Starburst Dendrimers :

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Control of Size, Shape, Surface Chemistry, Topology and Flexibility from Atoms to Macroscopic Matter

*Synthetic strategies have been developed for the preparation of precise macromolecular building blocks referred to as Starburst * dendrimers. Electro-spray ionization mass spectroscopy techniques have confirmed a typical polydispersity for a polyamidoamine (PAMAM) dendrimer (Generation = 4.0 ; MWT. = 10,632) to be ; $\frac{M_W}{M_N} = 1.0005$. The use of these building blocks to construct supramolecular structures such as membranes, rods, clusters, necklaces and microcrystallites will be reviewed.*

Molecular level construction (Aufbau) of Starburst * dendrimers involves the stepwise assembly of monomer units (〜〜) into branch cells (—⟨) which are organized into single trunked, tree-like ensembles referred to as dendrons. Multiples of these dendrons may be anchored to initiator cores ①, to produce a vast array of dendrimers differing in size and morphology. Depending on the multiplicity of the core (N_c) and the branch cells (N_b), one can produce a wide variety of precise macromolecular architectures. The 2-dimensional projections show a tridendron starburst dendrimer series with $N_c = 3$ and $N_b = 2$. Advancement from the initiator core to higher generations G = 1, 2, 3, etc, leads to branch cell and terminal group proliferations that mimic biological cell division (see *Figure 1*).

In this latter instance both "divergent" as well as "convergent" synthesis strategies have been successful as reported by Fréchet [10], and others [11]. These issues and other details have been reviewed elsewhere [12]. In either case, a reiterative branch cell assembly scheme is necessary for developing concentric generations and advancing the Starburst architecture. As a result of these reiterative branch cell assembly operations, it is apparent that these constructions follow systematic branching rules (geometric progressions), if the assembly is near ideal. This allows one to predict the number of repeat units assembled (N_{RU}, degree of polymerization) and calculate dendrimer theoretical molecular weight as a function of initiator core multiplicity, N_c,
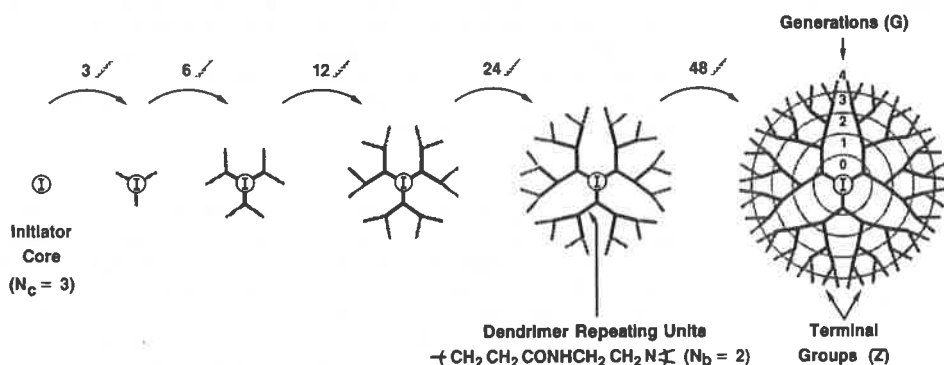

FIGURE 1. - *Time sequenced monomer self organization around ① to give a dendrimer ; Gen. = 4.0, $N_c = 3$, $N_b = 2$.*

To date, successful "divergent" synthetic strategies have involved either :

- (a) in situ construction of branch cells around an initiator core [1a,b,2-5] or

- (b) coupling of preformed branch cells (derived from branch cell reagents) around such an attractor [6-11].

branch cell multiplicity N_b, and generations (G), according to the following relationships :

$$N_{RU} = N_c \left[\frac{N_b^{G+1} - 1}{N_b - 1} \right]$$

$$MW = M_c + N_c \left[M_{RU} \left(\frac{N_b^{G+1} - 1}{N_b - 1} \right) + M_b N_b^{G+1} \right]$$

For example, *Figure 1* illustrates the time sequenced organization of monomer units around an initiator core with a multiplicity (N_c = 3), designed to produce in situ branch cells with multiplicities of N_b = 2. This step-wise dendrimer growth gives N_{RU} values of 3, 9, 21, 45 and 93 for generations = 0 - 4, respectively.

