Evolution of simple systems to complex behaviours

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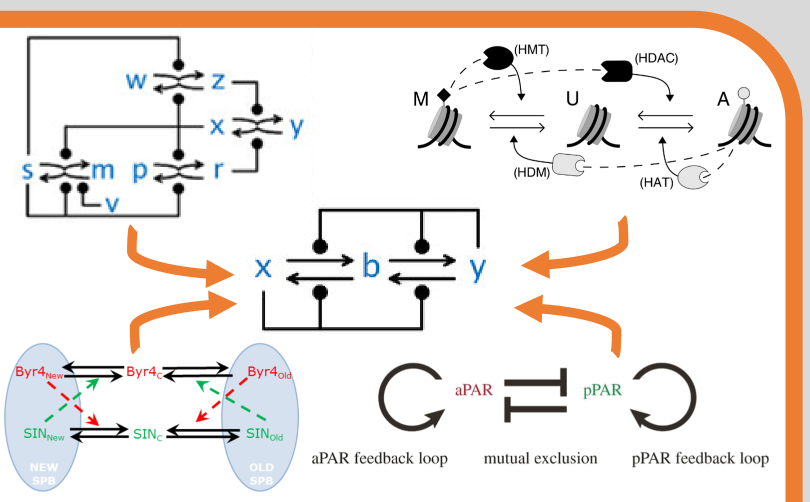
INTRODUCTION

Biological switches drive changes in the functional state of a system in an all-or-none fashion. These switch-like behaviours have been observed in different biological processes, like the transitions between phases of the cell cycle[1], the epigenetic changes[2], the regulation of polarity[3], or the septation initiation[4]. A simple model able to capture the dynamics of these complex processes is a population protocol, Approximate Majority[5] (AM), widely used in distributed computing. This algorithm describes how to drive a population of agents (molecules), initially in two different states, into a final population where all agents (molecules) are in the same state.



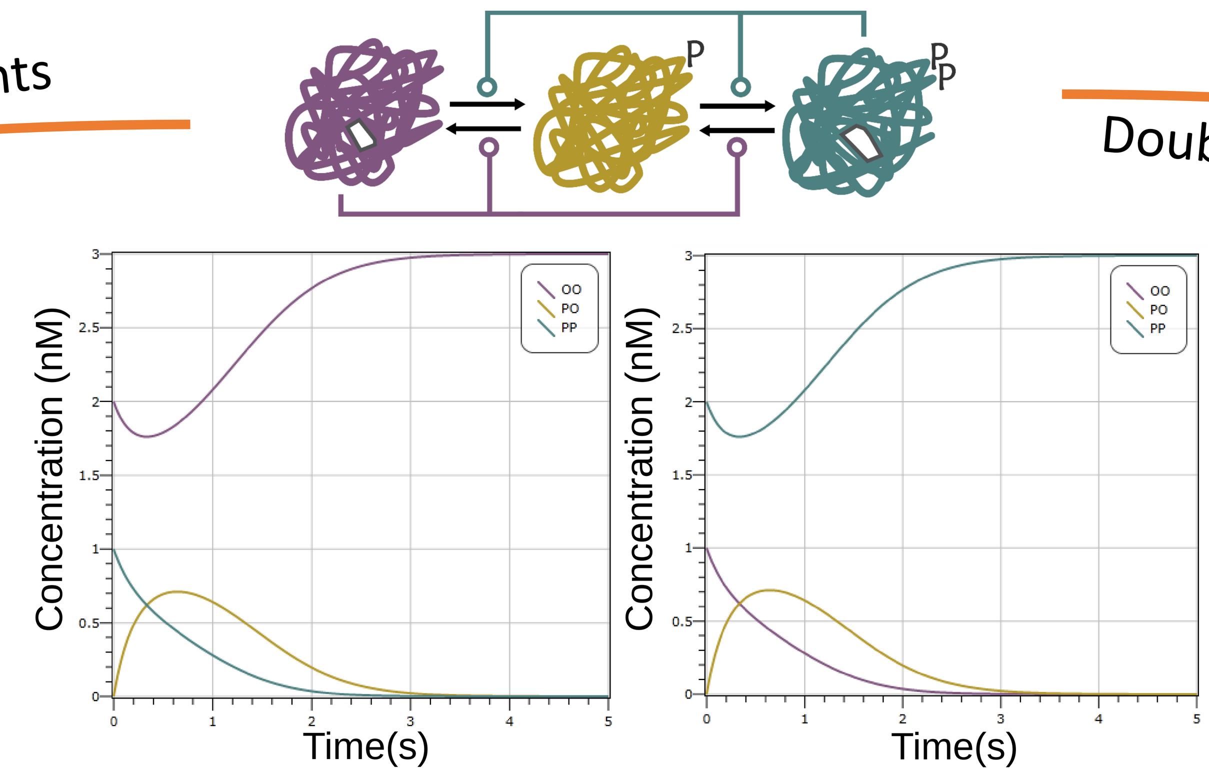
We investigate if this type of system could have been the ancestor of a class of biological switches, where the transitions between functional states should happen in a fast, reliable and robust way.

