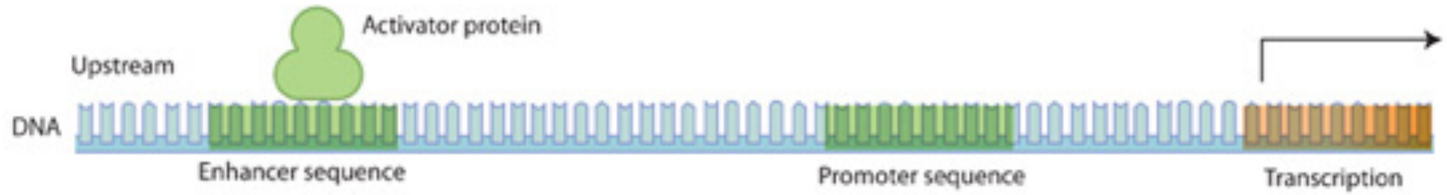
Gene Regulatory Networks

Paul Magwene

Transcriptional regulation: how are genes turned "on"?



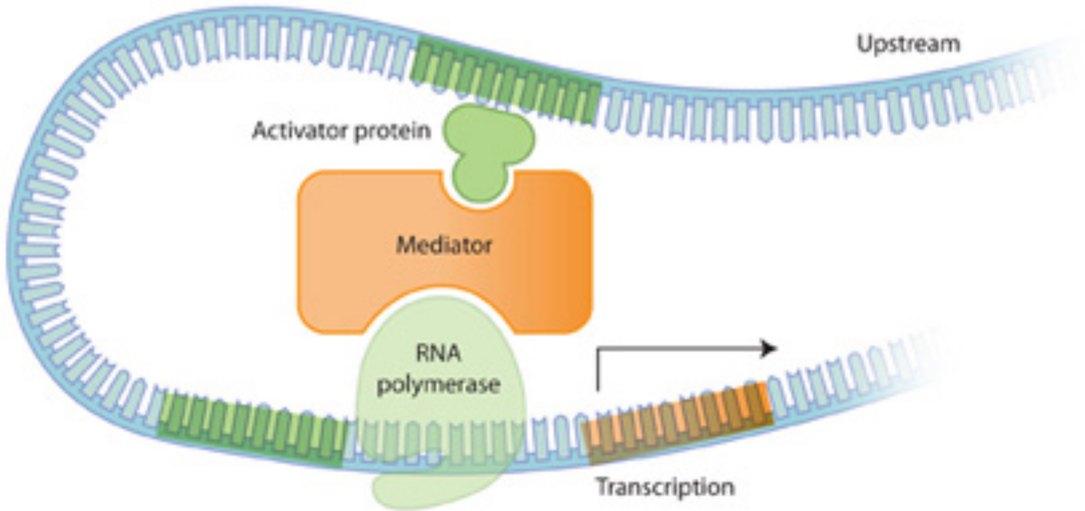


Image from: https://www.nature.com/scitable/topicpage/gene-expression-14121669/

Transcriptional regulation: repressor TFs

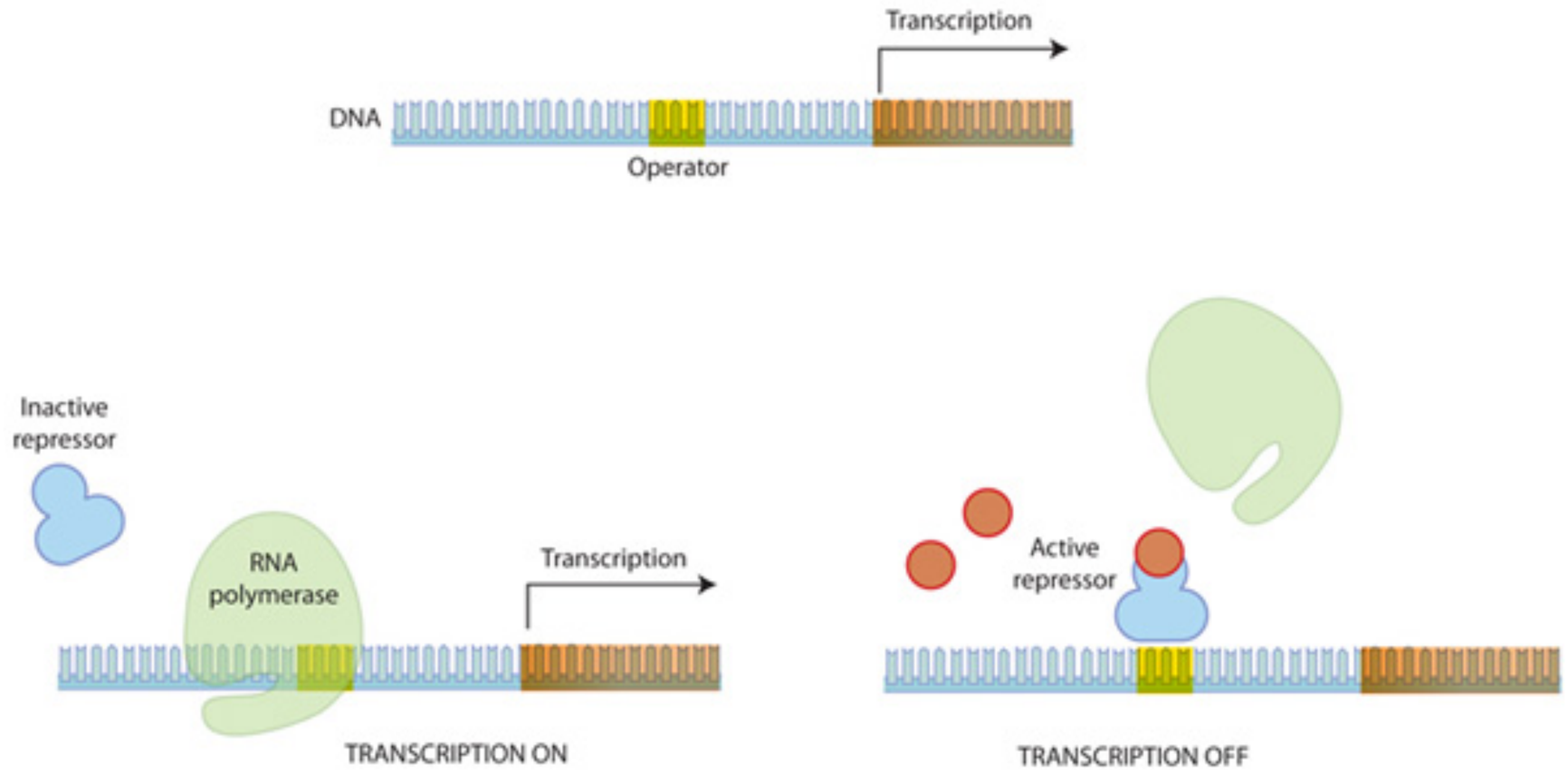


Image from: https://www.nature.com/scitable/topicpage/gene-expression-14121669/

Multiple TFs usually are often involved in the transcriptional regulation of any given gene

