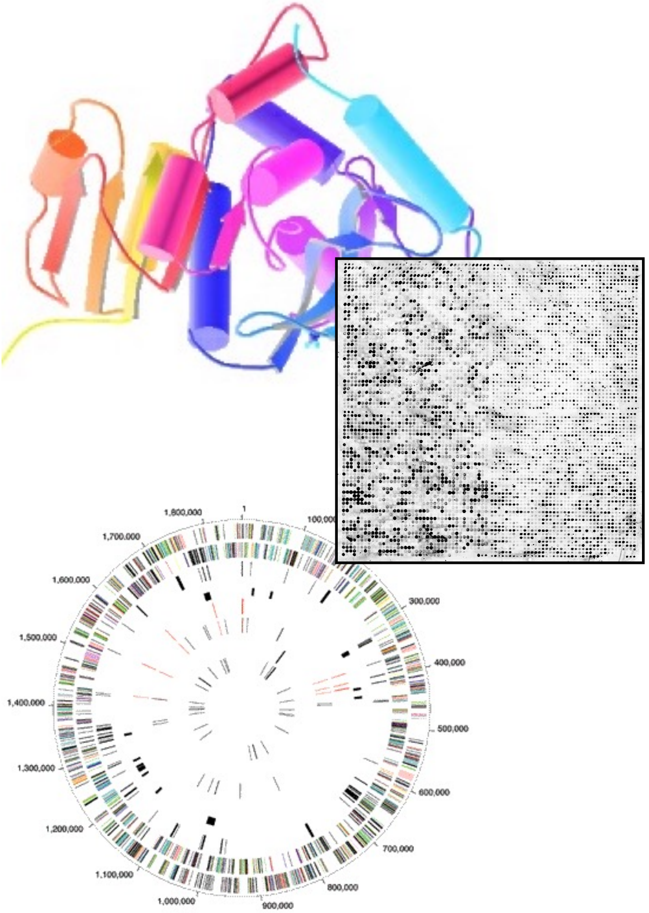
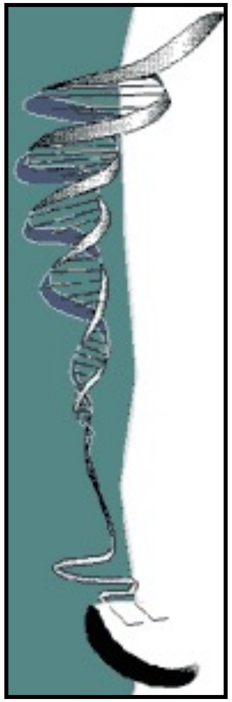
Biomed. Data Science:

Unsupervised Datamining C: SVD





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gersteinlab.org/courses/452

(last edit in spring ’21, pack #9c, final)

