



# Architecture and Dynamics of Biomolecular Networks Facilitate Evolution of Persistence Strategies in Living Organisms

Aishwarya Raj

Advisers: Dr. Liudmila Sergeevna Mainzer & Dr. Jay Mittenthal

University of Illinois Urbana Champaign

National Center for Supercomputing Applications

- I. Introduction to Persistence Strategies and Why it Matters
- II. Methods of Investigation and Rationale
- III. Future Direction of Investigation

# What is Life

life 

[lahyf]

Spell

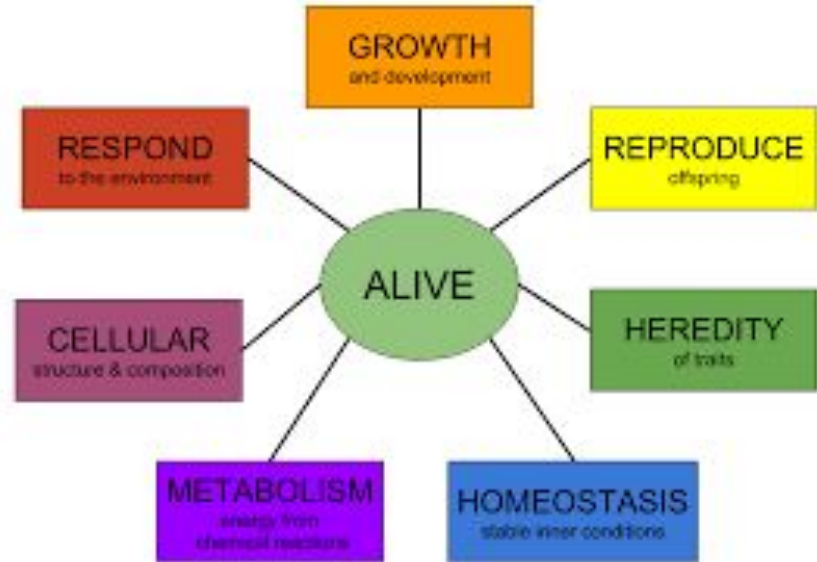
Syllables

[Synonyms](#) [Examples](#) [Word Origin](#)

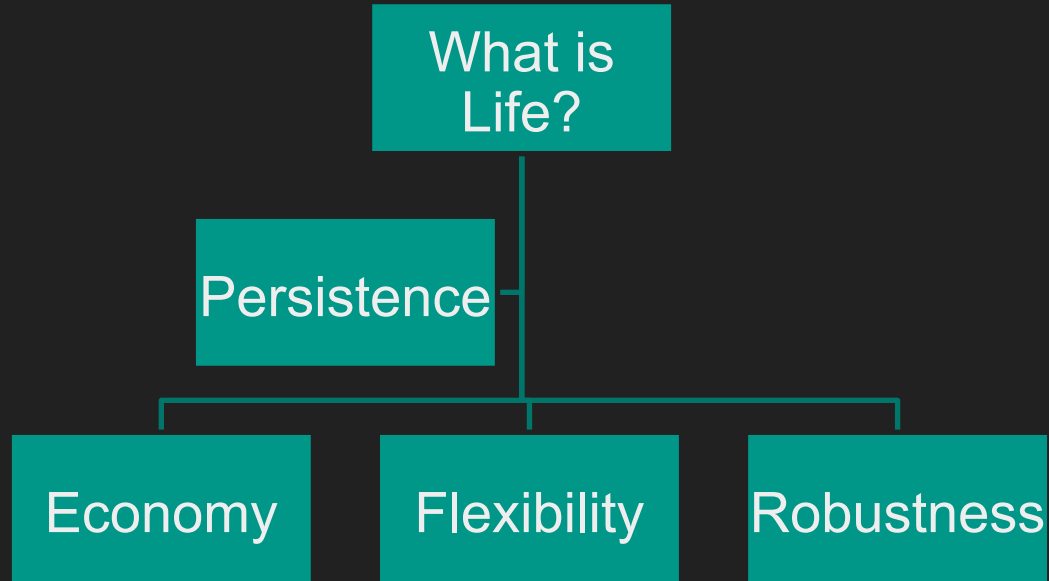
[See more synonyms on Thesaurus.com](#)

noun, plural **lives**  [lahyɪvz] ([Show IPA](#))

1. the condition that distinguishes organisms from inorganic objects and dead organisms, being manifested by growth through metabolism, reproduction, and the power of adaptation to environment through changes originating internally.
2. the sum of the distinguishing phenomena of organisms, especially metabolism, growth, reproduction, and adaptation to environment.
3. the animate existence or period of animate existence of an individual: *to risk one's life; a short life and a merry one.*



# What are Persistence Strategies



# Why Does it Matter

Understanding persistence strategies is important.



