

Hamlet on the Fly:

To be or not to be a Foreleg?



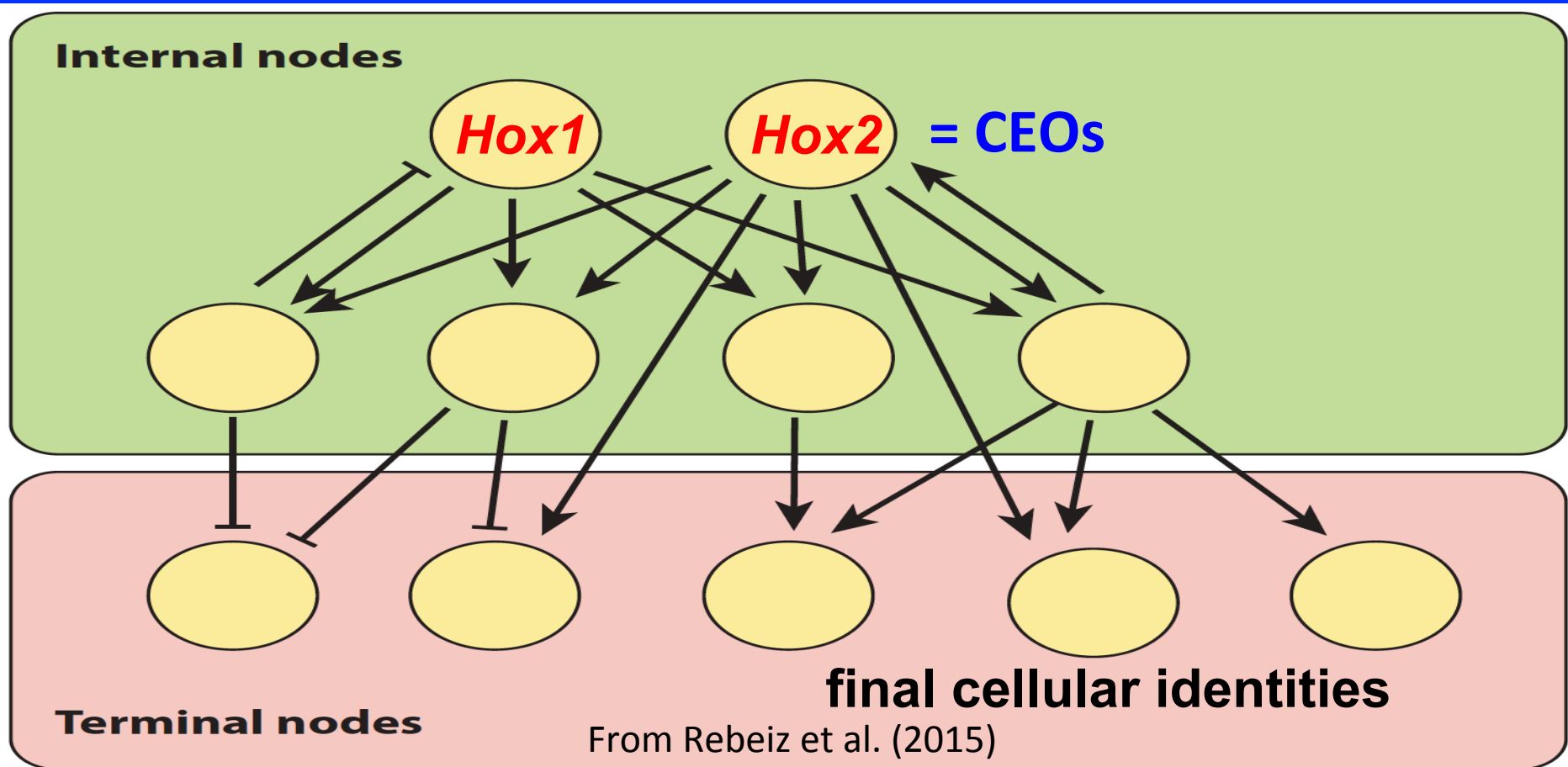
Lewis Held

Wed., February 7, 2018

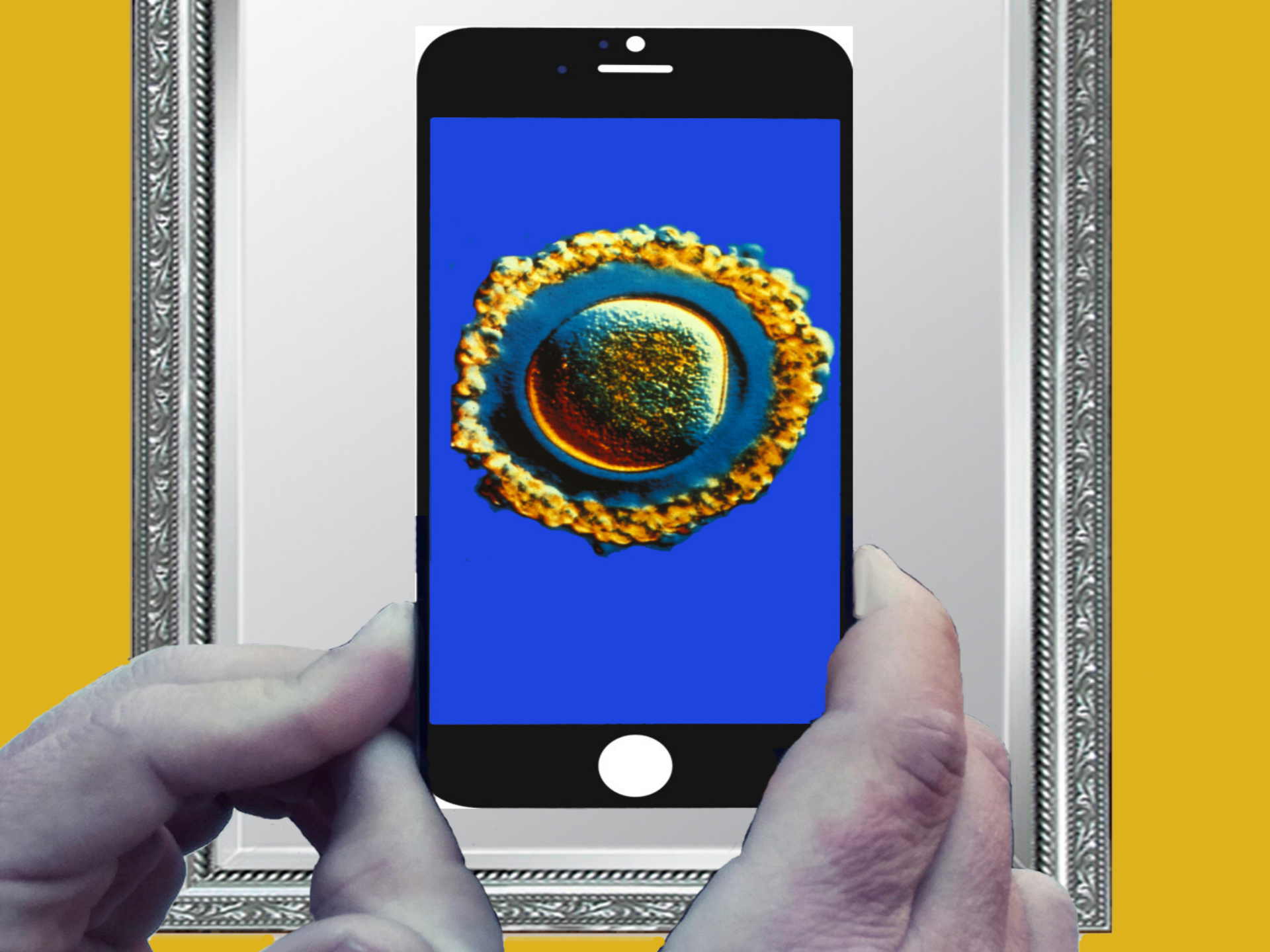
4 PM, Biology Room 101

Q: How do cells decide what to be?

A: They make a series of ~binary choices with “master” (Hox) genes as CEOs.





