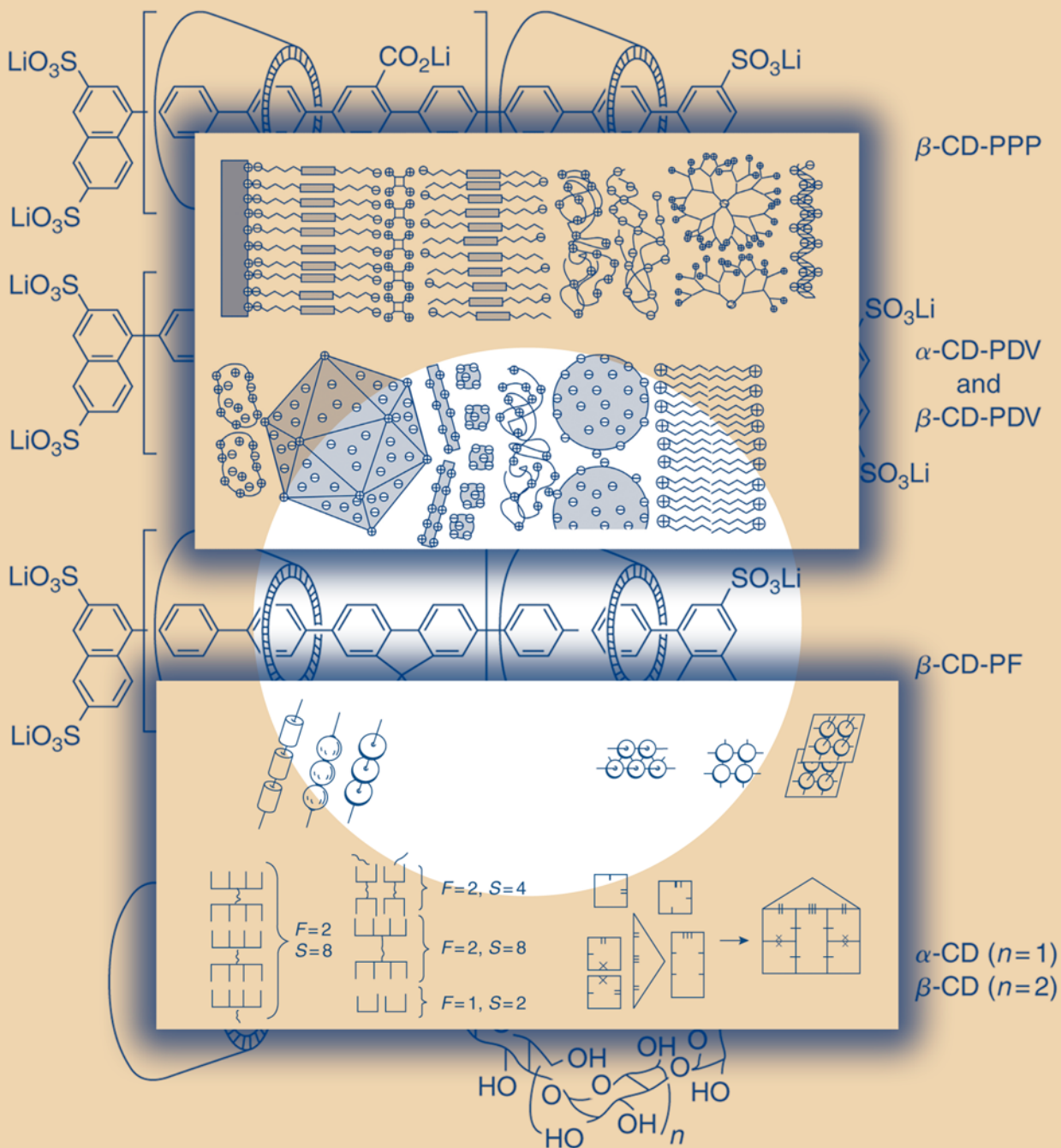


SUPRAMOLECULAR POLYMERS

SECOND EDITION



EDITED BY *Alberto Ciferri*

SUPRAMOLECULAR POLYMERS

Second Edition

EDITED BY
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Preface

The five years that have elapsed from the presentation of the first edition of the book have witnessed an unprecedented expansion of the area of supramolecular polymers (SPs). The organization of the present edition in two sections (Theory/Structure and Properties/Functions) highlights the directions of said expansion. The first section describes developments that have occurred in the synthesis of complex structures, arising from an understanding of chemical design principles that underline self-assembly (Chapters 1, 6, 7, 8, 10, and 11). These developments have been accompanied by the elaboration of theoretical models of growth processes, allowing predictions of the field of stability, degree of polymerization, and shapes of a variety of assemblies (Chapters 2, 3, 4, and 9).

The self-assembly of natural and synthetic multifunctional unimers occurs, in fact, by a combination of classical molecular recognition and growth mechanisms. Self-assembled, reversible structures include linear, helical, columnar, and tubular polymers; micelles; monolayers; and three-dimensional phases and networks. Self-assembled systems based on an interplay between covalent chains and supramolecular interactions are also important. Typical examples are side-chain SPs (Chapter 5), host-guest polymeric composites and dendrimers (Chapters 2 and 7), polymers with mechanical bonds (Chapter 8), and block copolymers (Chapters 9–11).

The second section describes properties and proposed applications of synthetic SPs of both the self-assembled and engineered types. Naturally occurring SPs are included, because they demonstrate the rich potential that may eventually be matched by synthetic systems. An impressive amount of work has indeed been reported. Chapter 19, for instance, documents the impressive threefold increase of references on layered polyelectrolytes that has occurred during the five years between the two editions.

Systems included represent a selection adequate to show both the potential applications of SPs and the relationship with the basic principles outlined in the first section. Bottom-up nanotechnology applications based on DNA templates (Chapter 12) include the self-assembly of electronic components, DNA actuators, and even molecular computing. Chapter 13 describes supramolecular amphiphiles forming membranes, hydrogels, and organic/inorganic nanocomposites. Opto-electronic devices (for instance, columnar π -stacks and molecular wires) are extensively described in Chapter 14. Linear SPs are receiving attention for tunable, adaptive features expressed by their rheological and self-healing properties (Chapter 15), while tubular SPs may host polymer molecules or act as ion-selective channels (Chapter 16). Planar SPs are applied as templates for immobilization and patterning in molecular biosensors and biocompatible surfaces (Chapters 17, 18, and 19). Molecular imprinting (Chapter 20) is a recognized approach to the preparation of tailor-made receptors, artificial enzymes, and catalytic antibodies. Helical SPs coupled to chemical stimuli allow motion or force generation (Chapters 21 and 22).

Several chapters from the first edition have been updated or rewritten, and an equal number of new chapters have been added. Rather than a collection of scattered chapters, the book is an attempt to provide a unified overview of the field, with an emphasis on fundamental principles, chemical design, and applications. This was made possible by the commitment and patience of the authors and their participation in minimeetings.

Supramolecular organization can be controlled at the nanometer level but can also be programmed to attain meso- and macroscopic levels through a hierarchical ordering sequence. Thus, the general principles outlined in the book, and their further elaboration, will be guidelines for the currently emphasized nanofabrication, for mimicking functional biological structures, and for bottom-up technologies where the “bottom” limit is based on molecules but the true extent of the “up” limit is wide open to future exploration.

About the Editor

Alberto Ciferri received a D.Sc. degree in physical chemistry from the University of Rome and performed postdoctoral work with H. Benoit in Strasbourg, Germany, and P.J. Flory in Pittsburgh, Pennsylvania. He held the positions of scientist at the Monsanto Company and director of research at the National Research Council. He is currently a professor of chemistry at the University of Genoa (from 1982 until 2005) and has been a visiting professor at Duke University since 1975. He received numerous visiting appointments and has been involved in the promotion of advanced education in developing countries through his JEPA Foundation. He has published over 200 papers as well as several books and patents in the areas of polymer mechanics, biopolymers, salt interaction, liquid crystals, and supramolecular assemblies.

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Contents

Part I: Theory and Structure

Chapter 1	
Supramolecular Polymer Chemistry — Scope and Perspectives	3
Jean-Marie Lehn	
Chapter 2	
Growth of Supramolecular Structures	29
Alberto Ciferri	
Chapter 3	
Theory of Supramolecular Polymerization	77
Paul van der Schoot	
Chapter 4	
Supramolecular Liquid Crystals: Simulation	107
Reinhard Hentschke, Peter Lenz, and Bernd Fodi	
Chapter 5	
Supramolecular Low-Molecular Weight Complexes and Supramolecular Side-Chain Polymers	131
Takashi Kato	
Chapter 6	
Hydrogen-Bonded Supramolecular Polymers: Linear and Network Polymers and Self-Assembling Discotic Polymers	153
Perry S. Corbin and Stephen C. Zimmerman	
Chapter 7	
Dendrimeric Supramolecular and Supramacromolecular Assemblies	187
Donald A. Tomalia	
Chapter 8	
Polymers with Intertwined Superstructures and Interlocked Structures	257
J. Benjamin Beck and Stuart J. Rowan	
Chapter 9	
Theory of Block Copolymers	301
Mark D. Whitmore	
Chapter 10	
Assemblies in Complex Block Copolymer Systems	351
Volker Abetz	

Chapter 11	
Microstructure and Crystallization of Rigid-Coil Comblike Polymers and Block Copolymers	393
Katja Loos and Sebastián Muñoz-Guerra	

Part II: Properties and Functions

Chapter 12	
DNA Structures and Their Applications in Nanotechnology	445
Jun Xu, Thom H. LaBean, and Stephen L. Craig	

Chapter 13	
Soluble Amphiphilic Nanostructures and Potential Applications	481
Nobuo Kimizuka	

Chapter 14	
Supramolecular Properties of Polymers for Plastic Electronics	509
Davide Comoretto	

Chapter 15	
Supramolecular Polymers in Action	555
Anton W. Bosman and Rint P. Sijbesma	

Chapter 16	
Columnar, Helical, and Tubular Supramolecular Polymers	571
Wei Zhang and Colin Nuckolls	

Chapter 17	
Crystalline Bacterial Cell Surface Layers (S-Layers): A Versatile Self-Assembly System	583
Uwe B. Sleytr, Margit Sára, Dietmar Pum, and Bernhard Schuster	

Chapter 18	
Self-Assembled Monolayers (SAMs) and Synthesis of Planar Micro- and Nanostructures	617
Lin Yan, Wilhelm T.S. Huck, and George M. Whitesides	

Chapter 19	
Layered Polyelectrolyte Assemblies	651
X. Arys, A.M. Jonas, A. Laschewsky, R. Legras, and F. Mallwitz	

Chapter 20	
Molecular Imprinting	711
Makoto Komiyama	

Chapter 21

Protein Polymerization and Polymer Dynamics Approach to Functional Systems	725
Fumio Oosawa	

Chapter 22

Force Generation by Cellular Polymers	741
George Oster and Alex Mogilner	

<i>Index</i>	753
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Part I

Theory and Structure

Chapter 1

Supramolecular Polymer Chemistry — Scope and Perspectives

Jean-Marie Lehn

CONTENTS

I.	Introduction	3
II.	Generation of Hydrogen-Bonded Supramolecular Polymers and Liquid Crystals	4
	A. Formation of Mesogenic Supramolecules by Association of Complementary Molecular Components	5
	B. Generation of Supramolecular Liquid-Crystalline Polymers and Fibers	6
	C. Mesophases from Combination of Monotopic and Ditopic Complementary Components	11
	D. Rigid Rod Supramolecular Polymers	12
	E. Cross-Linking of Supramolecular Polymers	14
	F. “Ladder” and Two-Dimensional Supramolecular Polymers from Monomers Containing Janus-Type Recognition Groups	14
	G. Supramolecular Coordination Polymers	14
III.	Basic Features of Supramolecular Polymers	16
IV.	Supramolecular Polymers as Supramolecular Materials	22
	A. Supramolecular Materials	22
	B. Supramolecular Chemistry: Constitutionally Dynamic	23
	C. Supramolecular Polymers as Constitutional Dynamic Materials, Dynamers	23
V.	Conclusion	24
	References	25

I. INTRODUCTION

Beyond molecular chemistry based on the covalent bond, lies supramolecular chemistry, the chemistry of the entities generated via intermolecular noncovalent interactions [1–3]. The objects of supramolecular chemistry are thus defined on one hand by the nature of the molecular components and on the other by the type of interactions that hold them together (hydrogen bonding, electrostatic and donor–acceptor interactions, metal–ion coordination, etc.). They may be divided into two broad,

partially overlapping classes: (1) *supermolecules*, well-defined oligomolecular species resulting from the specific intermolecular association of a few components; (2) *polymolecular assemblies*, formed by the spontaneous association of a large number of components into a large supramolecular architecture or a specific phase having more or less well-defined microscopic organization and macroscopic characteristics depending on its nature (films, layers, membranes, vesicles, micelles, mesophases, surfaces, solids, etc.).

The extension of the concepts of supramolecular chemistry [1–4] from supermolecules to polymolecular entities leads in particular, to the implementation of *molecular recognition* as a means for controlling the evolution and the architecture of polymolecular species as they spontaneously buildup from their components through *self-organization* [1–4]. Such recognition-directed self-assembly is of major interest in supramolecular design and engineering. In particular, its combination with the chemistry of macromolecules and of organized assemblies led to the emergence of the areas of supramolecular polymers and of supramolecular phases such as liquid crystals [1,3–17].

A very rich and active field of research thus developed involving the designed manipulation of molecular interactions and information through recognition processes to generate, in a spontaneous but controlled fashion, supramolecular polymers and phases by the self-assembly of complementary monomeric components, bearing two or more interaction/recognition groups. These systems belong to the realm of *programmed supramolecular systems* that generate organized entities following a defined plan based on molecular recognition events [1,3]. Three main steps may be distinguished in the process: (1) *selective binding* of complementary components via molecular recognition; (2) *growth* through sequential binding of the components in the correct relative orientation; (3) *termination* requiring a built-in feature, a *stop signal*, which specifies the end point and signifies that the process has reached completion.

In addition, supramolecular chemistry is a *constitutional dynamic chemistry* [4] due to the *reversibility* of the connecting events, that is, their kinetic lability allows the exploration of the energy hypersurface of the system. It confers to self-assembling systems the ability to undergo *annealing* and *self-healing* of defects and to manifest tunable degree of polymerization and cohesive properties (rheology). In contrast, covalently linked, nonlabile species cannot heal spontaneously and defects are permanent.

Since this book provides a wide selection of relevant topics presented by some of the major actors in the domain, we shall emphasize here the conceptual and prospective aspects, illustrated by a brief retrospective of our own work. It started with the exploration of the concept of supramolecular polymers, introduced in 1990 [3a], through the implementation of the principles of supramolecular chemistry to generate polymers and liquid crystals of supramolecular nature from molecular components interacting through specific hydrogen-bonding patterns. The chemistry of supramolecular polymeric entities based on these as well as on other types of noncovalent interactions has since then actively developed [3–17].

II. GENERATION OF HYDROGEN-BONDED SUPRAMOLECULAR POLYMERS AND LIQUID CRYSTALS

Intermolecular processes occurring in a material may markedly affect its properties. Thus, supramolecular polymerization could be expected to induce changes in phase organization, viscosity, optical features, etc. For instance, the interaction between molecular units that by themselves would not be mesogenic could lead to the formation of a supramolecular species presenting liquid-crystalline behavior. It might then be possible to take advantage of selective interactions so that the mesogenic supermolecule would form only from complementary components. This would amount to a *macroscopic expression of molecular recognition*, since recognition processes occurring at the molecular level would be displayed at the macroscopic level of the material by the induction of a mesomorphic phase.

A. Formation of Mesogenic Supermolecules by Association of Complementary Molecular Components

The most common type of molecular species that form thermotropic liquid crystals possess an axial rigid core fitted with flexible chains at each end. One may then imagine splitting the central core into two complementary halves, whose association would generate the mesogenic supermolecule, as schematically represented in Figure 1. This was realized with the derivatives P_1 and U_1 of the heterocyclic groups 2,6-diamino-pyridine P and uracil U presenting complementary arrays, DAD and ADA, respectively, of hydrogen-bonding acceptor (A) and donor (D) sites. Whereas the pure compounds did not show liquid-crystalline behavior, 1:1 mixtures presented a metastable mesophase of columnar hexagonal type as indicated by x-ray diffraction data. Its existence may be attributed to the formation of a supermolecule via molecular recognition-directed association of the complementary components U_1 and P_1 , followed by the self-organization into columns formed by stacks of disk-like plates each containing two units of the supermolecule, arranged side by side (Figure 2) [12].

Supramolecular discotic liquid crystals may be generated via the initial formation of disk-like supermolecules. Thus, the tautomerism-induced self-assembly of three units of the lactam-lactim form of disubstituted derivatives of phthalhydrazide yields a disk-like trimeric supermolecule (Figure 3). Thereafter, these disks self-organize into a thermotropic, columnar discotic mesophase [13].

Related processes are the formation of discotic mesogens from hydrogen-bonded phenanthridinone derivatives [14a] and especially of helical mesophases based on tetrameric cyclic arrangements (G-quartets) of guanine-related molecules [14b].

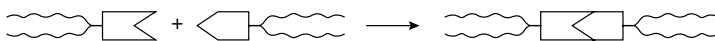


Figure 1 Formation of a mesogenic supermolecule from two complementary components.

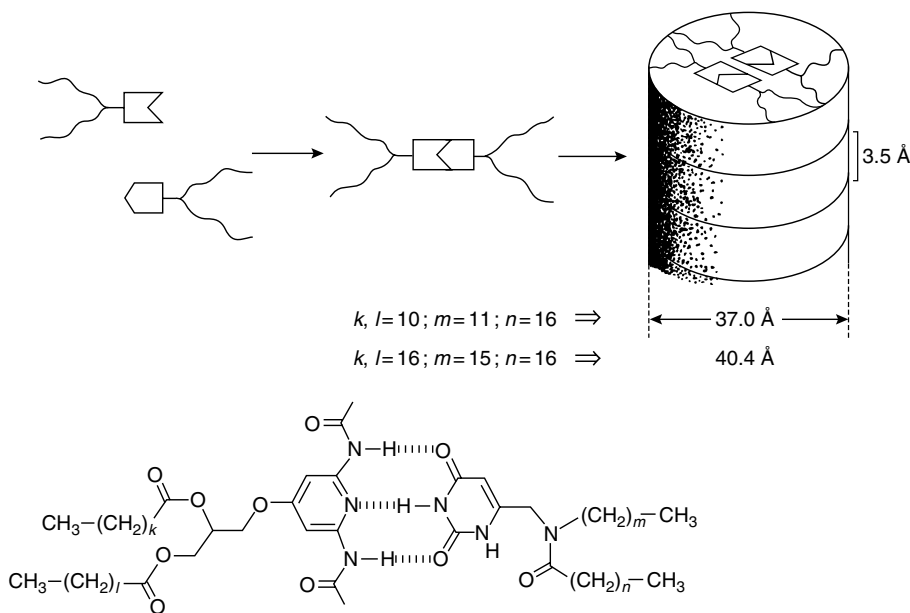


Figure 2 Formation of columnar mesophases (top) from disks constituted by the side by side arrangement of two units of a supermolecule (bottom) resulting from hydrogen bonding between the complementary components P_1 (bottom left) and U_1 (bottom right).

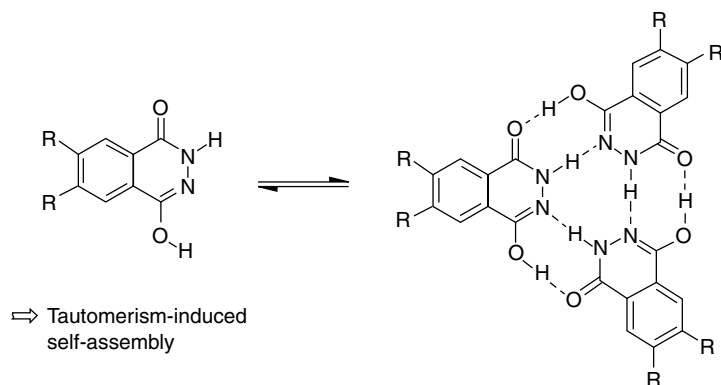


Figure 3 Tautomerism-induced self-assembly of a supramolecular cyclic trimer from the lactam–lactim form of phthalhydrazide derivatives.

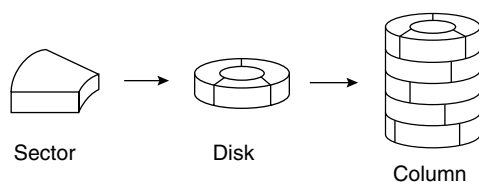


Figure 4 Hierarchical self-assembly. Self-assembly of sector components into a disk is a prerequisite for the subsequent self-assembly of the disks into a discotic columnar architecture; the case illustrated is that of a trimeric mesogenic supermolecule (see Figure 3).

All these cases represent overall examples of *hierarchical self-assembly*, a conditional process where the initial assembly of molecular components into a disk-like mesogenic supermolecule is a prerequisite for the subsequent formation of a discotic columnar architecture by stacking of the disks (Figure 4; also see Section II.B).

B. Generation of Supramolecular Liquid-Crystalline Polymers and Fibers

Mixing molecular monomers bearing two identical hydrogen-bonding subunits should lead to the self-assembly of a linear “polymeric” supramolecular species via molecular recognition-directed association. Figure 5 schematically represents such a process which served as the basis for the concept of supramolecular polymers [3c]. The resulting supramolecular polymeric material may be expected to present novel features resulting from its polyassociated nature, for instance, liquid-crystalline properties if suitable chains are introduced on the components.

Condensation of the complementary groups P and U with long-chain derivatives of tartaric acid T (T = L, D, or M) gave substances TP₂ and TU₂ each bearing two identical units capable of undergoing supramolecular polymerization via triple hydrogen bonding [3c]. Whereas the individual species LP₂, LU₂, DP₂, DU₂, MP₂, and MU₂ are solids, the mixtures (LP₂ + LU₂), (DP₂ + LU₂), and (MP₂ + MU₂) display *thermotropic mesophases* presenting an exceptionally wide domain of liquid crystallinity (from <25 to 220–250°C) and a hexagonal columnar superstructure, with a total column diameter of about 37 to 38 Å. The materials have the aspect of a highly birefringent glue that forms fibers upon spreading. The overall process may be described as the molecular recognition-induced self-assembly of a supramolecular liquid-crystalline polymer (TP₂, TU₂)_n **1** (Figure 6). Supramolecular telechelic polymers and block copolymers based on related hydrogen-bonding units have been described recently [15].

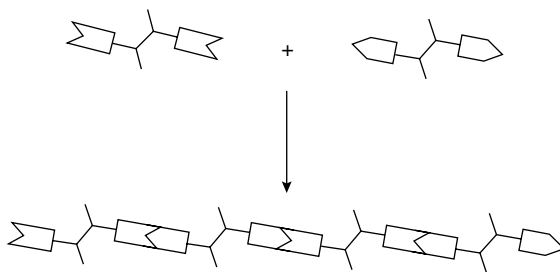


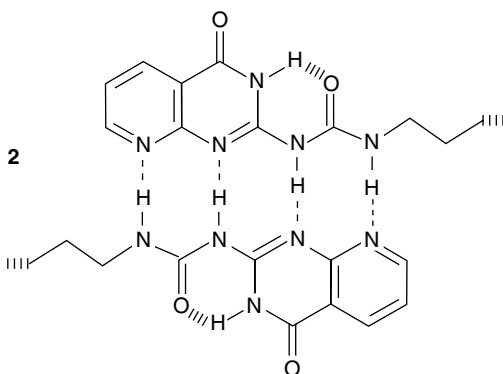
Figure 5 Formation of a polymeric supramolecular species by association of two complementary ditopic molecular components.

The x-ray patterns for $(LP_2, LU_2)_n$ are consistent with columns formed by three polymeric strands having a *triple helix superstructure*, whereas those for the $(MP_2, MU_2)_n$ mixture fit a model built on the three strands in a zig-zag conformation (Figure 7).

Electron microscopy studies revealed the successive states of self-assembly of **1** from nuclei to filaments and then to very long helical fibers of opposite chirality for the (L, L) **1** and (D, D) **1**, whereas the achiral (M, M) **1** material showed no helicity (Figure 8) [16]. Thus, molecular chirality is transduced into supramolecular helicity which is expressed at the level of the material on nanometric and micrometric scales.

The *racemic mixture* of all four components LP_2 , LU_2 , DP_2 , and DU_2 yielded long superhelices of opposite handedness that coexisted in the same sample, pointing to the occurrence of spontaneous *resolution* through *chiral selection* in molecular recognition-directed self-assembly of supramolecular liquid-crystalline polymers. Such chiral selection features of self-organized entities are of general significance in connection with the questions of spontaneous resolution and of chirality amplification. This was confirmed by subsequent studies on a variety of helical supramolecular polymers (see Chapters 2, 3, and 6).

