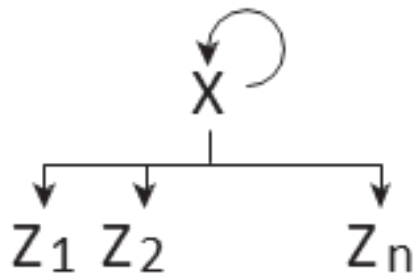


# Temporal programs and global structure of transcription networks

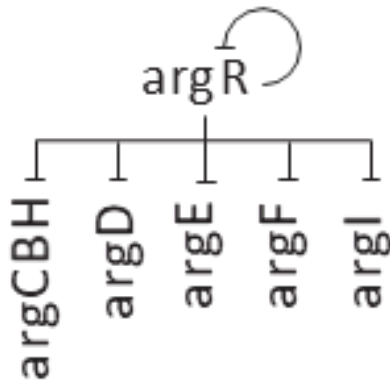
Typically, only 4 motives.

- the autorepressor,
- the feed forward loop (FFL),
- the Single input module (SIMs)
- the densely overlapping regulons (DORs).

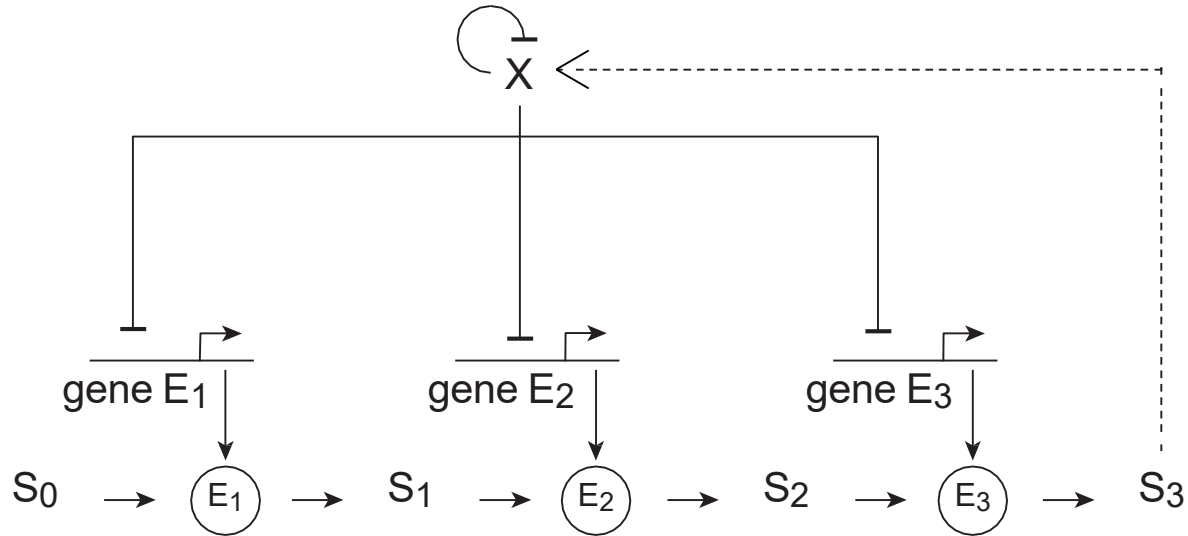
## Single Input Module (SIM)



Very rare in  
random  
networks!  
-> Finding them is  
very significant.

