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Porous polylactide prepared by the delocalized crazing as a template for nanocomposite materials

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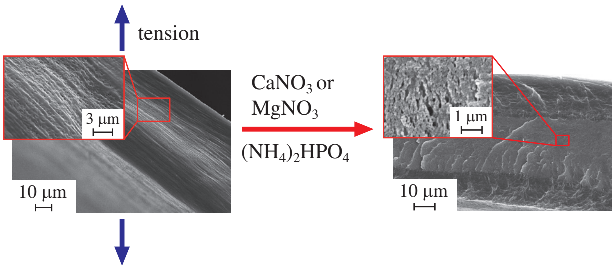
Experimental conditions have been established for the preparation of stable open-pore matrices with pore diameters of 10–20 nm on the basis of semicrystalline polylactide films by the delocalized crazing mechanism. The synthesis of phosphates of calcium (brushite) and magnesium (struvite) in the pores of such a polymer matrix allows one to tune the size of the formed crystallites, which has appeared to be about 30 nm, and to obtain nanocomposites with high dispersity of the components. The resulting nanocomposites were characterized by SAXS, SEM, TGA and XRD methods.



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The development of new 'organic matrix–mineral component' composite materials[1–4] for treating bone defects is a crucial problem in the modern regenerative medicine. An important task is the search for polymers applicable as the basis for composite materials[5] that would be nontoxic and bioactive, possess mechanical characteristics close to those of bone, and degrade at rates as close as possible to the rate of new bone tissue generation. Currently, polylactide (PLA) and its copolymers are among the most promising polymers used in the design of biomedical materials.[6–9] At the same time, there is a problem in combining incompatible hydrophilic calcium phosphates with hydrophobic PLA for the production of finely dispersed composites possessing the necessary mechanical properties.

Nowadays, there are many reports on methods for the preparation of PLA–calcium phosphate blends.[7–11] However, these approaches require to use compatibilizers,[10] *e.g.*, PLA–maleic anhydride copolymers, or to chemically modify the particle surface with L-lactide or PLA in the presence of tin compounds before the blending.[11]

As an alternative way to prepare the composites for biomedical purposes, it seems to be promising to employ a porous polymer matrix formed according to the crazing mechanism *via* the simultaneous action of tensile stress and physically active liquid media.[12] Such tension of solid polymers results in a high porosity (up to 60 vol%) with the pore diameters of 5–20 nm. Indeed, this approach was efficient for the preparation of nanocomposites based on PLA-films, deformed according to the so-called classic crazing mechanism,[13] and containing various forms of biologically active calcium phosphates (brushite, hydroxyapatite, *etc.*). The morphology of similar porous film was represented by alternating parts of a bulk polymer and crazes, *i.e.*, regions containing a finely dispersed fibrillar-porous structure loaded with the particles of calcium phosphates.[14] These nanocomposites exhibited a low cytotoxicity and facilitated the proliferation and differentiation processes of osteoblasts.[15]

The possibility of realizing another mechanism (delocalized or intercrystallite) for the crazing, which is inherent in semicrystalline polymers (*e.g.*, polyolefins),[16,17] was explored in the present work. The major condition for the realization of delocalized crazing is a microscopic structural heterogeneity of the polymer and a substantial difference in the mechanical properties of the amorphous and crystalline phases. In this case, a fibrillar-porous structure can be simultaneously formed in the intercrystallite regions throughout the sample volume. This mechanism is distinguished by the preservation of an open-pore structure in the polymer sample after the removal of liquid.[16] This feature represents a drastic difference between this and porous structures resulting from the classical crazing, which appears to be impermeable after the removal of liquid medium from the pores.

This work was aimed at the investigations of features of the mechanical behavior of semicrystalline PLA films in ethanol, the determination of conditions for the deformation development according to the delocalized crazing mechanism, and the applications of resulting porous PLA matrices as templates for the precipitation and crystallization of calcium and magnesium phosphates and for the preparation of nanocomposite materials.

Peculiarities of the mechanical behavior of semicrystalline PLA films[†] were explored in order to determine conditions for

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[†] Films of 80–85 µm thick obtained from PLA granules of the 4032D grade (M_W = 170 kDa, M_W:M_n = 1.8) by hot molding followed by fast quenching were used in the experiments. The initial amorphous polymer films were crystallized from the EtOH medium at 50 °C for 1–4 h. Mp of

