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A Conversation with Carol Robinson

Carol Robinson, Oxford University

Katharine Sanderson, *C&EN*

The analytical chemist discusses her career and pioneering work in mass spectrometry

Dame Carol Robinson, Professor of Chemistry at Oxford University, has excelled at pushing electrospray mass spectrometry to places thought impossible. With the technique, which analyzes aerosolized droplets of samples, she has studied the structure and function of membrane proteins—molecules that are present in all cells and are popular drug targets. Katharine Sanderson recently met with Robinson to talk to her about what drew her to this particular analytical method and the remarkable things it can do.

Your career path has been rather unconventional. Can you tell us the story?

I left school early at 16 to become a technician at Pfizer. I rotated around different labs, but when I got to the mass spectrometry lab, I just loved it. This was my passion; this is what I wanted to do. Then I studied part time, went to Cambridge to do a Ph.D., and worked with great people who really inspired me to carry on. I did something unusual in taking a career break, and then I came back eight years later to Oxford to do a postdoctoral research position. I went back to Cambridge to be a professor, then back to Oxford—a bit of a yo-yo!

What is it like to study membrane proteins with electrospray mass spectrometry?

Membrane proteins are incredibly difficult because of solubility problems. Electrospray is a technique whereby things have to be soluble initially. But once you're in the gas phase, this is the whole beauty of it: It doesn't matter if one part is soluble in a very hydrophobic substance, and one part is very polar, because the solvent is all gone. It's a really beautiful phase in which to examine membrane proteins.

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What did you realize you could do with this technique?

I was using electrospray to look at a protein and how it folded. Then I started to look at proteins with cofactors present. I saw—and I didn't expect to see—that the cofactors stuck to the proteins in the gas phase. I thought, "That can't be right, because we know proteins require water for interactions, and there's no water, so it's an artifact." But the more I looked into it, I started to think it was telling me something.

What has been one of the more impressive feats you've accomplished using electrospray?

In 1999, we studied an 800-kilodalton molecule. It was a molecular chaperone, a very big double-doughnut complex—a protein that has 14 subunits all held together by noncovalent forces. What it meant to us was that if we have large protein assemblies and don't have any crystal structures, we'll still be able to predict what's happening to them.

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What other molecules associated with the proteins can you study?

We're asking about what determines which lipids are important for protein structure. We'd like to figure out how you could preserve more of the natural membrane and get a lovely assembly of membrane proteins communicating with each other with the correct lipids between them.

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Have you had to deal with skepticism about your approach to mass spectrometry throughout?

Yes. I wonder if I will ever have to stop. For example, recently with three membrane protein complexes, we had to do functional assays in solution to show that the lipids we'd determined were the correct ones. I felt we had to go a lot further to convince than if we'd presented a crystal structure.

Katharine Sanderson is a freelance writer for C&EN, the weekly newsmagazine of the American Chemical Society.

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