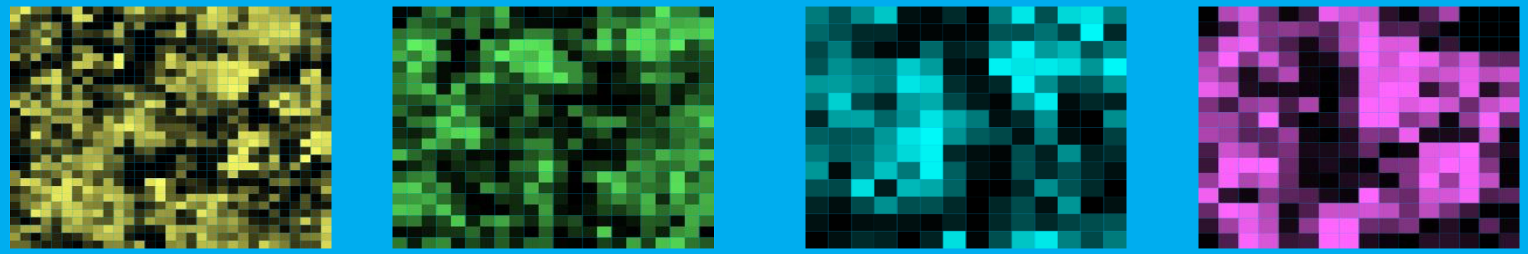
The Characteristic Direction: A Geometrical Approach to Differential Expression – Part Two



Network Analysis in Systems Biology

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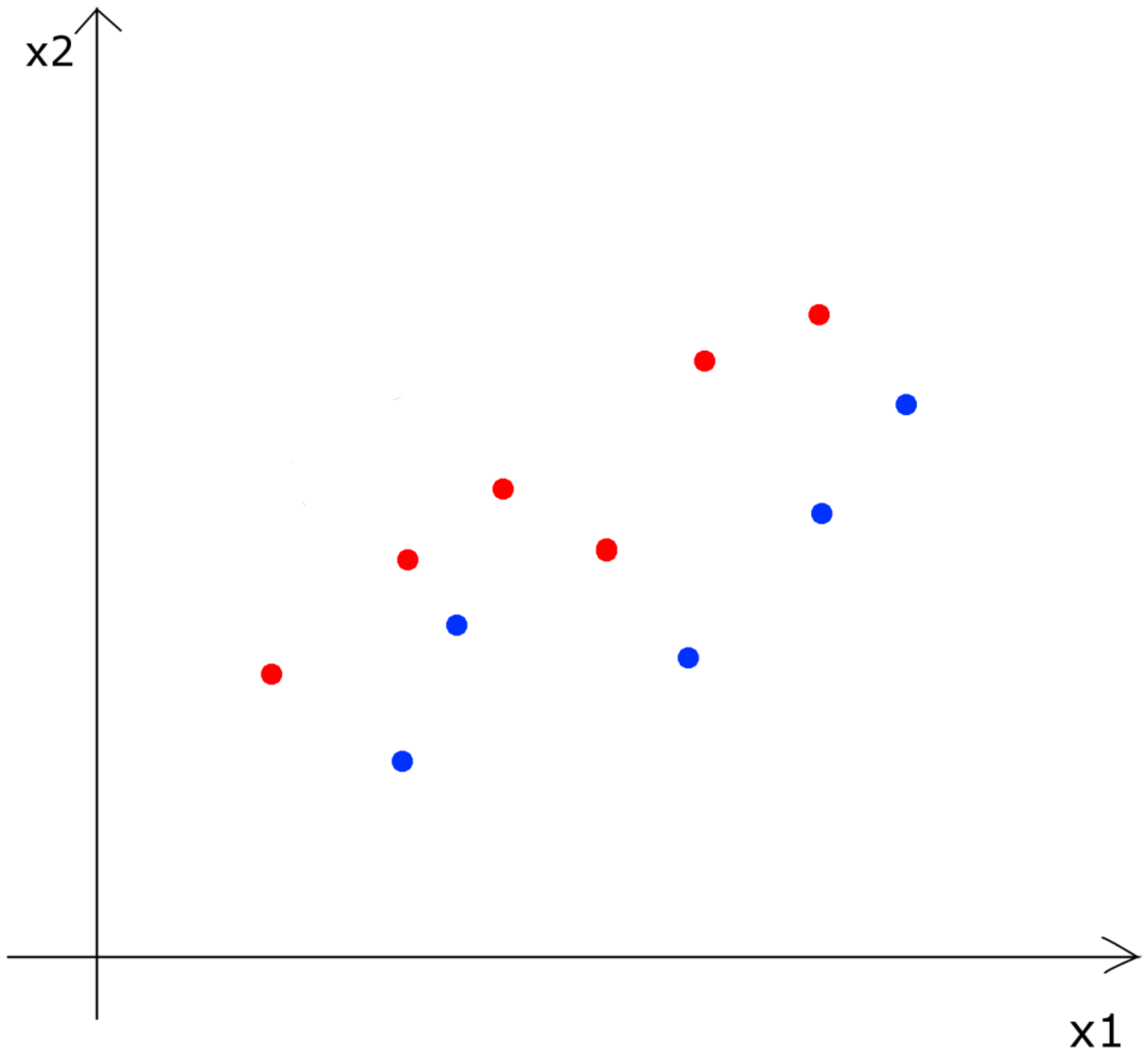
Linear Discriminant Analysis

