The Brain is the Client:
Designing a Back Door into the Nervous System

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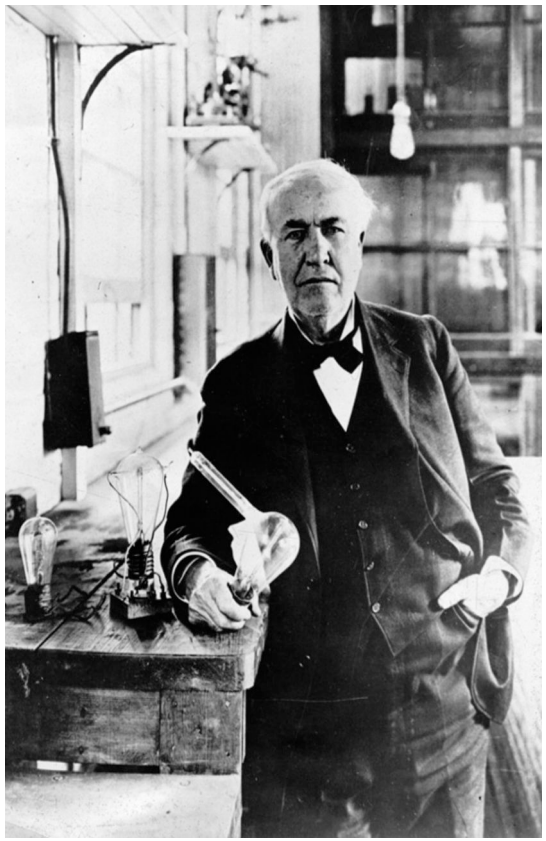
Brain-machine interface

No convention,
no consensus

“War of the Currents”

Thomas Edison

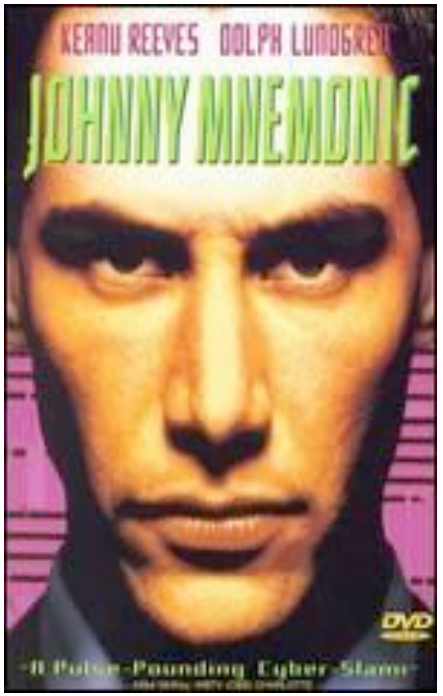


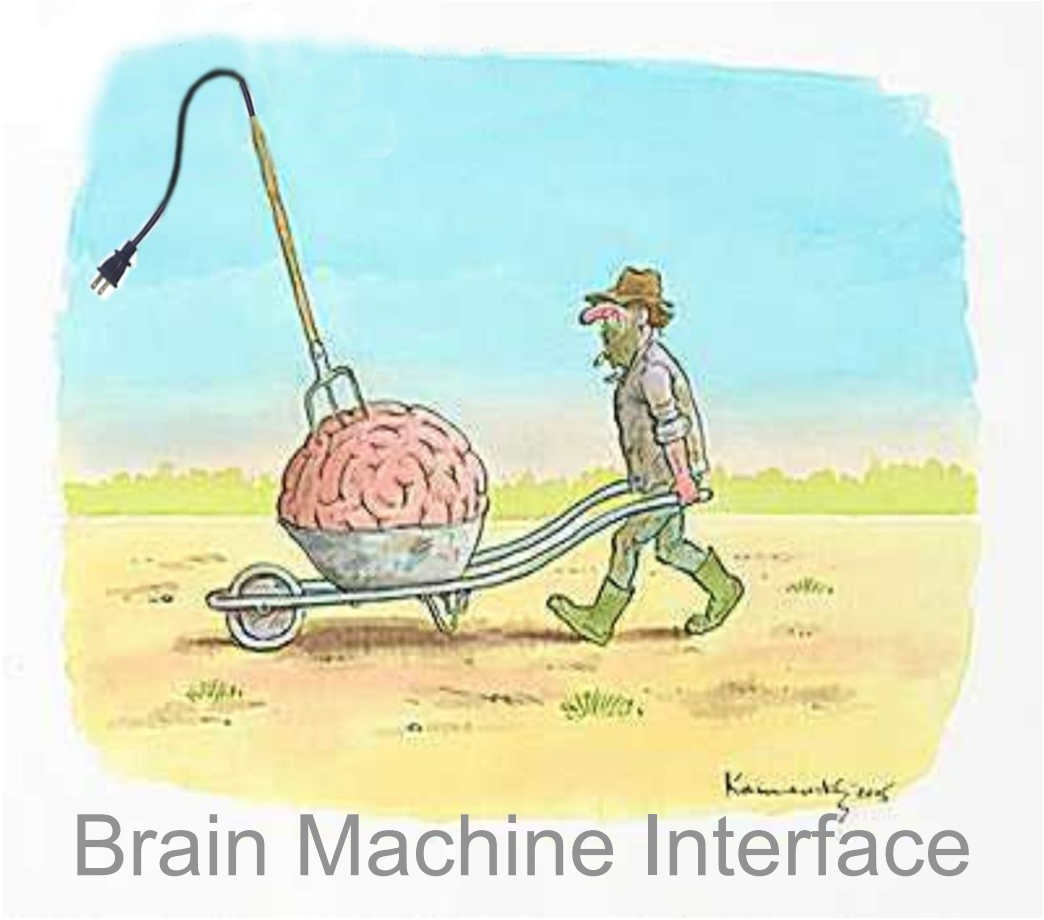
DC vs. AC

Nikola Tesla

Where and what is a neural interface?

The Matrix: Hooking into the Net





Brain Machine Interface

Where do you connect?

Do you cause damage?

Hard and/or sharp:
BAD

Wet and juicy familiar tissue:
GOOD

Cater to the promiscuous nature of the nervous system

The brain is the client; give it what it wants.

Direct or
Indirect interface?

Harness as much of the processing power of the nervous system

as possible

i.e., interface as far away from the brain as possible

Must have two way communication:

Transfer sensory and motor signals

Elephant in the room

PROPRIOCEPTION

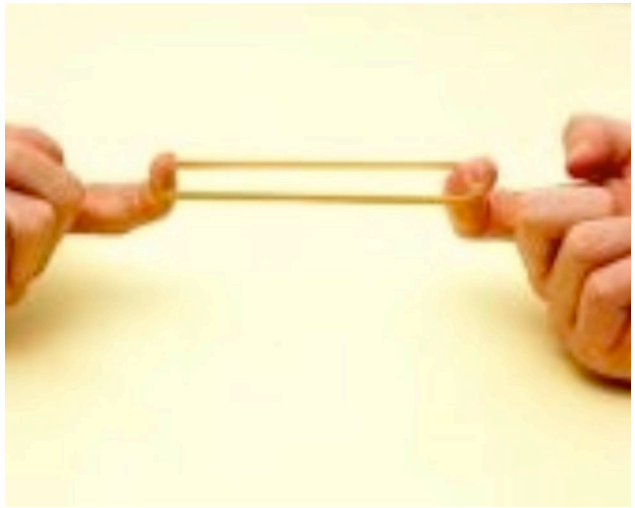
PROPRIOCEPTION

One-way exception:

Sensory devices -
Vision and Hearing

Still, interface should be as far away as possible from final processing site in the brain

Engineering a nervous tissue interface via stretch growth of integrated axon tracts



How fast, and to what length

can you stretch an

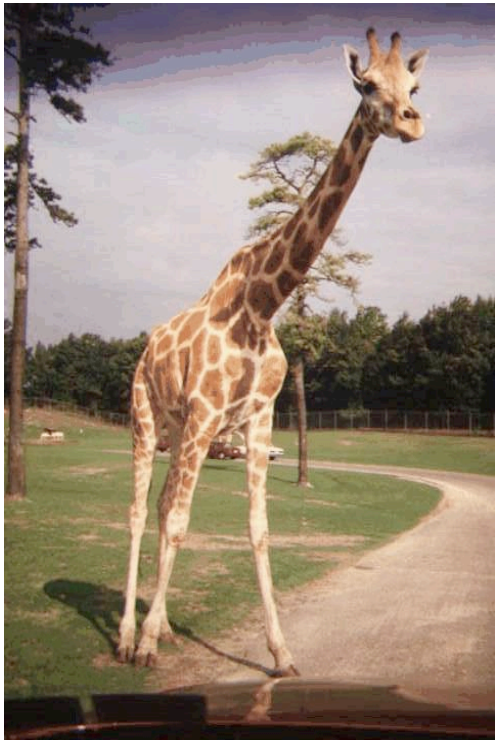
axon without damage?

Current Dogma:

Neurofilament protein transport = 1-2 mm/day

Axon outgrowth in culture = 1-2 mm/day

Nerve regrowth in vivo = 1-2 mm/day



A giraffe's neck can grow by 20mm a day!

Baobabfarm, 2002

Blue whales grow 40mm a day!

