

integrated

expression

DNA analysis

The GeneChip® System

An Integrated Solution for Expression and DNA Analysis

genomics

pharmacogenomics

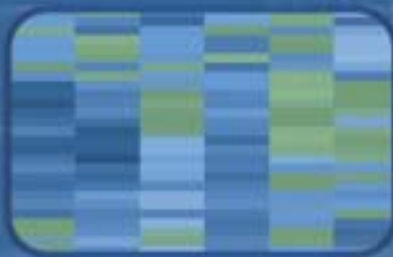
quality





G C C A A T A T
 A G C A T A C C
 G A A T A C C A
 C G A C C C C T
 A G C A T A C G
 G A A T A C C A
 T A A T A C C C
 G G A C C C C T
 T G C A T A C G
 G A A T A C C A
 G G A C C C C T
 A G C A T A C G
 G A A T A C C A

The DNA microarray is a technology that allows scientists to study the expression of thousands of genes simultaneously. It is a powerful tool for understanding the complex interactions between genes and the environment. The DNA microarray is a chip that contains thousands of small spots of DNA. Each spot represents a specific gene. When a sample of RNA is added to the chip, the RNA molecules bind to the complementary DNA sequences on the chip. This binding process is called hybridization. The intensity of the fluorescence signal at each spot indicates the level of expression of the corresponding gene.



The Affymetrix GeneChip® System Provides a Global View of ■ Systems Biology

To understand the complex mechanisms and networks involved in biological processes and diseases, it is no longer sufficient to focus on isolated pathways or single genetic events. Instead, scientists are embracing a systems biology approach for a more complete knowledge of intricate regulatory networks and complicated pathways.

The Affymetrix GeneChip® System provides a systems biology perspective for both expression profiling and DNA analysis. This integrated system gives you the flexibility to view the genome at a global level or focus on a specific subset of genes.

The GeneChip Advantage

■ **Power of the Probe Set** The key to the GeneChip advantage is that each high-density array provides multiple, independent measurements for each transcript and genotype call. Multiple probes mean that you get a complete data set with accurate, reliable, reproducible results from every experiment.

■ **Multiple Applications for a Genomic Perspective** By integrating gene expression and DNA analysis on a single platform, the GeneChip System provides a total solution to elucidate complex mechanisms and networks underlying biological processes and diseases.

■ **Parallel Manufacturing for Results You Can Trust** Photolithographic manufacturing, paired with strict process controls, results in flexible array formats with unsurpassed quality, reproducibility, and consistency.

■ **Open Access to a View of Systems Biology** All GeneChip microarray content is designed from genomic information in the public domain. The research community has the opportunity to openly collaborate and share data obtained on a single, standardized platform.



■ The GeneChip® System

■ Microarrays

■ Reagents and Assays

Experimental
Design

Sample
Preparation

Array
Hybridization

Scanning

Data
Management

Data
Analysis



- Available in a comprehensive selection of catalog products and custom options for RNA and DNA applications
- Flexible array formats for the freedom to conduct whole-genome analysis or focus on a subset of genes
- Array design processes using advanced bioinformatics algorithms from genomic sequence analysis to probe selection—you can focus on science, not array design
- Unique photolithographic manufacturing, with built-in process controls at each synthesis step, for unsurpassed data accuracy and reproducibility
- Standardized and validated for robust, reproducible experimental results, including GeneChip® microarray-specific controls for critical assay steps
- Optimized assays integrated with array design and analysis
- Continuous development of new assays and reagents for streamlined sample preparation and new applications



▄▄ Instruments



- Easy-to-use, integrated system for rapid adoption of both RNA and DNA applications
- Automated processing for increased data reproducibility and reduced hands-on time
- The most cost-effective approach for multiple applications through a single, flexible system

▄▄ Software



- Provides data analysis capabilities for both RNA and DNA applications
- Offers scalable data management options for low- and high-throughput requirements
- Enables seamless, customizable data analysis and third-party software integration with a unique, open architecture

