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And I, of course, would return the favor by using the harsh light of reason to make Charlotte’s proposed experiments shrivel at a similar rate. Perhaps, after a month of jousting, exactly two nearly perfect experiments would have been done, only to fail because of flaws that neither of us could foresee.

The other extreme is American exuberance, something I absorbed in graduate school. The fundamental idea is that doing more experiments means more results, that flawed experiments can be helpful too, and that stopping for tea and coffee is silly, when you can work frenetically till 10 p.m. and still have the bars open for another four hours to discuss life and science. Like the English Patient, this is a caricature, but every scientist I know will admit that they’ve had this sinking 11 p.m. sensation: “Oh fiddlesticks, I’ve just seen the fatal flaw of the experiment I’m about to finish that essentially guarantees that I can learn nothing from it!”

My claim is that you can hold that sinking feeling at bay and increase your post-Covid-19 productivity by doing two things: dissect and critique every experiment that you’ve done over the last six months, and find good jousting partners to poke English-style holes in these old experiments and all the new ones that you’re going to rush to do the moment your lab reopens. Their lashes will force you to admit that many, and possibly most, of the last six months’ failures should, at least with the perfect vision of hindsight, have been avoided. You should also be asking whether the inferences and conclusions that you drew from the experiments are really supported by the data. Again, if you’re honest with yourself, you’ll discover that there are logical flaws and alternative interpretations. And if you’re not, your jousting partners force you to open your eyes when you try to defend the evidence that supports your future plans.

When you discuss the experiments that you’re planning to do, things are likely to be even worse. Your intellectual motivation for individual experiments, entire strategies, and perhaps your overall project will be vigorously questioned. Missing controls will proliferate like desert wildflowers after the spring rain, and convincing arguments for the fallibility of experiments that you thought were guaranteed to succeed will pop up like molehills on the parental lawn.

One especially useful group of people to talk to are the folks who run core facilities and help with data analysis. In modern science, a lot of work is done by such core facilities: for example, cell-sorting, mass spectrometry, sophisticated microscopy, and DNA and RNA sequencing. Normally, you’re too busy to seek the advice of the people who run these facilities until the first and second attempts have failed and your PI is yelling at you about the cost of these experiments. But now you have nothing but time and the staff of the core facilities are in the same boat. Ask them to look over your plans, tell you what quantity and purity of material are needed to produce the data you need, and critique your calculations and assumptions about how your experiments will produce that material.

Doing everything I’ve advocated will take serious time and effort and it won’t be as fun as learning Python. As your plans for your first three months back in the lab and your expectations about what they will reveal shrink, the initial effect on morale may not be positive. But pain and suffering now should have a dramatic payoff in the halcyon world when experimental scientific research begins again. Ask an experienced experimentalist what fraction of their experiments either made it into a paper, or were directly necessary to produce the data in the paper: their answer will be between 5 and 10%. Imagine that three months of rigorous self-flagellation might increase that fraction 1.5-fold, that you will be working at the bench for another eight years, and that it takes two years of work (the optimism of scientists never dies!), at your pre-pause level of productivity, to make a paper. As things were, you would have produced four papers, but if you become 50% more productive, you will, instead, produce six papers. In retrospect you might even think that the three months that you spend in this socially distanced, Zoom-filled hell, were the most valuable ones of your scientific life.

Mala Murthy

What follows is the transcript of interviews with Mala Murthy by the graduate students and postdocs of the Murthy lab (Sama Ahmed, Christa Baker, Adam Calhoun, David (Dudi) Deutsch, Xiping (Lily) Li, Edna Normand, Diego Pacheco, Talmo Pereira, Nivedita Ranagraganj, Shruthi Ravindranath, Fred Roemschied, and Megan Wang). These interviews were conducted over Zoom in April 2020, during the coronavirus pandemic. Mala is grateful to her lab for participating in the Q & A.

Mala Murthy is Professor of Neuroscience at Princeton University, leading the Murthy lab in the Princeton Neuroscience Institute. She grew up in Texas and received her BS in Biology from MIT in 1997. She received her PhD in Neuroscience from Stanford University in 2004, working with Thomas Schwarz and Richard Scheller. Her postdoctoral work, which she completed with Gilles Laurent at Caltech, centered on odor coding in Drosophila mushroom bodies and opened a new area of investigation into neuronal stereotypy. In 2010, she started her own lab at Princeton University. Her research group consists of computational neuroscientists and experimentalists, who collectively study the many neural processes that underlie animal communication, including detection and recognition of multisensory cues, decision-making, and execution and patterning of motor actions. They discovered that flies engage in dynamic ‘conversations’: their ongoing actions (for example, courtship song sequences and changes in locomotion) are continually patterned by feedback that they receive from a partner. By leveraging the tools of Drosophila, in combination with predictive models of behavior, they have dissected the neural activity and circuits underlying the back-and-forth exchange of information between individuals.

