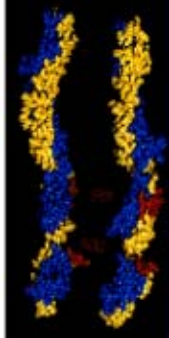
Mining Phenotypes and Informative Genes from Gene Expression Data



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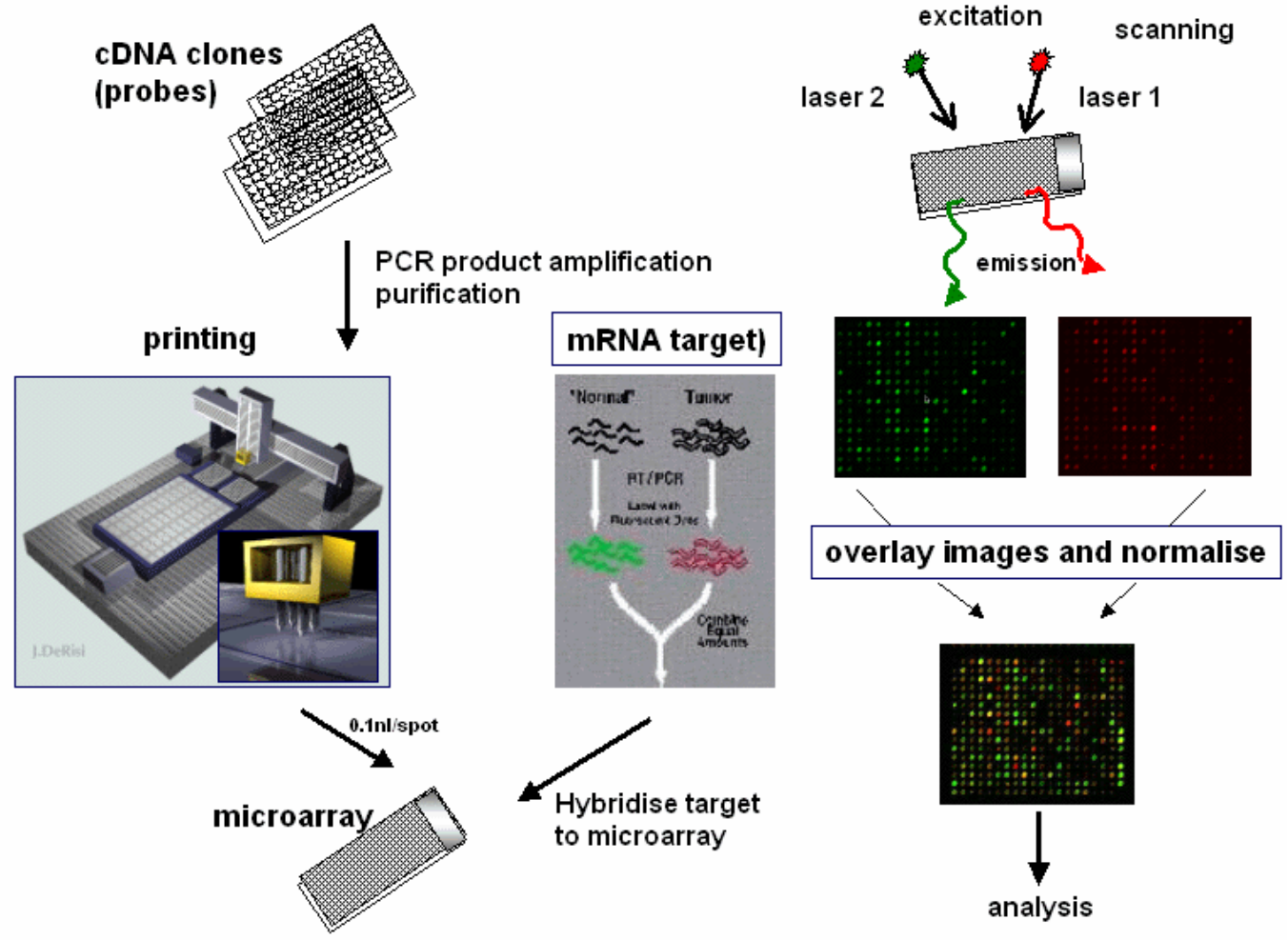
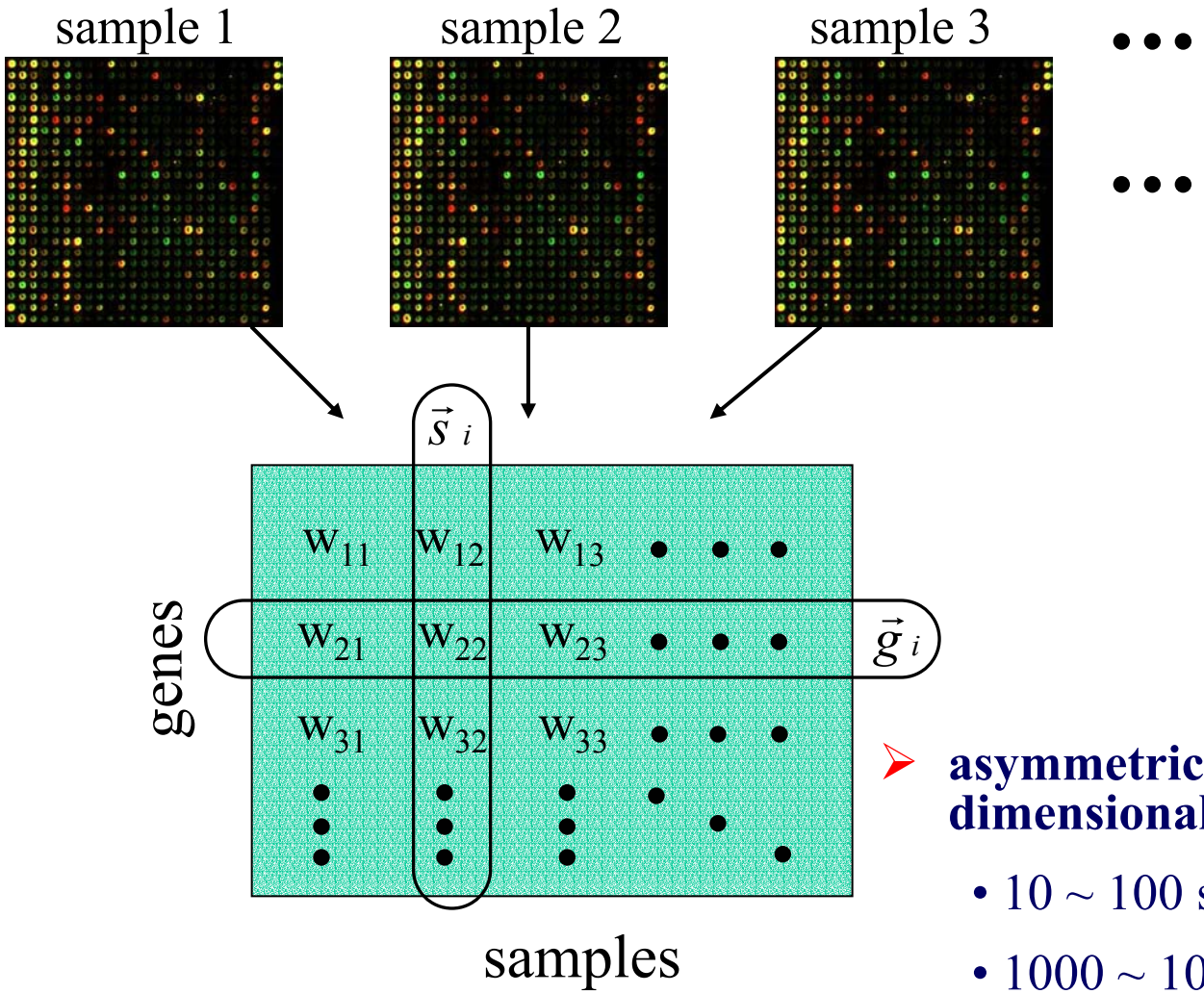
cDNA Microarray Experiment



