Progress in Polymer Science 35 (2010) 278–301

Contents lists available at ScienceDirect

Progress in Polymer Science

journal homepage: www.elsevier.com/locate/ppolysci

Future perspectives and recent advances in stimuli-responsive materials

Debashish Roy, Jennifer N. Cambre, Brent S. Sumerlin*

Department of Chemistry, Southern Methodist University, 3215 Daniel Avenue, Dallas, TX 75275-0314, USA

ARTICLE INFO

Article history:
Received 2 September 2009
Received in revised form 20 October 2009
Accepted 22 October 2009
Available online 3 November 2009

Keywords:
Stimuli-responsive polymers
Smart polymers
Drug delivery
Dynamic covalent chemistry
Hydrogels
Controlled release

ABSTRACT

Interest in stimuli-responsive polymers has persisted over many decades, and a great deal of work has been dedicated to developing environmentally sensitive macromolecules that can be crafted into new smart materials. However, the overwhelming majority of reports in the literature describe stimuli-responsive polymers that are sensitive to only a few common triggers, including changes in pH, temperature, and electrolyte concentration. Herein, we aim to highlight recent results and future trends that exploit stimuli that have not yet been as heavily considered, despite their unique potential. Many of the topics represent clear opportunities for making advances in biomedical fields due to their specificity and the ability to respond to stimuli that are inherently present in living systems. Recent results in the area of polymers that respond to specific antigen–antibody interactions, enzymes, and glucose are specifically discussed. Also considered are polymeric systems that respond to light, electric, magnetic, and sonic fields, all of which have potential in the area of controlled release as a result of their ability to be applied in a non-invasive and easily controlled manner. Thiol-responsive and redox-responsive polymers are also highlighted, with particular attention being devoted to their reversible dynamic covalent chemistry. It is our goal to emphasize these underutilized adaptive behaviors so that novel applications and new generations of smart materials can be realized.

Contents

Abbreviations: APBA, 3-acrylamidophenylboronic acid; ATRP, atom transfer radical polymerization; ConA, concanavalin A; CRP, controlled/"living" radical polymerization; DDOPBA, 4-(1,6-dioxo-2,5-diaza-7-oxamyl) phenylboronic acid; DTT, dithiothreitol; DMAPA, *N*,*N*-(dimethylamino)propylacrylamide; FITC, fluorescein isothiocyanate; GOx, glucose oxidase; GSH, glutathione; IgG, immunoglobulin G; IPN, interpenetrating network hydrogel; LCST, lower critical solution temperature; MBA, *N*,*N*-methylene-bis-acrylamide; NMP, nitroxide mediated radical polymerization; NSA, *N*-succinimidylacrylate; NIR, near-infrared; PAA, poly(acrylic acid); PMAA, poly(methacrylic acid); PNIPAM, poly(*N*-isopropylacrylamide); PHEMA, poly(2-hydroxyethyl methacrylate); PDMAEMA, poly(*N*,*N*-dimethylaminoethyl methacrylate); PEG, poly(ethylene glycol); PDMA, poly(*N*,*N*-dimethylacrylamide); PVA, poly(vinyl alcohol); PHPMA, poly(*N*-hydroxypropyl methacrylamide); PEO, poly(ethylene oxide); PNVP, poly(*N*-vinylpyrrolidone); PDEGA, poly(di(ethylene glycol)ethyl ether acrylate); PPO, poly(propylene oxide); RAFT, reversible addition-fragmentation chain transfer; TCEP, tris(2-carboxyethyl)phosphine; VPGVG, valine-proline-glycine-valine-glycine; UV, ultraviolet.

* Corresponding author.
E-mail address: bsumerlin@smu.edu (B.S. Sumerlin).

0079-6700/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.progpolymsci.2009.10.008

1. Introduction

At their most fundamental level, many of the most important substances in living systems are macromolecules with structures and behaviors that vary according to the conditions in their surrounding environment. A variety of biological processes rely on feedback-controlled communication involving nucleic acids, proteins, and polypeptides that have the ability to adopt conformations specific to their surroundings. Similar adaptive behavior can be imparted to synthetic (co)polymers such that their utility goes beyond providing structural support to instead allow active participation in a dynamic sense. Incorporating multiple copies of functional groups that are readily amenable to a change in character (*e.g.*, charge, polarity, and solvency) along a polymer backbone causes relatively minor changes in chemical structure to be synergistically amplified to bring about dramatic transformations in macroscopic material properties.

The "response" of a polymer can be defined in various ways. Responsive polymers in solution are typically classified as those that change their individual chain dimensions/size, secondary structure, solubility, or the degree of intermolecular association. In most cases, the physical or chemical event that causes these responses is limited to formation or destruction of secondary forces (hydrogen bonding, hydrophobic effects, electrostatic interactions, etc.), simple reactions (*e.g.*, acid–base reactions) of moieties pendant to the polymer backbone, and/or osmotic pressure differentials that result from such phenomena. In other systems, the definition of a response can be expanded to include more dramatic alterations in the polymeric structure. For example, degradation of hydrogels upon the application of a specific stimulus can occur by reversible or irreversible bond breakage of the polymeric backbone or pendant cross-linking groups. For the sake of this review, both concepts will be included, with particular attention being paid to those that hold promise in the areas of biomedical, sensing, and electronics applications.

Interest in stimuli-responsive polymers has persisted over many decades, and a great deal of work has been dedicated to devising examples of environmentally sensitive macromolecules that can be crafted into new smart materials. However, the overwhelming majority of reports in the literature describing stimuli-responsive polymers are dedicated to macromolecular systems that are sensitive to a few common stimuli, usually changes in pH, temperature, and electrolyte concentration. The purpose of this review is not to describe every stimulus being employed to induce a response in polymer systems. Rather, we aim to highlight recent results and future trends of a few particularly useful stimuli that have, in our opinion, not yet been exploited to a similar extent, despite their unique potential. In many cases, the topics represent clear opportunities for making advances in biomedical fields due to their specificity and the ability to respond to stimuli that are inherently present in biological systems. Indeed, designing synthetic polymers with the ability to adapt their properties in response to *specific* interactions with biomacromolecules and small molecules commonly associated with healthy or diseased states (*e.g.*, glucose) may facilitate the application of smart polymers in drug delivery, diagnostics, sensing, separations, etc. Additionally, it is often advantageous to utilize a stimulus that is specifically applied from an external source so that the location and rate of response can be easily adjusted, as opposed to a stimulus that is encountered as an inherent feature of the system under consideration (*e.g.*, change in pH occurring upon endocytosis). The ability to apply these sorts of stimuli in a non-invasive manner particularly lends itself to applications *in vivo*. The discussion that follows will focus on recent research in the area of smart materials by emphasizing these underutilized adaptive behaviors that have the ability to affect polymer conformation, solubility, degradability, and self-assembly behavior in aqueous media. The first areas covered will pertain to specific responses that may be encountered in biological systems. Polymers that alter their properties in response to glucose, enzymes, antigens/antibodies, and thiol/redox conditions are described. Secondly, we highlight recent results in the areas of field-responsive polymers, specifically macromolecules that exhibit adaptive behaviors when exposed to irradiation with light, electric, magnetic, or sonic energy.

2. Biologically responsive polymer systems

Smart polymers are becoming increasingly important in the context of biomedical applications. Whether for the purpose of controlled drug delivery, biosensing/diagnostics, smart films/matrices for tissue engineering, or for the *in situ* construction of structural networks,