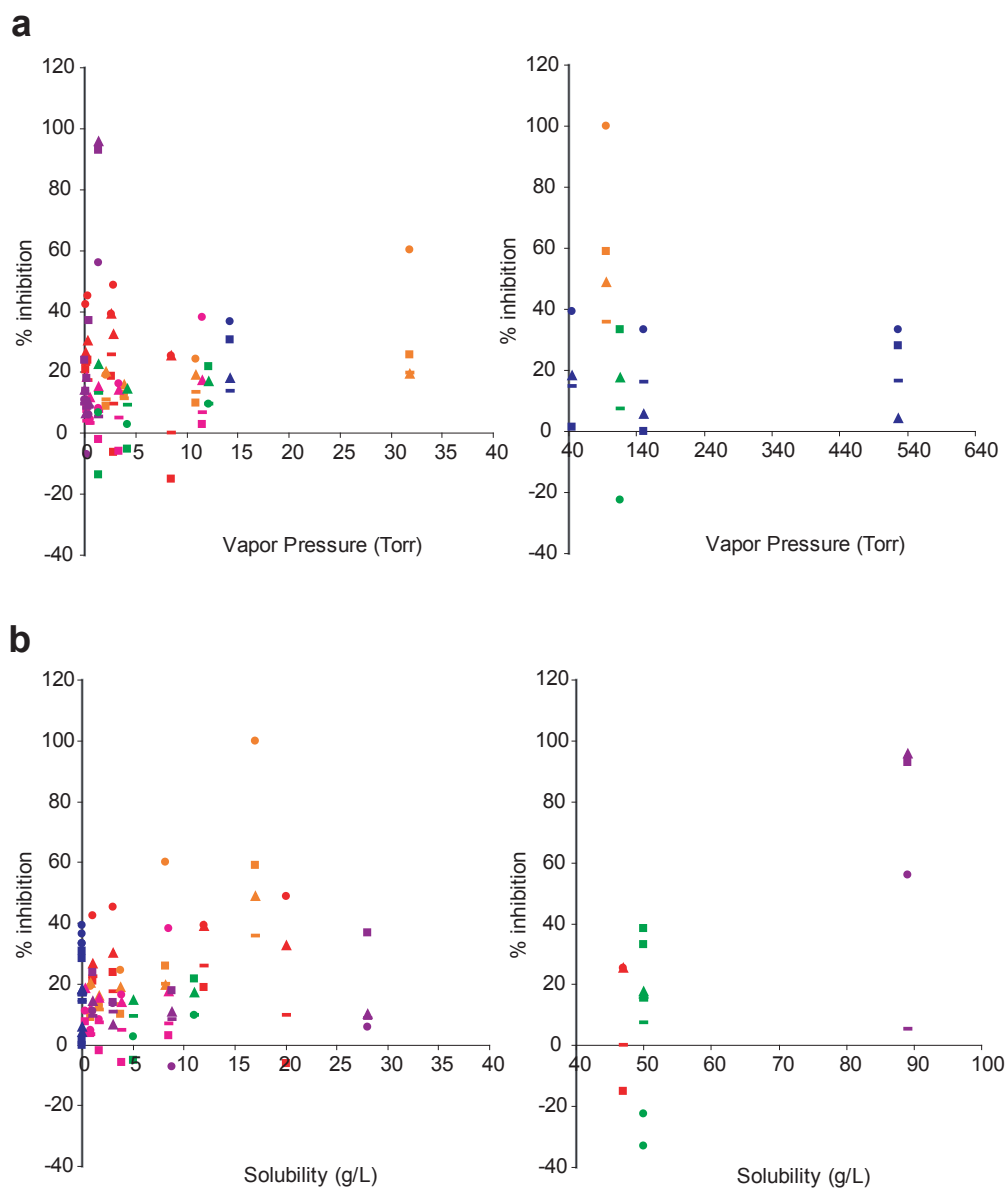
Supplemental figure 2: Volatility and solubility of CO_2 response inhibitors
Percentage inhibition of the CO_2 response as a function of **a,** vapor pressure, or **b,** solubility. Information obtained using Scifinder Scholar. Differing shapes indicate same compounds across different insects; *A. gambiae* (□)*, A. aegypti* (▲), C. *quinquefascitus* (▬)*, D. melanogaster* (◊). Differing colors indicate chemical class; alcohol (red), aldehyde (orange), ester (pink), alkane (blue), ketone (green), acid (purple). n=3.