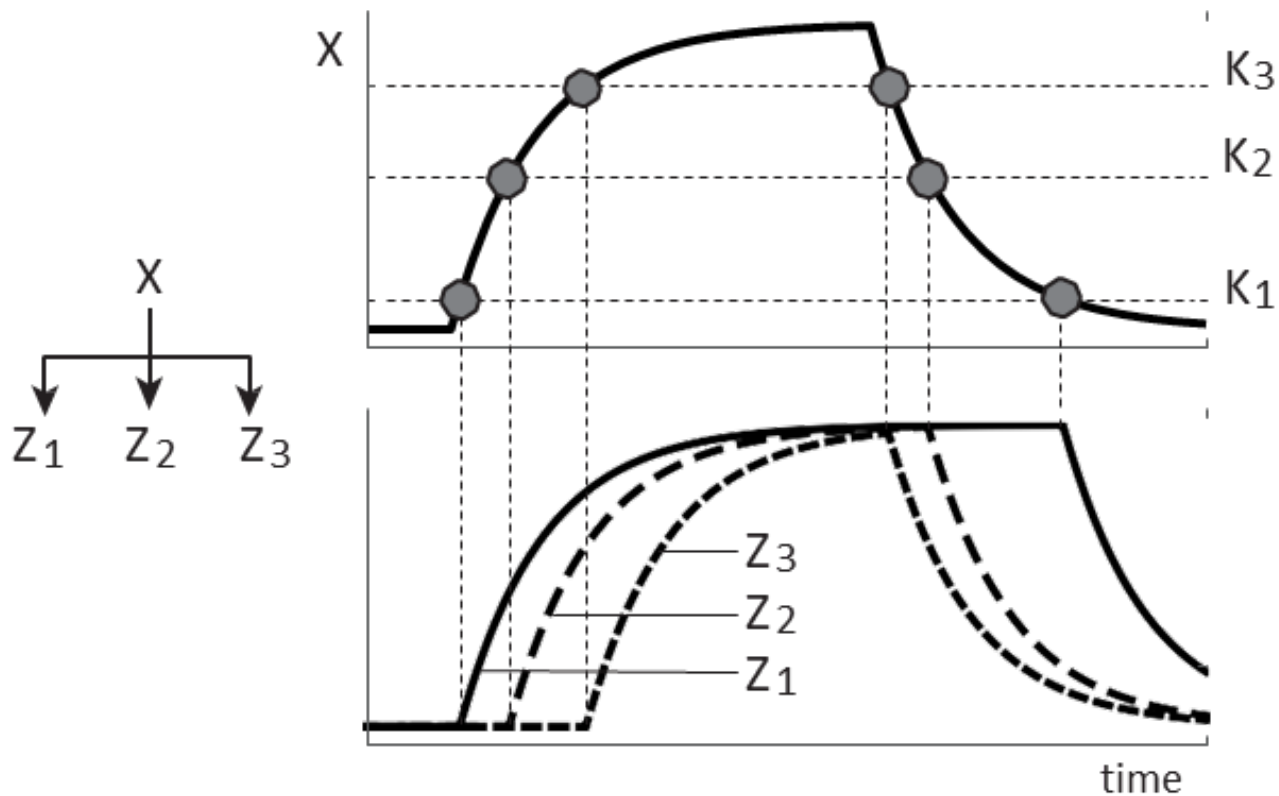


Function: Typically encode for genes with common biological function



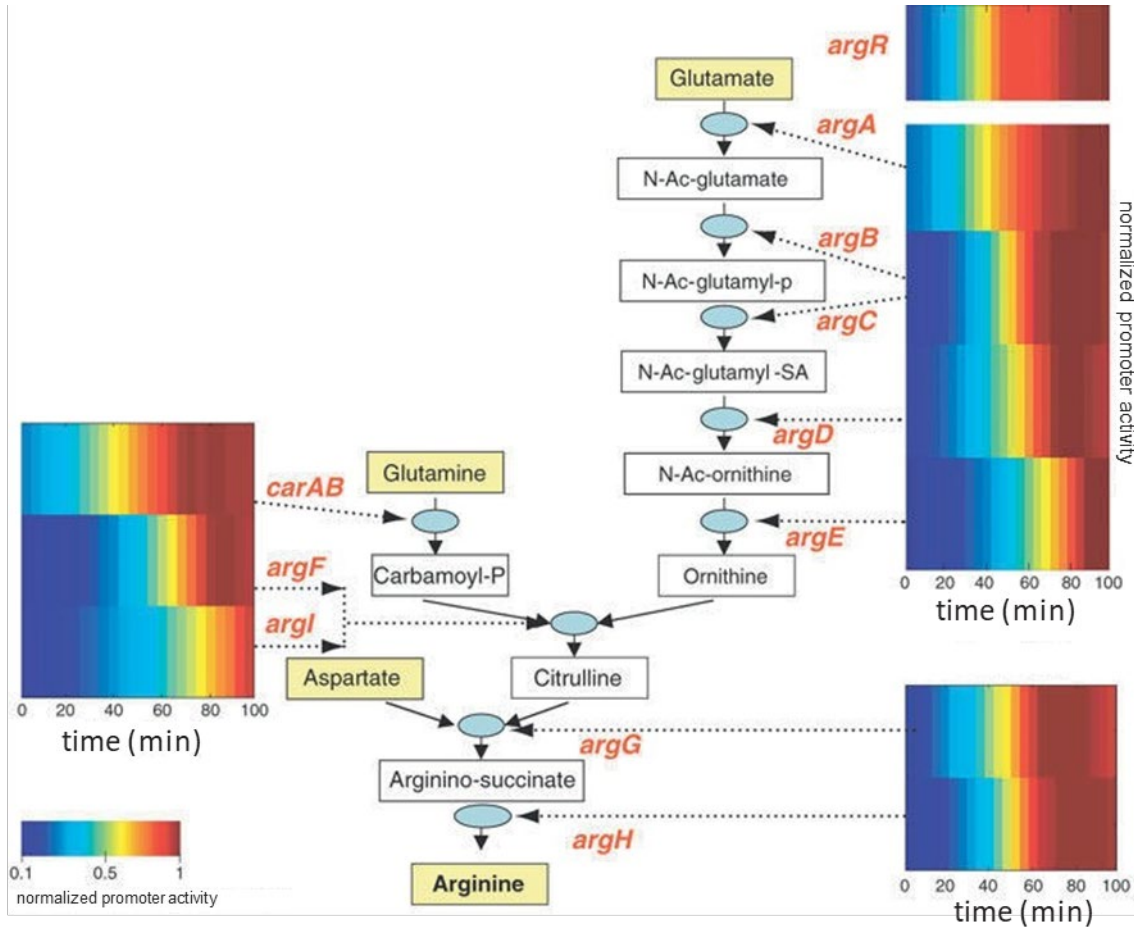
Metabolic line, where final product regulates the enzymes required for generating it.

