Profile of Julian I. Schroeder

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Julian Schroeder's research career might have unfolded differently if he had not run into Linus Pauling in the coffee room. Schroeder was a graduate student at the Max Planck Institute for Biophysical Chemistry in Göttingen, Germany, and was torn between attending a seminar on plant science and a speech by Linus Pauling on nuclear disarmament. As he pondered this dilemma, Schroeder took a break to grab a cup of tea. "I opened the door to our lab's coffee room, and who's sitting there? Linus Pauling!" says Schroeder. Pauling was by himself, and Schroeder got to discuss everything from nuclear disarmament and physics to chemistry.

Thanks to his chance encounter with Pauling, Schroeder decided to forgo Pauling's speech and attended the plant science seminar, which would set the ball rolling for a long and fruitful career studying plants. Schroeder has spent most of his career characterizing plant ion channels and elucidating the mechanisms by which their regulation helps plants resist environmental stresses. He has described the signaling pathways that regulate stomatal guard cell movements and has improved our understanding of how plants protect themselves from drought, high salt, and heavy metals, with practical implications for improving crop plants. Now a Novartis Distinguished Professor in Plant Sciences at the University of California, San Diego, Schroeder was elected to the National Academy of Sciences in 2015. In his Inaugural Article (IA), Schroeder describes a mechanism by which guard cells sense carbon dioxide, which is relevant for understanding how plants cope with increasing levels of atmospheric carbon dioxide (1).

Circuitous Path to Plant Research

Schroeder says his mother instilled a sense of self-sufficiency in him. She became separated from her Bulgarian/Czech family in Bulgaria during World War II at the age of 15 years and ended up on her own in the West at the end of the war. She eventually immigrated to the United States by herself and has retained a positive and accepting outlook.

Schroeder says he has long been interested in plants, beginning with the time he and a friend cultivated a vegetable garden as undergraduates at the University of Göttingen. "I bought an old truck and converted it into a tiny house," he says. "I lived for a year-and-a-half in this abandoned overgrown apple- and plum-tree orchard, and that's where we had our vegetable garden and where I first started working with plants."


Julian I. Schroeder. Image courtesy of Erik Jepsen (University of California, San Diego, La Jolla, CA). Copyright Regents of the University of California.

It would take a few years before plants became the focus of Schroeder's research. Schroeder studied physics as an undergraduate, and after completing the second-year examination, decided to take a semester off and get a job, an experience that would guide him toward a new interest. "I worked with physically and mentally handicapped persons, and I became fascinated by the question of how the brain works."

Upon resuming his studies, Schroeder started doing internships in biophysics and neurophysiology laboratories. "I realized I could focus on the area of biophysics that looks at the inner workings of neurons," he says. Schroeder began work on a master's degree at the Max Planck Institute with biophysicist Erwin Neher, who had recently developed the patch-clamp technique for studying electric currents in individual cells. Neher would later share the Nobel Prize in Physiology or Medicine with colleague Bert Sakmann for developing this technology. "I was

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This is a Profile of a recently elected member of the National Academy of Sciences to accompany the member's Inaugural Article on page 11129.

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planning a possible PhD project studying hippocampal neurons," says Schroeder. "So I was on a path very different from plants."

It was the view from the laboratory window that precipitated a change in Schroeder's research direction. One day, Schroeder was staring out at the forested countryside with a colleague, Julio M. Fernandez. "Julio pointed out that not much was known about electrical ion channels in land plants at that time," says Schroeder. Intrigued, Schroeder and Fernandez decided to look at ion channels in plants.

Shortly after, Schroeder attended the plant science seminar in lieu of Linus Pauling's speech, and found out that hardly any voltage-clamp electrophysiology had been done on higher plants. The duo met Klaus Raschke, an international expert on plant stomata. Raschke referred Schroeder to his graduate student Rainer Hedrich, who was studying metabolism in protoplasts. "With that, we started doing electrophysiology experiments on plant protoplasts," says Schroeder.

"We found that there are potassium channels in guard cells," says Schroeder (2, 3). "The community was quite excited about our findings," he says. "The first time I presented our findings at a meeting in Vienna, the speaker before me stated that land plants don't have ion channels, which encouraged me that we were on to something."

Neher gave Schroeder the option of focusing his PhD work on plant cells rather than his original goal. "I decided I wanted to move into this new direction of plant sciences."

Uncovering the Secrets of Plant Stress

After a postdoctoral stint at the University of California, Los Angeles, Schroeder developed an interest in the signaling mechanisms by which plants respond to abiotic stresses. When he started his own laboratory at the University of California, San Diego, he decided to merge plant electrophysiology and genetics to explore how plants respond rapidly to drought.

Schroeder was particularly interested in stomatal guard cells. "These are cells in the leaves that form stomatal pores through which plants lose water through transpiration or evaporation, and, at the same time, take in carbon dioxide for photosynthesis," he says. "When plants experience drought, they would preferably close these pores, if they are more drought-resilient," says Schroeder.

Figuring out how these cells work was a challenge. *Arabidopsis*, a plant species with well-developed genetic tools, happened to have tiny guard cells. "It was thought that they would be too small to apply patch-clamp techniques," says Schroeder.

