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LOADING AND COATING WATER SOLUBLE POLY (ETHYLENE OXIDE)
SUBSTRATES UNDER ETHANOL USING THE LAYER-BY-LAYER TECHNIQUE

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LOADING AND COATING WATER SOLUBLE POLY(ETHYLENE OXIDE)
SUBSTRATES UNDER ETHANOL USING THE LAYER- BY-LAYER TECHNIQUE

by

Sudha Ramachandra

A Thesis

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ABSTRACT

Ramachandra, Sudha. MS. The University of Memphis. May/2010. Loading and Coating Water-Soluble Poly(Ethylene Oxide) Substrates under Ethanol Using the Layer-by-Layer Technique. Major Professor: Dr. Tarek Farhat.

A poly(ethylene oxide) (PEO) and poly(acrylic acid) (PAA) layer-by-layer (LBL) coating was self-assembled on a PEO substrate under non-aqueous conditions using ethanol. After lysine, ferricyanide, and Prussian blue (PB) had been loaded into the PEO granules, the resulting PEO polymer gel was dried to obtain strips that could be dip-coated onto silica wafers to obtain planar base coats with a bilayer thickness of 115 Å at pH = 6 and 350 Å at pH = 2. Further analysis revealed that upon coating, retention in the PEO core was > 95% for PB, ~80% for ferricyanide, and ~73% for lysine. A dissolution test of PB loaded on coated and uncoated PEO strips showed that the former remained intact under an aqueous solution of $\text{pH} \leq 6.5$ for at least 20 minutes whereas the latter dissolved within 3 minutes. These hydrogen-bonded *eth*PEO/PAA LBL films degrade at $\text{pH} \geq 4.5$ under aqueous conditions.

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ABBREVIATIONS

PSS	Poly(styrene sulfonate)	Pg. 9
PAH	Poly(allyl amine) hydrochloride	Pg. 9
PDAC	Poly(diallyl dimethyl ammonium chloride)	Pg. 9
THF	Tetrahydrofuran	Pg. 9
DMF	Dimethylformamide	Pg. 9
HCl	Hydrochloric acid	Pg. 9

INTRODUCTION

Layer-by-layer (LBL) assemblies of polyelectrolytes (PEs) have captured much research attention because of the ease with which their properties (e.g., size, composition, and surface property) can be altered for potential use in drug-delivery systems [1]. This study examined a method of coating the substrate core of poly(ethylene)oxide (PEO), a non-ionic high molecular weight water-soluble polymer, with an ultra-thin polymer film under non-aqueous conditions. Obtained in the form of powder or granules of a whitish or off-white color that produce an ammonia-like odor, PEO is capable of forming association complexes with monomers and polymers through hydrogen bonding. Dilute solutions of PEO at pH ~ 6.5 are available in a wide range of molecular weights of up to 7×10^6 , with those of molecular weights 2500 and below classified as poly(ethylene glycols).

The viscosity of an aqueous PEO solution increases directly with its increasing molecular weight. This study examined a PEO solution of a molecular weight of 4×10^6 , of which an aqueous 1% solution has been reported to have a viscosity of 1650 to 3500 cP [2]. The dilute PEO aqueous and ethanolic solutions prepared in this project were $\leq 0.05\%$. One advantage of using PEO in a controlled molecular release application, such as that examined here, is its low toxicity and biocompatibility [3]. It is due to these characteristics that PEO has been investigated for pharmaceutical applications [4], with its use in oral delivery systems having already been established [5-8].

This study attempted to use PEO as a substrate core in LBL deposition, testing the LBL coating on both PEO granules and on gels transformed from granules, with

the latter dried into PEO pellets, sheets, or films. Such procedures allowed for characterization using spectroscopic techniques, such as Fourier transform infrared spectroscopy (FTIR) and attenuated total reflection-Fourier transform infrared spectroscopy (ATR-FTIR) on free-standing PEO strips or smeared PEO base coats on silicon (Si-100) wafers. The ethanolic solutions of PEO and poly(acrylic) acid (PAA) (see Fig. 1.) were carefully prepared using volumetric titration analysis. The ethanolic solutions were used to coat the PEO core substrate either as a planar strip or a base coat on an Si-100 wafer using the LBL technique to produce a substrate material coated with the same polymer. By performing and analyzing these processes, this study investigated the concept of the polymer couple (i.e., PEO/PAA) and its corresponding PEO substrate, represented as $\text{PEO}_{\text{subs}}/(\text{PAA}/\text{PEO})_{\text{LBL}}$. The advantage of using an ethanolic solution is the possibility of using a water- soluble polymer as a substrate for LBL deposition. Consequently, molecular probes that are loaded into the water- soluble polymer would be released the moment that the coating ruptures. The LBL film, whose thickness can vary from 50 nm to several microns, is formed through hydrogen bonding likely induced by the low tendency of polymers to dissolve in a non-aqueous environment.

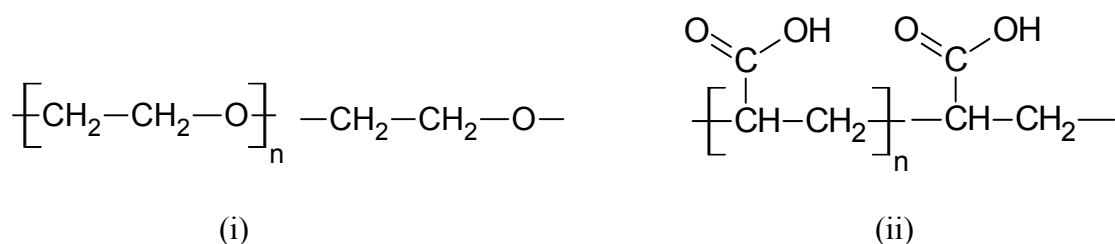


Fig. 1. Chemical structures of the polymers (i) poly(ethylene oxide) and (ii) poly(acrylic acid).

HISTORICAL BACKGROUND

Layer-By-Layer Technique

The oldest technique used for building multilayer films is the Langmuir and Blodgett (LB) technique, developed by Langmuir and Blodgett in the 1920s [9]. Since this initial development, newer characterization techniques have led to significant progress. In the LB technique, amphiphiles are spread on water and compressed to obtain a 2D solid-like film, which is then transferred from the water/air interface onto a solid substrate. In 1991 Decher and Hong developed the electrostatic self-assembly (ESA) technique to form multilayer films from the numerous polyanions and polycations produced by the alternate dipping of a substrate into anionic and cationic amphiphiles [10]. The adsorption of these molecules promoted the surface-charge reversal needed to form the film. For example, if a charged substrate, such as an Si-100 wafer, is dipped into an aqueous solution of an oppositely charged PE, the charge neutralization that initially occurs upon adsorption later results in the reversal of the surface charge. After the substrate is then washed in water to remove excess PE, it is dipped into another PE solution with a charge opposite to that of the first solution, which reverses the surface charge once again. These steps are repeated several times to obtain multiple layers (see Fig. 2.). The ESA method was quickly recognized as a highly versatile technique for the self-assembly of organic and inorganic substances. Interactions other than those among electrostatic charges have subsequently been applied to produce multilayered assemblies.

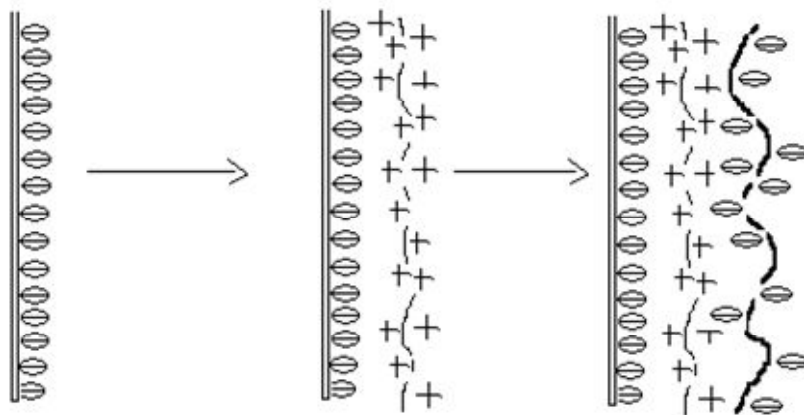


Fig. 2. Schematic representation of a silicon wafer adsorbed with polycation resulting in charge reversal and a second layer of polyanion adsorbed over the polycation to form the bilayer.

The production of hydrogen-bonded films from various non-ionic water-soluble polymers, such as poly(vinyl pyrrolidone) (PVP), poly(acrylamide) (PAAm), and PEO have also been attempted [11-13]. Films produced using the LBL process are formed one molecular layer at a time, providing a great degree of control over their composition and surface functionality [14]. The most widely used commercial PEs are poly(allyl amine), poly(ethylene imine), poly(styrene sulfonate), poly(diallyl dimethyl ammonium chloride), poly(vinyl sulfate), and poly(acrylic acid), with aqueous solutions having been mainly used for LBL depositions [10]. The assembly of weak PEs has attracted considerable interest in recent years because of their pH-dependent characteristics [15]. These PEs allow greater control over the thickness, conformation, and degree of ionic bonding by changing the linear charge density based on pH values [14]. The stability of these films depend on factors such as the thickness and nature of the film, such as whether it is acidic, basic, hydrophilic, hydrophobic, thermo-sensitive, or pH-sensitive. These self-assembled molecules have many applications in many fields as components of biosensors

and optical devices. The LBL technique can be applied to nano-sized particles, permitting their use in encapsulation techniques [16], and permits a wide range of functional molecules, such as electro-active polymers, organic dyes, and biologically active molecules, to be incorporated [17] into the films, thus providing an economical means of forming films of tailored compositions [18].

Types of Forces

Different kinds of forces are used in forming multilayer films, including electrostatic interaction, hydrogen bonding, adsorption, covalent bonds, stereo-complex formation, and specific recognition [19]. Hydrogen-bonded self-assembled polymers are formed when two soluble polymers of nearly equal molar concentrations interact to form a complex, with multiple hydrogen bonds formed along the polymer backbone [17]. The formation of hydrogen-bonded polymer complexes in aqueous solutions [20, 21] and the use of organic solvents or combinations of organic solvents and water for the construction of hydrogen-bonded films have been studied for many years [22]. Researchers have found that hydrogen-bonded films formed from weak PEs are sensitive to pH changes [15, 16], as well as that electro-statically formed films can be used to coat particulate substrates to produce pH-sensitive erasable capsule walls [23]. However, unlike electro-statically formed multilayered films, hydrogen-bonded multilayered films can be formed in organic solvents, permitting the use of non-ionic and water insoluble polymers [24]. Polymer blends in which the composition and physical properties are controlled at the molecular level, such as the polyacrylamide blends produced using the hydrogen-bonding approach [25], can be used for the controlled release of molecules [26], and may have applications in controlled drug-delivery systems [15].

History of PE Capsules

Since the LBL technique was first introduced in 1998 [27, 28], capsules made using this technique [29] have been researched for their use in various fields due to the ease in tailoring properties such as size, shape, and composition. These capsules can be made from a variety of starting materials, including natural and synthetic PEs, biomacromolecules, and nanoparticles [30]. PE LBL films can also act as carriers for therapeutic molecules. The vast majority of PE-based capsules have been made by alternating deposition of complementary PEs, facilitated by electrostatic force, hydrogen bonding [31, 32], hydrophobic bonding [33], and hybridization [34, 35]. The advantage of using LBL fabricated PE capsules is in its simplicity and possibility to obtain multifunctionality in their shells. The advantage of capsules in drug delivery is that they prevent drug degradation and its side effects in the body [36].

