Polymer Protein Conjugation Via A Grafting To Approach

Since the publication of Atherton and Sheppard's volume, the technique of Fmoc solid-phase peptide synthesis has matured considerably and is now the standard approach for the routine production of peptides. The focus of this new volume is much broader, and covers the essential procedures.

Even after significant advances in polymerization and protein modification chemistries, the majority of polymeric biomaterials focus on poly(ethylene glycol) (PEG)-based monomers. Despite their widespread use, these polymers present concerns due to their non-biodegradable nature, the possibility of toxicity and immunogenicity, and their limited chemical functionality. Therefore, there is significant interest in the rational design of alternative polymers with specific chemical or biological properties. Specifically, approaches that allow for the rapid and divergent synthesis of a large number of biodegradable polymeric materials capable of functionalization would be broadly applicable. This dissertation focuses on novel degradable and modifiable polymers with applications in protein conjugation and stabilization. In Chapter 1, the history of protein-polymer conjugates for therapeutic use is outlined, from PEGylation techniques to next-generation conjugation strategies. Alternative polymer technologies and future directions of the field are also presented. In Chapter 2, the synthesis and biological application of a degradable trehalose glycopolymer is described. The polymer is shown to stabilize the therapeutic protein granulocyte colony stimulating factor (G-CSF) against heat stress. While the polymer was noncytotoxic, its degradation products inhibited cell proliferation at high concentrations. Chapter 3 details the development of poly(caprolactone)-based polyesters for protein stabilization. An alkene-substituted polyester was synthesized and modified using thiol-ene chemistry with thiols containing glucose, lactose, trehalose, PEG, and carboxybetaine units. The relative stabilizing ability of these side-chains toward G-CSF was assessed. Trehalose and carboxybetaine were found to maintain the most protein activity upon exposure to heat stress. We varied the size of these polymers and found a dependence on molecular weight, where longer polymers were more effective protein stabilizers. These materials and their degradation products were cytocompatible, yet exhibited minimal degradation in aqueous conditions. Chapter 4 describes the synthesis of trehalose- and carboxybetaine-funcitonalized polyesters and polycarbonates with tunable degradability, with half-lives from 10 hours to over 4 months. We expect these materials will be useful in the development of novel protein-polymer therapeutics. We also describe the development of novel PEG analogs using ring-opening metathesis polymerization (ROMP). Chapter 5 describes the synthesis of these PEG analogs and subsequent conjugation to the model protein lysozyme. Exploration of post-polymerization modifications to install thiols onto the unsaturated polymer backbone are also described.

Nanomedicine is a developing field, which includes different disciplines such as material science, chemistry, engineering and medicine devoted to the design, synthesis and construction of high-tech nanostructures. The ability of these structures to have their chemical and physical properties tuned by structural modification, has allowed their use in drug delivery systems, gene therapy delivery, and various types of theranostic approaches. Colloidal noble metal nanoparticles and other nanostructures have many therapeutic and diagnostic applications. The concept of drug targeting as a magic bullet has led to much research in chemical modification to design and optimize the binding to targeted receptors. It is important to understand the precise relationship between the drug and the carrier and its ability to target specific tissues, and pathogens to make an efficient drug delivery system. This book covers advances based on different drug delivery systems: polymeric and hyper branched nanomaterials, carbon-based nanomaterials, nature-inspired nanomaterials, and pathogen-based carriers.

Contemporary approaches to the synthesis of chemically modified biomacromolecules (proteins, nucleic acids, lipids, and carbohydrates) not only require efficient means to control conjugation and the specific site of attachment of the conjugated moiety but also the effective use of recent developments in the fields of pharmaceutical chemistry, biomolecular/polymer engineering, and nanobiotechnology. In this second edition of Bioconjugation Protocols: Strategies and Methods, expert researchers update the classic methods and introduce valuable new approaches that go beyond basic conjugation techniques to include elements from advanced organic synthesis, molecular biology, surface biotechnology, materials science, and nanobioscience/engineering. These readily reproducible methods cover the preparation of biomolecular conjugates using a variety of labeling techniques and semisynthetic approaches. Additional chapters address the biofunctionalization of surface structures, including organic/inorganic thin films, as well as various types of nanostructures (magnetic nanoparticles, quantum dots, carbon nanotubes, and silicon nanowire devices). All the protocols follow the successful Methods in Molecular BiologyTM series format, each one offering step-by-step laboratory instructions, an introduction outlining the principle behind the technique, lists of the necessary equipment and reagents, and tips on troubleshooting and avoiding known pitfalls. Cutting-edge and highly practical, Bioconjugation Protocols: Strategies and Methods, Second Edition offers both novice and experienced researchers access to the broad array of techniques needed to carry out the semisynthesis of functional biomolecular reagents and/or the biofunctionalization of surfaces and structures of unique interest for a wide variety of applications, ranging from novel biomedical diagnostics to powerful new therapeutics to advanced biomaterials.

