Phase transitions and structural formation of PEG-PCL-PEG copolymer in the processes of fused deposition 3D printing

A Dunaev¹, A Mariyanac¹, A Mironov¹,³, O Mironova¹, V Popov¹ and M Syachina¹,²
¹Institute of Photonic Technologies, Federal Research Centre Crystallography and Photonics’, RAS, Moscow, Russia
²I.M. Sechenov First Moscow State Medical University, 8/2 Trubetskaya St., Moscow, Russian Federation.
³Author to whom any correspondence should be addressed

E-mail: scftlab@gmail.com

Abstract. In present work the analysis of thermal field distribution and thermal analysis were used to study phase and structural transformations in the block copolymer of polycaprolactone and polyethylene glycol in the process of scaffolds fabrication for tissue engineering using fused deposition modeling. It was shown that the intact polymer has a noticeable thermal history and formed degree of crystallinity which is close to its equilibrium value, while the microstructure of the polymer stays unchanged.

1. Introduction
Nowadays one of the actual task of regenerative medicine is the creation of tissue engineering constructs (TEC) using three-dimensional printing. Main concept of tissue engineering was published in 1993 [1], where one of the basic elements of TEC - artificial bioresorbable (gradually dissolving in the body) volumetric porous matrix-frames of certain sizes, shapes and internal structure where described. In general, TECs are a system consisting of living functional cells, artificial scaffolds and biologically active compounds. Currently, there are many research works is focused on different 3D printing methods adaption to create TEC, designed and targeted to repair damaged tissue. They are used for partial or complete restoration of the functions of damaged or lost tissues. The choice of material and technology for these scaffold manufacturing is determined by the set of desired physical, chemical and mechanical properties for TEC. In addition, there are very stringent requirements for scaffold materials. They should neither provoke any negative cellular response nor exhibit immunogenicity or toxicity. These materials should provide mechanical strength and stability of the TEC, both during its implantation and in subsequent processes of tissue regeneration [2-5].

Biocompatible aliphatic polyesters (polylactides, polylactoglycolides, and poly-ε-caprolactones) and its copolymers are widely used both in biomedical research and clinical practice. The physicochemical properties of these polymers allow their processing in various ways, including 3D printing via Fused Deposition Modeling (FDM) [6-8]. However, the process of fused deposition printing is able to influence the properties of the selected material. Thus, there are detailed studies of the physicochemical processes during the FDM printing is needed. The present work is devoted to the study of phase transitions and structure formation processes during fabrication of the polyethylene glycol-poly-ε-caprolactone-polyethylene glycol copolymer (PEG-PCL-PEG) scaffolds by FMD 3D
printing. This block copolymer has a number of advantages for biomedical applications in comparison with poly-ε-caprolactone alone [9-11]. PEG-PCL-PEG also has significant crystallinity, which greatly simplifies the studies using thermal analysis methods.

2. Materials and methods
The combined method including studies of the dynamics of the thermal fields distribution during the process of three-dimensional printing of polymer melt and the subsequent model study of thermal effects was applied to study phase transitions and structure formation in the process of FDM printing.

2.1. Materials
In experiments a polyethylene glycol-poly-ε-caprolactone-polyethylene glycol (PEG-PCL-PEG) block copolymer was used as a model compound. PEG-PCL-PEG with four different molecular weights (Mₙ) 10 kDa, 20 kDa, 30 kDa and 40 kDa was synthesized by the method described in [10]. In all cases, the molecular weight of the polyethylene glycol end blocks was 550 Da. The molecular weight of synthesized polymers was characterized by gel permeation chromatography (GPC) using a polystyrene standard.

2.2. 3D printing
The study of the three-dimensional printing was carried out using a specially designed 3D printer based on polymer pellet melt deposition technology (figure 1).

![Figure 1. 3D printer for thermal fields distribution analysis: 1 - main frame; 2 - positioning system; 3 - drive of the piston extruder; 4 - extruder with heater and nozzle; 5 - cooling table.](image)

The melting zone of the printer extruder is limited to a small (about 10 mm³) volume immediately before the nozzle to reduce the negative effect of prolonged thermal stress on thermo labile polyesters. The powder is fed into the melting zone in a solid state at a pressure of up to 1.5 MPa by means of a piston driven by a precision stepping motor. In order to improve the adhesion of the sample and increase the thermal contrast, the microporous steel substrate with a mass of 300 g was used as a working table of the printer.
As a test sample a hollow single-walled cylinder with a diameter of 10 mm was used during experiments. The generatrix of cylinder was printed layer by layer in the spiral way. This provided sufficient time for the transition of the polymer from melt to solid at any point of the sample.

