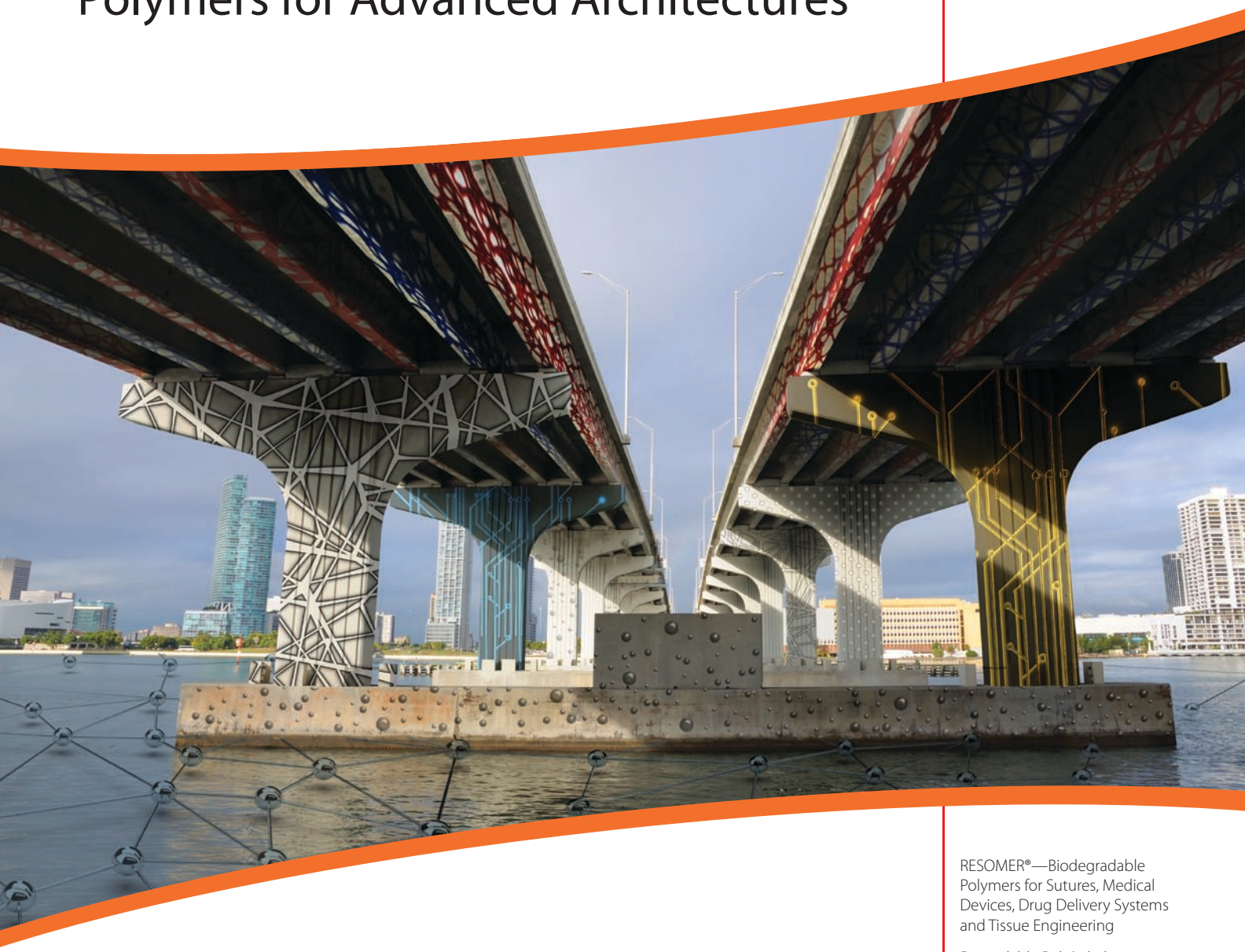
Material Matters™

Volume 6, Number 3

ALDRICH® Materials Science

Polymers for Advanced Architectures



Supporting Your Drive to Future Technologies

RESOMER®—Biodegradable Polymers for Sutures, Medical Devices, Drug Delivery Systems and Tissue Engineering

Degradable Poly(ethylene glycol) Hydrogels for 2D and 3D Cell Culture

Polyelectrolyte Multilayer Films and Membrane Functionalizaton

The Use of Block Copolymers in Nanoscale Patterning

Introduction

Sebastian Grajales, Ph.D.
Aldrich® Materials Science
Sigma-Aldrich Co. LLC

Welcome to the third 2011 issue of ***Material Matters***™, which focuses on polymers for advanced architectures. This issue contains a central theme on the use of polymers to create certain structures or environments which then provide functionality or an ability to further manipulate this environment. For some applications, precise control of macromolecular architecture and distribution of chain lengths is necessary, while others are dependant on tailored functionality on the polymer. The review articles in this issue serve to illustrate the effect of the polymer structure on the resulting architecture properties, with examples from biomedical, membrane, and nanolithography applications.

Degradation time is a critical structural-dependant property in several biotechnology applications such as biomedical devices, tissue engineering, and drug delivery. The first article reviews polyesters, such as polylactide and polyglycolide, and their applications in biodegradable sutures and implants. The RESOMER® polymers are specifically designed for controlled degradation, with lifetimes from a few days to a few years.

The second article describes poly(ethylene glycol) (PEG)-based hydrogels with tunable degradability primarily intended for tissue engineering and drug delivery. Functionalized PEGs provide an opportunity for formation of a gel with certain properties, and then the ability to degrade via hydrolysis, enzymatic cleavage, or light. These gels are useful models of tissue culture due to their ability to form in the presence of cells, proteins, and DNA.

The third article describes the layer-by-layer deposition of complementary polyelectrolytes to form functionalized films and membranes. This technique provides tailored permeability and selectivity, as well as an opportunity to incorporate particles such as enzymes and catalysts to influence chemical reactions.

The fourth article reviews the use of block copolymers in nanoscale patterning. The precise control of the ratio and length of blocks dictate the resulting film thickness and morphologies. These can be controlled to form lamellae or cylinders of either block component as well as assemble into device-oriented structures.

This issue purposefully did not include polymerization tools, but you may notice that some of the polymers have functionality suited for controlled radical polymerization (CRP), such as ATRP or RAFT. We are devoted to meeting your CRP needs and recommend that you visit our website at Aldrich.com/crptools to browse our offering.

Each article in this issue is accompanied by a list of polymers available from Aldrich® Materials Science. Please contact us at **matsci@sial.com** if you need any material that you cannot find in our catalog, or would like a custom material for your development work. We welcome your new product requests and suggestions as we continue to grow our polymer offering.

About Our Cover

Polymers support advancements in many areas of research, including medical devices, drug delivery, tissue engineering, advanced separations and nanolithography. Researchers are continually discovering new innovative ways to design macromolecules to form specialized physical architectures, such as block copolymers to pattern surfaces, functionalized poly(ethylene glycol)s for biodegradable hydrogels, polyesters to create biodegradable medical implants, and polyelectrolytes for membranes and membrane reactors. The cover represents how these specialty polymers with diverse functionality serve as a foundation, which supports researchers on the path to scientific understanding.

Material Matters™

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Jeff Thurston, President
Aldrich Chemical Co., Inc.

Do you have a compound that you wish Aldrich® Materials Science could list to help materials research? If it is needed to accelerate your research, it matters—send your suggestion to ***matsci@sial.com*** *and we will be happy to give it careful consideration.*

Dr. Nikzad Nikbin of Professor Steve Ley's group at the University of Cambridge, U.K. kindly suggested that we offer 1,4-*bis*(4-vinylphenoxy)butane (**Aldrich Prod. No. 730262**) as a product in our catalog. This bis-styrene is commonly used as a crosslinker to form swellable resins, such as JandaJel™. These gels have been shown to provide a microenvironment for the Mitsunobu reaction and for alcohol bromination.[1] Additionally, it was used in a series of triphenylphosphine loaded resins which catalyzed aza-Morita-Baylis-Hillman reactions of *N*-tosyl arylimines and a variety of Michael acceptors.[2] The cross-linked resins have been shown to swell in a wide variety of both polar and non-polar solvents.[3]

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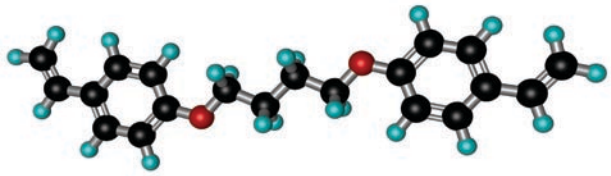
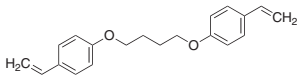


1,4-Bis(4-vinylphenoxy)butane, >90%

JandaJel™ crosslinker
[112309-98-5] $C_{20}H_{22}O_2$ FW 294.39



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Featured Products

RESOMER®—Biodegradeable Polymers for Sutures, Medical Devices, Drug Delivery Systems and Tissue Engineering

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Introduction

The ability for synthetic polymers to degrade in a controlled manner was developed for environmental reasons in the late 1960s. Interest in utilizing biodegradable polymers for biomedical applications rapidly followed and research focused on designing novel materials has continued to grow. Biodegradable polymers can be tailored for controlled degradation through numerous functional groups including esters, amides, anhydrides, and others. Among these, polyesters synthesized from lactide (1) and glycolide (2), shown in **Figure 1**, are of particular interest because they are well tolerated in biological systems and display distinct tunable physicochemical and mechanical properties. Synthetically, poly(glycolide) (PGA) (3) and poly(lactide) (PLA) (4) are typically prepared via ring-opening polymerization of lactide and glycolide, respectively. Their degradation products are predominantly glycolic acid (5) and lactic acid (6), respectively.

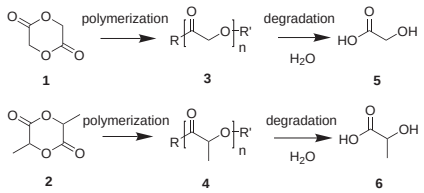

Figure 1. Chemical structures of glycolide (1) and lactide (2); the corresponding polymers polyglycolide (PGA) (3) and polylactide (PLA) (4); and glycolic acid (5) and lactic acid (6).

Most biomedical applications have specific requirements and high quality materials are crucial in order to obtain reliable and predictable behavior. The quality of these polymers is characterized by a narrow molecular weight distribution, a low residual monomer content, minimal impurities, and a well-defined chemical structure. The desired parameters can be controlled via living ring opening polymerization to design polymers with well defined properties specific to the application need. Historically, polyhydroxyester was the first biodegradable polymer utilized in a biomedical application as a biodegradable suture material. Other biodegradeable polymers and applications followed which include their utilization for biodegradable medical devices (screws, plates, stents), as drug carriers, and as material for tissue engineering. Depending on the desired application the required degradation rate can range from a few days to a few years.

RESOMER® polymers are bioresorbable aliphatic polyesters comprised of a range of different ratios of lactide and glycolide monomers, PLA stereochemistries, and end-group functionalization. These biodegradeable homopolymers and copolymers of lactide and glycolide afford a variety of properties that range from very stiff, hard semi-crystalline materials with long degradation times, to softer, amorphous materials with faster degradation rates. The general trends are summarized in **Table 1**.

Table 1. Key parameters and corresponding effects on RESOMER® properties.

Parameter	Influence
Molecular Weight	High M_w increases the degradation time
Ratio Lactide/Glycolide	Polymers with one monomer degrade more slowly. Degradation times: PLA > PGA > PLGA 50:50
Stereochemistry	L-PLA: semicrystalline D,L-PLA: amorphous
Blockage of Acidic Endgroups	Polymers with free -COOH groups are more hydrophilic (e.g., R503H compared to R503)
PEGylation	Increase in hydrophilicity, change of degradation and release behavior

Degradation

The presence of water leads to hydrolysis of the RESOMER® polymers. **Figure 2** illustrates the steps involved in the biodegradation processes of RESOMER® polymers. In the first step water wets the surface and diffuses into the polymer. The rate of the diffusion depends on porosity, pore size and surface tension. In the second step, ester linkage hydrolysis cleaves the chain into smaller chain lengths (polymer degradation). As the degradation proceeds, smaller chain segments (<100 g/mole), start to dissolve and polymer erosion takes place (step 3). The solubilized monomers/oligomers are then excreted via the kidney or metabolized into carbon dioxide and water (step 4). At the end of the process the polymer is completely absorbed and eliminated from the body. The complete disappearance of biodegradable polymers after the duration of their lifecycle (e.g., fixation or drug release) is a highly desired feature. The complete disappearance is an intrinsic characteristic of RESOMER® polymers due to the high water solubility of the monomers. In contrast, hydrophobic monomers of polyanhydrides tend to reside locally long after the polymer has degraded due to their poor solubility.[1,2]

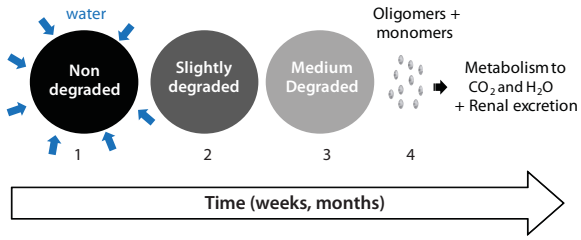

Figure 2. The biofate of RESOMER® polymers includes several steps: (1) Wetting and water diffusion, (2) Decrease of the molecular weight = Polymer degradation (3) Mass loss = Polymer erosion and (4) Renal excretion or metabolism to carbon dioxide and water.

