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## Supramolecular Polymers: General Considerations\*

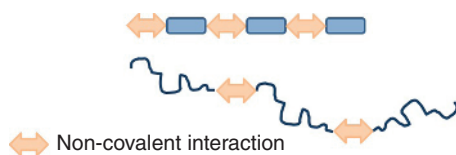
### 1.1 Introduction

In 1920, Staudinger proposed that polymers are indeed long chains built from repeating molecular subunits (the so-called monomer), which are linked by covalent bonds [1]. Only a few years later, Carothers developed a classification of macromolecules taking into account both types of compounds that one can polymerize and the polymerization techniques themselves [2]. About 80 years later, this classification is still contemporary and widely utilized to explain the differences between macromolecules made via different polymerization mechanisms (e.g. step-/chain-growth or ring-opening polymerization [ROP]). A broad range of polymers has been prepared over the last few decades, generally following these three basic mechanisms. More recently, the actual controlled/living techniques have widened the synthetic toolbox, but nevertheless, these metathesis, ionic, and radical polymerizations obey Carothers' taxonomy.

The interactions of macromolecules on the molecular level give rise to the materials' properties on the macroscopic scale. Such secondary or non-covalent interactions, commonly referred to as supramolecular interactions, are responsible for the programmed function of natural (e.g. DNA and enzymes) as well as synthetic polymers [3–20]. Moreover, the emerging field of supramolecular chemistry gave answers to the question if covalently linked macromolecules are necessarily required to generate polymeric materials. Considering a supramolecular polymer, i.e. a polymer whose monomeric building blocks are connected by directional and reversible non-covalent bonds, the field of polymer chemistry is no longer limited to conventional (i.e. covalent) macromolecules. The self-assembly of appropriate monomers via moderately strong, reversible, and highly directional non-covalent interactions into linear polymers of high molar mass is known as supramolecular polymerization.

The field of supramolecular chemistry was pioneered by Cram, Pedersen, and Lehn, who received the Nobel prize in chemistry in 1987 for their fundamental

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**Figure 1.1** Schematic representation of a polymer based on non-covalent interactions.

and groundbreaking studies in this respect. Today, supramolecular chemistry also deals with the formation of larger entities that are beyond the classical molecular covalent chemistry but still involve intermolecular non-covalent interactions [21–23]. Several types of weak interactions are known that can keep the whole assembly together: metal-to-ligand coordination, hydrogen-bonding (H-bonding), halogen-bonding (X-bonding), ionic interactions,  $\pi$ – $\pi$ -stacking interactions, and host–guest complexation. In principle, two different types of these assemblies can be distinguished: (i) supermolecules, which are well-defined oligomeric structures and (ii) polymolecular assemblies, which consist of a large number of monomeric species. The latter could be covalent molecules, even macromolecules [24]. Therefore, it is apparently difficult to precisely define supramolecular polymers. If the only criterion is that a supramolecular polymer “consists of non-covalently linked monomers,” polymeric micelles, even a simple crystal formed by an organic compound, would already be a “supramolecular polymer” [25]. In contrast, Meijer and coworkers coined a new definition [26, 27]: “Supramolecular polymers are defined as polymeric arrays of monomeric units that are brought together by reversible and highly directional secondary interactions, resulting in polymeric properties in dilute and concentrated solution as well as in the bulk. The directionality and strength of the supramolecular bonding are important features of systems that can be regarded as polymers and that behave according to well-established theories of polymer physics.”

In simple terms, a long sequence of units (i.e. monomers or polymers) connected by secondary (non-covalent) interactions can be considered as a supramolecular polymer when the overall (macromolecular) structure can also exist in solution or in the melt (Figure 1.1) [28]. The covalent counterparts of the depicted supramolecular polymers are macromolecules, which are formed by polyaddition and polycondensation reactions, respectively.

## 1.2 Classification Schemes

According to Meijer and coworkers, three main different aspects have to be considered when classifying supramolecular polymers [27]: first, the physical nature of the non-covalent interaction (i.e. the origin/type of the reversible interaction, “physical origin classification”), the type of molecular component or monomers utilized (“structural monomer classification”), and, finally, the Gibbs free energy of the polymer expressed as a function of the monomer conversion (“thermodynamic classification”). It has been under discussion if even a fourth classification scheme can be applied taking into account the dimensionality of the resultant assembly. However,

**Table 1.1** The strength and directionality of non-covalent interactions.

Type of non-covalent interaction	Strength (kJ mol <sup>-1</sup> )	Directionality
van der Waals interactions	1–5	Low
Charge–transfer interactions	7–20	Medium
Hydrogen-bonding interactions	10–20	High
Hydrophobic–hydrophilic interaction	12–15	Low
Ion-pairing interactions	12–20	Medium
Metal-to-ligand coordination	40–120	High
Covalent bond	150–1000	High

Source: Friese and Kurth [38]. © 2009 Elsevier.

it needs to be emphasized that the addition of a second (or even third) dimension is expected to introduce additional interaction energies which, in turn, will have a considerable influence on the Gibbs free energy ( $\Delta G^0$ ) of the supramolecular materials [26]. Thus, the understanding of how changes in certain parameters, such as concentration and/or temperature, impact the 3D structure of the material is no longer straightforward.

However, supramolecular polymers are typically classified according to the nature of the non-covalent interaction(s) on whose basis they have been assembled from, thus taking into account the main chemical driving force for the formation of large assemblies [26]; several reviews have dealt with these types of materials [29–37]. Non-covalent interactions are intrinsically much weaker (i.e. ranging from c. 1 to 120 kJ mol<sup>-1</sup>), in particular when compared to the strong covalent bonds (150–1000 kJ mol<sup>-1</sup>). Table 1.1 summarizes the strength of the different interactions, ranging from rather weak (van der Waals and charge–transfer) through medium (H-bonding, hydrophobic–hydrophilic, and ion-pairing interactions) to strong (metal-to-ligand coordination). Accordingly, one can correlate the strength of the supramolecular interaction(s) to the virtual molar mass and, thereby, to the degree of polymerization (DP, *vide infra*).

As a result, from their comparably low strength and non-covalent character, most of these interactions feature a certain degree of reversibility. In other words, the monomeric units of a supramolecular polymer can readily be assembled and disassembled resulting in new, interesting properties and potential applications that are not (or only hardly) accessible for covalent polymers. Utilizing all of these different types of non-covalent interactions allows one to assemble “tailor-made” supramolecular polymers, which reveal the key property, i.e. reversibility of binding [29].

Moreover, with respect to the synthesis of any type of supramolecular polymer, the directionality of the utilized non-covalent bond is of utmost relevance. In classical polymers, the covalent bonds with their perfect directionality represent the linkage of two monomeric units. On the contrary, supramolecular polymers often rely on interactions, which feature a much lower degree of directionality (e.g. ion-pairing

or charge–transfer interactions). Only hydrogen-bonding interactions, certain types of metal-to-ligand coordination, and host–guest inclusion complexes offer very high directionalities, which are comparable to those of conventional covalent bonds. In summary, the directionality and strength of the non-covalent interactions represent crucial parameters when dealing with (linear) supramolecular polymers.

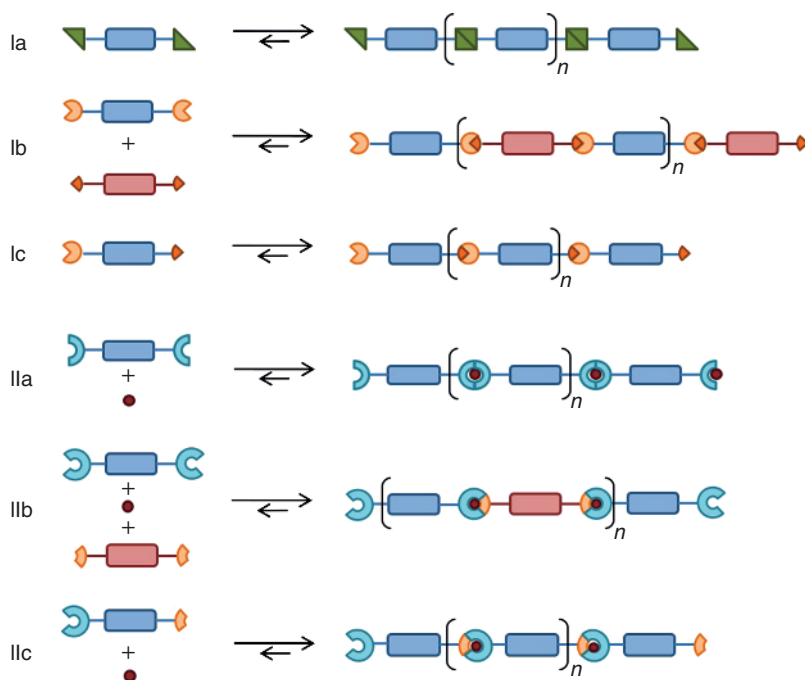
Taking the aforementioned “structural monomer classification” scheme, one can distinguish between two cases: first, a single molecular component is equipped with supramolecular binding site of either a self-complementary or a complementary nature. For instance, the reversible association into an  $A_2$ -system in solution is based on the self-complementary **A:A** interactions (accordingly, an **A–B**-type system is formed by reversible complementary **A:B** interactions). Second, the two different homoditopic monomers **A–A** and **B–B** may exhibit only one type of interaction; in this case, the supramolecular polymerization process is driven solely by the complementary interactions between **A** and **B**.