SUMMARY

We assumed that dynamical behaviours must be kept to obtain new systems with new functions, while keeping original features. Evolving AM, we have shown that:

- An increasing of complexity from AM is feasible. We obtain the mutual inhibition system (MI), a system usually observed in biological networks. It resembles a kinase – phosphatase pair
- From a switch-like behaviour an oscillatory behaviour can arise, keeping the dynamical properties of a switch in previous steps.

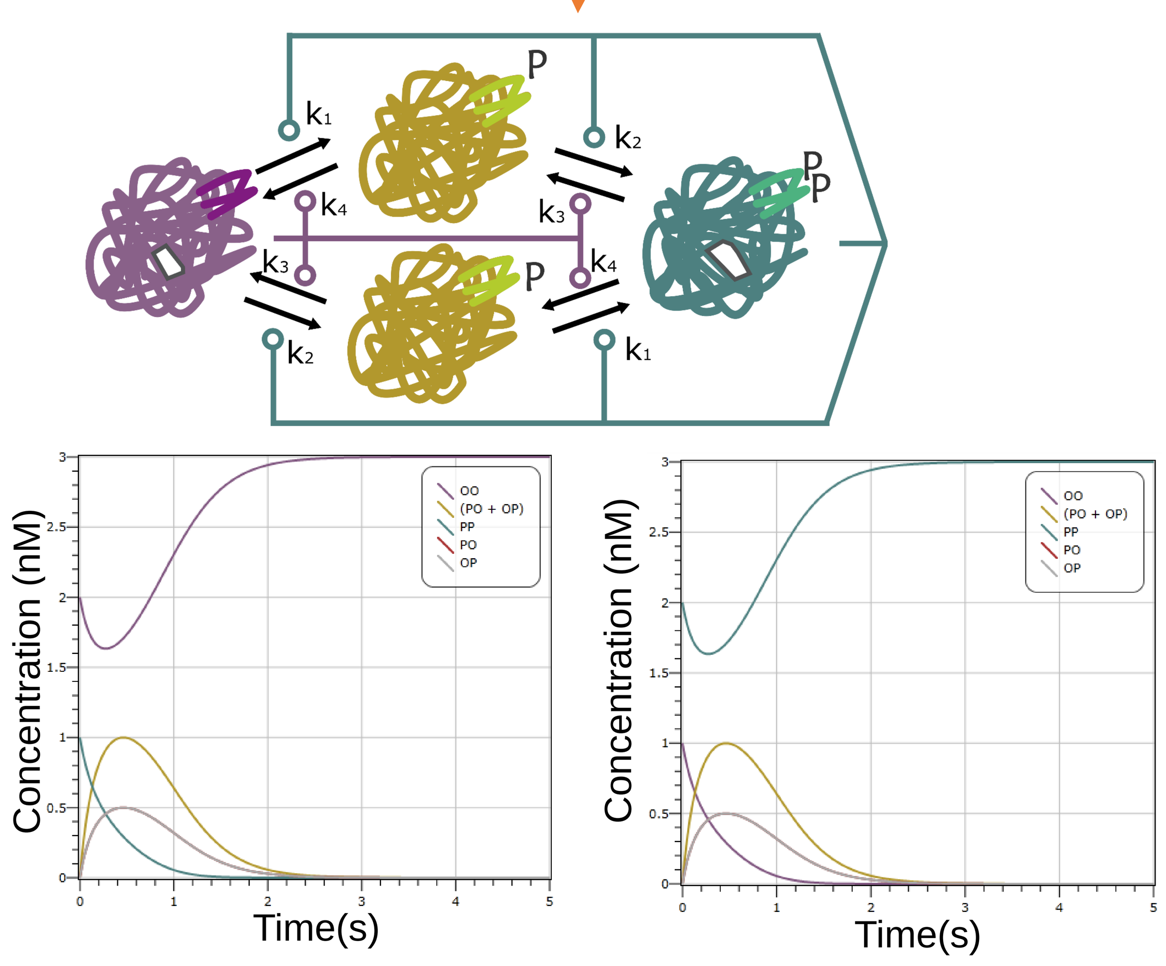
RESULTS



Time-course diagrams of Approximate Majority (AM).
Initial conditions: OO=2 PP=1; OO=1 PP=2
The system was solved using a deterministic method
All kinetic rates are equal to 1.

