Dynamic wettability study on the functionalized PEGylated layer on a
polylactide surface constructed by the coating of aldehyde-ended
poly(ethylene glycol) (PEG)/polylactide (PLA) block copolymer

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Abstract

A block copolymer of $\alpha$-acetal-poly(ethylene glycol) and polylactide(PEG/PLA) was prepared and utilized as a surface modifier to construct a functionalized PEG layer on a PLA substrate by simple coating. An active functional group, aldehyde, was readily prepared by the derivatization of an $\alpha$-acetal group at the tethered PEG-chain end and can be further utilized to link bioactive functionality molecules such as sugars and proteins. The PEGylated surface thus prepared was characterized by the method of dynamic wetting using the Wilhelmy plate technique and by the surface/interfacial free energy calculation. The results of the dynamic wetting study suggested that the interactions of PEG on the surface with water induce the reorientation of the hydrophilic PEG component to accommodate itself optimally with the water phase, resulting in a significant reduction in the interfacial free energy. By employing the extended Fowkes' equation, the polar interactions are accurately estimated in the free energy calculation of PEGylated surface: the polar components in surface free energy may be divided into two contributions with distinctive characteristics; one is the $\gamma^p_s$ component reflecting water-interactive Lewis sites and the other is the $\gamma^s_p$ component reflecting the dipole moment on the surface. The $\gamma^s_p$ component, related to the PEG conformation via the dipole moment on the substrate, was suggested to be a determinant factor in the protein adsorption. Because these surfaces have both non-fouling and ligand-binding properties, they might support the selective binding and the growth of particular cell populations, and eventually, they are expected to have a high utility in biomedical fields including the field of tissue engineering. © 2000 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Modification by polymers is widely used to control the surface properties of devices for biological and biomedical applications [1–3]. Particularly, poly(ethylene glycol) (PEG) coating is the most common way to minimize non-specific fouling of a material surface with biocomponents [4,5], including plasma proteins, and has been performed by a wide variety of methods [6–11]. However, most of the PEG-coated surfaces so far reported possess no reactive group on the PEG chain end. To provide further functionality on the PEG-coated surface, we designed a block copolymer having end-functionalized PEG as a hydrophilic segment. Polylactide (PLA) was chosen as the hydrophobic segment because it is biodegradable and non-toxic and is widely utilized as an implant material. Further, an acetal group is installed at the $\alpha$-chain end of poly(ethylene glycol)/polylactide (PEG/PLA) block copolymers, which apparently is able to be derivatized to an aldehyde group by a moderate acid treatment. These block copolymers have been utilized as surface modifiers to construct the functionalized PEG layer on the biodegradable PLA surface by simple coating [12,13]. Various ligands including proteins and sugars can be covalently immobilized to aldehyde groups by reductive amination; therefore, these PEGylated PLA materials are expected to have high utility in biomedical fields such as tissue engineering (Fig. 1).

To attain successful control of biological interaction on the PEGylated materials, an accurate analysis of their surface properties is the key issue. Relatively mobile surfaces composed of amphiphilic block copolymers tend to organize themselves in water so as to achieve the lowest possible interfacial free energy [14]. In the case of highly mobile systems, the process is appreciably fast and readily detected by advancing and receding contact angle experiments. Note that surface or interfacial free energy plays a
key role in several biological events such as fouling of biomaterials with proteins [15]. In addition, such polymer surfaces can lead to several specific and non-specific interactions, which may significantly modify the interface with an aqueous exterior due to adsorbed water and polar/non-polar organics. Thus, the study on surface energetics is considered to provide detailed insight into the fouling mechanism of polymer surfaces. Under physiological conditions, the hydrogen bonding capacity of the surface is obviously of major importance in its interaction with water. In the context of surface energy calculation, this contribution has been lumped into the $\gamma^p$ (polar component) term in the previously reported two-component calculations such as the Owens approach [16], resulting in an ambiguous estimation. A separate term should be utilized for the hydrogen-bonding interactions. By employing the extended Fowkes’ equation [17], the surface/interfacial free energies of the usual organic substances can be calculated, e.g. the PEG layer in the present study, including intermolecular interactions of nonpolar, polar, and hydrogen bonding characteristics. This approach, in turn, provides an accurate estimation of both nonpolar and polar energy components.

