Computational Biology LU 2014

Biomolecular Network Analysis

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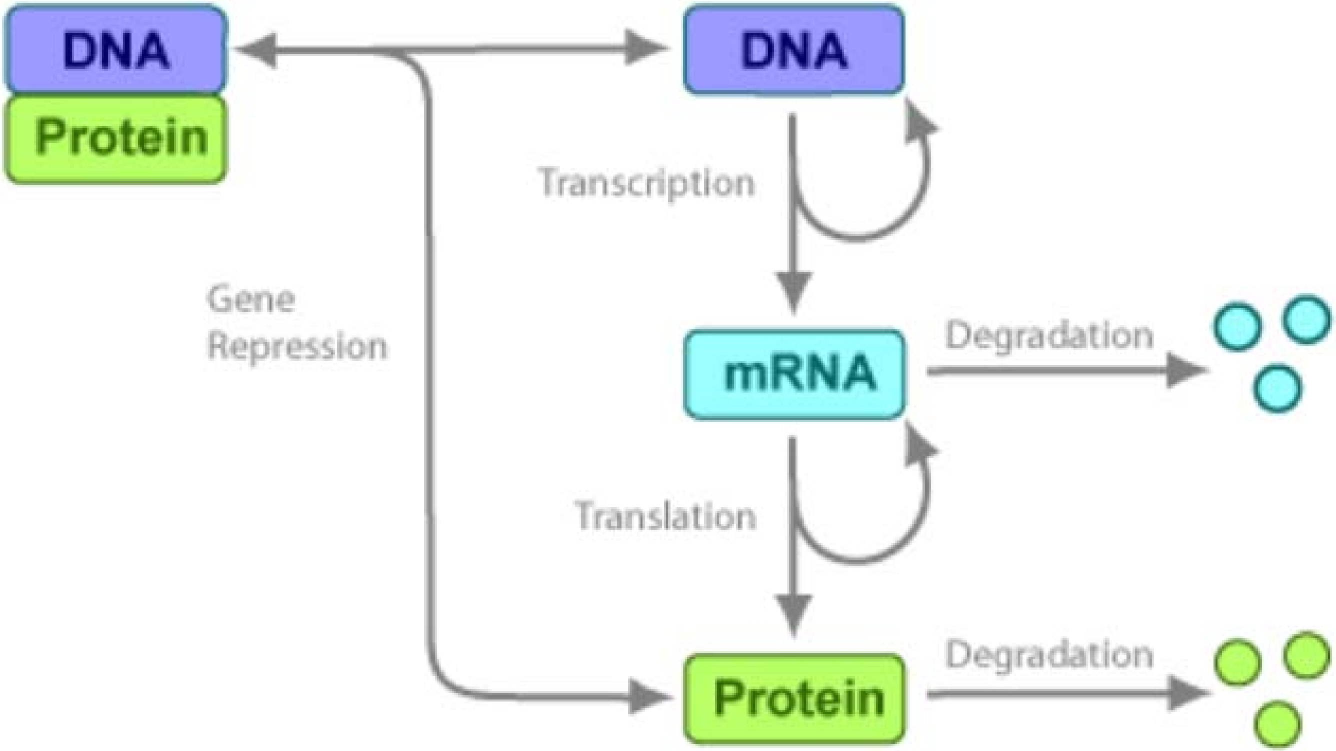
Outline

- Biomolecular network analysis
  - Introduction
  - Network motifs
  - Visualisation
- Exercise