Supramolecular polymers have been obtained with other types of interaction patterns between monomers, from a single hydrogen bond between a carboxylic acid and a pyridine unit [9] to four hydrogen bonds between self-complementary heterocyclic groups. The latter case is represented, for instance, by the supramolecular unit **2**, that reaches degrees of polymerization up to 1000 in isotropic (nonliquid-crystalline) solutions. It has led to especially broad and fruitful developments, yielding a variety of extended entities, which display a number of interesting physico-chemical properties [11,17]. Modifications of the liquid-crystalline properties have been induced in ternary mixtures by means of chiral additives [18a] and nanofibers are formed from ditopic complementary nucleose monomers [18b]. DNA-based supramolecular polymers are generated by duplex formation between complementary bis-oligonucleotide modules [18c].



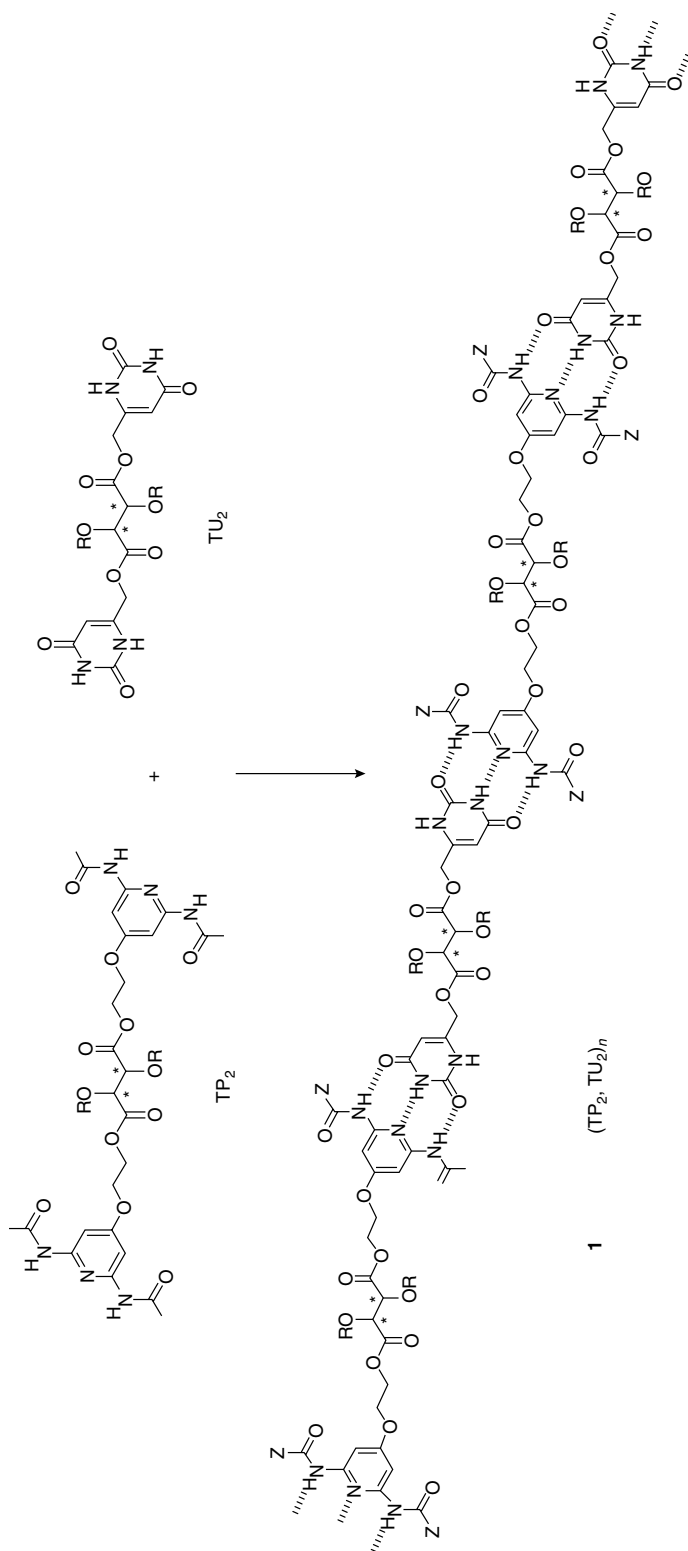


Figure 6 Self-assembly of the polymolecular supramolecular species $(TP_2, TU_2)_n$ **1** from the complementary chiral components TP_2 and TU_2 via hydrogen bonding; T represents L-, D-, or M-tartaric acid; R = $C_{12}H_{25}$.

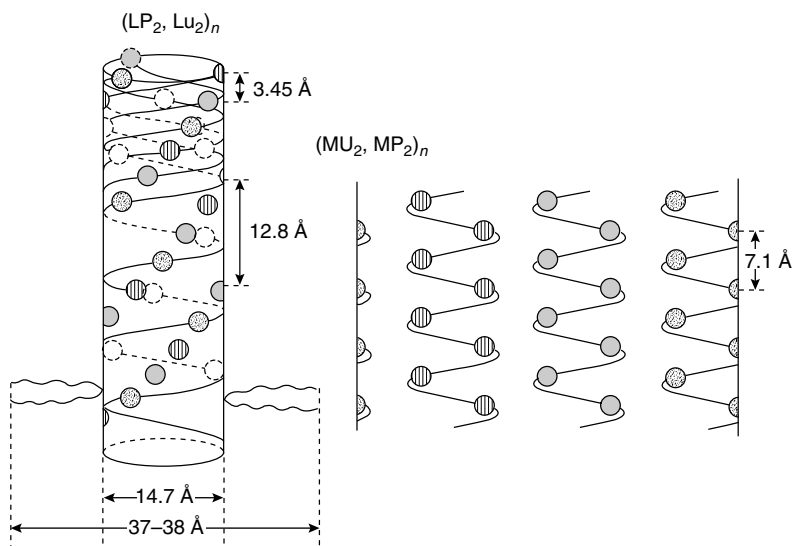


Figure 7 Schematic representation of the columnar superstructures suggested by the x-ray data for $(LP_2, LU_2)_n$, (left) and $(MP_2, MU_2)_n$ (right); each spot represents a PU base pair; spots of the same type belong to the same supramolecular strand; the dimensions are compatible with an arrangement of the PTP and UTU components along the strands indicated; the aliphatic chains stick out of the cylinder, more or less perpendicularly to its axis. For $(LP_2, LU_2)_n$, a single helical strand and the full triple helix are respectively represented at the bottom and at the top of the column. For $(MP_2, MU_2)_n$, the representation shown corresponds to the column cut parallel to its axis and flattened out.

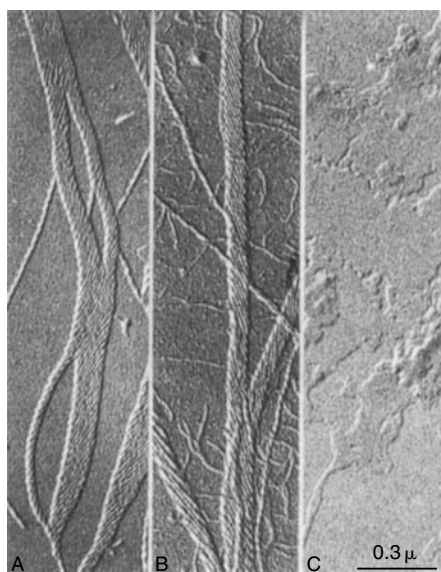
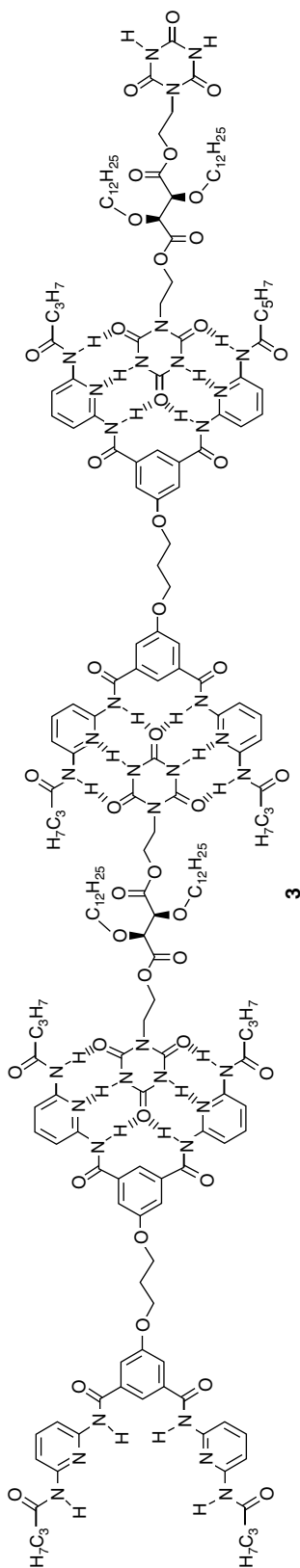
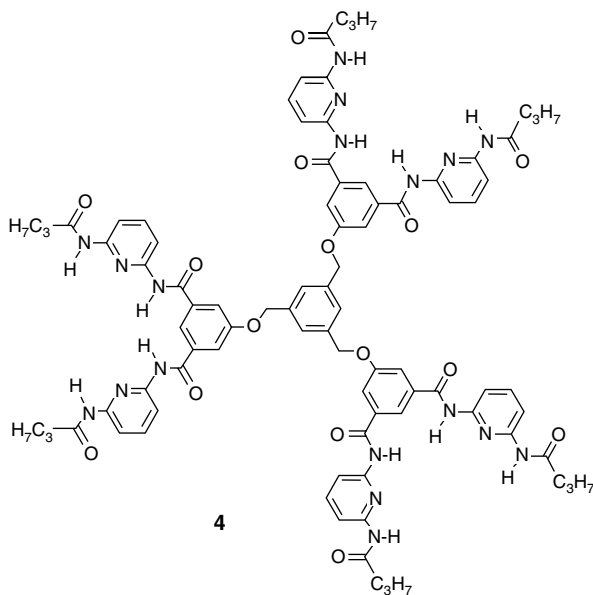


Figure 8 Helical textures observed by electron microscopy for the materials formed by the mixtures (A) $LP_2 + LU_2$, (B) $DP_2 + DU_2$, and (C) $MP_2 + MU_2$.

Supramolecular polymeric chains **3** have been obtained [19a] from the association of two homoditopic heterocomplementary monomers through sextuple hydrogen bonding [19]. They form fibers and a variety of different materials depending on conditions. Fiber formation was shown to be strongly influenced by stoichiometry, as well as by the addition of end-capping agents and of the tritopic cross-linking unit **4**.



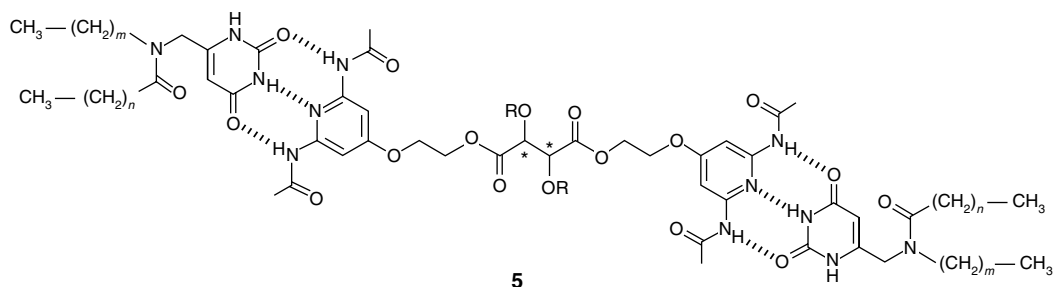


Multiple hydrogen bonding between calixarene-derived groups yields polymeric capsules [20].

C. Mesophases from Combination of Monotopic and Ditopic Complementary Components

In line with the processes described earlier, it may be possible to obtain liquid-crystalline materials from 2:1 mixtures of species containing, respectively, one and two recognition sites as represented schematically in Figure 9.

Indeed when an uracil component U_1 is combined with the complementary LP_2 unit in 2:1 ratio a mesophase is obtained; its occurrence may be attributed to the formation of mixed 2:1 supermolecules such as **5**, which forms a mesophase having a columnar structure of rectangular section and a very wide domain of liquid crystallinity (from <20 to $111\text{--}116^\circ\text{C}$, for $R = C_{12}H_{25}$, $m = C_{11}H_{22}$, $n = C_{16}H_{32}$ in **5**). Similar observations were made for the 2:1 combination of a diaminopyridine unit P_1 with the complementary LU_2 component [21].



One may note that the U_1 and P_1 components (Figure 2) represent *chain termination* groups inducing a control of chain length via end-capping on addition to the polymeric entities **1** [19a,22]. Related effects are induced when nonstoichiometric amounts of the two homoditopic monomeric components in **3** are used, the component in excess acting as chain-capping agent [19a].

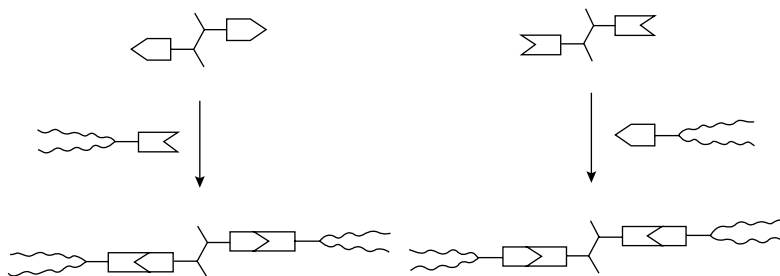


Figure 9 Formation of mesogenic species by 2:1 association of complementary monotopic and ditopic components.

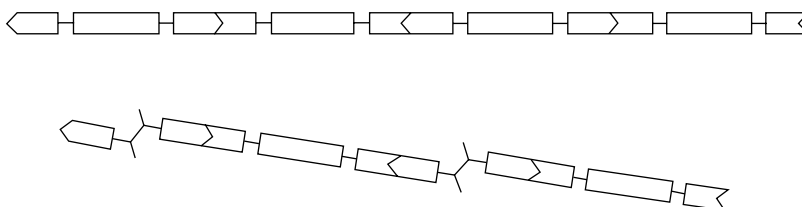
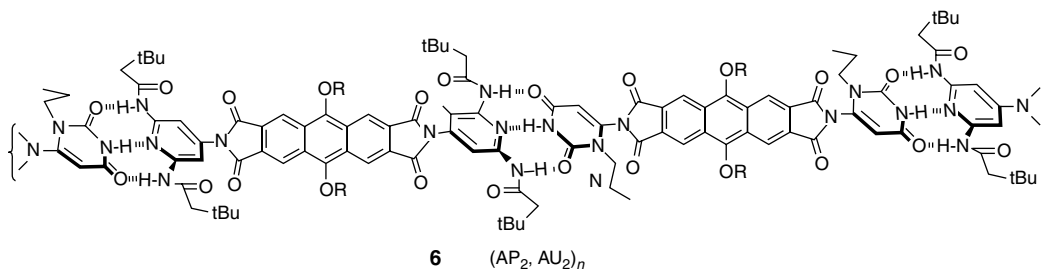


Figure 10 Schematic representation of: (top) a self-assembled rigid rod supramolecular system from two rigid complementary components, and (bottom) a self-assembled mixed system from a rigid unit and a complementary flexible one.

D. Rigid Rod Supramolecular Polymers

The introduction of rigid molecular units into macromolecular species has been extensively pursued in view of the novel physico-chemical that the resulting rigid rods may present. Self-assembling rigid components may be designed by attaching recognition groups to a rigid core. Combination of two such complementary components may result in the formation of rigid rod supramolecular systems (Figure 10). Mixed materials would be formed by combining a rigid unit with a complementary flexible one, such as the LP₂ or LU₂ species described in Section II.C. The two complementary rigid components AP₂ and AU₂, each containing two identical recognition groups linked to an anthracenyl core, self-assemble to yield the rigid rod supramolecular polymeric entity **6** which was found to present a lyotropic mesophase whereas AP₂ and AU₂ themselves are solids [23].



Hairy rigid rod polymers in which flexible side chains are attached to a rigid core, present attractive features [24]. A supramolecular version of such materials may be devised on the basis of components containing two recognition sites and on the capability of forming “hairy” ribbon-like structures. Thus, hydrogen-bonding recognition between double-faced Janus-type recognition units, such as barbituric acid and triamino-pyrimidine derivatives, leads to ordered molecular solids through formation of polyassociated supramolecular strand bearing lateral chains

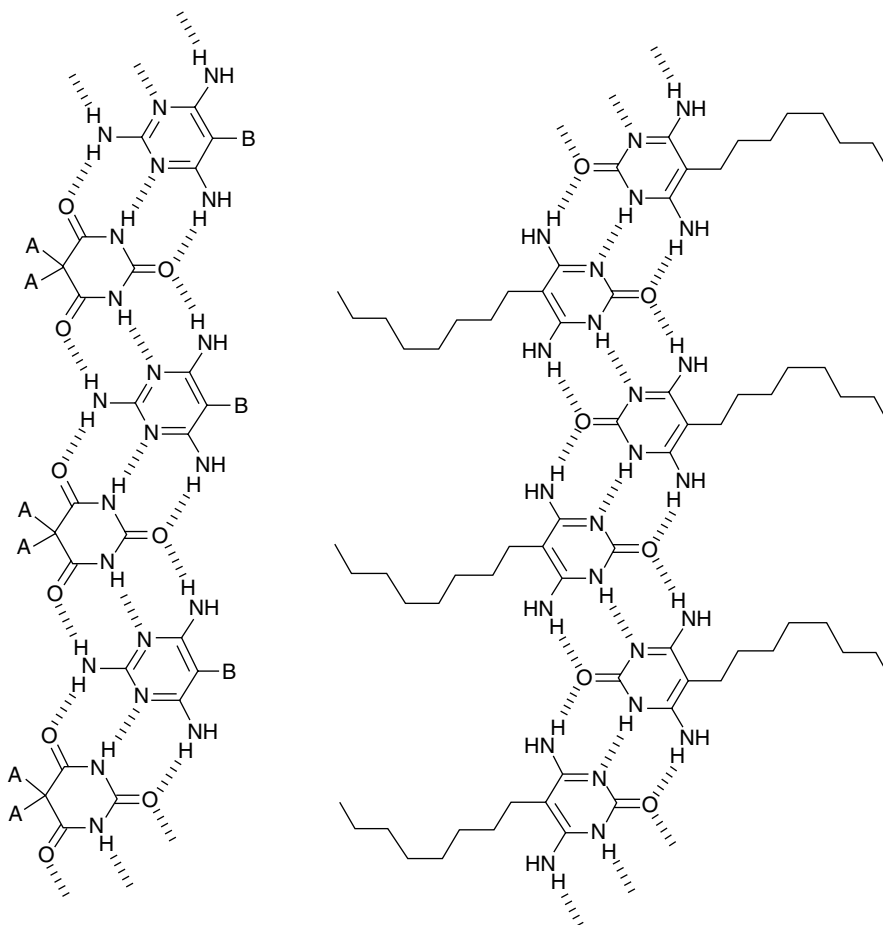


Figure 11 Self-assembled supramolecular “hairy” strands derived from components bearing side chains and containing heterocomplementary (left) or self-complementary (right) recognition sites; A and B: aliphatic chains; for the corresponding crystal structures [24a,b].

(Figure 11, left) [25a]. In the process molecular sorting out and left–right differentiation occurs, so that it is possible to obtain extended structures carrying identical or different chains of various lengths on each side.

A similar type of species bearing identical chains on each side is formed from components containing self-complementary recognition arrays of diamino-pyrimidone type (Figure 11, right) [25b]. However, whereas the (barbituric acid, triamino-pyrimidine) combination may in principle yield either a linear strand or a cyclic entity [25b,c], this latter recognition group enforces the formation of a strand only. Furthermore, one may also point out that, in this case, the arrangement of interaction sites presents some relationship with the Oosawa model of chain growth (see Figure 6 in Chapter 2, this volume).

One may note that the triple helical supramolecular species described above (Figure 7, left) displays the features of a hairy cylinder. The self-assembled species **6** bearing long R chains represent supramolecular hairy rigid rods. Mesoscopic supramolecular assemblies of cylindrical rigid rod-type, of about 150 Å diameter and several tens of micrometers length, have been obtained from a tricyclic bis-imide Janus molecule and a long-chain triaminotriazine derivative [26]. Numerous variations in the nature of the side chains of these compounds may be envisaged, giving in principle access to a variety of materials.

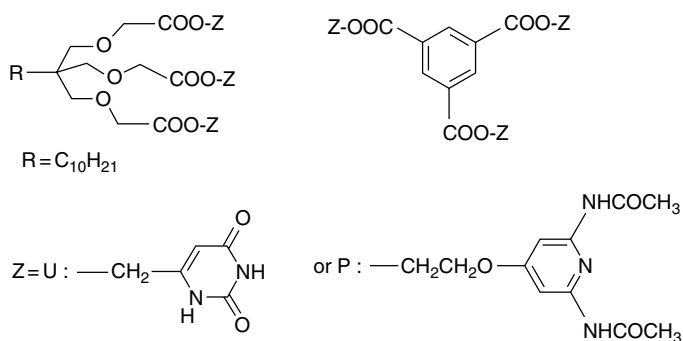


Figure 12 Ternary recognition components for the cross-linking of supramolecular polymeric species.

E. Cross-Linking of Supramolecular Polymers

Extending further the procedures of polymer chemistry to supramolecular species, one may envisage to devise supramolecular cross-linking agents. Thus, tritopic components containing three equivalent recognition subunits may be expected to establish two-dimensional networks when mixed with linear polyassociated species such as those described in Section II.D, yielding cross-linked supramolecular polymers (Figure 12) [27a]. For instance, addition of **4** to **3** leads to marked changes in the material obtained, from initial long fibers to much shorter ones and to loss of structure, as observed by electron microscopy [19]. Of course, one may also imagine corresponding tetravalent components bearing four interaction groups which would then yield formally three-dimensionally cross-linked entities. Such polytopic monomers may also generate supramolecular branched species, in particular, of dendrimeric type (see Section II.F) [28].

F. “Ladder” and Two-Dimensional Supramolecular Polymers from Monomers Containing Janus-Type Recognition Groups

Janus-type recognition groups, such as barbituric or cyanuric acid and triamino-pyrimidine or triazine derivatives (see also Figure 11), represent a special type of cross-linking units by virtue of their ability to interact through their two hydrogen-bonding faces. The incorporation of two such groups into ditopic molecular monomers provides entries toward the generation of “ladder” or double-ribbon polyassociations (when only a single ditopic component is used) or of two-dimensional supramolecular polymeric networks (from two complementary ditopic components). This is schematically illustrated in Figure 13.

Indeed, monomers in which two such groups are grafted onto tartaric acid units (e.g., replacing P and U units in TP₂ and TU₂, see Figure 6) generate very high molecular weight aggregates that may be characterized by various physical methods [27b].

G. Supramolecular Coordination Polymers

When the monomeric components carry metal-ion binding subunits, polyassociation occurs on addition of a suitable ion, yielding a supramolecular coordination polymer [29]. This is the case for the L-tartaric acid derivative **7** bearing two methylated bipyridine groups. The binding of Cu (I) ions may *inter alia* generate chains where the components **7** are connected through [Cu (I) (bipy)₂] centers of tetrahedral coordination. Indeed, addition of Cu(CH₃CN)₄PF₆ to **7** resulted in the formation of organized phases, in particular *self-assembled inorganic nanotubes* of very regular structure, resulting presumably from the helicoidal winding of a large tape-like entity, as revealed by electron microscopy (Figure 14) [29a].

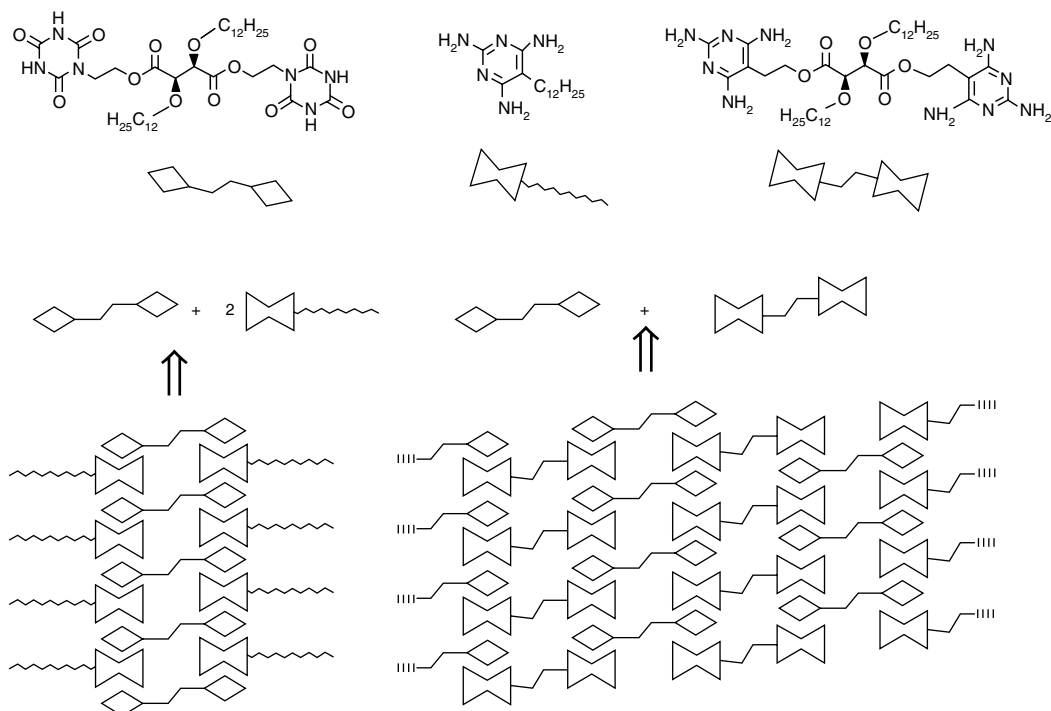


Figure 13 Schematic representation of the H-bond-mediated self-assembly of monomer components bearing Janus-type complementary recognition groups (e.g., cyanuric acid and 2,4,6-triaminopyrimidine); forming supramolecular polymers: (left) of “ladder” or double-ribbon type from a double-Janus and a single-Janus component, (right) of two-dimensional cross-linked nature from two double-Janus components.

