

Chapter 1

Promising Dendritic Materials: An Introduction to Hyperbranched Polymers

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1.1 IMPORTANCE OF BRANCHING

In nature and universe from living to nonliving things, branching occurs anywhere and anytime, such as the Crab Nebula, forked lightning, river basins, trees, nerves, veins, snow crystals, nervures, and proteoglycan ranging from light-years to kilometers, and to microscale and nanoscales (see Figure 1.1 for selected branching patterns). Hence, branching is a general and important phenomenon that could result in faster and more efficient transfer, dissipation, and distribution of energy and/or matter.

1.2 POLYMER ARCHITECTURE

The past century has witnessed pioneering work and blossoming of polymer science and industry, for which various star scientists like Staudinger, Flory,

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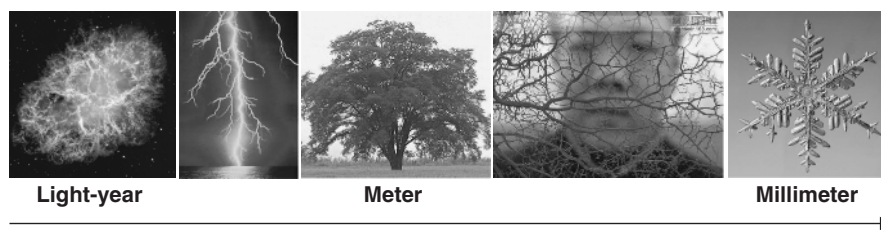


Figure 1.1 Selected branching patterns observed in universe and nature (from left to right: Crab Nebula, forked lightning, tree, vascular network, snow crystal). The images were obtained from the Internet.

Ziegler, Natta, de Gennes, Shirakawa, Heeger, MacDiarmid, Noyori, Sharpless, Grubbs, and others have made great contributions. Notably, their focus has mainly concentrated on linear chains. Since the first beacon publication of “Über Polymerisation” (on Polymerization) in 1920,¹ and the definition of “macromolecules” as primary valence chain systems in 1922 by Staudinger,² numerous types of macromolecules with various architectures have been synthesized successfully. Figure 1.2 shows besides linear polymers that seem to approach a period of fatigue nowadays,³ new paradigms including chain-branched, cross-linked, cyclic, starlike, ladderlike, dendritic, linear brush-like (or comblike), cyclic brush-like, sheetlike, tubal, and supramolecular interlocked architectures keep coming to the fore, promising an unlimited future for and sustainable development of polymer science and technology. Except the linear, cyclic, and interlocked polymers, all other architectures possess branched structures, also indicating the significance of branching in the molecular construction.

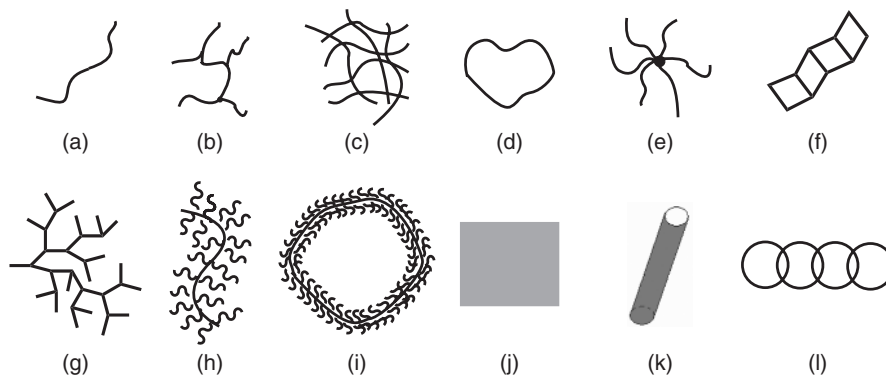


Figure 1.2 Architectures of synthesized macromolecules: (a) linear, (b) chain-branched, (c) cross-linked, (d) cyclic, (e) starlike, (f) ladderlike, (g) dendritic, (h) linear brush-like, (i) cyclic brush-like, (j) sheetlike, (k) tubelike, and (l) interlocked.

1.3 DENDRITIC POLYMERS

In the 1980s, a kind of highly branched three-dimensional macromolecules, also named *dendritic polymers*, was born, and gradually became one of the most interesting areas of polymer science and engineering. Despite the 12 architectures shown in Figure 1.2, dendritic architecture is recognized as the main fourth class of polymer architecture after traditional types of linear, cross-linked, and chain-branched polymers that have been widely studied and industrially used.⁴ Up to now, eight subclasses of dendritic polymers have been developed: (i) dendrons and dendrimers, (ii) linear-dendritic hybrids, (iii) dendronized polymers, (iv) dendrigrafts or dendrimer-like star macromolecules (DendriMacro), (v) hyperbranched polymers (HPs), (vi) hyperbranched polymer brushes (HPBs), (vii) hyperbranched polymer-grafted linear macromolecules, and (viii) hypergrafts or hyperbranched polymer-like star macromolecules (HyperMacro) (Figure 1.3), of which the first four subclasses have the perfect and ideally branched structures

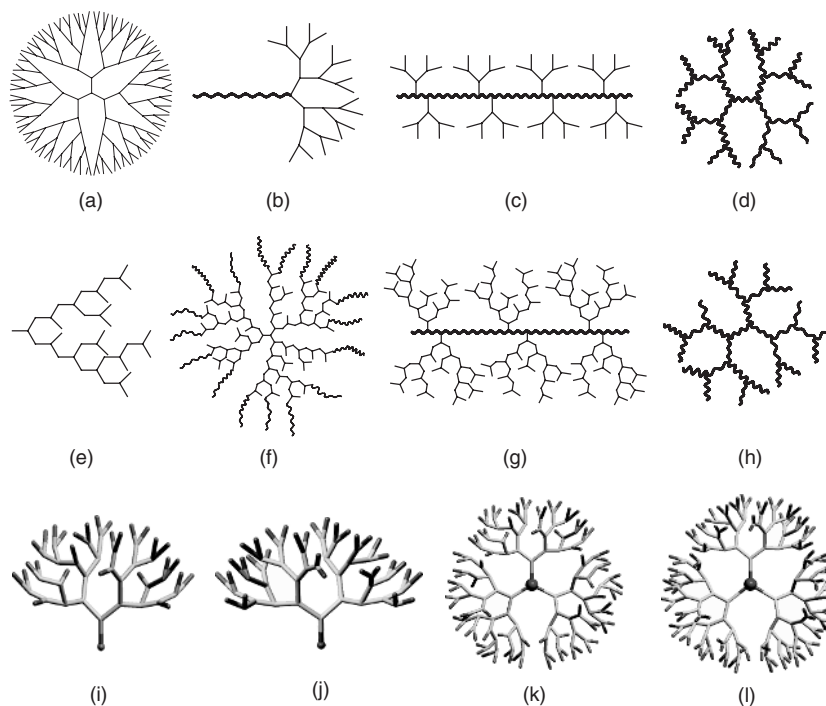


Figure 1.3 Dendritic polymers with different structures. (a) Dendrimer, (b) linear-dendritic hybrid, (c) dendronized polymer, (d) DendriMacro, (e) hyperbranched polymer, (f) multiarm star polymer or hyperbranched polymer brush, (g) HP-grafted polymer, (h) HyperMacro, (i) 3D model of HP with initial unit, (j) 3D model of dendron, (k) 3D model of HP with a core, and (l) 3D model of dendrimer.

