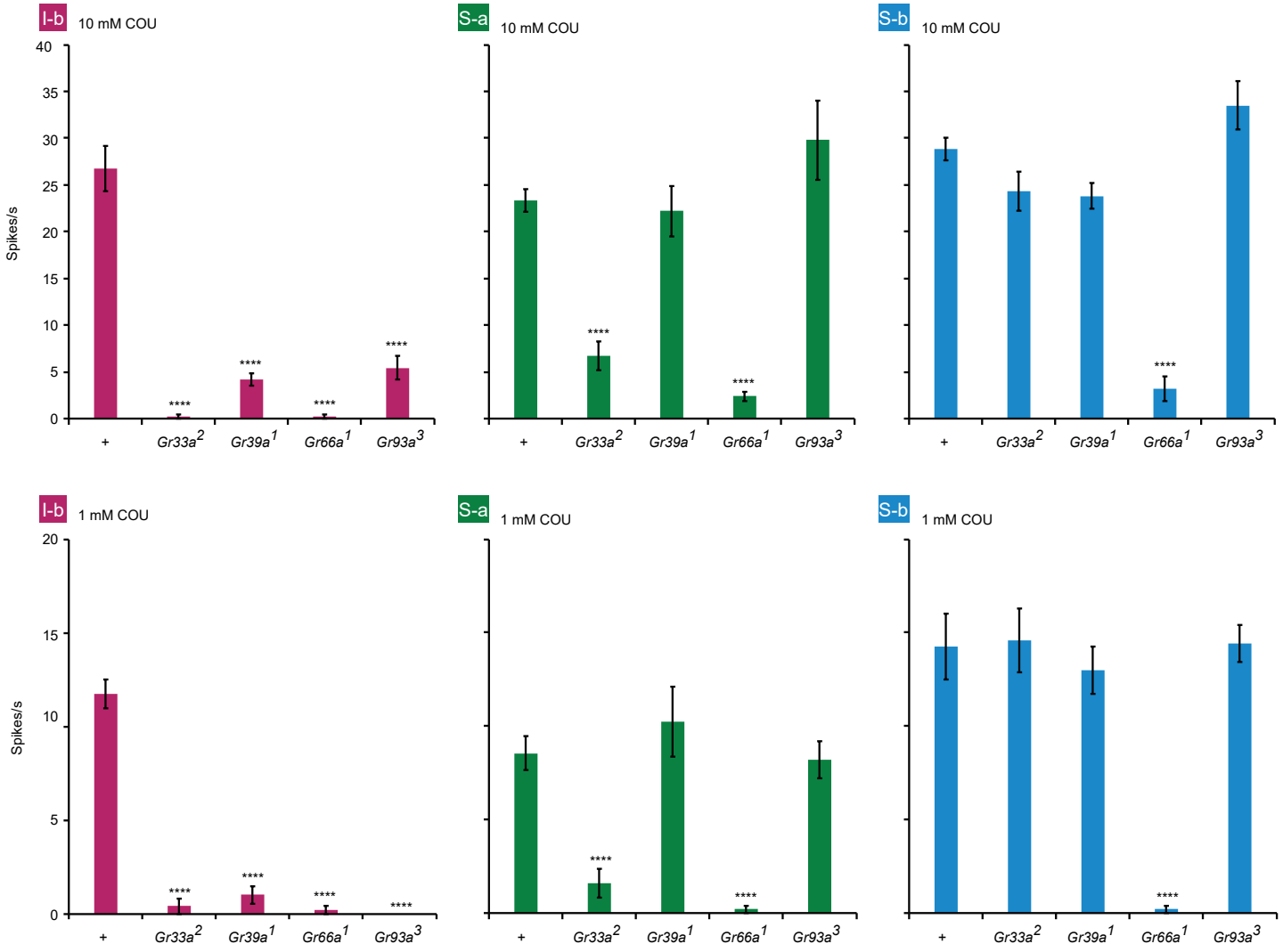


Figure S1. Requirements for responses to COU differ in different classes of sensilla. Related to Figure 2. One-way ANOVA followed by Dunnett's multiple comparison test, n = 8-28, *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001. We note that a study of three individual S sensilla found a phenotype for 1 mM coumarin in Gr33a and Gr66a mutants, in agreement with our results, but also in a Gr93a mutant [S1].

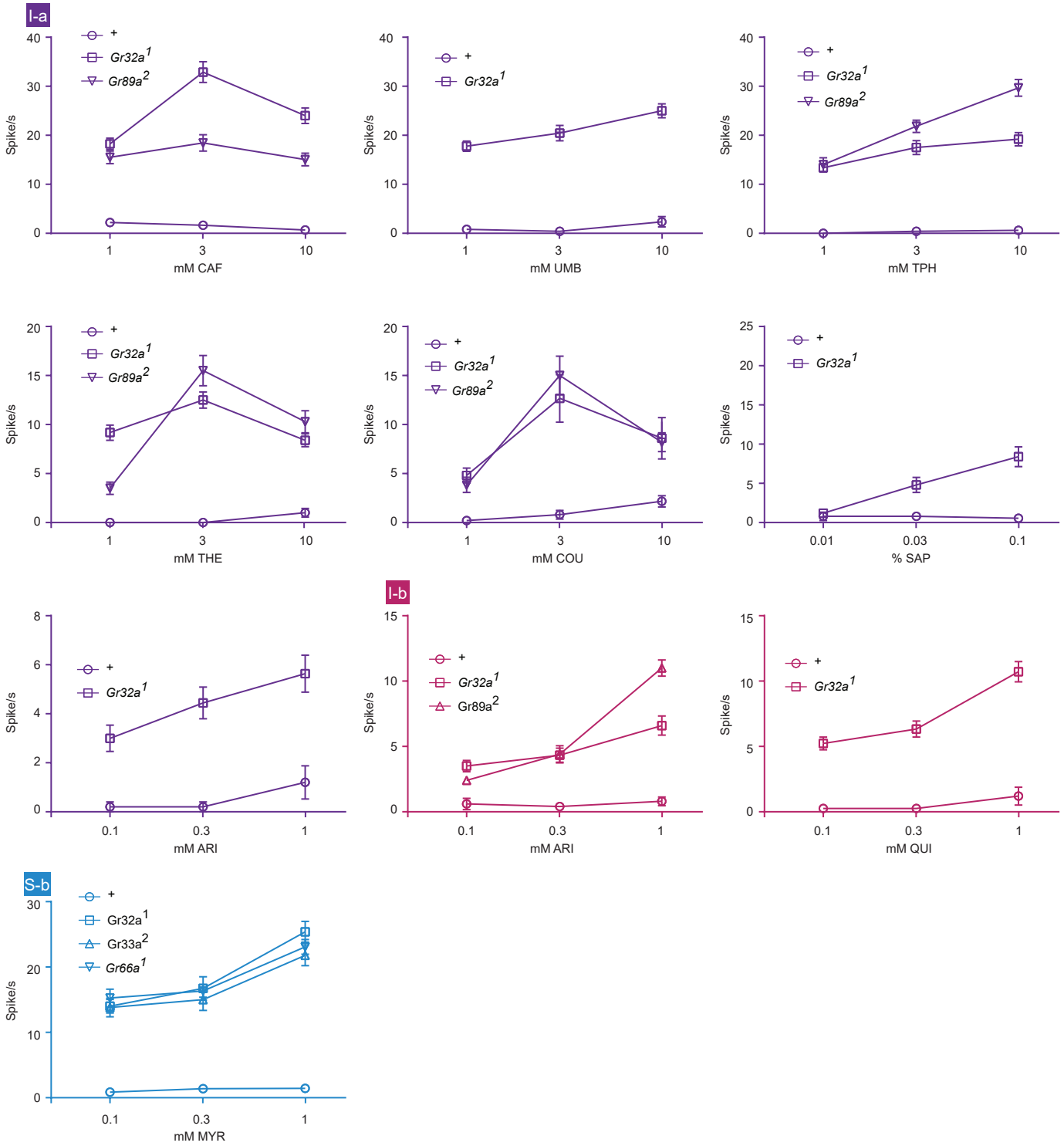
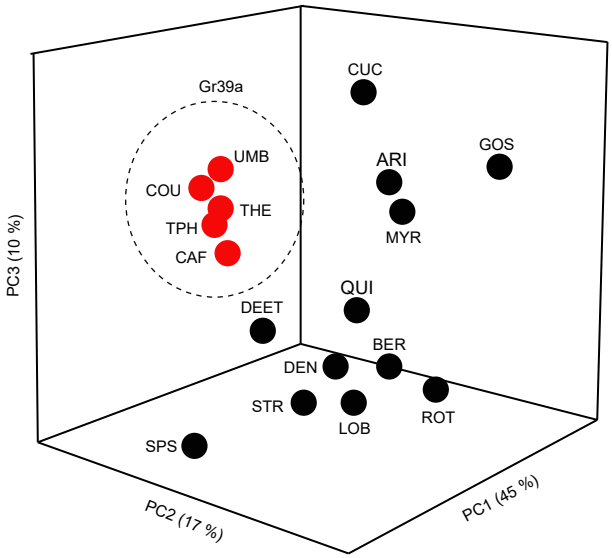


