

Profile of George Oster

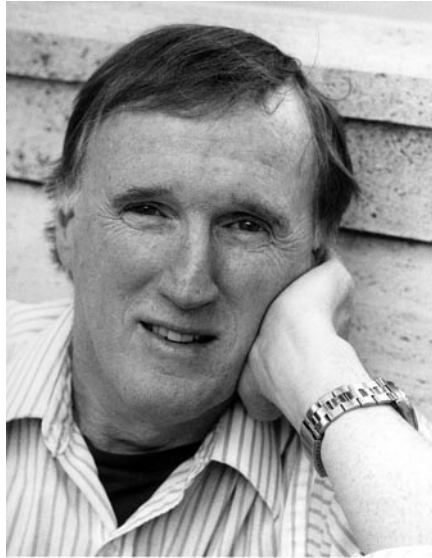
In 1980, when biophysicist George Oster submitted a paper to an esteemed developmental biology journal, he received a reply with a rather Orwellian overtone. “The authors are attempting to apply Newton’s laws to embryos,” the anonymous reviewer wrote, “but as all biologists know, biological systems don’t obey the laws of physics.” Luckily, an astute editor found that remark suspicious, and the paper, coauthored with Garry Odell and Beth Burnside, was published (1). “But that was the atmosphere of the day,” Oster says.

Biologists’ skepticism about math and physics is only one of many changes Oster has seen in the field over the years. Through collaborations and “staying close to the experiments” of the day, as he says, Oster has enjoyed a front-seat view of a tour through biology over the last three decades. From saving whales in the 1970s to modeling molecular motors today, Oster’s research interests often have reflected the scientific spirit of the times. He is now a professor in the Departments of Molecular and Cellular Biology and the College of Natural Resources at the University of California, Berkeley, where he has made a place as a theoretician among experimentalists.

Elected to the National Academy of Sciences in 2004, Oster brings knowledge of physical principles to bear on scientific problems in a variety of disciplines, including ecology, evolution, cell biology, and molecular biology. His models reveal underlying principles in biological systems at all levels of complexity, from population dynamics to bacterial propulsion. In his Inaugural Article (2), published in a recent issue of PNAS, Oster continued his previous work on molecular motors with the presentation of a model describing the synthesis of ATP by the enzyme ATP synthase.

Tying Knots at Sea

As Oster was graduating high school on Long Island, NY, in 1957, his father suddenly found himself out of a job. With no money to pay for college, Oster decided to attend the United States Merchant Marine Academy (Kings Point, NY) on Long Island. This federal military academy, modeled in the tradition of Army, Navy, and Coast Guard military academies, paid for tuition and trained young men for a career as officers on commercial ships. Moreover, Oster points out, it offered an opportunity



George Oster

attractive to a 17-year-old: a chance to see the world.

“But it turned out not to be a happy experience. I didn’t really fit in at the Academy,” Oster says. He spent his sophomore year sailing on freighters and tankers to various ports of call, including Casablanca, Morocco; Trieste, Italy; and Rio de Janeiro, Brazil. “I realized that my father was right when he told me that most things in life tell better than they live. So although I had a lot of ‘sea stories’ to tell, I didn’t always like being there. Sailing itself was mostly very boring,” he says.

Oster emerged from the 4-year program in 1961, with a U.S. naval officer commission and no academically useful skills, as he says. He applied to graduate school at Columbia University (New York), where a new department in Nuclear Engineering was eager for students. Says Oster, “The professors who interviewed me were amused by my transcript. They saw that I had courses like knot tying and marine seamanship. Nevertheless, they admitted me on probation, and I had to make up much of an entire undergraduate education during the first year.”

A Doctorate and then Some

Although nuclear energy was a booming field in the 1960s, Oster enjoyed its mathematical theory more than its applications. “I learned how to design reactors, which I didn’t find much more interesting than sailing on ships,” he says. Still, he counted on the degree leading to a better career. Oster continued to sail during the summers to pay

his tuition, until he was relieved to be awarded a graduate fellowship from the Atomic Energy Commission in 1964. He spent a summer in Berkeley, CA, while working in plasma physics at the Lawrence Livermore Laboratory, operated by the University of California. “That summer, I fell in love with the Bay Area,” he recalls.

As Oster wrote his thesis on the critical density and temperature of cesium, he knew that he wanted to return to Berkeley—but not as a nuclear engineer. “I didn’t know what I wanted to do, but I knew I didn’t want to design nuclear reactors,” he says. Oster had taught thermodynamics part-time at City College of New York and had sat in on a biophysics course at Columbia. It was not much to go on, but he decided biophysics was as good a career alternative as any. In 1967, with a doctorate in hand, Oster applied for the biophysics graduate program at University of California, Berkeley. “They said yes, although it wasn’t clear to them that I already had a Ph.D.,” he says, “then when I got there, and they saw that I had a Ph.D., it was too late for them to say no.”

