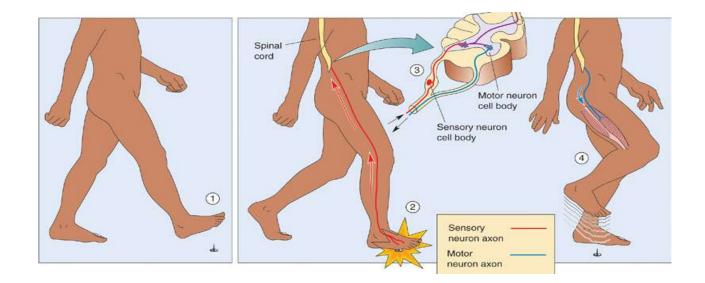
Drosophila Pheromones: From Reception to Perception

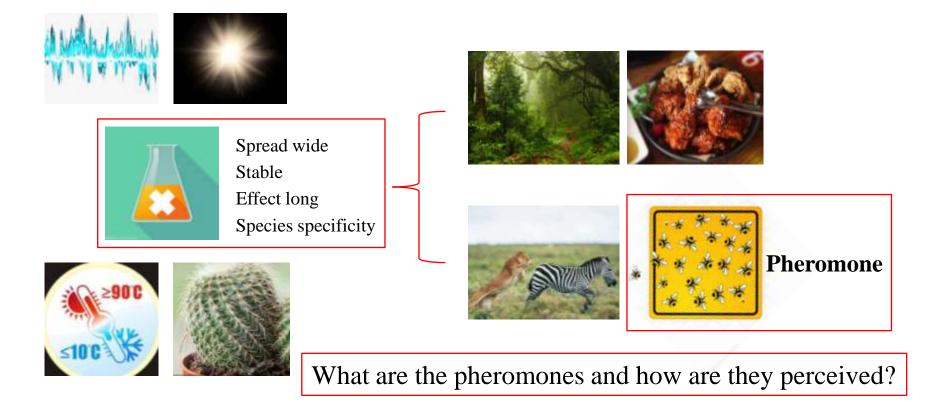
'Por Una Cabeza' Club 2021-3-25

神经系统的基本功能:感知环境、作出反应



一中枢(信息整合)——运动神经元 刺激——感觉神经元

Chemical senses are most used and probably the first to evolve



Content

Pheromones and their receptors

— JXY

Volatile- pheromonal information processing in olfactory system _____MMZ

Nonvolatile-pheromonal information processing in gustatory system _____SMS

Pheromones and their receptors

-0



ONE

What are the pheromones?

Pheromones are chemicals released by an organism to which
a conspecific responds either behaviorally or physiologically.a single moleculea mixture of many molecules

pherin (to transfer) + *hormon* (to excite)

1879



SOUVENIRS ENTOMOLOGICS

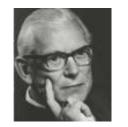


NO. 4653 January 3, 1959 NATURE

BIOLOGY

'Pheromones': a New Term for a Class of Biologically Active Substances

P. Karlson and M. Lüscher

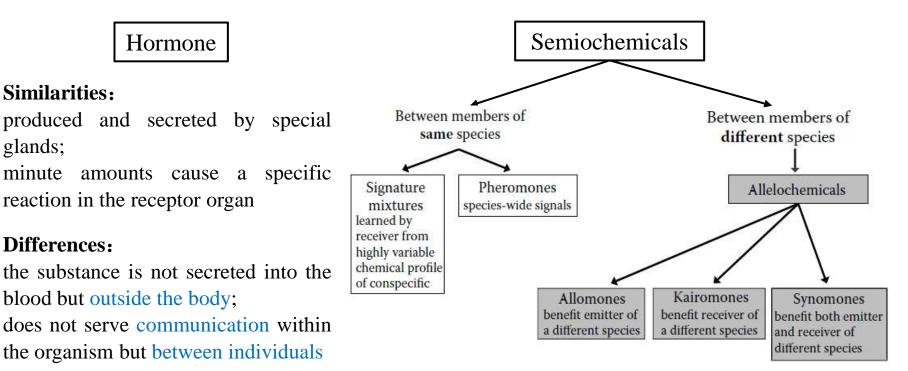


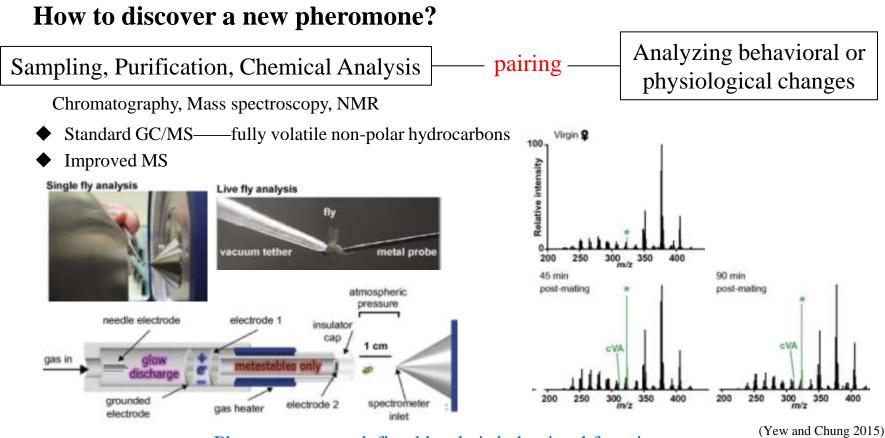
Aphrodisiac Silkmoth (*Bombyx mori*) OH bombykol

the first identified pheromone

Adolf Butenandt Nobel Prize in Chemistry in 1939 for the chemical synthesis of sex hormones

Be careful to distinguish the following chemical signals!





Pheromones are defined by their behavioral function

This really is the molecule and other similar molecules are not equally stimulating

How to discover a new pheromone?

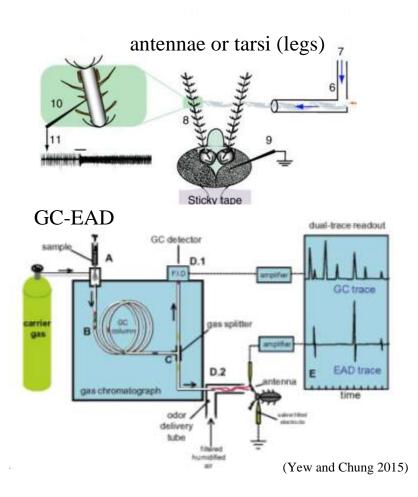
Characterize gene and function of pheromone receptors

Next generation sequencing RNA interference, transgenics and genome-editing tools Reconstitution in heterologous expression systems

Measuring neural responses to pheromones

Calcium imaging

Electroantennography or Single sensillum recording



The complexity of social functions mediated by pheromones is matched by the chemical diversity

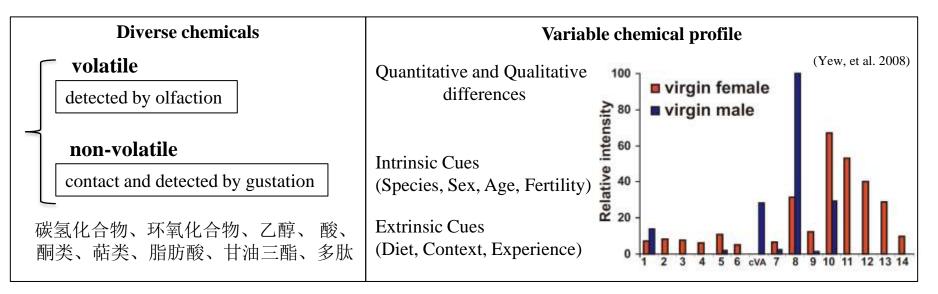
Interindividual recognition of species and gender

Role -

Aggregation Species identification Aphrodisiacs Anti-aphrodisiacs

Aggression

_ Additionally recognition of colony membership, nestmates, caste, and kin ——social insects



Pheromones in Drosophila —— cuticular hydrocarbons (CHCs)

produced in the specialized secretory cells: oenocytes

Male (Z)-7-Tricosene (7-T)

H,C CH,

Description: *D. melanogaster* male-prominent (female express low quantities) cuticular hydrocarbon that acts as male courtship inhibitor, in combination with cVA. *D. simulans* sex pheromone.

(Z)-9-Tricosene (9-T)

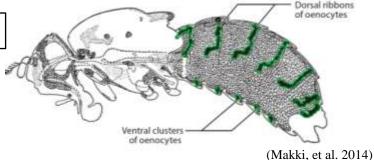
H,C CH,

Description: *D. melanogaster* cuticular hydrocarbon acting as aggregation pheromone and egg-laying attractant. **Receptor**: Or7a (Lin et al., 2015)

volatile

non-volatile

(Z)-4-undecenal



(Makki, et al. 2 (Z, Z)-7,11-Nonacosadiene (7,11-ND)

(Z, Z)- 7,11-Heptacosadiene (7,11-HD)



Description: *D. melanogaster* female- and species-specific cuticular hydrocarbon pheromone that inhibits courtship in males from other *Drosophila* species.

H,C~~~~

Description: Oxidization product of the *D. melanogaster* sex pheromone 7,11-HD. Long range *D. melanogaster* attractant. **Receptor**: Or69aB (Lebreton *et al.*, 2017).

