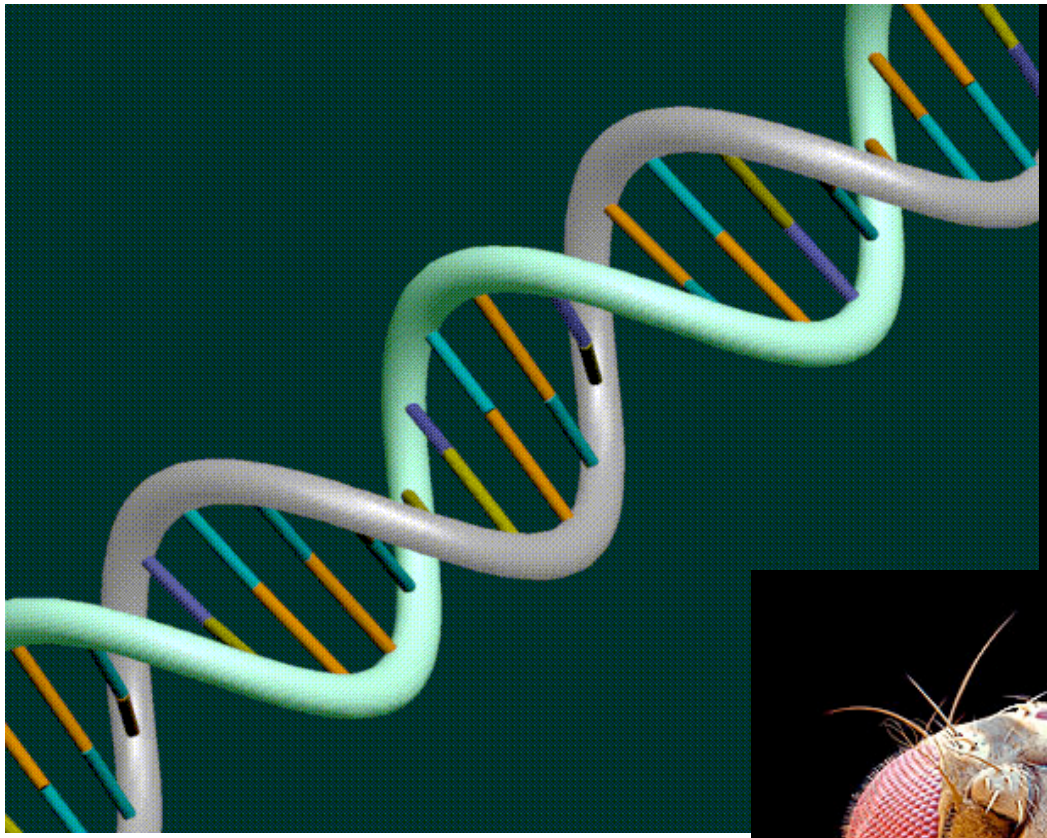
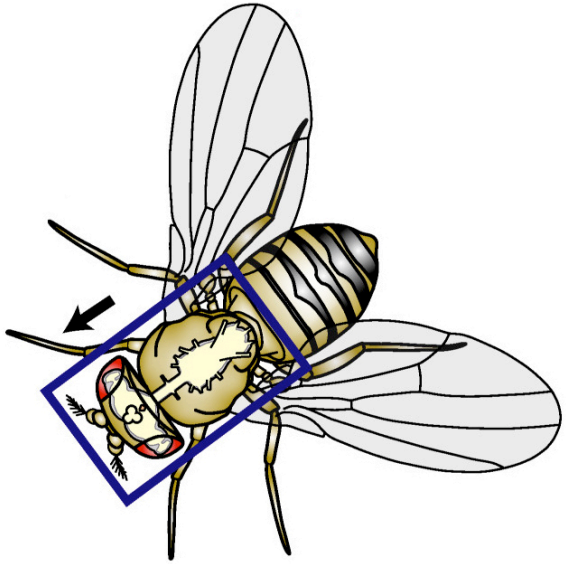
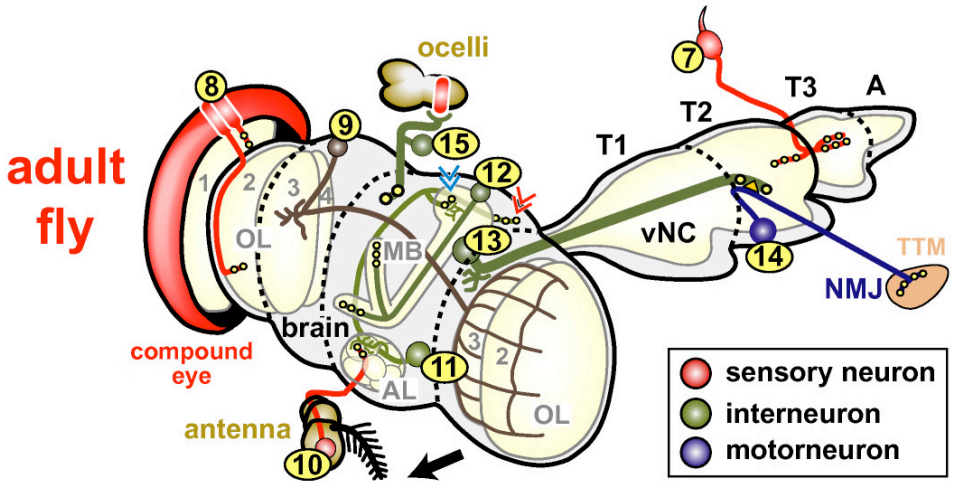
Genes, Brains and Behaviour: command neurons

Karl-Friedrich Fischbach, Neurogenetics, Freiburg



The giant fibre system of Drosophila as an example of command neurons





Escape response in Drosophila

http://www.youtube.com/watch?v=Tuf1kZDWeaw&NR=1

Escape response in wingless Drosophila

http://www.youtube.com/watch?v=WRK5kWKOHrc

PLoS ONE. 2009; 4(4): e5100.
Published online 2009 April 2. doi: 10.1371/journal.pone.0005100.
PMCID: PMC2660433

Manipulation of an Innate Escape Response in *Drosophila*: Photoexcitation of *acj6* Neurons Induces the Escape Response

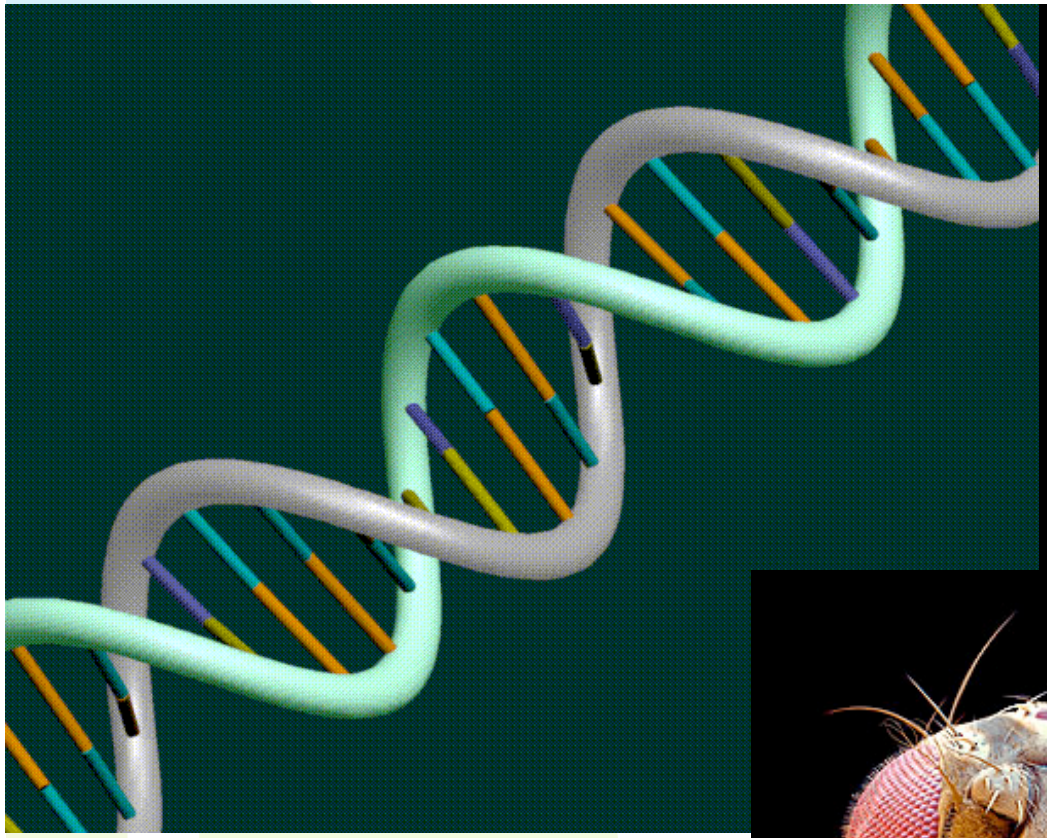
Gregor Zimmermann,[#1] Li-ping Wang,[#2] Alexander G. Vaughan,[#3] Devanand S. Manoli,[3] Feng Zhang,[2] Karl Deisseroth,[2] Bruce S. Baker,[3] and Matthew P. Scott[1*]

Adult female flies expressing ChR2 under the acj6-GAL4 driver.
Photostimulation induces a startle-like jump response,
dependent on supplementary Retinal

Adult flies expressing ChR2 in cholinergic neurons under cha-GAL4. Photostimulation results in a seizure-like response, which is dependent on supplementary Retinal.

