Molecule Matters

Dendritic Architecture

A Clever Route to Monodispersed Macromolecules

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Dendritic macromolecules are excellent examples for macromolecules that possess well-defined branching that develops from a core to the periphery. The pseudospherical structure of dendrimers has opened up numerous possibilities for interesting applications.

Introduction

Synthetic polymeric macromolecules occupy an important place in the development of modern materials. Understanding the molecular details is important in order to develop a material which can eventually find real-life application. Molecular structures hold the key to the properties that a material exhibits. Tuning molecular and macromolecular properties is essential to the functions and performance of a polymer. Apart from the constitution, factors such as sizes and shapes characterize a polymeric macromolecule. Several architectures as well as substructures have been derived within the major types of linear, cross-linked, branched and hyper-branched polymers. One may expect that macromolecular substances having the same building blocks in identical proportions, but in different architectural configurations will manifest different properties and macroscopic behavior.

In any polmerisation process, it is difficult to control the number of monomers that join together to form the polymer. Consequently, the end product is a material that contains molecules of different molecular weights. Thus polydispersity is inherent to polymers and the attendant bulk properties of a polymer are attributed to the extent of the polydispersity. Efforts to reduce or avoid polydispersity demand different approaches to the

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synthesis. Fine-tuning such approaches should, in principle, lead to creation of materials that are monodisperse, that is, all the molecules in the sample are of identical size and shape. Monodisperse samples would offer distinct physical features that, in essence, would be difficult to achieve through other polydisperse samples.

The Dendritic Architecture

An easy method to achieve a monodisperse macromolecule is through the formation of branches-upon-branches architecture throughout the macromolecule. It is important that 100% branching is achieved, so as to realize a perfect monodispersed material. This intention to generate monodispersed macromolecules is one of the primary motivations to develop the field of dendrimer chemistry [1]. The term 'dendrimer' refers to macromolecules possessing 100% branched architecture, with molecular weights of several kiloDaltons[1], which possess near spherical shapes. Developments in the field of dendrimer chemistry began from a few reports that appeared on the synthesis of well-defined dendritic macromolecules in the mid-1980's [2]. Most of these dendrimers are man made. However, natural dendritic architectures are also known, for example, glycogen, an energy-storage macromolecule in living organisms has a dendritic structure.

[1] Daltons refer to the unit of molecular weight of a compound. For example, molecular weight of methane is 16 g/mole and can be denoted as 16 Daltons. A kiloDalton in turn refers to one thousand Daltons.

A dendritic architecture could be defined by three distinct components, (i) the core, (ii) the interior branches and (iii) the exterior functionalities (*Figure* 1). The assembly of these components creates a dendritic structure, which is radially symmetric and has several tiers. A tier, more often called a generation, refers to a circle enveloped by a set of branch points located symmetrically around the core. The symmetric branching results in (i) exponential growth of the dendritic structure leading to an exponential increase in the molecular weights with increasing generations, (ii) dense exterior regions and (iii) relatively less-dense interior regions. The growth leads to dense exteriors and less dense interior regions within the structure, especially at higher generations. The molecular weights increase