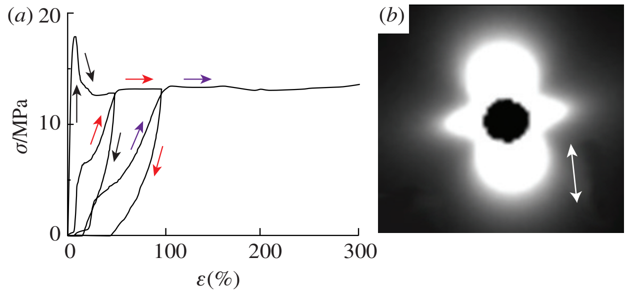

Figure 1 (*a*) Stress-strain curve for a crystalline PLA film and (*b*) SAXS pattern of the crystalline PLA film deformed by 100% in EtOH medium. Arrows indicate the stretching directions.

the development of deformation according to the delocalized crazing mechanism. Wet samples containing EtOH (9–12 wt%) were stretched. The necessary condition for the delocalized mechanism can be realized for these films, which consists in the combination of rigid crystallites possessing a modulus of several dozens of GPa and fairly soft amorphous moieties that are present in a rubberlike state with a modulus of several MPa due to the presence of EtOH that consequently reduces the glass-transition temperature of the polymer. Figure 1(*a*) shows the stress-strain curve‡ recorded for a crystalline PLA film during its uniaxial stretching in a cyclic mode of loading in EtOH at room temperature. Large reversible strains were observed upon the film shrinkage in the longitudinal direction reaching 70–80%. Therewith, the pore volume determined from the geometric sizes of the samples[18] at the strain of 100% has appeared to be nearly 40 vol%. Once the liquid medium is removed from the deformed samples under the isometric conditions, they become milk-white, while remaining permeable for liquid media and capable of being easily stained with dye solutions throughout their volume. The acquired results allowed us to assume that the uniaxial deformation of a crystalline PLA film in EtOH at room temperature proceeds according to the delocalized crazing mechanism.

Additional structural data on the porous matrix was acquired by the SAXS method.§ The scattering pattern [Figure 1(*b*)] is characteristic of polymers deformed according to the delocalized crazing mechanism. In this case, an intense wedge-shaped X-ray scattering was observed at the meridian due to the X-ray diffraction on a set of crazes. In the equatorial direction, there is a substantially less intense scattering on separate fibrils connecting craze walls. A fairly strong azimuthal smearing of the meridional reflection indicates that major axes of the crazes are not oriented strictly normally to the stretching direction. The normal to the craze surfaces is oriented in an angle range of nearly from –30 to +30° to the stretching direction. The pore width and fibril diameter determined from the curves of scattered X-ray intensity distribution[16] were about 10–20 nm. Moreover, scanning electron microscopy (SEM) data¶ has revealed that pores [Figure 2(*d*)] with submicron sizes (several hundreds of nm) are also present inside the film along with the pores resulting seemingly from the polymer frontal crystallization, which proceeds under non-equilibrium conditions from the film surface to its central part, *i.e.*, with the EtOH diffusion into the film bulk.

Thus, it has been demonstrated for the first time that the delocalized crazing mechanism can be realized upon the PLA deformation, which has a fairly high glass-transition temperature (markedly higher than the temperature in the experiment). The proposed approach allows one to obtain stable porous PLA-based matrices possessing an open nanoporous structure and to employ them as an organic matrix for the preparation of nanocomposite materials.

The counterflow diffusion method was employed to reveal the regularities for the formation of crystalline phases of Ca^{2+} and Mg^{2+} phosphates in PLA nanopores *via* an exchange reaction (see Online Supplementary Materials for details). According to this procedure, the reagents diffuse into the bulk of polymer matrix from the opposite sides and interact in a certain reaction zone, whose width and position are determined by a ratio between the rates of diffusion and chemical reaction. The morphology and phase composition of the obtained composites were studied and compared with the characteristics of powder precipitated under the same conditions. Figure 2(*b*),(*c*) shows the diffraction patterns†† for two composites containing Ca^{2+} and Mg^{2+} phosphates, while the diffraction pattern of pure crystalline polylactide is represented in Figure 2(*a*).

A comparison of the experimental reflections with the known values has revealed that brushite ($CaHPO_4{\cdot}2H_2O$) and struvite ($MgNH_4PO_4{\cdot}6H_2O$) are the major crystalline phases in the

