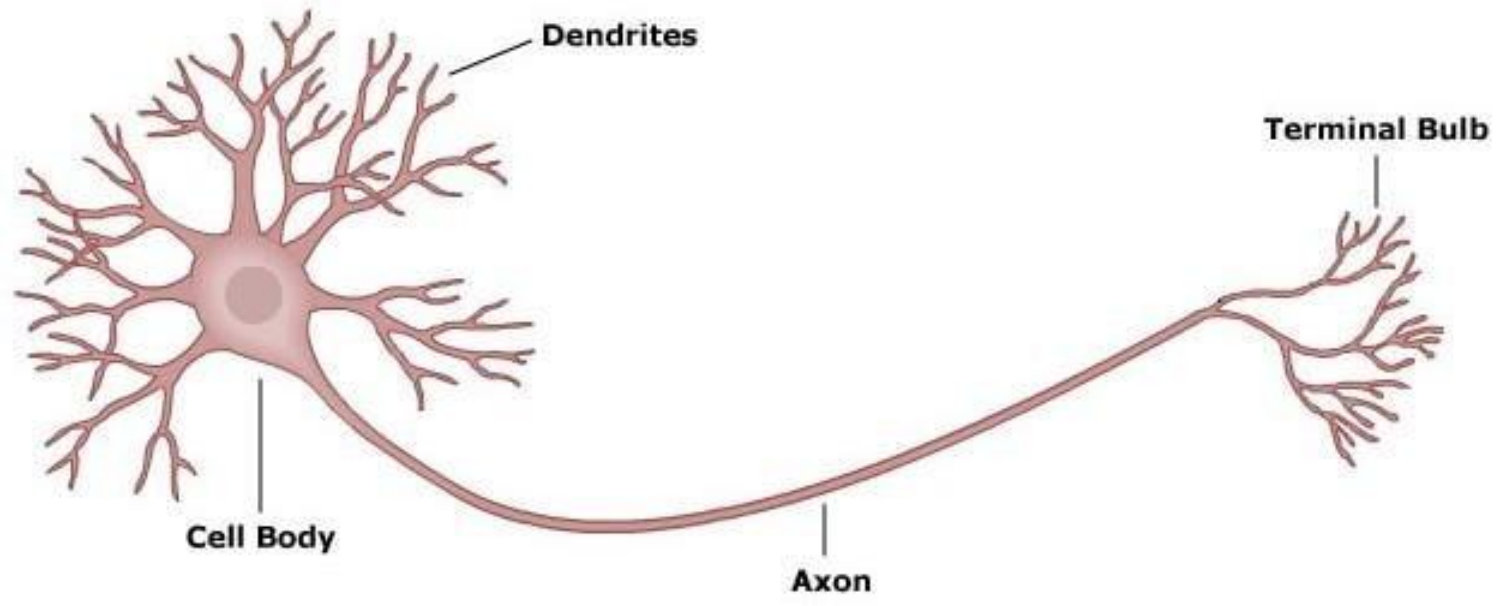


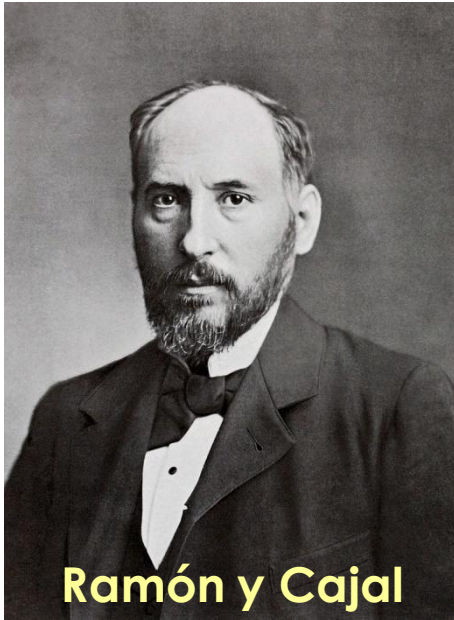
Polarización neuronas

Biología del Desarrollo 2022

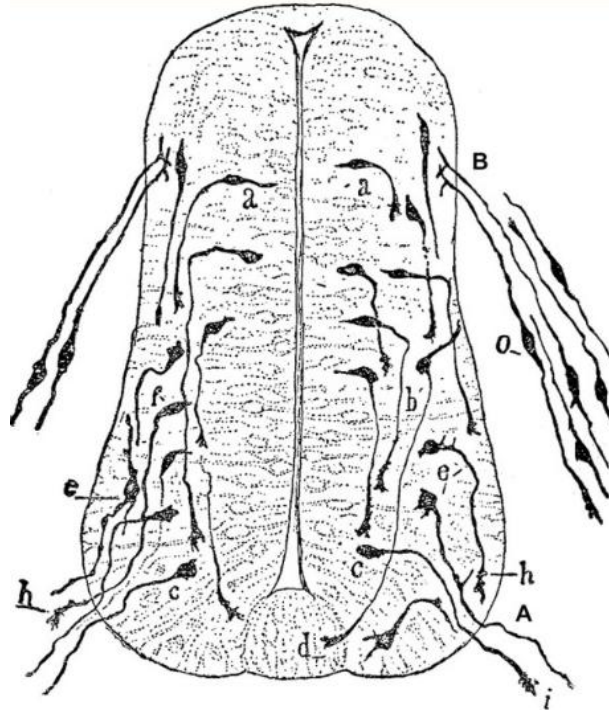
Polaridad neuronal



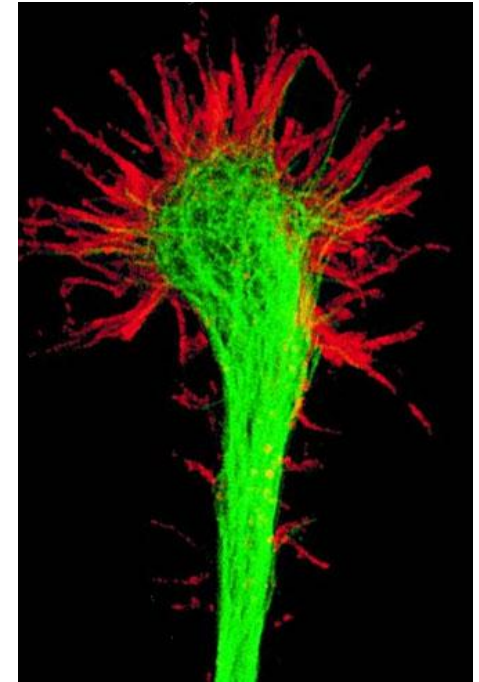
El cono de crecimiento



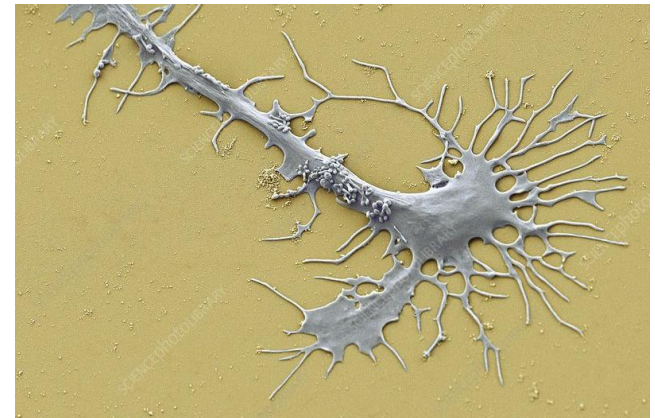
Ramón y Cajal



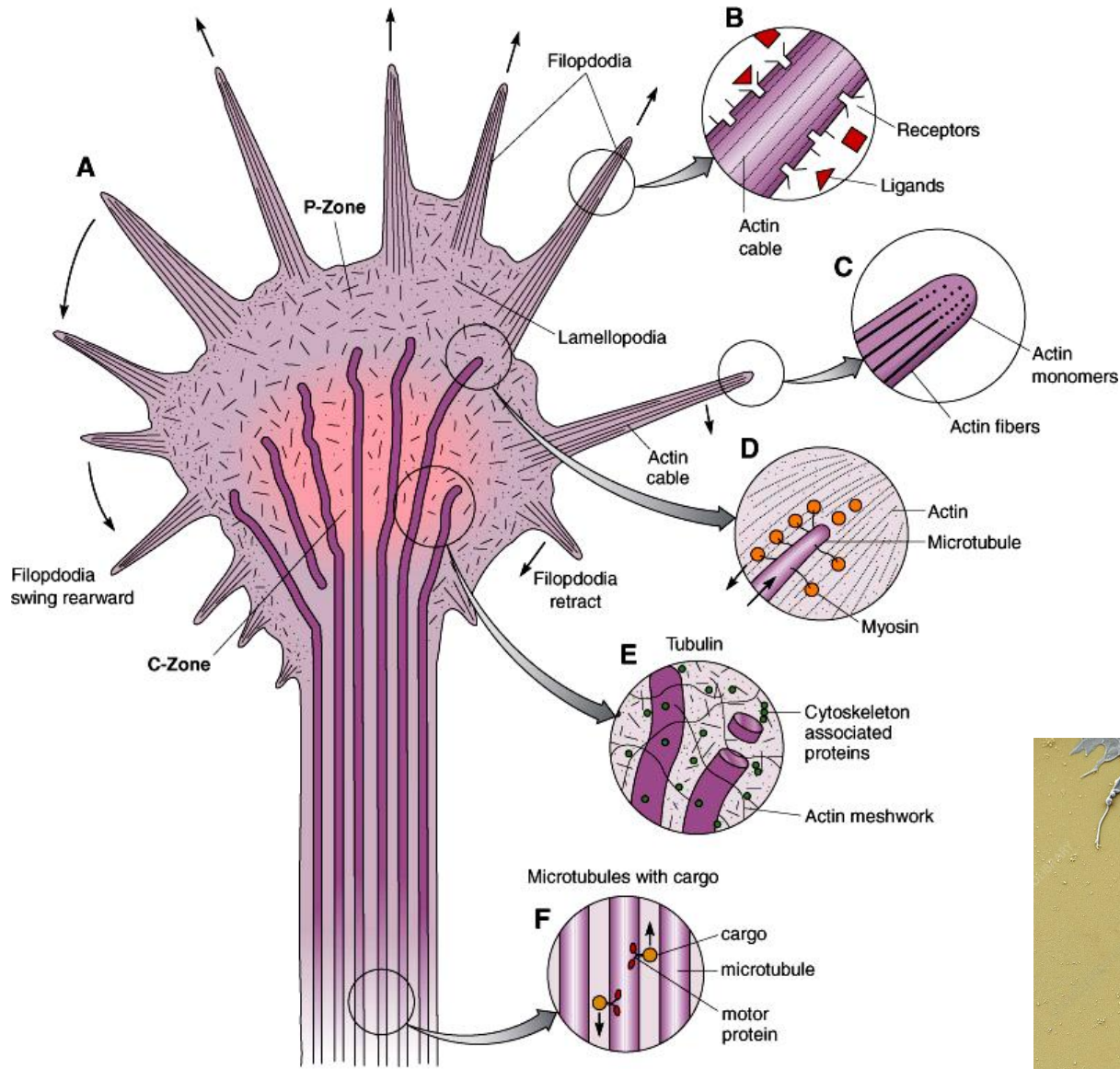
Cajal, 1890



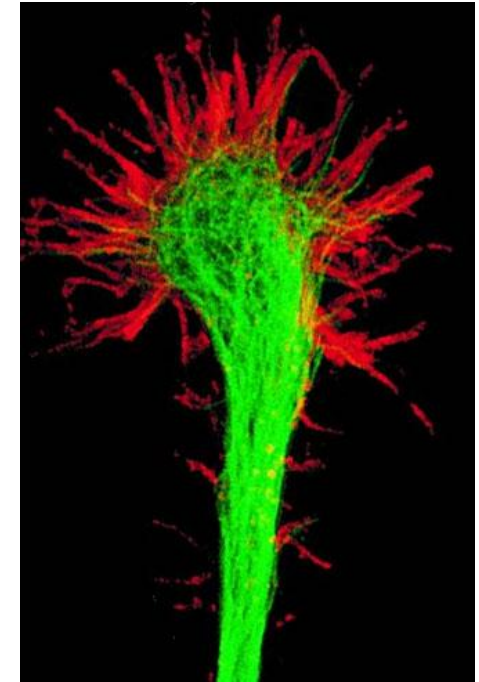
Microtúbulos
Actina



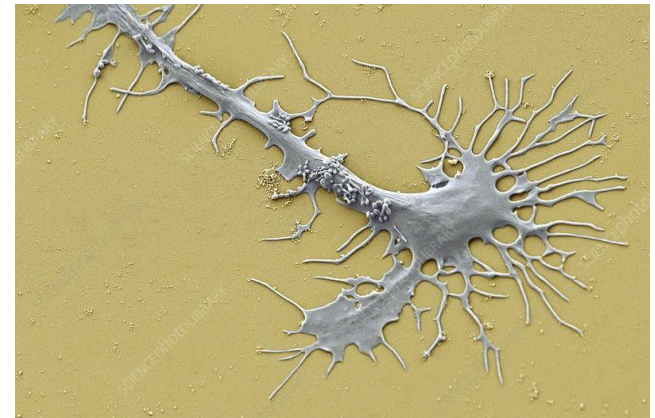
El cono de crecimiento



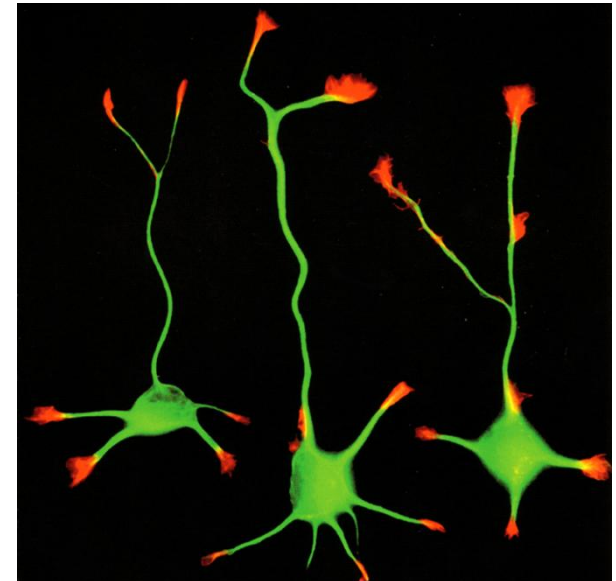
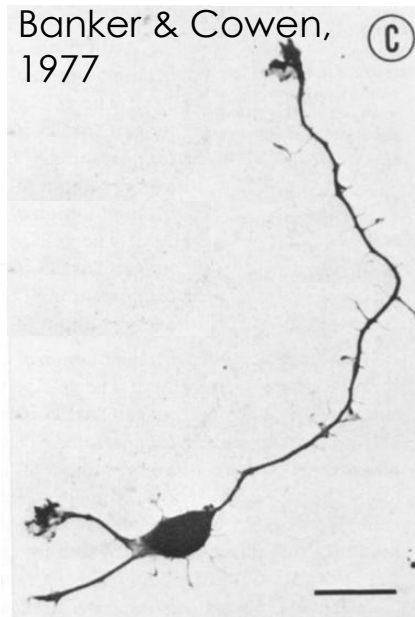
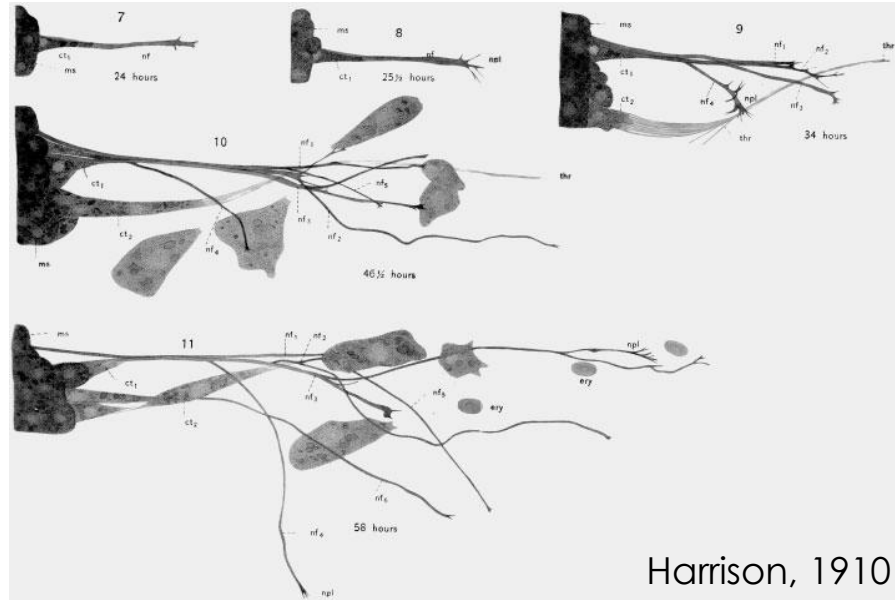
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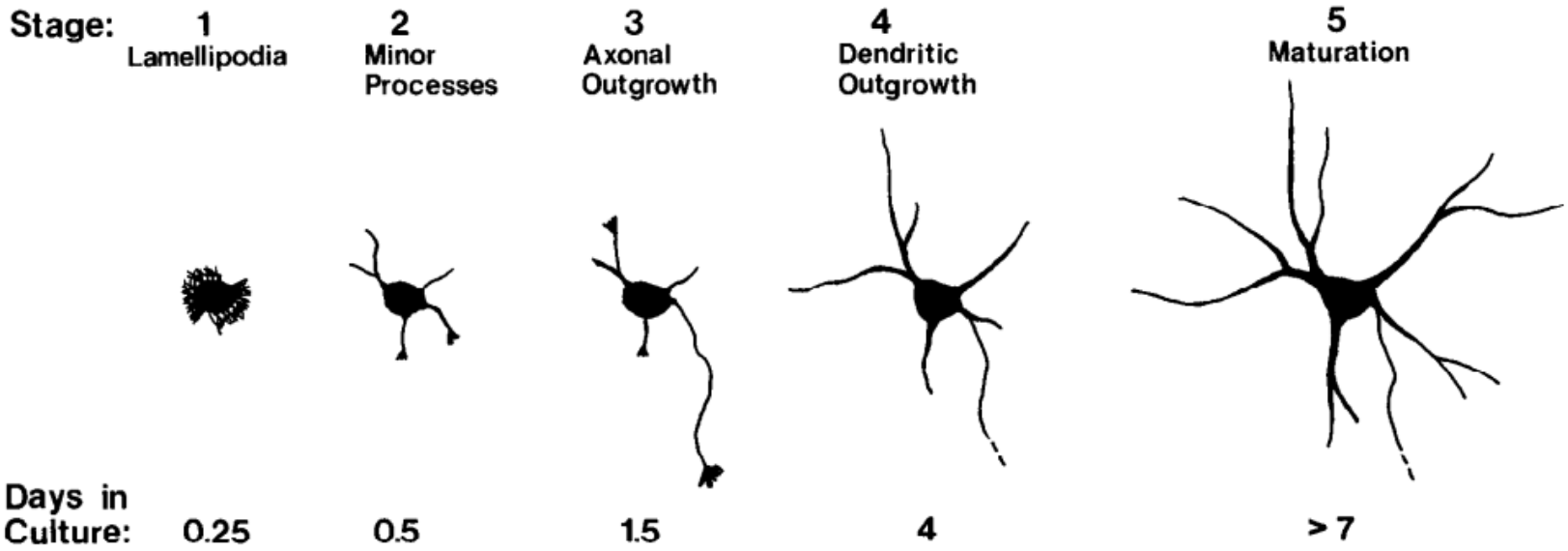
Microtúbulos
Actina



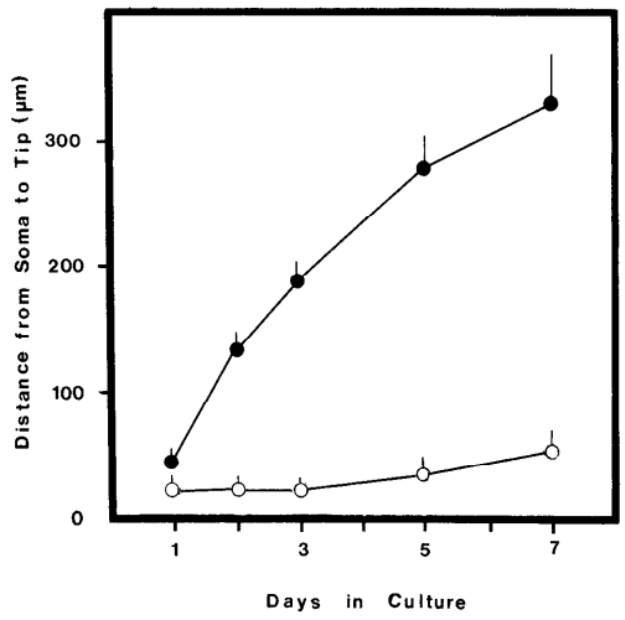
Polarización y crecimiento axonal in vitro



Polarización y crecimiento axonal in vitro



Dotti et al., 1988

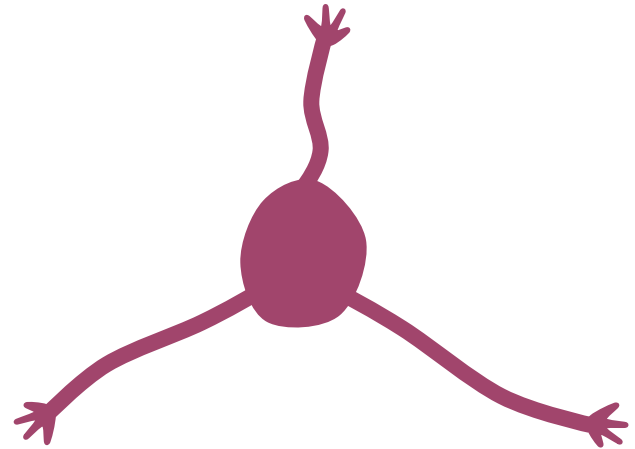
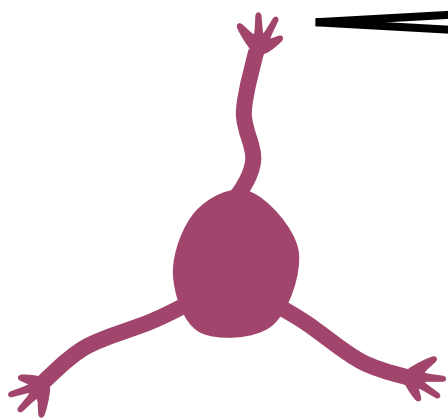


Entre el primer y segundo día de cultivo se observa la aparición de una neurita más larga. Esta neurita crece a velocidades más altas que el resto, y se identifica posteriormente como axón.

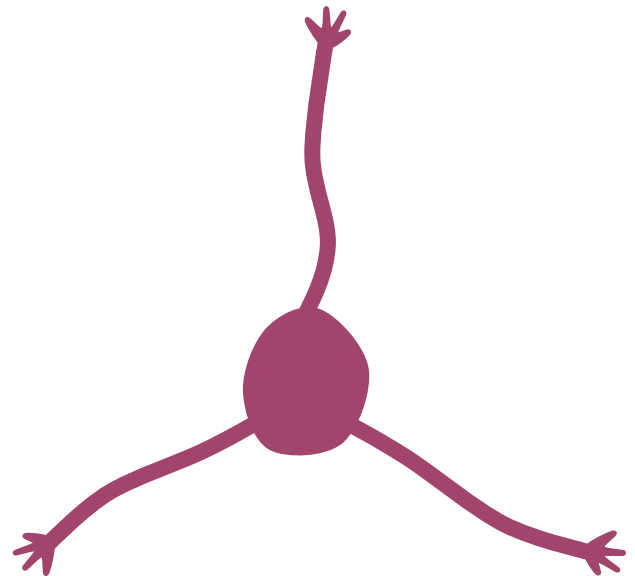
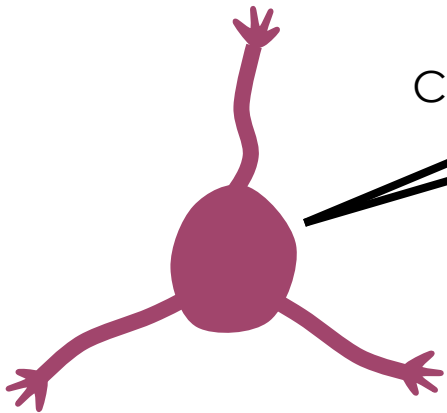
Polarización y crecimiento axonal: MTs

Bamburg et al., 1986

Colcemida



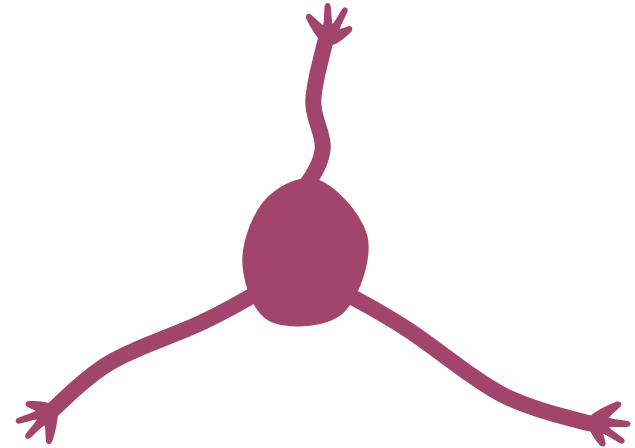
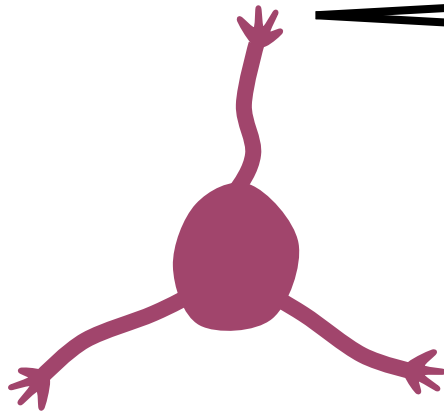
Colcemida



Polarización y crecimiento axonal: MTs

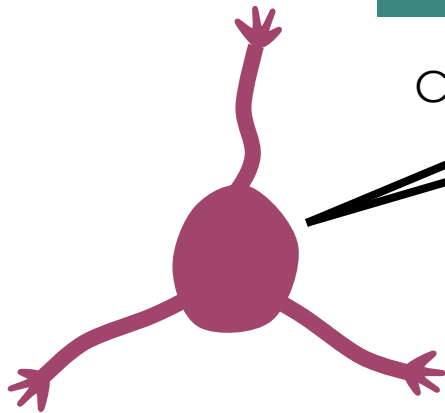
Bamburg et al., 1986

Colcemida

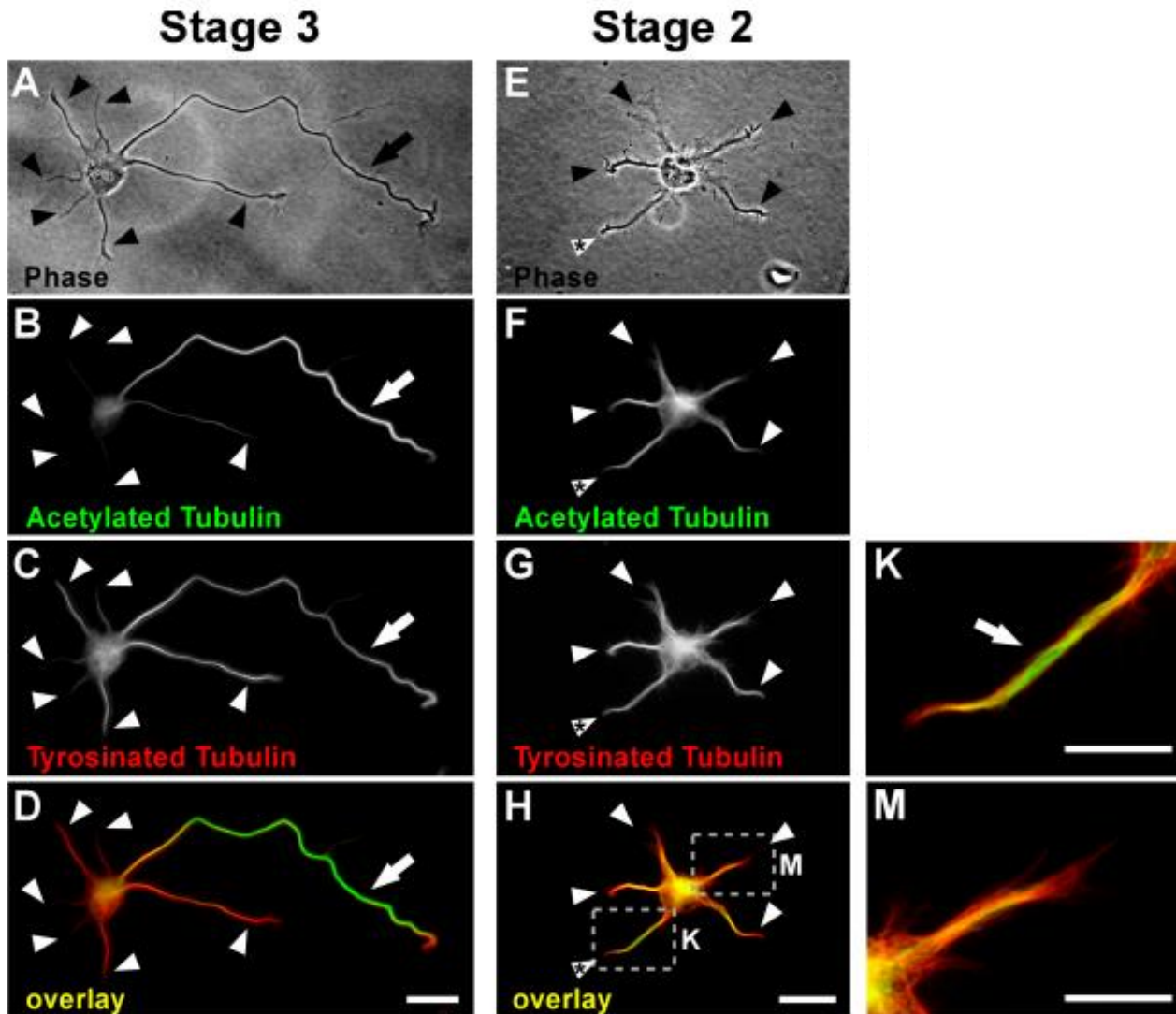


El ensamblaje local de MTs
permite el crecimiento de las
neuritas

Colcemida

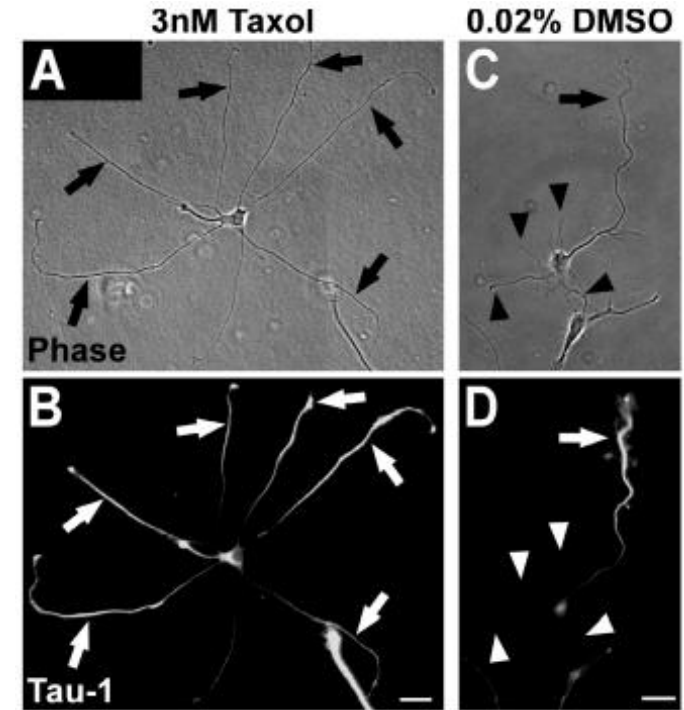
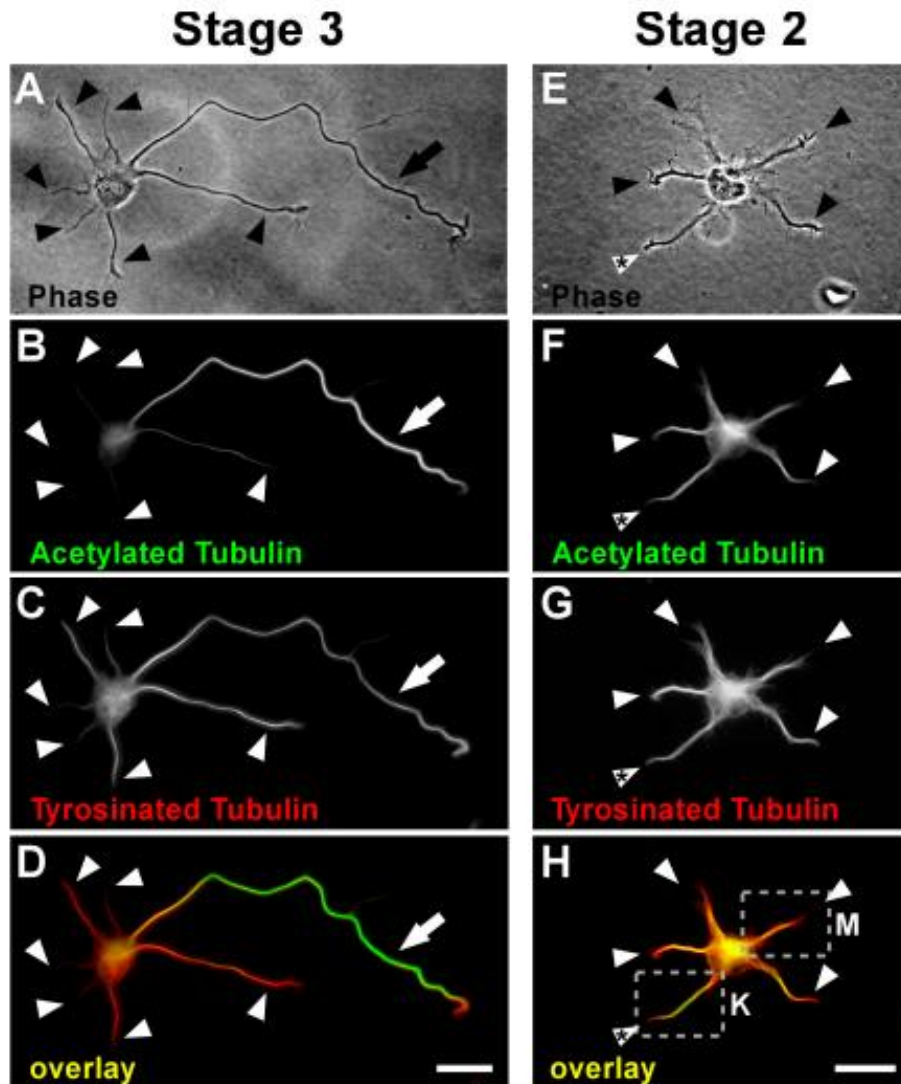


Polarización y crecimiento axonal: MTs

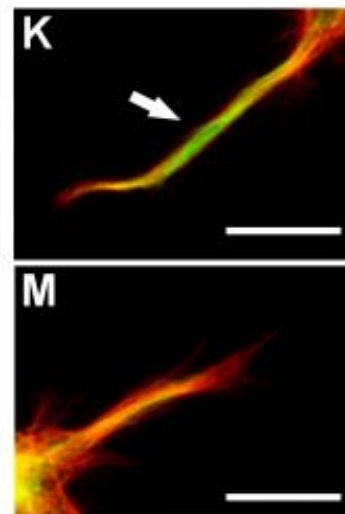


Witte et al., 2008

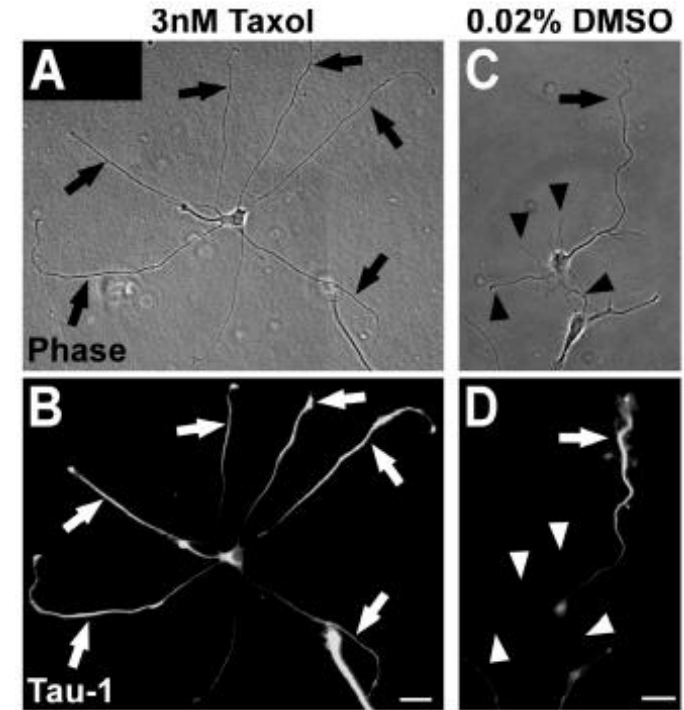
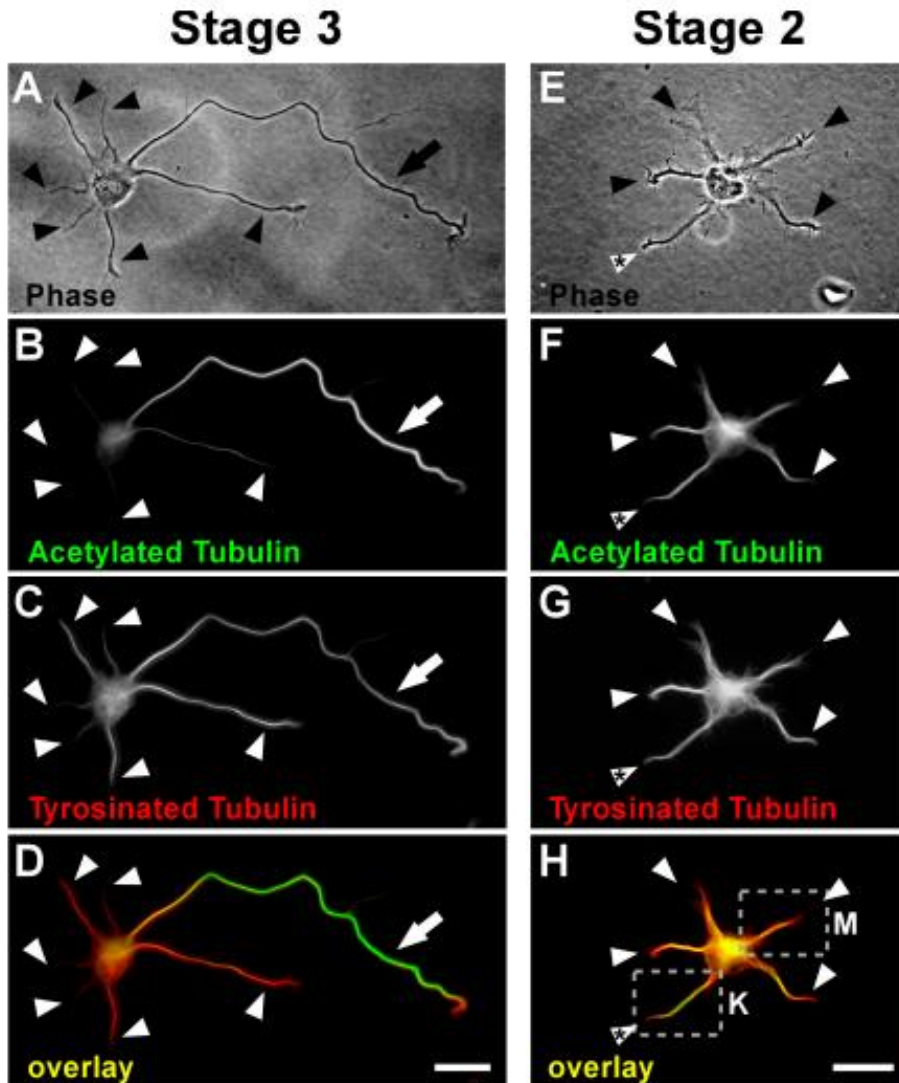
Polarización y crecimiento axonal: MTs



