Genomic data analysis with R

Macrogen Inc
김세환

Contents

- Biological background
- Methods for biological data measurement
- Example of biological data analysis
- Bioconductor
- Trend in Genomics

Where We Are

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- Example of biological data analysis
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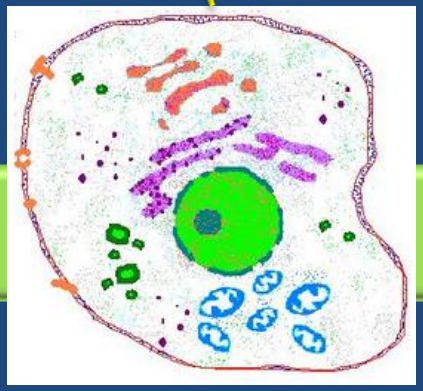
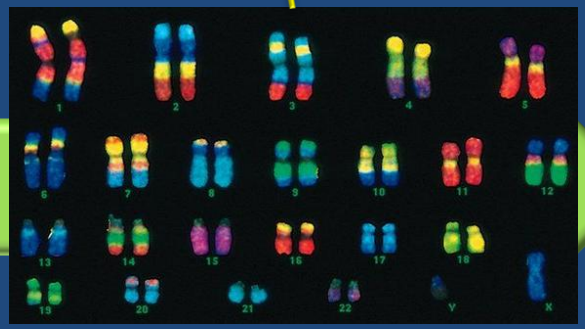
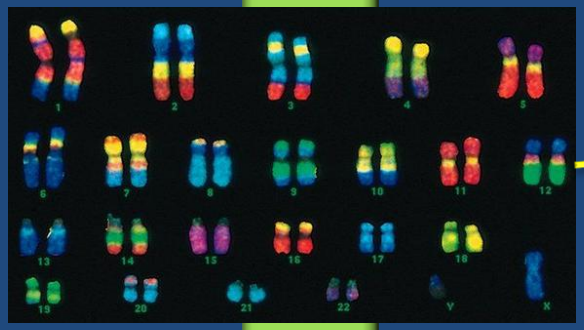
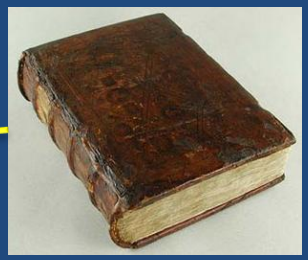
Biological Background for Genomics



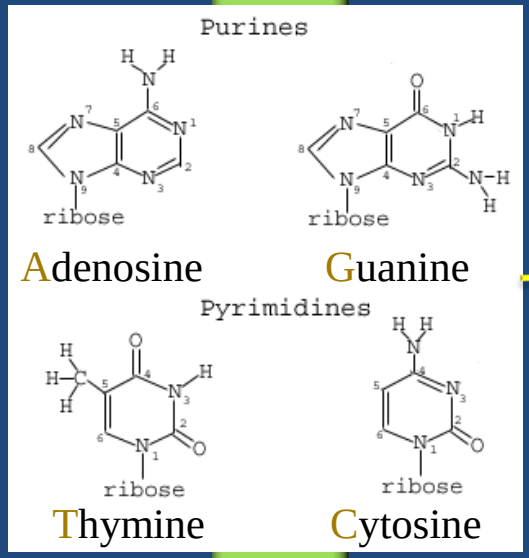


Biological Background for Genomics





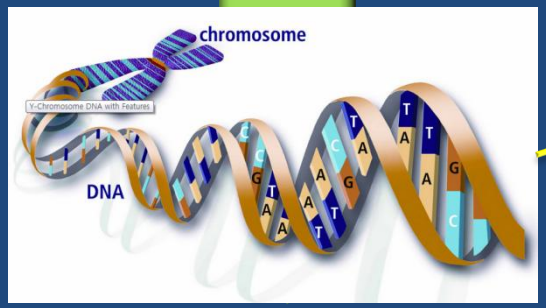
46 chromosomes = 22 * 2 + (1+1)



