

Functional Polymers and Dendrimers: Reactivity, Molecular Architecture, and Interfacial Energy

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The interaction of polymers with their environment depends largely on the functional groups they carry. Interfaces between different polymers or between polymers and other surfaces can be strengthened through the design of molecular interactions such as hydrogen bonding and through the control of polymer architecture. The placement of functional groups at polymer chain ends or in well-defined segments can determine the ultimate properties. Three-dimensional synthetic polymers such as dendrimers can be fashioned to encapsulate reactive sites or provide highly controlled surfaces and interfaces.

The term "functional polymer" is used to describe polymers that carry reactive functional groups that can participate in chemical processes without degradation of the original polymer chains. Although functional polymers are abundant in nature, this article focuses exclusively on synthetic functional polymers that are obtained by covalent polymerization of simple monomers. Given the nature of the processes used in covalent polymerizations, the reactive groups of functional polymers may be incorporated into the main chain, as pendant groups, or even as the chain ends of the macromolecule (1). Examples of functional polymers with reactive groups in the main chain or in the side chain are poly(isoprene) (natural rubber) and poly(acrylamide), polymers that have carbon-carbon double bonds or primary amide functional groups at regular intervals throughout their main chain or pendant to the main chain, respectively.

Functional Polymers: From Homopolymers to Block Copolymers

Although both poly(isoprene) and poly(acrylamide) are vinyl homopolymers containing a single type of monomer unit throughout the polymer chain, functional polymers frequently incorporate two or more different monomers A and B scattered randomly throughout the chain (a random copolymer) or distributed within the chain in a more ordered fashion. Indeed, copolymers in which two vinyl monomers A and B are connected to one another in a regularly alternating fashion throughout the chain do exist (1), but these highly regular copolymers are seldom encountered. However, polymer chemistry provides useful techniques for the preparation of precisely

structured block copolymers (2).

An AB diblock copolymer is characterized by polymer chains that each contain a sequence (block) of monomer A linked to a sequence of the second monomer B. In similar fashion, an ABA triblock would have a sequence of monomer A followed by a central sequence of B, itself attached to another sequence of A. The ability to prepare block copolymers with varying sequence lengths is of particular relevance to functional polymers because different reactive groups may be placed in well-defined and segregated sections of a single chain.

In addition, the placement of dissimilar sequences of monomers in close proximity to one another within the same chain often results in unique properties that cannot be matched by homopolymers. For example, the commercially available thermoplastic elastomer Kraton-D (3) is an ABA triblock copolymer in which short styrene blocks are on either side of a long central block of butadiene. This material is not only a rubbery elastomer at room temperature, but it also behaves as a thermoplastic when heated, allowing it to be molded and remolded whenever necessary. In contrast, classical elastomers (rubbers) owe their rubbery properties to cross-links that are introduced once and for all during their vulcanization (4). Once shaped into rubber objects and vulcanized, these materials cannot be reused or even reshaped. The thermoplastic elastomers do not require any chemical vulcanization as their cross-linking is physical in nature, entirely the result of aggregation of the glassy styrene blocks, a thermodynamic interfacial process that occurs spontaneously at room temperature and is thermally reversible.

Polymer Blends, Interfacial Interactions, and Hydrogen Bonds

The demand for new materials that meet the needs of very specific uses frequently suggests that a hypothetical structure com-

binning the features of two well-known polymers would be ideal. Although copolymerization is an attractive technique, the simplest intuitive approach would be to blend two polymers, as the physical properties of the blend might exceed the weighted average of the properties of each individual component (5). However, because most polymers lack miscibility (6), a problem may arise at their interface: High interfacial energy translates into very coarse phase structures with the formation of large domains of separate polymers that do not stick together. As a result, the blend or polymer alloy may have very poor properties. Improvements in material properties will therefore largely depend on the achievement of some control over interfacial parameters through the control of interaction forces at the interface.

One approach to improved miscibility is based on simple thermodynamic considerations. Two polymers will mix well if the change in Gibbs free energy, ΔG , resulting from mixing is negative

$$\Delta G_{\text{mix}} = \Delta H_{\text{mix}} - T \Delta S_{\text{mix}} \quad (1)$$

Little favorable contribution can be expected from the entropy term ΔS_{mix} , whereas the enthalpy of mixing ΔH_{mix} may well be favorable if specific interactions between complementary functional groups on the two polymers can be introduced.