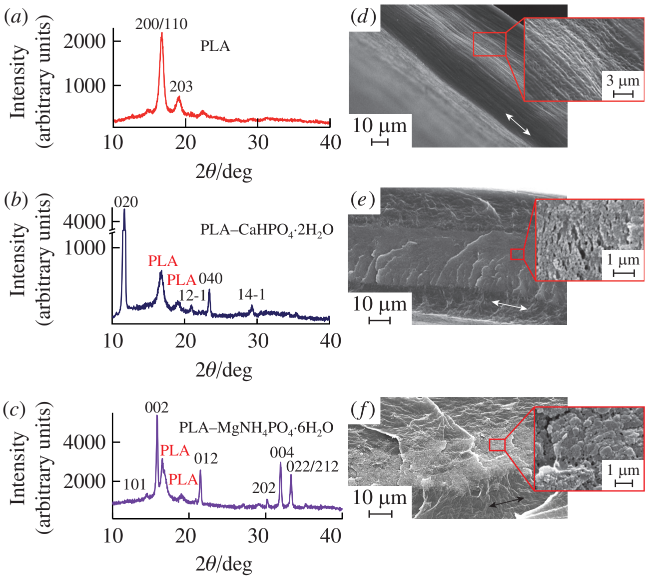

Figure 2 Diffraction patterns of (*a*) pure porous semi-crystalline PLA deformed by 100% in EtOH and its composites containing phosphates of (*b*) calcium (brushite) and (*c*) magnesium (struvite); and (*d*, *e*, *f*) their SEM micrographs, respectively. Indices [*hkl*] for the given crystalline phases are denoted at the peaks. The insets in parts (*d*), (*e*), and (*f*) show the magnified images of regions noted by the rectangles on micrographs.

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the PLA (168 °C) was determined using the DSC method, and the degree of crystallinity was 40–45%. The average size of polymer crystallites was about 11 nm according to the X-ray diffraction method.

‡ Mechanical tests of the film samples possessing the standard dog-bone shape and working part sizes of 6×20 mm were performed using an Instron 4301 tensile machine at the strain rate of 25% per 1 min and temperature of 22–24 °C in an EtOH (95%) solution under conditions of the cyclic loading.

§ The structure of polymer samples was studied at the DIKSI beamline station at the Kurchatov Centre of Synchrotron Radiation (Moscow, Russia) by the small-angle X-ray scattering (SAXS) method at the radiation wavelength of 0.16 nm and distance from a Dectris Pilatus3R 1M detector of 2.4 m. The sample exposure time was 180 s. Silver behenate was used as the reference. The pixel size in the scattering pattern was 172 µm.

¶ The SEM study was performed using an EVO 40 XPV microscope (Zeiss). Preliminarily, samples were prepared as cleavages by brittle fracture in liquid nitrogen and fastened to a microscopic stage with a carbon sticky tape. Then, a gold layer 50–70 nm thick was sputtered onto the samples using a Giko IB-3 experimental setup.

†† The phase composition of the samples was determined by X-ray diffraction analysis according to the θ–2θ procedure using a DRON3M instrument equipped with a Si(111) monochromator and a CuKα X-ray source (Ni filter) operating at $\lambda = 1.54$ Å. Reflections were assigned using the known data[19] and the MYNCRYST structural base. Crystallite sizes were calculated from the coherent-scattering region (CSR) according to the Scherrer equation.

composites.[19] The sizes of crystallites for Ca^{2+} and Mg^{2+} phosphates in a PLA film were almost the same (~30 nm) thus being markedly smaller than that in powdered samples (>100 nm).

It is known[20,21] that $CaHPO_4\cdot 2H_2O$ and $MgNH_4PO_4\cdot 6H_2O$ are stepwise transformed into the corresponding pyrophosphates ($Ca_2P_2O_7$ and $Mg_2P_2O_7$, respectively) upon heating. In addition, the PLA matrix is completely burned upon heating in air at 300–400 °C. Mass fractions of the residues remaining after heating of composites under conditions of their TGA investigation[‡‡] were 23 and 14 wt% for the Ca- and Mg-containing materials, respectively. The recalculation for initial forms of the phosphates has revealed that the initial composites contained 31 and 26 wt% of brushite and struvite, respectively.

Figure 2(*e*),(*f*) depicts SEM micrographs of the composites. As one can see, the calcium phosphate phase is localized in the central part of the polymer matrix as a rather wide layer nearly 30 μm thick. This layer consists of small spherical particles being in a close contact with each other, whose diameter is approximately 50 nm [see Figure 2(*e*)]. Magnesium phosphate phase is also localized in the bulk of polymer matrix [see Figure 2(*f*)]. The thickness of this layer is about 20 μm; however, filler particles (single satellites) have also been found outside of the layer. The layer itself consists of particles possessing different sizes, from very large aggregates (more than 500 nm in diameter) to small spherical particles (diameters of 50–150 nm). It should be noted that residual submicron pores, which were previously observed in the initial polymer matrix, have remained preserved in the obtained composites.

In conclusion, an approach has been developed for the preparation of nanocomposite film materials based on a semicrystalline polylactide film and an inorganic phase (25–30 wt%) represented by either brushite or struvite, which are bioactive precursors in the growth of bone tissue. A porous structure in the polylactide film was formed according to the delocalized crazing mechanism. It has been found that the synthesis of phosphates in the polymer matrix pores makes it possible to tune the size of their crystallites, which has appeared to be approximately 30 nm for both brushite and struvite. Therewith, the morphology of the obtained composites is determined by the structure of porous polymer matrix.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2020.03.013.

