Some novel facets of molecular and supramolecular systems

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This article surveys in brief the developments in the building up of supramolecules through non-covalent interactions between molecules and their various applications. The major topics included in the present review are: self-assembly and supramolecules; construction of supramolecules through non-covalent interactions; characterization of supramolecules; molecular recognition and sensors; supramolecular reactivity, catalysis and transport processes; photochemistry of supramolecules, and, drug design and supramolecules.

1.0 Introduction

Molecules that interact physically and react chemically in specific and selective ways are the basic constituents of this living world. One of the most exciting and potentially rewarding challenges the modern chemist faces today is the devising and realizing of wholly synthetic systems that may mimic the biological ones. It is therefore important to develop an understanding of the steps involved in molecular recognition process controlling the formation of multimolecular assemblies. The most sophisticated and effective examples of self-assembly occur in living systems, e.g., a virus, is basically a machine that makes copies of itself. The tobacco mosaic virus consists of a helical strand of RNA, which codes for the synthesis of 2130 identical protein molecules in the surrounding coat. If damaged, the viral capsule will rapidly self-assemble by mixing the protein and RNA components together. Mechanism of this self-assembly has been studied in detail.

Furthermore, the biological systems direct the construction and functioning of nanoscale structures with startling efficiency. Therefore, it seems logical that self-assembly should be the strategy of choice for synthetic chemists wishing to construct nanoscale assemblies. The initial step involves the covalent synthesis (conventional
self-assembly is increasingly becoming one of the most important synthetic tools for the construction of molecular devices. An example worth mentioning is the construction of rotaxane (a class of molecules in which a dumbbell shaped component is encircled by a macrocycle). As shown in Fig. 2, the two components are linked mechanically rather than by a covalent bond. The complex formed between these two species can then be modified with blocking groups to produce the \([2]\) rotaxane. The prefix \([2]\) indicates the number of mechanically linked components within the molecule. Ogino and coworkers\(^2\) reacted diaminoalkanes with \(\alpha\)-cyclodextrin (\(\alpha\)-CD) or \(\beta\)-CD which after the formation of inclusion complexes further reacted with the cobalt complex \([\text{CoCl}_2(\text{en})_2]\) (\(\text{en} = \text{ethylenediamine}\)) yielding \([2]\) rotaxane (Fig. 3).

The supramolecular chemistry has its own specific terminology; like ligands in coordination compounds, the supramolecular components have been named as receptor (\(\rho\)) and substrate (\(\sigma\)) (being smaller component). Also, 'inclusion compound', the "host-guest" that exist in solid state do represent the supramolecular solid state species. The selective binding of a specific substrate \(\sigma\) to its receptor \(\rho\) yields supramolecule \(\rho\sigma\) and involves molecular recognition process. In addition to binding sites, if a receptor also bears reactive functions, it may affect a chemical transformation on the bound substrate, thus behaving as a supramolecular reagent or catalyst.

Naming of such compounds poses some specific problems. Receptors and substrates themselves are covalent structures whose naming is governed by rules approved in the Geneva conference. Conventions used for coordination compounds may be a starting point, e.g., \(\kappa\), kappa (indicating coordinating atom), hapto, \(\eta\) (for coordinated group) or \(\mu\) (for bridging ligands). Spatial localization of bound substrate with respect to the receptor also requires some formalism. External addition complexes may be written as \([A, B]\) or \([A/B]\), the mathematical symbols of inclusion \(\subset\) and intersection \(\cap\) have been introduced for the inclusion \(\sigma\) into \(\rho\) [\(\sigma \subset \rho\)] and for the partial interpenetration of \(\sigma\) and \(\rho[\sigma \cap \rho]\). The vocabulary and syntax for supramolecular systems are progressively being developed.

2.0 Self-assembly and supramolecules

As mentioned earlier the self-assembly has now been recognized as a crucial component in the molecular events leading to the evolution of life\(^3\). A significant fraction of all chemical and biological processes falls within its realm which could be a synthetic protocol exclusively driven by non-covalent interactions. In biology, one of the best
examples of a self-assembly could be seen in hemoglobin comprising four separate components, two α and two β subunits. Though there is little contact between α and α or β and β components there are extensive non-covalent interactions between the α and β subunits in hemoglobin tetramer. The multitude of these precisely apportioned non-covalent interactions that exist between the individual subunits in hemoglobin control both structure and function. These non-covalent interactions are very influential in producing functionally active supramolecular complexes since a simple structural error could lead to terrible consequences. For example, in a sickle-cell anemic patient there is valine in a place normally reserved for glutamic acid. This causes deoxyhemoglobin to aggregate forming long fibres that deform the cell-membrane. These aggregated hemoglobin mutants are another example of self-assembly, though inappropriate, which results in the formation of a defective product. The self-assembly processes could be promoted by the following factors:

(a) Enhancing the strength of non-covalent interactions through the control of solvent; for example, if two or more species are to interact by hydrophobic interactions then self-assembly is promoted by an aqueous solvent. Other interactions like hydrogen bonding and electrostatic interactions are strongest in apolar aprotic solvents.