Oster’s graduate studies in biophysics were short-lived, however. Soon after the fall term, he met Aharon Katchalsky, a renowned Russian–Israeli biophysical chemist visiting from the Weizmann Institute in Rehovot, Israel. “For reasons that to this day I cannot fathom, he took me under his wing and said, ‘Don’t bother collecting another Ph.D. Come to Israel and work with me.’ And so I did,” says Oster. Katchalsky obtained some funding for Oster, and they worked together in Rehovot on the thermodynamics of biological networks (3). “It was through him that I became a scientist,” Oster says. “He was a world-famous scientist. He knew everyone and introduced me. It was sort of like being made by the mob,” he says of Katchalsky. Oster’s collaborations with his mentor were tragically cut short in 1972, when Katchalsky, on his way to take office as President of Israel, was shot and killed at the Tel Aviv airport by terrorists of the Japanese Red Army.

Six-Legged Spiders

At the time of Katchalsky’s assassination, Oster had finished his postdoctoral work and was back in Berkeley. “I had

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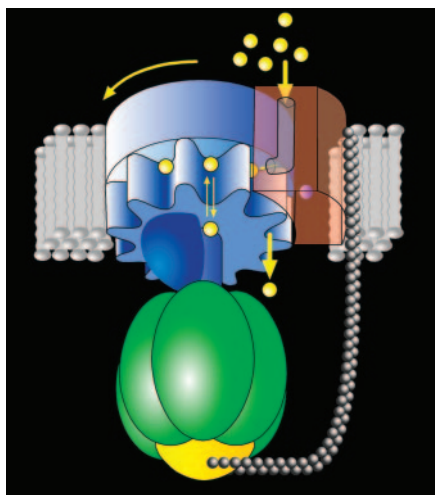
offers from other places, but I loved Berkeley and was looking for any reason to stay," he says. Oster had taken a 2-year position in the Mechanical Engineering department but soon developed an interest in population biology from his friend Roger Payne, a well known whale biologist. "That was during the Vietnam era, and Berkeley was very exciting. I was into saving the whales and saving the world," says Oster. Although Oster won the Levy Medal from the Franklin Institute for engineering papers in 1971 and 1974, the department chairman decided Oster's population biology work was too far afield.

As Oster was preparing to leave Berkeley, however, a spot serendipitously opened. The Entomology department was looking for a population biologist, and they had interviewed Simon Levin, an old friend of Oster's. Levin turned down the position but told the search committee, "What about my friend George?" The search committee liked Oster's research and welcomed the discipline-hopping theoretician without any entomology experience. "I remember they took me out to lunch, and as a joke I said, 'I really don't like spiders,'" he says. An awkward silence followed, until one of Oster's new colleagues pointed out that entomologists study insects, which spiders are not. Says Oster, "I responded lamely, 'I knew that.'"

Before too long, however, Oster found an insect he thought was rather appealing. "I was taking a course at Woods Hole Oceanographic Station in Massachusetts. One evening in a local bar, I ran into Ed Wilson," who was well known for his entomology work at Harvard University (Cambridge, MA), Oster recalls. "We started drinking, and he started telling me about ants. I was fascinated. So Wilson said, 'Look, I want you to come to Harvard, and we should write a book on the modeling of ant colonies,'" says Oster. Oster agreed, and Wilson's famous name helped persuade the Guggenheim Foundation to award them both with year-long fellowships to write their book, which was published in 1978 (4).

Theoretician in Camouflage

At Harvard, Oster landed in the center of the emerging academic firestorm surrounding the new science of sociobiology. On one side was its inventor, Wilson, who was applying biological and evolutionary principles to animal societies and who suggested the same could be applied to humans. Opposing him were eminent scientists, such as Richard Lewontin and Stephen Jay Gould, who pointed to eugenics and social Darwinism as dangerous examples of such



ATP synthase.

thinking. Says Oster, "It was one of the more vicious scientific fights I've witnessed. There was a AAAS meeting where people ran up on the stage and dumped water on Ed. I tried to remain on the sidelines, but there I was in the middle of it. In the mornings I would work with Ed on the fourth floor, and in the afternoons when he went home, I went downstairs and worked with people in Dick Lewontin's lab. It was an interesting year—in the 'Chinese-curse' sense."

After his year at Harvard, Oster continued to collaborate with scientific luminaries from a variety of fields. The trick to working well with experimentalists, according to Oster, involves a lot of preparation and a little disguise. "You listen. You try to figure out how they

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think. I had to teach biology, so I learned to talk the talk well enough," he says. Oster also learned how to make his mathematics friendly for even the most math-phobic biologists. "You have to put a lot of effort into trying to say it in pictures, without equations," he says.