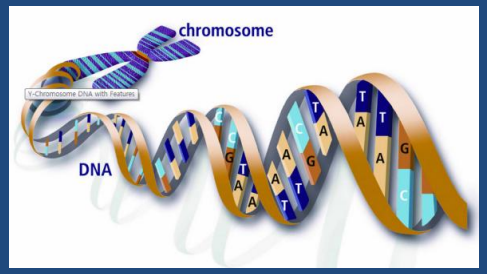
AGTC

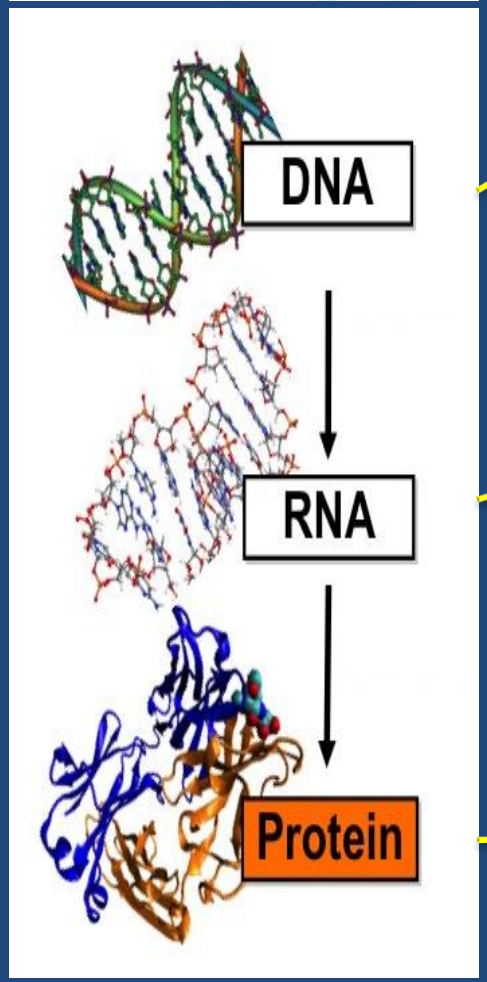
4 bases

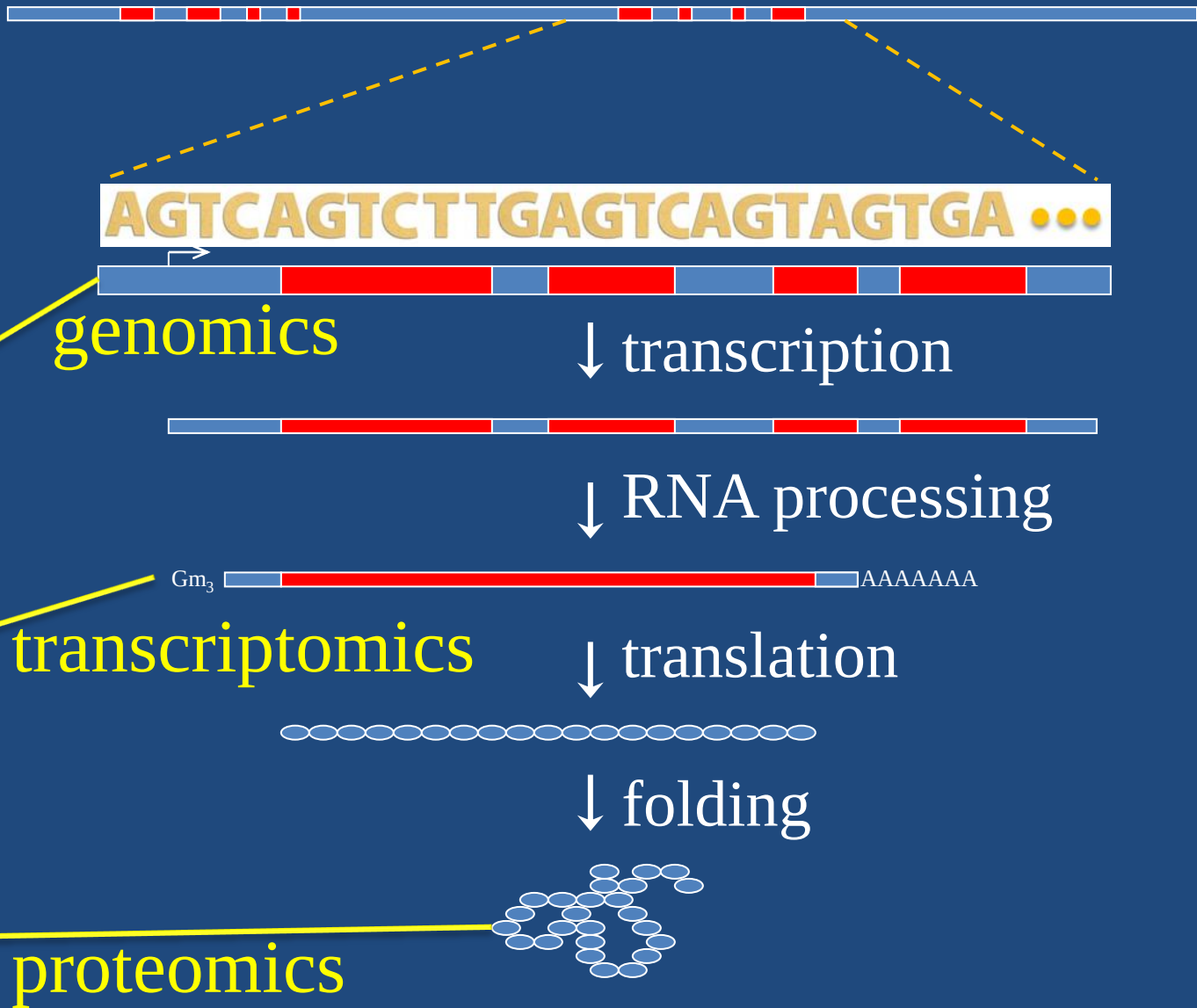
$3 * 10^9$ bp



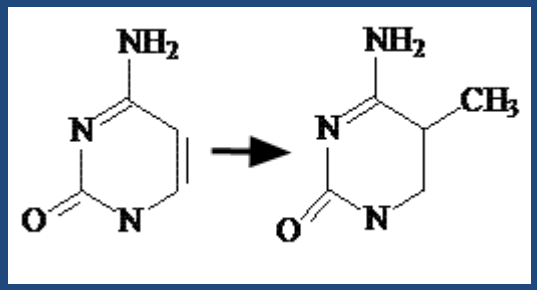
Central Dogma

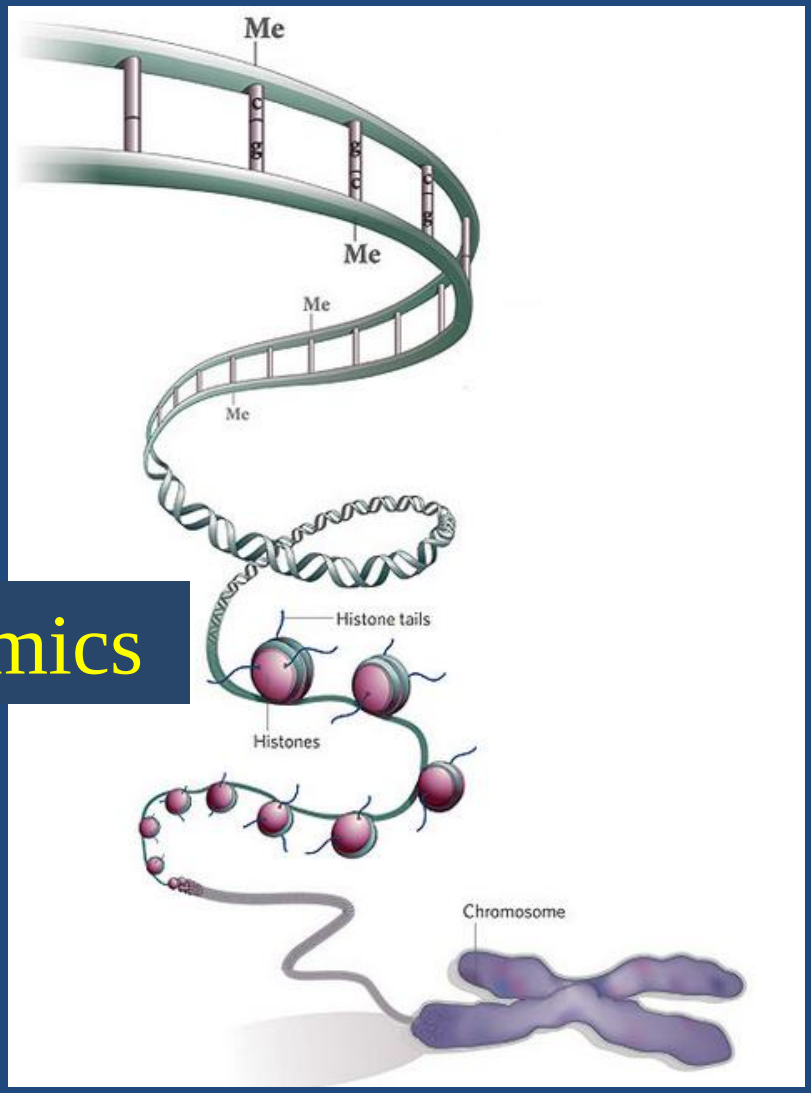




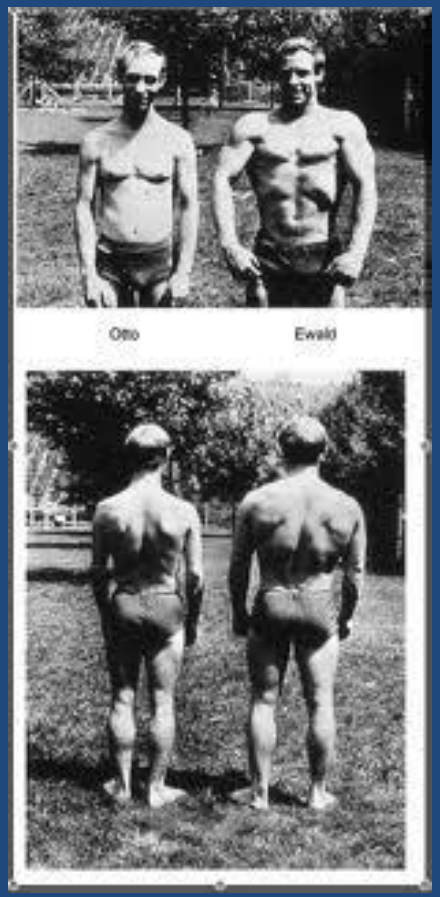


Methylated 5’ C ; Fifth base in DNA





epigenomics



Where We Are

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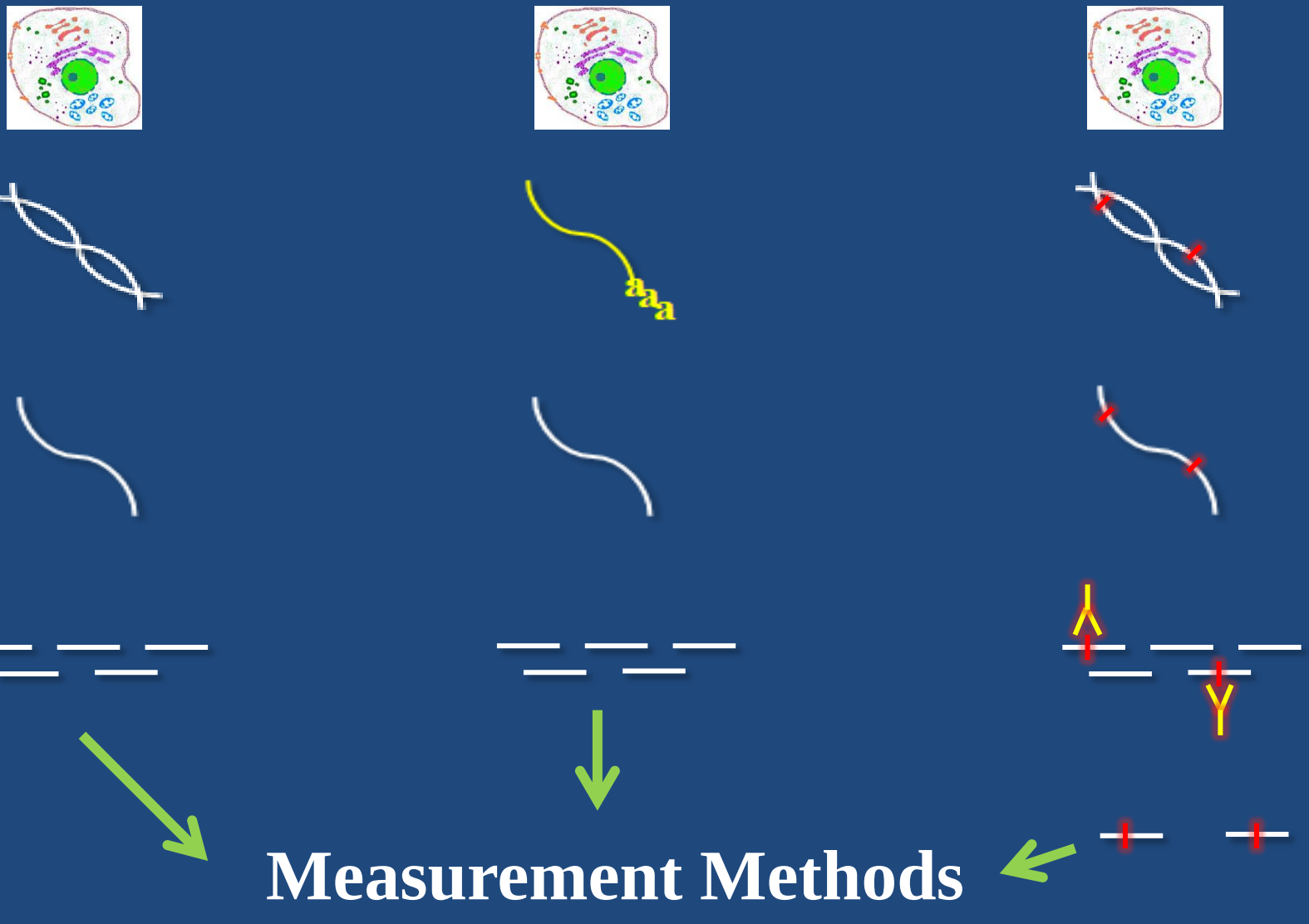
