COMSOL CONFERENCE 2016 BOSTON

How Finite Element Analysis Revolutionized a 100-Year Old Equation

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A TEACHING HOSPITAL OF HARVARD MEDICAL SCHOOL

Evolution of the Nervous System

- 100 lightning strikes per second globally
- Sets up background noise level
- Solutions evolved to achieve reliable signal transmission
  - Bandpass filters – e.g. thresholds
  - Integrate signal over time
  - Go digital
- Nervous system is digital-analog hybrid

Neuromodulation & ‘Electroceuticals’

- *Neuromodulation*
  - the application of electromagnetic fields to affect the nervous system
    - spinal cord stimulation for chronic back pain
    - vagus nerve stimulation for epilepsy

- *Electroceuticals paradigm (GSK, DARPA)*
  - an ambitious program to decipher signaling through the nervous system and build devices to modulate it at will

The Weiss-Lapicque Equation

Simple solution to 19th century puzzle

$$I_{th} = I_{rh}(1 + \frac{\tau_{ch}}{pw}) \quad (1)$$

Threshold current is measured externally through intervening tissue

G. Weiss, "Sur la possibilité de render comparable entre eux les appareils servant a l'excitation électrique," *Arch. Ital. Biol.*, vol. 35, pp. 413–446, 1901.

L. Lapicque, "Influence d'une variation locale de température su l'excitabilité du nerf moteur," *Comptes Rendus Soc: de Biol.*, vol. 62, pp. 35–37, 1907.

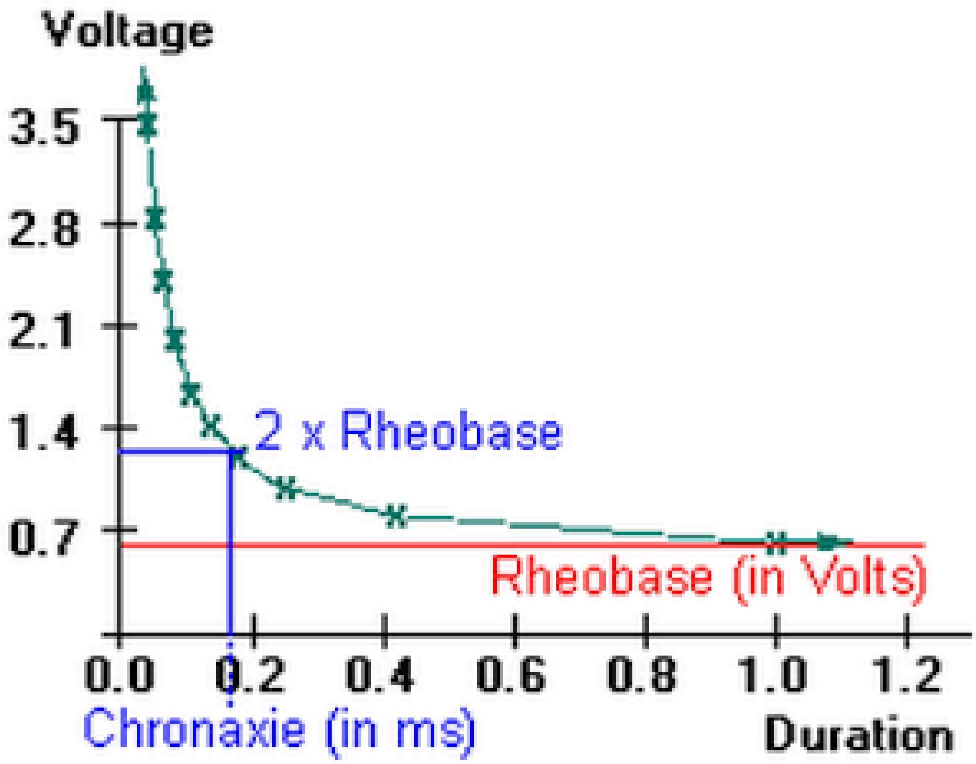
——, "Definition experimentale de l'excitation," *Comptes Rendus Acad. Sci. (Paris)*, vol. 67, no. 2, pp. 280–283, 1909.

——, *L'Excitabilite en Function du Temps*. Paris: Presses Universitaires de France, 1926.

