# The Art of Science

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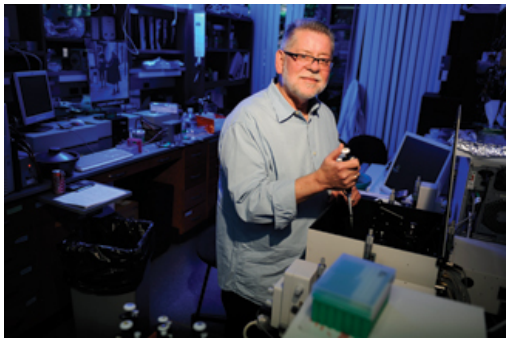

Professor of Pathology Paul Bock



## Whether biochemist Paul Bock is creating artwork or conducting research on blood coagulation, creativity is the name of the game

**by Joan Brasher**
*photo by John Russell*

As a boy growing up on Long Island, N.Y., in the 1950s, Paul Bock wanted to be a naturalist, harboring dreams of paddling a canoe down the Amazon River, discovering rare species of birds, fish and plants. He enjoyed doing experiments with his chemistry set and had an assortment of pets, including snakes, lizards, fish and bugs.

Science, it seemed, was in his blood. Bock's father was a consulting radio physicist who designed antennas for aircraft companies such as McDonnell Douglas and Lockheed. He also worked on highly secretive projects at the radiation research labs at Harvard University, as well as served in a classified countermeasures unit during World War II.

Paul Bock would one day graduate from chemistry sets to running his own laboratory, and would become known for the creation of a new method for tagging blood clotting enzymes that has advanced the study of life-threatening conditions such as strokes and acute bacterial endocarditis. But his journey from inquisitive boy to successful scientist has had a few unusual twists and turns.

The family relocated to Los Angeles for his father's work, and by the time Bock reached adolescence, like many young men, he struggled for acceptance among his peers. He describes his large L.A. high school – both figuratively and literally – as a battlefield. But there was one place Bock could turn his teenage frustrations into a productive outlet: art class.

"I was very good in art, and they didn't really give us assignments – they just let us paint or draw," he said. "I gravitated toward hot rods and Big Daddy Roth in my drawings, which was kind of counter-culture at the time."

"Divining Rod" by Paul Bock

College wasn't even on Bock's radar, but his parents pressed him to go. He enrolled at the University of California-San Diego, a two-and-a-half-hour drive from Los Angeles. He was glad he did.

"When I got away from high school and home I realized that there were people out there who were interested in intellectual things. I thought, 'Wow, this is paradise.'"

Bock excelled in his art classes but gravitated toward chemistry and biology where he was "curious about things and good at figuring things out."

He qualified for some graduate school-level classes and worked as a laboratory intern. A near-death experience during his senior year in college proved life changing. A misdiagnosed blood clot in his leg resulted in a pulmonary embolism that could have been fatal.

Bock recovered from the clot and returned to finish his senior year with enthusiasm. But unlike his other gifted classmates, he had not planned ahead for graduate school.

Although he had been accepted to an excellent school – Washington University in St. Louis – he had not applied to the right program. Upon hearing this, one of Bock's professors, John DeMoss, came to the rescue.

“He picked up the phone and called his friend Roy Vagelos, then chairman of the biochemistry department at Washington University in St. Louis, who later became the president of Merck Laboratories.

“He hung up the phone and said, ‘Well, I got you into the biochemistry program,’” Bock said.

In graduate school, Bock was mentored by professor of biochemistry and molecular biophysics Carl Frieden, a highly respected enzyme kinetics expert who is a member of the National Academy of Sciences.

Bock went on to three post-doctoral appointments, including a two-year stint in England on a fellowship focused on blood coagulation, which, ironically, included the study of the same kind of pesky clot that nearly took his life. The field became his lifelong passion.

“I’ve had a couple of really good ideas in my career, and there is no better narcotic than the ‘aha moment’ – that moment when you see something new and understand how it works,” he said.

