Introduction to complexity and biological networks

Analysis of Biological-Ecological Networks 2026

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Class goals

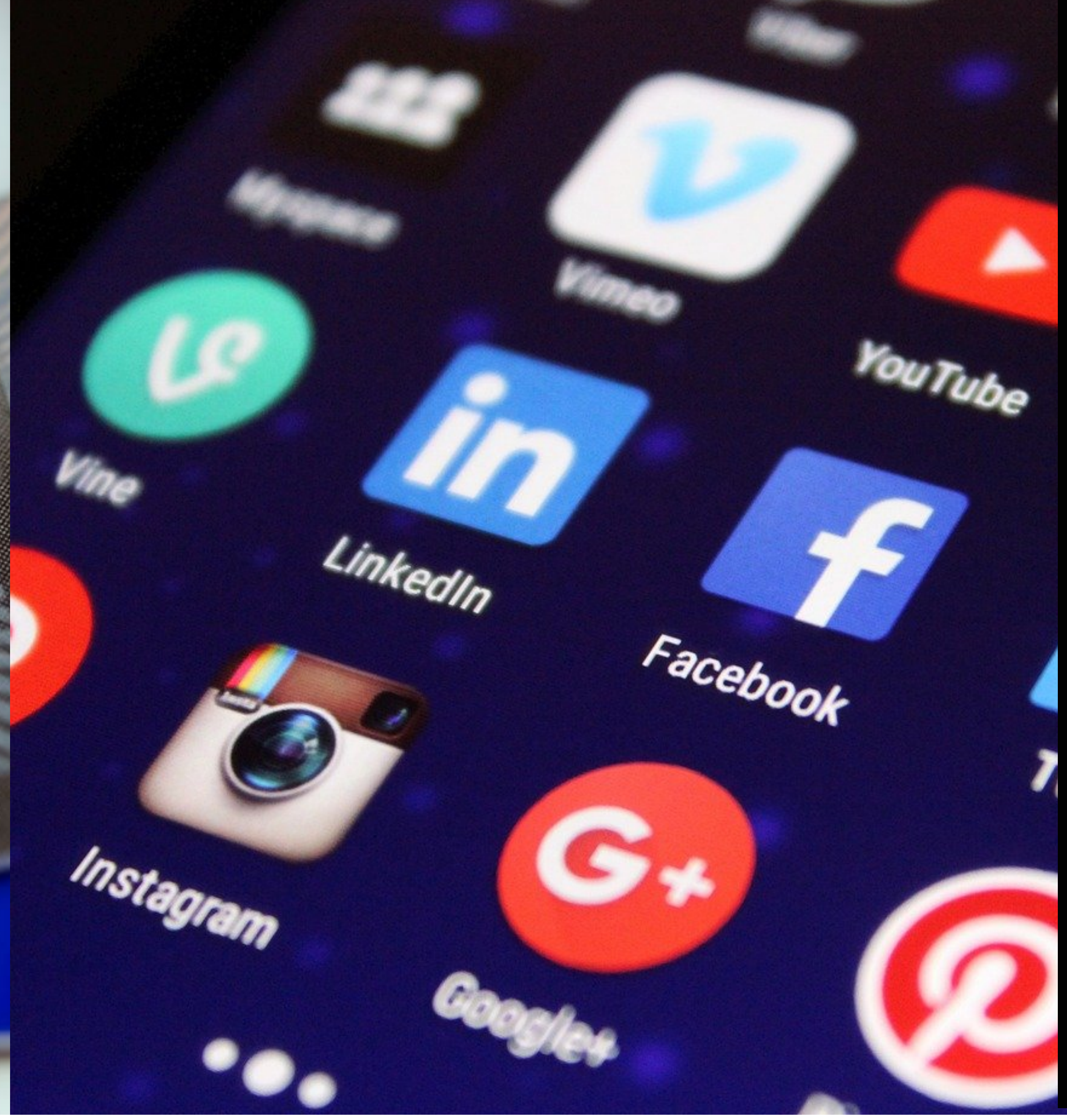
1. Introduce the basic ideas and concepts of complexity in biological systems.
2. Introduce the use of networks in biology.

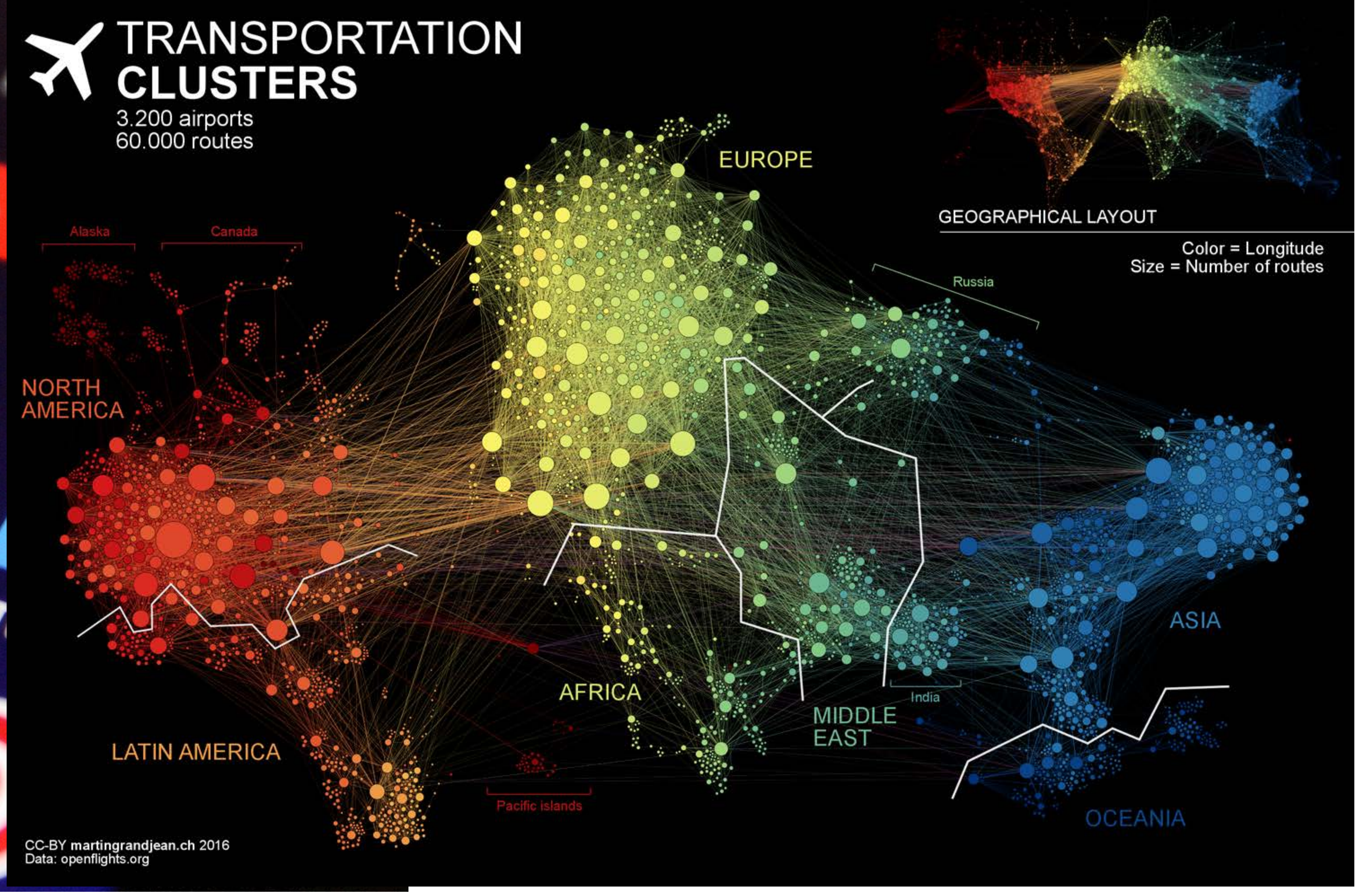
Our world is complex

I think the next century will be the century of complexity

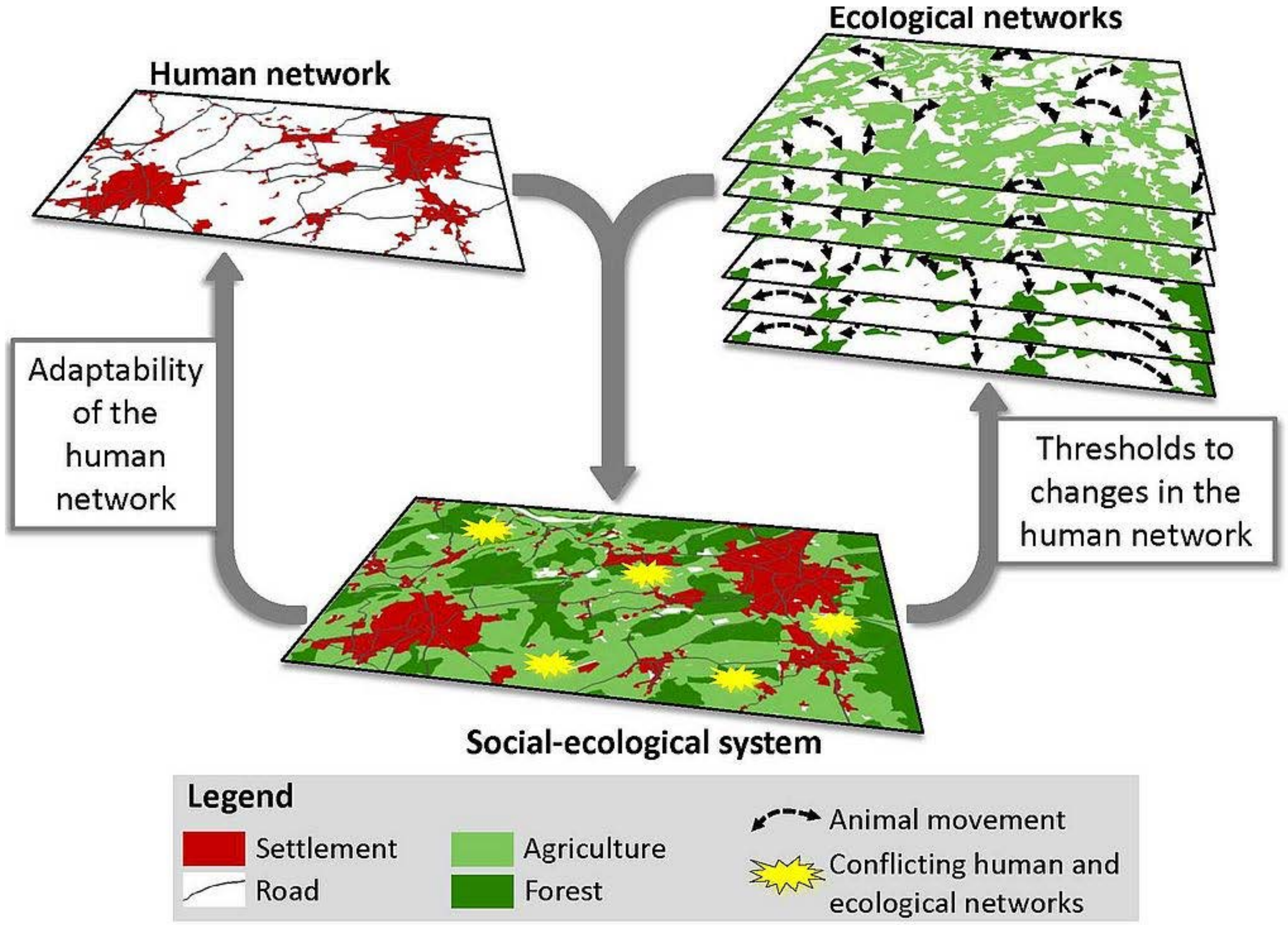
('millennium' interview 23/1/2000, San Jose Mercury News)

