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INTERVIEW
Neuroethologist Ron Hoy on College, Careers, and Crawdads

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In April 2006, at the Symposium for Young Neuroscientists & Professors of the Southeast (SYNAPSE), I had the honor of sitting down for breakfast with Dr. Ron Hoy, the David and Dorothy Merksamer Professor of Biology at Cornell University. In addition to receiving grants from the National Institute of Mental Health and the National Science Foundation, Dr. Hoy has been supported by the National Institute on Deafness and Other Communication Disorders (NIDCD) for 30 years. Dr. Hoy, who received the prestigious designation of Howard Hughes Medical Institute (HHMI) Professor in 2002 for his dedication to undergraduate science education, was intelligent and articulate, but perhaps what struck me most about him was his flexibility and excitement about following his curiosity to valuable discoveries.

JR: How did your career evolve, and what led you to neuroscience?

RH: Neither of my parents finished high school, and they wanted their kids to all go to college. I was the first member of my immediate family to go to college. My family had a business, a restaurant, and that's where I worked from when I was a little kid all the way up to getting into college. I liked chemistry sets, and I liked running around in the fields, because I grew up in the fields of southeastern Washington. I used to collect bugs and put them in jars, and I raised tropical fish on my own—this was all before I got to high school. In high school, I got to take science courses, which I really liked.

I went to Whitman College, which is a small liberal arts college in my hometown. This made my parents happy because I could live at home and we would save a bundle of money! I was a commuter student; I walked to college because it was three blocks away, so I really didn't get to know my classmates except in the context of classes. But I found a couple of wonderful professors at this liberal arts college. One was a psychology professor, one was a mathematics professor, and one was a professor in philosophy, and they were wonderful role models. I began to think teaching at a college seemed like a pretty cool thing to do. For one thing, you didn't have to teach every single day! I used to talk to my professors a lot after class, which is one of the things I really like about liberal arts colleges—the very relaxed pace.

The psychology class was particularly interesting because there I learned about the physiological correlates of behavior and that really resonated with me. But since I didn't have a social life at home, I transferred to Washington State, and there I really got caught by the science bug. I majored in chemistry for one year, but then I found that I really liked philosophy and changed my major to philosophy for one semester. After that, I decided to swap back, this time to psychology, and I stayed in psychology for a year. But then I really caught the bug in my senior year zoology courses! One was *Zoophysiology,* now called *Animal Physiology*, and the other was *Cell Biology* or *Cell Physiology*. They really got me into science. By this time, I really didn't have enough credits to major in any one subject. I was fortunate enough to get an NSF summer internship, so I spent my junior and senior year at NSF working in the lab of a membrane physiologist named Leonard Kirschner. Kirschner was a wonderful and generous man; he had graduate students in his lab, but he had a lot of undergraduates too, and I was one of those. I guess I'm an NSF science baby. I managed to eventually finish my degree; I had to go a fifth year to complete my credits, but I didn't mind, because I worked in the lab. I applied to several graduate schools. I knew I wanted to go to California, so I applied to Berkeley. My girlfriend was applying to Stanford, so I applied there and to the University of Washington, which is where my professor wanted me to go.

I got into all three, but ended up going to Stanford because the author of one of our textbooks was a professor there, and I loved the textbook. I went there and met a wonderful group of students. We formed a cohort all the way through our five years. I started out in developmental biology, working on the development of the mouse pancreas, but I developed an allergy—probably psychological—to mice. Socially, I started hanging out with people from Don Kennedy's lab, and took the neurophysiology course. I really liked neurophysiology, so as was my wont, I switched labs late in my third year to Don Kennedy's lab. The sociology of a lab has always been very important to me: the personality of the people, the lab culture. My developmental biology lab was very much regimented and hierarchical. There was the head professor and then there were his lab technicians who ran the lab, postdocs, and then the lowly peons, graduate students. It was very formal, whereas Don's lab was very informal. We'd meet every week and just talk at some coffeehouse or a bar. I liked the much freer exchange of information and the camaraderie.

I ended up doing my Ph.D. on crayfish. At that time in neurobiology, model systems were *just* coming into being, and people were looking broadly across the animal kingdom for good models for the biological understanding of behavior. Stanford has a marine biology station associated with it called Hopkins Marine Station, and I spent a summer there taking classes, and looking around at the various systems. I settled on crayfish because a lot was known about its nervous system. It has relatively few neurons compared to a vertebrate, and especially compared to humans.

In the summer of my third year, I went to Woods Hole for a Grass Fellowship. I worked independently on a project: regeneration in lobsters. I decided to do a postdoc. The regeneration project was great, but I wanted to do more behavior. My friend David Bentley who was a postdoc down the hall from me at Stanford said, "Why don't you join me and we can work on auditory behavior?" That sounded interesting to me, so I worked in his lab for a few years and learned about communication biology and neuroethology. I liked it so much that that's what I stuck to.

