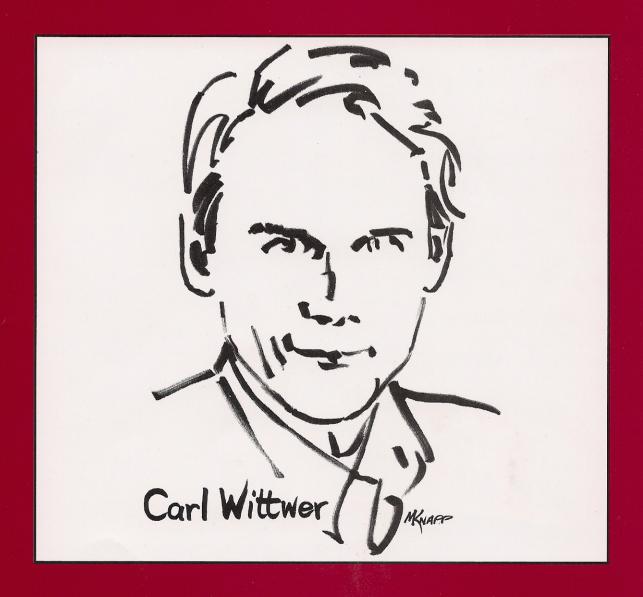
## Clinical Chemistry

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## Carl Wittwer

In the novel *Flatland*—one of Carl Wittwer's favorite books—a humble square living in a two-dimensional world journeys to a universe filled with spheres, cubes, and other filled-out shapes. Astounded, he returns home to share the news only to be thrown into prison for preaching the heresy of three dimensions.

It's not surprising that Wittwer counts the book among his favorites—even as a kid, he was known for his exotic taste. "Friends would make fun of me because I liked to read these very big books about seemingly obscure subjects," said Wittwer, professor of pathology at the University of Utah Medical School. He was a big fan of the *Gormenghast* trilogy by the British fantasy writer Mervyn Peake, which depicts a dark, cobwebbed, Byzantine world crumbling beneath the weight of centuries of treachery, corruption, and repressive ritual.

In sixth grade, while prowling around the local college bookstore, he was drawn to a big orange and black tome with the barely intelligible words, *Atomic Physics*, emblazoned on its cover. "For some reason I latched onto this," he said. The book would inspire a life-defining interest in science.

But *Flatland*, with its dimension-hopping hero, captures something quintessential about Carl Wittwer. Colleagues know him as a brilliant and pioneering scientist who turned polymerase chain reaction (PCR), a mainstay of molecular biological research, from a laborious and time-consuming task into a quick and easy method—overturning fundamental assumptions about how DNA behaves in the process.

He would transform PCR into a tool not just for replicating genes but for analyzing their differences. "He comes up with ways of seeing and using what is not obvious to other people," said Kirk Ririe, CEO of Idaho Technology, Inc. (ITI).

In 1990, he would take his innovations to market by partnering not with big business but old friends Ririe and Randy Rasmussen, turning out prototypes in a corner of a shed housing parts for potato harvesting machines owned by Ririe's father.

Though Wittwer's penchant for crossing boundaries is evident in his work, it is best appreciated in person. Reserved and deliberate in manner, he has a mind that is constantly active, moving between alternative possibilities, examining basic assumptions.

"He doesn't take for granted what everybody else takes for granted. He's always examining the underlying assumptions, asking if what everybody believes is true," said Rasmussen, president and chief operating officer of ITI, who has known Wittwer since childhood.

"It was fantastic working for him because you really had to think things through," said Ririe, who first met and worked for Wittwer as an undergraduate, adding that such freedom is not for everyone. "I'm telling you, to the wrong person, it would be terrifying working in Carl's laboratory because you're expected to just figure it out and do it."



The fact is, Wittwer's approach to teaching is defined by a passionate distrust of his own unexamined premises. "Who knows in whatever aspects of your interactions with people you're living in a Flatland and there's an entire dimension you haven't even dreamed of," he said. "What I've learned is you can't and you really shouldn't trust your own opinion to the exclusion of suppressing someone from the energy they have to follow their own path."

Examining assumptions, his own and others, is something Wittwer has been doing since childhood. Born in 1955 in East Lansing Michigan, he grew up in a somewhat paradoxical household. As the youngest of four children, Wittwer was treated with extraordinary lenience. He was allowed to convert the family basement into a shop where he would take apart and reassemble neighbor's old T.V. sets. "I made a grand mess of the room," he said. He was even allowed to buy mailorder electronic parts and chemicals, "some of which I would use to make my own pyrotechnics."

Nor did his father, a professor of horticulture at Michigan State University and a chemist by training, pressure his young son to follow in his professional footsteps. "Somehow I gravitated there relatively early on myself," he said.

