SUMMER INSTITUTE CALENDAR 2022

SUN	MON	TUE	WED	THU	FRI	SAT
						July 02
						Early Arrival Airport Arrivals and Check-in
July 03	04	05	06	07	08	09
Early Arrival Airport Arrivals and Check-in	Airport Arrivals and Check-in 6:00pm: 4th of July Celebrations	9:30am-12pm: Campus tour, Panther ID & ISSS Check-in 12-2pm Lunch 2:00-6:00pm, Shuttle to local grocery store	9:30am-11:30am ISSS, OII, & Housing Orientation & Presentation **2:30-4:30pm:-Welcome Reception and Buddy Meet & Greet Event**	**Classes begin!** 9-11:20am: Morning course 11:20am-2:00pm: Lunch break **1:30-4:30pm: BIOL4905 INTRO - TRAINING**	9-11:20am: Morning course 11:20am-2:00pm: Lunch break **1:30-4:30pm: BIOL4905 DNA PREPARATION**	Free Day
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31	August 01	02	03	04		
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Note: Students may arrive prior to the program date with an extra charge of $35 per night. Earliest day to check-in to University Commons is July 2.

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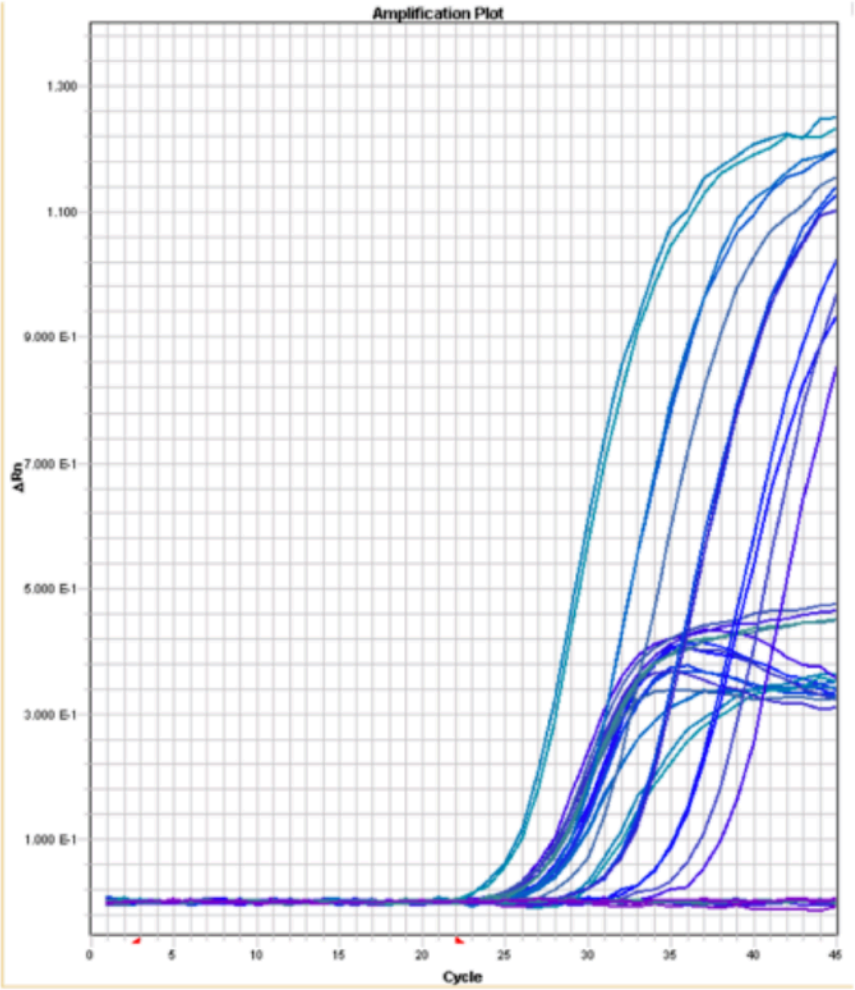
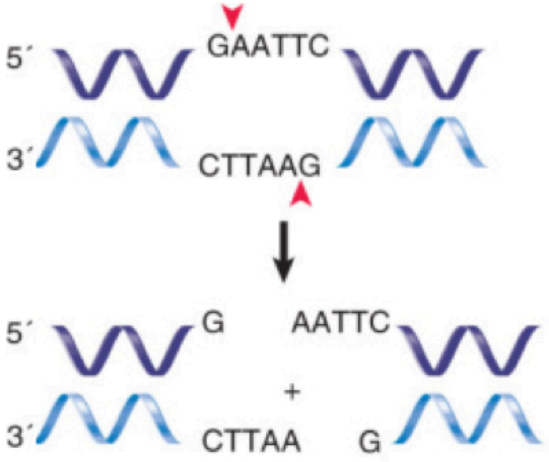


Is this a good qPCR plot of data?

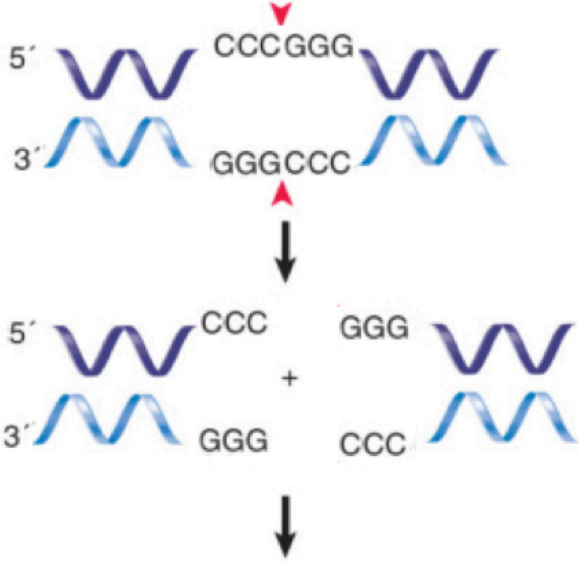
Explain your answer in your notebook.

Questions

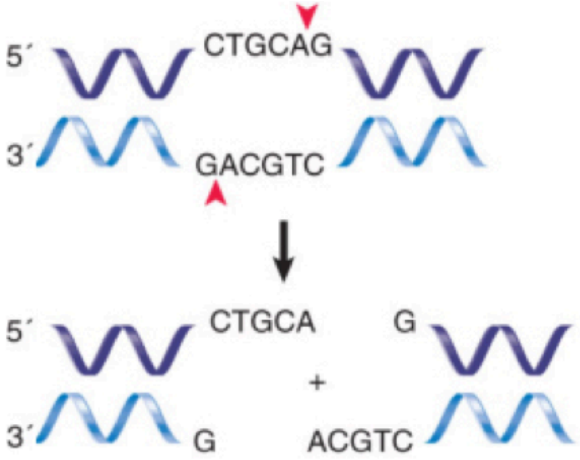
EcoR I



Sma I



Pst I



Which of these Type II REN can you find in YOUR sequence (next page). If you find the site, after which base number in the sequence does it cut?

Explain your answer by providing your analysis in your notebook.

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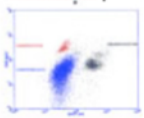
Georgia State University

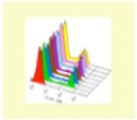
Flow Cytometry

Profiling Cells

Normal

Leukaemia patient

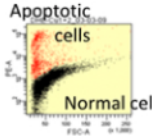




See effects of different drugs on Cell cycle

Apoptotic cells

Normal cells



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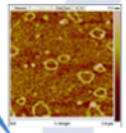

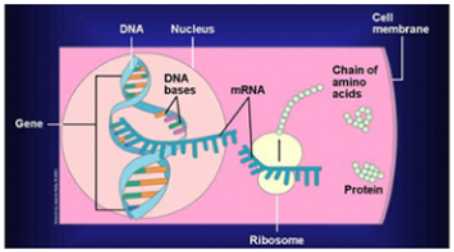

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Sanger Sequencing – >800 base pairs/run

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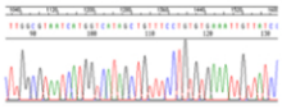
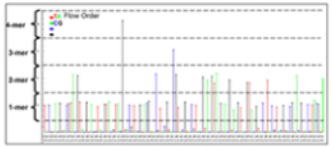


High Throughput Genomic Sequencing – 100,000,000,000 base pairs/run



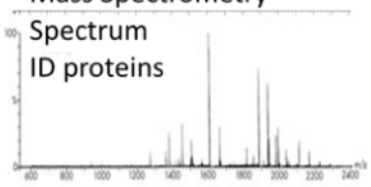
RNA Expression

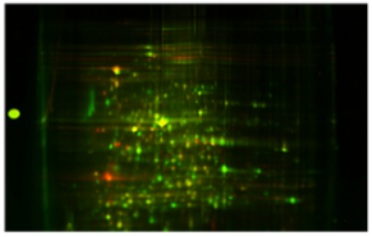
Cellular Functions

Protein Expression

Mass Spectrometry

Spectrum ID proteins





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2D Protein gel
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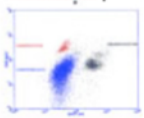

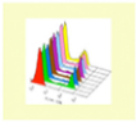

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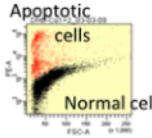

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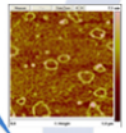

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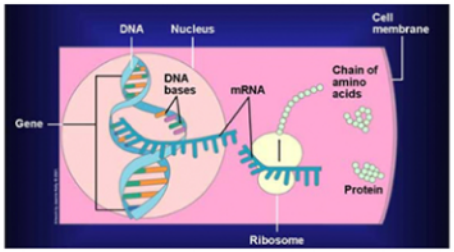

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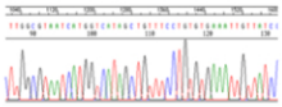

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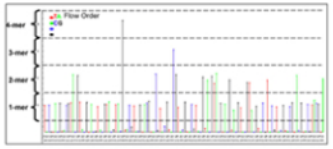

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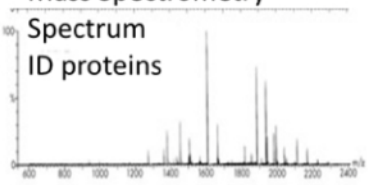

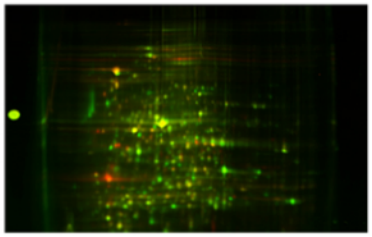

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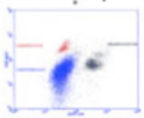

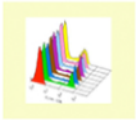

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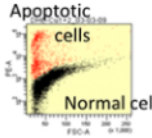

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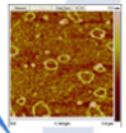

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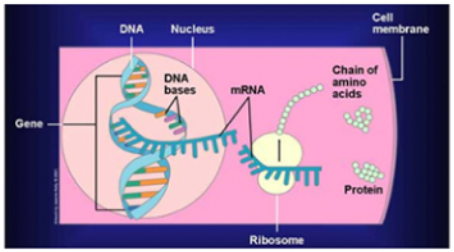

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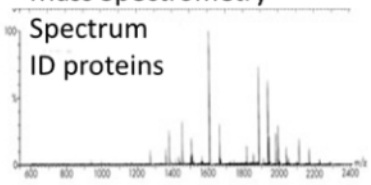

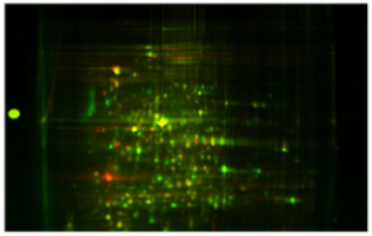

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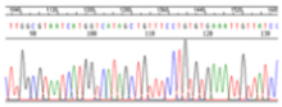
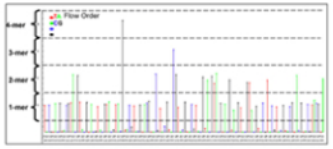


High Throughput Genomic Sequencing –

100,000,000,000 base pairs/run



Microarray:Analysis

Profiling mRNA

Colour of pin-point dots demonstrates the presence / absence of gene sequences

GSU Biology Core Facility

Supporting Life Sciences at GSU

http://biotech.gsu.edu/core_facility/index.html

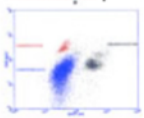
Georgia State University

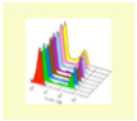
Flow Cytometry

Profiling Cells

Normal

Leukaemia patient

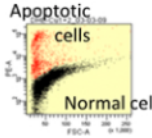




See effects of different drugs on Cell cycle

Apoptotic cells

Normal cells

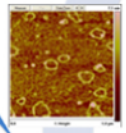


Apoptosis -programmed cell death

Atomic Force Microscopy

Imaging at the Ångström level

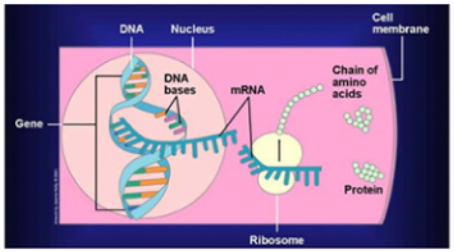
Protein structure analysis



Cellular Functions

DNA

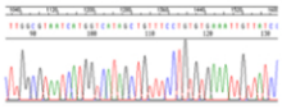
Replication



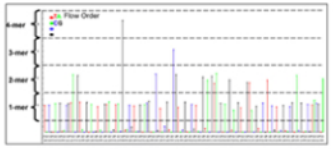
DNA Sequence Analysis:

Profiling DNA

Sanger Sequencing – >800 base pairs/run



High Throughput Genomic Sequencing – 100,000,000,000 base pairs/run



RNA Expression

Microarray:Analysis

Profiling mRNA

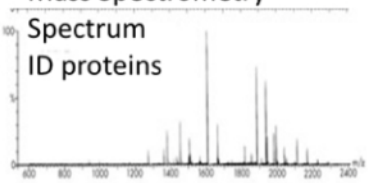
Colour of pin-point dots demonstrates the presence / absence of gene sequences

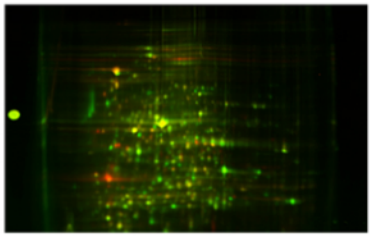
Protein Expression

Mass Spectrometry

Spectrum

ID proteins





Proteomics

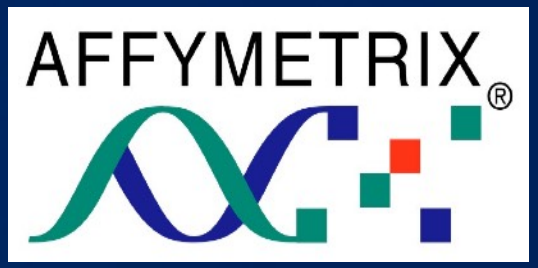
Profiling Proteins

2D Protein gel

Protein separation using

Electric charge and molecular weight

An Overview of GeneChip® Technology -



John Houghton, PhD
GSU ABCore Facilities

What is Microarray?

Microarrays
- circa 1991
- (Schena et al. (1995) *Science* **270**:467-70)

Probe DNA is attached to solid support
- plastic beads, glass slide, nylon
- or chip

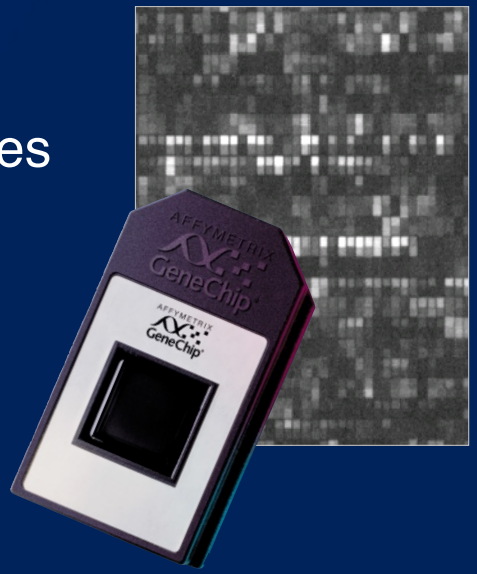
RNA is labeled (usually indirectly)

Arrays can detect
- mRNA
- microRNA
- Methylation
- SNP

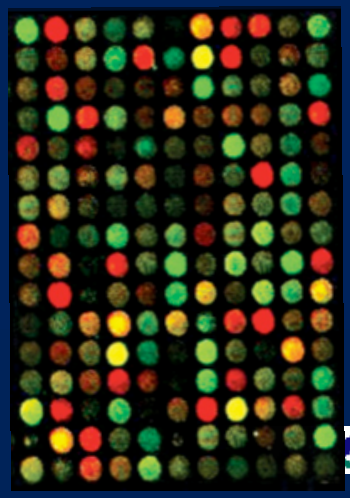
High throughput
- 10,000s of specific probes
- Measure global gene expression, SNP calls, LOH, amplification, methylation etc

GeneChip® vs. Spotted Arrays

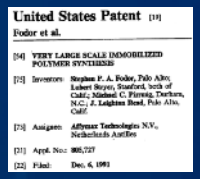
- Affymetrix GeneChip® Arrays use oligonucleotides
  - Oligos are built on a solid support



- Spotted arrays utilize nucleic acids made in solution
  - Solutions are then “spotted” onto a solid support
  - Competitive Hybridization

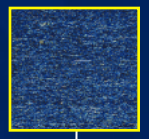


About Affymetrix


United States Patent [19]
Fodor et al.
[54] VERY LARGE SCALE IMMOBILIZED POLYMER SYNTHESIS
[75] Inventors: Stephen P. A. Fodor, Palo Alto; Robert Stryer, Stanford, both of Calif.; Michael C. Pirrung, Durham, N.C.; J. Leighton Read, Palo Alto, Calif.
[73] Assignee: Affymax Technologies N.V., Netherlands Antilles
[21] Appl. No.: 805,727
[22] Filed: Dec. 6, 1991

First Microarray Patent Issued

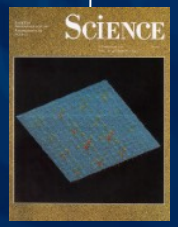
Commercial launch



Genetic MicroSystems™

neomorphic®

1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001



Cover of *Science*

AFFYMETRIX

Field Testing of GeneChip® System

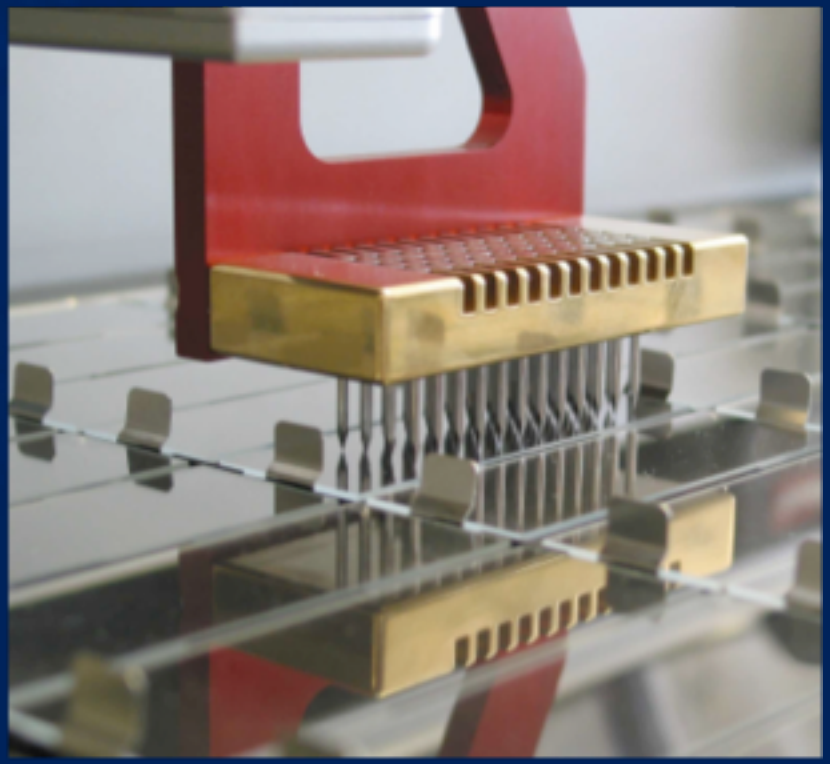
PERLEGEN SCIENCES


Sacramento Chip Plant

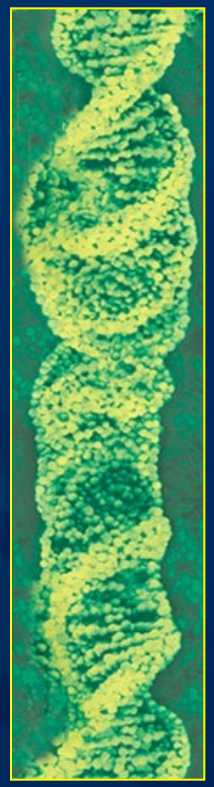
Historically....

DNA spotting

- DNA spotting usually uses multiple pins
- DNA in microtiter plate
- DNA usually PCR amplified
- Oligonucleotides can also be spotted

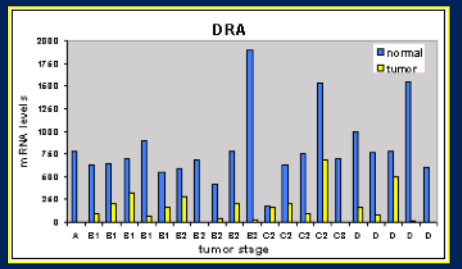


Afymetrix cornered the market

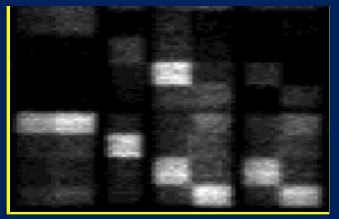


Sequence Database

Research Tools

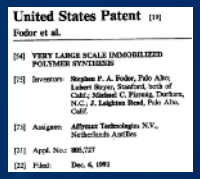


Expression Variability



Sequence Variability

About Affymetrix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[73] Assignee: Affymax Technologies N.V., Netherlands Antilles

[21] Appl. No.: 806,727

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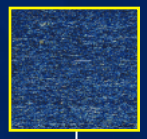
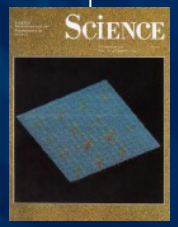


Genetic MicroSystems™

neomorphic®

1991 1992 1993 1994 1995 1996 1997 1998 1999 2000 2001



Cover of *Science*

AFFYMETRIX

Field Testing of GeneChip® System

PERLEGEN SCIENCES

Sacramento Chip Plant

Expression Arrays 2006

GeneChip Human Genome U133A 2.0 Array

The GeneChip® Human Genome U133A 2.0 Array is a single array representing 14,500 well-characterized human genes that can be used to explore human biology and disease processes.

Part #	Description	Unit Size	Your Price (USD)	Qty
900471	Human Genome U133A 2.0 Array	contains 2 arrays	Please Inquire	
900468	Human Genome U133A 2.0 Array	contains 6 arrays	Please Inquire	
900469	Human Genome U133A 2.0 Array	contains 30 arrays	Please Inquire	

Product Description | Technical Documentation | Required/Related Products

The GeneChip® Human Genome U133A 2.0 Array is a single array representing 14,500 well-characterized human genes that can be used to explore human biology and disease processes. New design and reduced feature size mean that you can use smaller sample volumes than the previous HG®U133A Array without compromising performance.

- Provides coverage of well-substantiated genes in the transcribed human genome on a single array
- Analyzes the expression level of 18,400 transcripts and variants, including 14,500 well-characterized human genes
- Comprised of more than 22,000 probe sets and 500,000 distinct oligonucleotide features
- Use the Power of the Probe Set and get multiple independent measurements for each transcript that deliver the greatest accuracy and reproducibility of any microarray platform
- All probe sets represented on the GeneChip® Human Genome U133A Array are identically replicated on the GeneChip Human Genome U133A 2.0 Array

Array Profile

Sequences used in the design of the array were selected from GenBank®, dbEST, and RefSeq. The sequence clusters were created from the UniGene database (Build 133, April 20, 2001) and then were refined by analysis and comparison with a number of other publicly available databases including the Washington University EST trace repository and the University of California, Santa Cruz Golden-Path human genome database (April 2001 release).