- Example of biological data analysis
- Bioconductor
- Trend in Genomics

How to get these biological data?

genomics transcriptomics epigenomics



Measurement Methods

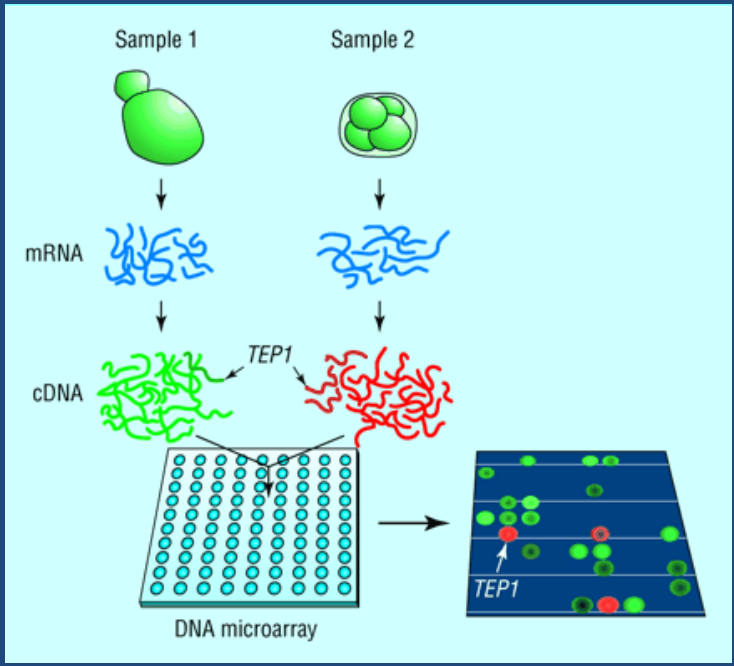
Measurement Methods

- Microarray

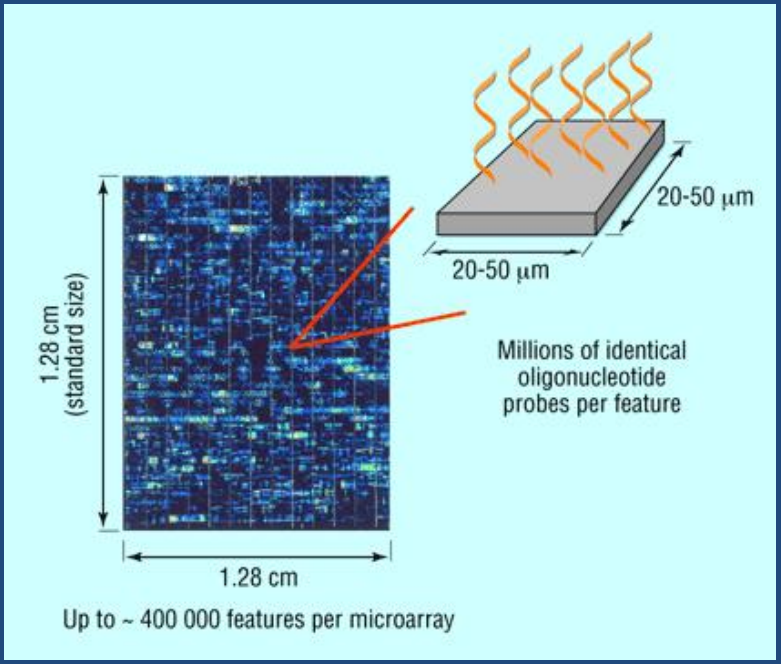
- DNA sequencer

Microarray

- Probe => Measurement
- Analogue signal
- oligonucleotide array VS two-color spotted array

