

# Wie der Neurit waechst.



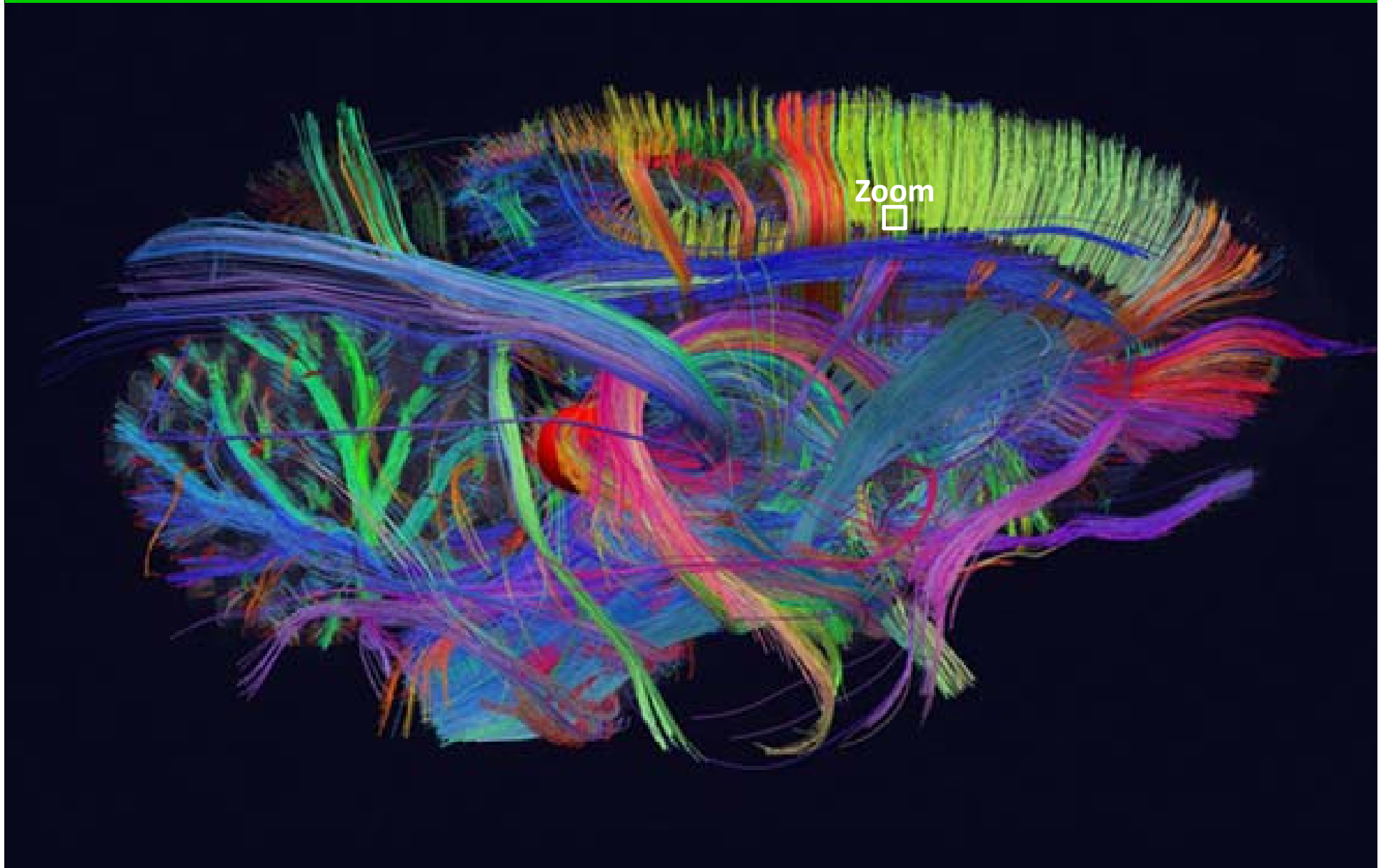
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# Komplexität der Verbindungen im Gehirn



**Auf der Zellebene sind die Neuronen durch  
Neuriten verknuepft.**

**Wie waechst der Neurit aus dem Zellkoerper?**

← Zell Extension = Neurit

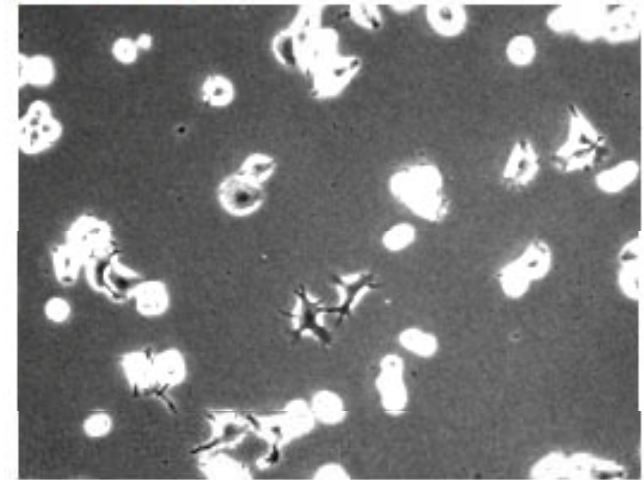
Zell Koerper = Soma



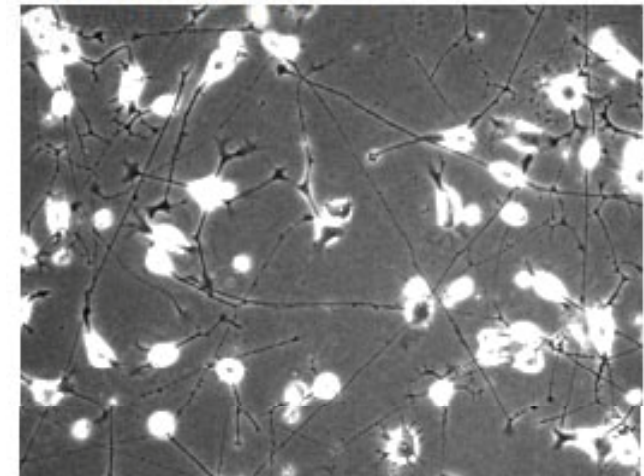
# Einzelne Neuronen leben auch in der “Petri Schale”