2.3. Thermal imaging analyses

In order to study the dynamics of the thermal process distribution, a three-dimensional printer was equipped with the Flir A655sc high-speed thermal imaging camera (FLIR, Sweden) and the compact thermal imaging module Thermal Expert TE-Q1 (I3System, Taiwan, ROC). The temperature profiles of the samples which described the temperature distribution in the layers of the printed object were gained directly during the printing process in 8-14 mkm radiation wavelength range.

2.4. TGA/DSC modeling

A combined differential thermal and gravimetric analysis (TGA/DSC Linesys PT1000, Liseis, Germany) was used to model the thermal effects of phase transitions during 3D printing process. To create a temperature profile (the curve of the temperature versus time, according to which the sample is heated and cooled) the data obtained in the analysis of thermal fields by the thermal visualization method were used. The conditions of DTA analysis were chosen as close as possible to the conditions of three-dimensional printing.

2.5. Structural analyses

The microstructure of the resulting samples was examined without further processing with a Phenom Scanning Electron Microscope (Phenom, The Netherlands).

3. Results and discussion

In order to obtain modeling parameters, a thermal imaging of a real 3D printing process was used. Each temperature profile represented a curve with peaks where width increased, till the height of sample did not exceed 1 – 1.2 mm. After that a new layers cooling process was not influenced by heat transfer to substrate and their temperature profiles becomes uniformal (figure 2). For investigated PEG-PCL-PEG samples the thermal profiles were nearly similar and were not affected by polymer molecular weight. The subsequent modeling differential scanning calorimetry (DSC) and thermogravimetry (TG) experiments were performed using measured temperature curves.

Figure 2. Thermal imaging and trace during extrusion of melt of PEG-PCL-PEG copolymer (A) and single layer temperature profile (B).
The thermal analysis results (figure 3) indicate the presence of significant thermal history of the original polymer because in the process of heating-cooling, the area of the crystallization peak decreases markedly. For example, for PEG-PCL-PEG with a molecular weight $M_n = 30000$, in the first heating-cooling cycle, the heat of fusion was 88.74 J/g, while the heat of crystallization was 62.53 J/g. In the second cycle, the heat of melting and crystallization had values of 61.36 J/g and 64.20 J/g, respectively.

For all investigated samples in the temperature interval from 30°C to 200°C two cycles of heating-cooling thermogravimetry analysis did not reveal any anomaly. The obtained data show that during short-term heating, studied polymers are not subject to significant thermal degradation and do not react with atmospheric components.

Combining the data of thermal field distribution (figure 2A) and PEG-PCL-PEG DCS curve (figure 3), shows that each printed layer completely passes into a crystallized state even for a small model sample. The cooling rate of any layer is generally identical and described by exponential law, so significant differences were not found in the thermograms of individual layers. This indicates close degrees of crystallinity, but the real degree of crystallinity of the model triblock-co-polymer was not calculated, because no data were obtained about the heat of fusion of 100% crystalline phase of PEG-PCL-PEG. Also thermal field distribution shows that the following passages of the nozzle re-melting underlying layers into a depth of from 200 to 400 microns. This effect was not observed for layers lying in the immediate vicinity (up to 1 mm) from the metal substrate, which is associated with a more intense heat transfer. As a result, of experimental modeling a picture of the phase and aggregate states of the model triblock-co-polymer during the fused deposition printing process was obtained.

There is no evidence of fundamental changes in the microstructure of the PEG-PCL-PEG in depend of different molecular weight and or layers position of the formed sample. The structure of all the samples is formed by spherulites with characteristic dimensions of 20-50 mkm (figure 4), which agrees well with literature data for block copolymers based on polyesters [12].

**Figure 3.** Typical thermogram of successive heating-cooling cycles of PEG-PCL-PEG. a - first cycle (intact PEG-PCL-PEG), b-second cycle (re-crystallized PEG-PCL-PEG).
4. Conclusions
For thermo-extrusion printing with a thermal imager, the data of thermal fields dynamics were obtained, as well as on peak temperatures during the layer-by-layer creation of a three-dimensional object from the melt of a crystallizing copolymer. Based on thermal modeling data, the DTA method established that: 1) the polymer used has a significant thermal prehistory and the heat of fusion of the starting polymer is 25% higher than that of the polymer subjected to fused extrusion, whether this is a feature of the synthesis of a PEG-PCL-PEG copolymer or cold crystallization processes were not established; 2) in the heating-cooling cycles, the identity of the heat of fusion and crystallization of the polymer from cycle to cycle was manifested.

5. Acknowledgments
This work was supported by the Federal Agency of Scientific Organizations (Agreement No 007-ГЗ/Ч3363/26) in part of thermal analyses and by the Russian Foundation for Basic Research (grant №16-29-11722 ofi_m) in part of analysis of 3D printing and thermal imaging.

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