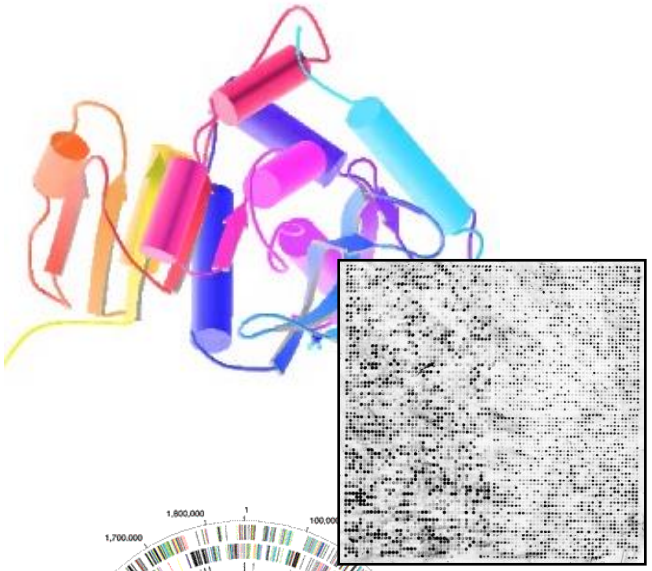
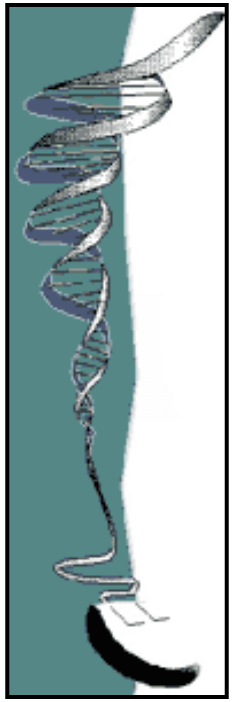
Biomed. Data Science:

Unsupervised Datamining -- General Clustering





Mark Gerstein, Yale University

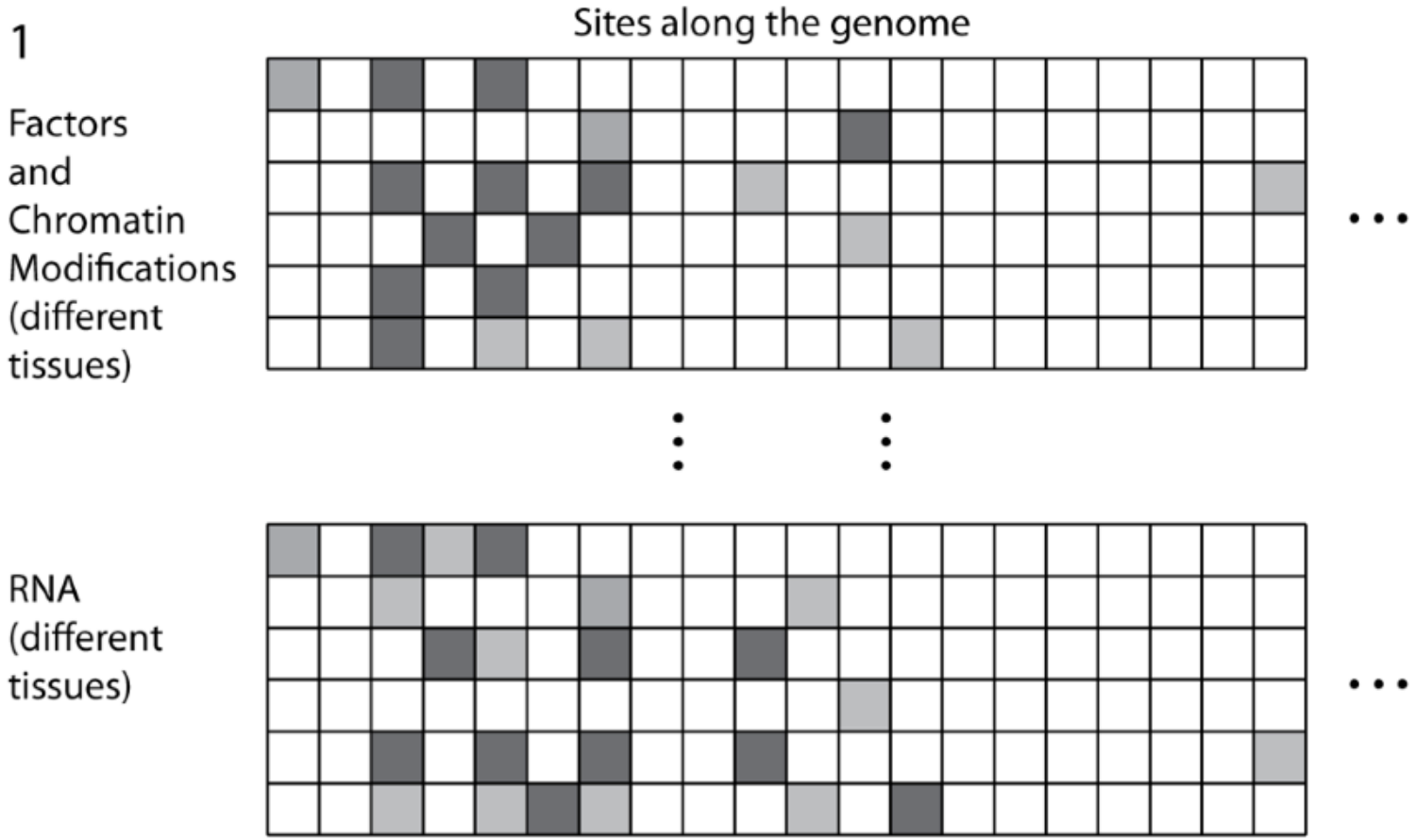
gersteinlab.org/courses/452

(Last edit in spring ’22, pack 22m9a, final; similar to last year’s M9a,
with one slide on agglomerative clustering removed & some other small edits.)

