Combining Neurosciences and Engineering for Fun and Profit
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1 Salutations

It is a pleasure to have been invited to address you this evening. My thanks to Cathy Smith-Maxwell and Dave Yamane for the invitation. This is a special occasion for me because, for reasons that I will elaborate at the end of my address, it might be the last Society for Neurosciences Meeting that I will attend.

2 Topic

I am going to be a bit old fashioned tonight and speak without PowerPoint, because instead of speaking to you about products or science I am going to speak to you about my experiences combining neurosciences and engineering for fun and profit. My goal is to illustrate how, with a bit of luck and hard work, one's interests and passions can be directed to commercial success in the world of technology.

3 Negative Feedback

Like all stories, there has to be a beginning. Most beginnings are arbitrary, so let me start when I was a graduate electrical engineering student. How did I end up doing neurosciences research and making instruments commercially for neuroscientists? While looking for a Ph.D. topic I was fortunate to come across Steve Redman, a professor of electrical engineering at Monash University in my home town, Melbourne, Australia. Steve was studying motorneuron synaptic transmission in spinal cord. What particularly fascinated me about Steve's work was that it involved negative feedback in the motor control system. Negative feedback was a subject I had already studied extensively as an undergraduate electrical engineering student.

As most of you know, negative feedback is a system of continuous adjustment based on information fed back from the environment, and it is the basis of many of today's engineering achievements.

But it isn't new. In fact, negative feedback was first invented more than 2,000 years ago by the ancient Greeks to control their water clocks, then it was re-invented 200 years ago by James Watt to control the speed of his steam engines. Today, negative feedback is essential to the operation of many systems we take for granted: in hi fi audio systems negative feedback eliminates distortion; in manufacturing plants negative feedback allows industrial robots to pick up parts first time and every time.

4 Inspiration

The remarkable thing I learned from Steve Redman was that negative feedback is prevalent in nature! Just like a robot picking up a part, you couldn't catch a basketball without negative feedback from your visual system to guide your muscle control.

What amazed me was that nature uses the same methods to control its creations as we engineers use routinely to control our sophisticated machines. But we didn't copy nature. We didn't even know about negative feedback in nature. James Watt and nature converged on the same solution; in the first case in a moment of insight, in the second case by billions of years of evolution. I was in awe of what engineers had achieved and I was inspired to pursue a career that combined neurosciences and electronics. Lesson learned? Follow your passion.

5 Postdoc

So during my Ph.D. I dabbled in both neurosciences and electronics, and after a while I discovered that I was a better engineer than I was a scientist. Both disciplines require talent, but different kinds of talent. I was good at designing. When I designed electronic circuits I was in charge of my own destiny. If the result wasn't what I hoped for I could refine it and make it better. But when I ran an experiment I was always frustrated by results that had a mind of their own. I didn't have the special ability of a great scientist to recognize the subtle patterns hiding in the data; to me it seemed like my destiny was in somebody else's hands.

I decided that I wanted to get out of research but I didn't know what to do instead. Playing it safe I accepted a postdoctoral research fellowship offered to me at the Australian National University in Canberra. There I concentrated on designing new research equipment, participating in experiments primarily for the thrill of seeing my creations in use. My efforts were appreciated by my colleagues because they knew very well that most scientific advances depend on breakthroughs in instrumentation.

Nearly every day I joined my colleagues in experiments, then at night I designed changes to accommodate what we learned during the day. Lesson learned? My experience then and later taught me that in the world of engineering, everything is possible, all that one needs is to believe in one's own ability to create a new design that is simpler, more elegant, more reliable and faster, all the while having fun in the endeavor.

6 Ticket Out

I was still committed to leaving research. But how could I reconcile my interests and my training? The defining moment for me was when Paul Adams from the State University of New York visited our labs in Canberra in 1981 and asked a question that changed my career. Looking at my hand-built voltage clamp he asked, "Wow, can I buy one of those?"

That was it, my ticket out. I could capitalize on my investment in neuroscience by doing what I loved best: designing electronic instruments for other neuroscientists.

Lesson learned? Do what you're good at. If you are about to start a business, build the business on something you enjoy and do well. And start it with a clear idea of what your first product will be.

7 To San Francisco

I left the university and started Axon Instruments in San Francisco, literally as a one man business, using $100,000 given to me by my family to cover living expenses and the establishment of the company.