JR: We typically use model organisms because they are easy to work with, easy to care for, well-characterized, and abundant, among other reasons. Why do you advocate for the study of non-traditional systems?

RH: I'm advocating for non-traditional model systems partly as a research strategy. First of all, animals solve all kinds of problems in locomotion, in detecting different kinds of sensory energy—for example, in vision, some animals are sensitive to ultraviolet light, other animals can sense polarized light. It's curiosity-driven research, and it's just wanting to know, "How does that work?" So you tinker. Another reason is that there's another branch of biomedical science which is of great interest to the biomedical engineers, and it's a strategy called biomimicry. Biomimicry means you want to solve engineering problems or problems that are relevant to humans, but you look to nature to inspire the result. Velcro is an example of biomimicry; the man who developed it was a hiker, an engineer, and a Swiss citizen who hiked in the Alps. He noticed that birds kept getting stuck on his wool lederhosen. He said, "That's really tight, really adherent; I wonder why." The answer to his question was informed by his knowledge of mechanical engineering. At a micro scale there were little hooks, and the weave of his lederhosen was comprised of loops. At a small enough scale, if you have a high density of hooks and loops, you could form a really tight bond. Thus was born the idea of Velcro. There are lots of other examples of inventions for which animals served as the model. You have to have a knowledge base; you have to be interested in a particular problem to be aware that there's an interesting solution there.

One of my friends at Berkeley, Robert J. Full, is interested in animal locomotion, and they are looking at a reptile called a gecko and wondering how they stick to ceilings and walls. He and his colleagues, again working with engineers, discovered that the foot pads of geckoes break down into finer and finer webs of hairs, which you can only see at electron microscopic scale.

It turns out that the very tips of the outermost hairs are forming molecular forces called van der Waals forces with the surface. And there is enough surface area from the continued branching and reticulation of the hairs that this holds the animal up. Now Bob and his colleagues have a patent out to make cements that are not adhesive, not based on a glue. A combination of engineering and biology have turned up something really interesting. Well, geckoes are non-traditional models.

Right now in research universities, research is driven by whether you can get a grant. And you have a step up if you're working on one of the four model systems. While they're wonderful model systems—I dearly love them, and I worked on two of them myself at one time or another—I think that that will shape the directions of careers, and it will give neuroscience tunnel vision. I think that overemphasis on biomedical models is unfortunate because we're closing ourselves off to other opportunities. You are looking at the world through the eyes of four model systems, when in fact there is a multitude of ways in which other animals have solved very interesting problems.

I think liberal arts colleges will be the reservoir where non-traditional models can prosper because your career is not contingent on the ability to get a NIH grant or a biomedical grant, and students can be free to follow their curiosity. If you're in a lab that is under grant contract, you have to work on what that grant entails. It is an opportunity lost.

JR: What projects are going on in your lab currently?

RH: Because of the HHMI, I started a *Drosophila* lab of my own. We are just beginning work on behavioral mutants in *Drosophila*. We are working on neural excitability, and working with various phenotypes. One thing that we are looking at is the effects of stress on the flies, and the relationship between the amount of stress a fruitfly is subjected to and its lifespan. We have different lines of flies that have different mutations affecting neural excitability and the ability to handle stress, and we relate that to lifespan. And if we can find double mutants, we ask if having the double mutation restores a normal lifespan, or if, in fact, it makes it worse. The students seem to be very interested in this project, and it is turning out to be a very tractable thing. That's going to feed not only into research that we're doing, but it will be a teaching module within FRUITFLY. Everything that I'm trying to do with *Drosophila* is a “two-for.” Number one, it has to result in a teaching exercise, but number two, if it results in research too, that’s good.

The other thing we’re working on is continuing our exploration of insect ears and insect hearing. We’re expanding that, and bottom line, we are looking at the smallest animals that I know of that have a sense of hearing, and I’m asking, how small can an ear be and still function as an ear?

JR: You are very concerned with the quality of undergraduate education in neuroscience; it’s one of your passions. What do you feel are the key components of successful undergraduate neuroscience programs?

RH: I think the most important element of undergraduate neuroscience today is a good background in basic chemistry, physics, and mathematics. I know people have been saying this for a long time, but now it’s really essential. My concern is that today’s neuroscience students are not getting quite enough math to be able to communicate with the mathematicians.