▄▄ The NetAffx™ Analysis Center

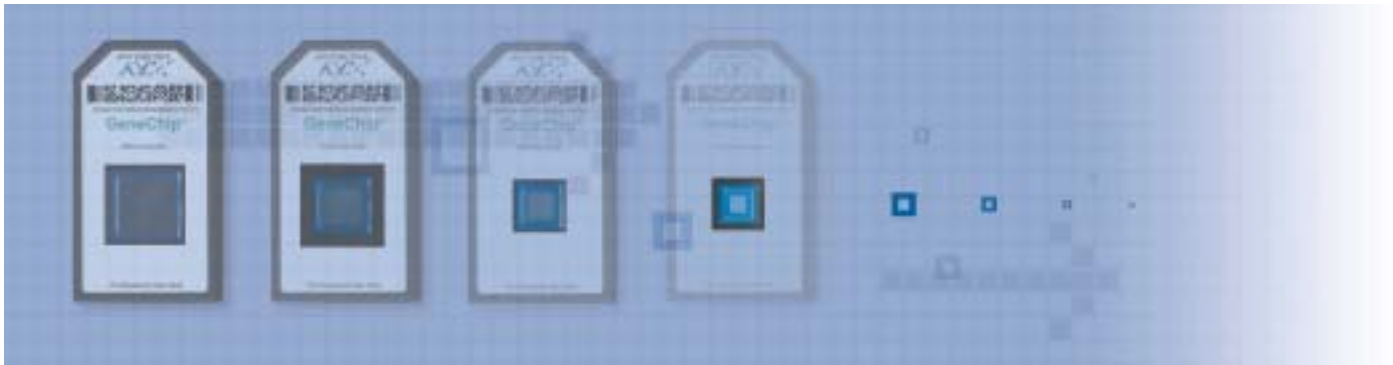


- Enables you to quickly derive biological significance from array data
- Allows you to preview array content before research begins for efficient experimental design
- Offers open access to comprehensive public domain and Affymetrix annotations via a single online interface



One System. Multiple Applications. Infinite Discoveries.

The GeneChip® System supports both DNA and RNA analysis, bringing the fundamental GeneChip advantages to multiple applications. This integrated platform allows you to conduct a wide range of experimental studies to gain a more complete understanding of your biological systems.

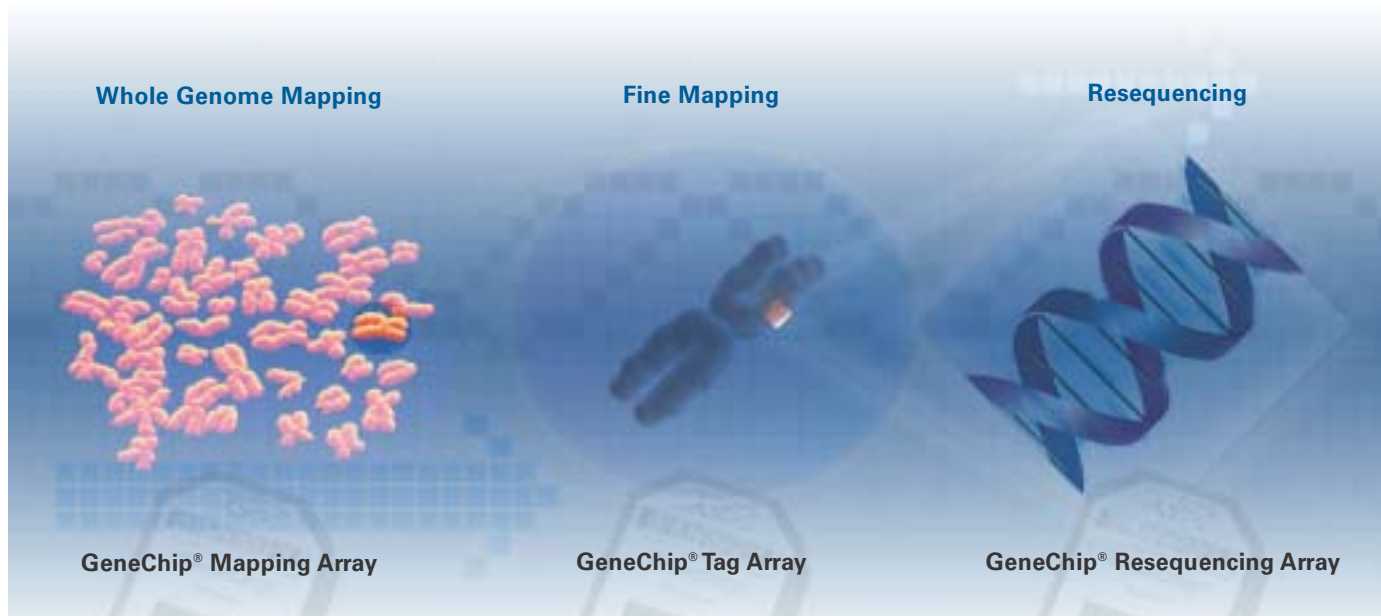


Gene Expression Analysis

GeneChip® catalog and CustomExpress™ arrays are widely recognized as the gold standard in expression analysis. They are used by leading research labs around the world for a broad and expanding list of applications, such as: uncovering new regulatory pathways, confirming mechanisms of action, validating drug targets, classifying diseases, analyzing toxicological responses, and developing diagnostics. Discover the unique GeneChip advantages for yourself:

- A large selection of catalog arrays enables you to study diverse organisms from *Arabidopsis* to Zebrafish.
- Custom options with CustomExpress arrays mean customers can study expression for any number of genes in any model organism.
- Multiple independent measurements of each transcript of interest provide reliable assessments of each data point with analysis of statistical significance. Other microarray technologies are typically limited by density and can only analyze each transcript with a single probe, compromising the robustness of the array.
- Multiple 25-mer probes offer an optimal balance of sensitivity and specificity for accurate evaluation of gene expression levels.





■ DNA Analysis

The GeneChip DNA analysis products are transforming traditional genotyping and resequencing in the same way GeneChip expression arrays revolutionized how gene expression is studied. This powerful new line provides:

- **More informative results for more discoveries.** High-density GeneChip arrays enable higher resolution whole-genome scans and large-scale sequencing projects, facilitating discoveries that would be difficult or impossible to make with other technologies.
- **Higher quality data.** Multiple probe sets provide highly accurate and automated genotype and sequence calling, reducing the need for manual quality control.
- **Simplified sample preparation for increased throughput.** Innovative assays allow for more efficient use of laboratory time and resources.

The unique advantages of GeneChip DNA analysis products will advance your studies of:

- **Whole-Genome Scanning:** Complete high-resolution scans with unprecedented power in a fraction of the time required by traditional technologies.
- **Cancer Genetics Research:** Analyze regions with loss of heterozygosity at high resolution.
- **Pathogen Subtyping:** Perform complete sequence analysis of microbial pathogens to track genetic evolution

and identify variations contributing to pathogenicity or drug resistance.

- **Pharmacogenetics:** Understand the molecular basis for differential drug response through whole-genome scans or target gene sequence analysis.



■ ■ Affymetrix. The Industry Standard in Quality and Experience

■ ■ State-of-the-Art Array Design

Affymetrix' strategies for array design result in sensitive and reliable sequence and transcript detection with the highest specificity.

- Sequence selection processes qualify, cluster, and screen through millions of raw sequences and SNPs from multiple databases in the public domain. Quality is rigorously assessed before any sequences are chosen for the array.
- Probe selection algorithms are based on large amounts of empirical data and extensive testing. This results in probes with the desired intensity and concentration-dependence, with minimal cross-hybridization.
- Probes are designed in sets to provide multiple, independent measurements for each transcript or SNP, resulting in increased data reliability.
- Probe sets are comprised of multiple 25-mer oligos for the optimal balance of sensitivity and specificity.
- Because all probe sequence descriptions and annotations are openly accessible through the NetAffx™ Analysis Center, the connection between array design and downstream analysis is seamless.



Quality-Controlled Manufacturing

Proven combinatorial chemistry and photolithographic technology consistently deliver unmatched array quality and reproducibility. Stringent quality-control processes ensure that GeneChip® arrays deliver a complete data set each and every time.

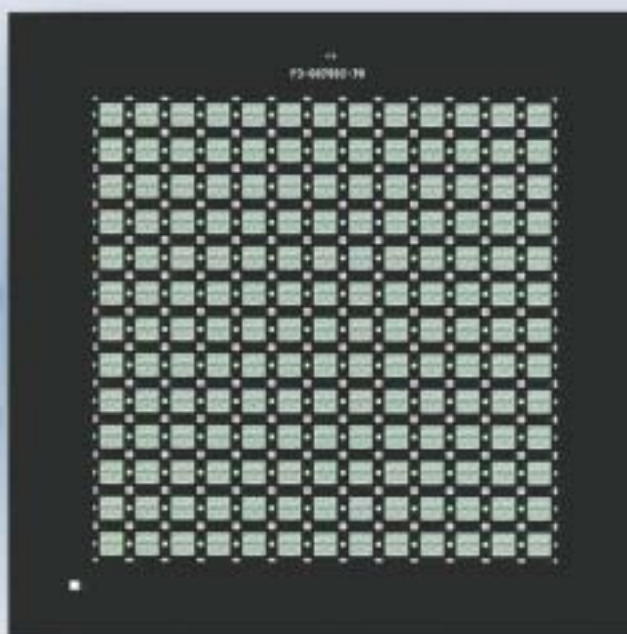
- This unique manufacturing process occurs on wafers, which are then diced into microarrays. This makes it possible to perform quality-control measurements of the entire manufacturing lot by sampling a few representative arrays

to ensure that each array meets high-quality standards.

