1.1. INTRODUCTION

Molecular self-assembly is the assembly of molecules into an organized structure with the aid of multiple intermolecular forces including relatively weak non-covalent interactions, such as hydrogen bonding, π-π stacking, electrostatic, van der Waals, coordination and ion-dipole interactions. On a molecular scale, the accurate and controlled application of intermolecular forces can lead to new and previously unachievable nanostructures. Hence, the molecular self-assembly is a highly topical and promising field of research in nanotechnology today. With many complex examples in nature, the molecular self-assembly is a widely observed phenomenon that
Chapter 1: Molecular self-assembly

is yet to be fully understood. Nature’s power to efficiently create diverse complex biological functions is based on the non-covalent interactions of covalently pre-fabricated building blocks including bilayered lipid liposomes, protein tertiary structures, DNA double helices, as well as the complex biological process. The molecular self-assembly is ubiquitous in nature and has recently emerged as a new approach in chemical synthesis, nanotechnology, polymer science, materials and engineering. The most illustrative and best understood examples of the molecular self-assembled structures occurring in nature are the tobacco mosaic virus and the formation of collagen (Figure 1.1).

![Image](image_url)

**Figure 1.1.** A) Hierarchical self-assembly of collagen. B) Schematic structure of the tobacco mosaic virus. [Adapted from the reference 3].

Through the molecular self-assembly it is possible to create a new class of materials at the molecular level. The functional hybrid materials based on this approach are very important from the fundamental as well as technology view points. For example, the non-covalently prepared combinations of organic and
inorganic systems have been of central role to the design of a variety of hybrid materials useful for optoelectronic and biological applications.\textsuperscript{2} The optical and morphological properties of these soft materials eventually depend on how these molecules are packed in the assemblies. The self-assembled architectures engineered from organic/polymer/biomolecules construct the novel hybrid materials with enhanced thermal, optical, electronic, and mechanical properties. In this chapter, an overview of the recent developments in the field of self-assembled functional materials is presented with a particular emphasis on nanostructures and their applications. Furthermore, the objectives of the present thesis are also briefly described in this chapter.

\textbf{1.2. SELF-ASSEMBLY PHENOMENON}

The self-assembly is a key tool in supramolecular chemistry in which the term ‘assembly’ connotes ‘to put together’ and the ‘self’ implies ‘without outside help or on its own’.\textsuperscript{1,2} The self-assembly can occur with components from the molecular to planetary scale with the aid of different kinds of interactions provided that appropriate conditions are met. The molecular self-assembly systems lie at the interface between molecular biology, chemistry, polymer science, materials science and engineering.\textsuperscript{2,3} The molecular self-assembly has proven to be a reliable approach based on multiple weak intermolecular forces leading to the creation of large, discrete, ordered structures from the relatively simple units. The formation of molecular crystals,\textsuperscript{4} colloids,\textsuperscript{5} lipid bilayers, and self-assembled monolayers\textsuperscript{6} are all
examples of the molecular self-assembly. It is believed that application of these simple and versatile molecular self-assembly systems will provide us with new opportunities to study some complex and previously unknown biological phenomenon.

The molecular engineering through molecular design and self-assembly of the biological building blocks is an enabling technology that will likely to play an increasingly important role in the future technology. This chapter primarily focuses on the recent progress of the molecular self-assembly that is inspired from naturally occurring materials, peptide self-assemblies and also based on synthetic molecules or amphiphiles bearing bioactive moieties. These larger systems also offer a level of control over the characteristics of the components and interactions among them that makes fundamental investigations especially tractable. In this context, the self-assembly of living systems is most important. The astonishing range of complex structures present in the cells offer countless examples of the functional self-assembly.\textsuperscript{3} The molecular self-assembly provides routes to a range of ordered structures for example molecular crystals,\textsuperscript{4} liquid crystals,\textsuperscript{5} semicrystalline\textsuperscript{5} and phase-separated polymers.\textsuperscript{6} And it is providing one of the general strategies for generating the ensembles of nanostructures. Finally, there is great potential for its use in smart materials, non-fouling properties, electrochemistry, protein binding, DNA assembly, corrosion resistance, biological arrays, cell interactions, and molecular electronics.\textsuperscript{7} Thus, the self-assembly is important in a variety of fields including chemistry, physics, biology, materials science and nanoscience.
1.2.1 Types of Self-Assemblies

The term self-assembly implies spontaneity, in which an ordered pattern forms itself from a disordered state. There are mainly two kinds of self-assemblies, viz., static (S) and dynamic (D). The static self-assembly denotes a process in which ordered structures are formed when the system reaches an energy minimum and do not dissipate energy. Classic examples are structured block copolymers, nanoparticles, nanorods, liquid crystals, and hierarchical supramolecular systems. In dynamic self-assembly (D) (Table 1.1), the interactions responsible for the formation of structures or patterns between components only occur if the system is dissipating energy. The components in dynamic self-assembling systems interact with one another in complex (and often nonlinear) ways and their behavior will often be complex.