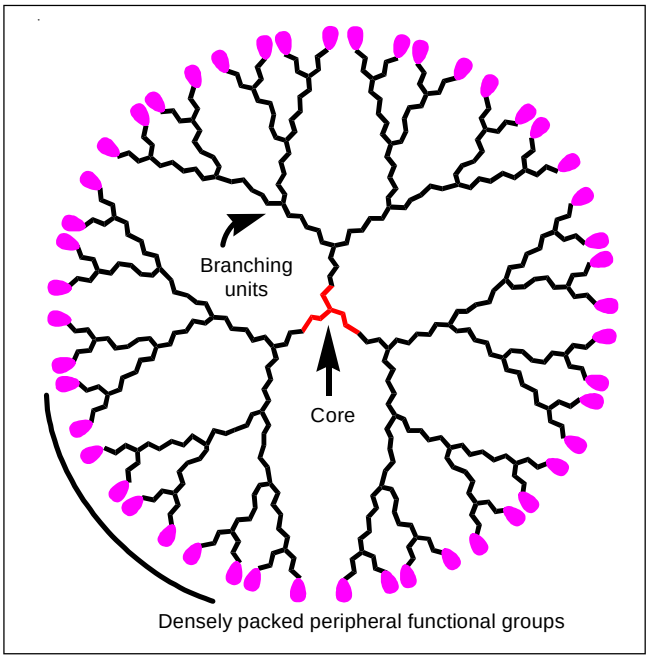

Figure 1. A dendritic architecture.

exponentially as the generations advance, but the molecular volumes do not increase exponentially. This unique architectural feature is one of the key aspects, which is exploited in order to realize new functions.

Synthesis of Dendrimers

The monodisperse nature of these macromolecules implies that the chemical synthesis needs to be step-wise in nature, as opposed to single-step polymerization reactions in a traditional polymer synthesis. Assuming that an AB_2-type of monomer grows into a dendrimer, the number of simultaneous reactions at each step, beginning from a trifunctional core would be 3, 6, 12, 24, 48, 96, … for the generations, 0, 1, 2, 3, 4, 5, … respectively. This exponential rise in the number of simultaneous reactions demands that the chosen reactions should be efficient and high-yielding. Thus, critical parameters to synthesize dendrimers are (i) the choice of a multifunctional monomer; (ii) the choice of reactions and (iii) considerations of purifications and yields. Each one of these parameters should be optimal in order to make

the synthesis of dendrimers efficient and advantageous.

The structures of poly(propyl ether imine) (PETIM) dendrimers are used herein to illustrate dendritic architectures [3]. This class of PETIM dendrimers is derived from the monomer, 3-amino propan-1-ol ($H_2NCH_2CH_2CH_2OH$). The assembly of this monomer through iterative chemical reactions, namely, etherification and functional group reduction in an alternating sequence, leads to the formation of the class of PETIM dendrimers of several generations. Generations (G) 1, 2, 3, 4, 5 and 6 present, respectively, 4, 8, 16, 32, 64 and 128 functional groups at the periphery (*Figure* 2). The above series of dendrimers are prepared by a divergent growth method, wherein G-1 grows outward, i.e. at the peripheries, to become G-2. The latter generation progresses to G-3 when monomers are appended symmetrically at their peripheries. The higher dendrimer generations form by the same iterative reactions involving the immediate previous generation.