- Affymetrix' parallel manufacturing can produce hundreds of thousands of probes in fewer than 100 steps. This is in contrast to other technologies, which may require well over one million independent synthesis events to generate 30,000-probe microarrays. As a result, the GeneChip platform is the only platform that can implement multiple in-process quality-control techniques to verify design, monitor correct reagent

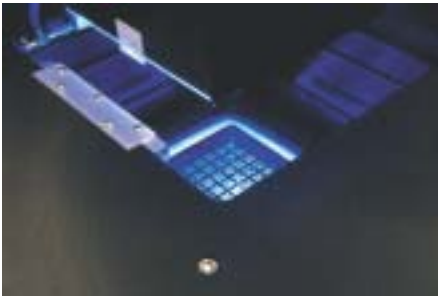
delivery time, and confirm precise synthesis of every step for every probe. These controls validate that all probes on all arrays are synthesized in the correct location and yield sufficient signal.

- Chemical synthesis takes place *in situ* on the wafer. This eliminates possible contamination—due to mishandling of clones, PCR products, or pre-synthesized oligos—that routinely occurs when producing spotted arrays.



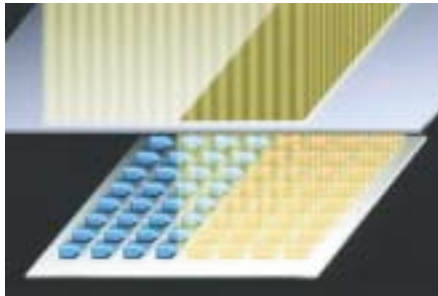
State-of-the-Art Photolithographic Manufacturing Process

1 | Photolithography



- A photolithographic mask set is designed to represent the information content on the array, and automated software tests verify the design by building the array *in silico*.
- After design validation, the mask is manufactured and aligned with a five-inch-square, quartz wafer.
- The mask set's patterns correspond to the desired sequence of each probe and either block or transmit light to the wafer.
- Oligo synthesis is activated only at locations where light is transmitted for precise and consistent feature construction.

2 | Probe Construction



- When ultraviolet light shines through the mask, the 5'-ends of the oligo-nucleotides in the exposed areas of the substrate become deprotected in preparation for the chemical coupling with the nucleoside phosphoramidite monomer.
- Once the desired features have been activated, a solution containing a deoxynucleoside phosphoramidite monomer with a light-sensitive protecting group is flushed over the wafer's surface.
- In the next synthesis step, a different mask is placed over the wafer for another round of oligonucleotide deprotection and monomer coupling.
- The process is repeated until all of the full-length probe sequences are completed.

3 | Cartridge Assembly



- Each wafer yields between 49 and 400 GeneChip® microarrays—depending on desired information content—and is cut so individual microarrays can be placed into GeneChip cartridges.
- The high-quality nature and parallel process of manufacturing results in arrays which generate highly reproducible data.
- Process controls at every step of manufacturing prevent feature loss and increase lot-to-lot array consistency.

■ The Way Ahead™

Affymetrix has invested significant time and resources towards developing optimal microarray design and manufacturing strategies. We remain dedicated to evolving GeneChip® technology to accelerate the understanding of complex biological systems. This combination of forward-thinking vision and cutting-edge technology will allow you to explore the genome in creative ways that were previously unimaginable.

As the GeneChip technology advances and microarray feature size continues to shrink, GeneChip applications will also expand to include additional genomics research, such as:

- Splice variant analysis
- Exon scanning
- Whole-transcriptome analysis
- Studies of regulatory mechanisms
- Whole-genome association studies

State-of-the-art microarrays, optimized assays, precision instrumentation, and open access to biological information together comprise an integrated solution, which delivers the most accurate and reproducible results possible today. Reliable data means you can make better decisions, and better decisions enable you to move your research forward with confidence. Whether your research requires whole-genome analysis or a focus on a specific subset of genes, Affymetrix will help you lead The Way Ahead.™



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