Probing coating morphology and polymer-drug segregation with novel environmental SPM methodology

Greg Haugstad,[1] Klaus Wormuth[2]
[1]Characterization Facility, University of Minnesota, and [2]Surmodics, Inc.

Statement of Purpose: Formulation of drug eluting coatings remains a challenge since the coating must be thin, conformal, and mechanically stable to deformations during medical device insertion; yet the polymer matrix needs to have a chemical and nanoscale structure conducive to controlled elution of drug. Thus a nanoscopic probe that reveals not only coating morphology but also polymer phase segregation, drug distribution and mechanical behavior is of high interest. A large part of our effort in this arena has been in developing novel scanning probe microscopy (SPM) methodologies. Here we present procedures for using Digital Pulsed Force Mode SPM in a study of the morphology and properties of poly n-akyl methacrylate blend coatings incorporating the drug dexamethasone. Full force-distance cycles collected at each image pixel location, and under controlled ultimate load, relative humidity and sample temperature, allow identification of drug and polymer phases.

Methods: Poly butyl/laurel methacrylate blend coatings (PBMA/PLMA) including dexamethasone were cast or sprayed onto glass slides. Examination of individual spray microdroplets using scanning probe microscopy revealed near-surface morphologies. Differences in viscoelastic memory were examined by varying the ultimate load achieved during force-distance cycles, and further by elevating the sample temperature and/or system water content (via humidity control) under a custom, feedback-driven system to provide a range of specific environmental conditions.

Results/Discussion: Figure 1 contains representative apparent height (Z piezoscanner position to reach selected upward cantilever deflection, i.e. load) and tip-sample adhesion (pull-off force) images for two cases of ultimate load, light (top) and heavy (middle, 5x greater). Corresponding raw oscilloscope traces (cantilever deflection during one 500-µs cycle of Z ramping, left) are shown for each case of ultimate load, as acquired on identified drug-containing regions. High frequency oscillations are due to cantilever ring-down following break of contact including the preceding time cycle as well as the shown time interval. Pull-off force (adhesion) on drug is relatively small (dark) and only weakly dependent on ultimate load (small rightward shift of histogram peak, bottom graph, from blue to sharp red peak), whereas high adhesion (bright) and strong viscoelastic memory of ultimate load (large rightward shift from blue to broad red peak) is observed on the predominately PLMA polymer. Changes in apparent height from light to heavy load conditions were consistent with observed adhesion changes: regions that "lowered" under higher load are mechanical softer, and these same regions exhibit higher viscoelastic memory and tip-sample adhesion. Assignment of the different materials in this two-polymer plus drug sample was made based on control experiments on simplified samples (drug only, polymer only, one polymer plus drug) and known material properties under variable environmental conditions (temperature, humidity).

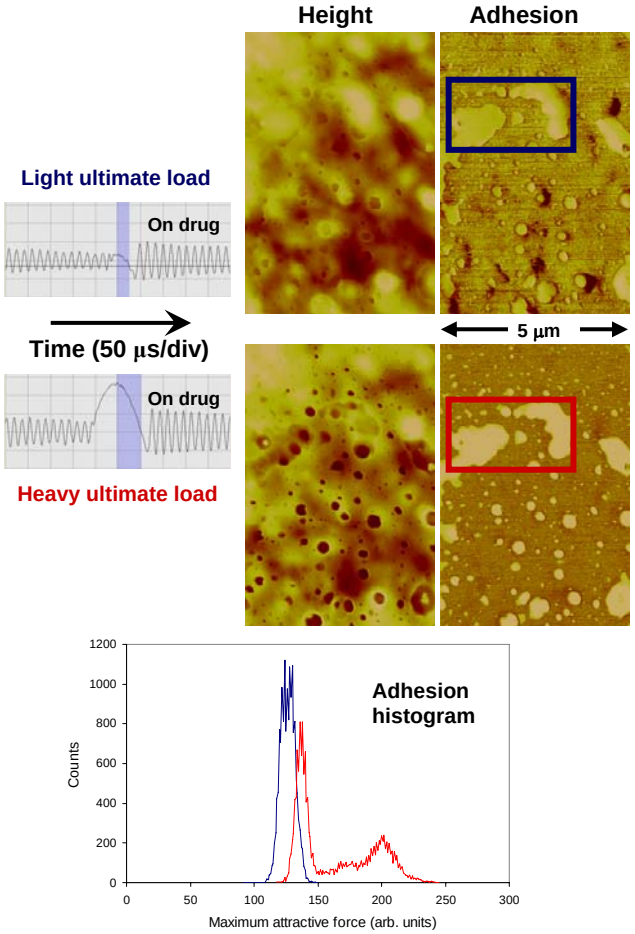

Figure 1. Load dependence of apparent height and tip-sample adhesion images with adhesion histograms from designated surface regions.

Conclusions: A combination of image types (apparent topography, adhesion, mechanical stiffness), environmental parameters (temperature, humidity) and measurement procedures (e.g., variable ultimate load) provided an understanding of component segregation in a complex polymer-blend-plus-drug coating. The ability to acquire full force-distance curves at high speed (2000 per second) enabled a detailed and elucidating examination of sample behavior at each pixel location.