In this study, a block copolymer of $\alpha$-acetal-PEG with PLA ($\alpha$-acetal-PEG/PLA) was synthesized and utilized to construct a functionalized PEG layer on a biodegradable PLA surface by simple coating. The effect of varying PEG molecular weight (MW) on the surface properties was investigated from a physicochemical (dynamic wetting and surface free energy) as well as biological (protein adsorption) point of view. Contributions of dispersion (nonpolar), polar, and hydrogen bonding forces to the surface/interfacial free energies were determined, and the role of these properties in protein adsorption was discussed. Such a study may lead to a better understanding of the mechanisms involving the low protein adsorption behavior of PEGylated surfaces.

2. Experimental

2.1. Materials

Commercial tetrahydrofuran (THF), 3,3-dithoxy-1-propanol (Aldrich), and L-lactide (LA) (Aldrich) were purified by conventional method [18]. Ethylene oxide (EO) (Saisan) was dried over calcium hydride and distilled.
under an argon atmosphere. Potassium naphthalene was used as a THF solution, whose concentration was determined by titration. Other reagents were used as received. Water used in this study was purified by a Milli-Q System (Nihon Millipore Co., Tokyo, Japan) to have a specific conductivity of less than 0.1 $\mu$S cm$^{-1}$.

2.2. Synthesis of acetal-PEG/PLA block copolymers

$\alpha$-Acetal-PEG/PLA was synthesized by a one-pot anionic ring-opening polymerization of EO followed by LA initiated with potassium 3,3-diethoxypropanolate (PDP) as an initiator at room temperature under argon (Scheme 1). Because the detailed procedure was described elsewhere [12,13,19], only a brief description is presented here; 1 mmol of 3,3-diethoxypropanol and 1 mmol of potassium naphthalene were added to dry THF to form PDP. After stirring, an appropriate amount of EO was added to the PDP solution. The polymerization of the EO proceeded for two days at room temperature. Potassium naphthalene was added to stabilize the living chain end. LA solution in THF $c_{\text{THF}}$ was then introduced and the mixture stirred for 120 min. The polymer was recovered by precipitation in cold isopropyl alcohol and centrifuged, followed by freeze-drying from benzene.

2.3. Polymer Characterisation

The molecular weight of the PEG segment was determined by both gel permeation chromatography (GPC) and matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI–TOF–MS) measurements at the end of EO polymerization. For GPC measurement, DMF containing 10 mmol l$^{-1}$ of lithium bromide was used as the eluent at a flow rate of 1.0 ml min$^{-1}$ at 40°C. MALDI–TOF–MS spectra were recorded using a Bruker Reflex II. 2,5-Dihydroxybenzoic acid (DHB) was used as the matrix for the ionization operated in the reflection mode. Cytochrome C was used for the calibration of the detected ions. The molecular weight of the PLA segment was determined using an $^1$H NMR spectrum by estimating the ratio of methine protons in the PLA segment and methylene protons in the PEG segment based on the number-averaged molecular weight (Mn) of PEG determined from the MALDI-TOF-MS results. $^1$H NMR spectra were obtained using chloroform-d as the solvent with a JEOL EX400 spectrometer at 400 MHz.