Witte et al., 2008



Polarización y crecimiento axonal: MTs

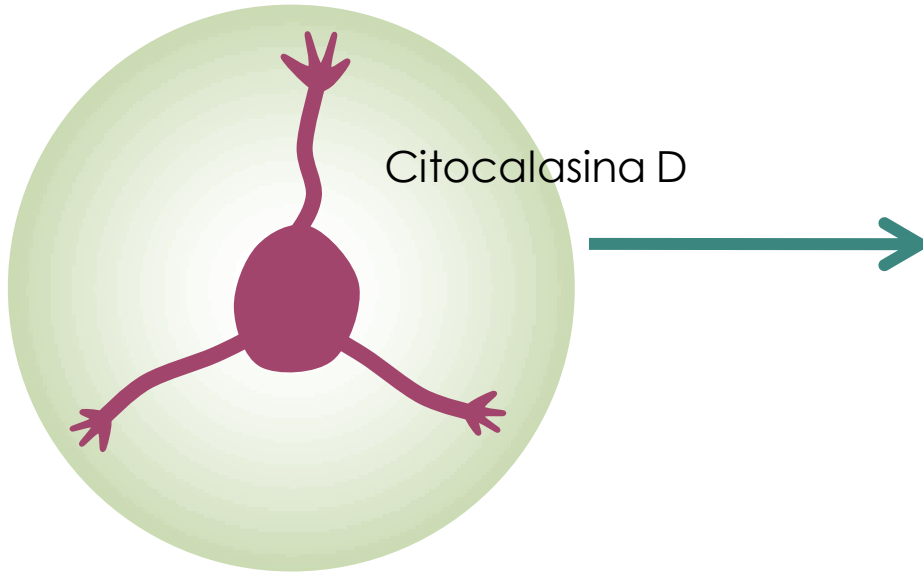


Witte et al., 2008

La
estabilización
de los MTs es
esencial para
la formación
del axón

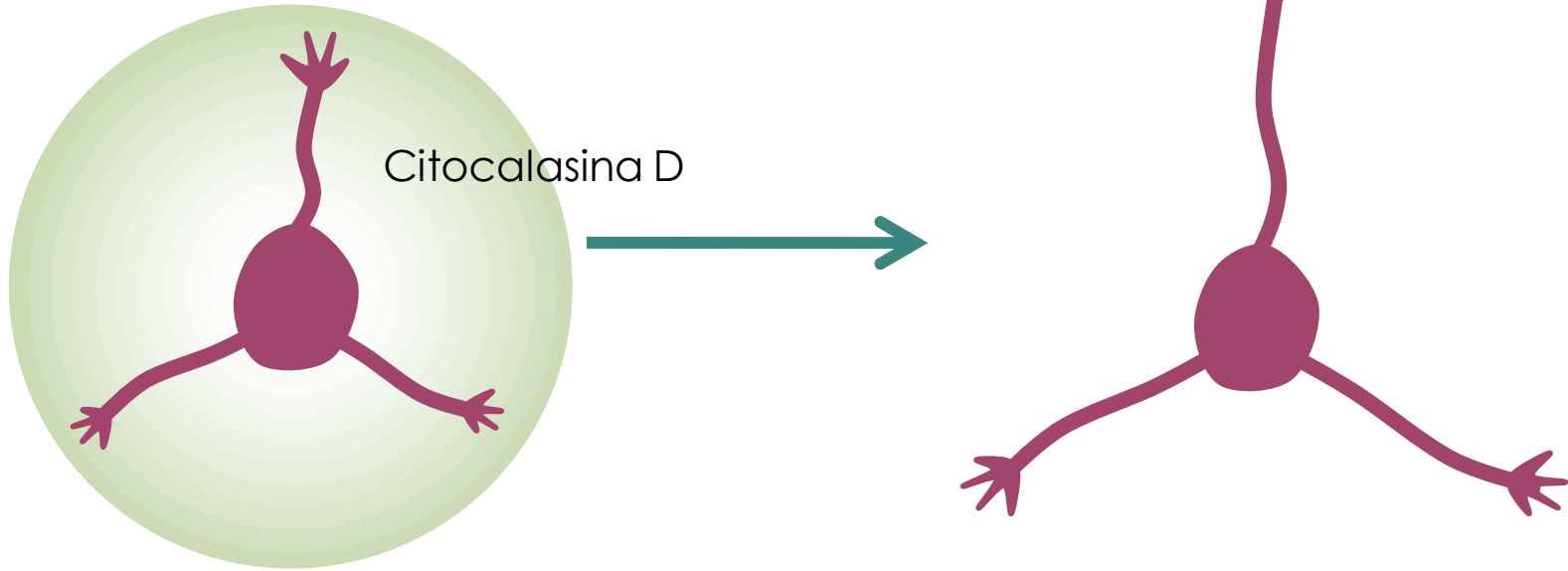
Polarización y crecimiento axonal: actina

Bradke & Dotti, 1999



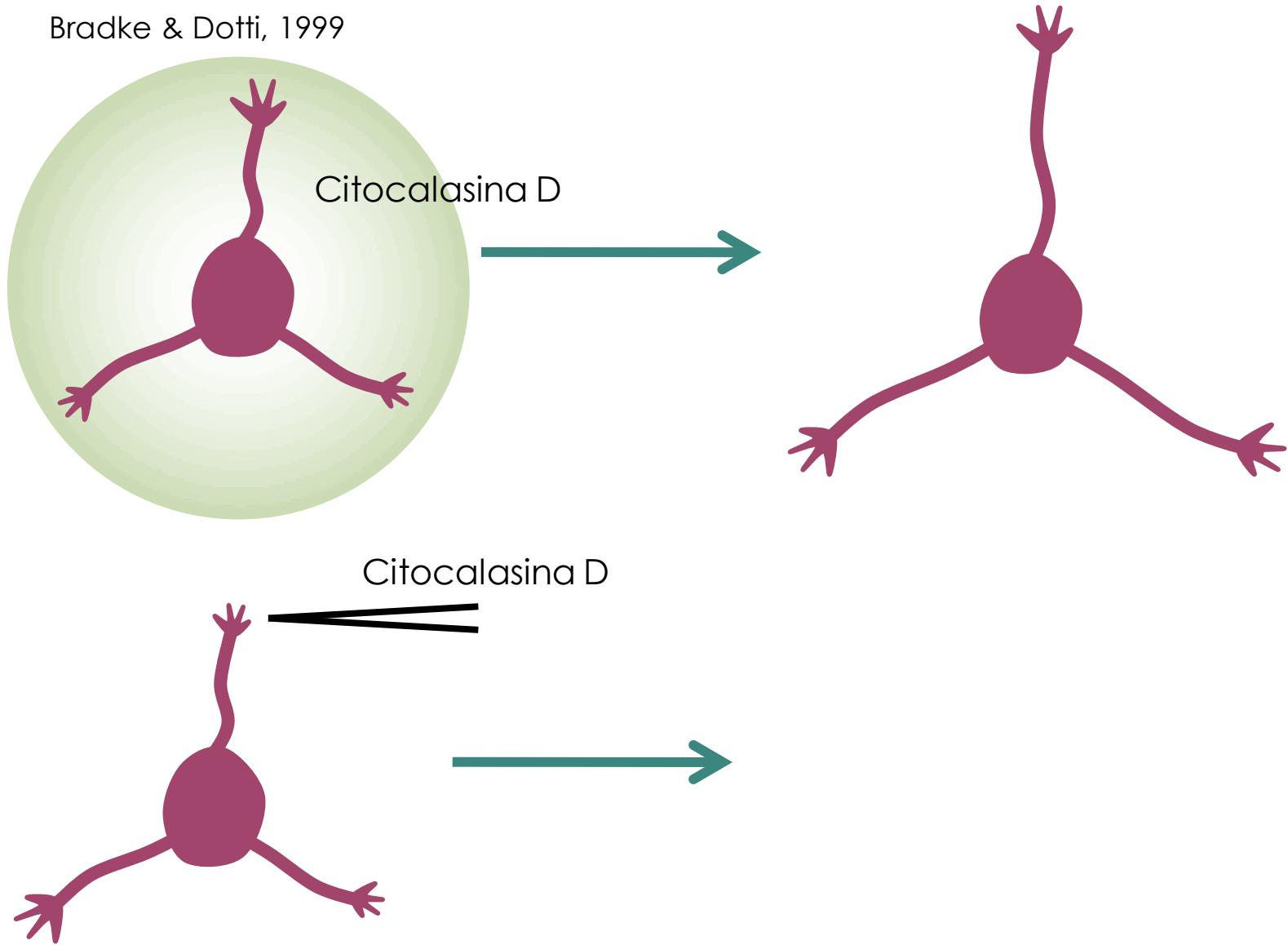
Polarización y crecimiento axonal: actina

Bradke & Dotti, 1999



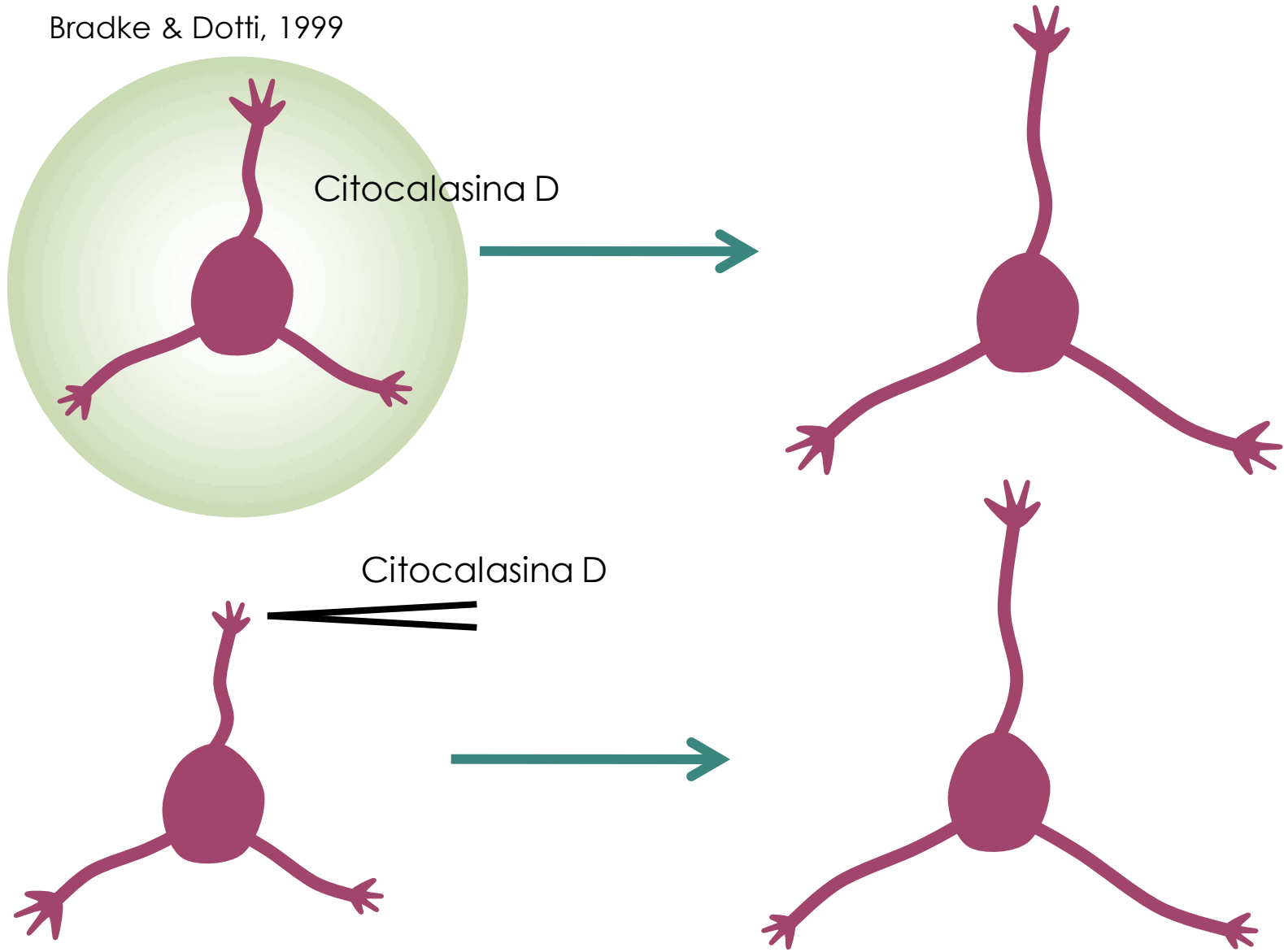
Polarización y crecimiento axonal: actina

Bradke & Dotti, 1999



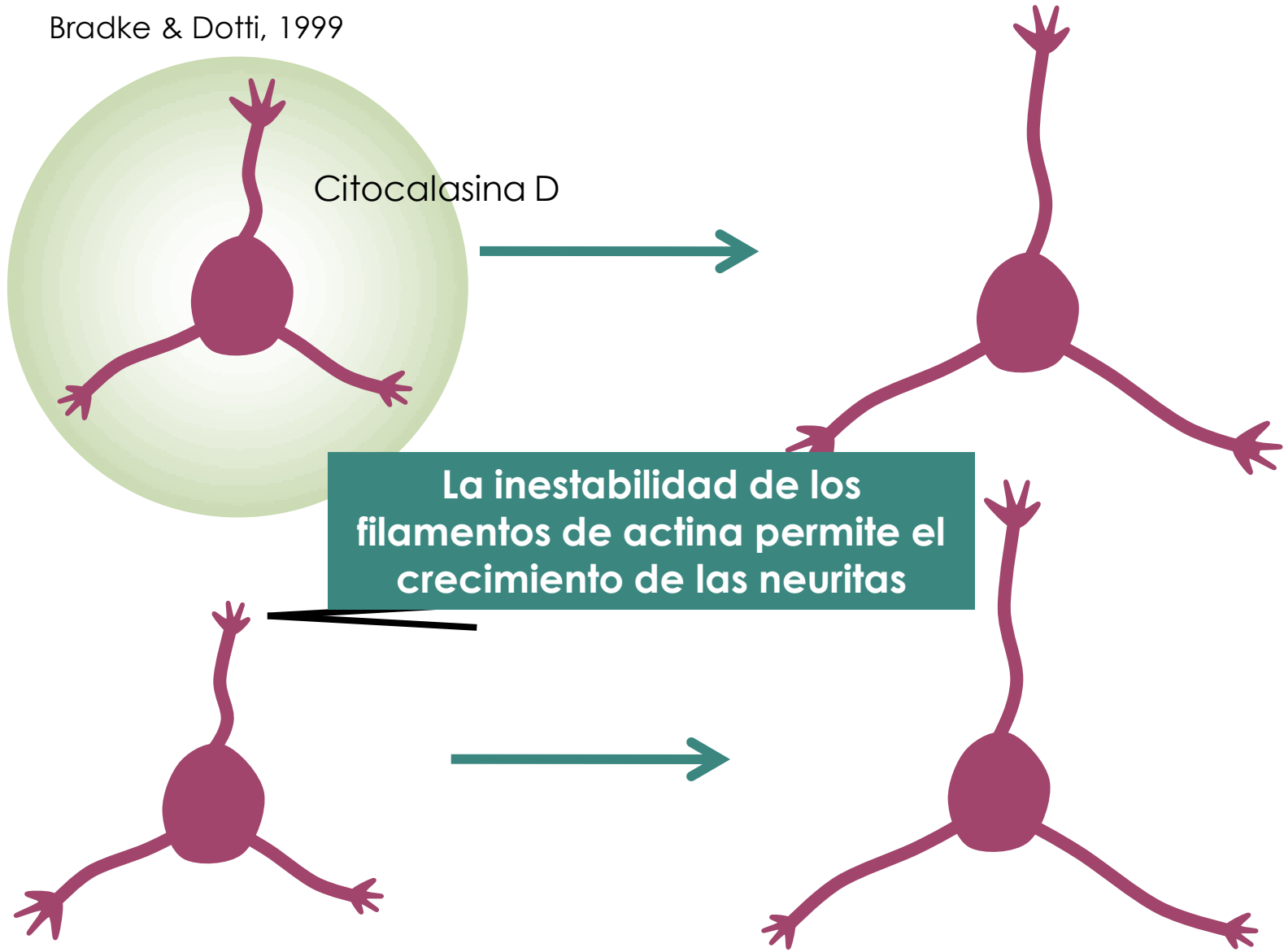
Polarización y crecimiento axonal: actina

Bradke & Dotti, 1999



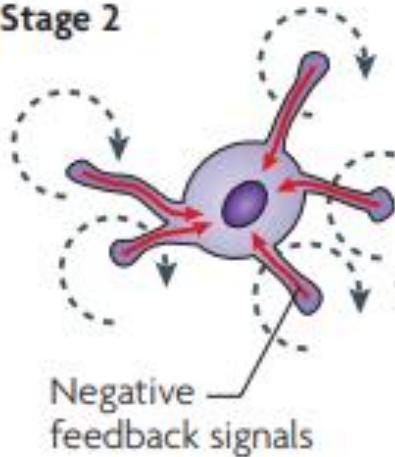
Polarización y crecimiento axonal: actina

Bradke & Dotti, 1999

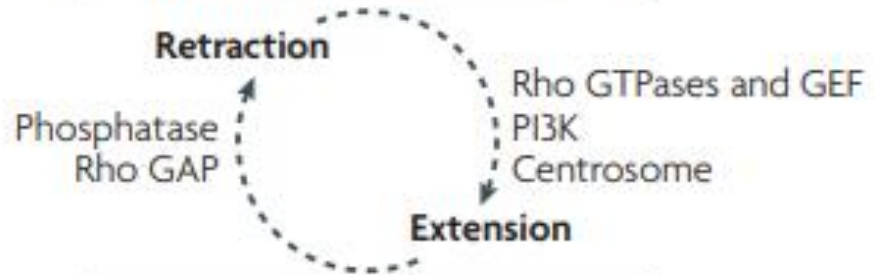


Especificación del axón

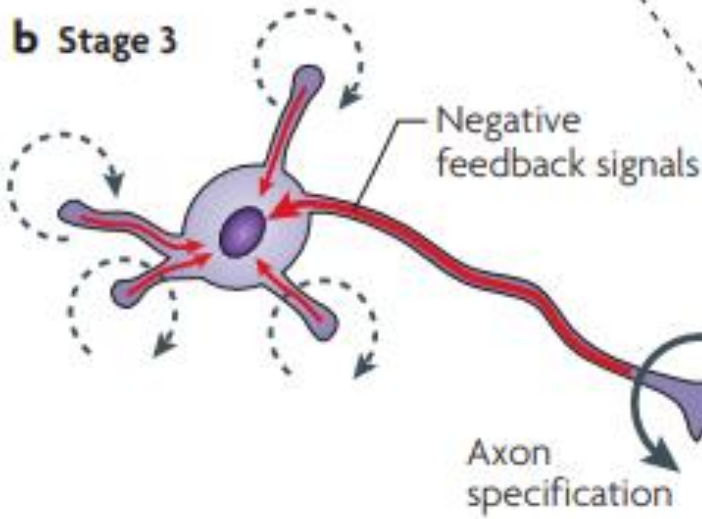
a Stage 2



- Negative regulation**
- Membrane elimination
 - Degradation of proteins
 - Decrease in dynamics of F-actin
 - Microtubule catastrophe



b Stage 3

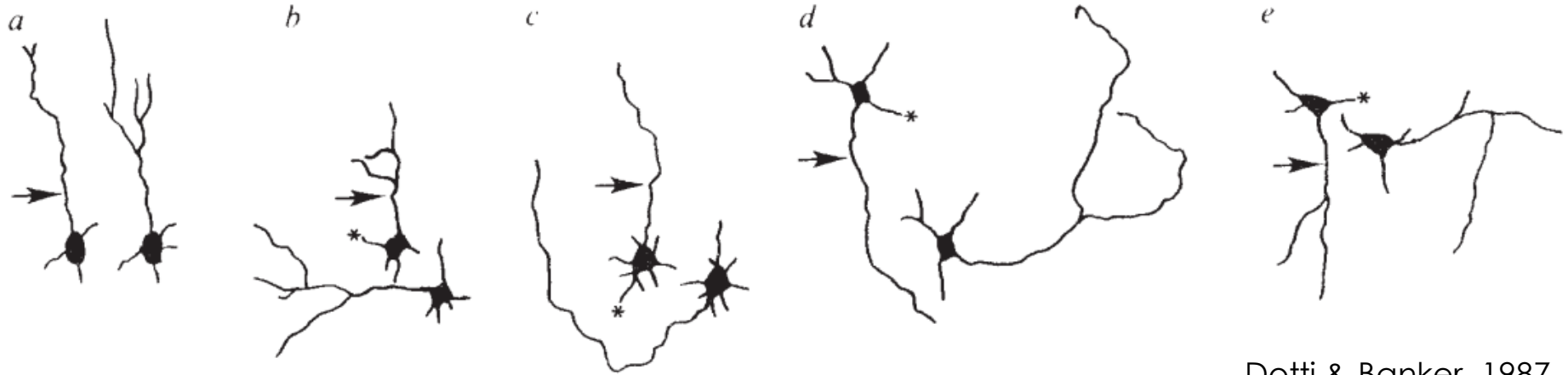


- Positive regulation**
- Membrane recruitment
 - Protein transport
 - Increase in dynamics of F-actin
 - Microtubule assembly



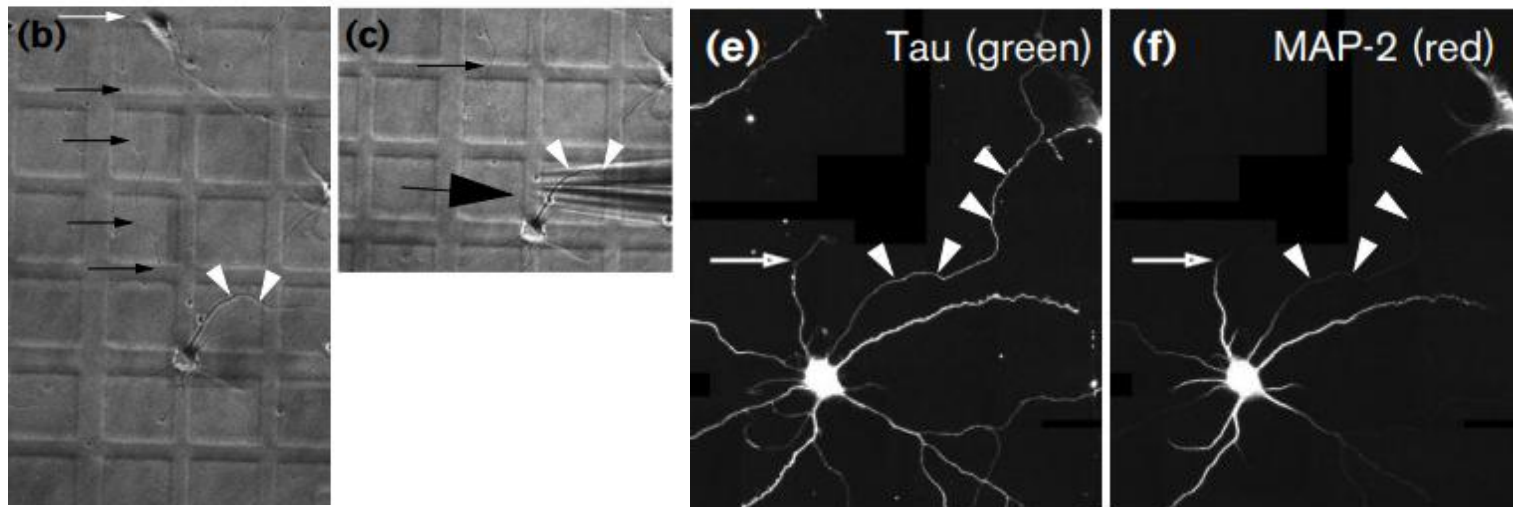
Plasticidad de neuronas en diferenciación

Neuronas en estadio 3



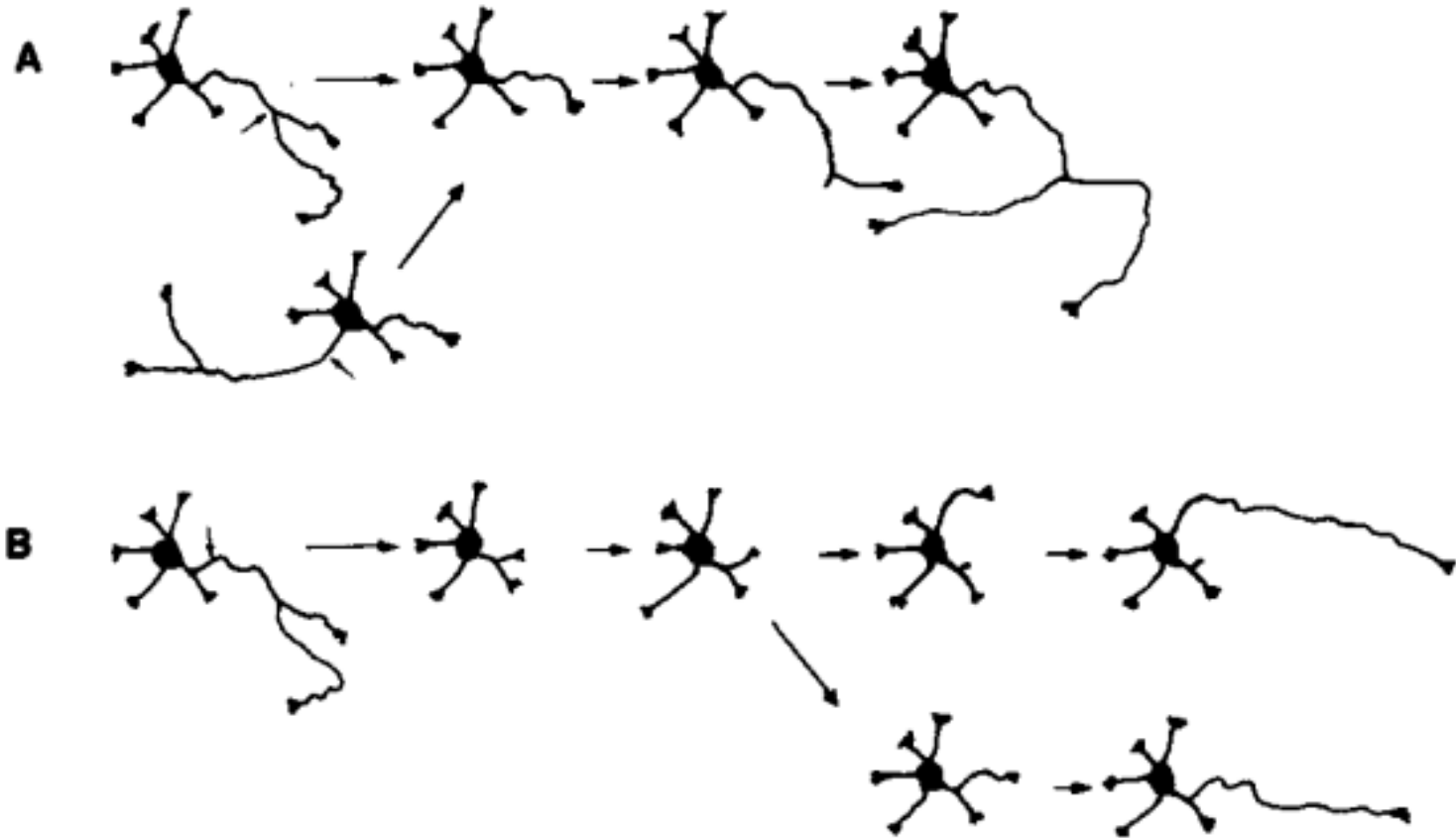
Dotti & Banker, 1987

Neuronas en estadio 4



Bradke & Dotti, 2000

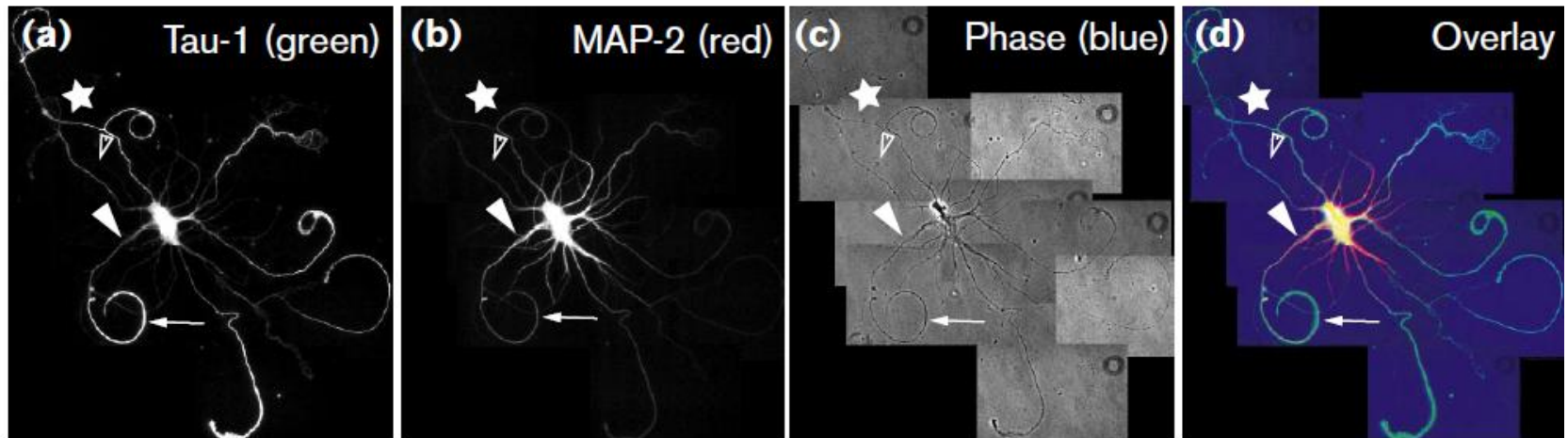
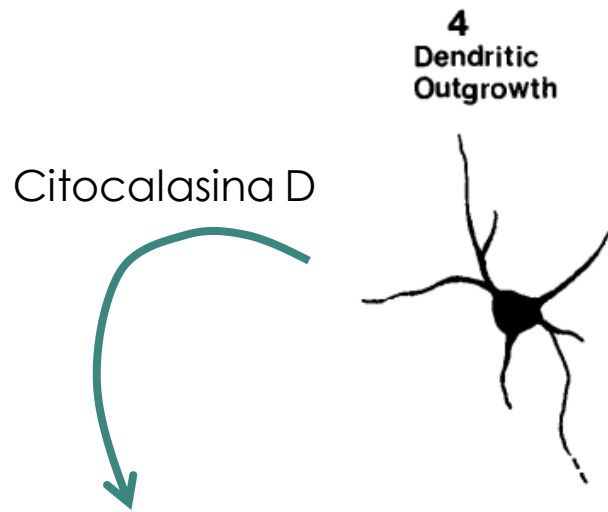
Plasticidad de neuronas en diferenciación



Goslin & Banker, 1989

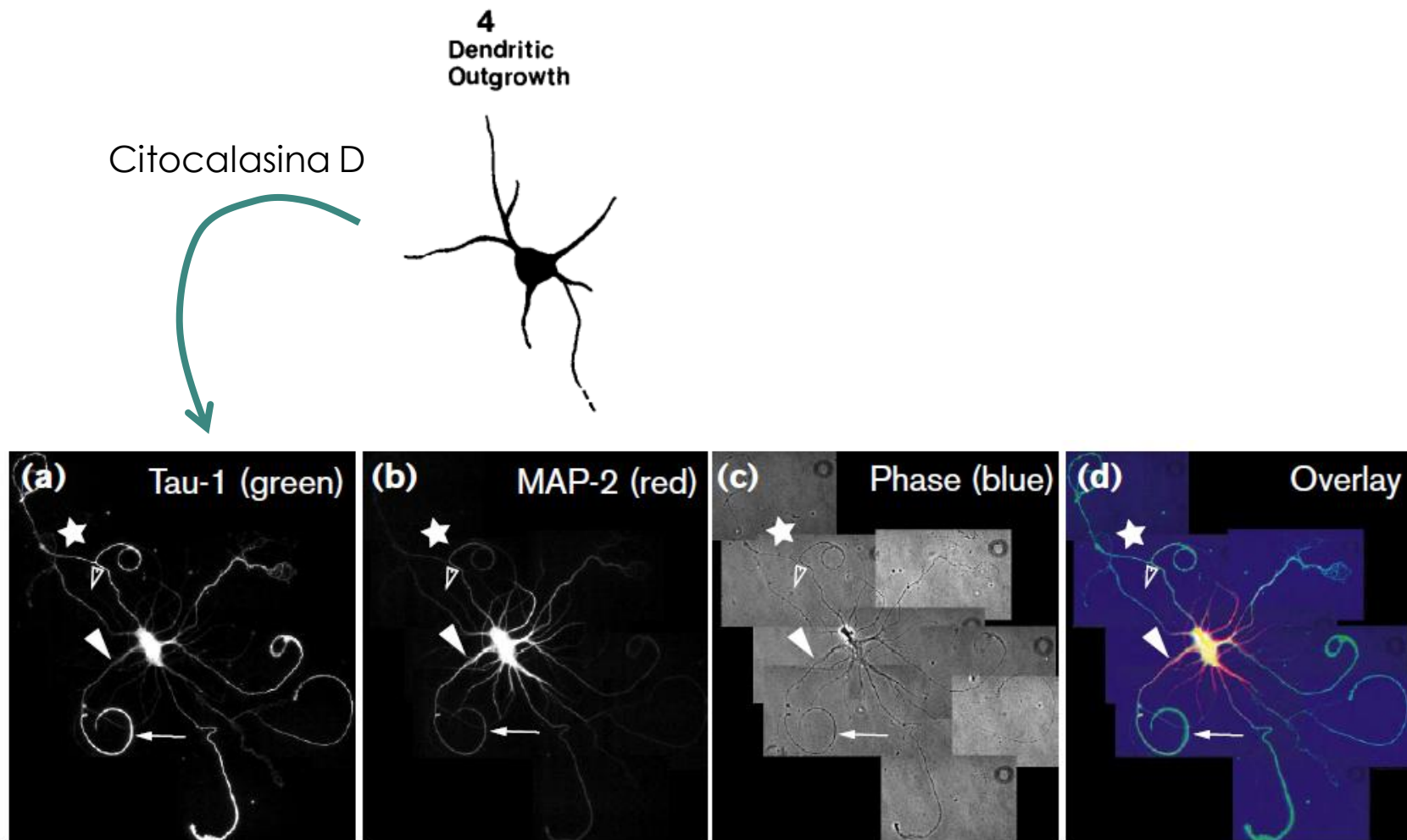
El proceso más largo da lugar al nuevo axón,
independientemente de si era o no el axón
previamente

Plasticidad de neuronas en diferenciación



Bradke & Dotti, 2000

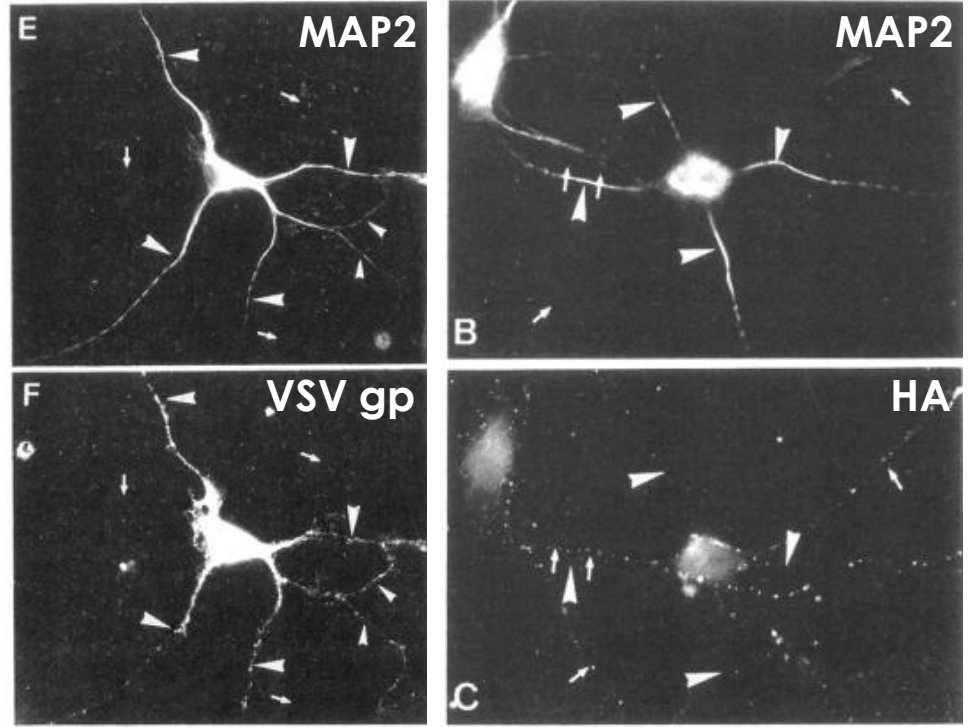
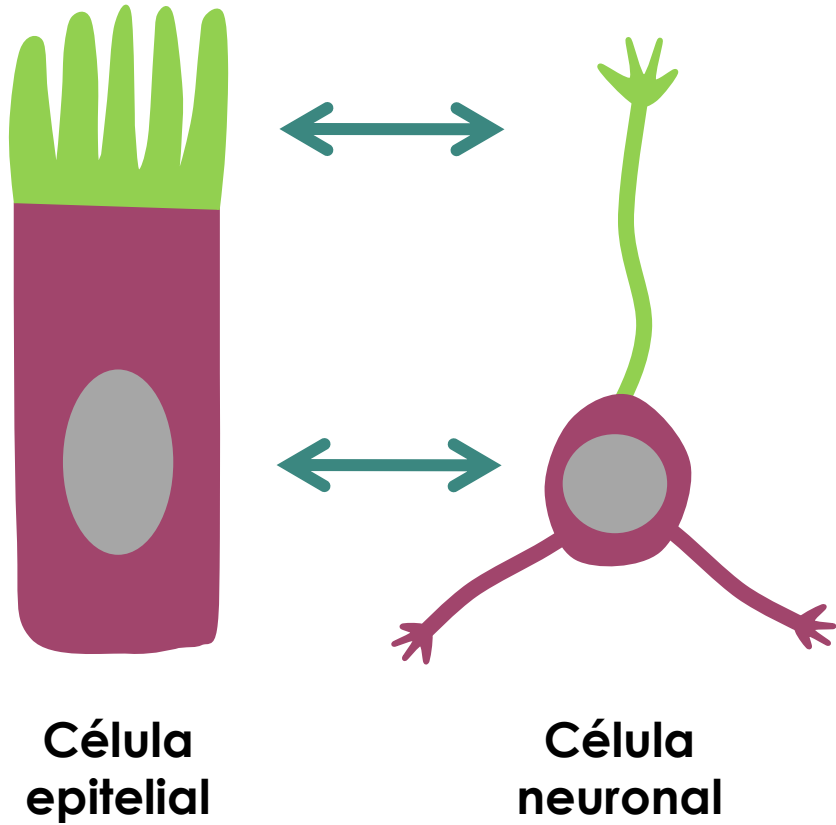
Plasticidad de neuronas en diferenciación