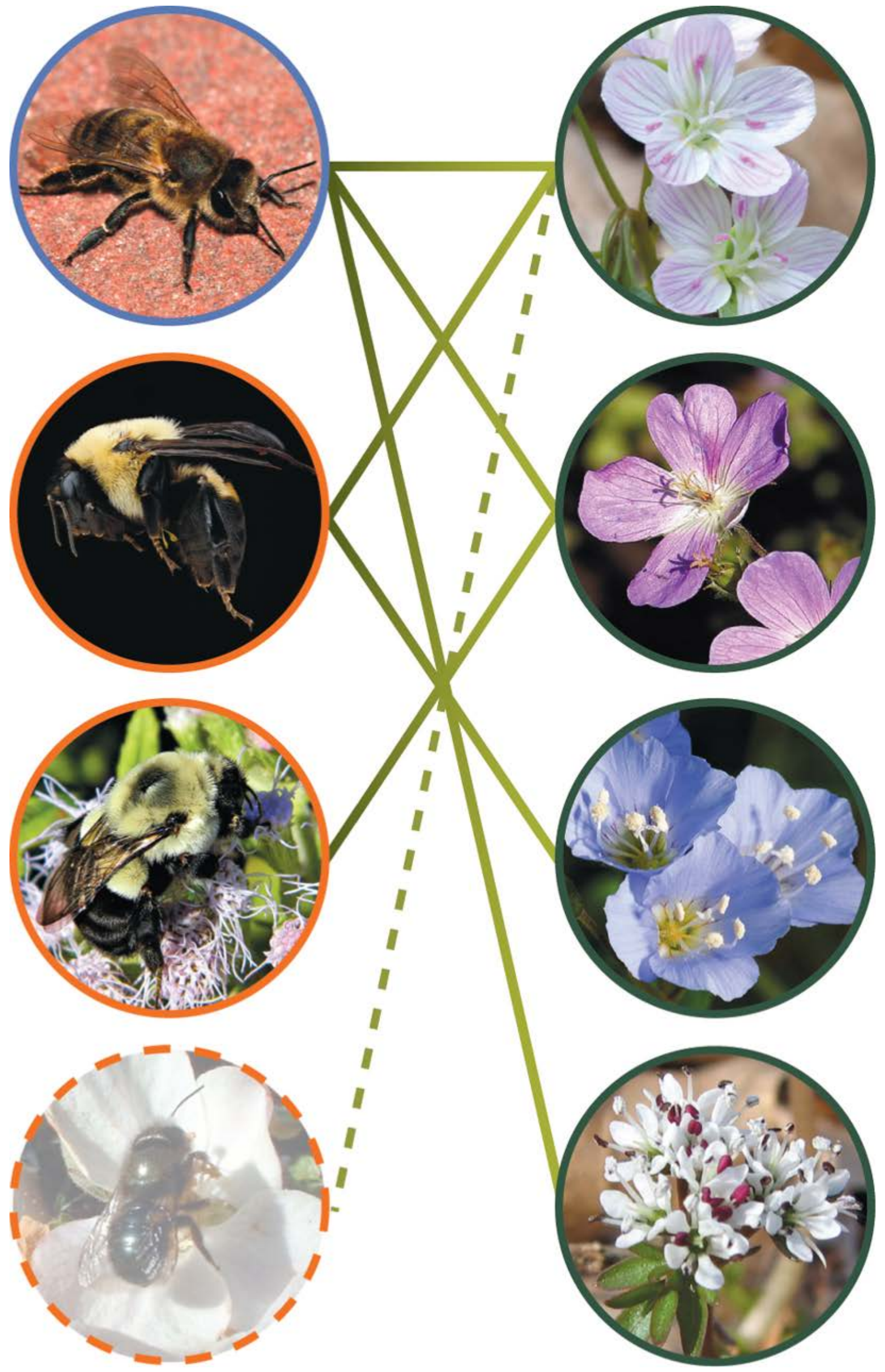
The understanding, mathematical description, prediction, and eventually control of complex systems is one of the major intellectual and scientific challenges of the 21st century.

