Biographical Sketch Bob ('Robert S.') Eisenberg

I have been interested in how physical things work as long as I can remember, and in how living things work nearly as long, from the day my father (a physician and then psychiatrist) showed me that was the best way to mold my interests to his approval.

Accidents have been kind to me: Sputnik came as I was in High School, so science became an easier career. I met John Pappenheimer (a Physiology Professor at Harvard) when I was asked to help interview him on a television show when I was 15 or 16 years old. He insisted I take a Medical School course on the physiology of channels (as we now call them) in my first semester at Harvard College, when I was just 17 and then introduced me to Steve Kuffler. I worked in Steve's Nerve Muscle Program at Woods Hole for two summers. Harvard assigned me John Edsall as a tutor, who did in fact tutor me, biweekly at first and then (nearly) weekly, nominally in biology, but really in the wisdom of science. (John Edsall was born the son of a Dean of Harvard Medical School, became a biophysical chemist, and was a fulcrum for the pivotal change from macroscopic to molecular biology at Harvard and elsewhere, training Bruce Alberts, David Eisenberg, and Jared Diamond among many other distinguished scientists.) My course work was in physics, chemistry, applied mathematics, and electrical engineering, but, if my memory serves me correctly, not in biology at all. (I actually love evolutionary and descriptive biology as I love collecting classical CD's but those loves are hobbies more than anything else.) My undergraduate thesis solved the cable equation of physiology (the transmission line equations of engineering) with a Green's function, reproducing in an elegant but useless way what I had learned from Morse & Feshbach about heat equations.

Young in many ways, I was eager to 'get to work', and left Harvard a year before I should have, to do experimental work in biophysics and physiology at University College London, where my department chairman Bernard Katz was to win the Nobel Prize a few years later. Fortunately, Andrew Huxley (Chair of Physiology at UCL, winner of the Nobel Prize with Alan Hodgkin in 1964 a year or two before Bernard Katz, if I remember correctly) had solved the cable equations the way I had, but much earlier and much more originally and insightfully, and so was happy to spend many hours teaching me, on the side, as if he didn't have enough else to do. Thus started a long string of interactions continuing to this day. My thesis supervisor Paul Fatt asked Alan Hodgkin to be my external examiner, and that nurtured a relationship that had started in The Mess (Dining Hall) at the MBL, Woods, in 1961, where and when I also met Clay and Clara Armstrong. Alan Hodgkin guided me—more than he ever knew, more by passive example than active guidance—for many years.

My experimental work measured the spread of current in crab muscle fibers over a range of frequencies, using impedance spectroscopy, as it is now rather pretentiously named. I was one of those students who was given an empty lab, to be filled with equipment however I could, by personal construction, borrowing, and even purchasing in small measure. Of course, I had to heat the space first, it being in England in the winter of 1962-3 still in post-war poverty (from an American's perspective). Doing these measurements taught me respect for stray capacitances; analyzing these measurements taught me respect for computers (the calculations were done by hand); interpreting these measurements taught me how to solve partial differential equations (or rather how to use other people's solutions, Carslaw & Jaeger's in particular).

I will not bore you with the many decades of experimental work I did analyzing the flow of current in muscle fibers and then the lens of the eye: the work included much traditional biophysics, and even some anatomy, as we learned to describe and then measure the structures seen in the electron microscope (using statistical sampling to avoid the labor and systematic errors of tracing profiles). The experiments also included measurements of flux of radioactive isotopes from single muscle fibers (around 50 μm in diameter) too dangerous to describe without cringing in our present more enlightened (and safer) world.

Accidents came to my rescue again, while I struggled to understand my impedance measurements. As I was walking down the long corridor one day at UCLA, Jared Diamond asked me into his office to meet Victor Barcilon, an applied mathematician who became quite interested in our problems, along with his friend Julian Cole, one of the founders of singular perturbation theory. Thus fertilized, my interests in physics and mathematics took a more professional turn and we wrote several papers showing how the systematic approximations of singular perturbation theory can lead directly to biological and physical insight.

I became a Department Chairman at Rush Medical College in Chicago in 1976: the temptation of an Endowed Chair was enough to make a 34 year old move from the perpetual spring of Brentwood (LA) to the recurrent vagaries of midwestern weather. Fortunately, the Medical School did not give me too much to do, and my faculty proved highly supportive and successful, so I have been able to continue spending nearly all my time trying to do science, as I did before I was a Chairman.

That is, I have spent my time struggling to understand nature, except when I was Chairman of the Physiology Study Section at the NIH, which provided a substantial fraction of the funding for physiology. While trapped in those duties, I watched enviously as my colleagues measured the current through single protein molecules. I could help as an administrator (at home, and at the NIH), and as an engineer, by helping to design the picoammeter (named the Axopatch) now used by most workers in the field, but I could not myself make the measurements that were so much fun to do.

When I finished at the NIH, I wanted to do something new, not as thoroughly descriptive, so I started thinking about the theoretical problem of describing ion movement through the water filled tunnels of charge we call ionic channels. Working with many gifted physical colleagues, and my close friends Duan Chen, Victor Barcilon, and Zeev Schuss, we derived and solved the nonlinearly coupled equations of electrodiffusion and electrostatics, only to learn that they had been thoroughly explored previously by workers in the computational electronics of the properties of semiconductors and semiconductor devices. Fortunately, we seem to have derived and solved them correctly. Unfortunately, we took years doing it.

The ionic channel is where we still are; but gazing through this narrow hole has proven to be rather like looking through a keyhole in a door. The closer you get to it, the further you can see, even glimpsing the horizon (of knowledge) occasionally, even seeing a star or two, when all else seems dark.

It turns out that studying ionic channels requires modeling nonequilibrium systems, dominated by electrostatics (because the charge density of the channel is so large), involving the theory of concentrated ionic solutions (because the finite volume of ions is such a large fraction of the volume of the pore of the channel.) While studying channels, we necessarily glimpse the horizon of knowledge in physical chemistry and computational electronics. We necessarily must go beyond the description of rates and states to the understanding of physical theories.

The issues raised in these theories will keep me busy for the rest of my career, I suspect; they certainly will not be solved quickly and completely, because they require prediction of long lived macroscopic phenomena arising and controlled by systems of atomic dimension. The questions are what part of the atomic detail is needed to explain biological phenomena; and what part of the atomic detail can be safely averaged; and how should that averaging be done.

Keeping me busy will be keeping me happy. The task itself is endlessly rewarding. It also can only be done with the help of bright, energetic colleagues, who know physical chemistry, computational electronics, applied mathematics, and biophysics. I will always have more to learn from the world and from them and that will always be fun (I hope and trust).