toid. Into this they introduce a population of mutant parasites that have different rates of locating hosts and converting them into offspring (efficiency) (Fig. 2). They find that even though selection (competition) within a patch favors parasites with higher efficiency, lower efficiency parasites can be maintained. This is because greater host dispersal occurs where hosts are regulated by lower efficiency parasitoids. The wave front is thus less inhibited by local extinction of the host. Faster rotating spirals gradually expand to take over the domain of slower ones and the less efficient parasitoids dominate (Fig. 2). Hence the direction of within-patch selection is contradicted by what Boerlijst and co-workers term "between spiral" selection. Such an outcome is reminiscent of the consequences of group structure on the outcome of selection much studied for the last few decades (*11*, *12*). And it was Wynne-Edwards' suggestion that group selection was responsible for population regulation and nonviolent contests that set Price and Maynard Smith to developing their ESS models in the first place.

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Supramolecular Chemistry

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When a substrate binds to an enzyme, a drug sticks to its target, or signals propagate between cells, highly selective interactions occur between the partners to control the process. Supramolecular chemistry is concerned with the study of the basic features of these interactions and with their implementation in specially designed nonnatural systems.

For more than 150 years, since the synthesis of urea by Friedrich Wöhler in 1828, molecular chemistry has developed a vast array of highly sophisticated and powerful methods for the construction of ever more complex molecular structures by the making or breaking of covalent bonds between atoms in a controlled and precise fashion. The time has come to do the same for noncovalent intermolecular forces. Just as there is a field of molecular chemistry based on the covalent bond, there is a field of supramolecular chemistry, the chemistry of molecular assemblies and of the intermolecular bond. It is "chemistry beyond the molecule," whose objects are supramolecular entities, supermolecules possessing features as well defined as those of molecules themselves (*1*, *2*).

Supramolecular chemistry is a highly interdisciplinary field of science covering the chemical, physical, and biological features of chemical species of higher complexity, that are held together and organized by means of intermolecular (noncovalent) binding interactions. This relatively young area has been rapidly defined, conceptualized, and structured into a coherent system. Its roots extend into organic chemistry and the synthetic procedures for receptor construction, into coordination chemistry and metal ion–ligand complexes, into physical chemistry and the experimental and theoretical studies of interactions, and into biochemistry and the biological processes that all start with substrate binding and recognition. A major feature is the range of perspectives offered by the cross fertilization of supramolecular chemical research, owing to its location at the intersection of chemistry, biology, and physics. Such wide horizons are a challenge and a stimulus to the creative imagination of the chemist.

The field started with the selective binding of alkali metal cations by natural (*3*) as well as synthetic macrocyclic and macropolycyclic ligands, the crown ethers and cryptands (*1*, *4*). This led to the emergence of molecular recognition as a new domain of chemical research that expanded over other areas and became supramolecular chemistry (*1*, *2*). It underwent explosive growth with the development of synthetic receptor molecules of numerous types for the strong and selective binding of cationic, anionic, or neutral complementary substrates of organic, inorganic, or biological nature by means of various interactions (electrostatic, hydrogen binding, van der Waals, and donor-acceptor). Molecular recognition implies the (molecular) storage and (supramolecular) retrieval of molecular structural information. Many types of receptor molecules have already been explored (crown ethers, cryptands, spherands, cavitands, calixarenes, cyclophanes, cryptophanes, and so forth) (*4*, *5*). Still others may be imagined for the binding of complementary substrates of chemical or biological significance; for instance, for the development of substrate-specific sensors or for the recognition of structural features in biomolecules (nucleic acid probes, affinity cleavage reagents, enzyme inhibitors, and so on).

The combination of recognition features with reactive functions generates supramolecular reagents and catalysts that operate in processes involving two main steps: substrate recognition followed by its transformation into products. Because of their relationship with enzymatic catalysis, they present protoenzymatic and biomimetic features. By nature, they are abiotic reagents that may perform the same overall processes as enzymes without following the same mechanistic pathways. More importantly, they may also effect highly efficient and selective reactions that enzymes do not perform. This represents a very important area for further development, which may lead to a range of reactive receptor molecules combining substrate specificity with high reactional efficiency and selectivity. Much work remains to be done that should contribute very significantly to the understanding of chemical reactivity and to its application in industrial processes.

Suitably modified receptors act as carriers for the selective transport of various types of substrates through artificial or biological membranes. Further developments may concern, for instance, the construction of selective membrane sensors or the transport of drugs through biological barriers, which may include targeting if suitable target selective recognition groups are introduced.