2.4. Silane activation of glass substrate

Prior to the silanation reaction, glass substrates (18 $\times$ 18 $\times$ 0.15 mm for the Wilhelmy plate method, 26 $\times$ 76 $\times$ 9 mm for the sessile drop method) were sequentially cleaned ultrasonically for 10 min in water, acetone, and hexane and then subjected to a Piranha etch [20] (boiling mixture of 50% (v/v) sulfuric acid and 50% (v/v) hydrogen peroxide) for 60 min and thoroughly rinsed in water. The cleaned glass plates were stored under pure water until further use. The clean plates thus obtained were left in the beaker filled with water for 1 h to allow for water absorption on the glass surface to equilibrate. The plates were then immersed into a 2% (v/v) solution of (3-(methacryloyloxy)propyl)trimethoxysilane in 95% (v/v) ethanol/water for 3 h, with the pH adjusted from 4.5 to 5.5 using acetic acid. The glass plates were thoroughly rinsed with ethanol and were dried at 160°C under high vacuum for 24 h. These glass plates were stored under vacuum until use.

2.5. Coating of silanized glass substrates with PLA followed by acetal-PEG/PLA /conversion of acetal group into aldehyde group

The film samples for dynamic contact angle measurement using the Wilhelmy plate method were prepared by a dip-coating method; silanized glass substrates were dipped into a toluene solution of the PLA homopolymers (4% (w/v)), followed by a toluene solution of the acetal-PEG/PLA (2% (w/v)). For dynamic sessile drop contact angle measurements, the film samples were prepared by successive spin coating on silanized glass substrates of 4% (w/v) PLA and 2% (w/v) acetal-PEG/PLA solutions in toluene [21]. The polymer-coated substrates were dried in a vacuum oven at room temperature for 24 h. To perform an on-surface conversion of acetal-PEG to aldehyde-PEG, the surface was immersed in aqueous media adjusted to pH2 using hydrochloric acid for 6 h.
2.6. Characterization of spin-coated samples with acetal-PEG/PLA

2.6.1. Dynamic study of wetting.

Wetting of the films by water with surface tension $\gamma$ was investigated by the Wilhelmy plate method, using a Cahn dynamic contact angle balance (DCA-315, Madison, WI) at 25°C. Successive cycles of immersion and emersion (advancing–receding) were performed employing three different rates of 33/100/264 $\mu$m/s, and the contact angle (advancing contact angle: $\theta_{\text{adv}}$; receding contact angle: $\theta_{\text{rec}}$) was deduced from the following equation:

$$F = mg + p\gamma \cos \theta - F_b$$

Table 1

| No. | Sample* | PEG Mn | PEG Mw | PEG Mw/Mn | PLA Mn |
|-----|---------|--------|--------|-----------|--------|
|     |         | GPC    | MS     | GPC       | MS     | GPC     | MS     | NMR  |
| 1   | PEG/PLA (0.65/11.0) | 685    | 650    | 770       | 720    | 1.12    | 1.10   | 11470 |
| 2   | PEG/PLA (1.8/7.0)   | 1920   | 1880   | 2110      | 1930   | 1.09    | 1.03   | 7020  |
| 3   | PEG/PLA (3.3/5.4)   | 3570   | 3340   | 3750      | 3470   | 1.05    | 1.04   | 5410  |
| 4   | PEG/PLA (5.0/4.6)   | 5100   | 5050   | 5670      | 5210   | 1.11    | 1.03   | 4640  |
| 5   | PEG/PLA (8.7/6.9)   | 8910   | 8730   | 9080      | 8810   | 1.02    | 1.01   | 6940  |

* Molecular weights (MW) of PEG/PLA segments were abbreviated as follows: PEG/PLA (0.65/11.0, 1.8/7.0, 3.3/5.4, 5.0/4.6, 8.7/6.9) where the numbers in parenthesis denote the MW $x 10^{-3}$ of the PEG segments and PLA segments in kg/mol, respectively.

Fig. 2. MALDI–TOF mass spectrum of the acetal-ended PEG (a) and its expanded spectrum in the region of 3190-3440 (b).
where $F$ is the force measured by the balance, recorded during the wetting cycle; $m$ and $p$ are the mass and the perimeters of the samples, respectively; and $g$ is the gravitational constant. The buoyancy $F_b$ was computed at each position during the accumulation of the balance.