Therefore, numerous approaches to improved miscibility (compatibility) have been developed, including the formation of hydrogen bond (7, 8), dipole-dipole (9), charge transfer (10), and even ionic interactions (11). For example, although poly(styrene) and poly(vinylpyridine) do not mix, it is possible to obtain a miscible blend by introducing phenolic functionalities into

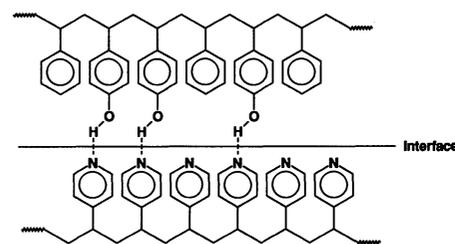


Fig. 1. Formation of hydrogen bonds between 4-hydroxystyrene and 4-vinylpyridine units at the polymer-polymer interface. The symbol \sim denotes the continuation of a polymer chain.

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the poly(styrene) structure (7). When a random copolymer of styrene and 4-hydroxystyrene is blended with poly(vinylpyridine), a favorable interface between the two polymers results from the enthalpically driven formation of hydrogen bonds between the pyridyl and phenolic moieties of the two polymers (Fig. 1).

A related approach involving the use of both block copolymers and enthalpically favorable interactions of functional groups has been used by Kramer and co-workers (12) to effect the strengthening of polymer-polymer interfaces. A known strategy (13) for interfacial strengthening of a system consisting of two immiscible homopolymers A and B has been to add a small amount of an AB block copolymer (14). Under appropriate conditions, the free energy of the system is minimized when the block copolymer segregates to the interface between the two homopolymers in such a way that each of its individual blocks becomes entangled with the corresponding homopolymer on either side of the interface. As a result, it acts as an adhesive joining together two homopolymers that normally have no affinity for each other. Obviously, the strengthening effect depends at least partly on the areal chain density of the copolymer at the interface and therefore on the ability of the copolymer to migrate to this interface (15).

Shull *et al.* (16) recently demonstrated that a high areal density is readily achieved by the introduction of an attractive interaction, such as hydrogen bonding, between one of the homopolymers and one of the blocks of the added copolymer. Therefore, Kramer and co-workers (12) strengthen the interface between poly(styrene) and poly(vinylphenol), two immiscible polymers, using a diblock copolymer containing connected blocks of styrene and vinylpyridine. In this system, the favorable enthalpic interactions between the vinylpyridine portions of the copolymer and the poly(vinylphenol) homopolymer help drive the copolymer to the interface, where a remarkably high areal density of the copolymer is observed with considerable concomitant strengthening.

Controlling the Chain Ends of Polymers

Functional groups may be introduced in reproducible fashion at one or both ends of a polymer chain. Polymers that contain two reactive end groups per molecule are termed telechelic polymers (17). Step growth polymers (such as nylon-6,6), obtained by the polycondensation of two bifunctional monomers (adipic acid and 1,6-hexanediamine), always have free functional groups at each end of the chain. The exact nature of the chain ends can be controlled through the stoichi-

ometry and reaction conditions (1). In contrast, the placement of specific functional groups at one or both chain ends of a polymer obtained by a chain growth process, such as a vinyl polymerization, is a much more demanding task that requires careful consideration of the initiation and termination steps, as well as possible side reactions. Because initiating species become incorporated into the polymer, the use of a functional initiator can provide control over the chain end at which polymerization is started. Similarly, the reaction that terminates polymer growth can introduce a specific functionality at the other terminus of the chain. Examples of functionalized initiators (Fig. 2) include azo compounds (18) (such as 1), used in free radical polymerizations to introduce a carboxylic acid terminus, and the reactive ether 2, used to introduce a masked alcohol functionality in the living polymerization of a vinyl ether (19). An example of functionalization by chain termination is the carboxylation (20) of living poly(styrene) (3) prepared by anionic polymerization (Fig. 2).

