

**Media Backgrounder – perspective and detail for journalists:**

## **AGILENT IN GENOMIC MICROARRAYS**



Agilent Technologies, Inc. a global leader in genomic microarrays, is providing researchers with high performance solutions to interrogate thousands of genes at once, rapidly, reliably and reproducibly. A typical DNA microarray or “biochip” is a one inch by three inch slide holding thousands of bits of genetic information used to analyze the processes of life. These microarrays represent many genes which are placed in precise locations on the slide. Each spot represents a gene for examination, Researchers use this powerful technology to establish associations between gene activity and health. In addition to microarrays, Agilent offers a full set of reagents, hardware, methods and bioinformatics software to run genomic experiments. These products are

complemented by a highly flexible service model for both microarray design and experiments - ranging from full service through local Certified Service Providers, to support from dedicated field engineers in helping customers establish and maintain microarray facilities.

### **GENE EXPRESSION**

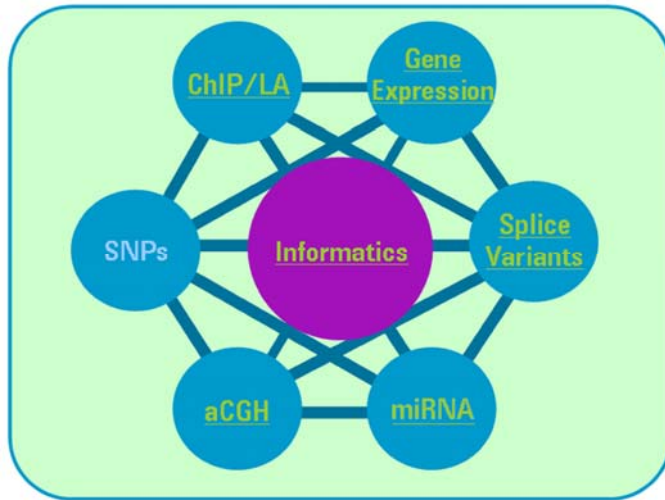
The first and most popular use of DNA microarrays is the study of gene expression, which genes and how many in a cell are “turned on and off.” The expression patterns of healthy cells, for example, can be compared to those of cancer cells. Researchers use gene expression studies to seek new therapeutics, identify early warning signs of diseases and even to investigate which drugs could work best for certain patients.

About half of gene expression analysis performed worldwide is for cancer research. Other important applications include study of cardiovascular disease, immune and inflammatory diseases (such as AIDS and asthma) and central nervous system disorders.

Agilent offers an 8-plex format microarray in which eight gene expression microarrays are printed on a standard slide. This is useful for researchers to profile large numbers of tissue samples at low cost with comparable accuracy and sensitivity. By running eight separate samples on one slide, cost-per-experiment can be reduced by a factor of eight.

### **Emerging Applications**

Agilent’s flexible manufacturing capability is well-suited for the next generation of genomic microarray applications enabling researchers to discover the mechanisms of health and disease. Agilent develops these new technologies through three avenues: development by Agilent Laboratories, acquisitions and strategic partnerships.



Researchers are increasingly comparing gene expression data to one or two additional genomic applications to look at complex biological questions from more than one point of view. A powerful bioinformatics capability is the key to deriving useful knowledge from this complex data.

### **Array-based Comparative Genomic Hybridization Arrays (aCGH), Copy Number Variations (CNV)**

In January 2005, Agilent introduced a breakthrough platform that enabled researchers to use microarrays to precisely study chromosomal gains and losses associated with cancer in a massively parallel manner. Previously they needed to use optical imaging of whole chromosomes, a technique with limited sensitivity, resolution, quantification and throughput.

“This advancement, along with the opportunity it provides to correlate genomic copy alterations with mRNA abundance and protein abundance, is going to incite a huge body of experimentation and publication among the cancer research community,” said Michael Bittner of the Translational Genomics Research Institute about the Agilent aCGH platform.

### **ChIP-on-chip (location analysis)**

Chromatin immunoprecipitation (ChIP) on microarray (chip) studies, also known as location analysis, use microarrays to pinpoint activity at regulatory regions of chromosomes. This provides insight into pathways for cancer, cardiovascular disease and central nervous system disorders. Regulatory proteins bind to genomic DNA to control DNA replication and gene expression. In other words, these proteins act as switches in cells’ regulatory circuitry. ChIP-on-chip is implicated in growing numbers of biomarker discoveries.

### **DNA Methylation**

This application detects events that regulate gene expression without changing the DNA sequence itself. This is considered an important step in many disease pathways, and an emerging area of study.