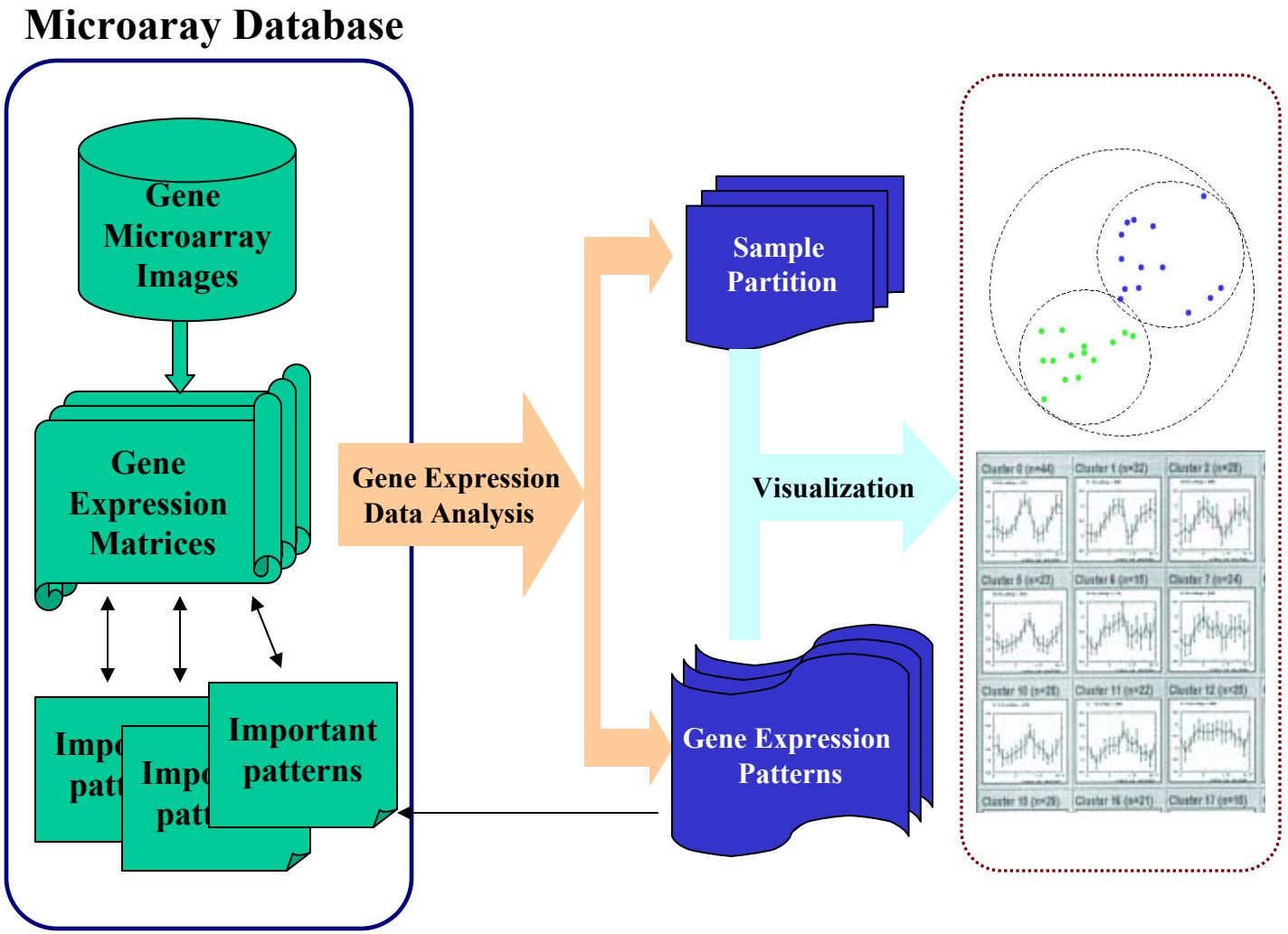
http://www.ipam.ucla.edu/programs/fg2000/fgt_speed7.ppt