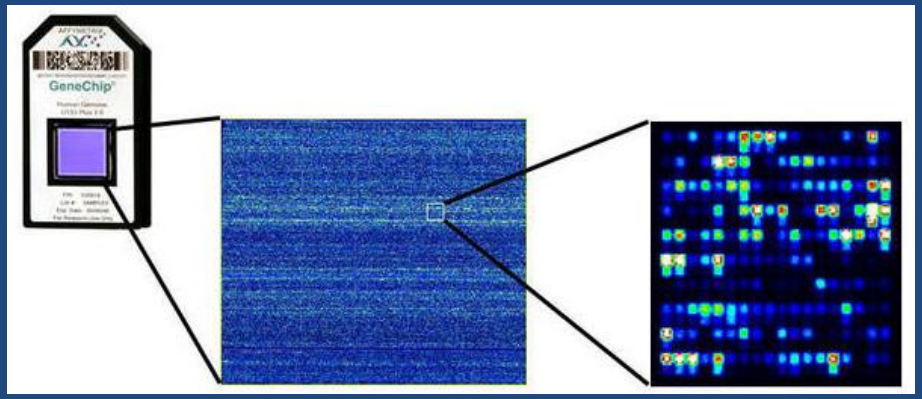


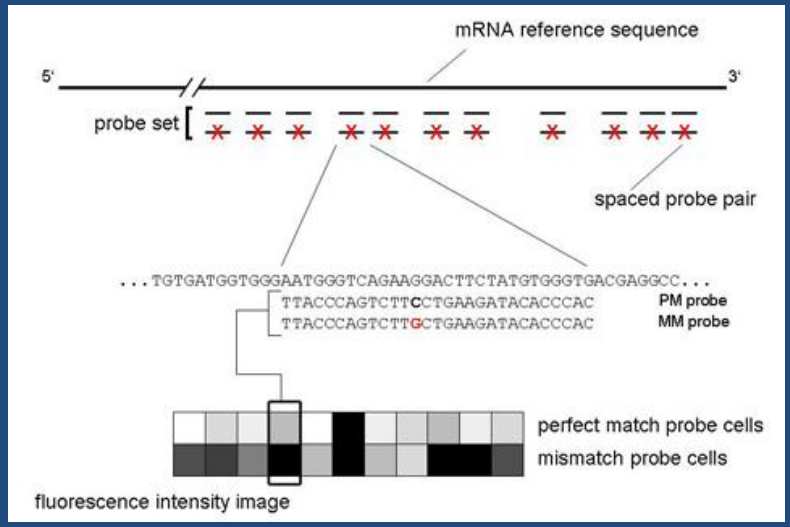
<two-color spotted array>



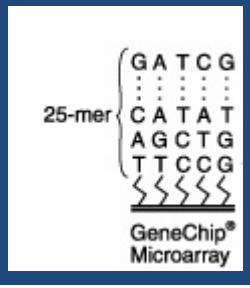
<oligonucleotide array>

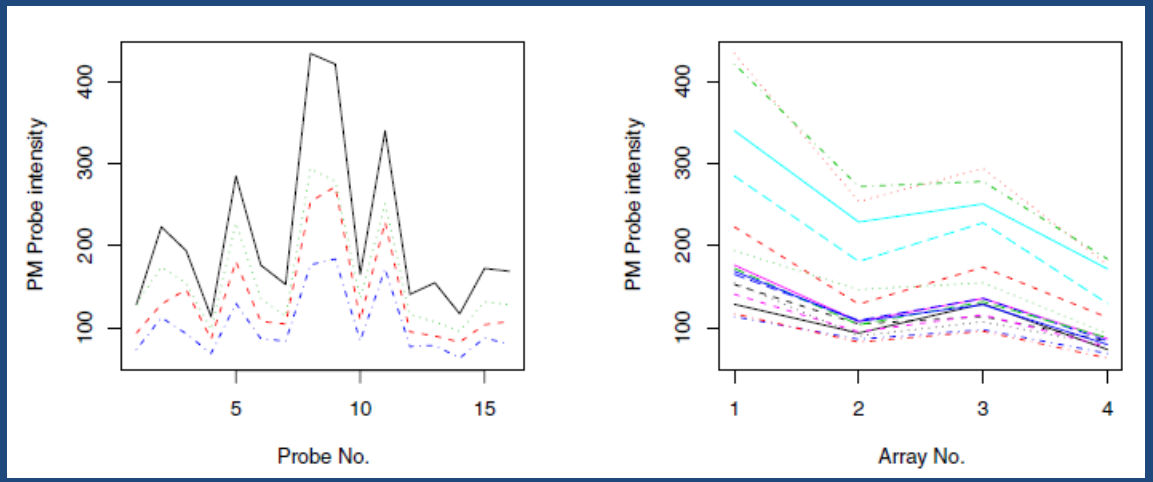
Preprocessing of Microarray Data

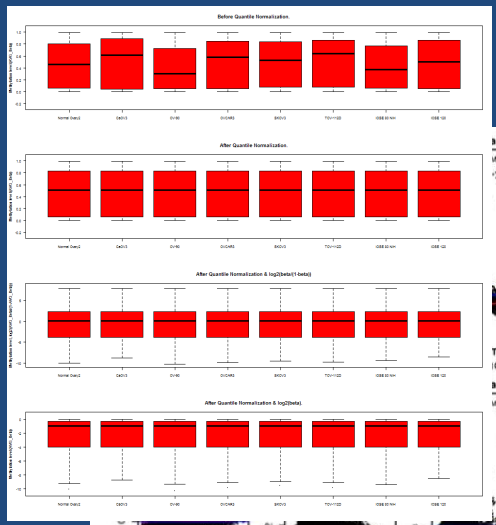




affy, affyPLM, affycomp, gcrma, affypdnn

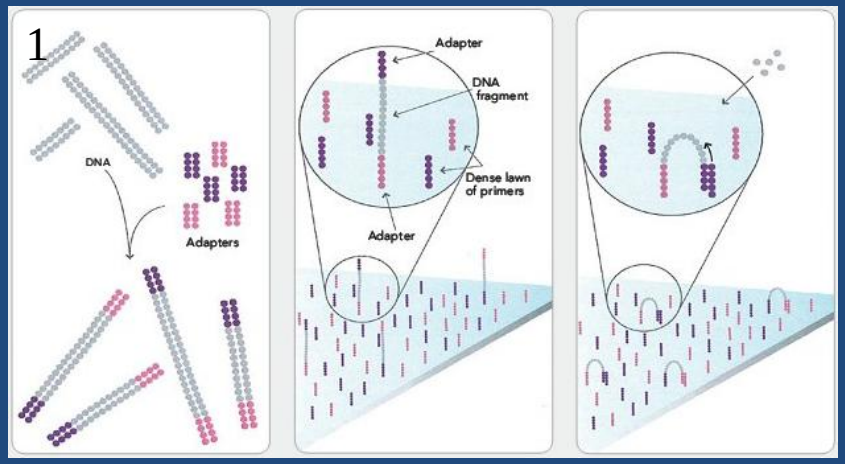


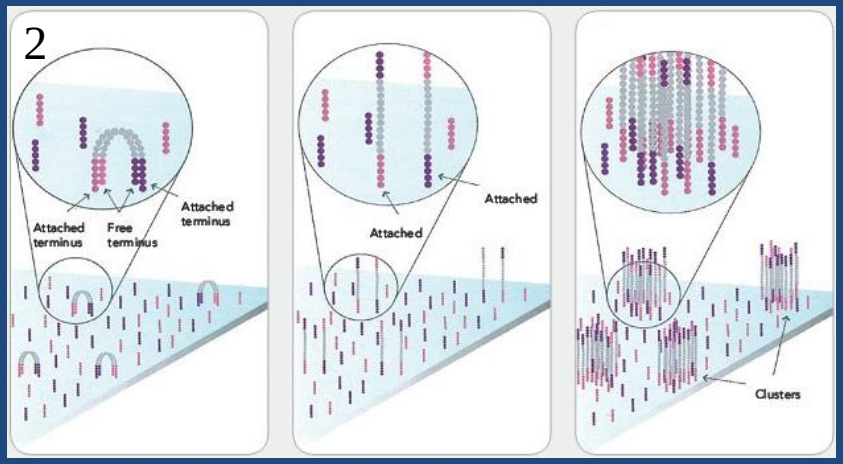


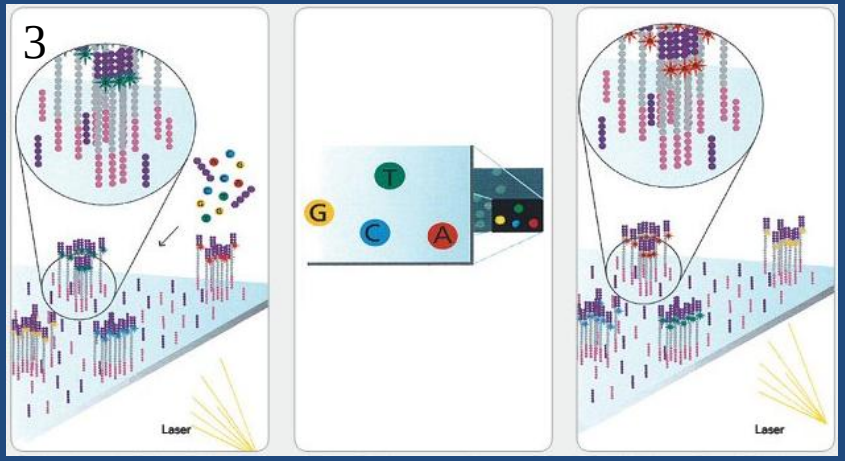


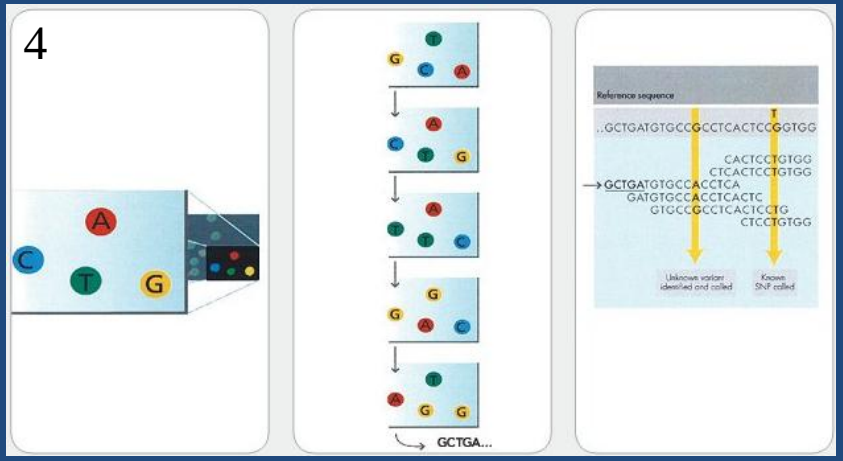
DNA sequencer

- Measurement => Probe
- Digital signal









Preprocessing of Sequence Data

@HWUSI-EAS052R_0029:3:1:4952:1104#1/1
CTATCATGATCACCAACATCACCATCACC
+HWUSI-EAS052R_0029:3:1:4952:1104#1/1
gggggfffefba_caB``abbbabaeeee