In addition to the inherent polymer properties, the final performance and residence time of a biodegradable device can be tailored by processing and introduction of copolymers or additives. For example, amphiphilic substances incorporated into the device will increase wettability, and processing that generates high porosity will increase the water penetration. The concentration and the size distribution of incorporated substances (e.g., therapeutic agents) can change the kinetic parameters of the degradation processes shown in **Figure 2**. Strong alkaline or acidic materials can enhance polymer degradation. The microclimate inside the polymers is a crucial factor for release and degradation processes. It has been shown, that the pH inside PLGA implants can drop to pH values as low as pH 2 *in vivo*.[3] Excellent work by the groups of Schwendemann, Siepmann, and Göpferich and others show that (i) degradation is often heterogeneous and occurs faster in the central part of the delivery systems, (ii) acidic pH environments are also present in microparticles and (iii) therapeutic agents and/or buffering substances can modify the microclimate and, therefore, the kinetics of polymer degradation and drug release.[4-7] An acidic microenvironment could also interfere with the performance of an incorporated drug. Recent studies show that an acidic microclimate favors the covalent modification of peptide drugs by polymer degradation products, but incorporation of appropriate salts avoided the pH drop and stabilized peptide and protein drugs.[8]

Implant Formulation

Several processing technologies can be applied to biodegradable polyesters to formulate coatings, implants, micro- and nanoparticles, or micro- and nanocapsules. Most commonly used are thermal-mechanical treatment or solution facilitated technologies (**Figure 4**).

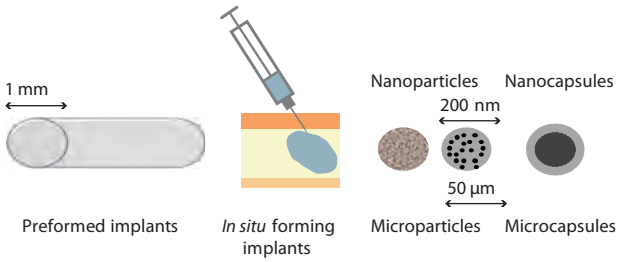

Figure 3. Most commonly used formulation principles and their typical sizes for controlled release applications for RESOMER® polymers.

Melt extrusion is one method that is utilized in the production of sutures and preformed implants. Moderate heat can be used to thermally process most RESOMER® polymers, for example X has a glass transition temperature (T_g) of ~50 °C. Peptide-loaded, preformed PLGA or PLA implants are widely used as 1 to 6 months depot formulations for the treatment of hormone sensitive prostate or breast cancer. A depot formulation is injected subcutaneously or intramuscularly and contains pharmacological agent which is released in a controlled manner over a long period of time. Recently, smaller sized dexamethasone-loaded PLGA intravitreal implants have reached the market to treat macular edema in the eye.[9]

An alternative approach to preformed implants is the *in situ* formation of implants. In this method biodegradeable PLGA or PLA polymers are dissolved in a biocompatible organic solvent and injected into the patient. *In situ* implant formation is easy and has low processing costs compared to preformed implants. In addition, smaller needles are used in this method that has a clear advantage to the patient. However, the size and the shape of the resulting implant shows significant variability and depends strongly on the application procedure and the local tissue conditions. In addition, the initial burst release is high and difficult to control.

Another route to deliver therapeutic agents is via microparticle encapsulation. Microparticles are commonly used for the parenteral delivery of hydrophilic or hydrophobic drugs. The loaded microparticles are commonly prepared via spray drying, coacervation or emulsification with solvent evaporation. The drug is either solubilized or dispersed within the microparticle. The release profile depends on the size distribution and porosity of the microparticles, the drug characteristics and concentration, and the release conditions. Often the release profiles show the following phases: (1) initial burst release; followed by a (2) slower release phase and (3) an accelerated final release phase. The accelerated final release phase is caused by the acidic microclimate inside the particle generated by the autocatalytic degradation of the polyester. The release profile can be adjusted by appropriate formulation parameters. For example, linear release, pulsed release (e.g., for vaccination) with no burst release, and a tunable lag phase release can be achieved.

RESOMER® polymers can also be formulated as nanoparticles or nanocapsules. The primary administration route of the nanoscaled systems is intraveneous injection. The nanoparticles can be used for diagnostic purposes or the treatment of tumors. Other administration routes of nanosized polyesters are oral, dermal, pulmonal or ocular drug delivery. The use of oral administration PLA/PLGA based nanoparticles permits a localized delivery to inflamed tissue, decreases the side effects and increases the efficacy of the treatment. Prolonged residence times on the tissue surface have been observed.

PEGylation

Although a significant range of applications are available with PLA and PLGA copolymers, the introduction of chemical modification by incorporating polyethylene glycol (PEGylation) to the polyesters opens new avenues for applications.

PEGylation has a measurable impact on degradation and erosion, as shown in **Figure 4**. For PLGA, degradation takes place for approximately three weeks before erosion occurs. Erosion commences once the molecular weight drops to ~7,000–8,000 g/mole, and occurs at a relatively rapid rate. However, PEGylated PLGA copolymers (PEG-PLGA) show both degradation and erosion without any lag time. Although erosion is faster at the initial stage, as expected for the more hydrophilic PEG-PLGA, PLGA reaches the final mass over a much shorter timeframe. This nonlinear behavior of PLGA is explained by the autocatalytic degradation and the acidic microenvironment inside PLGA.

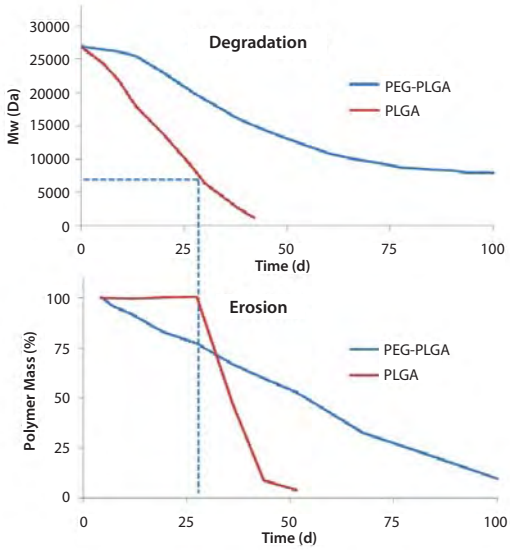

Figure 4. Typical time course of polymer degradation (top) and erosion (bottom) for PLGA and PEG-PLGA polymers.[10-12]

The incorporation of even low percentages of PEG accelerates water penetration and enables the rapid diffusion out of low molecular weight degradation products (typically acids). Therefore, the decrease in acidic microenvironments decreases the impact of autocatalysis and slows the degradation rate.

The rate of release of therapeutic agents can also be tailored with PEGylated RESOMER® polymers. Small molecular drugs are rapidly released from PEGylated RESOMER® polymers, but larger peptides and proteins can be released over days to several weeks. PEGylation increases the hydrophilicity of the polymers. The hydrophilicity can be tuned by the change of the chain lengths and the ratio of the hydrophilic PEG and the hydrophobic PLA/PLGA blocks. However, a high percentage of PEG leads to micelle forming copolymers. If the hydrophilicity is balanced, the polymers form lamellar phases. Polymers with lower PEG contents (<30 %) are not self-solubilizing and form nano- or microparticles or implants. However, due to the phase separation of PEG-PLA and PEG-PLGA, hydrophilic nanodomains exist. These nanodomains are a good environment for proteins. Many publications show that PEG-PLA and PEG-PLGA polymers are superior when compared to PLA and PLGA, for the controlled release of proteins as defined by a reduction of the initial burst release, for a much better control of the overall release profile, and for preservation of the protein activity. The introduction of PEG has a significant impact on the water penetration, polymer degradation and the release characteristics. It has been shown that water penetration into PEG-PLGA microparticles is very fast which leads to a fast solubilization of the protein. Low molecular weight compounds are immediately released; however, the protein is restricted in the PEG chains of the PEG-PLGA microparticles and a controlled release over days and weeks is achieved. PEG-PLGA polymers degrade initially faster and show often a more linear degradation and erosion profile. In contrast, pure PLA or PLGA polymers show often initial lag times due to the slow penetration of water. However, very often autocatalysis takes place and the degradation is accelerated due to the development of an acidic microclimate. Therefore, PLA and PLGA polymers can degrade faster despite their higher hydrophobicity. The desired release profile from PEGylated polymers can be achieved by the formulation process and the selection of the appropriate PEG content and/or chain length.

PEGylated RESOMER® has been used for the encapsulation of Bone Morphogenic Protein II (BMP II).[13] The microparticles showed a tunable and controlled release profile and were able to induce bone formation *in vivo* after subcutaneous injection. PEGylated RESOMER® can be used also for the formulation of emulsifier free nanoparticles and nano-capsules. The particles are known to show long circulation times due to the stealth effect of PEG which reduces the interaction with the system. In conclusion, RESOMER® polymers are biodegradable and diverse materials for a wide range of applications. The appropriate selection of the polymer chemical composition and tailored formulation process can be used to obtain the desired properties for a given application. The development of PEGylated RESOMER® polymers offers new applications in the field of the Biopharmaceutics.

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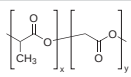
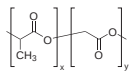
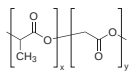
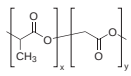
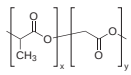
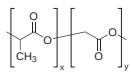
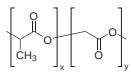
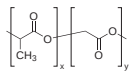
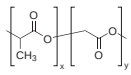
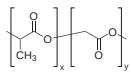
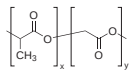
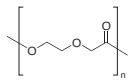
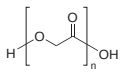
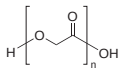
Biodegradable Polymers

For a complete list of available biodegradable polymers, visit Aldrich.com/biopoly

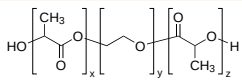
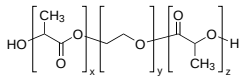
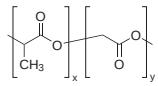
RESOMER® Products

Name	Synonym(s)	Structure	Molecular Weight	Prod. No.
Poly(L-lactide), ester terminated	RESOMER® L 206 S		-	719854-5G 719854-25G
Poly(D,L-lactide), alkyl ester terminated	RESOMER® R 202 S		M_w 10,000-18,000	719951-1G 719951-5G
Poly(D,L-lactide), acid terminated	RESOMER® R 202 H		M_w 10,000-18,000	719978-1G 719978-5G
Poly(D,L-lactide), alkyl ester terminated	RESOMER® R 203 S		M_w 18,000-28,000	719935-1G 719935-5G
Poly(D,L-lactide), acid terminated	RESOMER® R 203 H		M_w 18,000-24,000	719943-1G 719943-5G
Poly(D,L-lactide-*co*-glycolide), ester terminated, (50:50)	RESOMER® RG 502		M_w 7,000-17,000	719889-1G 719889-5G
Poly(D,L-lactide-*co*-glycolide), acid terminated, (50:50)	RESOMER® RG 502 H		M_w 7,000-17,000	719897-1G 719897-5G
Poly(D,L-lactide-*co*-glycolide), ester terminated, (50:50)	RESOMER® RG 503		M_w 24,000-38,000	739952-1G 739952-5G
Poly(D,L-lactide-*co*-glycolide), acid terminated, (50:50)	RESOMER® RG 503 H		M_w 24,000-38,000	719870-1G 719870-5G
Poly(D,L-lactide-*co*-glycolide), ester terminated, (50:50)	RESOMER® RG 504		M_w 38,000-54,000	739944-1G
Poly(D,L-lactide-*co*-glycolide), acid terminated, (50:50)	RESOMER® RG 504 H		M_w 38,000-54,000	719900-1G 719900-5G
Poly(D,L-lactide-*co*-glycolide), ester terminated, (50:50)	RESOMER® RG 505		M_w 54,000-69,000	739960-1G 739960-5G
Poly(D,L-lactide-*co*-glycolide), acid terminated, (65:35)	RESOMER® RG 653 H		M_w 24,000-38,000	719862-1G 719862-5G
Poly(D,L-lactide-*co*-glycolide), acid terminated, (75:25)	RESOMER® RG 752 H		M_w 4,000-15,000	719919-1G 719919-5G
Poly(D,L-lactide-*co*-glycolide), alkyl ester terminated, (75:25)	RESOMER® RG 756 S		M_w 76,000-115,000	719927-1G 719927-5G
Poly(D,L-lactide-*co*-glycolide), alkyl ether terminated, (85:15)	RESOMER® RG 858 S		M_w 190,000-240,000	739979-1G 739979-5G
Poly(dioxanone), viscosity 1.5-2.2 dL/g	RESOMER® X 206 S		-	719846-1G 719846-5G

Lactides and Glycolides

Name	Structure	Inherent Viscosity	Molecular Weight	Prod. No.
Poly(L-lactide)		~0.5 dl/g	M_n 50,400 M_w 67,400	94829-1G-F 94829-5G-F
Poly(L-lactide)		~1.0 dl/g	M_n 59,100 M_w 101,700	93578-5G-F
Poly(L-lactide)		~2.0 dl/g	M_n 99,000 M_w 152,000	81273-10G
Poly(L-lactide)		~4.0 dl/g	M_n 103,200 M_w 258,700	95468-1G-F 95468-5G-F
Polyglycolic acid		1.2 dl/g	-	46746-1G 46746-10G
Polyglycolide		1.4-1.8 dL/g	-	457620-5G

Other Biodegradable Copolymers

Name	Structure	Molecular Weight	Prod. No.
Polylactide-*block*-poly(ethylene glycol)-*block*-polylactide		PEG average M_n900 PLA average M_n3,000 (total)	659630-1G
Polylactide-*block*-poly(ethylene glycol)-*block*-polylactide		PEG average M_n10,000 PLA average M_n2,000	659649-1G
Poly(D,L-lactide-*co*-glycolide), 85:15 lactide glycolide		M_w 50,000-75,000	430471-1G 430471-5G

Degradable Poly(ethylene glycol) Hydrogels for 2D and 3D Cell Culture

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Introduction

Progress in biotechnology fields such as tissue engineering and drug delivery is accompanied by an increasing demand for diverse functional biomaterials. For decades, research in polymeric biomaterials has focused on testing the biocompatibility of polymers developed for other applications and/or their processing (e.g., electrospinning, solvent casting/porogen leaching, 3D printing). More recently, researchers have shifted towards synthesizing materials specifically for biomedical uses, including synthetic proteins, glycomimetics and polymers compatible with aqueous media, along with chemical modification of naturally occurring polymers (e.g., to allow gelation or increased *in vivo* stability). In the past decade, polymer chemists have created a niche for designed biomaterials to use as cell scaffolds and to deliver therapeutic agents.