Instrument and Software Requirements

- GeneChip® Scanner 3000, enabled for High-Resolution Scanning*
- GeneChip® Command Console® Software (AGCC) including the GeneChip® Scanner 3000 High-Resolution Scanning Patch

*GeneChip Scanner 3000 High-Resolution Update is standard on all instruments shipped starting in September 2003 with serial number series 502. Previous versions, serial number series 501, will require the 00-0110 GeneChip Scanner 3000 High-Resolution Update to be installed.

For more information, please review the data sheet (pdf, 169 KB).

For research use only. Not for use in diagnostic procedures.

Feline Gene 1.0 ST Array	30 arrays	Please Inquire	
Guinea Pig Gene 1.0 ST Array	Contains 6 arrays	Please Inquire	
Guinea Pig Gene 1.0 ST Array	Contains 30 arrays	Please Inquire	
Marmoset Gene 1.0 ST Array	6 arrays	Please Inquire	
Marmoset Gene 1.0 ST Array	30 arrays	Please Inquire	
Medicago Gene 1.0 ST Array	6 arrays	Please Inquire	
Medicago Gene 1.0 ST Array	30 arrays	Please Inquire	
Ovine Gene 1.0 ST Array	6 arrays	Please Inquire	
Ovine Gene 1.0 ST Array	30 arrays	Please Inquire	
Porcine Gene 1.0 ST Array	6 arrays	Please Inquire	
Porcine Gene 1.0 ST Array	30 arrays	Please Inquire	
Rabbit Gene 1.0 ST Array	Contains 6 arrays	Please Inquire	
Rabbit Gene 1.0 ST Array	Contains 30 arrays	Please Inquire	
Rhesus Gene 1.0 ST Array	6 arrays	Please Inquire	
Rhesus Gene 1.0 ST Array	30 arrays	Please Inquire	
Rice (Cn) Gene 1.0 ST Array	6 arrays	Please Inquire	
Rice (Cn) Gene 1.0 ST Array	30 arrays	Please Inquire	
901997	Rice (Jp) Gene 1.0 ST Array	6 arrays	Please Inquire
901996	Rice (Jp) Gene 1.0 ST Array	30 arrays	Please Inquire
901991	Rice (US) Gene 1.0 ST Array	30 arrays	Please Inquire
901992	Rice (US) Gene 1.0 ST Array	6 arrays	Please Inquire
902002	Soybean Gene 1.0 ST Array	6 arrays	Please Inquire
902001	Soybean Gene 1.0 ST Array	30 arrays	Please Inquire
902299	Tomato Gene 1.0 ST Array	6 arrays	Please Inquire
902300	Tomato Gene 1.0 ST Array	30 arrays	Please Inquire
901956	Zebra Finch Gene 1.0 ST Array	30 arrays	Please Inquire
901957	Zebra Finch Gene 1.0 ST Array	6 arrays	Please Inquire
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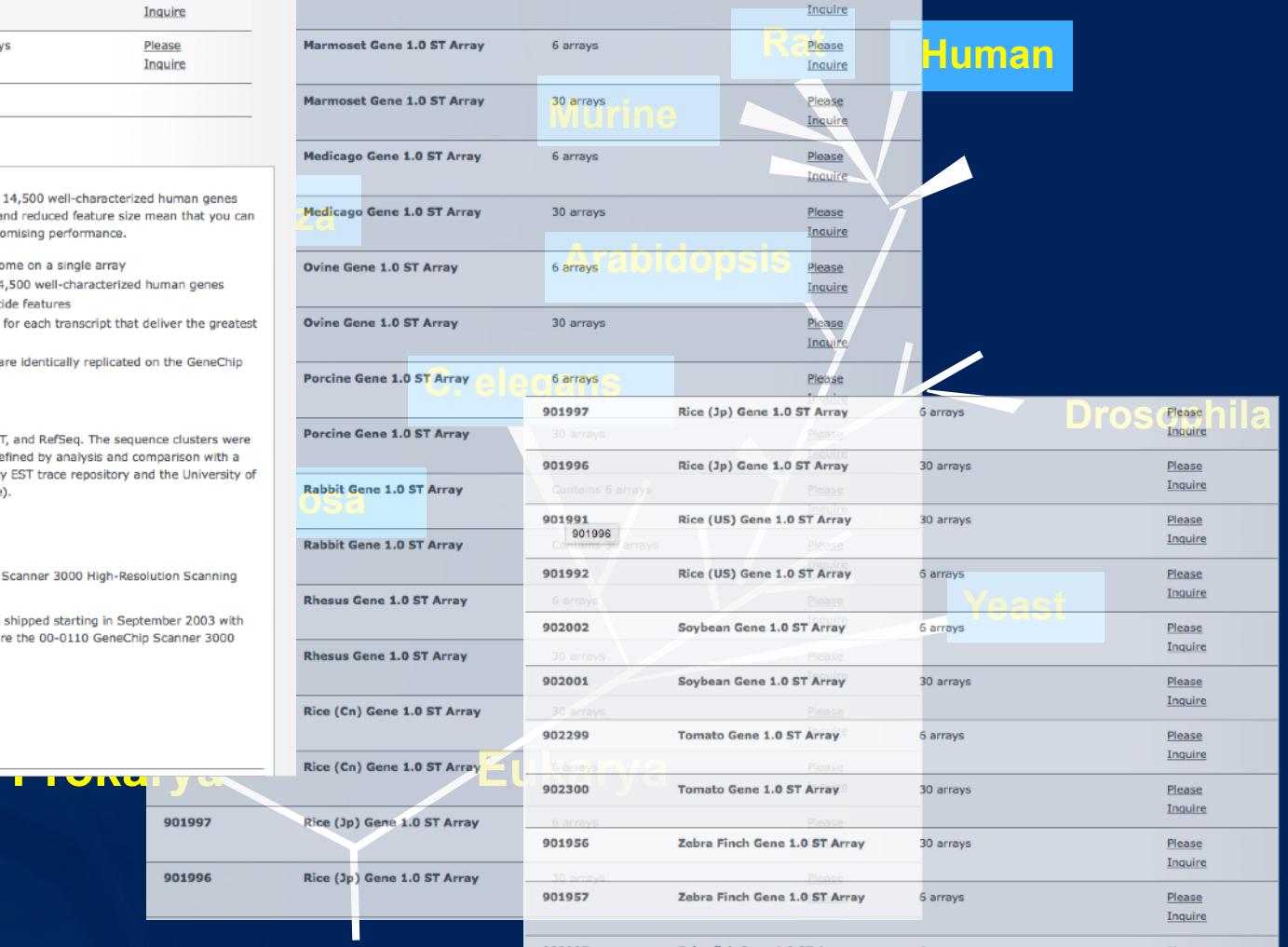
902006	Zebrafish Gene 1.0 ST Array	30 arrays	Please Inquire

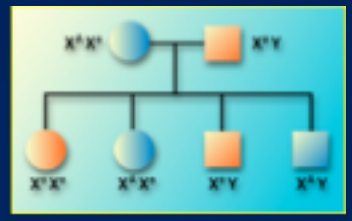


Enabling the Genetic Revolution

Food testing

Livestock diagnostics or grading

Environmental testing



Identity testing

Agricultural biotech

Individualized medicine

Basic Research

Human diagnostics

Understanding Information -Human Genome Project

Gene Functions at a Basic Level

- Gene Identification
  – Which genes are important and in which tissues?
- Pathway Characterization
  – Define relationships between genes
- Regulation
  – Examine motifs on a global scale

Specific Applications in Healthcare & Pharma

- Tumour Typing

  – Use expression patterns to complement classical histology to identify classes of tumors and predict disease development

- Drug ResponseDrug Response

  – Monitor impact of a therapeutic on disease state or toxicological effect

Understanding Cancer

Diagnosis → Classification → Prognosis → Therapeutic Choice

Is it benign?

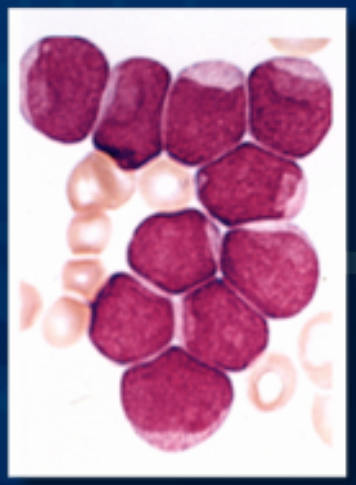
Which class of cancer?

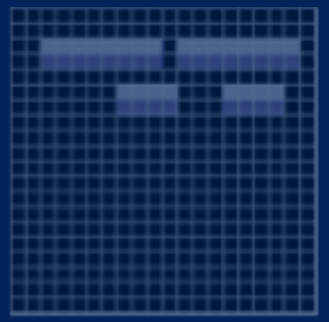
What are my chances?

Which treatment?

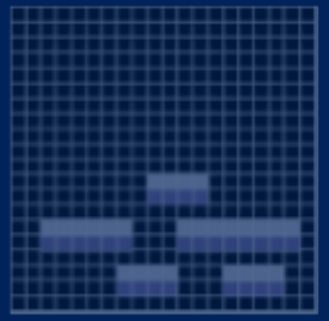
Distinguishing Between Leukaemias

Pediatric **A**cute **M**yeloid **L**eukaemia (**AML**)
T or B cell **A**cute **L**ymphoblastic **L**eukaemia (**ALL**)
Mixed **L**ineage **L**eukamias (**MLL**)





ALL



AML

MLL

Which class of leukemia?

Golub, T.R., et al. **Science** 286: 531-537, 1999; Armstrong, S.A., et al. **Nature Genetics** 30: 41- 47, 2002

Individual Variations in Drug Metabolism

Cytochrome P450, Detoxification Enzymes

Cytochrome P450 (CYP) enzymes are a superfamily of mono-oxygenases that are found in all kingdoms of life, and which show extraordinary diversity in their reaction chemistry. In mammals, these enzymes are found primarily in the membranes of the endoplasmic reticulum (microsomes) within liver cells (hepatocytes), as well as many other cell types. These enzymes use haeme iron to oxidise molecules, often making them more water-soluble for clearance.

They achieve this by either adding or unmasking a polar group. In general, the reaction catalysed by these enzymes can be summarised as:

Individual Variations in Drug Metabolism

"Intestinal cytochrome P450 proteins play an important role in the biotransformation of drugs and may significantly limit their oral absorption."

Drug Metabolism and Disposition, **June 2008** vol. 36 no. 6 **1039-1045**

Int J Clin Pharmacol Res. 2003;23(1):31-5.

Genetic polymorphism of cytochrome P450 enzymes in Asian populations: focus on CYP2D6.

Kitada M[1].

⊕ **Author information**

Abstract

Published studies demonstrate that significant ethnic differences can exist in the metabolism of some drugs. These differences are caused by cytochrome P450 polymorphisms and result in the potential for wide interpatient and interethnic variability in adverse events. One of the most common of these cytochrome P450 polymorphisms is related to the CYP2D6 isozyme. Many classes of commonly used drugs are metabolized by CYP2D6, creating the potential for significant adverse events. Due to the variety of genetic polymorphisms among Asian populations, this article focuses on this group rather than on other ethnic populations and discusses the clinical importance of genetic polymorphisms with regard to potential drug interactions. Polymorphism of CYP2D6 can either increase the rate of drug elimination (ultrametabolizers, leading to faster metabolic clearance potentially resulting in reduced effectiveness and need for higher doses) or decrease drug metabolism (poor metabolizers, which may increase the potential for drug interactions and adverse events). Although the CYP2D6 poor metabolizer phenotype is less frequent in Asian than in Western populations (e.g. about 1% in Thai, Chinese and Japanese populations and up to 4.8% in Indians versus 5-10% in Caucasians), the increased prevalence of the CYP2D6*10 allele in Asians does have an impact on drugs metabolized by CYP2D6. Enzyme activity is reduced, potentially increasing circulating drug doses and increasing the risk for drug interactions. Thus, in Asian populations it may be important to optimize pharmacotherapy either by assessing patients' CYP2D6 genotype, or by prescribing medications that are not metabolized by this isozyme.

PMID: 14621071

[PubMed - indexed for MEDLINE]

Individual Variations in Drug Metabolism

CYP450 genes metabolize more than 90% of commercially available drugs

Poor Metabolizers
- Two mutant alleles
- No enzyme activity

Intermediate Metabolizers
- One reduced activity allele
- One null allele

Extensive Metabolizers
- At least one normal allele

Ultrarapid Metabolizers
- Multiple functional alleles
- Excess enzymatic activity

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What is GeneChip® Technology?

GeneChip® System

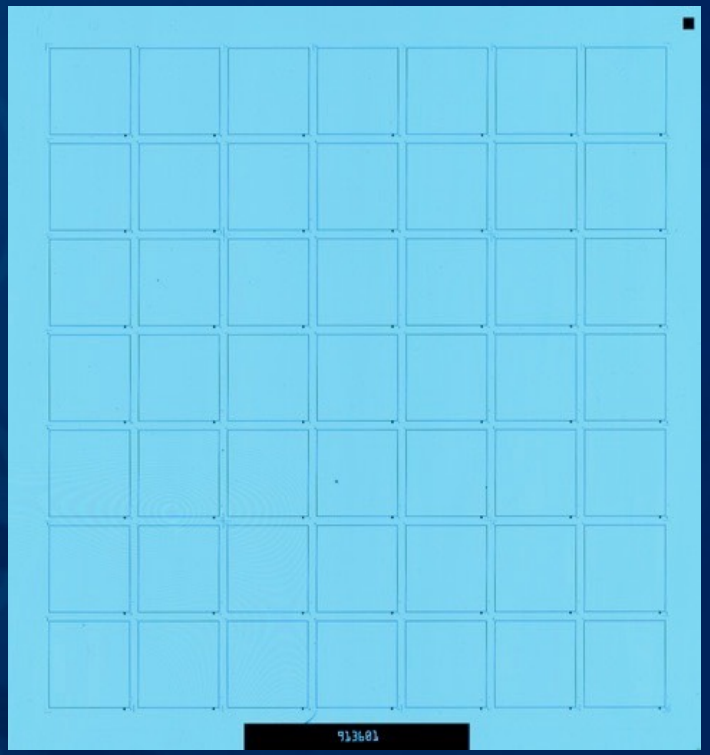
Probe Arrays (chips)

Fluidics Station

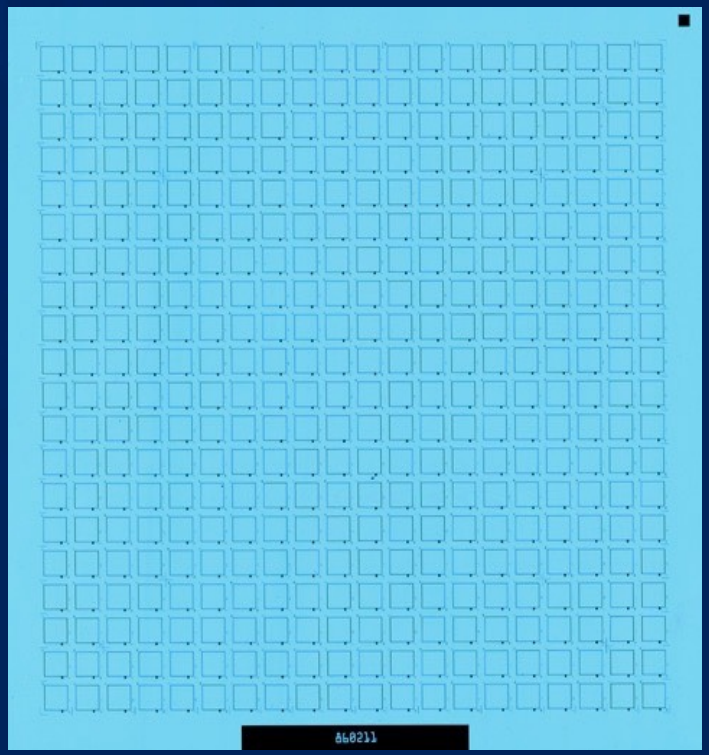
Scanner

Software Data Analysis

GeneChip® Technology?

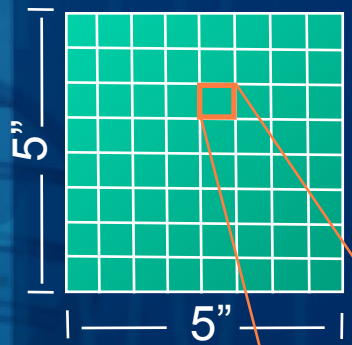


49 Chips per Wafer



400 Chips per Wafer

GeneChip Probe Arrays

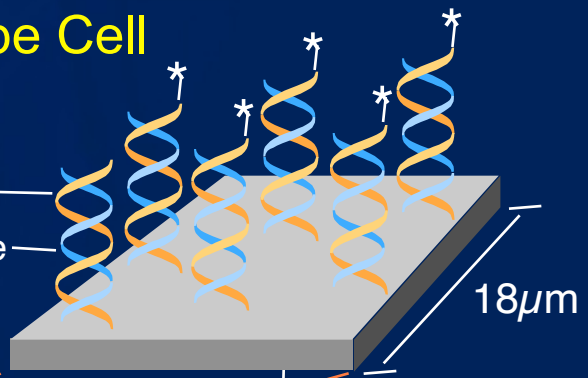


49 - 400
Chips/wafer

Hybridized Probe Cell

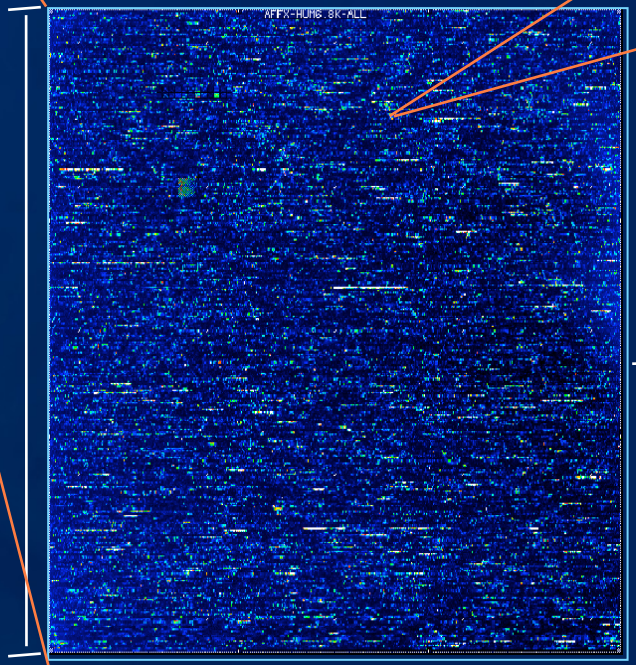
Single stranded, fluorescently labeled DNA target

Oligonucleotide probe



Each probe cell or feature contains millions of copies of a specific oligonucleotide probe

1.28cm



1.28cm

Over 500,000 different probes complementary to genetic information of interest

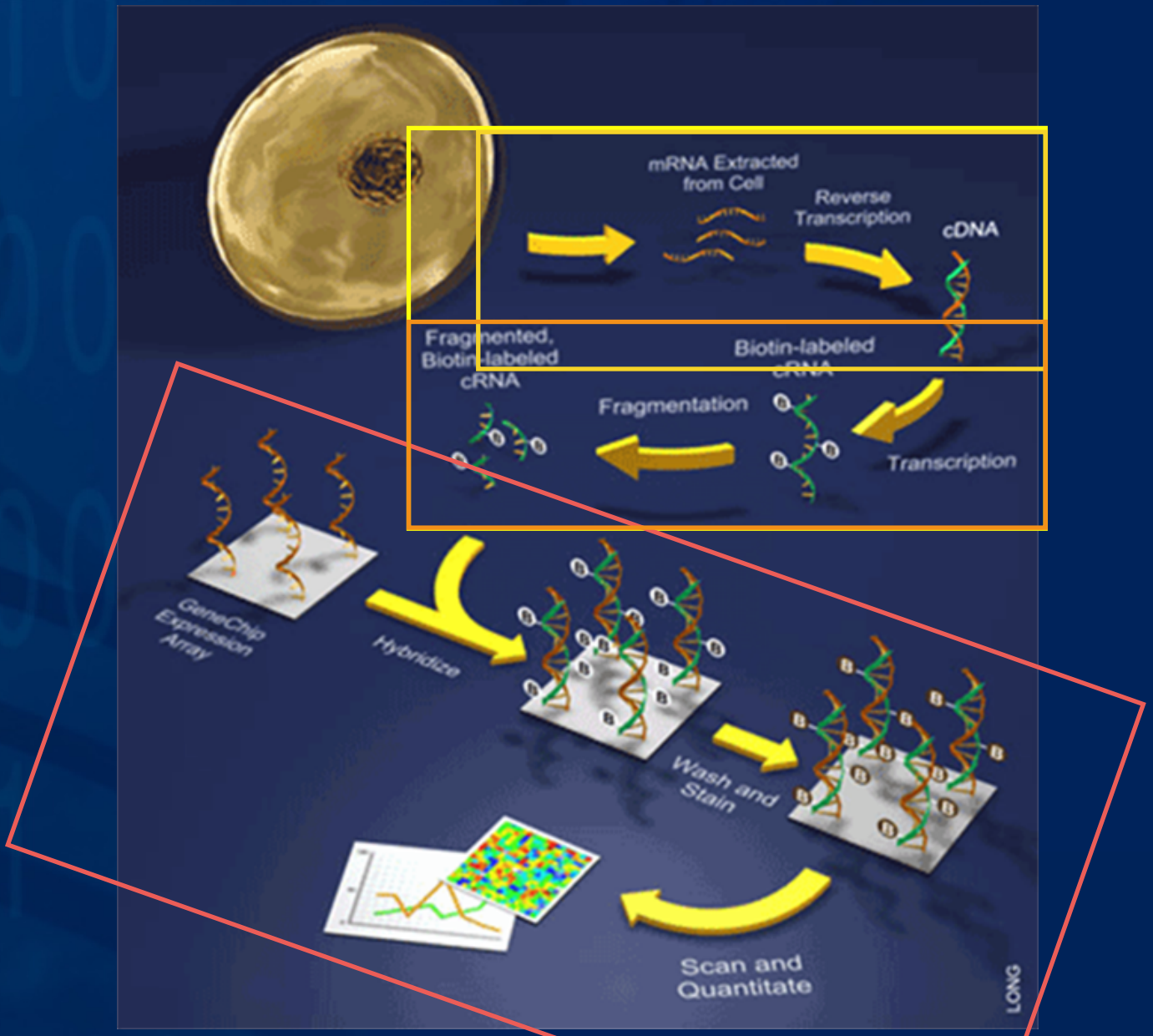
Image of Hybridized Probe Array

GeneChip® Array Advantages

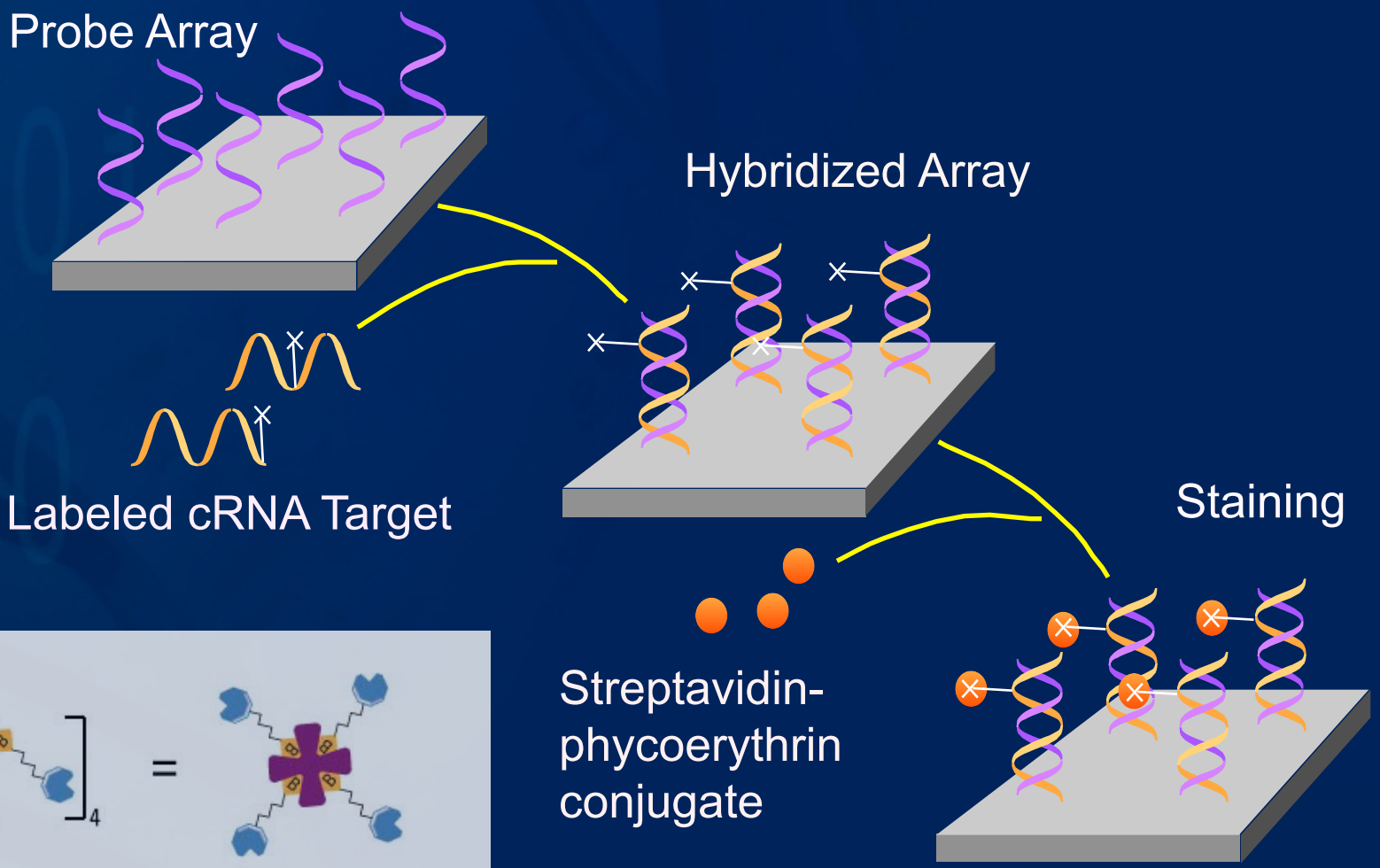
- Assume fixed array size, 1.28 x 1.28 cm