Finally, the classification of supramolecular polymerizations according to their thermodynamics has to be considered: for supramolecular polymers,  $\Delta G^0$  can be expressed as a function of the monomer conversion from zero ( $p = 0$ ) to full conversion ( $p = 1$ ). Here, the particular mechanism by which a supramolecular polymer is formed from monomeric components has to be considered (this process is dependent on various parameters, e.g. concentration, solvent, and temperature).

### 1.3 Supramolecular Polymerization Mechanisms

The conventional polycondensation and polyaddition reactions require monomers with (at least) two functional groups by which the covalent bonds are formed. Considering linear polymers, either a single type of monomer bearing two different functionalities (the so-called AB-type monomer) or two different monomers each equipped with two functionalities of the same kind (the so-called homoditopic AA- and BB-type monomers) can basically be employed in this context. Accordingly, supramolecular polymers can be formed by the polyassociation of monomers, which possess (at least) two appropriate binding sites to undergo non-covalent interactions (Figure 1.2) [39]. As for their covalent counterparts, AB-type monomers (e.g. Ic) as well as pairs of AA- and BB-type monomers (Ib) can be utilized for this purpose. In principle, one can further distinguish between two different monomer classes: directly interacting monomers (Ia–c) and those that are connected via metal ions (IIa–c). Supramolecular polymerizations according to type-I typically involve hydrogen-bonding or ionic interactions as well as host–guest complexation (however, ionic interactions can also be involved in type-II polymers where coordinative interactions are involved). The self-complementary monomers (e.g. Ia and IIa) give supramolecular polymers with only a single type of monomeric unit. Accordingly, complementary binding units can be employed to assemble homopolymers (i.e. Ic and IIc) as well as alternating copolymers (i.e. IIb and IIc).

In general, the formation of polymers, via a polycondensation or polyaddition, represents a kinetically controlled process [26]: the potential barrier for the forward

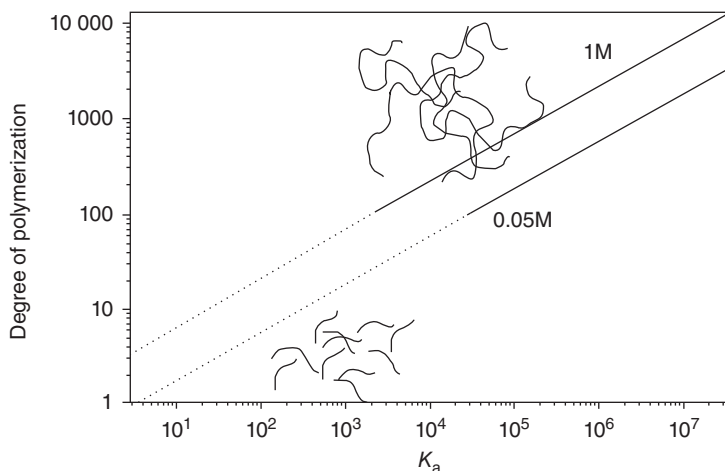


**Figure 1.2** Schematic representation of the different types of supramolecular polymerization. Source: Winter et al. [39]. © 2012 Elsevier B.V.

reaction (i.e. the polymerization) is much lower than for the backward reaction (i.e. depolymerization). As a consequence, neither changes in concentration (i.e. dilution) nor temperature (i.e. heating) will affect the molar mass or the degree of conversion. In supramolecular polymerizations, the situation is much more complicated – due to the (partially) reversible character, depolymerization must be considered. Thus, heating or dilution of a kinetically unstable supramolecular polymer will have a tremendous effect with respect to the molar mass – unlike for a common macromolecule, a decrease of  $M_n$  will be the result. According to Carothers' equation (Eq. (1.1)), the molar mass of polymers, which have been prepared by either a polyaddition or a polycondensation, can be correlated to the monomer conversion. However, for supramolecular polymers, featuring a certain degree of reversibility of the non-covalent interactions, the molar mass will mainly depend on the strength of these interactions, i.e. their association constants ( $K_a$  values). As depicted in Figure 1.3, both high  $K_a$  values and high monomer concentrations are required to obtain the supramolecular polymers with high DPs. Besides these considerations, other parameters, such as concentration, temperature, and the particular reaction conditions (i.e. presence of additives or reagents, etc.), will also have an impact on the entire assembly process.

$$DP = 1/(1 - p) \quad (1.1)$$

where DP: degree of polymerization,  $p$ : monomer conversion.



**Figure 1.3** Representation of the theoretical DP as a function of the association constant ( $K_a$  in  $M^{-1}$ ) for a typical supramolecular polymerization according to an isodesmic model at two different concentrations. Source: Brunsveld et al. [27]. © 2001 American Chemical Society.

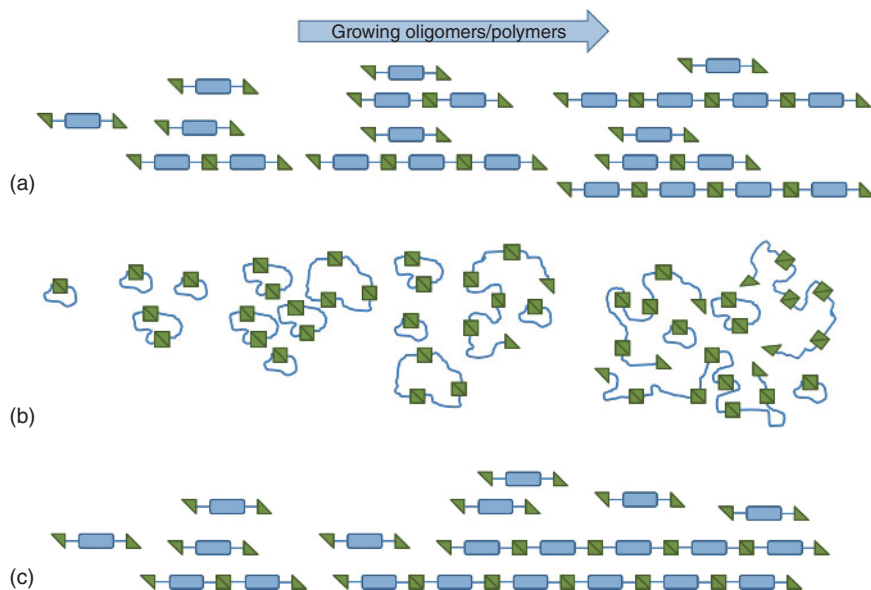
This assumption, however, represents only a simplification of the actual mechanism of a supramolecular polymerization – even when only considering the thermodynamic equilibrium state, where assemblies are formed that, ideally, retain their polymeric structure over time. In this respect, three main mechanisms can be listed (Figure 1.4) [26]:

1. The isodesmic supramolecular polymerization (IDP) is comparable to the step-growth polymerization of esters (i.e. showing a broad dispersity,  $\bar{D}$ ) and the DP is strongly dependent on the  $K_a$  value of underlying supramolecular interaction.
2. The ring-chain-mediated supramolecular polymerization features an equilibrium between supramolecular cyclic species and linear polymer chains.
3. The cooperative supramolecular polymerization shows a nonlinear growth of the polymer chains and is typically nucleated.

Going beyond the “traditional” equilibrium state, supramolecular polymerizations leading to assemblies in either dissipative nonequilibrium or even non-dissipative nonequilibrium states (i.e. kinetically trapped or metastable ones) have recently attracted substantial interest. In these cases, the progress of the polymerization is heavily dependent on the applied preparative method (the so-called pathway selection), and an in-depth knowledge of the kinetics is required. In particular, the association rates for each single step become more important. These issues have recently been discussed by Sorrenti et al. in a tutorial review [40].