Microarray Data



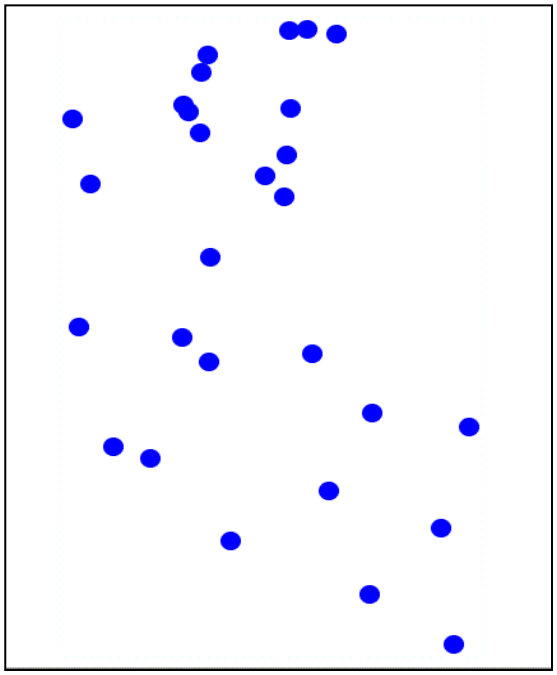
- **asymmetric dimensionality**
  - 10 ~ 100 samples
  - 1000 ~ 10000 genes

