Self Assembly of Surface Modifying End Groups™: Overcoming Limitations of SAMs Applied to Polymeric Medical Devices

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Introduction: All surfaces or interfaces will respond to an environment by minimizing their surface free energy. This can be achieved by either reducing its surface area, adsorbing contaminants, or in the case of polymers, by presenting functional groups that reduce the interfacial energy. During the synthesis of a polymer, surface modifying end groups (SMEs) can be appended to the end of polymer chains. Hydrophobic SMEs such as PDMS, fluorocarbon, and C_{18} alkane chains will be surface active in air while hydrophilic SMEs such as PEO and PVP will be surface active in water. Such SMEs are passive in that they present a favorable surface to enhance either biostability or blood compatibility without specific binding of biomolecules. Additionally, SMEs are robust as they are covalently bound to the bulk polymer network and as demonstrated in many medical devices with SMEs in clinical use, they can survive long-term implantation. A strategy to present bioactive SMEs is to provide a reactive terminal group that would allow the coupling of bioactive molecules after the device is formed. Such appended molecules could be peptides or drugs for permanent surface modification or time release. The reactive group can be brought to the surface by using a spacer chain that would self-assemble and form a stable surface structure through hydrophobic interactions.

The SAM literature has demonstrated that bioactive chemical groups can be appended to alkane chains as a method of modifying model surfaces for *in vitro* applications. Ideally, the chemistry used during such model studies could then be applied to actual medical devices to further improve clinical outcome. However, SAM technologies are not easily transferred to medical device applications. It is much more likely that SME technology can provide robust engineered surfaces for medical devices, similar to SAMs. The purpose of this work is to study the diffusion and packing of SMEs at material surfaces and relate them to SAM formation. These results will support the engineering of more complex surface chemistry to real medical devices.

Methods: Bionate® 55D with octadecane SMEs were synthesized using continuous reaction. The concentration of SME was 0.6 wt%. Film of the SME polymer was cast from solution on a continuous web coater with HEPA filtered oven. Film samples were then exposed to various solvents to study the diffusion effects of the SME. In addition, the samples were annealed and the diffusion of the SMEs was followed with Sum Frequency Generation (SFG).

Results: SFG was performed on film samples without treatment or conditioning of the material and on annealed film samples after various solvent exposures. The results are shown in Figure 1. Peaks at 2855 (CH_2 symmetric), 2875 (CH_3 symmetric), 2935 (CH_3 Fermi resonance), and 2960 cm^{-1} (CH_3 asymmetric) are observed. The methyl peaks are from the C18 SME. The fitted peak amplitude ratio of 2875/2855 indicates the relative concentration of CH_3/CH_2 while the 2875/2960 ratio indicates the orientation of the methyl group (larger the ratio the more perpendicular the methyl group is). Annealing the sample greatly increases the C_{18} concentration and the methyl groups orient more perpendicular to the surface. When the film is soaked in ethanol and annealed, the concentration of methyl groups is slightly less than the annealed-only sample with a similar methyl orientation. Annealing the sample after soaking in hexane shows a large increase in the relative concentration of methyl groups.

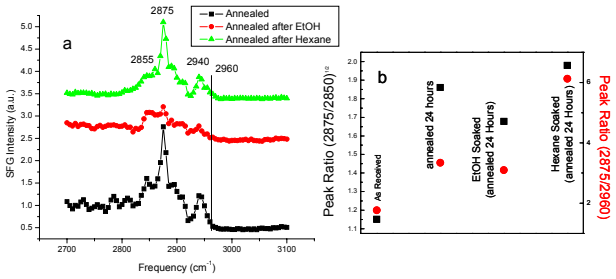

Figure 1: (a) SFG of as received, EtOH, and Hexane soaked Bionate 55D with C18 film. (b) Fitted peak ratios.

These results also indicate that as the concentration of C_{18} increases at the surface, the methyl groups orient more perpendicular to the surface. This ordering mechanism is very similar to what is observed for an octadecanethiol SAM on gold. At low concentration, the C_{18} adopts a planar orientation, but at high concentration becomes more perpendicular due to hydrophobic interaction and packing of the methylene chains.

Conclusions: SFG spectroscopy was used to monitor the diffusion and assembly of SMEs at a polymer surface. The results show that even at 0.6 wt% of C_{18} SME, the SFG spectra, and therefore the surface structure, are dominated by the terminal methyl groups. Consider that the overall concentration of the terminal methyl group is only 0.04 wt%, and yet dominates the surface chemistry. It is therefore very likely that the C_{18} chains are aligned and ordered through intermolecular hydrophobic interactions. This presents only the methyl group at the surface with adjacent methylene groups apparently adopting a centrosymmetric symmetry, thereby becoming SFG inactive. If the methylene groups were not aligned, it is likely that there would be a large signal from the methylene groups in the SFG spectra. This is also observed for alkane thiol SAMs and therefore it appears that the C_{18} SMEs order similarly to octadecane thiol SAMs. In other work we employ reactive groups at the end of alkane spacers as SMEs. The alignment of the alkane spacers as observed for C_{18} presents a means for coupling biologically relevant moieties to the surface.