Function: Different activation levels can lead to temporally coordinated expression



Turning off leads to “last-in-first-out” (LIFO)

## Example: Arginine system

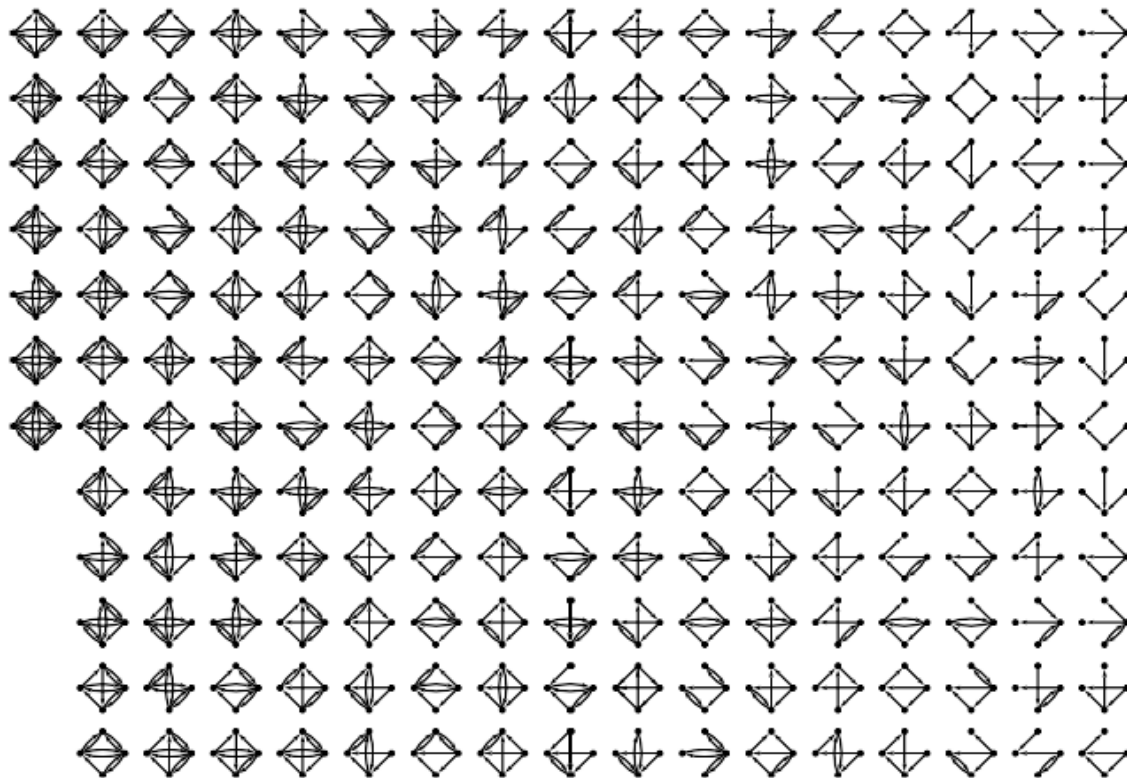


So LIFO works....  
But what about a  
FIFO?