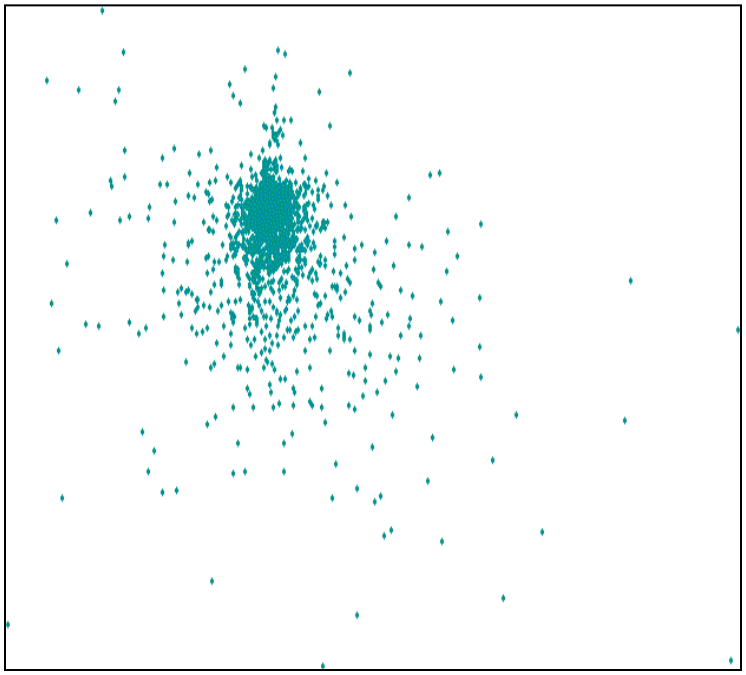
Scope and Goal



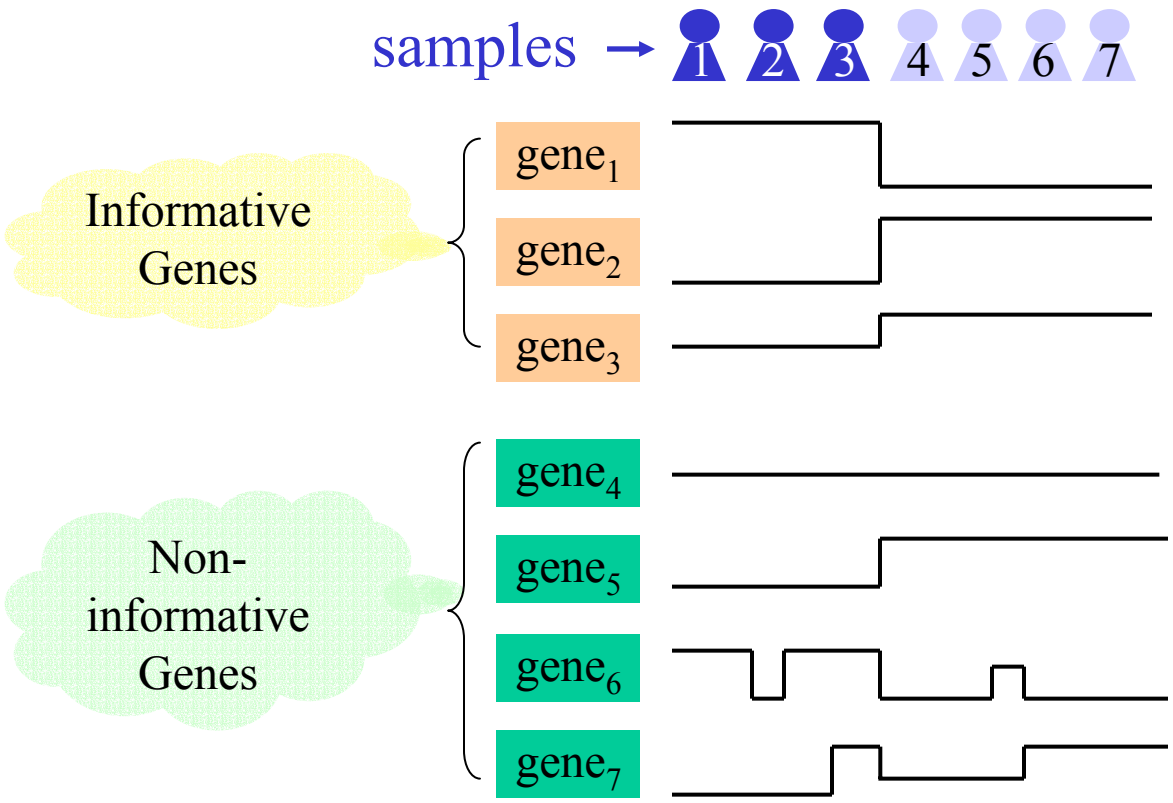
Microarray Data Analysis

- **Analysis from two angles**
  - **sample** as object, gene as attribute
  - gene as object, sample/condition as attribute





Sample-based Analysis



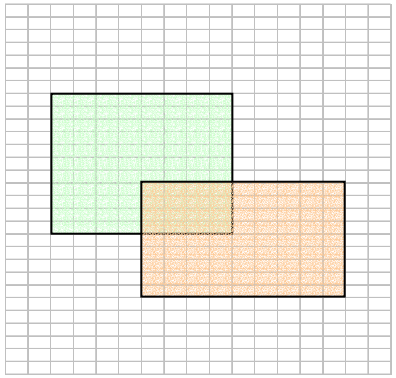
Related Work

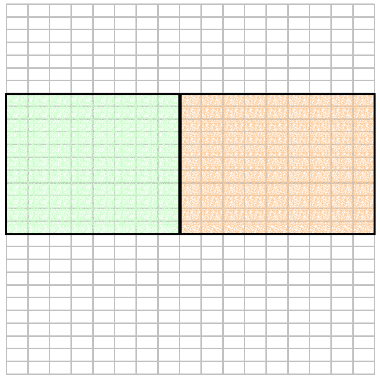
- **New tools using traditional methods :**

TreeView
CLUTO
CIT
SOTA
GeneSpring
J-Express
CLUSFAVOR

  - SOM
  - K-means
  - Hierarchical clustering
  - Graph based clustering
  - PCA

- **Clustering with feature selection:**
- **Subspace clustering**





Quality Measurement

- **Intra-phenotype consistency:**

$$Con\ (G', S') = \frac{1}{|G'| \bullet (|S'| - 1)} \sum_{\vec{g}_i \in G'} \sum_{\vec{s}_j \in S'} (w_{i,j} - \overline{w}_{i,S'})^2$$