Genes, Brains and Behaviour: aggression

Karl-Friedrich Fischbach, Neurogenetics, Freiburg



Genes, Brains and Behaviour: aggression

Karl-Friedrich Fischbach, Neurogenetics, Freiburg

Konrad Lorenz

KONRAD LORENZ

ZUR NATURGESCHICHTE
DER AGGRESSION

DAS
SOGENANNTE
BÖSE

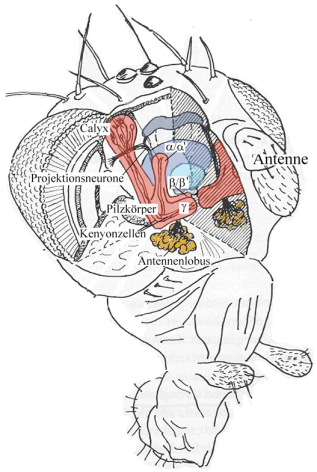
Not only humans are aggressive against members of the same species

Context, in which aggressive behavior can be observed?
What is the function of aggressive behavior?

- interspecific
  (aggression between species)
  - eating and being eaten, predator and prey
    - attack
    - defence

- intraspecific
  (conspecific aggression in social behavior)
  - in gaming behavior
  - sexual behavior
  - territorial behavior
  - competing behavior
  - frustration behavior
  - group aggression in social animals

aggressive behavior of Drosophila



What can Drosophila add to the study of aggressive behavior?

1. The nervous system is well known
2. The genetic tool box available in Drosophila is outstanding
   a) mutant analysis
   b) Groups of cells can be genetically manipulated
3. Sexually dimorphic aggressive behavior could be studied on the background of knowledge about sexual differentiation mechanisms.
4. But: Does Drosophila show aggressive behavior?

No emotions? Fighting Drosophila

Lab Works

Harvard Medicine News About HMS Feedback A window on Harvard Medical research

Fruit Fly Fight Club

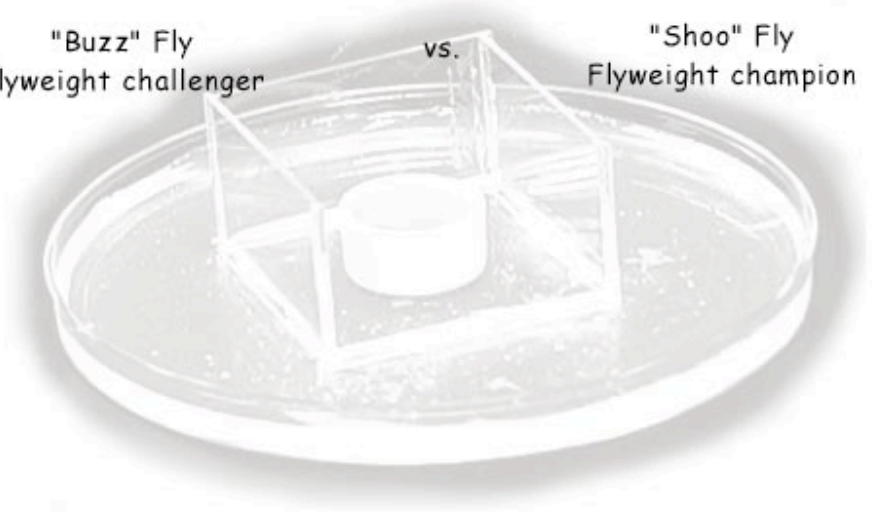
See top flyweights in the squared circle pound out a new model of aggression

"Buzz" Fly
Flyweight challenger

vs.

"Shoo" Fly
Flyweight champion

Prof. Kravitz



Thriller Championships

Official fight videos showing aggressive young males set new standards for winning and losing in hundreds of cliff-hanger fights.

Training Room

Exclusive sneak peek at how researchers are betting on future mutant fly fights to learn more about the biology of aggression, dominance, and defeat.

KF. Fischbach

male fighting

Table 1. Ethogram of offensive and defensive actions of male flies during agonistic encounters

Component	Description
Offensive actions	
Approach	One fly lowers body, then advances in the direction of the other
Low-Level fencing	Both flies extend one leg and tap opponent's leg
Wing threat	One fly quickly raises both wings to a 45° angle towards opponent
High-level fencing	One or both flies face each other, extend leg forward and push opponent
Chasing	One fly runs after the other
Lunging	One fly rears up on hind legs and snaps down on the other
Holding	One fly grasps the opponent with forelegs and tries to immobilize
Boxing	Both flies rear up on hind legs and strike the opponent with forelegs
Tussling	Both flies tumble over each other, sometimes leaving food surface
Defensive actions	
Walk away	Loser turns and retreats slowly from advance of winner
Defensive wing threat	Loser flicks wings at 45° angle while facing away from opponent
Run away/being chased	Loser runs away quickly from advance of winner
Fly away	Loser flies off food surface

Within each category the order of the components is roughly in increasing levels of intensity.

transition matrix

	Slow Approach	Fast Approach	Wing Threat	Fencing	Holding	Boxing Tussling	Retreat	Σ
Slow Approach	-	188	330	479	13	9	243	1262
Fast Approach	330	-	126	187	7	8	13	671
Wing Threat	437	148	-	213	6	5	35	844
Fencing	1437	112	214	-	8	20	421	2212
Holding	6	34	0	1	-	0	0	41
Boxing/ Tussling	19	4	4	14	1	-	4	46
Retreat	75	36	82	1059	1	7	-	1260
Σ	2304	522	756	1953	36	49	716	6336

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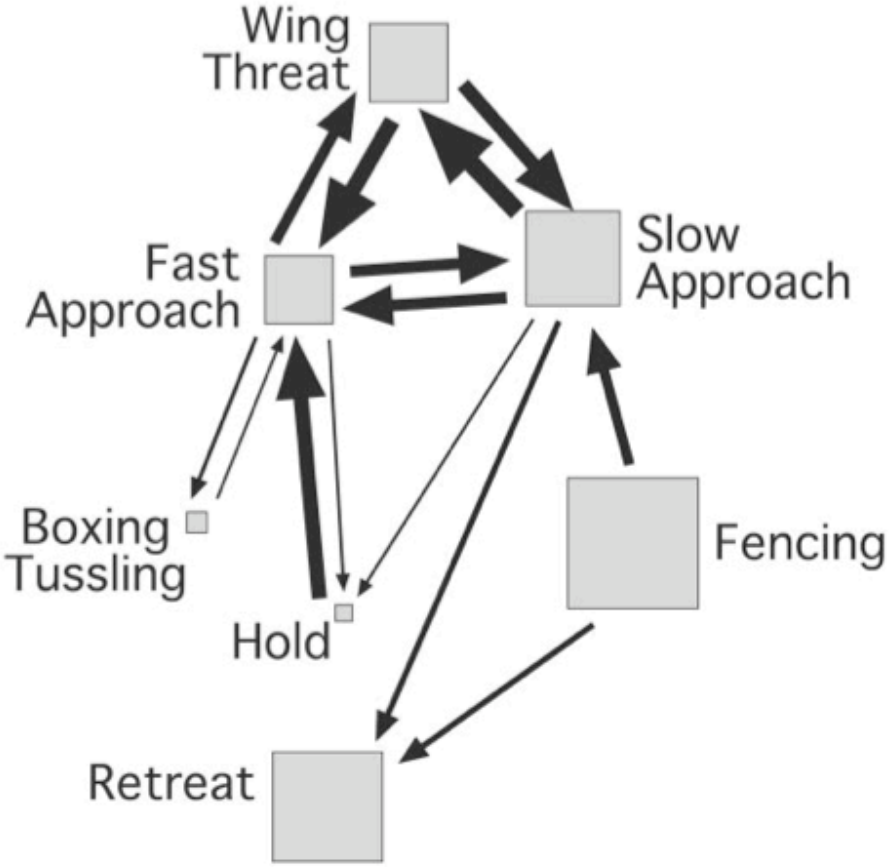
Markov chain of first order of fighting in Drosophila



