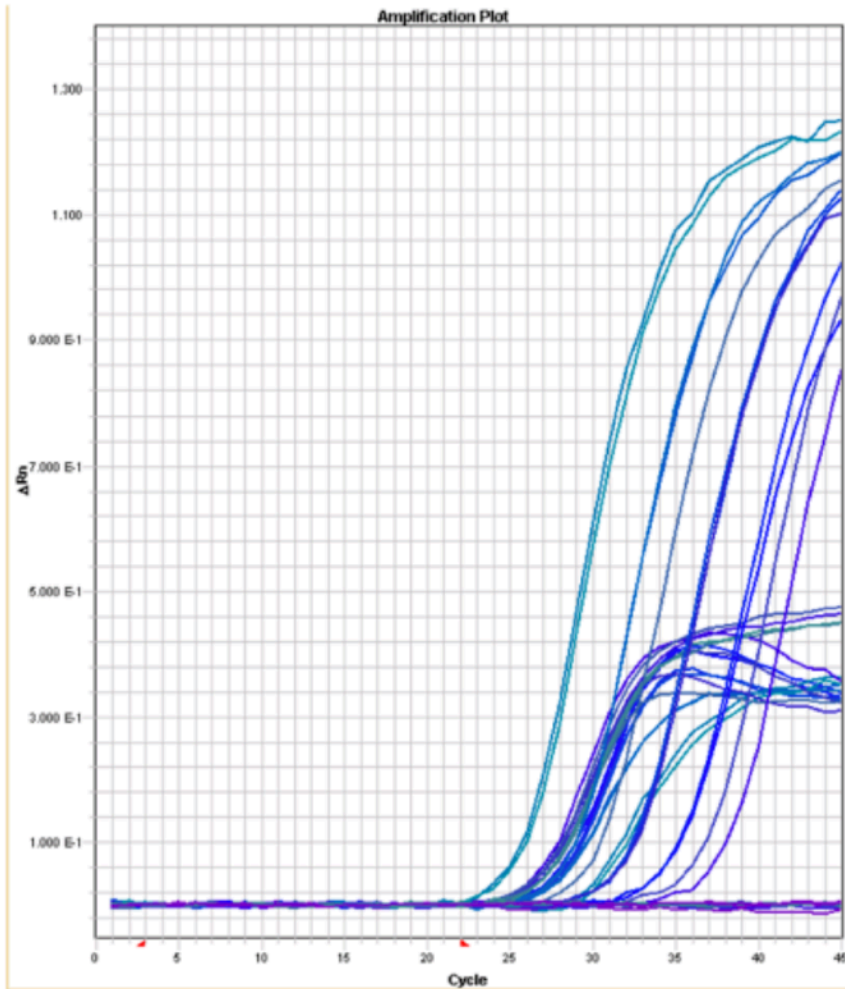


SUMMER INSTITUTE - ONLINE MODALITY CALENDAR 2022

SUN	MON	TUE	WED	THU	FRI	SAT
June 26	27	28	29	30	31	July 02
	9:00-10:00am Virtual Program Orientation for Summer Institute Online Modality					
July 03	04	05	06	07	08	09
	Holiday (Independence Day)	8:30-10:00am -Welcome Reception and Buddy Meet & Greet Event	Free Day	Classes begin! 8:30-11am: BIOL4905 INTRODUCTION 8-10:20pm: Afternoon course	8:30-11am: BIOL4905 DNA PREPARATION 8-10:20pm: Afternoon course	
10	11	12	13	14	15	16
	8:30-11am:BIOL4905 PROTEOMICS I 8-10:20pm: Afternoon course	8:30-11am:BIOL4905 PROTEOMICS II 8-10:20pm: Afternoon course	8:30-11am:BIOL4905 PROTEOMICS III 8-10:20pm: Afternoon course	8:30-11am: BIOL4905 RNA PREPARATION 8-10:20pm: Afternoon course	Virtual Independence Day Activity	
17	18	19	20	21	22	23
	8:30-11am:BIOL4905 qPCR / ROBOTS 8-10:20pm: Afternoon course	8:30-11am:BIOL4905 DNA Sequence Analysis 8-10:20pm: Afternoon course	Midterm Break	8:30-11am:BIOL4905 Next Gen. Sequencing 8-10:20pm: Afternoon course	8:30-11am:BIOL4905 Next Gen. Sequencing 8-10:20pm: Afternoon course	
24	25	26	27	28	29	30
	8:30-11am:BIOL4905 Microarray I 8-10:20pm: Afternoon course	8:30-11am:BIOL4905 Nanostring 8-10:20pm: Afternoon course	8:30-11am:BIOL4905 Automated Microscopy /AFM	8:30-11am:BIOL4905 Flow Cytometry 8-10:20pm: Afternoon course	FINALS	
31	August 01	02	03			
	9:00-10:00am: Closing Reception		Grades available in PAWS			

Legend:
Orange: Courses Blue: Activities

Questions

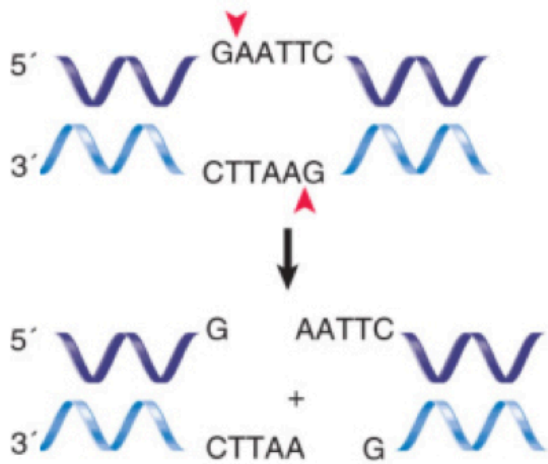


Is this a good qPCR plot of data?

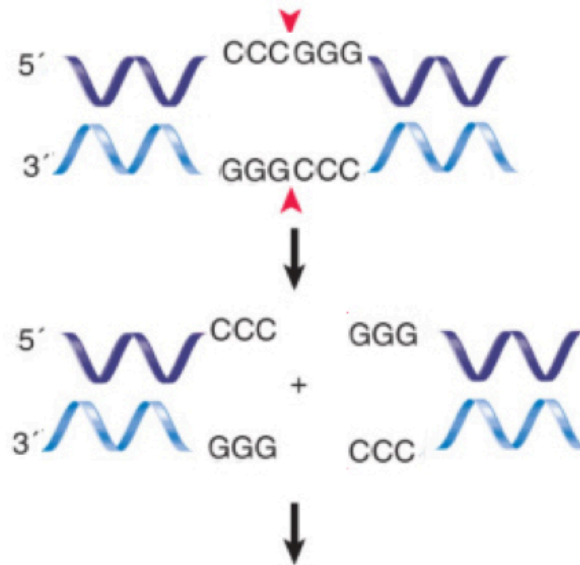
Explain your answer.

Questions

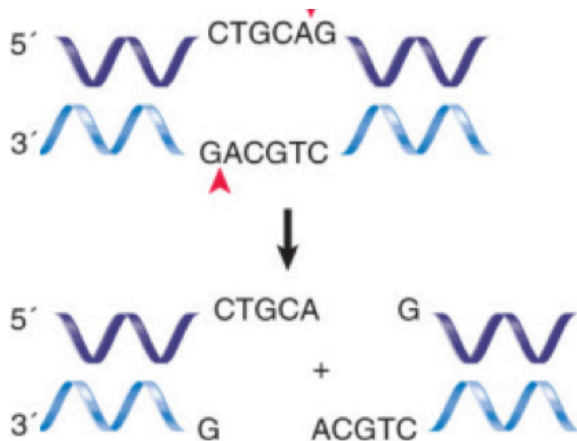
EcoR I



Sma I



Pst I

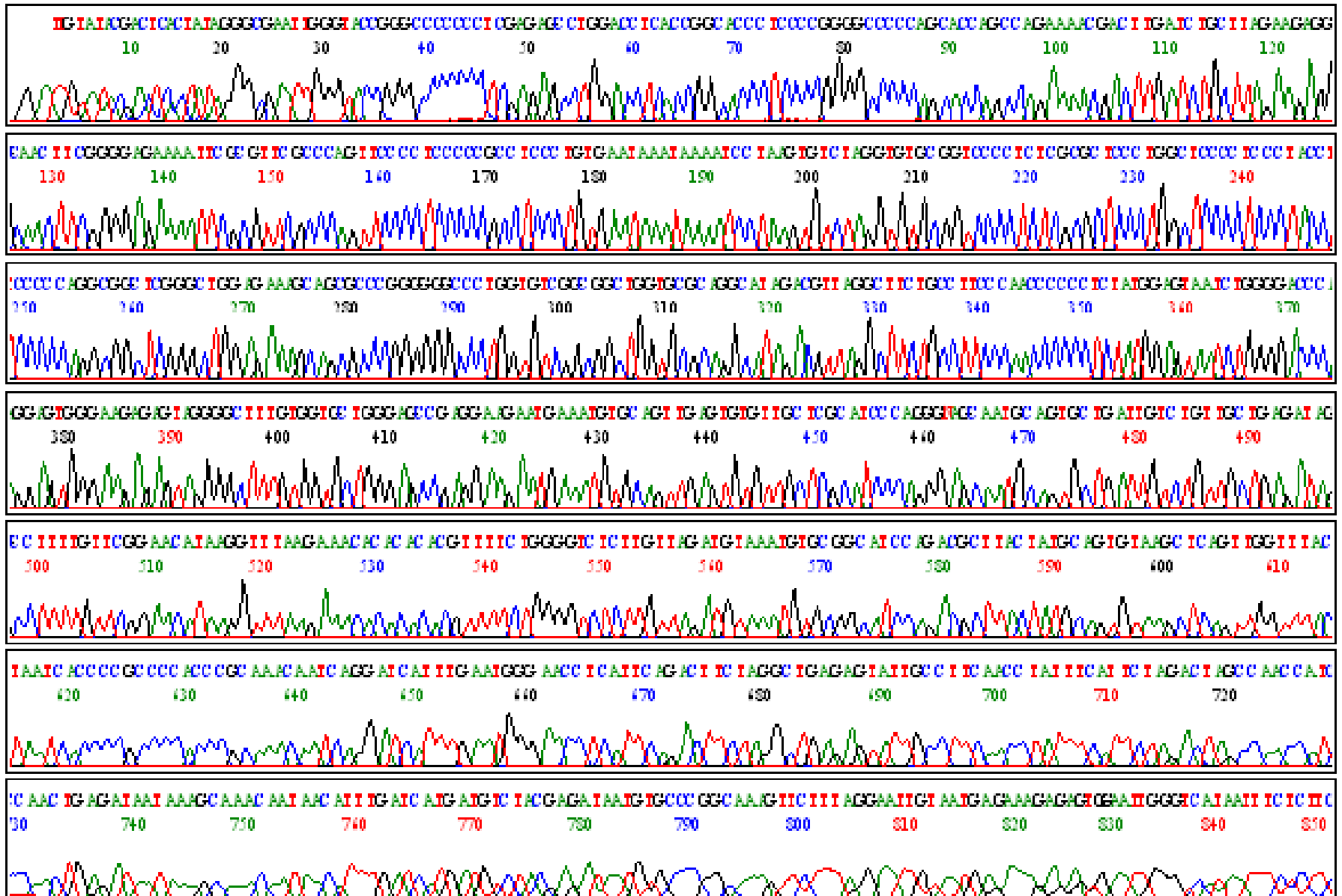


Which of these Type II REN can you find in the sequence (next page). If you find the sequence, after which base number in the sequence does it cut?

Is this DNA from pGEM-T Easy?

Explain your answer.

Questions



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

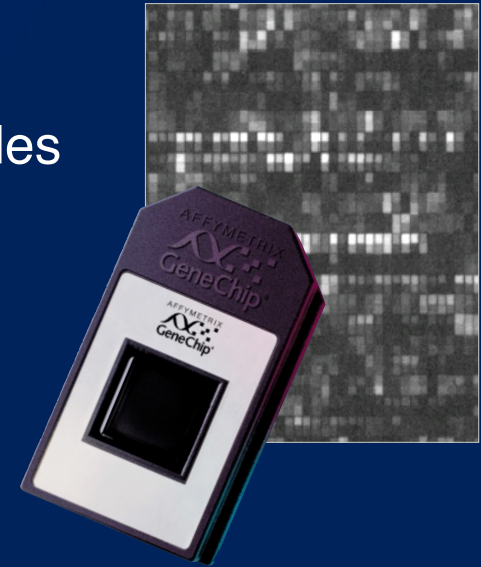
10,000s of specific probes

Measure global gene expression,
SNP calls, LOH, amplification, methylation etc

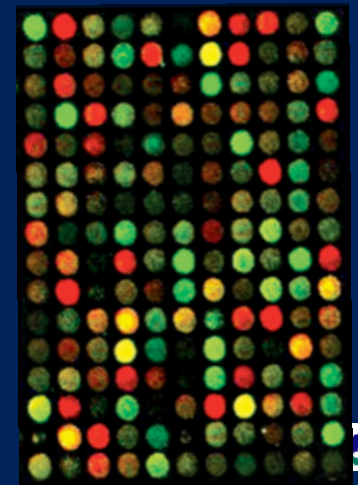


GeneChip® vs. Spotted Arrays

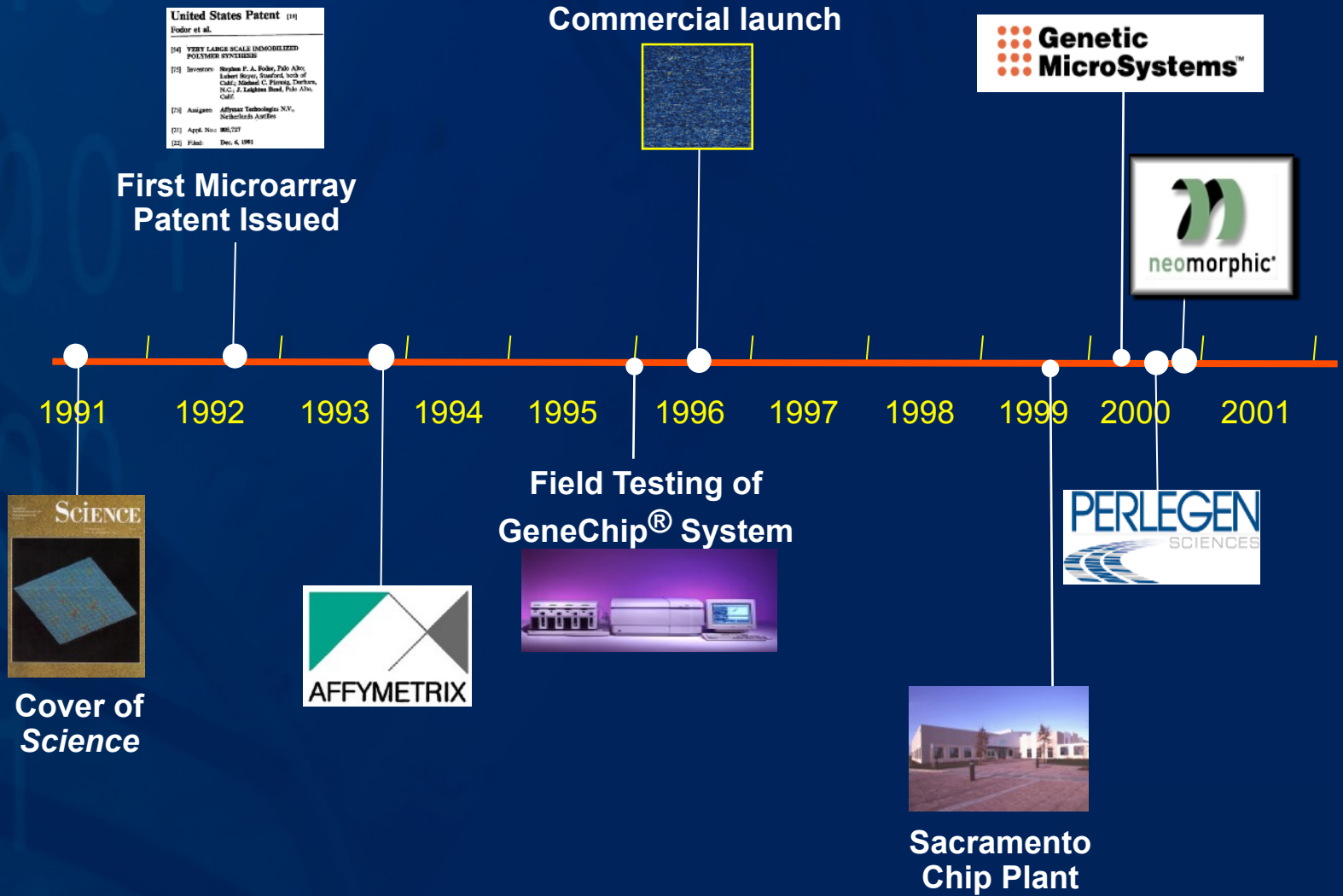
- Affymetrix GeneChip® Arrays use oligonucleotides
- Oligos are built on a solid support



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



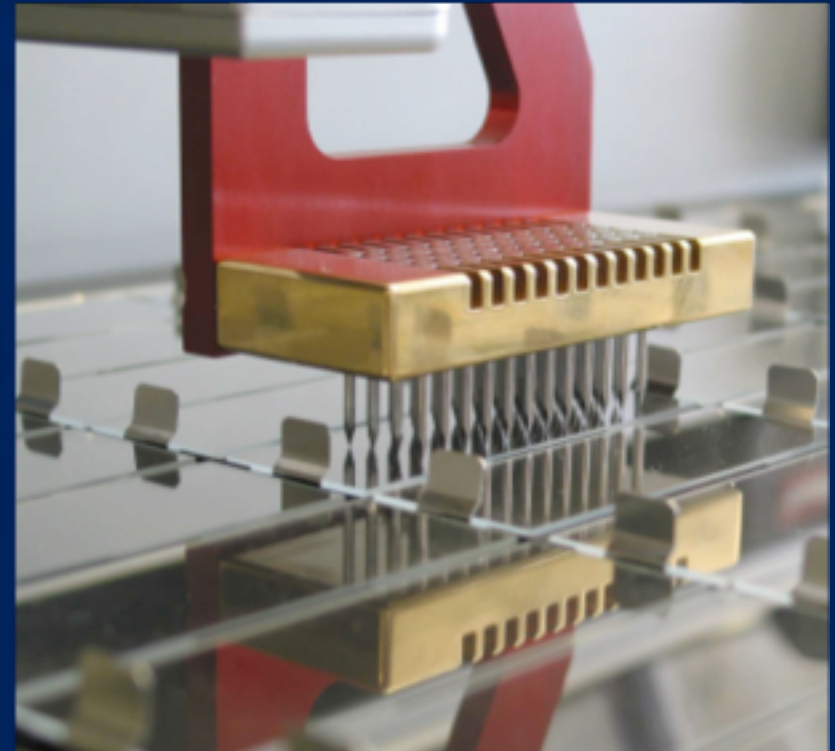
About Affymetrix



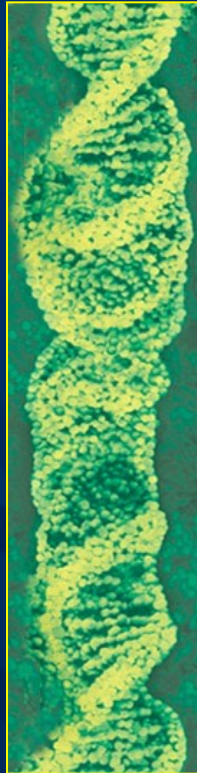
Historically....

DNA spotting

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



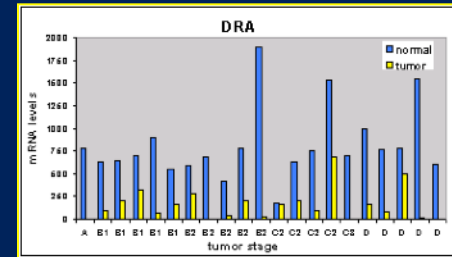
Afymetrix cornered the market



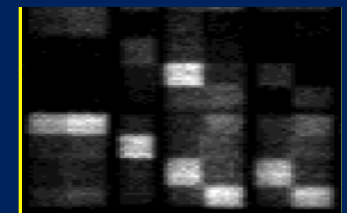
Sequence Database



Research Tools

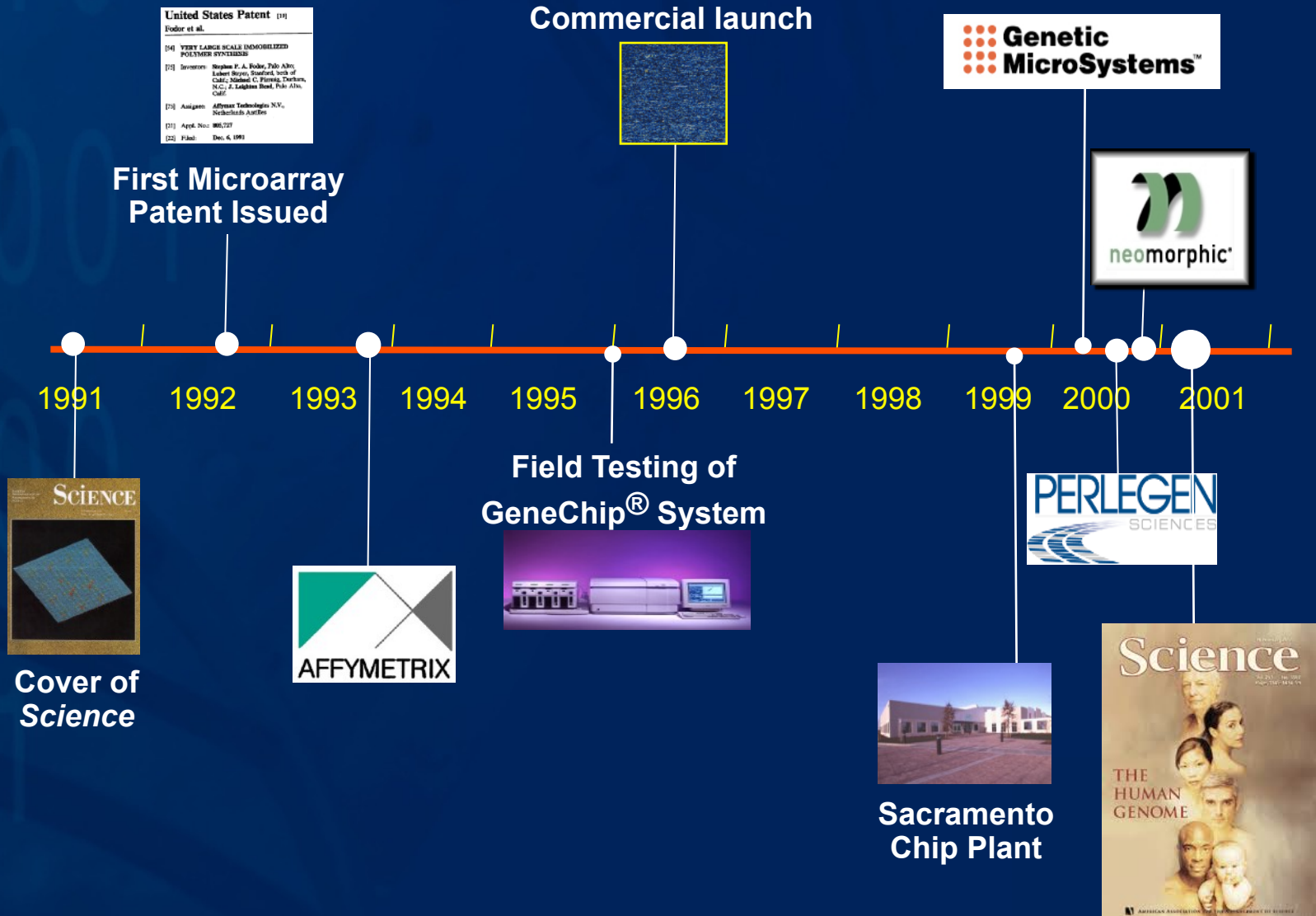


Expression Variability



Sequence Variability

About Affymetrix



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	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	30 arrays	Please Inquire
Rice (Cn) Gene 1.0 ST Array	6 arrays	Please Inquire
Rice (Cn) Gene 1.0 ST Array	6 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
901996	Rice (US) Gene 1.0 ST Array	6 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
902007	Zebrafish Gene 1.0 ST Array	6 arrays Please Inquire
902006	Zebrafish Gene 1.0 ST Array	30 arrays Please Inquire

