Combinatorial Methods for Rapid Screening of Biomaterials

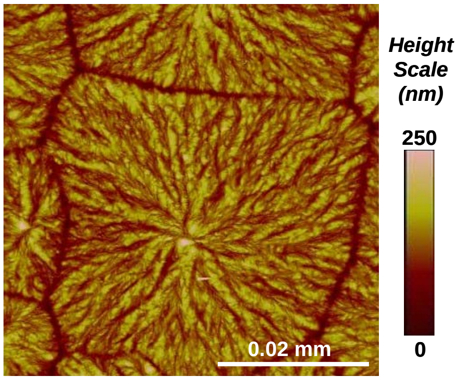
Carl G. Simon Jr.[1], Newell R. Washburn[1], Scott B. Kennedy[1], Naomi Eidelman[2], Yan Deng[3] & Eric J. Amis[1]

[1]Polymers Division, [2]American Dental Association Foundation, [3]Ceramics Division, National Institute of Standards and Technology, Gaithersburg, MD

Current methods for biomaterials development involve one-specimen-at-a-time characterization which is costly and time-consuming. Combinatorial and high-throughput methods hold the potential to enhance research and development in any field of scientific study. In the Polymers Division we are leading the way in the application of these approaches to the characterization of biomaterials. Towards this end, we have utilized gradient technology to create libraries with varying material properties focusing specifically on *surface energy, polymer crystallinity and polymer composition*.

Surface energy is a fundamental material property that affects cell interactions. This response may be through a direct cell-material interaction, but more often is an indirect effect where surface energy dictates protein adsorption which subsequently dictates cell response. To produce a gradient, an automated stage is used to move a silanized glass slide beneath a UV lamp such that the ends of the slide are exposed to the light for varying amounts of time. The differential exposure to the UV light creates a gradient in oxidation which ranges in water contact angle from 30° to 90°. Cell behaviors such as adhesion and proliferation are assessed on the gradients which provides us with a unique tool to probe the fundamental correlations between cell response and surface energy.

Polymer crystallinity: Surface topology can strongly influence the performance of tissue engineered medical products. Crystalline polymers used in biomedical applications, such as poly(ε-caprolactone) and poly(L-lactic acid), can have either rough or smooth surfaces depending on how they are processed. To make these gradients, polymer solutions are spread onto glass substrates to yield smooth, amorphous, thin films. The films are placed on a temperature gradient stage such that one end is held below the Tg at room temperature and the other end is heated above the Tg to 100 °C. This produces gradients in crystallinity along the PLLA films where the room temperature-end remains smooth and amorphous while the 100 °C-end becomes crystalline and roughened. When combined with cell culture, we have a high-throughput method for studying cell response to the surface roughness that results from polymer crystallinity.



Atomic force microscopy height image of a poly(L-lactic acid) spherulite.

Polymer Composition: Manufacturing industries have a long history of using polymer blending as an inexpensive method to create new materials with desirable properties. Blending can be used to optimize modulus, strength, morphology and crystallinity and for these reasons blending is also receiving attention from the tissue engineering community. A gradient library of two polymers is created using a three-syringe pump system and a translation stage. The library is a strip-shaped film and its composition is measured by FTIR microspectroscopy. A gradient in composition spans the long axis of the film being PLLA-rich on one end and PDLLA-rich on the opposite end. Cells are cultured on the gradients to yield a high-throughput method for screening cell response to polymer blends.

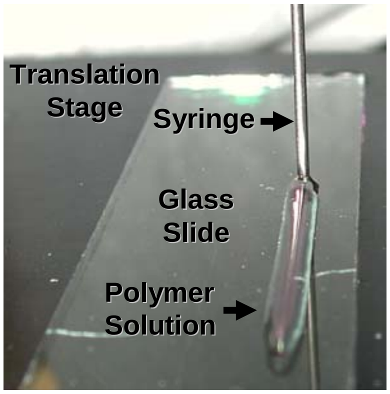


Image of a polymer solution being deposited from a syringe onto a glass substrate.

Gradients are characterized with atomic force microscopy, Fourier transform infrared microspectroscopy and contact angle. Cell functions such as adhesion, morphology, proliferation and differentiation can be evaluated across the gradients and correlated with material properties. In addition protein adsorption and conformation can be probed on the gradients. This unique array of high-throughput techniques provides a powerful platform to begin to understand the fundamental properties of cell-material interactions that are critical for the success of new biomaterials.