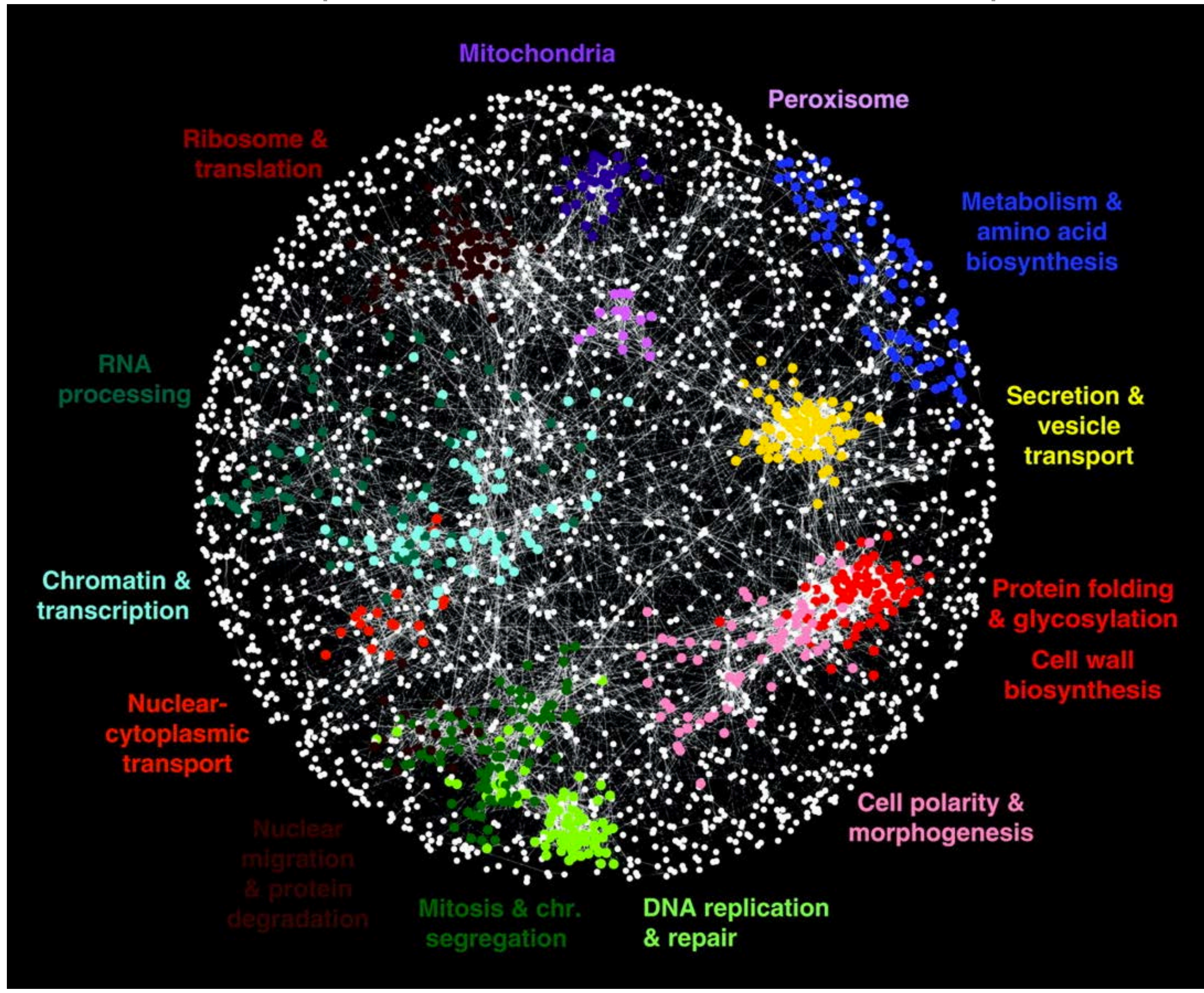




https://www.visualcapitalist.com/air-traffic-network-map/





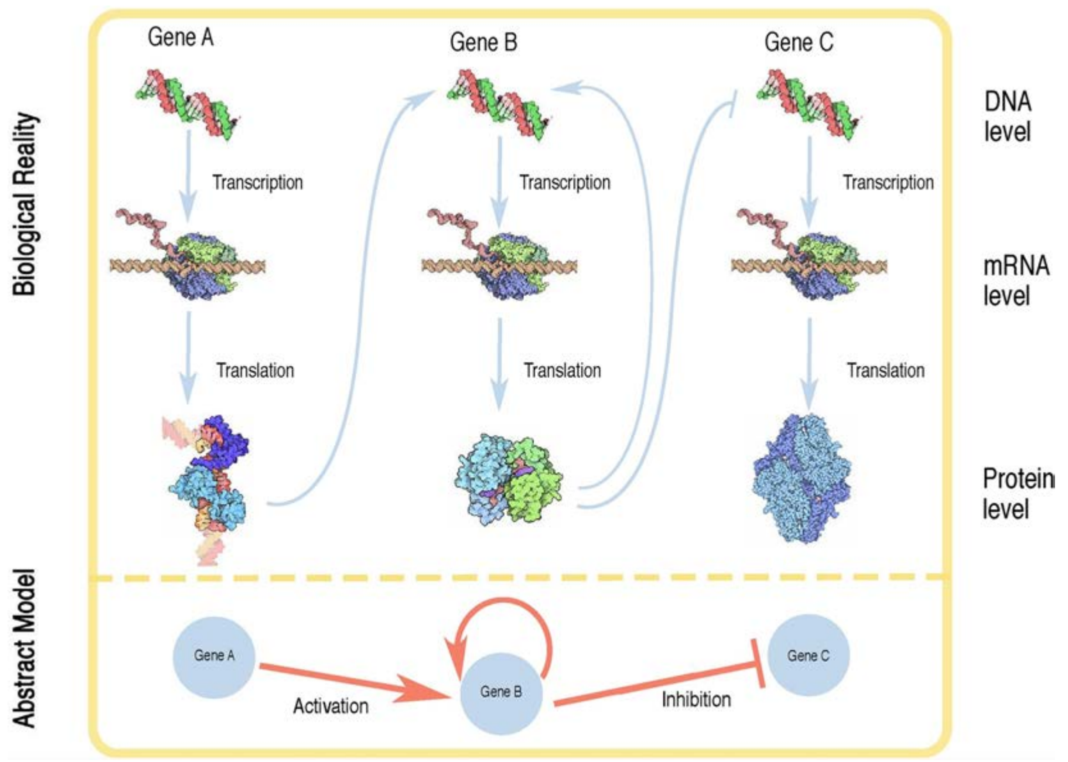


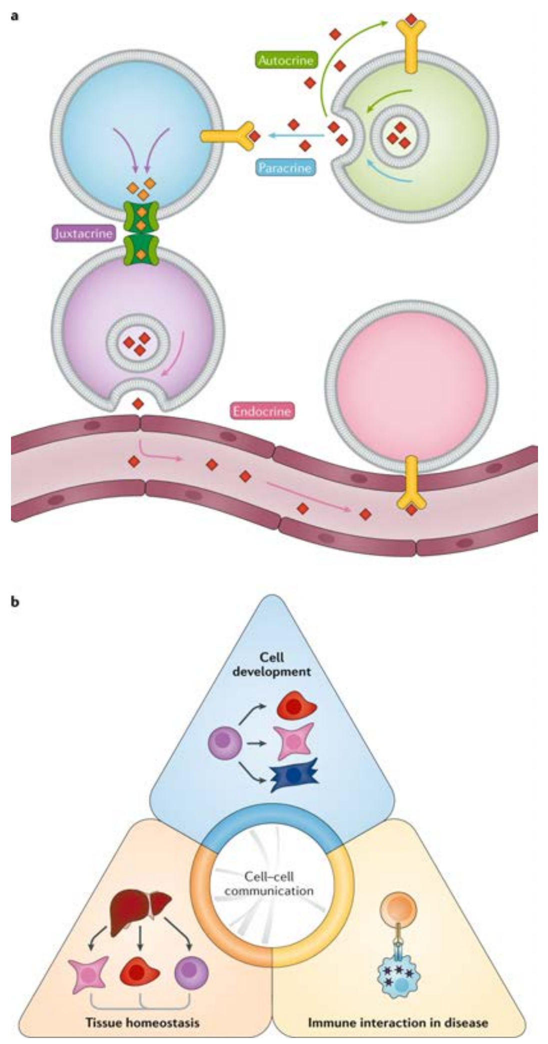
CHECNET project, WSL

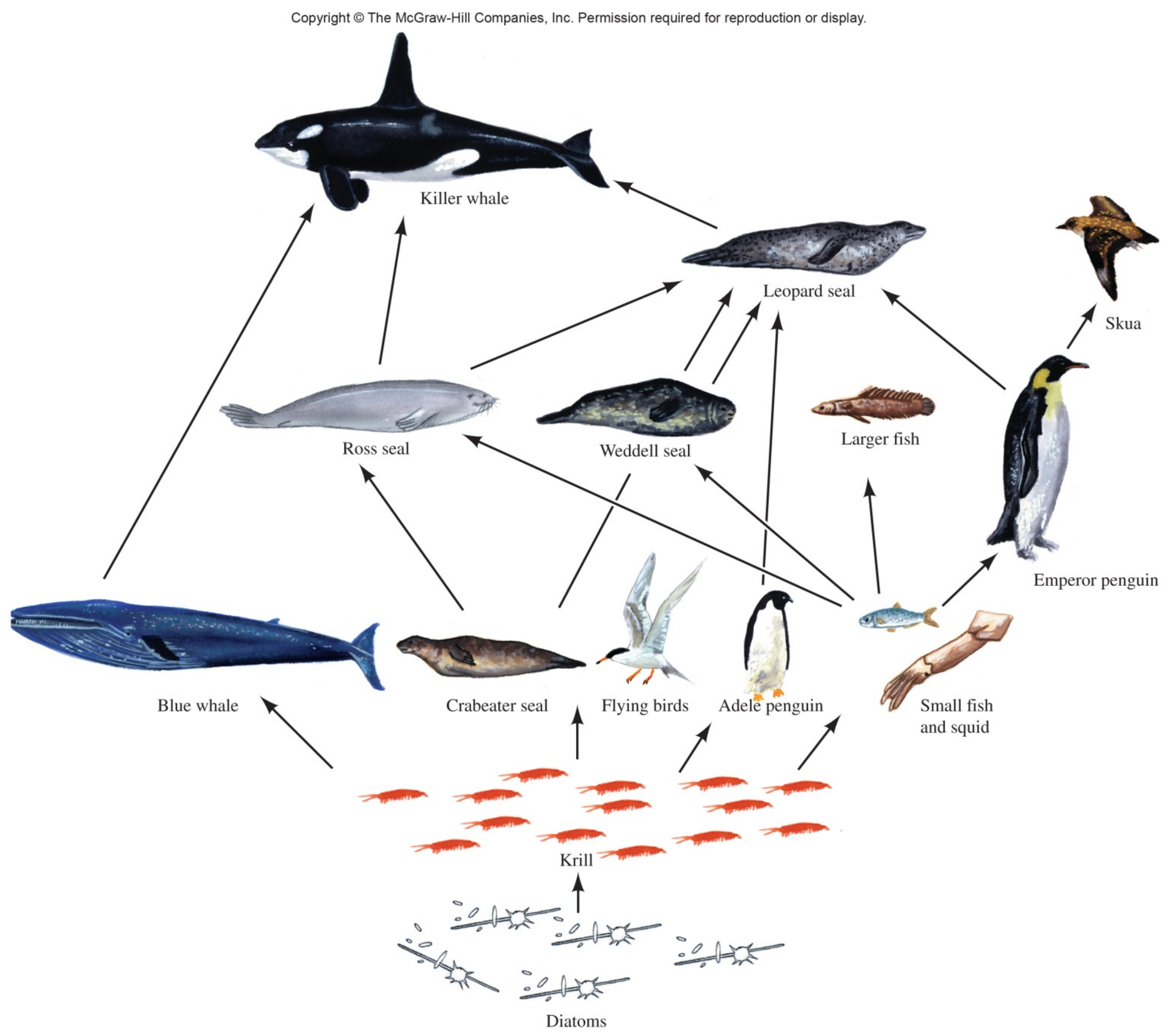
https://www.science.org/doi/10.1126/science.1235464