I was fortunate that my Australian colleagues, David Hirst and Steve Redman, sent word to their colleagues in the United States that I was coming, inventions in tow. My first product was the Axoclamp single electrode voltage clamp. It was more powerful and more capable than anything else on the market, but it was also more expensive. Nevertheless, scientists bought it and loved it. Lesson learned? Make a good product and your reputation will be assured and sales will follow. Or as my stepfather often said, "Quality is remembered long after price is forgotten."

8 Financial Nadir

That first year, 1983, was tough. My $100,000 startup equity went down, down, down till by the time it reached $20,000 I was starting to seriously worry. So I worked harder and faster, and suddenly the revenue from my first sale came in and the account balance started to be restored. In fact, we were profitable in the first year and nearly every year since. The lesson learned in this case was straight out of the Hitchhiker's Guide to the Galaxy: Don't Panic! Perseverance is rewarded.

9 Back to Melbourne

Axon grew. After five years, we employed fifteen people and sales were strong but my wife and I decided to return to Melbourne, Australia, for family reasons. This was the start of my life as a trans-Pacific commuter. I have now been traveling back and forth to the U.S. from my home in Melbourne about ten times a year for 18 years. I think of myself as the world's longest distance commuter, and I have the frequent flyer points to prove it.

Coming back to live in Melbourne meant that I had to manage the business in San Francisco remotely. This was one of the toughest and most enduring challenges for me personally and for the company. We were certainly successful and grew tenfold in the ensuing years, but collaborating with colleagues by email, by telephone and by courier pack doesn't come close to working under the same roof. The efficiency and synergies that come from corridor discussions and round table meetings cannot be approached by electronic communication. Nevertheless, by accepting that what we had was the best we were going to get we managed to make steady progress. Lesson learned? Don't let challenging circumstances turn into frustrations that will further undermine the chances of success.

10 Axopatch 200B

The first product we made after I returned to Melbourne became known as the Axopatch 200, a defining product in the success of Axon Instruments. Designed by Richard Lobdill with advice by Rick Levis and Jim Rae, the Axopatch 200B is well recognized as the most sensitive amplifier in the known universe. For more than ten years it has reigned supreme, measuring single-channel currents better than any competing amplifier, whether made by another company or constructed in a university lab. It operates at the limits of semiconductor device theory. How did we achieve this? What was the lesson learned? My own contribution to the Axopatch 200 series was small, but I claim lots of credit because I employed engineers who knew no bounds, advised by excellent consulting scientists, and together we exhibited absolute perseverance and commitment to perfection.

11 GenePix

By the mid 1990's Axon dominated the worldwide market for electrophysiology research equipment, achieving a 60% share in a mature market. This meant there was no way to ever double our sales. That was bad. Frankly, if there is no prospect to double sales there is no reason to be in business. So we needed to expand our markets.

To help us evaluate our opportunities in this field we established a dedicated task force to identify products that could take advantage of our imaging and data acquisition technologies. We met regularly and we brought in experts such as Stephen Smith from nearby Stanford University. The task force worked like a charm, leading to the identification of an opportunity to make a laser scanner for DNA microarrays. We decided to make the development of this DNA microarray scanner our number one priority. With a clever engineer named Yuri Osipchuk leading the

development, we iterated through three different design concepts and in approximately one and a half years we were shipping our first GenePix microarray scanners.

This expansion brought us international recognition in the rapidly emerging genomics field and to this day we are still the largest supplier worldwide of DNA microarray scanners. Lesson learned? Believe that there is always something better to be achieved and bring bright people together to work on fulfilling that belief.

12 Loss in 2002

In 2002 we underwent a unique experience in Axon's 21 year history—we made our one and only loss. In that year we over-invested to expand our genomics products, but the market did not grow as we assumed it would. We hadn't simply guessed at the market growth. Instead, we purchased a number of expensive market research reports to guide us. But they were all wrong! Lesson learned? You cannot rely on market research reports. It is difficult for market research companies to sell their reports for $5,000 each if the reports don't paint an optimistic picture. Who will buy a pessimistic report? More important, relying on a market research report distances you from the customer. What I used to know, forgot for a moment, and have learned again is that the best way to understand what customers need is to talk to them face to face. A face to face dialog with a small number of representative customers is far more important than the summary report from an impersonal survey of a thousand customers.

13 PatchXpress

Fortunately, 2002 was our only bad year and after some heart wrenching restructuring we recovered and returned to profitability.

