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# **Fibration symmetries uncover the building blocks of biological networks**

— Ian Leifer, Flaviano Morone, —  
Hernan Makse

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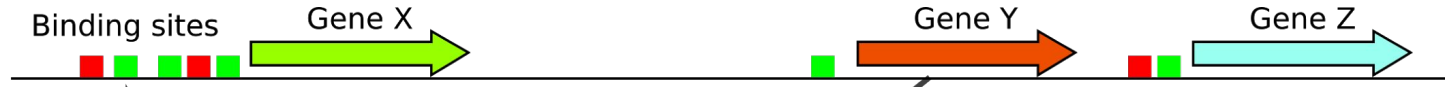
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# Introduction

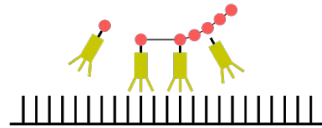
- The centerpiece in science is to decompose the complex system into the fundamental building blocks and study the way the collective behavior emerges from their interactions
- Two approaches are popular in biology: modularity by the biological function and network motifs
- Symmetry fibrations provide a novel way to look for building blocks originating from the synchronization in the network dynamics
- Fibrations have first been introduced in category theory by Alexander Grothendieck in 1958 and later studied in computer science, chaos theory and graph theory providing us with the well-developed mathematical machinery to be applied
- Disclaimer: we talk about applications to transcriptional regulatory networks and use examples from bacteria, but this approach can be applied to any directed network