- Bayes rule for the classification probability:

$$\Pr(G = k|X = x) = \frac{\overbrace{f_k(x)}^{\text{Class conditional density of X}}\overbrace{\pi_k}^{\text{Prior probability of class k}}}{\sum_{l=1}^{K} f_l(x)\pi_l}$$



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Class conditional density of X

Prior probability of class k

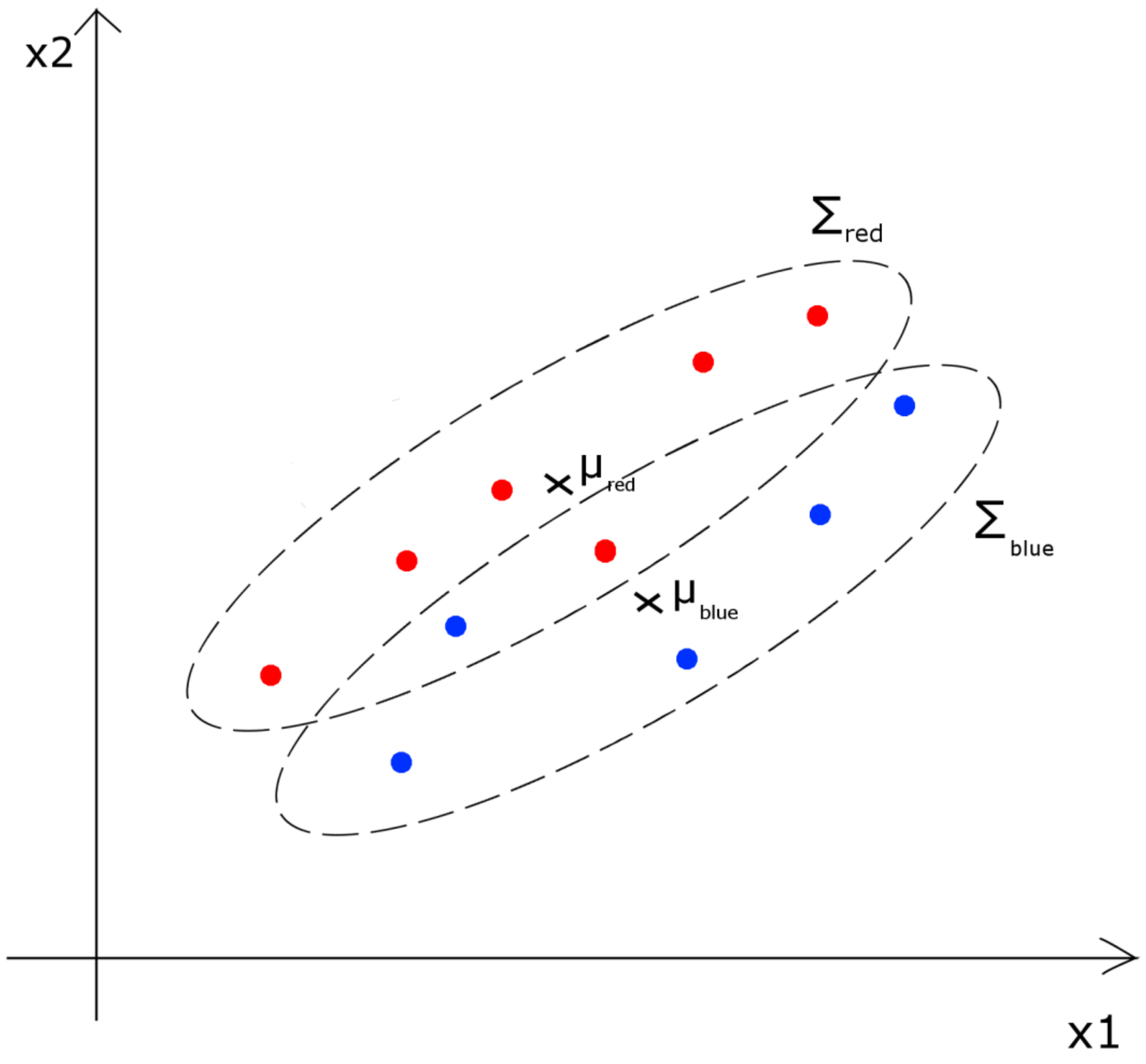
$$\Pr(G = k|X = x) = \frac{f_k(x)\pi_k}{\sum_{l=1}^{K} f_l(x)\pi_l}$$