Rat Human

Murine

Arabidopsis

Celegans

Drosophila

Usa

Yeast

Eukarya

Fungi



Enabling the Genetic Revolution

Food testing



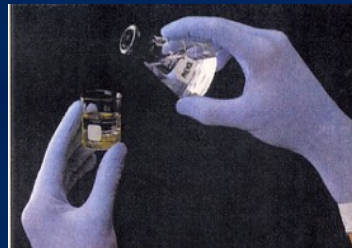
Livestock diagnostics or grading



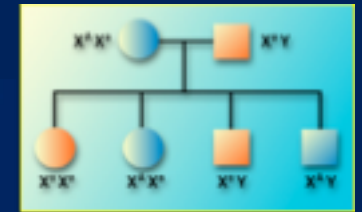
Environmental testing



Agricultural biotech



Basic Research



Identity testing



Individualized medicine



Human diagnostics

Understanding Information -Human Genome Project

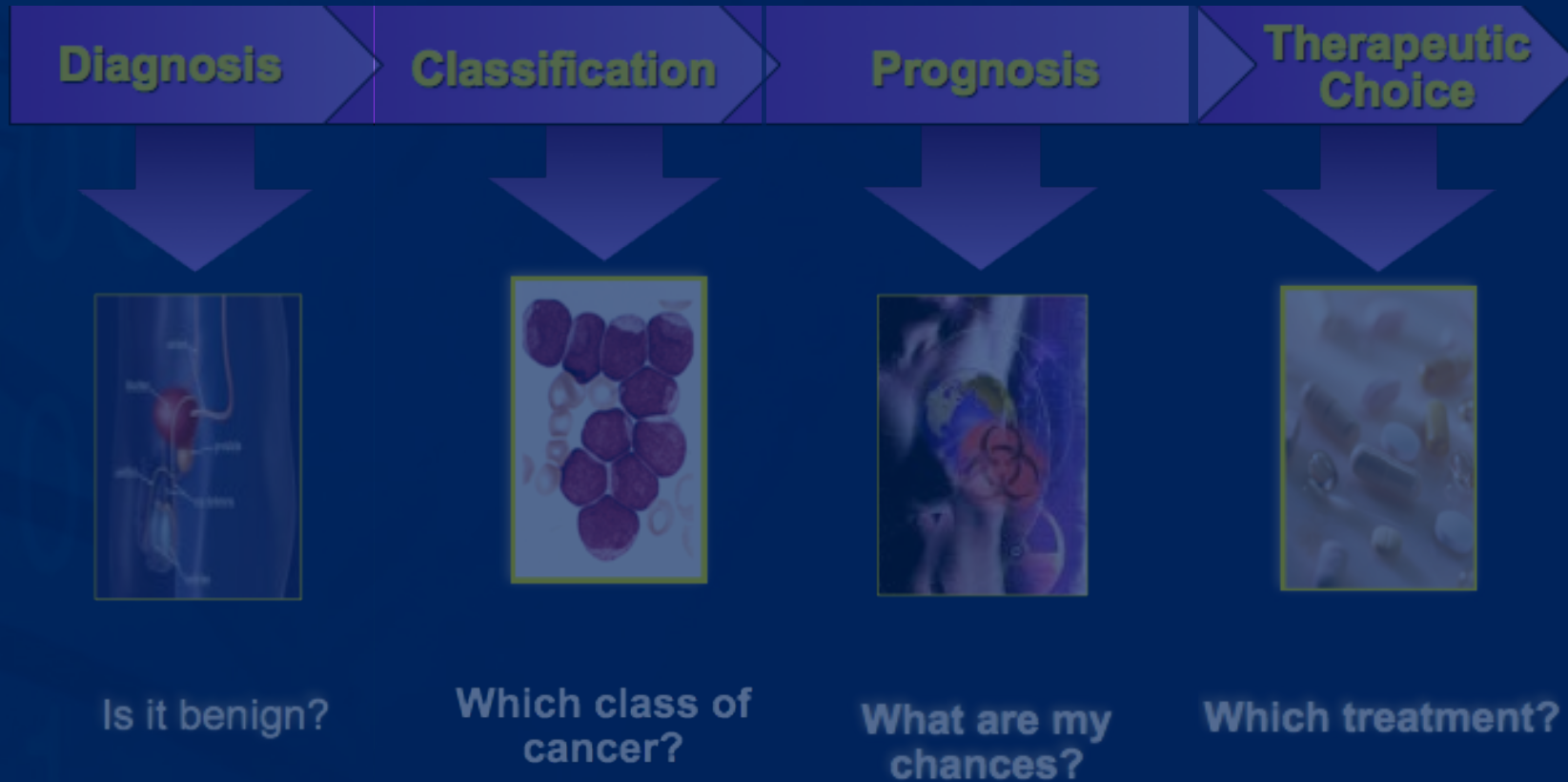
Gene Functions at a Basic Level

- 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

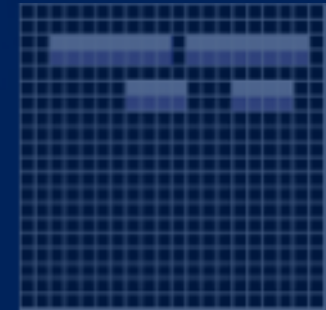
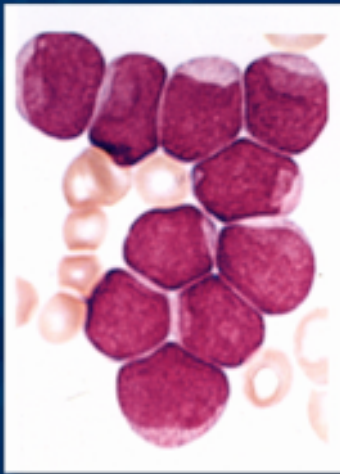
- Tumour Typing
 - Use expression patterns to complement classical histology to identify classes of tumors and predict disease development
- Drug Response
 - Monitor impact of a therapeutic on disease state or toxicological effect

Understanding Cancer

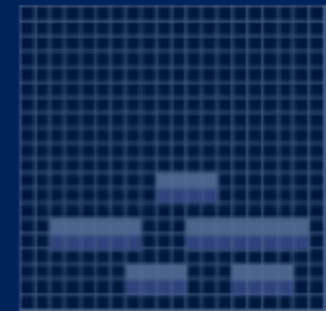


Distinguishing Between Leukaemias

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?

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 M¹.](#)

⊕ 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

Individual Variations in Drug Metabolism



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Individual Variations in Drug Metabolism



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 - One null allele

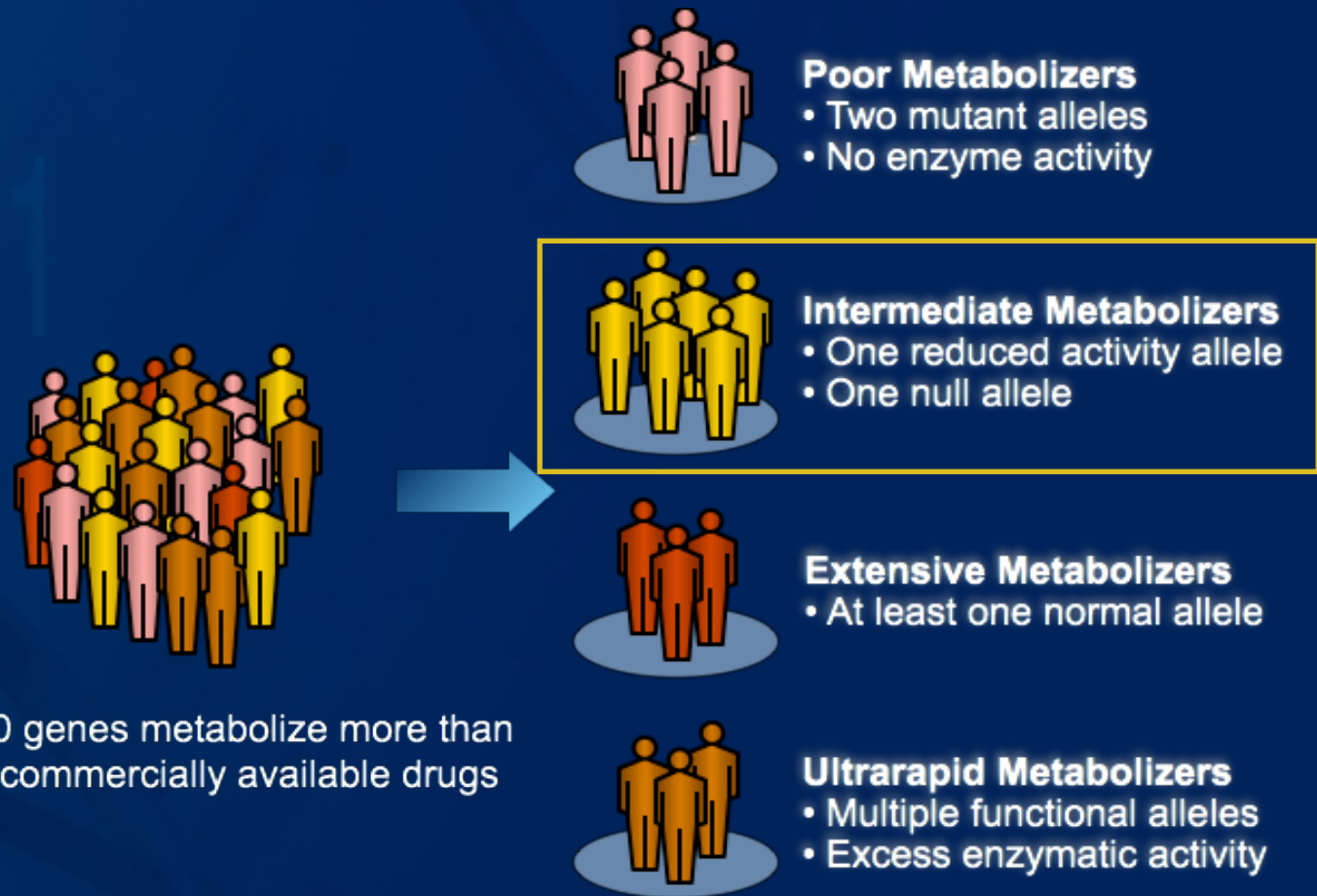


- Extensive Metabolizers**
- At least one normal allele



- Ultrarapid Metabolizers**
- Multiple functional alleles
 - Excess enzymatic activity

Individual Variations in Drug Metabolism



CYP450 genes metabolize more than 90% of commercially available drugs

What is GeneChip® Technology?



GeneChip® System



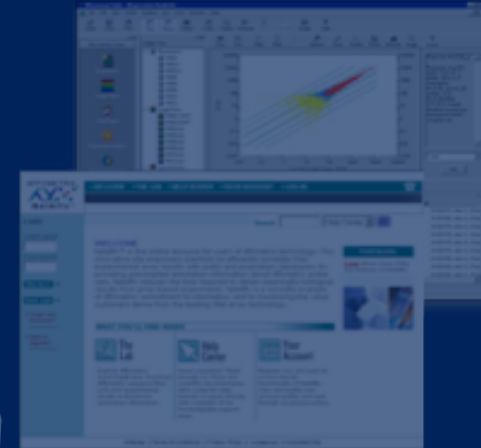
**Probe
Arrays
(chips)**



**Fluidics
Station**

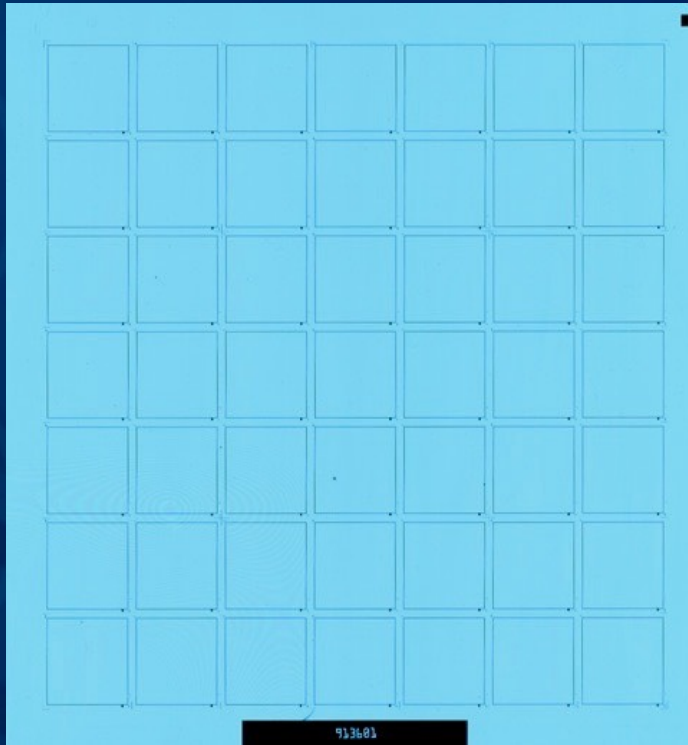


Scanner

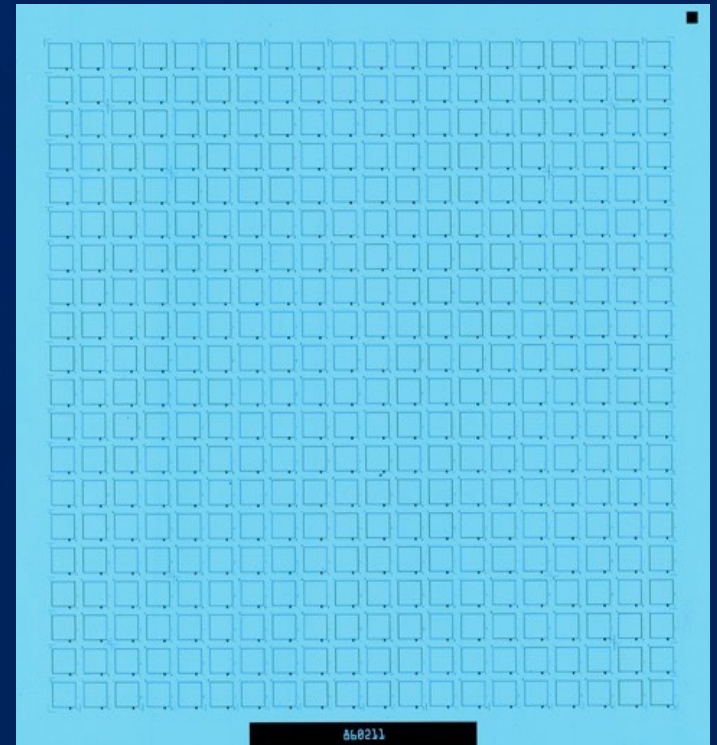


**Software
Data Analysis**

GeneChip[®] Technology?

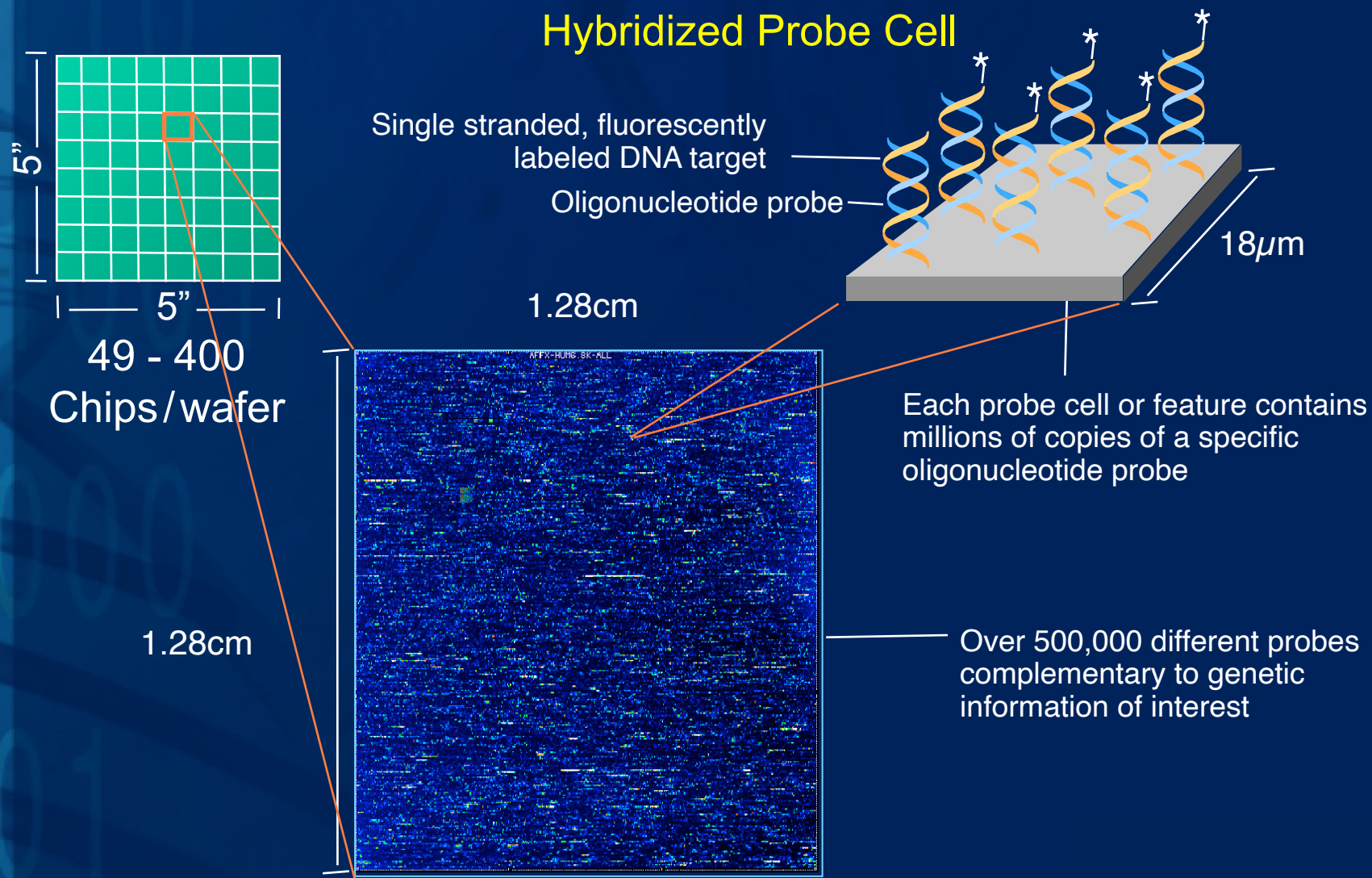


49 Chips per Wafer



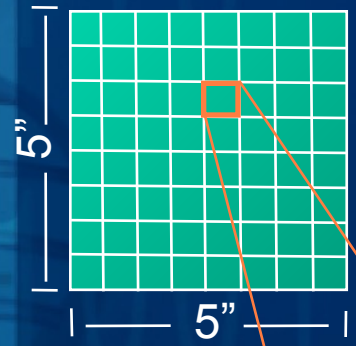
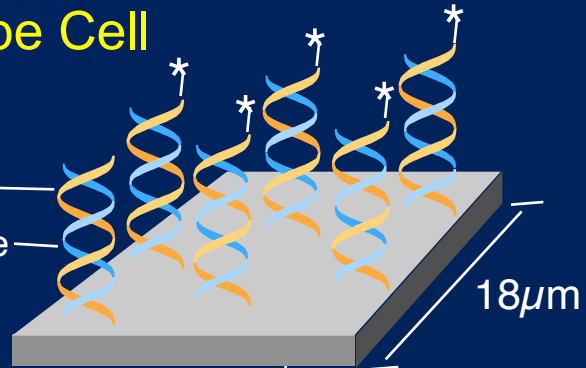
400 Chips per Wafer