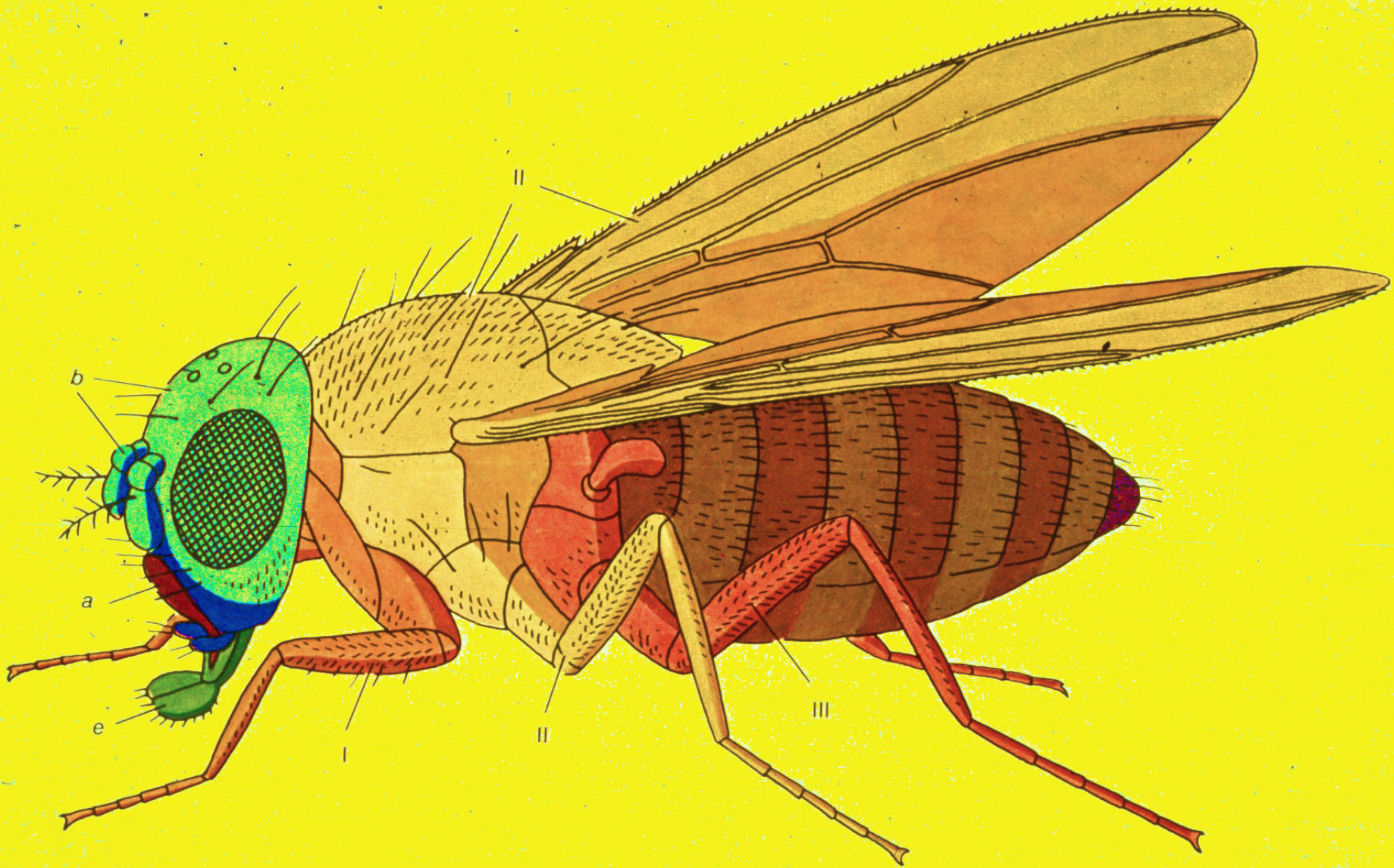




IN GOD WE TRUST

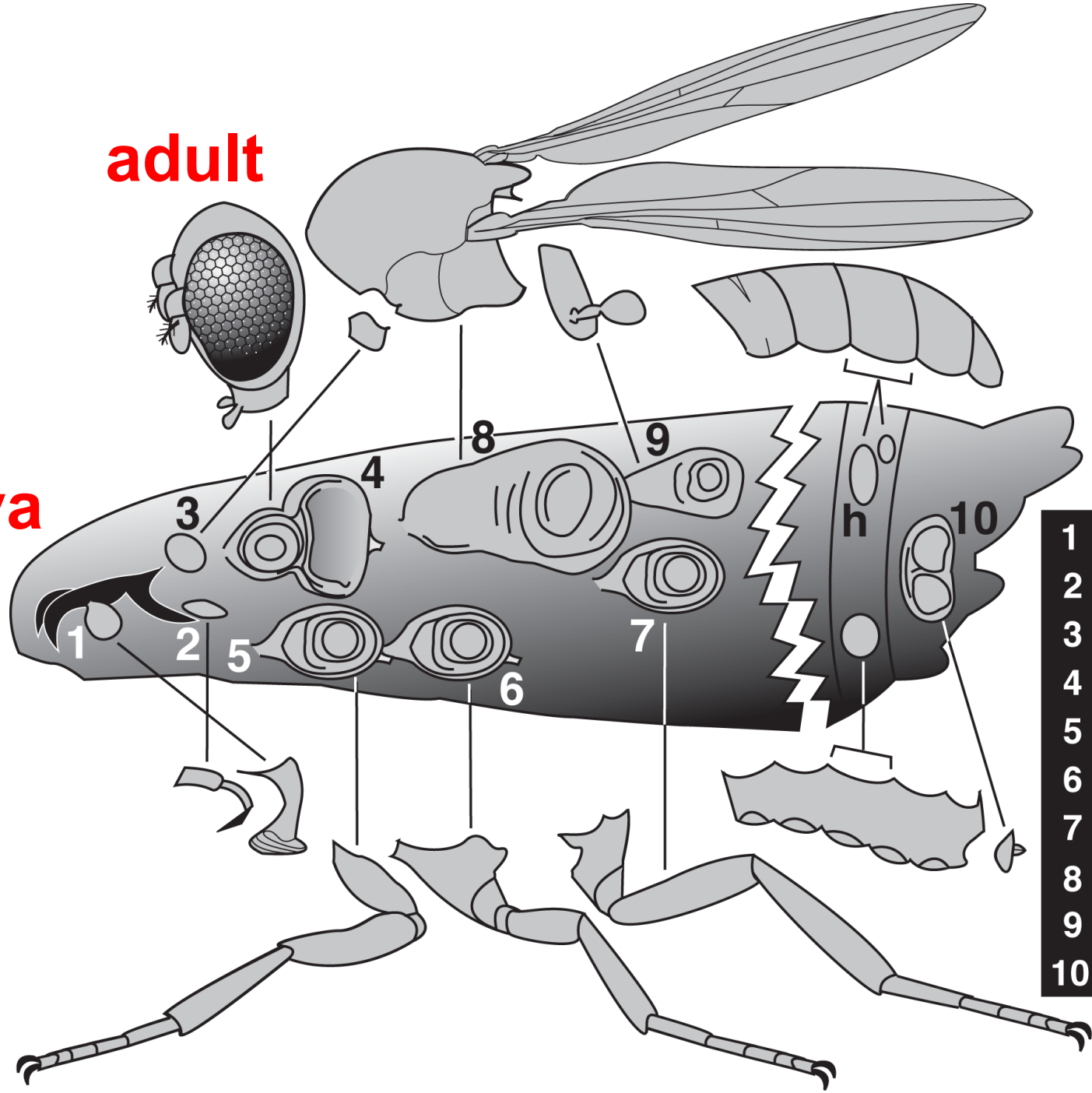
LIBERTY

1982



adult

larva

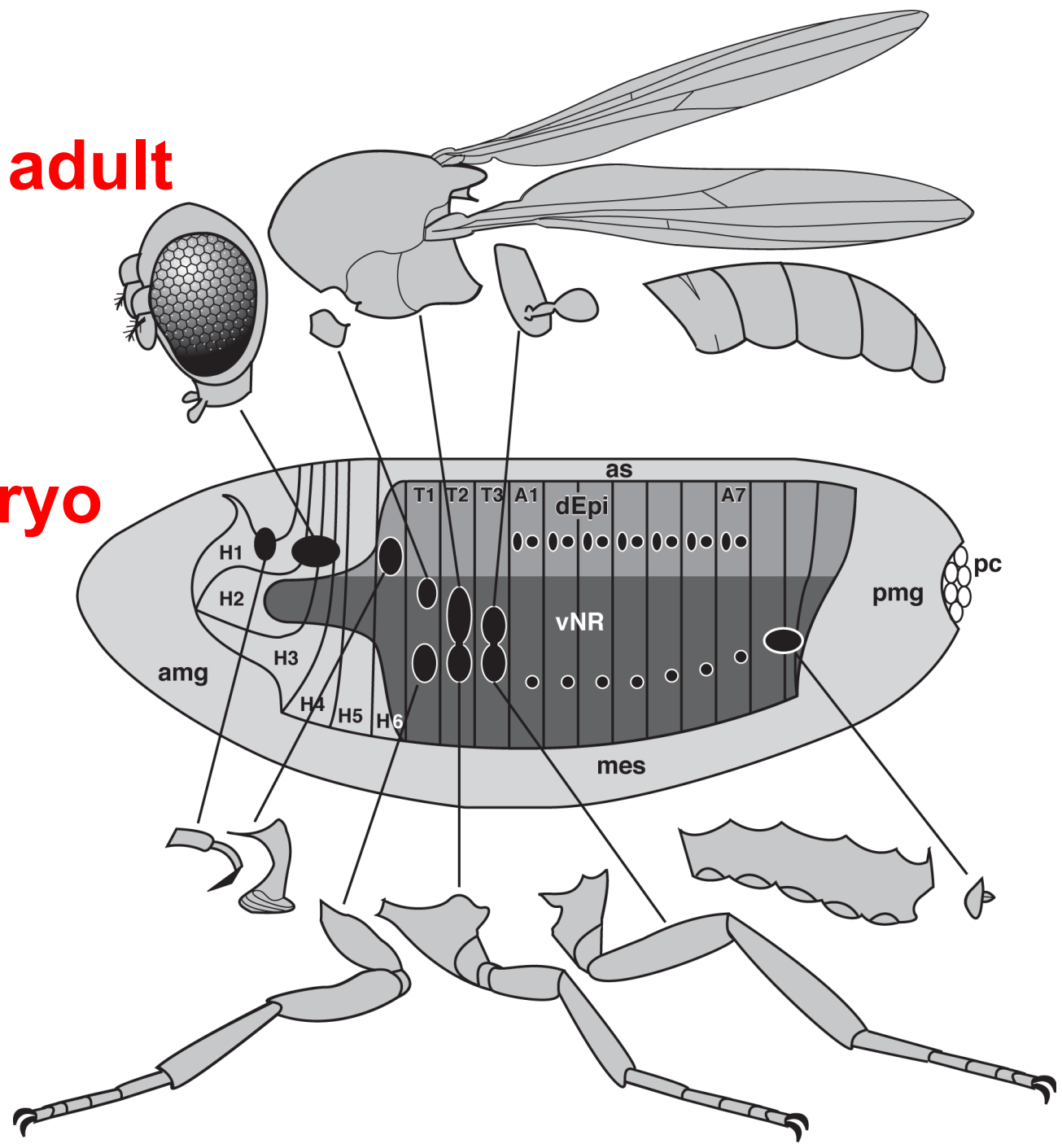


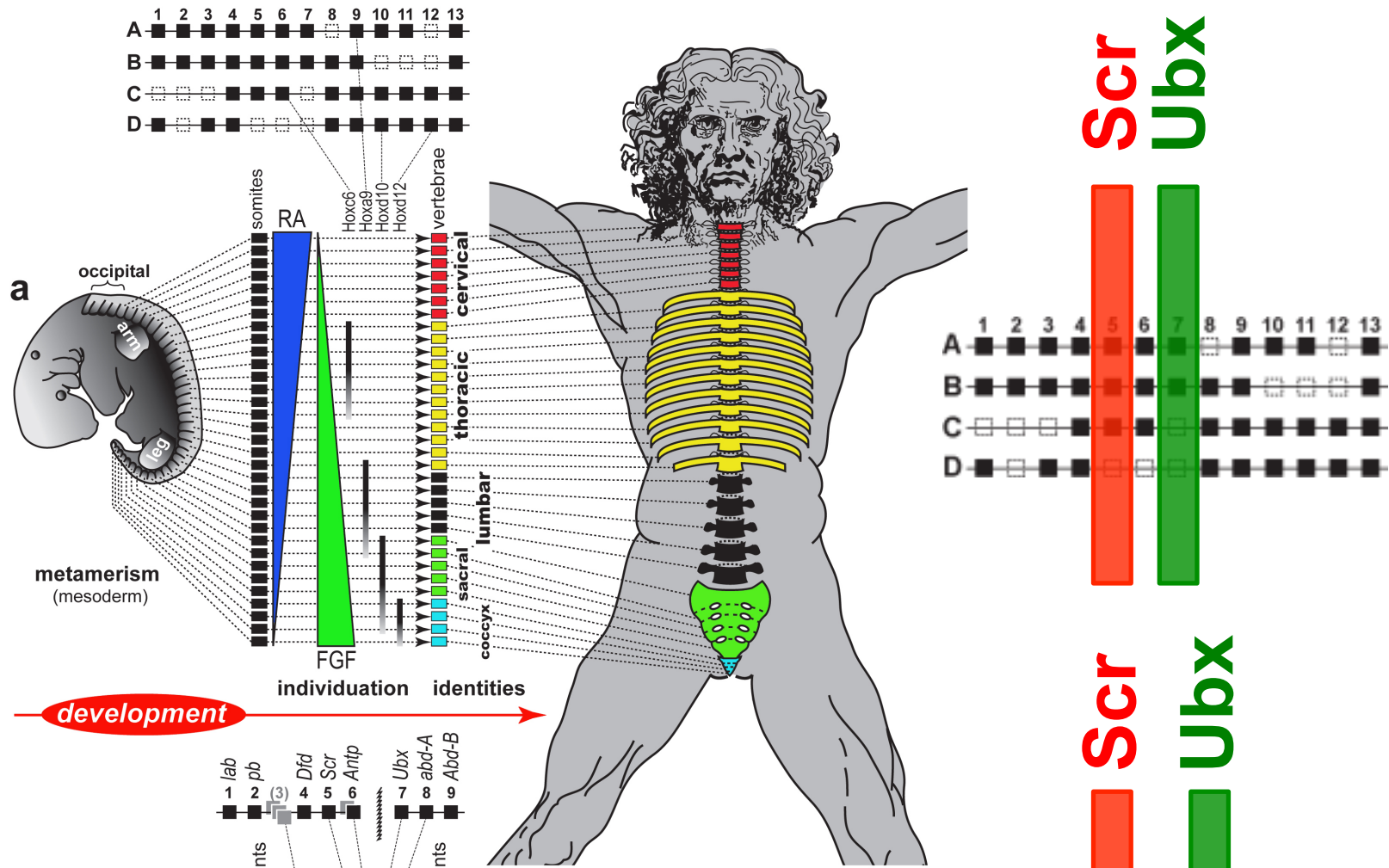
Discs

1	Labial
2	Clypeolabral
3	Humeral
4	Eye-antennal
5	1st Leg
6	2nd Leg
7	3rd Leg
8	Wing
9	Haltere
10	Genital

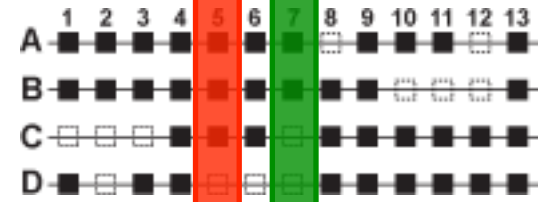
adult

embryo

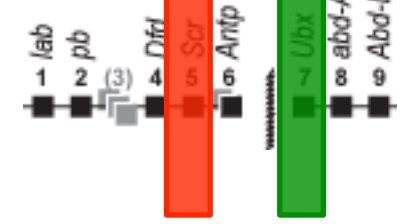
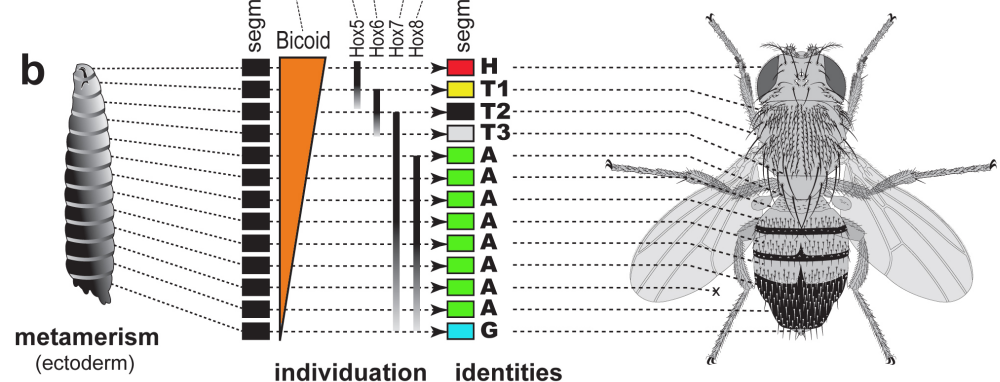




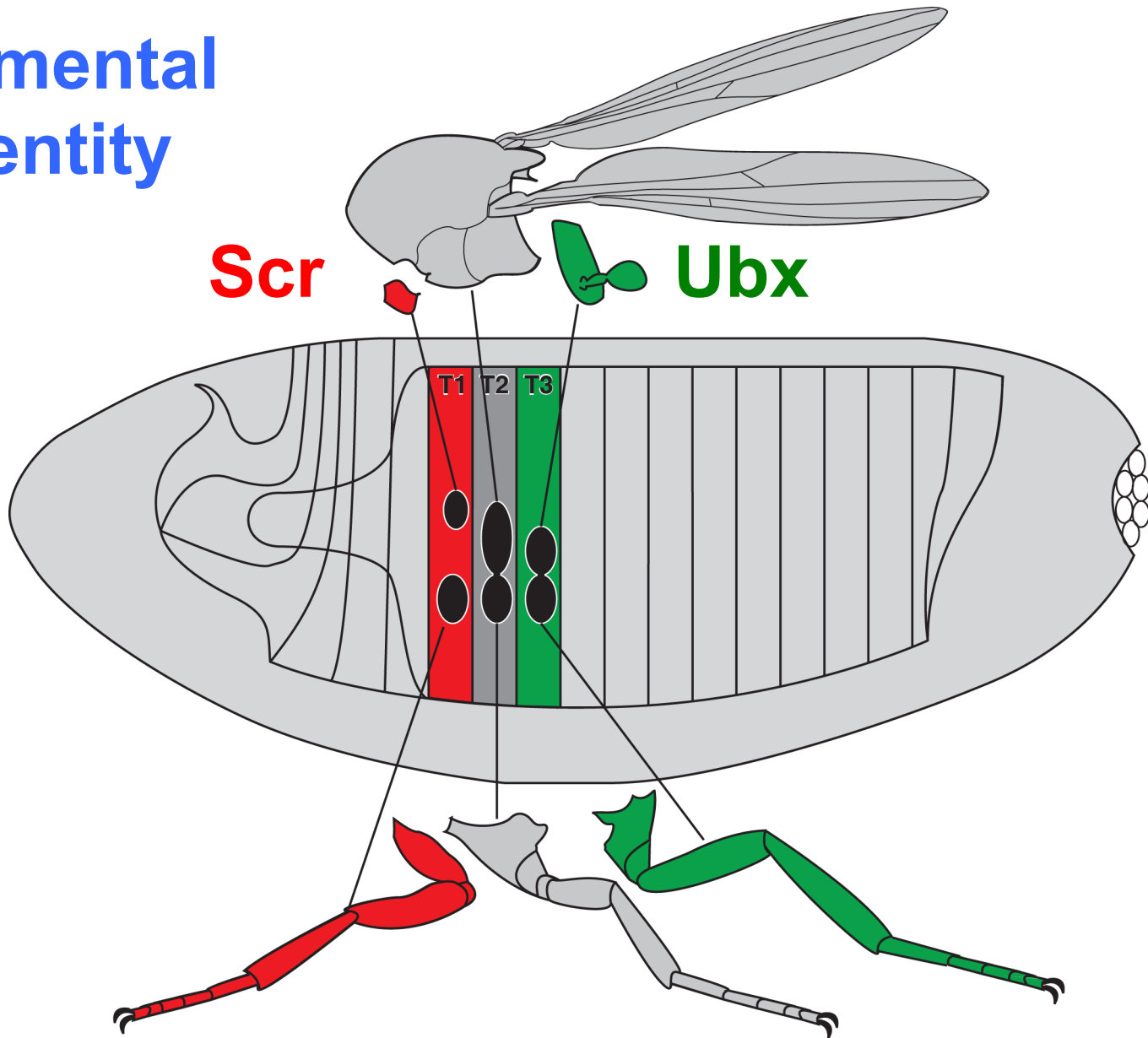
Scr
 Ubx



Scr
 Ubx



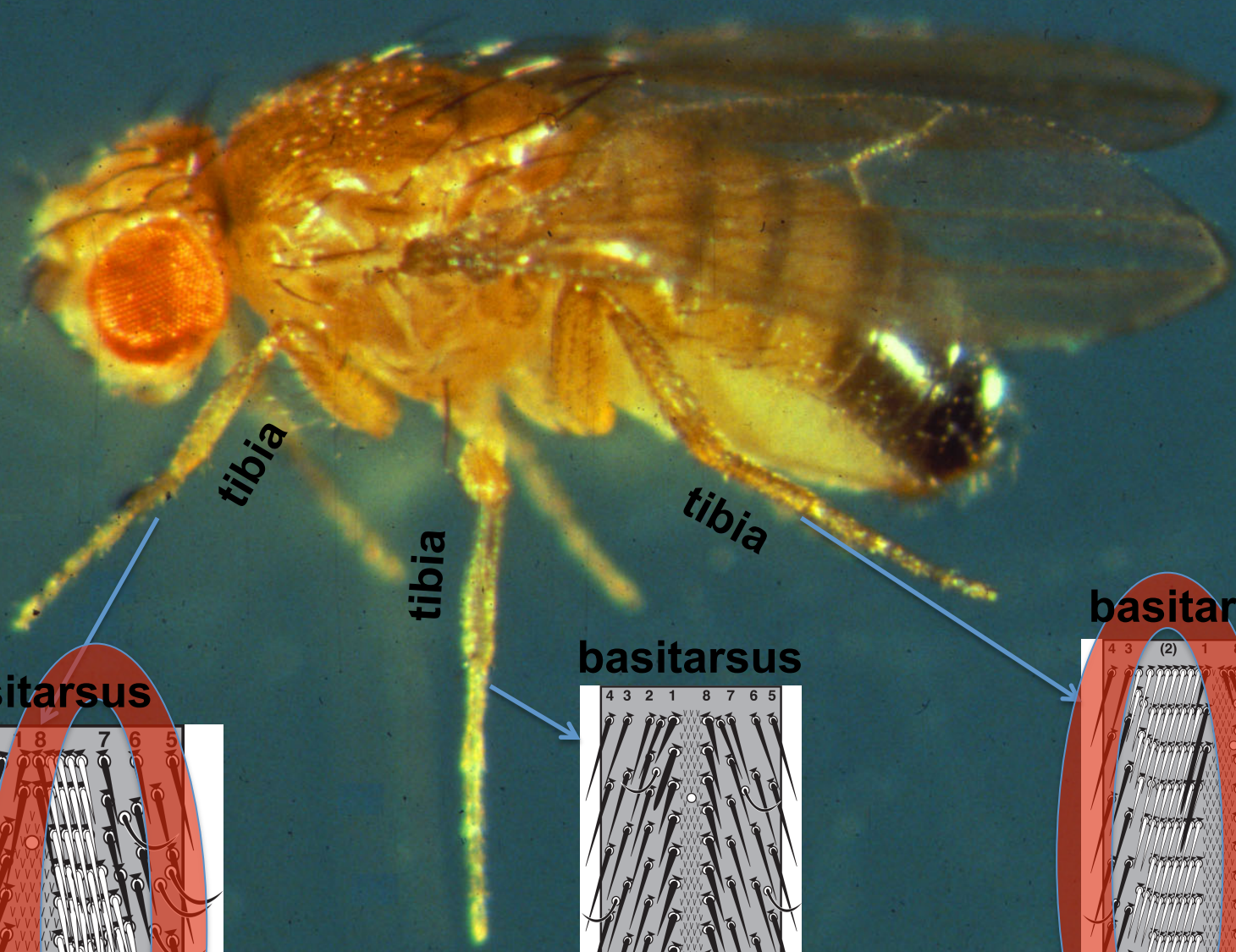
segmental identity



bithorax
mutant



~~Ubx~~



tibia

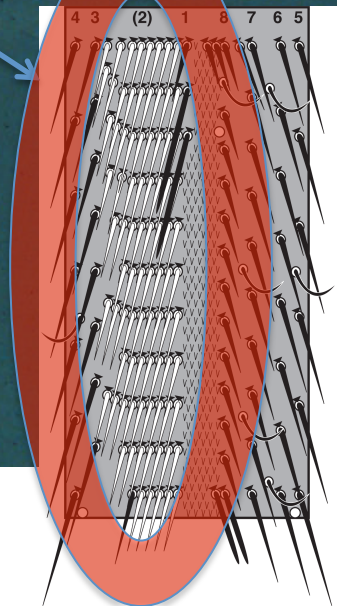
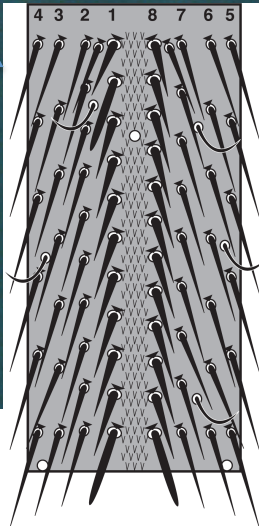
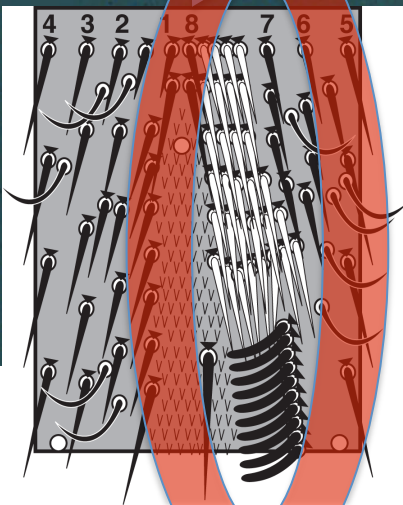
tibia