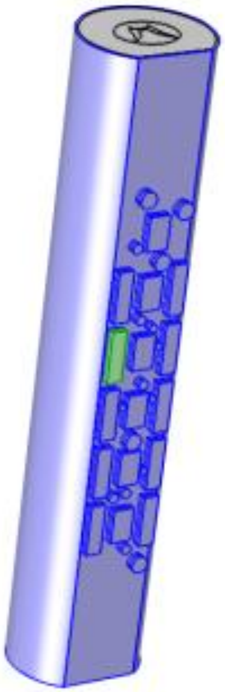
——, "Consideration préalables sur la nature du phénomene par lequel l'électricite excite les nerfs," *J. Physiol. Pathol. Génér.*, vol. 9, pp. 565–578, 1907.

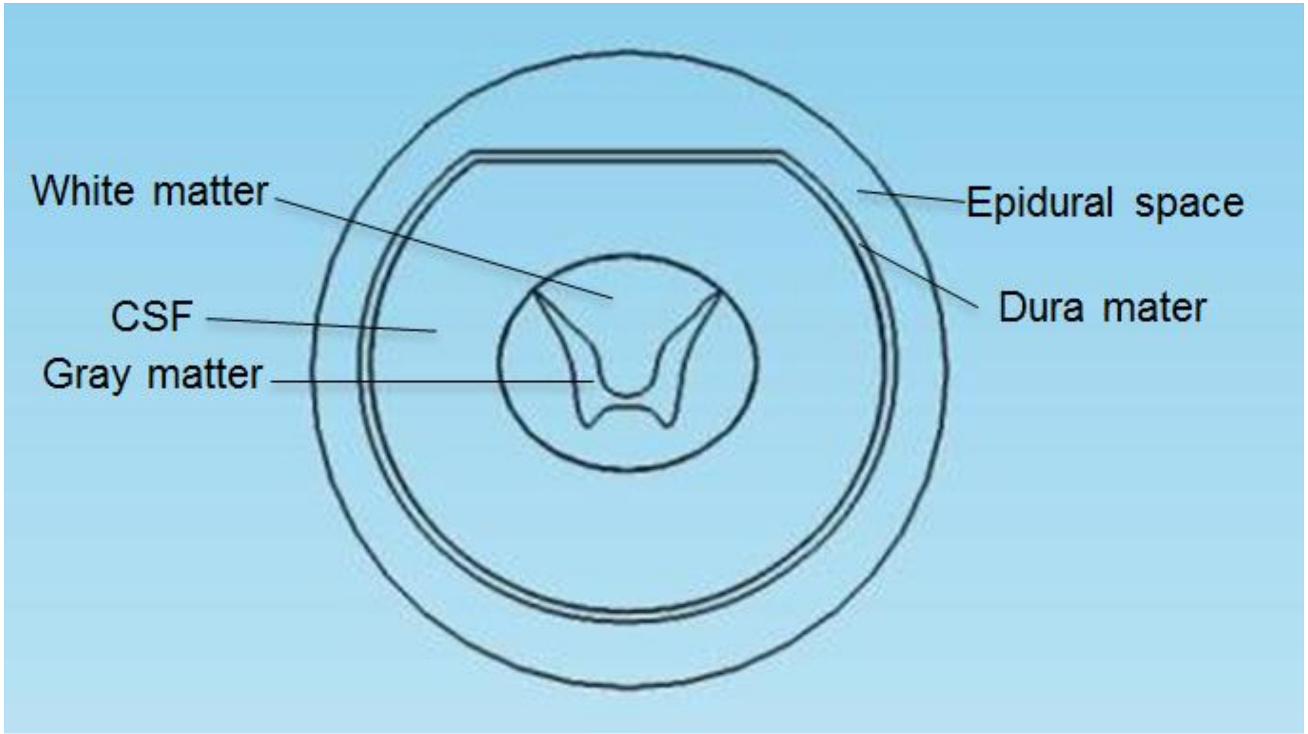
Relative Strength-Duration Curve

Relative to geometry, conductivities, electrode array, waveform



COMSOL Model of Spinal Cord Stimulation





Holsheimer active fiber model

Based on Hodgkin-Huxley model of the squid giant axon (Nobel Prize 1963)

