Computational model of the peripheral nervous system: PNPy

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Introduction

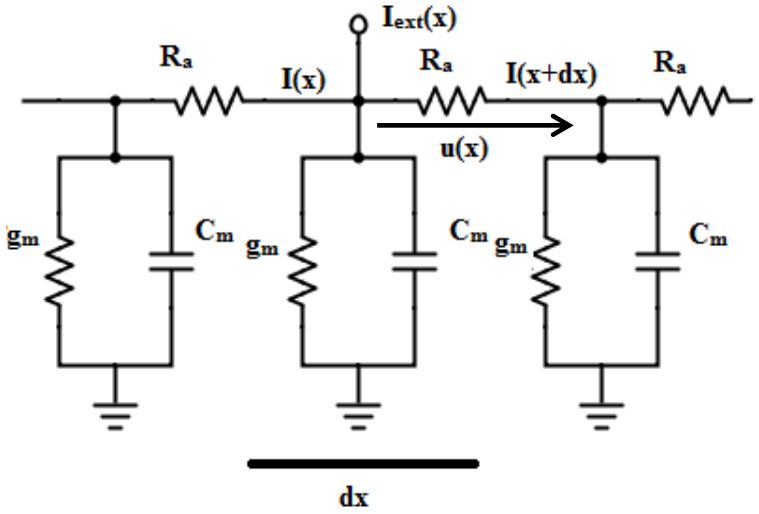
Motivation: **Improve understanding of anatomy and neurophysiology of peripheral nerves**

Hypothesis: **Axons can be modelled by electrical circuits**

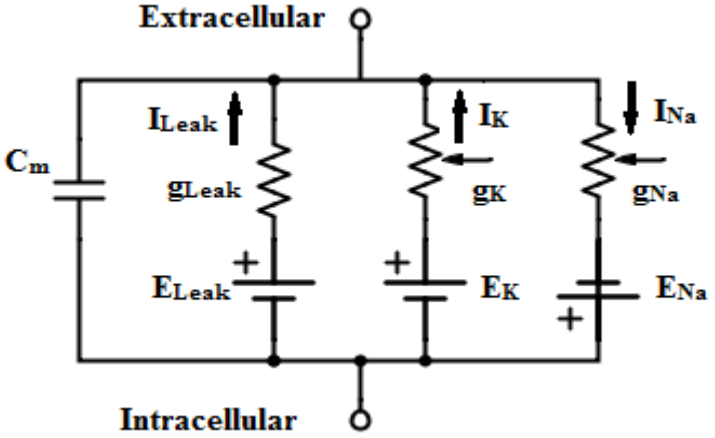
Objective: **Produce as an output the type of signals measured by nerve cuff electrodes**

Project applications: **Vagus nerve stimulation (VNS), bioelectronics medicines**