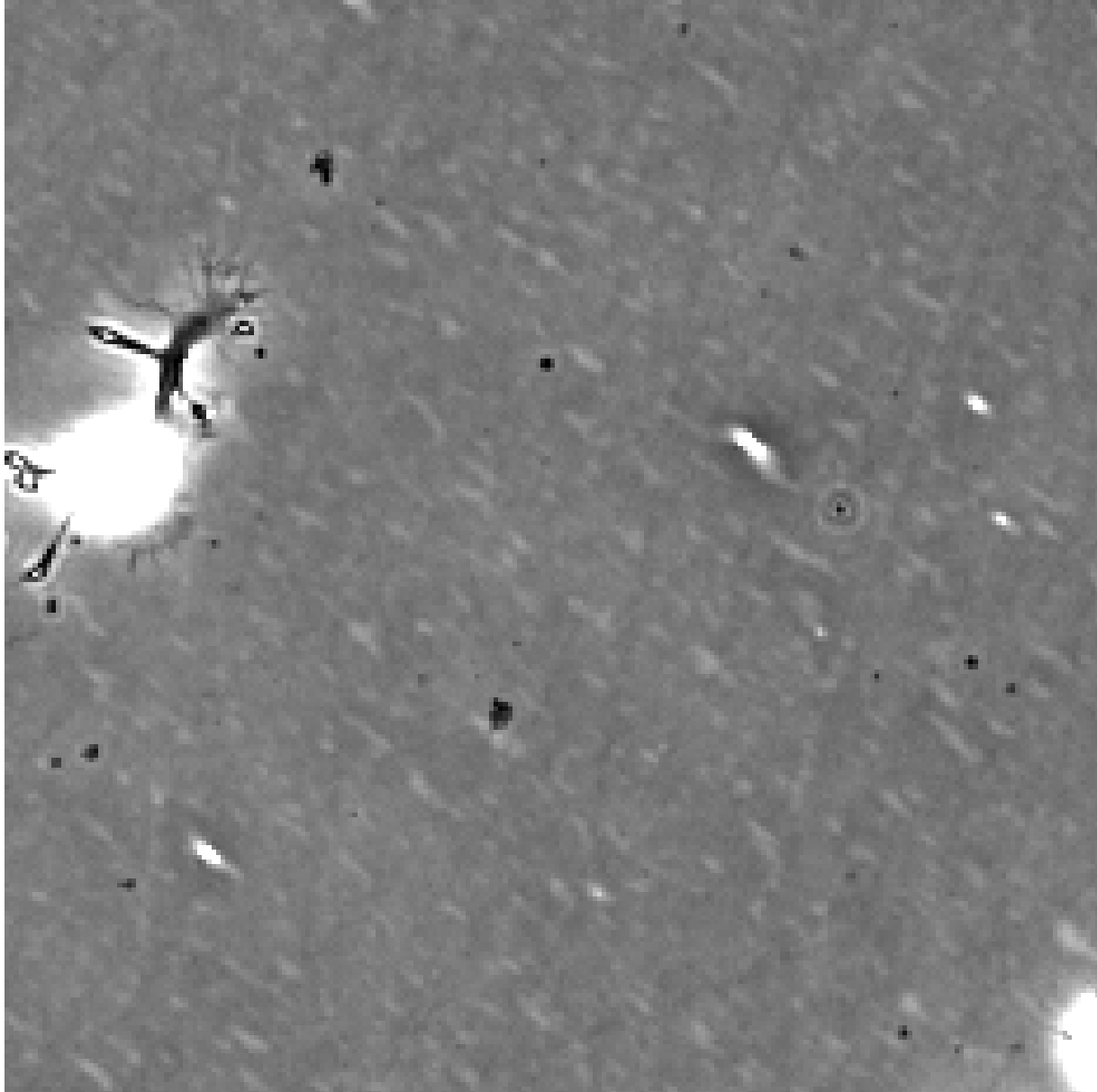
+ serum



serum-starved



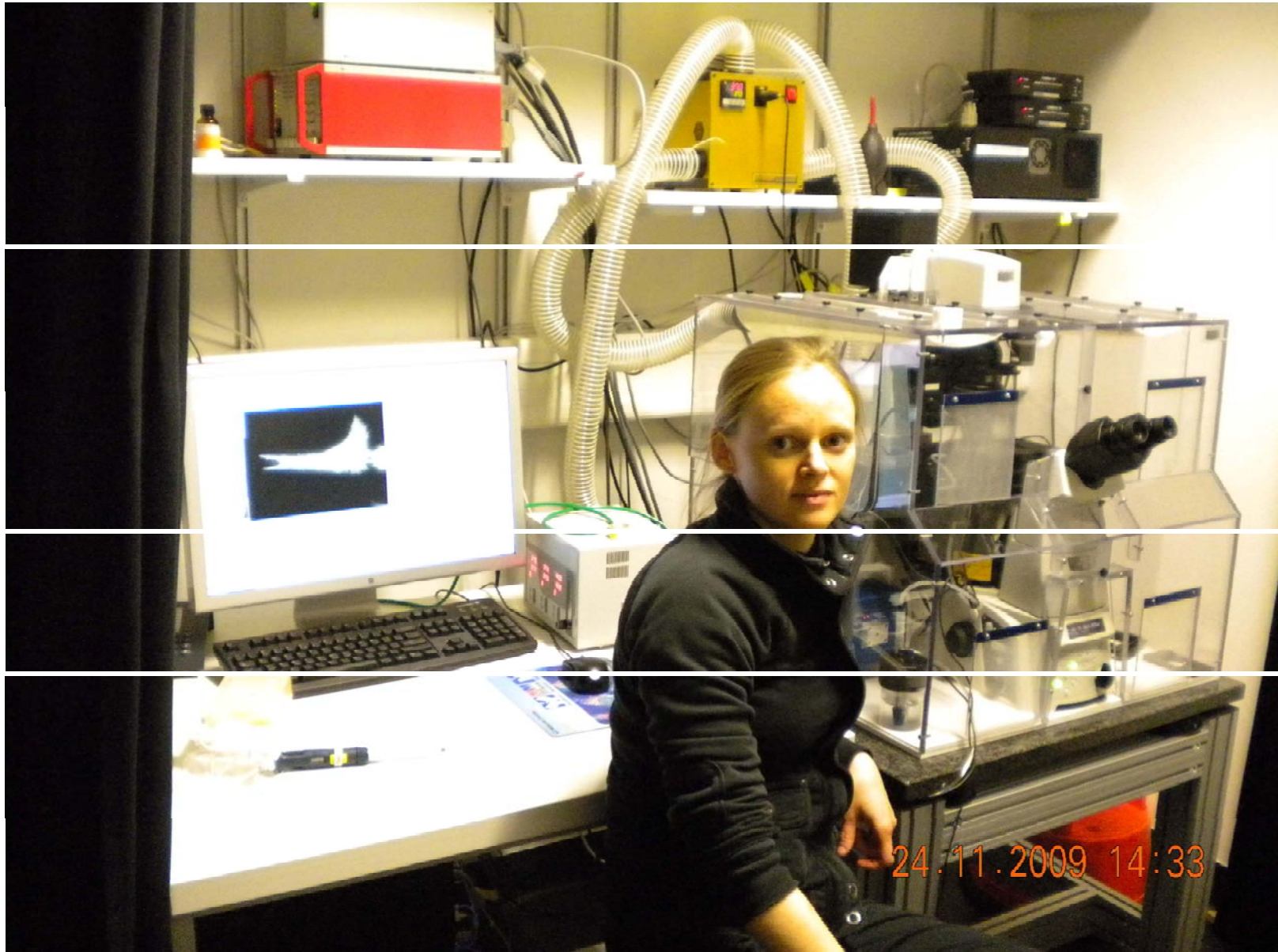
## Dynamik von Neuronen in der Petri Schale



**Neuronale  
Zelle  
auf dem  
Substrat  
Laminin**

**24 Stunden**

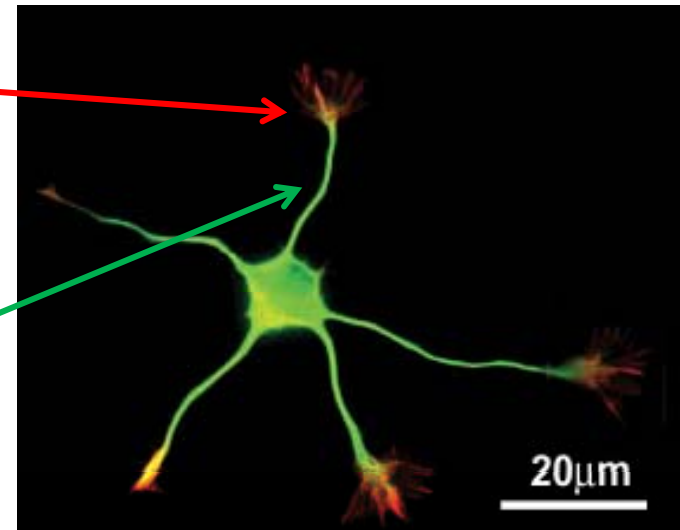
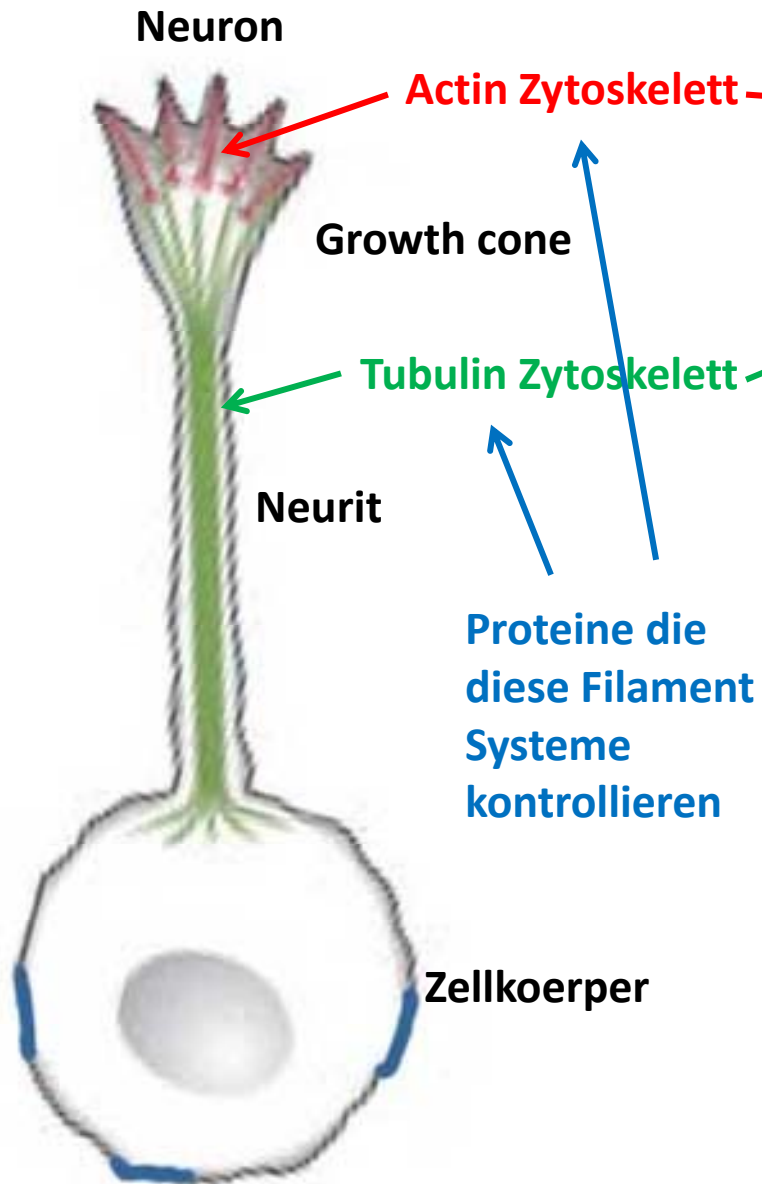
# Das Mikroskop, I



## Das Mikroskop, II



# Der Neurit hat einen komplexen molekularen Motor, der aus verschiedenen Filamenten gemacht ist

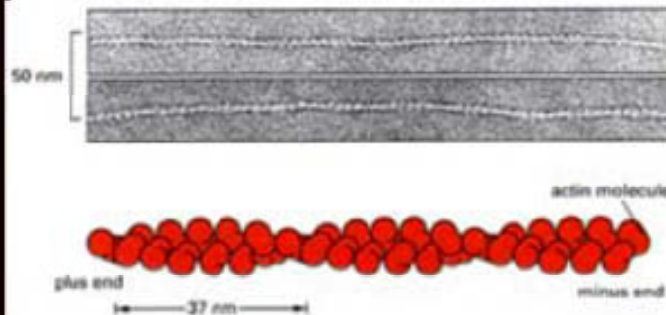


Ford  
Mustang  
1968  
Motor

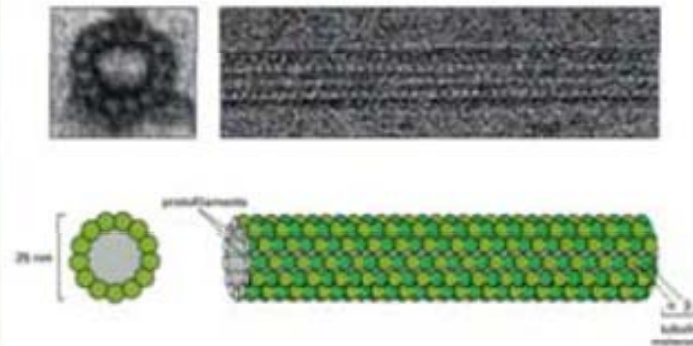
Proteine die  
diese Filament  
Systeme  
kontrollieren