Atom-transfer radical polymerisation (ATRP) and nitroxide-mediated polymerisation (NMP) have been used in the design of block copolymer micelles and polymersomes [3, 5]. Considered analogous to liposomes, polymersomes have been studied for their use as capsules in drug-release systems [37]. These structures, which are versatile due to their flexibility in design, release entrapped molecules in response to various factors, including changes in pH or changes in thermal or redox potentials. The incorporation of molecules (see Fig. 3.) into capsules for drug delivery has been studied [1]. The loading of molecules or encapsulation is typically achieved through (a) permeation of molecules into preformed PE capsules, (b) LBL coating over a crystal form of the molecule, or (c) adsorption of molecules to colloidal particles over which an LBL coating is deposited (see Fig. 3.). Permeation through preformed capsules is possible

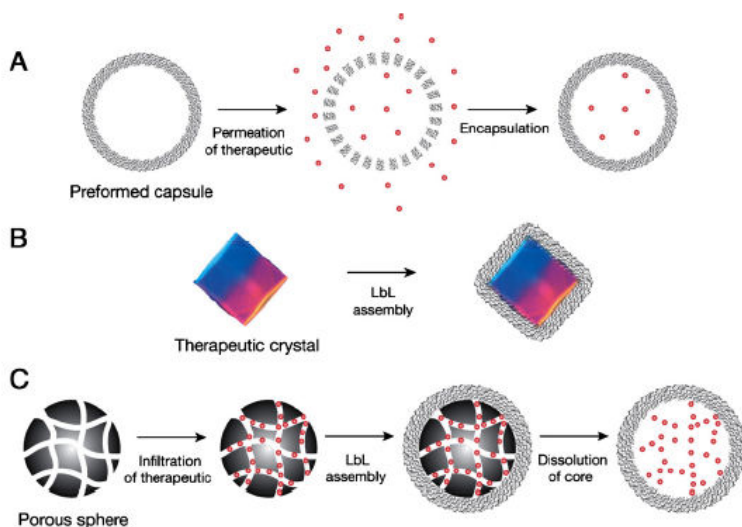


Fig. 3. Different methods for encapsulating therapeutics: (A) loading preformed capsules, (B) encapsulation of crystalline particles, and (C) incorporation into porous materials. Reproduced from [1].

when the capsule material responds to changes in salt concentration or to pH by opening the pores in the capsules. For example, (dextran sulfate/PAH), poly(allylamine hydrochloride) microcapsule responds to change in salt, and poly(styrene sulfonate) (PSS)/PAH capsule responds to changes in pH. [39,40] However, the amount of loading depends on the concentration in the solution into which the preformed capsules are dispersed, and the level of reproducibility is very low [41]. Sequestering agents of low molecular weight that have a high affinity for the therapeutic molecules introduced into the capsules permit increased adsorption of these molecules [42]. An example for this is the use of low molecular weight dextran sulfate as sequestering agent in capsules made from PSS/amidoamine dendrimer. [43]

Proteins and drugs that can form crystals are encapsulated by directly depositing LbL coating onto them [44, 45]. The most recent development is the use of colloidal particles such as calcium carbonate [46] and silicon [47-49] to adsorb the therapeutic

molecule, followed by LBL coating, which permits high loading of the molecule and low interaction between the sequestering agent and the loaded molecule. Release of molecules in a sustained manner could be achieved through diffusion across the highly permeable capsule wall [50] or by slow degradation of the capsule wall [51]. As demonstrated by Antipov *et al.* in their study of the impact of ionic strength and pH on the permeation of fluorescein in PSS/PAH multilayers, changing external factors such as ionic strength and pH can induce degradation of the capsule wall [52].

Core Substrates

Early research led to the production of capsules from organic templates such as polystyrene (PS), cross-linked melamine formaldehyde (MF) microparticles, and cross-linked alginates that hydrolyze under Ca^{2+} deprivation by which Ca^{2+} -crossed alginates degrade slowly in EDTA solutions [53-56]. However, MF complexes with the shell [57-60] and could be toxic, while PS is easily destroyed by organic solvents and disintegrates the capsule [61]. Later, they were replaced by inorganic carbonates such calcium carbonate and magnesium carbonate [2, 62-65], which have lower molecular weights and are more stable. Recently, cadmium carbonate [2, 66] has been used to fabricate PE capsules. Although silica particles (SiO_2) have been used for encapsulation [67, 68], the hydrofluoric acid used to dissolve the silicon core needs extreme caution while handling. Some of the recent work on PS and MF is summarized in **Table 1**.

Table 1. Release Study on PS and MF as Substrates

Number	Polyelectrolyte for Coating	Loaded Material	Core Substrate	Solvent	Citation
1	Chitosan and PSS		PS-Colloidal particle	THF	[69]
2	Benzophenone modified PAH and PSS	Rhodamine B	PS	THF	[70]
3	Diazo-resins (DZR) and PSS	Hollow	PS	THF	[71]
4	Per fluorinated ionomer (Nafion) and ferric ions	Fluorescein	PS latex particle	THF or DMF	[72]
5	(sodium+salt) PAA and PAH	Hollow	MF and PS	HCl	[73]
6	Tb ³⁺ /(PSS) and 4-Pyrene sulfate/ PAA	Hollow	PSS and MF latex particles		[74]
7	PSS,PAH,PDAC,DNA salt	Hollow	MF and PS spheres	pH<1.6	[75]

Because PEs release molecules in response to changes in factors such as pH, light, magnetic field, glucose level, and redox potential, they have been used to produce stimuli-responsive capsules for drug-delivery systems. Changes in pH causes the PE to change into its uncharged form, thereby disassembling the capsule. Rubner *et al.* described the change in charge and morphology of PAH-based planar multilayers [76] and proved that the integrity of these films was reversible by changing their pH. Similar studies were conducted on PE capsules by Masuer *et al.* [77] for poly(methacrylic) acid/poly(allyl amine) hydrochloride (PMA/PAH) and Dejugnat *et al.* [61] for PSS/PAH systems. This feature of the reversibility of capsule permeability with changes in pH was used by Dejugnat *et al.* for introducing and releasing large molecular weight substances such as rhodamine-labeled PSS and FTIC-dextran.

PEO, the core substrate used in this study, has also been used in several recent studies. Krogel and Bodmeier [78] used a chemical oscillator that released drugs in a pulsating manner from the formulation. The pulsatile drug delivery system had two layers, one impermeable capsule filled with drug and an erodible plug at the capsule opening. When they produced the plugs by directly compressing the PEO and placing the tablet into the capsule, they found that erosion time increased in tandem with an increase in the molecular weight of the PEO [79]. In another study, Ali Javed *et al.* achieved the release of celecoxib from the polymer microsphere using dichloromethane and ethanol. Many other studies have used organic solvents to release drugs from microspheres [75, 82, 83]. This study proposes that the use of PEO gels, *if coated*, could be part of an alternative encapsulation technique by which the loaded molecule could be released without the use of any harmful solvents or the necessity to fabricate hollow capsules.

Applications of PEO in the Pharmaceutical Industry

PEO complexes find varied applications in drug-delivery systems, enteric-coated drugs, and contact lenses [84]. Due to their ionic and hydrophilic nature and permeability to body fluids, they have many biomedical applications [84]. Dhawan and Sinha have reviewed the use of PEO in hydrophilic and hydrogel matrices and various other drug-delivery systems [85]. Kofinas *et al.* observed that PEO hydrogels can be used in the transportation of growth factors [87] and Abraham *et al.* reported that PEO hydrogels provide the right conditions for the diffusion of small polar molecules [88]. PEO complexes can deliver drugs across the skin, while PEO tablets and hydrophilic matrixes can be used in prolonged oral drug delivery. When Zhang and McGinity

studied the release of chlorpheniramine maleate from matrix tablets prepared by hot extrusion [89], they found that the release was controlled by the erosion of the PEO matrix and the diffusion of the drug across the gel at the surface of the tablet. Pillay and Fassihi described a new monolithic delivery system that follows a zero-order kinetics for metoprolol tartarate [90], is independent of pH changes, and has the potential for extended release of bioactive agents at a constant rate.

In this study PEO was used as a swellable matrix, as had Luber and Bunick, who described an immediate-release tablet that could be chewed or disintegrated in the oral cavity [91] with a matrix made from PEO. Berner and Louie [92] described the targeted and controlled delivery of ciprofloxacin to the upper gastrointestinal tract over a period of time from an erodible PEO matrix, a useful method when patients are in fed mode. Plotnikov *et al.* observed that intravenous injection of PEO reduced blood pressure in the stenosed vessel in narcotized cats [93]. According to Gutowska *et al.*, injectable PEO formulations, which can gel in-vivo in response to changes in temperature or pH or during ionic cross linking or solvent exchange, have the potential for minimally invasive implantation because they can assume a desired shape and permit the easy incorporation of drugs [94]. Anderson *et al.* have used PEO in targeted drug delivery, and anticipate that systemic drug delivery of poorly absorbed proteins and peptides will be improved by the use of targeted oral liposomes [95]. When Verma *et al.* compared the muco adhesion behavior of PEO versus carbopol matrices using a water-soluble drug, they found a marked increase in the swelling index of matrices with a high PEO content compared to the carbopol matrices [96]. While working on a sandwiched osmotic tablet system for delivering

Nifedepine, Liu *et al.* found that the PEO in the drug layer of a osmotic tablet core surrounded by cellulose acetate membrane with two orifices for Nifedepine release assisted in the Nifedepine release [97].

Previous research has demonstrated the significance of PEO as a core substrate in controlled molecular release and the capability of the LBL technique to form thin coating. Although Hammond and Sukhishvili [98-100] conducted research into PEO/PAA using aqueous solutions, the current study was the first to investigate the preparation of ethanolic solutions using polymer/water/ethanol combinations in which PEO and PAA segments do not precipitate out of the solution, as the prepared polymer/water/ethanol mixture must not dissolve the PEO polymer substrate or LBL deposition will fail. Under non-aqueous conditions, hydrogen bonding is the force most likely to cause LBL film assembly.

This study conducted several experiments to demonstrate that PAA is a highly protonated species prepared to H-bond with the oxy-ether of PEO. Under ethanol, the PAA segments can hydrogen bond with PEO segments at the surface of the PEO substrate or with loose PEO segments in solution. This study used FTIR to characterize the free PAA and PEO segments as well as monitor LBL deposition on Si-100 wafers and PEO substrates. Molecular and colloidal loading was also examined using FTIR and colorimetric analysis. Environmental scanning electron microscopy (ESEM) and atomic force microscopy (AFM) were used to examine the topography, cross-sectional features, and thickness of the deposited films. For ease of handling and characterization, PEO granules were made into polymer gels, then molded into strips and base coat substrates. Based on the results of this study, it is anticipated that $\text{PEO}_{\text{subs}}/(\text{PEO/PAA})_{\text{LBL}}$ systems

will have many applications in the field of controlled molecular release within the chemical and pharmaceutical industries.