Bradke & Dotti, 2000

La desestabilización de los filamentos de actina en neuronas maduras transforma las dendritas en axones

Polaridad epitelial vs polaridad neuronal

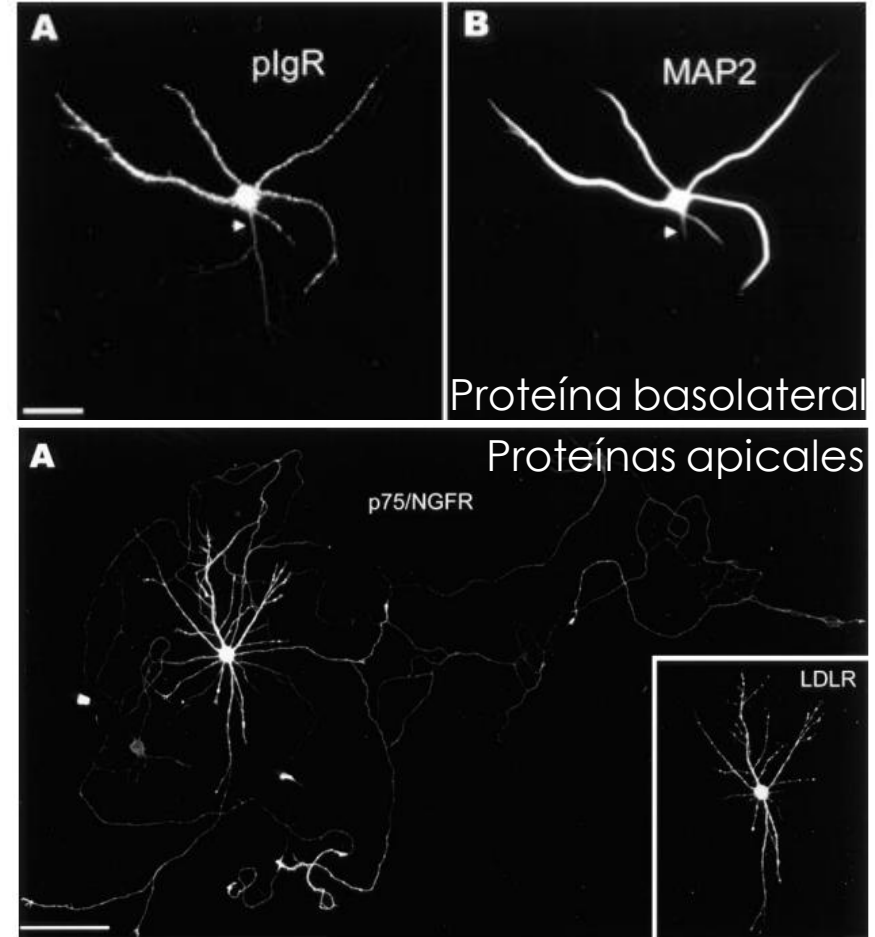
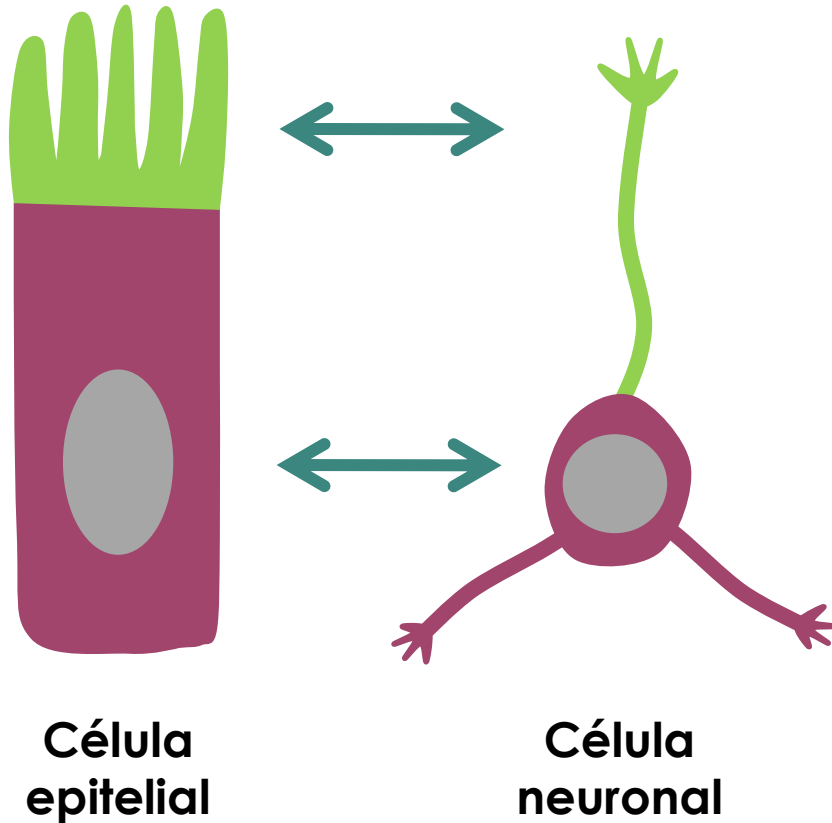


Dotti & Simons, 1990

Glucoproteínas VSV → Membrana basolateral → Dendritas y soma

Hemaglutinina Influenza → Membrana apical → Axón

Polaridad epitelial vs polaridad neuronal



Jaber & Banker, 1998

Glucoproteínas VSV → Membrana basolateral → Dendritas y soma

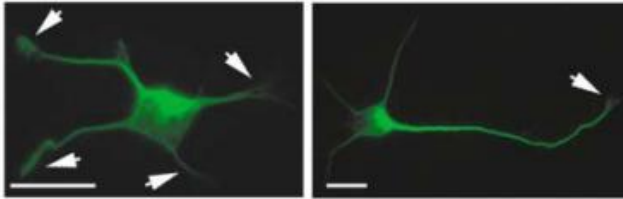
Hemaglutinina Influenza → Membrana apical → Axón

Componentes celulares y axonogénesis

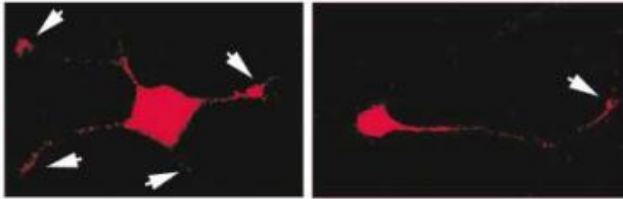
Stage 2

Stage 3

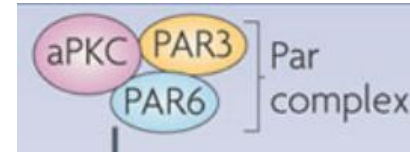
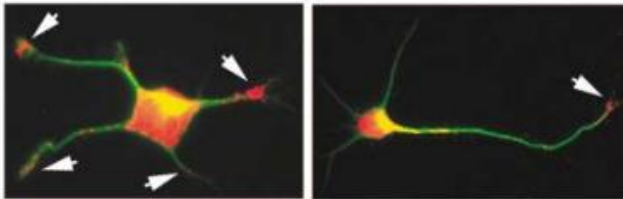
Anti-Tuj1



Anti-mPar3



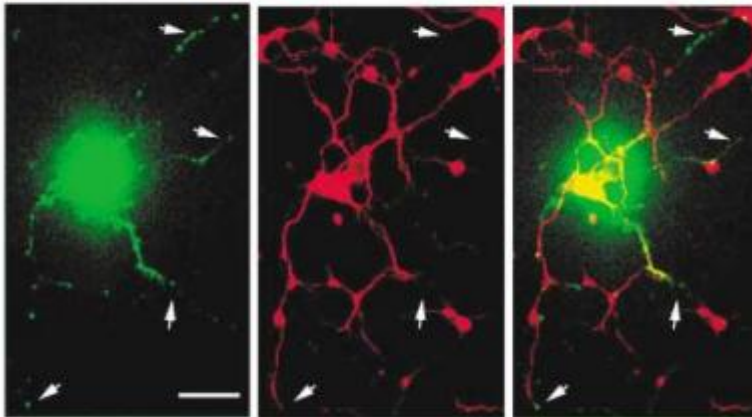
Overlay



EGFP-mPar3

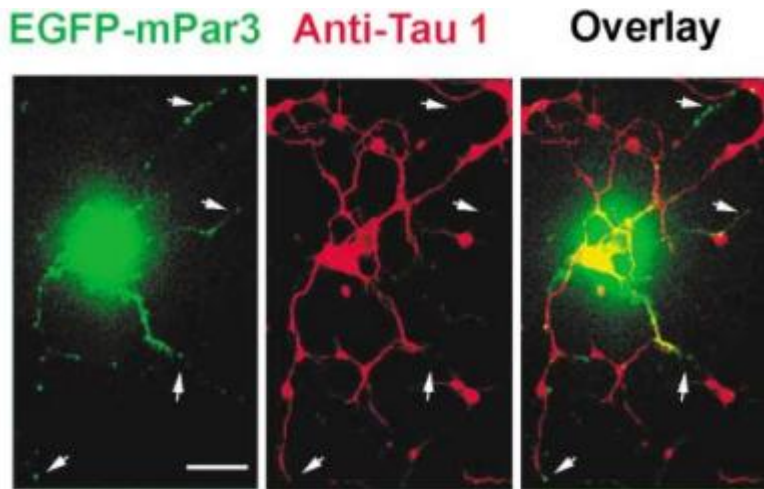
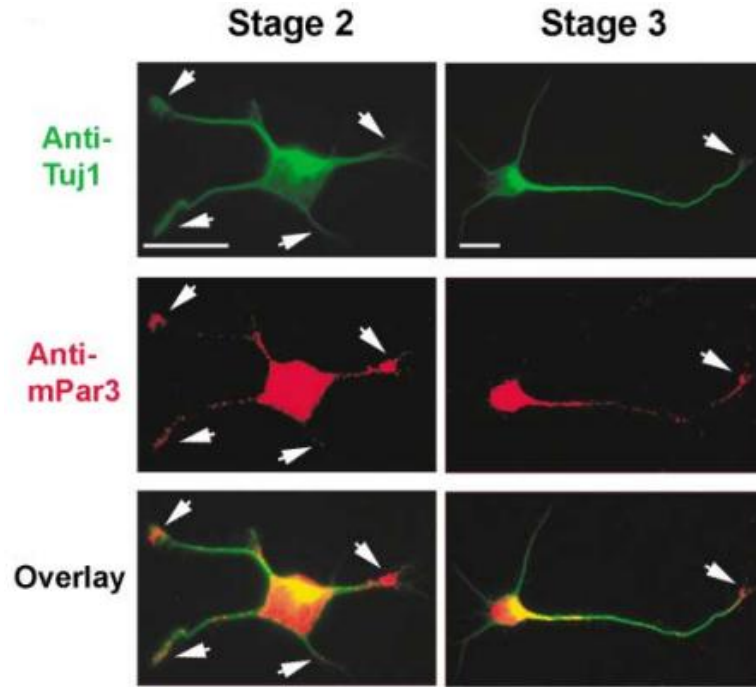
Anti-Tau 1

Overlay

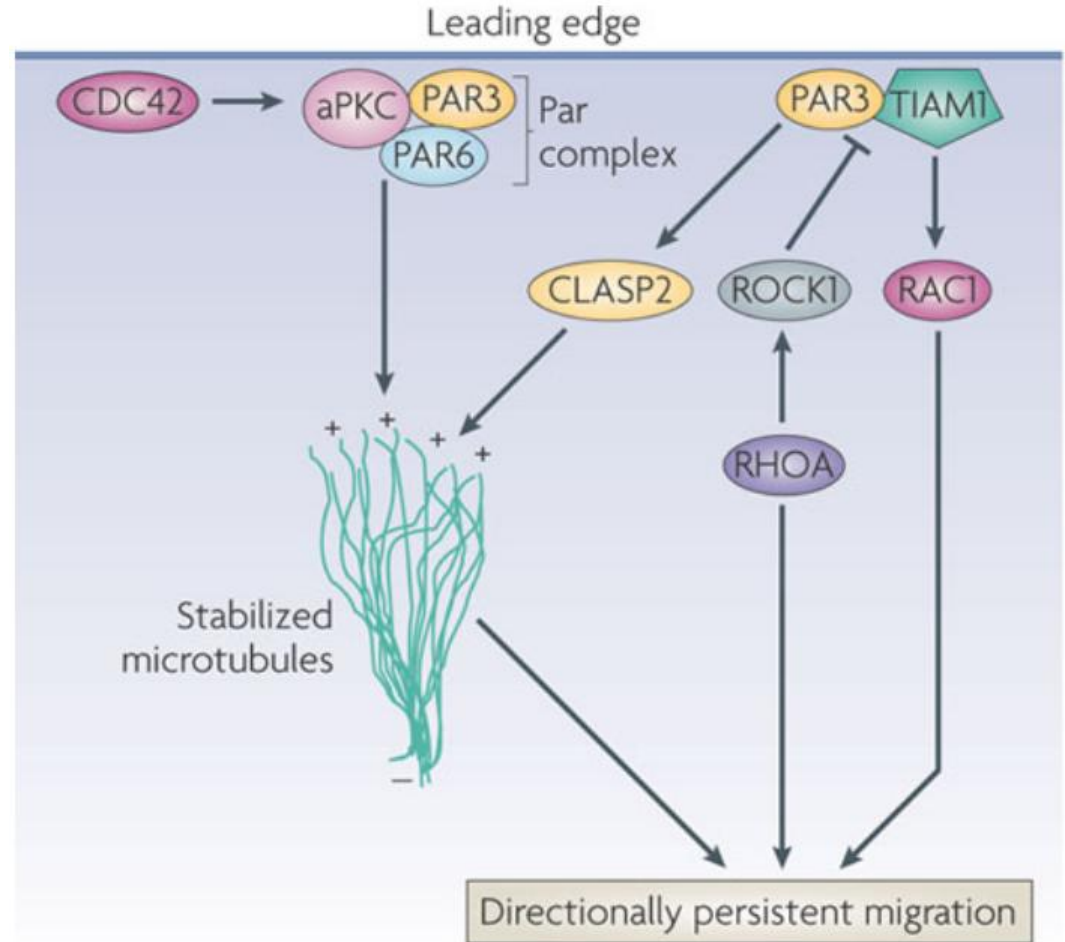


Shi et al., 2003

Componentes celulares y axonogénesis

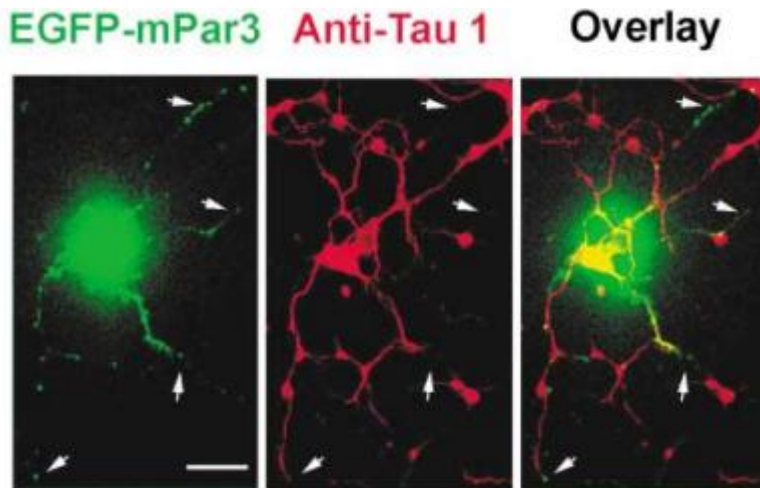
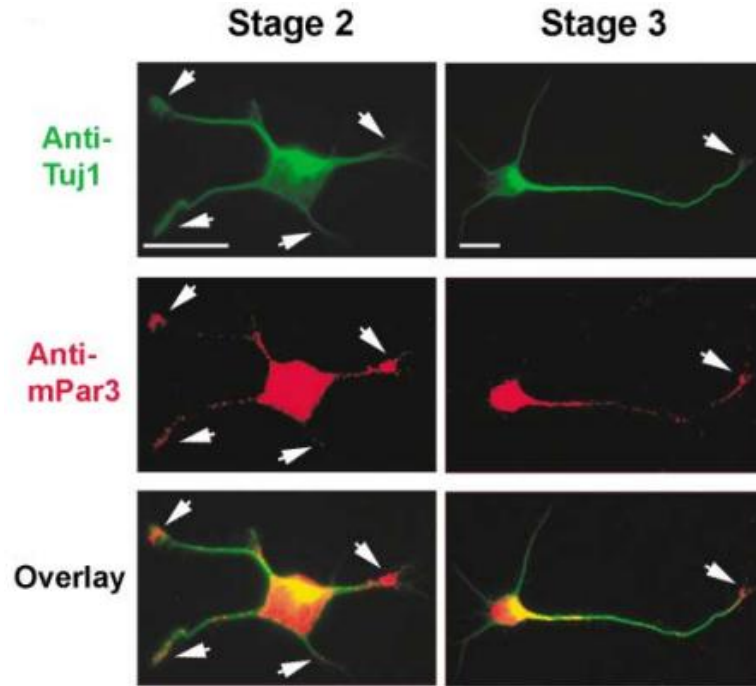


Shi et al., 2003

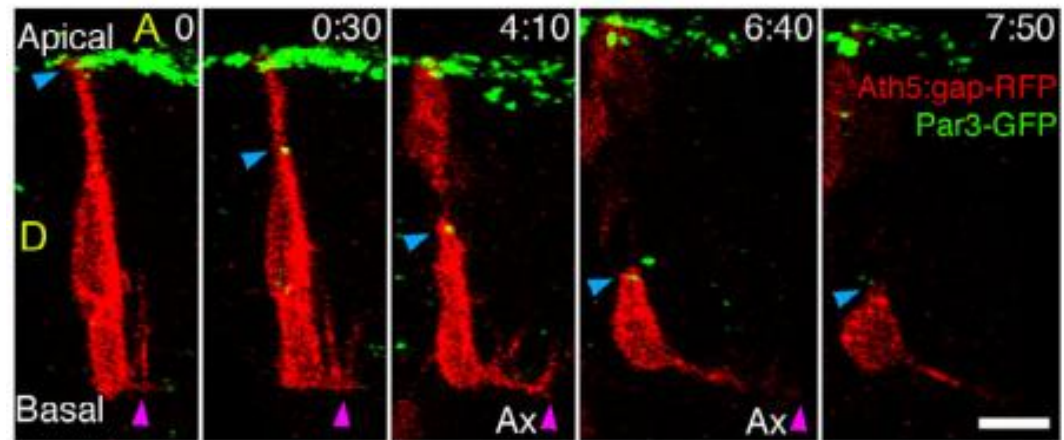
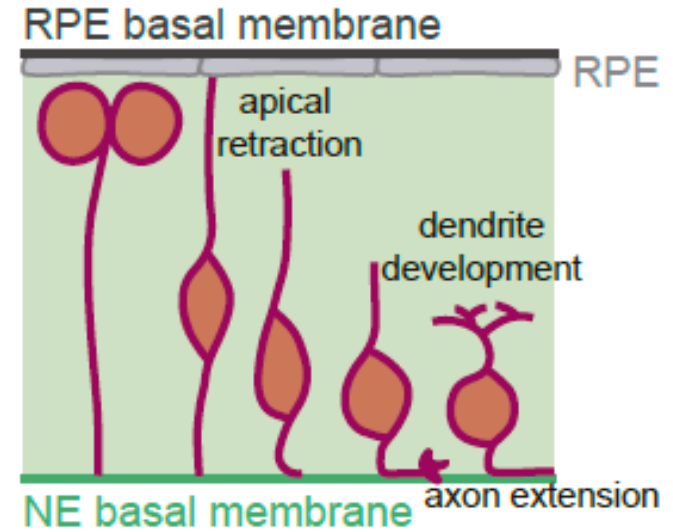


Petrie et al., 2009

Componentes celulares y axonogénesis



Shi et al., 2003



Zolessi et al., 2006

Componentes celulares y axonogénesis

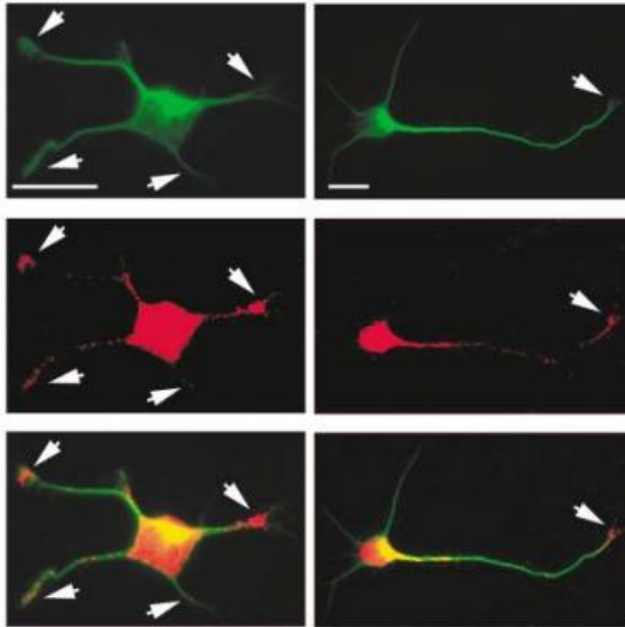
Stage 2

Stage 3

Anti-Tuj1

Anti-mPar3

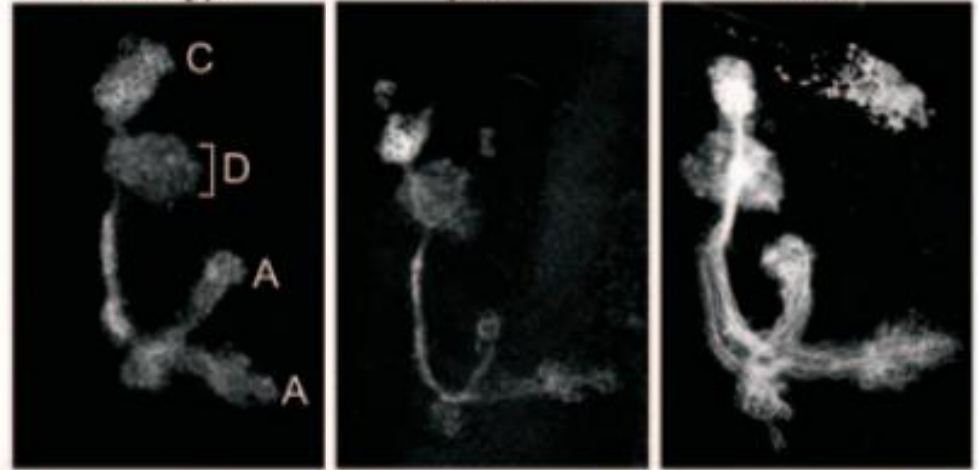
Overlay



Wild type

par-6

aPKC

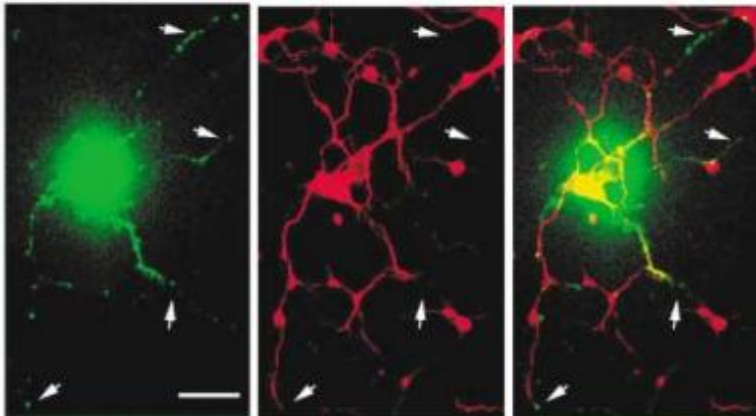


Rolls & Doe, 2004

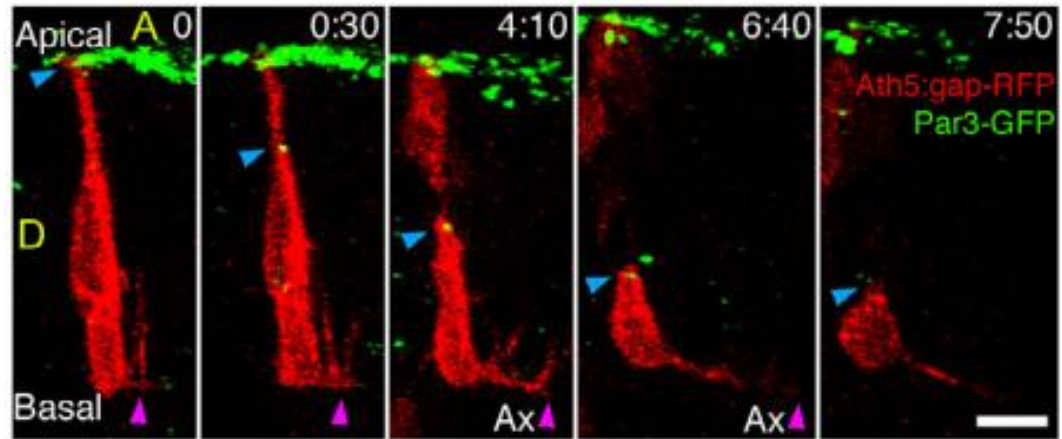
EGFP-mPar3

Anti-Tau 1

Overlay

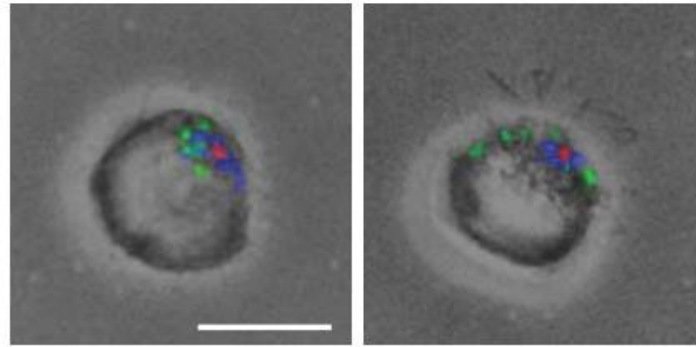


Shi et al., 2003



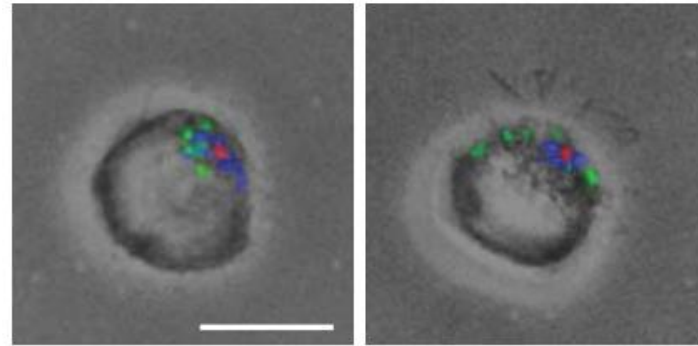
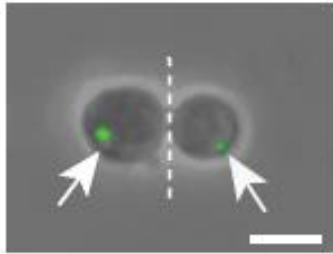
Zolessi et al., 2006

Componentes celulares y axonogénesis

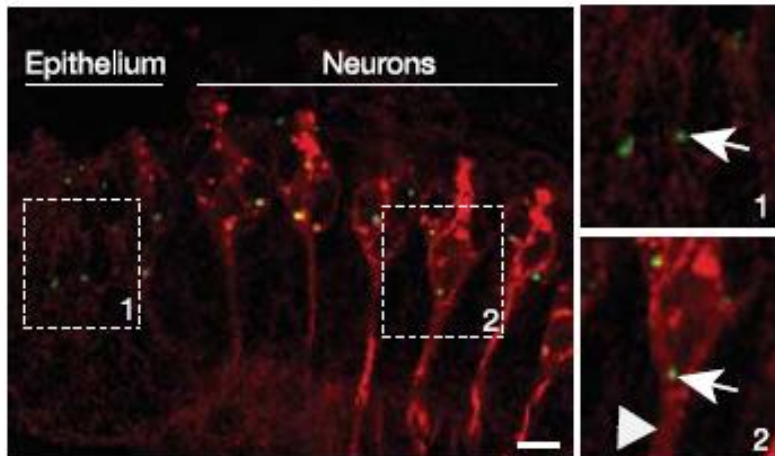
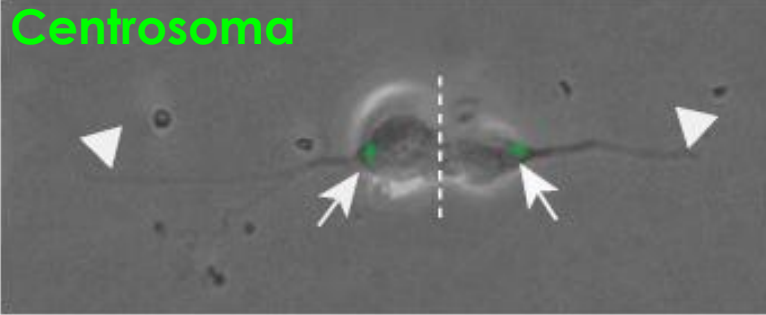


Centrosoma
Golgi
Endosomas

Componentes celulares y axonogénesis

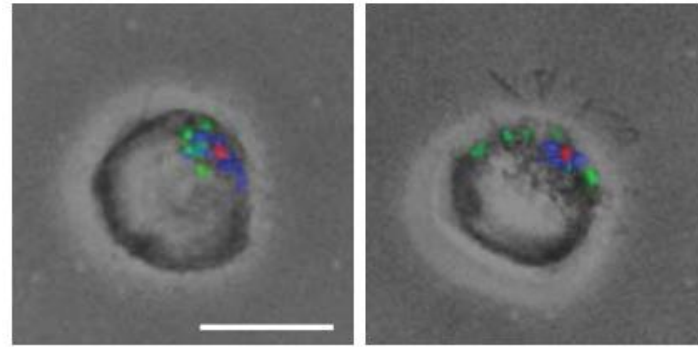
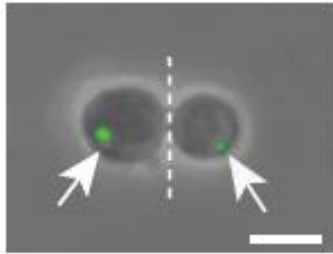


Centrosoma
Golgi
Endosomas

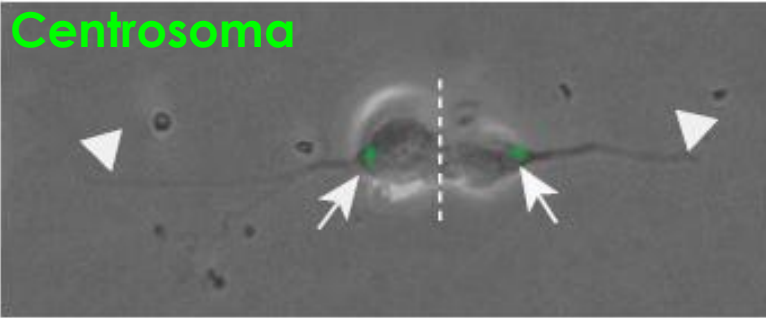


Calderón de Anda et al., 2005

Componentes celulares y axonogénesis

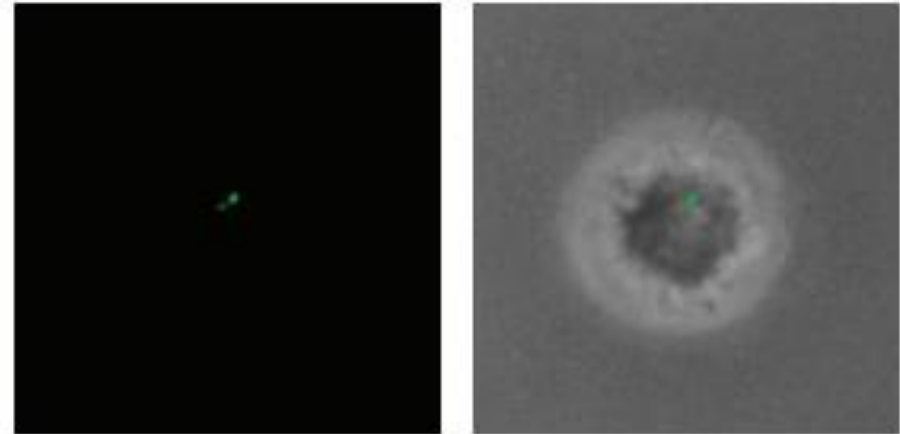
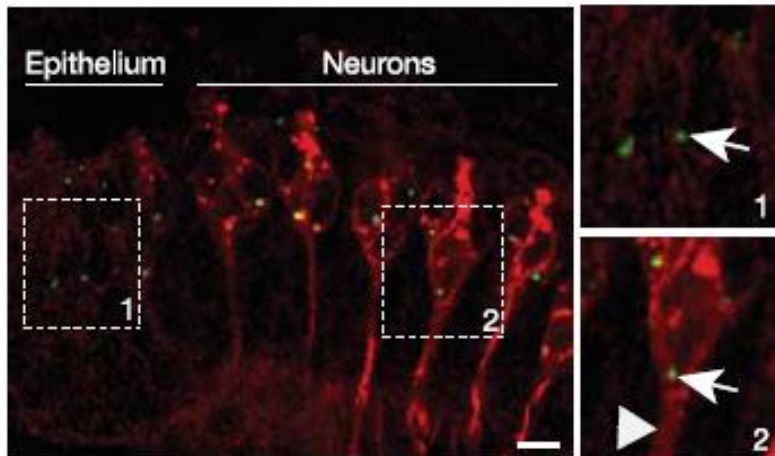


Centrosoma
Golgi
Endosomas



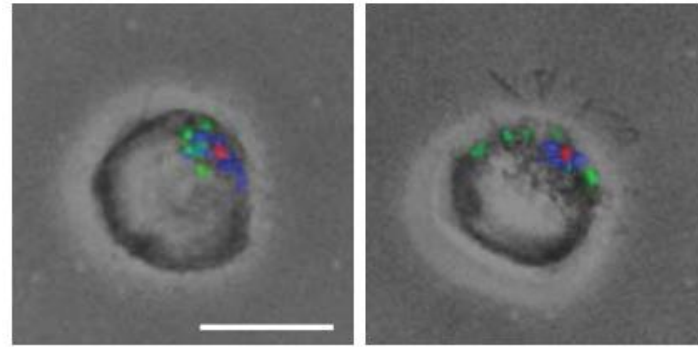
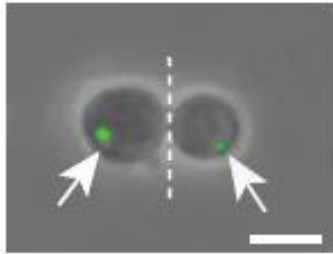
~~Microtúbulos
Golgi/endosomas
Centrosoma~~

} ~~Axón~~

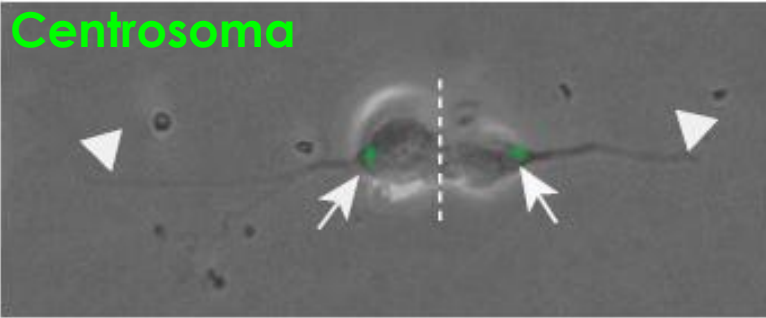


Calderón de Anda et al., 2005

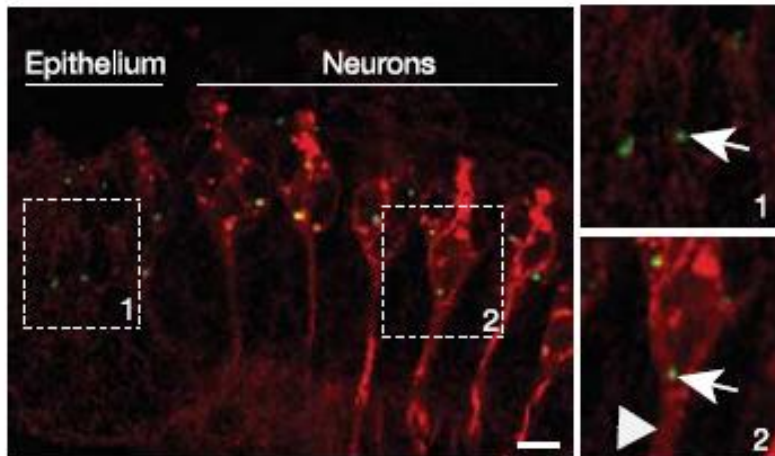
Componentes celulares y axonogénesis



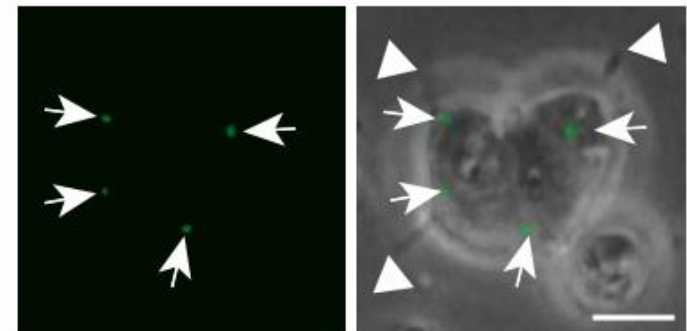
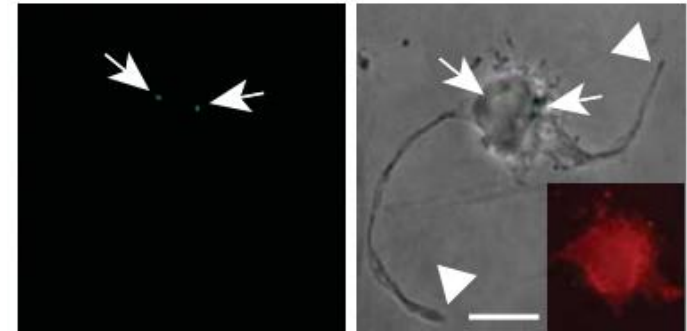
Centrosoma
Golgi
Endosomas



