Cellular networks

Combinatorial complexity of gene regulation

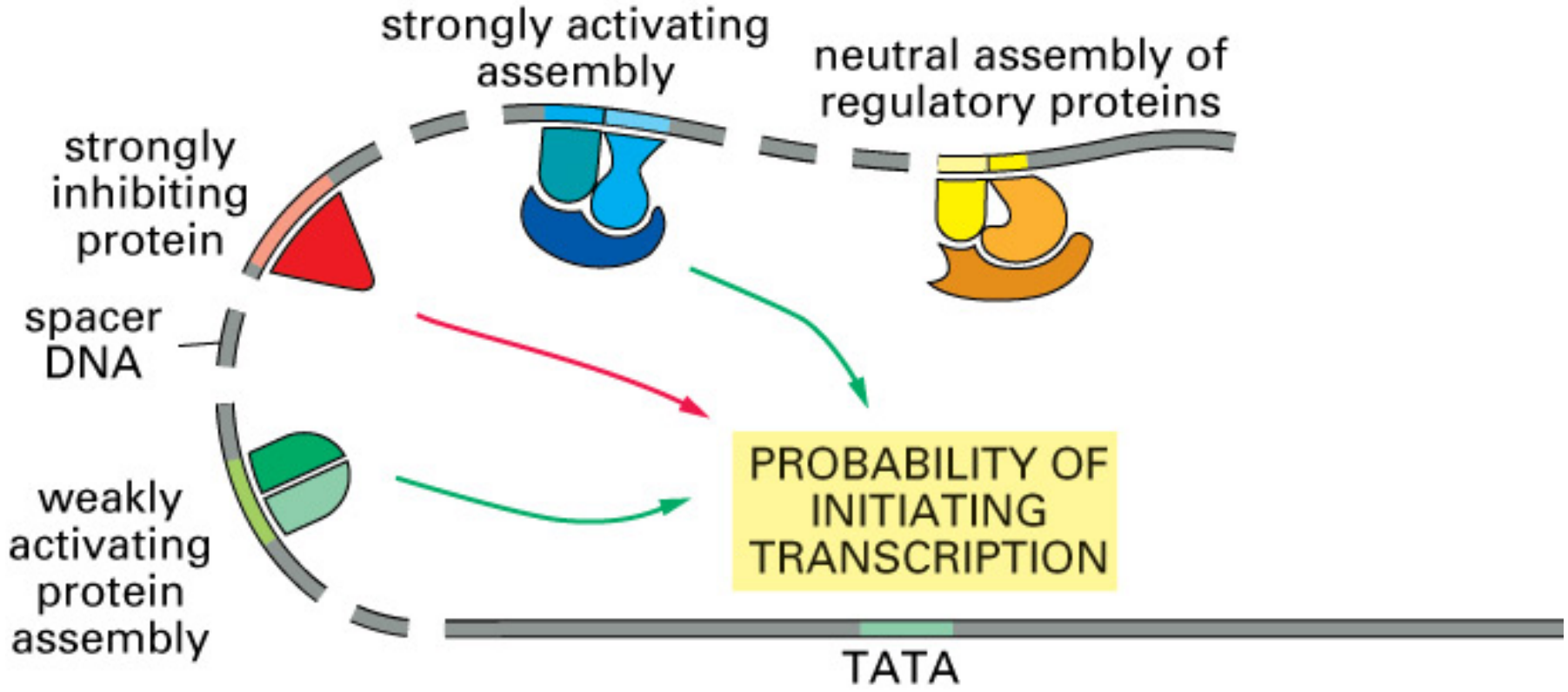
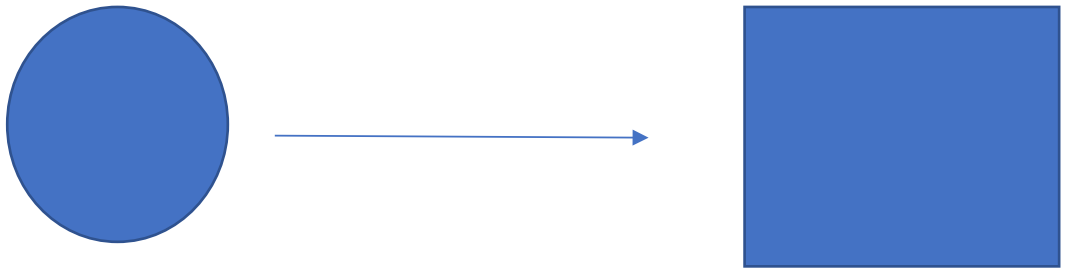


Figure 7–57. Molecular Biology of the Cell, 4th Edition.

Transcription regulatory networks (TRN)



Components of TRNs (also known as Gene Regulatory Networks (GRNS)):

Transcription regulatory network patterns

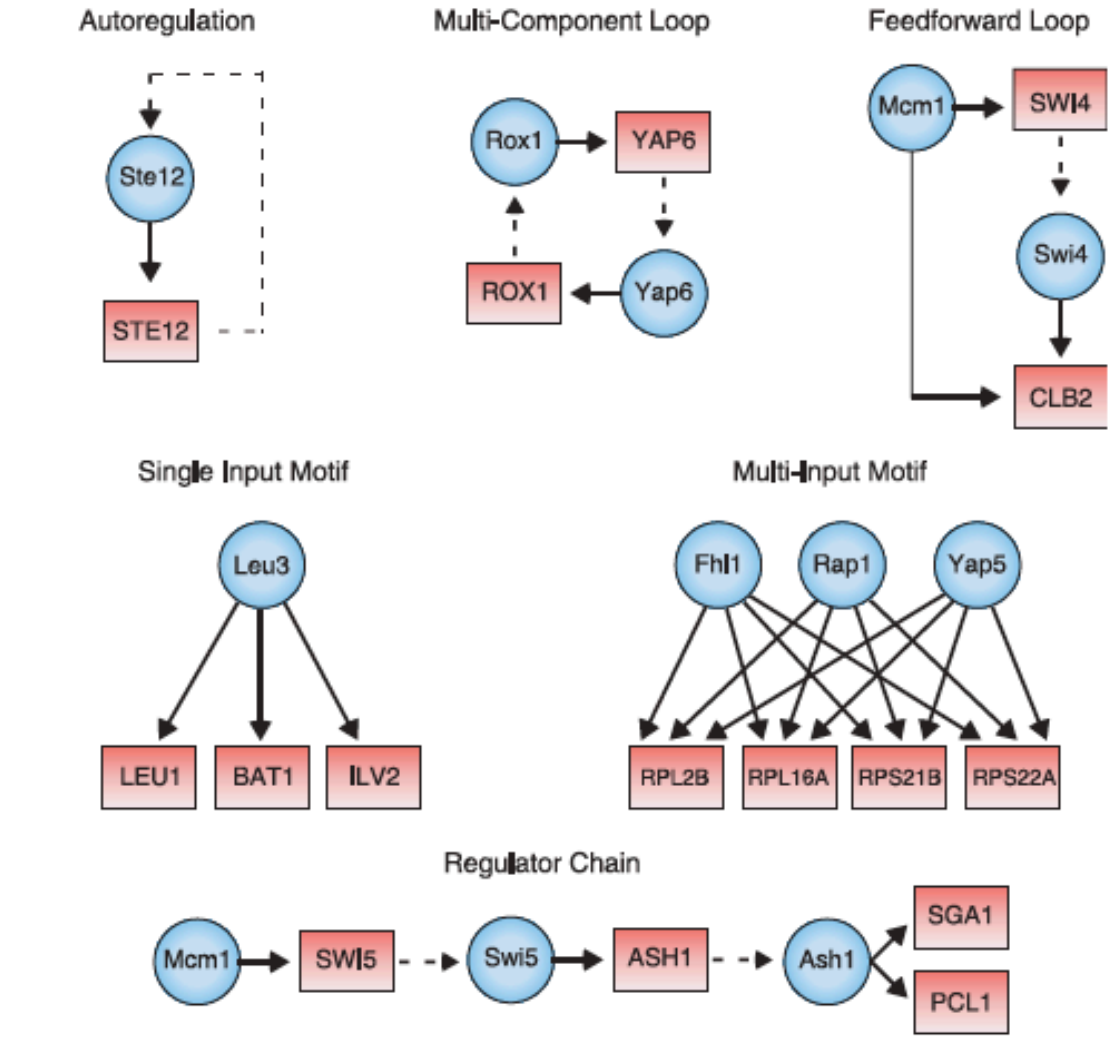
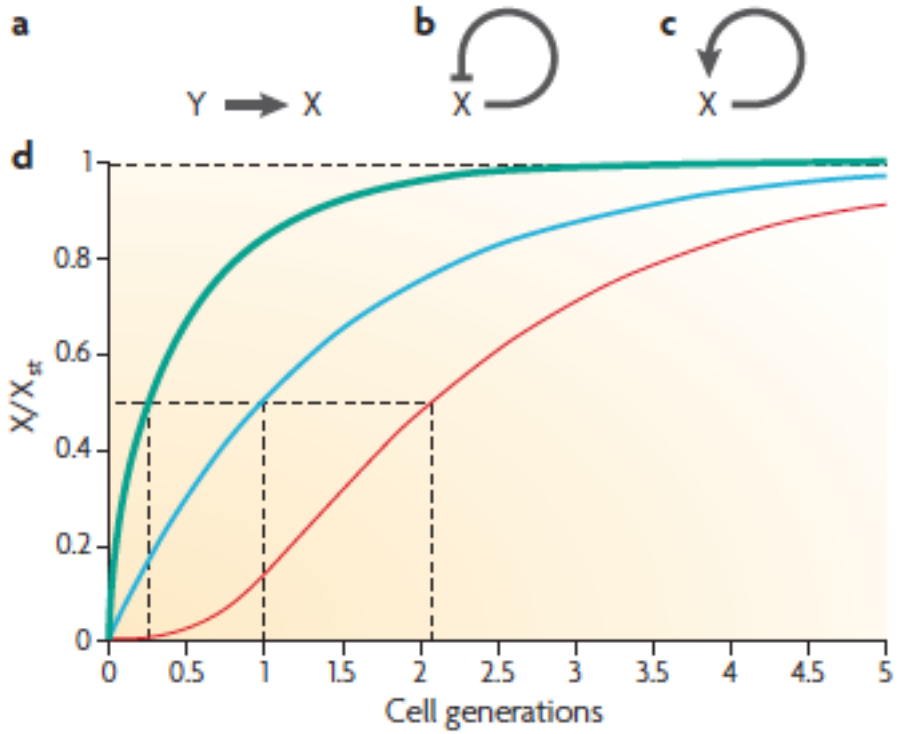
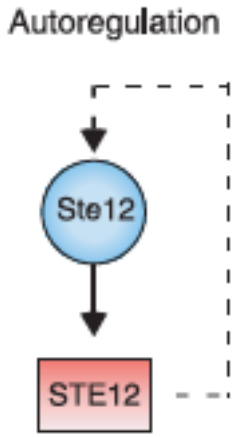