# Filamente: Actin und Microtubuli



- Ø 5-9 nm
- polar filaments (+/- end)
- actin monomers
- ATP/ADP nucleotide binding

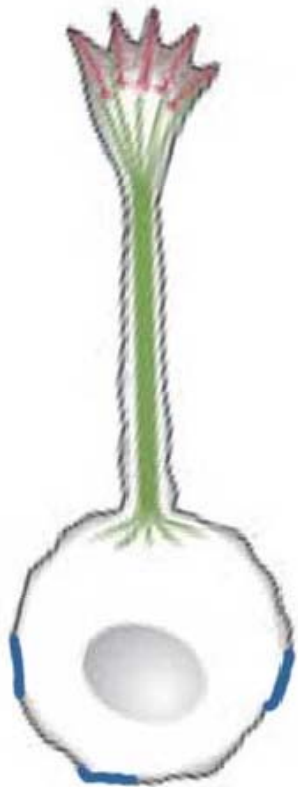


- Ø 24 nm
- polar filaments (+/- end)
- $\alpha/\beta$  tubulin hetero-dimers
- GTP/GDP nucleotide binding

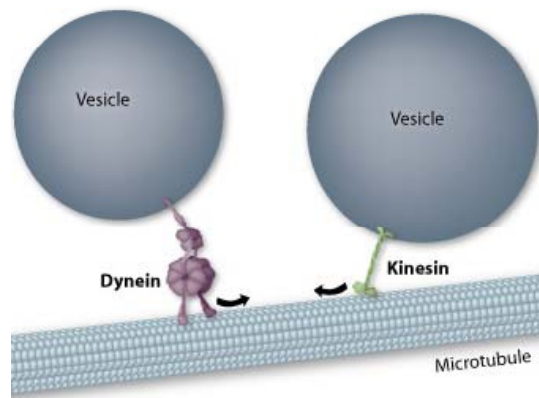
# Rolle der Microtubuli

- Microtubuli bilden einen Widerstand gegen Kompression, wichtig fuer die Stabilitaet der Struktur

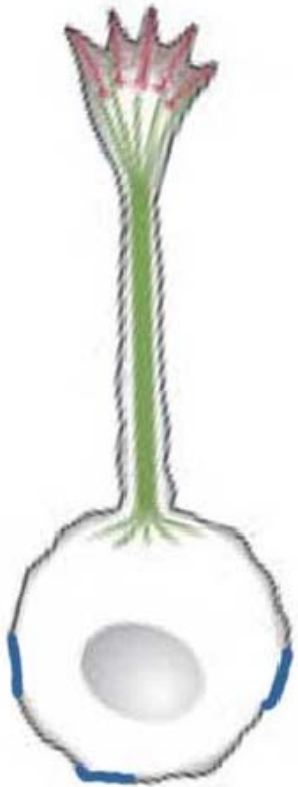
-Microtubuli dienen als Schienen fuer den Transport von Molekuelen und Vesikeln



Vesicles Travel Cellular Highways

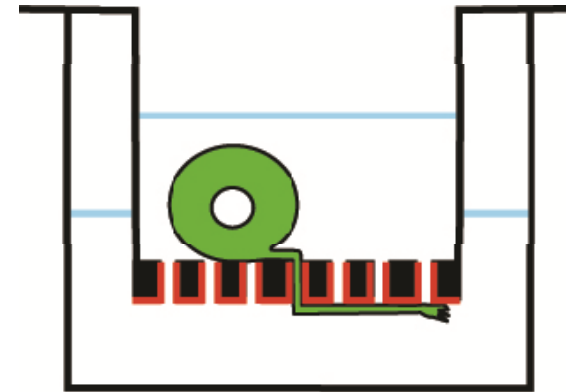
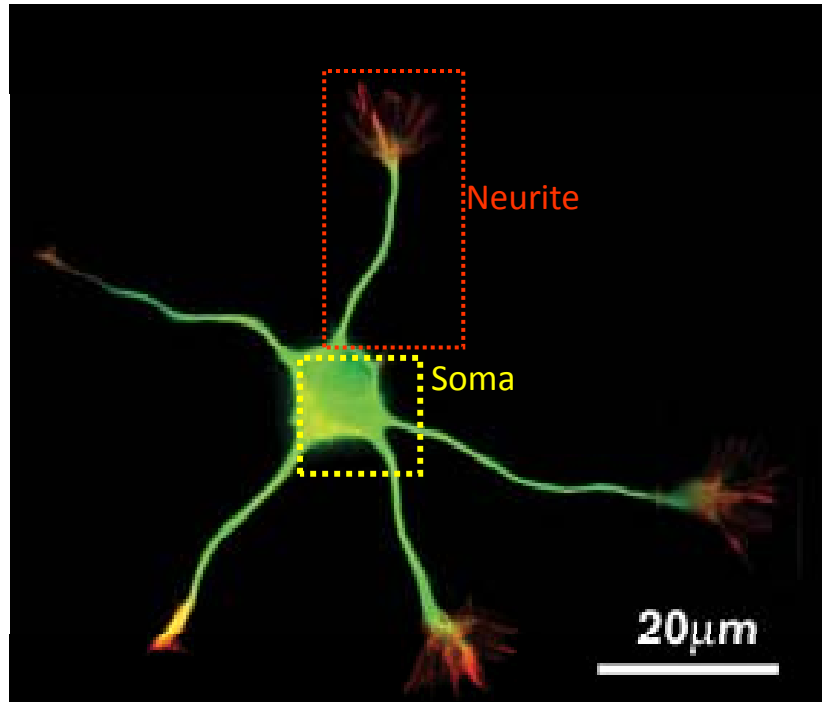


# Rolle des Actins



Actin Polymerization entwickelt  
Kontraktion Kräfte,  
welche die Bewegung des  
Growth cone ermöglichen