- **Inter-phenotype divergency:**

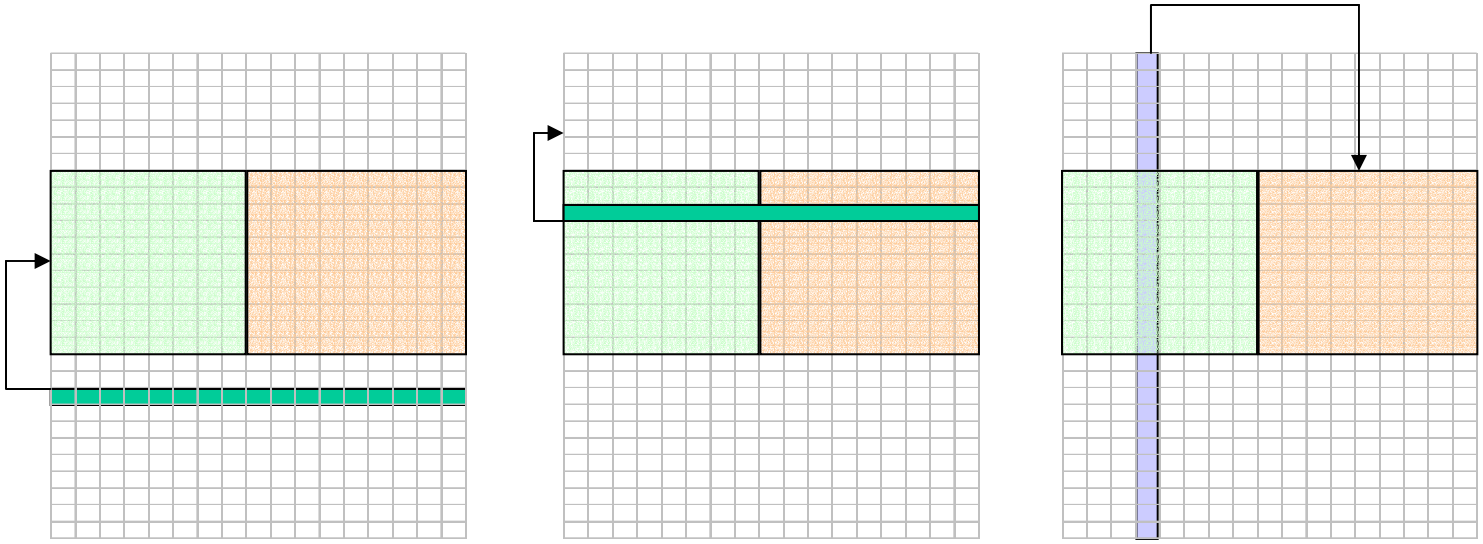
$$Div\ (G', S_1, S_2)) = \frac{\sum_{\vec{g}_i \in G'} \left| \overline{w}_{i,S_1} - \overline{w}_{i,S_2} \right|}{|G'|}$$

- **The quality of phenotype and informative genes:**

$$\Omega = \frac{1}{\sum_{S_i, S_j (1 \le i, j \le K; i \ne j)} \frac{\sqrt{Con\ (G', S_i) + Con\ (G', S_j)}}{Div\ (G', S_i, S_j)}}$$

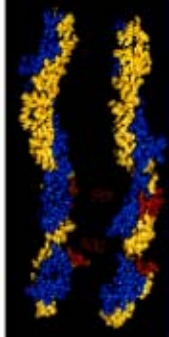
Heuristic Searching

- Starts with a random K-partition of samples and a subset of genes as the candidate of the informative space.
- Iteratively adjust the partition and the gene set toward the optimal solution.
  - for each gene, try possible insert/remove
  - for each sample, try best movement.



Mutual Reinforcing Adjustment

- Divide the original matrix into a series of exclusive sub-matrices based on partitioning both the samples and genes.
- Post a partial or approximate phenotype structure called a *reference partition* of samples.
  - compute *reference degree* for each sample groups;
  - select *k* groups of samples;
  - do partition adjustment.
- Adjust the candidate informative genes.
  - compute W for *reference partition* on *G*
  - perform possible adjustment of each genes
- Refinement Phase



Reference Partition Detection

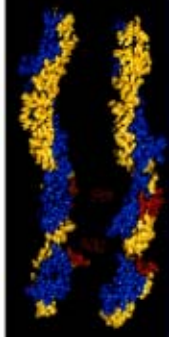
- *Reference degree*: measurement of a sample group over all gene groups

$$ref\ (S_j) = \log |S_j| \sum_{G_i \in G'} \frac{1}{Con\ (G_i, S_j)}$$

- The sample group having the highest reference degree – S_{p0} , S_{p1} , S_{p2} … S_{px} ,…