One class of biomaterials that has been the subject of intense research interest is hydrogels.[1] Hydrogels are extensively investigated as two- and three-dimensional scaffolds for cells because they closely mimic the natural environment of cells, both chemically and physically.[2] Hydrogels can be formed from synthetic (e.g., poly(ethylene glycol), poly (hydroxyethyl methacrylate)) and naturally occurring polymers (e.g., collagen, hyaluronan, heparin),[1b] and are useful 3D models of tissue culture due to their high water content and ability to form in the presence of cells, proteins and DNA. Depending on the reactivity of the constituent materials, gelation can be induced using pH[3], temperature[4], coulombic interactions, covalent bonding, non-covalent interactions[5], or polymerization.

PEG

Poly(ethylene glycol) is a hydrophilic polymer that, when cross-linked into networks, can have a high water content. PEG is a suitable material for biological applications because it does not generally elicit an immune response.[6] Since the 1970s, PEG has been used to modify therapeutic proteins and peptides to increase their solubility, lower their toxicity and to prolong their circulation half-life.[7] In the late 1970s, researchers began to experiment with PEG hydrogels for cell culture. PEG hydrogels are chemically well-defined, and multiple chemistries can be used both for their formation and chemical modification.

PEG Macromers

PEG is easily synthesized by the living anionic ring-opening polymerization of ethylene oxide; well-defined (low polydispersity) PEGs with a range of molecular weights and a variety of end groups (e.g., alcohol, methyl ether, amine, N-hydroxysuccinimidyl (NHS) ester) are widely available.

In order to form a hydrogel, PEG must be cross-linked. Initially, PEG was cross-linked non-specifically using ionizing radiation.[8] PEG hydrogels are now typically synthesized via covalent cross-linking of PEG macromers with reactive chain ends.

PEG macromers with reactive chain ends such as acrylate, methacrylate, allyl ether, maleimide, vinyl sulfone, NHS ester and vinyl ether groups (**Chart 1**) are easily synthesized from readily available starting materials. The alcohol chain ends of PEG can be esterified using acid chlorides (e.g., acryloyl chloride, methacryloyl chloride) in the presence of base. PEG chain ends can be etherified under basic conditions by reaction with alkyl halides such as 2-chloroethyl vinyl ether or allyl bromide. PEG divinyl sulfone is prepared by coupling PEG to a large excess of divinyl sulfone or by a multistep process to prepare chloroethyl sulfone chain ends that undergo basic elimination to form vinyl sulfone groups[9].

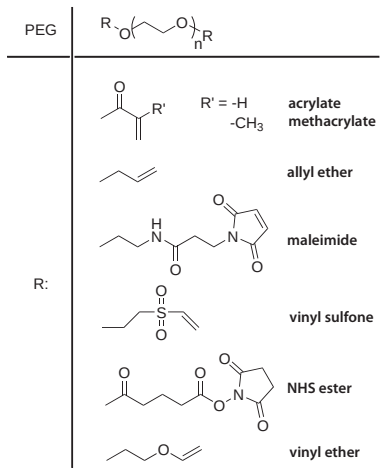
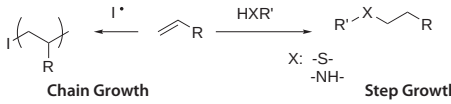


Chart 1. End groups of different PEG macromers.

Macromers can be homobifunctional or heterobifunctional. Homobifunctional macromers are typically used to form networks, while heterobifunctional macromers may be used to tether a therapeutic molecule into a hydrogel network.

Mechanisms of Hydrogel Formation

The cross-linking mechanism to form hydrogels depends on the identity of the chain ends of PEG macromers. In most cases, cross-linking occurs when the reactive vinyl chain ends are polymerized, usually with a free radical initiator. For example, polymerization of macromers can be initiated using redox-generated radicals (e.g., ammonium persulfate and TEMED), or radicals generated with light (e.g., Irgacure® 651, λ=365 nm **Scheme 1**). Acrylate and methacrylate chain ends undergo chain polymerization. In step growth network formation, a multifunctional (f>2) cross-linker reacts with the PEG chain ends in a stoichiometric manner; alternatively, multifunctional PEGs (f>2) can be crosslinked with difunctional crosslinkers (**Scheme 1**). Acrylate, methacrylate, vinyl sulfone, maleimide, vinyl ether and allyl ether are all capable of step growth network formation, through conversion to thiols depending on reaction conditions. Typical cross-linkers may include thiol or amine moieties. Mixed-mode polymerizations are the result of both mechanisms occurring in the same reaction vessel; acrylate and methacrylate groups can undergo mixed mode network formation. Both mechanisms of hydrogel formation can be used to encapsulate live cells, and both mechanisms allow for the reactive incorporation of peptides, proteins and other therapeutics.



Scheme 1. Chain growth and step growth reactions.

The mesh structure that results from different mechanisms is depicted in **Figure 1**. In chain growth networks, a kinetic chain is formed at the crosslink site, while in step growth networks, the crosslink sites bear the same functionality as the multifunctional cross-linker, neglecting defects. In both chain and step growth, network defects such as loops, permanent entanglements and dangling chain ends may exist.

The chemical identity of the macromer and the mechanism of hydrogel formation are both important as each influences the cross-link density of the hydrogel network. Material properties that are important to 2D and 3D culture are easily controlled through the chemistry of hydrogel formation. As cross-linking density increases, mesh size decreases, swelling ratio decreases, and storage modulus increases. Varying the molecular weight of the PEG macromer results in coarse control over hydrogel properties (large differences in cross-linking density). Varying the reaction mechanism used to produce the hydrogels results in fine control over hydrogel properties (can be used to tune cross-linking density of a system).

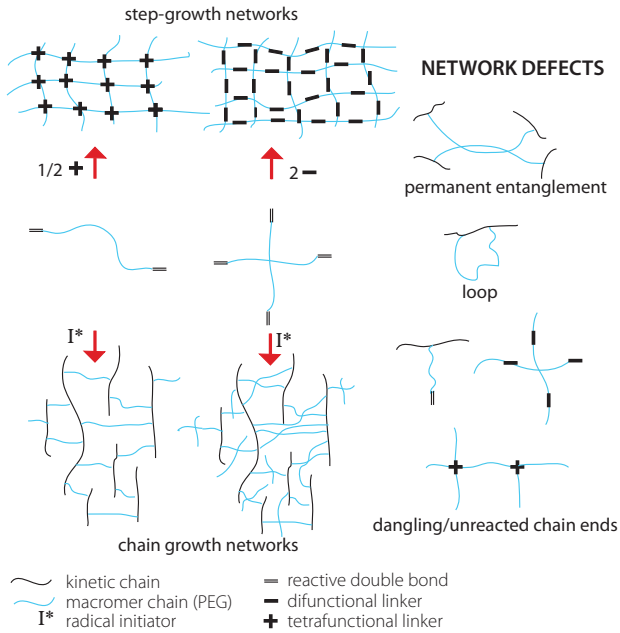


Figure 1. Formation mechanism affects hydrogel network structure and network defects.

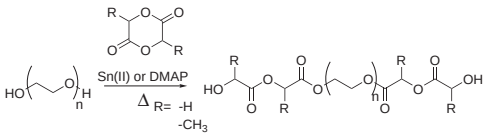
Degradeable Hydrogels

In order to use 3D hydrogel scaffolds to study cell differentiation and tissue evolution, it is critical to be able to control the physical and chemical properties of the gel in a spatially and temporally controlled manner.[10] Polymeric material properties are typically changed through polymerization/cross-linking (bond forming events) or through controlled degradation and/or release (bond breaking events). Bond forming events typically often use small molecule reagents (initiators, catalysts, monomers, ligands to be conjugated to the material) while bond breaking typically does not rely on exogenous reagents. Small molecules often have more adverse effects *in vitro* and *in vivo* than polymeric reagents so many research groups use degradation as a tool for *in situ* manipulation of polymeric biomaterials.

Hydrolytic Degradation

The mechanism of degradation most commonly utilized in hydrogels is hydrolysis, in which a molecule of water adds to the polymer backbone, causing chain scission. Anhydrides, esters and amides are all susceptible to hydrolysis. Anyhydrides typically hydrolyze too quickly, and the uncatalyzed hydrolysis of amides is too slow, so most hydrogels that degrade hydrolytically utilize ester linkages. In order to obtain hydrolytically degradable hydrogels with physiologically relevant time scales of degradation, researchers typically functionalize PEG with degradable ester linkages using lactide or glycolide segments.

Alcohol chain ends on PEG can initiate ring-opening reactions of 3,6-dimethyl-1,4-dioxane-2,5-dione and 1,4-Dioxane-2,5-dione to generate PEG-lactide and PEG-glycolide, respectively (**Scheme 2**).[11] The ring-opening reaction is typically catalyzed by tin(II)-2-ethylhexanoate,[12] although the reaction is also easily accomplished using dimethyl-aminopyridine as a catalyst,[13] which may be easier to remove than the residual tin. The alcohol chain ends of PEG-lactide or PEG-glycolide are easily functionalized with reactive double bonds such as acrylate and methacrylate.



Scheme 2. Synthesis of PEG-lactide and PEG-glycolide.

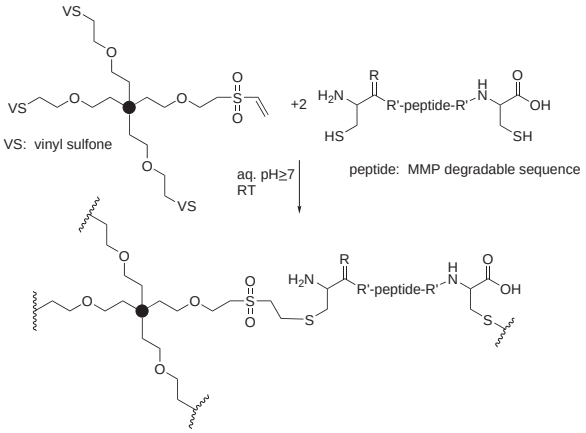
In addition to hydrogel degradation, hydrolysis of ester linkages can be used to deliver drugs to cells encapsulated in a hydrogel. For example, therapeutic agents such as dexamethasone[14] or statins[15] have been tethered into hydrogels through degradable lactide linkages; their sustained release has been used to induce the differentiation of mesenchymal stem cells (MSCs) into osteoblasts

Enzymatic Degradation

Although ester linkages are enzymatically degradable, most researchers utilize sequence-specific enzymatic degradation of peptides incorporated into hydrogels rather than non-specific enzymatic degradation of esters and amides. Hubbell's group pioneered this approach[16] by incorporating matrix metalloproteinase (MMP) sensitive linkages into hydrogels via Michael addition of cysteine-functionalized peptides across acrylates, maleimides and vinyl sulfones (**Scheme 3**).[17]

MMP-degradable linkages have also been used to tether therapeutic agents into hydrogels. For example, growth factors such as vascular endothelial growth factor (VEG-F) can be released via enzymatic degradation of an MMP-sensitive tether to induce angiogenesis.[18]

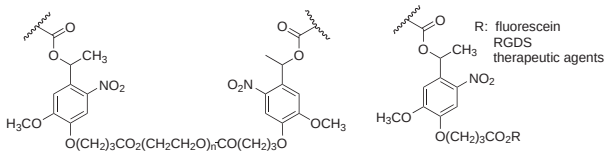
In both hydrolysis and enzymolysis, the rate of degradation is pre-determined by the chemistry of the macromer. In hydrolysis, the degradation rate of the material is pre-engineered through the identity (e.g., hydrophobicity or hydrophilicity) and number of the hydrolysable groups, and cannot be changed once the material is fabricated. In enzymolysis, the degradation typically occurs in an area local to the cells producing the enzyme. While hydrolysis and enzymolysis are both effective methods for sustained hydrogel degradation and sustained release of therapeutic agents, the rate of release cannot be adjusted or arrested after the hydrogel is fabricated, and release is not spatially controlled.