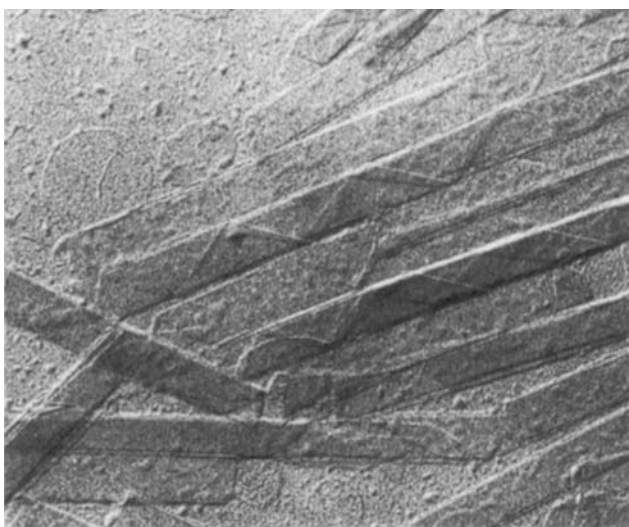
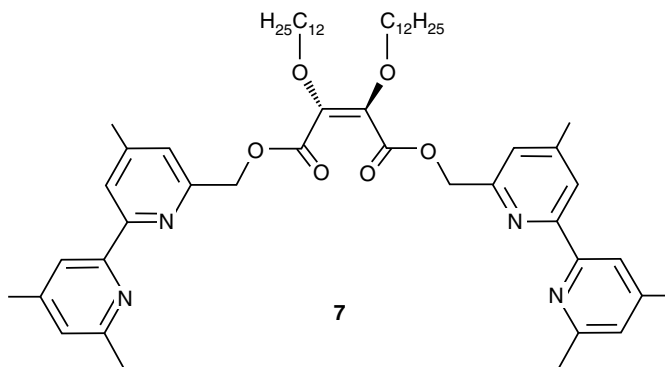


Figure 14 Inorganic nanotubes formed by the ditopic ligand **5** with $\text{Cu}(\text{CH}_3\text{CN})_4\text{PF}_6$ observed by electron microscopy [29a].

Soluble coordination polymers of variable degrees of polymerization have been obtained from bis-bipyridylketone and Cu (II) ions in different solvents; they have been characterized by electrospray mass spectrometry revealing molecular weights reaching >60,000 Da [29b]. More recent examples of coordination polymers are discussed in Chapter 6 (see also Refs. 29c,d).



III. BASIC FEATURES OF SUPRAMOLECULAR POLYMERS

The results presented earlier illustrate the rich domain that emerges from the combination of polymer chemistry with supramolecular chemistry. It involves the generation of polymeric superstructures by the designed use and manipulation of molecular interactions and information through molecular recognition processes. Figure 15 presents some of the different types of such

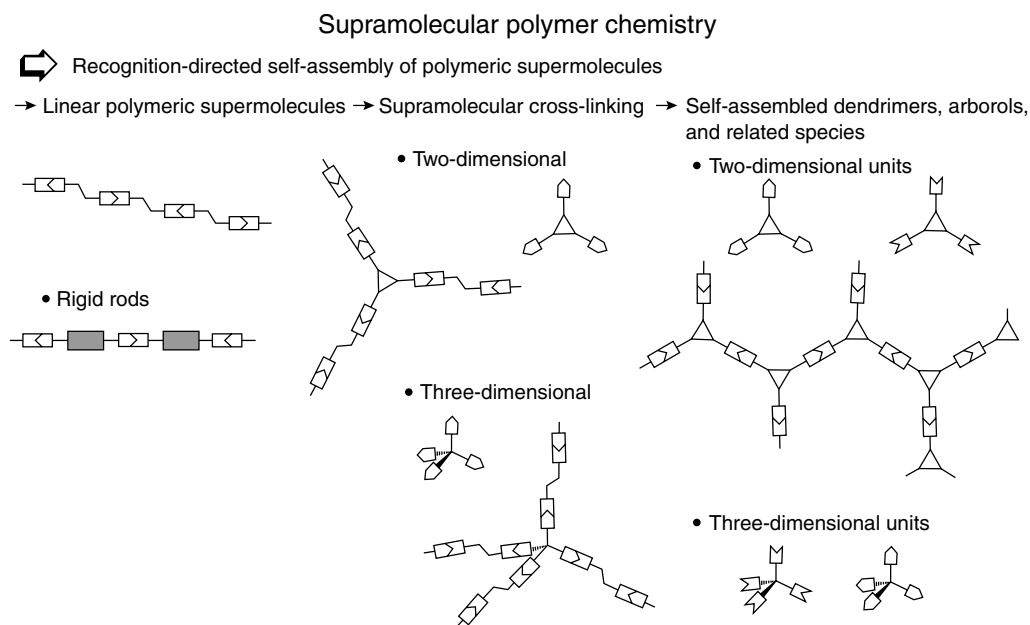


Figure 15 An aspect of the panorama of supramolecular polymer chemistry; formation of different types of polymeric supermolecular entities by recognition-directed self-assembly of monomers through noncovalent interactions, such as hydrogen bonds.

“informed” supramolecular polymers that may be generated by recognition-directed self-assembly of complementary monomer species.

Broadening the scope, we may briefly consider a nonexhaustive panorama of various types and features of supramolecular polymers depending on their constitution, characterized by three main parameters: the nature of the core/framework of the monomers, the type of noncovalent interaction(s), and the eventual incorporation of functional subunits. The interactions may involve complementary arrays of hydrogen-bonding sites, electrostatic forces, electronic donor–acceptor interactions, metal–ion coordination, etc. The polyassociated structure itself may be of main-chain, side-chain, or branched, dendritic type, depending on the number and disposition of the interaction subunits. The central question is that of the size and the polydispersity of the polymeric supramolecular species formed. Of course their size is expected to increase with concentration and the polydispersity depends on the stability constants for successive associations. The dependence of the molecular weight distribution on these parameters may be simulated by a mathematical model [19]. These features are detailed in Chapters 2, 3, and 6 for various growth mechanisms.

The basic characteristics of *main-chain supramolecular polymers* are presented schematically in Figure 16. Designating the monomer core residues by R_i , monomers bearing two identical interaction/recognition groups (homoditopic), may yield either *homopolymers*, when $R_i = R_j$ or regularly alternating *copolymers* when $R_i \neq R_j$.

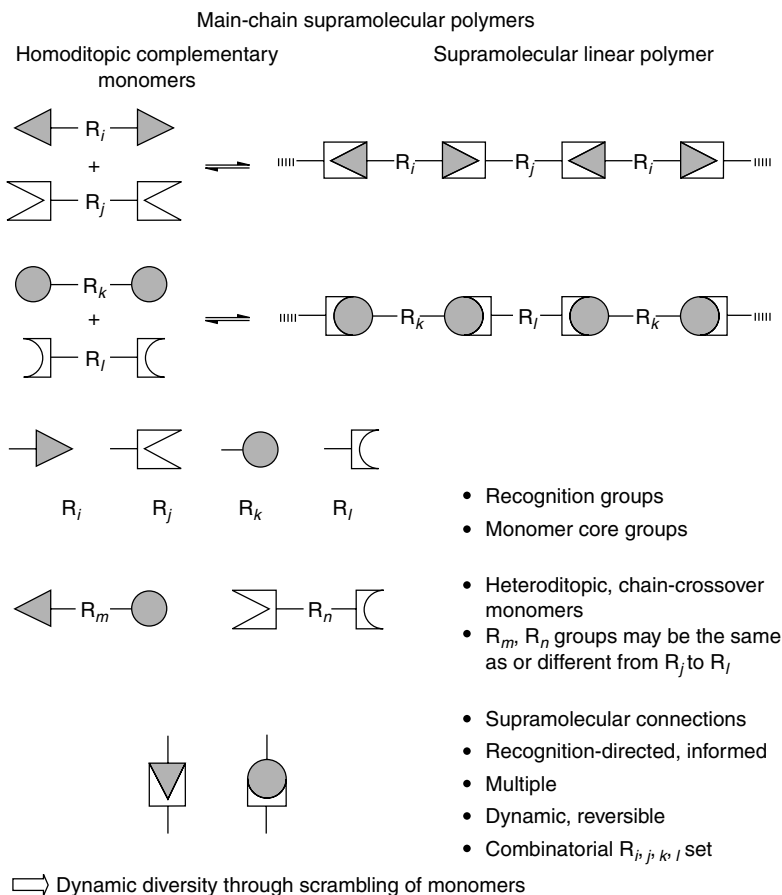


Figure 16 Schematic representation of the formation of linear main-chain supramolecular polymers from complementary homoditopic monomers, and of the constituting subunits. Dynamic diversity may be generated by scrambling of monomers containing different core groups.

When several different core residues are used, a large number of polymeric objects may be generated. Thus, for a chain $(R_i R_j)_k$ of k pairs length, formed from m different monomers R_i and n different monomers R_j , the total number of different sequences is $(m \times n)^k$. Since chains of any length ($k = 1$ to p) can be formed, the total number of different objects that can be present, comprising all possible sequences of all lengths (i.e., the full virtual combinatorial diversity [see Section IV.C]) is $mn[(mn)^p - 1]/(mn - 1)$. The fractions of the species as a function of chain length follow the size distribution curve of the system considered.

Initiation and chain growth occur on mixing of the complementary monomers. Chains of different compositions may be formed side by side, in principle without crossover, when several different pairs of complementary recognition groups are put to use (see Figure 16, top). Heteroditopic monomers combining recognition groups from different pairs may act as chain-crossover components, allowing the combination of two different chains.

Self-complementary monomers where the R units bear two complementary recognition groups yield homopolymers (only a single R_i) or random copolymers (two or more different core units $R_i, R_j, R_k, \dots$). Initiation and growth occur immediately after generation of the interaction groups.

In all cases, chain growth can be initiated by setting free one of the recognition groups by an external stimulus (e.g., light) from a derivative bearing a protecting group. Chain length may be altered/reduced by the addition of substances bearing a single recognition group, which act as *chain termination component* by end-capping [22].

Side-chain supramolecular polymers result from the binding of residues bearing recognition groups to complementary groups attached to the main chain of a covalent polymer (Figure 17) [9,11,30]. Of course, such main-chain covalent polymers may be cross-linked in a supramolecular fashion by means of double-headed complementary additives establishing bridges between the side groups of two different chains.

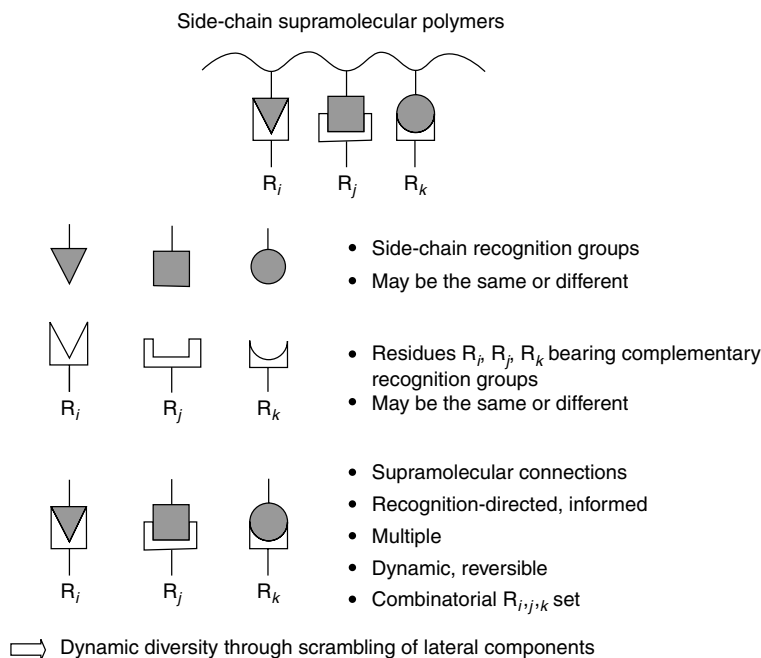


Figure 17 Schematic representation of the formation of side-chain supramolecular polymers from a covalent polymer bearing recognition groups, that bind complementary components, and of the constituting subunits. Dynamic diversity may be generated by scrambling of lateral components containing different residues R.

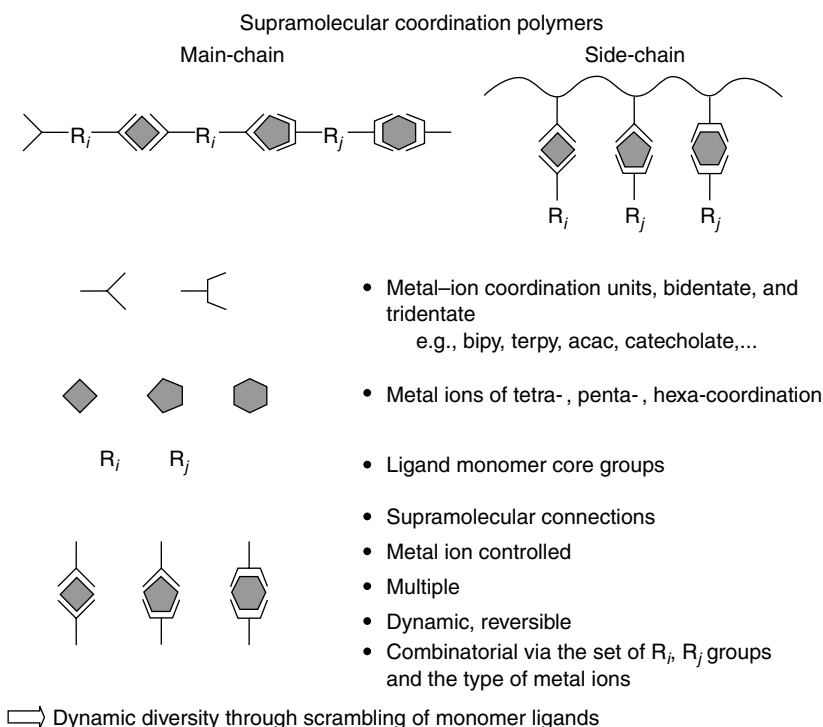


Figure 18 Schematic representation of the formation of supramolecular coordination polymers of main-chain or side-chain type from ligands containing bidentate and/or tridentate complexation subunits (such as bipyridine and terpyridine) binding metal ions of tetra-, penta-, or hexa-coordination, and of the constituting subunits. Dynamic diversity may be generated by scrambling of different ligand monomers.

Supramolecular coordination polymers represent a special class where the monomers are ditopic ligand molecules possessing two metal binding groups and where the connection is provided by metal–ion coordination (Figure 18). The metal ions play the role of association mediators enabling one to select the ligand components and to direct the polyassociation according to the combination (metal–ion/ligand binding site) in operation. One may take advantage of the vast set of metal binding units available and of their more or less selective coordination with specific ions. Initiation and growth occur only on addition of given metal ions and preferentially between specific ligands. Thus, in the presence of a mixture of ditopic ligands bearing different metal binding subunits, the nature of the “monomers” participating in the formation of main-chain coordination polymers may be determined/directed by the choice of the ion introduced. For instance, with bidentate (B) tridentate (T) metal binding sites, metal ions (M) of tetra-, penta-, and hexa-coordination are expected to yield (BMB), (BMT), and (TMT) connections, respectively (Figure 18). Of course, side-chain coordination polymers can also be obtained, as well as discotic-type coordination assemblies, such as the columnar mesophases formed from trimeric gold complexes of pyrazole derivatives [31] in a fashion similar to the processes shown in Figure 3 and Figure 4. Components combining organic (e.g., hydrogen bonding, etc.) and metal–ion binding sites may be expected to yield mixed organic/inorganic composite polymers. (For metallosupramolecular polymers combining hydrogen bonding and metal–ion binding sites see Ref. 32).

Similar considerations hold for *supramolecular organometallic polymeric* entities [33]. *Supramolecular cross-linking* may be achieved by introducing molecular monomers bearing more than two organic or metal–ion binding subunits. Such compounds provide links between chains in a way directed by the nature of the interacting groups. Figure 19 schematically represents cross-linking

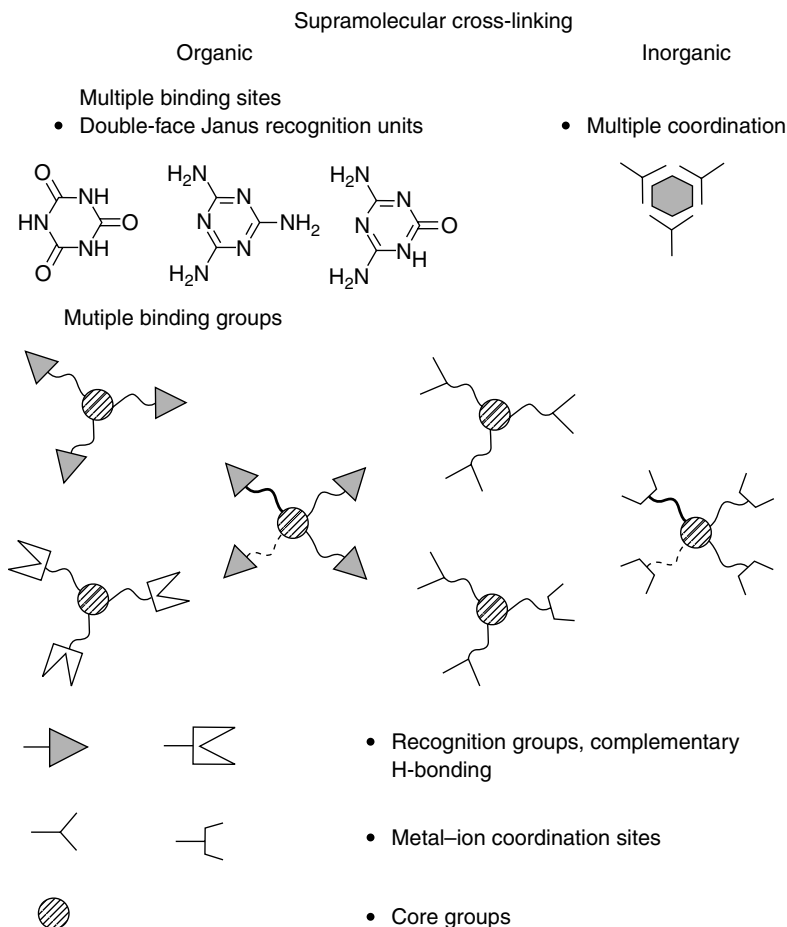


Figure 19 Schematic representation of supramolecular cross-linking agents of organic and inorganic types, and of the constituting subunits.

components of organic and inorganic types. An intriguing case is that of diamino-triazinone which possesses three different H-bonding faces DAA, ADD, and DAD, a sort of triple-Janus! Of course one may also envisage combining organic and inorganic interaction sites, which would allow the cross-linking of organic and inorganic supramolecular polymeric chains.

The use of suitable components containing multiple recognition groups should allow the designed generation of supramolecular species possessing a desired architecture. On the other hand, such components also greatly increase the dynamic combinatorial diversity of the system (see Section IV.C).

As in the case of covalent macromolecules, the supramolecular associations may also present internal (intrasupramolecular) interactions between sites located either in the main-chain or in side-chain appendages, thus leading to chain folding and structuration of the supramolecular entity.

Branched supramolecular polymers are obtained by means of cross-linking monomers. Of special significance is the fact that equimolar mixtures of complementary ternary or quaternary components lead in principle to the spontaneous generation of tree-like species that represent recognition-directed, *self-assembling supramolecular dendrimers* of the usual dichotomic as well as of trichotomic types (see also Figure 15). This holds both for organic and inorganic dendritic entities [28]. Mixed organic/inorganic dendrimers would be accessible from tri- and tetra-topic monomers bearing both organic and metal-ion binding sites.

Hierarchical self-assembly takes place when several self-assembling events occur in sequence via a conditional process, a given step being a prerequisite for the subsequent one. This is, for instance, the case in the formation of discotic-type columnar liquid crystals from self-assembled supramolecular disks (see Figure 4). One may distinguish three steps in the generation of the liquid-crystalline entities described in Section II.B: formation of a supramolecular strand (1), assembly of three strands into columnar superstructures (Figure 7), and finally generation of fibers (Figure 8) by association of several columnar entities. The control of hierarchical organization at different scales in supramolecular polymeric materials has been described [34].

A basic common feature of all these types of supramolecular polyassociations is that they are *reversible polymers* due to the lability of the noncovalent connections, and as a result they also possess the ability to generate dynamic diversity through scrambling of the monomer components (see Section IV). Furthermore, since only correct recognition-directed complementary pairing is expected to occur, *self-selection* [35] between compatible units should take place and control of the self-assembly process is in principle possible.

In view of the lability of the associations, supramolecular polymers present features of “living” polymers capable of growing or shortening, of rearranging their interaction patterns, of exchanging components, and of undergoing annealing, healing, and adaptation processes.

Growth control and regulation of structure and composition may be achievable by means of external effectors (temperature, pH, metal ions, competing ligands, end-capping units, etc.). A relevant case is that of a molecular strand which undergoes a structural reorganization upon recognition-directed binding of a complementary effector to give a coiled disk-like object which thereafter self-assembles into extended fibers (Figure 20) [36].

All these most interesting features displayed by supramolecular polymers, however, raise important but difficult questions of *characterization* concerning composition, size, persistence length,

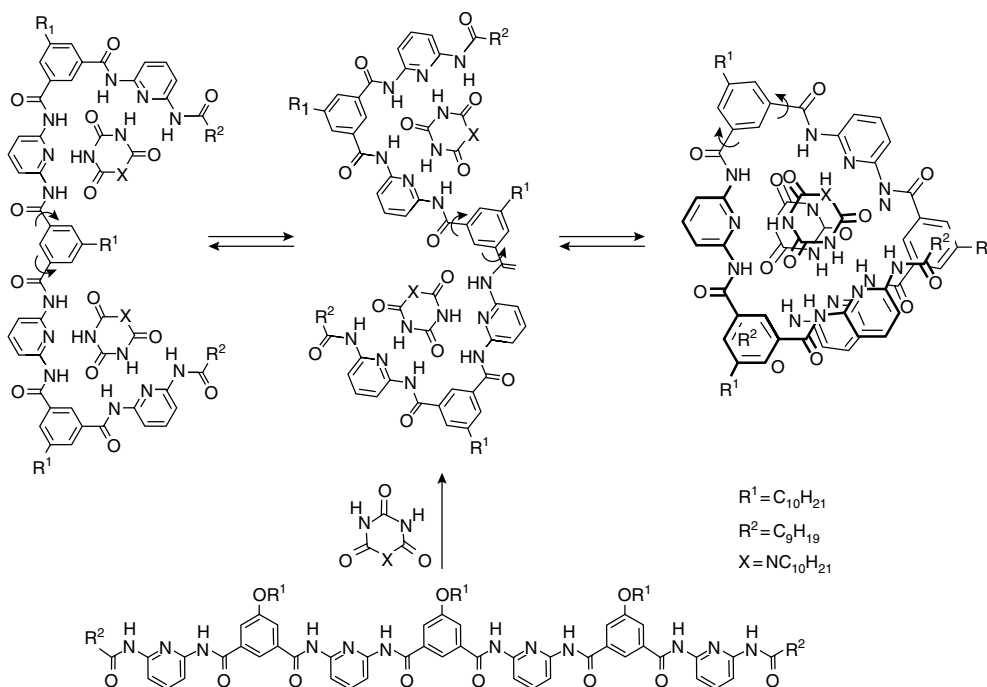


Figure 20 Folding of a molecular strand (bottom) induced by the binding of a cyanuric acid-derived template, generates different possible conformers (top) and leads to the formation of fibers from the helical conformer (top right).

shape, structure, etc., of the entities formed. To this end, an array of physico-chemical methods is required and must be put to use, such as vapor-phase osmometry, differential scanning calorimetry, electrospray mass spectrometry, NMR spectroscopy, gel permeation chromatography light scattering, electron microscopy, near field microscopies, etc. (For a relevant case, see Refs. 17 and 37.)

Supramolecular versions of the various species and procedures of molecular polymer chemistry may be imagined and implemented providing a wide field of future investigation that offers a wealth of novel entities and functionalities. Possible extensions concern, for instance, the introduction of various central cores, in particular those already known to yield molecular liquid crystals, the incorporation of photo-, electro-, or iono-active functional units, the potential use for detection devices as well as the extension to various other recognition components particularly those of biological nature (see, for instance, the case of the guanine-type quartets [14b]). Recently suggested applications are presented in Chapter 14.