### 2.6.2. Estimation of surface free energy

The advancing and receding contact angles were measured by the sessile drop technique [12,13] using a CA-W contact angle meter manufactured by Kyowa Kaimen Kagaku Co. Surface free energy values as the sum of dispersion, polar, and hydrogen bonding components were calculated from contact angles using the geometrical mean method according to the equation derived by Kitazaki and Hata [17]. Testing liquids were water, $n$-hexadecane, and diiodomethane.

### 3. Results and discussion

#### 3.1. Synthesis of acetal-PEG/PLA

An aldehyde group was selected as a reactive group at the PEG chain end, because the aldehyde function is very useful for the present purpose due to its stability in water and its high reactivity with primary amino groups. For the introduction of an aldehyde group at the PEG end, an acetal group was employed as a protective group (Scheme 1). When PDP is used as an initiator for anionic polymerization of EO, PEG with an acetal moiety at the $\alpha$-terminus is obtained quantitatively. Because potassium alkoxide has the ability to initiate LA polymerization, a PEG/PLA with an acetal group at the PEG chain end can be prepared. The molecular weight of each segment was controlled by changing the initial monomer/initiator ratio, resulting in the preparation of five PEG/PLA block copolymers with varying PEG lengths. One of the objectives in this study was to investigate the effect of the variation in PEG chain length on surface properties. The molecular weight data for the acetal-PEG/PLAs are summarized in Table 1. The molecular weight of the PEG segment was determined from both GPC and MALDI–TOF–MS measurements at the end of the EO polymerization. The chain end of the acetal-PEG is in the form of potassium alkoxide, which quantitatively initiates the following LA polymerization. It is essential to obtain evidence that each PEG molecule quantitatively possesses one acetal group at the $\alpha$-chain end and one hydroxyl group at the $\omega$-chain end, to obtain an acetal-PEG/PLA with the desired size and structure. The MALDI–TOF–MS analysis makes this feasible by analyzing the molecular mass of the individual polymer molecule. Fig. 2, for example, shows one of the results of MALDI–TOF–MS measurements for acetal-PEG(3.3). The numbers in parenthesis are referred to in Table 1. In the MALDI–TOF–MS analysis, only the parent ions of each polymer molecule are generally observed with no fragment signals. From the spectrum shown in Fig. 2(a), the mass of the products appears around 3500 (Mn = 3340, Mw/Mn = 1.04), which is in a good accordance with the GPC results (Mn = 3570, Mw/Mn = 1.05, see Table 1). The difference in mass of each signal was roughly estimated to be 44, indicating that the signals are assignable to the PEG homologues.

In consideration of the MW of the EO monomer and both end groups, the MW of each heterobifunctional PEG should be expressed by the following equation.

$$\text{MW}_{\text{MS}} = 44.053n(\text{EO}) + 147.194(\text{acetal}) + 1.008(\text{H})$$

(1)

The detected signals were 23 mass units larger than those calculated from Eq. (1). This is generally known as an effect of sodium ions adducts. The center peak in the expanded spectrum (Fig. 2(b)) showed a mass of 3299.0, which agreed well with 71-mers. Small signals appearing at 17 mass units higher than each large signal can be assignable to the potassium adduct, which originated from the counter ion of the initiator for the polymerization. On the basis of the MALDI–TOF–MS results, the poly(ethylene glycol) synthesized in this technique was confirmed to quantitatively possess an acetal group at one end and a hydroxyl group at the other end. Thus, the following LA polymerization is indeed initiated from the $\omega$-end of PEG having an acetal moiety at the $\alpha$-end.