In the meantime, we were working on a device that for the first time would automate gigaseal planar patch clamping. We knew that if we could make an automated version of the patch clamp we would be able to deliver the holy grail of test instruments for the development of nervous system drugs. Pursuing this was a big deal for us. We had a lot riding on it. Our machine, called the PatchXpress, was being developed by a wonderful team of creative engineers and applications scientists but it was incredibly complex and the pieces were refusing to come together as a functioning whole. Eventually, my friend and fellow Board member Henry Lester, called me in Melbourne and said, "Alan, do you want to continue with your current schedule or are you prepared to spend the next six months away from your family to steer the company to a new era by helping the PatchXpress project?" Henry's logic was unassailable, so for the next nine months I increased my travel schedule and assumed the role of systems analyst for the PatchXpress project. In this role I coordinated every technical aspect of this complex project and found it to be more thrilling than anything I had done during the prior ten years. Better than that, the PatchXpress opened up a whole new market for us, one in which the technology we had developed for academic research could be applied at an industrial scale to drug discovery. Lesson learned? Sometimes CEOs have to get their hands dirty.

14 Acquired

By the time we released the PatchXpress, our corporate profile was soaring and we started to be of interest to potential acquirers. Which was good, because I have to tell you that after twenty years as the CEO I was tired of the job. Everybody deserves a break but CEOs don't get breaks. It is a full time worry job. I needed a change and the company needed a change. The two options I had were to bring in a new CEO or to sell the company. The Board of Directors and I explored both, and acquisition came to our doorstep first.

15 Population Patch Clamp

Life changed dramatically for me on July the first last year, the day Axon was officially acquired by Molecular Devices and I changed from being the CEO of Axon to being the Chief Technology Officer of the combined firm. This gave given me the opportunity to concentrate on projects in a way that I never could before. For example, after Axon's acquisition was assured I was able to relax and sit in the audience at a Molecular Devices users' conference at the beautiful Claremont Hotel in Berkeley. This was the first time I sat still at a conference for twenty years. The end result was that I thought of something new, the population patch clamp, an important improvement that takes whole cell patch clamp for screening applications to a new height of efficiency. The population patch clamp became the basis of the IonWorks Quattro that we released this year, allowing pharmaceutical companies to screen compounds at higher quality, and faster and cheaper than ever before. Conventional wisdom is that when it comes to faster, cheaper and better you can have any two, but not all three. Well, we delivered on all three. I could never, ever have had the insight that led to this invention if I had still been the CEO. Lesson learned? That you need balance in your professional life. You need to balance the demanding, short-term, daily responsibilities with intervals for long-term thinking in a stimulating environment.

16 People

What else have I learned on my journey? Above all, success depends on people. Our employees worked hard, intelligently and selflessly. When I sold Axon, employees cried, because they felt like teenagers leaving the security of their family home. Lesson learned? Invest in the wellbeing of your employees and they will repay that investment with loyalty and hard work.

17 Change

One of the hallmarks of being a design engineer is being comfortable with change. I've enjoyed the changes in my life since we were acquired and I'm looking forward to more changes. At the end of this year I will retire from Molecular Devices and I will start the next stage of my life. At this moment, I don't know what I will be doing, but my goal is to operate in areas that fundamentally interest me, such as science, technology and education.

18 Neurosciences Course

In the education area, I recently had the opportunity to play a key role in the establishment of an advanced neuroscience course in Australia that introduces young scientists to the latest and greatest research techniques in international neuroscience. Similar to the summer courses at Woods Hole and Cold Spring Harbor, and sometimes referred to as "Woods Hole Down Under", this Australian course was held on a beautiful, almost tropical island off the coast of Queensland. The instructors and students worked extremely hard for six days and nights each week for three weeks, but they also had time to explore sandy beaches and crystal-clear inland lakes. It is hard to think of a better way to convey to those students the lesson that hard work and science can be fun.

19 Grab Bag

There are lots of other lessons learned in starting and then running a company for 25 years, but I do not have time to give examples. Without elaboration, these include the need to always be enthusiastic, to believe in your own products, to respect your customers, to respect your colleagues, to fix every problem when it occurs, and to give the engineers and scientists in the company a vision then let them turn their heads loose.

20 Defining Moment

Two months from now when I retire I will be facing a defining moment in my life. Hopefully I will be able to utilize my experience gained over the last twenty five years and apply the lessons learned to new endeavors. Above all, I will be looking for opportunities that combine fun and profit, for what I have learned more than anything else over the years is that both are equally important and contrary to the belief of many they are not mutually exclusive.