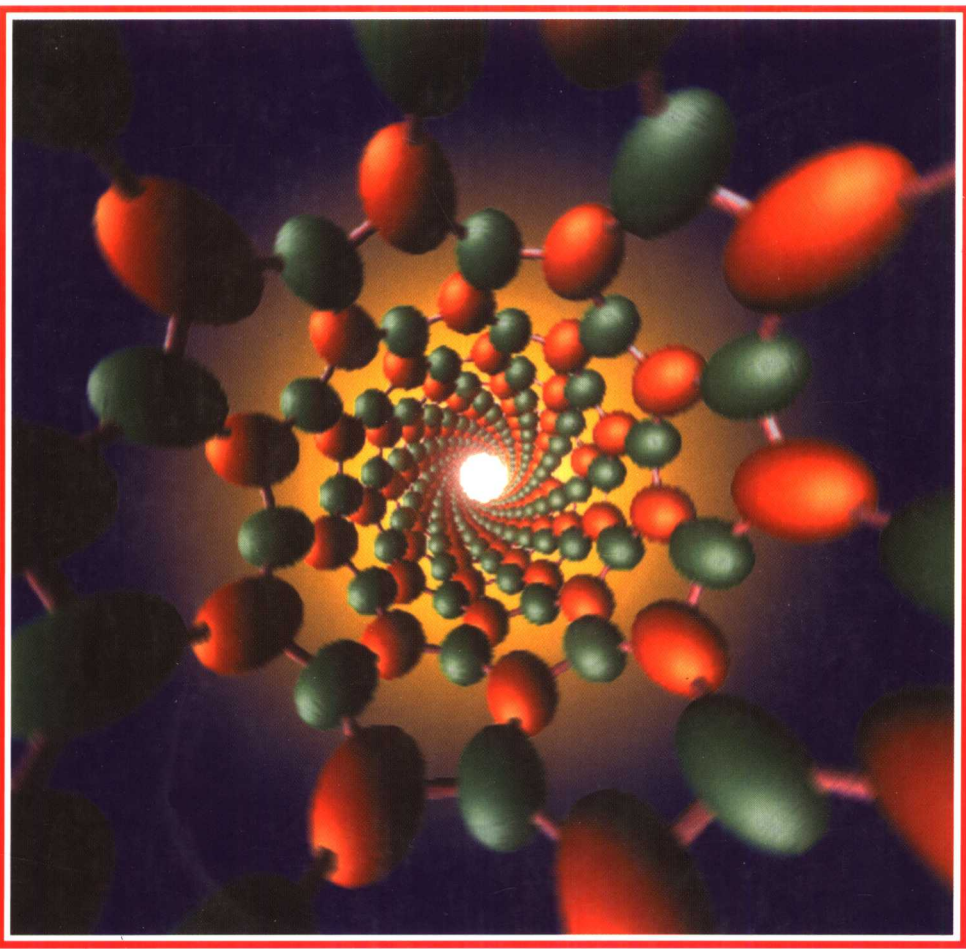


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CHEMISTRY FOR THE 21st CENTURY



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Chemistry for the 21st Century

Edited by

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Preface

"Creative thinking in science is mainly concerned with searching for fresh meaningful combinations of old pieces of information."

W. I. B. Beveridge

"Novelties come from previously unseen association of old material. To create is to re-combine."

François Jacob

On May 11–12 1998, the Israeli scientific community staged a very special event celebrating both the 20th anniversary of the Wolf Prize and the 50th anniversary of the State of Israel. The scientific program of that event included many lectures by Wolf Prize Laureates in all five scientific disciplines of the Prize: Agriculture, Chemistry, Mathematics, Medicine and Physics. This program, which was sponsored by Novartis AG, highlighted a revolutionary trend that characterizes science at the turn of the 20th century – the unification and integration of science.