# What is a transcriptional regulatory network?

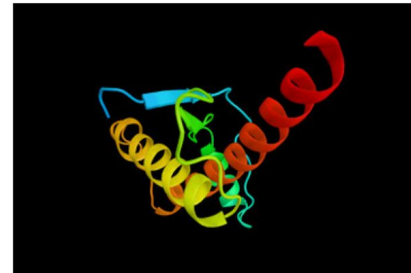
DNA



mRNA



Protein



Transcription

Translation

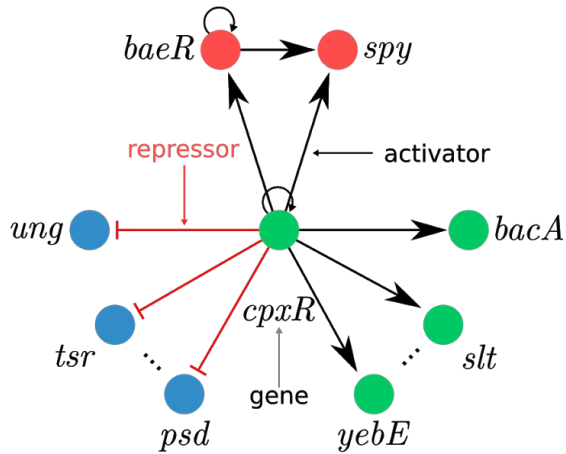
Protein folding

Metabolism

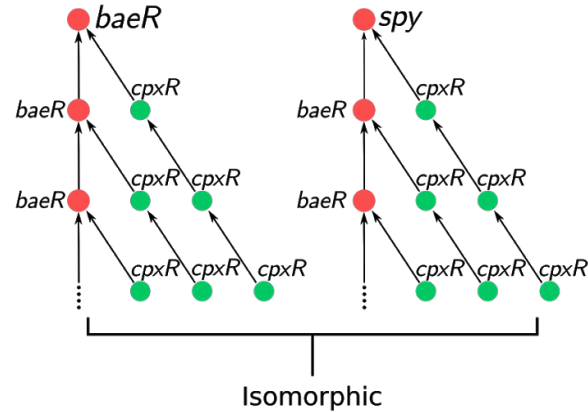


# Input-trees, fibers, synchronization

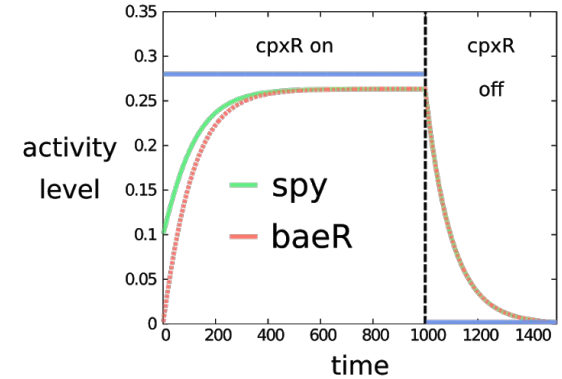
cpxR circuit



Input trees



Synchronization



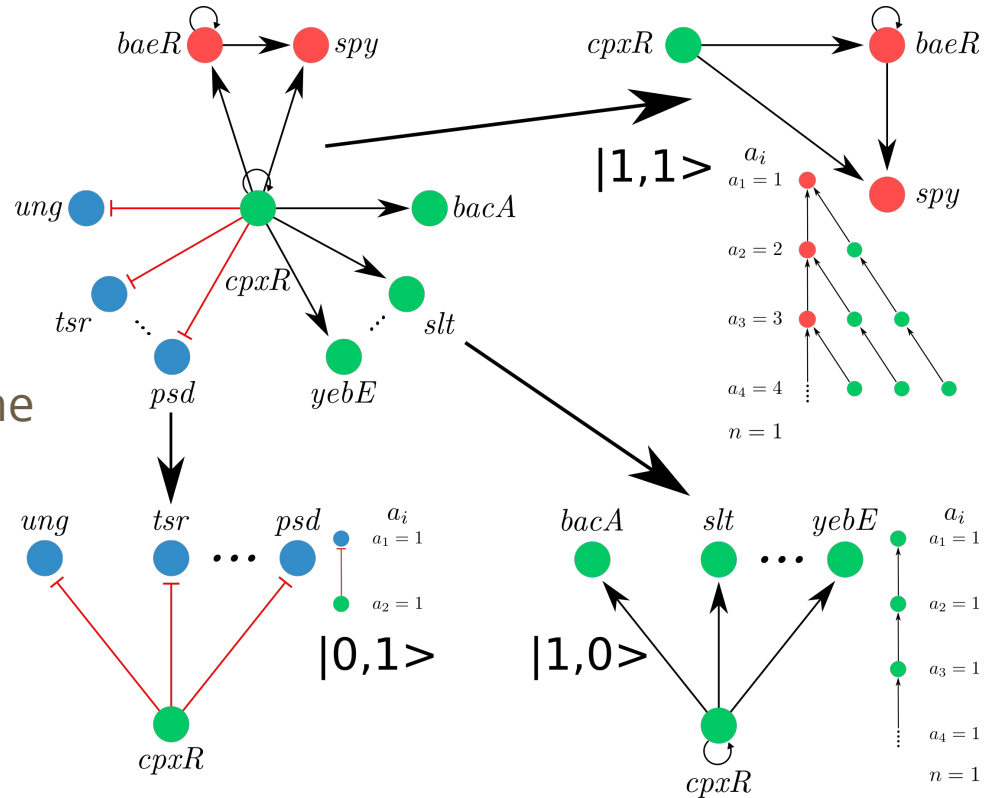
# Building blocks and fiber numbers

Building block is comprised by the genes in the fiber plus all regulators that are needed to establish the synchronization.

