

# Polymeric Nanocubes Spontaneously Formed from Poly( $\epsilon$ -caprolactone)

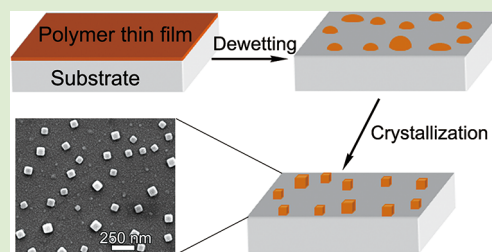
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## S Supporting Information

**ABSTRACT:** A facile and economical approach was successfully developed to prepare polymeric nanocubes from poly( $\epsilon$ -caprolactone) (PCL). Nanocubes which are rarely achieved with polymer were obtained simply by a proper thermal treatment on PCL thin film on a glass slide or silicon wafer. The results of scanning electron microscopy (SEM) and atomic force microscopy (AFM) observation showed that the nanocubes were as small as  $\sim 70$  nm with high yield (up to  $\sim 130\,000$  nanocubes in  $1\text{ cm}^2$  area). The combination of high-resolution transmission electron microscopy (HRTEM) and fast Fourier transform (FFT) demonstrated that these particles were single nanocrystals. We suggest that the formation of these nanocubes is based on a dewetting and crystallization mechanism. In addition, the size and yield of nanocubes could be controlled by the solution concentration and architecture of polymer as well as substrate. This work might not only facilitate gaining further basic knowledge about nucleation and crystalline growth mechanism of PCL but also provide a new way to fabricate nonspherical polymeric nanoparticles.

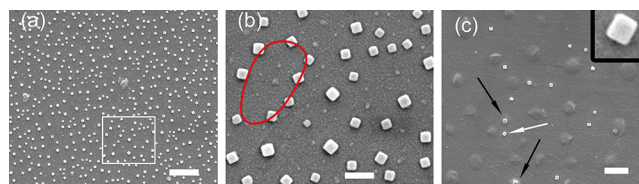


Polymeric particles with precise size and shape have been widely applied in many fields such as optical materials, drug delivery systems, and biomaterials, and so forth.<sup>1–3</sup> The shape of these particles determines their functions to a great extent. For example, the *in vivo* circulation time for polymeric nonspherical filomicelles was about 10 times longer than their analogous spherical counterparts.<sup>4</sup> Champion et al. reported another example that, instead of particles of lowest volume, rod-like PEG-based particles showed kinetically preferential cell uptake.<sup>5</sup> Noteworthy progress has been made in synthesizing inorganic and metallic nanoparticles in a variety of nonspherical shapes since the past decade.<sup>6–10</sup> However, methods for polymeric particle fabrication, especially for particles at the nanoscale are dominantly for spherical systems up to now.<sup>3,11</sup> Although the fabrication of nonspherical nanoparticles was reported using some special techniques, such as stretching of spherical particles,<sup>5,12–15</sup> particle replication in nonwetting templates (PRINT),<sup>16</sup> and nanoimprint lithography,<sup>17</sup> there is still limited success to date in preparing nanoparticles in polygonal shapes like a triangle, rectangle, and hexagon, and so forth, especially with sizes less than 100 nm. In 2007, Weber et al. reported a template-free approach to synthesize hexagonal nanoparticles from polyethylene (PE) under a very mild condition in aqueous solution.<sup>18</sup> This aroused great interest among polymer scientists as these particles are the smallest PE nanocrystal ever reported and have great potential for further understanding of polymer science and for some interesting applications as well.<sup>19</sup>

In this article, we proposed another simple strategy to fabricate polymeric cubes at nanoscale from poly( $\epsilon$ -caprolac-

tone) (PCL), a semicrystalline polyester widely used in medical field due to its excellent biodegradability and biocompatibility. The process is simply dripping polymer solution at a very dilute concentration onto a proper substrate and then heating and cooling the substrate in an appropriate manner (experimental details are described in the Supporting Information).