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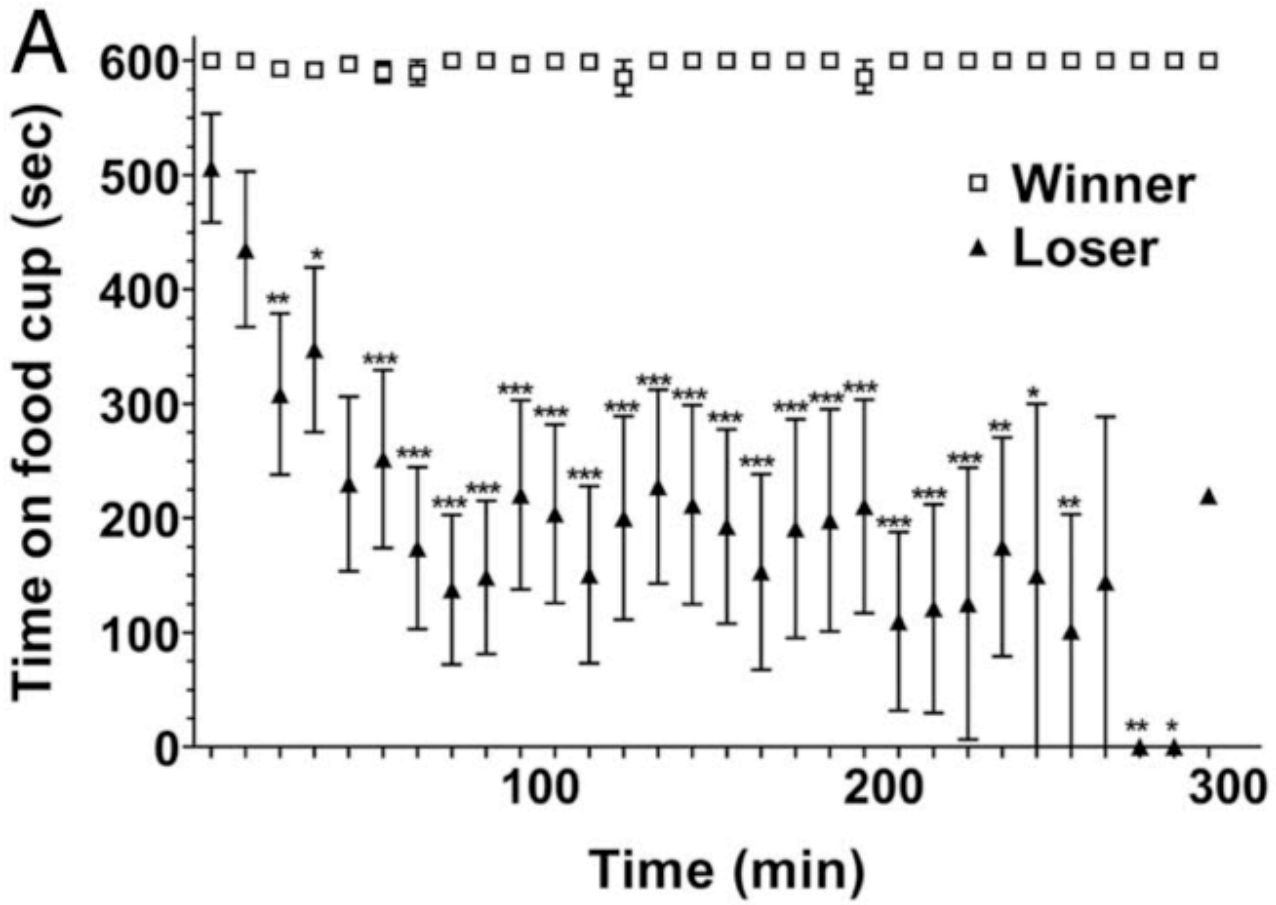
The biological advantage of winning



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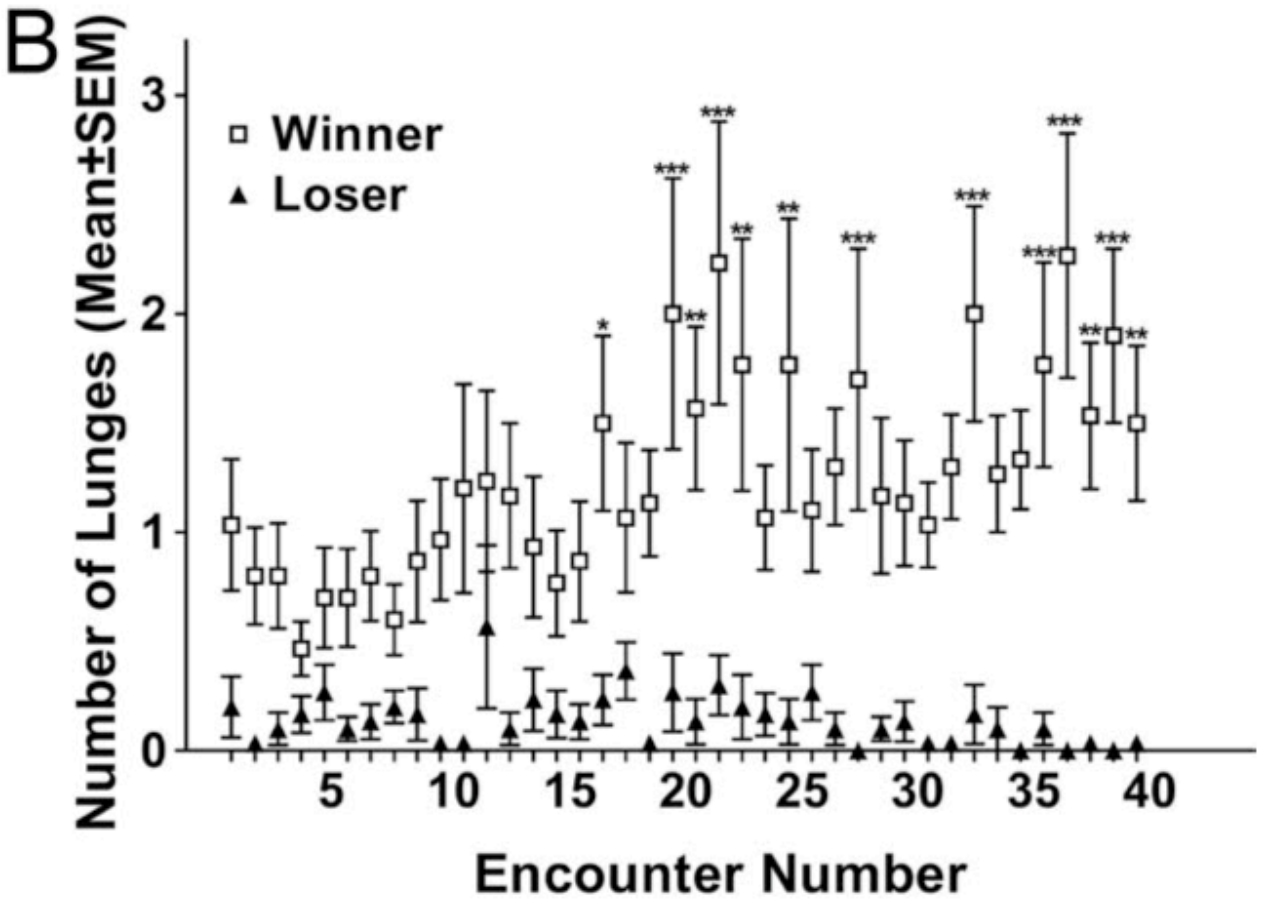
The winner likes to attack more



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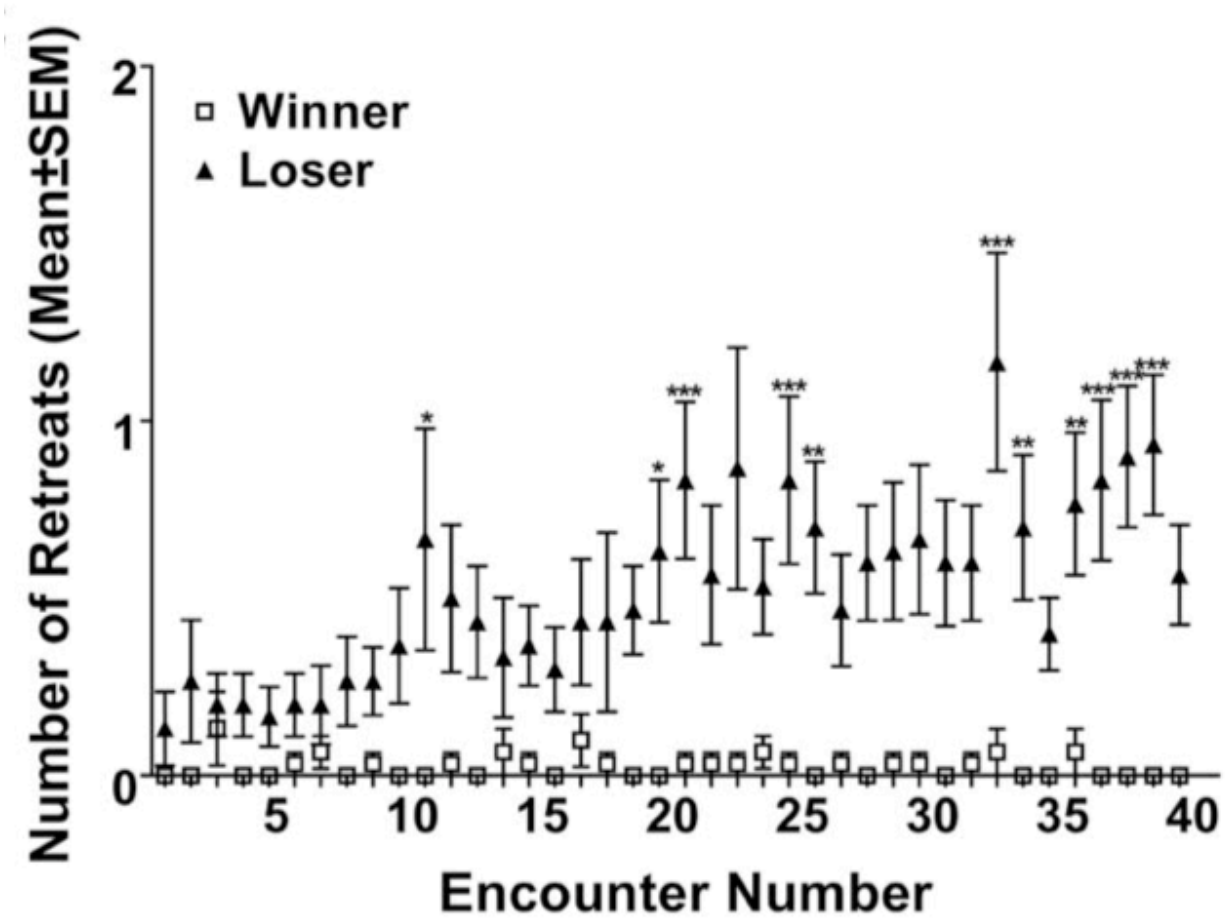
losing makes you cautious



