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3-D Characterization of Biomaterials with Cluster SIMS

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Secondary Ion Mass Spectrometry (SIMS) has proven to be a useful tool in the analysis of biomaterials and drug delivery systems. With SIMS, the distribution of components in biomaterials systems can potentially be determined with a high degree of spatial resolution (<1 μm) and sensitivity (as low as ppm (μg / g)) when compared to other analytical methods such as Raman and IR spectroscopies [1]. Unfortunately, the widespread use of SIMS for imaging and depth profiling of organic constituents in drug delivery systems has been severely limited by low secondary ion yields and beam-induced damage effects that result from the use of monatomic primary ion beams, resulting in low sensitivity and precluding compositional depth profiling. One potential solution to this limitation is to use cluster or polyatomic primary ion bombardment. Cluster primary ion sources (such as SF_5^+ and C_{60}^+) have already generated considerable interest for organic SIMS analysis, where they have resulted in significant improvements (up to 1000 fold) in characteristic molecular secondary ion yields and in some cases have resulted in decreased beam-induced damage [2,3,4]. This decreased beam-induced damage coupled with an increased sputter rate has led to the ability to depth profile through some organic and polymeric materials without the characteristic rapid signal decay observed with monatomic primary ion sources [2,4].

Figure 1 illustrates an example of successful polymeric depth profiling in a model drug delivery system comprised of poly(lactic acid) (PLA) doped with 20 % (w/w) acetaminophen cast on Si. Characteristic secondary ion signals are observed from both PLA and acetaminophen as a function of increasing SF_5^+ primary ion dose (increasing depth). These characteristic secondary ion signals remain stable throughout the depth profile until the Si substrate is reached. Intensity variations in the surface and bulk regions are consistent with domain formations within the film and a surface depleted drug region. This capability can be combined with the ability to obtain secondary ion images to obtain information on the 3-D molecular structures within these films. An example of this is shown in Figure 2, which represents the surface and in-depth distribution in three component blend films of poly(L-lactic acid) (PLLA) containing Pluronic surfactant [poly(ethylene oxide) (A) poly(propylene oxide) (B) ABA block copolymer] and insulin. It can be clearly seen from this figure that there is a surface enriched P104 region. In the subsurface region, domains on the order of 40 μm – 50 μm are observed. These domains disappear shortly thereafter until after 210 s of sputtering where there is complete removal of the organic material as indicated by the intense Si signal intensity and corresponding loss in organic signals.

References

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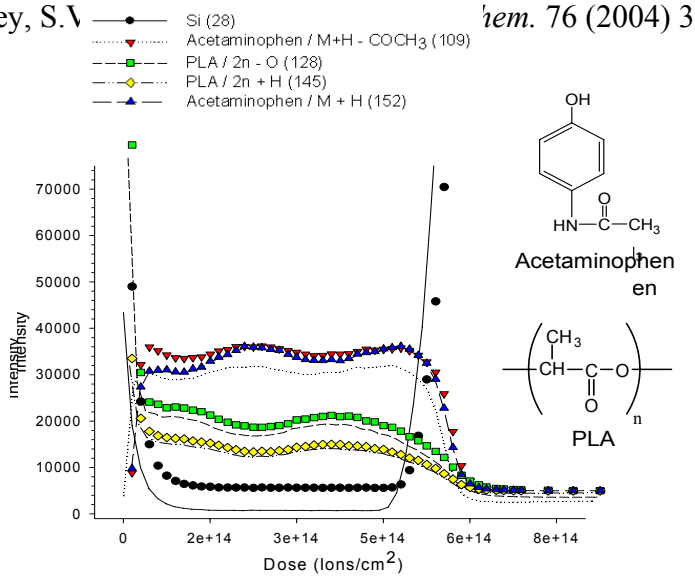

Fig 1. Secondary ion intensities plotted as a function of increasing SF_5^+ primary ion dose for PLA films (~200 nm) containing 20% (w/w) acetaminophen.

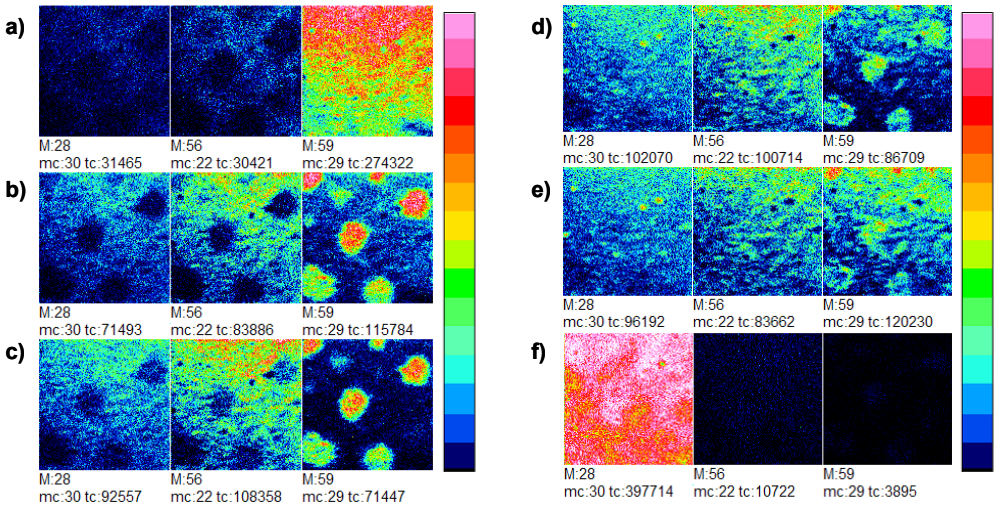

FIG. 2. Positive secondary ion images (300 µm x 300 µm) of a P104/PLLA blend film (15 % P104, w/w) containing 5 % (w/w) insulin on Si (~200 nm). a) 0 s sputtering, b) 5 s sputtering, c) 10 s sputtering, d) 20 s sputtering, e) 25 s sputtering, and f) 210 s sputtering. Sputter gun: 5 keV SF_5^+, 2 nA continuous current, 500 µm x 500 µm raster. Analysis Gun: 25 keV Ga^+ , 2 pA pulsed current, 300 um x 300 um raster. **M** denotes the mass of the ion being imaged, **mc** denotes the maximum counts per pixel in the image and **tc** denotes total counts per image. Color scale bar to the right of the images represents (0 – 30) counts.

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