Neuroscience in the future is not going to require that biologists be able to solve the complex equations of Fourier analysis or gain of velocity transforms, but I do think they need to know about Fourier analysis and transforms so that they can communicate. In other words, I think it’s important that biologists have mathematic function sense. They may not be great at solving problems involving functions, but they need to understand how those functions behave at various scales, and what happens when functions go discontinuous or non-linear, because much of biology is about that. And you don’t have to be an expert mathematician to get function sense. You don’t need to be as good at solving problems as a mathematician to understand the functions that seem to govern nature, including biology. But right now, that is not the way mathematics is taught. Mathematics is taught in terms of achieving mastery, and that mastery is defined by how well you solved the problem. The assumption is that if you can’t solve the problem, you just don’t understand the whole process. To me that’s just plain wrong. I believe that you can have a deep understanding, or at least a reasonable understanding, of how functions work, and of how variables change in nature, as other variables change.

If a course could be invented in which students build a certain intuition about mathematics, even the complex functions of mathematics, so they can set up a problem but not necessarily drive it to its solution, many biologists would get over the math phobia. And, of course, all of this has to be taught in the context of meaningful problems. Genomics and computational biology provide plenty of context to take on problems.

JR: What is CRAWDAD, and how does it fit in with your ideas on neuroscience education?

RH: CRAWDAD grows out of my Ph.D. thesis on crayfish. I was a TA when I was a graduate student, and I really liked teaching. I always thought that you could teach a whole neurophysiology course on the motor and sensory systems of the crayfish. So when I actually did get a job, I did such a lab and it worked! The students really liked it. It doesn’t matter whether you’re working with the sciatic nerve of a frog, or hippocampal slices, or neurons from a crayfish or a leech—if you see an action potential on the oscilloscope, you can’t tell me where in the animal kingdom that action potential came from... the same ions are moving, the same molecular machinery generates a spike. They are very similar, sometimes even in quantitative detail. That’s also true for networks; the interactions within the network of a crayfish involve the same synaptic arithmetic, if you will, as in our neural networks—it’s excitation, inhibition, and neuromodulation, adjusting the gain of excitation and inhibition. The same sorts of actions take place at the communication port between two neurons, which is the synapse. I use that as justification for saying that you can use crayfish to teach principles of neurophysiology all the way from high school classes to medical school classes, because principles are very similar.

Given that spark of an idea when I was a graduate student, I was determined to bring the crayfish into teaching labs, although it took an awfully long time for me to do it. I taught it on my own at Cornell and at Woods Hole. But not until the mid-1990s did I decide that I wanted to work this up on a broader scale, to make video. I applied to NSF and we got a wonderful rating. They made me feel as good as any paper I’ve ever written. I put together a wonderful team of colleagues, Bob Wyttenbach and Bruce Johnson, which helped me realize my dream. The idea was to put together 12 modules, 12 afternoons of neurophysiology using invertebrate models. We expanded beyond crayfish to include some snail nervous systems and then one plant that generates action potentials. The most important thing about CRAWDAD was that we held three workshops for 12 teachers each—the teachers were neurophysiology or psychobiology teachers from all over the country, and they came to Cornell for one week where we worked intensively on showing each of them each of the labs. Then they wrote their *own* NSF grants to replicate the experience, and many of them were successful, so we managed to take advantage of the multiplier principle. That was one of my most satisfying teaching experiences—to teach teachers—what a blast! Even though I’ll never know their students, to realize that through the eyes and hands and minds of these teachers we’re going to extend our reach is extremely satisfying.

We found a wonderful publisher, Andy Sinauer. It is used now in Germany, England, New Zealand, Australia, and Asia. Of course, it’s being used to supplement most labs. Nobody’s crazy enough to want to do a whole semester’s course on crayfish! But it’s doing well. I’m grateful again to NSF for their program in undergraduate education to sponsor this.

JR: You are one of only 20 Howard Hughes Medical Institute Professors in the country, an honor awarded to innovative leading scientists invested in undergraduate education. What plans do you have for that award?

RH: One of them is a direct outgrowth of CRAWDAD, and it is called FRUITFLY. We are planning a series of teaching modules for laboratories that would be based on *Drosophila*, one of the four canonical models. Everybody takes a genetics lab, or should, and in almost every one of those labs, you deal with fruitflies. The phenotype is always eye color, whether it's got wings or not, whether its body is dark or light, the morphology of the wings (whether they're frizzy, stubbled, short, or forked), whether the antennae are absent or missing, *et cetera*. None of those labs feature behavior as a phenotype, which I think is an opportunity missed. The behavioral mutants, of which there are hundreds, if not thousands by now, can be studied in the laboratories. One of my goals with the Hughes is to bring behavior to the genetics laboratory through *Drosophila*. Then students can understand that not only structure, which is an anatomical phenotype, but function, which would be behavior, can be studied there. For instance, epilepsy can be modeled in the fruitfly because there are flies that have seizures under certain conditions.

JR: Your plans sound so exciting! Dr. Hoy, on behalf of *JUNE* readers, I thank you for taking the time to give us a glimpse of your professional development and work as a neurobiologist. I hope that all educators are inspired by your dedication to undergraduate science and your commitment to follow interesting and uncharted leads in the lab!