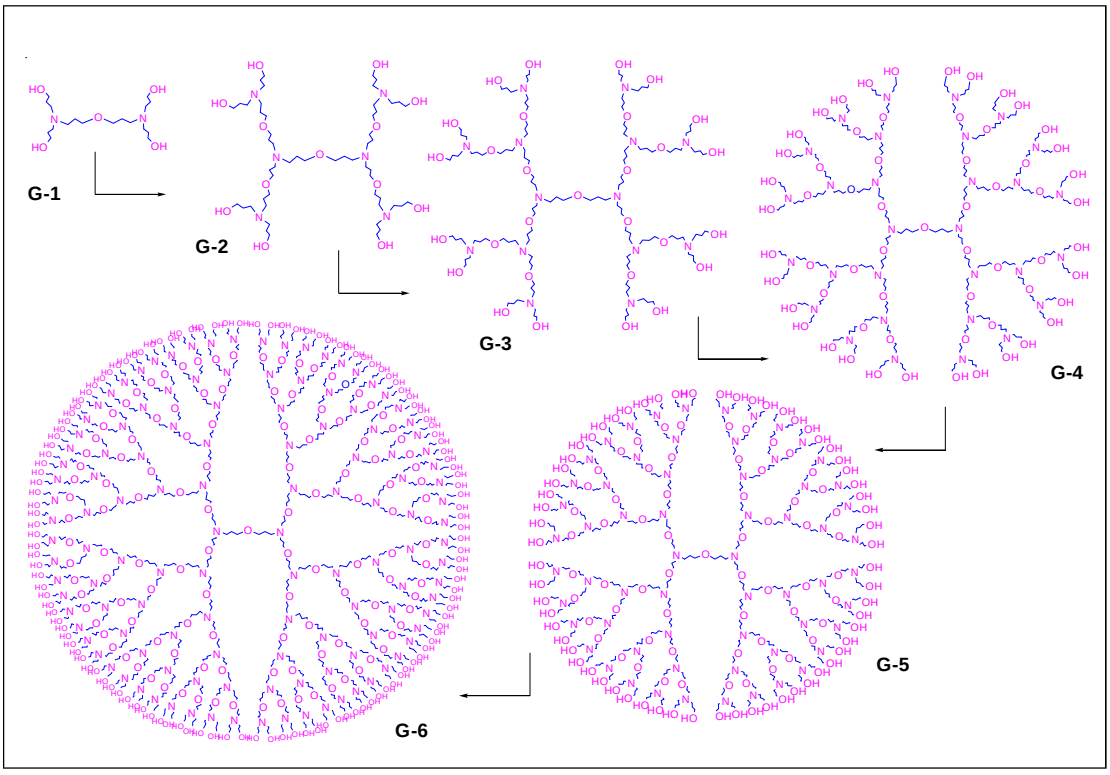

Figure 2. Molecular structures of poly(ether imine) (PETIM) dendrimers.

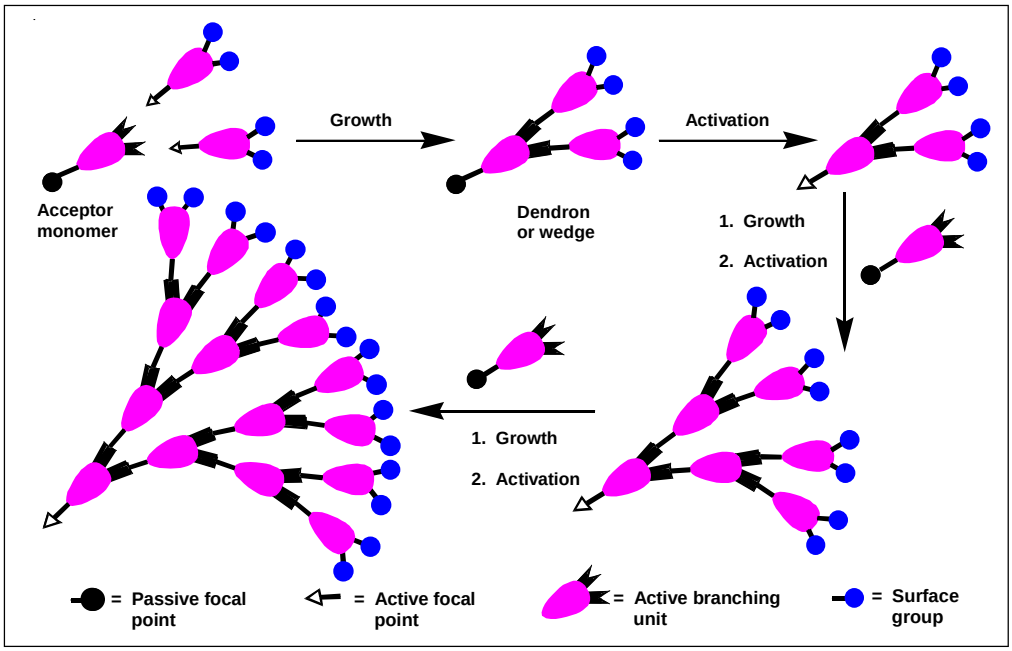

Figure 3. Schematic representation of a convergent method to construct dendrons.