Conjugation of synthetic materials with cell-responsive biologically-active molecules, in addition to providing structural support and release of biomolecules in the regenerating region, can provide the signaling factors required to initiate the cascade of cell migration, adhesion, differentiation, maturation, growth factor modulation, maintenance of matrix integrity, and tissue morphogenesis. Nanoparticles conjugated with ligands that preferentially interact with cell surface receptors in the tumor environment have the potential to drastically improve bioavailability, selectivity and residence time of the chemotherapeutic agent in the tumor microenvironment, while limiting their peripheral toxicity. Multivalent presentation of tumor-associated antigens on a targeted delivery system containing T and B cell epitopes can result in strong, long-lasting, self-adjuvant immunity against cancer and other diseases in vaccination. These examples demonstrate that cell-responsive conjugate biomaterials have profoundly impacted the medical field. This book is divided into three sections. In the first section, synthesis and characterization, conformation, structure-activity, self-assembly, and host response of conjugate hybrid biomaterials are covered. The second section is dedicated to the applications of conjugate biomaterials in drug delivery and vaccination while the last section is devoted to tissue engineering applications including cell adhesion, control of the stem cell niche, cartilage regeneration, neural and vascular tissue engineering, and dynamic cell culture systems for functionalized biomaterials. There is no doubt that biologically-responsive conjugate biomaterials play a key role in the design of biologics and medical devices, and this pioneering reference book provides a comprehensive review on synthesis, characterization, structure-activity, 3D assembly/fabrication, host