Figure S2. Novel responses over a range of concentrations. Related to Figure 3. Purple graphs are from I-a; red graphs are from I-b; the blue graph is from S-b. n = 6-22.

A



B

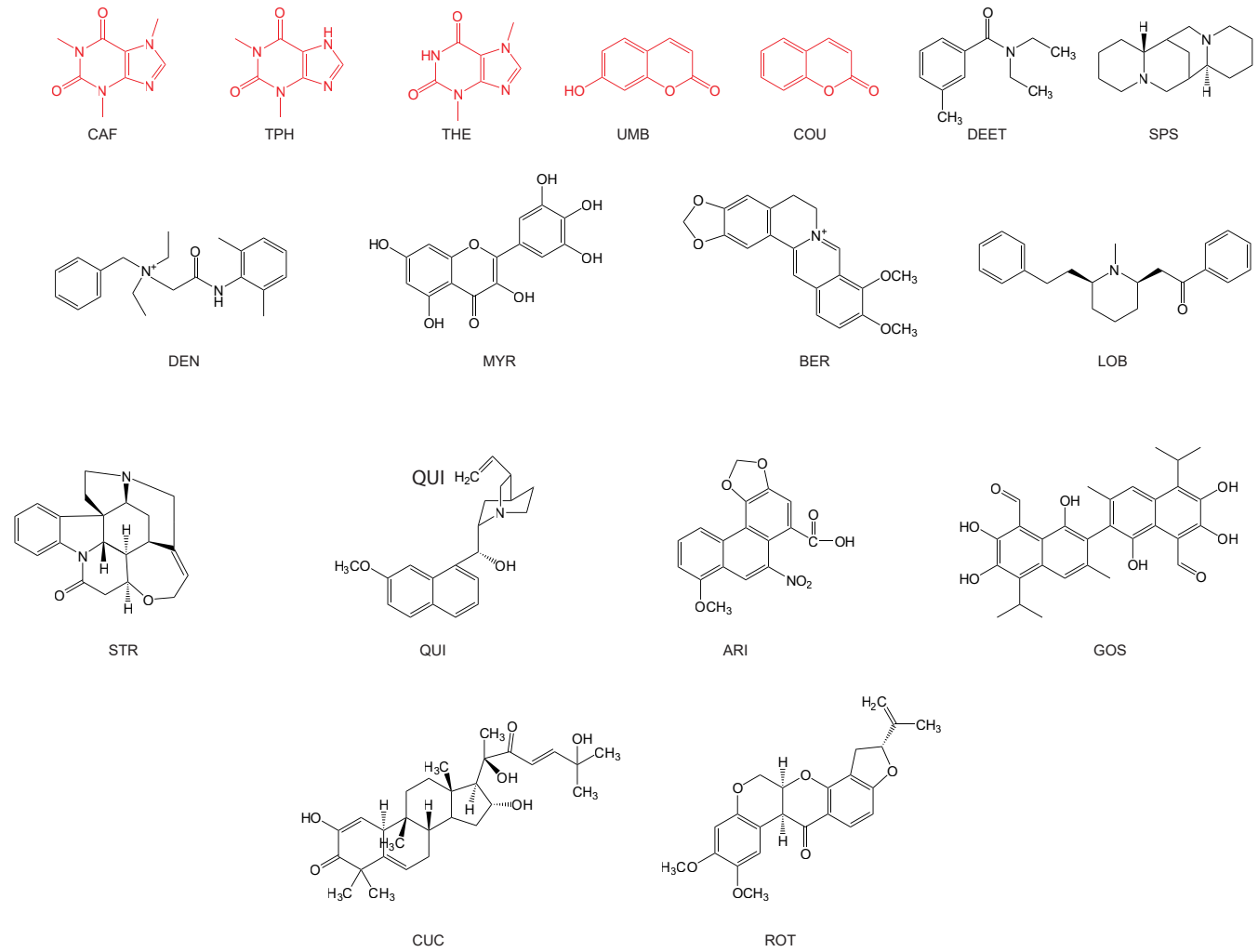


Figure S3. The five compounds that depend on Gr39a.a all cluster together in a physicochemical tastant space. Related to Figure 4. (A) A 32-dimensional tastant space visualized by a principle component analysis. CAF, COU, THE, TPH, and UMB, depicted in red, cluster together. Four tastants are not included because the physicochemical parameters needed to map them are not available. (B) Structures of CAF, COU, THE, TPH, and UMB, containing exactly two fused rings, are depicted in red. The other mapped tastants are depicted in black.

