HIGHLIGHT

Discovery of Dendrimers and Dendritic Polymers: A Brief Historical Perspective*

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ABSTRACT: A brief historical perspective relating the discovery of dendrimers and other dendritic polymers is presented. Dendritic polymers are recognized as the fourth major class of macromolecular architecture consisting of four subclasses, namely, (1) random hyperbranched, (2) dendrigrafts, (3) dendrons, and (4) dendrimers. The previous literature is reviewed with anecdotal events leading to implications for dendrimers in the emerging science of nanotechnology.

Keywords: dendrimers; nanotechnology; telechelics; artificial proteins; dendrigrafts; hyperbranched

DONALD A. TOMALIA

Donald A. Tomalia completed his undergraduate chemistry degree at the University of Michigan, Flint College and obtained his Ph.D. degree (physical-organic chemistry) from Michigan State University. He joined the Dow Chemical Company as a synthetic polymer chemist with a focus on functional monomers and polymers, where he held various research and management positions (1962–1989). During that time, he discovered the cationic polymerization of 2-oxazolines (1966) (J Polym Sci, A-1, 2253, 1966) and Starburst® dendrimers (1979) (Polym J, Tokyo, 17, 117, 1985). The oxazoline breakthrough was recognized by I.R.-100 Awards (1978, 1986), and the first dendrimer synthesis was noted by an R&D-100 Award (1991) and the Leonardo da Vinci Prize (Paris, 1996). In 1990, he joined the Michigan Molecular Institute (MMI) as Professor and Director of Nanoscale Chemistry & Architecture (1990–1999). In 1992, he co-founded Dendritech, Inc., the first commercial producer of dendrimers, and was named founding President and Chief Scientist (1992–2000). In 1998, he became Vice President of Technology for MMI (1998–2000) while simultaneously serving as Scientific Director for the Biologic Nanotechnology Center, University Michigan

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JEAN M. J. FRÉCHET

Medical School (1998–2000). In 2001, Dr. Tomalia founded Dendritic Sciences, Inc., which has joined with Starpharma (Melbourne, Australia) to form a dendrimer-based nanotechnology venture called Dendritic Nanotechnologies Inc. He serves as President and Chief Technical Officer of this dendritic polymer company with production and laboratory facilities located at Central Michigan University, Mt. Pleasant, Michigan. Other positions currently held by Dr. Tomalia include Distinguished Visiting Professor (Columbia University), Distinguished Research Scientist (Central Michigan University), and adjunct professor (Michigan Technological University).

He is listed as the inventor of over 100 U.S. patents and is author/coauthor of more than 180 peer-reviewed publications. Over 150 papers are focused in the dendrimer/dendritic polymer field, including a monograph entitled "Dendrimers and Other Dendritic Polymers" (Wiley) he co-edited with J. M. J. Fréchet (2001). Dr. Tomalia is a member of the American Chemical Society, Sigma Xi, The American Association for the Advancement of Science, and serves on the editorial advisory boards of Bioconjugate Chemistry (1999–) and NanoLetters (2000–).

Jean M. Fréchet obtained his first degree at the Institut de Chimie et Physique Industrielles (now CPE) in Lyon, France, and Ph.D. degrees at SUNY-CESF and Syracuse University. Following academic appointments at the University of Ottawa (1973–86) and Cornell University (1987–96), where he was the IBM Professor of Chemistry and later the holder of the Peter Debye Chair of Chemistry, he joined the Department of Chemistry at the University of California, Berkeley. He is currently Professor of Chemistry at UC Berkeley as well as head of Materials Synthesis at the Lawrence Berkeley National Laboratory. In 2001 he returned to Cornell University to give the George Fisher Baker Non-Resident Lectures in Chemistry. Jean Fréchet is the recipient of both the ACS Awards in Polymer Chemistry and in Applied Polymer Science. He is a member of the National Academy of Science, the National Academy of Engineering, and the American Academy of Arts and Sciences. His research is concerned with both fundamental and applied aspects of macromolecular science with emphasis on functional polymers from their design and synthesis to their applications.