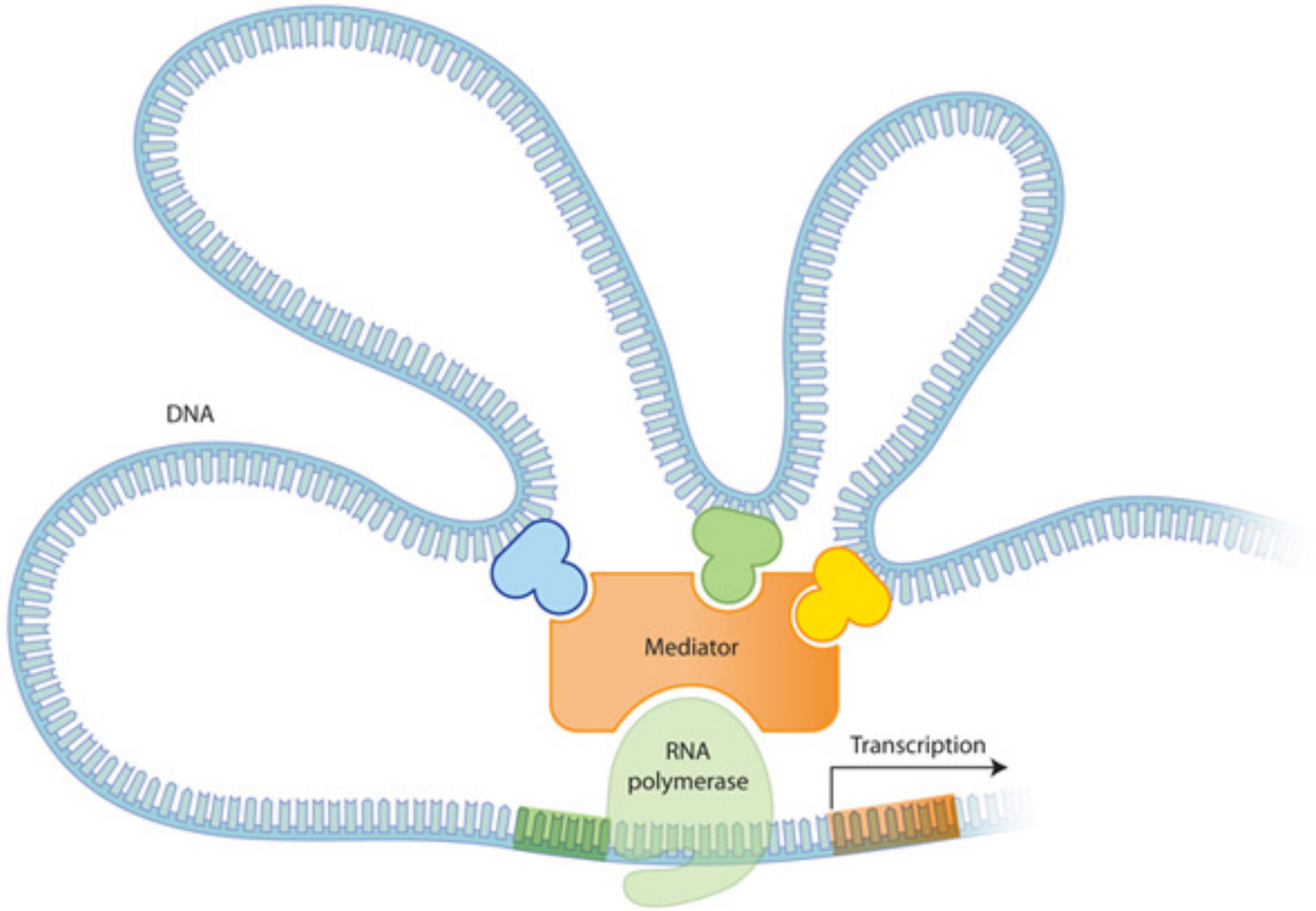


Image from: https://www.nature.com/scitable/topicpage/gene-expression-14121669/

Eukaryotic transcriptional regulation also involves chromatin remodelling

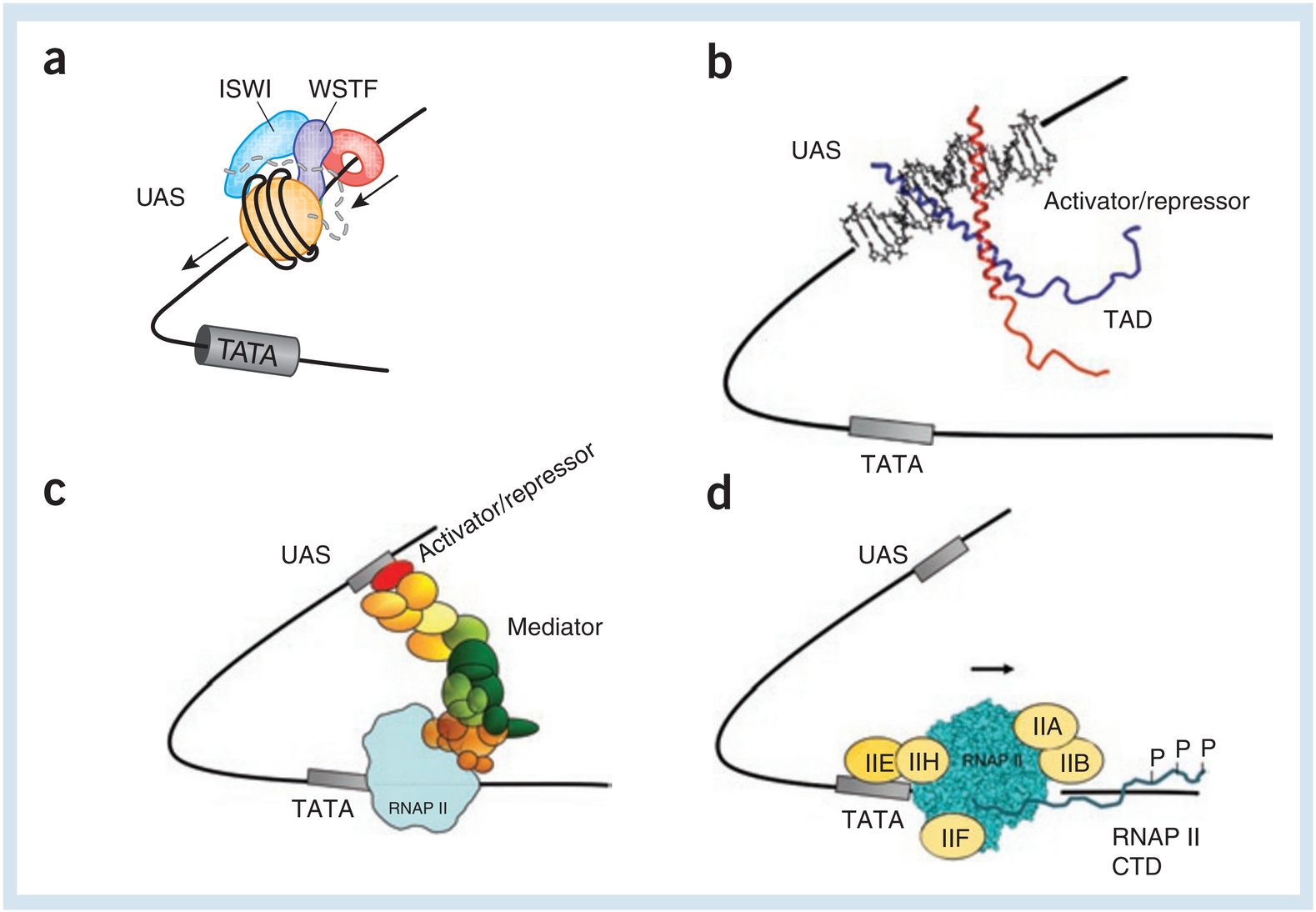