Fig. 3. Examples of network motifs in the yeast regulatory network. Regulators are represented by

Lee et al., Science 1999.

Connection: molecular mechanism → motif topology → gene expression dynamics

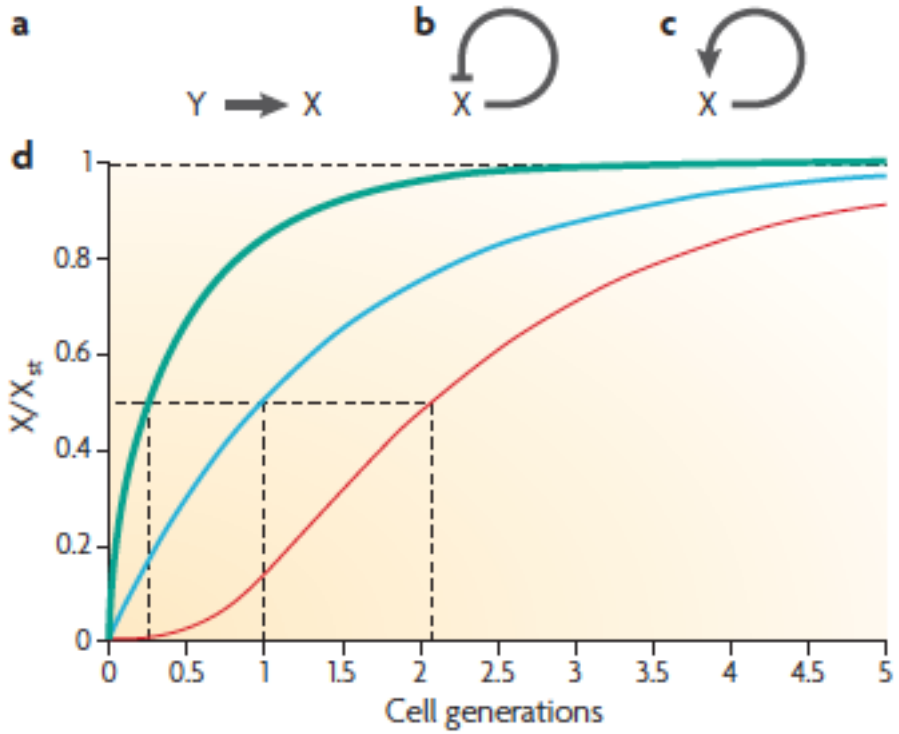


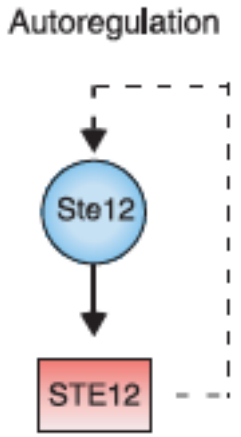


Positive autoregulation slows gene expression response time.
Negative autoregulation speeds gene expression response time.

Shen-Orr et al., 2002 Nature Genetics
Lee et al., Science 1999.

Autoregulation



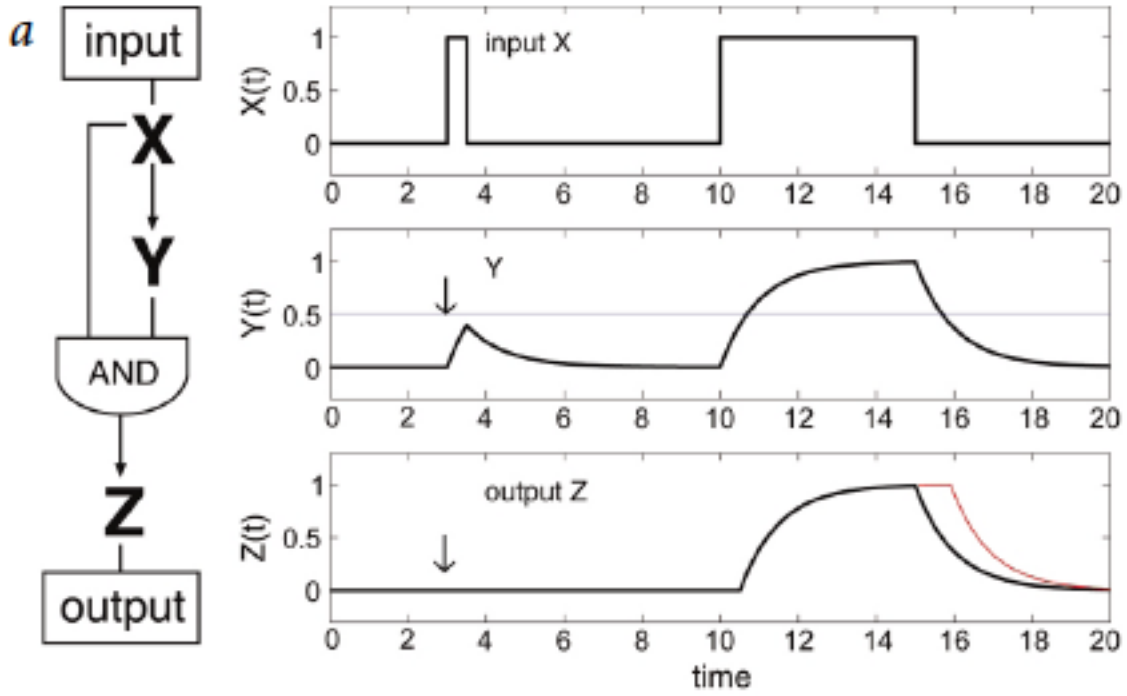


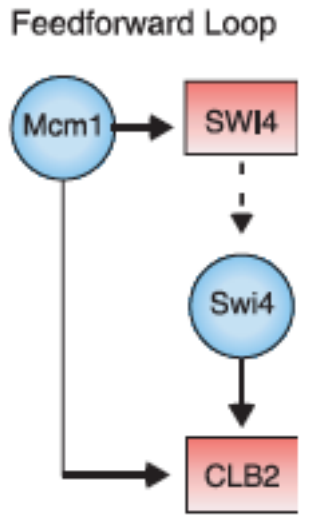
Positive autoregulation _____

Negative autoregulation _____

Shen-Orr et al., 2002 Nature Genetics
Lee et al., Science 1999.

Feed forward loops.