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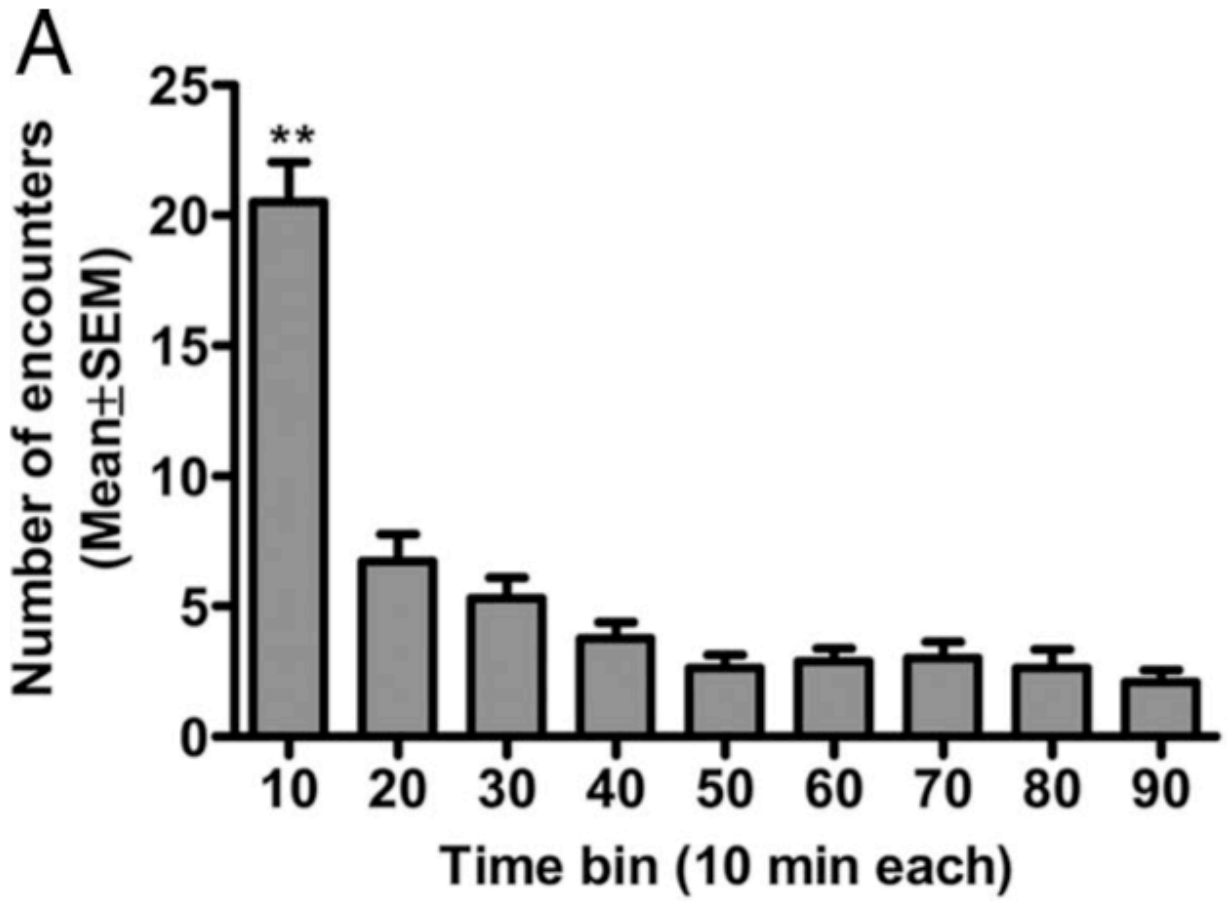
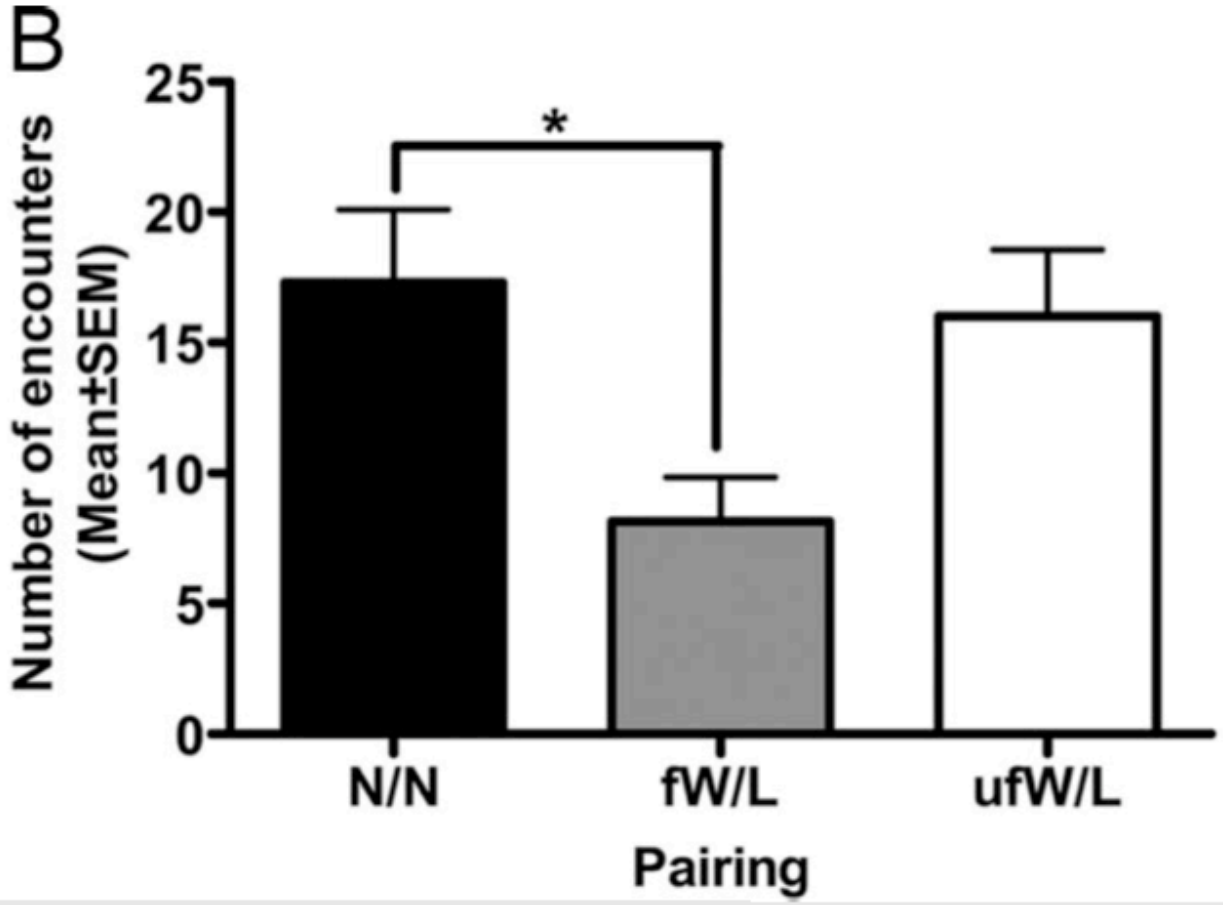
number of fights decrease due to the establishment of a pecking order (hierarchy)



knowledge of pecking order prevents fighting



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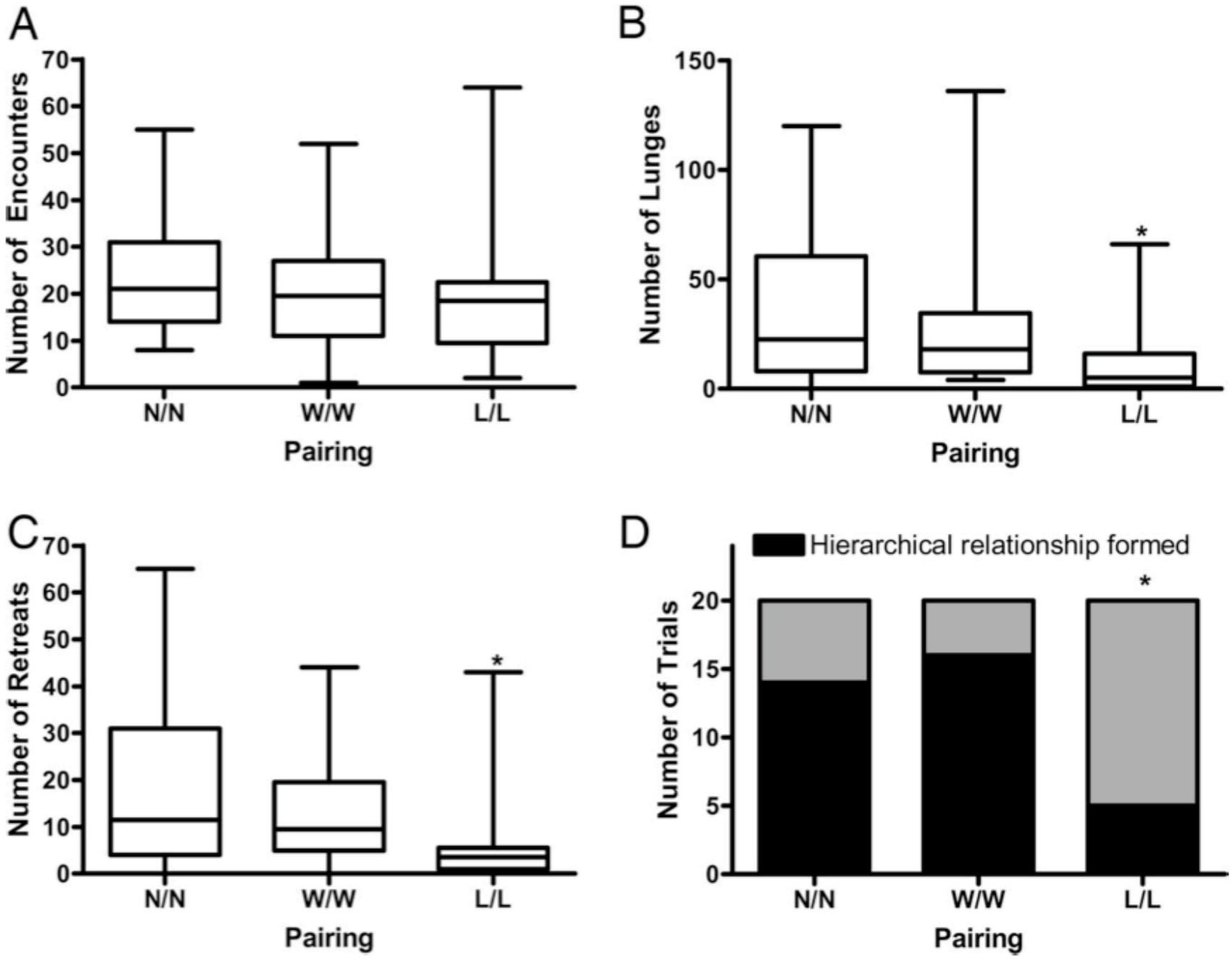
Losers and winners develop different strategies