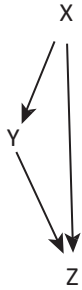
Look at more complex motifs... random variability diverges

- 199 different 4 node directed patterns

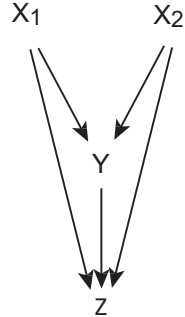
- >9000 5 node patterns



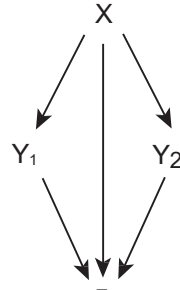
# Idea: Topological generalization of motifs



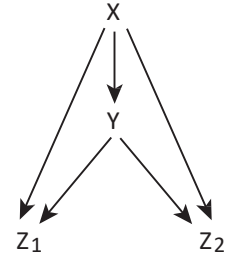
Feedforward Loop



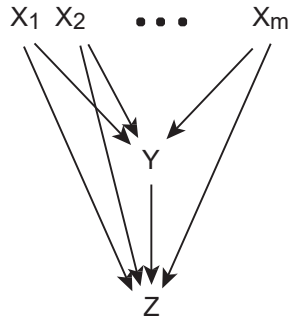
Double input FFL



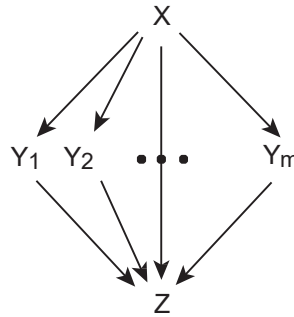
Double YFFL



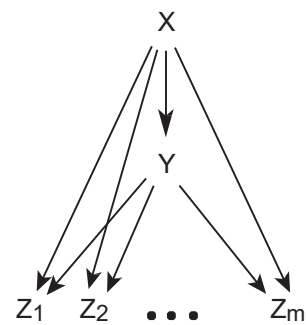
Double output FFL



multi input



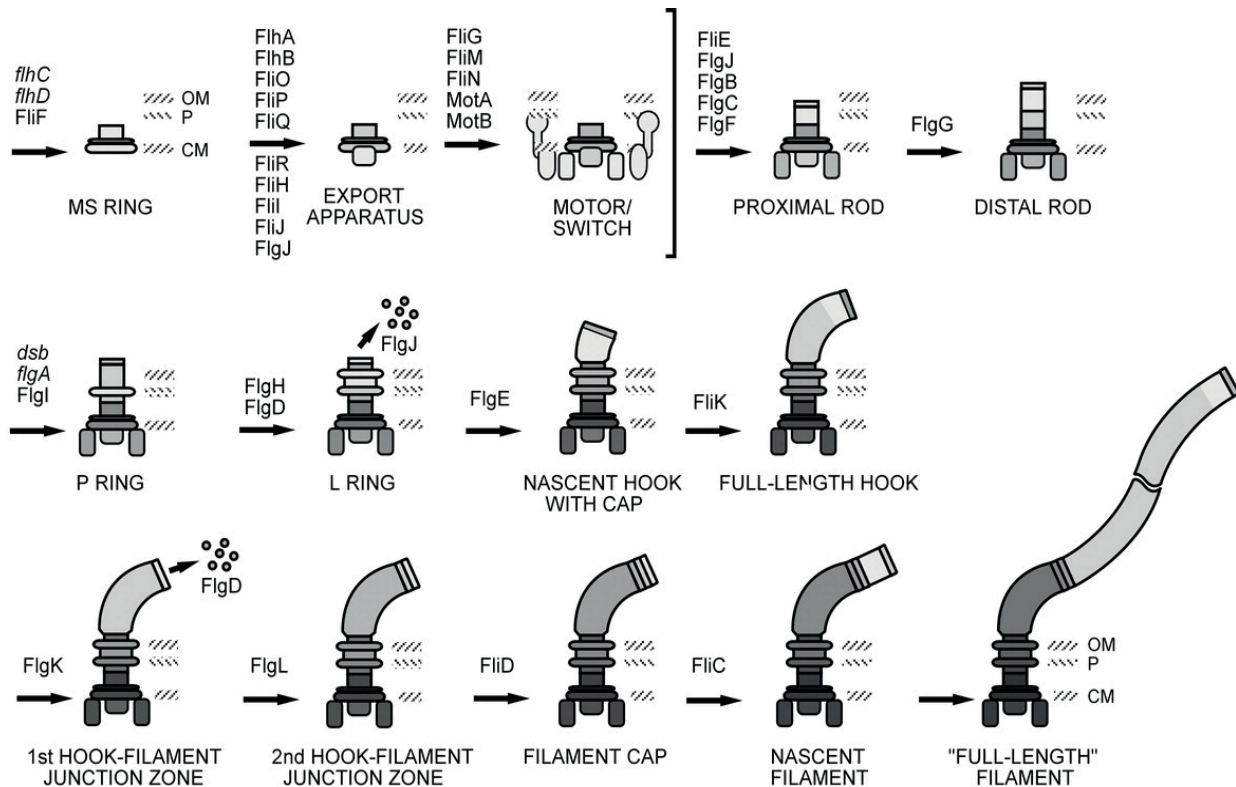
multi-Y



multi output

All are variation of FFL,  
but only  
**multi output FFL**  
is generation in  
transcription networks

