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For Self-Starting Scientists A "Model" Career Awaits

Dustin Hoffman's character in *The Graduate*, Benjamin Braddock, wasn't exactly overwhelmed when he heard that his professional future might lie in one word—"plastics." Neither was Mark Murcko.

Murcko, an organic chemist by training, says that when he was an undergraduate at Fairfield University in Connecticut, he attended a talk by a researcher who was designing plastics for hair curlers. "It struck me that maybe what he was doing, while useful, wasn't quite as stimulating as it might be," says Murcko with dry understatement. "And it occurred to me that I didn't want to spend my life designing hair curlers or a better nonstick coating for a Teflon frypan."

So if plastics didn't do it for Murcko, what did? The answer: computer modeling of biomolecules. Today, Murcko is a vice president at Vertex, a pharmaceutical company in Cambridge, Massachusetts, and he specializes in computer modeling.

Modeling, which is closely related to another hot field—bioinformatics—is a rapidly growing part of the pharmaceutical and biotechnology industries. It's an interdisciplinary field that draws people with many types of scientific training, from computer science to structural biology. And there aren't many formal training programs, so tailoring your own training is important. But what skills do you need to succeed? What qualities are employers looking for? Those questions are answered in the latest "New Niche" feature on *Science*'s Next Wave. From 1 August to 3 October, this New Niche will allow you to interact online with people who are already established in this field.

The reason computer modeling is so important now is that it forms a crucial element of structure-based drug design, a method that many companies are relying on to speed up the process of drug development. Structure-based drug design allows a "more targeted approach" to designing new pharmaceuticals, says Andrew MacBride, a staff programmer in the computer science division at the University of California, Berkeley. In the past, says MacBride, "you'd get a lot of candidate molecules," and people would try to figure out what to do with them. These days, he continues, researchers try to come up with the key biochemical pathways in a disease. Then, using a computer, they try to design molecules specifically targeted to those particular pathways.

But this does sound a bit like bioinformatics, another hot field that was the subject of a Next Wave New Niche that began on 12 July 1996 and a special issue of the Next Wave on 14 February. Dennis Underwood, director of molecular systems at Merck, says there is a large area of overlap between bioinformatics and computer modeling. He adds that there is an important difference in emphasis. In bioinformatics, researchers are interested in identifying and cataloging DNA sequences. Modelers, on the other hand, work with three-dimensional (3D) structures of proteins and other biomolecules. "Because it's really the 3D structure that's important [for function] and not the linear sequence," says Underwood, "we bring the 3D side to bioinformatics."

This is one of a series of pages in *Science* about features on *Science*'s Next Wave, the AAAS/*Science* Web site for young scientists (www.nextwave.org). This story highlights an alternative career feature on "Computer Modeling in Biology" in the "New Niches" section of the site, which begins on 1 August and runs until 3 October.

Regardless of the precise definition of computer modeling, there's no question about it—the field is growing rapidly. Insiders have seen this growth coming for several years. Chris Lee and Michael Levitt, for example, bet their futures on this growth 4 years ago by founding a company, Molecular Applications Group, that designs software for the pharmaceutical industry. "The whole idea in starting the company was that the human genome data were really going to change the way people work," says Lee, "and that the key was being able to relate that vast body of data to structure and function, the things that make it have meaning biologically—and that's not a trivial task." In fact, it was a task that Lee and Levitt thought would require new science and new tools.

Not only is the field of computer modeling growing; it's also an exciting area to be in. "The challenges are extraordinary," says Murcko. "No one has a black box solution. You can't punch a button and have a little sheet of paper pop out with the structure of the drug written on it." Lee agrees: "The problems are hard. It's very difficult to do calculations that will connect with an experiment that will test whether what you're doing is real or not." Because the problems are difficult and interdisciplinary, computer-modeling groups are composed of many different kinds of scientists.

As a result, assembling a team can be a challenge. "There are very few individuals that you can hire to spec, right out of the box," says Lee. A typical modeling group might consist of computer scientists, molecular biologists, structural biologists, physicists, mathematicians, and computational chemists. Lee says that although nonbiologists may be involved in modeling, "it's important to be able to understand what matters biologically." Frequently, the field becomes broken down into two worlds, says Lee: biologists who don't really understand modeling, and modelers who don't understand the underlying biology. "Someone who has the background," says Lee, "or the will to put in the effort to immerse themselves in both halves really has a leg up on the problems."

Hiring managers in computer modeling are looking for technical skills as well as the ability to understand multiple disciplines. "It's important to have people in [a modeling] group who are flexible, creative, and can take on new ideas and develop them very quickly—we try to look for these qualities in résumés," says Underwood.

Underwood says that in hiring, his problem is not finding applicants—it's finding the right applicants. He says a recruitment advertisement in *Science* typically produces 200 responses—but only 75 of those applicants might have the appropriate background. "From those, we weed it down to about 20 and then begin to prioritize them by the kind of personality that would fit the group, background, range of experience a person has, flexibility, and some indication of creativity."

With the amount of genetic information being churned out daily and the continuing demand for new drugs, it's clear that computer modeling will continue to be an important growth area. Because the field accommodates a wide variety of scientific backgrounds, there's almost no place that you can be specifically trained. This means that there is plenty of room for researchers to take the initiative and self-train. And if you take that initiative, you will make yourself attractive to an employer, says Lee, because it shows you're a self-starter who is savvy enough to pick the right skills to learn. So check out the New Niche and find out what those skills are—it might lead to a very rewarding new career path.

–Nicole Ruediger