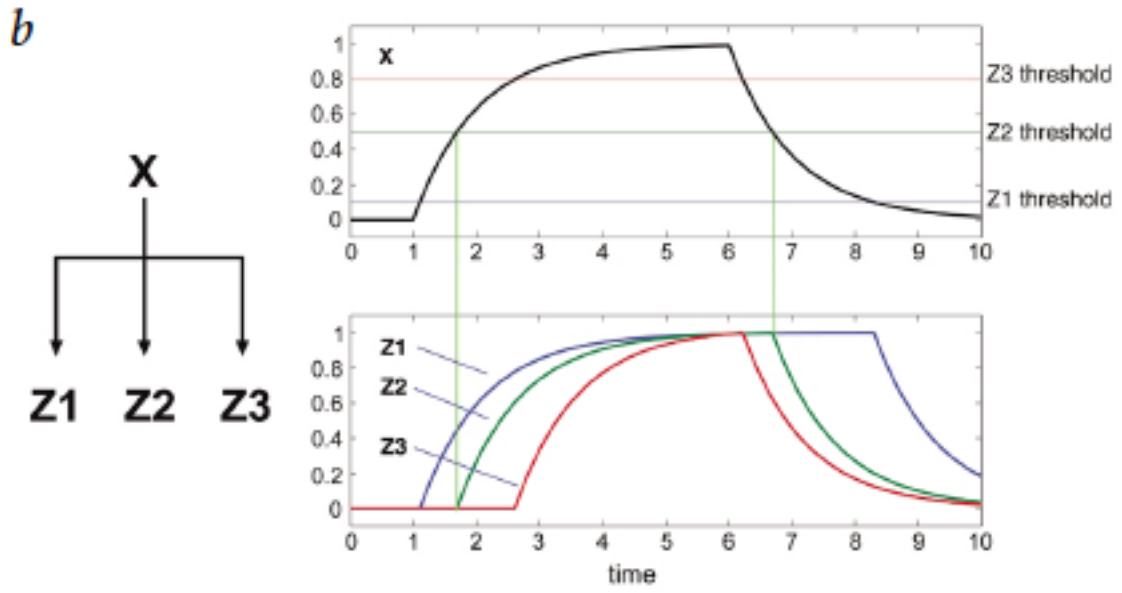


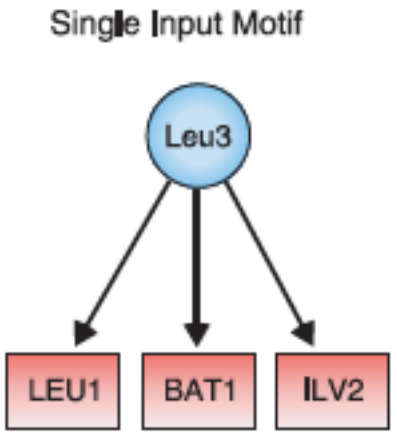


Most common is coherent FFL. Dynamic behavior is _____.

Shen-Orr et al., 2002 Nature Genetics
Lee et al., Science 1999.

Single input motifs co-regulate genes that have similar functions.

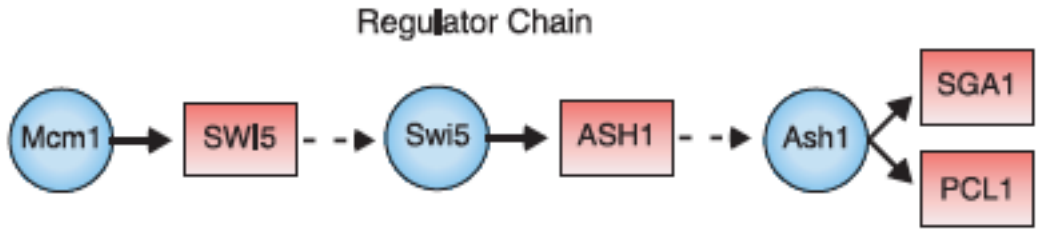




Shen-Orr et al., 2002 Nature Genetics
Lee et al., Science 1999.

Allows for _____of expression with a single regulator.
Good for _____processes or need for specific _____in complexes.
If Z1, Z2, Z3 all have same _____, allows for same timing of expression

Connection: molecular mechanism → motif topology → gene expression dynamics and function



Inter-TF gene regulatory network of yeast

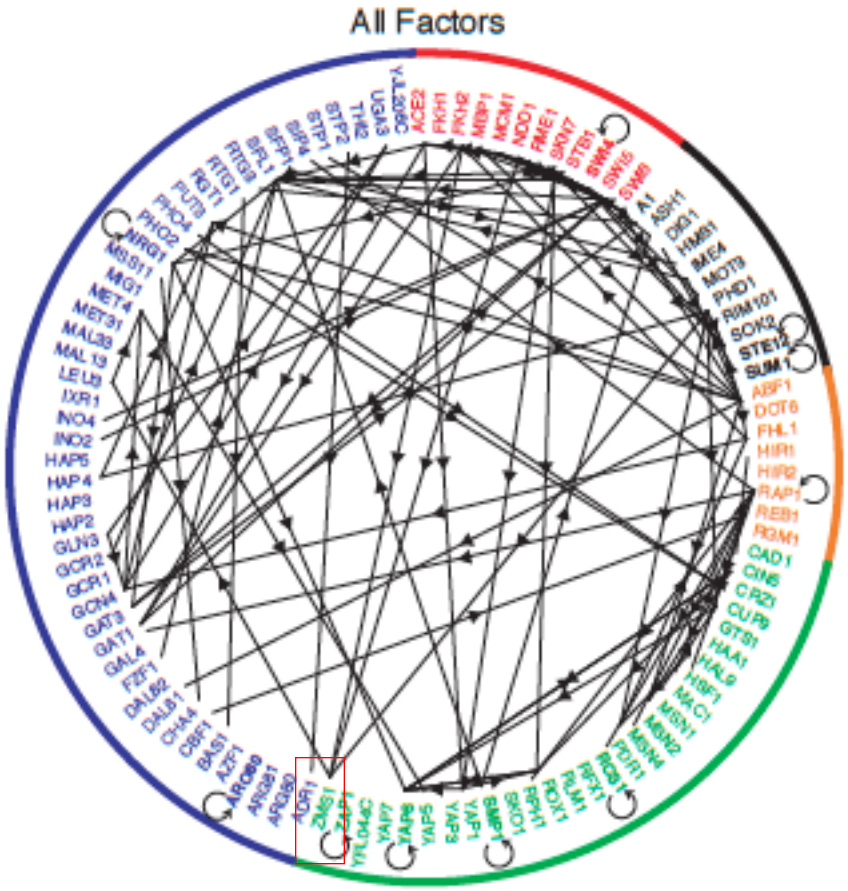


Figure 5, Lee et al., 2002

Transcription regulatory networks can produce _____ in gene expression

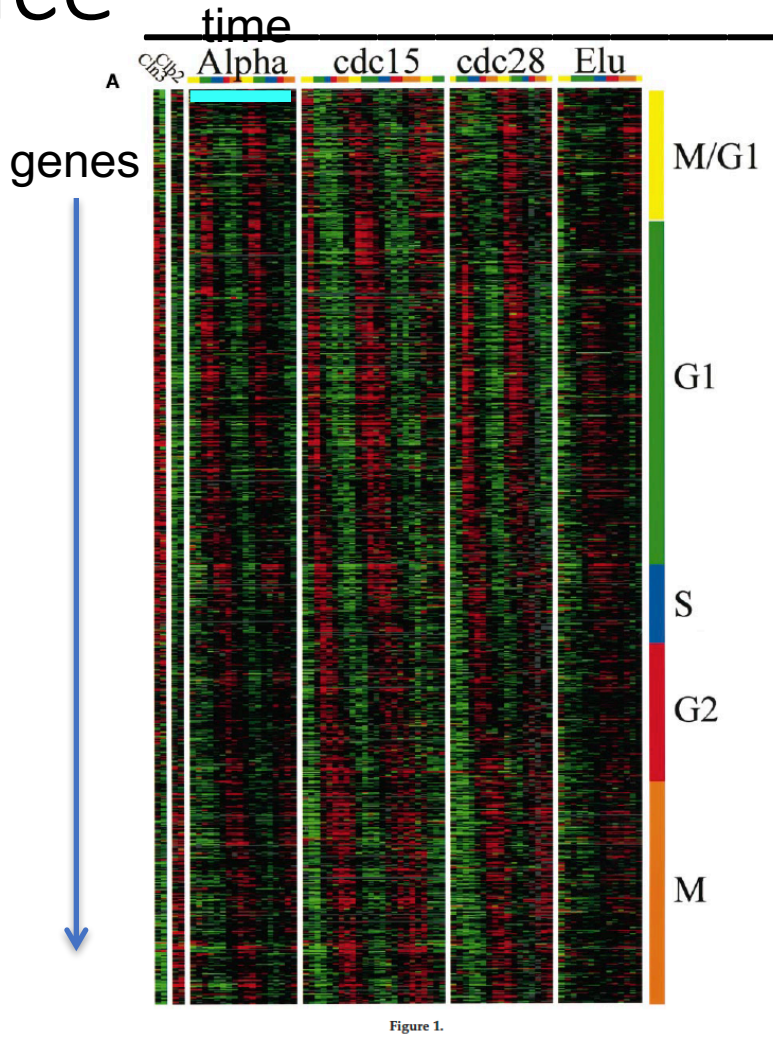
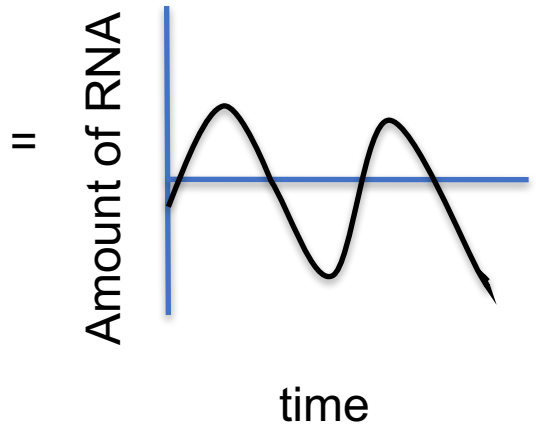


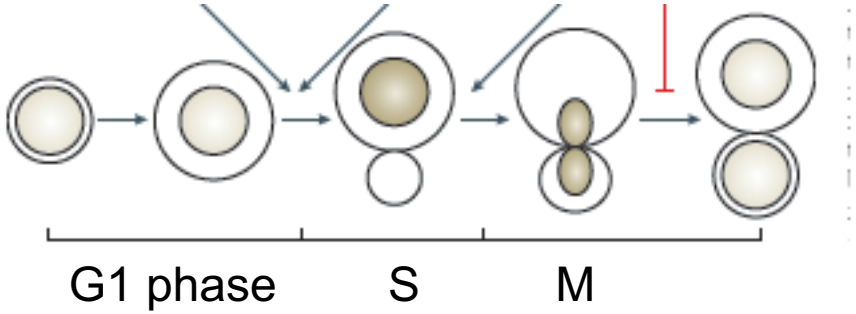
Figure 1.