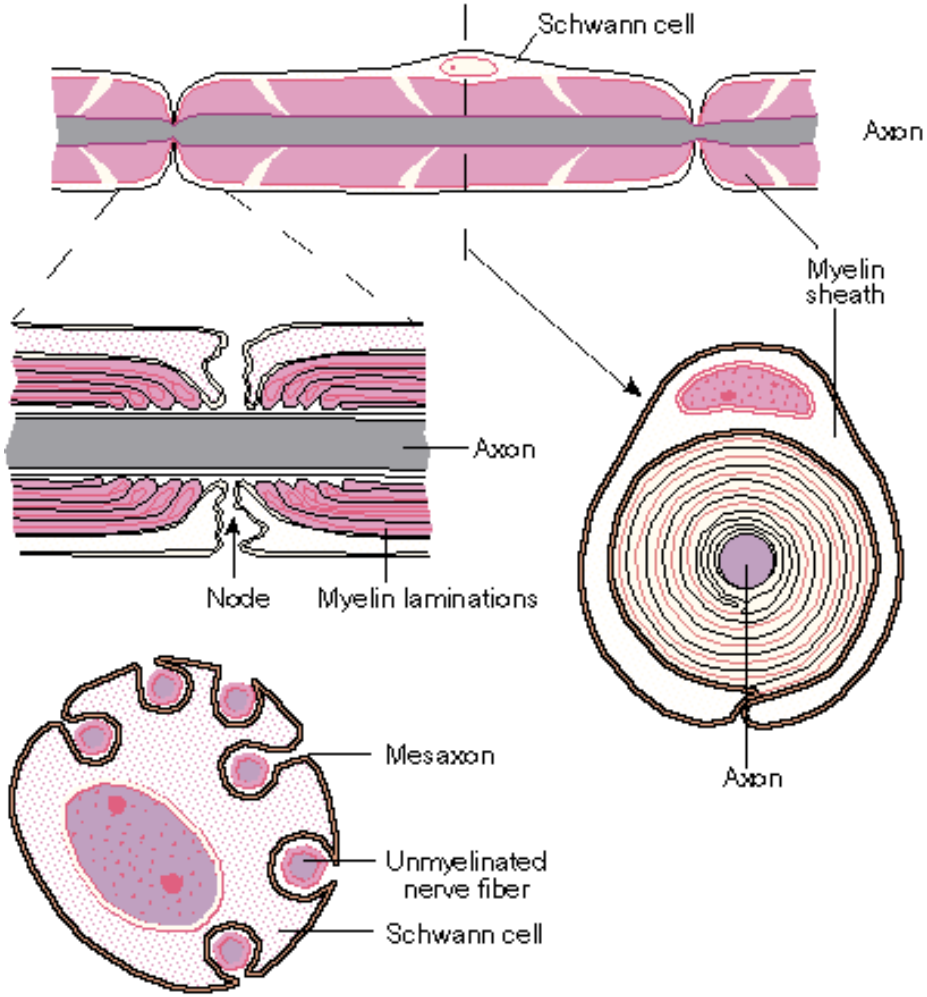
Background



Cable model schematic



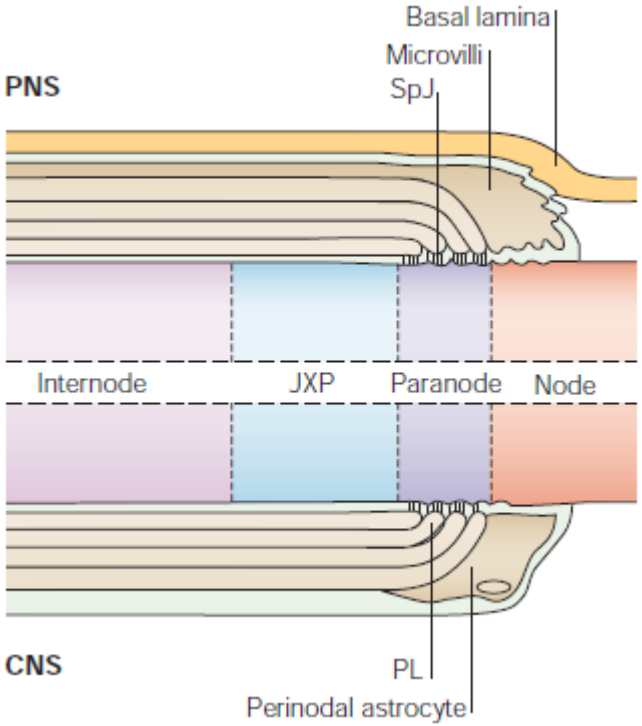
Hodgkin & Huxley model schematic



Credits: Queen Margaret University Edinburgh, Applied Sciences website

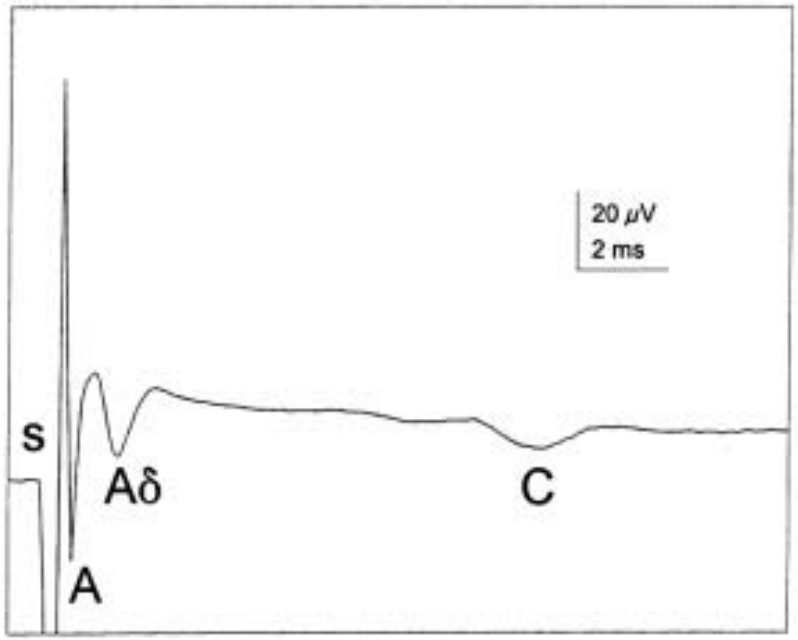
Representation of myelinated and unmyelinated nerve fibres