Appendix

The fibre model and its parameters at 37°C

Fibre geometry

d axon diameter [m]
D fibre diameter [m]
L internodal length [m]
l nodal width, 1.5 μm
πdl nodal area [m^2]
$d = C_d D - D_d$, $C_d = 0.76$, $D_d = 1.81 \times 10^{-6}$
$L = C_L \ln(D/D_L)$, $C_L = 7.87 \times 10^{-6}$, $D_L = 3.44 \times 10^{-6}$

Gating variables

$a_m = 4.6 \times 10^3 (V + 18.4)/(1 - e^{(-18.4-V)/10.3})$
$b_m = 0.33 \times 10^3 (-22.7 - V)/(1 - e^{(V+22.7)/9.16})$
$a_h = 0.21 \times 10^3 (-111 - V)/(1 - e^{(V+111)/11})$
$b_h = 14.1 \times 10^3 /(1 + e^{(-28.8-V)/1.1})$
$a_n = 51.7(V + 93.2)/(1 - e^{(-93.2-V)/1.1})$
$b_n = 92(-76 - V)/(1 - e^{(V+76)/10.5})$
gating coefficients a, b in ms^{-1}
$dm/dt = a_m(1 - m) - b_m m$
$dh/dt = a_h(1 - h) - b_h h$
$dn/dt = a_n(1 - n) - b_n n$
$m(0) = 0.0382$
$h(0) = 0.6986$
$n(0) = 0.2563$
membrane potential V in millivolts (mV)

Parameters

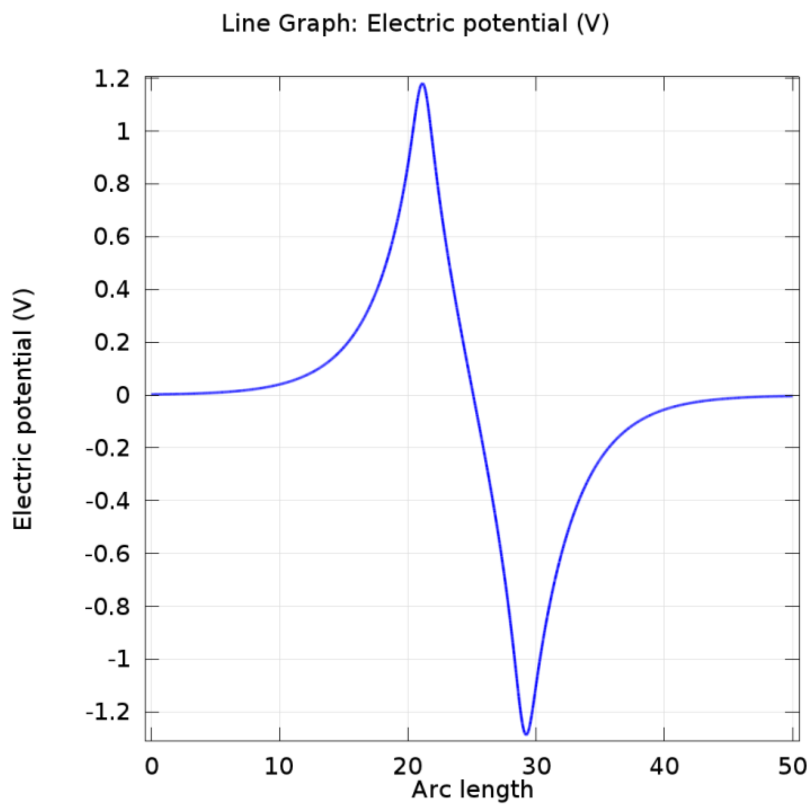
c_m membrane capacity, 0.028 F/m^2
g_L leakage conductance, 600 S/m^2
p_{Na} sodium permeability, 0.0704 dm^3/m$_2$s
g_K potassium conductance, 300 S/m^2
ρ_a intra-axonal resistance, 0.33 Ωm
V_L leakage equilibrium potential, −84.14 mV
V_{Na} sodium equilibrium potential, 43.7 mV
Na_o sodium concentration outside cell, 154 mM
Na_i sodium concentration inside cell, 30 mM
V_K potassium equilibrium potential, −84 mV
V_r resting membrane potential, −84 mV
F Faraday constant, 96485 C/mole
R gas constant, 8.3144 J/K mole
T absolute temperature, 310.15 K