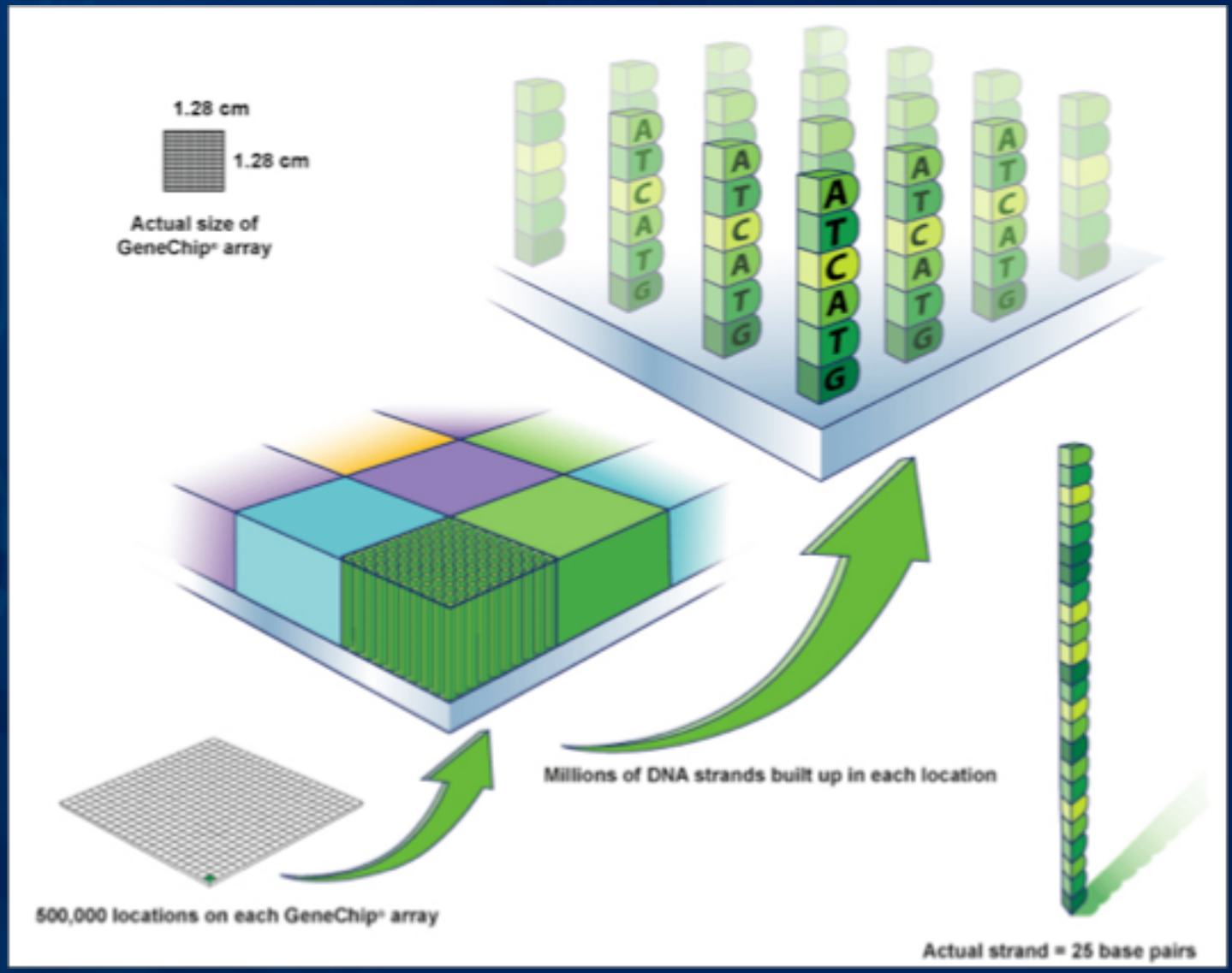
Feature Size	Features/Chip	Genes/Chip
100 µm	16,384	409
50 µm	65,538	1,638
24 µm	284,444	7,111
20 µm	409,600	12,800
18 µm	506,944	~ 22,500
10 µm	1,600,000	>200,000

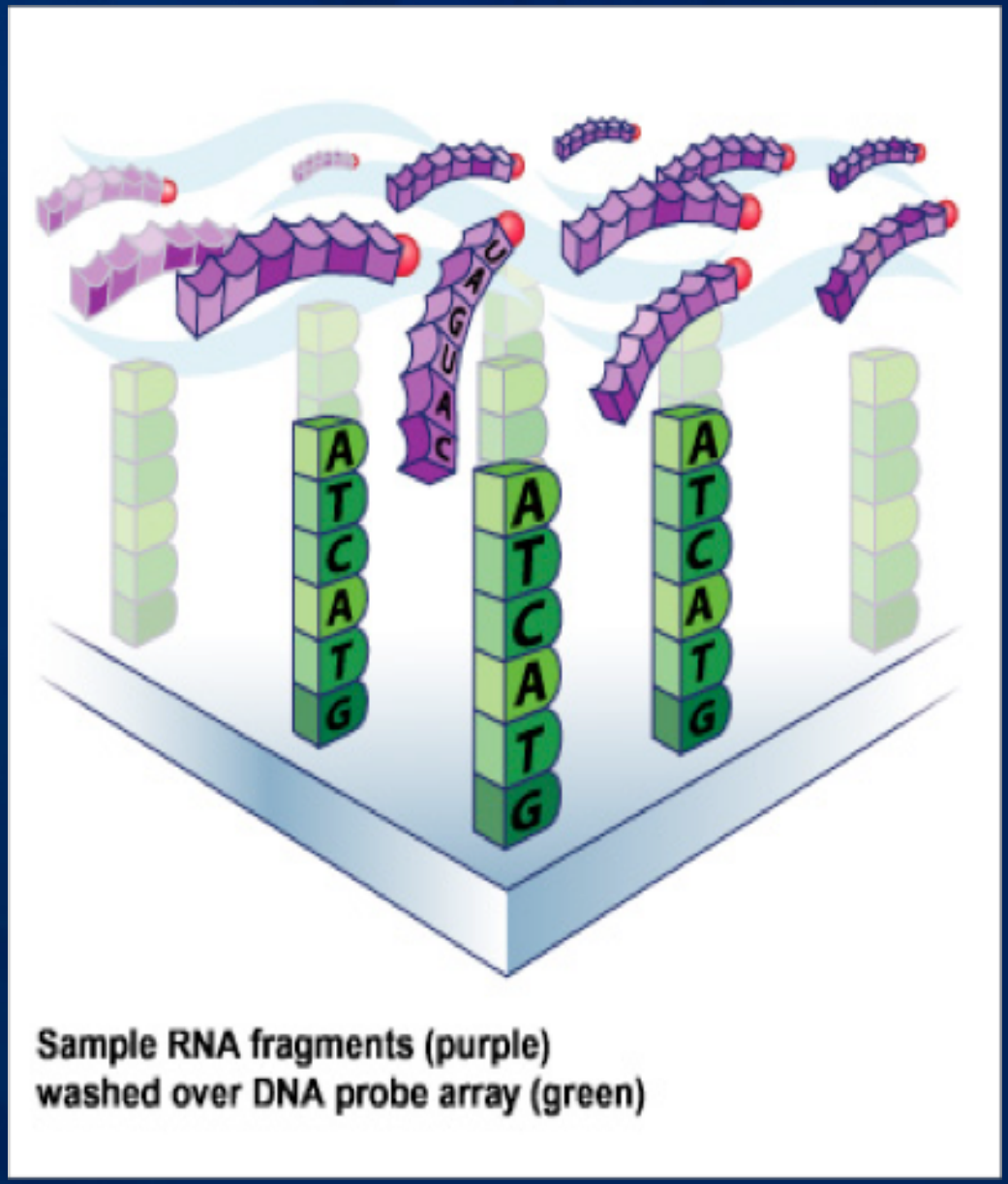
GeneChip® Expression Analysis
Hybridization and Staining



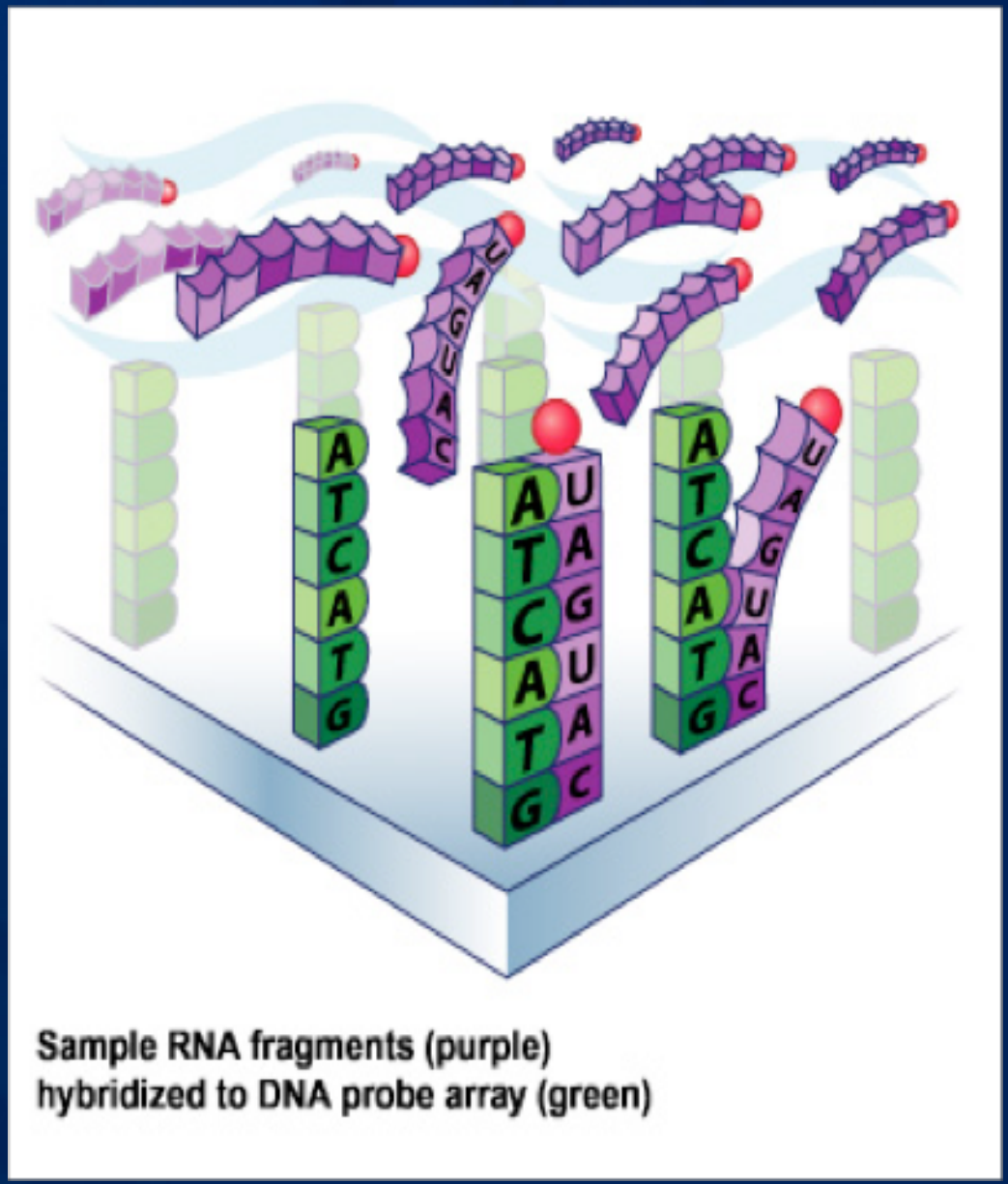
GeneChip® Expression Analysis
Hybridization and Staining



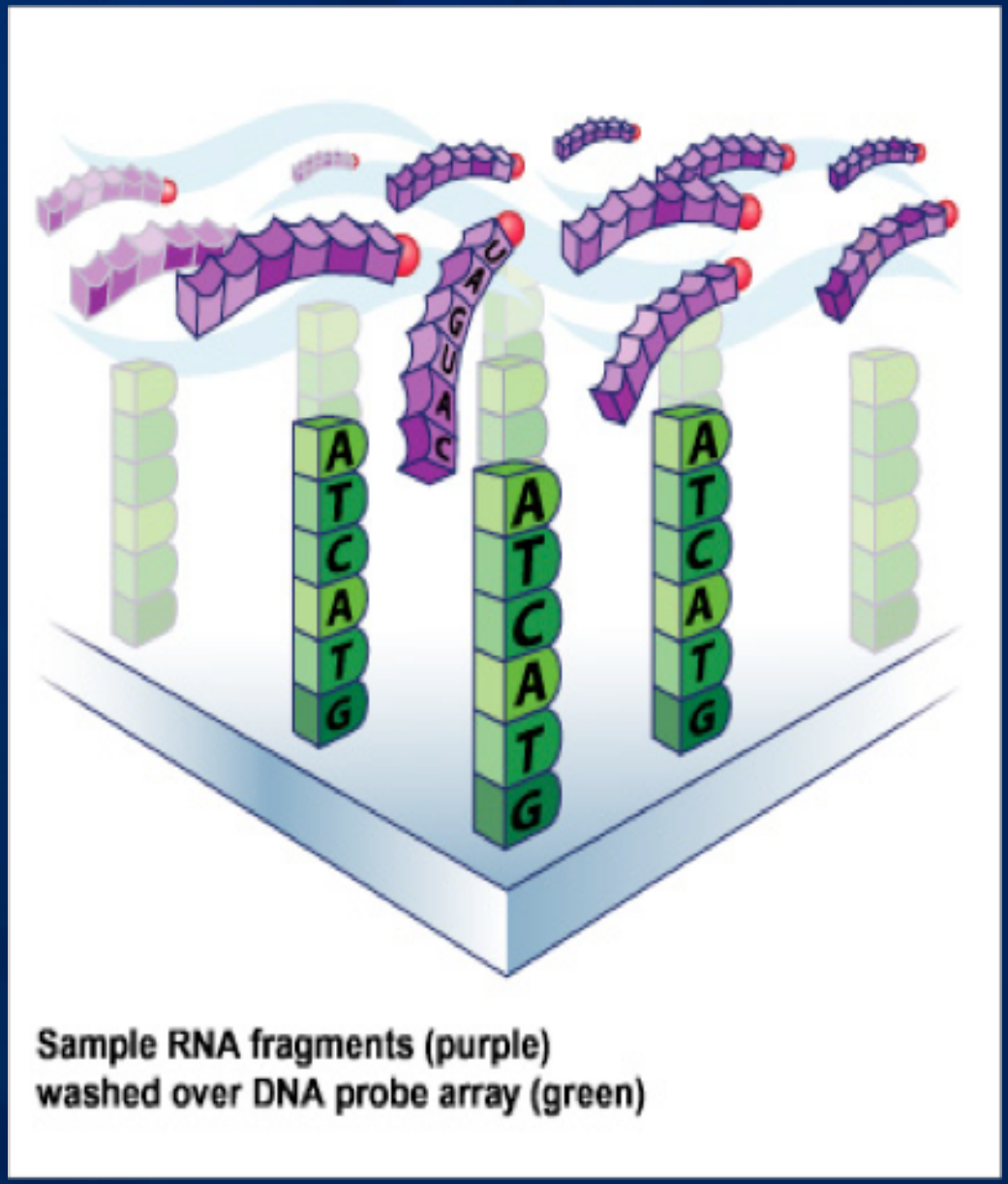

1.28 cm
1.28 cm
Actual size of GeneChip® array
A T C A T G
Millions of DNA strands built up in each location
500,000 locations on each GeneChip® array
Actual strand = 25 base pairs



Sample RNA fragments (purple)
washed over DNA probe array (green)



Sample RNA fragments (purple)
hybridized to DNA probe array (green)



Sample RNA fragments (purple)
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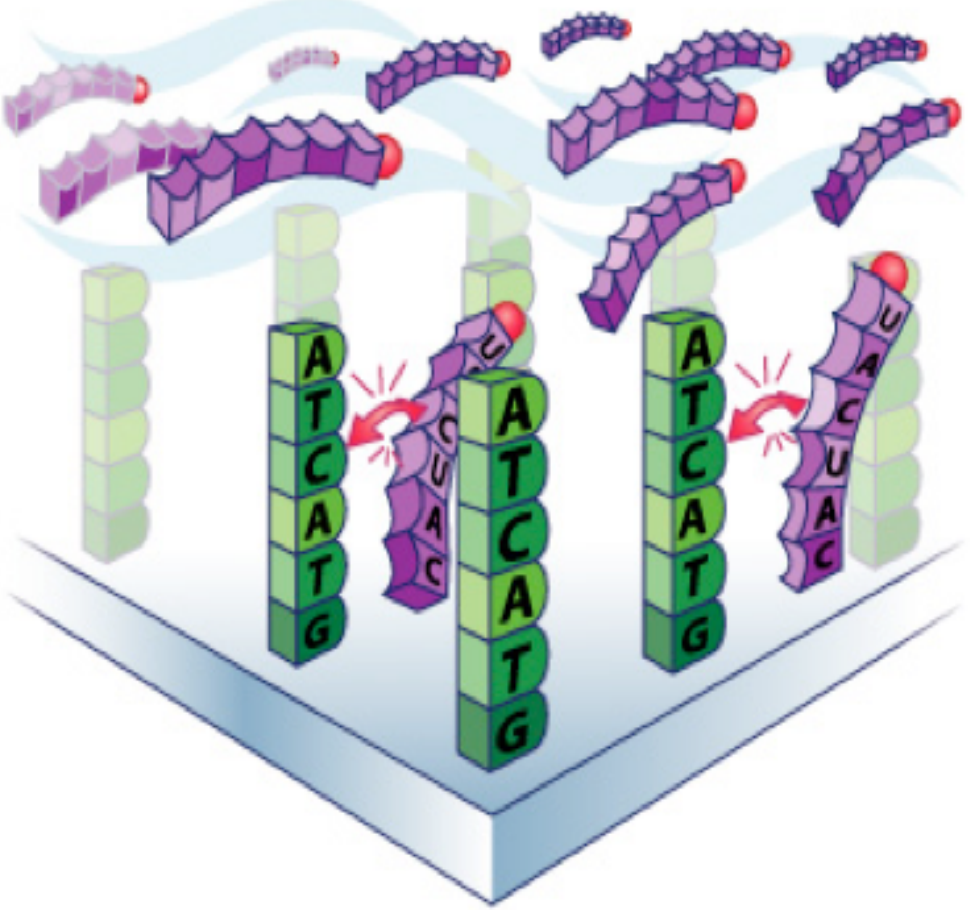
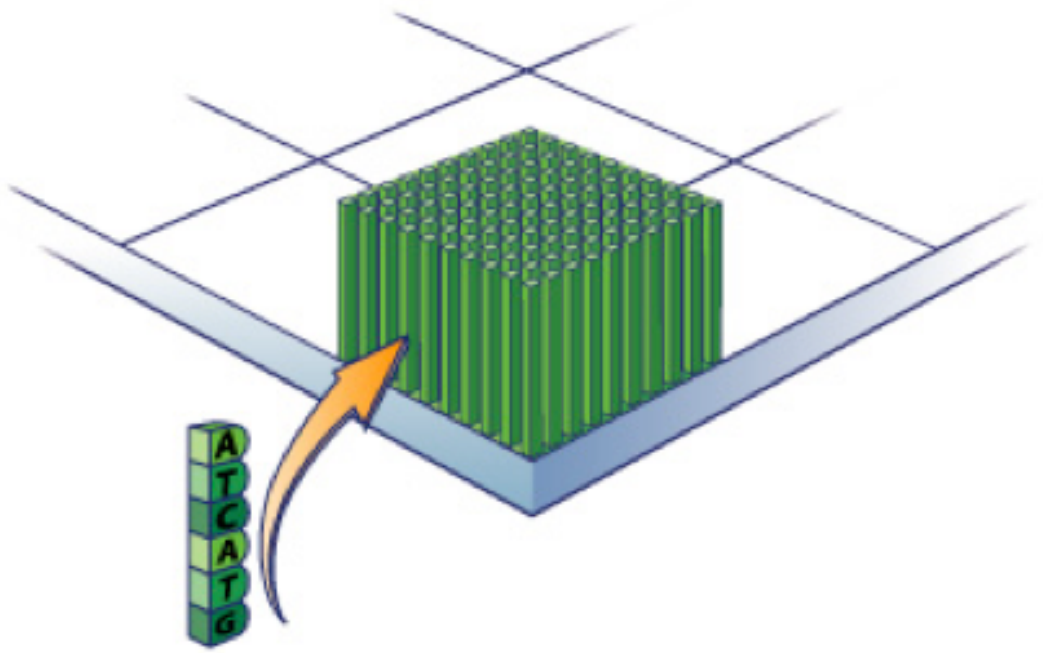
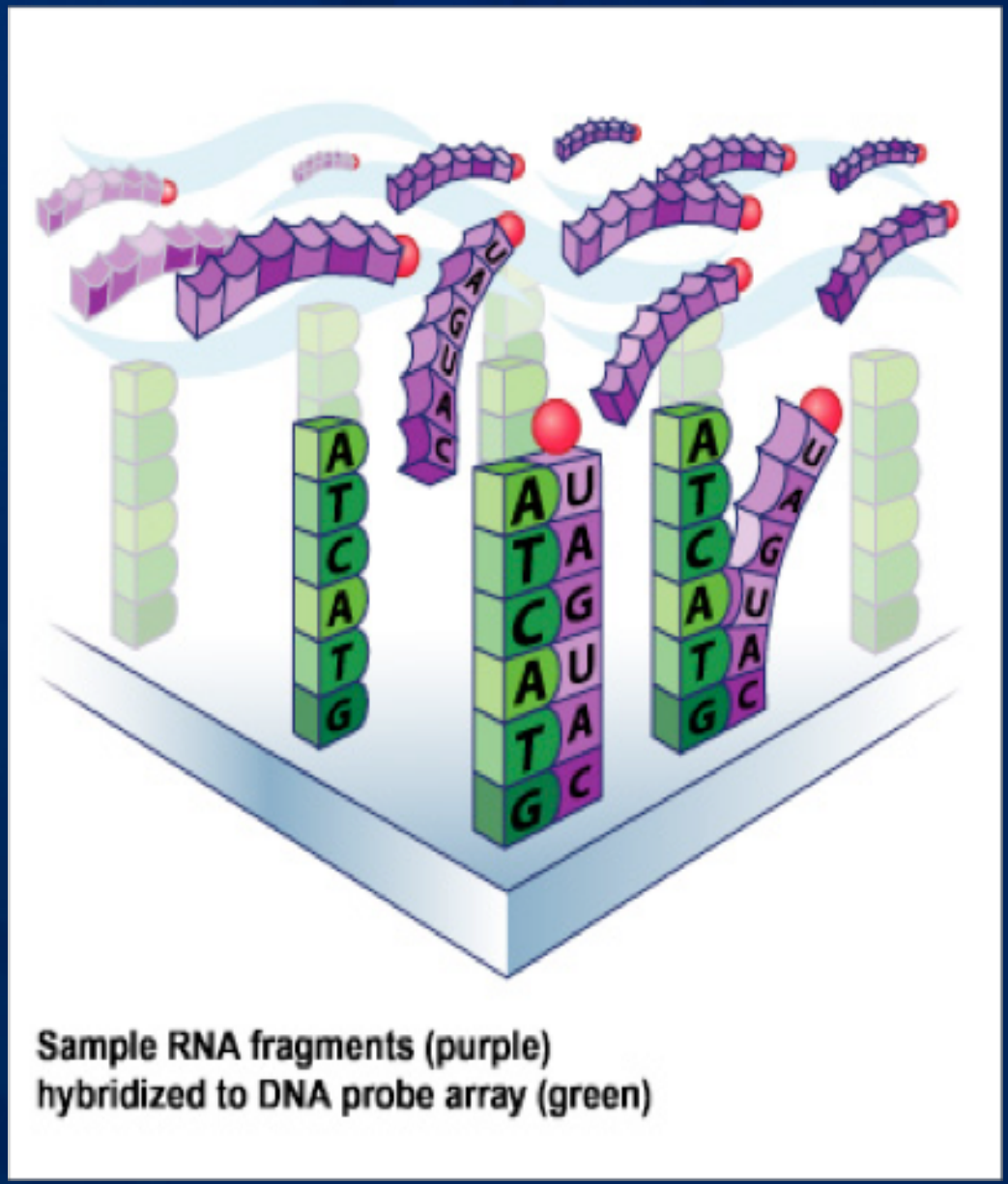


