Functional Polymers with Controlled Molecular Architecture: Design, Synthesis and Applications

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Introduction

The importance of functional polymers has increased significantly over the past few decades as macromolecules have found more and more applications beyond their traditional uses in commodity fibers and plastics. Some specialized areas of endeavor have included toners and inks for personal and business printing, plastic lenses and other corrective vision products, supported catalysis, plastic electronics, polymer therapeutics, artificial bone or prostheses, etc. Because polymer architecture plays a great role in determining the properties of functional polymers, this lecture will explore the design and the synthesis of polymers with controlled architecture and functionality. Especially featured will be star and dendritic architectures where the functional group placement and the molecular shape can be controlled. This will be followed by examples of applications illustrated with a few model systems of functional polymers specifically designed for use in areas such as organic electronics (photovoltaics, light emitting diodes, etc), catalysis, surface patterning, separation and molecular recognition, and polymer therapeutics [1-2].

Discussion

Controlling the molecular architecture of linear and star polymers. The advent of living radical polymerization has drastically changed our ability to produce block copolymers, once only available through extremely precise but technically challenging anionic processes. Today, techniques such as atom transfer radical polymerization (ATRP) [3], alkoxyamine-mediated living radical polymerization [4], and reversible addition-fragmentation chain transfer (RAFT) polymerization [5] have considerably enhanced our ability to produce polymers with controlled size, polydispersity and architecture.

Important advances have also been made in the area of ring-opening metathesis polymerization with the latest generations of easily handled and functional group tolerant Grubbs catalysts [6].

An important application of these new and readily accessed living polymerization techniques has been their use in the preparation of star and comb polymers and copolymers. For example, in collaboration with Hawker, we have used a combination of alkoxyamine-mediated living radical polymerization and high throughput experimentation to prepare a variety of star polymers [8, 9].

Time allowing, some applications highlighting the importance of controlled structure and architecture in linear, block, and star copolymers in self-assembled materials [10], or electroactive polymers for organic electronics [11-12] may be presented.

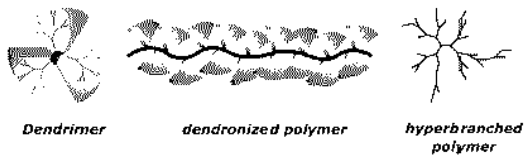

Figure 1. Three types of dendritic architecture.

Dendritic macromolecules. Over the past two decades dendrimers have attracted much attention due to their unique architecture and properties that are not matched by any other type of synthetic macromolecules. In 1985, Tomalia and coworkers [13] introduced the first important family of dendrimers, the so-called PAMAM dendrimers, prepared by an iterative divergent approach. It was in Seoul at an IUPAC sponsored International Symposium on Macromolecules [14] that we first disclosed the convergent synthesis [15-16] of dendrimers in 1989. Since that time several other important families of dendrimers as well as other classes of dendritic structures have been explored. While dendrimers tend to adopt a globular structure in solution - which is preserved to some extent in the solid state for high generation materials - dendronized linear polymers are forced into a tubular configuration by the sheer bulk of their side-chain. Both dendrimers and dendronized linear polymers offer opportunities for the use of their "interior" volume and the special nanoenvironment it provides for applications such as catalysis or drug delivery.

Controlling the placement of functionalities for applications. In addition to architecture, both the type and placement of functional groups affect the properties of functional polymers. For example dendritic polymeric catalysts that mimic the function of enzymes in their ability to both promote catalysis and effect mass transfer have been reported [17].

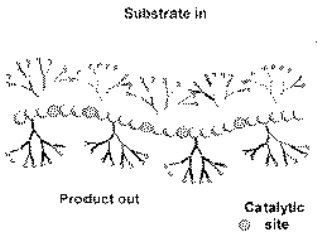

Figure 2. Nanoscale "tubular" reactor based on dendronized linear polymer with a radial gradient of polarity.

Figure 2 shows the schematic representation of a dendronized linear polymer in which the catalytic sites are randomly located along the main chain of the linear "core", which is surrounded by encapsulating dendrons. A radial gradient of polarity is built into the dendrons to drive reactants inside the tubular molecule thereby considerably increasing their local concentration and thus the rate of reaction. As the catalytic transformation is accompanied by a change in polarity, the product then migrates out of the dendronized catalyst back into the surrounding medium. Thus, it is the nanoenvironment afforded by the very structure of the dendronized polymer that is responsible for its action in a free-energy driven process.

