

SELF-ASSEMBLED MICROARRAYS OF ATTOLITER MOLECULAR VESSELSD.Stamou¹, C.Duschl², E.Delamarche³ & H.Vogel¹¹ISB-VO, EPFL, Lausanne, Switzerland. ²Fraunhofer Institute, AMBT, Berlin, Germany.³IBM Research, Rüschlikon, Switzerland.

INTRODUCTION: We believe that combining self-assembly (SA) principles with the use of biologically important building blocks, is key to the development of functional nano-sized architectures of far greater complexity than the one attainable by “conventional” microstructuring. In this context we describe a method that allows the massively parallel isolation of attoliter experimental volumes and their self-assembled positioning with 100-nm precision in ordered arrays on surfaces.^[1]

RESULTS: The strategy employed to realize arrays of surface-immobilized single vesicles (SVs) is illustrated in Figure 1. Using high resolution micro contact printing^[2] (μ CP), we defined regions on the substrate that specifically bind vesicles and are surrounded by areas that prevent nonspecific attachment. In this manner, the positioning of vesicles and their content becomes a diffusion-limited SA process guided by the patterned surface functionalisation.

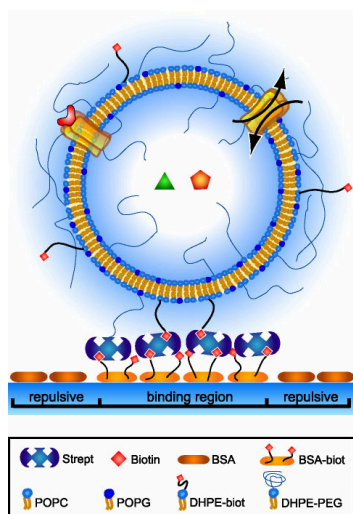


Fig. 1: Biotinylated bovine serum albumin (BSA-biot) is patterned on the surface by means of μ CP. The nonprinted regions are passivated by adsorbing BSA from solution. Streptavidin is then bound to the printed BSA-biot. Biotinylated lipids mediate the specific immobilization of vesicles. The vesicles carry charged and PEG-derivatised lipids to prevent their nonspecific interactions with the surface.

The μ CP technique allowed us to create patterns with feature sizes from a few microns down to 100 nm. These patterns were used to immobilize groups of vesicles and most importantly to isolate single individual vesicles and their content, Figure 2 A and B.

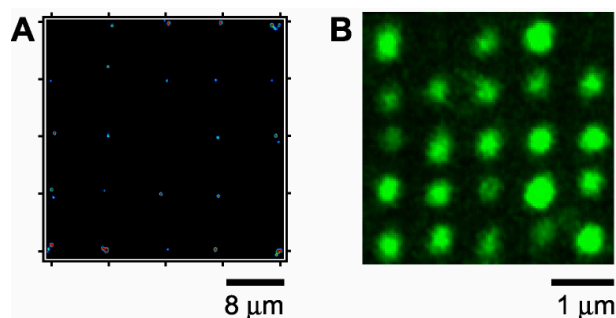


Fig. 2: Confocal fluorescence microscopy characterization of vesicles arrayed on a glass surface. Binding sites in A) and B) were $2\ \mu\text{m}$ in diameter and $100 \times 400\ \text{nm}^2$ respectively. Vesicles were labeled with 1% rhodamine-lipid in the bilayer and carboxyfluorescein in their interior.

DISCUSSION & CONCLUSIONS: In this work we combined hierarchical SA and receptor-ligand interaction first to define attoliter volumes, and then to order them on surfaces. The lipid-bilayer vesicles we used as molecular vessels are arrayed at high densities, $\sim 10^6$ per mm^2 . Nevertheless, each one maintains its cargo dissolved in a protective environment of defined chemical composition (pH, ionic strength etc.). Such ultra-small volume libraries allow simultaneous screening of (bio)chemical properties, molecular function or confined chemical reactions over millions of samples, while consuming total reagent volumes of a few picoliters.

REFERENCES: ¹D. Stamou, C. Duschl, E. Delamarche, H. Vogel, *submitted* 2003. ²J. P. Renault, A. Bernard, A. Bietsch, B. Michel, H. R. Bosshard, E. Delamarche, M. Kreiter, B. Hecht, U. P. Wild, *J. Phys. Chem. B* 2003, 107, 703.