Dendritic architecture is perhaps one of the most pervasive topologies observed on our planet. Innumerable examples of these patterns[1] may be found in both abiotic systems (e.g., lightning patterns, snow crystals, and tributary/erosion fractals) as well as in the biological world (e.g., tree branching/roots, plant/animal vasculatory systems, and neurons).[2] In biological systems, these dendritic patterns may be found at dimensional length scales measured in meters (trees), millimeters/centimeters (fungi), or microns (neurons) as illustrated in Figure 1. The reasons for such extensive mimicry of these dendritic topologies at virtually all dimensional length scales is not entirely clear. However, one might speculate that these are evolutionary architectures that have been optimized over the past several billion years to provide structures manifesting maximum interfaces for optimum energy extraction/distribution, nutrient extraction/distribution, and information storage/retrieval.

The first inspiration for synthesizing such molecular level treelike structures evolved from a lifetime hobby enjoyed by one of the authors (D. A. Tomalia) as a horticulturist/tree grower.[3] Although perhaps first conceptualized by Flory,[4–7] the first successful laboratory synthesis of such dendritic complexity did not occur until the late 1970s. It required a significant digression from traditional polymerization strategies with realignment to new perspectives. These perspectives utilized major new synthesis concepts that have led to nearly monodispersed synthetic macromolecules. This was the first time in the history of synthetic polymer science that precise abiotic macromolecules could be synthesized without the use of a biological system. The result was a unique core-shell

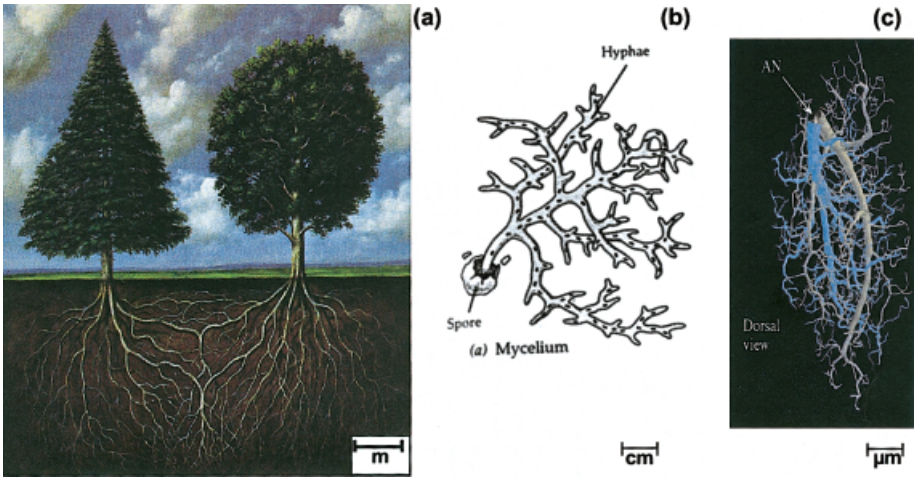

Figure 1. Coniferous and deciduous trees with root systems (a), fungal anatomy (b), and giant interneuron of a cockroach (c).

macromolecular architecture, now recognized as *dendrimers*.

The concept of repetitive growth with branching was first reported in 1978 by Buhleier et al.[8] (University of Bonn, Germany) who applied it to the construction of low molecular weight amines. This was followed closely by the parallel and independent development of the divergent, macromolecular synthesis of "true dendrimers" in the Tomalia group[9,10] (Dow Chemical Co.). The first article[9] using the term "dendrimer" and describing in great detail the preparation of poly(amidoamine) (PAMAM) dendrimers was presented in 1984 at the 1st International Polymer Conference, Society of Polymer Science, Japan (SPSJ). It was then published[10] in 1985, the same year a communication reported the synthesis of arborols by Newkome et al.[11] (Louisiana State University).

The divergent methodology based on acrylate monomers was discovered in 1979 and developed in the Dow laboratories during the period of 1979–1985. It did not suffer from the problem of low yields, purity, or purification encountered by Voegtle in his "cascade" synthesis and afforded the first family of well-characterized dendrimers. PAMAM dendrimers with molecular weights ranging from several hundred to over 1 million daltons (i.e., generations 1–13) were prepared in high yields. This original methodology was so successful that today it still constitutes the preferred commercial route to the trademarked Starburst® dendrimer family.