(b) Selective sequestering of supramolecules in solution in order to avoid their dissociation back to the components.

(c) Using excess of the components to drive the self-assembly process to completion. This approach is, however, restricted since it would be critical that the free subunits do not disturb the ability of the desired complex to perform the task for which it was designed.

3.0 Construction of supramolecules through different non-covalent interactions

In the synthetic self-assembling systems, three approaches, namely, (i) hydrogen bonding, (ii) the stacking (π-π) interactions of aromatic rings and (iii) metal-ligand bonding have been extensively exploited.

3.1 H-Bonding

Base pairing within nucleic acids as formulated by Watson and Crick could be quoted as a classical form of molecular recognition, e.g., the complementary hydrogen bonding surfaces shown in Fig. 4 for adenine (A) and thymine (T) provide a vehicle for information transfer while stacking interactions between adjacent base pairs provide additional stability for the helical structure.

H-bonding aspects shown in Fig. 4 have been examined in detail by Rich and Hammes using derivative of A and T in CDCl₃ while stacking of individual bases in H₂O has been observed by Chan.

Besides holding together the complementary strands of DNA in living organisms, hydrogen bonding is also a powerful tool in designing artificial self-assembling systems. The key to such successful synthesis is designing of complementary hydrogen bond donors and acceptors that match up...
both in number and spatial arrangements. The best example could be seen in the work of A.D. Hamilton who first noted that barbiturates possess three carbonyl hydrogen-bond acceptor sites and two NH hydrogen-bond donors; so Hamilton designed a fully complementary partner containing two 2,6-pyridine diamide groups, each of which is complementary to a O=C=NH-C=O set of the barbiturate. A stable host-guest complex (Fig. 5) comprising six hydrogen-bonds forms when the receptor is mixed with the barbiturate.

Similarly George Whitesides and coworkers selected cyanuric acid possessing similar H-bonding properties as Hamilton's barbiturate, and triamino syn-triazine as the complementary host and prepared a complex (Fig. 6) possessing multiple host-guest interactions.

The self-assembling of supramolecular complexes through hydrogen bonding has been recently reviewed by Lawrence et al. It was noted that lactam functionality is absolutely critical for self-recognition and obviously an amide moiety can serve as both a hydrogen-bond donor and acceptor. Thus, it is not surprising that several groups have utilized the lactam motif to create compounds that can spontaneously assemble into multimeric complexes.

It was also noted that in both the solid state and in solution, minor differences in subunit structure have a profound effect on aggregation behaviour. Amide functionality was also exploited by Zimmerman and his group to create cyclic aggregates especially the trimerization of quinoline derivative a to b (Fig. 7) and the product has been investigated by vapour pressure osmometry and $^1$H NMR data.

J.M. Lehn and his group have also synthesised heterocycles 1 (hydrogen bond-acceptor/acceptor/donor, and 2 (hydrogen bond donor/donor/acceptor).

They proposed that an equimolar mixture of 1 and 2 should assemble to form the disk-like structure (Fig. 8).

Like their amide counterparts, carboxylic acids do exhibit a strong tendency towards dimer formation in aprotic solvents. Consequently carboxylic acid functional group has also been employed for the assembly of various supramolecules.

### 3.2 Stacking interaction

The importance of $\pi-\pi$ interactions in biological systems is seen in the extra stabilisation of the DNA double helix through stacking of the aromatic base points. Generally, the $\pi-\pi$ stacking and charge transfer interactions between $\pi$-electron-rich and $\pi$-electron-deficient systems are the basis of the systems composed of interlocked rings (catenanes, beads and threads rotaxanes). The potential of $\pi-\pi$ interaction in the assembly of supramolecular system could be seen in the work of Gunter et al. who reported recently that naphthoquinol strapped porphyrin (c) mixed with bis(bipyridinium) dication (d) and 1,4-bis-(bromomethyl)benzene (e) yielded...
The driving force in this assembly is derived from the π-electron-rich character of naphthoquinol and π-electron-deficient character of bipyridinium rings. The potential of π-interaction in such an assembly could be visualized furthermore by the low yield (20%) of the catenanes obtained by changing the naphthalene ring by benzene ring in ether linkage which of course reduces the strength of π-interactions and consequently reduces the yield of catenane (f).

