果蠅：一個生物學家的工具箱

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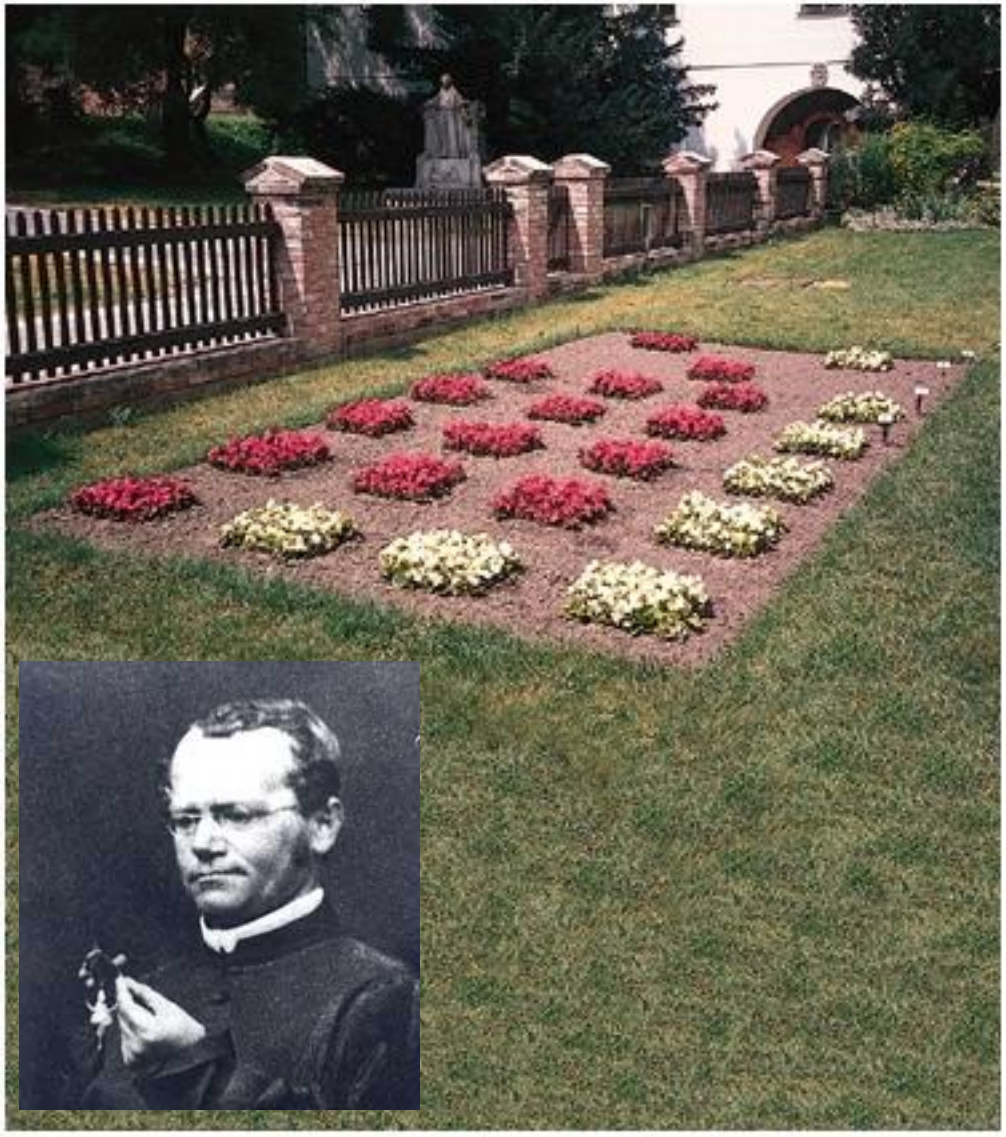
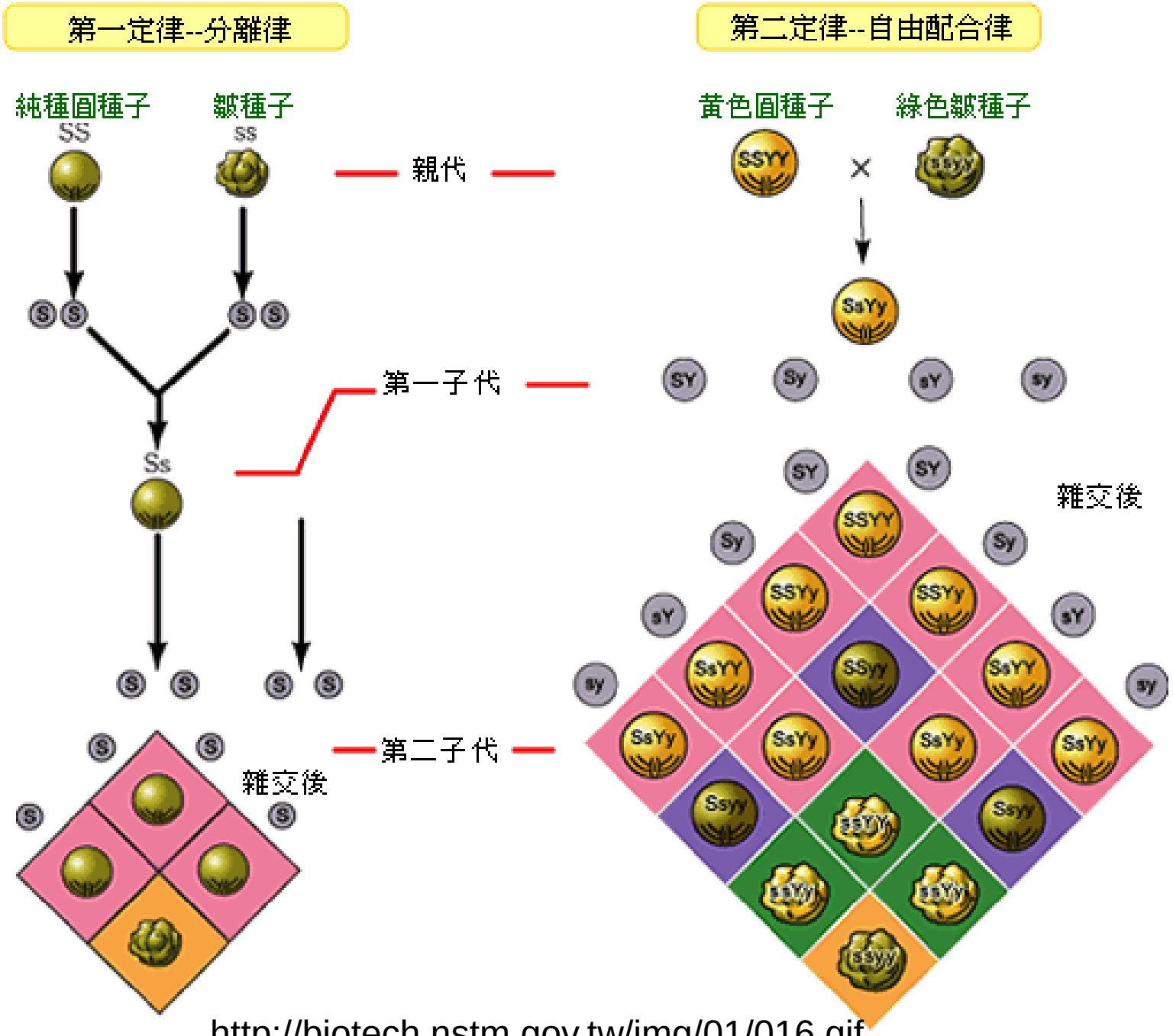
內容

- 遺傳學
- 發育生物學
- 行為科學
- 生物醫學

孟德爾跟他的豌豆實驗

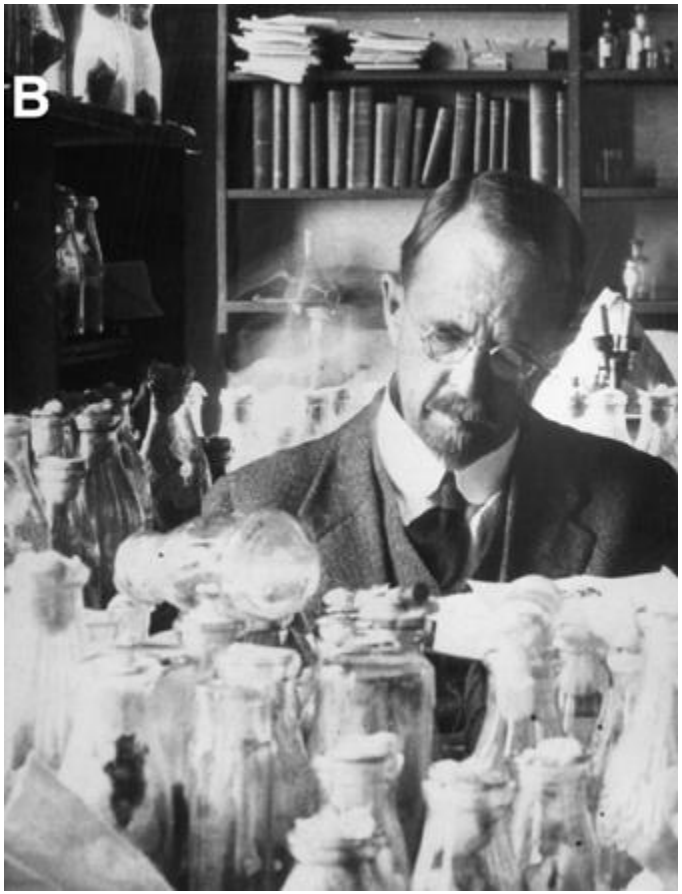


Character	Contrasting traits	
Seeds	round/wrinkled	
	yellow/green	
Pods	full/constricted	
	green/yellow	
Flower color	violet/white	
Flower position	axial/terminal	
Stem length	tall/dwarf	

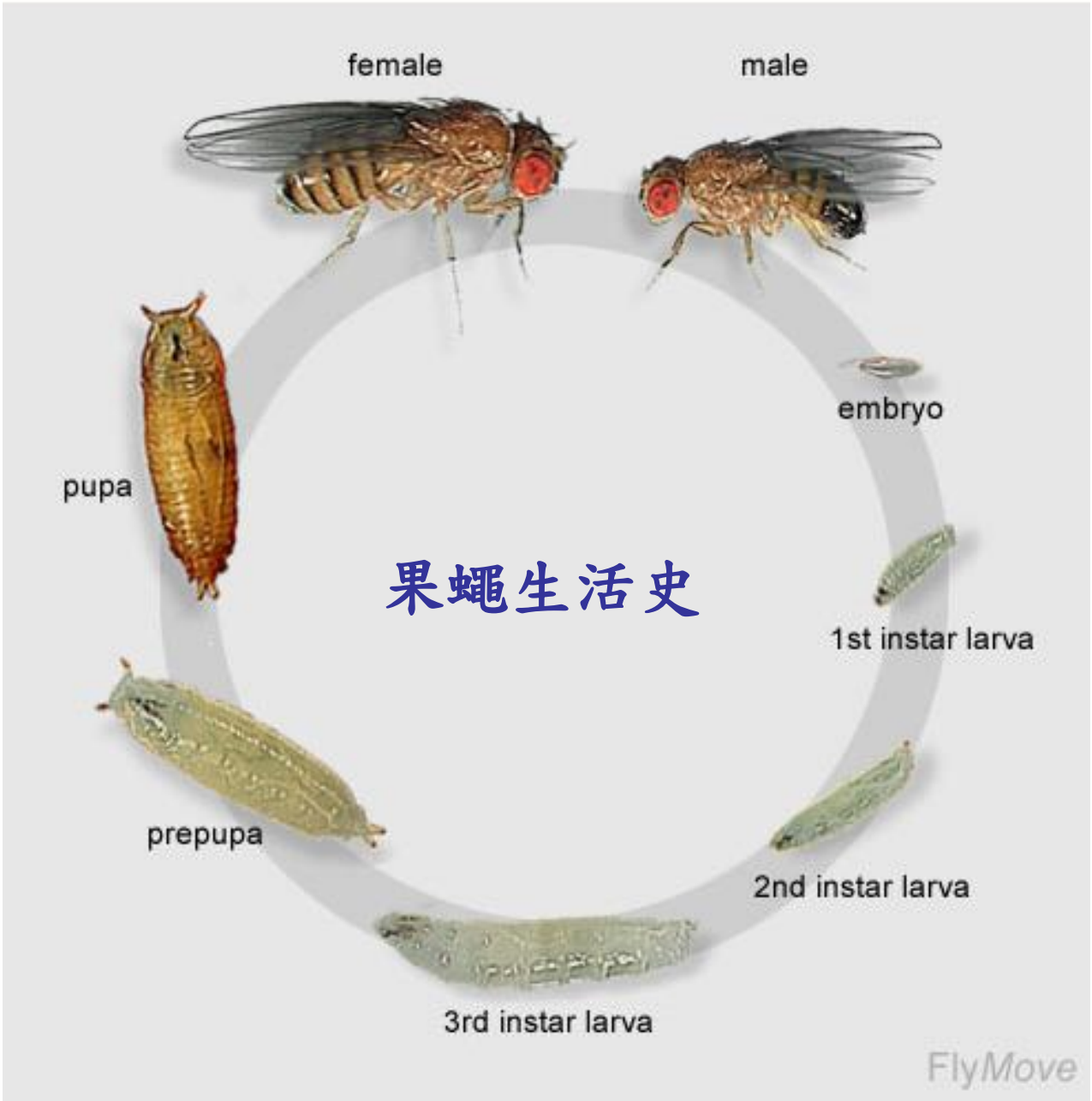


http://biotech.nstm.gov.tw/img/01/016.gif

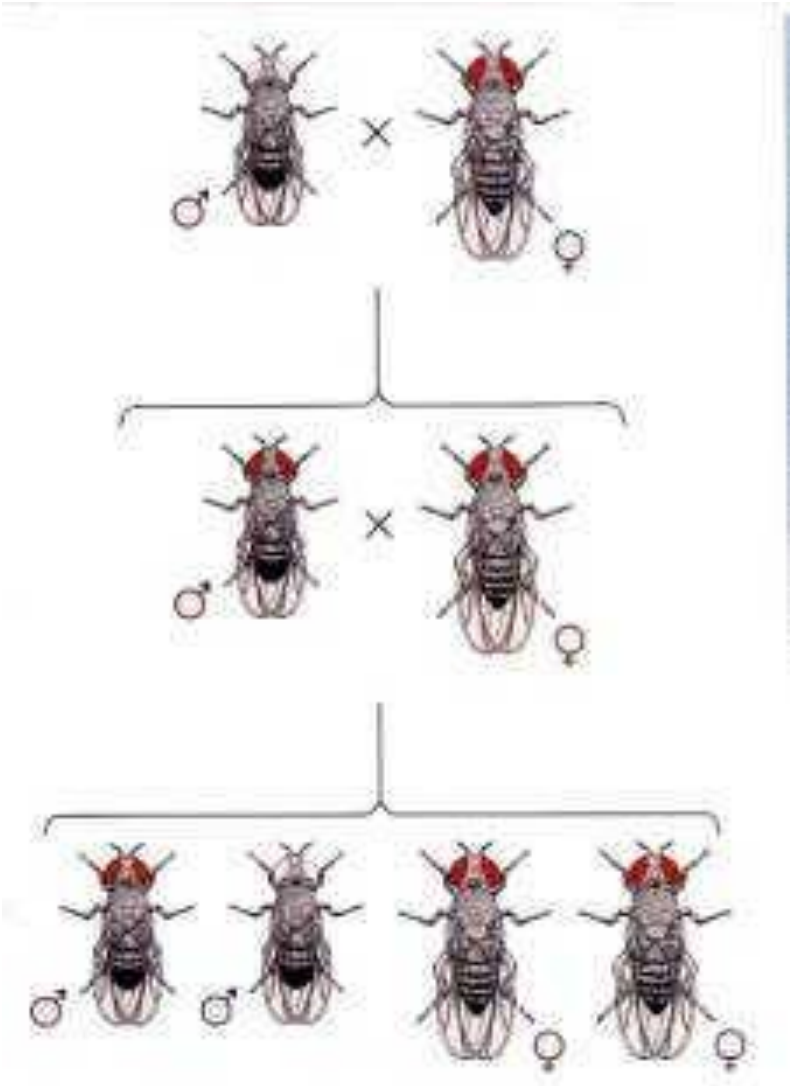
摩根和哥倫比亞大學的果蠅房



The life cycle of *Drosophila melanogaster*



首先有了白眼果蠅

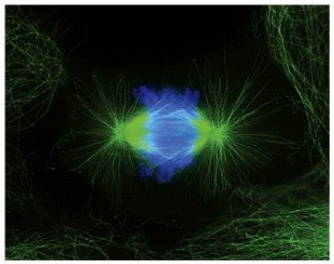


親代：X^wY（白眼）× $X^{w+}X^{w+}$（紅眼）

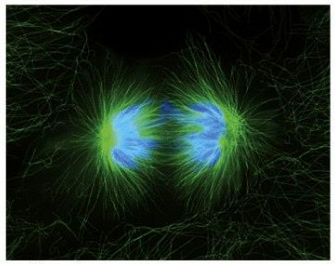
第一子代：$X^{w+}Y$（紅眼）× $X^{w+}X^{w}$（紅眼）

第二子代：$X^{w+}Y$（紅眼）：$X^{w}Y$（白眼）：
$X^{w+}X^{w+}$（紅眼）：$X^{w+}X^{w}$（紅眼）

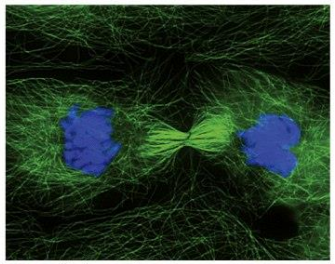
http://vschool.scu.edu.tw/biology/content/genetics/ge030201.htm