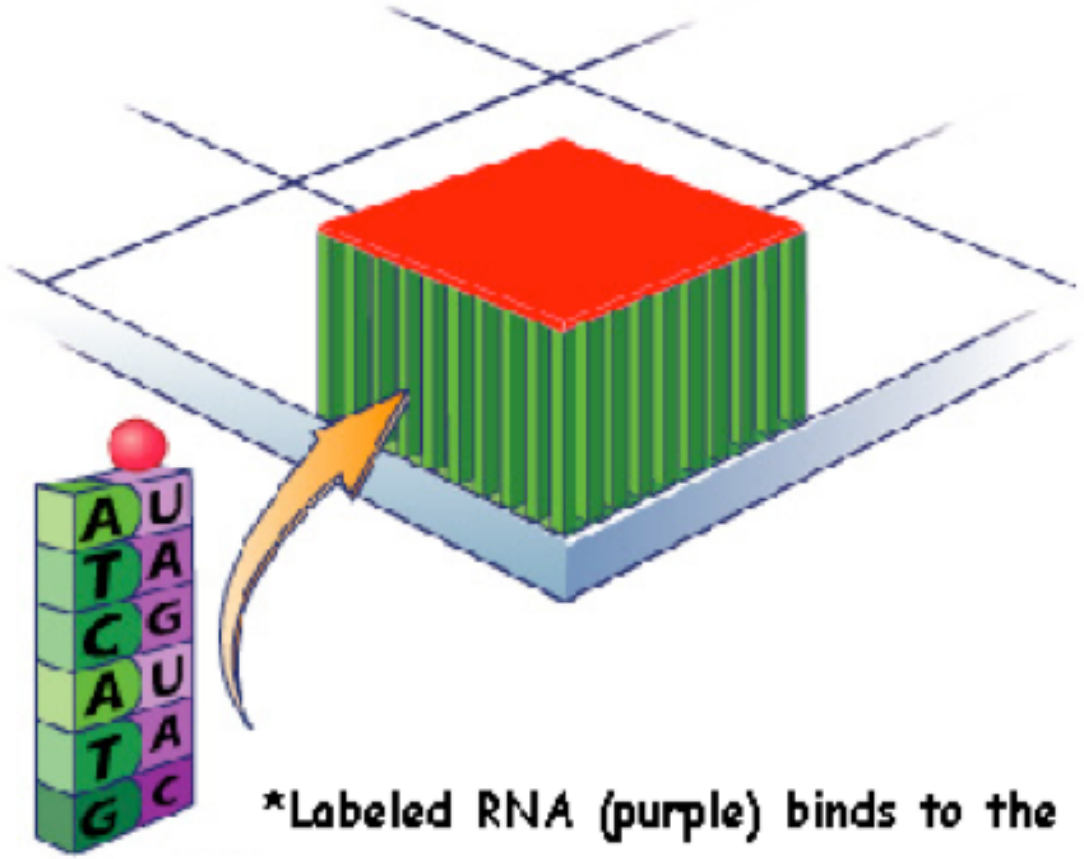
C does not stick to another C,
so no match is made



We know there was no match because
there is no fluorescent RNA bound to the probe.



Sample RNA fragments (purple)
hybridized to DNA probe array (green)

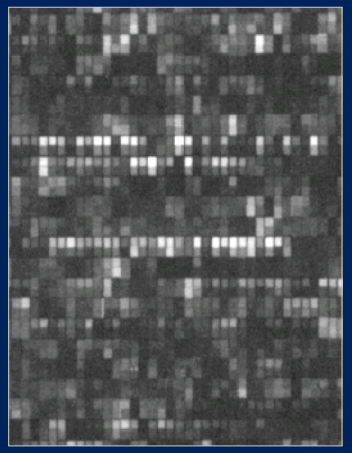


*Labeled RNA (purple) binds to the matching probes in the single feature.

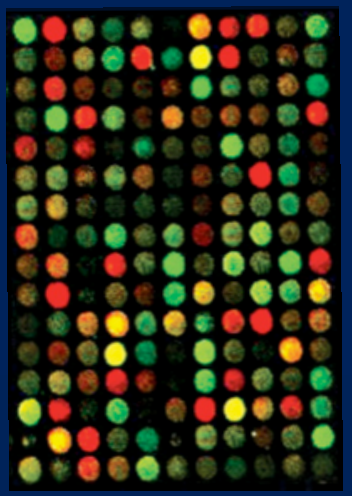
*The feature will now fluoresce

GeneChip® vs. Spotted Arrays

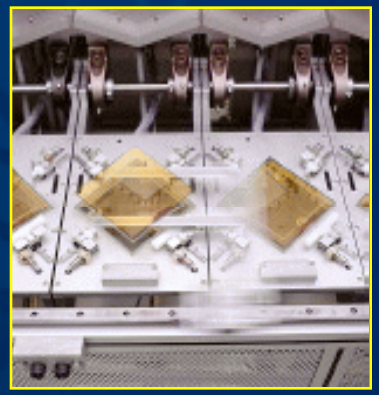
- Affymetrix GeneChip® Arrays use oligonucleotides
  - Oligos are built on a solid support



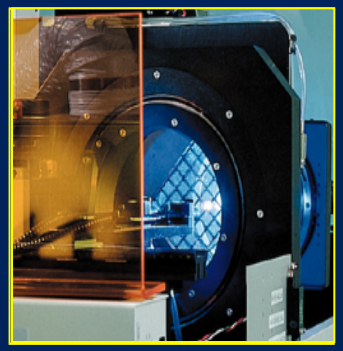
- Spotted arrays utilize nucleic acids made in solution
  - Solutions are then “spotted” onto a solid support
  - Competitive Hybridization



Proven Manufacturing Systems



Wafer Prep

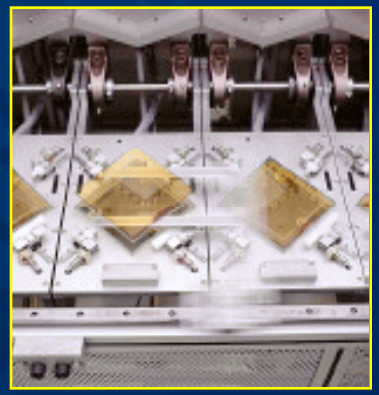


Photolithography

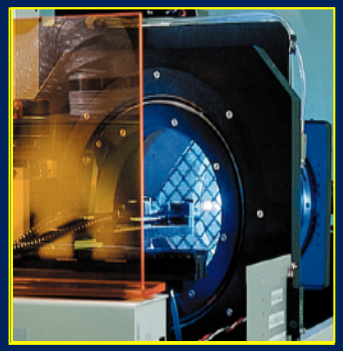
Cartridge Assembly

Finished GeneChip
Probe Array

Proven Manufacturing Systems



Wafer Prep



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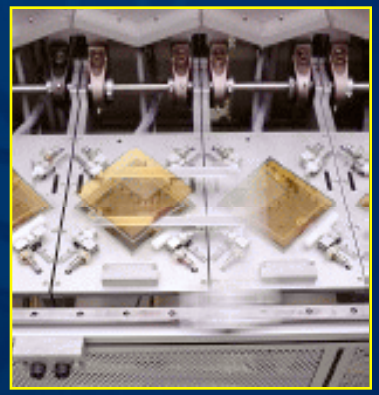

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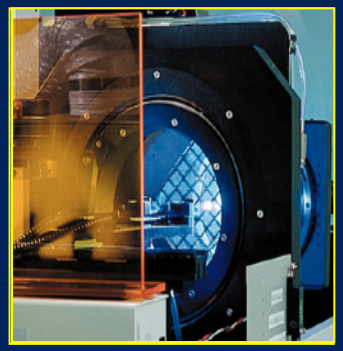

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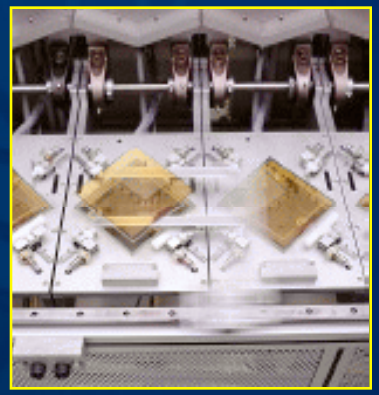
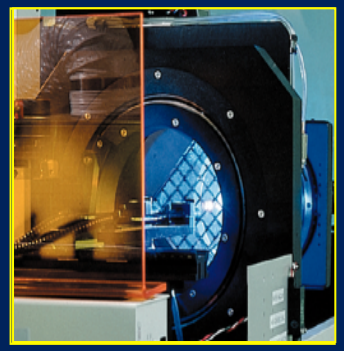