hbach

fighting is sex specific

The fly standing on the left is the beloved female

female fighting

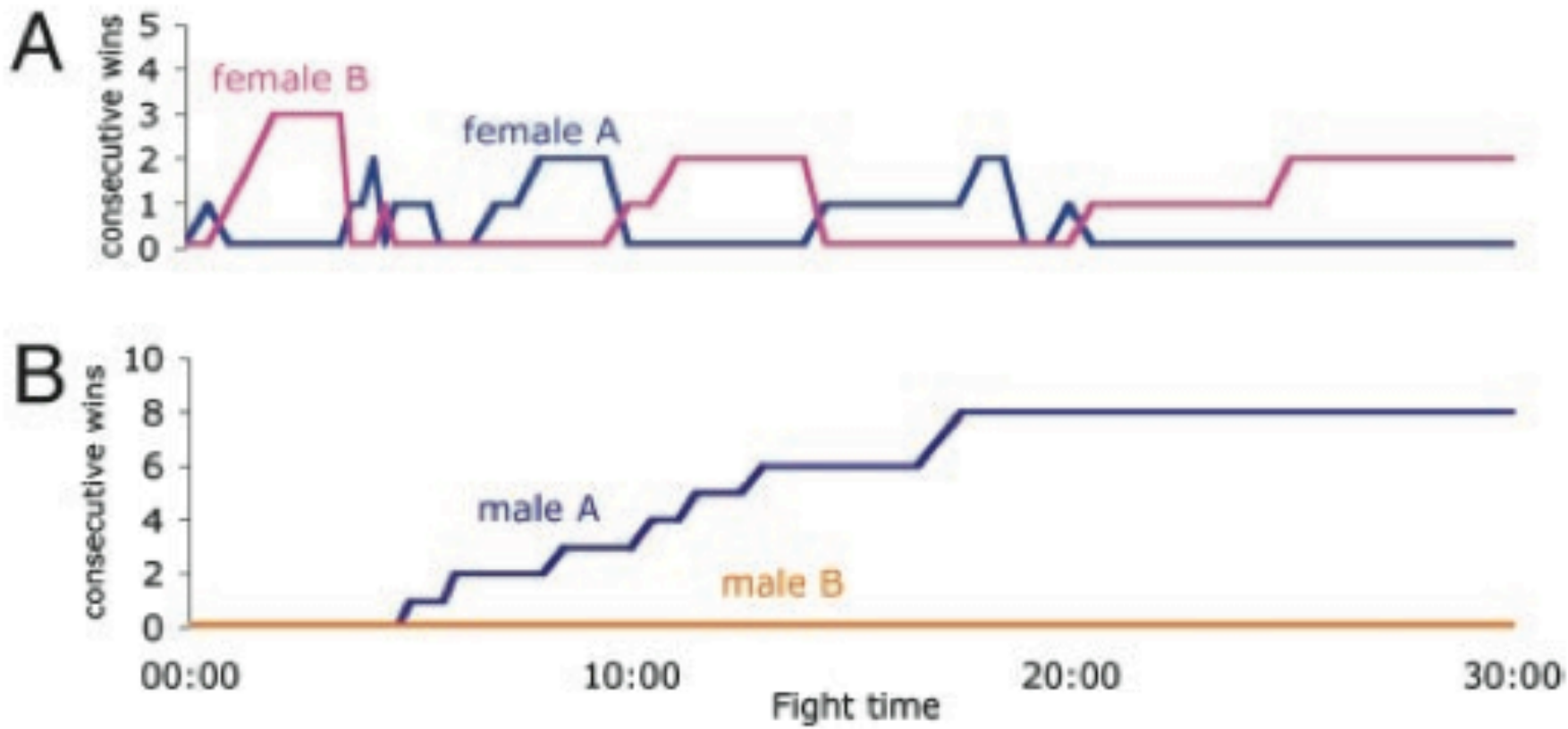


Fig. 3. An example of a fight between a pair of virgin females (*A*) and a pair of males (*B*). In the male fight, the subordinate fly retreated from the food cup without returning after the last encounter. In the female fight, both females were on the food cup for the 30-min period, and there were five reversals in the pattern of consecutive wins.

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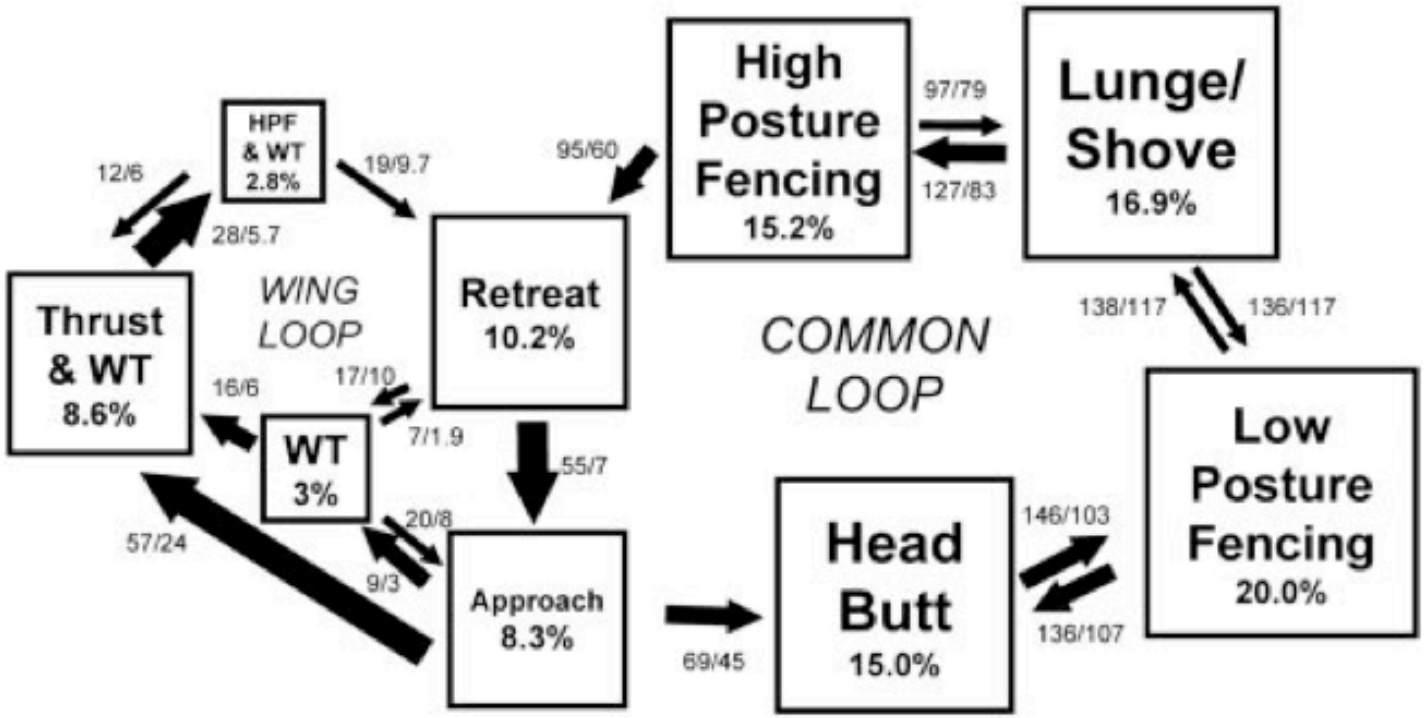
transition probabilities between behavioral subroutines in females