Scheme 3. Enzymatically degradable hydrogels via Michael addition of cysteine-containing peptides to vinyl sulfone groups.

Photodegradable Hydrogels

In contrast to hydrolytically and enzymatically degradable linkages, photodegradable linkages allow precise spatial and temporal control over degradation and release. While many researchers have reported photopolymerizable hydrogels, and photofunctionalizable hydrogels, very few reports exist of biocompatible photodegradable hydrogels. Kloxin and Kasko reported photodegradable hydrogel networks formed from 2-methoxy-5-nitro-4-(1-hydroxyethyl) phenoxybutanoate-containing PEG macromers (**Scheme 4**)[19]; the photodegradation behavior of the *ortho*-nitrobenzyl (*o*-NB) linker group is well-characterized. Hydrogels formed from the photodegradable macromer show bulk degradation upon exposure to light that is dependent on exposure time, wavelength, and light intensity. When the light is shuttered, degradation is arrested; the sample continues photolyzing once light exposure resumes. hMSCs (human mesenchymal stem cells) encapsulated in a hydrogel containing the photo-releasable cell-adhesive ligand RGDS (Arg-Gly-Asp-Ser) differentiate down the chondrogenic pathway when the RGD is released at day ten (corresponding to the downregulation of fibronectin during chondrogenesis). Surface erosion and through-gel lithography of this degradable hydrogel can be used to form features over a range of lengths scales, from 10^{-7} m to 10^{-2} m or larger.[20] Partial degradation in a local area results in decreased cross-link density and increased swelling, providing a means to etch softer features onto a hydrogel that protrude out from the gel.



Scheme 4. Photodegradable *o*-NB moieties incorporated into hydrogel backbone and for therapeutic agent release.

In addition to single photon photolysis, the *o*-NB containing hydrogels are also susceptible to two-photon photolysis, allowing for 3D etching.[19-20] In single photon reactions, any area exposed to the light will react. In contrast, multi-photon lithography should occur only where multiple photons are simultaneously absorbed, which occurs at the focal volume of the light source (inset). Typical wavelengths in single photon lithography of biomaterials range from long wave UV (≥365 nm) into the visible region, while two-photon lithography uses IR light (typically ~740–800 nm). IR light is more biocompatible and less destructive to live tissues and offers greater penetration depth. The probability of two-photon absorption occurring is also tightly limited to the focal point of the focused light, rather than along the entire path of the light, providing 3D control over excitation. Both single- and multi-photon reactions have the potential to pattern materials with features smaller than 500 nm, much smaller than the size of a mammalian cell.[21] This represents an unprecedented level of spatial control over hydrogel scaffold structure and chemistry.

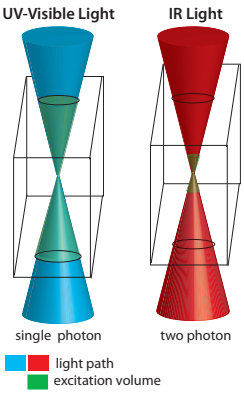


Figure 2. Single photon photolysis (left) occurs in the entire area of the hydrogel exposed to UV-visible light, and two photon photolysis (right) results only in the area where simultaneous absorption of two photons of IR light occurs.

The *o*-NB linker can also be used to tether therapeutic agents into hydrogels for delivery to live cells. Griffin *et al.* demonstrated the controlled release of fluorescein tethered into a hydrogel through an *o*-NB-PEG macromer.[22] The release of this model therapeutic as a function of light exposure at multiple wavelengths (365–436 nm), intensities (5–20 mW/cm^2) and durations (0–20 minutes) was quantified. While the fastest release occurs at 365 nm (which corresponds to a higher molar absorptivity of the *o*-NB linker at that wavelength), significant release is also seen at 405 nm; the release is easily modeled from physical constants of the molecules (such as molar absorptivity). Light attenuation allows the facile formation of chemical and mechanical gradients in these systems.

Conclusion

Poly(ethylene glycol) is a readily available, easily modifiable polymer. It has found widespread use in hydrogel fabrication, including as 2D and 3D scaffolds for tissue culture. Degradable linkages are easily introduced into PEG hydrogels. Hydrolytically degradable gels allow for sustained material degradation and/or therapeutic agent release. Degradation and release is cell-dictated in enzymatically degradable gels. Photodegradation allows for real-time user tailored external manipulation of the chemical and physical properties of hydrogels.

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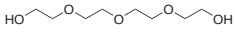
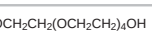
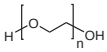
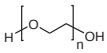
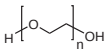
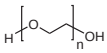
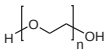
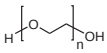
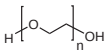
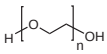
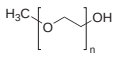
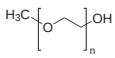
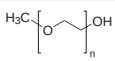
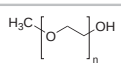
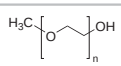
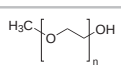
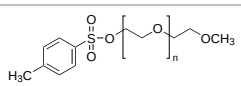
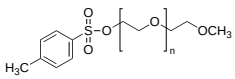
Polyethylene Glycols

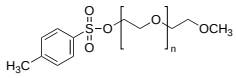
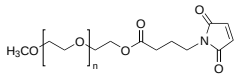
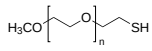
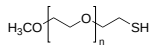
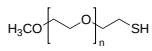
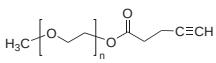
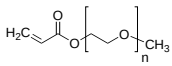
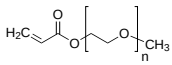
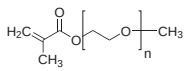
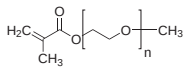
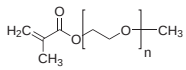
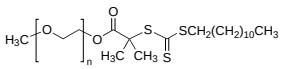
For your convenience, we list the polymers using the terms α and ω to refer to the terminal end groups of the polymer.
For a complete list of available PEG and PEO materials, visit Aldrich.com/poly

Oligo and Poly(ethylene glycol)

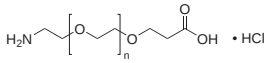
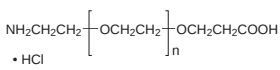
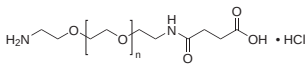
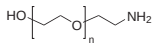
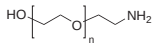
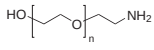
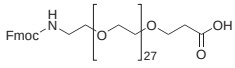
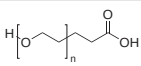
Name	Structure	Molecular Weight	Prod. No.
Tetraethylene glycol		194.23	110175-100G 110175-1KG 110175-3KG 110175-20KG
Pentaethylene glycol		238.28	335754-5G 335754-25G
Hexaethylene glycol		282.33	259268-5G 259268-25G
Poly(ethylene glycol)		mol wt range 1400-1600	81210-1KG 81210-5KG
Poly(ethylene glycol)		M_n 1,900-2,200 average M_n 2050	295906-5G 295906-250G 295906-500G
Poly(ethylene glycol)		M_n 3,015-3,685 average M_n 3,350	202444-250G 202444-500G
Poly(ethylene glycol)		M_n 8,500-11,500 average M_n 10,000	309028-250G 309028-500G
Poly(ethylene glycol)		M_n 16,000-24,000 average M_n 20,000	81300-1KG 81300-5KG
Poly(ethylene oxide)		average M_v 100,000	181986-5G 181986-250G 181986-500G
Poly(ethylene oxide)		average M_v 200,000	181994-5G 181994-250G 181994-500G
Poly(ethylene oxide)		average M_v 600,000	182028-5G 182028-250G 182028-500G

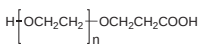
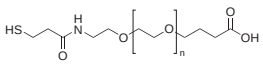
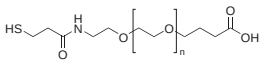
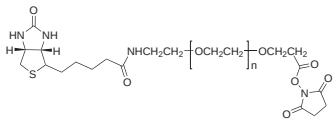
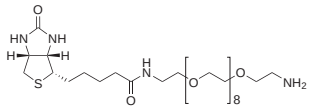
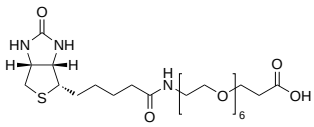
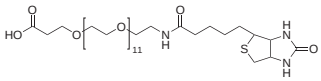
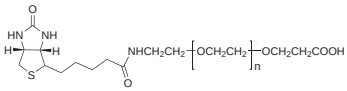
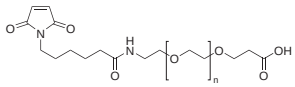
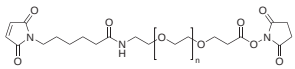
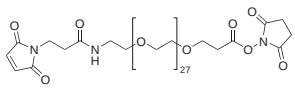
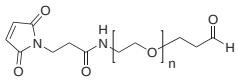
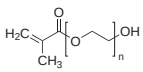
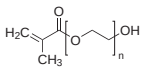
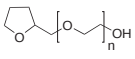
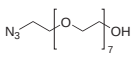
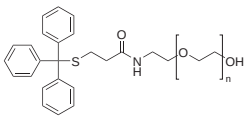
Monofunctional PEGs

α-end	ω-end	Molecular Weight	Structure	Prod. No.
CH_3	OH	average M_n 550		202487-5G 202487-250G 202487-500G
CH_3	OH	average M_n 750		202495-250G 202495-500G
CH_3	OH	average M_n 5,000		81323-250G 81323-1KG
CH_3	OH	average M_w 2,000		81321-250G 81321-1KG
CH_3	OH	M_n 10,000		732621-5G 732621-25G
CH_3	OH	M_n 20,000		732613-5G 732613-25G
CH_3	Tosylate	average M_n 1,000		729116-5G
CH_3	Tosylate	average M_n 2,000		729124-5G

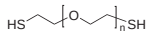
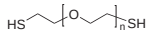
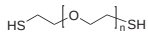
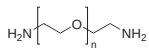
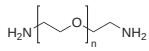
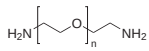
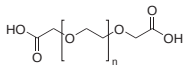
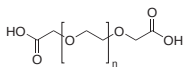
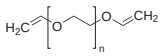
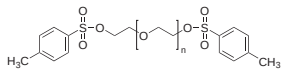
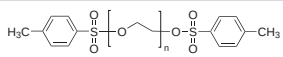
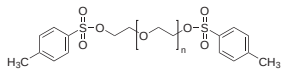
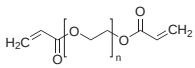
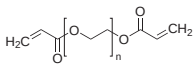
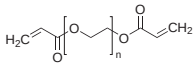
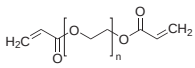
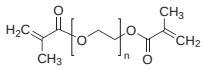
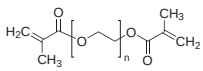
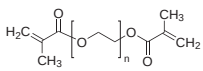
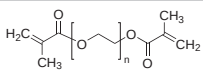
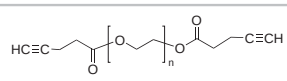
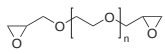
α-end	ω-end	Molecular Weight	Structure	Prod. No.
CH_3	Tosylate	average M_n 5,000		729132-5G
CH_3	Maleimide	average M_n 2,000		731765-1G 731765-5G
CH_3	SH	average M_n 1,000		729108-1G 729108-5G
CH_3	SH	average M_n 2,000		729140-1G 729140-5G
CH_3	SH	average M_n 5,000		729159-1G 729159-5G
CH_3	Acetylene	average M_n 2,000		699802-500MG
CH_3	Acrylate	average M_n 2,000		730270-1G
CH_3	Acrylate	average M_n 5,000		730289-1G
CH_3	Methacrylate	average M_n 950		447951-100ML 447951-500ML
CH_3	Methacrylate	average M_n 2,000		730319-1G
CH_3	Methacrylate	average M_n 5,000		730327-1G
CH_3	DDMAT	average M_n 1,126		740705-1G

Heterobifunctional PEGs

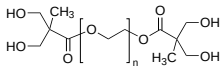
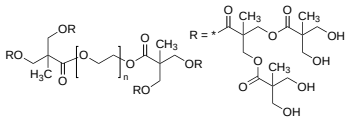
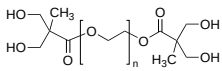
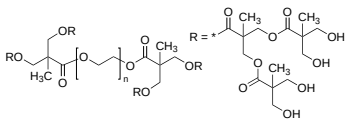
α-end	ω-end	Molecular Weight	Structure	Prod. No.
NH_2	COOH	M_p 3,000		671487-100MG 671487-500MG
NH_2	COOH	M_p 5,000		671592-100MG 671592-500MG
NH_2	COOH	M_p 10,000		672165-100MG 672165-500MG
NH_2	OH	M_p 10,000		671924-100MG 671924-500MG
NH_2	OH	M_p 3,000		07969-250MG 07969-1G
NH_2	OH	M_p 5,000		672130-100MG 672130-500MG
COOH	Fmoc	1544.80		689653-100MG
COOH	OH	M_p 10,000		671037-100MG 671037-500MG