Pheromones in *Drosophila* — male-specific signals

produced in the ejaculatory bulb

volatile

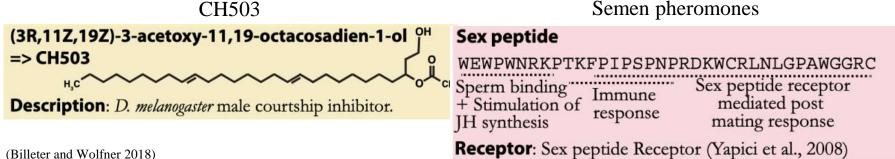
non-volatile

cis-vaccenyl acetate (cvA)

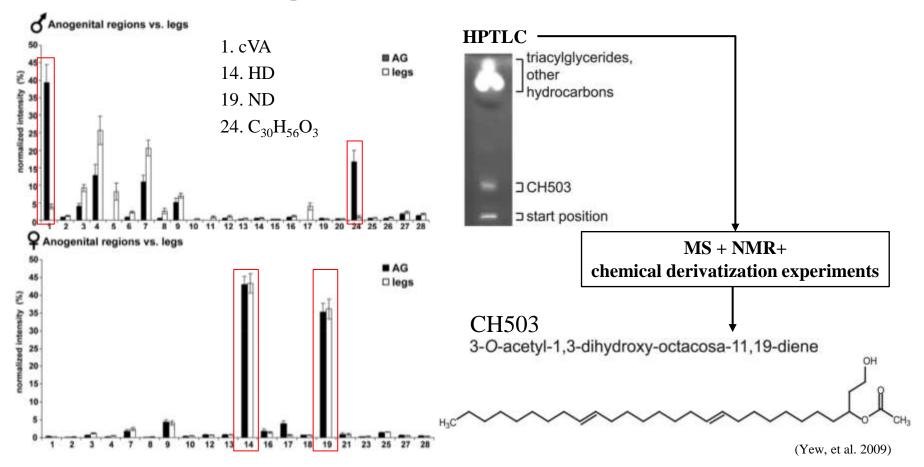
Description: *D. melanogaster* male courtship inhibitor, in combination with 7-T. Aggregation pheromone, in combination with food odors.

111 cVA from distance aggregation aggression(3-3) - cVA on a star little cVA on ₽ no cVA on 2 courtship(3) courtship inhibition(3) mated female copulation(?) cVA on courting of (Ejima 2015)

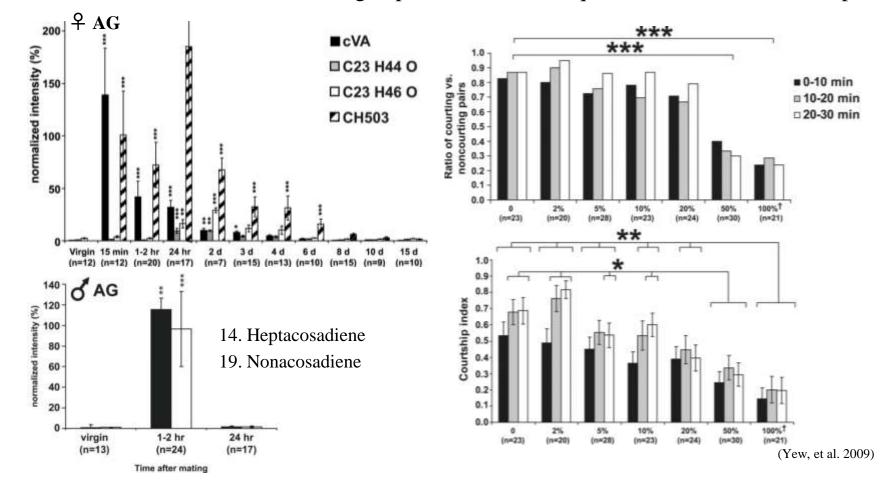
Semen pheromones

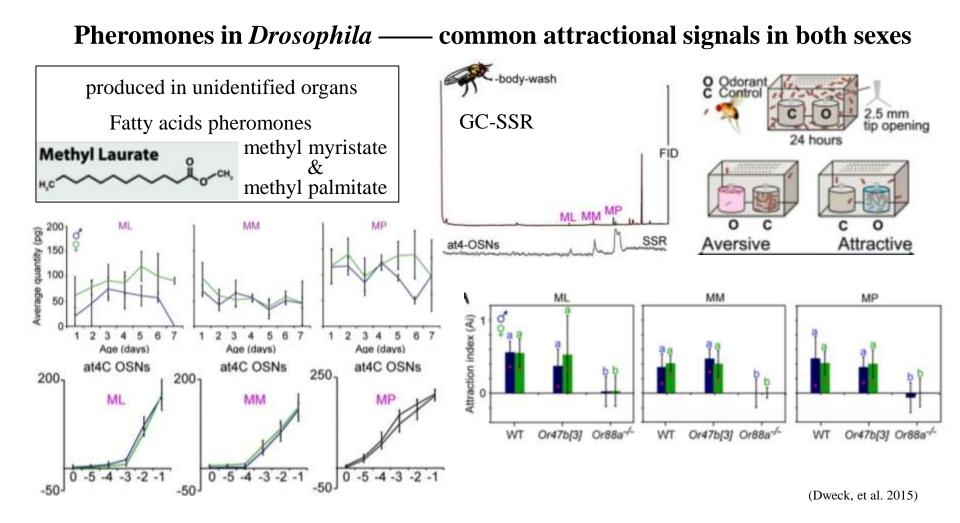


A new male pheromone CH503 in Drosophila is identified



CH503 is transferred to females during copulation and subsequent inhibits male courtship



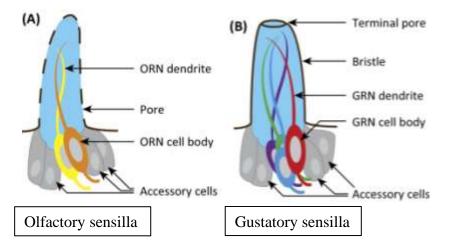


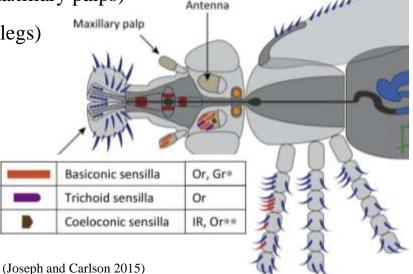
How are candidate pheromones received by the sense organs? ——The sensory organs house the pheromone receptors.

To ensure specificity, insects have evolved highly specialized channels of communication, both on the sending as well as the receiving side.

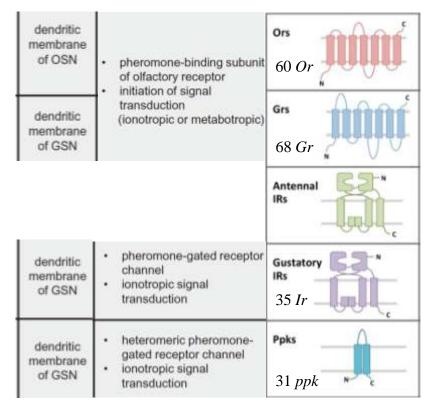
chemosensory units: sensilla ——cuticular, hair-like structures equipped with an array of sensory neurons and specialized proteins

Olfactory ——on head appendages (antennae and maxillary palps) Gustatory ——on various body parts (proboscis and legs)





There is a large repertoire of distinct pheromone receptors in Drosophila.



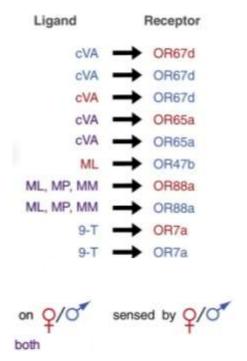
(Fleischer and Krieger 2021)

PRs mediate the specific recognition of pheromone components and

trigger subsequent ionotropic or possibly metabotropic signal transduction processes

There is a large repertoire of distinct pheromone receptors in Drosophila.