Background



Credits: S. Poliak and E. Peles, Nature, December 2013

Detailed myelinated axon structure around the nodes the of Ranvier



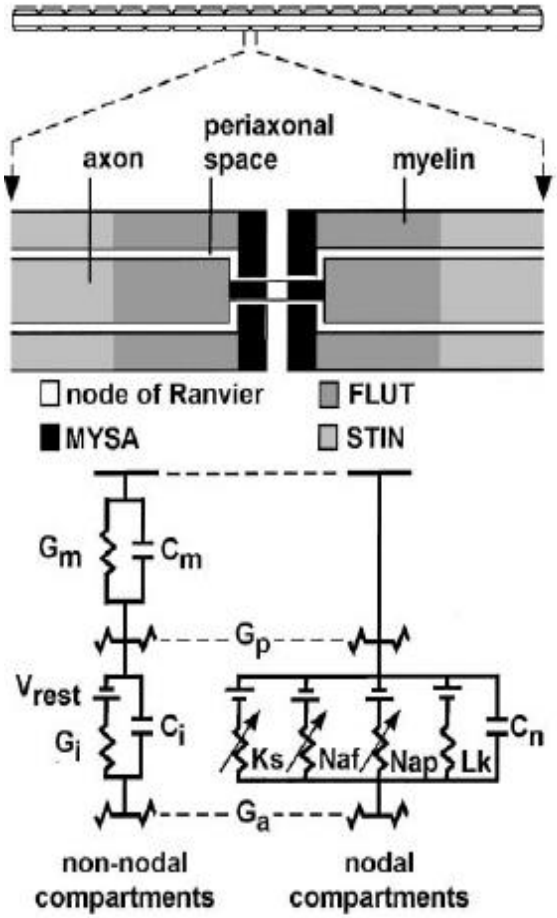
Credits: M. S. Evans et al, Acta Neurol Scand, 2004

Example of a compound action potential recorded from the cervical portion of left vagus nerve.

Methods

1. Axons parameters

Unmyelinated axon	*Myelinated axon*
Distribution of densities & diameters	Distribution of densities & diameters
Axon length (µm)	Number of nodes
Specific axial resistance (µF/cm²)	



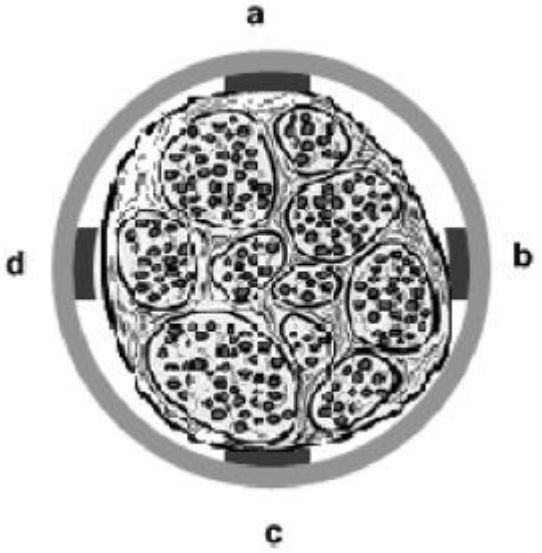
Credits: C. McIntyre et al, J Neurophysiol, 2002

Myelinated axon model used in PNPy

Methods

2. Electrodes parameters

Stimulating electrode	*Recording electrode*
Stimulation type	Number contact points
Coordinates	Position along nerve
Frequency and duty cycle	Number of electrodes
Amplitude (nA)	Simulation duration (ms)
Jitter parameters	
Stimulus duration (ms)	



Credits: SC. Ordelman et al 2003

Schematic of a multi-contact electrode cuff around a nerve

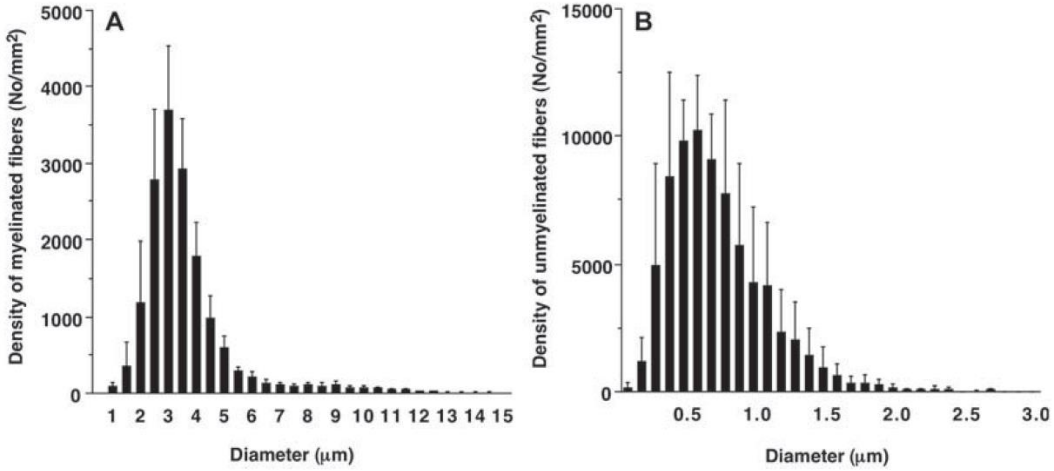
Point source model:

$$V(r,t) = \frac{1}{4\pi\sigma}\sum_{n=1}^{N}\frac{I_n(t)}{|r-r_n|}$$

Line source model:

$$V(r,t) = \frac{1}{4\pi\sigma}\sum_{n=1}^{N} I_n(t)\int\frac{dr_n}{|r-r_n|}$$

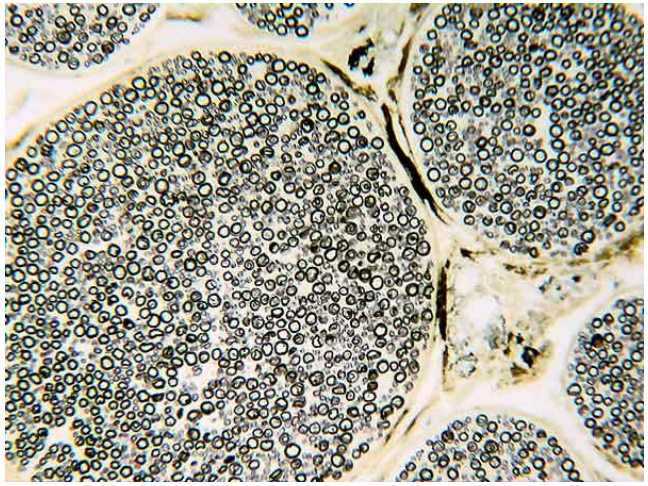
3. Diameter distributions and bundle parameters



Credits: T. Shimizu et al 2011

Histogram of myelinated and unmyelinated fibre densities of the human vagal visceral branch

Bundle parameters
Bundle radius
Proportion myelinated axons
Proportion unmyelinated axons
Number of axons



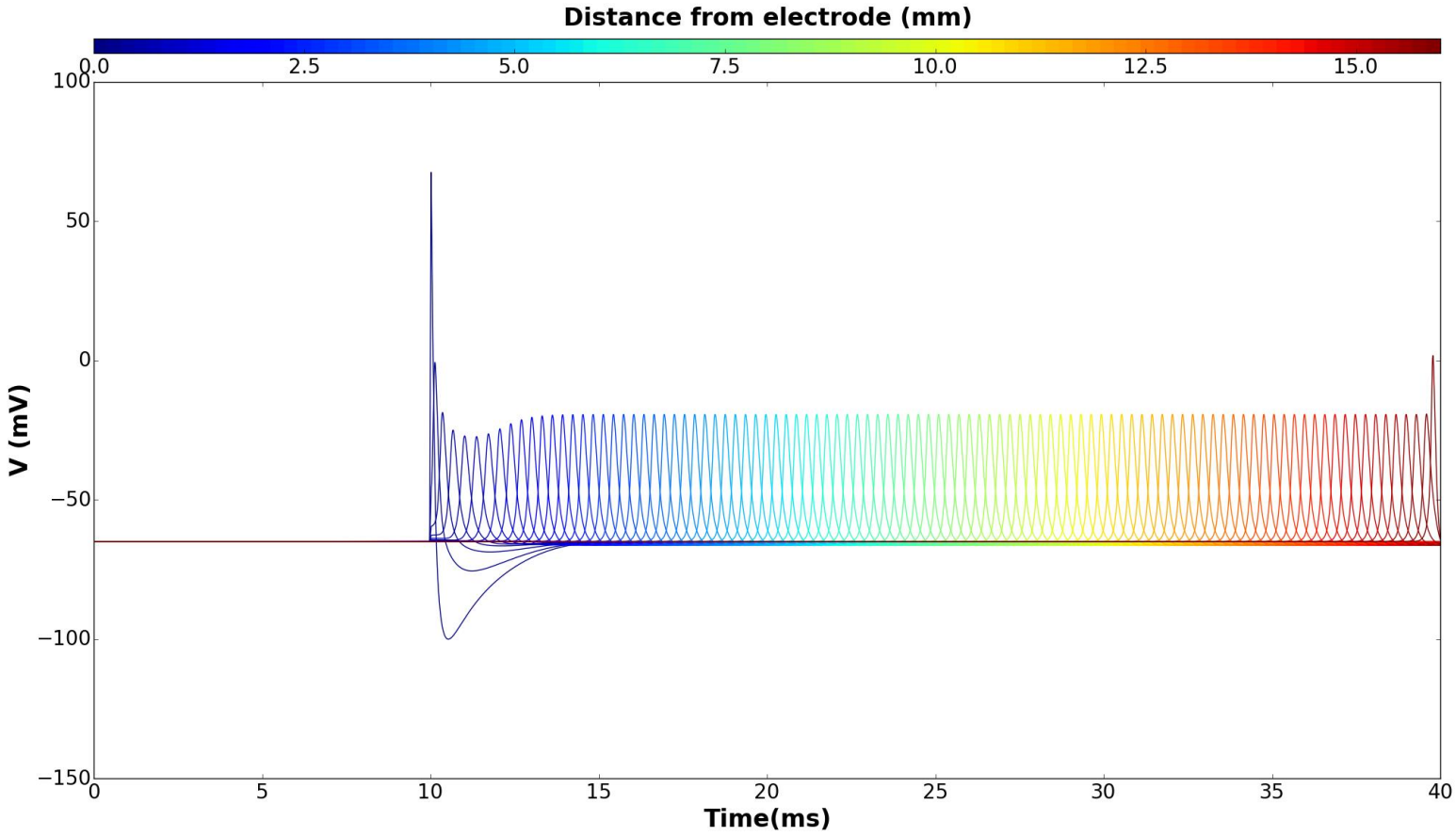
Credits: University of Minnesota, College of Veterinary Medicine website

Transverse section through a canine vagus nerve.