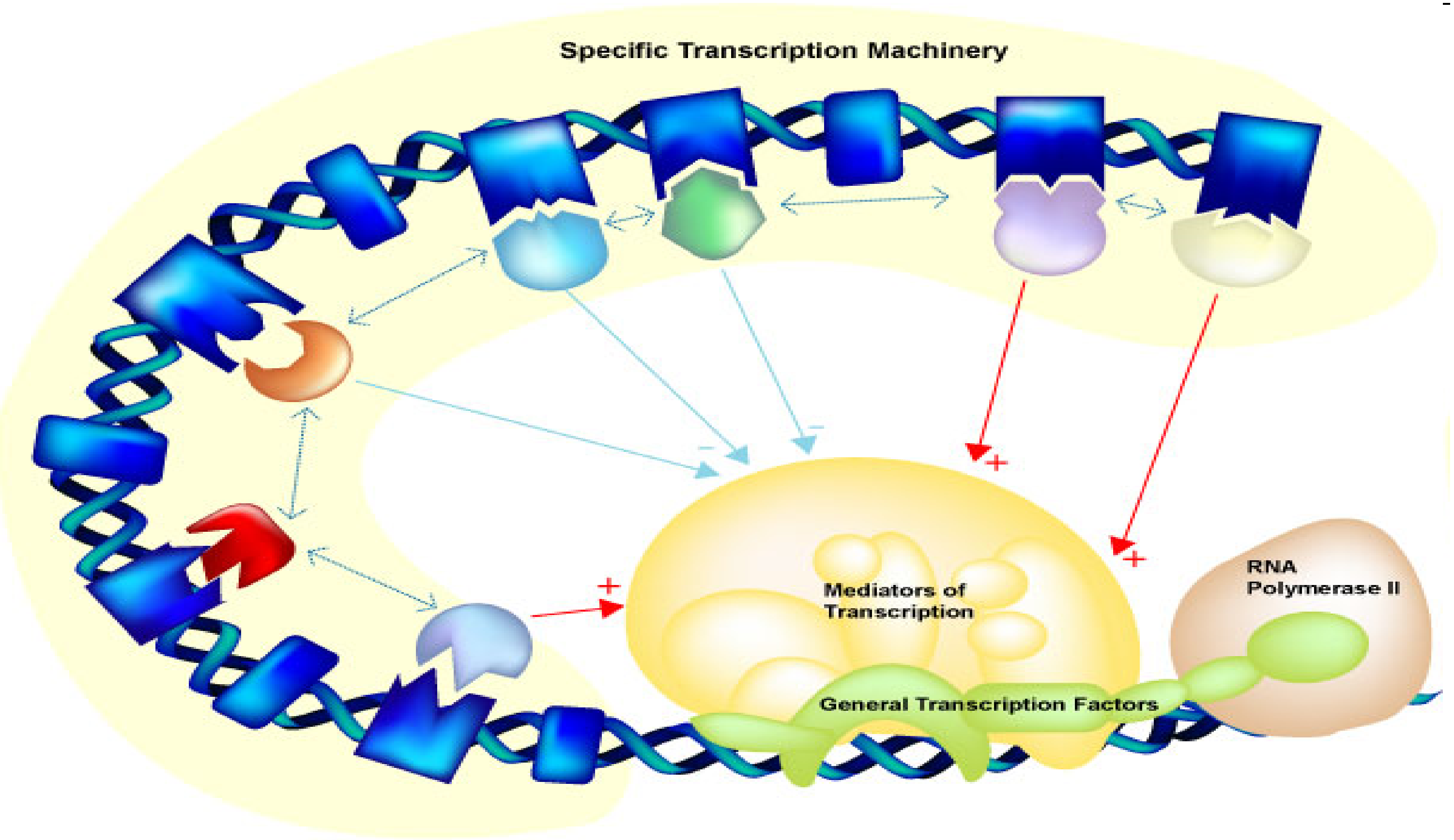
Introduction – Gene Regulation

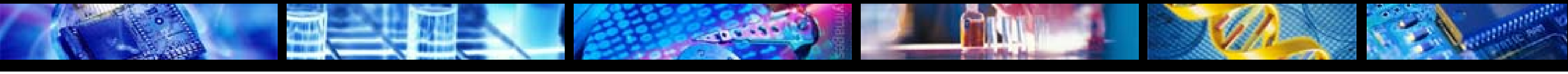


Transcription Factors (TF)

- Def: a protein that binds to a specific DNA sequence and controls in this way the flow of genetic information from DNA to RNA.
- They contain one or more DNA-binding domains which attach to specific sequences of DNA adjacent to the genes that they regulate.
- Play an important role in the gene regulation

Transcription



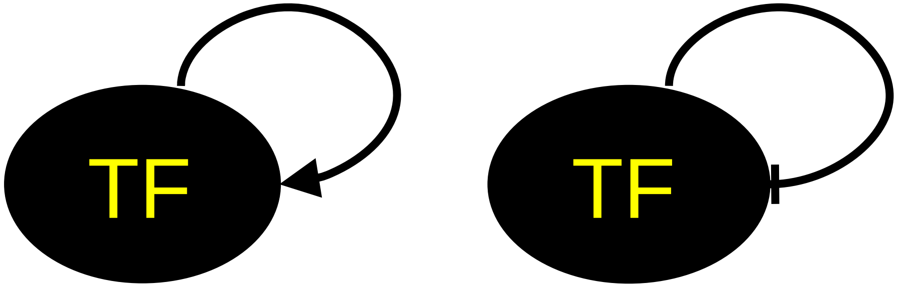


Transcription regulation networks

- Interactions between transcription factors and the genes they regulate
- Contain network motifs – patterns that occur more often than in random networks