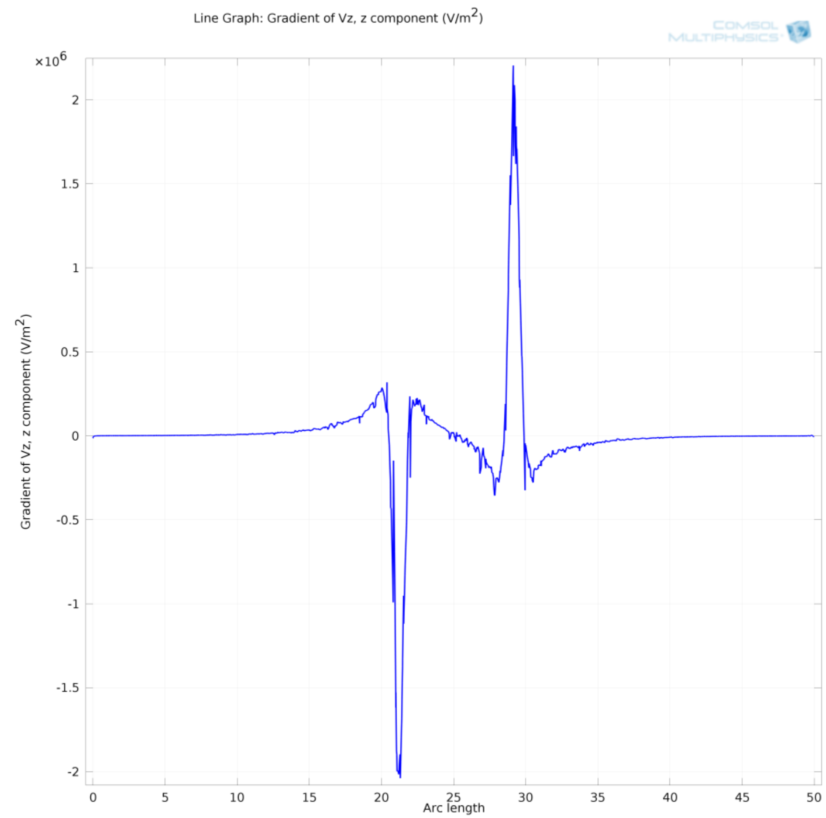
Membrane currents

i_{Na} sodium current [A/m^2]
i_K (fast) potassium current [A/m^2]
i_L leakage current [A/m^2]
i_{ion} total ionic current [A/m^2]
i_c capacitive current [A/m^2].
I_{mem} total nodal membrane current [A]
$i_{Na} = m^3 h\, p_{Na} VF^2/RT\,(Na_o - Na_i e^{VF/RT})/(1 - e^{VF/RT})$
$i_K = n^4 g_K(V - V_K)$
$i_L = g_L(V - V_L)$
$i_{ion} = i_{Na} + i_K + i_L$
$i_c = c_m\, dV/dt$
$I_{mem} = (i_{ion} + i_c)\pi dl$