PCL with either a star shape (SPCL) or a linear shape (LPCL) was used to prepare nanocubes (the synthesis of PCL polymers and characterization results are shown in Table S1 and Figures S1 and S2 in the Supporting Information). The scanning electron microscope (SEM) images in Figure 1 clearly



**Figure 1.** SEM images of nanocubes formed from: (a and b) SPCL; (c) LPCL. Nanocubes were prepared by evaporating  $20\ \mu\text{L}$  of polymer solution at  $0.02\ \text{mg/mL}$  at  $100\ ^\circ\text{C}$  on a glass slide ( $0.5\ \text{cm} \times 0.5\ \text{cm}$ ) and subsequently cooling at  $0.3\ ^\circ\text{C/min}$  to room temperature ( $10\text{--}15\ ^\circ\text{C}$ ). Part b is a detailed view of the boxed region in part a. The image inset of part c is a detailed view of the nanocubes indicated by the white arrow. The scale bars are  $1\ \mu\text{m}$  for a and c and  $250\ \text{nm}$  for b.

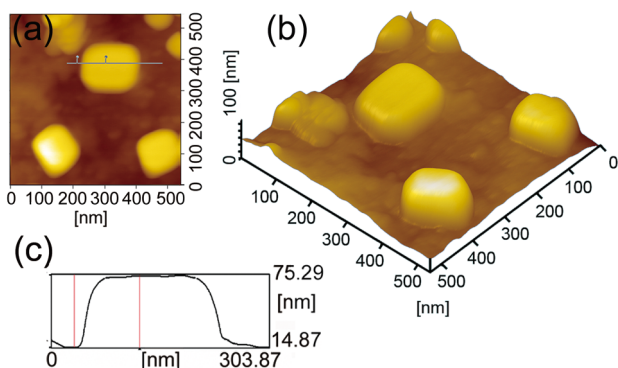
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confirmed the successful preparation and high yield of well-defined polymeric nanocubic particles based on PCL. Figure 1a,b shows the nanocubes prepared from SPCL. There are about 560 nanocubes in an area of  $7 \times 6.1 \mu\text{m}^2$  (Figure 1a), that is, about 130 000 nanocubes in  $1 \text{ cm}^2$ . The edge of the nanocubes is  $78.4 \pm 8.5 \text{ nm}$  long (calculated from 100 nanocubes). In an image of higher magnification (Figure 1b), we can see that the surfaces of the nanocubes are smooth, and their edges and corners are slightly truncated. Moreover, no nanocubes are interestingly interconnected with each other, and the nanocubes are arranged into irregular circles (e.g., red circles in Figure 1b). A similar morphology was observed when the polymer was LPCL (Figure 1c). However, the number of nanocubes formed from LPCL is evidently smaller than those from SPCL. Meanwhile, there are some noncubic droplets with diameters about 200–500 nm (Figure 1c). A transition state between the well-shaped nanocubes and the droplets could also be observed (pointed out by black arrows in Figure 1c, also shown in Figure S2 in the Supporting Information). We believe that this phenomenon sheds light on the growth process of the nanocubes. This will be discussed in detail in the latter part of this communication.

The morphology of the nanocubes was further verified by an atomic force microscope (AFM) (Figure 2). The three-

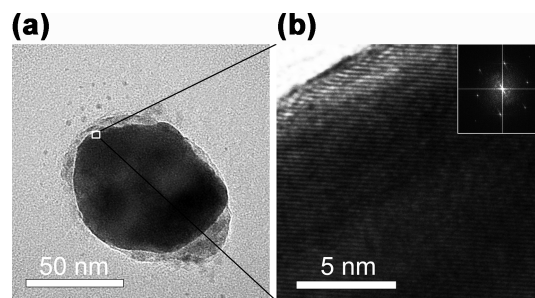


**Figure 2.** AFM images of nanocubes formed from SPCL. Nanocubes were prepared by evaporating  $20 \mu\text{L}$  of polymer solution at  $0.02 \text{ mg/mL}$  at  $100 \text{ }^\circ\text{C}$  on a glass slide ( $0.5 \text{ cm} \times 0.5 \text{ cm}$ ) and subsequently cooling at  $0.3 \text{ }^\circ\text{C/min}$  to room temperature ( $10\text{--}15 \text{ }^\circ\text{C}$ ). (a) Top view, (b) surface plot, and (c) section analysis of image a.

dimensional structure of the nanocubes can be clearly discerned from the AFM images which are consistent with the SEM images. According to the section analysis, the height of a typical nanocube is about 60 nm.