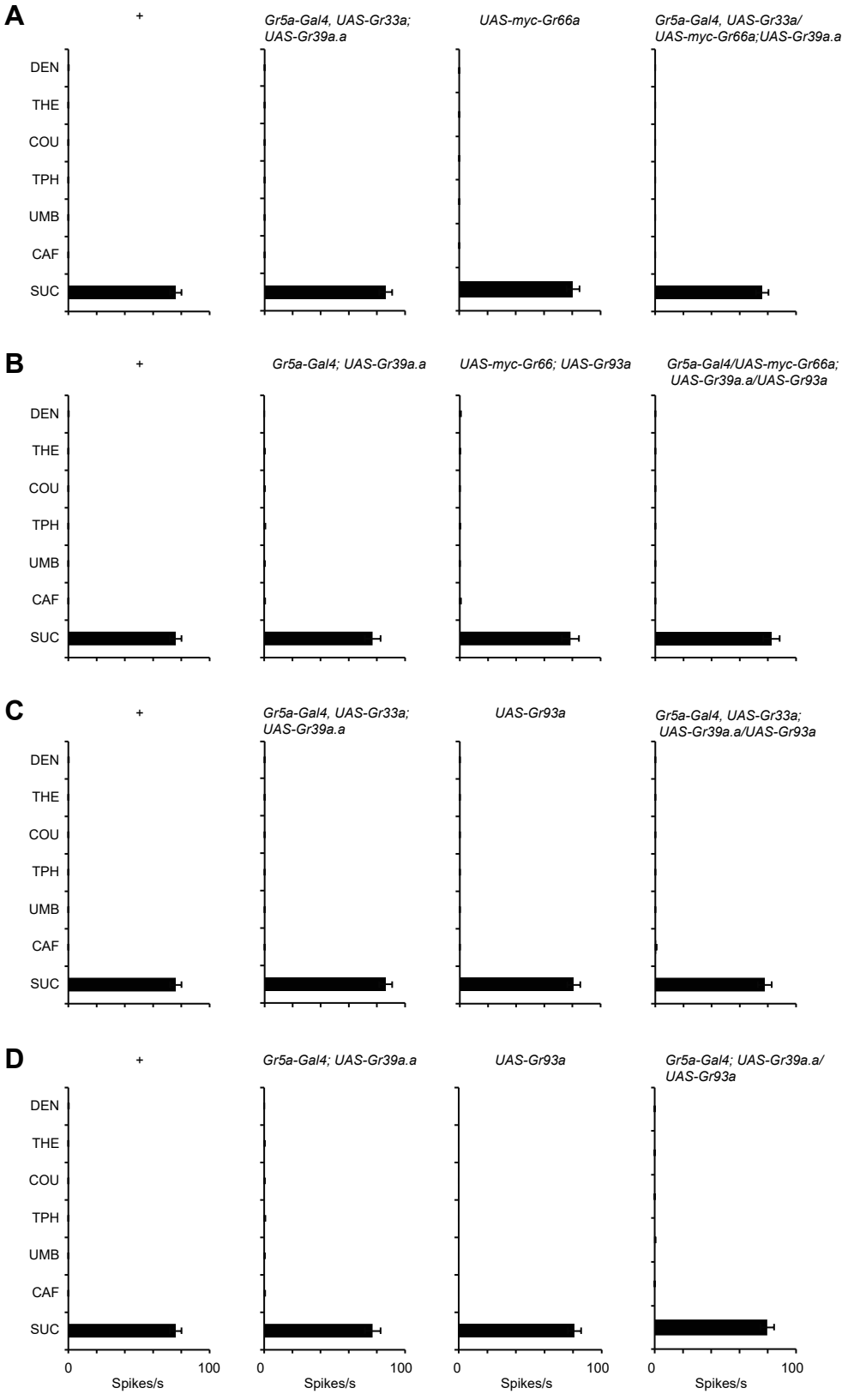


Figure S4. Coexpression of Grs in sugar neurons. Related to Figure 5. Neither the combination of Gr33a, Gr66a, and Gr39a.a. (A), nor the combination of Gr66a, Gr39a.a and Gr93a (B), nor the combination of Gr33a, Gr39a.a, and Gr93a (C) are sufficient to confer response to the indicated bitter compounds in a sugar-sensing neuron. Neither is Gr39a.a and Gr93a, nor Gr39a.a alone sufficient (D). n = 10-13.

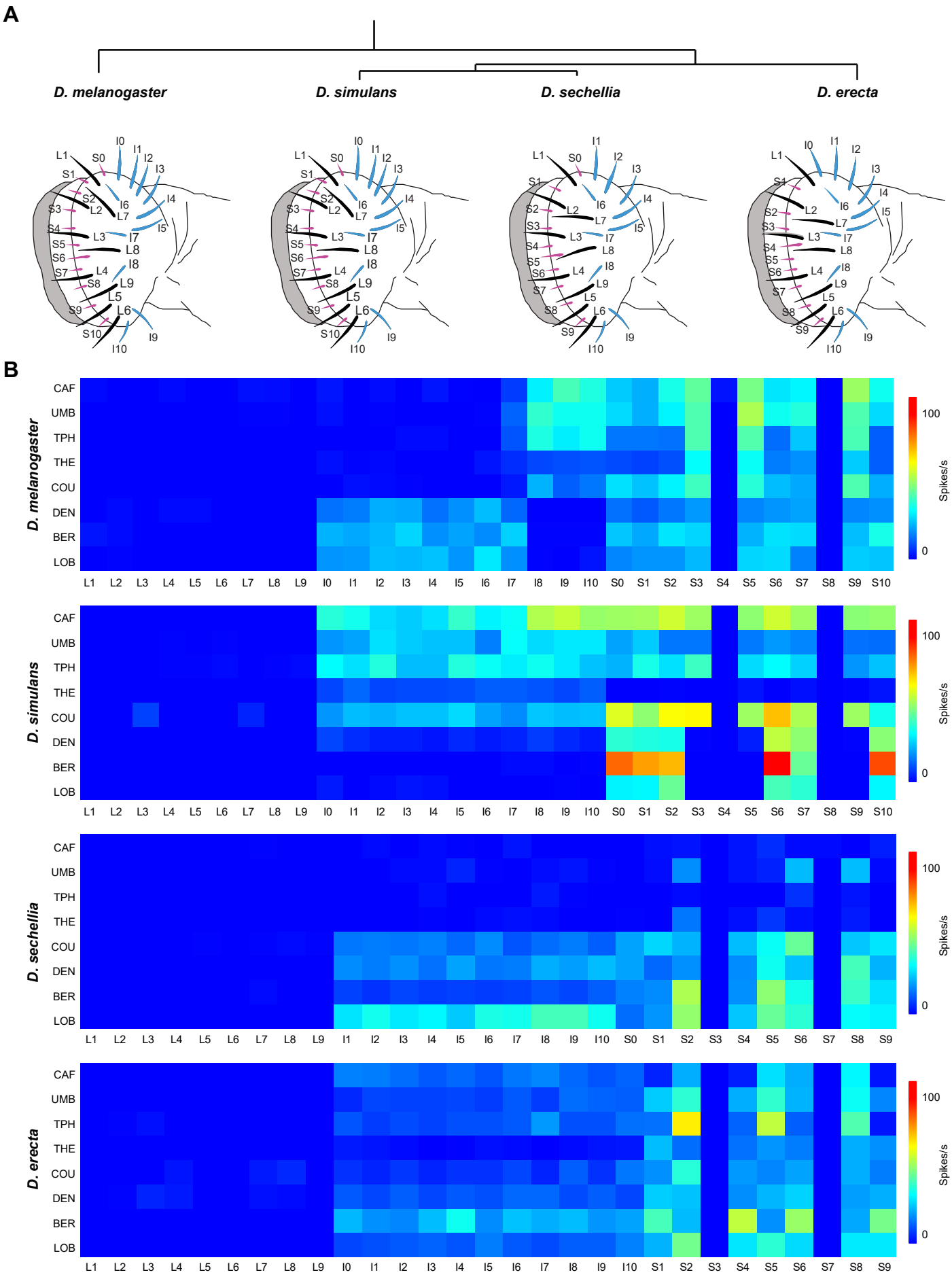


Figure S5. Anatomy and coding of bitter taste in labella of four Drosophila species. Related to Figure 6.
(A) Phylogenetic relationship and organization of labellar sensilla in four species. The D. melanogaster used here was Canton-S, without the w mutation contained within the genetic background control used in other experiments.
(B) Heat map of physiological responses to bitter compounds in all labellar sensilla infour species. n=3-10.