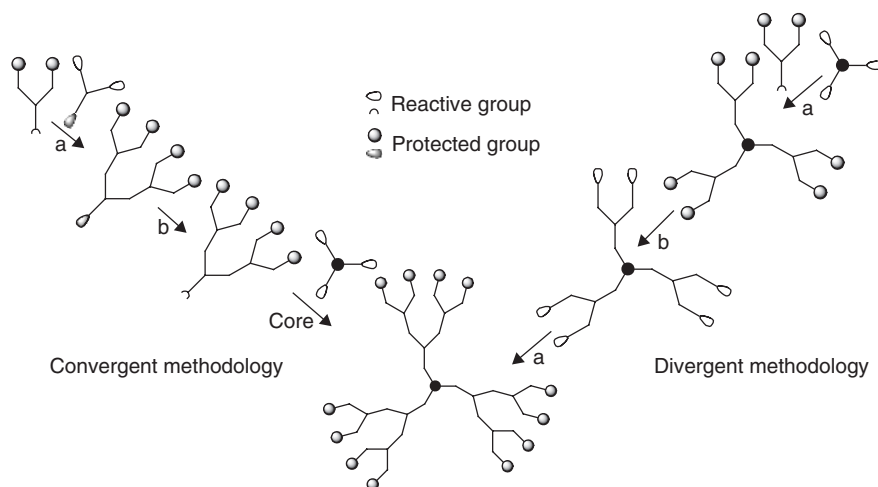


Figure 1.4 Convergent and divergent methodologies for synthesis of dendrimers.

with the degree of branching (DB) of 1.0, and the latter four exhibit a random and irregular branched configuration with lesser DB (normally, 0.4–0.6).⁵ Dendrimers and HPs have been extensively studied as the representative regular and irregular dendritic polymers, respectively.

Dendrons and dendrimers can be synthesized by divergent and convergent methodologies (Figure 1.4).^{4,6} Generally, step-by-step synthesis, purification, protection, and deprotection are needed for accessing dendrimers with controlled molecular structure, shape, size, and functions and functional groups. Nevertheless, the employment of “click” chemistry, especially the Cu(I)-catalyzed Huisgen 1,3-dipolar cycloaddition between azides and acetylene derivatives (also called *azide–alkyne click chemistry*)⁷ and thiol–ene click chemistry possessing the merits of specificity, fast reaction, tolerance to common functional groups and water, greatly furthers the progress of dendrimer synthesis because the tedious protection/deprotection and chromatography-based purification steps are not required any more.⁸ There is no doubt that the facile availability of dendrimers would boost their real applications. However, the accessible varieties and structures through click chemistry are still limited at present.

A backbone of linear polymer attached with high density of side dendrons is called a dendronized polymer, which can be prepared by four approaches: direct polymerization of dendron–monomer (macromonomer approach), grafting dendrons to a linear polymer (attach to approach), divergent step-growth from a core of linear polymer (divergent approach), and their combinations (Figure 1.5). The cylindrical dendritic polymers can be easily visualized and manipulated using atomic force microscopy (AFM), affording the chance for the fabrication of complex structures via molecular fusion techniques.⁹

Dendrigrfts¹⁰ and hypergrfts¹¹ are highly branched star polymers constructed with linear polymeric blocks via controlled and random branching

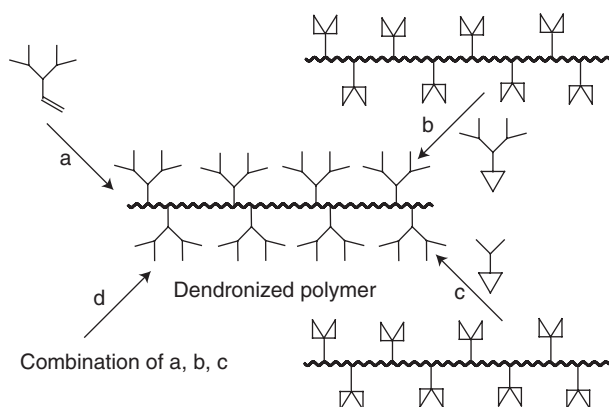


Figure 1.5 Synthesis approaches to dendronized polymers: (a) macromonomer approach, (b) attach to approach, (c) divergent approach, and (d) combination of a, b, and c.

approaches, respectively. They can be prepared through three strategies: divergent “grafting onto,” divergent “grafting from,” and convergent “grafting through.” The sizes of both kinds of macromolecules can range from tens to hundreds of nanometers, which is 1–2 orders of magnitude larger than their counterparts of dendrimers and HPs. Because of the building blocks of linear polymers, dendrigrafts and hypergrafts may show crystallization behavior, which is also essentially different from the classic dendrimers and HPs, which are normally amorphous due to the lack of chain entanglements.

More details on dendrimers, dendronized polymers, and dendrigrafts can be obtained from relevant review papers and books. This book will focus on synthesis, characterization, properties, and applications of HPs.

1.4 HYPERBRANCHED POLYMERS

1.4.1 Concept and History

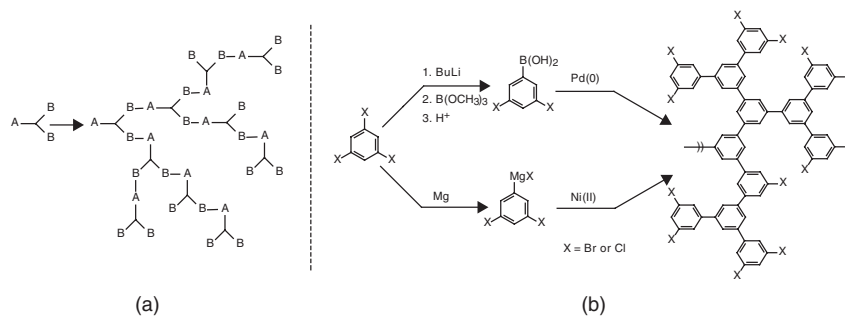
It is known that the DuPont researchers, Kim and Webster, coined the term *hyperbranched polymers* to define dendritic macromolecules that have a random branch-on-branch topology prepared by single-step polycondensation of AB_2 -type monomers in the late 1980s.^{12–16} The first intentional preparation of the HP (hyperbranched polyphenylene) was warranted as a patent in 1987,¹² and presented to the public at the 1988 American Chemical Society Meeting at Los Angeles.^{13,16} Around this period, Tomalia¹⁷ and Fréchet *et al.*¹⁸ also reported their work on highly branched structures independently. But the history of HP is quite long and complex (Table 1.1); it can be dated to the end of the nineteenth century, the gestation period of the synthesized polymer, when Berzelius reported the formation of a resin from tartaric acid (A_2B_2 -type monomer) and glycerol (B_3 -type monomer).^{5,19} In 1901, Watson Smith attempted the reaction of

Table 1.1 History of Hyperbranched Polymers⁵

Year	Case	Lead Authors	Reference
Before 1900	Tartaric acid + glycerol	Berzelius	[19]
1901	Glycerol + phthalic anhydride	Smith	[19]
1909	Phenolic + formaldehyde	Baekeland	[22]
1929–1939	Glycerol + phthalic anhydride	Kienle	[19–21]
1941	Molecular size distribution in theory	Flory	[23–27]
1952	AB _n polymerization in theory	Flory	[28]
1982	AB ₂ + AB copolymerization	Kricheldorf	[29]
1987–1991	AB ₂ homopolymerization	Kim/Webster	[12–16]
		Odian/Tomalia	[17]
		Fréchet/Hawker	[18]

phthalic anhydride (latent A₂-type monomer) or phthalic acid (A₂-type monomer) and glycerol (B₃-type monomer).¹⁹ Following his report, Callahan, Arsem, Dawson, Howell, and Kienle *et al.* investigated that reaction further, obtaining some interesting results.^{19–21} Kienle showed that the specific viscosities of samples prepared from phthalic anhydride and glycerol were lower than those of linear polymers (e.g., polystyrene) given by Staudinger.²⁰ In 1909, Baekeland produced the first commercial synthetic plastics and phenolic polymers, in his Bakelite Company through the reaction of formaldehyde (latent A₂ monomer) and phenol (latent B₃ monomer).²² Notably, the soluble precursors of phenolic thermosets obtained just prior to gelation would have the randomly branched topology.