Encapsulation of guests within dendrimers. Dendrimers have long been known to be able to encapsulate guests within their interior. This property can be exploited in the development of state-of-the-art imaging agents for magnetic resonance imaging. Therefore a dendrimer containing internal amine groups can be used to encapsulate several copies of a cryptophane, each of which can act as a cage for the transport of hyperpolarized xenon gas. We have now demonstrated a novel supramolecular biosensor based on a polyamidoamine dendrimer equipped with a single targeting group and capable of encapsulating multiple cryptophane-based ^{129}Xe cages (Figure 3) that is highly effective in amplifying the NMR signals obtained from polarized xenon [18].

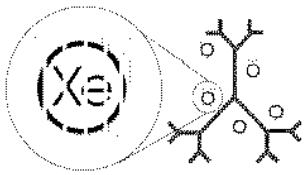

Figure 3. Encapsulated Xe biosensor

Controlling macromolecular architecture for polymer therapeutics. Early work in the use of polymers as carriers or solubilizing groups in therapeutic applications has been entirely focused on linear polymers. Several of these polymers have now been approved for human use by regulatory agencies. Early examples include slow-eroding encapsulating polymers such as Langer's polyanhydrides, used in the formulation of Gliadel wafers for the treatment of brain tumors. These wafers, impregnated with the DNA crosslinking drug carmustine, are implanted into a tumor cavity after the tumor has been removed by surgery. As the polyanhydride wafers dissolve, Carmustine is slowly released directly at the tumor site in a concentration much greater than is possible by intravenous

delivery. Another linear polymer that has gained acceptance in therapeutics is poly(ethylene glycol), frequently conjugated with protein drugs, thus vastly improving their efficacy through reduced renal clearance and prolonged in vivo persistence.

While poly(ethylene glycol) could also be used for the systemic delivery of conventional low molecular weight drugs, the macromolecule only has two functional groups – one at each chain-end – thus affording little opportunity for the conjugation of multiple copies of a drug or a combination of drug and targeting agent.

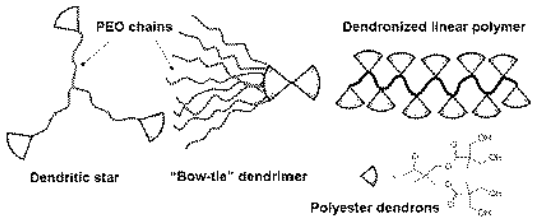

Figure 4. Three types of dendritic carriers developed for cancer chemotherapy and other therapeutic applications.

We have now developed several families of dendritic carrier molecules that can carry multiple copies of a drug and release them at a specified target site. Conjugation of the drug to the dendritic macromolecule enhances its solubility and bioavailability and increases its residence time in the body also enabling the targeting mechanism of the drug conjugate to operate [18]. In a series of animal studies we have shown that the "bow-tie" dendrimer carriers shown schematically in Figure 4 are remarkably effective in the treatment of some cancers.

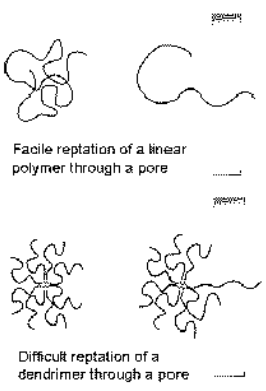

Figure 5. The importance of architecture in renal filtration.

The importance of architecture in the design of polymeric drug delivery system is shown in the schematic drawing of Figure 5. Because residence time in the body is an important factor, the rate of renal filtration is directly affected by the ability of the polymer to reptate through the pores of the kidney. Therefore once a certain size threshold is met, the highly branched architecture of a dendrimer hinders reptation and slows elimination where a comparable linear polymer would be rapidly eliminated. This concept has now been proven with a variety of polymer architectures and the bow-tie architecture, in which the drug payload is located near the core of the dendritic molecule and is surrounded by many solubilizing polyethylene oxide arms, has been shown to be particularly favorable at molecular weights in the range of 40-50 KDa.

Conclusions

These examples illustrate how polymer functionality as well as architecture influence the properties of macromolecules and enable new, more advanced applications. It is clear that the continued development of new synthetic techniques allowing the fine control of polymer structure is an important target for today's polymer scientists as material-dependent applications emerge in fields as varied as electronics, catalysis, printing, and even medicine.

Acknowledgements.

The author thanks his many coworkers, in particular those cited in the references, for their critical contributions to the research outlined herein. Financial support of our research in the area of dendritic macromolecules was initiated by an unrestricted gift from IBM Corporation and a grant from the National Science Foundation (Division of Materials Research). Further support from the National Institutes of Health, the US Department of Energy (Basic Energy Sciences), the Office of Naval Research, the Air Force Office of Scientific Research, and the Semiconductor Research Corporation is acknowledged with thanks.

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