EXPERIMENTAL SECTION

Materials and Methods

Chemicals Used

All polymers were used as purchased without further purification. Lysine, potassium ferricyanide, PEO (MW = 4000,000; FW 44g/mol), and poly(diallyldimethyl ammonium chloride) (PDAC, MW~200,000, 20% wt., FW 161.1g/mol) were purchased from Sigma Aldrich. PAA (MW = 90,000, 25 wt. %, FW 72.06g/mol) was purchased from Polysciences Inc. Ethyl alcohol anhydrous USP grade (ethanol 200 proof) used as solvent was purchased from Pharmco-Aaper. A millipore (system) dispenser for 18 M Ω ultra-pure water was used in all experiments.

Instruments Used

A plasma cleaner/sterilizer PDC-32G purchased from Harrik was used to clean Si-100 wafers by plasma etching before treatment with 10-mM PE (PDAC or PAA) solution as a base layer. The treated Si-100 substrate was then subjected to multilayer deposition from the respective polymers using a robotic dipper purchased from Nanostrata, Inc. A Nicolet 550 Series-II/Avatar 380 FTIR was used to monitor LBL assembly. Spectral and quantitative analysis on low-polymer solution concentrations was performed using a ATR/FTIR optical box and trough purchased from Specac, Inc. The interferogram was collected with a 4-cm⁻¹ resolution gain of 1 and an average number of

scans of 30. The signals were obtained on absorbance mode against corresponding backgrounds. A spectrum of Si-100 was obtained first and the sample spectrum of coated Si-100 was obtained against the former as background to obtain the IR spectrum of the LBL assembly.

Absorbance values for the carboxylate and carboxylic acid of PAA were estimated by examining the absorbance bands at ~ 1550 and $\sim 1700\text{ cm}^{-1}$, respectively. Each peak height was assumed to be the maximum of a Gaussian absorbance curve for its respective chemical species. Signature peaks of PEO was observed at $2900, 1100\text{ cm}^{-1}$, lysine was observed at ~ 1420 and ferricyanide at $\sim 2120\text{ cm}^{-1}$. Spectra were also obtained for various number of bilayers applied on a PEO base coat that had been cast on Si-100 wafers. In one method, spectra were sampled for a combined PEO base coat and LBL film, while in another method the spectra of PEO base coat on Si-100 wafers was used as the background and to obtain the full spectrum of only the LBL film.

The film thickness of various LBL films was measured using a Stokes ellipsometer purchased from Gaertner Scientific, where $K_s = -0.319$, $N_{\text{LBL}} = 1.5$, and $N_{\text{Si}} = 4.5$. An environmental scanning electron microscope (ESEM) Philips XL 30 and atomic force microscope (AFM) purchased from Digital Instruments, Veeco metrology, Dimension 3100 were used to examine topological and cross-sectional views of the PEO substrate coated with the PEO/PAA LBL film and to estimate the film thickness. The SEM-EDAX instrument has a field emission gun operating at 1 or 4kV. All samples were dried before analysis. A small piece of the sample was placed in the field using a stainless steel specimen stub. The signals from secondary electrons were obtained using accelerating voltage of 500kV. The images were obtained at an inclination of 45° and at a

magnification between x580 and x2500. AFM topographical images of samples were obtained under an imaging mode at a scan rate of 0.28Hz with the instrument set for 512 scan points and a scan size of 100 μ m. The thickness and roughness of the films on the Si-100 were also obtained. The PEO/PAA LBL films on PEO substrates were detected using transmission FTIR and ESEM.

Preparation of PEO Gel for Base Coat on Si-100 Wafers

A 0.01% water based PEO gel was obtained by dispersing 0.2 g of PEO granules in 20 mL of pure water to obtain a polymer gel under stirring. The resulting gel was cast on glass Petri dishes and left to dry overnight. The dry PEO film was cut into strips for LBL deposition. For the base coat, clean rectangular silicon plates were dip coated into the PEO gel, which was left to dry on Si-100 wafers before LBL deposition. The PEO base coat on the Si-100 wafers was sufficiently thin to allow transmission of IR radiation.

Substrate Preparation

To obtain free-standing strips, 0.7g of PEO was weighed and dispersed in 12.5mL of ethanol, then 12.5mL of water was added under high stirring to obtain a uniform pourable gel. The gels were then poured onto glass Petri dishes and left to dry to obtain dry PEO strips. In another experiment, Si-100 wafers were used as the substrate after first being cleaned in boiling water and then in boiling ethanol. To avoid alteration on Si surface, chromic acid was not preferred for cleaning. Washing wafers in chromic acid increased the number of oxygen groups available on the Si-100 surface. The wafers were plasma etched (Plasma Cleaner PDC-32G, neon lamp) under medium intensity for 5 min

each to render the silicon surface slightly hydrophilic before being coated with polymers in an LBL fashion using a robotic mechanical deposition system.

Loading of Chemicals

Water-soluble chemicals can be dissolved in water before loading them into PEO. To produce an ethanol -water based PEO gel, the ethanol-insoluble chemicals potassium ferricyanide and the amino acids lysine and arginine were loaded into PEO by dissolving them in water and adding to the dispersion of PEO in ethanol. 0.05 g of lysine and arginine were dissolved in 1mL of water and added to 15mL of the prepared PEO gel. A 30mM solution of ferricyanide in water was used for maximum loading. 0.03g of PEO granules were dissolved into 3mL of this ferricyanide solution. About 17 to 18 drops of the resulting PEO gel was dried on Si-100 substrates, and IR signals were obtained before any LBL coating was deposited on the surface. Ferrous sulfate was added to a 10mL solution of ferricyanide to obtain a Prussian blue (PB) solution. This solution was added to a dispersion of 0.7g of PEO granules in 10mL of ethanol under stirring to obtain a thicker gel.

Robotic Mechanical Deposition

The LBL deposition was performed with an automated dipping system controlled by a robotic Stratosmart software program. Eight beakers, two filled with polymer solutions placed diagonally opposite to each other and separated by six beakers of ethanol, were placed in a circle inside the robotic chamber. The desired substrate (i.e., PEO strips, PEO base coats on Si-100 wafers, and Si-100 wafers) was dipped into beakers filled with polymer solutions to obtain a specified number of bilayers. The two

solutions used were PAA and PEO in their aqueous or ethanol forms and the adsorption time was set to either 5.0 or 10.0 minutes. After deposition, the substrate underwent three rinsing of one minute each with either water or ethanol to remove surplus polymer solution. (Note: During manual deposition, the PEO granules were gently stirred in their respective solutions and left to settle before decanting the solution. Although slight centrifugation had to be applied to the first two bilayers, the coated granules settled quickly during subsequent bilayer deposition). For both aqueous and ethanolic polymer depositions, the pH was adjusted within two pH ranges ($\text{pH} = 6$ to 7 and $\text{pH} = 2$ to 2.5) using either concentrated HCl or concentrated NaOH.

Preparation of PEO and PAA Ethanol Solutions and Automated LBL Deposition

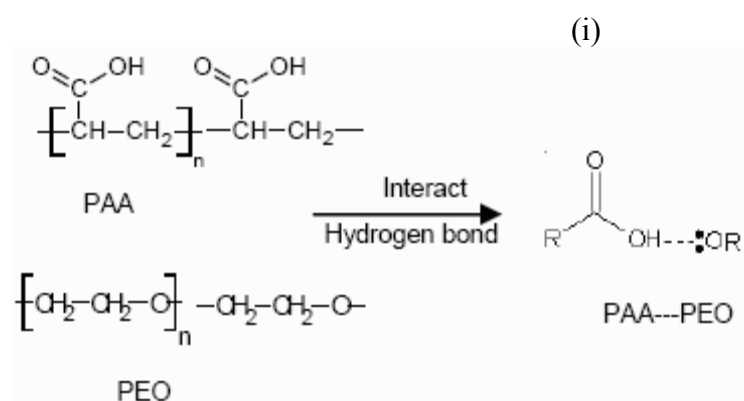
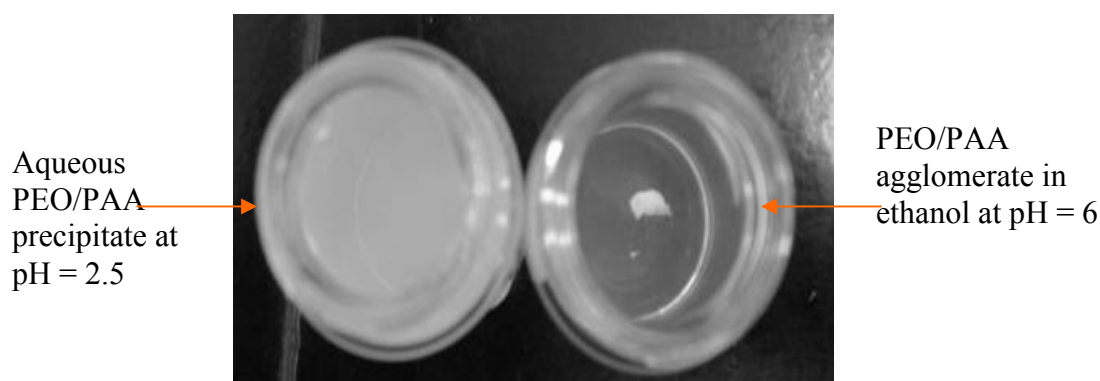
A mass of 1.0 g of the as-prepared PEO polymer gel was dispersed in 20 mL of ethanol, yielding approximately 10.0 to 12.0 mM of clear PEO-PE solution. A PAA (10mM) PE ethanol solution was prepared by carefully dissolving 0.7 to 0.72 g of stock 25% PAA in 250 mL ethanol. The ethanolic PEO and PAA solutions were adjusted to $\text{pH} \leq 2.5$ by adding 1 to 3 drops of concentrated HCl solution, followed by filtering with a 0.45 to 1.2 μm syringe filters. The effective solution preparation was set aside for several hours to ensure that no precipitates formed. An ethanolic polymer solution was considered stable if no precipitate formed when stored.

As the core for the loading of probe molecules, PEO obtained in granular form was first transformed into a gel then dried to obtain PEO strips or base coats. Transforming PEO granules into gel allows for easy loading of probe molecules and easy characterization of PEO flat substrates using instruments such as the FTIR, ATR-FTIR, or ellipsometer. Although the PEO substrates are nonconductive, ESEM analysis can be

performed on these substrates, as the microscope can operate the sample chamber at ambient conditions. After loading the probe molecules into the PEO substrates, the PEO substrate was coated by a protective layer so that it would neither decompose at $\text{pH} < 2.5$ nor degrade quickly at $\text{pH} > 4$. The coating assembled was possible due to formation of hydrogen bonds between the polymer couple PEO/PAA. Preparing the coating required preparing the ethanolic polymer solutions. Ethanol was used as a solvent in the experiments because it allows preparation of the polymer solutions of PEO and PAA with a minimum amount of water, which is especially important when using PEO as a substrate for LBL assembly, and is a safe and economical solvent. A combination of water and ethanol is needed because pure ethanol cannot be used to prepare a PEO solution, as PEO does not dissolve in pure ethanol. After several volumetric experiments, the volumes of ethanol and water that would dissolve a specific mass of PEO to produce a stable PEO solution were determined. The prepared PEO and PAA polymer solutions were used as coating solutions for LBL assembly. However, obtaining a stable PEO coat solution proved challenging. Above a critical volume of ethanol, PEO precipitates out of the solution, and excess moisture in the coat solution leaches the PEO from the base coat during the deposition cycle. The stability of the PEO solutions depended on the proportion of alcohol to water content.