a

PO

Butanone

b
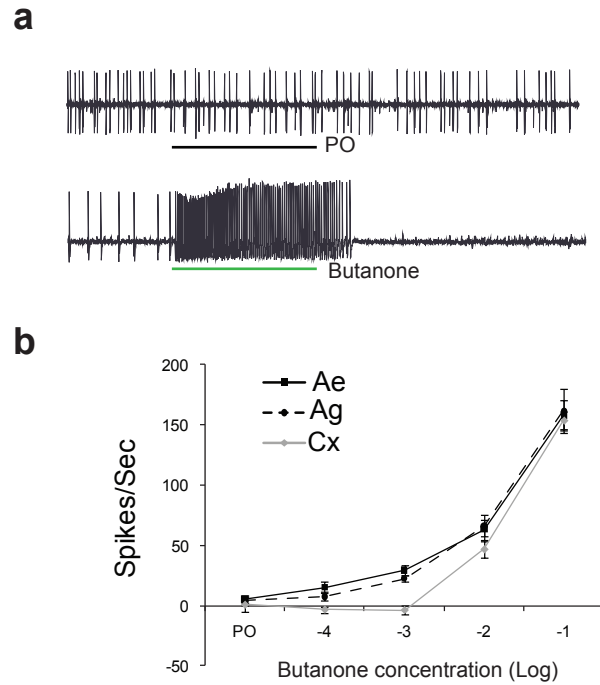
**Supplemental figure 3: Butanone activates cpA neuron in mosquito and mimics CO_2.**
a, Representative trace from *A. gambiae* peg sensillum to a 1-sec stimulus of solvent (PO) or 2-butanone (10^{-1} dilution). **b,** Mean responses of the cpA neuron to 1-sec 2-butanone at indicated dilutions on *A. gambiae* (Ag), *A. aegypti* (Ae), and *C. quinquefasciatus* (Cx). n=5, error bars=s.e.m.
