Questions and Answers – Ted Berger

Q1. ***When did you decide you wanted to be a scientist?***

At the end of my undergraduate education, i.e., when I began graduate school. There was no great "ah ha" moment – my decision to become a scientist was more a matter of decision by default. It gradually became clear to me that there was nothing else besides science and research that I could ever tolerate as a career!

Q2. ***Did you face many obstacles on achieving that [a scientific career], and what made you choose medical research?***

In hindsight, the obstacles were many and they were substantial, but in the course of developing a scientific career I hardly ever gave thought to the obstacles themselves. I only thought about what was interesting to me and what problems captivated my thinking. I did sometimes think about how fortunate I was that I could be paid to think about and investigate how the brain works – I thought that was amazing! And I did give thanks to whatever process it was that allowed me to have such a career. I choose medical research because very early on I became interested in the brain, how the brain controlled thought processes and behavior, and how the adaptive properties of the brain were what allowed organisms [mammals] to learn and change over time.

Q3. ***What came first, your interest in engineering or your interest in] biology?***

My interest in biology definitely came first. I have a deep interest in biological systems, and how those systems are structured hierarchically, i.e., how higher level functions (at the levels of systems and behaviors) depend on lower level functions (at the level of cellular and molecular mechanisms). Such a hierarchical organization of multiple, complex subsystems leads to dynamics that are difficult to understand and to quantify, particularly when those (sub) systems breakdown and become in need of treatment. It is when neurobiological systems require mathematical representation for better quantifiable prediction, and improved re-organization to provide for treatment, that engineering approaches become essential. Systems level analyses, particularly for the nonlinearities so characteristic of the nervous system, have become critically useful tools in understanding the nervous system and in leading toward next-generation treatments, such as neural prostheses.

Q4. ***How important is transdisciplinary/convergence science to your work and to all science generally?***

With respect to my own research into neural prostheses to correct for neurological disorders, interdisciplinary and convergent science is essential for developing the new breakthrough tools that will allow the integration of micro-electronic circuitry, biomedical modeling, and neurobiological circuitry. The essential components of the device-based treatments we are considering all involve bi-directional communication between the brain and biomimetic microelectronic models of the damaged brain regions we are attempting to repair. To accomplish this goal requires a coordinated effort between neuroscientists, biomedical engineers, materials scientists, electrical engineers, computer scientists, neurologists, and neurosurgeons, to identify just the major disciplines. Interdisciplinary work of this kind is becoming more typical as global scientific issues of greater social consequence are more frequently becoming the targets of scientific efforts.

Q5. ***What do you hope to achieve through your advisory work with the National Space Biomedical Research Institute (NSBRI)?***

The NSBRI is charged in part with developing and implementing medical technologies that can be used in outer space (and/or in low-earth orbit) to counter the physiological effects of low-gravity conditions. The conditions of use in space require that such technologies be operable by personnel with less than extensive medical training, occupy a minimal spatial footprint, utilize minimal power consumption, operate wirelessly with respect to home control and database components, and take advantage of the latest in "smart" analytical technology, i.e., store and evaluate individual data, recognize aberrant medical conditions, suggest treatment regimens, evaluate the course of conditions and/or treatments over time, communicate with expert systems, etc. Many of the conditions imposed by use in space are highly similar to those imposed by use as a neural prosthesis, i.e., low-power, small footprint, smart analytical technologies, etc. Thus, meeting the needs of smart medical technologies for the NSBRI requires designs that overlap substantially with those required to meet the needs of medical neural prostheses of the future, on earth or in space environments.

Q6. ***Cognitive impairment has become a huge health issue over the past decade or so. It is a complex disease with no cure [at present]. Was this the catalyst for [many of] your inspirations?***

Not directly. My interest in developing neural prostheses originated from a more general interest in brain-computer interfaces and bi-directional brain-computer communications. Neural prostheses are really just one example of this more general category of interactions between biological computing systems and silicon computing systems. In thinking about real-world applications, however, neurological disorders rapidly rise to the top in terms of motivating a continued and extended research focus. Nonetheless, bi-directional brain-computer interactions should be pursued in their most general sense to more completely explore generalized computing structures and generalized computing paradigms, and particularly to gain a better understanding of the fundamental differences between biological and non-biological computing systems.

Q7. ***Your work is truly innovative, what were the clues that you could transform memory into a code that could then be predicted using mathematics and retransmitted to help with long-term memory?***

The conceptual breakthrough that allows the vision for our cognitive neural prosthesis is that all brain functions, no matter how complicated, can be reduced to a system of multi-input, multi-output pulse-coded processors. In other words, all neurons transmit information in terms of all-or-none pulse codes, i.e., information is coded in terms of temporal patterns. Because all objects and events are represented by populations of neurons, information is coded in terms of spatio-temporal patterns. These principles apply to all sensory and motor modalities, and to feature-elements of all cognitive representations. By extension, all cognitive operations can be represented by linear and or nonlinear transformations of all spatio-temporal patterns. By reducing all neural computations to these fundamentals, there is the potential for treating all cognitive operations with a common set of mathematical operations.

Q8. ***You mention the team; how were you able to assemble the right parts of the team and did you face many obstacles to get the balance right? What are the essential elements?***

To achieve a cognitive prosthesis, assembling the correct team is fundamental to success and is remarkably difficult. Team members must come from disciplines spanning neuroscience, biomedical engineering, materials science, electrical engineering, computer science, neurology, and neurosurgery, among others Each member of the team must share two essential traits: they each must have a high level of expertise in their "home" discipline, and they also must be capable of "reaching across the divide" to other disciplines required to achieve a prosthesis. Each member must be able to push the envelope of their own discipline, and at the same time be capable of translating their own disciplinary fundamentals into a language that members of other disciplines can understand, so that the total team can find the maximum superset of disciplinary boundaries suitable for the best prosthesis solution. Finding team members with both of these two traits is difficult; finding team members with both of these two traits for all of the requisite disciplines is, of course, extraordinarily difficult. It is for this reason that our team now spans five different universities in the USA and Hong Kong.

