Optimization-Based Model Fitting for Latent Class and Latent Profile Analyses

Guan-Hua Huang, Su-Mei Wang and Chung-Chu Hsu

12/17/2010

Breast cancer data

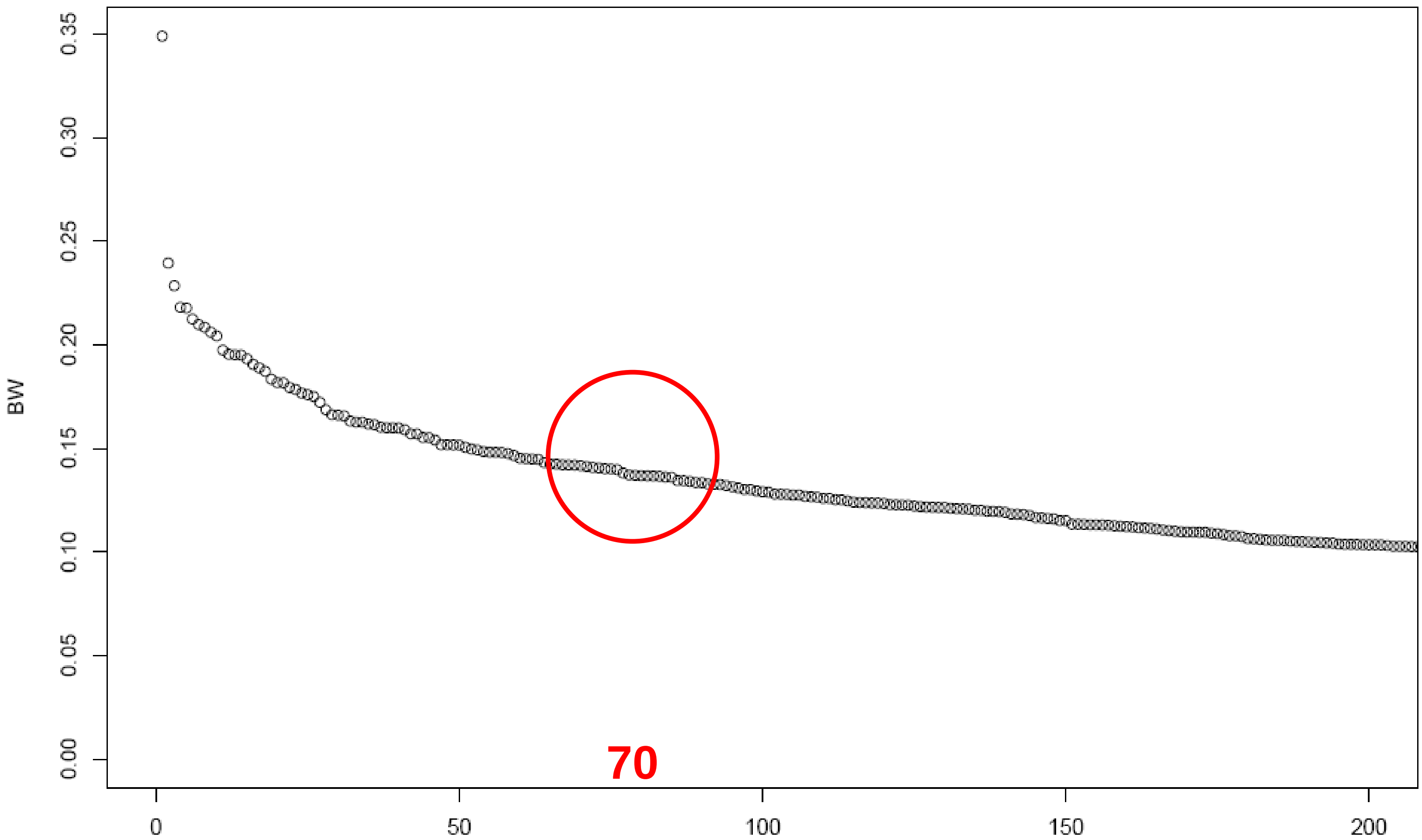
- van't Veer *et al*. Nature 2002
- The 78 sporadic lymph-node-negative breast cancer patients
  - 44 remained free of disease for an interval of at least 5 years (good prognosis group)
  - 34 had developed distant metastases within 5 years (poor prognosis group).
- Aim to predict good and poor prognostic patients through gene expression profiling

Breast cancer data (cont'd)

- A preliminary two-step gene selection process (from 24481 genes):
  - 4741 genes with the intensity ratio more than two-fold difference and the significance of regulation p-value < 0.01 in more than 3 patients
  - Apply a selection of genes based on the ratio of their between-group to within-group sums of squares

$$BW(m) = \frac{\sum_i \sum_c I(d_i = c)(\bar{y}_{cm} - \bar{y}_{.m})^2}{\sum_i \sum_c I(d_i = c)(y_{im} - \bar{y}_{cm})^2}$$

BW plot



Breast cancer data (cont'd)

- Using 70 selected gene expression ratios as observed surrogates, a finite mixture model was fitted.

