



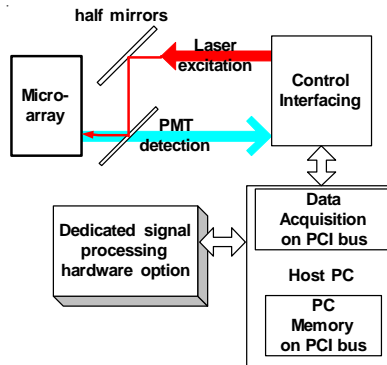
# Gene Expression Microarrays and Biochips: Electronic Measurement Solutions for High Throughput

Gene expression analysis is performed in the lab with a glass or silicon based microarray. The arrays are searched for photo-fluorescence of labelled probes under multiple wavelength laser excitation, and a complex image is acquired on a low cost PC platform.

Such biochip readers are presently quite slow and expensive. Plextek's signal processing, optoelectronics and regulatory expertise can help speed up and cost reduce the process.

## Overview

The diagram shows the main blocks of a microarray scanner.



Scanner Block Diagram

## Signal Acquisition

Current microarray scanners perform the basic task, but are neither speed nor cost optimised, especially in the light of the high performance electronics now readily available as commodity parts.

For example many analog to digital converters used on data acquisition cards perform at only 500 kilo-samples per second (kS/s), yet a performance up to one hundred times this level is available. With today's array complexity, even a ten times faster coverage would remove this measurement bottleneck.

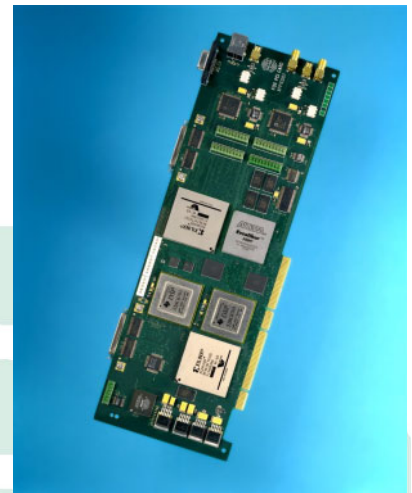
## Exploiting Low Cost PCs

Low cost PCs are now equipped with a very fast PCI bus architecture. With this exists the possibility of quickly writing the large amounts of microarray image data directly to PC memory, obviating a second acquisition memory or interruption of the host Athlon or Pentium processor. Yet present commercial data acquisition equipment does not universally take full advantage of this fast architecture.

## Faster Image Processing

Whilst low cost PCs can capture data well via the PCI bus, dedicated image processing hardware can always be made considerably faster than the host PC processor for subsequent analysis. This can lead to a truly high throughput screening process.

A Plextek Digital Signal Processing PCI card (FOX) which can be used to speed up image processing is shown below.



Fox Dedicated Hardware

## Better Optical Control

Control of the intensity of the laser excitation sources is important to strike a balance in achieving a good signal to noise ratio without photobleaching the sample. Cy3 and Cy5 are common labels which can be excited with a frequency doubled YAG laser (532nm) and a Helium Neon laser (633nm). The resultant fluorescence is simultaneously yet independently measured, typically by photomultiplier tubes.

Some applications require four fluorescent labels, for example signal sequencing work. In this case signal quality and signal-to-signal interference (crosstalk) may become greater issues.

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Current confocal scanning methods address signal quality issues optically. However electrical signal processing methods can also be designed to reduce interference. These include crosstalk cancellation and multiplexing schemes.

Plextek could offer further specific improvement to usability by the design of a linearised detector sensitivity control. Without such correction, any multiplication detector (photomultiplier tube, avalanche photodiode) normally has non-linear gain.

### Scanning Versus Staring

Staring systems can be lower cost since they remove the need for scanning optics. The trade off between scanning and staring is sensitivity versus complexity, although long measurement integration times can offset staring sensitivity issues in some applications. Plextek have design experience with the charge coupled device (CCD) elements often used in staring systems.

### Novel applications

For genotyping studies it might be sufficient to simply detect an 'on' or 'off' fluorescence state, in other words simple binary detection of fluorescence with respect to a user definable threshold. The simple CCD staring method gains merit in such an approach since the poorer typical sensitivity is less relevant. A further option would consider low cost solid state photodiodes as detectors.

### Proteomics

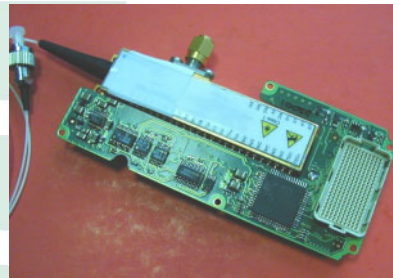
Protein arrays for protein expression testing involve arrays which are presently harder to make, but the scanners may be expected to be very similar in principle.

### Conclusions

Plextek can offer a competitive advantage in microarray reader electronic design, resulting in higher sensitivity, higher throughput, lower cost and bespoke application to novel requirements.

### Plextek Previous Work

Plextek have previously worked on many client projects encompassing lasers and imaging systems. Some examples are shown below.



Tunable Laser Controller



X-ray Image Processor

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