In the 1940s, Flory *et al.* introduced the concepts of “degree of branching” and “highly branched species” when they calculated the molecular weight (MW) distribution of three-dimensional polymers in the state of gelation.^{23–27,30} In 1952, Flory pointed out theoretically that highly branched polymers can be synthesized without the risk of gelation by polycondensation of a monomer containing one



Scheme 1.1 Flory's theoretical model of highly branched polymer prepared by polycondensation of AB₂-type monomer (a)²⁸ and Kim-Webster's hyperbranched polyphenylene prepared by Suzuki polycondensation of AB₂ monomer (b).¹³

A functional group and two or more B functional groups capable of reacting with A (AB_g-type monomer, $g \geq 2$) (Scheme 1.1).²⁸ This work, primarily, lays the theoretical foundation of highly branched polymers. Intrigued by the stronger mechanical property, higher heat-resistant temperature, and other better strength-related performance of highly-branched polymers, the subsequent three decades have led to the witnessing of the fast and incredible development of linear polymers, cross-linked plastics, and chain-branched polymers. Accompanying the focus shift from strength to functionality in polymer science and technology, cascade molecules or dendrimers were successfully synthesized via multistep reactions by Vögtle,³¹ Tomalia *et al.*,³² Newkome *et al.*,³³ and Fréchet *et al.*³⁴ Following the discovery of dendrimers with regular branched units, another kind of dendritic polymer, the HP with random branched units, was prepared by one-step polycondensation of AB₂-type monomer in the late 1980s (Scheme 1.1), as mentioned above.^{12–16} Prior to Kim's definition, Kricheldorf and coworkers even prepared highly branched copolymers by one-step copolymerization of AB- and AB₂-type monomers, in 1982.²⁹ Since the pioneering work of Kim and Webster, HPs have drawn much attention of both scientists and engineers, and has become one of the hottest fields in polymer science and engineering, as demonstrated by the increasing number of related publications (Figure 1.6), due to their unique properties, highly reactive and numerous terminal groups, and wide range of potential applications.^{5,35} Till date, various HPs have been prepared, comparable with the library of linear polymers, including polyesters, polyethers, polyamides, polyimides, poly(ether ketone)s, polystyrenes, polyacrylates, polyolefins, and so forth. The details will be discussed in the subsequent chapters of this book.

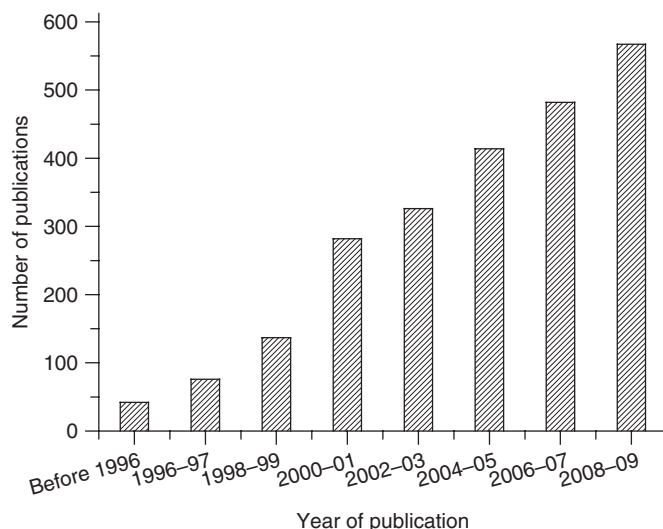


Figure 1.6 Publication numbers during 1988 and 2009 with the topic of “hyperbranched polymers” searched by ISI Web of Science.

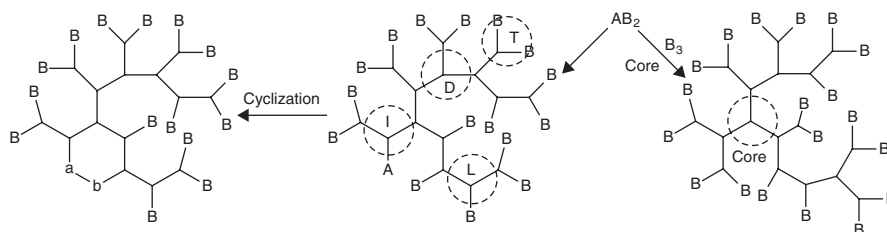


Figure 1.7 Schematic structure of hyperbranched polymer prepared from AB_2 -type monomer. Reprinted with permission from Ref. [36].

1.4.2 Structure and Properties

Generally, there are initial (I), linear (L), dendritic (D), and terminal (T) repeating units in a hyperbranched macromolecule prepared from an AB_2 -type monomer.³⁶ After polymerization, A HP contains, at most, one A group at the initial unit that could be converted into another bond (e.g., ab bond) by reaction either with intramolecular B group via cyclization or with extra-added multifunctional core molecules (Figure 1.7). The units with one unreacted B group, two reacted B groups, and two unreacted B groups represent linear, dendritic, and terminal units, respectively. Two types of linear units may exist for a HP prepared from an asymmetric AB_2 (or ABB') monomer.

To correlate the units of HP and describe the structure of HPs quantitatively, Fréchet and coworkers gave an equation for the DB at first, as shown in Eq. (1.1).¹⁸

$$DB = \frac{(\text{no. of dendritic units}) + (\text{no. of terminal units})}{\text{total no. of units}} = \frac{D + T}{D + T + L} \quad (1.1)$$

Here, D is the total number of dendritic units, T the total number of terminal units, and L the total number of linear units. For a HP with large MW, the number of terminal units (T) is very close to that of dendritic units (D). Accordingly, Eq. (1.1) can be simplified as Eq. (1.2).³⁶

$$DB = \frac{1}{1 + L/2D} \quad (1.2)$$

Equation (1.2) is quite useful since L/D or L/T could be easily calculated from the corresponding nuclear magnetic resonance (NMR) spectrum, whereas it is always difficult to know the exact numbers of units.

From the theoretical point of view, Frey, Müller, and Yan *et al.* obtained more strict expressions of DB as a function of conversion (Eq. 1.3) upon the condition of equal reactivity of all B groups,^{37,38} which is very helpful in the prediction of DB at a given MW or degree of polymerization (DP).

$$DB = \frac{2x}{5 - x} \quad (1.3)$$

Here, x is the conversion of the A group. When the reaction approaches completion, x would be approximately equal to 1, and thus DB would approach 0.5. The detailed calculations will be discussed in Chapter 13. Most of reported HPs prepared from AB_2 monomers have DBs close to 0.5, indicating the coincidence of theory and experiments.

On the other hand, DB could be altered or even tuned to some extent.³⁹ To increase DB, the five methods can be attempted: (i) enhancement of the reactivity of the functional group associated with linear units;⁴⁰ (ii) addition of multifunctional core molecules (B_f) to the polymerization system of AB_n ;⁴¹ (iii) polycondensation of dendrons without linear units;⁴² (iv) postmodification of the formed HPs to convert linear units to dendritic ones;⁴³ and (v) using special catalyst.⁴⁴ Through these techniques, DB could be obviously higher than 0.5 or even approach 1 in some cases.^{44–48} Attentively, HPs still contain many isomers with different MWs even though DB is equal to 1, which is different from dendrimers that have the same MWs. For tuning DB, four methods can be attempted: (i) copolymerization of AB_2 and AB monomers with different feed ratios;⁴⁹ (ii) changing the polymerization conditions such as temperature, feed ratio of monomer to catalyst, and solvent;^{50–52} (iii) host–guest inclusion of AB_2 or multifunctional monomer;⁵³ and (iv) combination of the above ones.