Yet his dad, who was born in Southern Utah, had been raised a Mormon and expected his own family to attend church and follow Mormon customs—practices that Wittwer would question and secretly reject while in high school.

"I believe that anybody who goes through a period of examining the principles they're raised with is

forever somebody who is questioning assumptions," said childhood friend Rasmussen.

Wittwer was at the end of his second year at Middlebury College in Vermont—the age when young Mormon men are expected to go off on proselytizing missions—when he finally told his father. In an unspoken compromise, Wittwer transferred to the school his siblings had attended, Utah State University (USU) in Logan, Utah, and began working almost immediately in a biochemistry laboratory.

The fit was so good that, after graduating, Wittwer embarked on a PhD project there, trying out different ways to measure a particular enzyme, pantetheinase. Working on this project over the next few yearsalternated by stints at medical school—he discovered a career-defining impatience.

"The techniques for measuring took a couple of days and that drove me crazy. So people would joke that I actually spent about two of the three years of my PhD training trying to turn those assays into assays that could be done in about 15 to 30 minutes. But for me that time was worth it," Wittwer said.

In the late 1980s, as an assistant professor and director of the flow cytometry laboratory at the University of Utah, he would apply a similar approach to the newly invented PCR, speeding the process and ultimately showing that DNA responded much more nimbly to manipulations than believed.

Wittwer would balance his laboratory persona in an offbeat way. Soon after arriving at USU, he began studying the slow deliberate movements of pantomime. "I liked the rigor and the exercise and perhaps the nonverbal piece. And the instructor liked me," he said. That instructor, a kind but "socially unacceptable," six times-married gentleman, invited Wittwer to join a small mime troupe that met every morning at 7 AM. "The practice was less for performance and more a self-group exploration in communication," said Wittwer.

He did take his acting skills into the real world a few years later. As a graduate student, he would disguise himself as a freshman and attend the honors beginning students' retreat, "just to see what it was like being a freshman," said Ririe. "He had sort of a baby face that let him get away with it," said Rasmussen.

Wittwer possessed another feature that contributed to his success in mime—and the laboratory. "Carl has beautiful hands, though he would be embarrassed to hear me say that," said Ririe. "His handwriting is minute and carefully crafted. And watching him work in the lab—he works with this deft precision."

His success in the laboratory would put Wittwer much in demand. In the early 1990s, as the field of clinical chemistry was moving in a more molecular direction, David Bruns, then the editor of Clinical Chemistry, wanted to recruit Wittwer to the editorial board. "He was the guy I wanted," said Bruns, professor of pathology at the University of Virginia. Wittwer eventually said yes. "Oh my god, we celebrated," said Bruns.

Hearing that might embarrass Wittwer. "Carl doesn't like being honored as an authority," said Rasmussen. "The prestige that many people are after—that feeling that you're important and that other people know it-Carl seems somewhat repulsed by that. He will get a major award and not tell anyone. He got the governor's award here and didn't tell a soul. He's not comfortable being the authority figure that he's been preaching people should question."

Wittwer must have appreciated his status as an authority on at least one occasion. In 1993 he was invited to consult with a company in Maine, a supplier of agarose, and met Noriko Kusukawa, who had just come over from her native Kyoto. Wittwer, who had spent almost all his waking hours in the laboratory and had rarely thought about marriage or family, kept in touch with her over the next few years. "Later I convinced her to follow me back to Salt Lake City," he said. They married and, in 2001, had a son, Tori. It has been a perspective-altering experience.

"You do get personal insights both of yourself and other people through your children," said Wittwer. He finds his son's intense fascination with toy trains "hauntingly familiar."

According to Ririe, Tori shares his father's reserved manner, as much as is possible for an eight-yearold. "It's a contemplative household," Ririe said. "We don't own a television set-we refuse to watch," said Wittwer.

He wakes around 7:00 and leaves soon after, usually without eating breakfast. "I can't imagine why anyone would want to do that," he said. Wittwer heads straight for his lab, except on Thursday mornings when he runs 2000 feet up a nearby mountain, Big Beacon, with his business partners, Ririe and Rasmussen. "We have a moving meeting," Ririe said. "We climb this mountain, going as fast as we can while our brains still work."

In the evening, after Tori has gone to bed, Wittwer and Noriko may watch a DVD. "I used to love watching Fellini movies but now it's mostly recreational—sci fi or junk adventure films," he said. One of his all time favorites is Cabaret, which Joel Grey played in mimelike white face. "The whole Nazi Germany cabaret scene—again, you have very strict versus very outward devil-may-care attitudes," he said.

It is a resonant theme for Wittwer. When he was in graduate school, he directed a play written by a close friend "—a very avant-garde play. I'm afraid it was not necessarily to the taste of Logan, Utah," said Ririe.

## **Inspiring Minds**

What was it about? "Fighting authority, of course," said Rasmussen.

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