Effect of Molecular Architecture on Functional Polymers

Most polymers consist of "linear" chains that are randomly coiled and entangled with their neighbors. These chains are frequently branched, as a result of synthetic planning, grafting reactions (1), or side reactions. Star polymers, in which several linear chains originate from a central core, can be prepared by attaching linear polymer chains to a multifunctional core through a reactive group placed at one end of each chain (21) or by initiating the polymerization of several polymer chains from an activated multifunctional core (22). Branching is always accompanied by substantial changes in rheological properties: Both branched and star polymers have significantly lower viscosities than linear polymers of the same molecular weight. Another effect of branching is the multiplication of reactive chain ends.

The control of molecular architecture is important even for well-established commodity polymers. For example, a recently developed "star-branched butyl" polymer takes advantage of well-designed carbocationic chemistry to afford a new poly(isobutylene) rubber that is easier to handle than classical butyl rubber because its star shape results in a lower melt viscosity. In the approach pioneered by Wang and co-workers (23), the product obtained in the cationic copolymerization of isobutylene with a small amount of isoprene, a typical "butyl" rubber, is grafted onto the double bonds of a short triblock copolymer consisting of connected blocks of styrene-butadiene-styrene. The grafting process is a simple electrophilic addition involving the cationic ends of the growing butyl rubber chains with the double bonds of the poly(butadiene) block of the triblock. These additions produce new carbocationic centers that terminate readily by abstracting hydride from some of the isoprene monomer still present in the reaction medium. Although a true star topology is not obtained, the "star-branched" product has a high density of branches on a short central chain, approximating the shape and matching the properties of a true star polymer. In practice, the extent of star formation is limited to less than 25%, affording a mixture of star-branched and linear butyl rubber with near ideal rheological properties. The entire process can be carried out in the existing butyl reactors that operate at the very low temperature (near -90°C) required for this type of carbocationic rubber chemistry.

In recent years, several types of functional polymers with highly unusual architectures have appeared. These include sheet-like two-dimensional polymers (24) as well as three-dimensional structures such as dendrimers (25-28), hyperbranched polymers (29, 30), and the threaded linear polymers, polyrotaxanes (31).

Dendrimers are highly branched three-dimensional macromolecules with a branch point at each monomer unit. Therefore,

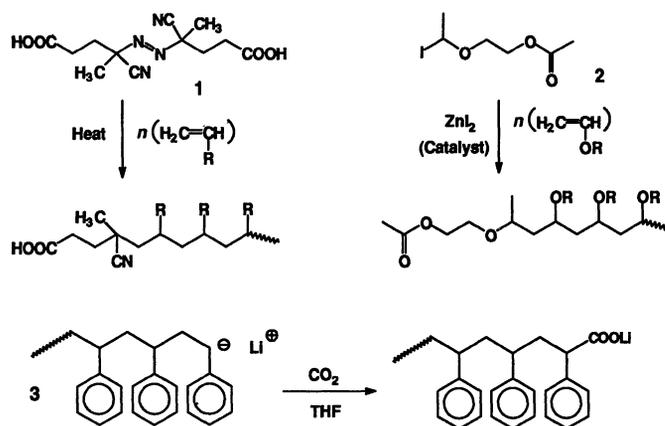


Fig. 2. Introduction of reactive groups at a chain end by use of functional initiators (top structures) or chain termination (bottom). Each polymer is shown with three repeating units; ~ denotes the continuation of the chain.

they are potentially the most highly branched structures that exist. As a result of this high degree of branching, large dendrimers adopt a globular shape in which all bonds converge to a focal point or central core unit. Of particular interest in the context of functional polymers is the fact that dendrimers possess a very large number of chain ends. For example, polyether dendrimers prepared by our convergent growth method (26) (Fig. 3) have two branches at each monomer unit and therefore possess

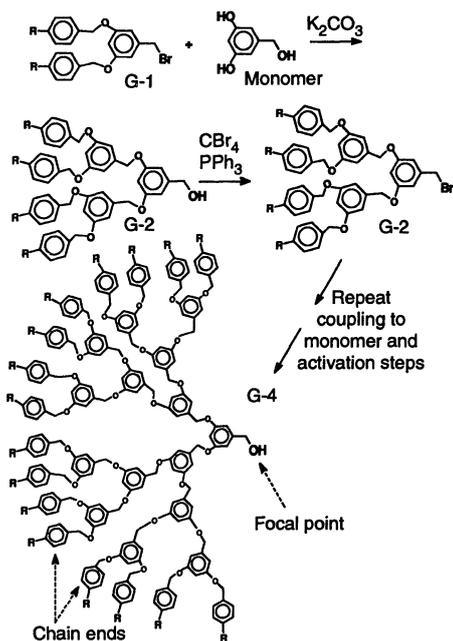


Fig. 3. Convergent growth of a fourth generation dendrimer (G-4) (30).

