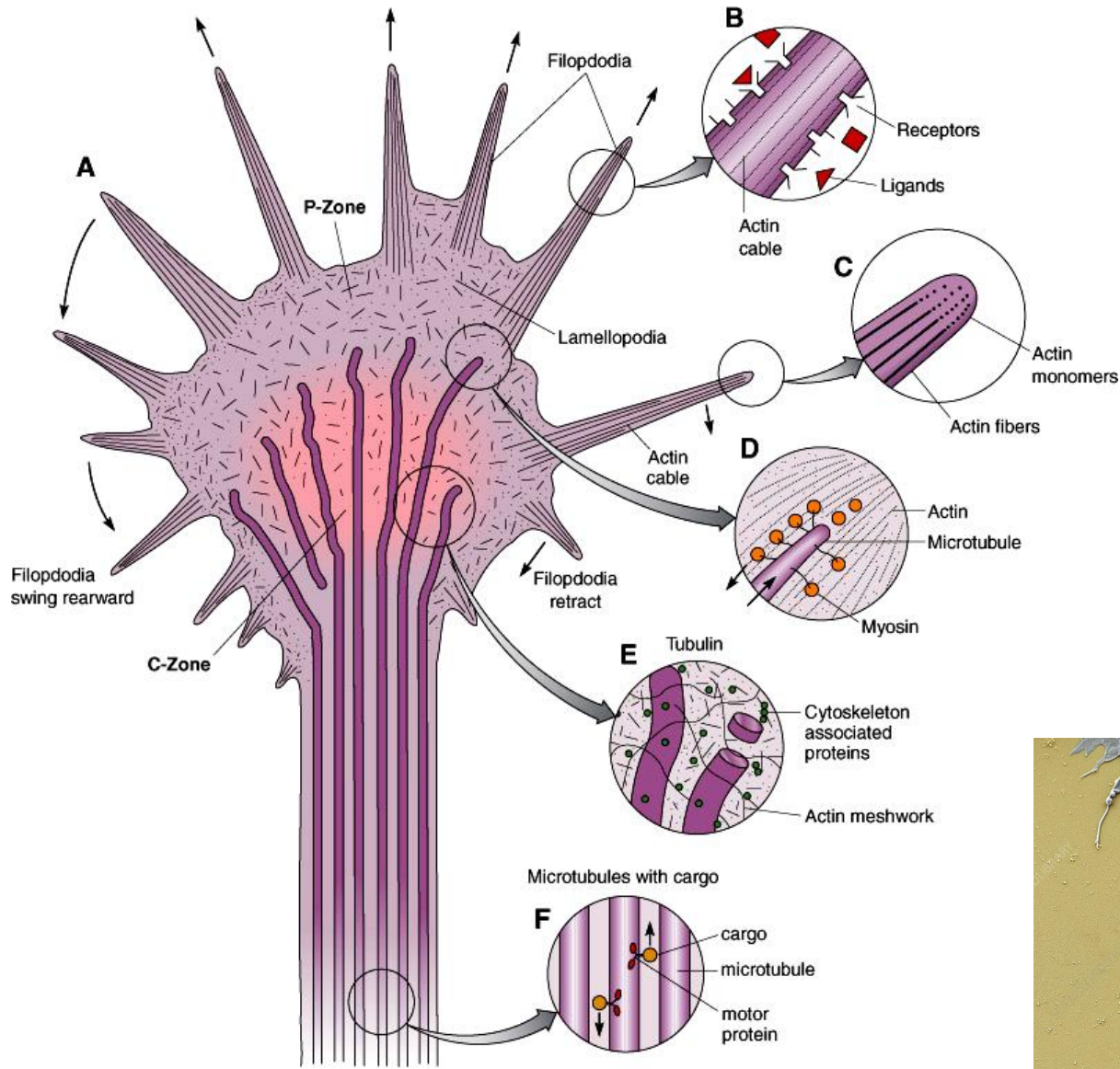


*Guiado  
axonal*

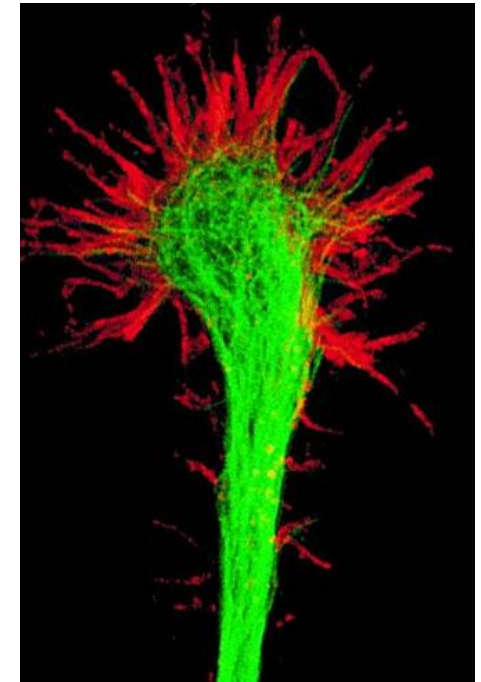


**Biología del Desarrollo 2022**

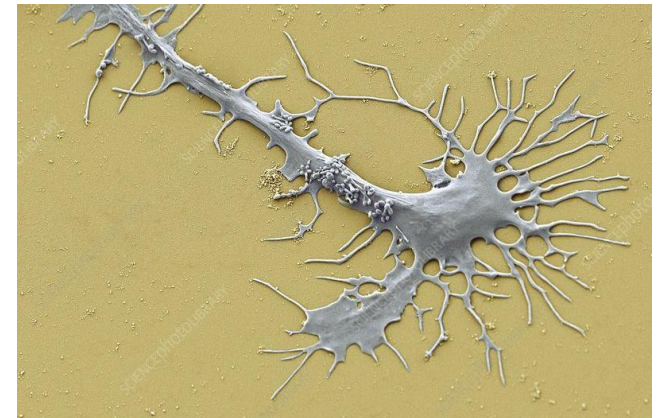
# El cono de crecimiento



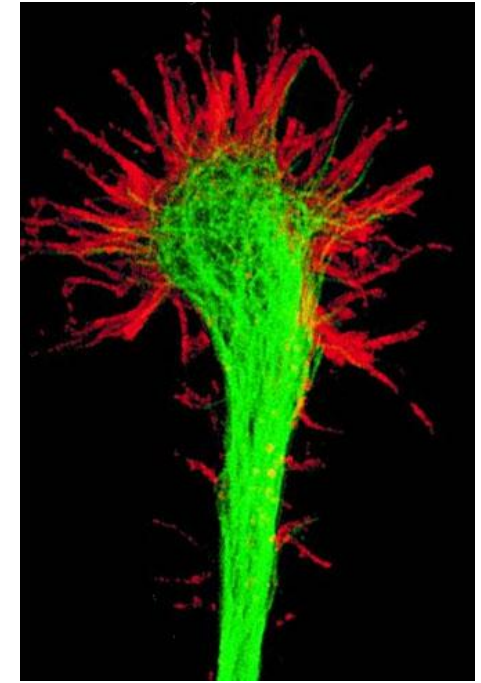
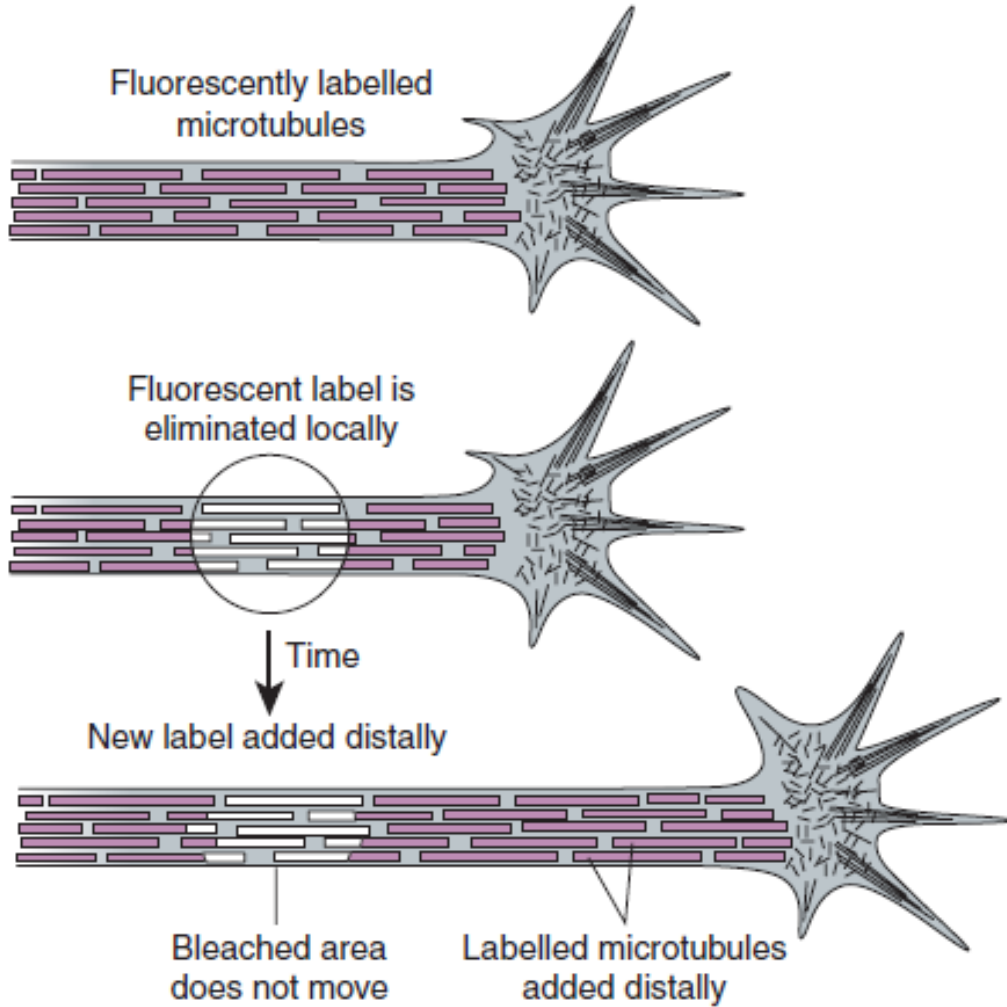
Copyright © 2006 Elsevier, Inc.



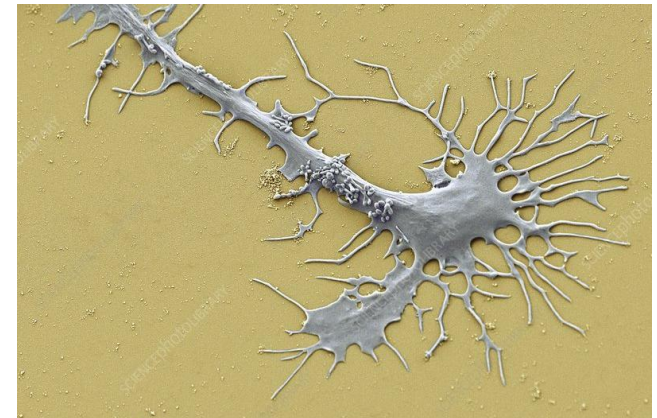
**Microtúbulos**  
**Actina**



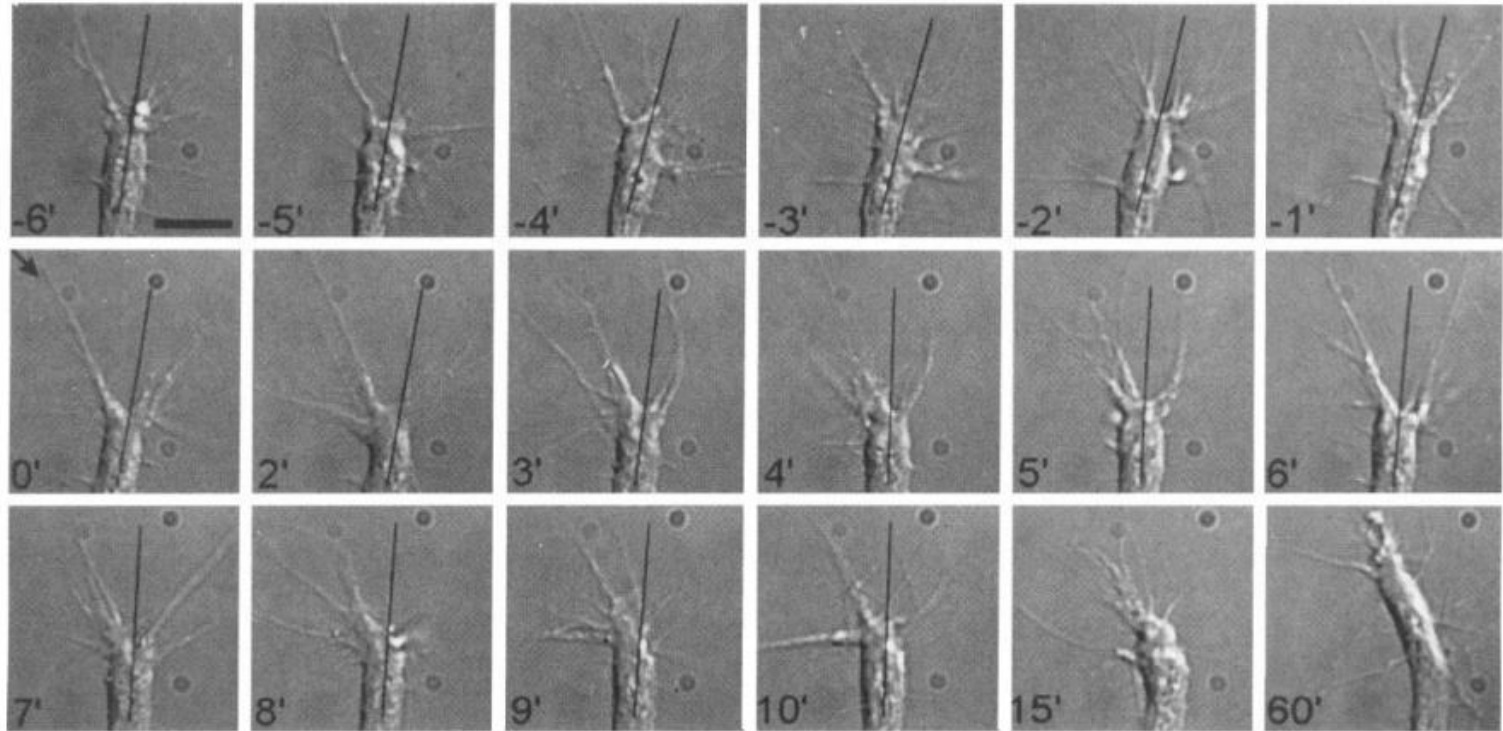
# El cono de crecimiento



**Microtúbulos**  
**Actina**

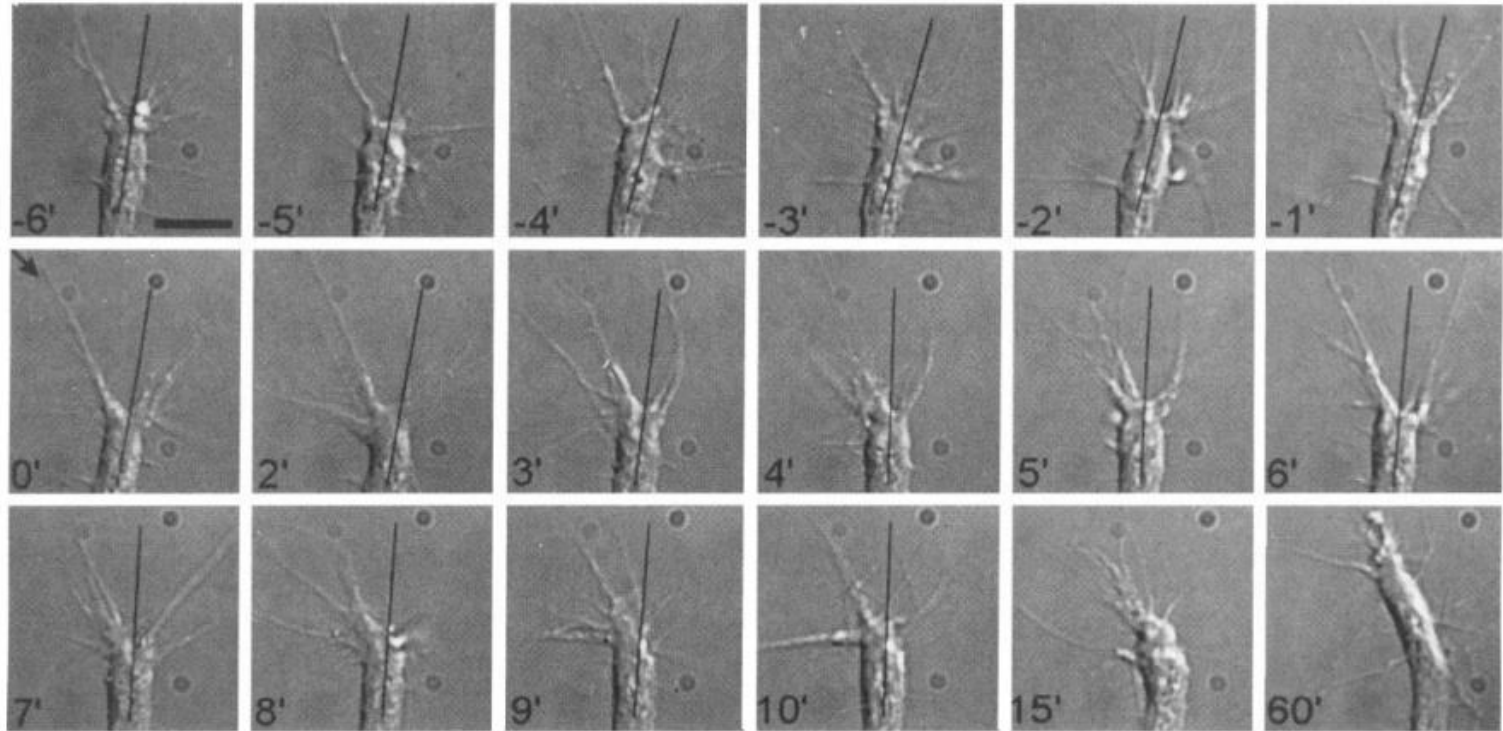


# Los filopodios

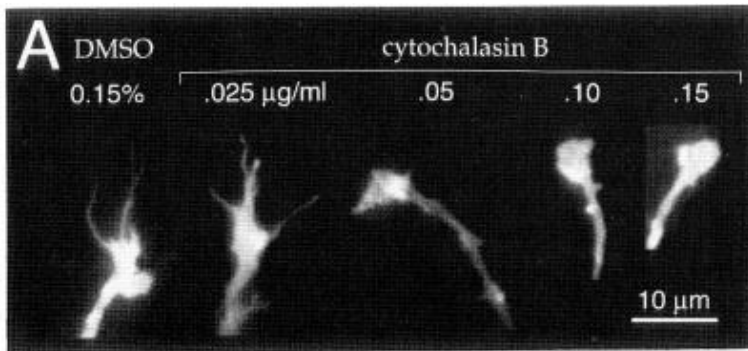


Zheng et al., 1996

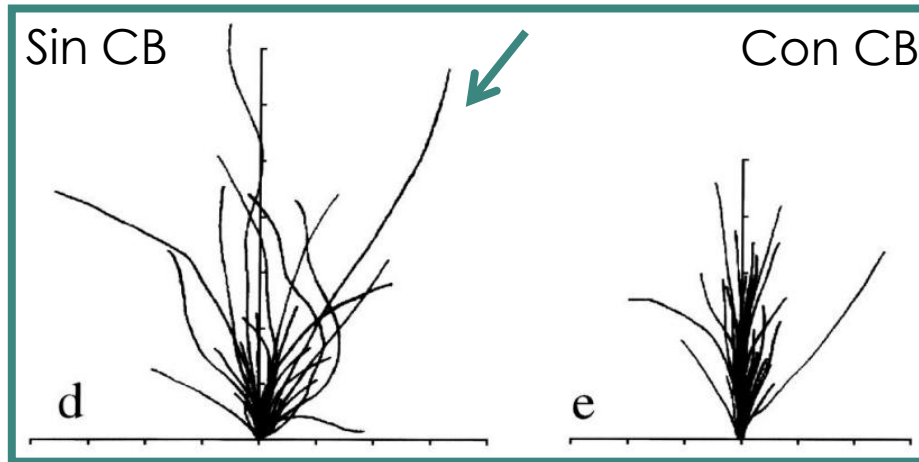
# Los filopodios



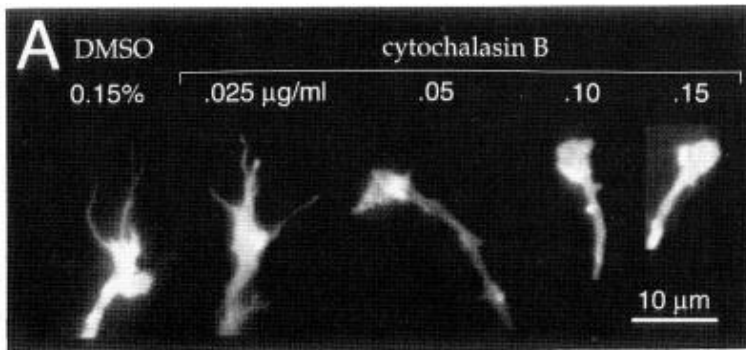
Zheng et al., 1996



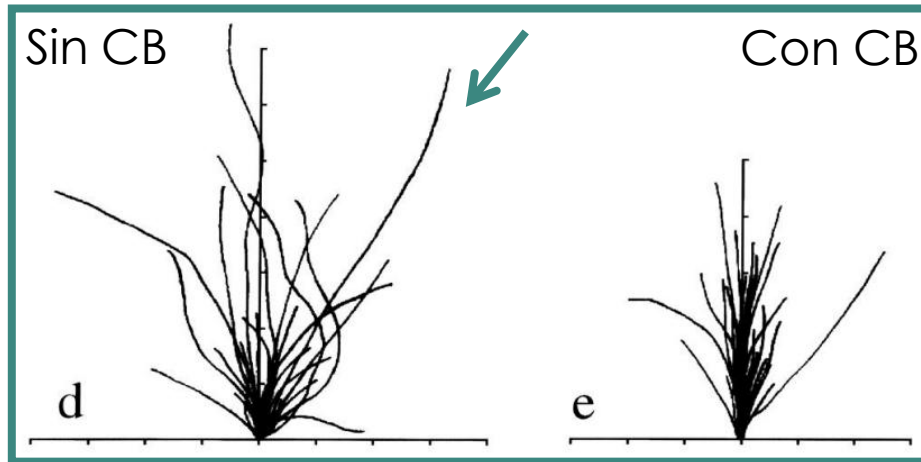
# Los filopodios



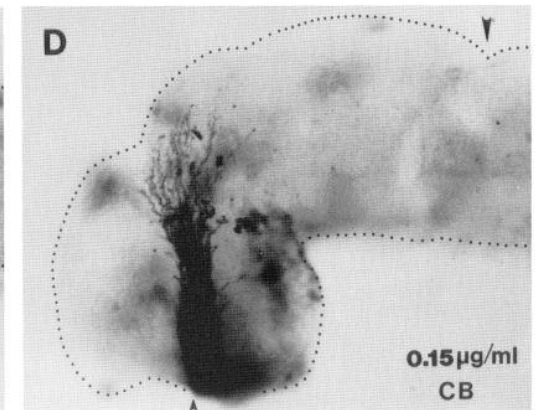
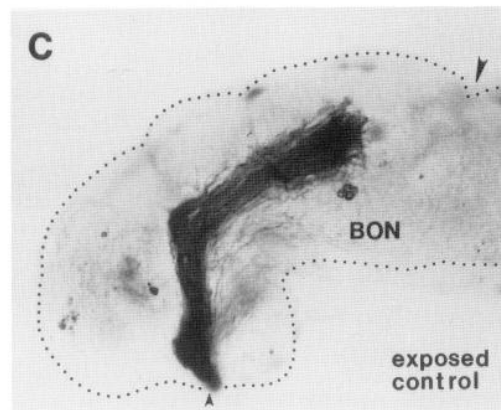
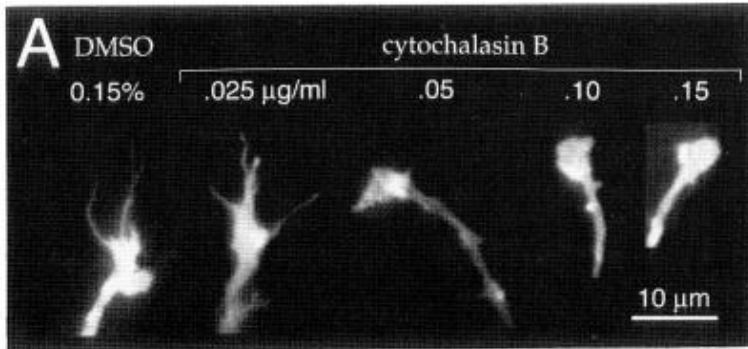
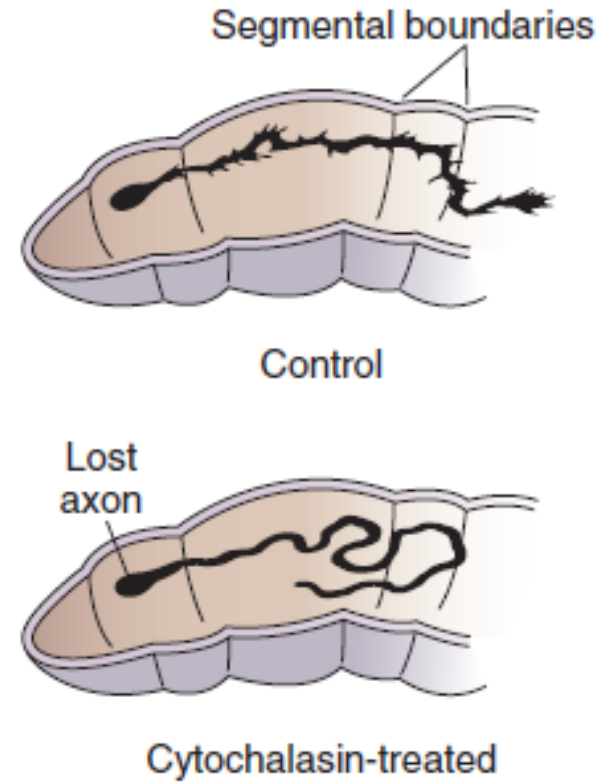
Zheng et al., 1996



# Los filopodios

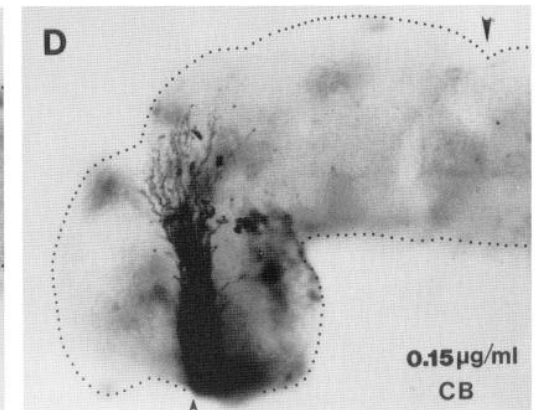
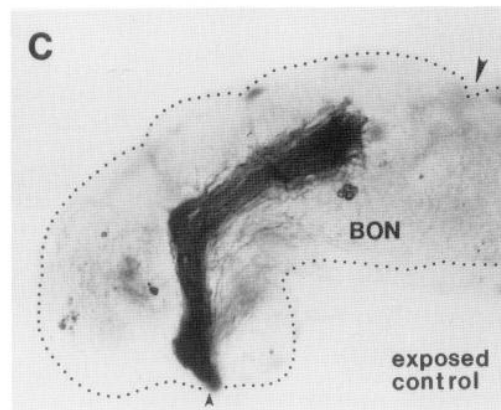
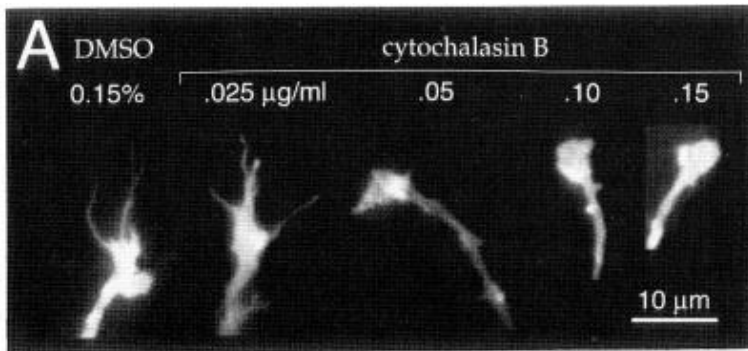
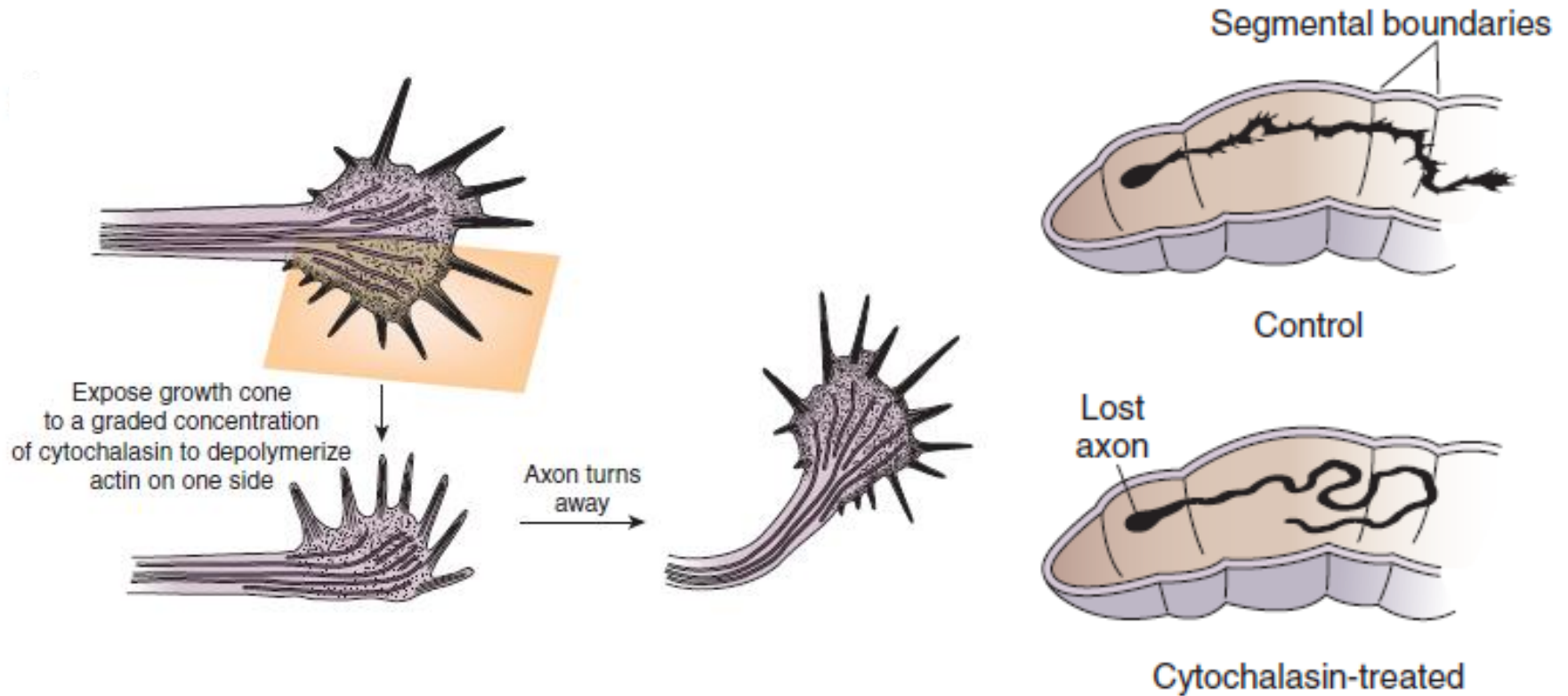


Zheng et al., 1996



Chien et al., 1993

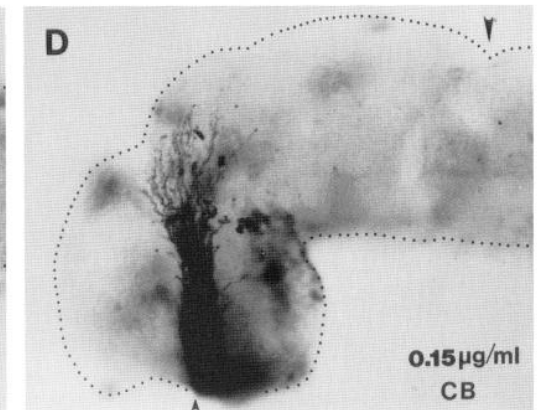
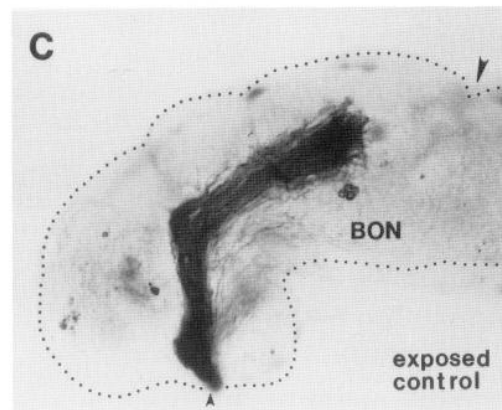
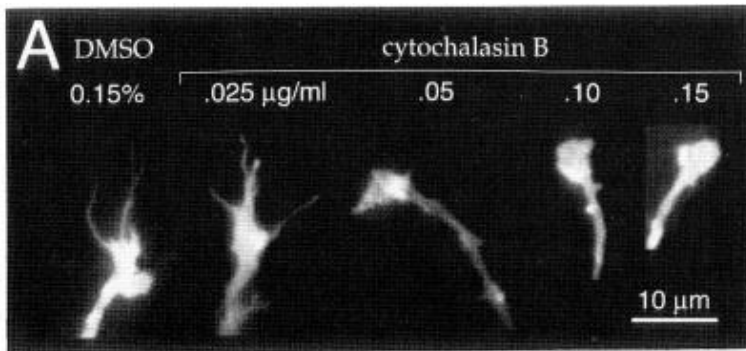
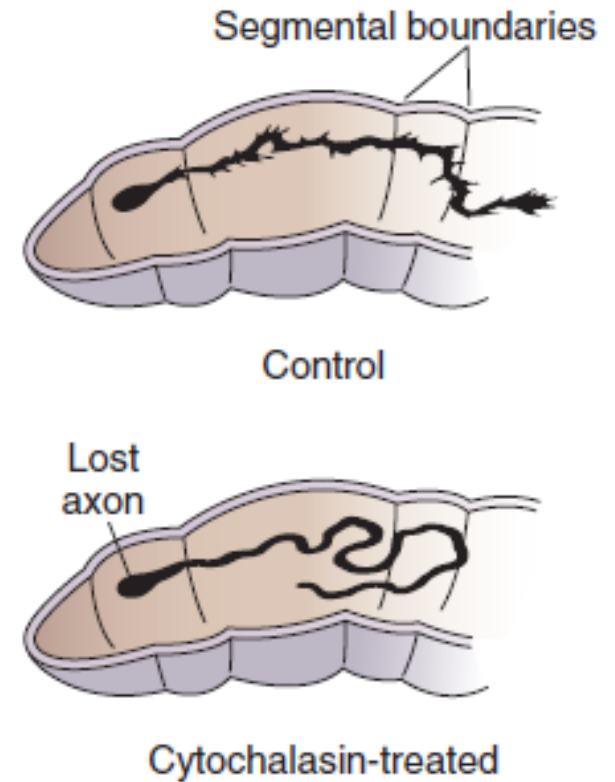
# Los filopodios