Image from Fuxreiter et al. 2008, Nature Chem Biol, doi:10.1038/nchembio.127

Measuring TF-DNA interactions using ChIP-Seq

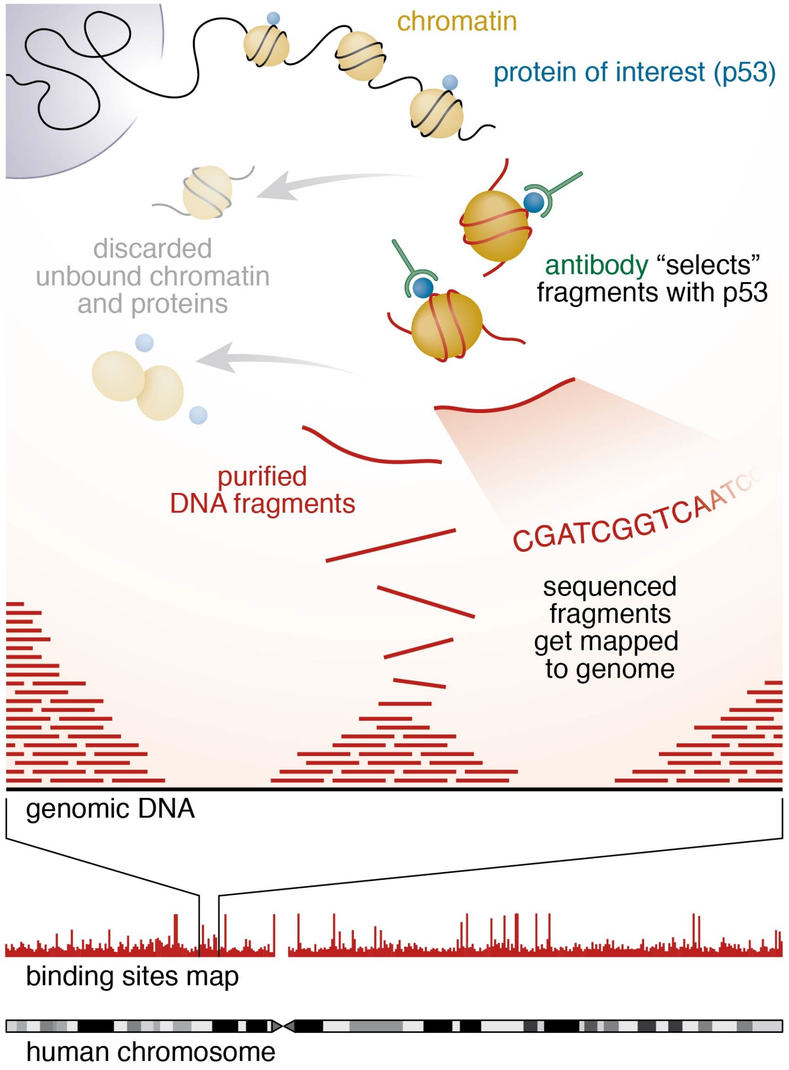
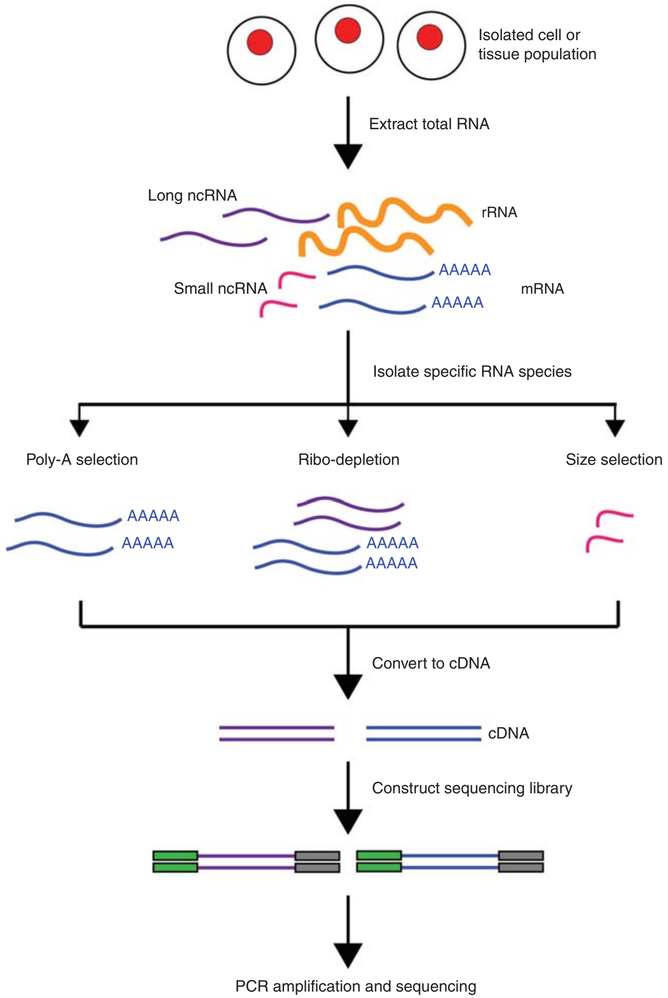
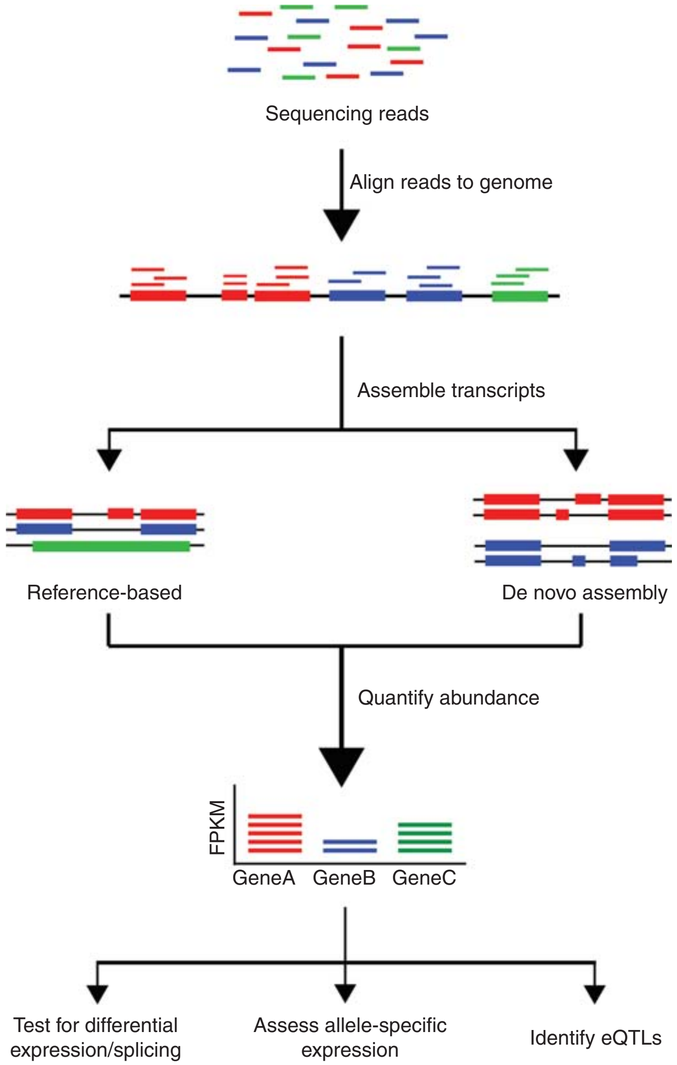


