Biologically Active Micropatterns of Biomolecules and Living Matter Using Microbubble Lithography

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Making microscopic patterns out of biomolecules (including proteins such as antigens and antibodies) can be a game-changer in rapid, low-cost diagnostics. This is because such patterning can, in principle, facilitate the development of user-friendly Rapid Antigen Test (RAT)-like kits which can detect several diseases with a single patient sample. Now, patterning biomolecules by conventional methods (photolithography, e-beam lithography, or self-assembly based methods) have limitations in efficacy for various reasons ranging from damaging the biospecimens to being slow and inflexible. In this context, Microbubble lithography (MBL) is a comparatively recent (about a decade-old, being developed at the Light Matter lab, IISER Kolkata) micro-patterning technique that uses laser-generated and manipulated microbubbles to self-assemble and pattern a large range of materials in real time. MBL has been used to pattern numerous organic and inorganic materials, allowing for various applications including the fabrication of plastic electronics, catalytic chips, and even biosensing. In this work, we have employed MBL for the first time in developing continuous patterns of a wide range of living organisms of biomolecules, including both bacterial and viral samples, at varying concentrations. Most importantly, we also performed experiments to determine the activity of the bacteria and virus post patterning – and obtained conclusive evidence of them retaining their activity. Overall, this study may open a new paradigm in designing multi-disease sensitive RAT kits, though significant work still remains to be done.

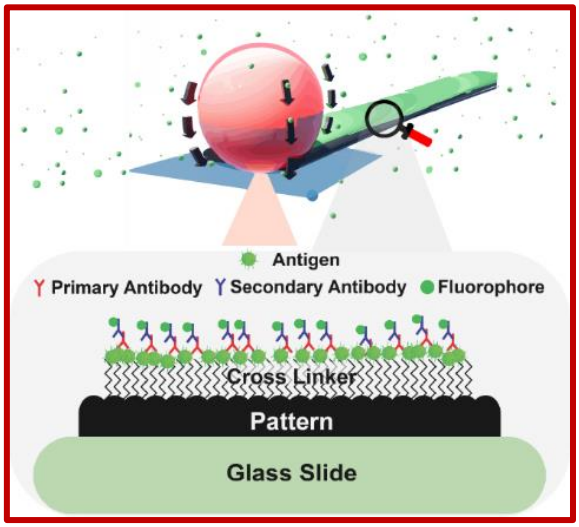

Figure: Schematic of MBL for patterning living matter – first an organic substrate is patterned on a glass cover-slip, followed by a cross-linker to enhance adhesivity of the biomolecules, after which biomolecules in the form of a primary antibody, and then a secondary antibody/antigen tagged with fluorophores is patterned. Fluorescence is observed on laser illumination, demonstrating the retention of activity of the species patterned.