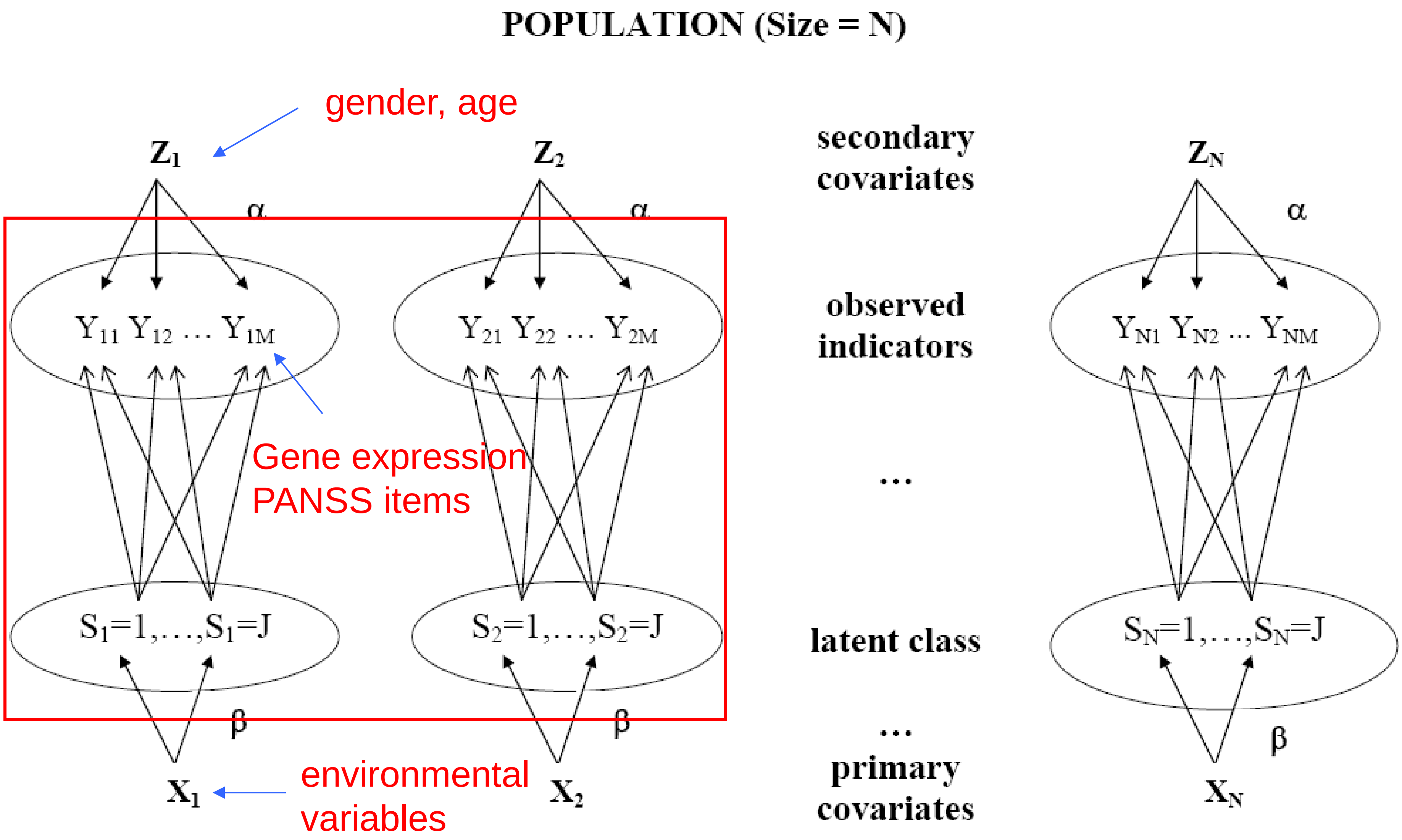
Schizophrenia data

- The data were collected from a series of projects for schizophrenia (Dr. Hai-Gwo Hwu).
- The analyzed data include
  - 169 acute patients of schizophrenia who were recruited within one week of index admission
  - 160 subsided state patients who were living with community and under family care
- Aim to
  - explore the subtypes of schizophrenia patients
  - predict patients' phases of chronicity