"_____gene expression"

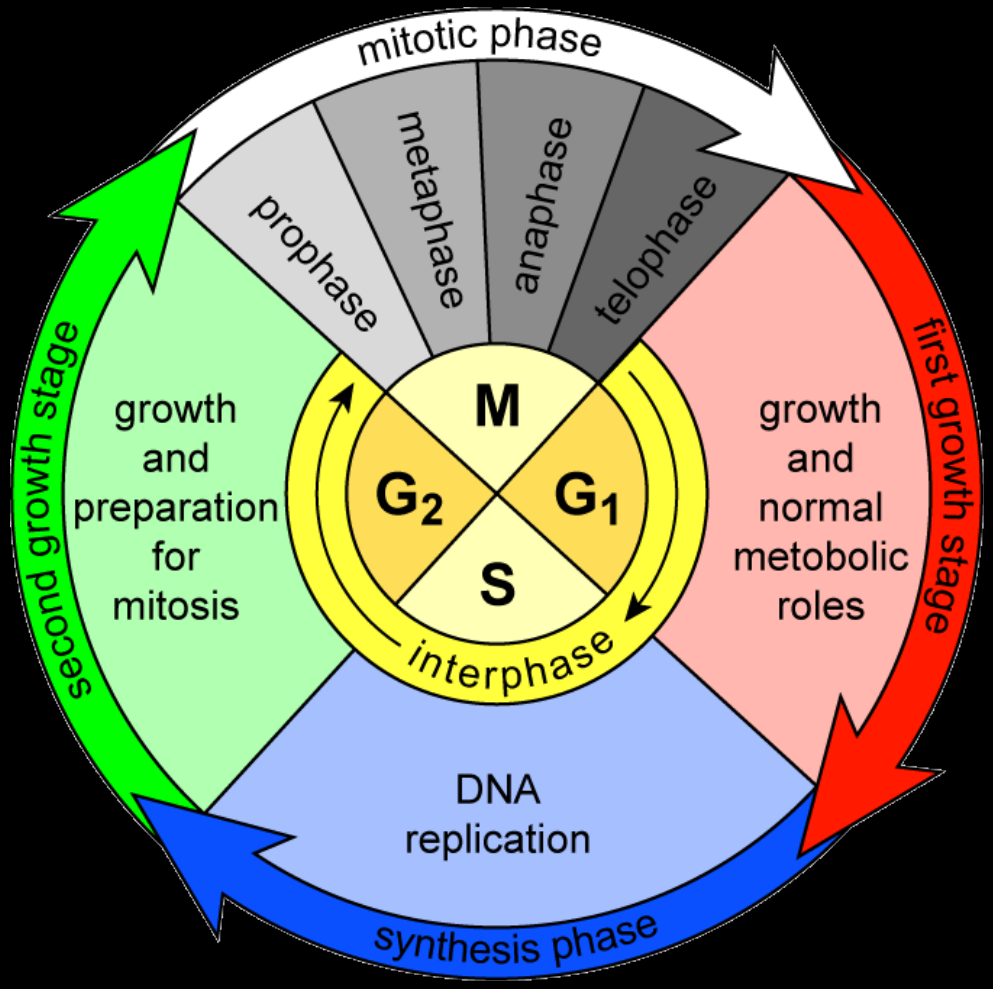
Spellman et al., Mol Biol Cell, 1998

Transcription networks produce gene expression oscillations to regulate the _____



from Bloom and Cross 2007

The cell cycle



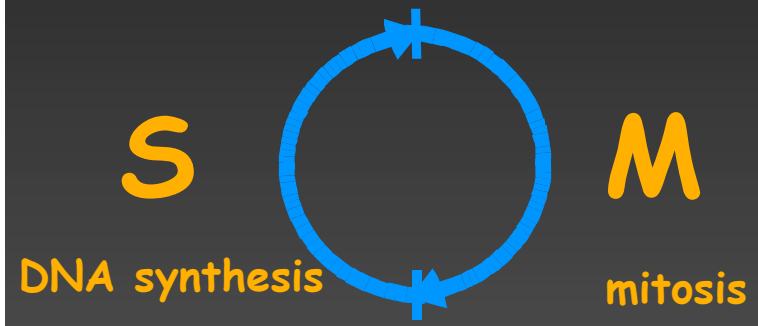
6.1

Mitosis

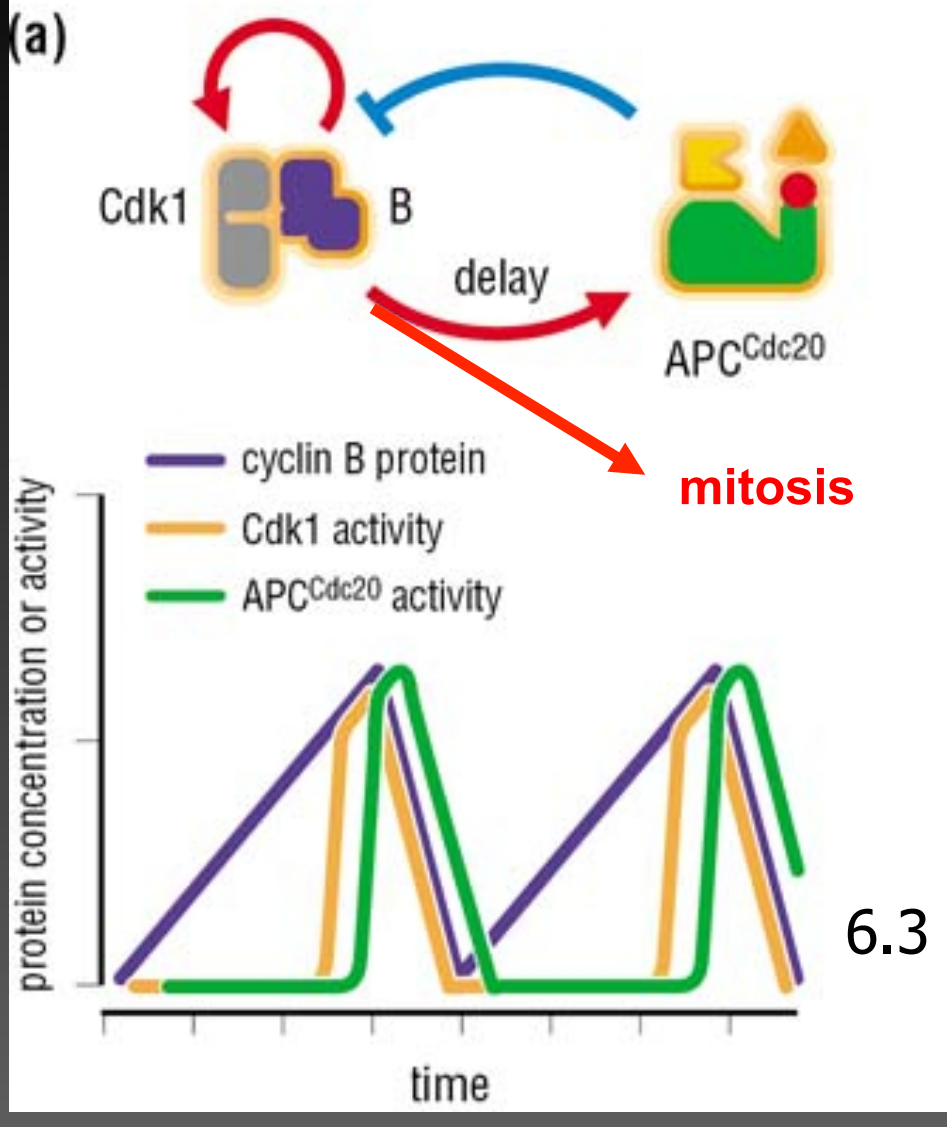
- Replicated _____, partitioning to two daughters.
- Mitosis in action: https://www.youtube.com/watch?v=2J65DoinDKU
- Think / pair / share: what would happen if cell division happened before mitosis was finished?
- How is progress through the cell cycle regulated?