OLFACTION



7,11
7,11
7,11

CONTACT CHEMOSENSATION

Ligand	Receptor	Behavior			
7-T	Gr32a	increases female receptivity			
7-T	→ Gr32a	male-male/interspecies repulsion			
9-T, 11-P	→ Gr32a	male-male/interspecies repulsion			
9-T, 11-P	→ Gr33a	male-male/interspecies repulsion			
2	→ Gr33a	preference for younger females			
2	→ Gr39a	sustaining male courtship			
7-T	→ Gr66a	male-male/interspecies repulsion			
CH503	→ Gr68a	courtship suppression			
7-T, cVA	-> Ppk23	male-male repulsion			
7,11-ND, 7,11-HD	-> Ppk23	courtship initiation			
7,11-ND, 7,11-HD	Ppk25	courtship initiation			
7-T	-> Ppk29	male-male repulsion			
7,11-ND, 7,11-HD	Ppk29	courtship initiation			
?	- Ir52c/d	potentially courtship initiation			
on \$10 s	sensed by Q/C	behavior of 9/0*			

Other molecules are also required for proper pheromone detection

Pheromone binding proteins (PBPs): Or76a

Small, soluble proteins in the sensillum lymph, Synthesized and secreted by support cells Binding hydrophobic pheromones for transport across the lymph towards pheromone receptors (PRs) in the dendritic membrane of OSNs

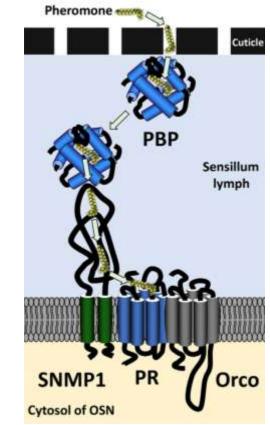
Sensory neuron membrane protein 1 (SNMP1):

Enriched in dendritic membrane

Co-receptor that may take over pheromones from PBPs and pass them on to nearby PRs

Odorant receptor co-receptor (Orco): Or83b

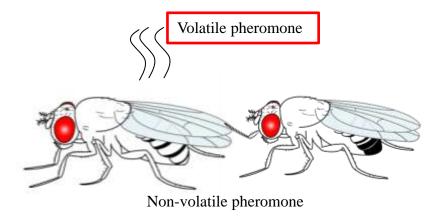
A noncanonical member of the OR family Present in all OR-expressing OSNs Forming heteromers with ORs; heteromeric OR/Orco complexes operate as ligand-gated ion channels



Summary

- Substances which are secreted to the outside by an individual and received by a second individual of the same species, in which they release a specific reaction.
- Pheromones are defined by their behavioral function. But the complex background of chemicals makes it challenging to identify pheromones. It will be necessary to perform better technologies to more fully characterize the chemical composition of fly cuticles.
- While several PRs have been reported, the results are partly controversial. Identifying certain pheromone-receptor pairs and relevance to social behavior, and characterizing their biochemical regulation are important next steps
 - How flies use their senses of smell and taste to communicate?
 - Why can the same pheromone elicit different types of behaviors?

Volatile- pheromonal information processing in olfactory system

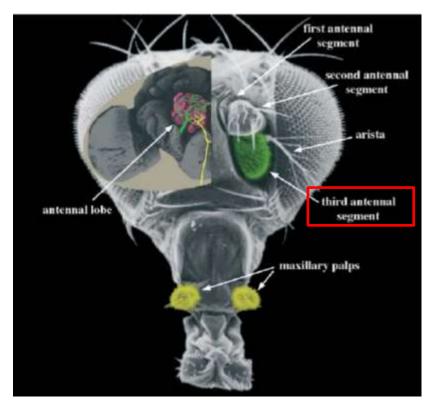


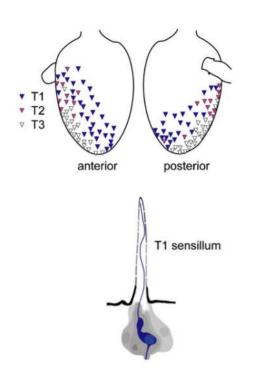
How volatile pheromones are perceived?

How to cause diverse behavioral output?

Sensillas and receptors response fly odors
cVA regulates behaviors in two sexs
Sexually -specific cVA perceiving circuit

An important olfactory sensor—Trichoid sensilla





Martin F, et al., The Anatomical Record, 2013.

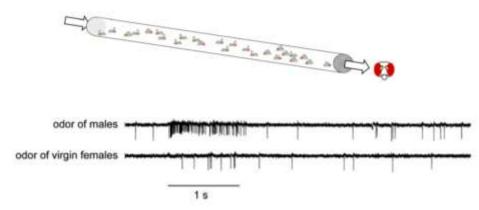
Distribution of responses to extracts and to cVA

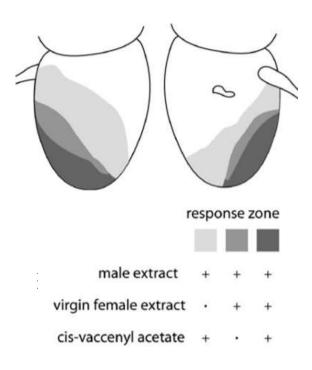


Report

Receptors and Neurons for Fly Odors in Drosophila

Wynand van der Goes van Naten 1, John R. Carlson 1 A #



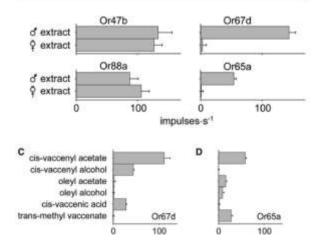


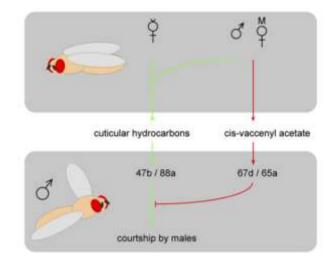
Model of the olfactory basis of mate recognition

Table 1. Responses Mediated by Ectopically Expressed Receptors

	Or47b	Or88a	Or67d	Or65a
Male extract	++	+	++	+
Virgin-female extract	++	++	14	÷.
Male genital material	•	++	+++	++
Virgin-female genital material	+		a ann an a	() (*)
Mated-female genital material	i i	++	+++	++
cis-vaccenyl acetate	÷.		++	+

 $\cdot, n <$ 50 impulses/s; +, 50 \leq n < 100 impulses/s; ++, 100 \leq n < 150 impulses/s; +++, 150 impulses/s \leq n.





Or67d responses cVA in Drosophila

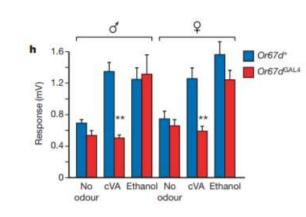
manuny

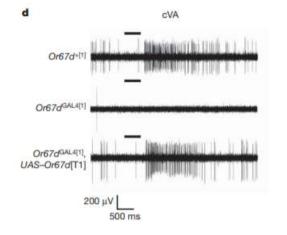
Vid 446.39 March 2007/JMI/M08/2008/S060

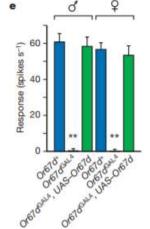
LETTERS

A single class of olfactory neurons mediates behavioural responses to a Drosophila sex pheromone

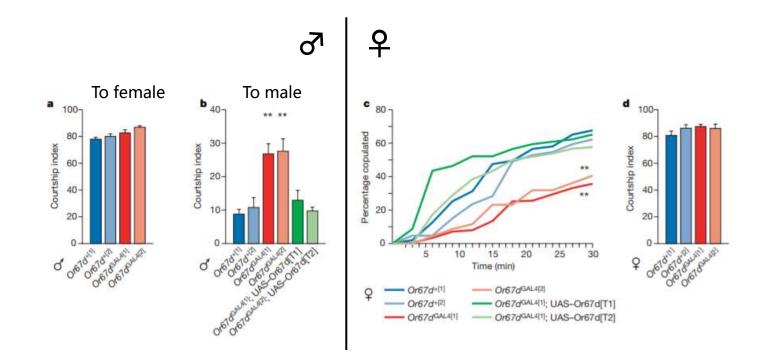
Amina Kurtovic¹⁺, Alexandre Widmer¹⁺ & Barry J. Dickson¹







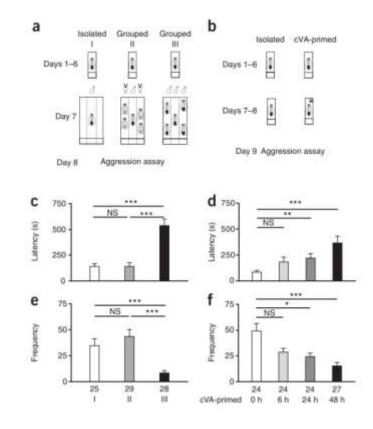
Same receptor mediates distinct behaviors in both sexs



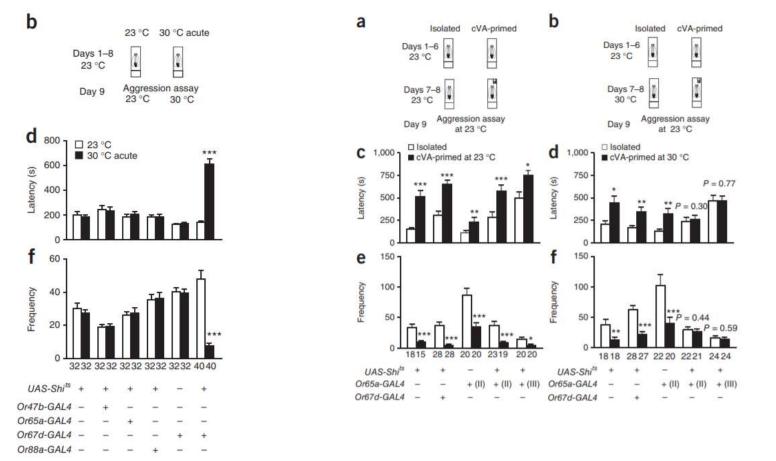
Perception of cVA is related to male aggression

Social regulation of aggression by pheromonal activation of Or65a olfactory neurons in *Drosophila*