The molecular weight of the PLA segment was determined using a $^1$H NMR spectrum [19] based on the Mn of PEG determined from the MALDI–TOF–MS results. ($\alpha$-acetal-PEG/PLA was then spin-coated on the PLA surface, followed by an immersion into aqueous media

| Sample         | 264 $\mu$m/s |          |          | 100 $\mu$m/s |          |          | 33 $\mu$m/s |          |          |
|----------------|--------------|----------|----------|--------------|----------|----------|-------------|----------|----------|
|                | Adv. | Rec. | Hys. | Adv. | Rec. | Hys. | Adv. | Rec. | Hys. |
| PLA            | 78.1 | 51.2 | 26.9 | 79.3 | 51.1 | 28.2 | 79.2 | 52.3 | 26.9 |
| PEG/PLA (0.65/1.10) | 79.8 | 50.0 | 29.8 | 80.1 | 51.1 | 30.0 | 80.6 | 50.1 | 30.5 |
| PEG/PLA (1.8/7.0) | 77.0 | 45.2 | 31.8 | 78.0 | 44.8 | 33.2 | 77.2 | 46.0 | 31.2 |
| PEG/PLA (3.3/5.4) | 65.9 | 30.1 | 35.8 | 64.9 | 30.9 | 34.0 | 66.3 | 31.4 | 34.9 |
| PEG/PLA (5.0/6.6) | 63.2 | 41.2 | 22.0 | 62.0 | 41.1 | 20.9 | 59.1 | 42.1 | 17.0 |
| PEG/PLA (8.7/6.9) | 58.2 | 40.1 | 18.1 | 58.5 | 41.2 | 17.3 | 57.3 | 41.2 | 16.1 |

Table 2

Water contact angle and corresponding hystereses for various polymer surfaces measured at immersion speeds of 264, 100, 33 $\mu$m/s
adjusted to pH2 using hydrochloric acid to successfully transform the acetal group at the PEG chain end to an aldehyde group. The presence as well as the reactivity of the aldehyde groups on the surface was experimentally confirmed using a model reaction with an ESR labeling agent, 4-amino-TEMPO (2, 2, 6, 6-tetramethyl-1-piperidinyloxy) [13].

3.2. Dynamic contact angle measurements

The dynamic wetting of the surfaces covered with α-acetal-PEG/PLA was estimated by a dynamic contact angle measurement at three different immersion/emersion speeds of 264/100/33 μm/s. Samples were immersed to a depth of 10 mm and then retracted. The advancing (θ_adv) and receding (θ_rec) contact angles and the corresponding hystereses for all the samples were calculated from the surface tension at zero immersion depth and are summarized in Table 2. A PLA-coated surface served as control. Coating of α-acetal-PEG/PLA on the PLA surface progressively increased its wettability with increasing PEG molecular weight, as indicated by the decreasing values in θ_adv. This is consistent with the results of static contact angle measurements, as reported in a previous paper [13]. In the Johnson and Dettre model [22], the factor θ_adv is most closely associated with the lower surface free energy component of the surface. In addition, one of the most sensitive methods that provide information on the outermost polymer surfaces of a few angstroms is the contact angle measurement [23]. The large magnitude of the θ_adv in the region of lower PEG MW may be due to the strong contribution from a hydrophobic domain on the surface, indicating incomplete coverage of the underlying hydrophobic PLA surface due to the relatively small size of the PEG chains. On the other hand, the θ_rec is most closely associated with the higher surface free energy component. Once the surface is entirely immersed in aqueous solution and one makes a receding measurement, there is a tendency for the high energy and low-angle phase to prevent the liquid from being pulled away. The high-energy regions function as pinning points to prevent the liquid from receding. As a result, a marked difference between θ_adv and θ_rec was observed. Worth noticing is that this depends on the molecular weight of PEG blocks in the copolymers. It is clear from Table 2 that the block copolymers used in this work exhibited a relatively large contact angle hysteresis on all sample surfaces. Such factors responsible for the hysteresis of a polymer include surface contamination, surface roughness, heterogeneity of the surface structure, reorientation or mobility of the surface segment, swelling, and deformation [24–27]. Because the amount of polymer on the glass substrate is very small, the variation in sample weight due to water sorption is negligible for the estimation of surface tension. The important factors in this study seem to be the heterogeneity, short time-scale molecular reorganization, and mobility of the segment of the polymer surface. The large hysteresis of the PEG/PLA samples was previously shown to cause the reorientation of hydrophilic PEG segments from a position just below the surface to the outermost surface to accommodate with aqueous phase [13]. Hydrophilic segments are turned away from the solid/air interface in the dried state, but upon immersion into an aqueous solution, they are exposed to the polymer/water interface [14]. The hysteresis increases with PEG MW and then reaches a maximum at a medium PEG chain length (PEG/PLA(3.3/5.4)), followed by an appreciable decrease. A similar trend was observed in the previous study using the sessile drop technique [13]. Comparing the dynamic wetting behavior of the PEG/PLA surfaces based on a difference in PEG MW, the most striking change is the marked decrease in the receding contact angle on the PEG/PLA(3.3/5.4) surface, causing the maximum hysteresis. This indicates that the molecular reorganization of the PEG/PLA(3.3/5.4) surface proceeds most rapidly. From the results obtained above, one can conclude that the interaction of the PEG/PLA surfaces with water provides a strong driving force to reduce the interfacial free energy by reorientation of the hydrophilic PEG component to interact optimally with the water phase. However, there is no significant dependence of immersion/emersion speed on the θ_adv and θ_rec values and the corresponding hystereses, showing almost the same values at the three speeds employed. Our previous study revealed [13] that a very rapid and distinctive relaxation in the measured contact angle with time appeared within 4.5 s on all the samples and then became almost constant. On the other hand, the time required for the present study is ca. 80 s at the shortest, and hence it cannot differentiate this fast surface reorientation. This is the reason for no significant difference in the dynamic wetting with the applied speed of immersion/emersion.

