Auto-Fluorescent Polymer Brushes for Glucose Detection

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Primary CNF Tools Used: E-beam Resist Spinners, JEOL 9500, Oxford 81, Zeiss Ultra SEM, Optical Microscope

Abstract:

Polymer brushes possess considerable potential for designing smart surfaces suited for a diverse range of applications, such as controlled cell adhesion, self-cleaning surfaces, and smart actuators. Introduction of luminescent properties to polymer brushes has facilitated novel characterization techniques and opened up new applications in sensing and optoelectronics. In this study, we introduce a fluorescent glucose sensing platform that utilizes auto-fluorescent copolymer brushes functionalized with phenylboronic acid (PBA). These brushes exhibit conformational changes upon binding with glucose, leading to alteration in aggregation-induced emission (AIE). An integrated process involving electron-beam lithography, surface-initiated polymerization, and post-polymerization modification was employed to create nanopatterned polymer brushes.

Summary of Research:

Smart polymeric materials that exhibit prompt feedback when exposed to external stimuli hold great potential, particularly in biomedical field. These materials find applications in drug delivery, sensing, and diagnostics [1]. Consequently, the development of smart (bio) interfaces capable of sensing and responding to changes in the local environment presents intriguing possibilities for surface-based sensing concepts [2]. Polymer brushes are highly suitable for designing adaptive and responsive interfaces due to their diverse range of functional and structural options. Notably, these thin polymeric coatings offer rapid response times while minimally affecting the physical properties of the underlying cores or substrates [3]. By integrating these systems with sensing and reporting entities, such as colorimetric or luminescent components, efficient transduction mechanisms can be achieved [4].

Previously, we demonstrated that polymer brushes built from AIE polymers can generate optical signals from pH-induced conformational changes without conventional fluorophores [5]. In this work, we extend the application of AIE polymers to design glucose responsive surfaces by combining auto-fluorescent poly(styrene-*alt*-maleic anhydride) (pSMA) copolymer brushes with boronic acid receptors. This work builds on the nanopatterning process reported earlier [6]. Preparation of boronic acid containing pSMA brushes was achieved via an integrated fabrication process of area-selective deposition of initiator, surface-initiated polymerization, and post-polymerization modification (PPM). Polymer brushes were grown from both patterned and non-patterned substrates.

E-Beam Resist Mask Preparation. E-beam resist was patterned via JEOL 9500, which was later used as the mask for the vapor deposition of silane coupling agent. Prior to the deposition, the substrate was descummed via the Oxford 81 etcher to remove residual debris in the unmasked area.

Initiator Immobilization. The vapor deposition of the silane coupling agent was carried out in a closed chamber at 1 torr and 70°C for 18 hours. The substrate was cleaned with organic solvents to remove the resist mask and then transferred into a sealed flask with a solution of azo-initiator. The immersion time was 24 hours.

Brush Synthesis and Modification. Polymer brushes were synthesized via surface-initiated radical polymerization in acetonitrile at 85°C, using equimolar amounts of styrene and maleic anhydride. PPM with 3-aminophenylboronic acid with was conducted at room temperature and the degree of functionalization was adjusted through the reaction time.

Characterization and Results:

The patterned e-beam resist was characterized using Zeiss Ultra scanning electron microscopy. Patterned

brushes, thickness and morphology of non-patterned samples were analyzed by atomic force microscopy (AFM) after each step using the Asylum Research Cypher ES (Figure 1). The fluorescence characteristics and the response of the brushes to changes in pH and glucose levels were monitored using two-photon confocal microscopy (Zeiss LSM i880) (Figure 2). Fluorescence images were scanned in λ mode from 413 to 693 nm (λex = 800 nm) and the corresponding emission spectra were generated through 64 spectral sections. Figure 3 illustrates the changes in emission intensity observed when brushes were subjected to the buffer solutions with varying glucose concentrations. An increase in glucose concentration led to a substantial change in fluorescence intensity, wherein the increase in brush height from 136 to 460 nm corresponded to 83% decrease in fluorescence intensity. The steep decline in fluorescence intensity is attributed to the hydration and highly extended conformation of the polymer chains. In this state, the intra- and interchain interactions are constrained, limiting cluster formation, and subsequently affecting the fluorescence properties.