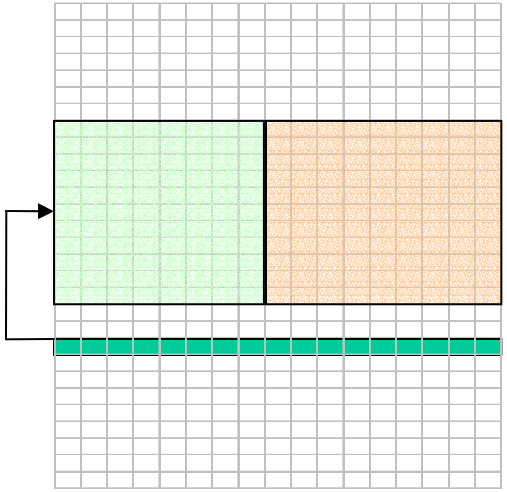
$$Ran\ (S_{px}) = \log |S_{px}| \sum_{G_i \in G'} \frac{\sum_{t=0}^{x-1} Div\ (G_i, S_{px}, S_{pt})}{Con\ (G_i, S_{px})}$$

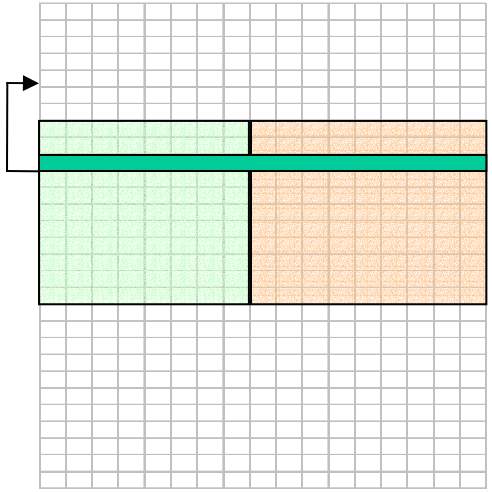
- Partition adjustment: check the missing samples



Gene Adjustment

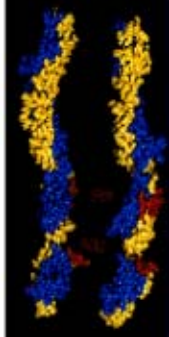
- For each gene, try possible insert/remove





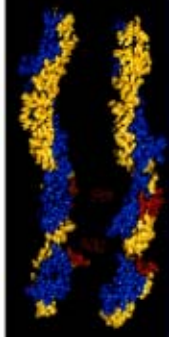
Refinement Phase

- The partition corresponding to the best state may not cover all the samples.
- Add every sample not covered by the reference partition into its *matching* group – the phenotypes of the samples.
- Then, a gene adjustment phase is conducted. We execute all adjustments with a positive quality gain – informative space.
- Time complexity $O(n*m^2*I)$