Schizophrenia data (cont'd)

- Schizophrenia symptoms were assessed by the PANSS:
  - 30 items and consists of three subscales: positive, negative and general psychopathology
  - Each item was originally rated on a 7-point scale (1=absent, 7=extreme), but we reduced the 7-point scale by merging the points that had the response percentages less than 10%

Models



POPULATION (Size = N)
gender, age
Z_1
Z_2
secondary covariates
Z_N
α
α
α
Y_{11} Y_{12} … Y_{1M}
Y_{21} Y_{22} … Y_{2M}
observed indicators
Y_{N1} Y_{N2} … Y_{NM}
Gene expression
PANSS items
…
$S_1=1,\ldots,S_1=J$
$S_2=1,\ldots,S_2=J$
latent class
$S_N=1,\ldots,S_N=J$
β
β
β
…
X_1
environmental variables
X_2
primary covariates
X_N

Introduction

- Finite mixture model is an analogy of cluster analysis.
- Finite mixture model classifies objects based on their responses to a set of surrogates.
- Measured surrogates are assumed independent of one another within any category of the underlying latent variable.
- Use k-means and hierarchical clustering methods with covariance among surrogates as the distance measure.

Finite mixture model

$$\mathbf{Y}_{\mathrm{i}} = (\mathrm{Y}_{i1}, \cdots, \mathrm{Y}_{iM})^T : \text{M observable surrogates}$$

$$f(y_{i1}, \ldots, y_{iM}) = \sum_{j=1}^{J} \left\{ \Pr(S_i = j) f(y_{i1}, \cdots, y_{iM} \mid S_i = j) \right\}$$

$$= \sum_{j=1}^{J} \left\{ \Pr(S_i = j) \prod_{m=1}^{M} f(y_{im} \mid S_i = j) \right\}$$

Latent Class Membership Estimation

Background

- The key is to estimate the latent class membership.
- Use K-means and hierarchical clustering methods to group the objects such that observed variables are statistically independent within latent classes.
- Use sample covariance matrix as the independence measurement.

Independence measurement

- Supposed $\tilde{\mathbf{Y}}_{\mathrm{i}} = (\mathrm{Y}_{\mathrm{i1}}, \mathrm{Y}_{\mathrm{i2}}, \cdots, \mathrm{Y}_{iM})$

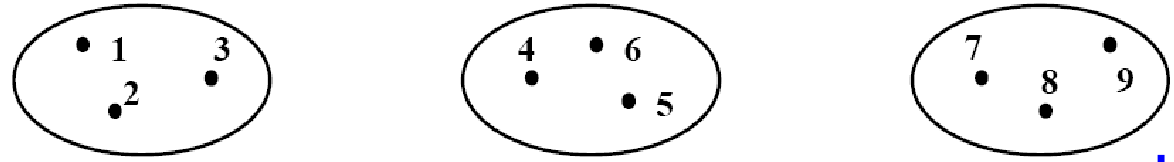
  Then,

$$\mathrm{Cov}(\tilde{\mathbf{Y}}_{\mathrm{i}}) = \begin{bmatrix} \mathrm{cov}(\mathrm{Y}_{\mathrm{i1}}, \mathrm{Y}_{\mathrm{i1}}) & \mathrm{cov}(\mathrm{Y}_{\mathrm{i1}}, \mathrm{Y}_{\mathrm{i2}}) & \cdots & \mathrm{cov}(\mathrm{Y}_{\mathrm{i1}}, \mathrm{Y}_{\mathrm{iM}}) \\ \mathrm{cov}(\mathrm{Y}_{\mathrm{i2}}, \mathrm{Y}_{\mathrm{i1}}) & \mathrm{cov}(\mathrm{Y}_{\mathrm{i2}}, \mathrm{Y}_{\mathrm{i2}}) & \cdots & \mathrm{cov}(\mathrm{Y}_{\mathrm{i2}}, \mathrm{Y}_{\mathrm{iM}}) \\ \vdots & \vdots & \ddots & \vdots \\ \mathrm{cov}(\mathrm{Y}_{\mathrm{iM}}, \mathrm{Y}_{\mathrm{i1}}) & \mathrm{cov}(\mathrm{Y}_{\mathrm{iM}}, \mathrm{Y}_{\mathrm{i2}}) & \cdots & \mathrm{cov}(\mathrm{Y}_{\mathrm{iM}}, \mathrm{Y}_{\mathrm{iM}}) \end{bmatrix}$$