Wafer Prep

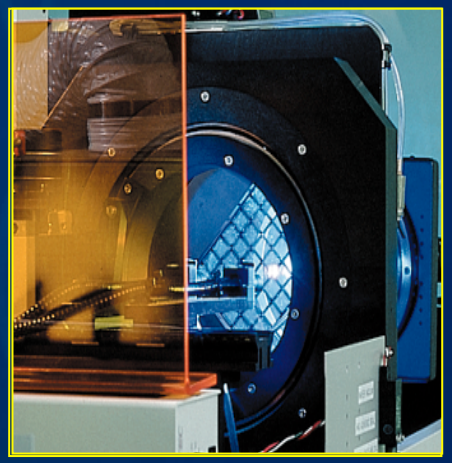


Photolithography

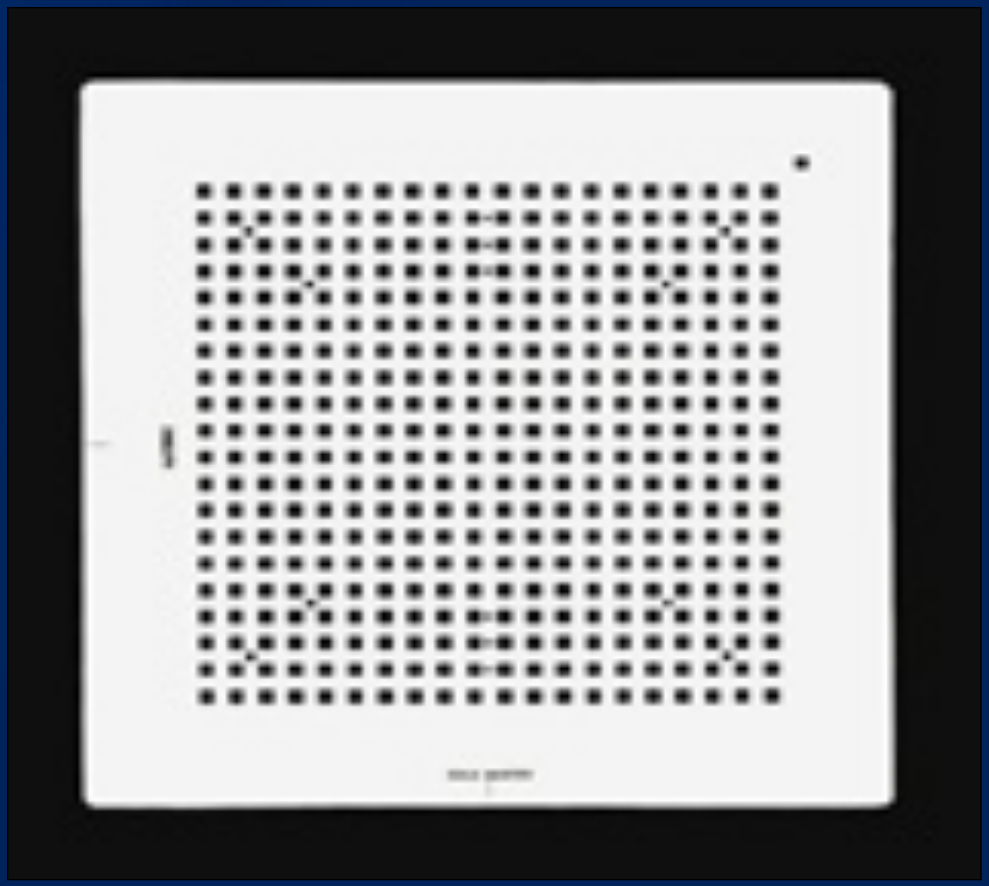
Cartridge Assembly

Finished GeneChip
Probe Array

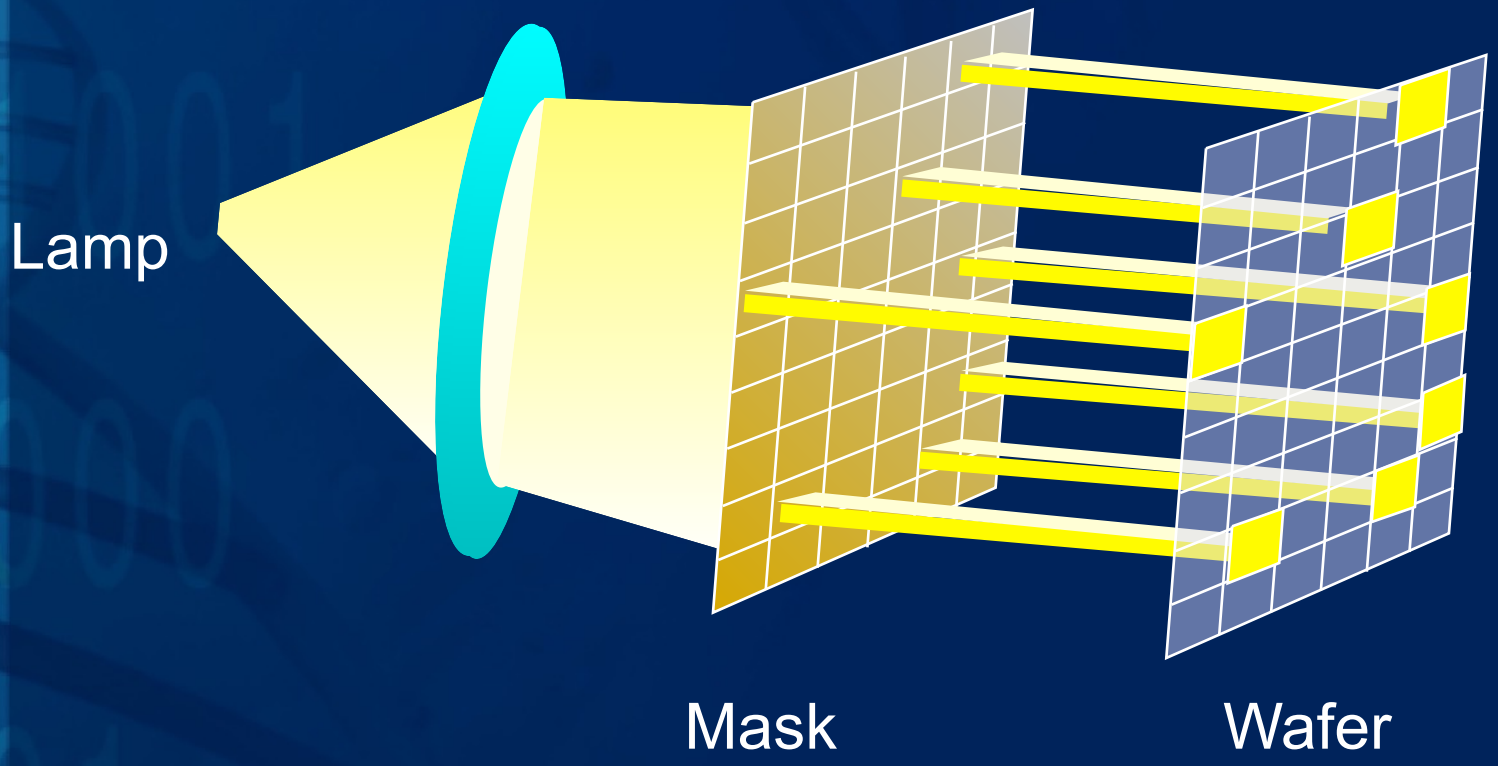
Photolithographic Synthesis



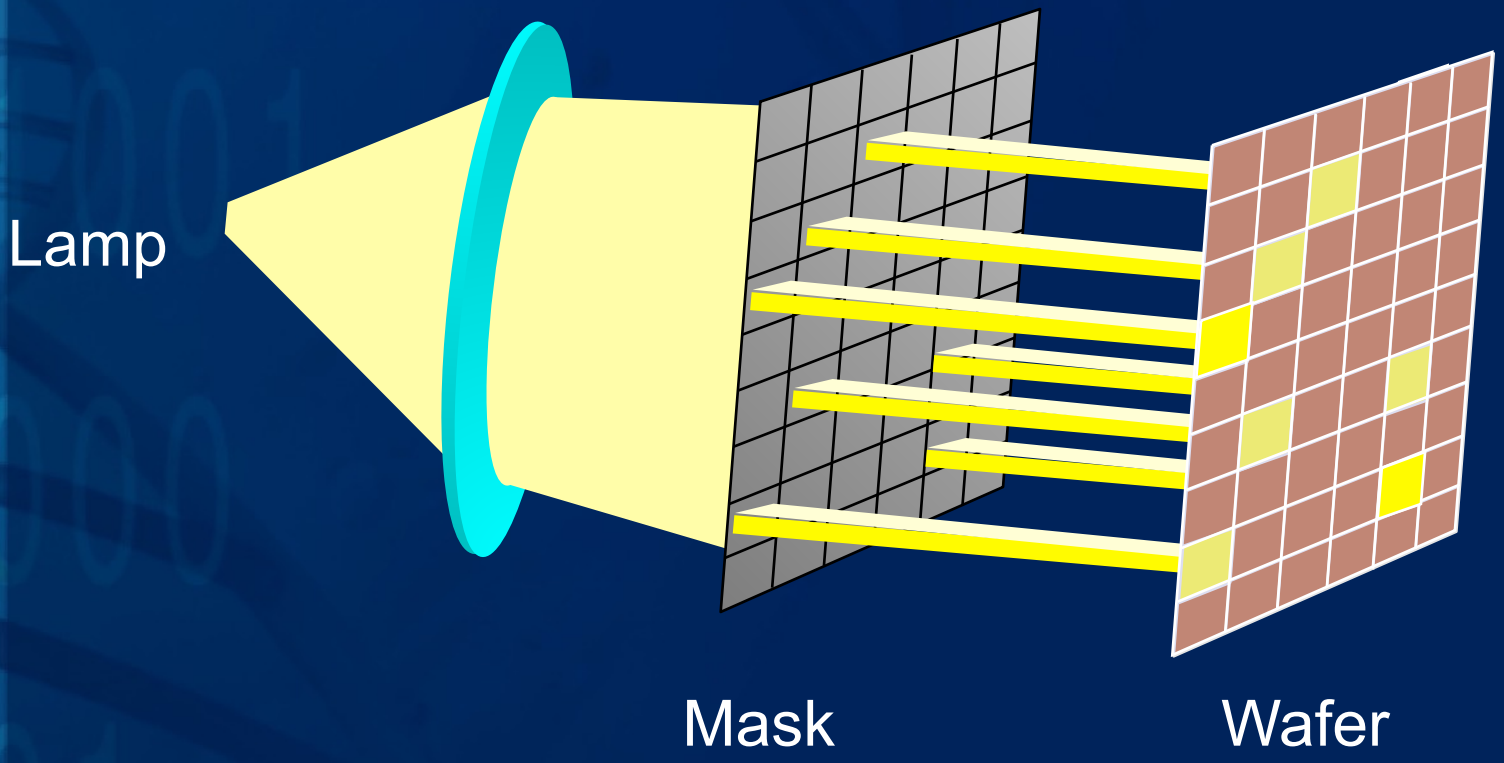
Photolithography



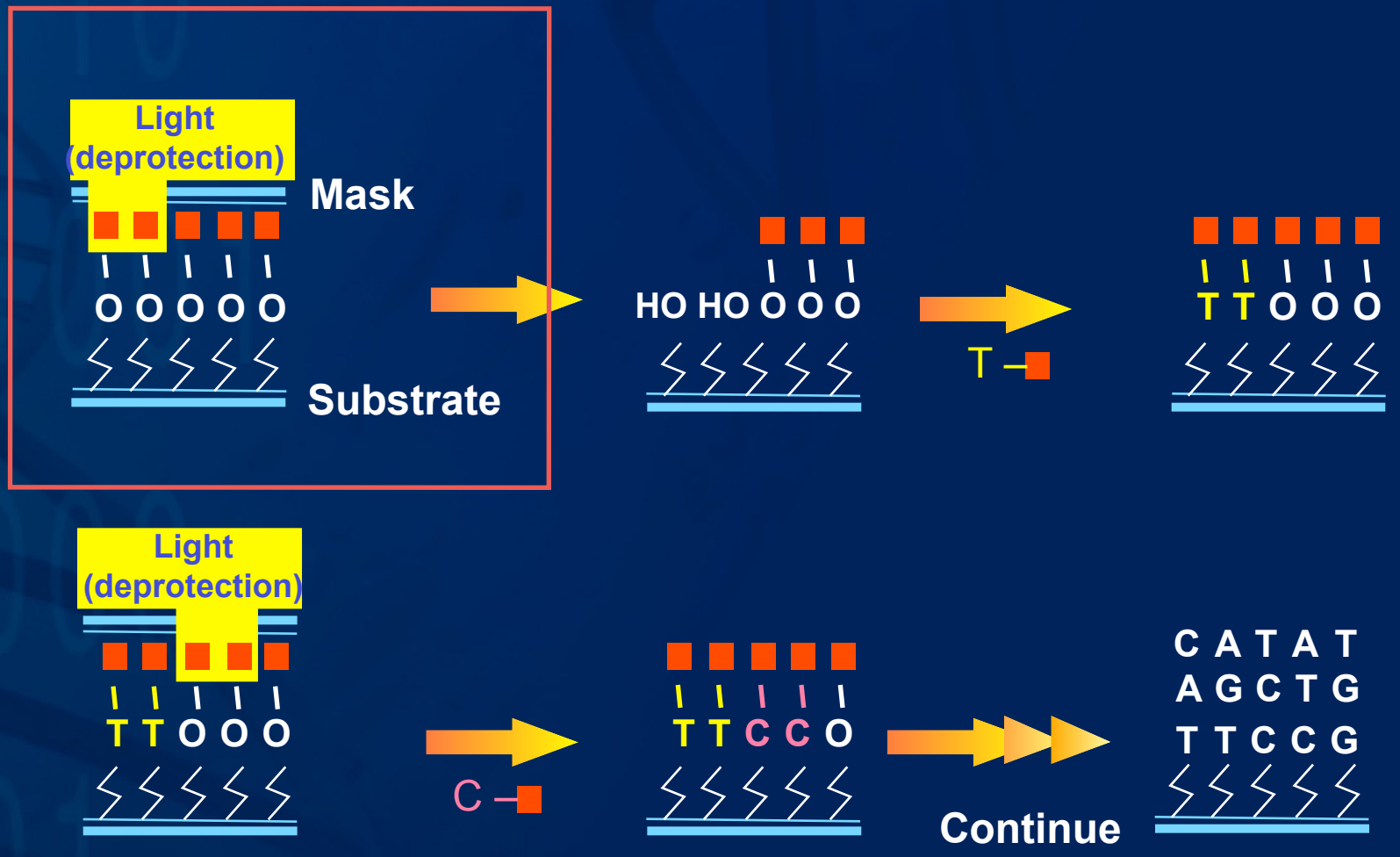
Photolithographic Synthesis



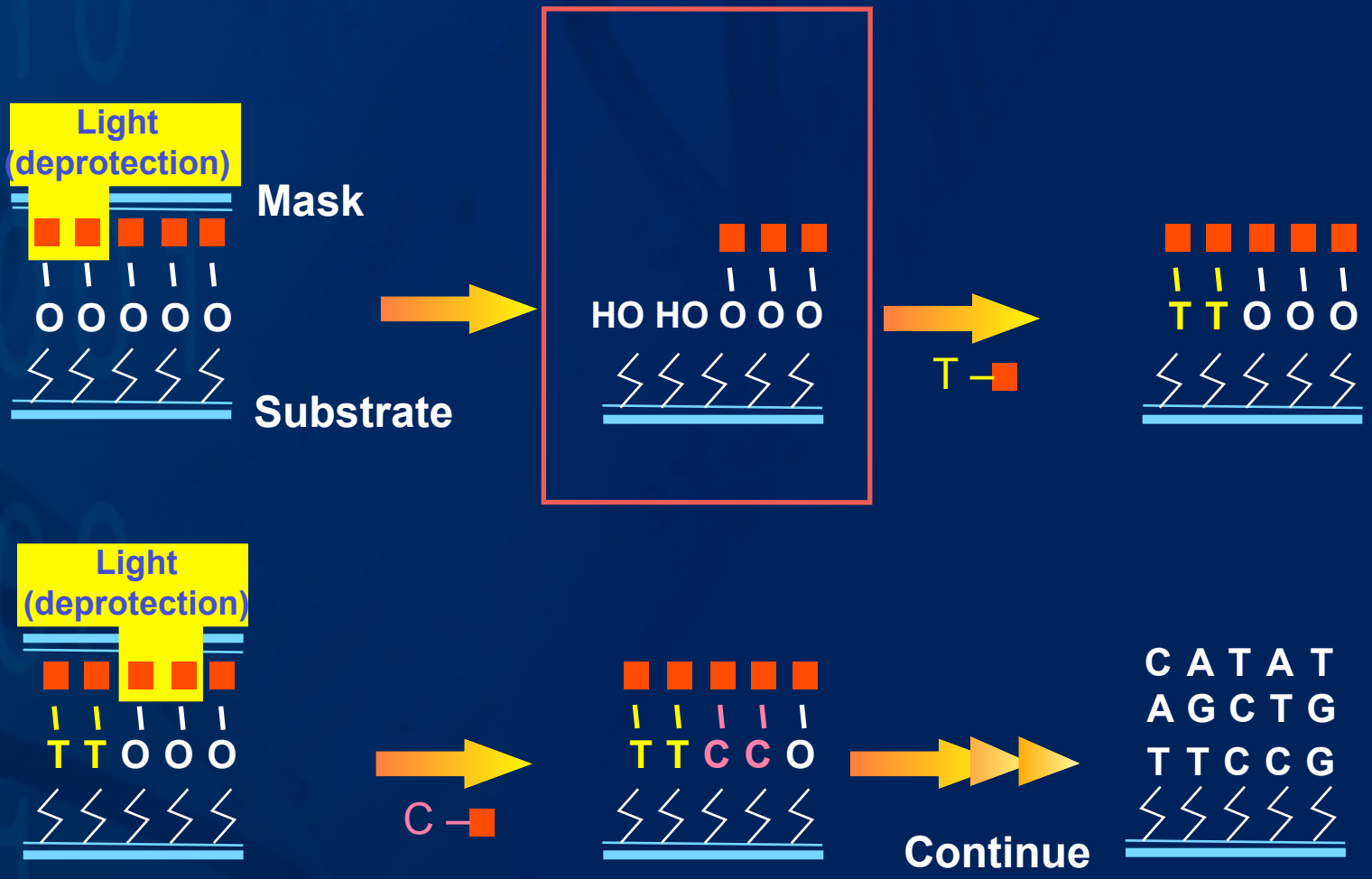
Photolithographic Synthesis



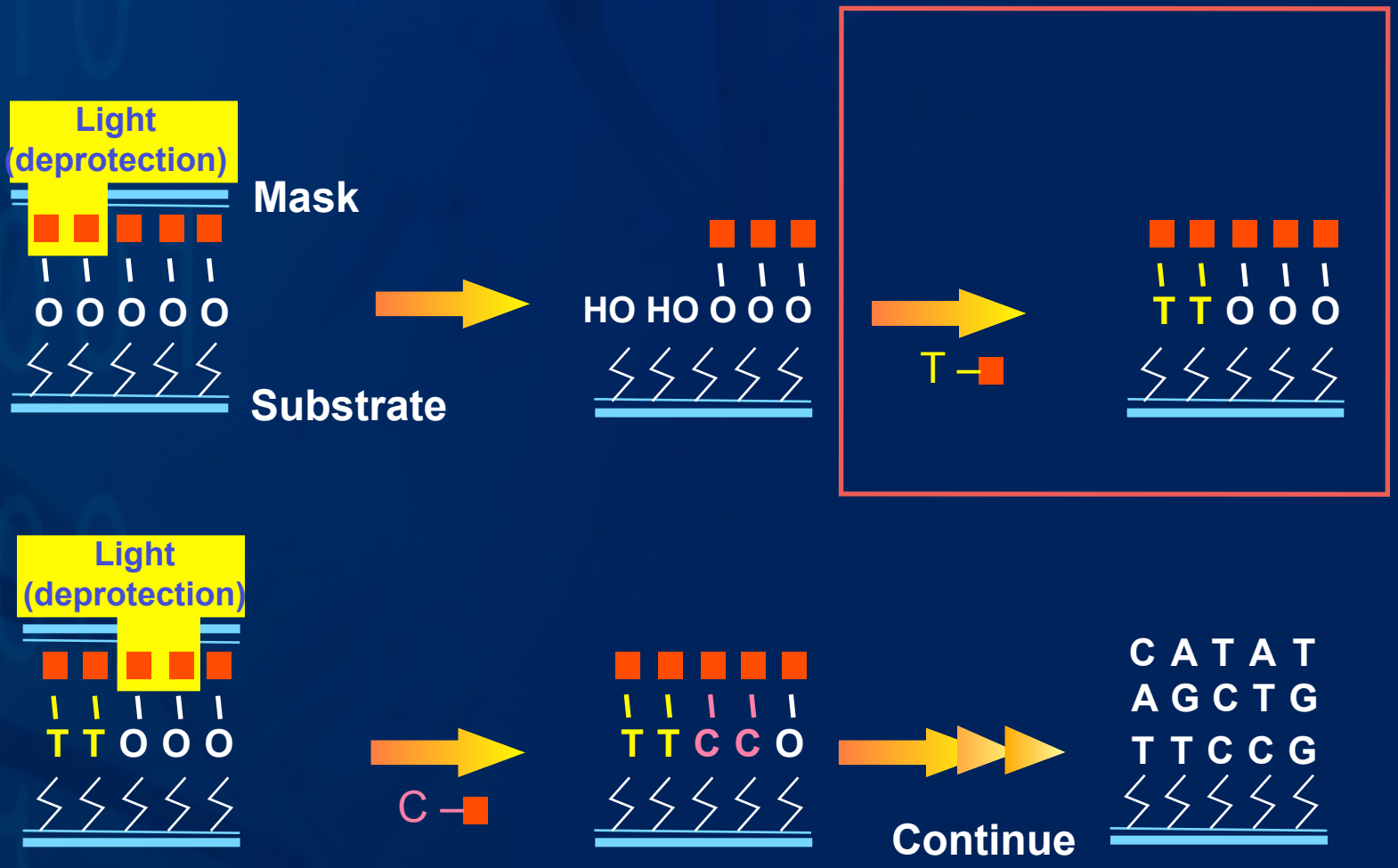
How Probes Are Synthesized



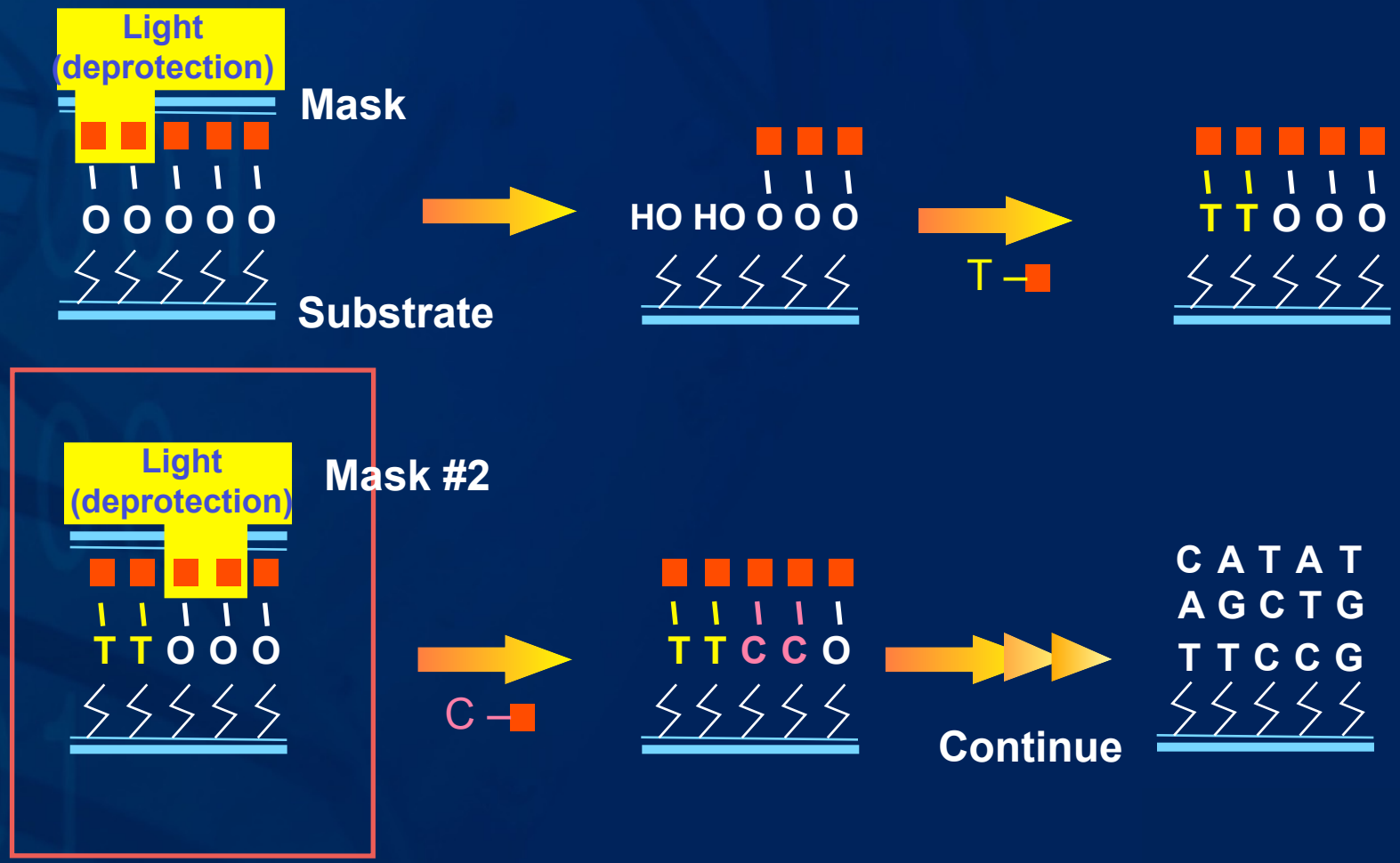
How Probes Are Synthesized



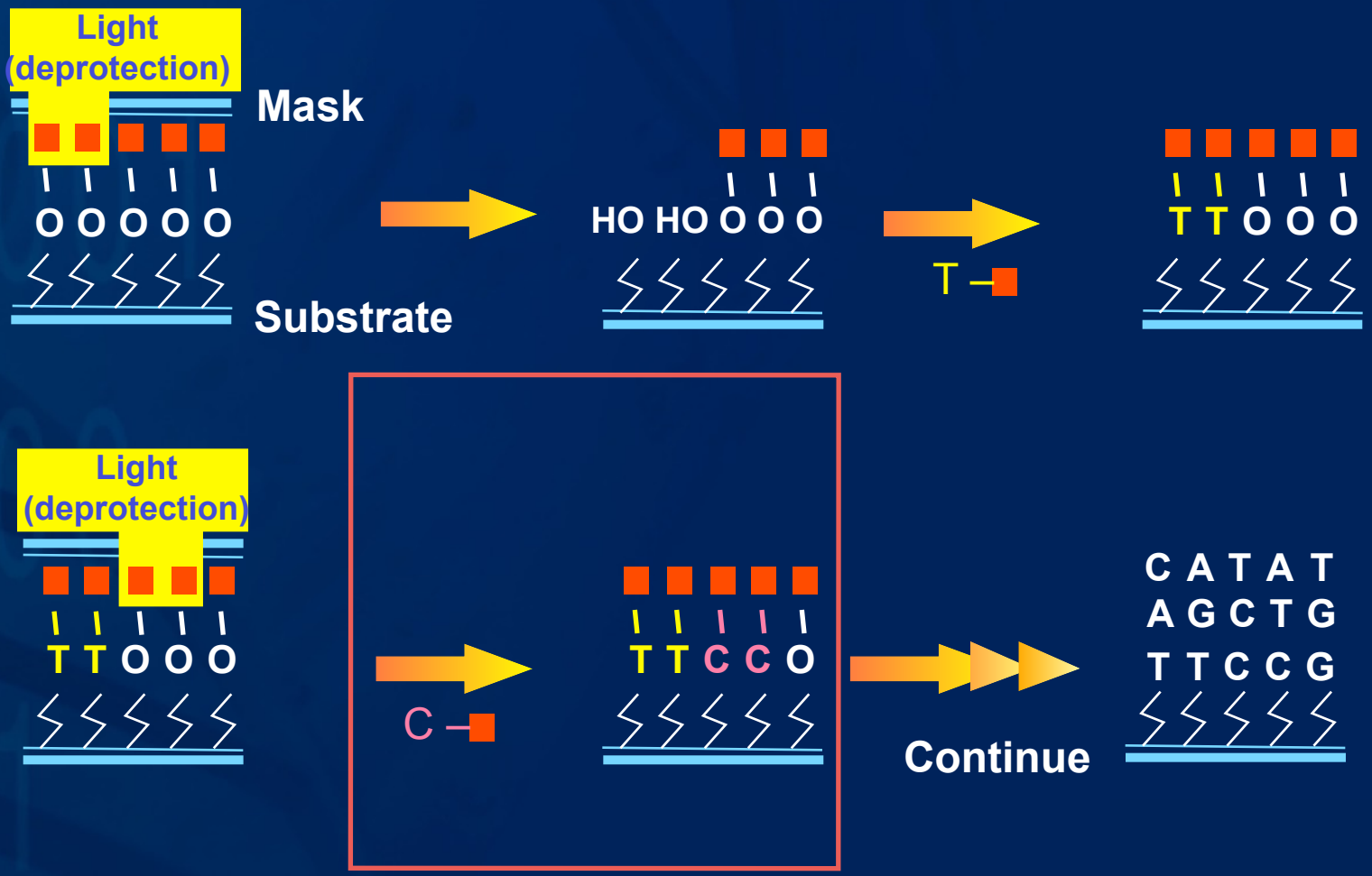
How Probes Are Synthesized



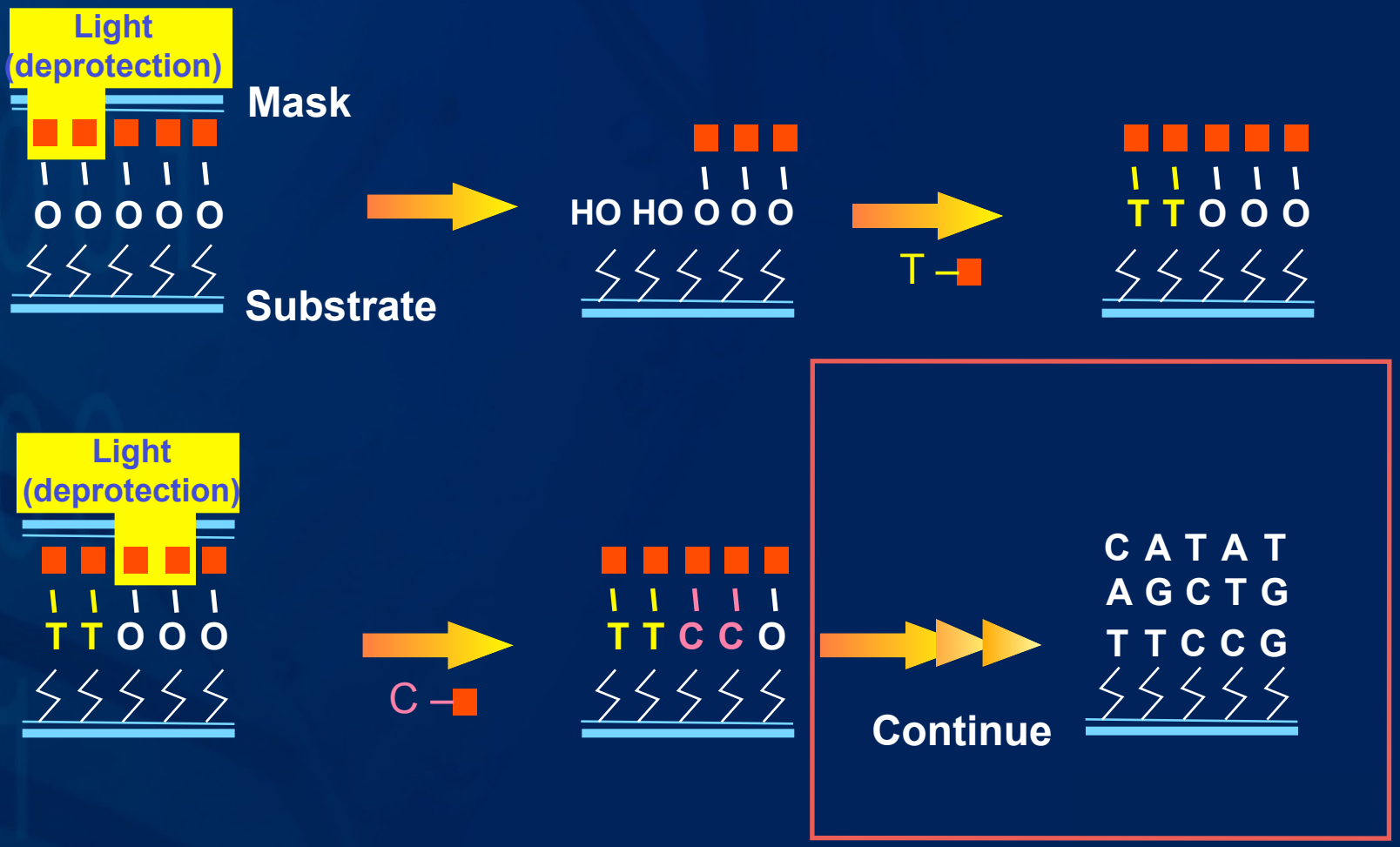
How Probes Are Synthesized



How Probes Are Synthesized



How Probes Are Synthesized

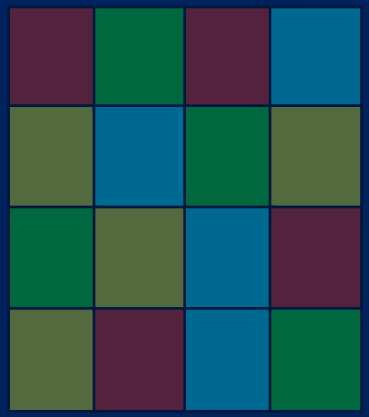


Combinatorial Synthesis

Any N-mer can be synthesized in 4 x N steps

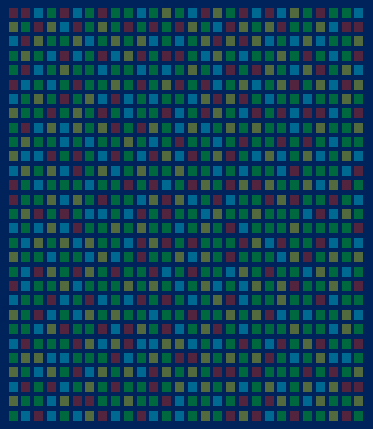
Example:

Sixteen 20-mers



< 80-step synthesis

~10^{12} 20-mers



< 80-step synthesis

Applications of Gene Expression

- Basic Research
- Cell Cycle
- Signaling Pathways
- Regulation of cell differentiation

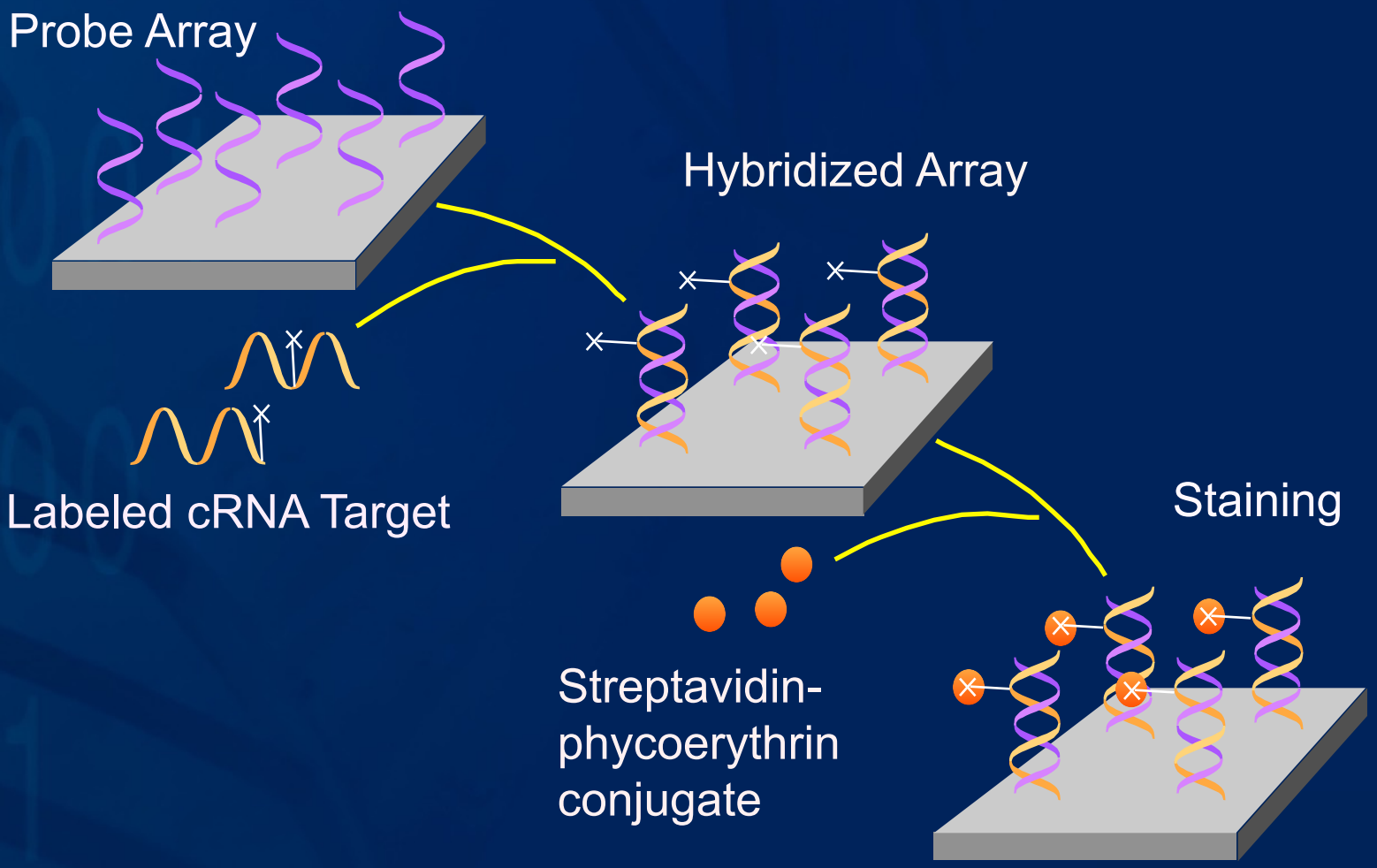
- Genetic Basis of Disease
- Genetic changes in cancer; classification
- Metabolic diseases
- Aging-related biological pathologies
- Immune system pathologies
- Infectious diseases