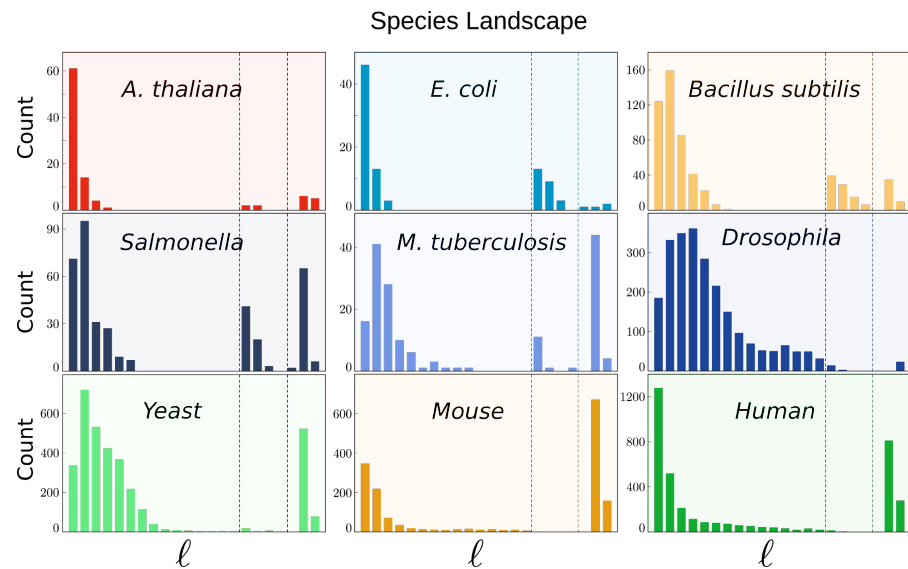
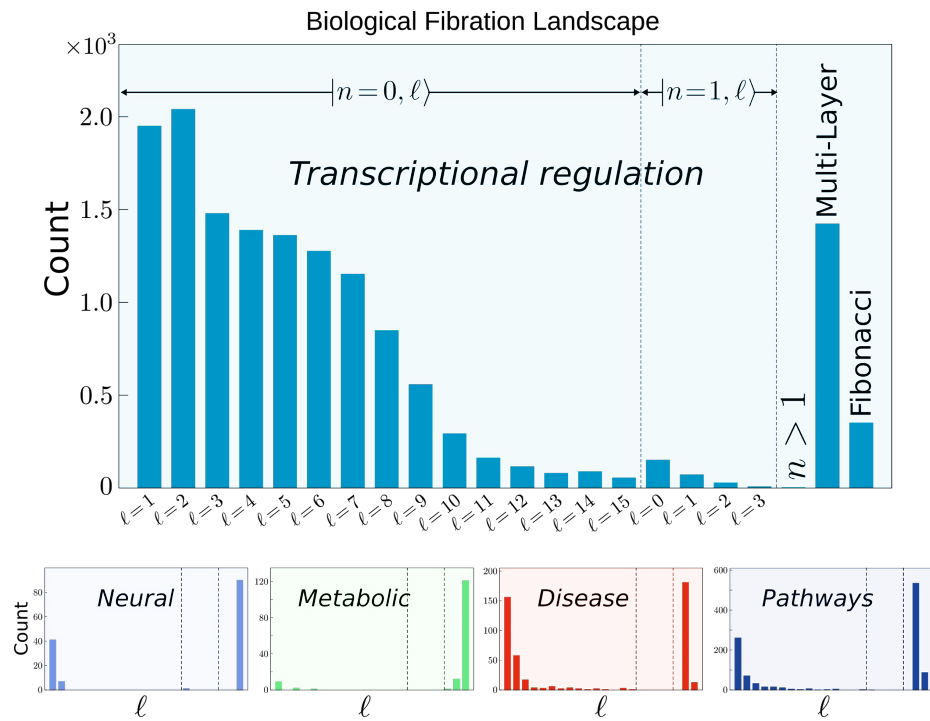
Building blocks are classified using 'fiber numbers' denoted  $|n, l\rangle$ .  $n$  is the branching ratio of the input tree

$$n = \lim_{i \rightarrow \infty} \frac{a_{i+1}}{a_i}$$

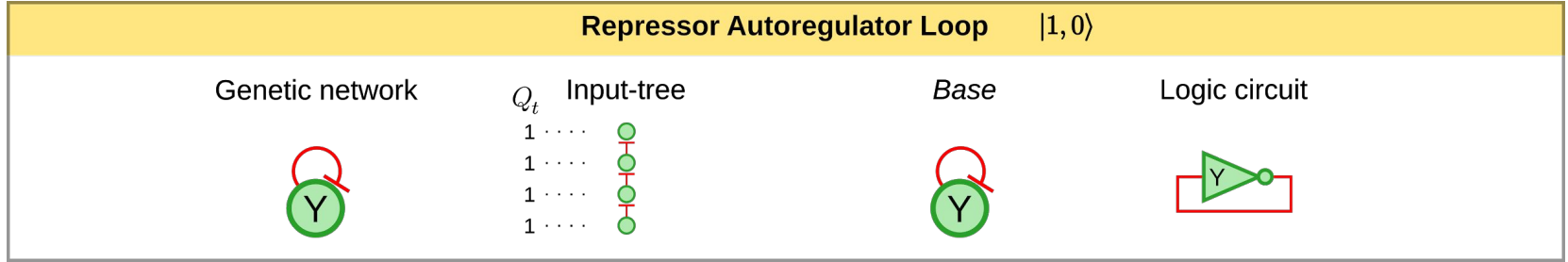
and  $l$  is the number of external regulators of the fiber