Dimensionality Reduction & Spectral Methods Outline & Papers

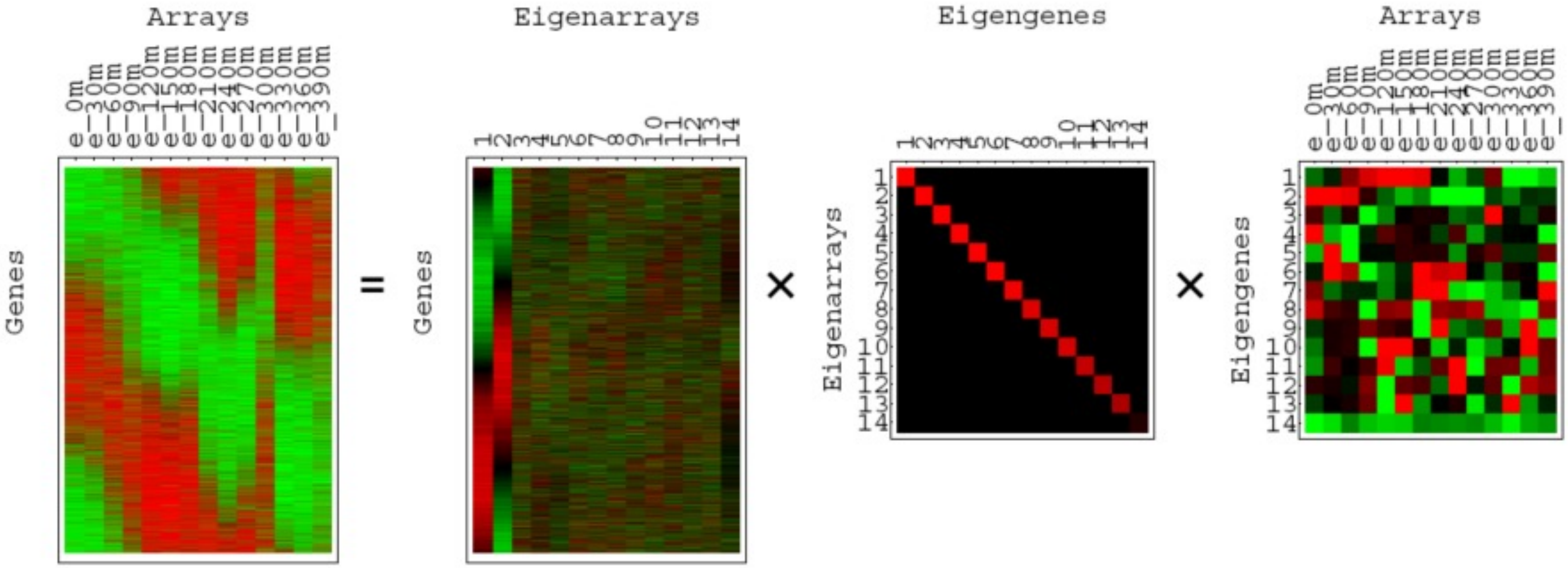
- PCA/SVD
- Extensions: biplot, RCA, CCA….
- Expression Clustering
- Application to
  - O Alter et al. (2000). "Singular value decomposition for genome-wide expression data processing and modeling." PNAS 97: 10101
  - Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between co-expression modules. BMC Systems Biology 2007, 1:54
  - Z Zhang et al. (2007) "Statistical analysis of the genomic distribution and correlation of regulatory elements in the ENCODE regions." Genome Res 17: 787
  - TA Gianoulis et al. (2009) "Quantifying environmental adaptation of metabolic pathways in metagenomics." PNAS 106: 1374.

Unsupervised Mining

SVD

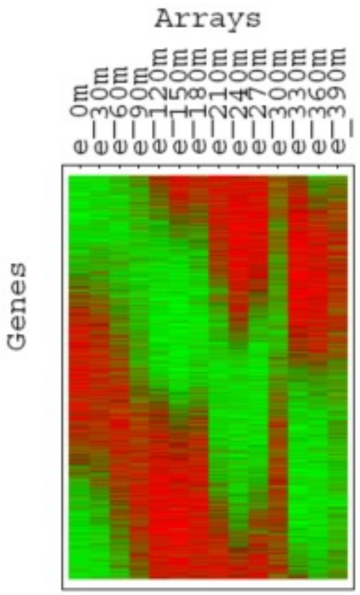
Puts together slides prepared by
Brandon Xia with images from
Alter et al. papers

SVD for microarray data (Alter et al, PNAS 2000)



$$A = USV^T$$

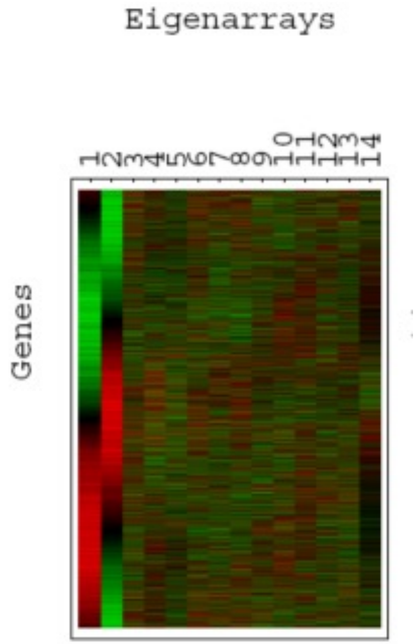
- A is any rectangular matrix (m ≥ n)
- Row space: vector subspace generated by the row vectors of A
- Column space: vector subspace generated by the column vectors of A
  - The dimension of the row & column space is the rank of the matrix A: r (≤ n)
- A is a linear transformation that maps vector x in row space into vector Ax in column space