To verify that these nanoparticles in cubic shape is formed from polymer rather than inorganic or metal materials, in situ energy dispersive X-ray (EDX) characterization was performed to analyze the elements of the nanocubes. The result (Figure S3, Supporting Information) shows that there is no signal of an inorganic element other than Cu from the copper grid, which powerfully suggests that the nanocubic structure is originated from PCL polymer.

The highly symmetric shape of these nanoparticles implies that they might form by crystal growth. High-resolution transmission electron microscopy (HRTEM) was thus employed to study the structure of nanocubes. The results in Figure 3 confirmed the hypothesis: well-resolved, continuous diffraction fringes with the same orientation strongly suggested that the nanocube is a piece of single crystal. Furthermore, a

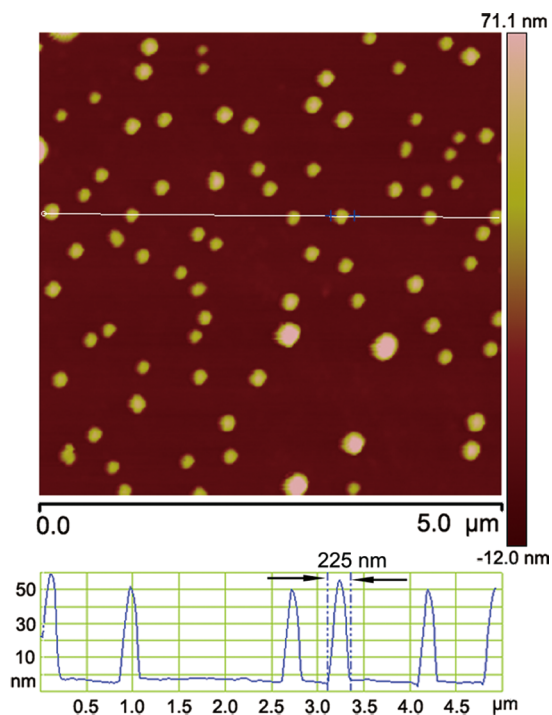


**Figure 3.** TEM images of nanocube formed from SPCL. Part b is HRTEM image of the boxed region in part a. The inset is the FFT pattern taken from part b. The three dents observed on the nanocube in part a were created by electron beam when performing HRTEM characterizations. The nanocubes prepared on the glass slide were floated onto the surface of a 5 vol % hydrofluoric acid solution and transferred to a copper grid for TEM observation.

fast Fourier transform (FFT) analysis of the HRTEM image showed a dotted pattern, in which all of the spots corresponding to the  $(hk0)$  projection of the PCL reciprocal lattice,<sup>20,21</sup> indicating the presence of flat-on lamellae. That is to say, the PCL chains orient normally to the substrate surface.

To evaluate the generality of our approach, we varied the concentration of polymer solution and substrate. The nanocubes were still successfully obtained at an increased concentration of SPCL solution at  $0.1 \text{ mg/mL}$  (Figure S4, Supporting Information). However, compared with that of nanocubes formed with a  $0.02 \text{ mg/mL}$  solution (Figure 1a), the mean size of the resulting nanocubes increases to  $310.8 \text{ nm}$ , with a standard deviation of  $63.7 \text{ nm}$  (calculated from 100 nanocubes), while the number within  $7 \times 6.1 \mu\text{m}^2$  (the same area as Figure 1a) decreases dramatically. When the concentration was further increased to  $0.5 \text{ mg/mL}$  or  $1 \text{ mg/mL}$ , no nanocubes could be observed (Figure S5, Supporting Information). A silicon wafer and carbon film were chosen to study the influences of substrates. Particles in cubic shape were also observed on a silicon wafer, although the cubes are not as perfect as those on a glass slide (Figure S6(a), Supporting Information). In contrast, no nanocube appears on a carbon film (Figure S6(b), Supporting Information).

