CSci 8980: Advanced Topics in Graphical Models

Application: Gene Expression Analysis

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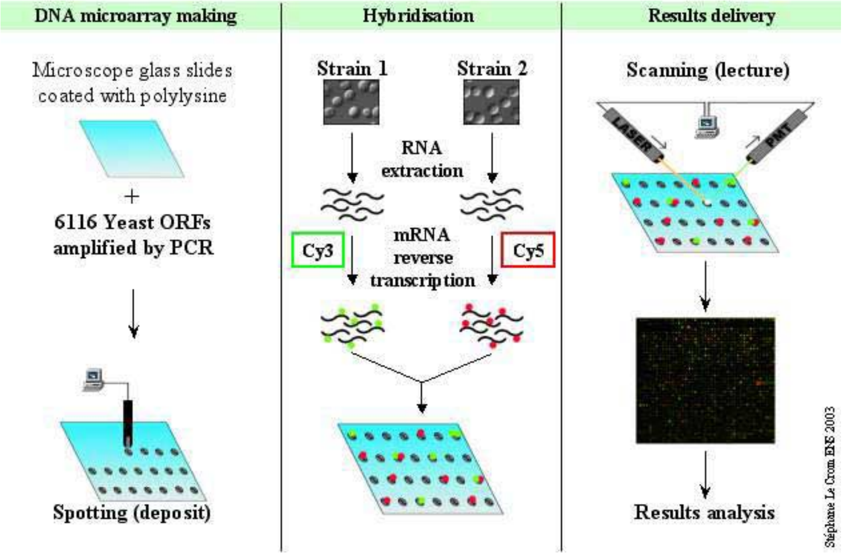
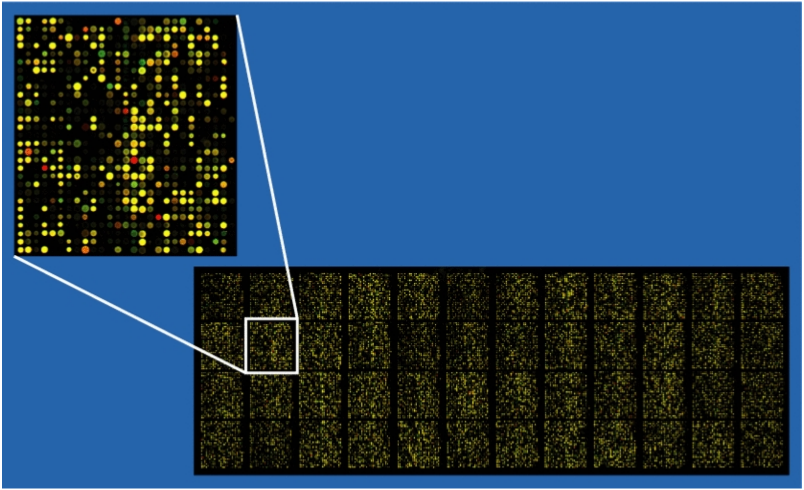
Microarray Technology



Microarray Data



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- Idea: Use a Bayesian infinite mixture model

Infinite Mixture Model for Gene Expression

- Level 1: Data generation

$$p(x_i|c_i = j, \mu_h, \sigma_h^2, [h]_1^Q) = \mathcal{N}(x; \mu_j, \sigma_j^2 \mathbb{I})$$

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- Level 2: Priors for parameters

$$\begin{aligned} p(\mu_j|\lambda, r) &= \mathcal{N}(\mu; \lambda, 1/r\mathbb{I}) \\ p(\sigma_j^{-2}|\beta, w) &= f_G(\sigma^{-2}; \beta/2, \beta w/2) \end{aligned}$$

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- Level 2: Prior for clustering $c_i \sim Discrete(\pi)$

Infinite Mixture Model for Gene Expression (Contd.)

- Prior for hyper-parameters

$$
\begin{aligned}
p(w|\sigma_x^2) &= f_G(w; 1/2, 1/(2\sigma_x^2)) \\
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\end{aligned}
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Infinite Mixture Model for Gene Expression (Contd.)