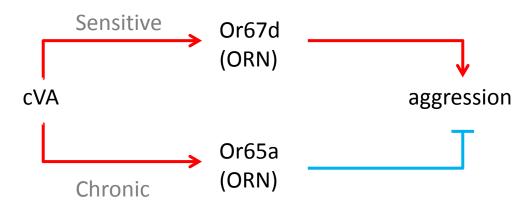
Weiwei Liu^{2,3,7}, Xinhua Liang^{1,3,7}, Jianxian Gong⁴, Zhen Yang⁴, Yao-Hua Zhang⁵, Jian-Xu Zhang⁵ & Yi Rao^{3,6}



Two specific receptors of cVA regulate aggression in different ways



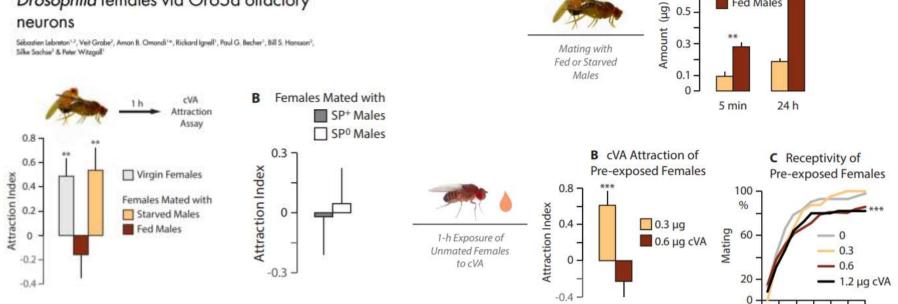
cVA regulates male aggression model



Perception of cVA is related to female receptivity

Love makes smell blind: mating suppresses pheromone attraction in Drosophila females via Or65a olfactory neurons

Sébastien Lebreton12, Veit Grabe?, Amon B. Omondi1*, Rickard Ignell1, Paul G. Becher1, Bill S. Honsson7,



A cVA Extracted from

30

60 min

10

Females Mated with

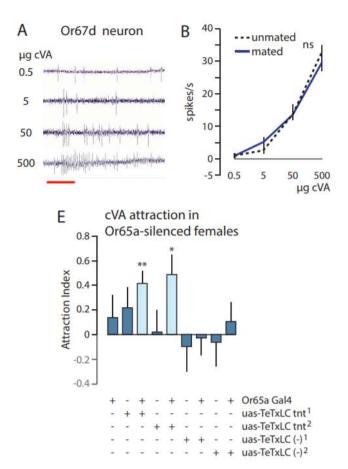
Starved

Fed Males

0.7 -

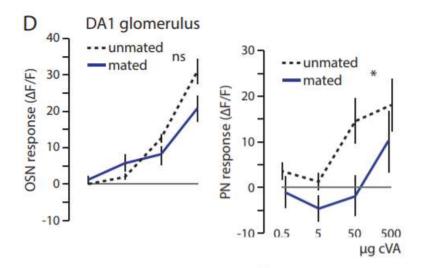
0.5

Two specific receptors of cVA regulate receptivity in different ways

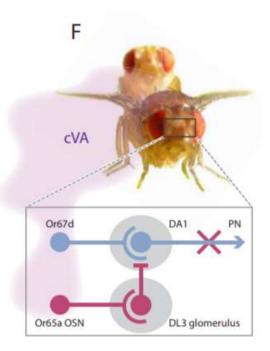


Or67d → DA1

Or65a → DL3



cVA regulates male receptivity model



Why the same signal input has different outputs in both sexes?

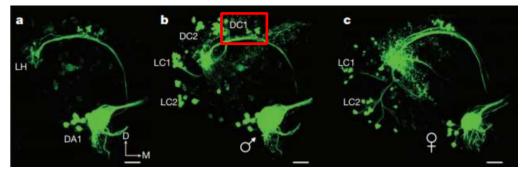
Sex-specific neurons response to DA1

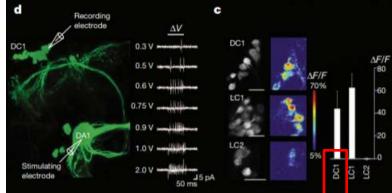
LETTER

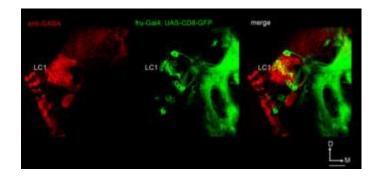
doi:10.1038/nature09554

A dimorphic pheromone circuit in Drosophila from sensory input to descending output

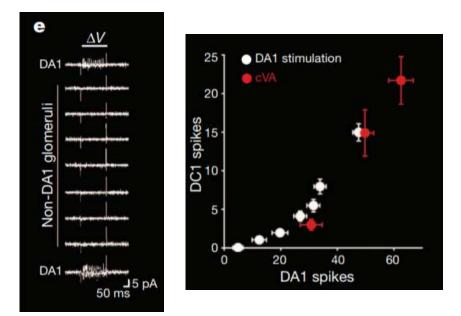
Vanessa Ruta¹, Sandoep Robert Dutta¹†, Maria Luisu Vasconcelos¹†, Jessica Freeland¹, Loren L. Looger² & Richard Axel¹

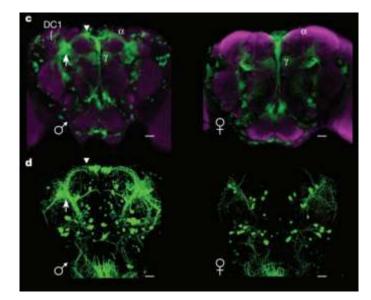






Excitatory neuron DC1 responds to cVA signal

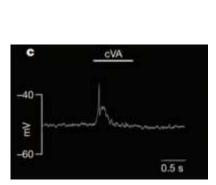


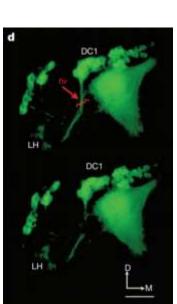


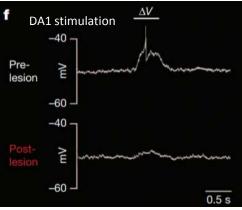
DN1 involved in male-specific circuit of processing cVA

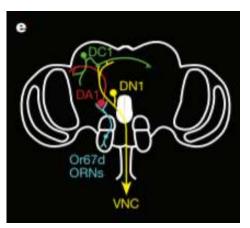
DN1



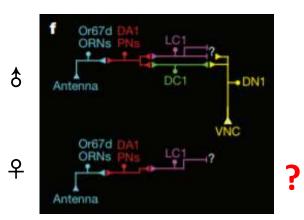


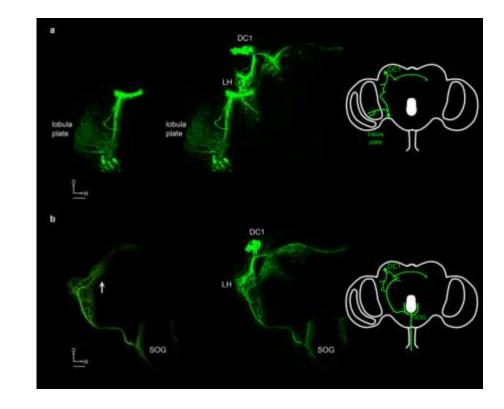






The dimorphic pheromone circuit in Drosophila male





How the same signal is transmitted in different brains?

A Bidirectional Circuit Switch Reroutes Pheromone Signals in Male and Female Brains

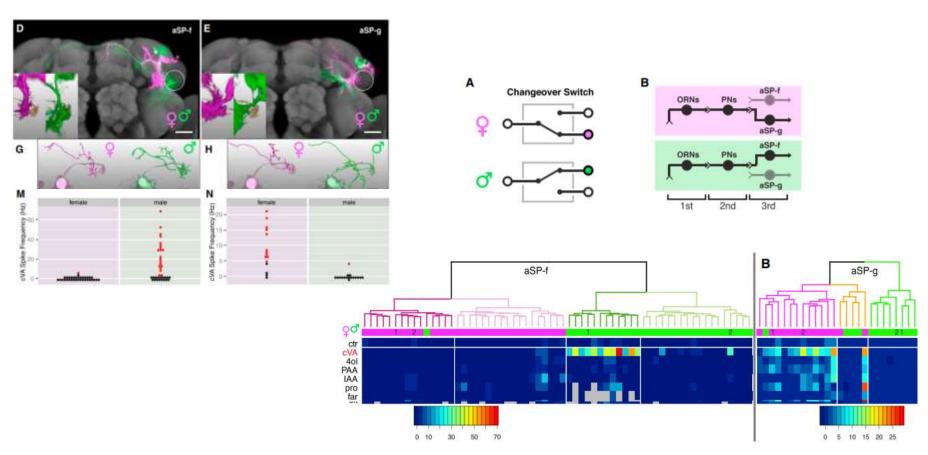
Johannes Kohl,12 Aaron D. Ostrovsky,123 Shahar Frechter,1 and Gregory S.X.E. Jefferis14