Among these, the study of dynamic self-assembly is in its infancy while the static type has found various applications. The processes of static and dynamic self-assemblies can be sub-divided into two further variants, templated and biological self-assembly. In a templated self-assembly (T), the interactions between the components and regular features in their environment determine the structures that form. Some examples include, crystallization on the surface, which determine the morphology of the crystal as well as crystallization of colloids in three-dimensional optical fields. Thus the biological self-assembly has emerged over times as a hybrid methodology and the characteristic of the biological self-assembly (B) is the variety and complexity of the functions that it produces due to the organization.
**Chapter 1: Molecular self-assembly**

**Table 1.1.** Examples of static (S), dynamic (D), template (T), and biological (B) self assemblies.

<table>
<thead>
<tr>
<th>Systems</th>
<th>Type</th>
<th>Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atomic, ionic, and molecular crystals</td>
<td>S</td>
<td>Materials, optoelectronics</td>
</tr>
<tr>
<td>Phase-separated and ionic layered polymers</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>Self-assembled monolayers (SAMs)</td>
<td>S/T</td>
<td>Microfabrication, nanoelectronics, sensors</td>
</tr>
<tr>
<td>Lipid bilayers and lipid films</td>
<td>S</td>
<td>Biomembranes, emulsions</td>
</tr>
<tr>
<td>Liquid crystals</td>
<td>S</td>
<td>Displays</td>
</tr>
<tr>
<td>Colloidal crystals</td>
<td>S</td>
<td>Band gap materials, molecular sieves</td>
</tr>
<tr>
<td>Macro- and mesoscopic structures</td>
<td>S/D/T</td>
<td>Electronic circuits</td>
</tr>
<tr>
<td>Fluidic self-assembly</td>
<td>S/T</td>
<td>Microfabrication</td>
</tr>
<tr>
<td>Oscillating and reaction-diffusion reactions</td>
<td>D</td>
<td>Biological oscillations</td>
</tr>
<tr>
<td>Bacterial colonies</td>
<td>D/B</td>
<td></td>
</tr>
</tbody>
</table>

Of the diverse approaches reported for the molecular self-assembly, two strategies have received significant attention. These include, electrostatic self-assembly (or layer-by-layer assembly) and “self-assembled monolayers” (SAMs). The electrostatic self-assembly involves the alternate adsorption of anionic and cationic electrolytes onto a suitable substrate, whereas for SAMs, the basic building blocks (that is, the constituent molecules), and weaker intermolecular bonds such as
van der Waals bonds were utilized to synthesize a defined structure. Figure 1.2 shows the representative examples of dynamic and static self-assembly.

**Figure 1.2.** Examples of A) dynamic self-assembly, an optical micrograph of a cell with fluorescently labeled cytoskeleton and nucleus and B) static self-assembly, crystal structure of a ribosome. [Adapted from the reference 8].

### 1.2.2. Non-Covalent Interactions in Self-Assembly

The self-assembly is a process in which components, either separated or linked, which spontaneously form ordered structures. The characteristic properties such as shape, surface, charge, polarizability, magnetic dipole, mass, etc of the individual components determine the interactions among them. The design of components that organize themselves into desired patterns is the key to applications of the self-assembly.\(^9\) In the self-assembly of larger components (meso or macroscopic objects), the interactions can often be selected and tailored, and can include gravitational attraction, external electromagnetic fields, and magnetic, capillary, and entropic interactions, which are not important in the case of the
molecules. The molecular self-assembly involves the non-covalent interactions such as van der Waals, electrostatic, hydrophobic interactions, hydrogen and coordinate bonds. While a covalent bond normally has a homolytic bond dissociation energy that ranges between 100 and 400 kJ mol\(^{-1}\), the non-covalent interactions are generally weak and vary from less than 5 kJ mol\(^{-1}\) for van der Waals forces, to approximately 50 kJ mol\(^{-1}\) for hydrogen bonding and 250 kJ mol\(^{-1}\) for Coulomb interactions (Table 1.2). Our ability to predict the structural features from combinations of such interactions in the self-assembled materials is still in its early stage and, most of the learning is done in retrospect that is, after the discovery of structures and their functions.