Image from https://www.bnl.gov/bnlweb/pubaf/pr/photos/2011/11/chip_seq_illustration_final-hr.jpg

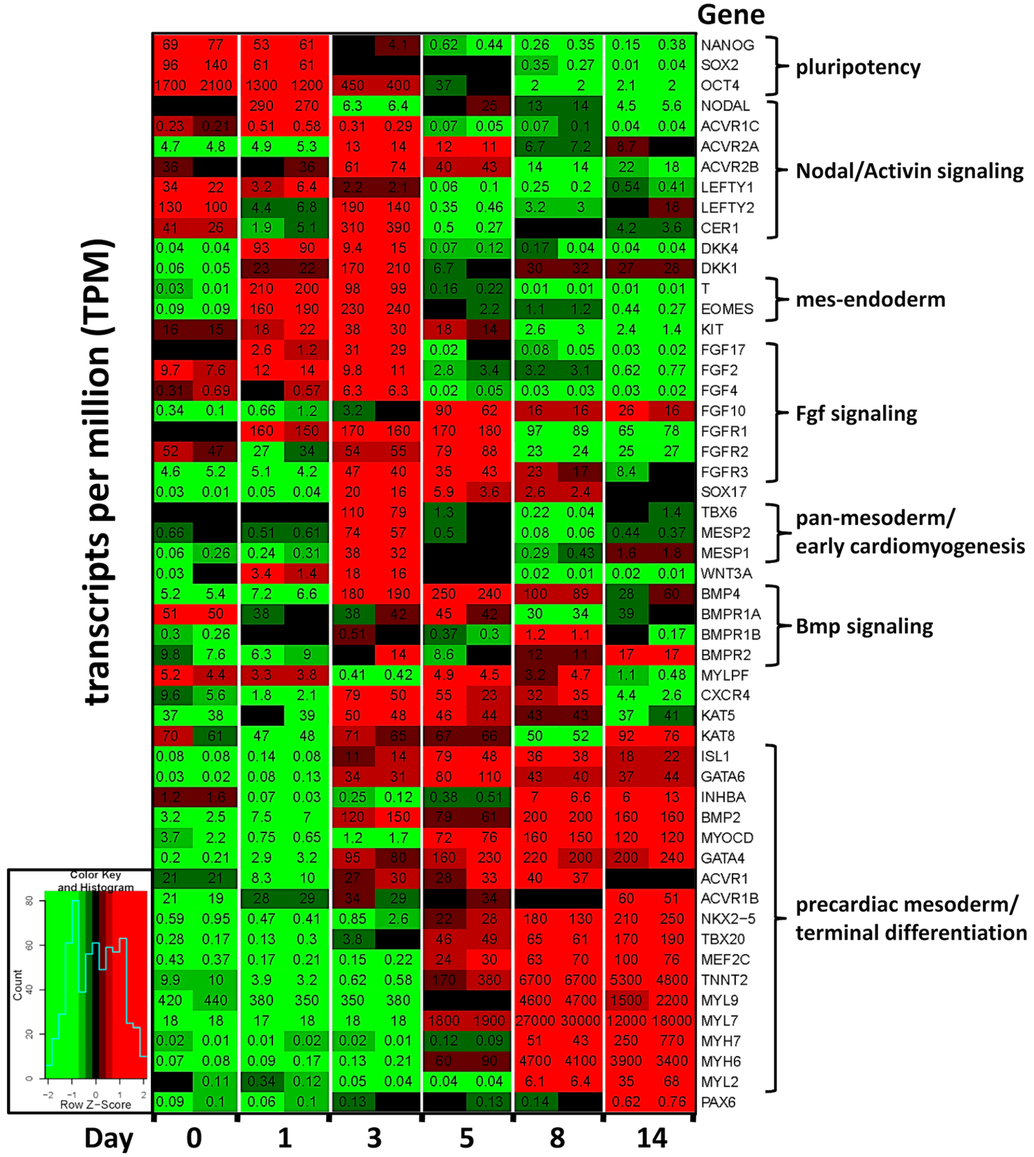
Measuring transcriptional abundance via RNA-seq





