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Exploring the World of Plant Biology: An Interview with Dr. Elizabeth Sattely

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Dr. Elizabeth Sattely is an Associated Professor and HHMI Investigator in the Department of Chemical Engineering at Stanford and a Stanford ChEM-H Faculty Fellow. Dr. Sattely is interested in understanding how plants use creative chemical maneuvers to adapt to environmental stresses and communicate with other kingdoms of life as well as each other. Dr. Sattely's research focuses on identifying and engineering plant metabolic pathways which allows for exploration of possibilities in enhancing plants' fitness. Further, Dr. Sattely's lab investigates the impact of food chemistry on health and develops innovative ways of investigating plant pathways.

Dr. Sattely attended Boston College for her graduate degree followed by post-doctoral work at Harvard Medical School where she worked on biosynthesis of antibiotic and bacterial natural products. Dr. Sattely and her lab has been recognized by an NIH New Innovator Award, a DOE Early Career Award, an HHMI-Simons Faculty Scholar Award, a DARPA Young Investigator Award, and a AAAS Mason Award for Women in the Chemical Sciences.

JH: Could you tell us a little bit about your educational journey [and] your research journey?

ES: Sure, I'll start with my educational journey that began with coursework and incorporated research over time. My undergraduate degree is in chemistry. Towards the end of my time as an undergraduate, I started doing research in the lab and worked on organic synthesis. I pursued my PhD in organic chemistry: developing new reactions, reaction methods, as well as working on total synthesis of natural products. So, I was very interested in compounds that were found in nature, and how chemists might be able to develop synthetic routes to produce those molecules.

After my PhD which was strictly in synthetic chemistry, I got more interested in how molecules are assembled in the context of nature using enzymes. So, I was really excited to have an opportunity to work with Chris Walsh at Harvard Medical School, who at the time was looking at antibiotic and bacterial natural product biosynthesis. I worked in his lab as a postdoc trying to identify enzymes that could put together the small molecules that bacteria use for defense against other bacteria or for acquiring nutrients like iron from the surrounding media.

JH: You mentioned that your undergrad degree was in chemistry. How do you think that has impacted your current research in chemical engineering?

ES: I didn't know at the time that, as a PhD student, I was really learning a language of thinking about molecules, intrinsic reactivity, and molecular structure. At the time, I was very focused on organic synthesis, but I was really learning about how atoms bond, how reactions take place, and a language which I now see can be applied in so many different areas. It has forever changed my perspective of the world because I now view the world through the lens of molecules.

I never thought I would be working in the area of plants. I thought ‘that's a hobby,’ and I never saw how those two things could meet. The impact certainly is the perspective I can offer in different areas of biology. And hopefully, as I'm learning so much from my colleagues who have deep expertise in biology or botany or different aspects of plants, I can offer the perspective of chemistry.

JH: What did you originally think you're going to focus on?

ES: I followed, at the time, amazing and inspiring instructors and professors I had in class. I just liked doing the work and thinking about organic chemistry and organic synthesis. I thought it was interesting that all these molecules are there, and even though I can't see them with my eyes, they're running the show. I didn't really know where that was going to take me—I followed my interest every step of the way. It was at the time when I was applying for faculty jobs where I really took stock of everything I had learned and what I thought would keep me motivated and excited throughout the duration of my career. That brought me to thinking about plant chemistry.

JH: I understand that you do a lot of exciting work in understanding plant metabolic pathways; could you tell us a little bit more about your research?

ES: Yeah, sure. When I started my own lab, I was still very interested in biological chemistry and the different types of diverse molecules that have evolved in nature to enable organisms to survive environmental stress. And I got really interested especially in the chemistry of plants given that we rely on plants for food for medicine, renewable energy—so many things that are critical. To me, it was really fascinating to understand how they use their chemistry to cope with the fact that they are sessile—they can't run from predators or pathogens or move to a new environment. How do they use chemistry to cope with those stresses and also to communicate either with other plants or between kingdoms of life such as microorganisms growing the roots or fungi growing in the soil? And so that's what I decided to focus my research program on—to dissect this really fascinating chemistry that comes from plants.