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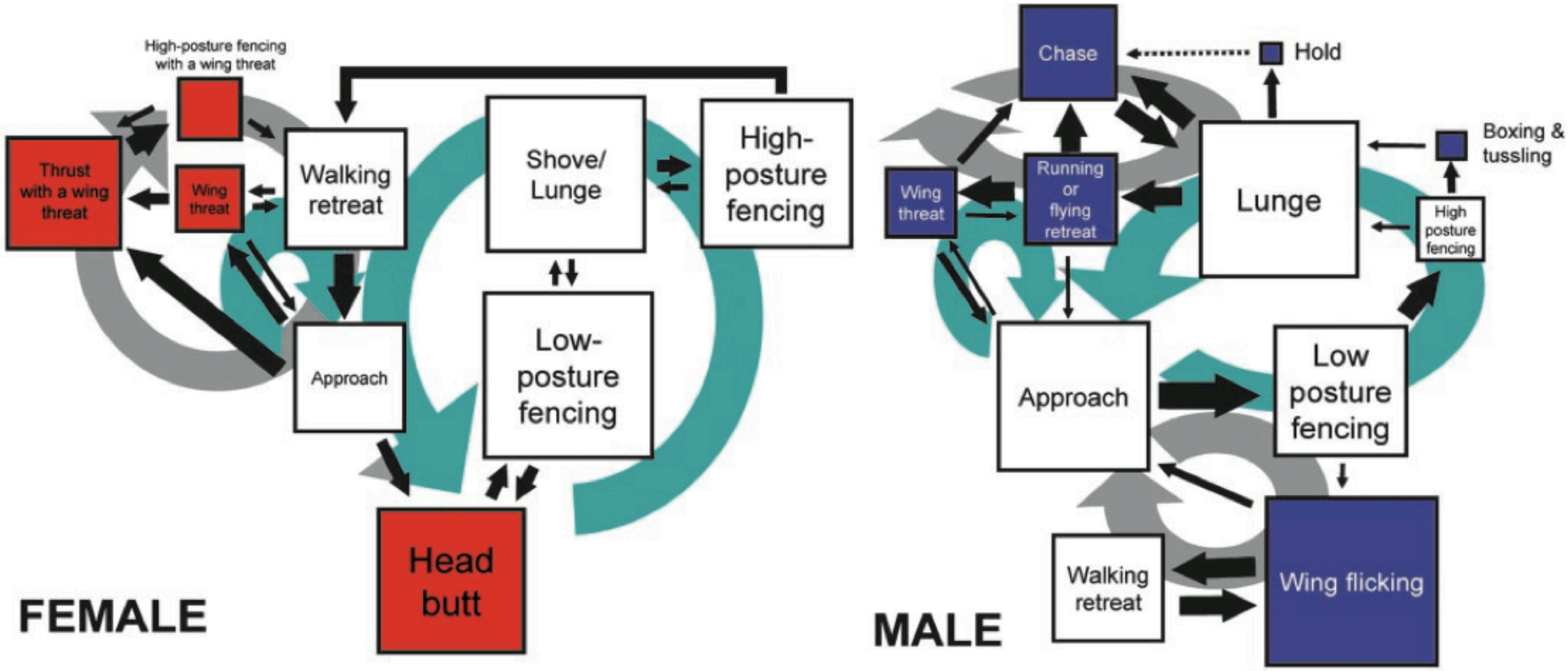
Gender-differences in aggressive behavior



Red: female-specific

Blue: male-specific

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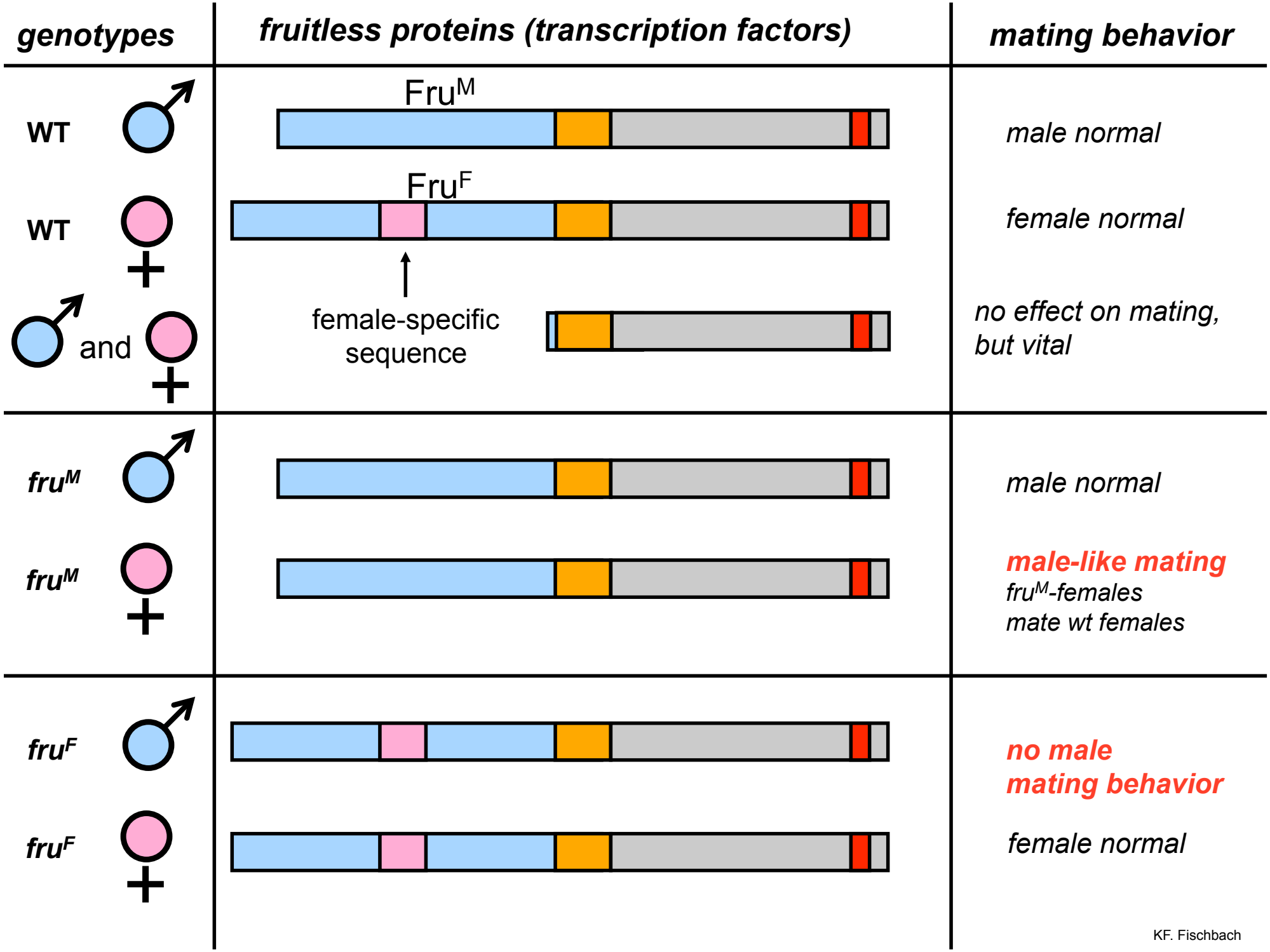
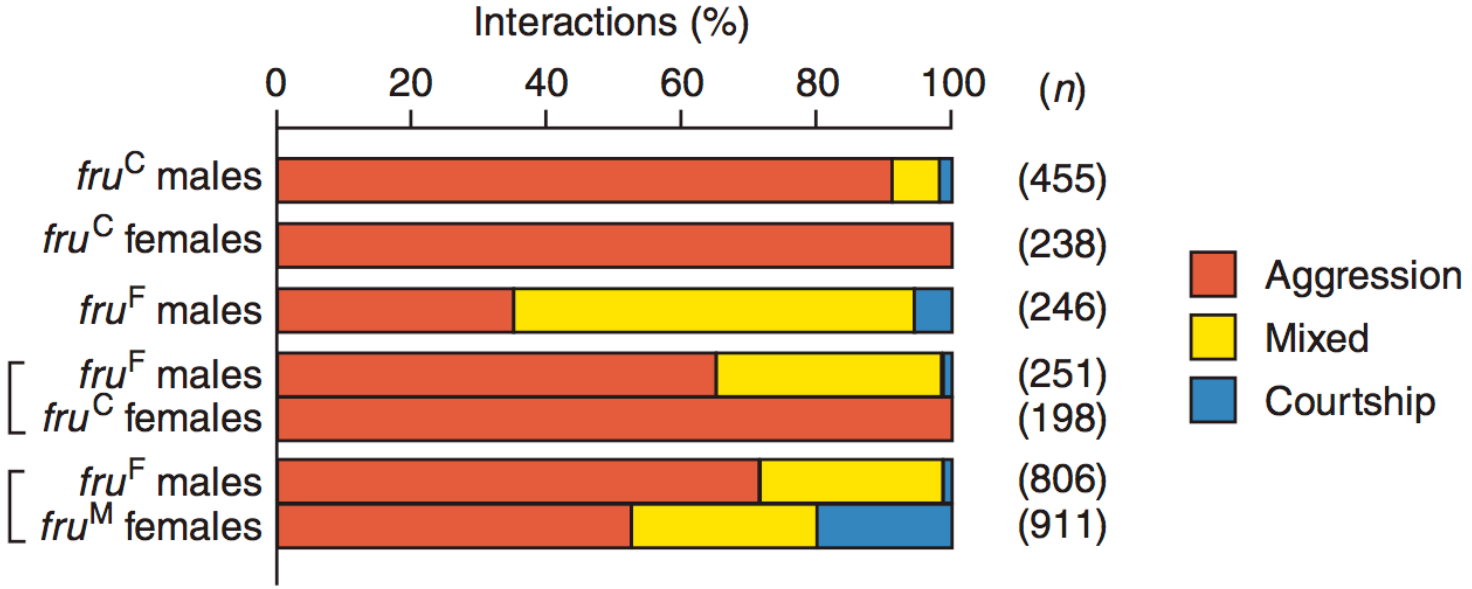
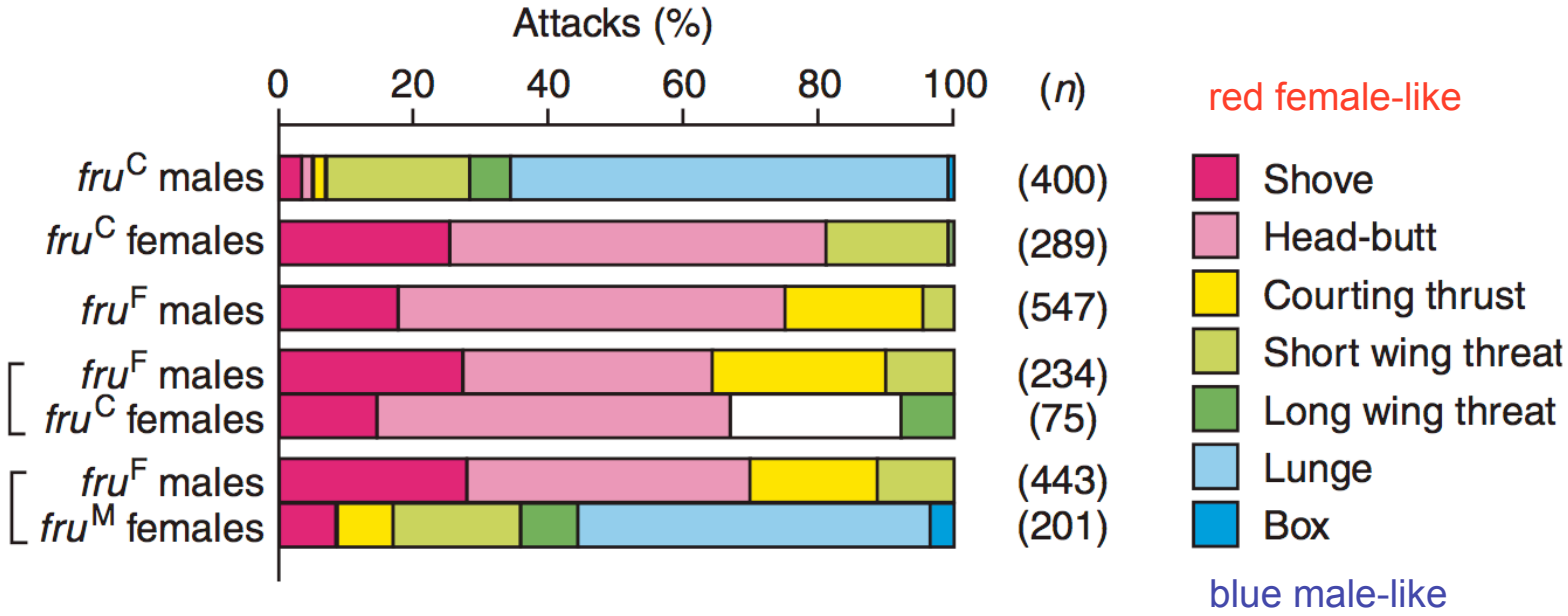
aggressive behavior and the fruitless gene


