

STAT588/BIOL588: Genomic Data Science
Lecture11: Introduction to Microarray Technology
(Chapter 5 in Gondro's book)

Dr. Yen-Yi Ho (hoyen@stat.sc.edu)

Objectives of Lecture 11

- ▶ Types of Arrays
- ▶ Expression Microarrays
 - ▶ General Experiment Protocol
 - ▶ Hybridization, Target, Probe, Probe Set
 - ▶ Commercial Microarrays
 - ▶ Common Issues
- ▶ aCGH
- ▶ ChIP-chip

Genomics in the Real World



- ▶ Currently used to assess the risk of breast cancer recurrence in women ≤ 61 with stage 1 and II, lymph node-negative, ER positive or negative primary breast cancer
- ▶ About 14,000 patients test as of mid 2011
- ▶ Uses the 70-gene expression profile

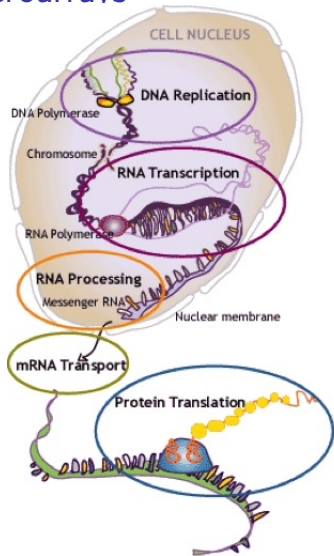
*Image: Mamaprint Logo, <http://www.agendia.com/mamaprint>

Data: van't Veer et al. (2012) Nature

Microarrays

- ▶ Microarrays (or just arrays) allow the simultaneous measurement of the mRNA of thousands of genes (gene expression)
- ▶ Why “micro”? Measuring things on a small scale means less mRNA is necessary to be extracted
- ▶ The simultaneous measurement is important, so that various factors/conditions are all common to the array, and relative gene expression can be measured with less variability
- ▶ Still microarray? Microarray is still used for clinically diagnostic tests.
- ▶ Similar problems are presented in newer technologies such as RNA-seq, and similar statistical approaches can be applied.

Microarrays



Microarrays can be used for many purpose including:

- ▶ genotyping: SNP arrays
- ▶ measure gene expression
- ▶ determine DNA copy number: aCGH
- ▶ determining transcription factor binding sties: Chip-chip

source:

<http://www.nobelprize.org/educational/medicine/dna/index.html>

Co\$t

Micorarray

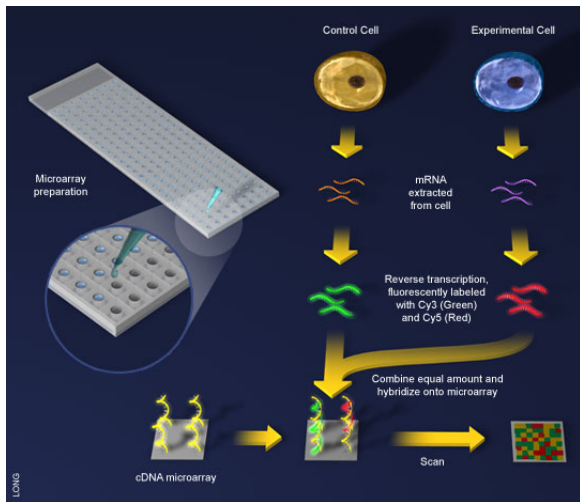
Affymetrix Cost: \$425/per array

Illumina BeadChip Cost: \$ 80 ~ \$250 /per strip $\times 12 = \$960 \sim$
\$3,000 /chip

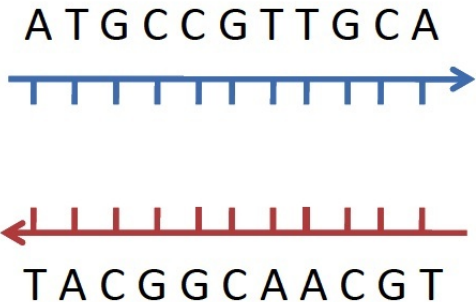
Next-Generation Sequencing

Illumina \sim \$2,000 per samples (for 1-7 samples)