~~Micotúbulos
Golgi/endosomas
Centrosoma~~ } ~~Axón~~

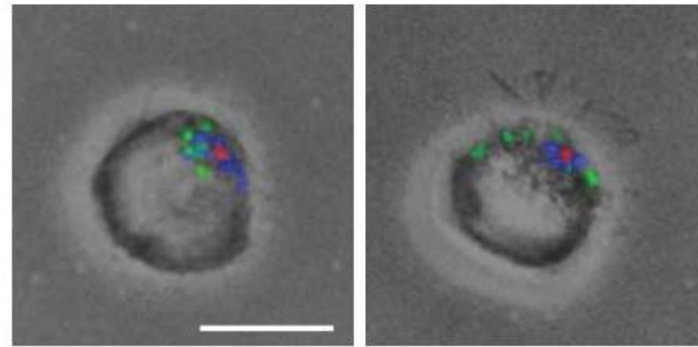
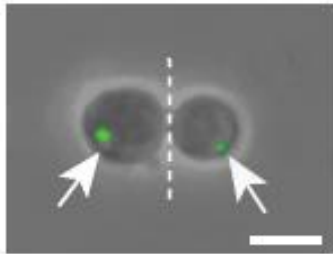


Más de un centrosoma

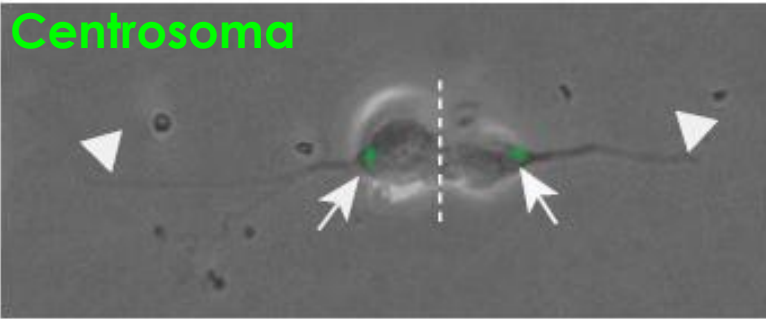


Calderón de Anda et al., 2005

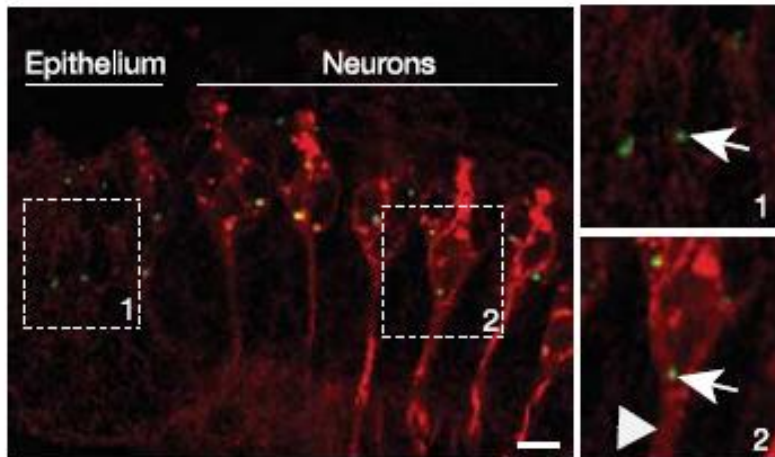
Componentes celulares y axonogénesis



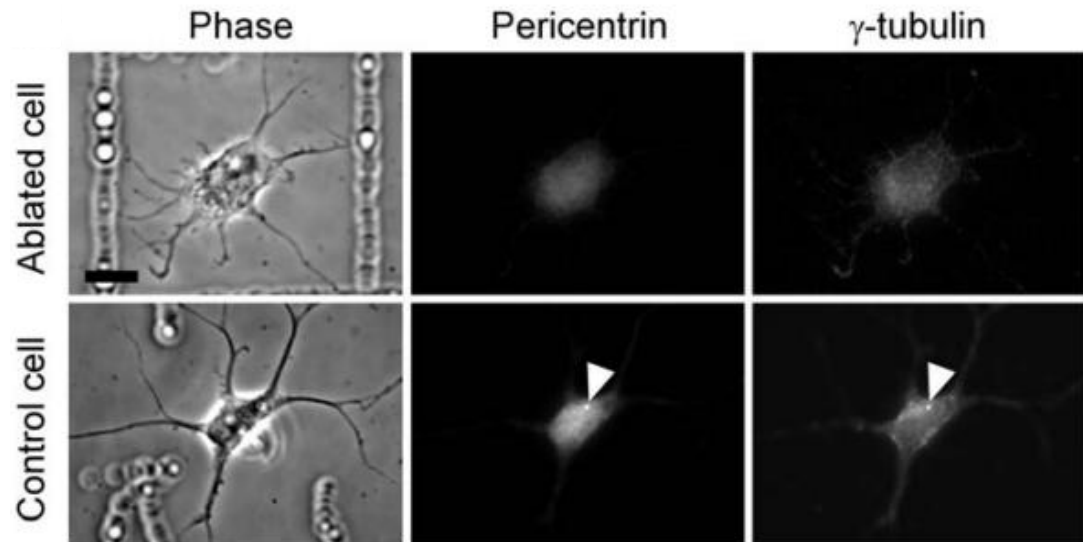
Centrosoma
Golgi
Endosomas



~~Microtúbulos
Golgi/endosomas
Centrosoma~~ } ~~Axón~~

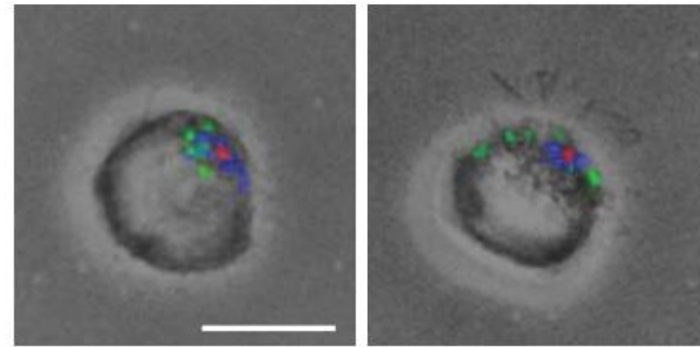
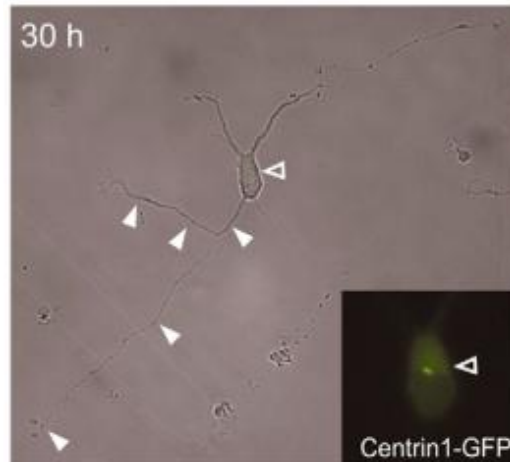
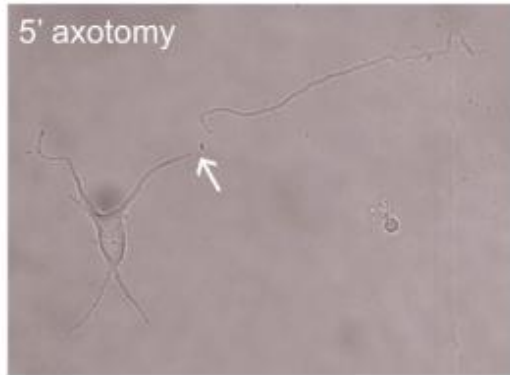
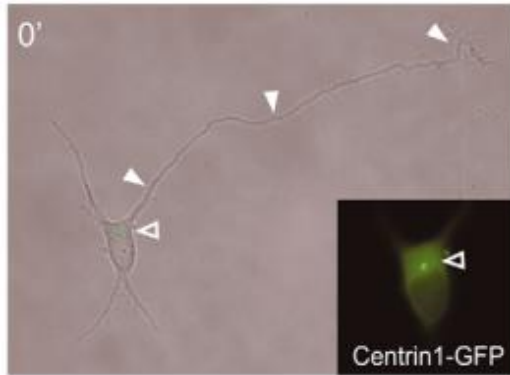


Calderón de Anda et al., 2005



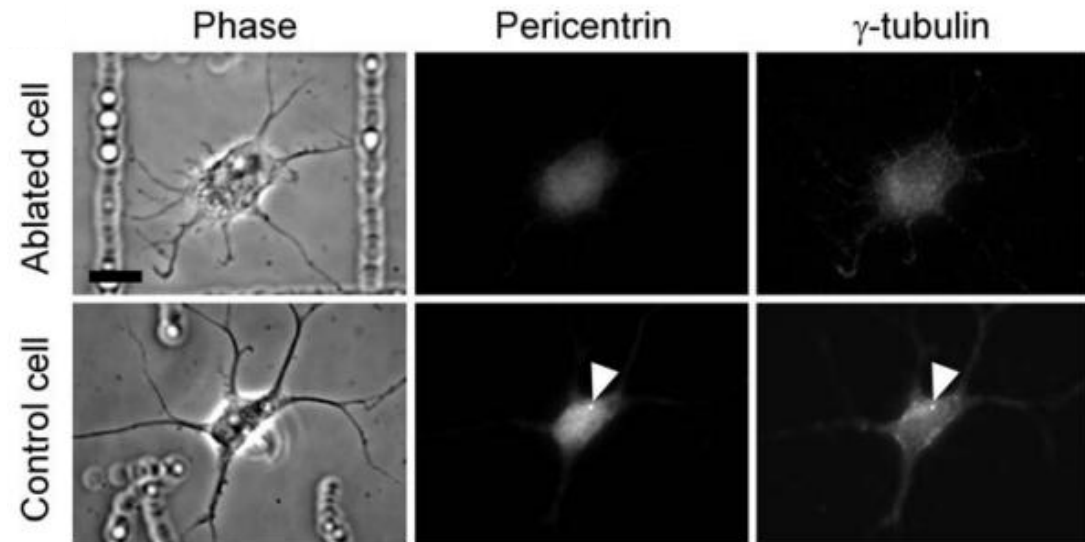
Stiess et al., 2010

Componentes celulares y axonogénesis



Centrosoma
Golgi
Endosomas

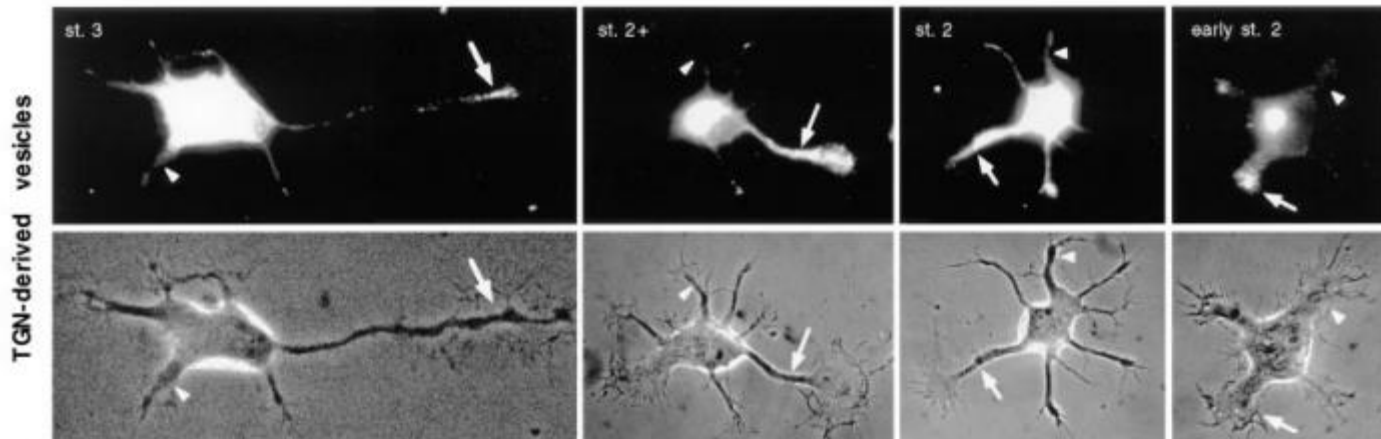
~~Microtúbulos
Golgi/endosomas
Centrosoma~~ } ~~Axón~~



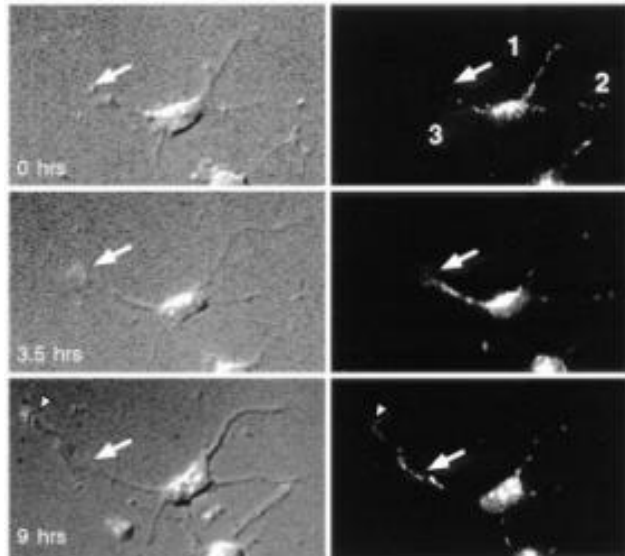
Stiess et al., 2010

Componentes celulares y axonogénesis

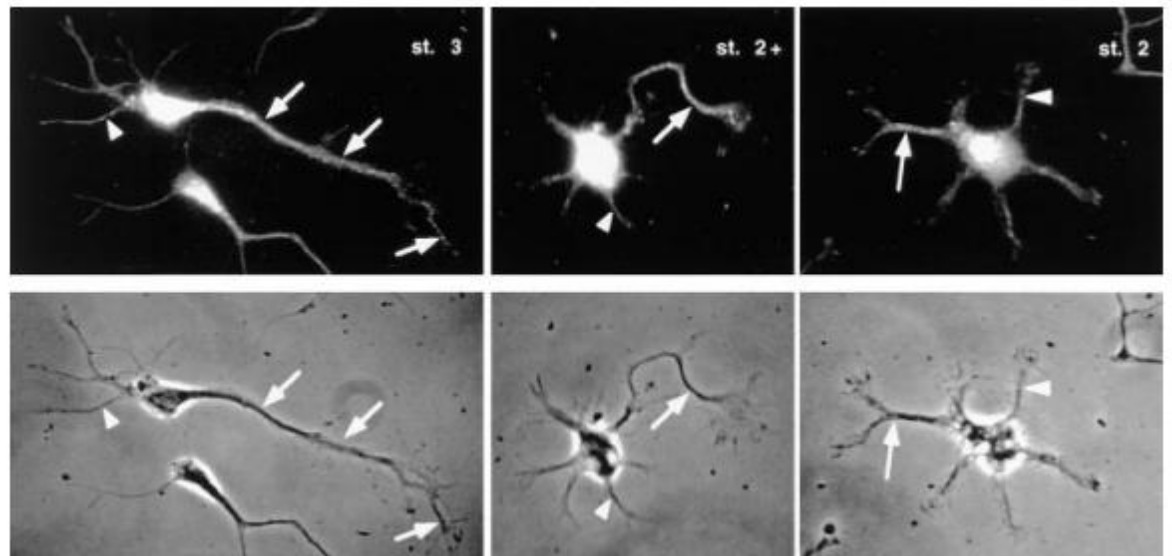
Vesículas del Golgi



Mitocondrias

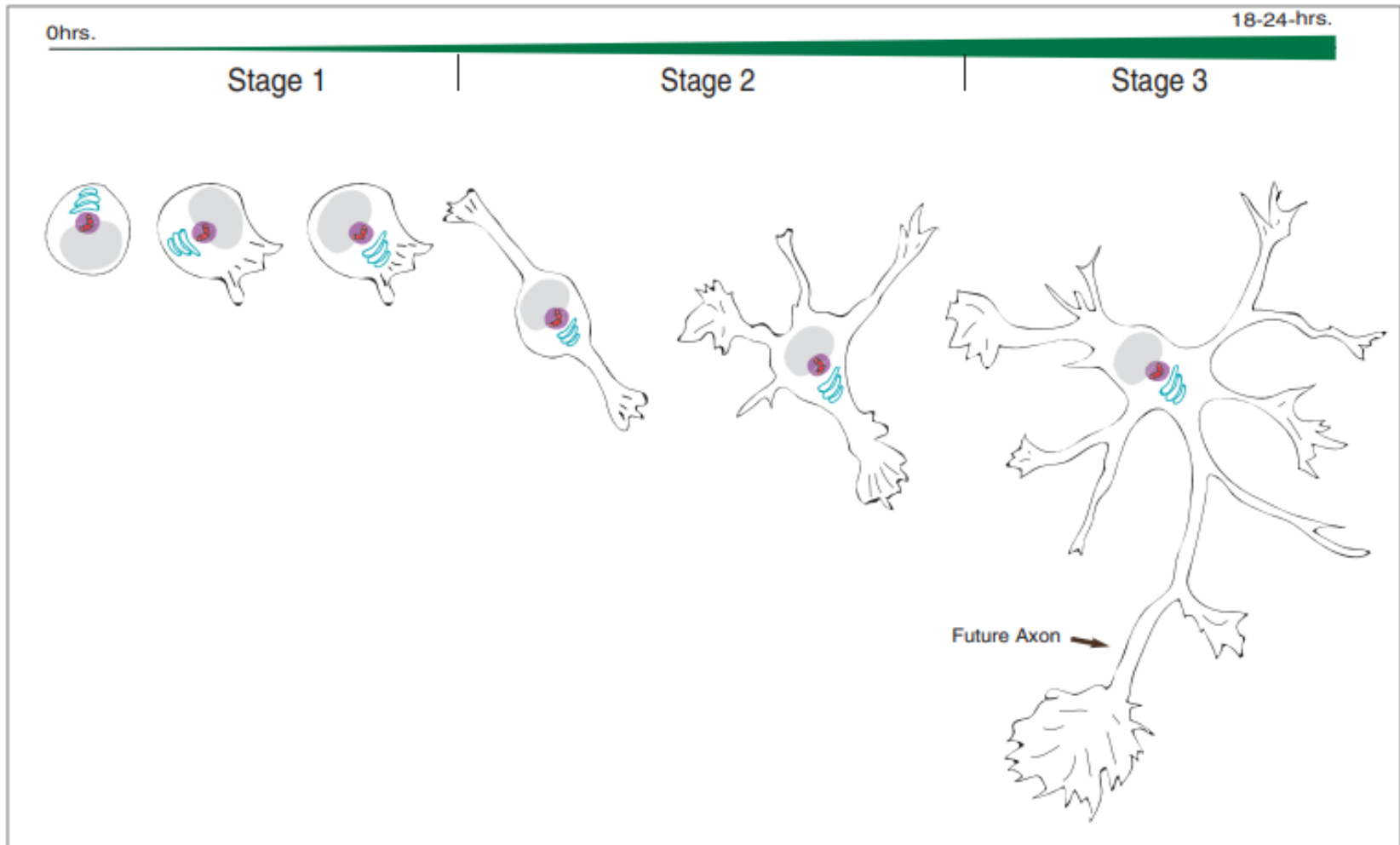


Peroxisomas



Bradke & Dotti, 1997

Componentes celulares y axonogénesis



Centrosome (pair of Centrioles surrounded by Pericentriolar Material (PCM))

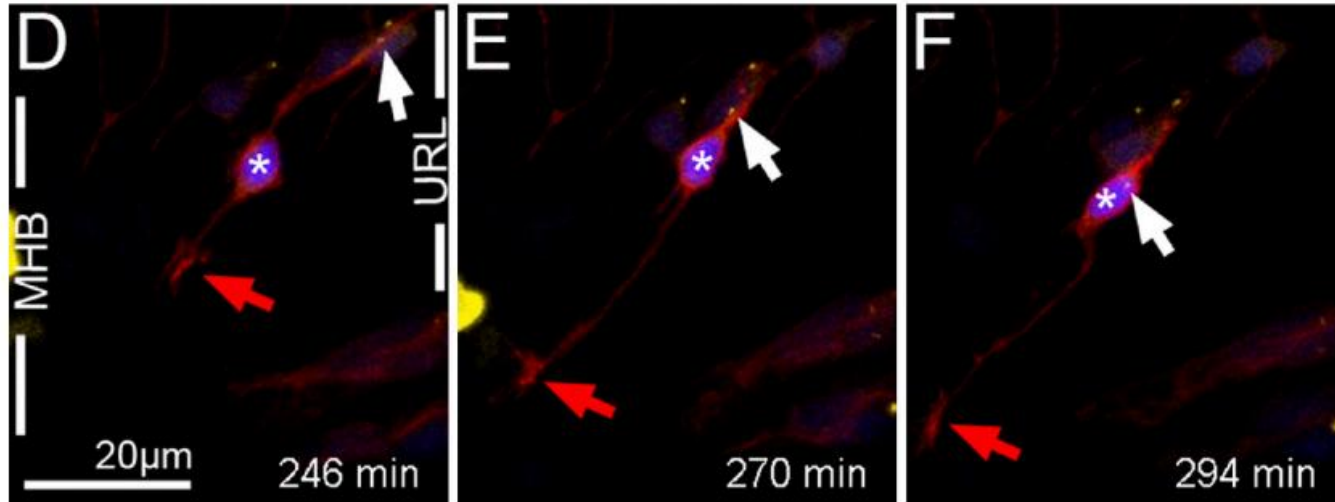


Golgi Tubules



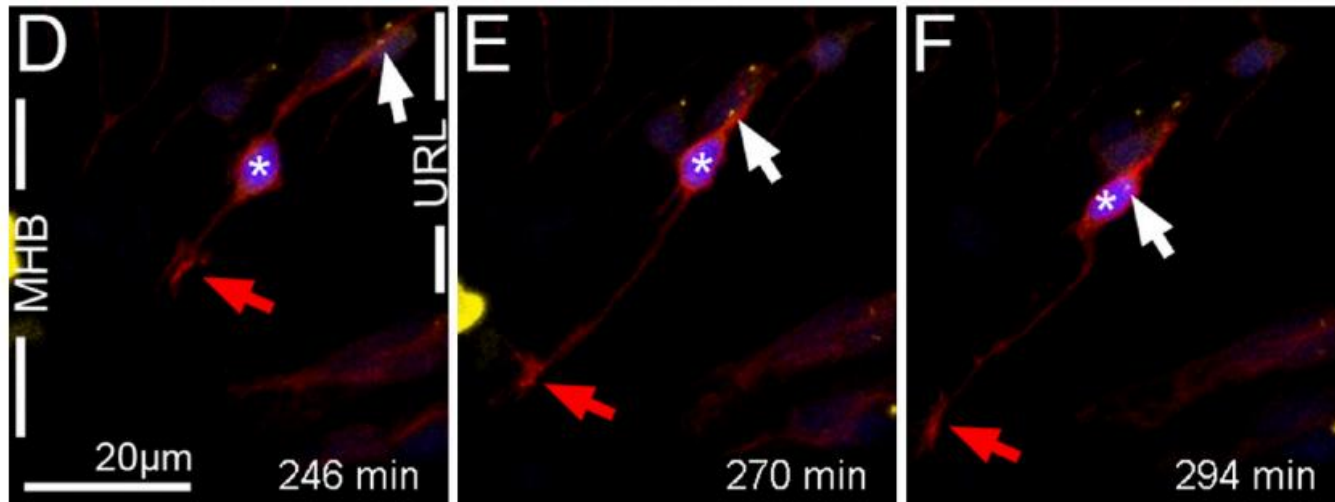
Nucleus

Componentes celulares y axonogénesis

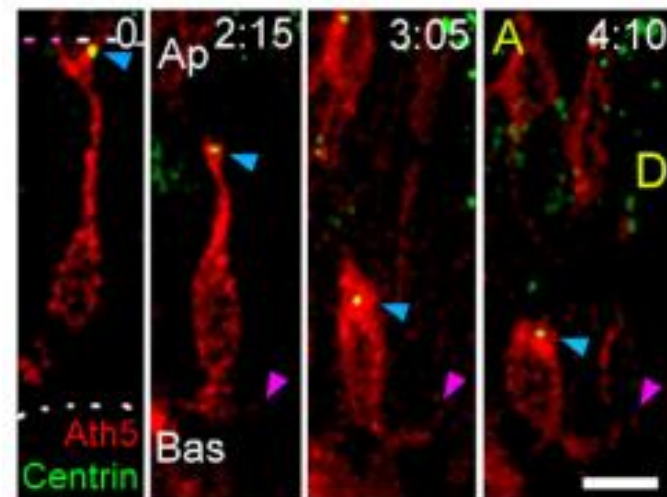
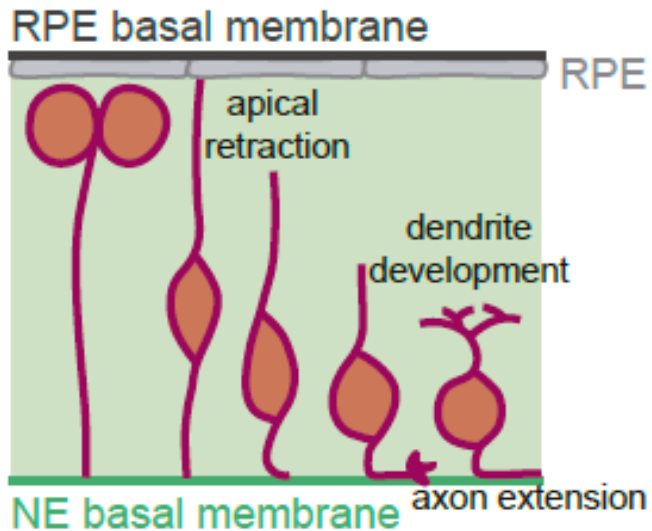


Distel et al., 2010

Componentes celulares y axonogénesis

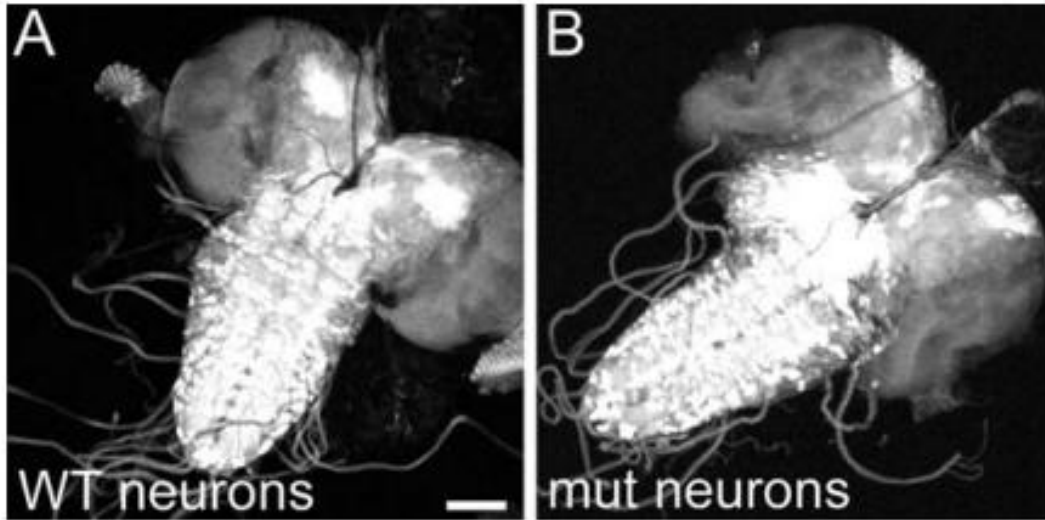


Distel et al., 2010

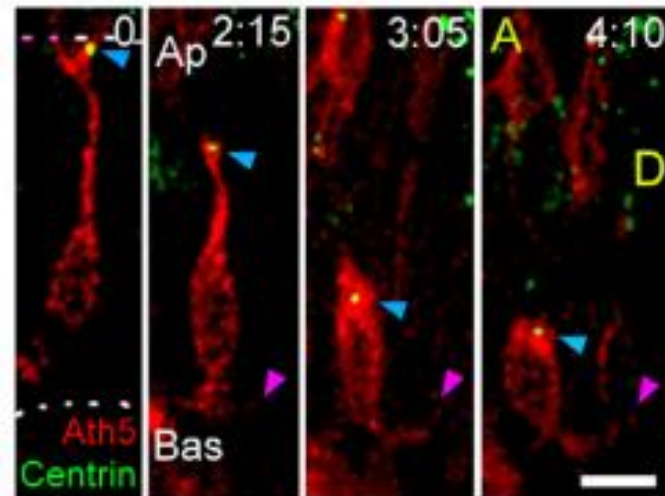
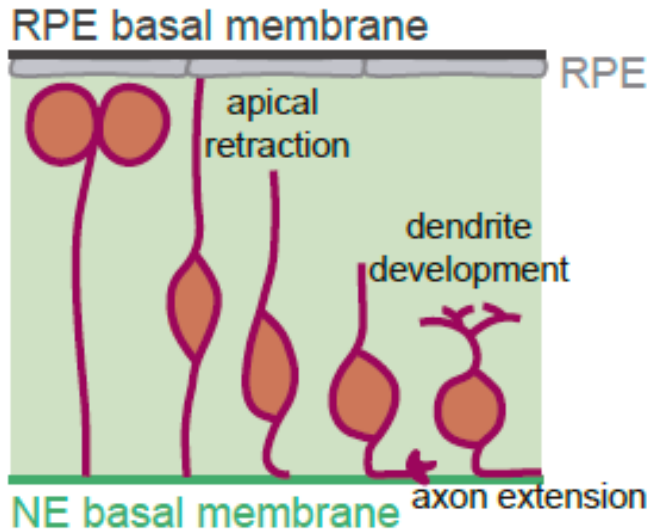


Zolessi et al., 2006

Componentes celulares y axonogénesis

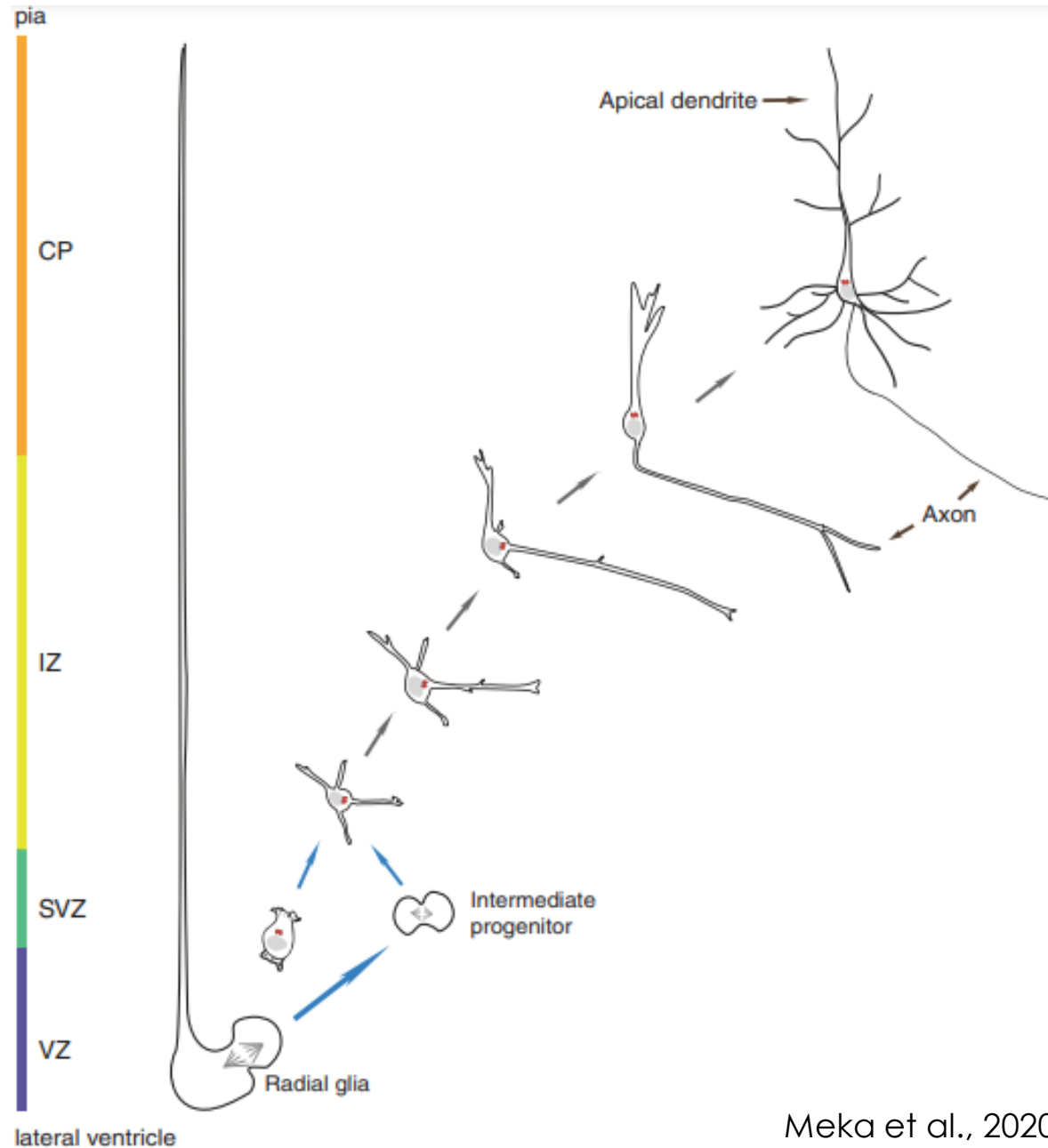


Basto et al., 2006

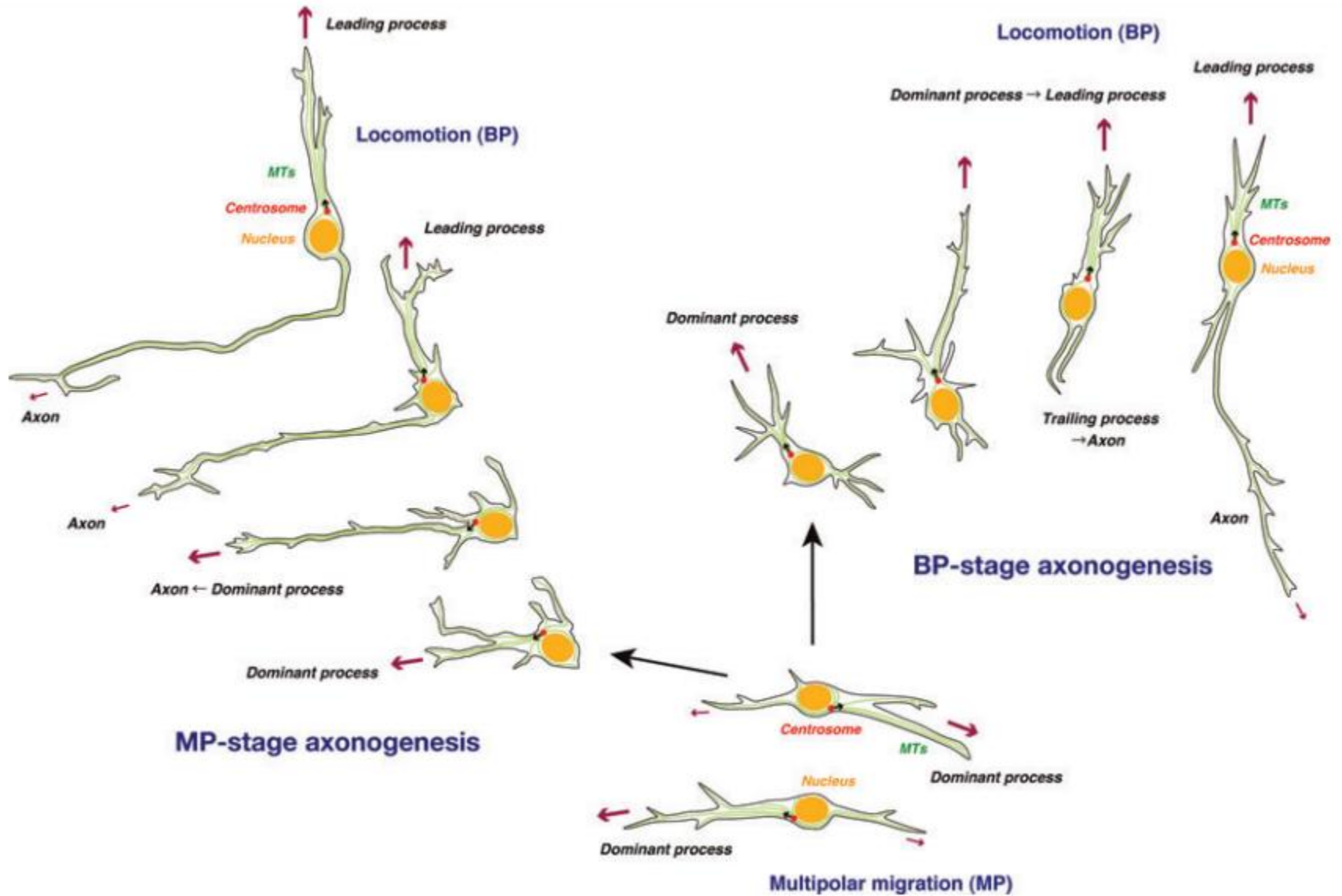


Zolessi et al., 2006

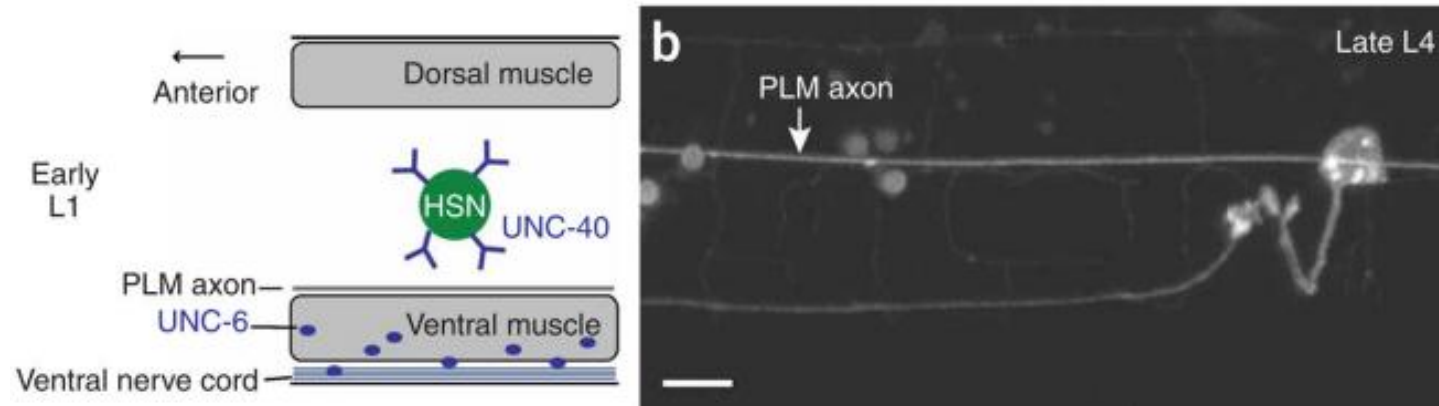
Componentes celulares y axonogénesis



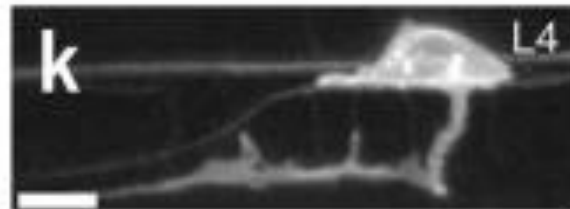
Componentes celulares y axonogénesis



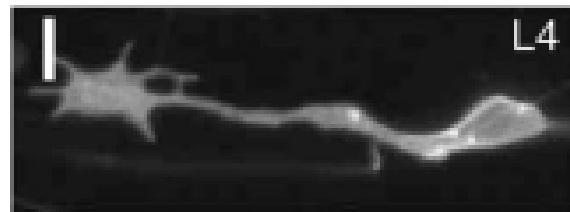
Interacciones celulares y axonogénesis



Adler et al., 2006

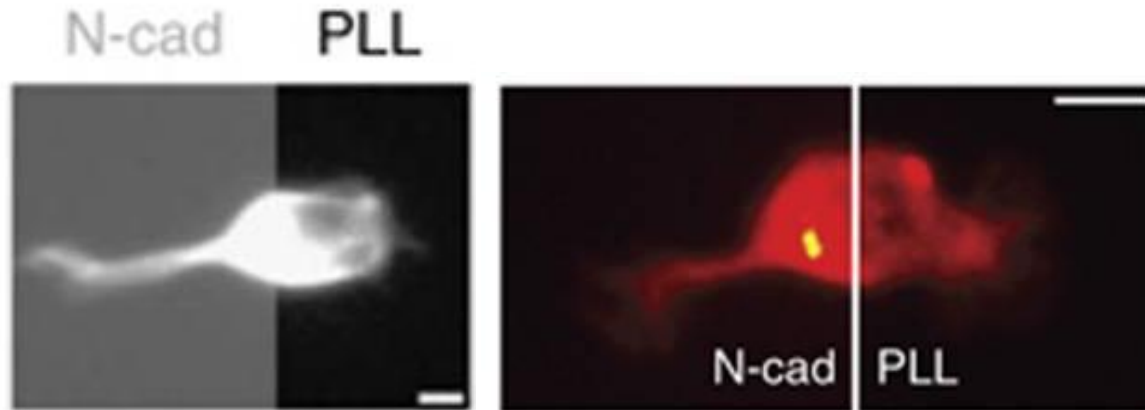
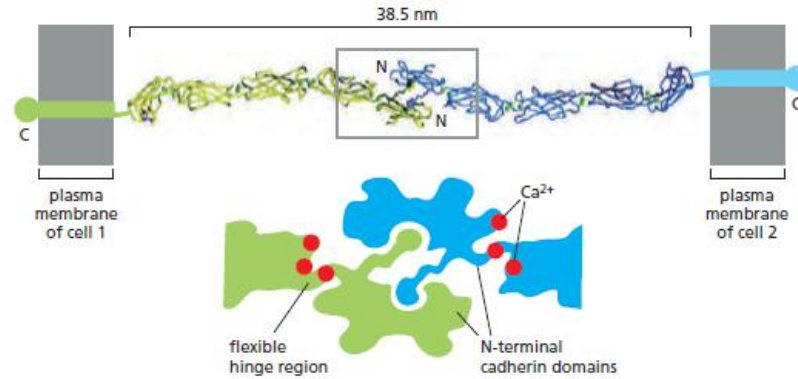