Schroeder and coworkers (4) eventually developed patch clamping of *Arabidopsis* guard cells. "That was really important because we were able to do electrophysiology on mutants, and we started characterizing genes and mechanisms by which plants close their stomata," says Schroeder.

Schroeder was simultaneously using other experimental systems to identify genes involved in plant ion channels and transporters. "We used *Xenopus* oocytes as an expression system to express plant ion channels and study their function," says Schroeder. His laboratory also identified potassium and sodium transporters, and, together with collaborators at UCSD, characterized a plant aquaporin and a nitrate transporter-encoding gene. Schroeder also showed that a clade in a sodium/potassium transporter family that he and his colleagues isolated, the HKT transporters, protects *Arabidopsis* from salt stress via a unique sodium transport mechanism (5–7).

Schroeder's research has helped elucidate many of the mechanisms and pathways involved in guard cell signaling. One of the key signaling molecules that Schroeder worked on was abscisic acid (ABA), a plant hormone produced in response to abiotic stresses, such as drought and salinity. "ABA downregulates growth to protect the plant from these stresses, and, among other things, it closes stomatal pores so plants lose less water," says Schroeder. "We were able to resolve early signaling mechanisms at a temporal resolution, so our research has led to an understanding of a number of early mechanisms of how ABA signals."

How Stomata Sense Carbon Dioxide

Another important signal for stomatal closing that Schroeder has been working on is elevated levels of carbon dioxide. "At night, photosynthesis is inactive and respiration inside leaves leads to higher CO_2 concentrations, which tells the stomata it's night-time and they might as well close their pores," he says. "We want to identify how CO_2 regulates water loss through the stomatal pore apertures."

It is a question of current relevance. "We're experiencing this very steep rise in atmospheric CO_2 that, on a global scale, is narrowing stomatal pores in plants," says Schroeder. "How is that affecting crop plants and trees, and how does CO_2 control how plants lose water?"

Schroeder found that enzymes called carbonic anhydrases inside guard cells accelerate the CO_2 response by producing bicarbonate, suggesting that bicarbonate is an important intracellular messenger that signals this response. That raised another question: What are the actual bicarbonate or carbon dioxide sensors inside the plant?

Schroeder previously identified slow anion channels in guard cells, encoded by the slow anion channel-associated 1 (*SLAC1*) gene (8–10). "With collaborators we found that in *SLAC1* mutants, the slow anion channels are disrupted and the stomata don't close very well because you've removed a major mechanism through which guard cells reduce their turgor and close stomata," he says (10).

"Some of our recent research is pointing to the hypothesis that slow anion channels may be one of the bicarbonate-responsive proteins in guard cells, although not the only sensor," says Schroeder. He investigated the involvement of SLAC1 in carbon dioxide/bicarbonate sensing in plants, and describes his results in his IA (1).

The researchers used a combination of computer-aided molecular dynamics modeling and experimental assays providing evidence for the model that SLAC1 plays an important role in carbon dioxide/bicarbonate sensing in guard cells. They found that mutating some predicted putative bicarbonate-interacting sites in the SLAC1 channel impaired the carbon dioxide/bicarbonate response in *Xenopus* oocytes. Using patch-clamp and gas exchange analyses in transgenic plants, the researchers identified a specific SLAC1 residue required for carbon dioxide/bicarbonate enhancement of slow anion channel activity and carbon dioxide-induced, but not ABA-induced, stomatal closing.

These findings point to SLAC1 being one of the carbon dioxide/bicarbonate sensors that mediates carbon dioxide signaling during control of stomatal movements, and provide important insights into how plants respond to rising carbon dioxide. Understanding the pathways involved may aid the development of plants that can adapt to climate change.

Basic Research with Applications

Studying carbon dioxide in guard cells is not the only avenue of Schroeder's research with practical applications. "We are often motivated by questions that are relevant for present-day problems, and we focus on the fundamental underlying mechanisms," he says.

Schroeder's research on the HKT sodium transporter family has helped plant scientists and breeders boost the salt tolerance of crop plants, such as rice and wheat. "It turns out that this HKT1 transporter mechanism is of major importance in crops for breeding enhanced salt tolerance, as others have now shown," he says.

Schroeder and collaborators also discovered plant transporters that could play a role in how plants accumulate and protect themselves from heavy metals. "Some of the genes and mechanisms could potentially be used to avoid accumulation of toxic metals and arsenic in the edible portions of plants, or could have an impact on removing heavy metals or arsenic from soils," says Schroeder.

Additionally, Schroeder and his colleagues have long been working on how plants resist drought. "The research community has discovered various mechanisms that you can manipulate to obtain plants that are more drought-resistant," he says. Applying these mechanisms to crop plants could have a huge impact, but Schroeder notes that translational research is in its early stages.

"There are many avenues to affect the way a plant responds to drought emanating from this research, but it could take 5 to 10 years or so to see which ones may be working best in combination in which crops in the field," Schroeder says. "Clearly, there will be many useful tools that build on basic discovery and knowledge."

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