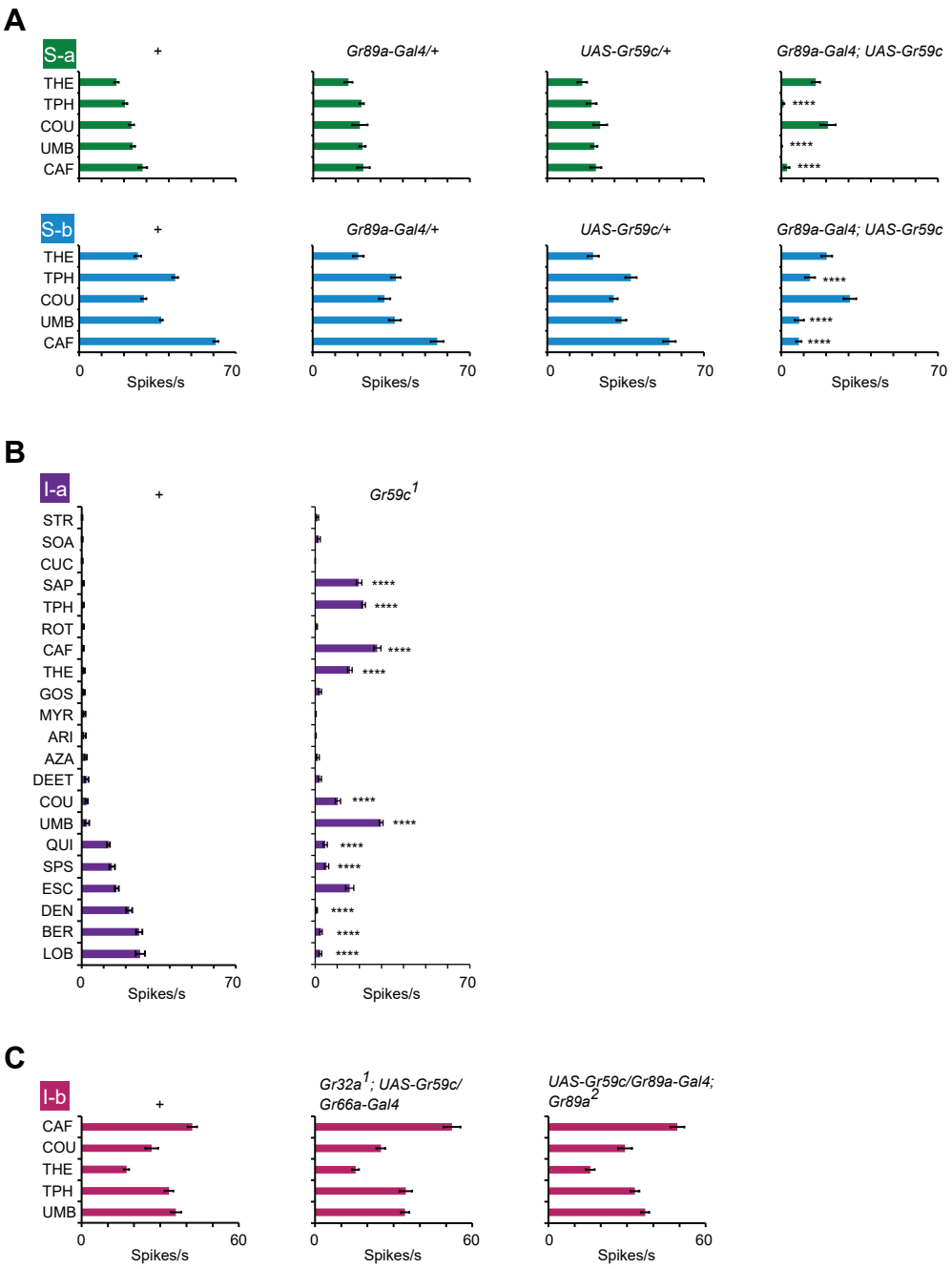


Figure S6. Regulation of the identity of I-a. Related to Figure 7. (A) Responses of S sensilla that ectopically express Gr59c. The control responses ("+") are from Figure 2. One-way ANOVA followed by Dunnett's multiple comparison test. n=10. (B) Responses of I-a in Gr59c- to the full tastant panel. Data for the control are from Figure 2. Mann-Whitney test, n=10-23. (C) Expression of Gr59c in I-b did not suppress response to these bitter compounds in Gr32a or Gr89a mutants. The control panel "+" is from Figure 2. One-way ANOVA followed by Dunnett's multiple comparison test. n=10.

A

Target	Name	Sequence (5'-3')
Gr32a	Gr32agRNAF	TATATAGGAAAGATATCCGGGTGAACTTCGGCCATGTCCCCGAACACTTGTTTTAGAGCTAGAAATAGCAAG
	Gr32agRNAR	ATTTTAACTTGCTATTTCTAGCTCTAAAACTCACAACATACTTGGTAATCGACGTTAAATTGAAAATAGGTC
Gr33a	Gr33agRNAF	TATATAGGAAAGATATCCGGGTGAACTTCGTTCACAGAGAAAAGTTATAGTTTTAGAGCTAGAAATAGCAAG
	Gr33agRNAR	ATTTTAACTTGCTATTTCTAGCTCTAAAACACATAGTGCTTCGACTATGCGACGTTAAATTGAAAATAGGTC
Gr39a	Gr39agRNAF	TATATAGGAAAGATATCCGGGTGAACTTCGGCCGCTCTGTTGGGAGCACGTTTTAGAGCTAGAAATAGCAAG
	Gr39agRNAR	ATTTTAACTTGCTATTTCTAGCTCTAAAACCATTGTAGCCCTGGTGCTCCGACGTTAAATTGAAAATAGGTC
Gr59c	Gr59cgRNAF	TATATAGGAAAGATATCCGGGTGAACTTCGATCGTGTGCCAGTACTACTGTTTTAGAGCTAGAAATAGCAAG
	Gr59cgRNAR	ATTTTAACTTGCTATTTCTAGCTCTAAAACGTAACCGGCATGAATTCTACGACGTTAAATTGAAAATAGGTC
Gr66a	Gr66agRNAF	TATATAGGAAAGATATCCGGGTGAACTTCGGCTTGTTCCTGACCTATATGTTTTAGAGCTAGAAATAGCAAG
	Gr66agRNAR	ATTTTAACTTGCTATTTCTAGCTCTAAAACCGACCATGACACCGGCGGTCGACGTTAAATTGAAAATAGGTC
Gr89a	Gr89agRNAF	TATATAGGAAAGATATCCGGGTGAACTTCGTTTCGGACTTCCGAGCCAAGTTTTAGAGCTAGAAATAGCAAG
	Gr89agRNAR	ATTTTAACTTGCTATTTCTAGCTCTAAAACTGGCCTGAGAAAATATCAACGACGTTAAATTGAAAATAGGTC

B

Target	Name	Sequence (5'-3')
Gr32a	Gr32aH1F	cgaaagactgggcctttcgcTGAAAATGTTTCCAATTATCCATTAAAACCTTTAATAGTTTAACTAATAAAAC
	Gr32aH1R	attagcccggTGTTCGGGGACATGGCCAAC
Gr32a	Gr32aH2F	ccttctgcagCAACATACTTGGTAATCTTGATTC
	Gr32aH2R	attgacggaagagcctcgagAGAAAAGCATTTGAATTGATAATTTG
Gr33a	Gr33aH1F	cgaaagactgggcctttcgcTCCCTTTCCAACCCGCGC
	Gr33aH1R	attagcccggAACTTTTCTCTGTGAACTGCCACTAGTTTG
Gr39a	Gr39aH1F	cgaaagactgggcctttcgcAGTCGAGTTCCCCGACTTTTTC
	Gr39aH1R	attagcccggCTCCCAACAGAGCGGCCA
Gr39a	Gr39aH2F	ccttctgcagTGTAGCCCTGGTGCTCCTG
	Gr39aH2R	attgacggaagagcctcgagATGTTCACGGTTACATTACATTACAGATCTG
Gr59c	Gr59cH1F	cgaaagactgggcctttcgcGTCGAGTTTGGCAGCAAG
	Gr59cH1R	attagcccggACCGGCATGAATTCTACG
Gr59c	Gr59cH2F	ccttctgcagAGTACTGGCACACGATCATG
	Gr59cH2R	attgacggaagagcctcgagGTTTCAGCCAGGTCTGGATC
Gr66a	Gr66aH1F	cgaaagactgggcctttcgcCAAAGGCACATAAACTTCAAAAGACACATTTAG
	Gr66aH1R	attagcccggCCATGACACCGGCGGTCT
Gr66a	Gr66aH2F	ccttctgcagTAGGTCAGGAACAAGCCAATC
	Gr66aH2R	attgacggaagagcctcgagTTGCAAAAGCTTCCAGTATAAAATTC
Gr89a	Gr89aH1F	cgaaagactgggcctttcgcCATAATCTGCAGTTTGGTGGC
	Gr89aH1R	attagcccggCCATGGCTTCGACTCCATTTC
Gr89a	Gr89aH2F	ccttctgcagGCTCGGAAGTCCGAAACG
	Gr89aH2R	attgacggaagagcctcgagGCTGTGATGACCAGGGAAC