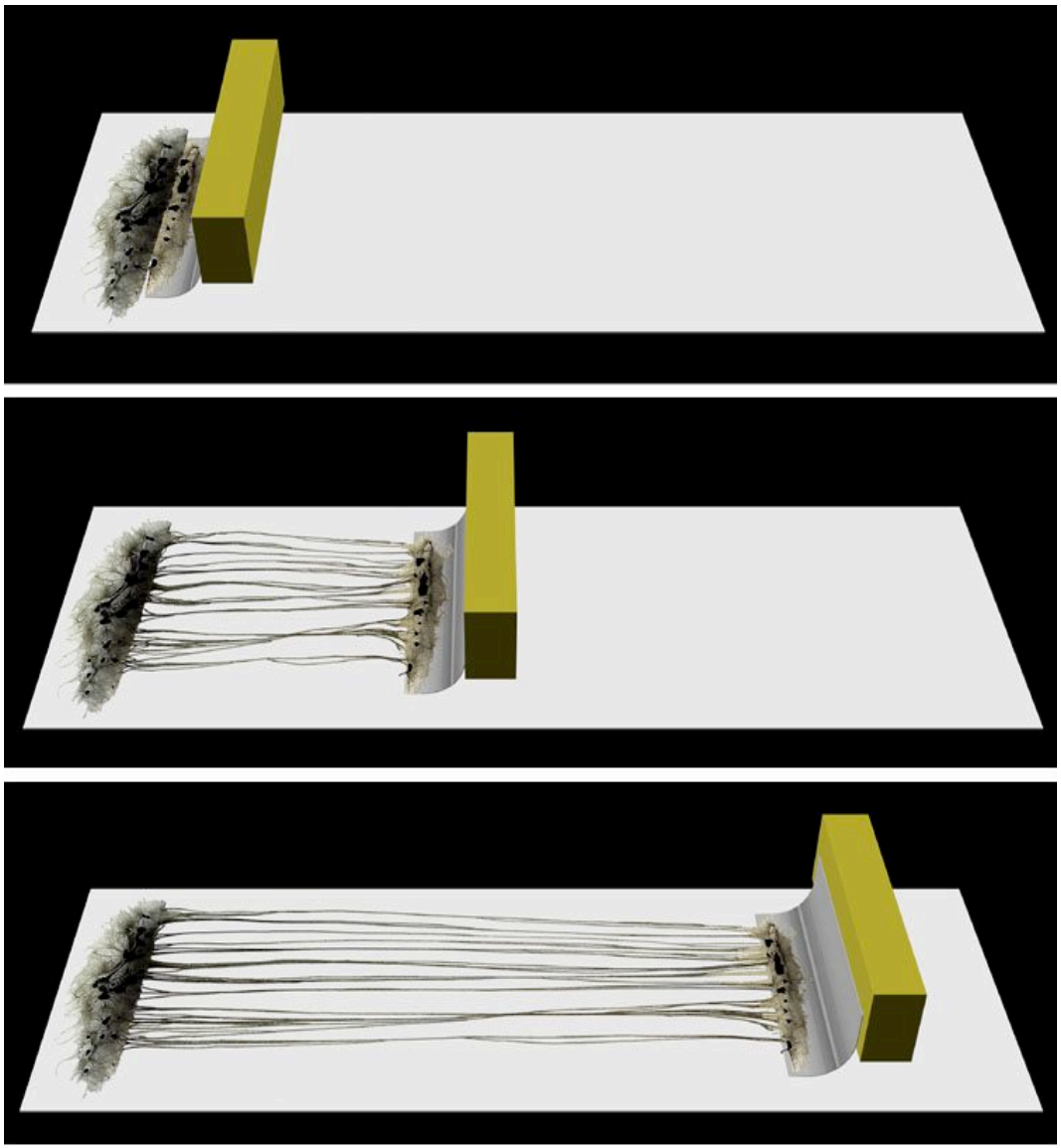
Kato, 1994

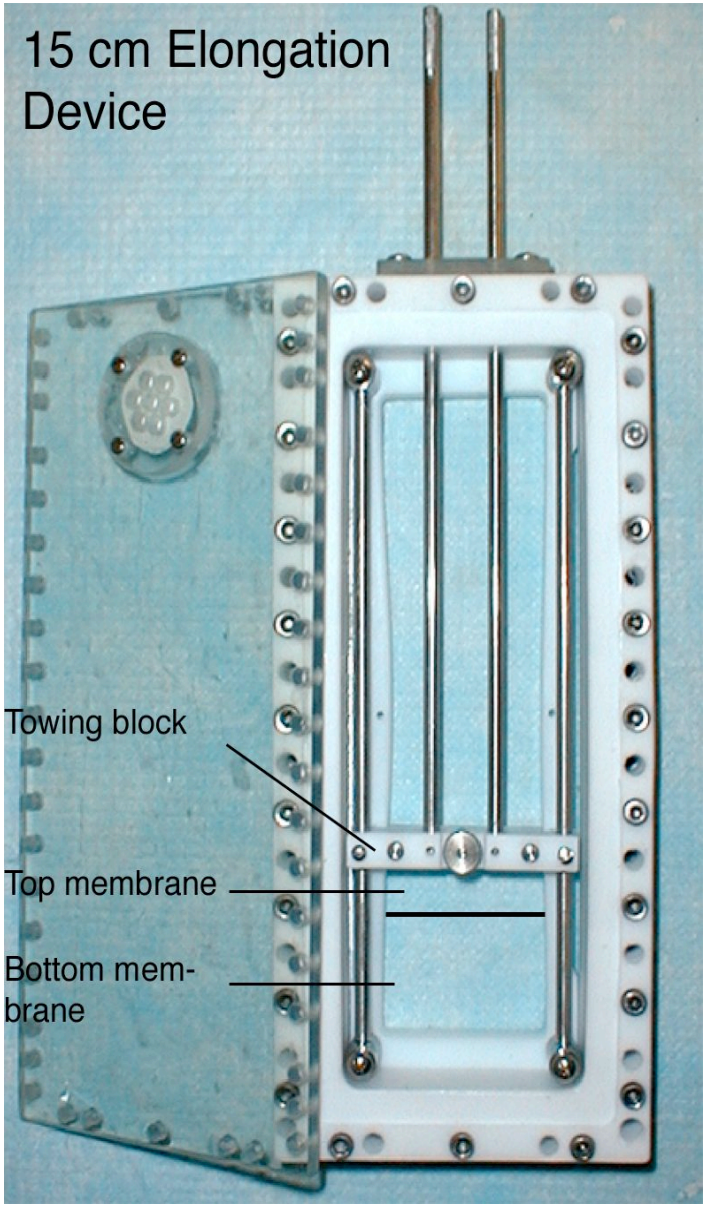
Deer antler sensory axons grow up to 18mm a day!

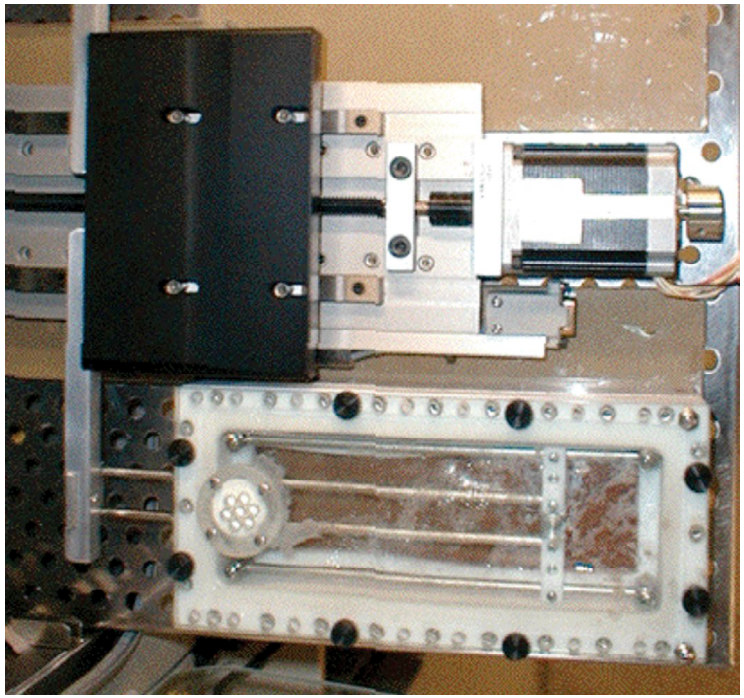
Gray et. al. 1992

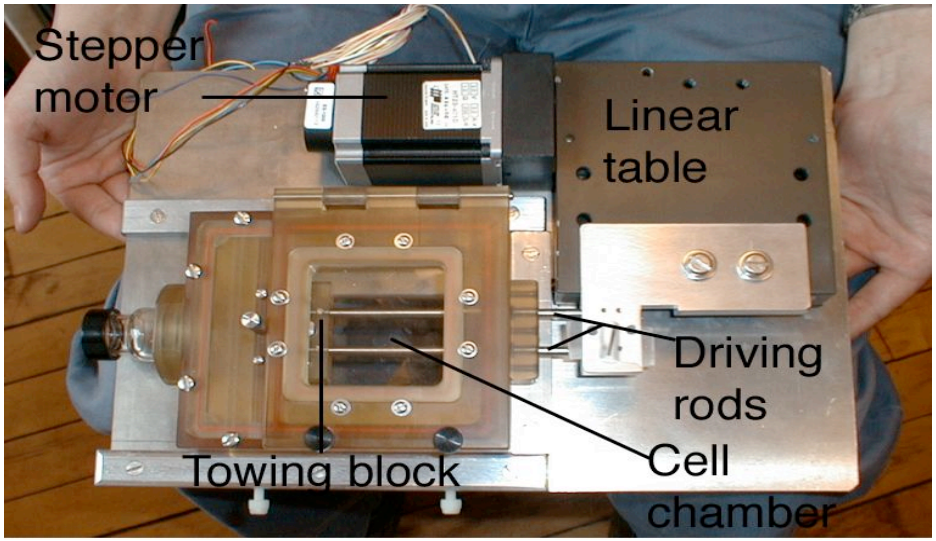
During development, there must be growth along the central portion of integrated axon tracts