References

1 M. Okamoto and B. John, *Prog. Polym. Sci.*, 2013, **38**, 1487.
2 M. Neumann and M. Epple, *Eur. J. Trauma Emerg. Surg.*, 2006, **32**, 125.
3 Z. Kang, X. Zhang, Y. Chen, M. Y. Akram, J. Nie and X. Zhu, *Mater. Sci. Eng., C*, 2017, **70**, 1125.
4 M. A. Goldberg, V. V. Smirnov, O. S. Antonova, D. R. Khairutdinova, S. V. Smirnov, A. I. Krylov, N. S. Sergeeva, I. K. Sviridova, V. A. Kirsanova, S. A. Akhmedova, S. N. Zhevnenko and S. M. Barinov, *Mendeleev Commun.*, 2018, **28**, 329.
5 J. D. Currey, *Bones: Structure and Mechanics*, Princeton University Press, Princeton, NJ, 2002.
6 T. A. Egiazaryan, V. M. Makarov, M. V. Moskalev, D. A. Razborov and I. L. Fedushkin, *Mendeleev Commun.*, 2019, **29**, 648.
7 D. M. Zuev, E. S. Klimashina, P. V. Evdokimov, Ya. Yu. Filippov and V. I. Putlyaev, *Inorg. Mater.*, 2018, **54**, 87.
8 H. Zhou, J. G. Lawrence and S. B. Bhaduri, *Acta Biomater.*, 2012, **8**, 1999.
9 I. E. Nifant'ev, A. V. Shlyakhtin, V. V. Bagrov, P. D. Komarov, A. N. Tavtorkin, M. E. Minyaev and P. V. Ivchenko, *Mendeleev Commun.*, 2018, **28**, 412.
10 S. M. Nainar, S. Begum, Z. Hasan, M. N. M. Ansari and H. Anuar, *Regenerative Research*, 2012, **1**, 32.
11 J. Li, X. L. Lu and Y. F. Zheng, *Appl. Surf. Sci.*, 2008, **255**, 494.
12 A. L. Volynskii and N. F. Bakeev, *Surface Phenomena in the Structural and Mechanical Behaviour of Solid Polymers*, CRC Press, Boca Raton, 2016.
13 E. S. Trofimchuk, A. V. Efimov, T. E. Grokhovskaya, N. I. Nikonorova, M. A. Moskvina, N. G. Sedush, P. V. Dorovatovskii, O. A. Ivanova, E. G. Rukhlya, A. L. Volynskii and S. N. Chvalun, *ACS Appl. Mater. Interfaces*, 2017, **9**, 34325.
14 E. S. Trofimchuk, A. V. Efimov, M. A. Moskvina, O. A. Ivanova, N. I. Nikonorova, S. B. Zezin, A. V. Bakirov and A. L. Volynskii, *Polym. Sci., Ser. A*, 2018, **60**, 845 (*Vysokomol. Soedin., Ser. A.*, 2018, **60**, S3).
15 I. V. Fadeeva, E. S. Trofimchuk, M. Giretova, D. K. Mal'tsev, N. I. Nikonorova, A. S. Fomin, J. V. Rau, L. Medvecky and S. M. Barinov, *Biomed. Phys. Eng. Express*, 2015, **1**, 045011.
16 A. O. Dudnik, E. S. Trofimchuk, A. V. Efimov, N. I. Nikonorova, E. G. Rukhlya, L. N. Nikitin, I. V. Yaminsky and A. L. Volynskii, *Macromolecules*, 2018, **51**, 1129.
17 A. A. Efimova, T. E. Grokhovskaya and A. V. Efimov, *Mendeleev Commun.*, 2017, **27**, 315.
18 A. Yu. Yarysheva, D. V. Bagrov, A. V. Bakirov, L. M. Yarysheva, S. N. Chvalun and A. L. Volynskii, *Eur. Polym. J.*, 2018, **100**, 233.
19 H. E. Swanson, H. F. McMurdie, M. C. Morris and E. H. Evans, *Standard X-ray Diffraction Powder Patterns: Section 7*, UNT Digital Library, Washington, DC, 1969, p. 95.
20 E. J. Duff, *J. Appl. Chem.*, 1971, **21**, 233.
21 M. V. Ramlogan and A. A. Rouff, *J. Therm. Anal. Calorim.*, 2016, **123**, 145.

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[‡‡] The thermogravimetric analysis (TGA) was carried out using an STA 449 F3 Jupiter instrument (Netzsch, Germany) in the mode of linear heating to 700 °C in air at the rate of 10 deg min^{-1}.