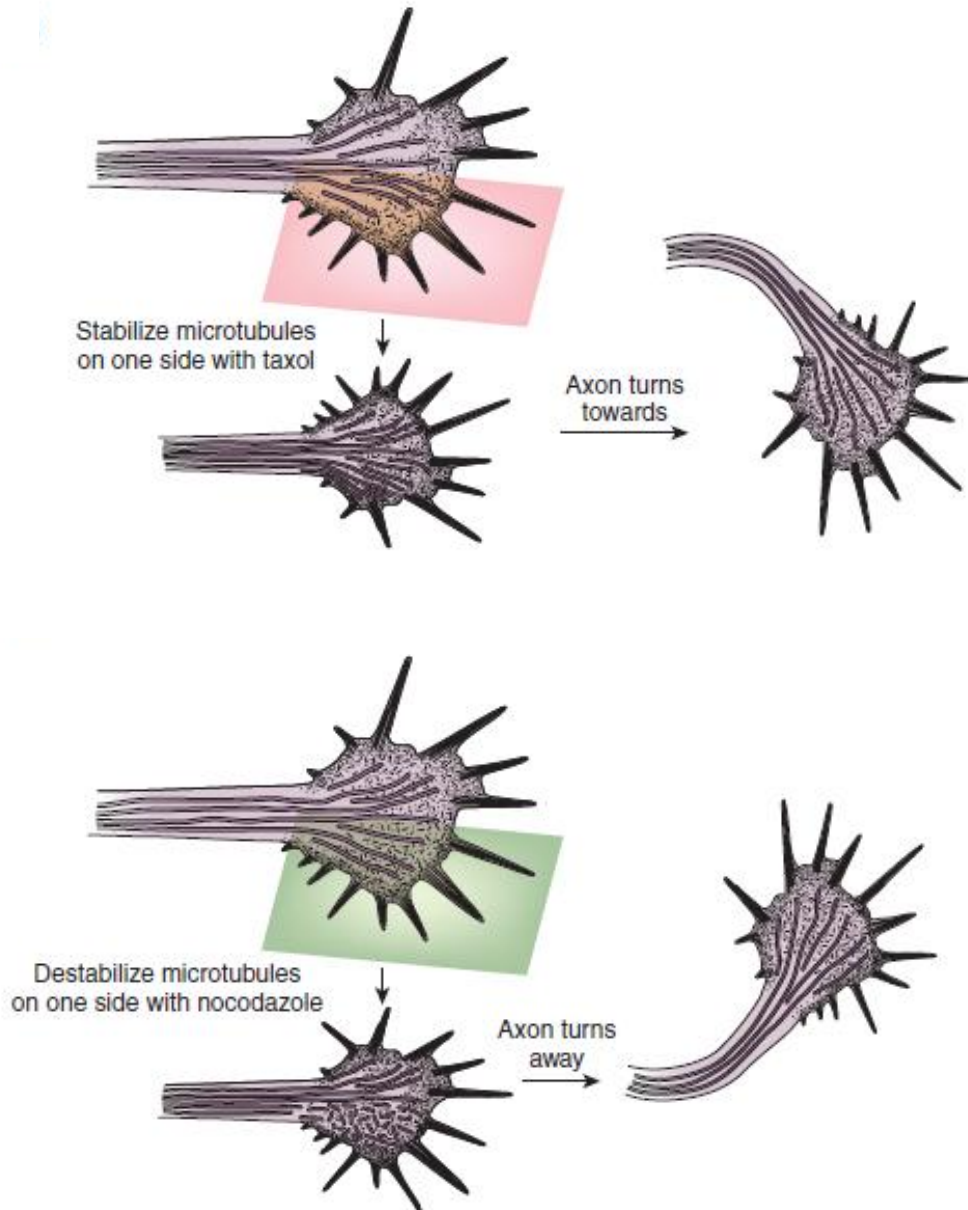


# Los filopodios

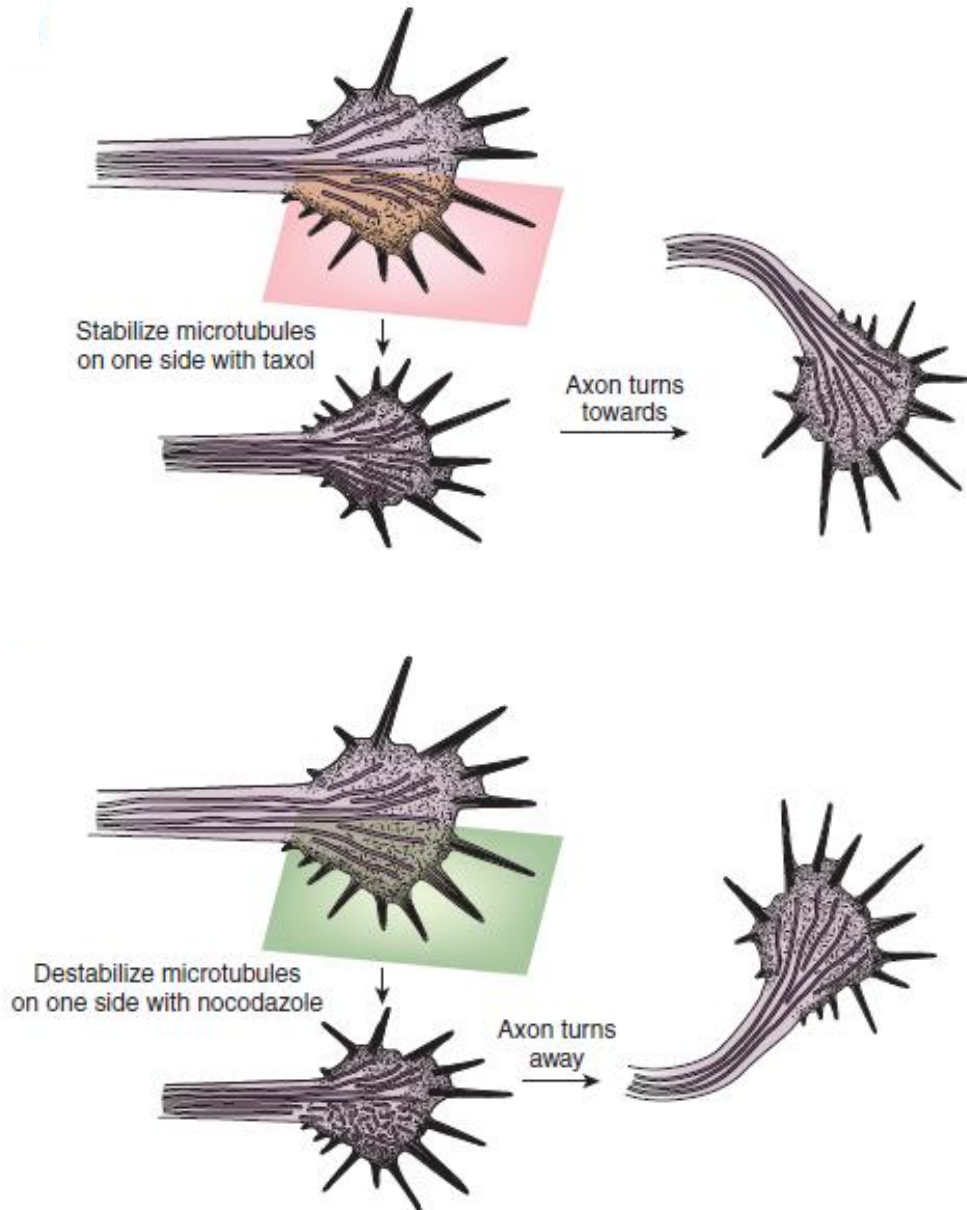
Los filopodios son esenciales para la navegación del cono de crecimiento



# Los microtúbulos



# Los microtúbulos



La polimerización de los MTs es esencial para la navegación del cono de crecimiento

# ¿A quién sigue el cono?

Señales químicas

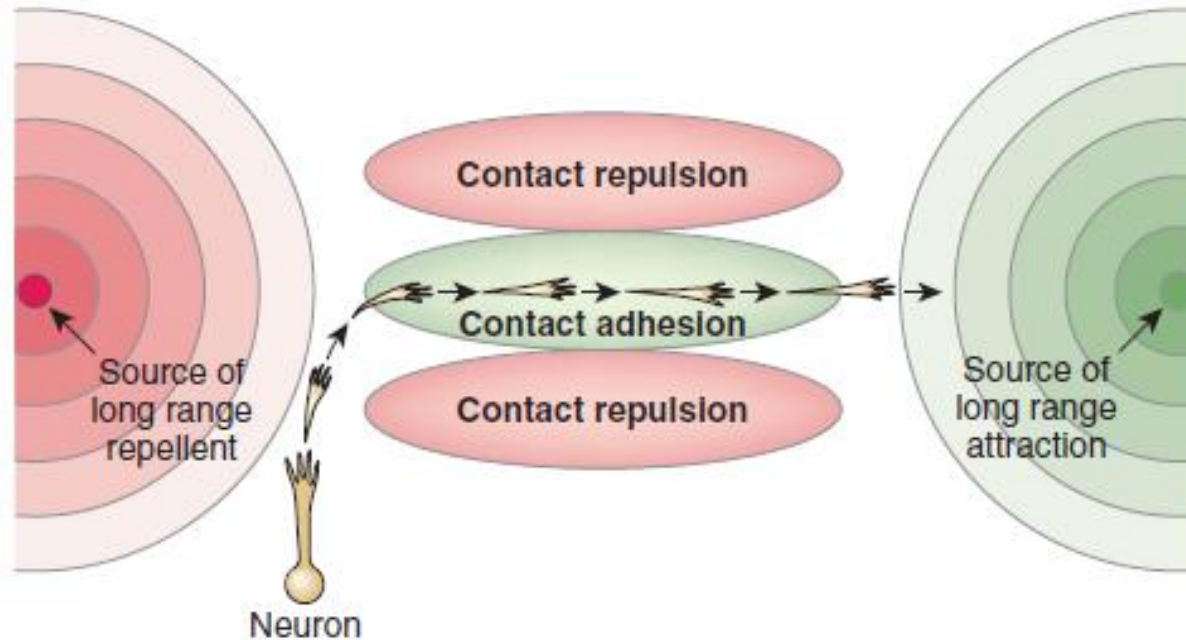


A distancia



De contacto

Estímulos mecánicos



# ¿A quién sigue el cono?

Señales químicas

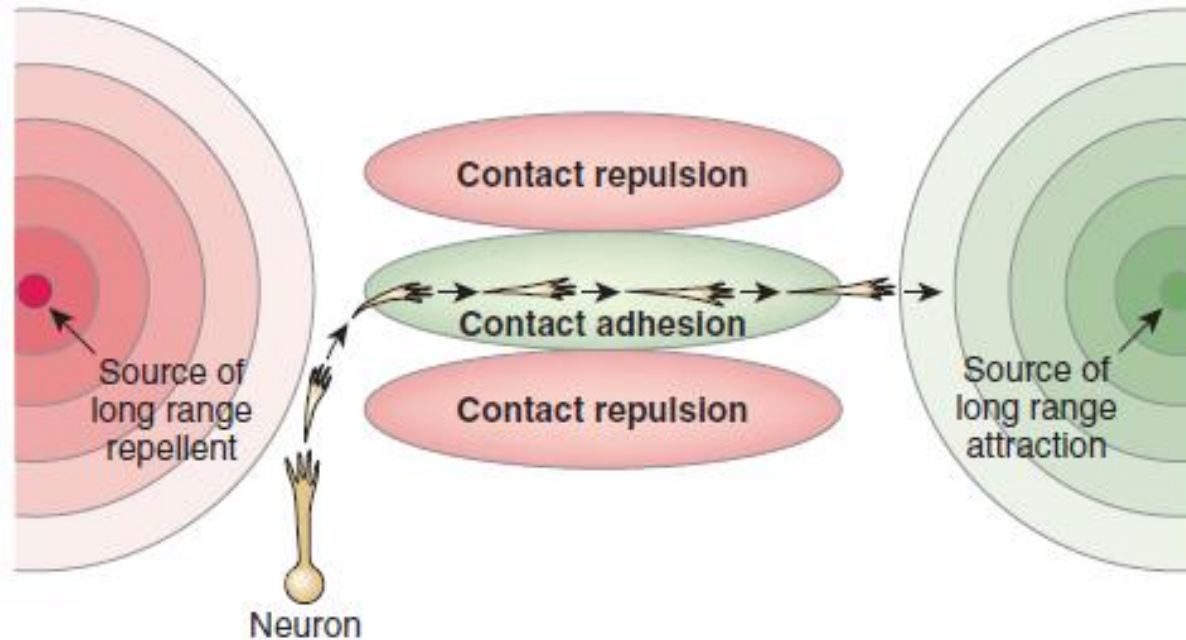


A distancia

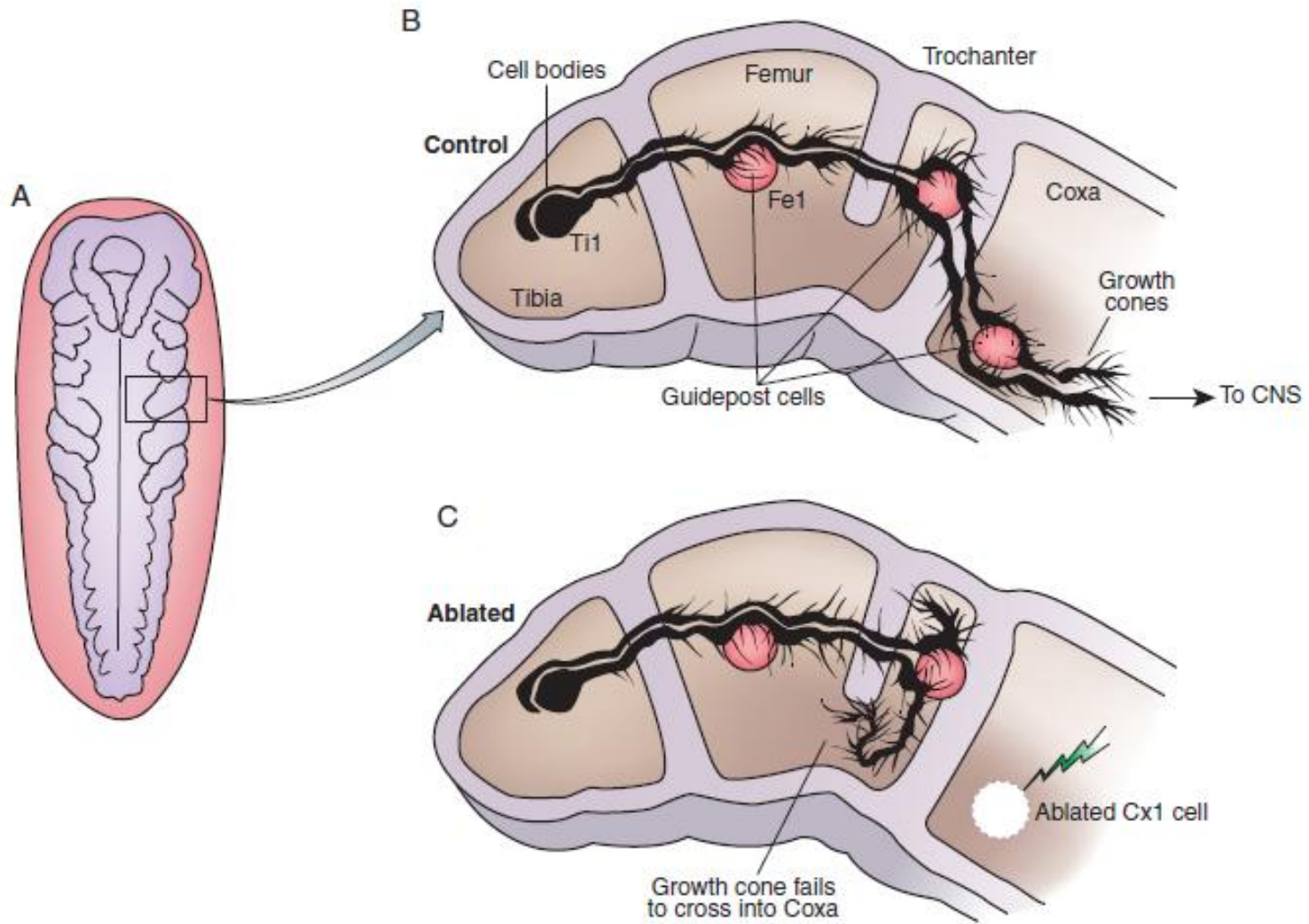


De contacto

Estímulos mecánicos

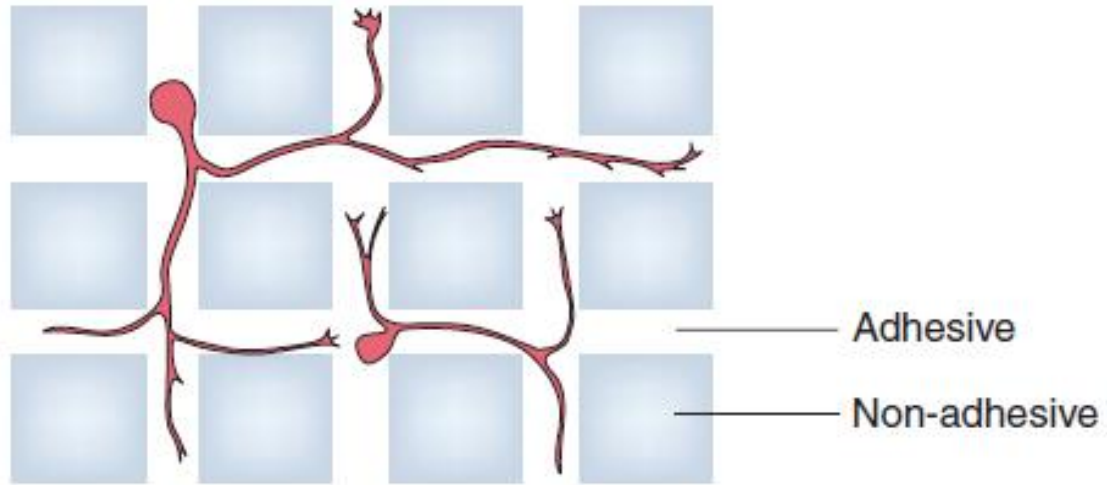


# Señales locales para el guiado axonal

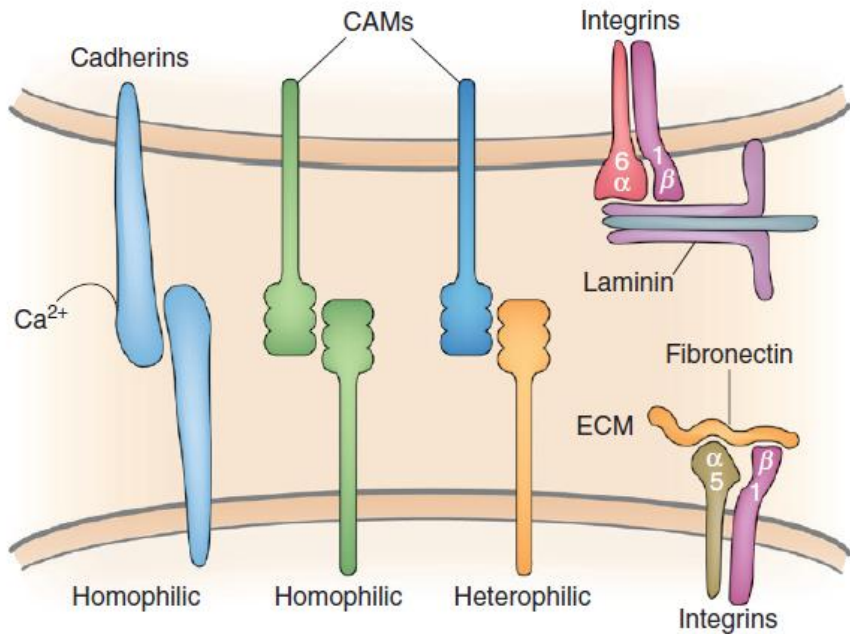
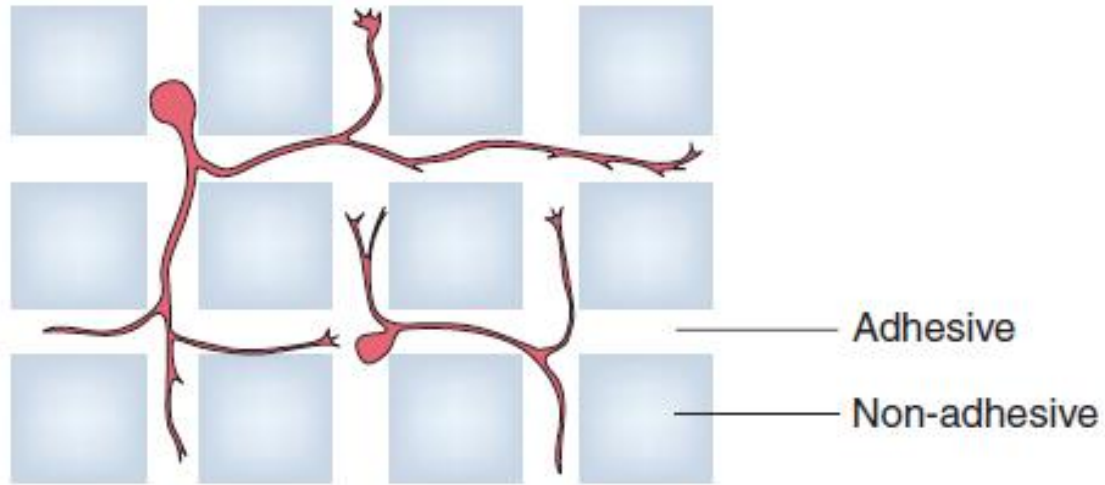


Bentley & Caudy, 1983; Caudy & Bentley, 1986

# Moléculas adhesivas

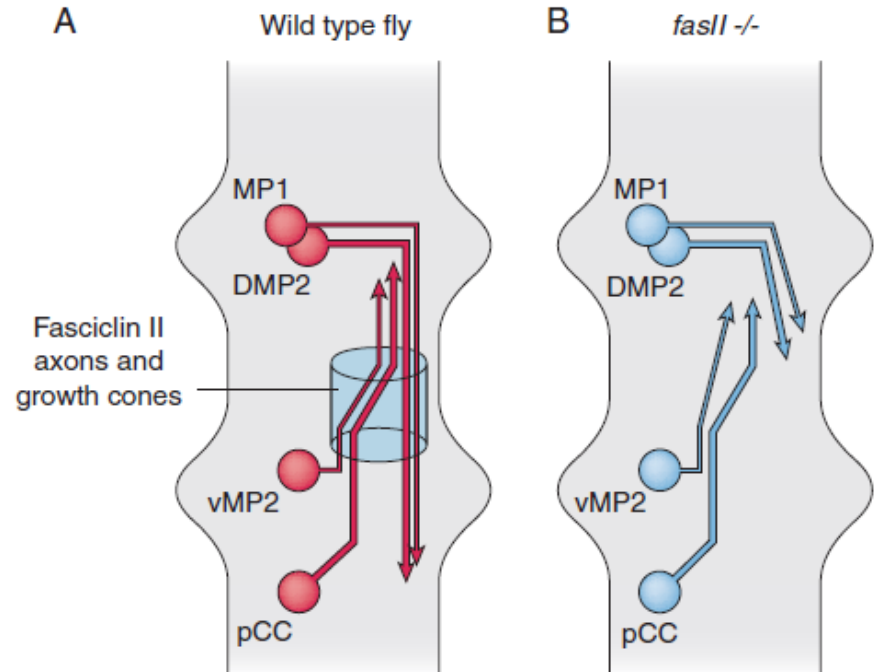
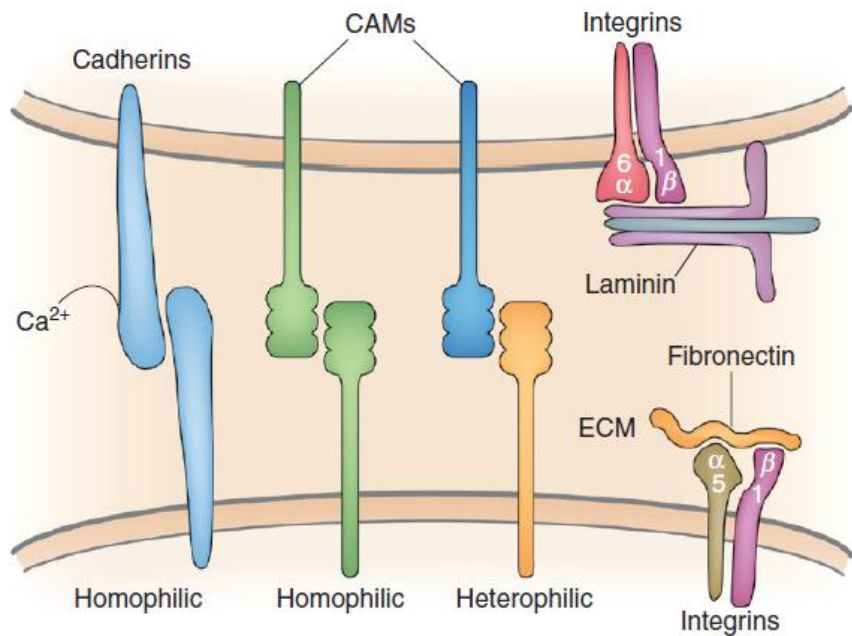
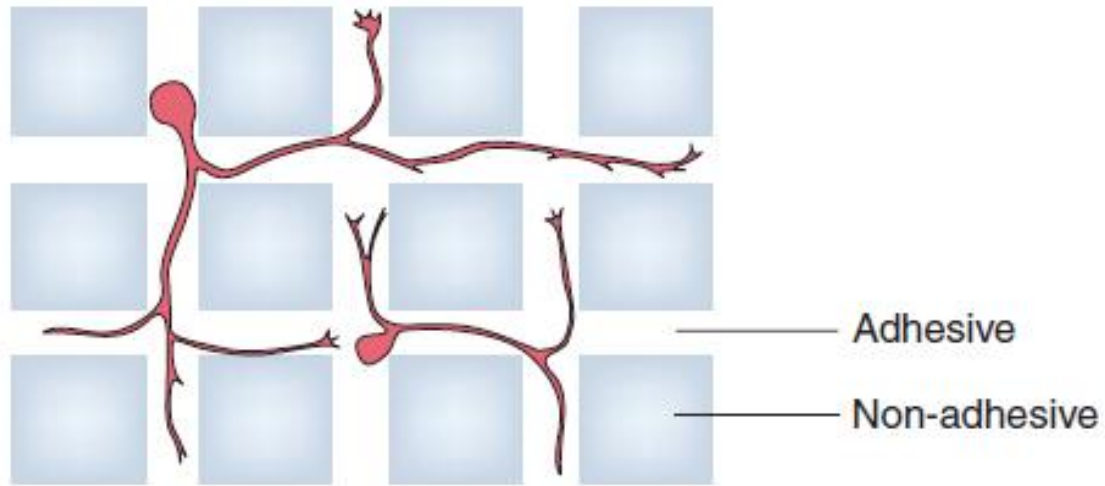


# Moléculas adhesivas

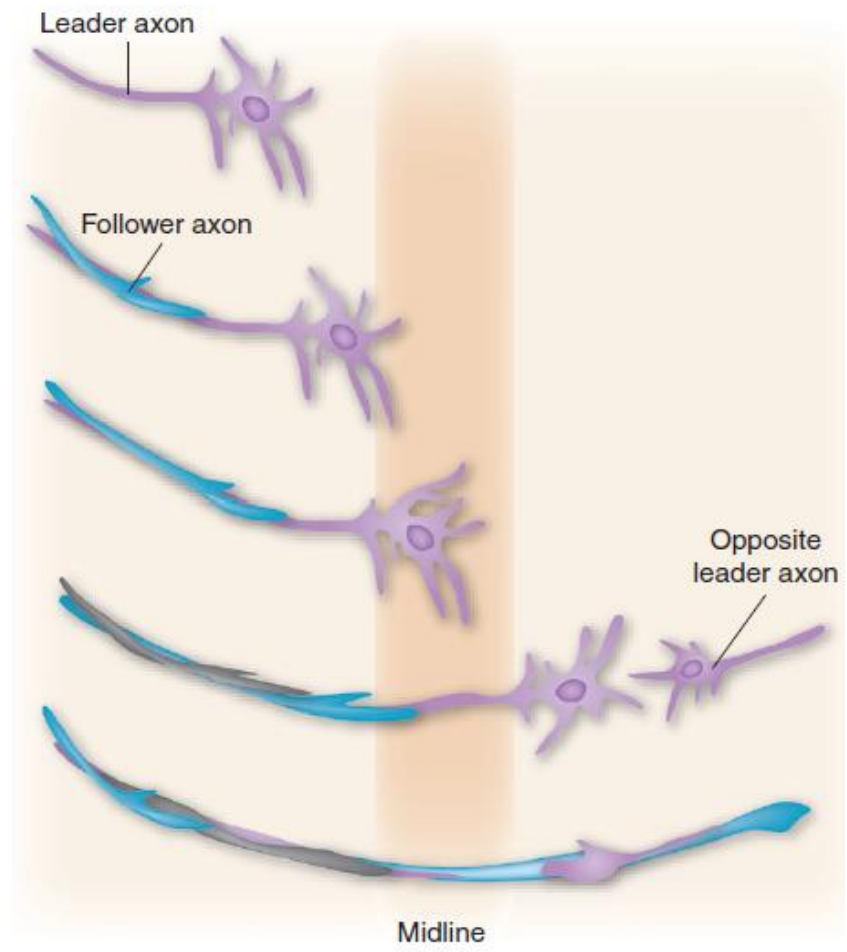
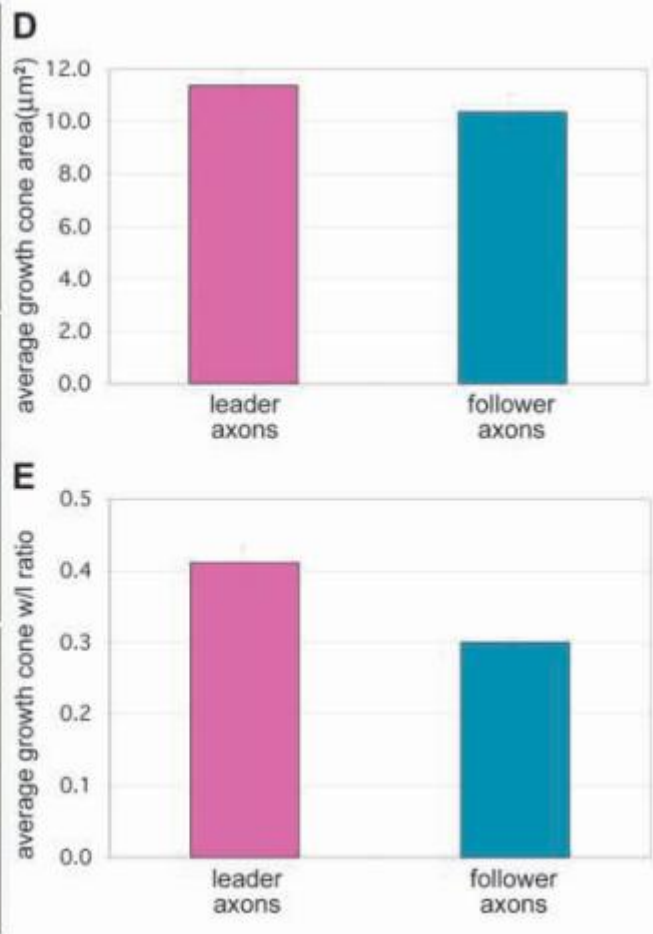
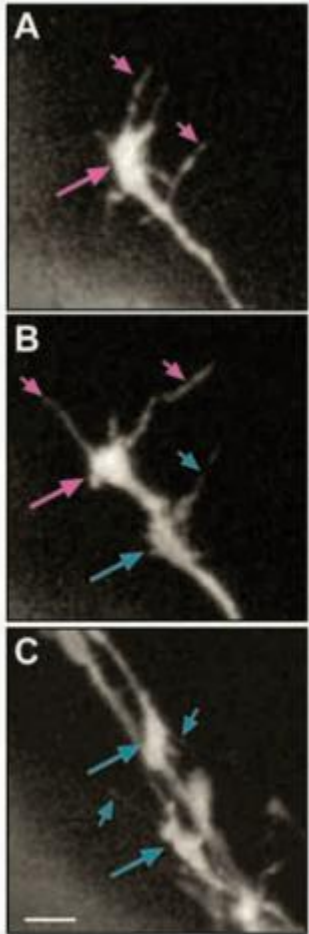




# Moléculas adhesivas

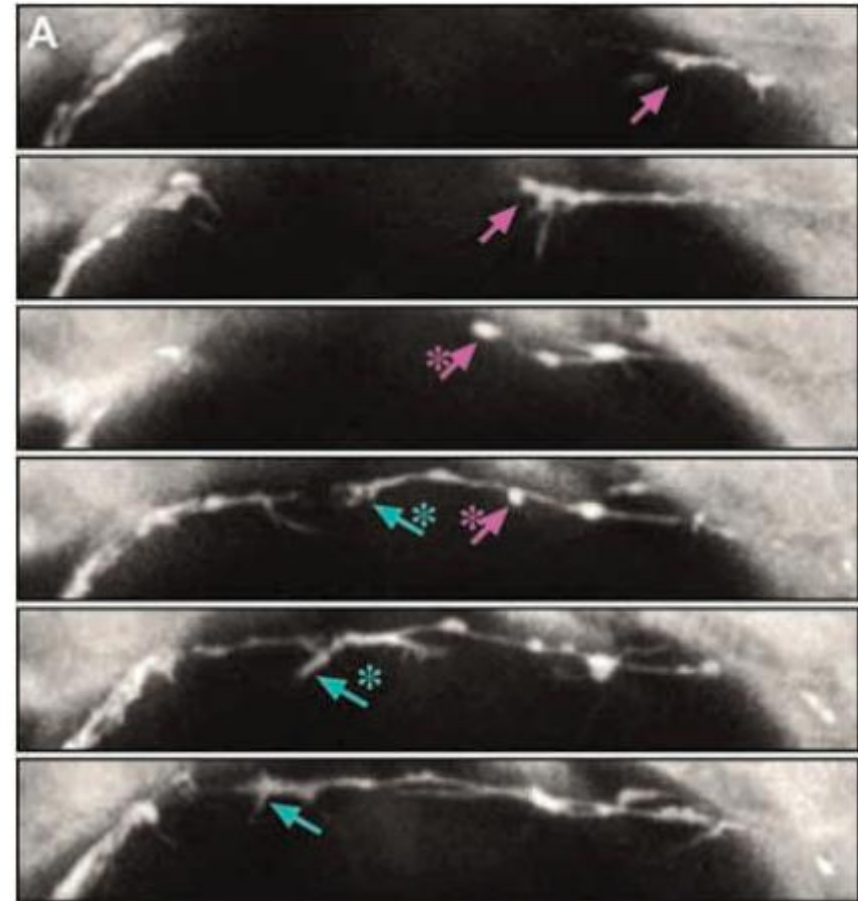
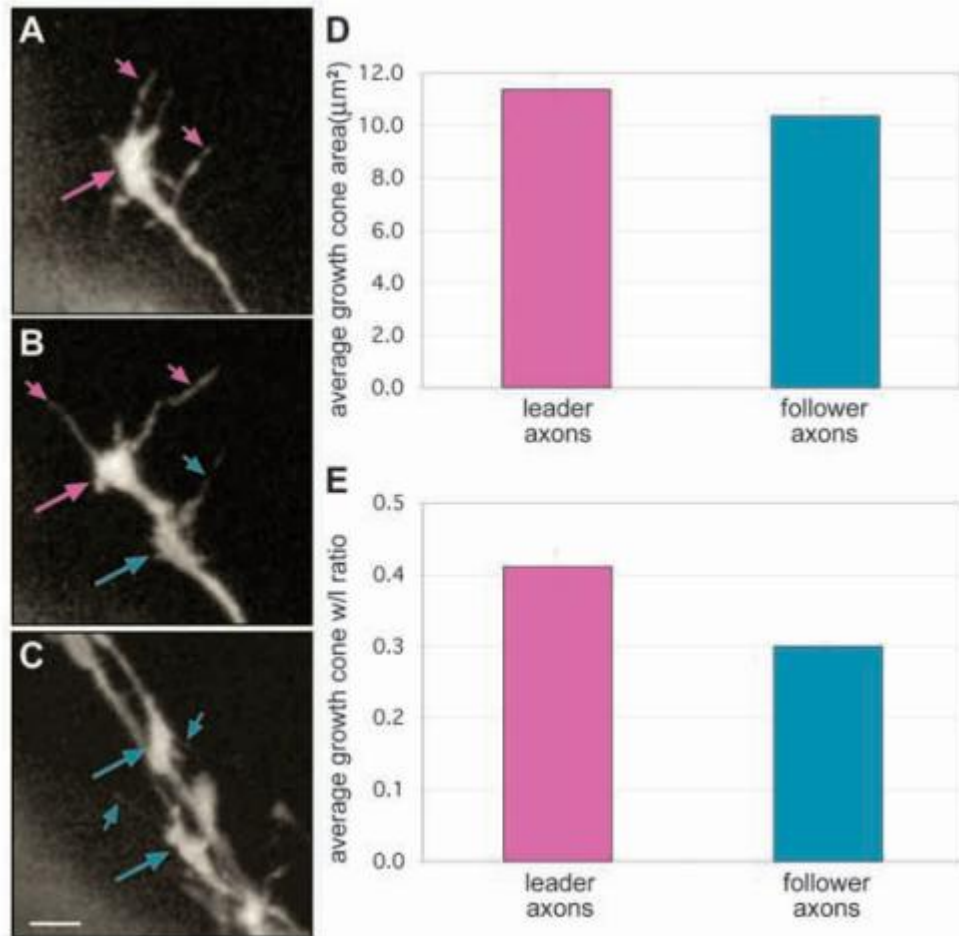