The first evidence of the forming of a multilayer under alcoholic conditions was obtained during the blending of equimolar volumes of ethanolic PEO and PAA to form a precipitate (see Fig. 4[i]). At a high pH (~ 5 -6), a white colloidal agglomerate was formed, whereas at a low pH ($= 2.5$), a precipitate that was similar to the precipitate under aqueous condition (i.e., pH 2.5) was obtained [101]. The agglomeration at high pH

may be due to the screening effect of COO^- groups in PAA from the ethanol. At a low pH, COOH groups predominate, which allows uniform interaction and dispersal of the PEO-PAA complex in ethanol. Water with a dielectric constant of 80, can easily accommodate charged groups like COO^- because the hydrogen which is a leaving group can be easily form hydronium ions, which cannot occur in Ethanol with a dielectric



(ii)

Fig. 4. (i) In water or ethanol at pH = 2.5, equimolar polymer solutions of poly(ethylene oxide) and poly(acrylic acid) produced white colloidal precipitates, while neutral ethanolic poly(ethylene oxide) and poly(acrylic acid) solutions formed agglomerates. (ii) Depicts the interaction between poly(ethylene oxide) and poly(acrylic acid) in ethanol at a low pH.

constant of 30. After succeeding in isolating the PEO/PAA insoluble complex, the preliminary experiments were conducted on Si-100 wafers to provide evidence of PEO

and PAA multilayer deposition while obtaining thickness measurements of the LBL films deposited, the latter of which was necessary before making any PEO/PAA LBL deposition on a PEO base coat or free PEO strips. The coating or deposition was achieved by a long-range hydrogen-bond interaction between PEO and PAA (see Fig. 4[ii]). The evidence for the base coat, LBL coating, and loaded molecules was obtained in the form of infrared (IR) spectra and scanning electron microscope (SEM) images, with further AFM investigation revealing the thickness and roughness of these films.

RESULTS AND DISCUSSIONS

PEO and PAA LBL Films on Si-100 Wafers

The FTIR spectrum of a PEO base coat on Si-100 wafers (see Fig. 5) can be obtained if the thickness of the PEO substrate does not exceed 500 microns. The samples of base coats on Si-100 wafers in this study were either 100 to 200 microns or 20 to 30 microns in thickness, as measured using a micrometer at a resolution of 0.0001. It was necessary to obtain measures of the PEO FTIR spectrum to identify any PEO losses or gains during LBL deposition as well as identify any background spectral interference. The spectra showed a strong absorbance at 1120 cm^{-1} associated with the symmetric and asymmetric C-O-C vibrations [102]. The spectrum had contributions from smaller peaks at 1060 cm^{-1} and 1150 cm^{-1} due to -C-C stretch and CH_2 rocking vibrations [103]. A second band was observed at 2900 cm^{-1} from the alkyl -C-H vibrations.

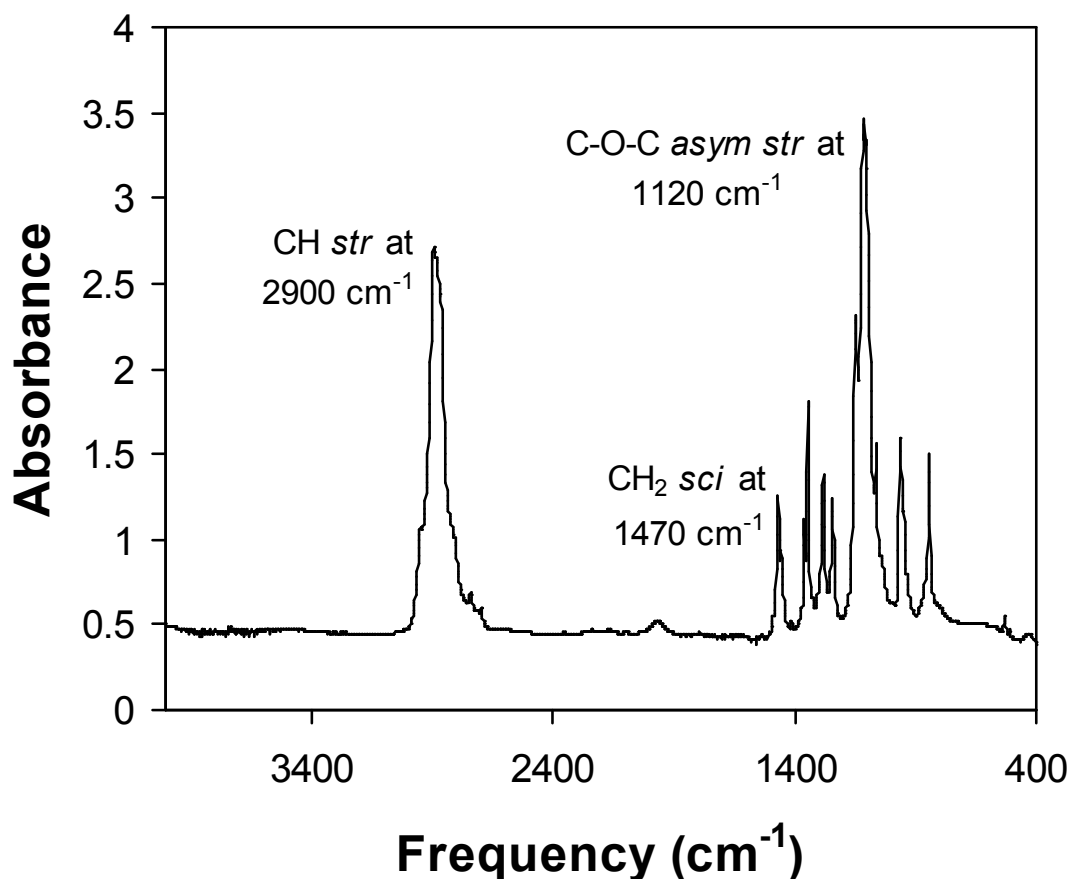


Fig. 5. Fourier Transform Infrared spectrum of poly(ethylene oxide) base coat on Si-100 wafers with an estimated thickness of 150 to 200 μm .

The pH of the polymer solutions and the rinsing solvents had a pronounced effect on the extent of LBL deposition. Prior research into PEO/PAA in aqueous media (i.e., *aqu*PEO/PAA) had verified that changing the pH affected LBL deposition. This study further verified the pH effect by succeeding in the LBL assembly of 20 bilayers on Si-100 wafers by adjusting the pH of the ethanol/water solutions at pH = 6.5 and pH = 2.5, using ethanolic PAA and PEO (i.e., *eth*PEO/PAA) at pH = 6.5 starting with PAA (on Si-100) as the first layer. When measured using AFM, the 20-bilayer *eth*PEO/PAA LBL film assembled at pH = 6.5 measured $\sim 2300 \text{ \AA}$ in thickness and 60 \AA in roughness, whereas the LBL film at pH = 2.5 measured 7500 to 7800 \AA in thickness and 450 \AA in

roughness (see Fig. 6 [i and ii]). A 20-bilayer *aqu*PEO/PAA film using aqueous solutions (PAA and PEO) at pH = 2.5 that measured $\sim 7300 \text{ \AA}$ in thickness was also assembled, a value 1/3 that reported by Hammond *et al.* [98, 99]. It should be noted that

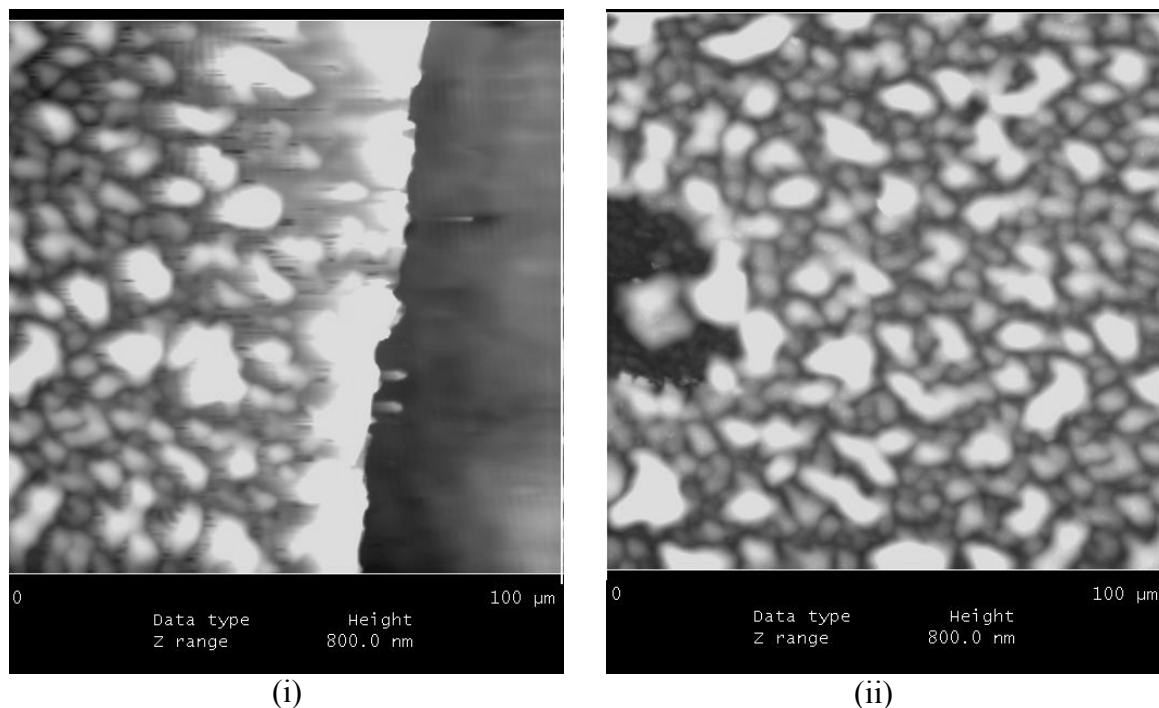


Fig. 6. Atomic force microscope pictures of 20 bilayers of ethanolic poly(ethylene oxide)/poly(acrylic acid) Layer-by-layer film showing (i) a scratch on the surface for thickness and roughness measurements (thickness of 7500 \AA , surface roughness of $\sim 450 \text{ \AA}$) and (ii) a topographical view.

in general poly(ethylene imine) used instead of PAA as the base layer. However, Sukhishvili reported a measurement of $\sim 2000 \text{ \AA}$ for a 10-bilayer assembly of PMAA/PEO [104]. The difference in the thickness of the alcoholic and aqueous films is related to the pH conditions. The thickness of an aqueous PEO/PAA film assembled at pH = 3.5 is 1/3 the thickness of a film obtained at pH = 2 (9). Similarly, a 20-bilayer ethanolic PEO/PAA film assembled at pH ≤ 2.5 with a thickness of 7650 to 7700 \AA has an IR absorbance 3 times stronger than that of a film obtained at pH ≤ 6 (see Fig. 7 [i, ii])

with a thickness of $\sim 2300 \text{ \AA}$. The mass and thickness increment with each bilayer applied at $\text{pH} \leq 2.5$ is $4.2 \mu\text{g}$, corresponding to a $\sim 350 \text{ \AA}$ /bilayer, assuming that the LBL film density is 1.2 g cm^{-3} [102].