- Target Discovery and Drug Development
- Analyze disease models to discover drug targets
- Profile drug candidates using expression data
- Analyze drug toxicity in various model systems

GeneChip® Array Advantages

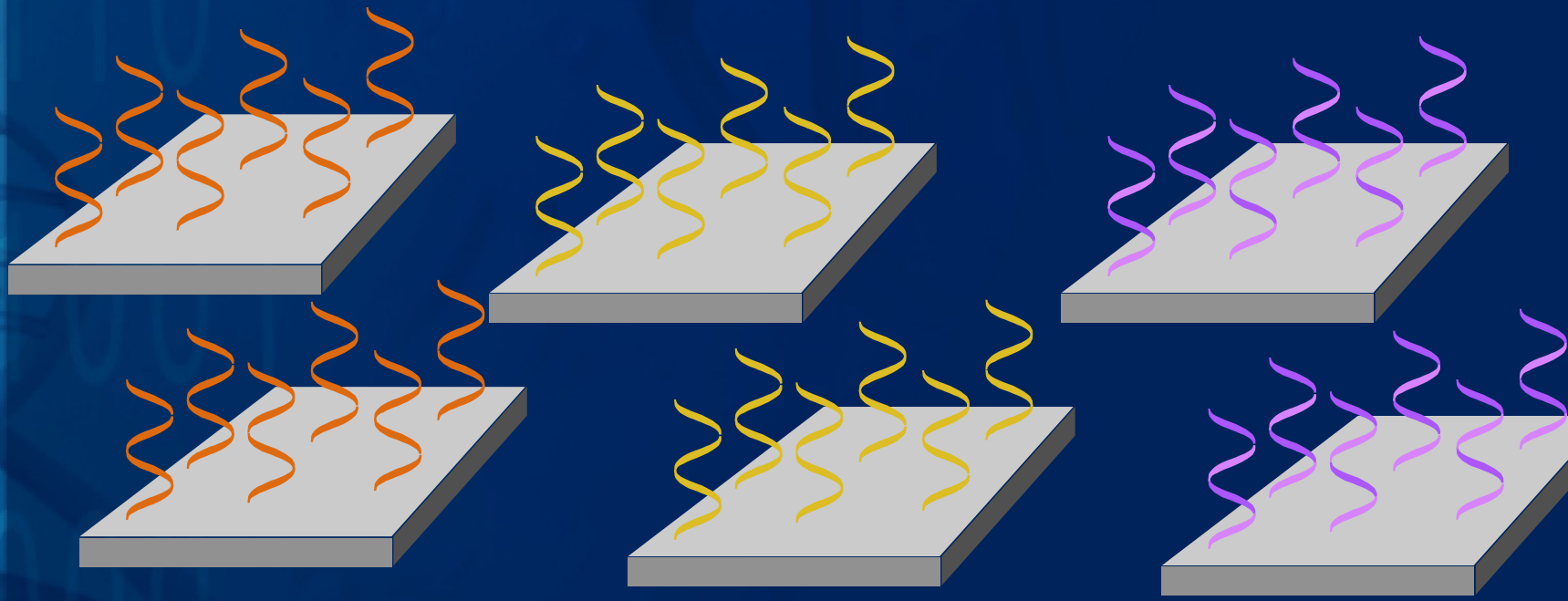
- Multiple Indicators for the Same Target Ensures:
  - Specificity
  - Quantitative accuracy
  - Low false positive rate
  - High sensitivity

GeneChip® Expression Analysis
Hybridization and Staining



GeneChip® Array Advantages

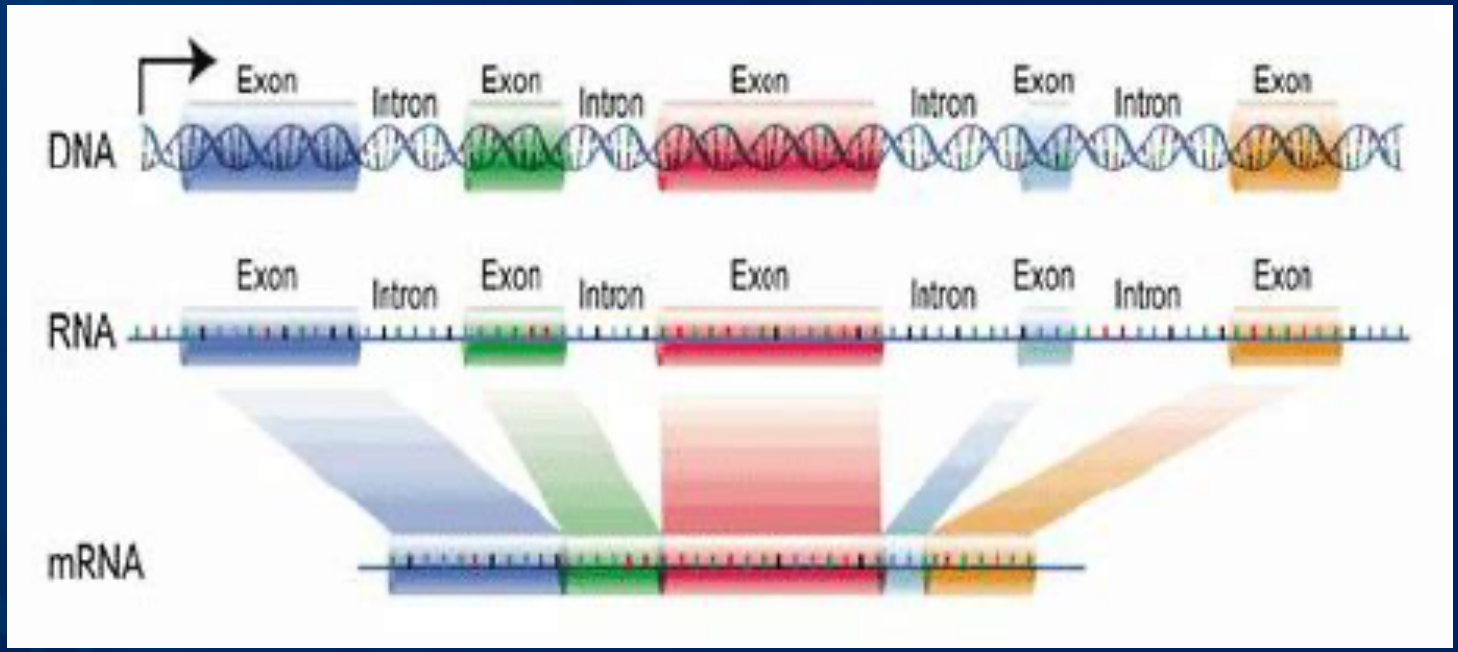
Specificity



Oligo probes for Increased Gene Specificity

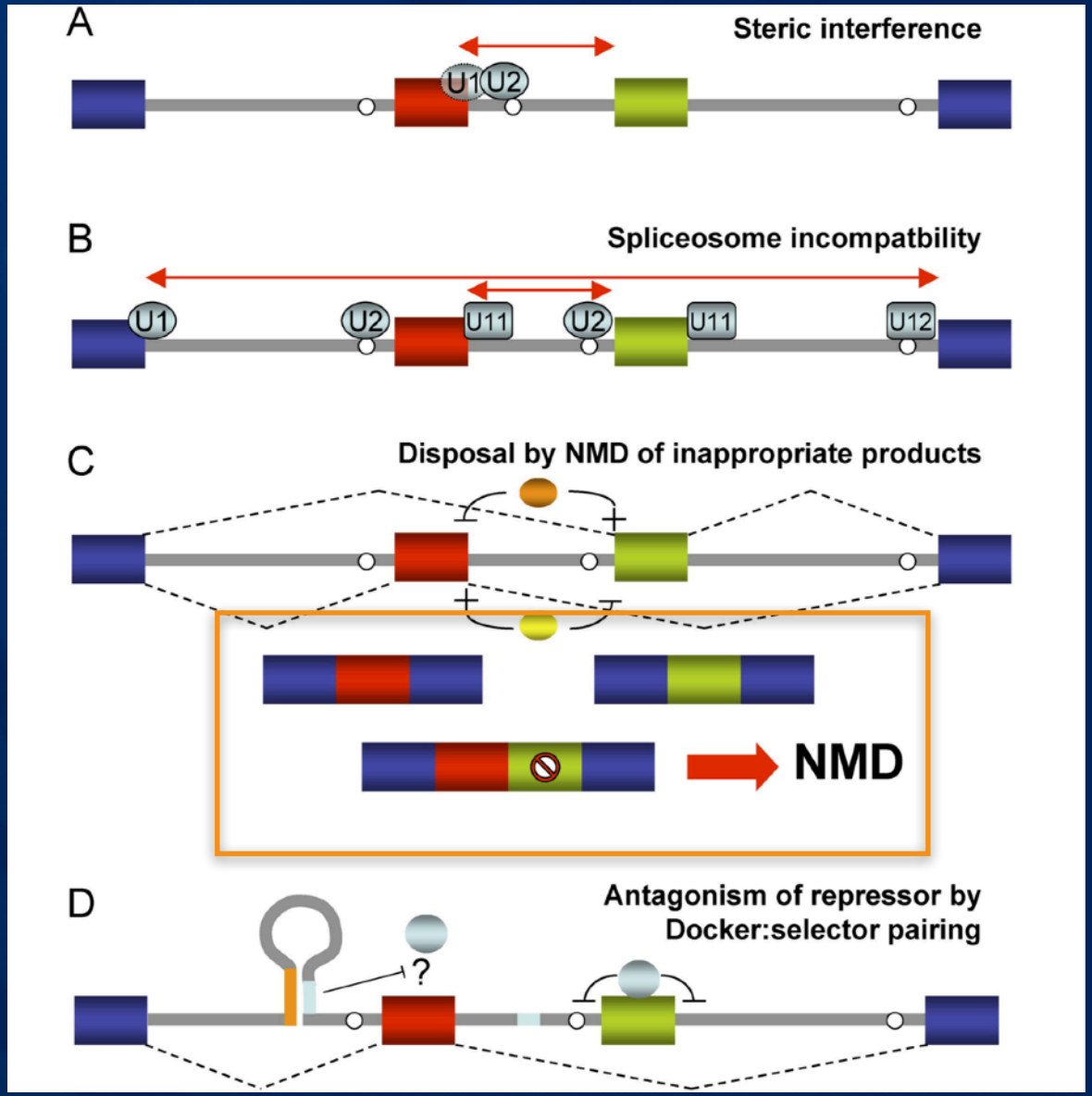
GeneChip® Array Advantages

Specificity



GeneChip® Array Advantages

Specificity

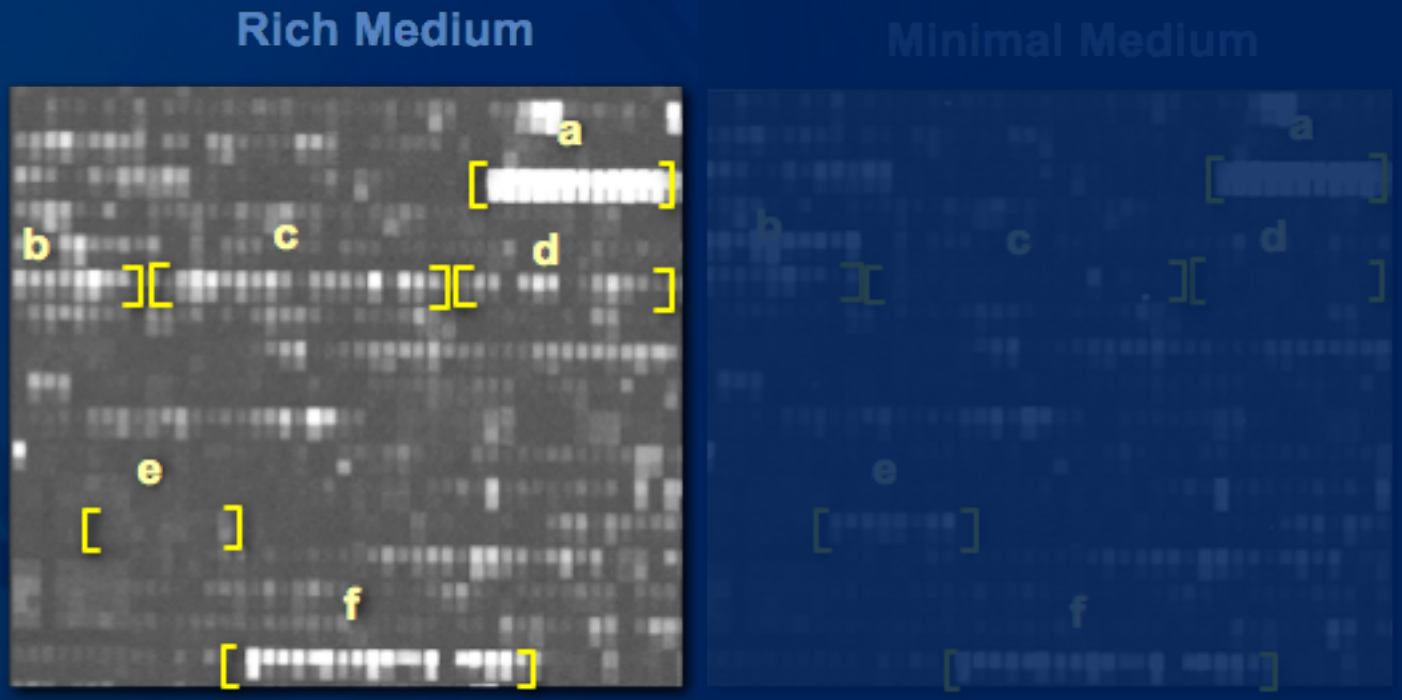


GeneChip® Array Advantages

Specificity

Detecting Change in Gene Expression

Yeast grown in different conditions

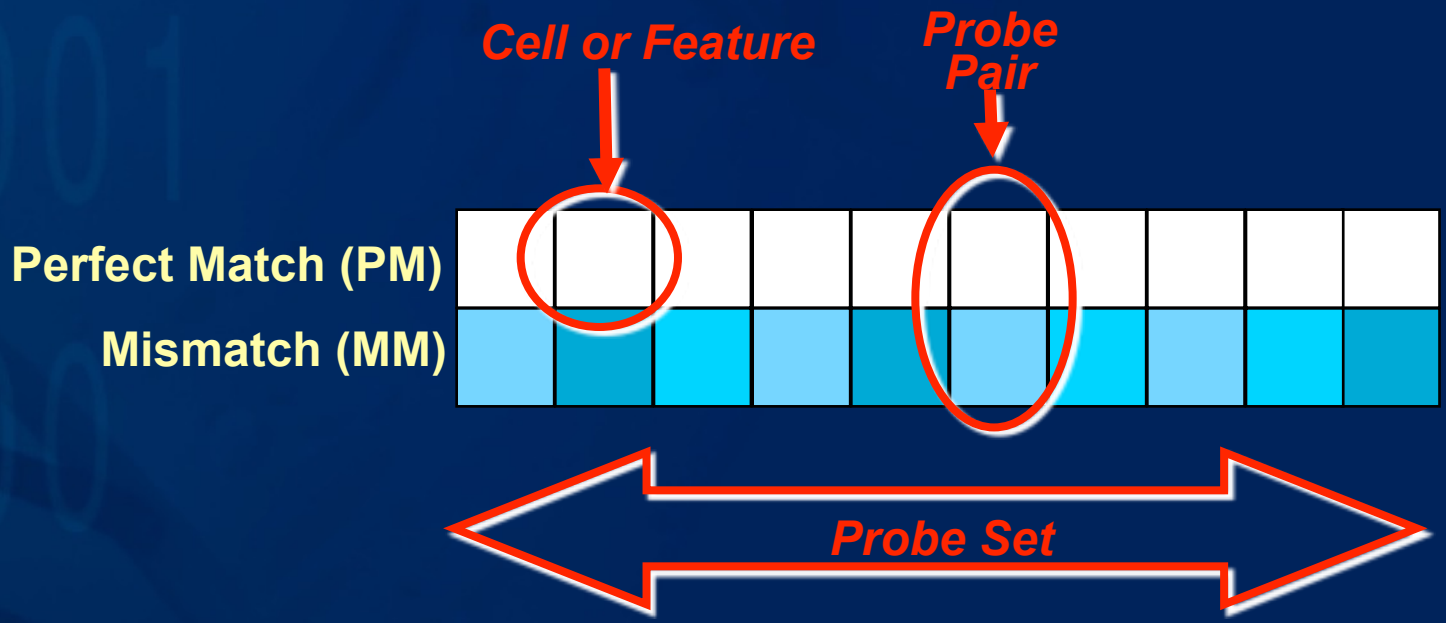


Wodicka, L., et al. 1997
Nature Biotechnology 15:1359-1367

Genes

a = RPL2A
b = TIP1
c = BAP2
d = VAP1
e = YBR147W
f = SUP46

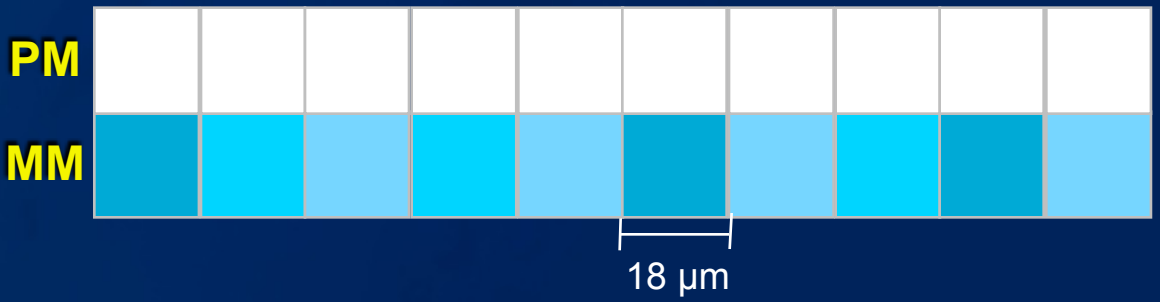
GeneChip® Probe Nomenclature



GeneChip® Array Advantages

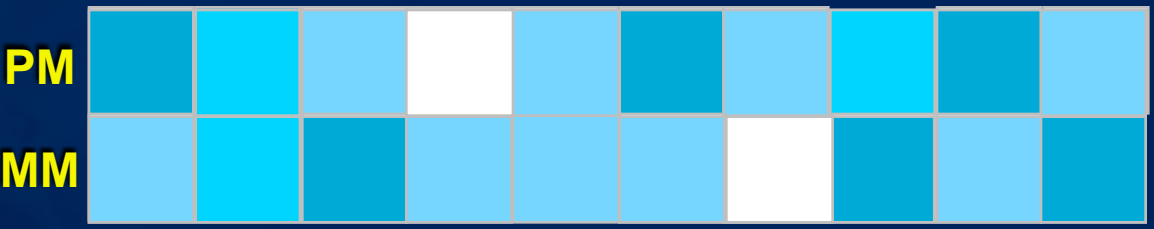
Specific Hybridization

Called "Present"

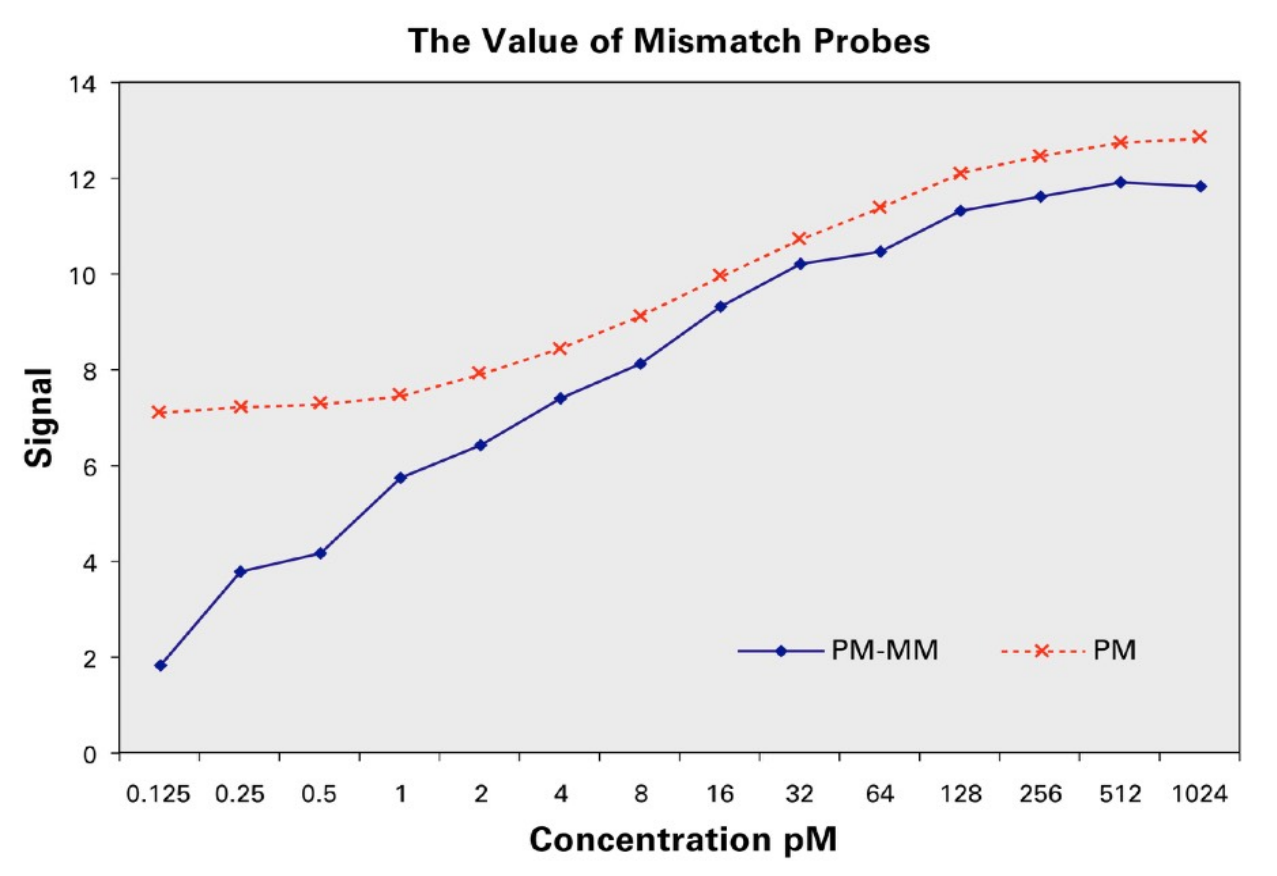


Non-specific/Cross Hybridization

Called "Absent"

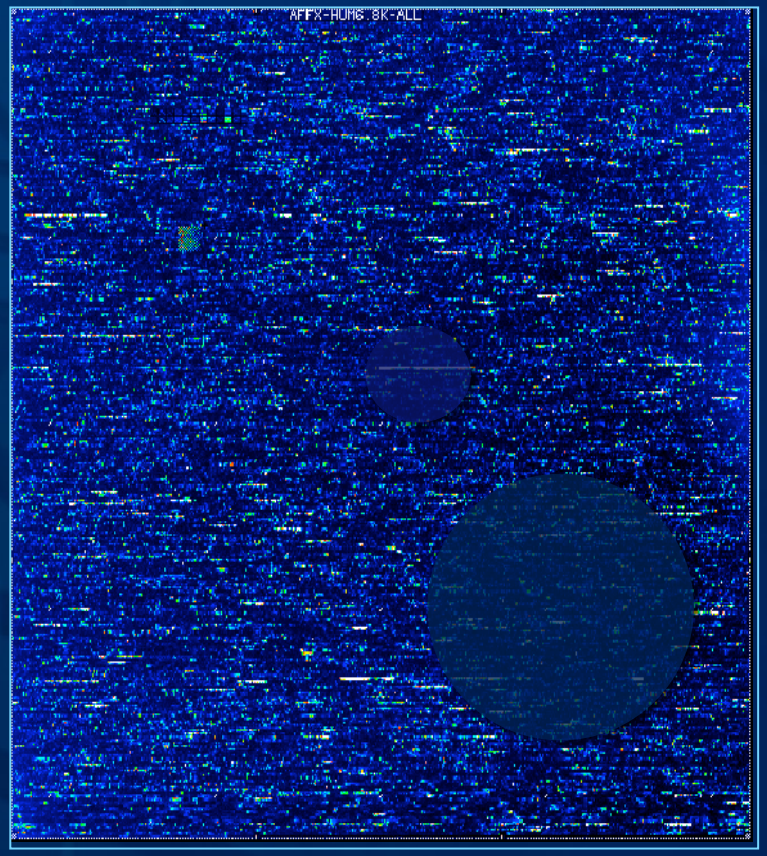


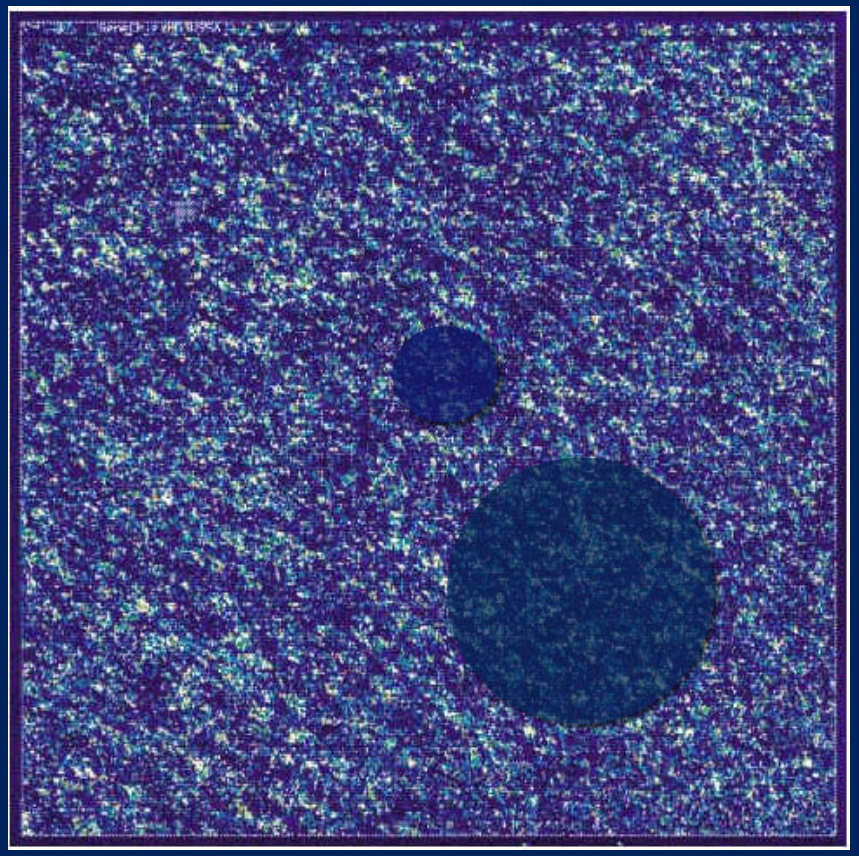
25-mer PM-MM Probe Pairs Offer Increased Specificity



Discrimination between target and stray signal at low (<8pM) target concentrations facilitated by the use of MM probes.