3.3. Calculation of surface/interfacial free energy and work of adhesion.

It is generally known [28] that the amount of protein adsorbed on the surface decreases with increasing hydrophilic of the substrate, i.e. surface free energy. However, numerous exceptions, which are not in line with this rule, have been found and reported. This study was performed to estimate whether the surface free energy could be correlated with the relative extent of protein adsorption on these PEG/PLA coated samples. Because the hydration or solvation of the surface PEG layer is of main importance in the wettability behavior related to protein adsorption, polar interactions including dipole and hydrogen bonding characteristics should be accurately estimated in its interaction with water. A separate estimation of the dipole (polar) interactions from the hydrogen bonding interactions may provide a novel insight into the mechanism contributing to the high wettability as well as the low protein adsorption behavior. According to Kitazaki and Hata [17], Fowkes’ equation for interfacial free energy can be
extended to an interface which includes intermolecular interactions of polar and hydrogen bonding characteristics, besides a nonpolar one. Their study shows that the surface free energy of the usual organic substances comprises of three components (nonpolar, polar, and hydrogen bonding) and thus its decrease is expressed by the sum of the geometrical means of their components. On the basis of these assumptions, we calculated the surface free energy of the PEGylated surface which includes a substantial contribution from the polar and hydrogen bonding components. In the calculation of the surface free energy, the contact angle data for three series of liquids (L), whose components are known, are used. A set of the testing liquids used for the determination of the surface free energy components of the solid has to include purely nonpolar liquids (d) such as an n-alkane and a di-n-alkylether, polar liquids (p) such as halogenated liquids and esters, and hydrogen bonding liquids (h) such as water, glycerol and formamide. The surface free energy of the solid, \( \gamma_s \), was calculated by formally extending from Fowkes' equation to the following equations:

\[
\gamma_s = \gamma_s^d + \gamma_s^p + \gamma_s^h
\]

where \( \gamma_s^d \), \( \gamma_s^p \), and \( \gamma_s^h \) are components of the surface free energy \( \gamma \) arising from the dispersion force, the polar (permanent and induced) force, and the hydrogen-bonding force, respectively. This extension of Fowkes' equation has many advantages over the extended two-component force, respectively. This extension of Fowkes' equation proposed by Owens et al. [16] and Kaelble et al. [17] have many advantages over the extended two-component force, respectively. This extension of Fowkes' equation to the following equations:

\[
\gamma_S = \gamma + \gamma_S - 2\sqrt{\gamma_d^h \gamma_S^d} - 2\sqrt{\gamma_p^h \gamma_S^p} - 2\sqrt{\gamma_h^h \gamma_S^h}
\]  

where \( \gamma_d^h \), \( \gamma_p^h \), and \( \gamma_h^h \) are components of the surface free energy \( \gamma \) arising from the dispersion force, the polar (permanent and induced) force, and the hydrogen-bonding force, respectively. This extension of Fowkes' equation has many advantages over the extended two-component force, respectively. This extension of Fowkes' equation proposed by Owens et al. [16] and Kaelble et al. [28]. It is useful, particularly, when one considers the wetting properties of biomaterials used under physiological conditions due to the crucial importance of \( \gamma_d^h \) and \( \gamma_h^h \) components under such conditions. Furthermore, combination of the geometric mean approximation (Eq. (3)) with the Young–Dupre equation (Eq. (5)) gave the work of adhesion for the solid and the liquid in contact, \( W_{SL} \), and the interfacial free energy between the solid and the liquid, \( \gamma_{SL} \) (liquid is water in the present study).

\[
W_{SL} = W^d_{SL} + W^p_{SL} + W^h_{SL} = 2\sqrt{\gamma_d^h \gamma_S^d} + 2\sqrt{\gamma_p^h \gamma_S^p} + 2\sqrt{\gamma_h^h \gamma_S^h}
\]  

(4)

\[
W_{SL} = \gamma_L + \gamma_S - \gamma_{SL} = \gamma_L(1 + \cos \theta) \quad \text{(Young–Dupre equation)}
\]  

(5)

The nonpolar, polar, and hydrogen bonding components of n-hexadecane (d), methylene iodide (p), and water (h) were calculated (Table 3) by introducing into Eq. (2) the measured values (obtained by the Wilhelmy method) of the liquid surface tension for each liquid and the values of interfacial tension for each liquid pair; n-hexadecane-methylene iodide, n-hexadecane-water, and methylene iodide-water. On introducing into Eq. (2) the values in Table 3 and values of the contact angle for these three liquids, the surface free energy components of PEG/PLA-coated surfaces were then calculated as summarized in Table 4. The results of BSA adsorption from Dulbecco PBS(−) solution on various PEG/PLA surfaces are also shown in Table 4 [13]. A portion of the data is presented in Fig. 3 where the surface properties are shown as a function of PEG MW. As shown in Fig. 3, the estimated \( \gamma_s^d \) values remain almost constant for the PEG MW of 650-8700. The \( \gamma_s \) values increased with the increase in PEG MW due to the substantial increase in \( \gamma_s^h \) values, playing a major role in the variation in \( \gamma_s \). This is in line with an increase in wettability or a decrease in contact angle values, which consequently increased the work of adhesion with water and decreased the interfacial free energy.