Results

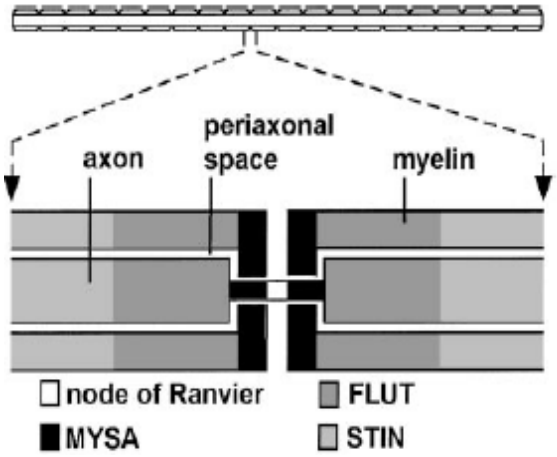
AP propagation along an unmyelinated axon

Axon diameter 1,8 cm - Conduction velocity ≈ 0,5 m/s



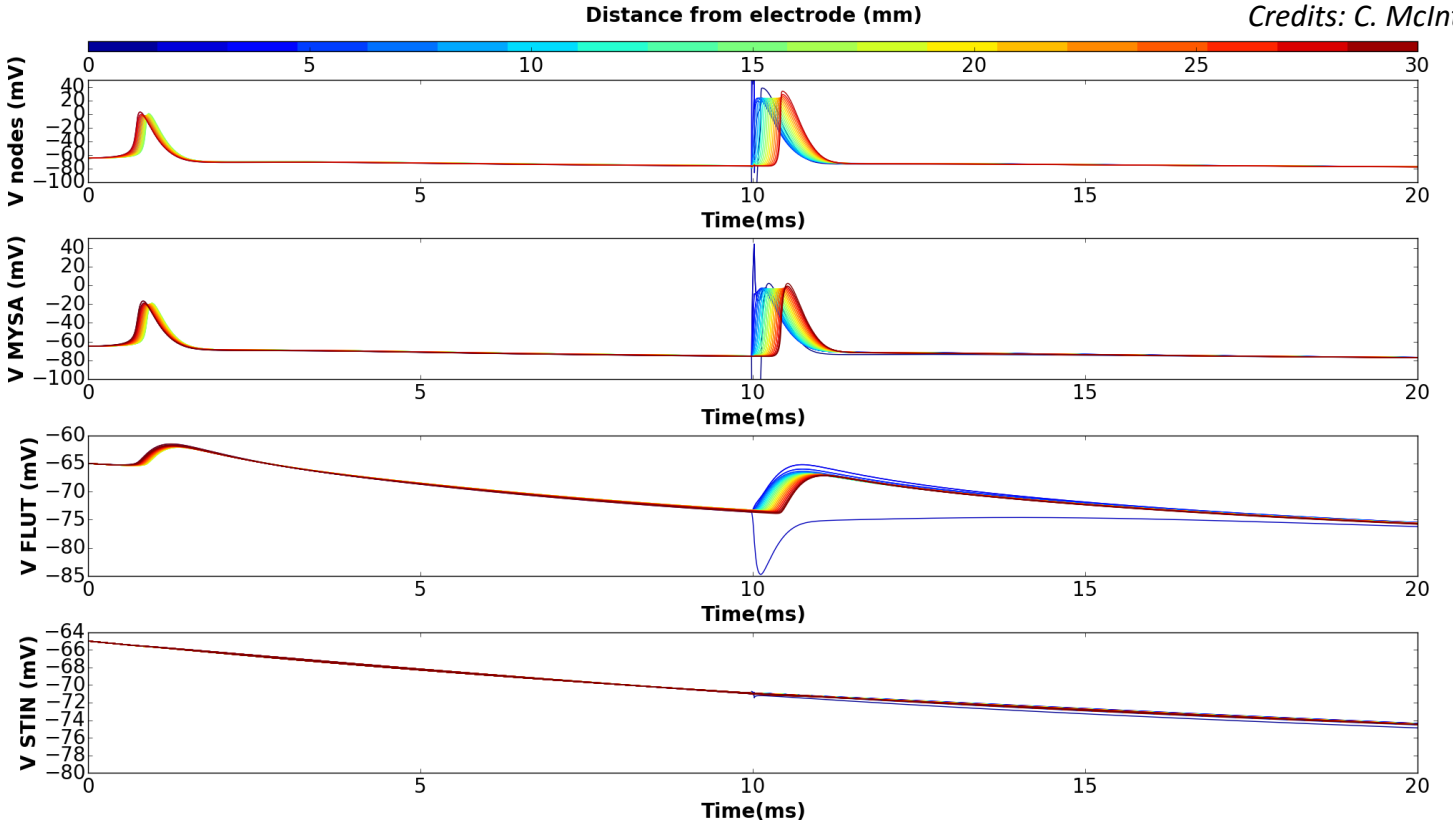