Because the self-assembly requires that the components be mobile, it usually takes place in fluid phases or on smooth surfaces. The environment can modify the interactions between the components and the equilibration is usually required to reach the ordered structures. The self-assembly requires that the components either equilibrate between aggregated and non-aggregated states, or adjust their positions relative to one another in an organized state.\(^8\) There are three ranges of sizes of components for which self-assembly is important: molecular, nanoscale (colloids, nanowires, nanospheres, and related structures), and meso to macroscopic (objects with dimensions from microns to centimeters). The rules for self-assembly in each of these ranges are similar but not identical. The new types of self-assembled structures, especially those with potential for application in microelectronics,\(^{20,21}\) photonics,\(^{22,23}\) near field optics\(^{24}\) and the emerging field of nanoscience\(^{25,26}\) have
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gained technological importance. In the following headings, we describe the nanostructures that are formed from the self-assembly of various molecular systems as well as their properties and applications.

Table 1.2. Bond energies in kJ mol⁻¹ of non-covalent interactions.

<table>
<thead>
<tr>
<th>Type of interaction or bonding</th>
<th>Strength (kJ mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covalent bond</td>
<td>100-400</td>
</tr>
<tr>
<td>Coulomb</td>
<td>250</td>
</tr>
<tr>
<td>Hydrogen bond</td>
<td>10-65</td>
</tr>
<tr>
<td>Ion-dipole</td>
<td>50-200</td>
</tr>
<tr>
<td>Dipole-dipole</td>
<td>5-50</td>
</tr>
<tr>
<td>π-π</td>
<td>0-50</td>
</tr>
<tr>
<td>van der Waals forces</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Hydrophobic effects</td>
<td>difficult to assess</td>
</tr>
<tr>
<td>Metal-ligand</td>
<td>0-400</td>
</tr>
</tbody>
</table>

1.2.3. Self-Assembly of Peptides and Proteins

The ability of peptides and proteins to adopt specific secondary, tertiary and quaternary structures provides unique opportunities for the design of nanoscale materials. The covalently linked amino acids with specific sequence give rise to
peptides, which can undergo distinctive self-assembly\textsuperscript{34-37} and exhibit recognition function.\textsuperscript{37,38} Depending on the conformation and stereochemical configuration of the constituent amino acids, these peptides exhibit different structures, such as $\alpha$-helices and $\beta$-sheets. A number of peptide molecular self-assembly systems have been designed and developed. Their systematic analysis has provided insights into the chemical and structural principles of peptide self-assembly, which are simple to design and easy to synthesize. This class of biological materials has considerable potential for a number of applications, including scaffolding for tissue repair and tissue engineering, drug delivery, and biological surface engineering.

The first engineered structures at the nano-scale were the cyclic peptide nanotubes 1, which were developed by Ghadiri and co-workers (Chart 1.1).\textsuperscript{39a} In their elegant work, the concepts of natural peptides were translated into technological applications. The authors have used the concept of alternating D- and L-amino acids in the context of a cyclic peptide to form a planar ring that could be self-assembled, one on top of the other, to form tubular structures of a desired diameter. Another cyclic peptide that was shown to self-assemble into tubular structures is the lanreotide (2) growth hormone inhibitor reported by Valery and co-workers (Chart 1.1).\textsuperscript{39b} Importantly, this naturally occurring cyclic peptide self-assembled into well-ordered structures at the nano-scale through hydrophobic and aromatic interactions. Similar systems have also been described where these peptide systems exhibited self-assembly to form a gel with regular $\beta$-sheet tapes of well-defined structures.\textsuperscript{39-42} The self-assembly of peptide nanotubes, which allowed
ions to pass through and to insert themselves into lipid bilayer membranes were also described.\textsuperscript{42} The peptide-amphiphiles (PA), which were attached with hydrophobic tails were found to self-assemble into highly organized nanostructures, which can in principle promote cell adhesion, spreading, migration, growth and differentiation.\textsuperscript{43-47} For example, Stupp and co-workers have synthesized a peptide amphiphile (PA) 3, consisting of different functionalities (Chart 1.1).\textsuperscript{48} Upon acidification of the solution, PA spontaneously aggregated into birefringent hydrogels. The cryo-TEM studies have revealed a network of fibers with a diameter
of ~7.6 nm and lengths up to several micrometers. Furthermore, a number of fascinating bio-mimetic peptide and protein structures have been reported in the literature, which exhibited helical coils and di-, tri-, and tetra-helical bundles.\textsuperscript{49}

The protein-protein interactions play an important role in metabolic and degradation processes and in the self-assembling of large biological structures.\textsuperscript{50} The self-assembly in biology was popularized by the cross-fibril formation, also known as formation of amyloids.\textsuperscript{51} There were about 20 different human diseases that are associated with the formation of these 7-10 nm amyloid fibrils. These fibrils show remarkable order, as indicated by X-ray fibre diffraction at 4.6-4.8 Å. They also exhibit a typical β-sheet conformation and strong interactions with thioflavin.\textsuperscript{52,53} The cross-fibre consists of peptide chains that align perpendicular to the fibril axis as shown in Figure 1.3.\textsuperscript{51} Basically, the amyloid fibres were a bundle of highly

\begin{figure}
\centering
\includegraphics[width=\textwidth]{cross_beta_structure.png}
\caption{Schematic representation of the cross beta structure perpendicular to fibril axis [Adapted from the reference 51].}
\end{figure}
ordered filaments composed of ladders of β-strands that run perpendicular to the fibre axis and are arranged in hydrogen-bonded β-sheets. The ability to construct biocompatible peptide-based molecular architectures with anisotropic shapes should expand the possibilities for the design of molecular machines for diverse applications in biological and materials science.