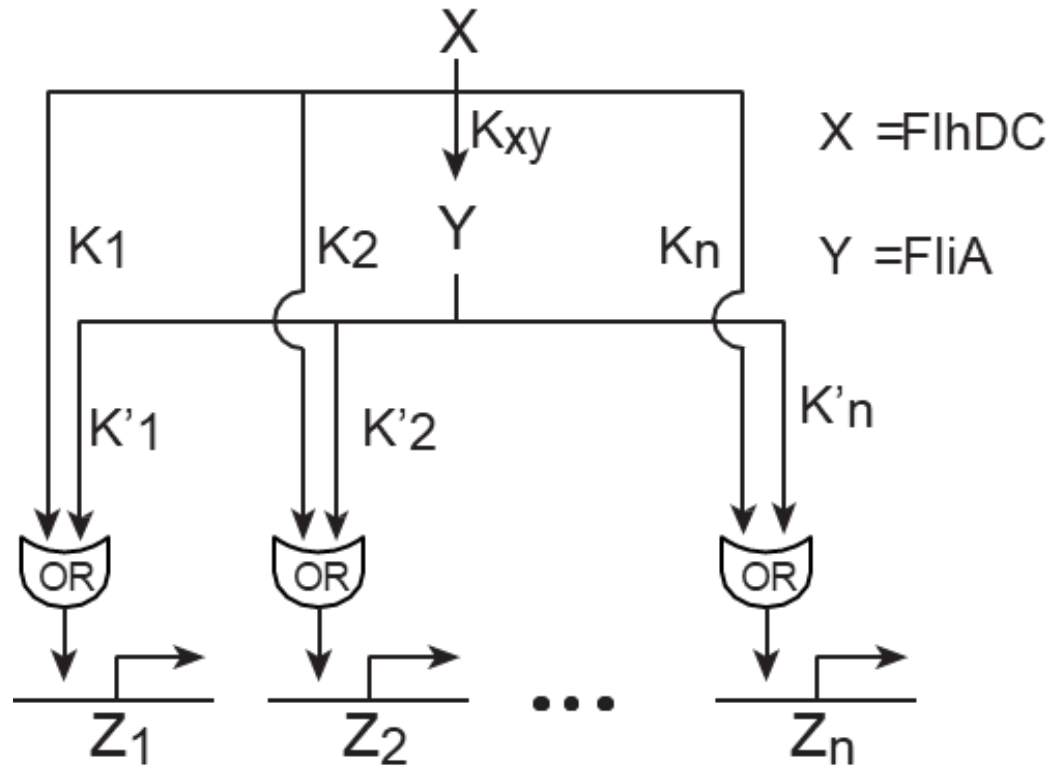
## Example of a FIFO: E.coli flagellar motor