@HWUSI-EAS052R_0029:3:1:4952:1104#1/1
CTATCATGATCACCAACATCACCATCACCANGAACN
+HWUSI-EAS052R_0029:3:1:4952:1104#1/1
gggggfffefba_caB``abbbabaeeeecB_\ZaB

Fastq file format

Reference genome

```
@HD VN:1.3 SO:coordinate        } Header section
@SQ SN:ref LN:45
r001 163 ref  7 30 8M2I4M1D3M = 37  39 TTAGATAAAGGATACTG *
r002   0 ref  9 30 3S6M1P1I4M *  0   0 AAAAGATAAGGATA     *
r003   0 ref  9 30 5H6M       *  0   0 AGCTAA    *   NM:i:1
r004   0 ref 16 30 6M14N5M    *  0   0 ATAGCTTCAGC       *
r003  16 ref 29 30 6H5M       *  0   0 TAGGC     *   NM:i:0
r001  83 ref 37 30 9M         =  7 -39 CAGCGCCAT         *
```

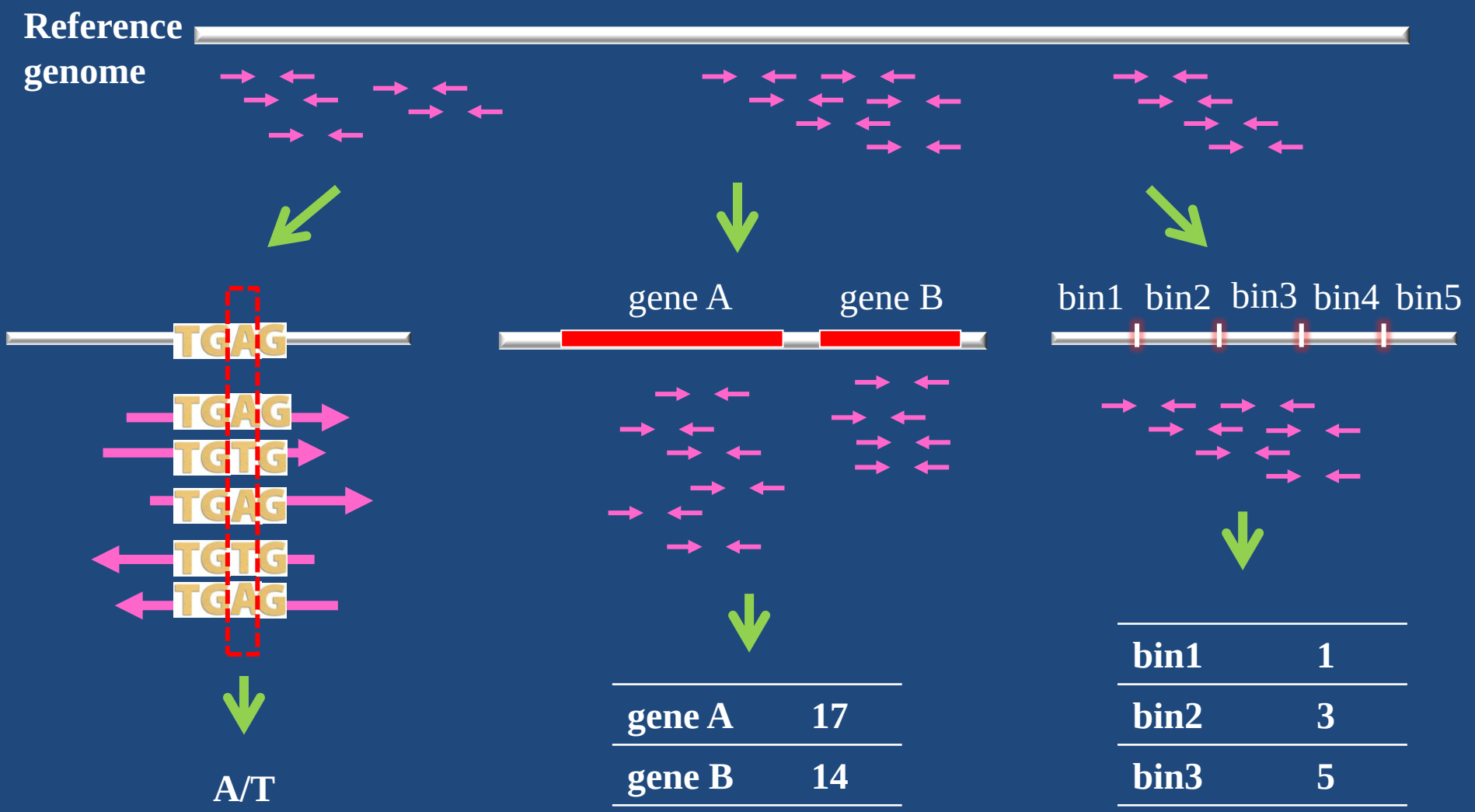
Alignment section

QNAME FLAG RNAME POS MAPQ CIGAR RNEXT PNEXT TLEN SEQ QUAL

sam format

shortRead, Rsamtools

Data from Sequencer



Data Formats

- SNP (A, C, G, T) : categorical
  - Genotype (AA, AB, BB)
  - Sample x Genotype for each SNP locus
  - Genetic Model(dominant, recessive, co-dominant, additive, allele models)
- Expression
  - Signal to noise for each sample and probe (continuous)
- Methylation : categorical or continuous
  - Avg_beta, methylation level for each CpG site(continuous)
  - methylated/unmethylated (categorical) or hypo methylated, medium methylated, hyper methylated (categorical)

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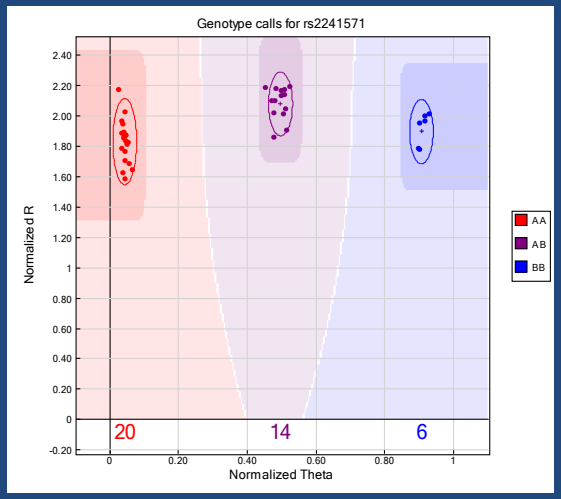
Genomics Data Analysis

A	A	A	SNP1	A	A	A
T	T	T	SNP2	T	T	T
G	G	G	SNP3	G	G	G
C	C	C	SNP4	A	A	A
G	G	G	SNP5	G	G	G
G	G	G	SNP6	G	G	G
C	C	C	SNP7	C	C	C
.	.	.	.	.	.	.
.	.	.	.	.	.	.
.	.	.	.	.	.	.
C	C	C	SNP8	C	C	C
T	T	T	SNP9	T	T	T
T	T	T	SNP10	T	T	T