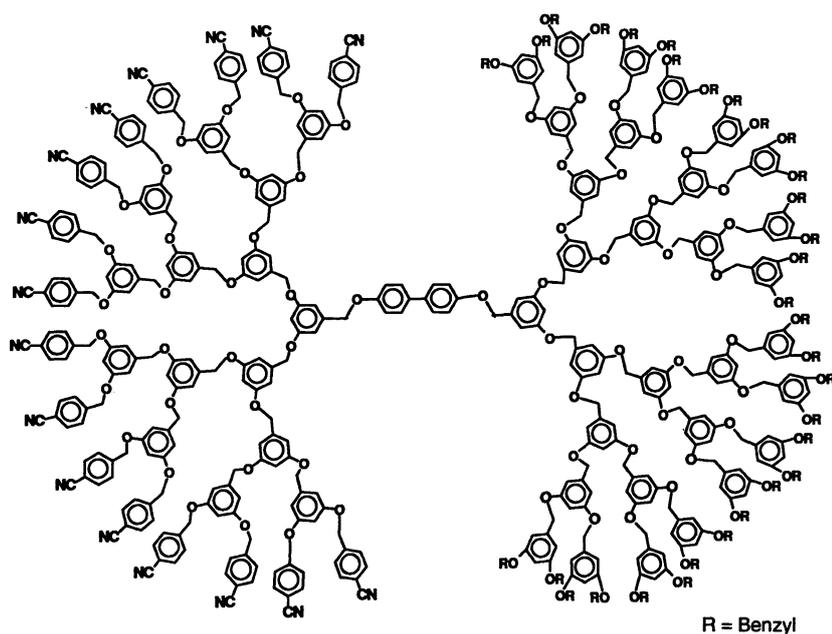


Fig. 4. Dendrimer obtained by the coupling of two dissimilar fragments to a central 4,4'-dihydroxybiphenyl core.

essentially the same number of chain ends as they have monomer units. The synthesis itself proceeds in steps, with each addition of monomer (a generation growth step) resulting essentially in the doubling of both the mass of the dendrimer and the number of its chain ends. Once large dendrimers have been prepared, the remaining reactivity of their focal point may be used to couple two or more fragments (or "dendrons") to a central core leading, for example, to structures with two dissimilar halves (32) (Fig. 4).

The steric considerations that dictate the globular shape of dendrimers also affect their ability to interact with neighboring molecules. A macroscopic (culinary) illustration for comparison of linear polymers and dendrimers is "cooked spaghetti" and "green peas," respectively. The former is heavily entangled, but the latter clearly is not. A similar situation prevails for Tomalia's well-known poly(amidoamine) Starburst dendrimers (25, 27) prepared by a divergent approach.

Because of their shape, dendrimers have very unusual physical as well as chemical properties (27, 33-35). As the molecular weight increases within a homologous series of dendrimers, the molecules undergo a transition from an extended to a globular shape. This transition is readily observed in a plot of intrinsic viscosity versus molecular weight (Fig. 5) (33). For classical linear polymers such as poly(styrene), the viscosity increases sharply with molecular weight according to the Mark-Houwink-Sakurada equation: $[\eta] = K M^a$, in which $[\eta]$ is the intrinsic viscosity of the polymer, M is its molecular

weight, and K and a are constants for a given polymer. Unlike almost all other macromolecules, including branched and star polymers, dendrimers do not obey this relation once a threshold molecular weight is reached. This deviation is easily understood if one considers that during generation growth, the volume of dendrimers increases cubically whereas their mass increases exponentially, a relation that does not hold true for other polymers. The existence of a molecular weight threshold that corresponds to the transition from an extended to a globular shape can be predicted by molecular modeling (36) and has also been demonstrated through solvatochromic (37) and other measurements (38).