Similar potential of π-π interaction in the assembly of supramolecules could also be seen in the recent work of Fraser Stoddart in the construction of system comprising five interlocked rings called olympiadane (j) (Fig. 10) initiated by the template reaction of trisnaphtho [5] crown-15, (g) with bipyridine salt (h) and 1,1-bis(bromomethyl)-4,4'-biphenylene (i).

A decade earlier Rebek et al. synthesized a model compound (m) (Fig. 11) where both H-bonding and stacking interaction are operative simultaneously. This new structure is provided by the derivative of Kemp's triacid (k) in which shape-selective relationship that exists between any two carboxyl functions is enforced by the equatorial methyl groups. This triacid (k) could be converted into various derivatives by different reactions leading to the formation of 1 (a'-d') which with aromatic amines yielded (m).

3.3 Metal-ligand bonding

In the assembly of supramolecules based on metal-ligand interactions, the inherent properties of the transition metal ions, like characteristic coordination numbers and geometries are matched
with the inherent bonding properties of polydentate ligands (number, type and spatial distribution of donor atoms). Fujita et al. have described the palladium and platinum assisted assembly of binding sites in which the bipyridine derivative (3) is rapidly converted to the cyclophanes (5 a"-e") which are found to bind a variety of aromatic guests. Furthermore, the palladium complex of the type (o) drives the self-assembly of (p) in presence of pyridine (Fig. 12). Jean-Marie Lehn also produced a molecular cylinder using hexaaazatriphenylene possessing three coordination sites as the key component and bipyridine derivative along with Cu(I) ion. The use of metal ions also allows the self-assembly of double helical molecules. The origin of double helix is latent within the structural framework of the organic ligand. Lehn has described a series of functionalized ligands that give rise to double helical complexes of varying nuclearity and has demonstrated a high degree of selectivity and cooperativity in the assembly of these helicates.

4.0 Characterization of supramolecules

As pointed out earlier, self-assembly leading to the formation of supramolecules is driven by weak non-covalent reversible interactions so this poses a unique challenge with regard to structural characterization. Structural information can be readily obtained if the desired complex yields X-ray quality crystals upon purification; otherwise, characterization will be difficult. First of all, the stoichiometry of the complexes is estimated employing titration techniques assuming that the components in the complex exhibit some measurable physical characteristics that are distinct from the uncomplexed components. One common approach is the method of continuous variation though it is impossible to apply it for systems in which three or more species are in equilibrium. Thus, assuming that the relative ratio of the individual components could be obtained, absolute stoichiometry must be supported by the molecular weight measurements. Molecular weight is readily obtained by mass spectrometry if the molecular ion peak is stable enough. Unfortunately, for supramolecular systems, mass spectroscopy is unlikely to be applicable due to loosely coordinated components. Vapour pressure osmometry and low resolution solution phase method have been extensively employed.

Colligative properties (elevation in boiling point and depression in freezing point) can also be used for molecular weight determination. However, these techniques have limitations for high molecular weight complexes which may produce effects that are too small to be measured. Finally, beside the cryoscopic and ebullioscopic measurements, light scattering measurement, sedimentation velocity, gel filtration and small angle X-ray scattering are commonly applied techniques. These analytical methods are described in detail by Cantor and Schimmel as well as by Bell and Bell.

Fig. 12 - The reaction of compound (n) with [Pd(en)(NO3)2]
During the self-assembling process, the subunits may aggregate either in a cyclic or a linear fashion; since cyclic structures are generally more ordered than the linear counterparts, entropy considerations should favour cyclic structures. However, the greater number of non-covalent interactions per subunit in cyclic species as compared to that in linear complex, would favour cyclic structure from enthalpy point of view. Thus enthalpy and entropy of complex formation have been used to distinguish between the linear and cyclic aggregates. For example, tetramerization of aniline is found to be consistent with the cyclic structure. In spite of this, thermodynamic data are typically not employed to differentiate between cyclic and linear structures. The best way to address such issues is via X-ray crystallography. For the sake of structural clarification, let us take an example of the macrocycle (6) synthesized by A.D. Hamilton et al. which contains 2,6-diaminopyridine and naphthalene components and shows two point binding to thymine derivatives. The host (7) was also designed to test the possibility of inducing a conformational change on substrate binding. The structure of macrocycle (6) was confirmed by single crystal X-ray analysis (Fig. 13A) which shows an open conformation with the naphthalene poised away from the pyridine ring at an interplane angle of 127.5°. The amide hydrogen lies in the plane of pyridine and projects under the naphthalene ring to provide a partially organized substrate binding region. Characteristic changes in the 1H-NMR spectrum were observed when one equivalent of (7) was treated with a CDCl3 solution of (6). The NH protons of both (6) and (7) were shifted down field by 2.25 and 2.6 ppm respectively reflecting the formation of a triple hydrogen-bonded complex. However, upfield shifting by ~0.3 ppm was seen in the thymine-6-proton, ring methyl and N-methylene resonances while no significant shift was found for the alkylmethyl group. The selective upfield shift of certain substrate protons is consistent with the close approach of the naphthalene to the substrate and its participation in binding.