Images from Kukurba and Montgomery 2015, Cold Spring Harb Protoc; doi:10.1101/pdb.top084970

Heat maps are often used to depict patterns of gene expression



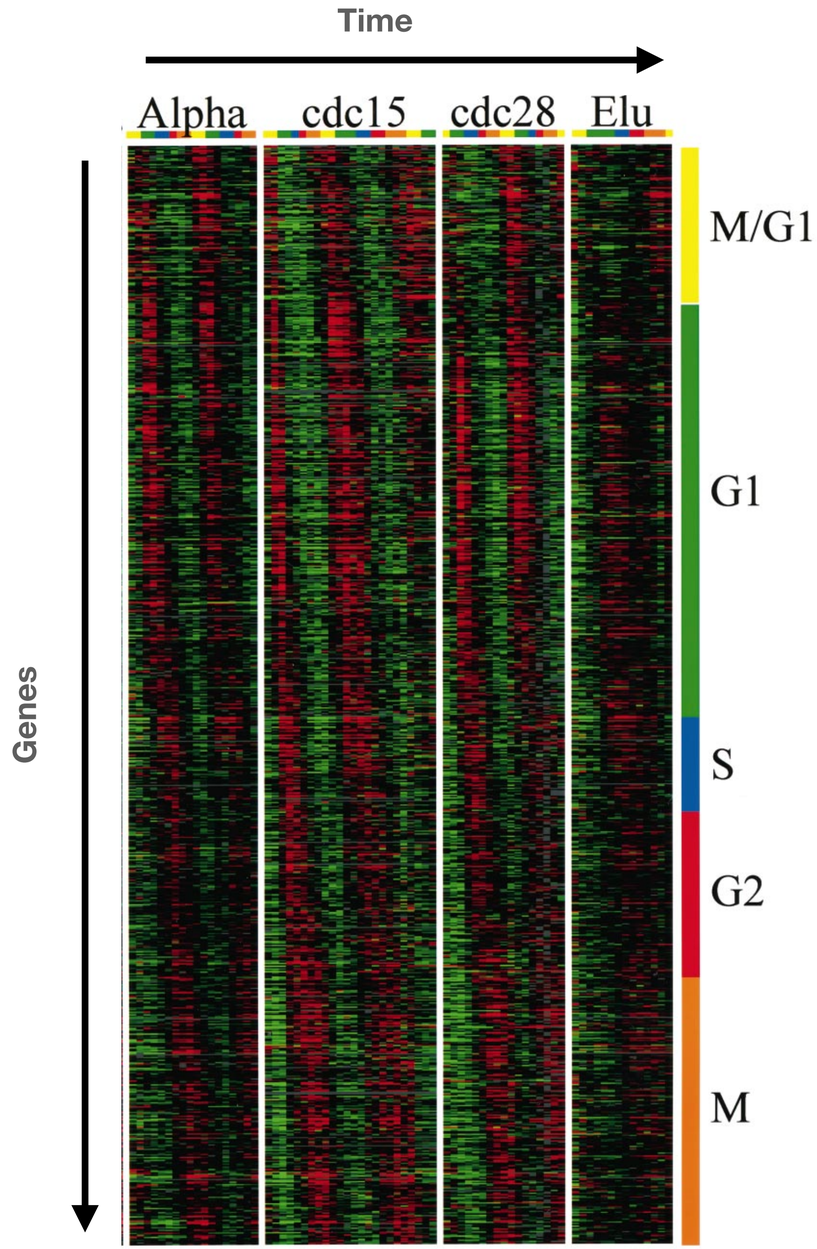


Image from Kim et al. 2015, PLoS One, https://doi.org/10.1371/journal.pone.0118670

Combining information about TF-binding and transcript abundance leads to Gene Regulatory Network (GRN) models