A simple cell-cycle oscillator model:

embryonic systems

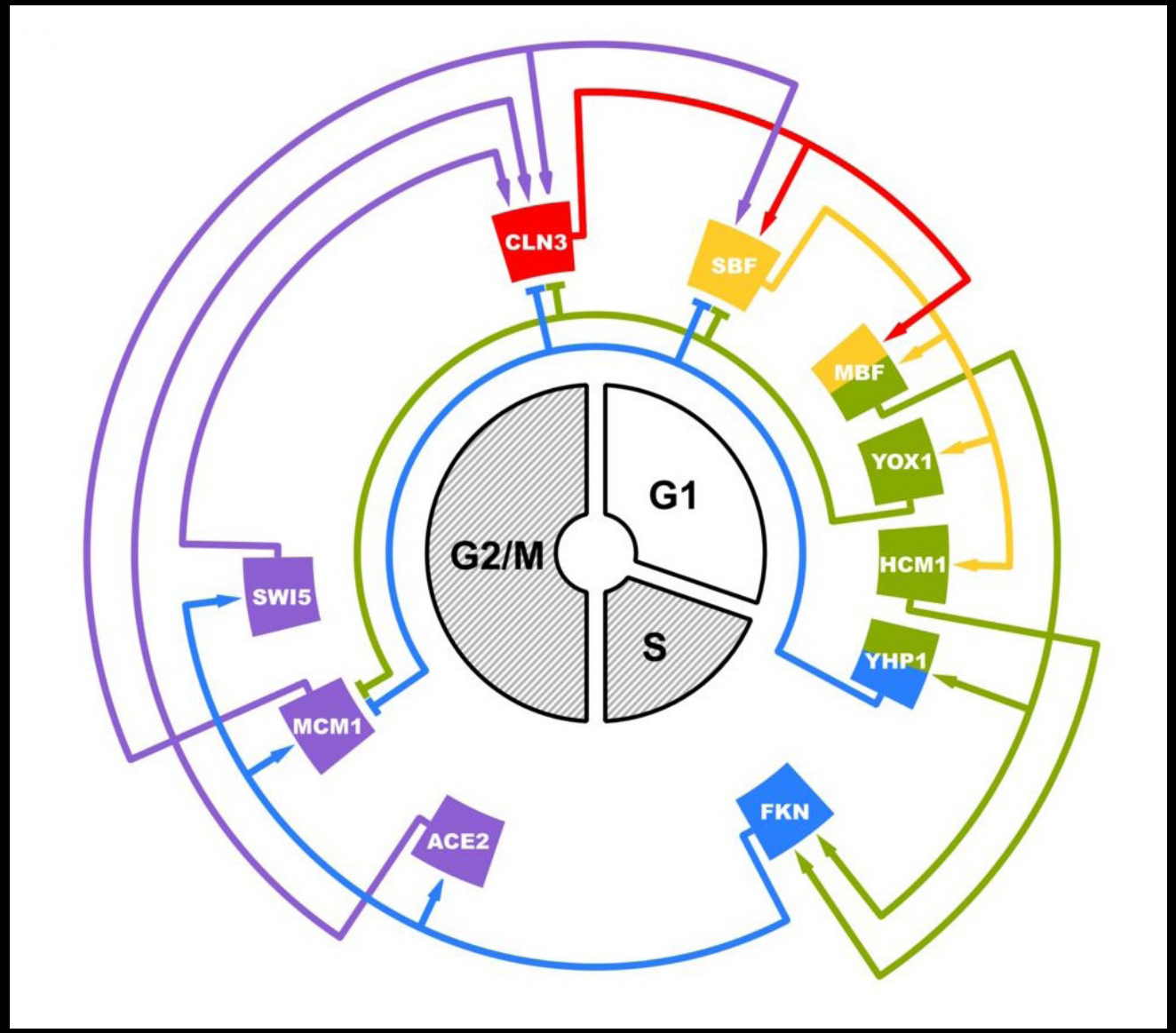


From The Cell Cycle: Principles of Control
by David O Morgan

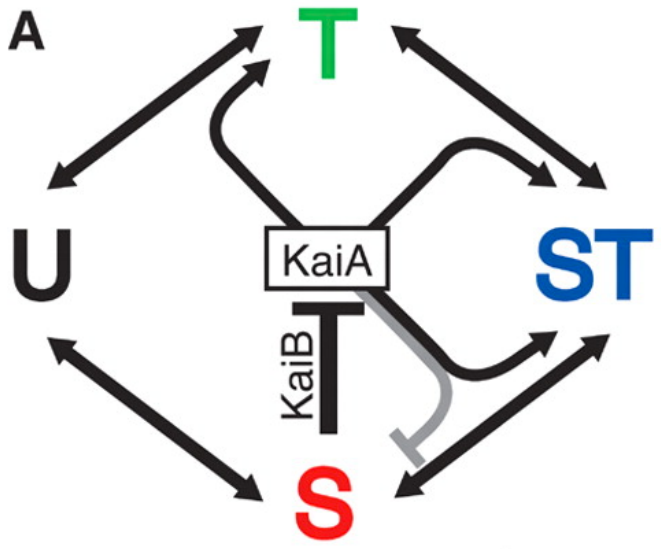


6.3

A synchronously updating Boolean model

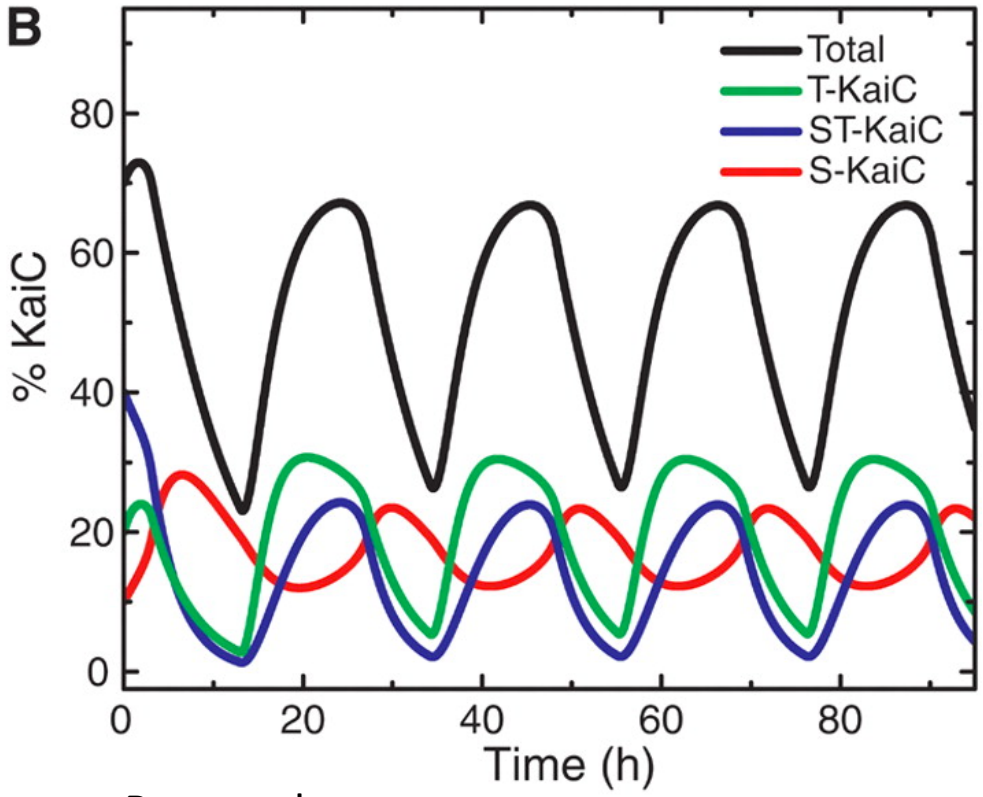


Transcription networks produce oscillations in _____ to regulate _____



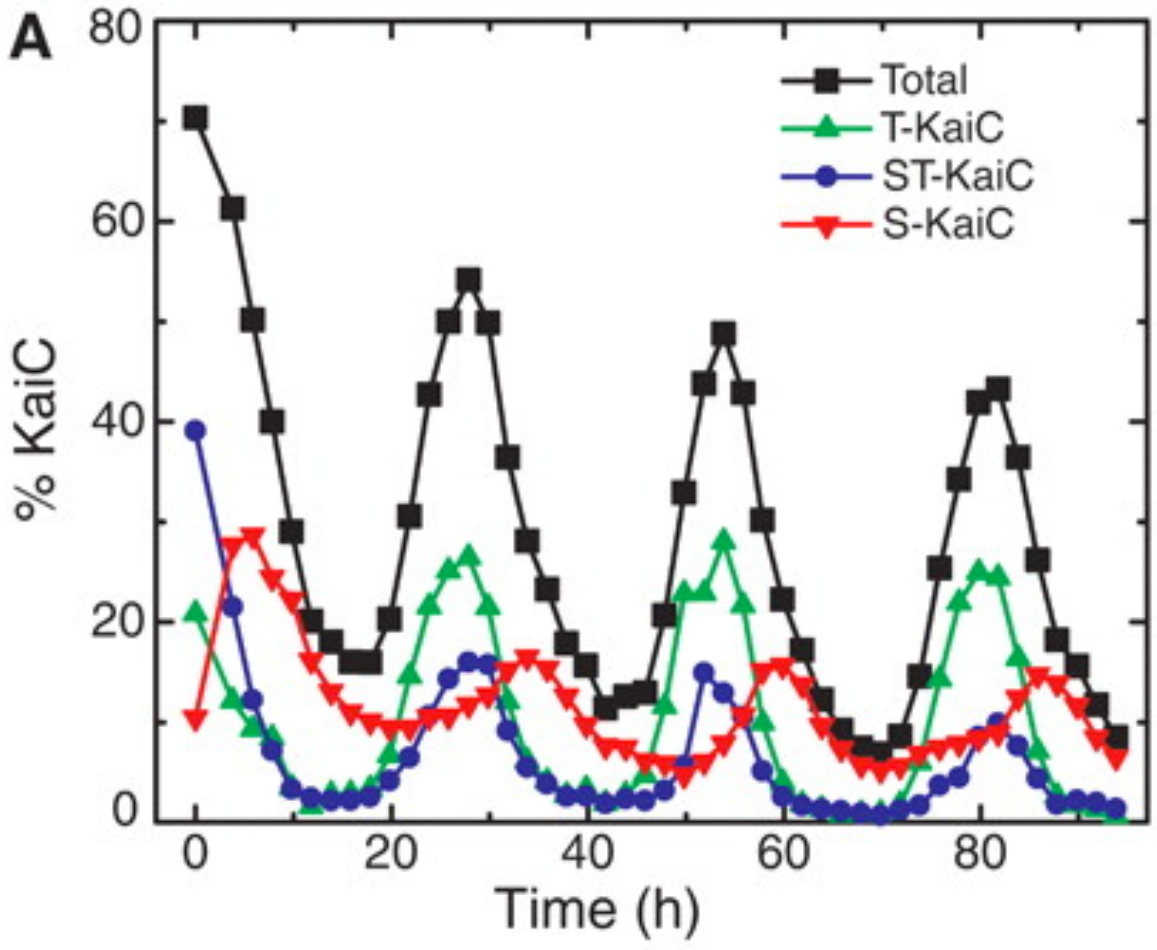
$$k_{XY}(S) = k^0_{XY} + \frac{k^A_{XY}\, A(S)}{K_{1/2} + A(S)}$$