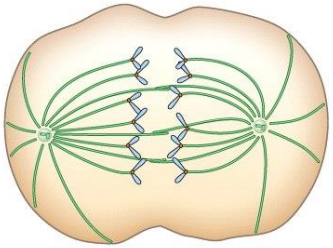
Anaphase



Telophase



Cytokinesis

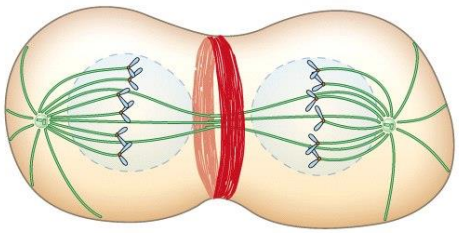


APC/C activated and cohesins degraded

Anaphase A: Chromosome movement to poles

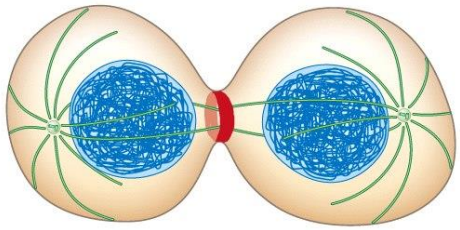
Anaphase B:

Spindle pole separation



Nuclear envelope reassembly

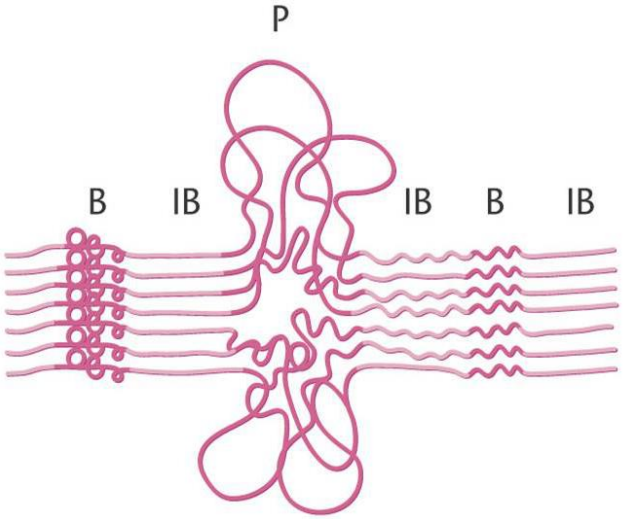
Assembly of contractile ring

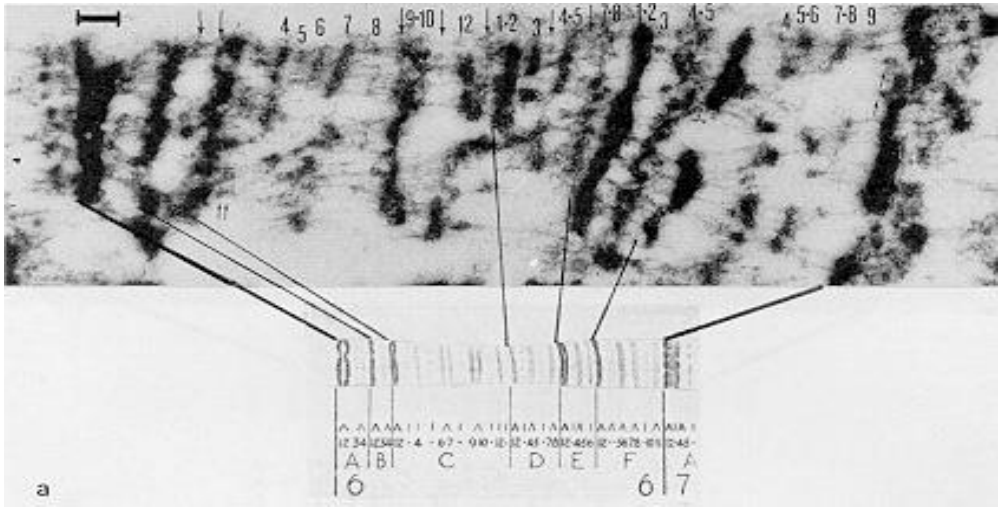


Reformation of interphase microtubule array

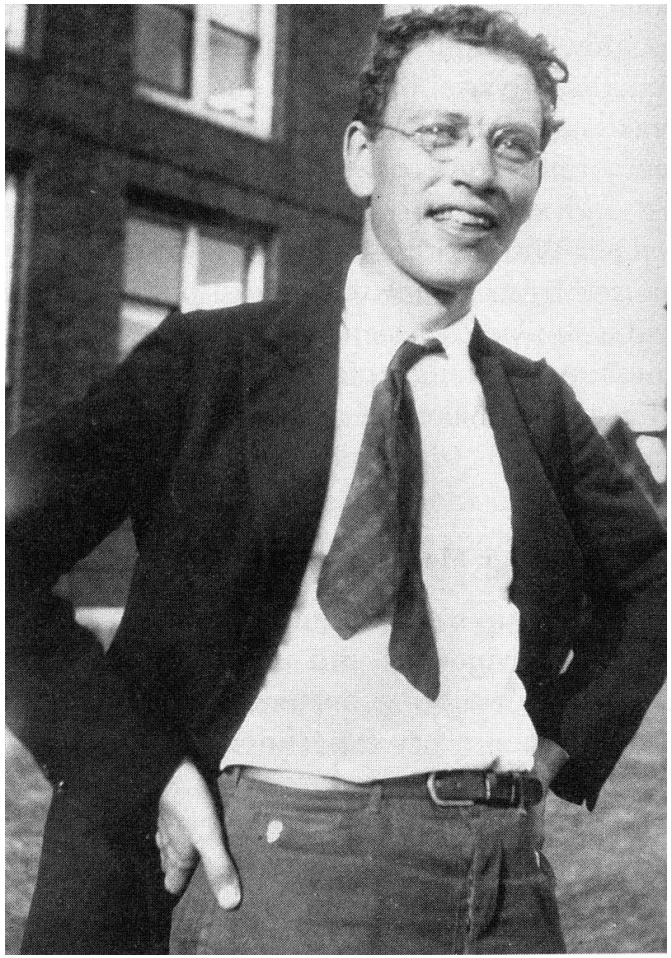
Contractile ring forms cleavage furrow

果蠅唾腺細胞的巨大染色體

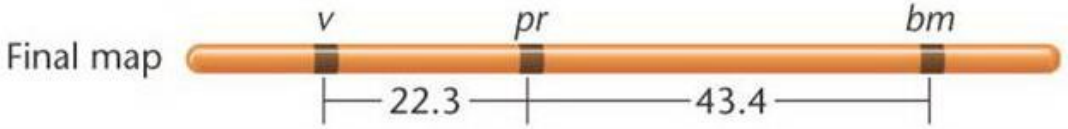




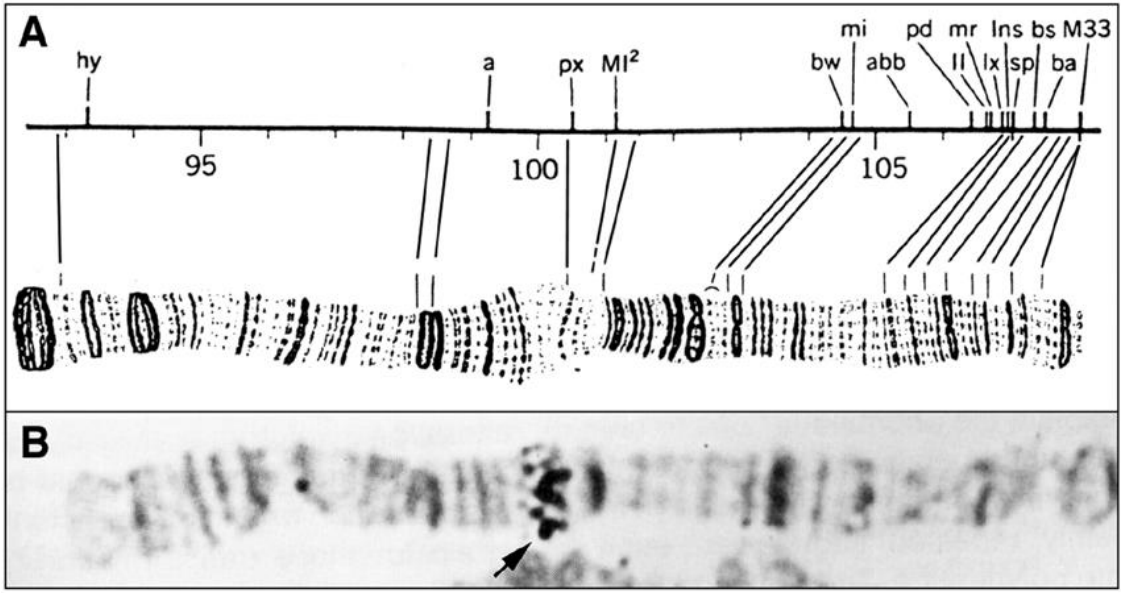
基因間的距離與其重組的比例成正比



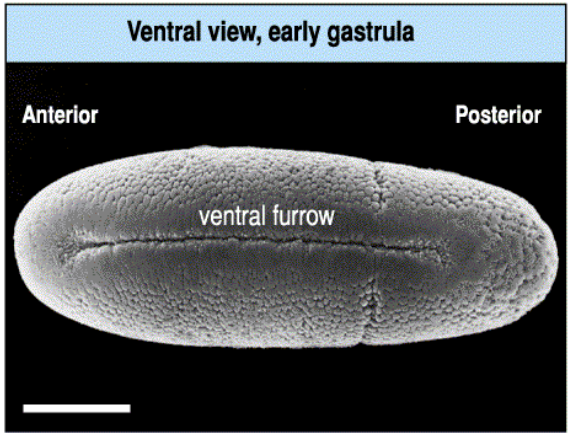
Alfred Sturtevant

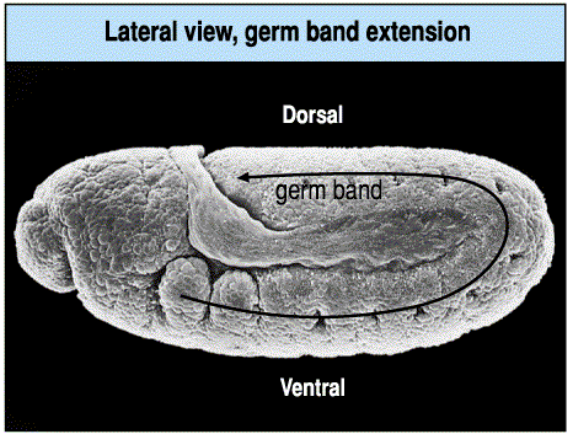


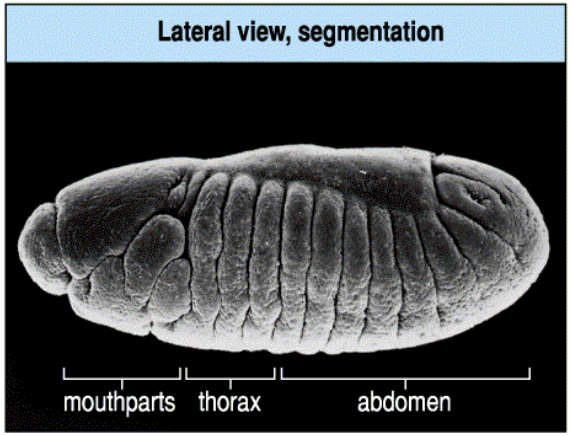
基因距離的單位：centiMorgans（cM）

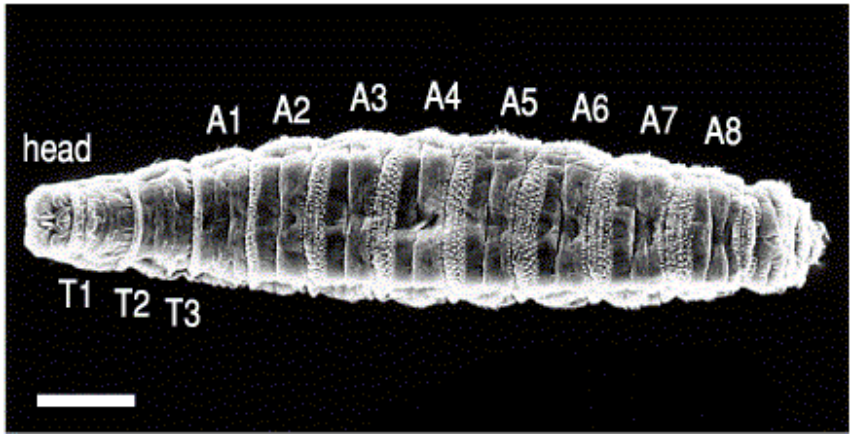


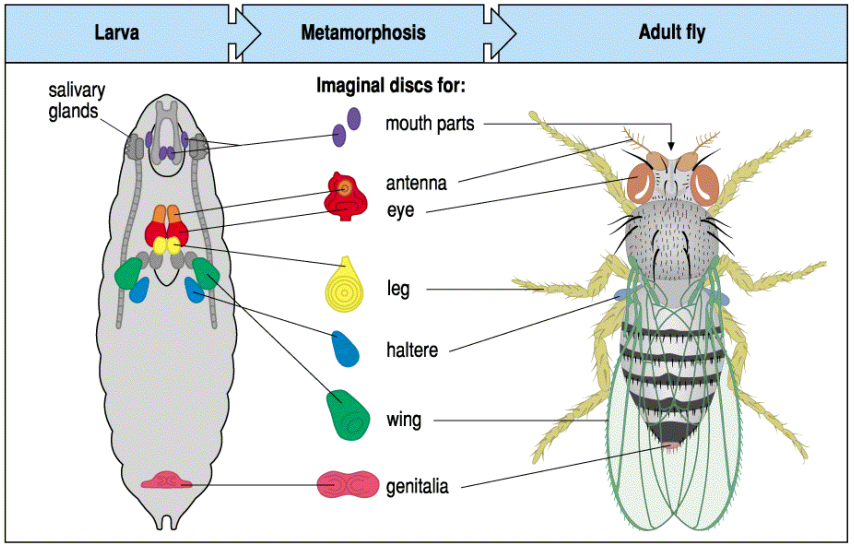
發育生物學: Right place at right time in right dosage