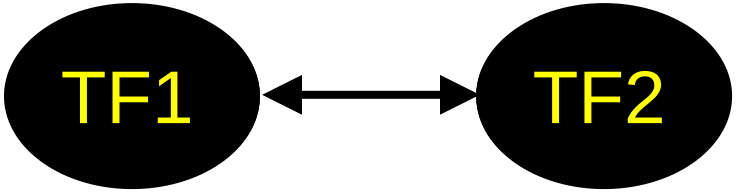
Transcription regulation network motifs

- TF autoregulation
- a TF regulates its own expression level
    - positive autoregulation
    - negative autoregulation



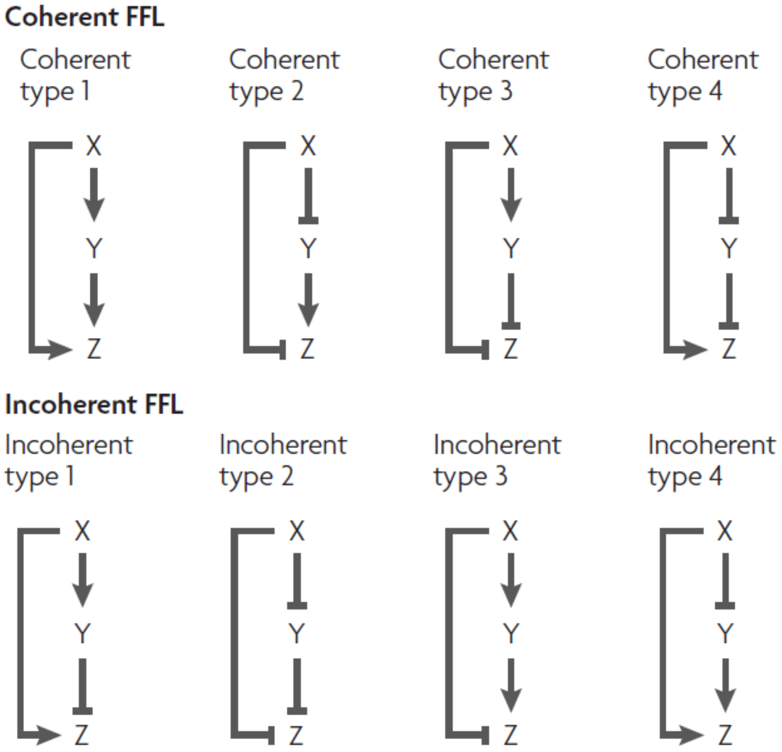
Transcription regulation network motifs

- TF crosstalk
- a TF regulates the expression level of another TF



Transcription regulation network motifs

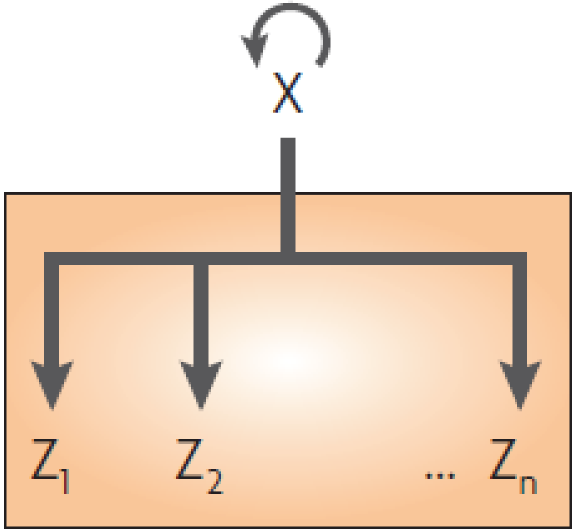
- Feed forward loops
  - TF X regulates expression level of TF Y and gene Z
  - TF Y regulates expression level of gene Z



Transcription regulation network motifs

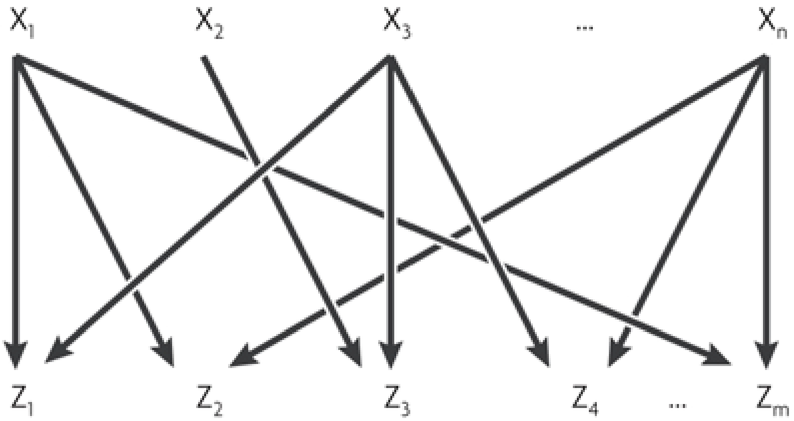
- Single input module (SIM) network motif
  - a single TF X regulates

