Q & A

John McCutcheon

John McCutcheon is an Associate Professor of Biology at the University of Montana in Missoula. He is interested in how symbioses form, are maintained, and sometimes break down. He and his collaborators mostly use insects that host intracellular microorganisms as model systems.

What turned you on to science in the first place? I did not have an innate interest in science as a kid. I was mostly interested in soccer, bikes, skateboards, and generally messing around in the neighborhood. I liked sports.

But my dad is an enthusiastic science and technology nerd, and so we always had ‘sciency’ things around the house: copies of *Scientific American*, encyclopaedias (translation for younger readers: encyclopaedias are like a tiny old internet but printed in dozens of volumes), and the latest Texas Instruments and Apple computers. I liked these things and did a bit of programming but never really took any of it very far. The first time that I can remember being drawn to science in any sustained way was in my senior year during high school. I had a terrific teacher who really sparked my interest in chemistry. I can distinctly remember thinking that the ideal gas law was so cool — it explained so much!

So I started my undergraduate studies as a chemistry major, based almost exclusively on thinking that $PV = nRT$ was interesting. My first friends in college were a group of second-year chemistry and physics undergraduates who were fun but also really serious students. We went to study in the library together and I was shocked to see them working on problem sets for hours. Two hours! *Four* hours! I couldn’t believe it. Somehow, I had never imagined that people would work this hard at learning things. But I also don’t think that I would have made it through college without the study skills that I learned from these four people.

So why aren’t you a chemist? For the first two years of college, I took lots of chemistry classes (somehow, I didn’t have any biology classes), but it was an organic chemistry lab course that began to sour me a bit on the subject. I didn’t find mixing various foul-smelling, explosive, corrosive, and acidic solutions together to generate various white powders particularly interesting, so when the time came to find a summer job between sophomore and junior year I looked for a research job that didn’t involve chemistry. Somehow, I ended up working as a field tech for a lab that studied the effects of biological control agents against various potato pests. Really what this meant was that I was driven around Wisconsin in a station wagon to farm potatoes in very peculiar ways. But it was a good summer because I earned some much-needed money as well as had some time to read and think about what I should do if I weren’t going to be a chemistry major.

What did you decide? That summer, in the back of the wagon, I read *The Lives of a Cell* by Lewis Thomas. I don’t know from where this book came. Did I buy it? Was it a gift from my dad? I have no idea, but I *loved* it. I read it twice. It was probably the first time in my life that I had thought seriously about biology. It was also probably the first time that I had read anything even remotely ‘literary’ on purpose.

In answering this question, I went back and reread *The Lives of a Cell* to see if I could figure out why it excited the 19-year-old version of me. It’s beautifully written, yes. It’s entertaining, even hilarious in places. It clearly conveys Thomas’s sense of wonder about biology. I still love it. But what shocked the 45-year-old version of me was how Thomas obsessed over the things that I now study in my own lab. In the very first chapter, on the second page, Thomas mentions mitochondria, chloroplasts, and symbiosis. In the second chapter, he writes:

> “The bacteria that live in the tissues of insects, like those incorporated into the mycetocytes of cockroaches and termites, have the appearance of specialized organs in their hosts. It is not yet clear what they accomplish for the insect, but it is known that the species cannot survive long without them. They are transmitted, like mitochondria, from generation to generation of eggs.”

Reading this again, I just about fell out of my chair. *The great scientist–philosopher–poet Lewis Thomas knew that insect symbiosis was cool*. I am not trying to say that reading this book in 1994 magically imprinted its ideas deep in my brain and that it inevitably destined me to study insect endosymbiosis with an eye on mitochondria. I am just saying that Thomas clearly had good taste in science.

So Lewis Thomas made you a biologist? Eventually, yes, I suppose, but it took a long time. Since it wasn’t until the summer before my junior year that I read *The Lives of a Cell*, I was a bit too far along the chemistry path to switch to biology without adding another year of college. So I came up with a compromise: I would be a *bio*chemistry major. I signed up for the first semester of biochemistry for majors and by about two weeks in I was completely hooked. It was chemistry but with a purpose. I loved the Krebs cycle. I loved the chemiosmotic theory. I loved lipid biochemistry.

But even at this point, starting my third year in college, I didn’t know what people actually *did* with college degrees. I knew that Lewis Thomas had been a medical doctor, so I thought this might be good. I signed up to volunteer in a hospital emergency room because this is what people told me premeds are supposed to do. In my case, 'volunteer' meant stand in the corner and be terrified for four hours. Injured and sick people seemed to be coming and going in a chaotic and relentless steady state. On the walk home that night, I decided that medical school was not for me (and that ER nurses and doctors are saints).

I was complaining to my roommate about my problem of not wanting to be a potato farmer but also not wanting to be a doctor, and he said, "why don't you work in a lab?" *Wait, what? I could work in a lab?* This somehow had never occurred to me. I suppose that I just had no concept of what chemists or biochemists actually did, what research really meant, or that there were approximately 15,000 labs to choose from at the University of Wisconsin.