The Nobel Prize in Physiology or Medicine 1995

Edward B. Lewis, Christiane Nüsslein-Volhard, Eric F. Wieschaus

The Nobel Prize in Physiology or Medicine 1995

Nobel Prize Award Ceremony

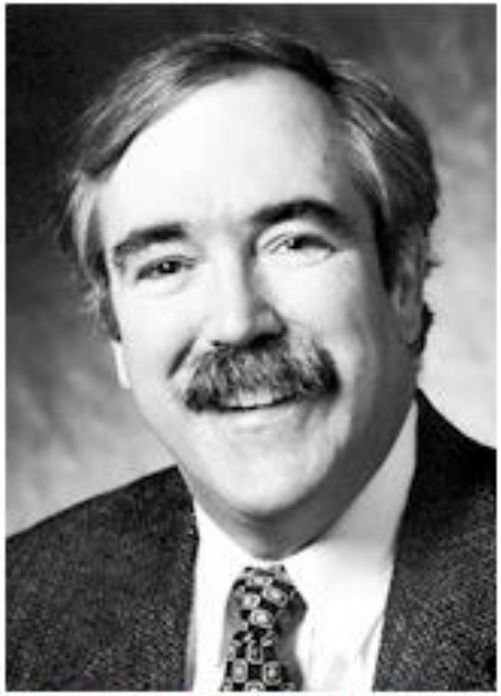
Edward B. Lewis

Christiane Nüsslein-Volhard

Eric F. Wieschaus

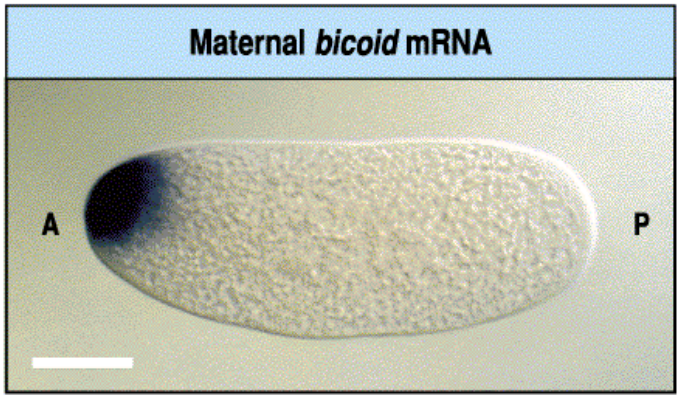
Edward B. Lewis

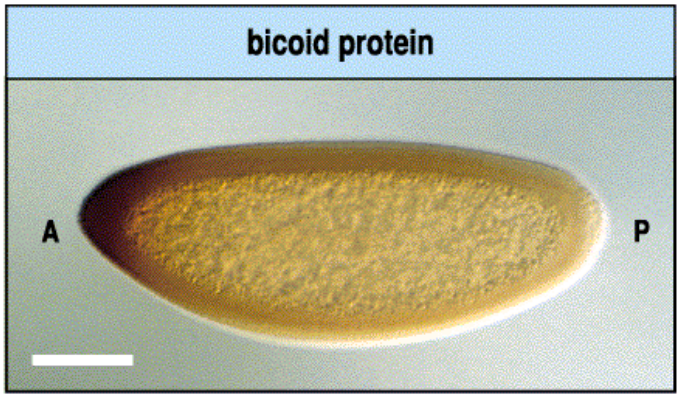
Christiane Nüsslein-Volhard

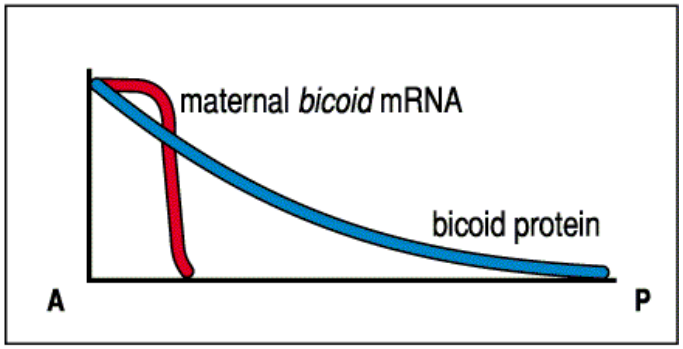


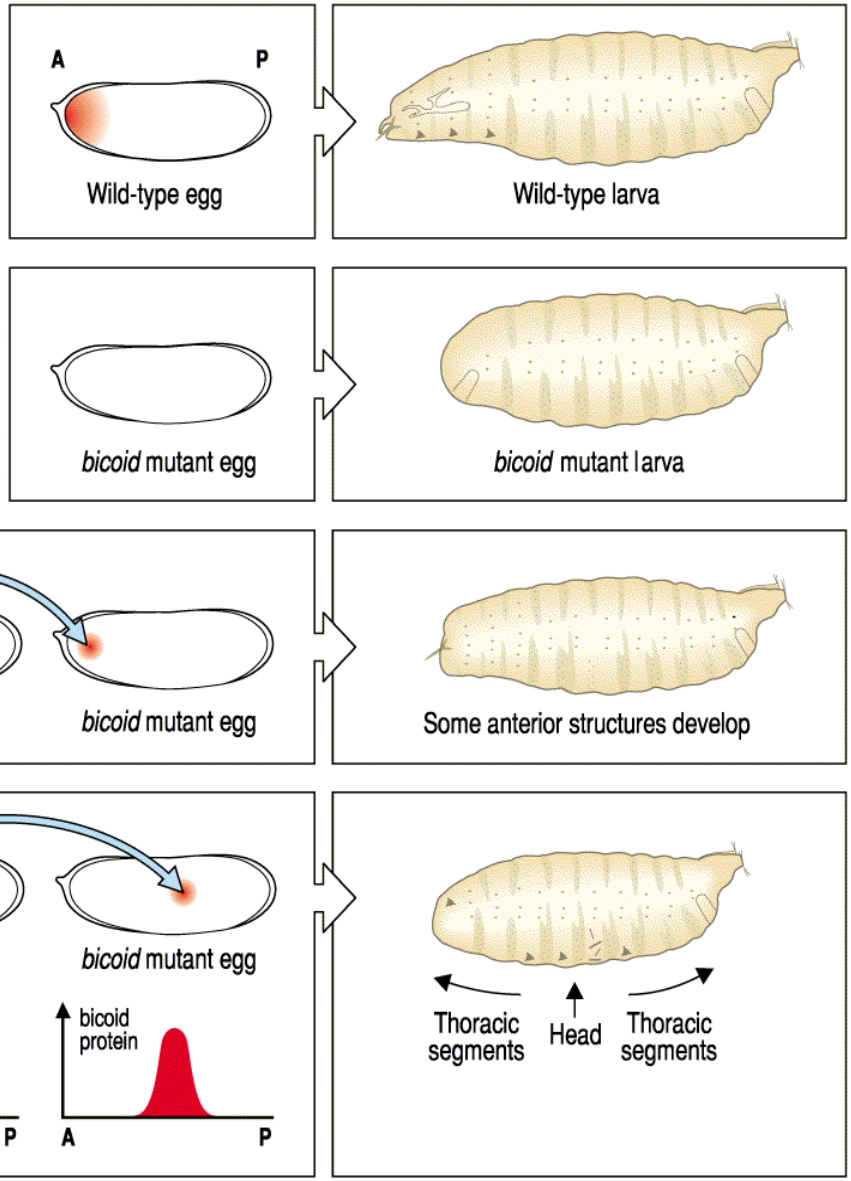
Eric F. Wieschaus

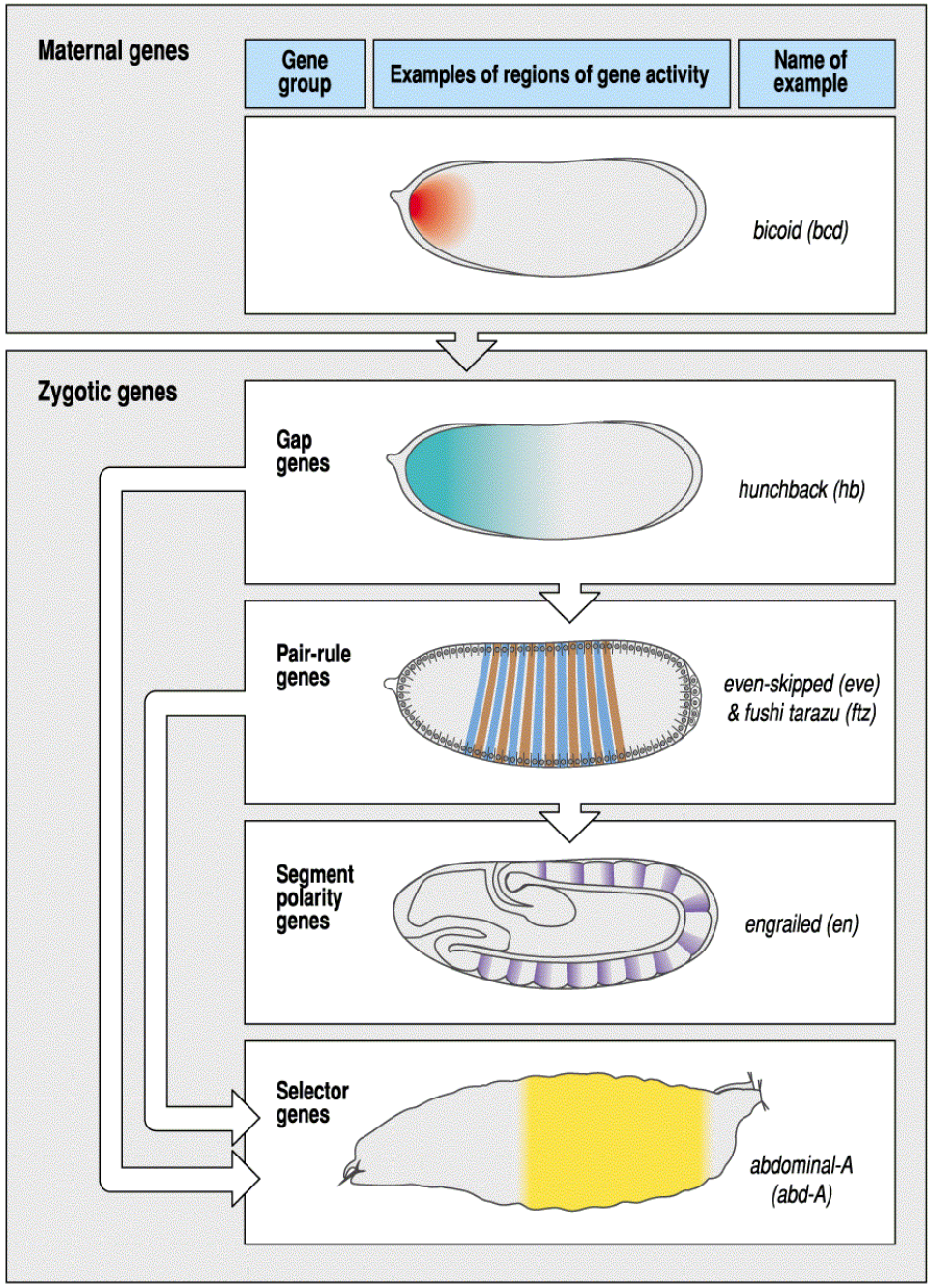
母源基因控制體軸的特性



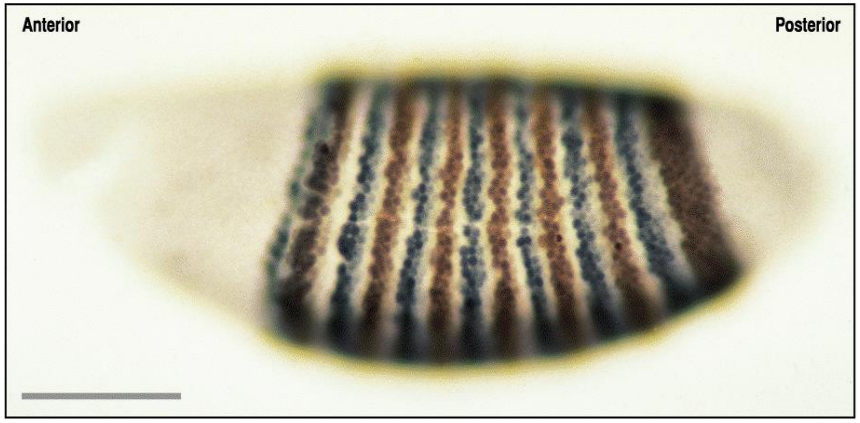






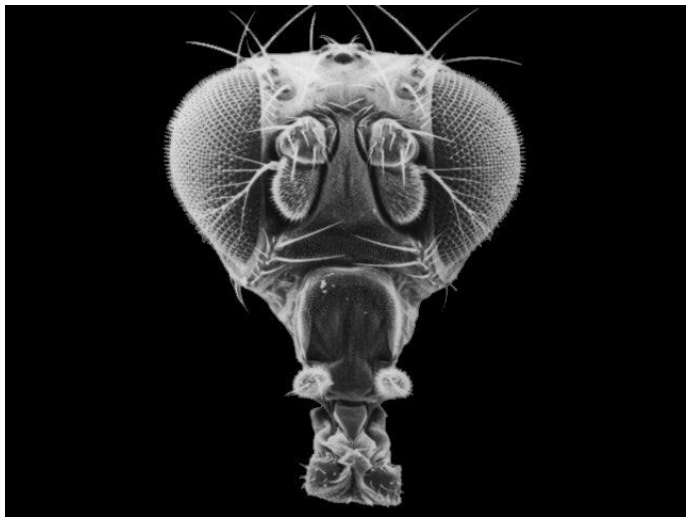


合子基因進一步分割與篩選特定體節成為特定器官

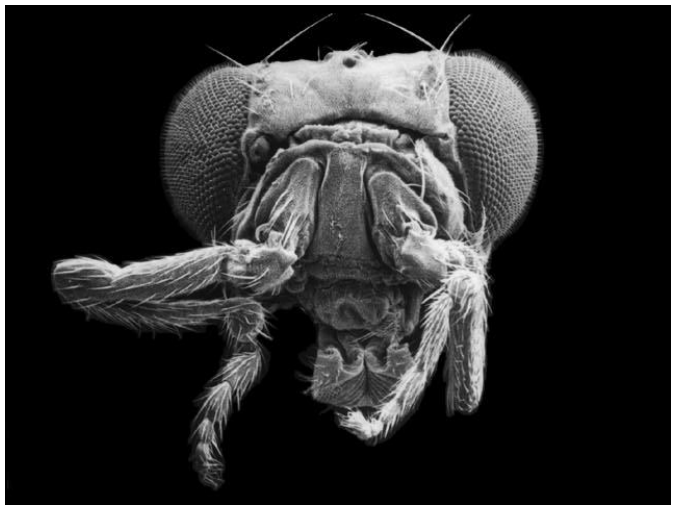


Homeotic transformation

野生型



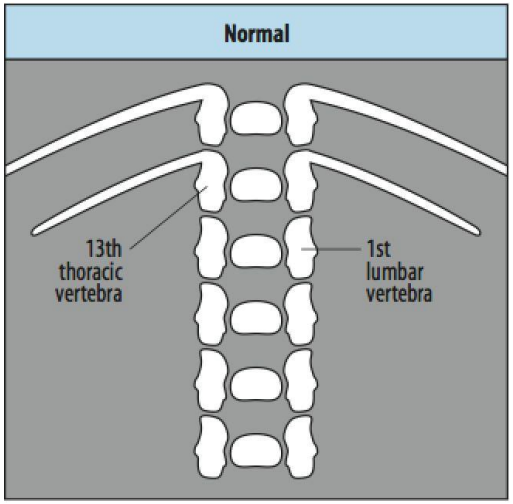
Antennapedia 觸角轉化成腿

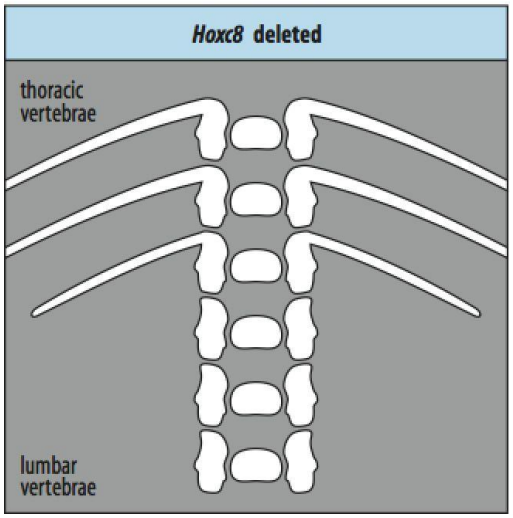