In contrast, the divergent iterative methodology involving acrylonitrile used by the Voegtle group[8] was initially plagued by low yields and product isolation difficulties and could not be used to produce molecules large enough to exhibit the unique properties that are now associated with the term "dendrimer." It is only a decade and a half later that two research groups Wörner/Mülhaupt[12] (Freiburg University) and de Brabander-van den Berg/Meijer[13] (DSM) were able to develop a vastly enhanced modification of the Voegtle approach to prepare true poly(propyleneimine) dendrimers. The route developed by the DSM group is particularly notable because it also constitutes a viable commercial route to this family of aliphatic amine dendrimers.

Since the "dendrimer" discovery occurred in a Dow corporate laboratory, the period 1979–1983 was spent filing many of the original dendrimer "composition of matter" patents.[64–73] The key Dow Starburst® dendrimer research team members associated with this initial research and development effort are shown in Figure 2 . It was not until 1983 that corporate approval was given for

Figure 2. Original Dow dendrimer research team (l.–r. back row: Pat Smith, Steve Martin, Mark Hall, and John Ryder; front row: Jim Dewald, Donald Tomalia, George Kallos, and Jesse Roeck [photo taken (1982) in Dow's Functional Polymer Research Laboratory, 1710 Bldg., Midland, MI where first complete series of PAMAM dendrimers (G = 1–7) were synthesized].

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A New Class of Polymers: Starburst-Dendritic Macromolecules

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ABSTRACT: This paper describes the first synthesis of a new class of topological macromolecules which we refer to as "starburst polymers." The fundamental building blocks to this new polymer class are referred to as "dendrimers." These dendrimers differ from classical monomers/oligomers by their extraordinary symmetry, high branching and maximized (telechelic) terminal functionality density. The dendrimers possess "reactive end groups" which allow (a) controlled moelcular weight building (monodispersity), (b) controlled branching (topology), and (c) versatility in design and modification of the terminal end groups. Dendrimer synthesis is accomplished by a variety of strategies involving "time sequenced propagation" techniques. The resulting dendrimers grow in a geometrically progressive fashion as shown: Chemically bridging these dendrimers leads to the new class of macromolecules—"starburst polymers" (*e.g.*, $(A)_n$, $(B)_n$ or $(C)_n$).

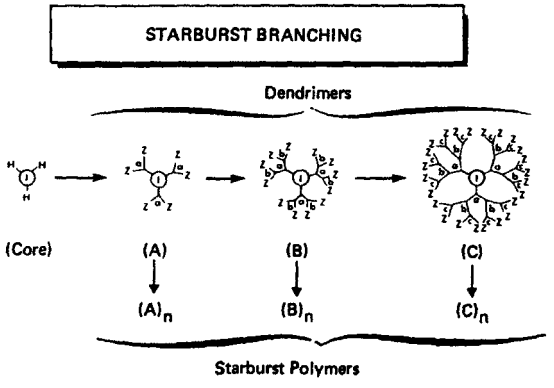

Figure 3. Abstract of first full article (ref. 10) describing dendrimers.

the first public presentation of this work (by D. A. Tomalia) at The Winter Polymer Gordon Conference in January (1983) (Santa Barbara, CA). It was after attending this Conference that Prof. Pierre de Gennes (College de France) predicted the fundamental dendrimer surface-congestion properties that are now referred to as the "de Gennes dense packing" phenomenon.[14,24,25,74] Excitement and controversy generated at this Gordon Conference concerning this new class of monodispersed dendritic architecture led to an intense schedule of invited lectures during 1984–1985 that included the following: The Akron Polymer Lecture Series (April 1984), American Chemical Society Great Lakes/Central Regional Meeting (May 1984), and the 1st International Polymer Conference, Society of Polymer Science Japan, in Kyoto (August 1984). The first use of the term "dendrimer" to describe this new class of polymers appeared in the form of several abstracts published during that year. The first SPSJ International Polymer Conference preprint[9] and the seminal full article[10] that followed describe the preparation of dendrimers and their use as fundamental building blocks that may be covalently bridged to form poly(dendrimers) or so-called "starburst polymers" as shown in Figure 3. These poly(dendrimers) are now referred to as "megamers."[74,75,76]