C

Target	Name	Sequence (5'-3')
Gr32a	Gr32aF	TTTCGAGGACATTCGCACCA
	Gr32aR	ACAGAACTTGCAGTACATCCCA
Gr33a	Gr33aF	CACTGAATCGCCAGCAATCG
	Gr33aR	TCATGGTGGTGAAGCTCCAAA
Gr39a	Gr39aF	CGGCCAACCTGCTACTTACA
	Gr39aR	GACCAGAGATCAGATCGCCC
Gr59c	Gr59cF	TGGCCAGTTGCAGTTGGAAG
	Gr59cR	TGCAGGTGATTGGGCTCTAC
Gr66a	Gr66aF	GTGGTGACGAAATCACGCAG
	Gr66aR	CGCGTTACGAAACCAGGGTA
Gr89a	Gr89aF	TCAACGAAAATTAGTCCCCTTACA
	Gr89aR	CCAGCGATGGATGACCTTGA

Table S1. Oligonucleotides. Related to Figure 1. (A) Oligonucleotides used to generate gRNA vectors. Black letters indicate vector sequence; red letters indicate genomic DNA sequence. (B) Oligonucleotides used to generate donor vectors. Small letters indicate vector sequence; capital letters indicate insert sequence. (C) Oligonucleotides used to confirm Gr deletions.

l-a	+	*Gr32a*[1]	*Gr33a*[2]	*Gr39a*[1]	*Gr66a*[1]	*Gr89a*[2]	*Gr93a*[3]
TCC	0.4 ± 0.3	1.3 ± 0.5	0.0 ± 0.0	0.4 ± 0.3	0.0 ± 0.0	0.2 ± 0.2	0.0 ± 0.0
STR	0.2 ± 0.2	0.2 ± 0.2	1.2 ± 0.5	0.2 ± 0.2	0.2 ± 0.2	1.2 ± 0.5	21.3 ± 1.4
SOA	0.2 ± 0.2	0.8 ± 0.3	0.4 ± 0.3	1.0 ± 0.6	0.2 ± 0.2	0.4 ± 0.3	22.0 ± 1.1
CUC	0.2 ± 0.2	0.0 ± 0.0	0.0 ± 0.0	0.6 ± 0.3	0.0 ± 0.0	0.0 ± 0.0	18.4 ± 1.2
SAP	0.5 ± 0.4	8.4 ± 1.3	0.7 ± 0.5	0.8 ± 0.4	1.0 ± 0.5	1.6 ± 0.5	15.7 ± 2.2
TPH	0.6 ± 0.4	19.2 ± 1.3	1.0 ± 0.6	0.2 ± 0.2	1.0 ± 0.4	29.7 ± 1.7	16.0 ± 1.6
ROT	0.6 ± 0.4	0.6 ± 0.4	1.0 ± 0.5	0.0 ± 0.0	0.0 ± 0.0	1.0 ± 0.5	14.0 ± 1.7
CAF	0.6 ± 0.4	24 ± 1.6	1.0 ± 0.5	1.8 ± 0.6	0.2 ± 0.2	15.1 ± 1.3	0.2 ± 0.2
THE	1.0 ± 0.4	8.4 ± 0.7	0.5 ± 0.4	0.4 ± 0.2	0.9 ± 0.5	10.3 ± 1.1	1.5 ± 0.4
GOS	1.0 ± 0.4	1.0 ± 0.4	0.8 ± 0.3	0.2 ± 0.2	1.0 ± 0.5	0.4 ± 0.3	1.2 ± 0.8
MYR	1.2 ± 0.5	2.2 ± 0.7	2.5 ± 0.5	0.6 ± 0.4	0.4 ± 0.3	0.4 ± 0.3	0.4 ± 0.4
ARI	1.2 ± 0.7	5.6 ± 0.8	0.0 ± 0.0	0.2 ± 0.2	0.8 ± 0.4	2.2 ± 1.1	0.2 ± 0.2
AZA	1.8 ± 0.5	0.2± 0.2	2.8 ± 0.7	0.9 ± 0.5	2.2 ± 0.7	1.0 ± 0.5	0.3 ± 0.3
DEET	2.2 ± 0.8	3.6 ± 1.0	3.3 ± 0.8	3.4 ± 0.6	1.0 ± 0.4	3.3 ± 0.8	0.0 ± 0.0
COU	2.2 ± 0.6	8.6 ± 2.1	0.2 ± 0.2	3.4 ± 0.5	0.4 ± 0.4	8.2 ± 1.0	0.0 ± 0.0
UMB	2.4 ± 1.0	25.0 ± 1.4	1.1 ± 0.6	2.4 ± 0.9	1.1 ± 0.6	6.8 ± 0.9	0.0 ± 0.0
QUI	12.1 ± 0.7	5.2 ± 0.8	2.8 ± 0.6	10.6 ± 0.6	3.4 ± 0.4	12.0 ± 1.2	0.3 ± 0.3
SPS	13.8 ± 1.2	5.8 ± 1.3	0.2 ± 0.2	16.6 ± 1.1	1.6 ± 0.7	12.0 ± 1.1	0.0 ± 0.0
ESC	15.9 ± 0.9	1.5 ± 0.7	0.9 ± 0.3	17.4 ± 1.4	0.2 ± 0.1	18.9 ± 1.5	2.3 ± 1.0
DEN	21.6 ± 1.4	1.6 ± 0.4	1.8 ± 0.9	24.3 ± 1.6	1.2 ± 0.5	24.9 ± 1.8	0.0 ± 0.0
BER	24.6 ± 1.8	1.5 ± 0.6	1.8 ± 0.7	24.2 ± 1.8	1.8 ± 0.6	22.9 ± 1.3	0.0 ± 0.0
LOB	26.1 ± 1.4	1.3 ± 0.4	0.3 ± 0.1	35.3 ± 1.4	0.7 ± 0.3	26.5 ± 1.2	0.8 ± 0.5