DB is one of the most important parameters for HPs because it has a close relationship with polymer properties such as free volume, chain entanglement, mean-square radius of gyration, glass-transition temperature (T_g), degree of crystallization (DC), capability of encapsulation, mechanical strength, melting/solution viscosity, biocompatibility, and self-assembly behaviors.^{54–62} Hence, the properties of HPs can be controlled to some extent by adjusting DB. For instance, Yan and coworkers found that T_g decreased almost linearly and DC decreased exponentially with the increase of DB of poly[3-ethyl-3-(hydroxymethyl)oxetane] (PEHMO) (Figure 1.8).^{56–58} Frey and coworkers revealed that hyperbranched polyglycerol (HPG) showed much higher capacity in supramolecular encapsulation of guest dyes than its linear analog.⁶¹ Haag *et al.* demonstrated that a moderate DB (0.5–0.7), rather than too low or too high, is beneficial to gene transfection in the gene delivery using the carrier of

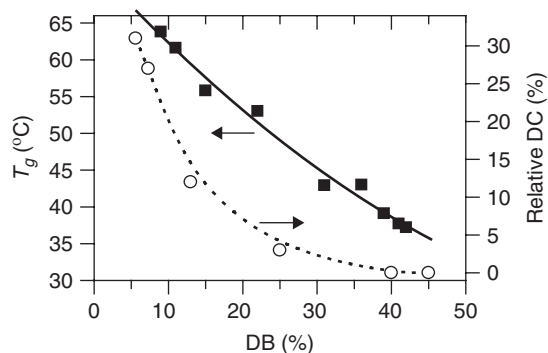


Figure 1.8 Relationship between glass-transition temperature (T_g) or relative degree of crystallization and degree of branching (DB) for poly[3-ethyl-3-(hydroxymethyl)oxetane]s.^{56–58}

Table 1.2 Average Degree of Polymerization and Polydispersity Index of Polymers Prepared from AB_g-Type Monomers ($g \geq 1$)^{63,64}

Monomer Type	AB	AB ₂	AB _g
P_n	$1/(1-x)$	$1/(1-x)$	$1/(1-x)$
P_w	$(1+x)/(1-x)$	$(1-x^2/2)/(1-x)^2$	$(1-x^2/g)/(1-x)^2$
PDI	$1+x$	$(1-x^2/2)/(1-x)$	$(1-x^2/g)/(1-x)$

modified hyperbranched poly(ethyleneimine) (PEI).⁶² The correlation of DB and properties will be explained in detail in Chapter 12. So the research on this aspect would be a promising direction, which will discover the essential difference and intrinsic similarity among linear polymers, HPs, and dendrimers. The uncovered rules can be then used to design new materials with desirable applications.

MW is another important parameter for HPs. Theoretically, the equations of number- and weight-average degrees of polymerization (P_n and P_w) and the polydispersity index (PDI) for polymers prepared from AB_g-type monomer ($g \geq 1$) are calculated as Eqs. (1.4)–(1.6).^{63,64}

$$\overline{P_n} = 1/(1-x) \quad (1.4)$$

$$\overline{P_w} = (1-x^2/g)(1-x)^2 \quad (1.5)$$

$$\text{PDI} = \overline{P_w}/\overline{P_n} = (1-x^2/g)/(1-x) \quad (1.6)$$

Here, x is the conversion of A group. If $g = 1$ or 2, we obtain the corresponding equations of linear polymers prepared by polycondensation of the AB monomer or the HP prepared from the AB₂ monomer, as shown in Table 1.2.

Therefore, we can see that PDI increases linearly for linear polymers but exponentially for HPs with increasing the conversion (x). So, the PDI of HP would be much higher than that of linear polymers, especially when the reaction approaches completion (i.e., x approaches 1). If $x = 0.99$, for example, the theoretic PDI approximates to 50 for HPs prepared from AB₂ monomers, while PDI is only about 2 for linear polymers. In experiments, nevertheless, PDI is usually smaller than the calculated value because residual monomers and oligomers might be removed from the product during the purification. The HPs with a broad PDI could be used as plasticizers to improve the processability of other polymers. On the other hand, the PDI could be narrowed by the techniques of (i) slow addition of monomers during polymerization,^{65–69} (ii) polymerization in the presence of core molecules,^{67–73} and (iii) classification of HPs via precipitation or dialysis.

The relationship between MW and viscosity for various polymer topologies is schematically depicted in Figure 1.9.⁷⁴ The intrinsic viscosity of HP is normally lower than that of its linear analog but higher than that of dendrimers.

For comparison, the characteristics and properties of HPs are summarized in Table 1.3 with both linear polymers and dendrimers as shown in Ref. [36]. Usually, HPs show ellipsoid-like 3D architecture, randomly branched structure

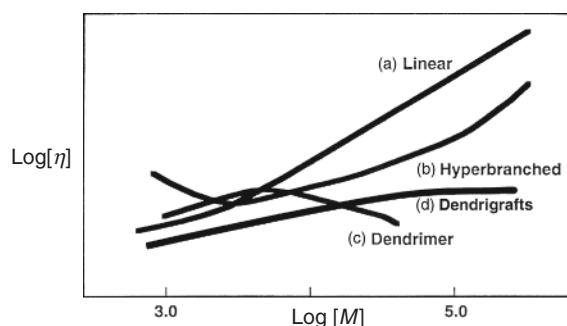

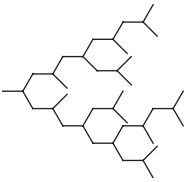
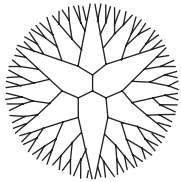


Figure 1.9 Schematic plots for the relationship between intrinsic viscosity ($\log[\eta]$) and molecular weight ($\log[M]$) for various polymer topologies. Reprinted with permission from Ref. [74].

Table 1.3 Comparison of Hyperbranched Polymer with Linear Polymer and Dendrimer³⁶

Polymer	Linear	Hyperbranched	Dendrimer
Structure			
Topology	1D, linear	3D, ellipsoidal	3D, globular
Synthesis	One-step, facile	One-step, cost-effective	Multistep, laborious
Purification	Precipitation	Precipitation	Chromatography
Scaling-up	Already, easy	Already, easy	Already, difficult
MW	Mixed MWs	Mixed MWs	Same MW
PDI	>1.1	>3.0	1.0 (<1.05)
DB	0	0.4–0.6	1.0
Molecular cavity	No	Reversible box	Irreversible box
Entanglement	Strong	Weak	Very weak or no
Viscosity	High	Low	Very low
Solubility	Low	High	Very high
Functional group	At two ends	At linear and terminal units	At terminal units
Reactivity	Low	High	Very high
Strength	High	Low	Very low

with $DB < 1.0$ (normally 0.4–0.6), wide polydispersity of MW (normally, $PDI > 3.0$), little molecular entanglement, low viscosity, high solubility, and plenty of functional groups linked at both the linear and terminal units; dendrimers exhibit globular architecture, perfectly branched and regular structure with $DB = 1.0$, extremely narrow polydispersity of MW (ideally, $PDI = 1.0$; normally, $PDI < 1.05$), no molecular entanglement, very low viscosity, high solubility, and

plenty of functional groups at the terminal units. Thus, dendrimers, synthesized via multistep controlled manner, are more close to pure molecules with precise molar mass and exact chemical units and bonds, while HPs, prepared by one-step polymerization, are more close to conventional polymers with distributions of MW and DB. Despite the differences, HPs have very similar properties such as low viscosity, high solubility, weak strength, highly reactive functional groups, and good capacity of encapsulation for guest molecules to dendrimers. On the basis of their cost-effective and large-scale productivity, HPs are preferred in industrial applications as compared with dendrimers.