tibia

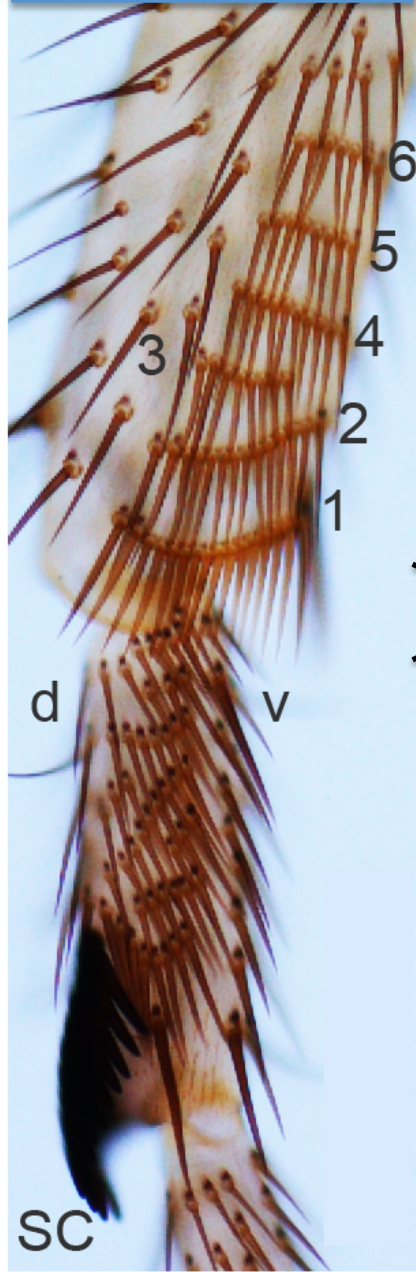
basitarsus

basitarsus

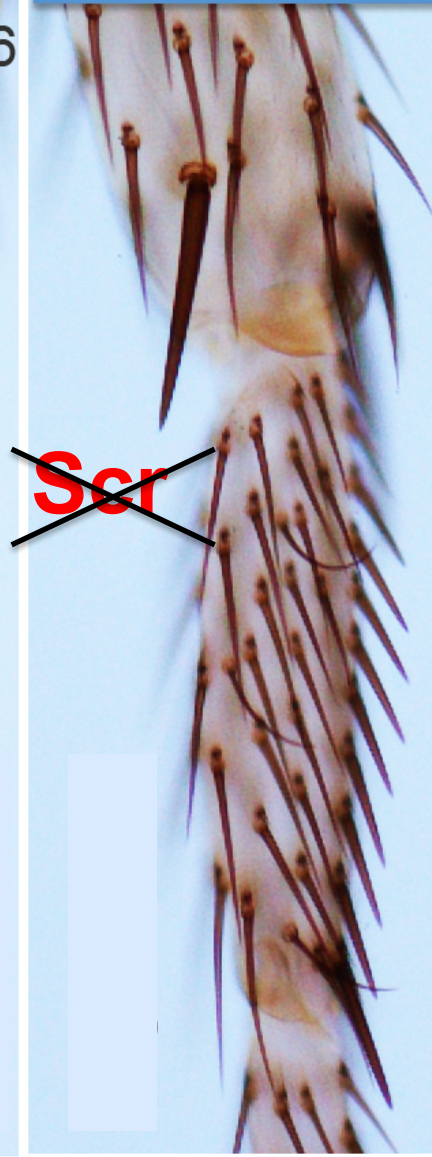
basitarsus



foreleg

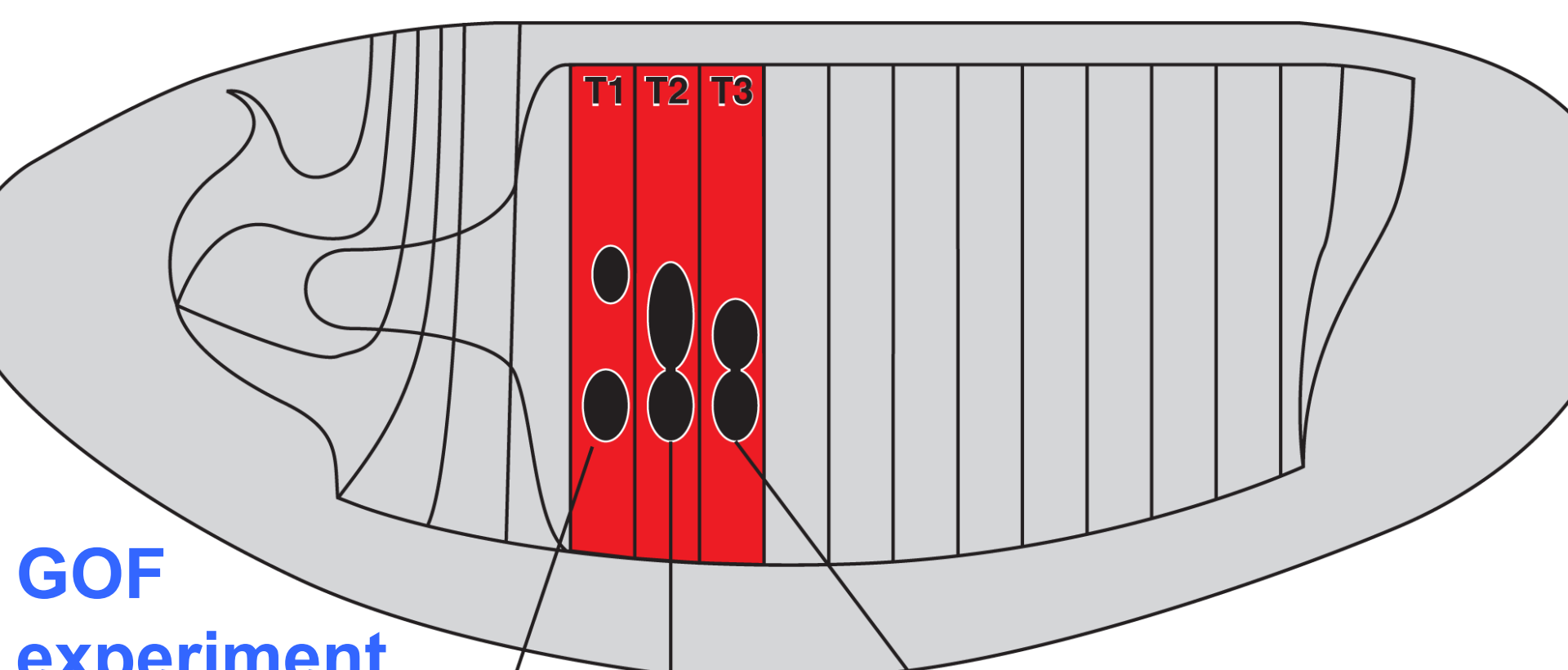


foreleg
Scr-null

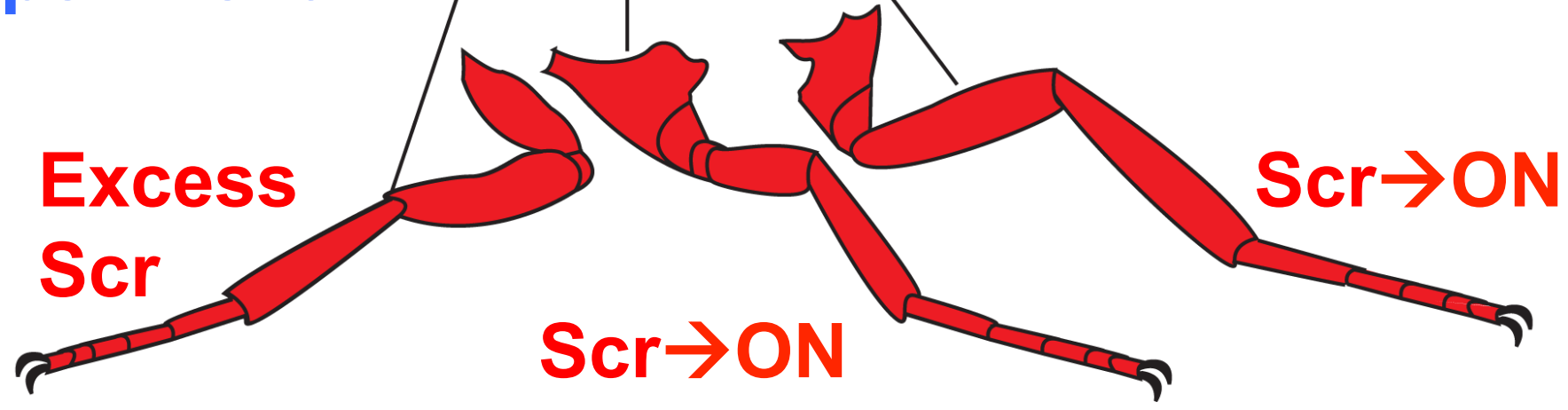


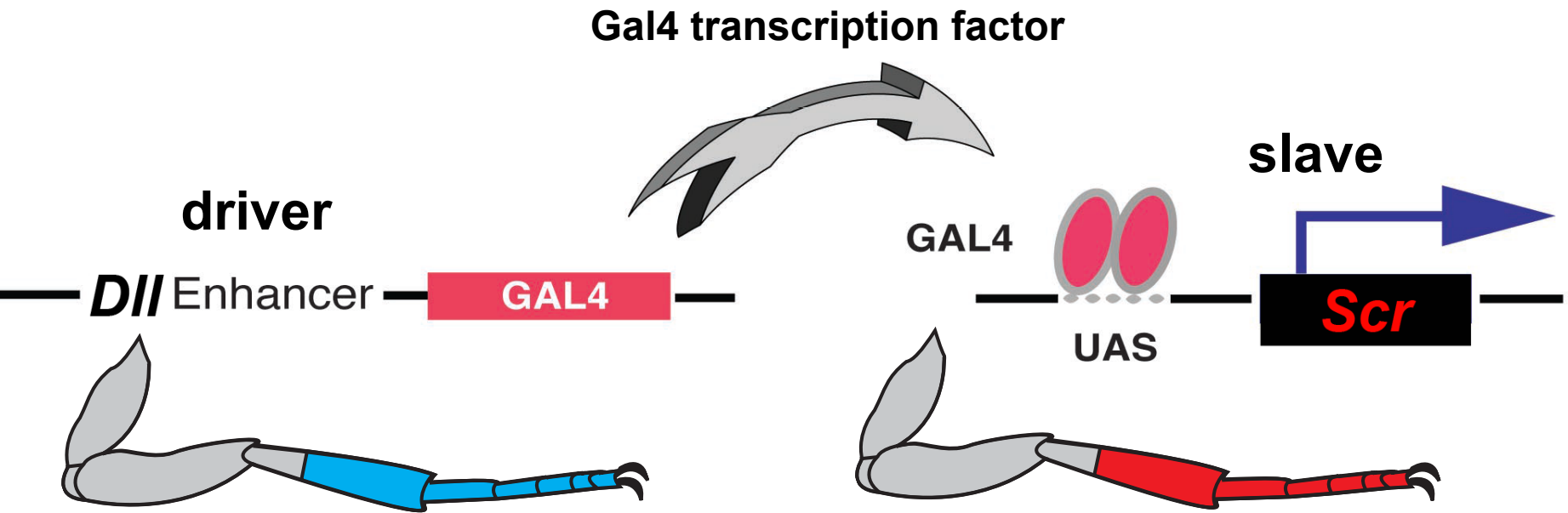
midleg



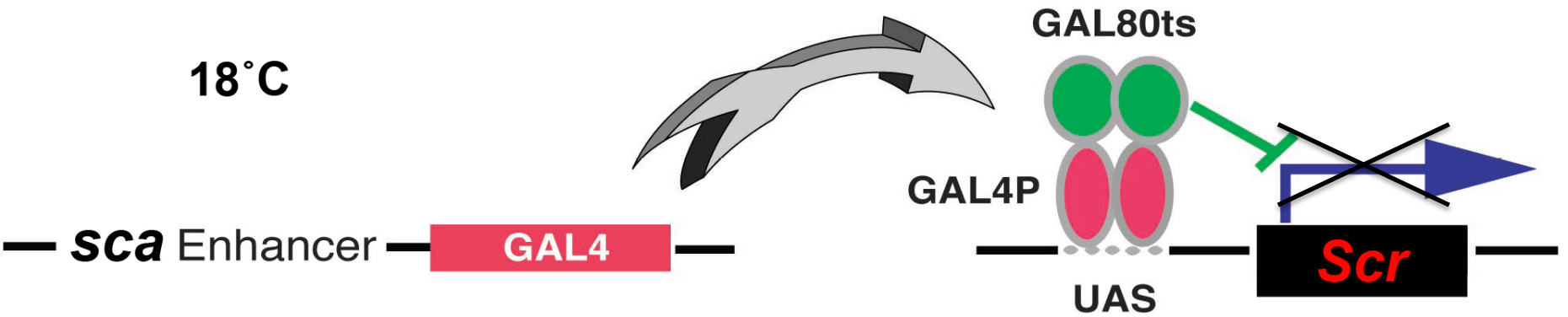


**GOF
experiment**

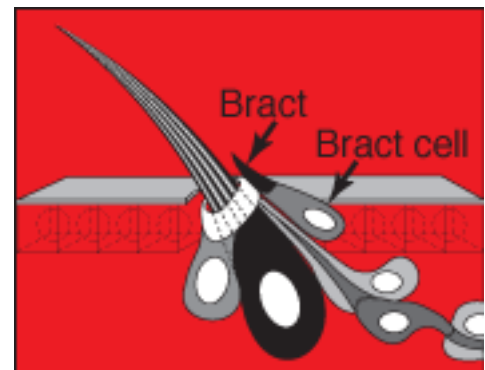
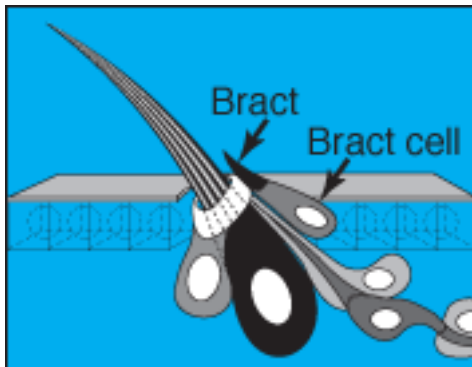
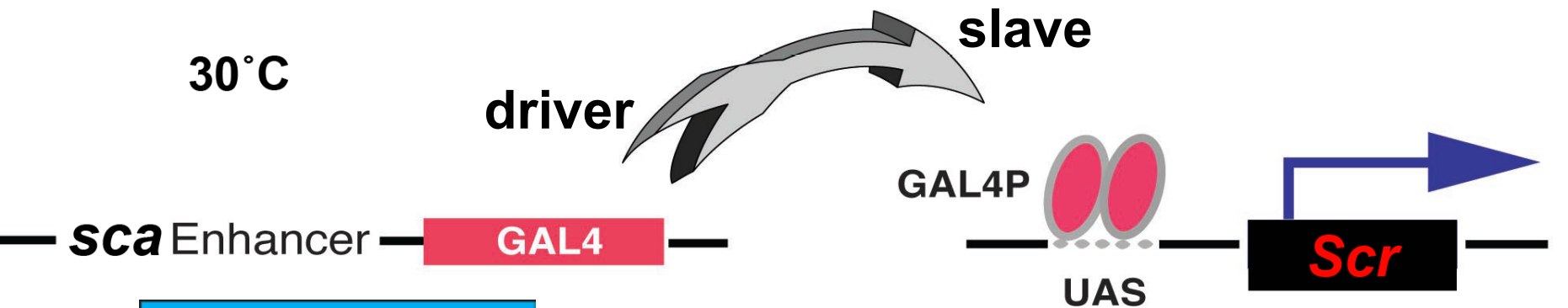




18°C



30°C



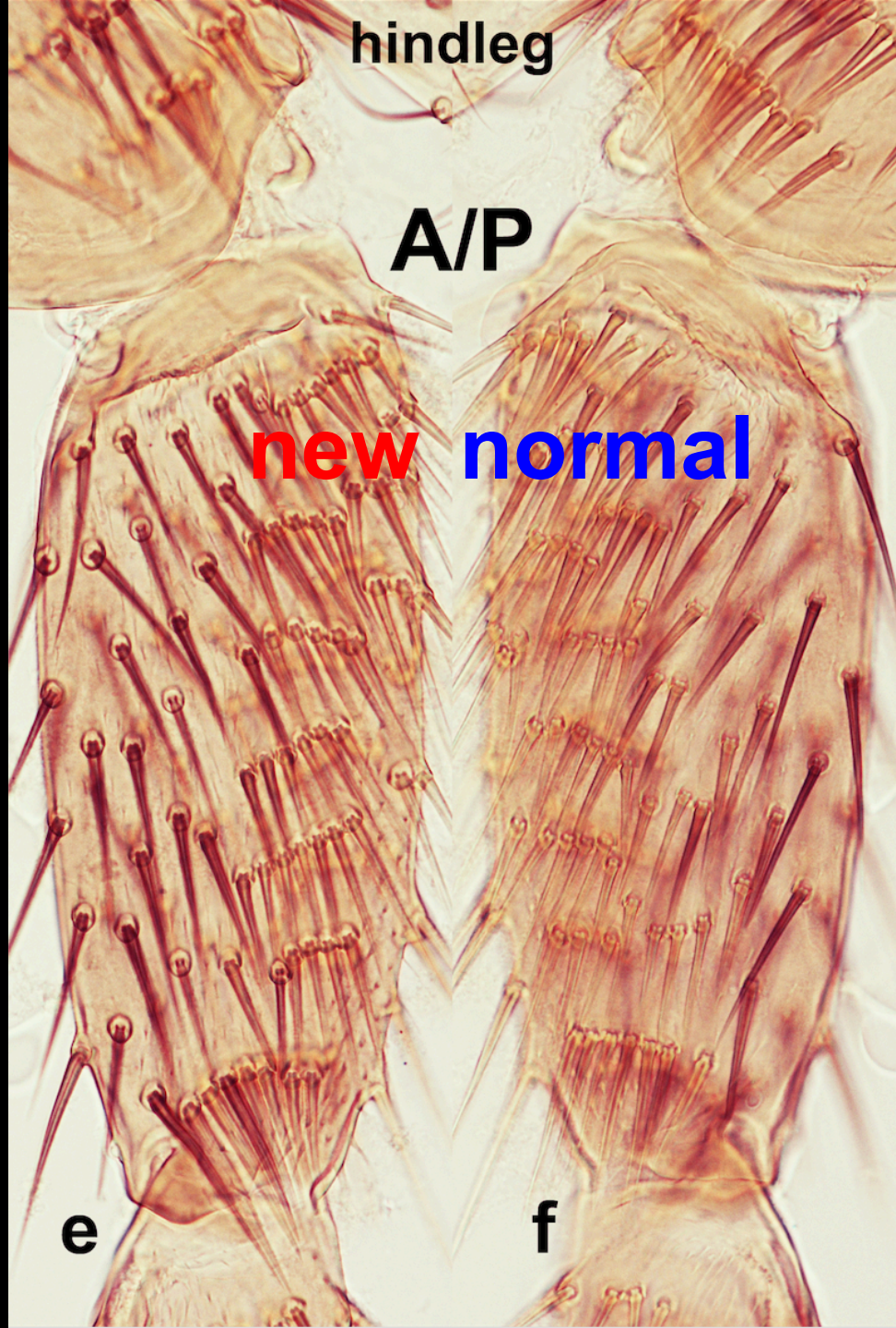
hindleg

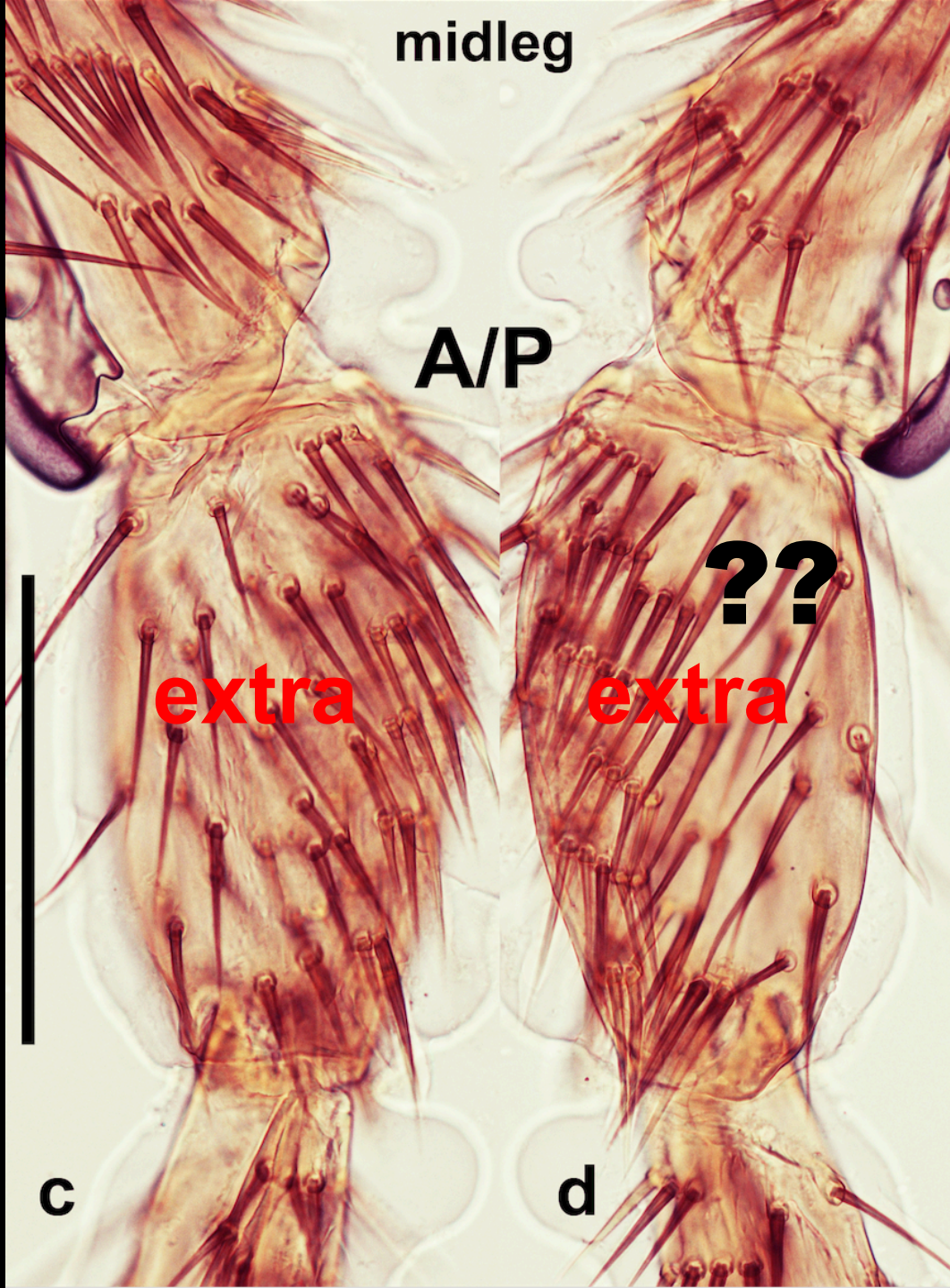
A/P

new normal

e

f





midleg

A/P

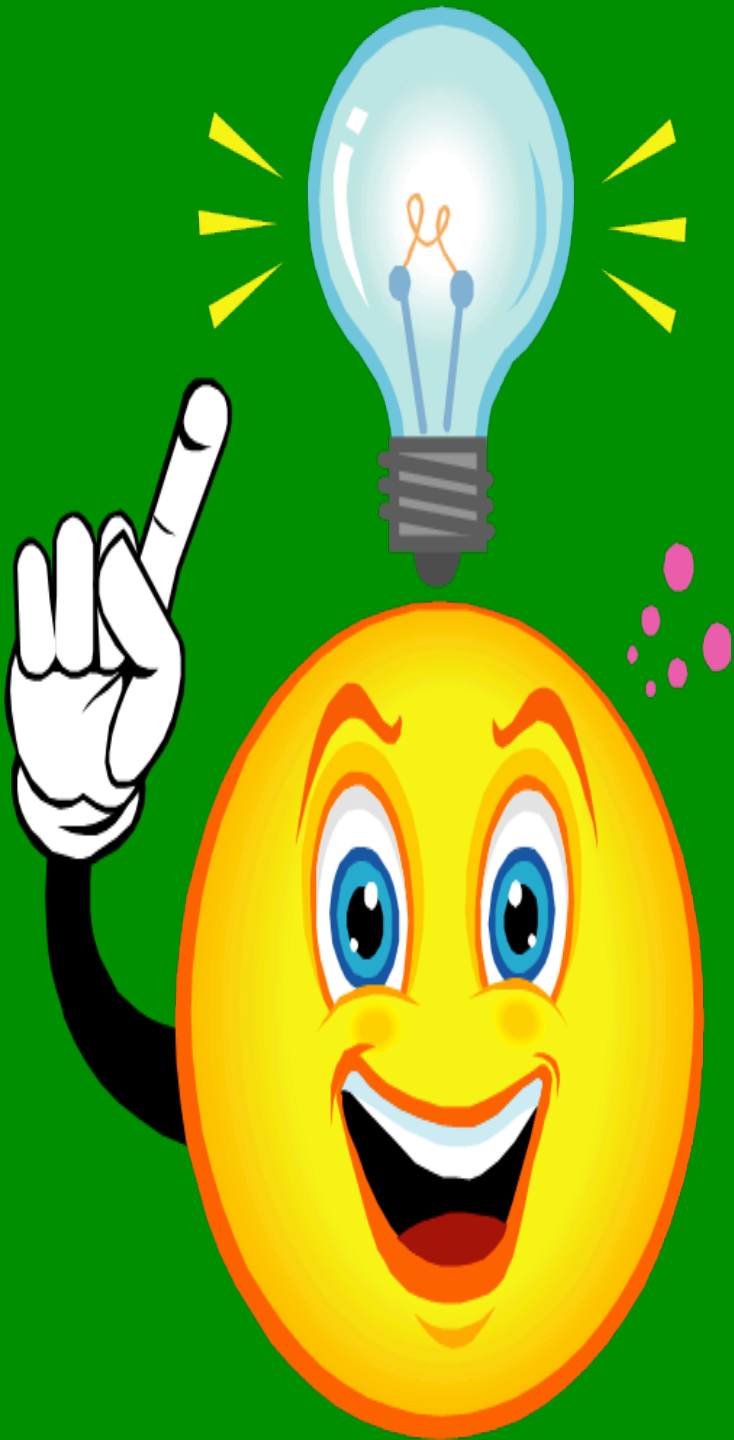
extra

???

