# A HAND-HELD DEVICE TO COPY DNA TO PROTEIN MICROARRAYS

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## ABSTRACT

The DNA Array to Protein Array (DAPA) system presented in 2008 by He et al. [1,2] allows to replicate protein microarrays from one master DNA microarray by cell-free expression and diffusion. We improved the basic idea by designing a hand-held microfluidic device replacing the porous membrane used in [1,2] by a microfluidic gap of ~50 µm in height. Hence any mechanical damage inflicted by the membrane is prevented as only the cell free system is in physical contact with the microarrays. The capillary priming of the microfluidic gap leads to a defined protein expression start. Protein translation and microarray formation only needs 30 minutes at 25 °C, the amount of cell free system needed is reduced significantly. The DNA master array can be re-used for multiple protein expressions.

**KEY WORDS:** protein microarray, microfluidics, cell-free protein expression

## INTRODUCTION

In order to further simplify the generation of protein microarrays and to increase the accuracy of the protein expression process itself we modified the DAPA system (fig. 1). The DAPA system as originally described is rather undefined (fig. 2). First the membrane soaked with cell-free translation system itself is non-woven fiber material and therefore undefined in structure isotropy and biased to thickness tolerances. Second the protein expression is immediately starting after putting the membrane in contact with the DNA array. This happens whilst the DAPA system assembly and therefore is in principle undefined. With our microfluidic system a defined distance between the DNA master array and the protein capture surface by a precise spacer (fig. 3) is guaranteed. The point of time for starting the protein expression is simply given by priming the cell-free translation system. There is no inhomogenous diffusion caused by the membranes pore structures, nor any risk of contamination or inhibition by substances of the membrane or violation of the slide surfaces by physical contact of the membrane to the arrays.

## EXPERIMENTAL RESULTS

First protein microarrays were produced with microfluidic gaps of ~80 µm in height realized by laser-cutting polyester adhesive foils (fig. 4 A+B) or spin-coated, laser-cut and vacuum-transferred PDMS layers (fig. 4 C). The DNA master array is produced by spotting PCR-amplified DNA featuring an amino linker onto an epoxy coated PMMA or glass slide. The protein microarray slide is Ni-NTA coated to capture $(His)_6$-tagged proteins. Analysing the result of the protein expression with this setup reveals deficiencies such as intrusion of air bubbles and fluid loss by leaks [3]. Further a certain violation of the integrity of the epoxy coating by the self-adhesive polyester foil and the laser-cutting process was observed. Therefore we modified the system by changing the design of the incubation chamber. We incorporated the sealing edge into a PDMS body as DNA microarray slide (Fig. 5+6) allowing various 3-dimensional moulded structures. We got a significantly better air and water tightness of the seal and no inhibitory effects on neither DNA spotting nor protein expression. A simple hand-held clamping both the DNA spotted PDMS slide and the Ni-NTA coated protein slide (fig. 7) lead to promising protein microarrays in less than 30 minutes at room temperature (fig. 8).

## CONCLUSION

We presented a membrane free hand-held DNA to protein translation device that circumvents the original membrane and thus improves the DAPA-system. Each of the different layouts under study replaces the membrane by a microfluidic gap and allows the defined priming and therefore starting of the protein expression. This avoids effects of membrane irregularity, allows a better and more defined expression of proteins and avoids any physical damage of either the DNA or the protein microarray.

## OUTLOOK

Ongoing optimisations of the hand-held devices will further ease the handling of this manual process for rapid generation of protein arrays and aim to increase the spot density of the microarray. Finally a simple disposable hand-held for daily laboratory routine is aimed to be developed.

## ACKNOWLEDGEMENT

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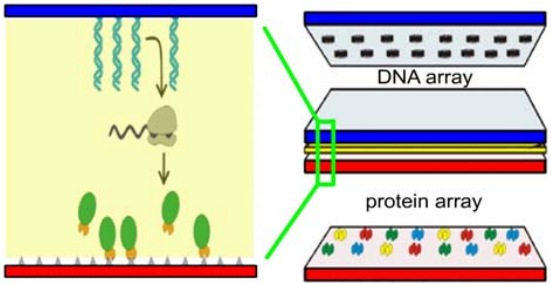


