Fabrication of Metallic Nanostructure Substrate by Templated Electrodeposition for Laser Desorption/Ionization Mass Spectrometry Detection

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Surface-assisted laser desorption ionization (SALDI) is a matrix-free soft ionization technique in mass spectrometry similar to matrix-assisted laser desorption/ionization (MALDI), which uses a laser energy absorbing surface to transfer laser energy to the analyte to produce ions.[1] MALDI is a commonly used technique in mass spectrometry detection, however, there are still unavoidable disadvantages of using organic matrices. First, organic matrices generate matrix interference noise in the low molecular-weight range. The crystallization of organic matrix with analytes is also irregular in size and form, which reduces reproducibility. Third, it is time consuming to select a certain matrix and do the optimization. The SALDI method using nanostructured surfaces instead of organic matrix has been shown to have good salt tolerance, minimal background noise, and high reproducibility.[2] Small molecules including metabolites, amino acids, glucose, and drugs can be found with SALDI.

We report herein the use of metal nanopillar arrays fabricated by interference lithography and electroplating for mass spectrometry (MS)-based small molecules profiling. Figure 1 shows the fabrication flow. The photoresist is patterned with a two-beam fiber-optic interference lithography system to fabricate two-dimensional hole array nanopatterns. Patterned metal films are formed by electroplating on the patterned photoresist-covered ITO surface and transfer to the target plate as a SALDI substrate for mass spectrometry detection. Figure 2 shows the surface morphology of the patterned metal film.

We evaluated the metal pillar array assisted LDI-MS for the analysis of glucose. One microliter of glucose (1 nmol) was deposited on the metal pillar array for LDI-MS analysis. The mass spectrum is shown in Figure 3a, where the peak at m/z = 203 could be assigned to glucose. Compared to the often-used organic matrix such as 2,5-Dihydroxybenzoic acid (DHB) (Figure 3b), detection of glucose using metal pillar array largely eliminated the background interference in the m/z range of 100–450 (Figure 3a). Our method shows a promising path towards a cost-effective, mass-producible substrate platform for SALDI technique.

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[1] *H. He, Z. Guo, Y. Wen, S. Xu, and Z. Liu, Recent Advances in Nanostructure/Nanomaterial-Assisted Laser Desorption/Ionization Mass Spectrometry of Low Molecular Mass Compounds, Analytica Chimica Acta **1090**, 1 (2019).*
[2] *K. P. Law and J. R. Larkin, Recent Advances in SALDI-MS Techniques and Their Chemical and Bioanalytical Applications, Anal Bioanal Chem 399, 8 (2011).*

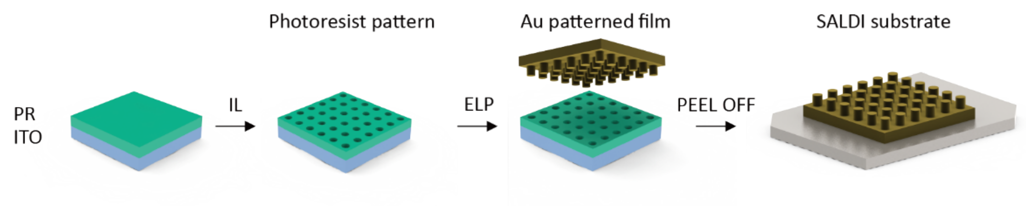

Figure 1: Fabrication flow chart of metal pillar array as the SALDI-MS substrate.

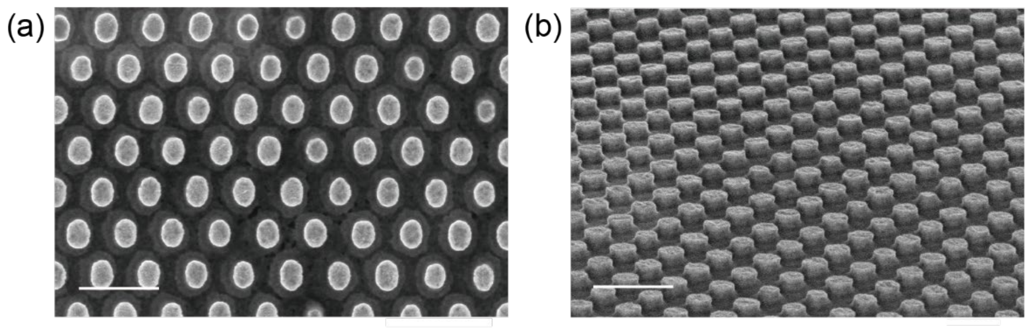

Figure 2: Scanning electron microscopic image of the metal pillar arrays film. The scale bar is 1 μm.

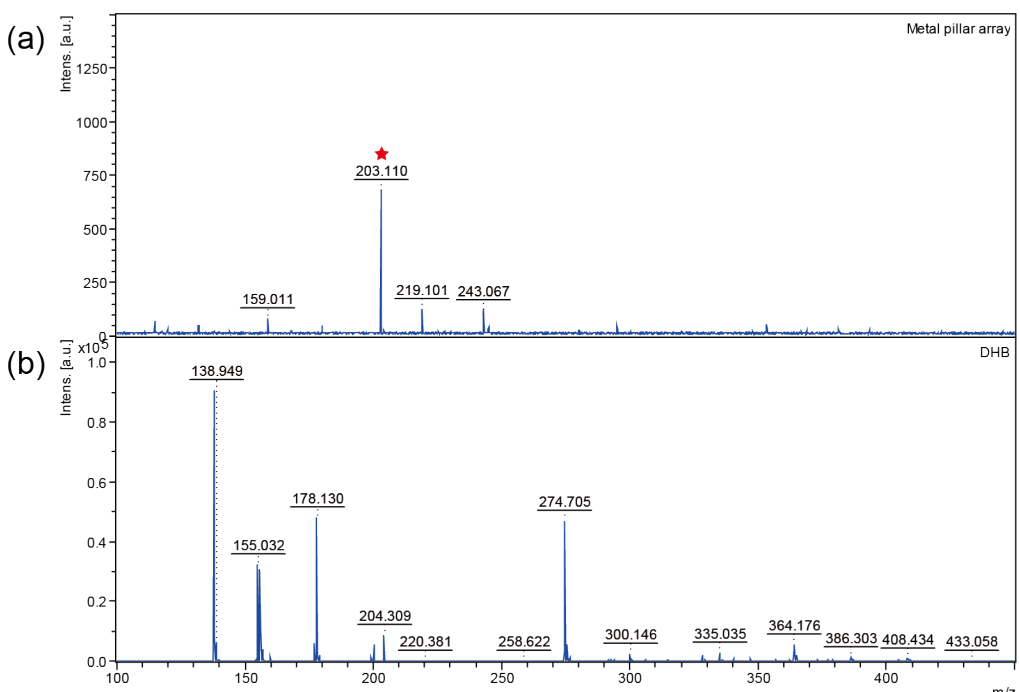

Figure 3: LDI-MS detection of (a) glucose with metal pillar film, (b) glucose with DHB.