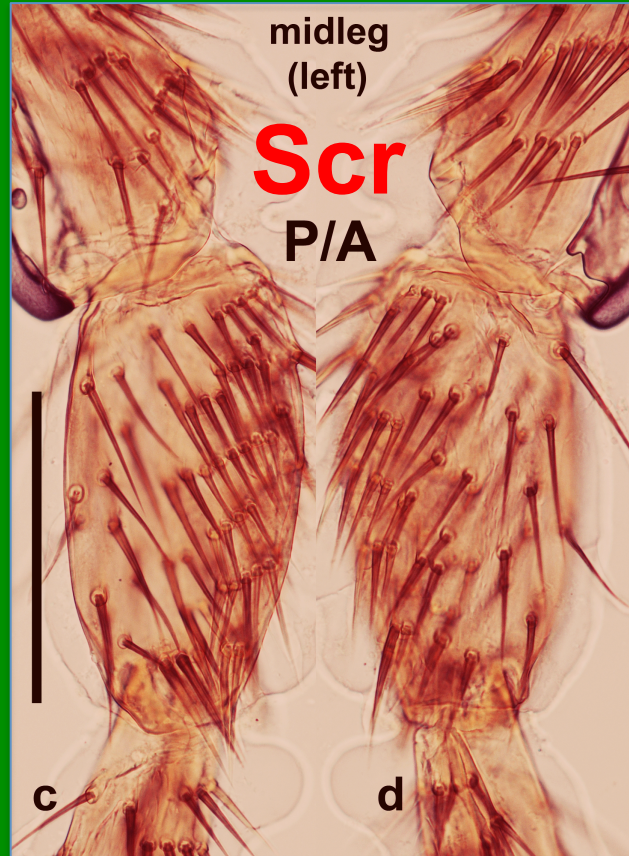
extra

c

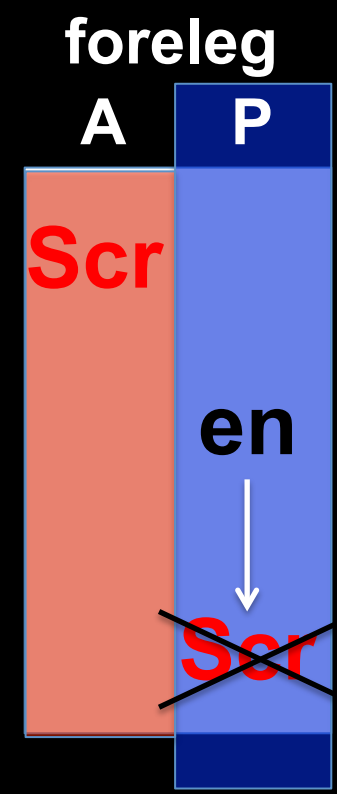
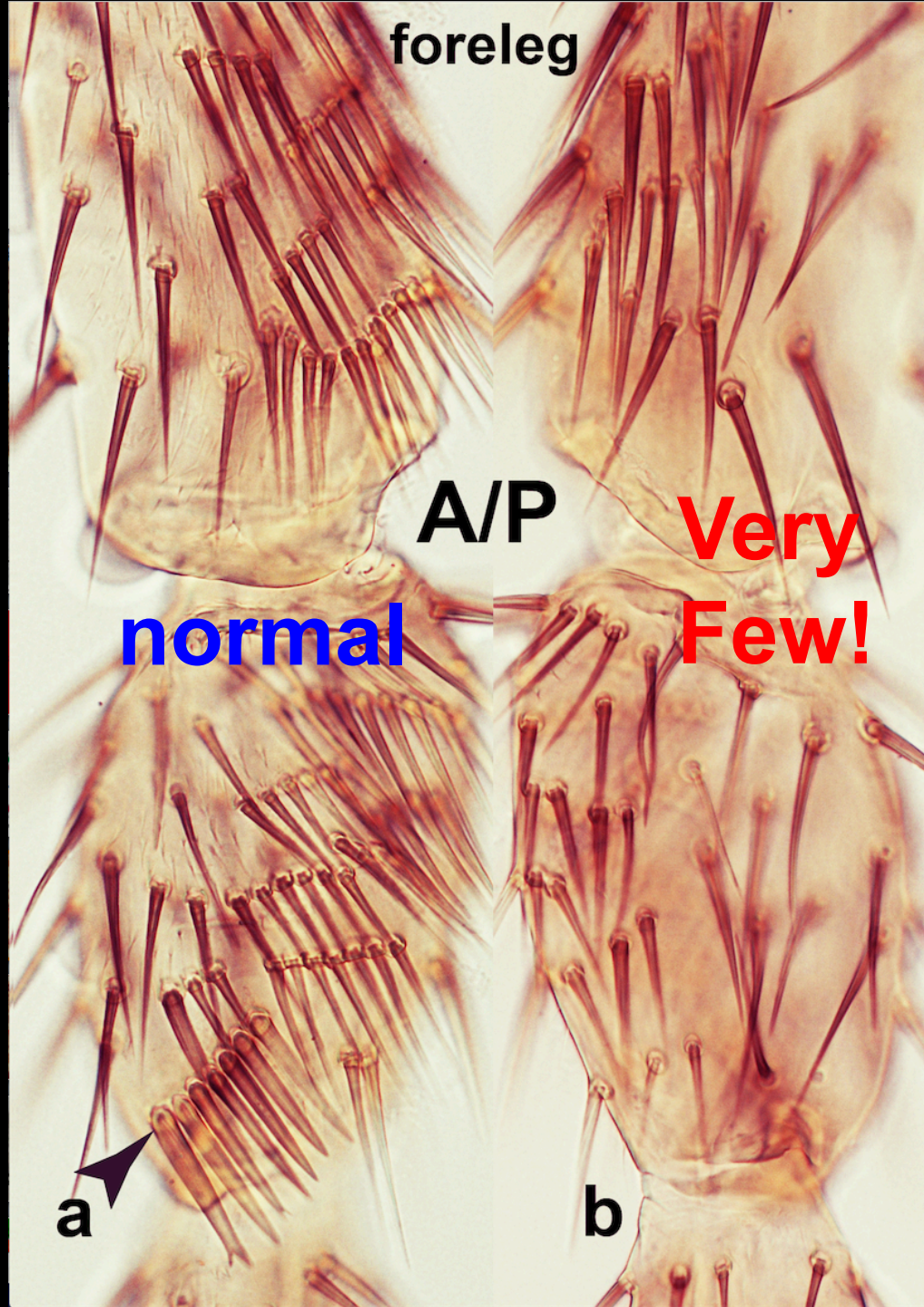
d



Maybe *Scr* is able to induce transverse rows ~anywhere?

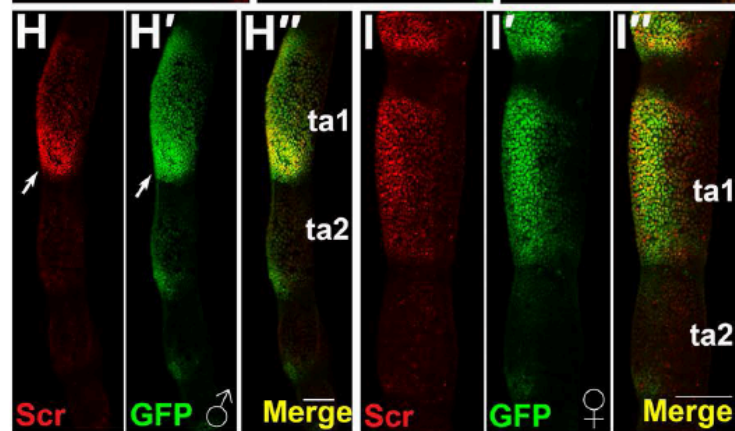
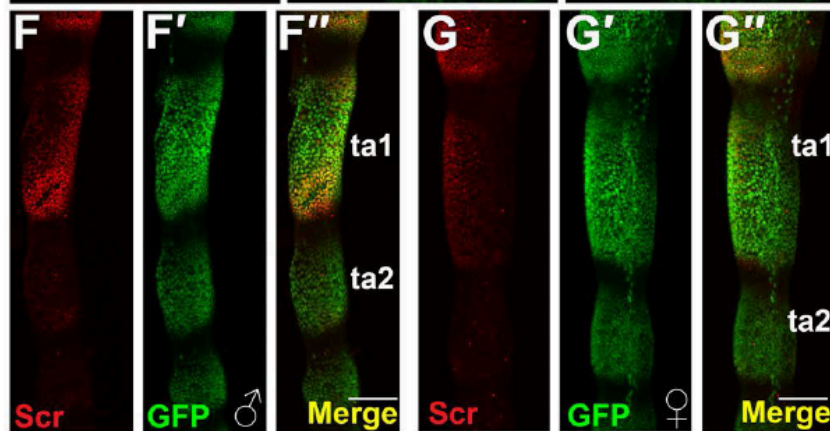
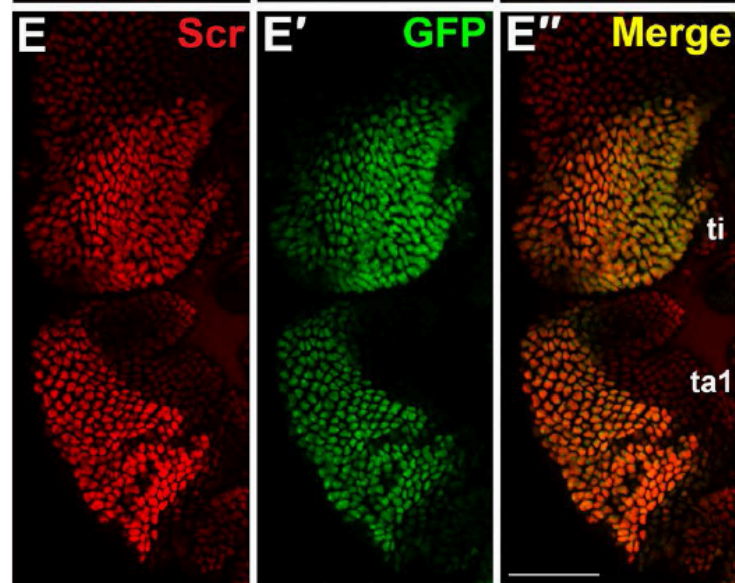
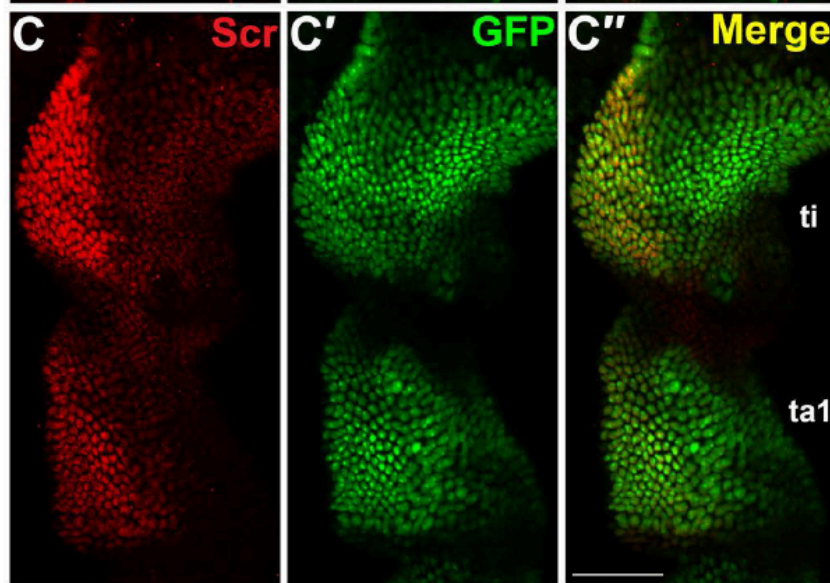
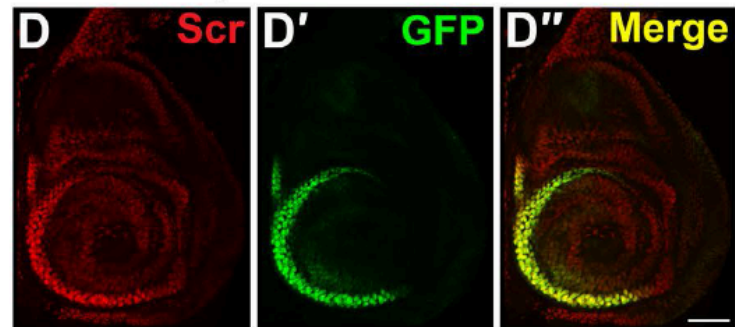
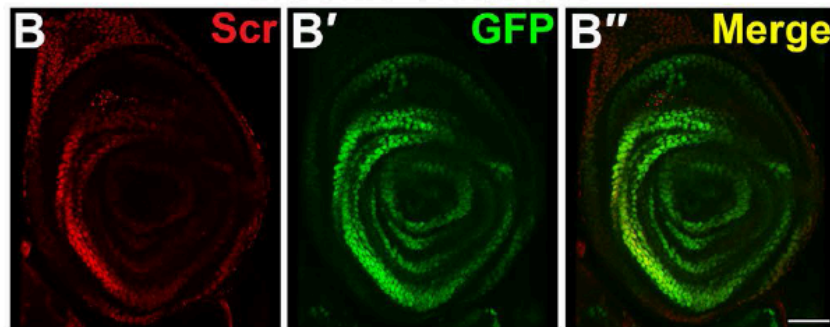


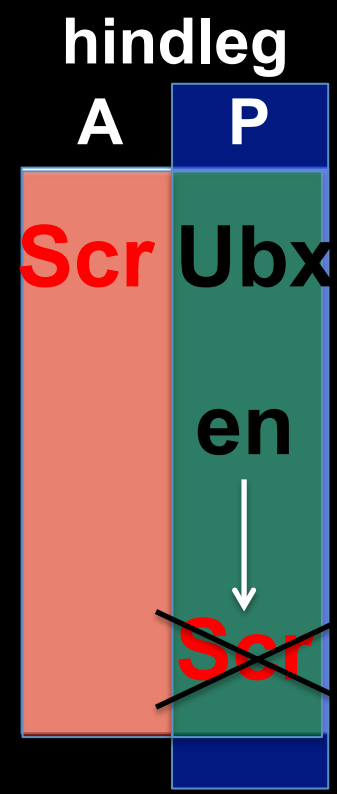
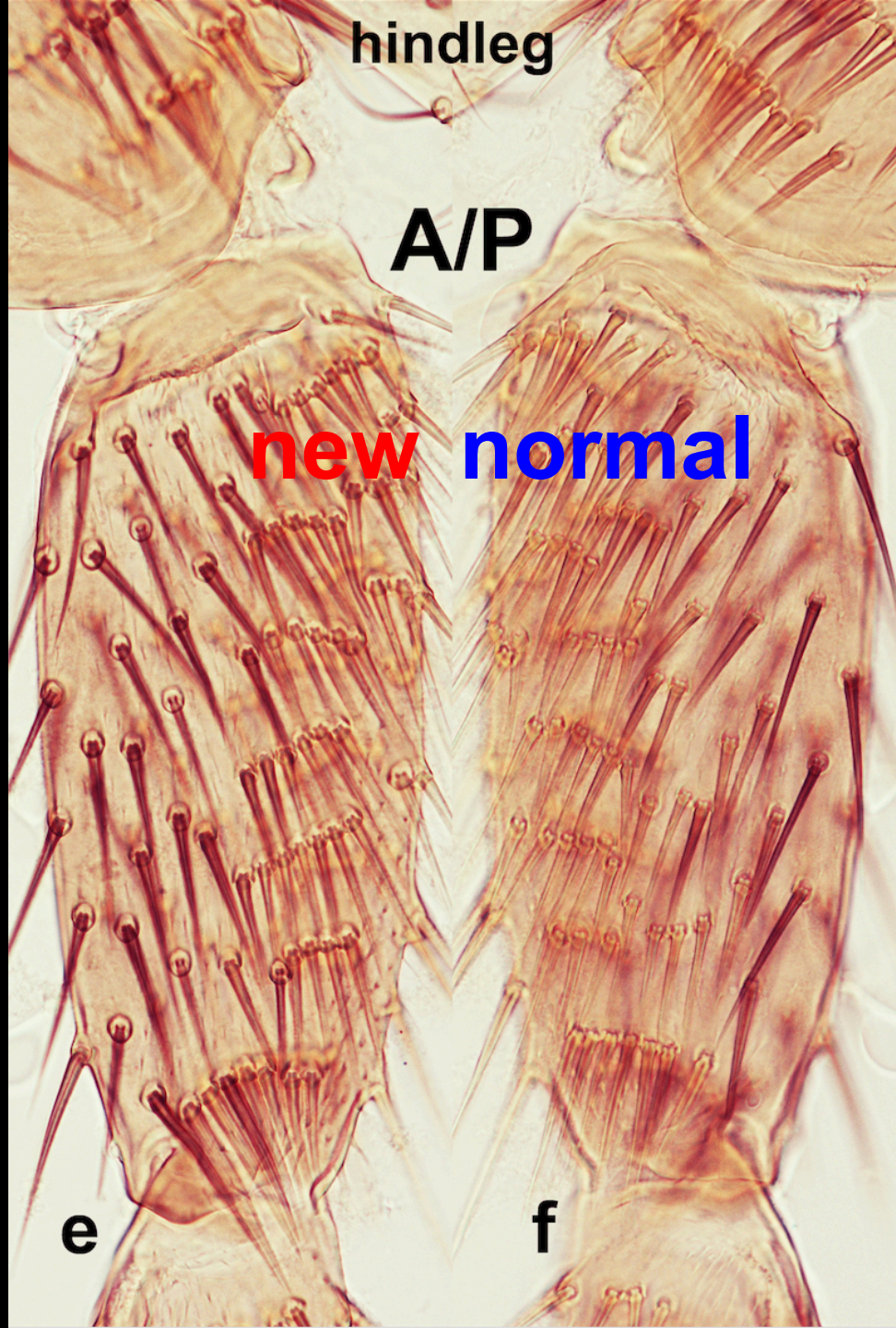
If so then extra *Scr* should also put t-rows on P side of foreleg?