There exists another popular strategy to assemble dendrimers. This strategy, known as 'convergent method', requires the dendrimers to grow inward from the peripheries to the core of the molecule. A schematic depiction shown in *Figure* 3, illustrates this method. Dendrons of progressively varying sizes are prepared in the process of the 'inward' growth, wherein a focal point functionality of a wedge or a dendron is activated periodically and is then attached to the acceptor monomer, in order to prepare a larger dendron. The dendrons can be attached to a multifunctional core molecule, leading to the completion of the dendrimer growth.

The molecular structures of dendrimers become progressively denser and may appear to become more complex as the generations advance. However, relatively simple, repetitive chemical reactions are sufficient to construct the macromolecule. It can be seen that the structures of the series of generations resemble each other, only the sizes differ between generations. These relations reflect that when the peripheral functional groups undergo further reactions, a new tier is formed which essentially

duplicates the previous generation. Alternately, when an outer tier is removed, a structure is generated similar to the initial structure, differing only in the size. In these instances, a dendritic structure may be compared to structures of fractal[2] objects.

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Future Prospects for Dendritic Macromolecules

Dendrimers are compact, globular and spherical macromolecules and more importantly, they are formed by iterative processes leading to highly optimized structures. Based on these molecular and macromolecular features, avenues for application of dendrimers in varied disciplines are emerging [4]. Primary among them are in utilizing dendrimers (i) for biological applications [5], (ii) as organometallic catalysts to mediate carbon-carbon bond formations [6] and (iii) as hosts for encapsulation of metals and aromatic compounds [7].

The dendrimer based drug delivery possibilities are likely to reach the first ever direct application of dendrimers (*Figure* 4). Some of the advantages associated with the dendritic macromolecule are the high drug-loading capacities, abilities to optimize the dendritic components to meet the needs of physiological requirements and flexibilities to incorporate specific targeting devices advantages associated with the dendritic macromolecule. Drugs can be attached directly to the dendrimers. Alternatively, the drugs can be encapsulated into the dendritic

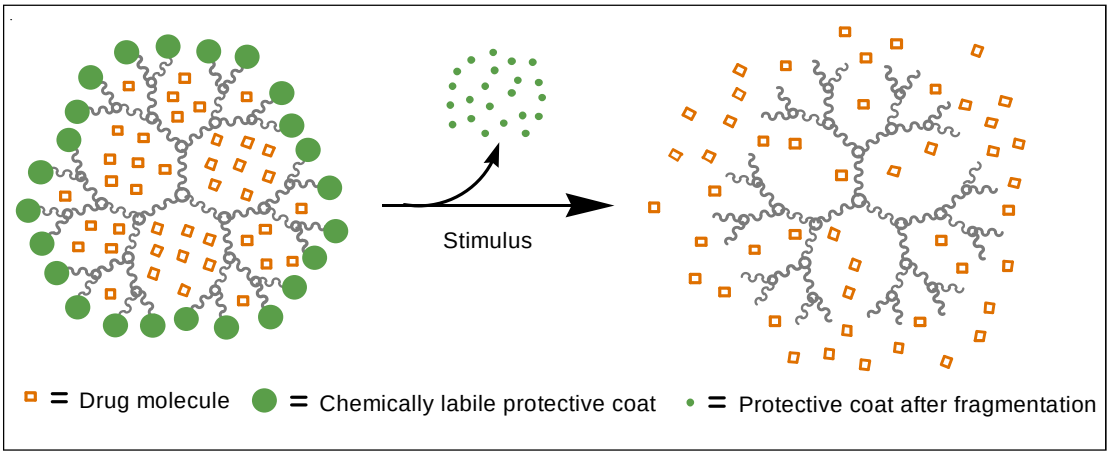

Figure 4. Dendrimers act as containers for loading drug molecules that can be released by an appropriate stimulus.

structure, which can then be released at the required cellular site for pharmacological action by an applied stimulus (see *Figure* 4). Another possibility is the degradation of dendrimer structure into smaller fragments by an enzyme or light or chemical action, so as to release the drug molecules. All these possibilities are being pursued aggressively to bring up medicines based on the dendrimer technology [8].

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Suggested Reading

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