genotypes
fruitless proteins (transcription factors)
mating behavior
WT
WT
and
Fru^M
Fru^F
female-specific sequence
male normal
female normal
no effect on mating, but vital
fru^M
fru^M
male normal
male-like mating
fru^M-females mate wt females
fru^F
fru^F
no male mating behavior
female normal
KF. Fischbach

aggressive interactions in fru splicing mutants paired to maximally exclude courtship components



aggressive interactions in fru splicing mutants : How are „male“ and „female“ fighting components distributed?



fruitless regulates aggression and dominance in flies

here female-like fighting in fru^F males

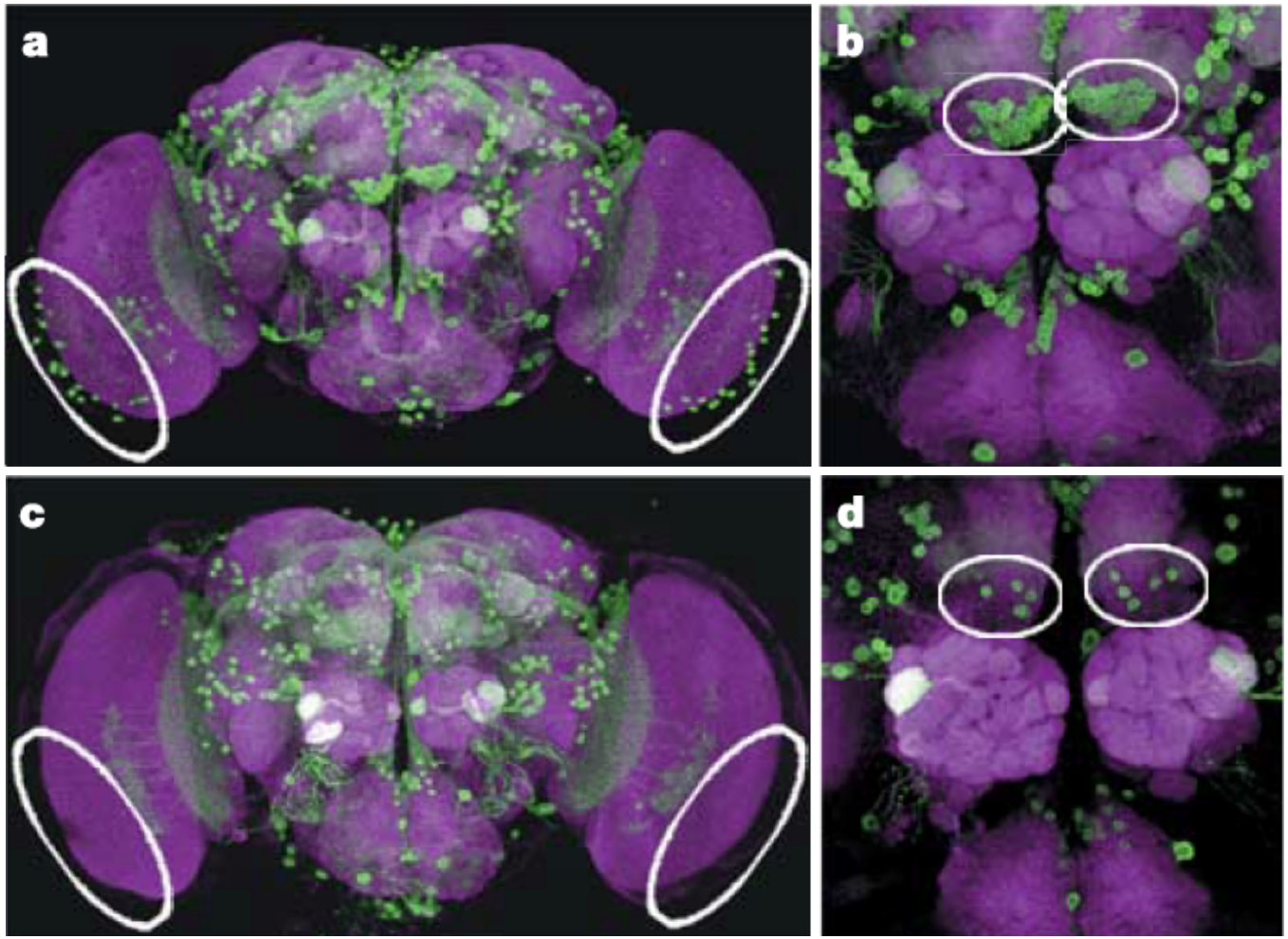
fruitless regulates aggression and dominance in flies

fru^M-female aggressively chases fru^F male: for her the male is a male rival. For him she is just a strong dominant other female)