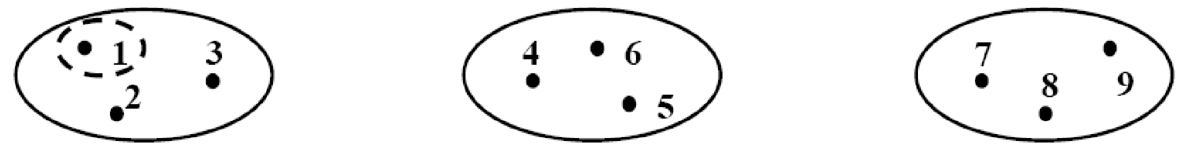
- $\mathrm{ACov} = mean(|\, entries \text{ in } non-diagonal-block \,|)$

K-means

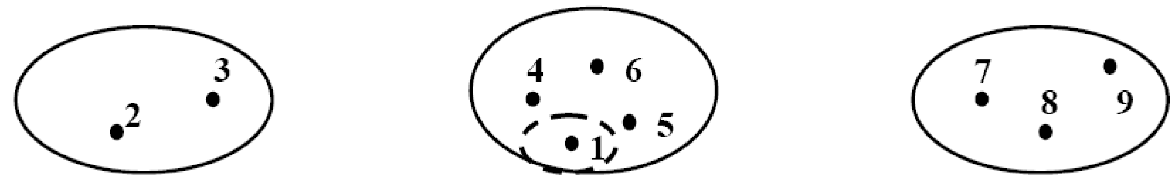
Initial classes



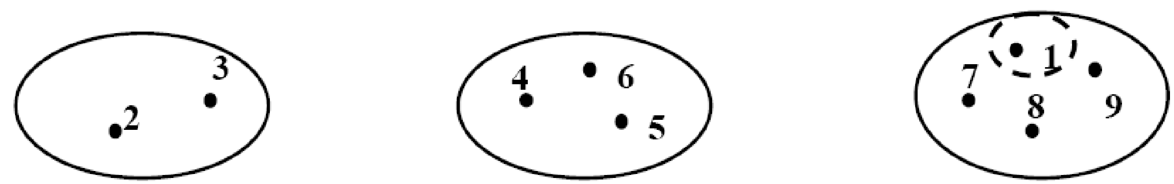
For object 1:



assign to class 1 $(3/9)\ ACov_1^{(1)} + (3/9)\ ACov_2^{(1)} + (3/9)\ ACov_3^{(1)} = LoI^{(1)}$



assign to class 2 $(2/9)\ ACov_1^{(2)} + (4/9)\ ACov_2^{(2)} + (3/9)\ ACov_3^{(2)} = LoI^{(2)}$

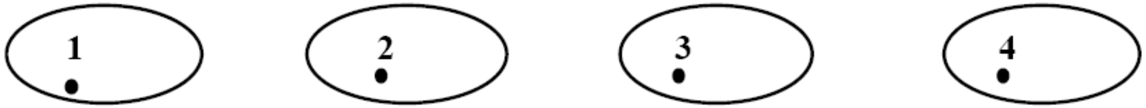


assign to class 3 $(2/9)\ ACov_1^{(3)} + (3/9)\ ACov_2^{(3)} + (4/9)\ ACov_3^{(3)} = LoI^{(3)}$

=> Assign object 1 to the class corresponding to minimum LoI

Agglomerative hierarchical

Initial



merge 1, 2 $\quad (2/4)\mathrm{ACov}_{(12)} + (1/4)\mathrm{ACov}_3 + (1/4)\mathrm{ACov}_4 = \mathrm{LoI}^{(12)}$

merge 1, 3 $\quad (2/4)\mathrm{ACov}_{(13)} + (1/4)\mathrm{ACov}_2 + (1/4)\mathrm{ACov}_4 = \mathrm{LoI}^{(13)}$

$\vdots \qquad \vdots \qquad \vdots \qquad \vdots \qquad \vdots$

merge 3, 4 $\quad (1/4)\mathrm{ACov}_1 + (1/4)\mathrm{ACov}_2 + (2/4)\mathrm{ACov}_{(34)} = \mathrm{LoI}^{(34)}$