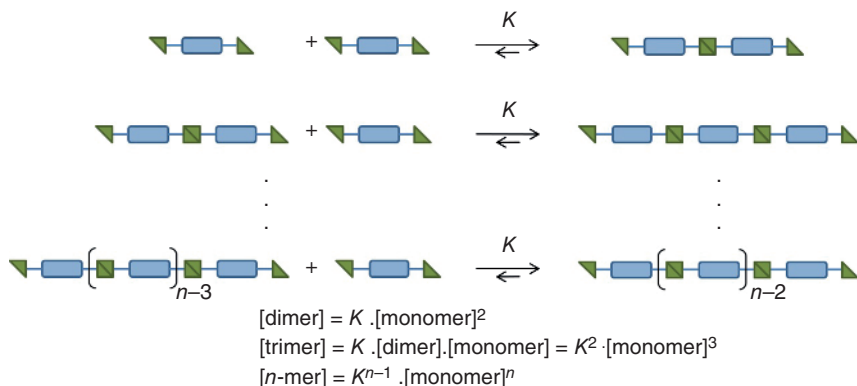
### 1.3.1 Isodesmic Supramolecular Polymerization

The isodesmic supramolecular polymerization (IDP, *isos*: equal, *desmos*: bond), also often referred to as the “multi-stage open association” mechanism [28, 41, 42],

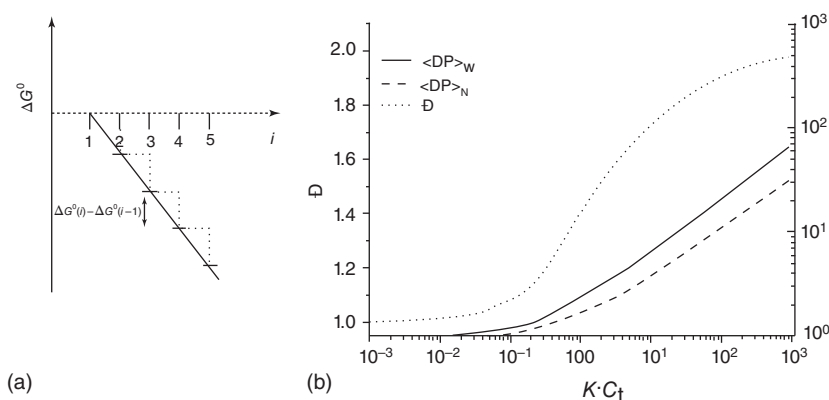


**Figure 1.4** Schematic representation of the three main mechanisms known for the supramolecular polymerization processes: (a) isodesmic, (b) ring-chain mediated, and (c) cooperative supramolecular polymerization. Source: Winter et al. [39]. © 2012 Elsevier B.V.

involves the formation of one type of reversible, non-covalent interaction between monomers, oligomers, and eventually even polymer chains (Figure 1.5). All supramolecular bonds, which are formed throughout the entire process, are considered to be identical, and thus, the reactivity of all species present is considered to have the same reactivity (i.e. monomers, oligomers, and polymers). Thereby, the neighboring group effects or additional interactions with non-adjacent sites are neglected. Each single step of the process is characterized by the intermolecular



**Figure 1.5** Schematic representation of the IDP in which the intermolecular equilibrium constant ( $K$ ) is independent of the length of the assembly (the mechanism is shown for a bifunctional monomer of the Ia-type, see also Figure 1.2). Source: Winter et al. [39]. © 2012 Elsevier B.V.



**Figure 1.6** (a) Schematic drawing of an energy diagram for an IDP ( $i$ : size of the oligomer,  $\Delta G^0$ : free energy in arbitrary units). (b) Evolution of the number- and weight-averaged DP ( $\langle DP \rangle_N$  and  $\langle DP \rangle_W$ ) and the dispersity ( $\bar{D}$ ) as a function of equilibrium constant and total concentration of monomer ( $K \cdot c_t$ ). Source: de Greef et al. [26]. © 2009 American Chemical Society.

equilibrium constant  $K$  (Figure 1.5) – regardless of the chain length. As a result, from the equivalence of each individual polymerization step, IDPs do not exhibit any critical values for the concentration or temperature of the supramolecular polymerization (cpc: critical polymerization concentration, cpt: critical polymerization temperature) [41, 43]. Unlike for the ring-chain-mediated polymerization (*vide supra*), no cyclic species can be found during the self-assembly process. The counterpart to IDP in “traditional” polymer science is the step-by-step reversible polycondensation where intramolecular cyclizations are absent and Flory’s “principle of equal reactivity” is obeyed [44, 45]. Detailed investigations have shown that, for example, the polycondensation of decanedioyl chloride with 1,10-decamethylene glycol in dioxane meets these requirements [46].

According to the rules of thermodynamics, the free energy of the system constantly decreases when the monomeric units are successively added to the growing polymer chain; this, in turn, further supports the assumption that binding of a monomer to the terminus of a polymer chain is independent of its length (an idealized energy diagram, in which kinetic barriers within the self-assembly process are neglected, is depicted in Figure 1.6a) [26].

The number- and weight-averaged DPs (i.e.  $\langle DP \rangle_N$  and  $\langle DP \rangle_W$ , respectively) can be derived from the monomer concentration and equilibrium constant  $K$  according to Eq. (1.2) (though only valid for  $K \cdot [\text{monomer}] < 1$ ) [43]. In the ideal case,  $\bar{D}$  converges to the limiting value of 2.0, and thus, the monomer concentration approaches  $1/K$  (Eq. (1.2)); this scenario is comparable to a standard step-growth polymerization as known from traditional polymer chemistry [27, 33]. The correlation of these parameters with the dimensionless concentration  $K \cdot c_t$ , where  $K$  represents the equilibrium constant and  $c_t$  the total monomer concentration, is shown in Figure 1.6b. Apparently, high DPs can only be reached for high  $K \cdot c_t$  values; thus, high monomer concentrations and high  $K$  values are both required.



Disadvantageously, the intrinsically poor solubility of monomers often excludes high concentrations, and thus, the equilibrium constants must be very high ( $K > 10^6$ ) to compensate for this when aiming for supramolecular polymers with high molar masses. As a typical feature of IDP-type processes, increasing  $c_i$  automatically leads to a gradual and simultaneous increase of the concentration of monomers and polymer chains; thus, the monomer and polymer chains of various length coexist in solution. Finally, the equilibrium concentration of monomers converges to its maximum value, corresponding to  $K^{-1}$ , when increasing the concentration further. Thereby, the monomer remains the most abundant species in solution, independent of the values of  $K$  and  $c_i$ . As for their covalent counterparts, the precise stoichiometry of the functional groups in an IDP represents a prerequisite to obtain polymers with high molar masses: self-complementary AB-type monomers inherently bear the ideal stoichiometry, whereas complementary monomers (i.e. using a combination of AA and BB) require an exact 1 : 1 ratio. Moreover, the molar masses of the resultant polymers can be adjusted by the addition of appropriate chain-stopping agents [47–49].

$$\begin{aligned} \langle DP \rangle_N &= \frac{1}{1 - K \cdot [\text{monomer}]} \langle DP \rangle_w = \frac{1 + K \cdot [\text{monomer}]}{1 - K \cdot [\text{monomer}]} \mathcal{D} \\ &= 1 + K \cdot [\text{monomer}] \end{aligned} \quad (1.2)$$

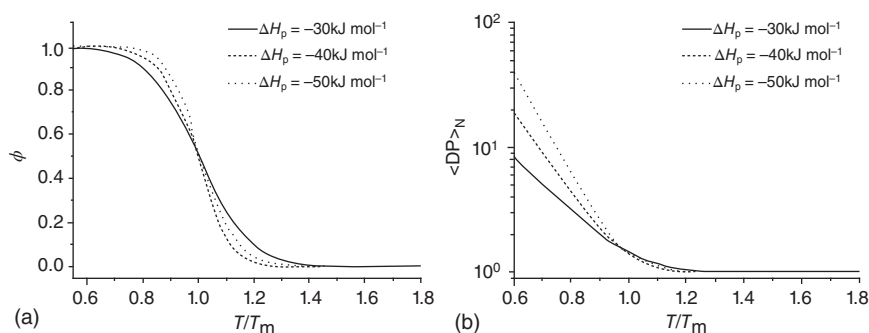
where  $\langle DP \rangle_N$ : number-averaged DP,  $\langle DP \rangle_w$ : weight-averaged DP,  $\mathcal{D}$ : dispersity,  $K$ : equilibrium constant,  $[\text{monomer}]$ : monomer concentration.

