Example data sets – already preprocessed

- Yeast cell-cycle data
  ~679 genes (exhibiting periodic behavior)
  15 time points – cdc time course
  no missing entries
  normalized (to green) log-ratios, from spotted arrays
  regular (15) and row-standardized columns (only first 12)
  Spellman et al. (1998)

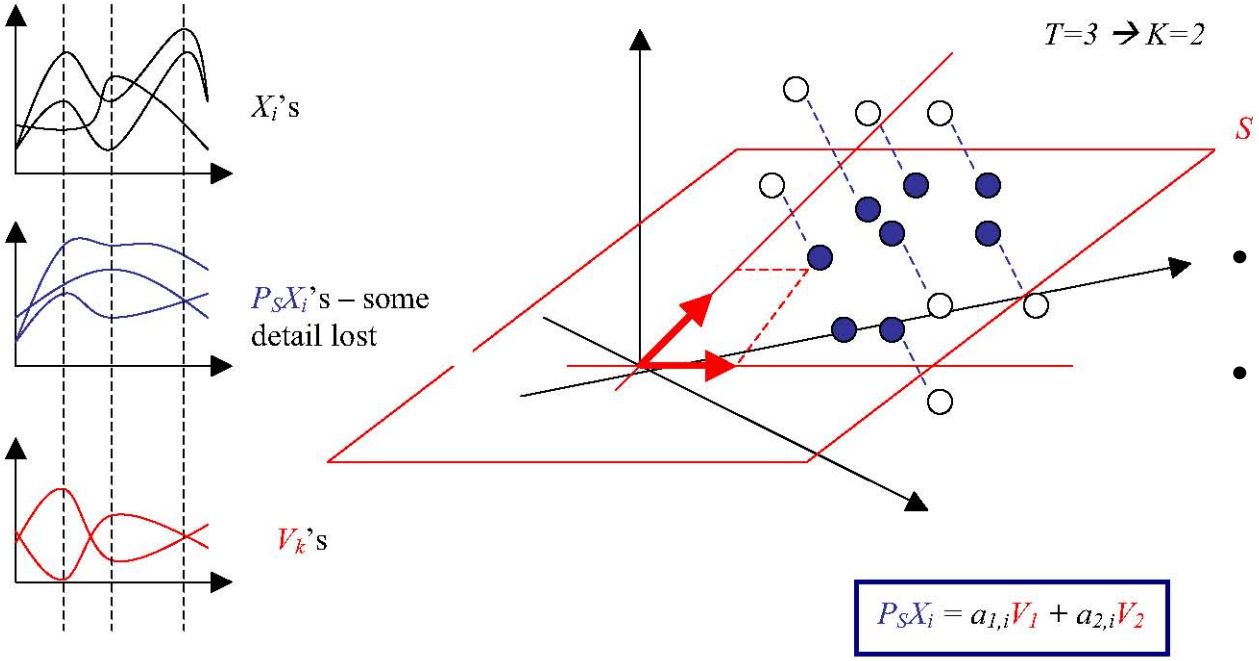
- Mouse tissues data
  ~459 genes (present in tissues under consideration, sequence info available)
  25 tissues
  no missing entries.
  logs of signals, normalized to overall average, from affy.
  regular and row-standardized columns
  Su et al. (2002)

Principal Components (PCA or equivalently Singular Value Decomposition)

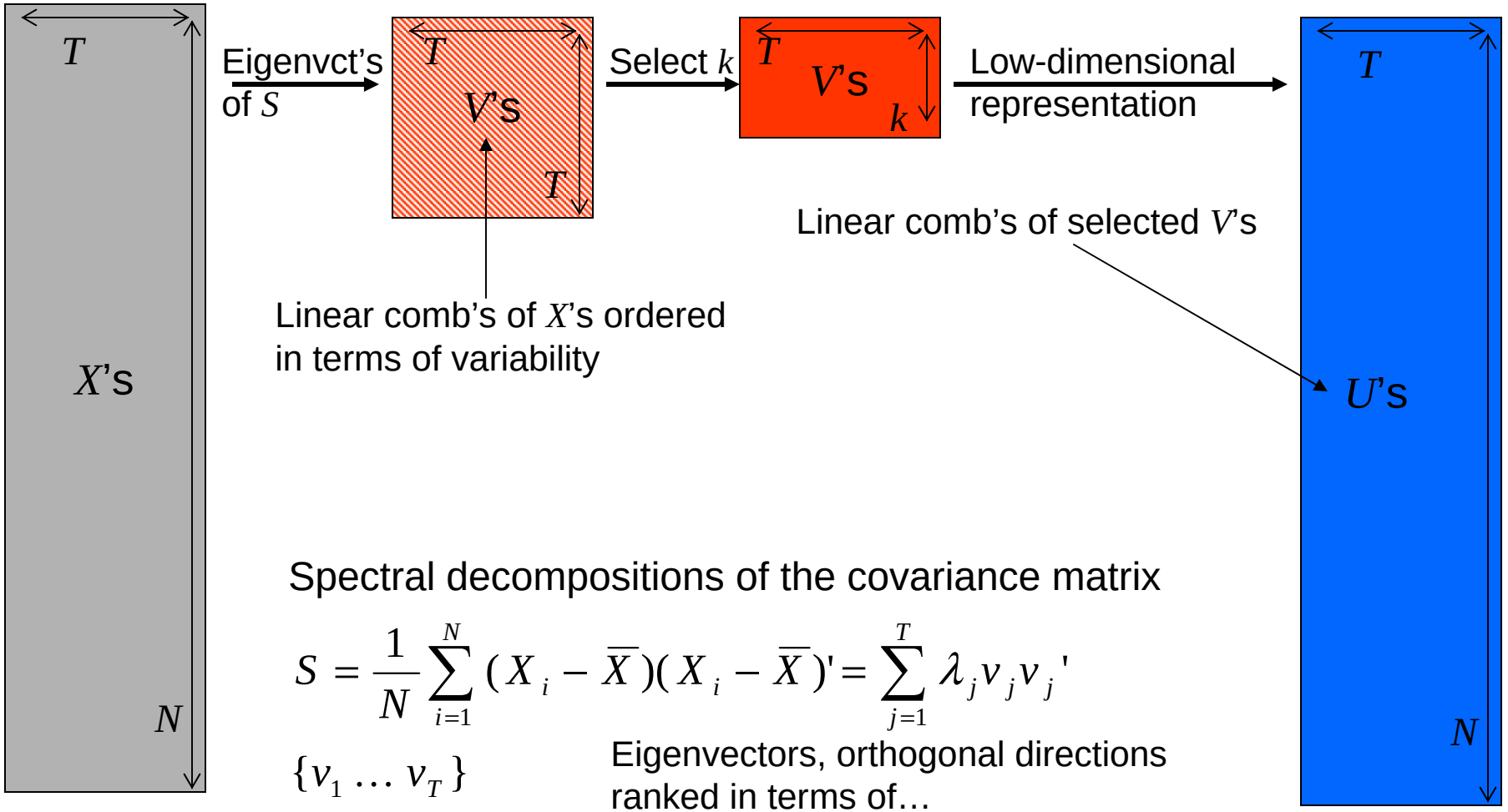
N points in R^T (N = # of genes, T = # of conditions)

based on the variability of the data cloud:

- Extract a few basic expression patterns (find a subspace).
- Give a low-dimensional reconstruction of the gene expression profiles (project the points)



- As a "structural summary" of the data
- As a "cleaning" step prior to further analyses



Spectral decompositions of the covariance matrix

$$S = \frac{1}{N}\sum_{i=1}^{N}(X_i - \overline{X})(X_i - \overline{X})' = \sum_{j=1}^{T}\lambda_j v_j v_j'$$

$\{v_1 \dots v_T\}$ Eigenvectors, orthogonal directions ranked in terms of…

$\lambda_1 \geq \lambda_2 \dots \geq \lambda_T$ Eigenvalues, variability

$$a_{1,i} = W_{i,1} = v_1' X_i \quad \dots \quad a_{T,i} = W_{i,T} = v_T' X_i$$

$$S = Span(v_1 \dots v_k)$$

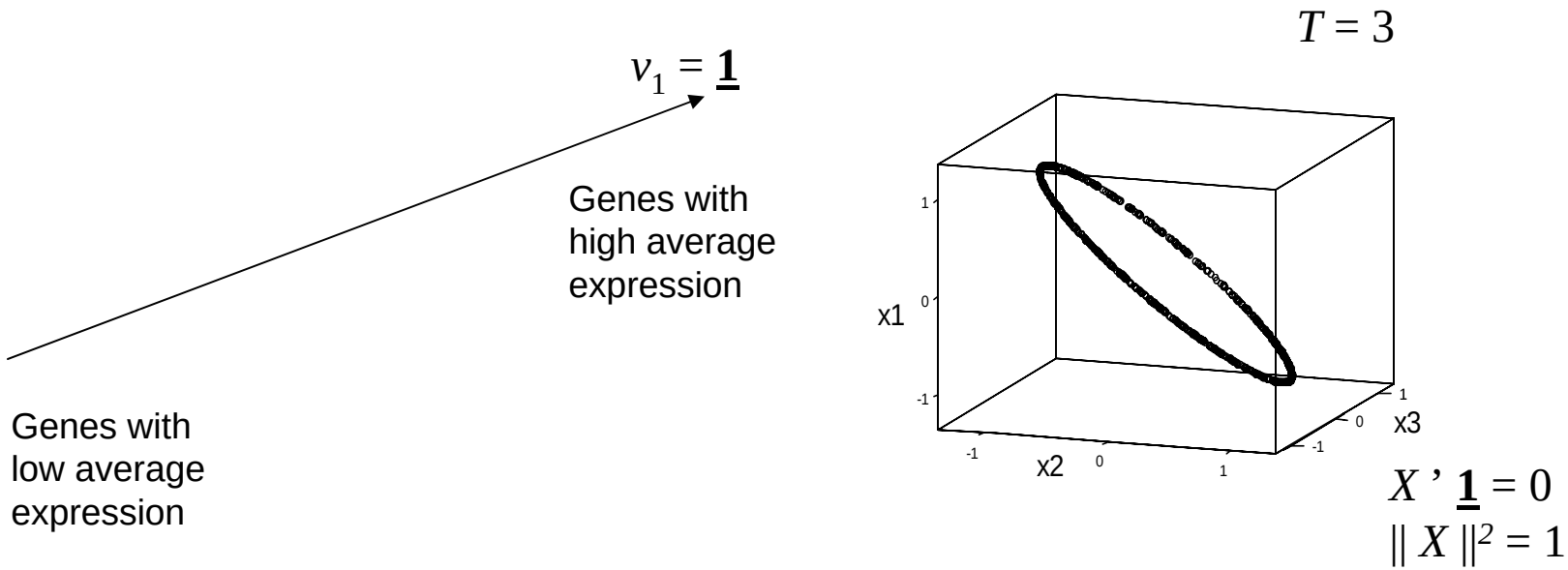
$$P_S X_i = U_i = W_{i,1} v_1 + \dots + W_{i,k} v_k$$

k-dimensional projection preserving most of the variability structure of the data cloud.

For both data sets, row (gene) **centering and standardization**:

• eliminate average expression and variation magnitude effects

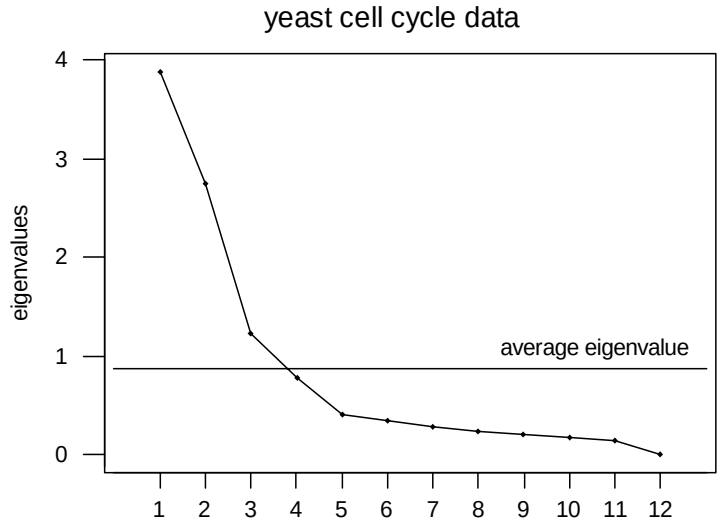
• restrict analysis to “pure shapes” of gene expression profiles.



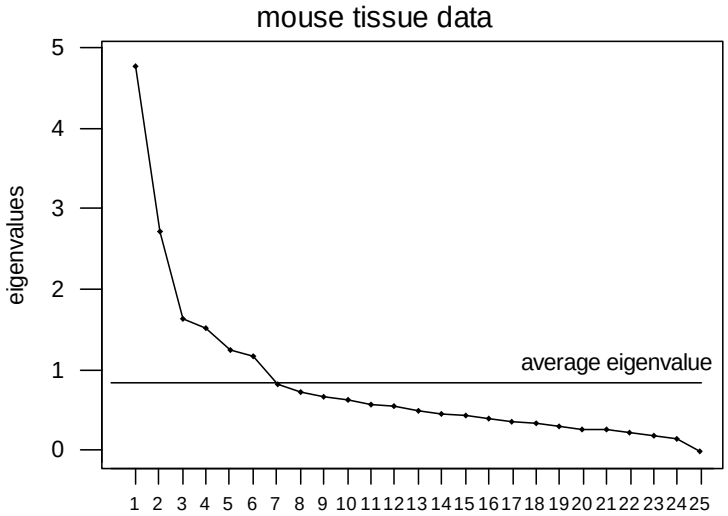
Before: cloud variability dominated by average expression magnitude

After: we have “created” a shape; points are on a (T-1)-hyperball surface

How complex is the data? (dimension)



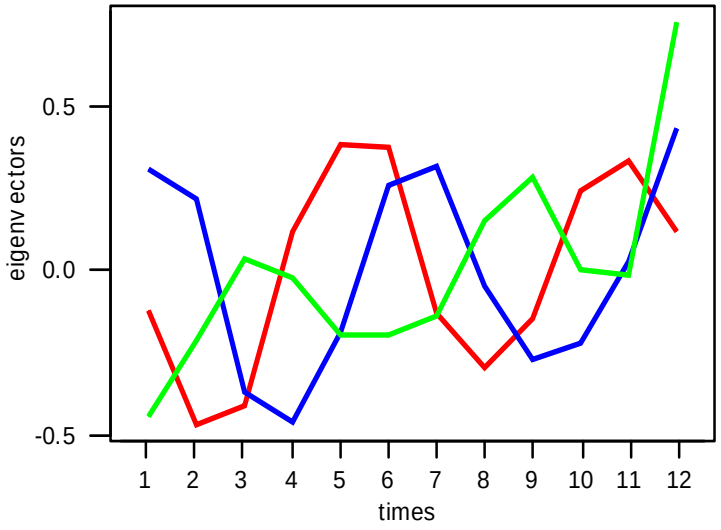
PC(1,2) ~ 63% ; PC(1,2,3) ~74%



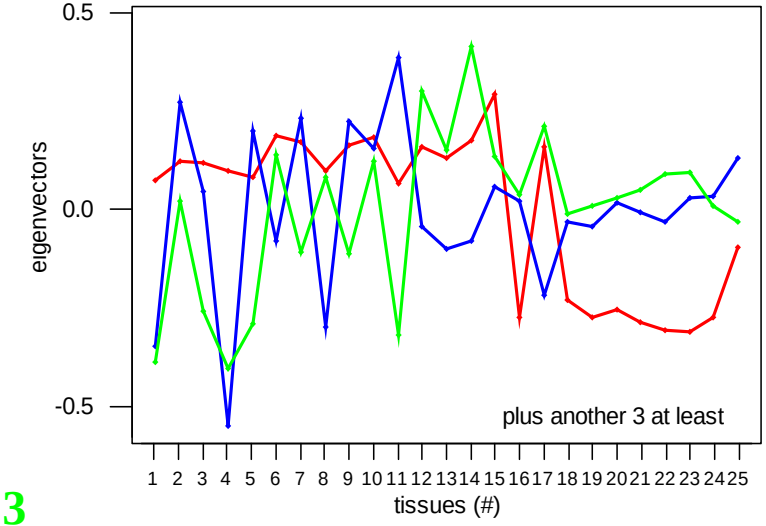
PC(1,2,3) ~ 47% ; PC(1,2,3,4,5,6) ~62%

(the V's)

Basic patterns

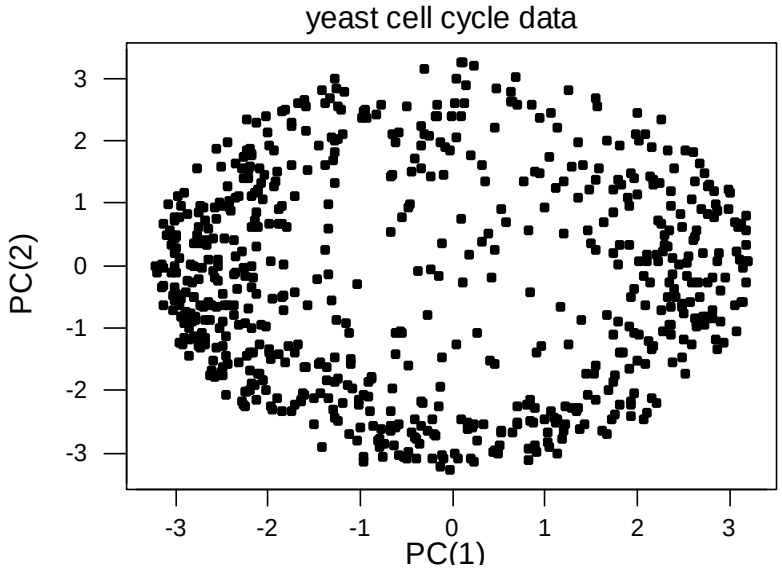


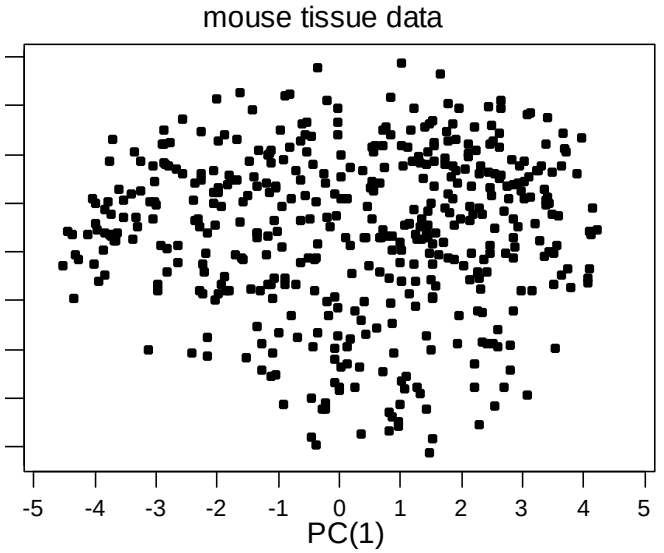
1 2 3



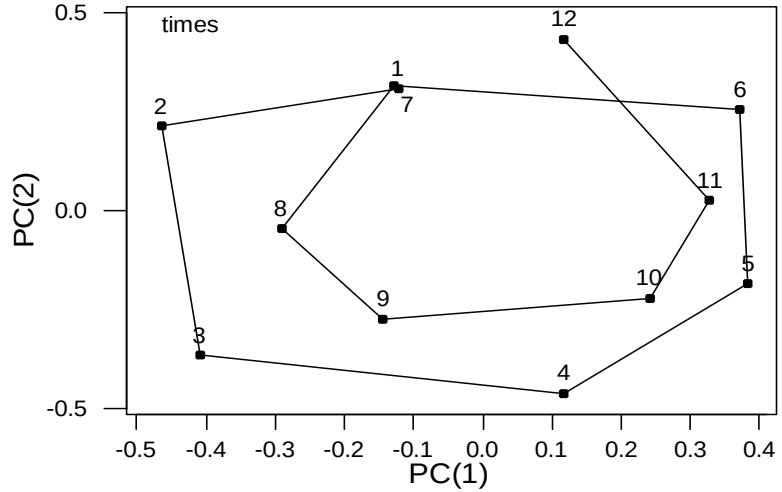
Low dimensional representations (visualization)

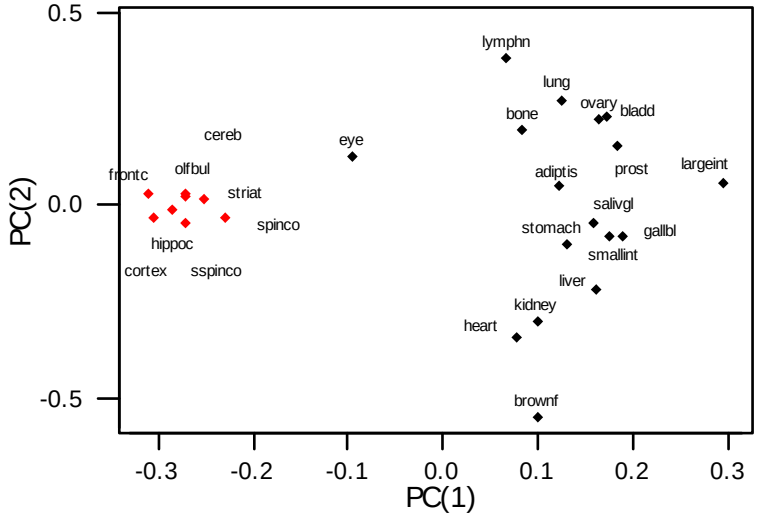
(the W's)





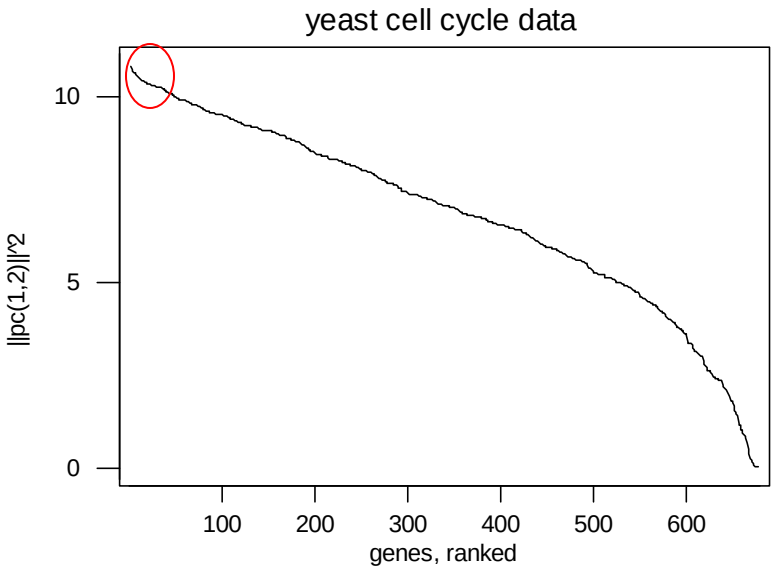
(the V's)

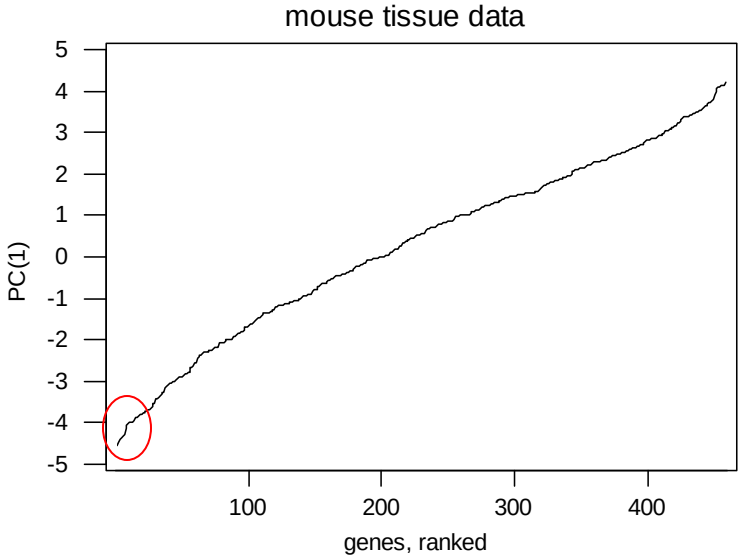




Identifying genes that "drive" patterns (ranking on projections)

(functions of the W's)





Genes closest to "pure" cycling behavior?

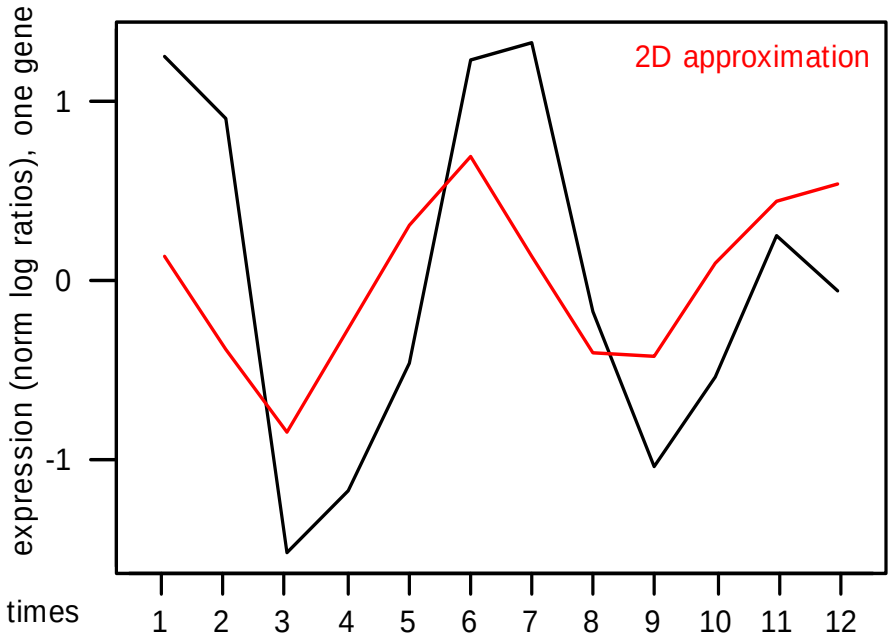
YLR190W **top ORFs**
YOR391C
YKR037C
YML058W
YHR005C
YDR191W
YKL185W
YNL058C
YGR042W
YLR326W …

Genes relevant to brain&spine?

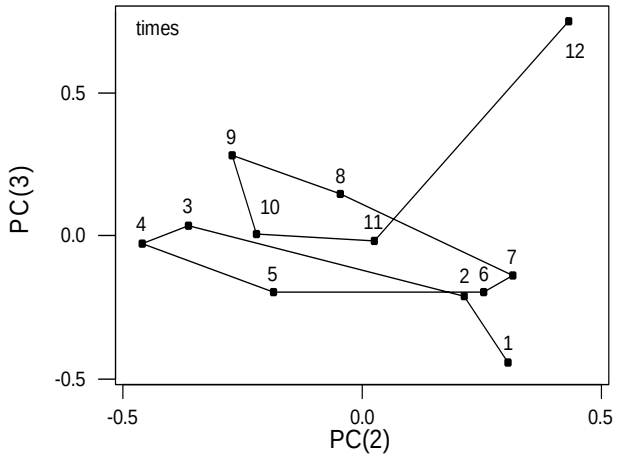
NM_013670 **top RefSeqs**
NM_019634
NM_019675
NM_053076
NM_020012
NM_053076
NM_024287
NM_018794
NM_019999
NM_023429 …

Principal components for reducing noise and artifacts

(the X's and U's, one instance)



(the V's)



Yeast cell cycle data:
emiliorate dampening in amplitude, and trend…

- dis-synchronization
- expression reaction to synchronization drugs, "crowd" effects?