## 1. Crops in Extreme Environments, and meeting growing economical needs

Martins, L. M. V., Xavier, G. R., Rangel, F. W., Ribeiro, J. R. A., Neves, M. C. P., Morgado, L. B., & Rumjanek, N. G. (2003).

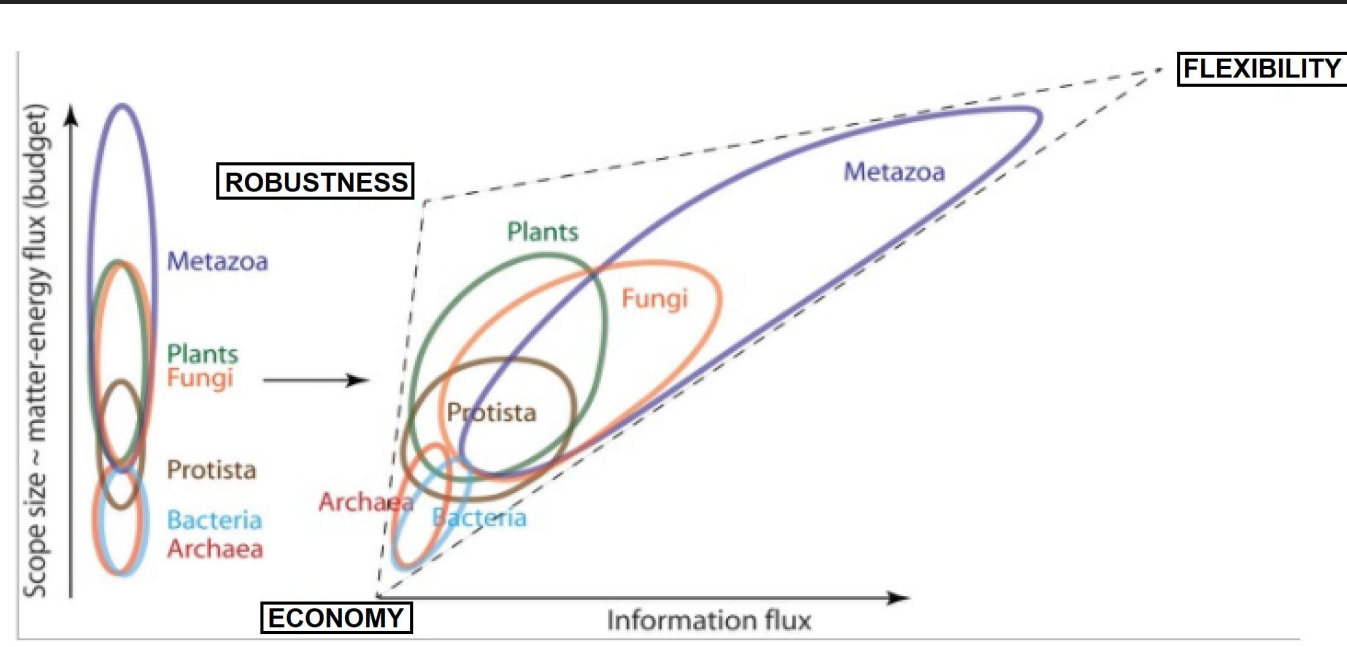
## 2. Growing Resistance of Bacteria to Most Antibiotics

Andersson, D. I. (2003).

## 3. Synthetic Biology and Astrobiological Systems

Andrianantoandro, E., Basu, S., Karig, D. K., & Weiss, R. (2006).