# Interacción axón-axón



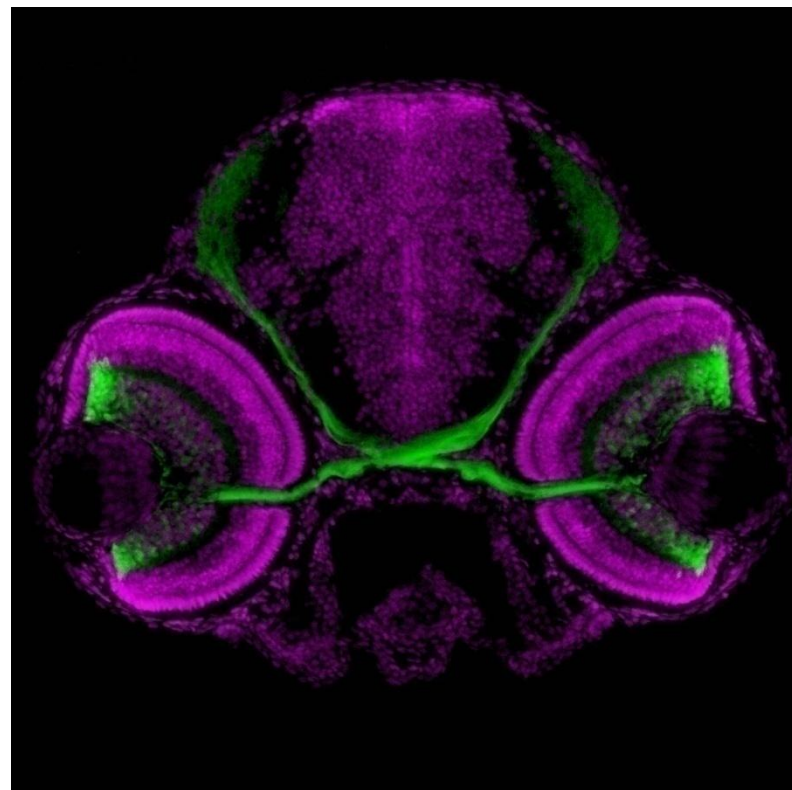
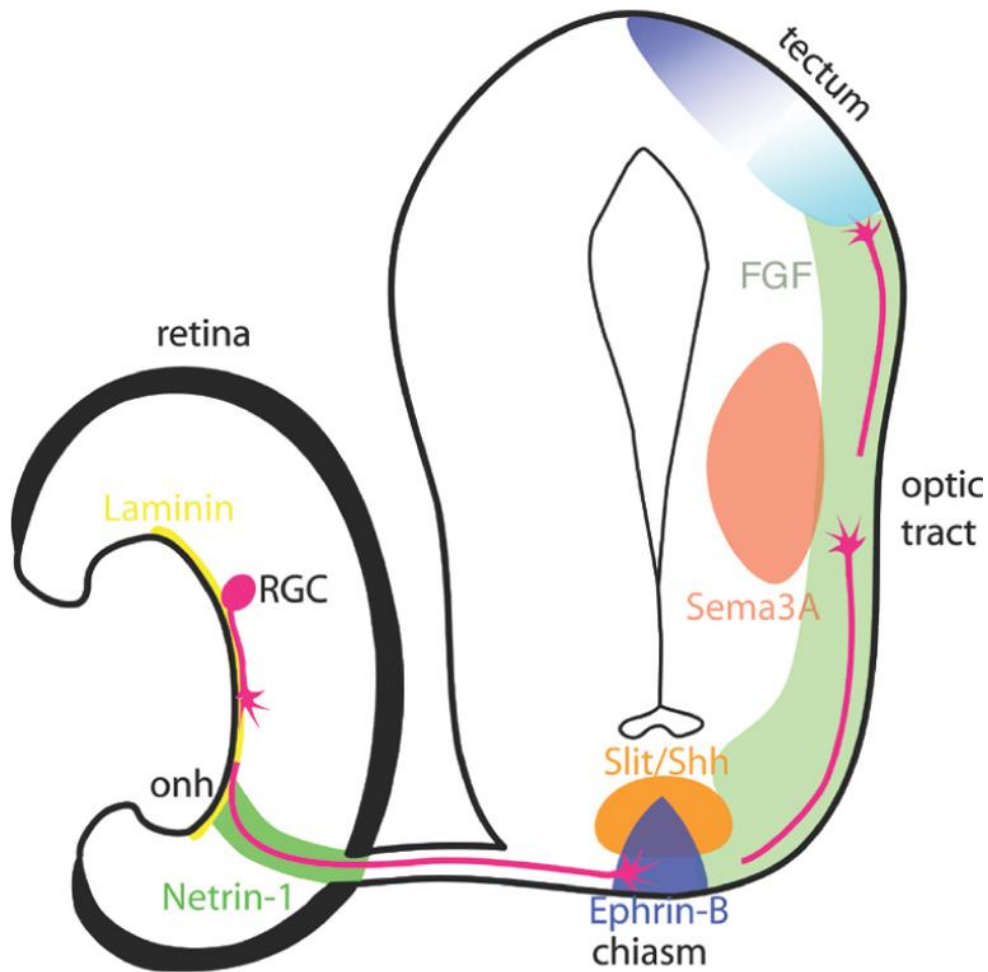
Bak & Fraser, 2003

# Interacción axón-axón

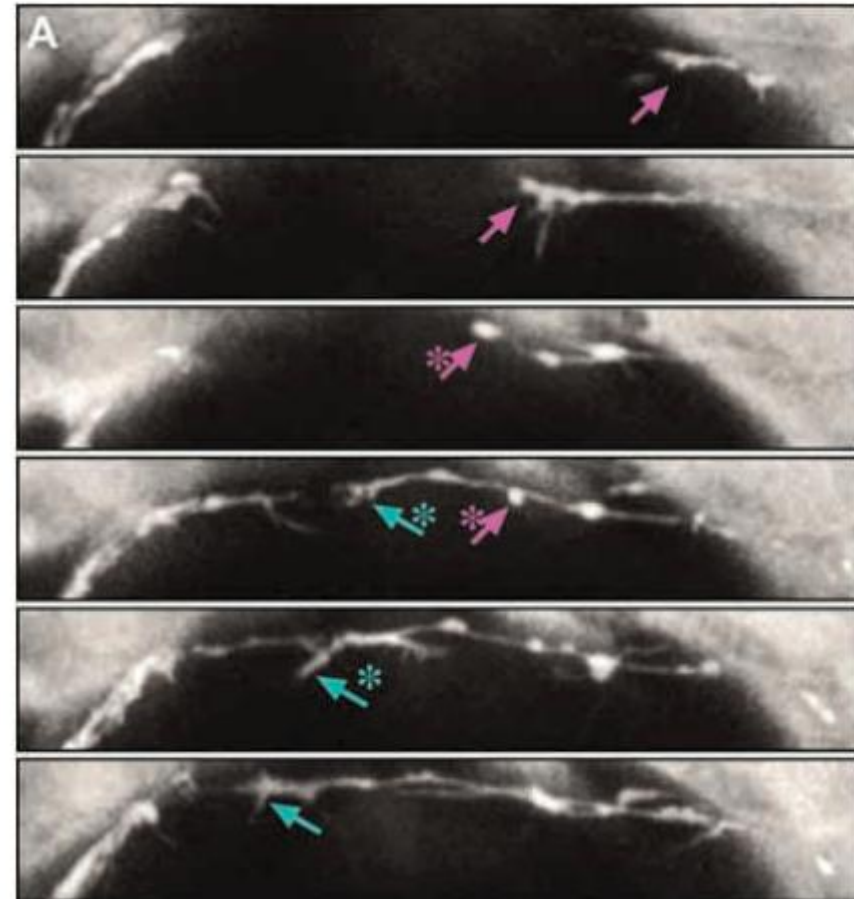
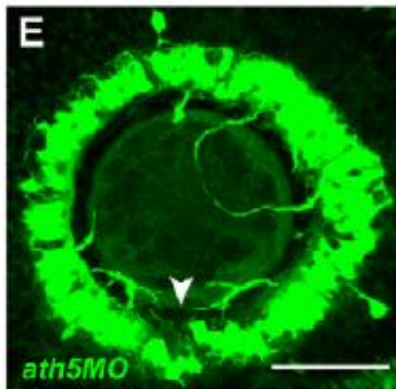
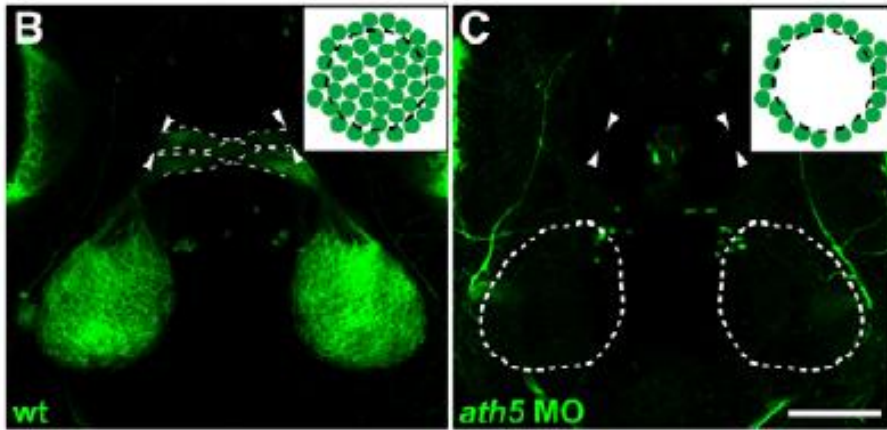
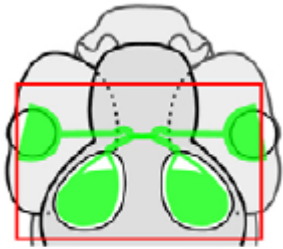


Bak & Fraser, 2003

# El sistema visual como modelo

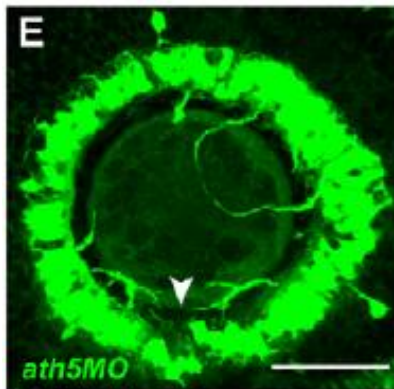
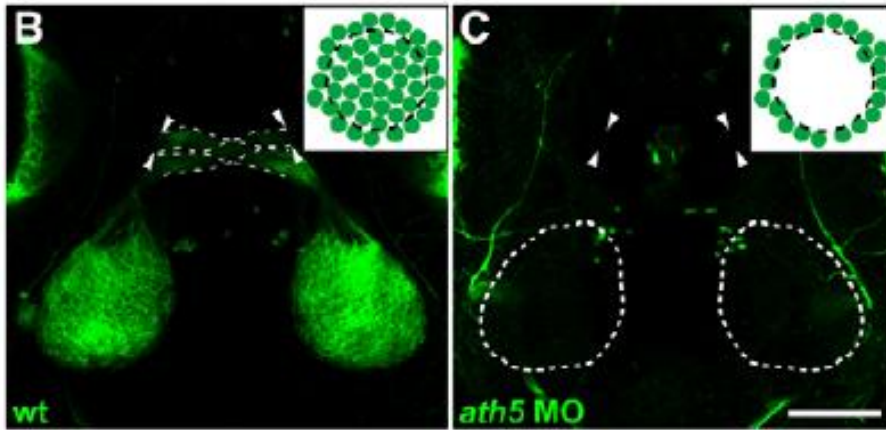
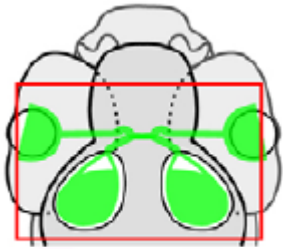


# Interacción axón-axón

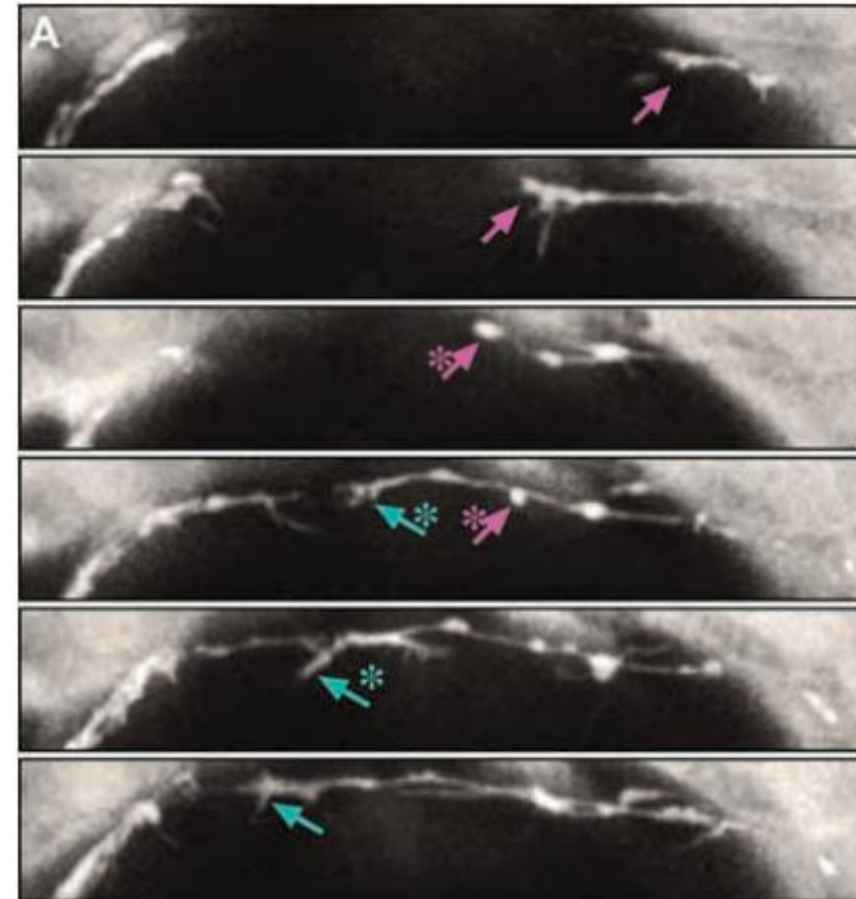


Pittman et al., 2008

# Interacción axón-axón

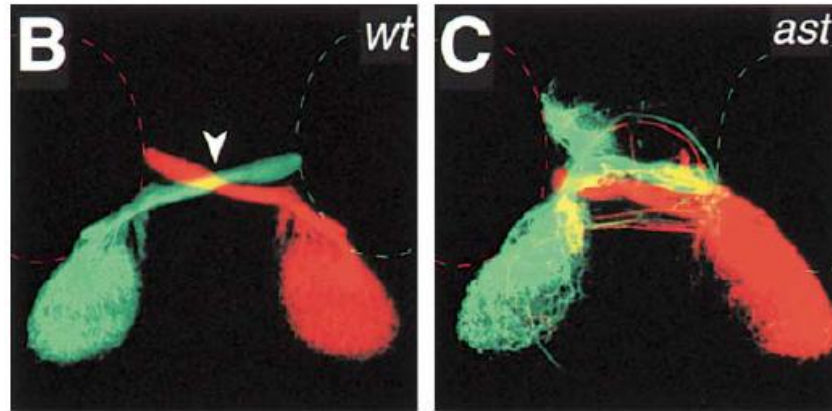


Pittman et al., 2008

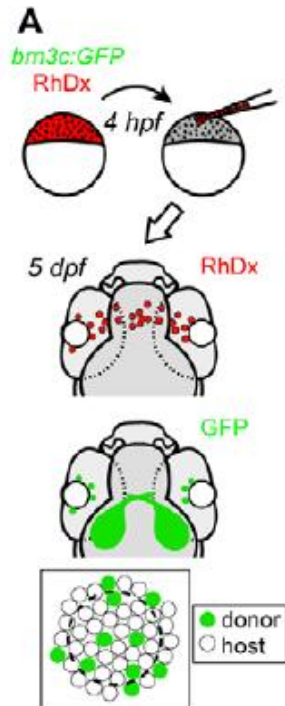


La eliminación de los axones pioneros es variable de acuerdo al tipo neuronal y la cantidad que se elimine

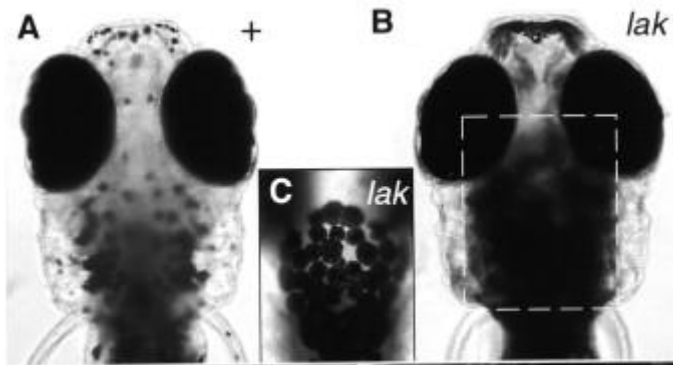
# Interacción axón-axón



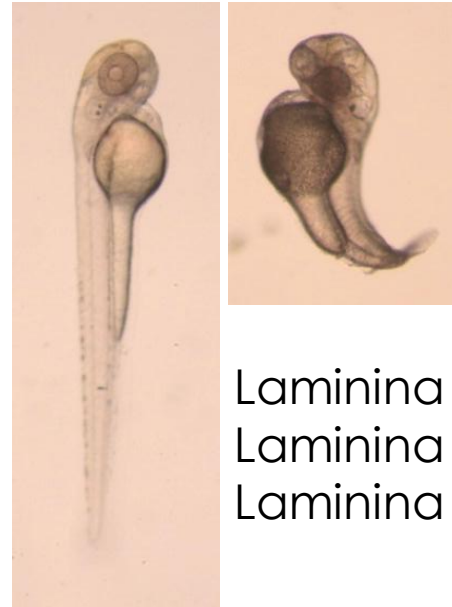
Hutson & Chien, 2002



# Un pequeño paréntesis



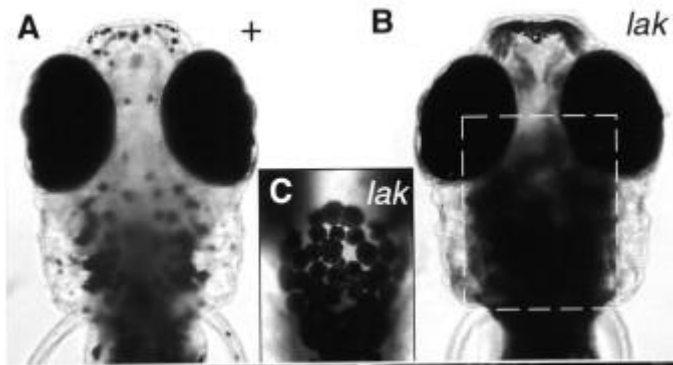
Kay et al., 2001



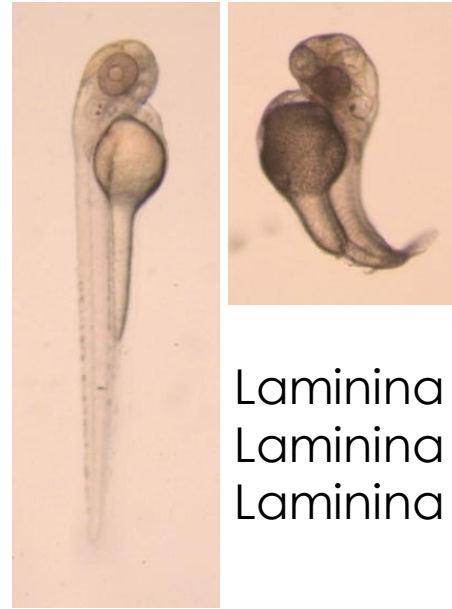
Laminina  $\alpha$ 1  
Laminina  $\beta$ 1  
Laminina  $\gamma$ 1



# Un pequeño paréntesis



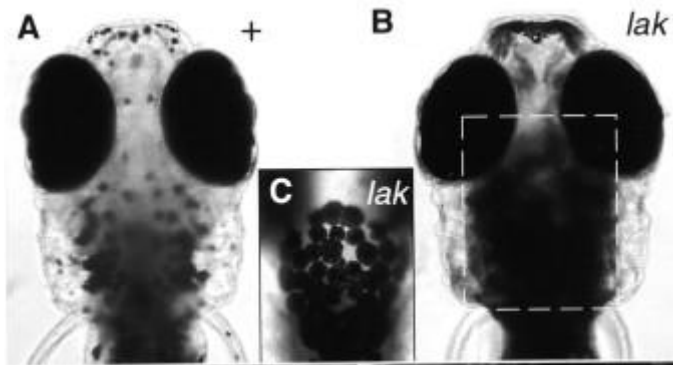
Kay et al., 2001



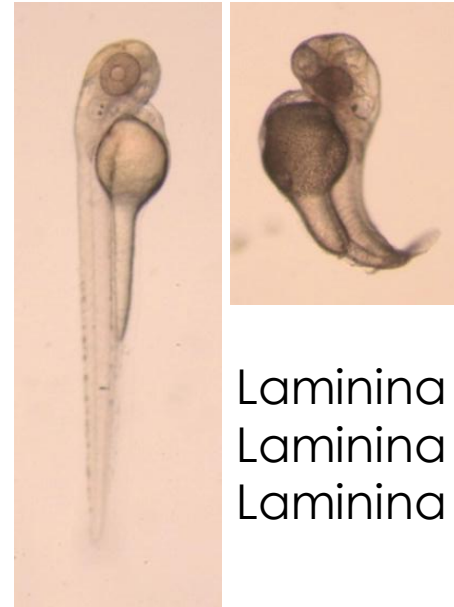
Laminina  $\alpha$ 1  
Laminina  $\beta$ 1  
Laminina  $\gamma$ 1



# Un pequeño paréntesis



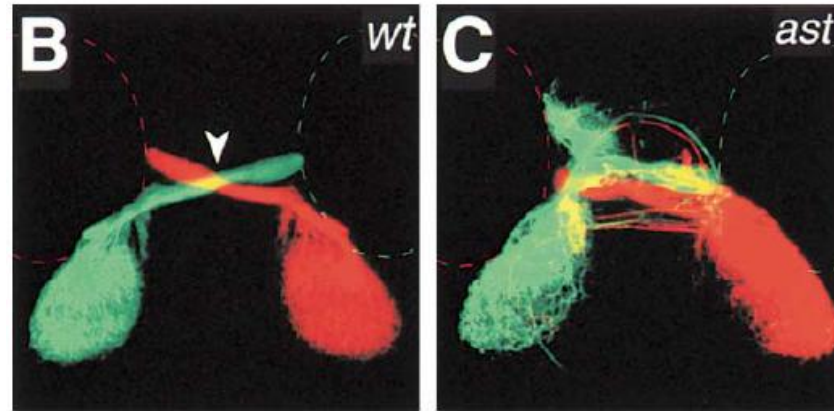
Kay et al., 2001



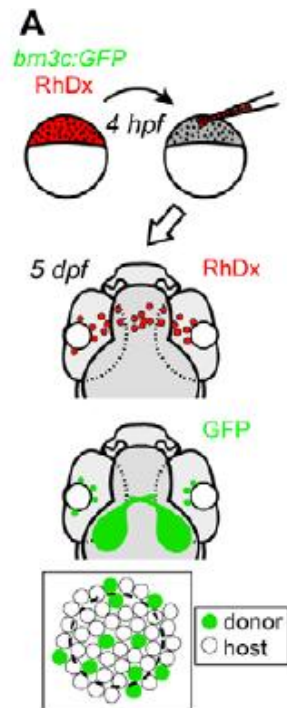
Laminina  $\alpha 1$ : bashful  
Laminina  $\beta 1$ : grumpy  
Laminina  $\gamma 1$ : sleepy



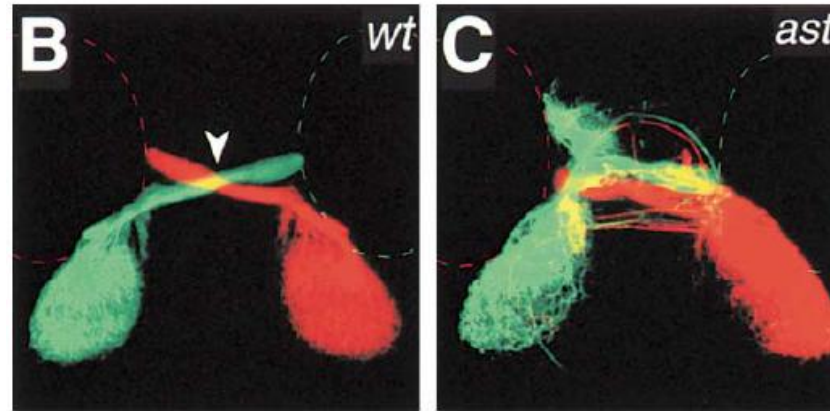
# Interacción axón-axón



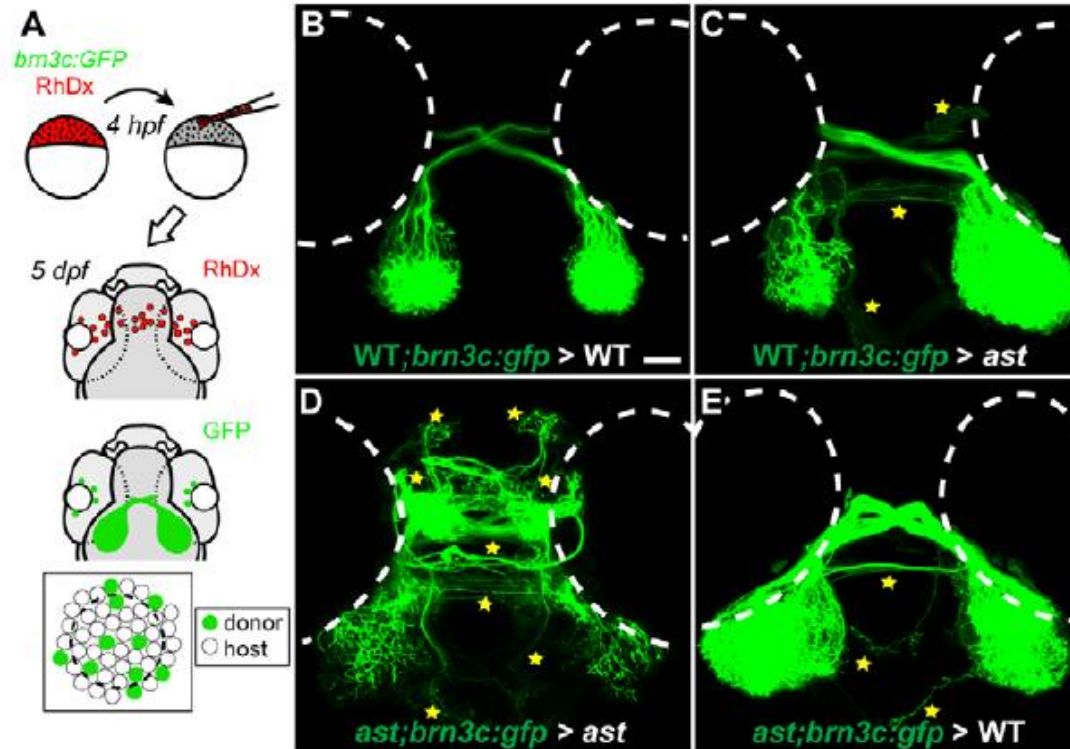
Hutson & Chien, 2002



# Interacción axón-axón

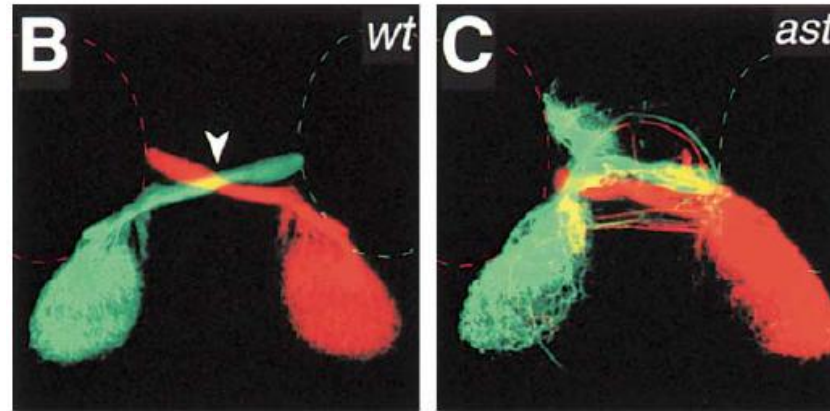


Hutson & Chien, 2002



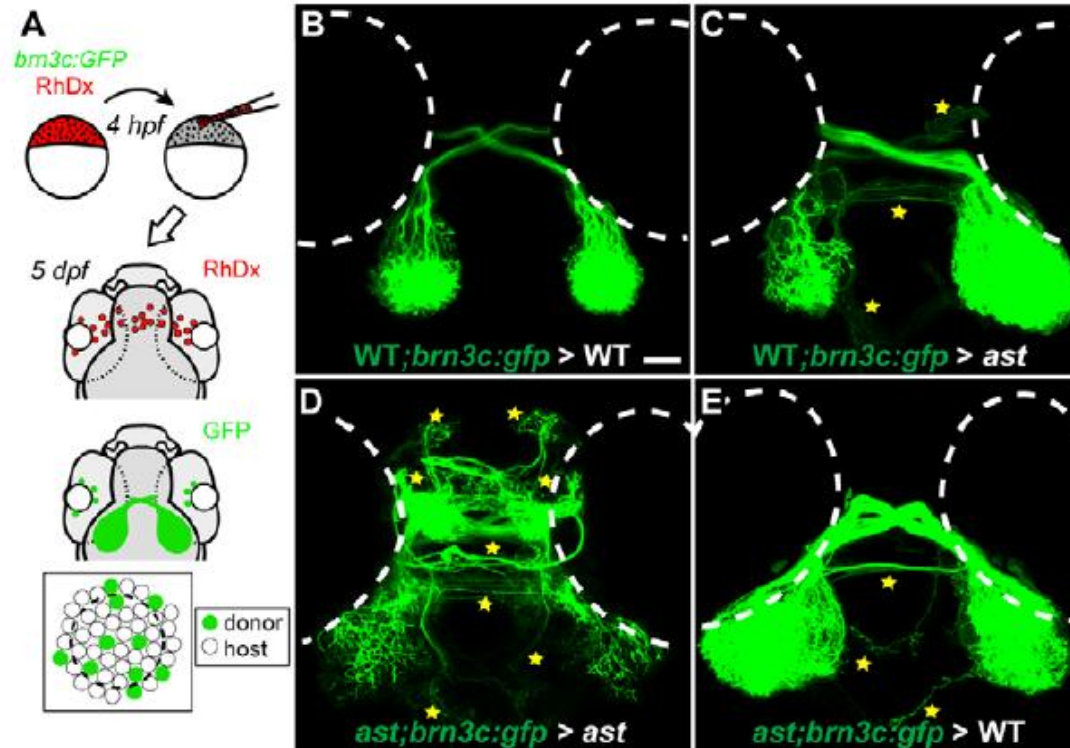
Pittman et al., 2008

# Interacción axón-axón



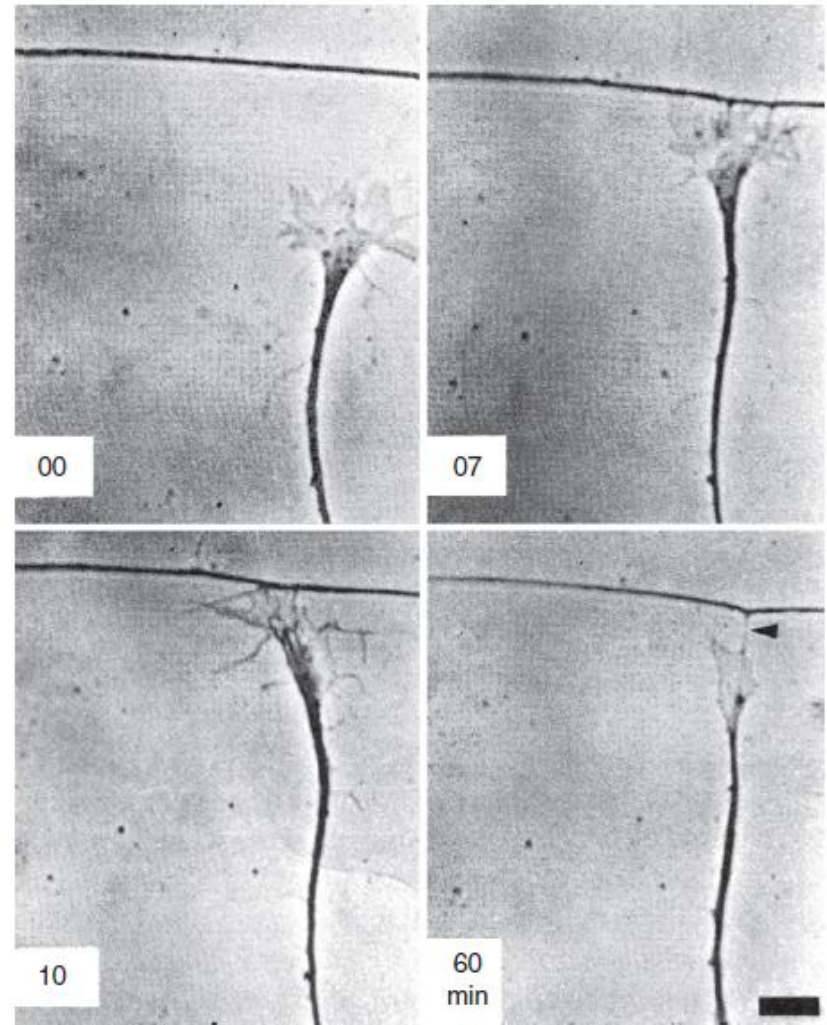
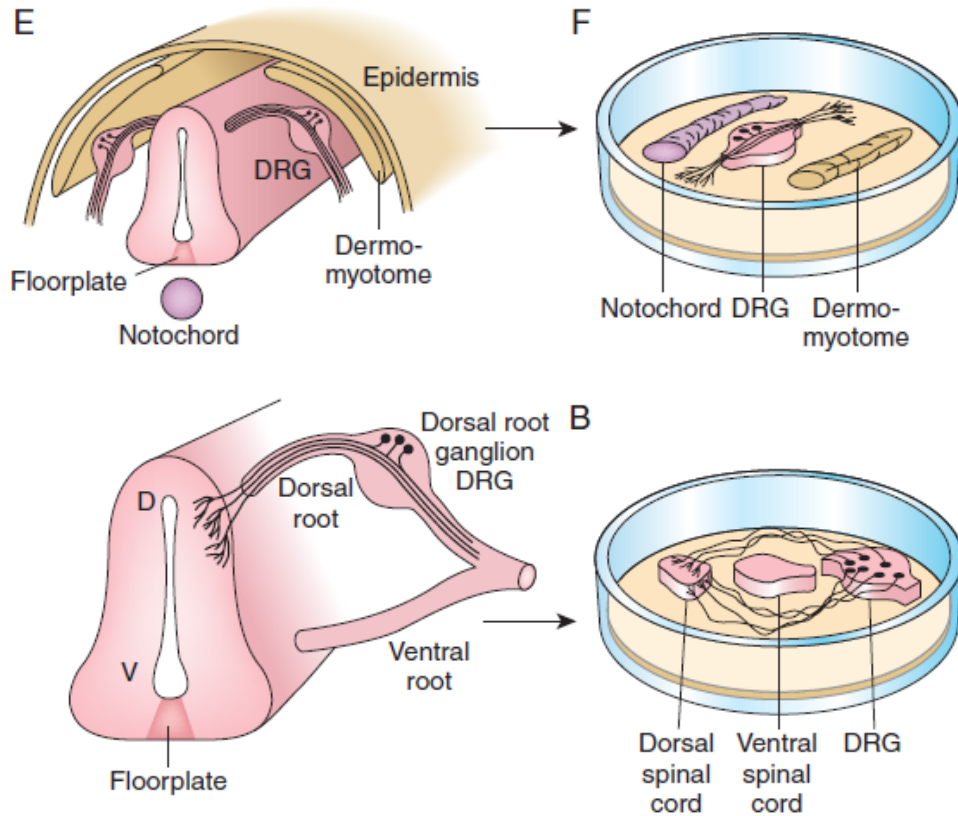
Los axones salvajes pueden equivocarse si siguen a un axón errado, y viceversa