Cachero et al. (2010)		aSP-f	aSP-g	aSP-h	aSP-k	alP-e
Cell Number	male	23.2 (2.6)	13.4 (0.9)	5.0 (0.8)	29.2 (3.3)	27.0 (4.2)
	female	18.6 (5.0)	13.4 (4.9)	5.0 (0.5)	20.2 (3.5)	27.0 (2.2)
Overlap DA1	male	+++	-	+	note 1	++
	female	1.00	++	±	note 1	++
PA-GFP Prediction	male	yes	no	yes	yes	yes
	female	no	yes	note 2	yes	yes
Ruta et al. (2010)		DC1	r/a	DC2	LC1	LC2
Cell Number	male	19.7 (2.3)	n/a	Note 3	25.8 (3.4)	13.0 (2.8)
	female	n/a	n/a	n/a	15.8 (3.0)	13.3 (2.1)
PA-GFP Observed	male	yes	no	yes	yes	yes
	female	no	no	no	yes	yes
DA1 Stim. Response	male	+++	n/a	-	+++	±
	female	n/a	n/a	n/a	n/a	n/a
cVA Response	male	+++	n/a	n/a	n/a	n/a
	female	n/a	n/a	n/a	n/a	n/a

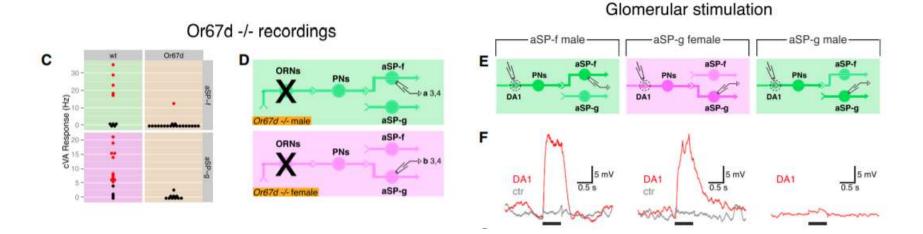
\$

★

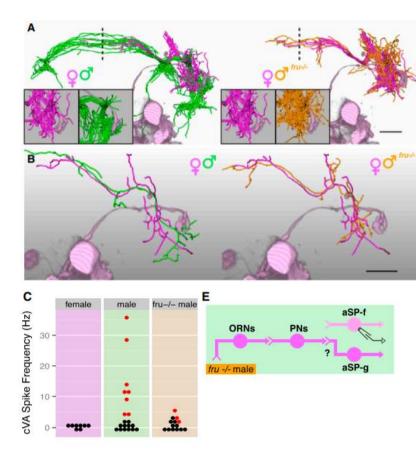
Two fru+ LHNs may be involved in sexually-specific circuits

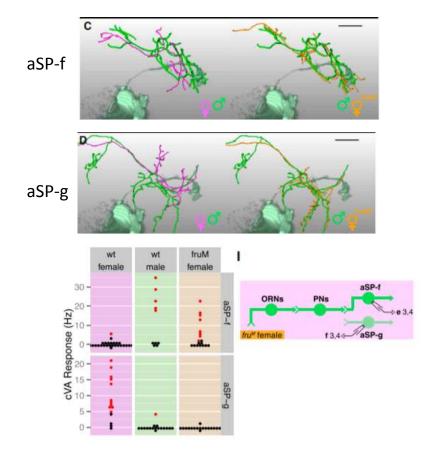


DA1 PNs form sex-specific connections with *fru*+ LHNs

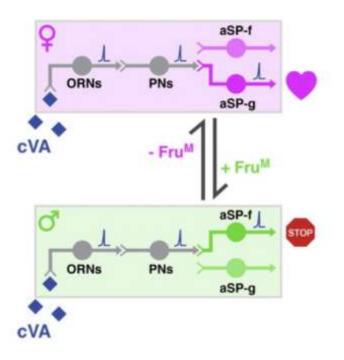


Fru^{M} is necessary and sufficient for the male form of the switch





A bidirectional circuit switch reroutes pheromone signals in *Drosophila* brains



Take home messages

•Or65a and Or67d are specific receptors for cVA

•There are sexually dimorphic neural circuits downstream of third order neurons

•*fruitless* is necessary and sufficient in the formation of the sexually dimorphic circuit

References

Ruta, V., Datta, S. R., Vasconcelos, M. L., Freeland, J., Looger, L. L., & Axel, R. (2010). A dimorphic pheromone circuit in drosophila from sensory input to descending output. *Nature*, *468*(7324), 686-690.

Kohl, J., AD Ostrovsky, Frechter, S., & Jefferis, G. (2013). A bidirectional circuit switch reroutes pheromone signals in male and female brains. *Cell*.

Lebreton, S., Grabe, V., Omondi, A. B., Ignell, R., Becher, P. G., & Hansson, B. S., et al. (2014). Love makes smell blind: mating suppresses pheromone attraction in drosophila females via or65a olfactory neurons. Rep, 4, 7119.

Liu, W., Liang, X., Gong, J., Zhen, Y., & Yi, R. (2011). Social regulation of aggression by pheromonal activation of or65a olfactory neurons in drosophila. Nature Neuroscience, 14(7), 896-902.

Naters, W., & Carlson, J. (2007). Receptors and neurons for fly odors in drosophila. Current Biology, 17(7), 606-612.

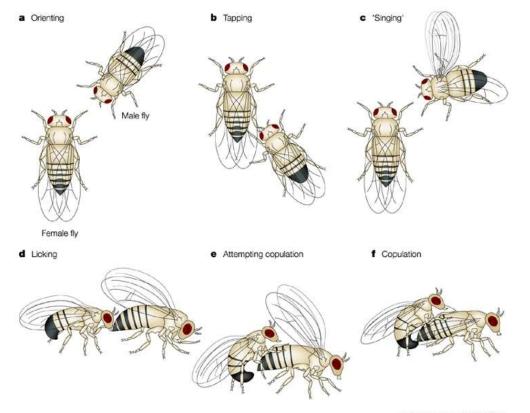
Amina Kurtovic, Alexandre Widmer& Barry J. Dickson.(2007). A single class of olfactory neurons mediates behavioural responses to a Drosophila sex pheromone. Nature.

Nonvolatile-pheromonal information processing in gustatory system in male courtship behavior

SMS

THREE

Sequence of courtship behaviors shown by Drosophila melanogaster males towards females.



Nature Reviews | Genetics

From: Drosophila: Genetics meets behaviour

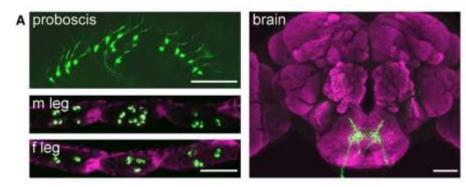


Contact Chemoreceptors Mediate Male-Male Repulsion and Male-Female Attraction during *Drosophila* Courtship

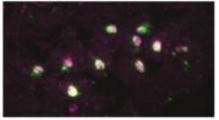
Robert Thistle,^{2,3} Peter Cameron,^{2,3,4} Azeen Ghorayshi,² Lisa Dennison,² and Kristin Scott^{1,2,*} ¹Howard Hughes Medical Institute ²Department of Molecular and Cell Biology and Helen Wills Neuroscience Institute ¹⁶ Barker Hall, University of California, Berkeley, Berkeley, CA 94720, USA ³These authors contributed equally to this work ⁴Present address: The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA ^{*}Correspondence: kscott@berkeley.edu DOI 10.1016/j.cell.2012.03.045

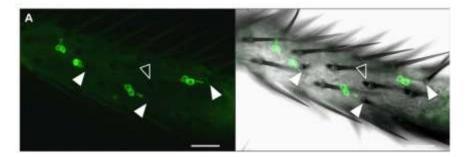
ppk23+ & ppk29+ neurons

PPK23-Gal4>uas-myrGFP









ppk23-GAL4 x UAS-CD8::GFP

B. Lu, A. LaMora, Y. Sun, M. J. Welsh, Y. Ben-Shahar, Plos Genet. 8, e1002587 (2012).

A to H-M Courtship Silencing H-F Courtship Silencing

PPK23+ cells are necessary to inhibit male-male courtship and promote female courtship.

Activation of ppk23+ cells drives appropriate courtship behavior.

ppk23-Gel4

Gr66p-LexA

AnxAnp-Gall0

UAS-TNT

Inv-LinxA

+

+

+

+

+

+

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Appk23

Appk23

ppk23-Gwl4

Grttda-LexA

InxAop-Gal80

UAS-TNT

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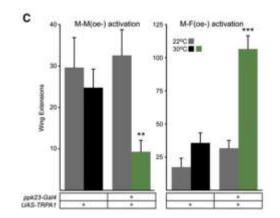
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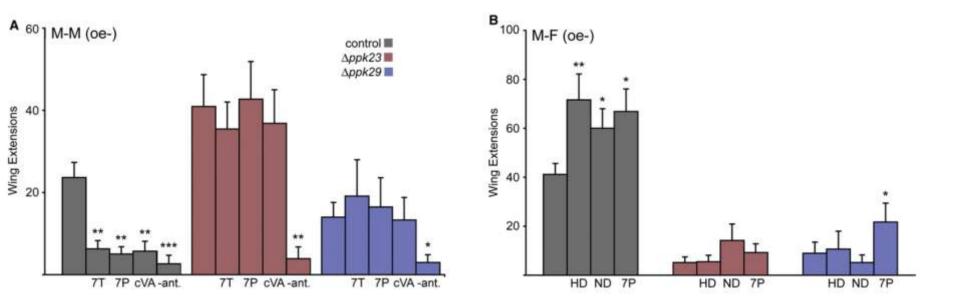
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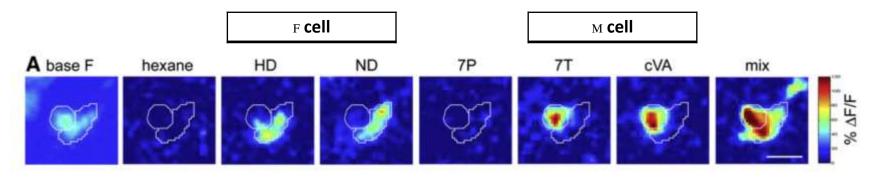


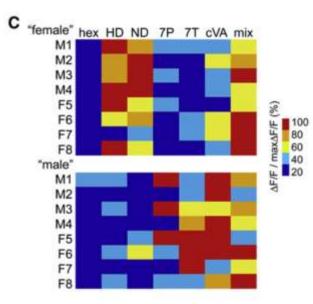
7T and cVA are inhibitory compounds on males.