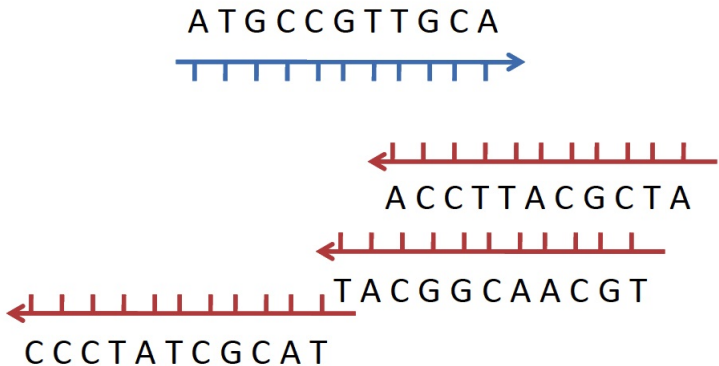
On Type of Microarray Experimental Procedure



Denaturation



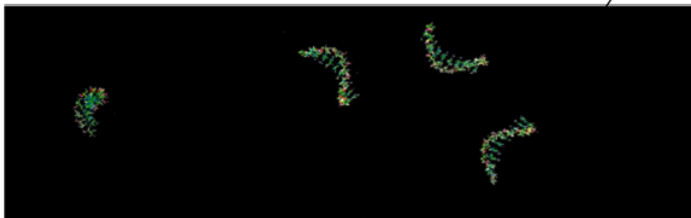
Hybridization



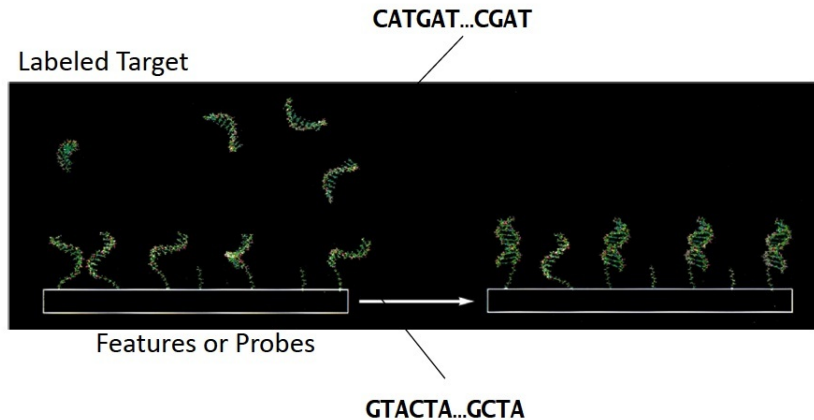
Target

Target

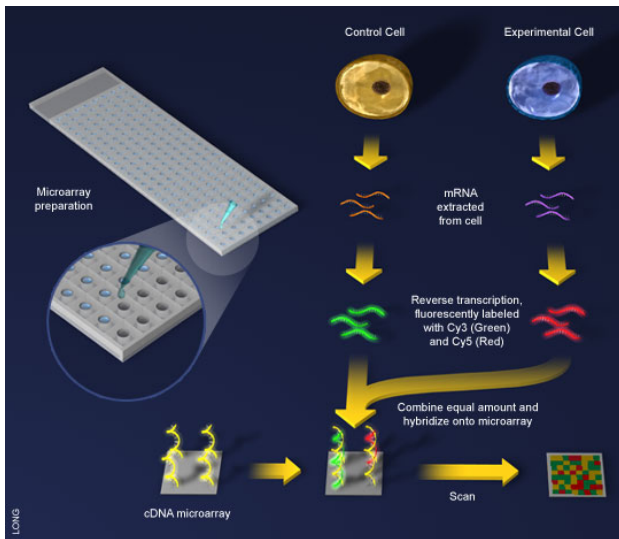
CATGAT...CGAT



Probes



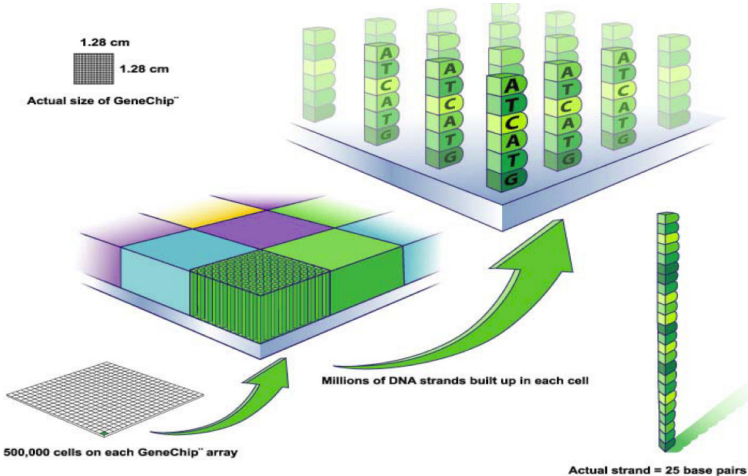
On Type of Microarray Experimental Procedure