Unsupervised Mining

Columns & Rows
of the Data Matrix

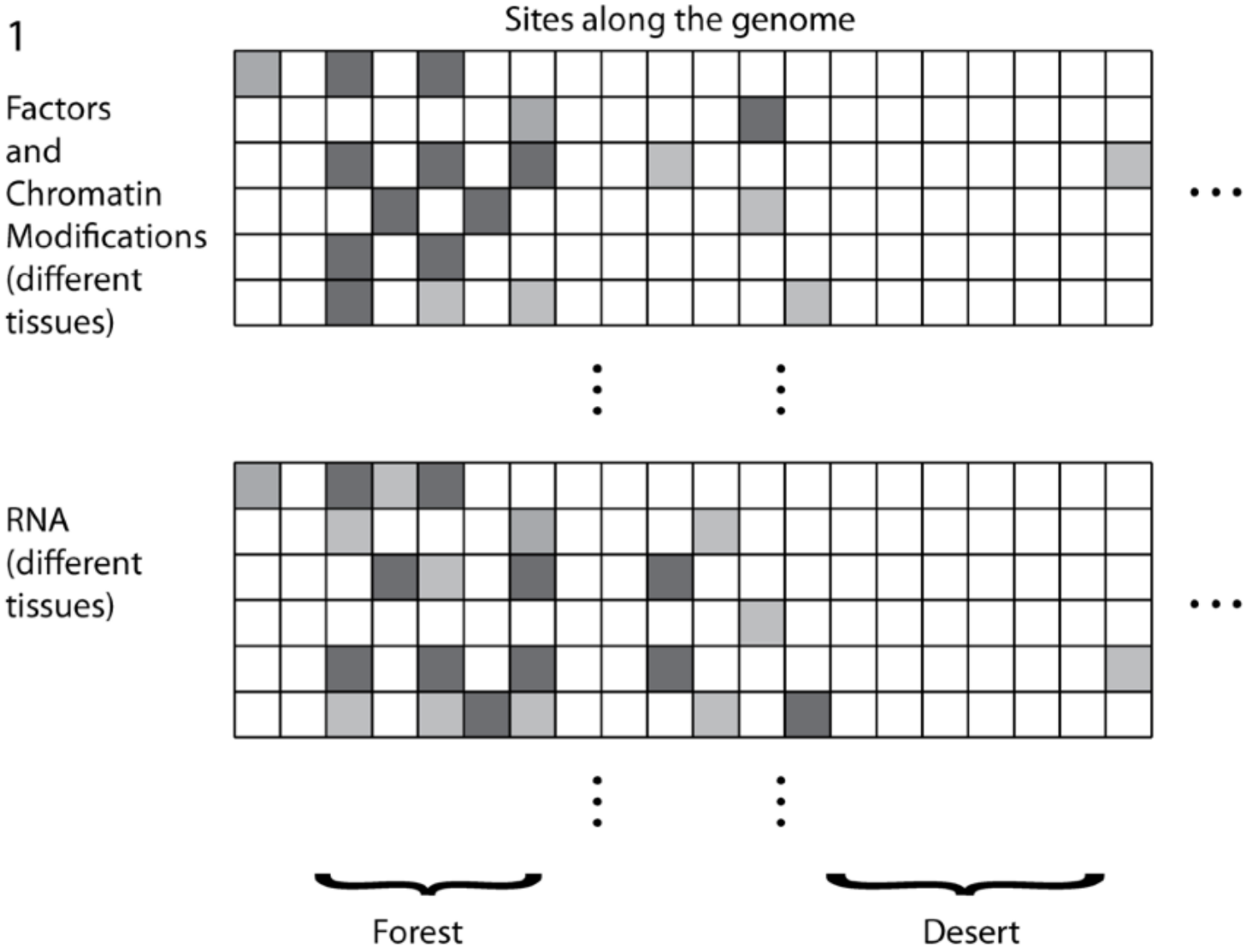
Structure of Genomic Features Matrix



Unsupervised Mining

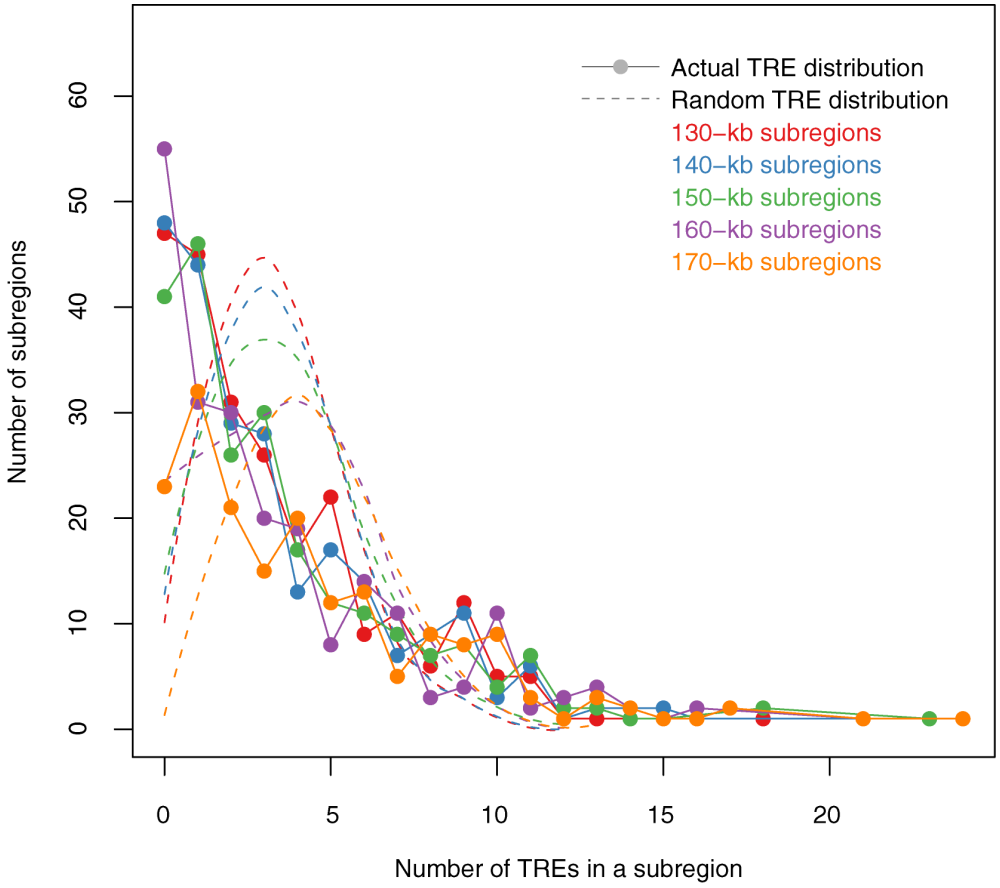
- Simple overlaps & enriched regions
- Clustering rows & columns (networks)
- PCA/SVD (theory + appl.)
- Biplot
- RCA
- CCA
- tSNE
- LDA
- (Variational Autoencoders)