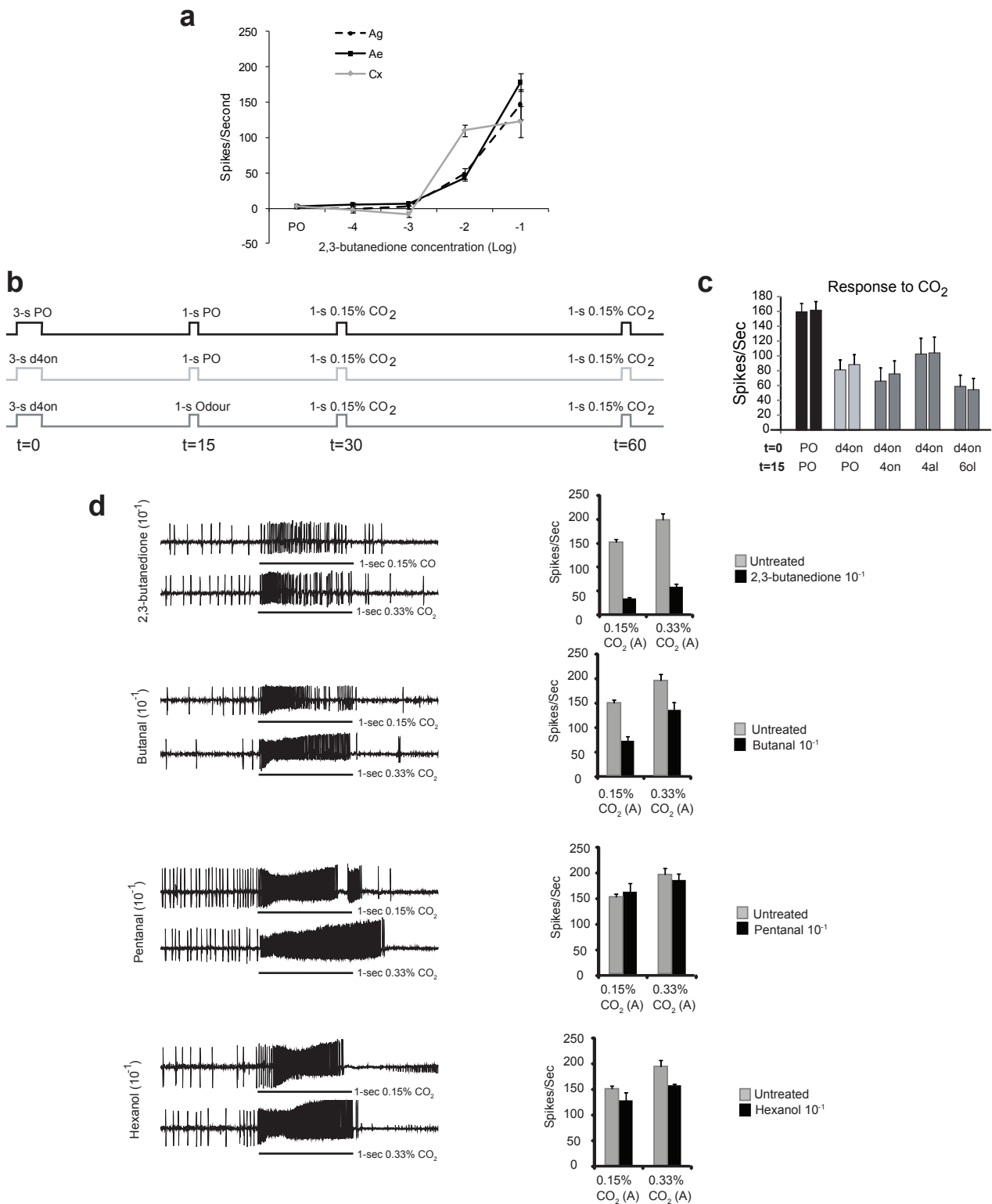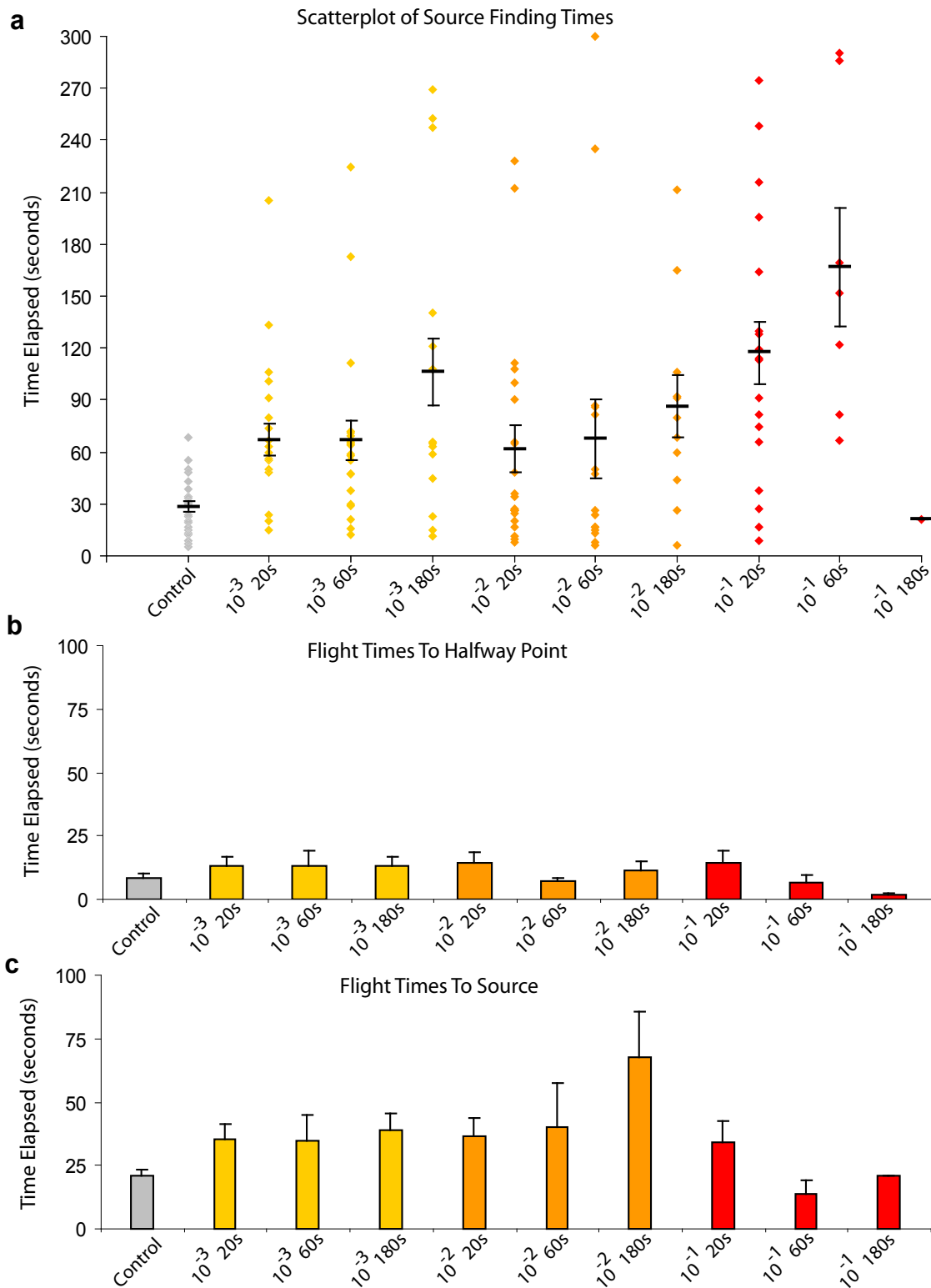
Supplemental Figure 4: Effect of individual odor mixture components on ultra-prolonged activation.
a, Mean responses of the cpA neuron to 1-sec 2,3-butanedione at indicated dilutions on *A. gambiae* (Ag), *A. aegypti* (Ae), and *C. quinquefasciatus* (Cx). n=5. error bars=s.e.m. **b,** Schematic of odour exposure sequence. **c,** Mean response of *A. aegypti* cpA neuron to a 1-sec CO_2 stimulus after pre-exposure