Wild type

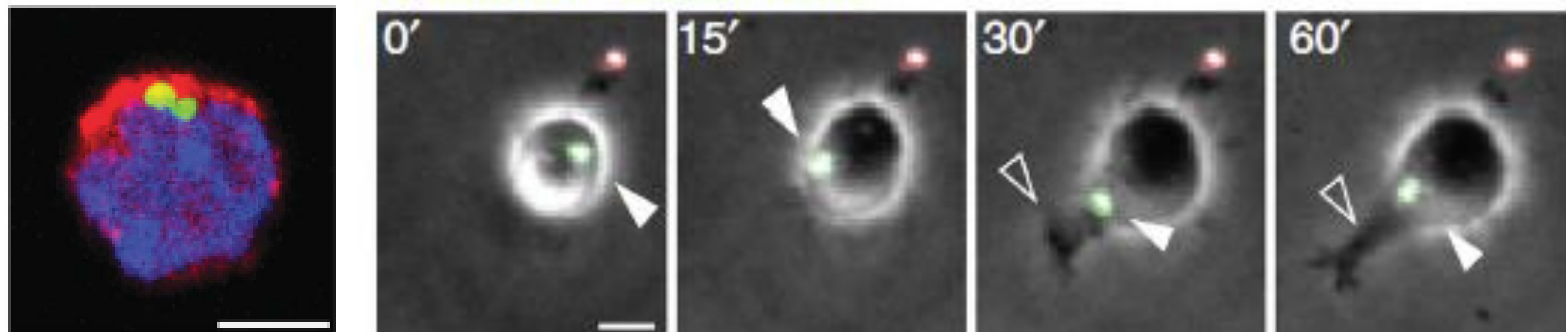


unc-6

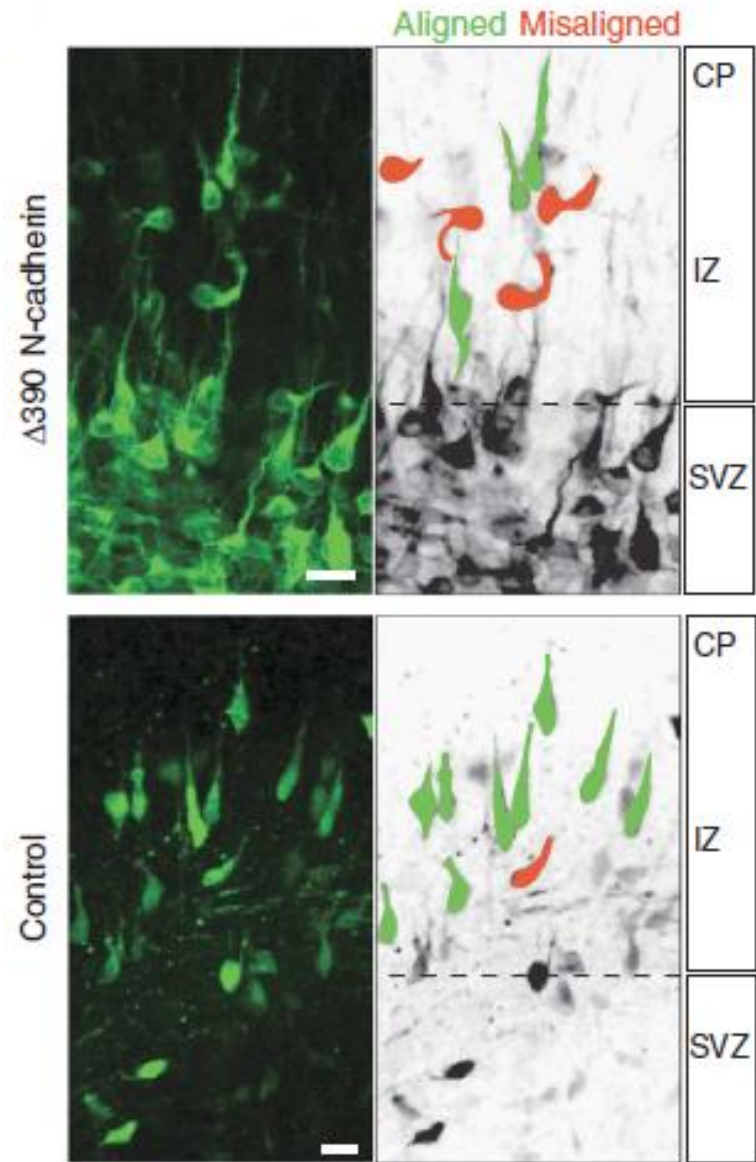
Interacciones celulares y axonogénesis



N-cadherin-coated bead

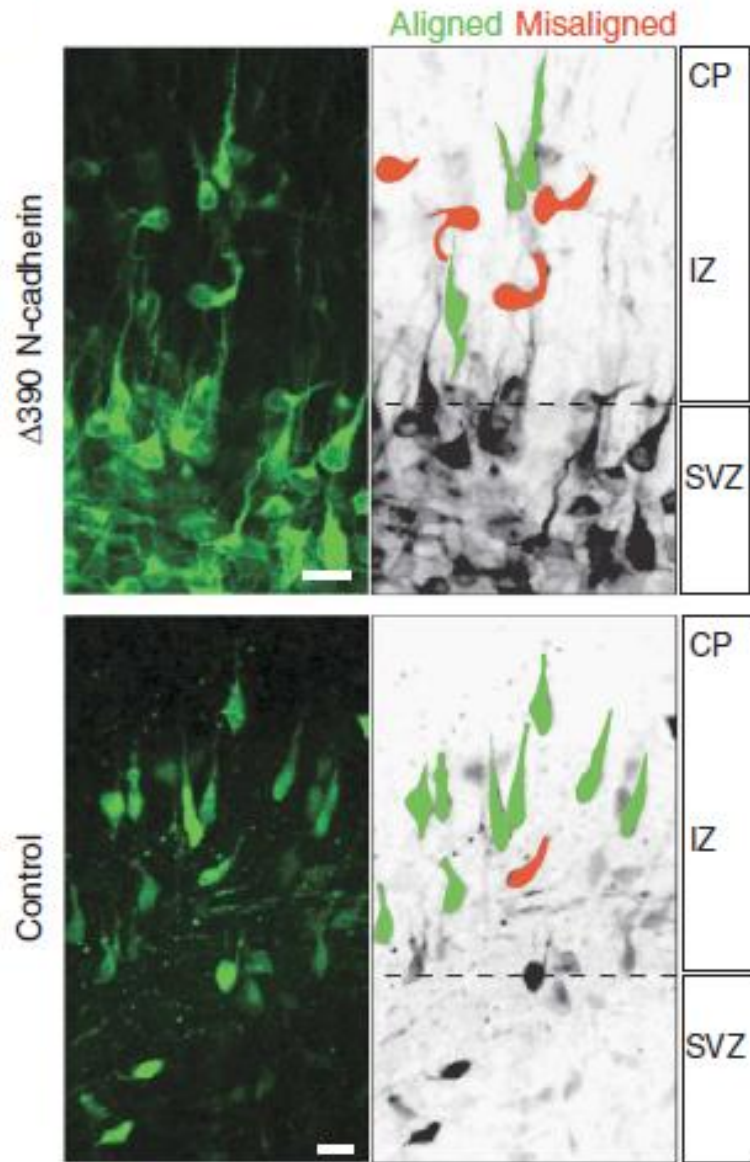


Interacciones celulares y axonogénesis



Gärtner et al., 2012

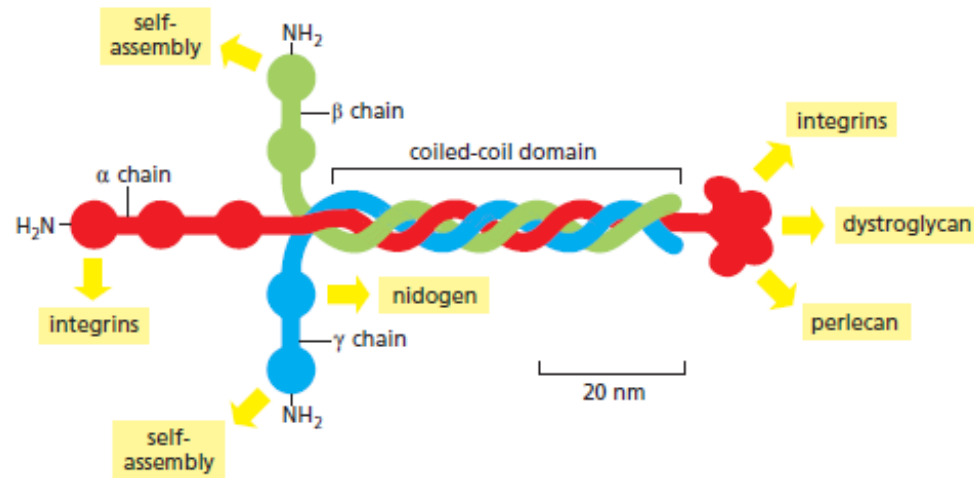
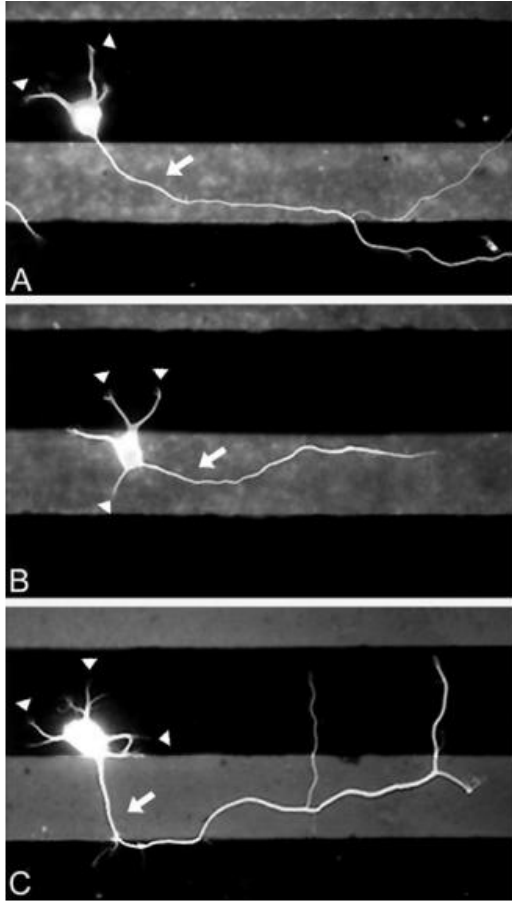
Interacciones celulares y axonogénesis



La N-cadherina es un determinante del sitio donde surge la primera asimetría

Interacciones celulares y axonogénesis

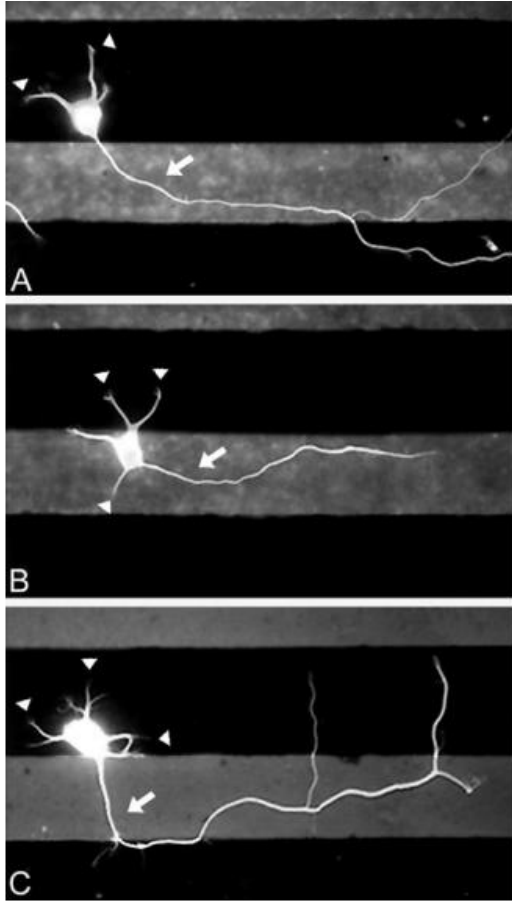
PLL/Laminina



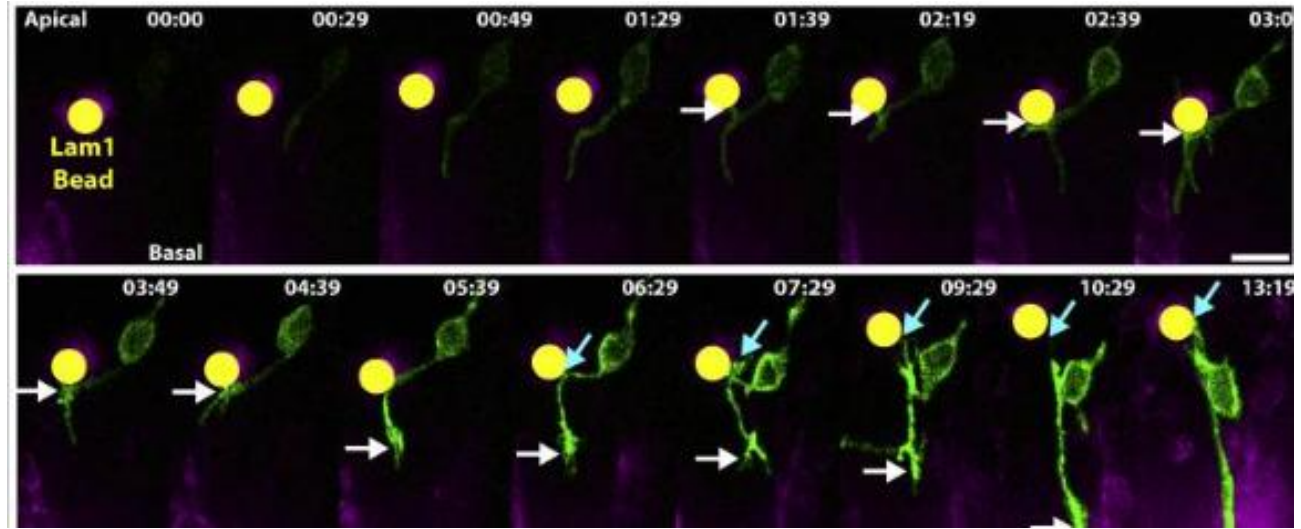
Esch et al., 1999

Interacciones celulares y axonogénesis

PLL/Laminina



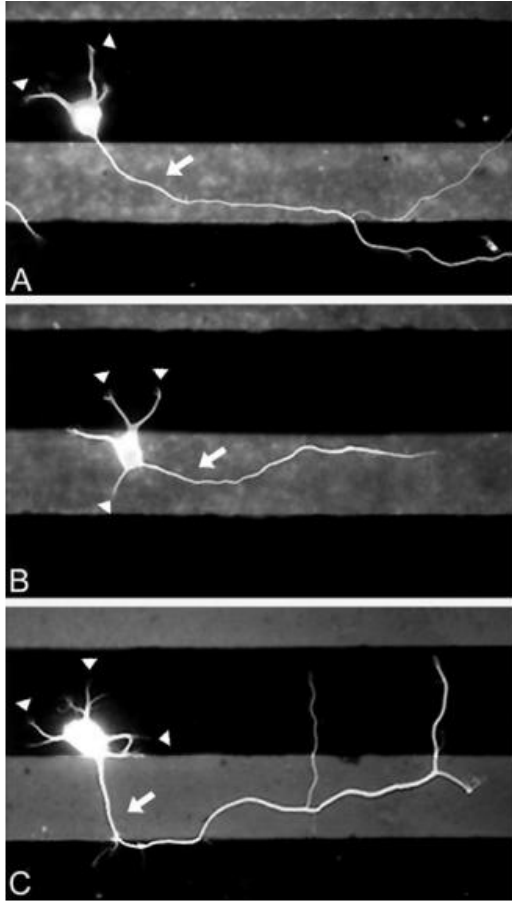
Esch et al., 1999



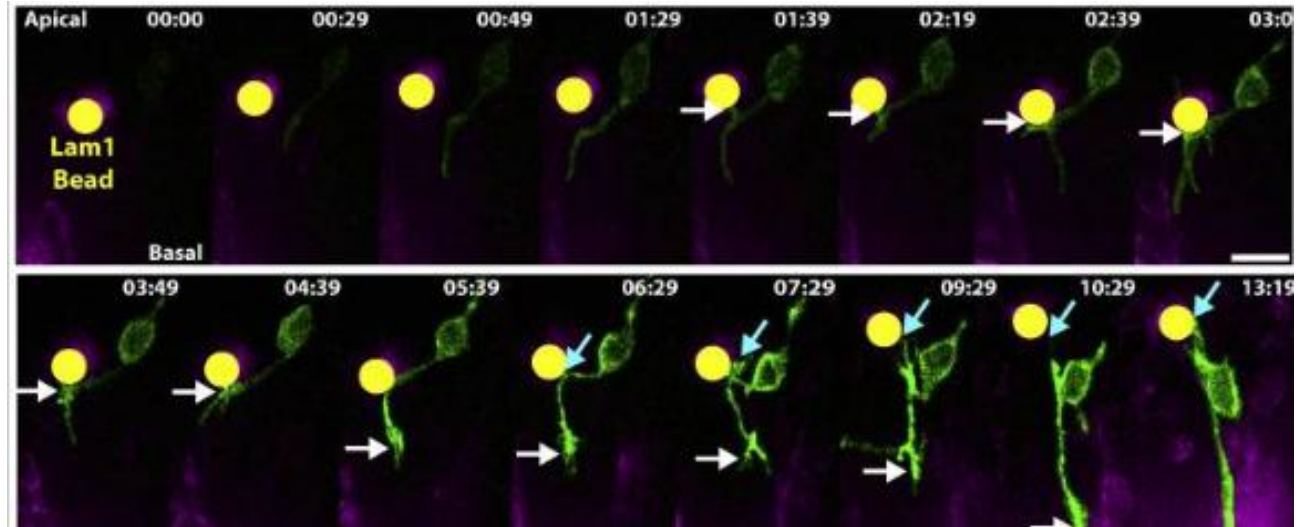
Randlett et al., 2011

Interacciones celulares y axonogénesis

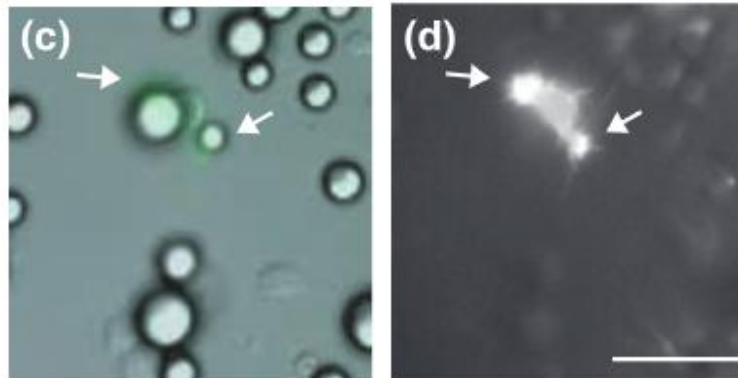
PLL/Laminina



Esch et al., 1999



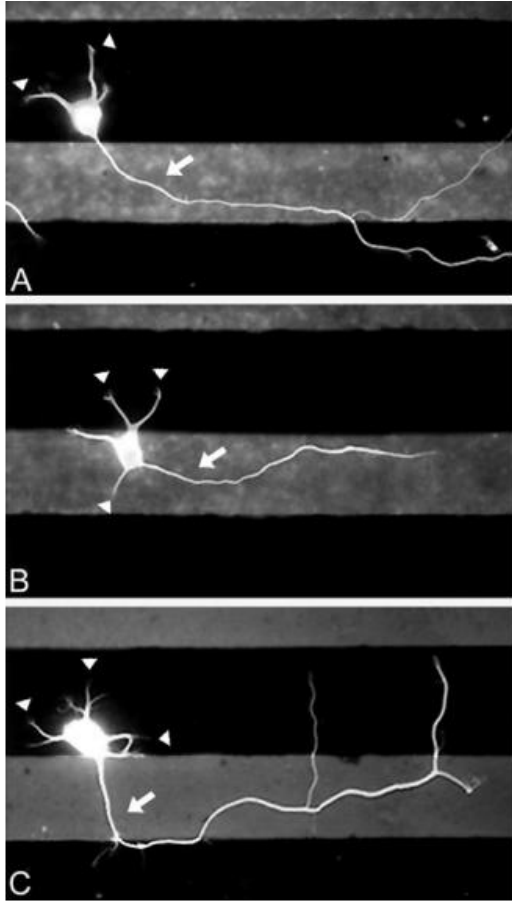
Randlett et al., 2011



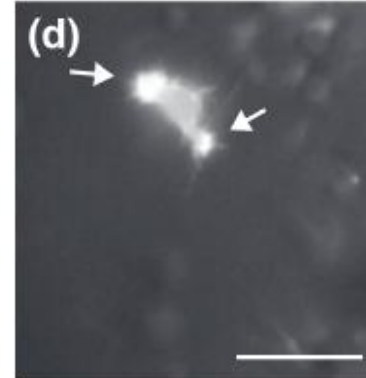
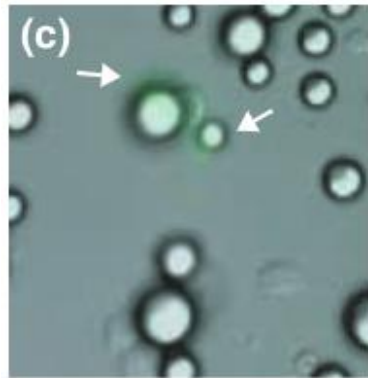
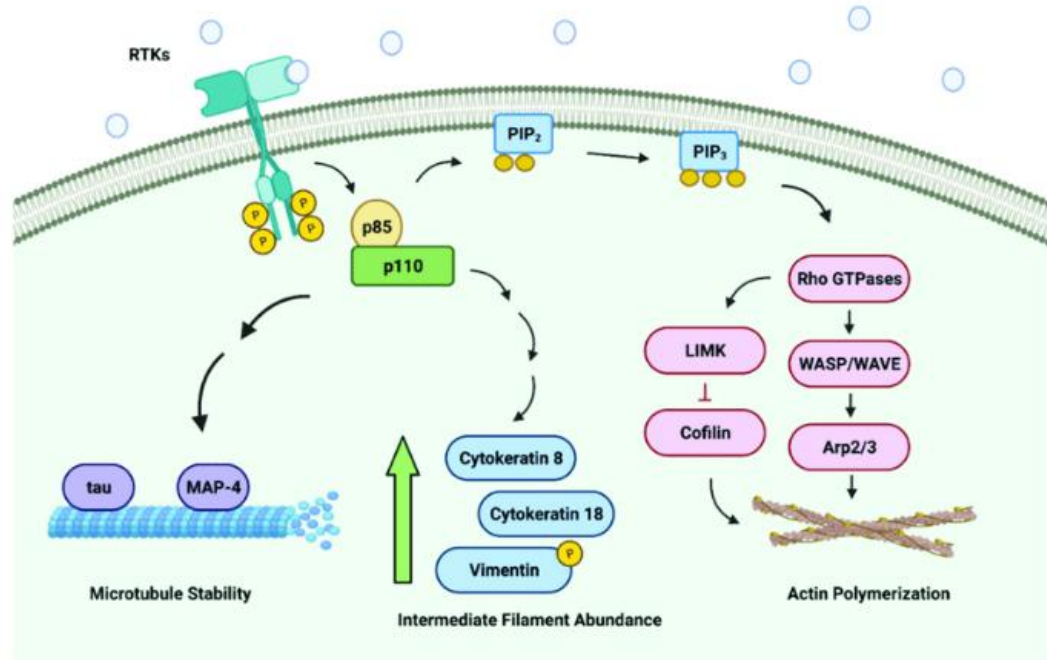
Ménager et al., 2004

Interacciones celulares y axonogénesis

PLL/Laminina

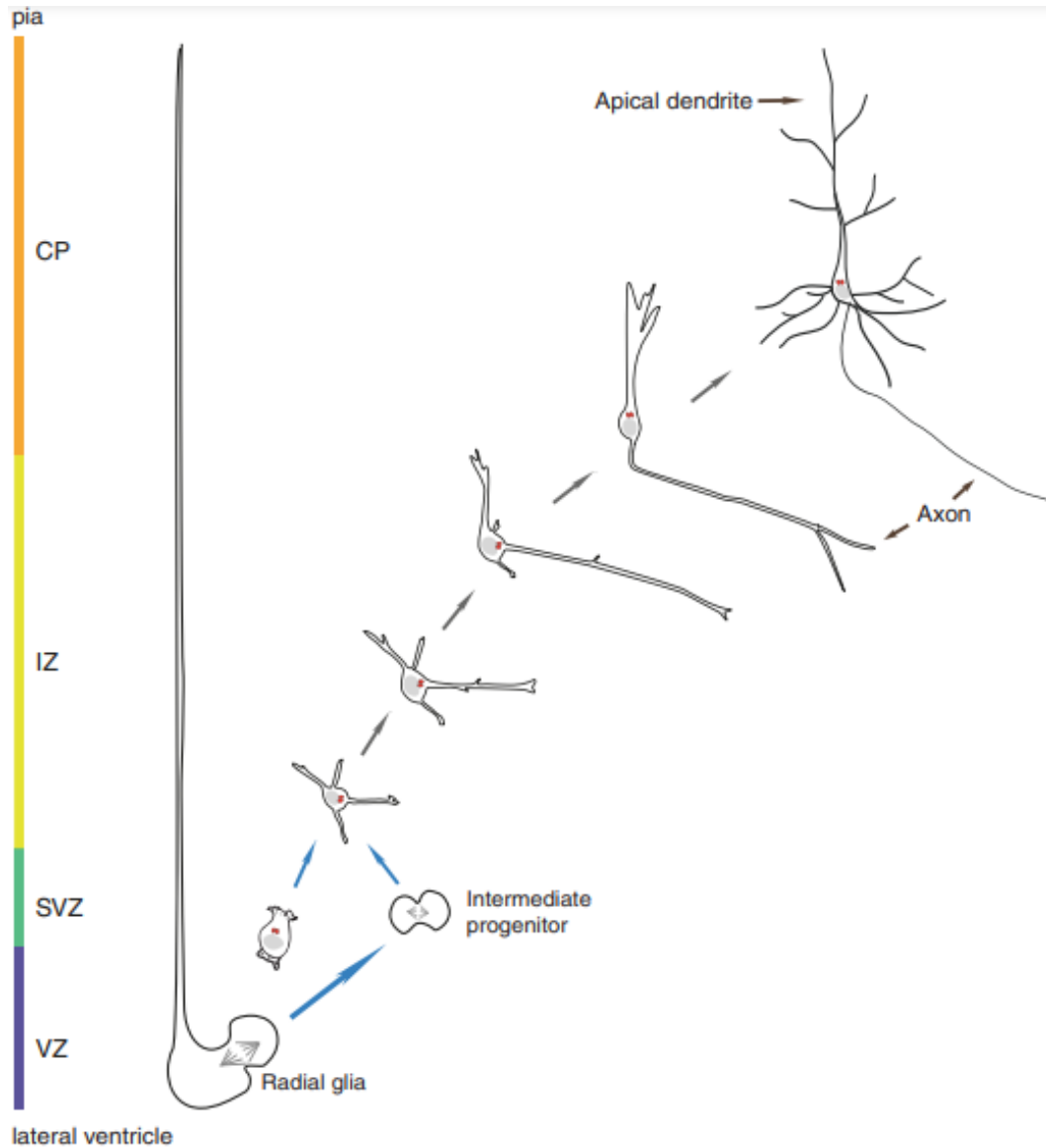


Esch et al., 1999

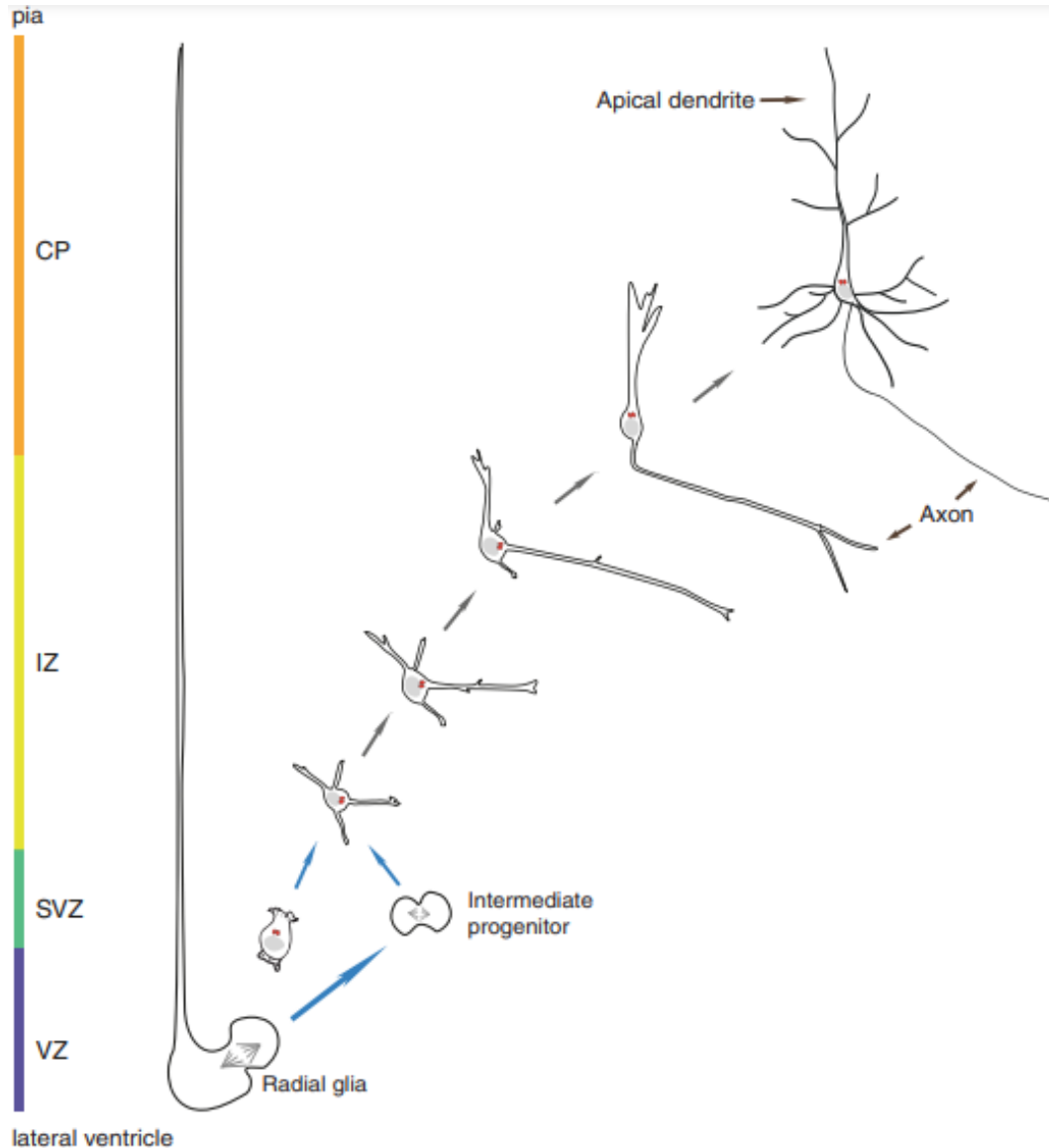


Ménager et al., 2004

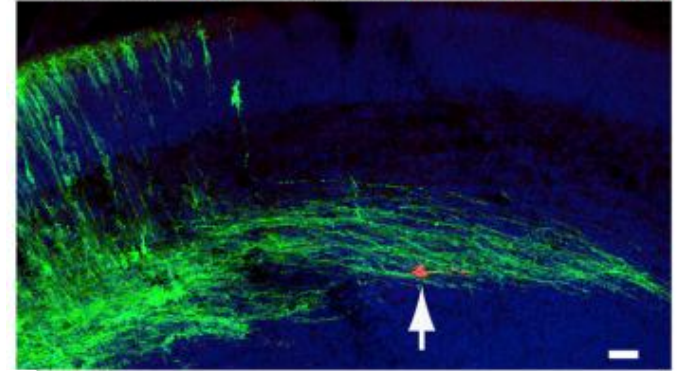
Interacciones celulares y axonogénesis



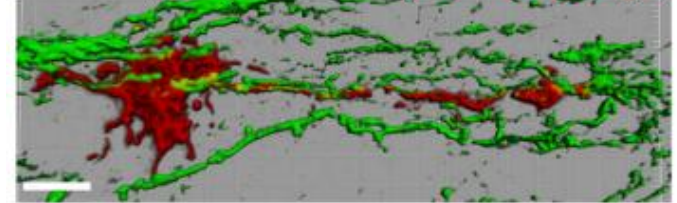
Interacciones celulares y axonogénesis



1st EP (GFP) -> 2nd EP (Kusabira Orange)

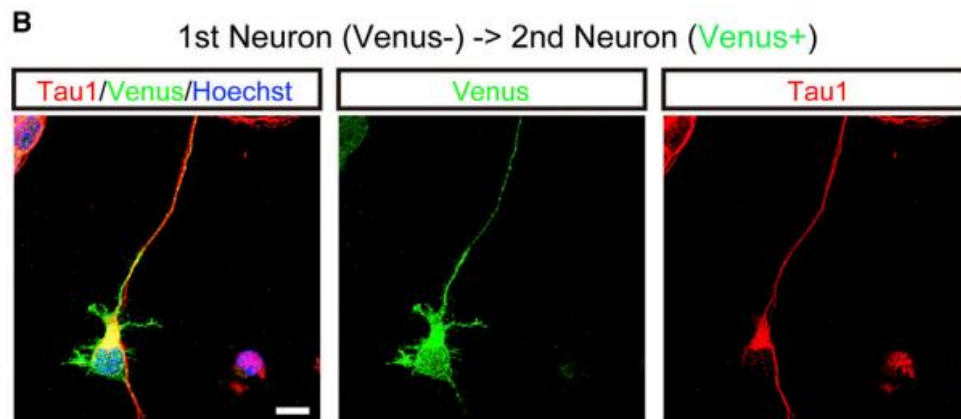
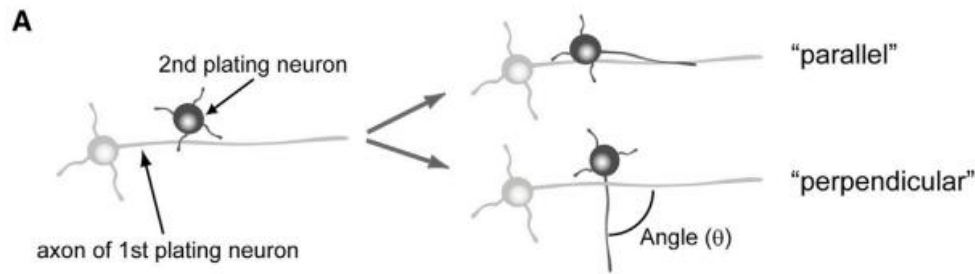


1st EP (GFP) -> 2nd EP (Kusabira Orange)

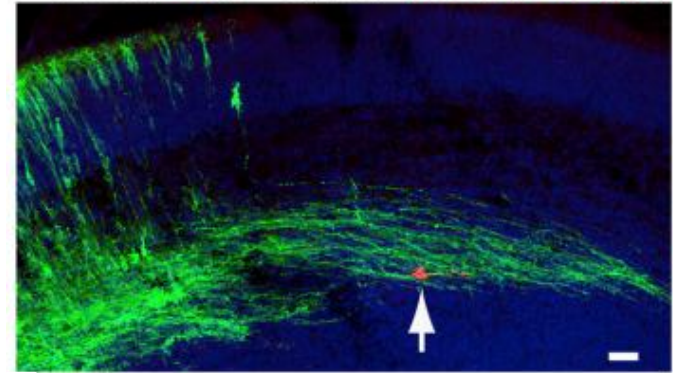


Namba et al., 2004

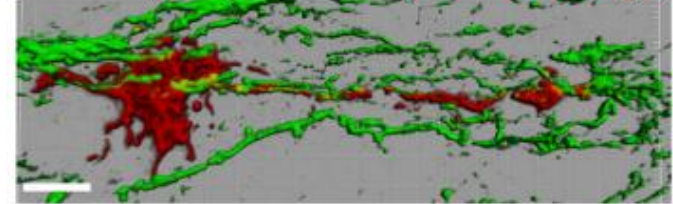
Interacciones celulares y axonogénesis



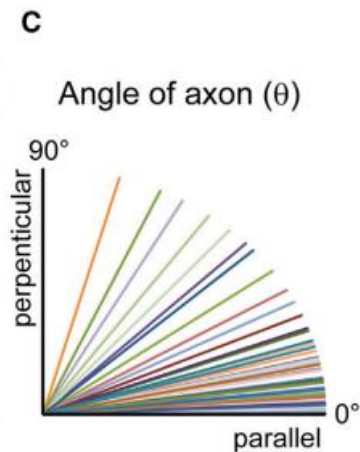
1st EP (GFP) -> 2nd EP (Kusabira Orange)