# Spectrum of EFR



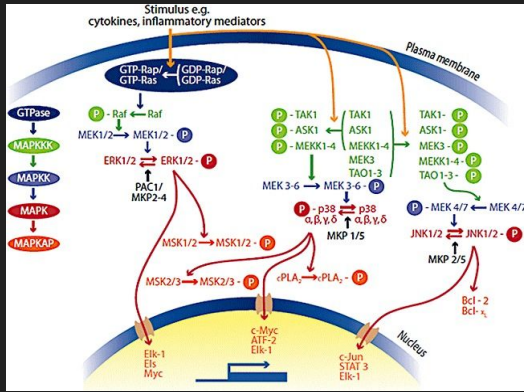
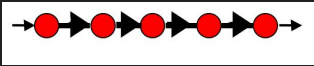
- Prokaryotes tend to gravitate towards the Economic vertex
- Single cell organisms tend to gravitate towards the robustness vertex
- Eukaryotes gravitate toward trade offs between economy and flexibility

- I. Introduction to Persistence Strategies and **Why it Matters**
- II. Methods of Investigation and Rationale
- III. Future Direction of Investigation

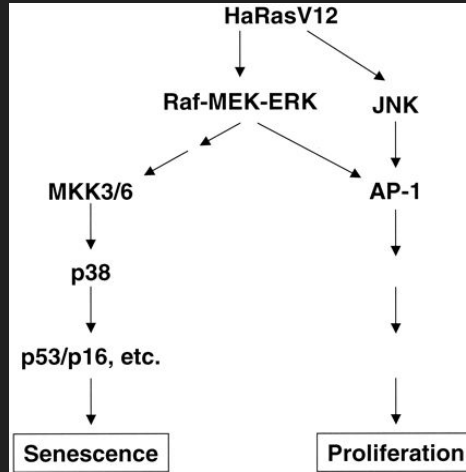
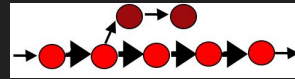
# Implementation & Analysis

Persistence

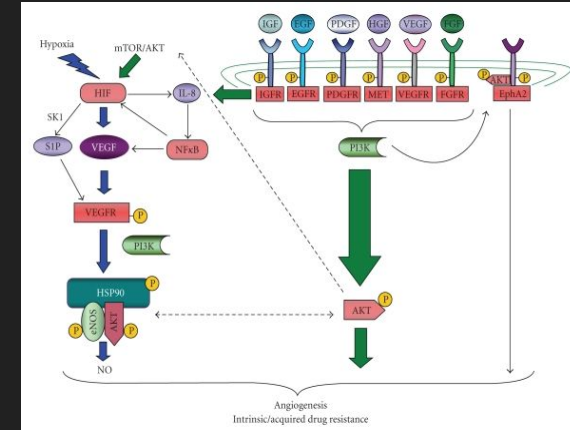
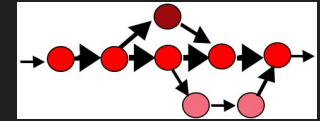
Economy