**Sama:** Do you remember the first time that you thought “I could be a scientist”?

**Mala:** Actually, in high school, everyone (including me) thought that I would become a lawyer (my tendency for not backing down...
from arguments, I suppose). But then I worked in a molecular biology lab for a summer at Texas Tech University and my trajectory shifted. I had always had a passion for math and science but had never worked in a lab before — it was thrilling. In addition, when I presented and defended my research project at the end of the summer, in front of student peers and faculty, I became aware of the role of skillful presentation in being a scientist — it was incredibly important to have good ideas and high-quality data, but communicating those ideas effectively was also critical.

**Sama:** What did you work on during your first lab experience? Mala: I helped to clone genes from *Arabidopsis* plants and put them into cotton plants to make them more resistant to oxidative stress. I know, it’s a little different from what our lab focuses on now.

**Sama:** So you could have been a lawyer. What other profession would you have liked to attempt? Mala: I would have loved to be a professional dancer or musician. I used to be a hip-hop dancer, and in a parallel universe maybe I would have been touring with Beyoncé! I think that music and dance have a lot in common with how we do science: they are all incredibly collaborative and there’s a joy that comes from discovering a new movement, expression, or idea with someone else. Music still fills my life and lately I have been playing the flute with my daughter. I have also recently taken up the banjo. It is not an accident that our lab studies the song and dance routines of *Drosophila*!

**Sama:** You also considered a career in art history, no? Mala: During college, I spent a semester in Rome, Italy. I learned Italian and studied art history and archaeology — it was amazing. While I could enjoy doing research in any field, there is something special about generating new knowledge with my own hands: being the first person to discover something new about the world from the comfort of your own electrophysiology rig.

**Edna:** What turned you on to biology? And what drew you to systems neuroscience? Mala: I majored in Biology at MIT because I was curious about the human body and motivated to cure diseases, such as cancer. But through working in Lenny Guarante’s lab I developed a love for tackling fundamental questions about cell biology. The lab had just started working on the cellular mechanisms of aging (in yeast!), and I found it extremely exciting to be at the forefront of a new emerging field. I moved from single-cell biology to the cell biology of neurons in graduate school, but along the way I could not stop thinking about perception — how individual neurons give rise to sensory percepts. I found myself drawn to papers about this topic in graduate school (when I should have been reading papers about synaptic transmission!), and this led me down the path to becoming a systems neuroscientist.

**Edna:** How did you figure out that you wanted to be a PI? Mala: There is an equality in the lab that I love, in that good ideas can come from anyone (from student to PI). But I was always looking at my boss and thinking “I am going to be that person”: running the lab, teaching, giving talks, writing papers. The more I learned about what the job entailed, the more I wanted to do it. I never really considered something else in science. I’m very lucky. Being an academic scientist gives me incredible freedom — to pursue the questions that most excite me each day.

**Shruthi:** So you wanted to be like your graduate and postdoc advisors? Mala: In a sense, yes. Both are talented scientists and gifted writers, and they are also good role models when it comes to work–life balance. They both taught me by example that one does not have to give up one’s personal or family life for a successful life in science and that success should be measured by one’s own standards.

**Lily:** Were there things that pushed you away from the field that you ultimately decided were worth the trouble? Mala: The harder aspects of the job have come more recently: managing a large team while still finding time and space to think about science. Management isn’t often part of our training in grad school, and I believe that’s a mistake. Of course, grad programs shouldn’t be exclusively for training academics, but management skills would be useful in any field.

**Diego:** How did you decide what to study in your own lab? Mala: During my postdoc with Gilles Laurent, I was working on olfactory coding and the degree of stereotypy across identified neurons in the *Drosophila* mushroom body. While in Gilles’s lab, I was thinking about what I would focus on in my own lab and was drawn to auditory coding because of the highly quantitative nature of the stimulus — and the fact that the natural sound space for flies was thought largely to consist of courtship songs, which could be easily parameterized (although I did not know at the time how variable we would discover these songs to be!). I was also really taken by a set of papers from Barry Dickson that came out in 2005 and succeeded at labeling with GAL4 all neurons in males and females that expressed the sex-specific fruitless transcripts. This provided the first genetic handle on the neurons relevant for song processing (and other aspects of social behavior), and it seemed like the right time to work on this new issue. Of course, there are always risks associated with starting a new research area in your own lab, but the payoff seemed well worth the risks.