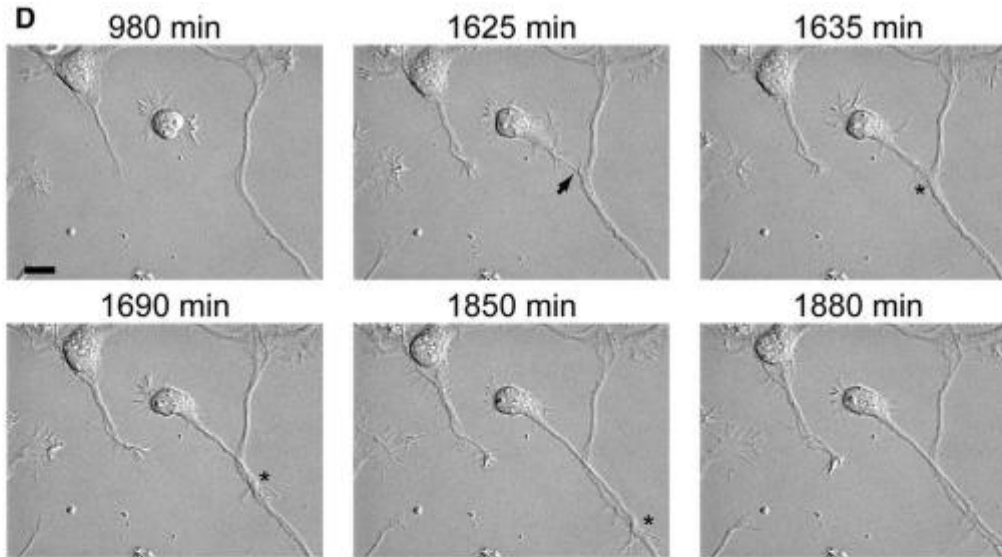
1st EP (GFP) -> 2nd EP (Kusabira Orange)



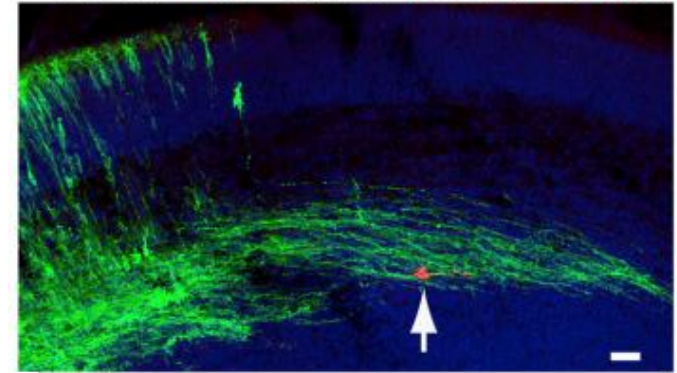
Namba et al., 2004



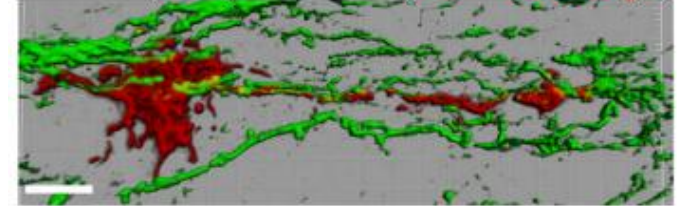
Interacciones celulares y axonogénesis



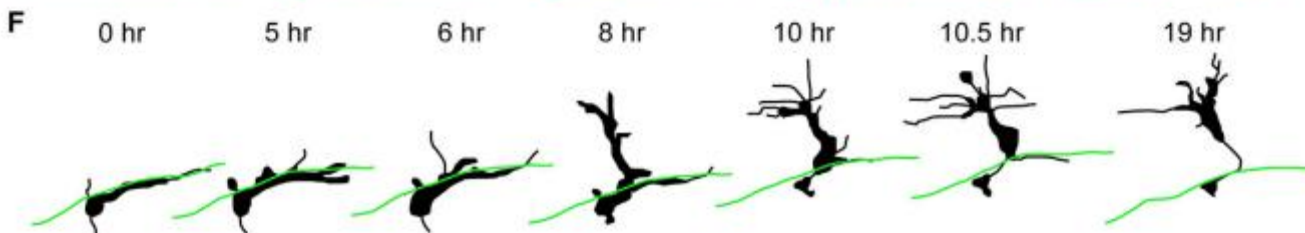
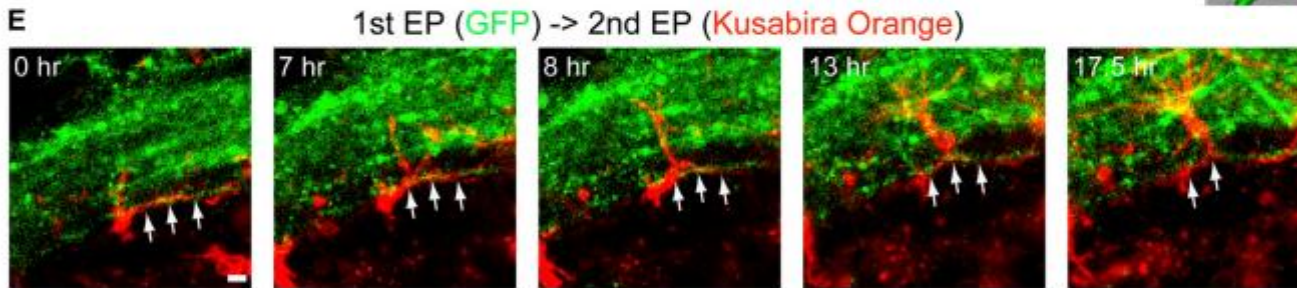
1st EP (GFP) -> 2nd EP (Kusabira Orange)



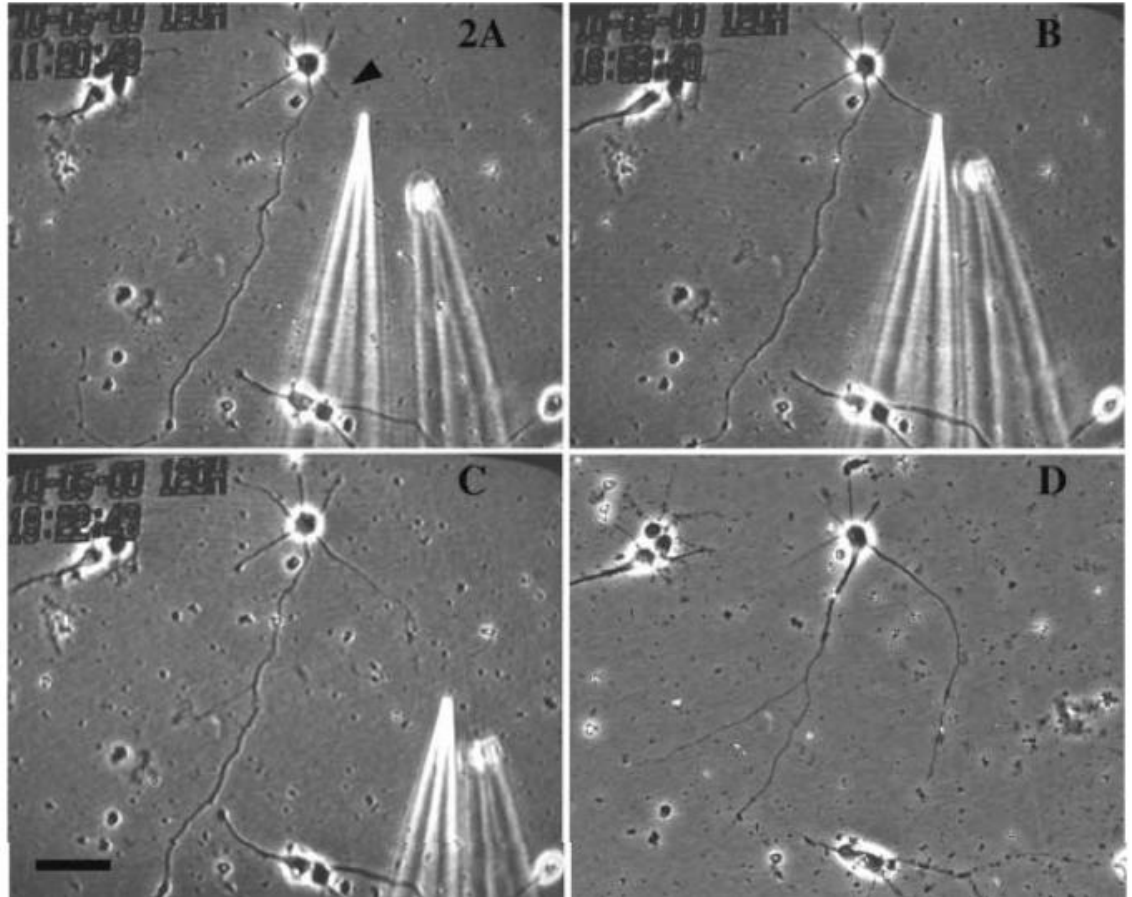
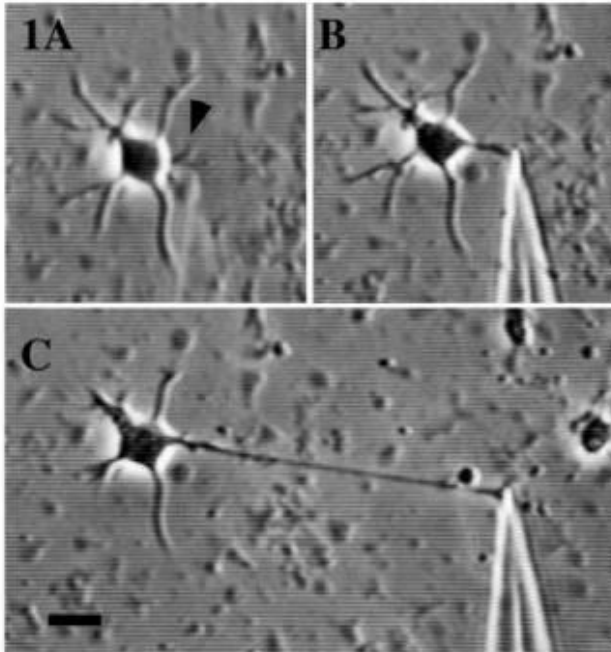
1st EP (GFP) -> 2nd EP (Kusabira Orange)



Namba et al., 2004



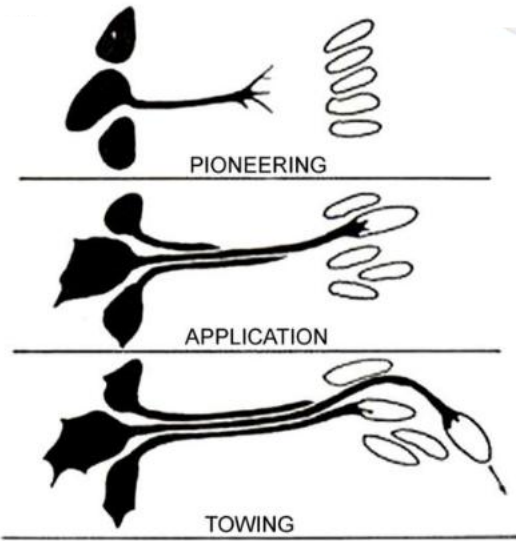
Tensión y axonogénesis



La tensión a la que está sometida una neurita puede ser un determinante de su especificación como axón

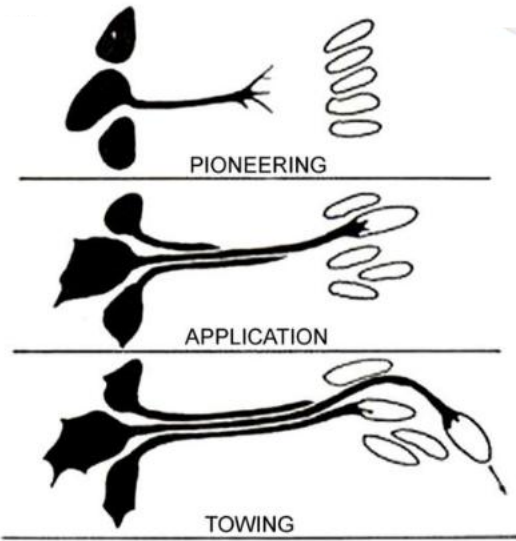
Lamoureux et al., 2002

Crecimiento por estiramiento

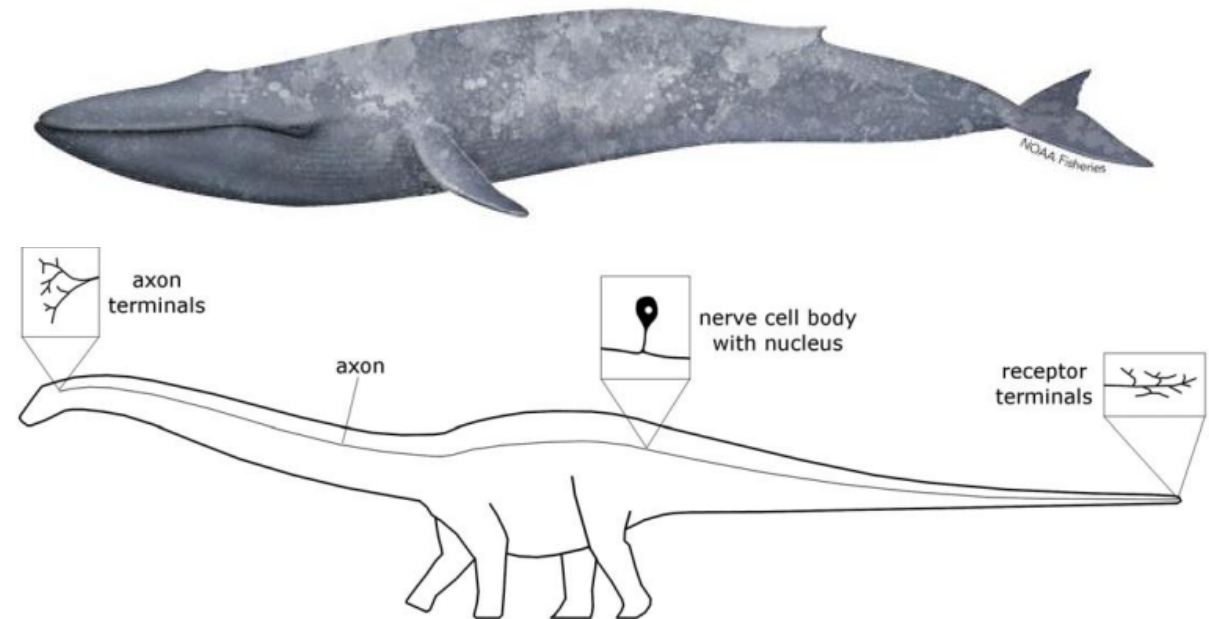
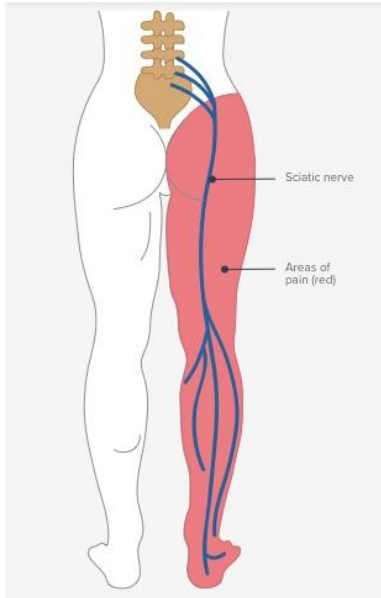


Smith, 2009

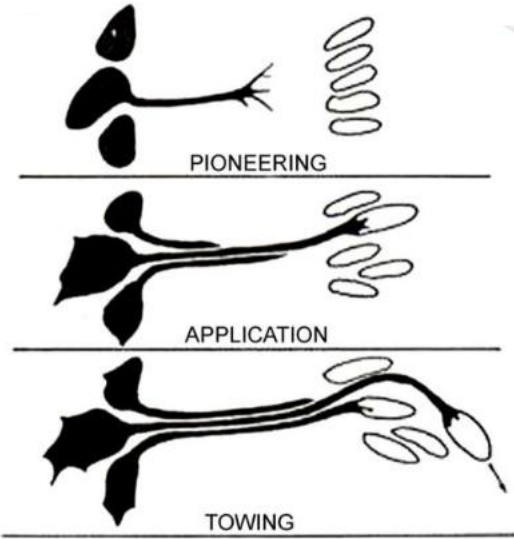
Crecimiento por estiramiento



Smith, 2009



Crecimiento por estiramiento

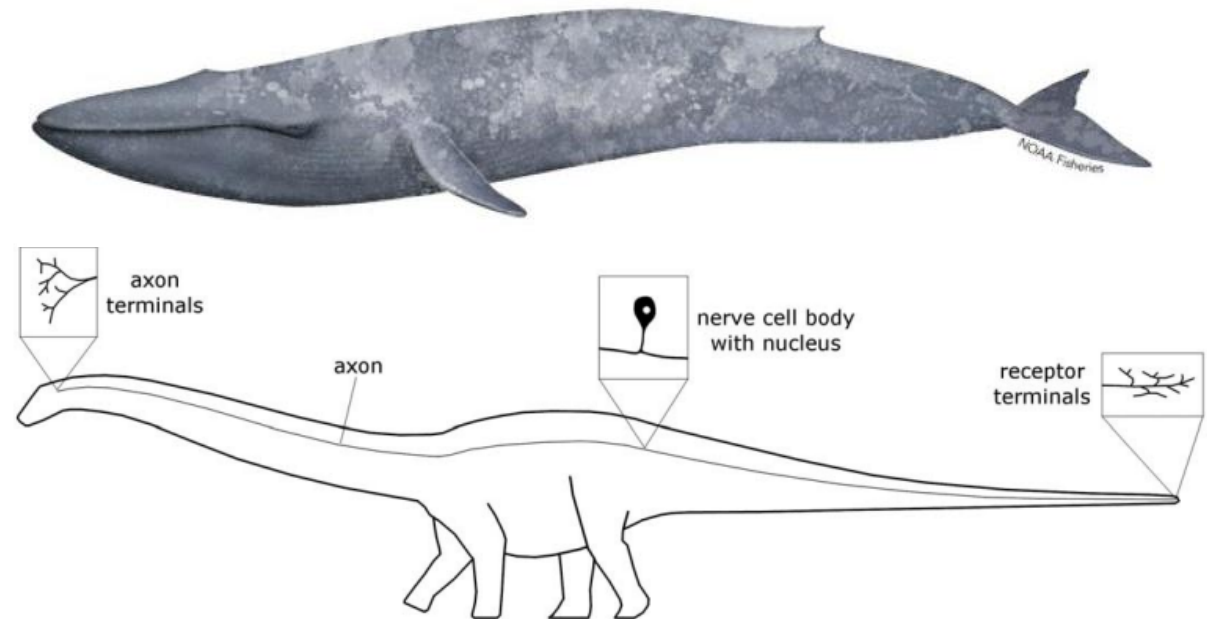
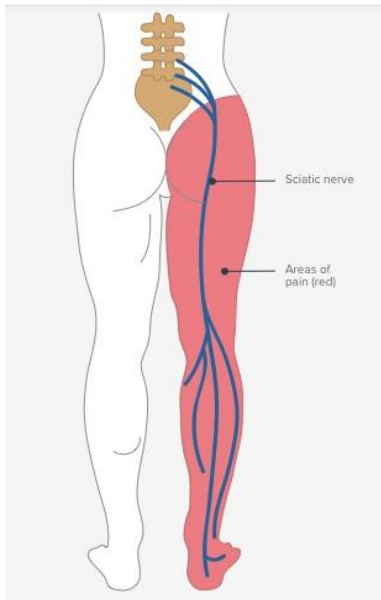


Smith, 2009

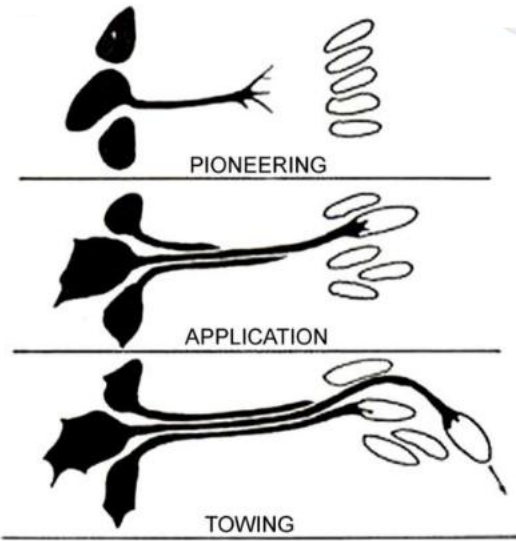
En la ballena azul: 3 cm/día



Doble de volumen celular!



Crecimiento por estiramiento

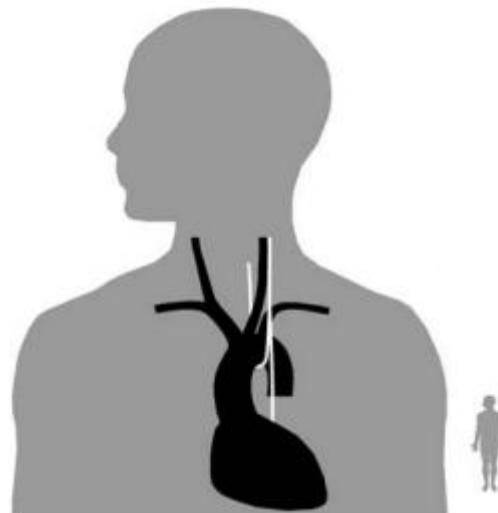
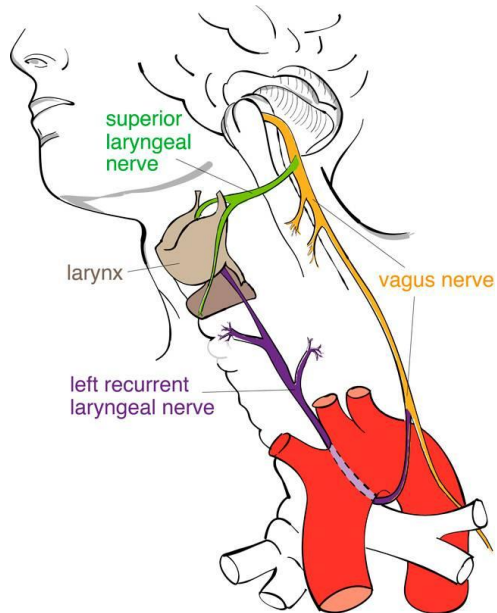


Smith, 2009

En la ballena azul: 3 cm/día

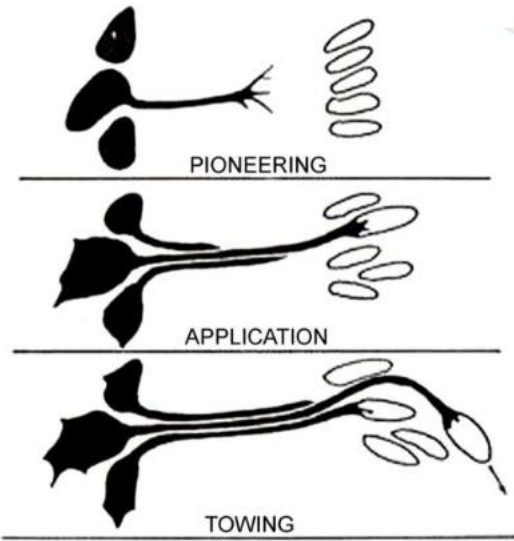


Doble de volumen celular!



Wedel, 2011

Crecimiento por estiramiento

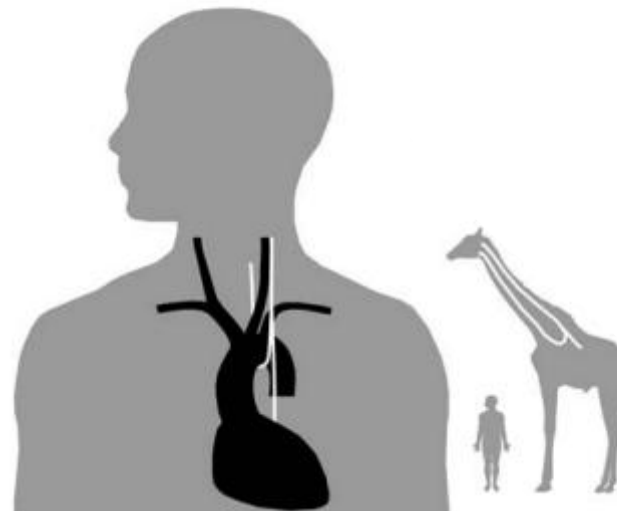
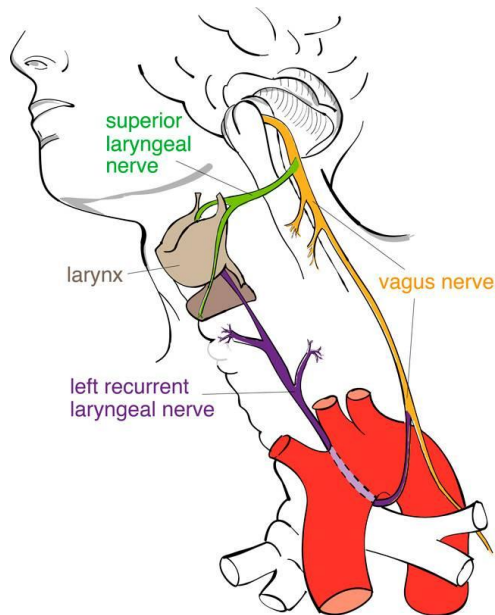


Smith, 2009

En la ballena azul: 3 cm/día

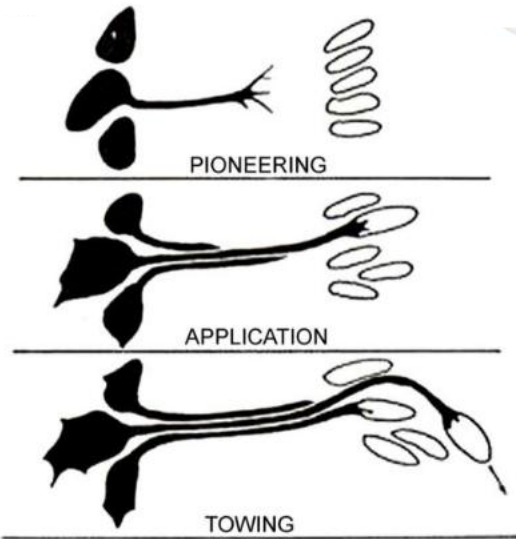


Doble de volumen celular!



Wedel, 2011

Crecimiento por estiramiento

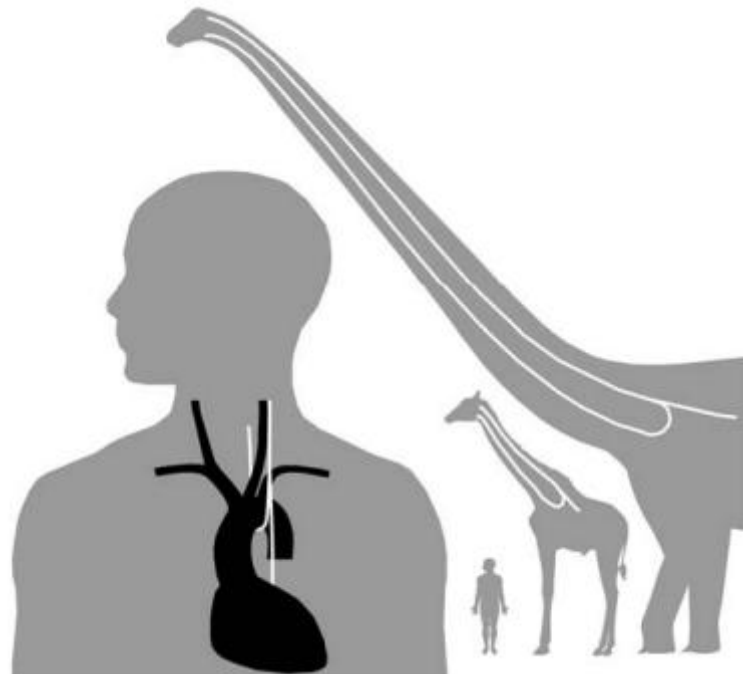
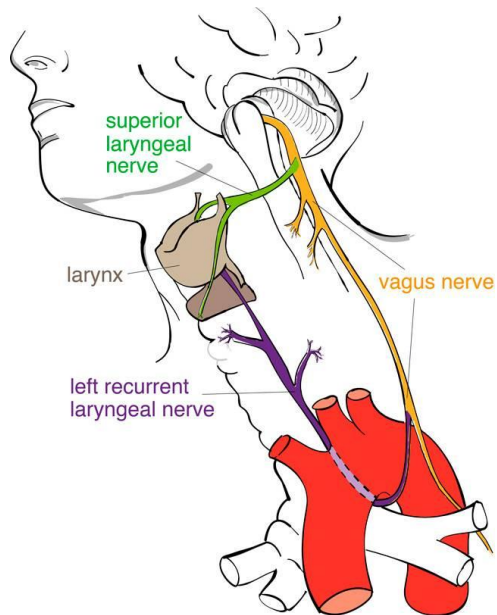


Smith, 2009

En la ballena azul: 3 cm/día

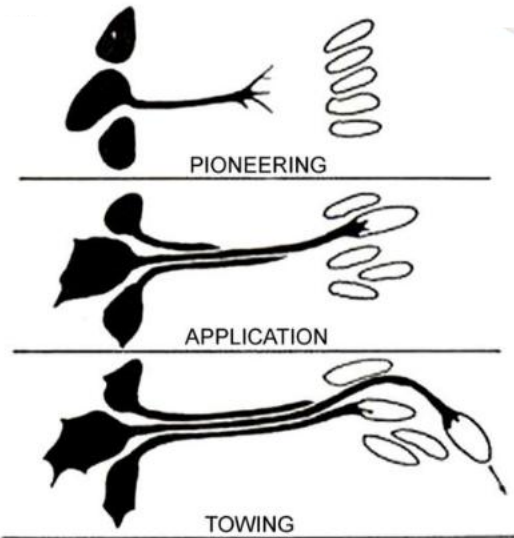


Doble de volumen celular!

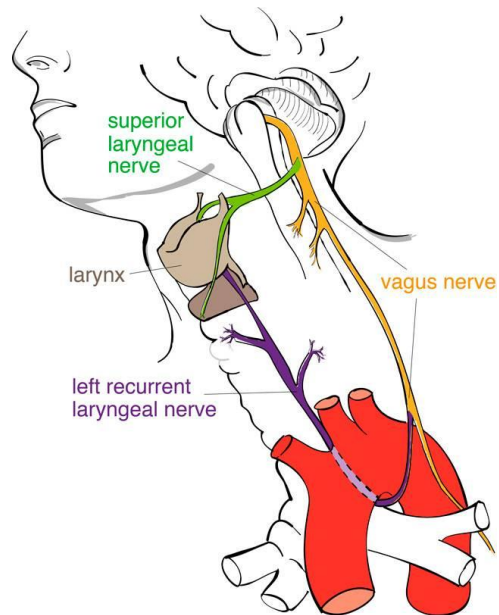


Wedel, 2011

Crecimiento por estiramiento



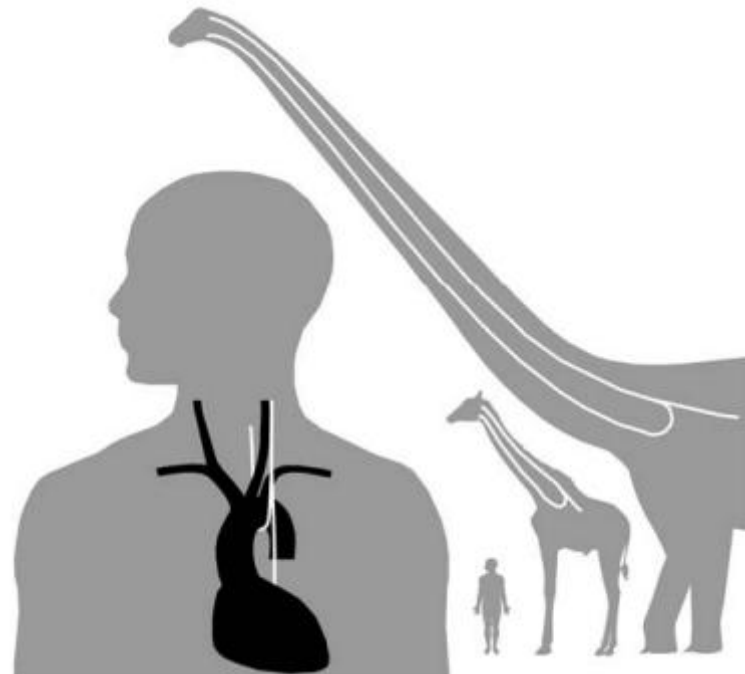
Smith, 2009



En la jirafa: 5 cm/día

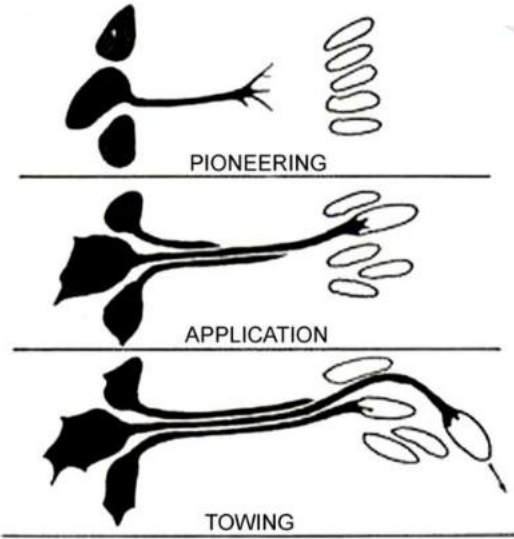


Mucho más del doble de volumen celular!



Wedel, 2011

Crecimiento por estiramiento

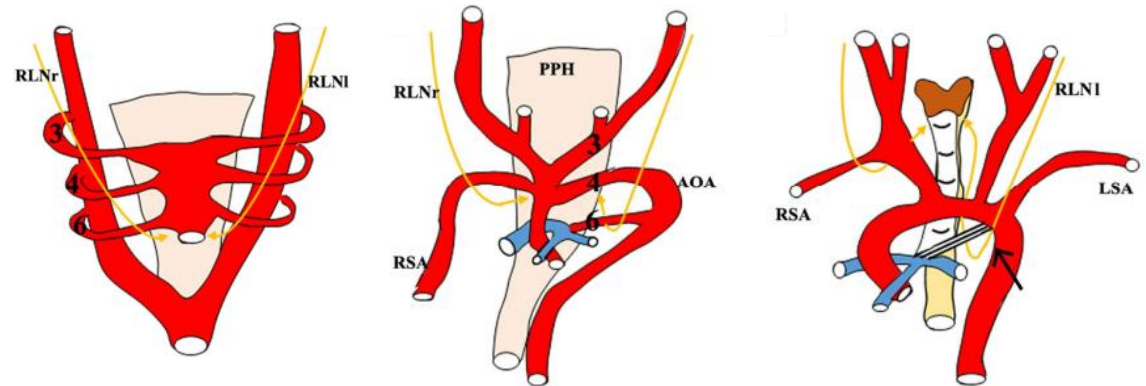
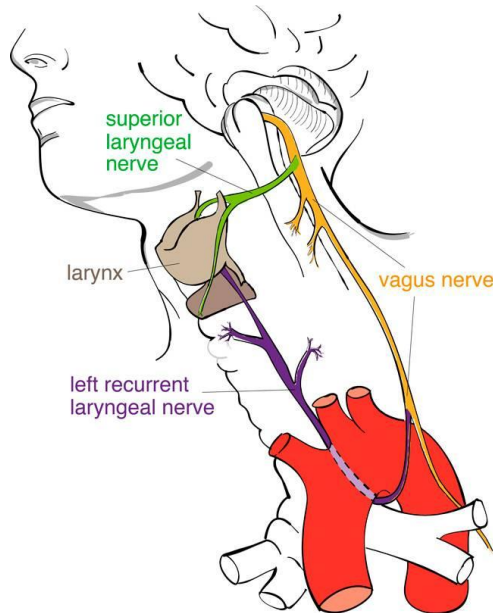


Smith, 2009

En la jirafa: 5 cm/día

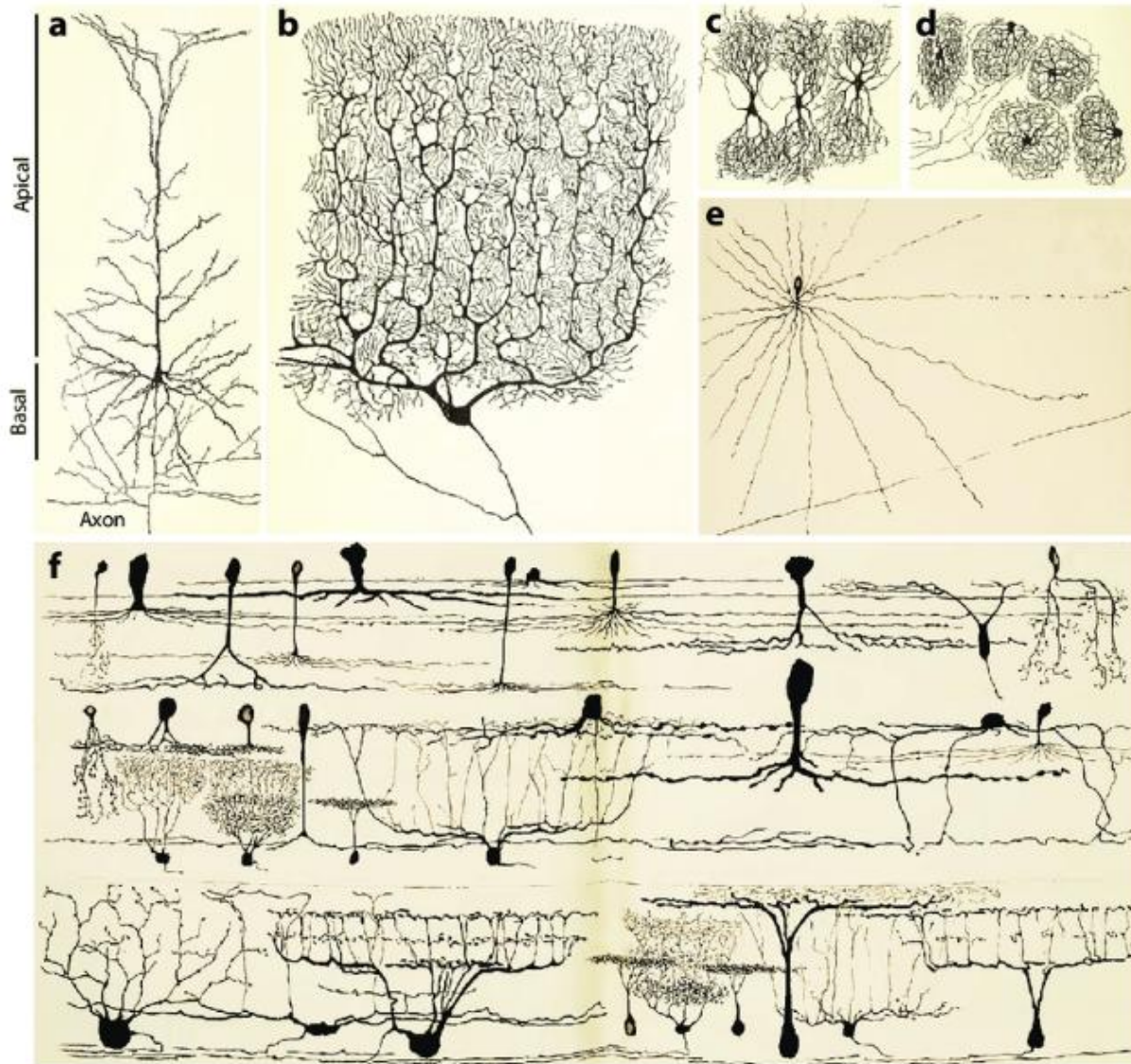


Mucho más del doble de volumen celular!



