

Ivano Bertini

Building on his contributions to NMR methodologies for studying metalloproteins, Bertini has been instrumental in bringing together inorganic chemists and biologists interested in metals in biology.

In Italy—just outside the center of Florence—sits one of the premier NMR centers in the world. Ivano Bertini is the director of the Center of Magnetic Resonance (CERM; <http://www.cerm.unifi.it/home/>) at the University of Florence—a center that has been, quite literally, built around NMR spectrometers. Bertini and his colleagues have been exceptionally successful in developing methods for looking at metalloproteins by NMR and have turned these methodological advances into significant new insights into the structure and function of these proteins. Along the way, Bertini has been an important force in advancing the field of metals in biology.

After receiving his doctorate at the University of Florence in 1964 studying coordination chemistry under Luigi Sacconi, Bertini first went to the ETH in Zurich to learn NMR spectroscopy and then on to Princeton University to work with Bill Horrocks, who was using NMR to look at paramagnetic metal ions. Bertini then began work in his own lab on inorganic complexes. It was a few years later, in 1974 during a sabbatical with Harry Gray at Caltech, that Bertini first became engaged in bioinorganic chemistry. Gray remembers, “I could tell right away when Ivano came to my lab that he was going to shake up the chemistry world.” Bertini was drawn to studying the inorganic chemistry of biomolecules, rather than coordination complexes, because he saw that “metalloenzymes were becoming a frontier field.” Bertini notes that he has “always tried to focus on frontier fields, using whatever techniques are necessary, rather than focusing on a single technique. Therefore,” he laughingly adds, “NMR has been a constant in my life.”

Following his return to Florence as a full professor in 1975, Bertini began working on developing solution NMR methods for looking at proteins containing paramagnetic centers, such as Cu(II) ions and Fe-S clusters. This was a significant challenge, he describes, because the paramagnetic center influences the nuclear relaxation of neighboring atoms and is a point of discontinuity in a network of structural restraints. This is particularly problematic because it causes you to be “half blind,” Bertini explains, “just at the site where the enzymatic function or important events occur.” However, continual efforts by Bertini and his colleagues at CERM to develop new methods for visualizing the protein structure around paramagnetic centers culminated in the first solution structure of a paramagnetic metalloprotein in 1994. As Gray describes, these advances were “truly pioneering.”

Currently, Bertini and his colleagues continue to work on methodological advances in NMR, while at the same time using this structural expertise to understand the functions of metalloproteins. For instance, Claudio Luchinat, a professor at CERM, is looking at the potential of solid-state NMR as a tool for determining the structure of proteins that would be difficult to solve by X-ray crystallography, such as membrane proteins and protein aggregates. In solid-state NMR, solving structures is difficult because unlike solution NMR there are fewer NOE-like structural restraints; however, paramagnetic ions may turn out to be an advantage in this case because they provide “pseudo-contact shifts” that can make structure determination possible. Lucia Banci, another professor at CERM, is using solution NMR to understand cellular copper trafficking pathways and their misfunction in

disease. In a complementary approach, Antonio Rosato, an associate professor at CERM, develops bioinformatic tools for understanding how metals are distributed within cells. As Luchinat notes, one thing that is unique about this center is that “we have a critical mass of senior people who really work together.”

Bertini and his colleagues are engaged in an impressive array of international collaborations. “Bertini reaches out by the nature of his personality,” says Tom O’Halloran, a professor at Northwestern and longtime collaborator. O’Halloran adds, “Ivano loves to connect—he is a very broad thinker who keeps his eye on the big picture.” Joan Valentine, a professor at UCLA, is another longtime collaborator who periodically spends time in Florence. “Ivano saw where ‘metals in biology’ was going before anyone else,” says Valentine. “He really understood the revolution that would come from genomic and structural information.” What is it like to collaborate with Bertini? “When Ivano

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is around, the kinetic energy in a room immediately doubles,” says O’Halloran. The scientists at CERM are “just like an Italian family,” notes Valentine, and collaborators are welcomed into this.

In addition to creating a network of collaborators, Bertini has played an important role in drawing together the field of bioinorganic chemistry. In the early 1980s, the importance of metals in biology was growing, but according to Bertini, “mainly in America.” So Bertini flew first to New York City for the National American Chemical Society meeting in 1981, then to Sweden and finally to Switzerland to enlist coorganizers for an international meeting. Following this tour, Bertini, together with Gray, Bo Malmström and Helmut Sigel, organized the first International Conference on Biological Inorganic Chemistry (ICBIC) in Florence in 1983. As Bertini remembers, with Malmström, “I had the power of the president of the Nobel Prize committee in chemistry,” so when Bertini invited speakers to attend the meeting, “no one could say no.” Following the success of this first meeting, ICBIC (<http://www.sbichem.org/meetings.php>) has become the major international conference for bioinorganic chemists, with the 14th biannual meeting to be held 25–30 July 2009 in Nagoya, Japan.

Florence may seem an unlikely spot to be the home of a state-of-the-art center for NMR. Even more surprisingly, many of the professors at CERM are native Florentines, including Luchinat, Banci and Rosato. Bertini himself originated more distantly—from Pisa. Bertini says that in a country where there are few resources, “we need synergy to survive.” At CERM they have clearly done much more than survive—the institute has served as a magnet, drawing scientists from around the world to Florence for the opportunity to have a structural glimpse at their metalloproteins.

Joanne Kotz, Cambridge, Massachusetts