Positioning of primer probes can be important





Images of Hybridized Probe Arrays

Over 500,000 different probes complementary to genetic information of interest

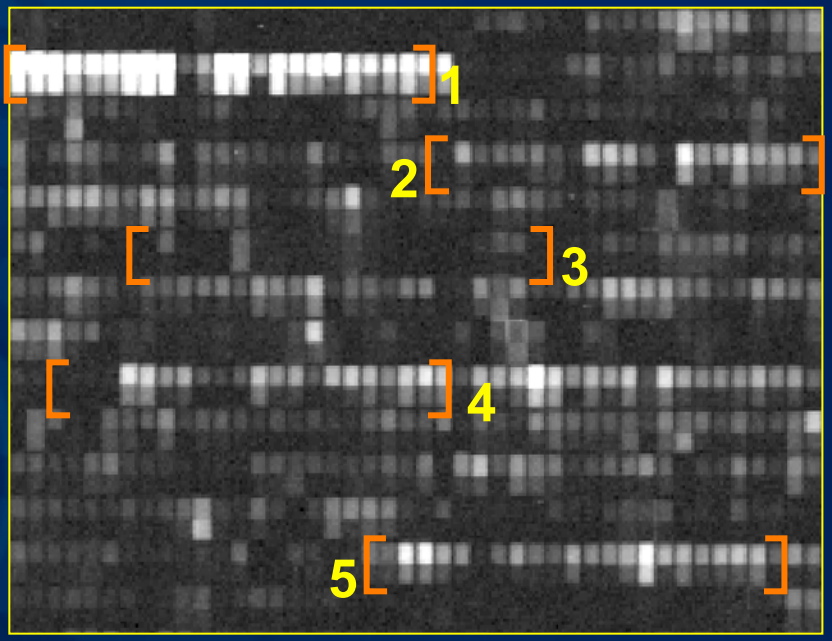
Sensitivity vs. Specificity

- Sensitivity
  - Identifying low abundance transcripts
  - Tolerate some miscalls to achieve greater sensitivity
  - Avoid false negatives
- Specificity
  - Accuracy of detection
  - Tolerate missing some calls to achieve accuracy
  - Avoid false positives

Reproducibility

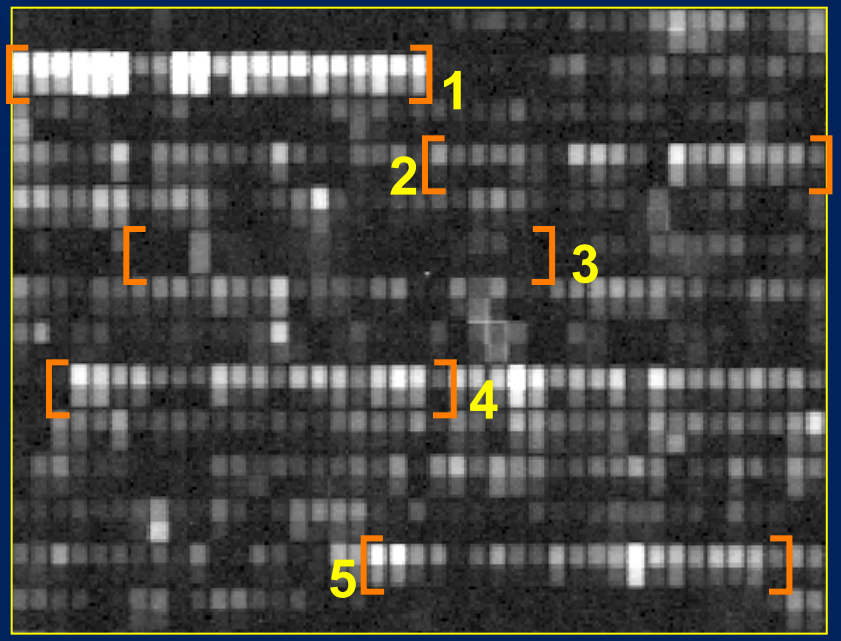
Independent cell growth and prep

Sample 1



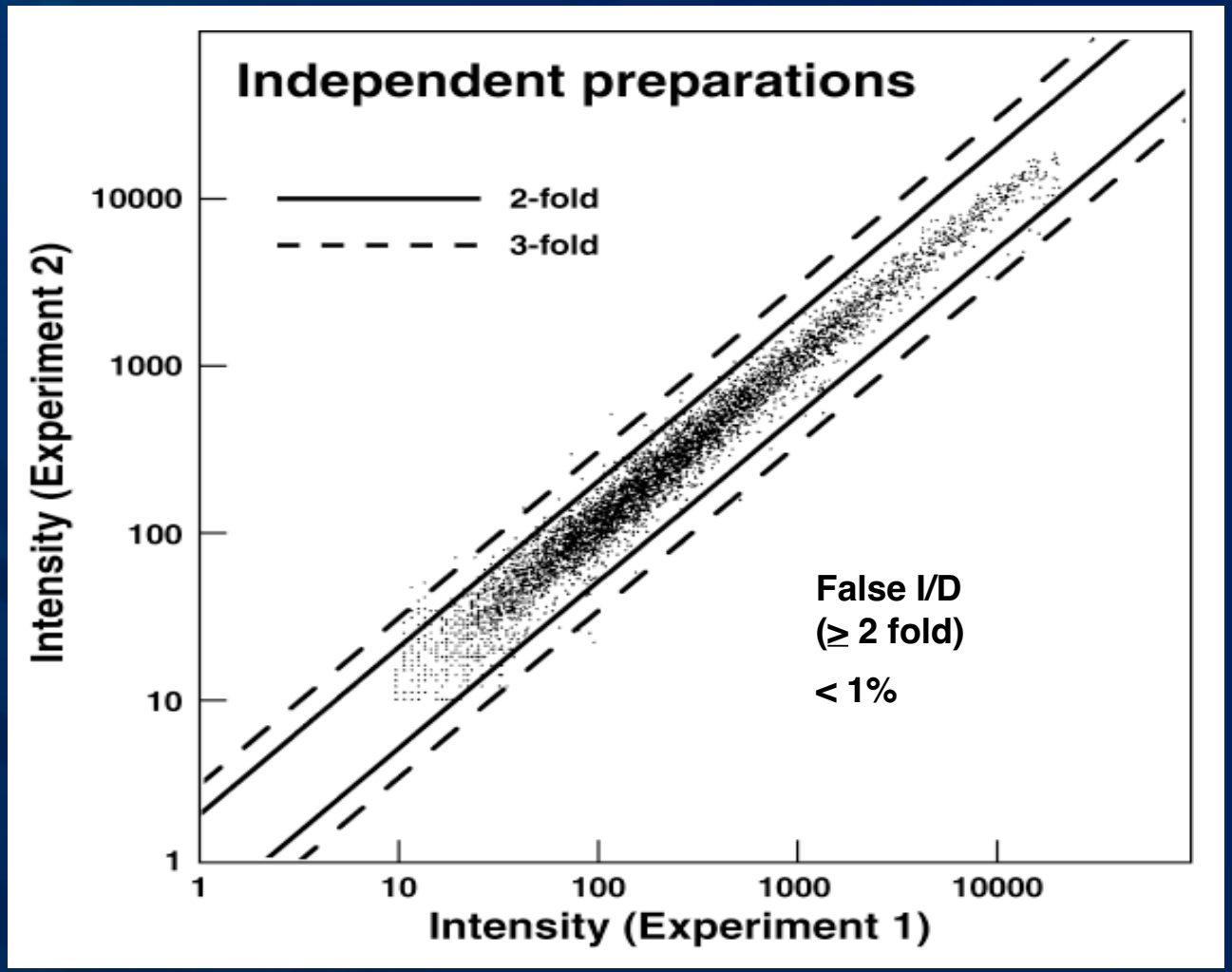
Signal Intensities: 1 13,400
2 1,280
3 1 (absent)
4 1,840
5 1,700

Sample 2



Signal Intensities: 1 11,670
2 1,250
3 9 (absent)
4 2,010
5 1,450

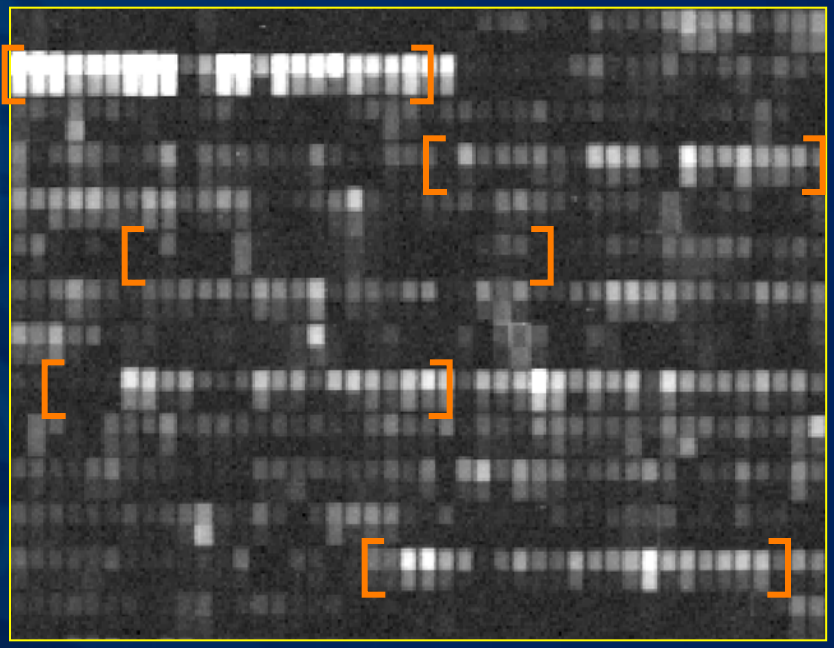
Reproducibility



Reproducibility

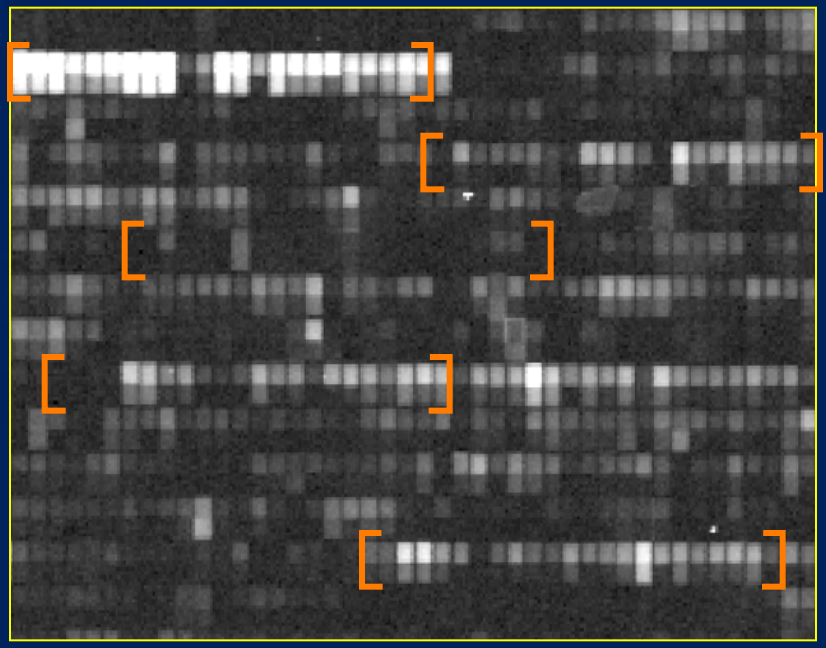
Same sample, different arrays

Sample 1



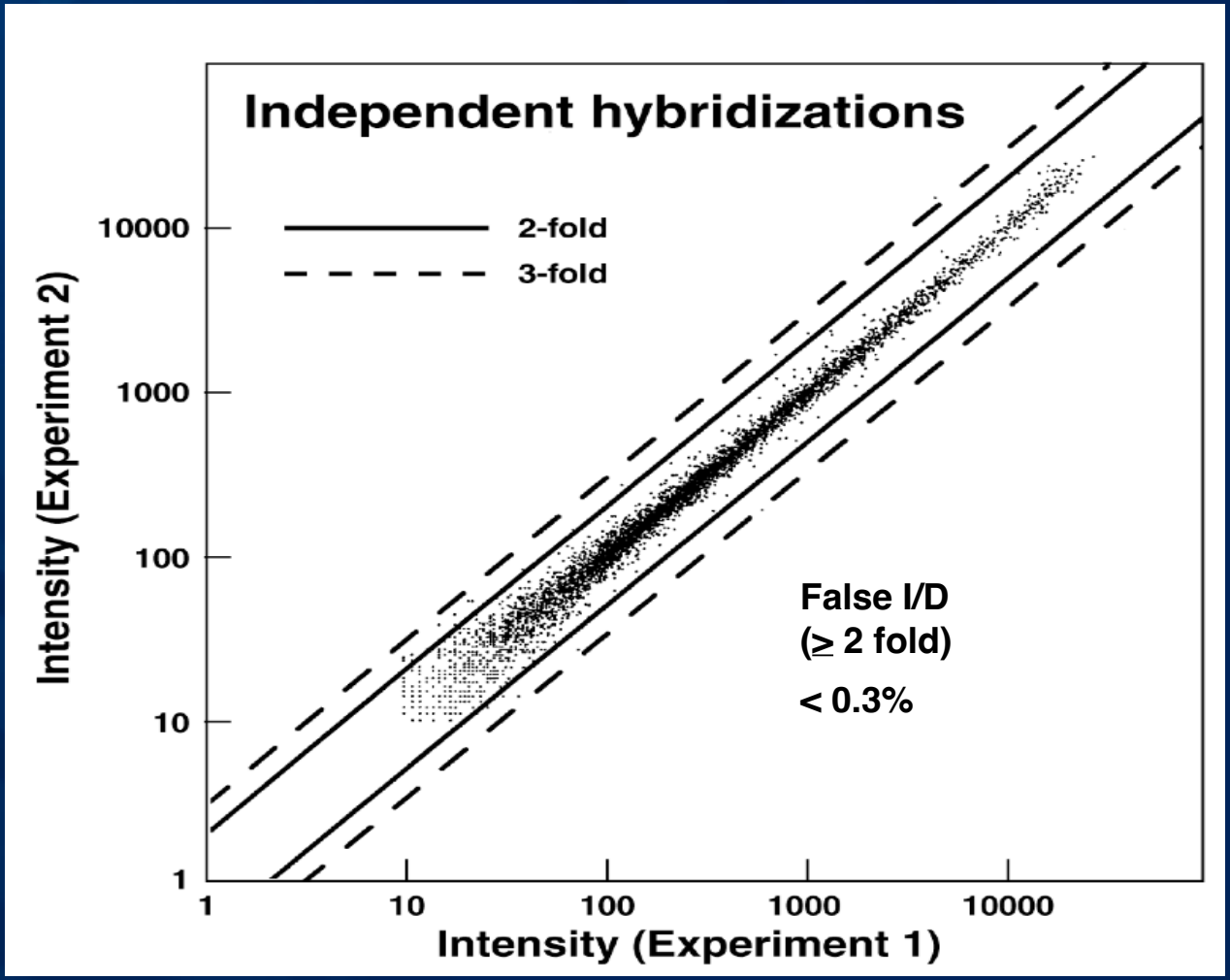
Signal Intensities:
13,400
1,280
1 (absent)
1,840
1,700