response and the emerging applications of conjugate hybrid biomaterials.
Emphasizing four major classes of polymers for drug delivery-water-soluble polymers, hydrogels, biodegradable polymers, and polymer assemblies-this reference surveys efforts to adapt, modify, and tailor polymers for challenging molecules such as poorly water-soluble compounds, peptides/proteins, and plasmid DNA.
This thesis covers the synthesis of conjugates of 2-Deoxy-D-ribose-5-phosphate aldolase (DERA) with suitable polymers and the subsequent immobilization of these conjugates in thin films via two different approaches. 2-Deoxy-D-ribose-5-phosphate aldolase (DERA) is a biocatalyst that is capable of converting acetaldehyde and a second aldehyde as acceptor into enantiomerically pure mono- and diyhydroxyaldehydes, which are important structural motifs in a number of pharmaceutically active compounds. Conjugation and immobilization renders the enzyme applicable for utilization in a continuously run biocatalytic process which avoids the common problem of product inhibition. Within this thesis, conjugates of DERA and poly(N-isopropylacrylamide) (PNIPAm) for immobilization via a self-assembly approach were synthesized and isolated, as well as conjugates with poly(N,N-dimethylacrylamide) (PDMAA) for a simplified and scalable spray-coating approach. For the DERA/PNIPAm-conjugates different synthesis routes were tested, including grafting-from and grafting-to, both being common methods for the conjugation. Furthermore, both lysines and cysteines were addressed for the conjugation in order to find optimum conjugation conditions. It turned out that conjugation via lysine causes severe activity loss as one lysine plays a key role in the catalyzing mechanism. [...]
Protein-polymer hybrid nanomaterials, designed for the targeted delivery of therapeutic anti-cancer agents, are at the forefront of research in biotechnology, nanotechnology, and cancer therapy. Conventional chemotherapeutics exhibit non-specific toxicity due to broad biodistribution; therefore developing nano-sized drug delivery vehicles for the targeted delivery of chemotherapeutics to tumors and cancer cells is important. Nanoparticles (ranging from 10-100 nanometers in size) accumulate in solid tumors and can be functionalized in order to encapsulate therapeutics and target cancer cells. Herein, the development of two classes of protein-polymer nanomaterials is described. Vaults are naturally occurring protein-cages measuring 42 x 42 x 75 nm in dimension with a hollow internal cavity. Vaults are non-immunogenic, readily expressed, and can be engineered. We have developed stimuli responsive vault-polymer conjugates. A protein reactive thermo-responsive poly(N-isopropylacrylamide) was prepared via reversible addition-fragmentation chain transfer (RAFT) polymerization and conjugated to the vault, resulting in a thermo-responsive vault nanoparticle (Chapter 2). Dual responsive vault nanoparticles have also been developed via conjugation of a pH- and thermo-responsive polymer, poly(N-isopropylacrylamide-co-acrylic acid), prepared by RAFT polymerization (Chapter 3). The design of nanoparticles was further explored by conjugating proteins to disulfide cross-linked poly(poly(ethylene glycol) methyl ether methacrylate) (pPEGMA) nanogels. Thiol-reactive nanogels were conjugated to thiol-enriched proteins via a simple disulfide exchange reaction (Chapter 4). Additionally, the development of new methods for protein-polymer conjugation is described. Ring opening metathesis polymerization (ROMP) was used for the preparation of protein-reactive unsaturated poly(ethylene glycol) (PEG) analogs (Chapter 5). These unsaturated PEG analogs were conjugated to proteins. Due to olefins present in the polymer backbone, the polymer can be degraded from the conjugated protein by exposure to Grubbs type metathesis catalysts. Furthermore, a ROMP grafting from approach has also been developed, whereby the protein streptavidin (SAv) was functionalized with a biotinylated ruthenium metathesis catalyst. The SAv macrocatalyst was then used in the ROMP of a tetraethylene glycol modified norbornene monomer to yield a well defined protein-polymer conjugate (Chapter 6). Lastly, the preparation of a telechelic, protein-reactive polymer by RAFT polymerization is described (Chapter 7). A Boc-protected aminooxy RAFT chain transfer agent (CTA) was synthesized and utilized in the polymerization of poly(ethylene glycol) methyl ether acrylate (PEGA). The resulting aminooxy functionalized pPEGA was then functionalized post-polymerization to install cysteine-reactive vinyl sulfone functionality on the polymer.
Polymer–Protein Conjugates: From Pegylation and Beyond helps researchers by offering a unique reference and guide into this fascinating area. Sections cover the challenges surrounding the homogeneity of conjugates, their purity and polymer toxicity on long-term use, and how to deal with the risk of immunogenicity. These discussions help researchers design new projects by taking into account the latest innovations for safe and site selective polymer conjugation to proteins. PEG has been the gold standard and likely will play this role for many years, but alternatives are coming into the market, some of which have already been launched. After five decades of improvements, the ideas in this book are entering into a new era of innovation because of the advances in genetic engineering, biochemistry and a better understanding of the results from clinical use of PEG conjugates in humans. Provides an overview on the state-of-the-art of protein polymer conjugation Presents both the pros and cons of polymer-protein conjugates from the point-of-view of their clinical outcomes Outlines advantages and potential risks of present technology based on PEG Offers new alternatives for PEG and new approaches for on site-selective protein modification Identifies future direction of research in this field
Bioconjugate Techniques, 3rd Edition, is the essential guide to the modification and cross linking of biomolecules for use in research, diagnostics, and therapeutics. It provides highly detailed information on the chemistry, reagent systems, and practical applications for creating labeled or conjugate molecules. It also describes dozens of reactions, with details on hundreds of commercially available reagents and the use of these reagents for modifying or crosslinking peptides and proteins, sugars and polysaccharides, nucleic acids and oligonucleotides, lipids, and synthetic polymers. Offers a one-stop source for proven methods and protocols for synthesizing bioconjugates in the lab Provides step-by-step presentation makes the book an ideal source for researchers who are less familiar with the synthesis of bioconjugates Features full color illustrations Includes a more extensive introduction into the vast field of bioconjugation and one of the most thorough overviews of immobilization chemistry ever presented
The unique physico-chemical properties of cationic polymers and their ability to be easily modified make them attractive for many biological applications. As a result there is a vast amount of research focussed on designing novel natural or synthetic cationic polymers with specific biological functionality. Cationic Polymers in Regenerative Medicine brings together the expertise of leading experts in the field to provide a comprehensive overview of the recent advances in cationic polymer synthesis, modification and the design of biomaterials with different structures for therapeutic applications. Chapters cover recent developments in novel cationic polymer based systems including poly(L-lysine), Poly(N,N-dimethylaminoethyl methacrylate) and cationic triazine dendrimers as well as cationic polymer-coated micro- and nanoparticles and cationic cellulose and chitin nanocrystals. Applications discussed in the book include drug and gene delivery, therapeutics in thrombosis and inflammation as well as gene therapy. Suitable both for an educational perspective for those new to the field and those already active in the field, the