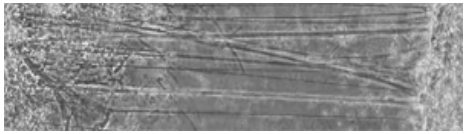
Stretch Growth Concept



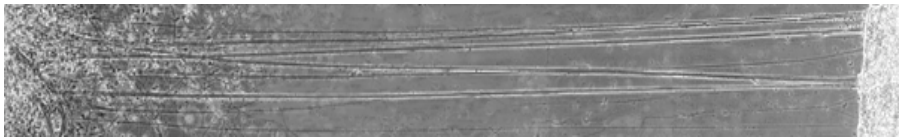

15 cm Elongation Device
Towing block
Top membrane
Bottom mem-brane




Stepper motor
Linear table
Driving rods
Towing block
Cell chamber

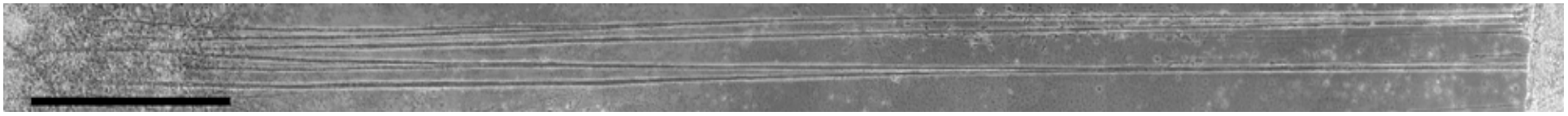


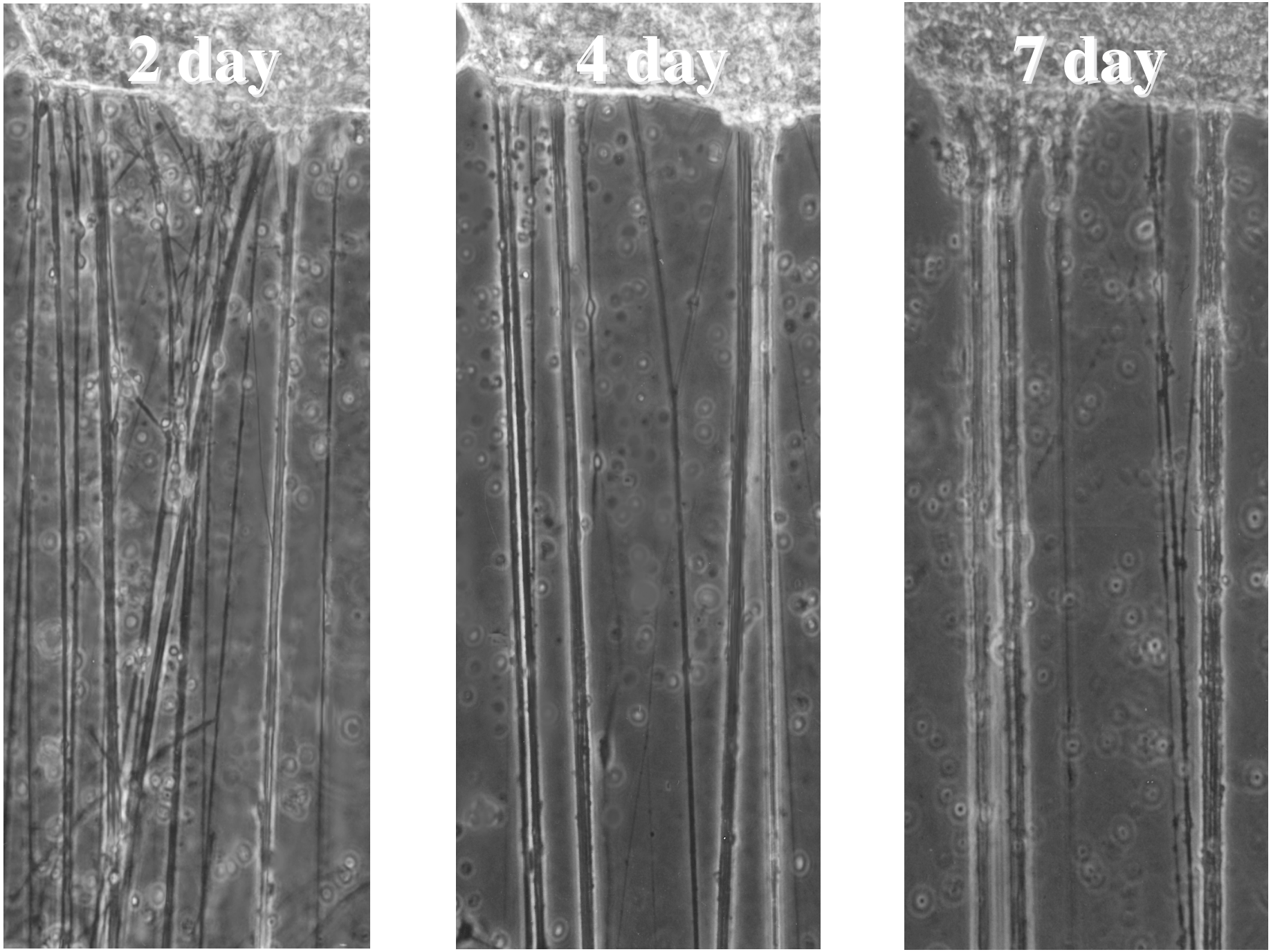
2 days of elongation



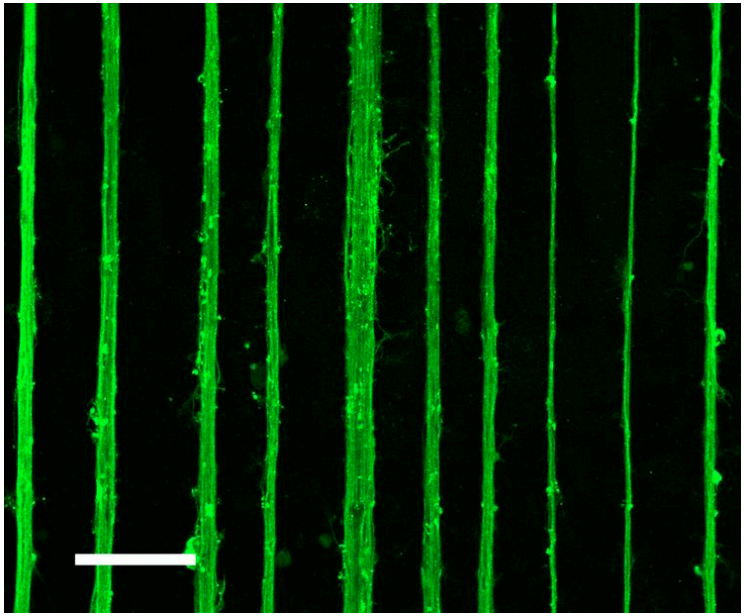
4 days

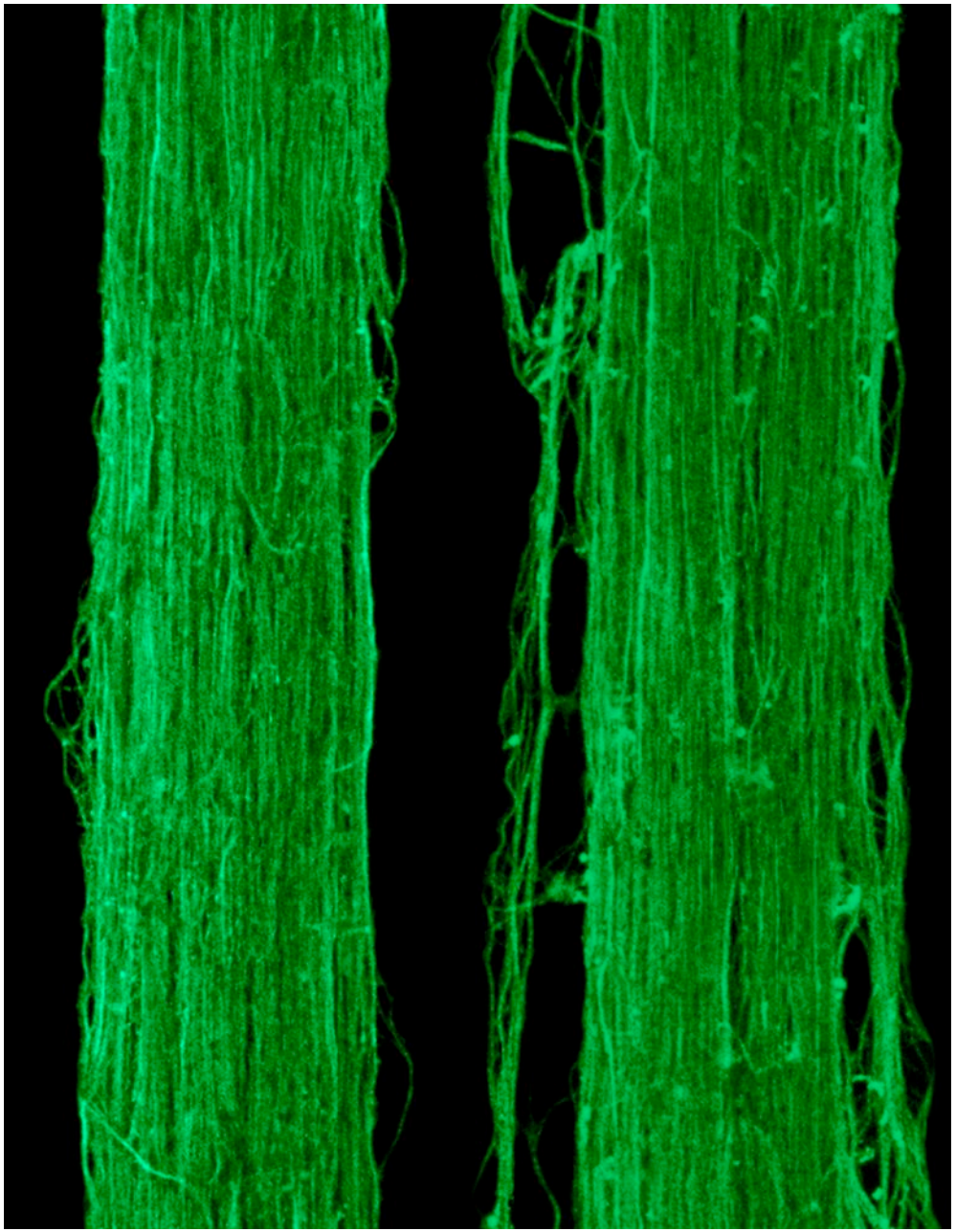
7 days

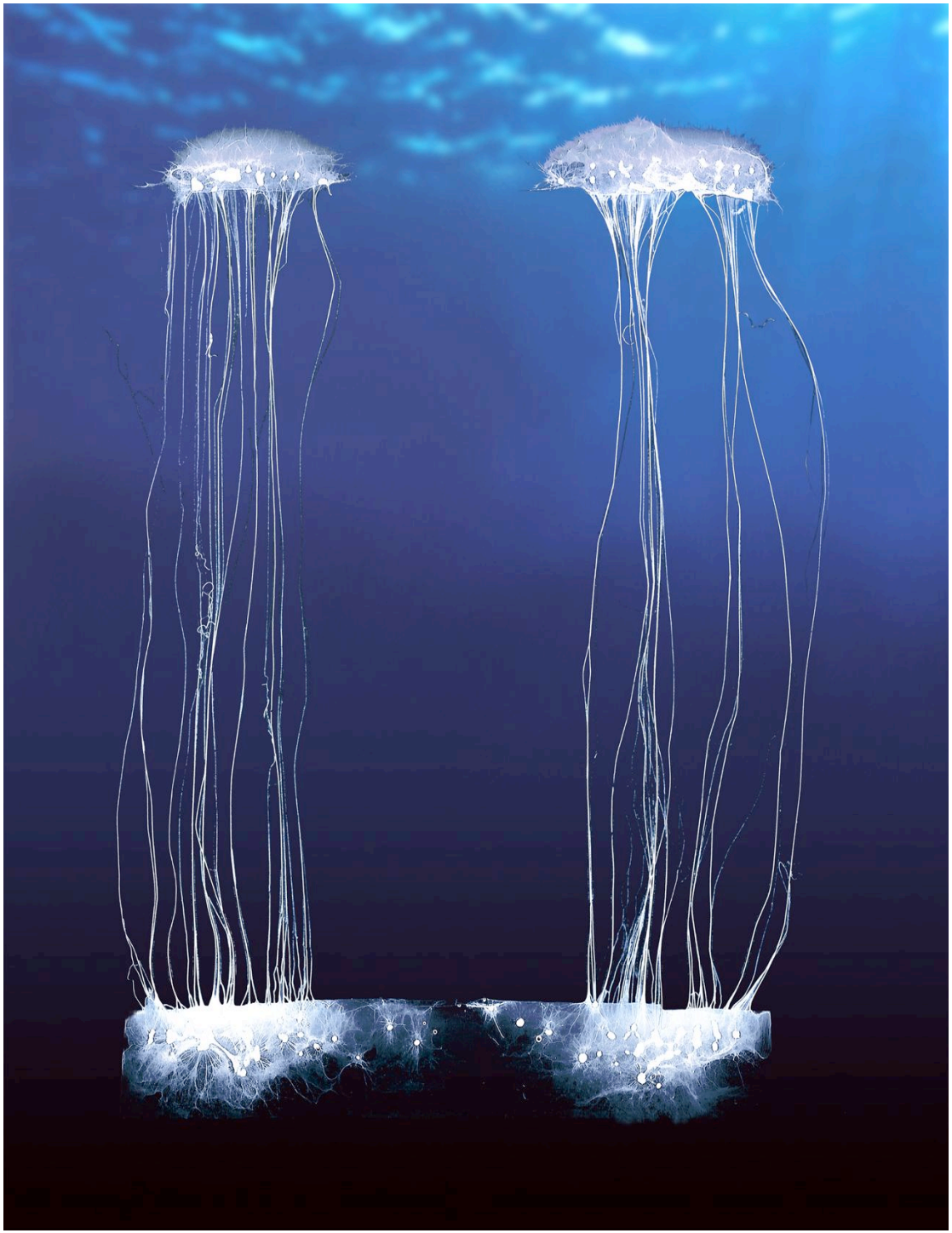



2 day
4 day
7 day

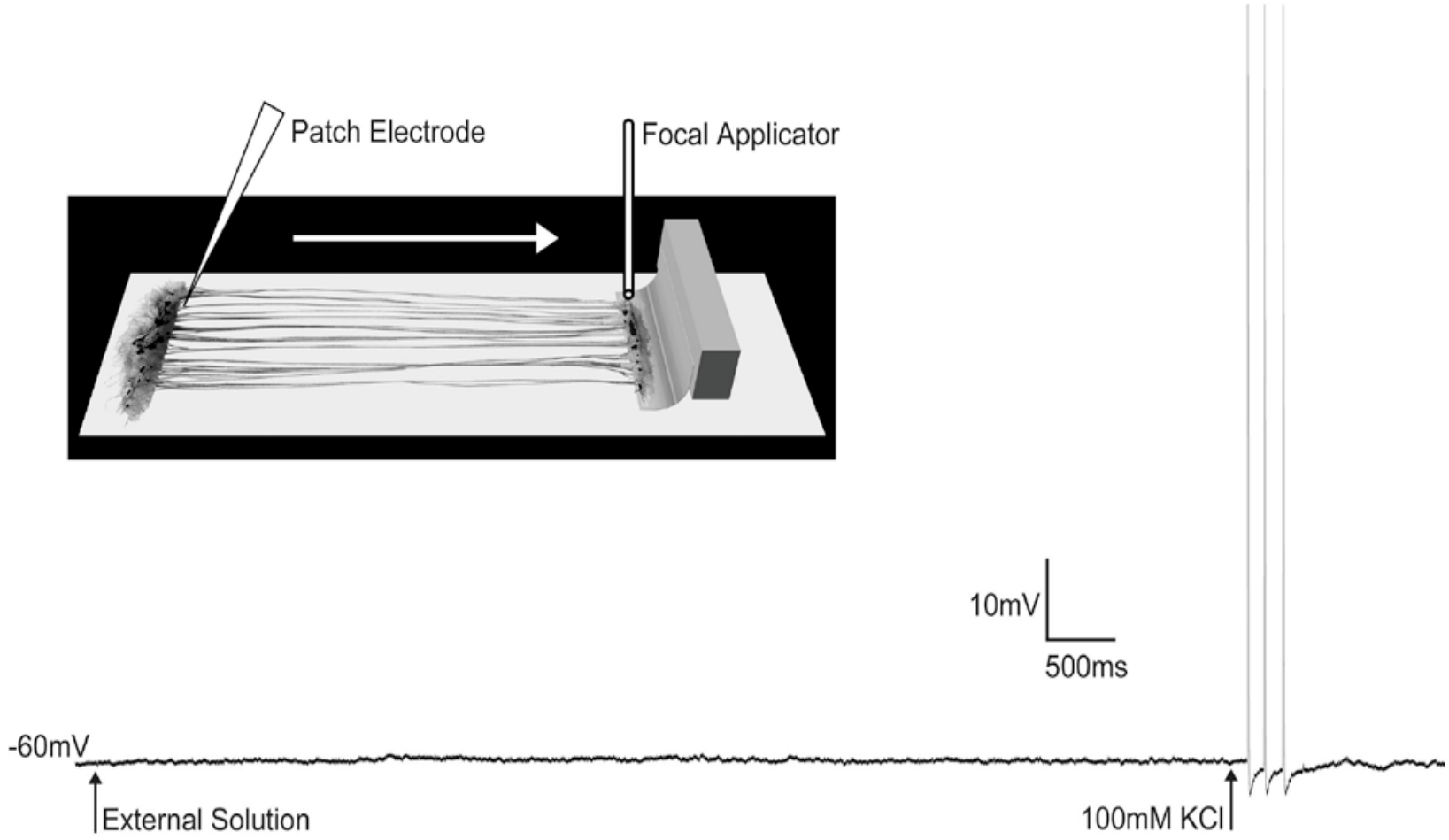
Parallel alignment of stretch-grown axon fascicles