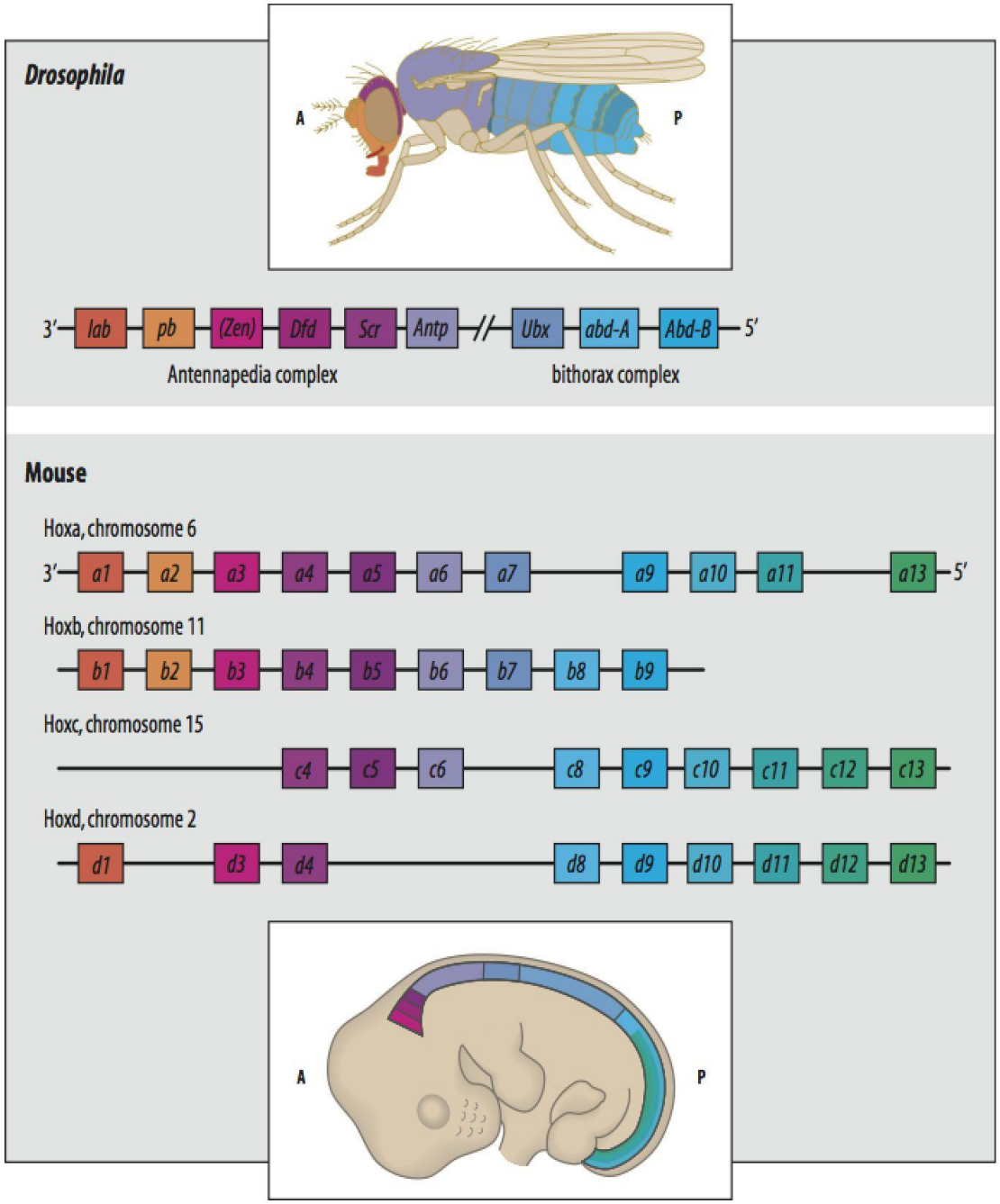
野生型

雙胸果蠅第三胸節轉化成第二胸節

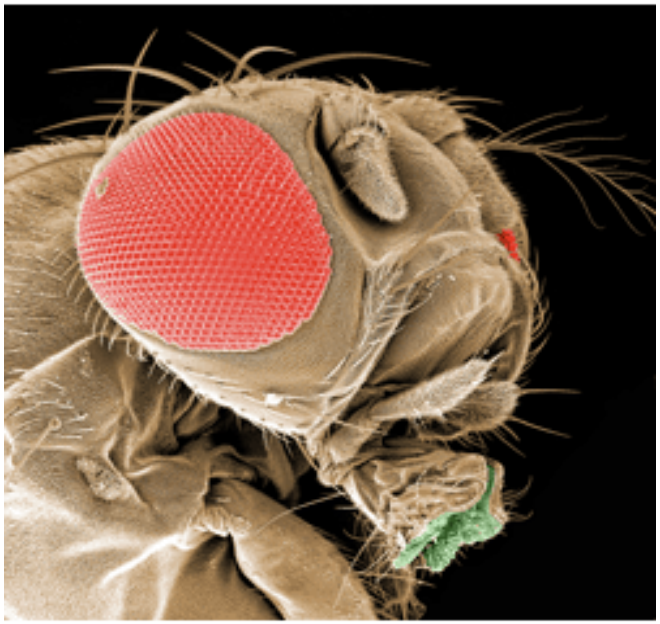
同源箱基因組的保守性


Normal
13th thoracic vertebra
1st lumbar vertebra


Hoxc8 deleted
thoracic vertebrae
lumbar vertebrae

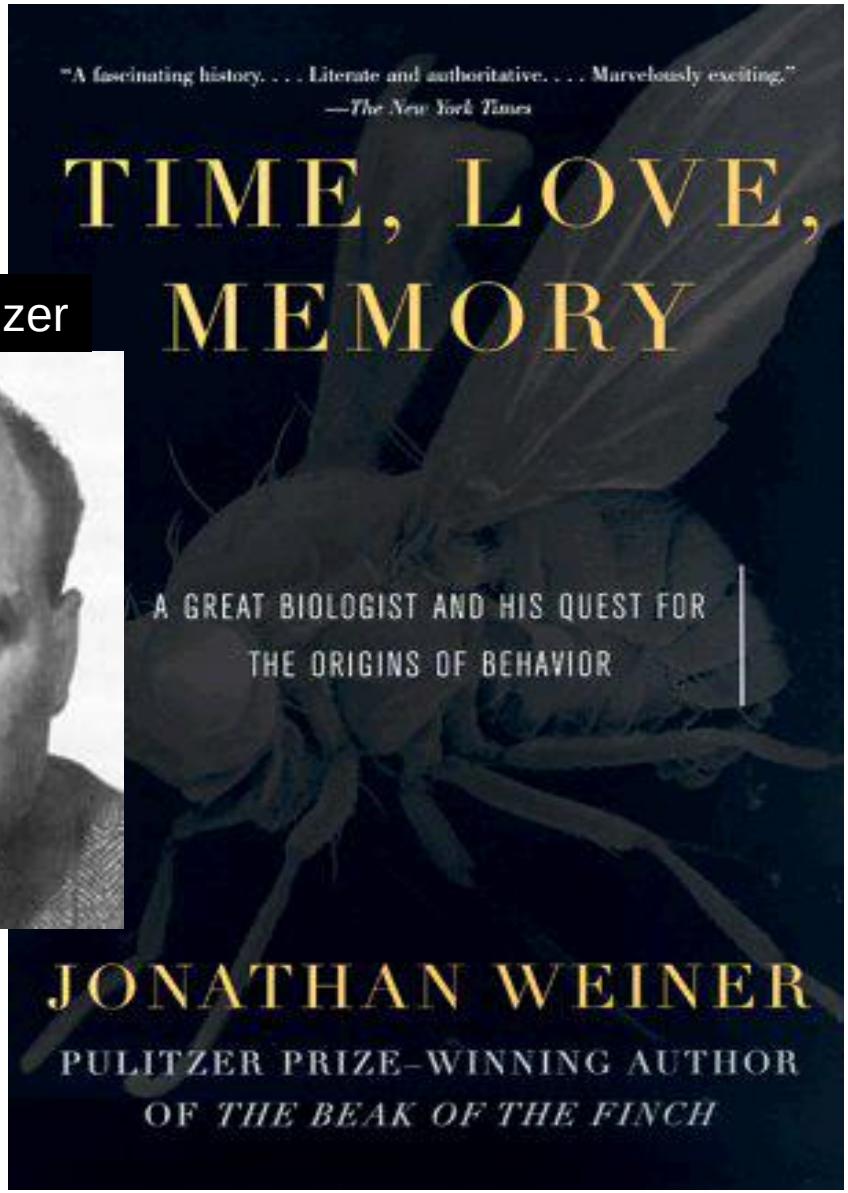

Drosophila
A
P
3′
lab
pb
(Zen)
Dfd
Scr
Antp
Ubx
abd-A
Abd-B
5′
Antennapedia complex
bithorax complex
Mouse
Hoxa, chromosome 6
3′
a1
a2
a3
a4
a5
a6
a7
a9
a10
a11
a13
5′
Hoxb, chromosome 11
b1
b2
b3
b4
b5
b6
b7
b8
b9
Hoxc, chromosome 15
c4
c5
c6
c8
c9
c10
c11
c12
c13
Hoxd, chromosome 2
d1
d3
d4
d8
d9
d10
d11
d12
d13
A
P

主控基因

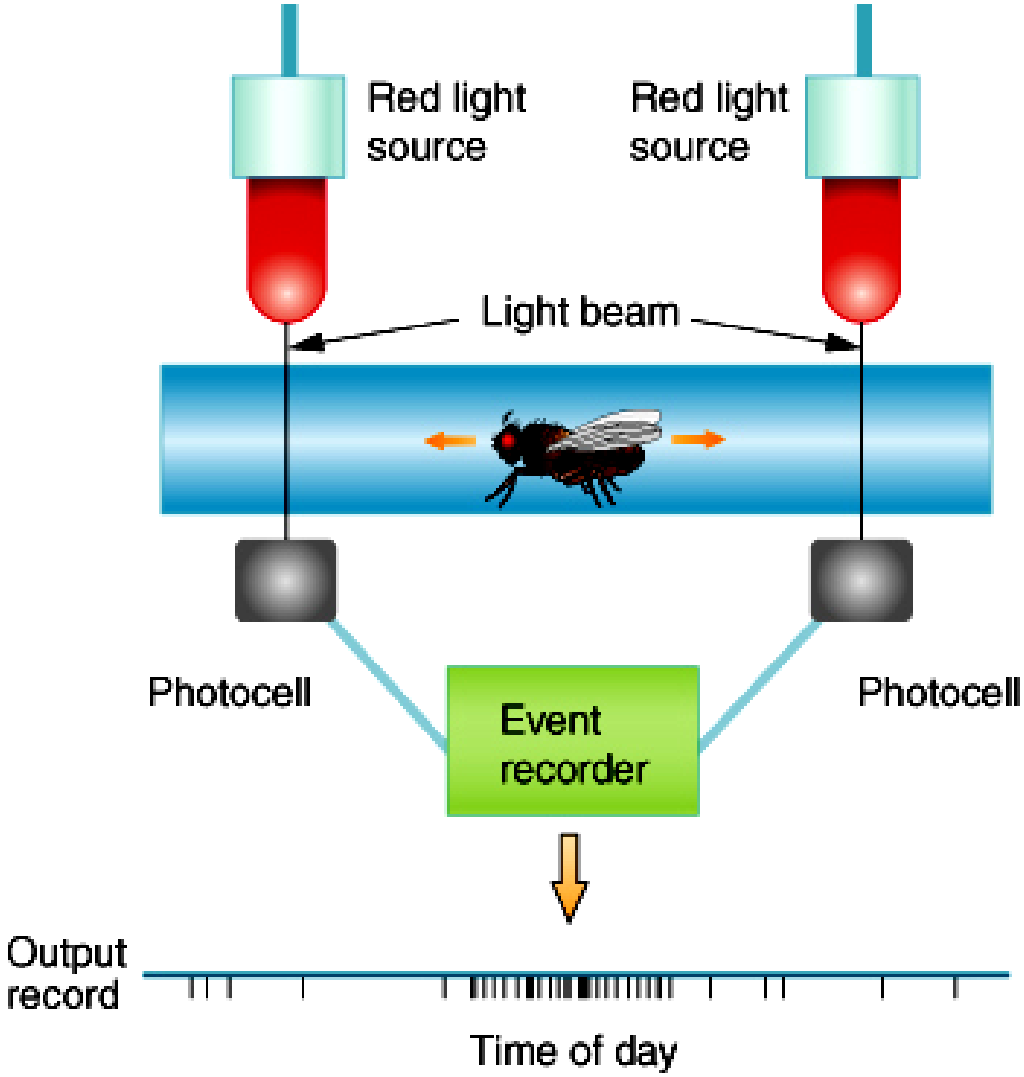


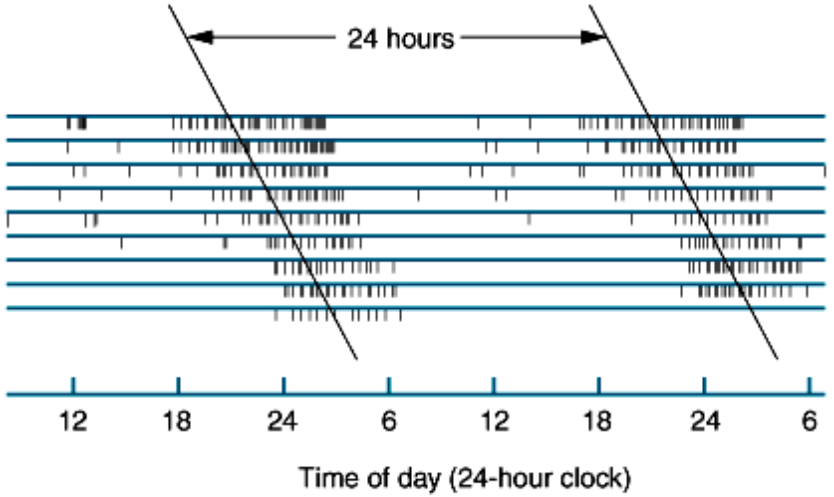
行為科學：是天性還是教養

Seymour Benzer

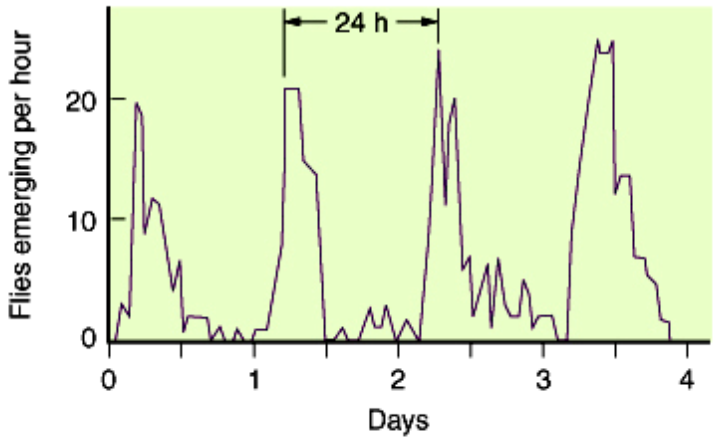


Circadian Rhythms：
日夜週期

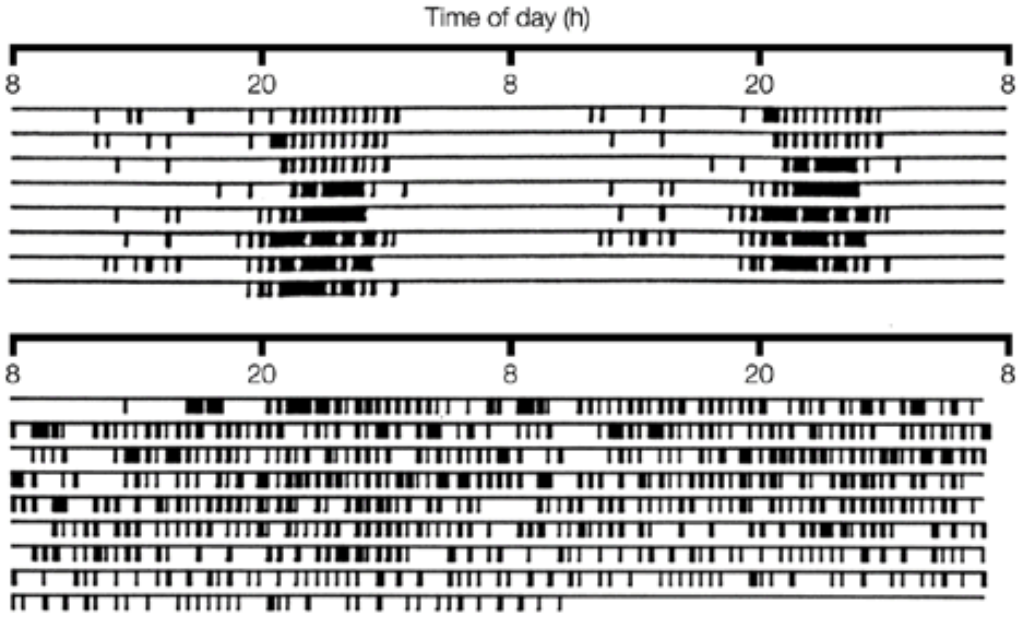




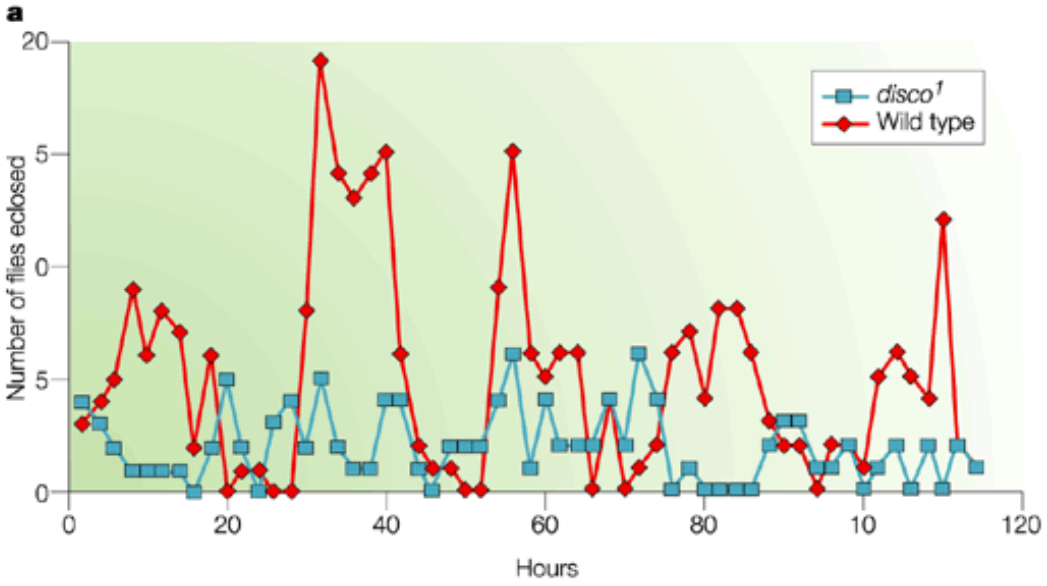
(b)



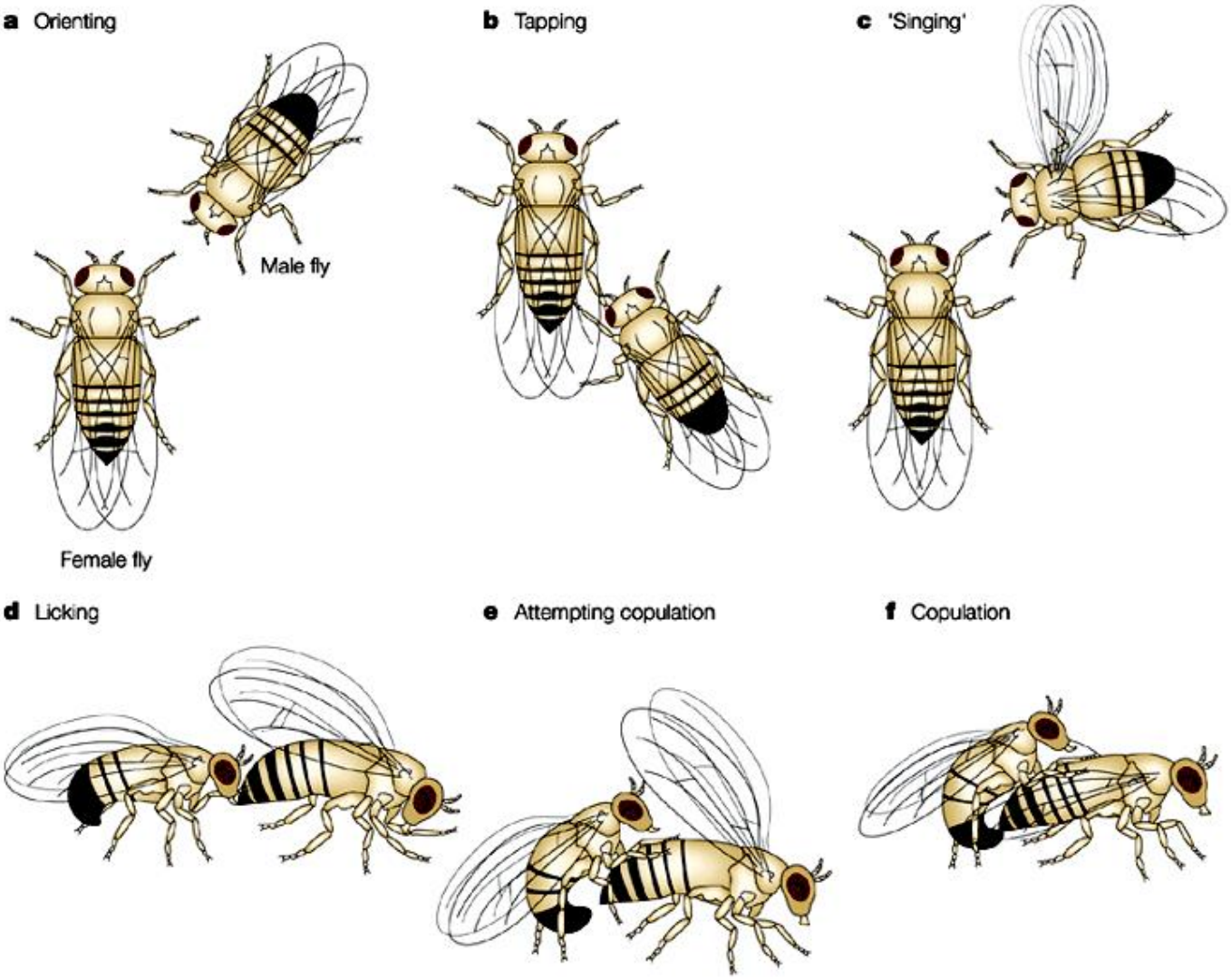
(c)