Accumulation of variants

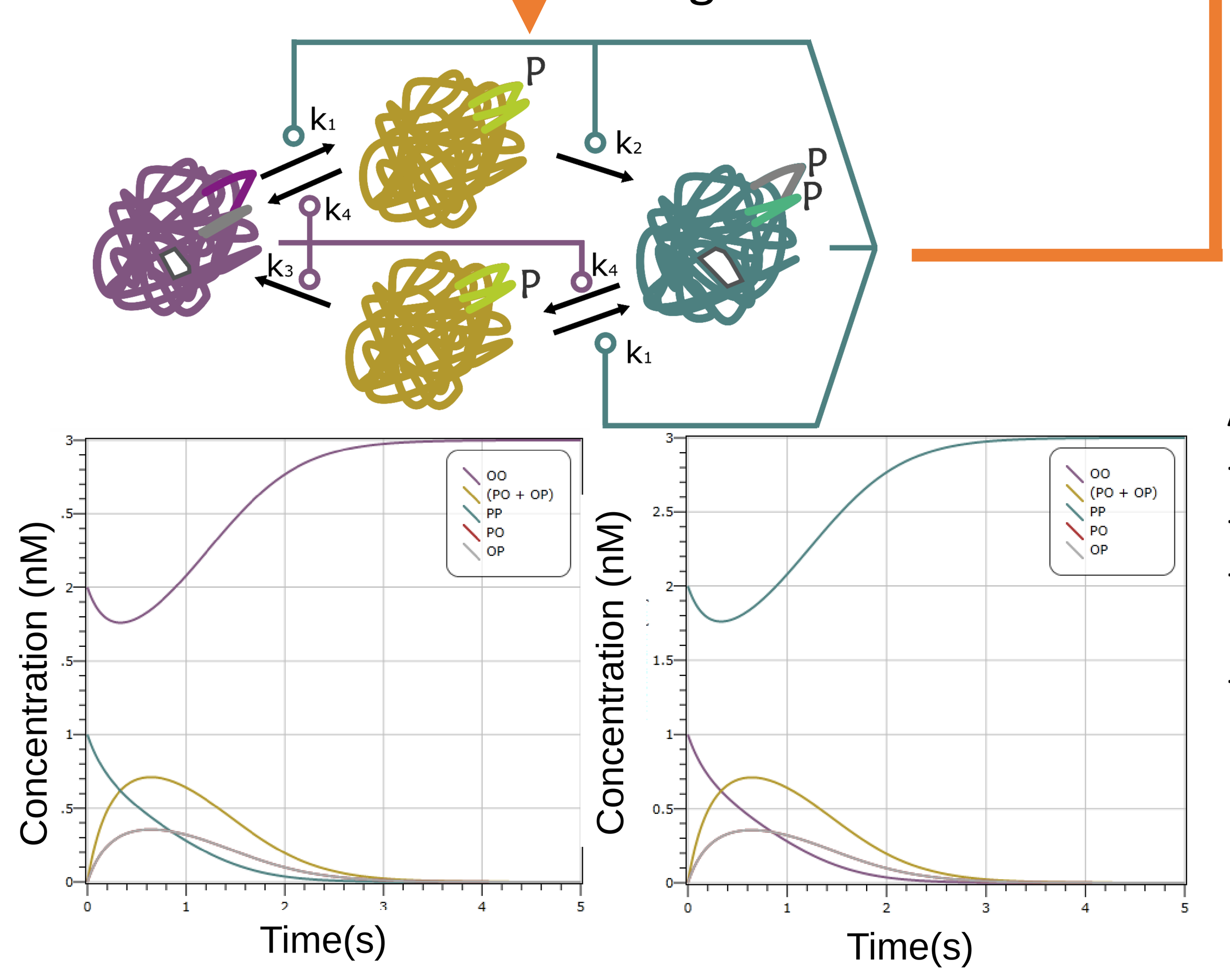
Allosteric changes



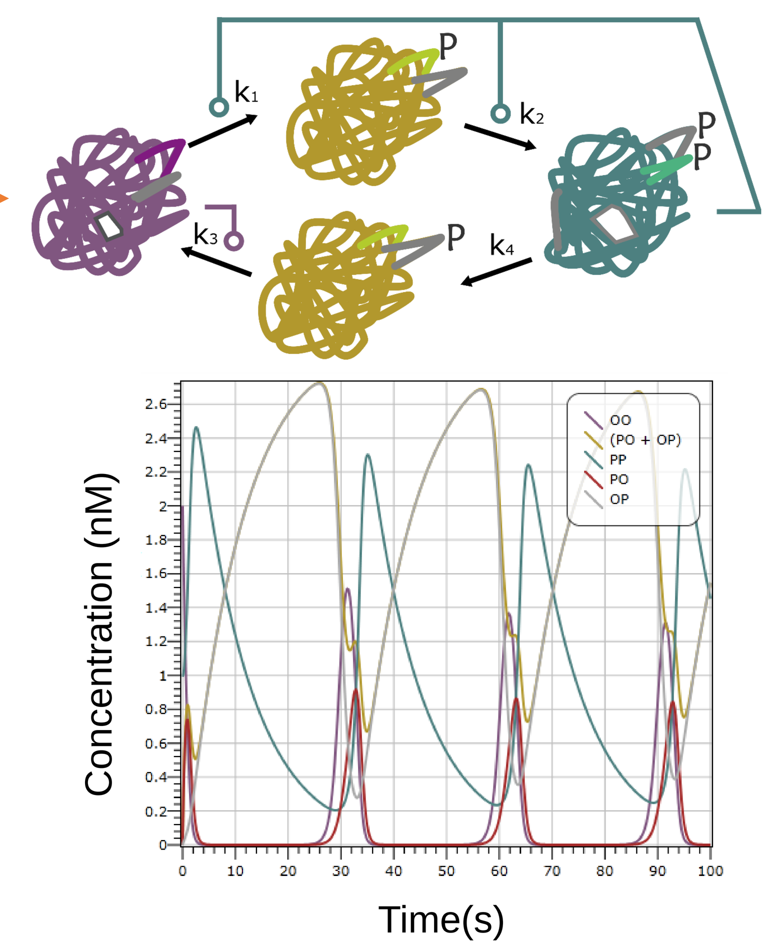
Introduction of a new conformation (OP).
The system is faster. Bistability is kept. $k_1=k_2=k_4=k_3=1$

Accumulation of variants

Allosteric changes



Allosteric changes in the catalytic conformations.
Bistability is kept. It restores AM's dynamics. $k_1=k_2=k_4=k_3=1$