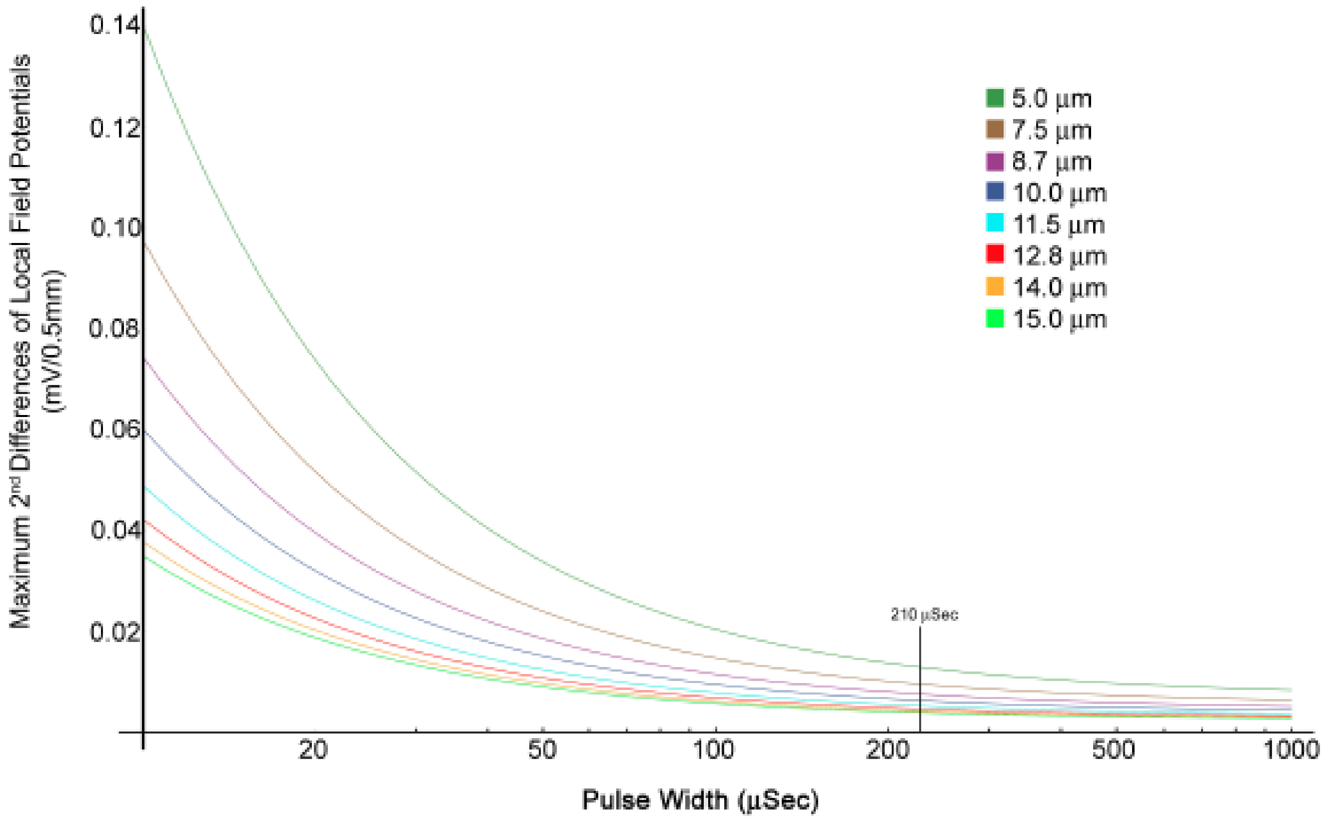
Wesselink et al. A model of the electrical behaviour of myelinated sensory nerve fibres based on human data. Med Bio Eng Comp 1999, 228-235.