Not jellyfish - approx. $1x10^6$ stretch-grown axons



Conductance across elongated axons

Extreme growth of axons:

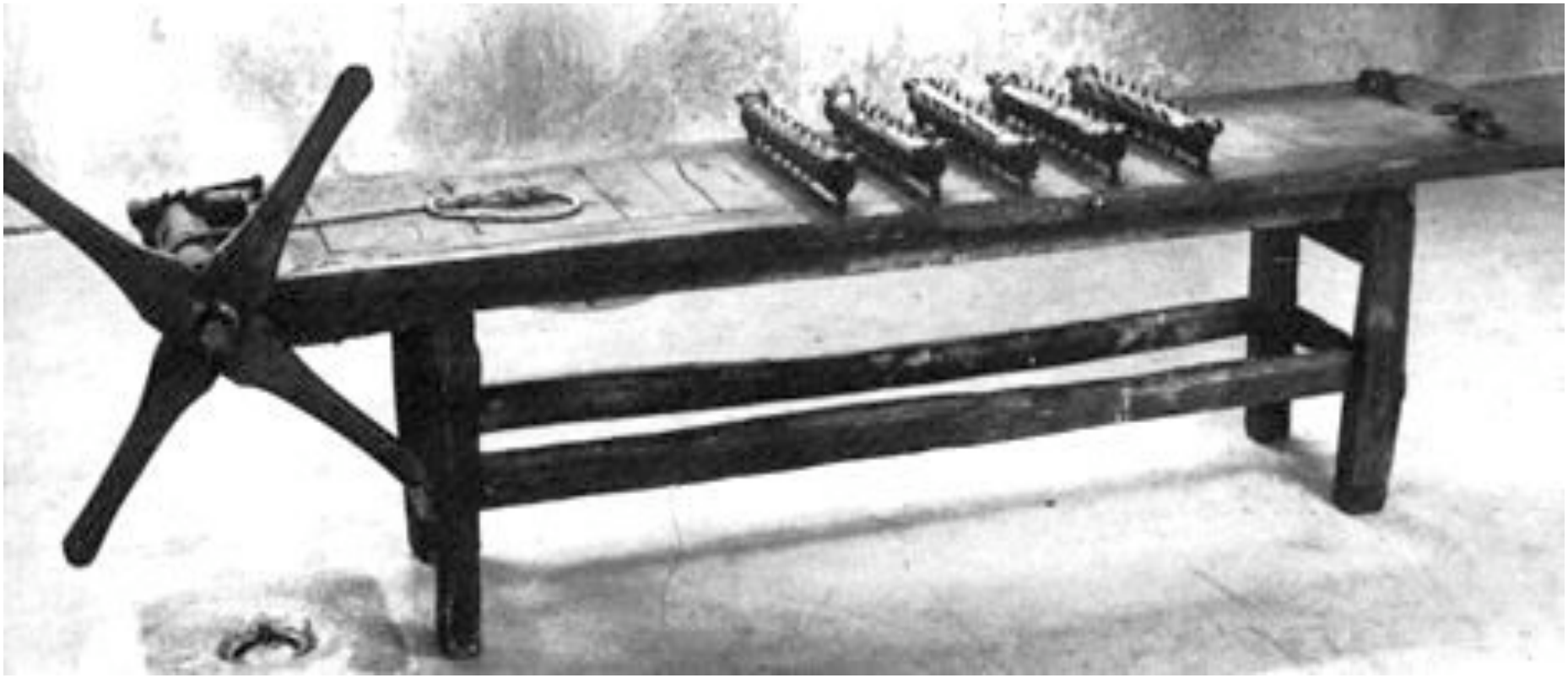
Rate of 1cm/day

World record!

Length of 10 cm

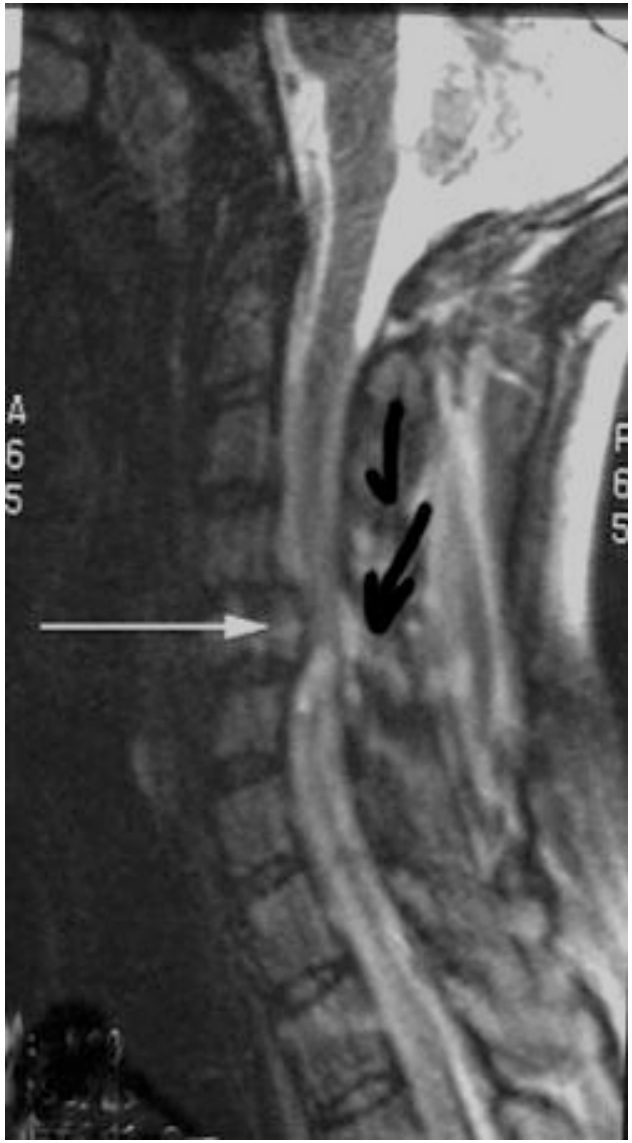
Maintain function

Tension can be good for your nerves



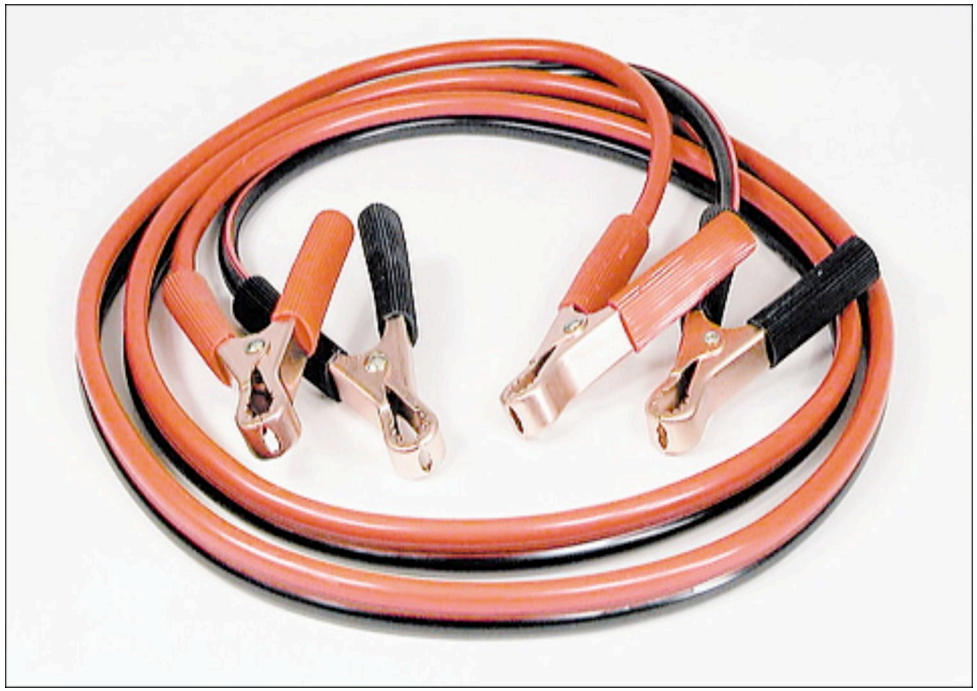

corbis.com

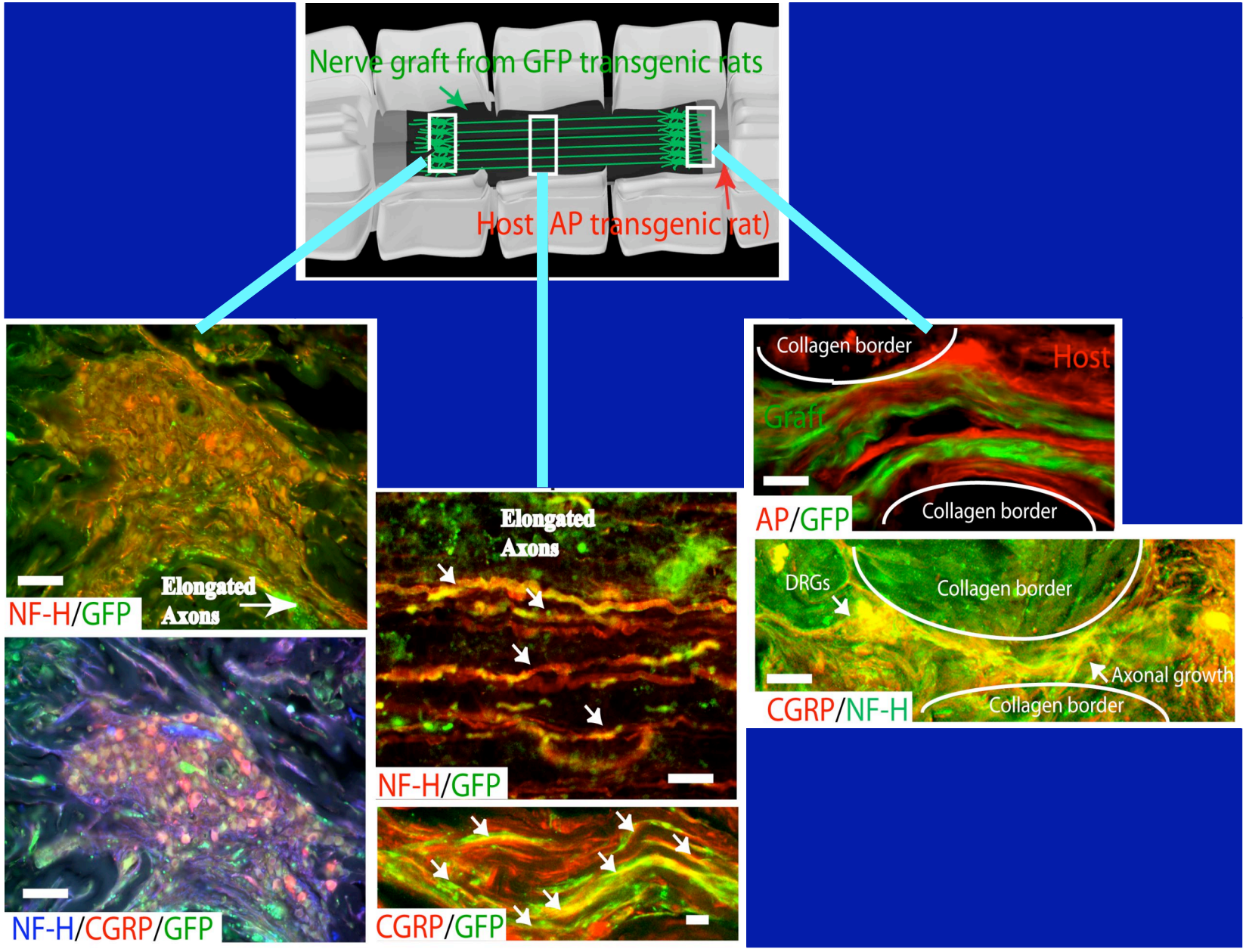
Can mechanical elongation of integrated axons be exploited to restore function?