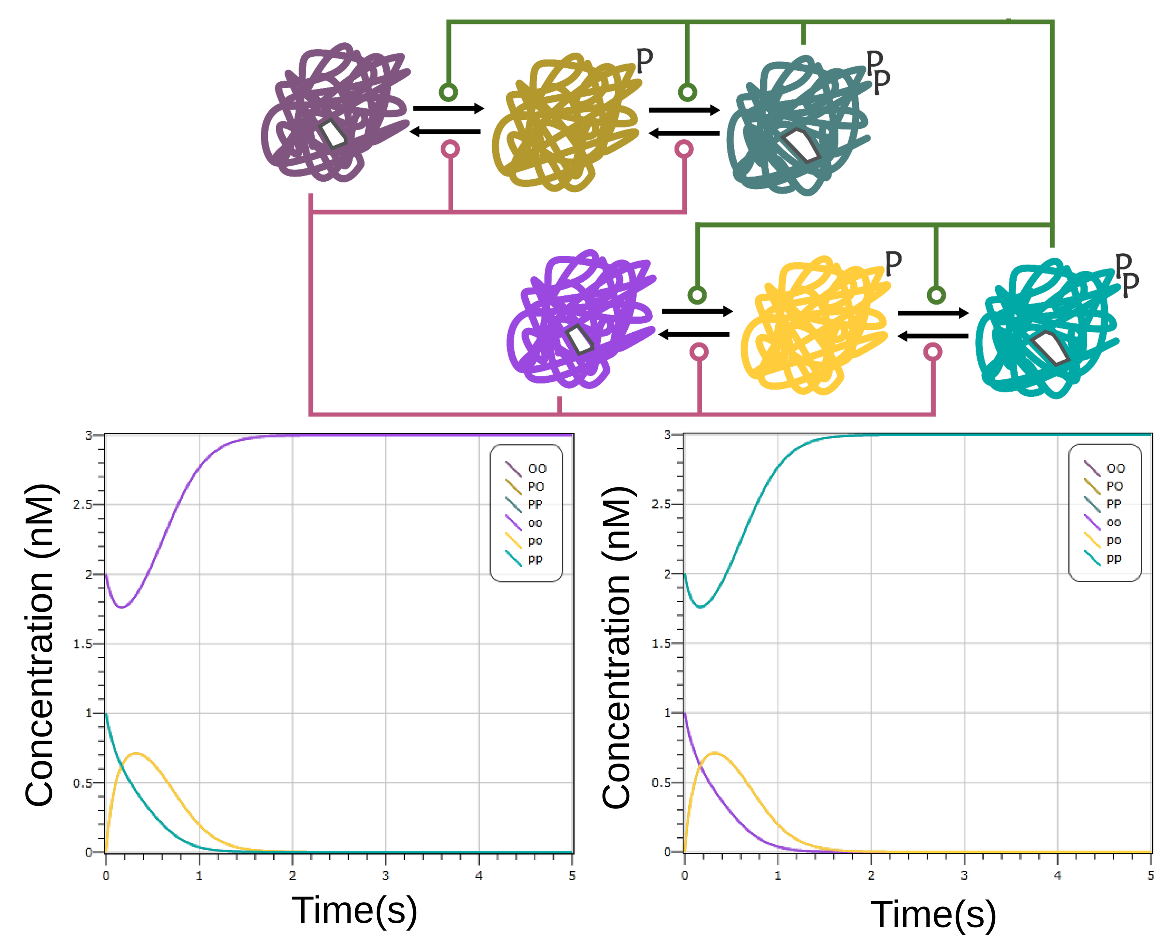


Allosteric changes in the intermediary conformations

- OO cannot dephosphorylate buried sites (PO)
- OO reduces its activity over OP (k_3=1 -> k_3=0.5)
- Allosteric changes in PP block the dephosphorylation by OO and allow the autodephosphorylation (k_4=1 -> k_4=0.1)
- PP cannot phosphorylate buried sites (OP)