Another class of peptide nanostructures was based on the use of short aromatic peptides to form well-ordered nanostructures. The simpler analogues, diphenylalanine (4) and diphenylglycine (5) peptides, form nanotube and nanospherical structures in the aqueous solution (Figure 1.4). Other end-termini analogs such as the Fmoc-diphenylalanine forms macroscopic hydrogels with nano-scale order, whereas the Fmoc-diphenylalanine exhibited fibrils that were very

![Diagram of self-assembly and nanostructures](image)

**Figure 1.4.** Formation of ordered nanostructures by simple aromatic dipeptides, 4 and 5.
similar to the amyloid fibrils.\textsuperscript{54} It was demonstrated that the dipeptide nanostructures were formed by vertical arrays in the form of a “nano-forest” of tubes or could be aligned horizontally upon modification with either magnetic nanoparticles or by the application of an external magnetic field.\textsuperscript{54}

1.2.4. Self-Assembly of Polymers and Small Organic Molecules

Over the past decades, the molecular self-assembly has become a powerful tool for making functional and self-assembled organic nanostructures. In 1990s, Whiteside and co-workers have pioneered the concept of self-assembly of nanoscale structures.\textsuperscript{54} Similarly, Stupp and co-workers have developed the concept of self-assembly of the functional bulk materials.\textsuperscript{55} The influence of the self-assembly strategies in polymeric materials research was reflected in the strong interest on the organization of well-defined block copolymers into defined superlattices and patterns.\textsuperscript{56} Most notably the exciting new field of supramolecular polymers\textsuperscript{57} was based on the control of non-covalent interactions among monomers and processes of self-assembly to generate ordered 1D structures. In organic nanoscience, the supramolecular chemistry is key in the design of self-assembled monolayers,\textsuperscript{58} and nanostructures with diverse shapes and dimensionalities.\textsuperscript{59-61} In all these cases, the programmed self-assembly of the \(\pi\)-conjugated oligomers has been achieved using supramolecular design rules.

One of the first examples of the self-assembly of the supramolecular material was reported by the Stupp’s group in the form of nanostructure lattices.\textsuperscript{55} In 1997, a
triblock molecule labeled as a rod-coil was reported to assemble into mushroom like objects that were fairly monodisperse. Inspired by this earlier work on rod-coil molecules that self-assemble into non-centrosymmetric nanostructures, the authors have designed another molecule 6 (Chart 1.2) with a dendritic block at the end of the rod segment that they refered to as a dendron rod-coil. These molecules assembled into 1D ribbons that were of ~10 nm wide and ~2 nm thickness. Later, synthetically modifying each of the dendron, rod, and coil segments revealed the importance of each portion on the self-assembly behavior. Around the same time, complementary approaches to 1D nanostructures with potential electronic function have also been proposed.

![Chart 1.2](image)

For example, Meijer’s group found that molecules functionalized at each end with ureidopyrimidinones 7 (Chart 1.3), assemble through self-complementary hydrogen bonding into supramolecular polymers that display effective mechanical properties similar to the covalent polymers at room temperatures. This structures
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were also incorporated with conjugated aromatic oligo(phenylene vinylene) groups to form different nanoarchitectures.\textsuperscript{56b,c} Importantly, 1D structures have been reported based on disk-shaped aromatics like hexabenzocoronene, which exhibited strong $\pi$-$\pi$ stacking interactions and required no additional interactions for the assembly.\textsuperscript{57} For example, Hill and co-workers have reported hexabenzocoronene 8 (Chart 1.3), with ethylene glycol tails on one side and alkyl tails on the other. These systems exhibited self-assembly to form a hollow tube.\textsuperscript{57} A solution of these graphitic tubes can be drawn into macroscopic fibers with anisotropic conductivity along the fiber’s long axis. This family of molecularly engineered graphite with a one-dimensional tubular shape and a chemically accessible surface constitutes an important step towards molecular electronics.\textsuperscript{57}

Recently, Stupp and co-workers have reported a hairpin-shaped molecule based on thiophene-capped diketopyrrolopyrrole units and the self-assembly motif
trans-diamidocyclohexane 9 (Chart 1.4). The authors have demonstrated that the self-assembly of 9 involving hydrogen bonding and π–π stacking interactions, led to long supramolecular electron donor nanowires. The authors have observed that the stepwise cooling process with minimal stirring of solutions was necessary to create robust wires through the self-assembly process.