IV. SUPRAMOLECULAR POLYMERS AS SUPRAMOLECULAR MATERIALS

A. Supramolecular Materials

The properties of a material depend both on the nature of the constituents and on the interactions between them. Supramolecular chemistry may thus be expected to have a strong impact on materials science via the explicit manipulation of the noncovalent forces that hold the constituents together. These interactions and the recognition processes that they underlie, allow the design of materials and the control of their buildup from suitable units by self-assembly.

Through recognition-directed association, self-assembly, and self-organization processes, supramolecular chemistry opens new perspectives in materials science toward an area of supramolecular materials whose features depend on molecular information and which involve “smart” materials, network engineering, polymolecular patterning, etc. As shown in Section III, liquid-crystalline polymers of supramolecular nature presenting various supramolecular textures may be obtained by the self-assembly of complementary subunits. This amounts to a macroscopic expression of molecular information via a phase change which, being a highly cooperative process, also corresponds to an amplification of molecular recognition and information from the microscopic to the macroscopic level.

Supramolecular engineering gives access to the molecular information-controlled generation of nanostructures [38,39] and of polymolecular architectures and patterns in molecular assemblies, layers, films, membranes, micelles, gels, colloids, mesophases, and solids as well as in large inorganic entities, polymetallic coordination architectures, and coordination polymers.

Molecular recognition processes may be used to induce and control processes between polymolecular assemblies such as organization of, and binding to, molecular layers and membranes [10,40], selective interaction of lipidic vesicles with molecular films [41], aggregation and fusion of *recosomes*, vesicles bearing complementary recognition groups [42,43], etc.

The buildup of supramolecular architectures and materials may involve several steps and proceed in particular via hierarchical self-assembly processes (see also above). On the one hand such sequential conditional processes enable the progressive buildup of more and more complex systems in a directed ordered fashion; on the other hand, they offer the intriguing possibility to intervene at each step so as to either suppress the following ones or to reorient the subsequent evolution of the system into another direction, toward another output entity.

Molecular recognition-directed processes also provide a powerful entry into *supramolecular solid state chemistry* and *crystal engineering*. The ability to control the way in which molecules associate may allow the designed generation of supramolecular architectures in the solid state. Modification of surfaces with recognition units leads to extended exo-receptors [1,3] that could display selective

surface binding on the microscopic level, and to recognition-controlled adhesion on the macroscopic scale [41,44].

B. Supramolecular Chemistry: Constitutionally Dynamic

Supramolecular chemistry is intrinsically a dynamic chemistry in view of the lability of the interactions connecting the molecular components of a supramolecular entity. Moreover, and most significantly, the reversibility of the associations allows a continuous reorganization by both modification of the connections between the constituents and incorporation or extrusion of components by exchange with the surroundings, conferring therefore *combinatorial* features to the system.

Supramolecular chemistry thus has a direct relationship with the highly active area of combinatorial chemistry, however in a very specific fashion. Indeed, reversibility being a basic and crucial feature of supramolecular systems, the dynamic generation of supramolecular diversity from the reversible combination of noncovalently linked building blocks falls within the realm of the emerging area of *dynamic combinatorial chemistry* (DCC) which involves dynamic combinatorial libraries, of either virtual (VCL) or real nature depending on the system and the conditions [45,46]. The concepts and perspectives of the DCC/VCL approach have been outlined, *inter alia* with respect to supramolecular polymers [45].

Consequently, *supramolecular materials* are by nature *dynamic materials*, defined as materials whose constituents are linked through *reversible* connections (covalent or noncovalent) and undergo spontaneous and continuous assembly/disassembly processes in a given set of conditions [47]. Because of their intrinsic ability to exchange their constituents, they also have combinatorial character so that they may be considered as *dynamic combinatorial materials* (DCMs). Supramolecular materials thus are *instructed*, *dynamic*, and *combinatorial*; they may in principle select their constituents in response to external stimuli or environmental factors and therefore behave as *adaptive materials* [45].

In an other vein, DCMs may be considered as *five-dimensional materials* with three dimensions of space, one dimension of time/dynamics, and one dimension of constitution, representing the different constitutional combinations.

C. Supramolecular Polymers as Constitutional Dynamic Materials, Dynamers

It follows from the previous considerations that supramolecular polymer chemistry is both dynamic and constitutionally diverse. Supramolecular polymers present dynamic constitutional diversity and are therefore *constitutional dynamic materials* (CDMs) belonging to the realm of *constitutional dynamic chemistry* (CDC) [4]. They are based on *dynamic polymer libraries* whose constituents have a constitutional diversity determined by the number of different monomers (see Section III). Similar views apply to supramolecular liquid crystals.

The components effectively incorporated into the polyassociation depend in particular on the nature of the core groups and on the interactions with the environment, so that supramolecular polymers possess the possibility of *adaptation* by association/growth/dissociation sequences. The selection of components may occur on the basis of size commensurability [18], of compatibility in chemical properties, in charge, in rigidity/flexibility, etc. An example is given by the formation of homochiral helical fibers with chiral selection from a racemic mixture of monomeric tartaric acid derivatives: $LU_2 = LP_2 + DU_2 + DP_2(LU_2LP_2)_n + (DU_2DP_2)_n$ (see Section II.C) [16].

On the other hand, the selective incorporation of components presenting specific functional properties (energy transfer, electron transfer, ion binding, etc.) may be brought about in a recognition-controlled fashion. In particular, the use of suitable monomers allows to envisage applications for such diverse purposes as drug delivery, gene transfer, mechanical action (e.g., triggered changes in shape or size), viscosity adjustment, hydrophilicity/hydrophobicity modulation, optical and electronic effects, etc.

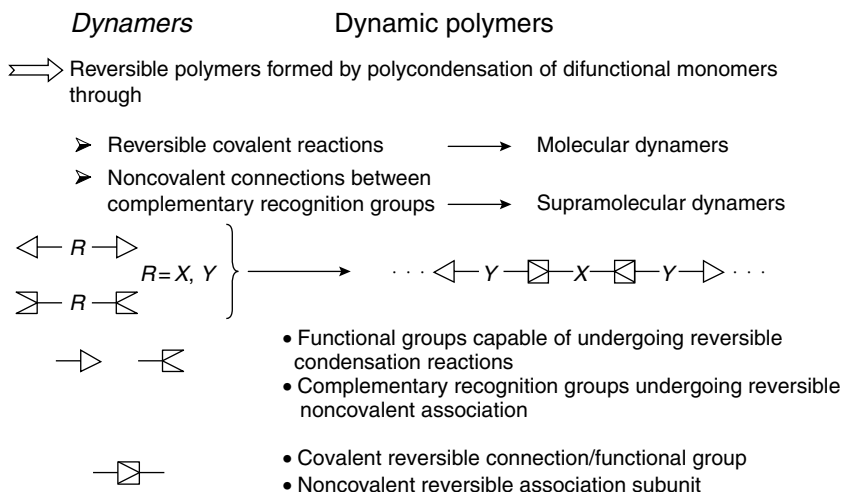


Figure 21 Dynamers: dynamic polymers defined as reversible polymeric entities of either molecular or supramolecular nature.

Broadening the scope, one may also consider covalent polymers formed from difunctional monomers that may undergo polycondensation through reversible chemical reactions (for instance, imine formation or others see Ref. 45). Such entities, where the reversible connections are covalent, are also dynamic and generate constitutional diversity [48–50]. Taken together, supramolecular polymers, dynamic by nature, and reversible molecular polymers, dynamic by design, define the class of dynamic polymers or “dynamers” [49a] (Figure 21), which may display a range of novel properties, merging molecular and supramolecular features both in main-chain and side-chain processes [51].

Depending on the nature and variety of core/interaction/functional groups in mixtures of several different monomeric components, the dynamic features give access to higher levels of behavior such as healing, adaptability, and response to external stimuli (heat, light, pressure, shear, additives, etc.).

V. CONCLUSION

Molecular information-based recognition events represent a means of performing programmed materials engineering and processing of biomimetic or abiotic type and may lead to *self-assembling nanostructures*, organized and functional species of nanometric dimensions that define a *supramolecular nanochemistry*, an area to which supramolecular polymer chemistry is particularly well suited and able to make important contributions.

Nanoscience and *nanotechnology* have become and will remain very active areas of investigation, in view of both their basic interest and their potential applications. Here again, supramolecular chemistry may have a deep impact. Indeed, the spontaneous but controlled generation of well-defined functional supramolecular architectures of nanometric size through self-organization offers a very powerful alternative to nanofabrication and to nanomanipulation, providing a chemical approach to nanoscience and technology [1]. One may surmise that rather than having to stepwise construct bottom-up or top-down prefabricated nanostructures, it will become possible to devise more and more powerful *self-fabrication* methodologies resorting to self-organization from instructed components. The results described above give an aspect of possible routes toward self-organized nanostructures. The dynamic features and constitutional diversity of such supramolecular architectures confers to them the potential to undergo healing and adaptation, processes of great value for the development of “*smart*” *nanomaterials*.

Widening the perspectives, one may consider that the science of five-dimensional supramolecular materials in general and supramolecular polymer chemistry in particular, as part of dynamic constitutional chemistry [4], will strongly contribute to the emergence and development of *adaptive chemistry* [47] on the way toward complex matter.

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Chapter 2

Growth of Supramolecular Structures

Alberto Ciferri

CONTENTS

I.	Classes of Supramolecular Polymers	30
A.	Definitions	30
B.	Classification	30
C.	Self Versus Engineered Assemblies: Reversibility and Stability	31
D.	Open Versus Closed Systems	32
II.	Principles of Supramolecular Organization	33
A.	Unimer Functionality and Assembly Dimensionality	33
1.	Site Distribution	33
2.	Shape Effects	34
3.	Dimensionality and Growth	35
B.	Localized Interactions	35
1.	The Supramolecular Bond	35
2.	Assembling via MSOA (Isodesmic Polymerization)	38
3.	Assembling via HG (Cooperative Helical Growth)	39
C.	Nonspecific Interactions	43
1.	Assembling by Incompatibility Effects	43
2.	Assembling by Orientational Fields	49
III.	Self-Assembled Polymers	53
A.	Linear Chains and Columnar Stacks: MSOA	53
B.	Helices and Helical Columns: HG	56
C.	Liquid Crystallinity in Supramolecular Polymers	61
1.	Liquid Crystallinity for Molecular and Closed SPs	62
2.	Liquid Crystallinity Uncoupled to Growth	62
3.	Liquid Crystallinity Coupled to Growth	63
4.	Discotic SPs	65
5.	Thermotropic SPs	66
D.	Multidimensional Assemblies	67
1.	Planar Assemblies	67
2.	Three-Dimensional Assemblies	69
	Acknowledgment	71
	References	71

I. CLASSES OF SUPRAMOLECULAR POLYMERS

A. Definitions

The broadest definition of a supramolecular polymer (SP) is that of a system based on the association of many unimers through supramolecular (noncovalent) interaction. The unimers may be covalent molecules and macromolecules, and also supramolecular entities such as supermolecules (cf. Chapter 1) and complex micellar structures. Although such a broad definition includes all the systems that have been described as SPs, it does not readily illustrate structural features and potential applications of this exciting class of new materials. For instance, even an organic crystal might be regarded as a SP [1] and supramolecular interactions play a controlling role on the intramolecular conformation and the intermolecular ordering of covalent polymers.

Attempts to restrict the definition of SPs have been made. The most restrictive definition was proposed by Meijer and coworkers [2] to regard SPs as only those systems exhibiting chainlike behavior in diluted solutions. Such a definition is of interest since linear SPs do have peculiar properties (e.g., rheological ones) that widen possible applications of conventional polymers. However, a significant degree of supramolecular polymerization (DP) may not occur in dilute solutions while novel properties may appear in concentrated phases or in the bulk. Moreover, a less restrictive definition of SPs may highlight important features of supramolecular polymer chemistry better, in particular the use of approaches that cut across traditional boundaries between colloid, polymer, and solid-state science.

A definition that may be proposed (not as broad, nor as restrictive as the two discussed above) is based on the distinction between *self-assembling* and *engineered* SPs. The former type of assemblies is the main focus of the present chapter and is characterized by thermodynamically controlled structures. By contrast engineered SPs, important for a variety of applications, are materials assembled by controlled deposition or synthesis. A more detailed definition of all systems that have been described as SPs (including self-assembling and engineered ones) is presented in Section I.B [3].

B. Classification

Figure 1 schematizes several classes of systems described as SPs. The reference model at the top of the figure represents the classical covalent chain resulting from molecular polymerization of small bifunctional monomers. The covalent chain is an open one, meaning that it could in principle grow to a large DP distribution, irreversible in solution and under a wide range of external variables.

Class A. The major components of this class are *equilibrium polymers* based on processes that can appropriately be regarded as *supramolecular polymerizations* [4,5]. Uni- and multidimensional growth mechanisms are coupled to molecular recognition processes typical of supramolecular chemistry. The linear chains are self-assembled, open, growing to a distribution of DP, and in a state of thermodynamic equilibrium sensitive to solvent type, concentration, and external variables. The geometrical shapes of the unimers in class A (Figure 1) bring to bear that repeating units in supramolecular polymerization can be of several forms and sizes. Specific chemical structures will be discussed in Section III. At variance with molecular polymers all interaction, including those stabilizing the main chain, are of supramolecular nature. Therefore we include in class A polymers based on unimers with functionality ≥ 2 , when a variety of multidimensional assemblies (linear, planar, three-dimensional) becomes possible. Examples of linear systems are hydrogen-bonded polymers, coordination polymers, and micelles (cf. Chapter 6). Examples of more complex geometries are helical, helical-columnar, and tubular structures (cf. Chapters 2, 16), protein layers (cf. Chapter 17), and composite systems such as block copolymers (cf. Chapters 10, 11). Random networks and blends stabilized by multifunctional supramolecular linkages (cf. Chapter 6) may also be included.

Class B. This class includes self-assembled structures based on supramolecular binding of monofunctional unimers. These unimers cannot undergo open supramolecular polymerization, but can form closed assemblies involving low- or high-MW species. Classical host-guest complexes, base pairing of simple nucleosides, and supermolecules are low-MW examples. Polymeric examples include side-chain binding of

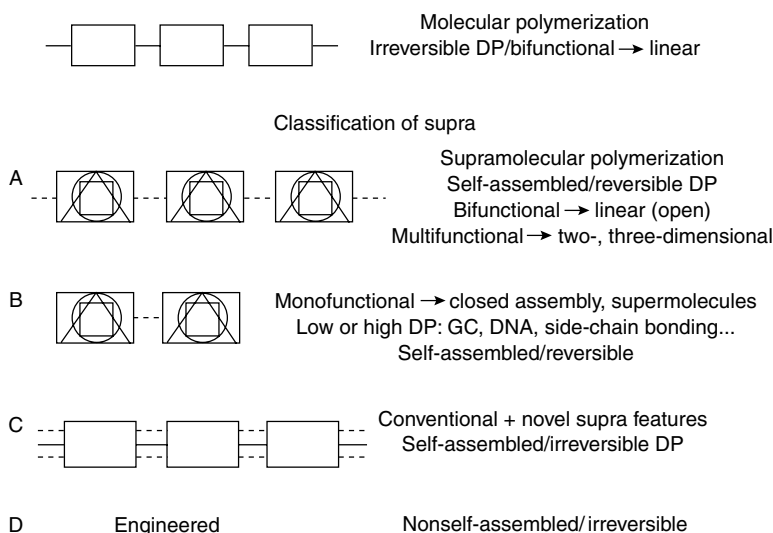


Figure 1 Classification of supramolecular polymers. Class A (reversible polymers obtained by supramolecular polymerization) is the main topic of this chapter. (From A. Ciferri. *Macromol. Rapid Commun.* 23:511, 2002a. Copyright Wiley-VCH 2002.)

a monofunctional unimer to a covalent chain (e.g., binding of low-MW mesogens to a covalent polymer, cf. Chapter 5, counterion binding), double- and triple-chain assemblies, and globular structures unable to further growth when complementary monofunctional sites are internally saturated.

Class C. SPs displaying novel supramolecular features have been obtained by a combination of covalent and supramolecular bonds. Such systems are self-assembling but the covalent component will not show reversible association–dissociation equilibria. The supramolecular organization may either precede, be simultaneous to, or follow the formation of covalent bonds. Examples of the first type are the rotaxane and catenane polymers described by Stoddart and coworkers (cf. Chapter 8), the growth of dendrimers through successive generations, and other attempts to stabilize a supramolecular assembly by subsequent formation of covalent bonds (cf. Chapters 7, 12). The final covalent system may retain supramolecular features. Alternatively, the precursor organization may just be a step of a supramolecularly assisted synthesis of a complex structure. Examples in which the supramolecular and the molecular order are simultaneously established include the synthesis of dendrons possessing polymerizable functionality at their focal points, noticeably reported by Percec and Schlüter (described in Chapter 7). These assemblies display most interesting composite architectures such as columns of disks based on dendrons with a main covalent chain running in the center of each column. Cases in which the covalent structure precedes the formation of the supramolecular one include the dendronization of a covalent polymer, reported for instance by Tomalia and Majoros (cf. Chapter 7), and the self-assembled monolayers (SAMs, cf. Chapter 18) regarded as supramolecular assemblies of short hydrocarbon chains covalently grafted to a gold surface.

Class D. The class of engineered assemblies includes systems that do not spontaneously form ordered structures under normal conditions. Their classification as SPs can be justified since elements of supramolecular interaction still assist the final organization. Some examples are layered assembly of complementary polyelectrolytes obtained by stepwise deposition under kinetic control (cf. Chapter 19), and polymer brushes prepared by grafting a polymer chain over a SAM of an initiator [6]. Both approaches allow a fine-tuning of surface properties and patterning possibilities. Tailored performance in applications, such as biocompatibility, biocatalysis, integrated optics and electronics have been considered. Additional differences between self-assembled and engineered SPs are discussed in Section I.C.

C. Self Versus Engineered Assemblies: Reversibility and Stability

Self-assembled systems may undergo association $\leftrightarrow$ dissociation equilibria under the influence of state variables, composition, and external conservative fields. Note that structural reversibility

applies only to the component assembled via secondary interaction. Reversible DP is shown by systems in class A, but not by systems exhibiting covalent main chains in class B and C.

In engineered systems the supramolecular interaction component is still important but the shape of the assembly or the distribution of components may be controlled by specific deposition techniques. For instance, random aggregates or double-helical structures may be produced by molecular recognition of complementary polyelectrolytes in solution [7]. The same recognition process allowed the engineered formation of spherical skins or layered films in the following engineered examples. Larez et al. [8] reported the formation of spherical assemblies (diameters up to 500 μm) by letting drops of a chitosan solution free-fall into a solution of oxidized scleroglucan. The skin of the assembly, separating the external polyanion from the internal polycation solution, acted as a semipermeable membrane. Laschewski and coworkers (cf. Chapter 19) reported a stepwise, layer-by-layer adsorption of oppositely charged elements enabling the engineered growth of these assemblies on suitable substrates. Due to the kinetically controlled deposition, interfacial complexation gives rise to stratified supramolecular structures that strongly differ from the ones obtained by direct polyelectrolyte complexation.

Deposition techniques may also allow the fabrication of functional assemblies of incompatible components such as rod and coiling polymers. This is the case of high-performance composites and natural systems such as connective tissue or the vitreous body of the eye [9]. Engineered systems may exhibit even greater stability than self-assembled ones since use of compatibilizers, fast quenching techniques, or covalent cross-linking may prevent or retard the dissipation of their organization.

D. Open Versus Closed Systems

All the examples cited for class A (Figure 1(A)) refer to supramolecular systems for which the addition of successive repeating units exposes sites at the end of the growing chain to which additional units can bind, a situation typical of the polymerization of molecular polymers. These systems are classified as *open assemblies*. Planar and three-dimensional assemblies growing by a mechanism similar to a phase transition may also be classified as open assemblies (cf. Section II.A.3). The examples cited for class B represent instead *closed assemblies* for which the binding sites are internally compensated and the complexes have a definite stoichiometry. A too strict classification of open or closed assemblies should nevertheless be avoided since some closed assemblies may have residual sites allowing growth to occur. For instance, although the stoichiometry of the collagen triple helix is strictly defined, it is difficult to observe a stable solution of tropocollagen at neutral pH. Side-by-side or head-to-tail aggregation continue until phase separation occurs.

On the other hand, some supramolecular assemblies may have a large number of repeating units but their growth is strictly limited. These systems are not oligomeric ones and it is convenient to classify them as open systems undergoing supramolecular polymerization once a proper termination step is recognized. Several situations may occur, for instance, a size limitation and a size distribution may be the natural result of the stochastic nature (cf. Section II.B.2) of the assembly mechanism. Size limitation may also result from termination by a monofunctional unit unable to grow further (Figure 3(c)). Situations of this type are encountered even in biological polymerizations (e.g., termination of actin growth by gelsolin; cf. Section III.B). The growth of cylindrical micelles slows down when the length of the assembly attains the value of the persistence length (cf. Section II.C.2). Giant mesoscopic vesicles based on either simple surfactants [10] or block copolymers [11] (cf. Chapter 11) are structures that may be conceived as arising from the closing up of extended bilayers exhibiting randomly fluctuating local curvature [12,13]. Spherical surfactant micelles have the typical aggregation number 100, their growth to infinite size being prevented by the peculiar nature of amphiphilic molecules (cf. Section II.C.2). The size of virus capsids may be controlled by the polynucleotide guest [3,14,15] (cf. Section III.B).

II. PRINCIPLES OF SUPRAMOLECULAR ORGANIZATION

A. Unimer Functionality and Assembly Dimensionality

1. Site Distribution

The number of complementary sites per unimer (S) and their distribution control the functionality of the unimer (F) and the dimensionality of the assembly [3,15]. Figure 2 illustrates the above concept in the case of a unimer schematized by a small square. Monofunctional unimers are those with one or more sites pointing in just one direction. Such unimers cannot linearly polymerize and form closed host–guest complexes, a subject of classical supramolecular chemistry. Bifunctional unimers, those with two or more sites pointing toward opposite (North and South) directions, can form linear polymers or closed rings (Figure 3(a)). Tetrafunctional unimers with four or more sites pointing toward azimuthal directions (N, S, E, W) form planar polymers. However, helical polymers are expected even in the case $S = 4$, $F = 4$ when two sites are located on the same surface (pointing toward NE and SE, Figure 3(b)). Three-dimensional ordered networks are expected if N–S sites longitudinally increase the functionality of the planar system. It appears that the dimensionality of the final assembly is crucially dependent upon site distribution.

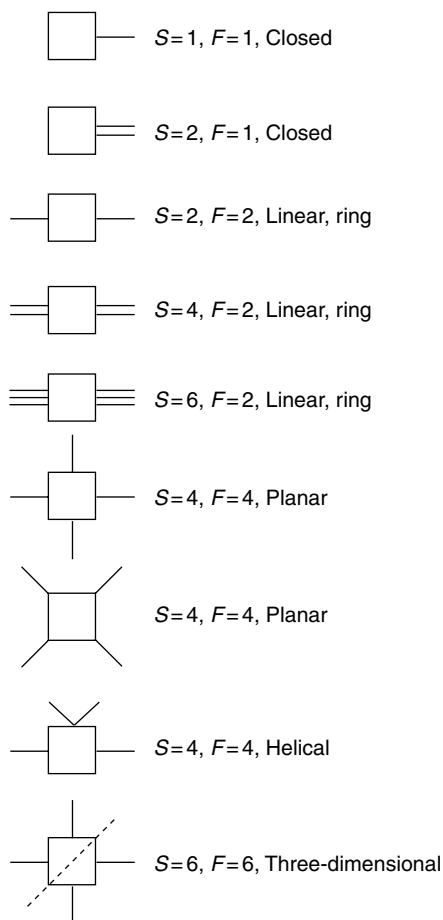


Figure 2 Schematic representation of unimer functionality (F), site number (S), and distribution. The geometry of the resulting assembly is indicated.

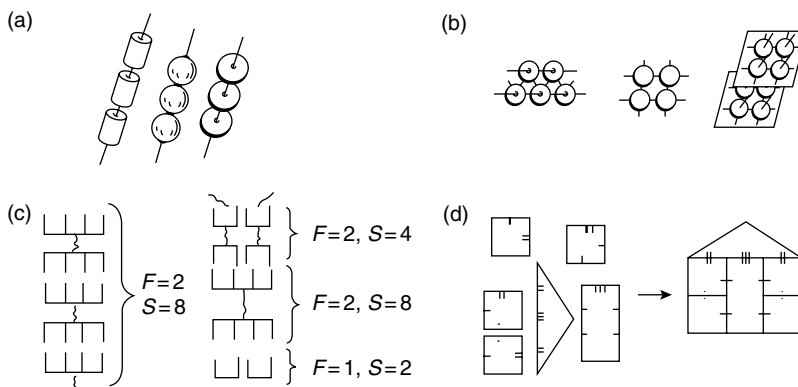


Figure 3 Shapes and functionality: (a) linear assemblies of bifunctional rodlike, spherical, disklike unimers ($F = 2$, $S = 2$); (b) helical, planar, three-dimensional assemblies ($F > 2$, $S > 2$); (c) linear polymers, branching, and termination for various F and S ; (d) assembly of unimers with different shapes and functionalities (note two square unimers not consistent with the final structure). (From A. Ciferri. *Encyclopedia of Supramolecular Chemistry*, J.L. Atwood and J.W. Steed Eds., New York: M. Dekker, 2004. With permission www.tandf.co.uk/journals)

Supramolecular unimers can be large in size, and often more than one binding site occurs over each complementary surface (Figure 3(c)). If full compensation occurs, there will be no alteration of the functionality of the unimer, or the dimensionality of the assembly. Multiple sites on properly designed complementary surfaces have a high probability of being mutually compensated. Should a mismatch occur, or unimers with different functionality or number of sites be mixed, alterations in the above assembling patterns are expected, that is, termination or random network formation, as shown schematically in Figure 3(c). More complex patterns are expected upon mixing unimers differing in shape, functionality, and bond type (Figure 3(d)). These situations are not yet under active investigation. Computational and simulation methods might be used for describing assemblies of increasing complexities (cf. Chapter 12). The algorithmic feature of the assembling process schematized in Figure 3(d) is evidenced by the two unimers indicated as an improper choice. These unimers might be included in the growing assembly, but should eventually be rejected by the final structure.