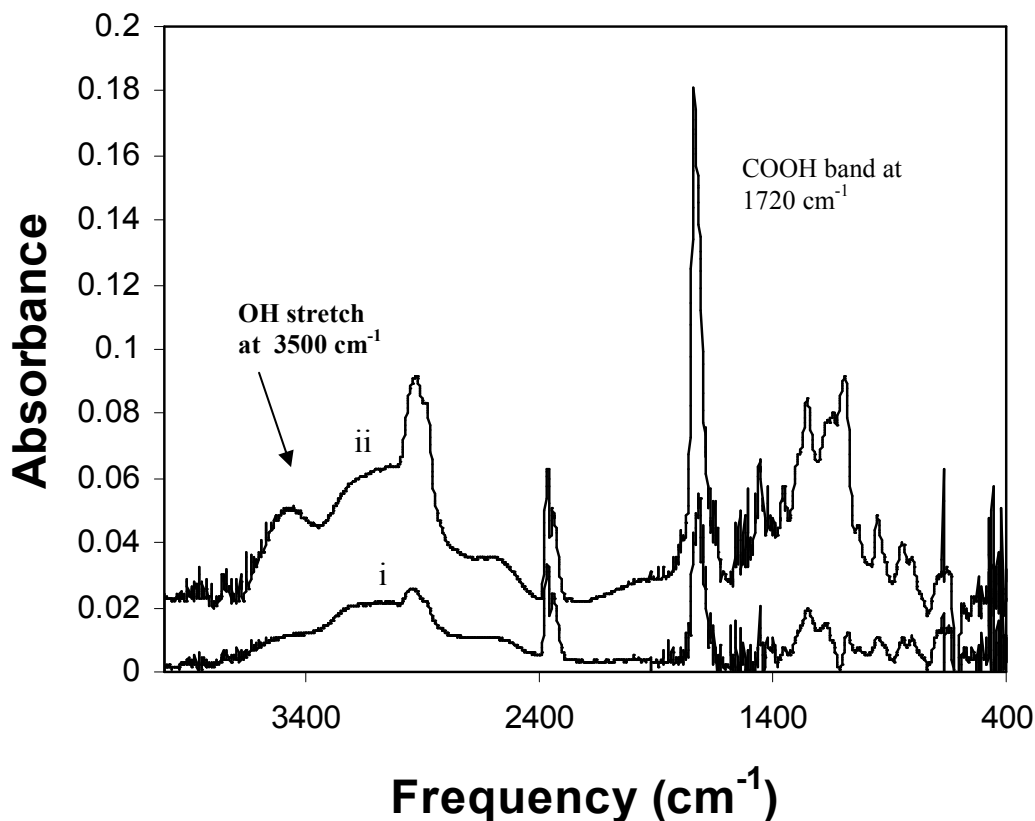


Fig. 7. Fourier Transform Infrared spectra of 20-bilayer ethanolic poly(ethylene oxide)/poly(acrylic acid) Layer-by-layer film deposited on Si-100 prepared at (i) $\text{pH} = 6-7$, (ii) $\text{pH} \sim 2.5$.

PEO and PAA LBL Films on PEO Core Substrate

After performing the successful deposition of ethanolic PEO/PAA LBL on Si-100 wafers, its deposition on PEO substrates was attempted. It had been observed that a 10- to 11-mM PEO solution does not dissolve the PEO base coat or a PEO strip; in fact, increased absorbance of the PEO signal after the deposition of the 2nd bilayer had been

observed. The drop in PEO signal or the absorbance of the base coat measured at 2900, 1470, and 1120 cm^{-1} was less than 1% with a PAA ethanolic solution and less than 3% with a PEO ethanolic solution after 3 hours of exposure. After FTIR subtraction and weight change in analytical balance, it was found that the loss in the PEO base coat on Si-100 did not exceed 1% after an estimated 20 PEO/PAA bilayers deposition or 3 1/2 hours of dipping. Change in the substrate mass is an important factor, as continuous loss of the surface could prevent LBL assembly.

Using a robotic dipper, 10, 15, and 20 bilayers were applied on a PEO base coat on Si-100. The assembly of *eth*PEO/PAA LBL film on PEO base coats was confirmed by FTIR as changes in peak absorbance of the C=O stretch of the COOH band at 1720 cm^{-1} for 10, 15, and 20 bilayers on PEO strips (see Fig. 8). The presence of the COOH group in its protonated form, which is involved in the hydrogen bonding in the ethanolic *eth*PEO/PAA LBL film, is seen in the spectra of Fig. 9 (ii) (**black line**). The COOH bands in the *eth*PEO/PAA LBL film and the ethanolic free PAA film are similar to the COOH band in aqueous free PAA at pH < 2 with less than 10% ionization (Fig. 9 [ii],[i]) [105]. At pH = 9, more than 80% of the COOH groups of aqueous free PAA ionizes to form COO⁻ groups, which appear as asymmetric and symmetric stretches at 1570 and 1410 cm^{-1} (Fig. 9 [i], [**black line**]). Compare to the aqueous

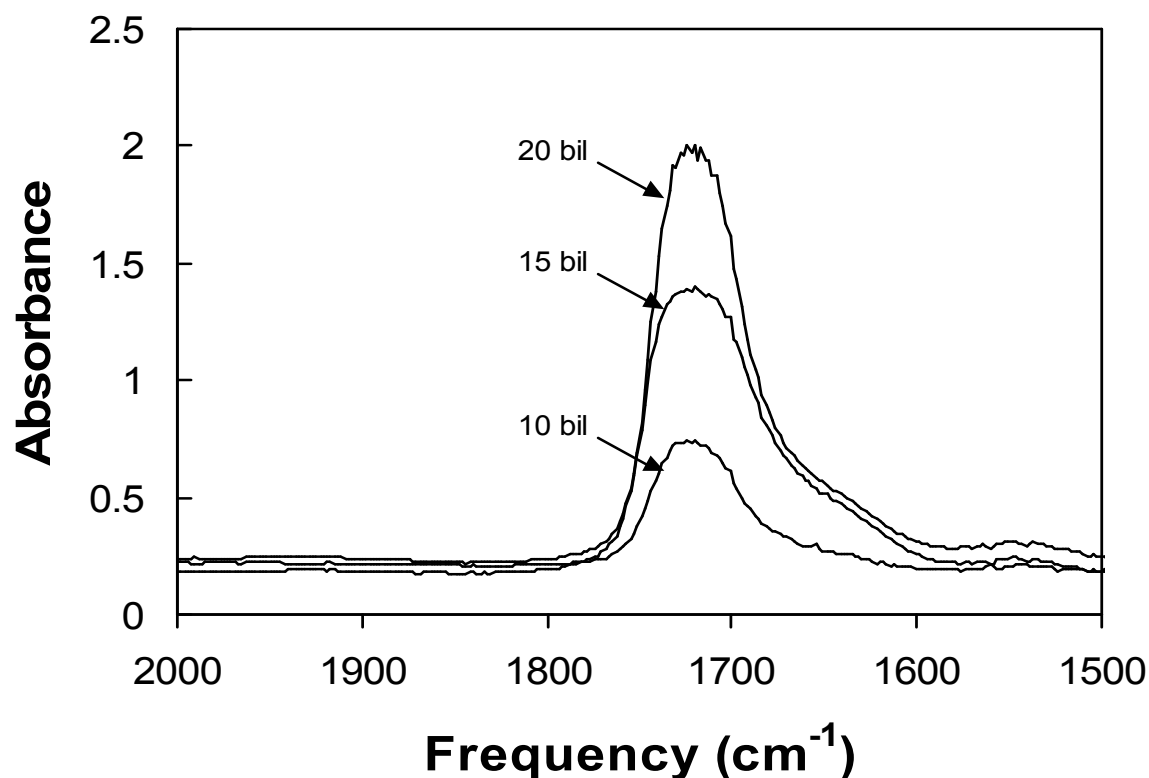


Fig. 8. Change in Fourier Transform Infrared peak absorbance (i.e., carbonyl stretch of the carboxylic acid band at 1720 cm^{-1}) for 10-, 15-, and 20-bilayer sequential assembly of ethanolic poly(ethylene oxide)/poly(acrylic acid) Layer-by-layer film on poly(ethylene oxide) strips.

PDAC/PAA LBL film at pH ~ 5 , where PAA shows $\sim 40\%$ protonation of the COOH band at 1710 cm^{-1} and of the COO^- bands at 1570 and 1410 cm^{-1} (Fig. 9 [iii]). Therefore, FTIR strongly indicates the strong protonation of the COOH group (i.e., $< 5\%$ ionization), which allows hydrogen interaction ($-\text{CO}-\text{O}-\text{H}\cdots\text{:O}-\text{C}$) between the COOH group of PAA and the oxy-ether group of PEO. The small amount of ionization of COOH in ethPEO/PAA was attributed to the presence of water in the PEO coat solution. Note that the small peak of the OH stretch at 3510 cm^{-1} in the ethanolic PEO/PAA LBL film replaces the broad OH bands due to water surrounding the COO^- groups in free aqueous PAA segments at pH = 9 and in the aqueous PDAC/PAA LBL film