Cytoscape

Types of biological networks





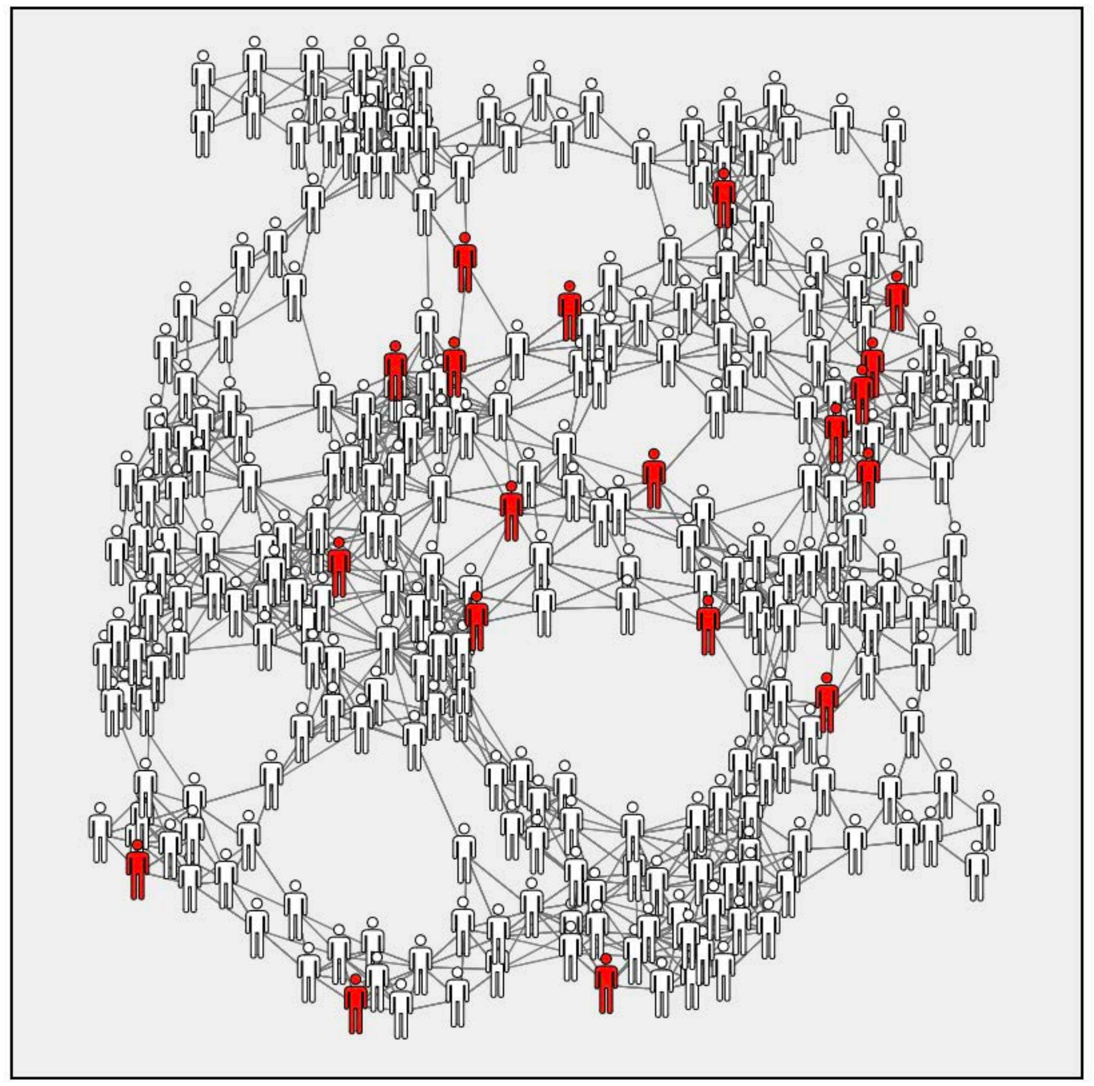


Delgado et al 2019

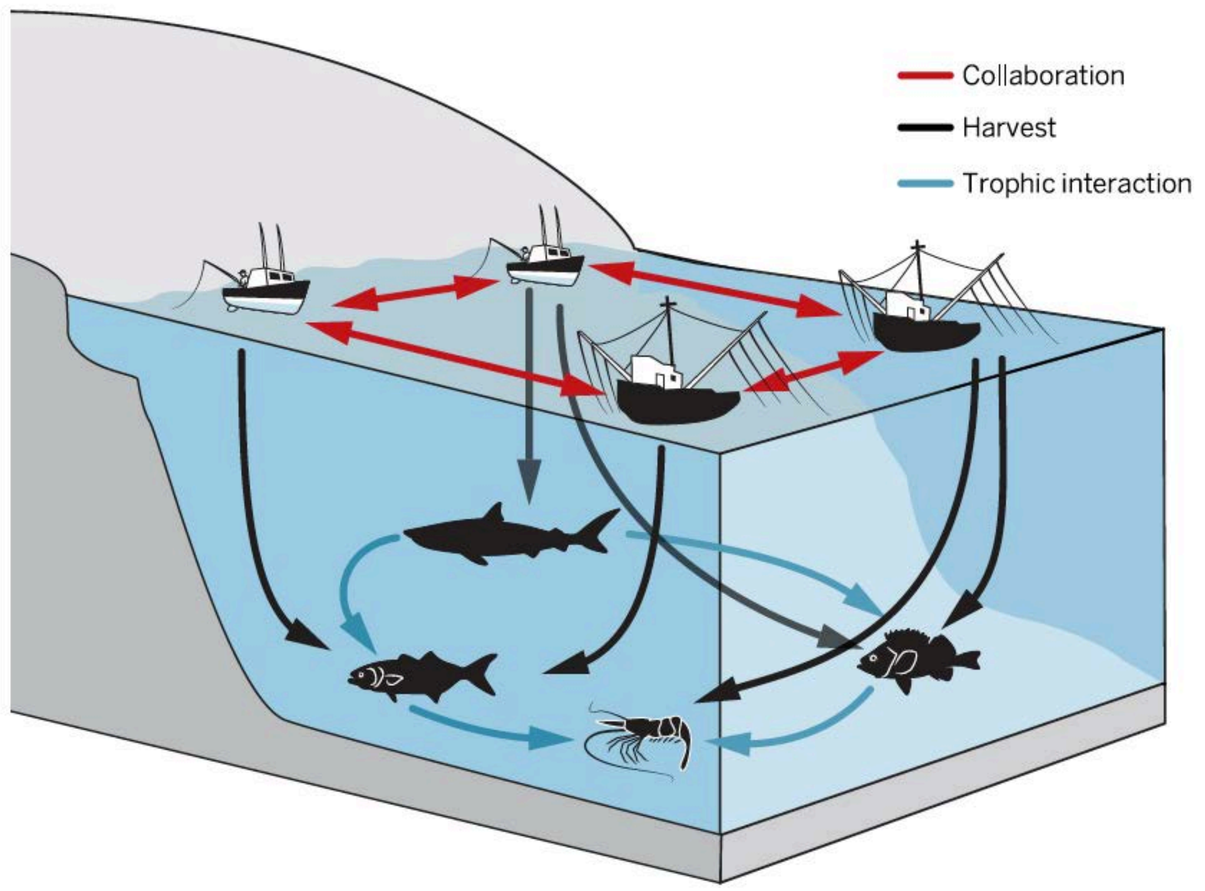
Armingol et al 2021

Shizuka et al 2020

Epidemiological networks

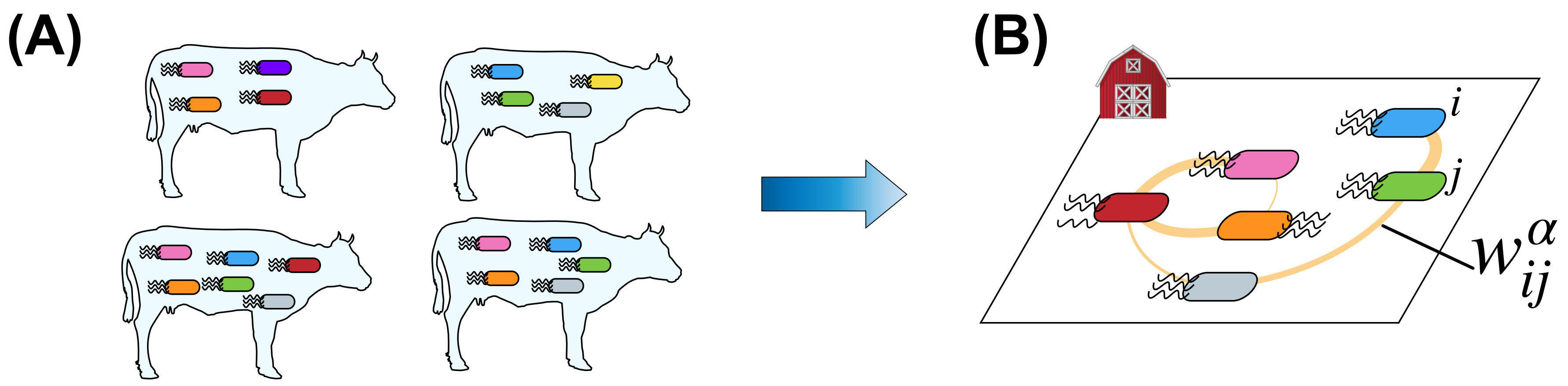


Socio-ecological networks



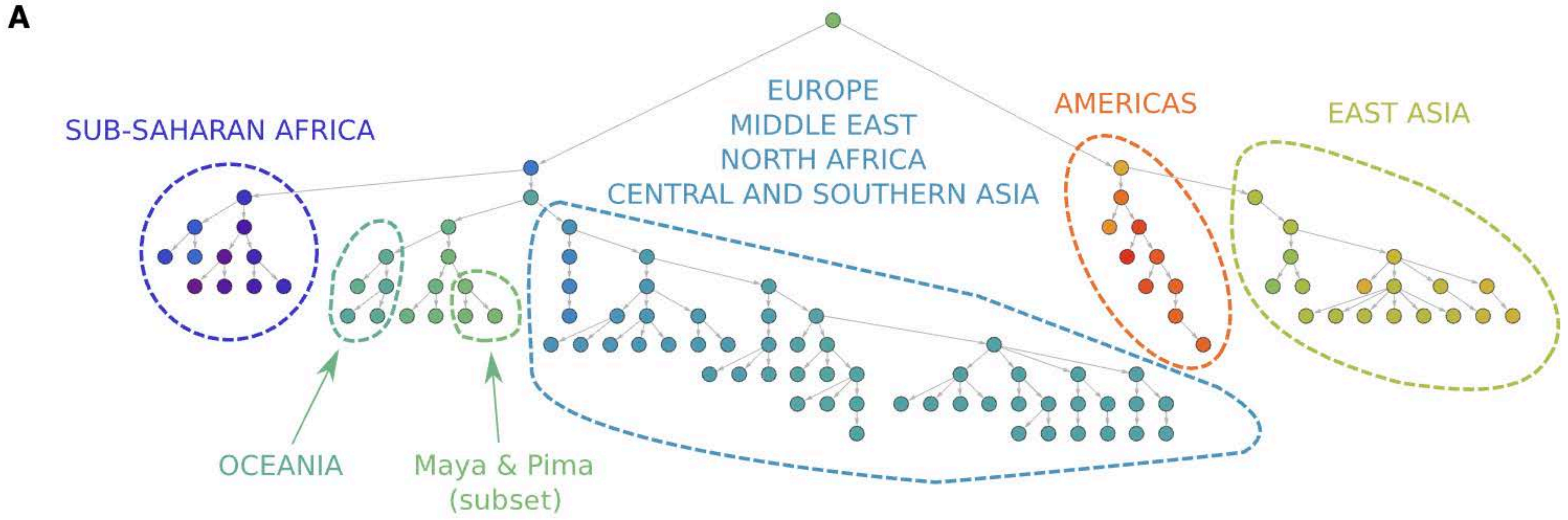
Bodin 2017, Science

Co-occurrence networks



Galai, …, Pilosof (in review)