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- (μ_x, σ_x^2) are empirical mean, variance
- Priors on cluster-prior π

$$\pi \sim Dirichlet(\alpha/Q)$$

Gibbs Sampler

- As $Q \to \infty$, we get a DPM

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$$p(c_i = j | c_{-i}, \mathbf{x}_i, \mu_j, \sigma_j^2) \quad \propto \quad \frac{n_{-i,j}}{T - 1 + \alpha} \mathcal{N}(x_i; \mu_j, \sigma_j^2 \mathbb{I})$$

$$p(c_i \neq c_j, j \neq i | c_{-i}, x_i, \mu_x, \sigma_x^2) \quad \propto \quad \frac{\alpha}{T - 1 + \alpha} \int \mathcal{N}(x_i | \mu, \sigma^2 \mathbb{I}) p(\mu, \sigma$$

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- Pairwise probability of being generated by the same pattern

$$P_{ij} = \frac{\#\text{ samples after `burn-in' with } c_i = c_j}{S_B}$$

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$$P_{ij} = \frac{\#\text{ samples after 'burn-in' with } c_i = c_j}{S_B}$$

- Distance $D_{ij} = 1 - P_{ij}$

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$$p(x_{i1}, \ldots, x_{ik}|c_i = j, \mu_j, \sigma_j^2, \psi_i) = \prod_k \mathcal{N}(\bar{x}_i; \mu_j, (\sigma_j^2 + \frac{\psi_i^2}{G})\mathbb{I})$$

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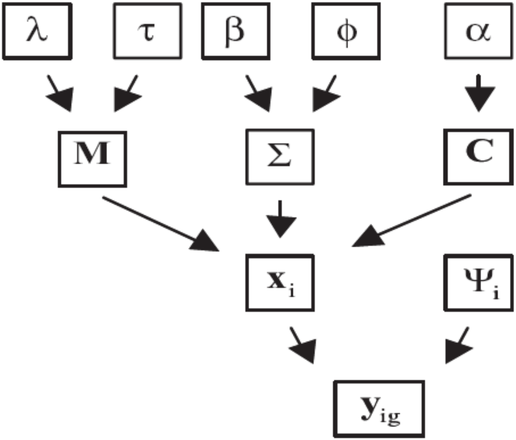
- Gibbs sampler used for inference

Experimental Results

- Move to paper for results

Results



Gibbs Sampler

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$$p(c_i \neq c_j, j \neq i | C_{-i}, x_{ik}, \psi_i, \alpha)$$
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- Let $\xi \to 1$ as iterations $n \to \infty$

Results

Table 2. (A) Average adjusted RAND indices for the 'elliptical' simulated data and (B) average number of clusters induced by different IMM algorithms with Auto cluster creation

Method	Number of replicates							
	Low Noise				High Noise			
	1	2	3	4	1	2	3	4
A								
Heuristic methods								
Average link; correlation	0.76	0.76	0.80	0.90	0.20	0.34	0.32	0.43
Average link; distance	0.86	1.00	0.96	1.00	0.00	0.00	0.00	0.00
Complete link; correlation	0.70	0.71	0.75	0.82	0.26	0.39	0.44	0.52
Complete link; distance	0.96	0.93	0.96	0.96	0.07	0.27	0.27	0.53
k-means; correlation	0.76	0.76	0.80	0.90	0.31	0.52	0.57	0.62
k-means; distance	0.86	1.00	0.96	1.00	0.00	0.21	0.16	0.48
SD-adjusted heuristic methods								
Average link; correlation	NA	0.32	0.59	0.61	NA	0.18	0.48	0.59
Average link; distance	NA	0.96	1.00	1.00	NA	0.13	0.47	0.67
Complete link; correlation	NA	0.29	0.46	0.63	NA	0.18	0.48	0.57
Complete link; distance	NA	0.96	1.00	1.00	NA	0.24	0.67	0.83
k-means; correlation	NA	0.47	0.59	0.71	NA	0.22	0.44	0.51
k-means; distance	NA	0.95	1.00	1.00	NA	0.49	0.78	0.77
Model-based methods								
IMM—elliptical	0.93	1.00	1.00	1.00	0.41	0.98	1.00	1.00
IMM—elliptical Auto	0.60	1.00	1.00	1.00	0.34	0.99	1.00	1.00
IMM—spherical	0.93	1.00	0.96	1.00	0.41	0.48	0.66	0.75
IMM—spherical Auto	0.60	0.98	0.99	1.00	0.34	0.82	0.85	0.92
IMM—averaged	0.93	0.93	0.99	1.00	0.41	0.47	0.67	0.77
IMM—averaged Auto	0.60	0.61	0.62	0.64	0.34	0.45	0.46	0.50
FMM—elliptical	0.98	1.00	1.00	1.00	0.30	0.98	1.00	1.00
FMM—spherical	0.98	1.00	1.00	1.00	0.30	0.86	0.89	0.95
FMM—averaged	0.98	0.80	0.95	1.00	0.30	0.44	0.50	0.57
MCLUST-HC	0.97	0.97	0.99	1.00	0.36	0.44	0.57	0.51
MCLUST-FITTS	0.97	0.96	0.97	1.00	0.36	0.38	0.43	0.50
B								
IMM—elliptical Auto	16.2	6.0	6.0	6.0	15.6	6.0	6.0	17.6
IMM—spherical Auto	16.2	7.6	7.8	7.0	15.6	10.4	10.2	6.0