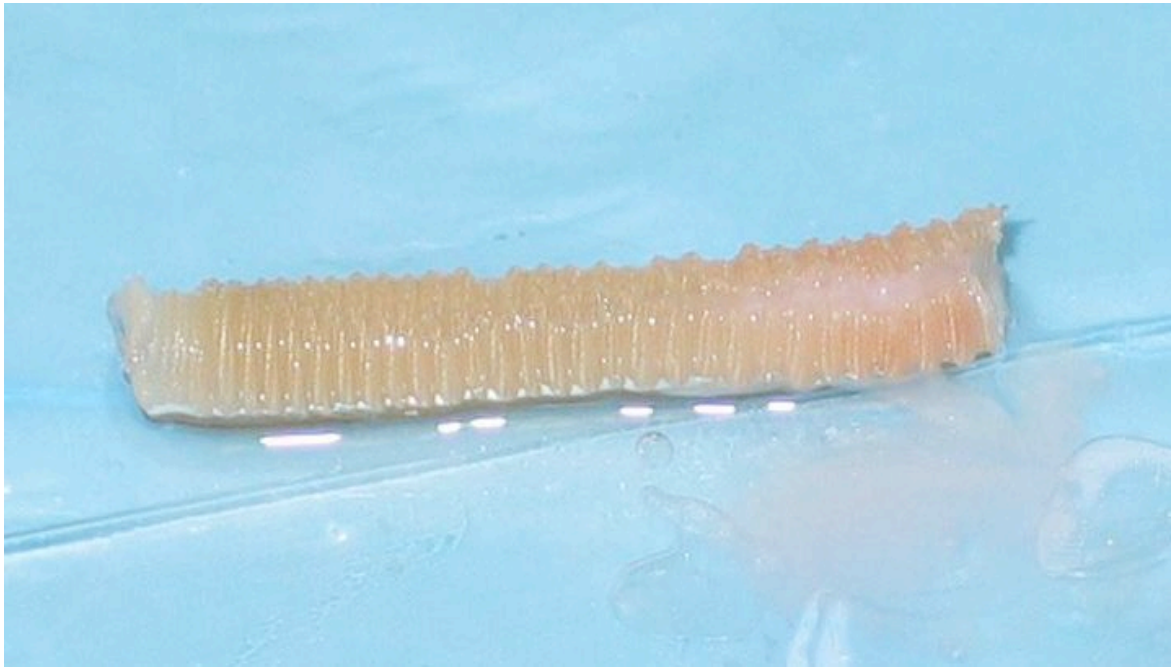
Can current approaches bridge spinal cord injury lesions often greater than 3cm?

Transplant of Stretch-Grown Nerves For Spinal Cord Injury

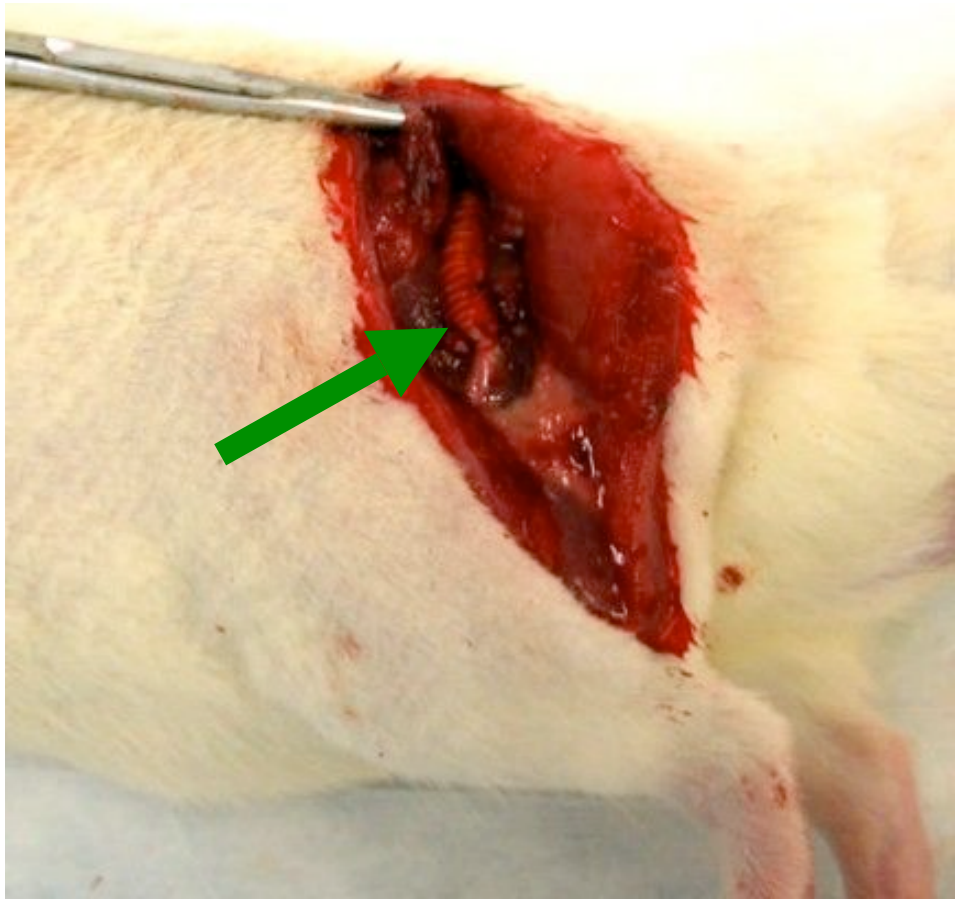



Nerve graft from GFP transgenic rats
Host (AP transgenic rat)
NF-H/GFP
Elongated Axons
NF-H/CGRP/GFP
Elongated Axons
NF-H/GFP
CGRP/GFP
Collagen border
Host
Graft
AP/GFP
Collagen border
DRGs
Collagen border
Axonal growth
CGRP/NF-H
Collagen border

Peripheral nerve repair with stretch-grown axons/ nervous tissue constructs

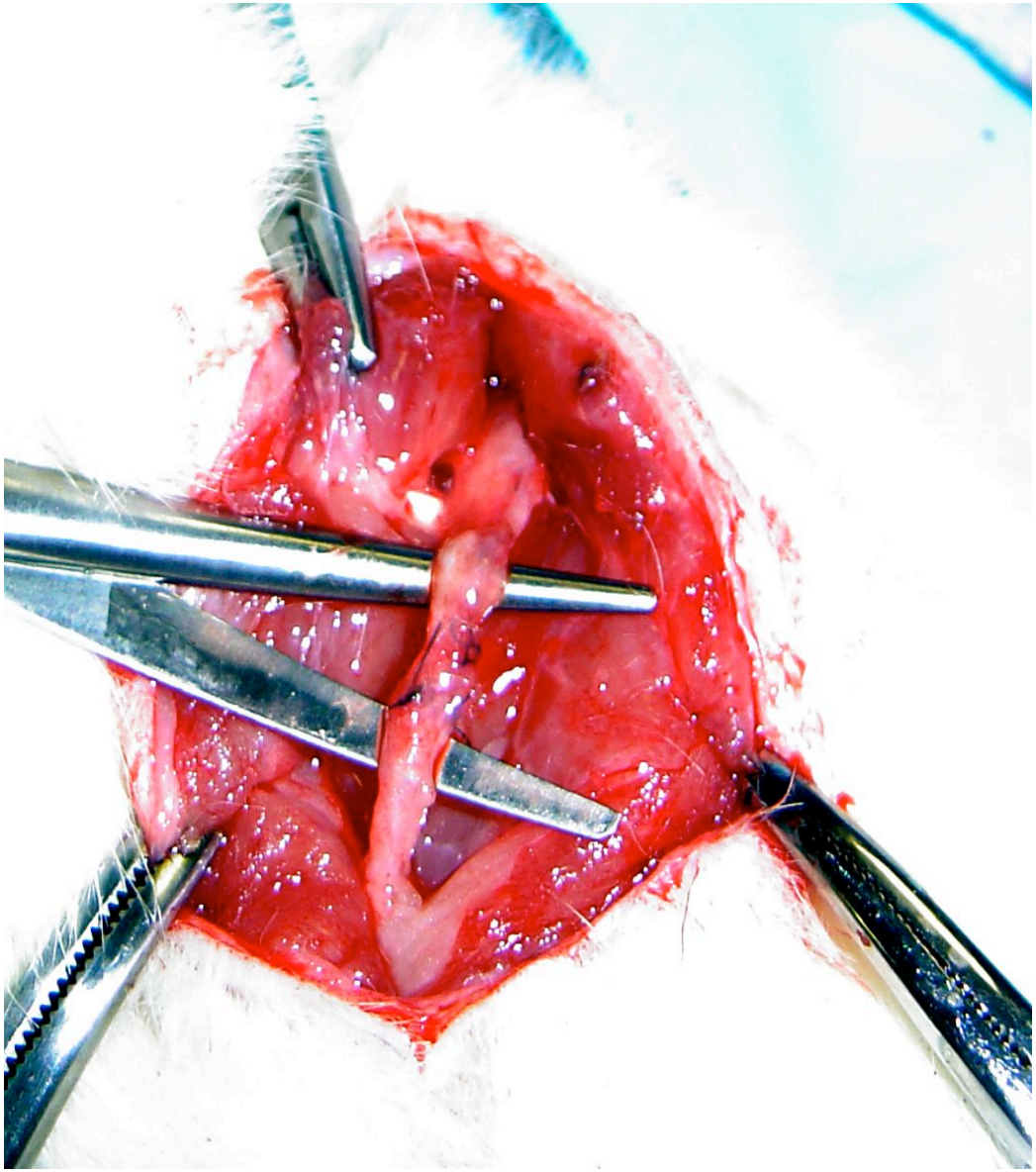


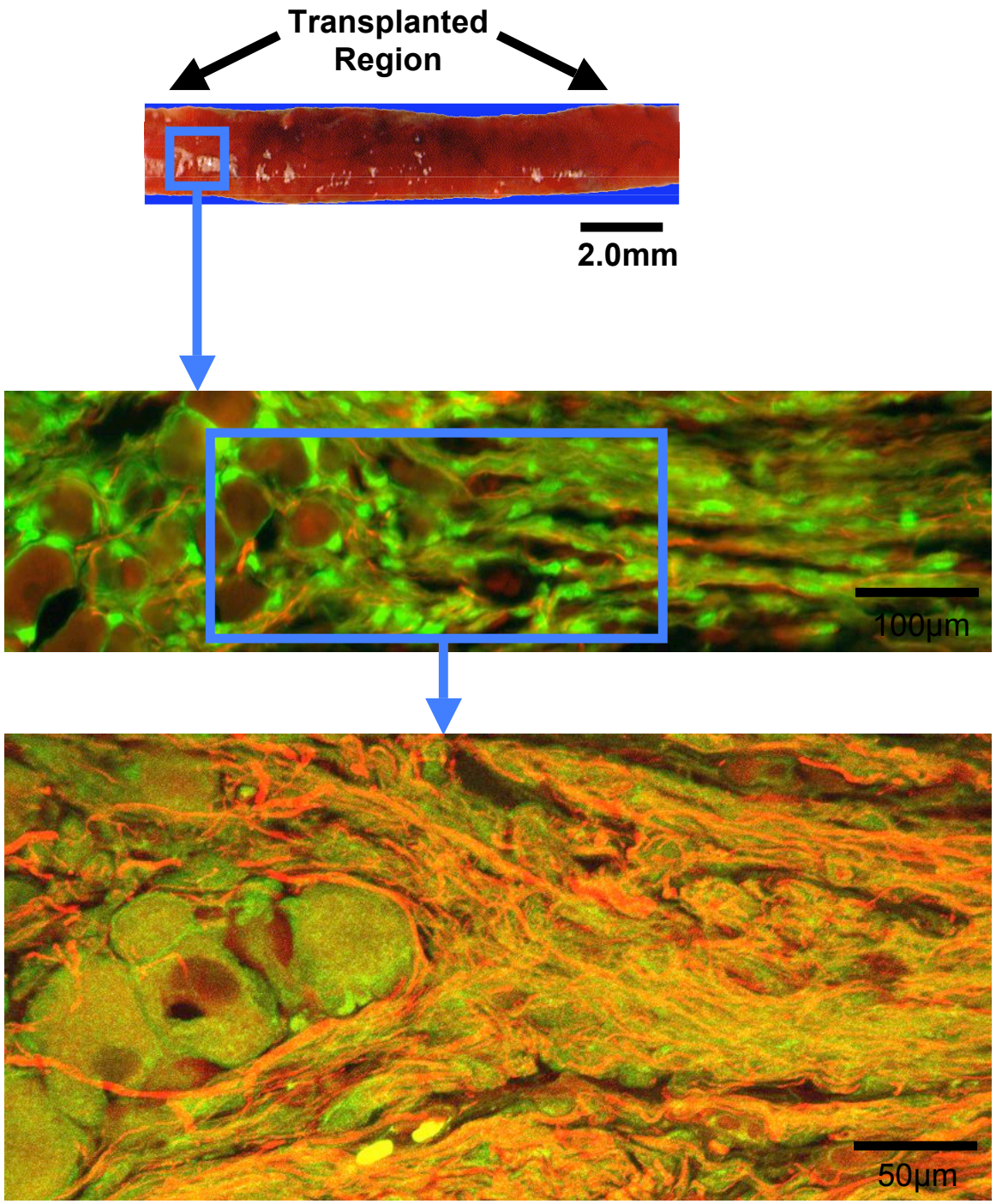
Nervous tissue construct: Stretch-grown axons encased in collagen and inserted in PGA tube