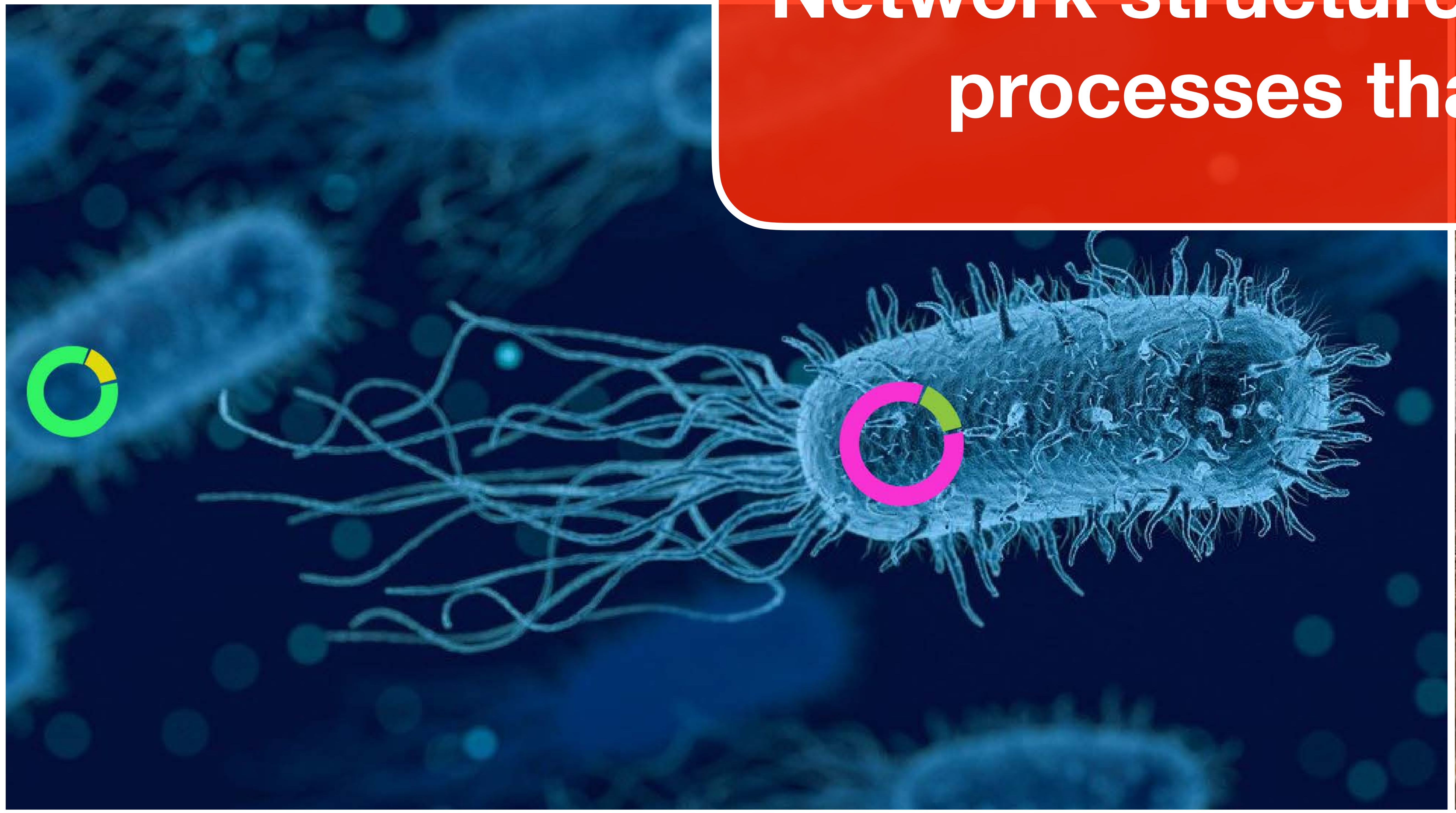
Population-genetic networks



Greenbaum et al. 2019, Genome Res.



Network structure influences biological processes that affect our lives




Biological systems are complex adaptive systems

- Components + interactions
- Emergence of patterns and behaviors
- Self-organization
- Dynamics and stability
- Adaptation and evolution
- Universality

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- **Components + interactions**
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Key concepts: nodes, links, interactions, networks

Interaction: a relationship or connection between two or more components, which can affect each other's behavior or state.

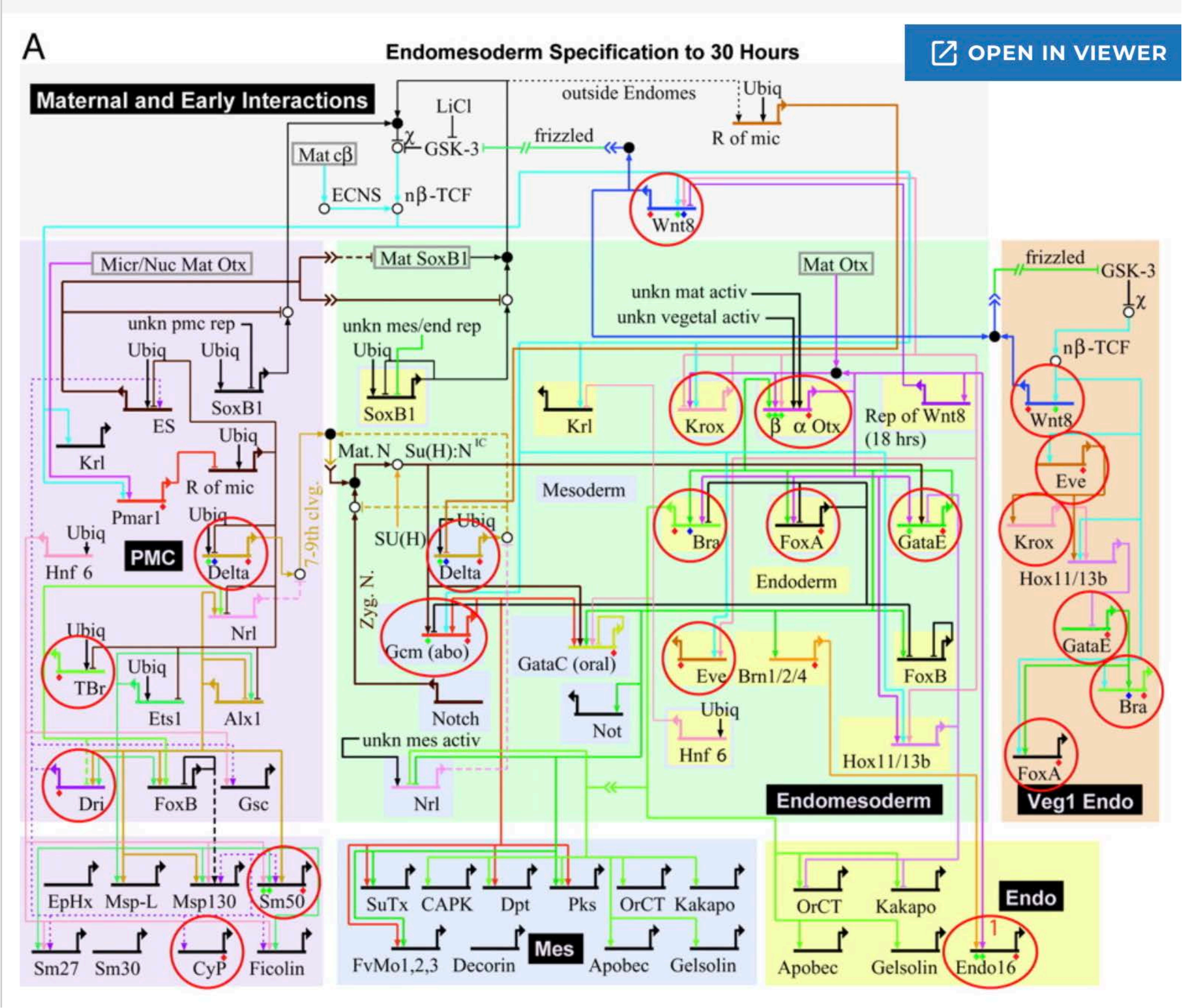
Can be physical, or functional (e.g., transcription factors on genes).

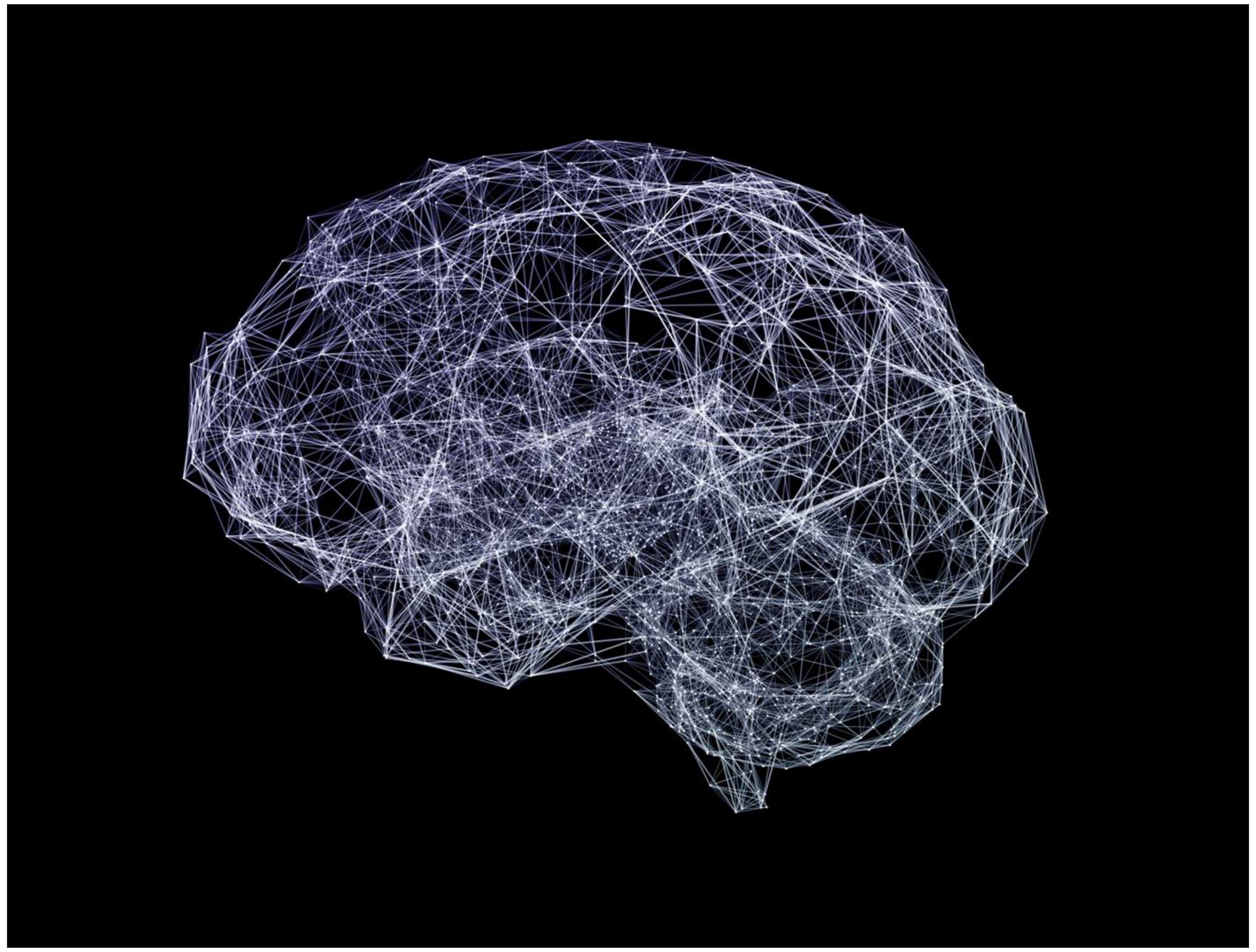
Components: molecules, genes, cells, organisms, species, etc.