1.4.3 Synthesis Philosophy

From the philosophy viewpoint, HPs can be accessed via three avenues: bottom up (i.e., polymerization of monomers), top down (i.e., degradation of giant networks or biomacromolecules), and middle upon (modification of as-prepared hyperbranched polymeric-precursor), as illustrated in Figure 1.10.³⁶ Figuratively, a tree is grown from a sapling (like bottom up), cuttings of branches (like top down), or grafting new branches on a tree (like middle upon) (Figure 1.10b). Most HPs are prepared through the bottom up avenue and modified as amphiphilic polymers, multiarm star polymers (or HPBs), and other polymers with dendritic architecture through the middle upon avenue.⁵

Four methodologies have been developed to prepare HPs via the bottom up ideology: (i) polycondensation of AB_g -type monomers, ($g \geq 2$)

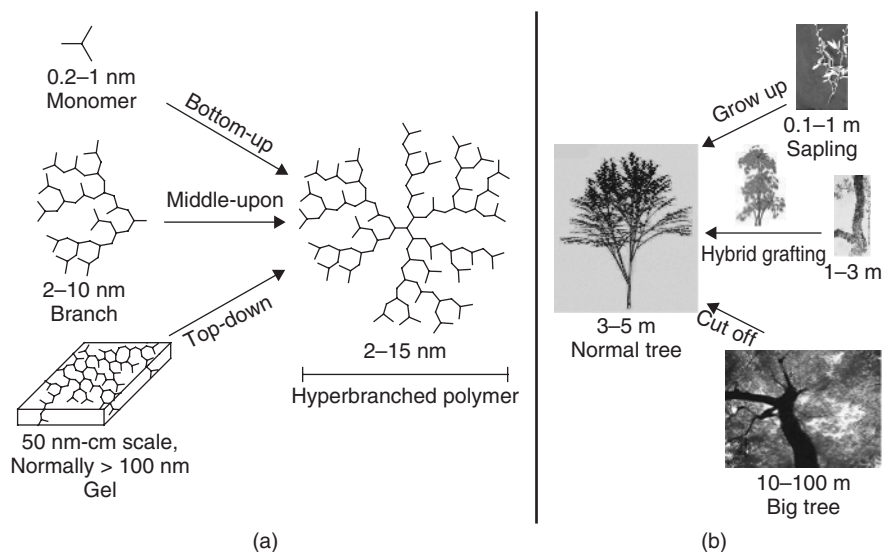


Figure 1.10 Three avenues to obtain hyperbranched polymers (a) and three manners to get a tree (b). Reprinted with permission from Ref. [36].

(ii) self-condensing chain-growth polymerization of AB*-type (latent AB₂) monomers, (iii) polycondensation of symmetric monomer pairs of A₂ and B₃ monomers under the rule of Flory's equal reactivity, and (iv) polymerization of asymmetric monomer pairs (coupling-monomer methodology, CMM) with the principle of nonequal reactivity (Table 1.4). The first two methodologies can also be ranged as "single-monomer" strategy, and the last two ranged as "double-monomer" strategy.⁵ The details will be shown in the following chapters respectively. Polycondensation of AB_g-type monomers gave rise to various HPs without the risk of gelation.^{5,75} However, most of AB_g monomers are not commercially available, limiting the large-scale production of HPs. Alternatively, polymerization of AB* monomers including vinyl and cyclic molecules can result in HPs capable of controlling DB by employing self-condensing vinyl polymerization (SCVP),⁷⁶ atom transfer radical polymerization (ATRP),^{77–81} ring-opening polymerization (ROP),^{82–86} and proton-transfer polymerization (PTP)⁸⁷ techniques. Polycondensation of A₂ and B₃ monomers may achieve soluble HPs with the advantage of commercial availability of monomers.^{88,89} But it should be noted that high risk of gelation exists during reaction, and special skills such as slow addition

Table 1.4 Synthesis Approaches for HPs via Bottom Up Ideology

Strategy	Methodology	Approach	Lead author	Year	Reference
Single-monomer	AB _g polymerization	Condensation model	Kim/Webster	1987	[12–14]
		Addition model	Hobson/Feast	1997	[75]
	AB* polymerization	SCVP	Fréchet	1995	[76]
		ATRP	Matyjaszewski	1997	[77–80]
		ROP	Suzuki	1992	[82]
			Penczek	1999	[83]
			Hult	1999	[84]
			Frey	1999	[85]
			Yan	1999	[51,86]
		PTP	Fréchet	1999	[87]
Double/multiple-monomer	Symmetric monomer pair	A ₂ + B ₃	Jikei/Kakimoto	1999	[88]
			Emrick/Fréchet		[89]
	Asymmetric monomer pair (CMM)	AA' + B'B ₂	Yan/Gao	2000	[92]
		AA' + B' ₂ + B'B ₂	Gao/Yan	2000	[94]
		A ₂ + CB _g	Gao/Yan	2001	[95–97]
		ABA ₂ + CD _g	Gao/Yan	2001	[95,98]
		A* + CB ₂	DSM Research	2001	[99]

of A_2 monomers to the diluted solution of B_3 and moderate catalysts are needed to delay the gelation point.^{90,91} In the CMM, based on the rule of nonequal reactivity of functional groups in specific monomer pairs such as AA' and $B'B_2$, AB_2 -type intermediate would predominantly form *in situ* in the initial stage of polymerization if the reactivity of A' is faster than that of A or the reactivity of B' is faster than that of B ; further reaction would produce hyperbranched macromolecules without gelation.^{5,92–95} More than 10 families of HPs including hyperbranched poly(sulfoneamine)s, poly(ester-amine)s, poly(amidoamine)s, poly(amido-ester)s, poly(urethane-urea)s, and polyesters have been prepared via CMM in various research groups and companies.^{96–99} Most recently, the kinetic analysis was also done for the reaction system of “ $A_2 + CB_2$ ”, obtaining theoretical results that are in accordance with the experiments.¹⁰⁰ The newly developed CMM possesses both the merits of commercial availability of monomers and no risk of gelation, facilitating the large-scale production and industrial application of HPs.

Through the middle upon ideology, various new polymers derived from HPs can be obtained by the “attach to,” “grafting from,” “grafting through,” and “building block” approaches (Figure 1.11).^{5,36} The details have been published in a comprehensive review.⁵ Modification of HPs by the “attach to” approach could dramatically change the nature of the polymer such as the T_g and thermal decomposition temperature (T_d) values, because of the significant

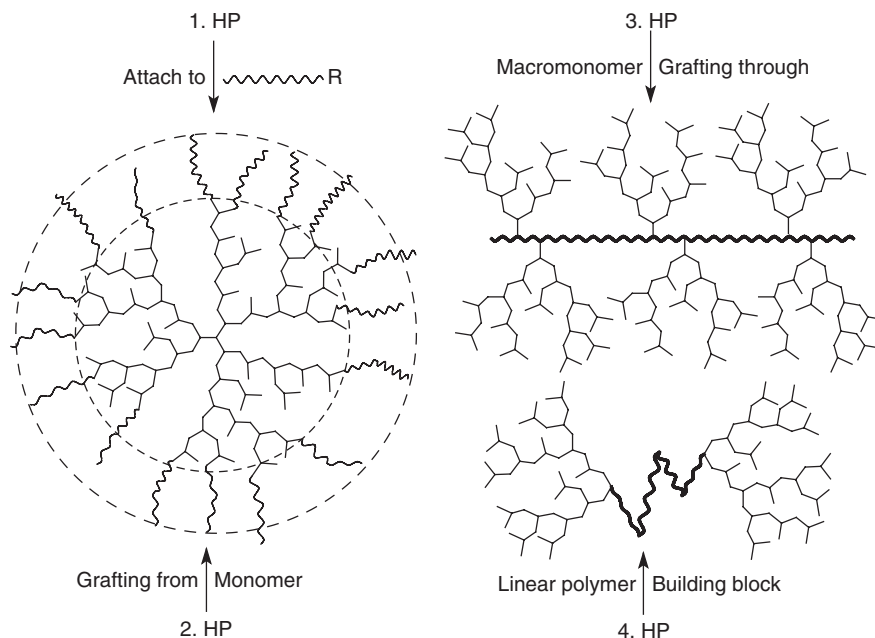


Figure 1.11 Four approaches to modify HPs and construct complex dendritic structures via middle upon ideology.³⁶

effect of terminal groups on the properties of HPs. For instance, T_g of hyperbranched polyphenylene can be varied over a wide range, from 96 °C for the polymer with α -vinyl phenyl end groups to 223 °C for the polymer with *p*-anisole end groups.¹⁵ Through the “attach to” approach, functional HPs such as liquid crystalline,¹⁰¹ fluorescent HPs,^{102,103} and amphiphilic HPs^{61,104} were prepared by immobilization of mesogenic, fluorescent molecules, and suitable molecules or chains with opposite polarity on HPs, respectively. Amphiphilic HPs can play the role of a dendritic box to load guest compounds such as dyes and drugs.