as indicated on X-axis with odorants at t=0 and t=15 sec. **d,** Representative traces (left) from peg sensillum and mean responses (right) from the cpA neurons to 0.15% and 0.33% CO_2 after a pretreatment to 3-min of paraffin oil, or individual odor mixture components indicated. n=5, error bars=s.e.m.
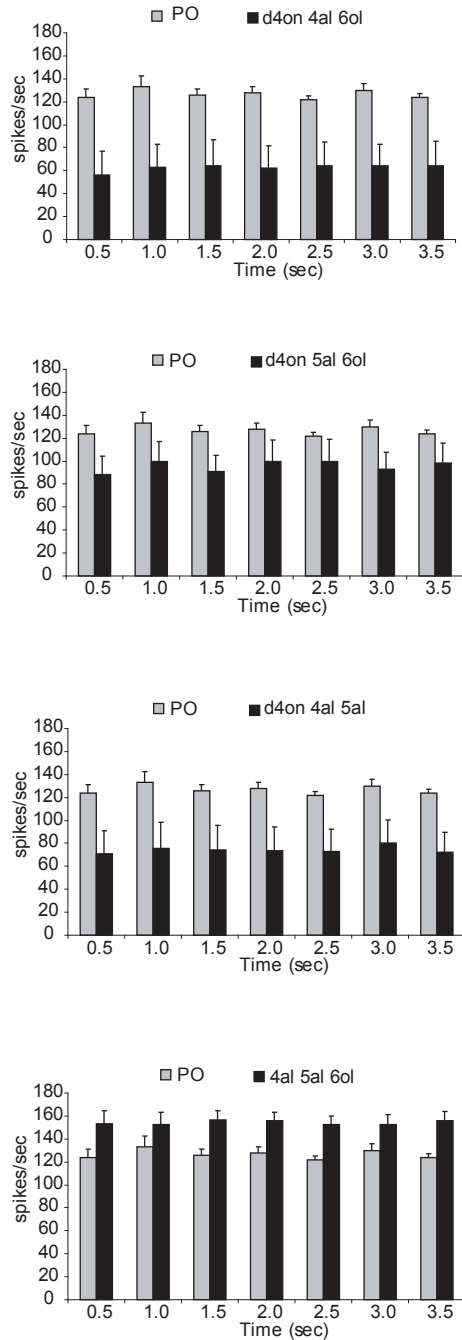
Supplemental figure 5: Long-term Inhibition of CO_2 response in *A. aegypti* after pre-exposure to combinations of odorants.