# Ein Beispiel aus unserem Labor: Wie studiert man, wie verschiedene Proteine die Neuriten regulieren

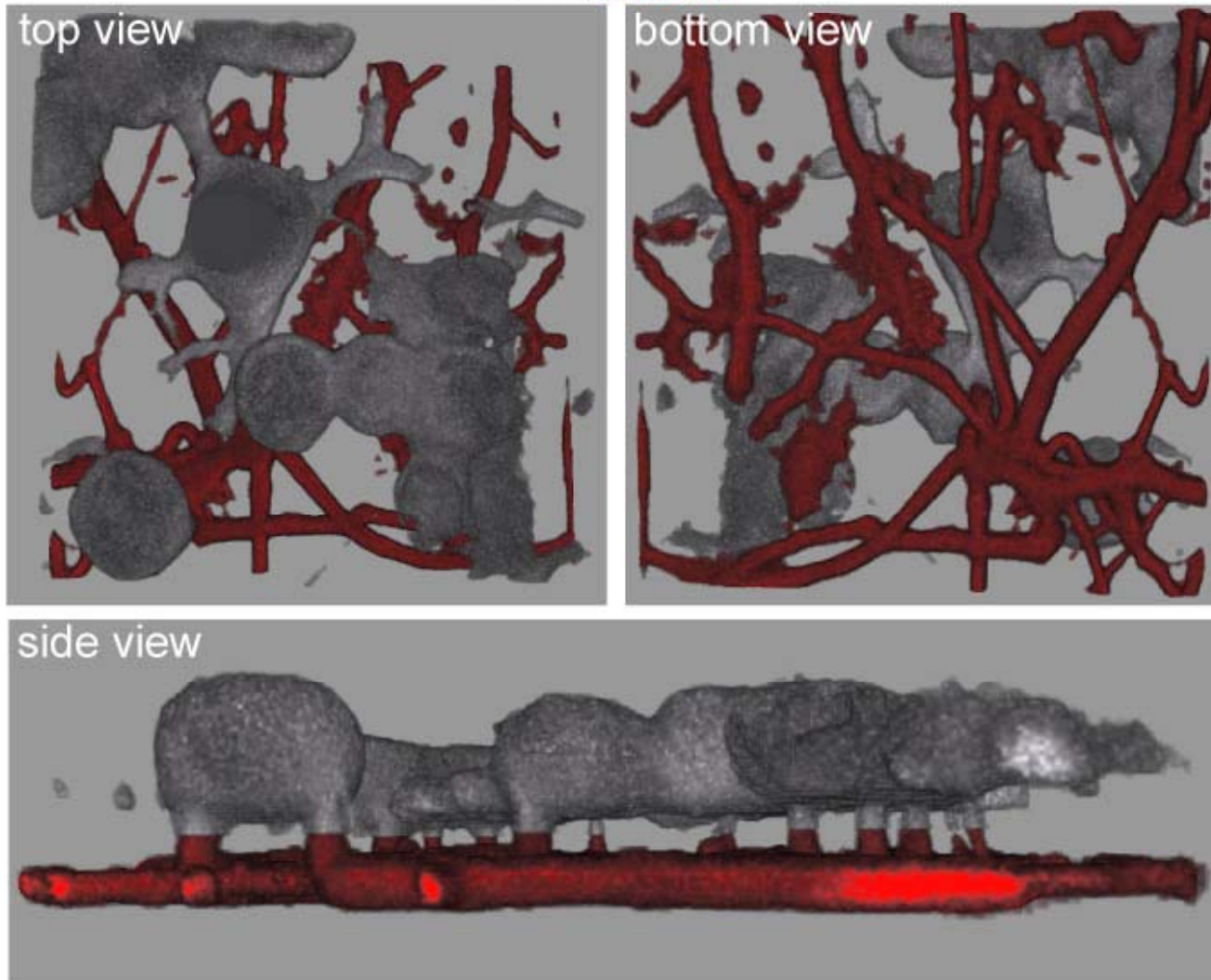


**Actin, tubulin und  
welche andere Proteine ?**

# Neuronen auf dem Filter: Bilder

3D reconstruction of neurons on filter

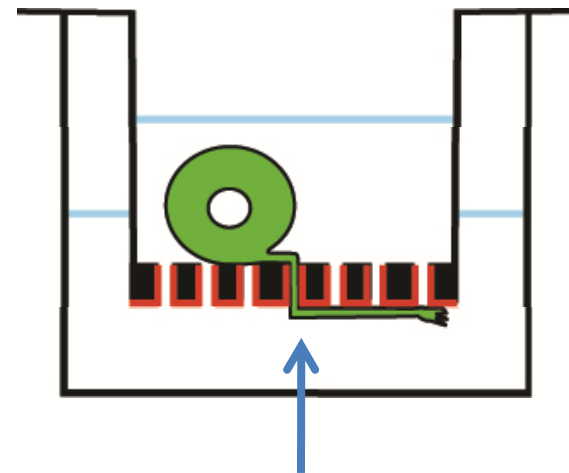
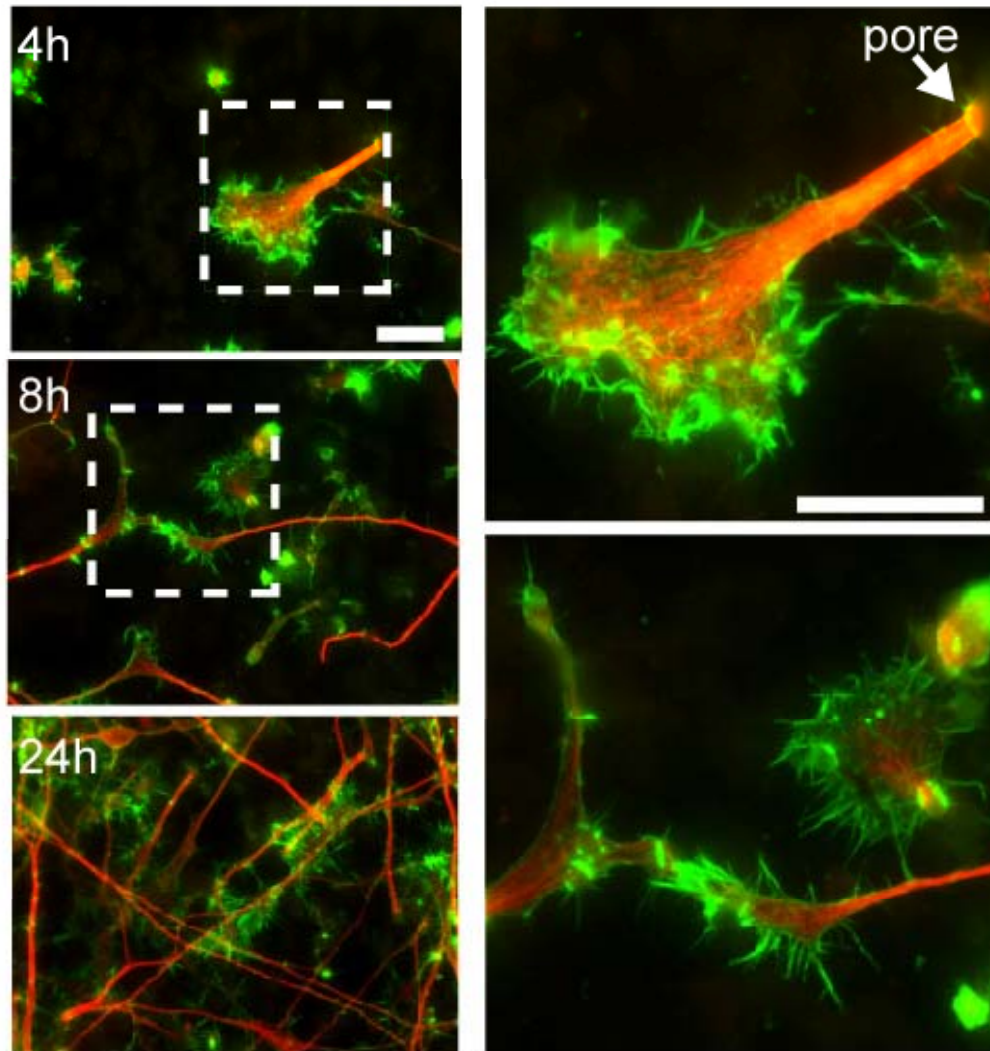
soma/neurite