2. Shape Effects

The process of molecular recognition, underlining the interaction of complementary sites discussed above, implies both chemical and shape recognition. Although molecular and shape recognition are closely related, it is often convenient to distinguish them. With supramolecular polymers it is further convenient to distinguish two types of shape effects. The first type (shape I effect) pertains to the shape of the molecules or of the assembly forming the repeating unit. Shape II effects pertain instead to the assembled polymer. The overall assembly process may start as a molecular and shape I recognition. Eventually this process produces well-defined shapes. Thereafter, the evolution toward more complex structures may be simply described by shape II recognition and geometrical shape parameters (cf. Section II.C.2).

Shape I effects are important at the molecular recognition level. *Endo* recognition occurs when binding sites are oriented into a molecular concavity. A well-known example is the enzyme–substrate catalysis when the specificity toward the hydrolysis of a particular peptide bond is controlled by the binding of the adjacent side chain inside a pocket of the enzyme [16]. The great selectivity and complex stability observed in closed cavities is attributed to an enhancement of the strength of pairwise attraction (particularly of the dispersive and hydrophobic type) with respect to binding over flat surfaces [17]. Site distribution within a cleft may favor the convergence of groups capable of directional binding, thus enhancing the strength of H-bonds [18]. On the other hand, *exo* recognition

occurs when binding sites are directed outward to flat surfaces. Similarity of size of the surfaces and multiple pairwise interactions enhance the binding free energy.

Shape II effects are particularly relevant to excluded volume and liquid crystallinity, and also suggest intriguing correlations between macroscopic and molecular design concepts. The dendrimers (cf. Chapter 7) may be regarded as a growing sequence of similar chemical steps exhibiting fractal shapes around an initiator core [19]. Dendrimers in the nanometric range may assemble further through a repetition and composition of the basic geometrical design. Macroscopic analogies are the growth of corals, branching of trees, nesting of spheres into a large sphere, and so on [20]. Intracellular networks reflect a supramolecular assembly design of protein chains that display occasional pentagonal meshes within a hexagonal topology [21]. The pentagons determine the curvature of the network and stabilize the discocyte shape of the erythrocytes. Similar design strategies are found in both molecular systems such as fullerenes [22], and in macroscopic objects such as bamboo vases and football spheres [23].

3. Dimensionality and Growth

Israelachvili [13] summarized general thermodynamic considerations with regard to the growth of supramolecular aggregates. The growth process is strongly determined by the dimensionality of the assembly. Dimensionality indexes $p = 1$, $p = \frac{1}{2}$, $p = \frac{1}{3}$ describe, respectively, unidimensional, planar, and three-dimensional growth. Following the formation of a critical aggregate nucleus at a critical aggregate concentration (CAC), further growth upon increasing unimer concentration produces macroscopic aggregates (aggregation number $\rightarrow \infty$) whenever $p < 1$. Finite-size distributions of assemblies are instead produced whenever $p = 1$. Spherical micelles share the latter feature of the $p = 1$ system due to the amphiphilic nature of constituent molecules [13]. The predicted phase diagrams (aggregation numbers versus free unimer concentration) include a critical concentration above which the concentration of aggregates increases and that of the free unimer remains constant.

On the above basis, supramolecular polymerization can be discussed within a general context that cuts across traditional boundaries between colloid, polymer, and solid-state science. The aggregation of two- and three-dimensional systems can be described as a none or all (crystallization) process, whereas the formation of unidimensional assemblies (linear, columnar, helical, cf. Figure 3) may display large cooperativity, but not a true phase transition. For unidimensional systems, different growth mechanisms (cf. seq.) have been identified within the above framework.

B. Localized Interactions

1. The Supramolecular Bond

For all types of SPs, the stabilization of well-defined structures is due to combinations of interactions that may be localized at specific atomic groups of the unimers, or more uniformly distributed over the assembly surface. In all cases, shape complementarity is an integral part of the process of molecular recognition. The present section discusses the role of localized interaction; smoothed-out interaction will be discussed in Section II.C. Detailed quantitative assessment of the role of classical localized interactions is described in the literature of low-MW host–guest complexes [17]. In the case of SPs, most important types of localized interactions are based on H-bonds, π – π stacking, charged groups, or metal–ion coordination. Several combinations of these interactions may additively contribute to the overall contact energy [17]. Solvents may compete or enhance the formation of localized bonds through localized effects. For instance, H-bonds are stronger in apolar not exchanging solvents and ionizable groups are sensitive to pH. Solvents also display nonlocalized effects (solvophobic/solvophilic interaction) on the formation of supramolecular bonds

(to be described in Section II.C). Localized interactions are described by the respective sets of potential functions involving point charges, dipolar interaction, and separation distances.

(a) Hydrogen bonds

These occupy a major role in the assemblies of both synthetic and biological molecules due to their strength and directionality. The H-bond involves a proton donor (C–H, O–H, N–H, F–H) and a basic acceptor (O, N) atom with distance of separation of ~ 3 Å and a strong directionality that primarily reflects the anisotropy of charge distribution (lone pair) of the acceptor atom. The bond results from an interplay of van der Waals and Coulombic interactions with the latter playing a predominant role. Potential functions have been given using either the point charge or the dipole interaction. The expression [24]

$$V = C[(r_0/r)^{12} - (r_0/r)^6] - (\mu_1\mu_2/r^3)g(\theta_1\theta_2, \phi_1\phi_2) \quad (1)$$

includes the steric or dispersion interaction terms of the Lennard–Jones potential where r_0 and r are, respectively, the van der Waals and the actual NH $\cdots$ O separation distances. The second term in Eq. (1) represents the Coulombic interaction for the dipoles attached to the NH and O=C bonds, as illustrated in Figure 4(a). The NH $\cdots$ O distance is thus a predictable function of the NH $\cdots$ O=C angle and azimuthal orientation. The strength of a H-bond can be determined from

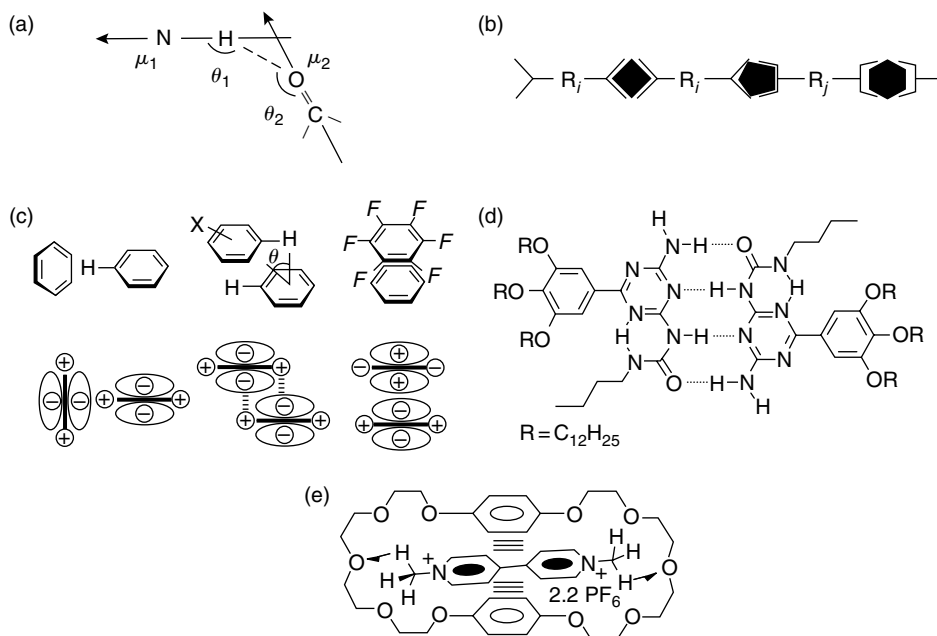


Figure 4 (a) Dipole–dipole interaction parameters for H-bonds; (b) scheme for coordination of SPs based on bidentate/tridentate complexation unit with metal ion and tetra- to hexa-coordination. (From J.-M. Lehn. *Supramolecular Polymers*. A. Ciferri, Ed., New York: Marcel Dekker, 2000. With permission.); (c) Geometries of aromatic interactions: edge-to-face, offset stacking, face-to-face stacked. (From M.L. Waters. *Curr. Opin. Chem. Biol.* 6:736, 2002. With permission.); (d) Monofunctional ureidotriazines assemble via quadruple hydrogen-bonding in a disk capable of columnar stacking. (From L. Brunsveld, B.J.B. Folmer, E.W. Meijer, and R.P. Sijbesma. *Chem. Rev.* 101:4071, 2001. Copyright 2001 ACS.); (e) π – π stacking interaction plus H-bonds contribute to the stabilization of a complex between paraquat [PQT] $^{2+}$ and a cyclophane-like macrocyclic polyether with hydroquinol rings. (From M.C.T. Fyfe and J.F. Stoddart. *Acc. Chem. Res.* 30:393, 1997. Copyright 1997 ACS.)

simple dimers forming a single bond, or by the analysis of data for complexation of compounds forming multiple H-bonds. The observed linear increase of ΔF for the complexation of amide-type complexes in CDCl_3 with the number of H-bonds is a verification of the important principle of additive binding increments mentioned above. The strength of a single H-bond in a particular solvent was evaluated to be 7.9 kJ/mol (~ 2 kcal/mol). The parallel or antiparallel arrangement of multiple H-bonds (e.g., AAA-DDD, ADA-DAD) in a given complex may increase or reduce the product of single-bonding constants due to secondary electrostatic interaction (cf. Chapter 6 and also Ref. 25). Other data quoted by Schneider [17] suggest a broader range of strength between ~ 2 and ~ 20 kJ/mol per amide link. It is important to note that polar solvents compete and destabilize H-bonds of supramolecular structures.

(b) π - π or arene-arene stacking

These attractions are also introduced by proper chemical design in SPs. The geometries of π - π interactions are schematized in Figure 4(c) [26b]. Quadruple moments arise due to the uneven electron density on the face and on the edge of rings. The nature and size of rings and substituents, and also the solvent interactions, are the variables. The offset stacked geometry (typical of DNA base stacking) maximizes buried surface area and thus dispersive and solvophobic interactions. Face-to-face stacking is favored by different substituents (opposite quadruple moments) and also by solvents or divalent cations. π - π interaction between two π -poor aromatic systems could be even more favorable than in the case of two π -rich, or one poor and one π -rich systems [26]. Stacking interaction in planar aromatic systems (discotics) occurring in polar solvents appears strengthened by solvophobic interaction [27] (cf. also Chapters 14, 16). However, the strength of stacking is not as strong nor as directional as for the H-bond in apolar solvents. Therefore, combinations of arene-arene and H-bonding have been exploited to produce columnar assemblies of discotic unimers characterized by strong contact energies (and thus large DP) in a variety of solvents [2]. The supermolecule in Figure 4(d) illustrates a coupling of several interactions. Dimerization by H-bonding stabilizes an extended core discotic supermolecule favoring π - π longitudinal stacking interaction and producing an apolar environment for stabilizing the H-bonds. Electrostatic components modulate the strength of the DDDA sequence of H-bonds. Interaction with solvents (solubility, solvophobic/solvophilic) can be modulated by the proper use of polar or apolar side chains R.

Figure 4(e) illustrates an example of superimposition of H-bonds and charge transfer in a 1:1 complex between the crown ether (host) bisparaphenylene-34-crown-10 having electron-rich hydroquinol rings, and the bipyridinium derivative paraquat $[\text{PQT}]^{2+}$ (guest) with electron-poor rings [28]. The complex is a good example of stabilization due to a variety of interactions such as charge transfer, hydrogen bonds (involving a hydrogen atom of $[\text{PQT}]^{2+}$ and the polyether oxygen atom of the crown ether), ion-dipole, and dispersive forces. The occurrence of charge transfer bands in the electronic spectra should be verified for a conclusive proof of electron transfer from high-level occupied to low-level unoccupied molecular orbitals for a given complex in a given solvent.

(c) Other electrostatic interactions

The electrostatic interactions between fixed and complementary ionizable groups are also frequently exploited (binding energies up to 10 kJ/mol) for both host-guest complexes and SPs. In line with the general features of the Debye-Huckel theory, a decrease of the association constants with increasing charge separation, solvent polarity, and ionic strength was frequently observed [29-31]. Stabilization of columnar SPs (Section III.B) by formation of salt bridges between discotic unimers was also exploited [32,33]. Triphenylenes form alternating donor-acceptor SPs in solution when doped with equimolecular amount of electron donors favoring unidirectional charge transfer along the columnar axis [34]. Metal-ion coordination favors linear association of unimers

having two metal binding sites. Figure 4(b) illustrates the coordination scheme between metal ions with tetra- to hexa-coordination and bidentate or tridentate binding terminals of a covalent segment.

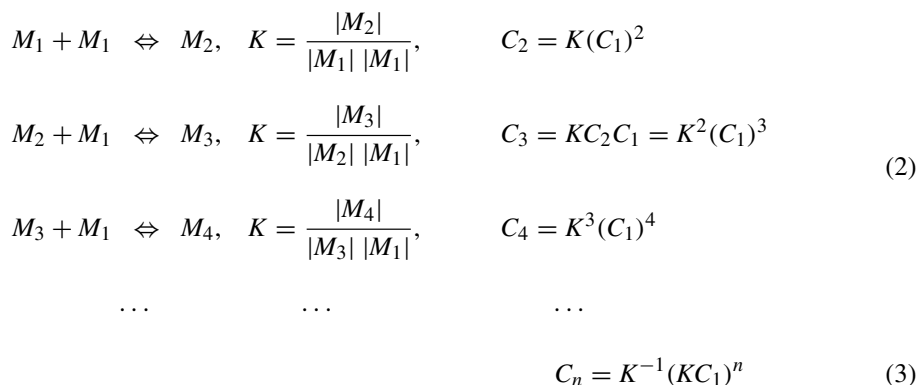
(d) Dispersive forces

The dispersive forces in host–guest supramolecular chemistry do not have the same all-important significance manifested by the conformation of molecular polymers. This type of interaction lacks the selectivity of other attractive interactions such as the H-bond. Nevertheless, dispersive interactions can be rather strong. The gas-phase calculated interaction between two C–H bonds amounts to ~ 0.2 kcal/mol, but the cumulative effect of the bonds occurring in two *n*-hexane molecules amounts to ~ 6 kcal/mol [17]. The interaction is reduced in polarizable organic solvents but is not much affected by water. Dispersive interactions can therefore be expected to play an essential role in situations (cf. seq.) in which long aliphatic segments undergo a molecular recognition that is not as specific, or pointlike directed, as other types of interactions.

The complex balance of localized interactions is the main component of binding constants and contact forces that promote supramolecular polymerization. Accordingly, the two main assembly mechanisms based on localized interactions will be presented below. Assembly mechanisms prevalently based on nonspecific (smoothed-out) interactions will instead be presented in Section II.C within the context of the latter type of interaction.

2. Assembling via MSOA (Isodesmic Polymerization)

The scheme of supramolecular association of *n* monomeric units (unimers) M_1 into a linear sequence (multistage open association (MSOA)) is [35–41]



where C_n is the concentration of the *n*-mer and the identical equilibrium constant K for each step (no cooperation) is assumed. The total concentration (C_p) of all species coexisting at a given polymerization degree (unimers, oligomers, polymers) and the total initial concentration of unimers (C_0) are

$$\begin{aligned}
 C_p &= \sum C_n = \sum K^{-1}(KC_1)^n = \frac{C_1}{1 - KC_1} \\
 C_0 &= \sum nC_n = \sum nK^{-1}(KC_1)^n = \frac{C_1}{(1 - KC_1)^2}
 \end{aligned} \tag{4}$$

The above equations show that $C_0 > C_p$ and $KC_1 \leq 1$. The extent of growth can thus be expressed as

$$DP_n = \frac{C_0}{C_p} = \frac{1}{1 - KC_1} \quad (5)$$

showing that the number average degree of polymerization, $DP_n \rightarrow \infty$ when $KC_1 \rightarrow 1$. Note that the dominant variables are C_0 and K . $C_0 = C_1$ only at the beginning of the polymerization and the various $C_1, C_2, \dots$ could only be assessed by fractionation. It is easy to show that the corresponding weight average can be expressed as

$$DP_w = \frac{1 + KC_1}{1 - KC_1} \quad (6)$$

and the width of the length distribution $DP_w/DP_n = 1 + KC_1$ widens to the limit of 2 when $KC_1 \rightarrow 1$ or C_1 approaches K^{-1} .

It is important to note that the above polymerization scheme applies to supramolecular polymerization when bond formation occurs *without byproducts*, in contrast to the case usually observed with molecular polycondensation [35,41]. The most significant difference is that DP increases with the initial unimer concentration (C_0 or C_1) in the supramolecular case, while it is independent of concentration for conventional isodesmic polycondensation. In the latter case, using the extent of reaction p (<1) and $C_p = C_0(1 - p)$ the Carothers equation yields $DP_n = 1/(1 - p)$. In both polymerizations, DP increases with increasing K . Plots illustrating the role of unimer concentration and equilibrium constants in supramolecular polymerization are shown in Figure 5(a) [41] and Figure 5(b) [2]. In the bulk phase (volume fraction = 1) DP is simply related to K by the approximate relationship (valid for $K \gg 1$)

$$DP \approx K^{1/2} \quad (7)$$

3. Assembling via HG (Cooperative Helical Growth)

A new situation is expected when binding of one unit promotes binding of successive units along a helical pattern. This type of cooperation was introduced by Oosawa [4,37] to interpret the occurrence

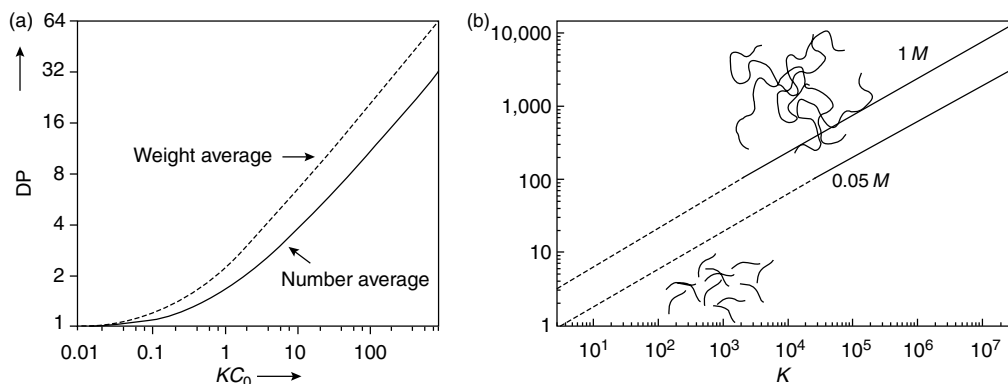


Figure 5 (a) Plots of DP_n and DP_w as functions of KC_0 for isodesmic polymerization without byproduct. (From D. Zhao and J.S. Moore. *Org. Biomol. Chem.* 2003. Copyright 2003 RCS.); (b) Theoretical relationship between the association constant K and DP according to the multistage open association model. (From L. Brunsveld, B.J.B. Folmer, E.W. Meijer, and R.P. Sijbesma. *Chem. Rev.* 101:4071, 2001. Copyright 2001 ACS.)

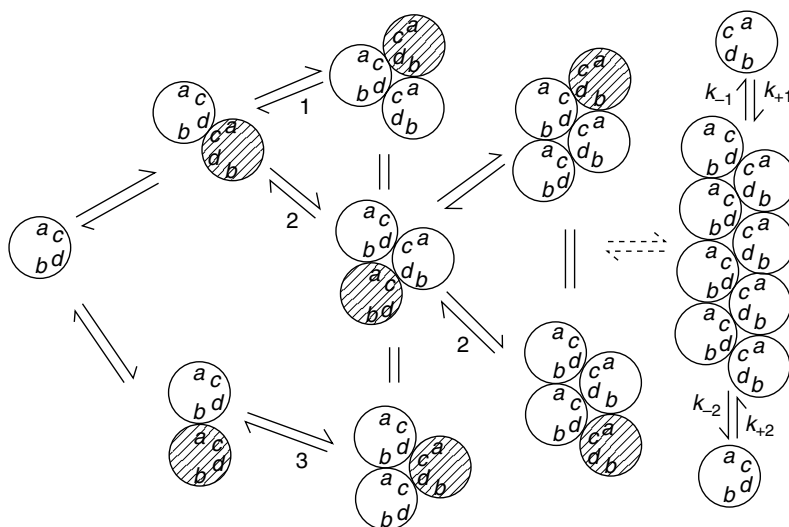


Figure 6 Scheme for the polymerization of actin-ADP. Two dimers (cd and ab bonds) originate identical trimers that may elongate by addition of unimers at either end through the simultaneous formation of ab and cd bonds. A steady-state situation is eventually reached with each end independently at equilibrium with unimers. (From E.D. Korn. *Physiol. Rev.* 62:672, 1982. With permission.)

of extremely large linear assemblies during the $G \leftrightarrow F$ (globular $\leftrightarrow$ fibrous) transformation in proteins. The approach is a simple thermodynamic treatment inspired by the statistical mechanical treatment of Zimm and Bragg [42] for the coil $\rightarrow$ helix transformation in linear polypeptides. In the α -helix, each amino acid residue is bound to two residues by main-chain covalent bonds and to two additional residues by H-bonds. In analogy, Oosawa imagines a helical assembly in which each unit can make two kinds of supramolecular bonds with four neighboring units: two along a linear sequence and two along a helical pattern [43]. In this case the shortest oligomer having a helical sequence is composed of four units (Figure 6 and Figure 3(b)). Only linear aggregates (or a transformation from helical to linear assemblies) are expected under conditions disfavoring the formation of one type of bonds.

The distinctive features of the Oosawa mechanism, in particular a large DP of the supramolecular polymer, emerge upon detailed consideration of the model. The formation and growth of the basic helical nucleus of four units (Figure 6) is characterized by the fact that the addition of the fourth (and successive) unit involves a larger number of bonds per unit, and a larger binding constant (K_h) relative to the constant K of the linear sequence. Thus, in analogy with Eq. (1),

$$\begin{aligned}
 M_1 + M_1 &\rightleftharpoons M_2 \rightarrow K = \frac{|M_2|}{|M_1||M_1|} \rightarrow C_2 = K(C_1)^2 \\
 M_2 + M_1 &\rightleftharpoons M_3 \rightarrow K = \frac{|M_3|}{|M_2||M_1|} \rightarrow C_3 = KC_2C_1 = K^2(C_1)^3 \\
 M_3 + M_1 &\rightleftharpoons M_4 \rightarrow K = \frac{|M_4|}{|M_3||M_1|} \rightarrow C_4 = K_h C_3 C_1 = K_h K^2(C_1)^4
 \end{aligned} \tag{8}$$

...

...

...

$$C_n = \sigma K_h^{-1} (K_h C_1)^n \quad n \geq 4 \tag{9}$$

where

$$\sigma = (K/K_h)^2 \quad (10)$$

is the key parameter of the theory accounting for the low probability of initiating the helical sequence and the cooperativity of the multiple equilibria process. The total initial concentration C_0 can be written as

$$C_0 = C_1 + \sum n\sigma K_h^{-1} (K_h C_1)^n \approx C_1 + \frac{\sigma C_1}{(1 - K_h C_1)^2} \quad (11)$$

and a plot of $K_h C_1$ versus C_0 is given in Figure 7(a) [41].