GeneChip Probe Arrays

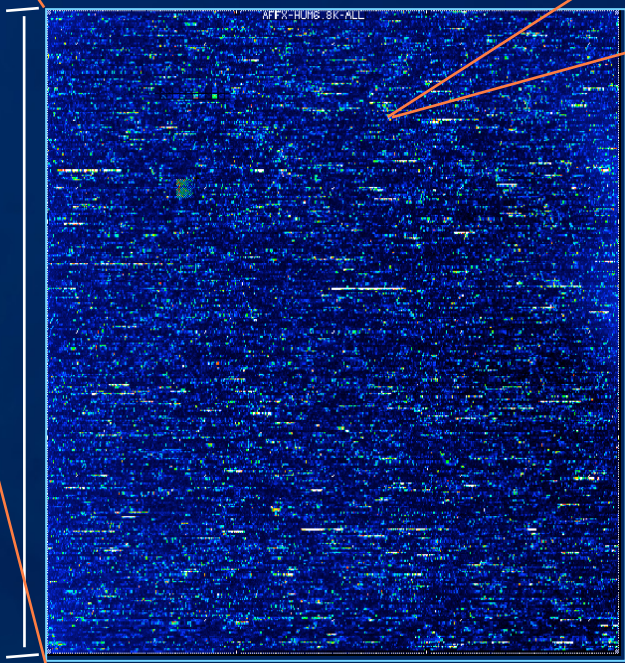


Hybridized Probe Cell

Single stranded, fluorescently labeled DNA target
Oligonucleotide probe



49 - 400
Chips/wafer



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

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

Image of Hybridized Probe Array

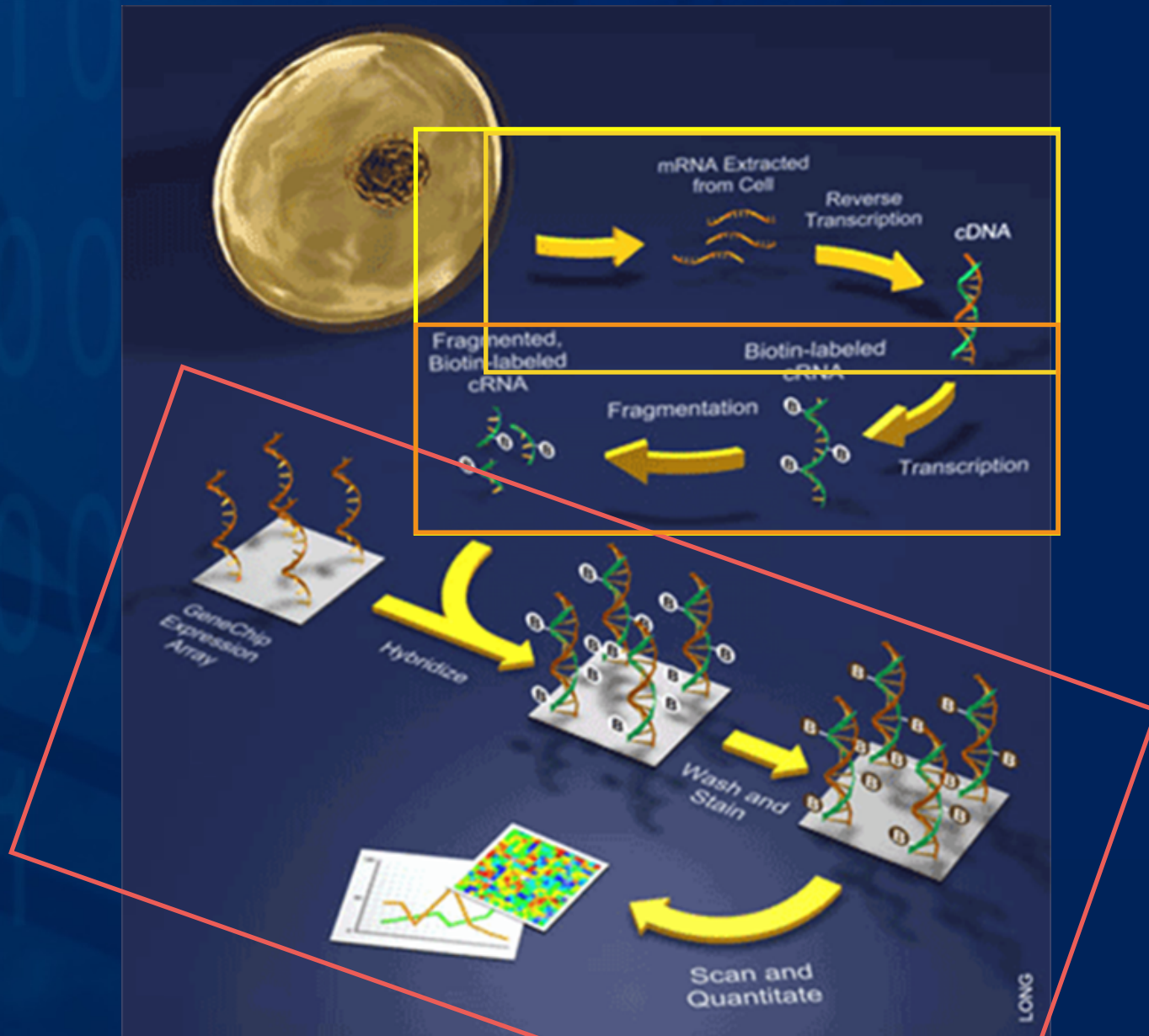
GeneChip[®] Array Advantages

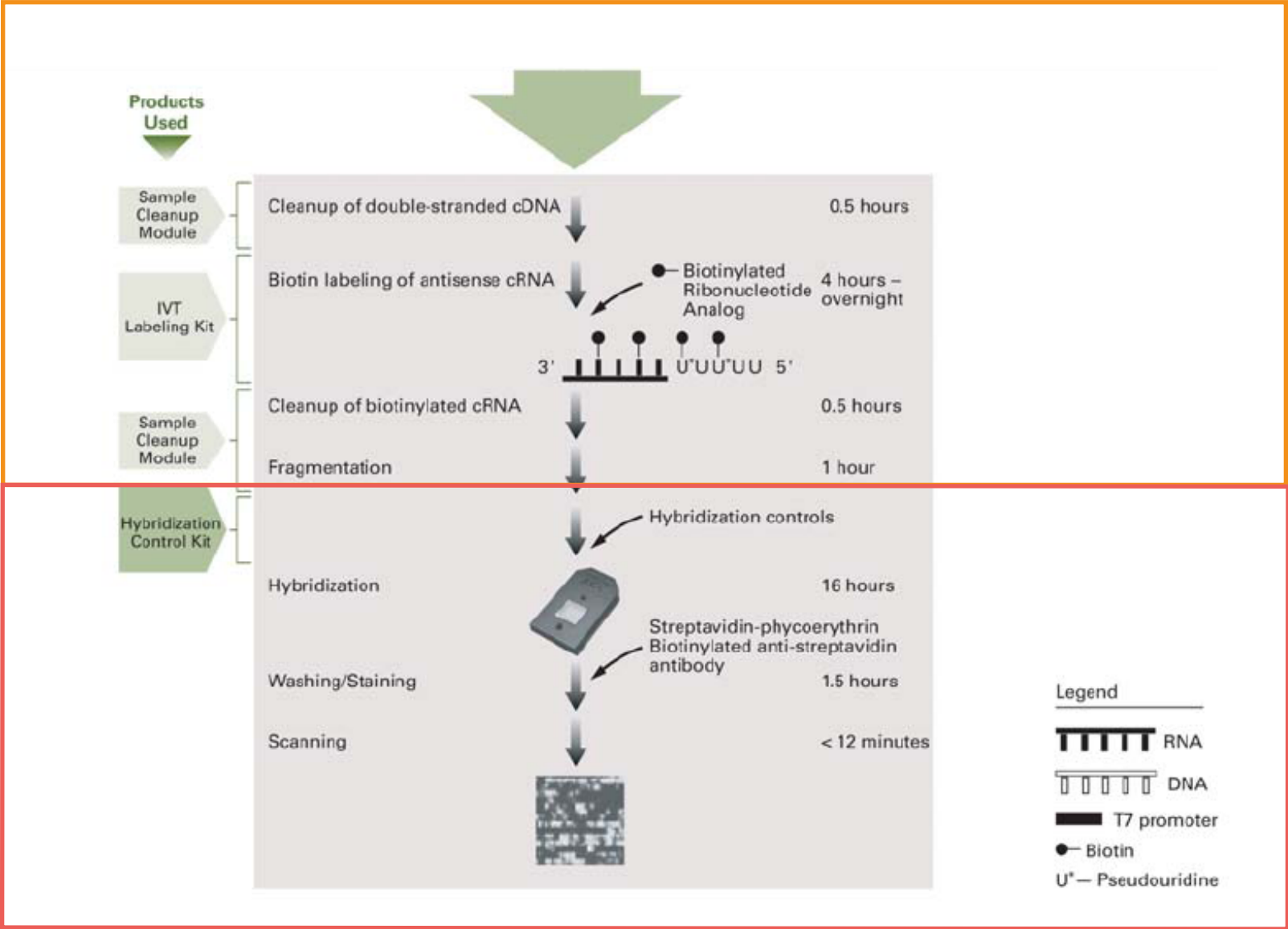
- Assume fixed array size, 1.28 x 1.28 cm

<u>Feature Size</u>	<u>Features/Chip</u>	<u>Genes/Chip</u>
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

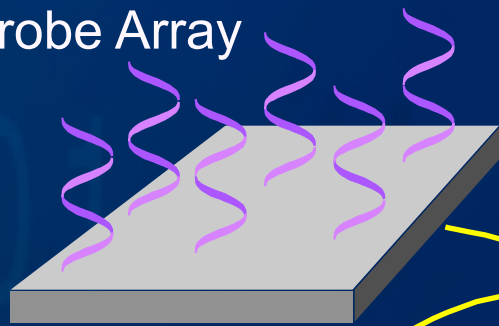




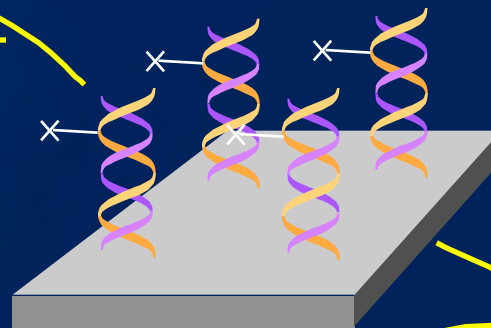
GeneChip[®] Expression Analysis

Hybridization and Staining

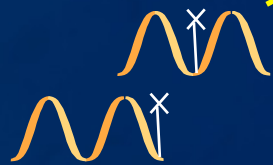
Probe Array



Hybridized Array

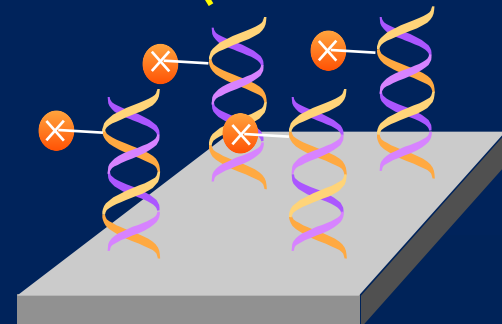


Labeled cRNA Target



Staining

Streptavidin-
phycoerythrin
conjugate



Avidin

+



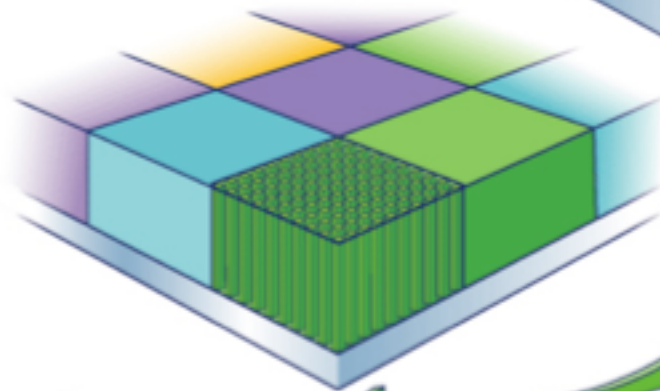
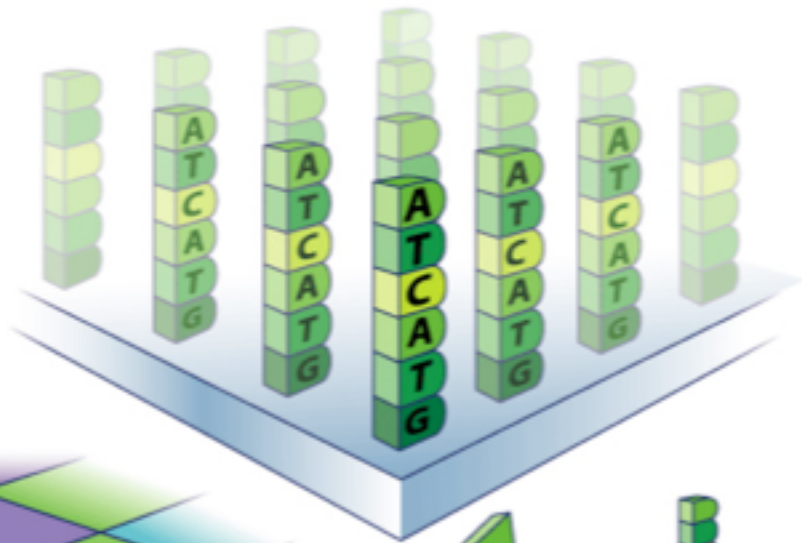
Biotin conjugate

=



Avidin-Biotin Complex

1.28 cm
1.28 cm
Actual size of
GeneChip[®] array

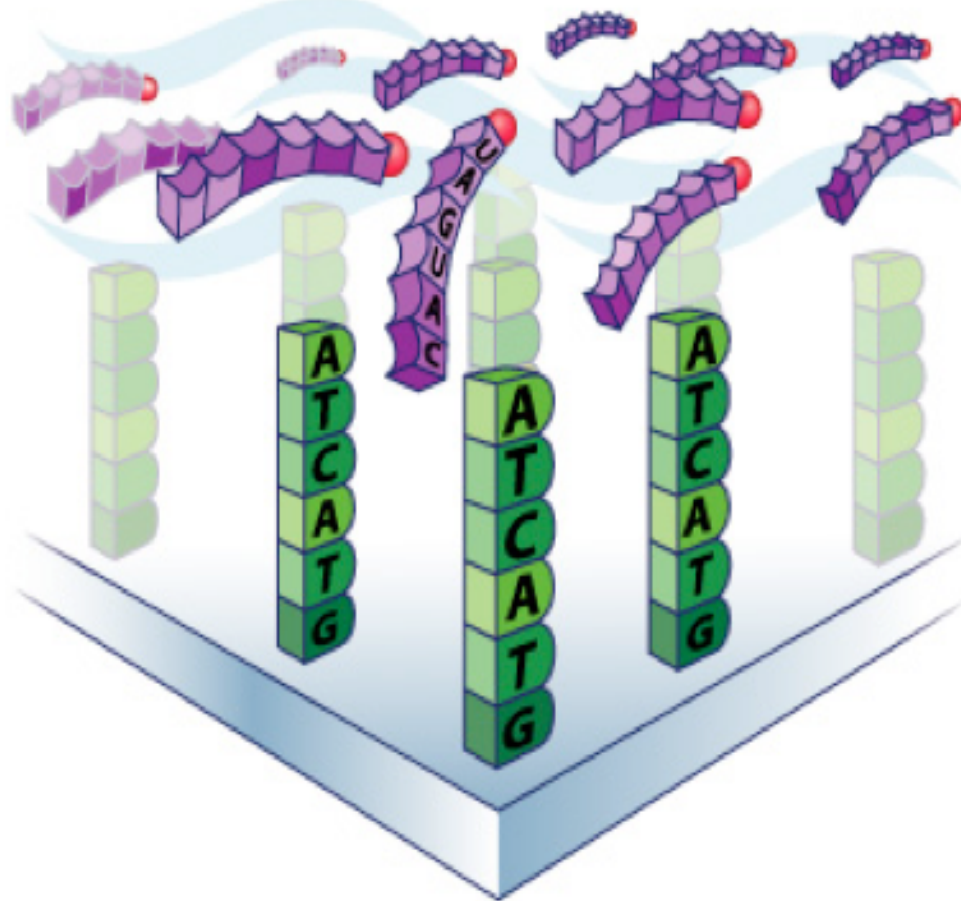


Millions of DNA strands built up in each location

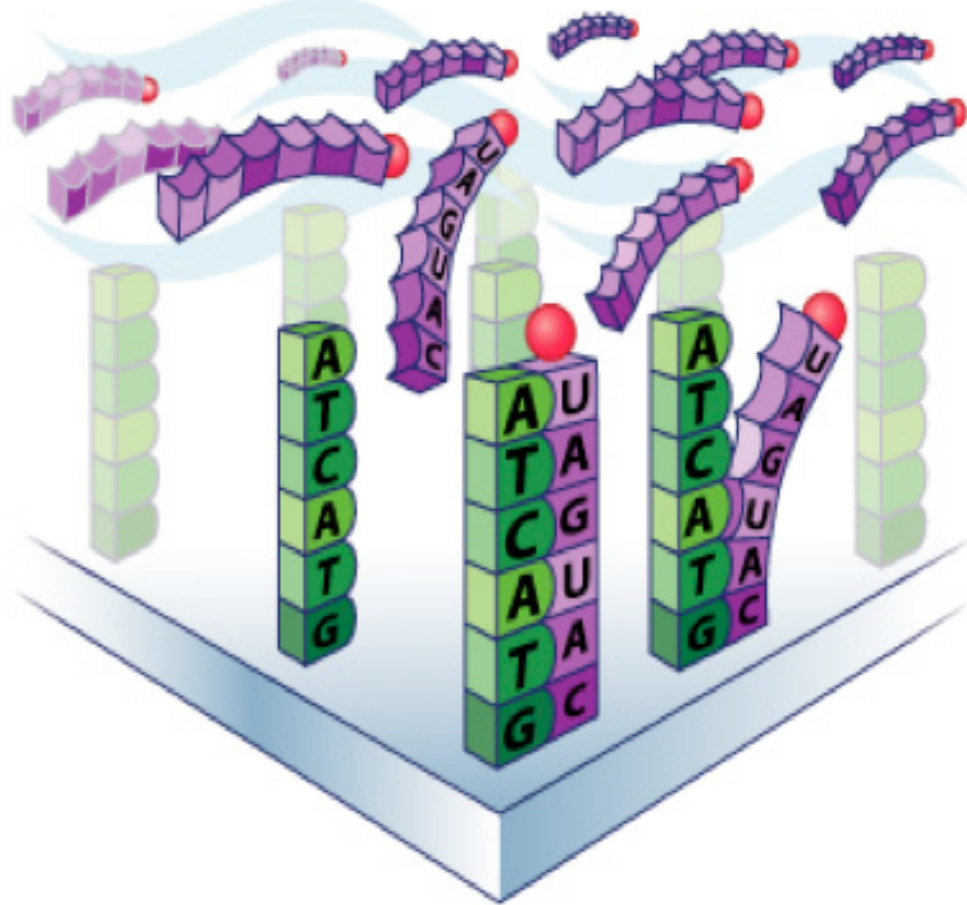
500,000 locations on each GeneChip[®] array



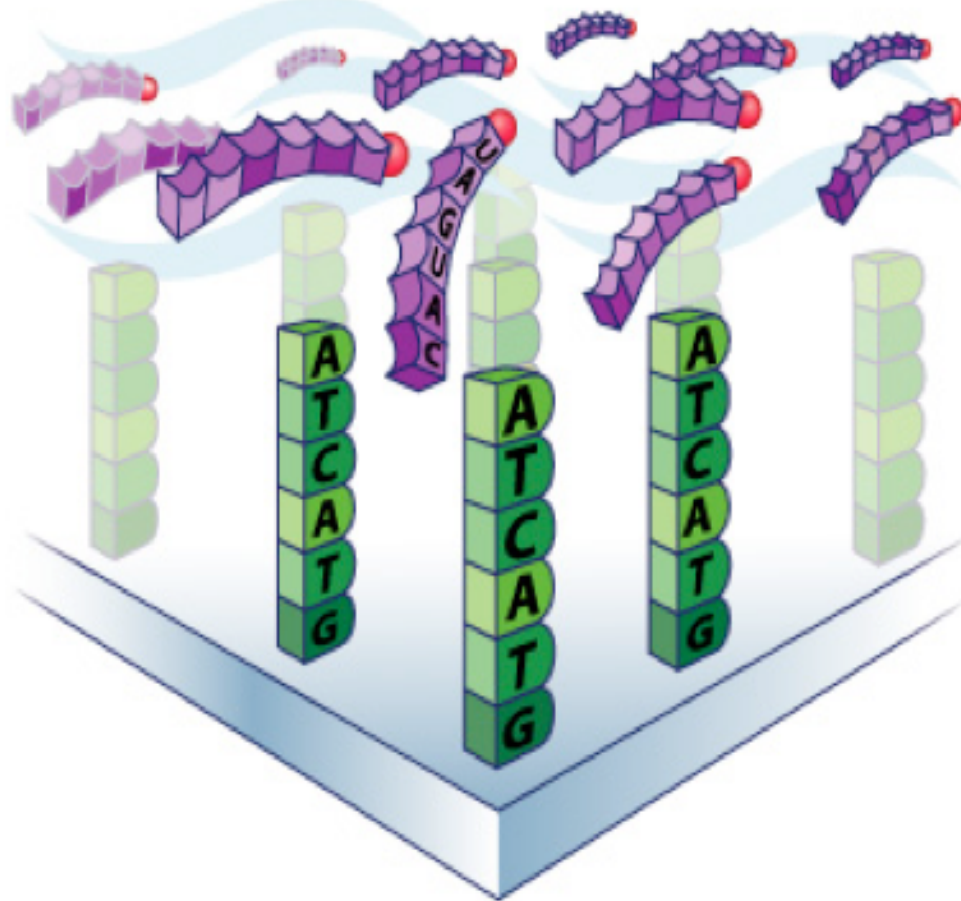
Actual strand = 25 base pairs



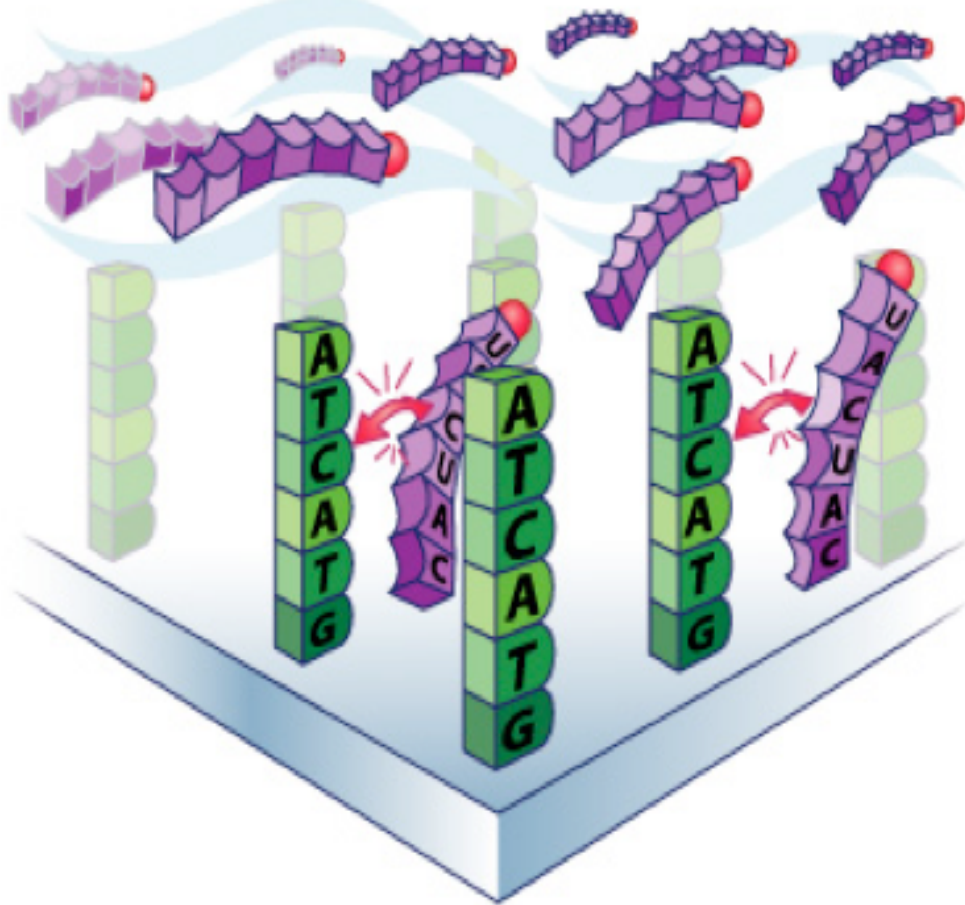
**Sample RNA fragments (purple)
washed over DNA probe array (green)**