The structure of the complex (6+7) was further confirmed by X-ray crystallography (Fig. 13B). Three hydrogen bonds are formed between pyridine and thymine rings with distances of (N-N) 3.06, (N-O) 2.87 and 2.97 Å. The naphthalene now lies approximately parallel (14°) to the plane of thymine substrate at a closest interplane distance of 3.37 Å. The position of the naphthalene directly above the substrate accounts for the upfield shift of those protons on the periphery of the thymine and the absence of a shift of those protons that are distant...
from the naphthalene ring current. The angle between the pyridine and naphthalene plane is now 161.6°. Thus on substrate completion, macrocycle (6) acts like a "molecular hinge" and swings the naphthalene unit through a 34.1° arc to within V der Waals distance of the thymine ring. This induced fit behaviour in a synthetic molecule mimics the recognition of nucleotides by ribonuclease in which a tyrosine residue moves into plane above the bound guanine. Similarly, X-ray crystallographic studies along with NMR, mass spectroscopic techniques and other cryoscopic and ebullioscopic techniques as mentioned earlier have been found very useful in elucidating the structure of supramolecules. However, it is worth mentioning that NMR spectroscopy, though commonly very useful technique for structural elucidation of even very complex molecules, is restricted for the determination of relative orientation of identical nearest neighbours. Consequently, characterization of small assembling molecules especially those containing several copies of single subunit, represents a major challenge that has yet to be resolved in a satisfactory fashion.

5.0 Molecular recognition and sensors

Molecular recognition is one of the cornerstones of supramolecular chemistry and implies the molecular storage and supramolecular read-out of molecular information. Though the notions of recognition and information were used in connection with the biological systems, they effectively pervaded in the realm of chemistry during 1970 in connection with the selective complexation of metal ions.

The basic principle of molecular recognition (Fig. 14) for any given substrate is the design of a receptor (ligand) possessing geometrical and bonding features for specific interaction.

Thus, recognition implies the geometrical and interactional complementarity, i.e., presence of complementary binding sites (electrostatic such as positive/negative, charge/dipole, dipole/dipole, hydrogen-bond, donor/acceptor etc.) between the associating partners.

In order to achieve a high degree of recognition, following factors must be taken into account while designing the receptors:

1. Steric factors (shape and size), i.e., presence of convex and concave domains in substrate and receptor molecule,
2. Interactional complementarity (which depends on well-defined three-dimensional architecture with correct arrangement of binding sites),
3. Large contact areas between receptor and substrate
4. Multiple interaction sites
5. Strong overall binding

In addition to above, medium effects play an important role through the interaction of solvent molecule with receptor and substrate as well as with each other.

In the above context, macrocyclic structures are of special interest for designing artificial receptors as they are large (macro) and may therefore contain cavities of appropriate size and shape. They also possess branches, bridges, connections that allow construction of a given architecture endowed with specific dynamic features.

These receptors may be mentioned as crown ethers, corrinand or torands; clathrochelates and

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<th>Table 1 — Different receptors in recognition of ions.</th>
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<td>Receptors</td>
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<tr>
<td>1 Crown ethers and cryptates</td>
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<td>2 Polyaaza, polythia- ligands</td>
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<tr>
<td>3 Hexapyridine torands</td>
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<tr>
<td>4 Inorganic cryptates</td>
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<td>5 Macrotricyclic cryptands and oxaaamacrocyecles,</td>
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<tr>
<td>(triaza trioxo macrocycle)-N₃O₃</td>
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<td>6 Polyammonium macrocycles</td>
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<tr>
<td>7 Guanidines, natural cyclodextrins</td>
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<td>8 Metallo receptors (heterotropic co-receptors)</td>
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Fig. 14 - The basic principle of molecular recognition for any given substrate, a receptor possessing geometrical and bonding features for specific interactions can be designed.

Fig. 15 - Designing a receptor for which the substrate has specific affinity may not suffice; something should signal to the operator that recognition has occurred. Assembling a receptor and a signalling unit makes a sensor.

Fig. 16 - A PET sensor for K⁺. Metal coordination stops the electron transfer process from the tertiary amine group to the photo-excited anthracene fragment and restores fluorescence.

coordinate clathrates, cryptands as speleants, spherands, cavitands calixarines, cyclophanes and cryptophanes, etc. The different recognition processes using these receptors could be shown in Table 1 (ref. 29a).