After the appearance of the seminal 1985 article from the Tomalia group, there was an enormous amount of intrinsic interest in dendritic polymer architecture. On the other hand, there was substantial resistance to accepting the supporting research results for publication by many of the major scientific journals. Some of the reasons cited by the critics of that period included the following:

1. How can one be certain the higher molecular weight dendrimers (i.e., $>G = 2$) are as monodispersed as proposed?
2. Dendrimers are no different than "microgels"—

Table 1. Early Peer-Reviewed Publications on Dendritic Molecules (1978–1991)

Year	Lead Authors	References
	From Cascade Growth to Dendrimers	
1978	Voegtle	8
1982	Maciejewski	15
1983	de Gennes	14
1985–1990	Tomalia/Turro/Goddard	9, 10, 16–27
1985–1990	Newkome/Baker	11, 28–30
1990–1991	Fréchet/Hawker	31–34
1990	Miller/Neenan	35–36
	Random Hyperbranched Polymers	
1988	Odian/Tomalia	37
1990	Kim/Webster	38
1991	Fréchet/Hawker	39
	Dendrigraft/Arborescent Polymers	
1991	Tomalia	40
1991	Gauthier/Möller	41

they are probably highly crosslinked particles akin to latexes.

3. It is difficult to believe that one can chemically advance from generation to generation (i.e., especially $>G = 2$) without substantial intramolecular cyclization and crosslinking.
4. Dendrimers are not really discrete chemical structures—they are nondescript materials.
5. Dendrimers are not expected to manifest any unique properties that cannot be found in microgels or latexes.
6. Backfolding of terminal chain ends into the interior of dendrimer will prohibit any "guest–host" properties—expectations for unimolecular micellelike properties are absurd!
7. Because little chain entanglement would be expected from these structures, one would expect poor bulk properties as compared with traditional linear, random coil polymers.

Despite this difficult acceptance, it is quite remarkable that by the end of 1990 about two-dozen publications on dendrimers had appeared in refereed journals. By the end of 1991, the rate of publication of dendrimer articles began to climb markedly while there were still only three articles on random hyperbranched polymers[37,38,39] and two articles on dendrigraft[40] or arborescent[41] polymers. The courage, persistence, and credibility of many key scientists listed in Table 1 during that period set the stage for the explosive acceptance and recognition of dendritic polymers over the next decade.

Several key events also contributed to this transformation. One such event included an invitation by Profs. D. Seebach (ETH, Switzerland) and H. Ringsdorf (Mainz, Germany) to present these new "dendritic polymer concepts" at the prestigious Bürgenstock Conference in Switzerland (May 1987). This lecture exposed these rather revolutionary concepts to the "elite scientific community" in Europe. Second, an invitation by Dr. P. Golitz (Editor, *Angewandte Chemie*) to publish an important review[24,25] entitled "Starburst Dendrimers: Molecular-Level Control of Size, Shape, Surface Chemistry, Topology and Flexibility from Atoms to Macroscopic Matter" provided broad exposure to the basic concepts underlying dendrimer chemistry. Finally, important contributions by key researchers significantly expanded the realm of dendrimer chemistry with the "convergent synthesis" approach of Fréchet et al.[42] (then at Cornell University) (Fig. 4) as well as the systematic and critical photophysical characterization of Turro et al.[26,43] (Columbia University).

Influenced by Tomalia's seminal 1985 article and stimulated by discussions with Dr. Richard Turner, then of the Eastman Kodak Co., dendrimer work at Cornell University was initiated by one of the authors (J. M. J. Fréchet) in 1987–1988. These were exciting times as the generous $2M gift by IBM Corp. to spur research in polymer chemistry had enabled the assembly of an outstanding team leading to discoveries that included Itsuno's polymer-supported chiral catalysts,[44,45] Stover's NMR method for the characterization of crosslinked reactive polymer beads,[46] Kato's self-assembly[47,48] of functional small molecules and polymers by hydrogen bonding, Cameron's photogeneration of base,[49] Matuszczak's new design for chemically amplified photoresists,[50] and of course Hawker's convergent synthesis[31,32,42] of dendrimers.