HPBs are accessible by *in situ* polymerization of monomers with HPs as macroinitiators, via the “grafting from” or the “terminal grafting” approach. The physical properties such as polarity, solubility, and flexibility as well as the self-assembly capability of HPs, can be readily tailored by selection of desired monomers. The techniques of controlled radical polymerization such as ATRP, anionic polymerization, and cationic polymerization have been introduced to make HPBs via reaction processes of macromolecular initiator-first and *in situ* one-pot grafting.^{105–112} The generally used HP macroinitiators include HPG, PEHMO, hyperbranched polyester of Boltorn, PEI, and so on.

The “grafting through” approach refers to polymerization of hyperbranched macromonomers to prepare cylindrical HPs or HP-grafted combburst polymers.¹¹³ Alternatively, with HPs as building blocks, more complex macromolecules can be constructed.¹¹⁴ After the pioneering work of Fréchet *et al.* on multibranched polystyrene,¹¹⁵ Frey and coworkers have studied complex branched polymers comprehensively.^{116–119} However, more efforts are required to further their remarkable development in terms of synthesis, purification, properties, and applications, as compared with dendronized polymers.

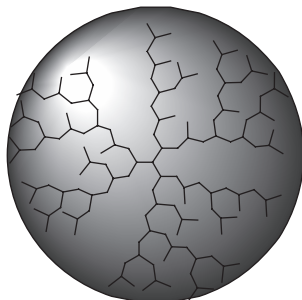
1.4.4 Applications

On the basis of their unique structures and properties aforementioned, HPs are promising in many applications such as additives, coatings, gene/drug carriers, nanoreactors and nanocapsules, and multifunctional platforms, as listed in Figure 1.12, of which bio- and nanorelevant applications will be discussed in Chapters 15 and 16, respectively.³⁶

Recently, the application of HPs in supramolecular chemistry is arousing the tremendous interest of researchers. For one thing, just like birds and nests in a tree, core-shell amphiphilic HPs can be used in supramolecular encapsulation to load guest molecules owing to their intramolecular cavities (Figure 1.13). Dyes, drugs, metal–ion complexes, and inorganic nanoparticles have been successfully filled into hosts of amphiphilic HPs including HPG,^{61,120–122} poly(amidoamine) (PAMAM),¹²³ poly(sulfoneamine),¹²⁴ PEI,¹²⁵ and poly(ester amide).¹²⁶ For the loading of dyes and drugs into the mixture of water and oil, phase transfer occurs generally with the indicative change of the color getting thinner for the guest phase and thicker for the host phase (Figure 1.13). Thus, the loading capacity (C_{load}) can be easily obtained from the UV–vis measurements for either the

Nature and properties:

1. Controllable size, 2–15 nm
2. Highly reactive groups
3. Tailor-made properties
4. Scaling-up production
5. No aggregation in bulk
6. High solubility in solvent
7. Possibly biodegradable
8. Low to no toxicity
9. Intramolecular cavities
10. ...



Potential applications:

1. Additives
2. Reactive nanoplatform
3. Coatings
4. Supramolecular encapsulation
5. Functional self-assembly
6. Electron/energy/light-harvesting
7. Nanoreactor
8. Gene/drugdelivery
9. Sensor, catalyst
10. ...

Figure 1.12 Characters and potential application fields of HPs.

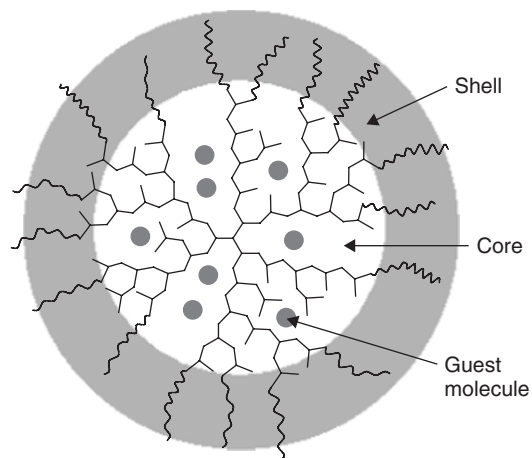
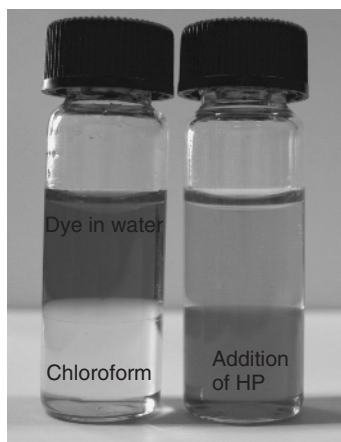


Figure 1.13 Supramolecular encapsulation of hyperbranched polymer to guest molecules (top), and photographs of nests and a bird in a tree (bottom). The bottom photographs are obtained from Internet.

water or the oil phase. By design of special structures, HP hosts can be used to selectively trap particular guests from mixtures and then release them under certain surroundings, declaring that HPs are a promising option in the separation and purification of mixtures as well as in the collection of wastes and in environmental protection.

Besides single-guest encapsulation, double or multiple-guest encapsulation, especially synergistic encapsulation, was found by Gao and coworkers, suggesting that the C_{load} of one sort of guests can be considerably increased in the presence of other sorts of guests.¹²³ Such a synergistic encapsulation indicates the unicity and complexity of HP-based host–guest chemistry as compared with the relatively smaller hollow hosts such as cyclodextrins, cucurbiturils, and calixarenes. It has been found that the C_{load} of HPs is dependent on the factors of (i) polarity difference between core and shell layers (the larger difference, the higher C_{load}), (ii) size or MW of the HP core (the bigger size, the higher C_{load}), (iii) DB (usually the greater the DB, the higher the C_{load}), (iv) degree of modification (a moderate modification facilitates guest loading, and either too high or too low is unfavorable), and (v) interaction force between the host and the guest (polyelectrolyte host promotes the loading of guests with opposite charges), etc.³⁶

