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MACROMOLECULAR ARCHITECTURE—NATURE AS A MODEL FOR DEGRADABLE POLYMERS

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ABSTRACT

Nature usually combines polymers with short degradation times with polymers having long degradation times in an energy and material optimized process involving hierarchical systems. Sometimes a natural system of polymers has evolved to degrade in a month, sometimes in many years. The building blocks of the plant and animal kingdom are biopolymers which are either oxidizable or hydrolyzable. In natural composites, combinations of the two are common, e.g., in wood. Current trends in polymer research and marketing of plastics indicate an increasing demand for the development of a diversity of degradable polymer products with a predetermined service-life. We identify four main routes to design degradable polymers. The goal is to tailor-make a material which is more susceptible to environmental degradation factors (e.g., hydrolysis, biodegradation, photooxidation). The most convenient route is to use cheap synthetic bulk polymers and add a biodegradable or photooxidizable component. A more expensive solution is to change the chemical structure by introducing hydrolyzable or oxidizable groups in the repetitive chain of a synthetic polymer. The third route to degradable polymers is to use biopolymers or derivatives of these where the bacterial polyhydroxyalkanoates are perhaps the most studied material of them all. The fourth route is to tailor-make new hydrolyzable structures e.g., polyesters, polyanhydrides, and polycarbonates.

INTRODUCTION

Modern polymer (macromolecular) materials science is interdisciplinary and demands an understanding of the basics of chemistry, physics, mathematics, mechanics, materials science, engineering, and, in many cases, electronics, biology, and medicine. Many fundamental questions concerning the relationships between primary chemical microstructure, supramolecular organization, and physical properties are only beginning to be addressed. Modernization of the laboratory has drastically changed both the nature and expectations of polymer science research. New experimental techniques now permit critical testing of theories on small-scale quantities of materials never before possible. Computer simulations and molecular modeling are increasingly powerful tools which allow the rational exploration of the molecular-level criteria for "polymer architecture" as it relates to higher ordered structures and properties. The enlarged knowledge of the fundamentals of polymer mechanics, solidification kinetics, thermodynamics, etc. and the access to powerful computers have made simulation of very intricate processing conditions possible and form a powerful basis for engineering design.

An objective of molecular architecture is to control the material's properties. For example, large changes in properties such as mechanical strength and heat resistance have been affected by making only small changes in the primary chemical structure of the polymer. Improved barrier properties of polymer films have been obtained through subtle changes in the chemical structure and molecular weight distribution. Materials with increased mechanical strength may require the use of liquid crystalline polymers and other ordered structures.

The structures of more demanding materials necessary for newly emerging fields such as opto-electronics and molecular electronics will only be possible via the application of the principles of molecular architecture. Sophisticated biological properties for new materials, such as biocompatibility and membrane functionality, will demand additional, and as yet unexplored, changes in molecular architecture. There is great need for these biofunctional materials for the development of medical devices, biosensors, and in the field of tissue engineering.

TERTIARY AND QUARTENARY STRUCTURE—NEW AREAS OF MOLECULAR ARCHITECTURE IN MATERIALS SCIENCE

Presently, there is little control of the resulting tertiary and quaternary structure of synthetic polymers. However, in nature these two microstructural modes govern most fundamental processes associated with material "intelligence," i.e., the ability of materials to respond to changes in their environment. Proteins and other biopolymers are characterized by a higher order of structures. For example, enzymes and other proteins can exhibit one type of tertiary structure in an inactive state but when exposed to a specific small molecule an interaction can occur with effects change in the higher-order structure that produces an active material. The first step in the synthesis of new polymers is the building of different structures in space, i.e., stars, dendrimers, combs, etc., where the molecules are held together by covalent bonds. If materials in the future can be made to react to molecules approaching from the outside of the polymer, then we in fact have "intelligent" or

“smart” materials. Today synthetic polymers are made which can change color or can be conductive. In Japan, PMMA has been prepared where isotactic and syndiotactic chains fit together in a pair which is the beginning of the phenomenon associated with the quaternary structure of proteins.

Knowledge and experience in polymer chemistry and physics, characterization of polymers, and biochemistry and analytical chemistry are necessary to take a fundamental approach toward the design of new, tailor-made polymers based on the structure of natural polymers. The macromolecular research of tomorrow will focus on changing existing synthetic polymers to behave more like natural polymers; blending synthetic polymers with natural polymers and building new “intelligent” materials with Nature as the model (i.e., biomimetic-chemistry).

BIOMIMETRIC CONSTRUCTION OF NEW MATERIALS

Interest in the polymers of Nature has grown in recent years due to both concern for the environment and eagerness to use renewable resources. The most important thing is, however, recognition of the superior qualities of native polymers. Most biopolymers demonstrate multifunctionality, i.e., separate components have more than one function.

This hierarchical structure is evident in a tissue like a tendon where the protein collagen is arranged into microfibrils which further arrange themselves to fibroblasts and end up with the tendon. Another example is the wood cell where cellulose, hemicellulose, and lignin together provide fiber, matrix, and cement, thus building up to a very strong wood material. The fibers are arranged in helices embedded in hemicellulose and lignin. These two examples clearly demonstrate how highly specialized materials are created by Nature.

New polymer materials will use Nature as a model, and the next generation of polymers will offer well-organized structures, bio- and environmentally adaptable materials, use of renewable resources to a larger extent than today, thus forming highly specialized materials with multifunctionality as well as adaptability. By learning from the microstructure of natural polymers, it is possible to design and synthesize new specialized polymers with superior functionalities and properties compared with the polymers of today. The integration of polymer chemistry and biochemistry together with molecular genetic engineering will provide a sound base for this research.