Although repetitive syntheses of both linear and branched[8,51] small molecules and even macromolecules were not new [e.g., preparation of linear oligopeptides, namely, branched poly(lysine)], Tomalia's dendrimers clearly had something special to offer; namely, features and properties that developed as a function of size (generation). We now know that the "dendritic state" and the properties derived from it are only accessed with certain symmetrical geometries[17] once a critical size has been reached and the molecule adopts a globular shape encapsulating its core or focal point.[24,25] Initial "learning" efforts were directed toward divergent syntheses of aromatic poly(amide) and poly(propyleneimine) dendrimers. These were soon abandoned as a result of severe problems of purification and the prevalent occurrence of stunted growth or structural defects. Only a few structures, such as Tomalia's PAMAM dendrimers, would lend themselves to controlled divergent growth.[24,25,74]

The "convergent" methodology for dendrimer synthesis was developed in the period 1988–1989 soon after two very gifted postdoctoral fellows, Craig Hawker and Athena Phillipides, joined Jean Fréchet at Cornell. The convergent growth approach, first demonstrated with

poly(ether) dendrimers, is probably best described as an "organic chemist" approach to globular macromolecules because it affords outstanding control over growth, structure, and functionality. Instead of expanding a core molecule "outward" in divergent fashion through an ever-increasing number of peripheral coupling steps, the convergent growth starts at what will become the periphery of the molecule proceeding "inward" to afford building blocks (dendrons) that are subsequently coupled to a branching monomer through reaction of a single reactive group located at its "focal point." This allows both for a drastic reduction in the amount of reagents used and for intermediate purification at each step of growth. More importantly, the convergent growth allows unparalleled control over functionality at specified locations of the growing macromolecule, and it provides access to numerous novel architectures through the attachment of dendrons to other molecules. This has led to innovative dendrimers consisting of different blocks, dendrimers with chemically varied layers or encapsulated functional entities, dendrimers with differentiated "surface" functionalities, and the opportunity to produce hybrid linear dendritic macromolecules and "dendronized" macromolecules.

The initial presentation[42] of convergently grown dendrimers was made in 1989 at the IUPAC Symposium on Macromolecules in Seoul, Korea. Here again, following initial patent filings, publication of the work was delayed very significantly by the thoroughly negative reception of the work by one referee, said to be "an expert in the field" who thought it "improbable that such precise molecules could actually have been prepared by the process described." Soon after initial publication[31,32] of the work by Hawker and Fréchet that finally took place in 1990, the convergent synthesis of an aromatic polyester was reported by Miller and coworkers,[35,36] whereas Hawker, working with a bright young graduate student, Karen Wooley, demonstrated the versatility of the convergent method with the preparation of dendrimers having differentiated functionalities.[33,34] Within a few months, the Cornell "dendrimer" group now including Hawker, Wooley, Uhrich, Gitsov, Boegeman, and Lee made use of the convergent synthesis to prepare and polymerize the first dendritic macromonomers,[52,53] develop hybrid macromolecules[54,55] consisting of a linear polymer block with either one or two dendrimers chain ends, develop the first double-stage convergent synthesis, and a variety of novel polymer architectures on the basis of dendritic building blocks.[56,57] Closely related work also produced the first solid-phase synthesis[58] of a dendritic molecule as well as a hyperbranched polyester[39] obtained by one-step polycondensation.

Today the convergent approach to dendrimer synthesis has taken its place alongside Tomalia's divergent approach as one of the two seminal routes to this important new class of macromolecules. Within the past decade alone, hundreds of publications making use of the convergent synthesis have appeared.[80] Figure 5 illustrates dendrimer growth by both the divergent and the convergent methodologies.

Among numerous events that contributed to the further acceptance of the dendrimers as discrete entities with remarkable structural precision was the development of mass spectrometric (MS) techniques for application in protein characterization. MS was useful for the precise determination of protein molecular weights (up to 1 M Da) using electrospray[81,83] and later matrix-assisted laser desorption/ionization time-of-flight techniques. With these techniques, it was possible to demonstrate unequivocally that all dendrimer constructions obeyed mathematically defined mass-growth rules that could be documented routinely by MS techniques.[90,91] This technological breakthrough as well as critical size exclusion chromatography,[20,25,59] light scattering/viscosity,[62] photophysical,[26,43,74] electron microscopy,[10,61] gel/capillary electrophoresis,[62] atomic force microscopy,[63,74] and other assorted measurements have exhaustively verified the principles of "dendritic growth and amplification" while also illustrating some of the unusual properties that result from the dendritic state.[74]