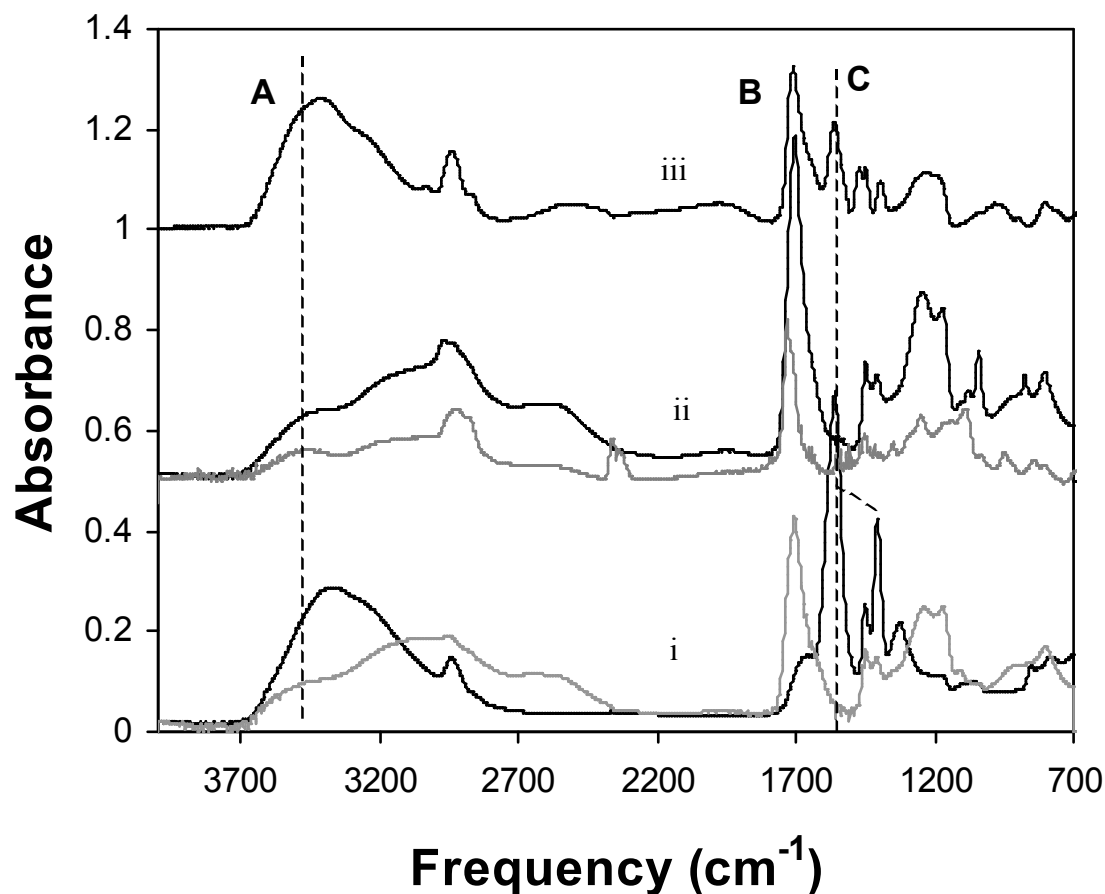


Fig. 9. Evidence of protonated carboxylic acid group in the ethanolic poly (ethylene oxide)/poly(acrylic acid) layer-by-layer film. Infrared spectra of the (i) carboxylic acid band of free aqueous poly(acrylic acid) segments at pH < 2 (gray line), carboxylic acid band of free aqueous poly(acrylic acid) segments at pH = 9 (black line) where carboxylic acid transforms to the carboxylate form (i.e. > 80% ionization) with characteristic asymmetric and symmetric stretch at 1570 and 1410 cm^{-1} , (ii) ethanolic poly(ethylene oxide)/poly(acrylic acid) layer-by-layer film and the free poly(acrylic acid) segments in ethanol, (iii) aqueous poly(diallyl dimethyl ammonium chloride)/poly(acrylic acid) layer-by-layer film at pH ~ 4.5-5 when poly(acrylic acid) is ~ 40% protonated showing both the carboxylic acid band at 1710 cm^{-1} and the carboxylate bands at 1570 and 1410 cm^{-1} . (A) hydroxyl band at 3510 cm^{-1} , (B) carboxylic acid band at 1720 cm^{-1} , (C) carboxylate bands at 1570 and 1410 cm^{-1} .

A sample FTIR spectrum of a 10-bilayer PEO/PAA LBL film of ethanolic *eth*PEO/PAA on a PEO strip after subtracting the IR spectrum of the PEO strip is shown in Fig. 10. The above spectra can be compared to the spectra of ethanolic and aqueous PEO/PAA LBL film deposited directly on Si-100. The FTIR spectra of *eth*PEO/PAA and *aqu*PEO/PAA

LBL film were similar because PAA under ethanol is largely in its COOH form, which analogous to its status at $\text{pH} < 2.5$ under aqueous conditions. However, some peak shifts were detected. The C=O stretch of ethanolic and aqueous free PAA and the *qu*PEO/PAA LBL film at $\text{pH} = 2$ observed at 1710 cm^{-1} is blue shifted by $\sim 15\text{ cm}^{-1}$ to $1720\text{--}1730\text{ cm}^{-1}$ in *eth*PEO/PAA LBL (see Fig. 11), a direct indication of hydrogen bonding.

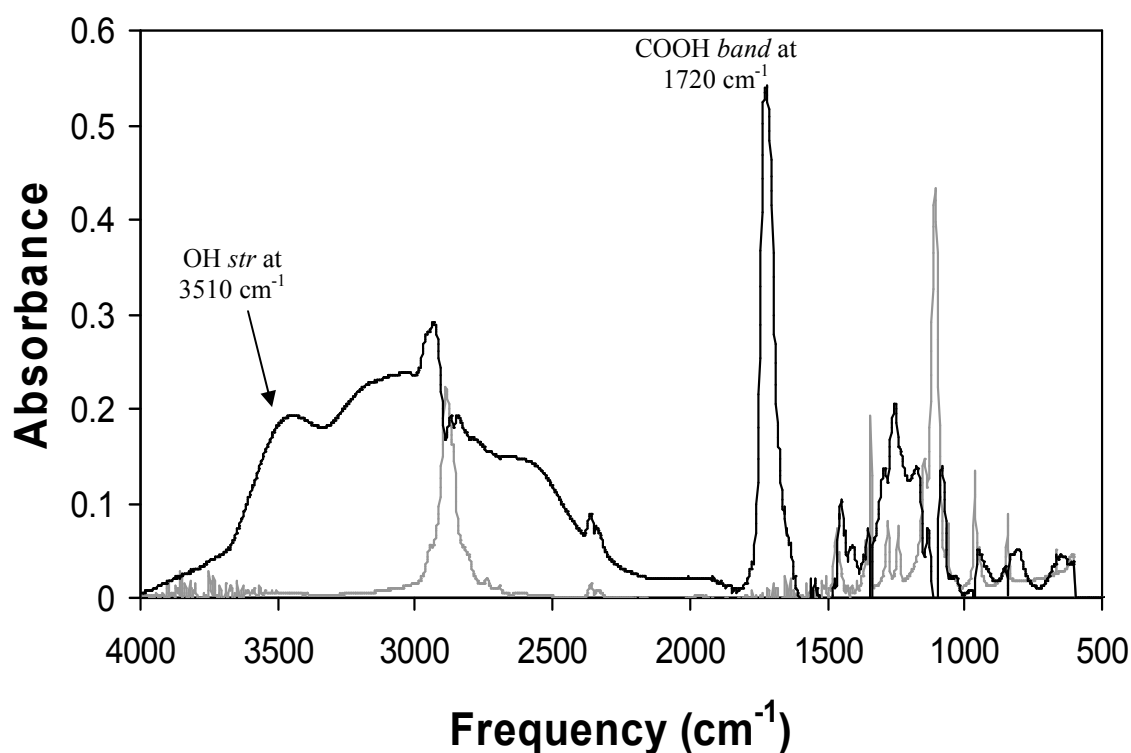


Fig. 10. An ethanolic poly(ethylene oxide)/poly(acrylic acid) 10 bilayer-film on a poly(ethylene oxide) strip. The Fourier Transform Infrared spectrum of the poly(ethylene oxide) base coat can be subtracted out, leaving the spectrum of poly(ethylene oxide)/poly(acrylic acid) Layer-by-layer film.

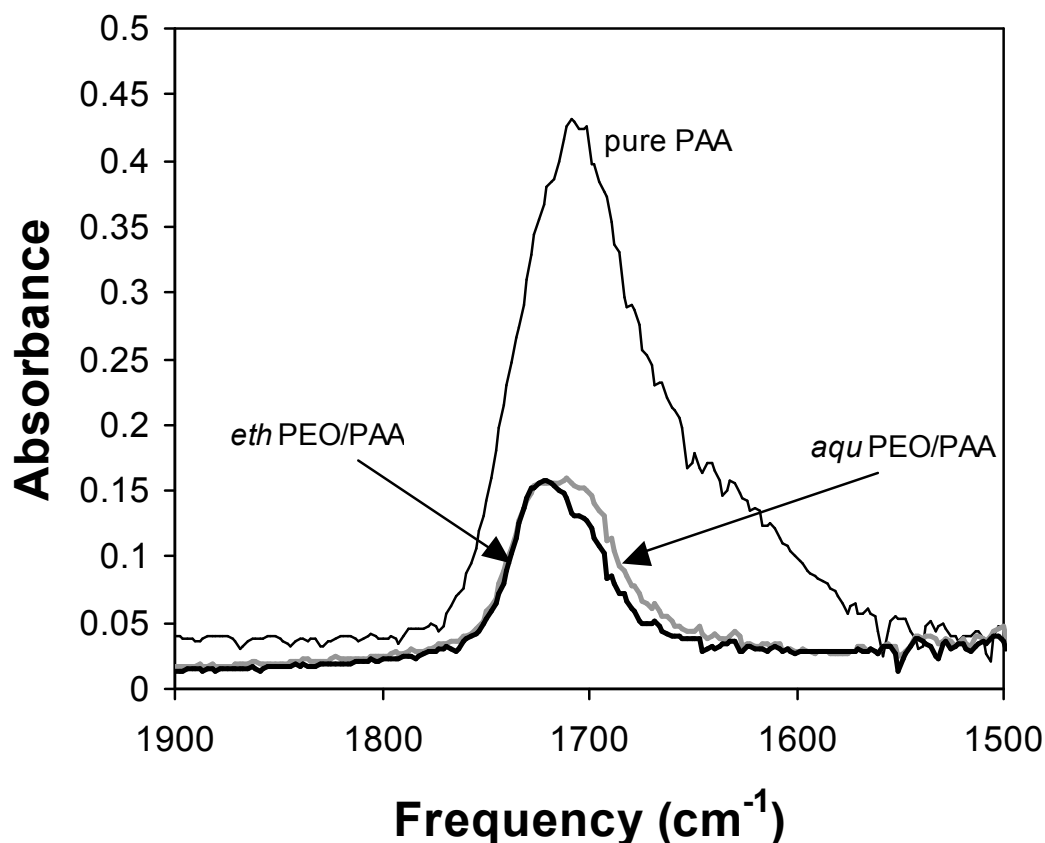


Fig. 11. Fourier Transform Infrared spectrum showing carboxylic acid stretch at 1720-1730 cm^{-1} in the ethanolic poly(ethylene oxide)/poly(acrylic acid) layer-by-layer film that is blue shifted by $\sim 15 \text{ cm}^{-1}$ when compared to the carboxylic acid stretch at 1710 cm^{-1} of pure aqueous poly(acrylic acid), free ethanolic poly(acrylic acid), and aqueous poly(ethylene oxide)/poly(acrylic acid) layer-by-layer film treated at pH = 2.

The blue shift is a strong evidence of hydrogen bonding ($\text{C-O} \cdots \text{H-O-OC}$) between PEO and PAA segments in ethanol. The COOH group acts as a proton donor while the C-O-C group in PEO acts as a proton acceptor. Moreover, the C-O-C band of PEO is red shifted by $\sim 20 \text{ cm}^{-1}$, from 1120-1110 cm^{-1} in pure PEO to 1090 cm^{-1} in the *eth*PEO/PAA LBL film [99, 104]

Disintegration Study of *eth*PEO/PAA LBL Films

Similar to an *aqu*PEO/PAA LBL film, an *eth*PEO/PAA LBL film remains intact in a pH = 2 solution but completely degrades in a neutral (pH = 7) solution. This was verified when a 20-bilayer *eth*PEO/PAA LBL film on silica exposed to pH = 8 decreased in thickness from 6300 Å to 40 Å, and the C=O *str* at 1720 cm⁻¹ of the PAA nearly disappeared when examined under ellipsometry and FTIR. This pattern of disintegration of the *eth*PEO/PAA LBL film was similar to the disintegration of *aqu*PEO/PAA LBL film reported by Hammond [9]. Starting with pH = 2 and increasing the pH in increments of 0.5, a 7500 Å thick Lbl film was exposed to different buffer solutions for 5 minutes and the change in IR absorbance of a 7500 Å was monitored. It was found that the *eth*PEO/PAA LBL film remained intact up to pH = 4, after which it started to disintegrate, with only < 30 % of its original thickness retained at pH = 5 (see Fig. 12), compared to *aq*PEO/PAA LBL film, which remains intact up to pH = 2.7 [9]. The stability of the *eth*PEO/PAA LBL film when exposed to pH changes is important in PEO_{subs}/(PAA/PEO)_{LBL} systems because pH stimuli could be used as control mechanisms in molecular release systems.