Budding Yeast Transcriptional Network

All Factors

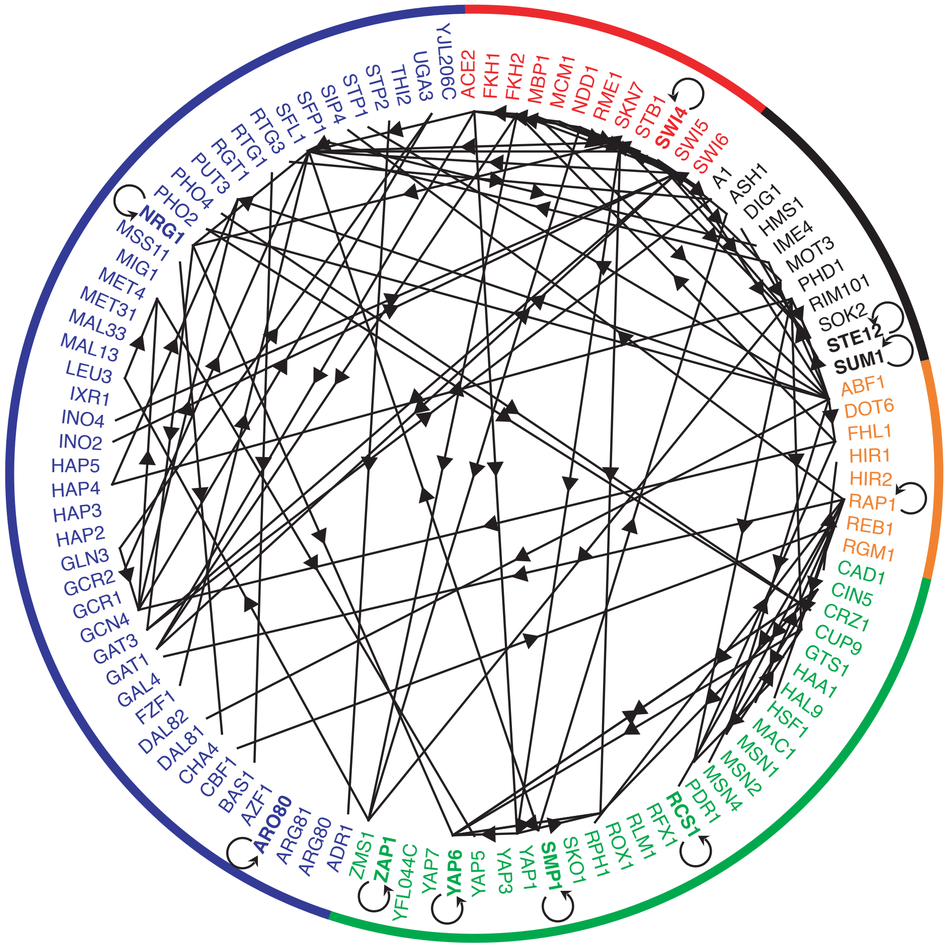
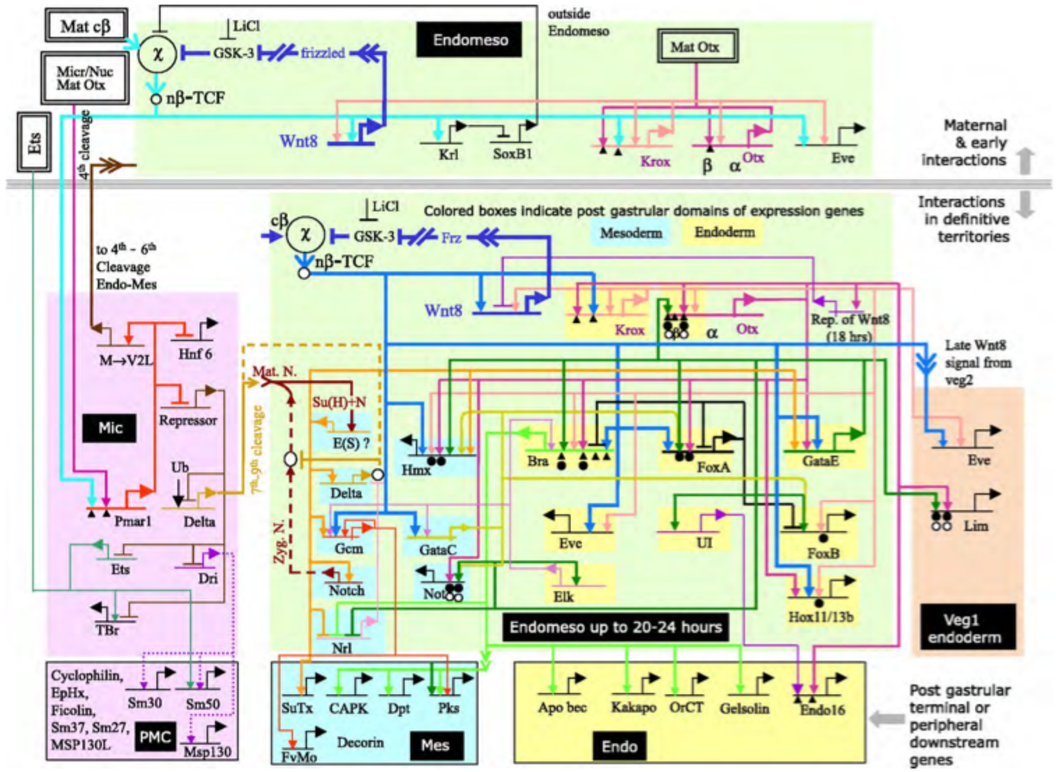