*Fig.1: DNA array to protein array (DAPA) system*

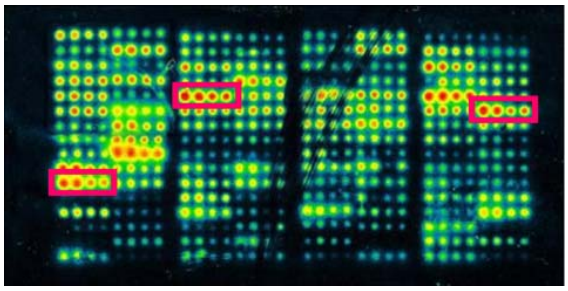

*Fig.2: DAPA expressions- significant inhomogenities*

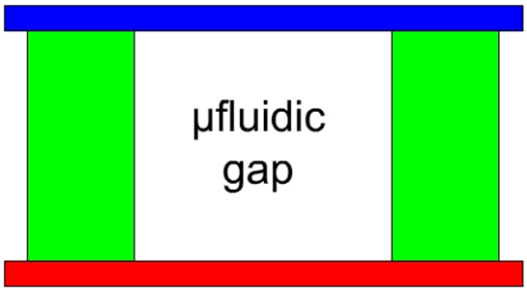


*Fig.3:Schematic of microfluidic gap with spacer*

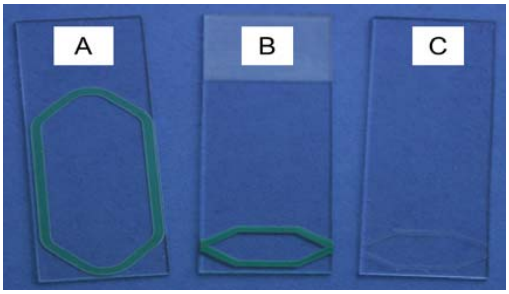


*Fig.4:Spacer of polyester foil-(A+B) / PDMS (C)*

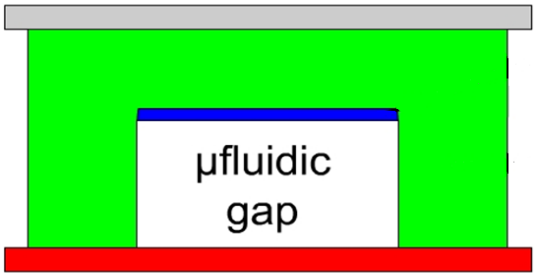


*Figure 5: Schematic of microfluidic gap with PDMS slide*

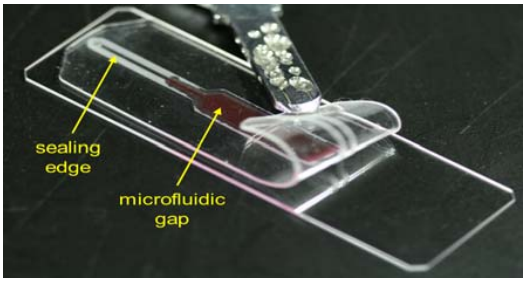


*Figure 6:Priming experiment with PDMS slide*

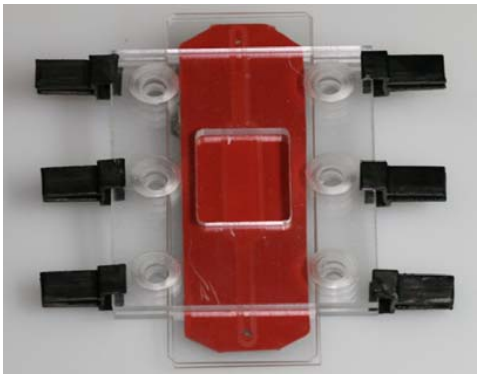

*Figure 7:Hand-held for PDMS slide*

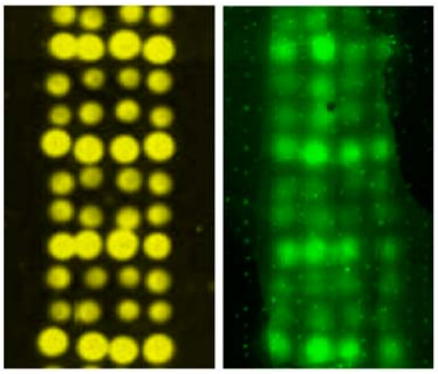

*Figure 8:DNA (left) and protein (right) array*

## REFERENCES

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