Links in the network: Can represent interactions, but not necessarily.

- Correlation in gene expression.
- Social ties for potential pathogen transmission.

Discuss: Examples for biological interactions?

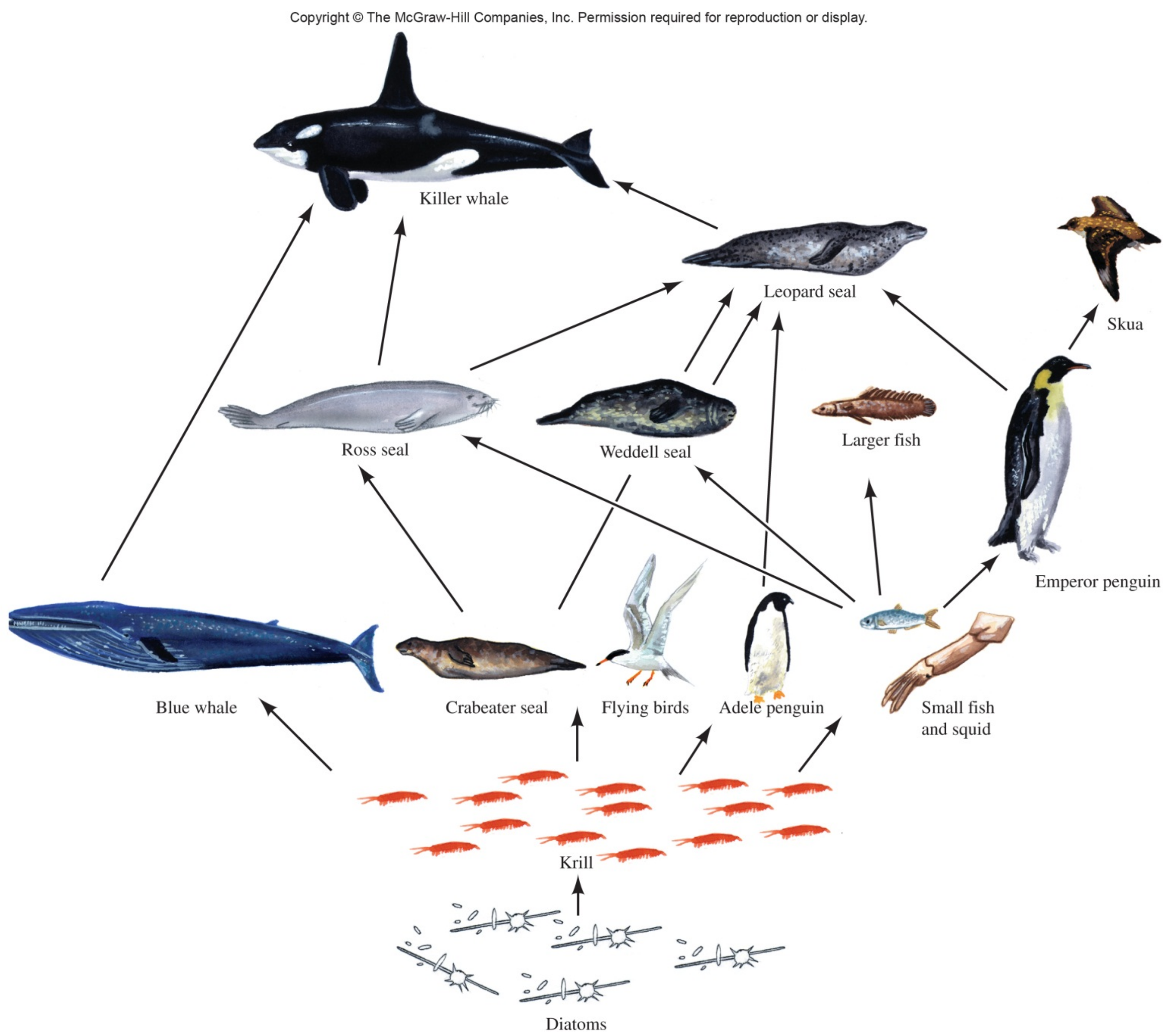




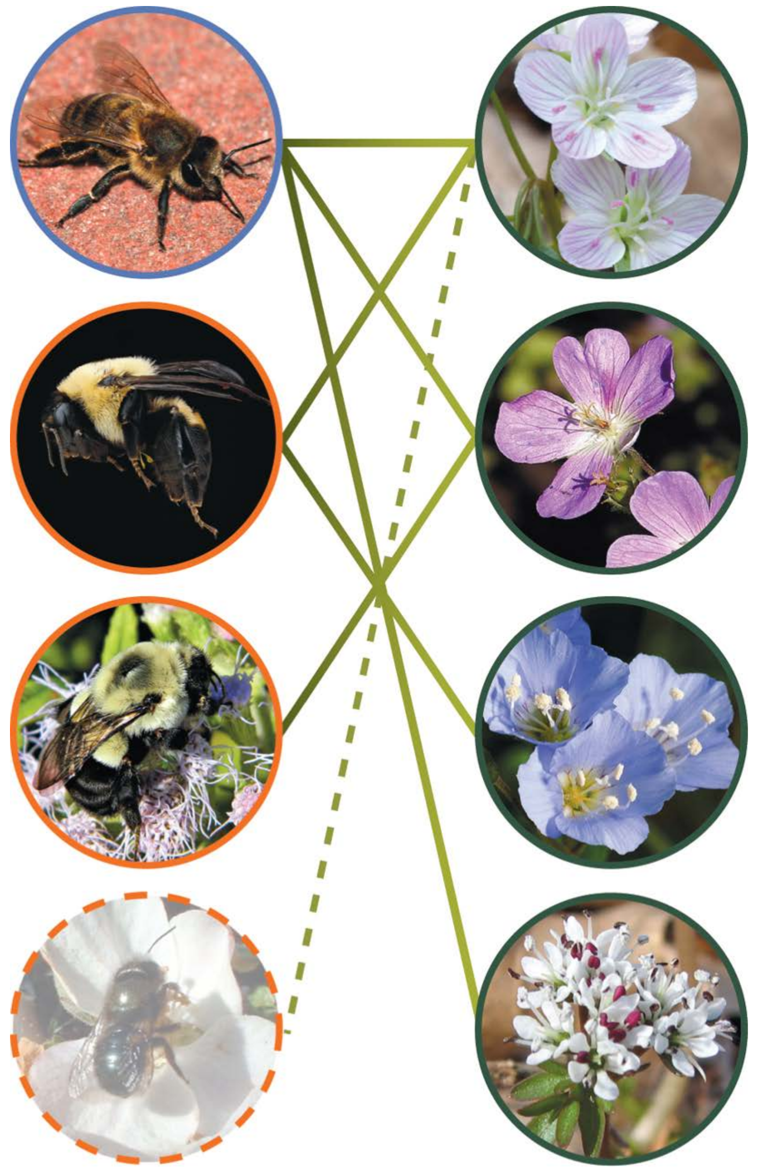
https://research.gatech.edu/new-neural-network-makes-decisions-human-would