Platforms that dominate market

- ▶ Affymetrix
- ▶ Agilent
- ▶ Illumina
- ▶ NimbleGen

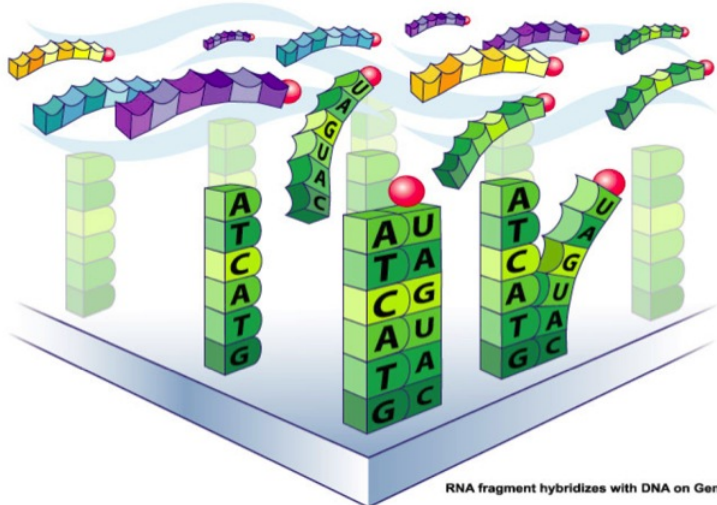
Affymetrix GeneChip



source: Affymetrix

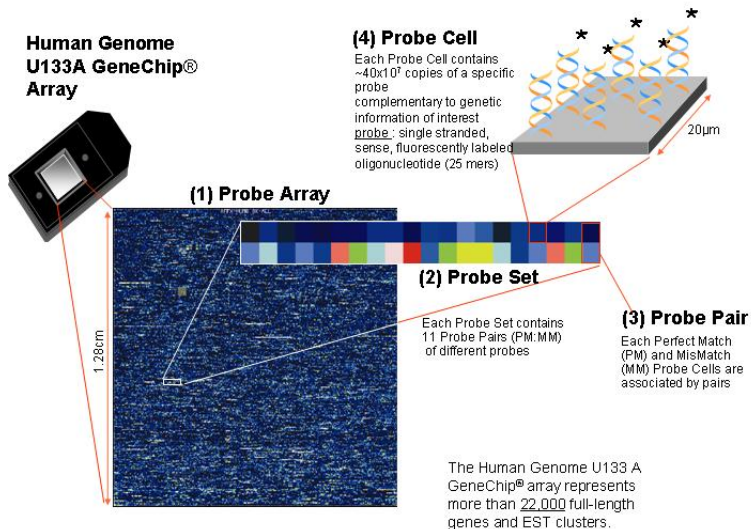
Affymetrix GeneChip

RNA fragments with fluorescent tags from sample to be tested



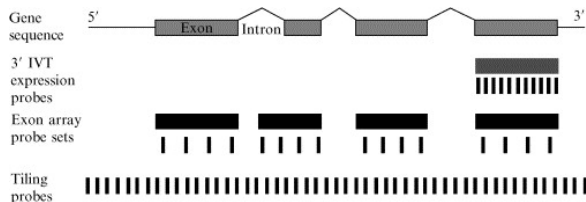
source: Affymetrix

Affymetrix GeneChip

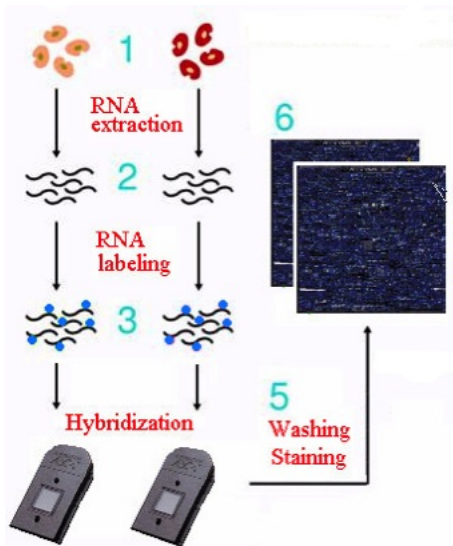


Probe Set

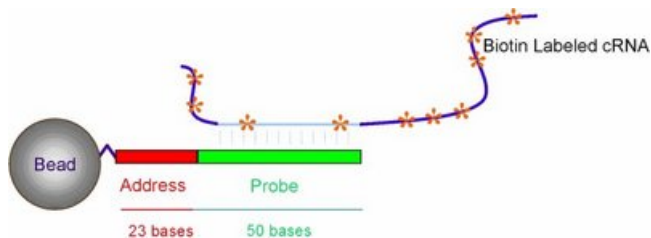
A probe set is a collection of probes designed to interrogate a given sequence.



