



# Terrence J. Sejnowski

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**“My goal is to discover the principles linking brain mechanisms and behavior. My laboratory uses both experimental and modeling techniques to study the biophysical properties of neurons and synapses, the sites at which neurons connect with each other, as well as the population dynamics of large networks of neurons.”**

Multiple sclerosis affects an estimated 400,000 Americans and more than 2.5 million people worldwide. A chronic, often disabling disease that attacks the central nervous system, it is characterized by a baffling range of neurological symptoms, including numbness, tingling, motor weakness, paralysis, and vision loss. It is thought to result when the immune system attacks the myelin sheath that insulates axons, the nerve fibers that conduct electrical impulses to and from the brain and between neurons within the brain. Ordinarily, the myelin speeds up the signals the axons transmit, but when axons lose their insulation, either signal conduction fails because the demyelinated axons are unable to generate an impulse, or the axons become hyperexcitable and overcompensate by firing even in the absence of an input.

The first computer model of axonal transmission, developed in the 1950s for the giant axon of the squid, which lacks myelin, tracked positively charged sodium and potassium ions, whose movements across the neuronal membrane generate the necessary electrical signals. Building on that model,

Sejnowski and his team included myelin in their own model, then demyelinated one of the sections and incorporated all the changes known to take place as a result. Most prior studies had focused on the sodium channel because it is responsible for initiating the electrical signal, but to everyone's surprise, Sejnowski's group found that it was the ratio of densities between the sodium channel and a previously ignored but ubiquitous voltage-insensitive potassium current, called the leak current, that determines whether neurons can fire properly. If the sodium level drops, an accompanying drop in the leak current will maintain the signal, whereas if the sodium drops but the leak current doesn't, signal transmission may fail. Conversely, if the sodium level is too high and the leak current doesn't increase, a patient may experience twitching.

Sejnowski's model not only offers an explanation for many of the bizarre symptoms that multiple sclerosis patients experience but could also provide a new target for drugs that increase or decrease the potassium leak current to maintain a constant ratio and offer relief.

For more information, please visit  
[salk.edu/faculty/sejnowski.html](http://salk.edu/faculty/sejnowski.html)

#### Left to right:

*Standing:* Justin Kinney, Chris Hiestand, Antonio Pinto Duarte, Jay Coggan, Maxime Bonjean, Samat Moldakarimov, Jorge Aldana (in red), Ben Huh, John Jacobson, Tiger Lin, Tanya Baker, Mike Arnold, Lee Campbell, Roger Bingham, Vlad Volman, and Ben Regner

*Seated:* Terrence J. Sejnowski, Mary Ellen Perry, Marga Behrens, John Reynolds, and Brian Nielsen