book appeals to postgraduates and researchers. The broad aspects of the topics covered are suitable for polymer chemists interested in the fundamentals of the materials systems as well as pharmaceutical chemists, bioengineering and medical professionals interested in their applications.

Functionalized polymers are macromolecules to which chemically bound functional groups are attached which can be used as catalysts, reagents, protective groups, etc. Functionalized polymers have low cost, ease of processing and attractive features for functional organic molecules. Chemical reactions for the introduction of functional groups in polymers and the conversion of functional groups in polymers depend on different properties. Such properties are of great importance for functionalization reactions for possible applications of reactive polymers. This book deals with the synthesis and design of various functional polymers, the modification of preformed polymer backbones and their various applications.

Smart Polymers and Their Applications, Second Edition presents an up-to-date resource of information on the synthesis and properties of different types of smart polymers, including temperature, pH, electro, magnetic and photo-responsive polymers, amongst others. It is an ideal introduction to this field, as well as a review of the latest research in this area. Shape memory polymers, smart polymer hydrogels, and self-healing polymer systems are also explored. In addition, a very strong focus on applications of smart polymers is included for tissue engineering, smart polymer nanocarriers for drug delivery, and the use of smart polymers in medical devices. Additionally, the book covers the use of smart polymers for textile applications, packaging, energy storage, optical data storage, environmental protection, and more. This book is an ideal, technical resource for chemists, chemical engineers, materials scientists, mechanical engineers and other professionals in a range of industries. Includes a significant number of new chapters on smart polymer materials development, as well as new applications development in energy storage, sensors and devices, and environmental protection Provides a multidisciplinary approach to the development of responsive polymers, approaching the subject by the different types of polymer (e.g. temperature-responsive) and its range of applications

Newcomers to the field of biopharmaceuticals require an understanding of the basic principles and underlying methodology involved in developing protein- and nucleic acid-based therapies for genetic and acquired diseases. Biomaterials for Delivery and Targeting of Proteins and Nucleic Acids introduces the principles of polymer science and che

This contribution book collects reviews and original articles from eminent experts working in the interdisciplinary arena of novel drug delivery systems and their uses. From their direct and recent experience, the readers can achieve a wide vision on the new and ongoing potentialities of different drug delivery systems. Since the advent of analytical techniques and capabilities to measure particle sizes in nanometer ranges, there has been tremendous interest in the use of nanoparticles for more efficient methods of drug delivery. On the other hand, this reference discusses advances in the design, optimization, and adaptation of gene delivery systems for the treatment of cancer, cardiovascular, pulmonary, genetic, and infectious diseases, and considers assessment and review procedures involved in the development of gene-based pharmaceuticals.

The approaches in drug design are mainly comprised of these three multidisciplinary sciences. First, Bioinformatics has successfully gather biological data in form of biomolecular sequences, in order to construct knowledge on drug and vaccine design. It is of considerable importance for drug designers to comprehend the utilization of bioinformatics tools for resolving their research questions. Second, Nanotechnology has made possible the design and delivery of the nano-based drug. Third, Pharmaceutical Chemistry made it possible to investigate the adsorption, distribution, metabolism, and toxicology of the drug candidates in a fine-grained resolution.

Dendrimers are important molecules that are currently undergoing investigation for use in a variety of different biomedical applications. This book explores the use of dendrimers for a variety of potential functions, including antiamyloidogenic agents, drug delivery systems, nucleic acid and RNA delivery vectors and to produce hybrid fibre platforms for nantechnology. Following the work of COST action TD0802, the main objective of which is to improve existing therapies and find new drugs based on dendrimers, the book will provide comprehensive coverage of dendrimer applications. Coverage includes modelling and molecular dynamic studies of dendrimers and dendrons, anionic dendrimer polymers, cationic carbosilane dendrimers and self-assembled multivalent dendrimers. Providing clear indications for future research and applications, this text will appeal to chemists, biologists and materials scientists, working in both academia and industry.

