

# Simulating Spiking Neurons Using a Simple Mathematical Model

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# Introduction

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There are more than 1.2 million Americans with Spinal cord injuries (SCI) [1]

Patients with SCI can lose the ability to walk, stand, move their arms and SCI often leads to secondary complications in bladder and bowel functions, etc. Basic life activities become extremely difficult

Recent studies [2] have shown that spinal cord stimulation can enable voluntary motor function in patients with spinal cord injury



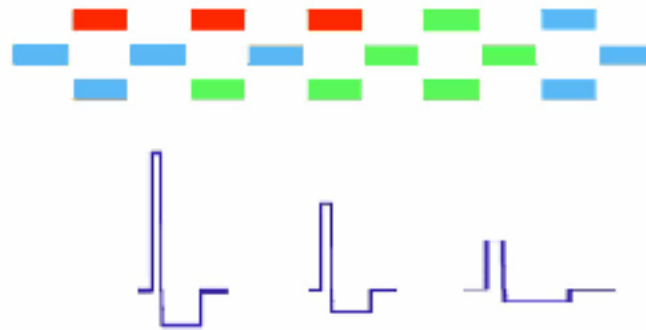
Since 2011, four individuals with SCI received epidural stimulation of the spinal cord. All regained the ability to independently stand, and acquire some voluntary control of the toes, ankles, knees and hips [3]



# Introduction

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Trial and error methods are frequently used to determine the stimulus parameters needed to activate specific motor neurons.



Simulations are useful in predicting the response elicited from particular stimulus parameters.

# Hodgkin-Huxley model

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In 1952, Alan Hodgkin and Andrew Huxley published a series of papers [4] describing mathematics behind propagation of action potentials in a squid axon

$$C_m \frac{\partial V_m}{\partial t} = \frac{r}{2R} \frac{\partial^2 V_m}{\partial x^2} + g_{Na} m^3 h (V_{Na} - V_m) + g_K n^4 (V_K - V_m) + g_L (V_L - V_m) \quad (1)$$

$$\frac{dw}{dt} = \alpha_w (1 - w) - \beta_w w \quad (2)$$

*w is m, n or h*

$$\alpha_m = \frac{2.5 - 0.1V}{e^{2.5 - 0.1V} - 1} \quad (3a)$$

$$\alpha_n = \frac{1 - 0.1V}{10(e^{1 - 0.1V} - 1)} \quad (3b)$$

$$\alpha_h = 0.07e^{-\frac{v}{20}} \quad (3c)$$

$$\beta_m = 4e^{-\frac{v}{18}} \quad (3d)$$

$$\beta_n = 0.125e^{-\frac{v}{80}} \quad (3e)$$

$$\beta_h = \frac{1}{e^{3 - 0.1V} + 1} \quad (3f)$$

Computationally challenging to use this model to simulate a complex system

# Izhikevich Model

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The Izhikevich model is a recently (2003) published simple mathematical model that is both computationally more efficient than the Hodgkin-Huxley model and is also capable of simulating multiple spiking and bursting patterns [5].

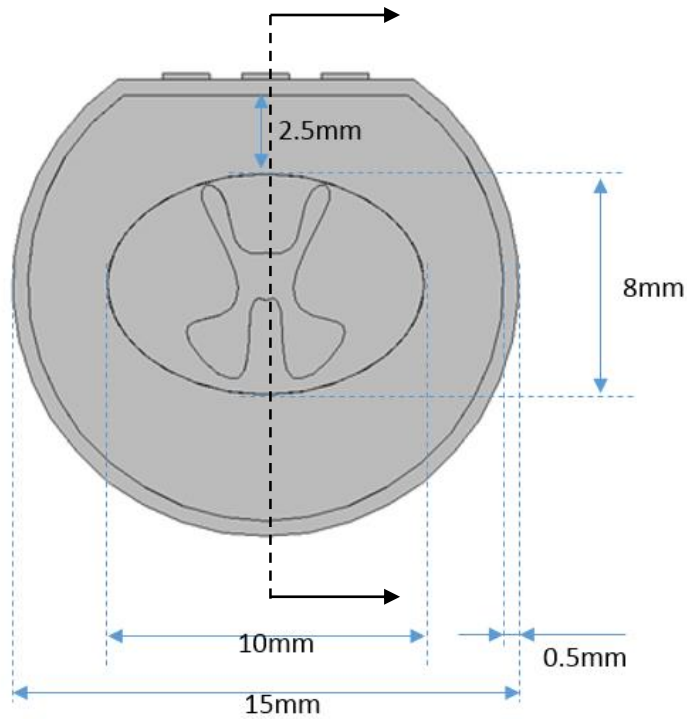
$$\frac{dv}{dt} = 0.04v^2 + 5v + 140 - u + I \quad (4)$$