Historically, divisions of the sciences evolved with the establishment of European universities during the Late Middle Ages. The medieval perception made clear distinctions between theology and physics, and even between terrestrial and celestial physics. Furthermore, it separated the mathematical sciences from natural philosophy and metaphysics. Institutional divisions separated the elevated sciences (which were based on philosophical principles) from the intellectually inferior arts (which were based on the various domains of craftsmanship). Interestingly, mathematics was considered at that time to be a craft and therefore unfit for explaining natural phenomena.

During the Renaissance and particularly during the Scientific Revolution of the 17th century, attempts were continuously made to shake this old perception. Many outstanding pioneers, including Copernicus, Kepler, Galileo, Bacon, Harvey, Descartes, Boyle, Newton, and Hooke, creatively endeavored to establish new theoretical and methodological links between previously separated scientific domains. Galileo took mathematics seriously and connected it with metaphysics; Bacon called the philosophers to come out of their libraries to the real world and learn from other disciplines. Promulgating the new "experimental philosophy", Boyle probably estab-

lished the most sophisticated laboratory in Europe. Craftsmen, meanwhile, started reading philosophical books and made their own contributions to science.

Interestingly, and probably not surprisingly, most of these geniuses operated outside the academic divisions of the university. Yet, the establishment of the modern universities at the beginning of the 19th century was again accompanied by the ordering, classification and partitioning of science. Understandably, the structure of universities around the world reflects their need to maintain comprehensive teaching programs and cover the entire base of scientific knowledge. Thus, the universities' commitment to provide scientific education has led to compartmentalization, hierarchy and even the formation of barriers between well-defined scientific disciplines, such as mathematics, physics, chemistry, biology and medicine, each of which is further divided into subcategories and subsections.

Now, at the turn of the 20th century we are witnessing a profound movement to change the traditional scientific arrangement that was so well preserved by our universities for almost 200 years. The current scientific revolution is reminiscent of the one that occurred at the beginning of the 17th century. As the contemporary explosion of information can cause further specialization and partitioning of scientific disciplines, integration of science sounds counterintuitive. Yet, the increased societal demand for novel technologies challenges the scientific community and pushes towards collaboration and cross-fertilization between seemingly remote scientific domains. There is now an interesting tendency to establish new academic as well as industrial institutions that break the walls between traditional disciplines and encourage creativity, brainstorming and heterogeneous teamwork in research.

Originally, we planned to publish a single volume compilation of scientific contributions that covers a wide range of active disciplines, entitled "Science for the 21st century". Publisher's preferences, however, lead us to arrange the material in the form of a three-volume set. While this first volume is dedicated to the chemical sciences, the second volume will focus on the life sciences and the third will deal with physics and the mathematical sciences.

The astounding history of science and technology of the 20th century testifies for the highly unpredictable nature of scientific developments. It is essentially impossible, and would be quite arrogant on our part, to make any prediction of which scientific disciplines will prevail in the future and therefore merit greater attention today. Consequently, this compilation represents a broad-scope sampling, but certainly not comprehensive coverage, of all scientific domains. All chapters are written by scientists who are well known in their fields and include their scientific achievements and a personal view of the perspectives and prospects in these fields. We hope that readers will have the opportunity to encounter new ideas and will be exposed to subjects well beyond that of their own scientific disciplines. However, our most important task is to provide the readers, now and in the future, with the "taste" and "flavor" of the science at the turn of the millennium.

August 2000

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1

Some Reflections on Chemistry – Molecular, Supramolecular and Beyond*

Jean Marie Lehn

1.1

From Structure to Information. The Challenge of Instructed Chemistry

In chemistry, as in other areas, the language of information is extending that of constitution and structure as the field develops towards more and more complex architectures and behaviors. And supramolecular chemistry is paving the way towards comprehending chemistry as an *information science*. In the one hundred years since 1894, molecular recognition has evolved from Emil Fischer's "Lock and Key" image of the age of mechanics towards the *information paradigm* of the age of electronics and communication. This change in paradigm will profoundly influence our perception of chemistry, how we think about it, how we perform it. Instructed chemistry extends from selectivity in the synthesis and reactivity of molecular structures to the organization and function of complex supramolecular entities. The latter rely on sets of instructed components capable of performing on mixtures specific operations that will lead to the desired substances and properties by the action of built-in self-processes.

