INTRODUCTION

The recent emergence of nanoarrays and ultramicro arrays as novel assay formats for small sample volumes has enabled a vast number of new applications. Some of these applications rely upon conventional far-field optical detection methods, while others employ techniques such as atomic force microscopy (AFM), near-field scanning optical microscopy (NSOM), and surface enhanced raman scattering spectroscopy (SERS). Despite their differences, all of these detection methods benefit from using surfaces that contain indexing features to facilitate the creation and subsequent read-out of the ultraminiaturized arrays. Although surfaces such as glass slides without an indexing system can be used for printing nano and ultramicro arrays, the localization of micron and submicron spots during detection can be problematic. We have developed a line of 4 mm x 4 mm silicon chips that possess a microfabricated grid of 100 µm or 200 µm raised square pads that are bordered by an alphanumeric indexing system (Figure 1). Tiny arrays of materials may be printed on these pads with the attainable goal of later returning to a specific location for analysis. These Sindex™ chips are available with a variety of application-specific surface chemistries.

DATA SUMMARY

We have developed proprietary instrumentation (The Nano eNabler™ system), surface patterning tools (SPT™ print cartridges) [1] and a methodology for delivering femtoliter to attoliter volumes of liquid precisely to a defined domain, enabling a variety of novel applications. These include the construction of ultramicro arrays for detection of analytes from very small volumes (as low as 100 - 500 nl) with very high specificity and sensitivity (on the order of pg/ml in the case of proteins). In brief, the Nano eNabler™ system consists of high precision X and Y stages (20 nm resolution), a video monitoring system, an environmental control system, a force feedback system to maintain consistent printing force, and a graphical user interface for easy pattern design and instrument control. The SPTs are microcantilever devices that have been specifically designed to facilitate fluid flow and transfer to surfaces with high reliability and efficiency. These can be used to precisely transfer attoliter volumes of liquids onto surfaces. Typical designs include features such as a reservoir for the material to be deposited, channels

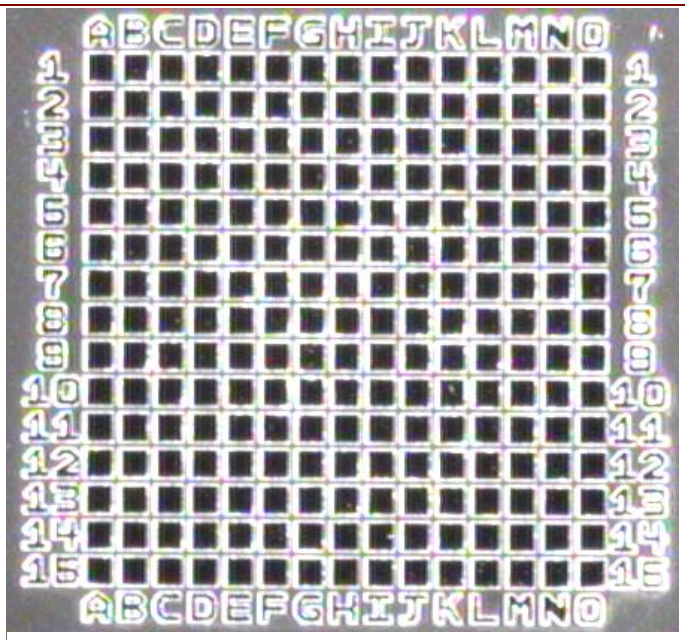

Figure 1: Optical image of the indexed grid portion of a 4mm Sindex™ chip. Individual silicon pads measure 100 µm x 100 µm and may be coated with metals or functionalized with additional surface chemistries.

to transport these materials to the distal end of the microcantilever and micron scale gaps at the distal end to control liquid flow. The Nano eNabler™ system and SPT™ print cartridges have been used to print arrays of proteins, DNA, nanoparticles, and other materials onto specific pads of Sindex™ chips. In the case of the biomolecules, a functional assay was performed with indexed grid locations assisting in the location of specific arrays. Read-out was typically performed via fluorescence microscopy or AFM.

CONCLUSIONS

The Nano eNabler™ system has been used to construct nano and ultramicro arrays of proteins on various surfaces including indexed silicon surfaces referred to as Sindex™ chips. These patent-pending chips are a valuable addition to the Nano eNabler™ system, as they provide an addressable grid of pads that simplifies the printing and subsequent re-location of micron and submicron features during detection.

REFERENCES

[1] Xu, J., Lynch, M., Huff, J., Mosher, C., Vengasandra, S., Ding, G., and E. Henderson. Microfabricated quill-type Surface Patterning Tools for the creation of biological micro/nano arrays. *Biomed. Microdev.* **6 (2)**: 117-123, 2004.