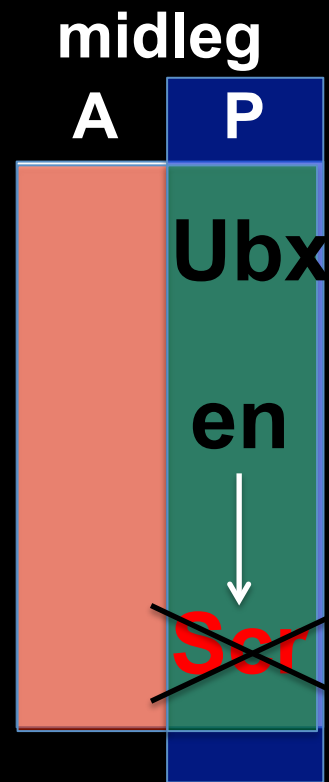
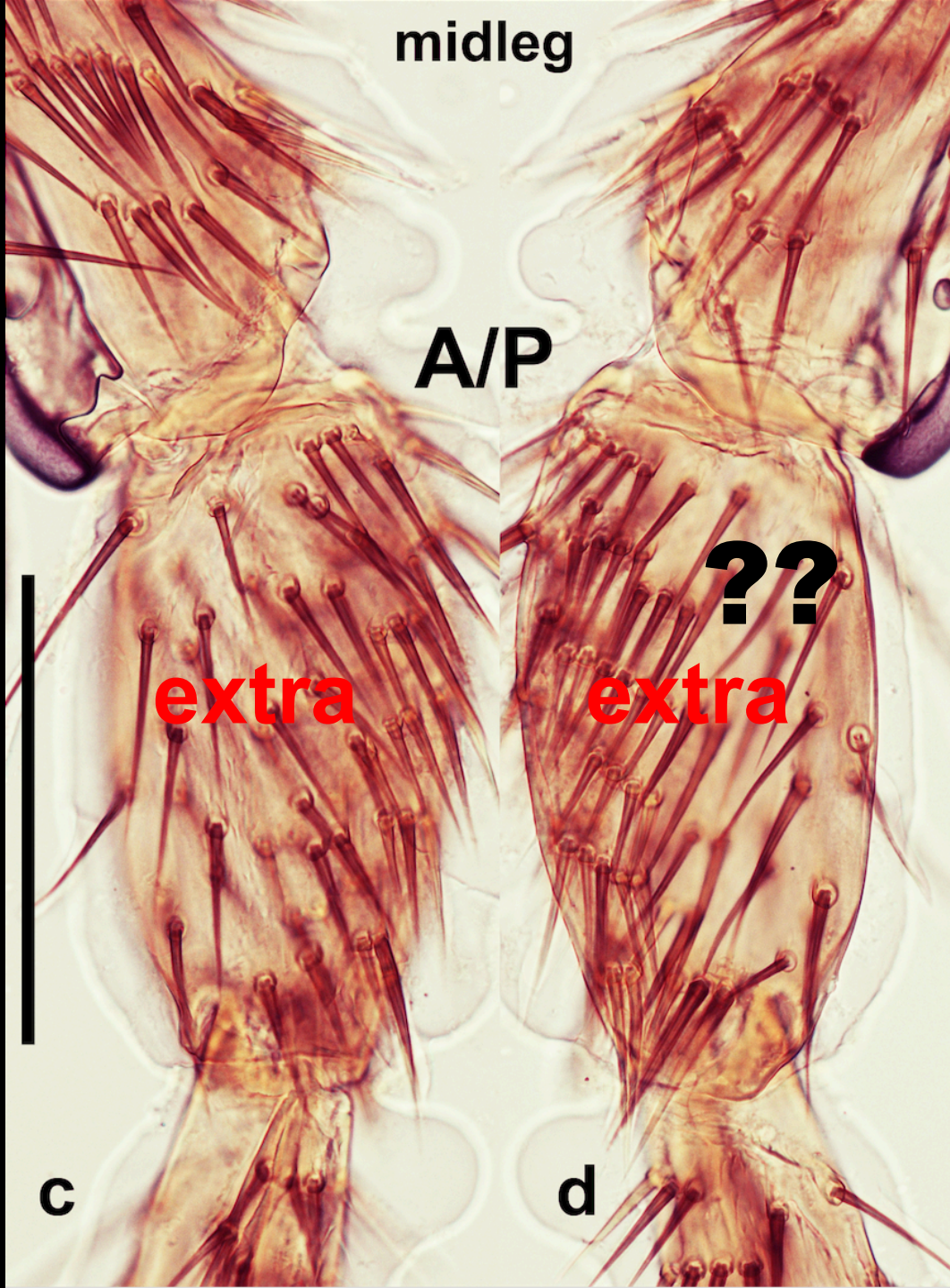


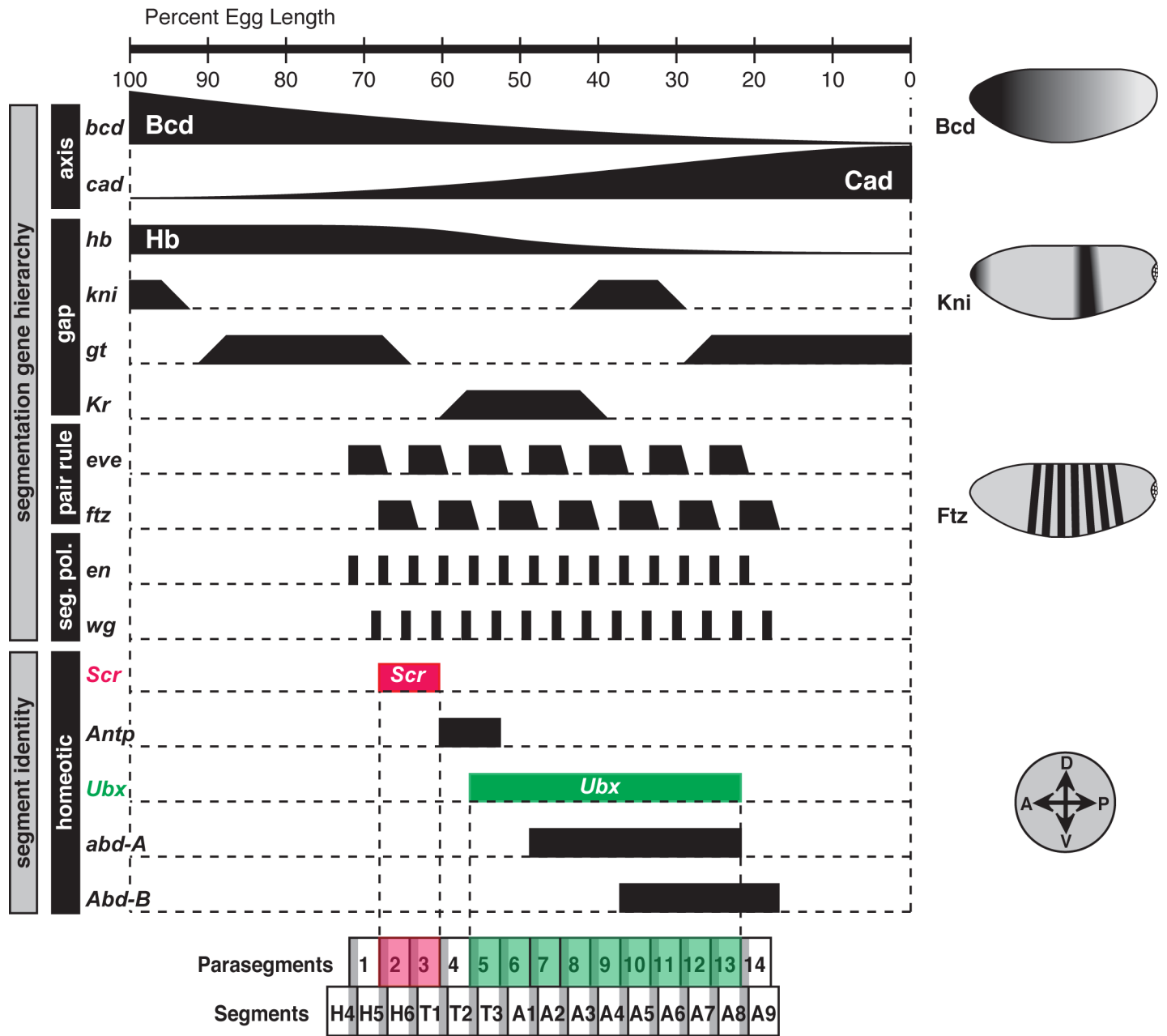
Intronic enhancer

Upstream enhancer

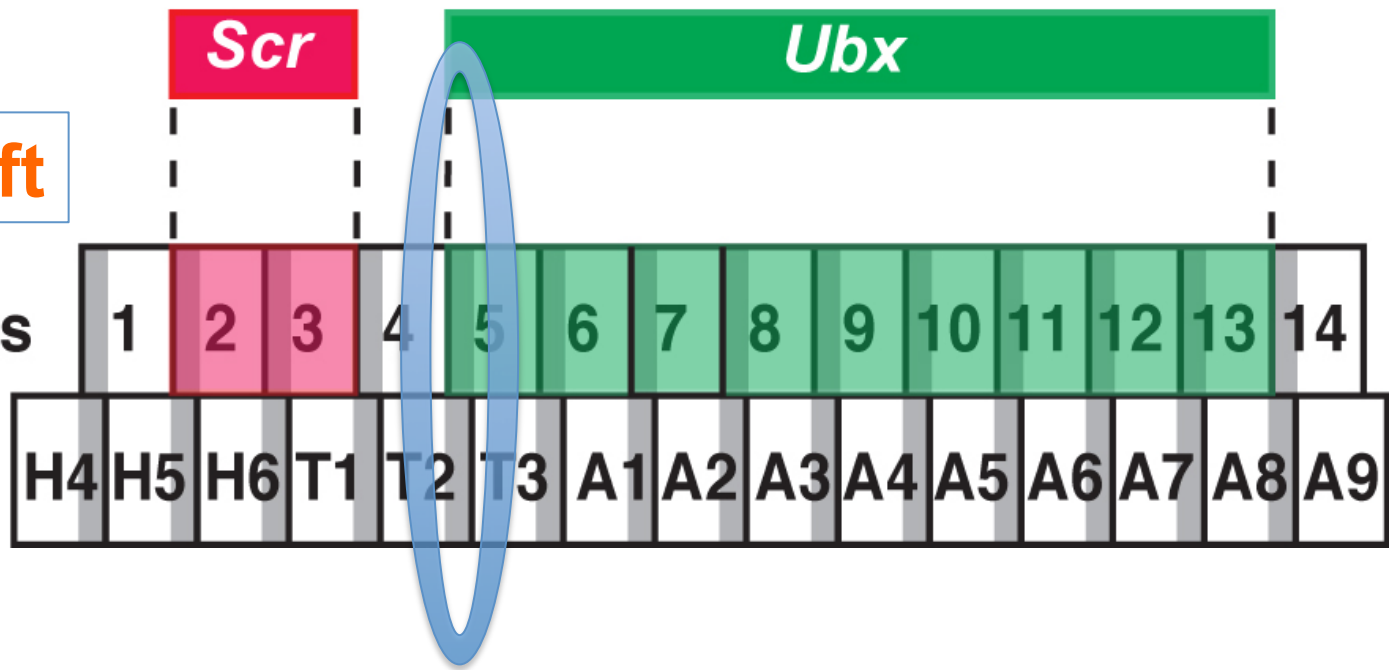






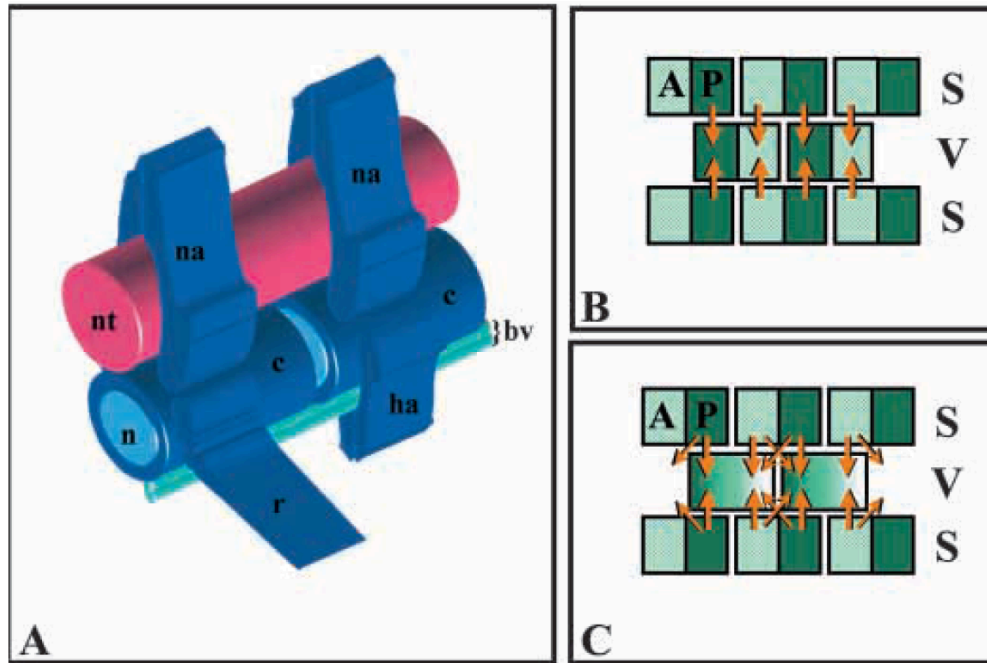


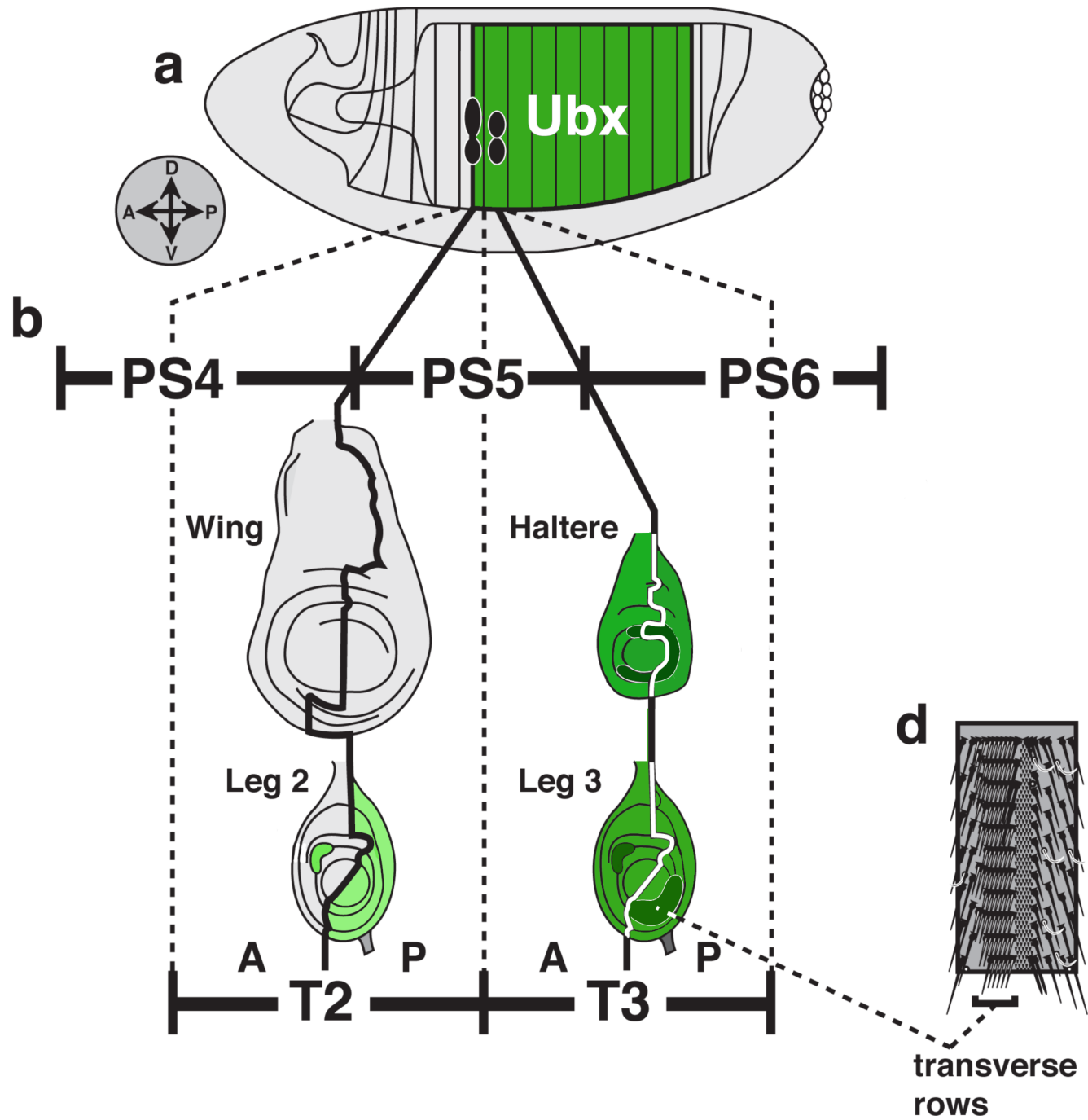
Phase Shift



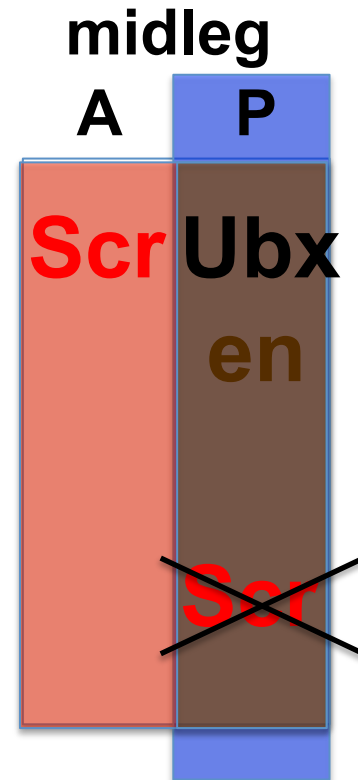
Phase Shift

Somites(S) vs. Vertebrae(V)





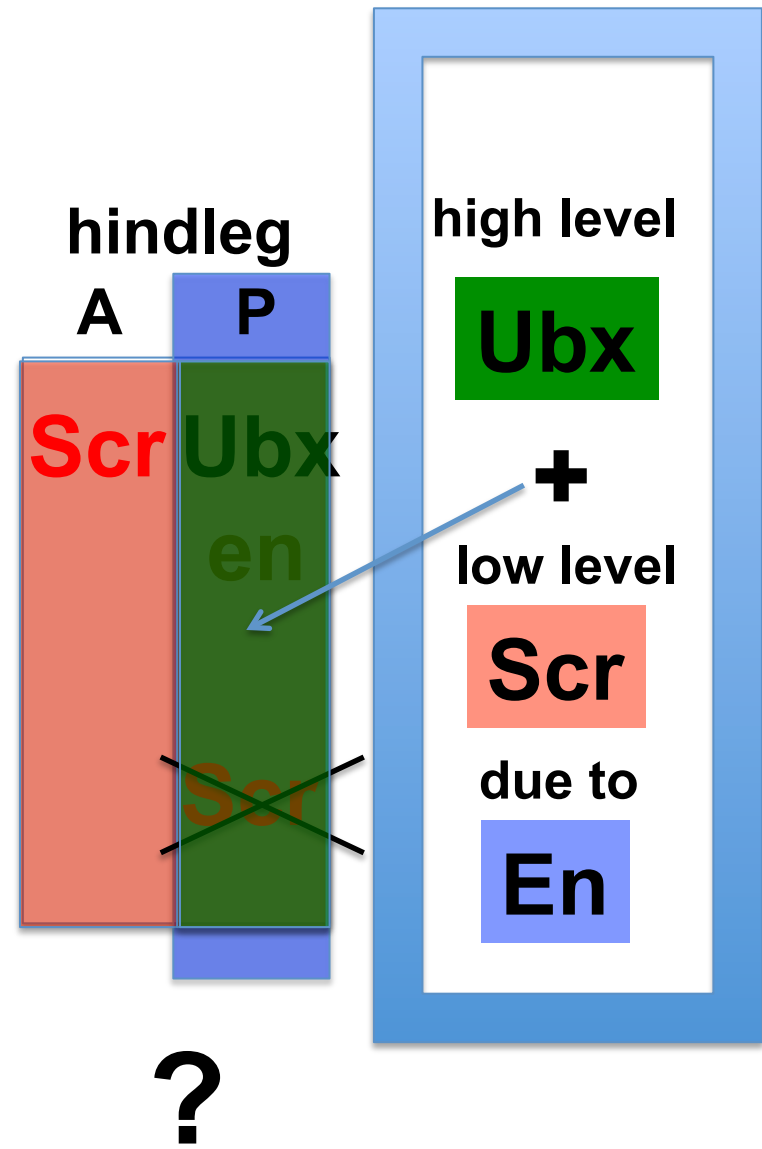
... so when we force *Scr* to be expressed on both sides, *en* partly suppresses *Scr*, but there might be enough *Scr* left to interact with *Ubx* so as to make t-rows on P side.