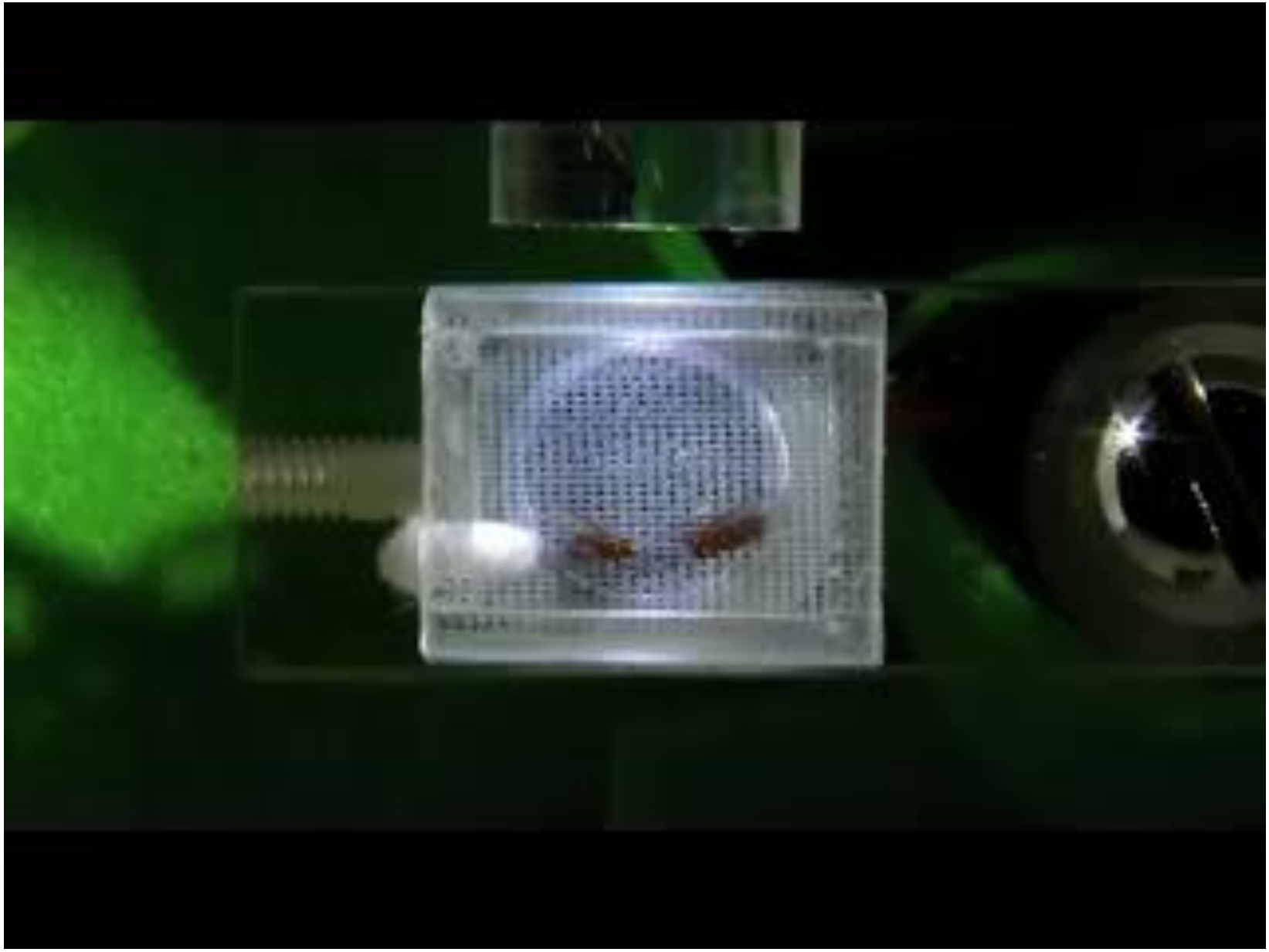
period or ***per***



果蠅的交尾行為


a Orienting
Male fly
Female fly
b Tapping
c 'Singing'
d Licking
e Attempting copulation
f Copulation
Nature Reviews | Genetics

Love song and mating



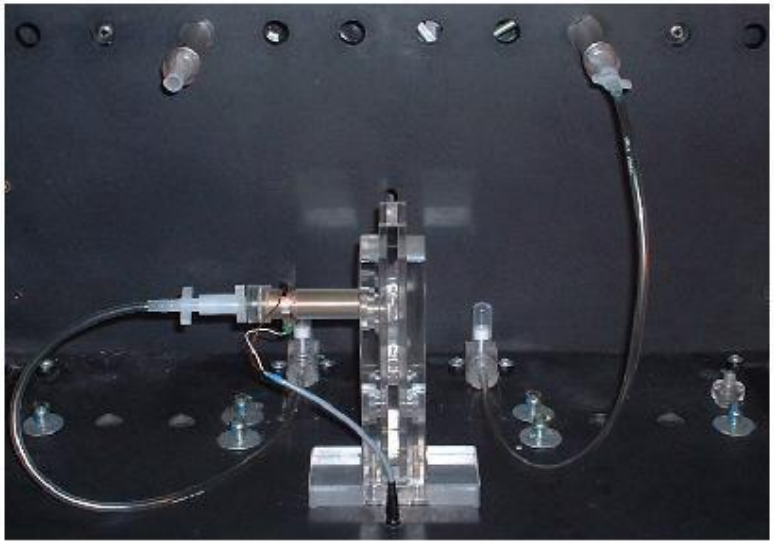
Fruitless gene and Mating chain

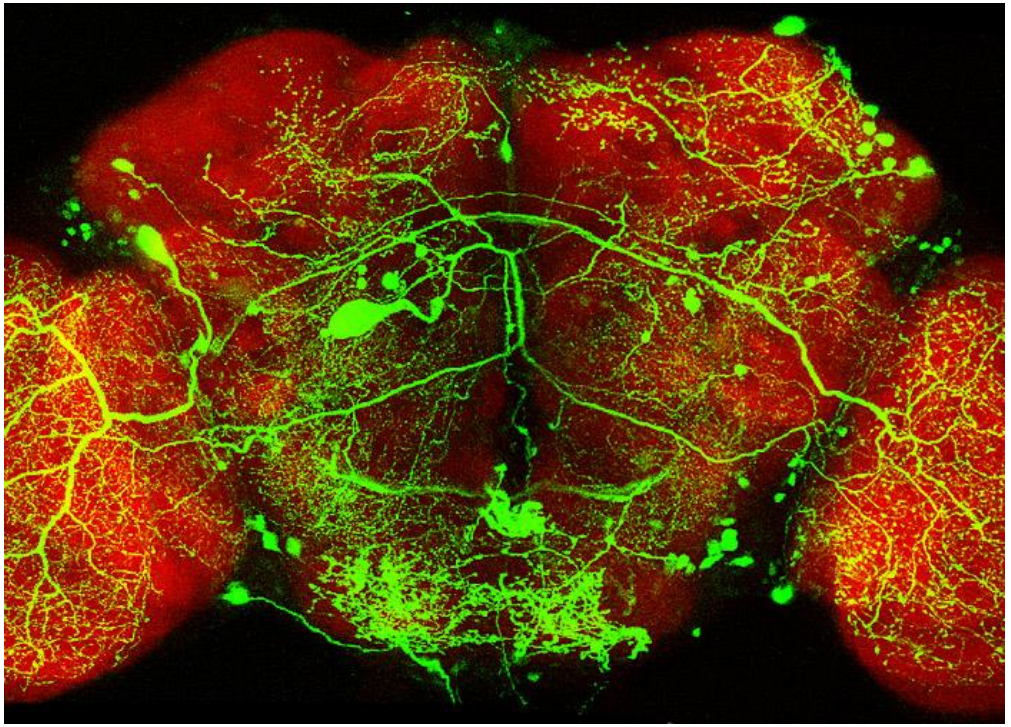
Sexual deprivation increases alcohol consumption in Fruit flies

Fighting behavior-I

Fighting-II

Drosophila olfactory classical conditioning paradigm



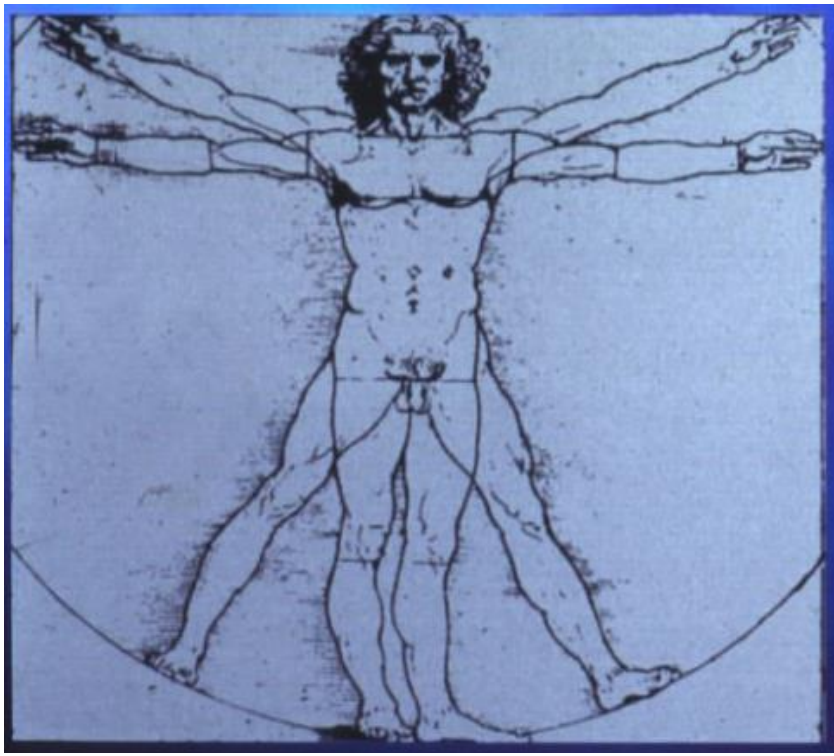


http://faculty.unlv.edu/debelle/dbs/debelle.html

Decision making

http://www.drosophila images.org/2009.shtml

生物醫學:果蠅疾病模式



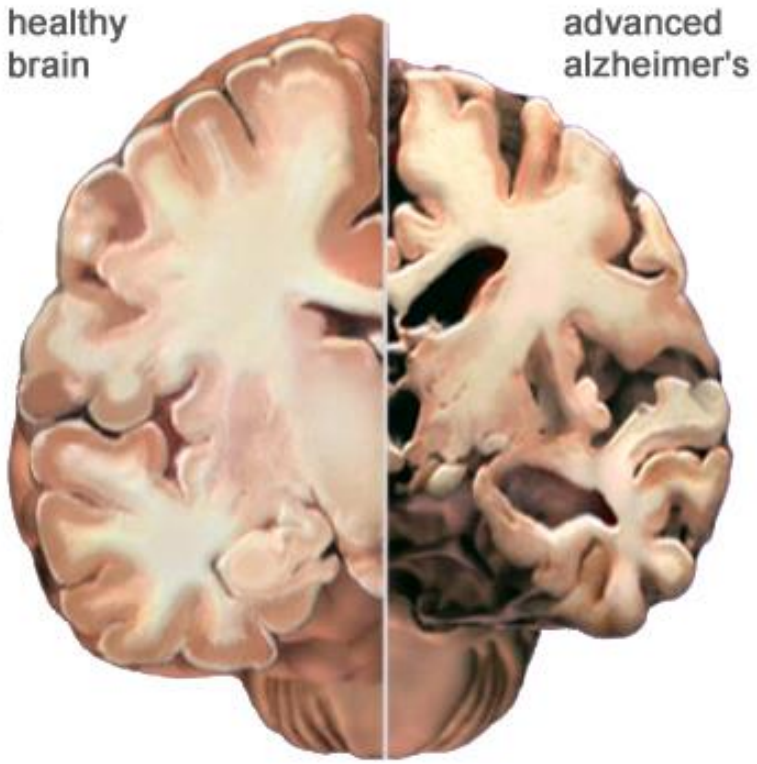
DISORDER	NUMBER OF GENES	DISORDER	NUMBER OF GENES	DISORDER	NUMBER OF GENES	DISORDER	NUMBER OF GENES
Neurological	**74**	**Ophthalmologic**	**43**	**Immunological**	**33**	**Skeletal Development**	**26**
Neuromuscular	20	**Anterior segment**	**(13)**	Complement mediated	11	Craniosynostosis	5
Neuropsychiatric	9	Aniridia	1	Other	22	Skeletal dysplasia	13
CNS/Developmental	8	Rieger syndrome	1			Other	8
CNS/Ataxia	9	Mesenchymal dysgenisis	2	**Hematologic**	**42**		
Mental Retardation	6	Iridogoniodysgenisis	2	Erythrocyte, general	29	**Soft Tissue**	**2**
Other	22	Corneal dystrophy	2	Porphyrias	7	**Connective Tissue**	**18**
		Cataract	3	Platelets	6	**Dermatologic**	**25**
Endocrine	**50**	Glaucoma	2			**Metabolic/mitochondrial**	**123**
Diabetes	10	**Retina**	**(30)**	**Coagulation abnormalities**	**28**	**Pharmacologic**	**12**
Other	40	Retinal dystrophy	1			**Peroxisomal**	**9**
		Choroiderimea	1	**Malignancies**	**79**		
Deafness	**13**	Color vision defects	4	Brain	3	**Storage**	**37**
Syndromic	7	Cone dystrophy	2	Breast	4	Glycogen storage	11
Nonsyndromic	6	Cone rod dystrophy	1	Colon	11	Lipid storage	13
		Night blindness	8	Other gastrointestinal	3	Mucopolysaccaridosis	10
Cardiovascular	**26**	Leber congenital amaurosis	2	Genitourinary	5	Other	3
Cardiomyopathy	10	Macular dystrophy	4	Gynocologic	3		
Conduction defects	4	Retinitis pigmentosa	7	Endocrine	3	**Pleitropic Developmental**	**35**
Hypertension	7			Dermatologic	3	Growth, immune, cancer	7
Atherosclerosis	3	**Pulmonary**	**4**	Xeroderma pigmentosa	6	Apoptosis	1
Vascular malformations	2	**Gastrointestinal**	**13**	Other/sarcomas	9	Other	27
		Renal	**13**	Hematologic Malignancies	29		
						Complex other	**9**
						TOTAL	**714**

77%造成人類遺傳疾病的基因與果蠅有相似性

老年人口成長愈來愈快速

- 經建會估算台灣在民國一百一十年的老年人口將翻倍數成長，從現今二一三萬增加到三九二萬人
- 老人每人每年醫療費用高達非老人的二．五倍以上
- 隨著老年人口增加退化性神經疾病之患者也以驚人速度攀升（以失智為例：台灣現約有9萬多，平均每天增加10位）

阿茲海默症（Alzheimer’s Disease）



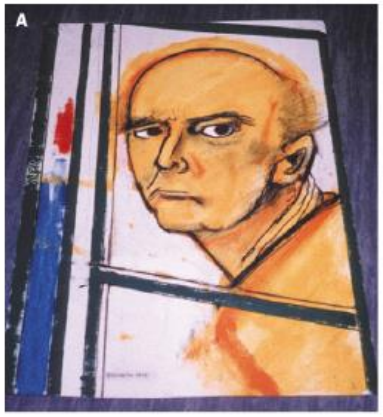
- 由一位精神科兼神經病理學家Alois Alzheimer在1906年在德國記錄了患者腦部細微的變化所發表的報告，並根據他的名字來作為此疾病的命名。
- 是一種腦部疾病，會造成腦部神經細胞功能的逐漸喪失，由於腦部神經細胞專責思考、記憶、運算及行動，所以，隨著時間一分一秒的過去，病人的心智功能逐步喪失，甚至最後連執行最基本的日常生活能力都會失去，像是刷牙、穿衣、洗澡及大小便等。

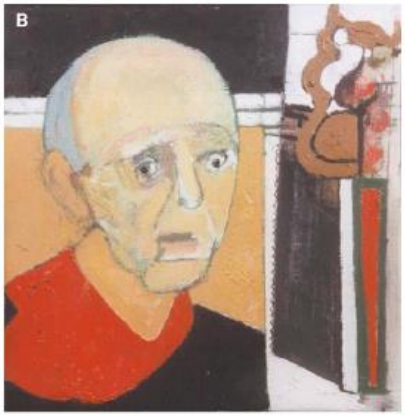
Six self-portraits by artist William Utermohlen chronicle his experience with Alzheimer's disease.
Utermohlen was diagnosed at the age of 60

http://www.csuci.edu/alzheimer/images/selfportraits.jpg

我不知道你是誰，但你一定是跟我很親近的人

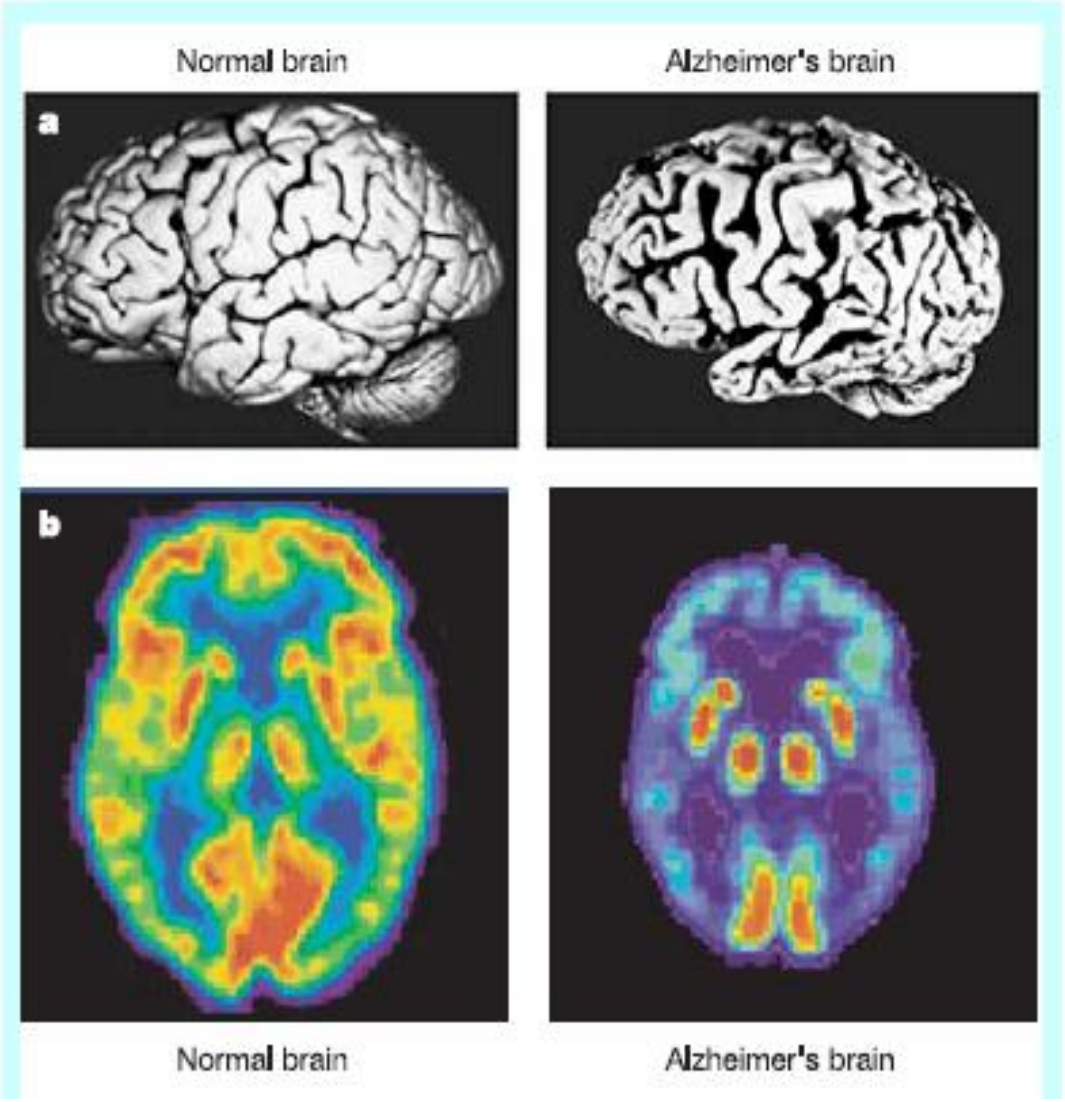
- 在美國，估計就有超過400萬人罹患此病，僅次於心臟病、癌症及腦中風
- 有些患者會變成偏執狂，常常懷疑照顧他們的人想毒害他們，或臆測伴侶不忠。患者也可能會喪失時間和空間觀念，半夜起床更衣，或漫無目的地走到街上，然後迷路，連自己本來熟悉的道路也認不出來。
- 這些改變會令病人的親屬和關心他的人壓力重重，非常苦惱，彷彿失去了一個他們曾經很熟悉的人。