$$\frac{du}{dt} = a(bv - u) \quad (5)$$

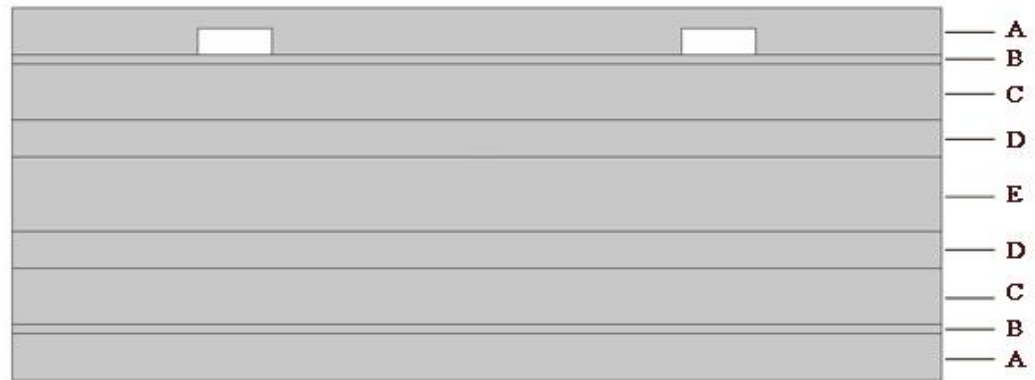
$$\text{if } v \geq 30\text{mV, then } \begin{cases} v \leftarrow c \\ u \leftarrow u + d \end{cases} \quad (6)$$

Computationally less complex model for simulating neurons

# Modeling in COMSOL Multiphysics



Cross section of the human spinal cord with average dimensions of L1-L5 region[6]



2D model used for simulations representing the longitudinal section of the spinal cord with two embedded electrode; where A, B, C, D and E represent epidural fat, Dura matter, CSF, white matter and gray matter, respectively.

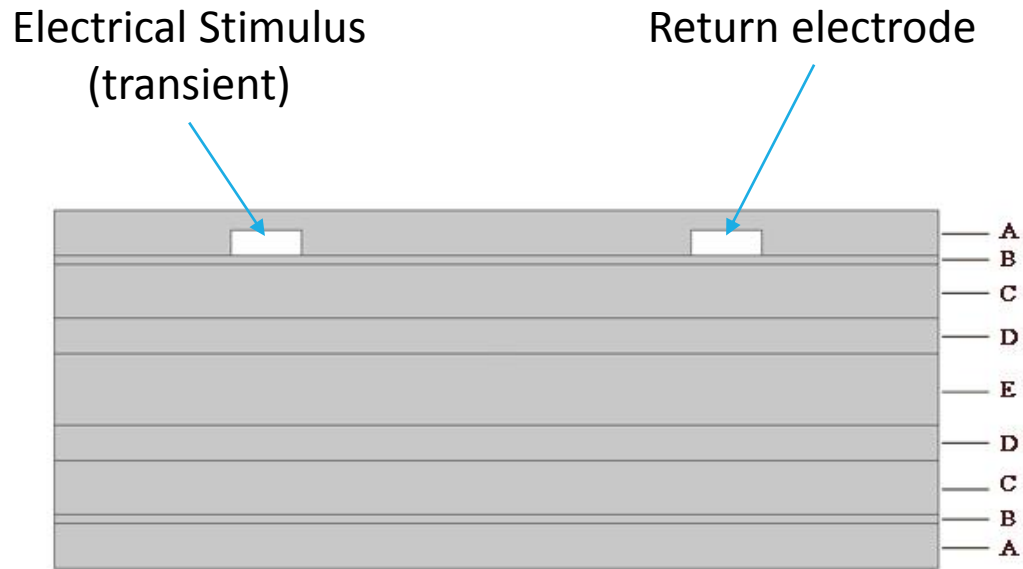
# Materials

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Item	Conductivity (S/m)	Permittivity
White matter (longitudinal)	0.6	38.79
White matter (transverse)	0.083	1846.05
Gray matter	0.23	458.89
CSF	2	108.89
Dura matter	0.6	141.25
Epidural fat	0.04	38.72