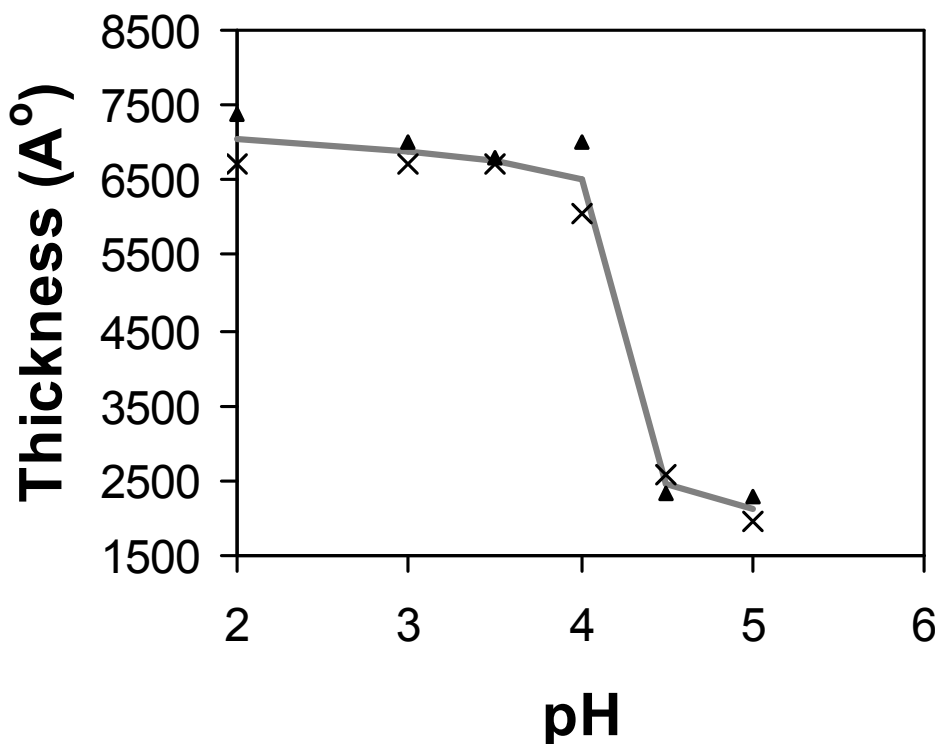


Fig. 12. Starting with pH = 2 and increasing the pH in increments of 0.5, the ethanolic poly(ethylene oxide)/poly(acrylic acid) layer-by-layer film remains intact up to pH = 4, after which it starts to degrade until it retains only < 30% of its original thickness at pH = 5.

ESEM Analysis on *eth*PEO/PAA Coating Assembled on a PEO Base Coat

Using ESEM, topological and cross-sectional views of the LBL coating on a PEO base coat were examined. The topological view of the PEO base coat showed a rough surface with holes and cavities due to the bursting of the air bubbles entrapped while applying the base coat on Si-100 wafers, leaving empty spaces (see Fig. 13 [i]). After 20 bilayers of *eth*PEO/PAA LBL film deposition on the base coat, the surface appears smooth and uniform (see Fig. 13 [ii]).

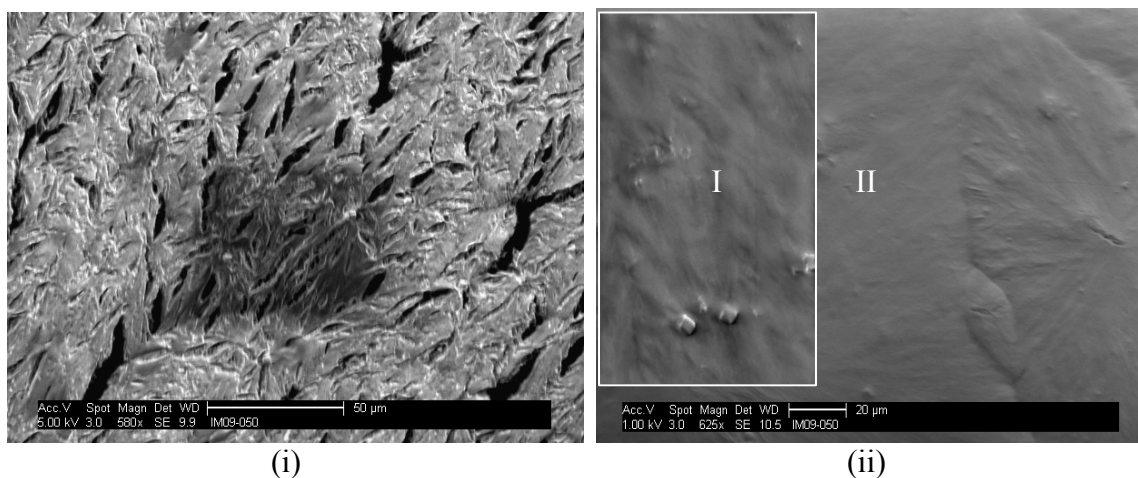


Fig. 13. Environmental scanning electron microscope showing, (i) a topological view of an uncoated base coat on a Si-100 plate. The topography of the poly(ethylene oxide) base coat is rough with cracks and cavities from entrapped air bubbles, (ii) topological view of a poly(ethylene oxide) base coat on a Si-100 plate coated with 20 bilayers of ethanolic poly(ethylene oxide)/poly(acrylic acid) layer-by-layer film at (I) pH = 2, (II) pH = 6.

A cross-sectional view of 20 bilayers of the *eth*PEO/PAA LBL film on a PEO base coat was obtained under ESEM by applying sharp cuts across the Si-100 wafers to sharply snap the LBL film. ESEM images show a 20- to 30-micron PEO base coat with a 0.7- to 0.8-micron thick *eth*PEO/PAA LBL film carpeting the PEO surface (see Fig. 14).

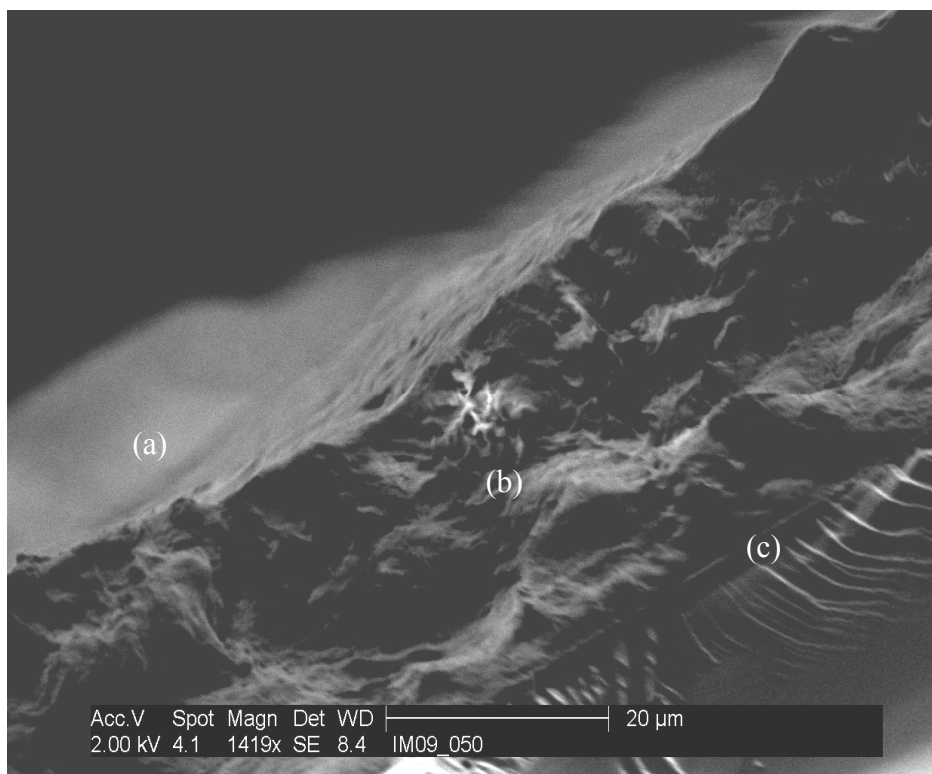


Fig. 14. Cross-sectional view of a poly(ethylene oxide) base coat on a Si-100 plate coated with an ethanolic 20-bilayer layer-by layer film of ethanolic poly(ethylene oxide)/poly(acrylic acid) (a) 20-bilayer (0.7 to 0.8 microns) ethanolic poly(ethylene oxide)/poly(acrylic acid) layer-by-layer film spread like a carpet over the rough surface of the poly(ethylene oxide) base coat, (b) 20-30 micron poly(ethylene oxide) base coat, (c) cut in the Si-100 wafer.

Thus, the ESEM results regarding the LBL film thickness correlate with results obtained by ellipsometry and AFM. ESEM photographs reveal an ethPEO/PAA LBL film spread like a carpet over the rough surface of the base coat due to the long-range hydrogen bonding between the PEO surface and the PAA base layer of the ethPEO/PAA LBL film, imparting a smooth and uniform surface (see Fig. 14). It was as difficult to examine the surface roughness of the LBL film on PEO strips or base coats using AFM as with ESEM because the PEO substrate surface was not uniform.

Retention Analysis after ethPEO/PAA LBL Film Deposition

The IR active molecules lysine and ferricyanide $\text{Fe}(\text{CN})_6^{3-}$ anion were loaded onto PEO substrates, and the $\text{C}\equiv\text{N}$ stretch at 2120 cm^{-1} in $\text{Fe}(\text{CN})_6^{3-}$ and COO^- sym stretch at 1420 cm^{-1} in lysine were used to measure their respective retention in the PEO substrate after LBL deposition. Although the presence of loaded molecules inside LBL film coated with PEO substrates was verified, a kinetic molecular release study was not conducted. The basecoat with the probe and LBL coating on it was abbreviated as [base coat]_B/[probe]_P/[LBL]_L system for easy representation. In the first system, in which lysine was loaded onto the PEO base coat (see Fig. 15[i]), the IR spectrum was compared to the IR spectrum after 10 bilayers of PEO/PAA had been deposited on the base coat [PEO]_B/[Lysine]_P/[PAA/PEO]_L system. The IR spectrum shows the characteristic peaks of the PEO base coat, the $\text{C}=\text{O}$ stretch of carboxylate in PAA, and the IR signature of the probe. In the above spectrum, the CH stretch at 2900 cm^{-1} and the C-O-C asymmetric stretch at 1110 cm^{-1} of the base coat, the OH stretch at 3520 cm^{-1} and the $\text{C}=\text{O}$ stretch at 1725 cm^{-1} of the PEO/PAA LBL film (10 bilayers), and the COO^- asymmetric stretch at 1420 cm^{-1} of the loaded lysine can be seen. The three peaks in lysine, due to NH_3^+ asymmetric deformation at 1620 cm^{-1} , NH_2 bend and COO^- asymmetric stretch at 1590 cm^{-1} , and NH_3^+ asymmetric deformation at 1515 cm^{-1} merged into two broad peaks at 1650 and 1560 cm^{-1} , likely due to weak amide formation leading to dimerisation of lysine molecules under the ethanolic medium [106]. As the COO^- symmetric stretch at 1420 cm^{-1} remained unaffected, it was used for retention analysis. Using the C-O-C asymmetric stretch at 1110 cm^{-1} of the PEO base coat as an internal reference, the amount of lysine retained after the LBL deposition was estimated as $\sim 74\%$. Problem of