Genomic Features Matrix: Deserts & Forests



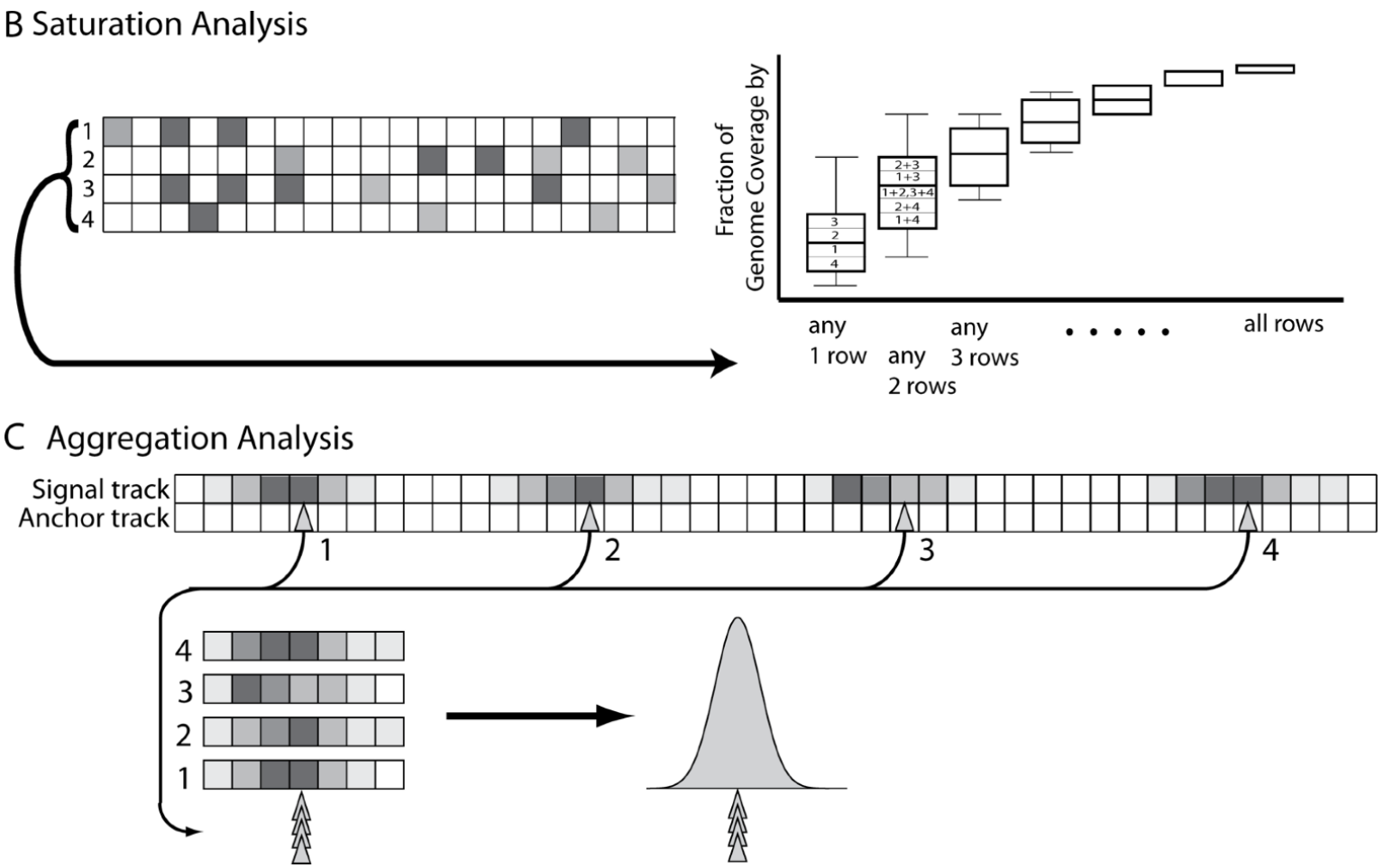
Non-random distribution of TREs

- TREs are not evenly distributed throughout the encode regions ($P < 2.2 \times 10^{-16}$).
- The actual TRE distribution is power-law.
- The null distribution is ‘Poissonesque.’
- Many genomic subregions with extreme numbers of TREs.



Zhang et al. (2007) Gen. Res.

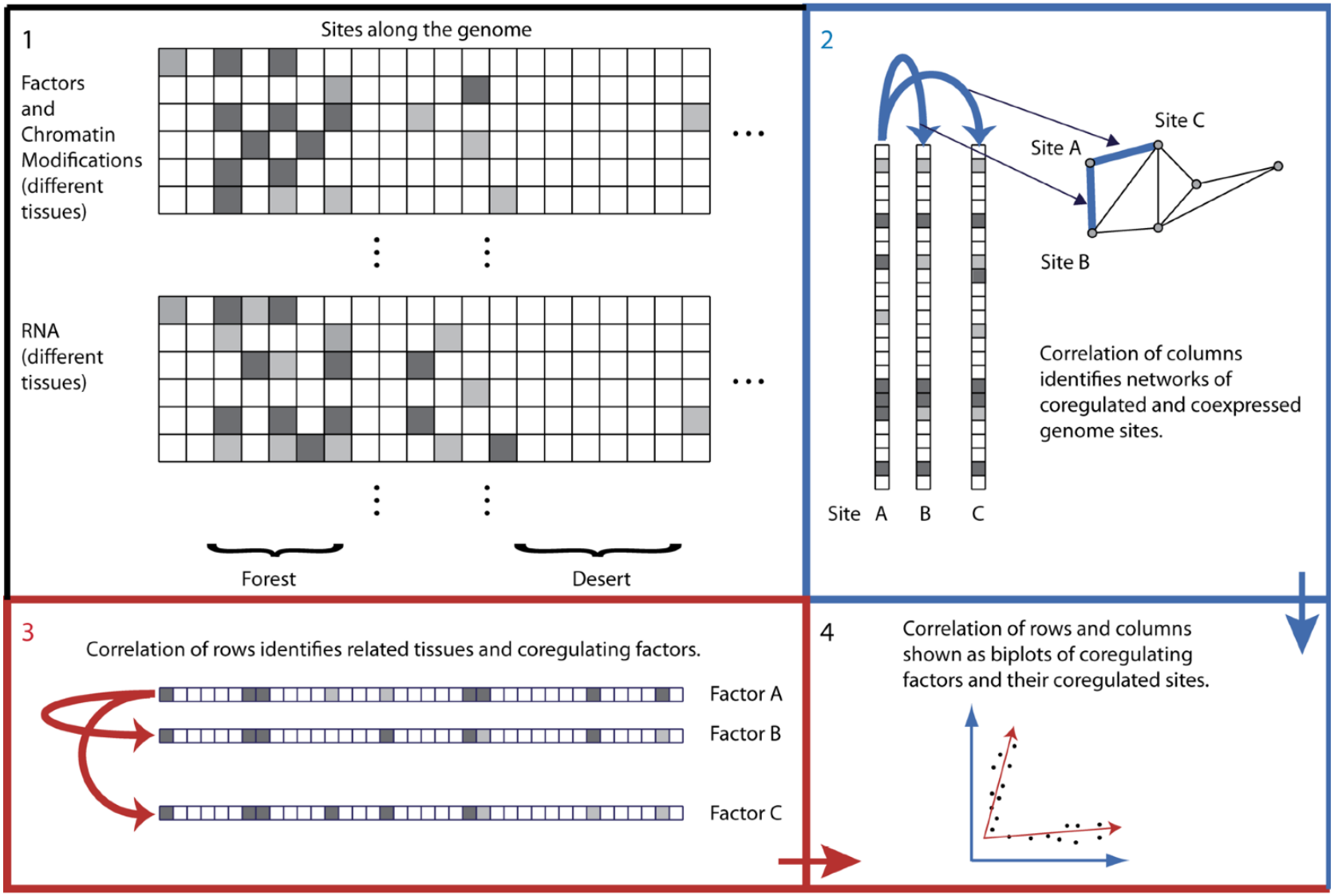
Aggregation & Saturation



[*Nat. Rev. Genet.* (2010) 11: 559]