Mean increase in frequency of response of the cpA neuron to stimulus of 1-sec 0.15% CO_2 applied approx. every 30-sec, following a 3-sec pre-exposure to odor mixtures (10^{-2} dilution) or paraffin oil (PO). d4on=2,3-butanedione, 4al=butanal, 5al=pentanal, 6ol=hexanol. n=5, error bars=s.e.m. Spontaneous activity subtracted.
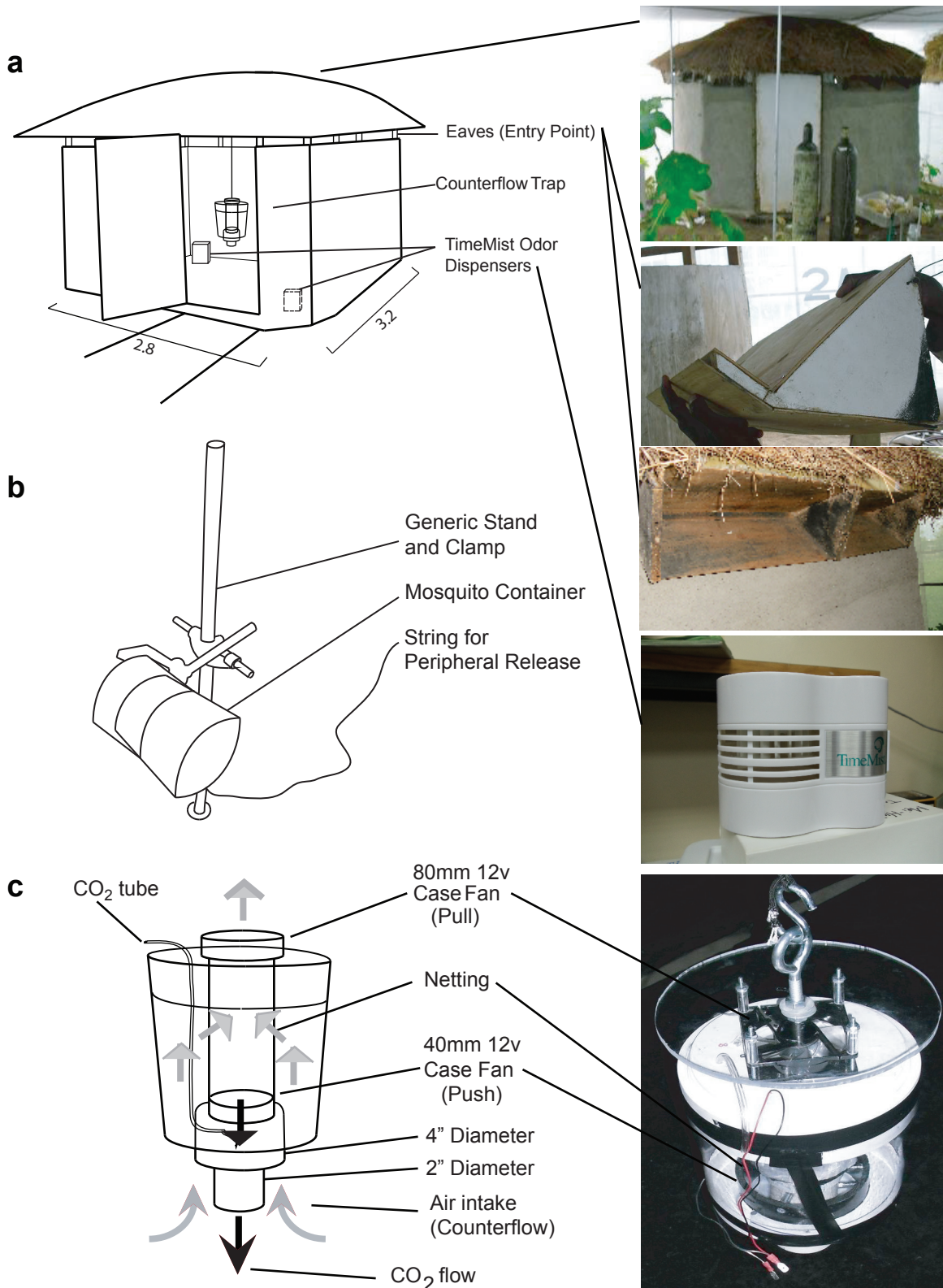
Supplemental figure 6: Behavior disruption in wind-tunnel