JH: What do you think are some practical applications of your research? How would that inform other fields of understanding?

ES: Plants as a kingdom are challenged with the same environmental stressors that we face but also so many different stressors. And to me, it's just fascinating to learn about different strategies that have evolved across the plant kingdom to deal with these common problems. How do you get micronutrients from the soil? How do you deal with aggressive viral pathogens or bacterial pathogens? How do you cope in drought conditions or high salinity? In my view, if we can understand what are some of these really cool strategies that have evolved in different parts of the plant kingdom, we can then potentially use engineering to take a solution to a problem that has evolved in an exotic plant and move it into one of the crops that we currently grow for food in a way that you could never accomplish by trying to breed those two plants together.

JH: What's an example of this sort of engineering?

ES: We're really only scratching the surface for how this might work. For example, to take immune receptors that enable plant to respond to a particular pathogen and put them into the crops and mostly monocots that we use for food might enable that plant to mount its own defenses against that pathogen if only it could perceive it. So that's just one idea. These kinds of things have been done in the academic literature, but I think our science and engineering is not quite there yet to be able to make these plants in a way that can be used in large scale agriculture.

JH: What do you think is one of most exciting challenge in the field of plant biology?

ES: They're certainly ones that surround my research. I think one of the biggest challenges that we face right now is: how do we produce food in a sustainable way with the minimum amount of chemical input, environmental destruction, minimizing waste? I think those are huge challenges in how we use plants for human needs, and there's a lot of room for metabolic engineering and chemistry to contribute there—to not only enable high yield output from plants and the growth of the food we need, but do it in a way that reflects environmental sustainability and acknowledgement of caring for ecosystems.

JH: These big issues you’ve mentioned require a lot of different fields to come together and solve, and chemical engineering is a very large, interdisciplinary field. How would you define chemical engineering or the type of problem that it's suited to help to solve?

ES: Yeah, I think that the problems that chemical engineers address have changed over time, but the foundational principles of chemical engineering—thermodynamics, kinetics, transport, and molecular analysis—stand. Those remain critical principles that we can apply to any problem that comes our way in the future. For example, as we shift and think about the generation of sustainable energy or sustainable agriculture, those foundational principles will enable us to serve all those new challenges going forward.

JH: In the context of Covid-19, I understand that there has been much development and research as well as higher demands for therapeutics and vaccines. How has that impacted your area of research or research in chemical engineering?

ES: A major strength of chemical engineers is to think very quantitatively about biological systems. And there's a huge need for that type of analysis in thinking about a pandemic: how a virus evolves, how populations are affected by a virus, and therapeutic modalities. Vaccine development requires all the skills of a chemical engineer.

In my personal research and the work that we do in the lab, Covid-19 has provided additional motivation to think about problems that might be coming our way that we might not anticipate. How do we get ourselves as prepared as possible?

In my lab, we're not focusing on COVID vaccines or pandemics of that nature, but certainly what we've gone through over the last few years has made me think more about vulnerabilities in our system. On one hand, that might be a virus that infects humans; and in another context, it might be pathogens and viruses that influence our food systems. I think the silver lining is just a reminder that we need to be thinking forward, and the challenges could be right around the corner.

JH: What do you think is the most effective way to comprehensively tackle environmental dangers such as pathogens? I understand we can engineer plants, and there's also a lot of conservation efforts—how do you see different strategies come together to promote sustainability?

ES: Interdisciplinary approaches are critical. There is no panacea of solutions—we need to have layers of security. The idea that we might be able to create one technology that will protect everyone from impending doom is short-sighted. We need to have layers of protection and security built in to help us slow a pathogen in its path. When it comes to food systems, we can't think, ‘we’ll create a plant that is resistant to a certain pathogen or a virus.’ We need to think about: how do we diversify our food systems? How do we distribute where we do food production and to have multiple layers of security built in?

JH: Where do you see other fields in these layers of protection?

