Jean-Marie Lehn

By questioning the very nature of how ion channels, brains and societies form and function, Nobel laureate Jean-Marie Lehn has changed our understanding of the chemical basis of self-organization.

As with many curious people, Jean-Marie Lehn has nursed a passion for many fields of study throughout his life. One of the earliest and most influential topics, perhaps, was philosophy. While Lehn took great interest in the big concepts and ideas in the field, his time as a philosopher was short; however, his exposure to philosophy did shape his passion for molecular recognition, or the idea of understanding and manipulating intermolecular interactions on an atomistic level. As he explains, "Knowledge comes out of the brain, and so you begin thinking about the brain, and then ultimately about sodium and potassium channels." Lehn's efforts using preorganized small molecules to mimic the exquisite selectivity manifested by those ion channels in recognizing specific metals led to a paradigm shift in chemical thinking, and ultimately to his receipt of the Nobel Prize in 1987 with Donald Cram and Charles Pedersen. Indeed, Lehn's early enthusiasm for and continual commitment to the fields of molecular recognition and self-assembly have helped illuminate the importance of noncovalent interactions throughout chemistry and biology.

Lehn's early research on natural products gave him a strong appreciation for the general importance of individual molecular details. As a new professor at the University of Strasbourg, however, he was particularly intrigued by recent discoveries in neuroscience of ion channels that selectively transported specific metal ions. Though this research had a very biological basis, Lehn thought there might be a way that a chemist could contribute. He remembers, "This was a question of trying to selectively bind a sphere in a collection of spheres. Then you think about molecular recognition, because that's all this binding is—a recognition process." The molecules he developed, called cryptands, 'recognized' specific alkali metals based on the precise spatial organization of donor atoms. Julius Rebek, Director of the Skaggs Institute at The Scripps Research Institute, recalls that the "invention of the cryptands inspired a generation of chemists to create architectures for molecular recognition."

Following Lehn's initial discoveries regarding the selective binding of metal ions, he continued to explore atomic interactions, creating two- and three-dimensional structures controlled by forces such as hydrogen bonding and charge-charge interactions, and endowed with a variety of functional properties. His motivation throughout was the idea that "like other chemists have learned to handle the covalent bond, we have to learn how to manipulate the noncovalent bond." Although he had always thought that the development of the cryptands was quite interesting, as the various systems he explored grew in number he started to realize that the concept of molecular recognition would be part of a more general phenomenon. Indeed, as these new architectures became more complex and incorporated additional kinds of noncovalent, intermolecular interactions, it became clear that the principles he was using to cause molecules to self-assemble could define a new field. Vince Rotello, a chemistry professor at the University of Massachusetts in Amherst, accentuates this point in saying, "This was the birth of supramolecular chemistry."

Recalling Lehn's early contributions, Rotello comments, "Before anyone else was thinking about this sort of self-assembly, he was pursuing it, and kept taking it down new paths." In his current research, Lehn is still looking for new paths to explore, but has shifted his emphasis to focus less on the individual interactions that occur between molecules and more on the results of those interactions. In particular, his lab is extending their investigations in self-assembly to study labile covalent bonds such as imines and oximes, and how these may be used to drive selection of optimal assemblies for biological or materials applications. In addition, his lab is trying to make molecules report on the interactions they experience by creating materials that selectively fluoresce upon binding.

After years of thinking about how molecules assemble into different groups and structures, Lehn is intrigued by assemblies and mixtures that have novel properties. As a general example, he puts forward that "a single water molecule cannot boil or freeze, but a glass of water can. What's the difference? It's still water. But it's water interacting." As the systems become more complex, these properties also become more interesting. Indeed, pondering this complexity, and the way in which these properties emerge from the chemical properties of the constituent molecules, brings the conversation to an interesting mix of science and philosophy. Lehn concludes, "The most basic process is self-organization. This is why, from the big bang to human beings, matter has become complex. How has this happened? That's what we must try to understand."

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In Lehn's world, organization doesn't just happen on an atomic level. In conceiving the Institut de Science et d'Ingénierie Supramoléculaire s (ISIS, part of the Université Louis Pasteur in Strasbourg), his vision began with the idea that a 'university is universal'—it deals with all branches of knowledge. However, Lehn acknowledges that "in present days, that is illusory, of course. You have to make choices and be good at a given thing." In discussing the unusual organization of the fledgling institute, inaugurated in December 2002, Lehn stresses the multidisciplinarity of the scientists, the focus on junior faculty and the inclusion of private industry labs within the building. Sylvain Ladame, one of the junior professors at the institute, agrees: "The ISIS represents a unique opportunity in France for young and dynamic scientists to be offered some laboratory space, students and financial support to develop their own research project with total scientific independence." In particular, Ladame hopes that the academic structure developed at ISIS "will be inspiring and contribute to the necessary modernization of French academic research."

Since winning the Nobel Prize, Lehn remains dedicated to his research, but is also committed to reaching out more broadly: "A more scientific approach to a number of problems would help a lot. I'm interested in trying to convince the public about the value of science in general, and chemistry specifically." As one of only two modern-day Nobel laureates from France, Rebek says "he's an outstanding spokesman for chemistry—particularly in France and western Europe." Lehn enjoys these chances to engage a general audience, but says "it's difficult to tell the audience that 'you are a bunch of molecules', even though a complex bunch at that! It's difficult for them to accept that." Perhaps the audience members are just hoping that they are more than the sum of their self-organized parts.

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