Levine et al 2005 PNAS

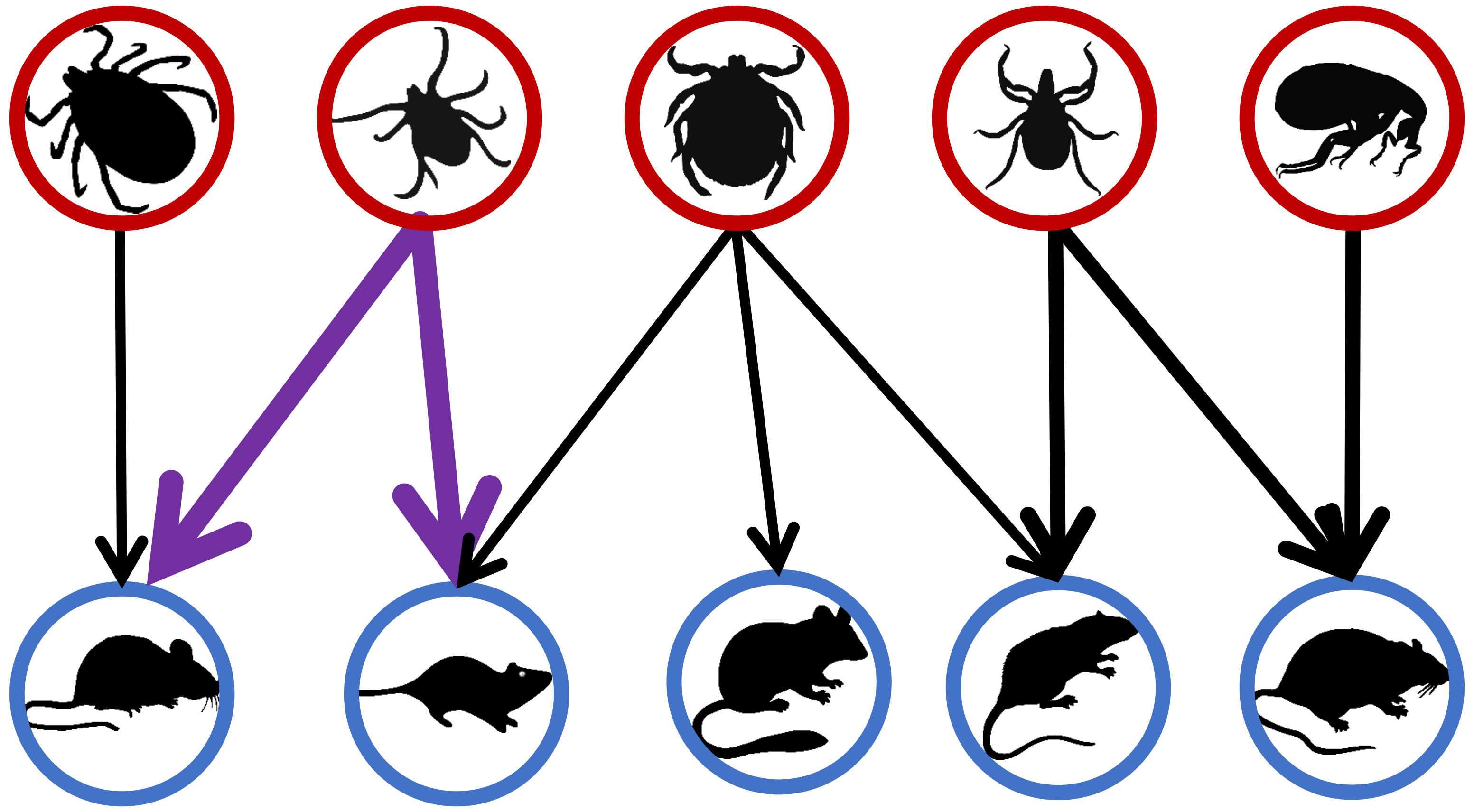
Energy flow



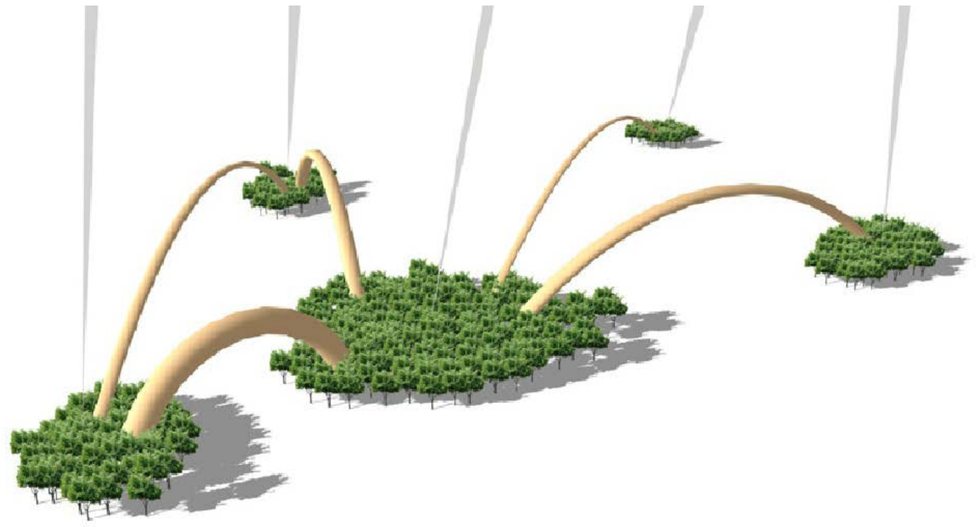
Plant-pollinator



Host-parasite

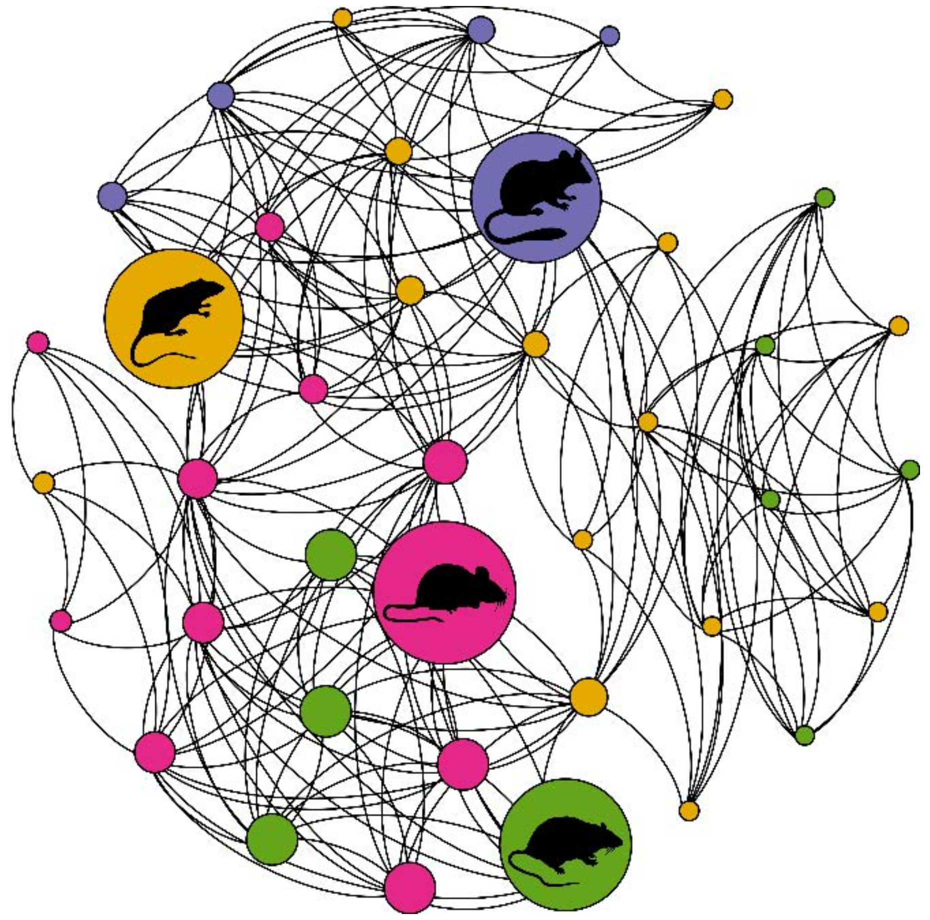


Dispersal



Hagen et al 2012

Parasite transmission



Pilosof et al 2015

Social interactions

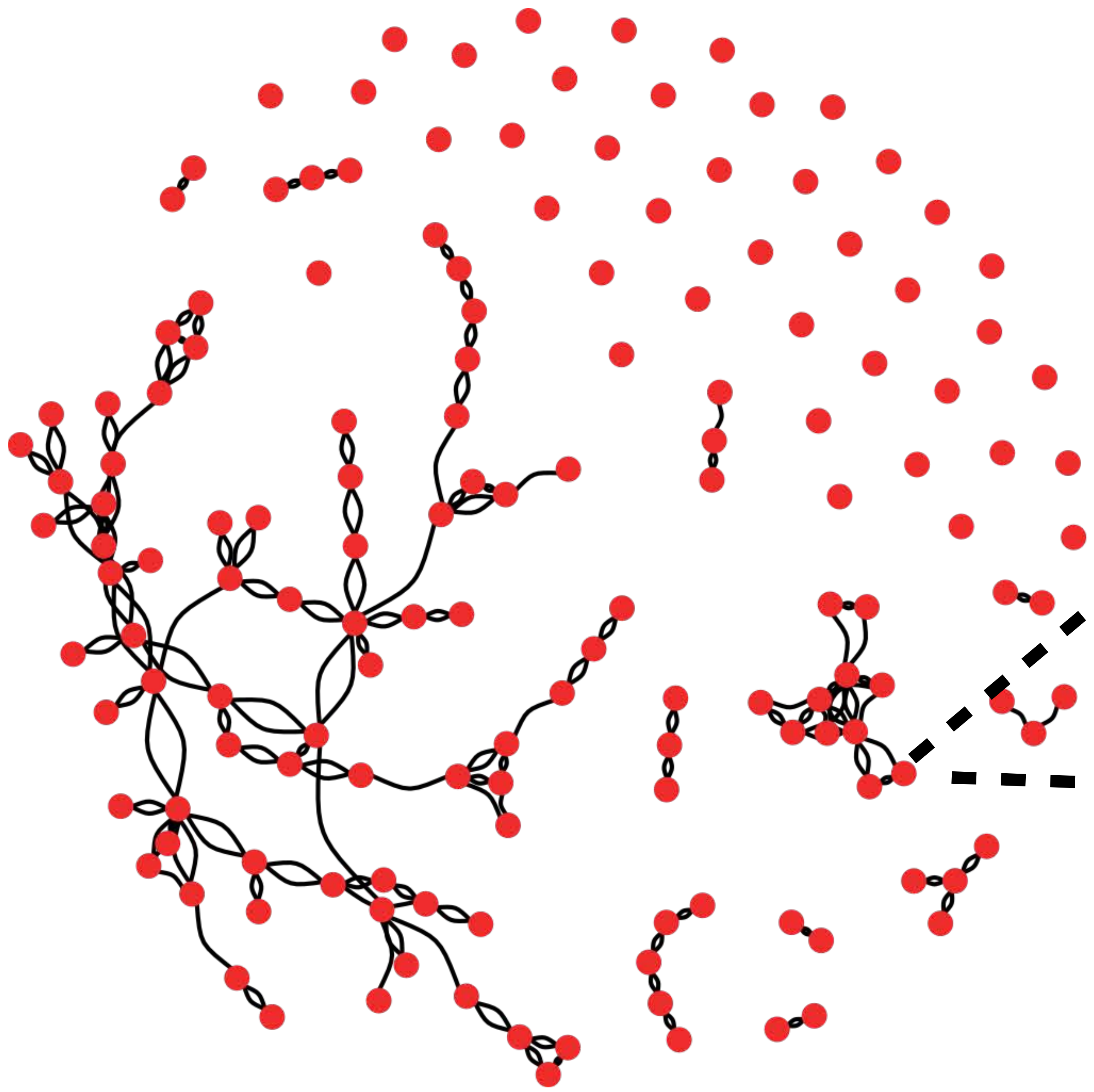