Besides the concentration dependency, the influence of the temperature on the IDP also needs to be addressed. Basically, any type of supramolecular polymerization using a bifunctional monomer represents the polymerization of monomers by equilibrium bond formation and features an ideal polymerization temperature ( $T_p^0$ ) [50–54]. The Dainton–Ivin equation, initially introduced to describe the thermodynamics of ROP and polyaddition reactions, correlates the enthalpy and entropy of propagation ( $\Delta H_{pr}$  and  $\Delta S_{pr}$ ) as well as the initial monomer mole fraction to  $T_p^0$  (Eq. (1.3)) [55, 56]. There are two fundamental cases that one must distinguish:

1. The polymerization only occurs at a temperature so high that the entropy term exceeds the enthalpy term and the system exhibits a floor temperature ( $\Delta H_{pr}$ ,  $\Delta S_{pr} > 0$ ).
2. The polymerization represents an enthalpically driven process, which is only allowed below a certain ceiling temperature ( $\Delta H_{pr}$ ,  $\Delta S_{pr} < 0$ ).

The so-called polymerization transition line, separating monomer-rich phases from polymer-rich ones, can be constructed by plotting  $[M_i]$  vs. the polymerization temperature, which can be determined experimentally. However, this model is only valid in those cases where a sharp monomer-to-polymer transition can be found (in general, applicable only for ring-opening, living, or cooperative polymerizations) [50]. For most of the reported IDPs, this transition is, however, very broad and the two phases rather coexist. Thus, for such a supramolecular polymerization, the polymerization transition line as a boundary appears less appropriate.

$$T_p^0 = \Delta H_{pr} / \Delta S_{pr} + R \cdot \ln [M_i] \quad (1.3)$$

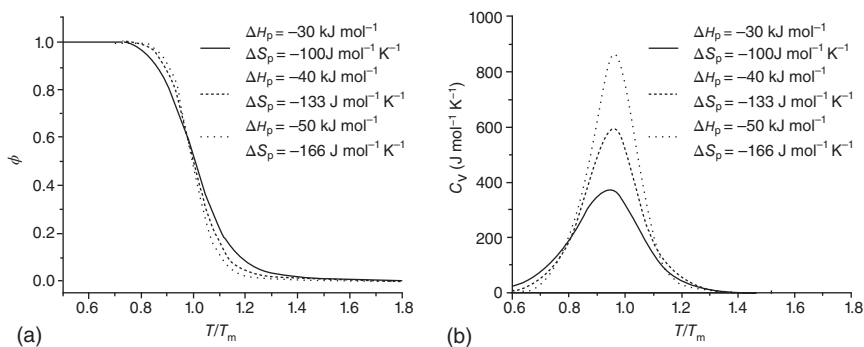


**Figure 1.7** Illustration of the characteristic properties of a temperature-dependent IDP according to van der Schoot's model: (a) fraction of polymerized material ( $\phi$ ) vs. the dimensionless temperature  $T/T_m$ ; (b)  $\langle DP \rangle_N$  vs.  $T/T_m$ . In both plots, the curves obtained for different enthalpies are shown ( $\Delta H_p = -30$ ,  $-40$ , and  $-50 \text{ kJ mol}^{-1}$ , respectively). Source: van der Schoot et al. [57]. © 2005 Taylor & Francis.

where  $T_p^0$ : ideal polymerization temperature,  $\Delta H_{pr}$ : enthalpy of propagation,  $\Delta S_{pr}$ : entropy of propagation,  $R$ : gas constant,  $[M_i]$ : initial mole fraction of a monomer.

Historically, the temperature dependency in isodesmic self-assembly processes has been explained by means of statistical mechanics [52]. More recently, mean-field models that are free of restrictions concerning the actual mechanism of chain have been applied for the same purpose. In such models, the chain growth can occur by either the addition of a single monomer or the linkage of two existing chains. van der Schoot proposed a model, where the temperature-dependent melting temperature ( $T_m$ ; in essence, the temperature at which the monomer mole fraction in the supramolecular polymer is 0.5) and the temperature-independent polymerization enthalpy ( $\Delta H_p$ ) were considered [57]. As one example, a system that polymerizes upon cooling is analysed by plotting the fraction of the already polymerized material ( $\phi$ ) against  $T/T_m$  for various  $\Delta H_p$  values; (Figure 1.7a) in such an IDP, the steepness of the transitions of the curves only depends on  $\Delta H_p$  and contributions arising from cooperativity effects can be excluded. Moreover, a gradual increase of  $\langle DP \rangle_N$  with decreasing temperature can typically be observed (Figure 1.7b).

Dudovich et al. introduced an alternative approach, commonly referred to as the “free association model,” which is based on a mean-field incompressible lattice model derived from the Flory–Huggins theory (for the Flory–Huggins model, see [58, 59]). In this approach, the flexibility of the polymer chains and the van der Waals interactions between the monomer and solvent molecules (quantified by the parameter  $\chi$ ) are taken into account [50, 51]. A variety of temperature-dependent properties can be calculated from the lattice model (e.g.  $\langle DP \rangle_N$  and the specific heat at constant volume  $[C_v]$ ). It has been shown that neither of these (as well as the  $\bar{D}$  value) is sensitive to  $\chi$  when the temperature is changed; however, the situation is different if the  $\chi$  value for the polymer–solvent interaction is different from the one for the monomer–solvent interaction [50]. On the other hand, a variety of thermodynamic properties do show a strong temperature dependency of  $\chi$ ; these include the osmotic pressure and the critical temperature at which phase



**Figure 1.8** Illustration of the characteristic properties of a temperature-dependent IDP according to the “free association” model: (a) fraction of polymerized monomers ( $\phi$ ) vs.  $T/T_m$  (assuming fully flexible polymer chains and a cubic lattice); (b) heat capacity at constant volume ( $C_v$ ) vs.  $T/T_m$ . In both plots, the curves obtained for various enthalpy ( $\Delta H_p = -30$ ,  $-40$ , and  $-50 \text{ kJ mol}^{-1}$ , respectively) and entropy values ( $\Delta S_p = -100$ ,  $-133$ , and  $-166 \text{ J mol}^{-1} \text{ K}^{-1}$ , respectively) are shown; in all cases, the initial volume fraction of the monomers has been set to 0.1. Source: Modified from Dudowicz et al. [50]; Douglas et al. [51].

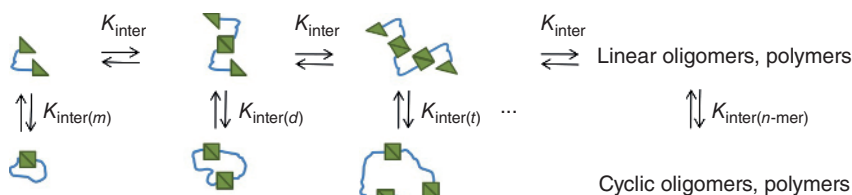
separation between monomer and solvent occurs. Two free energy parameters describe the reversibility of the supramolecular polymerization: the polymerization enthalpy ( $\Delta H_p$ ) and entropy ( $\Delta S_p$ ), which are both temperature independent. Representatively, the fraction of polymerized monomers ( $\phi$ ), as a function of the dimensionless temperature  $T/T_m$ , for a system that reversibly polymerizes upon cooling, is shown in Figure 1.8a [51]. In accordance with van der Schoot’s model (*vide supra*), the curve is of sigmoidal shape and, with the values of  $\Delta H_p$  and  $\Delta S_p$  becoming more negative, the steepness of the curve becomes more pronounced. For fixed monomer concentrations, the  $C_v$  vs.  $T/T_m$  plots show broad and highly symmetric transition (Figure 1.8b). This feature is indicative of an IDP in which the equilibrium constant  $K$  for the addition of each monomer to the growing polymer chain has always the same value. On the other hand, the temperature dependency of  $C_v$  in ring-chain or cooperative supramolecular polymerizations shows a much sharper transition (see also Sections 1.3.2 and 1.3.3).

In the field of supramolecular polymers, independent of the nature of the involved non-covalent linkage, their formation via IDP is by far the most common mechanism. Many examples involving hydrogen-bonding (Chapter 3) or host–guest interactions (e.g. by crown ether or calixarene recognition; Chapters 6–10) as well as metal-to-ligand coordination (Chapter 4) are discussed there. It has to be pointed out that the determination of the molar mass of all these supramolecular polymers is generally nontrivial, since the established direct analytical methods commonly used for traditional, i.e. covalent, macromolecules (e.g. size-exclusion chromatography [SEC] or mass spectrometry) can often not be applied due to the weak nature of the supramolecular bonds: already small changes in temperature, solvent composition, and concentration might lead to significant changes of the DP [60, 61]. However, several spectroscopic techniques (e.g. nuclear magnetic resonance (NMR)

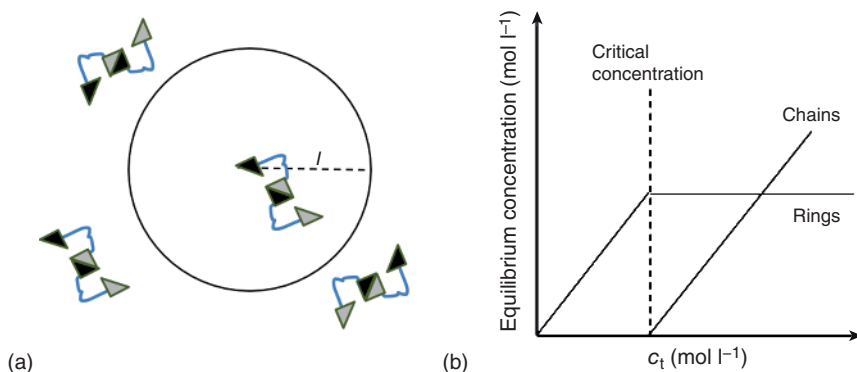
or UV/vis absorption), calorimetry, and analytical ultracentrifugation (AUC) can be applied in many cases to determine the molar masses [33, 36, 37]. A summary of the scope and limitations in characterizing supramolecular polymers is given separately in Chapter 12.