Having established that large dendrimers acquire a globular shape, it is interesting to compare their properties with those of linear polymers consisting of essentially the same building blocks. Therefore, two polyesters were prepared from the same monomer, 3,5-dihydroxybenzoic acid: dendrimer 4 with benzyl ether end groups (39) and linear polyester 5 obtained by polycondensation of the monobenzyl ether derivative of the monomer (35) (Fig. 6). Samples of the two polymers with molecular weights near 11,000 were selected to allow a realistic comparison: Both polymers contain approximately the same number of monomer units and the same number of benzyl ether functional groups. In a solubility test with tetrahydrofuran (THF) as the solvent, the solubility of the dendrimer was found to be remarkably high, reaching 1.15 g/ml compared with 0.025 g/ml for the analogous linear polyester. In contrast, a linear polyester derived from 3-hydroxybenzoic acid, therefore devoid of any benzyl pendant functional groups, is totally insoluble in THF. Miller, Neenan, and co-workers (40) have also reported solubility enhancements of more than 10^5 for dendritic poly(phe-

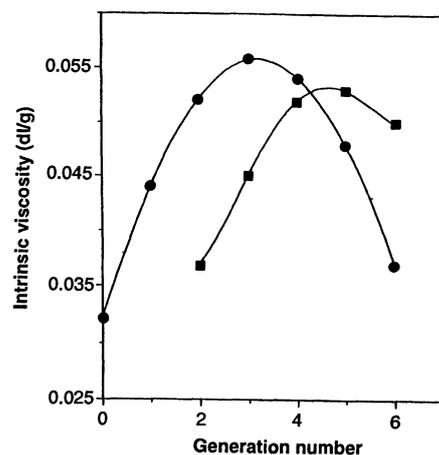


Fig. 5. Plot of intrinsic viscosity versus generation number for typical polyether dendrimers (30). (●) Tridendron on core; (■) monodendron.

nylenes) when compared to linear poly(*p*-phenylene). Although this figure may be excessive in that a more appropriate comparison would have involved the more soluble meta-linked poly(phenylene), it does confirm that the shape as well as the functionality of the molecule has a great effect on the molecular interactions and other parameters that control solubility and miscibility. A similar finding has been made by Gibson for polyrotaxanes (31).

A marked difference in chemical reactivity was also observed in the catalytic hydrogenolysis of both **4** and **5** with hydrogen gas and a solid Pd/C catalyst. Only the dendrimer **4** was debenzylated (39), whereas the linear polymer **5** was unreactive under a variety of reaction conditions (35). Although alternative explanations are possible, it is tempting to associate the unusually high solubility and reactivity of the dendrimer when compared with its linear analog to the globular architecture of the former.

The conformation of dendrimer molecules in the solid state and in solution is still controversial. In particular, conflicting predictions on the shape of dendritic molecules have been made on the basis of theory and of molecular modeling. The model of de

Genes and Hervet (41) suggests a density minimum at the center of the dendrimer and predicts that ideal dendritic growth will only occur until a certain generation is reached, at which point steric congestion will prevent further growth. Computer-assisted molecular modeling experiments by Goddard and co-workers (36) indeed suggest that as size increases, the shape of Starburst dendrimers (25, 27) progresses from open structures to closed spheroids with well-developed internal hollows and a dense surface. This view is not shared by Lescanec and Muthukumar (42), whose simplified kinetic model of dendritic growth predicts maximum density at the core of the dendrimer and a distribution of end groups throughout the structure. This model has some valuable features (33), but it fails to account for some of the properties of well-known dendrimers (27, 35, 43). A better model might not be based on a purely kinetic algorithm and would consider the geometric and other requirements of the bonds being formed as well as the thermodynamic feasibility of indiscriminate inward folding of chain ends. For example, would the free energy of polyester dendrimers such as **4** that contain multiple benzyl ether

chain ends be lower if the chain ends were folded in the ester monomer units rather than excluded to the periphery of the globule? The results of the comparative debenzylation experiments described above are consistent with readily accessible chain ends in this dendrimer.

As their name implies, hyperbranched polymers (29, 30) are also highly branched, but unlike dendrimers, their structure is neither regular nor highly symmetrical. Whereas dendrimers are obtained by careful stepwise growth of successive layers or generations, hyperbranched polymers are obtained in a single step by polycondensation of an A_2B monomer that contains two reactive groups of type A and one of type B. Functional groups A and B are selected in such a way that they can react with each other to form a covalent bond. Kim and Webster (29) have used the Pd-catalyzed polycondensation of 3,5-dibromobenzene boronic acid to prepare a hyperbranched poly(phenylene), and my group has used 3,5-dihydroxybenzoic acid to prepare a hyperbranched aromatic polyester (30, 44).