Affymetrix GeneChip Experiment Protocol



Illumina BeadArrays



- Each silica bead is 3 μ in diameter
- 700,000 copies of same probe sequence attached to each bead
- May have more than one bead for a particular gene

Illumina BeadArrays

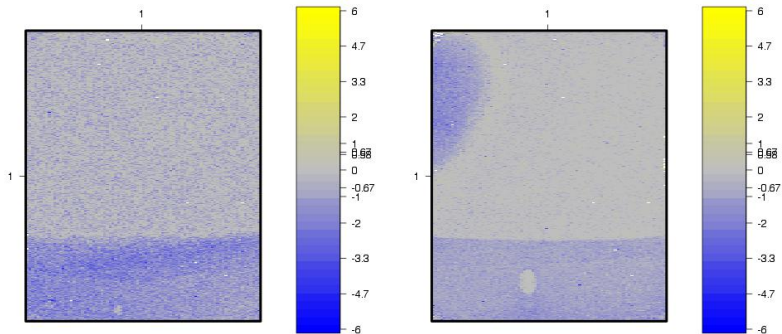


- RefSeq BeadChip (left) 8 arrays per chip, 1 strip= 1 array
- Whole Genome (right) 6 arrays per chip, 2 strip= 1 array

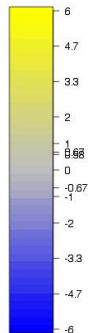
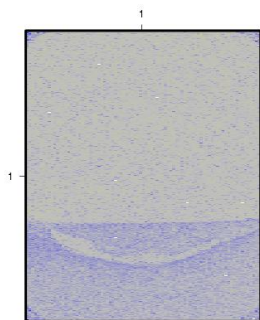
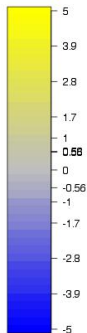
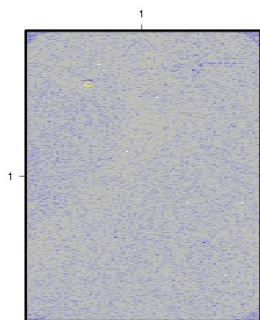
Commons Issues