Supramolecular self-assembly of HPs highlights the research progress of this subject, as demonstrated in a recent feature article from Zhou and Yan.¹²⁷ Classically, only regular molecules such as surfactants and polymers with well-defined structures such as block copolymers with narrow PDIs and dendrimers could self-assemble into ordered objects. On the contrary, HPs possess irregular structures and randomly branched units, implying that it would be difficult for HPs to perform supramolecular self-assembly behaviors. Nevertheless, HPs have been actually demonstrated recently as a versatile materials to show miraculous assembly behaviors after the landmark work of Yan and coworkers who discovered the macroscopic molecular self-assembly by using poly(ethylene oxide) (PEO)-grafted hyperbranched PEHMO.¹²⁸ Up to now, assembly objects covered from macroscopy to nanoscale have been achieved with various morphologies and functions, as shown in Figure 1.14,^{36,129–136} not only greatly enlarging the extension and intension of supramolecular chemistry, but also opening a promising new field. Being novel building blocks or precursors of self-assembly, HPs have several advantages over conventional molecules: (i) the cavities associated with HPs endow enough room for the adjusting of molecular configuration to form ordered structures; (ii) the multiarms or multifunctional groups afford strong multivalent interactions among primary assemblies making the resulting structures ultrastable; (iii) the globular topology favors the aggregation of macromolecules from any direction; and (iv) the functional groups at linear units may provide extra force for assembly by hydrogen bonding. Owing to the combined merits of big size, stable and flexible structures, the vesicles of multiarm HPs could be used as model membranes to mimic the fusion and fission behaviors of cells under optical microscopy in aqueous solution,¹³⁷ advancing the development of bionics that may give the answer for the highlighted question of “how far can we push chemical self-assembly” presented by Science in its 125th anniversary issue.¹³⁸

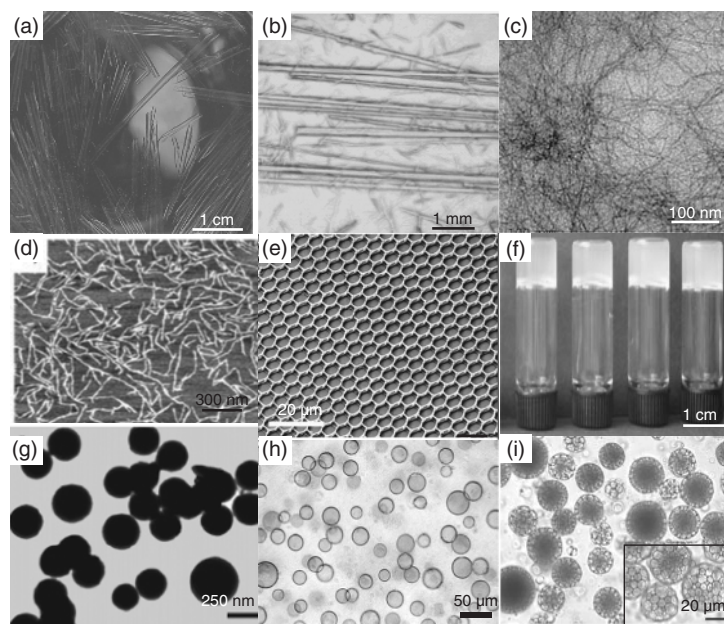


Figure 1.14 Selected self-assembled structures of amphiphilic hyperbranched polymers: macroscopic tubes (a),¹²⁸ mesoscopic tubes (b),¹²⁹ microscopic tubes (c),¹³⁰ nanoscale fibers (d),¹³¹ honeycomb films (e),¹³² physical gel (f),¹³³ spherical micelles (g),¹³⁴ vesicles (h),¹³⁵ and composed vesicles (i).¹³⁶

Furthermore, Liu *et al.* reported an interesting work by the combination of supramolecular encapsulation and self-assembly of HPs to fabricate large-area honeycomb-like films with strong fluorescence via self-assembly of dye-loaded hyperbranched PAMAM.¹³² The emission color or wavelength can be readily tuned by the encapsulated dyes, demonstrating the versatility and flexibility of the supramolecular chemistry of HPs.

Most recently, Gao *et al.* studied the self-assembly of miktoarm HPBs for the first time.¹³⁹ As shown in Figure 1.15, the dendritic brushes were synthesized by self-condensing atom transfer radical polymerization (SC-ATRP) of clickable initiator–monomer (click inimer), 3-azido-2-(2-bromo-2-methylpropanoyloxy) propylmethacrylate, followed by one-pot orthogonal multigrafting of PEO and poly(methyl methacrylate) (PMMA) heteroarms via click “attach to” and ATRP “grafting from” approaches, respectively. Self-assembly of the brushes with weight-average molecular weight (M_w) of 204,500 and PDI of 2.62 in DMF and water resulted in spherical micelles with diameters of 150–300 nm. In DMF and methanol, large assembled sheets can be observed. Significantly, the polymerization can be extended to copolymerization of click-inimer and 2-hydroxyethyl methacrylate (HEMA), affording HP with heterofunctional groups of azido, bromo, and hydroxyl. Further one-pot modification of the

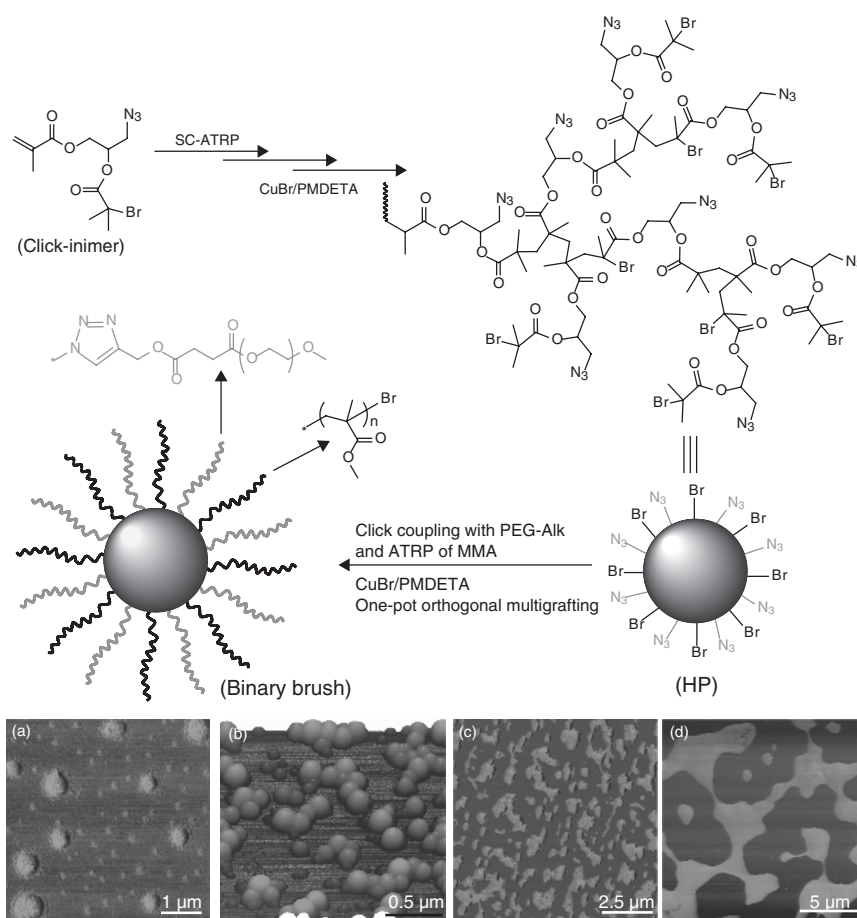


Figure 1.15 Synthesis of miktoarm hyperbranched polymer brushes by SCVP of click-inimer (top), and their dynamically self-assembled structures (bottom) in DMF/water system (a, b) and DMF/methanol system (c, d). Reprinted from Ref. [139] with permission.

multifunctional HP by click chemistry, esterification, and ATRP techniques gave rise to ternary hyperbranched brushes with hydrophilic PEO chains, and hydrophobic aliphatic and poly(*tert*-butyl acrylate) chains. In the DMF and water system, the ternary brushes can self-assemble dynamically into the dendritic tubes with dimensions of hundreds of micrometers. The dynamic assembly mechanism was speculated by the measurements of scanning electron microscopy (SEM), transmission electron microscopy (TEM), and NMR-tracing. The self-assembly of miktoarm HPs opens the door for construction of complex superstructures that may have multiple functions.