It is intriguing that such simple treatments on PCL solution on substrates can result in segregated and well-shaped cubic nanocrystals. Figure 4 shows the morphology of particles prepared by evaporating SPCL solution at  $100 \text{ }^\circ\text{C}$  for 10 min and then quenching at room temperature ( $10\text{--}15 \text{ }^\circ\text{C}$ ). Instead of particles in a cubic shape, lots of droplets are observed. Similar to that in Figure 1, these droplets are also segregated and arranged into irregular circles. In addition, the height of these droplets is  $50\text{--}60 \text{ nm}$ , close to that of nanocubes shown in Figure 1. Based on these similarities, we believe that the nanocubes observed in Figure 1 originate from these droplets, which is in agreement with the observation of transition state between nanocubes and droplets in Figure 1c. In fact, droplets arranged in such patterns are typical results of dewetting of polymer thin films.<sup>22</sup> Dewetting is a very common phenomenon when a polymer thin film has a negative spreading parameter  $S$  on substrate. A typical dewetting process is as follows: first, the thin film ruptures via a spinodal process forming some randomly distributed holes; then the holes grow, and the removed polymer accumulates along the holes' perimeters building up rims between holes; when the holes become large enough, their rims contact each other resulting in



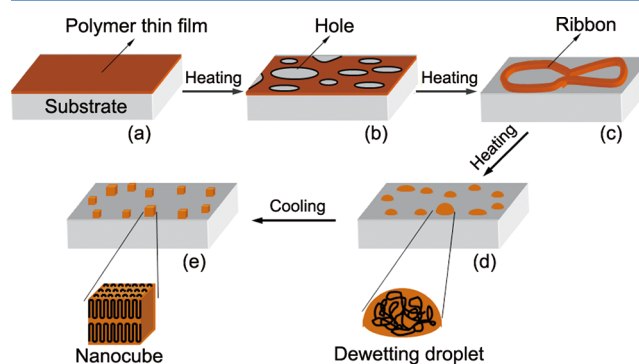
**Figure 4.** AFM image of nanoparticles formed by evaporating 20  $\mu\text{L}$  of SPCL solution at 0.02 mg/mL on glass slide at 100  $^{\circ}\text{C}$  and then quenching at room temperature (10–15  $^{\circ}\text{C}$ ).

irregular circle-shaped ribbons; these ribbons continue to decay due to Rayleigh instability and eventually create arrays of droplets which exhibit similar irregular circle-shaped arrangement and equivalent size to the ribbons.<sup>22–25</sup> Similar dewetting process was also observed in our study (see Figure S8 in the Supporting Information). Thus we suggest that the nanocubes are created through a dewetting mechanism. Based on this opinion, it is understandable that no nanocube was obtained on carbonate film (Figure S6(b), Supporting Information) or with high concentration polymer solution (Figure S5, Supporting Information), because dewetting of polymer thin film takes place only on its nonwettable surfaces, and the thickness of the film must be thin enough to allow the film rupture which initiates the dewetting process.<sup>22,23</sup>

The droplets do not transform into cubic shape until they are cooled to room temperature at a very slow cooling rate (0.3  $^{\circ}\text{C}/\text{min}$ ). This means the transformation of the droplets to the cubic nanoparticles takes place during the cooling treatment. The slow cooling rate allows crystallization of PCL polymers. In this context, the procedure of formation of the cubic nanocrystals can be divided into two stages: the heating stage where the isolated droplets form via dewetting and the cooling stage during which crystallization of the droplets takes place and consequently creates cubic nanoparticles. As we know, the first step for any crystallization is nucleation. In the case of this study, the nucleation event must have taken place within the limited volume of the segregated droplets independently.<sup>26</sup> Generally, there are two mechanisms by which nucleation occur: homogeneous and heterogeneous nucleation. The former has a high energy barrier of activation and requires a high supercooling condition,<sup>27,28</sup> which is clearly not implemented in our experiments. As the droplets are free of impurity due to the care taken in the sample preparation, and especially because the dewetting process is “self-cleaning”,<sup>26</sup> we

are confident that the nucleation in this study is not heterogeneous, either. Nevertheless, a high nucleation probability is evidently achieved in our work (as shown in Figure 1). This might be explained by an orientation effect induced by dewetting with a process called “molecular combining”.<sup>29</sup> In the process, the polymer chains were oriented by the receding air–droplet interface during dewetting, which act as a nucleus for the formation of polymer crystals. After the nucleation, the crystal growth progresses within the nucleus-containing droplets. The observation of facet-shaped nanocrystals indicates that the crystal growth follows the “nucleation-limited” mechanism,<sup>30–32</sup> in which crystal growth follows the planes of the crystal lattice.

