A well-engineered path into cell biology and academia

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ABSTRACT **Winning the American Society for Cell Biology's Women in Cell Biology Mid-career Award is incredibly meaningful to me, as it validates that someone focusing on engineering and applications can be a "real" cell biologist, too. Single-minded devotion to studying a particular biological process is not a prerequisite for a career in science and academia. The more diverse the scientific styles and demographics of scientists who feel welcome, the stronger science will be.**

When you ask folks how they ended up in their current careers, or within their specific fields of academia, they often laugh and say their paths were unconventional, too winding to be recommended—so much so, I have started to wonder if "unconventional" is the typical path. For myself, I transitioned from being an experimentalist to being a computational biologist during my postdoctoral fellowship period—a switch I described recently (Carpenter, 2020), along with its joys and challenges. To summarize: it is clear, in retrospect, that this circuitous route to where I am now was not an inefficient diversion but instead was quite critical for my being able to bridge the worlds of biology and computer science and do what I have done: create the CellProfiler software project, which serves thousands, and pioneer image-based profiling and Cell Painting, which are accelerating drug discovery.

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My path is unconventional in a second way, because I wholeheartedly did not intend to go into academia, and yet here I am, leading a research group at the nonprofit Broad Institute of Harvard and the Massachusetts Institute of Technology (MIT). How did that happen? As an undergraduate interested in biology, of course my first decision point was whether to be a medical doctor. This was an easy call: I was so squeamish, I always persuaded my lab partner to do dissections in biology labs. So the decision was made early on to avoid humans and their icky bodily problems; really, anything biological that did not fit into a test tube was out of the question. I also ruled out academia, as I was very driven to make an immediate impact in the world—comical, in retrospect. I thought a pharmaceutical or biotechnology company would be the best venue to improve human health. So I figured I would keep going to school until I was able to attain the sort of research position I wanted in industry. I had no clue as an undergrad that I would need a decade of training after college to get there!

My undergraduate public university, Purdue University, was so engineering-focused that English majors were termed "word engineers," but I managed to major in biology. Due to family circumstances I had only one choice for graduate school, the University of Illinois at Urbana–Champaign, which was a wonderful place to learn from dedicated and involved professors. It, too, has an international reputation for engineering but I still managed to remain focused on cell biology. I then went to a postdoc position at MIT, at which time it became clear that—whether by osmosis or natural inclination—I am more an engineer than a scientist. That is, I find figuring out *how* to answer a biological question to be much more interesting than actually answering biological questions. Although I was already inclined toward industry, this realization certainly solidified my choice to avoid academia.

I struggled to see myself as a biology professor for other reasons, too, not just my focus on engineering and technology. First, I literally did not see many people like me in such positions—and that is as a white American woman. Representation is so much lower for other demographics, that my guidance for young faculty in underrepresented groups is to balance their concern for outreach/mentoring

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Abbreviation used: MIT, Massachusetts Institute of Technology.

with a focus on doing well and succeeding. Simply existing and being visible is a big step forward for the next generation. Second, until late in my postdoctoral position, I had no clear passion to study a particular thing and no clear vision of how to create a niche for an independent laboratory. I was interested in too many things. I hear many researchers (especially those from underrepresented groups) use this as evidence they ought to avoid paths that involve their leading scientific research.

I had wanted to do a quick postdoc and then go to industry once the post-9/11 economy recovered. So how did I end up on the academic job market instead? The major driving factor was my realizing that I would not have the freedom in industry to make the sorts of technology advancements I thought the world needed. My faith has been an important part of my choices along the way. It was clear to me, once I discovered computational sciences applied to biology, that "the place God calls you to is the place where your deep gladness and the world's deep hunger meet" (Frederick Buechner). Discerning your calling, whether faith-based or not, involves assessing these two things. Hopefully you have the awareness or exposure to mentors to help you figure out what the world needs—and for most of us just as relevant: what the world is willing to pay you to do, and what funding agencies are willing to fund. As for your "deep gladness," the upside of the long path of training in the sciences is that you have time to deduce what kind of work really suits you personally.

I could not imagine devoting my life to working out the intricate mechanisms of some biological structure or process. But I am delighted that many people are passionate about doing so, and I collaborate with such people every day. It is very clear to me that science functions best as a whole organism, with each part carrying out very different roles in very different ways, rather than arguing about the right way to do science: whether to focus on basic research questions versus applied, generating data versus analyzing the data we already have, big science versus small. It typically does not take long, in any conversation with an academic, before you are treated to an explanation of why his or her kind of research is neglected and underfunded, and possibly why funding agencies spend far too much on some particular other sort. Sometimes we take for granted the very organic structure of science, with the moving and mixing of researchers every few years during training, the ease of collaborating across institutional boundaries; all this allows each person to identify his or her style and passions and find people with whom to work that complement them.

When launching my independent academic laboratory, I decided we would start modestly with something very straightforward: we would help biologists extract information from images and disseminate useful approaches through our open-source software, CellProfiler. Not exactly splashy, high-risk/high-reward Science with a capital "S," but perhaps enough to make a living and make a go of it. A few years in, I felt comfortable enough to begin working on a dream of mine, to see whether computers could see more in images than humans can, to detect aberrant pathway activity in cells or diagnose disease. It was too risky to be anyone's full-time project, so different people worked on it part-time over several years, and it was only possible due to unrestricted lab startup funds. I was not convinced that it would be fruitful, but it seemed just possible enough to keep things going. Still, I would lie awake at night thinking I had wasted my team's time, not to mention hundreds of thousands of dollars of salary money, developing a technology that might just not work all that well. Ten years later, I am happy to say that image-based profiling is a thing. It can detect disease in images, and evidence is mounting that it is more powerful (and cheaper) than transcriptional profiling. It has led already to four drugs entering clinical trials via a company, Recursion, based initially on my laboratory's technology. I cannot take credit for founding the company, but I am delighted to serve on its scientific advisory board and observe my dreams impacting the world in this way.

I worry that a lot of wonderful scientists are deterred from their chosen careers because they feel they don't fit, because of either their demographics or their working style—when in reality, differences among who scientists are, and how scientists do science, can synergize in beautiful ways. It is especially a responsibility for those of us who are in the mid-career to senior stage to put in the effort to enrich the scientific enterprise by making it more inclusive, and to encourage those who feel a bit out of place to stay, and to lead.

REFERENCE

Carpenter AE (2020). Bridging Domain and Data. Patterns 100064. Available at http://dx.doi.org/10.1016/j.patter.2020.100064.