- Model the class conditional density:

Class mean

Class covariance matrix

$$f_k(x) = \frac{1}{(2\pi)^{\frac{p}{2}}|\Sigma_k|^{\frac{1}{2}}} e^{-\frac{1}{2}(x-\mu_k)^T\Sigma_k^{-1}(x-\mu_k)}$$



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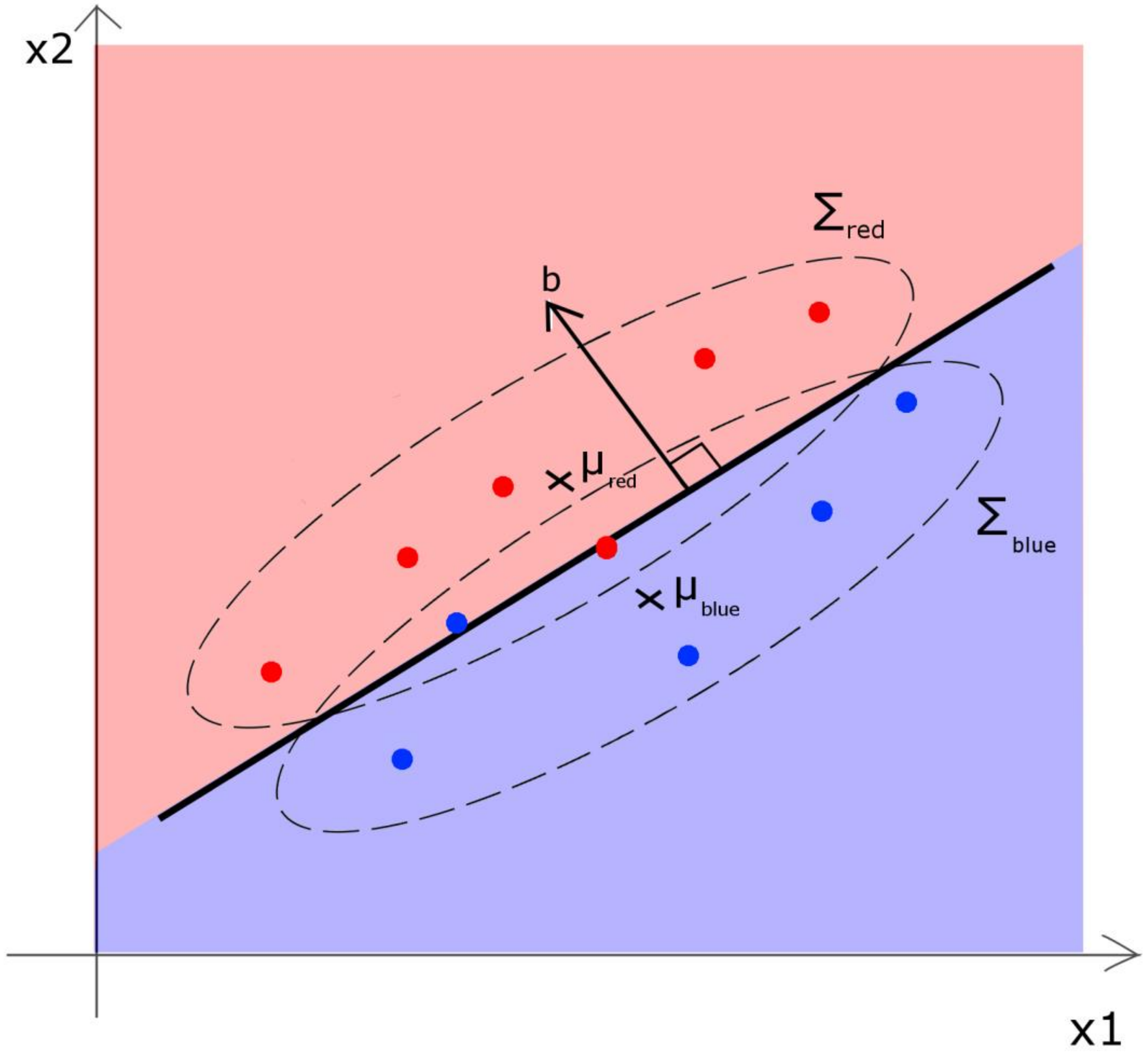
- Estimate classification probability:

$$log\frac{\Pr(G = k|X = x)}{\Pr(G = l|X = x)} = log\frac{\pi_k}{\pi_l} - \frac{1}{2}(\mu_k - \mu_l)^T\Sigma^{-1}(\mu_k - \mu_l) + x^T\Sigma^{-1}(\mu_k - \mu_l)$$