### 1.3.2 Ring-Chain-Mediated Supramolecular Polymerization

The so-called ring-chain-mediated supramolecular polymerization represents the second main mechanism to describe the growth of supramolecular polymer chains (Figure 1.4b). In general, a heteroditopic monomer is polymerized reversibly; this monomer as well as its oligomers and, eventually, polymer chains feature an equilibrium between a linear and a cyclic species (Figure 1.9). Ring formation occurs via the intramolecular reaction of the end groups, whereas intermolecular reactions will accordingly give longer chains. Flexibility of the monomer represents, thus, a prerequisite for this type of mechanism; for instance, flexible alkyl or even polymer chains can be used to link the terminal supramolecular binding sites of such a monomer [62]. It is generally accepted that the covalent step-growth polymerization of such monomers typically gives some wt% of macrocyclic oligomers (thereby, the polymerization can be performed under kinetic or thermodynamic control) [44, 63, 64]. Representatively, two classic cases in which also macrocyclic species are formed shall be named briefly: the bulk polymerization of triethylene glycol with hexamethylene-diisocyanate (polycondensation under kinetic control) [65] and, as an example for a thermodynamically controlled process, the catalyzed equilibrium polymerization of  $\alpha,\omega$ -disubstituted siloxanes (in particular, the later system was widely investigated by Scott [66], Brown and Slusarczuk [67], Carmichael and Winger [68], as well as Flory and Semlyen [69]). The entropically driven ring-opening metathesis polymerization (ROMP) of cyclic olefins [70] and the ring-chain polymerization of liquid sulfur [71–73] are further representatives for covalent ring-chain polymerizations under thermodynamic control. As a general characteristic for a step-growth polymer, the reversibility of bond formation establishes an equilibrium between macrocyclic and linear species. With respect to supramolecular polymers, where the formation/cleavage



**Figure 1.9** Schematic representation of the generalized mechanism of a ring-chain-mediated supramolecular polymerization. The intermolecular binding constants ( $K_{\text{inter}}$ ) are related to the intermolecular association of molecules, whereas the intramolecular binding constant  $K_{\text{intra}(n\text{-mer})}$  is assigned to the ring closure of monomers, oligomers, and polymers. Source: Winter et al. [39]. © 2012 Elsevier B.V.



**Figure 1.10** (a) Schematic representation of Kuhn's concept of effective concentration ( $c_{\text{eff}}$ ) for a heteroditopic oligomer (i.e. having two different end groups, A and B) [74]. In solution, the end group A will experience an effective concentration of B, if the latter one cannot escape from the sphere of radius  $l$ , which is identical to the length of the stretched chain. Thus, the intramolecular association between the termini becomes favored for  $c_{\text{eff}}$  values higher than the actual concentration of B end groups. (b) Illustration of how the equilibrium concentration of chains and macrocycles can be correlated to the total concentration ( $c_t$ ) of a ditopic monomer in dilute solution; such a ring-chain supramolecular polymerization typically features a critical concentration. Source: de Greef et al. [26]. © 2009 American Chemical Society.

of non-covalent bonds is typically fast, the macrocyclization pathway occurs always under thermodynamic control.

The first model to theoretically quantify the ratio of intra- and intermolecular association was provided by Kuhn already in the 1930s [74]: the effective concentration ( $c_{\text{eff}}$ ) correlates the length of a polymer chain (thereby, taking the mean squared end-to-end distance and assuming Gaussian statistics) with the probability of the end groups to react, i.e. to undergo macrocyclization; the latter one was predicted to decrease by  $N^{-3/2}$  ( $N$  denotes the number of bonds along the polymer chain [Figure 1.10]).

The toolbox of polymer physics, in particular utilizing random-flight statistics, enables one to calculate  $c_{\text{eff}}$  as a function of the length of the polymer chain [75]. In reasonably good approximation, the distribution function for random-coil polymers is of Gaussian shape [62]; however, this model only holds true for long, flexible chains [76]. In the same context, a particle-in-a-sphere model was utilized by Crothers and Metzger [77]. In a more realistic approach, Zhou employed a worm-like chain model to determine  $c_{\text{eff}}$  for short and, thus, semi-flexible polypeptides [78, 79].

For practical reasons, the rather theoretical concept of effective concentration, which basically relies on concentrations calculated from the physical properties of the terminal functionalities, is often replaced by a more empirical concept using effective molarities [80–85]. The effective molarity (EM) is defined as the ratio of intra- and intermolecular equilibrium constants (i.e.  $K_{\text{inter}}$  and  $K_{\text{intra}}$ , Eq. (1.4), see also Figure 1.9): cyclization is basically preferred for  $\text{EM} > 1$ , whereas linear chains are obtained for  $\text{EM} < 1$ . In addition, *EM can be considered as a pure entropic*

correction, which becomes relevant when an intramolecular process replaces the analogous intermolecular one (however, this only applies to unstrained, flexible chains linking the end groups) [86].

$$EM = \frac{K_{\text{intra}}}{K_{\text{inter}}} \quad (1.4)$$

where EM: effective molarity,  $K_{\text{intra}}$ : dimensionless equilibrium constant for the intramolecular reaction,  $K_{\text{inter}}$ : association constant ( $\text{M}^{-1}$ ) for an intermolecular reaction.

In the case of a supramolecular polymerization in which a heteroditopic AB-type monomer is used, *EM* defines the limit monomer concentration below which the (macro)cyclization pathway dominates the linear chain growth. This empirical approach allows one to predict the different cyclization reactions and, even more importantly, gives an absolute measure for a monomer's cyclization ability at the cost of its polymerization (valid only for reversible, non-covalent interactions).

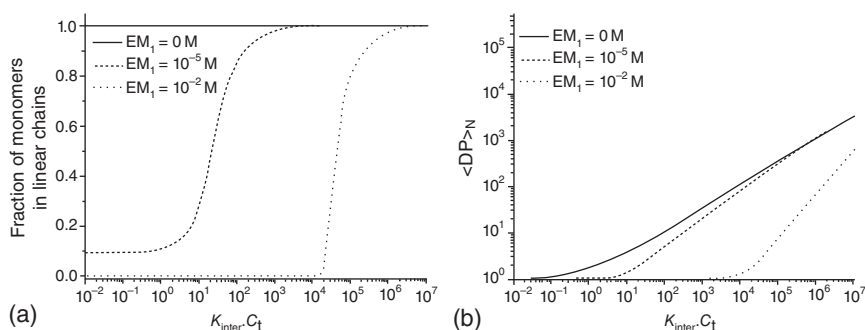
For thermodynamically controlled step-growth polymerizations, Jacobsen and Stockmayer predicted a critical concentration limit [87]: the system is exclusively composed of cyclic species below this value; above this value, an excess of monomer exclusively gives linear chains while the concentration of cyclic species stays constant (Figure 1.10b). These authors related the equilibrium constant for the cyclization to the probability for, thus directly connecting *EM* and  $c_{\text{eff}}$ . It was additionally shown that this constant would decrease with  $N^{-5/2}$ ; in other words, a macrocycle composed of  $N$  subunits can reopen in  $N$  different ways. This study was extended by Ercolani et al., who also considered the size distribution of macrocycles under dilute conditions; thereby, a broad range of  $K_{\text{a}}$  values for the supramolecular macrocyclization were taken into account [83]. According to this, only for high  $K_{\text{a}}$  values ( $>10^5 \text{ M}^{-1}$ ) can a critical concentration limit be observed.