Würthner and co-workers have also shown a strong pathway dependence in hairpin-shaped molecules bearing merocyanine dyes 10 (Chart 1.5). Accordingly, the authors have described the kinetically controlled self-assembly of merocyanine 10 into helical nanorods. A series of bis(merocyanine) dyes bearing alkyl substituents of different chain lengths and branching revealed that the small structural changes of the monomeric building block can have a considerable impact on the stability and structure of the nano structures formed. In addition, porphyrins, phthalocyanines, and perylenes were also investigated as molecular materials that possess unique electronic, magnetic and photophysical properties. These systems formed highly ordered aggregates with interesting morphology in solution such as micelles, vesicles, sheets, rods, tapes etc. For example, Wang⁶² and co-workers have reported nanotubes from the porphyrin derivative 11. This system exhibited the self-assembly in the aqueous solution involving ionic interactions (Chart 1.5).

Perylene bisimides (PBI) are one of the well studied classes of dyes for optoelectronic applications because of their promising optical properties such as the strong absorption in the visible range, high fluorescence quantum yields as well as their high stability towards photooxidation. Shinkai and co-workers⁶³ have reported
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Chart 1.4

Chart 1.5
the first cholesterol functionalized perylene bisimide organogelator 12 (Chart 1.6), which exhibited cascade of energy and electron transfer processes. SEM studies have suggested the formation of well-defined fibrous aggregates through π-π stacking and intermolecular hydrogen bonding between the constituent PBI molecules. The gelator also showed efficient electron transfer in organic solar cells upon mixing with p-type organic semiconductors. The authors have demonstrated that a new visible light-harvesting system that can be designed utilizing a superstructure created in an organogel medium. These nano-materials based on molecular assemblies can be applied as model systems for light-emitting diodes, signal amplifiers, fluorescence sensors, energy filters, and other photonic devices.

![Chart 1.6](image-url)
In another work, Würthner and co-workers have employed the perylene bisimide dye 13 (Chart 1.6), which exhibited gelation in a broad variety of organic solvents to afford well-defined nano and mesoscopic helical fibres and bundles.\textsuperscript{64} Such well-organized fibers and bundles were composed of extended $\pi$-stacks of the electron poor dye 13, which can have application as mobile n-type charge carriers. Shinkai and co-workers have reported the gelation of naphthalene diimide, 14 (Chart 1.7). The UV-vis absorption spectra of these derivatives showed charge-transfer band at 600 nm upon adding increasing amounts of the dihydroxy-naphthalene (15) in the gel matrix of 14.\textsuperscript{65} SEM analysis showed the presence of long 1D fibrous networks of 14, which transformed into a 2D sheet like structure by the addition of 15.

![Chart 1.7](chart.png)

### 1.3. APPLICATION OF SELF-ASSEMBLED STRUCTURES

The self-assembly paradigm in chemistry, physics and biology has emerged scientifically over the past two decades to a point of sophistication that one can
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begin to exploit its numerous attributes in nanofabrication. The self-assembled nanostructures are interesting because they offer new properties like conductivity and stiffness, and the broad range of fluorescent emission of CdSe quantum dots. These structures form a bridge between classical and biological branches of materials science, and thereby "materials-by-design". The nanomaterials can, in principle, be made using both top-down and bottom-up techniques. The self-assembly involving these two techniques allows materials to be designed with hierarchical order and complexity that mimics those seen in the biological systems.

Nanotechnology based device in its broadest terms refers to a device with dimensions in the range of 1 to 100 nm, while the nanofabrication involves the manipulation of matter at the nanoscopic length scale to provide by design structures and patterns with purposeful function. In the framework of nanofabrication by bottom-up synthetic chemistry, the self-assembly has provided a powerful way of making materials and organizing them into functional constructs designed for a specific purpose. The self-assembly, as a fundamental building principle, teaches that the matter of all kinds, exemplified by atoms and molecules, colloids and polymers, can undergo spontaneous organization to a higher level of structural complexity, driven by a map of forces operating over multiple length scales. With unique sequence-specific self-assembly and recognition properties, the peptides and proteins play critical roles in controlling the biomineralization of inorganic nanostructures in natural systems. These properties render them particularly useful molecules for the fabrication of new materials and devices.
In this context, substantial effort has been devoted to organizing nanoparticles (NPs) in one, two and three dimensions. The ability to create NP networks, arrays and composites, however, depends on our ability to fully understand and control the assembly process of these materials. Incorporation of both “bottom-up” (e.g., self-assembly) and “top-down” techniques (e.g., lithography) in patterning and controlling spatial assembly of NPs and their composites is a growing field of research. The synergy between these two approaches provides new directions for the creation of functional materials and devices. Of all the nanomaterials, gold based nanomaterials have attracted particular interest owing to their ease of synthesis and functionalization, chemical stability, low inherent toxicity (biocompatibility), and tuneable optical and electronic properties (absorption, fluorescence and conductivity). A number of efforts have been made in the field of biopolymer (proteins and DNA) mediated assembly of gold NPs (AuNPs) as well as their applications in sensors and devices (Figure 1.5). The protein or peptide scaffold in AuNP-protein composites can serve three purposes like assembling the NPs into composite material, serving as a matrix that induces ordering and anisotropic orientation in clusters and on surfaces, and acting as a functional element (e.g. possess an electronic property).

