

Cluster SIMS Depth Profiling in Polymeric Blends for Protein Drug Delivery Applications

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Poly(L-lactic acid) (PLLA) has shown particular promise as a biodegradable material because the degradation product, lactic acid, is readily metabolised by the body. In addition, the degradation rate can be easily controlled through variation of its relative mass. Polyethylene oxide (PEO)-containing copolymers, such as BASF's Pluronic[®] surfactants (containing polypropylene oxide (PPO) and PEO components) are also useful polymeric materials for biomaterial and pharmacological applications as they are neutral, highly biocompatible and pharmacologically inactive water-soluble polymers. The incorporation of PEO-containing copolymers into biodegradable PLLA-based drug delivery implant systems is expected to improve the interfacial biocompatibility of the polymeric devices as a result of the preferential migration of the PEO component to the surface. In addition, blend matrices of PEO and relatively hydrophobic PLLA is also expected to improve the three dimensional stability and the biological activity of water-soluble macromolecular drugs such as proteins or enzymes in the delivery systems via micelle formation. When used as drug-releasing matrices, these PLLA/Pluronic[®] blends have been proven to extend protein release and minimize the initial protein burst when compared to the pure PLLA homopolymers. The composition in the sub-surface region (10 nm -1000 nm) of these materials is highly important as it will determine the extent of initial burst release of any drugs present as well as the biocompatibility of the material. Until now, no methodology has been capable of yielding in-depth information from this region.

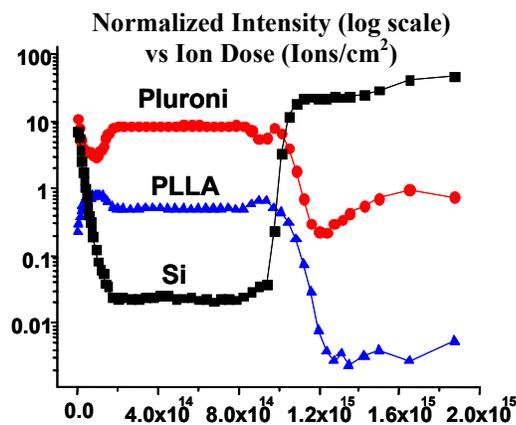


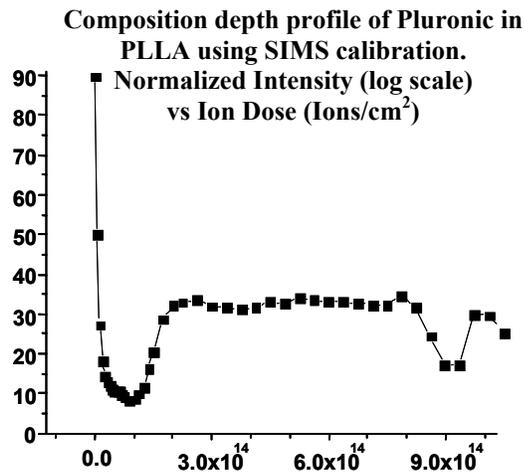
The surface chemistry as determined by both X-ray photoelectron spectroscopy (XPS) and time-of-flight secondary ion Mass spectrometry (TOF-SIMS) of these PLLA/Pluronic[®] blend materials indicates that there is an enrichment of the Pluronic[®] at the surface. However, these initial surface studies utilized monatomic primary ion beams, which cause significant subsurface damage particularly in organic and polymer samples. This increased beam-induced damage prevents the ability to obtain information as a function of depth in organic and polymer samples. Compared to conventional SIMS, "cluster SIMS" employing molecular rather than atomic primary ion beams often yields enhanced sensitivities, decreased accumulation of beam-induced damage, and increased sputter rates. These advantages have allowed us to obtain in-depth information from certain organic and polymeric materials for the first time.

The figure shows the resulting in-depth profiles obtained from a PLLA/Pluronic blend system containing a mass fraction of 25% Pluronic[®]. These profiles are consistent with a surface enrichment of Pluronic[®]-P104 surfactant, followed by a depletion zone, and then finally a constant bulk composition region. This effect was consistent over a range of concentrations (1% to 25%). Normalized signal intensities associated with Pluronic[®] ($m/z = 59$), PLLA ($m/z = 128$), and Si ($m/z = 28$) are plotted as a function of increasing SF_5^+ primary ion dose

The depth profile shown here represents the team's first successful attempt to obtain in-depth information from polymeric blend systems using SIMS.

Secondary Ion Mass Spectrometry (SIMS) methods developed at NIST provide in-depth information from polymeric blends and potentially relate the sub-surface composition to the performance characteristics in real devices.





Because of the well-behaved nature of these materials under cluster ion bombardment, we have also successfully obtained quantitative depth profiles. These results demonstrate that with cluster primary ion bombardment, we are now able to successfully monitor and quantify the preferential segregation that occurs within certain multi-component polymer blends.

The development of cluster secondary ion mass spectrometry (SIMS) for in-depth analysis of polymeric biomaterials has potential long-term impact for quality control and product development in the biomedical/pharmaceutical arenas.

Future plans include the determination of the 3-D molecular structure of these and other drug delivery systems (such as drug eluting stents and insulin delivery systems). We plan to monitor the diffusion and release of proteins and drugs from these systems using cluster SIMS technology. In addition to this, collaborations are being established with pharmaceutical and biomedical device manufacturing industries in order to relate the 3-D compositional structure to the performance characteristics in real devices.