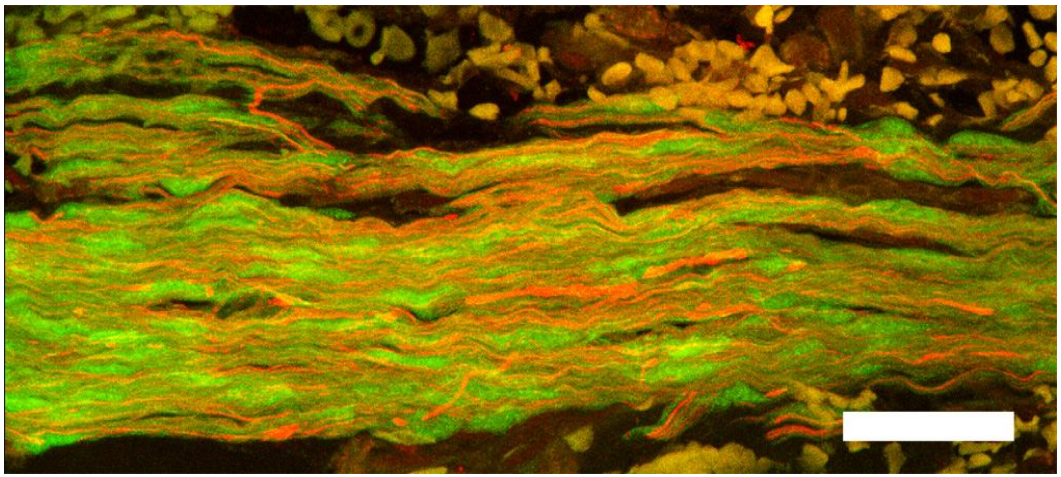


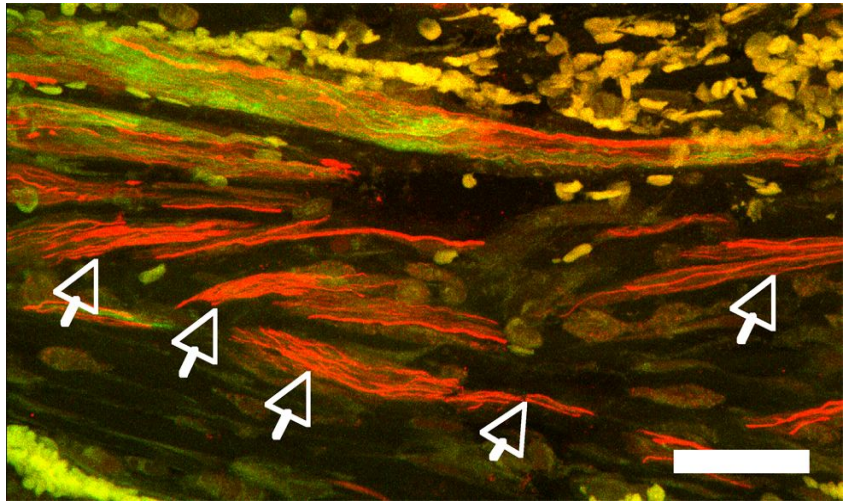
Nervous tissue construct repair of sciatic nerve

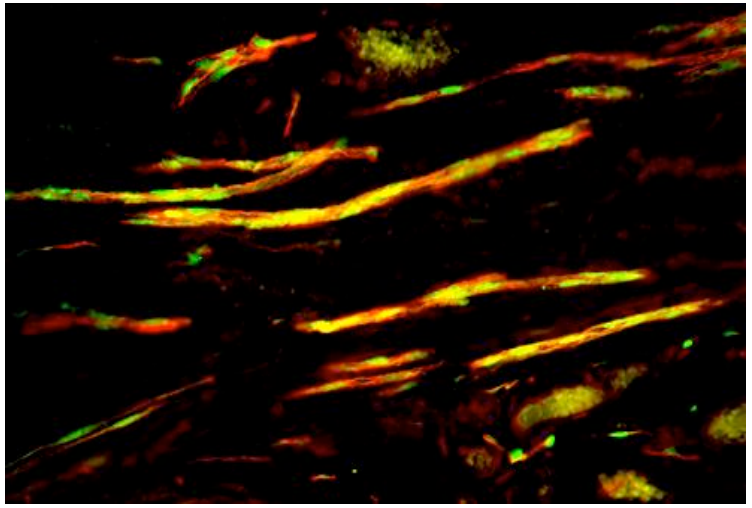
Nervous Tissue Construct 4mo Post-Transplantation




Transplanted
Region
2.0mm
100μm
50μm



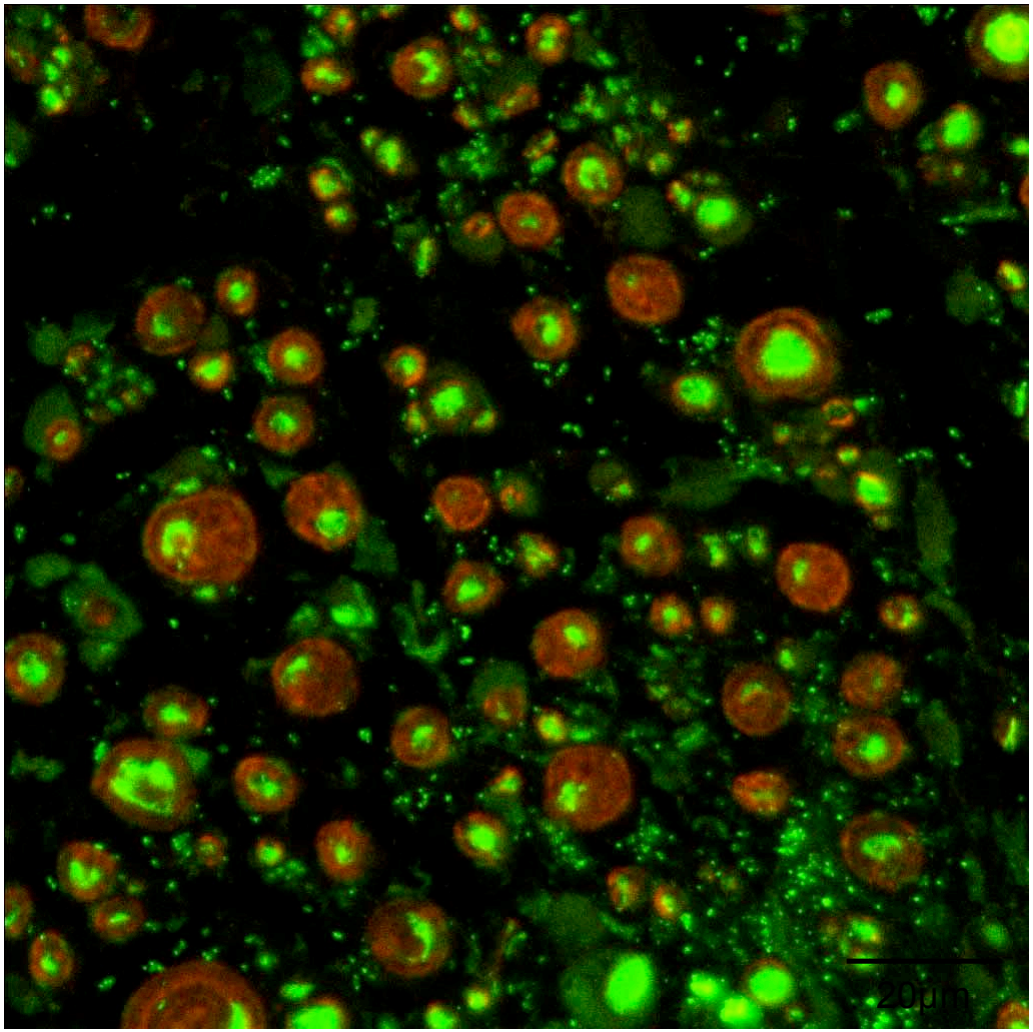




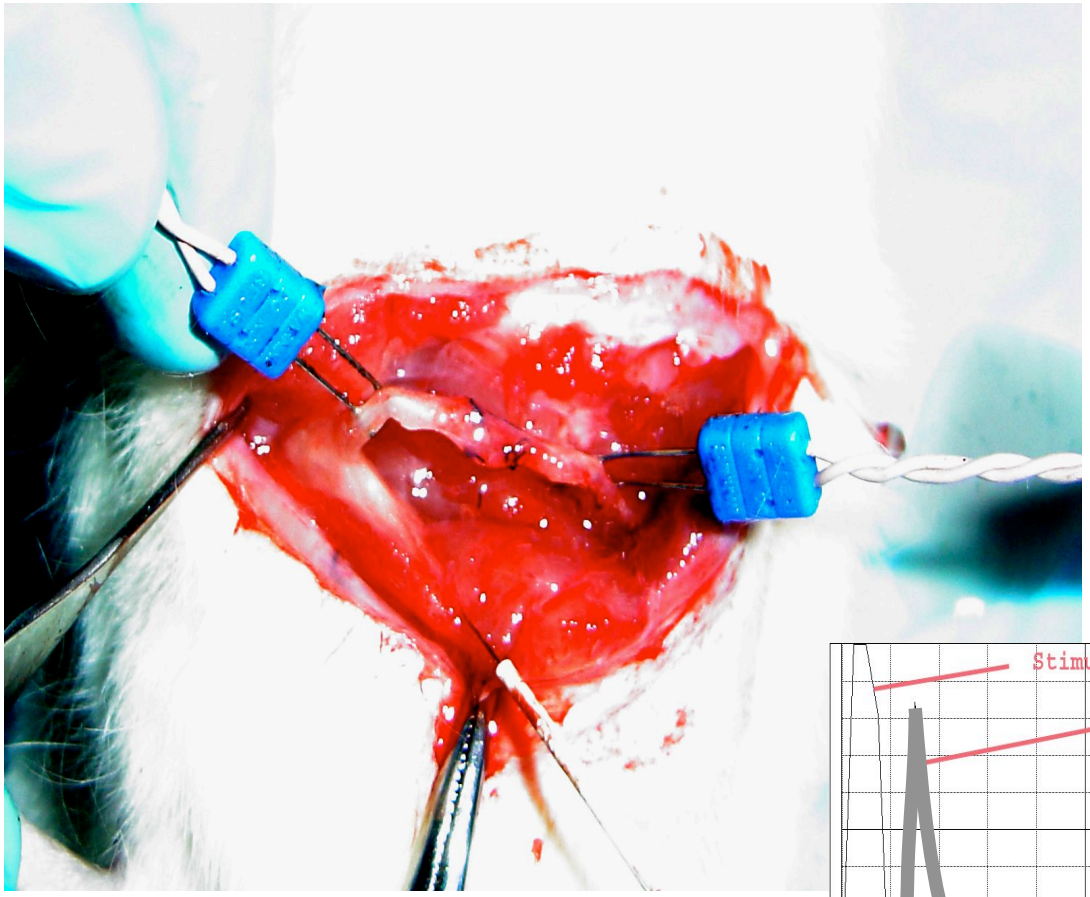
Red = host axons

Green = graft axons

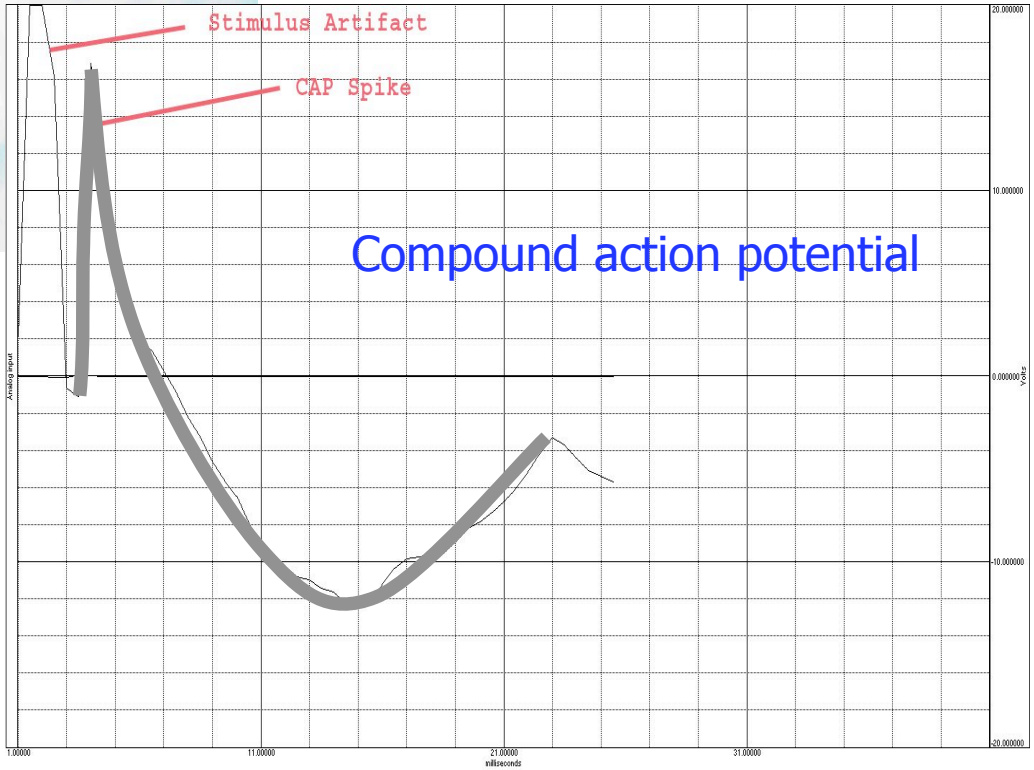
Cross Section Through Graft - Myelinated Axons 4mo Post-Transplant