Electrospun Nanofibers covers advances in the electrospinning process including characterization, testing and modeling of electrospun nanofibers, and electrospinning for particular fiber types and applications. Electrospun Nanofibers offers systematic and comprehensive coverage for academic researchers, industry professionals, and postgraduate students working in the field of fiber science. Electrospinning is the most commercially successful process for the production of nanofibers and rising demand is driving research and development in this field. Rapid progress is being made both in terms of the electrospinning process and in the production of nanofibers with superior chemical and physical properties. Electrospinning is becoming more efficient and more specialized in order to produce particular fiber types such as bicomponent and composite fibers, patterned and 3D nanofibers, carbon nanofibers and nanotubes, and nanofibers derived from chitosan. Provides systematic and comprehensive coverage of the manufacture, properties, and applications of nanofibers Covers recent developments in nanofibers materials including electrospinning of bicomponent, chitosan, carbon, and conductive fibers Brings together expertise from academia and industry to provide comprehensive, up-to-date information on nanofiber research and development Offers systematic and comprehensive coverage for academic researchers, industry professionals, and postgraduate students working in the field of fiber science

This book is devoted to the engineering of protein-based nanostructures and nanomaterials. One key challenge in nanobiotechnology is to be able to exploit the natural repertoire of protein structures and functions to build materials with defined properties at the nanoscale using “bottom-up” strategies. This book addresses in an integrated manner all the critical aspects that need to be understood and considered to design the next generation of nano-bio assemblies. The book covers first the fundamentals of the design and features of the protein building blocks and their self-assembly illustrating some of the most relevant examples of nanostructural design. Finally, the book contains a section dedicated to demonstrated applications of these novel bioinspired nanostructures in different fields from hybrid nanomaterials to regenerative medicine. This book provides a comprehensive updated review of this rapidly evolving field.

This book is intended to provide an overview and review of the latest developments in microencapsulation processes and technologies for various fields of applications. The general theme and purpose are to provide the reader with a current and general overview of the existing microencapsulation systems and to emphasize various methods of preparation, characterization,

evaluation, and potential applications in various fields such as medicine, food, agricultural, and composites. The book targets readers, including researchers in materials science processing and/or formulation and microencapsulation science, engineers in the area of microcapsule development, and students in colleges and universities.

Polypeptide-Polymer Conjugates, by Henning Menzel Chemical Strategies for the Synthesis of Protein-Polymer Conjugates, by Björn Jung and Patrick Theato Glycopolymer Conjugates, by Ahmed M. Eissa and Neil R. Cameron DNA-Polymer Conjugates: From Synthesis, Through Complex Formation and Self-assembly to Applications, by Dawid Kedracki, Ilyès Safir, Nidhi Gour, Kien Xuan Ngo and Corinne Vebert-Nardin Synthesis of Terpene-Based Polymers, by Junpeng Zhao and Helmut Schlaad

Polymer-Protein ConjugatesFrom Pegylation and Beyond

Polymer-Protein Conjugates: From Pegylation and Beyond helps researchers by offering a unique reference and guide into this fascinating area. Sections cover the challenges surrounding the homogeneity of conjugates, their purity and polymer toxicity on long-term use, and how to deal with the risk of immunogenicity. These discussions help researchers design new projects by taking into account the latest innovations for safe and site selective polymer conjugation to proteins. PEG has been the gold standard and likely will play this role for many years, but alternatives are coming into the market, some of which have already been launched. After five decades of improvements, the ideas in this book are entering into a new era of innovation because of the advances in genetic engineering, biochemistry and a better understanding of the results from clinical use of PEG conjugates in humans. Provides an overview on the state-of-the-art of protein polymer conjugation Presents both the pros and cons of polymer-protein conjugates from the point-of-view of their clinical outcomes Outlines advantages and potential risks of present technology based on PEG Offers new alternatives for PEG and new approaches for on site-selective protein modification Identifies future direction of research in this field

Recent important discoveries and developments in nanotechnology have had a remarkable and ever-increasing impact on many industries, especially materials science, pharmaceuticals, and biotechnology. Nanocarriers have been investigated for a wide variety of different medical applications. Some examples of these nanocarriers include polymersomes, liposomes, micelles and carbon-based nanomaterials. Within this book, the authors describe different features of carbon nanotubes (CNTs), survey the properties of both the multi-walled and single-walled varieties, and cover their applications in drug and gene delivery. In addition, the book explains the structure and properties of CNTs prepared by different method, and discussed their isolation and purification. The future of CNTs in the field of biomedical science will depend on minimizing their adverse effects by careful study of their structure and properties.