a, Scatterplot of time elapsed from start of assay required to find CO_2 source for individual female *Aedes* mosquitoes according to the various ultra-prolonged blend treatments as indicated. Mosquitoes that did not find source are not included. Mean times and s.e.m. are indicated with line and error bars. **b,** Mean flight-time (after takeoff from holding cage) to the half-way point, and **c,** mean flight-time (after takeoff from holding cage) to the CO_2 source. Error bars =s.e.m. Note the data for the 10^{-1} pre-exposure for 60-sec and 180-sec are severely skewed since very few individuals performed the behaviour, only 1 in the last condition. N=26 individuals for each condition were tested.
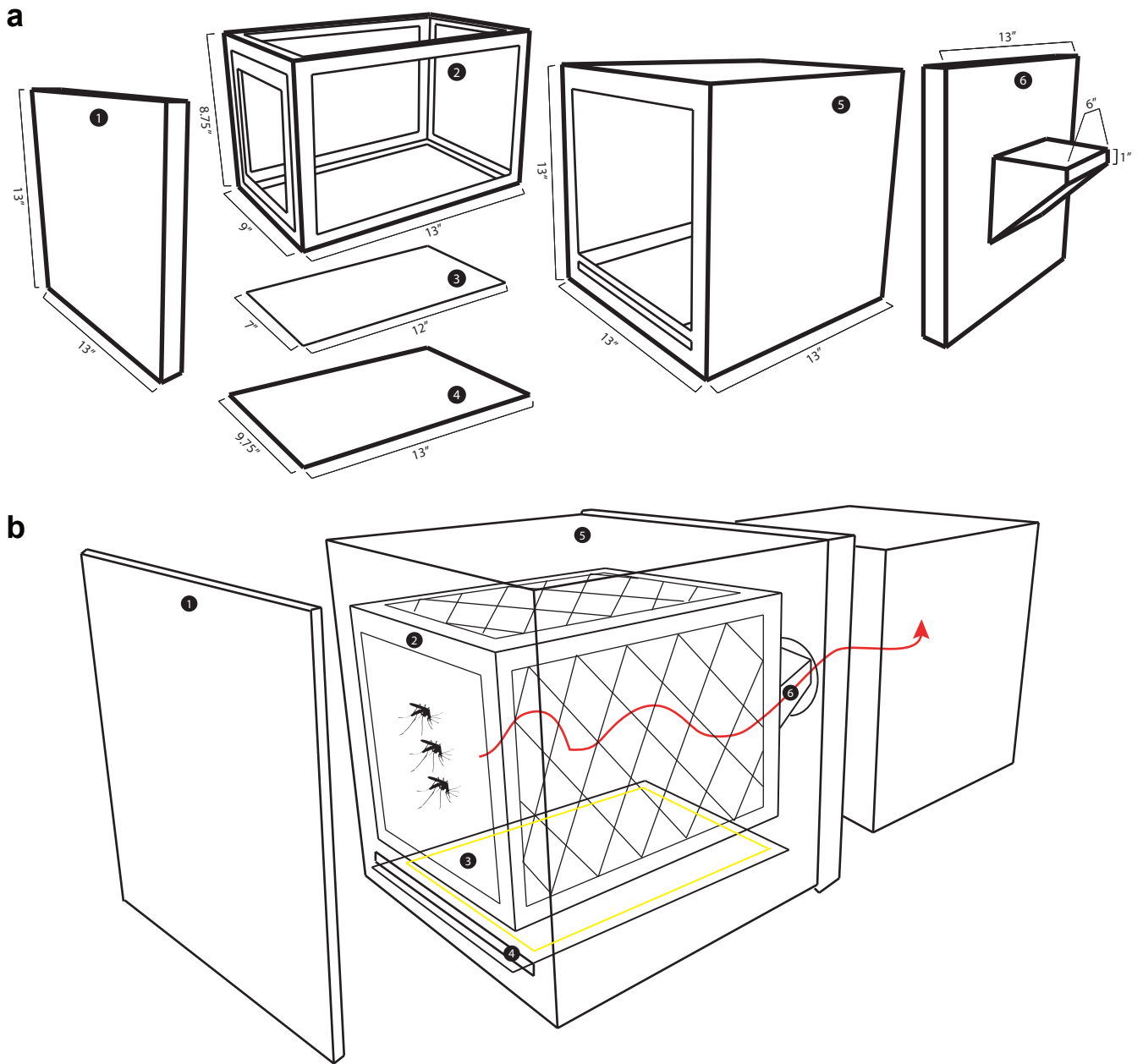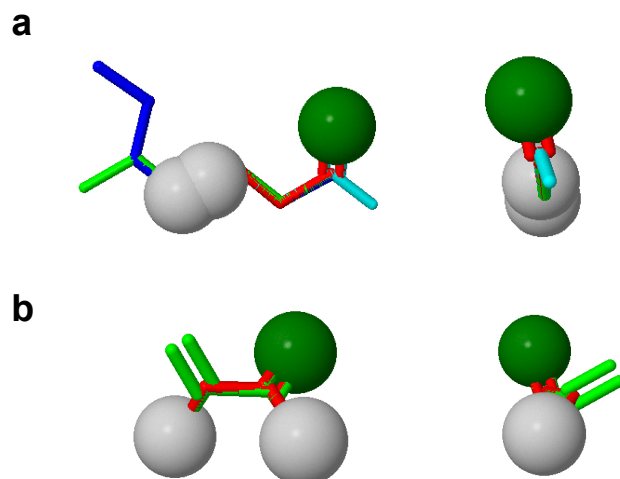
Supplemental Figure 7:
a,b Schematic diagram of the components of the stainless steel repellency chamber and use for the DEET avoidance assay.