7P is abundant on males, with more complex roles in courtship.

7,11-HD and 7,11-ND are excitatorycompounds on females.







Drosophila Pheromone-Sensing Neurons Expressing the ppk25 Ion Channel Subunit Stimulate Male Courtship and Female Receptivity

Vinoy Vijayan^{1,2}, Rob Thistle^{3,4}, Tong Liu^{1,2,5}, Elena Starostina^{1,2}, Claudio W. Pikielny^{1,2*}

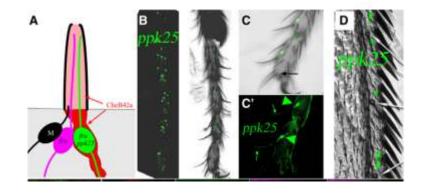
1 Department of Genetics, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire, United States of America, 2 Neuroscience Center, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire, United States of America, 3 Department of Molecular and Cell Biology and Helen Wills Neuroscience Institute, University of California, Berkeley, Berkeley, California, United States of America, 4 Howard Hughes Medical Institute, University of California, Berkeley, Berkeley, California, United States of America, 5 Institute of Neuroscience, Chinese Academy of Sciences, Shanghai, China

Cellular/Molecular

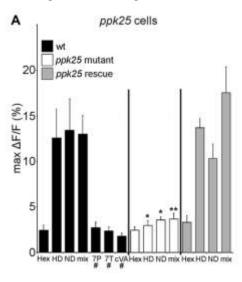
A *Drosophila* DEG/ENaC Subunit Functions Specifically in Gustatory Neurons Required for Male Courtship Behavior

Elena Starostina,^{1,2} Tong Liu,^{1,2} Vinoy Vijayan,^{1,2} Zheng Zheng,³ Kathleen K. Siwicki,³ and Claudio W. Pikielny^{1,2} ¹Department of Genetics and ²Neuroscience Center, Dartmouth Medical School, Hanover, New Hampshire 03755-1404 and ³Department of Biology, Swarthmore College, Swarthmore, Pennsylvania 19081

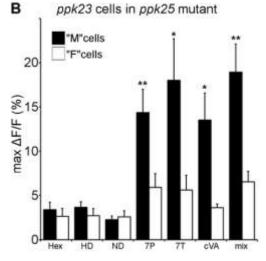
V. Vijayan, R. Thistle, T. Liu, E. Starostina, C. W. Pikielny, PLoS Genetics. 10, e1004238 (2014).



ppk25+ neuron respond to female pheromone

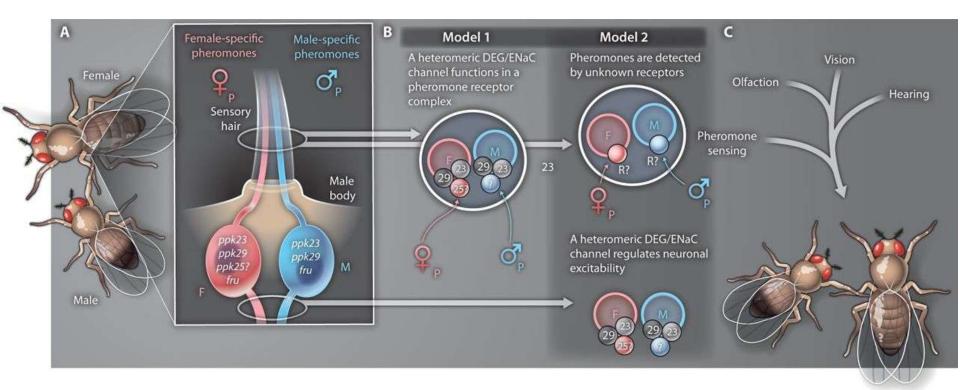


ppk25 is essential for the recognition of courtshipstimulating pheromone



E. Starostina et al., J Neurosci. 32, 4665-4674 (2012).

ppk25







Excitation and inhibition onto central courtship neurons biases *Drosophila* mate choice

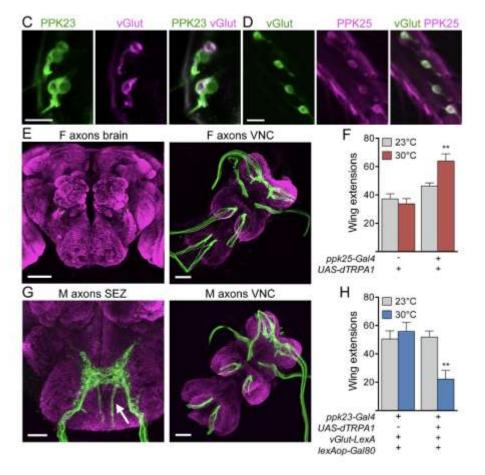
Benjamin R Kallman^{1,2}, Heesoo Kim^{1,2}, Kristin Scott^{1,2*}

¹Department of Molecular and Cell Biology, University of California, Berkeley, Berkeley, United States; ²Helen Wills Neuroscience Institute, University of California, Berkeley, Berkeley, United States

2015

(00)

F and M cells comprise distinct chemosensory neuron classes

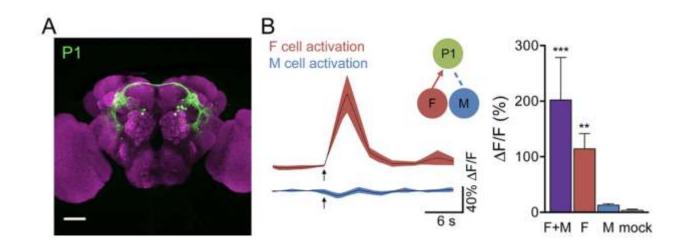


F cell, respond to female pheromone:

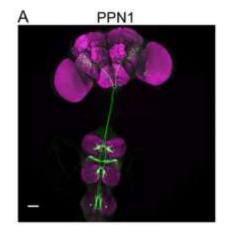
ppk25+, vGlut+

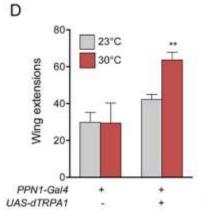
M cell, respond to male pheromone

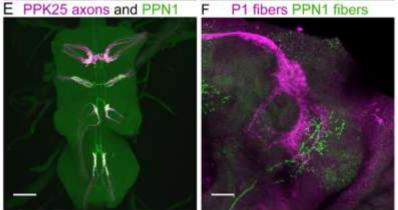
F cell stimulation activates P1 neurons

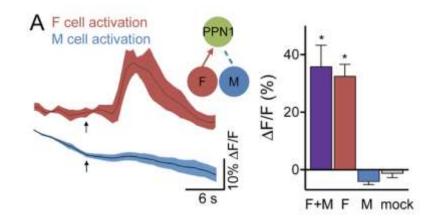


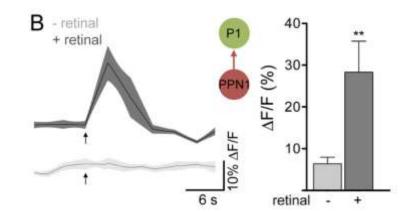
PPN1 neurons respond to F cell stimulation and activate P1 neurons