Beginning in the early 1990s, an overwhelming international interest in the dendritic polymer field has be-

Figure 4. Members of the 1988–1989 Cornell University team at a recent reunion. From right to left: back row, Dr. Craig Hawker (IBM Almaden Research Laboratory) and Prof. Takashi Kato (University of Tokyo); front row: Prof. Jean Fréchet (University of California, Berkeley) and Prof. Karen Wooley (Washington University).

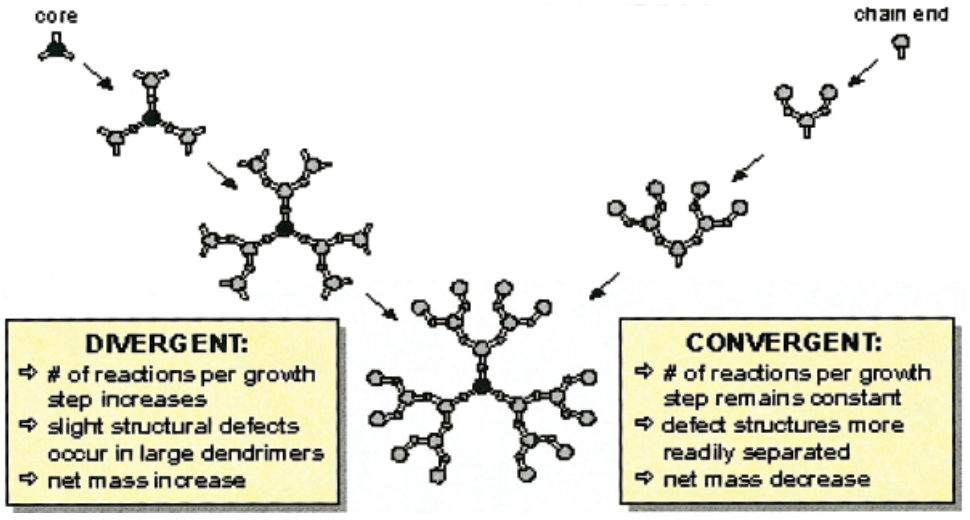

Figure 5. Representation of dendrimer growth by the divergent and convergent methods.

come apparent as manifested by research publications, reviews, monographs, and patents that numbered in the 100s during the period 1990–1995 then grew to thousands since 1995.[80] However, a decade ago lectures on dendrimers were still rather scarce, the last five to six years have witnessed two major "dendrimer" symposia at meetings of the American Chemical Society (ACS) in Chicago (1995) and Las Vegas (1998) that gathered very large international audiences. In 1999 the "First International Dendrimer Conference" was held in Frankfurt (Germany) under the auspices of DECHEMA. The year 2001 witnessed another international symposium including more than 150 invited lectures and communications devoted to dendritic polymers at the San Diego ACS meeting as well as the "Second International Dendrimer Conference," Tokyo, Japan (organized by Prof. T. Aida, University of Tokyo) with nearly 300 dendritic polymer scientists in attendance.