A schematic representation of the overall trend is given in Figure 7(b). At low C_0 , almost all units occur as dispersed unimers and short linear polymers ($C_0 = C_1$) since the second terms on the right of Eq. (11) can be neglected on account of the small value of σ . Upon further increase of C_0 , a critical concentration C^* is reached when

$$C^* = K_h^{-1} \quad (12)$$

For $C_0 > C^*$ the second term in Eq. (11) increases with C_0 and all excess units form helical supramolecular polymers coexisting with monomers and short linear sequences having constant concentration C_1 . The average DP of the helical polymer

$$DP_n = \sum DP_n C_{nh} / \sum C_{nh} = 1/(1 - K_h C_1) = (C_h/C^*)^{1/2} \sigma^{-1/2} \quad (13)$$

becomes very large near the critical concentration. For instance if $C_h/C^* \sim 1$ and $\sigma = 10^{-6}$, $DP_n = 10^3$. Comparison of Figure 7(a) and Figure 5(a) reveals the role of $\sigma \ll 1$ in increasing cooperativity ($K_h C_1$ reflects DP_n according to Eq. [13]). Cooperation is lost when $\sigma \rightarrow 1$ and the MSOA mechanism is recovered. Thus, the helical supramolecular polymerization exhibits

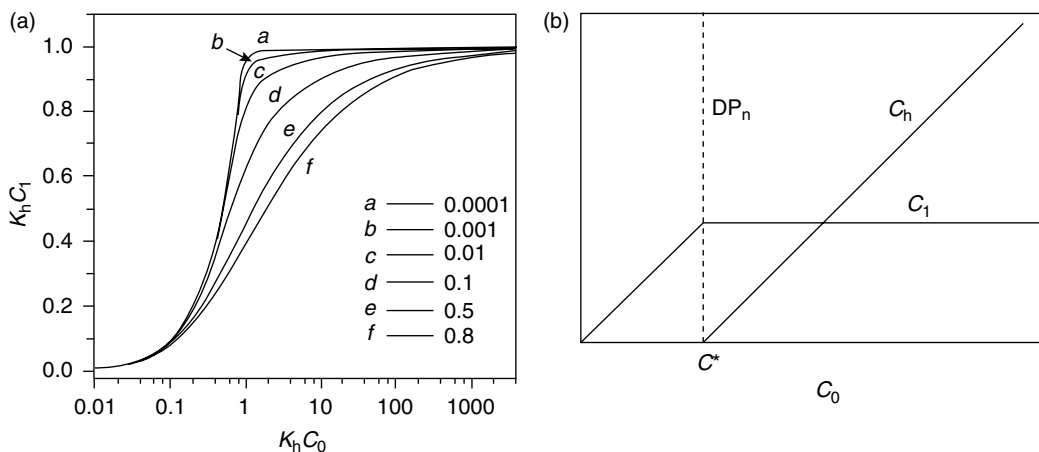


Figure 7 (a) Plot of $K_h C_1$ as functions of $K_h C_0$ for the indicated values of σ . (From D. Zhao and J.S. Moore. *Org. Biomol. Chem.* 2003. Copyright 2003 RCS.); (b) Features of helical supramolecular polymerization: ordinate: unimer + linear oligomer concentration C_1 ; helical polymer concentration C_h ; average degree of polymerization DP_n . Abscissa: total initial unit concentration. (From F. Oosawa and S. Asakura. *Thermodynamics of the Polymerization of Protein*. London: Academic Press, p. 25, 1975. With permission.)

a high degree of cooperativity and essentially involves two extremes: dissociated units (G) and very long assemblies (F). The enhancement of DP_n over the value predicted by isodesmic polymerization (Figure 5, compare Eqs. [4] and [11]) is determined by the cooperativity parameter σ . A broad equilibrium distribution can still be expected with an exponential decrease of C_n with DP and $DP_w/DP_n \approx 2$. The critical concentration is expected to depend upon temperature and solvent type through the value of K_h in Eq. (12). The $G \rightarrow F$ transformation is thus predicted to occur in isotropic solution before the liquid-crystalline phase is formed.

Oosawa emphasized the nucleation of the helix with $n = 4$ that appeared to best describe the experimental data for actin (cf. Section III.B). However, helix nucleation by critical nuclei having n smaller or larger than 4 is also described by Oosawa's theory. Recent work has considered the model with $n = 2$ for the $G \rightarrow F$ transformation [44] (see also [41]). In fact, the scheme in Figure 7(b) has general validity for a host of nucleation processes in solution including, for instance, the nucleation of spherical micelles and their sphere to rod transition (cf. Section II.A.3) [13].

Recently, a true statistical mechanical treatment of the nucleation of all supramolecular helices was presented by van der Schoot and coworkers (45, 46) and successfully applied to experimental data for columnar assemblies of chiral discotic molecules (cf. Section III.B). They elaborated a complete partition function for the nucleation process without an *a priori* specification of a molecular model or a critical nucleus, but included the role of chain-end conformation: confined helical (H), nonhelical (N), or free (F) [46b]. A typical phase diagram for the case in which both ends are unrestricted (FF) is reproduced in Figure 8. The diagram shows the field of stability of monomer, weakly aggregated species, and helical polymers as a function of the excess helical bond energy ($-P$) and the difference in the chemical potential of a monomer in free solution and in the aggregate ($\Delta\mu$). A transition to helical polymer is predicted for strong helical bonds, and nonhelical aggregates are predicted in a wide region of the diagram. Significant alteration, including a reentrance of the nonhelical aggregate (cf. Ref. 44) are predicted for other assignments of chain-end boundary. The partition function evaluated for the Oosawa model appeared to agree with the van der Schoot model only for the FF boundary and high cooperativity. A significant difference between the two approaches is that Oosawa considers a specific model for site interaction requiring an *a priori* specification of the nucleus size, whereas such a restriction is unnecessary with the generalized

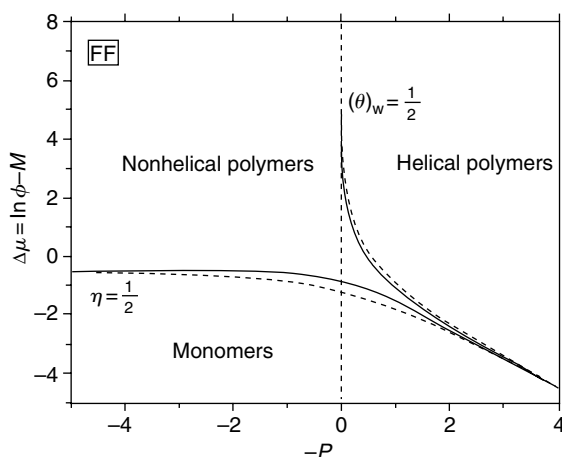


Figure 8 Theoretical state diagram under free boundary conditions (FF) for $\sigma = 1$ (dashed line) and $\sigma = 1.5 \times 10^{-3}$ (drawn line). Vertical axis: $\Delta\mu = -M + \ln \phi$; horizontal axis: $-P = \ln s$. The top line is the helical transition line, where half the bonds are helical and $(\theta)_w = \frac{1}{2}$. The bottom line is the polymerization line, where half the material is in the aggregated state and $\eta = \frac{1}{2}$. (From J. van Gestel, P. van der Schoot, M.A.J. Michels *Langmuir* 19:1375, 2003. Copyright 2003 ACS.)

theory. Consequently, the latter approach needs to be complemented by an *a posteriori* identification of a structural model.

C. Nonspecific Interactions

1. Assembling by Incompatibility Effects

The solute/solvent interaction is an important driving interaction in supramolecular assembling. Chemical compatibility or incompatibility between solution components affects the solubility, the solvation, and the conformation of polymers and oligomers. The well-known hydrophobic effect is due to the poor affinity of water for nonpolar molecules. Transfer of hydrocarbons from water to hydrocarbon solvents is accompanied by a large entropy increase, an often negligible enthalpy contribution, and a decrease of heat capacity [12,17]. The entropy gain has been attributed to a fluidification of the water shell surrounding the dispersed component although this interpretation disregards the role of attractive dispersion interaction within each component [47]. Macroscopic phase separation and ordering is eventually observed on increasing temperature.

The interaction of a particular segment with a poor solvent may be generalized to the interaction occurring when two incompatible segments are present. If the incompatible segments are chemically or supramolecularly connected, a selective solvent may promote solvation and exposure of the solvophilic component and association of the solvophobic one, a situation that leads to cases of globular proteins and micelles characterized by hydrophobic cores and hydrophilic shells. The solvophilic component actually prevents macroscopic phase separation of the solvophobic one. Even in the absence of the solvent, the segmental incompatibility will generate a supramolecular structure based on the *microsegregation* of segments in domains separated by the surface containing the intersegmental bonds.

In spite of their weakness, nonspecific interactions play a fundamental role in determining supramolecular architecture and properties. A relevant example is the possibility of carrying in solution even classical solid-state complexes by supramolecular association to anionic lipids (cf. Figure 12 in Chapter 13) thereby producing processable molecular wires. In fact, incompatible segments have been widely used in the design of amphiphilic molecules and supermolecules forming supramolecular structures in selective solvents. Relevant thermodynamic parameters deriving from the theory of polymer solution [48] describe the affinity of any pair of components down to the ultimate phase separation, also to be regarded as a self-assembly process. Therefore, we analyze the basis of assembly processes due to generic solvophobic interaction, phase separation, micellization, and microsegregation.

(a) Solvophobic interaction and macroscopic phase separation

The solubility of SPs in a given solvent is often controlled (cf. Section III.A) by the use of side chains compatible with the particular solvent. For instance, columnar assemblies of *m*-phenylene ethynylene rings having apolar aliphatic substituents are (poorly) soluble only in nonpolar solvents. More polar substituents result in increased solubility in polar solvents. While the side chain experiences a solvophilic interaction with the solvent, the core of the molecule experiences a solvophobic environment that may actually reinforce the contact forces.

This intricate scheme of interaction may be described in terms of sets of compatibility parameters easily calculated (or measured) for relevant binary systems (e.g., side chain/solvent, core/solvent, core/side chain) [49,50]. The knowledge of pairwise parameters is also necessary for a quantitative assessment of the temperature variation of solubility and demixing (two liquid phases or crystallization). According to an approximate treatment of binary solutions originally developed for mixtures of poorly interacting apolar polymers, a liquid–liquid phase separation is expected to occur at a critical temperature $T = \theta > 0$ at which a balance of the enthalpy (κ) and entropy (ψ) components

of dilution is achieved [48].

$$\theta/T = \kappa/\psi \quad (14)$$

The condition $\theta > 0$ is fulfilled provided both the heat and entropy of dilution parameters are of the same algebraic sign. Under normal situations the phases separate on cooling and an upper critical consolute temperature (UCST) corresponds to $\psi = \kappa$ with $\psi > 0$ and $\kappa > 0$. However, under the so-called *inverted* situations [51,52] the phases separate on heating and the lower critical consolute temperature (LCST) requires $\psi < 0$ and $\kappa < 0$. Inverted transitions are typical of hydrophobic interaction when more order may be said to occur in the solution than in the phase-separated system. Some degree of aggregation must therefore have occurred at least for one of the solution components. Moreover, the entropy gain due to the breaking of the aggregation must prevail over the entropy loss resulting from demixing. Liquid–liquid phase separation involving an isotropic and a liquid-crystalline phase can also be of the normal or inverted type [49] and conform to the above general principles [53]. For instance, the solvophobic effect in the binary system (hydroxypropyl)cellulose in H₂O produces the ultimate effect of an inverted transition leading to the formation of a liquid-crystalline phase at the smallest concentration ($\sim 0.4\%$ v/v, Figure 9) at which cholesteric order was ever detected [54,55]. Note that solution demixing into two coexisting phases (a diluted and a concentrated one), which cannot entail any DP alteration for a covalent polymer, will instead cause significant DP alterations for SPs. Phase transitions can thus be included among the mechanisms of supramolecular polymerization.

Inverted melting transition in the presence of a diluent has also been described [51]. It is characterized by an *increase* of the melting temperature with the amount of diluent, in contrast to the normal case of a depression of the melting temperature by a diluent. Even in this case entropy and enthalpy changes at the transition must each be described by contributions due to two components. The total enthalpy exchange is the sum [51]

$$\Delta H_{\text{tot}} = \Delta H^{\circ} + \Delta H_{\text{dil}} \quad (15)$$

where $\Delta H^{\circ} > 0$ is the melting enthalpy of a pure component, and ΔH_{dil} is its dilution enthalpy. The condition for normal melting requires $\Delta H_{\text{tot}} > 0$, whereas the condition for inverted melting is $\Delta H_{\text{tot}} < 0$. Therefore the inverted transition requires $\Delta H_{\text{dil}} < 0$ (or $\kappa < 0$) and also $|\Delta H_{\text{dil}}| > \Delta H^{\circ}$.

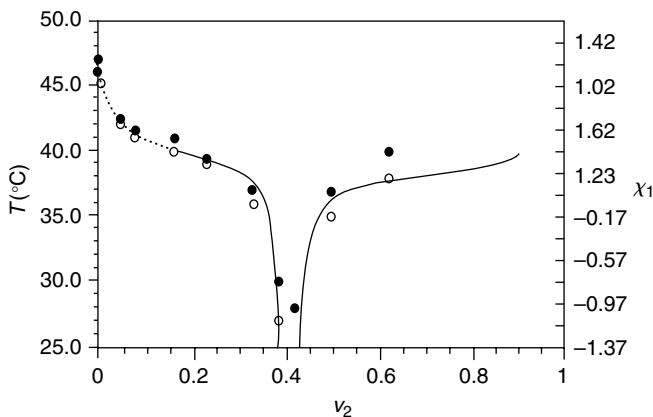


Figure 9 Macroscopic separation: inverted phase transition for (hydroxypropyl)cellulose in H₂O. An isotropic solution with polymer volume fraction $\gtrsim 0.05$ produces a biphasic (isotropic + liquid-crystalline) mixture at $T > 42^{\circ}\text{C}$. The condition $T = \Theta$ ($\chi \sim 0.5$) occurs at $T = 41^{\circ}\text{C}$. (From C.V. Larez, V. Crescenzi, and A. Ciferri. *Macromolecules* 28:5280, 1995. Copyright 1995 ACS.)

The mutual solubility, or compatibility, of two components 1 and 2 (polymer/solvent or polymer/polymer) may also be described in terms of cohesive energy density (CED) using the interaction parameter defined as [48,49]

$$\chi = z\Delta\omega/kT = V_{\text{seg}}(\delta_1 - \delta_2)^2/RT \quad (16)$$

where $\Delta\omega = \omega_{12} - \frac{1}{2}(\omega_{11} + \omega_{22})$ is the difference in energy for the formation of 1, 2 contacts out of 1, 1 and 2, 2 contacts, z is a coordination number, k is the Boltzmann constant, $\delta^2 = \text{CED}$ is the Hildebrand solubility parameter (calculated with QSPR methods), and V_{seg} the segment volume.

When large differences in the CEDs of the components occur, χ exceeds the critical value and the two components segregate into two macroscopic phases. Values of $\chi < \frac{1}{2}$ characterize instead thermodynamically good solvents in which polymer segments experience chain expansion and solvation. The term $\frac{1}{2} - \chi$ describes the excess mixing (dilution) free energy, which attains pseudo ideal values when [48]

$$T = \Theta, \quad \chi = \frac{1}{2}, \quad \psi = \kappa \quad (17)$$

Demixing for a ternary system is predicted to occur when $\chi > \frac{1}{2}(1/\text{DP}_2^{1/2} + 1/\text{DP}_3^{1/2})$. Solubility parameters for complex mixtures such as two block copolymers poly(A-co-B) + poly(C-co-D) x, y being volume fractions of A and C are evaluated according to [49]

$$\chi = xy\chi_{AC} + x(1-y)\chi_{AD} + (1-x)y\chi_{BC} + (1-x)(1-y)\chi_{BD} - x(1-x)\chi_{AB} - y(1-y)\chi_{CD} \quad (18)$$

(b) Micellization

The poor affinity of nonpolar hydrocarbons with water is manifested in a migration to the air–water interface and in a macroscopic phase separation equivalent to the formation of aggregates of infinite size, as discussed above. However, if a hydrophilic head group is attached to the hydrocarbon molecule the apolar tails can avoid phase separation by forming, above a critical concentration, micellarlike supramolecular structures stabilized by the exposure of the head group to water. Similar structures are expected if two incompatible segments A and B are chemically connected in an amphiphilic block copolymer and dissolved in a selective solvent for either A or B. Self-assembled supramolecular structures formed by surfactants, lipids [12,13,56], and block copolymers [57] in selective solvents have been extensively investigated. Structures involve spherical, cylindrical, and inverted micelles as well as bilayers and vesicles (Figure 10). In all cases the solvophilic groups point toward the solvent and in the case of vesicles there is also a solvent-filled cavity. The simplest structures in Figure 10 can be regarded as the repeating building blocks of larger assemblies. Suitable amphiphilic ABC triblock copolymers may form liposomic, vesicular structures and functional channels within copolymer membranes [58]. The relevance of these structures to the formation of biological membranes has been extensively discussed [12,13,56–58], and their relevance to supramolecular polymerization has been pointed out [5]. Supramolecular amphiphiles, when the solvophobic and solvophilic components are linked by a noncovalent bond, are also known. Kimizuka [59] has described hydrogen-bond-mediated bilayer membranes (cf. Figure 3 in Chapter 13).

The distinctive feature of block copolymer micelles is the occurrence of a polymer segment as the head group protruding from the core. Figure 11(a) illustrates cases in which the relative length of the two flexible blocks determines a large core and a thin corona, or vice versa. Cases in which the selective solvent was a homopolymer of the A or B type have been described [60]. In the case of micelles formed by a rod/coil copolymer (Figure 11[b]), a spherical core formed by the rigid block is not favored. Cylindrical cores or bilayers should be favored instead [57,60–62]. A lamellar sheet

typical of the microsegregation occurring with an ABA undiluted triblock copolymer is schematized in Figure 11(c). The formation of bilayers and giant vesicles has also been reported [10,11]. Micellar and microdomain structures are detailed in Chapters 9, 11, and 13.

The formation of spherical micelles occurs with a significant degree of cooperativity at very low amphiphile concentrations and should be regarded as a true phase transition only in the case of an infinite micelle [12,13]. The critical micelle concentration (CMC) marks the limit at which micellar aggregates are formed. Further addition of surfactant does not cause a large increase of free amphiphile molecules but rather an increase of number and average size of micelles (cf. figure 3

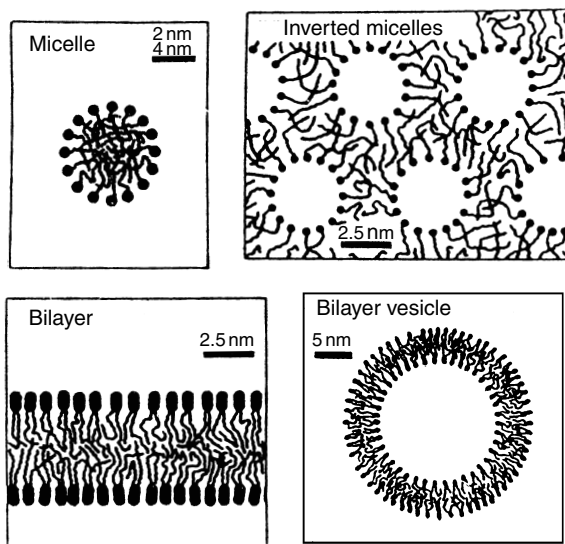


Figure 10 Micellization: micelles, bilayers, and vesicles formed by single- or double-chained surfactants in water. (From J.N. Israelachvili. *Intermolecular and Surface Forces*. London: Academic Press, 1992. With permission.)

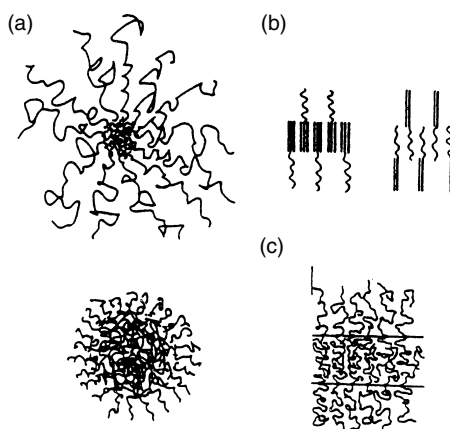


Figure 11 Micellization: (a) micelles in solutions of coil-coil diblock copolymers having different lengths of the solvophilic and solvophobic block. (From A. Halperin, M. Tirrel, and T.P. Lodge. *Adv. Polym. Sci.* 100:31, 1991.); (b) bilayers of rod-coil diblock copolymers in solvents affine for either block. (From A. Gabellini, M. Novi, A. Ciferri, and C. Dell'Erba. *Acta Polimerica* 50:127, 1999. With permission.); (c) microdomain structuration for a triblock copolymer in absence of a diluent. (From A. Halperin, M. Tirrel, and T.P. Lodge. *Adv. Polym. Sci.* 100:31, 1991. Copyright 1991 Springer-Verlag.)

and figure 4 in Chapter 4). A second CMC at which spherical micelles assume a cylindrical shape has often been discussed [63]. Spherical micelles thus exhibit a size distribution corresponding to variable numbers (n) of constituent amphiphilic molecules, and broadening with total surfactant concentration. Minimum (n) values range from 50 to 100 for typical ionic surfactants, average sizes are in the order of nm, and the CMC are in the order of mM, decreasing with charge screening and increasing with the size of the apolar tail. It is important to note that the essential features of micellar formation are similar to those illustrated in Figure 7(b) describing helical supramolecular polymerization. In fact, both phenomena follow the general thermodynamic considerations regarding growth of supramolecular aggregates discussed in Section II.A.3 [13]. Micellar parameters can be deduced from a balance between the attraction of apolar tails and the repulsion of charges at the rim, respectively decreasing and increasing with separation distance (64). The approach was recently expanded by Kegel and van der Schoot to describe the somewhat similar assembly of the hepatitis B virus capsid [14,65,66]. The stabilization of the core of micelles (or capsids) is driven by a cooperative association due to weak hydrophobic interactions (expectedly characterized by rather small equilibrium constants) counteracted by repulsive electrostatic interactions concentrated at the rim. The cooperative character of assembly formation is attributed to the high rim energy for conformations intermediate between the dispersed unimers and the fully formed micelle, coupled to the large translational entropy loss upon aggregation.

An alternative attempt in using geometrical parameters of the amphiphile to explain micellar shapes (without a detailed knowledge of specific interactions) is due to Israelachvili [13]. He describes the geometrical constraints that affect the interfacial surface area in terms of the area of the solvophilic head group (a_0), the volume (v), and extended length (l) of the aliphatic tail (Figure 12). The parameter v/a_0l controls the critical packing shape and the most stable structure for a given amphiphile in a given solvent environment. For instance, large head group areas (e.g., ionic amphiphiles in low salt) favor conical packing shape ($v/a_0l < \frac{1}{3}$) and spherical micelles (Figure 12). On the other hand, cylindrical packing shapes (i.e., double-chained lipids with small head group, $v/a_0l \sim 1$) favor planar bilayer, while a truncated cone ($v/a_0l \sim \frac{1}{2} - 1$) favors a vesicle.

Upon increasing the amphiphile concentration an evolution toward more asymmetric shapes (rodlike or disklike) and decreasing surface/volume ratio is observed. Eventually cylindrical (capped) micelles, bilayers (extended open sheet with rounded edges), and closed vesicles are formed.

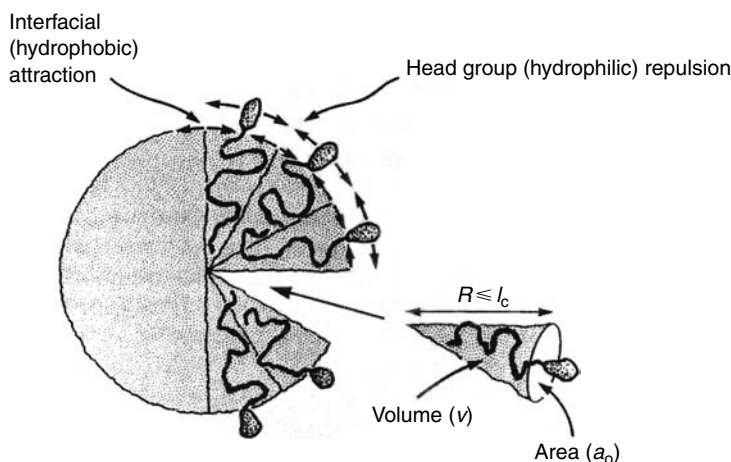


Figure 12 Micellization: the geometrical shape of the amphiphile, expressed by the ratio v/a_0l , determines the stability of micelles and bilayers. Spherical micelles are stabilized by conical shapes: $v/a_0l < \frac{1}{3}$ (single-chained, large head group area). (From J.N. Israelachvili. *Intermolecular and Surface Forces*. London: Academic Press, 1992. With permission.)

The prediction of the stability of the more complex geometrical shapes has been one of the outstanding goals of micellar studies. A simple treatment of the solvophobic core as a structureless continuum does provide a justification for all micellar shapes, including vesicles [12]. More complex, however, is the detailed description of how amphiphilic molecules can pack within the micellar structures. For instance, the external surface area of a vesicle is larger than the internal one, requiring a larger number of molecules in the section of the curved bilayer pointing outward.

Intermicellar forces are generally of a repulsive nature (i.e., charged amphiphiles) and a reduction of such repulsion accompanies the transformation from spherical to cylindrical micelles. Further increase of concentration results in the formation of linear assemblies and lyotropic mesophases (cf. Section II.C.2). Not only nematic (N_c and N_d for rodlike or disklike shapes, respectively), hexagonal, and smectic phases, but also biaxial (mixtures of N_c and N_d) and complex cubic phases (bicontinuous networks or plastics crystals) were reported by Israelachvili [67,68]. For block copolymers with long segments protruding from the core, interlocking may instead occur upon increasing concentration (cf. Chapter 9).

(c) Microsegregation

In the preceding section, AB block copolymers in solution were shown to produce micellar structures. If the same AB block copolymers are studied in the absence of a solvent, the chemical bond prevents the macroscopic phase separation expected for unconnected A and B. Supramolecular structures will instead occur in which all A-type and B-type segments microsegregate in domains separated by a surface that contains the intersegmental bonds.