Recent electrospray ionization mass spectrometry of higher generation polyamidoamine (PAMAM) dendrimers clearly supports the precision of these dendrimers as a function of their degree of polymerization (N_{RU}) and predicted molecular weights (MW). *Figure 2* illustrates the mass spectrum obtained for a PAMAM dendrimer ; core = NH_3 generation = 4.0, which would be expected to have 93 monomer units of N-(2-amino-ethyl) acrylamide organized around an ammonia attractor①. The polydispersity calculated from triplicate mass spectra runs of this dendrimer sample was found to be ; $\frac{M_W}{M_N}$ = 1.0005.

Control of cubic nanoscopic space and surfaces at the dendrimer level is determined by the design and modification of parameters that affect the three architectural components unique to all dendrimers, namely :

  I. the initiator core,

  II. the interior,

  III. the exterior.

Some of these parameters are listed in *Figure 4* and allow one to maintain control over the critical molecular design parameters (CMDP's) such as size, shape, surface chemistry, flexibility and topology which ultimately determine both interior as well as exterior properties of the dendrimers.

Generation = 4.0

N_c = 3; N_b = 2

① = NH_3

①$[CH_2 = CHCONHCH_2 CH_2 NH_2]_{n=93}$

M.W. = 10632.96

FIGURE 2. - *Electrospray ionization mass spectrum (deconvoluted) of G = 4.0 dendrimer.*

FIGURE 4. - *Dendrimer architectural components with molecular genealogy associated with CMDP's that effect interior and exterior properties.*

These properties have been designed and modulated to provide a wide variety of commercially interesting prototypes for use as submicron calibrators, virus mimics, micelle/liposome mimics, unimolecular synthetic cells for controlled/targeted drug delivery and macromolecular templates for controlling the topology of commodity polymer systems.

Cubic, nanoscopic space control within a dendron is determined by the branch cells which are defined by the following three construction parameters namely :

  I. repeat unit length (ℓ),

  II. branching angles (**a**),

  III. rotational angles (**b**).

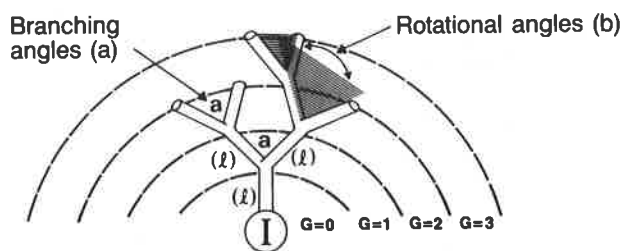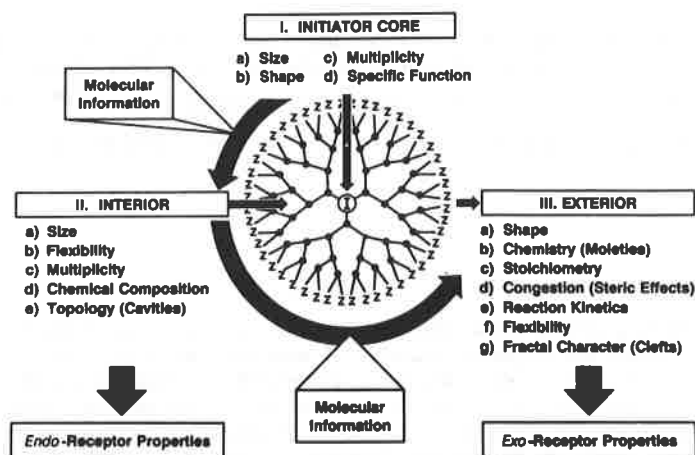These parameters are noted in *Figure 3* for a defective dendron, generation = 3.0.

Theoretically speaking, one might view these precise macromolecular structures as "nanoscopic analogues" of atoms. As such, they may be thought of as fundamental building blocks for the construction of a wide variety of new "supramolecular" and "macroscopic" structures not found in Nature. Such structures include membranes, rods, clusters, necklaces, microcrystallites and other morphologies. The range of structures may be as great as that which has been produced from the fundamental building blocks ; C, H, O, N, etc. This concept is illustrated in *Figure 5*.

In conclusion, comparing recent developments in dendrimer chemistry to more classical polymer efforts suggests a new frontier in nanoscopic synthesis and engineering of macromolecules may be emerging.