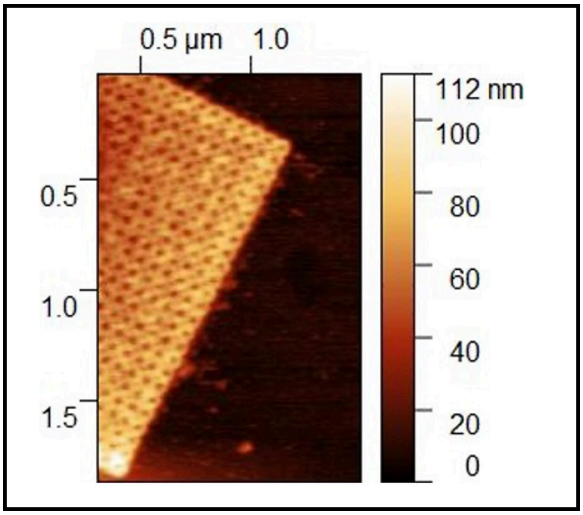

Figure 1: AFM height image of patterned pSMA brushes.

Conclusions and Future Steps:

Glucose responsive luminescent surfaces were prepared through an integrated process involving electron-beam lithography, surface-initiated polymerization, and post-polymerization modification. Utilizing auto-fluorescent polymer brushes, we have successfully demonstrated their ability to translate conformational transitions, triggered by binding events, into fluorescent readouts. Our primary objective is to optimize both sensitivity and pH parameters, thereby obtaining polymer brushes capable of operating within the physiologically relevant range.

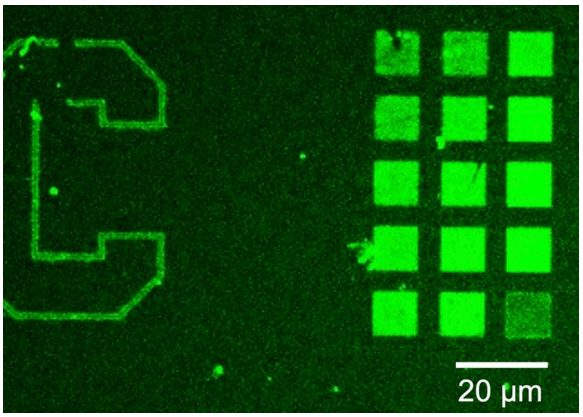

Figure 2: Confocal laser scanning microscopy images of the patterned brushes in collapsed state (pH 3).

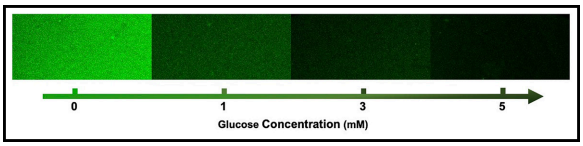

Figure 3: Confocal laser scanning microscopy images of brushes captured in solutions with varying glucose concentrations (pH 9).

References:

[1] Wei, M.; Gao, Y.; Li, X.; Serpe, M. J., Stimuli-responsive polymers and their applications. Polym Chem-Uk 2017, 8 (1), 127-143.

[2] Chen, W.-L.; Cordero, R.; Tran, H.; Ober, C. K., 50th Anniversary Perspective: Polymer Brushes: Novel Surfaces for Future Materials. Macromolecules 2017, 50 (11), 4089-4113.

[3] Li, D.; Xu, L.; Wang, J.; Gautrot, J. E., Responsive Polymer Brush Design and Emerging Applications for Nanotheranostics. Advanced Healthcare Materials 2021, 10 (5), 2000953.

[4] Poisson, J.; Hudson, Z. M., Luminescent Surface-Tethered Polymer Brush Materials. Chemistry - A European Journal 2022, 28 (32), e202200552.

[5] Aktas Eken, G.; Huang, Y.; Guo, Y.; Ober, C., Visualization of the pH Response through Autofluorescent Poly(styrene-alt-N-maleimide) Polyelectrolyte Brushes. ACS Applied Polymer Materials 2023, 5 (2), 1613-1623.

[6] Huang, Y.; Tran, H.; Ober, C. K., High-Resolution Nanopatterning of Free-Standing, Self-Supported Helical Polypeptide Rod Brushes via Electron Beam Lithography. ACS Macro Letters 2021, 10 (6), 755-759.