In bringing this historical perspective to closure, it is important to share an extraordinary moment that Donald Tomalia experienced at the First Society of Polymer Science Japan International Polymer Conference in Kyoto (August 1984). Prof. Paul Flory, who was not only the most prominent polymer scientist in attendance but also presented the key plenary lecture for the conference. All invited speakers were lodged at the Kyoto Grand Hotel. As such, many of us had the extraordinary opportunity to walk and talk with this celebrity on our many trips to the Kyoto Kaikan (lecture hall). On the other hand, I was one of the many eager, young scientists who had just presented some very intriguing, but nevertheless, "nontraditional" dendrimer data to an audience of largely traditional polymer scientists. Needless to say, during these group walks there was considerable discussion. Many questions were raised during these discussions. For example, "Is a dendrimer really a polymer?" "How could we possibly force monomers to bond according to mathematically defined rules?" Because of their dimensions, "Are dendrimers hazardous?" "Do we really need a polymer such as a dendrimer?" "Do dendrimers really exist?" Although I knew Flory attended the dendrimer lecture and he listened to these questions with interest, his comments were very sparse during these discussions. This troubled me until on one very special occasion as we were making the walk alone, he shared with me two memorable perspectives that have remained with me until this day. First, he consoled me by advising me not to be troubled by many of these questions. As he stated it, historically, few revolutionary findings in science are ever accepted without a predictable period of rejection. With a grin, he said dendrimers certainly qualify on that issue. Second, and perhaps more profound, were his perspectives on polymeric architecture. He stated it simply, "Architecture is a consequence of special atom relationships and just as observed for small molecules, different properties should be expected for new polymeric architectures." As such, dendrimers and other dendritic branched topologies should be expected to exhibit new and perhaps unexpected physical/chemical properties. He then challenged me with the following comment: "If you have indeed synthesized these new dendritic architectures and you believe in them, then your job and your destiny will be to demonstrate these new properties, understand them, and then attempt to predict the relationship between these parameters. Unfortunately, Prof. Flory passed away unexpectedly in the autumn of 1986, and the opportunity for further discussions was lost.

Some 17 years later, many of these predictions are turning into experimental reality as many of these questions are being answered in each new publication or patent that appears on dendritic architecture. Now den-

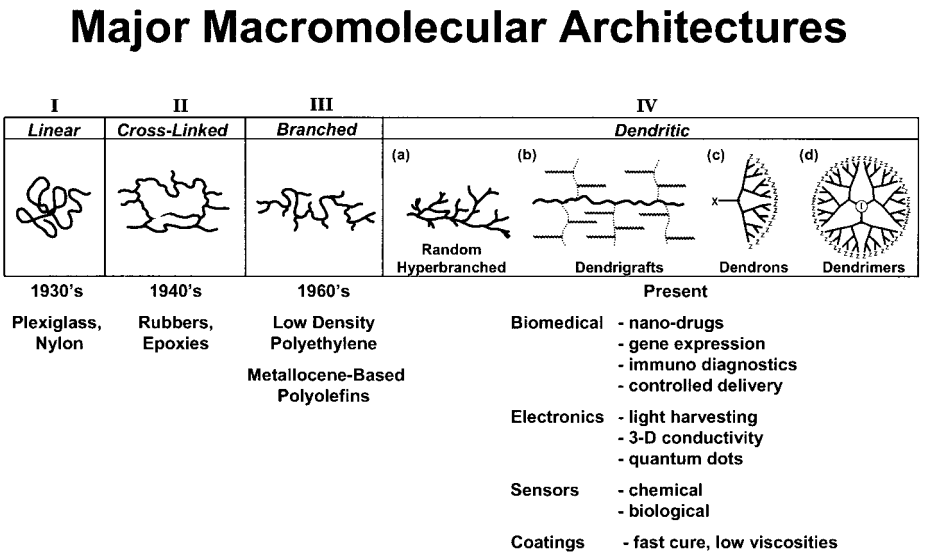

Figure 6. Representation of the four major classes of macromolecular architectures.

dritic polymers are recognized as the fourth major class of polymeric architecture, consisting of four subsets that are related to degree of structural control and are listed in ascending order: namely, (1) random hyperbranched polymers, (2) dendrigraft polymers, (3) dendrons, and (4) dendrimers (Fig. 6).

Three times this past century, chemists have developed major polymer architectures that have launched significant new industries and commerce.[77–79] The first two architectural classes [i.e., Class I (linear) and Class II (crosslinked) topologies] literally defined the origins of traditional polymer science, as well as major polymer property differences (i.e., thermoplastics vs thermosets). The third architectural class (i.e., Class III, branched) is now the focal point of dramatic growth related to new poly(olefins) topologies derived from "single-site," metallocene-type catalysts.[84] Historically, it has been widely recognized that macromolecular topologies significantly influence the determination of polymer properties and related new developments.