The later model is particularly suited for describing the equilibrium, which is established between cyclic and linear species during a supramolecular polymerization (they are typically conducted in relatively dilute solutions). In contrast to an IDP (*vide infra*), which commonly features  $K$  as the only thermodynamic constant, Ercolani's ring-chain model involves two such constants (Figure 1.9):  $K_{\text{inter}}$  and  $K_{\text{intra}(n\text{-mer})}$  (the latter represents the intramolecular binding constant for the  $n$ -th ring closure). Considering all cycles as unstrained and obeying Gaussian statistics, the  $EM_{n\text{-mer}}$  values can simply be expressed as a function of  $EM_1$  ( $EM_1$ : effective molarity of the bifunctional monomer itself; Eq. (1.5)). An additional aspect that needs to be briefly mentioned is the role of the solvent: thus, volume effects cannot be neglected, and the exponent in Eq. (1.5) needs to be adjusted [62, 88–90].

$$EM_{n\text{-mer}} = \frac{K_{\text{intra}(n\text{-mer})}}{K_{\text{inter}}} = EM_1 \cdot DP^{-5/2} \quad (1.5)$$

where  $EM_{n\text{-mer}}$ : effective molarity of the  $n$ -mer,  $K_{\text{intra}(n\text{-mer})}$ : intramolecular binding constant for the  $n$ -th ring closure,  $K_{\text{inter}}$ : association constant ( $\text{M}^{-1}$ ) for an intermolecular reaction,  $EM_1$ : effective molarity of the bifunctional monomer.

Due to an additional parameter, which is the critical concentration, the situation becomes even more complex when compared to the previously discussed IDP. To



**Figure 1.11** (a) Illustration of the fraction of polymerized monomer as a function of  $K_{\text{inter}} \cdot c_t$  for three different  $EM_1$  values and a fixed value of  $K_{\text{inter}}$  ( $10^6 \text{ M}^{-1}$ ). (b) Illustration of the evolution of  $\langle DP \rangle_N$  as a function of  $K_{\text{inter}} \cdot c_t$  for various  $EM_1$  values. Source: Flory and Suter [91].

account for this, the monomer fraction in linear species as well as the  $\langle DP \rangle_N$  and  $\langle DP \rangle_W$  values were calculated for a general ring-chain equilibrium, which only involved unstrained macrocycles (i.e. various  $K_{\text{intra}(1)}$  values were considered,  $K_{\text{inter}} = 10^6 \text{ M}^{-1}$ ) [26, 83]. As shown in Figure 1.11a, the transition between cyclic and linear species at the critical concentration becomes much sharper when  $K_{\text{intra}(1)}$  is increased. In addition, both  $\langle DP \rangle_N$  and  $\langle DP \rangle_W$  exhibit a steep increase for  $c_t > EM_1$  (the sharpness of the transition still depends on  $K_{\text{intra}(1)}$ ). In contrast, in an IDP, the DP gradually rises with increasing concentration. However, at high total concentrations, it is no longer possible to distinguish between the different modes of polymerization (i.e. the IDP or the ring-chain equilibrium polymerization), and the obtained DPs are almost identical at given concentrations that are much higher than the  $EM_1$  value (Figure 1.11b).

Dormidontova and coworker addressed the issue of the spacer's rigidity with respect to the ring-chain equilibrium of supramolecular polymers [92]. Applying Monte Carlo simulations on such supramolecular polymerizations, these authors showed that the critical concentration was strongly dependent on the rigidity of the spacer (in these modeling studies, H-bonding interactions were representatively studied). Keeping all further parameters constant (e.g. the length of the spacer or the energy for the interaction of the end groups), the critical concentration decreased in the following order: rigid > semi-flexible > flexible. Thus, for rigid and semi-flexible systems, the probability of their end groups meeting within a bonding distance and, thus, the formation of rings, is much smaller as for flexible systems.

Various groups have reported on critical temperatures in ring-chain equilibria ( $T_c$ ). These values define the transition between macrocyclic and linear species of high molar mass [71, 72, 93]. Like the supramolecular IDP elaborated in Section 1.3.1, one has to also distinguish two limiting cases for the ring-chain equilibrium polymerization [56]:

1. Above a certain ceiling temperature, polymers of high molar mass are thermodynamically less stable than cyclic monomers or oligomers.



- Below a certain floor temperature, polymers of high molar mass are thermodynamically less stable than cyclic monomers/oligomers.

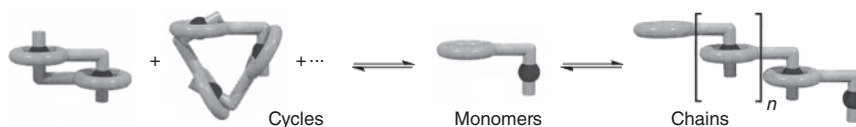
In other words, a ceiling temperature can be found in those (supramolecular) polymerizations where negative changes in the enthalpy and entropy of propagation occur; in the second case, the changes in these measures are positive and, consequently, the floor temperature defines the limit below which (supramolecular) polymerization cannot occur.

Covalent ROPs typically involve the opening of strained cycles (e.g. the cationic polymerization of tetrahydrofuran [THF] and dioxolane [42]). In general, such polymerizations represent enthalpy-driven processes for which ceiling temperatures can be observed (basically, all species are of cyclic nature above this value). Very few examples are known for ROPs exhibiting a floor temperature [94]. Examples for such processes that are characterized by a gain in entropy are the ROP of cyclic  $S_8$  in liquid sulfur [93] and the ROMP of unstrained, macrocyclic olefins [70].

Also in the “supramolecular world,” the ring-chain equilibrium polymerization is a common feature, independent of the type of employed non-covalent interactions. Representative examples in this respect are the formation of pseudorotaxanes (i.e. the supramolecular polymerization of crown ether derivatives equipped with a pending positively charged amine; Figure 1.12, see Chapter 6) [95–97], the polymerization of poly(dimethylsiloxane)s functionalized in  $\alpha,\omega$ -position with carboxylic acids (see Chapter 2) [98], and the equilibrium between linear, tape-like, and cyclic structures that can be observed in stoichiometric mixtures of cyanuric acid and melamine derivatives (see Chapter 3) [99].

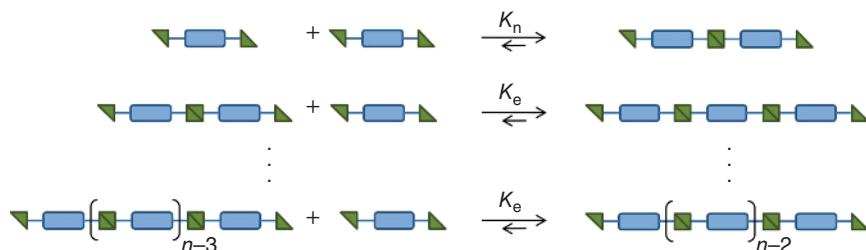
### 1.3.3 (Anti)-cooperative Supramolecular Polymerization

The third and last mechanism for supramolecular polymerization to be discussed herein involves (at least) two distinct stages, resulting in a cooperative or an anti-cooperative growth of the polymer chains. At first glance, the mechanism of the cooperative supramolecular polymerization is reminiscent to the one for the IDP; however, the polymerization initially occurs via the reversible binding of monomers to the growing chain (as for the IDP, all these steps basically possess the same equilibrium constant  $K_n$ ). At a certain DP, a nucleus is formed and, from this point on, the binding of monomers to the polymer chain features an association constant  $K_c$ , which is higher than  $K_n$  (Figure 1.13). In such a nucleation-elongation polymerization (NEP) model, the supramolecular polymerization proceeds via a



**Figure 1.12** Schematic representation of the formation of a poly(pseudorotaxane) via a ring-chain equilibrium. Source: Cantrill et al. [95]. © 2001 American Chemical Society.

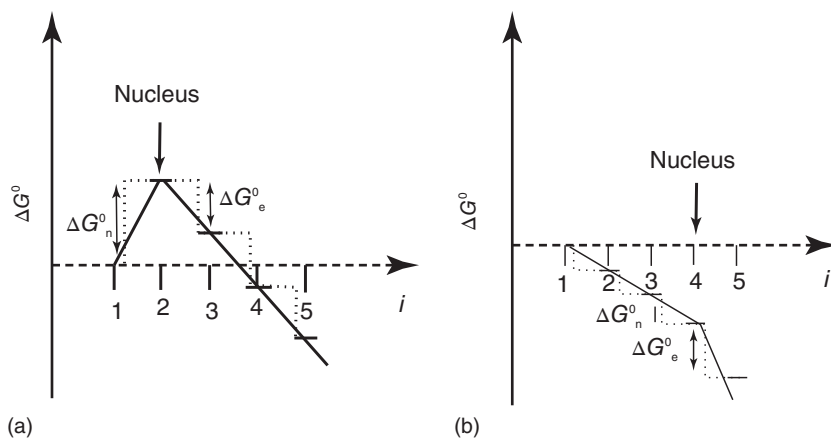




**Figure 1.13** Schematic representation of a typical cooperative supramolecular polymerization reaction (nucleation-elongation mechanism).  $K_n$  and  $K_e$  represent the association constants for the nucleation and the elongation phase, respectively ( $K_n < K_e$ ). Source: Winter et al. [39]. © 2012 Elsevier B.V.

linear IDP. In this elongation phase, the actual association constant is now  $K_e$  rather than  $K_n$  [26, 43, 100, 101].