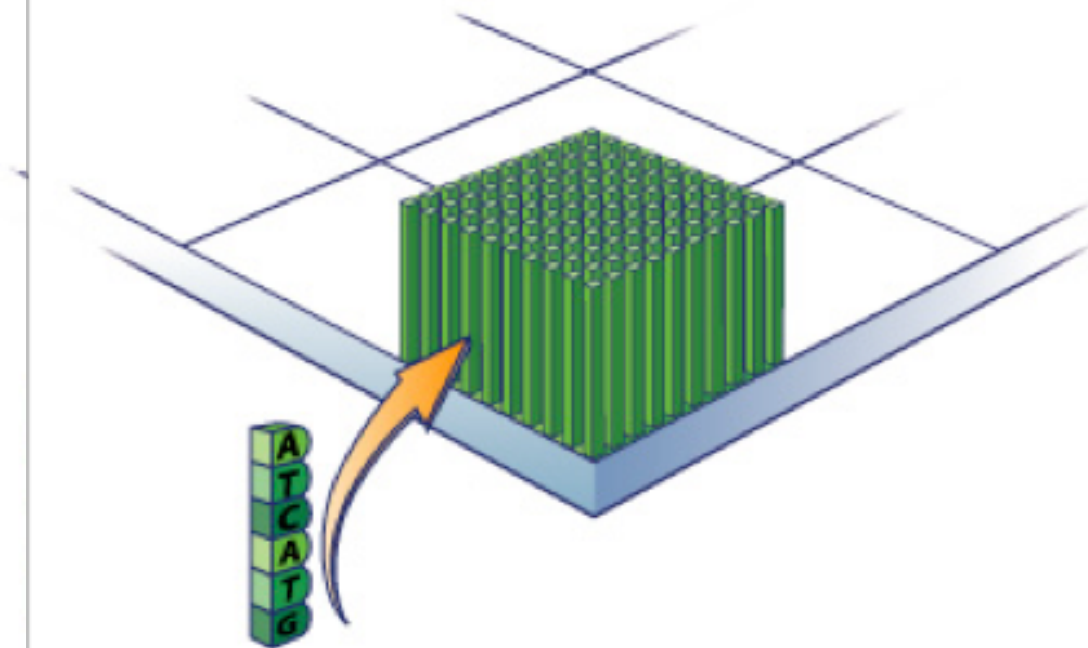
**Sample RNA fragments (purple)
hybridized to DNA probe array (green)**



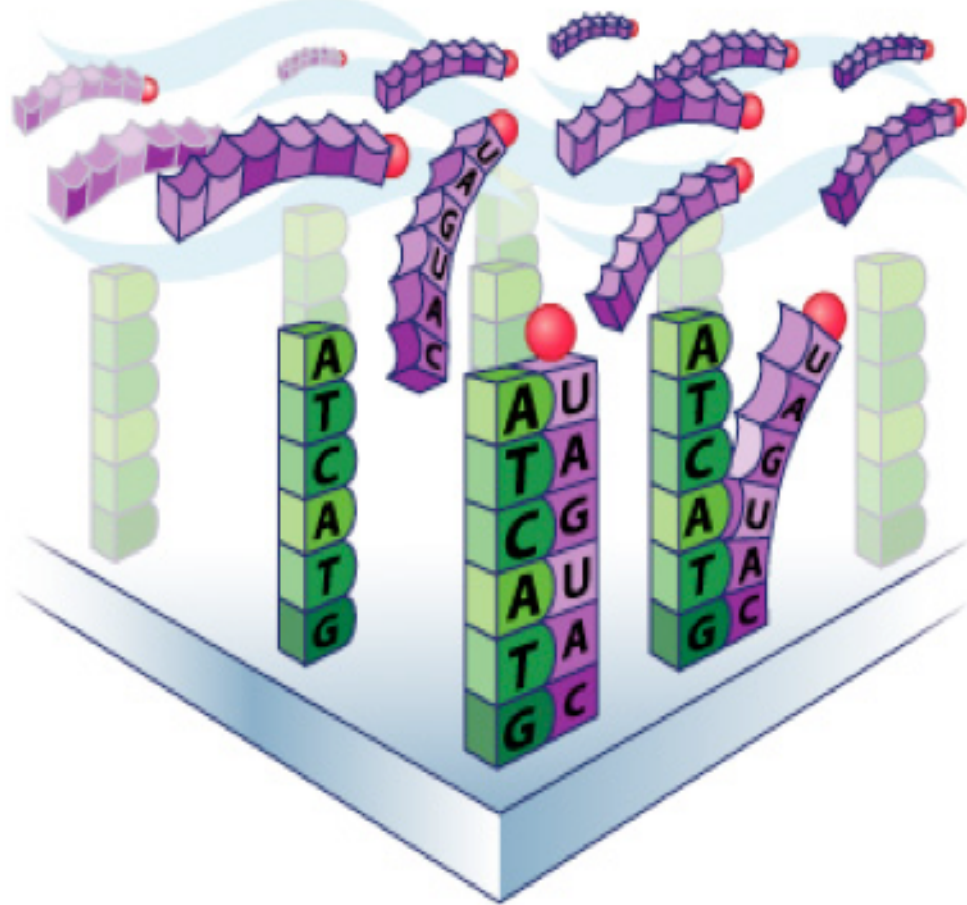
**Sample RNA fragments (purple)
washed over DNA probe array (green)**



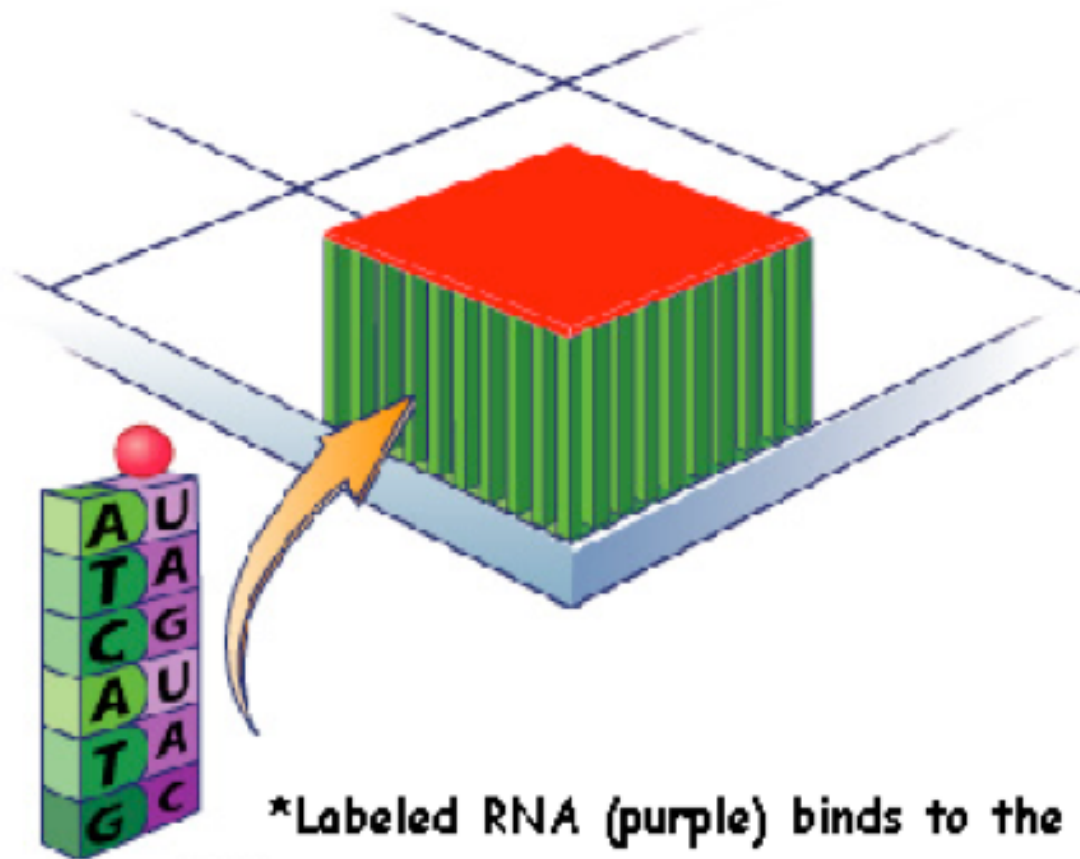
**C does not stick to another C,
so no match is made**



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)**

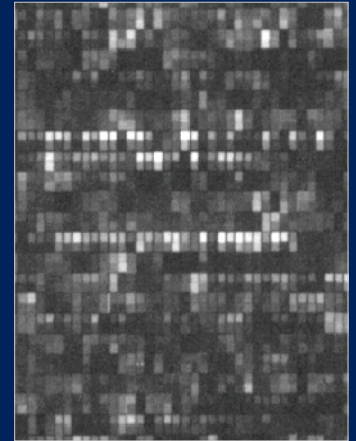


***Labeled RNA (purple) binds to the matching probes in the single feature.**

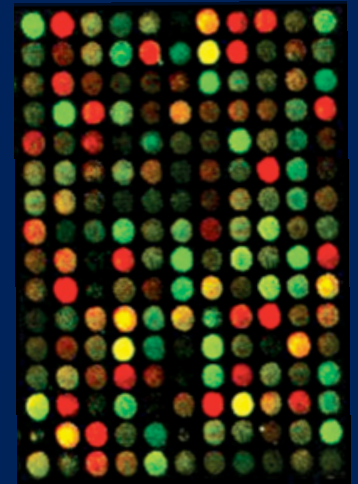
***The feature will now fluoresce**

GeneChip® vs. Spotted Arrays

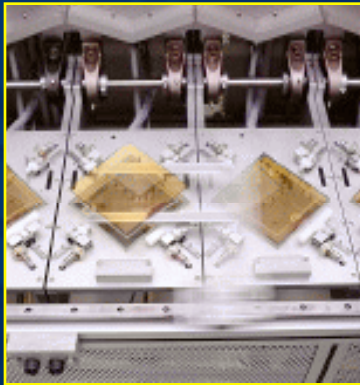
- Affymetrix GeneChip® Arrays use oligonucleotides
- Oligos are built on a solid support



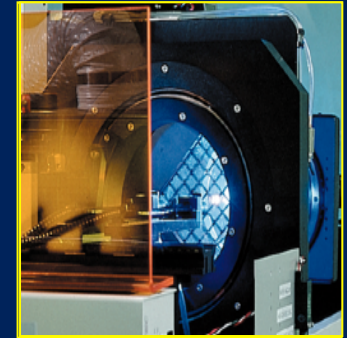
- Spotted arrays utilize nucleic acids made in solution
- Solutions are then “spotted” onto a solid support
- Competitive Hybridization