=> Merge the pair of classes whose combination results in the minimum LoI

Divisive hierarchical

Preliminary class

•1 •2 •3 •4
•5 •6 •7 •8

Split by 2-means

•1 •2 •3 •4   •5 •6 •7 •8

Split class 1 by 2-means

•1 •2   •3 •4   •5 •6 •7 •8

$$(2/8)\ \mathrm{ACov}_{(1)_1} + (2/8)\ \mathrm{ACov}_{(1)_2} + (4/8)\ \mathrm{ACov}_2 = \mathrm{LoI}^{(1)}$$

Split class 2 by 2-means

•1 •2 •3 •4   •5 •6   •7 •8

$$(4/8)\ \mathrm{ACov}_1 + (2/8)\ \mathrm{ACov}_{(2)_1} + (2/8)\mathrm{ACov}_{(2)_2} = \mathrm{LoI}^{(2)}$$

=> Split the class whose division results in the minimum LoI

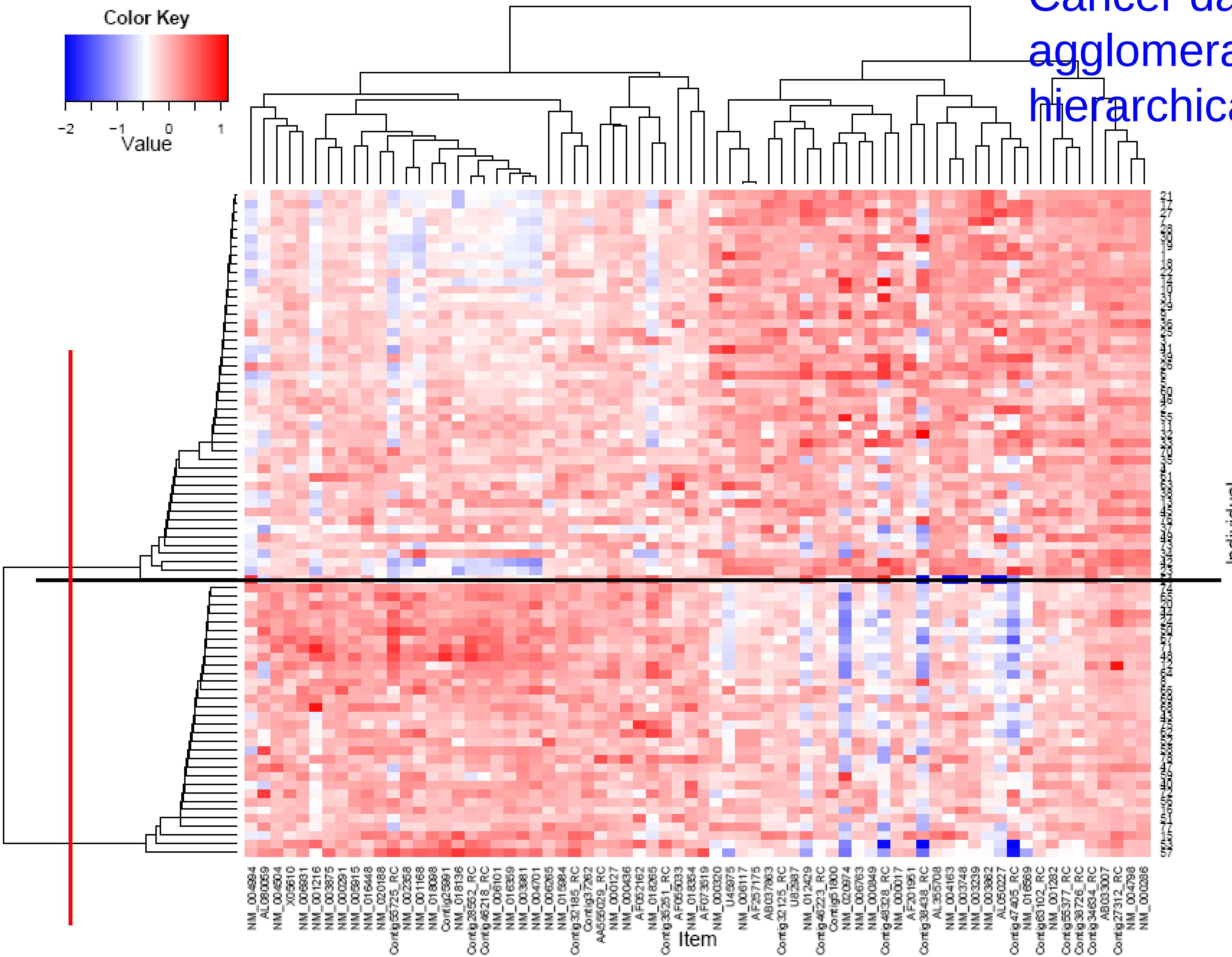
Classification using finite mixture models

