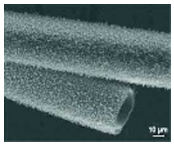

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The death of microarrays?

High-throughput gene sequencing seems to be stealing a march on microarrays. **Heidi Ledford** looks at a genome technology facing intense competition.

Faster, cheaper DNA sequencing technology is revolutionizing the burgeoning field of personal genomics. But it is having another, more subtle effect. Scientists are using the sequencers to tackle a wide range of research applications, including monitoring gene expression, mapping where proteins bind to the genome and cataloguing sites at which the DNA has been chemically modified. In doing so, they have enabled the technology to encroach on markets that have been dominated — and created — by microarray manufacturers.

The US$700-million market for expression arrays was becoming increasingly competitive even before high-throughput sequencing entered the scene. Once controlled entirely by Affymetrix, an array maker based in Santa Clara, California, the field is now populated by several companies jostling anxiously for position. Researchers initially flocked to microarrays to measure gene expression, then to assay the human genome for the presence of specific sequence variations.

Sequencing is still more expensive than arrays and many labs do not have access to sequencing equipment, which also requires a significant amount of computing infrastructure. But prices are expected to plummet, and the new sequencing platforms are already making their way out of specialized genome sequencing centres and into academic research labs. Californian firms Illumina in San Diego and Applied Biosystems in Foster City, as well as Connecticut-based 454 Life Sciences in Branford (now owned by Roche) all report that most new orders for their machines are coming from places other than sequencing centres.

Many researchers feel that sequencing sidesteps several technical limitations of microarrays, such as their failure to detect poorly expressed genes. And mounting dissatisfaction with results from genome-wide scans for genetic links to disease — a major market for genotyping arrays — has fuelled a call for sequencing targeted regions of the genome rather than full genotyping of study participants.

Some researchers predict that array makers who specialize in tailor-made, small-market arrays to suit more specific research needs — such as Roche NimbleGen based in Madison, Wisconsin — are best positioned to cater to the future microarray market. And the low cost and quick analysis of microarrays will ensure that the technology survives for some applications, especially genotyping, says biostatistician Xiaole Shirley Liu of the Harvard School of Public Health in Boston, Massachusetts. But the fact remains: "When possible, biologists are willing to spend more to get better data," says Liu.

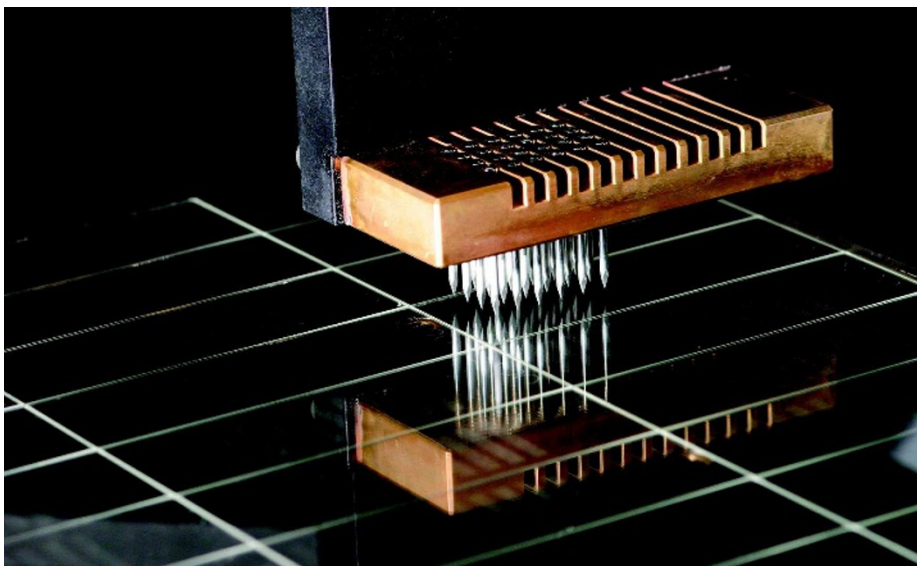
"Sequencing does put microarrays at risk in some areas of the life-sciences research market."

In the past two financial quarters, Affymetrix has acknowledged the growing threat from sequencing. On 13 October, the company said that its revenues for the third quarter of 2008 would come in well below analysts' estimates. "We are very deep into a transition phase of our business," said Affymetrix president Kevin King at the UBS Global Life Sciences Conference in New York last month. "It's going to take several quarters for us to restore the growth that we have had historically."

The company blames the declining growth — revenue was down 1.5% last quarter compared with the same time last year — on shrinking budgets in the pharmaceutical industry. But some analysts think that intrusion of sequencing into the gene-expression market could be having an effect. Although most of Affymetrix's growth is in the genotyping market, sales of expression arrays still account for almost 60% of the company's consumable sales revenue, says Douglas Schenkel, a vice-president at the Boston office of investment banking firm Cowen and Company.

Affymetrix and other microarray manufacturers are striking back with improvements designed to drive prices down and expand into clinical diagnostics, a growing field best suited for mature technologies and less likely to adopt sequencing in the near future. "Sequencing does put microarrays at risk in some areas of the life-sciences research market," says John Sullivan, a research analyst at Leerink Swann, a Boston-based health-care investment bank. "But improved genetic understanding of disease actually opens up the microarray platform to clinical diagnostics."

Manufacturers are also creating arrays that can be used to isolate specific regions of the genome for sequencing, so that researchers will not have to waste resources sequencing random fragments from the entire genome. These products, called 'capture arrays', have created a new market that, notably, is tied to the success of sequencing, says Kevin Meldrum, director of business development and genomics at Agilent, an array-maker in Santa Clara. It was a logical move, he says: "If we didn't do anything, we could be sitting here five to six years from now scratching our heads." ■



P. DUMAS/EURELIOS/SPL

DNA is deposited on a glass slide to make a microarray — but is the technology losing its allure?