$A = USV^T$

- U is an “orthogonal” matrix (m ≥ n)
- Column vectors of U form an orthonormal basis for the column space of A: $U^TU=I$

$$U = \begin{pmatrix} | & | & & | \\ \mathbf{u}_1 & \mathbf{u}_2 & \cdots & \mathbf{u}_n \\ | & | & & | \end{pmatrix}$$

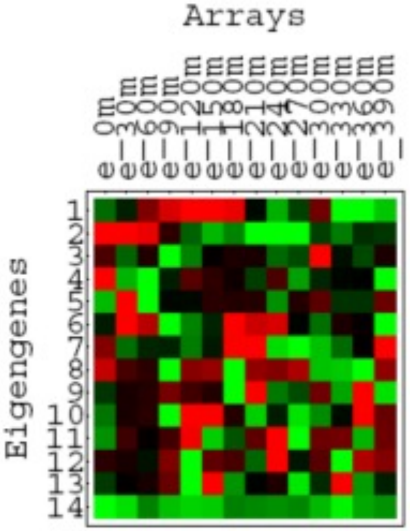


- $\boldsymbol{u}_1, \ldots, \boldsymbol{u}_n$ in U are eigenvectors of AA^T
  - $AA^T = USV^T VSU^T = US^2 U^T$
  - “Left singular vectors”

$$A = US\textcolor{red}{V}^T$$

- V is an orthogonal matrix (n by n)
- Column vectors of V form an orthonormal basis for the <span style="color:red">row space</span> of A: $V^TV=VV^T=I$

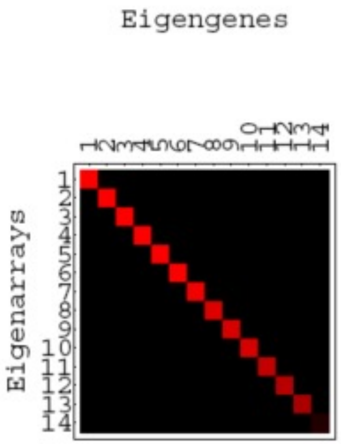
$$V = \begin{pmatrix} | & | & & | \\ \mathbf{v}_1 & \mathbf{v}_2 & \cdots & \mathbf{v}_n \\ | & | & & | \end{pmatrix}$$



- $\boldsymbol{v}_1, \ldots, \boldsymbol{v}_n$ in V are eigenvectors of A^TA
  - $A^TA = VSU^T USV^T = VS^2 V^T$
  - “Right singular vectors”

$$A = USV^T$$

- S is a diagonal matrix (n by n) of non-negative singular values
- Typically sorted from largest to smallest
- Singular values are the non-negative square root of corresponding eigenvalues of A^TA and AA^T



$$AV = US$$

- Means each $A\boldsymbol{v}_i = s_i\boldsymbol{u}_i$
- Remember A is a linear map from row space to column space
- Here, A maps an orthonormal basis $\{\boldsymbol{v}_i\}$ in row space into an orthonormal basis $\{\boldsymbol{u}_i\}$ in column space
- Each component of u_i is the projection of a row of the data matrix A onto the vector v_i

SVD as sum of rank-1 matrices

- $A = USV^T$
- $A = s_1 \boldsymbol{u}_1 \boldsymbol{v}_1^T + s_2 \boldsymbol{u}_2 \boldsymbol{v}_2^T + \ldots + s_n \boldsymbol{u}_n \boldsymbol{v}_n^T$
- $s_1 \geq s_2 \geq \ldots \geq s_n \geq 0$
- What is the rank-r matrix $\hat{A}$ that best approximates A ?
  - Minimize $\sum_{i=1}^{m} \sum_{j=1}^{n} \left(\hat{A}_{ij} - A_{ij} \right)^2$
- $\hat{A} = s_1 \boldsymbol{u}_1 \boldsymbol{v}_1^T + s_2 \boldsymbol{u}_2 \boldsymbol{v}_2^T + \ldots + s_r \boldsymbol{u}_r \boldsymbol{v}_r^T$
- Very useful for matrix approximation

an outer product (uv^T) giving a matrix rather than the scalar of the inner product

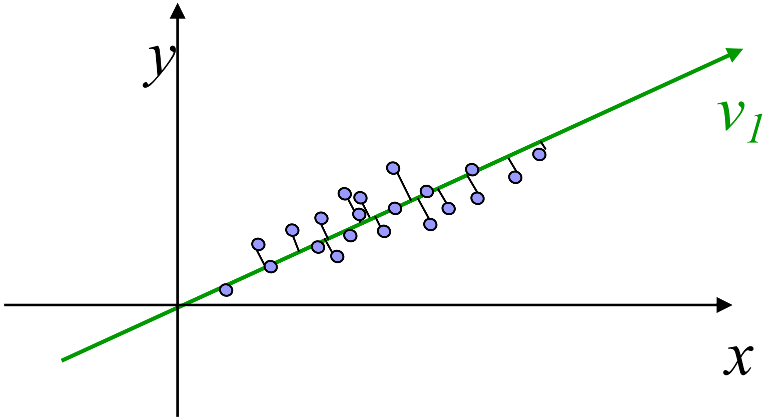
LSQ approx. If r=1, this amounts to a line fit.

Examples of (almost) rank-1 matrices

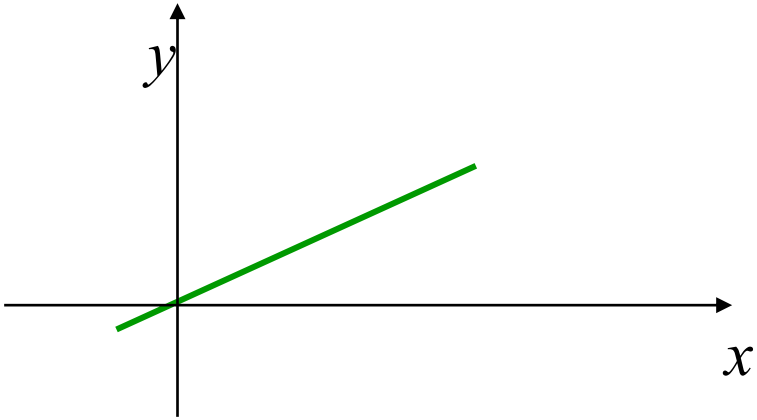
- Steady states with fluctuations $\begin{pmatrix} 101 & 103 & 102 \\ 302 & 300 & 301 \\ 203 & 204 & 203 \\ 401 & 402 & 404 \end{pmatrix}$
- Array artifacts? $\begin{pmatrix} 101 & 303 & 202 \\ 102 & 300 & 201 \\ 103 & 304 & 203 \\ 101 & 302 & 204 \end{pmatrix}$
- Signals?

$$\begin{pmatrix} 1 & 2 & -1 \\ 2 & 4 & -2 \\ -1 & -2 & 1 \\ 0 & 0 & 0 \end{pmatrix}$$

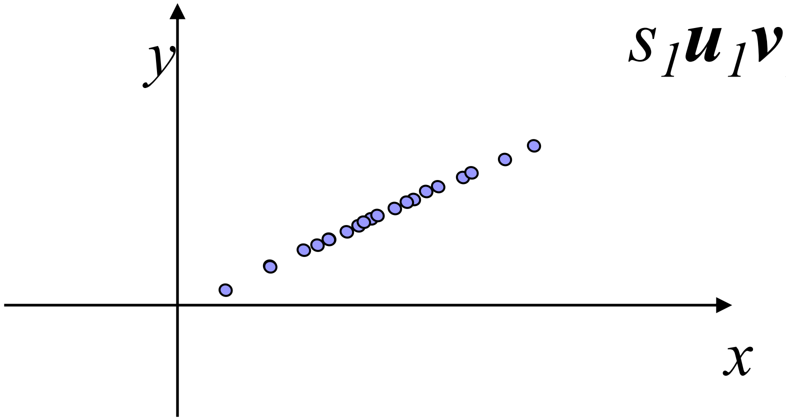
Geometry of SVD in row space



A



This line segment that goes through origin approximates the original data set

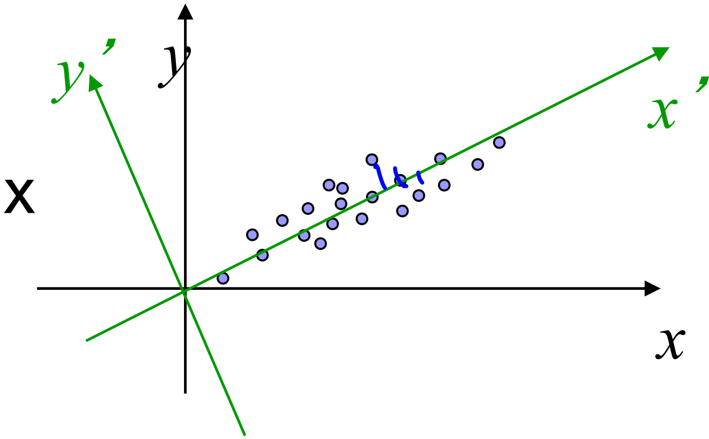


$s_1\boldsymbol{u}_1\boldsymbol{v}_1^T$

The projected data set approximates the original data set

Geometry of SVD in row space

- A as a collection of m row vectors (points) in the row space of A
- $s_1\boldsymbol{u}_1\boldsymbol{v}_1^T + s_2\boldsymbol{u}_2\boldsymbol{v}_2^T$ is the best rank-2 matrix approximation for A
- Geometrically: $\boldsymbol{v}_1$ and $\boldsymbol{v}_2$ are the directions of the best approximating rank-2 subspace that goes through origin
- $s_1\boldsymbol{u}_1$ and $s_2\boldsymbol{u}_2$ gives coordinates for row vectors in rank-2 subspace
- $\boldsymbol{v}_1$ and $\boldsymbol{v}_2$ gives coordinates for row space basis vectors in rank-2 subspace



$$\boxed{A\,\mathbf{v_i} \;=\; s_i\mathbf{u_i}}$$

$$\boxed{I\,\mathbf{v_i} \;=\; \mathbf{v_i}}$$

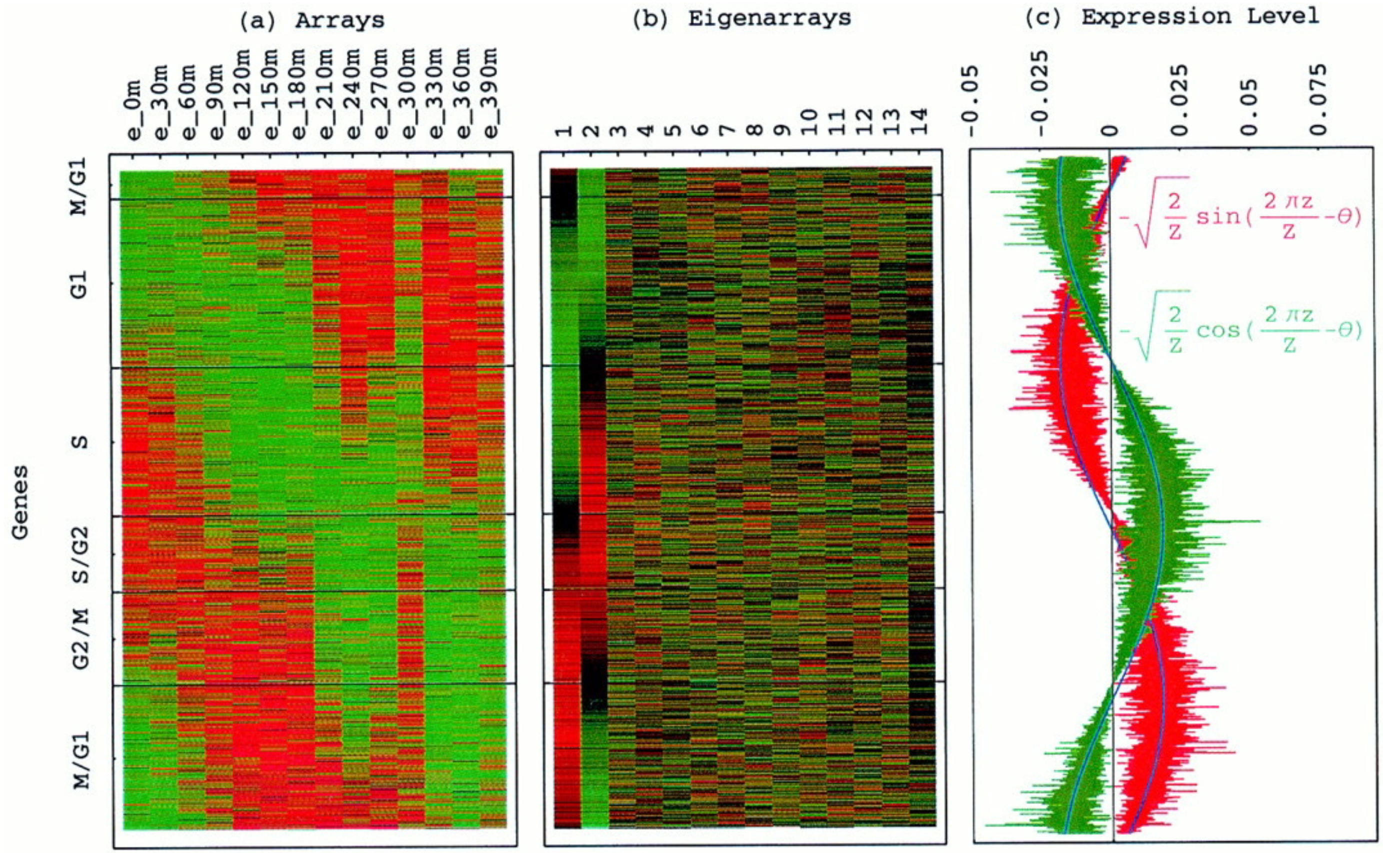
What about geometry of SVD in column space?

- $A = USV^T$
- $A^T = VSU^T$
- The column space of A becomes the row space of A^T
- The same as before, except that U and V are switched

Unsupervised Mining

Intuition on interpretation of SVD
in terms of genes and conditions

Genes sorted by correlation with top 2 eigengenes



Alter, Orly et al. (2000) Proc. Natl. Acad. Sci. USA 97, 10101-10106

Fig. 3. Genes sorted by relative correlation with $|\gamma_1\rangle_N$ and $|\gamma_2\rangle_N$ of normalized elutriation. (*a*) Normalized elutriation expression of the sorted 5,981 genes in the 14 arrays, showing traveling wave of expression. (*b*) Eigenarrays expression; the expression of $|\alpha_1\rangle_N$ and $|\alpha_2\rangle_N$, the eigenarrays corresponding to $|\gamma_1\rangle_N$ and $|\gamma_2\rangle_N$, displays the sorting. (*c*) Expression levels of $|\alpha_1\rangle_N$ (red) and $|\alpha_2\rangle_N$ (green) fit normalized sine and cosine functions of period $Z \equiv N - 1 = 5{,}980$ and phase $\theta \approx 2\pi/13$ (blue), respectively.

Normalized elutriation expression in the subspace associated with the cell cycle

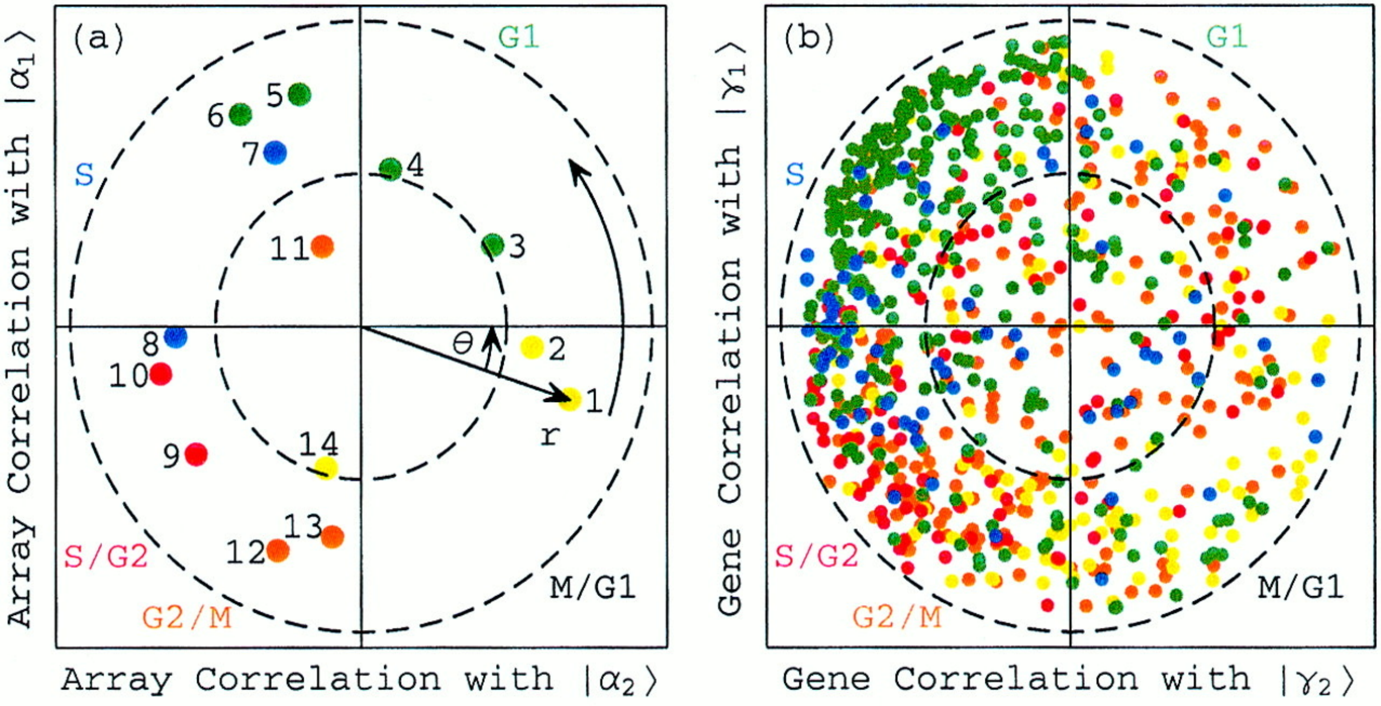


Fig. 2. Normalized elutriation expression in the subspace associated with the cell cycle. (*a*) Array correlation with $|\alpha_1\rangle_N$ along the *y*-axis vs. that with $|\alpha_2\rangle_N$ along the *x*-axis, color-coded according to the classification of the arrays into the five cell cycle stages, M/G_1 (yellow), G_1 (green), S (blue), S/G_2 (red), and G_2/M (orange). The dashed unit and half-unit circles outline 100% and 25% of overall normalized array expression in the $|\alpha_1\rangle_N$ and $|\alpha_2\rangle_N$ subspace. (*b*) Correlation of each gene with $|\gamma_1\rangle_N$ vs. that with $|\gamma_2\rangle_N$, for 784 cell cycle regulated genes, color-coded according to the classification by Spellman *et al.* (3).

Alter, Orly et al. (2000) Proc. Natl. Acad. Sci. USA 97, 10101-10106

PNAS