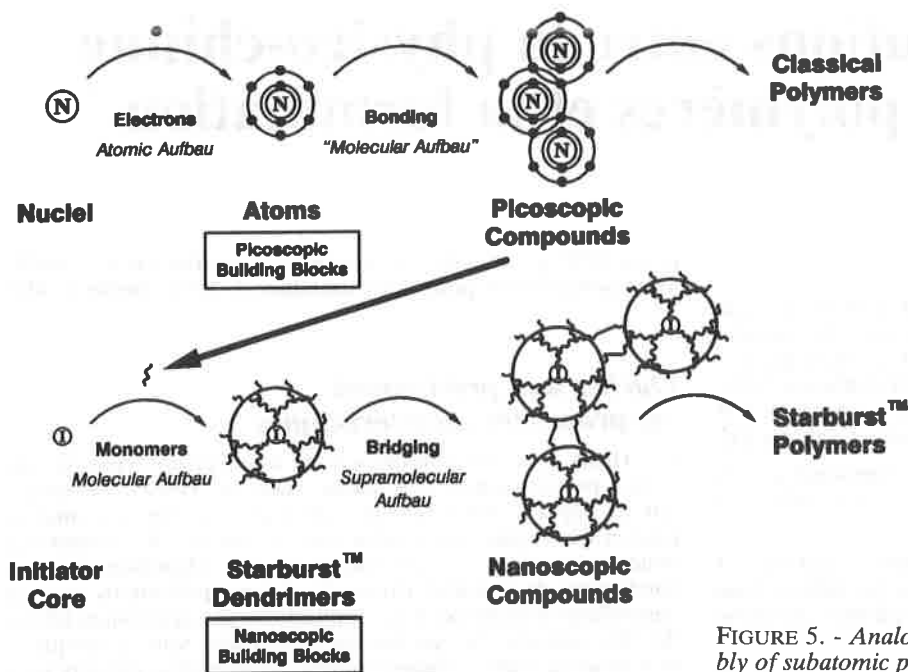FIGURE 3. - *Construction parameters controlling nanoscopic space in a dendron.*

FIGURE 5. - *Analogies between dendrimer assemblies and assembly of subatomic particles into atoms and molecules.*
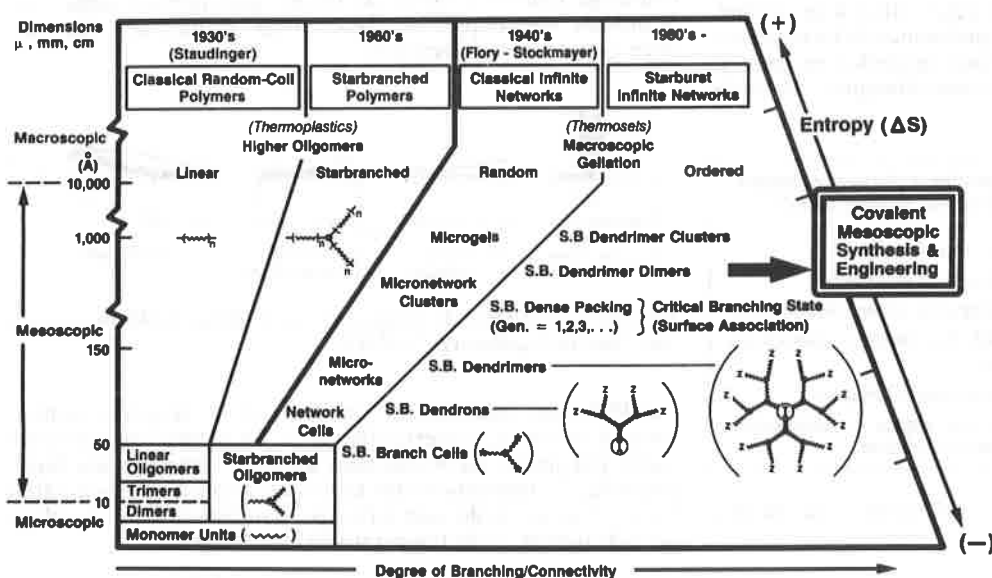

FIGURE 6. - *Architectural developments in polymer science.*

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