Hutson & Chien, 2002



Pittman et al., 2008

# Señales repulsivas



Kapfhammer & Raper, 1987

# ¿A quién sigue el cono?

Señales químicas

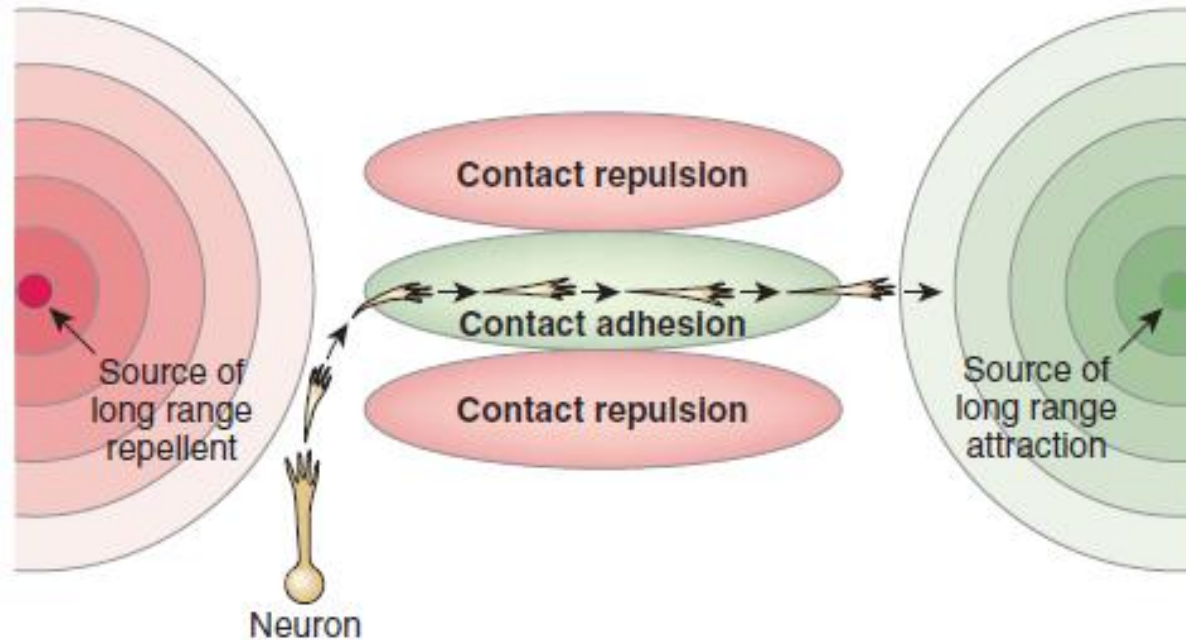


A distancia

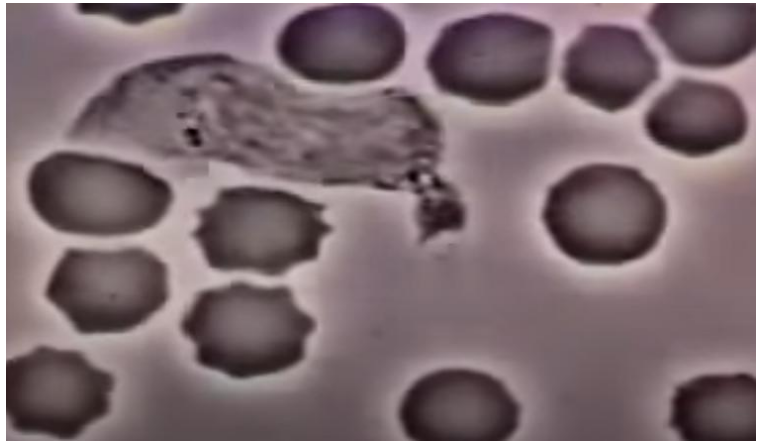
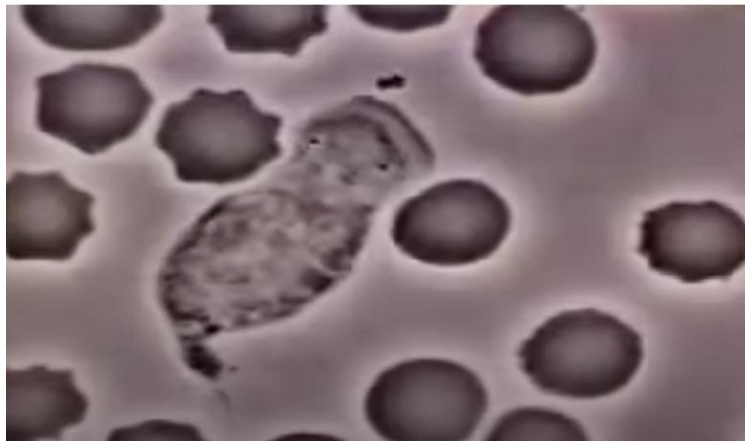
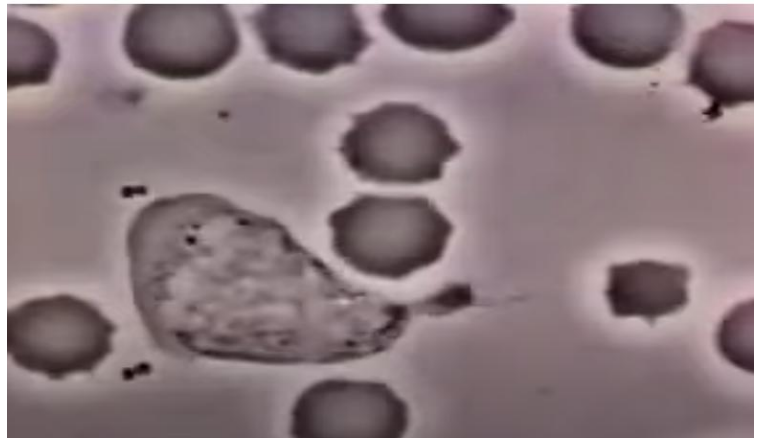
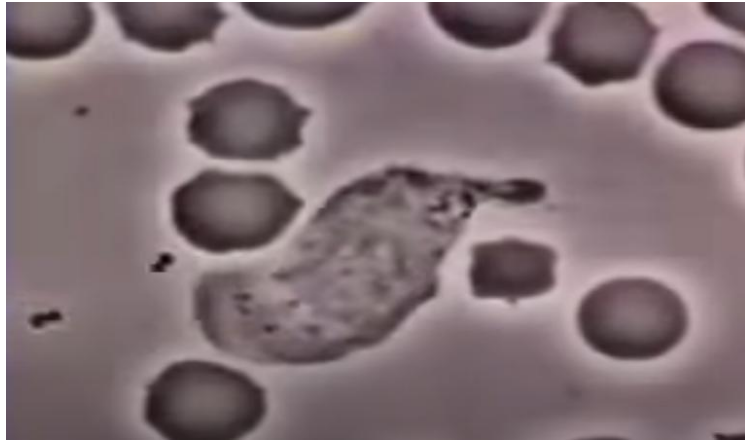


De contacto

Estímulos mecánicos



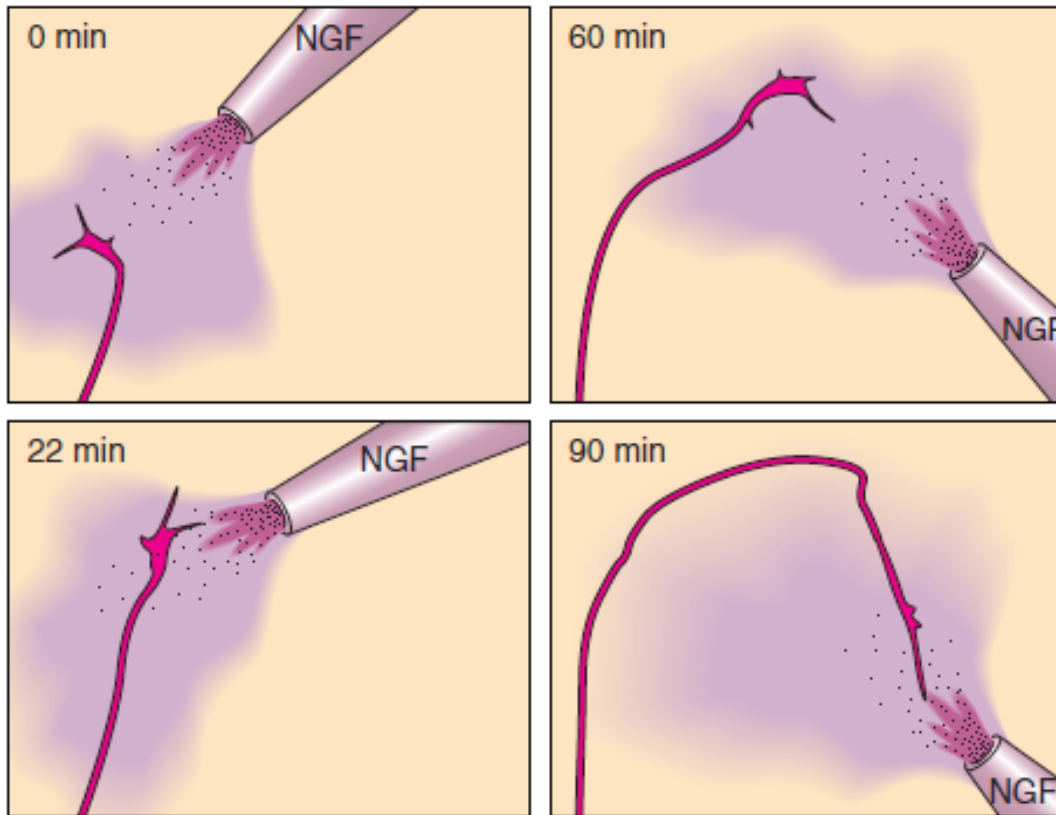
# Señales a distancia



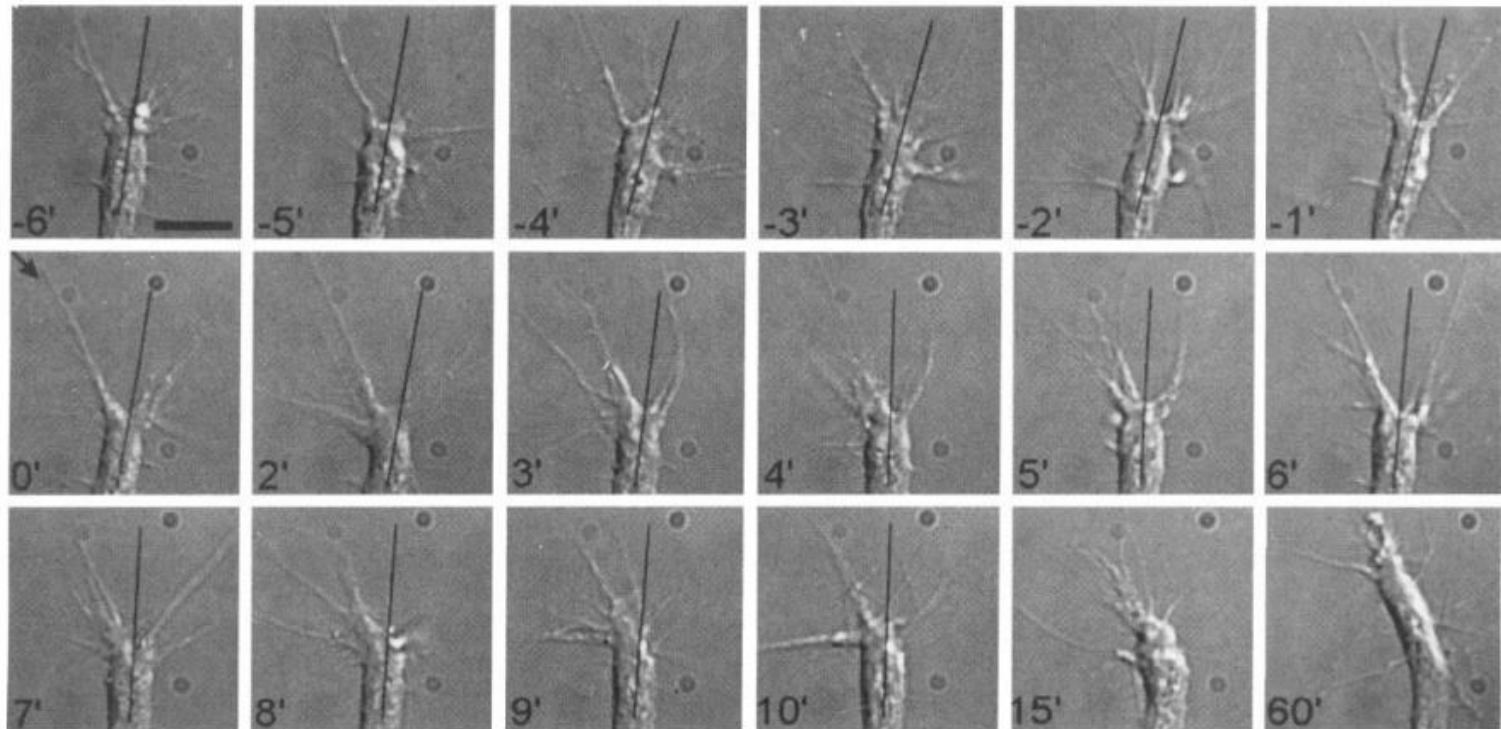
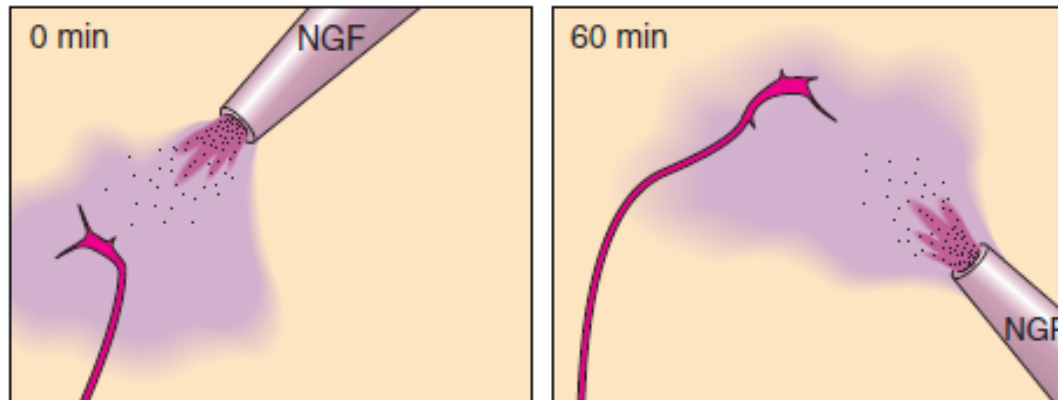
[https://www.youtube.com/watch?v=l\\_xh-bkiv\\_c](https://www.youtube.com/watch?v=l_xh-bkiv_c)



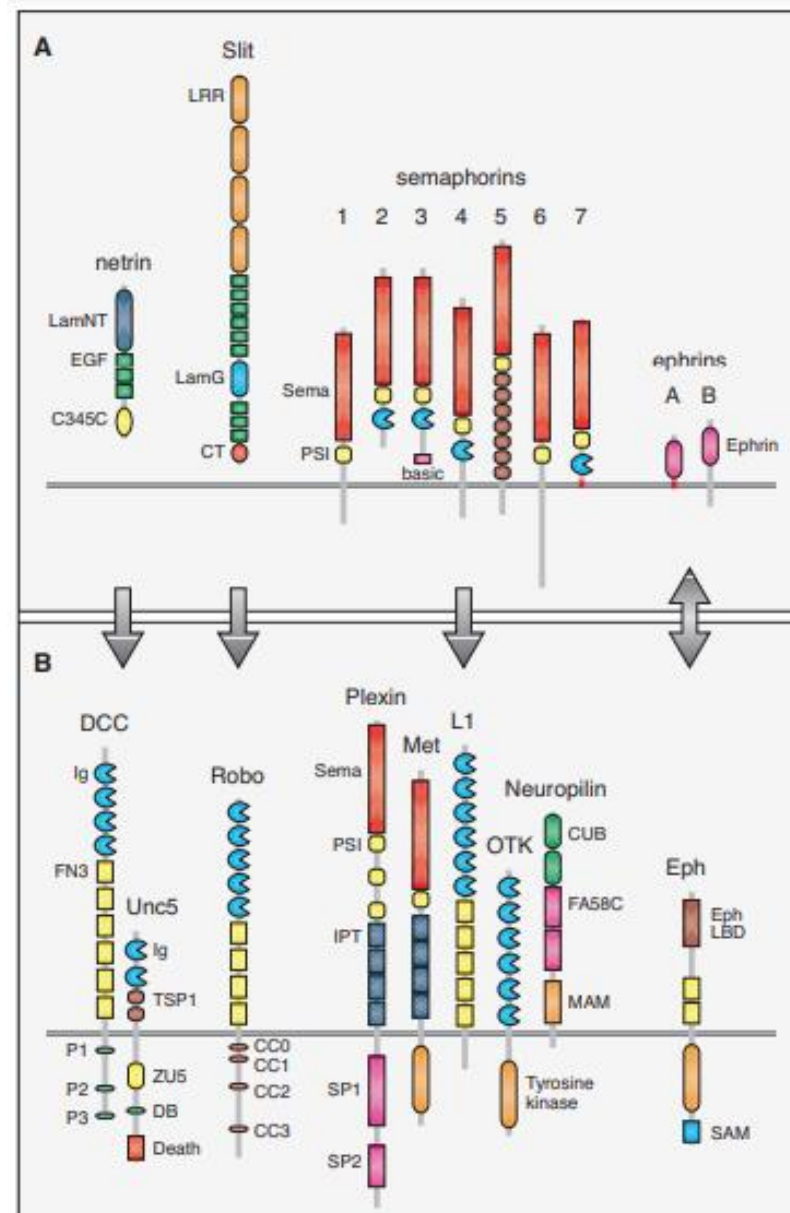
# Señales a distancia



# Señales a distancia



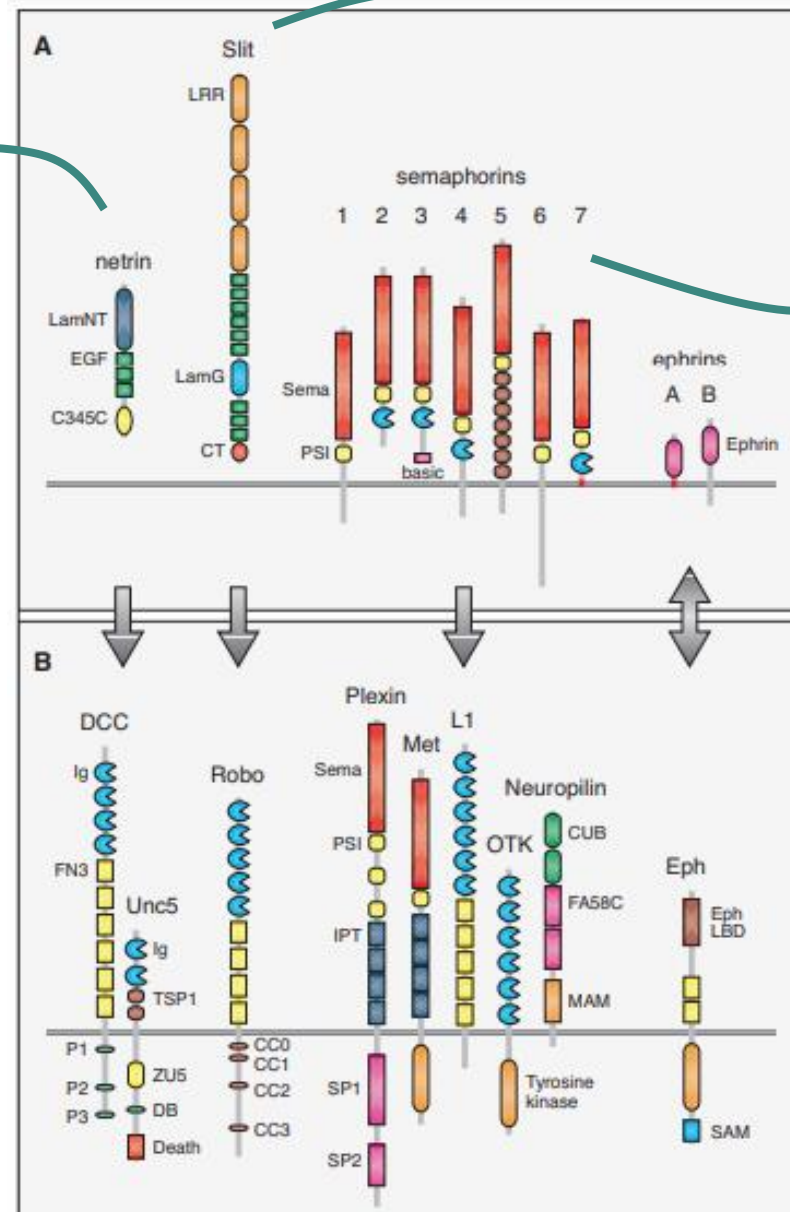
# Señales a distancia



# Señales a distancia

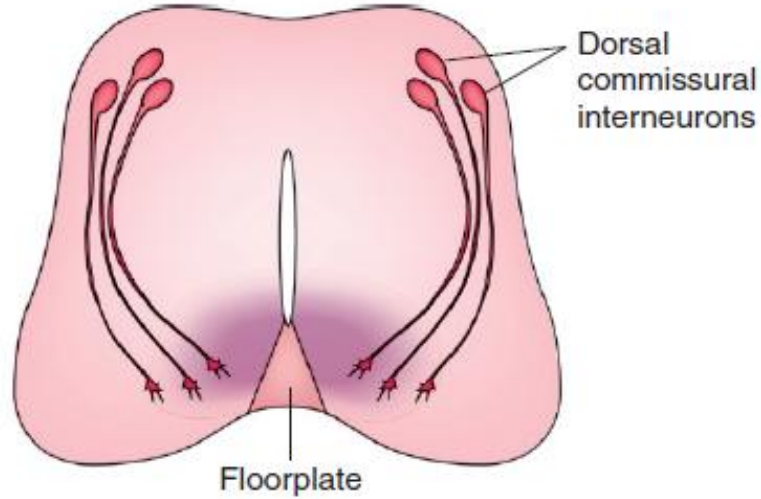
Atractiva

Repulsivas

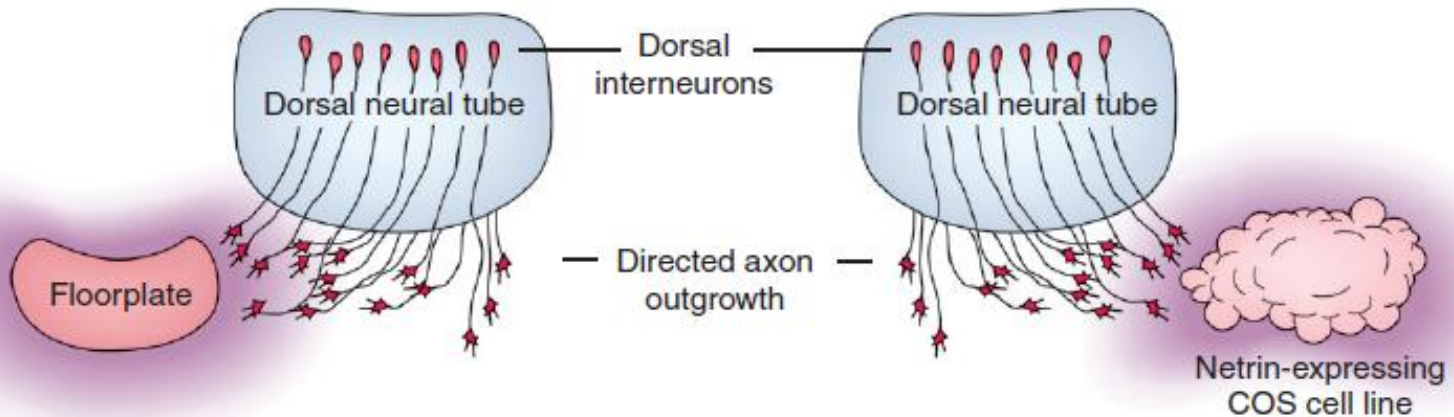


# Cruce de la línea media

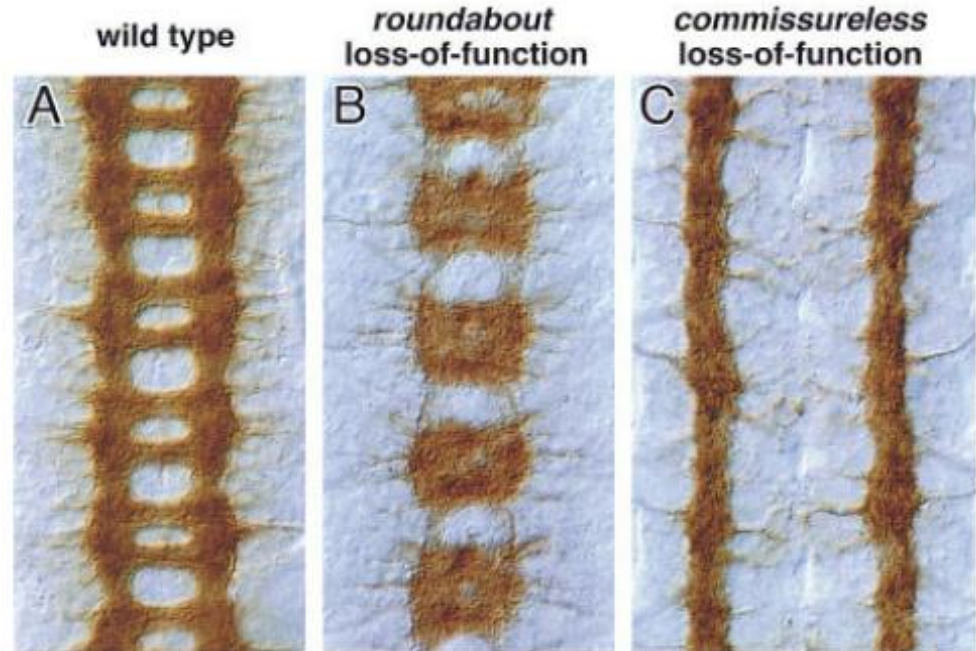
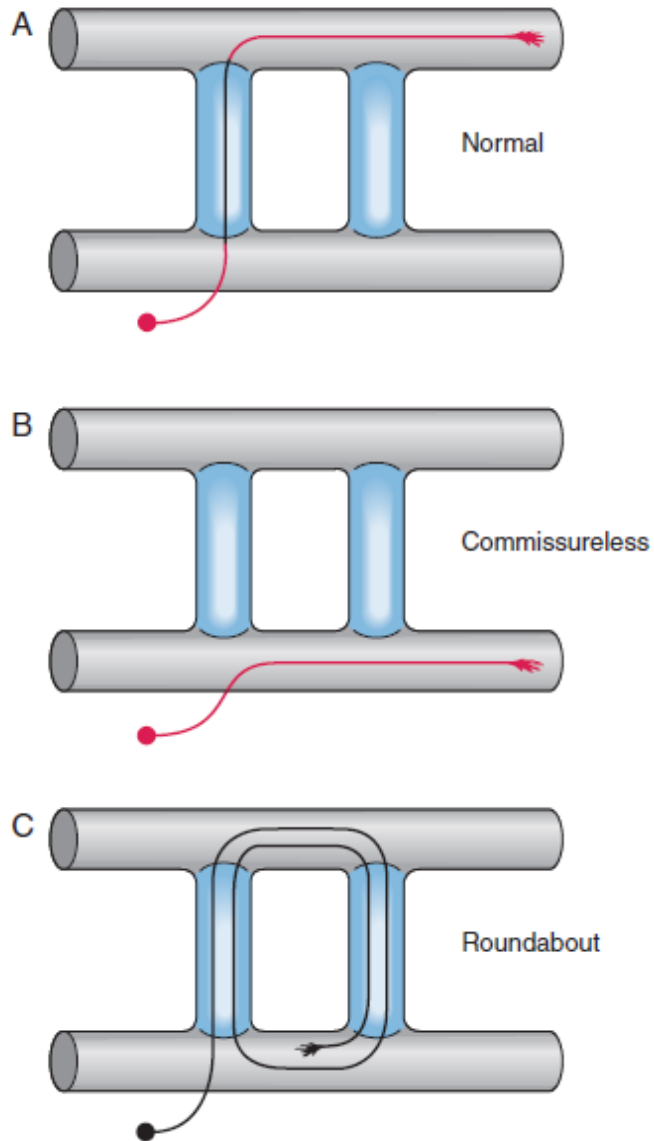
A Netrin-1 expression pattern in the floorplate



B *In vitro* assay of floorplate & Netrin-1

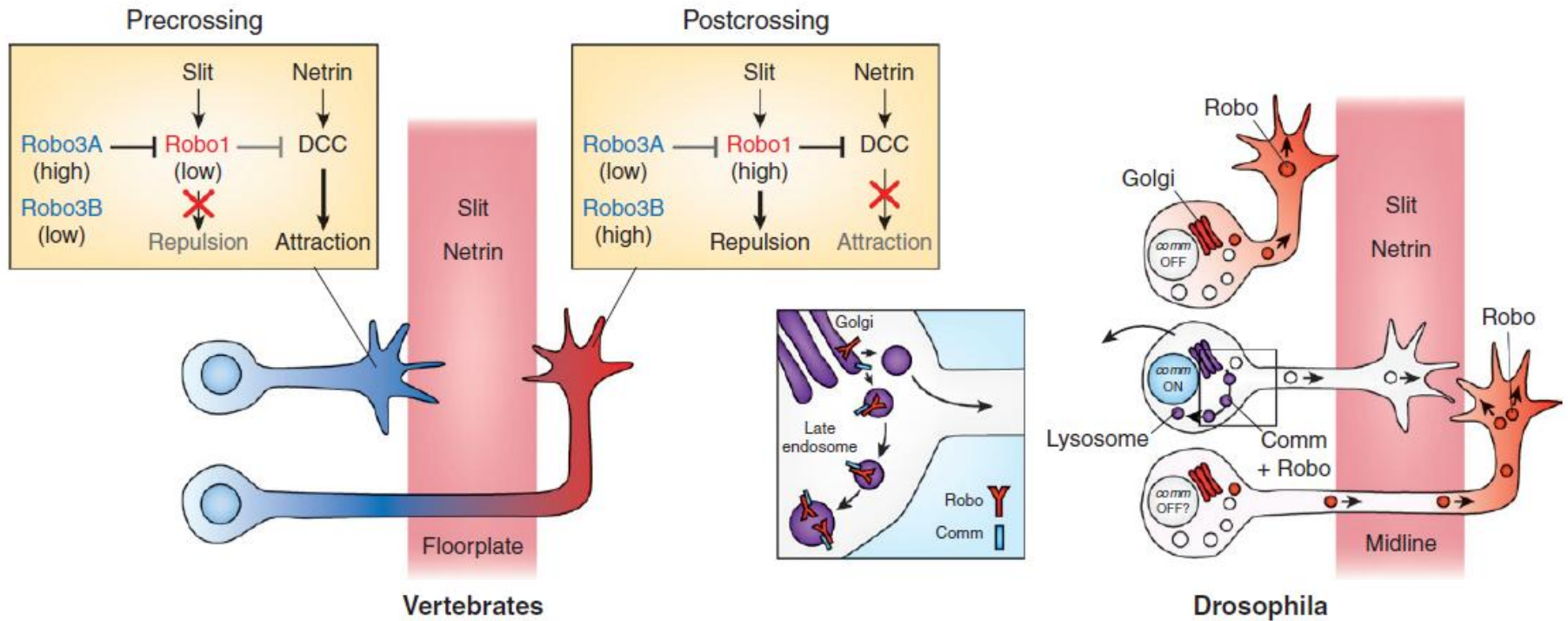


# Cruce de la línea media

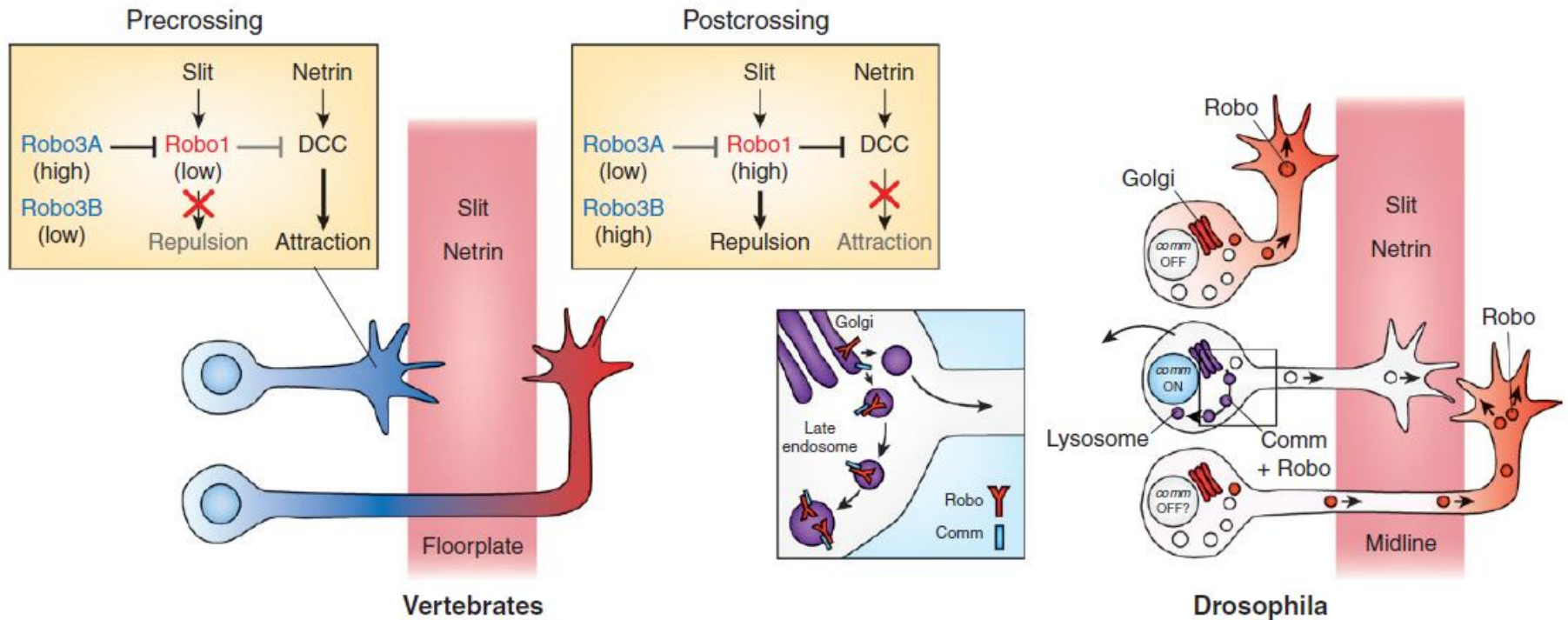


Kidd et al., 1998

# Cruce de la línea media



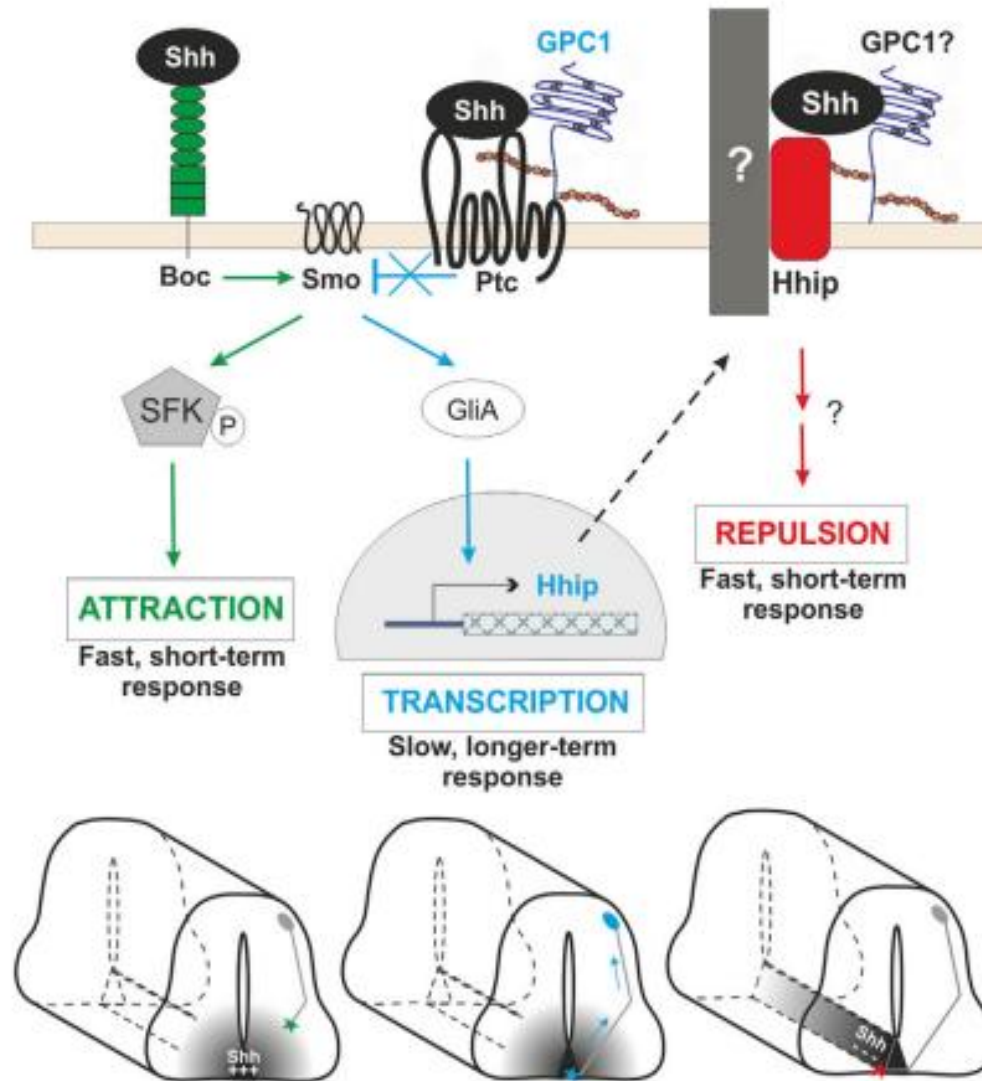
# Cruce de la línea media



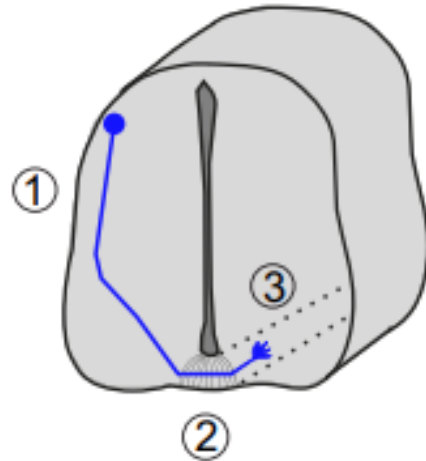
Los axones deben cambiar su respuesta a distintas moléculas a lo largo de su trayecto