**Fred:** Even though you trained as a physiologist, your lab’s work has involved the development of new computational methods for studying behavior. How did this happen? Mala: It is true, I started out as an electrophysiologist, first working on the
neuromuscular junction of Drosophila in graduate school, performing patch-clamp recordings on embryonic muscles, and later on neurons in the central brain during my postdoc with Gilles. I have always been drawn to computational data analysis methods, although I don’t have a lot of computational training myself. During my postdoc I chose to collaborate with a talented theorist, Ilia Fiete, who turned me on to modeling. When I started my lab, it became clear to me that we needed to pay attention to behavior. We needed to know what flies singing, how much variation was present in song, what aspects of song the brain tuned in to, and so on. This work was driven by two of the first people in the lab, Pip Coen and Jan Clemens. Pip collected large datasets, and then Jan and Pip worked together to model the data. The collaboration led to the breakthrough that the song of the fly was shaped by sensory feedback, and this opened doors to study how sensory information modulates behavior in real time, as communication unfolds. It also revealed that this approach was useful and that the behavior gives you the key to unlock what is interesting about the brain. This early work attracted excellent computational people to the lab, and that’s been essential.

Dudi: Why study Drosophila? Mala: Working in Drosophila offers a lot of advantages, given their extensive genetic and neural circuit toolkit. Any experiment that you can dream up can probably be performed already with the tools in Drosophila! In addition, flies perform rich behaviors. During courtship, both males and females make decisions, weigh sensory evidence, select the right behavior at the right time, and modulate behavior relative to ongoing feedback from a conversation partner — all complex cognitive processes with parallels to organisms with more complex brains.

Megan: What experiments have inspired you? Mala: I’m inspired by work that is ingeniously simple and not necessarily a product of brute force or fancy equipment. Examples include the manipulation of leg length to investigate pathfinding strategies in ants by Wittlinger, Wehner, and Wolf, the use of temperature to link neural activity to song structure in birds by Long and Fee, and the discovery of grid cells enabled by expansion of the behavioral arena by Hafting et al. I love when computational modeling can be used in clever ways to solve a biological problem, such as in the work of Prinz, Bucher, and Marder, who screened over two million models of STG circuit activity to show that many solutions could give rise to the right pattern of activity. Finally, it excites me when new technology facilitates a scientific breakthrough, such as the discovery of the compass neurons in flies (e.g., Seelig and Jayaraman) and the mapping of sensory and behavioral signals to whole brain neural activity in zebrafish (e.g., Ahrens et al.).

Fred: What’s your advice to junior scientists? Mala: If you want to do something well, you have to specialize. But how do you keep up as science becomes more interdisciplinary? Accept that you don’t know everything and this will lead to good collaborations — some of the best experiences I have had in science have been through collaboration.

Christa: Any other advice? Mala: Work on the questions of greatest interest to you and resist the temptation to work on what’s hot or trendy at the moment. It is never too early to start thinking about how you will carve out your own area and define yourself as a scientist. Think about what your unique vantage point is. My career has been defined by a bit of fearlessness in pursuing new ideas. For example, starting a new research area in my own lab was risky, but it had a huge payoff in terms of securing young investigator funding and attracting great people to the lab. All of this advice requires, to some extent, ignoring your inner critic, who suggests that your ideas are not good enough.

Nivedita: You work in the area of systems neuroscience. What do you think are the greatest challenges ahead for your field? In neuroscience, I would say that we face two big challenges. We’re collecting amazingly rich behavioral, sensory, and neurophysiological datasets and there is a challenge in making sense of these complex data, distilling meaning from them, and presenting the findings to others. We need more investment in developing tools that are suited for analysis of these kinds of new data. The other challenge lies in how to make meaningful comparisons of complex datasets across organisms. It is at the level of computations that we will find similarities between animals — to solve similar problems, animals may have evolved similar strategies. We could use more crosstalk between research on disparate model organisms and funding for this kind of comparative work.

Talmo: You have been heavily involved in the BRAIN Initiative ever since its inception. How do you feel that the BRAIN Initiative has transformed your research specifically and neuroscience more broadly? Mala: The BRAIN Initiative has been particularly effective in facilitating collaborations across disciplines. It created a large inclusive tent for neuroscientists, especially across model systems, and this now allows us to share expertise that would otherwise have taken longer to diffuse across model system boundaries. It’s remarkable to think about how quickly the field has shifted with the infusion of funding for technology development. Whereas just a few years ago it would have been unthinkable, today it’s nearly standard to use machine learning-based tools to study behavior, record from hundreds to thousands of neurons simultaneously, and use optogenetics to activate increasingly precise neural circuit targets. This emphasis on tool development has been particularly successful in bringing people with more quantitative backgrounds into our field.

One of the direct impacts that the BRAIN Initiative has had on my research is the creation of connections with colleagues in physics, such as Joshua Shaevitz and William Bialek, with whom I might not have struck up formal collaborations were it not for the quantitatively oriented objectives of the initiative. Subsequent collaborations with colleagues, such as Jonathan Pillow on computational modeling and Sebastian Seung on EM-level connectomics, have all sprung out of this type of bridge building across complementary approaches to systems neuroscience.

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