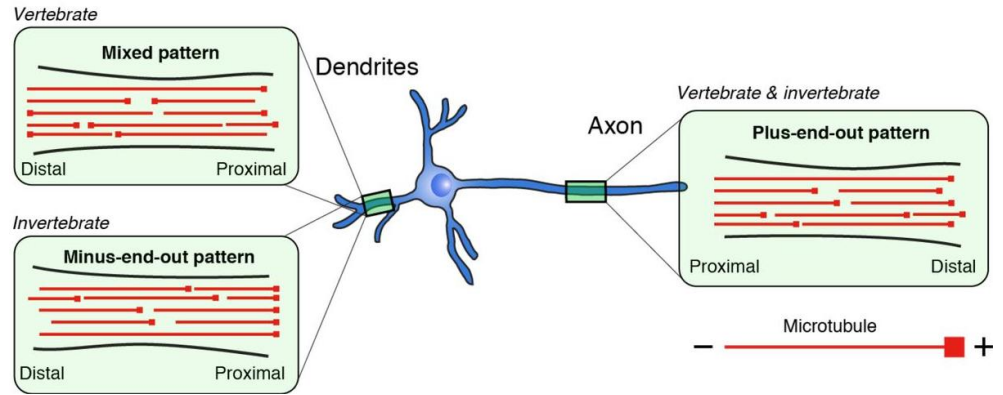
Yan et al., 2017

Dendritogénesis



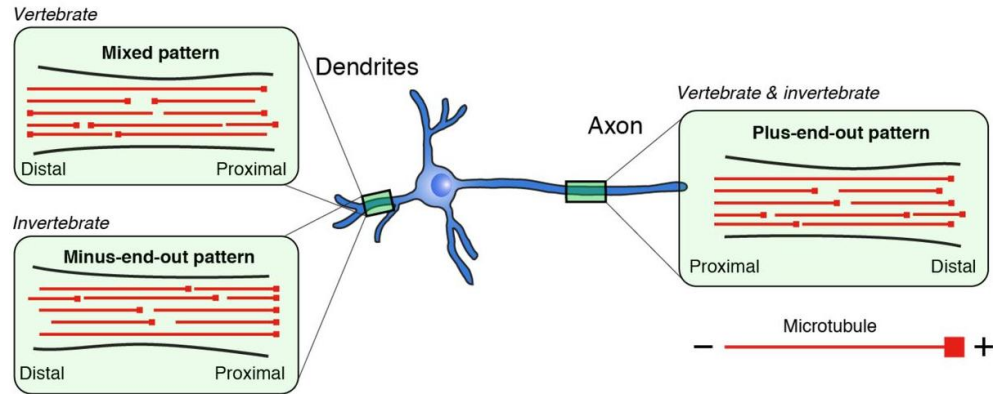
Ramón y Cajal, 1893; 1909

Dendritogénesis

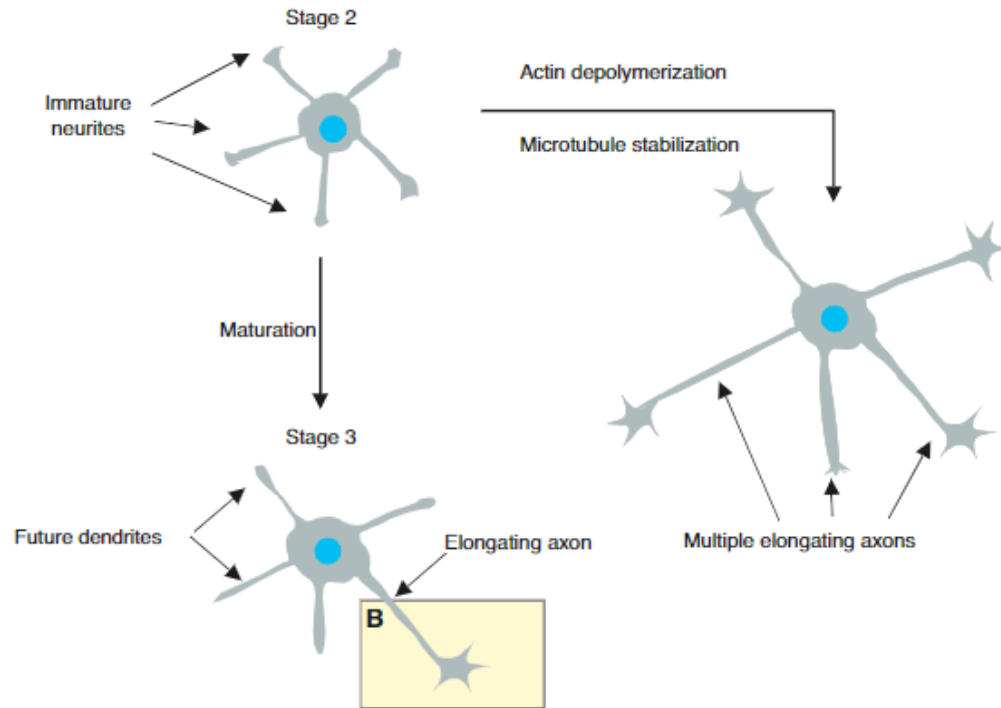


Naoki et al., 2017

Dendritogenesis

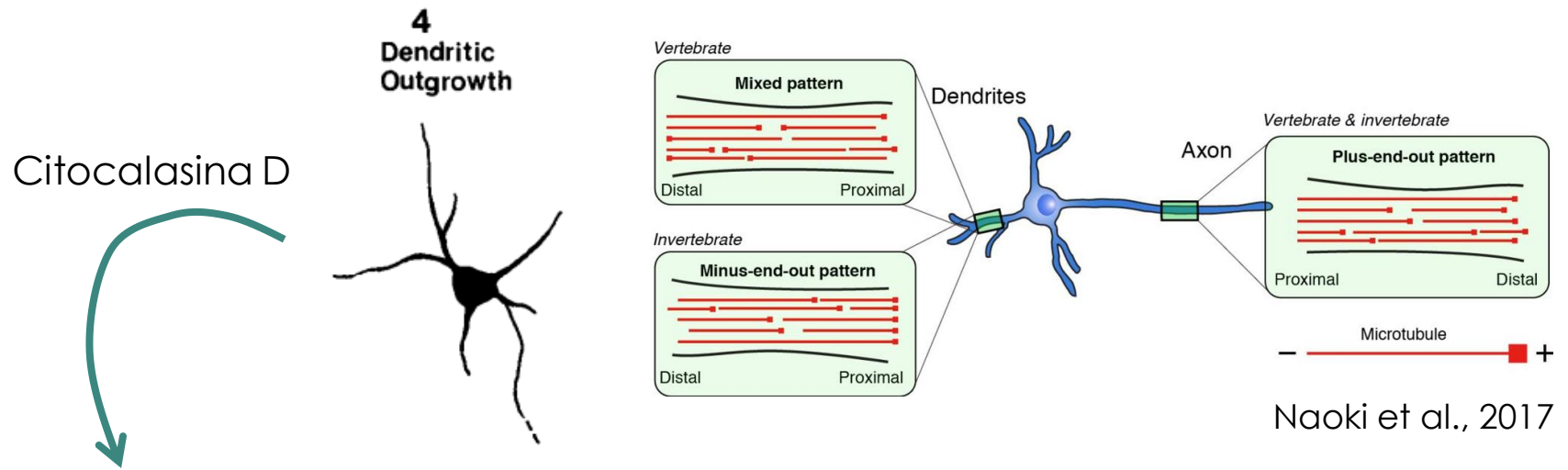


Naoki et al., 2017

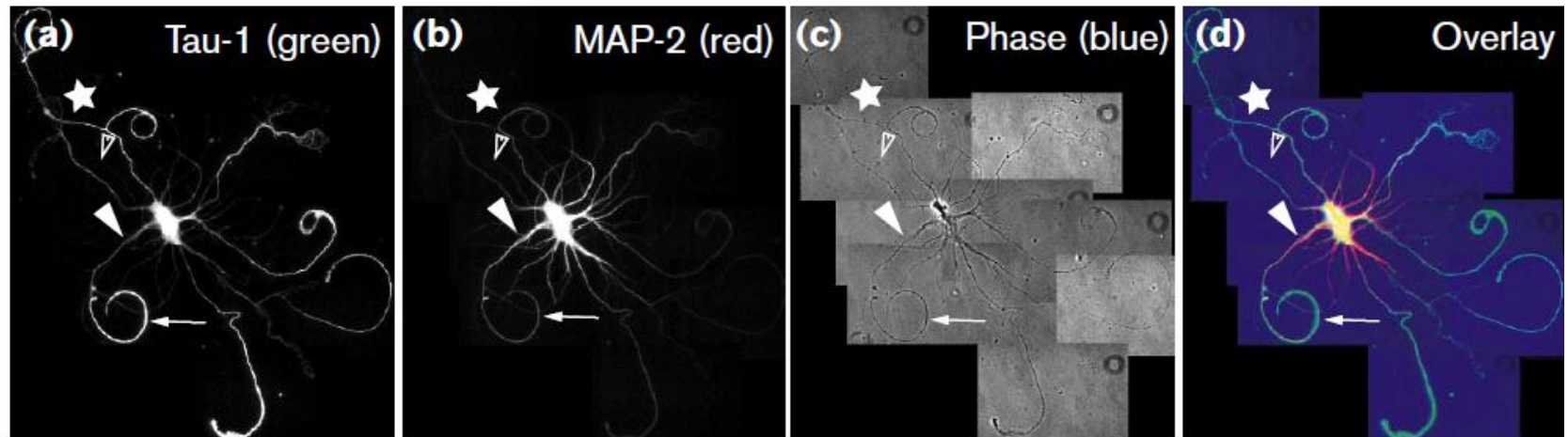


Blanquie & Bradke, 2018

Dendritogénesis

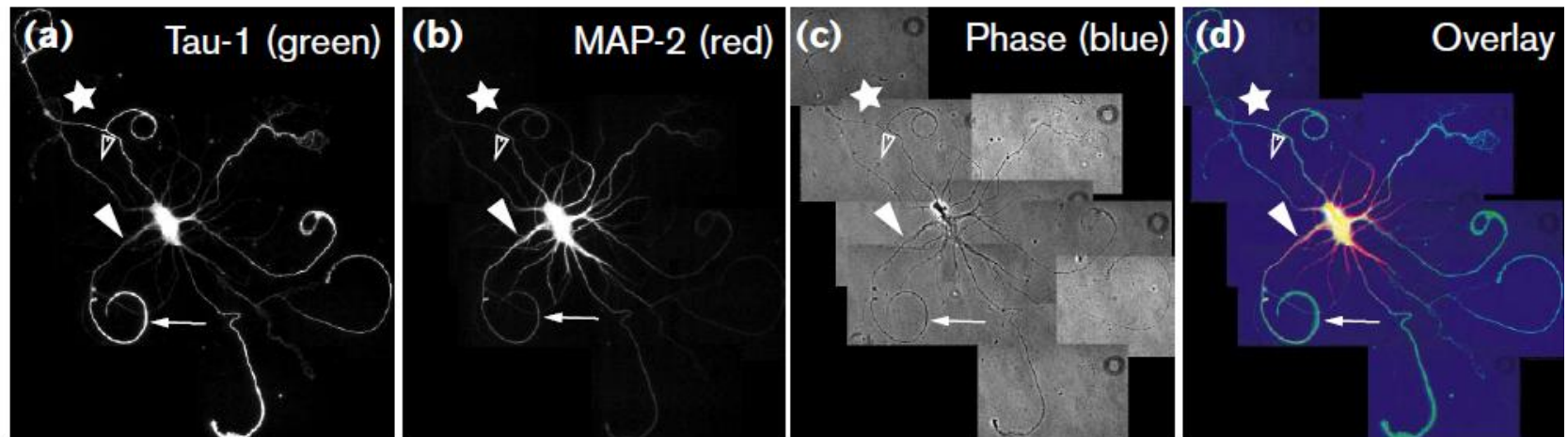
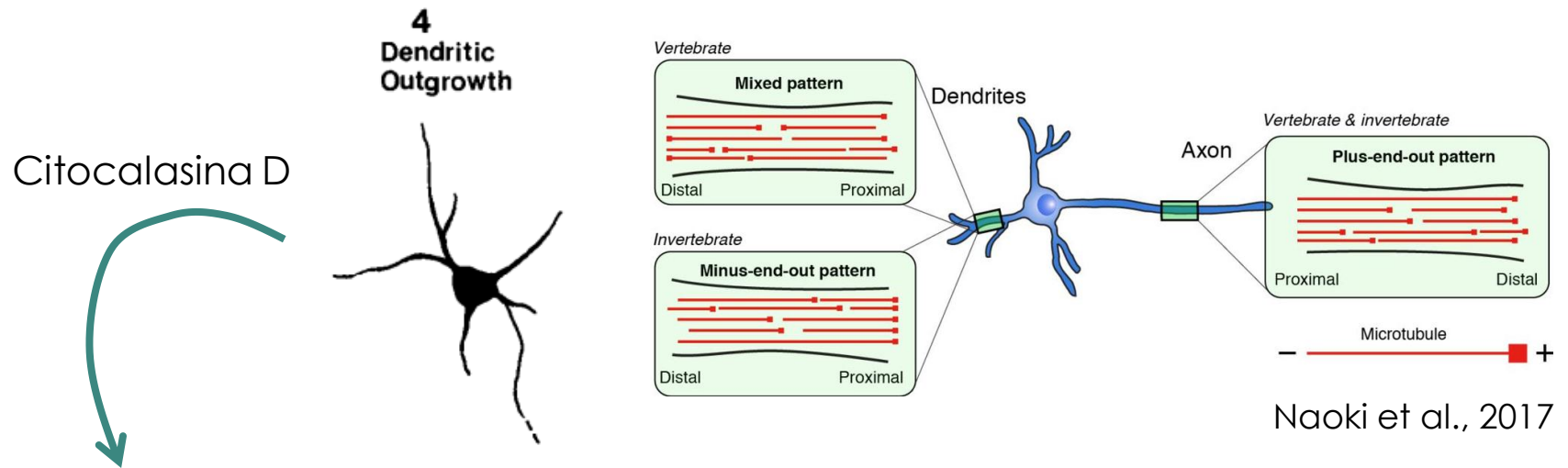


Naoki et al., 2017



Bradke & Dotti, 2000

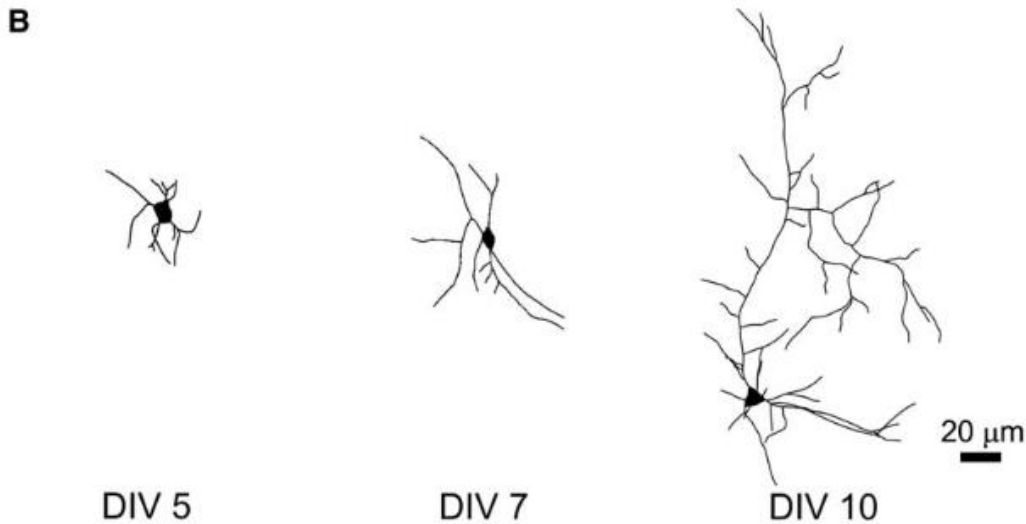
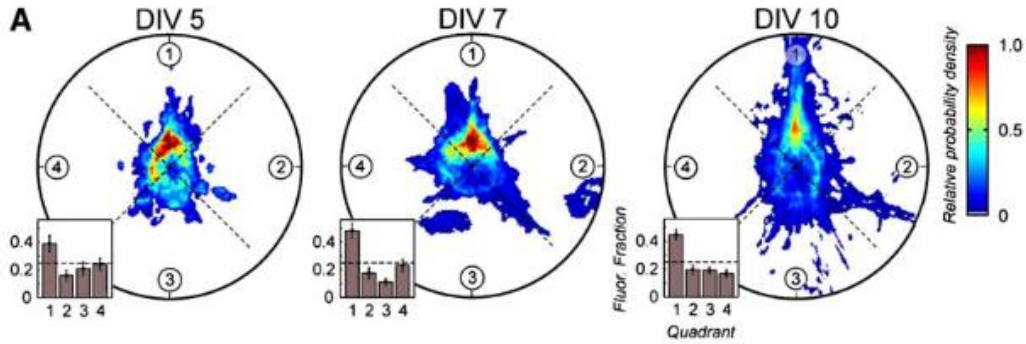
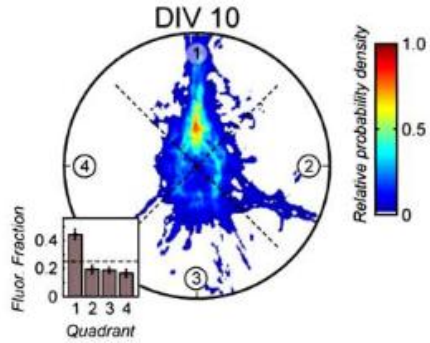
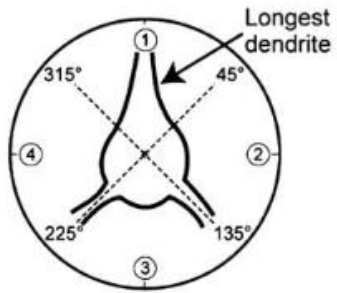
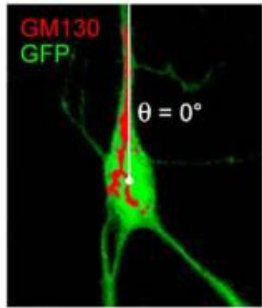
Dendritogénesis



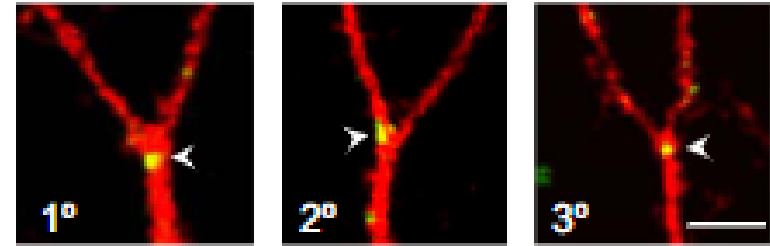
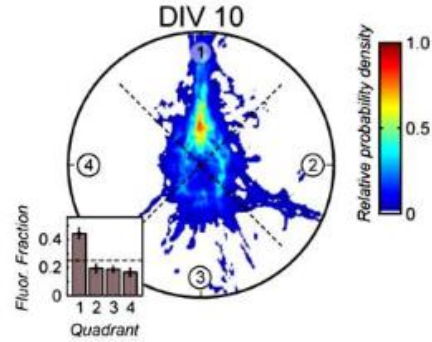
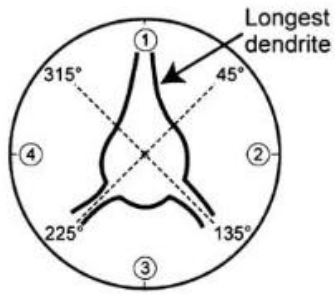
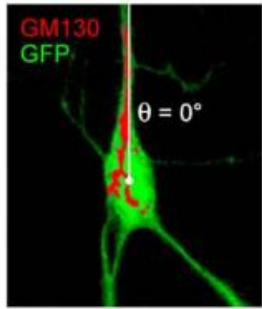
Bradke & Dotti, 2000

La estabilidad de los filamentos de actina es importante para el mantenimiento de las dendritas

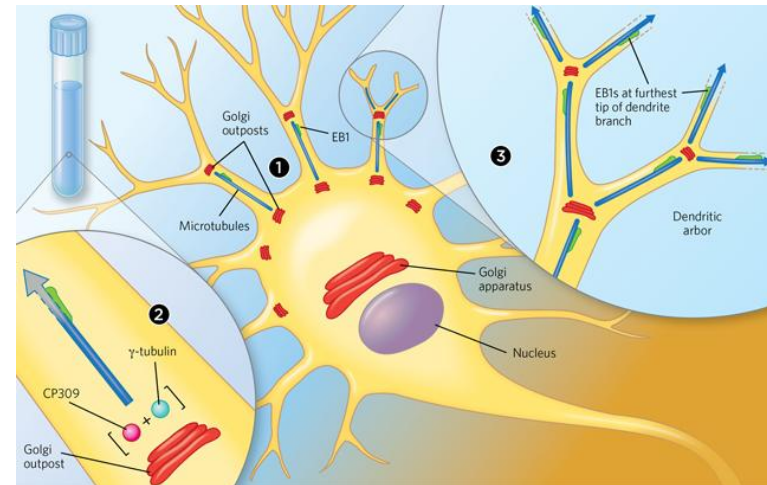
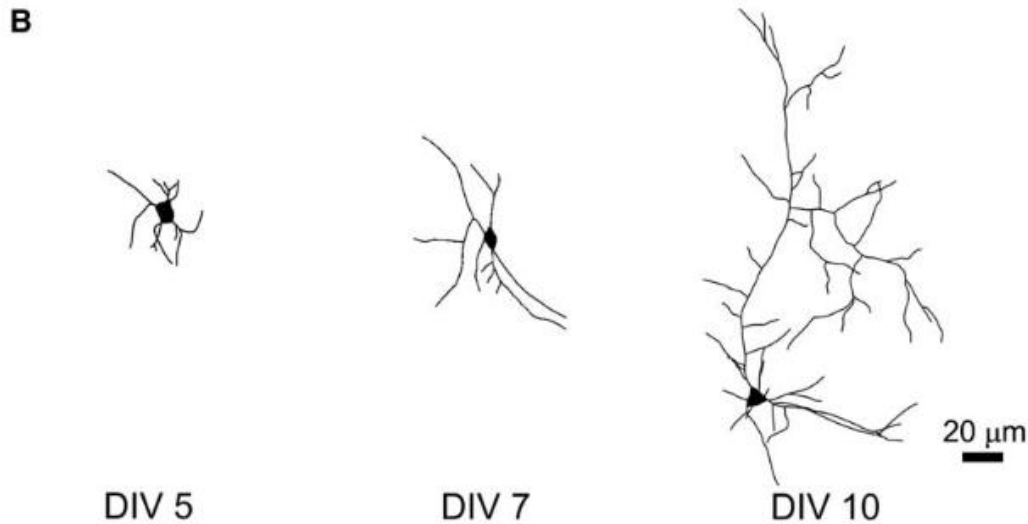
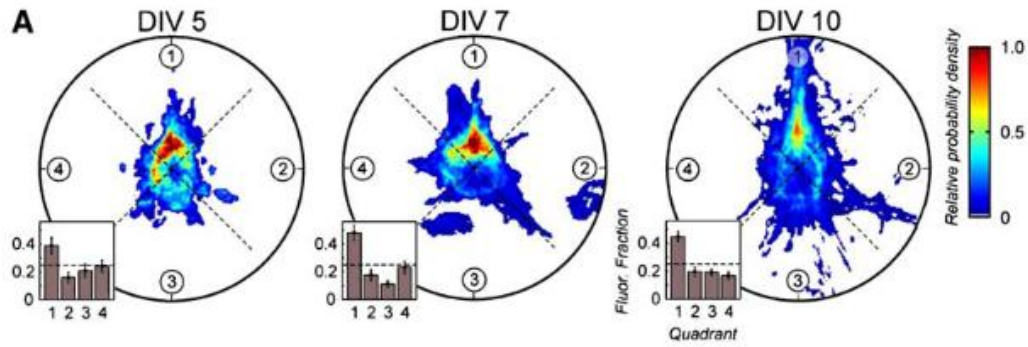
El Golgi y las dendritas



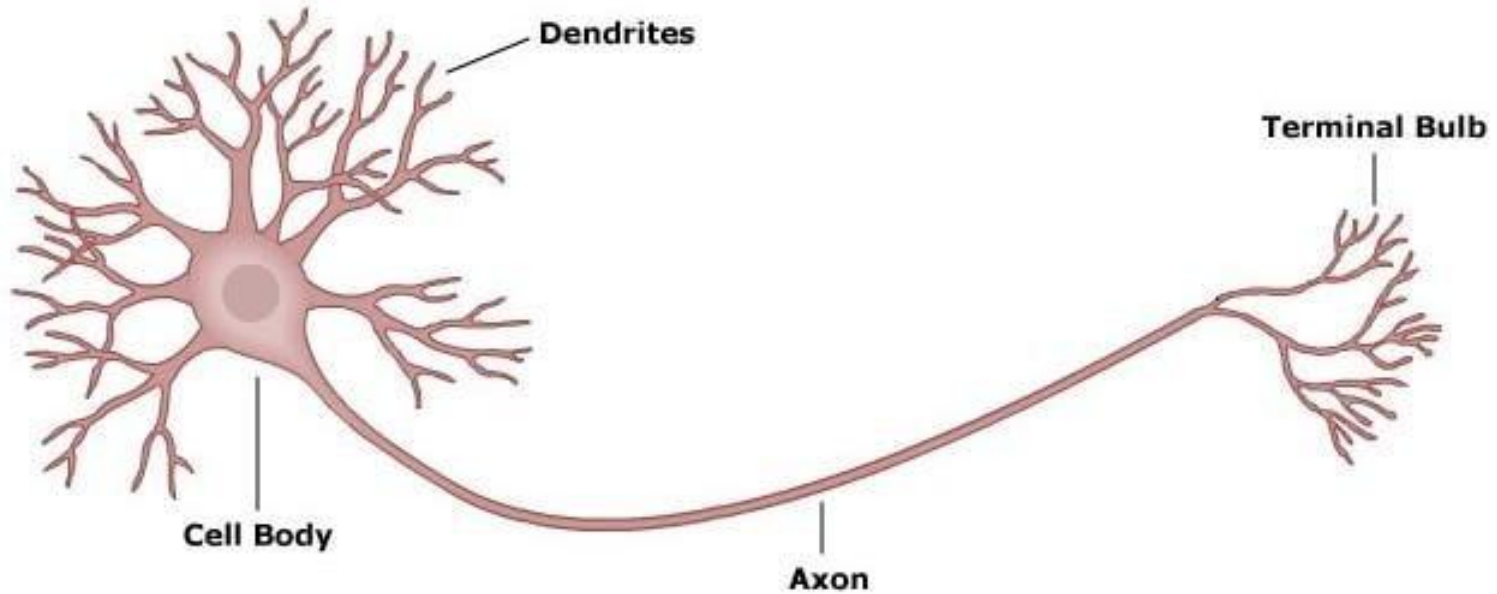
El Golgi y las dendritas



Horton et al., 2005



Dendritogénesis



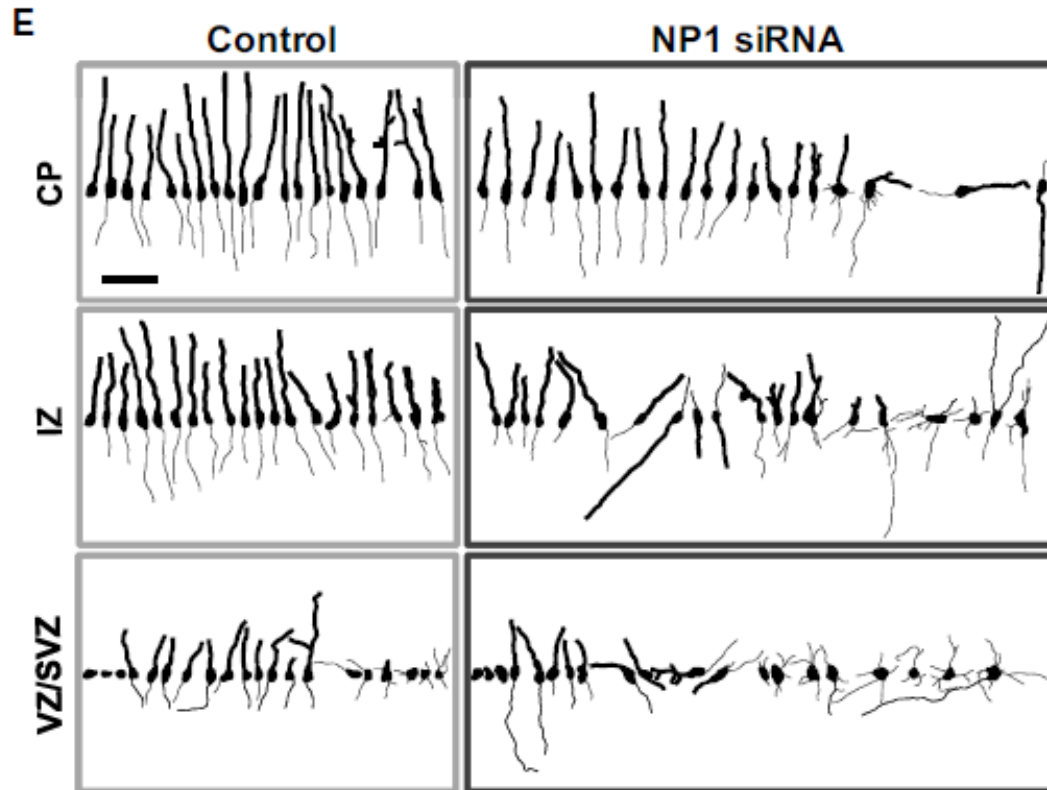
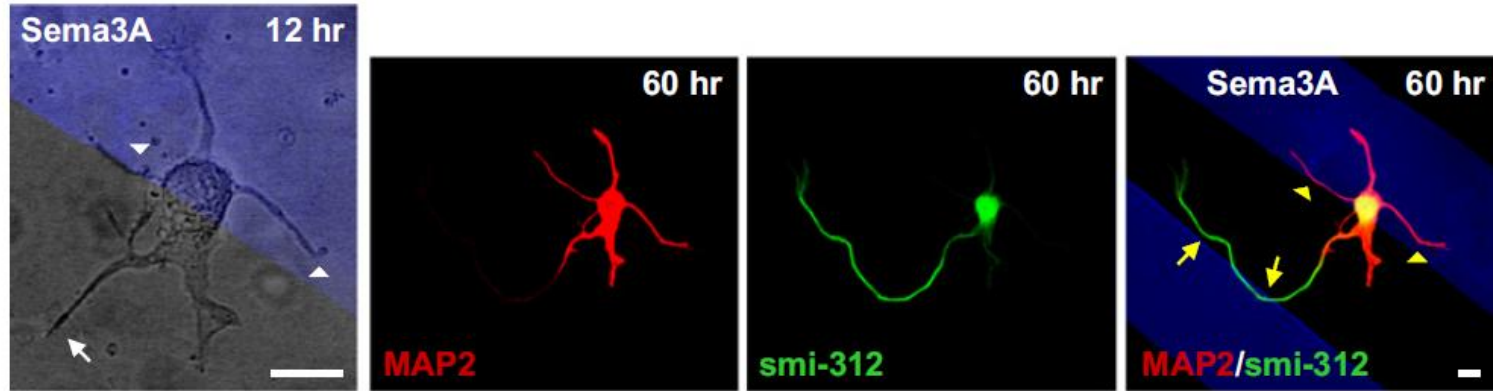
Señales difusibles:

- BDNF
- Semaforinas
- Slits

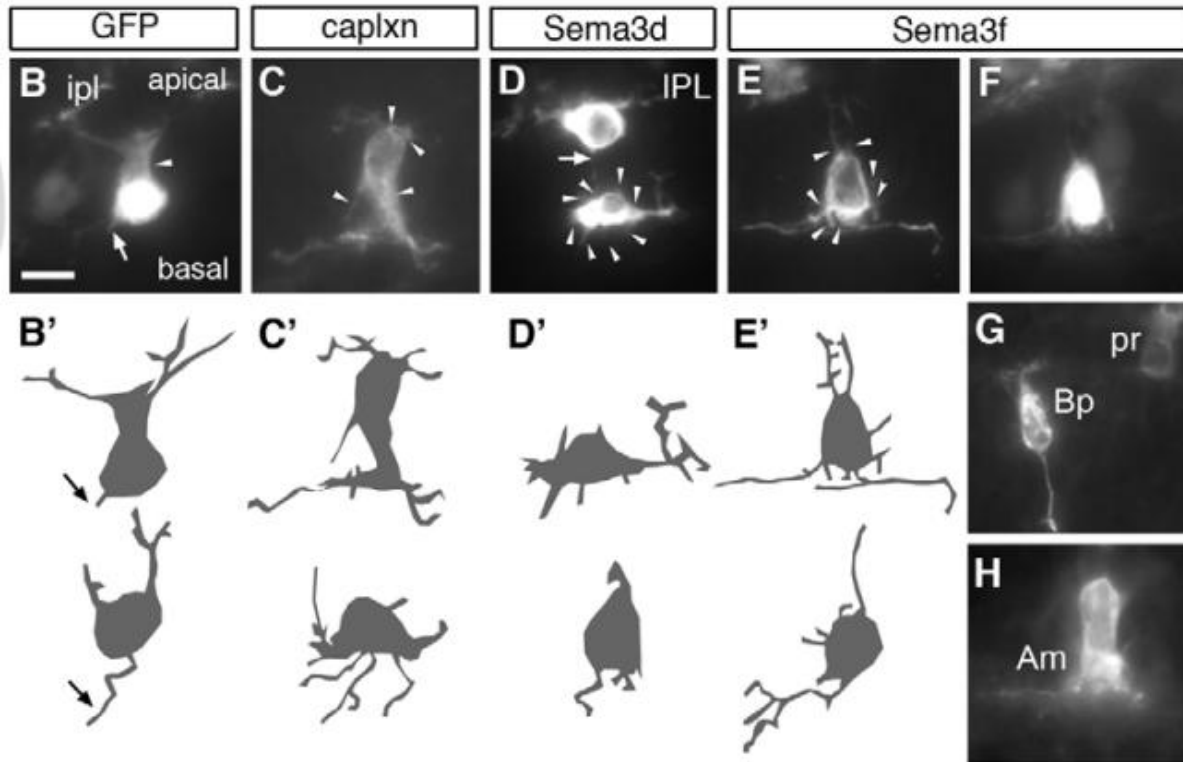
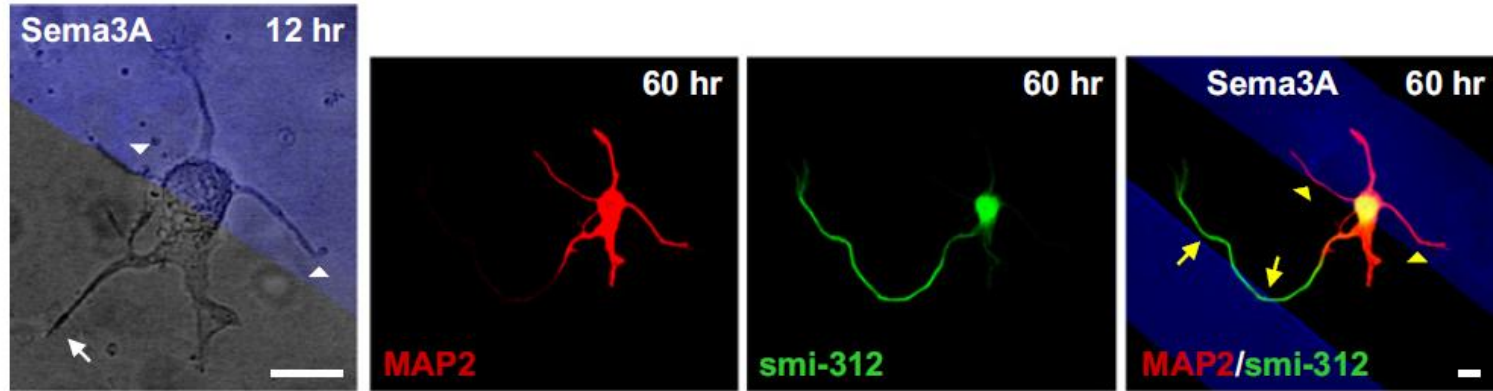
Señales de adhesión celular:

- Cadherinas
- Delta-Notch
- Efrinas

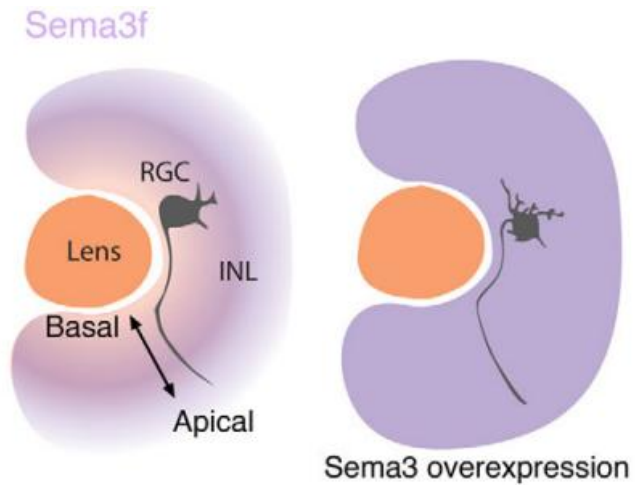
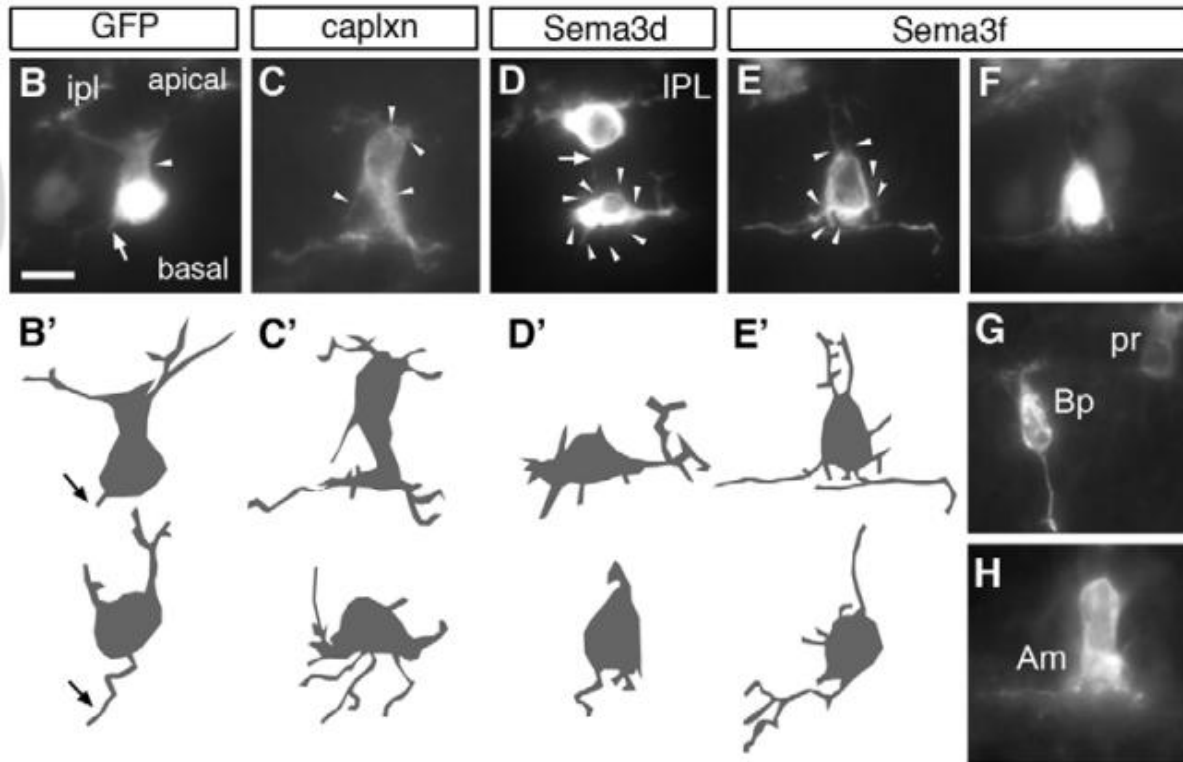
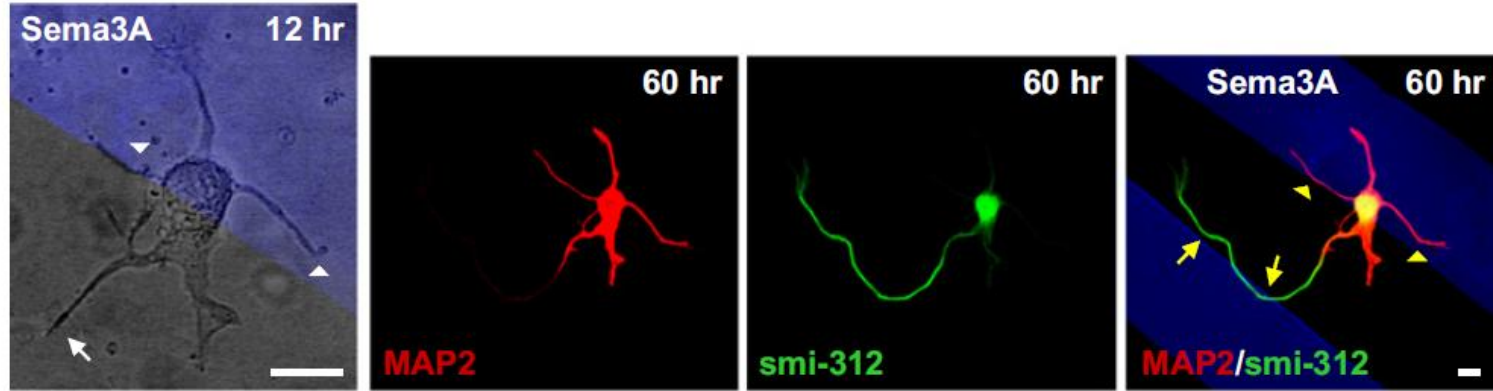
Dendritogénesis



Dendritogénesis



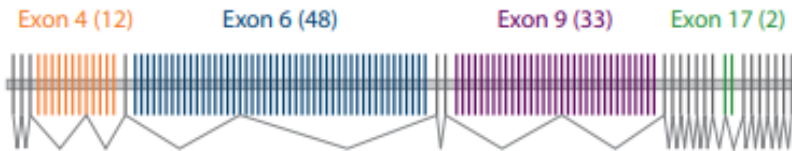
Dendritogénesis



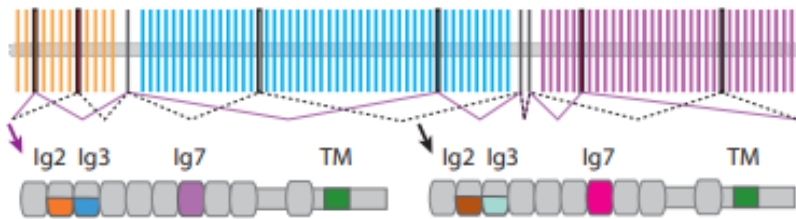
Auto-repulsión de las neuritas

Dscam1

a Genomic complexity



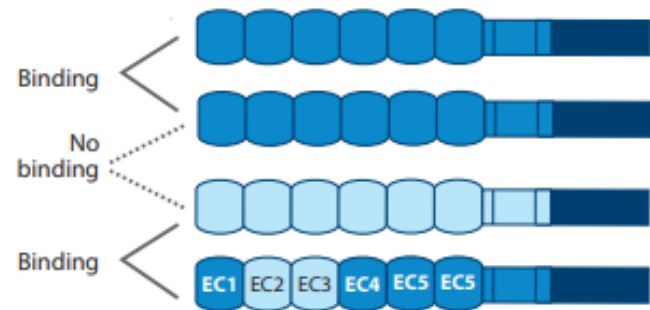
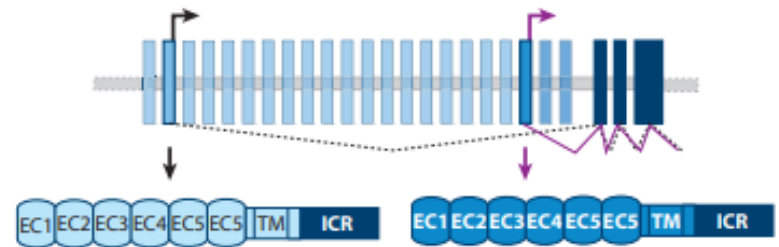
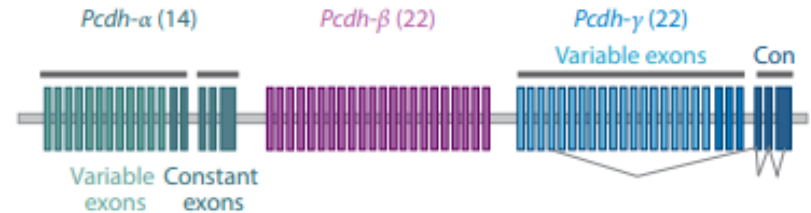
b Probabilistic control of isoform diversity



c Homophilic binding specificity



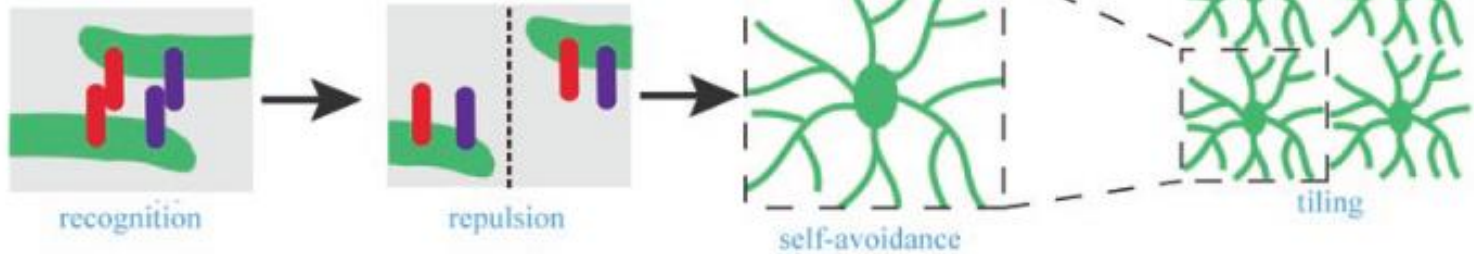
Clustered protocadherins



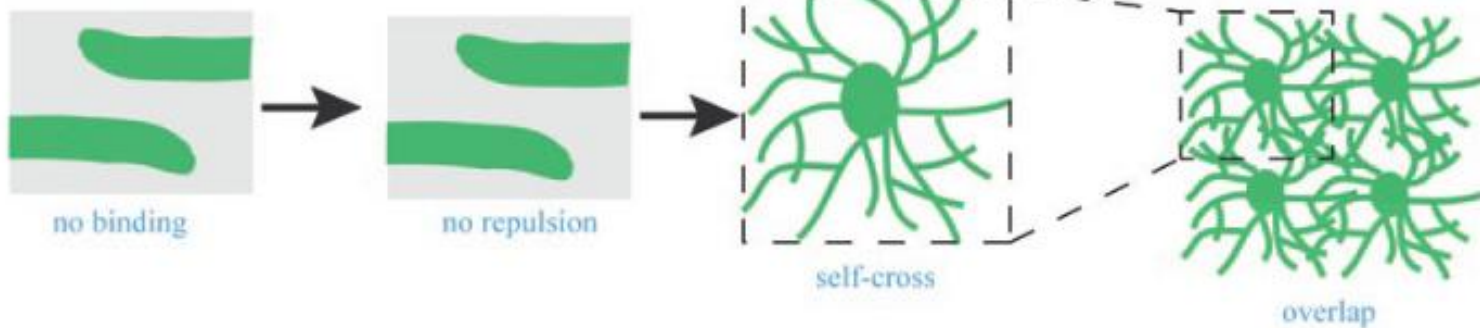
Lefebvre et al., 2015

Auto-repulsión de las neuritas

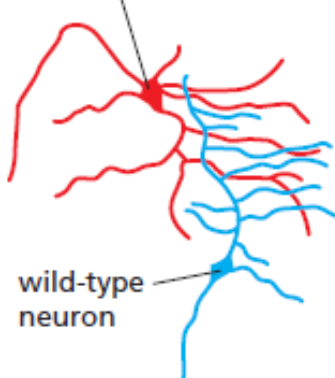
Wide type neuron



Dscam mutant neuron

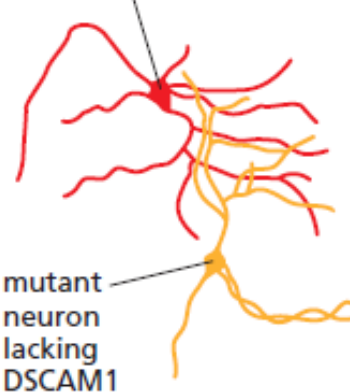


wild-type neuron

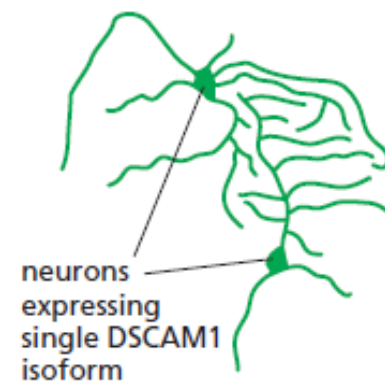


wild-type neuron

wild-type neuron



mutant neuron lacking DSCAM1

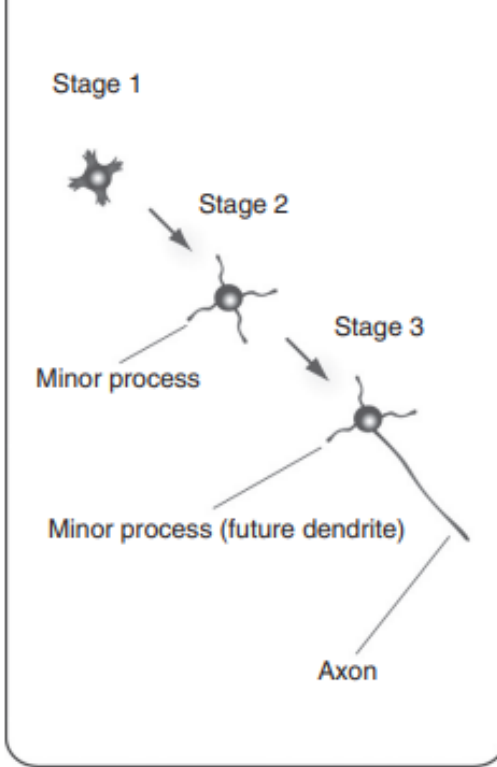


neurons expressing single DSCAM1 isoform

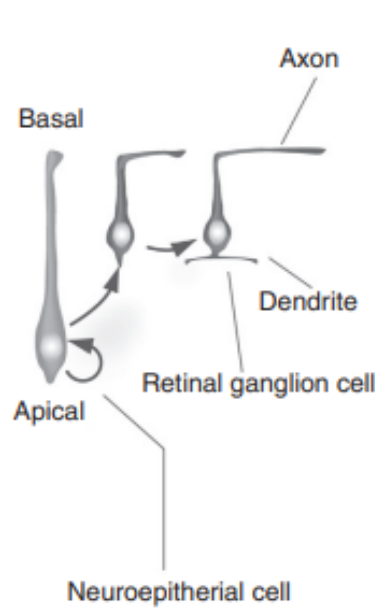
Polarización neuronal

Neuronas hipocampales

(a) Neuronal polarization *in vitro*
Cultured neurons

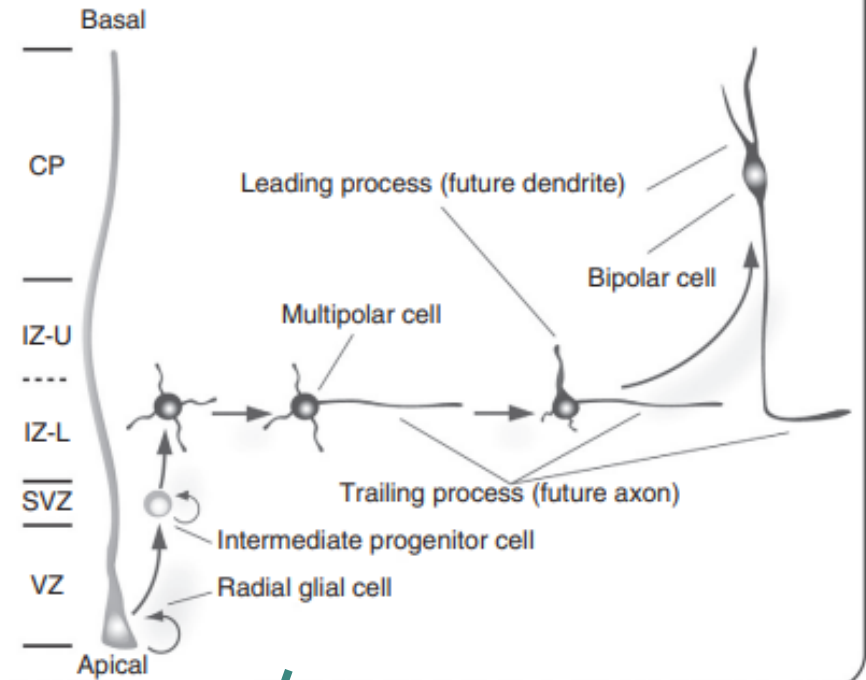


(b) Inheritance of polarity mode
Developing retina



Neuronal polarization *in vivo*

(c) Establishment of polarity mode
Late embryonic cerebral cortex

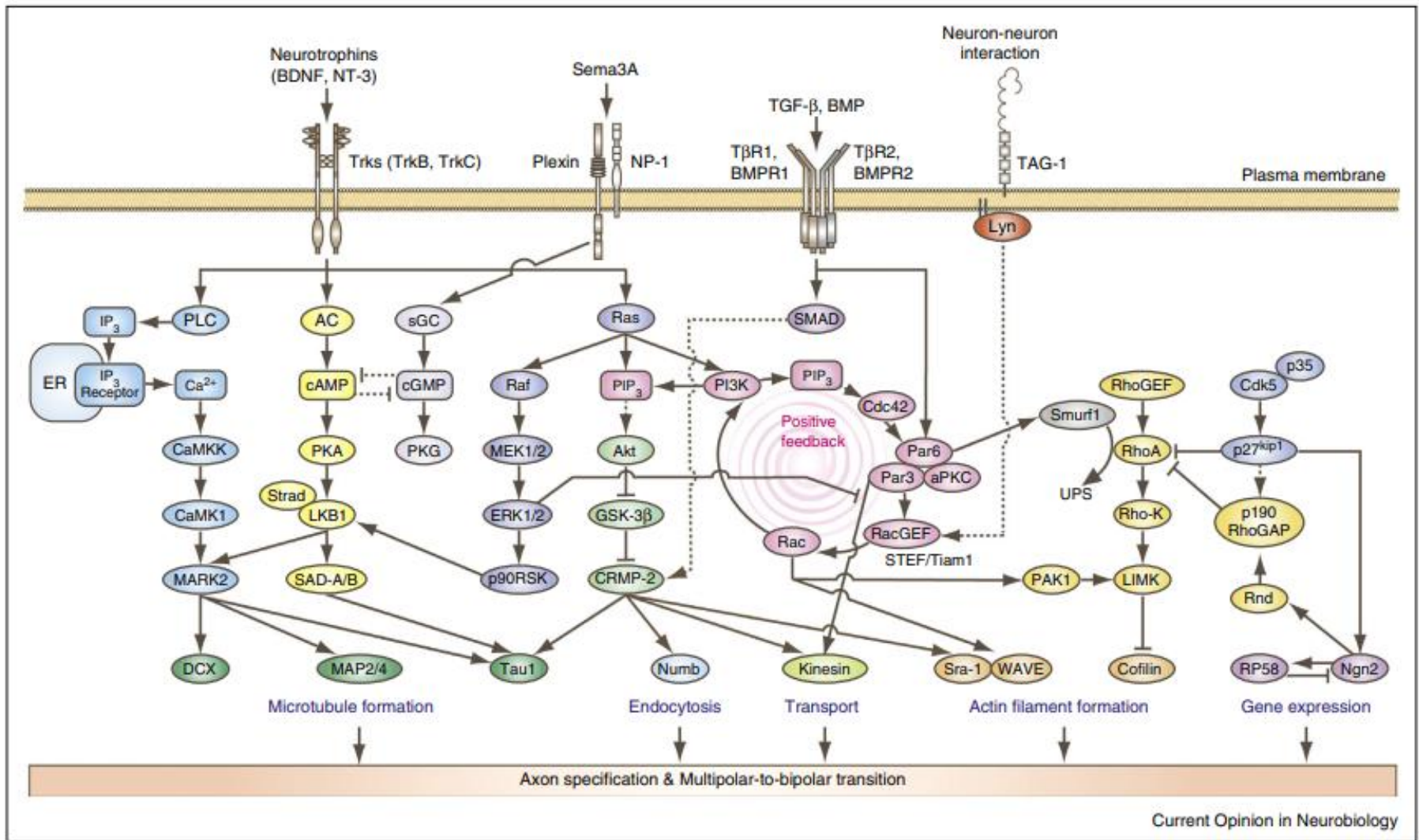


Funahashi et al., 2014

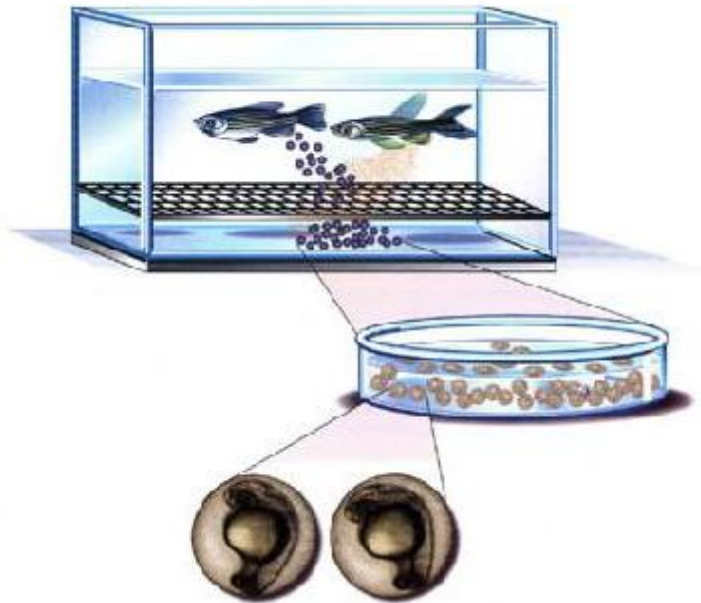
Células ganglionares de la retina

Neuronas corticales

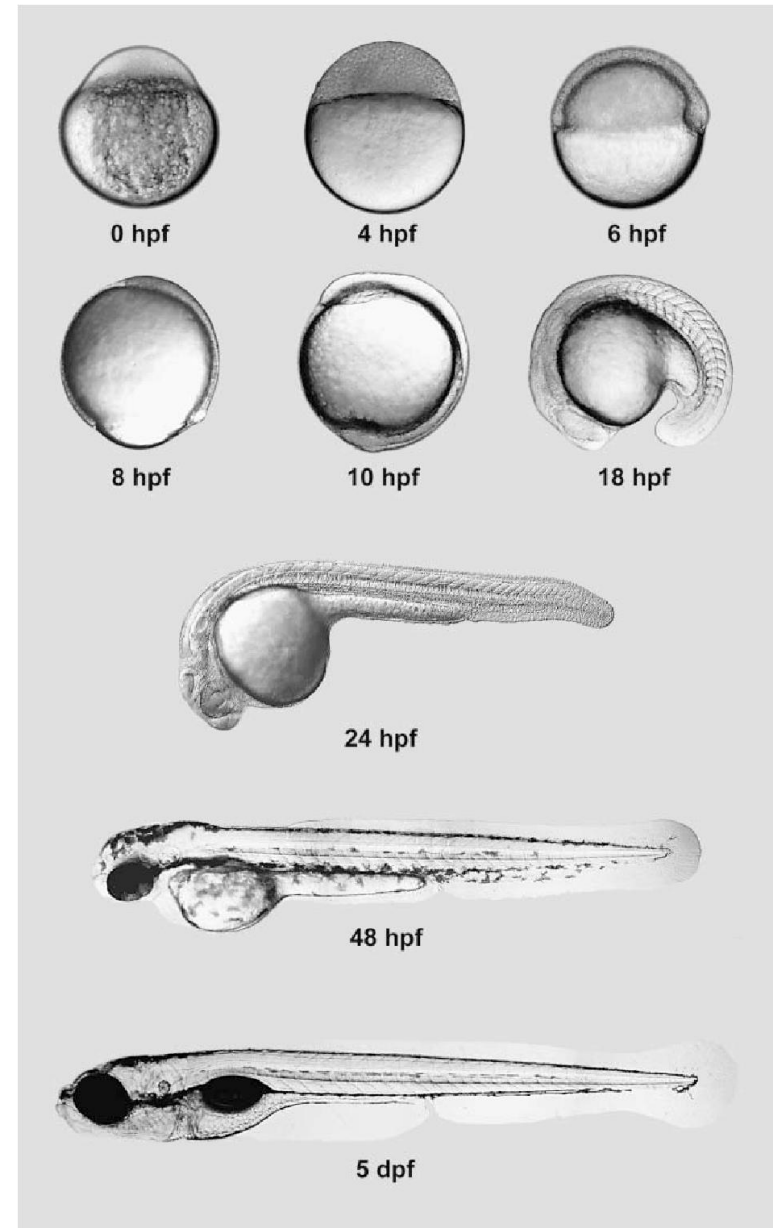
Polarización neuronal



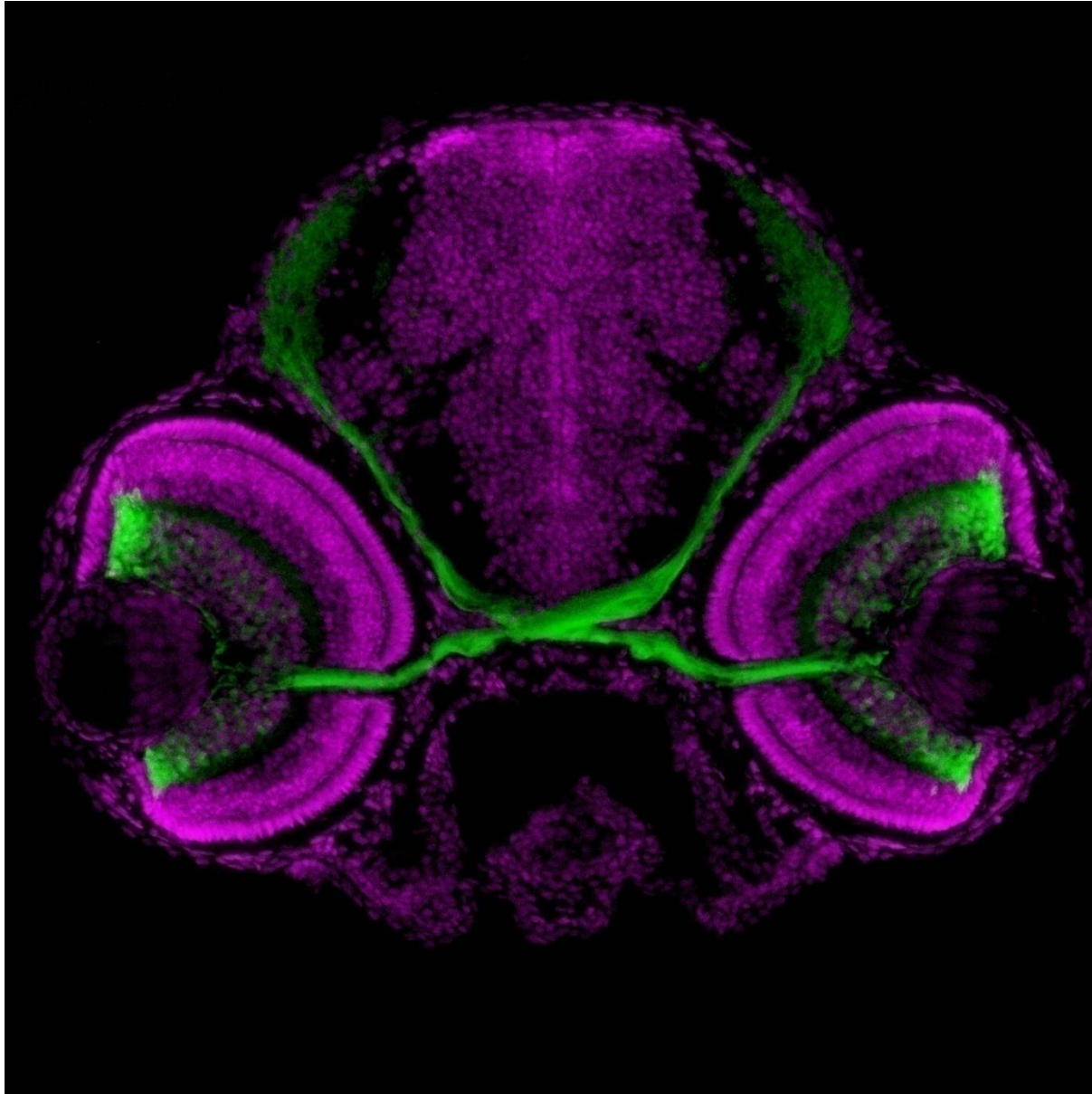
Introducción al práctico: zebrafish



Introducción al práctico: zebrafish



La vía visual








La vía Slit-Robo

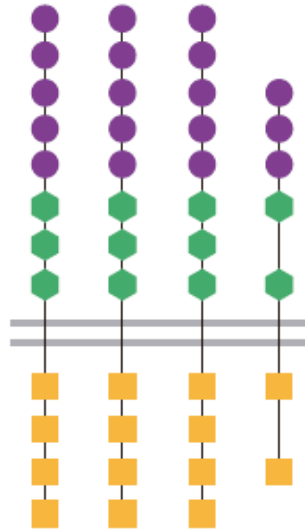
Slit ligands






Slit1a, 1b, 2 and 3

-  Signal peptide
-  LRR domains (1-4)
-  EGF-like domains (1-6/7-9)
-  Laminin-G-like domain
-  Cysteine knot

Robo receptors



Robo1 Robo2 Robo3 Robo4






-  Immunoglobulin domains
-  Fibronectin III domains
-  Conserved cytoplasmic domains

La vía Slit-Robo

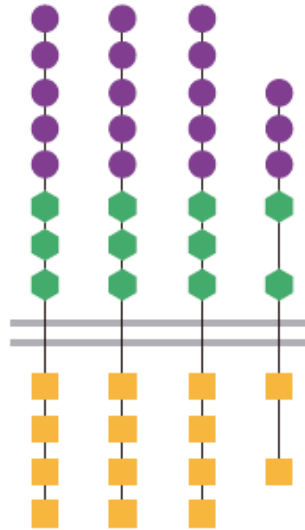
Slit ligands






Slit1a, 1b, 2 and 3

-  Signal peptide
-  LRR domains (1-4)
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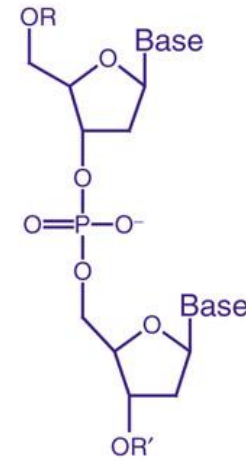
Robo receptors



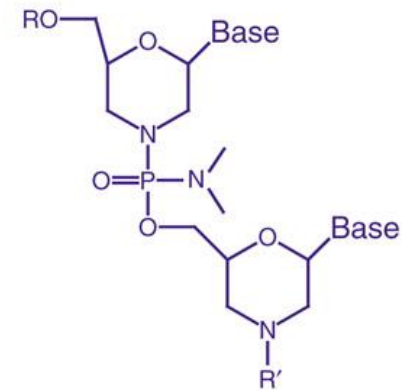
Robo1 Robo2 Robo3 Robo4

-  Immunoglobulin domains
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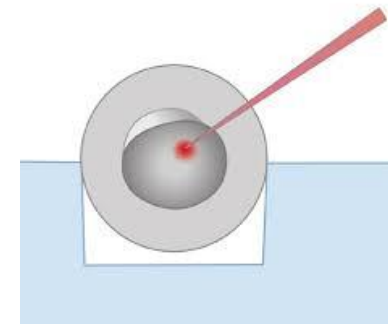
Slit2



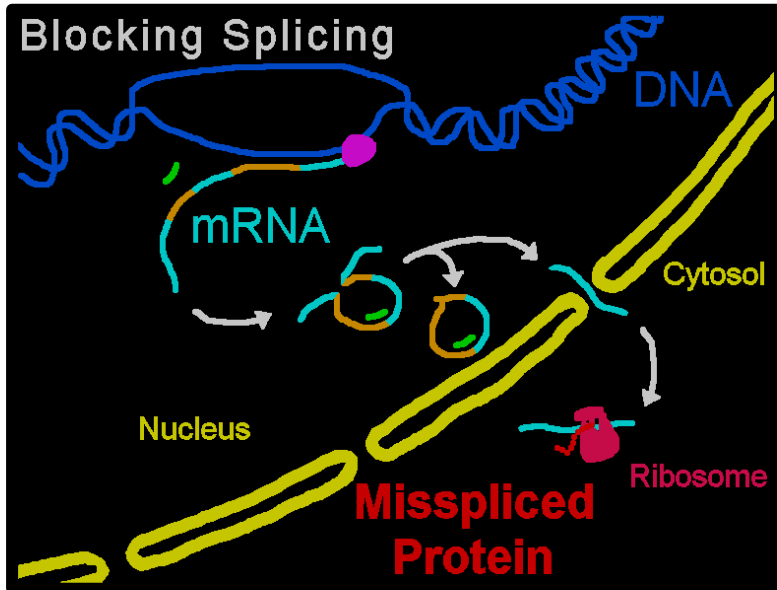
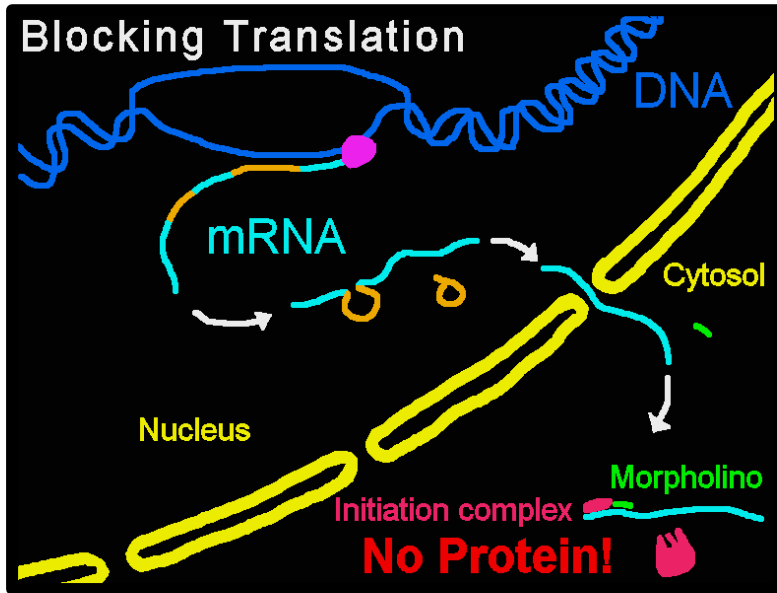
Phosphodiester
DNA



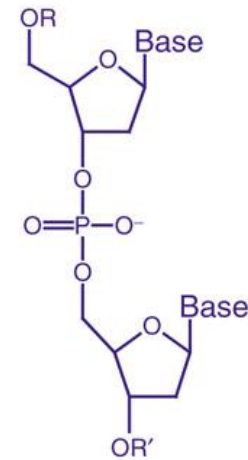
Morpholino



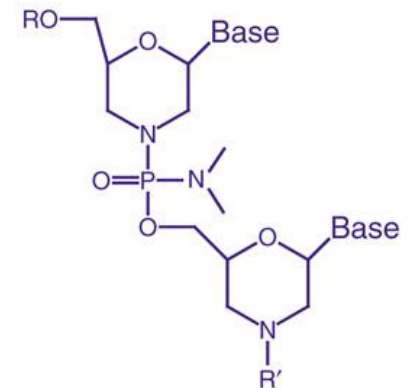
La via Slit-Robo



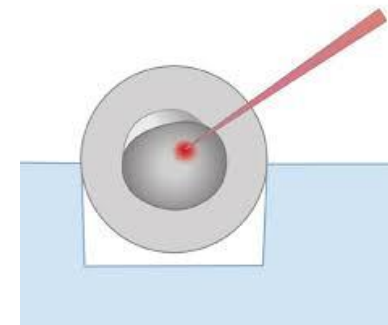
Slit2



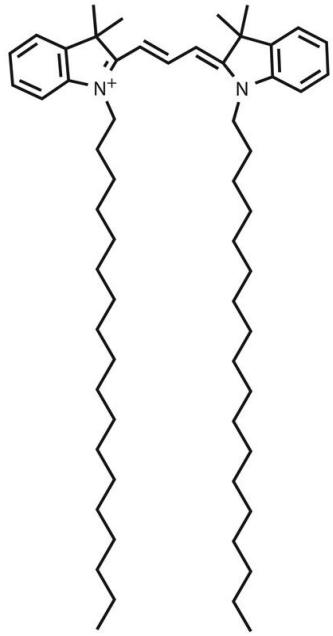
Phosphodiester
DNA



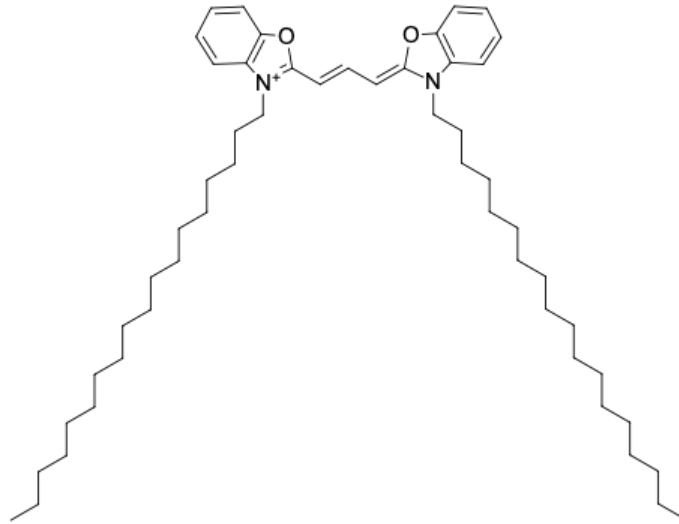
Morpholino



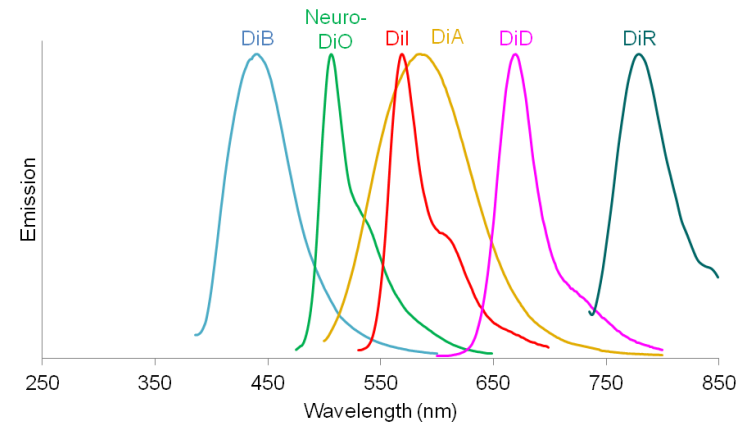
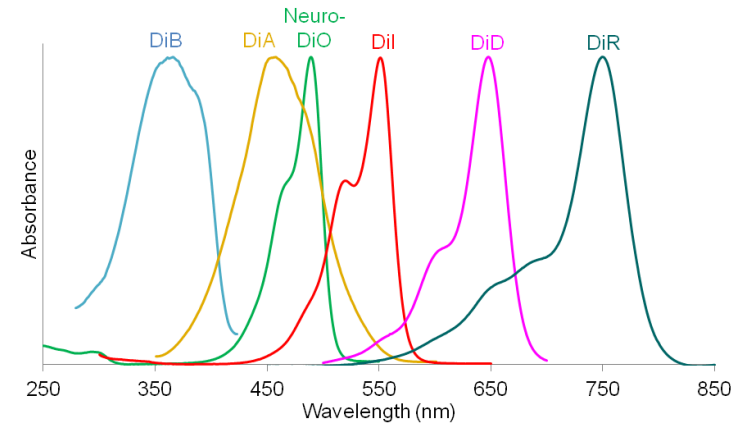
Marcadores lipofílicos



DiI



DiO



Marcadores lipofílicos

