Formation of Ordered Microporous Films with Water as Templates from Poly(D,L-lactic-*co*-glycolic acid) Solution

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ABSTRACT: Recently a method that uses water droplets at the air–solution interface as an ordered template was reported for the preparation of ordered micrometer-size honeycomb structures. Here we show that the method can also be used for formation of honeycomb-like porous films from random copolymers with certain hydrophilicity, besides those polymers with defined structures such as block copolymers, starlike homopolymers, amd amphiphilic polymers. This demonstrates that the stabilization of water droplets is the key factor for the regular structure. Also we indicate that size and structure of the films can be regulated by such variables as concentration and atmospheric humidity. © 2003 Wiley Periodicals, Inc. J Appl Polym Sci 90: 1846–1850, 2003

Key words: poly(D,L-lactic-*co*-glycolic acid) (PLGA); films; templates; solvent casting; structure

INTRODUCTION

Macroporous materials have been of great interest recently for a wide range of applications in chemistry.[1,2] They can be used, for example, as catalytic surface and supports,[3,4] biomaterials,[5,6] and separation and absorbent media.[7,8] Ordered porous films over a wide range of pore size can be applied to optical filters,[9] linear and nonlinear optics, and chemical sensors.[10,11] There are a number of techniques that have been studied for the production of well-controlled macroporous polymer matrices, such as emulsions[12] and silica particles as templates,[13] for instance. When François et al.[14] first described their honeycomb films with monodispersed pores, in which pores existed as hexagonal arrays, their method aroused great interest. These films are produced by evaporating carbon disulfide solutions of poly(styrene-*b*-polyparaphenylene) under a flow of moist gas. Later, Srinivasarao[15] reported that the ordered structure could also be formed by evaporating a solution of simple coil-like polymer with one end terminated by a carboxylic acid group in a volatile solvent in the presence of moisture. In all these studies, attainment of such structures seemed to need a special complex architecture of the polymer. Afterward, Karthaus et al.[16] extended the concept of such water-assisted patterning to amphiphilic polyion complex, even organic–inorganic hybrids, inspired by the ability of polyion complexes to form regular three-dimensional nanoscopic structures. However, the preparation of a honeycomb structure using simple random copolymers has not been previously reported.

In the present study, by copolymerizing polylactic acid (PLA) and polyglycolic acid (PGA) of different ratios, we obtained a poly(D,L-lactic-*co*-glycolic acid) (PLGA) series with different hydrophilicity values. We then successfully prepared porous polymer films with a narrow size distribution and a regular arrangement of pores using one kind of PLGA. By adding polyethylene-*block*-poly(ethylene glycol) (PE-*block*-PEG), one kind of polymer surfactant, into the solution of the other two PLGA solutions, we also attained a honeycomb-like structure. It can be concluded that the size distribution and arrangement of pores correlate significantly with the hydrophilicity of film-formation material. We also found that the size and structure of these pores could be controlled by varying conditions during the film-formation process. These results will definitely broaden the applicability of this porous film-formation method.

EXPERIMENTAL

Copolymerization

Glycolide was synthesized by the method described by Gilding and Reed.[17] The synthesis of D,L-lactide (LA) followed the literature.[18] Both glycolide (GA) and LA were recrystallized twice before further use. Other organic and inorganic chemicals were commercially available and used without further purification.

Predetermined amounts of LA and GA were placed in a tube, to which stannous octoate was added. After
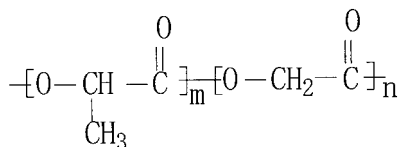
Figure 1 Chemical formula of the used copolymers.

deaeration by argon gas, the tube was sealed under vacuum, then heated to 180°C over a period of 18–20 h. The formula of the copolymer is shown in Figure 1. The composition of the polymer fraction was determined by 200-MHz proton nuclear magnetic resonance spectroscopy (NMR) in trifluoroacetic acid. Ratios of absorbances at 5.1 and 4.9 ppm were used to determine the composition. By varying the ratio of LA/GA introduced for reaction, the copolymer composition could be controlled. The 90 : 10, 70 : 30, and 50 : 50 LA/GA copolymers produced in this study were amorphous, as demonstrated by DSC thermograms.

The hydrophilicity of copolymers with different LA/GA ratios was characterized by the contact angle on a contact angle meter (FACE CA-D, Kyowa Kaimenkagaku Co.). The degree of water sorption was determined by the following procedure: after a sheet of polymer film had been immersed in deionized water for a period of 72 h, it was removed and cleared of superfluous water, then weighed (indicated as W_1). After the sample was dried under vacuum, it was again weighed (indicated as W_2). The degree of water sorption was estimated by $(W_1 - W_2)/W_2 \times 100\%$.