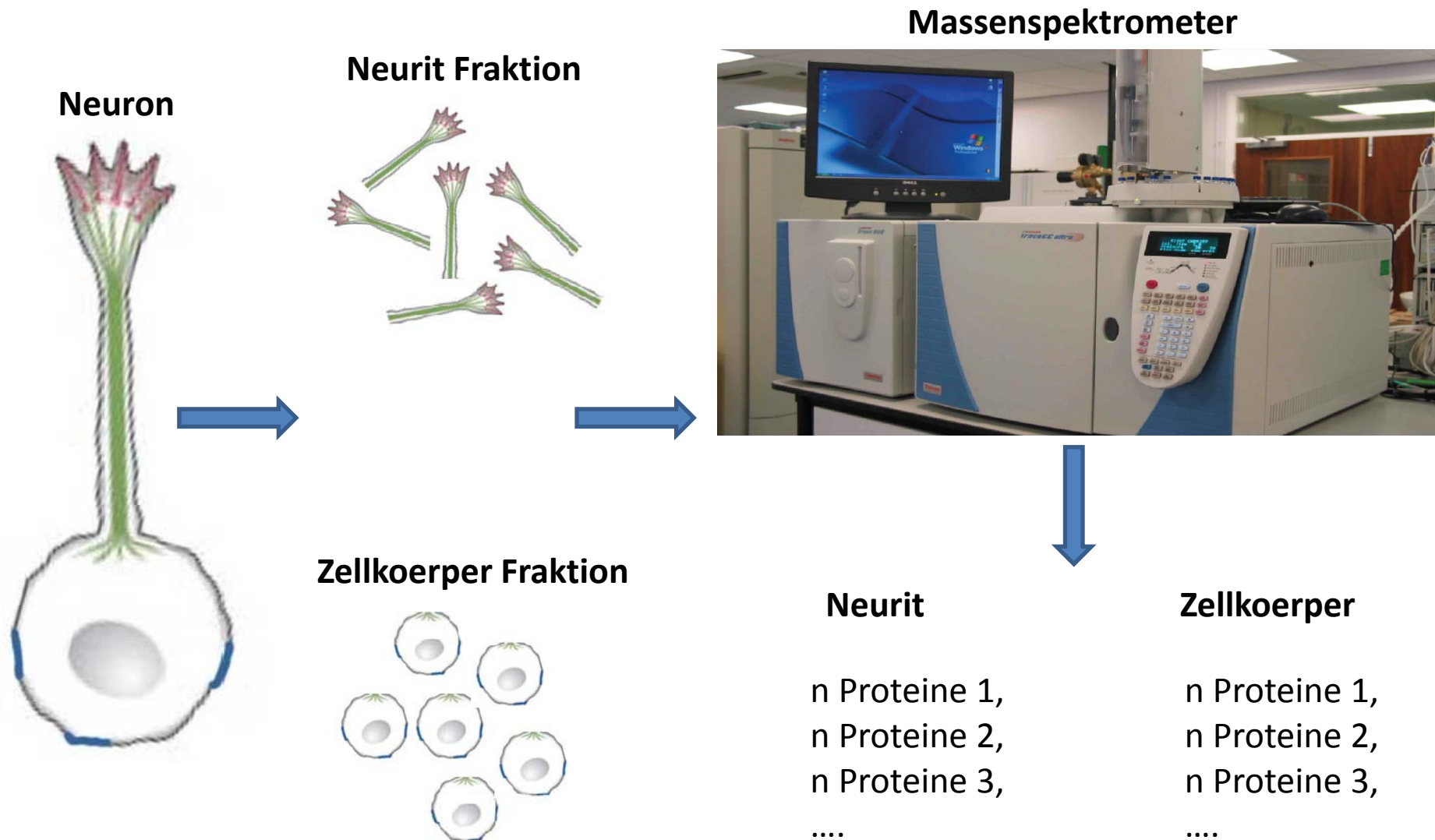
# Neuronen auf dem Filter: Bilder

Staining of neurites on filter bottom

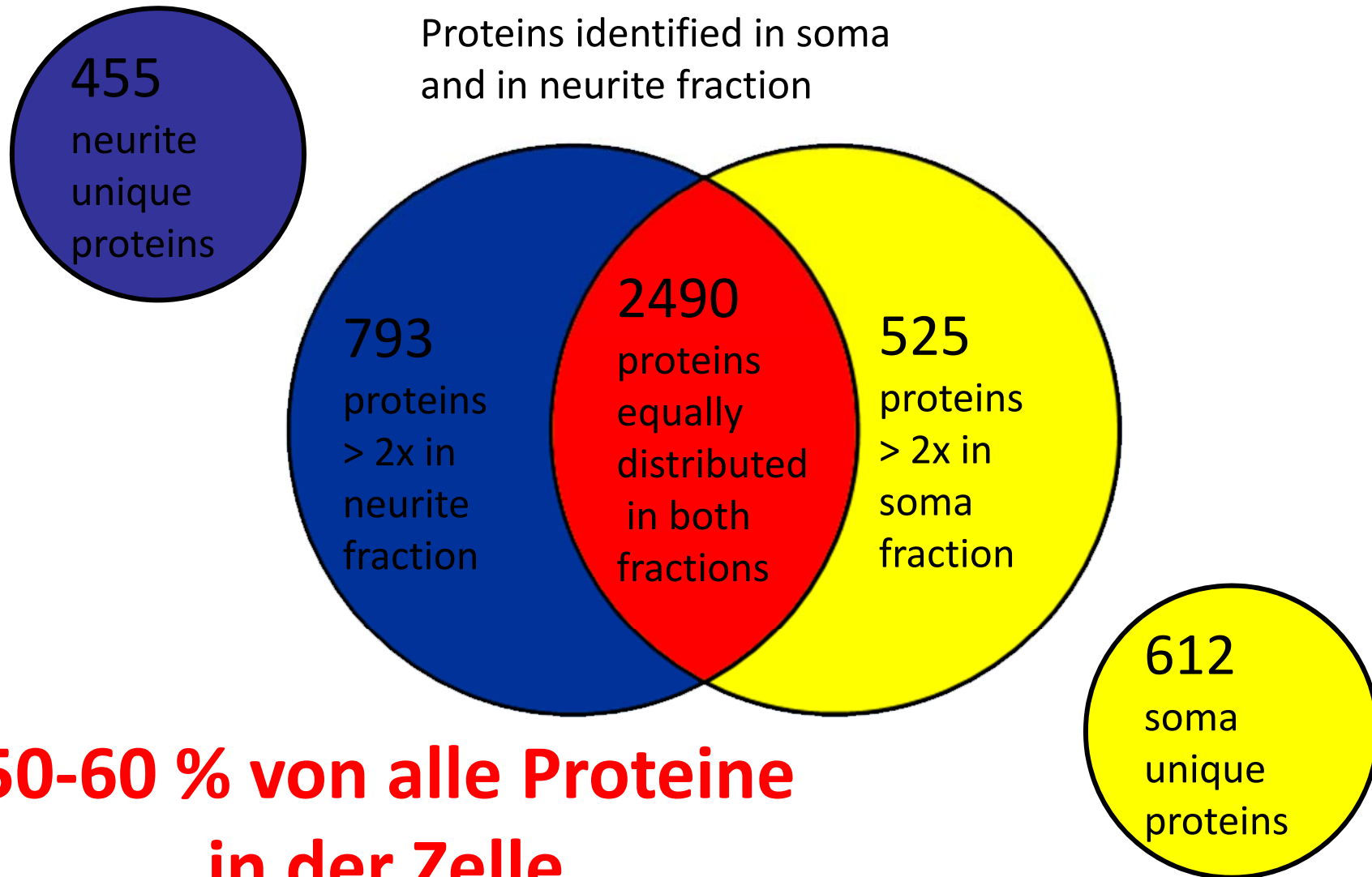
actin/tubulin



# Massenspektrometrische Analyse des Neuriten



# Wiewiele Proteine in Neurit und im Zellkoerper ?

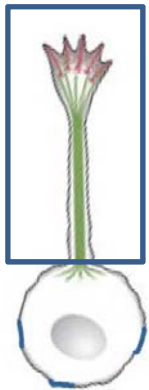




# Wieder die Analogie zum Auto Motor !

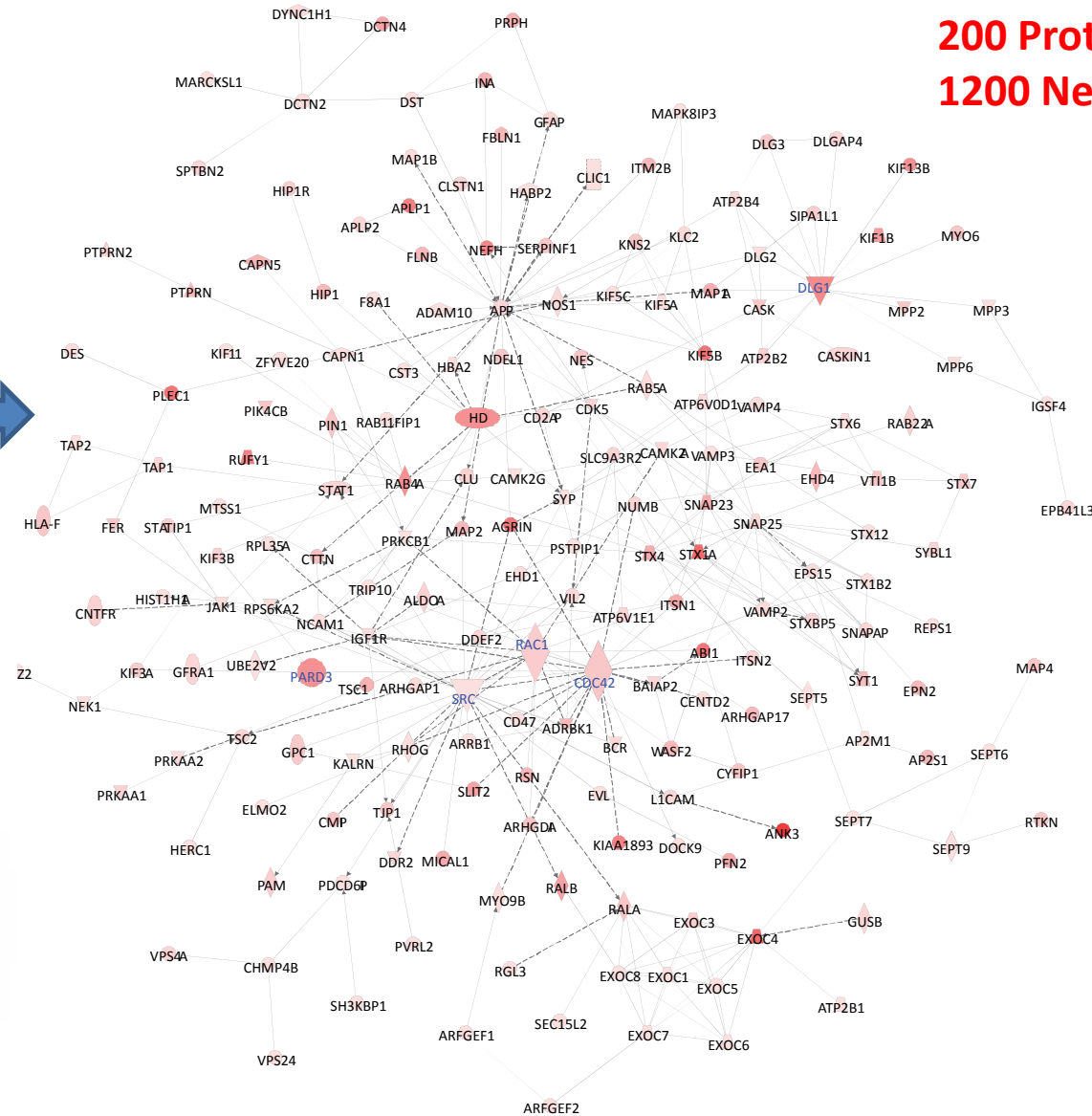
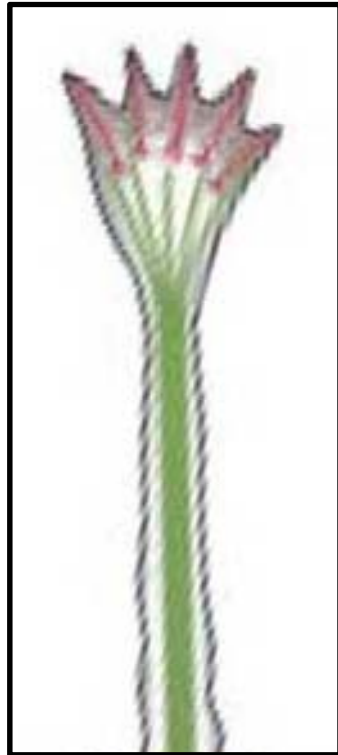
**Wir haben:  
Die Liste der Komponenten  
des Neuriten Motors**