- ▶ Background: print-tip, plate, print-order, spatial effects
- ▶ Between arrays: batches, plates, cross platform comparison, experiment protocols
- ▶ Within arrays: background noise, intensity dependent effect

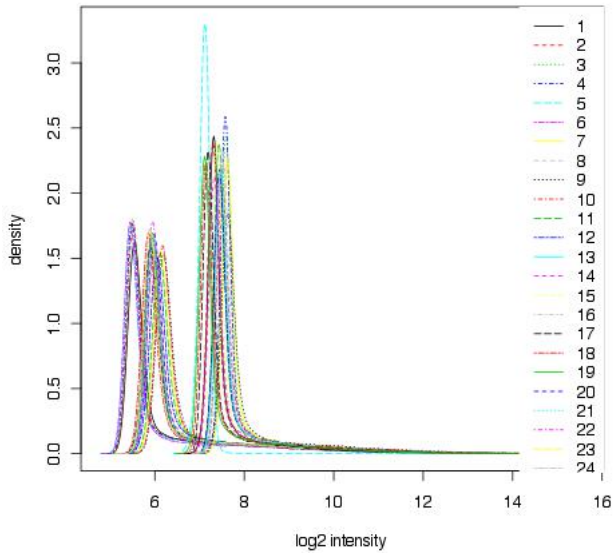
Spatial Effect



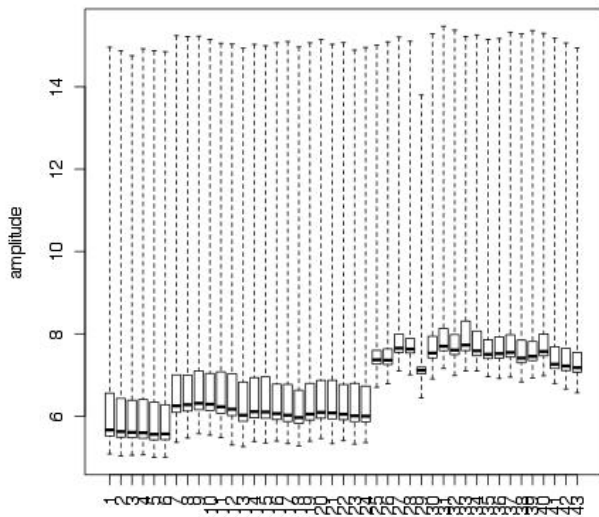
Spatial Effect



Batch Effect



Batch Effect

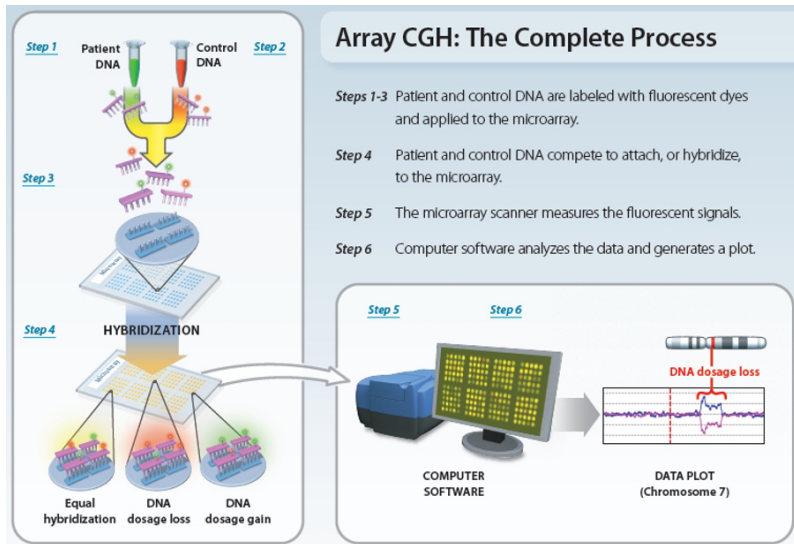


Microarrays

Microarrays can be used for many purpose including:

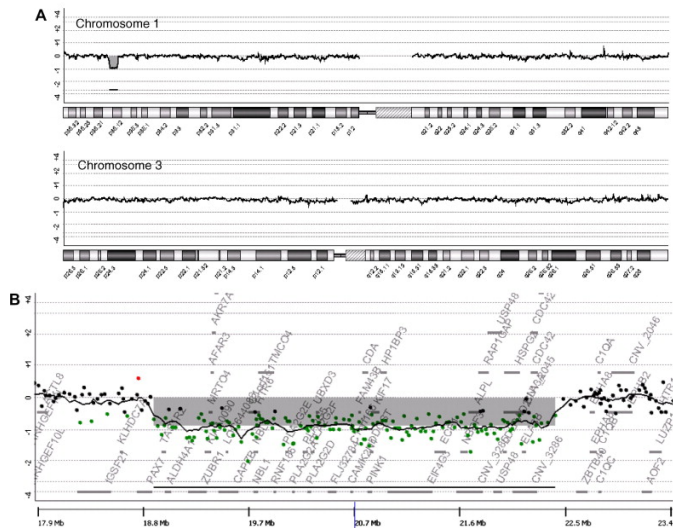
- ▶ genotyping: SNP arrays
- ▶ measure gene expression
- ▶ determine DNA copy number: aCGH
- ▶ determining transcription factor binding sties: Chip-chip

Array-comparative genomic hybridization (aCGH)



Nature Education1(1). Microarray-based Comparative Genomic Hybridization (aCGH)

array CGH



Brian and Development 31(6):629:633.

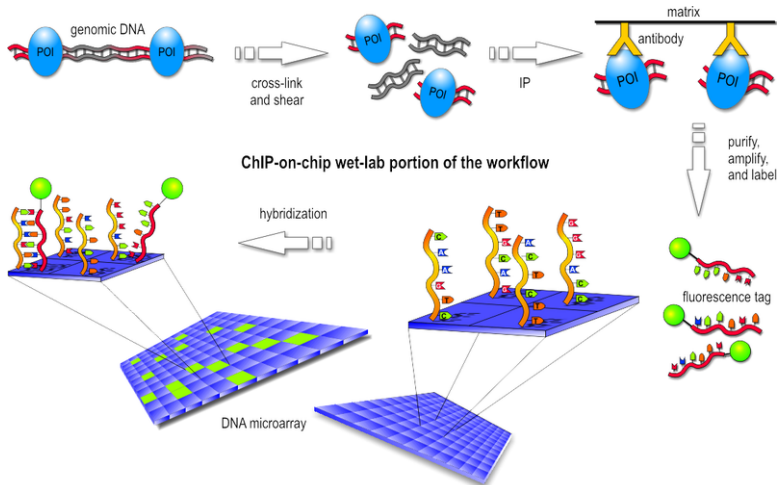
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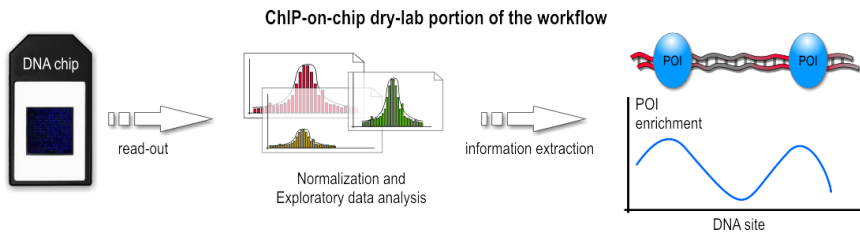
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ChIP-chip

Chromatin immunoprecipitation ("ChIP") with microarray technology ("chip")



ChIP-chip



Readings

Primer to Analysis of Genomic Data Using R (page 163 – 200).