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From Supramolecular to Systems Chemistry: Complexity Emerging out of Simplicity

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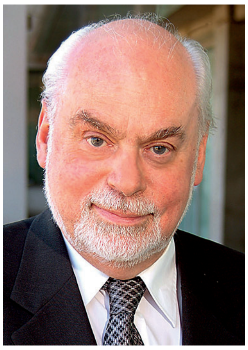

On 1 March 1967, I took my leave of Edinburgh University with a PhD degree firmly in my grasp to take to the air and cross "The Pond" in a jet liner bound for Canada, where I was to spend the next three years at Queen's University, as a postdoctoral fellow in the laboratory of Professor (JKN) Jones. During this, my first ever flight, the parting words of my PhD examiner, Sir Edmund Hirst, were still ringing in my ears, "Whatever you do, Stoddart, make sure you tackle a 'big problem' in chemistry".

My relocation from Edinburgh to Kingston had all the hallmarks of an arranged marriage by Sir Edmund and his former student, JKN. That said, the honeymoon period under the watchful eye of JKN was destined to be short-lived since I was to discover, on my arrival in Kingston, that he was leaving immediately to spend a full year on sabbatical in Brazil. Although I had been handed some lemon gum and asked to unravel its primary structure, I soon realized I could accomplish that task in my spare time, leaving me with ample opportunity to go in search of that "big problem". I was soon to discover it in the form of a Communication published in the spring of 1967 by Charles Pedersen in the *Journal of the American Chemical Society*. In the article, he described the relative ease with which he had synthesized a large ring compound—which subsequently became known as dibenzo[18]crown-6—in a respectable yield of 44–48 % for those times, as a consequence of the templating action of potassium ions present in the reaction mixture.

The rest, as they say, is history, which has already been more than adequately chronicled in a fine Editorial by François Diederich under the banner of "40 Years of Supramolecular Chemistry" (*Angew. Chem. Int. Ed.* **2007**, *46*, 68–69). All I would add some five years later, on the occasion of the Silver Jubilee of the award of the Nobel Prize in Chemistry to Charles Pedersen, Donald Cram, and Jean-Marie Lehn, is that the advent of supramolecular chemistry has helped to usher in a new age of "Beauty in Chemistry", the history of which has been captured quite magnificently in a book, edited by Luigi Fabrizzi, that appeared only a few months ago carrying this very title. As chemistry reached out beyond the molecule, not only did beauty continue to express itself in the shape of a crystal, or the color of a pigment, but it also started to surface in a number of trend-setting ways—for example, the architectural beauty evident as a result of the formation of a complex, or the nontrivial molecular topology revealed in catenanes and knots. Supramolecular chemists were quick to draw analogies between their supramolecules and works of art and architecture, sculptures and writings, emblems and logos, and everyday objects and activities.

These cultural developments were accompanied by a highly visual paradigm shift as the representation of small covalent molecular structures gave way to the need to portray superstructures of increasing size and sophistication, yet often still featuring simplicity with all its inherent elegance. Graphical representations (cartoons) started to appear with increasing regularity and color slowly but surely supplanted the austere black and white regime of previous times, but not without some spirited opposition in the early days.

As supramolecular chemistry witnessed the creativity of its first generation of practitioners in the presentation of their molecules, one could spot—while thumbing through the pages of the journals, a Busch or a Cram, a Gutsche or a Rebek, a de Mendoza or an Ungaro, a Cramer or an Etter, a Balzani or a Vögtle, a Desiraju or a Raymond, a Fujita or a Sessler, an Echegoyen or a He Tian, or a Lindoy or a Stang—a mile away before even setting eyes on the authorship of a paper. There were no followers, only inventors and innovators in the best tradition of chemistry, and I mean chemistry, for the reunification of chemistry was to begin under the supramolecular banner. As articulated so well by François Diederich, supramolecular chemists—whether they be a Tabushi or a Reinhoudt, a Nolte or a Sanders, a Shinkai or an Atwood, a Hamilton or a Stupp, an A. P. de Silva or a Kimoon Kim, or a Whitesides or a Lehn—have done much to unite the factions within chemistry and, in so doing, have reached out beyond its diffuse boundaries into the domains of physics, biology, materials science, engineering, and nanotechnology, to mention but a few of the key disciplines that have fallen under the spell of chemistry beyond the molecule. Supramolecular chemistry has also conspired in so many different ways to raise the intellectual appeal of chemistry, as well as attract some of the brightest young minds in our time into its alluring fold.