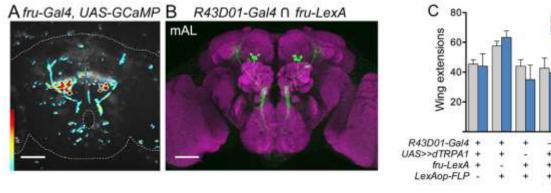


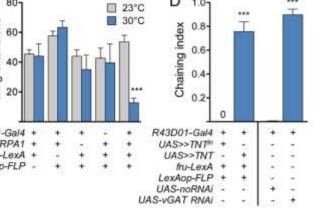




Activation of F+M cells

mAL neurons inhibit courtship via GABA



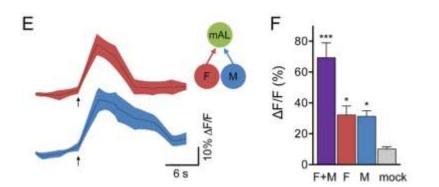


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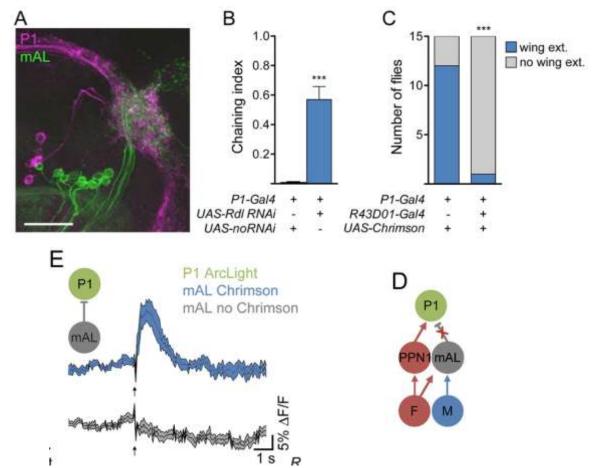
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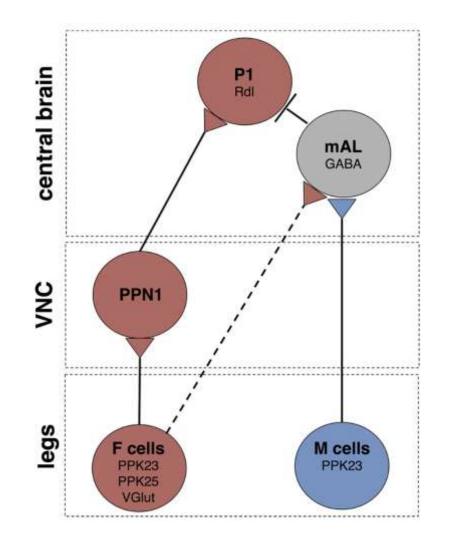
GABAergic neurons

M cells and F cells activate courtship-suppressing mAL neurons.



mAL neurons functionally and behaviorally inhibit P1 neurons.





Neuron Multimodal Chemosensory Circuits Controlling Male Courtship in Drosophila

Highlights

- P1 neurons are functionally tuned toward appropriate potential mates
- Gustatory and olfactory pheromone circuits converge on P1 neurons
- Pheromone signals are carried by parallel excitatory and inhibitory branches
- This neural architecture allows stringent and flexible control of courtship behavior

Authors

E. Josephine Clowney, Shinya Iguchi, Jennifer J. Bussell, Elias Scheer, Vanessa Ruta

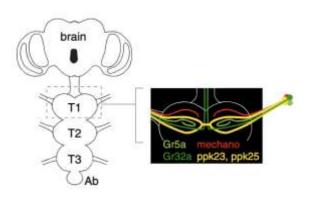
2015

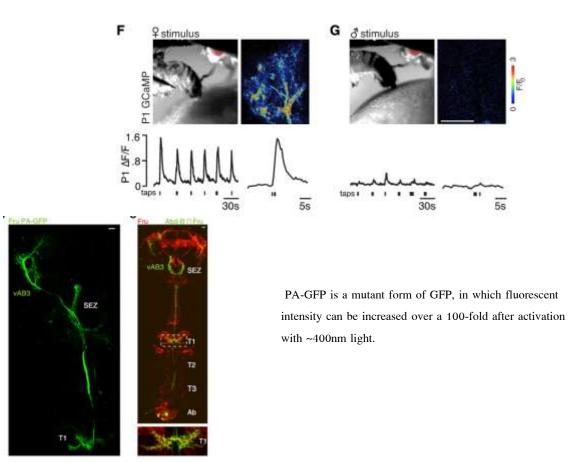
Article

P1 neuron chemosensory tuning correlates with mate preference

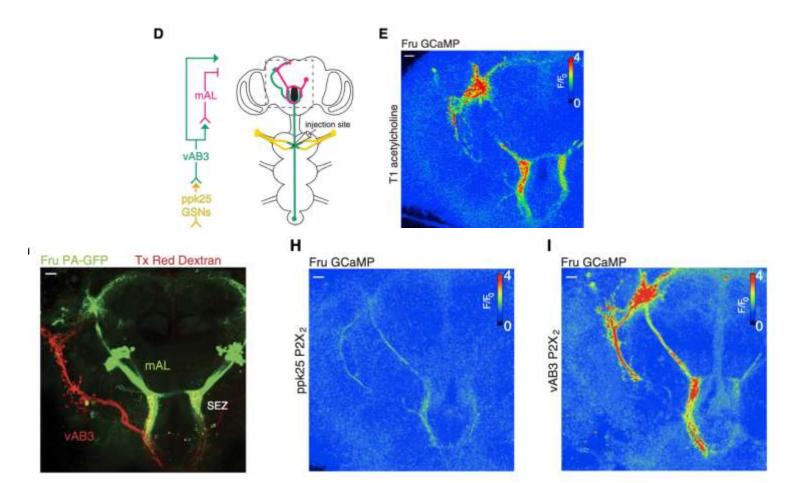
ABC



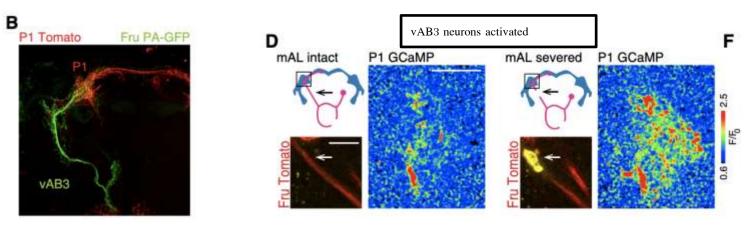




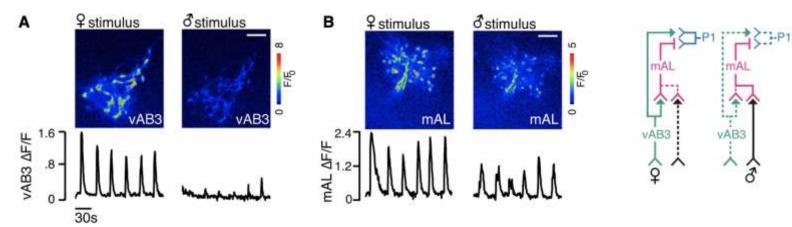
vAB3 neurons convey sensory signals from ppk25+ axons in the ventral nerve cord to mAL interneurons within the brain



Excitatory vAB3 neurons and inhibitory mAL neurons converge onto P1 Neurons



Differential pheromone tuning of vAB3 and mAL neurons



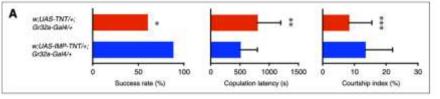
Article

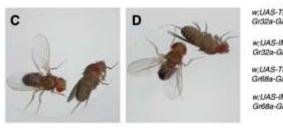
The Shaping of Male Courtship Posture by Lateralized Gustatory Inputs to Male-Specific Interneurons

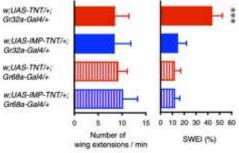
Masayuki Koganezawa,¹ Daisuke Haba,² Takashi Matsuo,² and Daisuke Yamamoto^{1,*}

¹Division of Neurogenetics, Tohoku University Graduate School of Life Sciences, Sendai 980-8578, Japan ²Department of Biological Sciences, Tokyo Metropolitan University, Hachioji, Tokyo 192-0397, Japan

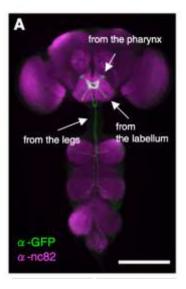
Effects of inactivation of Gr32-expression neurons on male mating behavior



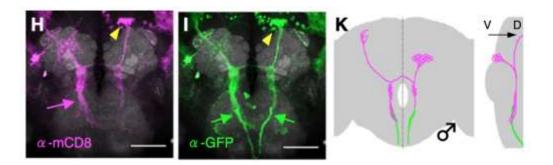




Central projection of Gr32a-expressing neurons

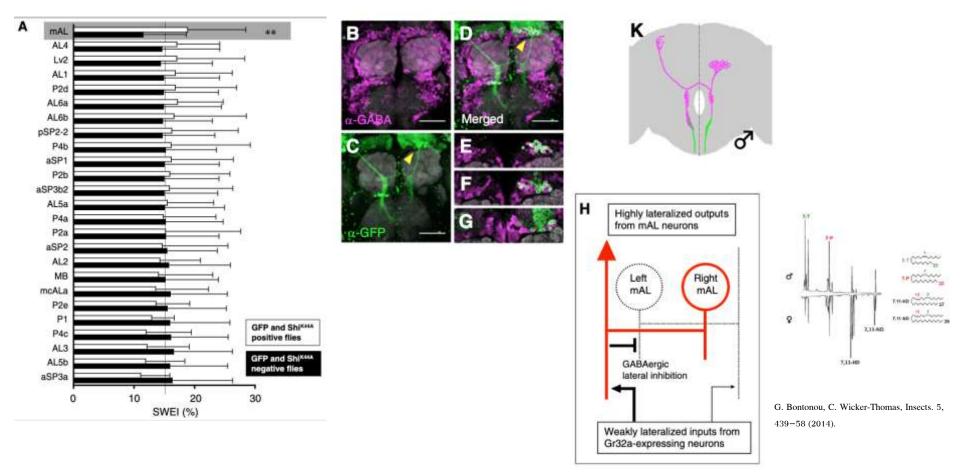


Double staining of Gr32a-expressing neurons and an mAL MARCM patch in male flies



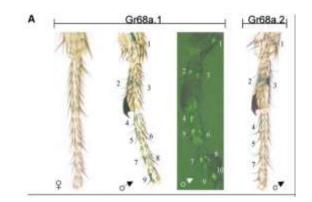
Gr32a>myrGFP

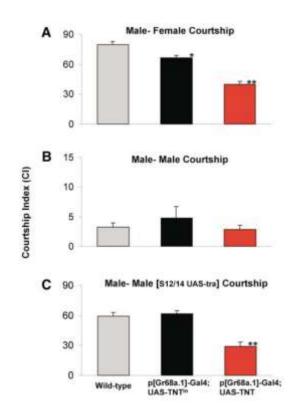
Contribution of mAL interneurons to unilateral wing extension