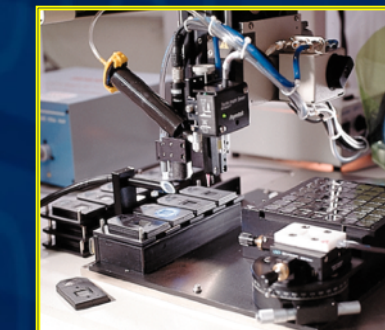
Proven Manufacturing Systems



Wafer Prep



Photolithography

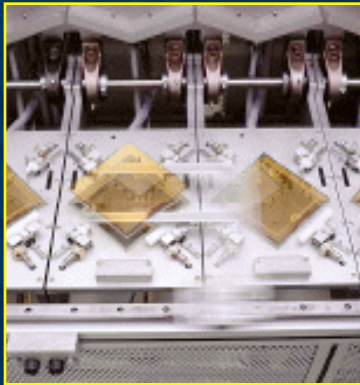


Cartridge Assembly

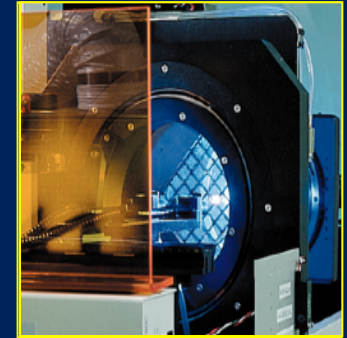


**Finished GeneChip
Probe Array**

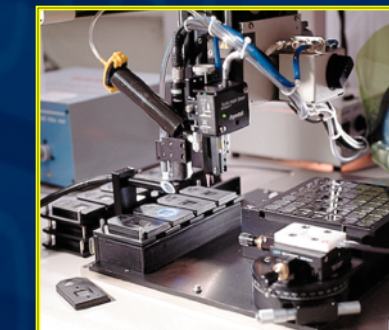
Proven Manufacturing Systems



Wafer Prep



Photolithography

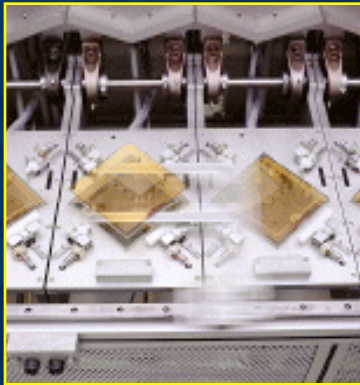


Cartridge Assembly

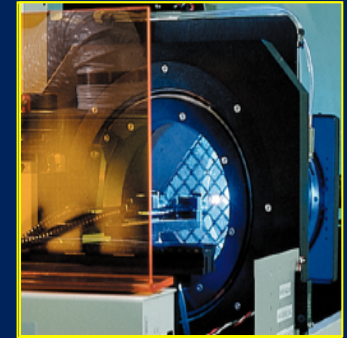


**Finished GeneChip
Probe Array**

Proven Manufacturing Systems



Wafer Prep



Photolithography

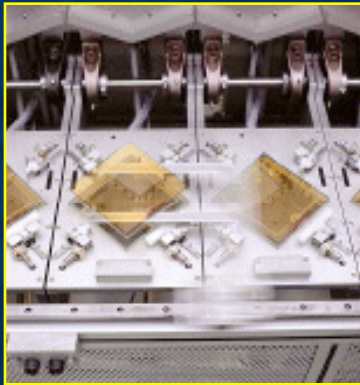


Cartridge Assembly

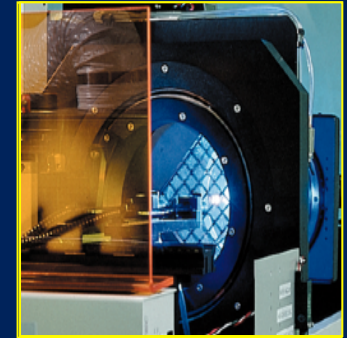


**Finished GeneChip
Probe Array**

Proven Manufacturing Systems



Wafer Prep



Photolithography

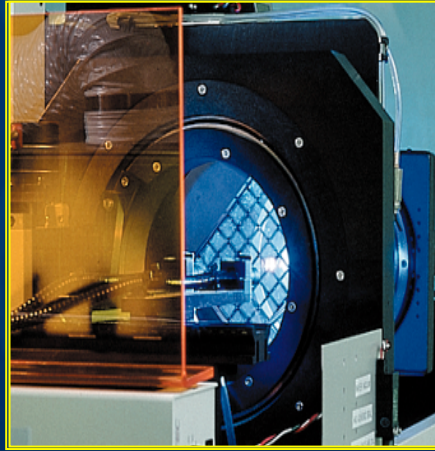


Cartridge Assembly



**Finished GeneChip
Probe Array**

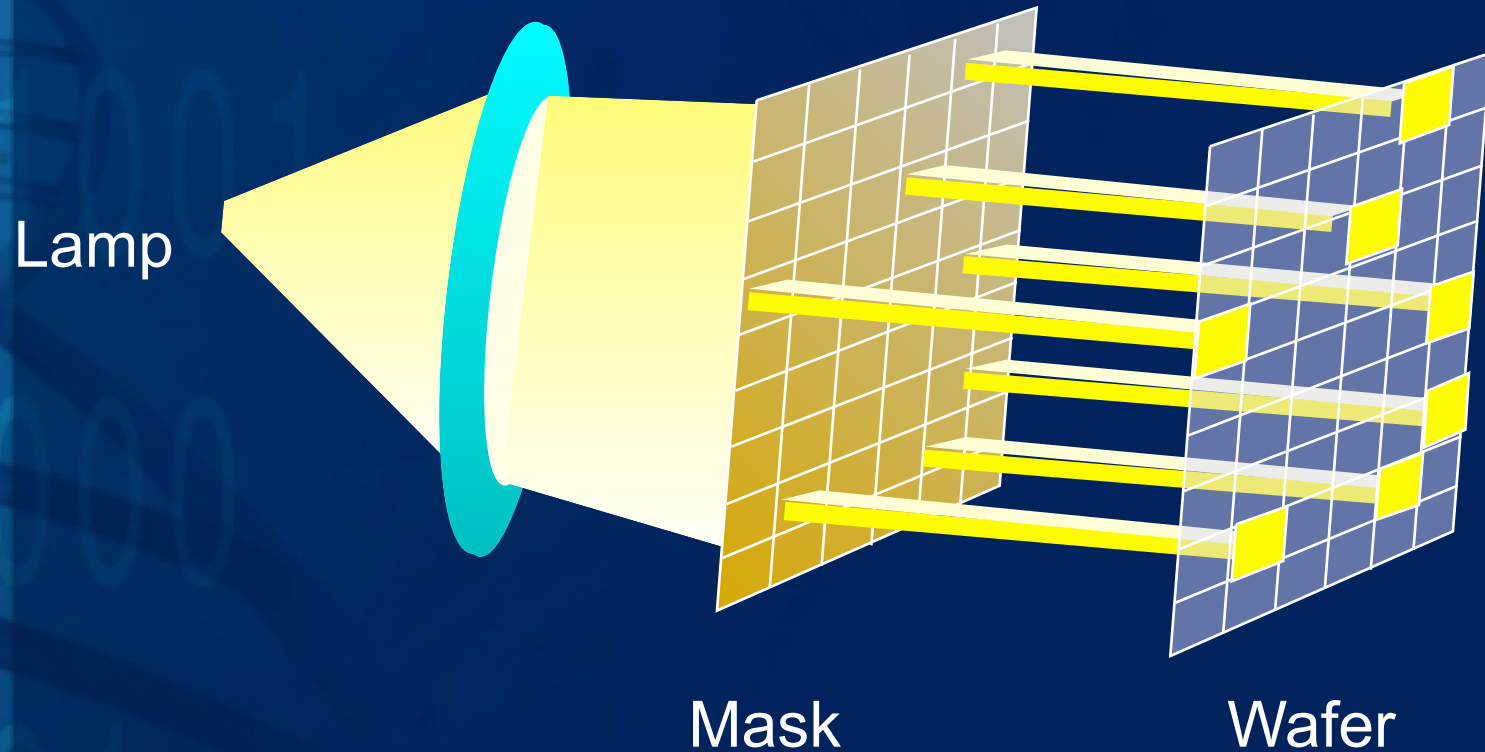
Photolithographic Synthesis



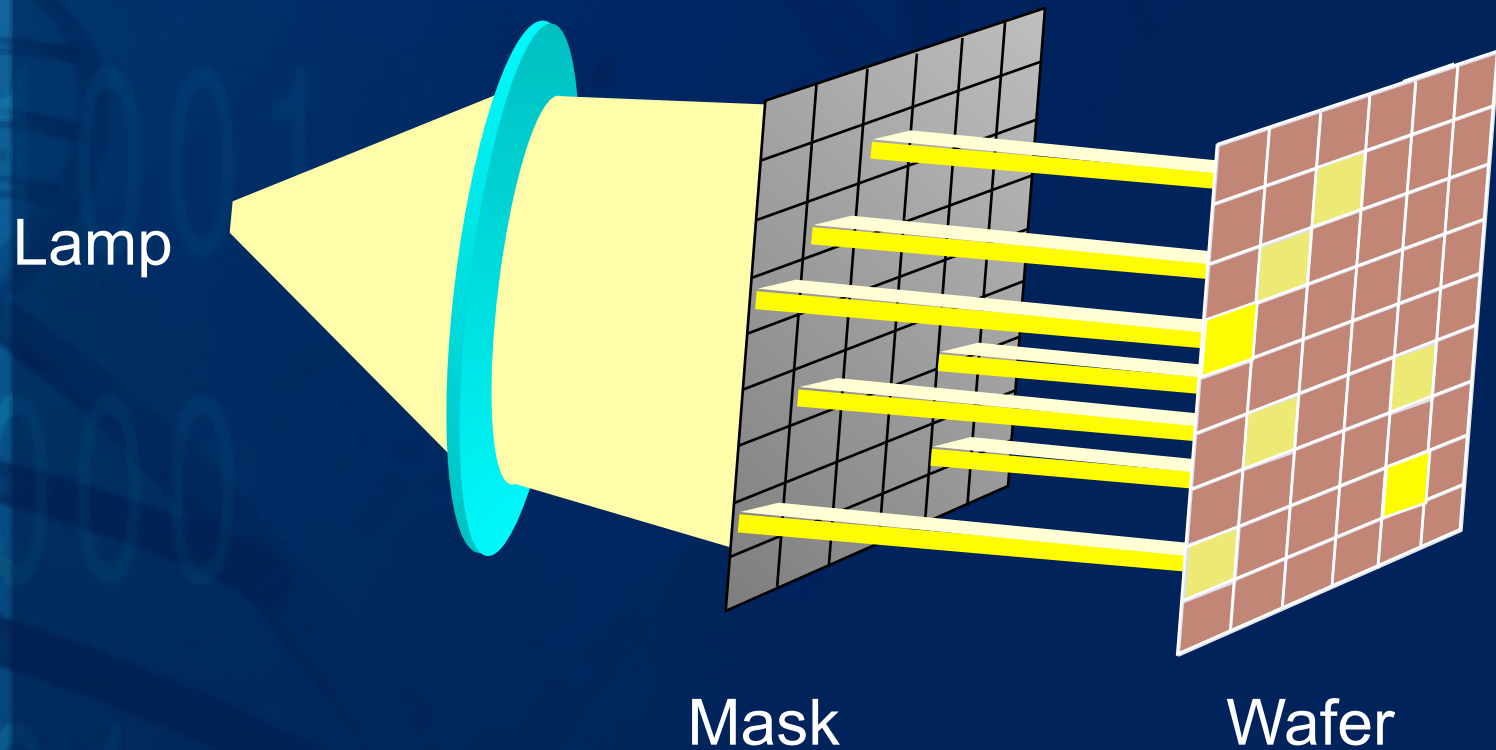
Photolithography



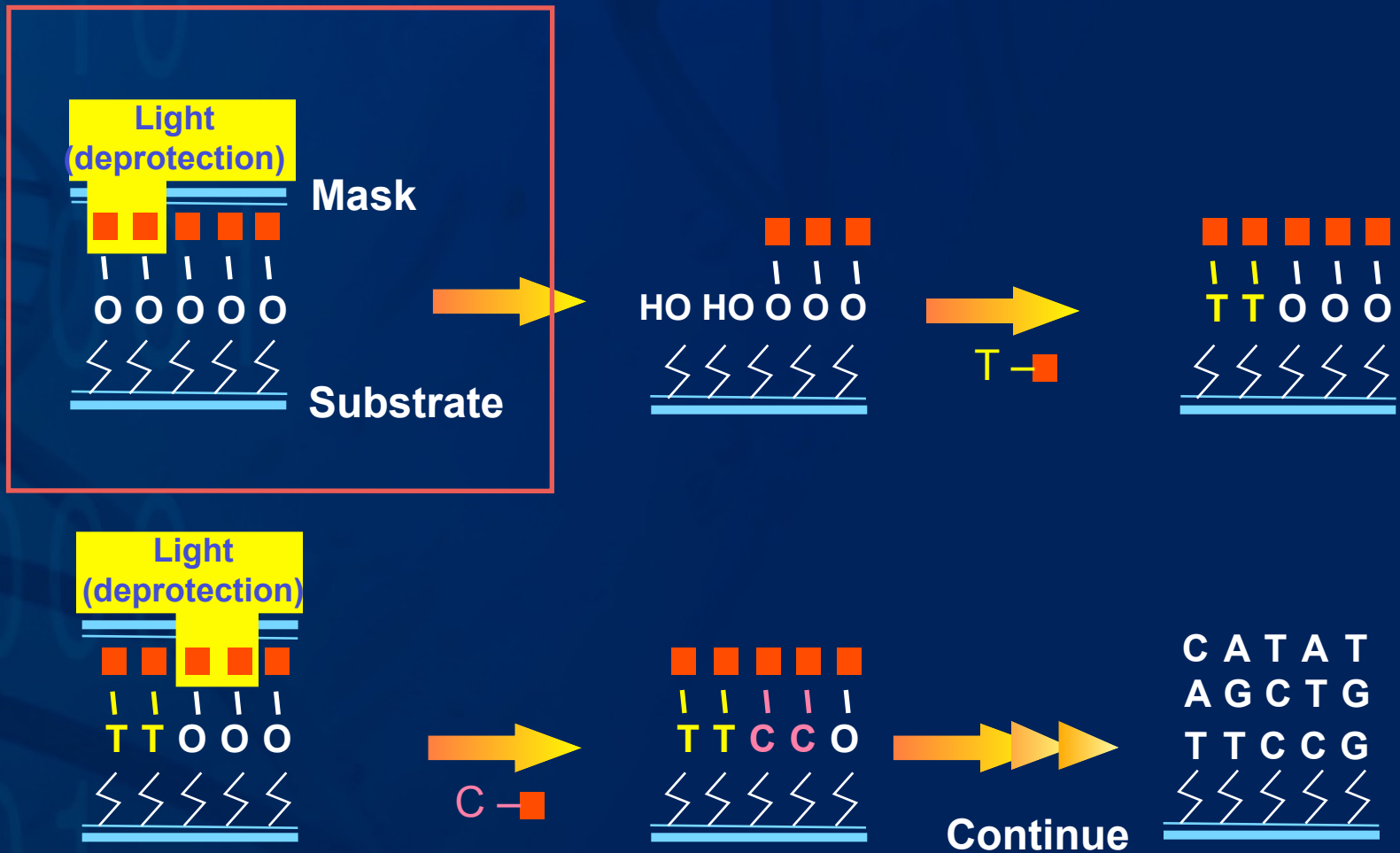
Photolithographic Synthesis



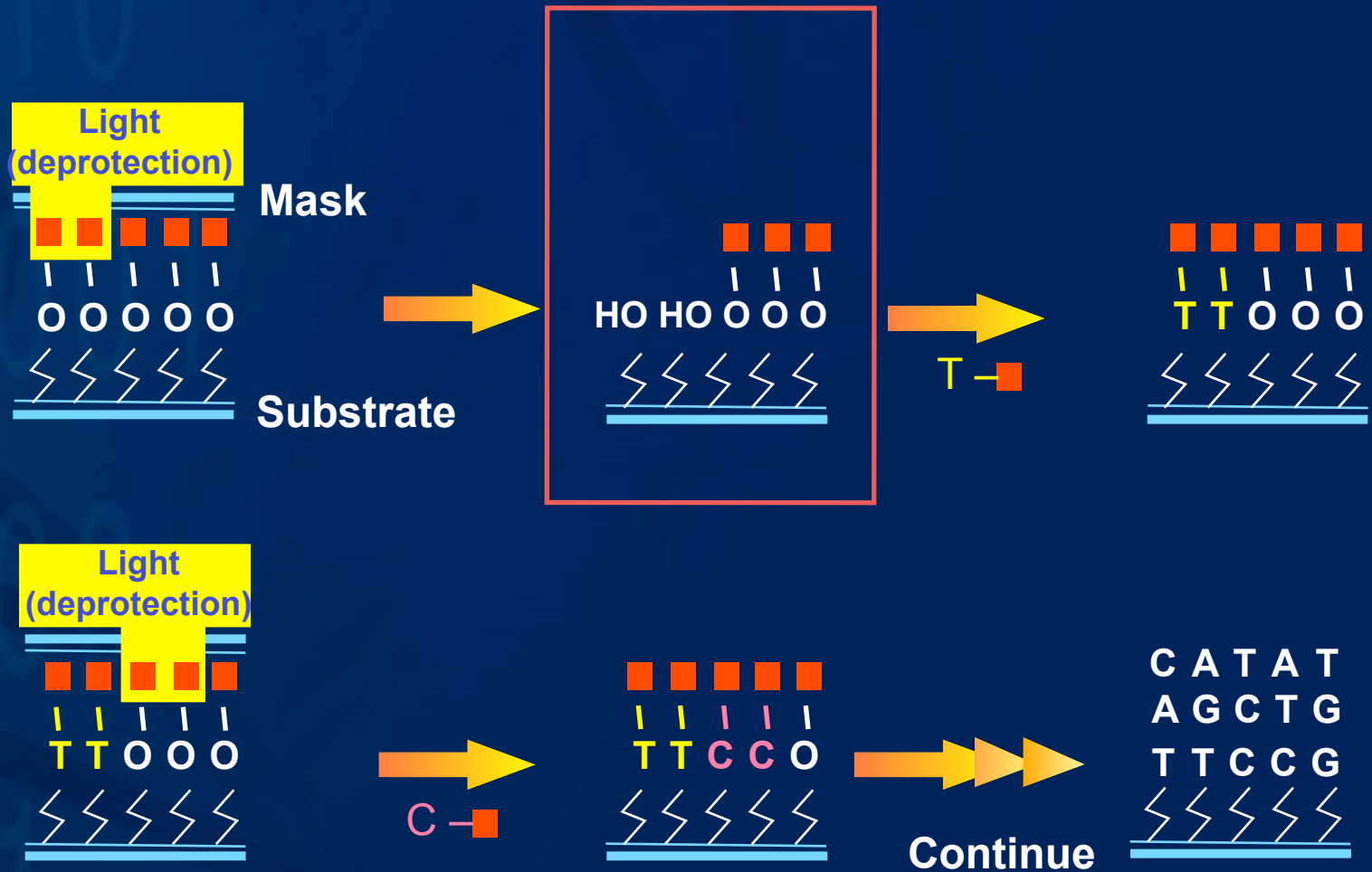
Photolithographic Synthesis



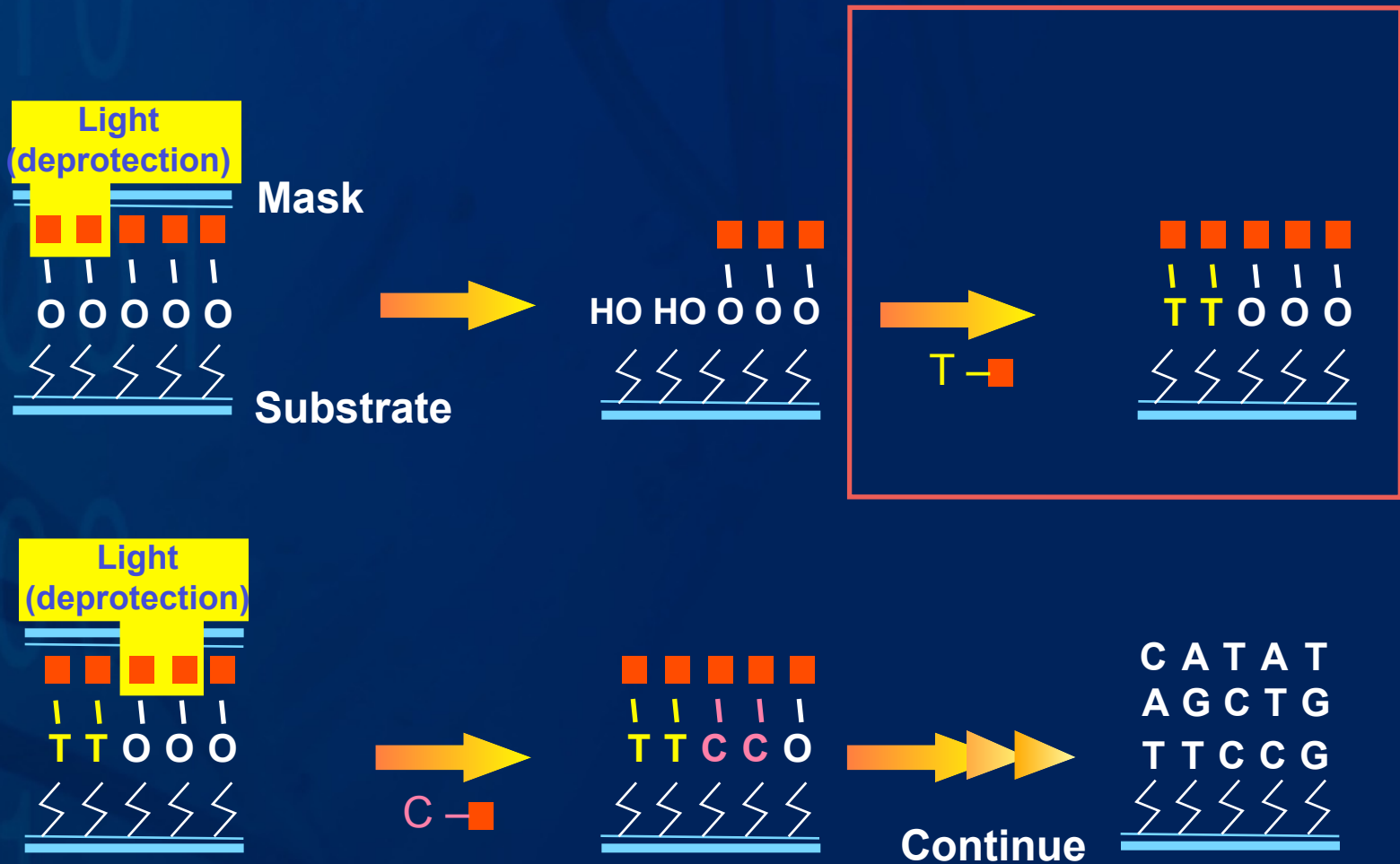
How Probes Are Synthesized



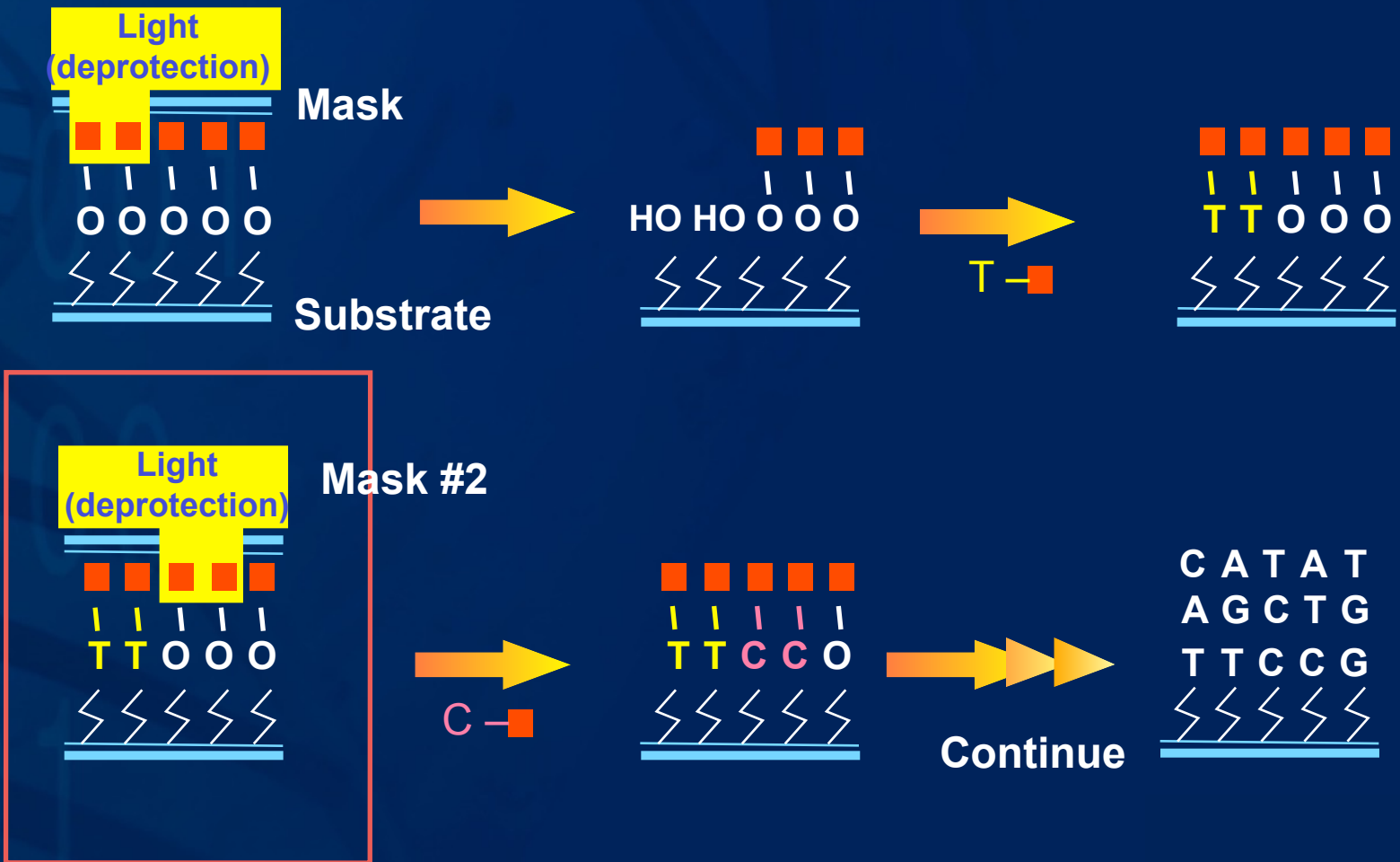
How Probes Are Synthesized



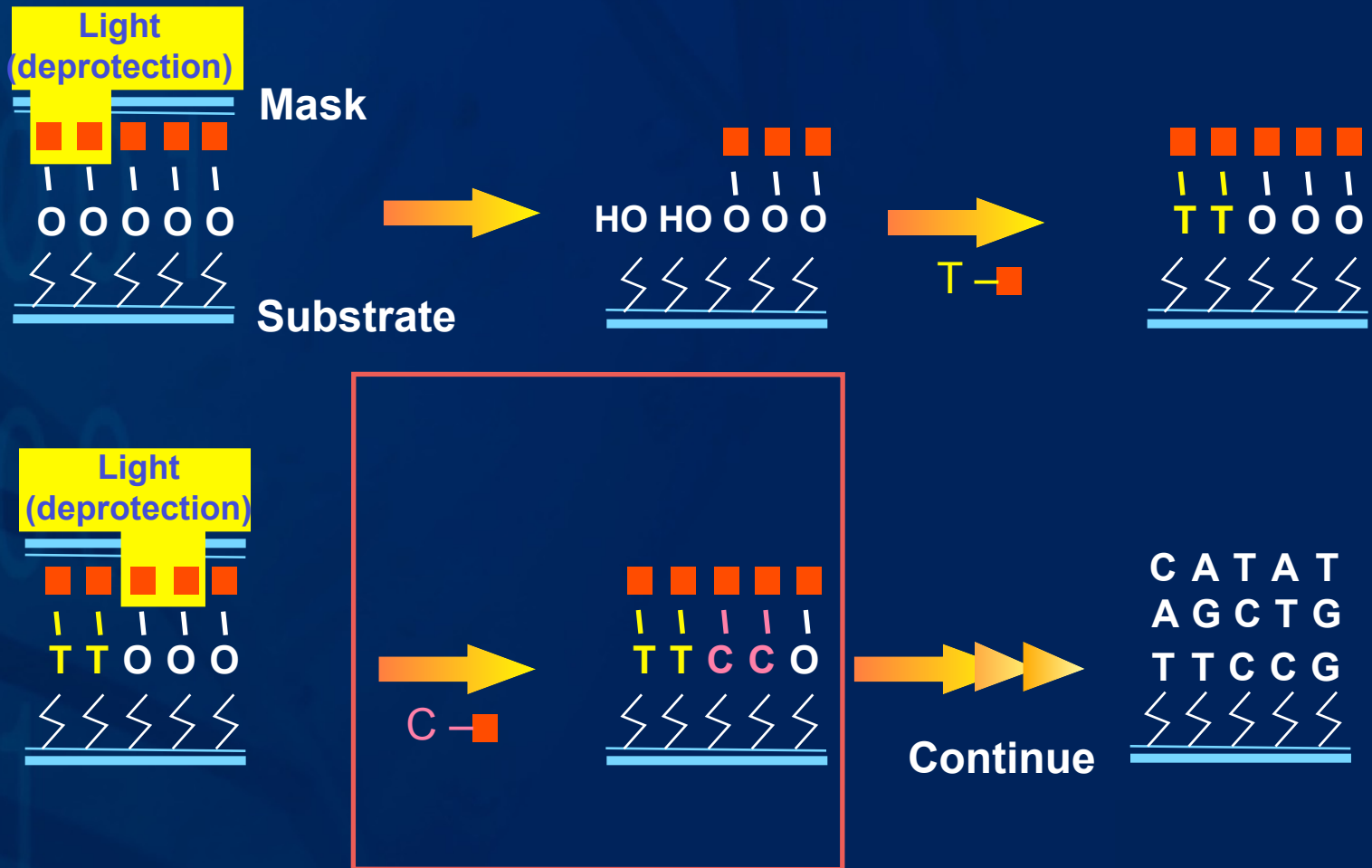
How Probes Are Synthesized



How Probes Are Synthesized



How Probes Are Synthesized



How Probes Are Synthesized

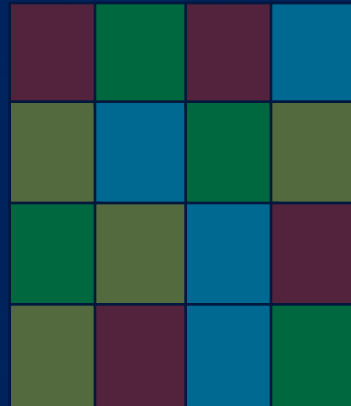


Combinatorial Synthesis

Any N-mer can be synthesized in $4 \times N$ steps

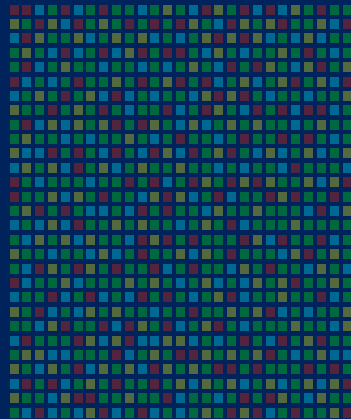
Example:

Sixteen 20-mers



< 80-step
synthesis

$\sim 10^{12}$ 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

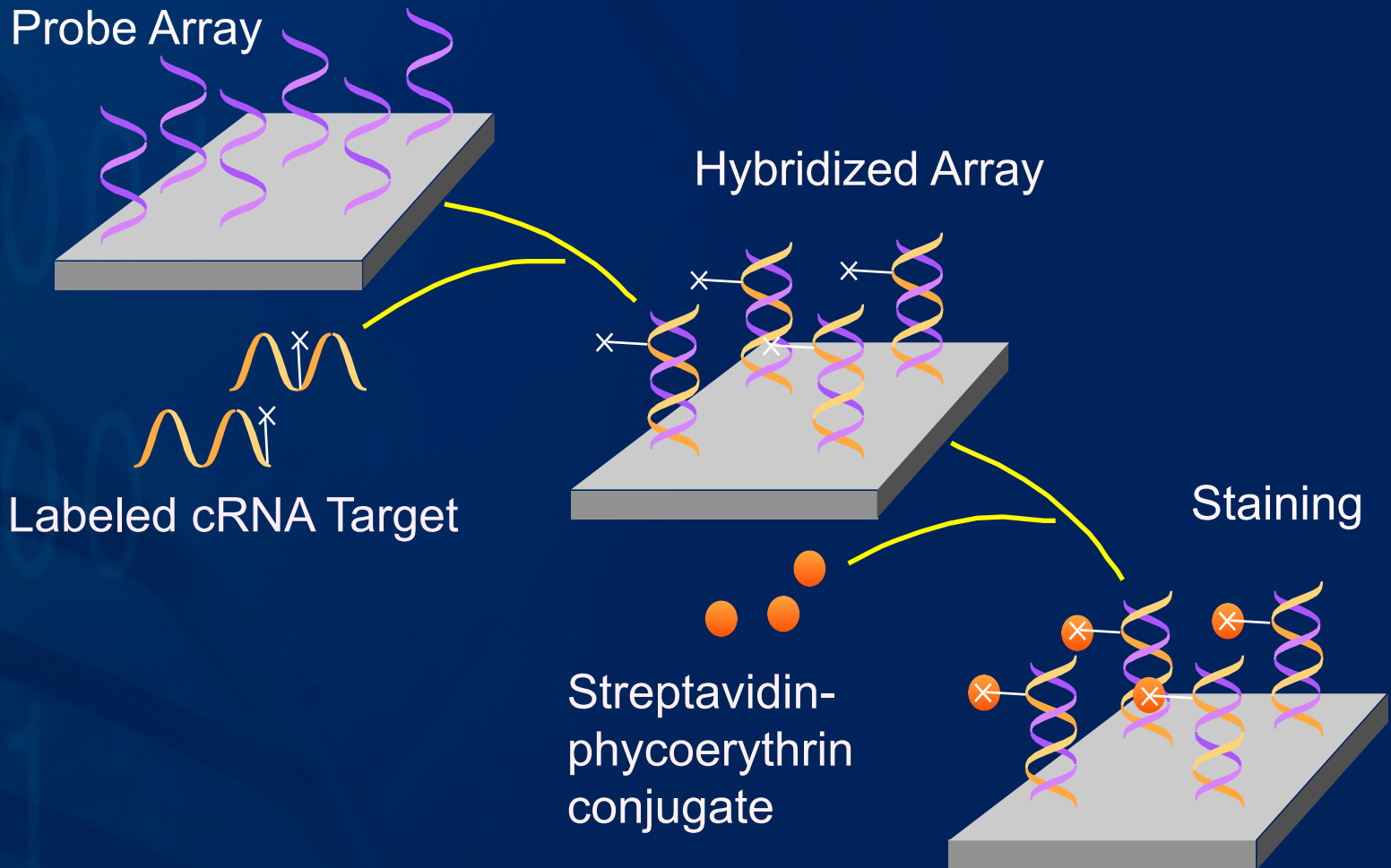
GeneChip[®] Array Advantages

- Multiple Indicators for the Same Target Ensures:

- Specificity
- Quantitative accuracy
- Low false positive rate
- High sensitivity

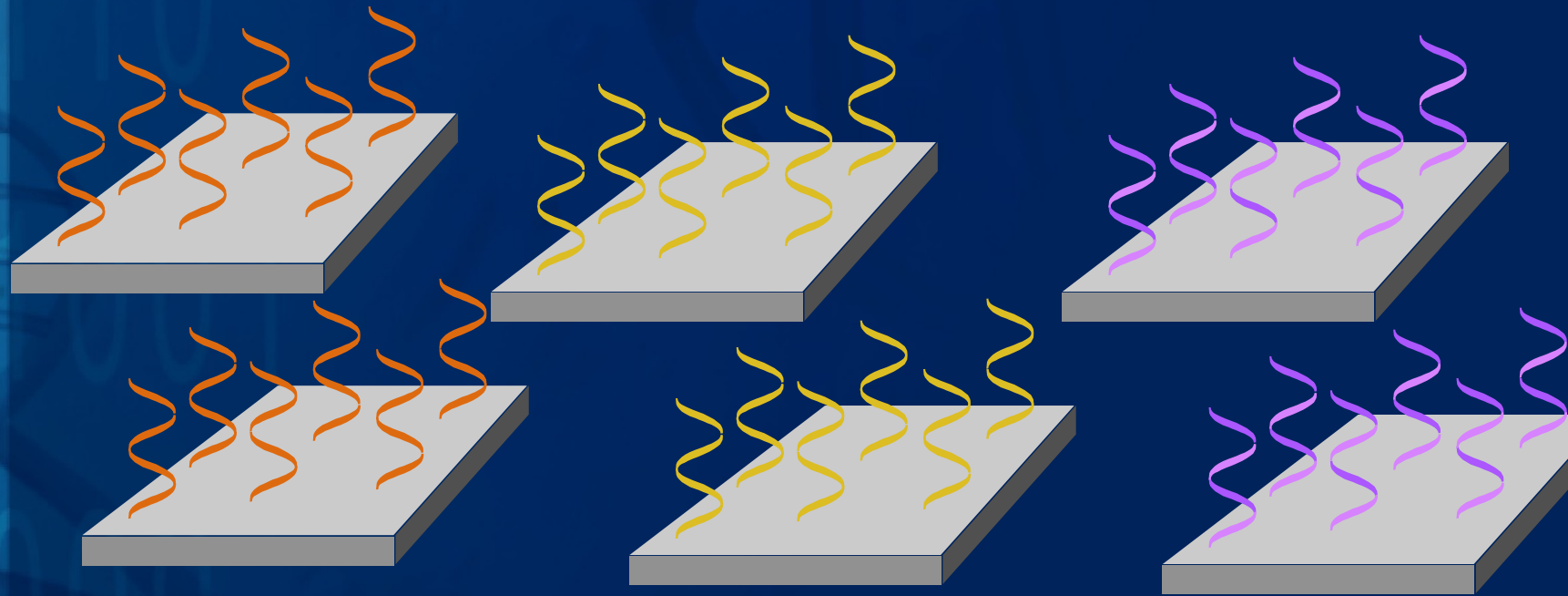
GeneChip[®] Expression Analysis

Hybridization and Staining



GeneChip[®] Array Advantages

Specificity



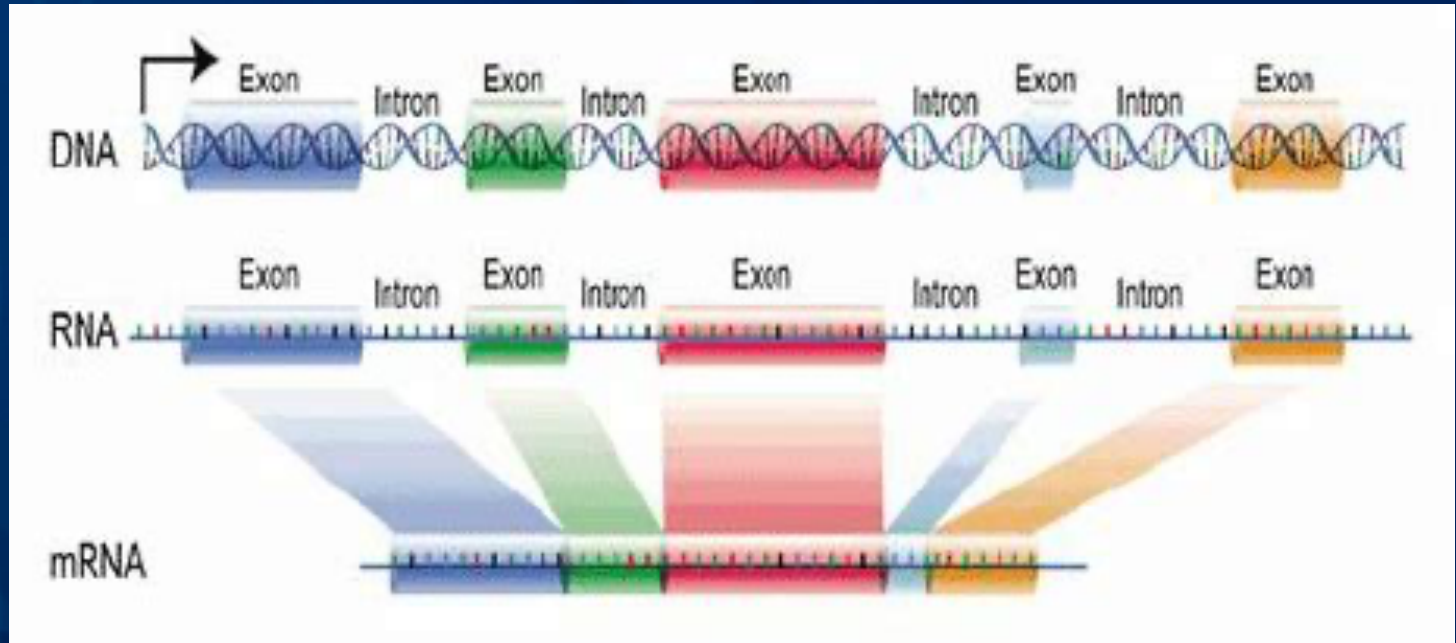
Gene



Oligo probes for Increased Gene Specificity

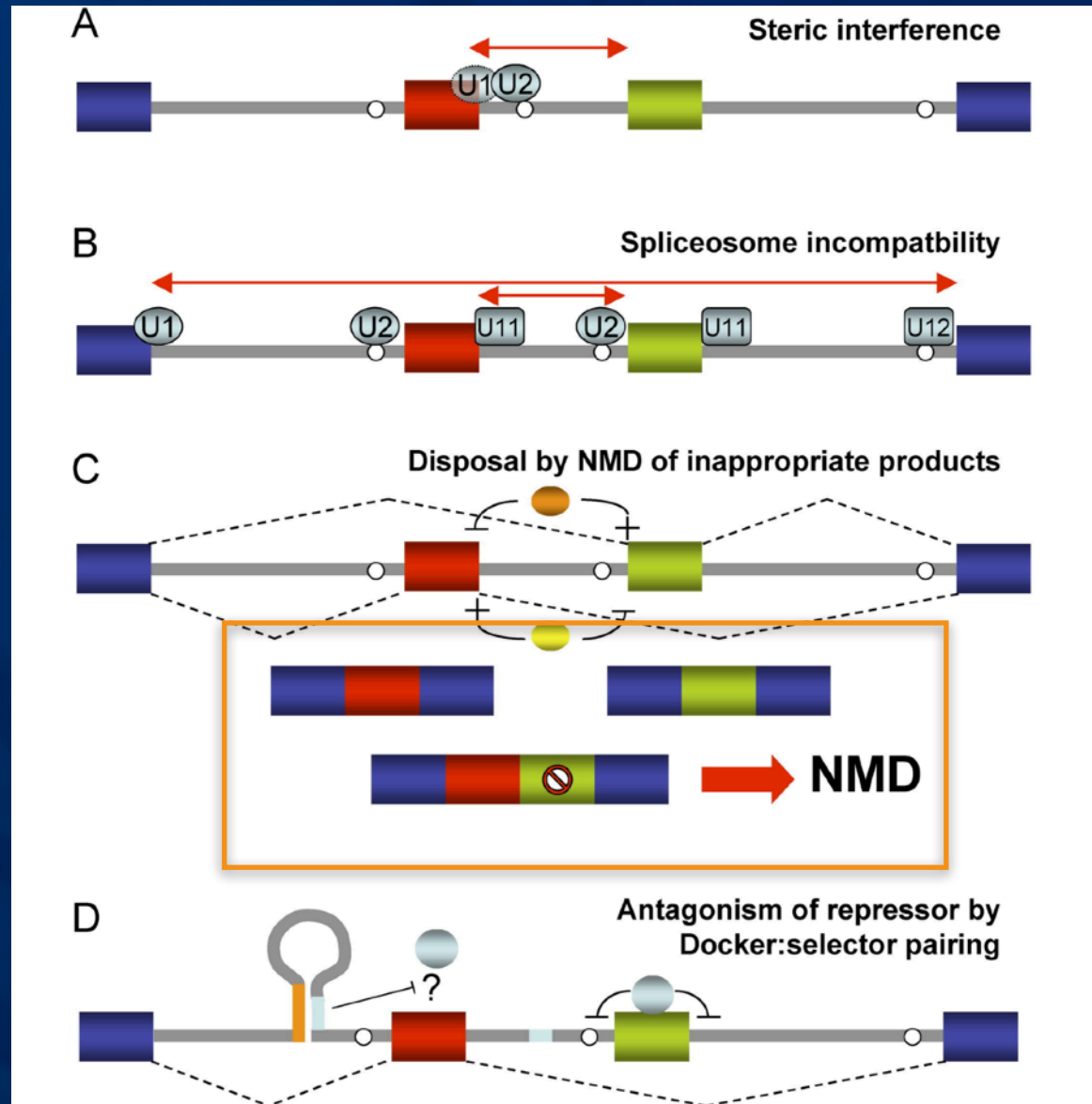
GeneChip[®] Array Advantages

Specificity



GeneChip[®] Array Advantages

Specificity



GeneChip[®] Array Advantages

Specificity

Gene 1



Oligo probes for Gene 1

Gene 2



Oligo probes for Gene 2

cDNA
for Gene 1



cDNA
for Gene 2

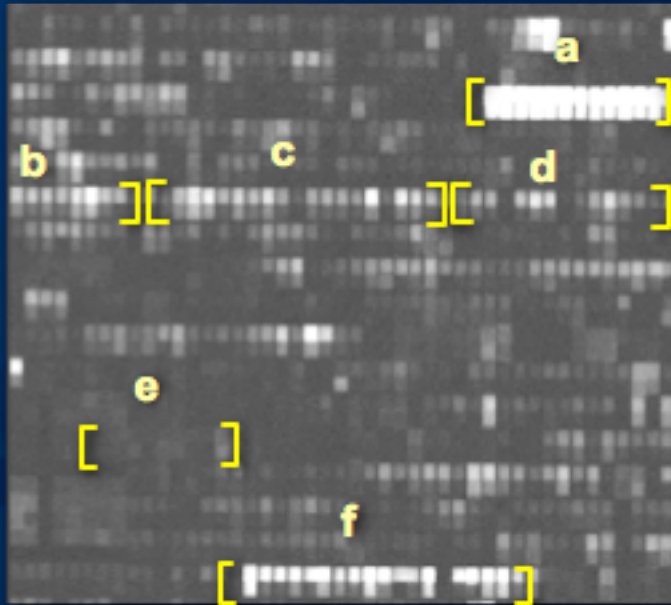


Spotted
cDNAs

Detecting Change in Gene Expression

Yeast grown in different conditions

Rich Medium



Minimal Medium



Genes

a = RPL2A

b = TIP1

c = BAP2

d = VAP1

e = YBR147W

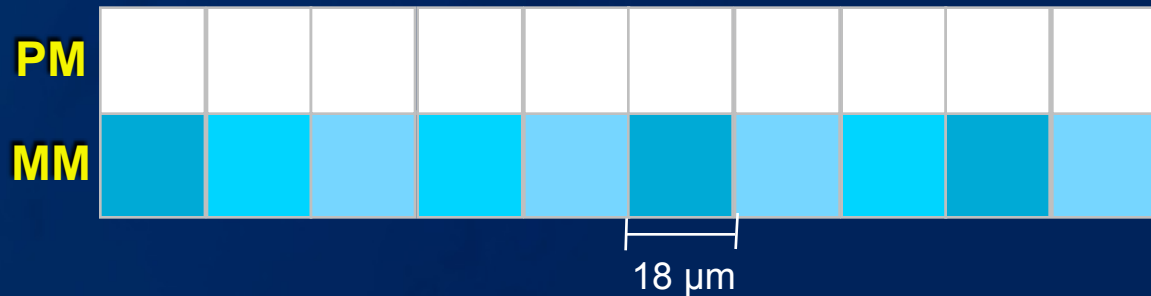
f = SUP46

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

GeneChip[®] Array Advantages

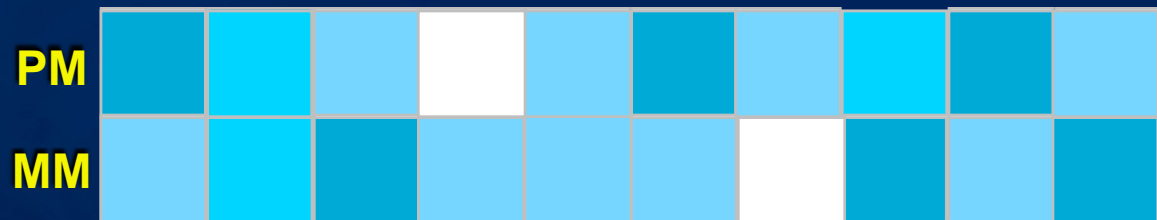
Specific Hybridization

Called
“Present”

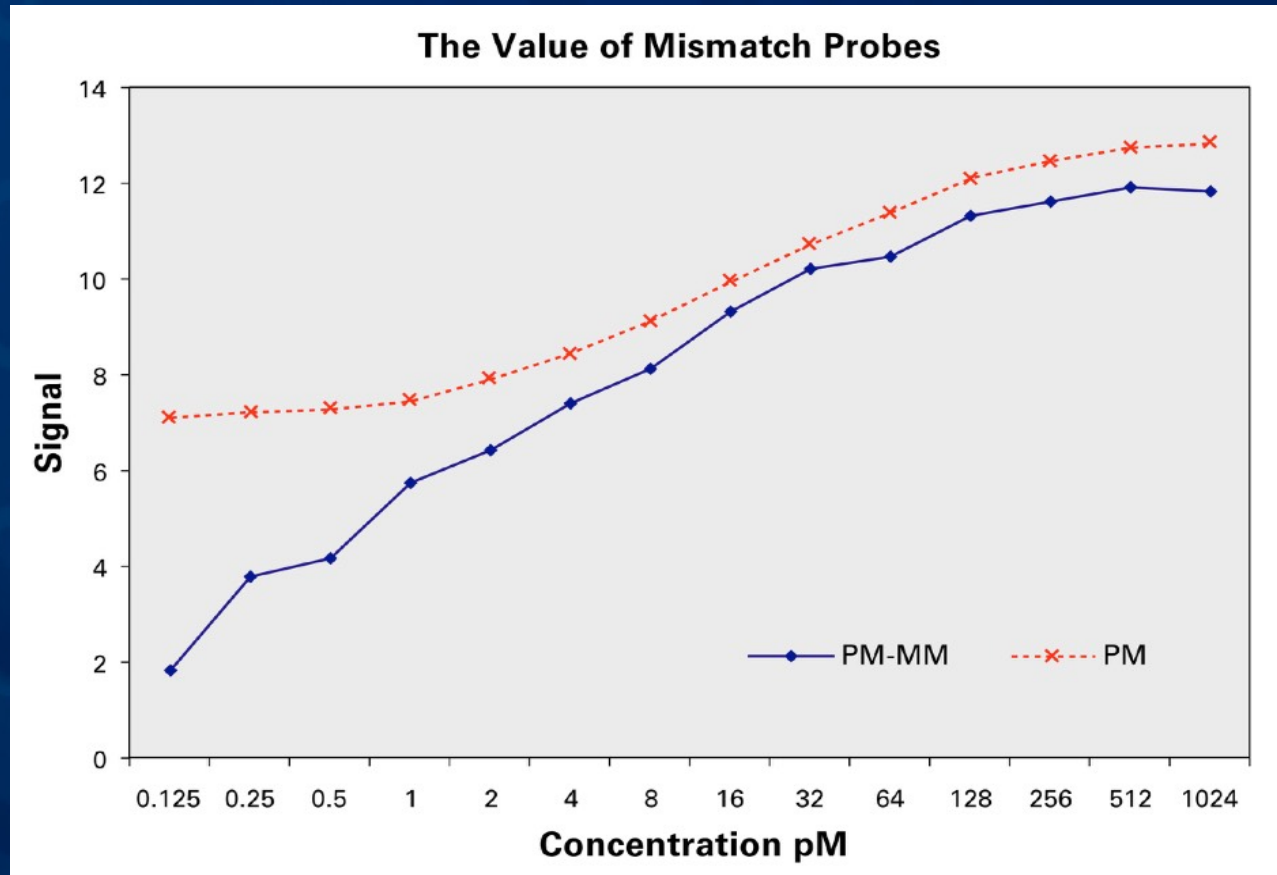


Non-specific/Cross Hybridization

Called
“Absent”

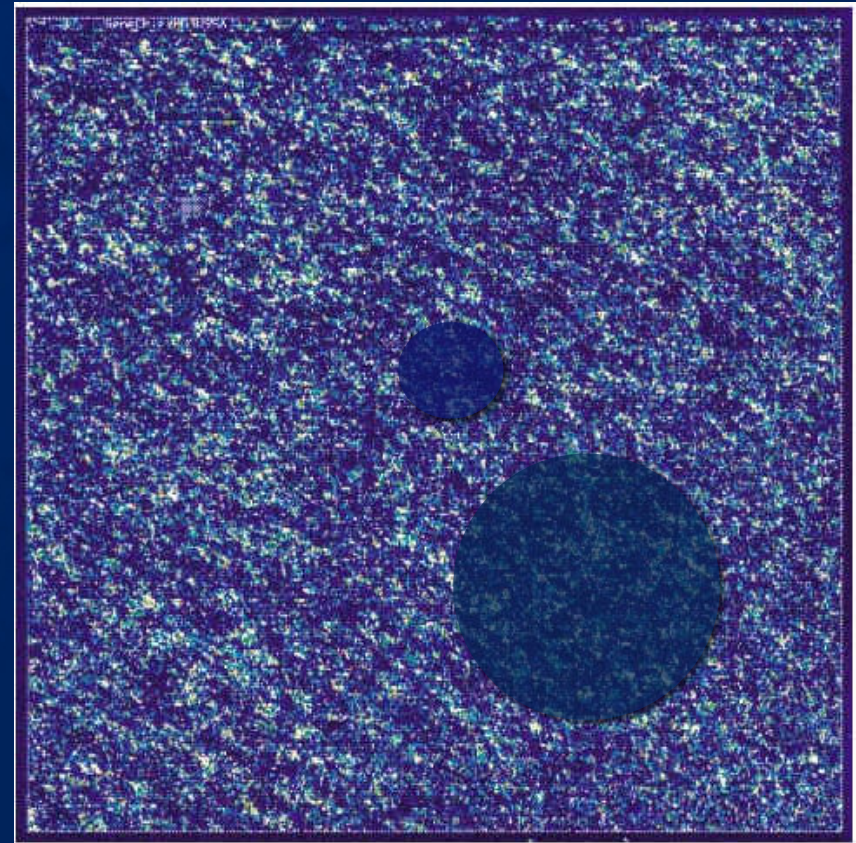
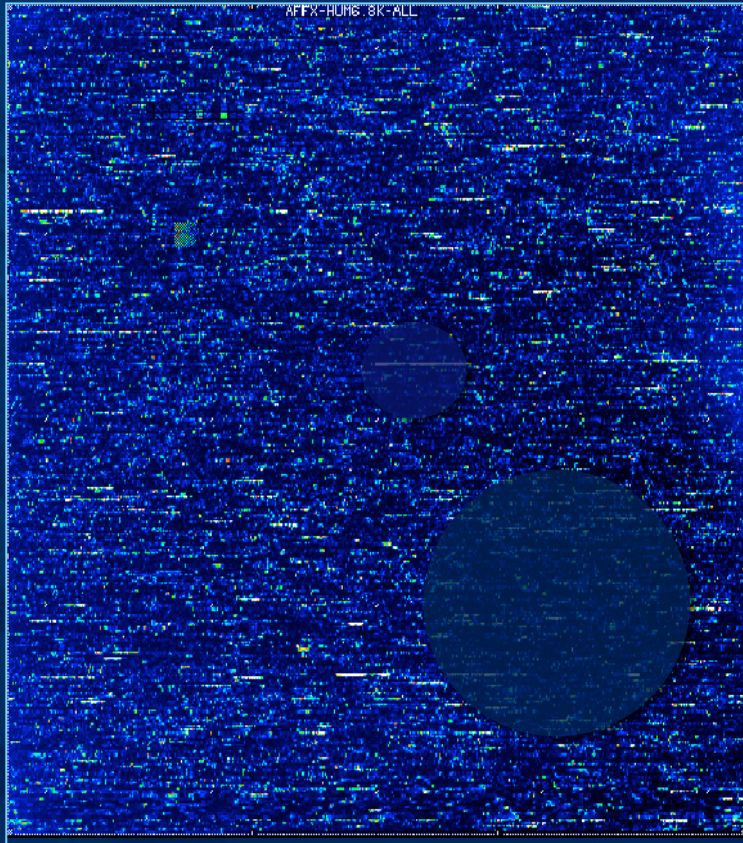