# Building block landscape

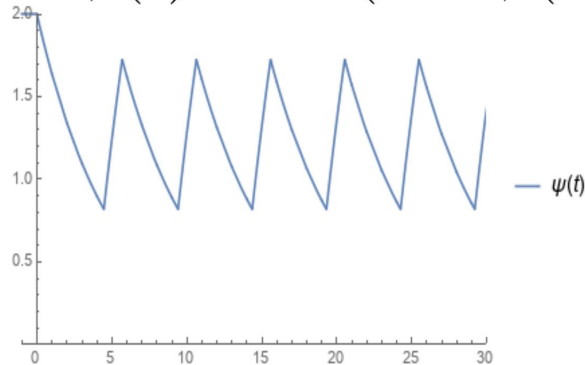


# Dynamics of the autorepression loop (clock)



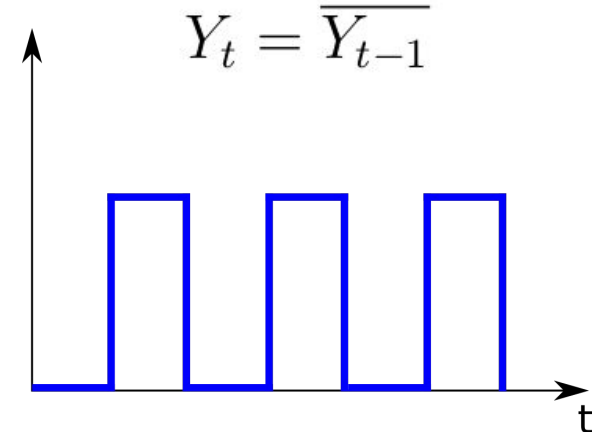
Continuous model

$$\dot{\psi} = -\alpha\psi(t) + \delta \theta(1 - \psi(t - \tau))$$

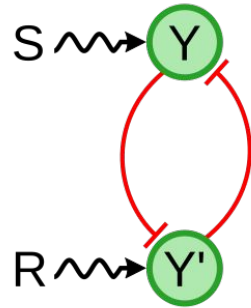


Boolean model

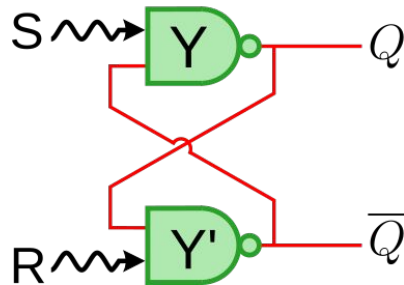
t	$Y_t$
0	1
1	0
2	1
3	0
4	1



# Dynamics of the genetic flip-flop (memory)



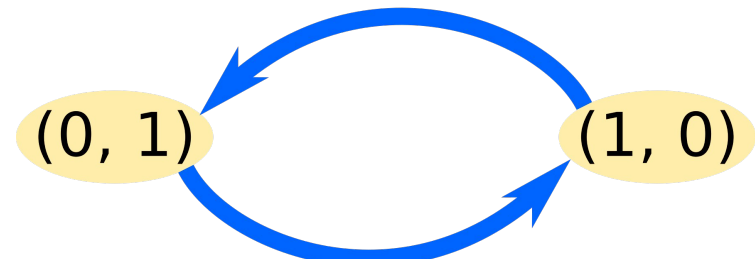
SR flip-flop



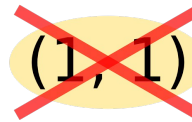
Boolean model



$S = 1, R = 0$



$S = 0, R = 1$





# Conclusion

- Fibration symmetry provides the novel way to analyze biological (or any other directed) network
- Symmetries of the network help uncover new functional building blocks related to synchronization
- Along with synchronization functional building blocks play the role of clock and memory
- This is a theoretically principled and algorithmically supported strategy to search for computational building blocks in biological networks

Further reading:  
Morone, Leifer, Makse, PNAS (2020)  
Leifer, et al. Plos. Comp. bio (2020)

Algorithm availability:  
<https://github.com/ianleifer/fibrationSymmetries>  
<https://github.com/makselab>

**Thank you for your attention!**