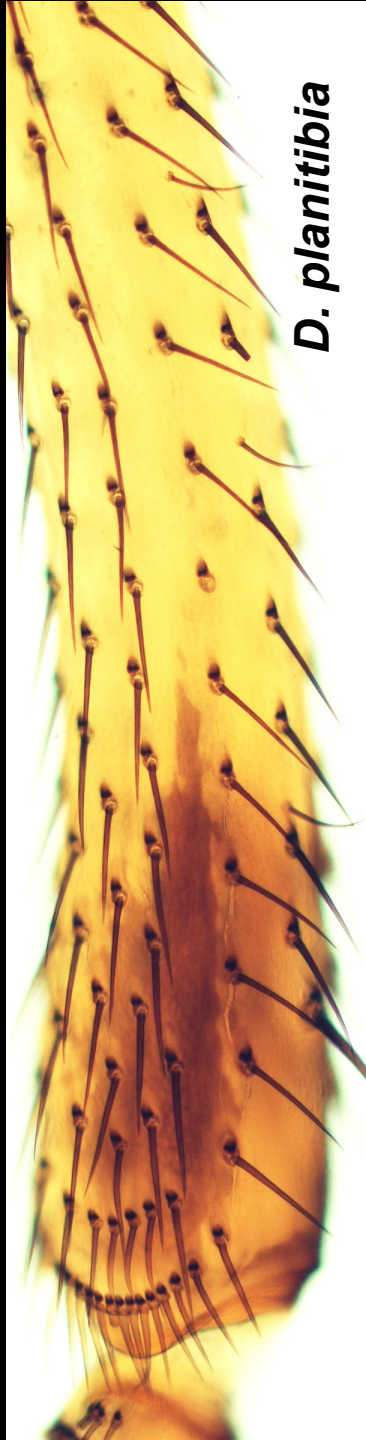


?

Test:

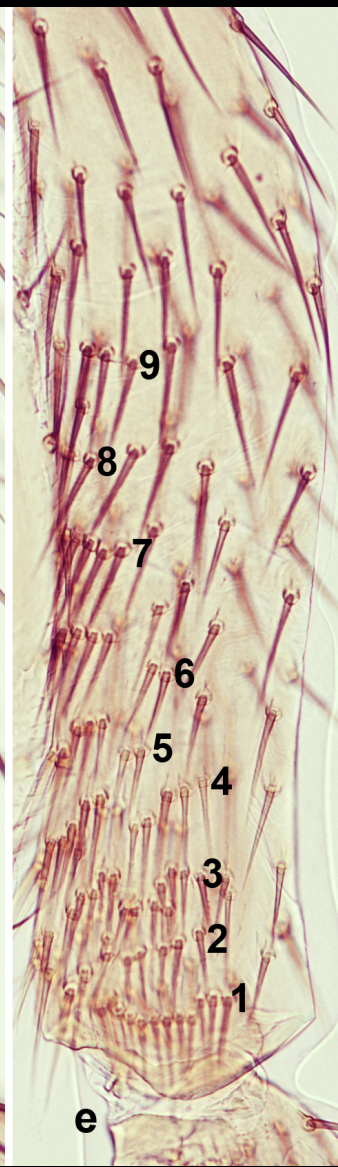
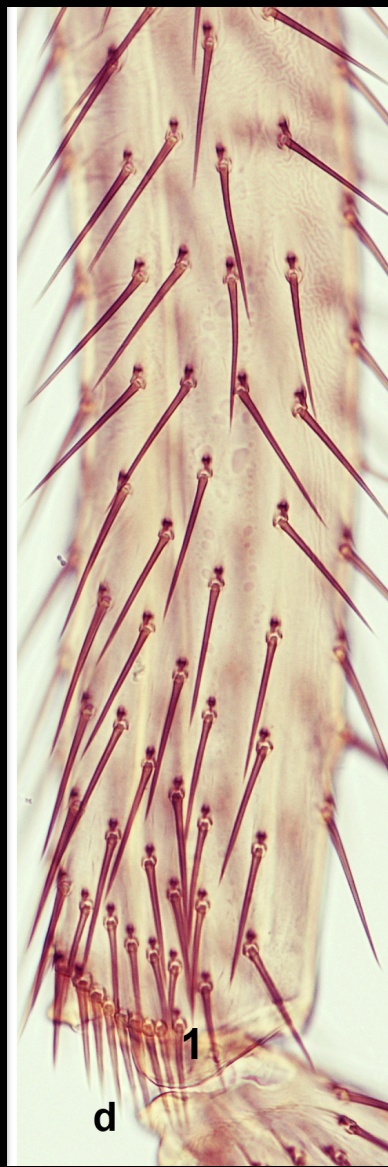
See whether there are excess t-rows on the P side on the hindleg.

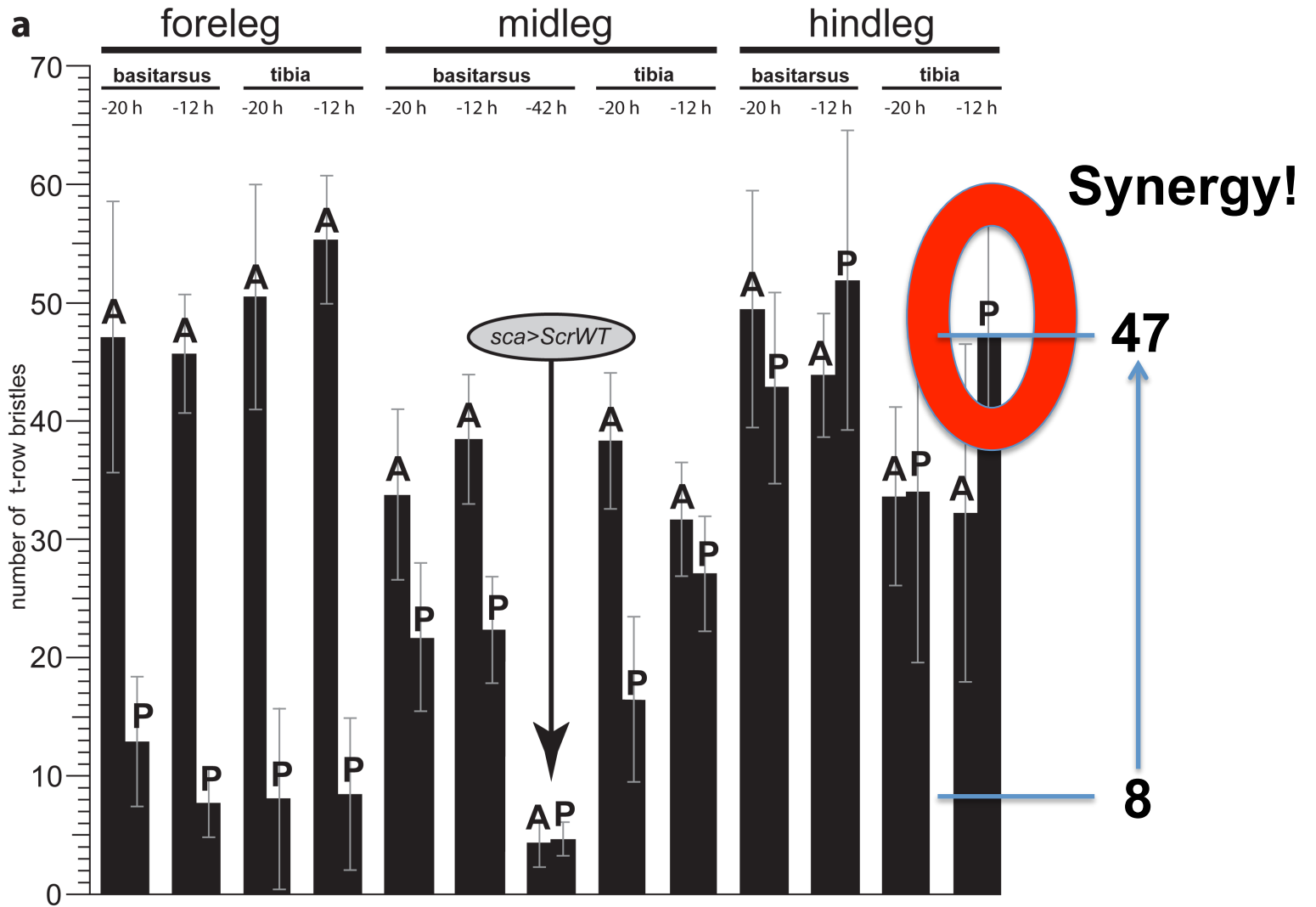




Ubx

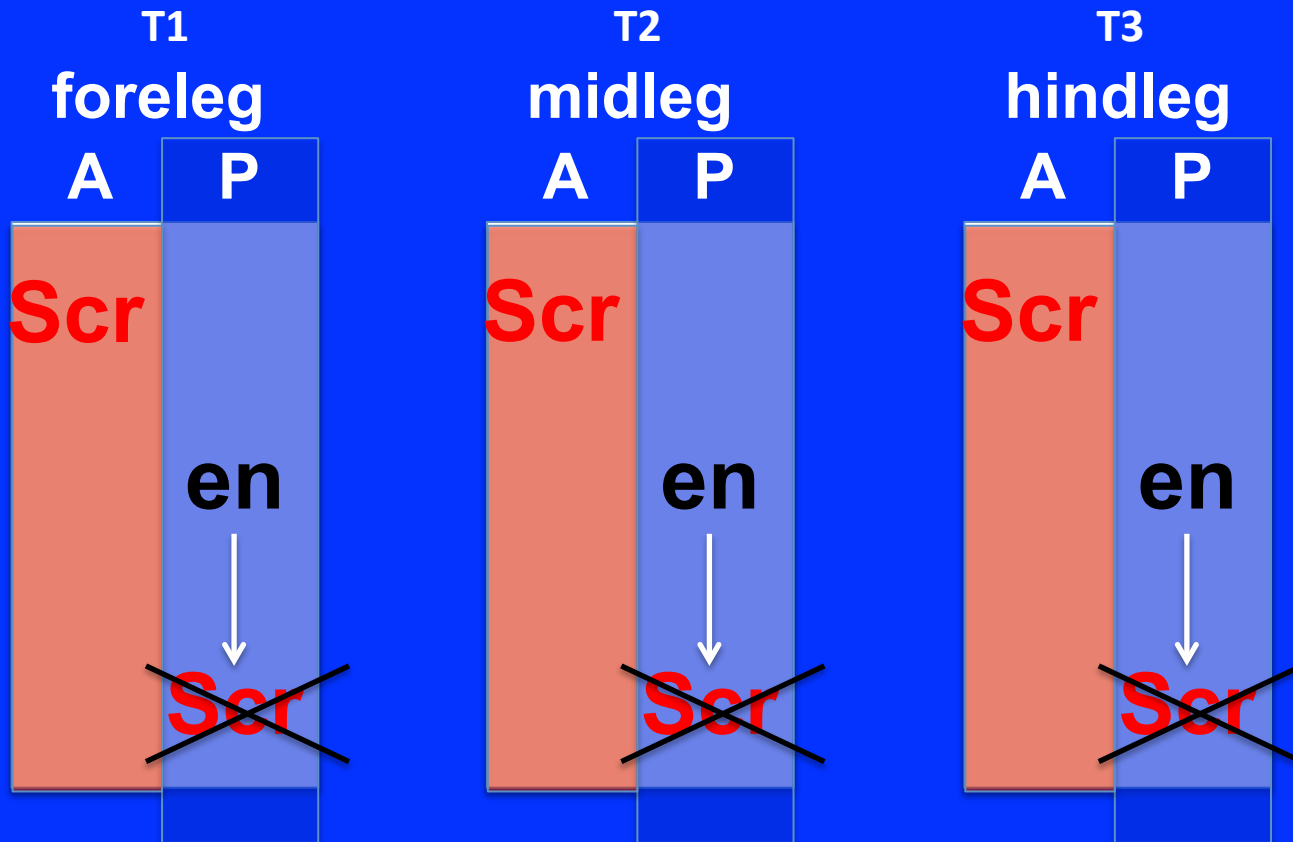
Scr
+
Ubx





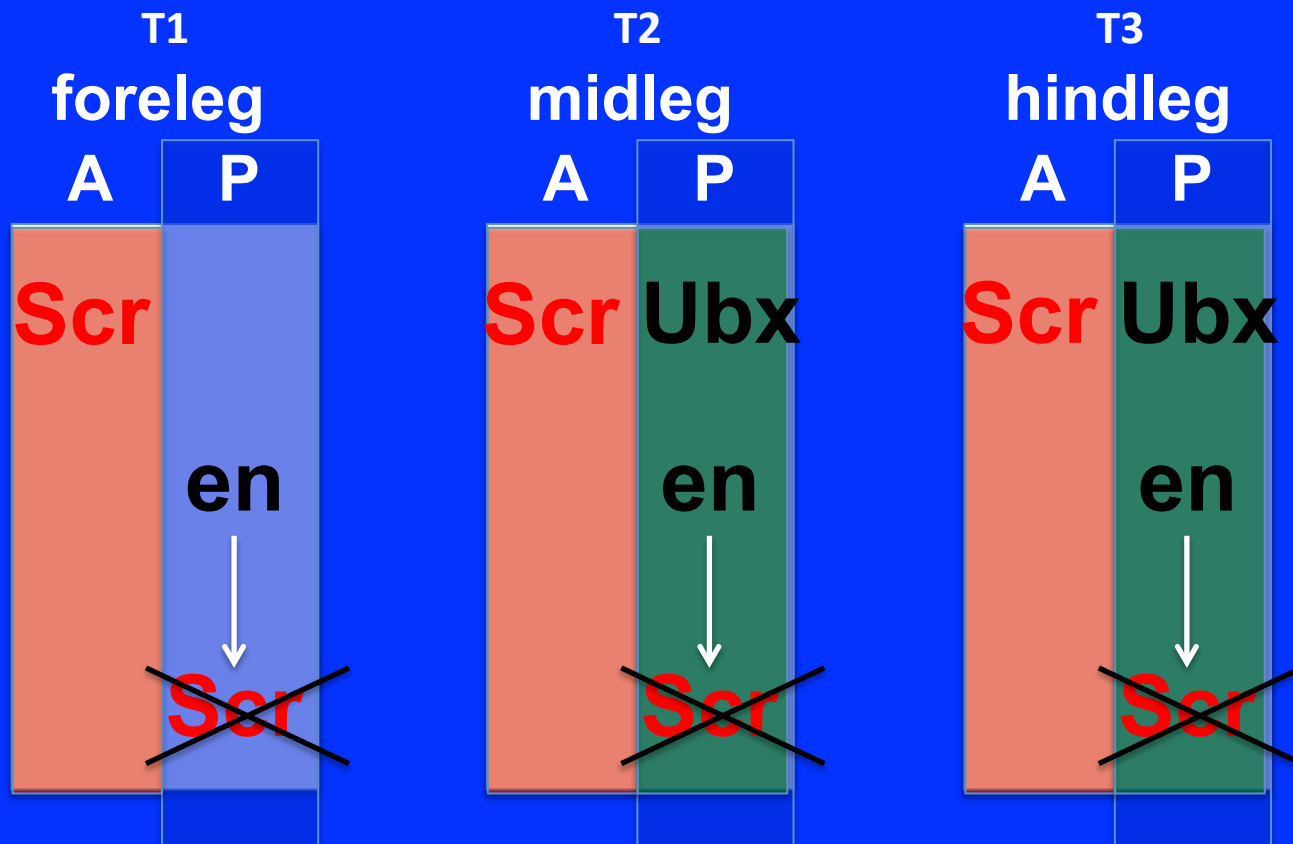
Conclusions:

1. En partly blocks Scr-GOF on POS of all legs.



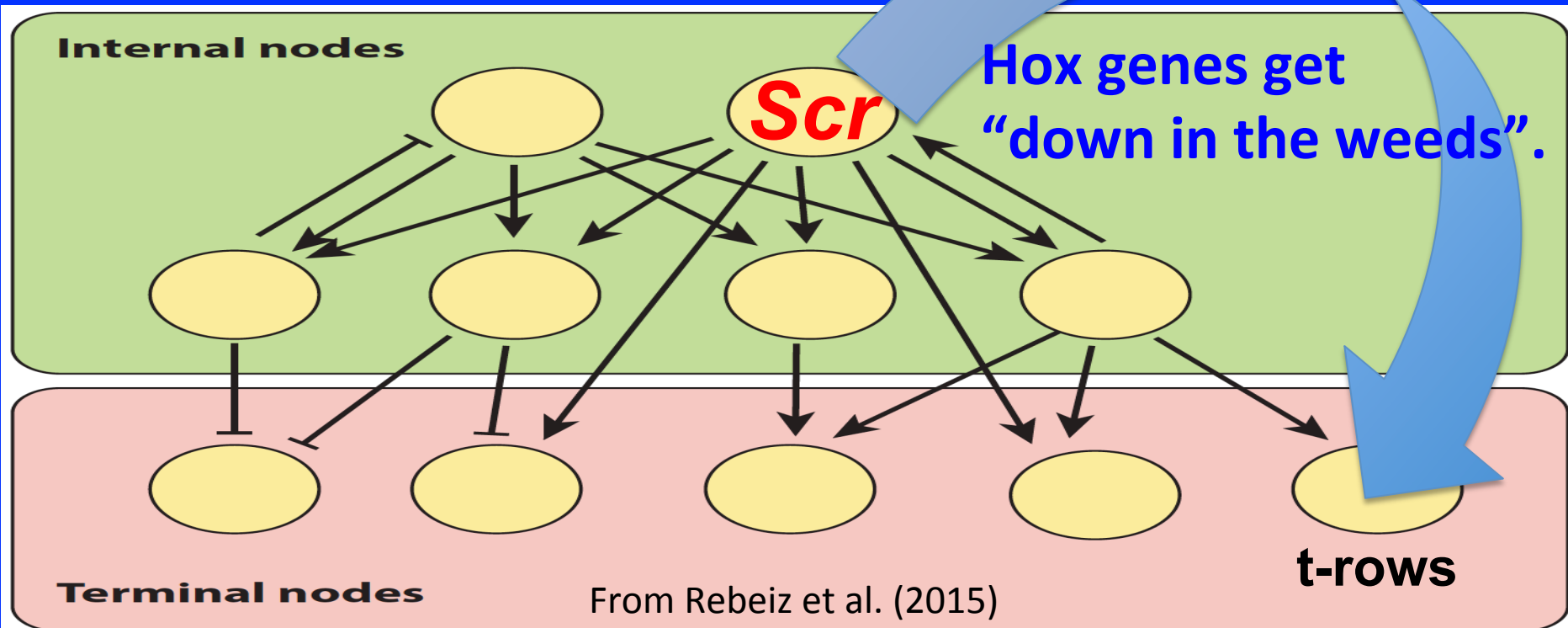
Conclusions:

1. En partly blocks Scr-GOF on POS of all legs.
2. Ubx makes up for this decrease on T2 & T3.



Conclusions:

1. En partly blocks Scr-GOF on POS of all legs.
2. Ubx makes up for this decrease on T2 & T3.
3. **Scr = a direct micromanager vs. an executive.**