Flexibility

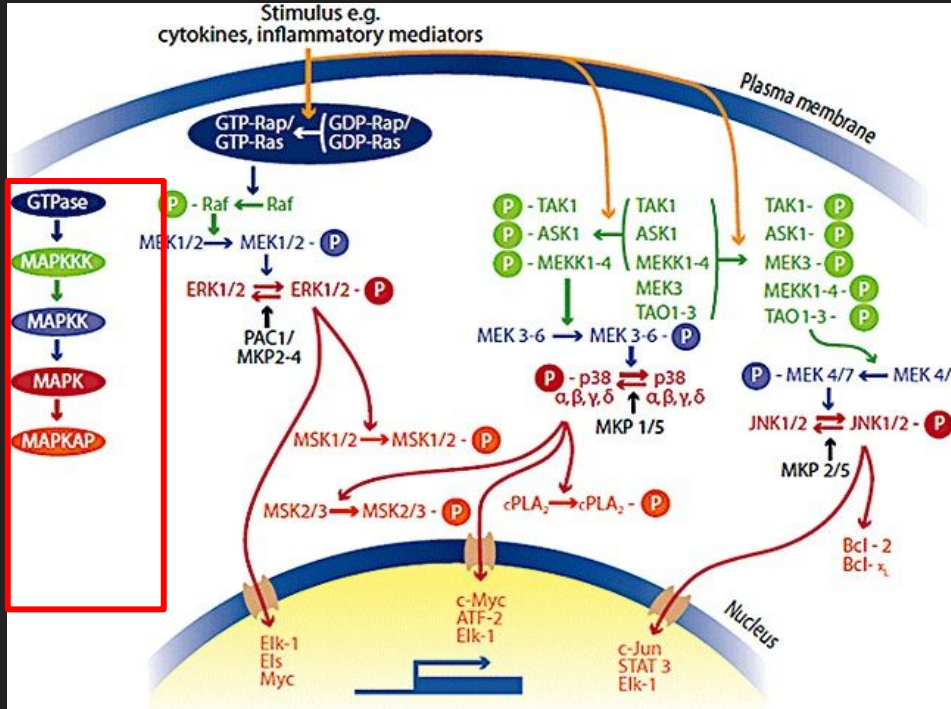


Robustness

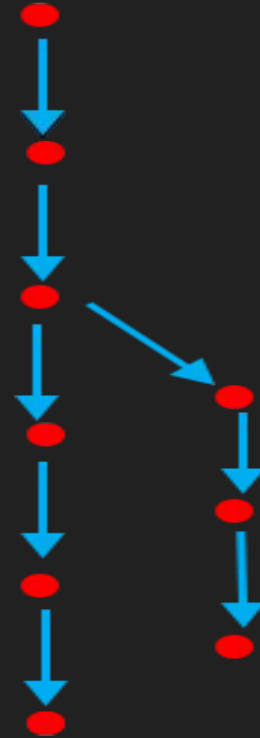
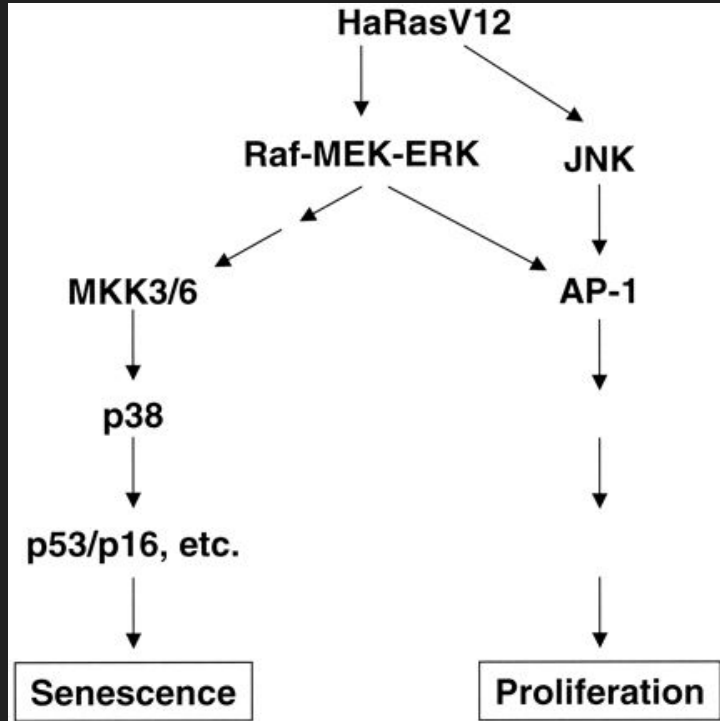




# Economy



# Flexibility

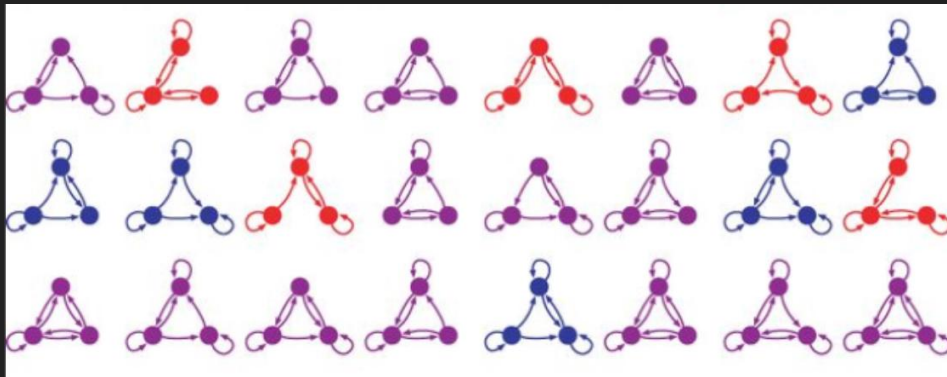
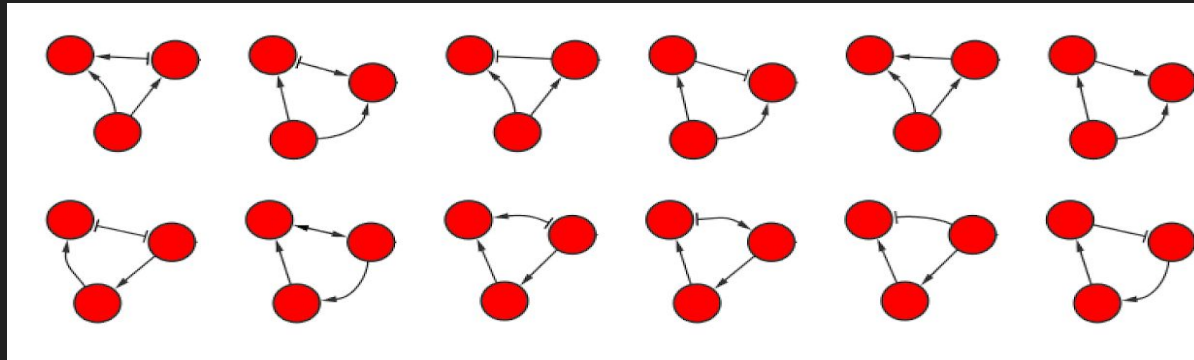