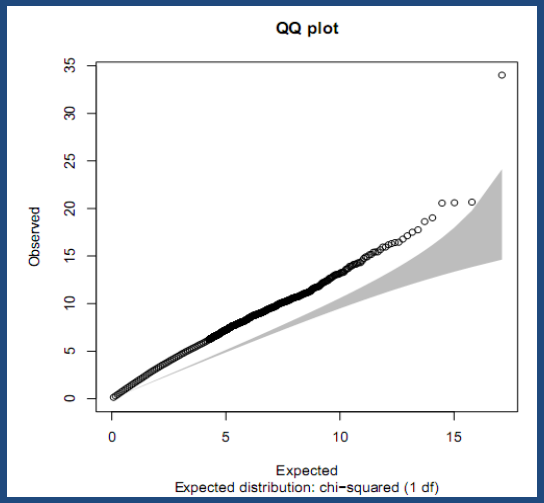
Genomics Data Analysis

→ SNPasoc, GenAbel

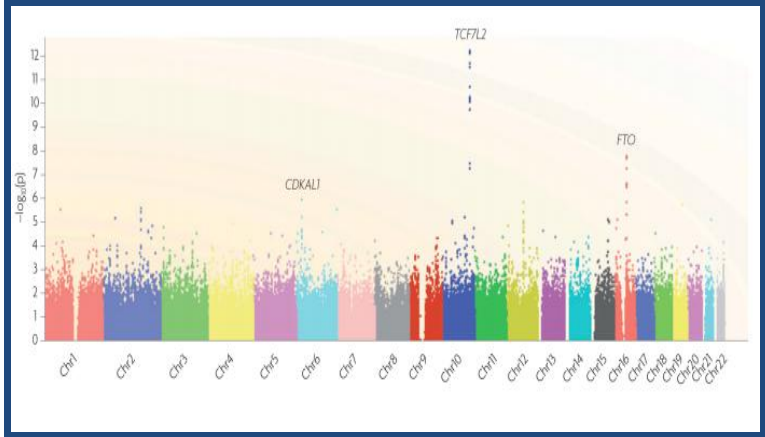
- Genotype clustering



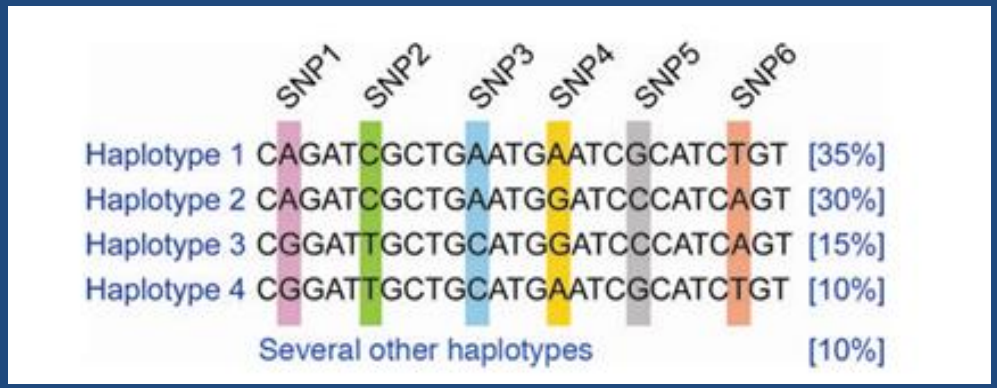
- HWE test

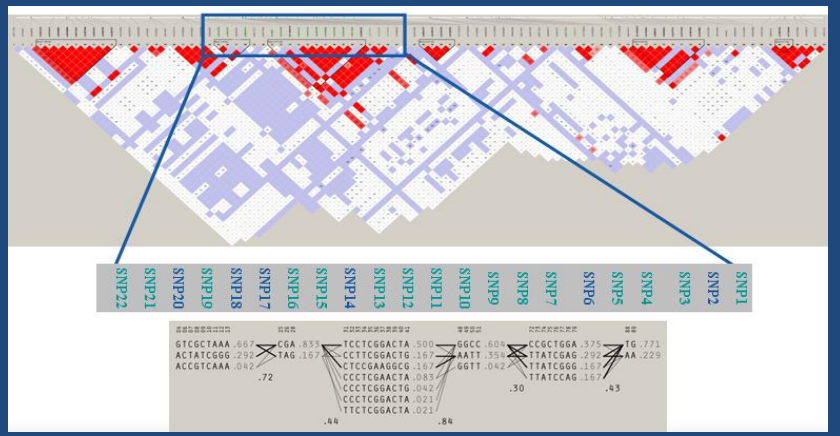


- Manhattan Plot

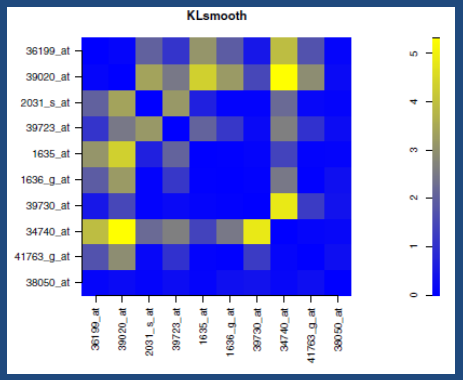


- LD & Haplotype

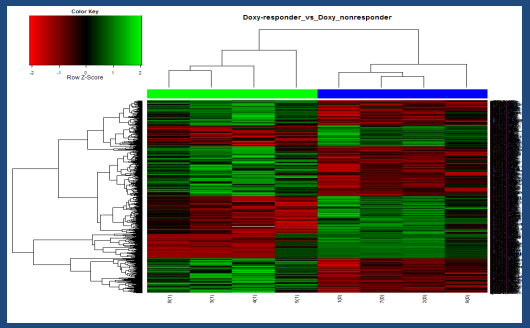




Transcriptomics/Epigenomic Data Analysis

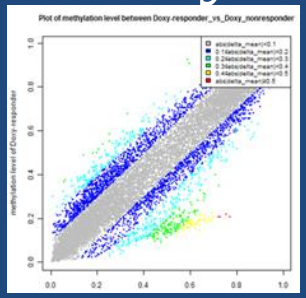


- Distance between Gene or Samples
  - Minkowski metric distance
  - Correlation-based distance
  - Distance between distributions
- Cluster analysis → cluster, hopach
  - Partitioning
  - Hierachical
  - Hybrid



- Analysis of Differential Gene Expression/methylation
  - parametric test
  - non-parametric test
  - multiple test adjustment