Furthermore, if the receptor also bears reactive functions beside its binding sites, it may effect a chemical transformation on the bound substrate and would behave as a supramolecular reagent or catalyst. Additionally, if the receptor is lipophilic membrane-soluble, it may act as carrier and affect the translocation of the bound substrate.

5.1 Sensors

The assembly of a specific receptor with a subunit capable of signalling the occurrence of receptor-substrate interaction constitutes a sensor (Fig. 15). Sensor efficiency is related to a comparable extent (i) to the selectivity of binding tendencies and (ii) to ease and simplicity of detecting and measuring the displayed signal. In this context, cheaper fluorescent sensors for metal ions are worth mentioning e.g., anthracene based sensors for S block metal ions developed by De Silva, where the receptor is an 18-membered macrocycle containing five ether oxygen atoms and amine nitrogen atom as donors, is suitable for selective interaction with K⁺.

Before metal incorporation, the supramolecular system (Fig. 16) is not fluorescent due to electron-transfer from fairly good reducing amine group to photoexcited anthracene. Upon metal incorporation, electron-transfer process is prevented (as the electron from N is transferred to metal) consequently fluorescence is restored.

Thus the interaction between the receptor and K⁺ is communicated in the form of intense emission spectrum of anthracene. In this context redox switchable fluorescent systems are worth mentioning. A two-component device combining a fluorescent centre and an electroactive unit may function as photoelectro switch in which the
emission properties are modulated by redox interconversion via energy or electron transfer quenching, i.e., in a system in which luminescent (tris bipyridine)ruthenium(II) centre is linked to a quinone unit through a \(-\mathrm{CH}_2-\mathrm{CH}_2-\) spacer (Fig. 17).

Since the appended quinone group takes the electron from the proximates photoexcited fragment, it quenches the fluorescence. However, if the quinone fragment in an acidic aqueous acetonitrile solution is reduced to hydroquinone form \(\text{H}_2\text{R-O} + 2\text{e}^- + 2\text{H}^+ \rightarrow \text{OHR-OH}^{-}\) the electron-transfer process is prevented and the fluorescence of \([\text{Ru(bipy)}]^{2+}\) fragment is initiated. Consecutive additions of reducing and oxidizing agents \((\text{S}_2\text{O}_4^{2-} \text{ and Ce}^{IV})\) switch the fluorescence on/off.

Multisensor devices may also be based on an array of sensing units that present different sensitivities for each component of a collection of substrates to be determined.

6.0 Supramolecular reactivity and catalysis

The functional properties of supramolecules control the reactivity and catalysis processes. The receptor bearing suitable reactive groups in addition to its binding sites, may complex a substrate, react with it and finally release the products regenerating the reagent for further cycling (Fig. 18). Thus, supramolecular reactivity and catalysis\(^{29a}\) involve two steps (a) binding of the substrate and (b) transformation of the bound species into products. Both steps require the correct molecular information in the reactive receptor and participation in the molecular recognition of the productive substrate.

The design of efficient and selective supramolecular reagents and catalysts may provide mechanistic insight into the elementary steps of catalysis, provide new chemical reagents and elucidate factors contributing to enzymatic catalysis. Many investigations in this regard, especially, based on functionalized \(\alpha\)-cyclodextrin, macrocyclic polyethers and cyclophanes have been made.

Macrocyclic polyethers fitted with side chains bearing thiol groups cleave activated ester with marked rate enhancement and chiral discrimination between optically active substrates. Additionally, the tetra-\(\alpha\)-cysteinyld derivative of macrocycle (8) binds \(p\)-nitrophenyl (PNP) esters of amino acids and peptides and reacts with bound species releasing \(p\)-nitrophenol as shown in (8). Similarly, the binding of pyridinium substrates to macrocycle of the type (8) bearing 1,4-dihydro-pyridyl side chains leads to enhanced rates of hydrogen transfer from dihydropyridine to pyridinium within supramolecular species formed.

6.1 Transport processes

The transport processes represent one of the basic functional features of supramolecular species\(^{29a}\) together with recognition. Design and synthesis of receptor molecules selectively binding the organic and inorganic substrates (if soluble in membrane) has been made and these have been used as carriers in the transport of bound species through membrane.

Carrier mediated transport is a cyclic process comprising four steps (Fig. 19):

(i) Formation of carrier-substrate complex at one interface

(ii) Diffusion of the complex through membrane phase

(iii) Release of the free carrier

(iv) Back diffusion

Carrier acts as a transport catalyst which increases the rate of passage of the substrate with respect to free diffusion and shows enzyme like features, saturation kinetics, competition and inhibition phenomena, etc.