Results

AP propagation along a myelinated axon



Axon diameter = 4,6 cm - Conduction velocity: ≈ 58 m/s

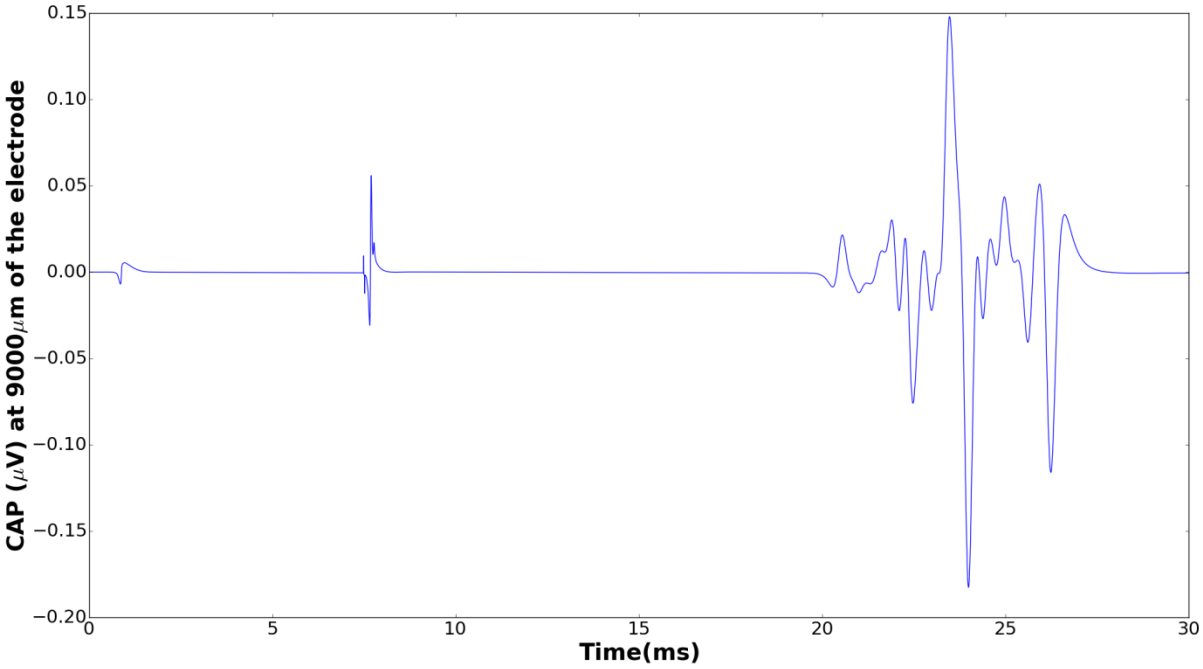
Credits: C. McIntyre et al, J Neurophysiol, 2002