Electric potential and 2nd difference along the axon



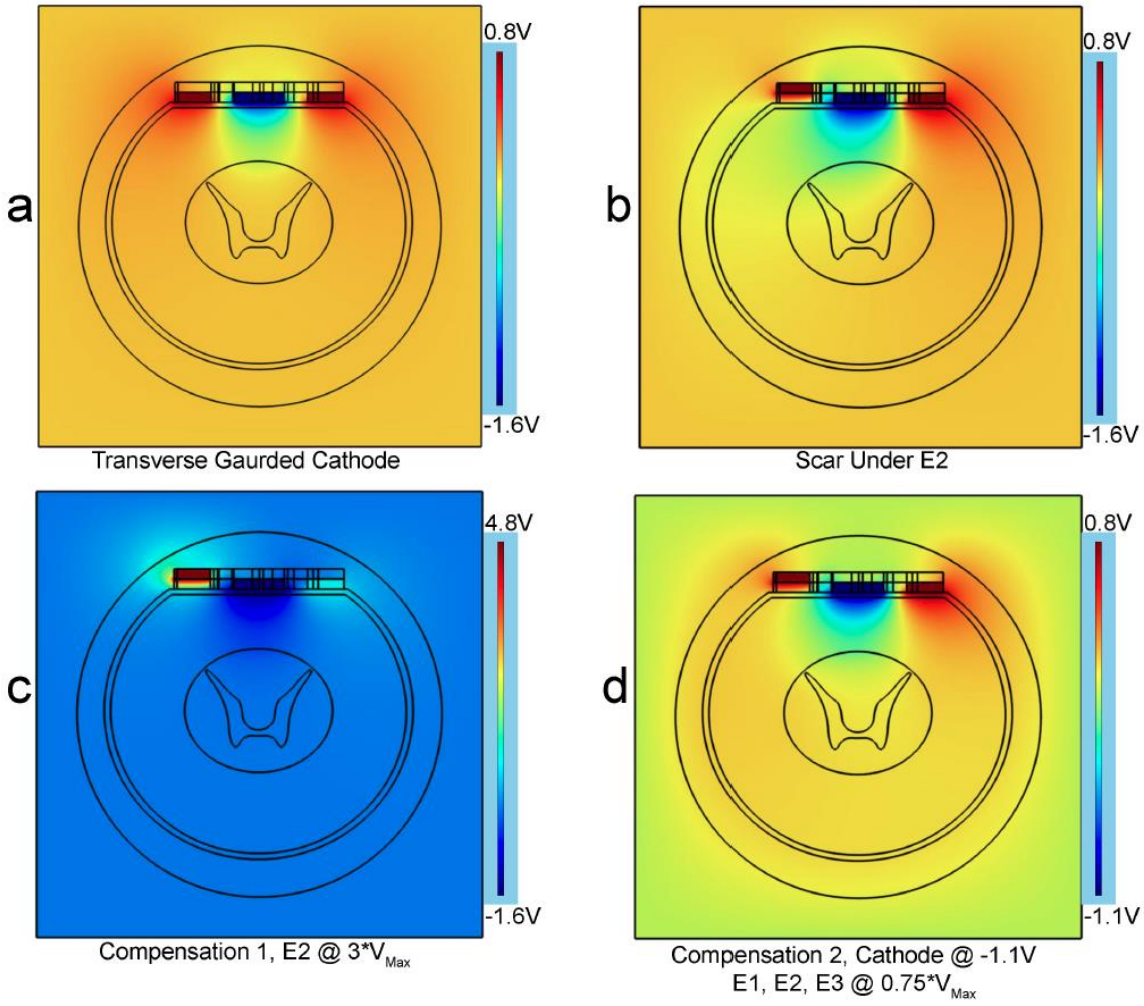


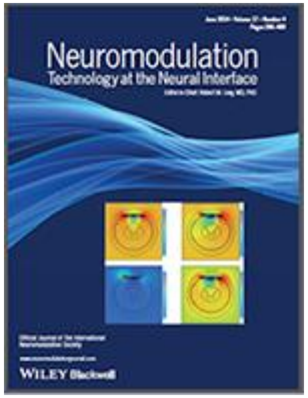
Absolute Strength-Duration Curve



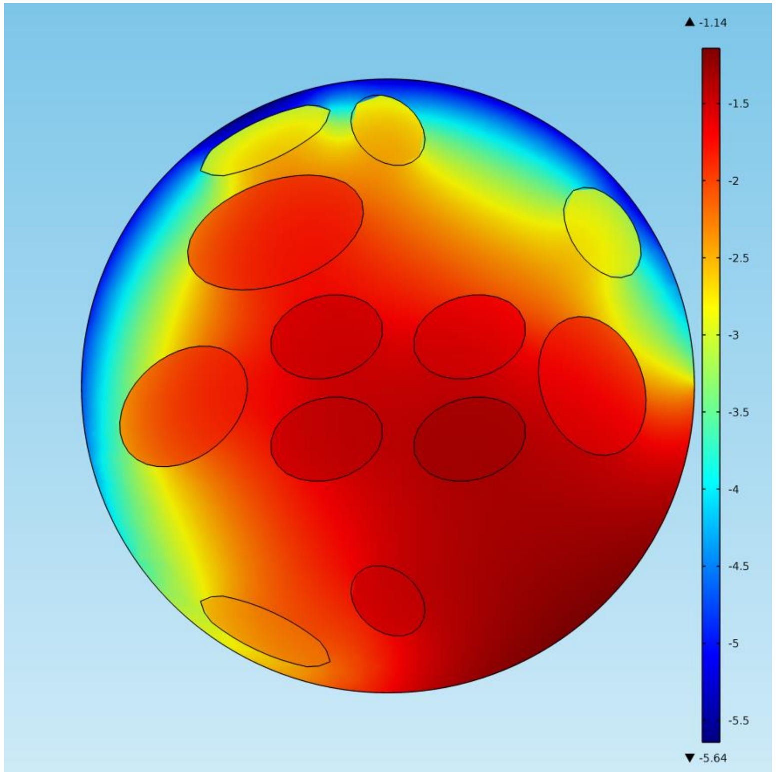
An *absolute* strength-duration plot of different diameter nerve fibers (legend) calculated from the Weiss equation in which 2nd differences of electric potential along the axons (y-axis), as predicted in a COMSOL FEM, are substituted for potential measured at the electrode, the traditional method. X-axis: duration of stimulating pulse.