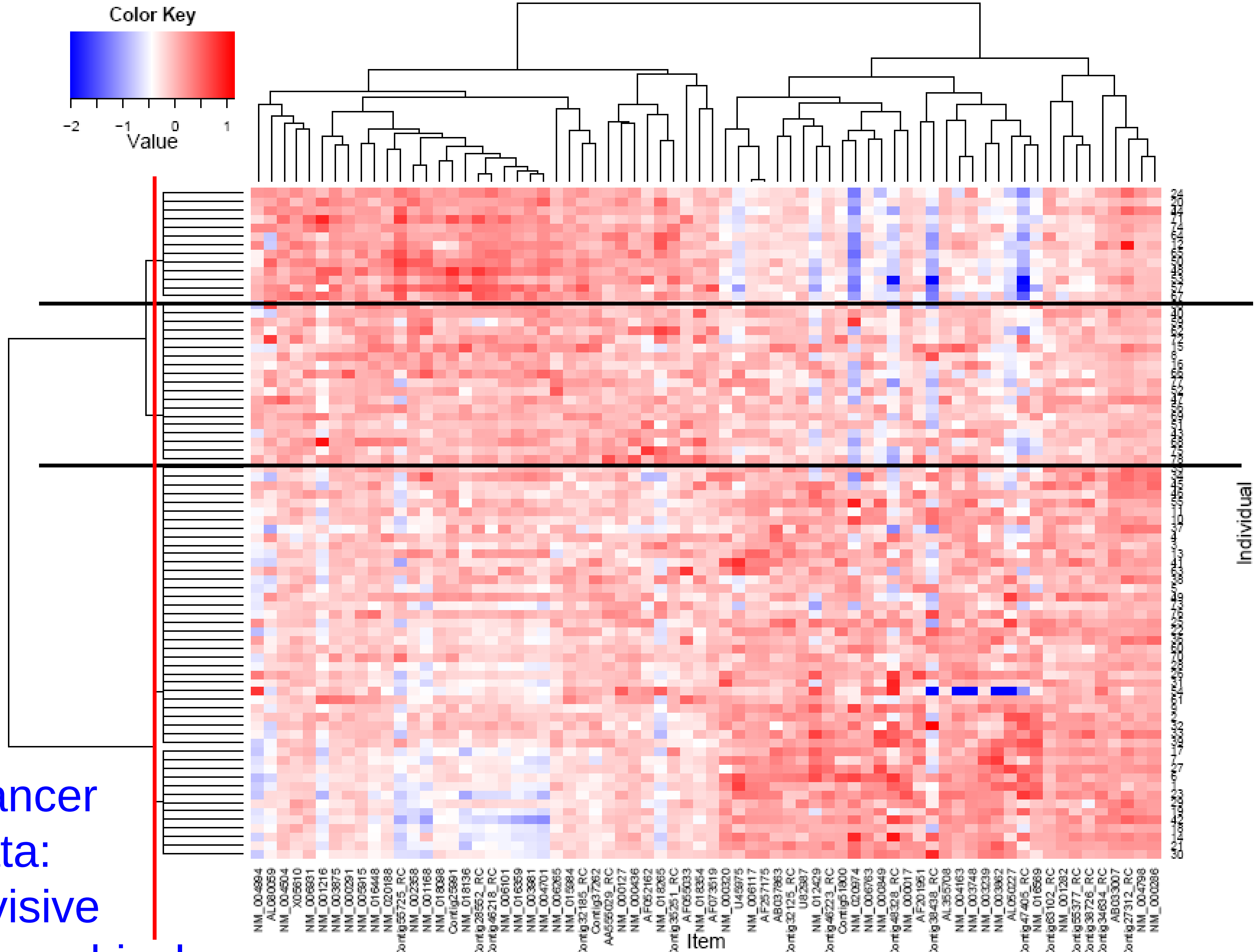
- For a new object $Y^* = (Y_1^*, \cdots, Y_M^*)$ with the disease status D^*

$$\Pr(D^* = c \mid Y^*) = \sum_{j=1}^{J} \left\{ \Pr(D^* = c \mid S^* = j, Y^*) \times \Pr(S^* = j \mid Y^*) \right\}$$

