P. Dubin · J. Bock · R.M. Davies
D.N. Schulz · C. Thies
Editors

# Macromolecular Complexes in Chemistry and Biology

Springer-Verlag

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With 196 Figures and 39 Tables



Springer-Verlag
Berlin Heidelberg New York
London Paris Tokyo
Hong Kong Barcelona Budapest

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ISBN 3-540-57166-3 Springer-Verlag Berlin Heidelberg New York
ISBN 0-387-57166-3 Springer-Verlag New York Berlin Heidelberg

Library of Congress Cataloging-in-Publication Data
Macromolecular complexes in chemistry and biology/P. Dubin ... [et al.], eds. p. cm.
Includes bibliographical references.
ISBN 0-387-57166-3
1. Polymer solutions. 2. Polyelectrolytes. 3. Complex compounds.
QD381.9.S65M32 1994 547.7'0454--dc20 93-38677 CIP



SPIN: 10076493 3020 5 4 3 2 1 0 Printed on acid-free paper

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# Preface

Throughout most of this century, progress in Polymer Science took place by way of studies of dilute polymer solutions and of the solid state. More recently, attention has been focused on the semi-dilute regime. The elucidation of transient network and temporal gel states under conditions of moderate concentration by numerous hydrodynamic and optical techniques is now well established and a solid theoretical underpinning for these phenomena is in place. However, in most of the systems studied, interpolymer interactions are relatively weak forces, because in solutions of typical polymers, strong interpolymer interactions lead to bulk phase separation. However, polymers that form highly associating structures in equilibrium solution now constitute an important class of synthetic macromolecules, and it is evident that strong intermacromolecular interactions – without accompanying phase separation – are prevalent in biopolymer systems as well. This behavior is generally characteristic of amphiphilic polymers, which contain both hydrophilic and hydrophobic repeat units. It is also characteristic of systems in which two macromolecular species are complementary, such as hydrogen-bond-donating and hydrogen-bond-accepting polymers, or polycations and polyanions.

Interest in associating polymer systems currently derives from both applied and fundamental questions. Synthetic water-soluble polymers bearing hydrophobic groups exhibit special rheological properties that make them well-suited as thickeners and viscosity-modifiers. Drag-reduction effects may arise in such polymer solutions, and may also be observed in polymer complexes based on hydrogen-bonding. Viscosity-modification has also been the motivation for many detailed studies of ionomer solutions, in which association via ion-pairing leads to aggregate formation in non-aqueous solvents. Complexes in which one component is a biological polymer also represent technological possibilities. These include protein separation via interactions with synthetic polyions, and modifications of the properties of DNA via complexation.

In this variety of associating polymer systems, a few central questions emerge as universal themes. One concerns the structure of multipolymer aggregates. In any system with strong interpolymer forces, one could anticipate interpolymer collapse, gelation, and phase separation as three reasonable consequences of these forces. Why then do many systems exhibit stable equilibrium aggregate states? In other words, the question "why do chains associate" must always be followed by another, often more difficult query: "how do they know when to stop?" If the association is at least partly open-ended, characterization of these complexes poses a set of related challenges. Since most techniques probe structure in a limited dimensional range (e.g. short range for absorption and fluorescence spectroscopy, medium range – long range for scattering methods, and long-range for rheology and viscometry) the use of a variety of experimental techniques becomes especially valuable.