α-end	ω-end	Molecular Weight	Structure	Prod. No.
COOH	OH	M_p 3,000		670812-100MG 670812-500MG
COOH	SH	M_w 3000		712515-100MG
COOH	SH	M_w 5000		712523-100MG
Biotin	NHS ester	M_p 3,000		670049-100MG
Biotin	NH_2	682.87		689882-100MG
Biotin	COOH	579.70		726265-100MG
Biotin	COOH	844.02		689998-100MG
Biotin	COOH	M_p 3,000		669946-250MG
Maleimide	COOH	M_p 3,000		670162-250MG
Maleimide	NHS ester	M_p 3,000		670278-100MG
Maleimide	NHS ester	1570.76		689777-100MG
Maleimide	Formyl	M_w/M_n <1.2 average M_n 3,000		579319-250MG
Methacrylate	OH	M_n 360		409537-5ML 409537-100ML 409537-500ML
Methacrylate	OH	average M_n 526		409529-100ML 409529-500ML
Tetrahydrofurfuryl ether	OH	M_n 234		309524-25G
Azide	OH	395.45		689440-250MG
Trityl	OH	M_p 3,000		712507-250MG

Homobifunctional PEGs

α-end and ω-end	Molecular Weight	Structure	Prod. No.
SH	M_n 900-1,100 average M_n 1,000		717142-1G
SH	M_n 3,060-3,740 average M_n 3,400		704539-1G
SH	average M_n 8,000		705004-1G
NH_2	M_w 2,000		14501-250MG 14501-1G
NH_2	M_w 3,000		14502-250MG 14502-1G
NH_2	M_w 20,000		14509-1G-F
COOH	average M_n 250		406996-100G
COOH	average M_n 600		407038-250ML 407038-1L
Vinyl	average M_n 240		410195-5ML 410195-25ML
Tosylate	average M_n 1,300		719080-5G
Tosylate	average M_n 3,500		701750-5G
Tosylate	average M_n 10,000		705047-5G
Acrylate	average M_n 258		475629-100ML 475629-500ML
Acrylate	average M_n 1,000		729086-1G
Acrylate	average M_n 6,000		701963-1G
Acrylate	average M_n 10,000		729094-1G
Methacrylate	average M_n 550		409510-250ML 409510-1L
Methacrylate	average M_n 6000		687537-1G
Methacrylate	average M_n 10,000		725684-1G
Methacrylate	average M_n 20,000		725692-1G
Acetylene	average M_n 2,000		699810-500MG
Glycidyl	average M_n 526		475696-100ML 475696-500ML

Dendron-functionalized PEGs

Name	Structure	Description	Prod. No.
Poly(ethylene glycol),4 hydroxyl dendron, generation 1		average PEG M_n = 20k esterified with 16 OH groups	752401-500MG
Poly(ethylene glycol),16 hydroxyl dendron, generation 3		average PEG M_n = 20k esterified with 16 OH groups	752371-500MG
Poly(ethylene glycol),4 hydroxyl dendron, generation 1		average PEG M_n = 20k esterified with 16 OH groups	752398-500MG
Poly(ethylene glycol),16 hydroxyl dendron, generation 3		average PEG M_n = 20k esterified with 16 OH groups	752363-500MG

Polyelectrolyte Multilayer Films and Membrane Functionalization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Introduction

Among the many methods for preparing thin films, layer-by-layer (LbL) deposition of complementary polymers has emerged as an especially versatile technique for controlling film thickness and functionality. **Figure 1** shows the most common form of the LbL method, which is the alternating adsorption of polycations and polyanions.[1]

Operationally, this method occurs through simple, consecutive exposures of a substrate to polycation and polyanion solutions, with rinsing to remove unadsorbed polymer after each deposition step. Typical polyanions employed for deposition of these films include ionized forms of poly(acrylic acid) (PAA), poly(styrene sulfonic acid) (PSS), and poly(vinyl sulfonic acid), whereas most polycations contain quaternary ammonium functionalities or protonated amines.[2] In addition, early studies showed that LbL methods can also use a much broader range of multiply charged species, including proteins, viruses, nanoparticles, and exfoliated inorganic materials.[2] In some cases, LbL methods also employ other interactions such as hydrogen bonding or covalent linkages.[3]

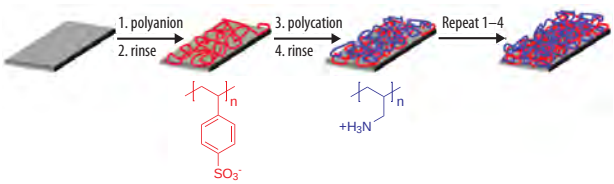


Figure 1. Schematic diagram of layer-by-layer adsorption of polyelectrolyte multilayers. The figure also shows the structures of two common polyelectrolytes, poly(styrene sulfonate) and protonated poly(allylamine).

The LbL strategy has a number of advantages over most thin film forming methods. First, this technique offers control over film thickness at the nanometer scale, because a single adsorption step can deposit as little as a few angstroms (Å) of polymer.[3] Second, conformal adsorption occurs on substrates with a wide range of geometries, allowing coating of 3-dimensional objects such as nanoparticles and porous membranes (see below).[4,5] Finally, the broad range of materials suitable for LbL adsorption and the ability to deposit species in a defined order can afford a wide variety of functional films. (We should note, however, that polyelectrolytes are frequently intertwined over several layers.[1]) Post-deposition reactions such as cross-linking and reduction of metal ions to form nanoparticles provide further ways to modify film properties. Prior studies of post-deposition reactions yielded functional films for catalysis,[6] corrosion prevention, anti-reflective coatings, optical shutters, and superhydrophobic coatings.

Film Formation

The key feature in the deposition of polyelectrolyte multilayers (PEMs) is charge overcompensation. The initial layer adsorbs onto the substrate by electrostatic or hydrophobic interactions and either creates a charged surface or reverses the substrate surface charge. Adsorption of subsequent layers again overcompensates the charge on the surface to reverse the substrate's charge and allow adsorption of the next layer.[7]

In many cases, the thickness of multilayer polyelectrolyte films increases linearly with the number of adsorbed layers. This suggests that the extent of charge overcompensation does not vary greatly with the number of adsorbed layers, so the amount of polyelectrolyte deposited in each step is approximately constant. However, for some polyelectrolyte systems, film thickness increases exponentially with the number of layers. Schaaf *et al.* suggest that the exponential growth occurs when one of the polyelectrolytes diffuses "into" the entire film during deposition.[8] Upon addition of the oppositely charged polyelectrolyte, the previously adsorbed polyelectrolyte diffuses "out" of the whole film to form a very thick polyanion-polycation complex at the surface. Because one of the polyelectrolytes, usually one with low charge density and high swelling in water, diffuses into the entire film, the thickness of each adsorbed layer increases with the number of layers.[9]

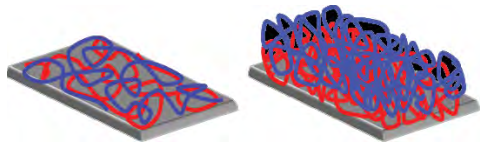


Figure 2. Schematic drawing of polyanion/polycation bilayers prepared without (left) and with (right) supporting salt.

In addition to the polyelectrolyte selected for deposition, a number of adsorption parameters such as supporting electrolyte concentration and composition, pH of the polyelectrolyte solutions, adsorption time, and temperature also influence the amount of polyelectrolyte deposited in LbL methods. Many studies show a dramatic effect of supporting electrolyte concentration on the thickness of PEMs. In the absence of added salt, polyelectrolytes are highly extended to maximize the distance between charged repeat units of the polymer. Under these conditions, adsorbed layers are thin and overcompensate the surface charge only slightly (**Figure 2**). For example, the thickness of a 10-bilayer PSS/poly(diallyl dimethyl ammonium chloride) film prepared without addition of salt is about 60 Å.[10] Thus, the average thickness per layer is only 3 Å. However, when deposited from solutions containing 2 M salt, the thickness of the corresponding 10-bilayer film is more than 3,000 Å.[10] Of course the film structure and composition also vary greatly with deposition conditions.

Film Permeability

Studies of film swelling and transport through polyelectrolyte multilayers demonstrate the wide range of structural variation available with these coatings. Remarkably, chitosan/hyaluronic acid films swell by 400% in water. Accordingly, these films are permeable to molecules as large as myoglobin (17 kDa).[11] In contrast, PSS/protonated polyallylamine (PAH) coatings swell by <100%, and these films can prevent transport of molecules as small as glucose. In general, coatings prepared from polyelectrolytes with a high charge density have a high degree of ionic cross-linking that leads to decreased permeability of small molecules along with relatively high transport selectivities between different molecules.[12]

Functionalized Membranes

PEMs are also attractive for coating surfaces with functional particles such as enzymes and catalysts. We are particularly interested in creating functionalized membranes (**Figure 3**) because they provide a relatively high surface area, and convective flow rapidly brings reactants to catalytic sites.[13] The micron-sized pores lead to minimal diffusion limitations, and variation of flow rates can limit the residence time in the membrane to control the extent of reaction.

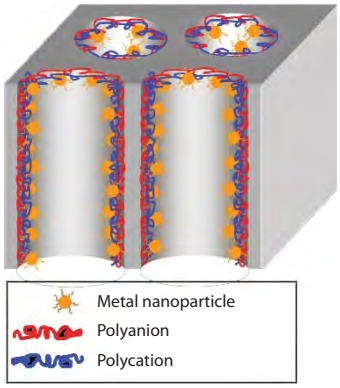


Figure 3. Schematic drawing of catalytic metal nanoparticles immobilized in a porous membrane using LbL deposition. Used by permission of the American Chemical Society.[14]

LbL adsorption in membrane pores occurs by simply flowing polyanion, polycation, and rinsing solutions through the membrane. When citrate-coated metal nanoparticles serve as the polyanion, this technique yields a high density of well-separated nanoparticles within membrane pores, as **Figure 4** shows.[14] This adsorption can occur in inorganic and polymeric flat sheet membranes as well as in polymeric hollow fiber membranes.[14-16] Avoiding particle aggregation is important to maintain both a high catalytic surface area and the unique electronic properties of nanoparticles.

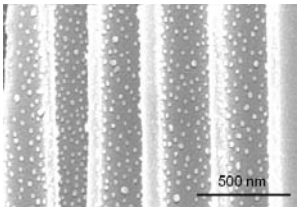
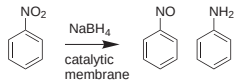


Figure 4. Cross-sectional SEM images of a porous alumina membrane coated with a PAA/PAH/Au nanoparticle film. The gold nanoparticles were stabilized by citrate. Used by permission of the American Chemical Society.[14]

Remarkably, the catalytic activity of the nanoparticles in LbL membrane coatings is essentially the same as that of nanoparticles in solution. Moreover, control over the flow rate through the membrane can alter product distribution. For example, reduction of nitrobenzene by $NaBH_4$ (**Scheme 1**) gives 24% nitrosobenzene and 73% aniline when the flux through the membrane is 0.015 mL/(cm^2s), but 47% nitrosobenzene and 49% aniline result from a ten-fold higher flux.[14] During the reduction step, less time in the membrane leads to higher amounts of the more valuable nitrosobenzene. Additionally, varying the flow rate reveals that nitrosobenzene is an intermediate in the reduction of nitrobenzene to aniline. Higher flow rates may yield even more nitrosobenzene, but a limit will eventually be reached and much of the starting material will remain unreacted.



Scheme 1. Reduction of nitrobenzene to nitrosobenzene and aniline.

LbL methods can also be used to immobilize enzymes in membranes.[17,18] In some cases, electrostatic interactions with the polyelectrolytes help stabilize the enzymes to maintain their activity. A few studies focused on LbL immobilization of trypsin in microfluidic chips to create systems that digest proteins prior to analysis by mass spectrometry.[19] However, in these chips, diffusion distances can reach up to 100 µm, which may limit digestion rates. In membranes, the diffusion distances are often <1 µm, so more complete, rapid digestion should be possible. We employed adsorption of only 1 layer of PSS and trypsin in nylon membranes (nominal 0.45 µm pore size) to construct membrane reactors that rapidly digest proteins.[18] This LbL process leads to deposition of ~11 mg of trypsin per cm^3 of membrane pores, which is about 450 times greater than the typical trypsin concentration in solution-based protein digestion. In-solution digestion employs low concentrations of trypsin to avoid self-digestion of the enzyme, whereas in the membrane immobilization limits self-digestion.