Often, casual chats with scientists over coffee at a conference or café would trigger more formal ventures. "I worked with people whom I liked and got along with and who had problems that were interesting. It evolved natu-

rally into a professional collaboration," says Oster. In all his research, Oster uses physical principles to understand biological phenomena. "Physics tells you what can't happen, and also what could happen, but it doesn't tell you what does happen. For that, you need experiments. Being in a biology department has forced me to stay close to the experiments," he says.

Darwin Meets Newton

As he was drawn by collaborations into a variety of fields, Oster's research interests broadened. With the physicist and biologist Robert May, Oster worked on issues of dynamic complexity in ecological models, including an early and influential paper on chaos theory (5). After meeting fellow modeler Garry Odell, Oster worked on models of embryology (1). With Jim Murray at the University of Oxford, he studied pattern formation and morphogenesis (6, 7). When the many biological departments at Berkeley were combined into two mega-departments, Oster's teaching appointment landed in the Molecular and Cell Biology department. The transition was smoothed considerably by being selected as a MacArthur Foundation Fellow in 1985.

From his work in embryology, Oster became interested in how individual cells behave, which led him to research into animal cell motility (8). Later, these interests would evolve into studying the exotic ways in which bacteria move. "Bacteria are very weird. Our cells move in pretty much the same way. But bacteria have found dozens of totally different ways of moving. Some of them get pushed along by slime. Some swim, some glide on surfaces by mysterious means," he says. Through a chance meeting with biochemist Dale Kaiser, Oster became interested in myxobacteria, cigar-shaped bacteria with no visible means of propulsion. With Kaiser, Oster constructed a model suggesting that myxobacteria move by exuding a polymer slime from nozzles in their back end—a mechanism known around Oster's laboratory as "the snot gun" (9).

Studying locomotion led Oster to think about the molecules that drive the locomotion. During a sabbatical sojourn in New York, a collaboration with Charlie Peskin prompted Oster to study the mechanochemical aspects of molecular motors (10). This research eventually led to a successful model of the motors comprising ATP synthase (11) and ultimately to his PNAS Inaugural Article (2), which centers on a model of the synthesis of ATP by this enzyme. Although Oster and other researchers previously studied the individual motors of

the enzyme, no one had constructed a mechanochemical model for the ATP synthase in its synthesis mode. He and his postdoctoral fellows Jianhua Xing and Jung-Chi Liao constructed such a model, which required structural, biochemical, and mutation analyses. "There are so many different kinds of experiments. It's a challenge to put them together into a mathematical model that is able to fit all those different kinds of data," says Oster. Their model shows how the stages in synthesis are related to the structure of the protein, and their approach may prove useful as a guide to modeling other protein motors.

From Engine Rooms to Berkeley Cafés

Students and fellows in Oster's research group hail from all parts of campus, including chemistry, engineering, physics, math, molecular biology, and even criminology, when a student once worked with Oster on fingerprint formation. The researchers never stray far from the tether of experimental data, through the work performed by either students or collaborators, Oster says. He

enjoys taking the group every morning to a Berkeley café for tea and coffee, much as he did with his mentor Katchalsky decades ago. Says Oster, "We spend an hour talking about each person's problem or a paper we read. That's my lab meeting. It's a free-thinking time. You're able to talk crazy ideas, and people don't criticize each other. This being Berkeley, some days we just end up talking politics. But most of the time, there is some puzzle to kick around. That's what is fun about doing science. There is this endless supply of intriguing puzzles."

Oster realizes that puzzle-loving students who want to follow in his footsteps may have a hard time finding the path in today's academic world. "When I was coming up, things were a lot looser, jobs were easier. Now it's quite tight, and I think that people have to specialize in ways that I didn't have to. It's hard to get away with being a dabbler like me these days," he says. Reflecting on his career path, he says, "I'm amazed at how lucky I've been. . . . I think I just met the right people at the

right time and worked on the right problems. I think of my career as a sequence of lucky accidents, of meeting people who were really smart. In fact, I think the story of my professional life is being able to work with people smarter than I am."

From fixing 20-ft turbines in ships to devising equations that explain how protons drive 20-nm molecular turbines, Oster has traversed wide academic ground. "When I was sailing in the engine room of ships, sweating, cursing my lot, and drinking coffee, not in a million years did I think I would be here. I remember Rod Laver, the tennis champion, once said to a reporter, 'I can't believe they pay me to do this.' Every day I look up at the Berkeley hills, and that's the way I feel. It is so much fun that I would pay them to do it," he says. Analyzing where he is today, Oster says, "The idea that I would end up in Berkeley as a professor, let alone in the National Academy? It never crossed my mind."

Regina Nuzzo, *Science Writer*

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