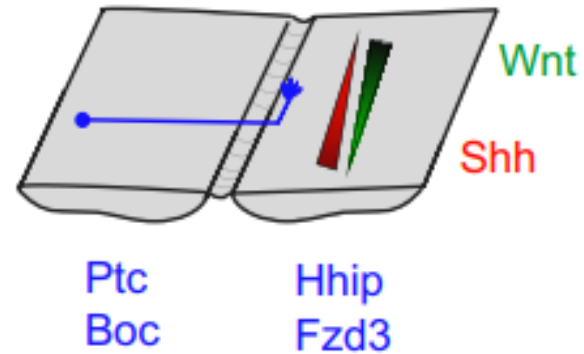
# Cruce de la línea media



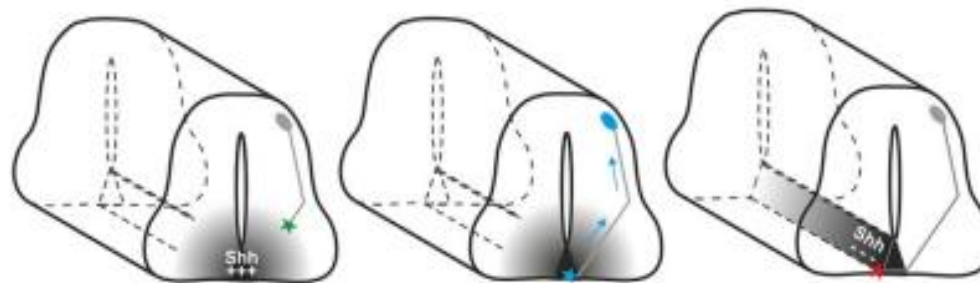
# Cruce de la línea media



## 3 Post-crossing turning

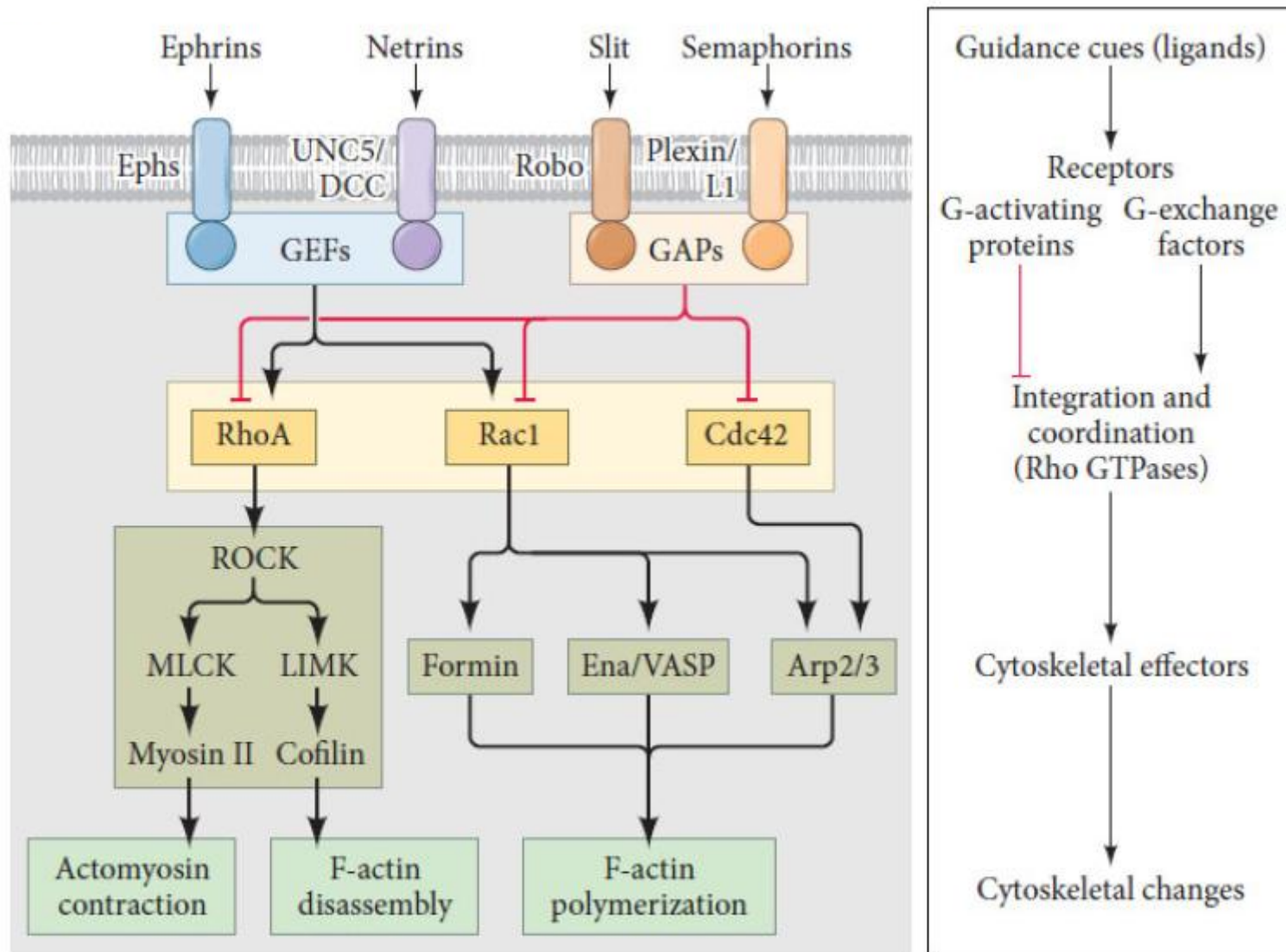


Stoeckli, 2018



Wilson & Stoeckli, 2018

# Transducción de las señales



# ¿A quién sigue el cono?

Señales químicas

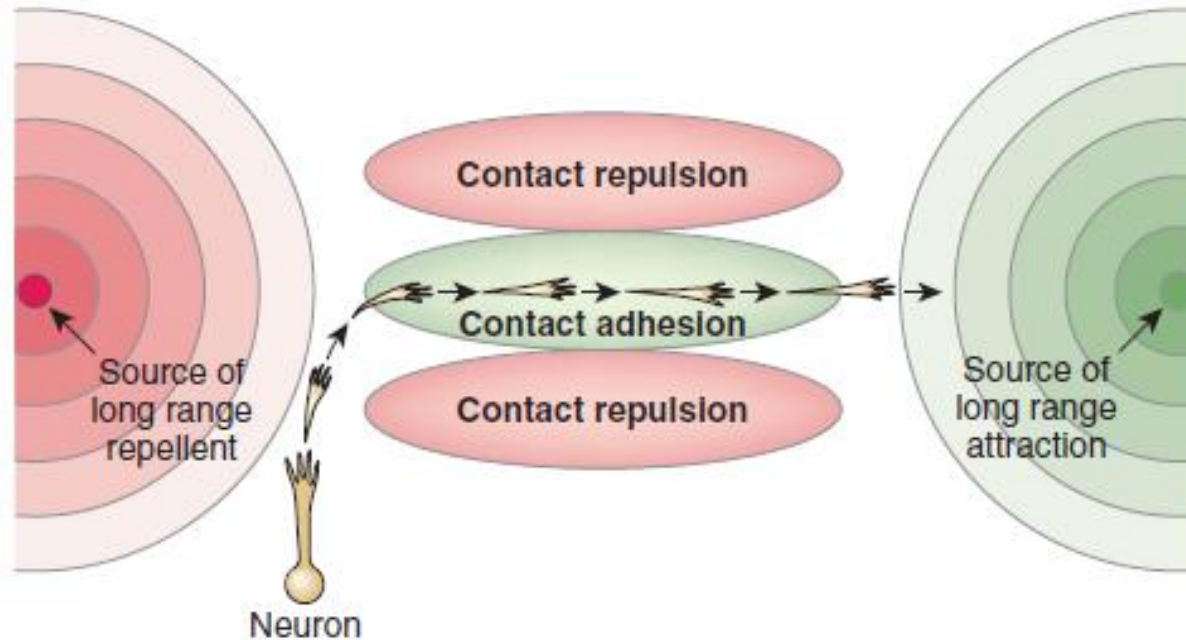


A distancia



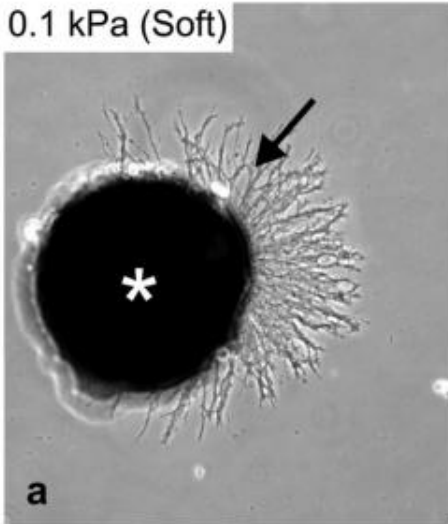
De contacto

Estímulos mecánicos

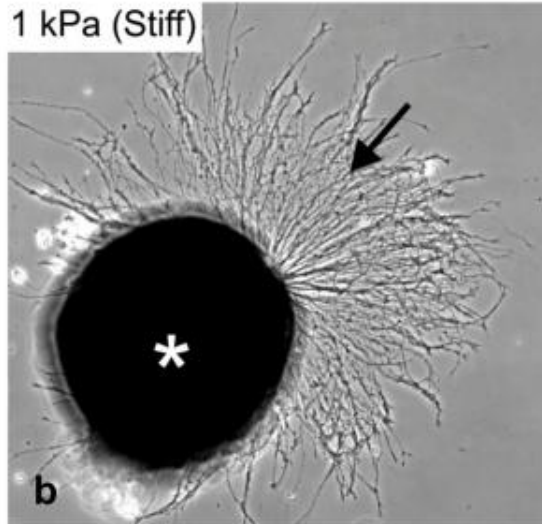


# Señales mecánicas

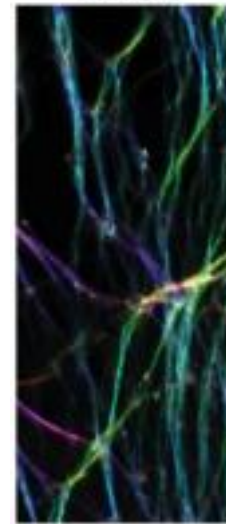
0.1 kPa (Soft)



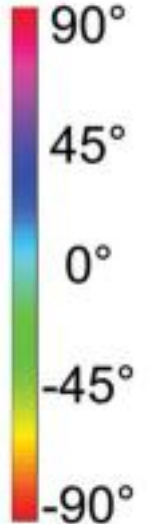
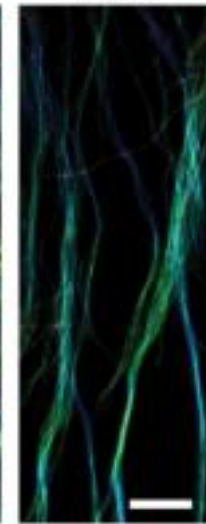
1 kPa (Stiff)



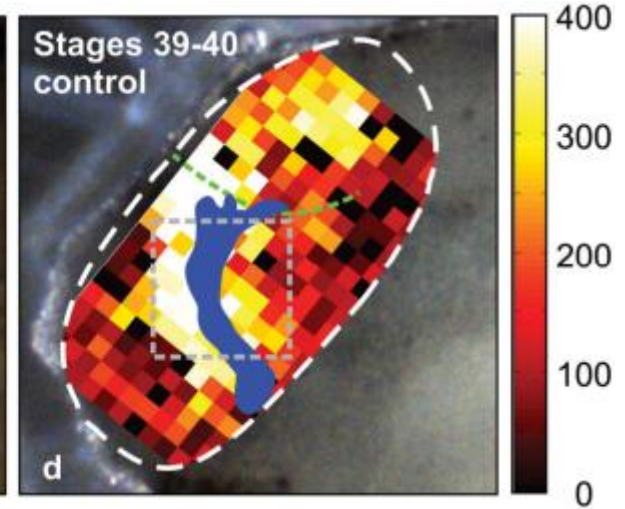
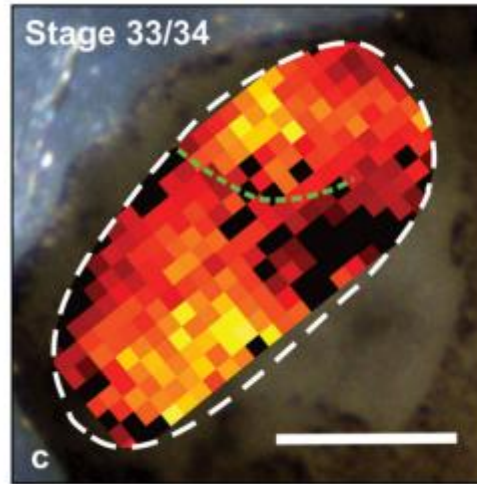
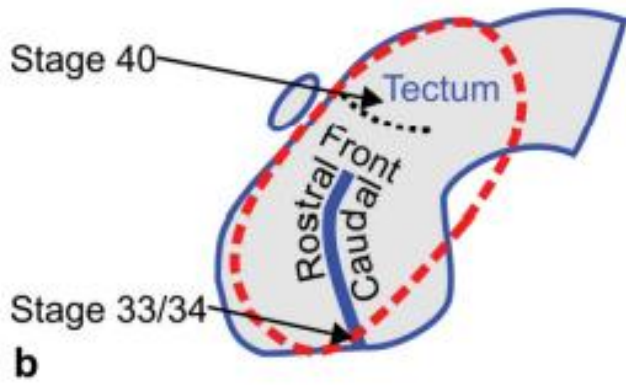
Soft



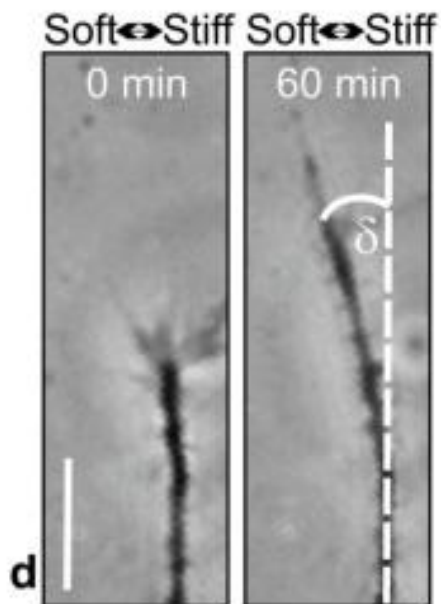
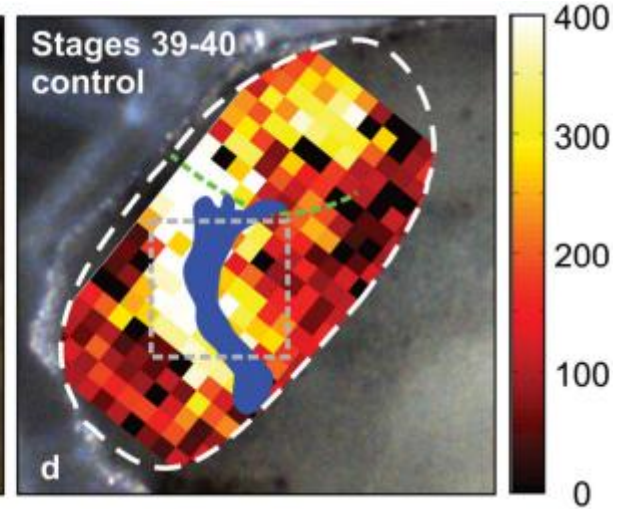
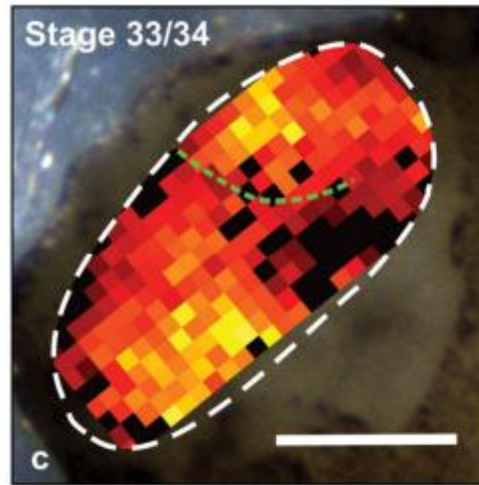
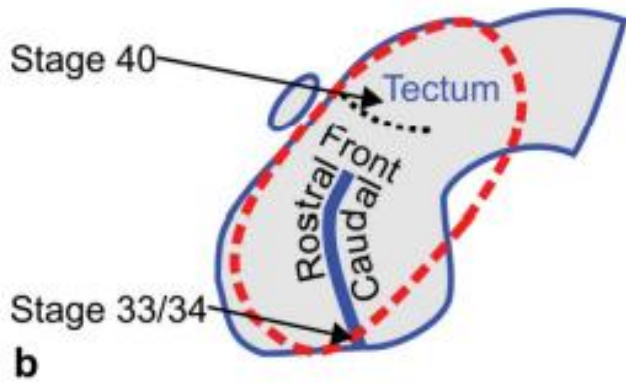
Stiff



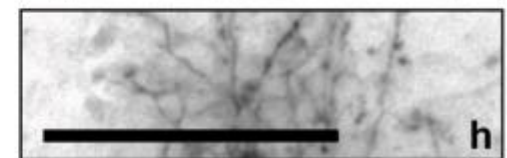
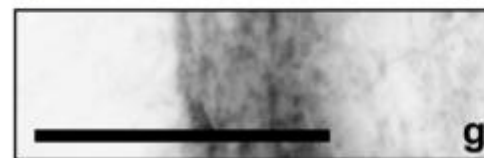
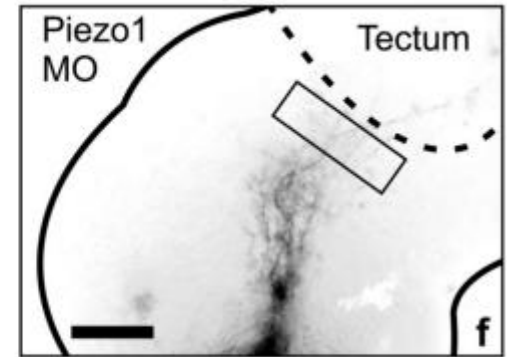
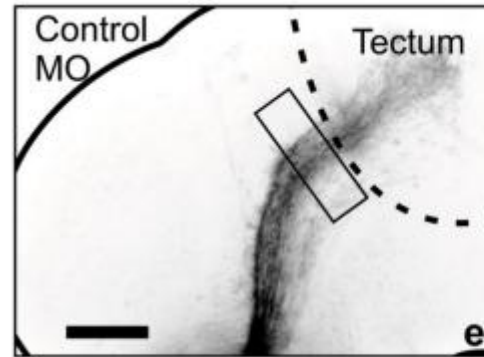
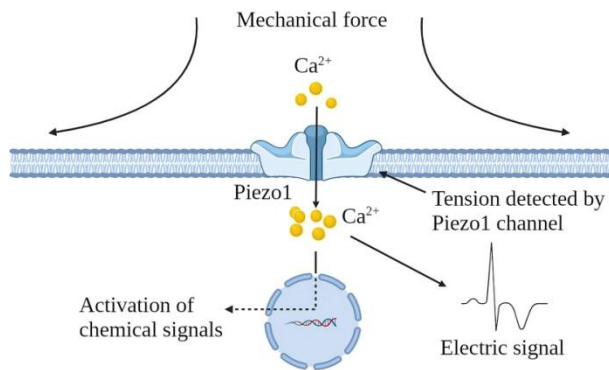
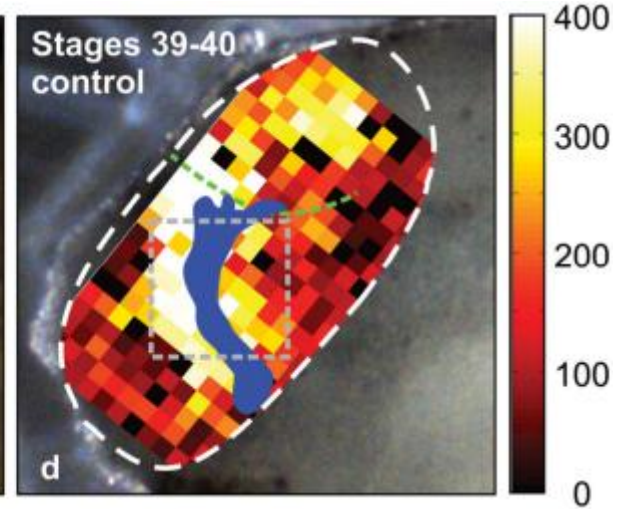
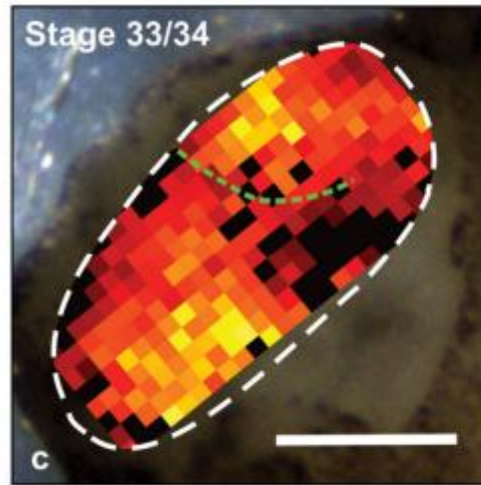
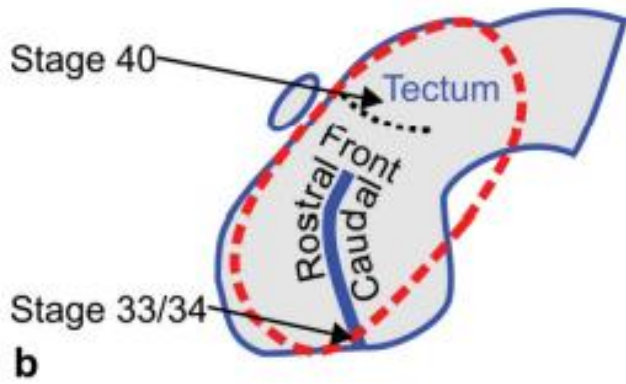
# Señales mecánicas



# Señales mecánicas



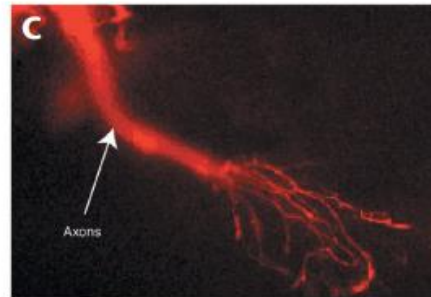
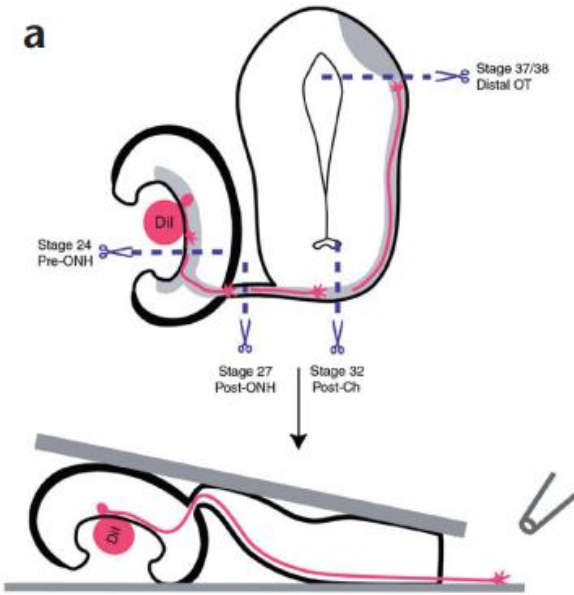
# Señales mecánicas





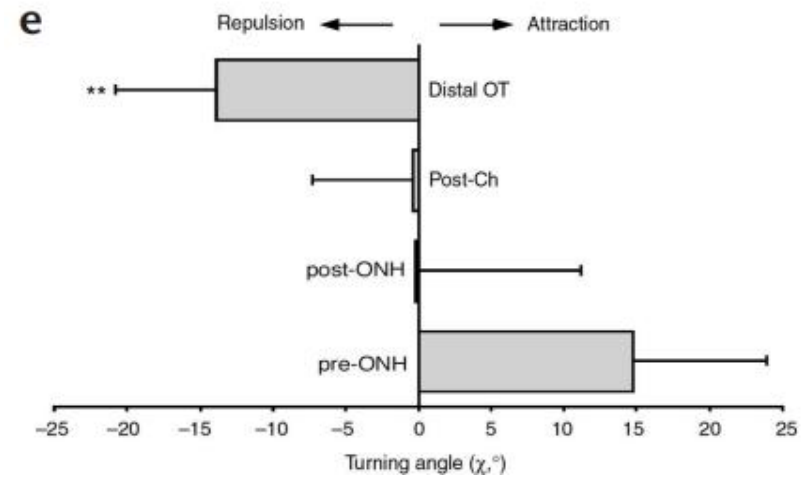
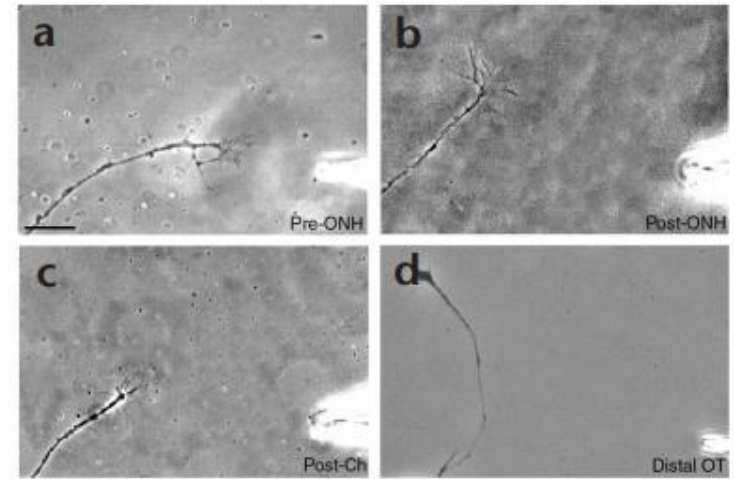
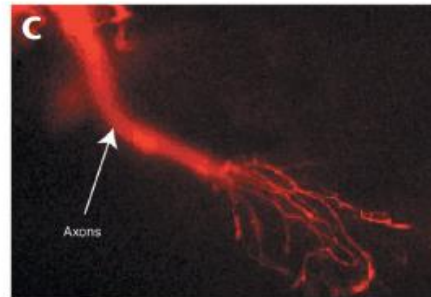
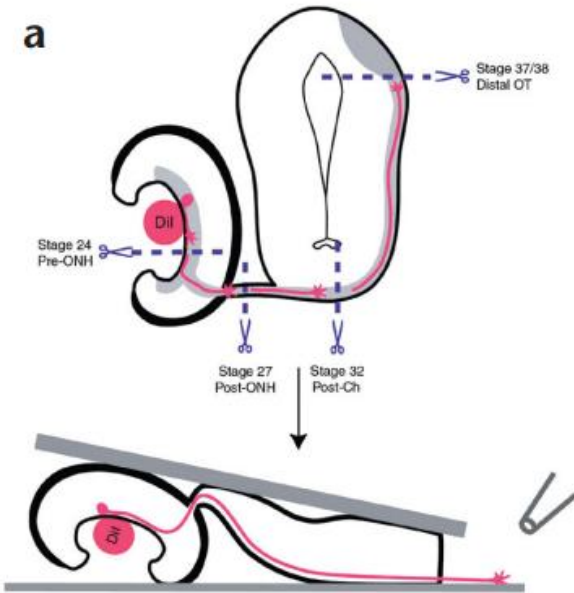
# El reloj de la neurona

Shewan et al., 2002



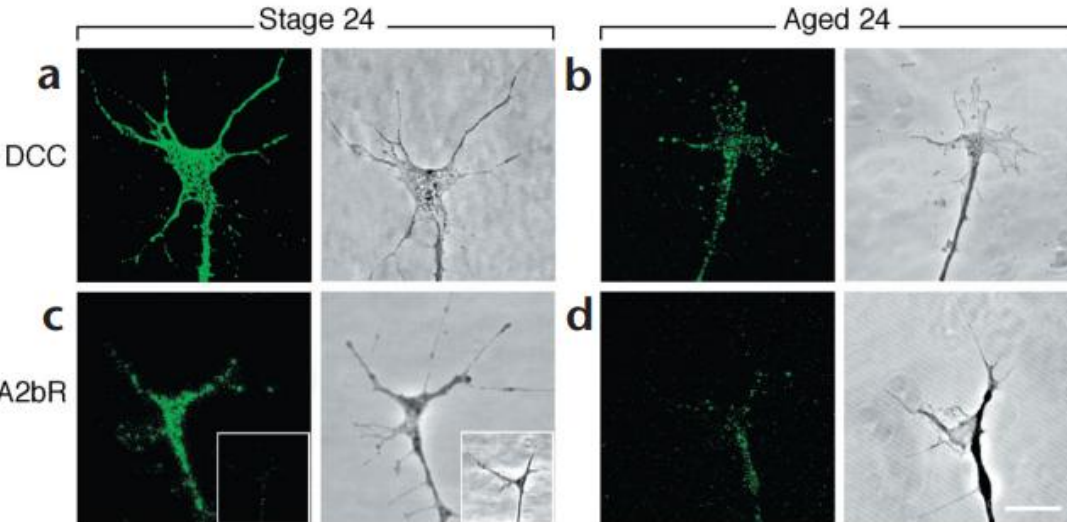
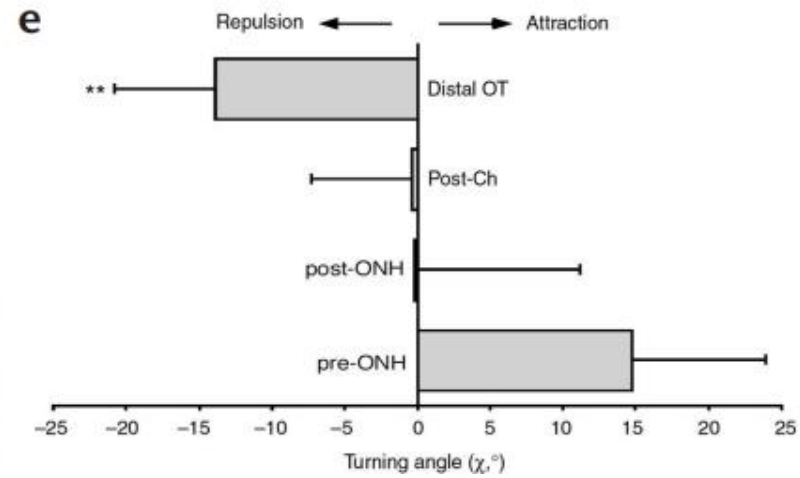
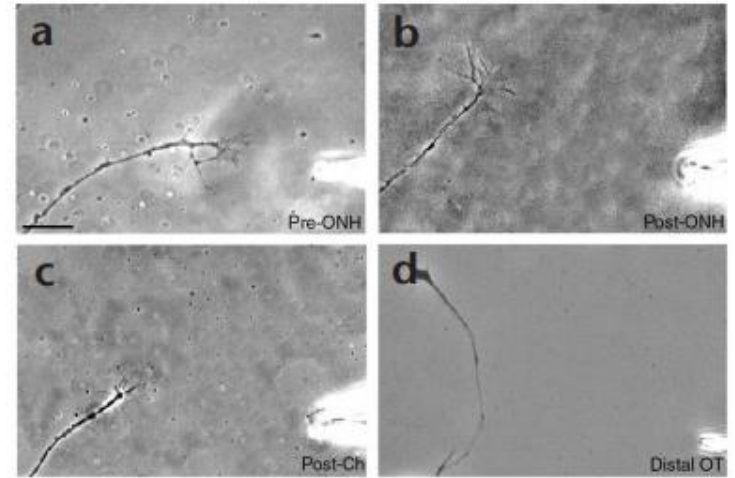
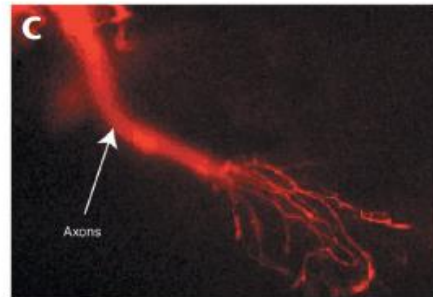
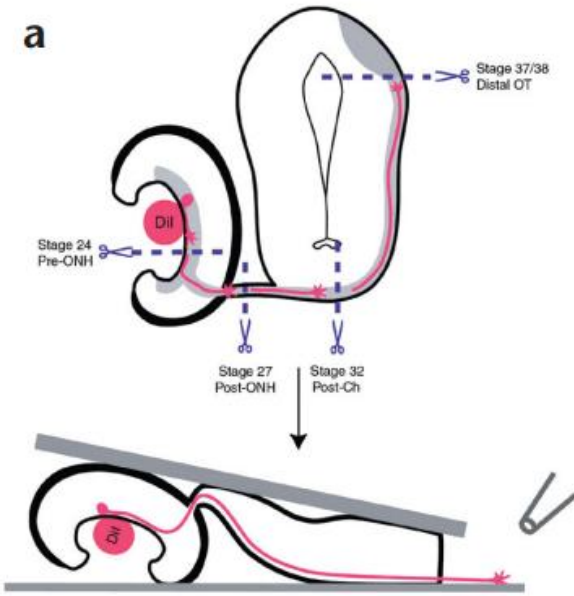
# El reloj de la neurona