The high concentration of trypsin in membranes modified using LbL deposition allows rapid, efficient protein digestion for mass spectrometry (MS). After digestion of α-casein in membranes, gel electrophoresis shows no residual protein even with residence times in the membrane as low as 0.8 seconds. Moreover, in matrix-assisted laser desorption/ionization-MS (MALDI-MS), membrane digestion leads to signals for 52 proteolytic peptides, whereas solution digestion reveals only 37 peptides. The larger number of peptides that result from membrane digestion leads to a high amino acid sequence coverage (84%), which facilitates identification of protein modifications. Very short residence times in membranes, on the order of microseconds, can lead to much larger peptides, which may prove useful in protein identification or structural studies.

Future Opportunities

In the laboratory, LbL deposition is extremely convenient and versatile. However, for films containing many layers, the technique becomes time consuming and cumbersome, especially from a manufacturing standpoint. Rinsing steps also produce waste streams that must be treated or recycled. Thus, although LbL deposition of polycations and polyanions began in earnest 20 years ago, practical applications of these films have not rapidly followed. Efforts to prepare coatings by spraying may simplify the LbL process,[20] but these methods may also sacrifice some control over resulting film structures. Future LbL applications may continue to expand by coupling nanotechnology to the process and lead to new innovations in sensors, where the film provides a unique function. A wide array of unique small-scale, functional and multifunctional coatings are possible.

Acknowledgment

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Polyelectrolyte Materials

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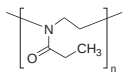
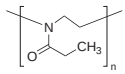
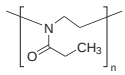
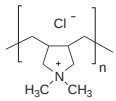
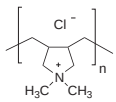
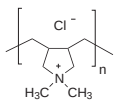
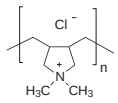
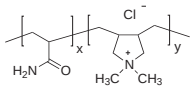
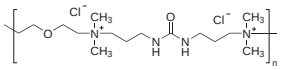
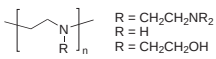
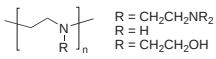
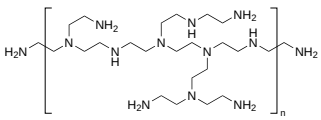
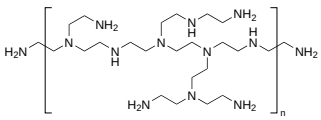
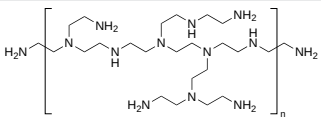
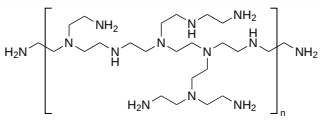
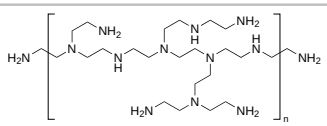
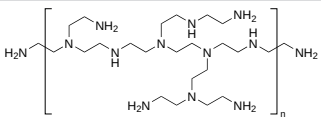
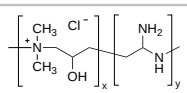
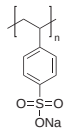
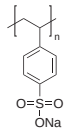
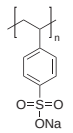
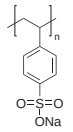
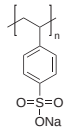
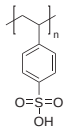
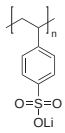
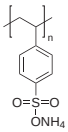
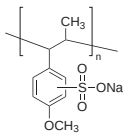
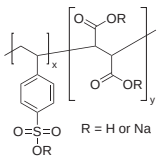
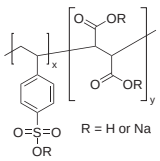
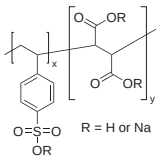
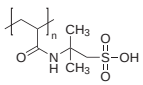
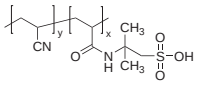
Polycations

Name	Structure	Molecular Weight	Prod. No.
Poly(allylamine), 20 wt. % in H_2O		average M_w ~17,000	479136-1G 479136-5G 479136-25G
Poly(allylamine), 20 wt. % in H_2O		average M_w ~65,000	479144-1G 479144-5G 479144-25G
Poly(allylamine hydrochloride)		average M_w ~15,000 (GPC vs. PEG std.)	283215-5G 283215-25G
Poly(2-ethyl-2-oxazoline)		average M_w ~50,000 (Polydispersity 3-4)	372846-100G 372846-500G
Poly(2-ethyl-2-oxazoline)		average M_w ~200,000 (Polydispersity 3-4)	372854-100G
Poly(2-ethyl-2-oxazoline)		average M_w ~500,000 (Polydispersity 3-4)	373974-100G 373974-500G
Poly(diallyldimethylammonium chloride), 35 wt. % in H_2O		average M_w <100,000 (very low molecular weight)	522376-25ML 522376-1L
Poly(diallyldimethylammonium chloride), 20 wt. % in H_2O		average M_w 100,000-200,000 (low molecular weight)	409014-25ML 409014-1L 409014-4L
Poly(diallyldimethylammonium chloride), 20 wt. % in H_2O		average M_w 200,000-350,000 (medium molecular weight)	409022-25ML 409022-1L 409022-4L

Name	Structure	Molecular Weight	Prod. No.
Poly(diallyldimethylammonium chloride), 20 wt. % in H_2O		average M_w 400,000-500,000 (high molecular weight)	409030-25ML 409030-1L 409030-4L
Poly(acrylamide-*co*-diallyldimethylammonium chloride), 10 wt. % in H_2O		-	409081-1L
Poly[bis(2-chloroethyl) ether-*alt*-1,3-bis[3-(dimethylamino)propyl]urea] quaternized, 62 wt. % in H_2O		-	458627-100ML
Polyethylenimine, 80% ethoxylated, 37 wt. % in H_2O		M_w 110,000	306185-100G 306185-250G
Polyethylenimine, 80% ethoxylated, 35-40 wt. % in H_2O		average M_w ~70,000	423475-50ML 423475-250ML
Polyethylenimine, ethylenediamine branched		average M_n ~600 by GPC average M_w ~800 by LS	408719-100ML 408719-250ML 408719-1L
Poly(ethyleneimine), 50 wt. % in H_2O		average M_n ~1,200 average M_w ~1300 by LS	482595-100ML 482595-250ML
Poly(ethyleneimine), 50 wt. % in H_2O		average M_n ~1,800 by GPC average M_w ~2,000 by LS	408700-5ML 408700-250ML 408700-1L
Polyethylenimine, branched		average M_n ~10,000 by GPC average M_w ~25,000 by LS	408727-100ML 408727-250ML 408727-1L
Poly(ethyleneimine), 50 wt. % in H_2O		average M_n ~60,000 by GPC average M_w ~750,000 by LS	181978-5G 181978-100G 181978-250G 181978-18KG
Poly(ethyleneimine), ~ 50% in H_2O		M_r 600,000-1,000,000	03880-100ML 03880-500ML
Poly(dimethylamine-*co*-epichlorohydrin-*co*-ethylenediamine), 50 wt. % in H_2O		average M_w ~75,000	409138-1L

Polyanions

Name	Structure	Molecular Weight	Prod. No.
Poly(acrylic acid, sodium salt), 45 wt. % in H_2O		average M_w ~1,200	416010-100ML 416010-500ML
Poly(acrylic acid sodium salt)		average M_w ~2,100	420344-100G 420344-500G
Poly(acrylic acid sodium salt)		average M_w ~5,100 by GPC	447013-100G 447013-500G
Poly(acrylic acid, sodium salt), 45 wt. % in H_2O		average M_w ~8,000	416029-100ML 416029-500ML
Poly(acrylic acid, sodium salt), 35 wt. % in H_2O		average M_w ~15,000	416037-100ML 416037-500ML
Poly(vinylsulfonic acid, sodium salt), 25 wt. % in H_2O		-	278424-250ML 278424-1L
Poly(vinyl sulfate)		average M_w ~170,000	271969-1G 271969-5G
Poly(sodium 4-styrenesulfonate)		average M_w ~70,000	243051-5G 243051-100G 243051-500G
Poly(sodium 4-styrenesulfonate), 30 wt. % in H_2O		average M_w ~70,000	527483-100ML 527483-1L
Poly(sodium 4-styrenesulfonate), 30 wt. % in H_2O		average M_w ~200,000	561967-500G
Poly(sodium 4-styrenesulfonate)		average M_w ~1,000,000	434574-5G 434574-100G 434574-500G
Poly(sodium 4-styrenesulfonate), 25 wt. % in H_2O		average M_w ~1,000,000	527491-100ML

Name	Structure	Molecular Weight	Prod. No.
Poly(4-styrenesulfonic acid), 18 wt. % in H_2O		M_w ~75,000	561223-100G 561223-500G
Poly(4-styrenesulfonic acid), 30 wt. % in H_2O		M_w ~75,000	561231-100G 561231-500G
Poly(4-styrenesulfonic acid), 30 wt. % in H_2O		M_w ~200,000	561258-250G
Polyanetholesulfonic acid		average M_v 9,000-11,000	444464-5G 444464-25G
Poly(4-styrenesulfonic acid-*co*-maleic acid)		average M_w ~20,000	434558-250G
Poly(4-styrenesulfonic acid-*co*-maleic acid), 25 wt. % in H_2O		M_w ~20,000	561215-500G 561215-4KG
Poly(4-styrenesulfonic acid-*co*-maleic acid)		average M_w ~20,000	434566-250G
Poly(2-acrylamido-2-methyl-1-propanesulfonic acid), 15 wt. % in H_2O		average M_w 2,000,000	191973-100G 191973-250G
Poly(2-acrylamido-2-methyl-1-propanesulfonic acid-*co*-acrylonitrile)		-	191981-10G 191981-25G

The Use of Block Copolymers in Nanoscale Patterning

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Introduction

For more than a decade, block copolymers have garnered significant interest as self-assembling materials for nanoscale patterning.[1] This interest stems from the propensity of block copolymers to assemble into distinct, nanometer-sized domains that exhibit ordered morphologies at equilibrium.[2] In thin films (<100 nm), these morphologies, which are typically lamellar, cylindrical, or spherical in nature, can form ordered arrays of lines or spots with feature dimensions of 5–50 nm. These ordered arrays can serve as templates for nanoscale patterning and other technological applications. Typically, one block of the copolymer is removed, and the remaining material serves as a soft etch mask. Block copolymer material systems that have been used in this context include polystyrene-*block*-polybutadiene ((PS-*b*-PB), with the polybutadiene selectively removed by ozone),[1] PS-*block*-polylactide (polylactide selectively chemically degraded),[3] PS-*block*-polydimethylsiloxane (PS selectively removed by reactive ion etching (RIE)),[4] and PS-*block*-polyferrocenyldialkylsilane systems (PS selectively removed by RIE).[5]

By far, the most common block copolymer that researchers have used in the study of nanoscale patterning is polystyrene-*block*-poly(methyl methacrylate) (PS-*b*-PMMA). The PMMA domains can be selectively removed by UV exposure,[6] and the remaining material can serve as templates for etching the underlying substrate.[7] PS-*b*-PMMA also has the advantage that the surface energies of PS and PMMA at the annealing temperature (190–230 °C) are remarkably similar.[8] Because of this similarity in surface energies, there is not a strong driving force for either block to reside at the surface of the film, and morphological patterns can go all the way through the film. Research with PS-*b*-PMMA has shown that the diameter of cylindrical domains can be selected to be 14–50 nm, depending on the molecular weight (M_n) of the block copolymer.[9] Addition of PS and PMMA homopolymer to the PS-*b*-PMMA to form a blend can also affect the diameter of the cylinders, resulting in diameters and domain spacings that are anywhere from 10% smaller to 150% larger than the corresponding values of the pure PS-*b*-PMMA, depending on the relative amount and M_n of the homopolymers added to the block copolymer.[6]

Self-assembled Arrays of Block Copolymer Domains

For pattern formation by assembled block copolymers domains, lines can be made either by lamellae that are perpendicular to the substrate, or by cylinders that are parallel to the substrate, and spots can be made by spheres or by cylinders that are perpendicular to the substrate. One advantage of PS-*b*-PMMA is that high aspect ratio, perpendicular domains can be achieved, which are preferable for pattern transfer. To assemble perpendicular structures, it is typically necessary to control the wetting interactions of the polymer on the surface,[8] the thickness of the film,[10] and the annealing temperature.[11,12] A standard method to chemically modify the surface to control the wetting interactions for PS-*b*-PMMA comes from the seminal work of Mansky *et al.*, who grafted random copolymer brushes comprised of styrene and methyl methacrylate (P(S-*r*-MMA)) onto silicon substrates.[8] With the appropriate fraction of styrene (F_{St}) in the P(S-*r*-MMA), the P(S-*r*-MMA) is non-preferential to wetting by either block of the PS-*b*-PMMA. P(S-*r*-MMA) can be easily synthesized via a combination of functional monomer and initiator, as outlined in **Figure 1**. Hydroxyl terminated polymer brushes can be synthesized from nitroxide-mediated polymerization (NMP) using functional initiators bearing a free hydroxyl group (**Figure 1a**).[13,14] Copolymers capable of grafting to native oxide surfaces or forming cross-linked mats via their side chain functionality can be achieved by either NMP or free radical polymerization techniques.[13,14] These materials are then easily used to form a non-preferential brush on the surface by dehydration or forming a cross-linked insoluble mat (Method 1 in **Figure 1b**). Alternatively, non-preferential surfaces can be achieved by exposure of octadecyl-trichlorosilane self-assembled monolayers (SAMs) to X-ray irradiation where the exposure dose defines the wetting characteristics of the SAM (Method 2 in **Figure 1b**).[15,16] For either method, once the substrate is treated to make it non-preferential, a block copolymer film is spin-coated onto the substrate, and then annealed so that it can assemble into its equilibrium morphology.