It is both remarkable and surprising to find that many of these Class IV dendritic structure-controlled macro-

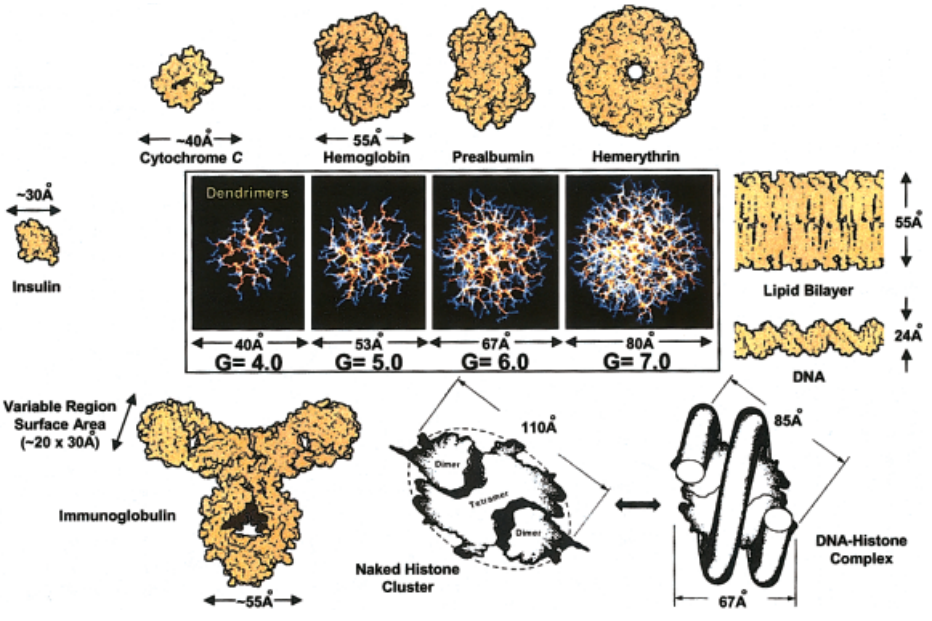

Figure 7. Dimensionally scaled comparison of a series of PAMAM dendrimers (NH_3 core; $G = 4–7$) with a variety of proteins, a typical lipid-bilayer membrane and DNA, indicating the closely matched size and contours of important proteins and bioassemblies.

molecules (i.e., dendrimers, dendrigrafts, etc.) possess topologies, function, and dimensions that scale very closely to a wide variety of important biological polymers and assemblies. In fact, they exhibit many properties reminiscent of proteins.[62,82] Figure 7 compares PAMAM dendrimers as a function of generation with important biological structures that are both conserved and essential in the life sciences. History has shown that the introduction of traditional synthetic polymer architectures (i.e., linear, crosslinked, etc.) by Staudinger,[78] Carothers,[79] Flory, and others[77] provided the basis for replacing many natural polymers (i.e., silk, rubber, cotton, etc.) while offering both improvements and advantages.

Now an international focus is emerging on nanotechnology. It has been described as the "ultimate scientific frontier" that will both define and lead the world into the next industrial revolution.[85] Although this description is surely exaggerated as today's ultimate quests become tomorrow's routine accomplishments, a very significant challenge facing the nanotechnology movement will be the development of structure-controlled methodologies that will enable cost-effective, controlled assembly of nanostructures in a very routine manner. Nature solved these problems and shattered this nanoscale synthesis barrier with its biological strategy for macromolecular structure control several billions of years ago. This set the stage for the dimensional scaling that today determines essentially all significant molecular level factors dealing with life. These same parameters that include nanoscale sizes, nanosurfaces/interfaces, nanocontainment, and nanoscale-transduction/amplification and information storage have important implications, not only in biology[86] but in critical abiotic areas such as catalysis, computer miniaturization, nanotribology, sensors, and new materials.[89] "Bottom-up" synthetic strategies that produce size-monodispersed, well-defined organic and inorganic nanostructures with dimensions ranging between 1 and 100 nm will be of utmost importance. Dendritic strategies allow the systematic construction of nanoscale structures and devices with precise atom-by-atom control as a function of: size, shape, and surface chemistry.[24,25,74,75,87]

Dendritic polymers, more specifically dendrimers, are expected to play a key role as an "enabling technology" in this challenge during the next century.[82,88,90–92] Just as the first three traditional, synthetic polymer architectures have so successfully fulfilled the critical material and functional needs for society during the past half-century, it is appropriate to be optimistic about such a role for the "dendritic state".

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