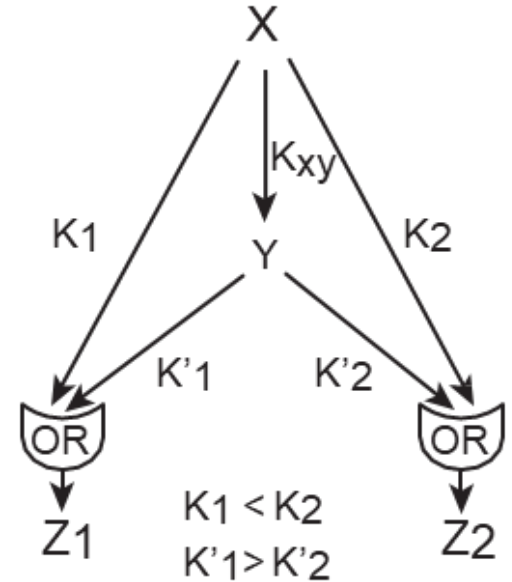
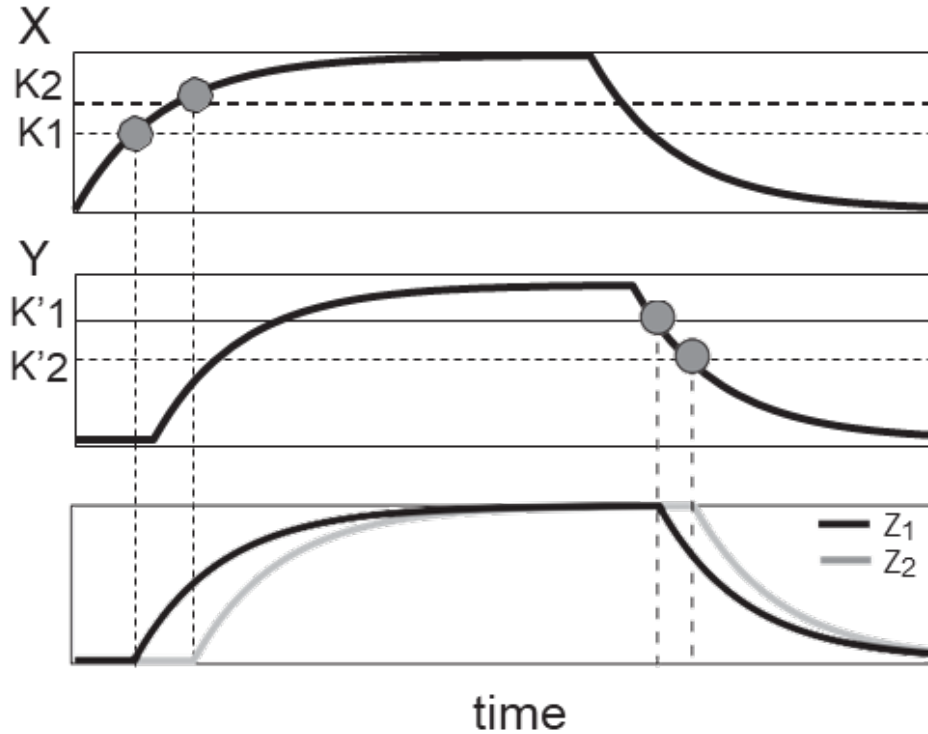
Produced on 6  
operons (one piece  
of mRNA coding  
more than 1  
protein)



Operons Z regulated by 2 activator X and Y, where X is master activator



Reversing thresholds for  $K_s$  and  $K'_s$  does the job of a FIFO  
(btw. Any arbitrary order for on and off can be realized!)

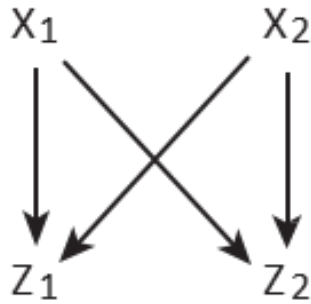


It also filter Fluctuations in OFF (low  $X$ )

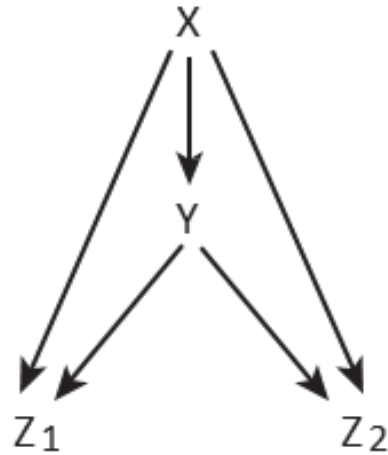
Multi Output FFL is most often fund motif in sensory transcription

## Four-node network motifs

(Of 199 possible, only 2 are significantly found in sensory transcription)



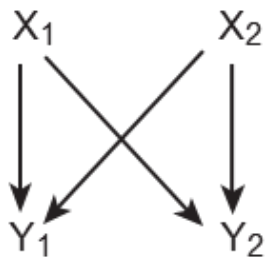
Bi-Fan



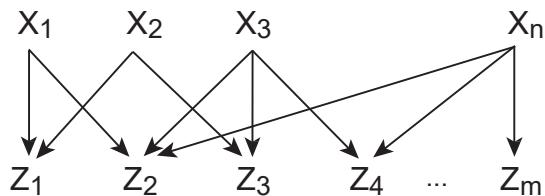
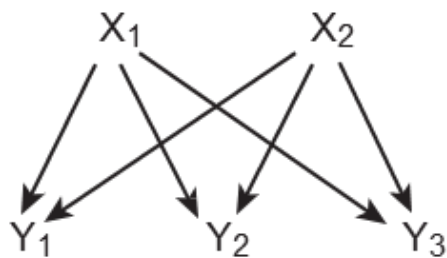
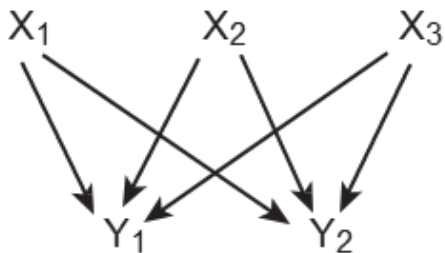
Two-output  
Feedforward Loop