The factors influencing the transport may be internal ones arising from the carrier and external ones due to medium. Carrier design takes into
account the factors specific for transport processes. Thus, whereas a receptor should display high stability, high selectivity and slow exchange rate towards its substrate, a carrier molecule should be highly selective, but not bind its substrate too tightly to be flexible enough to allow sufficiently fast exchange rates for loading and unloading and to avoid carrier saturation.

Natural acyclic and macrocyclic ligands such as monensin, valinomycin, enniatin and nonactin, etc, have been found to act as selective ion carriers- ionophores and have been extensively studied, particularly in view of their antibiotic properties. Besides cation transport, the carriers have also been designed and synthesised for the transport of anions\textsuperscript{29b,30}. For example, lipophilic transition metal complexes or organometallics like tin derivatives could serve as anion carriers by direct coordination of anions to the metal. The pair formed of course must be sufficiently kinetically labile. Anion binding to lipophilic porphyrin complexes is an interesting case of this type.

Liquid membranes\textsuperscript{29a} of the water-in-oil emulsion type have been extensively investigated for the separation and extraction of toxic species from biological fluids and regeneration of dialysates or ultrafiltrates, as required for artificial kidneys. Numerous facilitated transport processes have also been studied by us especially for cations mediated by carrier molecules\textsuperscript{31,32} through liquid membrane of the water in chloroform.

### 7.0 Supramolecular photochemistry and molecular photonics

Like catalysis, supramolecular photochemistry\textsuperscript{29a,33} may involve three steps (a) binding of substrate and receptor, (b) mediating a photochemical process, followed by either (c) restoration of the initial state for a new cycle or by a chemical reaction (Fig. 20). The photophysical and photochemical features of supramolecular entities form an extensive area of investigation into processes occurring at the level of intermolecular organization. Thus the formation of supramolecular species from photoactive and electroactive components may be expected to perturb the ground state and excited state properties of the individual species hence providing novel features that define supramolecular photochemistry.

Since the light excitation increases both the oxidizing and reducing power of a molecule, so in a multicomponent system, light excitation can often be followed by an electron-transfer process, viz.,

**Photoexcitation**

\[ A \rightarrow B + \text{hv} \rightarrow A^* \rightarrow B \]  

**Photoinduced oxidative electron transfer**

\[ A^* \rightarrow B \rightarrow A^+ \rightarrow B^- \]  

**Photoinduced reductive electron transfer**

\[ A^* \rightarrow B \rightarrow A^- \rightarrow B^+ \]  

The relevant thermodynamic parameters are the reduction potentials of \( A^+/A^* \), \( B/B^- \), \( B^+/B^- \) couples. To a first approximation, the reduction potential for the excited state couples may be calculated from the reduction potentials of the ground state couples and one electron potential corresponding to zero-zero excitation energy.

\[ E(A^*/A^+) \approx E(A^+/A) - E^{\infty} \]  

\[ E(A^*/A^-) \approx E(A^-/A) + E^{\infty} \]  

Consequently, feasibility of an excited state electron-transfer process can be assessed by the well known Weller equation, e.g., for the above process (ii).

\[ \Delta G^* \approx -E^{\infty} - E(B/B^-) + E(A^+/A^-) - EIP \]  

\( \Delta G^* = \) free energy change of the process

\( E^{\infty} = \) spectroscopic energy of the excited state

Fig. 20 - Representation of the processes involved in supramolecular photochemistry. Generation of \( R'S, RS^* \), \( R'S^* \) or \( R'S' \) may be followed by a chemical reaction.
E(B/B') and E(A'/A)' are one-electron energies corresponding to the reduction of two species (i.e. component of the supramolecule) involved in the process.

\[ \text{EIP} = \text{Coulombic stabilization energy of the products.} \]

However, in an absolute rate formalism (Marcus model) the rate constant for an electron transfer process, \( A \rightarrow B \rightarrow A^+ \rightarrow B^- \) can be expressed as

\[ k = \nu_N K_{exp} \exp \left( -\frac{\Delta G^*}{RT} \right); \quad \Delta G^* = \frac{1}{4} \left( 1 + \frac{\Delta G^0}{2} \right)^2 \]

(vii)

\( \nu_N = \) effective nuclear frequency factor;
\( K = \) electronic transmission coefficient;
\( \Delta G^* = \) free activation energy;
\( \Delta G^0 = \) standard free energy change of the reaction;
\( \lambda = \) reorganizational energy.

Furthermore, the electronic energy transfer processes can occur, either by Foster-type mechanism (based on coulombic interaction) or by Dexter-type mechanism based on exchange interaction

\[ A^* \rightarrow B \rightarrow A \rightarrow B^* \]

Forster-type mechanism is a long-range mechanism, its rate falls off as \( r^6 \) (r is separation distance between donor and acceptor). Dexter type mechanism is a short range mechanism (its rate falls as \( e^{-r} \)) that requires orbital overlap between donor and acceptor.