The assembly of inorganic nanoparticles using self-assembled peptide scaffolds generally involves several independent steps including peptide assembly, nanoparticle synthesis, nanoparticle functionalization with surface ligands suitable for interacting with the peptide-based template, and finally mixture of the template
structures with the functionalized nanoparticles to effect assembly of the nanoparticles. Pochan and co-workers have prepared sheets of gold nanoparticles (Figure 1.6), in which the assembled, non-twisted laminated β-sheet peptide fibrils acted as templates, and negatively charged gold nanoparticles intercalated within the fibril laminates. The formation of the aggregates was induced by the electrostatic interactions with the positively charged lysine side chains of the fibrils and negatively charged nanoparticles. The intercalation of gold nanoparticles was enhanced when the interfilament spacing increased from 2.5 nm to 3.9 nm.68
Rosi and co-workers have demonstrated that both the peptide self-assembly and peptide-based biomineralization of gold nanoparticles could be combined into one process.\textsuperscript{69} The authors have first selected the water-soluble peptide AYSGGAPPMPF, which had been identified by Naik \textit{et al.}, and was known to bind to both gold and silver surfaces. Moreover, this peptide was able to mineralize chloroauric acid to form monodisperse spherical gold nanoparticles in the presence of HEPES buffer.\textsuperscript{70} The authors have observed that the self-assembly process and the Au-based biomineralization of gold nanoparticles were successfully coupled into one simultaneous process to form structurally complex and highly ordered left handed double helices of gold nanoparticles.\textsuperscript{69}
Hutchinson and co-workers have demonstrated the use of DNA scaffolds to pattern closely spaced gold nanoparticle assemblies of lines, ribbons and junctions on surfaces (Figure 1.7). The nanoparticles thus formed close-packed linear assemblies along the DNA scaffold and showed extended linear structures that often reached nearly 1 μm in length. Furthermore, two-dimensional, ribbon-like structures were also observed, resulting from the cross-linking of DNA scaffolds by the polyvalent gold nanoparticles.71

Figure 1.7. Nanoassemblies of gold nanoparticles formed during solution phase assembly. Electrostatic assembly of cationic nanoparticles onto the anionic backbone of DNA produces a wide range of structures including A) linear arrays, B) ribbons, and C) branched assemblies. [Adapted from reference 71].

Encapsulation of noble-metal nanoparticles within dielectric matrices has been used to develop fast optoelectric response systems near the surface plasmon resonance (SPR) frequency.72 The light energy can thus be transported through nanoparticles whose sizes were substantially smaller than the wavelength of
corresponding light. Paik et al., have successfully constructed anisotropic AuNP chains within a dielectric protein matrix capable of exhibiting photoconductivity near the SPR frequency by taking advantage of molecular propensity of α-synuclein to form the protein fibrillar suprastructures (Figure 1.8). Their strategy employed a facile unit assembly procedure of novel self-interactive building blocks made of amyloidogenic α-synuclein encapsulating AuNPs to construct the high-order nanostructures, representing a typical bottom-up approach to fabricate a functional large structures of noble-metal nanoparticles.

Figure 1.8. A) TEM image of the pH induced AuNP chains. B) I-V response which revealed a nonlinear I-V curve in which the current increased linearly to the applied voltage only from 1.2 V after a non-responding lag phase. [Adapted from reference 74].