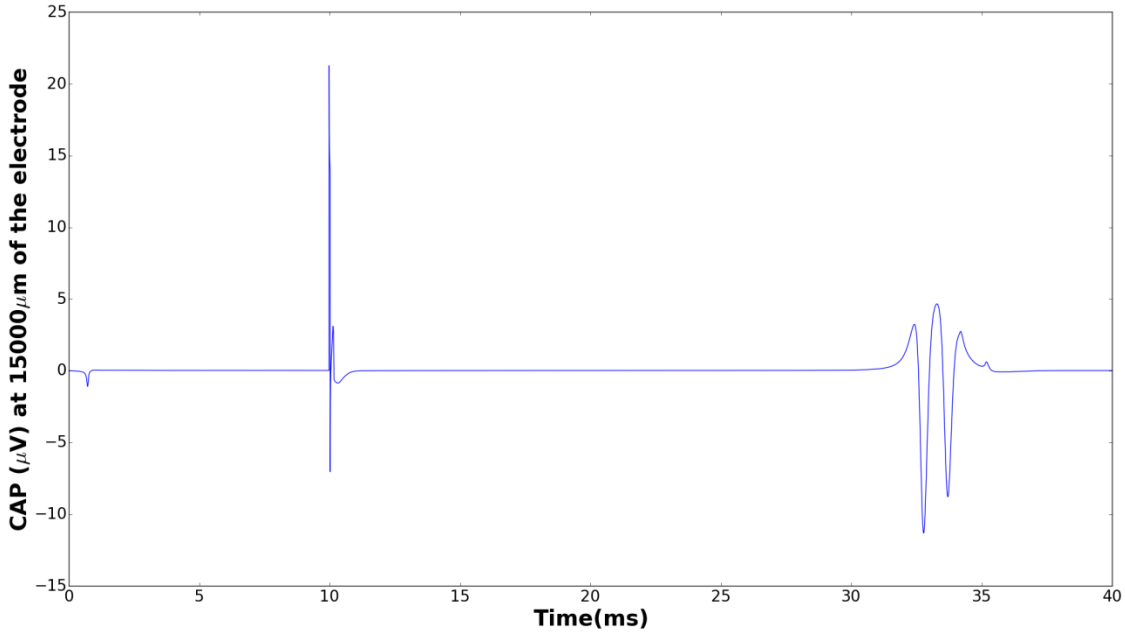


Results

CAP bipolar recording 9mm from stimulus

20% of myelinated axons



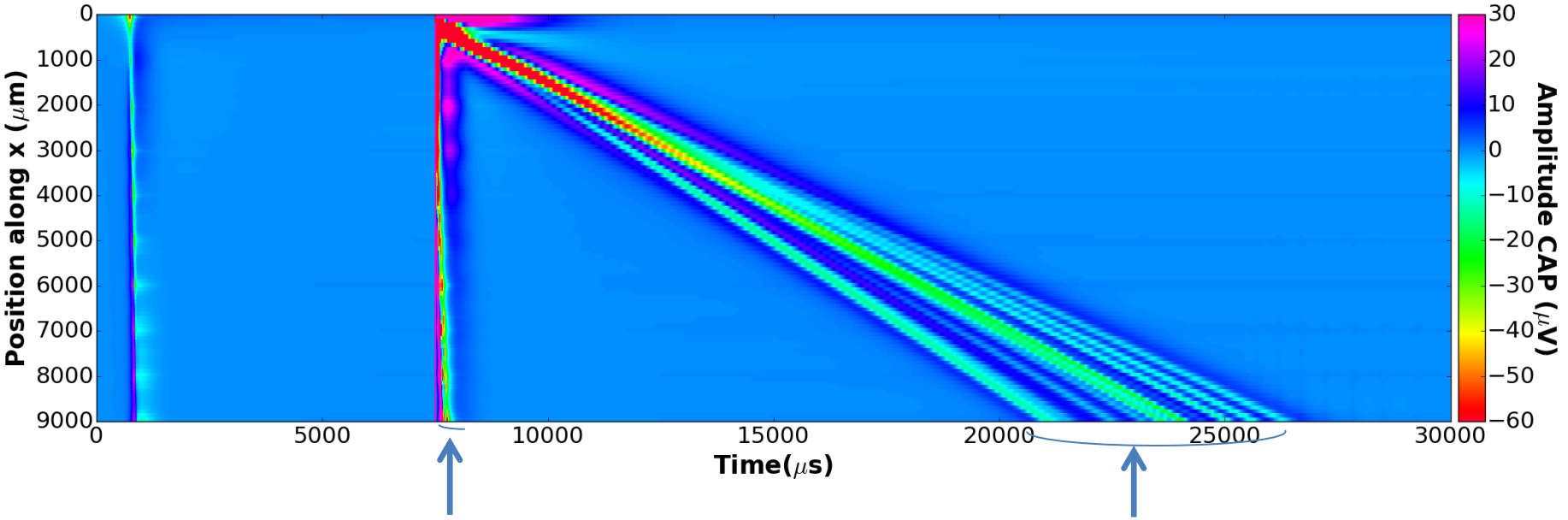


CAP monopolar recording 1,5cm from stimulus

17,5% of myelinated axons

Results

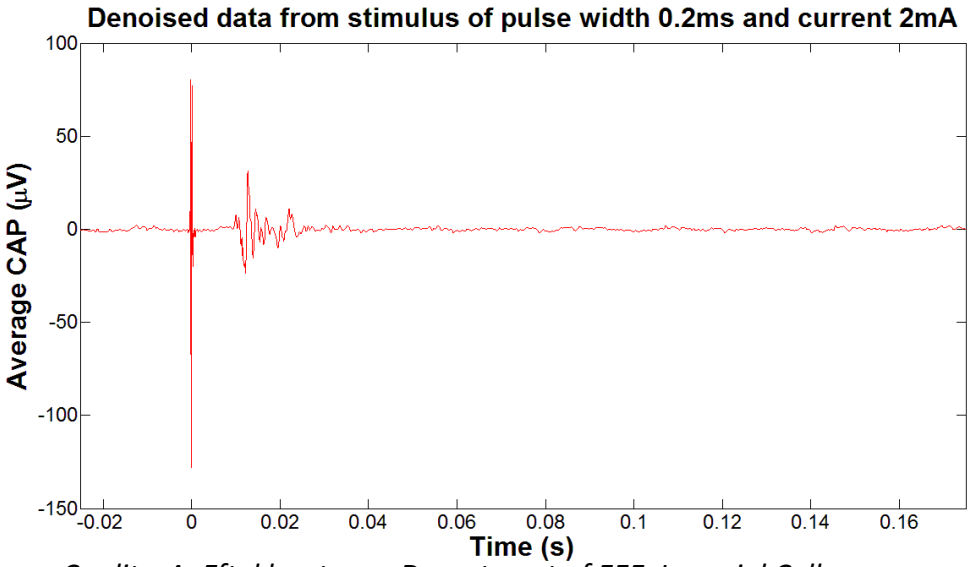
CAP temporal/spatial propagation



Distribution myelinated axons propagating at different conduction velocities

Distribution unmyelinated axons propagating at different conduction velocities

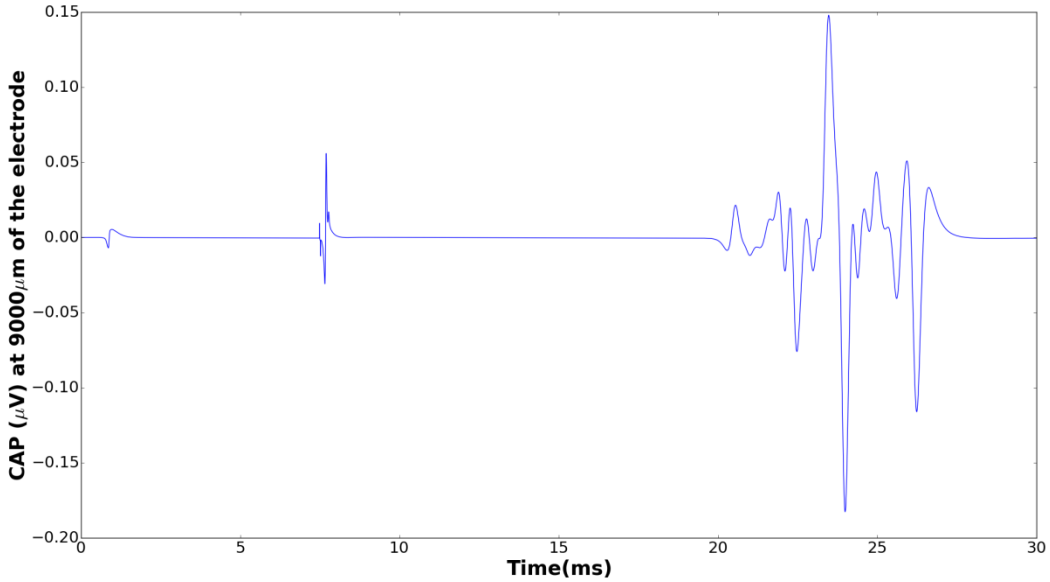
Discussion



Credits: A. Eftekhar team, Department of EEE, Imperial College

Cervical vagus nerve recording with bipolar electrode 8cm from the stimulus

<u>Objective:</u> To be able to back derive the composition of the nerve in term of myelinated and unmyelinated fibres from the CAP measurement using PNPy



References

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Annex

```
unmyelinatedDistribution = {
     'densities':[250,1250,5000,8000,9800,10200,8900,7600,5700,4000,3900,23
00,2000,1300,900,750,600,600,500,250], # Fibers densities
     'diameters': [ 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1., 1.1,
1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.], # Diameters for each densities
}

unmyelinatedParameters = {
     'name': "unmyelinated_axon", # Axon name (for NEURON)
     'L': 10500, # Axon length (µm)
     'diam': unmyelinatedDistribution, # Axon diameter distribution (µm)
     'cm' : 1.0, # Specific membrane capacitance (µF/cm²)
     'Ra': 200.0, # Specific axial resistance (Ohm cm)
     'rec_v': False, # Set voltage recorders True or False
}

myelinatedDistribution = {
     'densities':[100,300,1150,2750,3650,2850,1750,900,500,250,200,150,110,10
0,110,100,105], # Fibres densities
     'diameters': [ 1., 1.5, 2., 2.5, 3., 3.5, 4., 4.5, 5., 5.5, 6., 6.5,