l-b	+	*Gr32a*[1]	*Gr33a*[2]	*Gr39a*[1]	*Gr66a*[1]	*Gr89a*[2]	*Gr93a*[3]
TCC	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
STR	0.2 ± 0.2	1.2 ± 0.7	0.2 ± 0.2	0.2 ± 0.2	0.2 ± 0.2	0.4 ± 0.3	0.8 ± 0.3
DEET	0.2 ± 0.2	1.2 ± 0.6	0.4 ± 0.2	0.4 ± 0.4	0.4 ± 0.4	0.4 ± 0.4	0.2 ± 0.2
ROT	0.4 ± 0.4	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	1.0 ± 0.4	0.0 ± 0.0	0.2 ± 0.2
CUC	0.4 ± 0.4	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	1.0 ± 0.4	5.5 ± 1.2
SOA	0.6 ± 0.3	1.4 ± 0.7	0.4 ± 0.3	1.4 ± 0.3	0.2 ± 0.2	0.2 ± 0.2	14.9 ± 1.8
GOS	0.8 ± 0.8	0.6 ± 0.3	0.8 ± 0.3	0.2 ± 0.2	0.2 ± 0.2	1.8 ± 0.6	2.6 ± 0.9
ARI	0.8 ± 0.4	6.6 ± 0.7	2.0 ± 0.5	2.0 ± 0.7	0.0 ± 0.0	11.0 ± 0.6	15.3 ± 2.0
QUI	1.2 ± 0.7	10.7 ± 0.8	0.4 ± 0.3	0.6 ± 0.3	1.0 ± 0.3	2.7 ± 0.9	2.9 ± 0.6
DEN	1.2 ± 0.4	2.5 ± 0.5	0.2 ± 0.2	1.0 ± 0.3	0.4 ± 0.2	0.6 ± 0.4	1.8 ± 1.0
SPS	1.6 ± 0.6	0.4 ± 0.4	1.2 ± 0.7	0.4 ± 0.4	0.2 ± 0.2	0.2 ± 0.2	0.0 ± 0.0
AZA	2.4 ± 0.7	0.8 ± 0.4	2.8 ± 1.0	1.8 ± 0.6	4.0 ± 1.0	1.6 ± 0.5	0.0 ± 0.0
MYR	2.7 ± 0.8	1.6 ± 0.7	1.0 ± 0.6	2.0 ± 0.5	1.2 ± 0.8	1.0 ± 0.5	0.0 ± 0.0
LOB	3.7 ± 0.7	11.8 ± 0.6	4.7 ± 0.8	4.4 ± 0.7	3.6 ± 0.7	3.7 ± 0.4	1.4 ± 0.8
BER	5.1 ± 0.8	9.4 ± 0.7	4.4 ± 1.7	4.7 ± 0.8	2.6 ± 0.5	6.4 ± 0.9	0.0 ± 0.0
ESC	16.2 ± 1.2	1.4 ± 0.6	0.0 ± 0.0	16.6 ± 1.1	0.0 ± 0.0	16.2 ± 1.8	0.6 ± 0.4
THE	17.1 ± 1.0	17.5 ± 0.9	0.3 ± 0.3	0.2 ± 0.2	0.6 ± 0.3	16.0 ± 0.9	0.0 ± 0.0
SAP	18.7 ± 1.3	16.3 ± 2.0	6.2 ± 0.8	15.3 ± 1.2	3.5 ± 0.4	14.0 ± 0.8	0.4 ± 0.4
COU	26.7 ± 2.5	20.9 ± 2.5	0.2 ± 0.2	4.2 ± 0.7	0.2 ± 0.2	24.4 ± 1.8	1.6 ± 0.3
TPH	33.3 ± 1.7	30.6 ± 1.3	1.0 ± 0.3	1.6 ± 0.6	2.2 ± 0.6	36.8 ± 1.2	0.0 ± 0.0
UMB	36.0 ± 2.0	31.2 ± 2.5	2.0 ± 0.8	1.2 ± 0.6	2.8 ± 0.7	33.9 ± 1.2	0.4 ± 0.4
CAF	42.2 ± 1.8	43.8 ± 1.8	0.8 ± 0.4	1.9 ± 0.7	0.2 ± 0.2	46.4 ± 2.0	0.4 ± 0.4

S-a	+	*Gr32a*[1]	*Gr33a*[2]	*Gr39a*[1]	*Gr66a*[1]	*Gr89a*[2]	*Gr93a*[3]
TCC	1.4 ± 0.4	1.2 ± 0.9	0.0 ± 0.0	0.8 ± 0.4	0.0 ± 0.0	1.4 ± 0.5	0.8 ± 0.8
MYR	2.8 ± 1.0	4.7 ± 1.5	3.6 ± 1.4	2.1 ± 0.6	2.9 ± 0.5	1.3 ± 0.5	34.7 ± 2.5
ESC	4.0 ± 0.8	6.2 ± 0.7	4.9 ± 1.5	2.5 ± 0.9	5.5 ± 1.0	2.6 ± 0.8	27.3 ± 2.5
ROT	4.0 ± 0.7	4.8 ± 0.7	4.0 ± 0.5	4.3 ± 0.6	4.8 ± 0.8	5.6 ± 0.7	3.3 ± 0.4
GOS	4.4 ± 0.7	2.7 ± 0.5	10.7 ± 2.2	6.6 ± 1.1	5.8 ± 1.1	5.6 ± 1.2	33.6 ± 2.8
ARI	13.8 ± 1.2	16.7 ± 1.2	15 ± 1.9	14.6 ± 1.1	16.0 ± 1.7	16.0 ± 1.1	30.7 ± 3.6
DEET	14.5 ± 0.6	0.5 ± 0.4	0.0 ± 0.0	17.0 ± 1.8	1.0 ± 0.4	13.8 ± 0.8	26.2 ± 1.9
SAP	15.8 ± 1.6	20.7 ± 3.3	21.1 ± 1.4	22.1 ± 1.4	17.5 ± 1.7	18.4 ± 1.4	28.2 ± 2.0
THE	16.6 ± 1.0	20.2 ± 1.0	17.5 ± 1.0	19.2 ± 1.2	19.8 ± 1.2	12.2 ± 1.2	29.7 ± 2.4
QUI	19.4 ± 0.7	9.5 ± 1.6	5.8 ± 0.8	22.8 ± 1.3	19.2 ± 1.7	17.8 ± 1.1	29.8 ± 4.2
TPH	20.5 ± 1.0	22.6 ± 1.9	4.6 ± 1.2	9.2 ± 1.0	3.4 ± 0.7	23.8 ± 2.4	21.0 ± 2.1
CUC	21.3 ± 1.8	2.1 ± 0.9	1.9 ± 0.7	30.2 ± 1.4	4.7 ± 1.2	18.8 ± 1.5	20.0 ± 1.7
SOA	22.4 ± 1.0	1.1 ± 0.4	8.3 ± 1.4	26.0 ± 0.9	4.8 ± 1.1	20.0 ± 0.7	4.0 ± 1.8
COU	23.4 ± 1.2	20.2 ± 1.6	6.8 ± 1.5	22.2 ± 2.7	2.4 ± 0.5	17.8 ± 1.1	18.8 ± 1.7
STR	23.7 ± 1.0	0.4 ± 0.3	0.3 ± 0.2	41.1 ± 1.7	1.7 ± 0.9	30.9 ± 0.8	19.4 ± 2.1
UMB	24.0 ± 1.0	27.8 ± 1.7	12.4 ± 2.3	17.0 ± 1.5	3.2 ± 0.8	19.1 ± 1.1	19.3 ± 2.0
DEN	24.3 ± 0.9	0.6 ± 0.2	1.3 ± 0.5	35.3 ± 1.4	2.3 ± 0.6	24.1 ± 1.0	13.2 ± 1.0
SPS	26.7 ± 1.1	4.9 ± 1.5	12.3 ± 1.1	50.6 ± 3.1	15.4 ± 1.1	26.9 ± 1.0	13.3 ± 0.7
BER	26.9 ± 1.1	1.1 ± 0.4	0.5 ± 0.3	33.9 ± 1.9	6.2 ± 1.0	26.0 ± 1.7	6.0 ± 1.7
CAF	28.4 ± 1.9	36.9 ± 1.6	0.5 ± 0.3	2.3 ± 0.5	0.4 ± 0.3	27.9 ± 2.2	5.5 ± 1.7
AZA	29.9 ± 1.0	3.3 ± 0.6	33.6 ± 2.5	37.0 ± 1.9	15.0 ± 1.5	25.9 ± 2.2	5.0 ± 1.1
LOB	40.5 ± 1.5	2.5 ± 0.8	0.1 ± 0.1	38.0 ± 1.5	22.1 ± 1.3	34.4 ± 1.1	1.1 ± 0.6