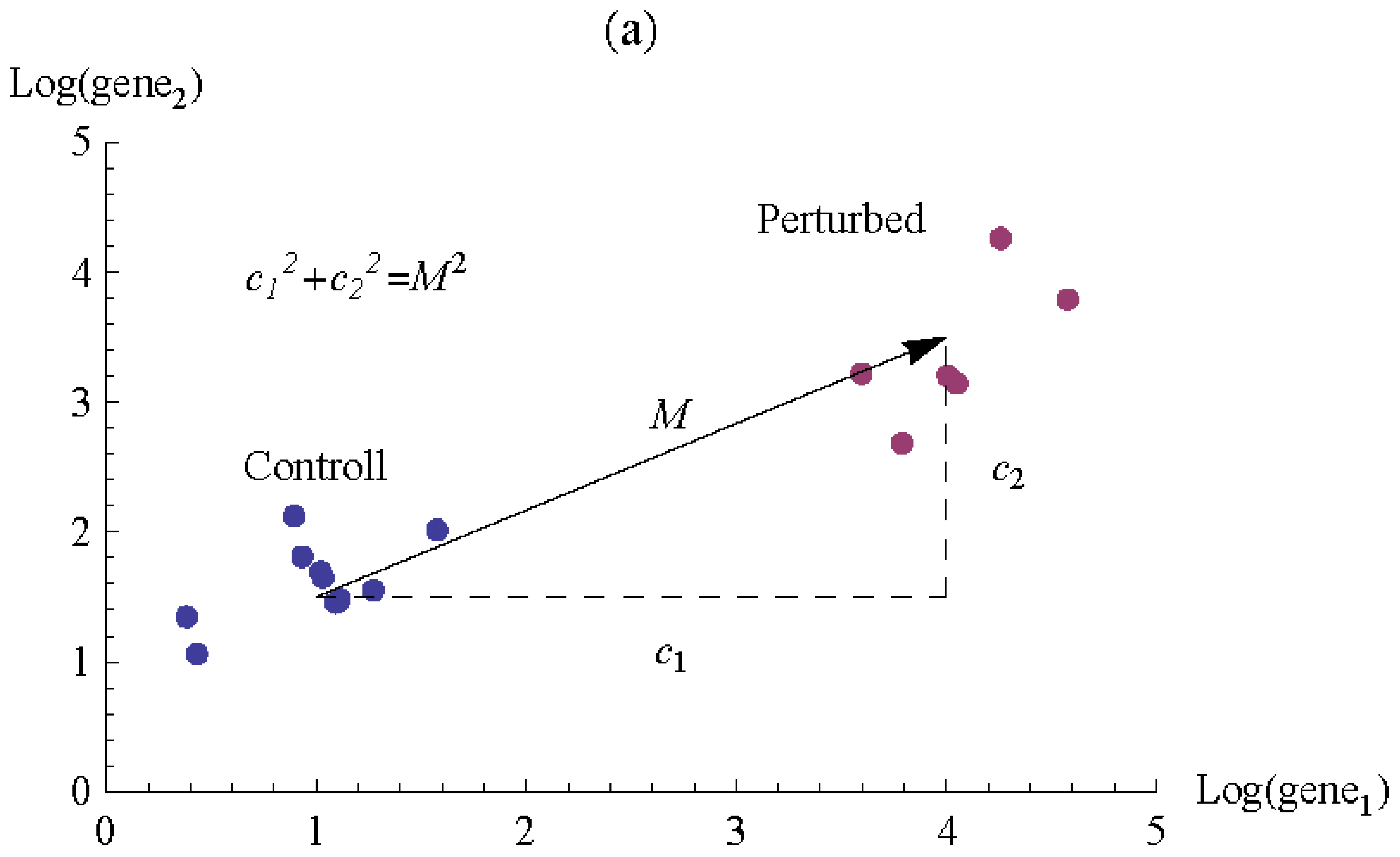
- The orientation of the separating hyper plane

  is given by: $b = \Sigma^{-1}(\mu_k - \mu_l)$



Interpreting the Characteristic Direction

- The square of the component corresponding to each gene is interpreted as a quantification of its significance in the total differential *M*



$$c_1^2 + c_1^2 + c_3^2 + \ldots c_n^2 = M^2$$

Use Shrinkage to Address the Curse of Dimensionality

- Our estimate of the covariance matrix is likely to be fraught with error because of the curse of dimensionality
- Attempt to smooth away the error while retaining the signal with shrinkage
- Shrink the covariance matrix to the scalar variance
  - $\hat{\Sigma}(\gamma) = \gamma\hat{\Sigma} + (1-\gamma)\sigma^2 I_p,$ with $\gamma \epsilon [0,1]$