In addition, HPs showed great potential in bioapplications. Owing to its water-solubility and biocompatibility, HPG has been widely researched as a

drug carrier.¹²² The MW could be improved to around half a million with controlled anionic polymerization in solution¹⁴⁰ and on solid surfaces,¹⁴¹ showing fascinating potential in bionanotechnology. After coating HPG on CdTe quantum dots (QDs), the cytotoxicity of QDs was remarkably decreased, and the biostability of QDs significantly improved since the fluorescence of HPG-grafted QDs could be clearly observed after incubating with cells for 24 h, whereas naked QDs were almost completely faded (Figure 1.16).¹⁴² Hyperbranched PAMAM is another promising material that could possibly replace the famous PAMAM dendrimer in bionanotechnology, as it shows nontoxicity and high efficiency in gene transfection when modified with phenylalanine as compared with PEI (Scheme 1.2).¹⁴³ Hyperbranched polyphosphates¹⁴⁴ (Scheme 1.3) and polylysines¹⁴⁵ were also reported for potential bioapplications.

Besides the aforementioned potential fields, various new applications can be extended and explored in terms of different demands on the foundation of unique structures and special properties of HPs.

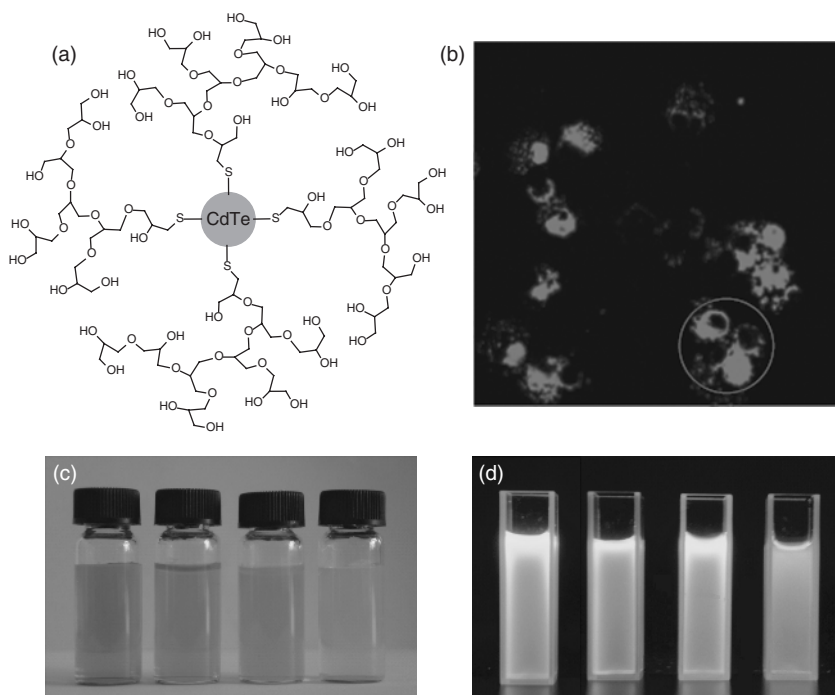
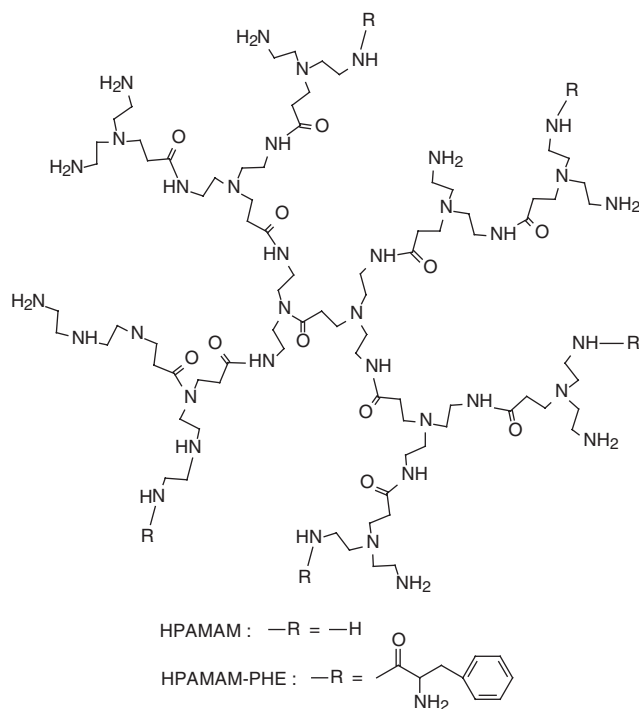


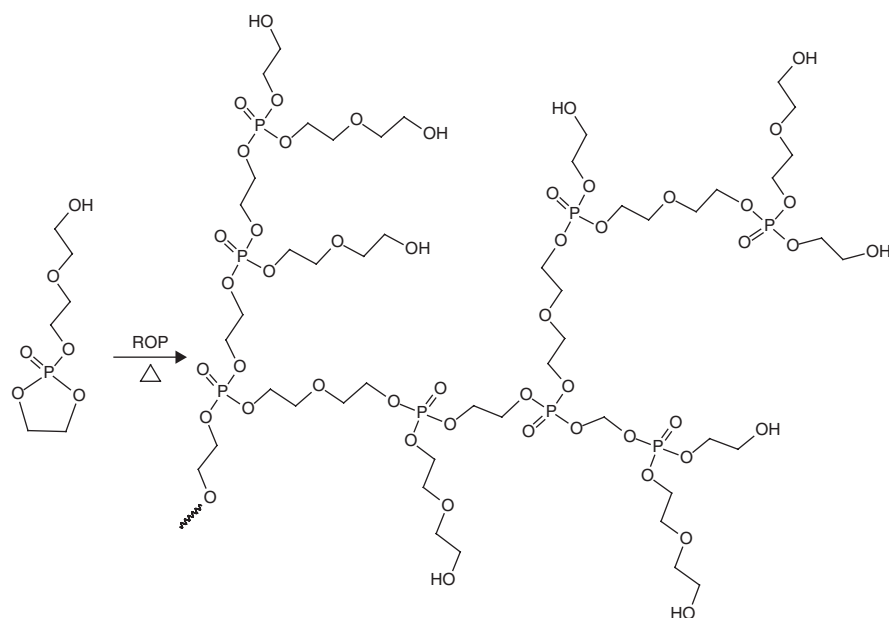
Figure 1.16 Schematic structure of hyperbranched polyglycerol-grafted CdTe quantum dot, QD@HPG (a), confocal microscopy image of A375 cells incubated with QD@HPG (at 2 mg/mL for 8 h) (b), photographs of pristine QDs and QD@HPGs with different amounts of HPG in aqueous solution under daylight (c), and irradiated at 365 nm (d). Reprinted from Ref. [142] with permission.



Scheme 1.2 Chemical structures of hyperbranched poly(amidoamine) (HPAMAM) and HPAMAM modified with phenylalanine (HPAMAM-PHE).¹⁴³

1.5 CONCLUSIONS

HPs are one of the major subclasses of dendritic architecture following linear, cross-linked, and chain-branched ones. Even though HPs have irregular structures with random branched topology, they still possess properties similar to dendrimers, such as low viscosity, high solubility, and large number of functional groups. From the philosophy viewpoint, the imperfect structure partly furnishes HPs with unlimited space for modification, functionalization, control over topology, tuning of DB, adjusting of MW and PDI, and hybridizing by copolymerization and terminal grafting, and so on. Such a flexibility makes the vitality of HPs inexhaustible. Hence, the progress of HPs can not only push the development of polymer science and engineering as well as related subjects, but can also inspire the thoughts of researchers and spread much wider the application realm than the prediction. Despite the limited products of commercialized HPs at present, we believe that more and more industrial applications would be achieved for HPs with their fast development in future, as linear polymers have exhibited in the past century.



Scheme 1.3 Synthesis of biocompatible hyperbranched polyphosphates by thermal ring-opening polymerization (ROP).¹⁴⁴

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