Neuron, Vol. 39, 1019–1029, September 11, 2003, Copyright ©2003 by Cell Press

A Putative *Drosophila* Pheromone Receptor Expressed in Male-Specific Taste Neurons Is Required for Efficient Courtship





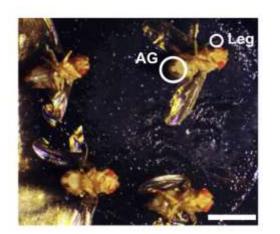
Male[S12/14 UAS-tra]:

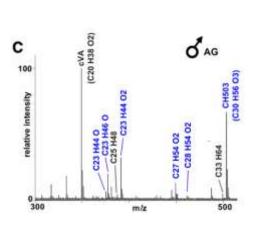
feminized oenocytes, produced female

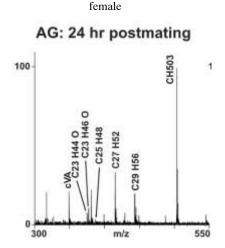
pheromone

A New Male Sex Pheromone and Novel Cuticular Cues for Chemical Communication in *Drosophila*

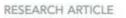
ultraviolet laser desorption/ionization orthogonal time-of-flight mass spectrometry(UV-LDIo-TOF MS)







Article



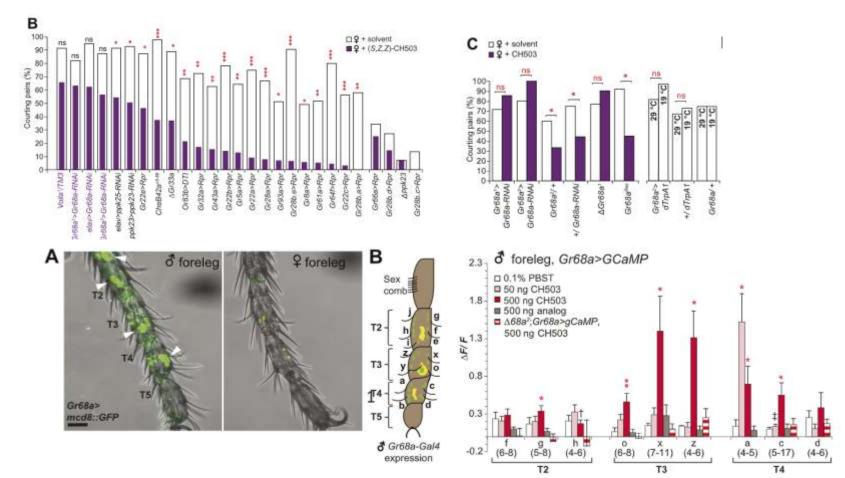


The neuropeptide tachykinin is essential for pheromone detection in a gustatory neural circuit

Shruti Shankar^{1,2}, Jia Yi Chua¹, Kah Junn Tan¹, Meredith EK Calvert^{1†}, Ruifen Weng³, Wan Chin Ng¹, Kenji Mori⁴, Joanne Y Yew^{1,2,5}*[‡]

¹Temasek Life Sciences Laboratory, Singapore, Singapore; ²Department of Biological Sciences, National University of Singapore, Singapore, Singapore; ³Institute of Molecular and Cell Biology, Singapore, Singapore; ⁴Photosensitive Materials Research Center, Toyo Gosei Co., Ltd, Chiba, Japan; ⁵Pacific Biosciences Research Center, University of Hawaii at Mānoa, Honolulu, United States

CH503: produced in male flies and transfer to female after mating

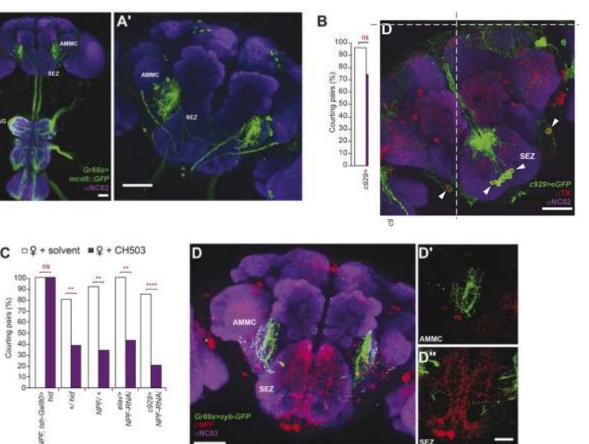


Gr68a expression in the male foreleg is required for CH503 detection.

Screen Gal4 and RNAi lines targeting central brain regions, neuropeptides and transmitter system.

С

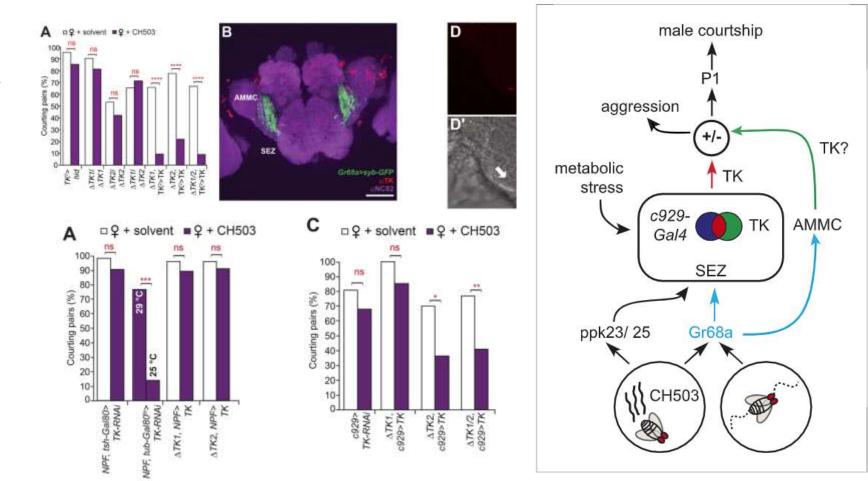
(%) 81



C929-Gal4 labeled brain region

NPF-Gal4 labeled neurons

Tachykinin-expressing cells in the SEZ are a second order circuit for Gr68a neurons

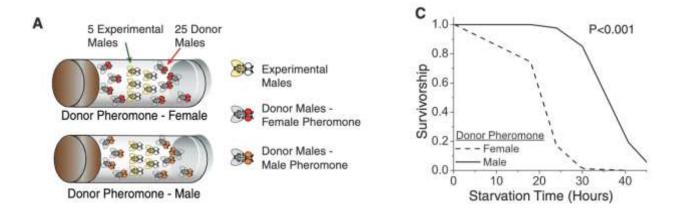




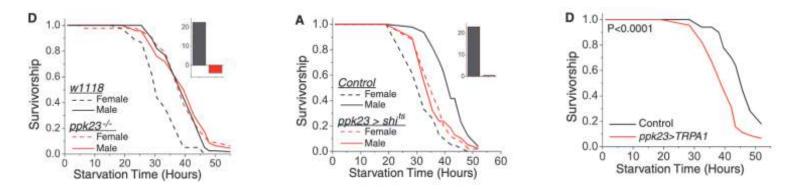
Drosophila Life Span and Physiology Are Modulated by Sexual Perception and Reward

Christi M. Gendron, Tsung-Han Kuo, Zachary M. Harvanek, Brian Y. Chung, Joanne Y. Yew, Herman A. Dierick and Scott D. Pletcher

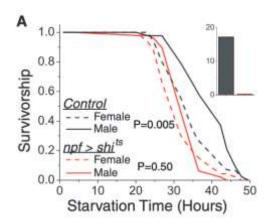
Science 343 (6170), 544-548. DOI: 10.1126/science.1243339originally published online November 29, 2013

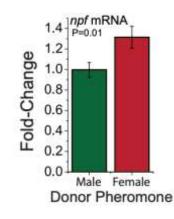


The effects of pheromone exposure are mediated by taste perception involving gustatory receptor ppk23.



Aging and physiology are modulated by neuralmechanisms of expectation and reward.





Exposure to female donor pheromones results in a significant increase in npf mRNA levels

Summary