Additionally, the molecular and supramolecular devices are formed from covalently and noncovalently linked components respectively. In this context, one may speak of photonics, electronic or ionic devices depending on whether the components are respectively photoactive, electroactive or ionic.

Molecular recognition (energy and information involved in the binding and selection of substrate (S) events) represents the basis of information processing at supramolecular level. It may give rise to change in electronic, ionic, optical and conformational properties which may translate into the generation of signal.

Molecular recognition processes thus play a role in key steps: (i) the binding up of device from its components, (ii) its incorporation into supramolecular arrays, (iii) the selective operation on given species (e.g., ions), (iv) the response to external physical or chemical stimuli (light electrons ions, molecules etc.) that may regulate the operation of devices and switch it on or off and (v) the nature of the signals generated and of the signal affected (photon-photon, photon-electron, electron-electron, electron-ions, ion-ion etc.). The resulting area is termed semiochemistry - the chemistry of molecular signal generation, processing transfer, conversion and detection.

Molecular recognition-dependent photochemical molecular devices may involve photochemical processes such as energy transfer or photoinduced electron transfer via association of two or more complementary units. The complementary units may be as small as heterocyclic bases or as large as gene-antibody conjugate. Pictorially the process may be represented as shown in Fig. 21.

Furthermore, conversion of light into emitted light of another wavelength occurs in a luminescent species. This is the basis of a light conversion

![Fig. 22 - Light-conversion photochemical molecular devices.](image1)

![Fig. 23 - Macro bicyclic ligand incorporating 2,2'-bipyridine(c') and its europium complex (d').](image2)
molecular device consisting of two discrete components, a light collector called antenna (formed by an array of strongly absorbing units), and an emitter, thus allowing the separate optimization of absorption and emission. In order to function intercomponent energy-transfer must occur as efficiently as possible. Such a device operates in three steps: absorption-energy transfer-emission (A - ET - E) (Fig. 22).

Cryptates of Eu(III), Tb(III) with macrobicyclic ligands\textsuperscript{29a} (Fig. 23) incorporating various heterobiaryl groups like 2,2'-bipyridine, phenanthroline, bithiazole, bipyrimidine, biisoquinoline and their N,N'-oxides (serving as light collecting antenna components) have been extensively realized as luminescent materials.

Polymetallic complexes presenting directional energy migration are of much significance for the design of photochemical molecular devices. Large arrays of multiple photoactive building blocks [of ruthenium and osmium - tris(bipyridine) type for instance] have been constructed for such purposes.

Recently we developed\textsuperscript{35} dinuclear Ru(II) complexes (Fig. 24) having extended conjugation within bridging ligand by coupling of the Ru(II) polypyridyl complex having a benzoyl substituted phenazine unit with diaminoanthraquinone in one step. Emission from the excited Ru(II) centre was efficiently quenched through the anthraquinone unit.

Molecules\textsuperscript{34} containing several chromophores such as pyrene, anthracene or porphyrin connected by various linkers have also been found useful in the intramolecular transfer of energy. Ultrafast energy hopping takes place in multichromophoric β-cyclodextrin derivative.

On the other hand, a possibility has also been envisaged to design electronic devices that would operate on the molecular and supramolecular level (molecular and supramolecular electronics). It is concerned with the properties of single molecules or oligomolecular associations and of polymolecular architectures such as Langmuir Blodgett films\textsuperscript{34} within and between which electron transfer processes may occur.

The possibility of designing devices such as molecular rectifiers, transistors, switches and photodiodes has been envisaged and some of the required features are present in compounds such as metal complexes or D-PS-A (D, donor; PS, photosensitizer; A, acceptor) that lead to photoinduced charge separation of the level of isolated molecule\textsuperscript{33} (Fig. 25). The D, A or PS units may be metal coordinating centres. Metal to ligand charge transfer (MLCT) in metal complexes such as Ru(III) or Re(I) - diimines centres has been extensively used for generating photoinduced electron transfer processes.

Inorganic and organic substances possessing a large electronic polarizability are likely to display optical nonlinear properties\textsuperscript{34} that depend first on molecular features but novel effects should arise on going to supramolecular level.

Non-linear optical (NLO) properties are considered to result from both the intrinsic
character of the molecules and from their arrangement in a material (solid, powder, monolayer or multilayer film). The design of material possessing NLO properties involves molecular and supramolecular engineering.

In this design, the push-pull polyenes composed of a polyolefinic chain being donor group on one end and an acceptor on the other (Fig. 26) are of special interest.