I ended up joining Jim Dahlberg's lab. I had just learned about RNA biochemistry, ribozymes, and the RNA world in my biochemistry class, and I got really into RNA. Jim was an RNA guru, and eventually (after much begging on my part) he let me join his lab. It was AMAZING. Jim was so smart and cool. Not only did he seem to know everything about science, he knew about wine and had traveled all over the world. I had never met anyone like him in my life. His lab had these things called 'postdocs' in it, and also 'graduate students', all of whom only seemed to do research all day. I loved it all — making solutions, learning and troubleshooting PCR, designing experiments. Also, exciting and mysterious things happened in Jim's lab. One day there was a giant message on the chalk board in the break room: "CONGRATULATIONS TO JIM ON BEING ELECTED TO THE NAS!!!!" I ran to Jim's office, "congrats, Jim! What's the NAS?"

Did you then go to graduate school to do biochemistry? Yes. I went to graduate school to study RNA and protein structural biology. Jim suggested the University of Utah as a place that I might like and that also had lots of good RNA people. I was especially interested in Venki Ramakrishnan's lab. I liked Venki because he had solved some really interesting structures of various ribosomal proteins, and both he and I were interested in doing protein–RNA structures. He also liked to cycle, and I thought that this was cool. I worked in Venki's lab for a few fun and exciting years, but he moved his lab to England and I decided not to go, instead staying in Utah.

What followed was a year of almost aimless wandering. During my dabbling with x-ray crystallography and cryo-electron microscopy in Venki's lab, I found that I really liked the computational parts of the work. So I took some computer science classes. I was also noticing in the news sections of *Science* and *Nature* that computational biology might be the next big thing, so I dug up some papers on it. I read — or rather tried to read — the classic pairwise alignment papers of Needleman and Wunsch (J. Mol. Biol. (1970) *48*, 443–453) and Smith and Waterman (J. Mol. Biol. (1981) *147*, 195–197) that form the basis for how BLAST works. I didn't get much out of them at the time, except that they seemed to be using the word 'matrix' a lot, so I thought I should take a linear algebra class because matrices also show up a lot there. If you know anything about either pairwise alignment or linear algebra, you will also know that the usages of the word 'matrix' in these two examples are completely nonhomologous. I clearly needed a bit more guidance.

I applied for a spot in the Computational Genomics course at Cold Spring Harbor Laboratory and was accepted. This course helped to get me oriented in the field, but it was mostly important because I met a young professor there named Sean Eddy. He was not only the best lecturer and teacher in the course by a wide margin, he was nice, funny, liked soccer, and was also obsessed with RNA. I decided over beers with him at the CSHL bar that I was going to try to do my PhD in his lab. So, after four terrific years at Utah, I moved to Washington University in St. Louis for try number two at my PhD.

So why aren't you a computational biologist? Because I was terrible at it.

Sean's lab was perfect for me. He taught me how to think creatively, rigorously, and independently. He gave me an enormous amount of rope to hang myself, and I did, many times over. My first spectacular failure in Sean's lab involved trying to become a computational biologist. I was an okay computer programmer, but this is not the most important skill for the job. Real computational biologists are applied mathematicians, and, while you might think that taking linear algebra for the wrong reason might qualify one for a career in computational biology, it does not. But, to Sean's credit, even though I was clearly going to fail at the computational biology thing, he still let me stay on and try out some different projects.

In the search for a new project, I began to notice that the papers I was reading for fun were not related to computational biology, structural biology, or technology development: they were about microbes. Three papers stand out as particularly influential, in that they got me so excited that I still remember exactly where I was when I read them. The first is Norm Pace's review of microbial diversity (Science (1997) *276*, 734–740), a paper that explained how microbes are everywhere, do everything, and are the most important entities on Earth. The next is Jeff Lawrence and Howard Ochman's analysis of the *Escherichia coli* genome (PNAS (1998) *95*, 9413–9417), which revealed that many sections of the genome seem to have come from other organisms due to horizontal gene transfer (HGT). The third is Ford Doolittle's review on the extent of HGT in biology and how this might affect our interpretation of the universal tree of life (Science (1999) *284*, 2124–2128).

Combining my interests in molecular biology and microbiology led to my second spectacular failure in Sean's lab. The details are unimportant and would take too long to explain, but essentially what I was trying to do was to develop a technique to find unusual bacteria and archaea, the kind that might be missed using 'universal' rRNA gene PCR primers. I eventually got the technology that I was developing to work. The problem was that, near the end of my PhD, I realized that the technique I had spent the last three years developing was now obsolete because the cost of DNA sequencing was rapidly decreasing and the ease of doing it was rapidly increasing. You didn't need fancy tricks to find weird microbes: you could just *sequence everything* and figure out what was there. Reading Susannah Tringe and colleagues' 'whale fall' paper

(Science (2005) *308*, 554–557) was thus both exhilarating and heartbreaking. I had been scooped by a paper, yes, but also by an entire nascent field.