S-b	+	*Gr32a*[1]	*Gr33a*[2]	*Gr39a*[1]	*Gr66a*[1]	*Gr89a*[2]	*Gr93a*[3]
TCC	3.0 ± 0.9	5.3 ± 1.5	5.2 ± 1.3	1.4 ± 0.6	0.0 ± 0.0	4.0 ± 0.6	4.4 ± 1.6
MYR	1.4 ± 0.4	25.4 ± 1.6	21.8 ± 1.6	3.0 ± 1.2	23.1 ± 1.1	2.2 ± 0.7	7.8 ± 1.8
GOS	5.8 ± 1.1	5.2 ± 0.9	14.8 ± 1.3	5.4 ± 1.2	5.7 ± 0.8	8.5 ± 1.4	0.7 ± 0.5
ROT	5.8 ± 0.6	6.0 ± 0.7	6.2 ± 0.8	5.3 ± 0.7	5.5 ± 0.5	4.7 ± 0.6	37.2 ± 3.3
ESC	13.5 ± 1.0	16.8 ± 1.7	17.9 ± 1.3	14.2 ± 1.3	15.0 ± 1.0	13.5 ± 1.1	4.5 ± 0.8
DEET	14.9 ± 1.1	0.8 ± 0.3	1.8 ± 0.7	23.1 ± 1.4	0.7 ± 0.3	15.0 ± 1.2	36.5 ± 2.9
QUI	15.3 ± 1.2	11.1 ± 0.7	13.7 ± 0.9	28.3 ± 1.8	4.2 ± 0.6	14.0 ± 1.3	34.7 ± 3.7
ARI	16.4 ± 0.9	21.2 ± 1.4	20.0 ± 1.1	17.1 ± 1.2	19.3 ± 1.4	19.5 ± 1.4	33.5 ± 2.6
BER	21.0 ± 1.2	8.3 ± 0.7	7.6 ± 1.0	36.8 ± 2.3	3.3 ± 0.6	20.8 ± 1.2	29.7 ± 3.8
DEN	21.5 ± 0.9	1.1 ± 0.3	0.8 ± 0.8	40.0 ± 1.8	0.3 ± 0.2	28.8 ± 1.1	24.8 ± 0.6
STR	22.5 ± 1.8	4.1 ± 1.1	2.6 ± 1.3	38.3 ± 1.6	0.6 ± 0.3	29.6 ± 1.7	29.1 ± 2.2
SOA	23.5 ± 1.3	8.0 ± 0.7	19.6 ± 0.7	22.1 ± 1.0	1.5 ± 0.5	22.7 ± 1.2	24.7 ± 2.2
SAP	23.6 ± 1.8	28.6 ± 1.0	28.5 ± 1.5	27.0 ± 1.5	28.7 ± 1.1	22.9 ± 1.3	26.0 ± 2.2
CUC	25.6 ± 2.4	3.1 ± 0.7	7.2 ± 1.9	36.8 ± 1.3	3.8 ± 2.1	21.4 ± 1.3	25.4 ± 3.2
THE	26.2 ± 1.4	31.5 ± 2.1	31.5 ± 1.3	25.0 ± 1.3	31.8 ± 1.6	30.2 ± 3.0	23.6 ± 1.8
COU	28.9 ± 1.2	30.3 ± 2.1	24.3 ± 2.1	23.8 ± 1.4	3.2 ± 1.3	29.2 ± 2.0	15.4 ± 1.8
SPS	33.3 ± 1.4	29.7 ± 1.1	24.5 ± 1.3	57.5 ± 3.1	17.4 ± 1.6	34.2 ± 1.6	13.7 ± 0.8
AZA	33.6 ± 1.1	6.6 ± 1.8	37.6 ± 1.7	41.4 ± 2.8	4.4 ± 1.7	32.0 ± 2.2	16.7 ± 1.6
UMB	36.7 ± 0.7	40.8 ± 0.7	22.6 ± 1.2	23.1 ± 1.6	4.2 ± 0.8	36.9 ± 2.8	14.7 ± 1.3
LOB	38.8 ± 1.6	5.5 ± 0.8	1.7 ± 0.5	41.2 ± 1.3	0.9 ± 0.3	39.4 ± 0.9	6.5 ± 1.0
TPH	42.9 ± 1.3	44.7 ± 1.7	30.6 ± 1.0	16.6 ± 1.6	18.6 ± 1.3	47.8 ± 2.0	6.3 ± 1.8
CAF	61.1 ± 1.2	58.7 ± 2.2	22.2 ± 1.7	7.0 ± 1.3	12.4 ± 1.2	59.4 ± 1.7	2.4 ± 1.2

Table S2. Responses in spikes/s of bitter neuron classes to tastants. Related to Figure 2. All errors are SEM. n>10 for 98% of the 587 genotype-tastant-sensillum class combinations; 7<n<10 for the remaining 2%.

A

	L1	L2	L3	L4	L5	L6	L7	L8	L9	I0	I1	I2	I3	I4	I5	I6	I7	I8	I9	I10	S0	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10
TCC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5	0	8	0	1	0	9	0
CAF	1	0	0	1	0	0	2	2	0	3	0	2	0	3	0	0	8	32	44	38	27	24	37	47	3	50	31	33	0	55	36
UMB	0	0	0	0	0	0	0	0	0	2	0	1	0	0	0	1	13	41	36	36	29	24	33	45	0	57	36	39	0	45	30
TPH	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	11	38	32	36	16	16	15	45	0	45	15	27	0	44	13
THE	0	0	0	0	0	0	0	0	0	2	1	1	0	0	0	3	6	10	11	11	10	9	11	34	0	35	17	19	0	27	13
COU	0	0	0	0	0	0	0	0	0	0	2	1	1	0	0	0	3	24	13	16	30	26	33	43	0	40	25	23	0	45	23
DEN	0	1	0	1	1	0	0	0	0	15	17	23	23	15	19	25	14	0	0	0	15	12	16	21	0	18	20	22	0	18	19
BER	3	1	0	0	0	0	0	0	0	24	23	25	29	19	22	19	28	1	1	1	27	23	31	29	0	24	31	30	0	26	37
LOB	0	1	0	0	0	0	0	0	0	20	21	25	25	26	20	31	19	1	0	3	18	20	20	25	0	29	29	18	0	28	27

B

	L1	L2	L3	L4	L5	L6	L7	L8	L9	I0	I1	I2	I3	I4	I5	I6	I7	I8	I9	I10	S0	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10
TCC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
CAF	0	0	0	0	0	0	0	0	0	39	37	29	27	30	41	33	35	58	61	55	55	56	62	55	0	53	62	55	0	53	54
UMB	0	0	0	0	0	1	0	0	0	20	22	30	27	26	26	17	35	29	31	31	22	27	16	16	0	17	21	18	0	15	15
TPH	0	0	0	0	1	1	0	1	1	34	30	39	25	25	39	35	32	36	31	26	24	37	30	42	0	29	34	28	0	20	26
THE	0	0	0	0	0	0	0	0	0	9	14	9	10	10	11	13	13	11	10	13	0	0	1	0	0	3	0	2	0	1	3
COU	0	0	9	9	0	0	5	0	0	20	25	24	26	26	29	22	19	27	25	26	64	53	68	69	0	55	77	57	0	55	37
DEN	0	0	0	0	0	0	0	0	0	9	6	4	4	3	5	3	5	8	5	3	40	39	37	1	0	4	60	53	0	1	53
BER	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	89	81	78	0	0	0	103	48	0	0	93
LOB	0	0	0	0	0	0	0	0	0	3	0	1	3	2	0	0	0	0	1	0	33	33	48	0	0	0	44	40	0	0	33

C

	L1	L2	L3	L4	L5	L6	L7	L8	L9	I1	I2	I3	I4	I5	I6	I7	I8	I9	I10	S0	S1	S2	S3	S4	S5	S6	S7	S8	S9
TCC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CAF	0	0	0	0	0	0	1	0	0	0	1	0	1	1	0	3	0	0	0	0	2	3	0	3	6	1	1	0	4
UMB	0	0	0	0	0	0	0	0	0	0	0	1	1	5	1	0	2	3	1	0	2	19	0	3	4	25	0	25	1
TPH	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	3	1	0	0	0	1	0	0	0	7	0	3	0
THE	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	2	1	0	0	1	0	16	0	2	7	2	0	4	0
COU	0	0	0	0	1	0	1	1	1	16	17	16	17	14	19	11	15	17	13	22	29	24	0	25	35	48	0	27	31
DEN	0	0	0	0	0	0	0	0	0	19	17	19	15	22	16	17	23	21	25	22	14	19	0	19	36	26	0	43	24
BER	0	0	0	0	0	0	1	0	0	9	7	9	8	9	8	9	11	9	13	17	19	57	0	19	53	37	0	42	30
LOB	0	0	0	0	0	0	0	0	0	31	37	31	33	27	38	37	43	43	36	15	20	54	0	27	48	40	0	35	33