$$A(S) = \max\{0, [\mathrm{KaiA}] - 2S\}$$



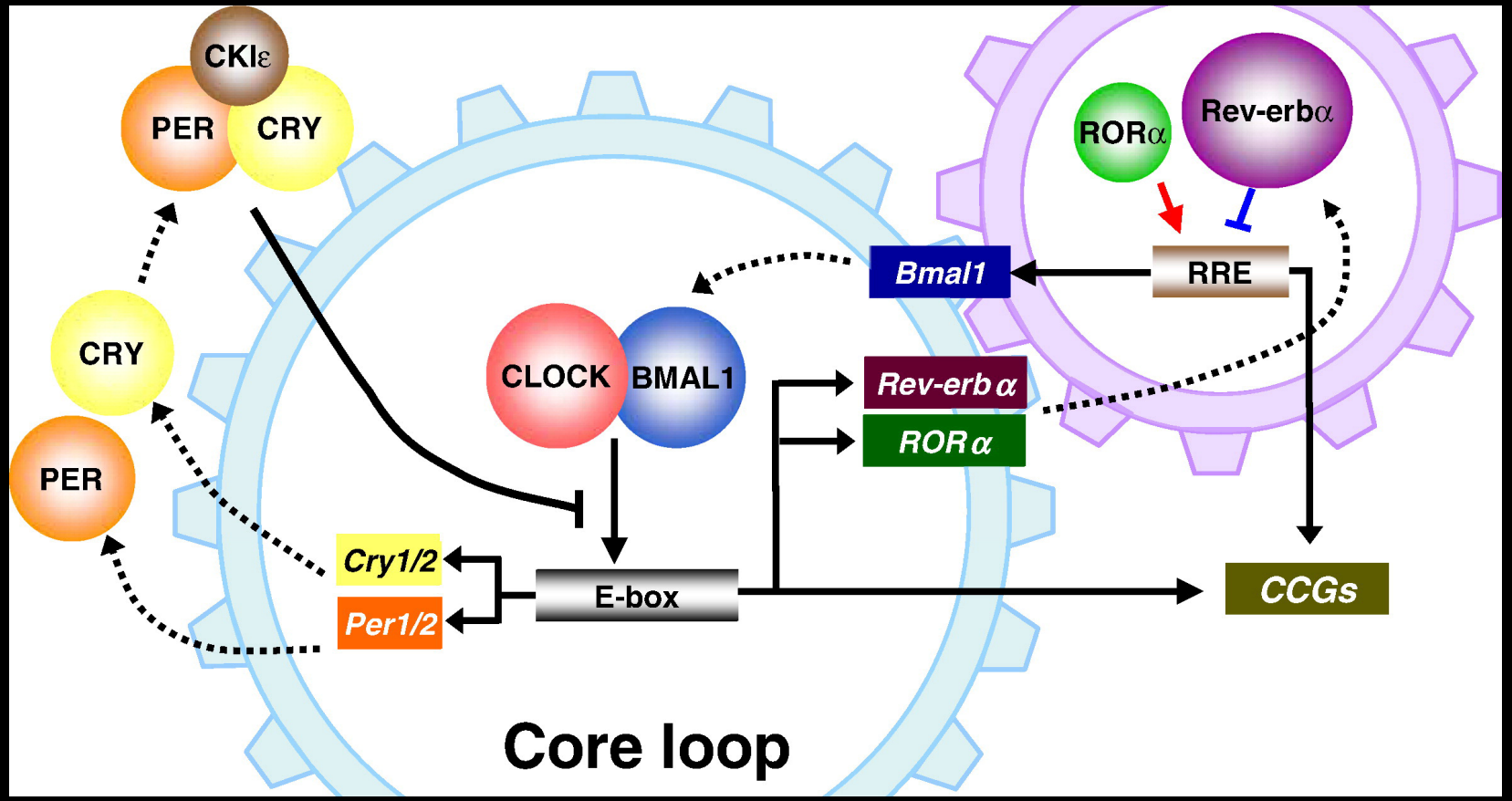
Rust et al.,
Science 2 November 2007:
Vol. 318 no. 5851 pp. 809–812
DOI: 10.1126/science.1148596

Oscillation requires phosphorylation control



Rust et al.,
Science 2 November 2007:
Vol. 318 no. 5851 pp. 809–812
DOI: 10.1126/science.1148596

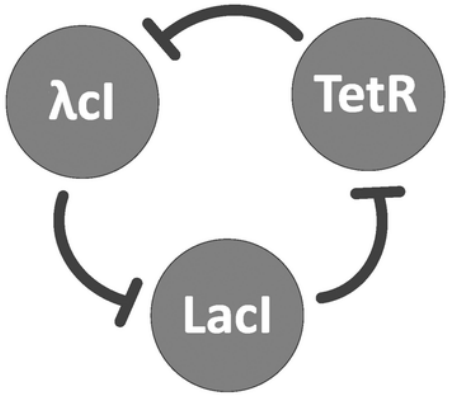
Circadian network



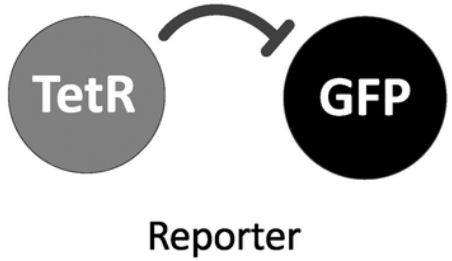
6.8

http://www.sciencedirect.com/cache/MiamiImageURL/1-s2.0-S0925443911000329-gr2_lrg.jpg/0?wchp=dGLbVlB-zSkWA&pii=S0925443911000329