Self-portraits of William Utermohlen

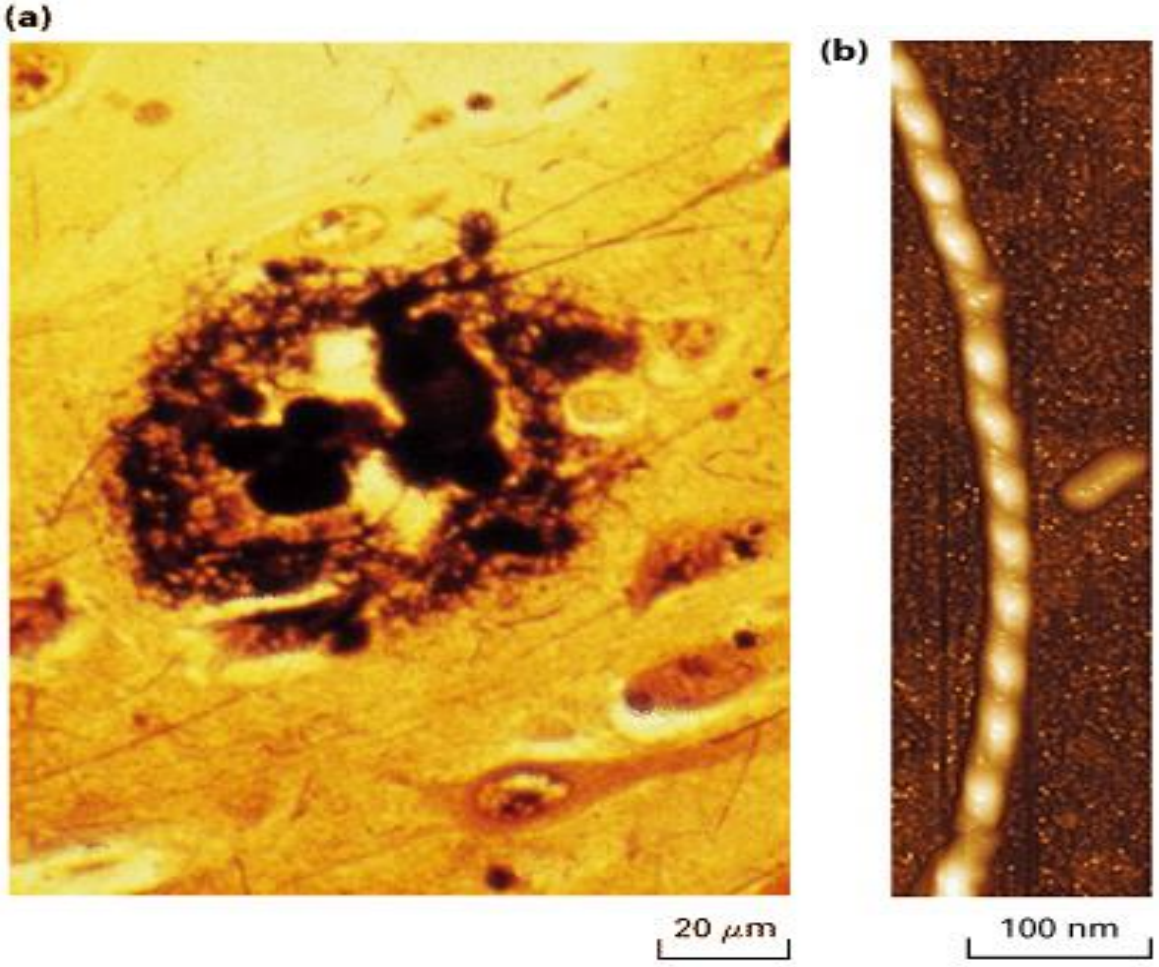
腦前葉萎縮代謝率降低



- 腦皮層萎縮。
- 神經傳導物(多巴胺)分泌細胞死亡。
- 多巴胺降低。

Nature 430 631

難溶解的蛋白質在阿茲海默症患者腦內形成類澱粉斑塊



- 類澱粉斑塊由纖維蛋白質糾結而成。
- 在原子力顯微鏡觀察下，纖維蛋白質由47個胺基酸規則排除而成。

常見疾病動物模式

- 線蟲
- 果蠅
- 斑馬魚
- 小鼠
- 大鼠
- 恆河猴

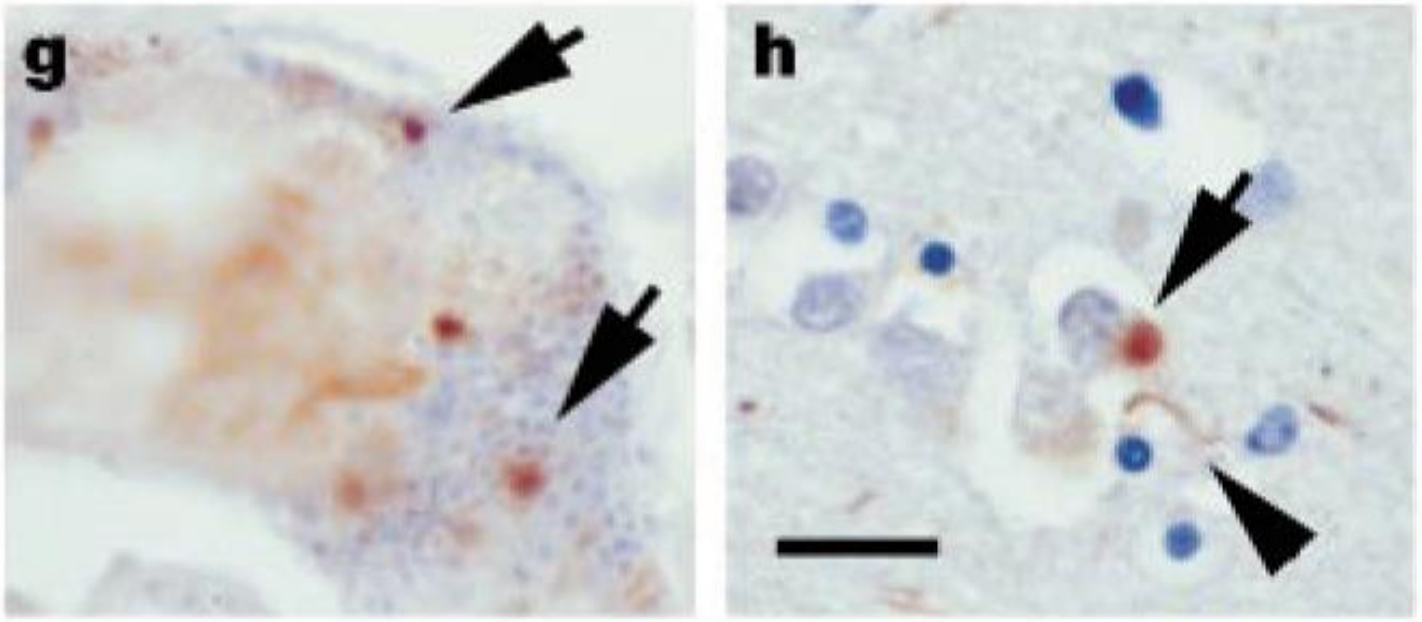
- 其它 (裸鼠、青蛙、天竺鼠、貓、狗...)

好動物模式具備的條件

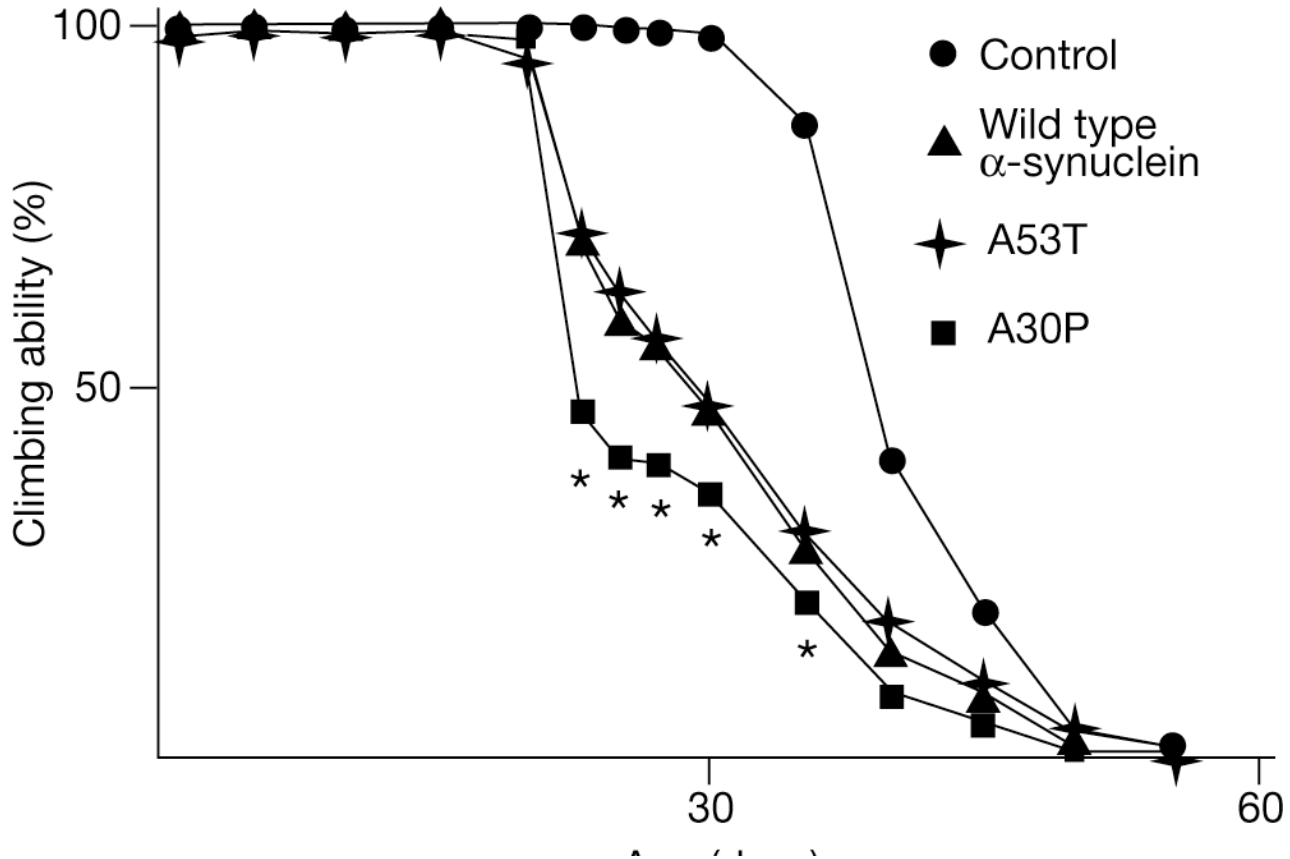
- 1. 能夠精確控制疾病或病變的再現性。
- 2. 發展出的動物模式，能供大多數的研究者使用。
- 3. 所使用的動物，可輸出至國外。
- 4. 如果是遺傳育種的研究，選擇多胎動物，如豬、鼠。
- 5. 動物夠大，能夠多次採取生檢材料。
- 6. 新發展出的動物能飼養於已有的動物房中。
- 7. 對研究者而言容易處理及保定。
- 8. 能夠發及應用於其他種動物。
- 9. 動物生命及使用期限夠長。
- 10. 品種特異性，不同的近親品系適合作不同的疾病研究。

http://animal.coa.gov.tw/html/?main=13h&page=13_labaratory_a08

細胞有相似的病理特徵



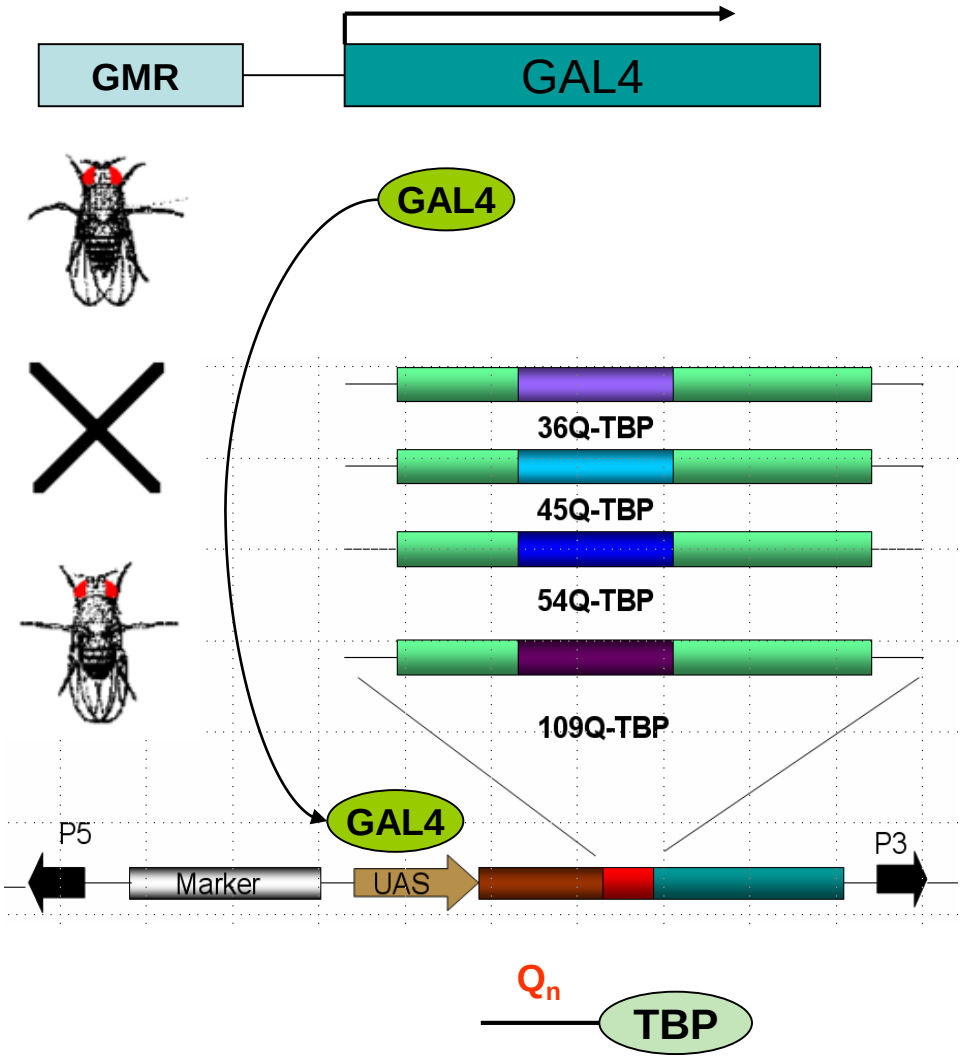
降低運動行為能力

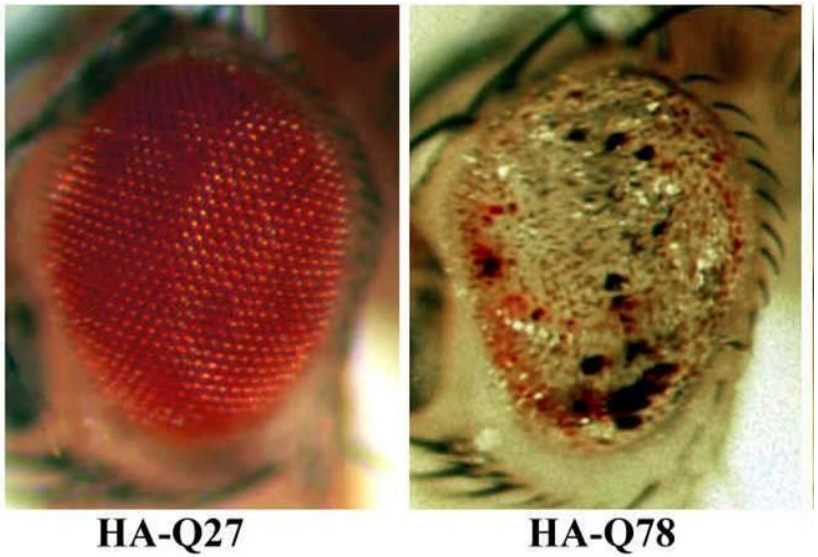

100
50
Climbing ability (%)
30
60
Control
Wild type
α-synuclein
A53T
A30P
*
*
*
*
*