Shewan et al., 2002



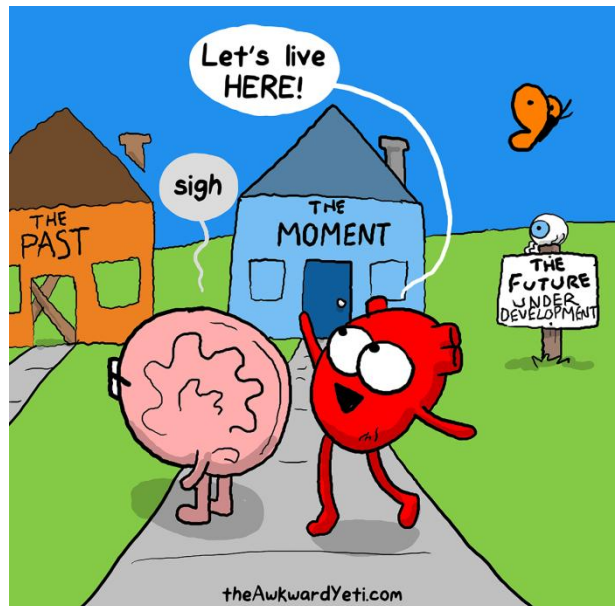
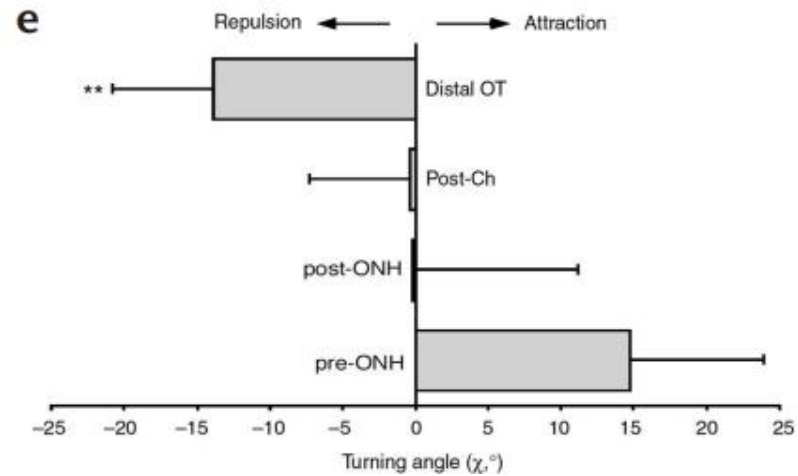
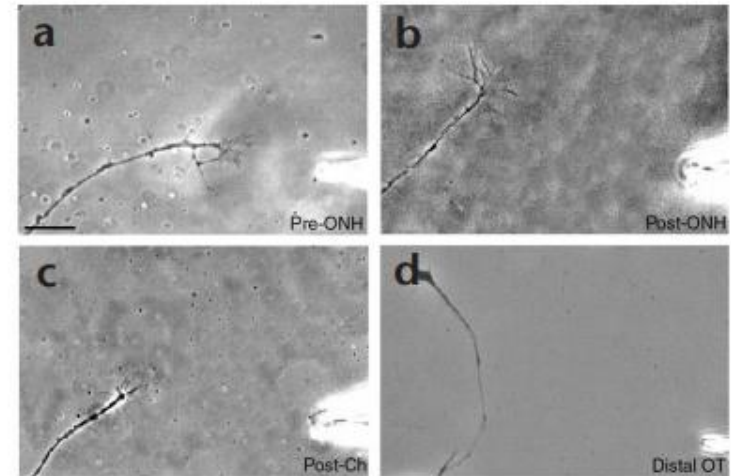
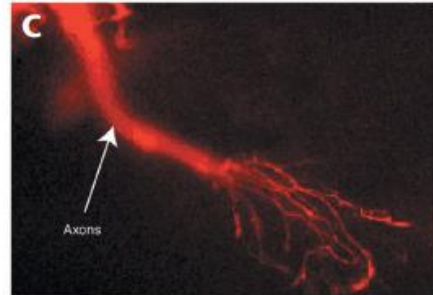
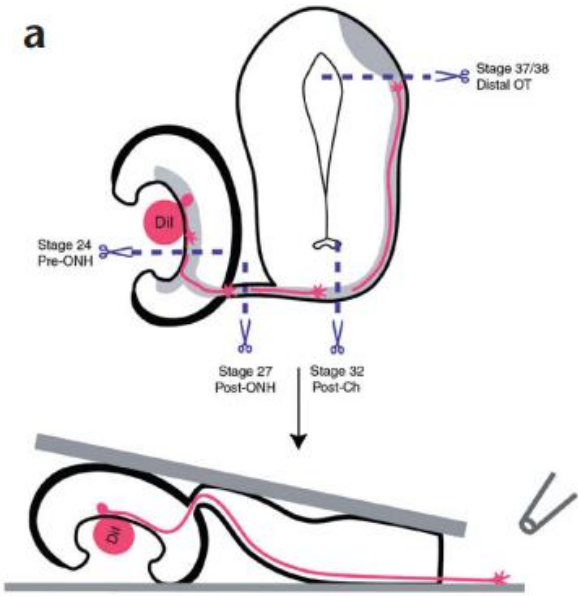
# El reloj de la neurona

Shewan et al., 2002



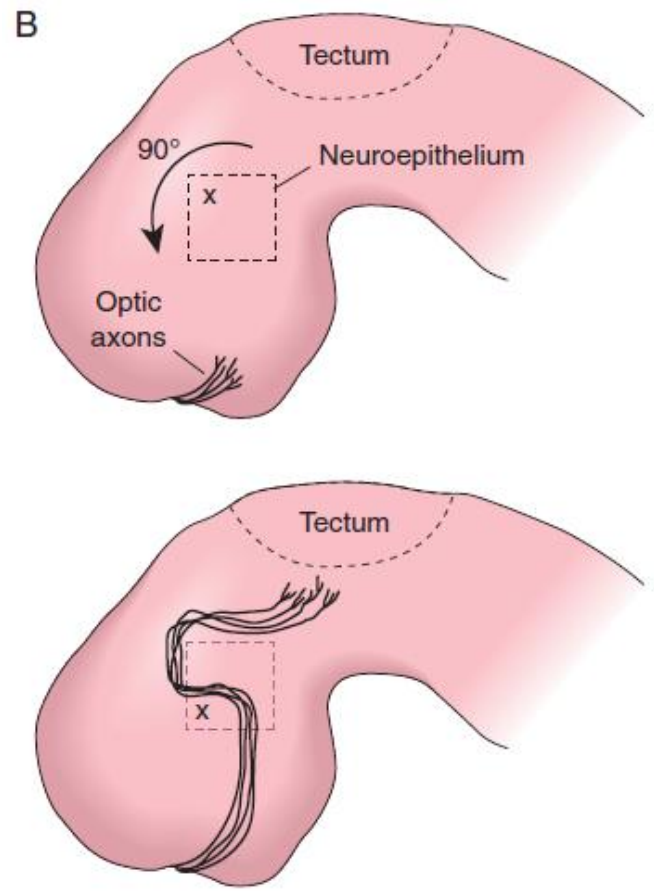
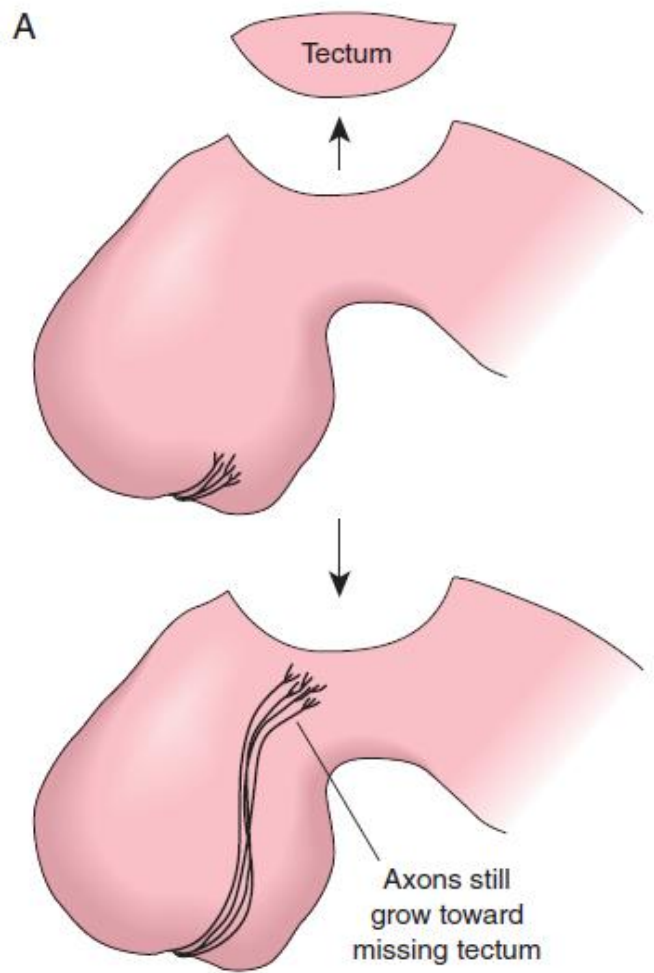
# El reloj de la neurona

Shewan et al., 2002



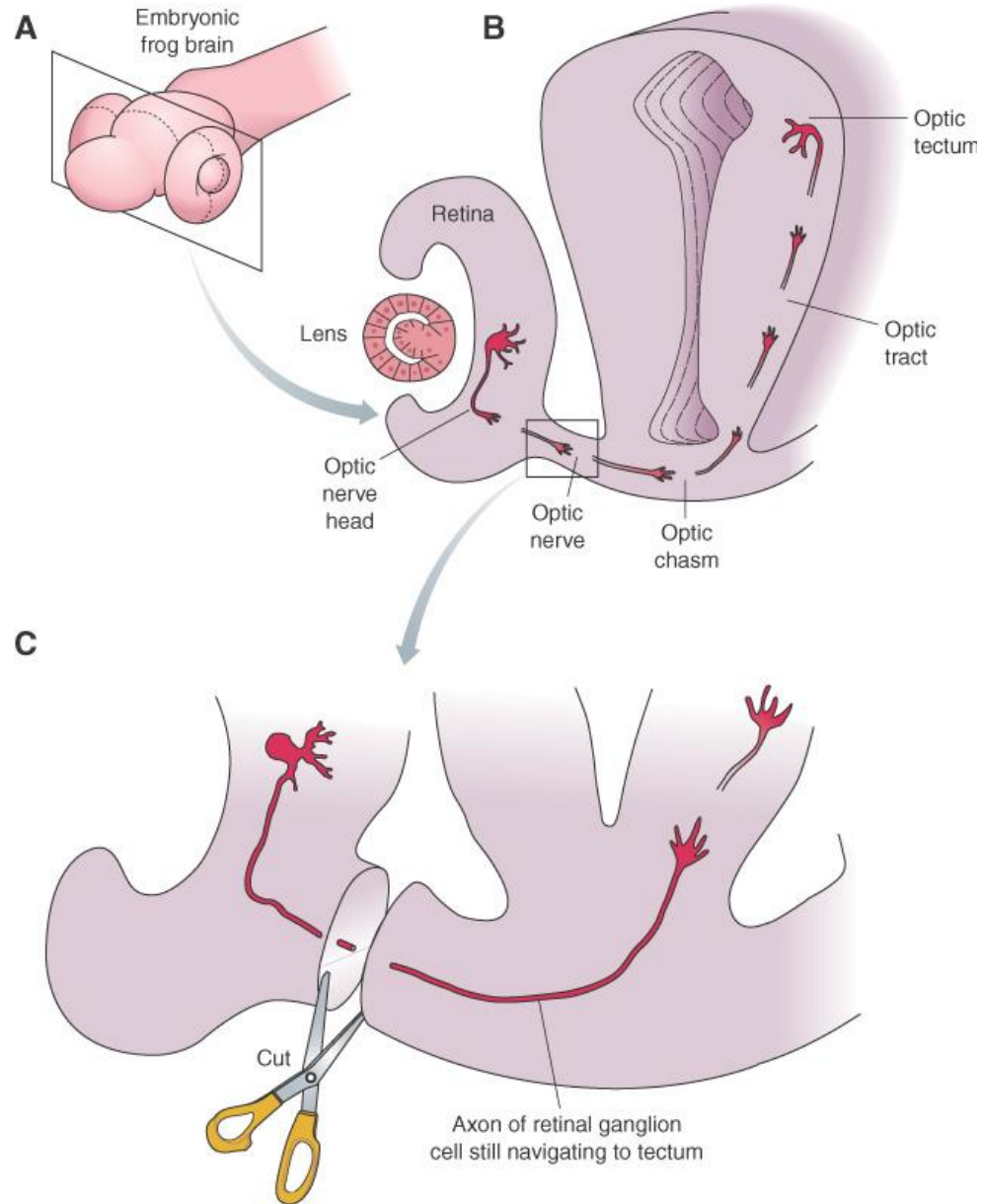
El cono de crecimiento se guía por las señales que tiene en el momento

# El reloj de la neurona

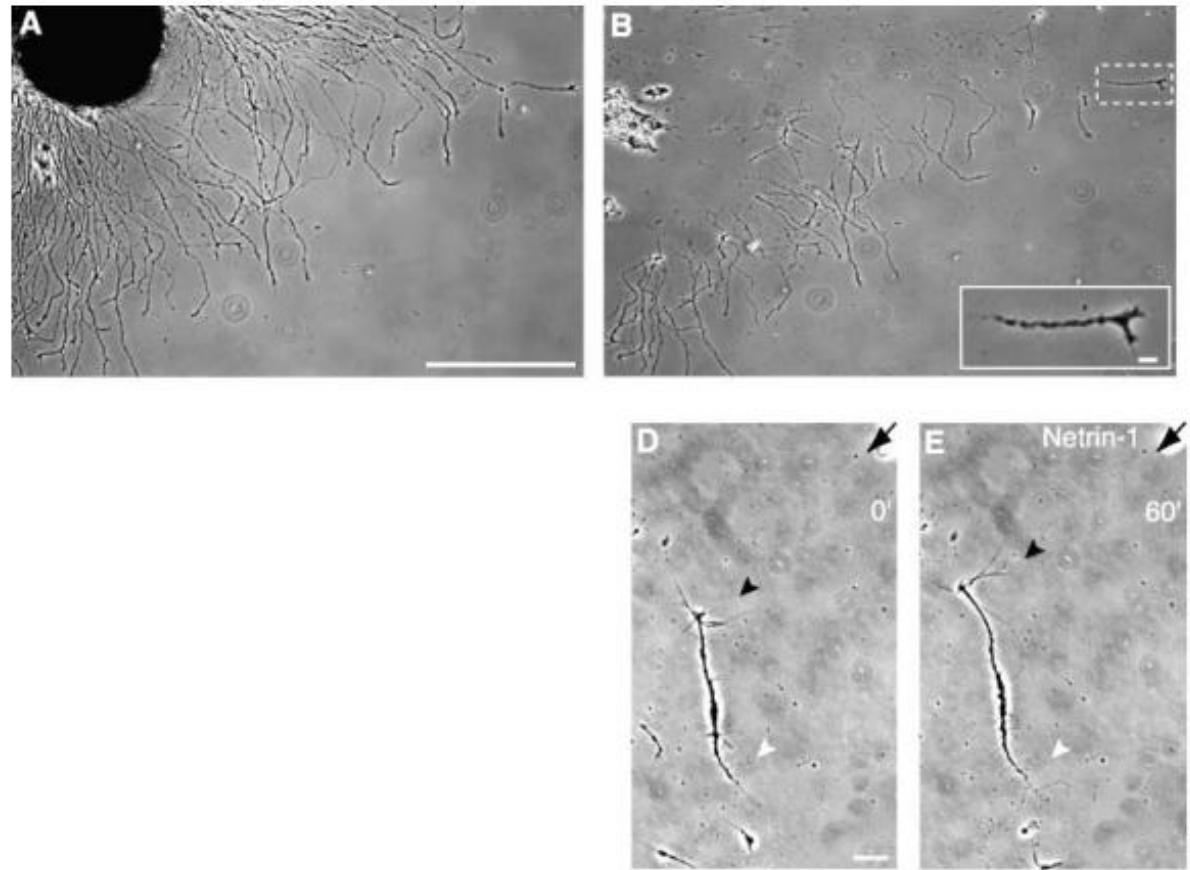


El cono de crecimiento se guía por las señales que tiene en el momento

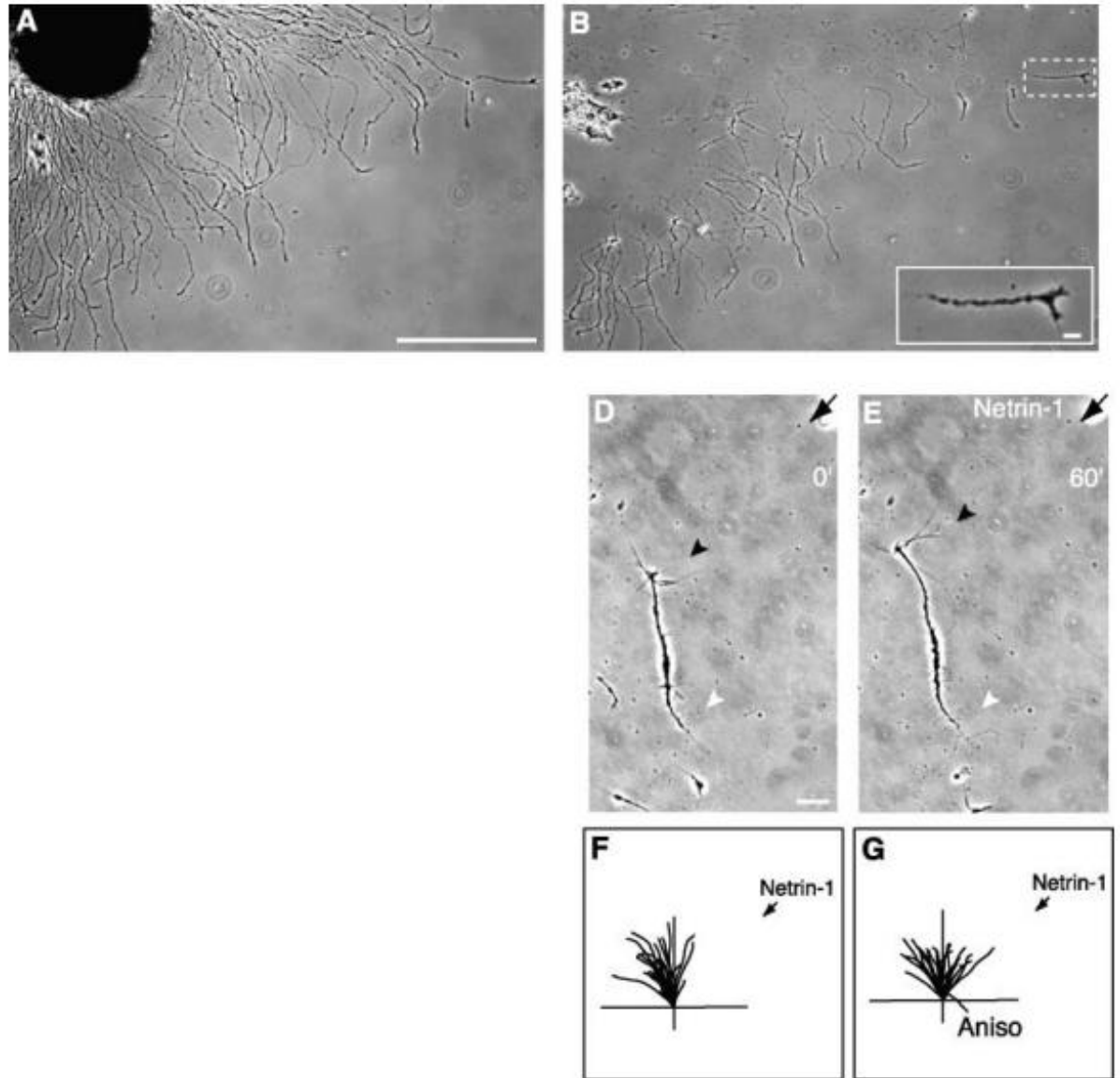
# La independencia del cono



# Síntesis local de proteínas



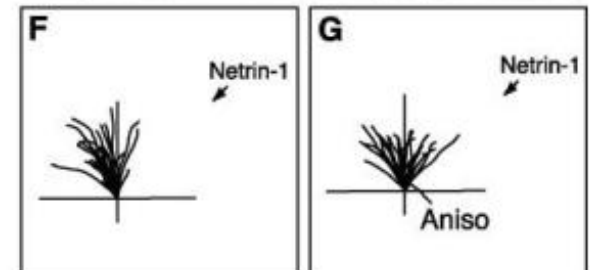
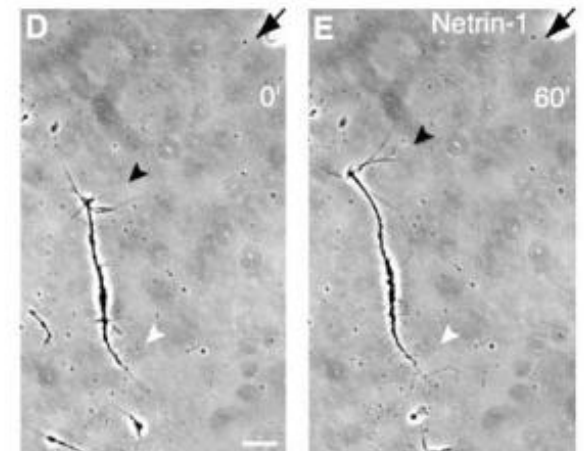
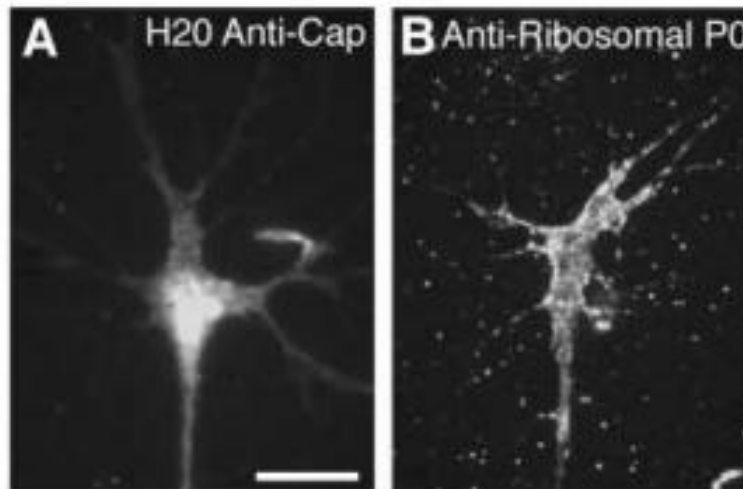
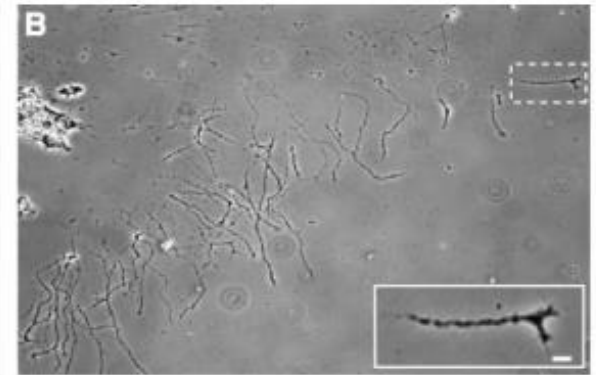
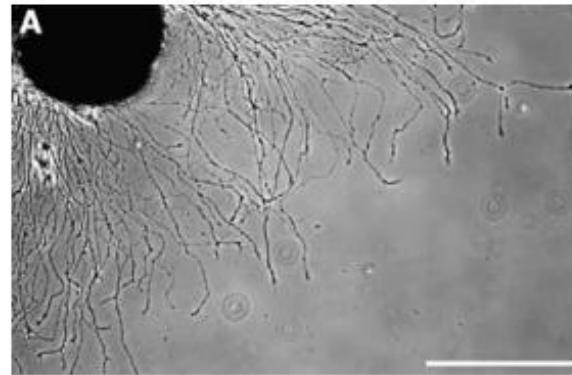
# Síntesis local de proteínas





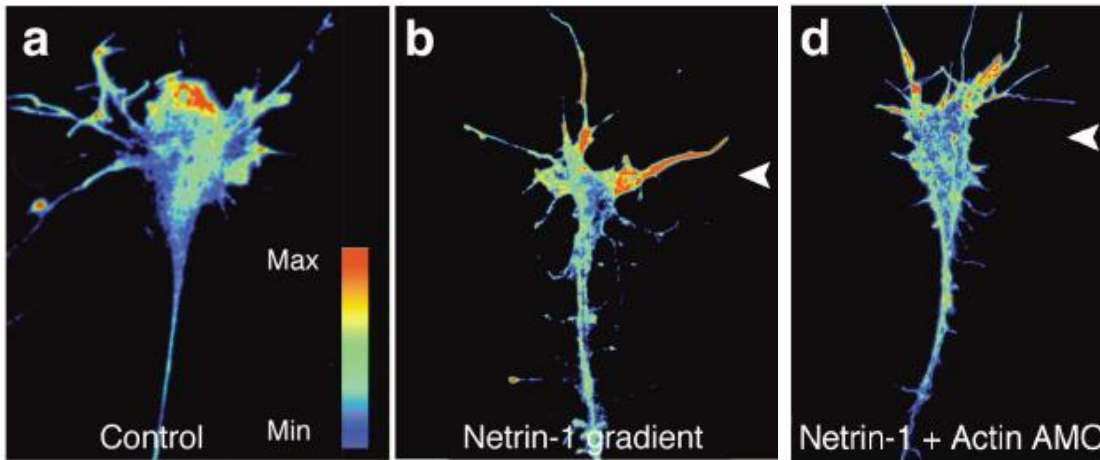
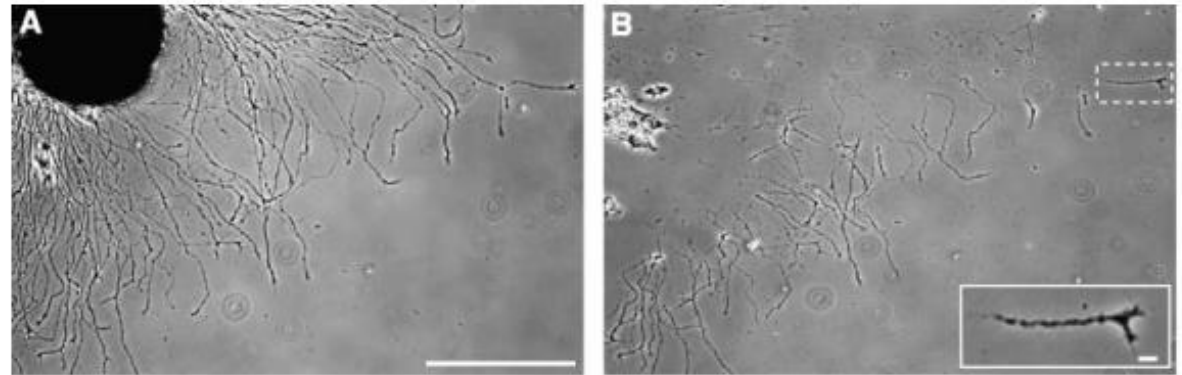
# Síntesis local de proteínas

El estímulo induce la síntesis local de proteínas

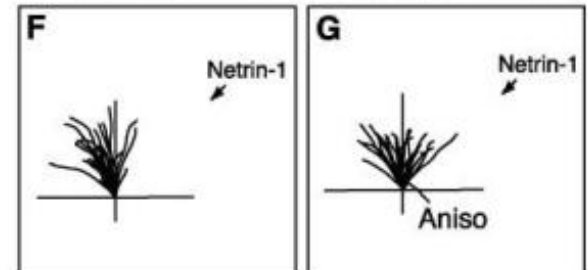
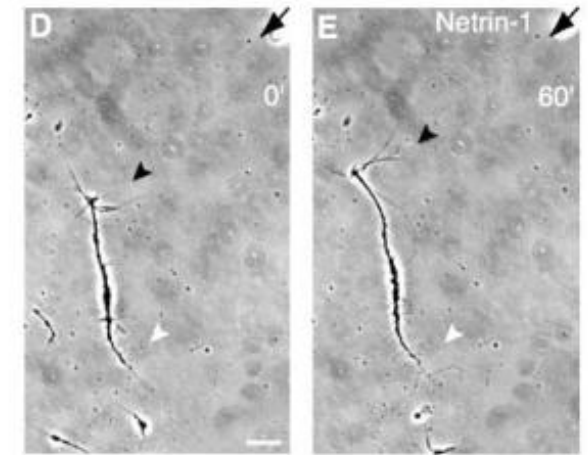


# Síntesis local de proteínas

El estímulo induce la síntesis local de proteínas

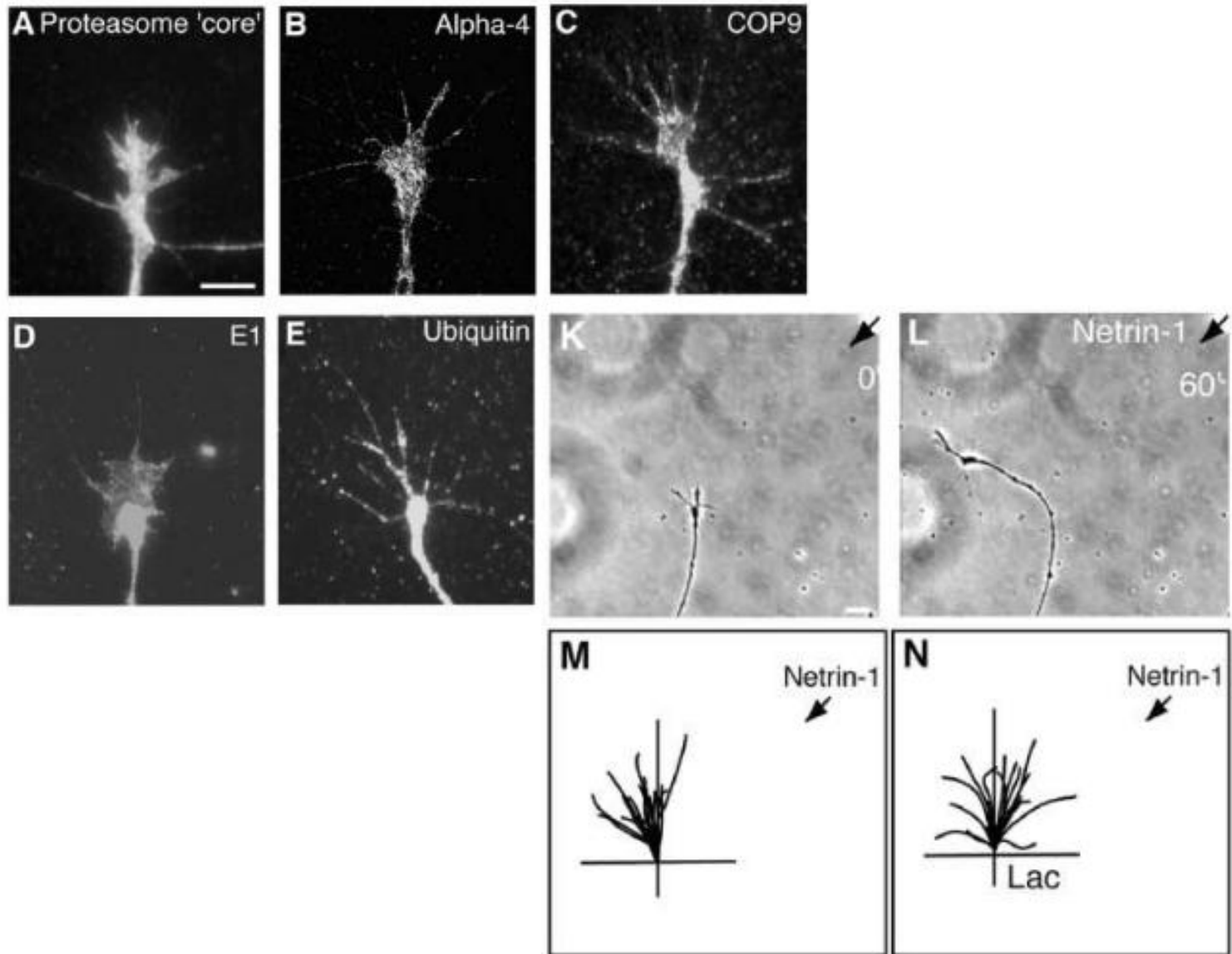


Leung et al., 2006

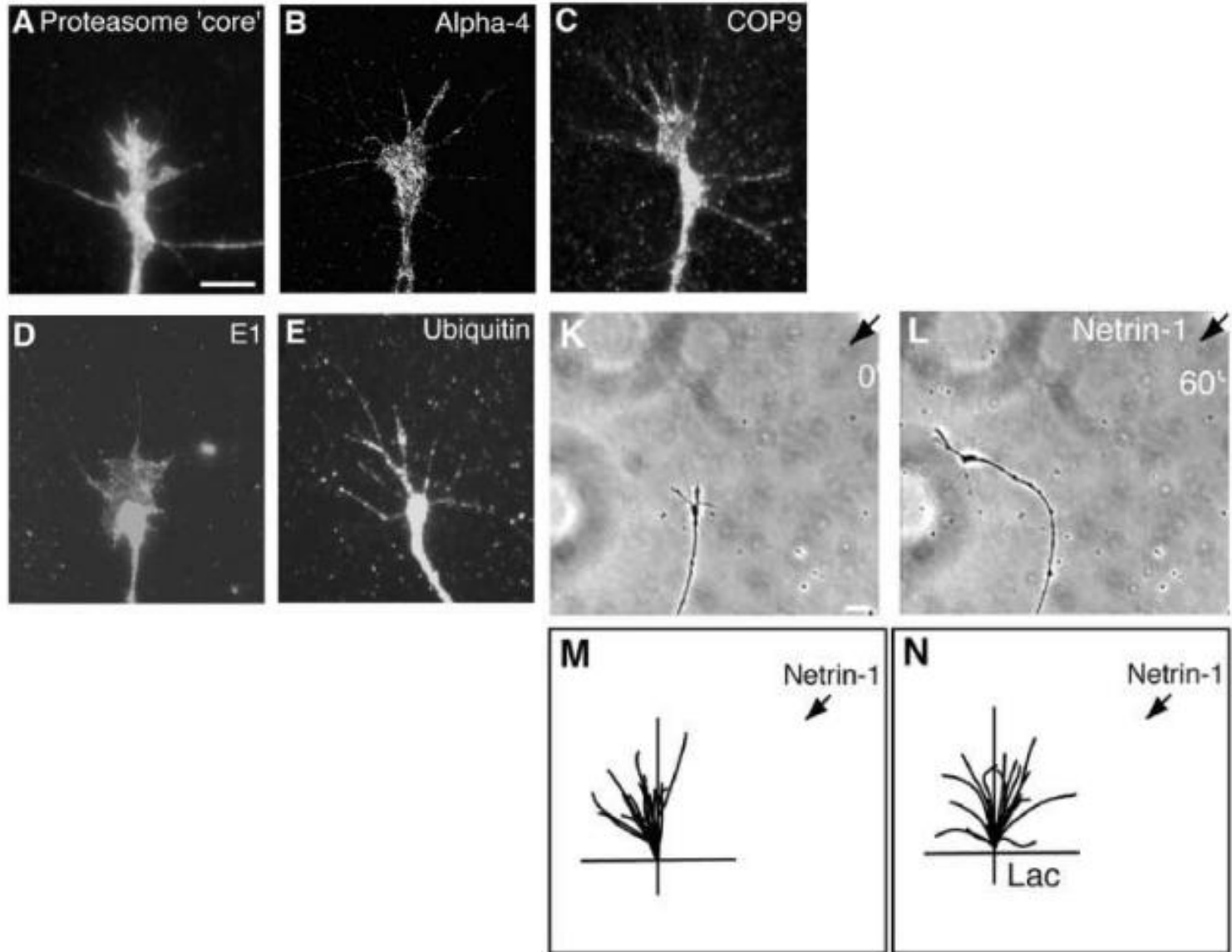


Campbell & Holt, 2001

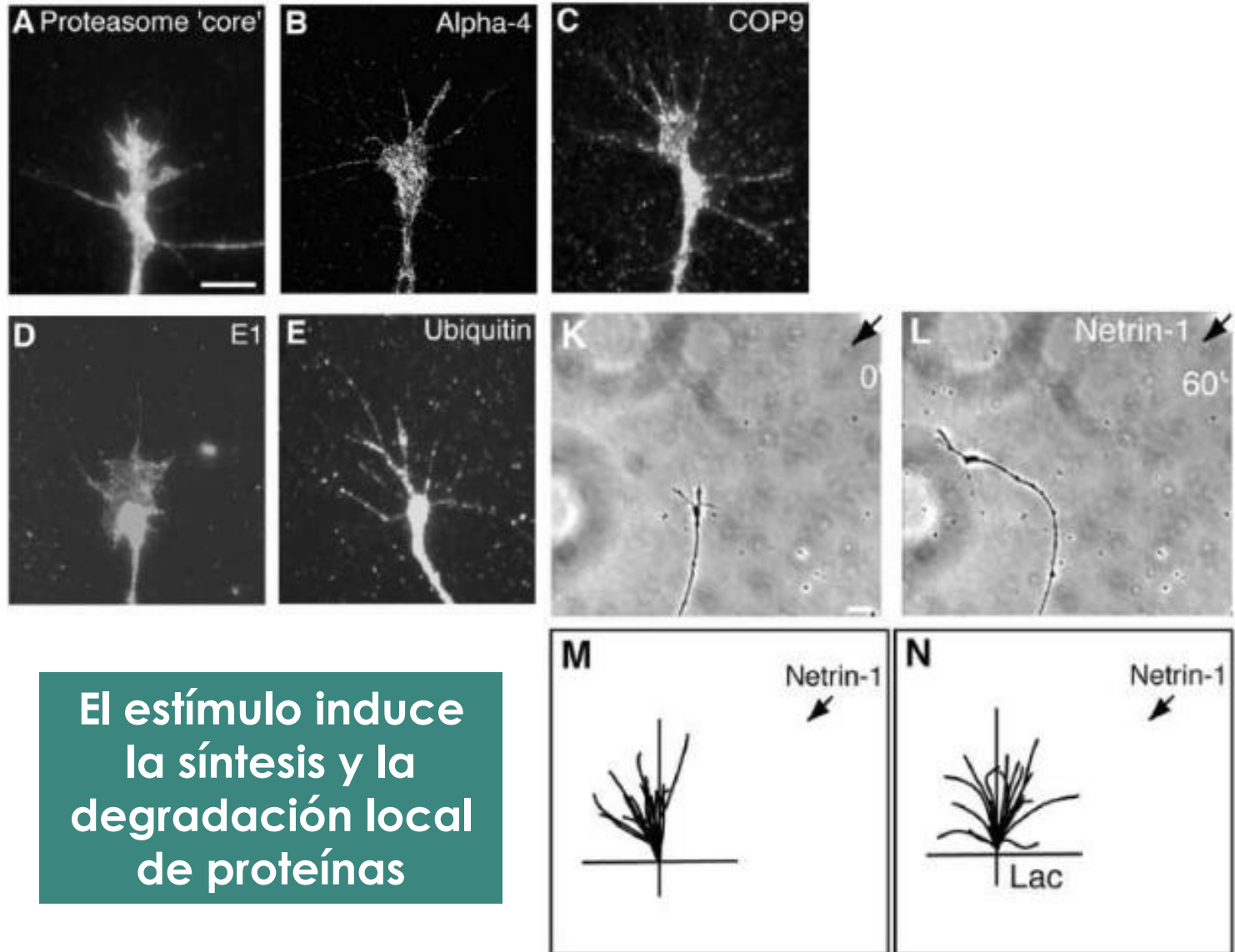
# Síntesis local de proteínas y degradación