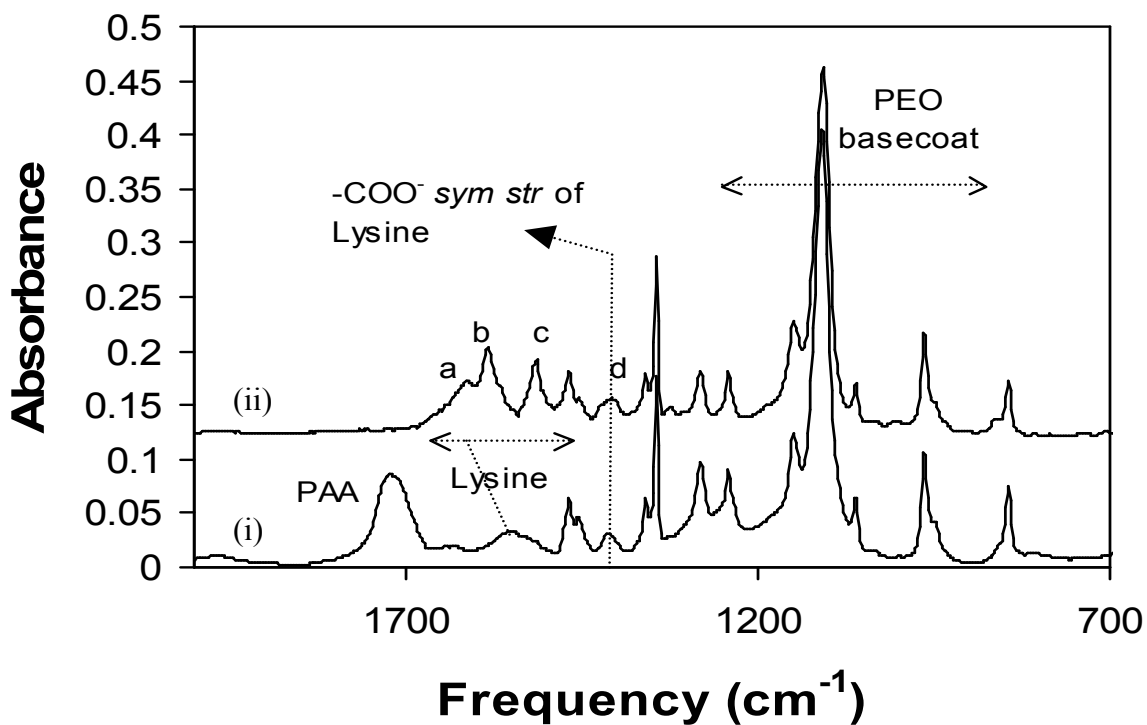


Fig. 15. Fourier Transform Infrared spectra of (i) poly(ethylene oxide) base coat loaded with lysine probes, (ii) poly(ethylene oxide) loaded with lysine and coated with 10 bilayers of ethanolic poly(ethylene oxide)/poly(acrylic acid) Layer-by-layer film. Note: the peak of the carboxylate symmetric stretch of lysine (peak-d) at 1420 cm^{-1} remained intact and was used for quantitative analysis of lysine retention. See poly(acrylic acid) carbonyl stretch at 1720 cm^{-1} , peaks (a,b,c,d) due to lysine.

leaching might be encountered during LBL assembly because the loaded probes would leach depending on its solubility in the *eth*PEO solution when the water content is $> 5\%$. To avoid or minimize leaching we saturated the *eth*PEO solution with the loaded probes (e.g. Lysine) by adding a small quantity ($< 0.01\text{g}$) of the probes that settled at the bottom of the beaker.

In the second system, in which ferricyanide ions were loaded with ferricyanide $\text{Fe}(\text{CN})_6^{3-}$ ion at a 30mM concentration, a major issue was the localization of the ions, as the ions segregated as yellow spots during the drying of the base coat. A certain amount of stress was expected due to stretching of the dry gel. An IR comparison between the

spectrum of the ferricyanide-loaded PEO base coat and the spectrum obtained after the deposition of 10 bilayers of PAA/PEO, $[\text{PEO}]_{\text{B}}/[\text{Fe}(\text{CN})_6^{3-}]_{\text{P}}/[\text{PAA}/\text{PEO}]_{\text{L}}$ shows a shoulder at CN peak (2120 cm^{-1}) instead of a sharp peak before the LBL deposition, most likely due to the formation of a salt complex similar to $\text{Fe}(\text{II})/\text{Fe}(\text{III})$ [107], which shows broad peaks in this region (see Fig. 16).

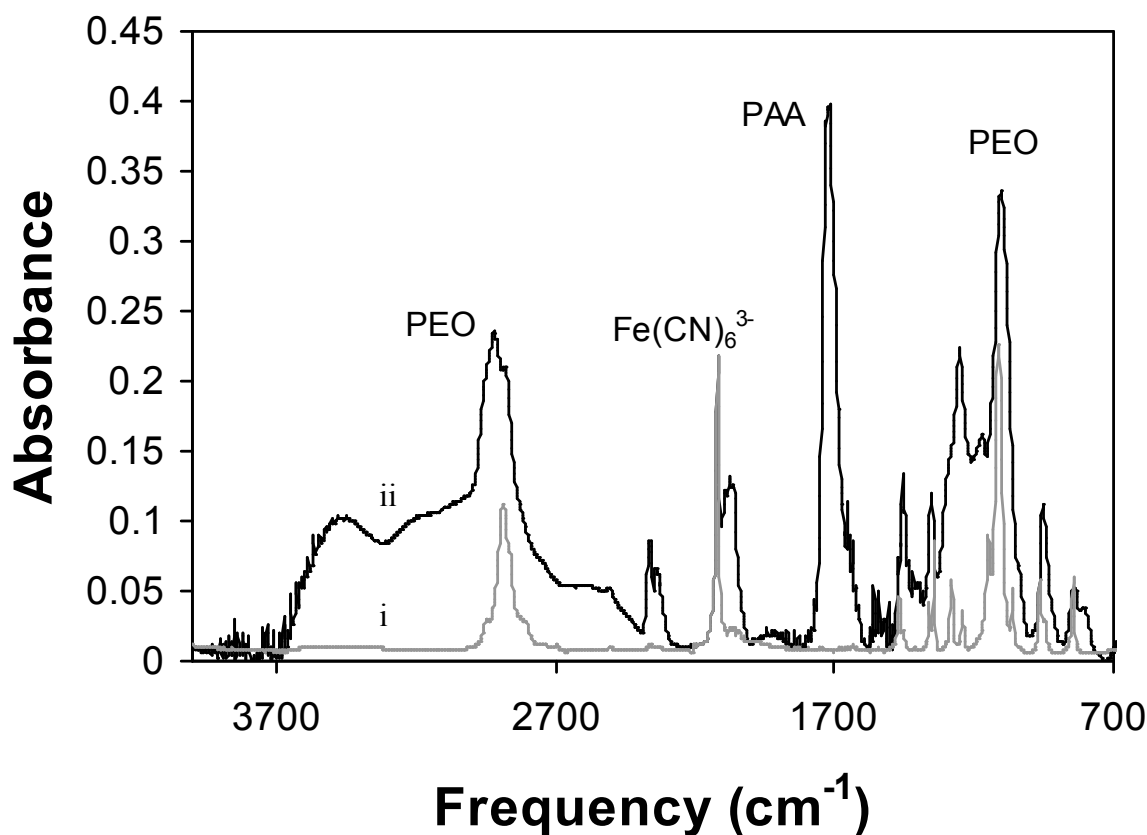


Fig. 16. Fourier Transform Infrared spectra of (i) poly(ethylene oxide) base coat loaded with ferricyanide probes, (ii) poly(ethylene oxide) loaded with ferricyanide and coated with 10 bilayers of ethanolic poly(ethylene oxide)/poly(acrylic acid) layer-by-layer film.

The change in the peak area excluding the shoulder indicated a $\sim 20\%$ loss in the probe on LBL deposition. Compared to an 11% increase in the amount of PEO deposited by LBL in the $[\text{PEO}]_{\text{B}}/[\text{Lysine}]_{\text{P}}/[\text{PAA}/\text{PEO}]_{\text{L}}$ system, the deposition in this system averaged a

36% increase. The amount of PEO deposition(11%: 36%) is roughly comparable to the ratios(1/4) of the C=O stretch of PAA at 1725 cm^{-1} in the two systems . This difference in the amount of film deposited and the hence the IR spectra in these two systems might be attributed to the presence and the kind of molecule loaded. Note that the average absorbance due to the C=O stretch of PAA at 1725 cm^{-1} in the absence of lysine in the base coat was ~ 3 to 4 times higher compared to the absorbance of LBL film when lysine was present.

In yet another system, PB colloid was loaded into PEO obtained as PEO strips rather than as loaded PEO base coats. Because PB gives an intense dark-blue color to the strips, IR analysis was not conducted on these strips; rather, disintegration of LBL film after coating on these strips was verified by dipping the LBL coated and uncoated strips in an aqueous solution at $\text{pH} \leq 6.5$. It was observed that a PEO strip loaded with PB and coated with 20 bilayers of PAA/PEO required more than 20 minutes to disintegrate, while the uncoated strip required only 3 minutes.

These systems demonstrated the possibility of using PEO, a water-soluble polymer, as a substrate in LBL deposition. Due to the ease with which PEO gels can be loaded with various materials, the versatile method of deposition described in this study would be very useful for applications in the field of controlled molecular release technology. Controlled release is achieved by the type of coating applied, with the PEO/PAA LBL coating having the capacity to be modified with other PEs sensitive to various physical effects (e.g., changes in pH and in thermal, shock, and ionic strength), thus providing an adaptable delivery technique. The assembly and loading method presented in this paper can be used by scientists who work with controlled-release

techniques to perform kinetic studies on LBL films of different capabilities. The loaded molecule can be inorganic, organic, and biological molecules, as well as nano- and micro-colloids, viruses, bacteria, and cellular organisms.

CONCLUSIONS

An LBL PEO/PAA film was successfully assembled on a water-soluble PEO substrate using ethanol as a medium of deposition. The ethanol-based LBL PEO/PAA film is pH dependent at a bilayer thickness of 115 Å at pH = 6 and at a bilayer thickness of 350 Å and pH = 2. ESEM revealed a film structure that appears as a 0.7-μm sheet over a 30-μm PEO base coat. Under ethanol, the *eth*PEO/PAA LBL film is highly protonated because its COOH *band* at 1720 cm⁻¹ matches the profile of the COOH *band* of PAA at a pH < 2. Because of the presence of moisture in the PEO solution, it was necessary to saturate the PEO solution with the probe molecules to minimize the leaching of the probes by dissolution. Disintegration of the *eth*PEO/PAA LBL film occurred at pH = 4.5. Of the three different types of probes loaded into the PEO substrate, colloidal PB was strongly retained, while ~80% of ferricyanide and ~73% of lysine were retained.

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