Sexual dimorphism in the Drosophila brain

male

female



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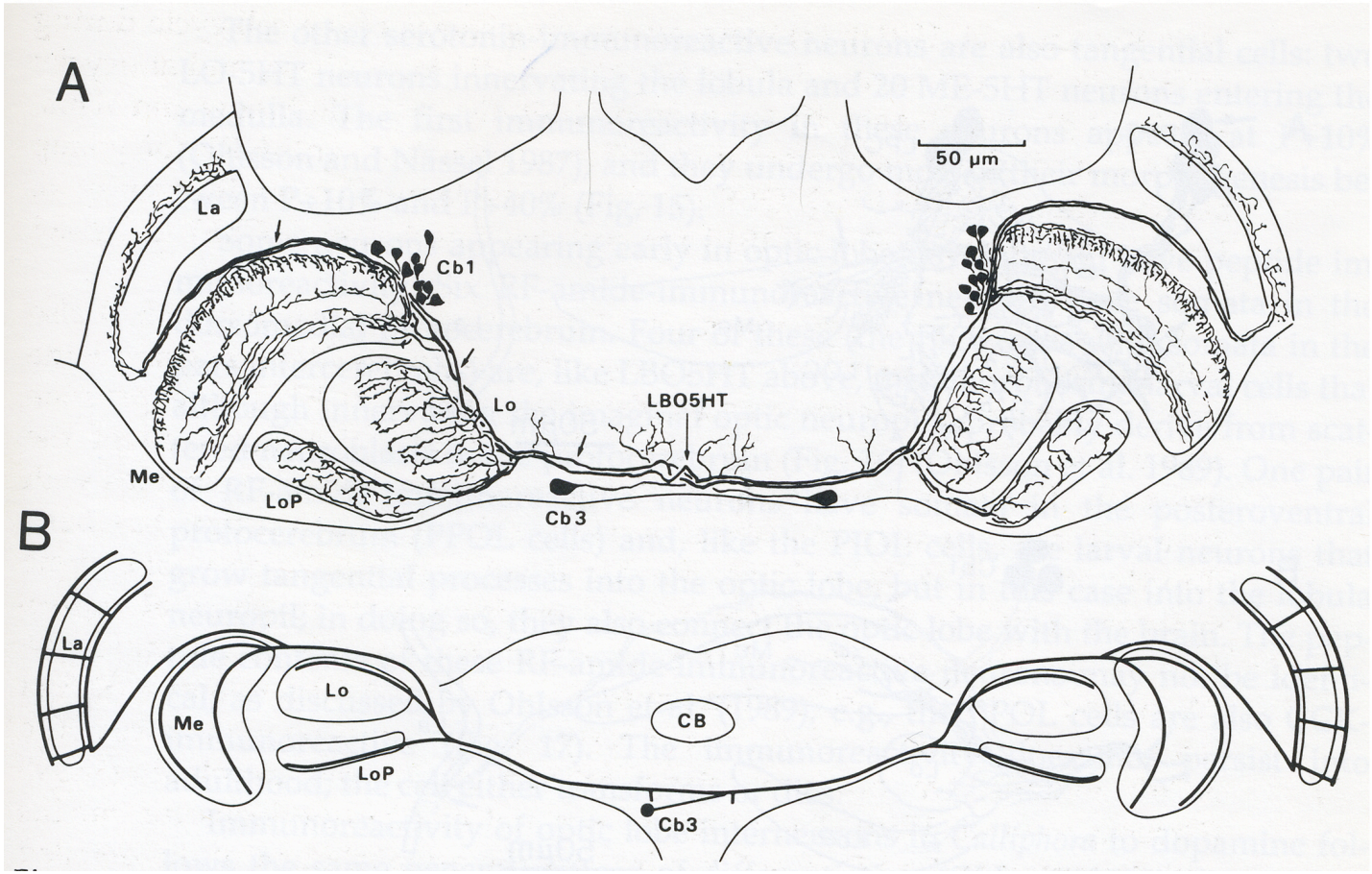
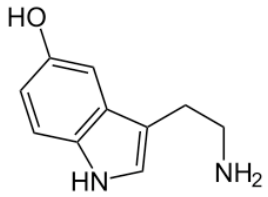
Serotonergic neurons in the Drosophila brain





Serotonine
= 5-Hydroxytryptamine (5-HT)

These neurons have been subjected to genetical and pharmacological manipulation

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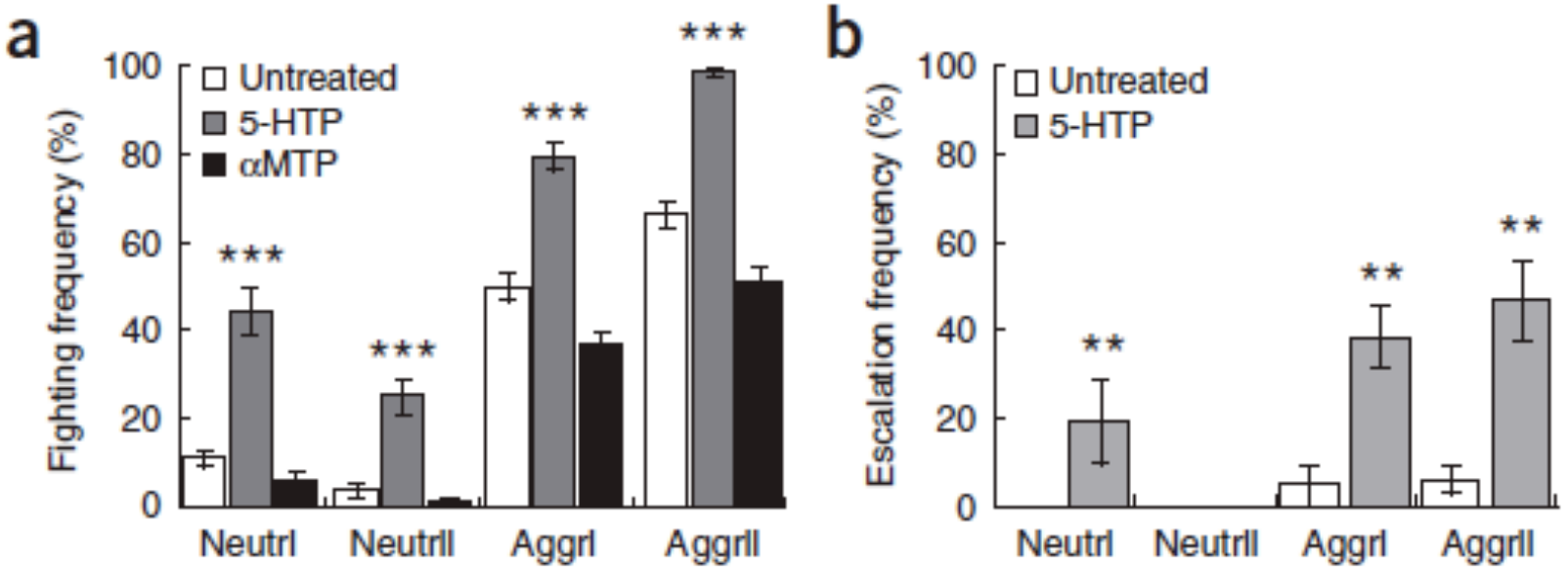
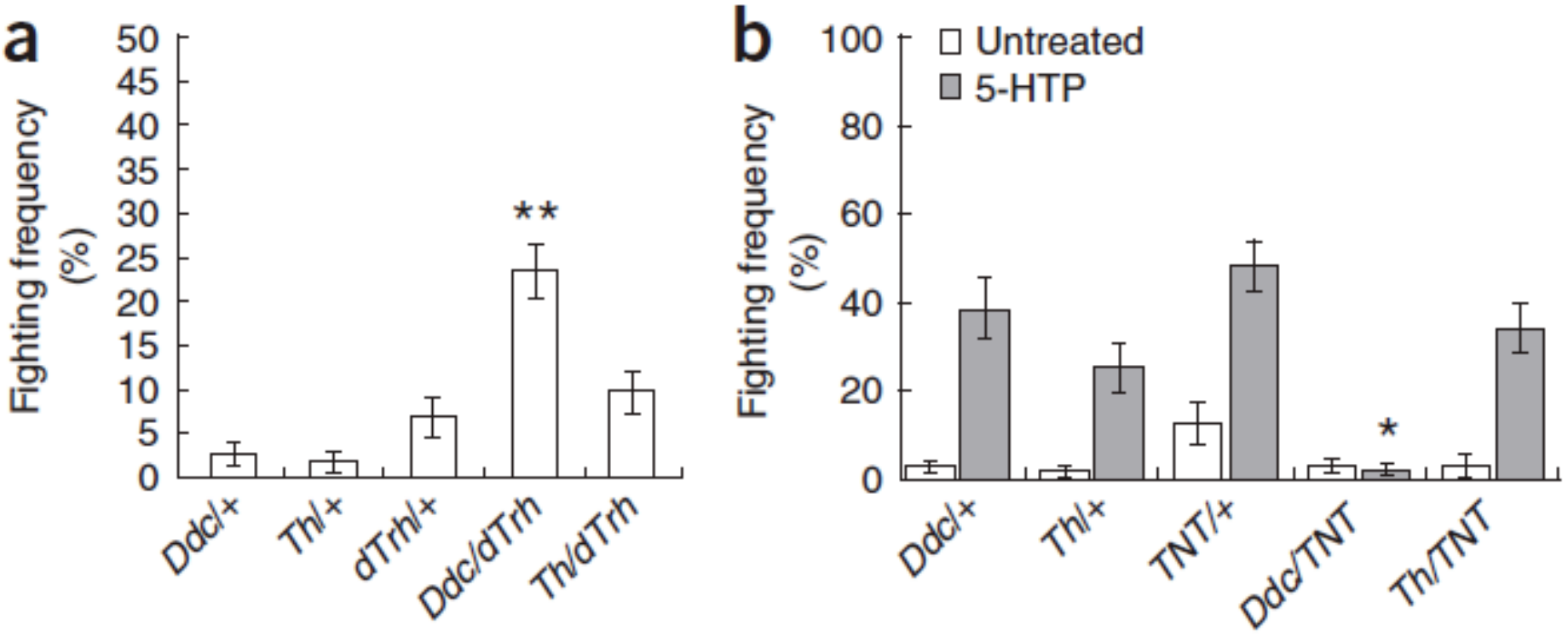
5-HTP (5-hydroxytryptophan, a precursor of 5-HT) increases linearly aggression in selected lines



αMTP = α-methyltryptophan = inhibitor of 5-HT metabolism

Dierick & Greespan Nature Genetics 39, 678-682

Genetic elevation of the 5-HT machinery on fighting and its silencing on 5-HTP responsiveness



Ddc-Gal4 drives in serotonergic and dopaminergic neurons
Th-Gal4 drives indopaminergic neurons only
No specific serotonergic Gal4 available
dTrh = tyrosin hydroxylase gene, rate limiting conversion of tryptophan to 5-HTP
TNT = tetanus toxin light chain

Dierick & Greespan Nature Genetics 39, 678-682

Summary

1. invertebrates are well suited for studies on aggression
2. drosophila is the most important model systems used
3. aggressive behavior is modified by experience (loser- or winner mentality)
4. aggressive behavior differs between the sexes
5. male flies develop territorial behavior, female flies do not
6. the *fruitless* transcription factor, which is active in about 2% of all neurons, switches sexual as well as sexually dimorphic fighting behaviour
7. Serotonin (5-HT) levels affect aggression

Thank you

for your attention