→ limma, multtest



Transcriptomics Data Analysis

normal

	Sample1	Sample2	Sample3
Gene A	13	14	15
Gene B			
.			
.			
Gene N			

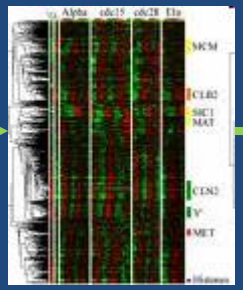
patient

	Sample1	Sample2	Sample3
Gene A	4	5	3
Gene B			
.			
.			
Gene N			

Non-specific filtering

	Sample 1	Sample 2	Sample 3
Gene A	13	14	15
Gene C			
.			
.			
Gene M			

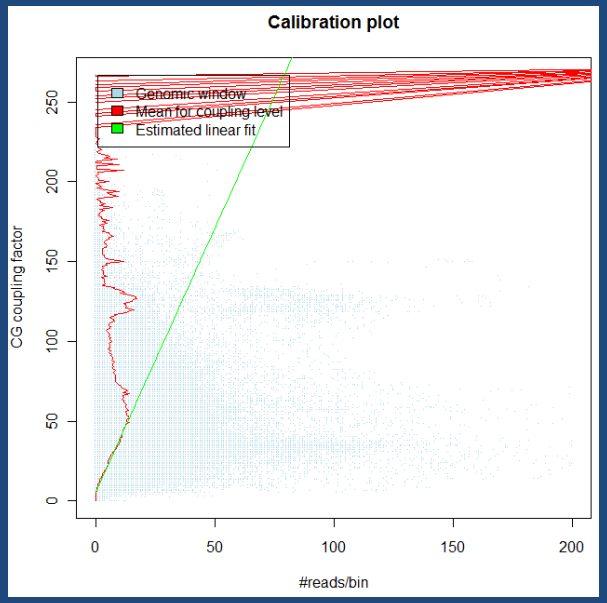
clustering

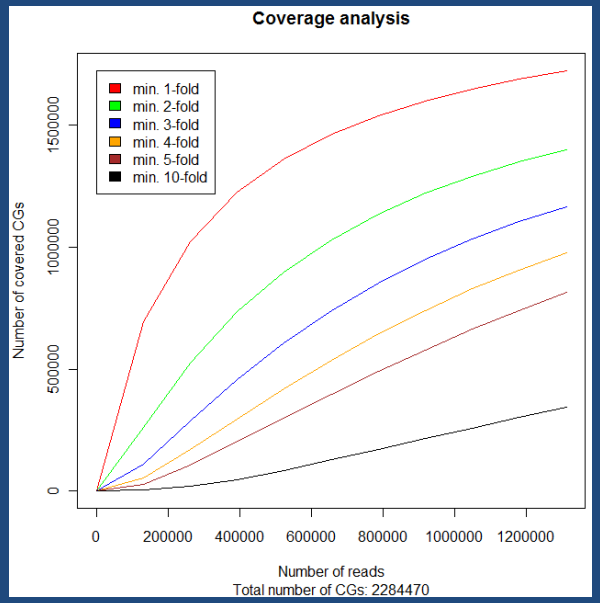


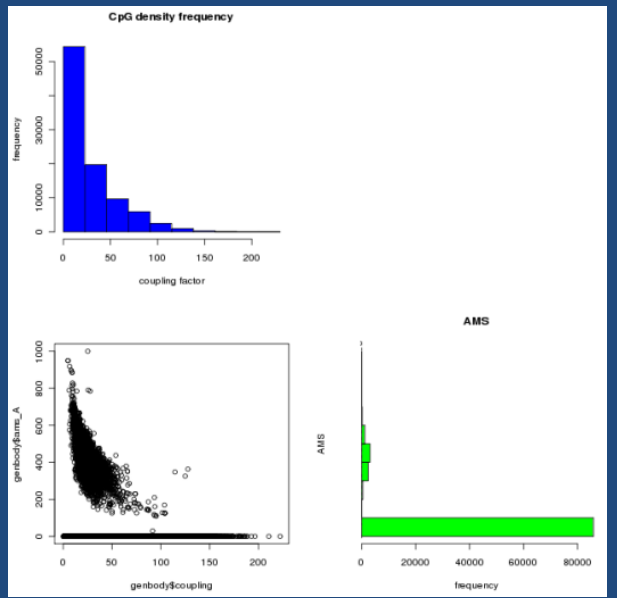
Finding DEG

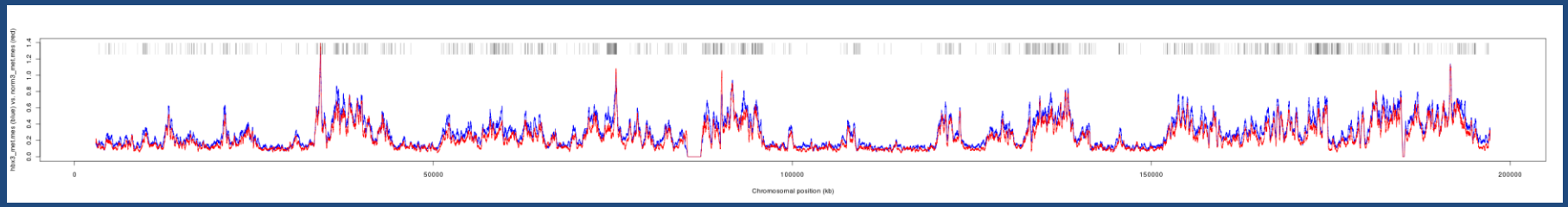
Gene K
Gene I
Gene M
.
.