The incorporation of such compounds into mixed Langmuir-Blodgett films built from a fatty acid or from an amphiphilic cyclodextrin produces oriented arrangements presenting marked NLO features. If a highly polarizable group is introduced into a receptor molecule, substrate binding would cause substantial perturbation so that recognition event would be converted into a non-linear optical signal. Other polyunsaturated compounds such as oligothiophenes or dyes as well as organometallic or coordination compounds may also exhibit pronounced NLO properties.

Among the various molecular scale electronic devices, the molecular wire is a crucial one. It operates as a connector permitting electron flow to occur between the different elements of a molecular electronic system. Basically three types of electron-transfer processes may be considered: (i) electron transport by redox active molecules acting as mobile carriers through membrane, (ii) electron hopping between suitable redox active groups attached to backbone or assembled through non-covalent interactions and (iii) electron conduction along a continuous conjugated path formed by π bonds. Components affecting these processes may be organic or inorganic. The design of molecular wire should satisfy three criteria: (i) contain an electron conducting chain, (ii) possess terminal electroactive and polar groups for reversible electron exchange and (iii) be long enough to span a typical molecular supporting element such as monolayer or bilayer membrane.

Electron transfer processes play major role in biology. The DNA double helix may serve as support for photoactive electron donor and acceptor groups. Such results do provide information of great value for the design of artificial electronic wire for oriented electron transfer over long distances in molecular and supramolecular systems.

Attachment of metal centres such as ferrocene groups, pyridine or 2,2'-bipyridine complexes at the end of a poly-conjugated chain (carotenoid chain) could provide molecular wires combining the rich electrochemical and photochemical activities of metal complexes with long range conjugation properties of the chain. A ferrocene unit introduced into donor-acceptor type conjugated system (Fig. 27) may serve as a donor centre or redox switch in films deposited on electrodes. Such substances which incorporate electro- and photosensitive switches at the end of or inside conjugated chains, represent switchable molecular wires responding to external stimuli.

In this context, it is worth mentioning that molecular electronics require not only molecular scale switches/transistors but also nano-scale interconnections that provide essential electronic communication between components while blocking undesirable interactions. There is at present a confluence of technological developments and basic...
research which has a good chance to create materials leading to new electronic devices. The work of Wada et al. on nano-scale devices could be a good start in making high memory chips. For this purpose ruthenium(II) and osmium(II) bipyridine type complexes are also found to be excellent components for building supramolecular species owing to their outstanding excited state and redox properties. In order to fulfill the demand of molecular electrician for nano-conductors, Lehn et al. linked two Ru(II) bpy complexes with a conjugate polyene spacer (Fig. 28) and observed long range electron delocalization whereas Barrigelletti et al. detected electronic interactions between complexes joined by rod-like polyphenylene groups (Fig. 29). The structural similarity of polyphenylenes to polyenes suggested that they might also provide a conjugated pathway that could act as a molecular wire. However, the steric interference between the hydrogen atoms on adjacent phenyl rings prevents the rings from lying in the same plane, and thus limits conjugation.

Molecular magnetic devices consist of another class of materials which are in essence supramolecular in nature. These result from the collective features of components bearing free spins and their arrangement in organized assemblies or solid lattices. Engineering of molecular magnets requires the search for high-spin components of organics such as free radicals, carbenes or charge-transfer salts, organometallics or inorganic compounds to incorporate them into supramolecular architectures inducing spin coupling and alignment.

8.0 Drug design and supramolecules

In the treatment of biological disorders, the role of metal ions and their complexes is now well established. The mode of action of these drugs especially as a DNA binder is also extensively studied. In this context, it would also be worthwhile to consider the ability of these metal complexes to form hydrogen bonds; however, this aspect of drug-activity is not well understood. But the development of bifunctional metal complexes showing covalent bond-forming capabilities of the metal ions, and ligand surface capable of recognizing nucleotide bases by means of hydrogen bonding would be of immense importance. Some of the complexes reported recently by Mingos group meet the above criteria and these are illustrated in Fig. 30.

Such interactions have potential implications for metal based drug design since triple hydrogen bonded complementary base pairs have been used for inducing the formation of supramolecular mesophases and as the basis for self-assembled nanostructures.

Thus, there is a clear vast domain of investigation into the design and properties of molecular and supramolecular devices as basis for the development of chemical information processing and signalling as well as for the exploration of their relationship with biological phenomenon.

Summary

Though the area of supramolecular chemistry is young yet extensive researches have been made currently with a variety of molecular interactions and transformations. It opens a new door to the understanding of molecular behaviour in individual entities and in populations. It forms the basis of specific recognition, transport processes, substrate binding to a receptor, enzymatic reactions, antigen-antibody association, entry of a virus into cell and so on. In short, it is a type of molecular engineering and lies at the forefront of modern chemistry.

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