This book originated from a symposium on "Soluble Polymer Complexes" sponsored by the Polymer Division of the American Chemical Society. To the editors of this volume it seemed clear that polymeric materials that can form ordered aggregates or complexes carry the potential for some novel commercial applications in both polymer chemistry and biotechnology. Consideration of the properties of these materials also raises some interesting scientific questions. These questions, which were formerly the basis for only hypothesis and speculation, appear now to be ideal subject matter for modern instrumental methods such as fluorescence probe studies and dyamic and total intensity scattering. Despite the fact that polymer complexes are of interest to a broad range of specialists, including chemical engineers, synthetic chemists, polymer physicits and biological chemists, the literature in this area is rather fragmented. Two previous books attempted to collect the material in this field. *Intermacromolecular Complexes*, by E. Tsuchida and K. Abe (Springer, 1982) surveyed the literature on both soluble and insoluble complexes and offer extensive descriptions of many specific polymer systems. *Microdomains in Polymer Solutions*, edited by one of us (PD) in 1985 (Plenum) contained reports about amphiphilic polymers and polymer-surfactant systems, about ordering in polyelectrolytes, and about association and aggregation in synthetic and natural polymers. Several new developments have taken place since the publication of those texts: the growth of biotechnology and the related interest in technological applications of polymer-protein interactions; the expansion of fluorescence and scattering techniques for the study of intra- and interpolymer association; and the study of ionomers in solution. These new developments reinforce two points about associating macromolecular systems: (1) they are important in both natural and abiotic systems, and (2) contrary to earlier thought, they are neither so inherently irreversible nor so heterogeneous as to preclude fundamental study.

In organizing the contributions to this volume, the editors first considered that the fundamental driving forces for association provide the best guide to sub-topical arrangement. Thus, we first discuss *hydrophobically* associating polymers, and secondly, *Coulombic* polyelectrolyte complexes. In the case of *Complexes involving proteins*, the subtleties of protein structure preclude the specification of a single type of interaction, but the motivation for grouping these papers together is clear, especially given the focus on protein separations. Lastly, we consider studies of the association of *Ionomers in organic media*, which occupies an important position between the long-standing literature on weakly ionic polymers in the bulk state and investigations of charged polymers in water.

The first seven chapters deal with complexes formed by the association of hydrophobic groups on water-soluble polymer backbones. These polymers pose a synthetic problem because of the incompatibility of the two monomer types. Characterization is also challenging, especially for polymers with low hydrophobe content.

*Schulz, Bock and Valint* begin by reviewing synthetic routes, through both direct copolymerization and post-polymerization reaction. NMR, UV and pyrolysis-GC methods of characterization are discussed. In the second chapter, *Varadaraj, Branham, McCormick and Bock* report on the use of emission and absorption probes to characterize the microstructure of hydrophobically associating polymers. The results suggest that interpolymer domains are more polar and less organized than conventional micelles. In chapter three, *Bock, Varadaraj, Schulz and Maurer* describe the unusual properties of hydrophobically associating water-soluble polymers. Examples of such properties are enhanced viscosification, shear thickening rheology, decreased sensitivity to salts, and increased mechanical stability. In chapter four, *Magny, Illiopoulos and Audebert* describe the dilute-solution viscometry and fluorescence of random copolymers of sodium acrylate and alkyl (octyl to octadecyl) acrylamide. Upon salt addition, a transition from nonaggregated to aggregated coils occurs. Interchain association and polyelectrolyte effects are superimposed in apparent molecular weight changes. *Varelas, Dualeh and Steiner* discuss, in chapter five, hydrogel networks formed from hydrophobically modified cellulose. Cluster formation is found to depend upon solvent composition, and the number of side-chains per cluster in turn influences the rheology of the network. The hydrophobic microdomains so formed act as solubilization sites for apolar solutes. In chapter six, *Fife* reviews the role of macromolecular association on the polymerization of alkylvinylpyridinium ions. For example, Coulombic interactions control copolymerization with anionic monomers, while hydrophobic forces influence copolymerization with water insoluble monomers. Lastly, *Zhang, Hwang and Hogen-Esch* describe, in chapter seven, the synthesis, characterization and viscosity behavior of "fluorophobe" modified polyacrylamide and cellulose derivatives. These polymers are found to be more efficient viscosity-enhancers than conventional alkyl hydrophobic polymers.

Soluble complexes involving polyelectrolytes are the subject of chapters seven through thirteen. These complexes display structural complexity and sensitivity to environment resulting from their ionic groups. The consequent structures range from colloidal droplets to semicrystalline fibers, in dilute solution, to gels and conducting solids at high concentrations. Two main classes of polyelectrolyte complexes (PEC) are discussed: those governed principally by Coulombic forces, and those strongly influenced by hydrogen bonding.