Bock said he got his best idea during his third post-doc, working in Detroit at an American Red Cross research laboratory. He wanted to attach fluorescent labels to blood coagulation enzymes so he could see how they interact with other proteins. But there were only three or four different labels at the time that he could use.

One day he was discussing with a crystallographer the process necessary to insert a mercury atom into the active site of an enzyme so that it would crystallize without chewing itself up. It occurred to Bock that he could do something similar with his fluorescent probes. By inserting a deactivating compound into his coagulation enzymes, he could attach dozens of different fluorescent tags with a few simple chemical steps.

“Nobody ever got famous creating a new method,” he said. “But I knew this would completely change the way things were being done.”

At first his peers were not keen on the idea. So Bock spent the next two years studying the process and documenting it so critics would take another look. At one point a chemistry friend told him, “If you hadn’t shown me the data, I would have said it was impossible. But you’ve done it.”

The first enzyme that Bock tagged was thrombin, which is the central enzyme in blood clotting. It’s the enzyme that chops fibrinogen – a protein in blood plasma that is synthesized in the liver – into fibrin, molecules that are insoluble in blood and form the threads that bind blood clots together.

Blood clotting is a complex process that involves the action of more than a dozen enzymes. Bock showed that his technique worked with five additional enzymes. “I demonstrated that anyone with a lab and a budget of $5,000 could make the key compound and label their enzyme with any probe that they wanted,” he said.

His technique was picked up and widely used in the community of researchers studying blood coagulation. For example, the Oklahoma Medical Research Foundation’s Charles Esmon has acknowledged that Bock’s technique played a key role in his discovery of an important protein in a critical anticoagulation pathway, a process the body uses to dismantle blood clots. This protein, called endothelial protein C receptor (EPCR), helps to generate activated protein C, which shuts off blood clotting.

Another career highlight came in 2003 when Bock, his graduate student and others co-authored a paper in *Nature* with Nobel Prize winner Robert Huber, his colleague Wolfram Bode and other members of the Max-Planck-Institut für Biochemie. The paper detailed their collaboration, which included the discovery that a protein called staphylocoagulase was a new type of activator of blood clotting and validated the “molecular sexuality hypothesis” that Huber and Bode made more than 25 years earlier.

“It was the most exciting thing I’ve been a part of,” Bock said.

Most recently Bock has been studying how bacterial proteins such as staphylocoagulase and its relatives attack the blood coagulation system.

A case in point is acute bacterial endocarditis, which accounts for about one case per thousand pediatric hospital admissions and has a mortality rate of 16 to 25 percent. It is caused when abnormal blood flow disrupts the cells covering a heart valve, resulting in platelets binding and fibrin forming at the site of injury.

If the patient has certain strains of staph bacteria in the blood, the bacterial cells attach themselves to the lesion and begin secreting staphylocoagulase that bypasses the body’s regulatory mechanisms and begins to produce fibrin, which attracts even more bacterial cells. That leads to the formation of a squishy mass about the size of a fingertip called a vegetation, which can break into pieces, travel through the body and attach to other organs. As a result, the patient can die of stroke, heart attack or multiple organ failure.

“This is a dire, but common, situation, so our research has a very real therapeutic application,” Bock said.

These days, Bock spends much of his time overseeing his lab in the Stallworth Building. He describes his work as “play.”

“I love trying my half-baked ideas in the lab, usually on Friday afternoons, just to see what’s going to happen,” he said.

He also plays with charcoal, pen and paint, never having lost his love for art. He even married an artist, Sue Mulcahy.

Creating art, he said, is not so very different from performing scientific research.

“Both are creative processes,” he said. “First you gather information. Then you find a corner to pull on and try to discover what it’s connected to. After a while, you start to see the pieces come together.

“Inevitably you go through the frustration stage and think, ‘I can’t do this.’ But when you keep working and trying and lifting the corners to see what’s there, you wind up with a beautiful end result.”

*Additional reporting by David F. Salisbury*

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