Results

Table 3. (A) Average adjusted RAND indices for the 'spherical' simulated data (B) average number of clusters induced by different IMM algorithms with Auto cluster creation

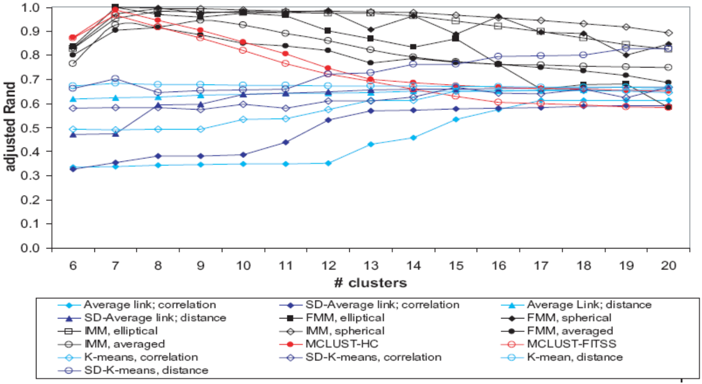
Method	Number of replicates Low Noise 1	2	3	4	High Noise 1	2	3	4
A								
Heuristic methods								
Average link; correlation	0.61	0.67	0.67	0.82	0.25	0.33	0.42	0.40
Average link; distance	0.28	0.70	0.73	0.90	0.00	0.00	0.00	0.00
Complete link; correlation	0.69	0.72	0.73	0.79	0.33	0.46	0.49	0.53
Complete link; distance	0.62	0.76	0.80	0.96	0.00	0.00	0.02	0.09
k-means; correlation	0.70	0.67	0.67	0.82	**0.38**	0.51	0.56	0.57
k-means; distance	0.44	0.70	0.73	0.90	0.00	0.00	0.00	0.00
SD-adjusted heuristic methods								
Average link; correlation	NA	0.35	0.64	0.73	NA	0.14	0.35	0.34
Average link; distance	NA	0.77	0.75	0.90	NA	0.00	0.00	0.00
Complete link; correlation	NA	0.33	0.70	0.77	NA	0.11	0.35	0.49
Complete link; distance	NA	0.77	0.85	0.96	NA	0.09	0.14	0.23
k-means; correlation	NA	0.52	0.75	0.75	NA	0.18	0.53	0.55
k-means; distance	NA	0.83	0.75	0.90	NA	0.14	0.17	0.28
Model-based methods								
IMM—elliptical	**0.90**	0.85	0.91	0.96	0.23	0.80	0.87	0.90
IMM—elliptical Auto	0.52	**1.00**	**1.00**	**1.00**	0.28	0.77	0.87	0.90
IMM—spherical	**0.90**	**1.00**	**1.00**	**1.00**	0.23	**0.84**	**0.90**	**0.93**
IMM—spherical Auto	0.52	**1.00**	**1.00**	**1.00**	0.28	**0.84**	0.89	**0.93**
IMM—averaged	**0.90**	0.94	0.91	0.92	0.23	0.42	0.46	0.64
IMM—averaged Auto	0.52	0.51	0.55	0.56	0.28	0.36	0.40	0.45
FMM—elliptical	0.71	**1.00**	**1.00**	**1.00**	0.23	0.78	0.87	0.90
FMM—spherical	0.71	**1.00**	**1.00**	**1.00**	0.23	**0.84**	**0.90**	0.92
FMM—averaged	0.71	0.89	0.93	0.96	0.23	0.32	0.39	0.48
MCLUST-HC	0.77	0.80	0.85	0.85	0.26	0.24	0.29	0.31
MCLUST-FITTS	0.77	0.90	0.95	0.95	0.26	0.27	0.38	0.35
B								
IMM—elliptical Auto	19.0	6.8	6.4	6.2	15.4	5.8	6.0	6.0
IMM—spherical Auto	19.0	6.0	6.0	6.0	15.4	6.0	6.0	6.0