Sample 1



Signal Intensities:
13,090
1,250
10 (absent)
1,750
1,430

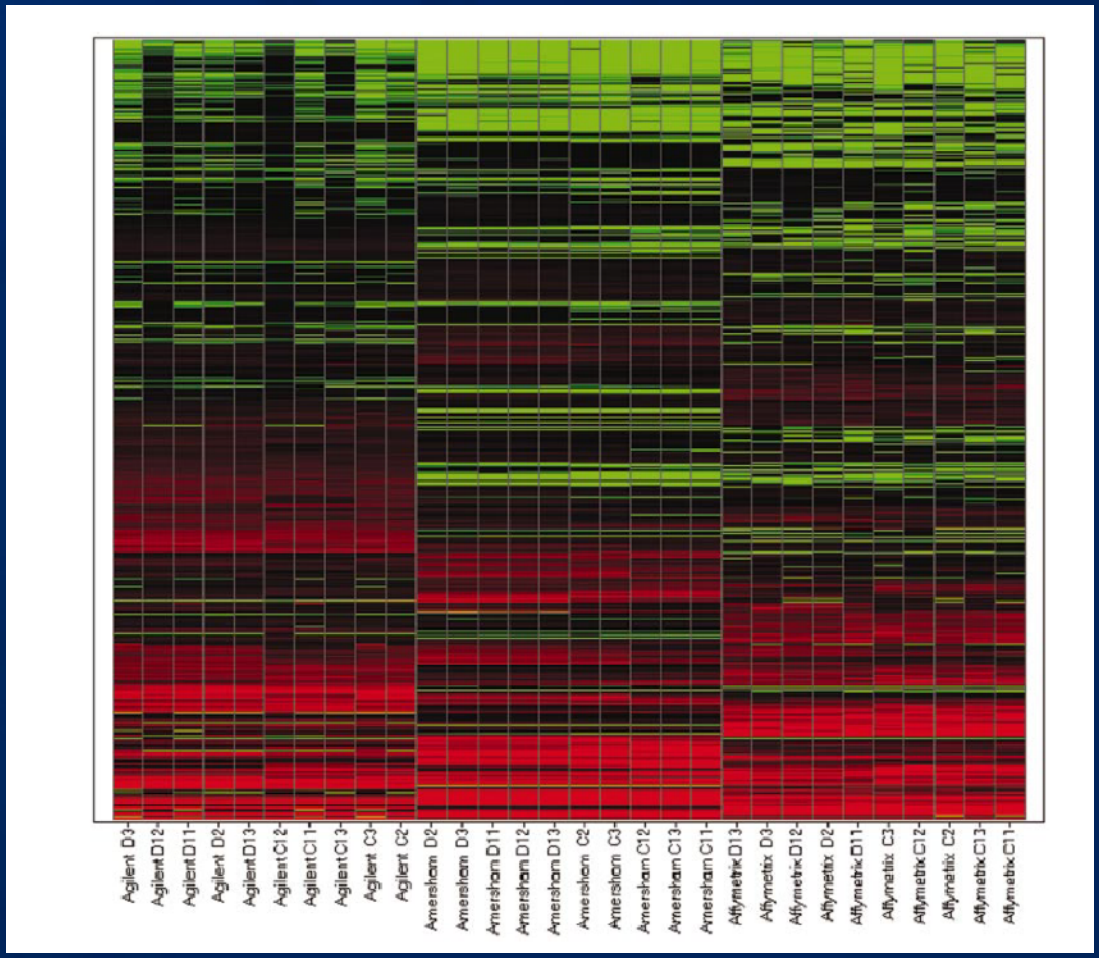
Reproducibility



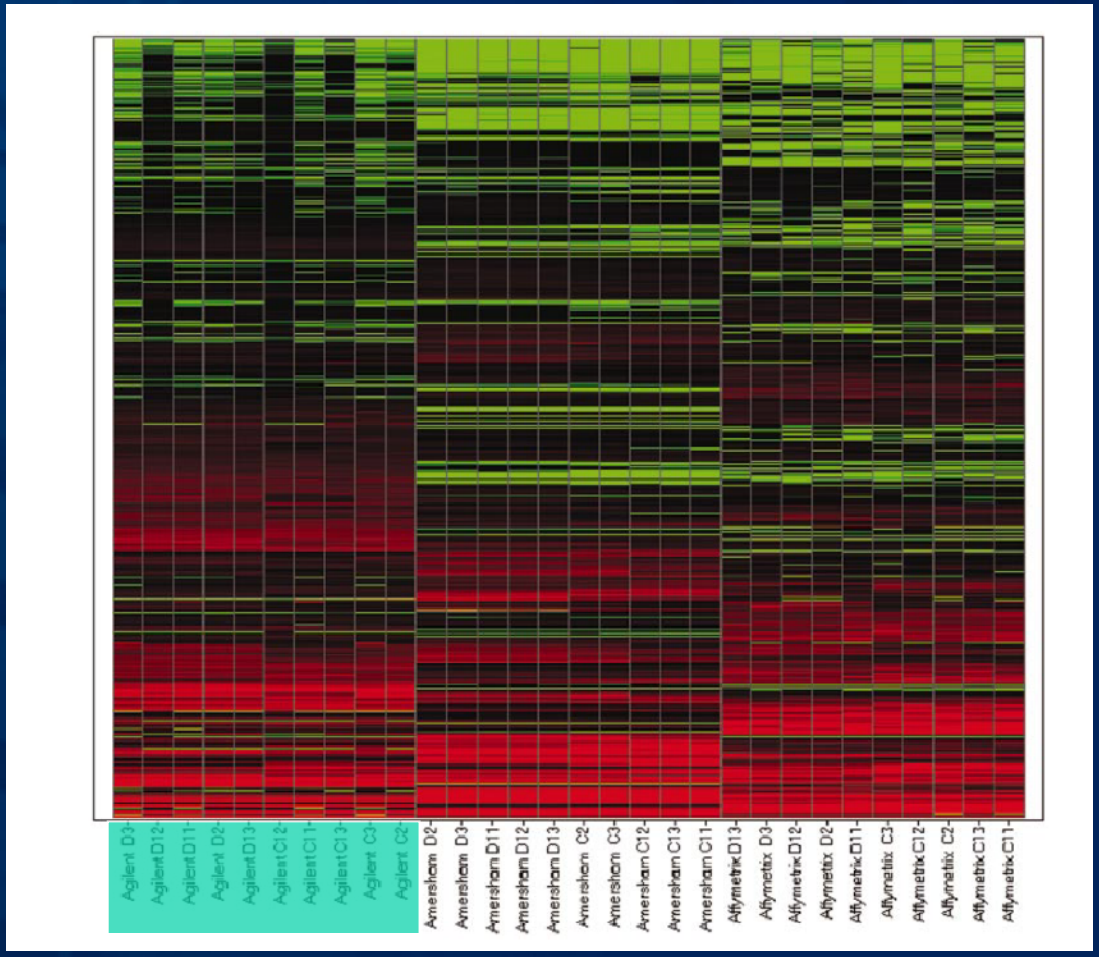
Differences Across Commercial Platforms

Increased Expression

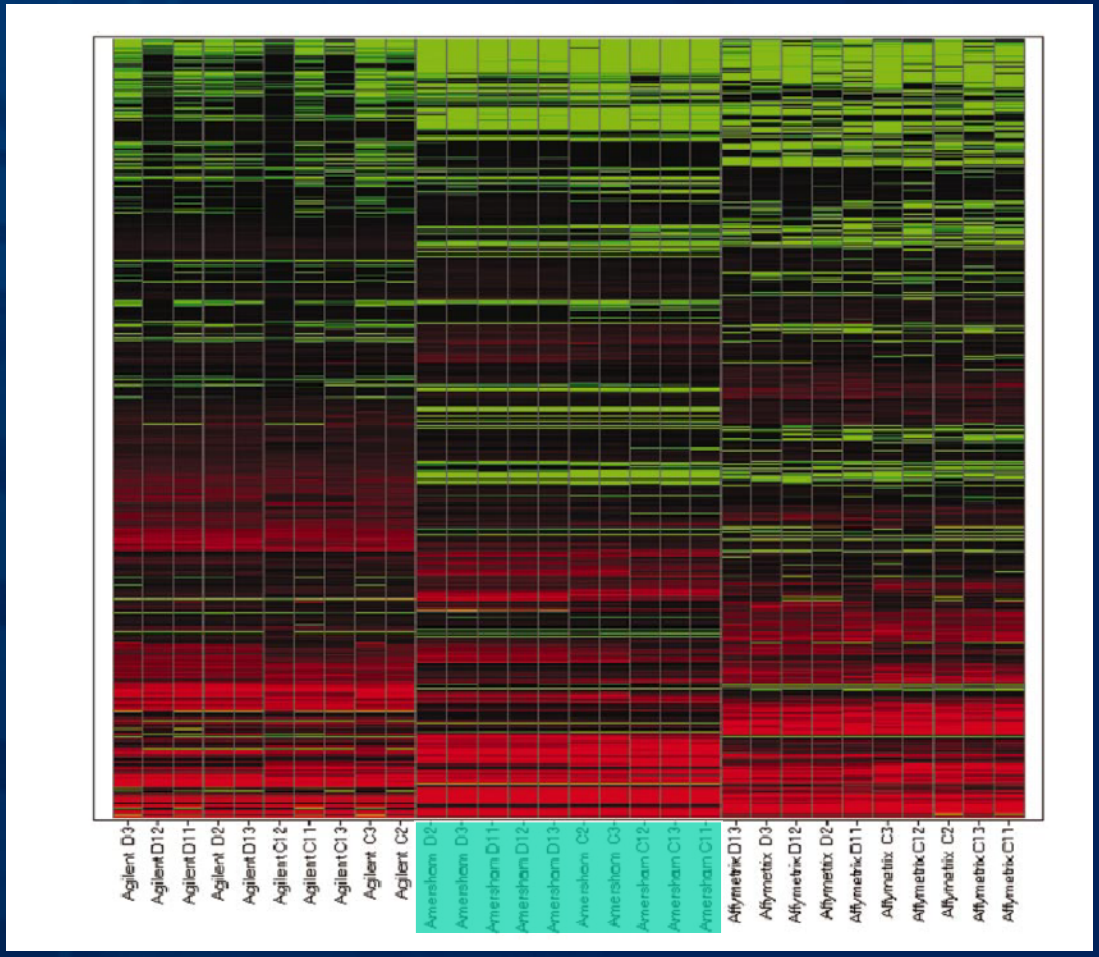
Decreased Expression



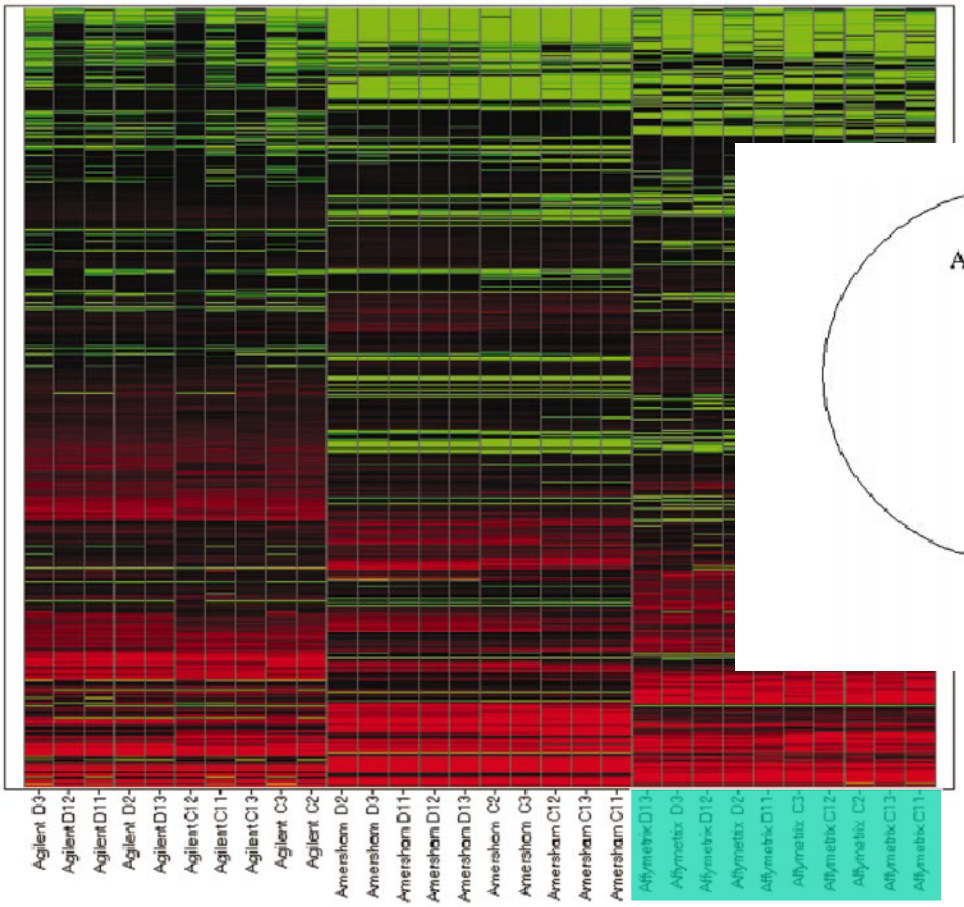
Differences Across Commercial Platforms

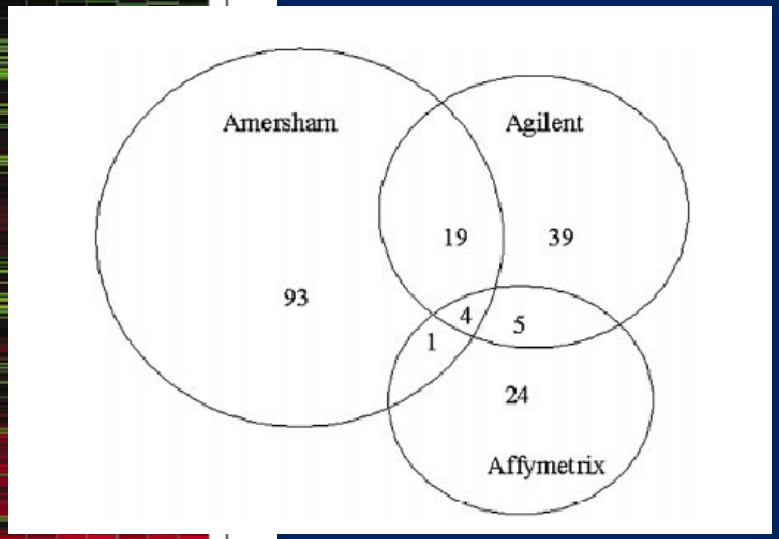


Differences Across Commercial Platforms

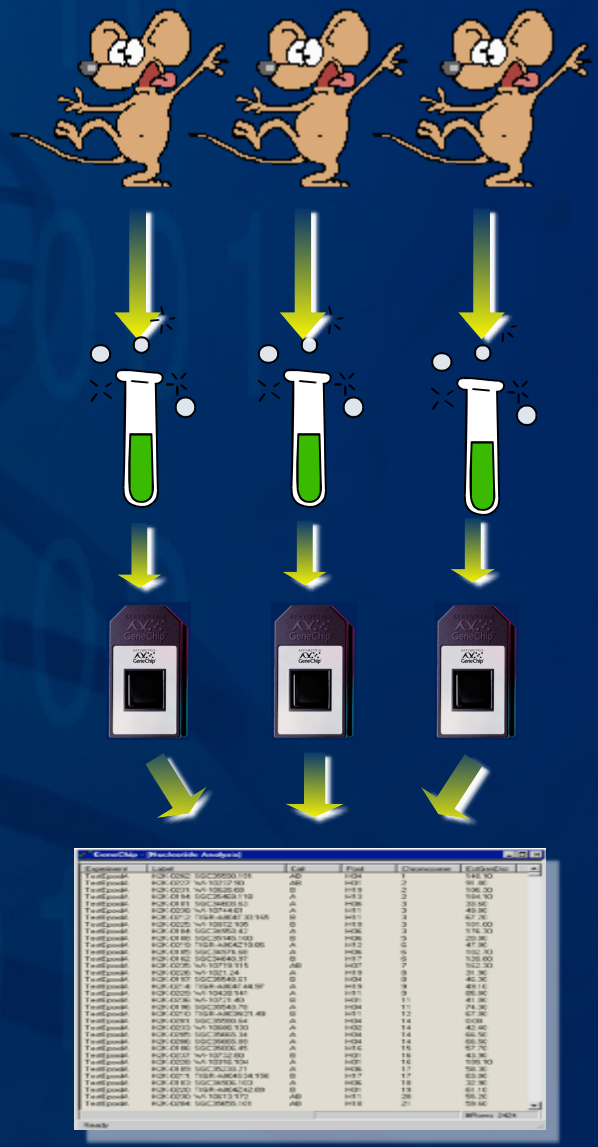


Differences Across Commercial Platforms





Sources of Variability



- Biology
  - The main source of variability
- Sample preparation
  - Technical variability depends on method and operator
- Probe array analysis
  - Standardized; relatively little variability
- Data analysis

GeneChip® System Work Flow

Design Experiment

Prepare Sample

Probe Array

Hybridize

Hybridization Oven

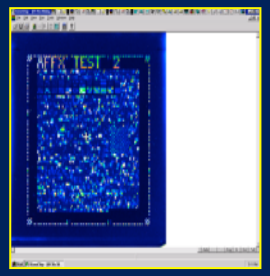
Wash & Stain

Fluidics Station

Scan

Scanner

Analysis



Software

GeneChip Expression Analysis

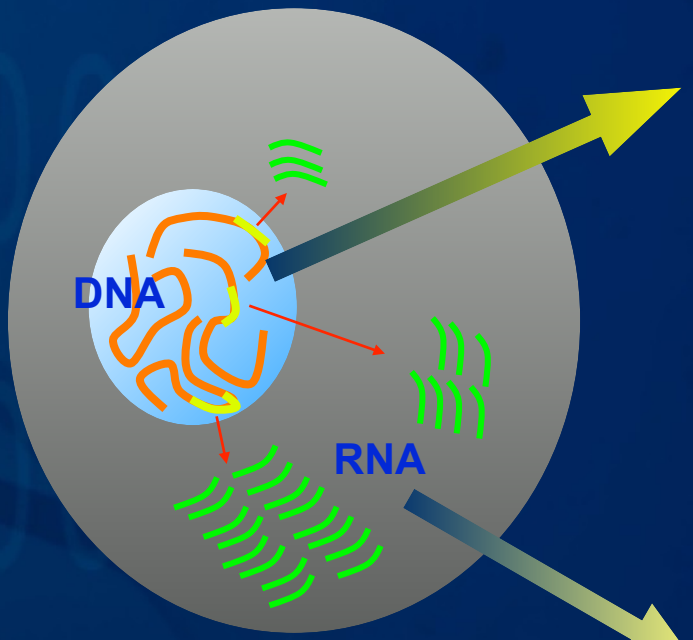
Absolute Analysis

- Detection (qualitative)
- Signal (quantitative)

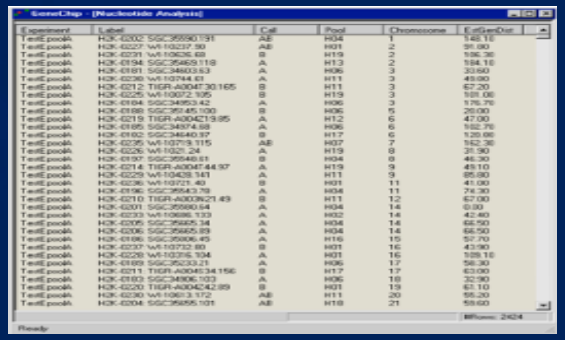
Comparison Analysis

- Change (qualitative)
- Signal Log Ratio (quant.)

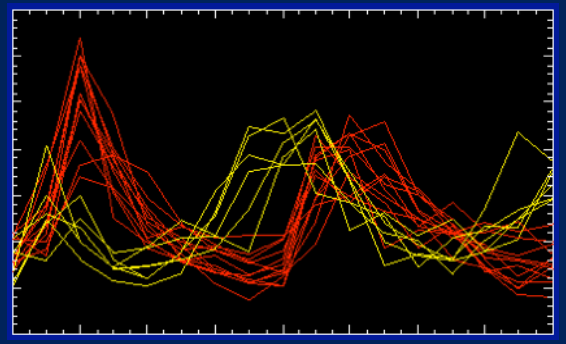
Genotyping or Gene Expression Monitoring



Eukaryotic Cell



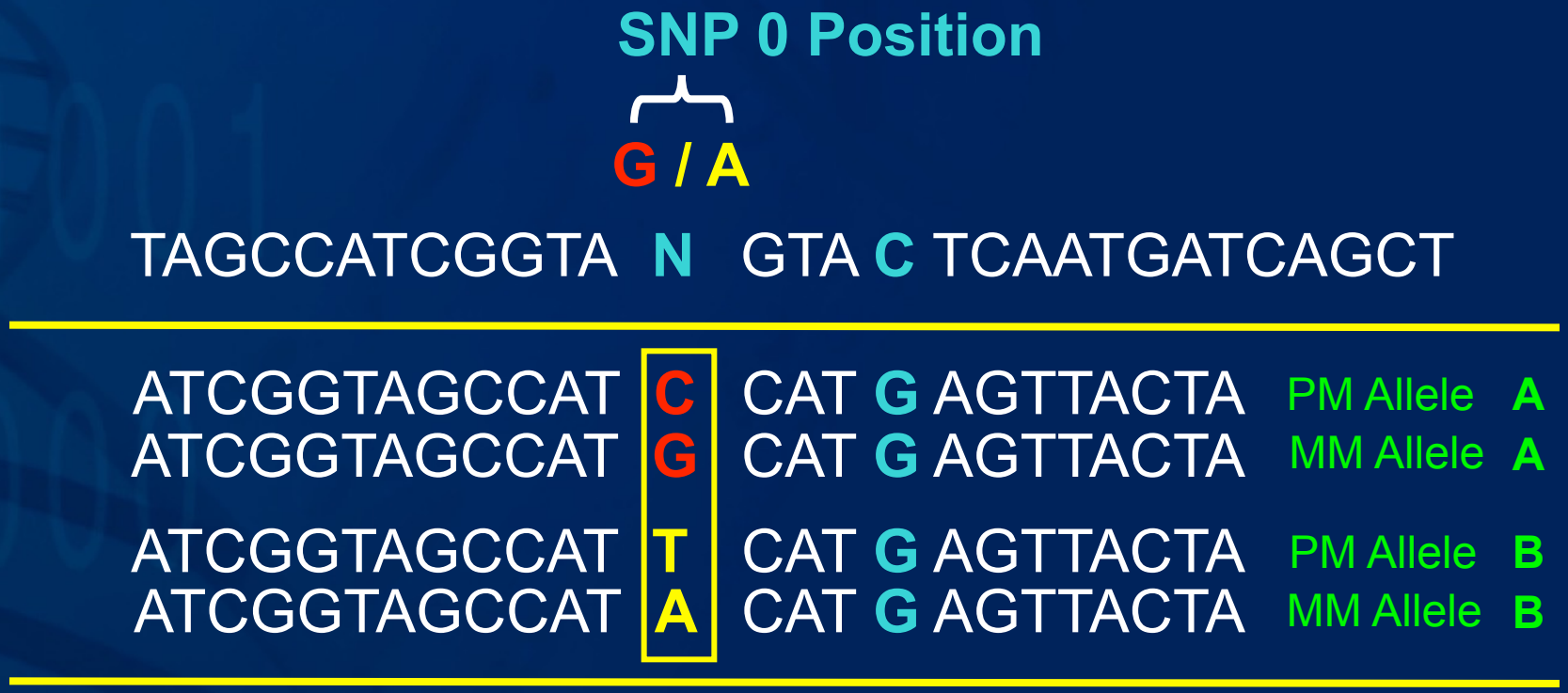
Genotyping: Is it A or B?



Gene Expression: How much of which, when?

GeneChip® Mapping 10K Probe Design

SNP Tiling Strategy



SNP Tiling Strategy

Single nucleotide polymorphisms: aging and diseases

B Bessenyei [1], M Márka, L Urbán, M Zeher, I Semsei

Affiliations + expand

PMID: 15547317 DOI: 10.1007/s10522-004-2567-y

Abstract

Differences of more than 3 million nucleotides can bee seen comparing the genomes of two individuals as a result of single nucleotide polymorphism (SNP). More and more SNPs can be identified and it seems that these alterations are behind of several biological phenomena. Personal differences in these nucleotides result for example in elevated disease susceptibilities, that is, certain nucleotides are more frequent in patients suffering from different diseases comparing to the healthy population. SNPs may cause substantial alterations in the cells, e.g. the enzyme activity of the respective gene changes, but in other cases the effects of the SNPs are not so pronounced. Later results indicate that SNPs can be rendered to individuals living a longer life than the average. Perhaps these results will not directly lead to the lengthening of the maximal life span; however, genes that play an important role in the aging process could be identified. In this respect SNPs are important factors in determining the information level of the cells of individuals which determines the maximal life span (I. Semsei On the nature of aging. Mech. Ageing Dev . 2000; 117: 93-108), in turn SNP is one of the factors that determine the aging process. Since there are certain age-related diseases, the discovery and the description of the SNPs as a function of age and diseases may result in a better understanding of the common roots of aging and those diseases.

SNP Tiling Strategy

Heart disease

Heart disease, in SNPedia as well as for the entry in Wikipedia, is a catch-all term including medical classifications such as coronary artery disease, myocardial infarction, atherosclerosis, etc. Heart disease overall is the #1 cause of death in developed countries, typically accounting for up to 40% of all deaths.

Many SNPs have been associated with increased risk for one or more types of heart disease. Before listing many of them, though, it is worth emphasizing that the risks associated with these SNPs add "relatively little to the current capacity of traditional, non-genetic risk factors to identify individuals with a high propensity to develop heart disease"[1]. This is generally true of most SNPs associated with other diseases as well.

SNPs and genes associated with altered risk for heart disease include the following:

- The most highly replicated associations to **heart disease** have been to SNPs in the chromosome 9p21 region. SNPs in this region include:
  - rs2383206
  - rs10757278
  - rs2383207
  - rs10757274

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rs2383206

rs10757274 and **rs2383206** can significantly increase the risk of heart disease[1]. About one in every four Caucasians are thought to carry the variants, and their risk of coronary heart disease is increased by 30 to 40%. rs10757278 in the same region has been linked to diabetes [2]. The chromosomal region where these SNPs are located is 9p21, and has no known genes.

a blog post about investigating rs10757274 and **rs2383206**

[PMID 18048766] This SNP was also associated with increased risk for coronary artery disease in a Korean population.

[PMID 18066490] Also found to be significant in a study of 416 Italian myocardial infarction patients.

A study of 1,000+ patients with early-onset angiographic coronary artery disease (CAD) concluded that **rs2383206**(G) was associated with an adjusted odds ratio of 1.39 (CI: 1.05-1.85) for (A;G) heterozygotes and 1.73 (CI: 1.26-2.37) for (G;G) homozygotes. This SNP alone accounted for 21% of the population attributable fraction and was independent of traditional risk factors, myocardial infarction risk, and the extent of disease.[19033013?dopt=Abstract PMID 19033013]

[PMID 19559344] Genetic variants on chromosome 9p21 and ischemic stroke in Chinese

Orientation	plus
Stabilized	plus

Geno	Mag	Summary
(A;A)		normal
(A;G)	2	1.4x increased risk for heart disease
(G;G)	3	1.7x increased risk for heart disease

Reference	GRCh38 38.1/141
Chromosome	9
Position	22115027
Gene	CDKN2B-AS1
is a	snp
is	mentioned by
dbSNP	rs2383206
dbSNP (classic)	rs2383206

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is a	snp
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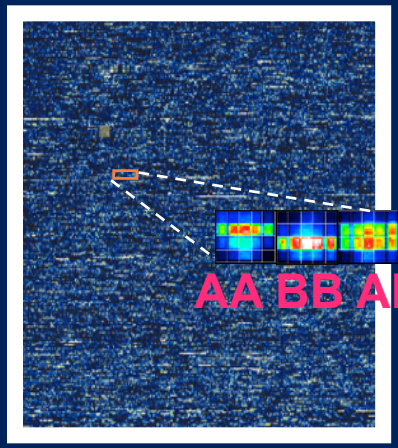
GeneChip Mapping 10K Assay

Single primer complexity reduction

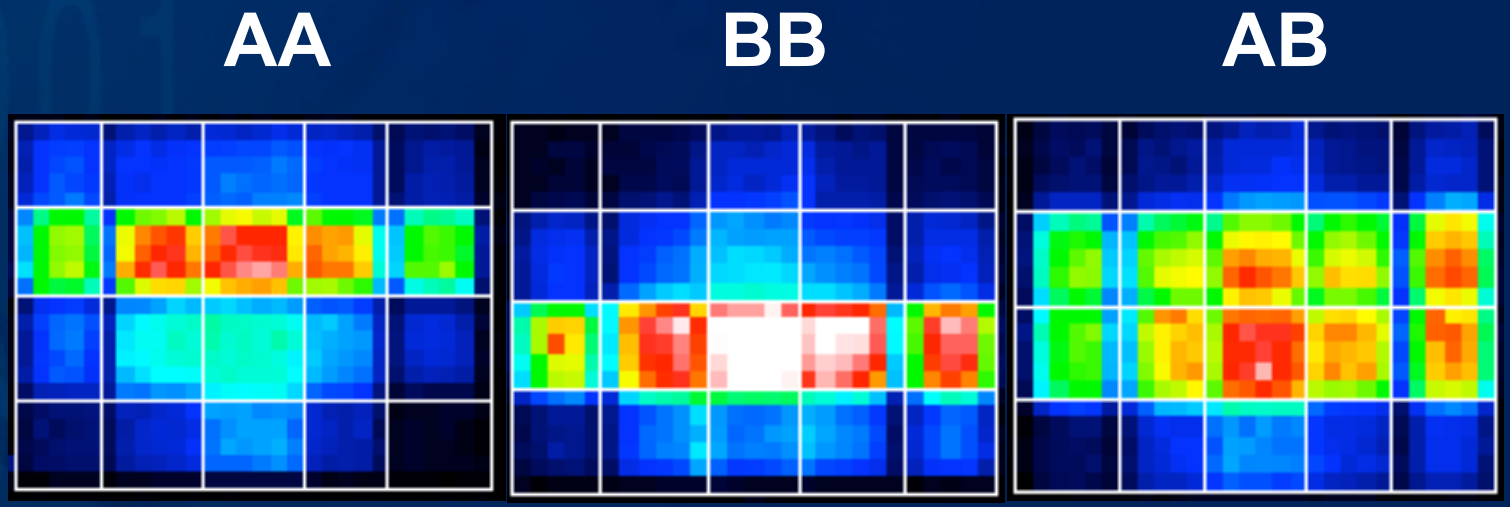
Allele-specific hybridization



- A single-primer,
- A single-amplification, and
- A cost-effective assay…

- …for simultaneously Genotyping

GeneChip® Mapping 10K Hybridization Patterns




PHASE TWO: INTERPRETATION
SHERMAN
I THINK I FOUND A CORNER PIECE.
3 BILLION PIECES
GENOME