Soft materials derived from organic molecules, through non-covalent interactions are extremely sensitive to the surrounding media and they exhibit reversible properties due to the dynamic nature of the non-covalent forces. As a
result, such soft materials are of great interest in chemistry, biology and material science. The chromophores based assemblies are of particular interest due to their inherent optical and electronic properties, which find application in organic electronics, light harvesting, as well as biological sensors. Therefore, design of chemosensors based on fluorescent molecules has been a subject of great interest to chemists. Among the diverse methods, the most common signal transduction schemes utilize optical or electrical properties. To produce a functional sensor, a highly sensitive optical transduction method such as fluorescence is of great advantage, where the analyte binding produces a reduction (turn-off), enhancement (turn-on), or wavelength shift in the emission. Recently, the molecular assemblies of \( \pi \)-systems have been investigated for their use in the sensing of analytes.\(^{75}\)

Zang and co-workers have fabricated nanofibres from a strongly fluorescent n-type organic semiconductor material and have employed for efficient fluorescent sensing of gaseous amines.\(^{76}\) The extended 1D molecular arrangement obtained for 16 (Figure 1.9A) was likely dominated by the \( \pi-\pi \) interactions between perylene backbones in cooperation with the hydrophobic interactions between the side chains having appropriate size (Figure 1.9B). These red fluorescence of nanofibers (Figure 1.9C) with quantum yield of ca. 15% showed quenching when exposed to aniline vapors. Such a porous and emissive nanofibres were found to be efficient in probing gaseous molecules with high sensitivity and fast time response. The emission intensity of the film monitored upon exposing to a saturated vapor of aniline (880 ppm) showed a decay lifetime of only 0.32 ns. The observed efficient
quenching has been attributed to the photoinduced electron transfer process having favorable energy difference between HOMO of aniline and 16.

![Chemical structure of 16](image)

**Figure 1.9.** A) Chemical structure of 16. B) SEM image of a nanofibril film deposited on a glass slide. C) Fluorescence optical microscopy image of a nanofibril film. [Adapted from reference 76].

Most of the organic dyes were intrinsically emissive but normally exhibit quenched emission at the higher concentrations due to the formation of their aggregates (self-quenching).\(^{77}\) Therefore, the fluorophores exhibiting aggregation-induced emission (AIE) have been increasingly attracting much attention because such effective systems can have potential optoelectronic applications.\(^{78}\) Importantly, the AIE molecules were endowed to exhibit the fluorescence “turn-on” switching in
response to the self-assembly, which makes them potential optical probes. Despite these advantages, only a few AIE examples have so far been reported which found use as probes for DNA,\textsuperscript{79} protein,\textsuperscript{80} and heparin,\textsuperscript{81} and as a chiral recognition host.\textsuperscript{82} Shinkai and co-workers have demonstrated that the AIE-based guanidinium bioprobe \textbf{17} (Chart 1.8), exhibited the nonlinear fluorescence response accompanying the self-assembly of TPE in the presence of ATP.\textsuperscript{83}

![Chart 1.8](image)

Recently, the self-assembly of nanoparticles have attracted attention in nanoformulations that showed many therapeutic advantages over conventional formulations. Liang \textit{et al.},\textsuperscript{84} developed traceable nano-formulations to closely monitor the drug delivery. They have developed a new drug delivery system (DDS) using tetraphenylethene \textbf{18}, to fabricate a self-assembled micelle with aggregation-induced emission (AIE micelle). AIE mechanism makes the nano-carriers visible for
high-quality imaging and the switching on and off of the AIE was intrinsically controlled by the assembly and disassembly of the micelles. This was tested for doxorubicin (DOX) delivery and intracellular imaging applications. For DOX-loaded micelles (TPED), the DOX content was reached as much as 15.3% by weight, and the anticancer efficiency was found to be higher than that observed for free DOX. At the same time, the high-quality imaging was obtained to trace the intracellular delivery of the TPED (Figure 1.10) using this system.

Figure 1.10. A) Chemical structure of 18. B) CLSM images of the distribution of DOX-loaded micelles. MCF-7 breast cancer cells were incubated with TPED (TPE–mPEG 75 μM and DOX 5.0 μM) for 4 h. Scale bars are 20 μm. [Adapted from reference 84].

With a view to develop organic and supramolecular assemblies for biological applications, Betsy et al.,\textsuperscript{85} have developed novel amphiphilic porphyrin systems containing the pyridine pincer systems and have investigated their photophysical and morphological transformations under different conditions. One of these systems, for example 19, exhibited vesicular structures in methanol, while in water
it showed time-dependent nanofibers, nano-networks and sheet-like structures (Chart 1.9). Interestingly, the authors have demonstrated that the vesicular structures formed in methanol can be utilized to encapsulate a hydrophilic guest molecule HPTS (8-hydroxypyrene-1,3,6-trisulfonate), which on demand can be released into the aqueous medium by varying the solvent polarity and time interval.