Mimicking natural biochemical processes, click chemistry is a modular approach to organic synthesis, joining together small chemical units quickly, efficiently and predictably. In contrast to complex traditional synthesis, click reactions offer high selectivity and yields, near-perfect reliability and exceptional tolerance towards a wide range of functional groups and reaction conditions. These ‘spring loaded’ reactions are achieved by using a high thermodynamic driving force, and are attracting tremendous attention throughout the chemical community. Originally introduced with the focus on drug discovery, the concept has been successfully applied to materials science, polymer chemistry and biotechnology. The first book to consider this topic, Click Chemistry for Biotechnology and Materials Science examines the fundamentals of click chemistry, its application to the precise design and synthesis of macromolecules, and its numerous applications in materials science and biotechnology. The book surveys the current research, discusses emerging trends and future applications, and provides an important nucleation point for research. Edited by one of the top 100 young innovators with the greatest potential to have an impact on technology in the 21st century according to Technology Review and with contributions from pioneers in the field, Click Chemistry for Biotechnology and Materials Science provides an ideal reference for anyone wanting to learn more about click reactions.

This volume of Macromolecular Symposia contains papers presented at the 1st International Symposium on "Reactive Polymers in Inhomogeneous Systems, in Melts and at Interfaces" held in Dresden Germany in July 2000. It includes 42 contributions from renowned scientists dealing with topics of current interest in the field of synthesis, characterization and application of reactive and functional polymers. The papers add significantly to the current understanding of the role of reactive polymers in phenomena such as adhesion, colloidal stability, corrosion resistance and biocompatibility - comprehension which is vital for improving the polymer technologies available today and for the development of new applications.

PEGylation technology and key applications are introduced by this topical volume. Basic physical and chemical properties of PEG as basis for altering/improving in vivo behaviour of PEG-conjugates such as increased stability, improved PK/PD, and decreased immunogenicity, are discussed. Furthermore, chemical and enzymatic strategies for the coupling and the conjugate characterization are reported. Following chapters describe approved and marketed PEG-proteins and PEG-oligonucleotides as well as conjugates in various stages of clinical development.

Proceedings of an ACS-PMSE Division Symposium held in Orlando, Florida, August 21-25, 1996

There is much interest in using biological structures for the fabrication of new functional materials. Recent developments in the particle character and behaviour of proteins and viral particles have had a major impact on the development of novel nanoparticle systems with new functions and possibilities. Bio-Synthetic Hybrid Materials and Bionanoparticles approaches the subject by covering the basics of disciplines involved as well as recent advances in new materials. The first section of the book focusses on the design and synthesis of different bionanoparticles and hybrid structures including the use of genetic modification as well as by organic synthesis. The second section of the book looks at the self-assembling behaviour of bionanoparticles to form new materials. The final section looks at bionanoparticle-based functional systems and materials including chapters on biomedical applications and electronic systems and devices. Edited by leading scientists in bionanoparticles, the book is a collaboration between scientists with different backgrounds and perspectives which will initiate the next generation of bio-based structures, materials and devices.

Nanoarmoring of Enzymes: Rational Design of Polymer-Wrapped Enzymes is the latest volume in the Methods in Enzymology series and focuses on nanoarmoring of enzymes and the rational design of polymer-wrapped enzymes. Focuses on the nanoarmoring of enzymes Covers the rational design of polymer-wrapped enzymes Includes contributions from leading authorities working in enzymology Informs and updates on all the latest developments in the field of enzymology

Many key aspects of life are based on naturally occurring polymers, such as polysaccharides, proteins and DNA. Unsurprisingly, their molecular functionalities, macromolecular structures and material properties are providing inspiration for designing new polymeric materials with specific functions, for example, responsive, adaptive and self-healing materials. Bio-inspired Polymers covers all aspects of the subject, ranging from the synthesis of novel polymers, to structure-property relationships, materials with advanced properties and applications of bio-inspired polymers in such diverse fields as drug delivery, tissue engineering, optical materials and lightweight structural materials. Written and edited by leading experts on the topic, the book provides a comprehensive review and essential graduate level text on bio-inspired polymers for biochemists, materials scientists and chemists working in both industry and academia.