**Wir moechten wissen wie:  
Der Motor assembliert ist  
und wie er funktioniert**



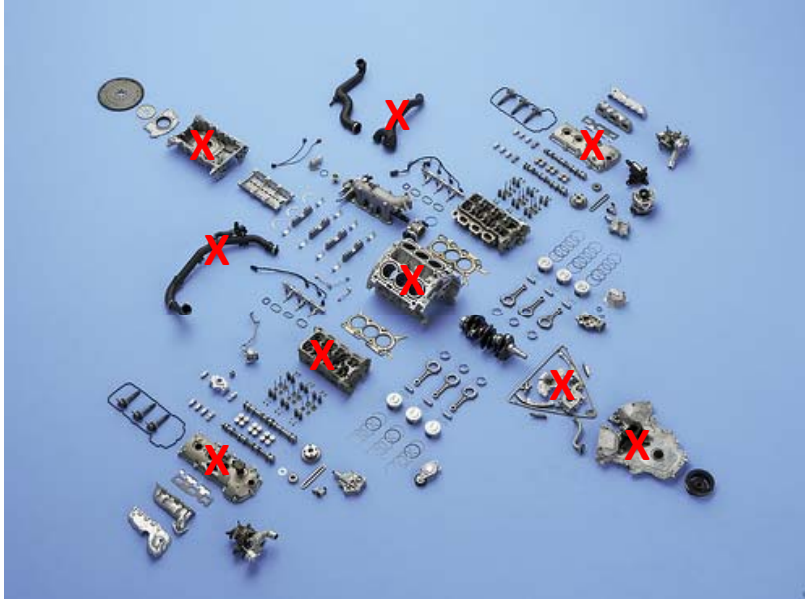
**Ford Ecoboost 3.5 Motor**

# Hypothese: Wie sind verschiedene Komponenten des Neurit "Motor" assembliert ?



200 Proteine von den  
1200 Neurit Proteine

# RNA Interferenz



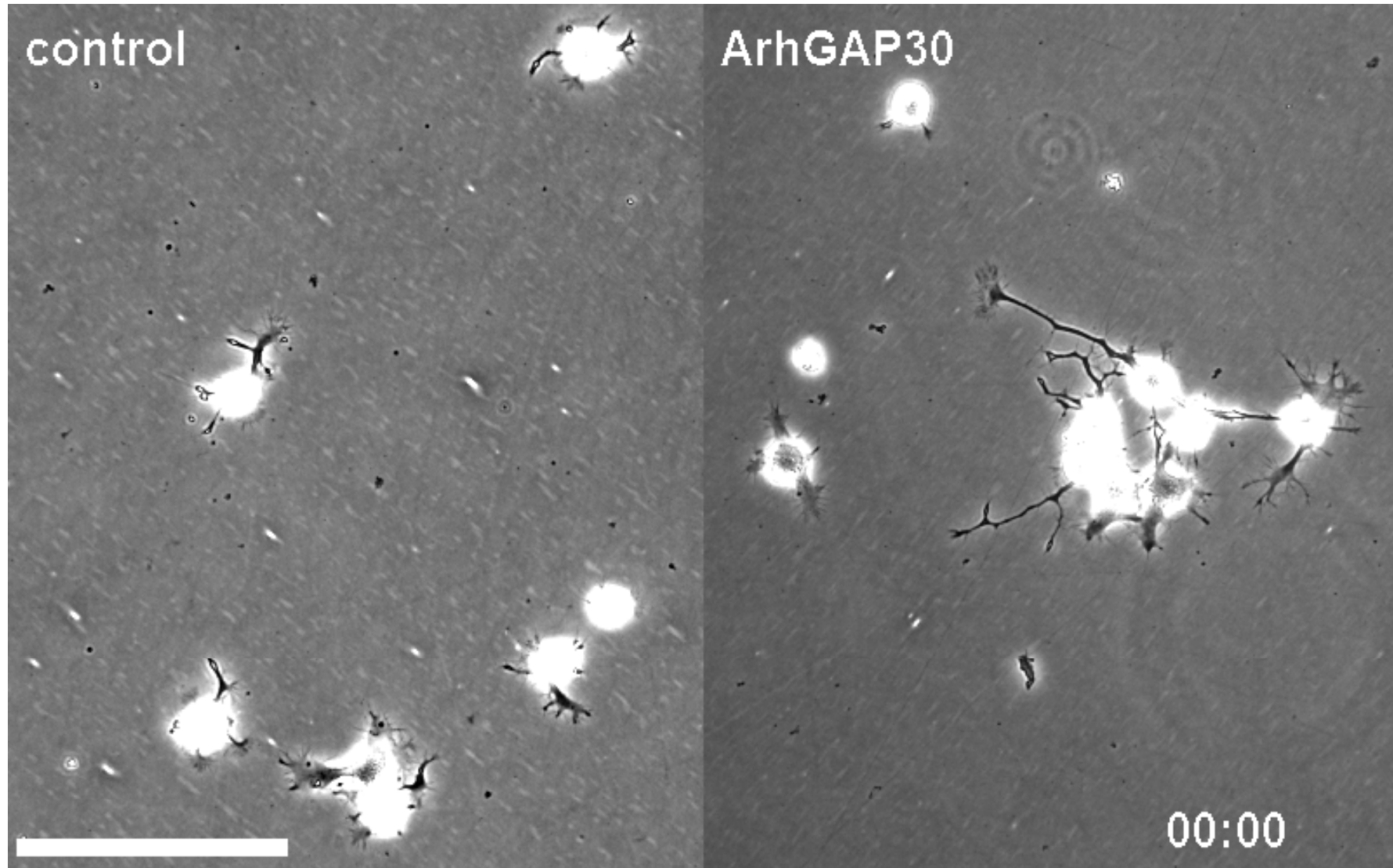
Neurit Komponente



Was ist den Effekt auf dem Motor ?

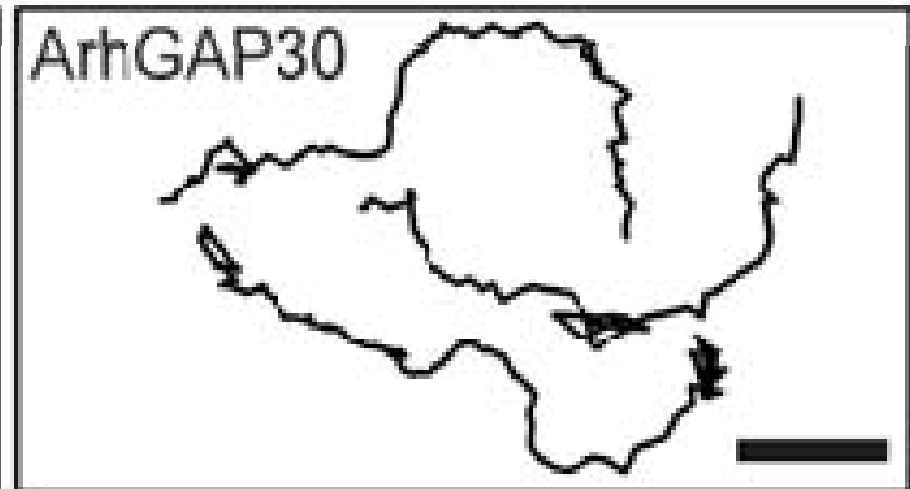
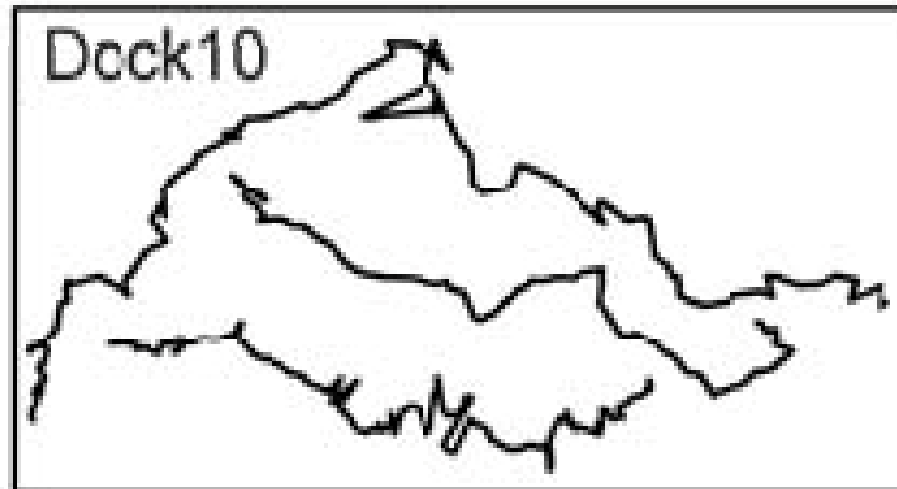
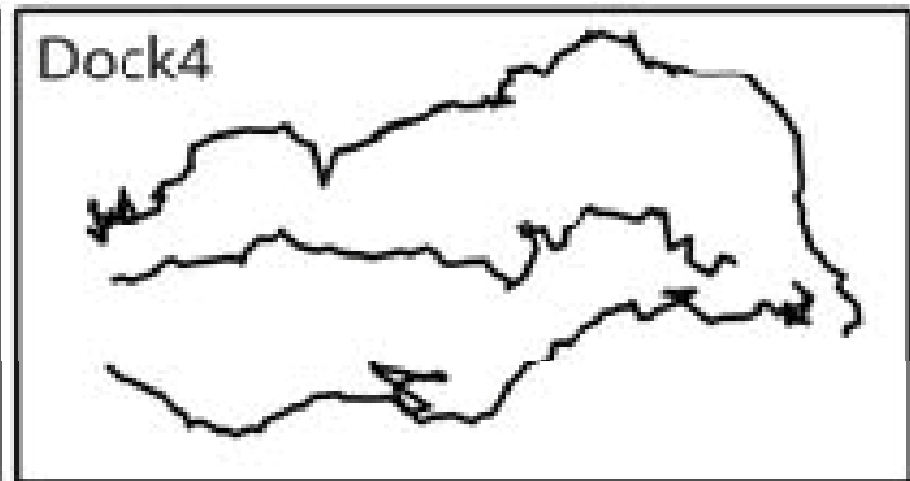
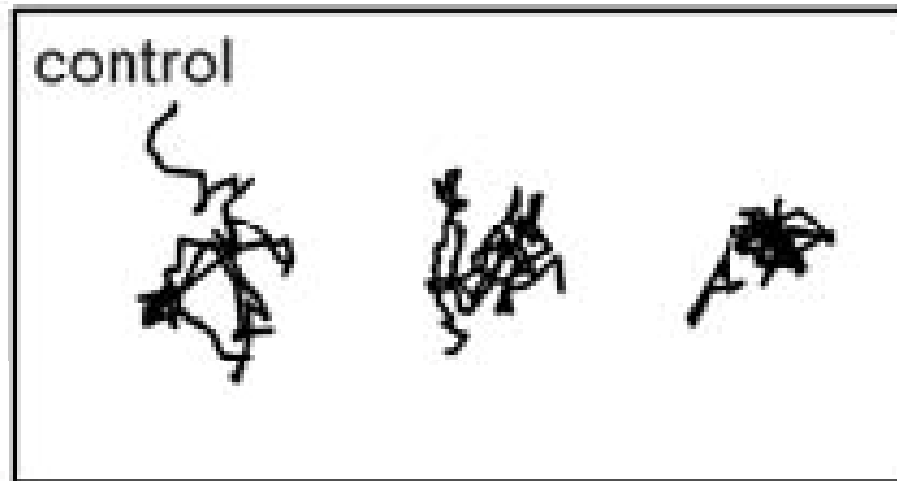


