

## Phase separation as the first step leading to hydrolytic degradation in PEG-containing polymers

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**Statement of Purpose:** Degradation and subsequent erosion of polymers is usually investigated following the changes in molecular weight, size, shape, surface topography and mass. Phenomenological models have been proposed to explain these observations.<sup>1</sup> But the mechanisms of degradation have not yet been investigated by comparing water-induced morphological changes across multiple length scales. Here we explore the initial effects of water penetrating into the dry polymer film by investigating the changes at nano- and meso-length scales in a model degradable polymer consisting of hydrophobic and hydrophilic segments. Hydrophobic segments are desaminotyrosyl tyrosine ethyl esters and the hydrophilic blocks are poly(ethylene glycol) (Fig. 1). The results will be used to map the evolution of hydration and erosion pathways that start from polymer-water interactions and lead to macroscopic erosion. Such studies provide the much needed fundamental insight into the degradation and erosion mechanisms of degradable implants.

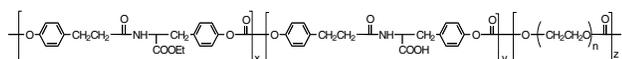


Fig. 1. Formula for the library of tyrosine-derived polycarbonates. In these terpolymers x is the mol% of desaminotyrosyl-tyrosine ethyl ester, (DTE), y is the mol% of desaminotyrosyl-tyrosine ester (DT), z is the mol% of poly(ethylene glycol) (PEG) and n is the length of the PEG block.

**Materials and Methods:** A family of poly(DTE-co-y%DT-co-z%PEG<sub>n</sub> carbonate)s shown in Fig. 1 were used (y: 0 to 50 mol%; z: 0 to 20 mol%; n: molecular weight of PEG from 1 to 35 kDa).<sup>2</sup> 200  $\mu\text{m}$ -thick compression molded flat films were used. The structure was examined using a combination of techniques including wide-angle x-ray scattering (WAXS), small-angle x-ray/neutron scattering (SAXS/SANS), and differential scanning calorimetry (DSC).<sup>3</sup>

**Results:** WAXS scans showed that the crystalline peaks of PEG that were present in the dry samples disappeared upon hydration, irrespective of their block size and crystallinity, indicating disruption of the PEG-DTE interactions and formation of PEG-water complexes. These complexes had a characteristic *d*-spacing of 3.5  $\text{\AA}$ , much different from the 4.5  $\text{\AA}$  *d*-spacing of DTE-PEG chains. These PEG-water complexes exhibited eutectic behavior, also seen in the DSC scans, which was extremely dependent on the water content.

SAXS, which is sensitive to structures at 10 nm length scales, showed that PEG at <50 wt%, even when crystalline, was uniformly distributed in the dry samples. Upon adding water, PEG segments phase separated into 10-20 nm size domains (Fig. 2a), irrespective of whether PEG was crystalline or not. The details of this hydration-induced microphase separation were investigated by simultaneous SAXS and WAXS and DSC. The state of

water, molten or frozen, rather than the  $T_g$ , was found to have a dramatic effect on the phase behavior. In most instances, phase separation developed as the ice melted.

SANS, which selectively probes the distribution of deuterated segments, was used to study the distribution of D<sub>2</sub>O (water) in these polymers. Dry polymers showed no scattering, consistent with the absence of any neutron-scattering contrast in the dry polymer. Samples with > 5 wt% water (D<sub>2</sub>O) always showed a diffraction peak, indicating that water is not uniformly distributed, but rather exists as clusters of  $\sim 100$   $\text{\AA}$  diameter domains (Fig. 2a). This is unexpected since the polymer is amorphous and the composition is expected to be homogeneous.

Effect of time and PEG content were investigated (Fig. 2b). Data show that the hydrated domains are packed closer together with increases in PEG concentration, and that the domains grow in size as the polymer degrades. Such increases in domain size will eventually lead to the formation of  $\mu\text{m}$  size erosion channels that were observed in electron micrographs..

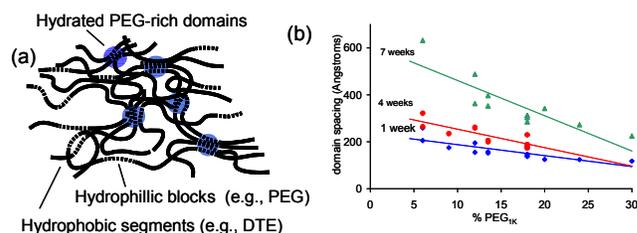


Fig 2. (a) Hydrophilic PEG segments that are uniformly distributed in the dry polymer segregate into a separate phases upon hydration. Shaded regions are the hydrated domains. (b) Changes in the spacing between the hydrated domains with time (1, 4 and 7 wks) and PEG content.

**Conclusions:** Our initial results demonstrate the utility of using multiple techniques for the investigation of structural changes that lead from initial hydration to erosion. Upon exposure to water, PEG segments phase-separate into 100-200  $\text{\AA}$  hydrated domains, and extrapolation of our initial studies suggest that these hydrated domains could evolve into erosion channels. Water mediated hydrogen-bonding rather than temperature-induced relaxation appears to bring about the observed phase behavior.

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### References:

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