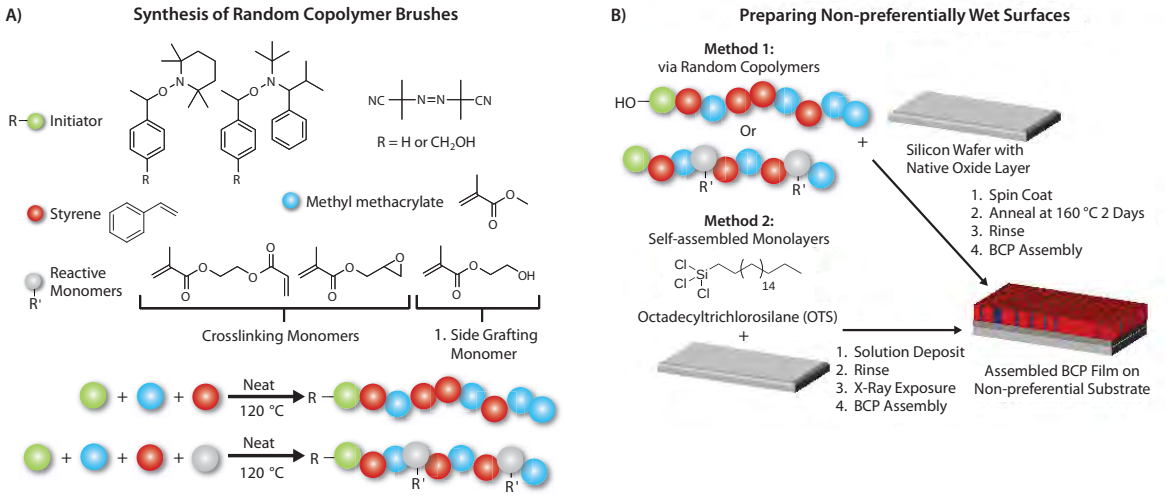

Figure 1. Synthesis of random copolymers **(A)** and the two methods of preparation of non-preferential surfaces **(B)**. Non-preferential surfaces are formed by either spin coating and annealing random copolymers (Method 1), or forming a self-assembled monolayer and exposing to x-rays (Method 2). After preparation of the non-preferential surface, a block copolymer (BCP) can be spin coated onto the surface, and then annealed to achieve its equilibrium morphology.

The F_{St} that is appropriate for use as a non-preferential surface treatment depends on the morphology of the PS-*b*-PMMA to be assembled on the random copolymer brush or mat. In the case of the self-assembly of lamellae-forming PS-*b*-PMMA, a random copolymer of styrene and methyl methacrylate (P(S-*r*-MMA)) must have F_{St} in the range of 0.45–0.78 to be non-preferential to the assembled PS-*b*-PMMA.[8,13,17] In contrast, the non-preferential F_{St} range for PS-*b*-PMMA that forms PS or PMMA cylinders is 0.55–0.57 or 0.59–0.72, respectively, as shown in the scanning electron microscope (SEM) images in **Figure 2**.[13] The thickness of the PS-*b*-PMMA film also plays an important role in the assembly of perpendicular domains that span the film thickness. Perpendicular domains can be readily achieved when the film thickness is 13–40 nm.[17] For thicker films (up to 300 nm), precise control of F_{St} and annealing temperature is required to achieve perpendicularly-oriented domains.[11] Porous films of block copolymer formed by the removal of the polymer in the cylindrical domains have been employed as a template for a host of applications, including the fabrication of MOSFET's,[18] quantum dots,[19,20] high surface area capacitors,[21] photovoltaic devices,[22] porous membranes,[23] magnetic nanowires,[24] and bit patterned media.[25]

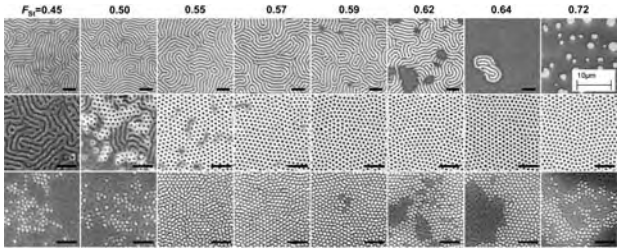

Figure 2. Effect of mole fraction of styrene (F_{St}) in a P(S-*r*-MMA) brush on the orientation of self-assembled films of PS-*b*-PMMA. The rows of top-down SEM images correspond to lamellae forming (top), PMMA cylinder forming (middle), and PS cylinder forming (bottom) PS-*b*-PMMA. Black scale bars correspond to 200 nm. Reprinted with permission from ACS.[26]

Directed Assembly of Block Copolymer Domains

Self-assembly of block copolymer domains has several technological applications and is of great scientific interest. However, some applications, such as bit patterned media and integrated circuits,[27] require control over the location and geometry of the assembled domains. Directed assembly with a chemical pattern provides a robust method of ordering the domains in a way that allows them to be registered to features on the underlying substrate. The directed assembly process starts with the formation of a lithographically defined chemical pattern. An example of a directed assembly process flow from previous work is shown in the left-most process flow in **Figure 3**.[28] In this process, a PS brush is uniformly grafted on a silicon wafer. The PS brush is then coated with a photoresist, which is subsequently lithographically patterned and developed. The substrate is then treated with an oxygen plasma, such that the exposed portions of the PS brush are oxidized. Removal of the remaining photoresist yields a chemical pattern in which the areas of the PS brush that were exposed to the oxygen plasma are preferentially wet in the PMMA block of PS-*b*-PMMA, and unexposed areas are preferentially wet in the PS block. Once the chemical pattern is formed, a thin film of PS-*b*-PMMA is spin coated on top of it, and then annealed. During annealing, the block copolymer equilibrates in the presence of the chemical pattern, and the preferential wetting of the different regions of the pattern directs the assembly of the domains of the PS-*b*-PMMA, as shown in the SEMs in **Figure 3** (for cylinders) and **Figure 4** (for lamellae).

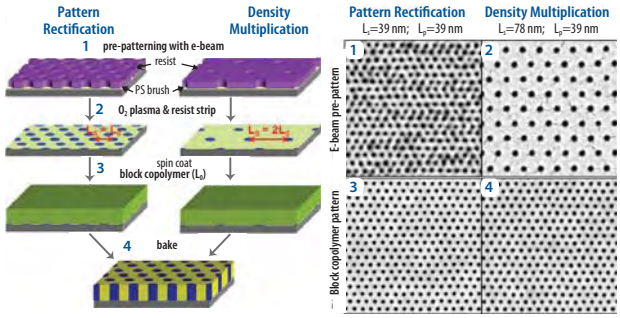

Figure 3. On the left is shown a schematic of the chemical pattern fabrication process for the directed assembly of cylinder-forming PS-*b*-PMMA, for both with (right) and without (left) density multiplication. **1-2)** SEM images of the patterned photoresist. **3-4)** SEM images of the block copolymer film on top of prepattern defined by the corresponding pattern above.[28]

It is also possible to make the chemical pattern using a cross-linked polymer brush as the starting material, as shown in the schematic in **Figure 4**.[29] The use of a cross-linked mat offers several advantages. First, it permits the use of a trim etch, so that the dimensions of the pattern features, such as the pattern line width *W*, can be finely controlled. Second, it dissociates the chemistry of the pattern features from the chemistry of the rest of the pattern. For example, in the schematic in **Figure 4**, the red guiding lines of the chemical pattern are cross-linked PS, and the rest of the chemical pattern is a P(S-*r*-MMA) brush, with a composition tailored specifically for directed assembly. Finally, because of the high cross-link density of the PS guiding lines, the chemistry of the cross-linked PS is unaffected by the photoresist patterning process and chemicals, and is therefore more robust.

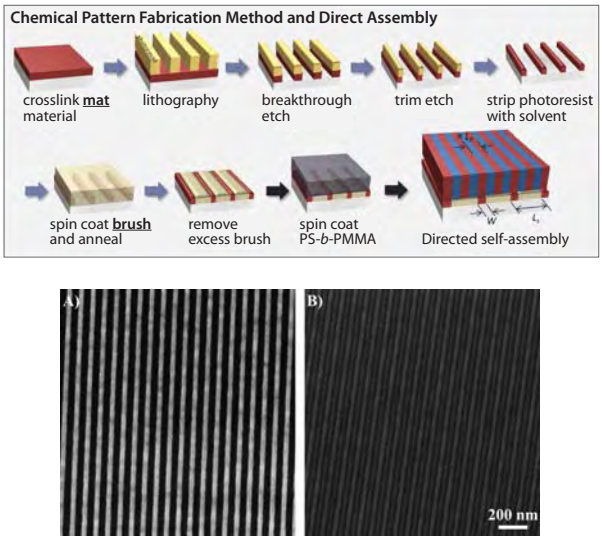

Figure 4. Schematic of the chemical pattern fabrication process for density multiplication using lamellae forming PS-*b*-PMMA. (Reprinted with permission from ACS.[29]) **A)** SEM image of the patterned photoresist (period = 80 nm), **B)** SEM image of the block-copolymer film (period = 40 nm) on top of the pattern in A).

Recent work has shown that chemical patterns can direct the assembly of block copolymers such that the density of features on the top surface of the assembled block copolymer is an integer multiple of the density of features on the chemical pattern.[7,30] The initial research on directed assembly focused on a 1:1 match of the assembled domains and the features of the chemical pattern, such as that shown in the left-most schematic in **Figure 3**, and in the SEMs in **Figure 3a** and **Figure 3c**.[31,32] While 1:1 directed assembly offers many potential advantages for advanced lithography related to uniformity of feature size and shape,[33,34] the ability to assemble block copolymers with a greater feature density than is on the chemical pattern is highly desired and would allow for increased resolution over current lithographic systems. General process schematics for directed assembly with density multiplication are shown on the right in **Figure 3** (cylinders), at the top of **Figure 4** (lamellae), and on the left in **Figure 5** (more complicated, device-oriented structures). In each case, the spacing of the features of the chemical pattern, L_s, is approximately equal to an integer multiple of the spacing of the domains in the bulk block copolymer, L_0. When the block copolymer domains assemble, the domains of a specific block of the copolymer will be registered to the guiding lines of the chemical pattern, and the same type of domains must assemble interpolated between guiding lines. As a result of directed assembly with density multiplication, the PS-*b*-PMMA cylinders in **Figure 3d** have a four-fold higher density than the patterned spots of the chemical pattern in **Figure 3b** that was used to direct the assembly. Similarly, the PS-*b*-PMMA lamellae in **Figure 4b** have a two-fold higher density than the cross-linked PS guiding lines in the chemical pattern in **Figure 4a**.

The alternating brightness and darkness of the assembled PS domains in **Figure 4b** is evidence of the cross-linked PS and the P(S-*r*-MMA) brush, respectively, of the chemical pattern underlying the assembled PS-*b*-PMMA.

Directed assembly with density multiplication is also shown in the SEMs in **Figure 5**, but in this case the assembled structures demonstrate another important capability of directed assembly of block copolymers: the ability to assemble into device-oriented structures.[35] While there are useful applications of naturally-occurring structures such as parallel lines and hexagonal arrays of spots, for many applications of advanced lithography it is necessary for more complex geometries, such as line segments, 90° bends, jogs, T-junctions, periodic arrays of spots, and isolated lines and spots.[36] Earlier research has shown the ability to direct the assembly of block copolymers on the chemical patterns to form each of these structures without density multiplication.[34,37] Recent research has shown that many of these features can also be assembled with density multiplication, as shown in the bends, jogs, T-junctions, and line terminations shown in the SEMs in **Figure 5**.[35]

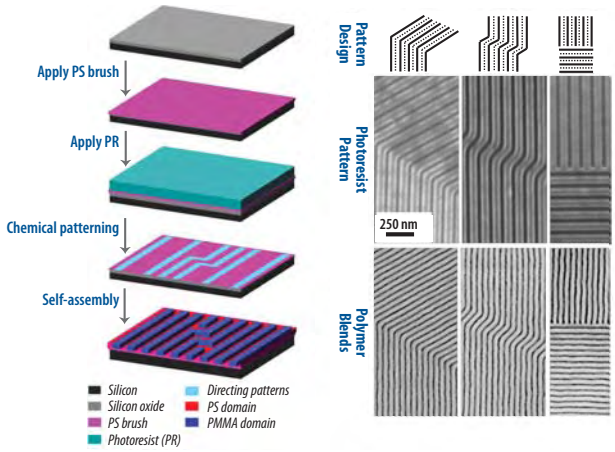

Figure 5. On the left is shown a schematic of the directed assembly process for the directed assembly of a block copolymer into device-oriented geometries with density multiplication. On the right is shown the chemical pattern design (top row), SEM images of the photoresist pattern (middle row), and the corresponding block copolymer-homopolymer ternary blends (bottom row) directed to assemble into device-oriented structures.[35]

Conclusion

The understanding and application of directed assembly has made huge gains over the past decade, but there are still many opportunity for research and innovation. For example, the bulk of the research on directed assembly, including the work described above, has been done with PS-*b*-PMMA. While significant advancements have been made, it is reasonable to assume that for some applications it would be beneficial to use other block copolymer systems, such as organometallic or silicon-containing block copolymers. Similarly, it may be valuable to use block copolymer systems that can assemble into smaller domain structures than PS-*b*-PMMA. Thus, directed assembly of block copolymers remains a rich field of exploration, both for new scientific discoveries and technological implementation of our current knowledge of the process.