Image from Lee et al. 2002, Science, DOI: 10.1126/science.1075090

Sea urchin embryogenesis



Network motifs

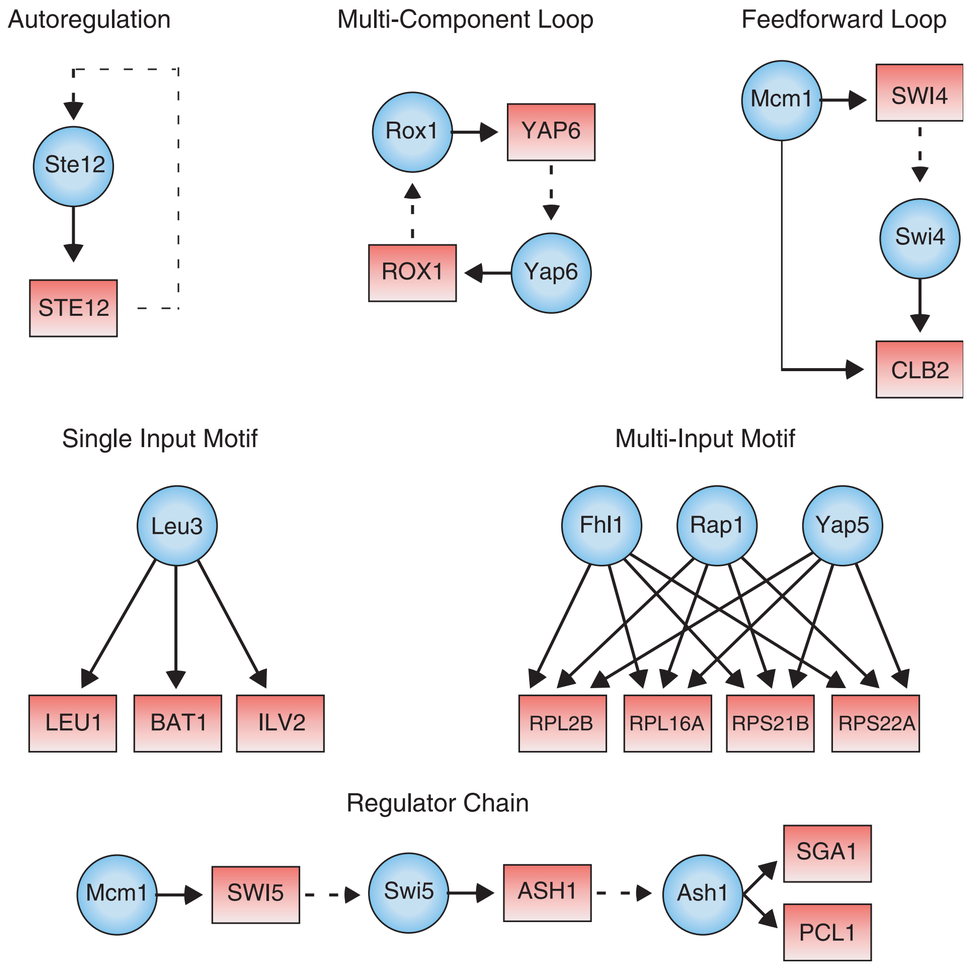
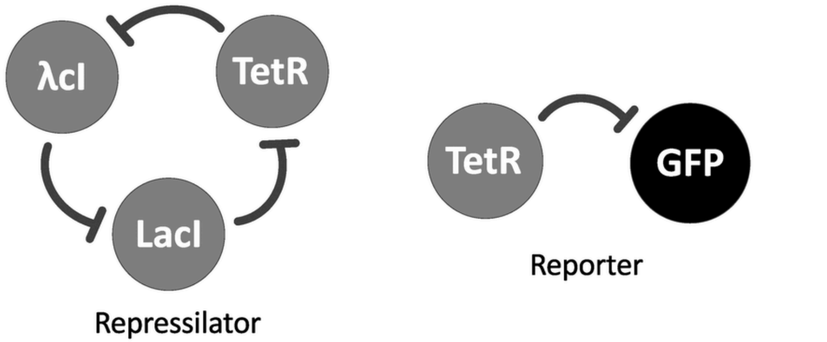
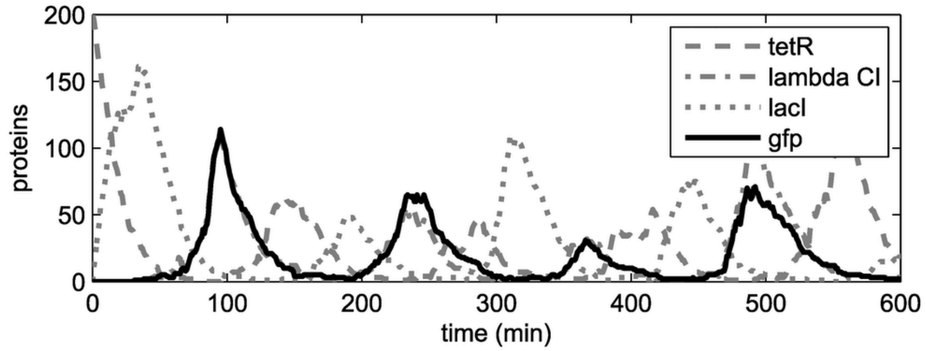


Image from Lee et al. 2002, Science, DOI: 10.1126/science.1075090

Network motif dynamics and functional behavior

Negative feedback loops
can generate oscillatory behavior





Elowitz et al., 2000. Nature. 403(6767):335-8.
Oliveira et al., 2015. Mol Biosyst. 11:1939-1945

Feed-Forward Loops
can act as noise filters

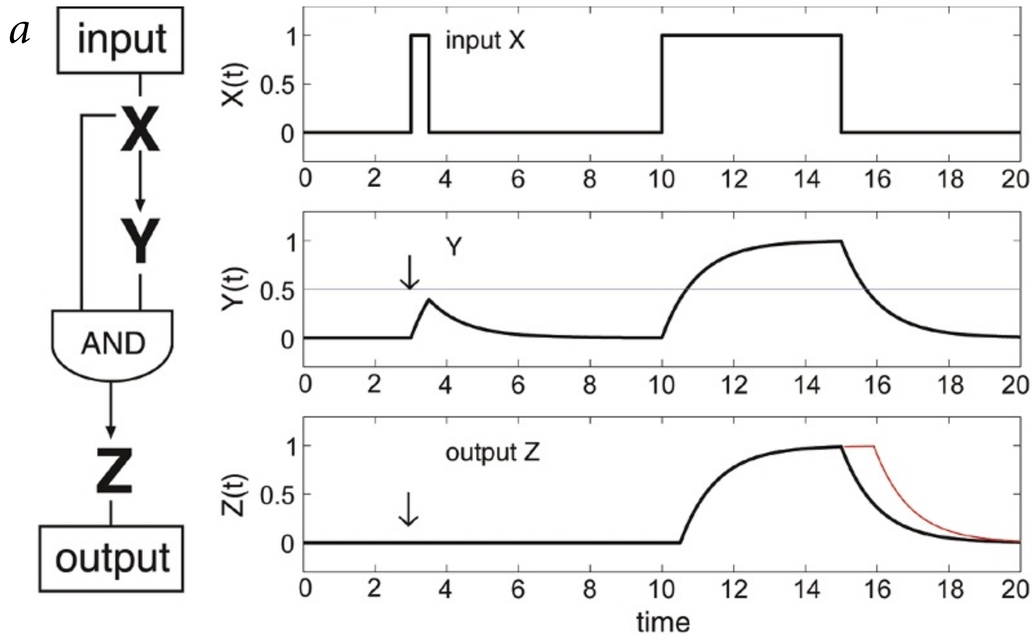


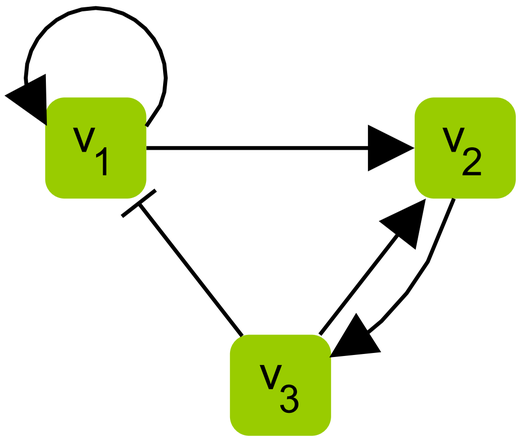
Image from Shen-Orr et al. 2002, Nat Genetics

