A chat with computational neuroscientist Terrence Sejnowski

Introduction | *Terry Sejnowski is one of the world's foremost theoretical neuroscientists and a pioneer in the field of computational neuroscience. Through the use of computational models and experimentation at multiple physiological levels, Dr. Sejnowski has contributed to our understanding of issues as diverse as the function of early sensory representations, neocortical dynamics, synaptic communication, and consciousness. He has co-invented machine learning algorithms such as the Boltzmann Machine and Independent Component Analysis and helped to produce MCell, software for constructing realistic simulations of cellular signaling. In addition to his research, Dr. Sejnowski has played a key role in the development of the field of computational neuroscience, which he continues to foster and promote. In 1989, he founded the journal Neural Computation, of which he his editor-in-chief, and he is currently President of the Neural Information Processing Systems Foundation, which organizes a prestigious interdisciplinary annual conference of the same name. In recognition of his contributions to the cognitive sciences, Dr. Sejnowski has received numerous accolades, including the Presidential Young Investigator Award from 1984-1989, the Hebb Prize in 1999, and in 2004 he was made a fellow of the American Association for the Advancement of Science. Dr. Sejnowski is currently a Howard Hughes Medical Institute investigator, the Francis Crick Professor at the Salk Institute for Biological Studies where he directs the Computational Neurobiology Laboratory, and a Professor of Biological Sciences at the University of California San Diego, where he heads the Institute for Neural Computation.*

You received your undergraduate and doctoral training in physics. What inspired you to move from physics to neuroscience?

I was a graduate student working on a thesis in general relativity at Princeton when I took a neuroethology course from Mark Konishi in the Biology Department. I was fascinated. The mysteries of the universe paled in comparison to the mysteries of behavior.

I also remember a lecture from Chuck Stevens, visiting from Yale, who reported that synapses in the cortex were unreliable. How could the brain reliably compute with such unreliable parts? I took a course from Charles Gross on the visual system and learned about recordings of Hubel and Wiesel from neurons in the visual cortex.

I went to a meeting of the Society for Neuroscience and was overwhelmed with the sheer size and energy of the field. Shortly after deciding to switch fields, I took the Neurobiology course at Woods Hole. This was an intense 10 week lab course that introduced me to dissections, action potentials and the culture of Biology. I made many lifelong friends there and never turned back.

Do you think that theoretical neuroscience will ever have something like the fundamental laws and awesome predictive power of theoretical physics? Or will a mature theoretical neuroscience be a very different kind of paradigm?

Biology is fundamentally different from physics and biological theory has a different role. Take, for example, the theory of evolution, which is explanatory but not predictive. A theory of the brain will explain behavior, not predict it. Nonetheless, understanding the brain will have amazing applications and profound implications for understanding ourselves as a species.

In the book, *Liars, Lovers, and Heroes* that you co-wrote with Stephen Quartz, you say "neuroscientists have learned more about the brain in the last decade than in all previous history." What do you think have been the most significant advances in our understanding of the nervous system in the past 10 years?

There are so many discoveries in neuroscience in the last decade that it is difficult to choose any of them as the most significant. Rather than pick one of them arbitrarily, let me rephrase the question and ask, instead, what is the most significant brain discovery that has not yet been made?

Leo van Hemmen and I recently edited a book entitled "23 Problems in Systems Neuroscience", which has 23 chapters by 23 authors on 23 big problems that neuroscientists have not yet solved, and may not in this century (we were inspired by Hilbert's 23 problems in mathematics at the turn of the 20th century). My question was what is the source of the brain's spontaneous activity and what impact can the firing of a single neuron have on the rest of the brain?

What do you think might be the most significant advances in the next 10 years?

Making predictions is always dangerous, especially about the future. I am pretty sure that the most important discovery in the next 10 years will be a surprise that no one anticipated.

Which area of neuroscience are you most interested in? (vision, sleep, subcortical structures, etc.) and what are you working on currently?

I can't think of a single area of neuroscience that I am not interested in, and I have been intensely interested in many research areas at one time or another. My lab is currently working on problems in the dynamics of neural signaling from the molecular to the systems levels. In particular, we are working on the hypothesis that large-scale communications in the cerebral cortex may be regulated by inhibitory interneurons –- not by suppressing activity but by enhancing it through spike synchronization.