Bi-fan is generalized to

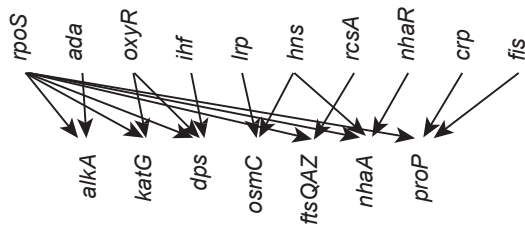
Dense Overlapping Regulons (DORs)



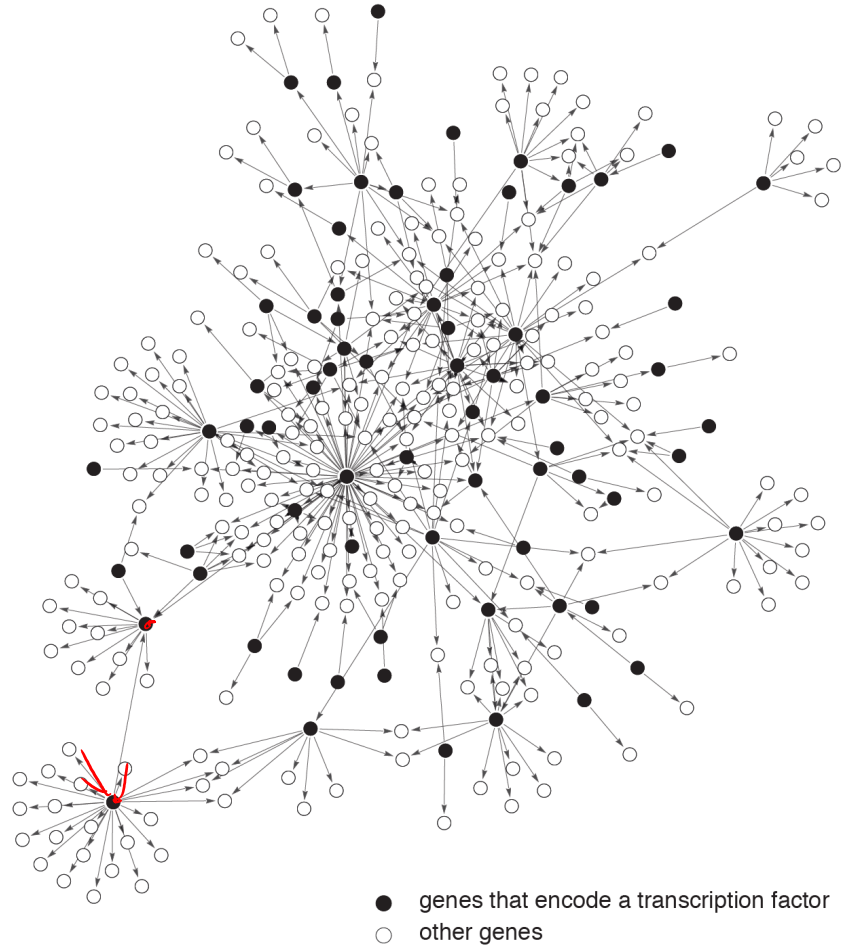
bi-fan



Example of stress response



Can motives help to get  
overview in networks?