Goal for next three class sessions

- Explore simple modeling frameworks for studying the behavior of gene regulatory networks
  - Boolean network models
  - Ordinary Differential Equation models using Boolean approximations
- Examine the kinds of dynamical behaviors that networks can generate
- Examine simple signal processing in networks

Boolean network modeling

(*a*) Network structure



(*b*) Boolean functions

$B_1(\sigma_1, \sigma_3) = \sigma_1$ OR NOT σ_3

$B_2(\sigma_1, \sigma_3) = \sigma_1$ AND σ_3

$B_3(\sigma_2) = \sigma_2$

(*c*) Truth tables

$B_1(\sigma_1, \sigma_3)$

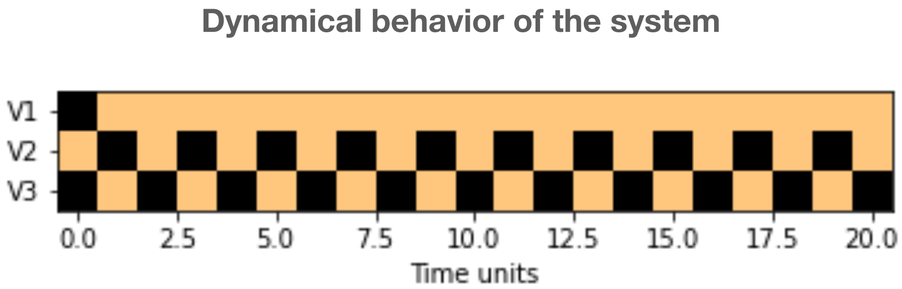
σ_1	σ_3	σ_1
0	0	1
0	1	0
1	0	1
1	1	1

$B_2(\sigma_1, \sigma_3)$

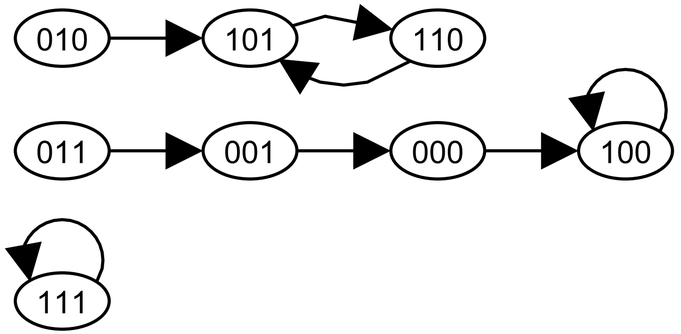
σ_1	σ_3	σ_2
0	0	0
0	1	0
1	0	0
1	1	1

$B_3(\sigma_2)$

σ_2	σ_3
0	0
1	1



(*d*) State transition graph



Images from Wang et al. 2012, Phys Biol, doi:10.1088/1478-3975/9/5/055001

A schema for Boolean modeling of biological systems

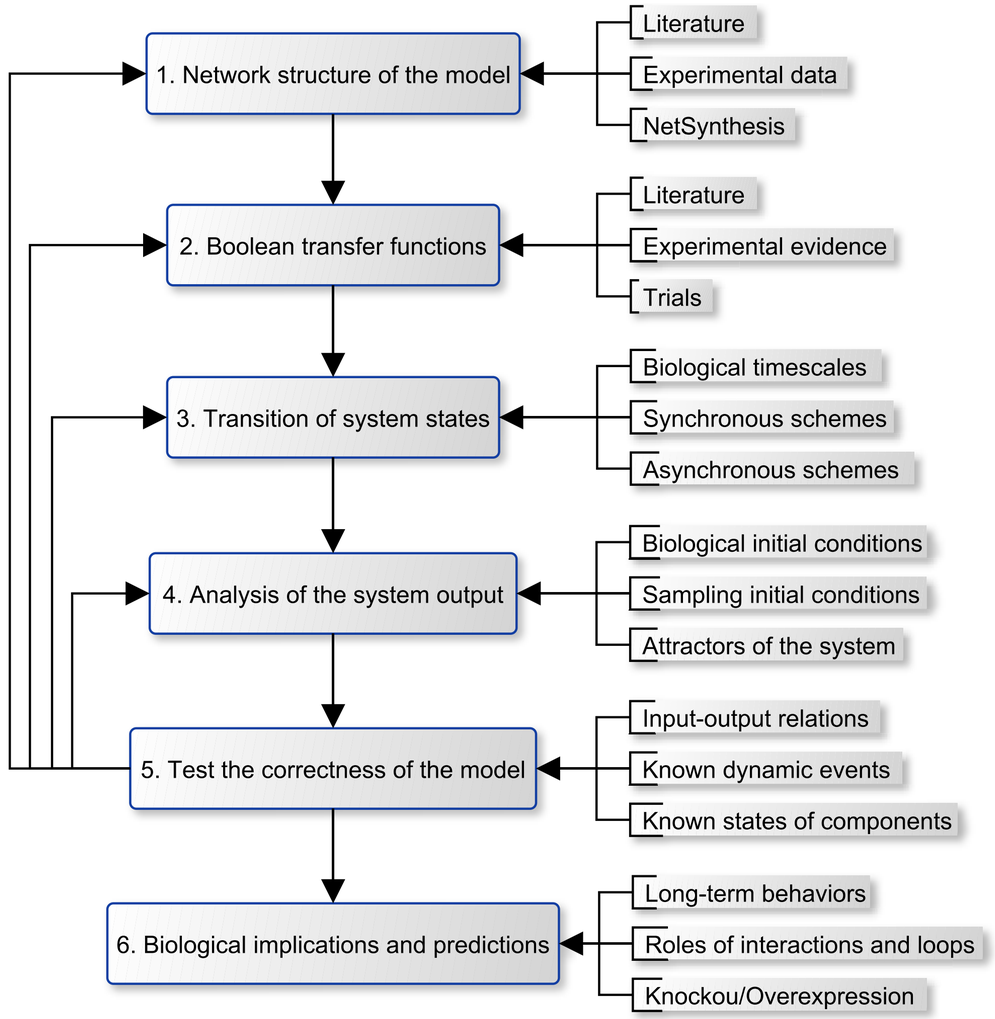


Figure 2. The main steps in Boolean dynamic modeling of biological systems.