How did you end up working on symbiosis, insects, and bacteria?
Near the end of my now 10-year-long PhD training, I tried to figure out what I was *really* interested in. As I mentioned before, I read microbiology for fun, so that seemed like a given. While I still loved technology and computing, I was pretty disillusioned with doing molecular technology development as a career. I wanted to do a postdoc with an evolutionary biologist, one who worked on critters in nature and knew about how these animals functioned in their environment. But I also wanted to use my computer skills and try my hand at genomics. At this time in 2006 there was really only one person who ran a lab that met these requirements.

As I've detailed elsewhere (in *Women in Microbiology*, R.J. Whitaker and H.A. Barton, eds), it is a small miracle that Nancy Moran let me join her lab as a postdoc given my deficiencies in microbiology, evolutionary biology, and entomology. But she did, and I got to study microbial diversity (in insects) and genomics. I also received a four-year crash course in evolutionary biology and microbiology from Nancy, Howard Ochman (Nancy and Howard have closely aligned labs), and their collection of amazing students and postdocs. I finally got to apply all the technologies that I'd been learning toward a super interesting biological problem, and I loved it. I'd finally found my field!

And why are you telling us all this?
Because I think it shows that there is no single way to do science and that everyone's path is different. It shows that you don't need to come from an academic family to end up an academic (but that it sometimes might take a bit longer) and that what you know when you start college has little to do with where you might end up in life. It also makes it clear that career advice (at least from me) should be viewed with extreme scepticism.

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Book review

The catch with global fisheries

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Vanishing Fish: Shifting Baselines and the Future of Global Fisheries
Daniel Pauly
(Greystone Books, Vancouver; 2019)
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Humanity is perhaps only now realizing that we inhabit an ocean planet that is shaping — and being shaped by — every aspect of our lives. Yet many people may only experience the global ocean's large footprint from the comfort of an airplane, admiring hours and hours of calming seascape below. In fact, this is where I find myself as I read *Vanishing Fish* by Daniel Pauly, one of the most widely known fisheries scientists of our time. Offering a very personal '30,000-foot view' of our blue planet, this book exposes in detail the transformational effects of fisheries on the global ocean. It is guided by a systems-thinking approach that treats individual fisheries not as isolated local phenomena but as elements of an interconnected global system that has affected almost every aspect of ocean life.

Over 288 pages (almost one third of which are endnotes and references), this tome offers a colorful *tour de force* through Pauly's thought universe, discussing a great variety of topics that range from detailed accounts of global fisheries expansion since World War II to thoughts about the proper role of scientists in society. Most of the material is derived from previously published essays that have been framed by new introductory and concluding chapters that revolve largely around the author's personal history, especially his work in tropical developing countries, and how this has shaped his approach and outlook on global fisheries. This wide range exemplifies Pauly's multidisciplinary approach, which embraces both natural and social sciences, and even philosophy.

The author presents several key ideas that have shaped his body of work. First is the above-mentioned conviction that fisheries are indeed a global enterprise and hence need to be assessed and understood at that level. Pauly points out that the only other activities that affect the ocean at a similar scale are marine transport and waste deposition (including of plastics, excess nutrients, and carbon). I would also add tourism and underwater noise to that list. But of all these, fishing certainly represents the longest-running activity and probably also the most impactful human pursuit throughout much of our history, reaching back at least 42,000 years [1].

This vast temporal dimension connects to another key idea that is highlighted in the book's subtitle, *Shifting Baselines and the Future of Global Fisheries*. The 'shifting baseline syndrome' suggests that each generation of fishermen, fisheries scientists or decision makers compares the state of the ocean and its resources with a personal baseline that largely reflects what was present when that generation first started to observe the ocean. Historical changes that predate our individual as well as collective memories are often lost and thus the baseline of what is 'normal' shifts over time. This concept, which was originally coined by Pauly in a short essay published in 1995 [2], has contributed to the emergence of a new field of inquiry, marine historical ecology, which has since matured into its own discipline [3,4], with important ramifications for marine management and conservation [5]. Pauly's work can be credited with helping to cure a 'collective amnesia' that had been caused by our lack of awareness of environmental history.

Another idea that is reflected in many chapters of this book is that fisheries catch represents a crucial measure of impact and that it needs to be estimated with great care, even in data-poor situations. Much of Pauly's work has revolved around the estimation of a total fish and invertebrate catch worldwide as opposed to other standard metrics, such as stock biomass or fishing mortality, which are often favored by other fisheries scientists. His multidecadal efforts have been shedding light on the oft-hidden impacts of unintended bycatch and discards, small-scale subsistence,