The concept of smart drug delivery vehicles involves designing and preparing a nanostructure (or microstructure) that can be loaded with a cargo, this can be a therapeutic drug, a contrast agent for imaging, or a nucleic acid for gene therapy. The nanocarrier serves to protect the cargo from degradation by enzymes in the body, to enhance the solubility of insoluble drugs, to extend the circulation half-life, and to enhance its penetration and accumulation at the target site. Importantly, smart nanocarriers can be designed to be responsive to a specific stimulus, so that the cargo is only released or activated when desired. In this volume we cover smart nanocarriers that respond to externally applied stimuli that usually involve application of physical energy. This physical energy can be applied from outside the body and can either cause cargo release, or can activate the nanostructure to be cytotoxic, or both. The stimuli covered include light of various wavelengths (ultraviolet, visible or infrared), temperature (increased or decreased), magnetic fields (used to externally manipulate nanostructures and to activate them), ultrasound, and electrical and mechanical forces. Finally we discuss the issue of nanotoxicology and the future scope of the field.

This authoritative book on MALDI MS, now finally available in its second edition and edited by one of its inventors, gives an in-depth description of the many different applications, along with a detailed discussion of the technology itself. Thoroughly updated and expanded, with contributions from key players in the field, this unique book provides a comprehensive overview of MALDI MS along with its possibilities and limitations. The initial chapters deal with the technology and the instrumental setup, followed by chapters on the use of MALDI MS in protein research (including proteomics), genomics, glycomics and lipidomics. The option of MALDI-MS for the analysis of polymers and small molecules are also covered in separate chapters, while new to this edition is a section devoted to the interplay of MALDI MS and bioinformatics. A much-needed practical and educational asset for individuals, academic institutions and companies in the field of bioanalytics.

The Concise Encyclopedia of Biomedical Polymers and Polymeric Biomaterials presents new and selected content from the 11-volume Biomedical Polymers and Polymeric Biomaterials Encyclopedia. The carefully culled content includes groundbreaking work from the earlier published work as well as exclusive online material added since its publication in print. A diverse and global team of renowned scientists provide cutting edge information concerning polymers and polymeric biomaterials. Acknowledging the evolving nature of the field, the encyclopedia also features newly added content in areas such as tissue engineering, tissue repair and reconstruction, and biomimetic materials.

For this ready reference, the internationally renowned authority in the field, Roland Kontermann, has assembled a team of outstanding contributors from industry and academia to convey the worldwide knowledge on modifying therapeutic proteins in order to optimize their pharmacological potential. The result is a comprehensive work covering all approaches and aspects of the topic in one handy volume, making this indispensable reading for companies and research institutions working on the development of biopharmaceuticals.

Nowadays, the implementation of novel technological platforms in biosensor-based developments is primarily directed to the miniaturization of analytical systems and lowering the limits of detection. Rapid scientific and technological progress enables the application of biosensors for the online detection of minute concentrations of different chemical compounds in a wide selection of matrixes and monitoring extremely low levels of biomarkers even in living organisms and individual cells. This book, including 16 chapters, characterizes the present state of the art and prospective options for micro and nanoscale activities in biosensors construction and applications.

This volume explores diverse protocols for peptide conjugation, and provides thoroughly tested and scientifically valid techniques that allow researchers and scientists to prepare, purify, characterize, and use peptide conjugation methods for chemical, biochemical, and biological studies. Some of the topics discussed in this book are gold nanoparticles, proteins, pegylated lipids, and vitamins. Chapters also cover enzymatic ligation using sortase A, construction of a phage-displayed cyclic-peptide library, quantum dot-peptide conjugates, and preparation of lipopeptides by CLipPA chemistry. Written in the highly successful Methods in Molecular Biology series format, chapters include introductions to their respective topics, lists of the necessary materials and reagents, step-by-step, readily reproducible laboratory protocols, and tips on troubleshooting and avoiding known pitfalls. Cutting-edge and comprehensive, Peptide Conjugation: Methods and Protocols is a valuable resource for experienced researches and undergraduate students alike who are interested in learning more about this exciting and developing field.