Expression Clustering

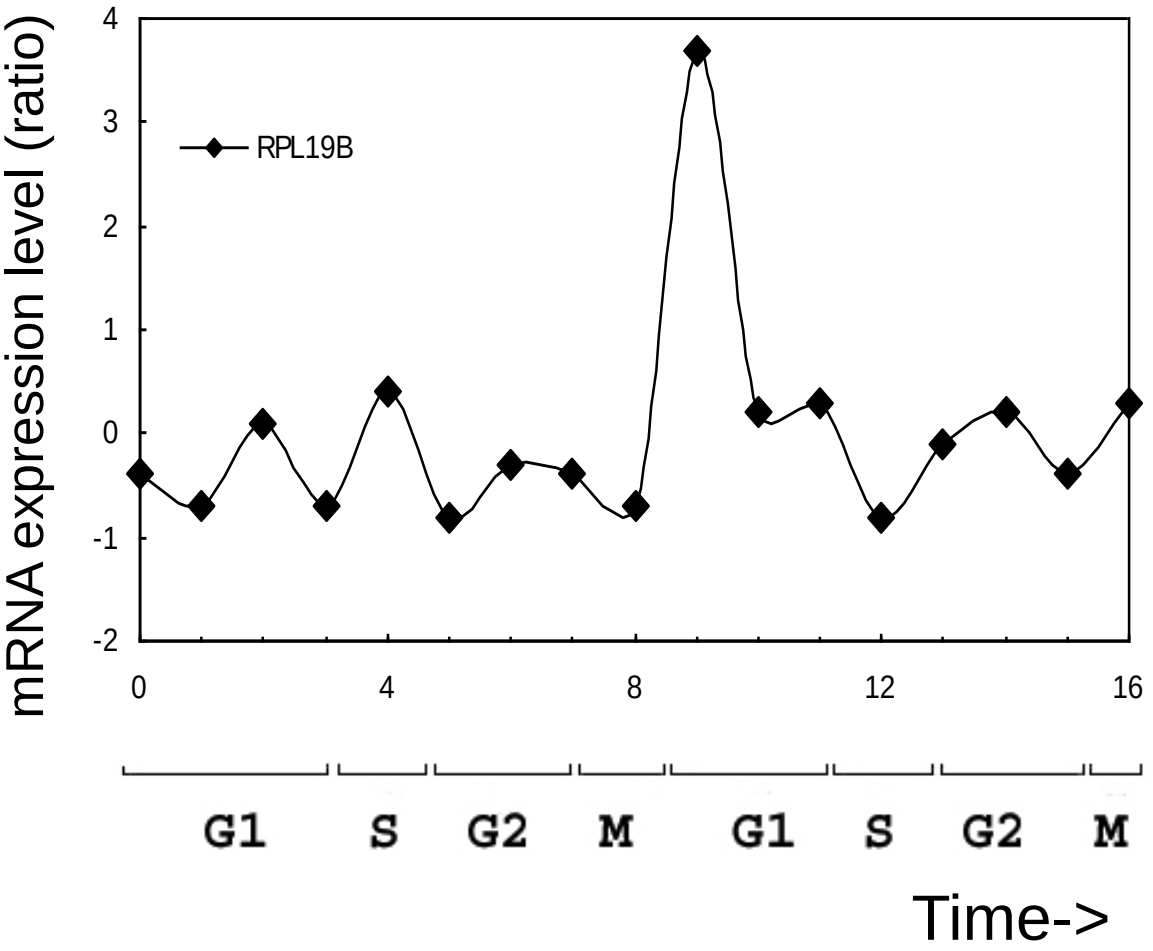
Correlating Rows & Columns

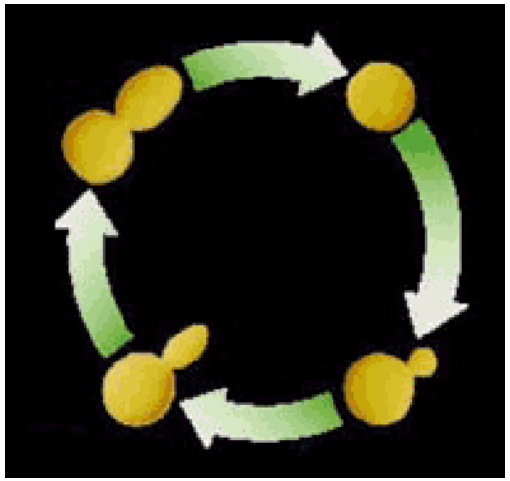


[*Nat. Rev. Genet.* (2010) 11: 559]

Clustering the yeast cell cycle to uncover interacting proteins

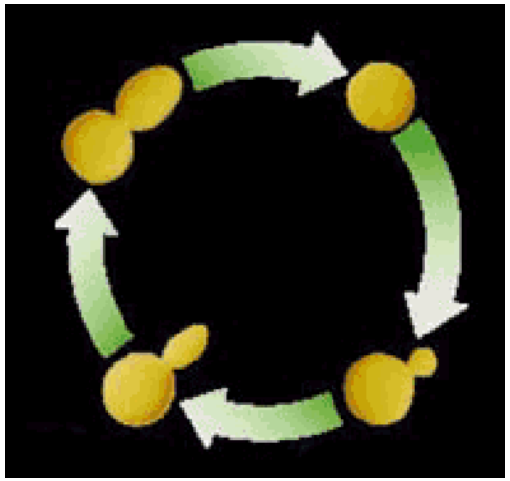
[Brown, Davis]