# Neurit (Motor) geht nur vorwaerts



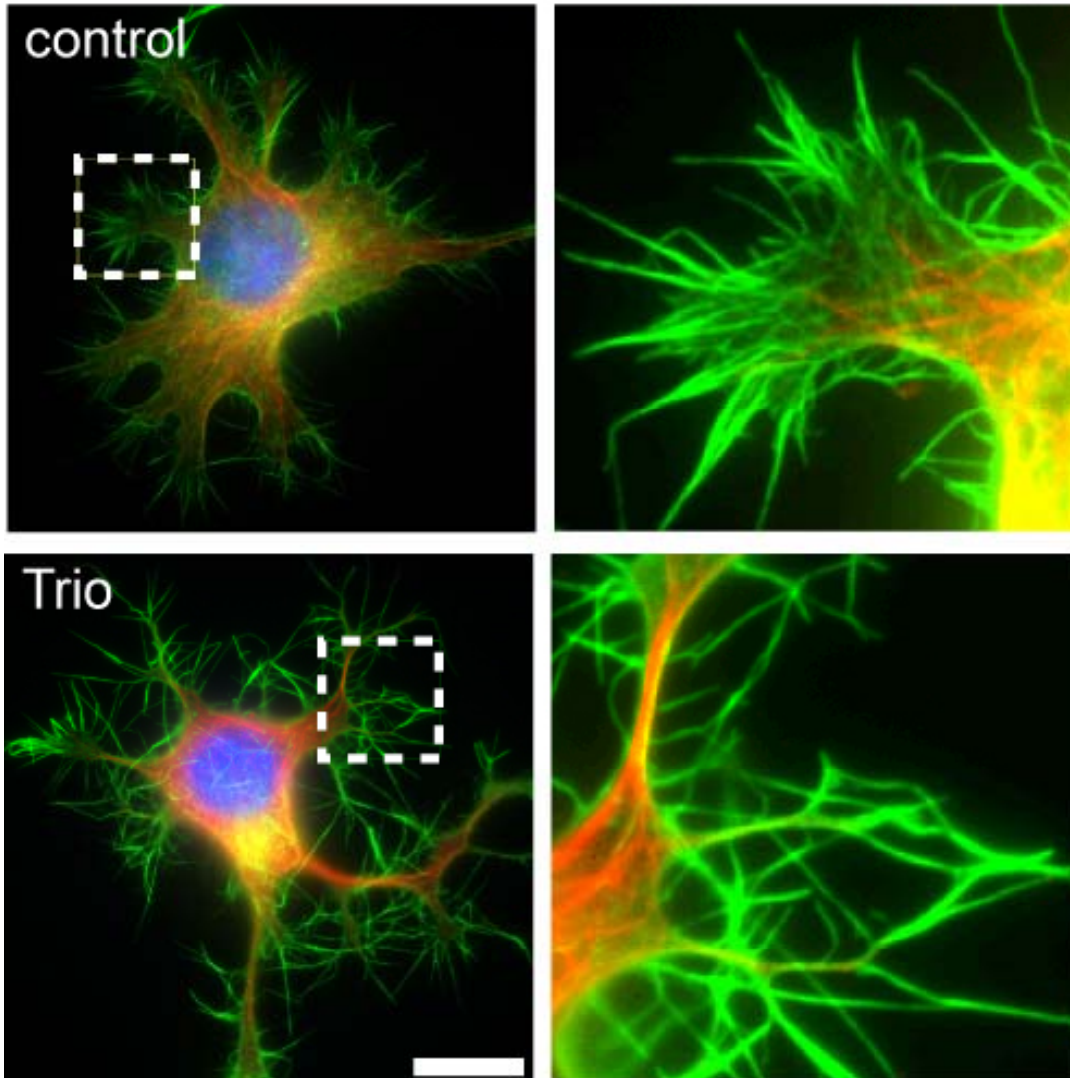
Scale bar = 100  $\mu$ m

# Motor geht vorwaerts !



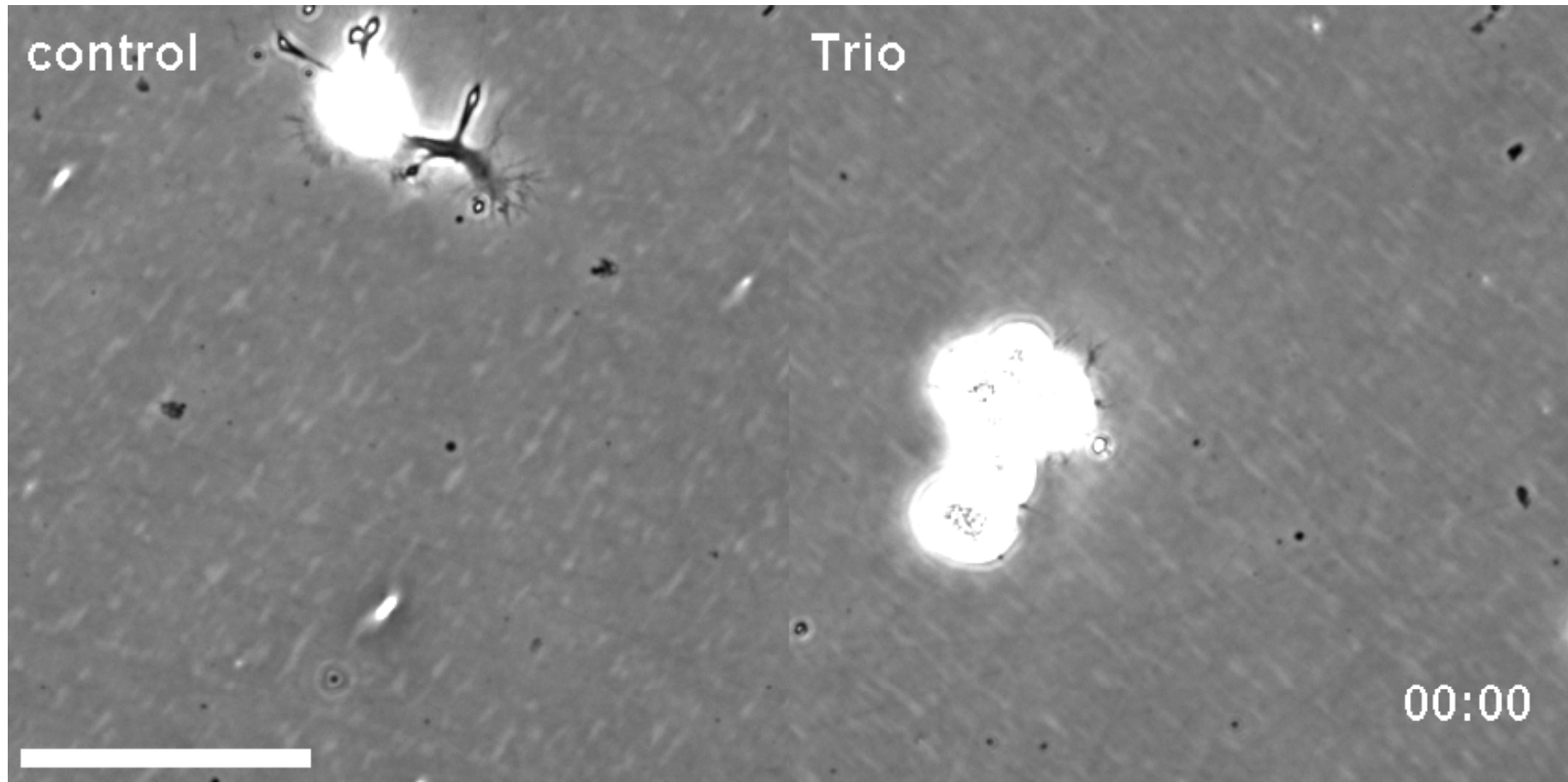
# Trio

actin/tubulin/nuclei



Filopodia  
Phenotyp

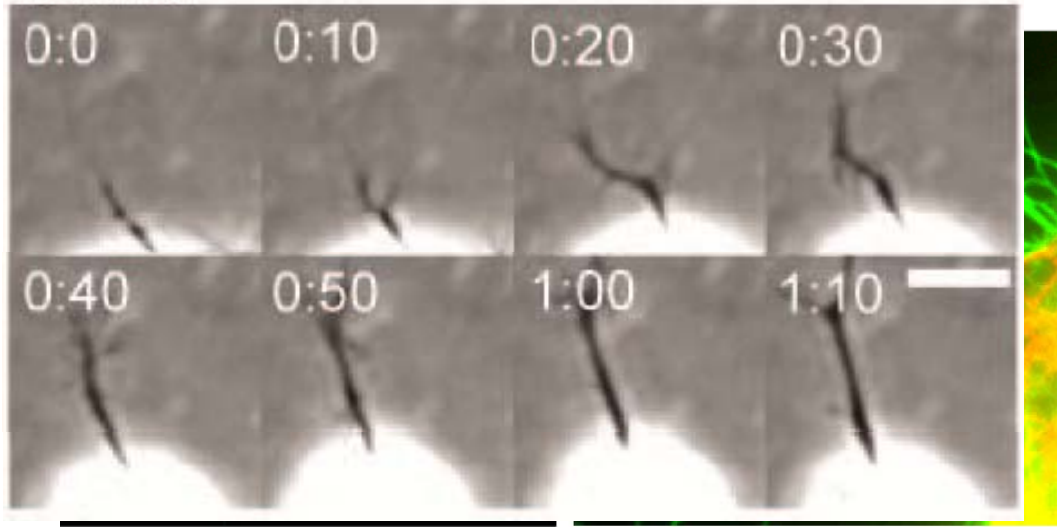
# Neurit Initiation Defekt



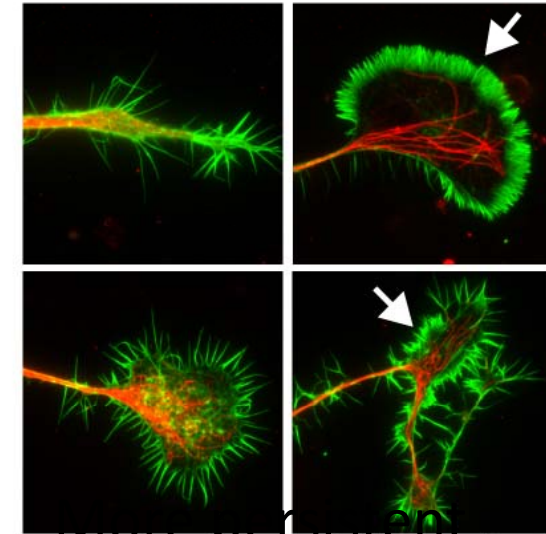
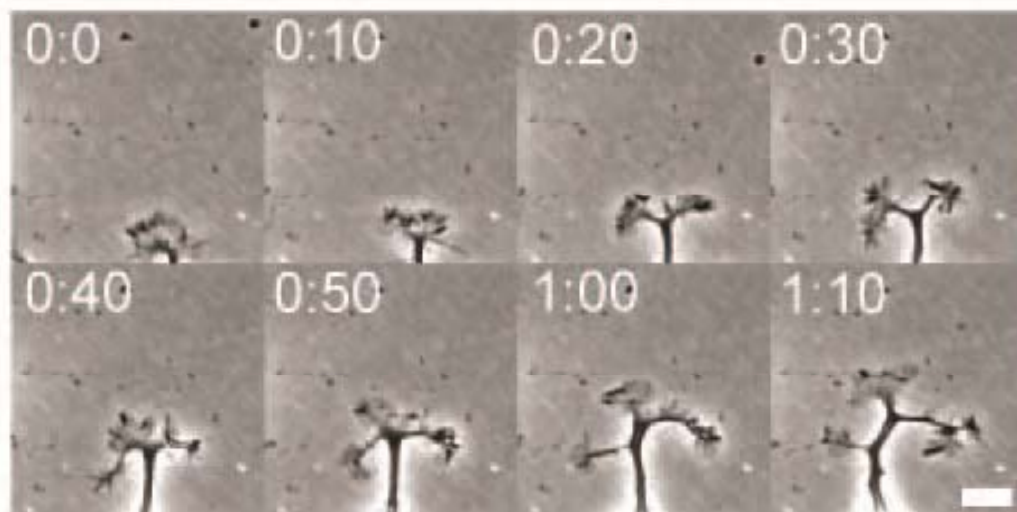
Scale bar = 100  $\mu$ m