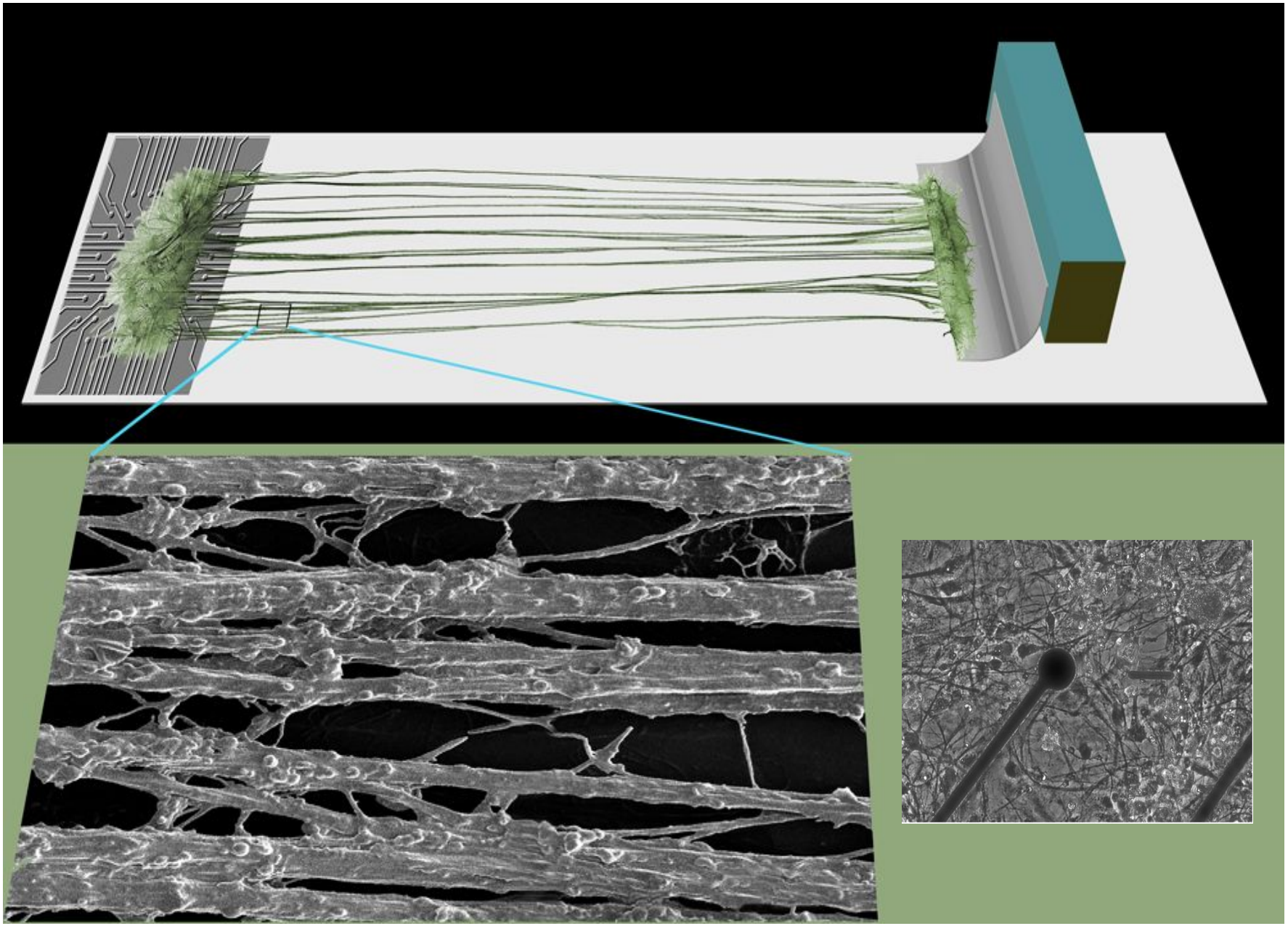


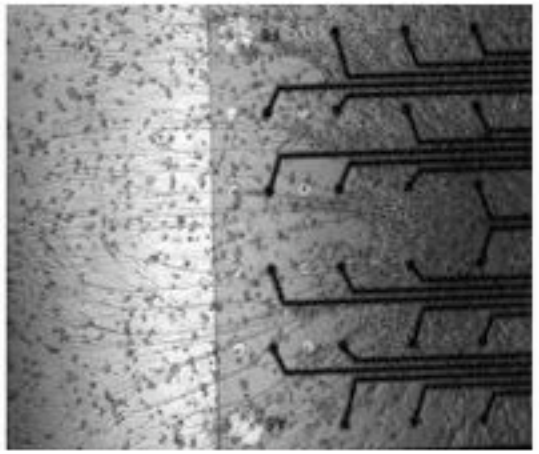
neurofilament myelin basic protein



Electrophysiological conduction through transplanted nervous tissue construct





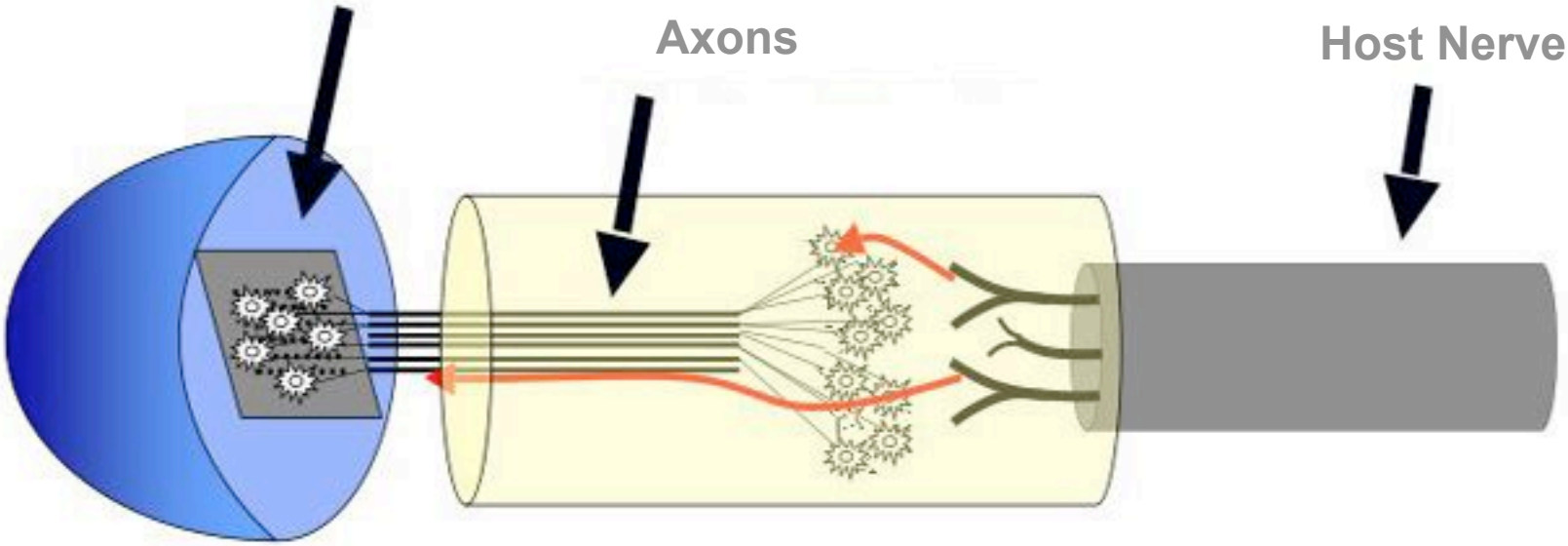


Neurons Grown on a Flexible Multi-Electrode Array

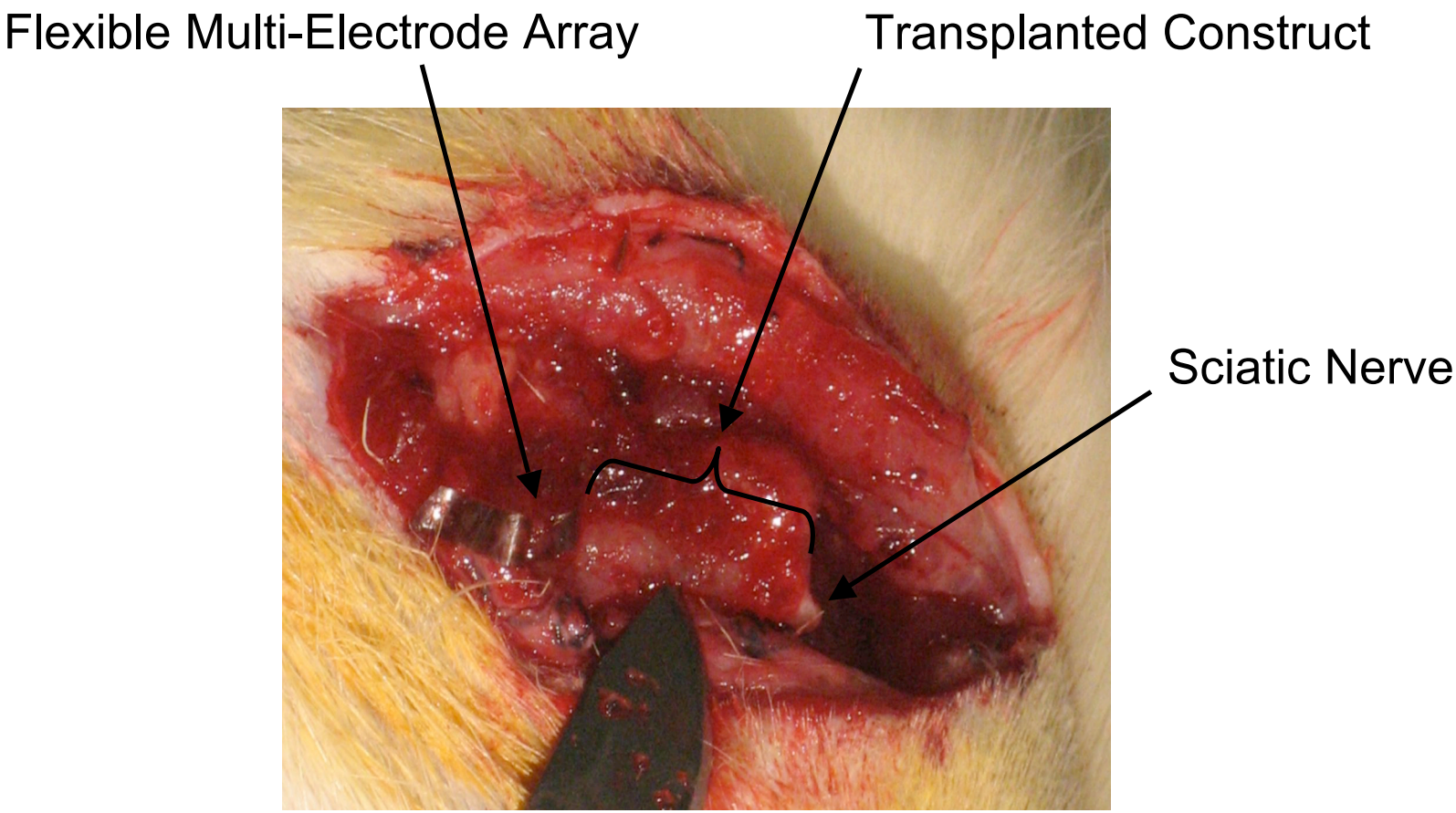
Stimulating / Recording Electrodes

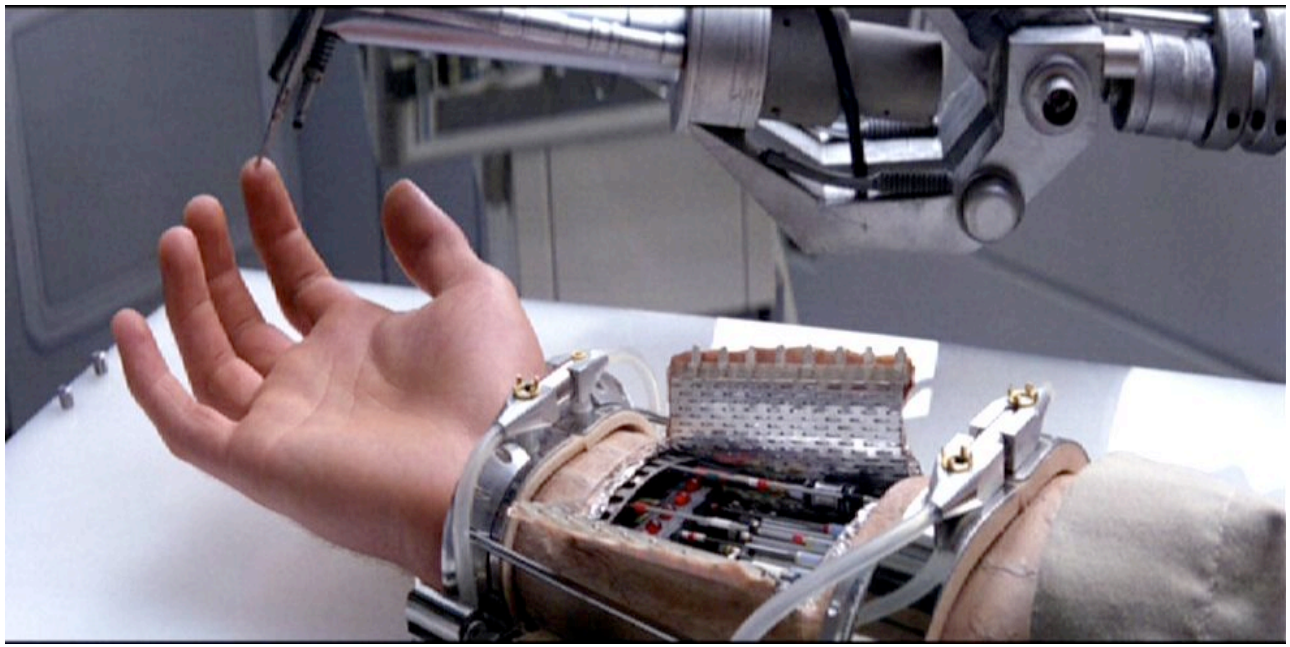
Stretch-Grown Axons

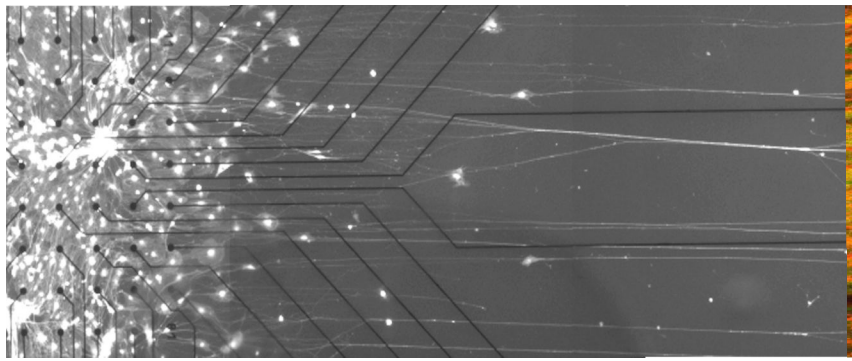
Host Nerve

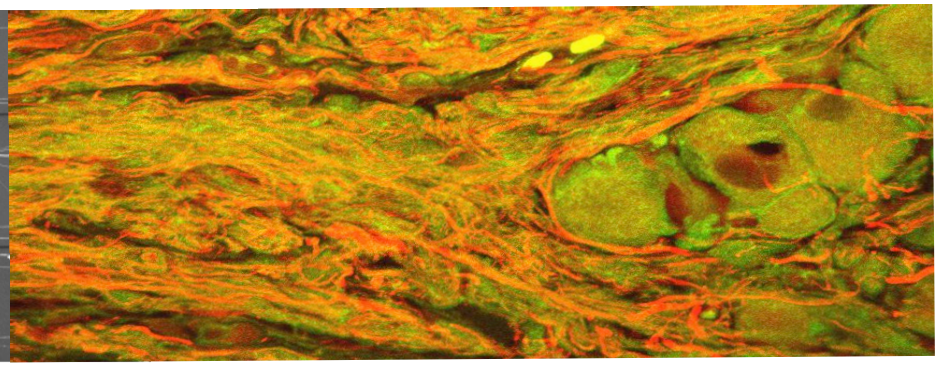


Gross Anatomy - Flexible Multi-Electrode Array 2wks Post-Transplant