Understanding the brain clearly requires integrating knowledge from disciplines as disparate as molecular biology, anthropology, and electrical engineering. There are two ways to do such interdisciplinary research. One is for researchers to be competent in multiple disciplines and the other is to foster collaboration between researchers who have specialized in a single discipline. In your experience, which method do you find the most productive? Or do you think the approaches have complementary strengths and weaknesses?

The farther away two insights are the longer it takes for them to come together and create a new discovery. If they are from two different disciplines it takes longer than if they are from the same discipline, and if they are in the heads of two different people it takes long than if they are both in the same head. The process can be speeded up by catalysis, which is what happens in my lab: bring creative researchers together from different disciplines and let them interact with each other.

Do you have any advice for young scientists beginning their careers?

I was asked by students in the neurosciences program to give a retreat talk on that theme. Ramon y Cajal, the great neuroanatomist, wrote a book on advice to the young scientist. I pointed out that there is no one way to have a successful career and each of us needs to find what we are good at and follow our instincts wherever that takes us. At the highest levels of achievement in science one often finds the highest levels of persistence.

More specifically, for a graduate student interested in computational neuroscience, which do you think is more important: having a background in programming and simulations, or having a background in biology and neuroscience?

Both are equally important. The goal of the computational neurobiology program that I direct in the Biology Department is to train students to be equally at home in the lab and in front of the computer.

Have there been any people or experiences that have particularly influenced how you think about the brain?

I have been inspired by many colleagues but I have learned the most about the brain from my students.

You've long been a pioneer and advocate of computational modeling in the cognitive sciences. How has computational modeling changed since the neural network explosion in the 1980s? What are hot topics in the discipline today and do you find that wet neuroscientists are increasingly willing to collaborate with modelers?

Alan Newell once said that when AI was founded not enough was known about the brain to be of any help and in the early 1980s, symbol processing was the only game in town. That has changed and we now know a lot about the brain, perhaps more than we need to know. Biology has undergone a profound shift toward quantitative analysis with the vast increase in knowledge of the genome and cellular mechanisms. The goal now is to mine that knowledge for a deeper understanding of how nature has solved difficult computational problems. This can only be done by using the tools of mathematics, physics, computer science and engineering, together with new molecular techniques. Francis Crick believed that the goal of theory is to design experiments that give the game away. So in the end the answers will come from doing new definitive experiments.

Do you believe scientists will one day be able to create an artificial brain that is similar to the biological one? Which level will we need to understand the brain at for this purpose? Single channels or systems of interconnected neurons? What "matters"?

Understanding the brain will lead to intelligent devices. These will be special purpose devices unlike human intelligence and more like insect intelligence. The recent victory of Stanley in the DARPA grand challenge autonomous vehicle race is case in point. Stanley is based on machine learning, a distant cousin of human learning. Human intelligence may someday be implemented as an afterthought but it is a luxury that will not be needed to create artificial intelligence.

As someone who's appeared multiple times in the mainstream media, what do you think about how the popular press covers neuroscience?

I respect what science journalists do and I am in awe of what the best ones can do. I am excited by the potential of the internet to create a new form of journalism: The internet will make open up high bandwidth access to the best that science has discovered about nature. The Science Network (www.thesciencenetwork.org), whose goal is to be the C-SPAN for science, is an example of what is now possible.

Do you think science and neuroscience in particular should be used to make ethical decisions (e.g. whether somebody should be kept alive)?

Science certainly raises new ethical problems but it does not make the decisions any easier. For example, science will someday make immortality possible, which raises the issue of whether we should live forever.

Has your knowledge of the brain had any impact on your lifestyle? For example, after you and members of Fred Gage's lab showed that running enhances neurogenesis and learning in mice, did you make more of an effort to go to the gym on a regular basis?

That experiment was done in Fred Gage's lab before we helped out by showing that long-term potentiation in the dentate gyrus of the hippocampus is enhanced by exercise. I get my best ideas running. Exercise is good for every system in your body, including your heart and circulatory system as well as your brain. If exercise were a medicine it would outsell all of the blockbusters. If exercise were more expensive, and if a profit could be made from it, there would be more advertising and more of us would exercise. ■