![Chart 1.9](image)

Recently, Anees and co-workers have demonstrated the versatility of an organic dye nanoparticle for the sensing of serum albumin proteins (SAP) in a pool of other biomolecules. The squaraine dye 20 in its native molecular form was reactive to a variety of thiol containing molecules. However, when the dye self-assembled to form nanoparticles, only SAP could selectively interact with the dye thereby opening the access for a thiol attack. Thus, the dormant fluorescence moiety
present in the squaraine dye 20 (Chart 1.10), gets activated latently, allowing the specific sensing of SAP by a “turn-on” green fluorescence mechanism. The selective covalent modification of SAP was achieved only with the self-assembled system and not with the monomeric dye. The enhanced selectivity of the squaraine nanoparticles allowed the authors to use them for the quantitative estimation of HSA in human blood samples. The described self-assembly approach using a small organic NIR dye having a dormant fluorophore, which was latently activatable through a nucleophilic attack was a model example for empowering a small molecular fluorophore to a reaction specific nanosensor by self-assembly.

Chart 1.10

Insights on the self-assembly of π-conjugated oligomers leading to nano-sized architectures, controlled size and shape are important in organic electronic devices due to their unique electronic properties. In this context, approaches for the preparation of 1D fibres of organic molecules have attracted the attention of chemists since these 1D structures are expected to have good electronic conductivity and high charge-carrier mobility, required for a variety of electronic applications. At the molecular level, conjugated systems represent the simplest
models of molecular wires, which together with their complementary functions either as molecular switches or logical gates.\textsuperscript{87}

For example, Park and co-workers have reported the semiconducting one dimensional nanowires (1D NWs) from the fused thiophene derivative 21 (Chart 1.10).\textsuperscript{87} Detailed UV-Vis, AFM and XRD analyses have revealed the strong self-assembling capability of these systems that led to the formation of 1D NWs exhibiting a drastic fluorescence emission enhancement upon the formation of NW aggregates. Further, the conducting probe-atomic force microscopy (CP-AFM) and space charge limited current (SCLC) measurements have revealed that the well-ordered 1D NWs exhibit good current flow along the crystals with an effective carrier mobility of up to 3.1 cm\textsuperscript{2} V\textsuperscript{-1} s\textsuperscript{-1}.

Aida and co-workers have made significant contribution to the self-assembly of hexa-\textit{peri}-hexabenzocoronene (HBC) derivatives. For example, they have reported the formation of nanotubes of an amphiphilic derivative 22 (Chart 1.11), from THF solution. These nanotubes showed an aspect ratio greater than 1000 and exhibited 14 nm width.\textsuperscript{61} The walls of the tubes consisted of helical arrays of \(\pi\)-stacked coronenes covered by hydrophilic glycol chains. Interestingly, an individual nanotube could be positioned across Pt nanogap electrodes (180 nm) on a SiO\textsubscript{2} substrate. The tube was essentially insulating, however, after oxidation with nitrosonium tetrafluoroborate (NOBF\textsubscript{4}), it showed an \(I-V\) profile with an ohmic behaviour having a resistance of 2.5 M\(\Omega\) at 285 K. This value was comparable to the inorganic semiconductor nanotubes reported in the literature.
As described above the self-assembled functional materials have attracted much attention in recent years and are being explored for a variety of applications. The elucidation of the assembly from the molecular level to small and large supramolecular nanosystems constitutes a bridge between molecules and their morphologies and functions, and thus provides a guideline for the design of advanced molecular materials. As can be deduced from this chapter, it is possible not only to study material properties at the supramolecular level, but also to tune their macroscopic properties for potential applications.

1.4. OBJECTIVES OF THE PRESENT INVESTIGATION

The molecular self-assembly is a key concept in supramolecular chemistry and which has been proven to be a reliable approach towards the synthesis of a variety of versatile nanomaterials. These self-assembled soft nanomaterials have been exploited in a wide range of areas from chemistry and biology to material
science. In this context, one of our objectives has been to synthesize the self-assembled nanostructures using biological and synthetic building blocks. We have synthesized biocompatible nano-biohybrid systems, using γ-globulin, a blood plasma protein as a capping, reducing as well as a templating agent. Our approach offered a way to understand the role played by the self-assembly of the protein in ordering and knocking out of the metal nanoparticles and also in the design of nano-biohybrid materials for medicinal and optoelectronic applications. Another objective has been the development systems based on water soluble near infrared absorbing squaraine dyes as protein labeling as well as anti-amyloid agents, wherein the amyloid fibres were believed to be involved in several disorders, such as Alzheimer's disease, cystic fibrosis, and prion diseases. The synthesized dyes showed efficient interactions with lysozyme and also acted as effective inhibitors of the amyloid fibres derived from lysozyme. Yet another objective of the thesis has been the synthesis and investigation of photophysical and self-assembly properties of novel electron donor and acceptor conjugates based on tetraphenylethene and benzothiazole chromophores. The nanoparticles derived from these conjugates exhibited high stability, fluorescence emission and good biocompatibility in the aqueous medium, thereby demonstrating their potential in cell tracing and imaging applications.
Chapter 1: Molecular self-assembly

1.5. REFERENCES


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