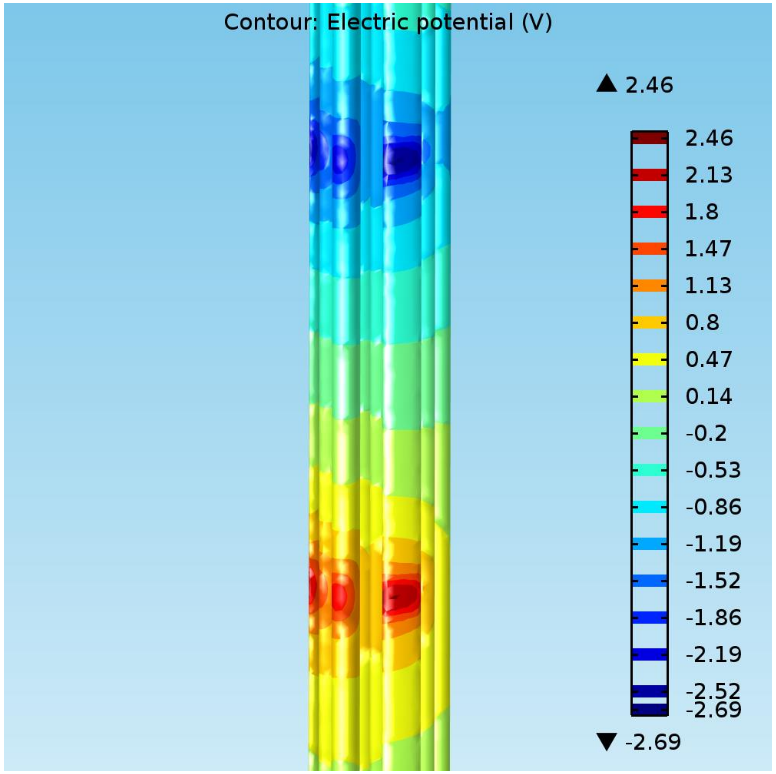
Effect of scarring under electrode array on spinal cord stimulation





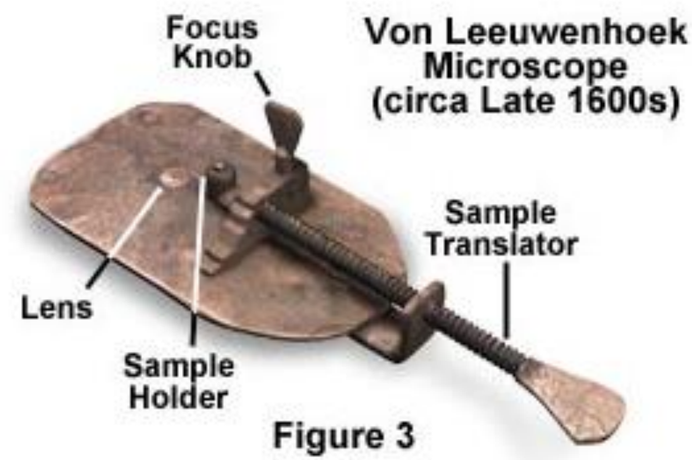
Vagus nerve stimulation for epilepsy





Finite Element Modeling

A tool as important as the telescope or microscope



Acknowledgments

- Jeff Arle, MD, PhD, Principal Investigator
- Jay Shils, PhD, Principal Investigator
- Longzhi Mei, MS, Research

- Sydney Family Trust
- Livanova Cyberonics
- Boston Scientific Corporation