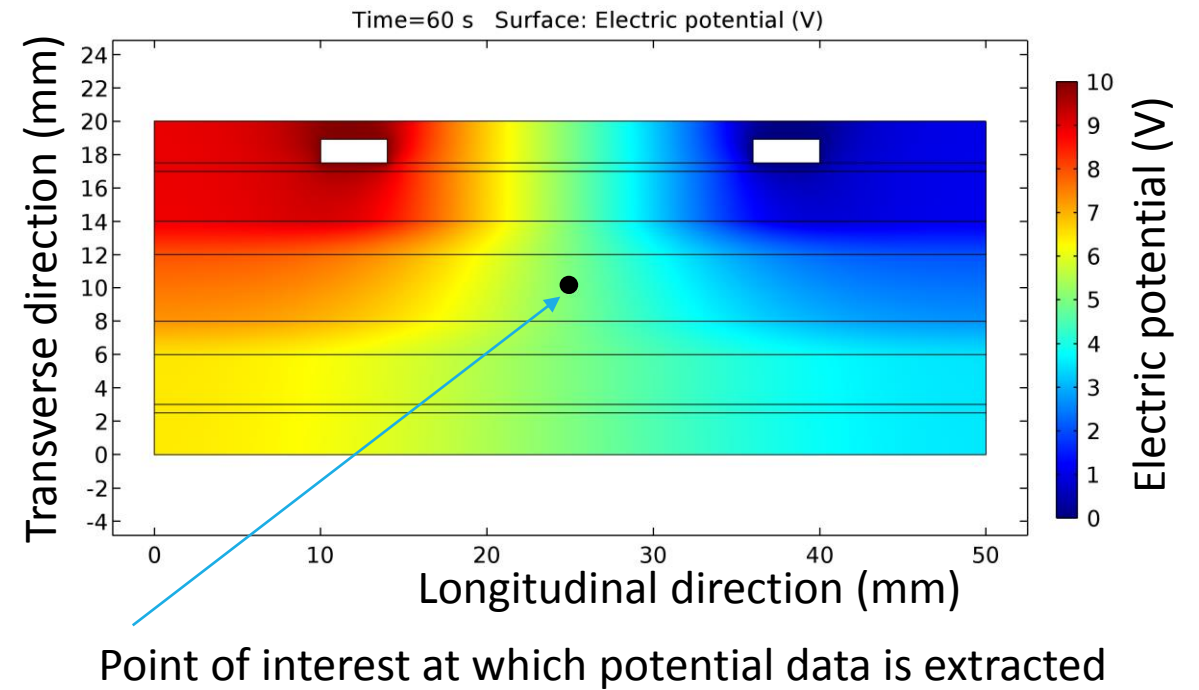
The dielectric properties [7, 8] used in this study.

# Simulation to find the electric potential at point of interest



Maxwell's equations to solve for the potential distribution

$$\nabla \cdot \mathbf{J} = -\nabla(\sigma \nabla V) - \nabla \left( \epsilon_0 \epsilon_r \nabla \frac{\partial V}{\partial t} \right) = 0 \quad (7)$$





# Simulation to find the action potential at point of interest

Use of previous solution operator

$$\frac{dv}{dt} = 0.04v^2 + 5v + 140 - u + I$$

$$\frac{du}{dt} = a(bv - u)$$

if  $v \geq 30\text{mV}$ , then

$$\left\{ \begin{array}{l} v \leftarrow c \\ u \leftarrow u + d \end{array} \right.$$

The screenshot shows the model tree in COMSOL Multiphysics. The following nodes are highlighted with red boxes:

- Global Equations 1
- Global Equations 2
- Previous Solution 1

Global Equations

Label: Global Equations 2

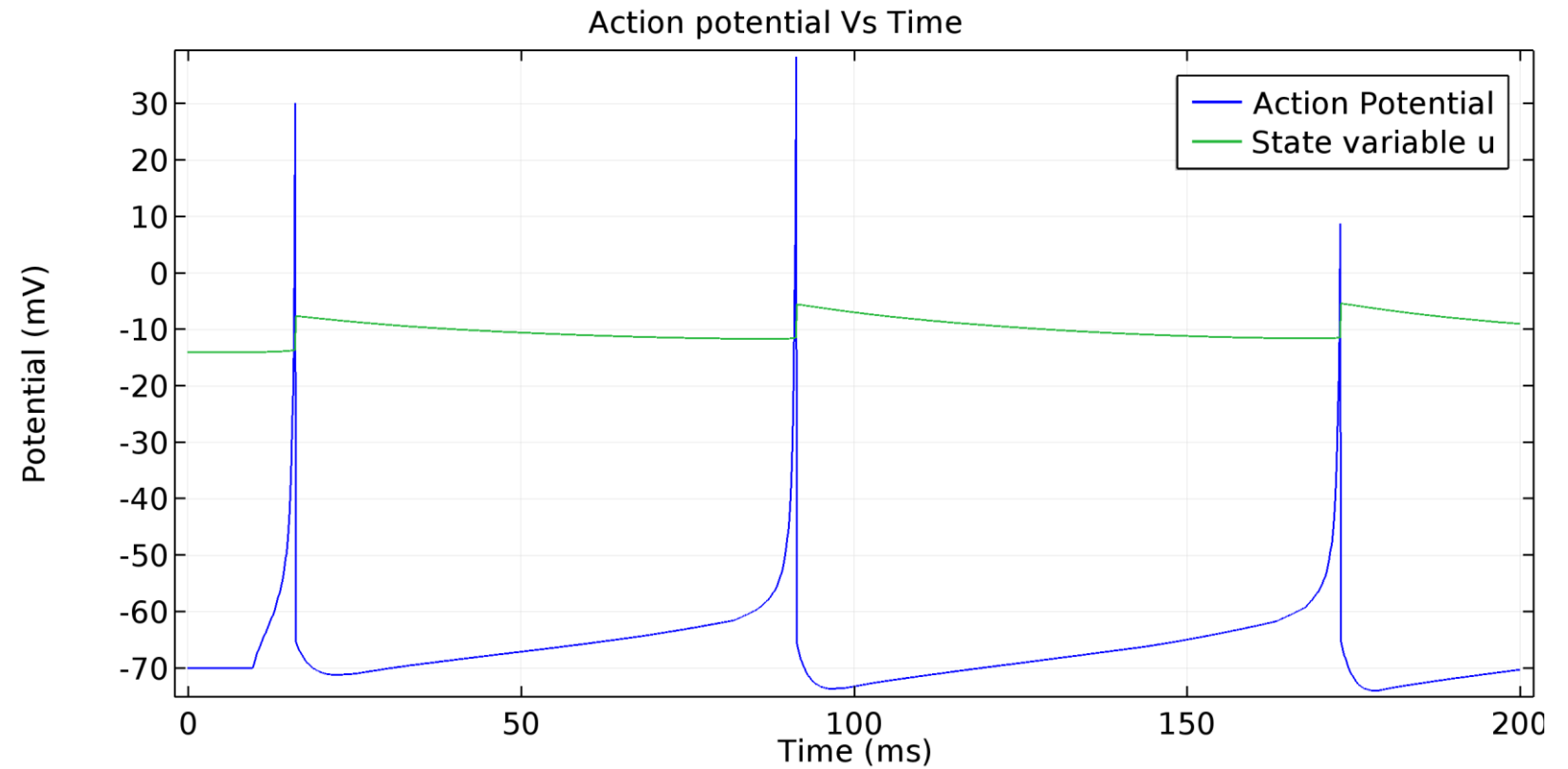
Global Equations

$f(u, u_t, u_{tt}, t) = 0, u(t_0) = u_0, u_t(t_0) = u_{t_0}$

Name	f(u, u_t, u_{tt}, t) (1)	Initial value	Initial value	Description
k	k-nojac(v)	0	0	
l	l-nojac(u)	0	0	
		0	0	

# Simulation results

Typical spiking pattern generated for the stimulus extracted from the previous step



# COMSOL app to simplify simulation process

The screenshot displays the COMSOL app interface for an AP Model simulation. The left sidebar contains several sections: 'AP Model Parameters' with input fields for 'a', 'b', 'c', 'd', 'v\_init', and 'u\_init'; 'Spiking Patterns' with buttons for 'Tonic Spiking', 'Phasic Spiking', 'Tonic Bursting', 'Phasic Bursting', and 'Mixed Mode'; 'Dendrite Position' with 'x Position' and 'y Position' fields; and 'Stimulus Parameters' with 'T1(s)', 'T2(s)', 'Voff', and 'Von' fields. A red box highlights the 'Simulation steps' toolbar, which includes 'Update Dendrite', '2D Potential', 'V Profile', 'Export Data', 'Import Data', and 'Action Potentials'. The main 'Results area' shows a plot of 'Potential (V)' versus 'Time (s)'. The plot features a blue line for 'Action Potential' and a green line for 'State variable u'. The blue line shows three distinct action potential spikes, while the green line shows a corresponding step-like response. Red arrows point from the text labels to the respective parts of the interface.