Gene Duplication

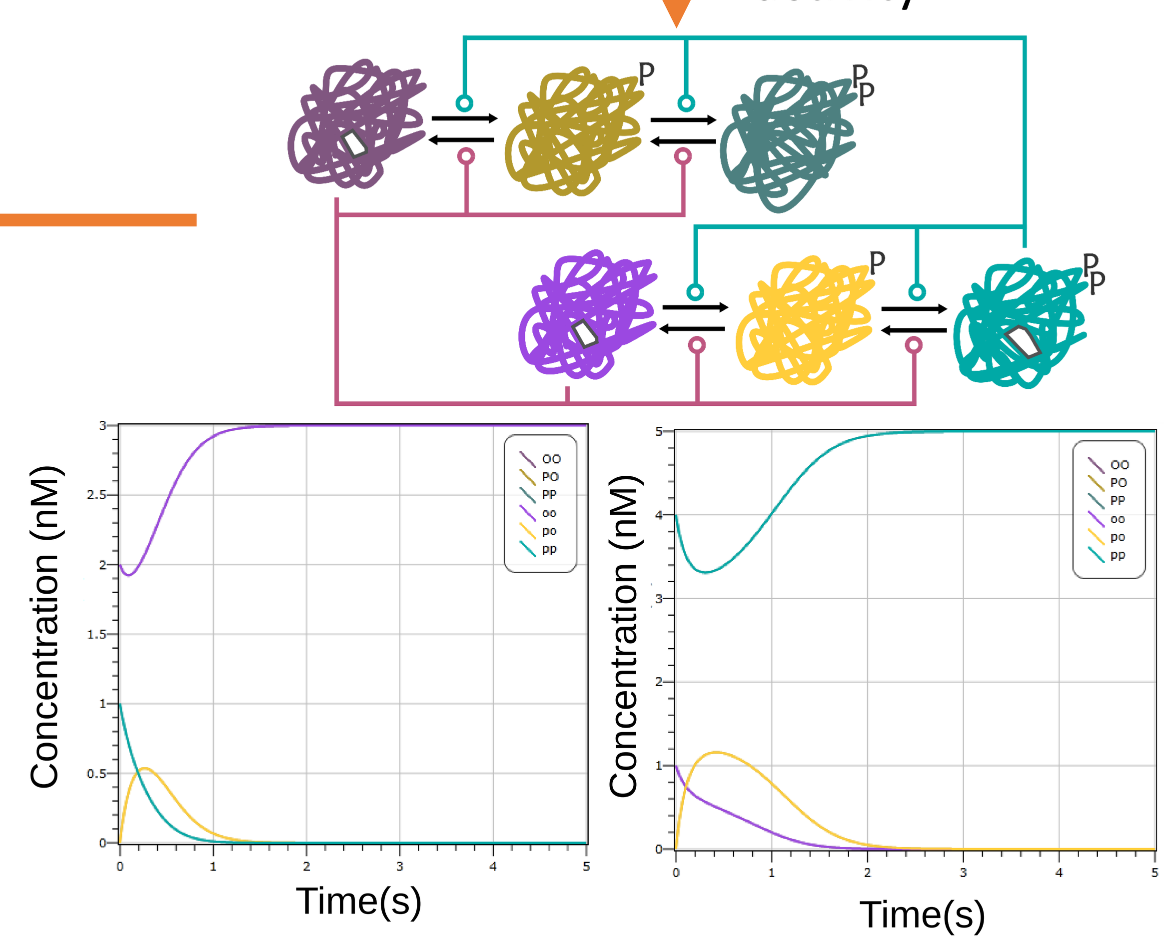
Double amount of protein



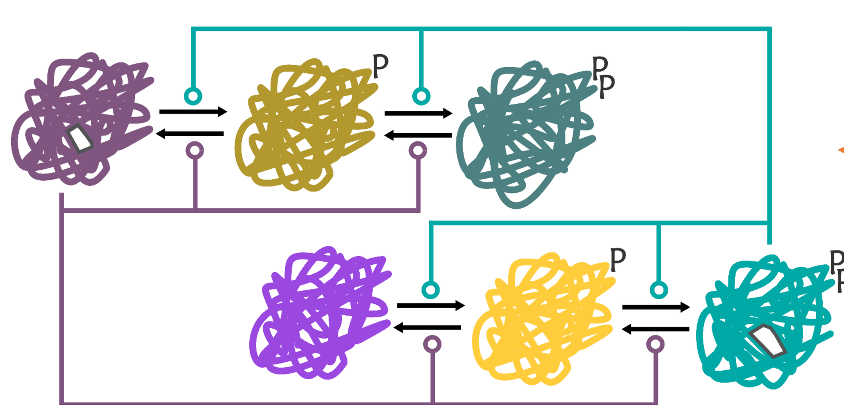
Gene Duplication. Double amount of protein
Faster system. Bistability is kept.

