Multiplexed Bioreceptors NanoPatterning Using Thermal Scanning Probe Lithography

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Achieving high-resolution multiplexed chemical nanopatterns on surfaces is crucial for biomedical applications, including lab-on-a-chip systems, biosensing, tissue engineering, and cell manipulation studies.

However, technology facilitating the precise nano-assembly of different biomolecules, such as antibodies or aptamers, at specified locations on a surface remains elusive. This challenge stems from resolution limitations, the diversity of biomolecule types, specificity, and the risk of non-specific binding of analytes to unintended locations. Thermal Scanning Probe Lithography (t-SPL), a nanofabrication technique using a heated probe to locally modify material on a substrate, addresses these issues by patterning thin film surfaces with nanoscale precision to locally activate chemical reactions in a polymer or resist layer, or remove material to expose chemically activate layers underneath a resist [1, 2].

To that end, we present a versatile process, implementing t-SPL, to conjugate different biomolecular receptors, including antibodies and aptamers, to targeted patterns on the nanometer scale with a minimum pitch of 200 nanometers [3]. In our study, thin polymer films are deposited on silicon wafers by spin coating. Using t-SPL patterning, the polymer is heated to locally deprotect amine groups for desired surface functionalization, including biotin-streptavidin interactions or click-chemistry. Consecutive patterning and functionalization steps with different bioreceptors create high resolution patterns with the ability to independently detect a variety of target molecules. Furthermore, *in-situ* t-SPL topographical imaging is used to demonstrate the specificity of each bioreceptor after functionalization steps by the changing in pattern depths.

1. Albisetti, E., et al., *Thermal scanning probe lithography.* Nature Reviews Methods Primers, 2022. **2**(1).
2. Liu, X.Y., et al., *Sub-10 nm Resolution Patterning of Pockets for Enzyme Immobilization with Independent Density and Quasi-3D Topography Control.* Acs Applied Materials & Interfaces, 2019. **11**(44): p. 41780-41790.
3. Wright, A., et al. *Transistors platform for rapid and parallel detection of multiple pathogens by nanoscale-localized multiplexed biological activation (Under Review)*. 2023.