# Síntesis local de proteínas y degradación

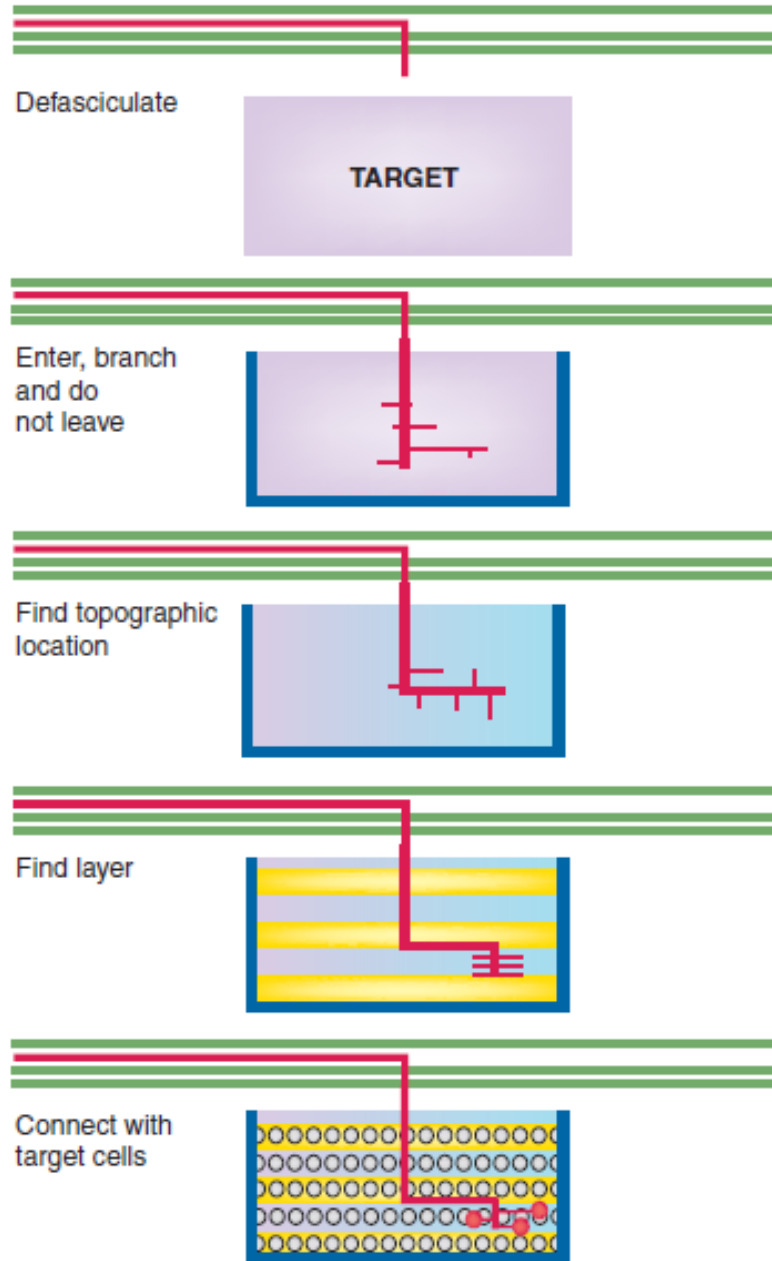


# Síntesis local de proteínas y degradación

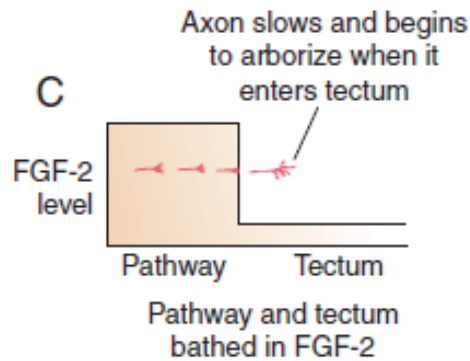
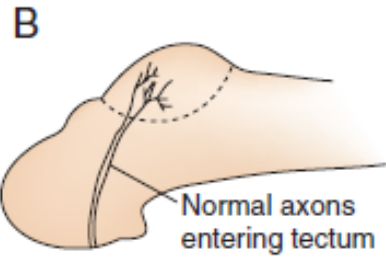
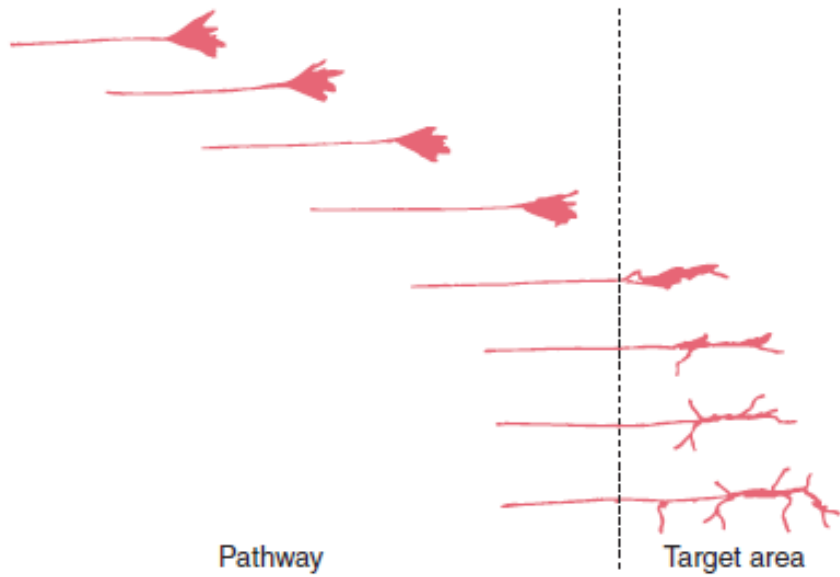


El estímulo induce  
la síntesis y la  
degradación local  
de proteínas

# Inervación del blanco

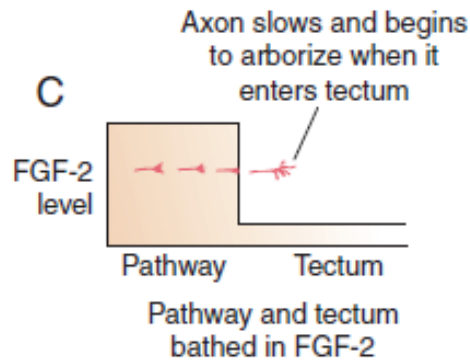
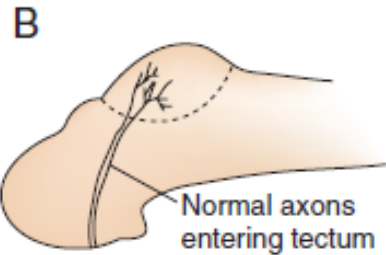
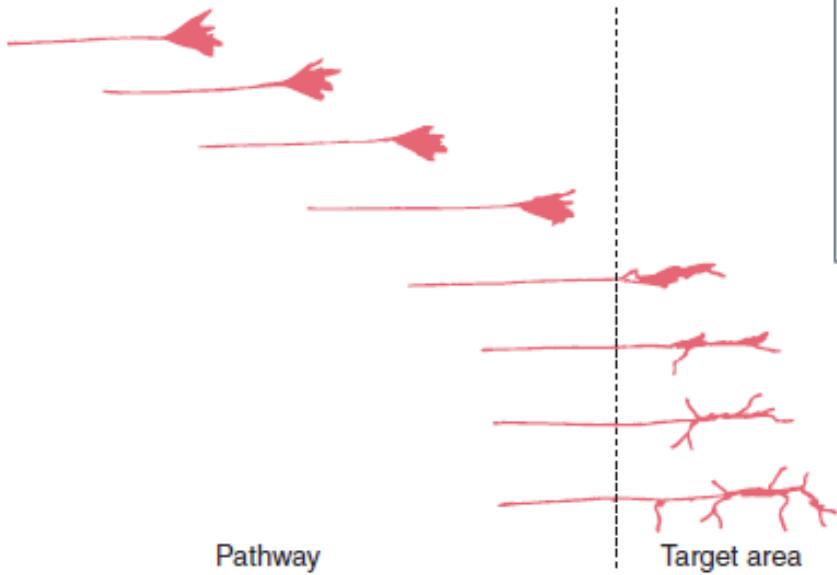
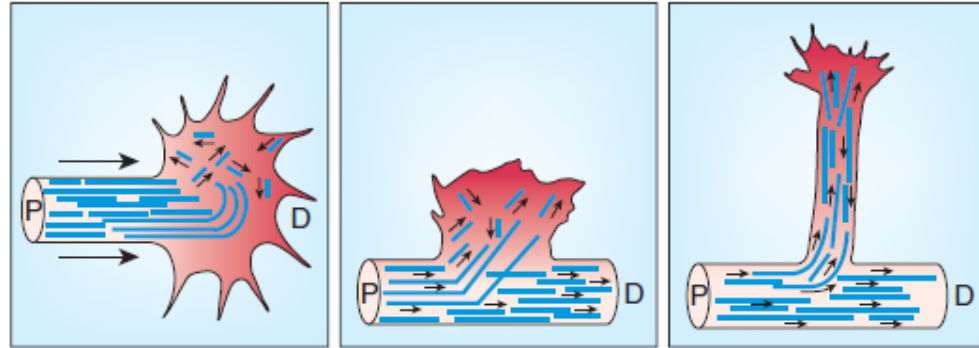


# Inervación del blanco



# Inervación del blanco

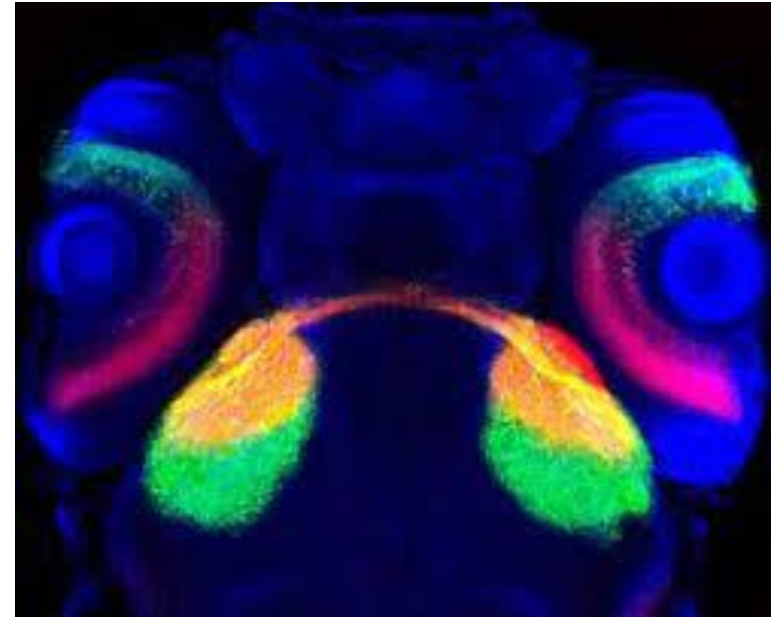
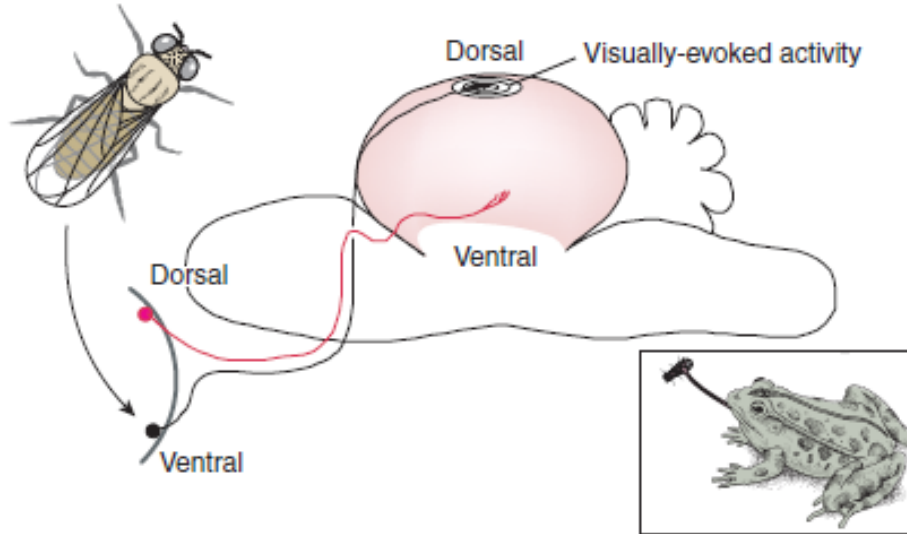
A Pausing growth cone B Developing branch C Elongating branch



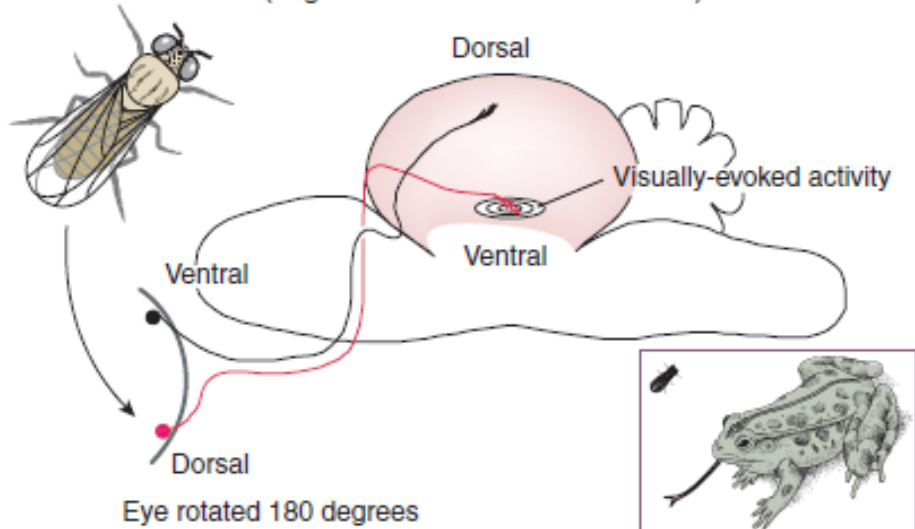


# Mapas topográficos

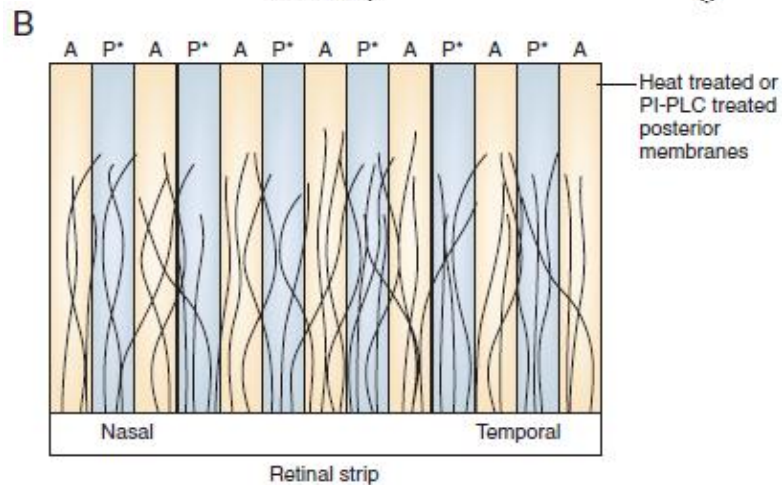
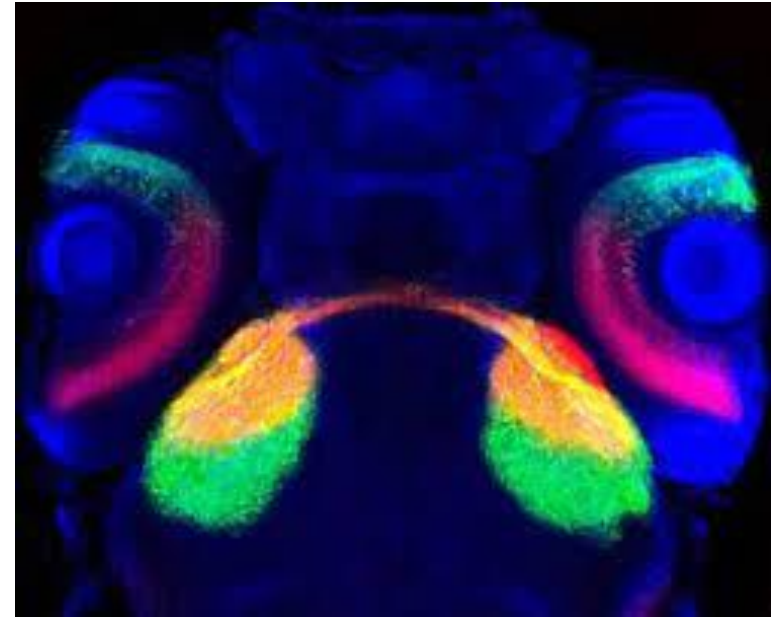
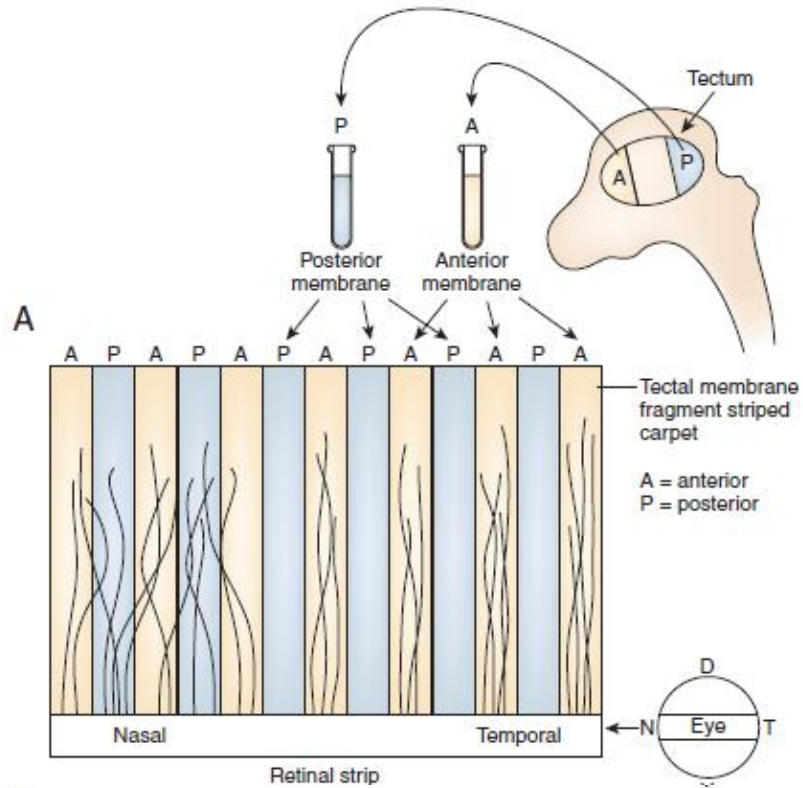
**A** Control: Fly is detected in the top visual field (ventral retina/dorsal tectum)



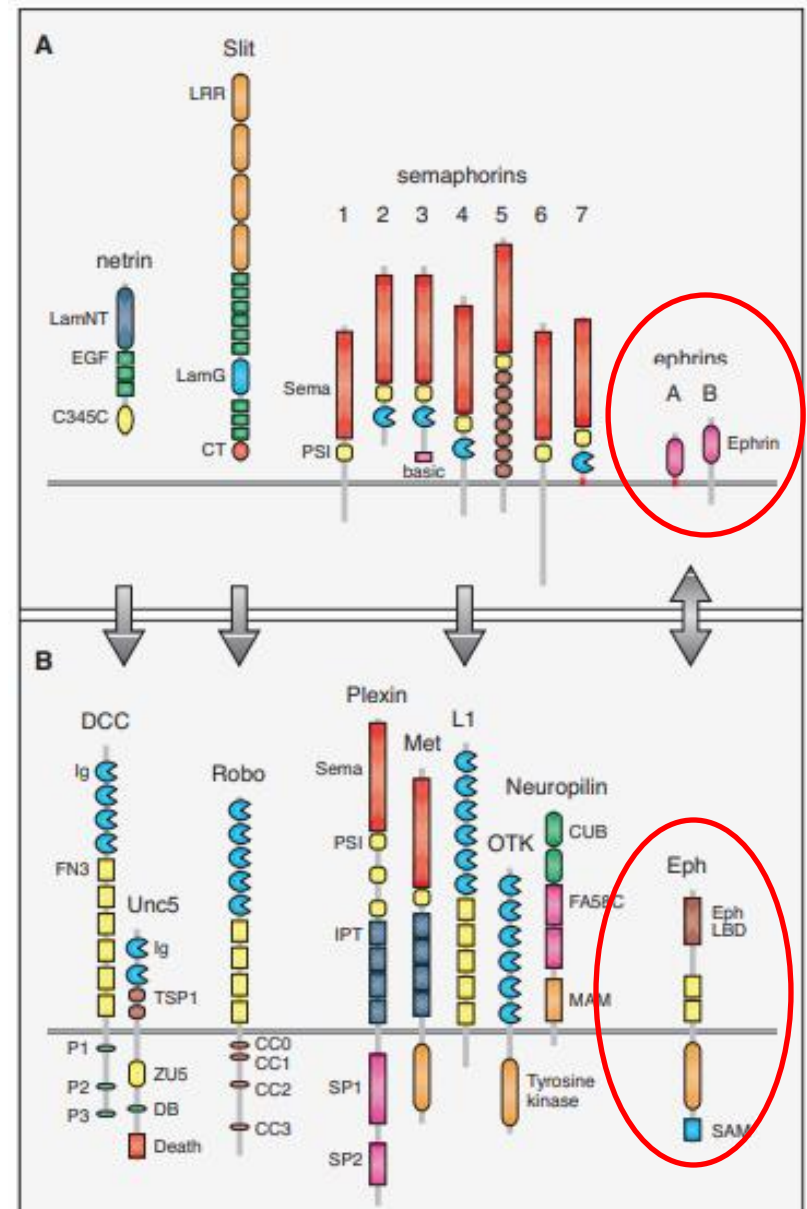
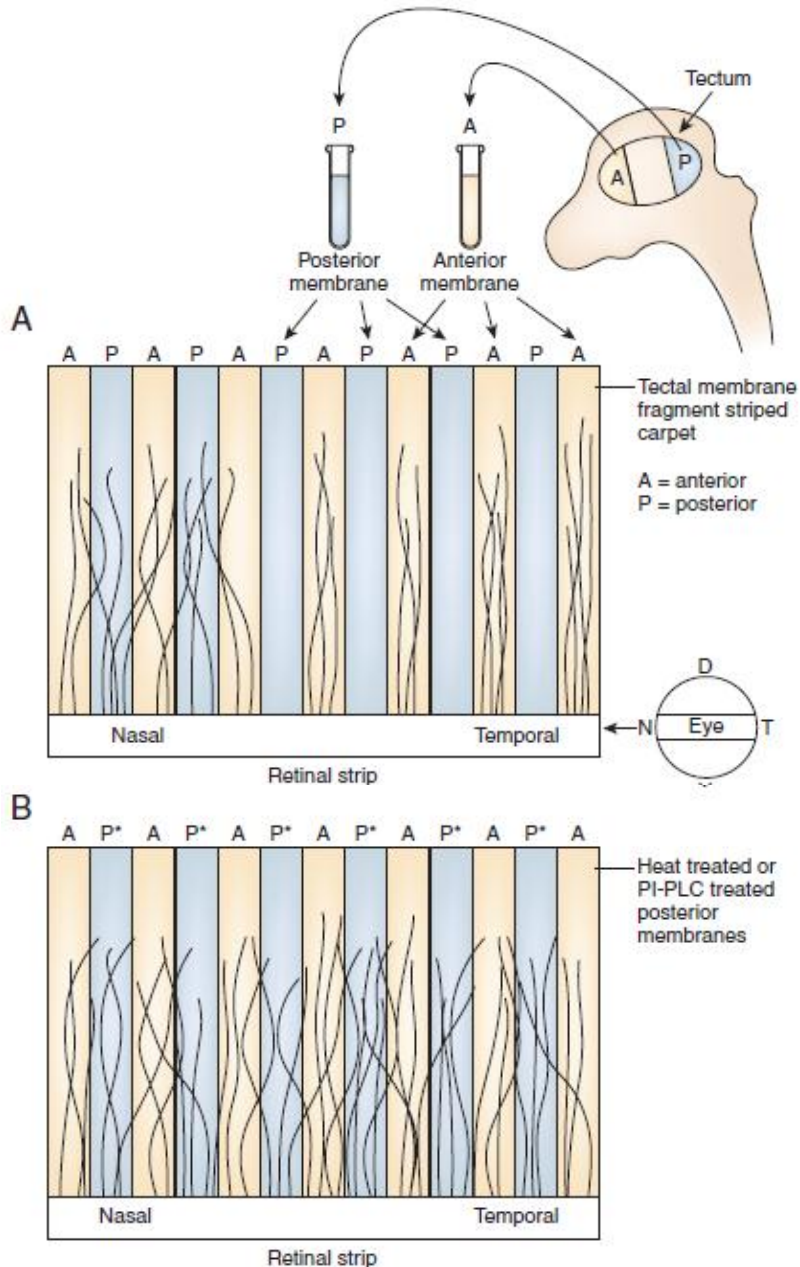
**B** Eye rotation: Fly is detected in the bottom visual field (original dorsal retina/ventral tectum)



# Mapas topográficos

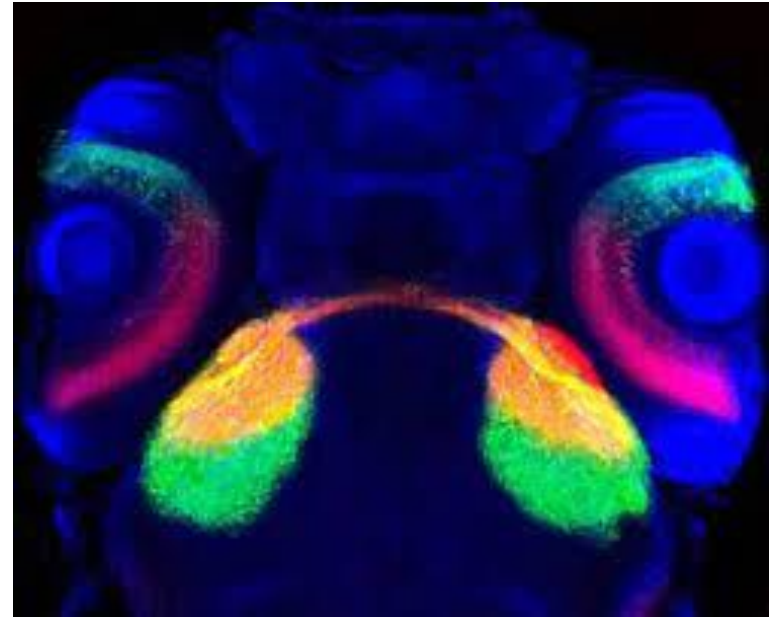
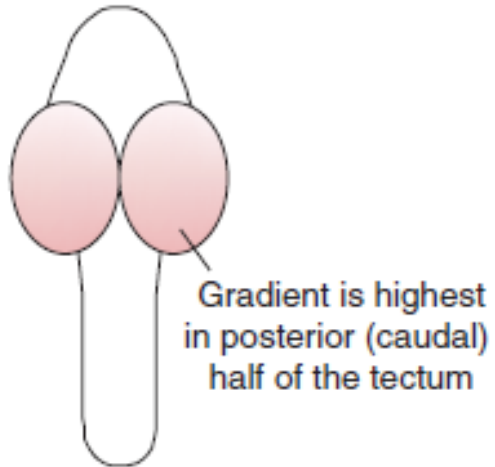


# Mapas topográficos

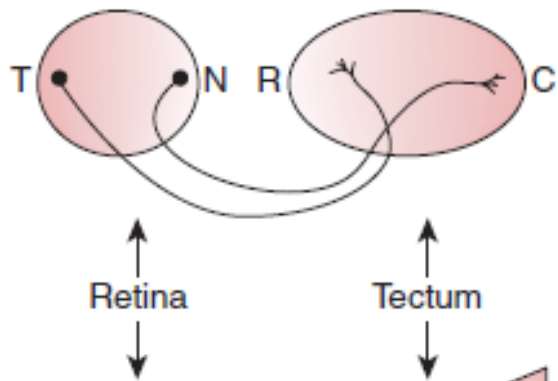


# Mapas topográficos

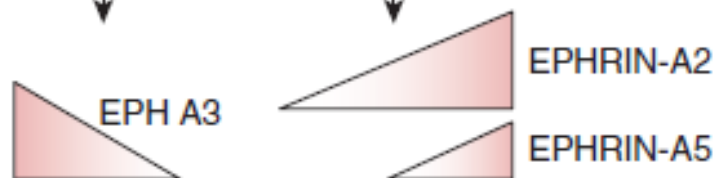
A Rostral to caudal gradient of tectal Ephrin



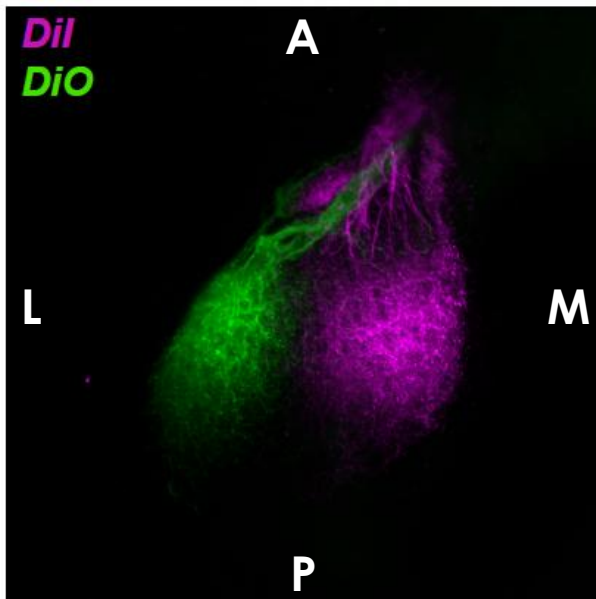
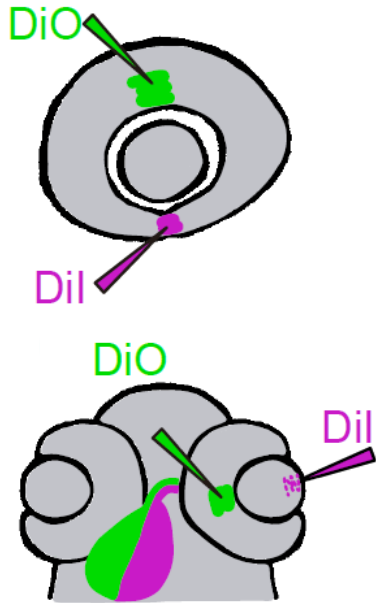
C