*Dautzenberg, Koetz, Linow, Philipp and Rother* describe in chapter eight the use of light scattering to probe the structure of PECs formed from oppositely charged polyacrylamides, thereby addressing what has been a long-standing problem. In chapter nine, *Frugier and Audebert* explore the solution behavior of oppositely charged polyacrylamides of low charge density, with special emphases on the effects of salt and polymer MW on phase separation. Their results point out the need for improved theories in this area. The kinetics of polyelectrolyte complexation and the role of PECs in biology are addressed in chapter ten by *Kabanov*. It is suggested that DNA complexed with polycations may be a "synthetic virus" with exciting applications in transgenic experiments. *Bystricky and Malovikova* examine the role of stereochemistry in a study of the complexation of D- and L-polylysine with anionic polysaccharides; their results in chapter may bear on the understanding of molecular recognition in biological systems. *Tsuchida and Takeoka* review, in chapter twelve, PEC formation – in both solution and solid states – between polyethylene oxide and polyacrytic or polymethacrylic acid. The intriguing application of the solid complexes in electrochromic devices is discussed. Interactions via hydrogen bonds are also the subject of *Kim and Choi's* work in chapter thirteen. Structures formed by high MW polyacrylic acid under high shear are elucidated by the use of fluorescent dyes.

The five subsequent chapters are devoted to protein-polymer complexes. These species are viewed in some cases as providing novel routes to protein separation, but in other situations the protein complex itself may have unique value.

In chapter fourteen, *Hubert and Dellacherie* review the features and limitations of several protein separation techniques based on complex formation. In one case, the hydrodynamic volume of the complex may be the key to enhanced separation. Complexation also can change the protein charge density, lead to the technique of affinophoresis. Two-phase polymeric aqueous systems allow the protein to exhibit preferential partitioning. In a fourth approach to protein separation, insoluble protein-polymer complexes may be isolated and then redissolved. In chapter fifteen, *Xia and Dubin* provide a review of "polyelectrolyte-protein" complexes, emphasizing the different experimental techniques that have been employed and discussing some of the molecular models put forward. *Shieh and Glatz* in chapter sixteen also describe similar phase separation methods for the case of lysozyme purification by precipitation with polyacrylic acid. The authors discuss the critical pH for precipitation, the stoichiometry of the complex, the precipitate's particle size, and the overall protein yield. The phenomenon of coacervation is reviewed by *Burgess* in chapter seventeen from both theoretical and experimental perspectives. The system of gum-arabic and serum albumin is the subject of experimental studies in microcapsule formation. In chapter eighteen, *Kokufuta* summarizes the complexation of proteins with strong polycations and polyanions in salt-free solution. Of special interest is the ability of precipitated proteins to display enzymatic activity.

The final section of the book deals with association of weakly ionic polymers (ionomers) in non-aqueous solvents. This area of study may bridge the gap between the fields of polyelectrolytes and ionomers. In the former case, the charged moieties are dissociated and ionized and their presence leads to chain expansion and interchain repulsion. In the latter case, the low dielectric environment in the solid state polymer precludes dissociation, and the ionic residues interact attractively through dipole-dipole forces, leading to intermacromolecular cohesion. Thus the ways these two systems behave are very different.

Ionomer solutions may display both types of behavior, depending on the dielectric constant of the medium. This question is specifically addressed in chapter nineteen by *Gebel.* The properties of lightly sulfornated polystyrene (LSPS) in polar and nonpolar solvents are discussed in terms of polyelectrolyte and ionomer behavior, respectively. In these two cases, rheological and scattering data are rationalized according to different structural models. Similar analyses are carried out for new data on perfluorinated ionomers. In chapter twenty, *Bodycomb and Hara* use dynamic and static light scattering to study the dependence of the aggregation of LSPS in toluene on ion content and ionomer concentration. They conclude that very large species can form at increased ion content.

We close this preface with expressions of appreciation for the support of the initial symposium from the American Chemical Society, for professional guidance from the staff of Springer, and for the extended cooperation of the contributors.

November 1993

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# Table of Contents

## Part II. Polyelectrolyte Complexes