A detailed mean-field theory [69,70] (namely, self-consistent field theory — SCFT) describes the supramolecular organization of block copolymers in terms of the favorable attraction of similar blocks (controlled by χ) counteracted by the conformational entropy loss by the other blocks confined in neighboring domains (controlled by chain flexibility and the total number of units N). Figure 13(a) illustrates the predicted range of stability of cubic, hexagonal, lamellar, and other phases in terms of the product $N\chi$ versus the fraction of A units in an A–B uncrystallizable block copolymer [71]. Instability modes generated in undiluted melt direct the formation of the various phases [71]. A review of the most recent elaborations of the SCMF theory that unifies the weak [72] and strong [73] segregation regimes was presented by Matsen [70]. Extension of the theory to the calculation of the relative stabilities of liquid-crystalline phases occurring in copolymer solutions was also attempted [74] and it is described in more detail in Chapter 9. A simple, qualitative description

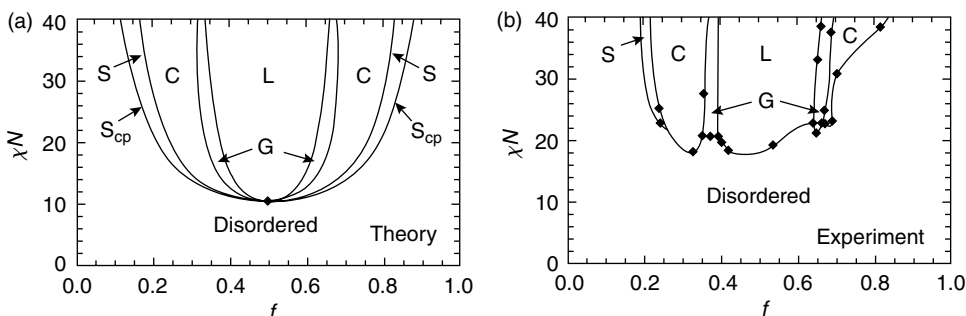


Figure 13 Microsegregation: (a) theoretical and (b) experimental equilibrium phase diagram for amorphous diblock copolymers $(A)_n-(B)_m$ calculated using SCFT and measured using polystyrene–polysoprene diblock copolymers. f is the fraction of A segments. L = lamellar, C = hexagonal cylindrical, S = spheres, G = gyroid phases. (From M.W. Matsen. *J. Phys. Condens. Matter* 14:R21, 2002. With permission.)

[3,15] of hexagonal and lamellar mesophases in solution and in the bulk, based on the supramolecular polymerization of suitable building blocks, will be described in Section III.D.

2. Assembling by Orientational Fields

The formation of liquid-crystalline phases by covalent rigid, wormlike, and segmented chains has been extensively described [50]. Anisotropy and orientation are characterized at the molecular level by the order parameter and at the mesoscopic level by director orientation. In the case of supramolecular polymers orientation and growth may occur according to the following mechanisms:

1. SPs pregrown in the isotropic phase by MSOA or HG subsequently forming a mesophase.
2. SPs growing simultaneously with the formation of their own nematic alignment.
3. SPs growing within a preexisting liquid-crystalline phase of another compound.
4. SPs growing under the action of external fields.

The difference between mechanisms 1 and 2 is illustrated in Figure 14 schematizing the transition from isotropic to nematic phase for molecularly dispersed rodlike polymers (Figure 14(a)), for closed (Figure 14(b)), and open (Figure 14(c)) supramolecular assemblies. Whereas molecular and closed supramolecular polymers are just oriented in the nematic phase, in the case of open SPs development of orientation is simultaneous with an enhancement of polymerization [5].

(a) Liquid crystallinity of molecular and closed SPs

The following interactions assist the formation of mesophases: *soft anisotropic attraction* that is the prevailing orienting component for low-MW mesogens and for segmented polymers in thermotropic melts (a segmented polymer is based on low-MW mesogens connected by flexible spacers along the main chain) [50,75]; *hard repulsion* (shape II recognition), which is the prevailing orienting component for rigid polymers in lyotropic solutions; *soft isotropic interaction* representing the role of solvent as expressed by χ parameters already discussed in connection with Figure 9. Soft attraction results from the orientation-dependent intermolecular energy $\varepsilon(\theta)$ of nonspherical molecules related

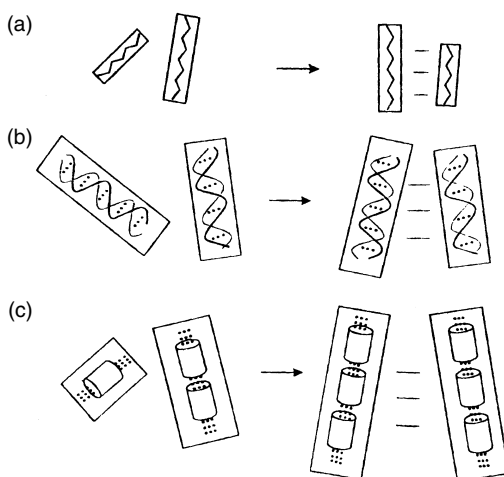


Figure 14 (a) Schematization of the isotropic $\rightarrow$ nematic transition for molecularly dispersed polymers; (b) closed supramolecular polymers; (c) open (linear) supramolecular assemblies. Coupling of contact interactions ($\cdots$) with hard and soft interactions ($-$) causes growth simultaneous to orientation for case (c). (From A. Ciferri. *Liq. Cryst.* 26:489, 1999. Copyright 1999 Taylor & Francis.)

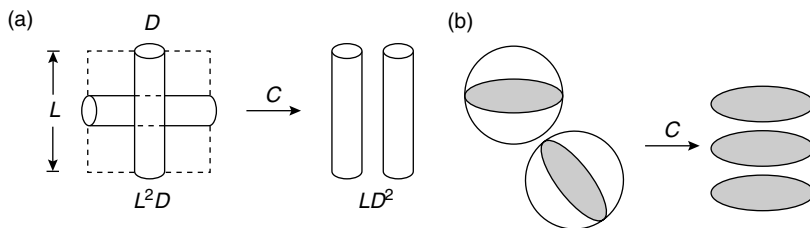


Figure 15 Excluded volume effects: a decrease of free volume favors the formation of (a) parallel assemblies of rods and (b) columnar assemblies of disks upon increasing unimer concentration. (From A. Ciferri, *Liq. Cryst.* 31:1487, 2004. Copyright 2004 Taylor & Francis. www.tandf.co.uk/journals)

to their anisotropy of polarization $\Delta\alpha$ [76,77]

$$\varepsilon(\theta) = C(\Delta\alpha/\bar{\alpha})^2 \varepsilon_{\text{iso}} \bar{V} S \left(1 - \frac{3}{2} \sin^2 \theta\right) \quad (19)$$

where C is a constant, θ is the angle between the molecular and the domain axis, $\bar{\alpha}$ is the mean polarizability, ε_{iso} the isotropic intermolecular energy, $\bar{V}$ the ratio of actual to hard core volume, and S is the order parameter. Hard interactions reflect instead the shape-dependent geometrical anisotropy of the molecules causing (Figure 15) a decrease of volume exclusion from random to parallel assembly of rods or columnar assembly of disks. The tendency to reduce excluded volume leads to a driving force for the orientation of rods or the stacking of disks. The effect begins to be detectable even in isotropic solutions (cf. Chapter 4) and eventually leads to a transition to a nematic mesophase at a critical concentration. The particle anisotropy is expressed by its axial ratio X (length/diameter > 1 for rods, thickness/diameter < 1 for disks).

Extensive theoretical and experimental investigation [50,75] has shown the limits under which the experimental behavior of low- and high-MW mesogens is described by the corresponding theoretical approaches. The following important conclusions are relevant to the present discussion.

1. A critical value of the axial ratio (X^i), varying from ~ 4 to ~ 8 for different theories of rigid chains [78], determines the limit at which an undiluted mesophase becomes “absolutely stable” [76], implying that when $X > X^i$ the mesophase is primarily stabilized by hard interaction and compositional changes (lyotropic systems). In this case a critical solute volume fraction (v^i) can be defined, decreasing with X according to

$$v^i \approx X^i/X \quad (3 < X^i < 8) \quad (20)$$

Critical values of axial ratio for hard rods have been obtained from simulation [79]. For the above system, the nematic $\rightarrow$ isotropic transition is not influenced by temperature changes meaning that $T_{\text{NI}} \rightarrow \infty$, unless a large temperature coefficient dX/dT of rigid conformation does occur [50]. The theory is well-developed for large rods ($L/D \gg 1$), but not for large disks ($L/D \ll 1$). However, simulation studies support the formation of nematic and columnar phases in solutions of thin disks characterized by $0 < L/D < 0.1$ [80]. Note from Figure 15 that disks exhibit a larger excluded volume than rods, if similar values of relevant dimensions are considered. On the other hand, when $X < X^i$ soft interaction prevails, the low-MW mesogens or the segmented polymers are thermotropic ($T_{\text{NI}} > 0$) and may admit only a small amount of isotropic diluent. For fully covalent low-MW mesogens, the T_{NI} temperature can be predicted from first principles (i.e., anisotropy of polarizability, cf. Eq. [19]). It is important to note that for mesogens including supramolecular bonds, a pronounced temperature dependence of the bond strength will play a significant role on T_{NI} .

2. The partial rigidity of long chain polymers is characterized by the persistence length P , which assumes the role of the limiting rigid segment stabilizing the mesophase. This implies that v^i will decrease with L to an asymptotic value. For the model of the freely jointed chain, the axial ratio in Eq. [20] is expressed in terms of the Kuhn segment [78]

$$X = 2P/D \quad (21)$$

Persistence lengths for molecular polymers are in the range 10–200 nm corresponding to rather large values [50] of the critical volume fractions (in the range 0.02–0.2 taking $X^i = 6$ and $D = 5\text{--}10 \text{ \AA}$). Within the mesophase, a wormlike chain may be forced to assume a more extended profile than in the isotropic phase due to the restriction imposed on the director by the order parameter [78,81]. Semirigidity in the nematic state is characterized by the deflection length λ .

$$\lambda = P/\alpha \quad (22)$$

where α is a parameter larger than unity, increasing with concentration and inversely related to the width of the angular distribution of the chain tangent vectors.

In the case of the closed supramolecular liquid crystal (SLC) (Figure 14(b)), when no further association $\rightarrow$ dissociation equilibria accompany the formation of the mesophase, their liquid-crystalline behavior is undistinguishable from that of a molecular liquid crystal (LC). The relevant axial ratio is determined by the geometry of the assembly with no need for account of contact interaction.

(b) Open SLC

Quite different is the case of open assemblies for which a coupling may occur between the contact forces that stabilize the assembly and the hard/soft interactions that stabilize the mesophase. Formally, it is necessary to add a term F_{intra} accounting for the stabilization of the assembly through the contact energy to the molecular LC terms describing hard interactions, soft interactions, and any conformational rearrangement of semirigid mesogens within the nematic field. The free energy of the open SLC becomes

$$F' = F'_{\text{ster}} + F'_{\varepsilon} + F'_{\text{el}} + F_{\text{intra}} \quad (23)$$

The result is an enhancement of growth of the assembly occurring simultaneously with the formation of the ordered mesophase (cf. scheme in Figure 14(c)). The detailed theory for *growth coupled to nematic orientation* was proposed by Herzfeld and Briehl [82] and by Gelbart et al. [83] to describe the assembly of micelles into linear particles. Odijk [84,85] revised the mechanism by recognizing that catastrophic growth in the nematic state is prevented by the flexibility of the linear assembly, resulting in a decoupling of growth in correspondence to the persistence or deflection length of the assembly. The theoretical expectations [5], schematized in Figure 16, show the encroachment of stepwise association to nematic ordering at the critical concentration C^i (generally larger than C^* in Figure 7(b)). The extent of increase of DP at C^i is related to the rigidity of the formed assembly, as expressed by its persistence or deflection length. The DP attained at C^i may be approximated by the ratio P/L_0 where L_0 is the length of the unimer.

The original theory [84], developed for linear assemblies of cylindrical micelles in nematic solutions, was later extended to discotic molecules displaying hard interactions and showing nematic, hexagonal, and higher order phases [86]. The theory predicts that the nematic phase may be skipped for particular combinations of contact energy and rigidity [87]. Extension to systems displaying soft interactions (thermotropic melts) was also considered [88]. A more detailed account of the theory is given in Chapter 4.

More recent considerations relating to the shape of the unimer and to the structure of SPs formed via the open SLC were presented by the author [89]. In particular, growth-coupled-to orientation needs not to be restricted to linear and discotic rigid assemblies. Helical SPs could also assemble by the open SLC mechanism. In fact, the stabilization of supramolecular helices (shown in Section II.B.2 to be due to a nucleation process) could be favored by the SLC even in the absence of nucleation. The process has some analogies with the selection of allowed ordered conformations occurring during crystallization. A related coupling between orientational and supramolecular order was discussed in

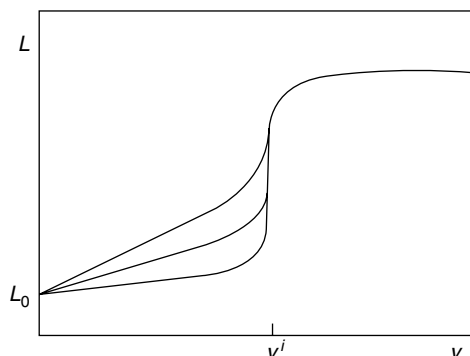


Figure 16 Schematic variation of the length L of a supramolecular polymer with the volume fraction of unimers having length L_0 . At the critical volume fraction v^i sudden growth is simultaneous with the formation of the nematic phase. At $v < v^i$ growth occurs according to the MSQA mechanism — three curves for increasing values of the contact energy being represented. (The expected biphasic gap for a first-order transition in lyotropic systems is omitted for clarity.) (From A. Ciferri. *Liq. Cryst.* 26:489, 1999. Copyright 1999 Taylor & Francis.)

the case of the H-bond scheme of the α -helical conformation when the coil $\rightarrow$ helix transformation was shown to be enhanced by the simultaneous formation of the mesophase [53,90]. Another interesting feature needing additional investigation is the possible coalescence of unimers to form a continuous filament. This possibility is supported by simulation studies on the growth of end-capped micelles of block copolymers [91]. Another recent suggestion [3,15] is the possibility of assembling extremely complex, composite, and functional structures by supramolecular polymerization of specifically designed *building blocks* as described in more detail in Section III.D.

(c) Spherical particles in a nematic field

Theoretical description of the assembly of small spherical particles of diameter σ within a nematic solution of rods ($D \ll \sigma \ll L$) has recently been presented [92]. The coupling of excluded volume of rods and spheres drives the spheres in a zone that is significantly depleted of rods. The depletion zone, oriented parallel to the nematic director, has the approximate shape of a cylinder of length L and diameter related to the average excursion of the rod tips from their aligned position. For low volume fraction of rods, an effective attraction between the spheres is induced, and the formation of their chainlike aggregates oriented along the nematic director is predicted (Figure 17). For a smectic A-type layered structure, the globules concentrate in the interlayer space. Larger spheres tend to demix (note that demixing is invariably predicted and observed for mixtures of rods and coiling polymers) [50]. Experimental results for mixtures of fd virus and PS spheres ($\sigma = 1000$ nm) [93] were consistent with the above theory.

(d) External fields

Orientation induced by elongational flow field has been shown to promote the formation of nematic order at concentration below the critical value in the absence of flow [94]. For covalent systems, the effect of local ordering (described by the order parameters) was shown to be not as dramatic as that occurring over a mesoscopic scale due to director orientation. It is known that application of flow, electrical, and magnetic fields may lead to perfectly ordered single LCs. Theoretical analysis for supramolecular polymers has so far been restricted to the relatively simpler case of helices in magnetic and electrical fields [46]. For polarizable helices in a quadrupole field, and for helices with a permanent dipole in a dipolar field, growth enhancement was predicted as more pronounced

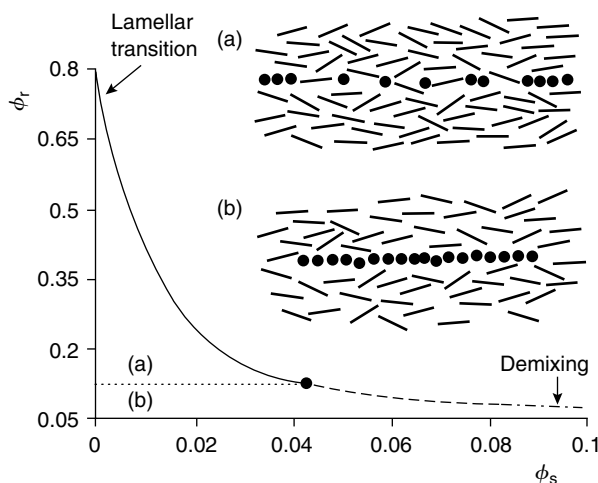


Figure 17 Calculated state diagram for hard globules with diameter σ dispersed in nematic rods with axial ratio $L/D = 100$. ϕ_s is the volume fraction of spheres, and ϕ_r that of the rods. $L/\sigma = 10$. The solid line marks the spinodal instability to the lamellar phase, and the dash-dotted line that to macroscopically demixed phases. The dotted line separates the region where self-assembled chains are of (a) the “open” type from that where they are of (b) the “dense” type. (From P. van der Schoot. *J. Chem. Phys.* 117:3537, 2002. With permission.)

the smaller the angle between chain axis and field direction (cf. Chapter 3). For linear micelles, a decrease of the critical concentration with flow gradient was experimentally observed [95,96]. Even in the absence of a nematic transition, an increase of DP under elongational flow can be related to an increased correlation between growing segments at an effectively larger local concentration.

An interesting example of growth promoted by the application of an electric field was reported [97,98]. A solution of (1,2-dimethoxybenzene) subjected to anodic oxidation (1.6 V) produced a discotic cation radical (1,2,5,6,9,10-hexamethoxytriphenylene). The presence of tetrafluoroborate counterions favored the next and subsequent additions of disklike units to the growing end, resulting in the formation of polyveratrole. Fibers emanating from the electrode surface could be isolated with no loss of properties (including paramagnetism) after several years.

III. SELF-ASSEMBLED POLYMERS

In this section selected data for synthetic and natural polymers in class A are analyzed making a systematic comparison between experimental behavior and theoretical mechanisms presented in Section II. Systems are grouped according to assembling mechanisms rather than chemical structure.

A. Linear Chains and Columnar Stacks: MSOA

Linear and columnar assemblies that were assembled by a noncooperative growth mechanism have been reported. Among earlier linear systems we find the association of glutamate dehydrogenase [38], tropomyosin [99], and synthetic SPs stabilized by a single main chain H-bond [100]. For glutamate dehydrogenase in diluted isotropic solutions an association constant $K = 9 \times 10^5/M$ was reported, and the experimental $M_w - C$ dependence in the oligomeric range ($DP \rightarrow \sim 15$) was well represented by the theoretical prediction illustrated in Figure 5(a). In the case of the SPs reported by Hilger and Stadler [100], undiluted (non LC) systems were considered and DP in the order of 15 was reported.

This result can be attributed to a much smaller association constant than in the case of glutamate dehydrogenase and is consistent with the theoretical plot in Figure 5(b), assuming $K \sim 500/M$ as determined for the pyridine/benzoic acid association [101].

The goal of obtaining large DP occurring in isotropic solution can be realized by the use of multiple H-bonds. A main chain link based on three H-bonds in the AAA-DDD configuration is expected to generate binding constants in the order of $500^3 \approx 10 \times 10^7$ adequate to attain DP in the order of 1000 according to Figure 5(b). This expectation was amply verified by Meijer and coworkers ([2,102], cf. Chapter 15) who studied systems (Table 1, polymer 1) based on the dimerization of ureidopyrimidone characterized by $K = 5 \times 10^7/M$ in CDCl_3 . A covalent segment (low- or high-MW linkers) was terminated by ureidopyrimidone forming a bifunctional unimer allowing four H-bonds on each terminal surface ($F = 2, S = 8$, cf. Figure 3(c)). The configuration AADD-DDAA reduced, by a factor in the order of 10^3 , the much larger value of K expected for the regular AAAA-DDDD configuration. These linear systems did attain DP in the order of 1000 in diluted isotropic solution, when contributions from the HG and SLC mechanisms were ruled out.

Evidence for large growth was also reported for coordination polymers [104,108]. One polymer based on functionalized porphyrin (Table 1, polymer 2) attained DP in the order of 100 in a $7 \times 10^{-3} M$ CHCl_3 solution. Preliminary reports have appeared describing SPs stabilized by DNA base pairing interaction. Rowan and coworkers [109] used only one nucleobase (A^P , C^P , G^P , T) as a terminal group of a short poly(tetrahydrofuran) segment. Solid-state properties were considerably altered but insignificant polymerization was detected in solution. Craig and coworkers [105] used oligonucleotides with partly complementary sequences involving seven or eight base pairs (Table 1, polymer 3). Nucleotide recognition promoted supramolecular polymerization rather than a closed double-helical system of class B type. Polymers formed in solution exhibited viscosity behavior typical of double-stranded DNA while scaling as expected for SPs (cf. Chapter 12).

It is noteworthy that DP obtained by the MSOA mechanism may reach values even larger than those obtained by ordinary polycondensation (DP ~ 100 can only be obtained using irreversible conditions for aliphatic polyamides) [35]. SPs may thus exhibit strong growth in spite of relatively weak bonds, allowing readjustment of donor/acceptor patterns and DP alteration in response to concentration, temperature, and other external variables. Novel properties are thus expected for this class of dynamic, adaptive, smart, self-healing, combinatorial materials (cf. Chapters 1,15). Meijer and coworkers [102] described the peculiar rheological features of networks cross-linked through a four H-bond scheme. Groups displaying supramolecular interaction have also been used to improve mutual compatibility in polymer blends, or in chain extension [103,110]. Supramolecular block copolymers have also been investigated [111] with supramolecular joints based on either metal complexes, e.g. bis(2,2':6,2''-terpyridine)ruthenium(II), [111a] or multiple H-bonds, e.g. UPy or base pairing, [111b-e]. Corresponding micellar, tubular structures were characterized. Electrostatic binding of copolymers having complementary charged block were also described [111f].

Polycaps based on H-bonded calixarene units functionalized with urea and hosting a small guest molecule were also reported. Isotropic solutions in *o*-dichlorobenzene revealed polymer like properties, notably strong normal forces supporting the permanence of a significant DP even under a flow field [112].

Columnar stacks are exemplified by the following systems. Triphenylenes with varying substitution (Table 1, polymer 4) form columnar stacks in isotropic solution of hexadecane or heptane ($<10^{-3} M$) due to arene–arene interaction. DP was determined using small-angle neutron scattering (SANS) by Sheu et al. [106], but no data are included in their paper. From the reported association constant, a maximum DP in the bulk phase is in the order of 300 according to Eq. (7). In very diluted solutions a loose stack of the unimer along the columnar axis was reported, and no helicity was detected for a chiral triphenylene in *n*-heptane [2]. Computer simulation [113] confirms that association in isotropic solution follows the MSOA mechanisms and is modulated by concentration and temperature changes [114]. Upon increasing concentration, a liquid-crystalline phase is formed causing a large DP increase due to encroachment with the SLC mechanism. This behavior will be

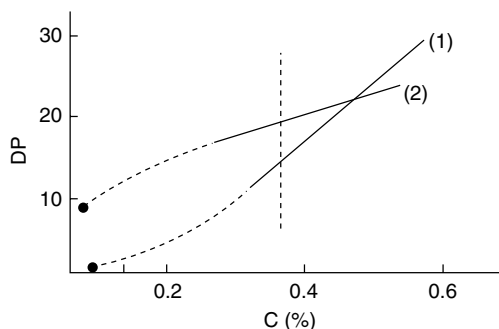


Figure 18 Variation of the number of stacked tetrameric disks (cf. Table 1, polymer 7) with folate concentration in pure H₂O (1) and 1 M NaCl (2) at 30°C. The vertical broken line indicates the I → H transition. (Plotted using data taken from G. Gottarelli, G.P. Spada, and A. Garbesi. *Crystallography of Supramolecular Compounds*. G. Tsoucaris, J.L. Atwood, and J. Lipkowski, Eds., Kluwer Academic Publishers), From A. Ciferri. *Macromol. Rapid Commun.* 23:511, 2002. Copyright Wiley_VCH 2002.

discussed in Section III.C using data for a triphenylene with polar substitution. These systems are attracting attention as molecular-scale wires endowed with charge carrier mobility that may be of use in electronic and optical devices (cf. Chapter 16).

Columnar stacks assembled by the MSOA mechanism include soluble *m*-phenylene ethynylene cycles adopting a completely flat conformation (Table 1, polymer 5). These SPs are stabilized by π – π stacking of the core and form isotropic solutions and thermotropic melts. A study by Moore and coworkers [27] clarifies the role of hydrophobic interaction and the nature of the substituent on the strength of π – π interaction and extent of association. Polar side chains such as tri(ethylene glycol) connected by an ester linkage to the macrocycle promoted solubility in a variety of solvents. Measured association constants varied from 50 to 15,000/*M*, respectively in chloroform and in acetone. In terms of Eq. (7) these values suggest corresponding theoretical DP from 10 to 120 in the undiluted phase. Solubility and association constants were affected by the polarity of the substituent and even by its linkage to the macrocycle.