D

	L1	L2	L3	L4	L5	L6	L7	L8	L9	I0	I1	I2	I3	I4	I5	I6	I7	I8	I9	I10	S1	S2	S3	S4	S5	S6	S7	S8	S9
TCC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	9	0	7	6	6	0	1	5
CAF	0	0	0	0	0	0	0	0	0	17	17	15	12	14	11	16	18	14	11	13	5	23	0	4	30	23	0	33	3
UMB	0	0	0	0	0	0	0	0	0	5	9	9	9	9	8	12	8	15	13	13	27	40	0	23	41	24	0	36	18
TPH	0	1	2	0	0	0	0	0	0	11	8	10	9	11	11	12	21	11	11	15	15	71	0	13	60	13	0	45	3
THE	0	0	0	0	0	0	0	0	0	3	3	1	0	1	2	1	0	1	3	3	25	15	0	15	20	17	0	23	19
COU	0	0	0	3	0	0	3	5	0	7	5	7	5	7	7	9	5	13	7	16	19	39	0	21	18	22	0	23	17
DEN	0	1	5	3	0	0	2	1	0	12	9	13	9	12	11	14	14	10	13	9	28	26	0	19	24	28	0	21	24
BER	0	0	0	0	0	0	0	0	0	25	19	18	25	36	19	26	23	25	20	22	44	25	0	60	19	55	0	23	50
LOB	0	0	0	0	0	0	0	0	0	9	11	12	13	11	17	12	10	13	13	17	24	50	0	31	40	29	0	32	31

E

	L1	L2	L3	L4	L5	L6	L7	L8	L9	I0	I1	I2	I3	I4	I5	I6	I7	I8	I9	I10	S0	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10
TCC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	1	0
CAF	0	0	0	1	0	0	1	1	0	1	0	1	0	1	0	0	0	5	3	3	4	1	3	2	1	4	3	4	0	4	6
UMB	0	0	0	0	0	0	1	1	0	1	0	1	0	0	0	1	2	3	1	1	1	4	3	1	0	1	3	1	0	2	2
TPH	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	1	1	1	1	1	6	0	2	1	3	0	4	1
THE	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	1	1	1	1	1	1	1	1	5	0	4	1	1	0	2	1
COU	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0	1	1	2	2	5	7	6	7	0	4	2	2	0	5	6
DEN	0	1	0	1	1	0	0	0	0	3	2	3	1	1	3	4	3	0	0	0	2	1	1	1	0	2	3	2	0	1	2
BER	1	1	0	0	0	0	0	0	0	4	3	5	3	5	1	1	4	1	1	1	5	2	4	4	0	4	1	3	0	2	7
LOB	0	1	0	0	0	0	0	0	0	3	4	3	3	1	2	4	3	1	0	1	1	1	2	4	0	4	7	1	0	5	2

F

	L1	L2	L3	L4	L5	L6	L7	L8	L9	I0	I1	I2	I3	I4	I5	I6	I7	I8	I9	I10	S0	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10
TCC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
CAF	0	0	0	0	0	0	0	0	0	2	3	1	1	1	1	2	6	1	2	1	4	6	4	8	0	7	2	7	0	1	4
UMB	0	0	0	1	0	1	0	0	0	7	3	6	2	4	1	1	2	3	5	4	4	2	2	2	0	1	2	5	0	1	1
TPH	0	0	0	1	1	1	0	1	1	4	7	6	4	6	9	4	5	2	6	1	1	4	5	3	0	5	4	4	0	1	2
THE	0	0	0	0	0	0	0	0	0	1	1	2	1	1	2	2	1	2	1	2	0	0	1	0	0	3	0	2	0	1	2
COU	0	0	1	0	0	0	2	0	0	2	4	6	4	3	2	3	6	2	2	1	3	4	2	4	0	10	6	8	0	8	3
DEN	0	0	0	0	0	0	0	0	0	3	2	2	4	1	3	1	2	2	1	1	2	4	4	1	0	2	7	2	0	1	6
BER	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	5	1	4	0	0	0	4	7	0	0	6
LOB	0	0	0	0	0	0	0	0	0	1	0	1	3	1	0	0	0	0	1	0	2	4	6	0	0	0	4	10	0	0	2

G

	L1	L2	L3	L4	L5	L6	L7	L8	L9	I1	I2	I3	I4	I5	I6	I7	I8	I9	I10	S0	S1	S2	S3	S4	S5	S6	S7	S8	S9
TCC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CAF	0	0	0	0	0	0	1	0	0	0	1	0	1	1	0	2	0	0	0	0	1	1	0	3	2	1	1	0	1
UMB	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	1	2	1	0	1	3	0	2	1	4	0	3	1	0	3	1
TPH	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0	0	1	0	0	0	2	0	1	0	0
THE	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	2	1	0	0	1	0	3	0	2	2	1	0	2	0	2	0
COU	0	0	0	0	1	0	1	1	1	2	1	3	1	1	2	1	1	2	1	5	5	8	0	3	6	10	0	2	7
DEN	0	0	0	0	0	0	0	0	0	4	2	1	2	2	4	2	1	1	1	5	1	5	0	2	3	6	0	6	1
BER	0	0	0	0	0	0	1	0	0	2	1	2	3	2	3	1	3	1	2	4	2	2	0	5	3	6	0	7	3
LOB	0	0	0	0	0	0	0	0	0	1	1	2	2	1	4	1	2	4	2	3	4	4	0	1	3	8	0	2	2

H

	L1	L2	L3	L4	L5	L6	L7	L8	L9	I0	I1	I2	I3	I4	I5	I6	I7	I8	I9	I10	S1	S2	S3	S4	S5	S6	S7	S8	S9
TCC	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	2	2	2	0	1	1
CAF	0	0	0	0	0	0	0	0	0	2	1	3	2	2	2	2	1	2	1	3	1	2	0	2	4	2	0	2	1
UMB	0	0	0	0	0	0	0	0	0	1	1	2	1	1	1	1	1	3	1	1	2	4	0	3	4	3	0	4	1
TPH	0	1	2	0	0	0	0	0	0	1	1	2	1	2	1	2	1	2	1	4	4	5	0	3	6	3	0	5	2
THE	0	0	0	0	0	0	0	0	0	1	1	1	0	1	1	1	0	1	2	1	1	1	0	2	4	1	0	5	4
COU	0	0	0	2	0	0	2	2	0	3	1	2	1	2	1	2	1	3	1	4	4	8	0	3	2	6	0	6	4
DEN	0	1	2	1	0	0	1	1	0	1	1	1	1	2	1	1	1	1	2	2	2	3	0	4	5	4	0	3	3
BER	0	0	0	0	0	0	0	0	0	3	3	3	3	2	2	2	2	1	3	1	6	4	0	4	5	5	0	1	2
LOB	0	0	0	0	0	0	0	0	0	1	2	2	2	2	1	3	1	2	1	1	3	4	0	3	5	4	0	3	7

Table S3. Responses in spikes/s of labellar sensilla of four species to bitter compounds. Related to Figure 6. (A), Drosophila melanogaster; (B) D. simulans; (C) D. sechellia; (D) D. erecta. n = 3-10. The D. melanogaster used here was Canton-S, without the w mutation contained within the genetic background control used in other experiments. Doses are provided in Materials and Methods. SEM, in spikes/s, for (E), Drosophila melanogaster; (F) D. simulans; (G) D. sechellia; (H) D. erecta.

Supplemental references

S1. Poudel, S., and Lee, Y. (2016). Gustatory Receptors Required for Avoiding the Toxic Compound Coumarin in Drosophila melanogaster. Mol Cells *39*, 310-315.