Epigenomics Data Analysis



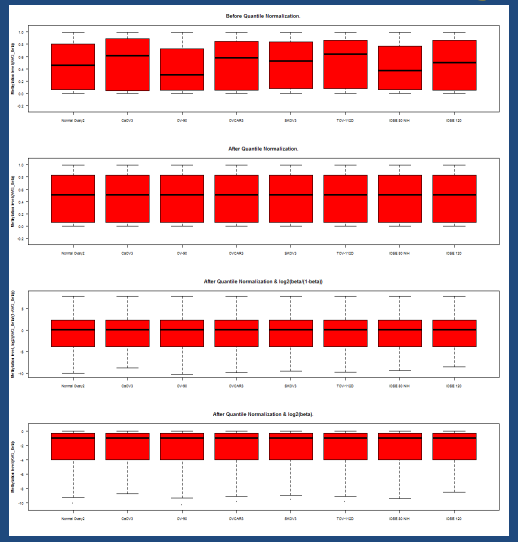


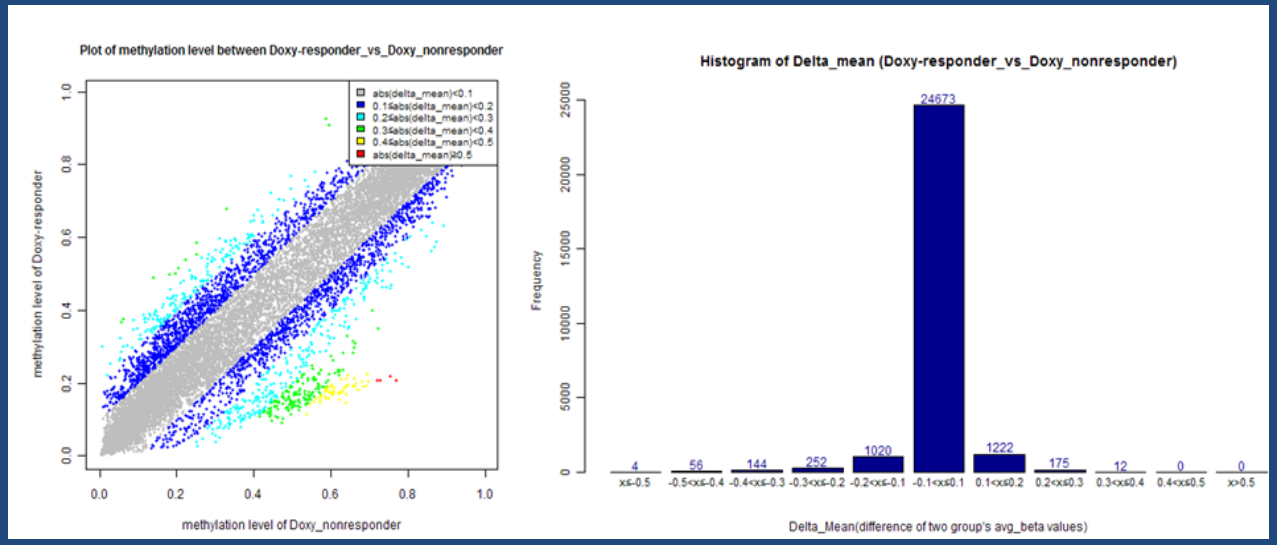


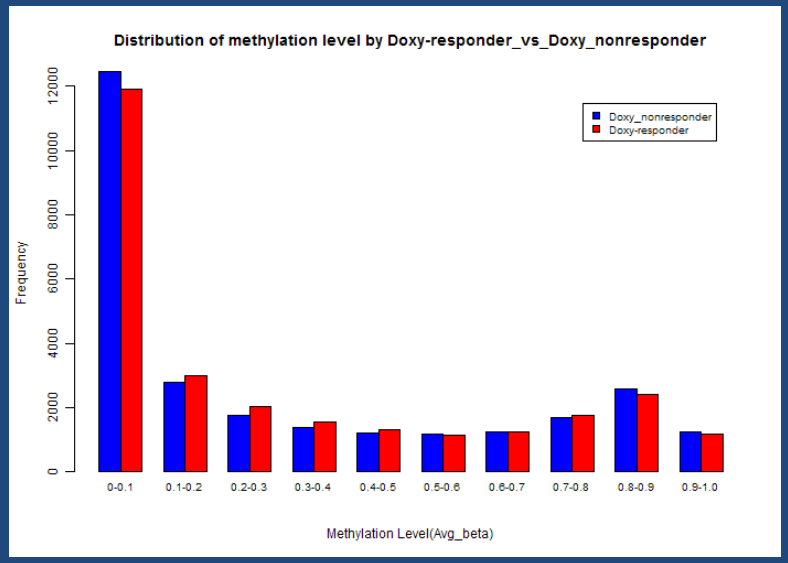


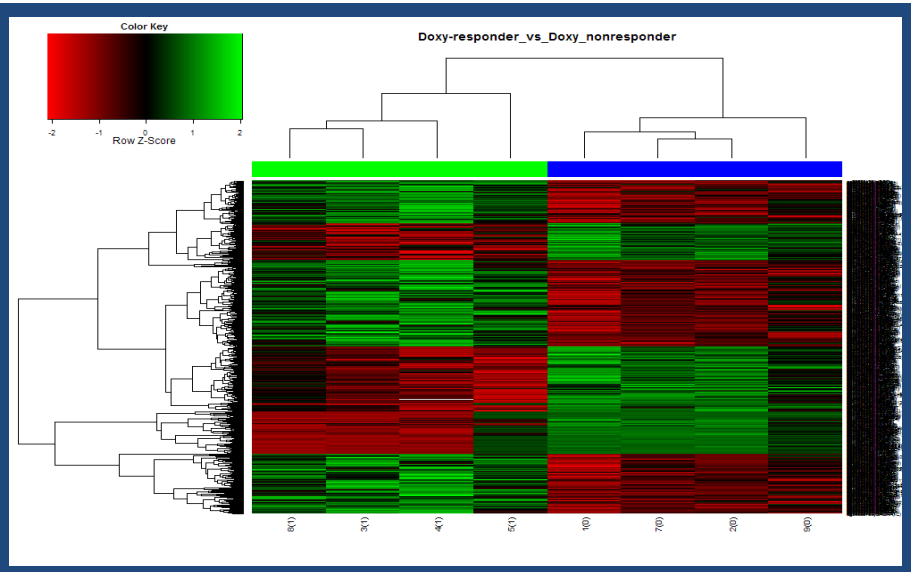
MEDIPS

Transcriptomics/Epigenomic Data Analysis

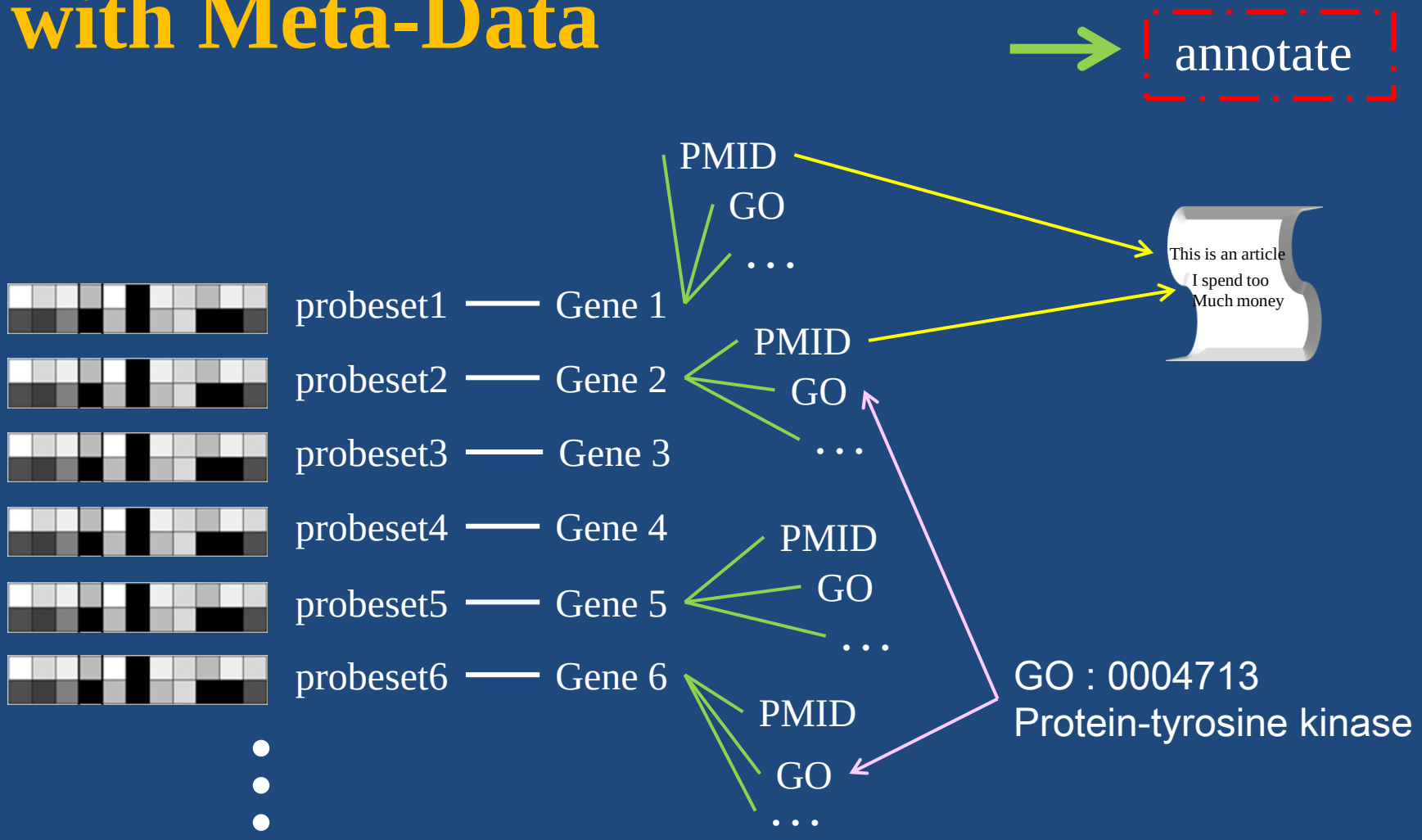








Association Genomic Data with Meta-Data



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Bioconductor

Method

Open Access

Bioconductor: open software development for computational biology and bioinformatics

Robert C Gentleman[1], Vincent J Carey[2], Douglas M Bates[3], Ben Bolstad[4], Marcel Dettling[5], Sandrine Dudoit[4], Byron Ellis[6], Laurent Gautier[7], Yongchao Ge[8], Jeff Gentry[1], Kurt Hornik[9], Torsten Hothorn[10], Wolfgang Huber[11], Stefano Iacus[12], Rafael Irizarry[13], Friedrich Leisch[9], Cheng Li[1], Martin Maechler[5], Anthony J Rossini[14], Gunther Sawitzki[15], Colin Smith[16], Gordon Smyth[17], Luke Tierney[18], Jean YH Yang[19] and Jianhua Zhang[1]

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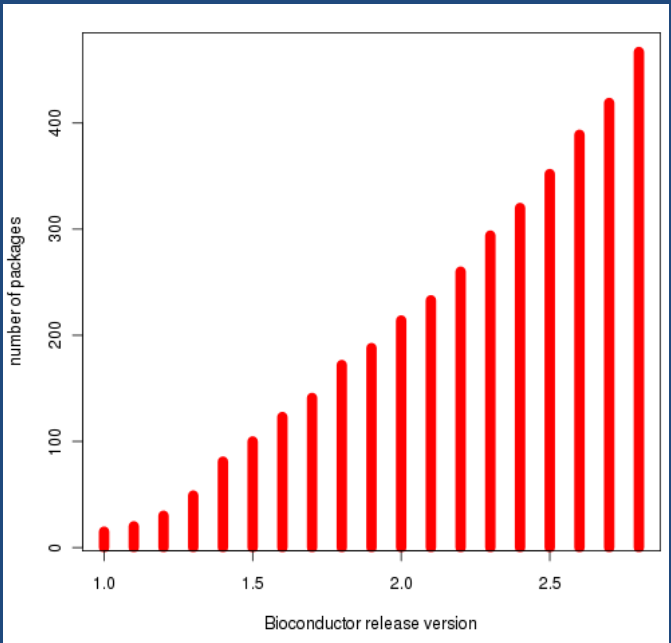
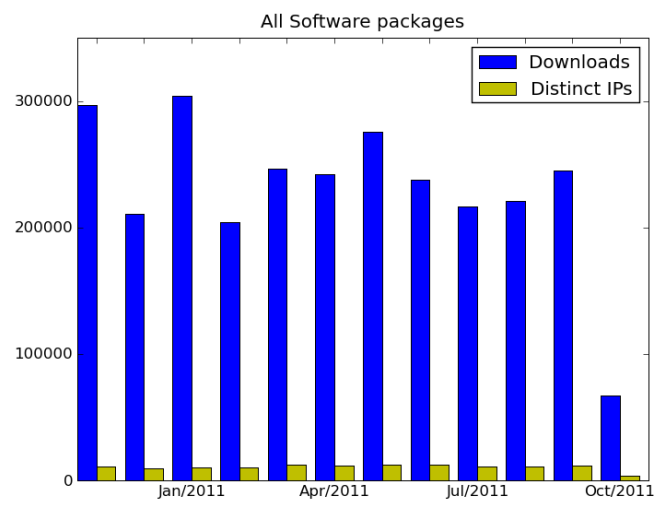
Purpose

Merit

expreSet class

Bioconductor





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Where We Are

- Biological background
- Methods for biological data measurement
- Example of biological data analysis
- Bioconductor
- Trend in Genomics

Why is genomics highlighted?

2001

Human Genome Project

2007

Next Generation Sequencer

1st generation sequencer

next generation sequencer

2011 ..

And 3rd …

Genomics in Business

Thank you

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