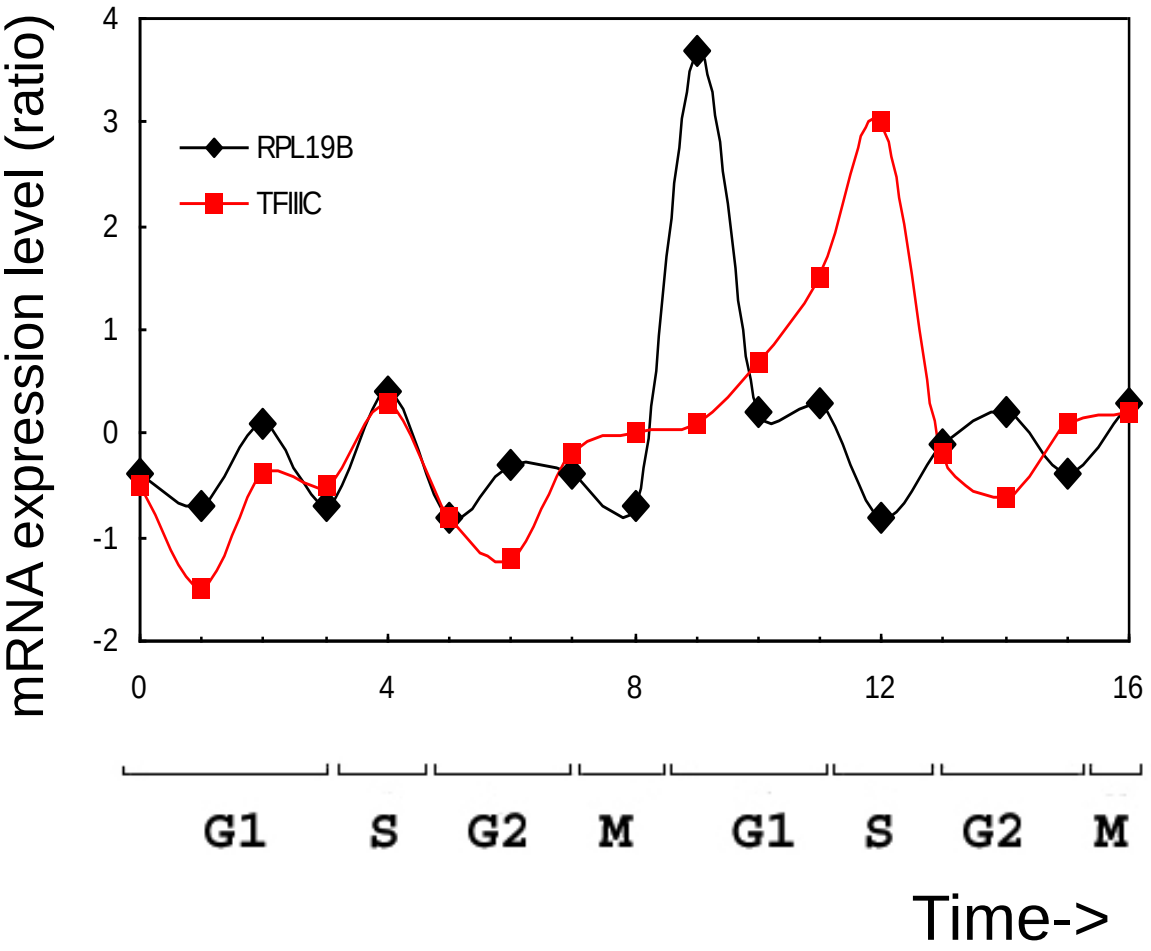




Microarray timecourse of
1 ribosomal protein

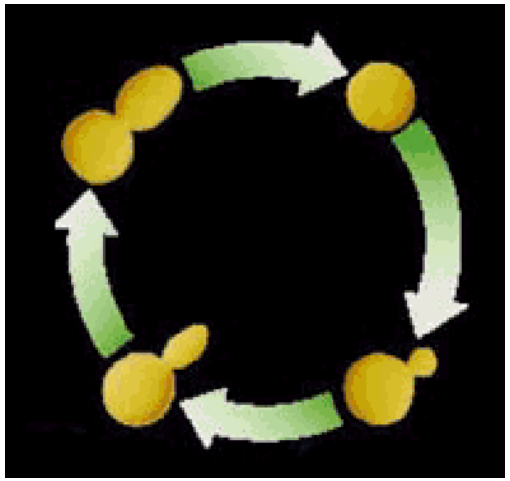
Clustering the yeast cell cycle to uncover interacting proteins

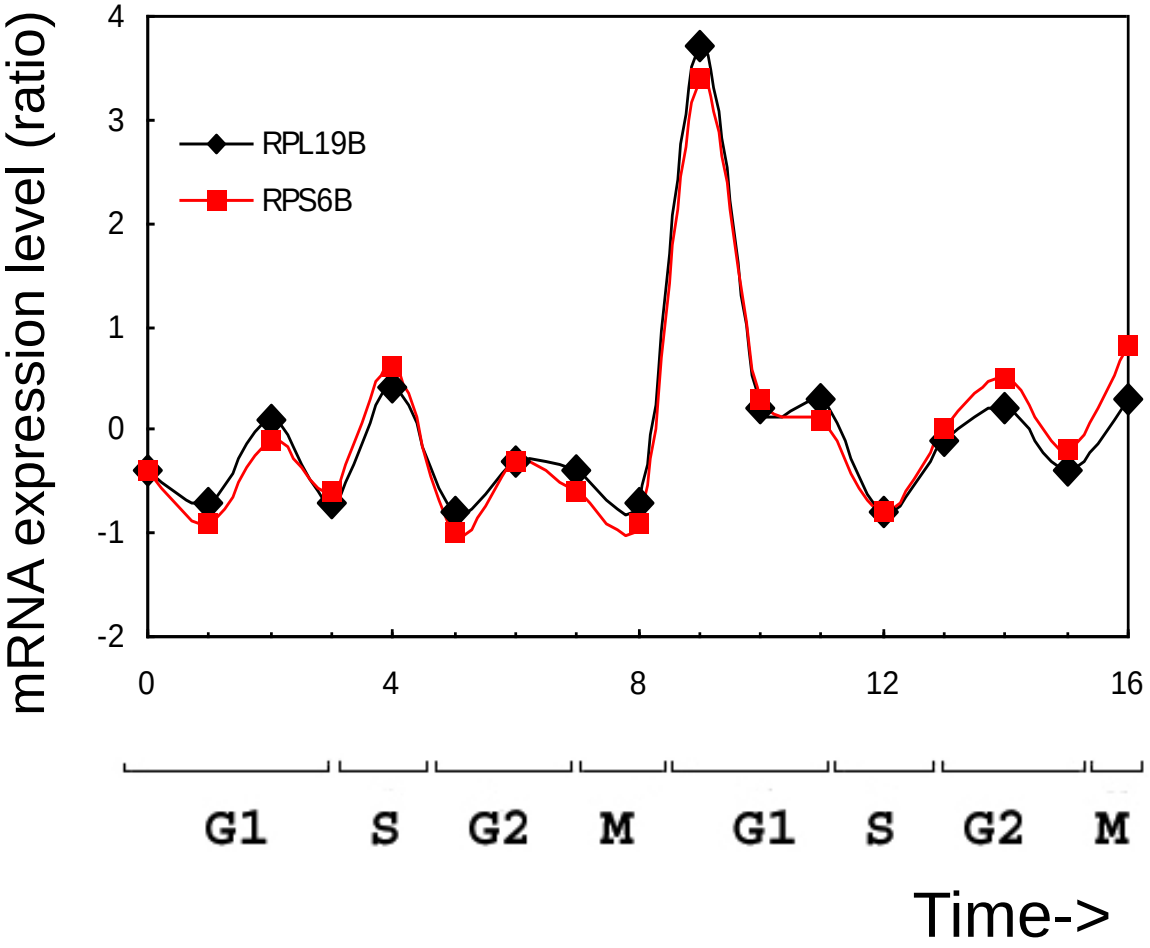




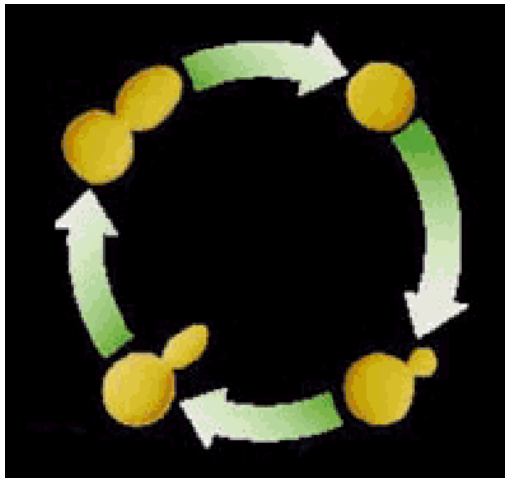
Clustering the yeast cell cycle to uncover interacting proteins