- Allocate Y^* to $D^*=c^*$ at which the maximum estimated posterior probability is reached

Cancer data: agglomerative hierarchical





Cancer data: divisive hierarchical

Leave-one-out cross-validation

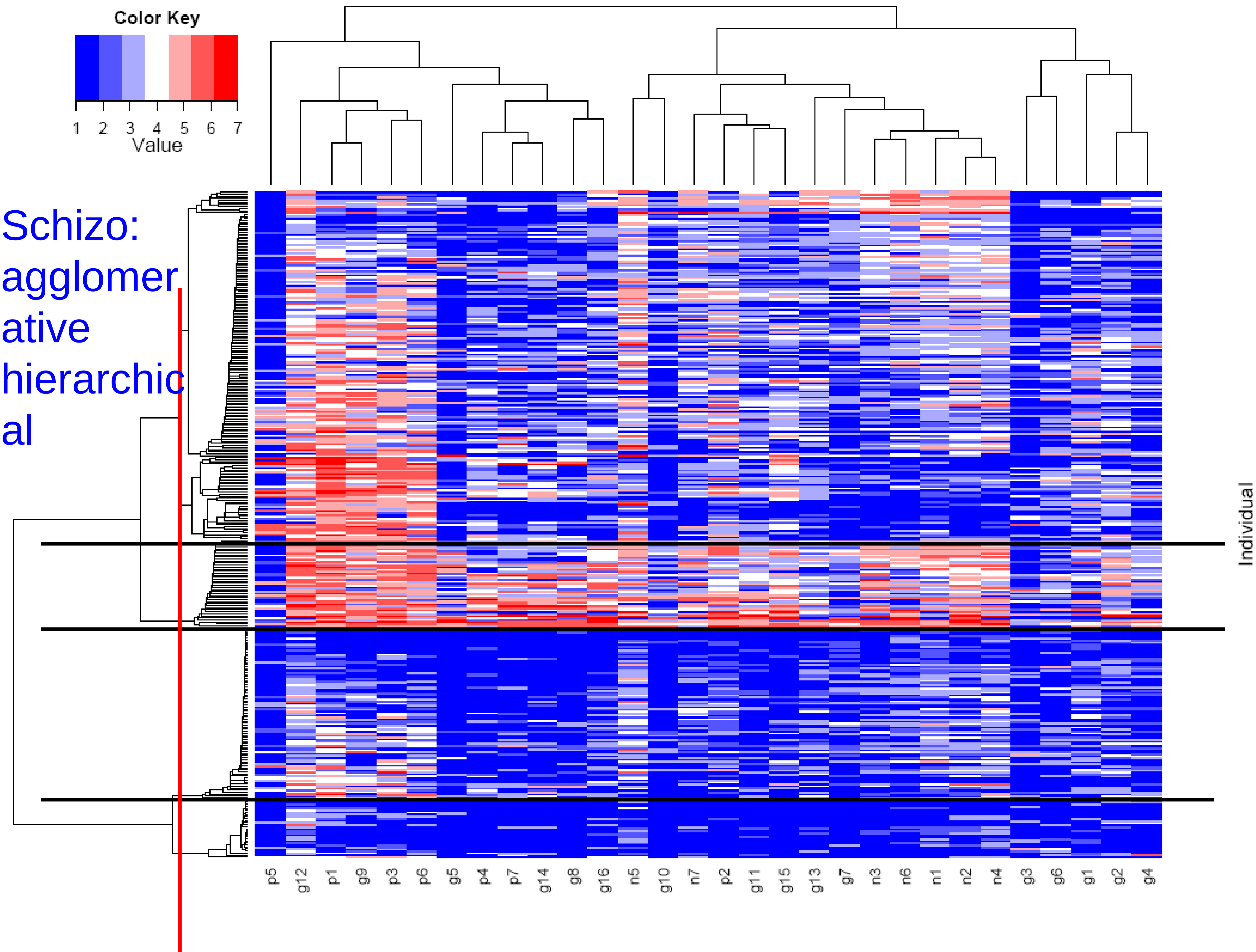
- Misclassification rates in predicting poor vs. good prognosis
  - k-means: 24.36%
  - agglomerative hierarchical: 26.92%
  - divisive hierarchical: 29.49%