The structure of hyperbranched polymers is thought to be intermediate between those of linear polymers and dendrimers.

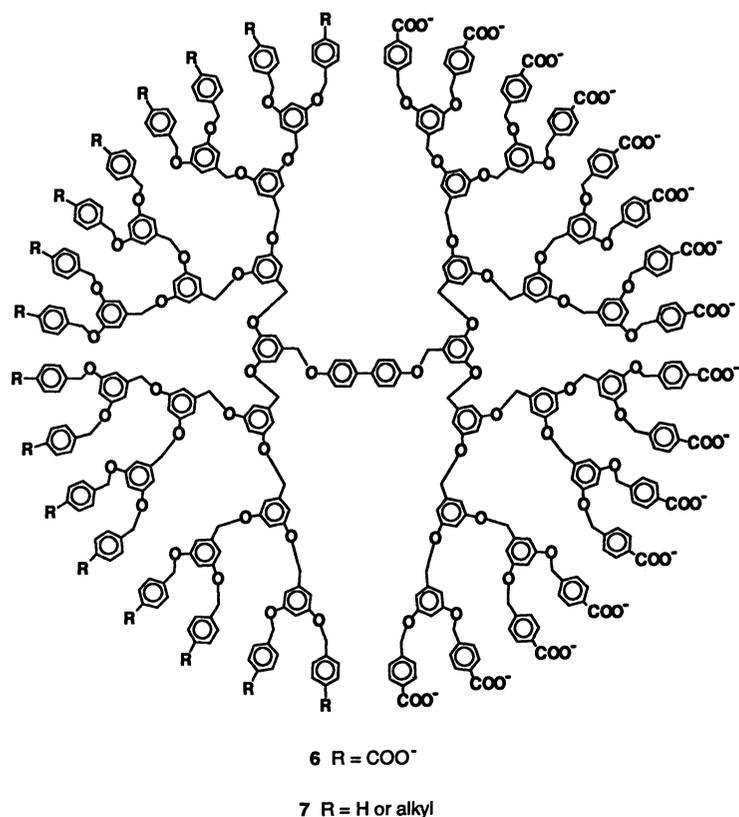
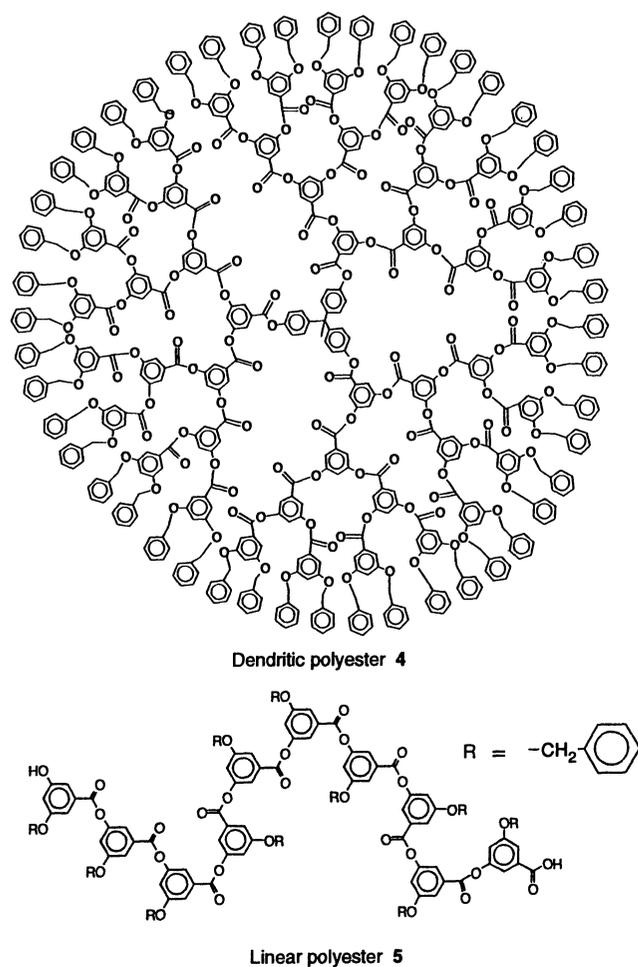
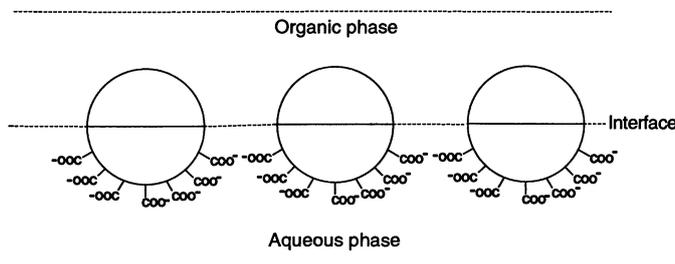