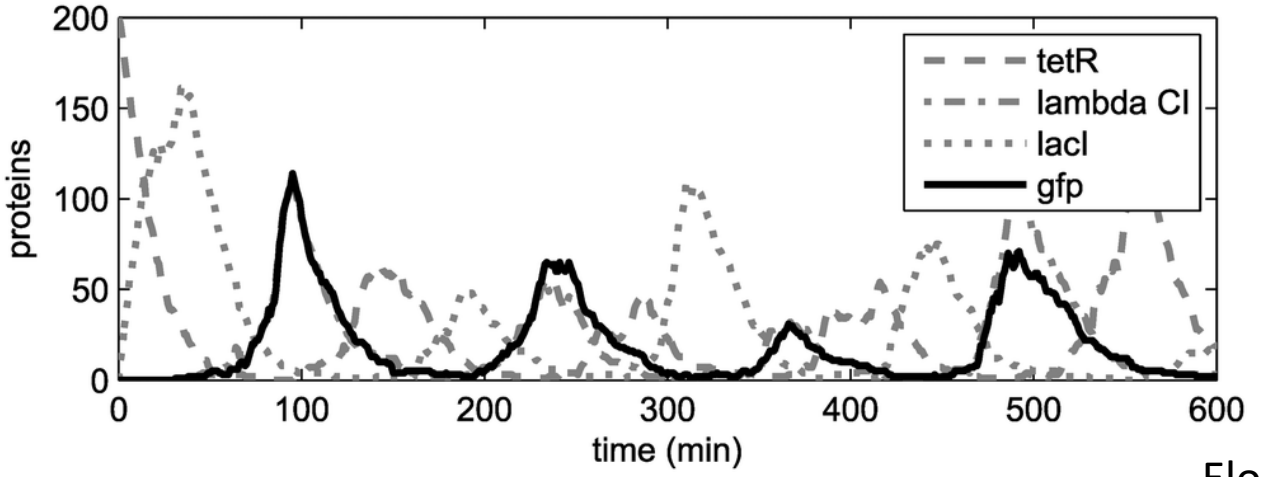
A synthetic TRN: the Repressilator



Repressilator



Reporter



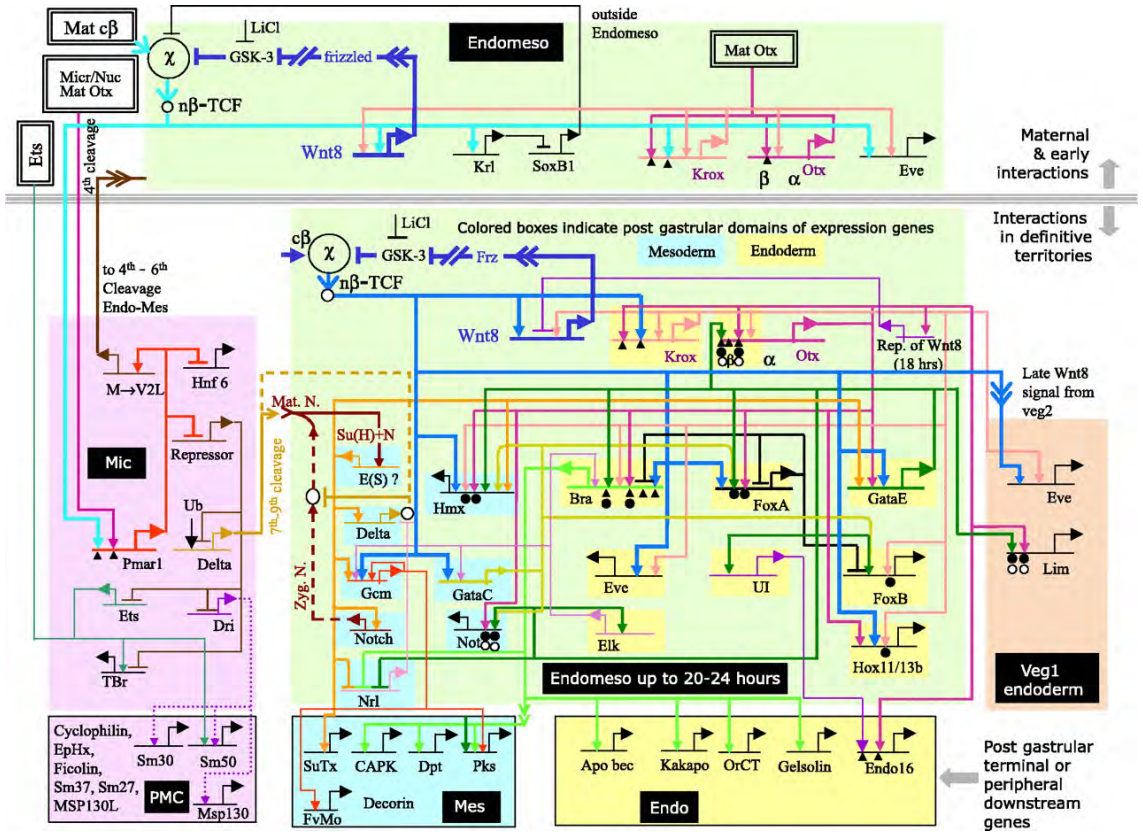
Elowitz et al., 2000. Nature. 403(6767):335-8.
Oliveira et al., 2015. Mol Biosyst. 11:1939-1945

Oscillations require negative feedback with delay

Transcriptional feedback
Protein degradation
Protein activity

Development: Ordered hierarchy

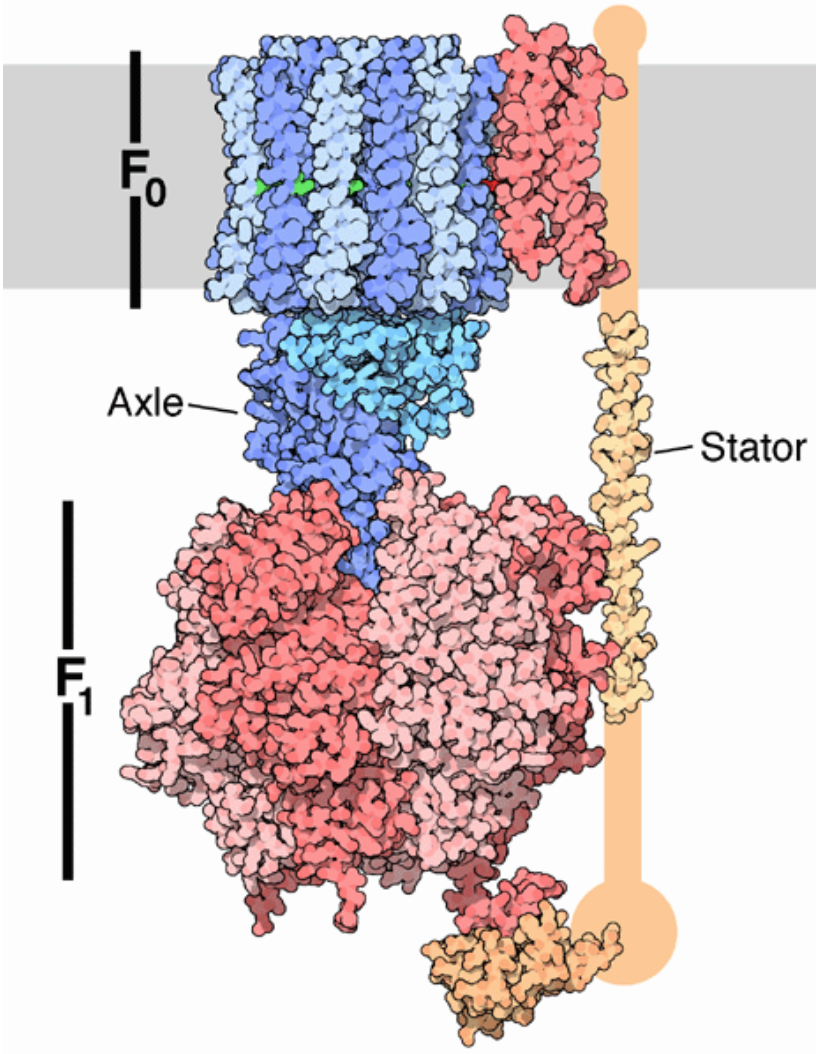
Sea urchin embryogenesis



7.1

Protein-protein interactions

- Describes how all the proteins in the cell are connected together to make functional complexes.