### **miRNA**

Agilent developed a new microarray-based application for studying microRNAs (miRNAs), a prevalent class of small single-stranded non-coding RNAs (19-30 nucleotides long). They’re associated with widespread regulation of gene expression, suspected to control as many as 30 percent of all human genes. Agilent’s miRNA microarray is the only commercially available high-throughput system that delivers the

optimal sensitivity and specificity for both sequence and size discrimination. The small size of the miRNA poses unique challenges regarding sensitivity, selectivity and sample consumption. Agilent's novel labeling method, probe design, and *in situ* synthesis overcomes these challenges.

### Alternative Splicing Arrays

Agilent collaborates with ExonHit Therapeutics to develop a microarray-based solution for monitoring the expression of splice variants. These are variable sequences of RNA produced from the same gene, affecting cell regulation. Scientists seeking new therapies are increasingly turning to splice variant analysis to find novel targets, detect disease states and observe the effects of drugs or toxins. Through a licensing agreement, customers can purchase the ExonHit content printed on Agilent microarrays directly from Agilent. ExonHit is also a Certified Agilent Microarray Service Provider.

### Competitive Landscape

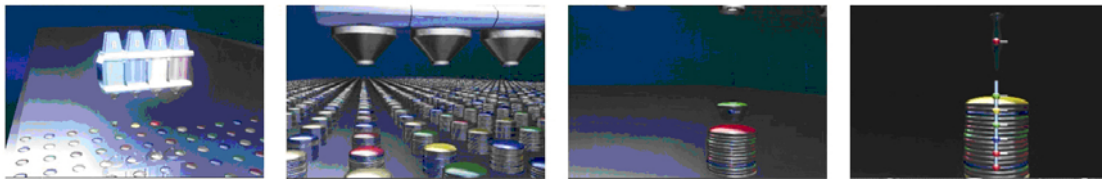
The use of microarrays began in 1991, with the publication of the chemical synthesis of oligonucleotides on glass chips by Fodor et al. The author went on to develop the first DNA microarray and founded Affymetrix. Other competitors include NimbleGen, ABI, and Illumina. GE Healthcare has exited the business. Agilent began manufacturing microarrays in 2000 and is a global leader, particularly in emerging applications.

### The Agilent Difference

Agilent's novel approach to microarray design and manufacturing offers substantial advantages over other techniques. Agilent's SurePrint manufacturing process is, basically, inkjet printing. Instead of ink, the print head deposits nucleic acids to synthesize nucleic acid probes known as "oligonucleotides." In contrast, Affymetrix uses photolithography, similar to methods used to fabricate semiconductors, to deposit layers of genetic material on their microarrays.

Photolithography is time consuming and thus expensive to set up, so it is best suited for large volume runs. Inkjet microarray printing is far more flexible and customizable, only requiring a different software file to print each array.

Agilent offers a new generation SurePrint technology which prints 244,000 features on a 1-in. x 3-in. slide with one million features being planned for next year.



In addition to flexibility, the Agilent technology enables the printing of probes that are 60 nucleotide bases long (60 mer). This provides a 5-8-fold increase in sensitivity of detection compared to the 25 mer probes dictated by photolithographic deposition.

### Open and Flexible

Agilent also offers the industry's first Web-based design tool for custom DNA microarrays. *eArray* incorporates the latest data from the major genomic databases, including approximately 4 million validated probes. *eArray* also enables researchers to collaborate on array design worldwide. Once an array experiment is laid out in the computer, it can be sent to Agilent to be

printed like a spreadsheet. Customer access to content leverages the flexibility of the printer so researchers can concentrate on their experiments rather than experiment design.

### **Agilent's Genomics Products and Services**

- Custom DNA Microarrays – probe design, layout, consulting, fabrication.
- Catalog DNA Microarray Kits – growing list of key model species
  - Agilent-designed
  - Collaboratively designed
- Reagent Kits
  - Sample preparation and isolation
  - Sample amplification and labeling
  - Microarray hybridization
  - Microarray wash
  - Individual reagents
- Data Analysis Software
  - CGH Analytics
  - Feature extraction
  - GeneSpring Gx
- Microarray Processing Hardware
  - QC using lab-on-a-chip Agilent 2100 Bioanalyzer
  - DNA microarray scanner
  - Hybridization oven, hybridization chamber, accessories
  - RT-PCR (Stratagene)
- Lab Automation
  - Velocity 11 liquid handling and microplate management instruments and systems.