NATURE AS A MODEL FOR DEGRADABLE POLYMERS

Environmentally degradable polymers are materials with built-in sensitivity to different degradation factors. Some polymers are sensitive to direct biodegradation by enzymes and/or microorganisms while others can be only degraded in the later stages after an initial hydrolytic or oxidative chain scission. The methods that have emerged to date for environmental adaptable polymers are: 1) photodegradable polymers, 2) directly biodegradable polymers, 3) autooxidizable polymers which then biodegrade, 4) water-soluble polymers, and 5) new forms of natural polymers. It will prove very fruitful to combine several modes for degradation in the same

material, e.g., photooxidizable and biodegradable. The demand in modern polymer technology is that every material should be especially adapted to the environment in which it will be used. The long-term properties should be predicted beforehand, i.e., controlling the degradation time is vital. Future research will be concentrated on modeling the precise degradation time by changing chemical groups in the repetitive unit of the polymer and/or different additives, by pretreatments of the polymer, etc.

Several of the new degradable polymers are produced from renewable resources rather than petroleum-based production of the bulk polymers (PE, PP, PS, PVC). Special research interest has been focused on the thermoplastic poly(hydroxyalkanoates) (PHA), with hundreds of copolymers prepared to date. Although these materials are still rather expensive, increased production along with new isolation schemes will undoubtedly lower the prices.

New research will be aimed at other natural polymers and the blending of natural polymers with synthetic commodity polymers to produce low cost environmentally friendly materials. Since the processing of natural polymers and degradable polymers has not been systematically studied, the influence of the processing parameters on the subsequent in-vivo degradation of these materials needs further analyses. Small changes in the processing may render the materials totally inert to environmental degradation. It is thus necessary to find optimum processing windows.

Some hydrolytically degradable polymers are useful for certain medical applications in which the use of the device is temporary. The advantage of using biodegradable (also referred to as bioresorbable) polymers in medical devices such as implantable drug delivery devices, sutures, ligature clamps, orthopaedic screws, and bone fixation plates is that the device does not have to be removed after its purpose has been fulfilled. The most successful class of degradable polymers so far has been the polyesters of aliphatic alpha-hydroxy acids. Extensive research is in progress to develop polymers in which the polymer properties can be altered for different applications.

The predominant procedure is ring-opening polymerization which provides a way to achieve pure and well-defined structures. We have used cyclic monomers of lactones, anhydrides, carbonates, ether-lactones, and specifically oxepane-2,7-dione, β -propiolactone, ϵ -caprolactone, 1,5-dioxepan-2-one, dilactide, and 1,3-dioxan-2-one [1-6]. The work involves the synthesis of monomers, studies of the polymerization conditions, development of crosslinked polymers and polymer blends, surface modification, and of course the characterization of the resulting materials. Future work will use simulations for obtaining very unique biomedical polymers.

THE INTERACTION OF POLYMERS WITH THE ENVIRONMENT

Reactions in polymers are often controlled by diffusion of reactive species. A great number of problems/questions, often involving multicomponent polymer systems, are asked by industry, authorities, and end users. Knowledge of the mechanisms determining migration and diffusion of additives and/or degradation products in materials will allow precise prediction of the useful lifetimes of the materials.

Environmental interaction of polymers is studied by resolving degradation product patterns and "chromatographic fingerprinting" which give clues to proposed degradation mechanisms [7-11]. By identifying degradation products of polymers in various environments, we are able to discuss the environmental interaction of polymers, i.e., the toxic properties of the products formed and how they influence the resulting degradation and the surrounding environment. Not all synthetic degradation products are dangerous, and not all natural degradation products are harmless. Knowledge about every degradation product formed gives valuable guidance to discuss the environmental interaction of polymers.

In Nature, biomolecules are transformed in anabolic and catabolic cycles. The reactions responsible for these cycles are collectively referred to as metabolism. Metabolism has four specific functions: 1) to obtain energy from the degradation of energy-rich nutrients; 2) to convert nutrient molecules into the building-block precursors of cell macromolecules; 3) to assemble these building blocks into proteins, nucleic acids, polysaccharides and other cell components; and 4) to form and degrade biomolecules required in specialized functions of cells. In principle, the central metabolic pathways are few in number and identical in most forms of life. The catabolic pathways converge to a few end products, e.g., ammonia, water, and carbon dioxide. The central metabolic pathways involve the cycling of perhaps several hundred grams of a substance per day, but there are other pathways where the flow of biopolymers is much smaller. Here, maybe milligrams of substance are formed or degraded every day, and these cycles are referred to as the secondary metabolism of the cells. Secondary metabolism leads to the formation of hundreds of highly specialized biomolecules, e.g., toxins, alkaloids, nucleotides, pigments, etc.

The formation of small molecules by the central metabolic pathways in Nature is self-regulated, i.e., overproduction of one product reduces the metabolism response of the product in question. Some of the most potent poisons in the world are biomolecules, e.g., botulin.

The degradation products of synthetic polymers are far less well-defined. In principle, some synthetic polymers form a monomer (e.g., polyester) during degradation while others form a series of different degradation products in varying amounts (e.g., polyolefins). We have identified degradation products in oxidizable (polyolefins) and hydrolyzable (polyesters and proteins) synthetic and natural polymers [7-11]. The degradation of a synthetic polymer is a continuous process, and the diffusion and migration of the degradation products are responsible for the interaction of polymers with the environment.

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