小腦萎縮症

- **共同症狀：** 步態失調，發音障礙
- **特有症狀：** 視覺的問題、錐體外路徑症狀、周邊神經病變、智力的問題、癲癇

Modeling of Neurodegenerative Disease using Fly

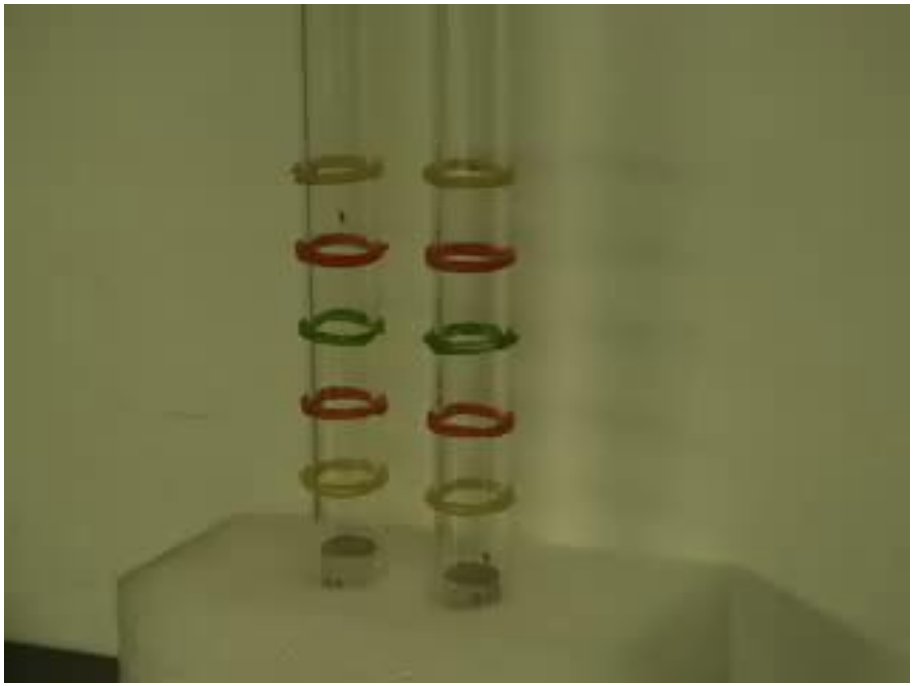




Fly model for SCA3

Warrick et al,1998

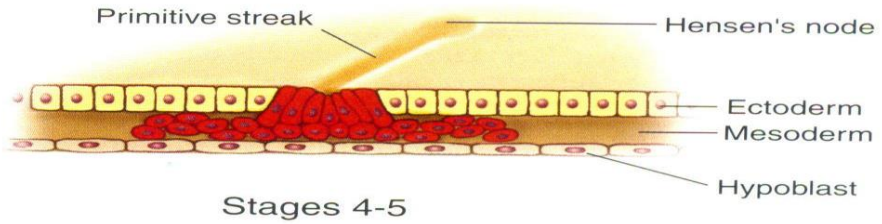
Motor dysfunction



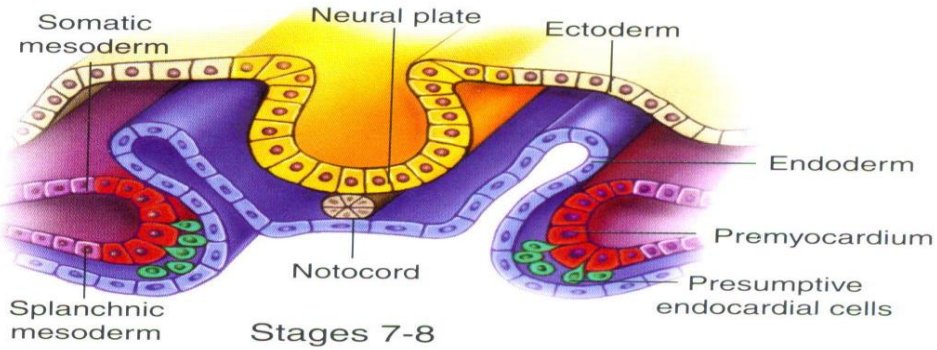
Can fly be a model for Cardiovascular disease?

- Cardiac parameter: heart beat, blood pressure, Heart volume ….
- Cardiac function
- Vascular parameters

