

Protein Chips As New Tools In Proteomics

SNF Researchers: P.-F. Indermuhle, M. X. Tan, F. G. Zaugg and P. Wagner
 Zyomyx Inc., Hayward, CA., USA

Abstract: *The study of protein activities and functions is a key element in life sciences, particularly in proteomics. Zyomyx developed a high-density protein profiling biochip™ for high throughput, low sample volume protein studies. As a first product, a human cytokine chip is commercialized, while various other products and technologies are under development.*

As a result of recent breakthroughs in genomics and proteomics, a new demand for high-density protein chips arose. However, the fabrication of biochips with immobilized active proteins may be technologically very complex and challenging. Using a multidisciplinary approach, Zyomyx Inc. has developed a high-density protein profiling biochip™ allowing the performance of multiplexed quantitative micro-assays with low sample volumes.

Zyomyx' platform consists of a three-dimensional pillar chip, an injection molded flow cell, a multiplexed workstation and a customized laser scanner (Fig1). In addition, a parallel, non-contact dispenser generates very reproducible and homogeneous spots on the pillar chip, allowing the performance of quantitative assays (Fig.2). This proprietary dispensing technology reduces denaturation of sensitive molecules and allows up to several thousands spots to be dispensed simultaneously. Both the dispenser and the pillar chip are fabricated by silicon micro-machining techniques and their surfaces are chemically engineered to optimize liquid behavior and biological compatibility.

The flexible architecture of Zyomyx' platform allows the performance of a wide range of assays. After preparation of a homogeneous reactive surface, any bio-molecule, e.g. capture molecules such as antibodies, can be reproducibly dispensed and immobilized in a selective and controlled manner on top of individual pillars. The pillar chips are then packaged in a plastic flow cell, which allows sample fluids and washing solutions to be applied in an automated assay station. A wide variety of incubation times and washing cycles can be selected. The interactions between the immobilized biomolecules and the analyte can be measured directly in liquid, using a sandwich assay or other kinds of assays (Fig.3). Thanks to miniaturization, 200 binding assays can be performed out of sample volumes smaller than 20 µl.

In the first commercial version of the Zyomyx protein profiling biochip™, multiplexed sandwich assays can be performed on 30 human cytokines with picomolar sensitivity and over a linear dynamic range of at least three logs. As an example, a cytokine expression profile of early rheumatoid arthritis will be presented. Other products using different cytokines are under development.

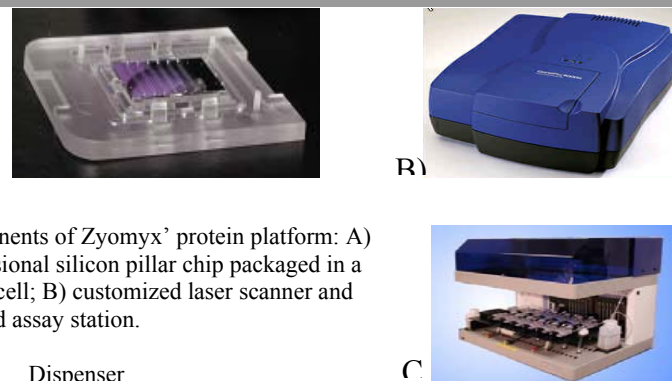


Fig.1 Three components of Zyomyx' protein platform: A) three-dimensional silicon pillar chip packaged in a plastic flow cell; B) customized laser scanner and C) automated assay station.

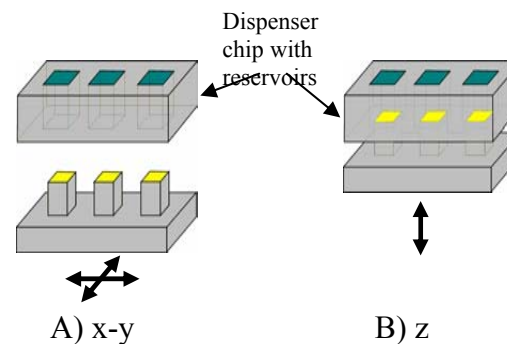


Fig. 2 Working principle of Zyomyx' parallel dispenser: up to several thousands different solutions can be dispensed simultaneously onto a pillar chip in a contactless, dropletless manner.

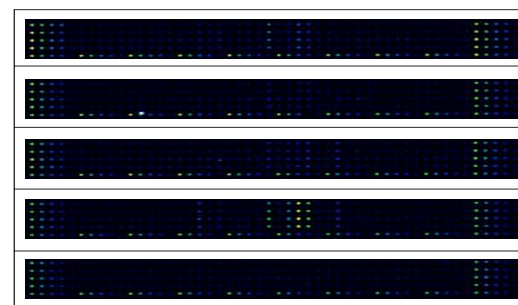


Fig.3 Results of a multi-channel assay performed with Zyomyx' protein profiling biochip™. the false color image represents the signal intensity measured by Zyomyx' customized laser scanner. Each dot corresponds to the top of one pillar.