25-mer PM-MM Probe Pairs Offer Increased Specificity



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

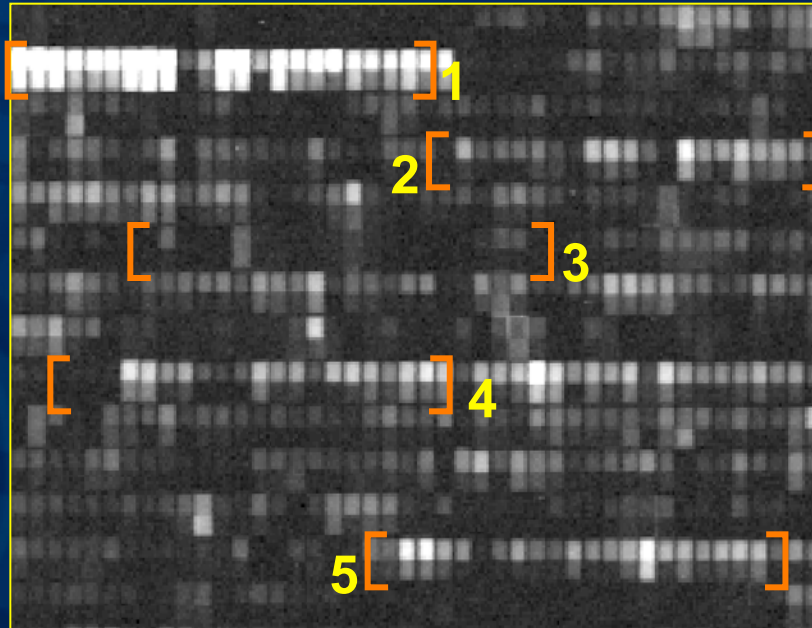
Sensitivity vs. Specificity

- 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

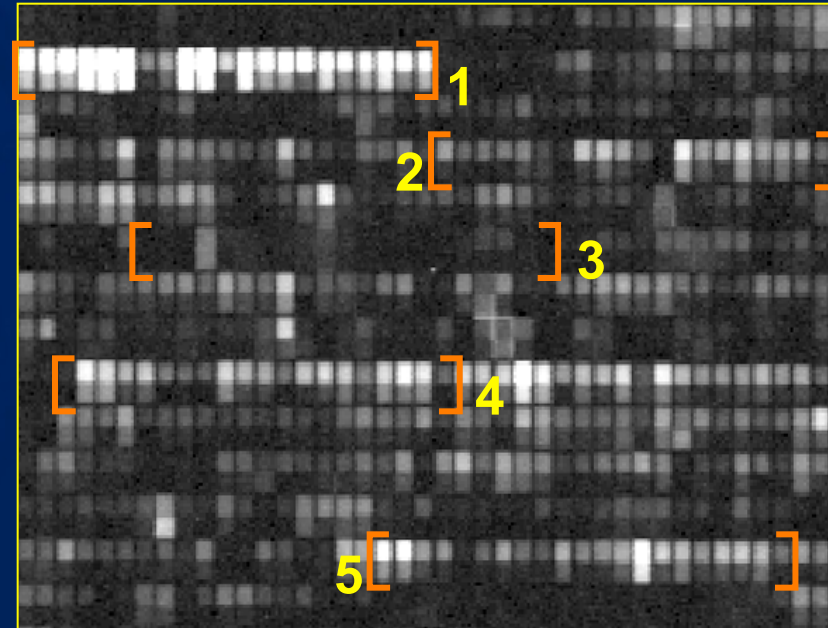
Independent cell growth and prep

Sample 1



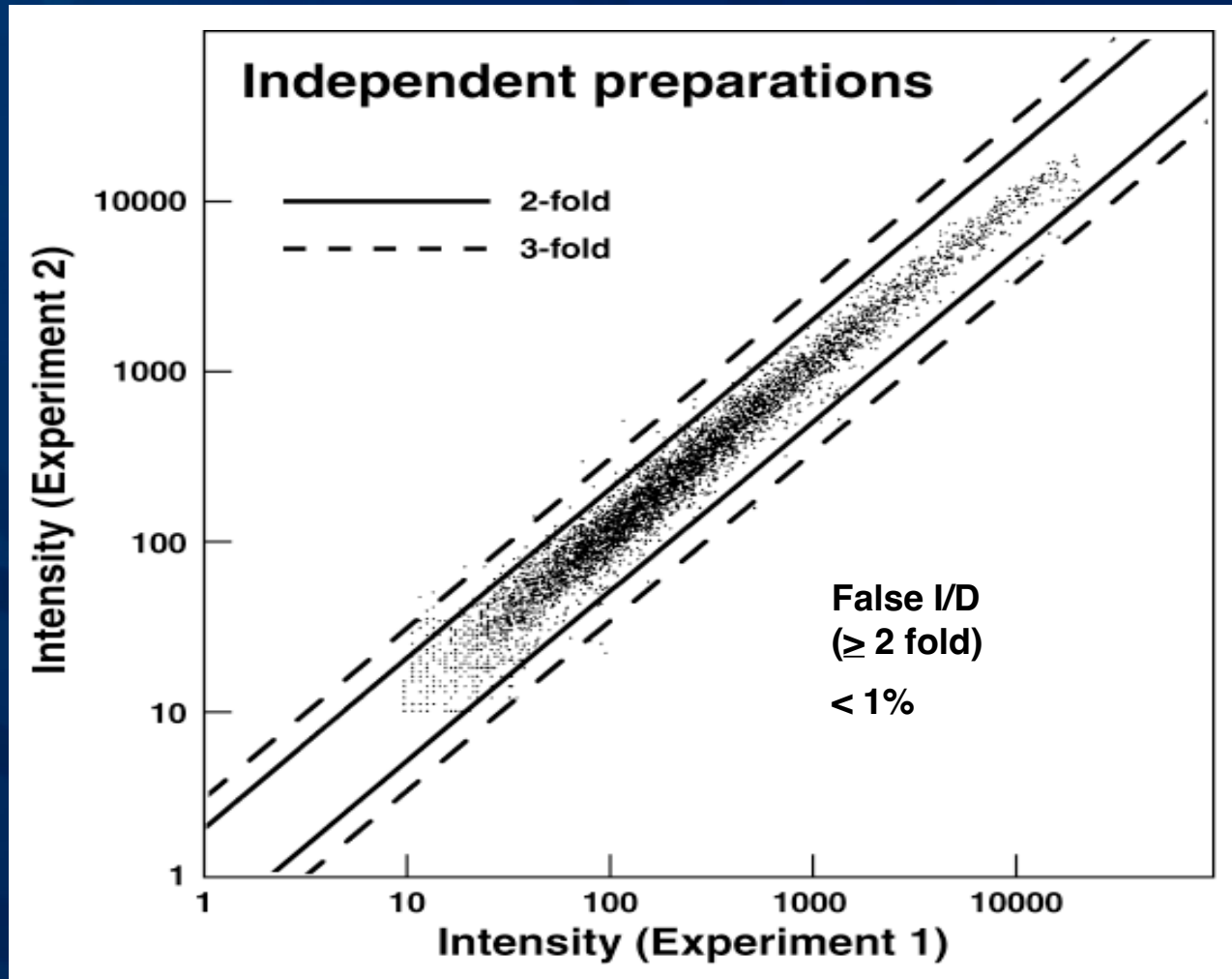
Signal Intensities: 1 13,400
2 1,280
3 1 (absent)
4 1,840
5 1,700

Sample 2



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

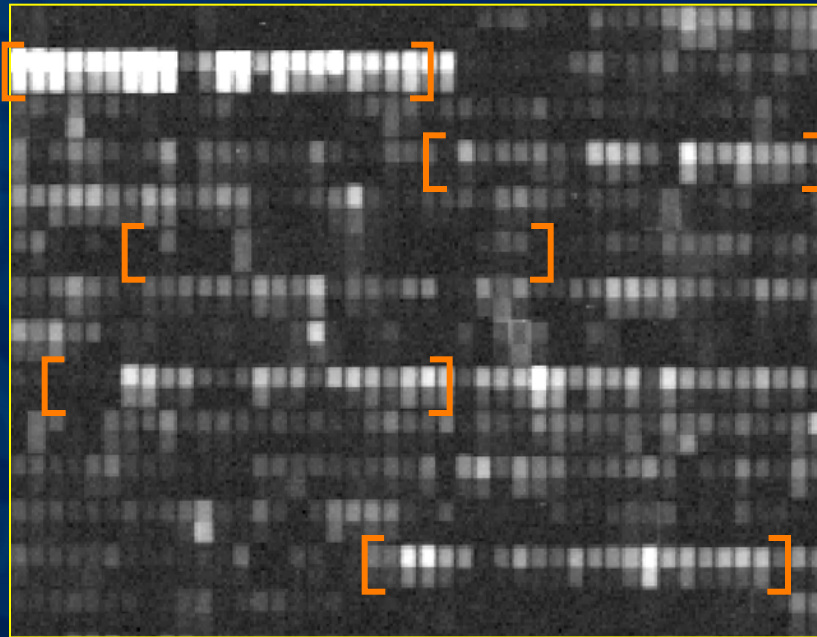
Reproducibility



Reproducibility

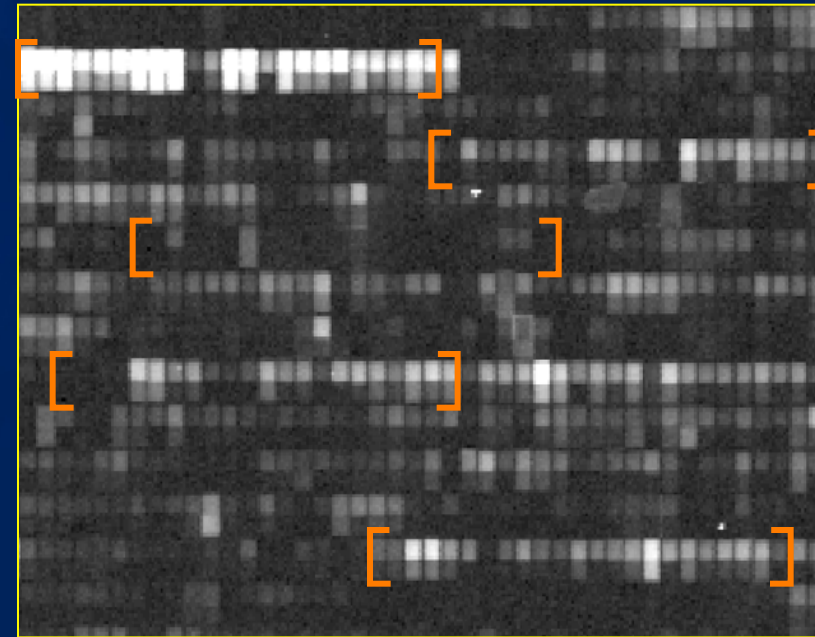
Same sample, different arrays

Sample 1



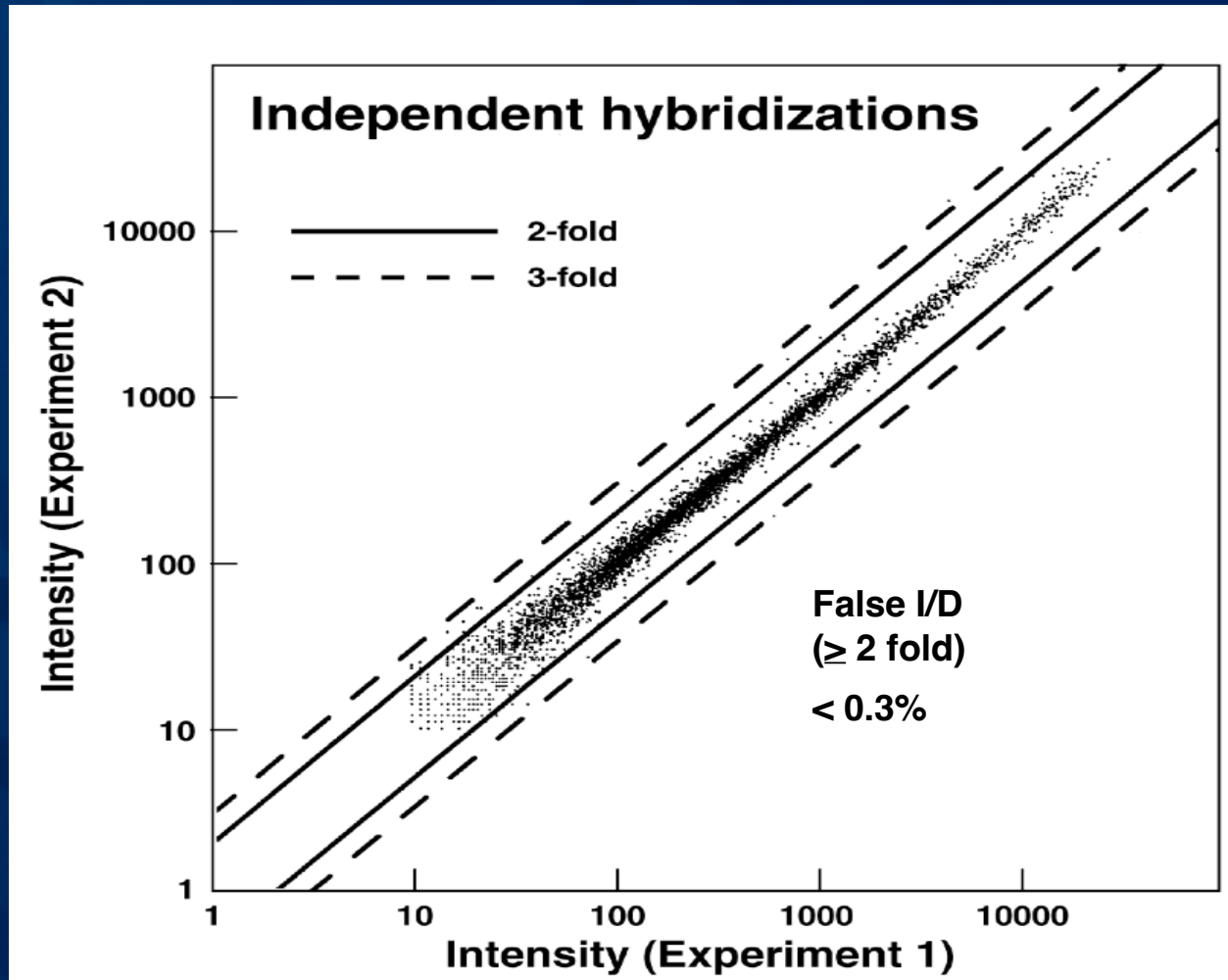
Signal Intensities: 13,400
1,280
1 (absent)
1,840
1,700

Sample 1

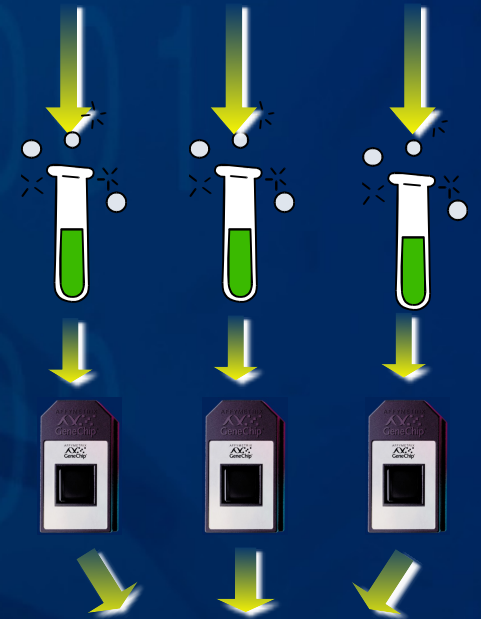


Signal Intensities: 13,090
1,250
10 (absent)
1,750
1,430

Reproducibility



Sources of Variability



Experiment	Label	Cell	Fluor	Channel	ExpType
Trial 1	1001	HEK293T	1	1001	1
Trial 2	1002	HEK293T	2	1002	1
Trial 3	1003	HEK293T	3	1003	1
Trial 4	1004	HEK293T	4	1004	1
Trial 5	1005	HEK293T	5	1005	1
Trial 6	1006	HEK293T	6	1006	1
Trial 7	1007	HEK293T	7	1007	1
Trial 8	1008	HEK293T	8	1008	1
Trial 9	1009	HEK293T	9	1009	1
Trial 10	1010	HEK293T	10	1010	1
Trial 11	1011	HEK293T	11	1011	1
Trial 12	1012	HEK293T	12	1012	1
Trial 13	1013	HEK293T	13	1013	1
Trial 14	1014	HEK293T	14	1014	1
Trial 15	1015	HEK293T	15	1015	1
Trial 16	1016	HEK293T	16	1016	1
Trial 17	1017	HEK293T	17	1017	1
Trial 18	1018	HEK293T	18	1018	1
Trial 19	1019	HEK293T	19	1019	1
Trial 20	1020	HEK293T	20	1020	1
Trial 21	1021	HEK293T	21	1021	1

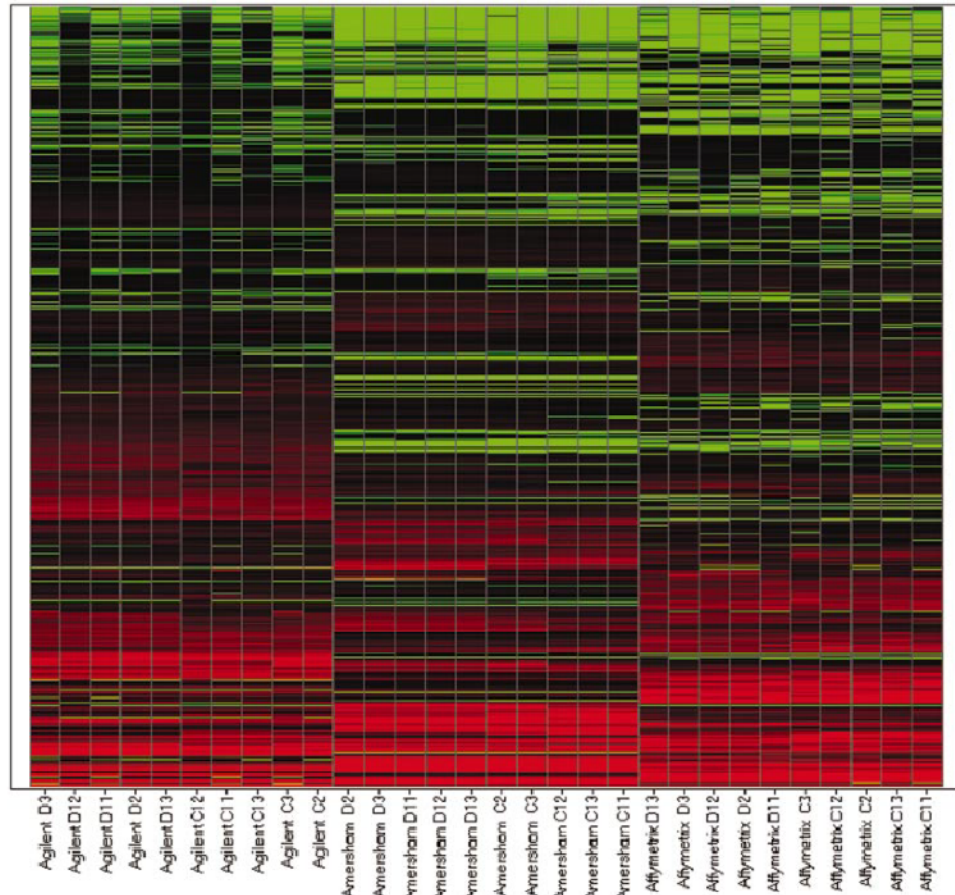
- **Biology**
 - The main source of variability
- **Sample preparation**
 - Technical variability depends on method and operator
- **Probe array analysis**
 - Standardized; relatively little variability