ES: One thing that we've learned in the agricultural area is that food is very closely tied to culture. Making changes to food systems involve really engaging different populations of individuals and understanding how they think about food, how they use plants for food and what might work in that area under those conditions. One thing that I really like about the School of Sustainability is bringing in experts from other non-engineering fields—sociologists, psychologists, economics experts—to think about all the different aspects of something as big and broad as agriculture and in the direct case of COVID health care.

JH: There’s much inherent complexity in biology, and it can be difficult to know something for certain. How do you deal with that element of uncertainty in research?

ES: Yeah, there're two sides to that coin. One, you can look at the complexities of biology and feel discouraged like you're never going to understand it all. On the other hand, it can just be endlessly fascinating. For example, you know there's this problem of fitness selection, and you've thought of all the possible ways a cell might be able to deal with it. And then when you look at a system, you find something that you never could have imagined—and it's just so endlessly fascinating. I try to stay on the side of being fascinated and surprised and enjoy the idea that there are solutions out there yet to be discovered. Constantly, we're taking what we understand as humans and weaving them into a story of how nature works. And that story is being rewritten every single day with every single experiment people do and new things they discover.

JH: What do you think has been the most surprising, impactful discovery in the field of biology in general?

ES: There're so many out there. There're a lot of tools that have been incredibly impactful because they've enabled our understanding of biological systems. In the course of my training, hearing the stories and the discoveries of the CRISPR system was exciting. When I was a graduate student, CRISPR wasn't a thing. There were some labs working on it perhaps as a curiosity—a process of someone poking around and saying, 'this is unusual sequence, a funny pattern presented by nature' and investigating whether that pattern have a purpose. More and more discoveries were made until we learn that this was a whole gene editing system that had been sitting there—right before our eyes—and nobody knew about it, and now it has completely changed how people do research in every single corner of life. To me, that's just fascinating. It makes me think about what's there right now that we don't see, but that we're going to learn about in the next five or ten years and will completely change the direction that science goes.

JH: How is CRISPR used in research?

ES: There're two major ways we can understand how a biological system works. We can break it and see which genes and components of an organism are necessary for a function, or you can try to rebuild it from scratch. Both those things are complementary and provide different ways to really understand how an organism works and give us our latest and greatest model of how it functions. CRISPR has enabled making changes in genomes that were completely unattainable. Precision gene editing has completely changed the game.

JH: I imagine CRISPR is at the frontier of current research. What are some other research areas at the edge of making very exciting discoveries?

ES: I think engineering and studying complex multicellular organisms and organs is one of the huge things going forward. So much of what we understand about biology has come from simple systems, but current developments allow for *in vivo* study of the most complex organ we know—the brain and the nervous system. Being able to do that in the context of a whole multicellular organism is the next frontier.

At the same time, making measurements on enormous scale with very low concentrations of molecules is another frontier. Sequencing is constantly changing where we're not just taking the most abundant things but really digging deep to understanding how life is working. Taking the field of immunology as an example, in the diversity of all the antibodies that are in a human is a footprint of what pathogens and antigens that person has encountered. Coupled to making measurements is our ability to use computation to mine those data.

JH: In a multi-component, complex biological system, how would we ascertain which specific stimuli led to which specific effect?

ES: It’s very hard to be certain about how a biological system functions. We're just building a case—a model for how something works—and we're constantly gathering more data that supports, refutes, or refines our model. We get closer and closer, but it's an asymptote. I don't think we're ever going to, at least in my lifetime, be able to completely recapitulate the complexities of a multicellular organism. But we get closer and closer as we go and at some point, using machine learning and AI—and this is already happening—will help us along that that path.

JH: Do you have some advice for students who might be interested in chemical engineering or plant biology?

ES: I think chemical engineering is just a fabulous set of quantitative, foundational tools that you can apply to any problem that really motivates you and that you feel passionate about. It's just such a great skill set and a privilege and opportunity to be able to learn those things, and then interact with folks that have a big problem on their hands and think about what kinds of engineering solutions you might be able to come up with. Even when you take a class that doesn’t necessarily seem relevant—when you don't see the connection to what you're working on—these classes build foundational skills that you will need for problem solving going forward. Keep an open mind as you're learning about all these different principles and think about how they might be synthesized later and inspire you to take a unique approach to addressing a grand challenge.