a

- Eaves (Entry Point)
- Counterflow Trap
- TimeMist Odor Dispensers

2.8

3.2

b

- Generic Stand and Clamp
- Mosquito Container
- String for Peripheral Release

c

- CO_2 tube
- 80mm 12v Case Fan (Pull)
- Netting
- 40mm 12v Case Fan (Push)
- 4" Diameter
- 2" Diameter
- Air intake (Counterflow)
- CO_2 flow

Supplemental Figure 8:
Schematic and pictures of the **a,** experimental hut inside MalariaSphere with close-up pictures of the one-way entry traps installed in the eaves and TimeMist odour; **b,** remote mosquito release system; **c,** counter-flow geometry trap.

Supplemental Figure 9:
Pharmacophores of **a,** antagonists (1-hexanol, 1-pentanol, 1-butanal, 1-butanoic acid), and **b,** agonists (2-butanone and 2,3-butanedione). Pharmacophores are shown in two orientations at right-angles. Grey=hydrophobic, green=acceptors. Pharmacophores generated using PharmaGist program as described in Inbar, Y., et. al.. Deterministic Pharmacophore Detection via Multiple Flexible Alignment of Drug-Like Molecules. In Proc. of RECOMB (2007), vol. 3692 of Lecture Notes in Computer Science, pp. 423-434. Springer Verlag.

Table 1a: Greenhouse Counter-flow Trapping Assay

Treatment	Solvent (Paraffin oil)	2,3-butanedione (0.1%)	2,3-butanedione (0.01%)	CO_2 (250ml/min)
Percentage of released mosquitoes trapped	19.2±5.7%	14±3%	9.2±2.3%	63.7±8.8%

Table 1b: Wind Tunnel Assay

Treatment	Solvent (Paraffin oil)	2,3-butanedione (0.1%)	CO_2 (1%)
Percentage of mosquitoes finding CO_2 source	0%	0%	100%

Supplemental Table 1:
a, Percentage of female *C. quinquifasciatus* mosquitoes trapped overnight in a counter-flow geometry trap using the indicated lures. N=5 trials per lure treatment, 50 mosquitoes/trial. **b,** Percentage of female *C. quinquifasciatus* mosquitoes flying through the odor emitting ring upwind in wind-tunnel assays. N= 20 per trial.