Q9. ***People must have laughed at you for proposing that you could use [electrophysiological data recorded from] electrodes to predict memory [codes]. How did you ever convince people to support your research and did you yourself ever doubt it could be done?***

From the earliest moments in proposing a cognitive neural prosthesis, I can recall others responding that we were "crazy," and that we would never be able to reach our goal! It was very difficult to obtain funding initially, though we have maintained a steady, uninterrupted stream of substantial funding for nearly 20 years. The reasons for this funding success has been several-fold. First, I broke up the problem into stages, each stage of which could be justified as an individual problem with its own goals, in terms of its scientific and budgetary needs. The whole problem of a cognitive prosthesis could be discussed and presented as background, but all of the multiple stages and their integration did not require justification in total. Second, I sought funding from sources (e.g., DARPA) that traditionally provided support for projects that were high-risk/high-payoff, and that did not shy away from funding interdisciplinary projects that by definition included multiple investigators with in total, higher budgets.

Q10. ***At what stage are you with [developing a cognitive memory prosthesis for] humans?***

There are three essential stages to application of a hippocampal memory prosthesis in humans: 1) record the electrical activity of memory codes for short-term memory (inputs to the hippocampus) and for long-term memory (outputs from the hippocampus); 2) use these data to develop a mathematical model that allows the prediction of long-term memory codes from short-term memory codes; 3) electrical stimulation of outputs of hippocampus to generate a new long-term memory in epilepsy patients with chronically implanted electrodes. We can now complete stages 1 and 2; we are currently attempting stage 3, which will require an additional 1-2 years of testing.

Q11. ***What is the lifespan of the current technologies?***

The most important critical lifespan of the current technologies is that of electrodes for electrophysiological recording and stimulation. Current electrode technologies have a lifespan of only 1-3 years, whereas a prosthesis system lifespan must be on the order of 10 years minimum to be commercially viable. Thus, the "weakest link" in the current brain prosthesis design concerns electrode technology, and substantial progress needs to be made in this arena for cognitive prosthesis systems to emerge from research and development into commercial markets.

Q12. ***How important is it to be brave in science?***

Given answers to the above questions, particularly #9, I can only say "very important." And if your goal is to accomplish something extraordinary in science, then the answer is that you need to be "unrelentingly courageous."

Q13. ***Do you have perspectives, systems, or even a model of how governments should invest in health and medical research, or how this should be managed?***

An answer to this question would be too involved given the limited space and time allowed here. Let me say that, in my opinion, the current model of how the United States invests in health and medical research, and the infrastructure that it provides for the translation of what emerges as "successful research" to commercialization is seriously flawed, and needs to be grossly overhauled.

Q14. ***It's not an ideal world; funding systems favor safe science. How do we get a balance?***

Set aside a significant percentage of funding for "high risk, high payoff" proposals, with separate evaluation committees and evaluation criteria. Maintain zero overlap with evaluation and payoff pathways for "safe" science.

Q15. ***Do you actively recruit investment from industry or big pharma and if yes, what other skills are required to collaborate with industry and/or venture capitalists (philanthropists)?***

I have in the past and continue to in the present recruit investment from both the technology and the pharmaceutical industry. In total, there have been four startup companies spun off from my lab's research. To mention two of those cases, one of my lab's mathematical platforms for modeling glutamatergic (excitatory) and GABAergic (inhibitory) synaptic transmission has been licensed by a group of investors for drug development (the lead investor being a former VP for drug development from Novartis, Inc.). Called Rhenovia Pharma, the company was formed first in Europe and later expanded to the United States. A second company was just recently formed in the United States, and will be dedicated to the development and commercialization of the cognitive memory prosthesis. This startup is being funded by private foundations belonging to Elon Musk (SpaceX, Tesla Motors, PayPal) and Bryan Johnson (Braintree, OS Fund), and soon will be organized to respond to venture capital.

Q16. ***If you're setting up an incubator to foster young researchers what would that look like?***

To create a playground, with the best toys and best minds, unrestricted in terms of discipline, let's get artists, engineers, physicists, people from across the scientific spectrum and give them freedom to play. Where experts from all over the world from diverse cultural and scientific backgrounds come together, and at these points of intersection where innovation occurs, get them to solve the big health and other questions, creating a new 'renaissance' for science across the board. Where the ecosystem for research is stable; job security is high and career opportunities are abundant. Where the culture for curiosity driven research and 'risky' projects encouraged and the translational and licencing end of the research pipeline are well supported.

Q17. ***What advice would you give young investigators with ideas that are right of center?***

Backing oneself is important. For the sceptics and cynics, bring them along with you, engage them, tell them the story. It can take years to change people's minds. Academics are often very conservative and data that shows a paradigm shift or challenges conventional wisdom can take a long time to be accepted. Allow the data to tell the story. Many brilliant ideas have been laughed at initially. Don't give up.

Q18 ***If you had a working crystal ball, what do you think science might achieve for health by 2066?***

Where longevity and wellbeing is increased. Where access to healthcare more equitable and indigenous and marginalized people from all corners of the globe have improved health outcomes. That cures, treatments and management regimes for escalating major health issues such a complex and chronic disease are combated. Lifestyle related disease is prevented through better promotion of health and knowledge transfer. That by 2066 cancer and HIV is not a death sentence. That aging and degenerative disease are curbed with innovative treatments/devices and preventatives.