Protein-protein interaction networks

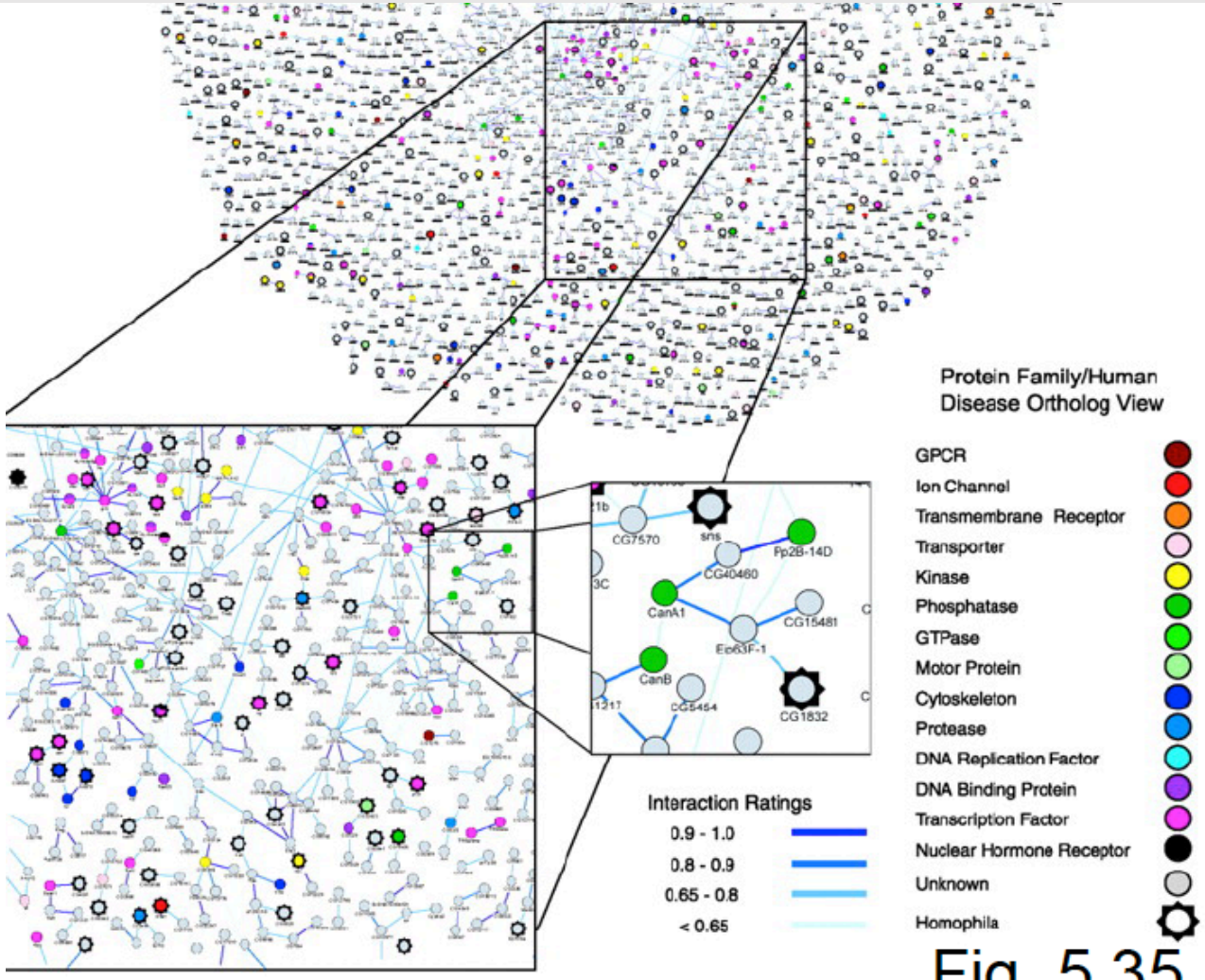
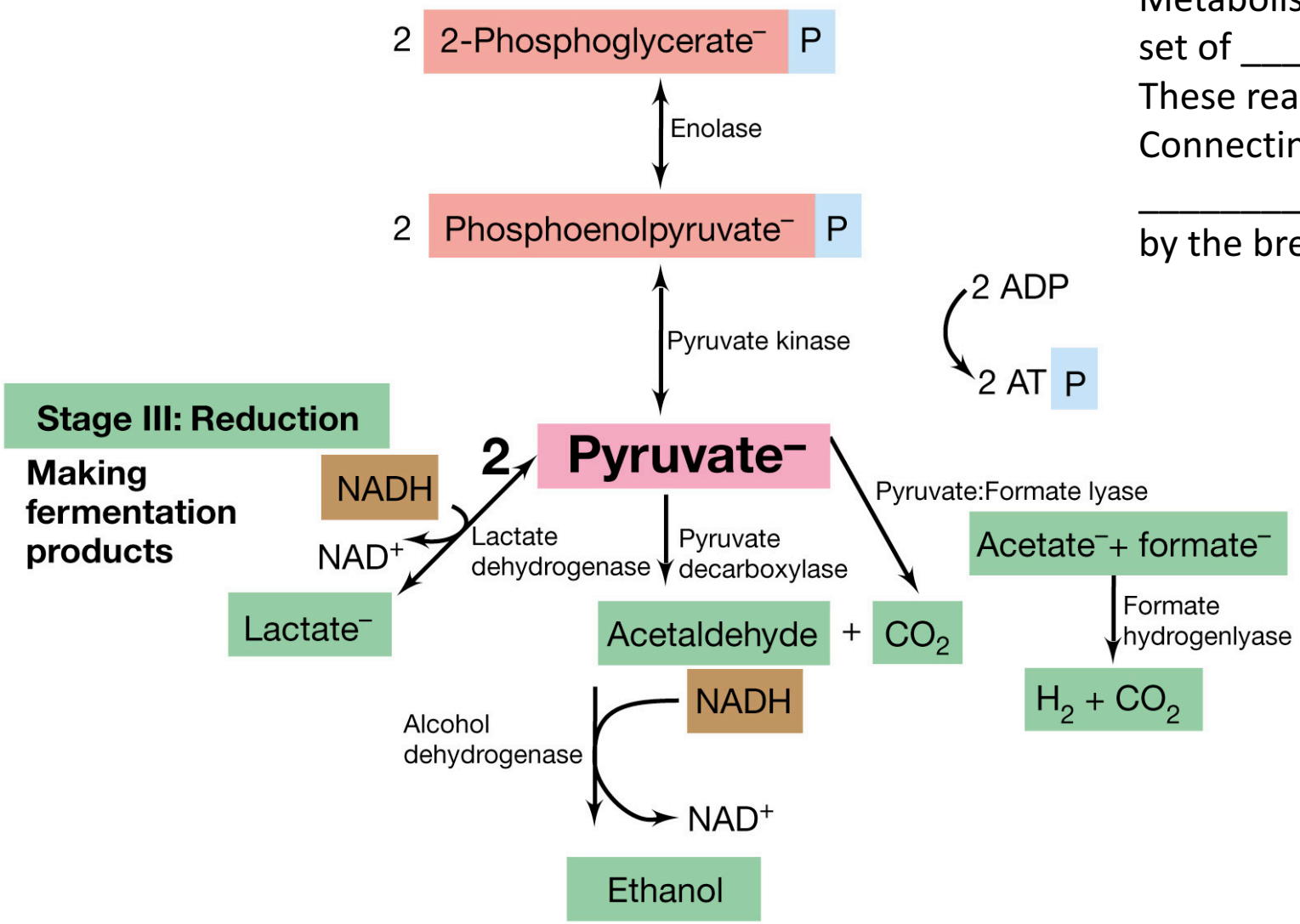


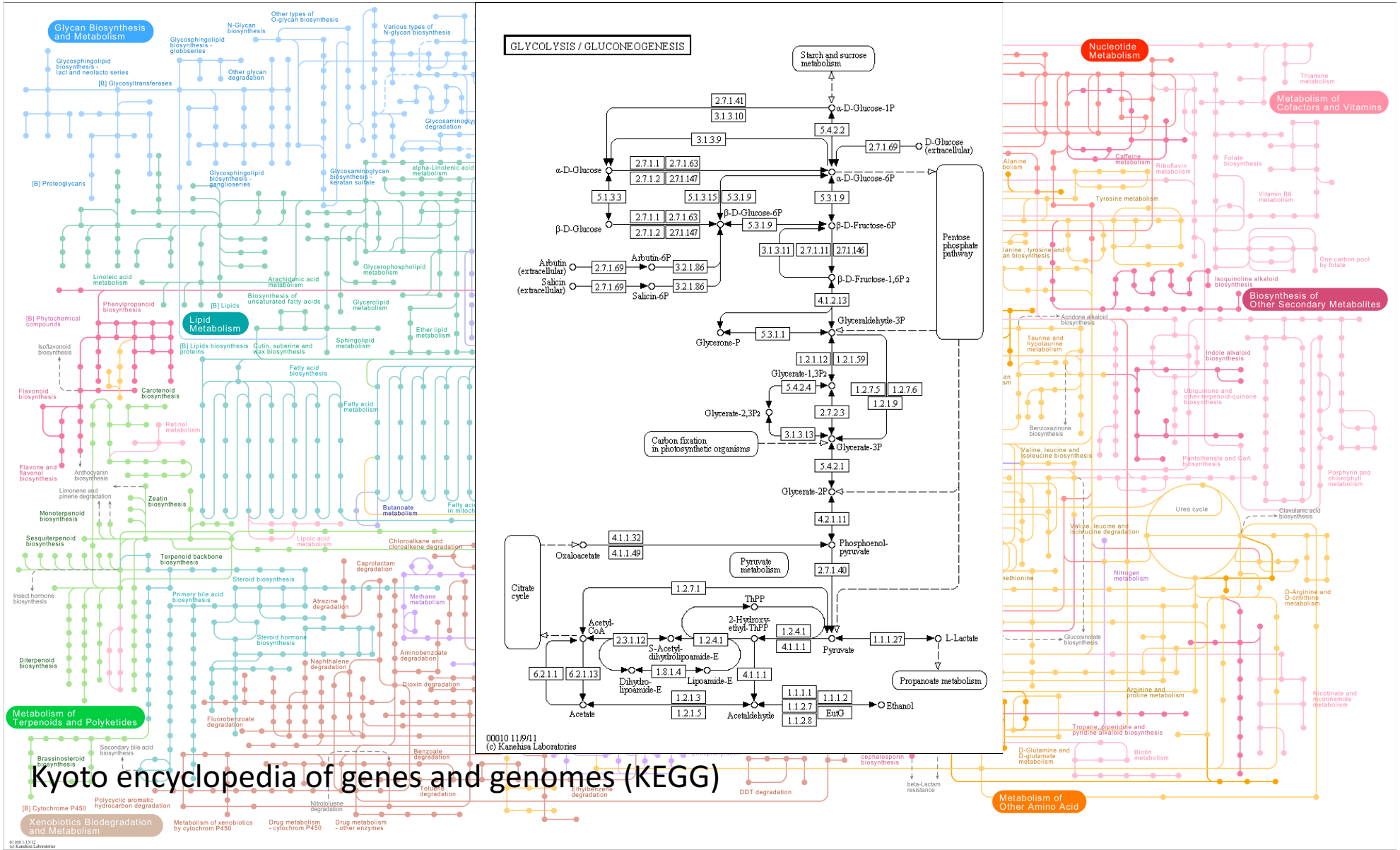
Fig. 5.35

Metabolism



Metabolism is defined as the set of _____in the cell. These reactions can _____by Connecting small molecules together or _____ by the breakdown of small molecules.

Metabolic network –



Kyoto encyclopedia of genes and genomes (KEGG)

Metabolic networks

- Describe chemical reactions for the production (anabolism) and breakdown (catabolism) of building blocks.
    - Amino acids
    - Sugars
    - Lipids
- Enzymes and energy required for synthesis and the processes by which the building blocks combine to make larger molecules
- Energy is released by catabolic reactions
- Metabolite profiling combined with gene expression analysis identifies how the TRN and metabolic networks are intercoordinated.