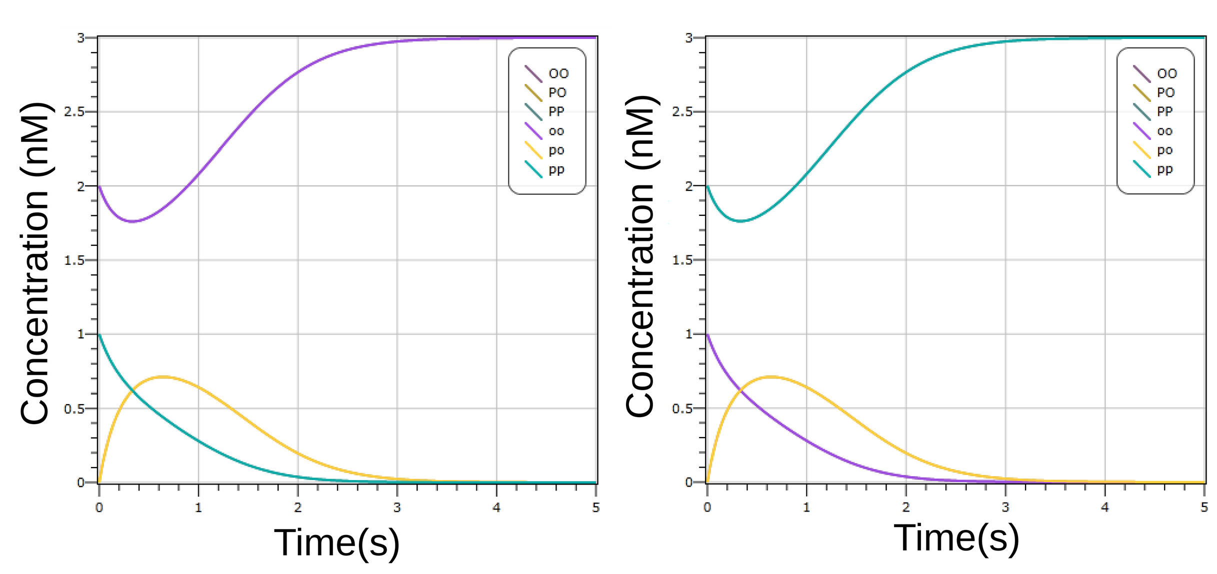
Accumulation of variants

Loss of catalytic activity



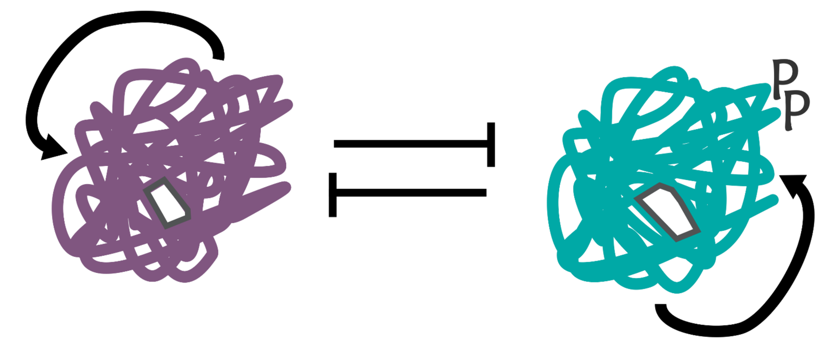
Loss of catalytic activity due to accumulation of variants
Bistability is kept but it is unbalanced.
Once state is a better attractor.





Lose of catalytic activity due to accumulation of variants

- Each species have one catalytic state and another inactive state.
- The system resembles a mutual inhibition (MI) system.
- OO active state autodephosphorylates and activates itself.
- OO active state dephosphorylates PP and inhibit it.
- PP active state autophosphorylates and activates itself.
- PP active state phosphorylates OO and inhibit it.



REFERENCES

1. Cardelli L, Csikász-Nagy A: The cell cycle switch computes approximate majority. *Scientific reports* 2012, 2: 656.
2. Arkin A, Ross J, McAdams HH: Stochastic kinetic analysis of developmental pathway bifurcation in phage λ-infected Escherichia coli cells. *Genetics* 1998, 149(4):1633-1648.
3. Motegi F, Seydoux G: The PAR network: redundancy and robustness in a symmetry-breaking system. *Philosophical Transactions of the Royal Society B: Biological Sciences* 2013, 368(1629):20130010
4. Bajpai A, Feoktistova A, Chen JS, McCollum D, Sato M, Carazo-Salas RE et al.. Dynamics of SIN asymmetry establishment. *PLoS Comput Biol* 2013, 9(7):e1003147.
5. Angluin D, Aspnes J, Eisenstat D: A simple population protocol for fast robust approximate majority. *Distributed Computing* 2008, 21(2):87-102