Protein therapeutics have become essential to the healthcare and pharmaceutical industries since the first recombinant proteins entered the clinic in the 1980s. Modification of proteins with polymers has traditionally been pursued as a means to improve protein stability and enhance pharmacokinetic properties. In addition to these benefits, polymer conjugation can also be utilized to control and modulate protein activity. The first polymer used for protein conjugation was poly(ethylene glycol) (PEG) in 1977. PEG is currently the only FDA-approved polymer for protein conjugation and 10 PEGylated protein drugs are currently on the market. This dissertation offers three modifications to traditional PEGylation, which allow for the modulation of protein activity. In the first example, masking and unmasking the activity of a model protein, lysozyme, was achieved by incorporating both a reducible disulfide linkage between the polymer and the protein as well as incorporating degradable cyclic ketene acetal (CKA) moieties throughout the backbone of a PEG-like polymer (Chapter 2). Specifically 5,6-benzo-2-methylene-1,3-dioxepane and poly(ethylene glycol) methyl ether methacrylate (PEGMA) were copolymerized by reversible addition-fragmentation chain transfer polymerization (RAFT) facilitated by a cysteine-reactive, pyridyl disulfide (PDS) modified chain transfer agent (CTA). Two polymers, a small (Mn GPC = 10.9 kDa) and a large (Mn GPC = 20.9 kDa) PDS-pPEGMA-co-BMDO, were synthesized with reasonable control (dispersities ( ) = 1.34 and 1.71, respectively). The polymers were then conjugated to a thiol-enriched hen egg white lysozyme by disulfide exchange. Conjugation with the 10.9 kDa polymer resulted in a conjugate, which exhibited high initial activity (63%) while the larger conjugate activity was highly attenuated (20%). Lysozyme release from both polymers by reduction of the disulfide linkage and by hydrolytic cleavage, in basic media, of the polymer backbone was visualized by gel electrophoresis. Reduction of the disulfide conjugation linkage with glutathione resulted in an increase in protein activity for both conjugates. In the next example, site-specific chemical dimerization of fibroblast growth factor 2 (FGF2) with a PEG linker, of optimized length, resulted in a FGF2 homodimer with wound healing ability at exceptionally low concentrations (Chapter 3). Homodimers of FGF2 were synthesized through site-specific conjugation to both ends of poly(ethylene glycol) (PEG). FGF2 was conjugated to 2, 6, and 20 kDa vinyl sulfone bis-functionalized PEG, as well as to a small molecule and mono-functionalized PEG controls. The optimal linker length was determined by screening FGF2 dimer-induced proliferation of human dermal fibroblasts (HDF). The inter-cyteine distance was calculated to be approximately 70 A , which is similar in length to a 2 kDa PEG. FGF2-PEG2k-FGF2 induced greater fibroblast proliferation than FGF2 alone, all other dimers, and all monoconjugates, at each concentration tested, with the greatest difference observed at low (0.1 ng/mL) concentration. FGF2-PEG2k-FGF2 further exhibited superior activity compared to FGF2 for both proliferation and migration in human umbilical vein endothelial cells, as well as improved angiogenesis in vitro. Efficacy in an in vivo wound healing model was assessed in diabetic mice. FGF2-PEG2k-FGF2 increased granulation tissue and blood vessel density in the wound bed compared to FGF2. The results suggest that this rationally designed construct may be useful in chronic wound healing. Lastly, a block copolymer capable of noncovalent and releasable conjugation to histidine-6 tagged proteins, consisting of a PEG-based block and a Ni(II) nitriolotriacetic acid (NTA)-based block was synthesized (Chapter 4). The first block was synthesized via RAFT polymerization of a NTA monomer. The resulting polymer was then utilized as a macro-CTA for the polymerization of PEGMA, resulting in a pNTAMA-b-PEGMA, containing 9 NTAMA repeats and 8 PEGMA repeats, with number average molecular weight (Mn) (GPC) = 9.9 kDa and dispersity ( ) = of 4.5. The high dispersity indicates a lack of control, and disproportionation was further confirmed by 1H-NMR. Initial

studies indicated that mono-NTA-His6 interactions are not sufficient for protein conjugation, therefore extension of this work towards a multi-valent approach may prove effective in the future.