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Block Copolymers

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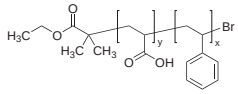
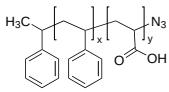
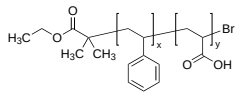
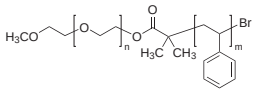
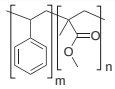
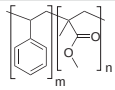
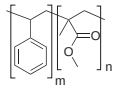
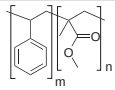
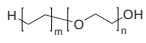
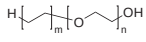
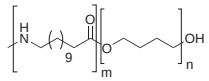
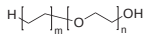
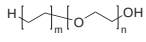
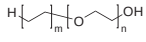
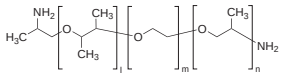
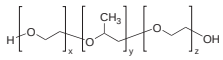
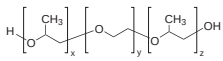
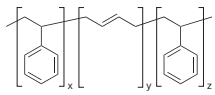
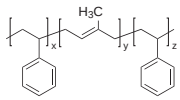
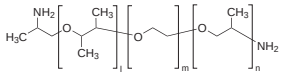
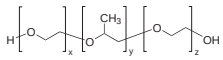
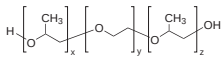
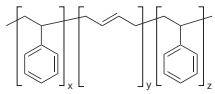
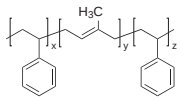
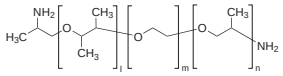
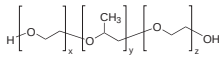
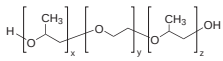
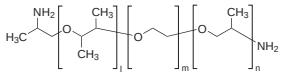
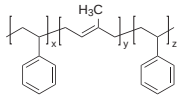
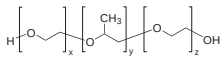
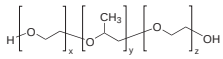
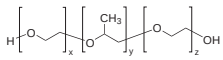
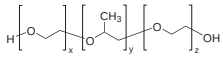
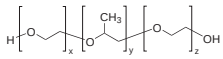
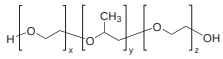
Diblock Copolymers

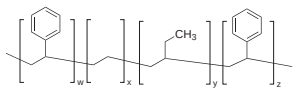
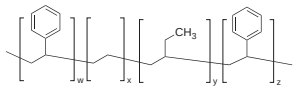
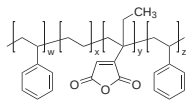
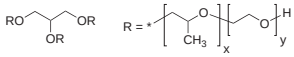
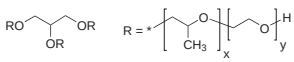
Name, Polydispersity	Structure	Molecular Weight	Prod. No.
Poly(styrene)-*block*-poly(acrylic acid), 1.1		M_n 7,470-9,130 M_n 1,890-2,310 (poly(acrylic acid)) M_n 5,580-6,820 (polystyrene)	686794-500MG
Poly(styrene)-*block*-poly(acrylic acid), azide terminated, 1.2		M_n 5,000 (poly(acrylic acid)) M_n 15,000 (polystyrene) M_n 20,000	735892-250MG
Polystyrene-*block*-poly(acrylic acid), 1.1		M_n 83,000 average M_n 70,000 (polystyrene) average M_n 13,000 (poly(acrylic acid))	725153-500MG
Poly(styrene)-*block*-poly(ethylene glycol), 1.1		M_n 21,000-30,000 (polystyrene) M_n 700-1,100 (PEG) M_n 21,000-31,000	686476-500MG
Poly(styrene-*block*-methyl methacrylate), <1.2		M_n 32,000 average M_n 10,000 (PMMA) average M_n 22,000 (polystyrene)	739553-1G 739553-5G
Poly(styrene-*block*-methyl methacrylate), <1.2		average M_n 15,000 (polystyrene) average M_n 15,000 (PMMA) average M_n 30,000	749184-1G
Poly(styrene-*block*-methyl methacrylate), <1.2		average M_n 104,000 average M_n 52,000 (polystyrene) average M_n 52,000 (PMMA)	749192-1G
Poly(styrene-*block*-methyl methacrylate), <1.2		average M_n 25,000 (PMMA) average M_n 57,000 (polystyrene) average M_n 82,000	749206-1G
Polyethylene-*block*-poly(ethylene glycol)		average M_n ~575	459003-250G
Polyethylene-*block*-poly(ethylene glycol)		average M_n ~875	458996-250G 458996-1KG
Polylauryllactam-*block*-polytetrahydrofuran		-	430803-100G
Polyethylene-*block*-poly(ethylene glycol)		average M_n ~920	458988-250G
Polyethylene-*block*-poly(ethylene glycol)		average M_n ~1,400	458961-250G
Polyethylene-*block*-poly(ethylene glycol)		average M_n ~2,250	525901-250G 525901-1KG

Triblock Copolymers

Name	Structure	Molecular Weight	Prod. No.
O,O'-Bis(2-aminopropyl) polypropylene glycol-*block*-polyethylene glycol-*block*-polypropylene glycol		M_r ~600	14526-500ML
Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol)		average M_n ~1,100	435406-250ML
Poly(propylene glycol)-*block*-poly(ethylene glycol)-*block*-poly(propylene glycol)		average M_n ~2,000	435473-250ML 435473-1L
Polystyrene-*block*-polybutadiene-*block*-polystyrene		average M_w ~140,000 by GPC	182877-250G
Polystyrene-*block*-polyisoprene-*block*-polystyrene		-	432415-500G
O,O'-Bis(2-aminopropyl) polypropylene glycol-*block*-polyethylene glycol-*block*-polypropylene glycol		M_r ~900	14527-500ML-F
Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol)		average M_n ~1,900	435414-250ML
Poly(propylene glycol)-*block*-poly(ethylene glycol)-*block*-poly(propylene glycol)		average M_n ~2,700	435481-250ML
Polystyrene-*block*-polybutadiene-*block*-polystyrene		-	432490-250G 432490-1KG
Polystyrene-*block*-polyisoprene-*block*-polystyrene		M_n 1,900	432407-500G
O,O'-Bis(2-aminopropyl) polypropylene glycol-*block*-polyethylene glycol-*block*-polypropylene glycol		-	14529-100G-F 14529-500G-F
Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol)		average M_n ~2,000	435422-250ML
Poly(propylene glycol)-*block*-poly(ethylene glycol)-*block*-poly(propylene glycol)		average M_n ~3,300	435503-250ML
Poly(propylene glycol)-*block*-poly(ethylene glycol)-*block*-poly(propylene glycol) bis(2-aminopropyl ether)		average M_n ~2,000	406635-250G
Polystyrene-*block*-polyisoprene-*block*-polystyrene		-	432393-500G

Name	Structure	Molecular Weight	Prod. No.
Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol)		average M_n ~2,800	435430-250ML
Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol)		average M_n ~2,900	435449-250ML 435449-1L
Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol)		average M_n ~4,400	435457-250ML
Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol)		average M_n ~5,800	435465-250ML 435465-1L
Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol)		average M_n ~8,400	412325-250G
Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol)		average M_n ~14,600	542342-250G 542342-1KG

Other Block Copolymers

Name	Structure	Molecular Weight	Composition	Prod. No.
Polystyrene-*block*-poly(ethylene-*ran*-butylene)-*block*-polystyrene		average M_w ~89,000 by GPC	-	200565-250G
Polystyrene-*block*-poly(ethylene-*ran*-butylene)-*block*-polystyrene		average M_w ~118,000 by GPC	-	200557-250G
Polystyrene-*block*-poly(ethylene-*ran*-butylene)-*block*-polystyrene-*graft*-maleic anhydride		-	maleic anhydride ~2 wt. %	432431-250G
Glycerol propoxylate-*block*-ethoxylate		average M_n ~4,000	ethoxylate 15% propoxylate 85%	373869-250G
Glycerol propoxylate-*block*-ethoxylate		average M_n ~5,300	ethoxylate 15% propoxylate 85%	373885-10G 373885-250G

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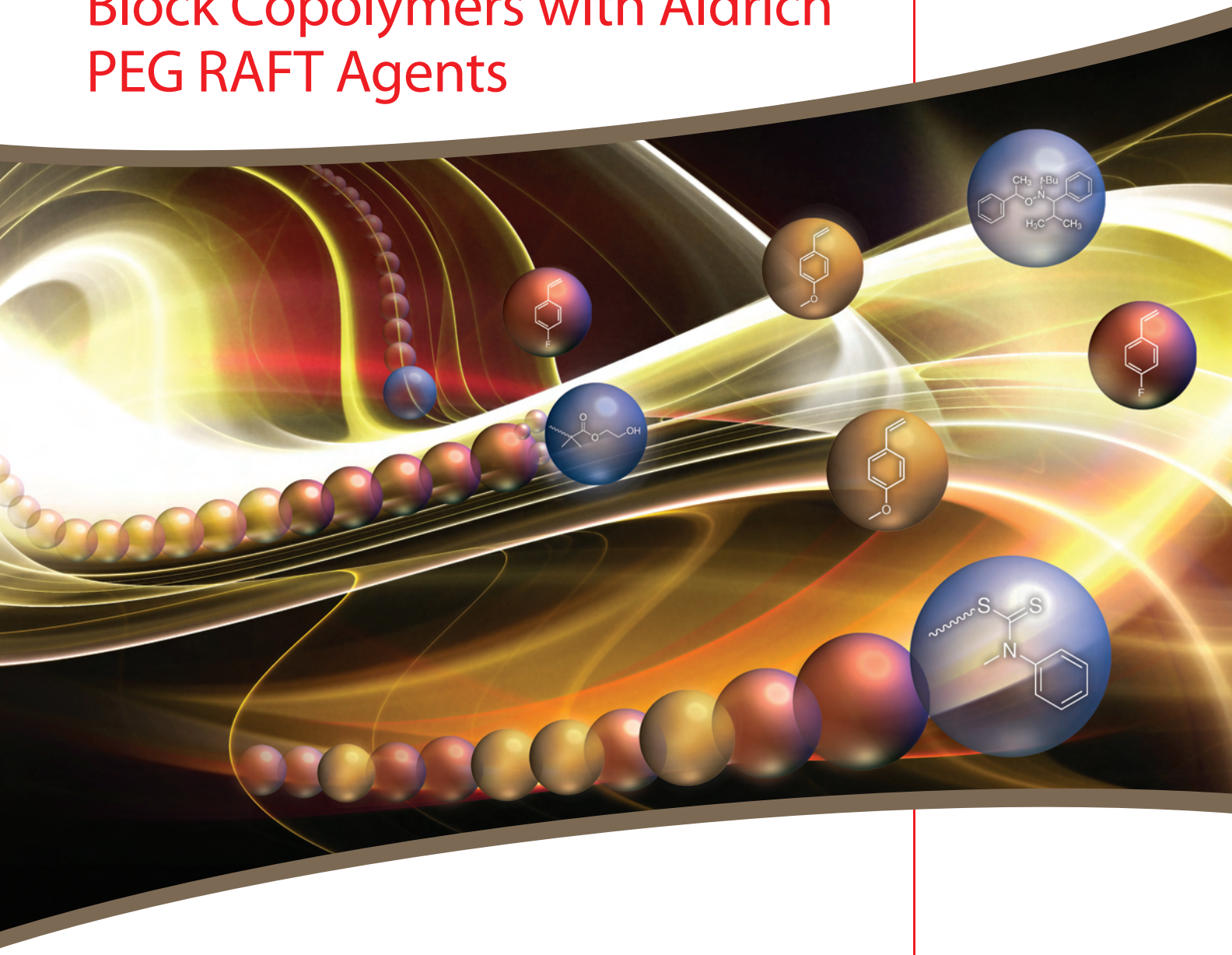

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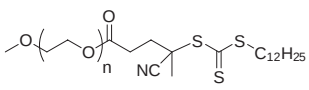

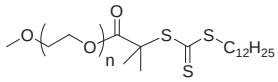

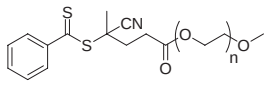

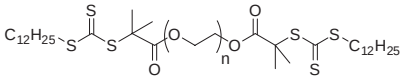

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