Results

Table 4. Automatic IMM clustering results for datasets with outliers

Noise level	Variance	RAND	No. of clusters
Low	Averaged	0.78	13.4
Low	Elliptical	0.99	7.6
Low	Spherical	0.99	8
High	Averaged	0.51	16.6
High	Elliptical	0.97	13
High	Spherical	0.89	8.8

Results


adjusted Rand
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
clusters
Average link; correlation
SD-Average link; correlation
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FMM, elliptical
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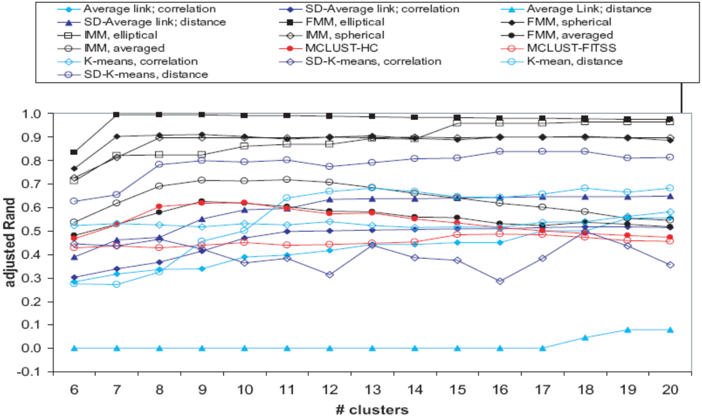
IMM, averaged
MCLUST-HC
MCLUST-FITSS
K-means, correlation
SD-K-means, correlation
K-mean, distance
SD-K-means, distance

Results



Average link; correlation
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1.0
0.9
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0.7
0.6
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0.3
0.2
0.1
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-0.1
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
clusters

Results

Method	Number of replicates 1	2	3	4
A				
Heuristic methods				
Average link; correlation	**0.88**	0.87	0.91	0.87
Average link; distance	0.67	0.90	0.92	0.86
Complete link; correlation	0.69	0.78	0.70	0.68
Complete link; distance	0.62	0.85	0.88	0.96
K-means; correlation	0.75	0.77	0.77	0.87
K-means; distance	0.86	0.92	0.91	0.86
SD-adjusted heuristic methods				
Average link; correlation	NA	0.68	0.82	0.82
Average link; distance	NA	0.84	0.86	0.86
Complete link; correlation	NA	0.52	0.67	0.72
Complete link; distance	NA	0.83	0.96	0.97
K-means; correlation	NA	0.63	0.75	0.64
K-means; distance	NA	0.79	0.85	0.86
Model-based methods				
IMM—elliptical	0.85	0.92	**0.97**	**0.97**
IMM—elliptical Auto	0.78	**0.94**	0.94	0.96
IMM—averaged	0.85	0.92	0.94	**0.97**
IMM—averaged Auto	0.78	0.93	0.96	0.96
FMM—elliptical	0.71	0.75	0.93	**0.97**
IMM—averaged	0.71	0.85	0.91	**0.97**
MCLUST-HC	0.68	0.90	0.96	**0.97**
MCLUST-FITTS	0.68	0.86	0.89	**0.97**
B				
IMM—elliptical Auto	2.8	4.2	4.8	5.0
IMM—averaged Auto	2.8	4.7	4.5	5.0