Figure 5 presents a schematic explanation as to how the nanocubes form. At first, a homogeneous thin film of PCL



**Figure 5.** Schematic description of the possible mechanism for the formation of nanocubes on substrate.

polymer develops after the solvent in the polymer solution on substrate is vaporized (Figure 4a). When being heated above melting temperature ( $T_m$ ), the film experiences a dewetting process including film rupture, ribbon development, and droplet formation (Figure 4b–d). Afterward, crystallization occurs within the droplet when the sample is cooled very slowly, which results in the transformation of droplets to cubic particles (Figure 4e). During the crystallization process, the isolated and irregularly circle-shaped arrangement of the droplets resulting from the dewetting process is preserved.

Structure formation and crystallization of the PCL thin film have been intensively studied by several groups.<sup>33–35</sup> Depending on the concentration of the solutions for film preparation, the PCL can crystallize into spherulites, dense-branching morphology (DBM), or dendrites.<sup>33</sup> When the solution was very dilute (0.1 wt %), dispersed droplets formed on glass substrate due to dewetting of PCL thin film.<sup>31</sup> The cubic shape morphology of PCL nanoparticles, however, has not been reported yet to our best knowledge. We hope that our finding might help us to understand the crystalline behaviors of PCL polymers at a more microcosmic level. Crystallization of a polymer such as poly(ethylene oxide) and polyethylene within droplets created by dewetting of polymer thin film has been noticed by Massa et al.<sup>26,27,36</sup> However, little attention has been paid to the shape changes induced by crystallization. Xu et al.<sup>37</sup> “cloned” rectangular shaped polymer single crystals at micro- and nanoscales. The formation of such single crystal is based on “self-seeding” instead of the dewetting mechanism; accordingly, the crystal orientation and distribution are quite different from the one in our work. Polymeric nanocubes can be also formed using top–down particle nanoreplication (PRINT) method<sup>16</sup>

or nanoimprint lithography.<sup>17</sup> However, the edge geometry of particles with precise size at sub 100 nm ranges is somewhat rounded due to the resolution limit of the e-beam lithography process.<sup>17</sup> Other limitations of the existing methods are the requirement of expensive devices and a complicated process. In contrast, our approach is facile and economical because the cubic shape formation is totally spontaneous and only routine instruments are needed. Nevertheless, the generality of this approach in other crystallizable polymers such as PE, PEO, and PET, and so forth is yet to be verified. Moreover, some other interesting issues may arise from the observed phenomenon in our approach. For example, can the final shape of particles be regulated by addition of nucleation agents or by other nonwetable substrates? Relevant studies are in proceeding in our laboratory now.

In conclusion, we have developed a facile and economical approach to prepare polymeric nanocubes (as small as ~70 nm) with high yield (up to ~130 000 nanocubes in a 1 cm<sup>2</sup> area) from PCL simply by a proper thermal treatment on thin polymer film on glass slide or silicon wafer. The combination of HRTEM and FFT demonstrates that these particles are single nanocrystals. We suggest that the development of these nanocubes is based on a dewetting and crystallization mechanism. In addition, the size and yield of nanocubes could be controlled by solution concentration and the architecture of the polymer as well as substrate. Our work might not only facilitate gaining further basic knowledge about nucleation and crystalline growth mechanism of PCL but also provide a new way to fabricate nonspherical polymeric nanoparticles.

## ■ ASSOCIATED CONTENT

### Supporting Information

Experimental details, characterization of PCL, and additional SEM data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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### Notes

The authors declare no competing financial interest.

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## ■ NOTE ADDED AFTER ASAP PUBLICATION

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