Supramolecular chemistry has started and developed as defined by its basic object: the chemistry of the species generated by non-covalent interactions. Through recognition and self-processes it has led to the concepts of (passive and active) information and of programmed systems, becoming progressively the chemistry of molecular information, its storage at the molecular level, its retrieval, transfer and processing at the supramolecular level.

*J) The present text is an adapted version of
Chapter 10 in : J.-M. Lehn, *Supramolecular
Chemistry – Concepts and Perspectives*, 1995,
VCH, Weinheim.

The outlook of supramolecular chemistry is towards a general *science of informed matter*, bringing forward in chemistry the third component of the basic trilogy matter–energy–information.

Chemical systems may store information either in an *analogical* fashion, in the structural features (size, shape, nature and disposition of interaction sites, etc.) of a molecule or a supermolecule, or in a *digital* fashion, in the different states or connectivities of a chemical entity. The evaluation of the information content of a *molecular recognition* process based on structural sensing in receptor/substrate pairs requires an assessment of the relevant molecular characteristics. Recognition is not an absolute but a relative notion. It results from the structural (and eventually dynamical) information stored in the partners and is defined by the fidelity of its reading, which rests on the difference in free energy of interaction between states, represented by different receptor/substrate combinations. It is thus not a yes/no process but is relative to a threshold level separating states and making them distinct. It depends on free energy and consequently on temperature. The parameter kT could be a possible reference quantity against which to evaluate threshold values, differences between states and reading accuracy. Both analogical and digital processing of chemical information depend on such factors.

Digital storage and retrieval of chemical information is found in the nucleic acids where the basic digital operation is a two state 2/3 process (2 versus 3 hydrogen bonds in A:T and G:C base pairs respectively) corresponding to the usual 0/1 commutation of electronic computers. It may also be envisaged for multisite receptors or multiredox systems possessing distinct states of site occupation or of oxidation.

A system of intriguing potential is represented by recently described inorganic superstructures where metal ions are arranged in grid-like arrays. These resemble grids based on quantum dots that are of much interest in microelectronics. They may be considered to consist of *ion dots* of still smaller size than quantum dots and do not necessitate microfabrication but form spontaneously by self-assembly. Such architectures may foreshadow multistate digital supramolecular chips for information storage in and retrieval from inscribed patterns that might be light or electrically addressable. For instance, the use of techniques of STM or AFM type to induce redox changes at specific locations in a single unit would then correspond to a sort of *single electronics* at ion dots. The grid-type arrangements also pose the intriguing question of performing matrix algebra operations on these inorganic superstructures. Extension into three dimensions through stacks of grids would lead to layered arrays in foliated spaces.

Molecular and supramolecular devices incorporated into ultra-micro-circuits represent potential hardware components of eventual systems that might qualify as molecular computers, whose highly integrated architecture and operation would not be of the von Neumann type. On the biological side, the fabrication of components for sensory and motor prostheses could be considered. All these entities may result from the self-assembly of suitably instructed subunits so that computing via self-assembly may be envisaged.

One may note that folding and structure generation in biological macromolecules could occur through parallel search with formation of local arrangements which

then interact with each other giving larger structured areas which will in turn interact, and so on, in a convergent fashion until the final superstructure is reached. For instance, protein folding, as a self-organizing process, would present characteristics of parallel computing.

Entities resulting from self-assembly and self-organization of a number of components may undergo *self-correction* and *adaptation*. This might also explain why large multisite protein architectures are formed by the association of several smaller protein subunits rather than from a single long polypeptide.

Beyond *programmed chemical systems*, the next step in complexity consists in the design of chemical "*learning*" systems, systems that are not just instructed but can be trained, that possess *self-modification* ability and *adaptability* in response to external stimuli. This opens perspectives towards systems that would undergo *evolution*, i.e. progressive change of internal structure under the pressure of environmental factors. It implies also the passage from closed systems to *open systems* that are connected spatially and temporally to their surroundings.