All the results of this series of copolymers are shown in Table I.

Film preparation and characterization

The films were prepared on cover glasses (Φ: 15 mm). Eighty microliters of copolymer–chloroform solution with different concentrations were cast onto the glass substrates in an atmosphere with controlled humidity and temperature. The surface morphology of the cast films was observed by using scanning electron microscopy (JSM-35CF; JEOL, Tokyo, Japan) and atomic
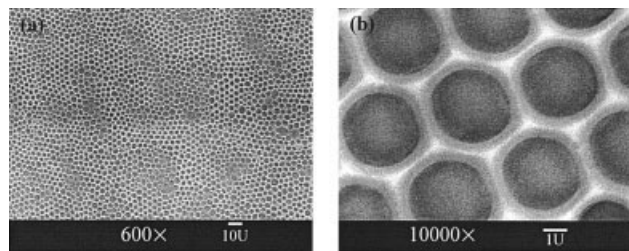

Figure 2 SEM micrograph of film surface prepared from 50 : 50 LA/GA copolymer (1.000 g/L). Atmospheric conditions: temperature, 30°C; relative humidity, 75%. Substrate temperature, 25°C.

force microscopy (AFM) with tapping mode (Nanoscope IIIa, Digital Instruments Co.).

RESULTS AND DISCUSSION

Effect of hydrophilicity

Table I shows that when the fraction of GA increases in the copolymer, the contact angle decreases with water sorption degree increasing at the same time, which means that the material becomes more hydrophilic. A typical SEM micrograph of films prepared from 50 : 50 LA/GA copolymer is presented in Figure 2(a). It can be seen that a layer of empty spherical cells with similar size makes up the surface of the film. For more detailed insight into the geometry, we display in Figure 2(b) a considerably magnified sample area from the film in Figure 2(a). It is evident that the circular holes organize upon a two-dimensional hexagonal network and the diameter of the pores amounts to about 3.5 μm.

It was recently proved by Pitois and François[19,20] and Nishikawa et al.[21] that water is indeed responsible for the regular structure where monodispersed water droplets closely pack in a hexagonal arrangement and act as a template around which the polymer assembles. The capacity of the polymer to precipitate at the solution/water interface is a key parameter in the establishment of the honeycomb morphology.