Fig. 6 (left). Dendritic and linear polyester with benzyl ether chain ends or pendant groups. **Fig. 7 (right).** Water-soluble dendrimer **6** (R = COO^-). Amphiphilic dendrimer **7** (R = H or alkyl).

Fig. 8. Liquid membrane of amphiphilic dendrimer **7** at the interface between water and an immiscible organic solvent.



Because of steric constraints and the statistical nature of the coupling steps, hyperbranched polymers have irregular structures, as some of the A groups remain unreacted, leading to the incorporation of "linear" segments (that is, monomer units coupled at two rather than three points) within a somewhat globular ensemble. Turner *et al.* (45) have shown that the viscosity-molecular weight behavior of the hyperbranched polymers does not show a maximum as observed with dendrimers; instead, they obey the Mark-Houwink-Sakurada relation, although their viscosities are anomalously low when compared to linear polymers of comparable size. In analogy to dendrimers, A_2B hyperbranched polymers have essentially the same number of reactive groups A as they have monomer units. However, unlike dendrimers, these functional groups are not all located at chain ends. The multiple functionalities of hyperbranched polymers coupled to their structure, which is frequently analogous to those of engineering plastics (1), make them particularly attractive for use as rheology modifiers, adhesives, components for reactive injection molding, and so forth (30, 45, 46). For example, we have recently reported the preparation of a hyperbranched polyurethane that can be isolated as a stable solid material but can be activated under mild thermal treatment to expose a large number of very active isocyanate groups (47). This type of functional polyurethane containing many masked isocyanate groups is likely to find applications in coatings and foams, where linear telechelic isocyanate-terminated polymers are in use today (48).

Defining Reactive Sites Through Steric and Interfacial Phenomena

Despite all the progress that has been made in the development of controlled methods (49) for the preparation of well-defined synthetic polymers, including living polymerization processes (50), spatially arranging functional groups in a predetermined fashion within functional polymers remains a challenge. Some very clever approaches involving the design of rigid "imprinted" surfaces prepared with the help of molecular

templates have been investigated (51). The pore size-specific introduction of functional groups within rigid macroporous polymers has opened new avenues formerly reserved to zeolites for applications in catalysis and biological separations (52). However, a common feature of these and other approaches to well-defined reactive sites is that they have all involved large monolithic entities consisting of aggregated and cross-linked polymers rather than single molecules. In contrast, dendrimers are isotropically soluble functional polymers with great potential for the precise arrangement or isolation of functional groups.

For example, Inoue and co-workers (53) reported the preparation of a porphyrin covalently encapsulated in a dendritic cage consisting of four "convergent" dendrimers attached to the porphyrin nucleus. Fluorescence quenching experiments showed that when large G-4 dendrimers (Fig. 3) were used to form the cage, the porphyrin core was effectively shielded from other relatively large molecules in solution while still remaining accessible to small molecules. This type of steric isolation of the metalloporphyrin, which is important to achieve certain biological functions, is most readily realized through the use of the functional dendrimers prepared by convergent growth (26).