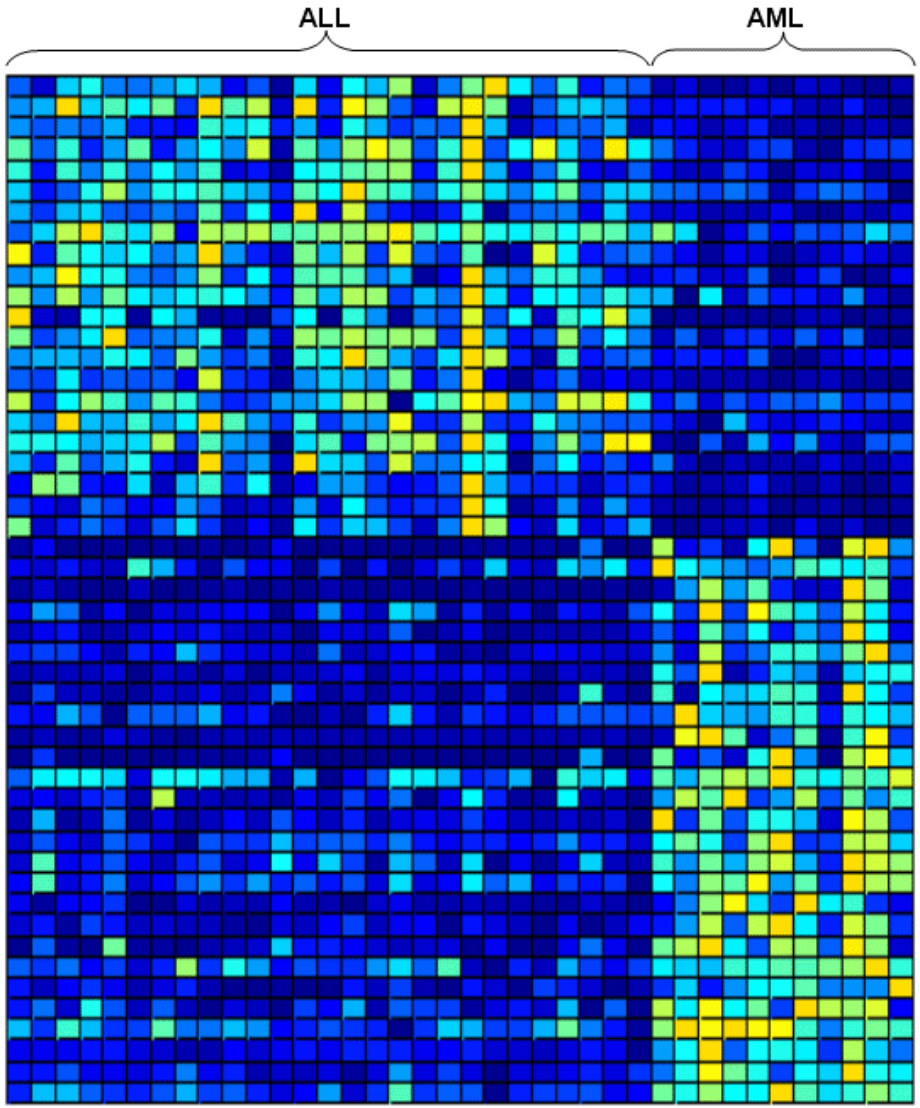


Phenotype Detection

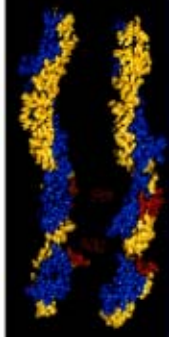
Data Set	MS-IFN	MS-CON	Leukemia-G1	Leukemia-G2	Colon	Breast
Data Size	4132*28	4132*30	7129*38	7129*34	2000*62	3226*22
J-Express	0.4815	0.4851	0.5092	0.4965	0.4939	0.4112
SOTA	0.4815	0.4920	0.6017	0.4920	0.4939	0.4112
CLUTO	0.4815	0.4828	0.5775	0.4866	0.4966	0.6364
Kmeans/PCA	0.4841	0.4851	0.6586	0.4920	0.4966	0.5844
SOM / PCA	0.5238	0.5402	0.5092	0.4920	0.4939	0.5844
δ-cluster	0.4894	0.4851	0.5007	0.4538	0.4796	0.4719
Heuristic	0.8052	0.6230	0.9761	0.7086	0.6293	0.8638
Mutual	0.8387	0.6513	0.9778	0.7558	0.6827	0.8749



Informative Gene Selection



Gene description	Probe	Match
C-myb	F009426	2
PROTEASOME IOTA	X59417	2
Myosin light chain	M31211	2
SNF2	D26156	2
Crystallin zeta	L13278	1
CTP synthetase	X52142	0
Cyclin D3	M92287	2
Actinin alpha 2	M86406	0
Thymopoietin beta	U09087	1
HKR-T1	S50223	2
Aldehyde reductase 1	X15414	1
MB-1	U05259	2
TFIIE beta	X63469	1
Clone 22	AF009426	0
RbAp48	X74262	2
CD19 CD19 antigen	M28170	0
Op18	M31303	2
ADH4	X56411	0
MCM3	D38073	2
Inducible protein	L47738	2
E2A	M31523	2
Topoisomerase II β	Z15115	2
IL8	M28130	1
M-CSF	M37435	0
Cystatin C	M27891	1
HU-K5	U67963	0
Cathepsin D	M63138	1
CD11C	M81695	1
p62	U46751	1
MAD3	M69043	1
HOX 2.2	X58431	0
adipsin	M84526	1
IL-8 PRECURSOR	Y00787	1
Neuromedin B mRNA	L08246	1
Catalase	X04085	1
MCL1	L08246	1
CyP3	M80254	2
Ferritin, light polypeptide	M11147	1
ATPase	M62762	2
CD33	M23197	2
LYN	M16038	2
Proteoglycan 1	X17042	2
Thrombospondin-1	U12471	1
Leptin receptor	Y12670	2
IGIF	D49950	1
HoxA9	U82759	2
Zyxin	X95735	2
LTC4 synthase	U50136	2
Fumarylacetoacetate	M55150	2



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