Recognition, reactivity, and transport represent the three basic functional features of supramolecular species. A further important line of development concerns the design of supramolecular devices built on photoactive, electroactive, or ionoactive components, operating with photons, electrons, and ions, respectively. Thus, a variety of photonic devices based on photoinduced energy and electron transfer may be imagined (*2*, *6*). Molecular wires, ion carriers, and channels facilitate the flow of electrons and ions through membranes. Such functional entities represent entries into molecular photonics, electronics, and ionics that can be used for stor-

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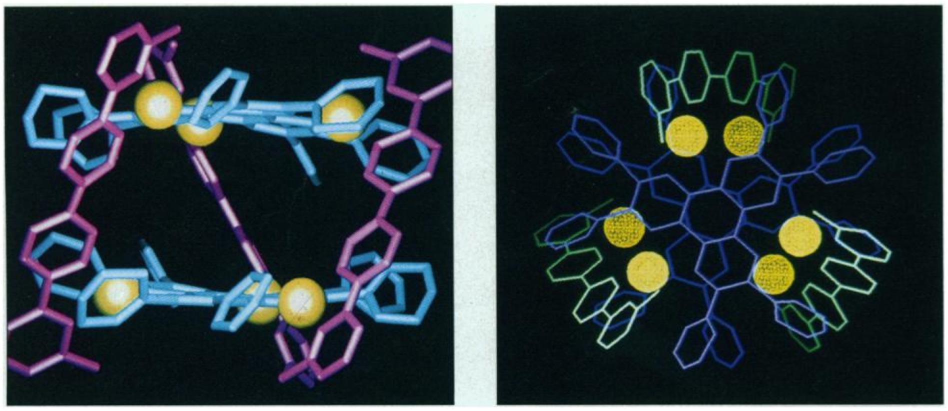

Supermolecules. Two views of a model of a self-assembled cylindrical complex. Copper ions, yellow; quaterpyridine ligands, purple; hexaphenyl hexaazatriphenylene ligands, blue.

age and processing and for the transfer of materials, signals, and information at the molecular and supramolecular levels.

An entire field lies here at the interface with physics, microelectronics, and micro-optics, a field that has barely been explored and remains wide open, presenting such intriguing goals as electrical storage, amplification, switching, and rectification. The chemistry of molecular signal generation, processing, transfer, conversion and detection—semiochemistry—touches upon both physical and biological signalization processes.

The most recent developments concern the implementation of molecular information and recognition as a means of controlling the evolution of supramolecular species as they are built up from their components. Thus, beyond the preorganization used in the construction of molecular receptors lies self-organization. It involves the design of systems capable of spontaneously generating well-defined supramolecular entities by self-assembly from their components in a given set of conditions (*2*, *7*). The information necessary for the process to take place and the program that it follows must be stored in the components and operate according to an algorithm based on molecular recognition events. Thus, these systems may be termed programmed supramolecular systems (*2*).

Self-assembly and self-organization have recently been implemented in several types of organic and inorganic systems (*2*, *7*, *8*). By clever use of metal coordination, hydrogen bonding, and donor-acceptor interactions, researchers have achieved the spontaneous formation of a variety of novel and intriguing species such as the inorganic double and triple helices termed helicates, catenanes, threaded entities (rotaxanes), cage compounds, and so forth. For instance, by the self-assembly of 11 particles—five ligands of two different types and six copper (I) metal ions—a closed, cage-like structure is obtained spontaneously and selectively in one stroke (see figure).

A further major development along these lines is the design of molecular species with the ability to self-replicate. This was realized with the use of components containing suitable recognition groups and reactive functions (*9*).

In a study of helicate self-assembly from a mixture of different ligands and metal ions, it has been found that only the "correct" helical complexes are formed through self-recognition. More broadly, this points to a change in paradigm from pure compounds to instructed mixtures—that is, from seeking chemical purity to designing programmed systems composed of mixtures of instructed components capable of spontaneously forming well-defined superstructures. One may venture to predict that this trend will represent a major line of development of chemistry in the years to come: the spontaneous but controlled buildup of structurally organized and functionally integrated supramolecular systems from a preexisting "soup" of instructed components following well-defined programs and interactional algorithms. Thus, the study of self-processes represents an area of rapidly increasing activity.

In addition to dealing with the oligomolecular supermolecules, well-defined species resulting from the specific intermolecular association of a few components, supramolecular chemistry deals also with polymolecular assemblies formed by the spontaneous association of a large number of components into a specific phase (films, layers, membranes, vesicles, micelles, mesophases, surfaces, solids, and such) (*10*). Here lies a vast and fertile domain of research. Molecular recognition between complementary components provides a means by which researchers can direct the architecture of polymolecular assemblies and endow them with novel properties, such as the selective binding of substrate molecules to layers and surfaces. It allows the design and engineering of supramolecular materials, in particular of a liquid crystalline and polymeric nature (*2*, *10*). A sort of supramolecular polymer chemistry is thus emerging and receiving more and more attention.

Processes directed by molecular recognition also provide a powerful entry into supramolecular solid-state chemistry and crystal engineering (*11*). The ability to control the way in which molecules associate may allow the designed generation of desired architectures in the solid state. Modification of surfaces with recognition units could lead to selective surface binding and to recognition-controlled adhesion.

The design of "programmed" systems, controlled by molecular information, represents a new horizon in materials engineering and processing that looks toward "smart," functional supramolecular materials, such as self-assembling nanostructures, which are organized and functional species of nanometric dimensions that define a supramolecular nanochemistry.

It has become clear that the key word of supramolecular chemistry is not size but information. In terms of size, "there's plenty of room at the bottom," as the celebrated aphorism of Richard Feynman goes. However, the ability of supramolecular species to spontaneously build up from their components and accomplish complex tasks on the basis of the encoded information and instructions, shows that through supramolecular chemistry "there's even more room at the top."

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