Instead of insulating a reactive site at the center of a dendrimer, it is possible to place functional groups at the periphery of the globular structure, thereby delineating an interface with a volume "inside" the den-

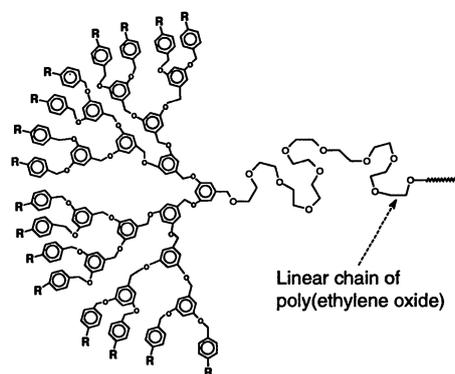


Fig. 9. Hybrid dendritic linear polymer obtained by attaching poly(ethylene oxide) to the focal point of structure G-4 (Fig. 3).

dimer and a space "outside." This goal is readily implemented through the construction of dendritic structures that have very polar or ionic chain ends and relatively nonpolar or hydrophobic building blocks (27, 43, 46, 54). Dendrimers with carboxylate chain ends (6, Fig. 7) are soluble in water and behave as static unimolecular micelles that retain their cohesion regardless of concentration. Because of its hydrophobic interior, dendrimer **6** is able to solubilize and concentrate organic molecules, such as pyrene, not normally soluble in water (43). The combination of a catalytic core with such a static micellar arrangement holds much promise for the development of organic chemistry in aqueous medium and for the mimicry of biological systems.

As discussed above, the versatile convergent method allows the construction of globular dendrimers that have an unsymmetrical but highly-controlled distribution of chain end chemistry (55). This approach enables the preparation of dendrimers that may be oriented at an interface or under the influence of an external stimulus. Indeed dendrimers can form monolayers at the air-water interface (56), and amphiphilic dendrimers such as **7** (Fig. 7) (43) are useful in forming interfacial liquid membranes or in stabilizing aqueous-organic emulsions (Fig. 8). A dendrimer built with two segregated types of chain ends—half electron donating and half electron withdrawing—(Fig. 4) can be oriented in an electrical field and has a very large dipole moment (32).

Finally, the combination of dendritic and linear polymers in hybrid block or graft copolymers, achieved recently (34, 57), affords an opportunity to optimize the structures of block copolymers for use as surface-active agents, compatibilizers, or adhesives. The small "footprint" of the dendrimer segment coupled to its multiple reactive chain ends (Fig. 9) make it an ideal candidate to maximize enthalpic interactions at an interface while allowing a high areal density of linear chains for entanglement with other polymers. These and other achievements in the preparation of functional polymers and copolymers with highly controlled architectures and precisely placed functional groups open new avenues for the preparation of well-defined molecular objects and devices.

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New Challenges in Biomaterials

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Significant opportunities and challenges exist in the creation and characterization of biomaterials. Materials have been designed for contact with blood, as replacements for soft and hard tissues, as adhesives, and as dental materials. Current methods of synthesis and characterization of these materials are outlined. Approaches for controlling the interface between tissue and biomaterials and ways in which the engineered materials may contribute to medicine are considered.

In general, biomaterials are substances other than food or drugs contained in therapeutic or diagnostic systems that are in contact with tissue or biological fluids. They are used in many pharmaceutical preparations—for example, as coatings for tablets or capsules or as components of transdermal patches. They play a central role in extracorporeal devices, from contact lenses to kidney dialyzers, and are essential components of implants, from vascular grafts to cardiac pacemakers (1). There are many current biomaterials applications (Table 1), found in about 2700 different kinds of medical devices, 2500 separate diagnostic products, and 39,000 different pharmaceutical preparations. Estimated annual sales of medical devices and diagnostic products in the United States is about \$24 billion, and that of pharmaceutical products exceeds \$80 billion (2, 3). Although biomaterials have already made an enormous health impact, the need exists for better polymer, ceramic,

and metal systems and improved methods of characterizing and testing them.

Synthetic Approaches to New Biomaterials

The development of biomaterials has been an evolving process. Many biomaterials in clinical use were not originally designed as such but were off-the-shelf materials that clinicians found useful in solving a problem. Thus, dialysis tubing was originally made of cellulose acetate, a commodity plastic. The polymers initially used in vascular grafts, such as Dacron, were derived from textiles. The materials used for artificial hearts were originally based on commercial-grade polyurethanes. These materials allowed serious medical problems to be addressed. Yet, they also introduced complications. Dialysis tubing may activate platelets and the complement system; Dacron-based vascular grafts can only be used if their diameter exceeds about 6 mm, otherwise occlusion can occur because of biological reactions at the blood-material and tissue-material interfaces; and blood-materials interactions can also lead to clot formation in an artificial heart, with the subsequent possibility of stroke and other complications.

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