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Yet times move on, just as they did for me in 1967. Chemists have to identify and tackle the next "big problem". It is more likely to happen if students shy away from continuing to pursue research lines promoted by their mentors, after the manner in which I forsook lemon gum for crown ethers! I don't pretend to have identified the next "big problem" for if I had, I would not be writing about it here, I would be wrestling with it in my laboratory. In general terms, however, I advocate forsaking simple systems for integrated ones, which, in practical terms, could mean our deserting, in large numbers, the comfort zones provided by solid and solution phases for the challenges posed by soft matter, not to mention surfaces and interfaces. We also need to encompass research directions that are function-oriented and application-driven. In this regard, there could be wisdom to be found in embracing robust hybrid materials in compartmentalized settings, where properties leading to commercialization stand a reasonable chance of emerging quite unexpectedly.

In the adventuresome act of going supramolecular, chemists took chemistry and widened its scope conceptually to encompass molecular recognition and self-assembly processes, not forgetting self-sorting and self-replication that are part and parcel of biology. The adoption of these concepts led to the development of template-directed syntheses and the birth, for all practical purposes in the hands of Jean-Pierre Sauvage, of a new chemical bond—the mechanical bond—which has led to the design and construction of artificial molecular switches by the hundreds. While their introduction into integrated systems has raised some expectations in the realm of molecular electronics, a lack of robustness continues to plague their performance. How to find the appropriate integrated system or hybrid material remains a vexed question that has still to be addressed.

Mention of artificial molecular switches begs the next question—do they earn the right to be described as artificial molecular machines/motors? The answer is, strictly speaking, no. Not until they have been designed and constructed to consume a fuel and perform work on their environments in a manner which has been enunciated theoretically by Dean Astumian, demonstrated practically by Ben Feringa, and highlighted in a landmark Review by David Leigh (*Angew. Chem. Int. Ed.* **2007**, *46*, 72—191). At a fundamental level we, as chemists, need to learn how to violate the principle of microscopic reversibility by addressing the issues raised by far-from-equilibrium processes and energy dissipation.

As if these challenges faced by post-supramolecular chemists are not enough, yet another major one has to be addressed in tomorrow's world. It is the need to be able to control the spatial ordering of molecular components in one-, two-, and three-dimensional space so that properties and functions can be expressed coherently on a size scale commensurate with nano-, micro-, and macroscopic objects. The rapid advances in our ability to fashion and exploit, increasingly with cooperativity in action as shown by Bert Meijer, supramolecular polymers on the one hand, and the extended structures associated with metal– and covalent organic frameworks on the other, constitute a good reason to feel optimistic. Nonetheless, chemists also need to come to terms with networks that are either aperiodic or completely random: the tools to study such extended structures are simply not available to us at this time. How often in the history of chemistry, however, has a new technique appeared on the scene in the nick of time, elevating the science to a completely new level?

Complex networks are everywhere to be found: they are all around us. Consider the world wide web or global stock markets. Reflect on the way birds adopt formations in the sky during migrations or the response of different ecosystems to climate change. In the superorganism formed by certain ant colonies, the ants operate as a unified entity, working together collectively to support the colony. Prediction in the case of complex networks is nigh impossible. Uncertainty rules the roost—and the unexpected is always just lurking around the corner. While research into complex networks is commonplace in mathematics, physics, and biology, as well as in computer science, economics and the engineering disciplines, when it comes to creating and understanding complex networks, chemists have been conditioned by their education and training to avoid them. We have an aversion to mixtures of molecules, yet complex mixtures no longer constitute an intractable problem with the rapidly growing access to modern analytical tools to probe and understand them within the context of what has become known as (dynamic) combinatorial chemistry.

The time has come for us to embrace complexity—despite the fact that everyone has their own definition of it—and put much more of our effort into studying complex mixtures of interacting molecules. An excellent reason for responding positively to the intellectual challenge posed by systems chemistry is that complexity very often gives rise to emergent properties that are not present in the components of a complex mixture but come to light *only* as a result of interactions between molecules. An example of emergent behavior from one of my group's recent forays into supramolecular systems is provided by a new class of organic materials which boasts the very attractive, but somewhat elusive property, of room temperature ferroelectricity. While the materials' behavior was unexpected, the molecular basis for it is simple and the superstructure leads directly to the complexity that emerges once an act of self-assembly has been completed. The result is a material with properties not shared by its components. Although one swallow does not make a summer, it does portend a bright future for systems chemistry, at least in my eyes.

If you are a chemist in your mid-20s and have your mind set on an academic career, then the only worthwhile advice I have to offer is "Whatever you do, tackle a 'big problem' in chemistry." Although the road you will travel along will be quite unpredictable, it will reveal an endless supply of surprises and the experience will be a rewarding one.