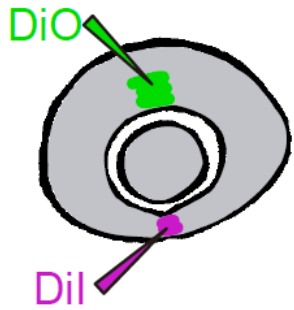
D



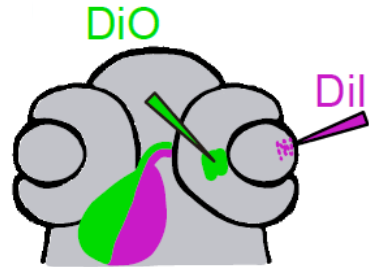
# Mapas topográficos



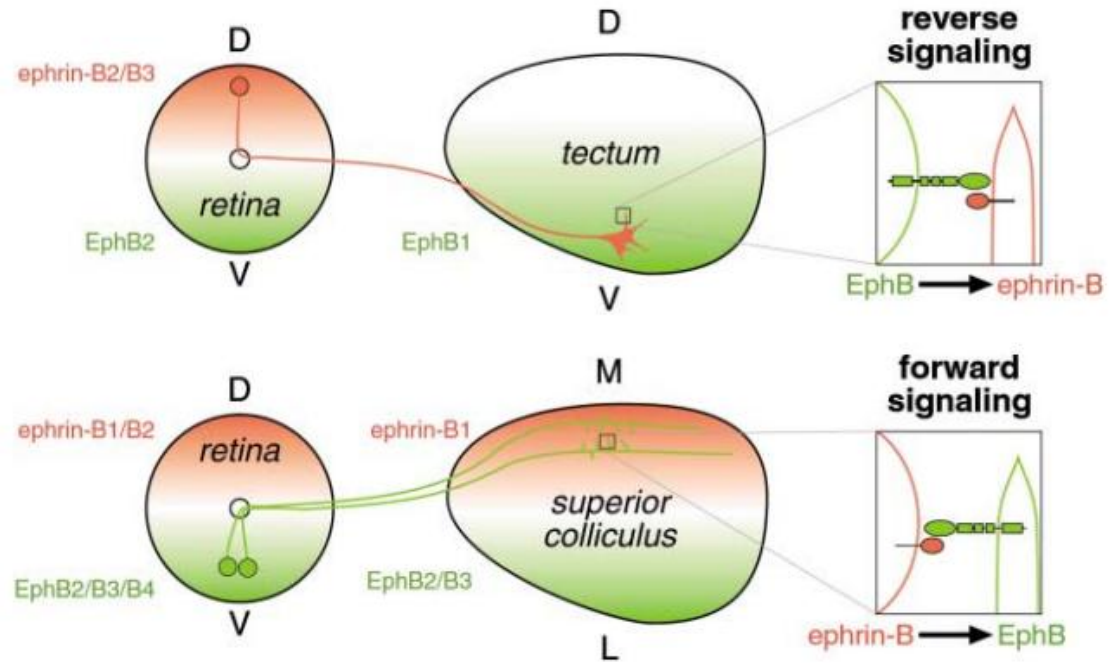
# Mapas topográficos



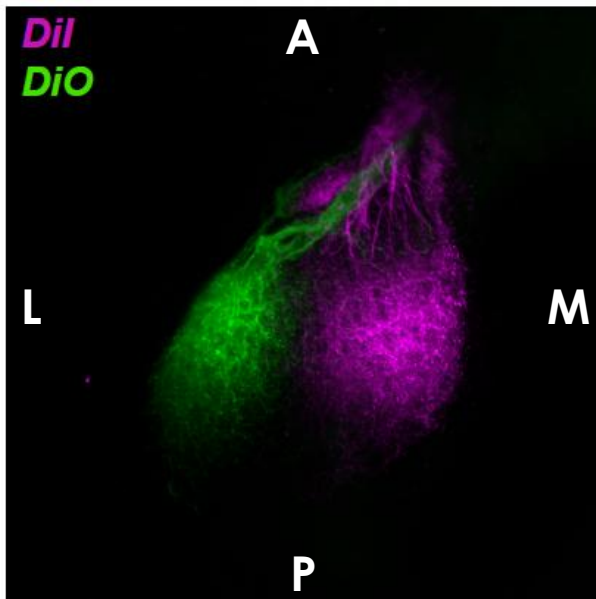
*Xenopus*



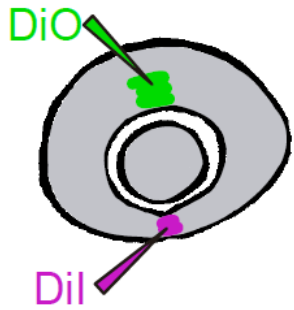
mouse



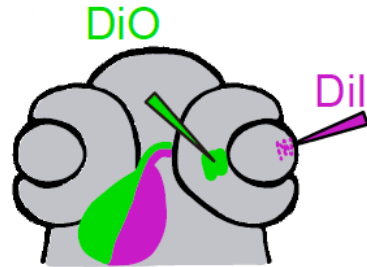
Pittman & Chien, 2002



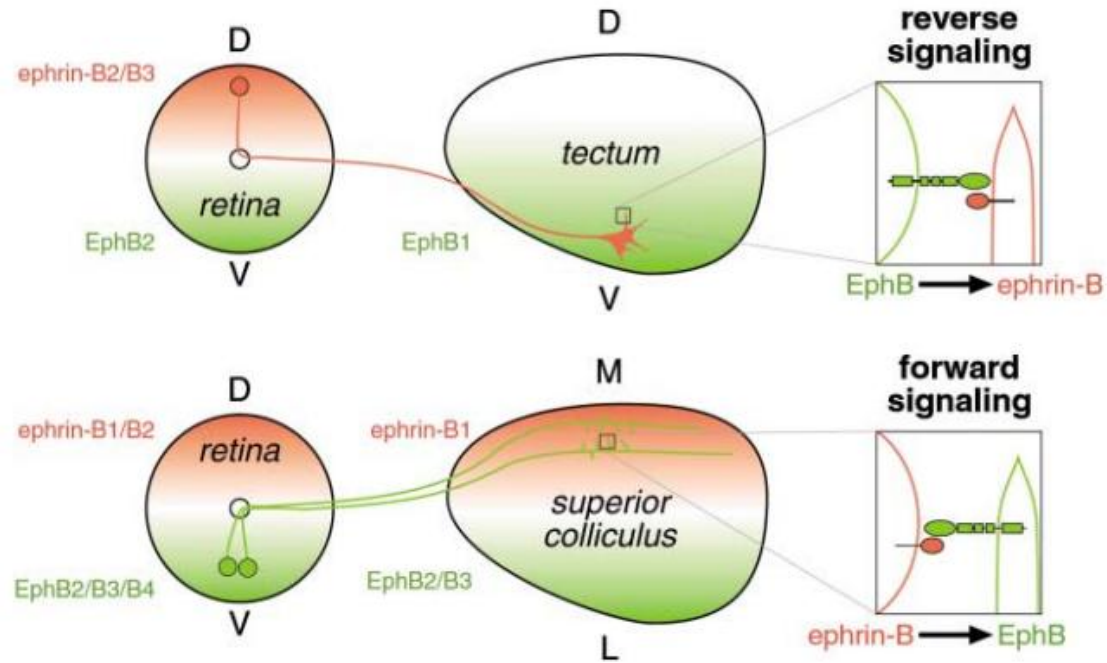
# Mapas topográficos



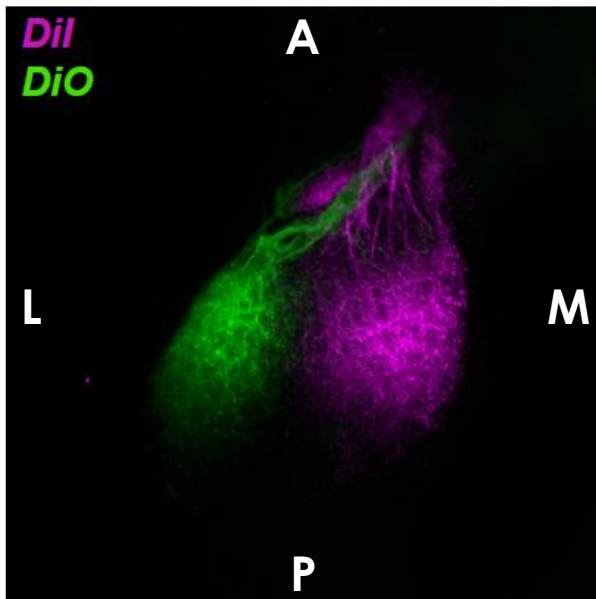
*Xenopus*



mouse

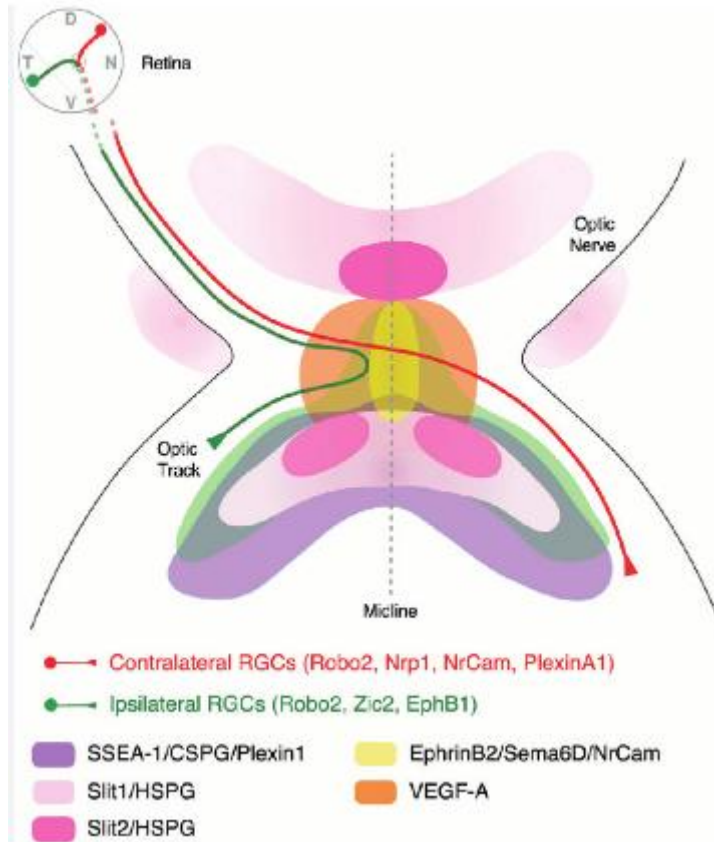


Pittman & Chien, 2002



Un gradiente de Efrinas en el tectum que permite la formación de los mapas retinotópicos

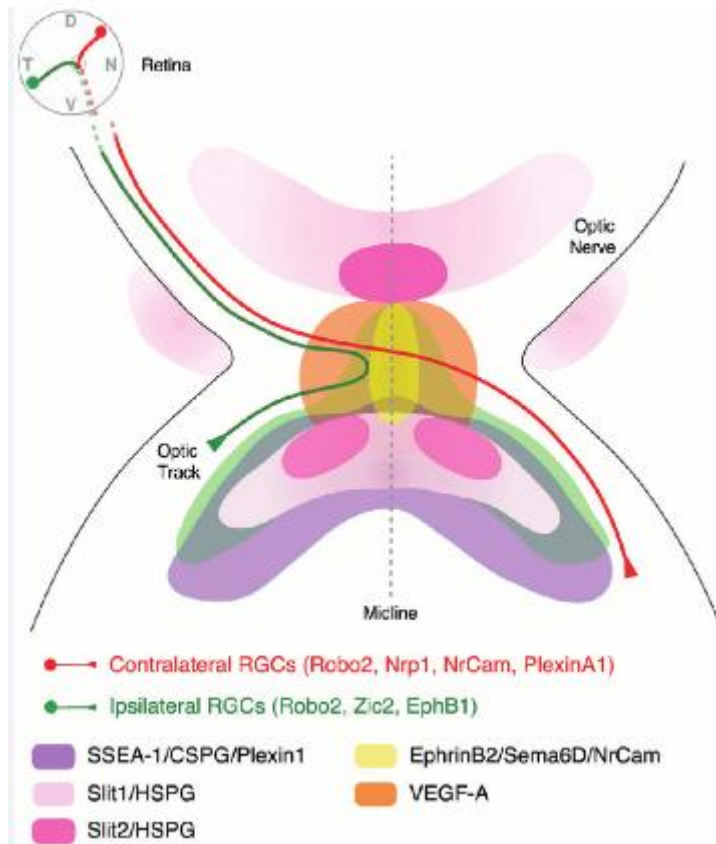
# Proyecciones ipsilaterales



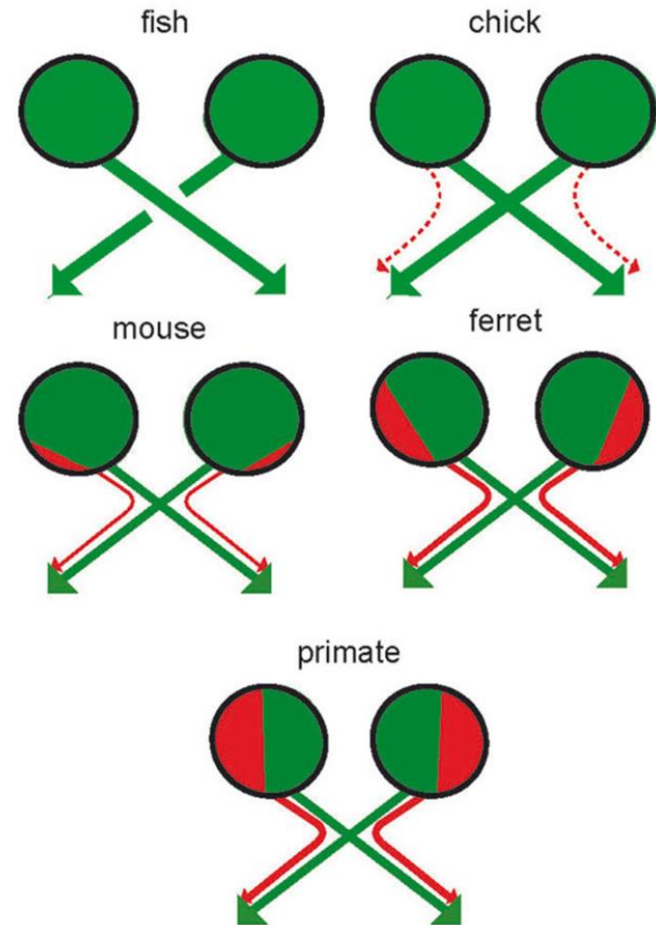
Erskine & Herrera, 2014



# Proyecciones ipsilaterales



Erskine & Herrera, 2014



— contralateral projection

— ipsilateral projection

Larsson, 2015

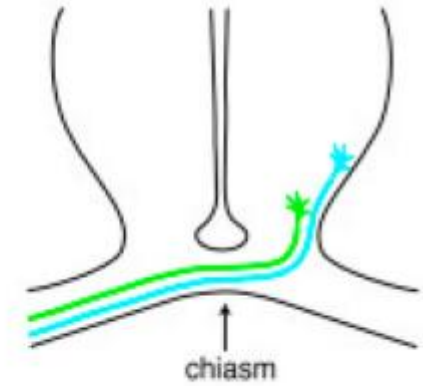
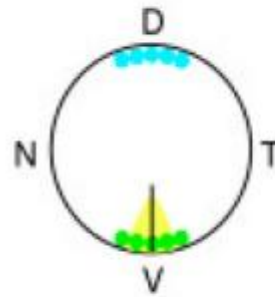
# Proyecciones ipsilaterales



# Proyecciones ipsilaterales



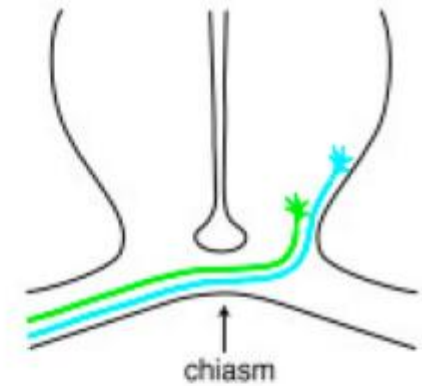
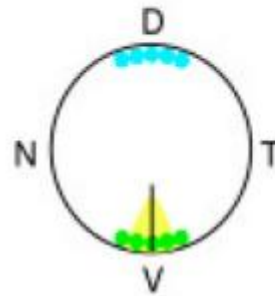
PRE-METAMORPHIC TADPOLE



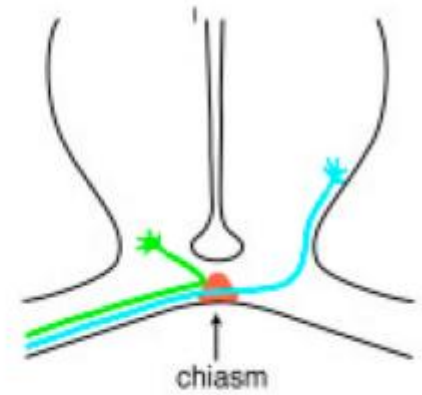
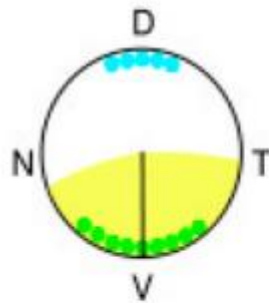
# Proyecciones ipsilaterales



PRE-METAMORPHIC TADPOLE



POST-METAMORPHIC FROGLET



■ EphB receptor

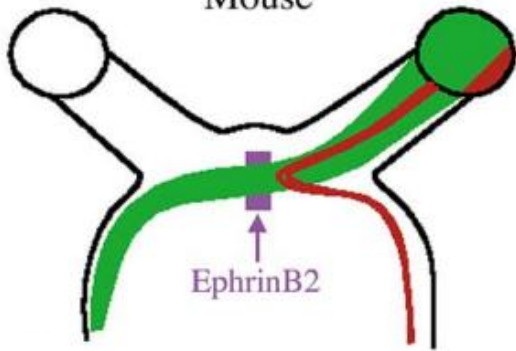
■ ephrin-B

# Proyecciones ipsilaterales

Zebrafish



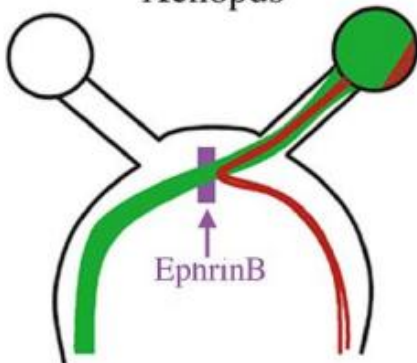
Mouse



EphrinB2

EphrinB

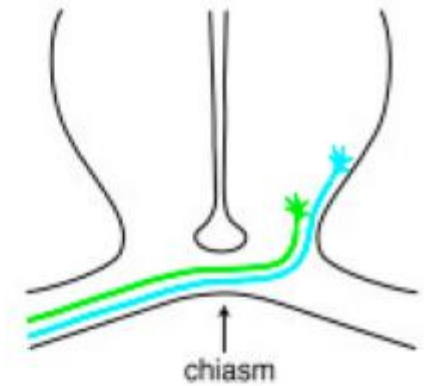
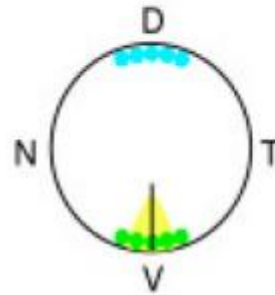
Xenopus



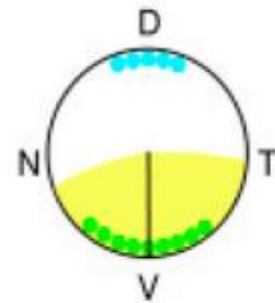
EphrinB

Jeffery & Erskine, 2005

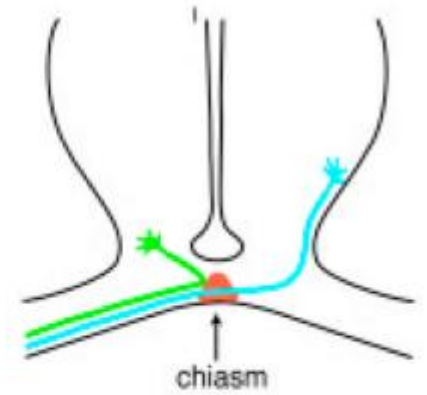
PRE-METAMORPHIC TADPOLE



POST-METAMORPHIC FROGLET



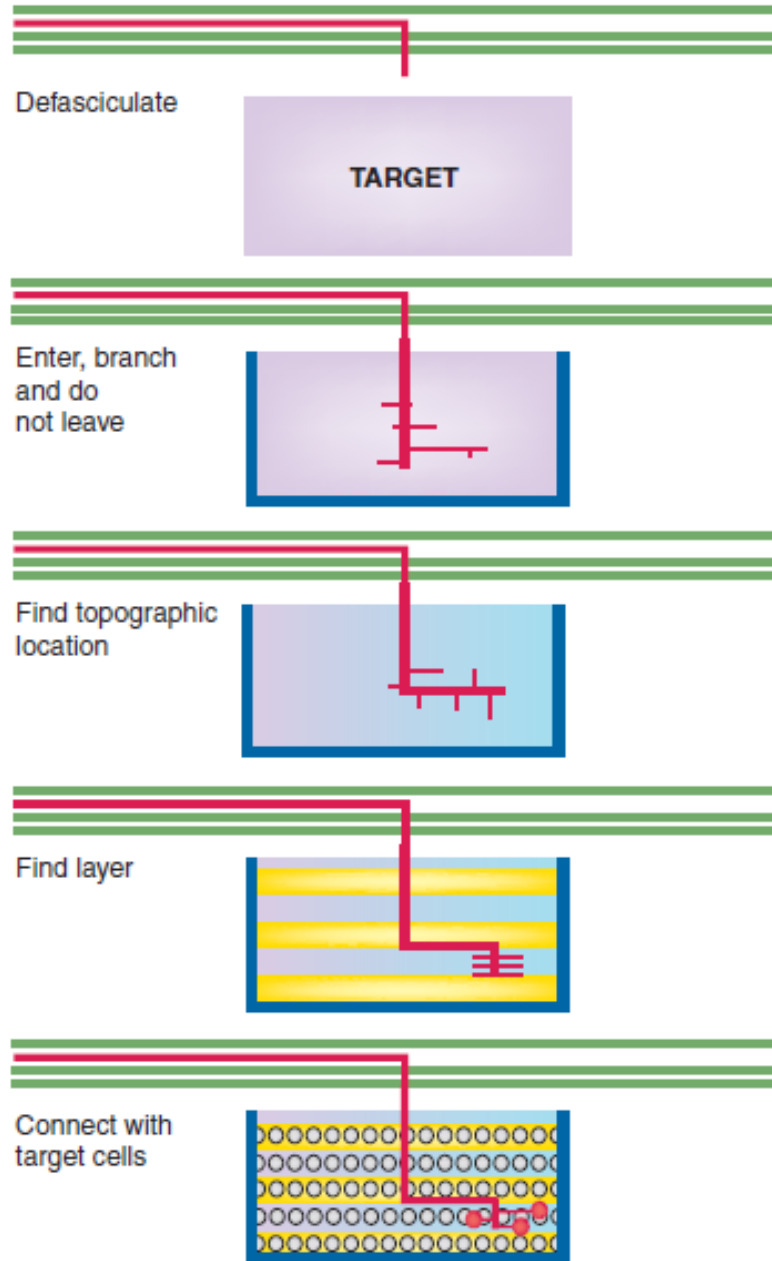
EphB receptor



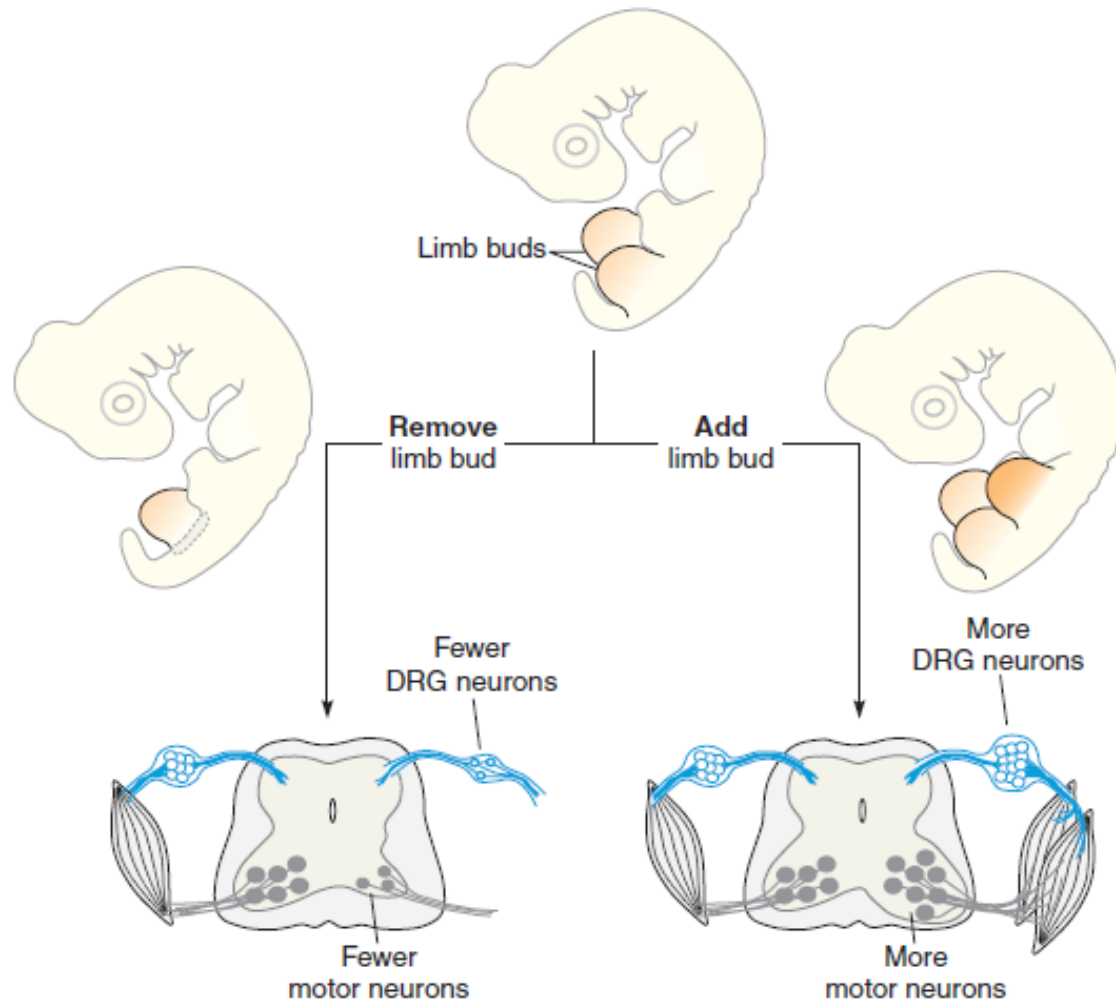
ephrin-B

Mann et al., 2004

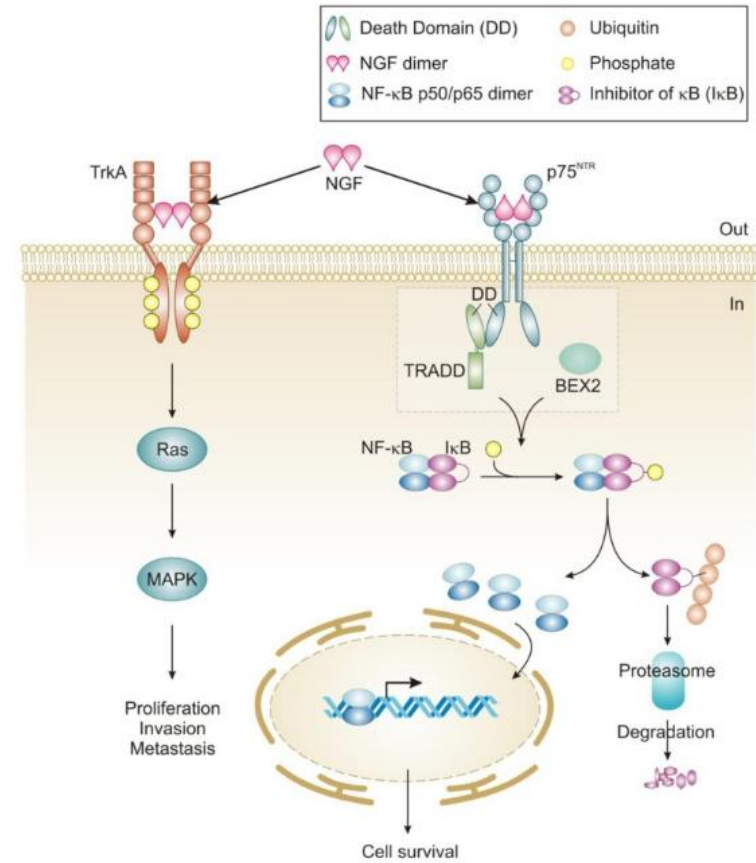
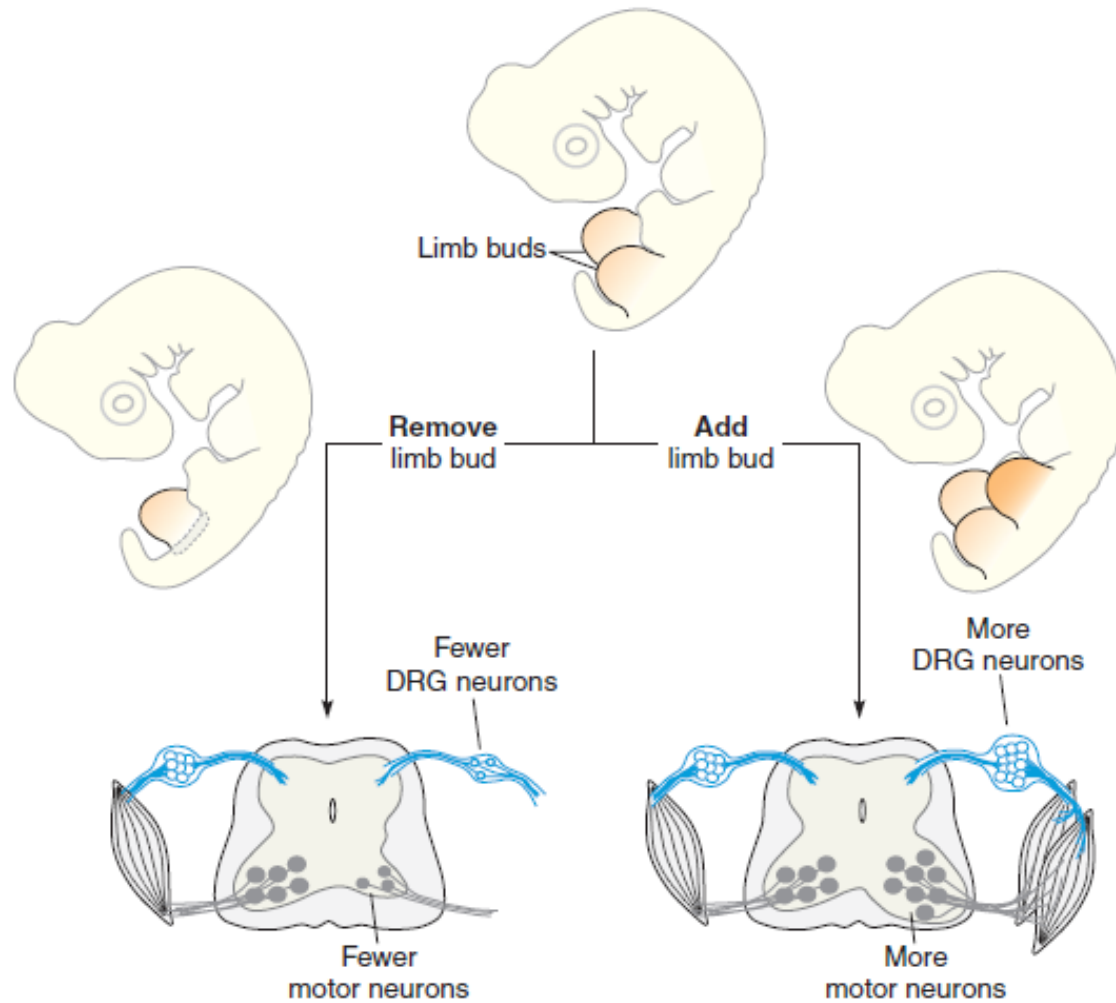
# Inervación del blanco



# Factores de supervivencia



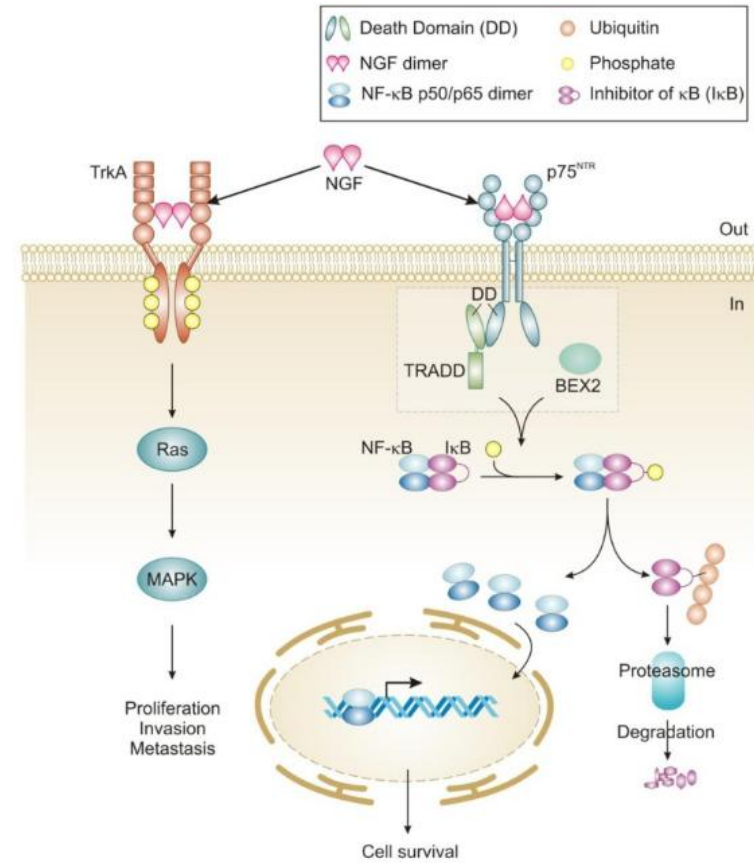
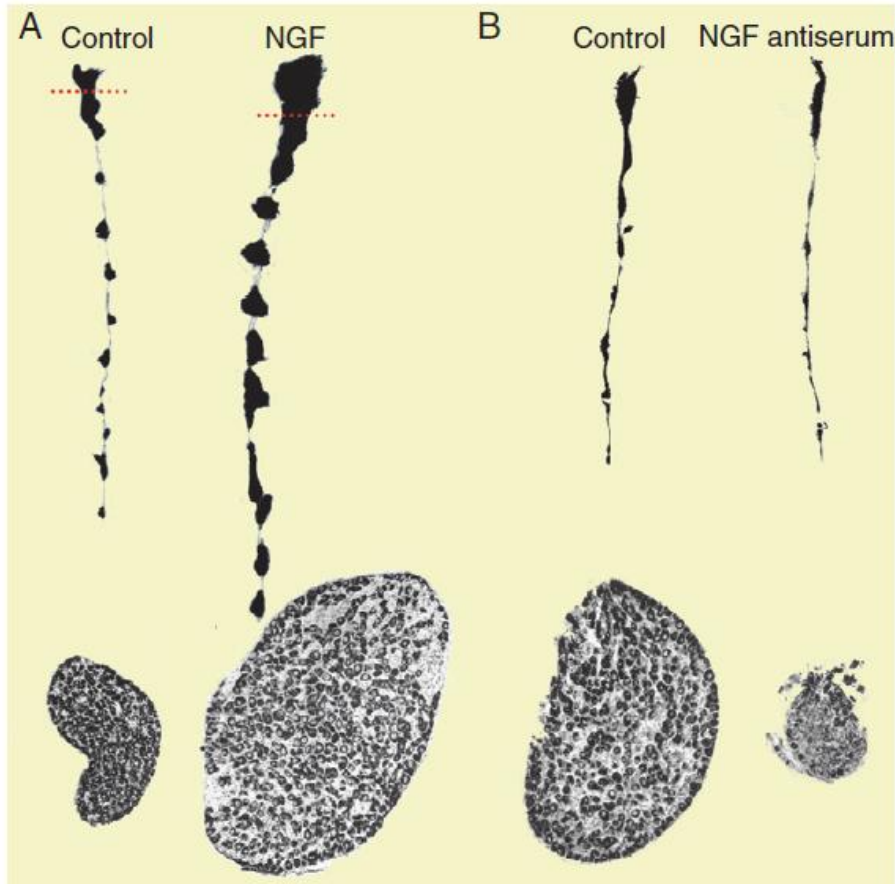
# Factores de supervivencia



Molloy et al., 2011

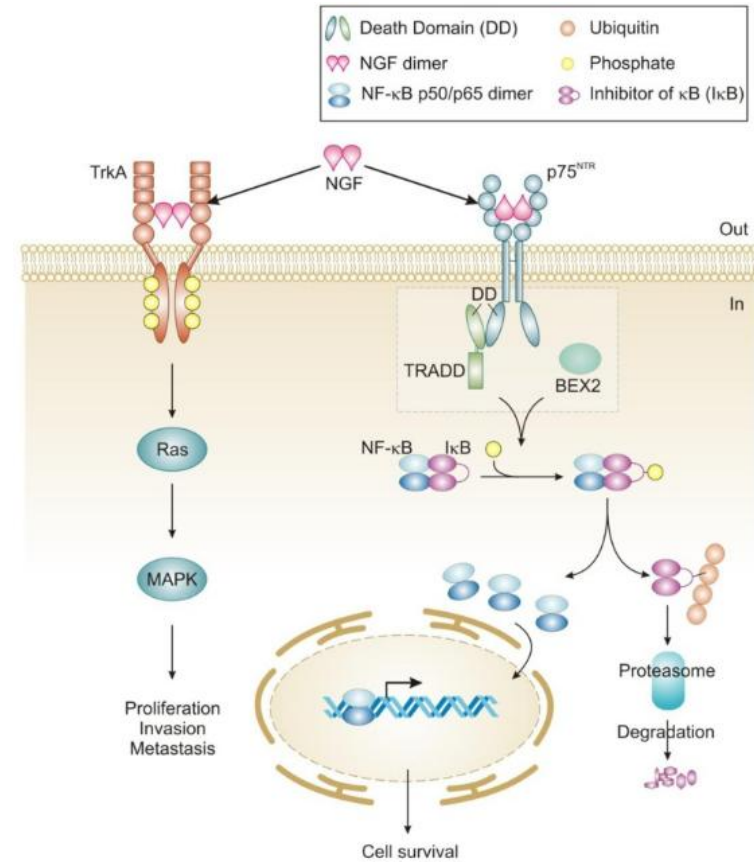
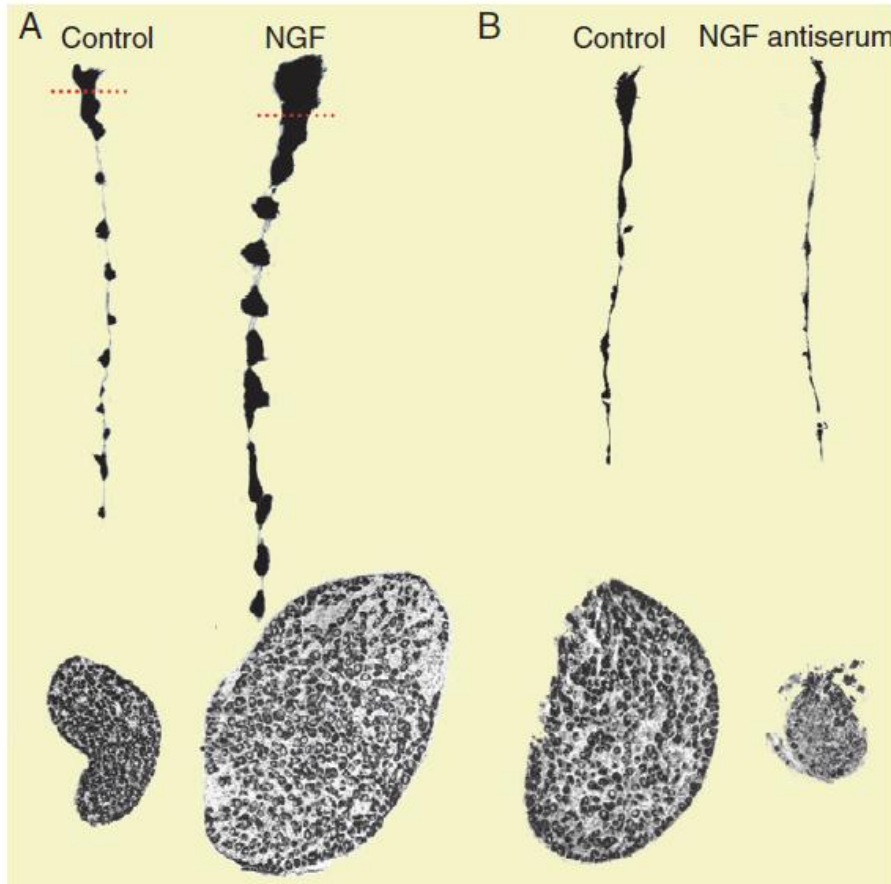


# Factores de supervivencia



Molloy et al., 2011

# Factores de supervivencia



Molloy et al., 2011

La neurona precisa recibir señales tróficas del tejido blanco para sobrevivir