There are generally known trends [27] also observed on these surfaces; the total energy \( \gamma \) increases sensibly with a decrease in water contact angle as summarized in Table 2 which is closely related to the \( \gamma_s^h \) values, reflecting the increasing surface density of water-interactive Lewis (polar) sites on the polymeric substrates. Accordingly, it
is feasible to consider that the observed $\gamma_s^h$ component may arise from hydrogen bonding between the ether groups in PEG and water. Optimal C–O···H–O bonds could form at the interface of the PEG-coated layer with a hydrogen bonding test liquid, water. It is further interesting to note that the surface free energy of the PEG/PLA(3.3/5.4) surface was significantly compensated by the strong and maximum polar interactions among these samples, resulting in almost the same $\gamma_s^p$ values as those of PEG/PLA(5.0/4.6) and PEG/PLA(8.7/6.9) surfaces. Note that there is a substantial increase in the $\gamma_s^p$ values (PEG/PLA(3.3/5.4)). The minimum adsorption of BSA at the PEG/PLA(3.3/5.4) (see Table 4) may be interpreted by this maximum contribution of polar components $\gamma_s^p$ to the $\gamma_s$ values. The EO building unit in PEG with nonionic character forms a dipole, and this dipole moment depends on the PEG conformation. According to the molecular dynamics simulation of PEG chains terminally attached to the surfaces [30], the oxygen atoms prefer a gauche conformation around the C–C bond and a trans conformation is preferred around the C–O bond. This leads to a high dipole moment for the segment and consequently a strong interaction with water. Maximum $\gamma_s^p$ values at PEG/PLA(3.3/5.4) suggests the strong interaction with water molecules through the dipole–dipole interactions. On the surface of PEG/PLA(3.3/5.4), the gauche–trans–gauche conformation may dominate to induce a maximum dipole moment, allowing to achieve an extensive hydration of the PEG chain. This surface property results in a dominating steric repulsion force (osmotic and excluded volume contributions) with a least contribution of the van der Waals force due to the extensive hydration, and consequently, minimum BSA adsorption was achieved on the PEG/PLA(3.3/5.4) surface.

The difference between surface energy values calculated from $\theta_{\text{adv}}$ and $\theta_{\text{rec}}$ reflects the alteration in the state of the surface due to contact with liquids. The values of $\gamma_s$ based on $\theta_{\text{adv}}$ tend to minimize the effects from the hydrophilic character of the surface. On the other hand, the $\theta_{\text{rec}}$ values reflect mainly the hydrophilic component and are preferred for the surface characterization contacting a water environment. Once the surface is wetted by water, the contribution from the hydrophilic PEG component should be appreciably enhanced. As a result of the minimum value in $\theta_{\text{rec}}$, the maximum value of $W_{\text{SL}}$ was attained on the PEG/PLA(3.3/5.4) surface, indicating that the adhesive energy of water is maximized at this surface to form a strongly bound water film (Fig. 4). Worth noting is that this surface provides the minimum adsorption of BSA. Presumably, a strongly bound water film can be displaced only through solute–interface interactions exceeding the adhesive energy of water. Since this mechanism, surface dehydration, is energetically prohibitive, the minimum adsorption of BSA may be attained on the PEG/PLA(3.3/5.4) surface. Thus, the maximized hydration power is reasonably indicated by $W_{\text{SL}}$ calculated from $\theta_{\text{rec}}$, i.e. the value in the water phase.

4. Conclusion

An AB type block copolymer of $\alpha$-acetal-$\omega$-hydroxy-PEG/PLA composed of PEG as a hydrophilic segment and PLA as a hydrophobic segment was prepared and coated on a polylactide surface to functionalize it. Acetal groups at the free end of tethered PEG chains were converted into aldehyde groups which are available in aqueous media for conjugation of functionality compounds such as proteins via Schiff base formation. The resultant interfacial structure, composed of brush-like or diffused layers of PEG-chains, appreciably minimized protein–surface interaction. In this way, a PEG-brushed layer with a terminal aldehyde group was readily prepared which has both non-fouling and
ligand-binding properties. The effect of varying the PEG molecular weight (MW) on the surface properties was investigated from a physicochemical (dynamic wetting and surface free energy) as well as a biological (protein adsorption) point of view. The results of a dynamic wetting study suggested that PEG/PLA formed a relatively mobile interface and that the restructuring process in contact with the water phase was appreciably fast. The surface free energy of the PEGylated surface comprises intermolecular interactions of three components (nonpolar, polar, and hydrogen bonding) and thus its decrease is expressed by the sum of the geometrical means of their components. The role of these properties in protein adsorption was then discussed. Note particularly that the protein adsorption seems to be predominantly affected by the polar component ($\gamma^p$) which is significantly related to the PEG conformation on the substrate. These studies provide novel insight into the effect of PEG molecular weight on the biocompatibility of a PEGylated surface, which is expected to have a high utility as a biomaterial.

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