Model parameters

Parameter presets

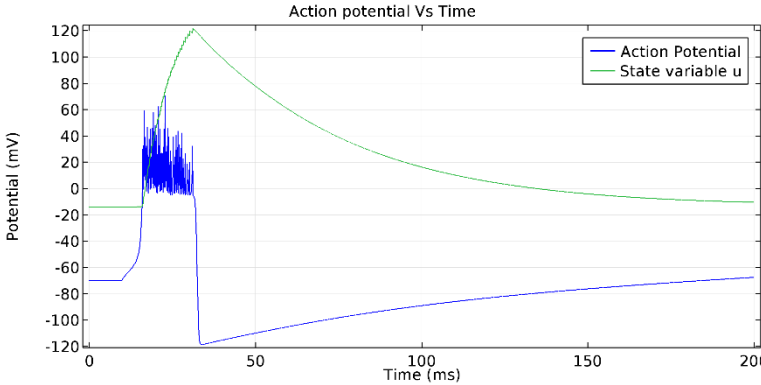
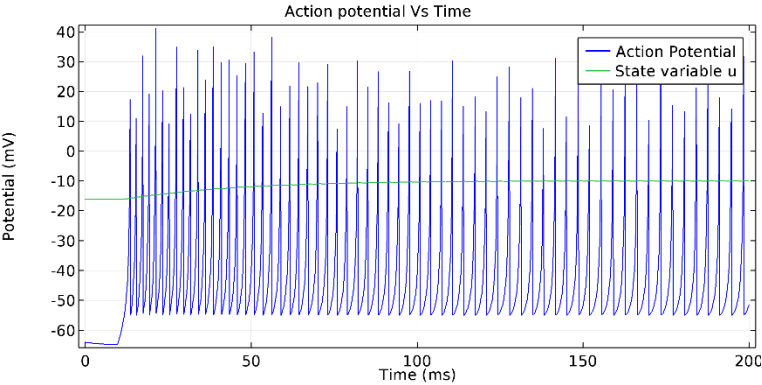
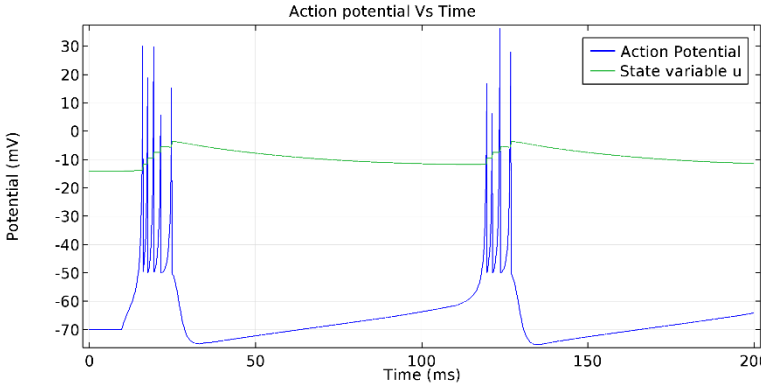
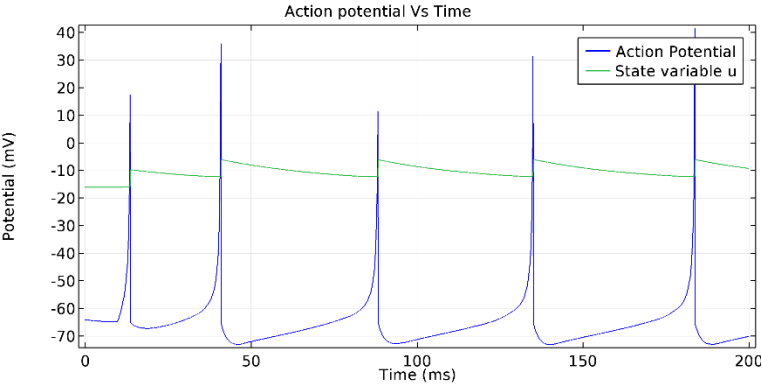
Dendrite position