The complex thermodynamics of the (anti-)cooperative supramolecular polymerization have already been summarized by de Greef et al.; the reader is referred to this review for a more in-depth discussion [26]. In the following, a few general aspects concerning the different types of cooperative supramolecular polymerization shall be named. First, one can distinguish between the nucleated and the downhill cooperative supramolecular polymerizations. Ferrone defined a nucleated supramolecular polymerization as a process wherein the initial steps of the chain growth are characterized by an increase of  $\Delta G^0$  of the oligomers relative to the monomer (Figure 1.14a) [102]. Beyond the point of nucleation, characterized by a maximum in  $\Delta G^0$ , polymerization becomes energetically favorable. Now, the nucleus represents the least stable and, thus, the least abundant species in the



**Figure 1.14** Schematic illustration of the energy diagrams of a cooperative nucleated (a) and a cooperative downhill supramolecular polymerization (b). In both plots, the axis of abscissae represents the oligomer's size ( $i$ ), whereas the ordinate measures the  $\Delta G^0$  in arbitrary units. In diagram (a), the size of the nucleus is 2 (i.e. dimeric nucleus); in diagram (b), a tetrameric nucleus is depicted. Source: de Greef et al. [26]. © 2009 American Chemical Society.

supramolecular polymerization; as a result, the formation of new polymer chains is retarded (the so-called bottleneck effect). It is widely accepted that formation of the nucleus occurs via homogeneous nucleation (the analysis of various examples of nucleated supramolecular polymerization has suggested this feature). Noteworthy, however, heterogeneous nucleation is also known, but commonly refers to the nucleation processes on foreign substrates [103]: foreign molecules (e.g. impurities) [104–106], external surfaces (e.g. substrates) [107], dust particles, or secondary nucleation of monomers. The latter eventually give a supramolecular polymer on an already existing one. In particular, the latter has been reported to be dominant in various bio-supramolecular polymerizations [26].

In summary, three key criteria can be listed according to Frieden to distinguish between an NEP and an IDP [280]:

1. The supramolecular polymerization process is retarded time dependently;
2. This delay of the polymerization can be compensated by adding a preformed nucleus (i.e. seeding); and
3. An equilibrium between the monomer and the supramolecular polymer is established at a certain critical concentration (or temperature).

In contrast to the cooperative nucleated supramolecular polymerization, the cooperative downhill counterpart does not exhibit any increase of  $\Delta G^0$  in the initial steps. Instead, the initial growth of the polymer is characterized by a lower association constant than the following elongation (i.e.  $K_n > K_e$ ; Figure 1.14b). Thus, the monomer is always the species of highest energy in such a cooperative polymerization for which Powers and Powers defined the “nucleus” as the critical chain length at which the absolute ( $d\Delta G^0/di$ )-increment steeply increases [108]. The distinction between the two aforementioned possibilities for cooperative polymerization is associated to the concentration, and, at high total monomer concentrations, a nucleated polymerization process can even be converted into a downhill one [108, 109]. Concentration-dependent kinetic measurements might, for example, be utilized to distinguish between the two different types of cooperative supramolecular polymerization [108]: in the downhill supramolecular polymerization, the nucleus will be different from the one to be found in a nucleated process (i.e. the nucleus represents a stable or an unstable species, respectively).

For the second type of mechanism, the anti-cooperative supramolecular polymerization, the initial oligomer formation features an association constant that is much higher than the one for the elongation process. So far, the anti-cooperative growth in supramolecular polymerizations has attracted less attention, though discrete objects of low dispersity might be obtained (on the contrary, cooperative growth typically gives supramolecular polymers with high  $\bar{D}$  values). For example, Mukerjee [110–114] as well as Tanford [115] reported the formation of large aggregates due to the self-assembly of the surfactants. Due to a high degree of cooperativity in the early stages of the micellar growth, the formation of molecular clusters (i.e. dimers and trimers) was almost fully suppressed. Moreover, (electro)static interactions between the polar head groups of the molecules were identified as the origin of the anti-cooperative effects, affording micelles of finite size.

What is the covalent counterpart to cooperative supramolecular polymerization? In typical chain-growth polymerizations (either ionic or radical), the initiation step is analogous to the formation of the nucleus in the NEP; both systems also feature a sequence of propagation steps; however, a conventional termination is generally absent in supramolecular polymerizations. One can still utilize that numerous features of the living ionic or the radical polymerization explain the cooperative supramolecular polymerization: e.g. in both cases, monomers and polymer chains are present halfway through the polymerization [26]. Furthermore, cooperative effects have also been observed in conventional polycondensation reactions: Flory's "principle of equal reactivity" [44] is disobeyed if the electronic properties of the termini are changed in course of the chain growth, in particular when the reactivity of the polymer end groups becomes higher as for the monomer (i.e. the reaction of monomers becomes retarded). The polycondensation of phenyl 4-(*N*-alkylamino)benzoate in THF under basic conditions, initiated by phenyl 4-nitrobenzoate, represents one example in this respect [116]: the reactivity of the remote phenyl ester moiety is strongly decreased as soon as the monomer is deprotonated; thus, individual monomers will not react with each other. The monomer anion will then only react with the initiator, thus generating an activated species which, in turn, contains phenyl ester moiety with increased reactivity (relative to the anionic monomer). Consequently, only the activated monomers will react, resulting in a polycondensation which shows a chain growth rather than a step-growth behavior [117, 118].

The cooperative supramolecular polymerization can be induced by electronic (as shown in the previous example), hydrophobic, as well as structural effects (e.g. the formation of helical structures). In the latter case, the initial polymerization is thermodynamically rather unfavored when compared to the elongation phase, and thus, polymerization is preferred only when a critical length of the growing polymer chain is reached; then, due to conformational and/or structural changes, the growth of the polymer chain eventually becomes more favorable. As pointed out above, the nucleus is defined as the critical oligomer at which length the elongation of the polymer chain becomes more favored compared to dissociation. If cooperativity is arising (mainly) from structural changes, the nucleus can be regarded as the smallest possible species at which an unstructured, disordered assembly is transformed into an ordered one. A typical example for such a covalent polymerization reaction is the acid-initiated polymerization of isocyanides, generating helical polymers. It has been proposed that the formation of an initial helical oligomer is required that, subsequently, serves as template for the attachment of further monomer units [119]. Remarkably, the anionic polymerization of triphenylmethyl methacrylate, using 9-fluorenyllithium, as initiator, can be conducted asymmetrically when additional chiral ligands are present. Nakano et al. reported the synthesis of a one-handed helical polymer [120]; the reactivity of each anionic oligomer was attributed to the DP and, thereby, to the specific chain conformation. The addition of further monomers to the chain occurred more readily when a stable helical conformation of the oligomer could be adopted (in this case, at a DP of 7–9).

Similarly, the Oya group reported on the cooperative chain growth of synthetic polypeptides via heterogeneous polymerization of amino acid anhydrides [121, 122]. Presumably due to the very short chains, preventing the formation of the anticipated *R*-helical structure, antiparallel  $\beta$ -sheet-type oligopeptide species were initially observed; however, at a DP of c. 8, a conformational change into the *R*-helix induced a more favorable chain growth via the addition of monomers to the active end of the helical structure.

Besides these representatives from the “covalent world,” various other examples for cooperative supramolecular polymerizations can be found. In particular, the structural cooperativity of H-bonding interactions has been addressed by the Lehn [123], Meijer [124], and the Würthner groups [125] (see also Chapter 3). Other examples include the aggregation of cationic and anionic porphyrins (see Chapter 2) [126] as well as the stacking of oligo(*p*-phenylene)s bearing dendritic ethylene glycol substituents [127], both driven by strong hydrophobic cooperativity effects. Moreover, metallophilic interactions have recently been identified to be the driving force in the supramolecular polymerization of oligo(phenylene ethynylene)-based Pd(II)–pyridyl complexes [128] or linear Pt(II)–acetylide complexes (Chapter 4) [129]. In contrast, anti-cooperative supramolecular polymerizations are rare: for instance, the polymerization of amphiphilic perylene derivatives in water [130] or cyclic peptides based on  $\alpha$ - and  $\epsilon$ -amino acids [131].