60 YEARS
DNA DISCOVERY

Hox 13

Hox 10,11,12,13

Hox 10,11,12,13

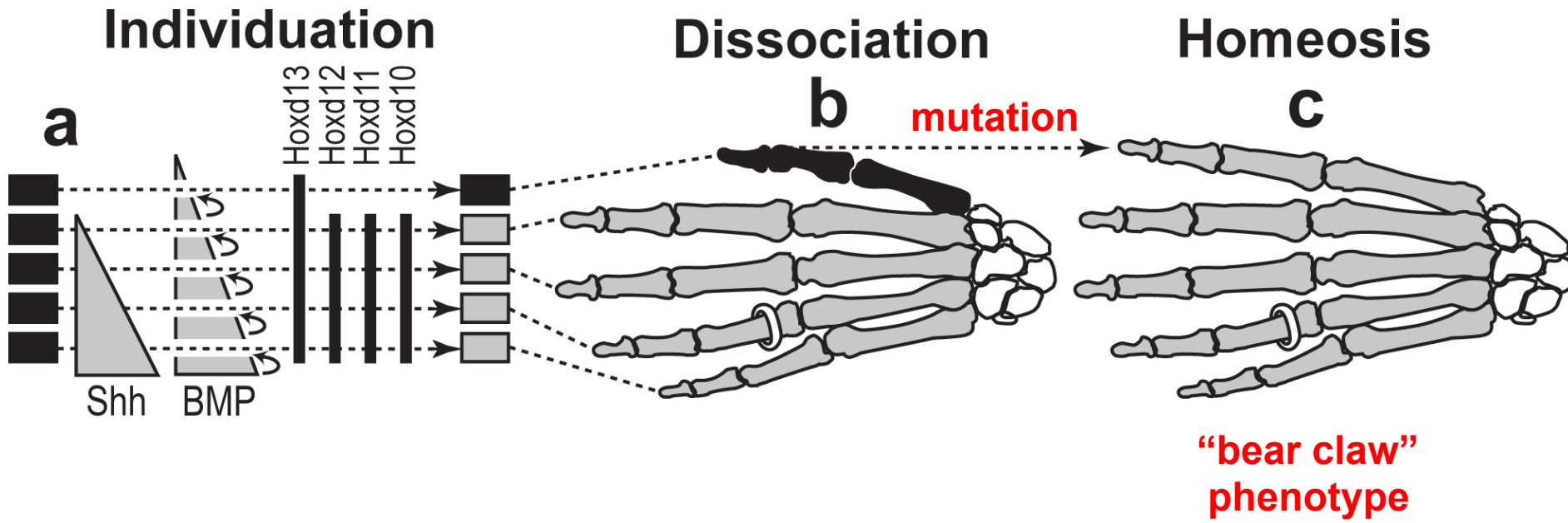
Hox 10,11,12,13

Hox 10,11,12,13

Reunion

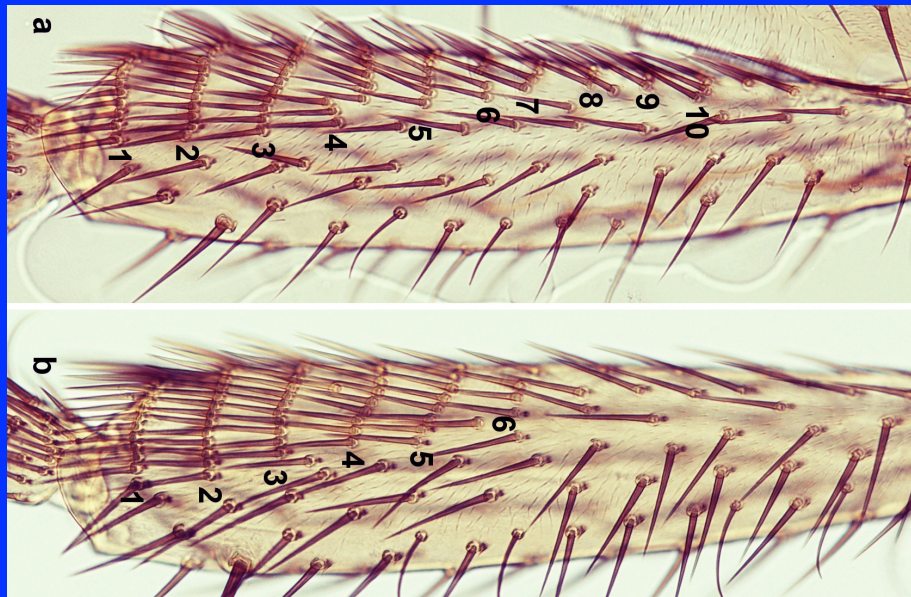
In 1983, Kary Mullis completed the invention of PCR, for which he was awarded the 1993 Nobel Prize.

Now, uses for PCR in human identification are becoming routine. Groups like DNA PROKIDS, a nonprofit organization dedicated to fighting human trafficking, make it possible to reunite kidnapped children with their parents.



Conclusions:

1. En partly blocks Scr-GOF on POS of all legs.
2. Ubx makes up for this decrease on T2 & T3.
3. Scr = a direct micromanager vs. an executive.
4. Scr acts as a knob (analog) vs. switch (digital).



**Excess
Scr-GOF**

**Normal
Scr**

Hamlet

By William Shakespeare



CAMBRIDGE SCHOOL

Shakespeare

Measure

FOR

Measure



Hamlet

By William Shakespeare



Much Ado About Nothing

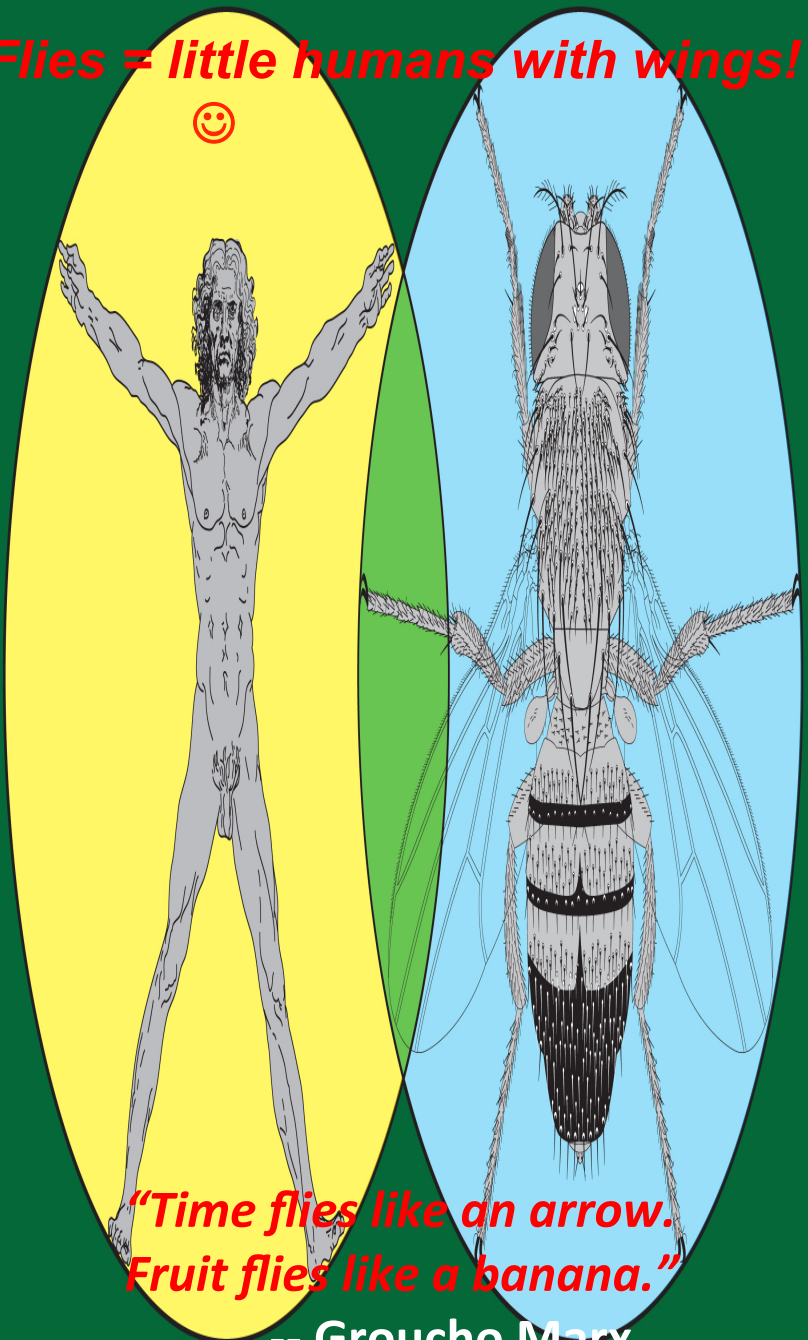
William Shakespeare

COMPLETE SCHOOL
EDITION



Macmillan
Modern
Shakespeare

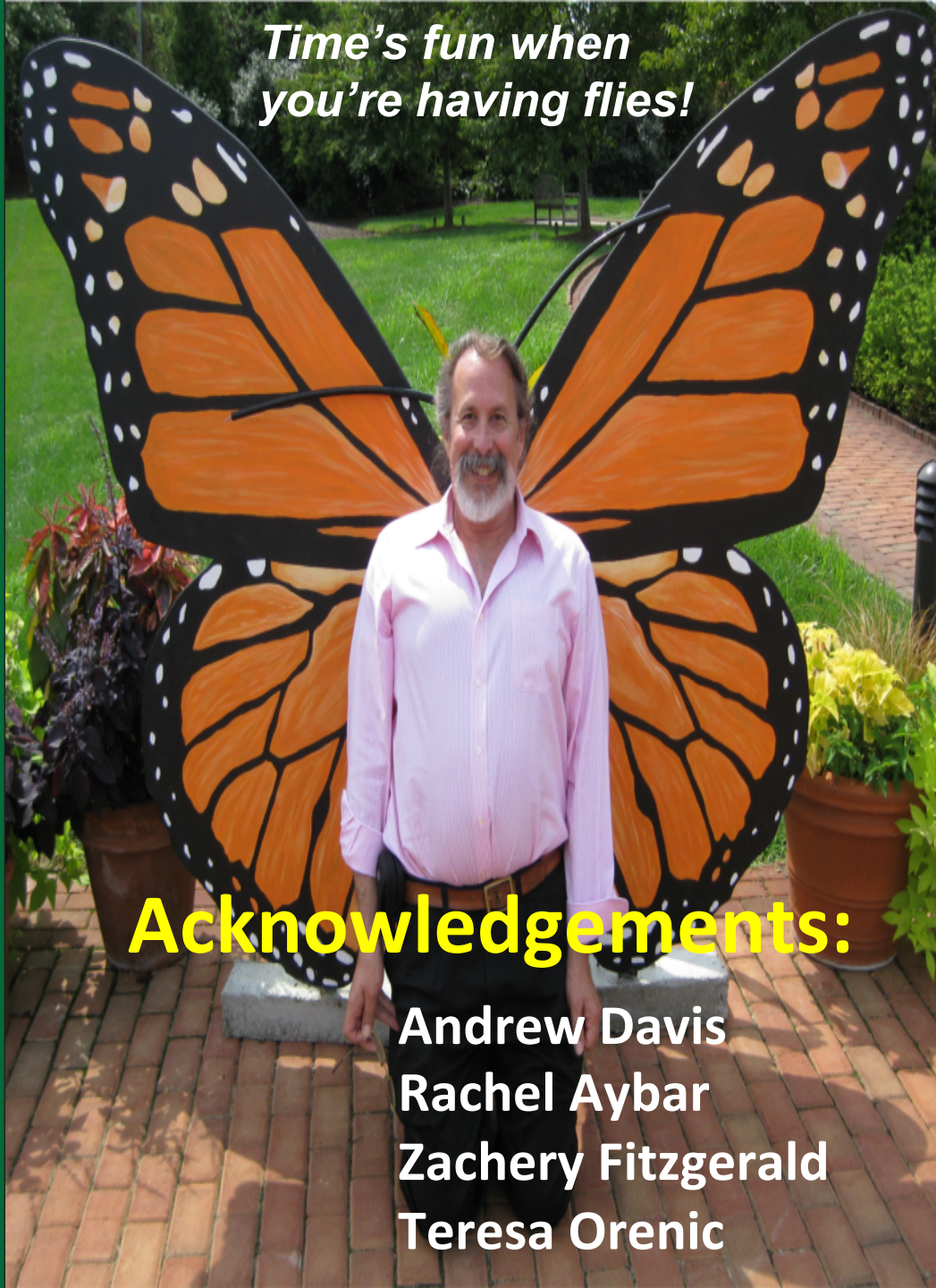
Flies = little humans with wings!



***"Time flies like an arrow.
Fruit flies like a banana."***

-- Groucho Marx

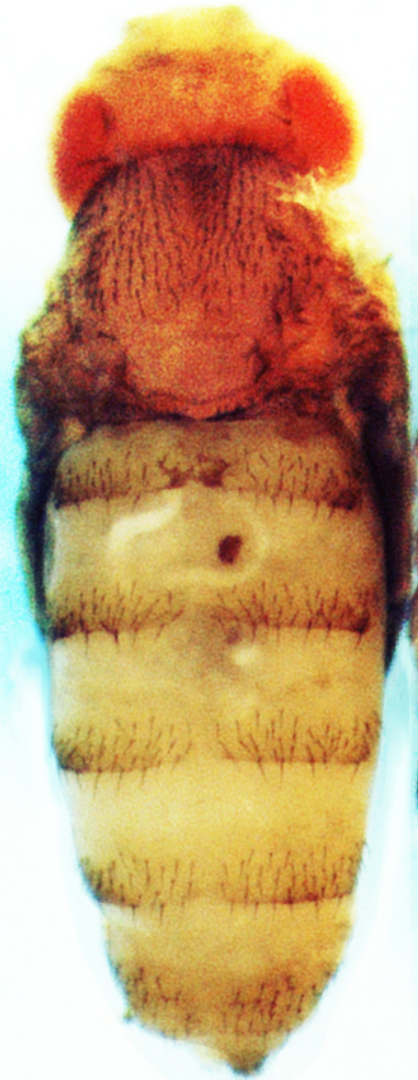
***Time's fun when
you're having flies!***



Acknowledgements:

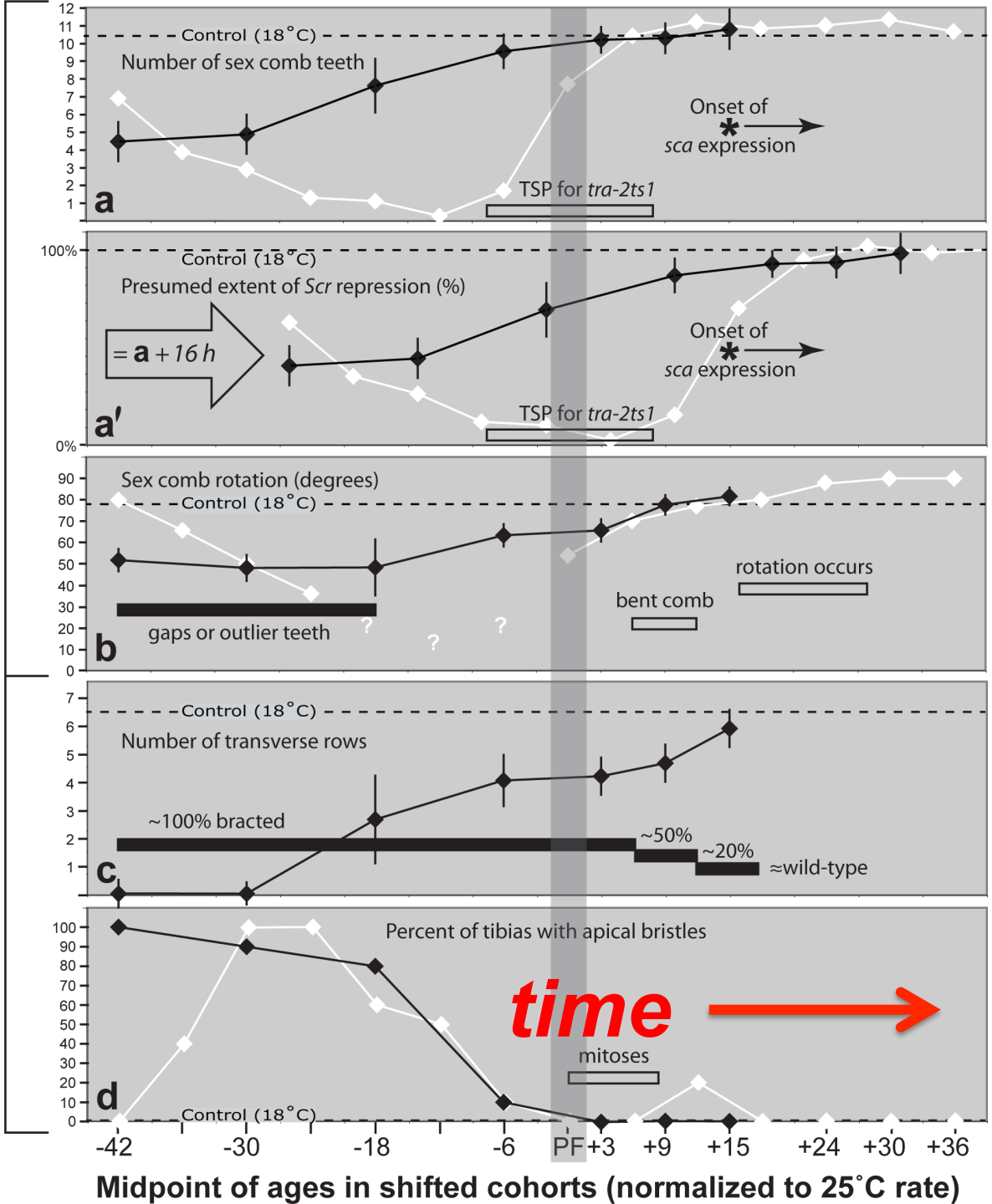
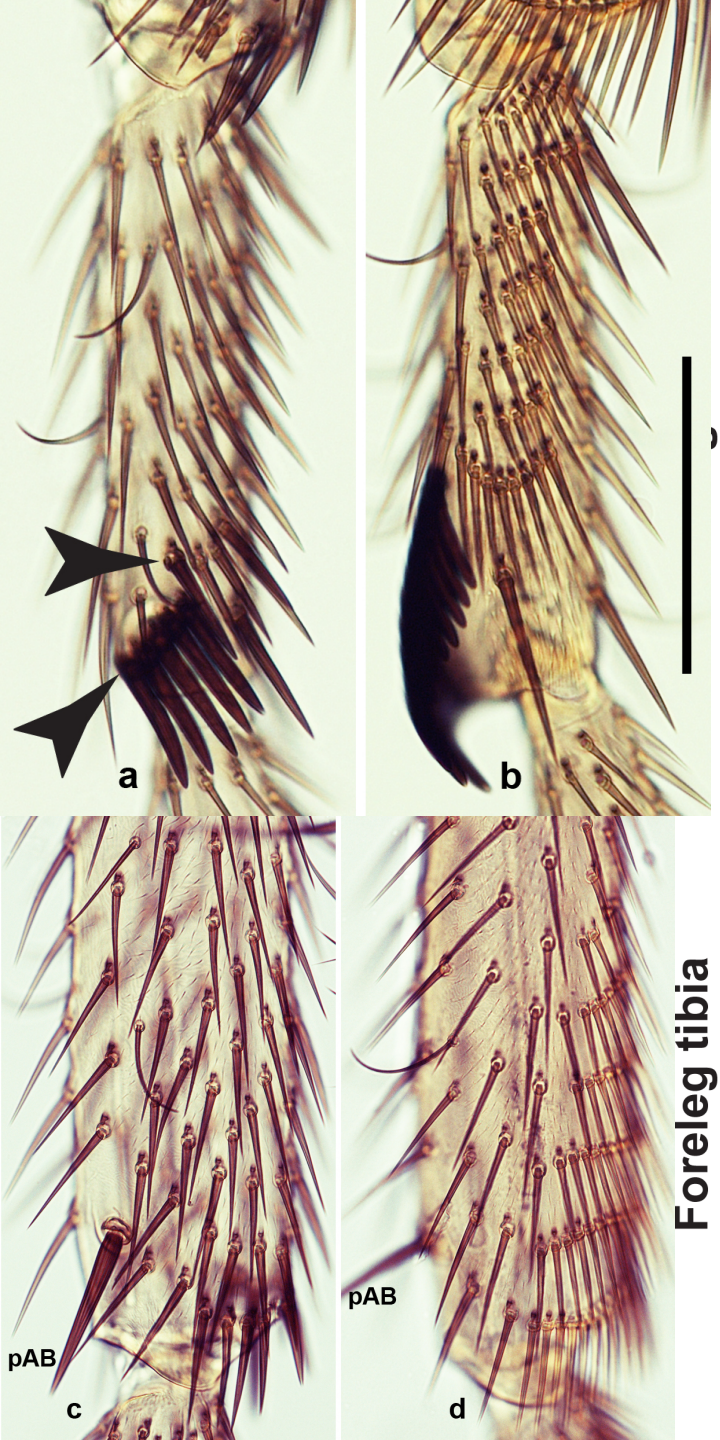
- Andrew Davis**
- Rachel Aybar**
- Zachery Fitzgerald**
- Teresa Orenic**