As shown in Figure 3, when the 70 : 30 and 90 : 10

TABLE I
Hydrophilicity of PLGA with Different LA/GA Ratios

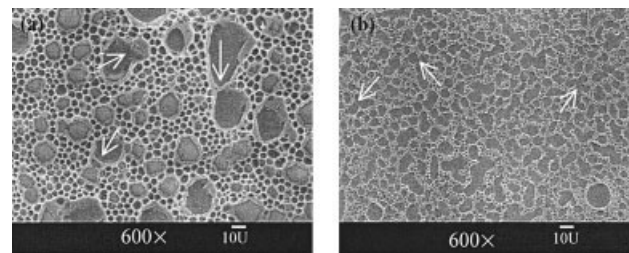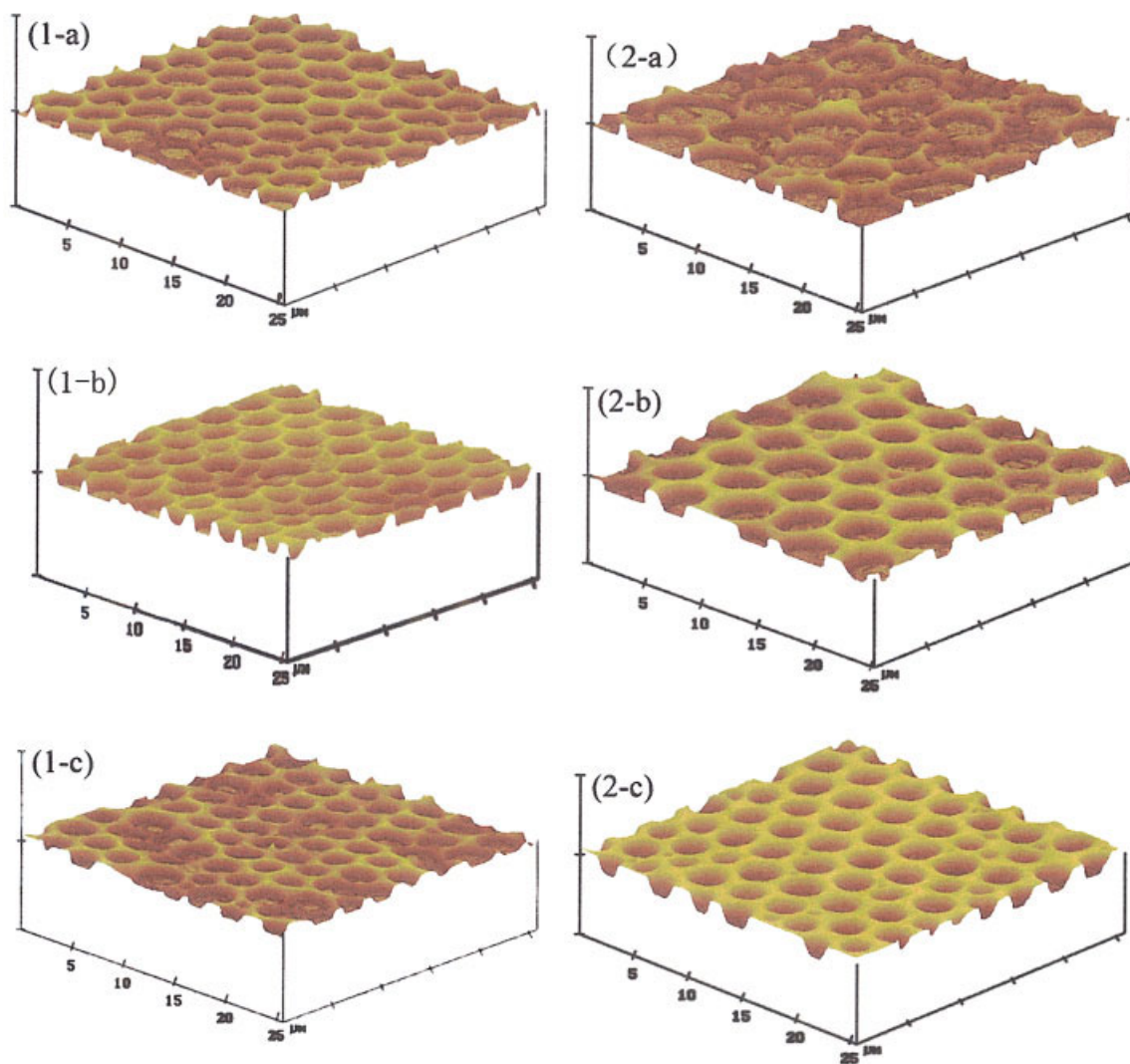|	PLGA		
	90/10	70/30	50/50
LA/GA			
Feeding dose	90/10	70/30	50/50
Product	85/15	67/33	47/53
T_g	49.1	47.4	45.8
Contact angle (°)	67	62	59
Water sorption degree	1.5	1.9	4.4

Figure 3 SEM micrograph of film surface prepared from (a) 90 : 10 and (b) 70 : 30 LA/GA copolymers (1.000 g/L). Atmospheric conditions: temperature, 30°C; relative humidity, 75%. Substrate temperature, 25°C.

Figure 4 AFM images of films prepared under different conditions from 50 : 50 LA/GA copolymer solution. Atmospheric temperature and substrate temperature are kept constant at 30 and 25°C, respectively. Relative humidity: (1) 75%, (2) 95%. Solution concentration: (a) 0.497 g/L, (b) 1.000 g/L, (c) 2.970 g/L. AFM images: X, Y, 5 μm/div; Z, 10 μm/div.

LA/GA copolymers were used for the film preparation, it was found that the films exhibited a broad pore size distribution and a disordered arrangement. Also some of the pores were greatly distorted. This clearly illustrates the traces of water droplets and fusion of some small water drops into larger ones during casting. The fusion action is indicated by those two neighboring holes sharing a sunken part of the hole wall, as marked by the arrows in Figure 3. Obviously, the fusion reflects that the initial condensed water droplets are not very stable in this case, attributed to the weak hydrophilicity of 90 : 10 and 70 : 30 LA/GA copolymers. After blending them with PE-*block*-PEG, which acts as the polymer surfactant, we attained a honeycomb-like structure under the same conditions. This could be attributed to the improvement of hydrophilicity of the membrane formation system toward condensed water droplets after adding PE-*block*-PEG.