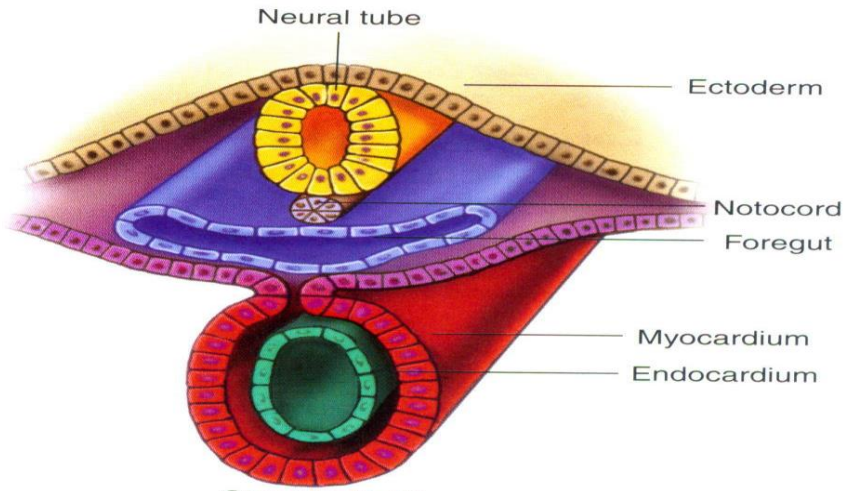
Heart morphogenesis of vertebrate



Stages 4-5

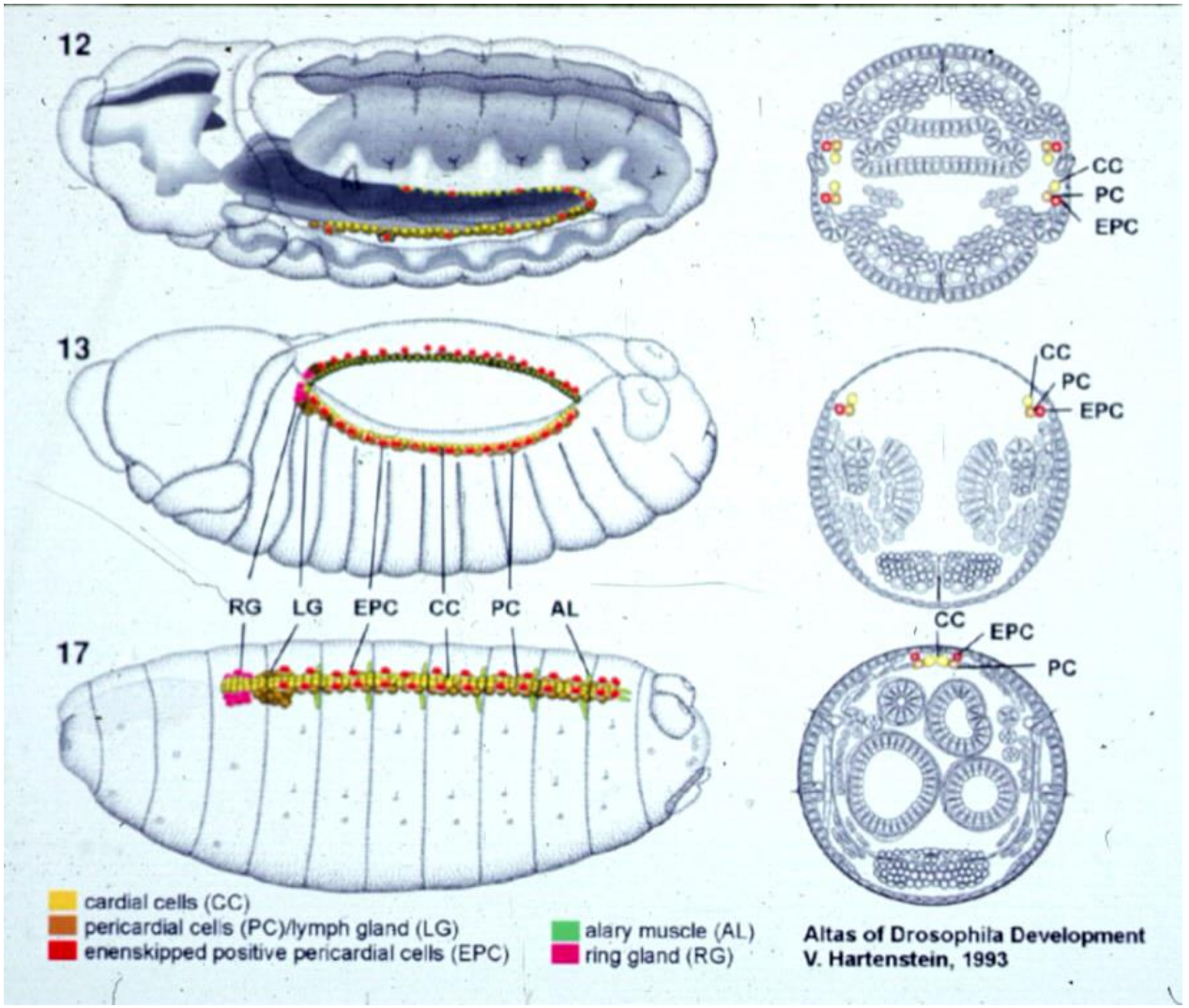


Stages 7-8

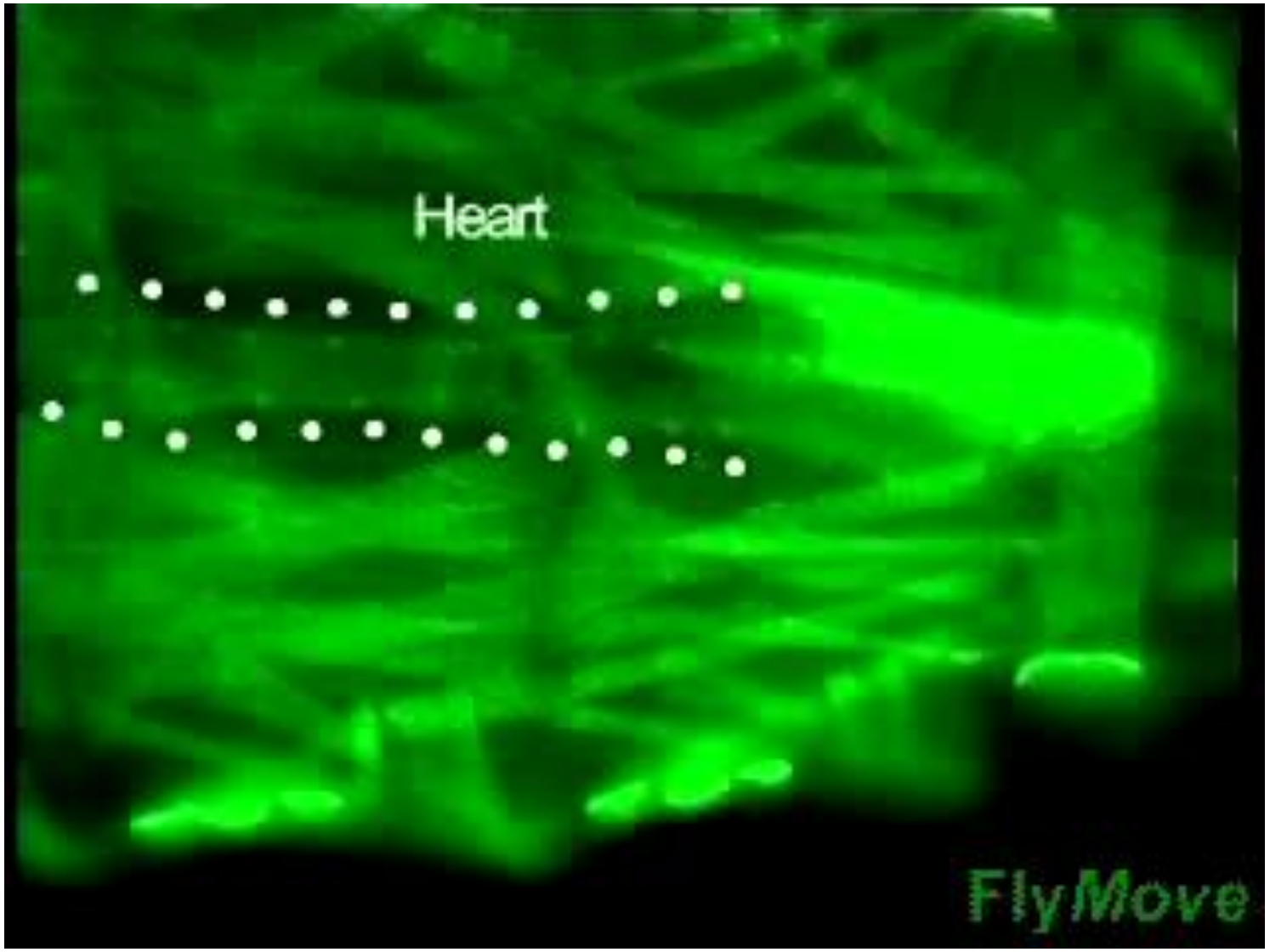


Stages 9-10

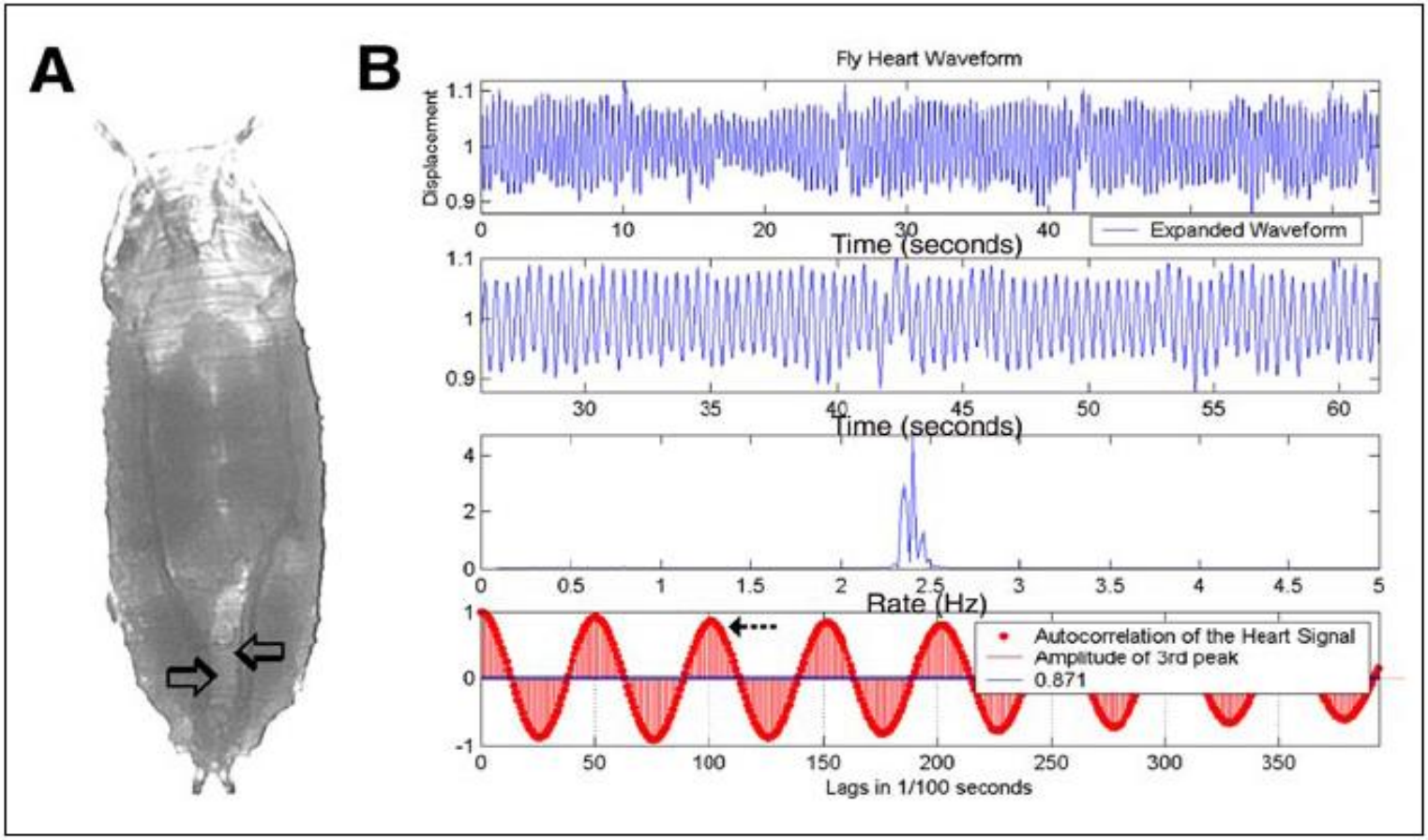
Cardiogenesis of Drosophila



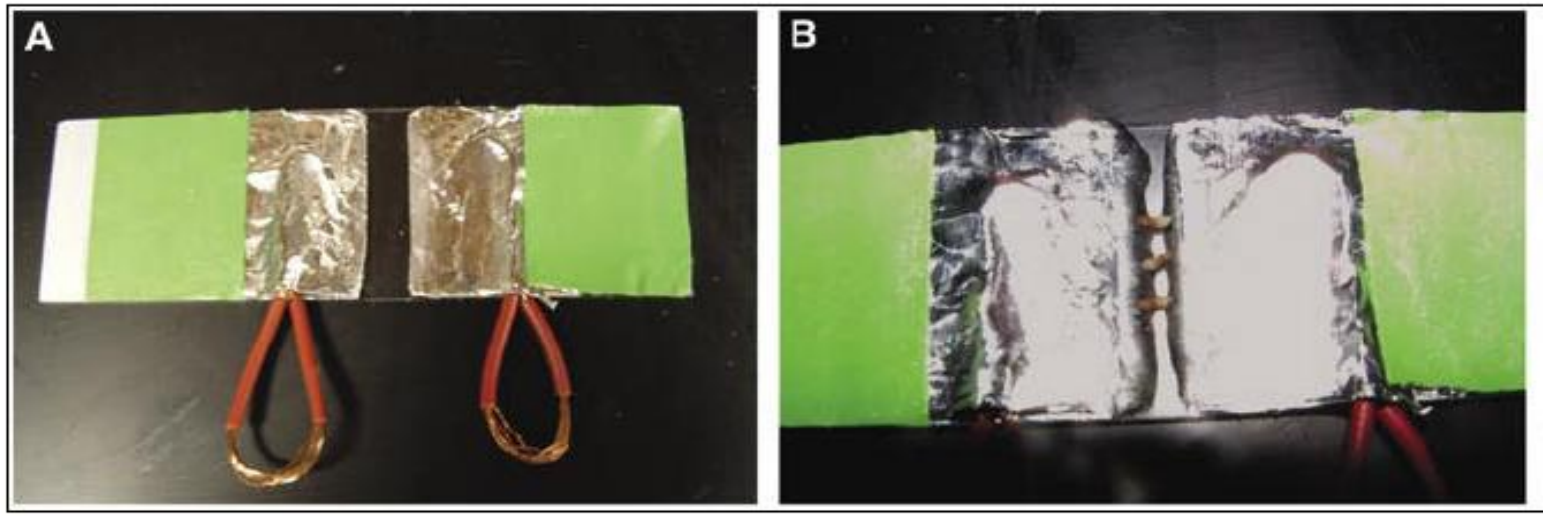
Heart beat of fly

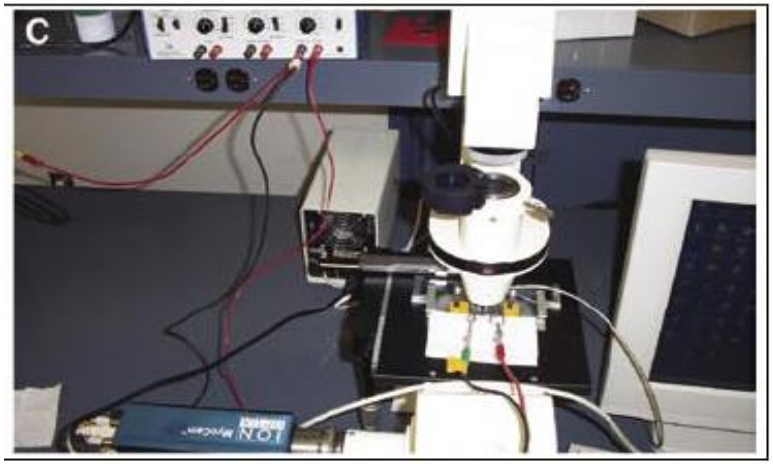


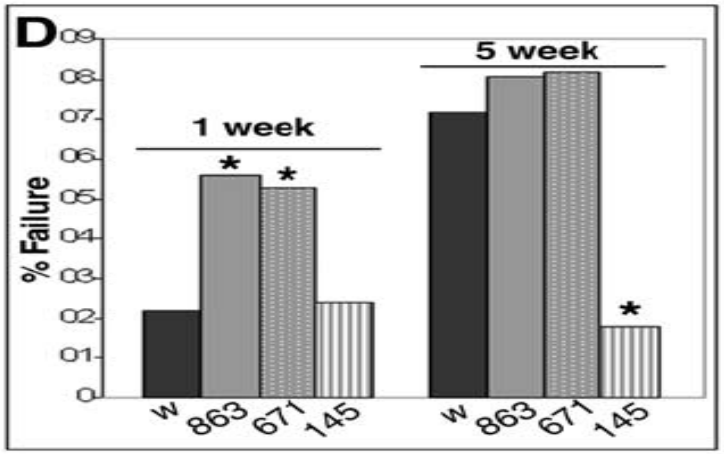
Transformation of heart beat of fly



Cardial performance

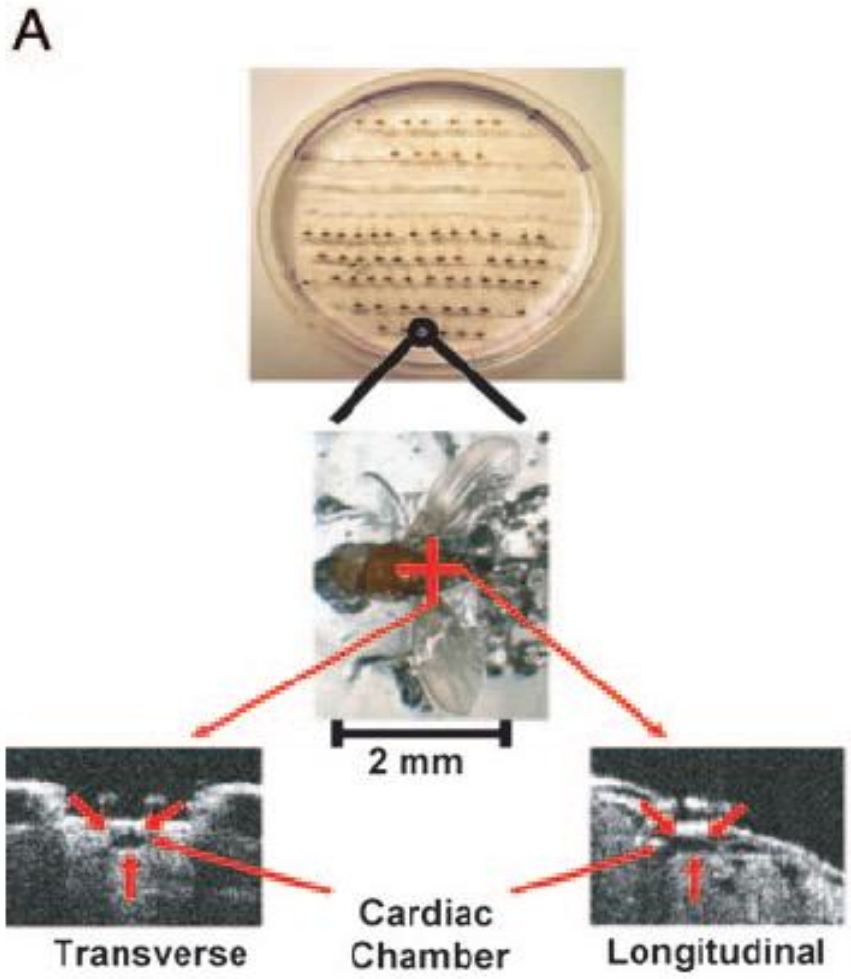


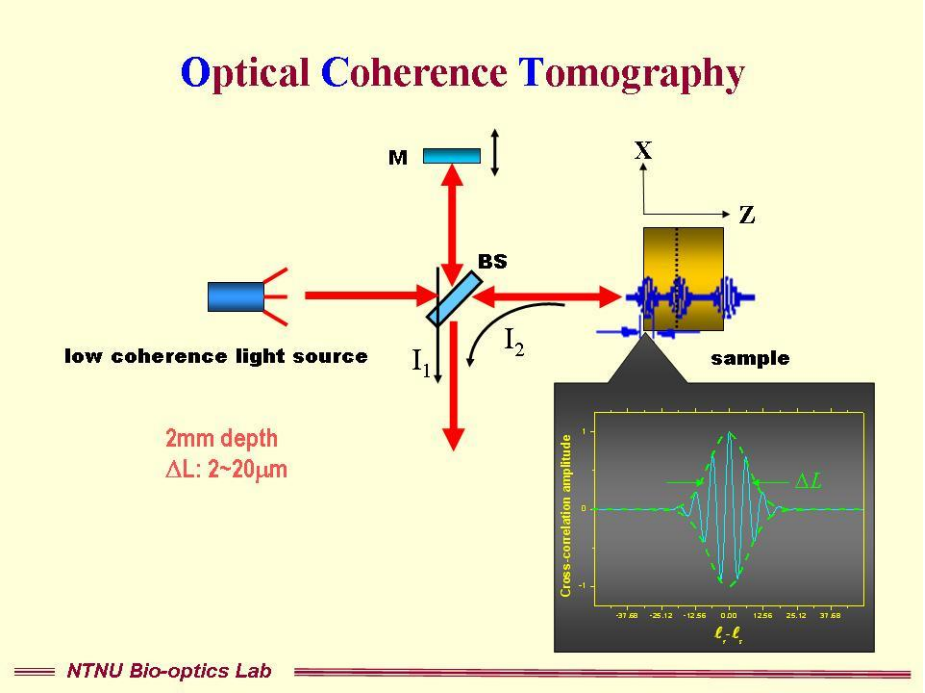




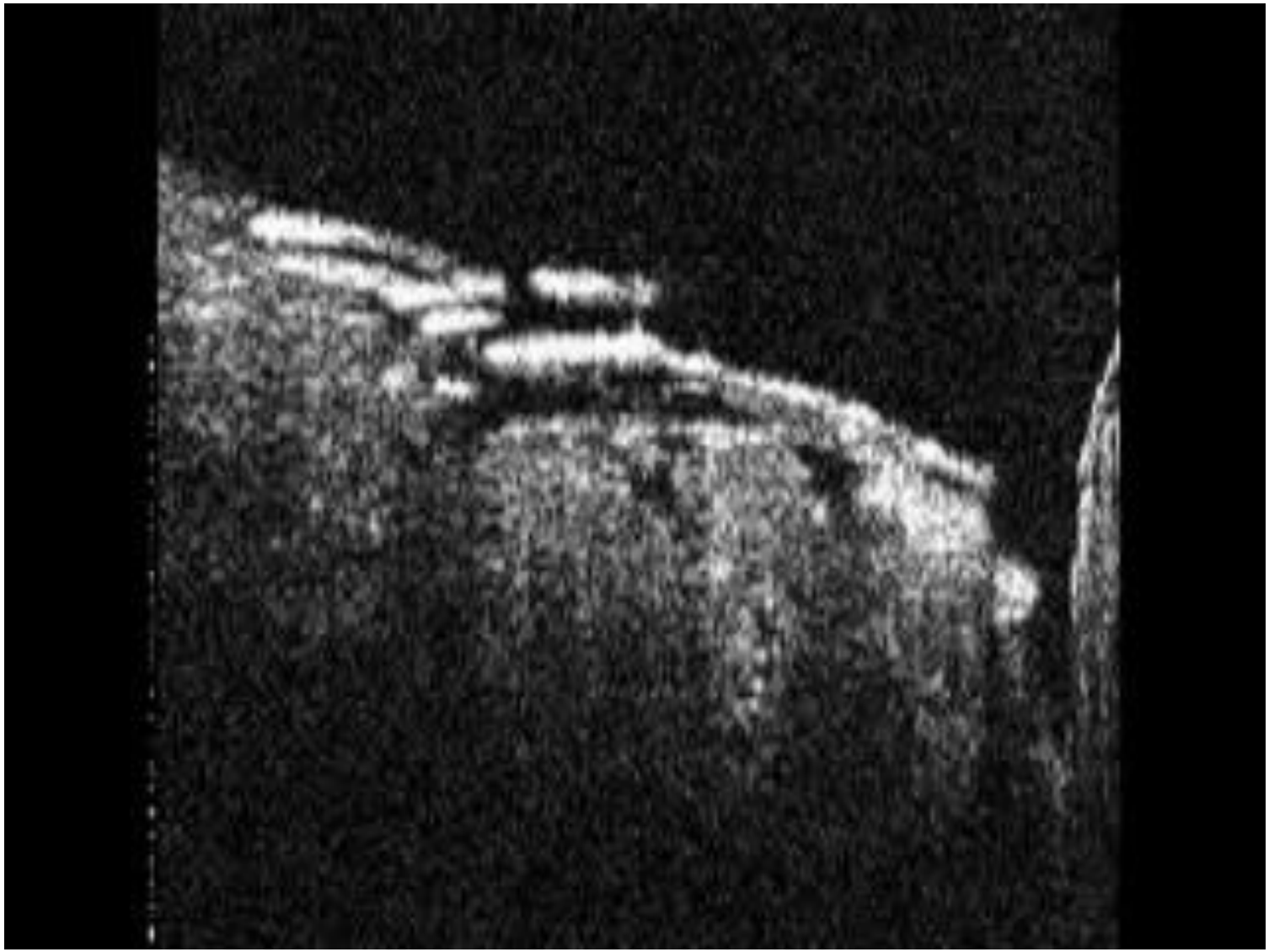
Optical coherence tomography (OCT)-

光學同調斷層攝影術

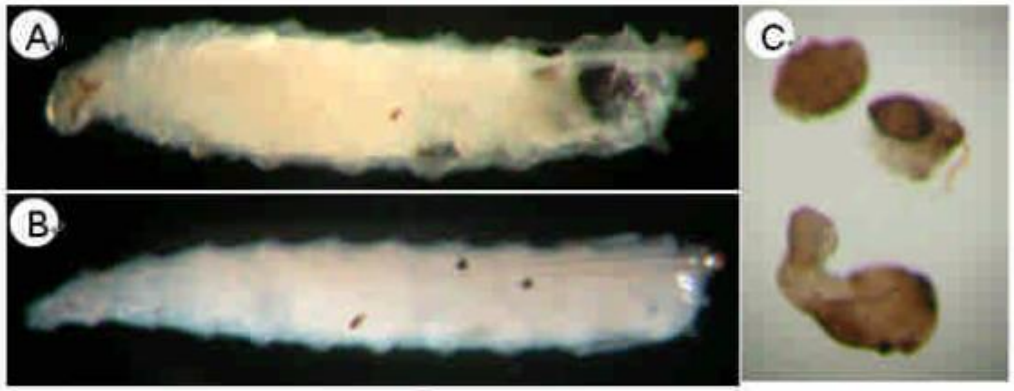




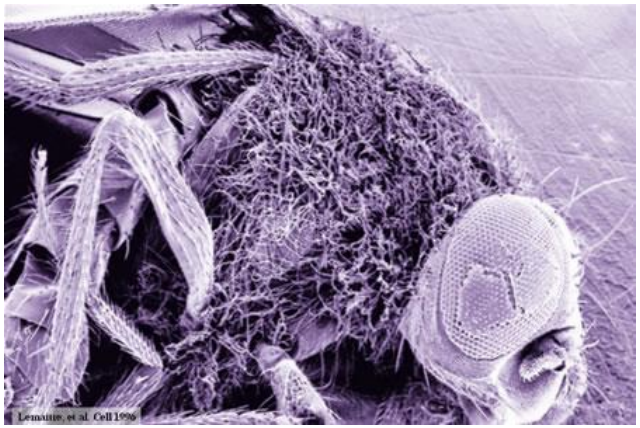
Fly model for dilated cardiomyopathy



Other applications



- Cancer
- Infectious disease
- Immunity
- Drug abuse (i.e. alcoholism)
- Speciation
- Ecology
- …more



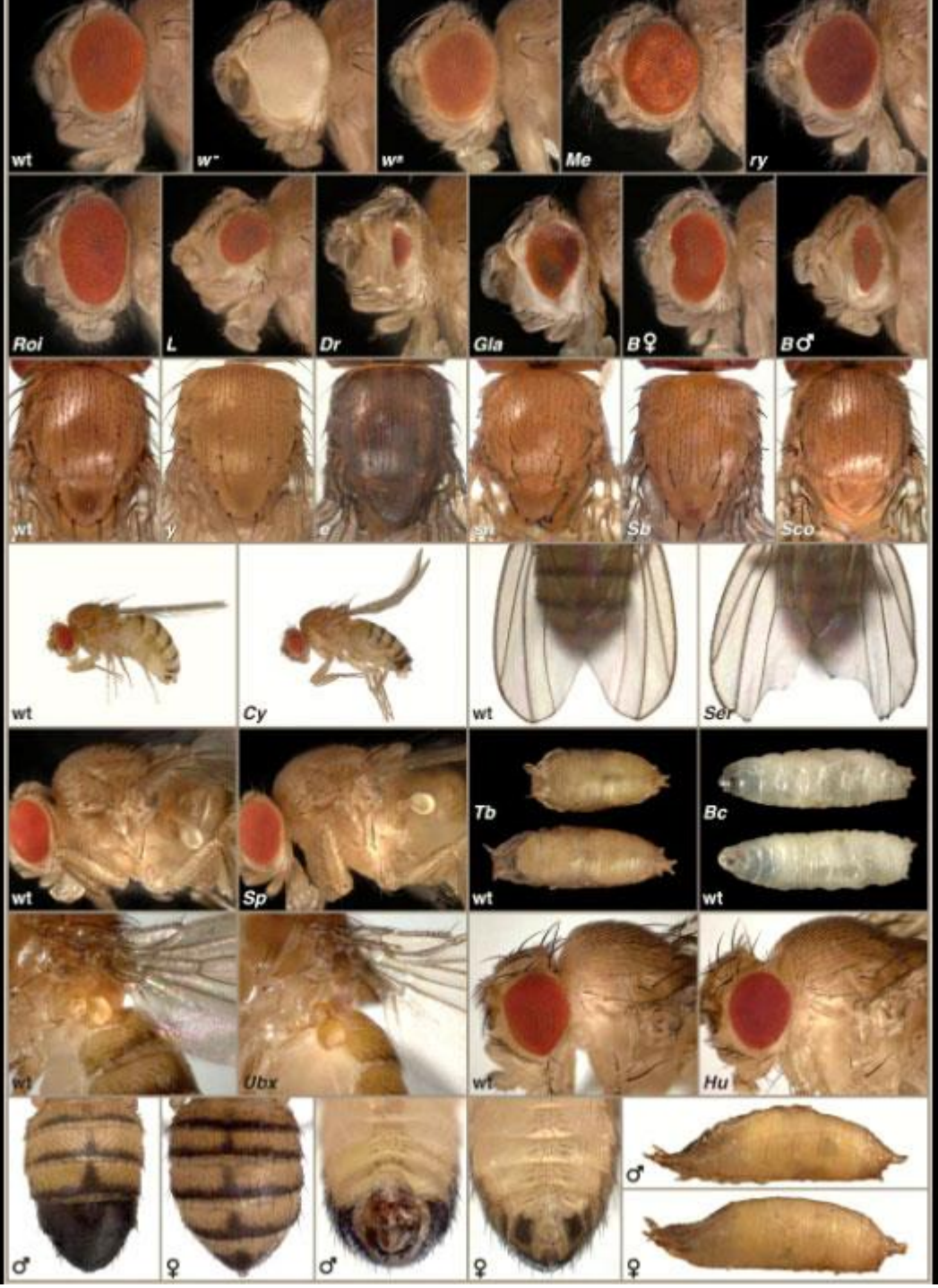
Jules A. Hoffmann: The Nobel Prize in Physiology or Medicine 2011

題外話:果實蠅 ≠ 果蠅

果蠅 (Drosophilidae 科，*Drosophila* 屬) ⇔
果實蠅 (Trypetidae 科，*Bactocera* 屬)

web1.nsc.gov.tw/ctpda.aspx?xItem=8036&ctNode=...

Thank



You!

http://www.drosophila-images.org/images-2006/14c-slide-F.htm