Scr-GOF



Control



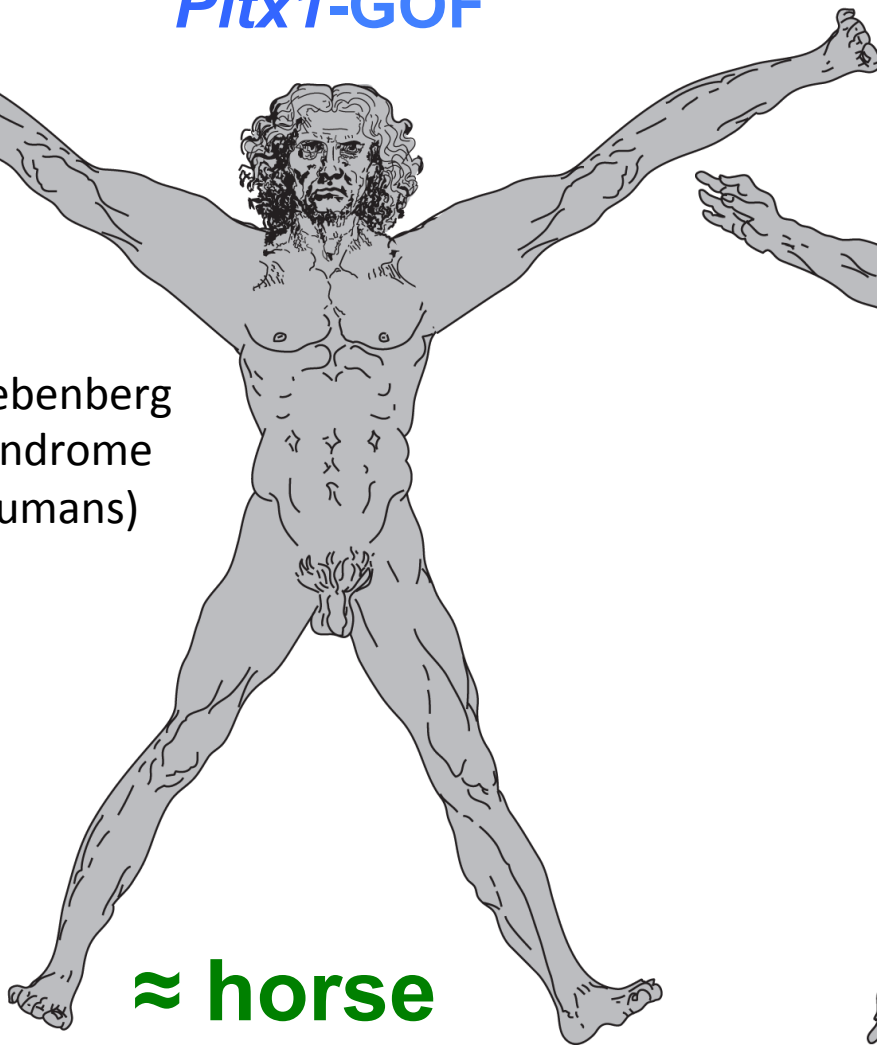


Relevance?

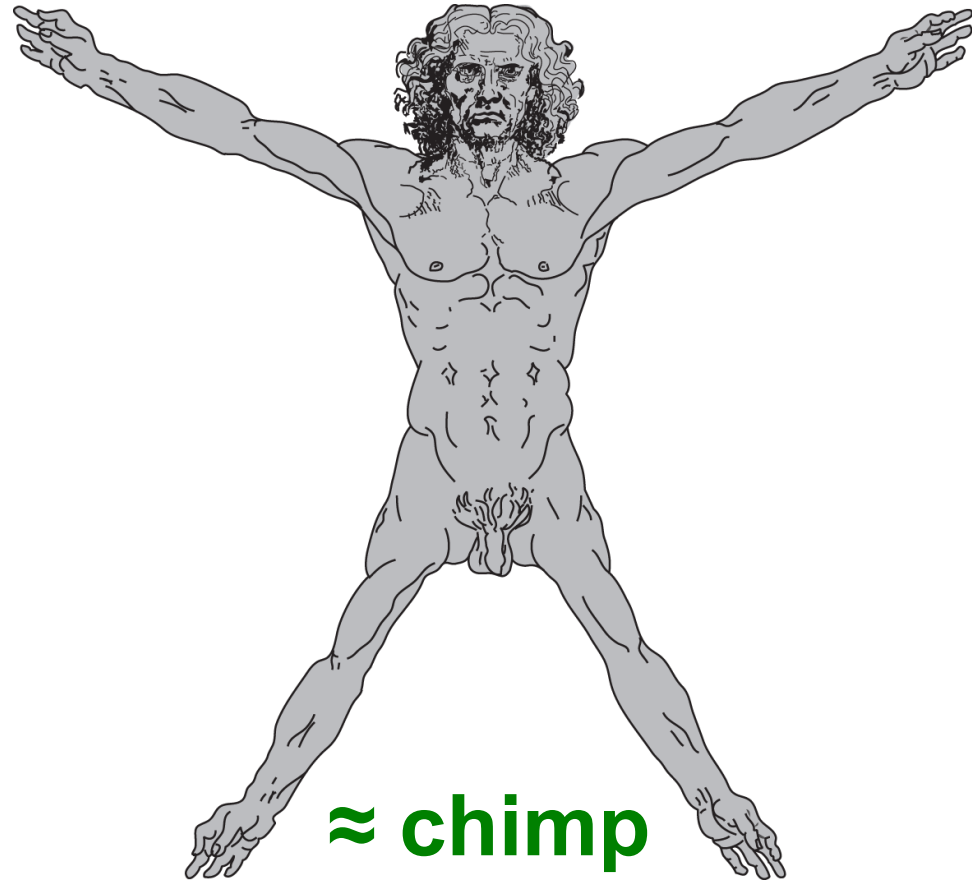
Pitx1-GOF

Pitx1-LOF

Liebenberg
Syndrome
(humans)



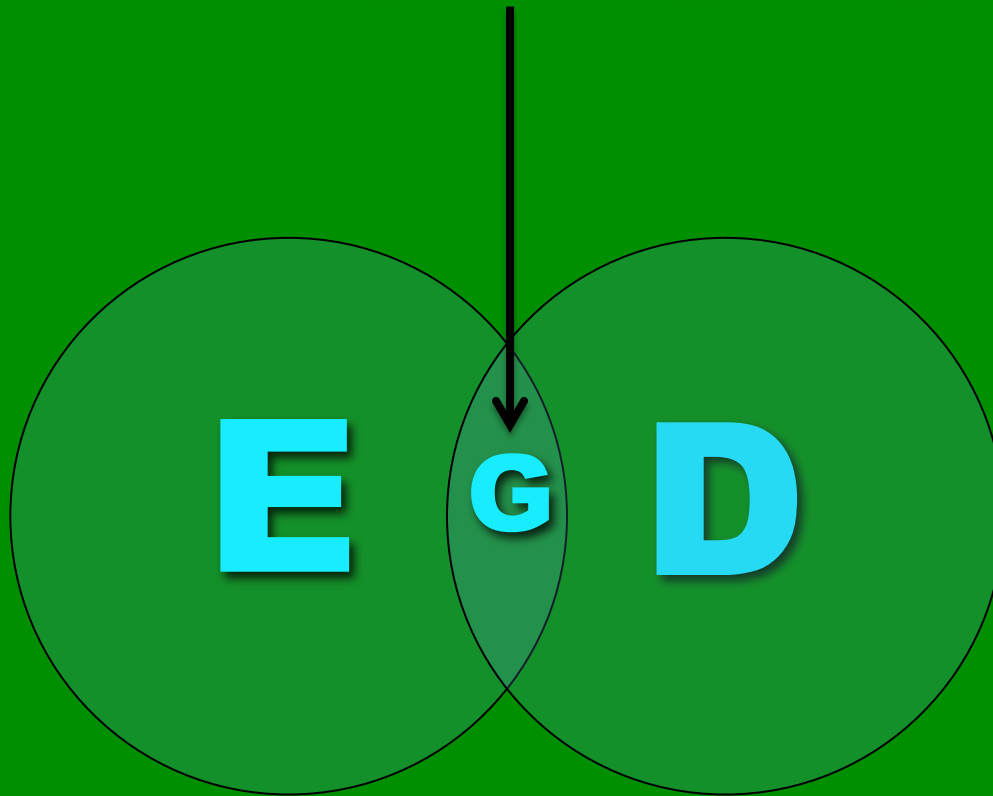
≈ horse

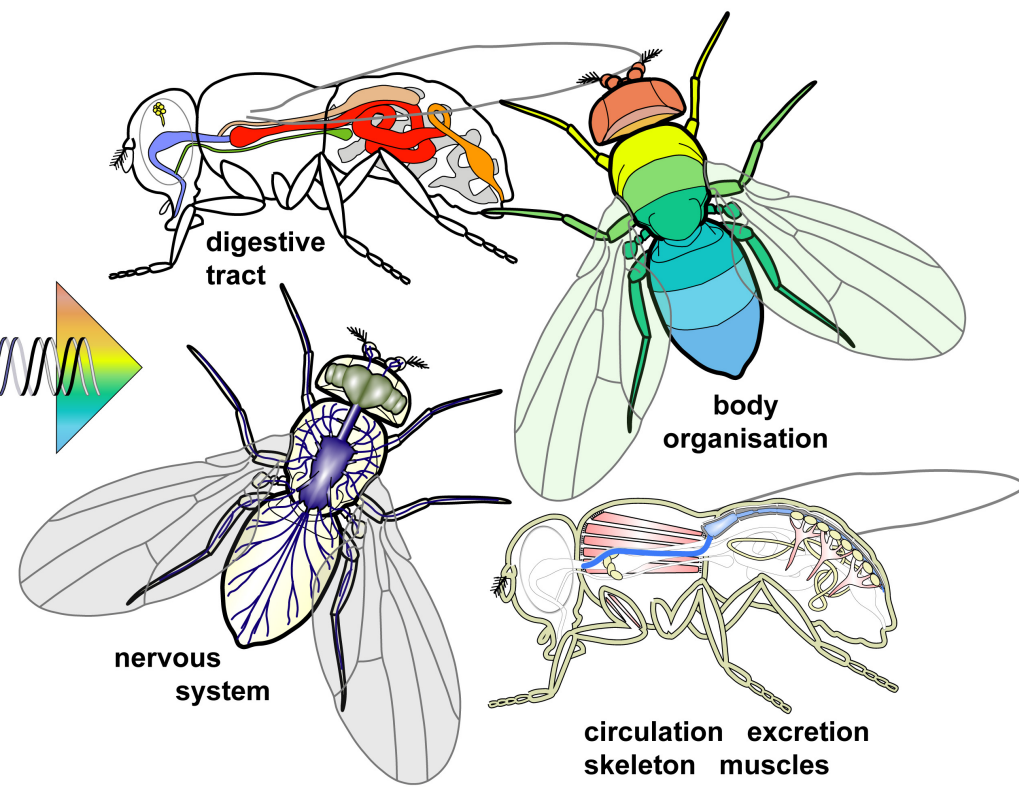
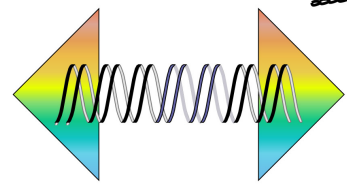
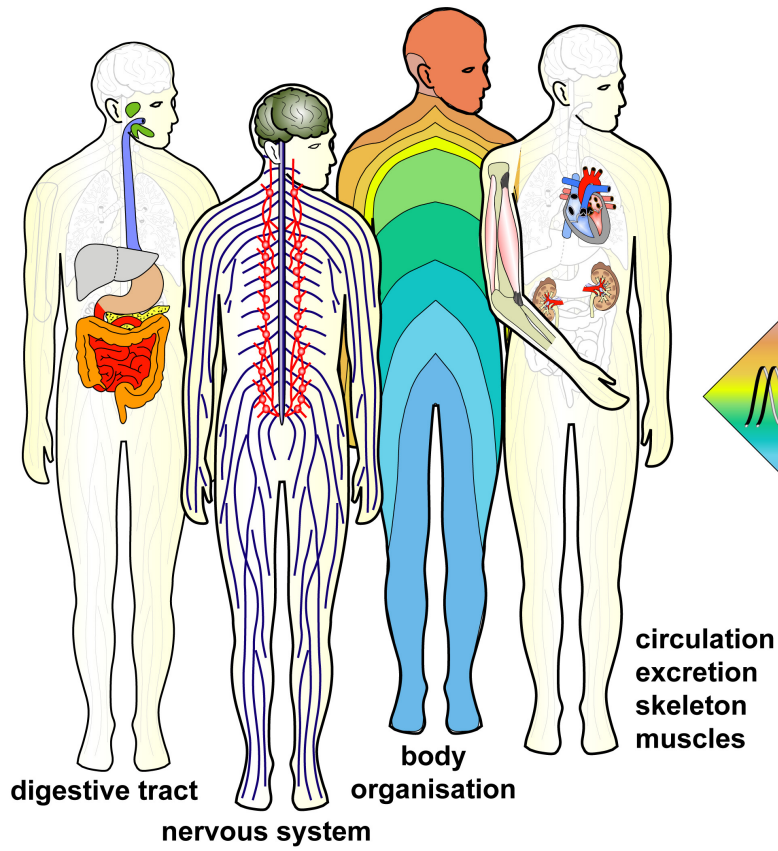


≈ chimp

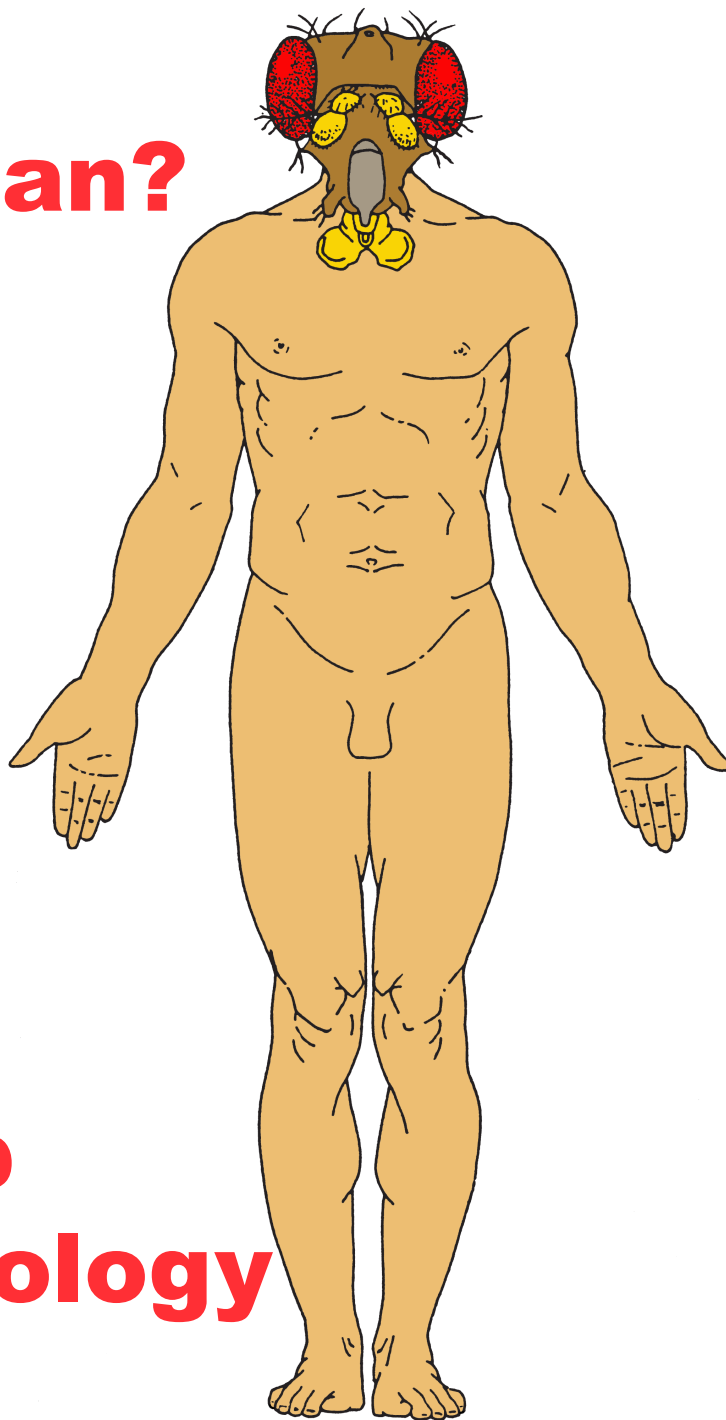
Homeosis

Evo-Devo





Flyman?



**Deep
Homology**

Fly Cell Language:

Hedgehog

Wnt

TGF-beta

EGFR

Notch

Human Cell Language:

Hedgehog

Wnt

TGF-beta

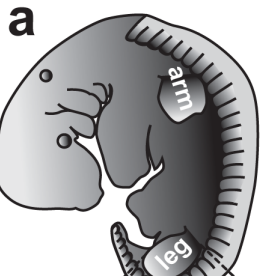
EGFR

Notch

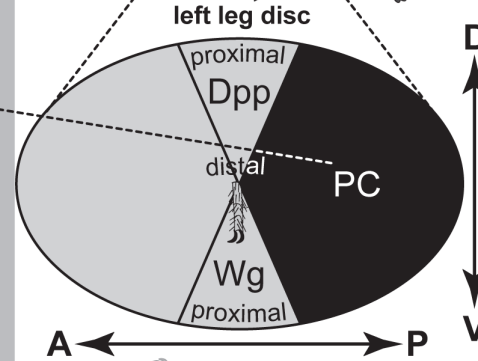
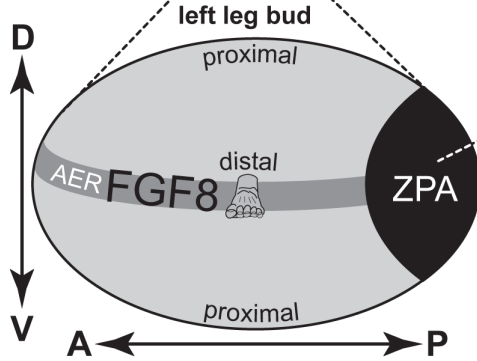
Limb Area Codes

Human quirks

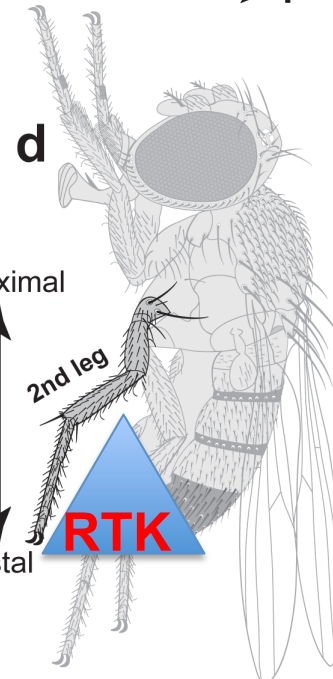
Fly quirks



Shared



Shh/Hh



c

d

proximal

proximal

{ Meis/Hth
mTsh/Tsh }

Dach/Dac

Dlx/Dll

distal

distal

Campbell (2002):
RTK Gradient

RTK

RTK

The End