Stimulus parameters

Simulation steps

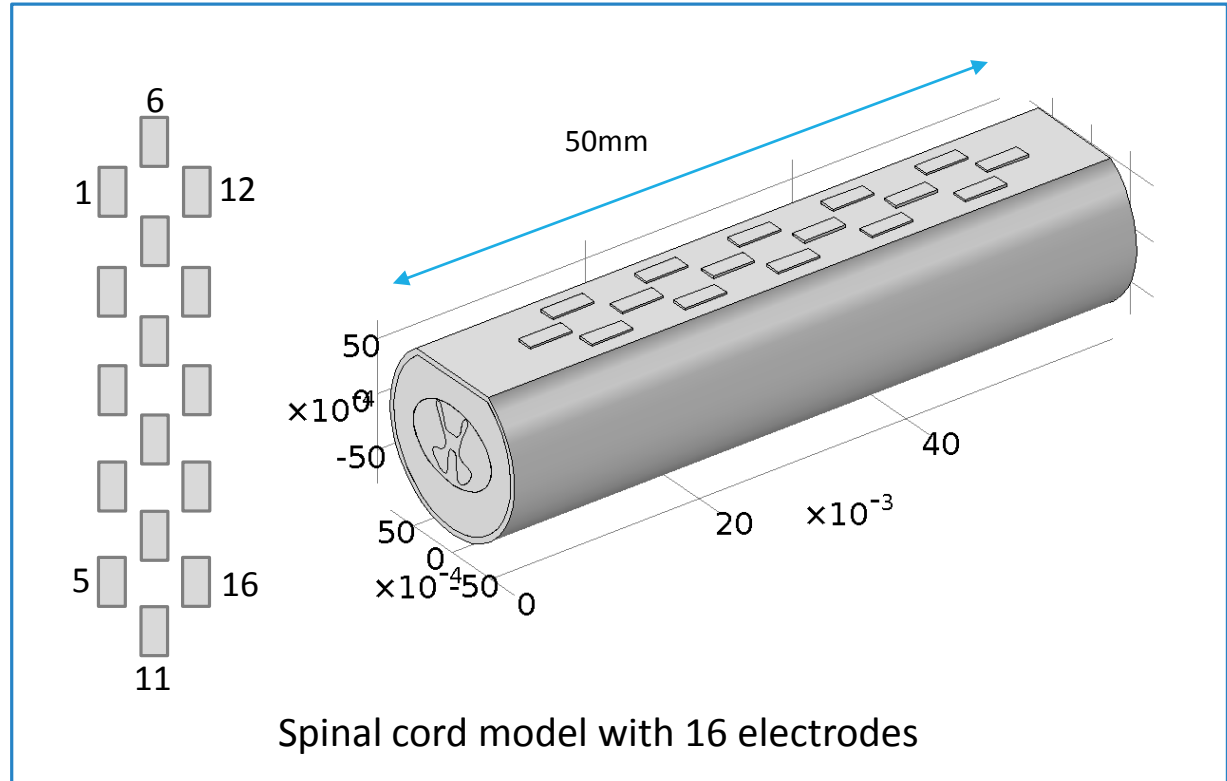
Results area

# Different spiking patterns



# Next steps

- Modeling with realistic 3D model
- Use of multiple neurons
- Introduce interaction between neurons



**Goal: To Improve the effectiveness of simulation**

# Conclusion

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- Izhikevich model was utilized to simulate spiking patterns of neurons due to external stimuli provided through a 2D spinal cord model
- COMSOL provides the ability to easily combine external electrical stimuli to a neural model
- COMSOL application builder was very useful in simplifying the simulation process

# References

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- [2] Harkema S, Gerasimenko Y, Hodes J, Burdick J, Angeli C, Chen Y, Ferreira C, Willhite A, Rejc E, Grossman RG, Edgerton VR. Effect of epidural stimulation of the lumbosacral spinal cord on voluntary movement, standing, and assisted stepping after motor complete paraplegia: a case study, *Lancet*, **377**, 1938-47 (2011)
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- [5] Izhikevich EM, Simple model of spiking neurons, *IEEE Trans. Neural Networks*, **14**, 1569–1572 (2003)
- [6] Ko HY, Park JH, Shin YB, Baek SY, Gross quantitative measurements of spinal cord segments in human, *Spinal Cord*, **42**, 35-40 (2004)
- [7] Min X, Kent AR, Rosenberg SP, Fayram TA, Modeling dermatome selectivity of single-and multiple-current source spinal cord stimulation system, 36<sup>th</sup> annual international conference of the IEEE, Chicago, 6246-6249, (2014)
- [8] Zengin R, Gençer NG, Küçükdeveci F, Numerical analysis of spinal cord stimulation with a 2-electrode percutaneous lead, 18<sup>th</sup> national biomedical engineering meeting, Istanbul, 1-4, (2014)

# Thank You

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