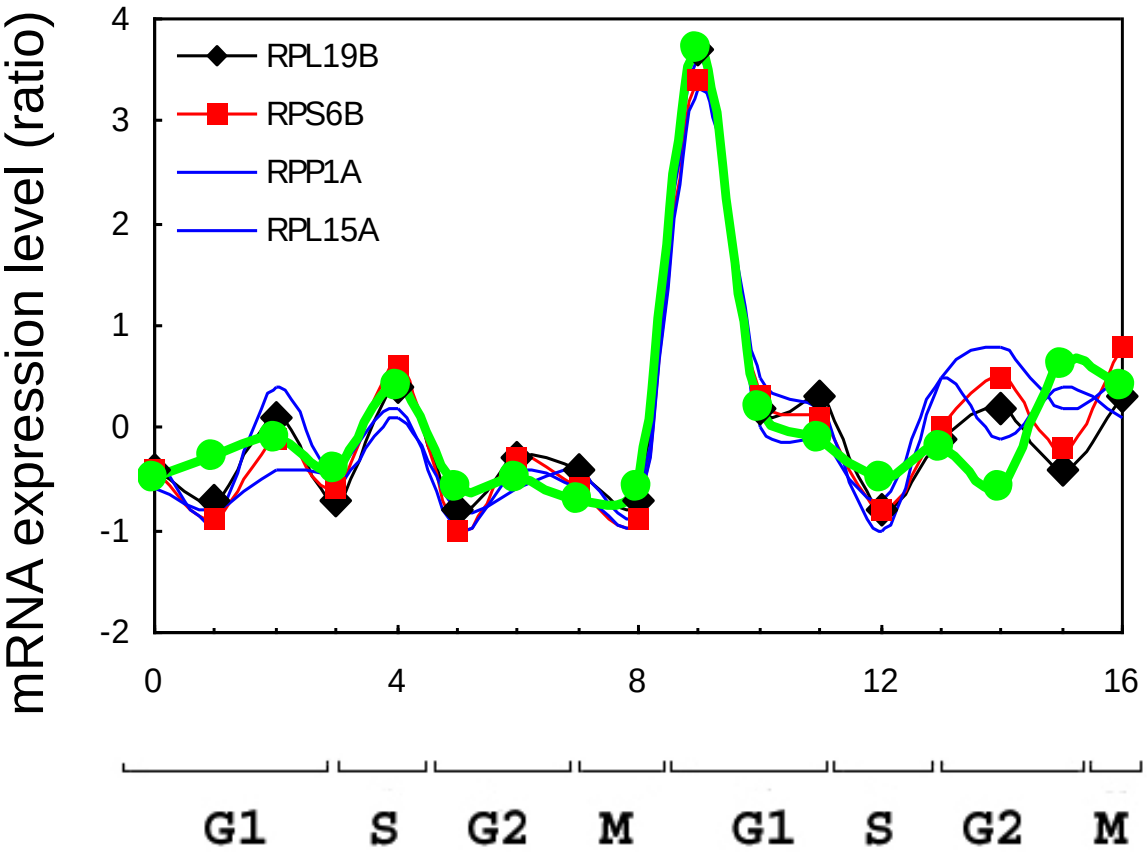
[Botstein; Church, Vidal]



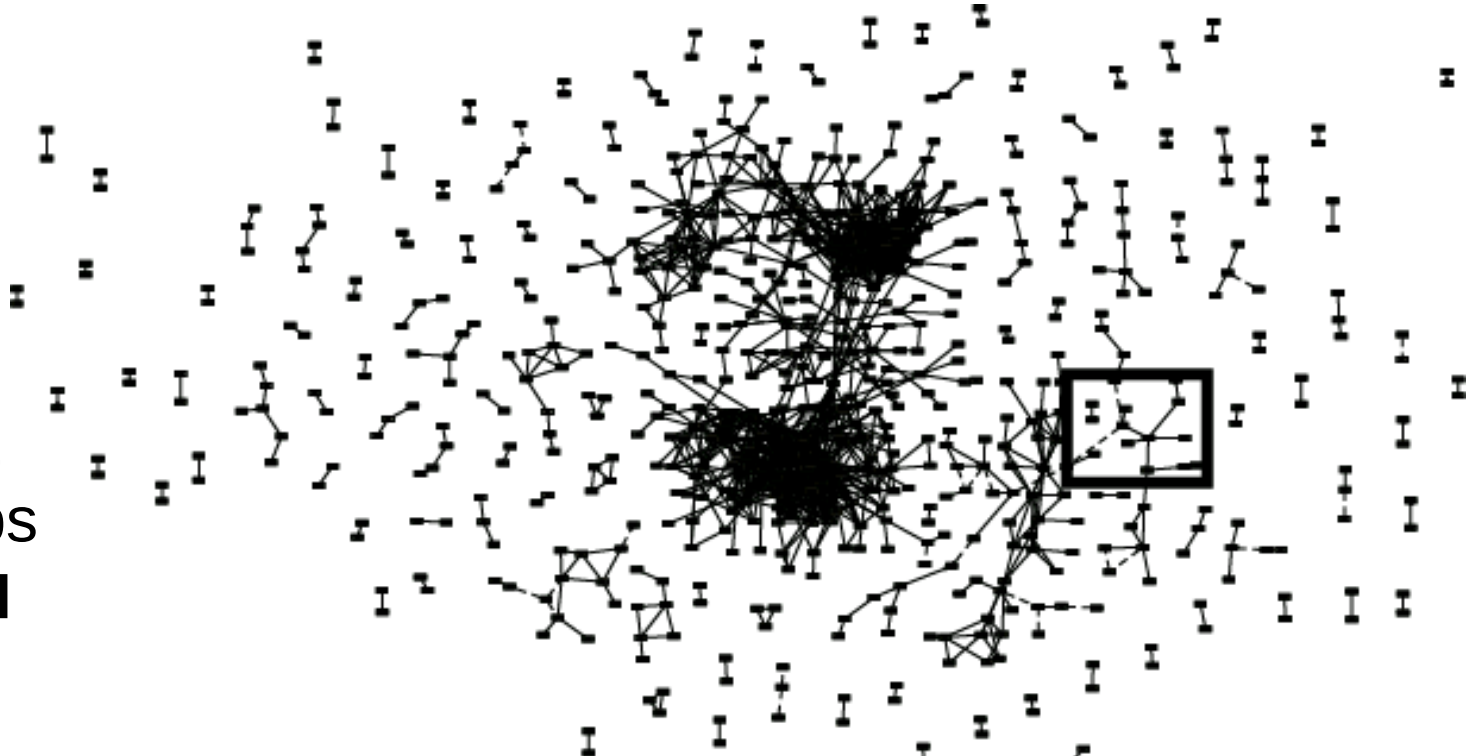


Clustering the yeast cell cycle to uncover interacting proteins





Global Network of Relationships



~470K significant relationships from ~**18M** possible

Unsupervised Mining

General Thoughts on Clustering

Overview of Clustering Methods (Very High Level)

- Connectivity-based
- Centroid-based
- Distribution-based
- Density-based
- Community Detection

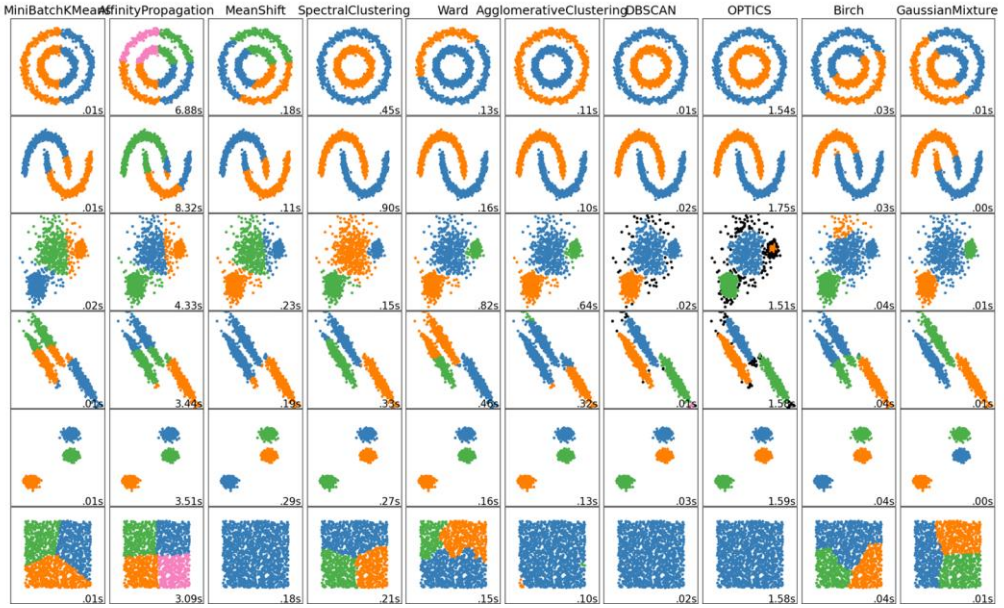


Image reference: https://scikit-learn.org/stable/modules/clustering.html

Centroid-based Methods

- Optimizes a center vector to find data clusters
- Clusters data into a Voronoi diagram, which is interpretable
- Assumes a spherical shape for the clusters centered around the center vector
- E.g. K-means clustering
  - Heavily parameterized by K
  - Optimized by Lloyd's algorithm

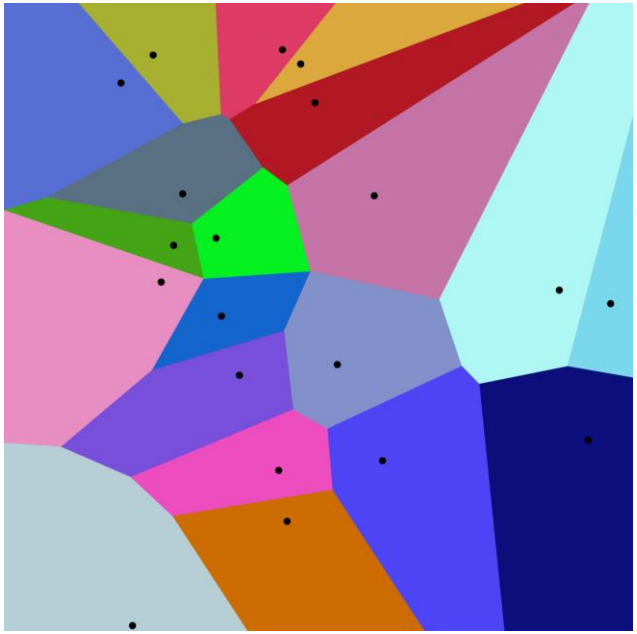
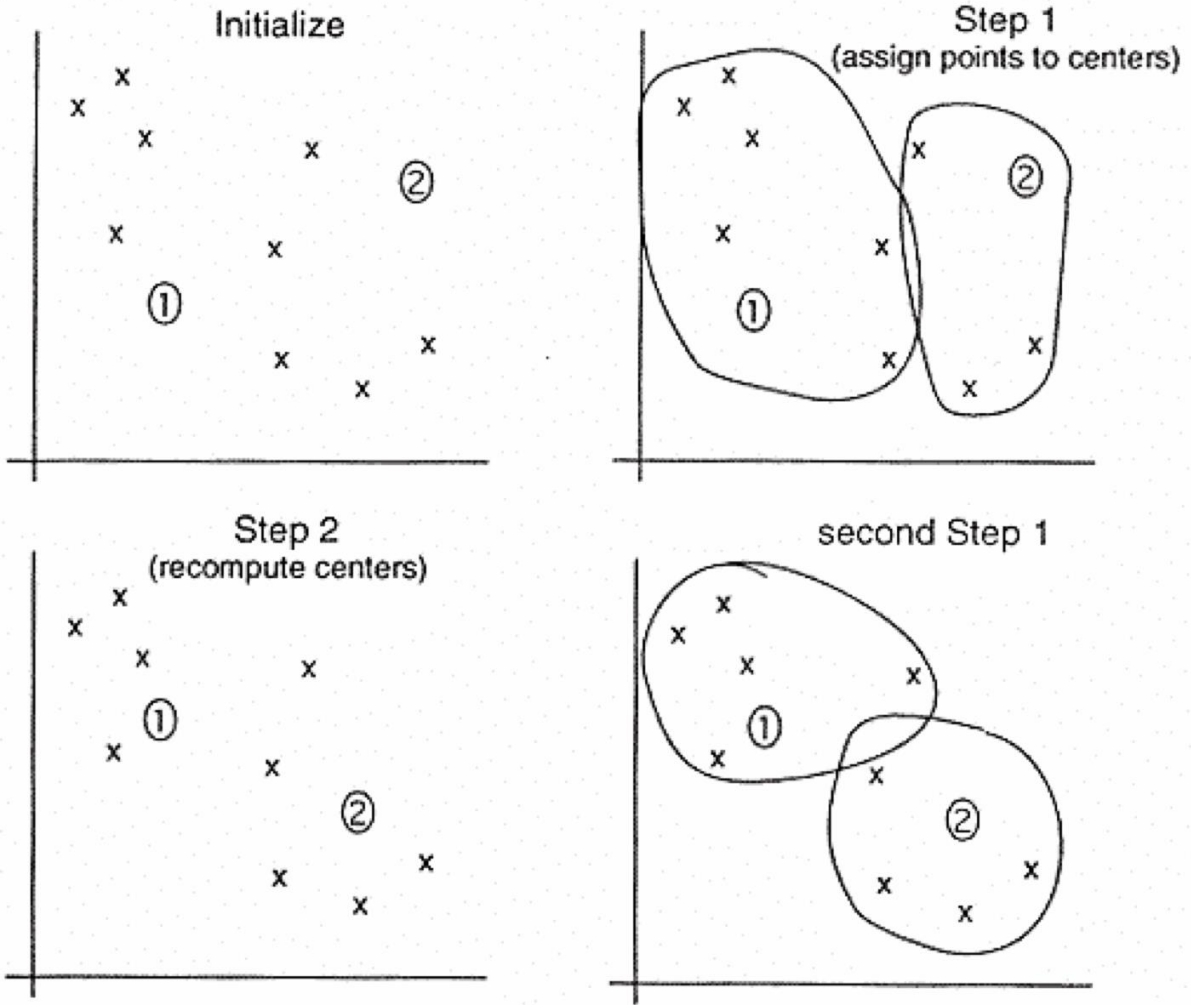


Image reference:
https://upload.wikimedia.org/wikipedia/commons/thumb/5/54/Euclidean_Voronoi_diagram.svg/1200px-Euclidean_Voronoi_diagram.svg.png

K-means



1) Pick ten (i.e. k?) random points as putative cluster centers.
2) Group the points to be clustered by the center to which they are closest.
3) Then take the mean of each group and repeat, with the means now at the cluster center.
4) Stop when the centers stop moving.

Distribution-based Methods

- Clusters are defined as samples from certain distributions
- Assumes the shape and number of distributions
- E.g. Gaussian Mixture Model Clustering
  - Can easily overfit by increasing the number of distributions

- LDA & tSNE (coming later)

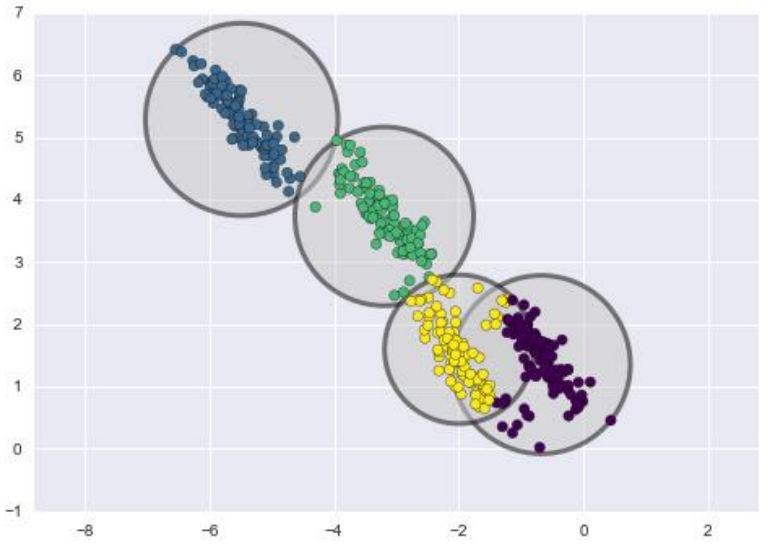
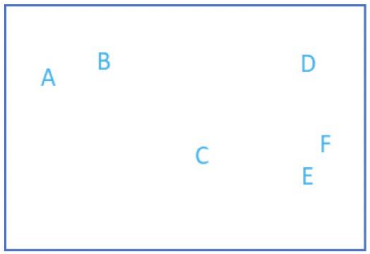
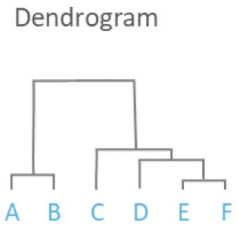


Image reference: https://towardsdatascience.com/gaussian-mixture-models-d13a5e915c8e

Connectivity-based Methods

- Each data point start in their own cluster
- Iteratively merge clusters together based on some evaluation of distance to form a hierarchical structure
- Can be represented by a dendrogram (data point on one axis while tracking merge history on another axis)
- No definitive cut off, but can be used to trace developmental pseudo-time
- E.g. Hierarchical clustering & sequence trees (such as those for multiple alignment [mentioned earlier])





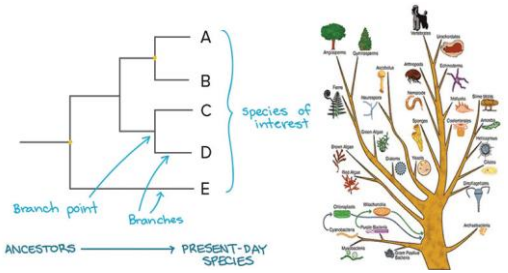


Image references:
https://46gyn61z4i0t1u1pnq2bbk2e-wpengine.netdna-ssl.com/wp-content/uploads/2018/03/Screen-Shot-2018-03-28-at-11.48.48-am.png
https://microbenotes.com/how-to-construct-a-phylogenetic-tree/

Density-based Methods

- Utilize sparse regions and reachability to define clusters
- Assumes some range parameter
- E.g. DBSCAN
- Pro: Fast - O(nlogn) runtime
- Con: Some data points will not be assigned a cluster (undefined) because they are unreachable

- Edge detection

- MSB (mentioned earlier)

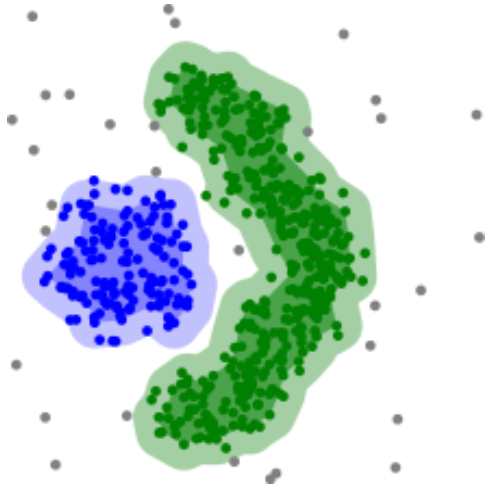


Image reference: https://upload.wikimedia.org/wikipedia/commons/thumb/0/05/DBSCAN-density-data.svg/440px-DBSCAN-density-data.svg.png