7.,7.5, 8., 8.5, 9.],  # Diameters for each densities
}
myelinatedParametersA = {
     'name': "myelinated_axonA", # Axon name (for NEURON)
     'Nnodes': 21, # Number of nodes
     'fiberD': myelinatedDistribution, # Fibre diameter distribution (µm)
     'rec_v': False, # Set voltage recorders True or False
}
```

Annex

```
stimulusParameters = {
    'stim_type': "EXTRA", #Stimulation type either "INTRA" or "EXTRA"
    'stim_coord': [[0,50,0]], # spatial coordinates  of the stimulating
electrodes, example for bipolar case=[[xe0,ye0,ze0], [xe1,ye1,ze1]]
    'amplitude': 2.0, # Pulse amplitude (nA)
    'freq': 0.1, # Frequency of the sin pulse (kHz)
    'duty_cycle': 0.001, # Percentage stimulus is ON for one period
    'stim_dur' : 1e1, # Stimulus duration (ms)
    'jitter_para': [0,0], # Mean and standard deviation of the delay
}
recordingParameters = {
    "number_contact_points": 8, #Number of points on the circle
constituting the cuff electrode
    'recording_elec_pos': [9000], #Position of the recording electrode
along axon in um, in "BIPOLAR" case should be given as a couple [x1,x2]
    'number_elecs': 100, #number of electrodes along the bundle
    'dur': h.tstop, # Simulation duration (ms)
    'rec_CAP': True, # Boolean stating if CAP is recorded
}
bundleParameters = {
    'radius_bundle': 150.0, # Radius of the bundle in µm
    'number_of_axons': 640, # Number of axons in the bundle
    'p_A': 0.2, # Percentage of myelinated fibre type A
    'p_B': 0, # Percentage of myelinated fibre type B
    'p_C': 0.8, # Percentage of unmyelinated fibre type C
    'myelinated_A': myelinatedParametersA, # Parameters for fibre type A
    'myelinated_B': myelinatedParametersB, # Parameters for fibre type B
    'unmyelinated': unmyelinatedParameters,# Parameters for fibre type C
}
```