- **Data analysis**

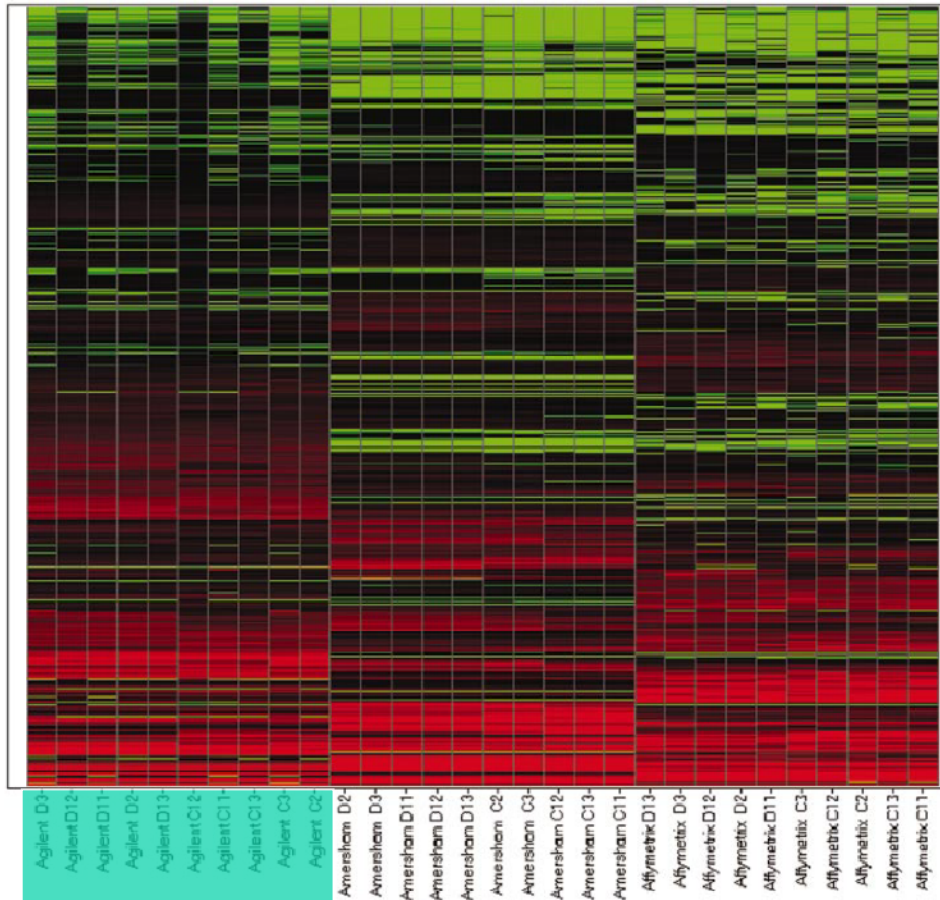
Differences Across Commercial Platforms

Increased Expression

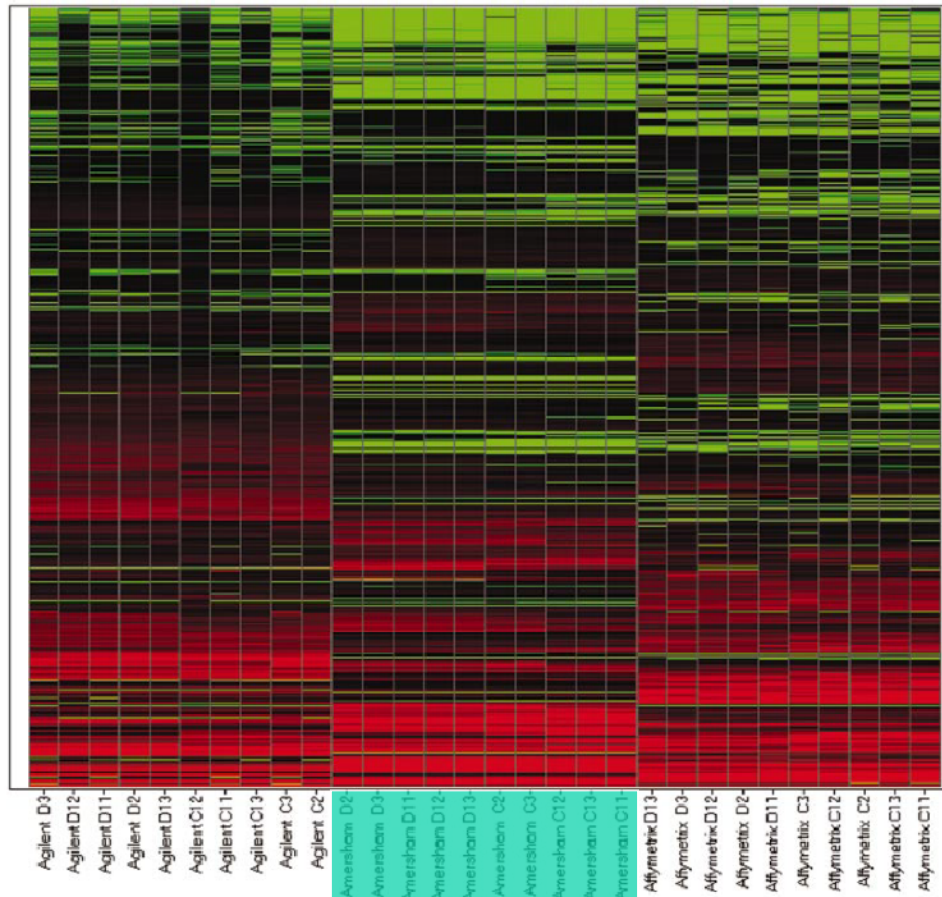
Decreased Expression



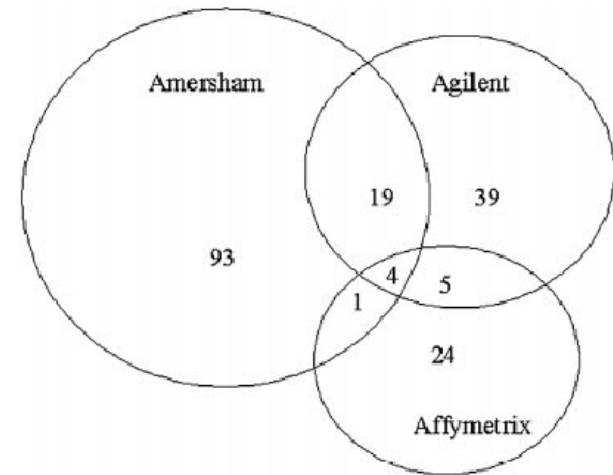
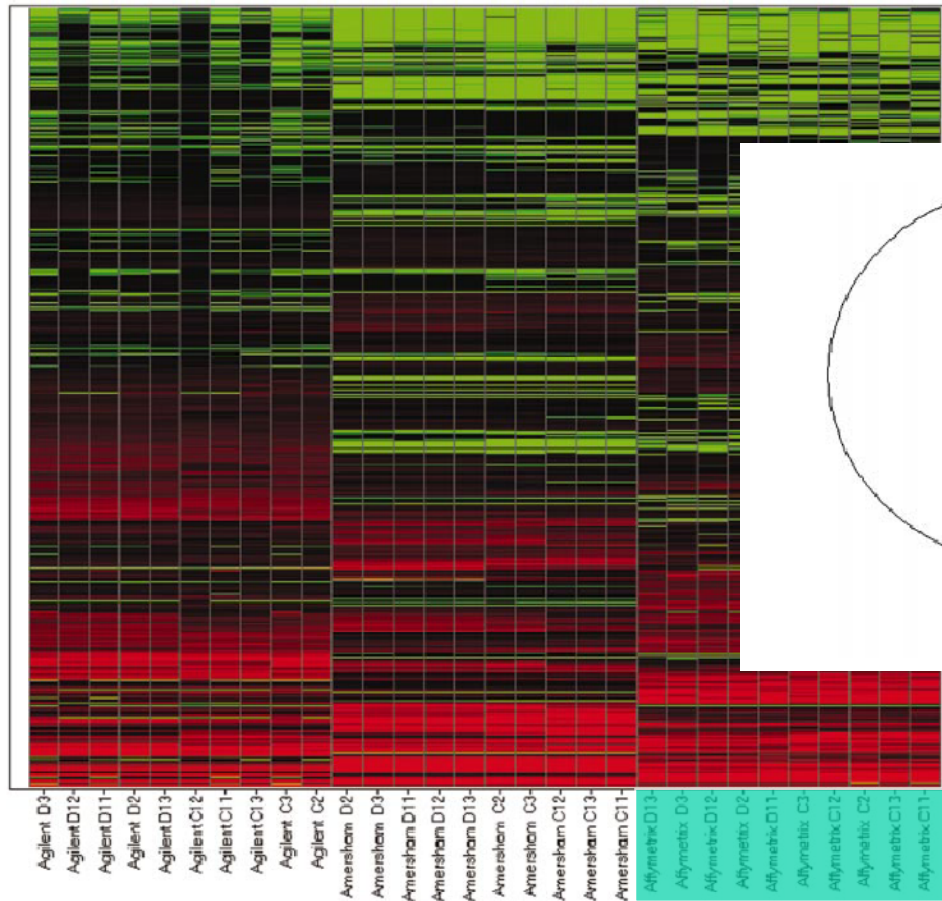
Differences Across Commercial Platforms



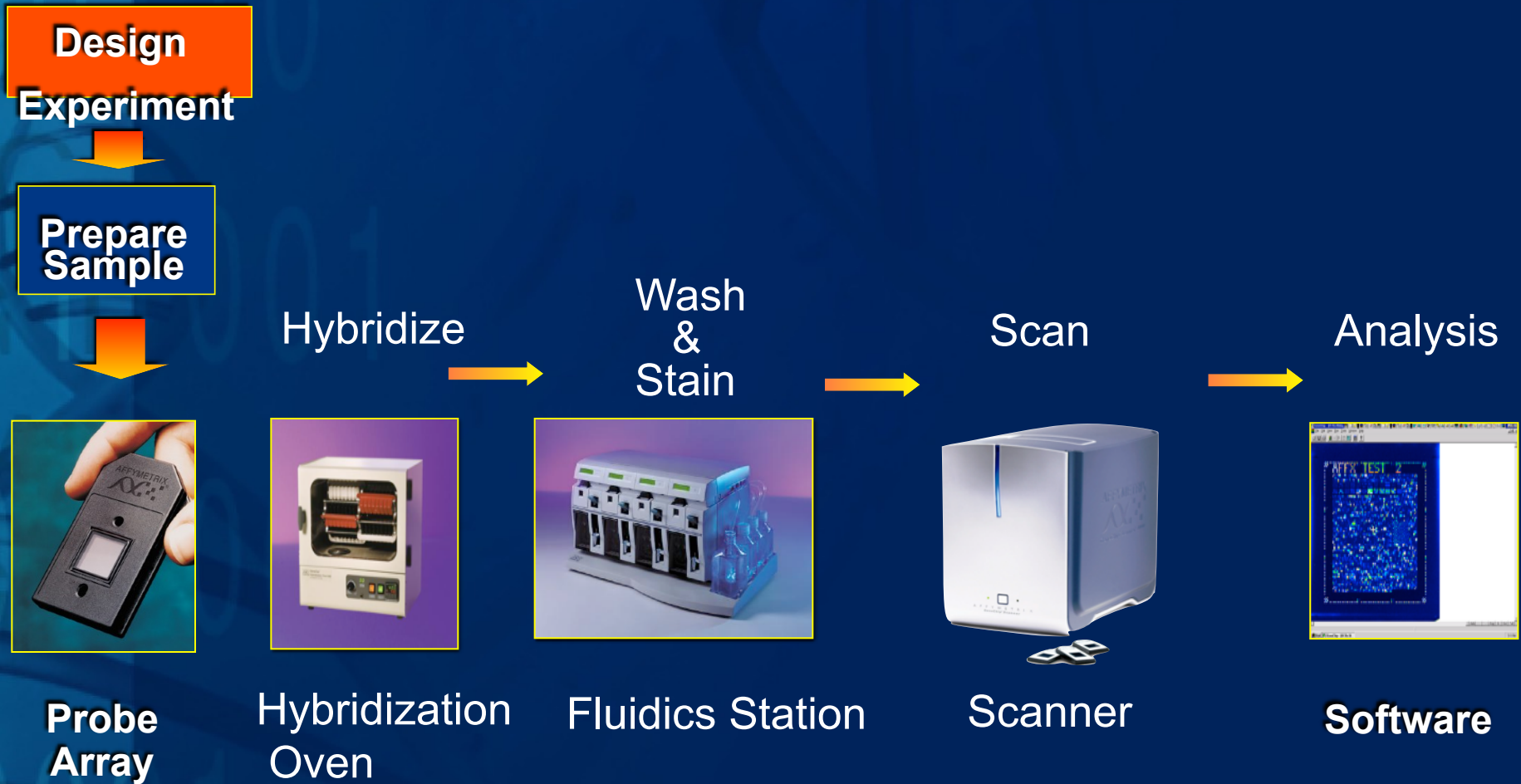
Differences Across Commercial Platforms



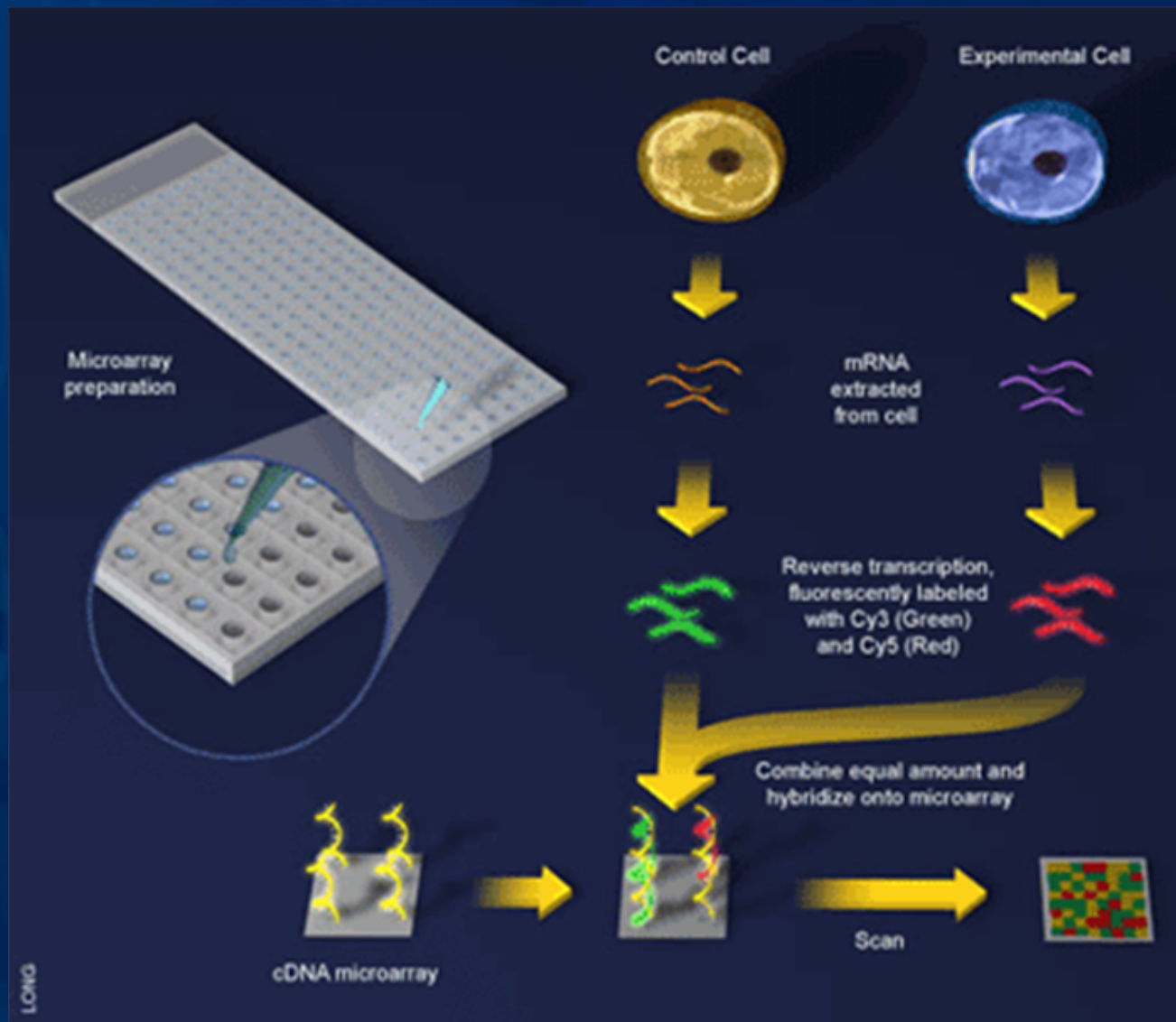
Differences Across Commercial Platforms



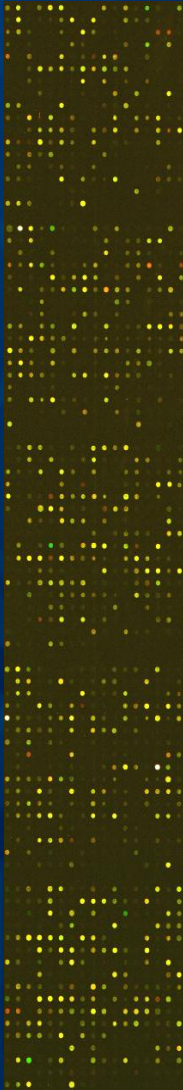
GeneChip[®] System Work Flow



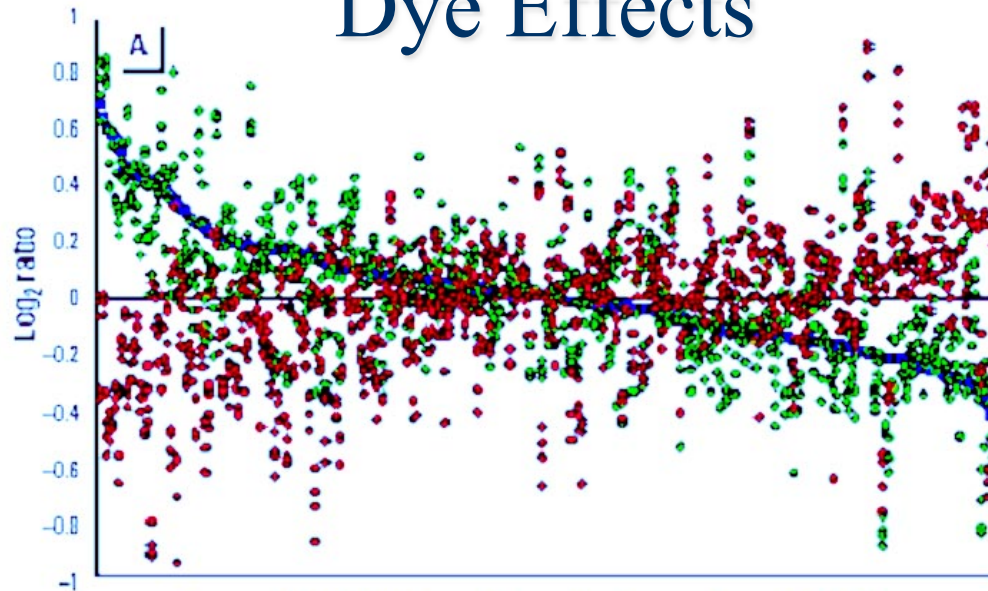
Two dye microarrays....



Two dye microarrays....



Dye Effects



Genes (ranked in descending order by mean \log_2 Cy3/Cy5 ratios of a pair of split-control hybridizations)

Environmental Health Perspectives • VOLUME 112 | NUMBER 4 | March 2004

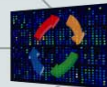
- Variation in quantum yield of fluorophores
- Variation in the incorporation efficiency
- Differential dye effects on hybridization



ParaBioSys

Parallel Biological Systems

Mass. General Hospital • Harvard Medical School • Boston University



GeneChip Expression Analysis



Absolute Analysis



- Detection (qualitative)
- Signal (quantitative)

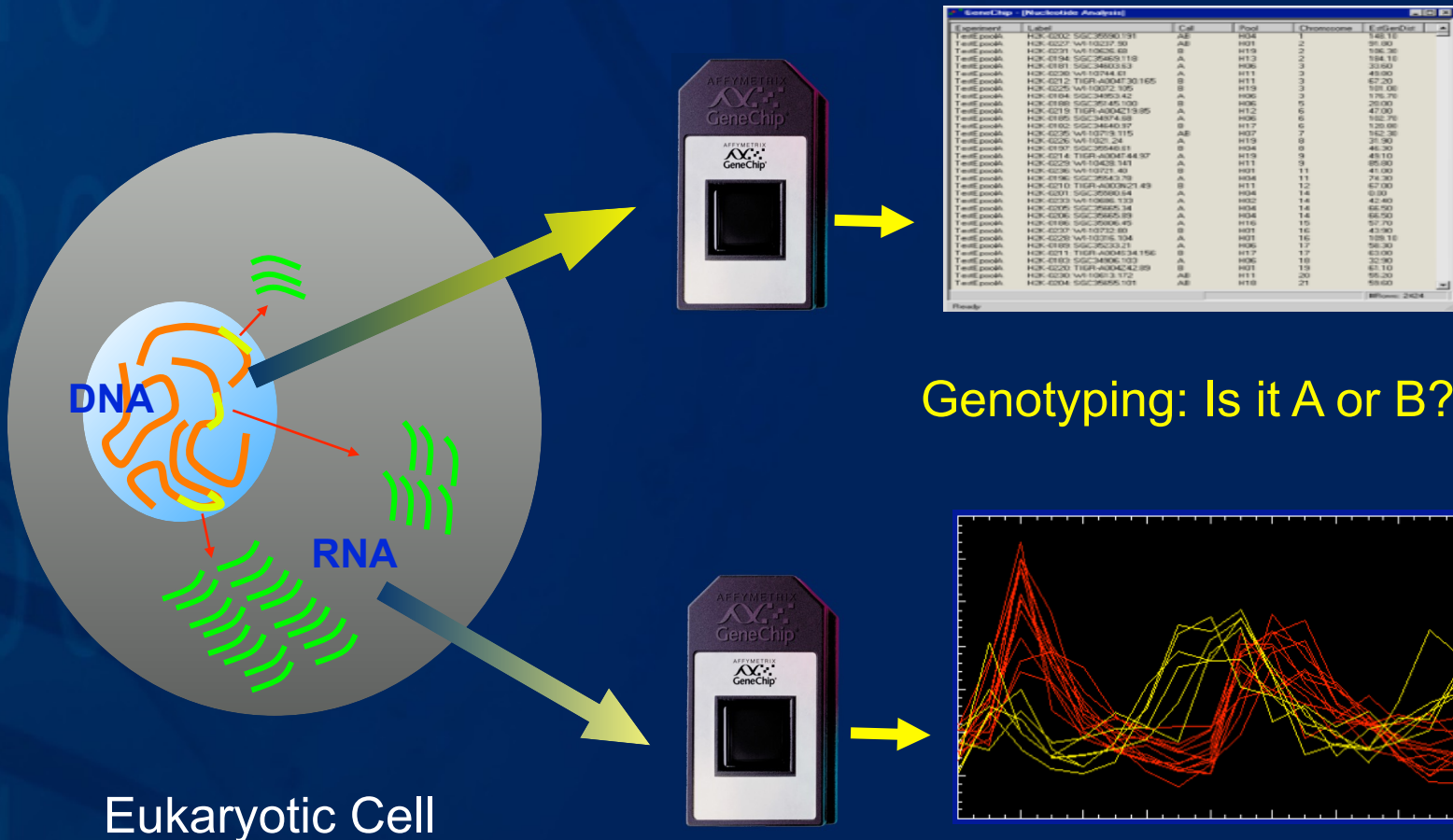


Comparison Analysis



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

Genotyping or Gene Expression Monitoring



GeneChip[®] Mapping 10K Probe Design



probes = 25 bases



SNP Tiling Strategy

SNP 0 Position


G / A

TAGCCATCGGTA **N** GTA **C** TCAATGATCAGCT

ATCGGTAGCCAT	C	CAT G AGTTACTA	PM Allele	A
ATCGGTAGCCAT	G	CAT G AGTTACTA	MM Allele	A
ATCGGTAGCCAT	T	CAT G AGTTACTA	PM Allele	B
ATCGGTAGCCAT	A	CAT G AGTTACTA	MM Allele	B

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](https://doi.org/10.1007/s10522-004-2567-y)

Abstract

Differences of more than 3 million nucleotides can be 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](#)

SNP Tiling Strategy

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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		
dbSNP (classic)	rs2383206		

SNP Tiling Strategy

Heart disease

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[[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)	1	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](#)

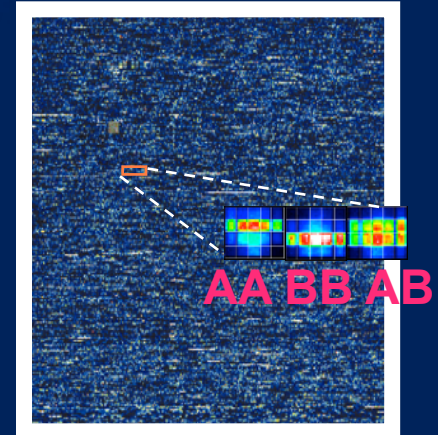
dbSNP [rs2383206](#)

dbSNP [rs2383206](#)

(classic)

dbSNP [rs2383206](#)

GeneChip Mapping 10K Assay



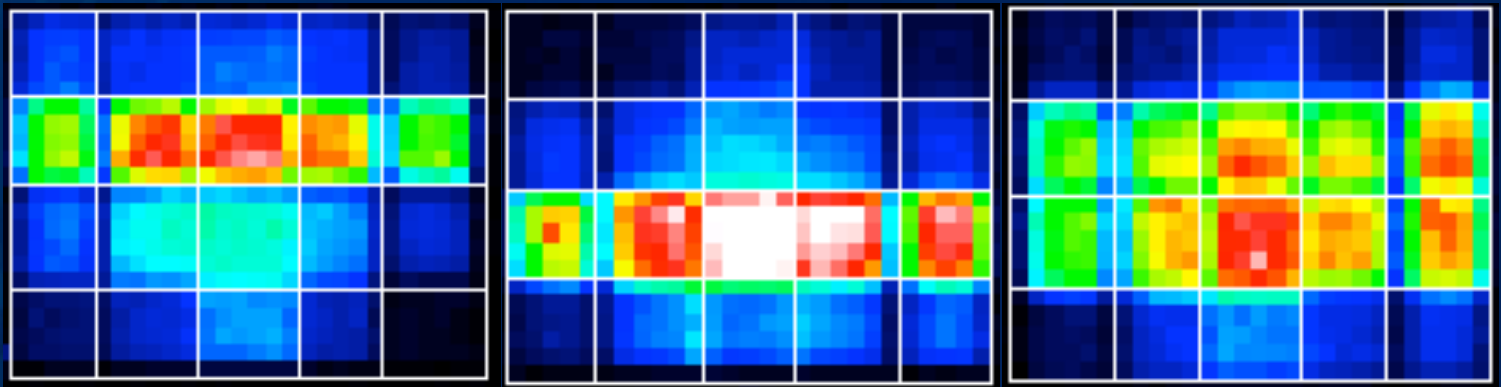
- A single-primer,
- A single-amplification, and
- A cost-effective assay...
- ...for simultaneously **Genotyping**

GeneChip[®] Mapping 10K Hybridization Patterns

AA

BB

AB



PHASE : INTERPRETATION
TWO

SEIDMAN *with* Leizer