- I. Introduction to Persistence Strategies and Why it Matters
- II. Methods of Investigation and Rationale
- III. Future Direction of Investigation

# Implementation and design constraints

- 3-node networks <https://github.com/Araj6/EFR>
- Connections: inhibitory, excitatory, self-activation, self-inhibition
- Only one node receives input



# Interesting network motifs

## Coherent FFL

Coherent type 1



Coherent type 2



Coherent type 3



Coherent type 4



## Incoherent FFL

Incoherent type 1



Incoherent type 2



Incoherent type 3



Incoherent type 4

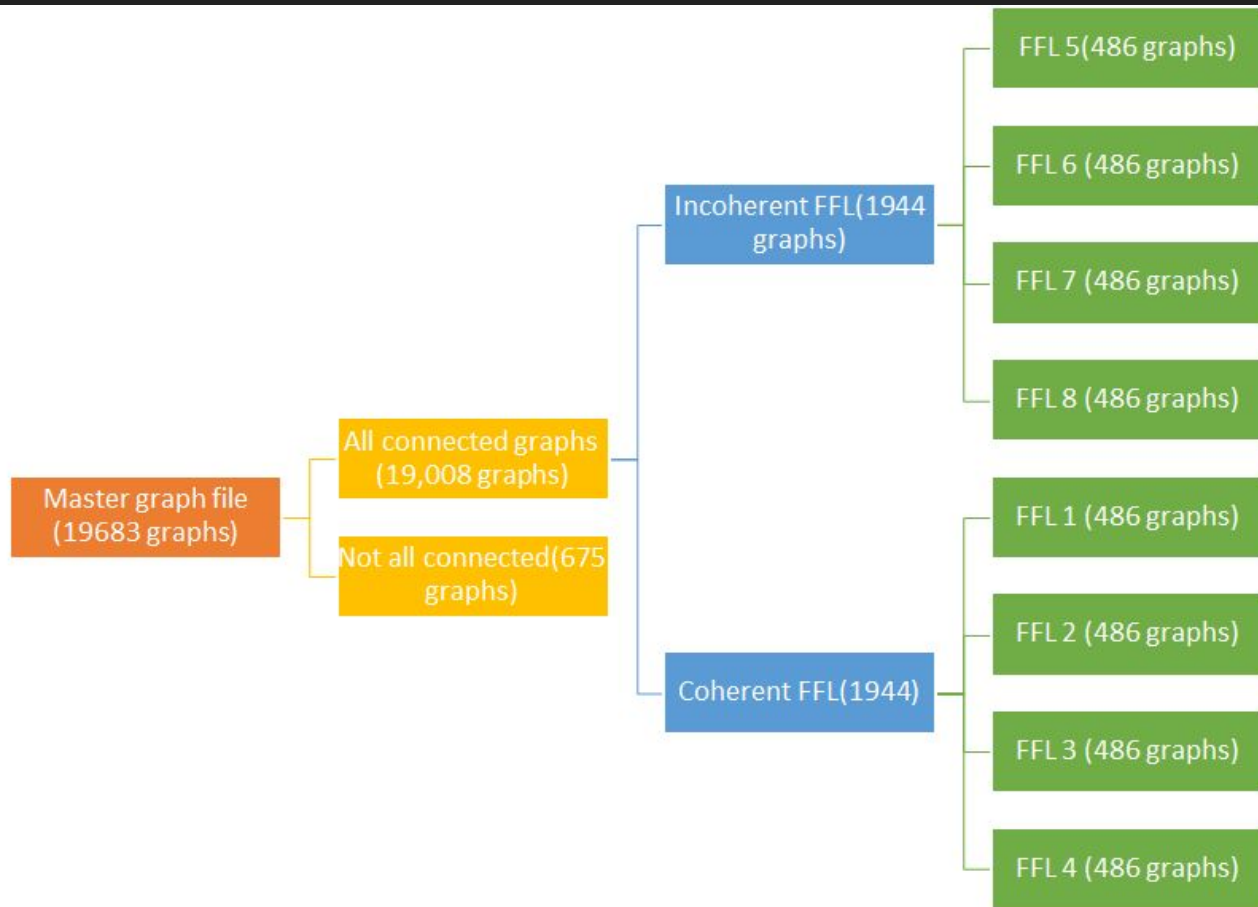


- direct
- Feed-forward
- Feed-back
- Coherent
- incoherent

# Grouping the graphs

Total number of  
3-node  
networks:19683

We looked for  
interesting motifs  
that could help us  
classify networks by  
persistence strategy



- I. Introduction to Persistence Strategies and Why it Matters
- II. Methods of Investigation and Rationale
- III. Future Direction of Investigation



# Takeaway and Next Steps

- **Group by Characteristics**
  - Patterns exhibiting certain traits(EFR)
  - Number of FFLs, FBLs, Coherent, Incoherent
- **Network Behavior & Dynamics**
  - Analysis beyond architecture via modelling
- **Expand Beyond 3 Nodes**
  - Are the patterns observed for 3-node diagrams present at higher level network topologies?

# Acknowledgments

I would like to thank both my advisers Dr. Mainzer and Dr. Mittenthal, as well as the National Center for Supercomputing Applications, the Informatics Department, and the Office of Undergraduate Research.



# References

- Ahnert, S. E., & Fink, T. M. A. (2016). Form and function in gene regulatory networks: the structure of network motifs determines fundamental properties of their dynamical state space. *Journal of The Royal Society Interface*, 13(120), 20160179.
