PREFACE

MY FIRST JOB IN THE SCIENCES WAS A WORK-STUDY POSITION AT Wesleyan University. I was a freshman at the time, and the way I remember it now, there were only a few job options available. Most of my dormmates went for positions at the library reshelving books. But I took a position as dishwasher for the department of biology.

It was the perfect job. I would arrive in the afternoon and the dishes would be waiting, prerinsed and sitting in big white plastic tubs, each tub labeled in bold black Sharpie marker with the last name of the professor who led the lab. I was asked to run the dishes from one lab separately from the next, filling the machine with the dishes from one tub at a time. Once I'd loaded the dishes into the industrial-grade washer, all I had to do was throw in a scoop of soap powder and get things going. After that, I could sit and study. Roughly an hour after I had pushed the start button, a buzzer would go off, at which point I would pull on a pair of heat-resistant gloves, unload that set of dishes, and set up the next run.

By the end of my freshman year I was being encouraged to join a lab as an undergraduate researcher. A biochemist whose lab was next door to the small room that held the dishwasher and a couple of autoclaves—high-pressure, high-temperature sterilization machines—would occasionally pop his head in to ask me about joining a lab. He seemed determined

to make sure I knew that I did not have to be sitting around all afternoon doing dishes. Instead, I could be doing hands-on research, either for course credit or for the same kind of work-study pay I was collecting for the dish-washing job. Eventually, and somewhat reluctantly—being paid mostly to do homework was a pretty plum job after all—I decided to take his advice and approach one of the professors in the biology department about a research position.

Starting out, I did not have a clear idea about what kind of research I wanted to do or whose lab I wanted to join. But I did have one firm "no" in my mind. I had decided, quite resolutely, that I would not work for the one lab in the department in which the researchers performed their studies with the fruit fly, *Drosophila melanogaster.*

Why was I so determined that I would not work in a fruit fly lab?

It was a decision based solely on the dishes.

After washing the dishes week after week for the dozen or so labs in the department, I had noticed a pattern. The dishes from most labs were varied: tall glass cylinders, low flasks, wide-mouthed beakers. Now and then a metal spatula or a magnetic stir bar. But there was one exception. Michael Weir was the only professor in the department at that time whose lab worked on fruit flies, and instead of containing the usual odd mix of sizes and shapes, the white trays marked "Weir," I noticed, contained rows and rows of same-sized, same-shaped, half pint glass bottles, many of which were marked "urine specimen" in raised letters.

It wasn't a gross-out factor for me—I knew that there was no urine involved, and the dishes arrived precleaned. No signs of flies or fly larvae. Not even any traces of fly food. Just the rinsed bottles, waiting for a deep mechanical scrub. So why did I object? For one simple reason: the dishes from that lab were too boring. Half pint bottle after half pint bottle loaded into the machine and then, sparkling clean, loaded back into the white plastic tray. I wanted to work for an exciting lab. A lab with a lot going on. A lab that did a lot of different things. I had a unique vantage point from which to judge. And bottle after bottle, all the same size, just didn't cut it.

The decision not to join a fly lab as an undergraduate seems now like the delay of something inevitable, the way two people who have just met and fallen in love might say, "And we lived just around the corner from each other for years!" Even in graduate school at the University of Colorado at Boulder, I circled around for a while before landing. I spent a couple of months working with *Chlamydomonas reinhardtii,* a one-celled green

alga that can breaststroke its way through a liquid with its pair of arm-like cilia, and another couple of months working with *Caenorhabditis elegans*, the small clear nematode worm that, like *Drosophila*, has become a common "model organism"—that is, a species many researchers use in their studies with the assumption (the justifiable assumption, I will argue) that what is learned using the model can be more widely applied to understanding the principles, mechanisms, and genetic underpinnings that control the development, growth, life, health, aging, behavior, and so on of other living creatures, including ourselves.

I was making a kind of Hail Mary throw when I approached Professor Robert Boswell in the early summer of 1994. I was nearing the end of my first year in graduate school—the only year in which classes, rather than lab work, were the main focus. I had been turned down at one lab, and I wasn't keen to join any of the others in which I had done rotations. I was nearly ready to give up on graduate school altogether and head back to the East Coast. I had a job lined up and everything.

But of course the reason quarterbacks still throw Hail Mary passes is that once in a while they pay off, and pay off big. The right things connect and the team makes that dream play. With the decision to give it one last try in Professor Boswell's lab—a *Drosophila* lab—I found the right fit for my graduate thesis and, as it turned out, far beyond. With that decision, I became a "fly person," as those of us who use *Drosophila melanogaster* in our research really do call ourselves.

As model organisms go, the fruit fly is, in my view—and I am not the first to propose this—the model of models. Left to its own devices, this innocuous little fly would be content to spend life doing nothing much more than hovering around a pile of rotting apples or wandering a vineyard. But research on this fly, which began more than a hundred years ago, has helped to reveal a surprising number of fundamental concepts related to biology, including fundamentals of human biology and disease. Although many years have passed since I was first introduced to the field, I continue to be amazed by what research on fruit flies reveals to us. I have gained a deep appreciation for this tiny sprite and for the many researchers who have used *Drosophila* to conduct studies in fields like genetics, genomics, cell biology, developmental biology, and neuroscience.

With this book, I hope to share some of that amazement and appreciation by telling some of the "first in fly" stories—that is, to present some of the key biological insights and discoveries for which *Drosophila* played a starring

role, starting researchers in other fields down a revealing new experimental path they might otherwise not have taken or not stumbled upon so quickly. My goal is not to present a comprehensive list of discoveries made first in the fly or to rigidly adhere to presenting only this type of discovery. Instead, my goal is to use "firsts" as jumping-off points to demonstrate some of the ways in which fly research has broadly impacted our understanding of biology and biomedicine, including our understanding of the functions of human genes. Indeed, for a surprisingly large number of human genes, the first hints of their biological functions—the cellular mechanisms of their action, the answer to "How does it work?"—came not from studies in human cells, mice, rats, or guinea pigs, but instead from studies performed with the lowly fruit fly.

At the 41st Annual *Drosophila* Research Conference in 2000, the opening session was centered around discussion of the newly released full-genome sequence for *Drosophila melanogaster,* the first full-genome sequence of any critter with eyes and legs. During that opening session of the conference, a leader in the fly field joked in front of the crowded auditorium that flies are basically "little people with wings."

They are not, of course.

But they are marvels. And they are connected to us. If by nothing else, then by a thread of evolution, by the fact that Nature tends to solve a problem once and then apply that solution over and over, rather than reinvent the wheel with each new species.

The reasons researchers came to study *Drosophila melanogaster* are to some extent a product of random chance and circumstance. But the reasons that research on fruit flies continues are anything but random. Once exposed to some of the "first in fly" stories—many of them closely connected to the story of our bodies, our behaviors, and our many plagues and diseases—one cannot help seeing that *Drosophila* is more than worthy of the attention it has been given and continues to receive.