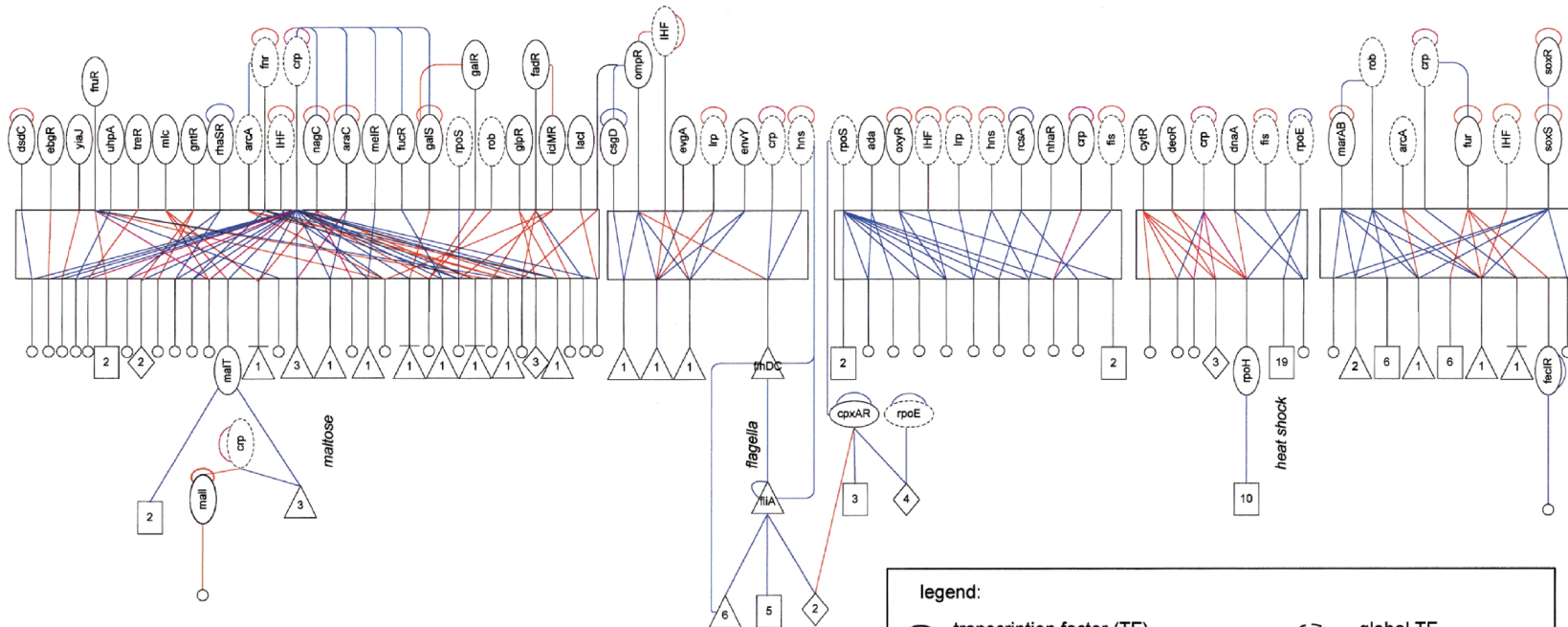
# carbon utilization DOR

# osmotic stress DOR

# stationary phase DOR

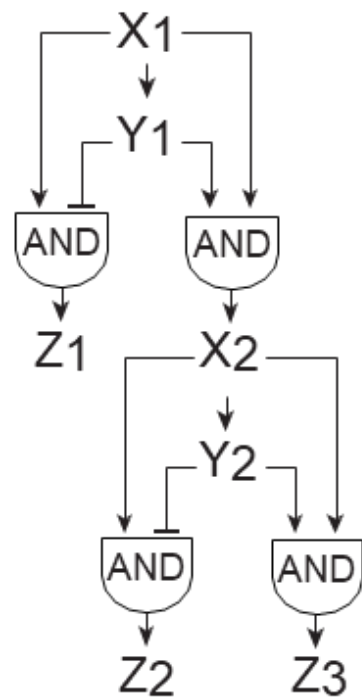
# DNA metabolism DOR

# drug and superoxide DOR



## legend:

- transcription factor (TF)
- global TF
- dense overlapping regulons (DOR)
- single input module (SIM)
- coherent feedforward loop
- incoherent feedforward loop
- single operon
- positive regulation
- negative regulation
- dual regulation
- multi-input module



# An overview of the motifs

Negative  
auto-regulation



Speeds response time,  
reduces cell-cell  
variability of X  
concentration

Positive  
auto-regulation



Slows response time,  
possible bi-stability

Coherent  
feed-forward loop  
(C1-FFL)



Sign-sensitive delay  
filters out brief ON  
input pulses  
when the Z-input function  
is AND logic, and OFF  
pulses when the input  
function is OR logic.

Incoherent  
feed-forward loop  
(I1-FFL)

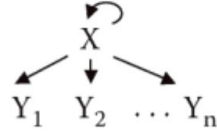


Pulse generation,  
sign-sensitive  
response acceleration



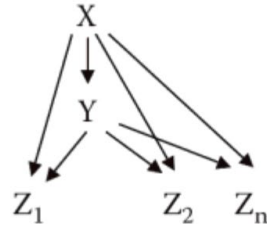
# An overview of the motifs

Single- input  
module (SIM)



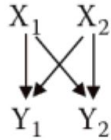
Coordinated control,  
Temporal (LIFO) order of  
promoter activity

Multi-output  
feed-forward loop  
(multi-output FFL)



Acts as FFL for each input  
(sign-sensitive delay, etc)  
FIFO temporal order of  
promoter activity

Bifan



Combinatorial logic  
based on multiple inputs,  
depends on  
input-function of each gene

Dense overlapping  
regulons (DOR)