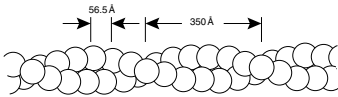
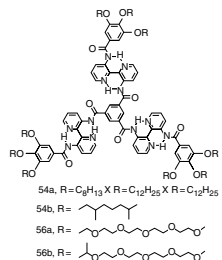
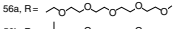
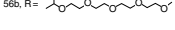
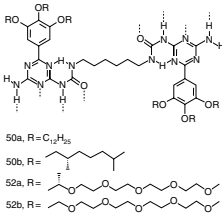
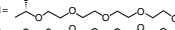
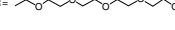
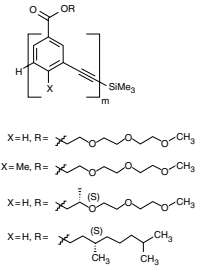
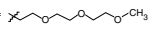
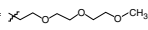
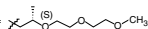
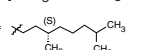
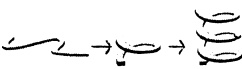
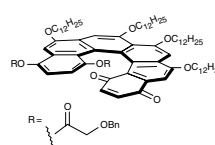
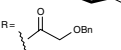
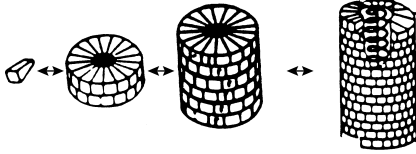
An additional example of ring-stacking motifs is based on cyclic peptides with alternating D- and L-amino acids giving rise to flat conformations stacking in nanotubes via antiparallel β -sheet H-bonding [107,115,116]. Due to their insolubility in non-H-bond breaking solvents, nanotubes were characterized in the solid state and in lipid bilayers where they formed transmembrane channels. To derive information on the assembling mechanism, Ghadiri and coworkers investigated soluble cylindrical dimers obtained by proper substitution at alternating residues. The dimer association constant for cyclo[(-L-Phe-D-^{NE}N-Ala)₄-] (Table 1, polymer 6) was 2540/*M* in chloroform (a somewhat larger value would have been expected in view of the large number of H-bonds). On the basis of this constant, we can predict values of DP in the order of 50 in the undiluted system according to Eq. (7).

The tetrameric H-bonded supermolecules of folic acid (Table 1, polymer 7) are thin disks of diameter $D \sim 30$ Å and thickness $L \sim 2.35$ Å ($L/D \sim 0.13$) forming columnar stacks of low DP. The plot in Figure 18 was constructed [3] selecting data for the stacked folate disks determined by SANS in both isotropic and liquid-crystalline aqueous solutions [33]. It is evident that no jump in the DP versus folate concentration occurs upon entering the mesophase region confirming that columnar growth is occurring by the MSOA mechanism. Contribution from excluded volume effects and the origin of mesophase will be discussed in Section III.C.

B. Helices and Helical Columns: HG

Several reports have illustrated the formation of helical SPs in isotropic solutions. Cases in which the helical structure nucleates from linear or from columnar sequences can be successfully described in terms of the HG mechanism. Table 2, polymer 8 schematizes the growth of actin F-filaments.

Table 2 Helices and Helical Columns in Isotropic Solutions (HG)

	Polymer	DP	Phase	Chirality	References
8		→ 4000	I	+	117
9	 54a, R = C₈H₁₃ X R = C₁₂H₂₅ X R = C₁₂H₂₅ 54b, R =  56a, R =  56b, R =  	→ 1000	I	+, -, !	118–121
10	 50a, R = C₁₂H₂₅ 50b, R =  52a, R =  52b, R =  	→ 100	I	+, -	2, 122
11	 X = H, R =  X = Me, R =  X = H, R =  X = H, R =  		I(A → T)	+, -, !	123, 124
12	 R =  		I(A → T)	+	125
13		→ 140	I	+	126

Notes: I: Isotropic soln, A: LC solution, T: Thermotropic melt. + = Chiral, - = Achiral, ! = Chiral amplification.

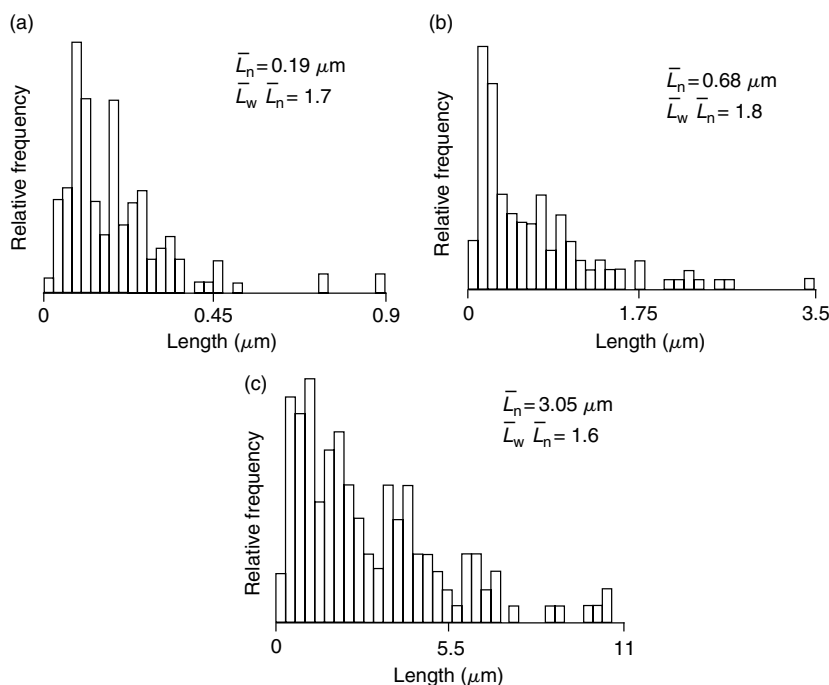


Figure 19 Length distribution determined from electron micrographs for filaments polymerized from solutions having actin/gelsolin mole ratio (a) 61:1; (b) 256:1; and (c) 2048:1. (From P.A. Janmey, J. Peetermans, K.S. Zanert, T.P. Stossel, and T. Tanaka. *J. Biol. Chem.* 261:8357, 1986. With permission.)

Verification of the theoretical HG mechanism (cf. Figure 7) was best performed on actin–ADP systems *in vitro* to avoid the complicating effect of the dephosphorylation reaction of ATP usually bound to the protein. In line with Oosawa's theory, the experimental phase diagram [117] reveals the occurrence of a critical concentration C^* at which HG begins and the concentration of unimers and oligomers attains a constant value. The double-helical structure conforms to the site distribution in Figure 6 [43,127]. In the few reports in which HG was not halted by a chain stopper (gelsolin), filaments in excess of 11 μm were reported in isotropic solutions at $C < 0.04$ mg/ml [127]. The latter value corresponds to a DP of ~ 4000 and is comparable to the persistence length of F-actin (cf. Section III.C). Note the much larger value of the critical concentration for appearance of the liquid-crystalline phase (~ 2 mg/ml) [128]. Figure 19 illustrates the length distribution of F-actin filaments polymerized at different actin/gelsolin ratios [127]. The ratio $L_w/L_n \sim 1.7$ and the theoretical exponential distribution was verified. $DP_n (= L_n/27 \text{ \AA})$ is usually close to the actin/gelsolin ratio. Sharp, Poisson type distributions can nevertheless be observed under nonequilibrium conditions in nucleation-controlled polymerization or *in vivo*. In the former case, the uniform length is controlled by the ratio nuclei/monomers and by a slow reverse (depolymerization) reaction that prevents a length redistribution [129]. In the *in vivo* case special controlling mechanisms may be involved [4].

The complexity of the growth process *in vivo* is related to a coupling between the polymerization and the $ATP \rightarrow ADP$ reaction resulting in a cycling of G unimers from one end to the other of the growing filaments [130]. As a result the polymer translates (treadmilling effect). A related dynamic instability controls the *in vivo* functioning of microtubules [131]. These effects are at the basis of molecular engines described in Chapters 21 and 22.

The disklike C_3 -symmetrical molecules synthesized by Palmans et al. [118] (Table 2, polymer 9) stack due to both arene–arene and H-bonding interaction and exemplify the stabilization of a helical structure of a columnar assembly. Side chains had either achiral or chiral character and varying polarity allowing study in either nonpolar or polar solvents. In isotropic solutions of *n*-hexane ($10^{-6} M$),

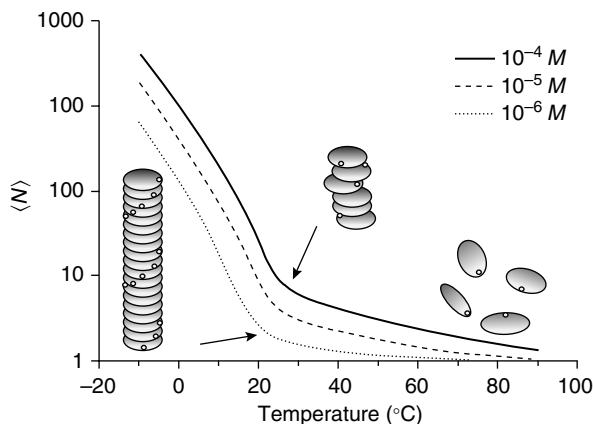


Figure 20 Helical columns: theoretical variation of the average DP ($\langle N \rangle$) of chiral C_3 symmetrical molecules (cf. Table 2, polymer 9) with temperature. Formation of achiral assemblies and transition to chiral helices occurs upon lowering T . (From J. van Gestel, P. van der Schoot, and M.A.J. Michels. *J. Phys. Chem. B* 105:10691, 2001. Copyright 2001 ACS.)

long chiral, helical assemblies with large binding constants ($10^8/M$) were detected [118]. Chirality is expected to favor helicoization but not necessarily a cooperative transition. The cooperative effect leading to helix formation was attributed to a conformational transition from flat to propeller shape of the arms of each disk, allowing a maximization of site interaction [45].

In the case of more polar homochiral C_3 molecules, studied in isotropic solutions of butanol (10^{-8} to $10^{-4} M$), the apolar core is shielded from the polar solvent by the polar side chains. These molecules showed a sequence of two assembly steps upon decreasing temperature (Figure 20). Low DP achiral stacks were stable in the $\sim 85^\circ\text{C}$ to $\sim 25^\circ\text{C}$ range, but were transformed below 25°C into large DP helical assemblies ($\text{DP} \rightarrow 1000$) with a simultaneous induction of the unimer chirality to the chirality of the whole assembly [119–121]. The chirality amplification extended to over 400 molecules before helix inversion was detected by sergeant and soldier [132] experiments. Helical order was strongly dependent upon solvent type. In water, helix inversion was detected after about 12 disks. The temperature variation of DP is reproduced in Figure 20. The theoretical lines represent the fitting of the van der Schoot and coworkers theory [45,46]. The two assembling steps may be described as the encroachment of MSOA to HG growth. Corresponding binding constants ($K < K_h$) and cooperativity parameters σ were derived from the theoretical fit. The role of boundary conditions was also discussed (cf. Section II.B.3 and Figure 8). Oosawa's theory does afford a good fitting of the data for actin (for a more detailed discussion, cf. Chapter 3).

The above results allow the definition of one important feature of the assembly of discotic molecules in isotropic solution. There seem to be conditions (controlled by temperature, concentration, and solvent type) in which contact forces are weak and loose binding of the unimers produces short columns with low DP and little or no chiral amplification. Cooperative growth ensues even though a detailed mechanism is often unclear. The critical nucleus size is not readily identified from theory (cf. Section II.B.3) but might be associated with the number of disks included in the pitch of the highly correlated helix forming when contact forces increase at low temperature.

The next case in Table 2 adds additional insight on helix formation by discotic components. Polymer 10 based on the bifunctional ureidotriazine unimer ($F = 2, S = 8$) is stabilized by quadruple H-bonds. At variance with the somewhat similar polymer 1 (Table 1), a very short spacer connects the two hydrogen-bonding terminals of each unimer. A coiling chain might be expected with H-bonded extended core discotics interconnected by the spacers. However, the arene–arene interaction should favor a columnar stacking of the disks externally connected by the spacers. In fact, SANS data for decane solutions (0.2% to 1.0%) of the achiral unimer ($R = C_{12}H_{25}$) revealed the occurrence of

cylinders with radii corresponding to the monofunctional ureidotriazine dimer and length between 100 and 190 Å (corresponding to $DP \rightarrow 100$ for a 2 Å disk thickness). The helical nature of the assembly was confirmed by the Cotton effect in decane when chiral alkyl chains were used for the R substituent. The increased correlation between unimeric disks due to the short linker favors cooperative helix formation. Simple columnar stacking was instead observed with the related monofunctional ureidotriazine units illustrated in Figure 4(d) [122].

The spontaneous formation of a columnar–helical structure based on disks interconnected by short covalent segments is significant for analogies with the new family of molecular foldamers and with complex biological assemblies. *Foldamers* are oligomeric segments able to fold into a programmed conformation in solution [133,134]. Their role is better understood in terms of the tertiary structure of proteins. The distribution of polar and apolar substituents along the polypeptide sequence does ultimately result in a globular structure with a solvophobic core and a solvophilic skin. For any specific structure, chain folds must be programmed to occur at particular locations along the sequence. Oligomeric foldamers have been studied mostly in connection with synthetic covalent sequences. However, polymers based on both supramolecular and covalent main chain sequences may also be induced to assume programmable structures, as indicated by the case of polymer 10.

An additional example of a conformationally programmed structure is offered by polymer 11 in Table 2. The unimers are short segments of *m*-phenylene ethynylene ($n = 8 \rightarrow 18$). The *m*-substitution of rigid subunits favors a change from the coiled to helical conformational for oligomers that are long enough ($n > 8$) to allow π – π stacking of aromatic rings [123]. The effect occurs in isotropic solutions of polar solvents inducing cooperative solvophobic packing of phenyl rings. Helical folding induces the simultaneous piling up of oligomers into helical SPs, evolving to lyotropic phases and hexagonal packing in the solid state [124]. The helical nature of the polymer was demonstrated by the Cotton effect revealing chiral amplification: a chiral oligomer amplified its chirality even to achiral foldamers supramolecularly following the helical pattern. The polymerization of helicenes is included in Table 2 (polymer 12) for comparison with polymer 11. Due to its fixed folded sequence, helicene is not considered a foldamer. Thus, the folding cooperative contribution is absent in the polymerization process. Its discotic shape allows the formation of liquid-crystalline phases exhibiting large DP and chiral effects [125]. However, the role of the mesophase might not be essential since nonliquid-crystalline helicenes were able to self-assemble in very diluted (0.0005 *M*) dodecane solutions [125].

Chromatin is an interesting foldameric assembly based on a sequence of discotic nucleosomes (histone protein octamers) wound up and interconnected by a long DNA superhelix (Figure 21) [135]. The final folded structure, often described by a solenoid-type model [136] is the result of histone–histone and histone–DNA interactions. The former can be studied by separating the histones from DNA either in 2 *M* NaCl or by enzymatic cleavage (the reassociation is not completely reversible [137]). Results showed that the discotic octamers formed loose stacks in isotropic solutions, eventually evolving to columnar and finally lamellar organizations [138]. The latter appears stabilized by interactions of electrostatic nature, and by nonspecific interactions in the transversal direction. The interaction by which DNA folds and wraps around the nucleosome is primarily of an electrostatic nature, as supported by the dissociation at high ionic strength. Note that the spacing between the nucleosomes (about 15 nm) is smaller than the persistence length of DNA. It is unlikely that rigid chains can wrap around spherical particles [139], and therefore strong interactions and possible local conformational alterations may be involved. A more detailed analysis of the folding mechanism and the final tertiary structure is still being investigated [140].

The last system included in Table 2, the tobacco mosaic virus (TMV), illustrates the induction of helicity in host–guest polymeric assemblies [3,126]. Columnar, helical, and helical–columnar assemblies often have a cavity in which guest molecules can be hosted. A cavity of only 6 Å diameter can host a polymer chain: for instance, stacks of α -cyclodextrin rings can host a poly(ethylene oxide) chain [141] without induction of helicity. Columnar stacks have also been observed with

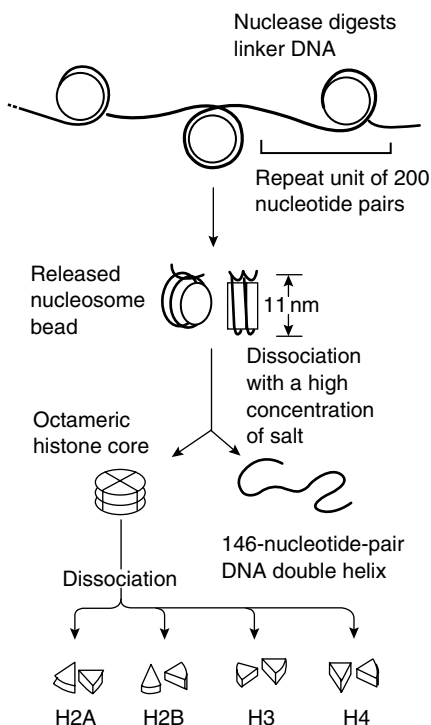


Figure 21 The chromatin assembly based on discotic supermolecules (histone octamers) linked by a DNA superhelix. (From B. Alberts, D. Bray, M. Raff, K. Roberts and J.D. Watson. *Molecular Biology of the cell*. 3rd Edition. New York: Garland Publishing 1995 page 343. With permission www.tandf.co.uk/journals)

covalent chains having dendritic side chains that self-assemble into disks [142]. No helicity is manifested by the above systems. Other known cases are those in which the polymeric guest induces helicization of tubular stacks of disks. In the case of TMV, the guest is a RNA molecule and the host is a helical-columnar assembly composed of identical tapered protein molecules. The structure can be disassembled and reassembled by pH changes in isotropic solutions with or without RNA. Without RNA, a population of dimeric disks, helical columns, and columnar stacks is observed, each disk comprising 17 protein units. However, the native helical structure based on 2310 proteins and 16.3 units per turn is reassembled when RNA is present. The complex role of RNA for the whole structure is evident. RNA acts like a crankshaft that stabilizes the proteins bound to it into a helical pattern and simultaneously provides the information for the proper length and DP of the host. The assembly mechanism of the overall TMV structure can thus be described in terms of a supramolecular polymerization of the external columnar assembly, coupled to the formation of monofunctional side chain bonds between host and guest [3]. A quantitative approach along the above lines was recently reported by van der Schoot and coworkers [14] for the spherical capsid of the hepatitis B virus.

C. Liquid Crystallinity in Supramolecular Polymers

Following the emphasis on the assembling power of the open SLC (Figure 14(c), [5,143]) several authors [2,144,145] have suggested an enhancement of growth associated with the formation of a mesophase for a large variety of SPs. It is therefore essential to critically distinguish cases in which growth is effectively coupled to orientation from cases in which the supramolecular polymerization is uncoupled to the occurrence of liquid crystallinity [89]. There is a need for more studies of the open SLC and several aspects of its theoretical mechanism have not yet been clarified.

1. Liquid Crystallinity for Molecular and Closed SPs

The closed SLC is exemplified in Figure 14(b) by a class B system when sites are internally compensated and no further growth accompanies the formation of the mesophase. The behavior of the closed SLC is thus indistinguishable from that of a molecular LC (Figure 14(a)). Relevant cases are DNA [146], adequately described by the theory of the molecular LC (Section II.C.2), and poly(*p*-benzamide) (PBA) in *N,N*-dimethylacetamide/LiCl solutions. An assembly of seven PBA molecules with a side-by-side shift of one fourth the molecular length was detected in both isotropic and lyotropic solutions. Even the axial ratio of the assembly (~ 104) was undistinguishable from the axial ratio (~ 100) of molecularly dispersed PBA [147].

2. Liquid Crystallinity Uncoupled to Growth

If strong growth, in isotropic solutions has produced at $C < C^i$ a wormlike chain with length comparable or exceeding the persistence length, no sudden growth due to the open SLC occurs at the critical concentration even though growth continues at $C > C^i$ driven by the MSOA or HG mechanism. In the case of actin (Table 2, polymer 8) the lowest critical concentration for appearance of the mesophase reported by Furukawa et al. [128] was ~ 2 mg/ml for a gelsolin terminated filament having DP ~ 1780 corresponding to a length of $\sim 5 \mu\text{m}$. Janmey et al. [127] were however able to grow filaments with a larger length at concentration of ~ 0.04 mg/ml suggesting that actin grows to a length comparable to the persistence length in isotropic solutions ($C^* < C^i$).

Figure 22 illustrates dynamic association–dissociation cycles of α - and β -tubulin into microtubules growing to a size visible under the polarizing microscope. The data by Hitt et al. [148] suggest a synchronous occurrence of growth and liquid crystallinity. The polymerization $\rightarrow$ depolymerization cycles are modulated by the reversible $\text{GTP} \leftrightarrow \text{GDP}$ reaction that uncovers sites on β -tubulin (cf. Chapter 21). A direct coupling between growth and alignment cannot be confirmed by these data (and similar cases in the literature) since the tubulin concentration (15 mg/ml) was larger than either the critical concentration at which the helix nucleates or the mesophase appears.

In the case of actin, and other systems characterized by strong binding constants, growth and mesophase are “uncoupled” but “hierarchically related” since liquid crystallinity arises as a consequence of a preassembling step in isotropic solution. Cases of growth totally uncoupled to liquid crystallinity have also been reported. One example is the tetrameric H-bonded supermolecule of folic

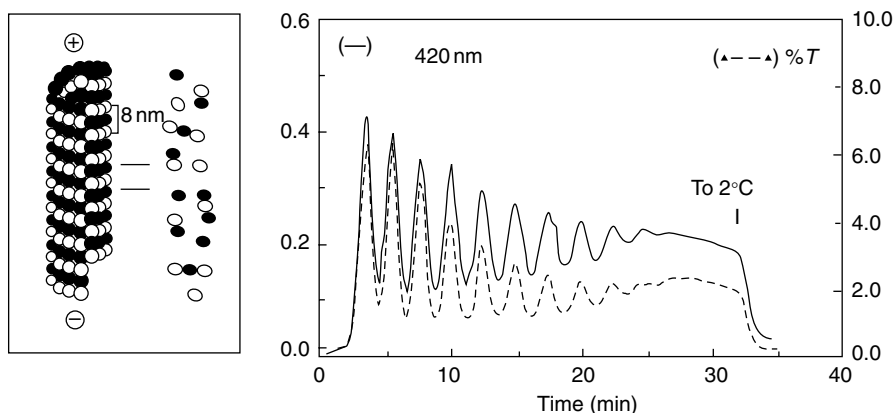


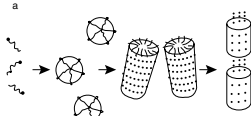
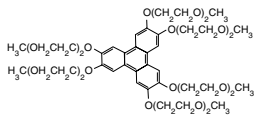
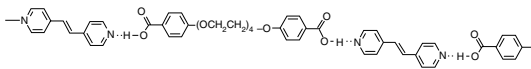
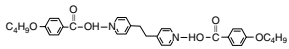
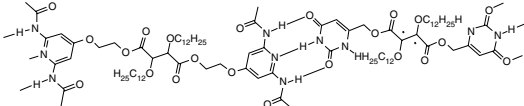
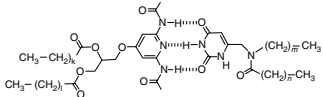
Figure 22 Dynamic assembly and disassembling of microtubules. Time variation of turbidity (right) and birefringence (left) at 420 nm for solutions of tubulin (15 mg/ml) in pH 6.9 buffer + 12 mM MgSO_4 + 2 mM GPT. Measurements at 37°C followed by quenching at 2°C . (From A.L. Hitt, A.R. Cross, and C.R. Williams Jr. *J. Biol. Chem.* 265:1639, 1990. With permission.)

acid (Table 1, polymer 7) for which the DP was determined by SANS. A continuous decrease of the number of stacked tetramers with concentration, undisturbed by the occurrence of the mesophase, is evidenced by the data collected in Figure 18. The intensity of contact forces or rigidity do not allow cooperative growth due to either the SLC or the HG mechanism. The occurrence of the mesophase can therefore be attributed to the large excluded volume of disks (cf. Figure 15). Similar behavior was reported by Ben-Shaul and Gelbart [149].

3. Liquid Crystallinity Coupled to Growth

Verification of the open SLC model is based on a sudden increase of polymerization when the nematic phase appears (Figure 16). Data regarding the rigidity (persistence length) of the assembly are desirable. Systems for which growth-coupled-to-orientation was adequately documented are described below [85,150–152,156]. In the case of micelles (Table 3, polymer 14), Odijk [85] has critically

Table 3 SPs in Lyotropic and Thermotropic Phases

	Polymer/complex	DP	Phase	References
14		→ 1000	A	84
15		→ —	A	152
16		→ 20 ^a	T	88
17		—	T	88
18		→ 100 ^a	T	153,154
19		—	T	155

Notes: A: LC solution, T: Thermotropic melt.

^a Theoretical in bulk.