Effect of concentration and humidity

The honeycomb film has been proved to form as follows[22]: after placing a droplet of chloroform solution on the substrate in a humid atmosphere [relative humidity (RH) > 50%], the chloroform starts to evaporate. This in turn leads to a cooling of the solution, and then the microsize water droplets condense onto the air–polymer solution interface. Polymer dissolved in the solution is absorbed to the interface between the water and the polymer solution. The presence of polymer stabilizes the water droplets and prevents their fusion. Then the water droplets are hexagonally packed by capillary flow generated in the evaporating solution. Finally, the water evaporates, leaving the observed honeycomb structure. So it can be concluded that the water vapor presented in the atmosphere and the concen-
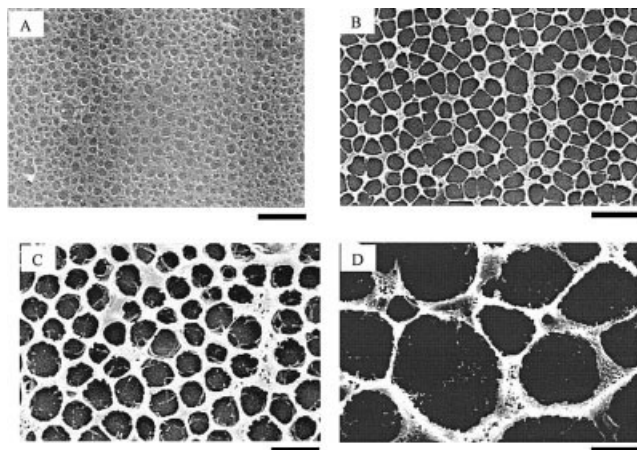
Figure 5 SEM micrographs of the surface of films obtained on substrates of different temperatures from 90 : 10 LA/GA copolymer blending with polyethylene-*block*-poly(ethylene glycol) (1 : 1) solution (concentration 1.000 g/L). Atmospheric conditions: temperature, 22°C; relative humidity, 75%. Substrate temperatures: (A) 20°C, (B) 15°C, (C) 10°C, (D) 5°C. Scale bar: 10 μm.

tration of polymer solution are two key factors influencing the pattern-formation process.

Figure 4 shows the dependency of the microporous structure on these two factors. As expected, higher humidity [Fig. 4, (1) → (2)] leads to larger pore diameters, whereas higher concentration [Fig. 4, (a) → (b) → (c)] leads to smaller pores. It is clear that when the ambient humidity is 95%RH, the change of concentration will have a more intensive effect on the pore size than at 75%RH. This is because the higher humidity not only forms larger water droplets but also slows the solvent evaporation speed at the air–solution interface, both of which favor the growth of droplets. In contrast, with increasing concentrations, the variation of the humidity will have a decreasing effect. Because water is the nonsolvent to the casting solution, It can be explained by the accelerated phase-inversion process when a higher solution concentration is used. Besides, we can see that the change of humidity and concentration can also influence the shape of the pores. When at 75%RH we changed the solution concentration from 2.97 to 0.497 g/L, we found the shape of the cells changed from circular pores to hexagonal pores. This change is the result of competition between surface tension, which favors a circular shape, and repulsion from neighbors, which leads to polygonal bubbles. Such a phenomenon was previously reported in the study of evolution of gas bubbles in lipid monolayers.[23]

Effect of substrate temperature

Because the film formation process involves the condensation of water droplets from the surrounding gas, which is initiated by a heterogeneous nucleation process on the substrate, this requires that the temperature T_s of the substrate be lower than that of the surrounding atmosphere T_r. It has been proved that the increase of the radius of droplets R per unit time t is proportional to the temperature difference $\Delta T_s = T_r - T_s$[24]:

$$dR/dt \sim \Delta T_s^{0.8}$$

In this solvent-casting method, the temperature difference is mainly caused by the rapid evaporation of solvent (a temperature of -6°C has been measured during evaporation of the solvent[25]). By adjusting the initial temperature of substrates, we found it had an important effect on the formation of the ordered macroporous structure. At 75%RH, when the temperature of substrates (25°C) was higher than the temperature (22°C) of the atmosphere, we attained a homogeneous nonporous film.

In Figure 5 we present the films formed from the solution of 90 : 10 LA/GA copolymer blending with PE-*block*-PEG on four different temperature substrates under an atmospheric temperature of 22°C and 75%RH. As displayed, the pore size of the films increased significantly with the decrease of substrate temperature. In particular, when the temperature of the substrate was kept at 20°C, the depth of the pores was much smaller than that of the other films. This suggested that at higher substrate temperature, it would be extremely difficult for the water vapor to condense onto the surface of the casting solution. The mechanism of the effect of substrate temperature on film structure is very complex, given that it will not only change the evaporation speed of solvent but also influence the interfacial character between substrate and casting solution. A more detailed understanding and description of its role is currently under investigation.

CONCLUSIONS

We successfully prepared ordered microporous films with random PLGA by a simple solvent-casting process. The ordered porous films can be seen to form using condensed water droplets as templates, which is supported by the observation of shape of the pores and the effects of atmosphere humidity, solution concentration, and substrate temperature on the pore structure. Moreover, by varying these conditions, we were able to control the size and structure of these films. Together with PLGA's excellent biocompatibility, we can expect this film to have great potential use not only for cell culture substrates but also as scaffolds for tissue engineering.

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