- Andersson, D. I. (2003). Persistence of antibiotic resistant bacteria. *Current opinion in microbiology*, 6(5), 452-456.
- Andrianantoandro, E., Basu, S., Karig, D. K., & Weiss, R. (2006). Synthetic biology: new engineering rules for an emerging discipline. *Molecular systems biology*, 2(1).
- Broom, Oliver & Widjaya, Budiman & Troelsen, J & Olsen, J & Nielsen, Ole. (2009). Mitogen activated protein kinases: A role in inflammatory bowel disease?. *Clinical and experimental immunology*. 158. 272-80. 10.1111/j.1365-2249.2009.04033.x.
- E Bohonowych, J & Gopal, U & Isaacs, Jennifer. (2010). Hsp90 as a Gatekeeper of Tumor Angiogenesis: Clinical Promise and Potential Pitfalls. *Journal of oncology*. 2010. 412985. 10.1155/2010/412985.
- Martins, L. M. V., Xavier, G. R., Rangel, F. W., Ribeiro, J. R. A., Neves, M. C. P., Morgado, L. B., & Rumjanek, N. G. (2003). Contribution of biological nitrogen fixation to cowpea: a strategy for improving grain yield in the semi-arid region of Brazil. *Biology and fertility of soils*, 38(6), 333-339.
- Wang, W., Chen, J. X., Liao, R., Deng, Q., Zhou, J. J., Huang, S., & Sun, P. (2002). Sequential activation of the MEK-extracellular signal-regulated kinase and MKK3/6-p38 mitogen-activated protein kinase pathways mediates oncogenic ras-induced premature senescence. *Molecular and cellular biology*, 22(10), 3389-3403.
- Yafremava, L. S., Wielgos, M., Thomas, S., Nasir, A., Wang, M., Mittenthal, J. E., & Caetano-Anollés, G. (2013). A general framework of persistence strategies for biological systems helps explain domains of life. *Frontiers in genetics*, 4, 16.