# Super stable Filopodia im Growth cone

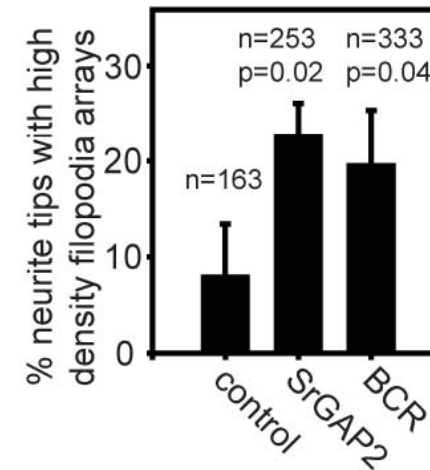
control



SrGAP2

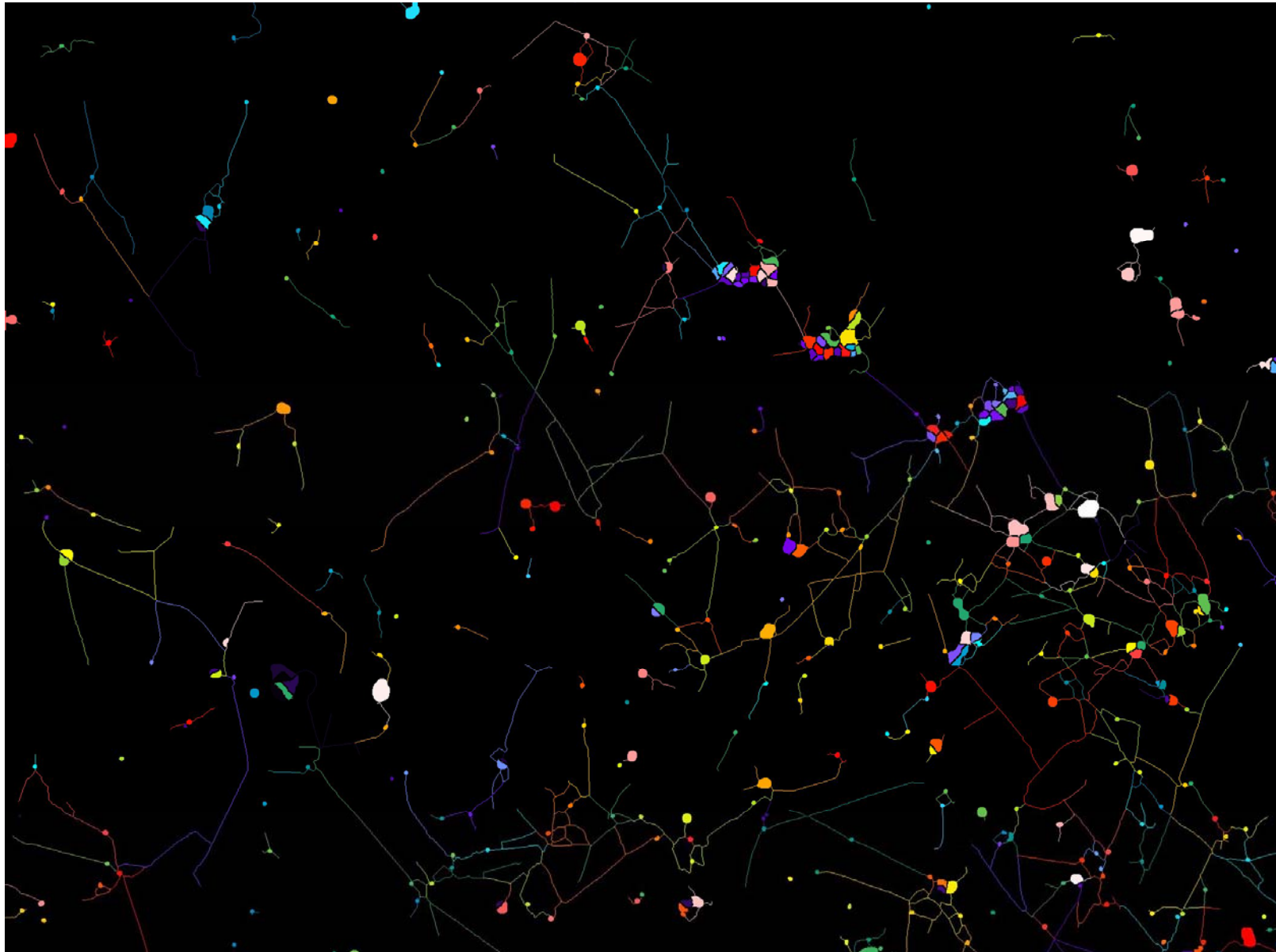


low density filopodia      high density filopodia  
 more persistent  
 Neurite outgrowth



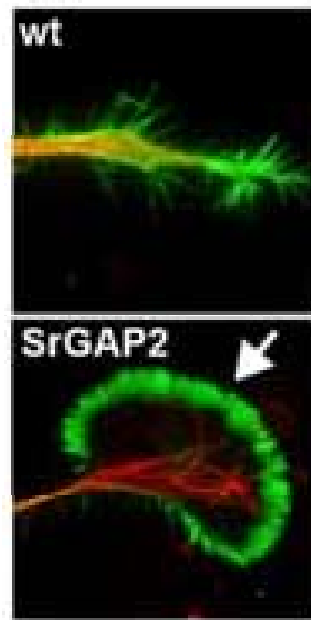


# Statische Bilder geben nur wenig Information

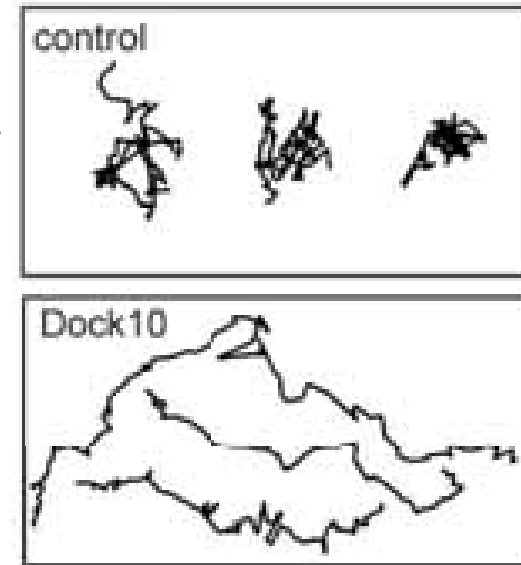


# Verschiedene Module im Motor

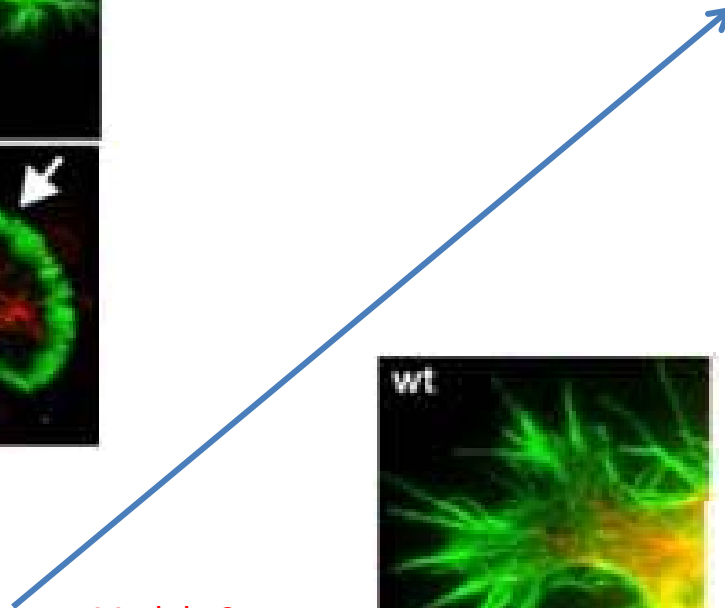
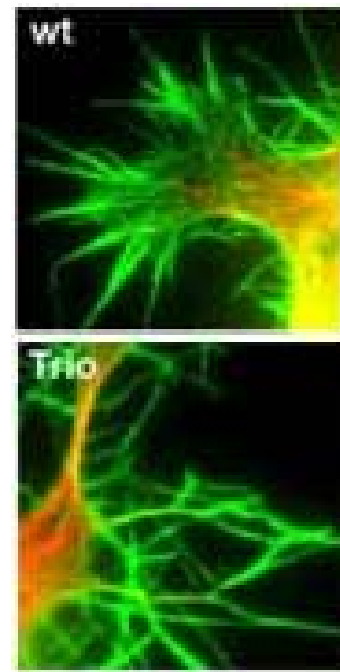
**Modul 3**  
Filopodia Stabilitaet



**Modul 1**  
Keine Retraction



**Module 2**  
Neurit Initiation  
und Filopodia  
Struktur



# Langfristiges Ziel: alle Komponenten in den Neuriten analysieren