    a set of genes Z_i



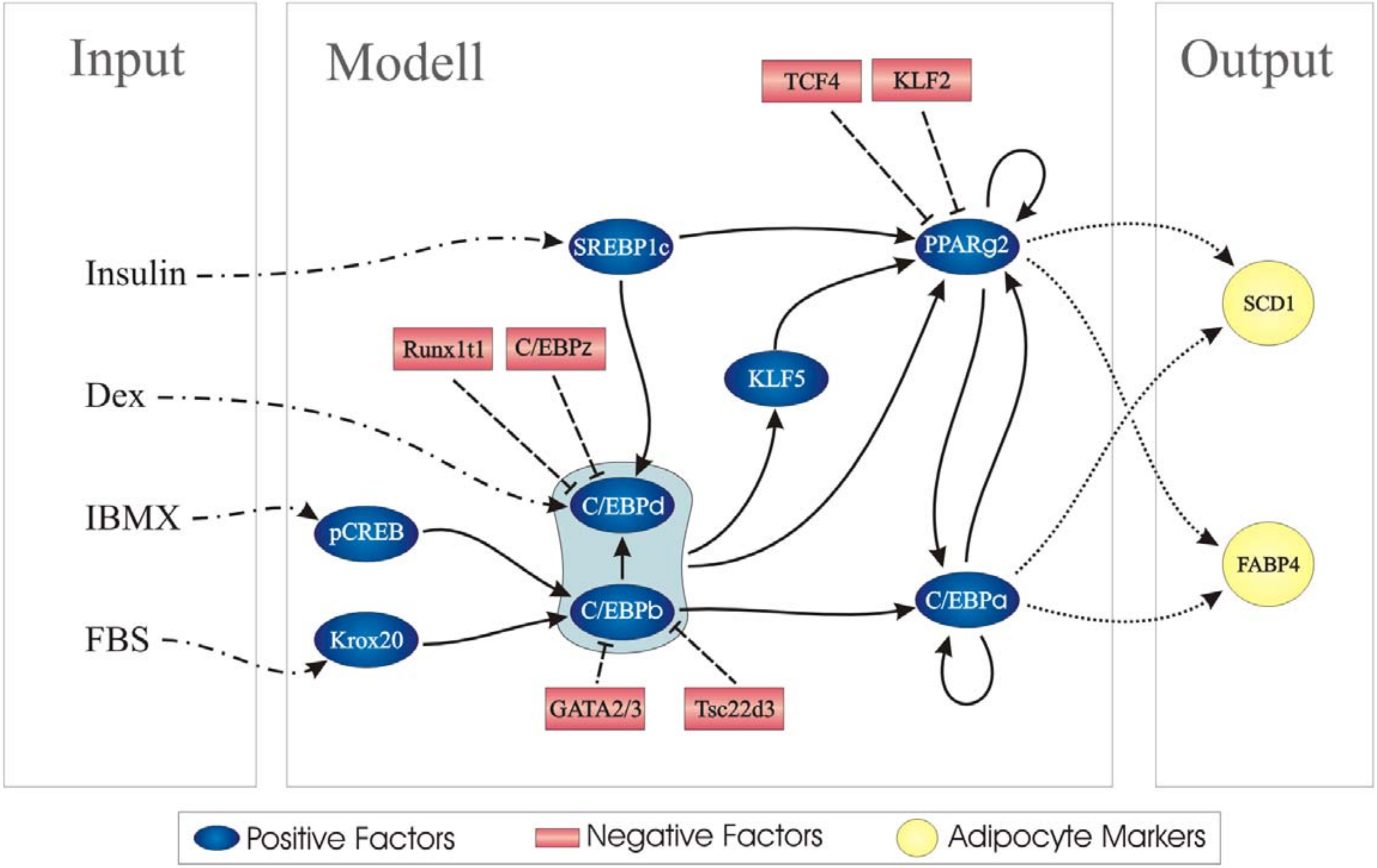
Transcription regulation network motifs

- Dense overlapping regulons (DOR)
  - several TFs X_i co-regulate the expression level of genes Z_i