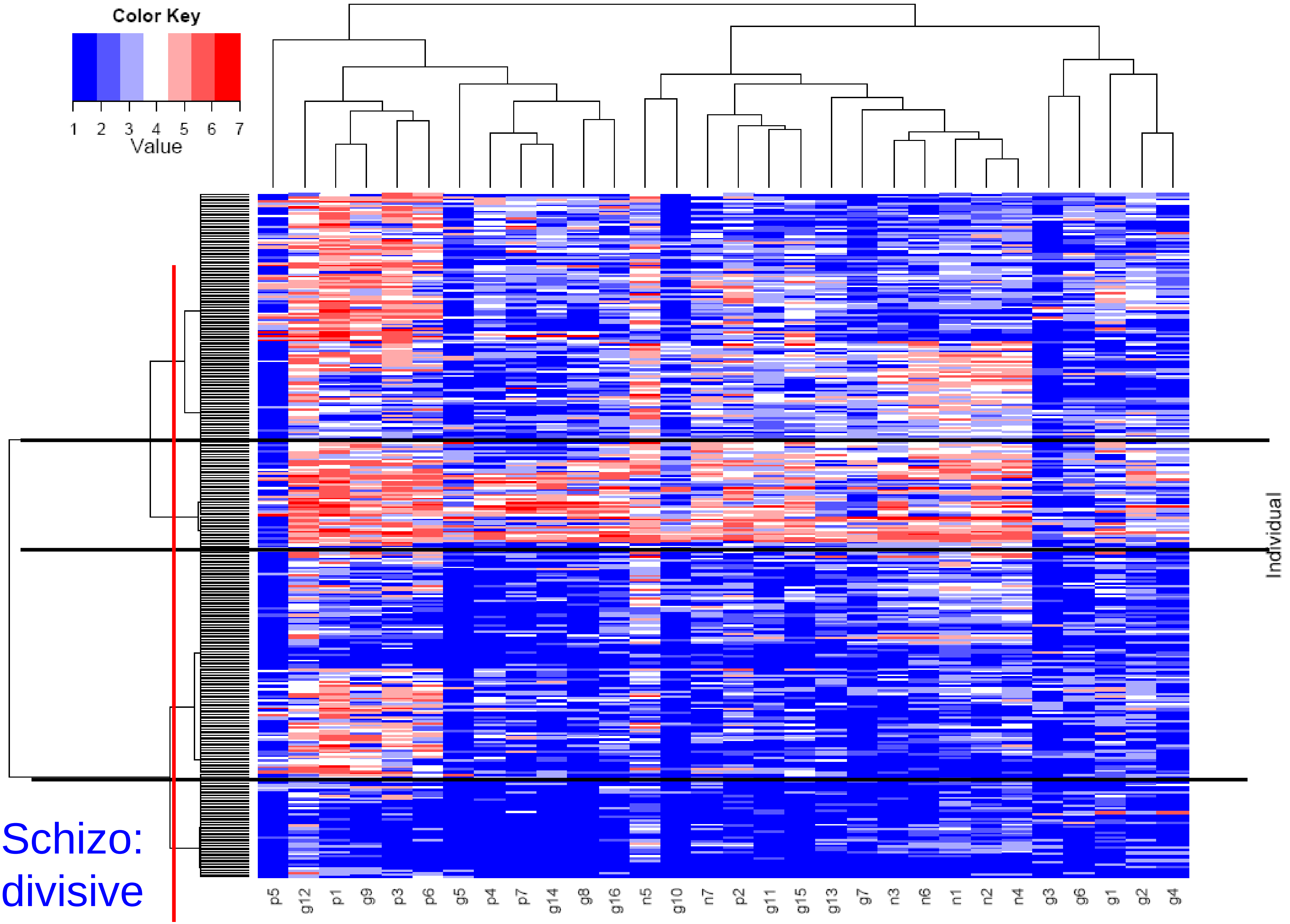
Additional independent test set

- Independent 19 young, lymph-node-negative breast cancer patients:
  - 12 poor prognosis
  - 7 good prognosis

No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
True	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1
KM	0	0	0	0	0	0	0	0	0	0	0	0	1	**0**	1	**0**	1	**0**	1
AH	0	0	0	**1**	0	0	0	0	0	0	0	**1**	1	1	1	1	1	**0**	1
DH	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	**0**	1	**0**	1

Schizo: agglomerative hierarchical





Schizo: divisive hierarchical

Leave-one-out cross-validation

- Misclassification rates in predicting acute vs. subsided schizophrenia
  - k-means: 23.10%
  - agglomerative hierarchical: 24.01%
  - divisive hierarchical: 28.27%