1.2

Steps Towards Complexity

The progression from elementary particles to the nucleus, the atom, the molecule, the supermolecule and the supramolecular assembly represents steps up the ladder of complexity. Particles interact to form atoms, atoms to form molecules, molecules to form supermolecules and supramolecular assemblies, etc. At each level novel features appear that did not exist at a lower one. Thus a major line of development of chemistry is towards complex systems and the emergence of complexity.

Very active research has been devoted to the development of complexity measures that would allow the quantitative characterization of a complex system. In the present context, complexity is not just described by the number of states, the multiplicity of a system, as defined in information science, or by the characteristics of the graphs representing a molecule or an assembly of molecules, or by structural complexity. Complexity implies and results from multiple components *and* interactions between them with integration, i.e. long range correlation, coupling and feedback. It is interaction between components that makes the whole more than the sum of the parts and leads to collective properties. Thus, the complexity of an organized system involves three basic features:

$$\text{Complexity} = (\text{Multiplicity}) (\text{Interaction}) (\text{Integration}) = \text{MI}^2$$

The species and properties defining a given level of complexity result from and may be explained on the basis of the species belonging to the level below and of their multibody interaction, e.g. supramolecular entities in terms of molecules, cells in terms of supramolecular entities, tissues in terms of cells, organisms in terms of tissues and so on up to the complexity of behavior of societies and ecosystems. For example, in the self-assembly of a virus shell, local information in the subunits is sufficient to "tell" the proteins where to bind in order to generate the final polyproteic association, thus going up a step in complexity from the molecular unit to the

supramolecular architecture. Ultimately one will have to go ever deeper and wider so as to link the structures and functions from the atom to the organism, along a hierarchy of levels defining the architecture of complexity.

The novel features that appear at each level of complexity and characterize it do not and even *cannot* conceptually *exist* at the level below but may be explained in terms of MI2, from the simplest particle to the highly complex multibody, multi-interactive societies of living organisms. Such an attitude is not reductionist, it is not a reduction of a level to the lower one(s) but an *integration*, connecting a level to the other ones by integrating species and interactions to describe and explain increasing complexity of behavior.

A simple but telling illustration is for instance the boiling point of a liquid. A single molecule of water has no boiling point, the concept of boiling itself does not, cannot even, exist for it. Only for a population of interacting water molecules is there such a thing as a boiling point, or a freezing point, or any other *collective property*.

A corollary is the question of how many individuals it takes to form a collectivity and to display the collective properties: how many molecules of water to have a boiling point, how many atoms to form a metal, how many components to display a phase transition? Or, how do boiling point, metallic properties, phase transition etc. depend on and vary with the number of components and the nature of their interaction(s)? In principle any finite number of components leads to a collective behavior that is only an approximation, however close it may well be, an asymptotic approach to the “true” value of a given property for an infinite number of units.

The path from the simple to the complex in behavioral space corresponds to that from the single to the collective and from the individual to the society in population space. A sum of individuals becomes a collectivity when there are interactions and at each level novel interactions appear leading to higher complexity. With respect to molecular chemistry, one may consider supramolecular chemistry as a sort of molecular sociology.

The global behavior of condensed matter may be described by phenomenological physical laws. An understanding of these macroscopic events will ultimately require their explanation in terms of the underlying molecular and supramolecular features, i.e. in terms of the chemical nature of the microscopic components and of their interactions. For instance, how is viscosity or a phase change related to the constituting molecules? How do individual partners synergetically cooperate to produce macroscopic spatial, temporal or functional features, inducing a transition from chaos to order through self-organisation? How does turbulent flow vary with the type of multibody interactions between them? Or how is structuration in a energy flow determined by molecular features of the components and their supramolecular interactions?

There is here a very exciting and fundamental field of investigation for supramolecular chemistry concerning the emergence of order and complexity, the passage from the microscopic to the macroscopic, from the isolated to the collective, with the aim of providing an etiological explanation of the phenomenological description. It requires bridging of the gap between and integration of the points of view of the