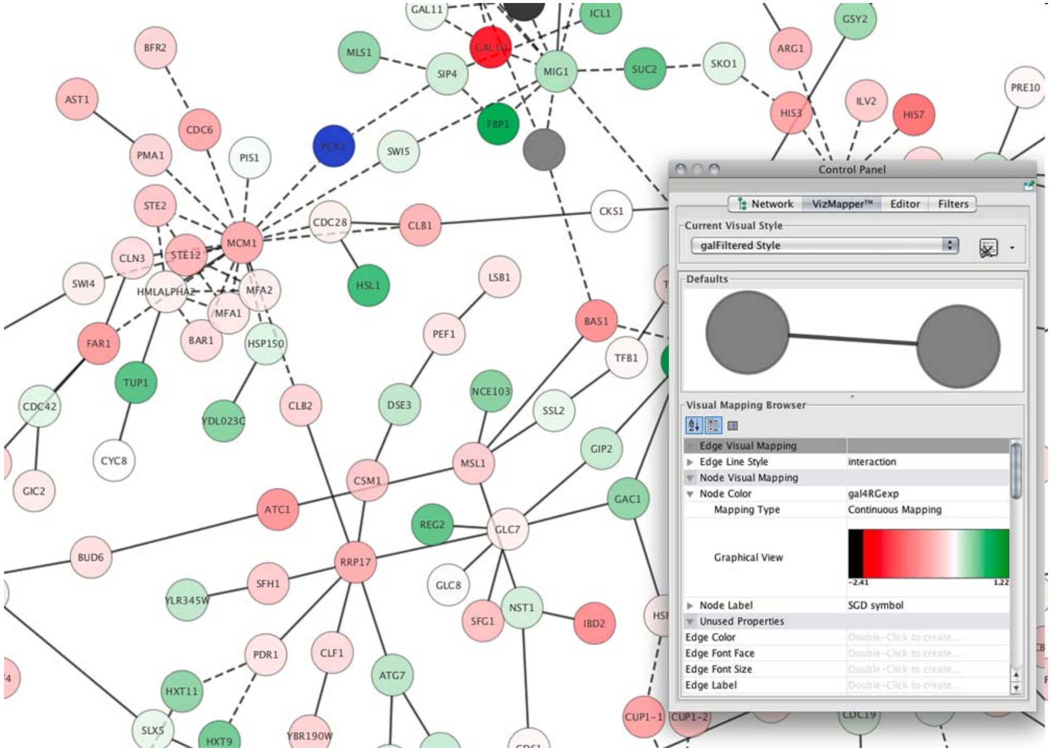
Uri A. Network motifs: theory and experimental approaches. Nature Reviews Genetics 8, 450-461 (June 2007)

Network Example - Adipogenesis



Network visualisation - Cytoscape

- open source software: http://www.cytoscape.org/



Current Visual Style: galFiltered Style

Edge Visual Mapping
Edge Line Style: interaction
Node Visual Mapping
Node Color: gal4RGexp
Mapping Type: Continuous Mapping
Node Label: SGD symbol
Unused Properties
Edge Color: Double-Click to create...
Edge Font Face: Double-Click to create...
Edge Font Size: Double-Click to create...
Edge Label: Double-Click to create...

Exercise

- Two independent parts
  - Transcriptional regulatory networks motifs
    - Transcription factor autoregulation
    - Transcription factor crosstalk
    - Feed forward loops
    - Co-regulated genes
  - Gene co-expression visualisation
    - Gene expression profiles → correlation matrix
    - Correlation matrix → find gene-protein interactions
    - Visualization of gene-protein interactions

Exercise – R hints

- Package igraph (CRAN)
- read.table() – read tab delimited files
- as.matrix() – converts data to matrix form
- cm <- cor(data, method=″pearson“) – calculate correlation coefficient
- cor.test() – calculate p value for each gene–gene correlation
- write.table() – writes data to file

Exercise – Cytoscape usage

- Import your .sif file:
  - File → Import → Network from Table
- Change network layout
  - Layout → yFiles → organic – better view of the network structure

Exercise – Sweave

- What is Sweave ?
  - Sweave is a tool that allows to embed the R code for complete data analyses in latex documents. The purpose is to create dynamic reports, which can be updated automatically if data or analysis change.
  - It is part of the R base (no package to be installed)
  - Depends on a LaTeX installation
- Install MiKTeX on the Lab PC via “Software Center”
- Test Sweave functionality using the supplied test file
- Use RStudio to create a skeleton for your report
- Sweave() – create a PDF from a .snw file