## 1.4 Beyond Classical Supramolecular Polymerization

The three aforementioned mechanisms represent the classical examples for how supramolecular polymerization might proceed. Going beyond these, various strategies have been developed to circumvent some limitations arising from the traditional approaches [37]. In particular, the control over the molar mass and the dispersity remain as major challenges. The living supramolecular polymerization aims to adopt the key features from covalent living polymerizations, i.e. good kinetic control over the initiation and propagation steps, and to transfer these into self-assembly processes [132]. Meijer and coworkers identified the NEP process (see Section 1.3.3) as the most appropriate mechanism for this purpose. It was shown that a finely tuned balance between attractive (i.e. a combination of various non-covalent interactions) and repulsive forces (i.e. electrostatic interactions) was crucial to enable control over the supramolecular polymerization [133]. Based on an interplay between isodesmic and cooperative pathways, Ogi et al. realized that the supramolecular self-assembly of a porphyrin monomer equipped with H-bonding entities and hydrophobic alkyl chains into nanofibers of narrow length dispersities (*D* value of 1.10) [134]. In the same context, the “living crystallization,” i.e. the seeded growth of block copolymers into micrometer-sized micelles, needs also to be mentioned [135]. In particular, the Manners and Winnick groups employed this strategy to assemble block copolymers in a highly controlled fashion.

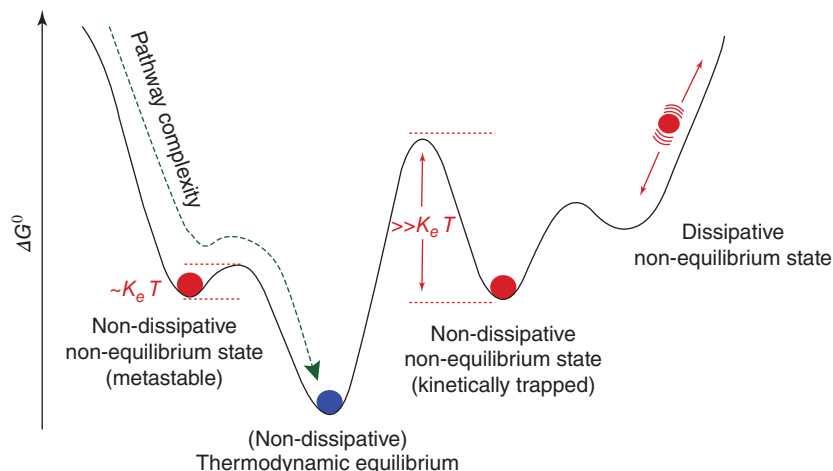
A “supramonomer,” i.e. a monomer that was formed via non-covalent interactions, can be polymerized using covalent or supramolecular polymerization

techniques [37]. The covalent polymerization of preformed metal complexes into metallopolymers represents one of the most common applications in this respect (see also Chapter 4) [36, 136]. However, these polymerizations (as well as other examples, e.g. [137, 138]) do not offer sufficient control over the molar mass (distribution) since the reactions typically follow a step-growth mechanism. Nonetheless, this approach provides an alternative to the direct supramolecular polymerizations and, thus, widens the options to prepare tailor-made polymers that incorporate supramolecular units.

The self-sorting of molecular components due to the selectivity of non-covalent binding represents an established approach to assemble alternating supramolecular polymers, in particular when making use of orthogonal types of secondary interactions (see Chapter 11) [139]. Huang et al. demonstrated that supramolecular self-sorting of two different cucurbit[*n*]uril derivatives ( $n = 7$  and 8), in the presence of an appropriate homoditopic guest, can even proceed with reasonable control (see also Chapter 7) [140]. At an equimolar ratio of all three components, a maximum molar mass ( $M_w$ ) of  $9.7 \times 10^4 \text{ g mol}^{-1}$  was obtained; the dispersity of the polymer was c. 1.5 and thus remarkably low for such a supramolecular polymerization.

As one further example, the stimuli-controlled supramolecular polymerization needs to be mentioned. Yang et al. proposed that supramolecular polymerizations, driven by external stimuli, might proceed with good control (assuming optimized reaction conditions) [37]. However, the broad range of stimuli-responsive polymers reported so far basically rely on the ability to reversibly polymerize/depolymerize when, e.g. the pH-switchability of ionic interactions (Chapter 2) or the redox-switchability of host-guest interactions (Chapter 7).

Not only supramolecular polymers are typically assembled under thermodynamic control, but also materials generated in kinetically trapped or metastable states have also been reported [40, 141]. For supramolecular polymers, which were assembled far from equilibrium, unique possibilities have been suggested: inherent dynamic nature, adaptivity, and spatiotemporal controllability [142–144]. Noteworthy, many natural self-assembled systems operate in such states and fulfill crucial functions [145]. Kinetic control of a supramolecular polymerization can be achieved utilizing strong non-covalent interactions; thus, materials in non-dissipative, nonequilibrium states can be formed (Figure 1.15). In such processes, the experimental details are of significant importance since nonlinear phenomena (e.g. nucleation or multiple competitive growth) are known to contribute to the outcome of the supramolecular self-assembly (e.g. the nanoscale morphology of the obtained materials) [40]. Remarkable progress has been made to understand the kinetics and pathway complexity, and, today, the selection of a specific self-assembly pathway is possible by cautious optimization of the experimental details. As a result, one can generate supramolecular materials with different functional properties, even from a single monomer. The fourth case, which is the dissipative nonequilibrium state, is known from living systems. In these supramolecular assemblies, energy is continuously consumed to account for their stability. In Nature, nucleobase triphosphates represent the main energy resources, which can control the nonequilibrium self-assembly process in a highly spatiotemporal fashion – a prerequisite for cells



**Figure 1.15** Illustration of the various thermodynamic states in supramolecular polymerizations on Gibbs free energy landscape. Source: Sorrenti et al. [40]. Licenced under CC BY 3.0.

to perform their complex functions (e.g. cell division, motility, and intracellular transport) [146]. The evolution of this field of research, an in-depth discussion of the underlying mechanisms, and selection criteria to assemble supramolecular polymers in nonequilibrium states can be found in various recent reviews [40, 145]. In a recent example, Xu and coworkers demonstrated that only a photo-reduced homoditopic viologen monomer gave a supramolecular polymer due to the formation of host–guest complexes with cucurbit[8]uril; whereas, under ambient conditions, depolymerization occurred due to a reoxidative process (see Chapter 7) [147].

## 1.5 Concluding Remarks

In polymer science, two types of materials are in the focus of research: conventional polymers and, with increasing interest, supramolecular polymers. Whereas the former ones are based on covalent bonds, the latter are formed via assembly of smaller entities by specific directional secondary interactions. Supramolecular polymers exhibit properties that are comparable to those of well-known traditional macromolecules; however, reversibility of the secondary interaction represents an additional feature that gives rise to new applications: supramolecular polymers typically represent species in their thermodynamic equilibrium and their properties can be adjusted by applying external stimuli (e.g. changes in temperature, concentration, or solvent). Moreover, supramolecular polymers in non-dissipative and/or nonequilibrium states also have to be considered and might be important in the future for the fine-tuning of, e.g. shape, molecular organization, chirality, and/or dispersity of supramolecular polymers [40]. These aspects have been proposed to be crucial for utilitarian applications, as in energy conversion or biomedicine areas [148].

The broad range of supramolecular polymers that has been published so far can be classified by mainly two approaches: the type of the secondary interaction involved (as noted in the following chapters) or the mechanism by which they have been formed (in accordance with Carothers' classification from the 1930s [2]). From the three main mechanisms discussed in this chapter, particularly the isodesmic and ring-chain-mediated supramolecular polymerizations are now well understood; however, various effects (e.g. hysteresis and heterogeneous nucleation) make cooperative supramolecular polymerizations much more difficult to understand. Insight into the kinetics and thermodynamics of supramolecular polymers can be gained by comparing these artificial systems to the well-documented protein aggregation. Moreover, one may compare these three mechanisms for supramolecular polymerizations to the three classes of covalent polymerization: step-growth, chain-growth, and ring-opening polymerizations. For covalent polymers, the field of application often dictates the way by which mechanism the polymer may be prepared. The same also holds basically true for the supramolecular polymers.

In recent years, new concepts have evolved addressing the issue on how to control supramolecular polymerizations regarding the molecular structure and even the dispersity of the self-assembled materials. From these, the so-called living supramolecular polymerization represents a highly promising approach to prepare novel, designer, supramolecular materials via control over, e.g. their shape, size, and dispersity.

Going beyond a rather theoretical discussion, various types of supramolecular polymers will be introduced in the subsequent chapters – differentiated by the nature of their underlying non-covalent/supramolecular interactions. Nonetheless, a detailed knowledge of the kinetic and thermodynamic driving forces for the formation of these materials remains a fundamental requirement.

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