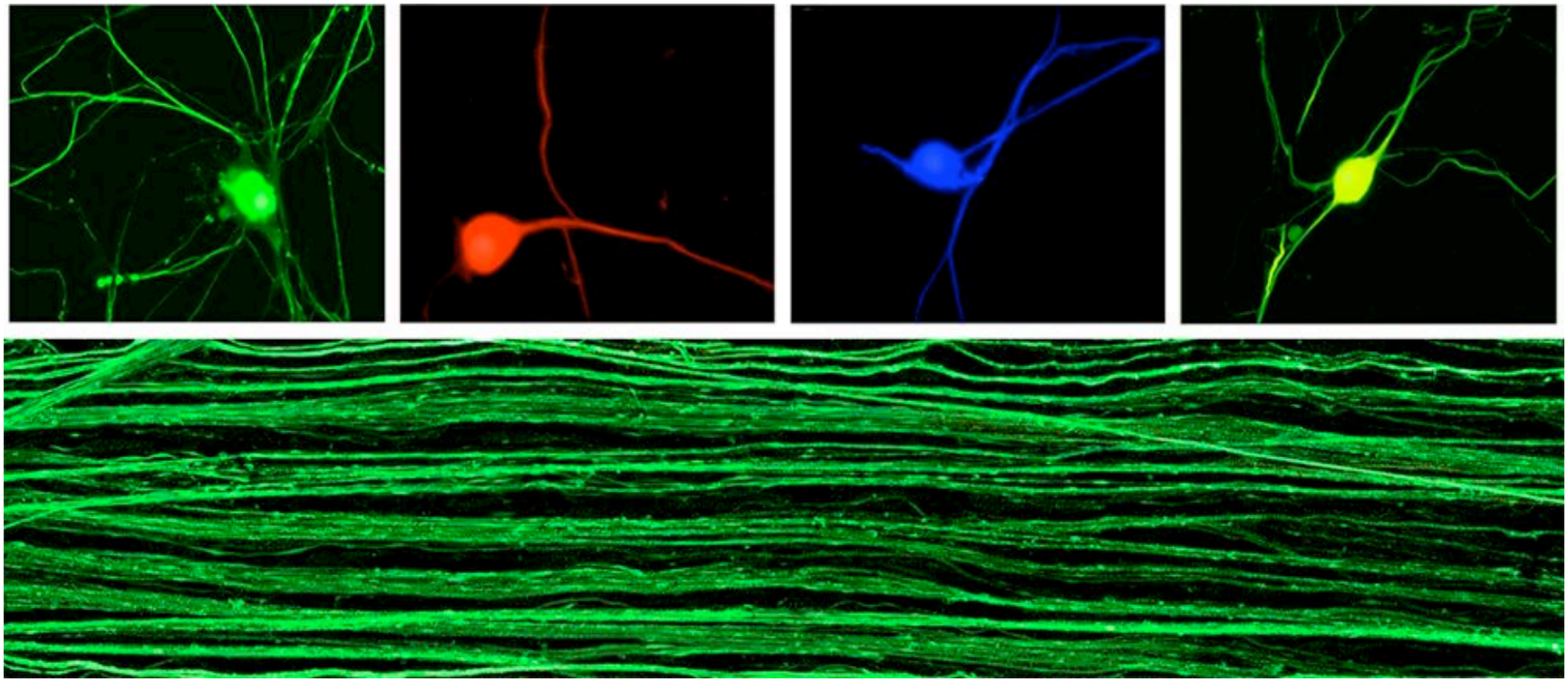






Human DRG neurons harvested from a patient

Surviving in culture for at least 3 months



Stretch-grown to produce human nervous tissue constructs

Interface check-list

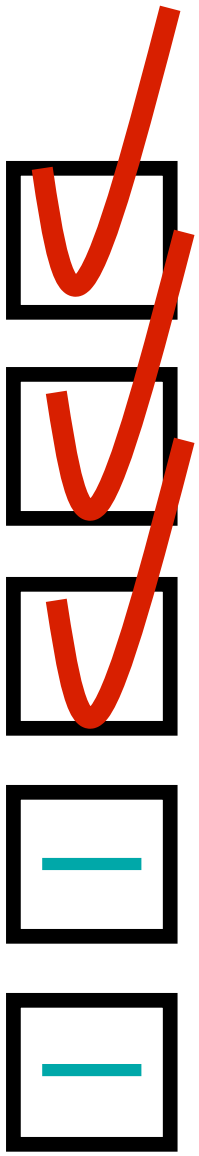
Integrate with nervous system

Demonstrate electrical signaling

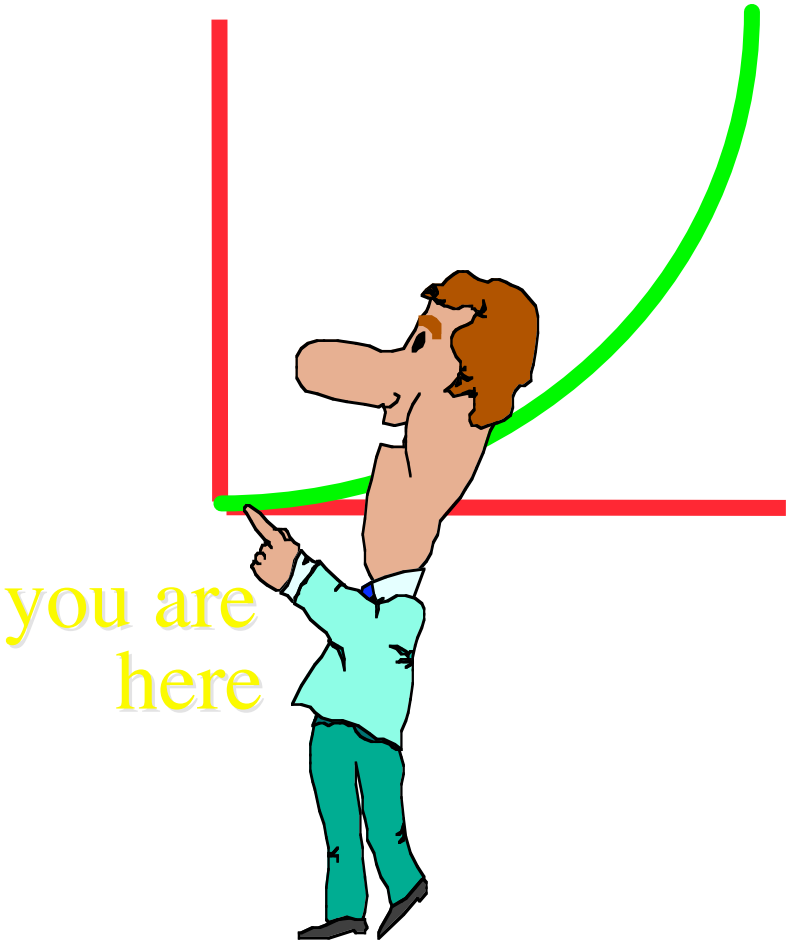
Design for two-way communication

Control a prosthetic device

Enable proprioception



Learning Curve



"That's amazing—I was just thinking the same thing."

The Elongators: