Non-parametric Bayesian Methods in Machine Learning

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May 9, 2014

Outline

- **FIX ME AT THE END**
- (My) Bayesian philosophy
- Gaussian Processes for Regression and Classification
  - GP preliminaries
  - Classification (including semi-supervised)
  - Regression application 1: clinical (dis)-agreement
  - Regressopn application 2: typing on touch-screens
- Dirichlet Process flavoured Cluster Models
  - DP preliminaries
  - Idenfitying metabolites
  - (if time) Cluster models for multiple data views

About me

- I'm not a statistican by training (don't ask me to prove anything!).
- Education:
  - Undergraduate Degree: Electrical and Electronic Engineering (Bristol)
  - PhD: Machine Learning Techniques for Microarray Analysis (Bristol)
- Currently:
  - Lecturer: Computing Science
  - Research Interests: Machine Learning and Applied Statistics in Computational Biology and Human-Computer Interaction (HCI)

Lecture 9: Infinte factorisaion of multiple non-parametric views

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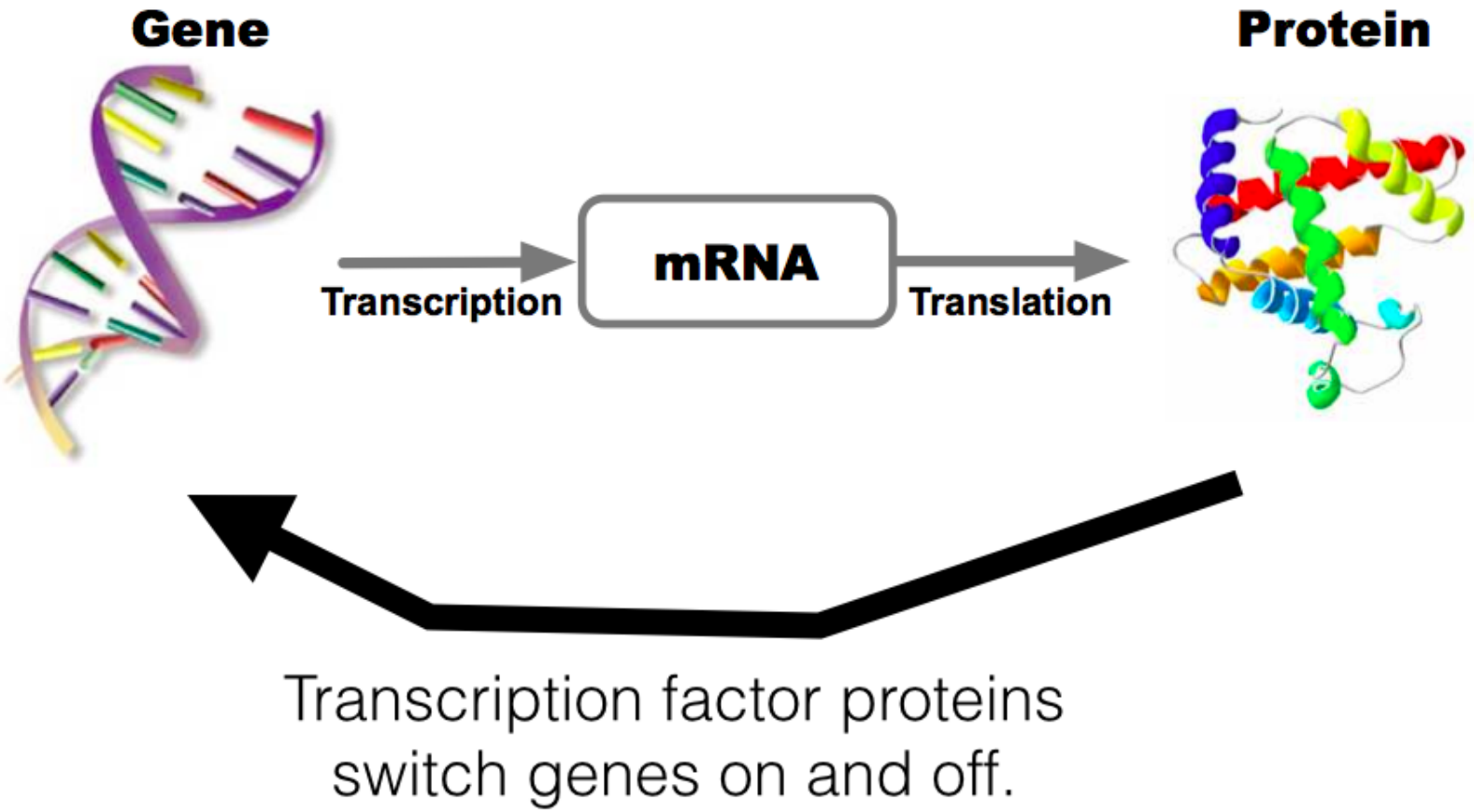
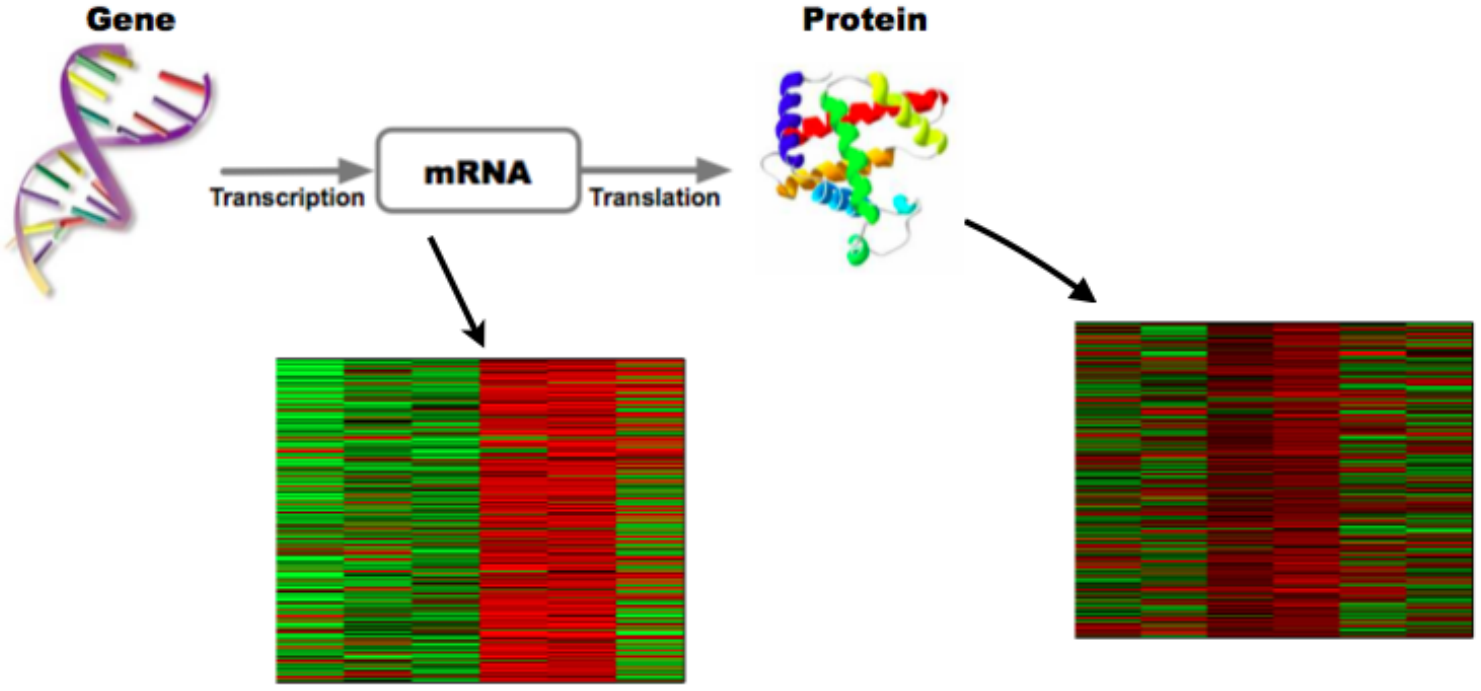
Introduction



- How related are mRNA and protein?
- **Where is the external control?**

Data

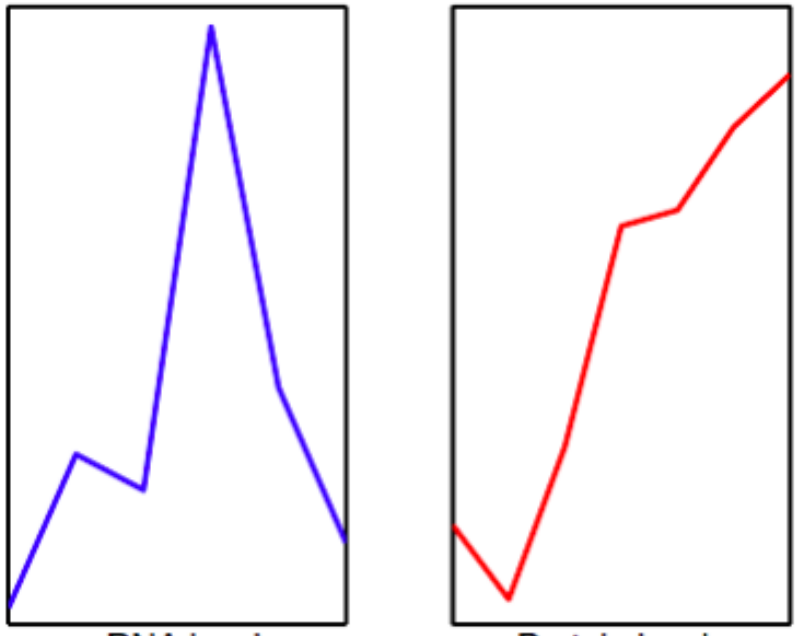
- mRNA and protein time series for $\sim$ 500 genes



mRNA & protein for ~500 genes

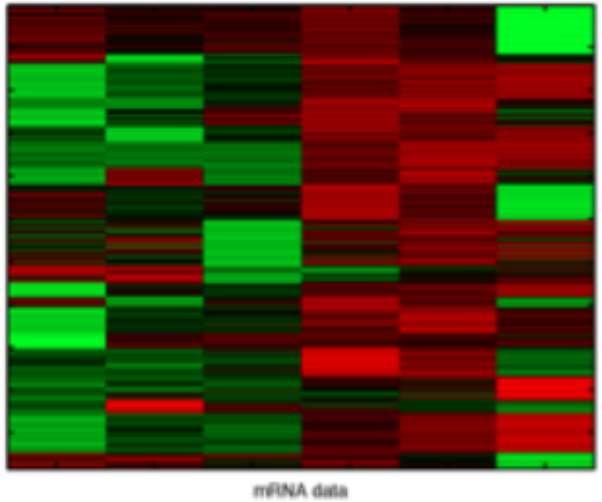
(rows in matrix correspond to one another)

Most don't look correlated

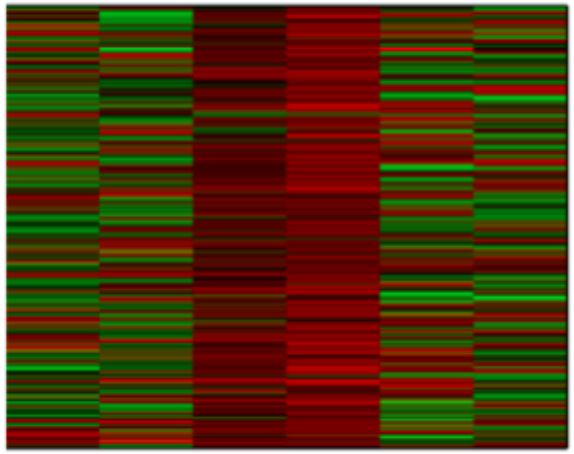


- Most don't look correlated.
  - Time delays? Saturation? Decay rates? Post-transcriptional control?

Non-parametric relationships



Cluster genes by mRNA



Cluster genes by protein

- Use clustering to define similarity.
- If genes A,B,C and D cluster together on both sides, then profiles are similar
  - They are controlled by similar processes

Generative coupled mixture model

- In Rogers et. al 2008 we developed a generative linked cluster model
- Prior membership of gene n in proteomic cluster j was dependent on assignment of mRNA to cluster k:

$$P(z_{nj} = 1, z_{nk} = 1) = P(z_{nj} = 1 | z_{nk} = 1) P(z_{nk} = 1)$$

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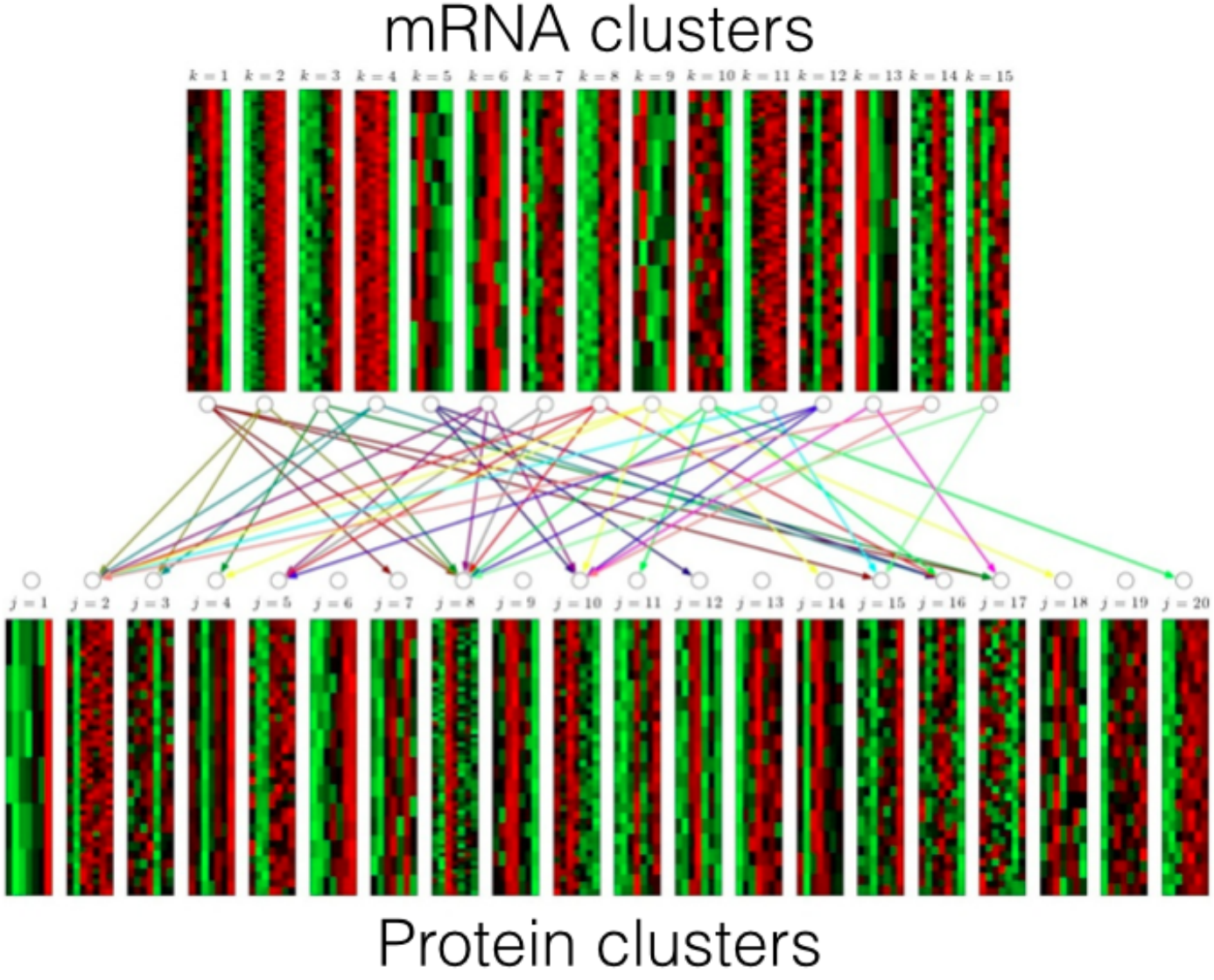
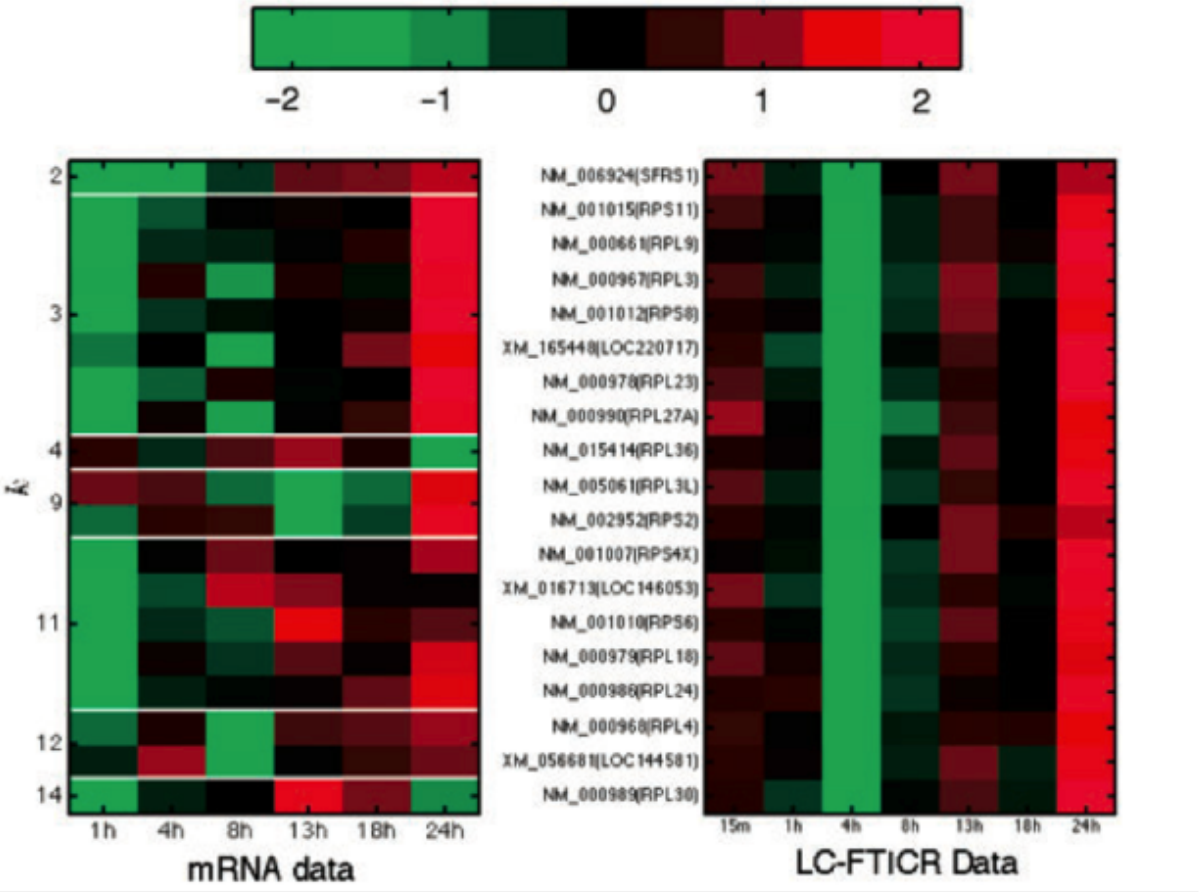
- When we do inference, we can find the links between clusters

Lots of links



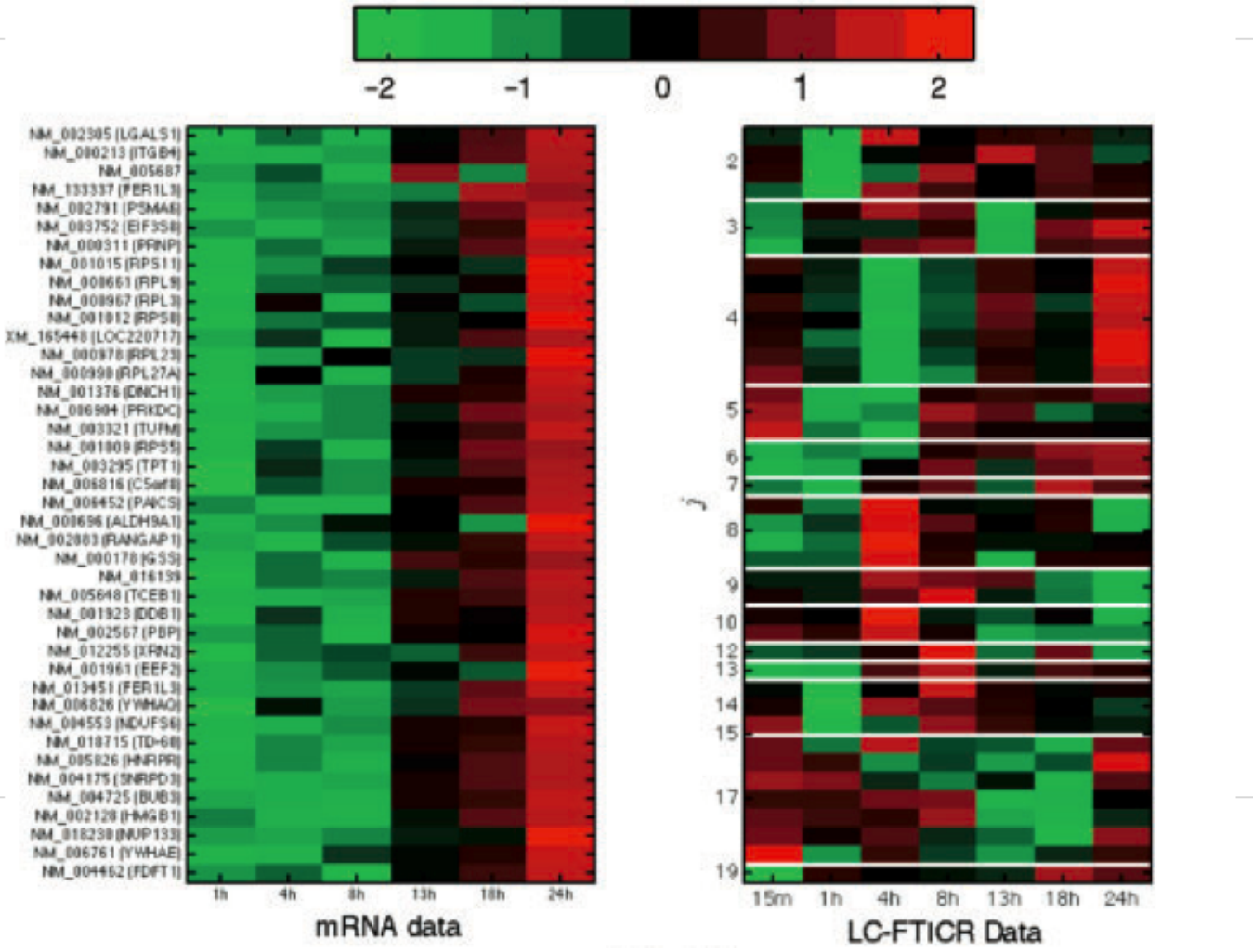
- If all control before transcription, we would expect sparse links.
- That doesn't happen!

Ribosomes



- Some strong links
- These are all ribosomal proteins
- The ribosome is where proteins are constructed
- Makes sense for them to be tightly transcriptionally controlled

Crazy genes



- In some cases, profiles were all over the place
- Here, highly conserved mRNA profiles, diverse protein profiles

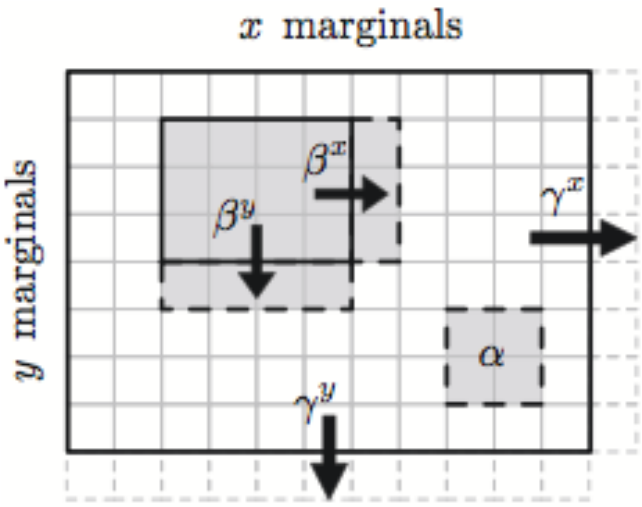
More flexible models

- At this point, we thought about more flexible models (!)
- In particular, how about decomposing the joint density as:

$$P(z_{nk} = 1, z_{nj} = 1) = \sum_i P(z_{nk} = 1|i)P(z_{nj} = 1|i)P(i)$$

- Each latent factor (i) defines a distribution over mRNA and protein clusters
- Use DP priors on i and the clusters in the two *views*

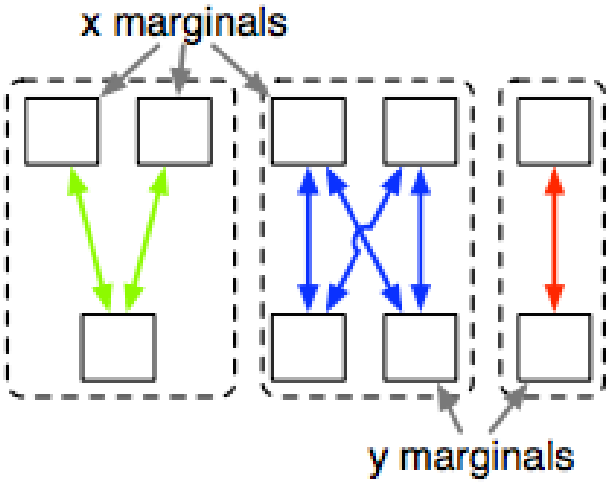
Contingency tables



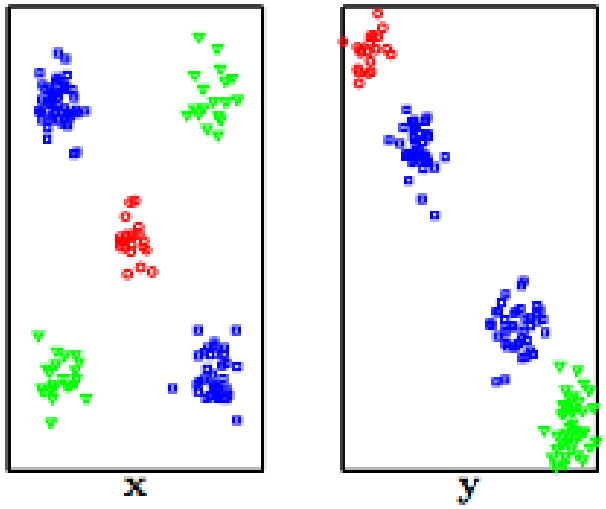
- Can visualise $P(j, k)$ as a table
- Each i is a block (if the clusters are ordered nicely)
- Numbers of rows, columns and blocks can all vary
- Restaurant analogies are possible but unhelpful

- Inference can be done with Gibbs sampling
- Details in Rogers et. al 2009

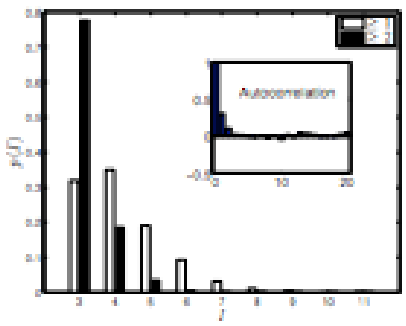
Synthetic example



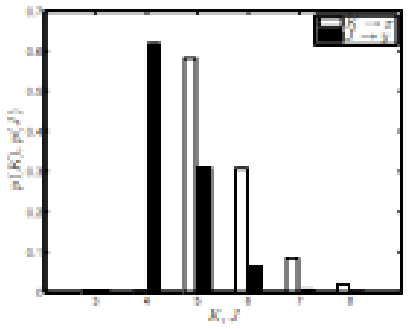
(a) Structure of Gaussian synthetic example. Top boxes represent x marginal components, bottom y. Arrows and dashed lines represent the block structure.



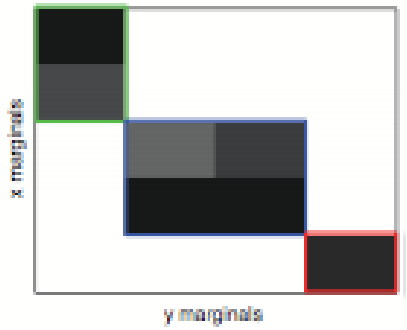
(b) Synthetic dataset for $\mathbf{x}$ (left) and $\mathbf{y}$ (right). Symbols/colors represent top-level clustering.



(c) Marginal posterior distribution over the number of top-level components, I. White bars show the histogram over all clusters, whereas black bars ignore singleton clusters. (Inset: autocorrelation)



(d) Posterior distribution over the number of marginal components. For both margins the mode corresponds with the true solution.



(e) Example contingency table from the sampler. Gray shades denote the count of samples in each cell, and the block structure corresponds exactly to that shown in subfigure (a).

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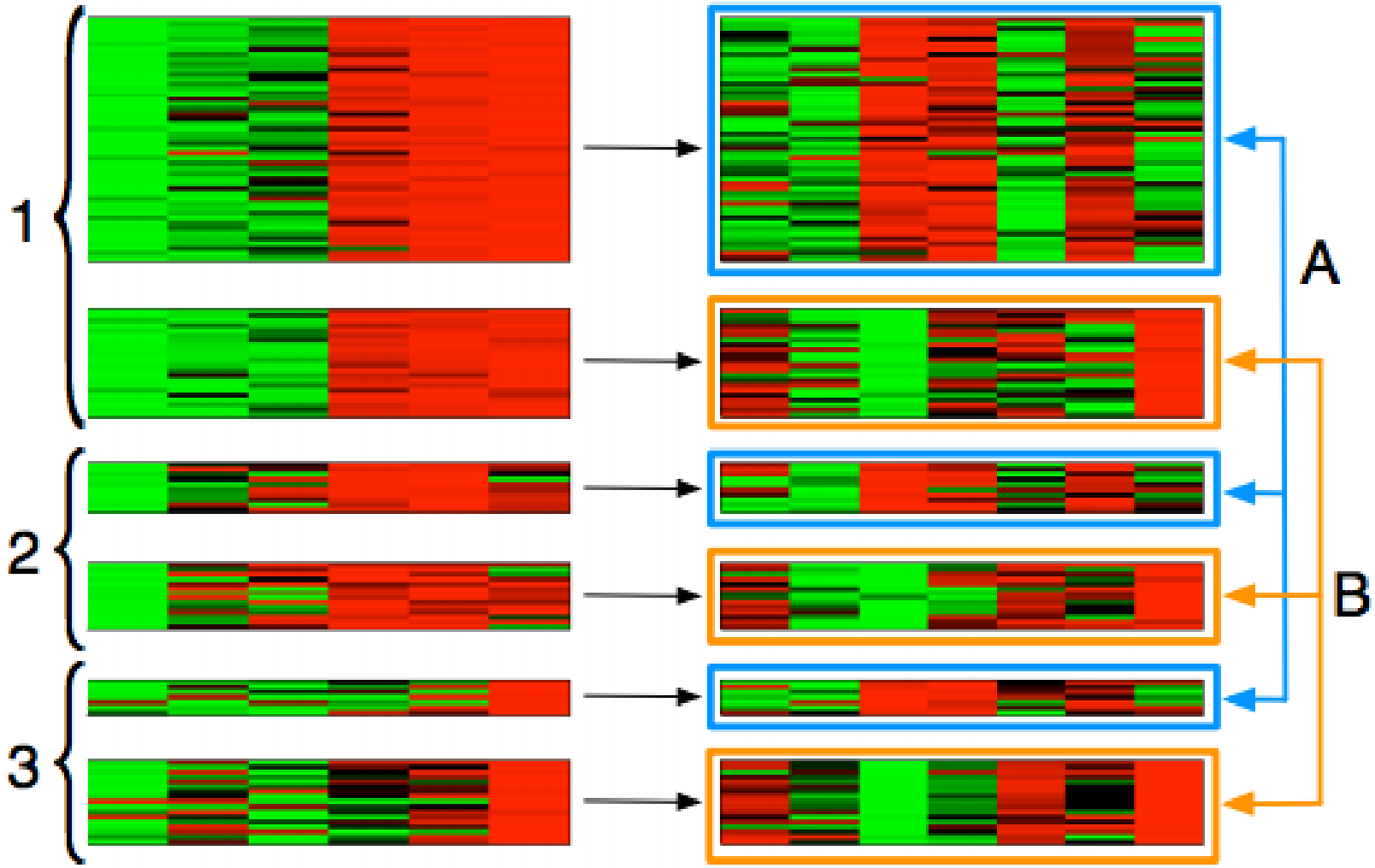
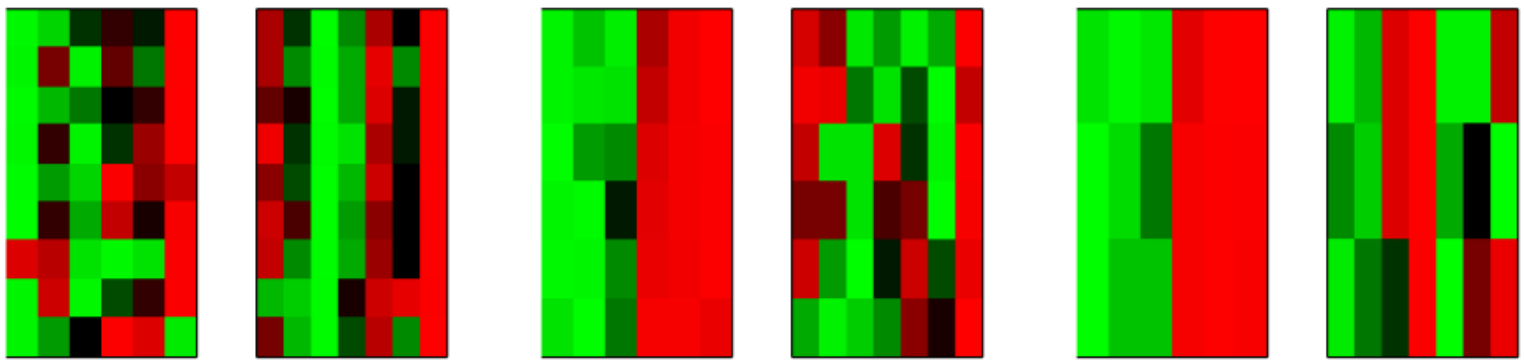
- As in previous example, the clustering is not our final goal!

Results 1: what kind of blocks are present



- Highly inter-connected. Clusters on left shown by numbers, on right by letters.

Results 2: what's enriched?

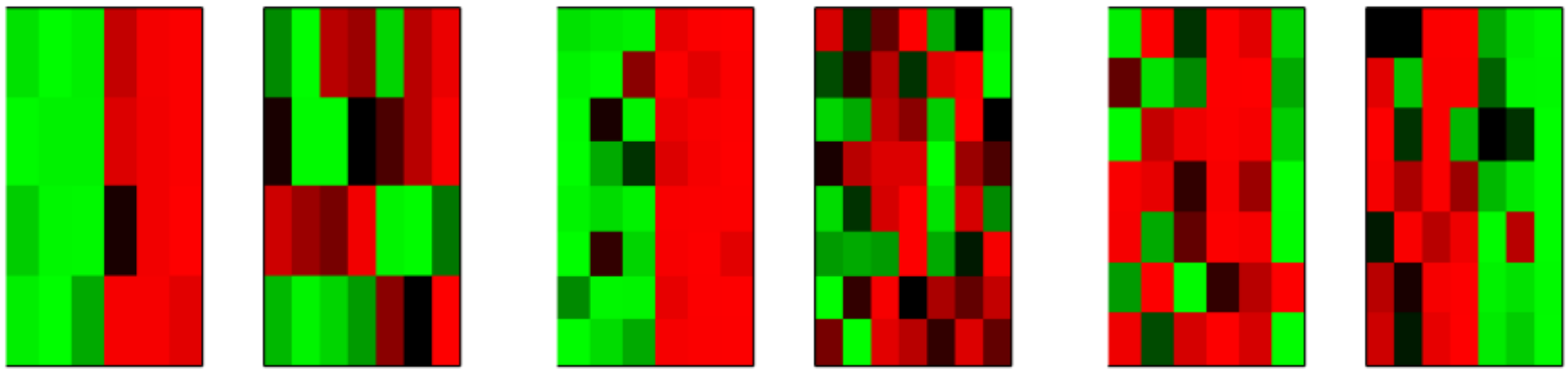


(a) GO:0003735 (b) GO:0008380 (c) GO:0000502

Fig. 8 3 examples of gene ontology terms significantly enriched in top level components. In all cases, left heat map is mRNA data, right is protein data.

- Some terms (and genes) enriched in the top components (i.e. for mRNA and protein)

Results 2: what's enriched?



(a) GO:0006281 (b) GO:0006457 (c) GO:0007155

- Some terms (and genes) enriched in one component and not the other (a,b: enriched in mRNC; c: enriched in protein)