Shizuka et al 2020

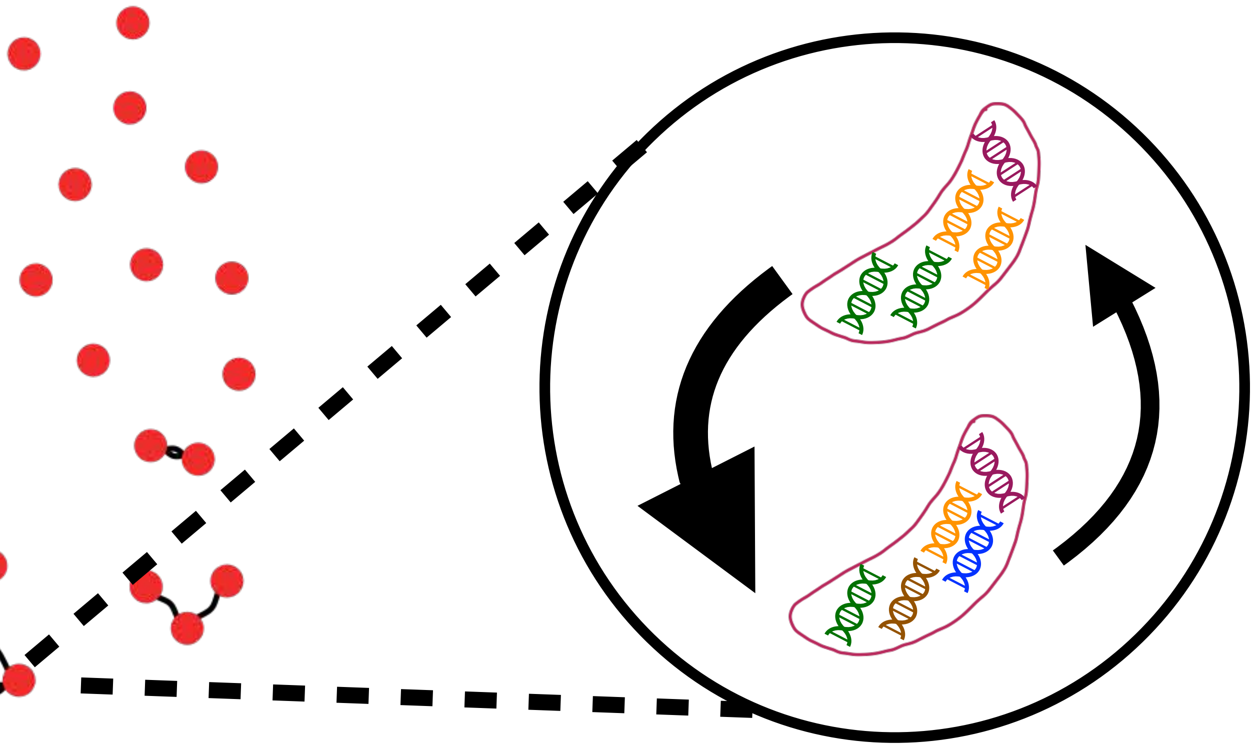
Tree connections

Simard et al 1997

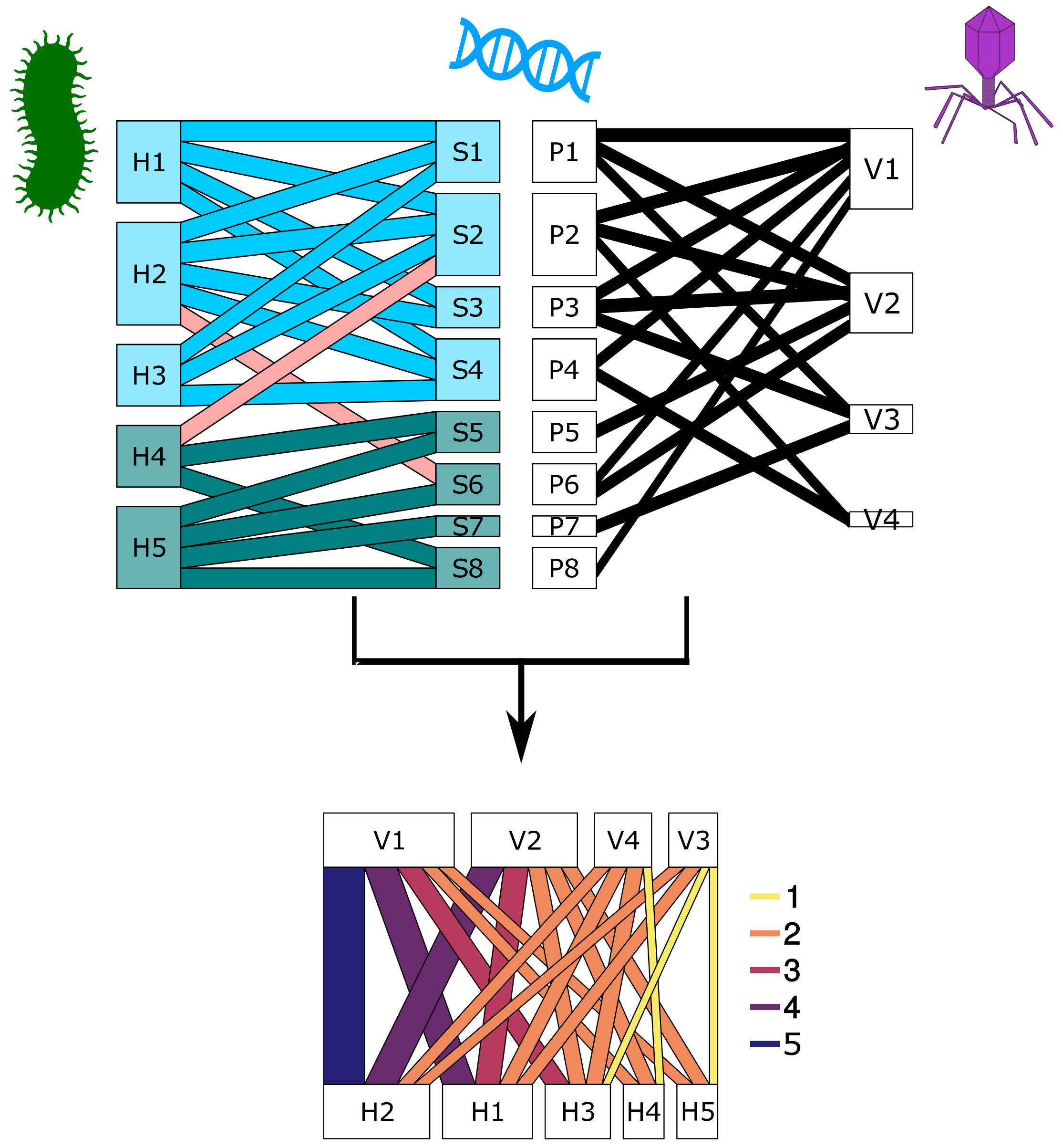
What is a link in the network?

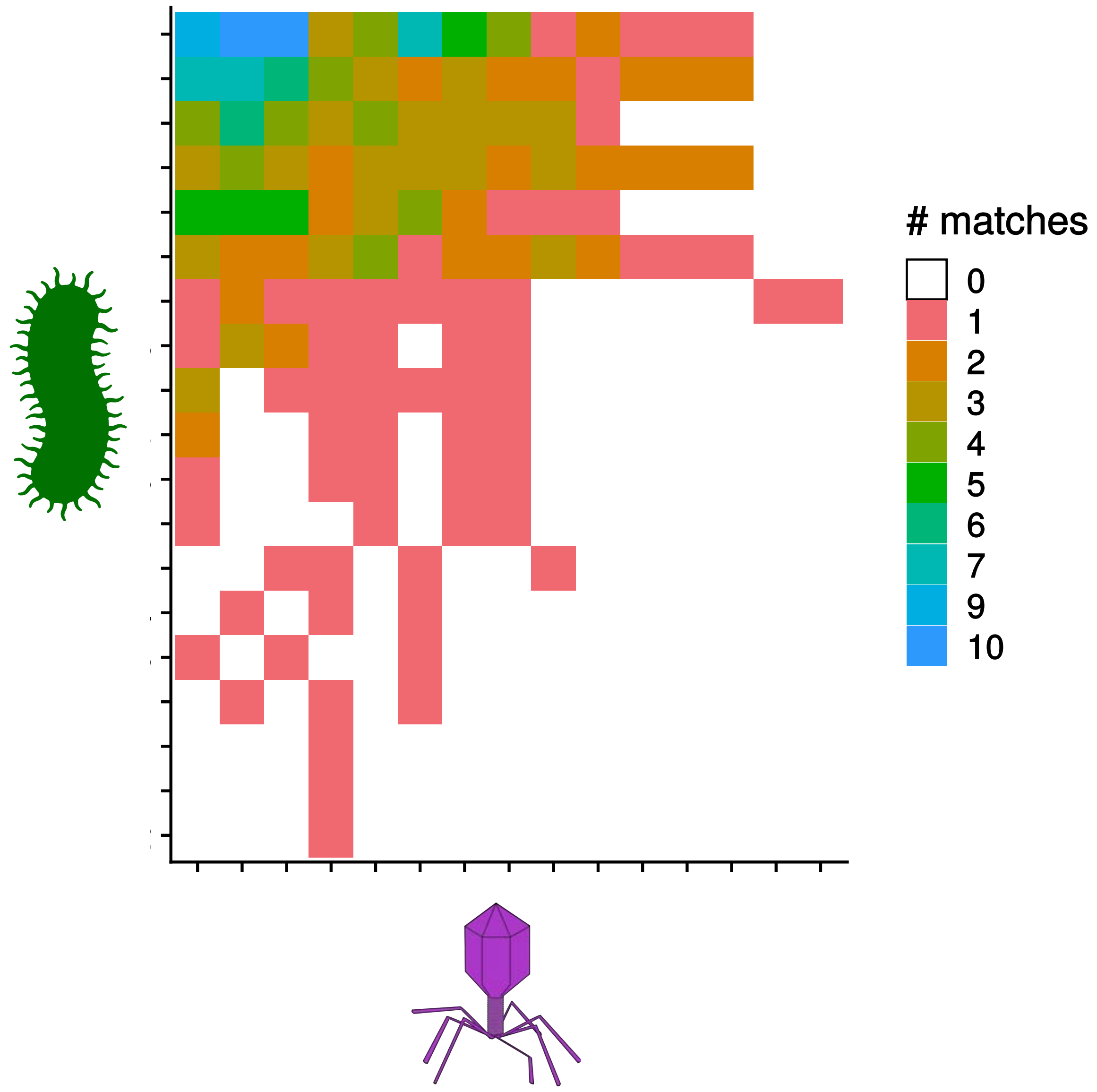
Does a link mean an interaction? How do we interpret the network?





$$S_{i \to j} = \frac{n_i \cap n_j}{n_i}$$

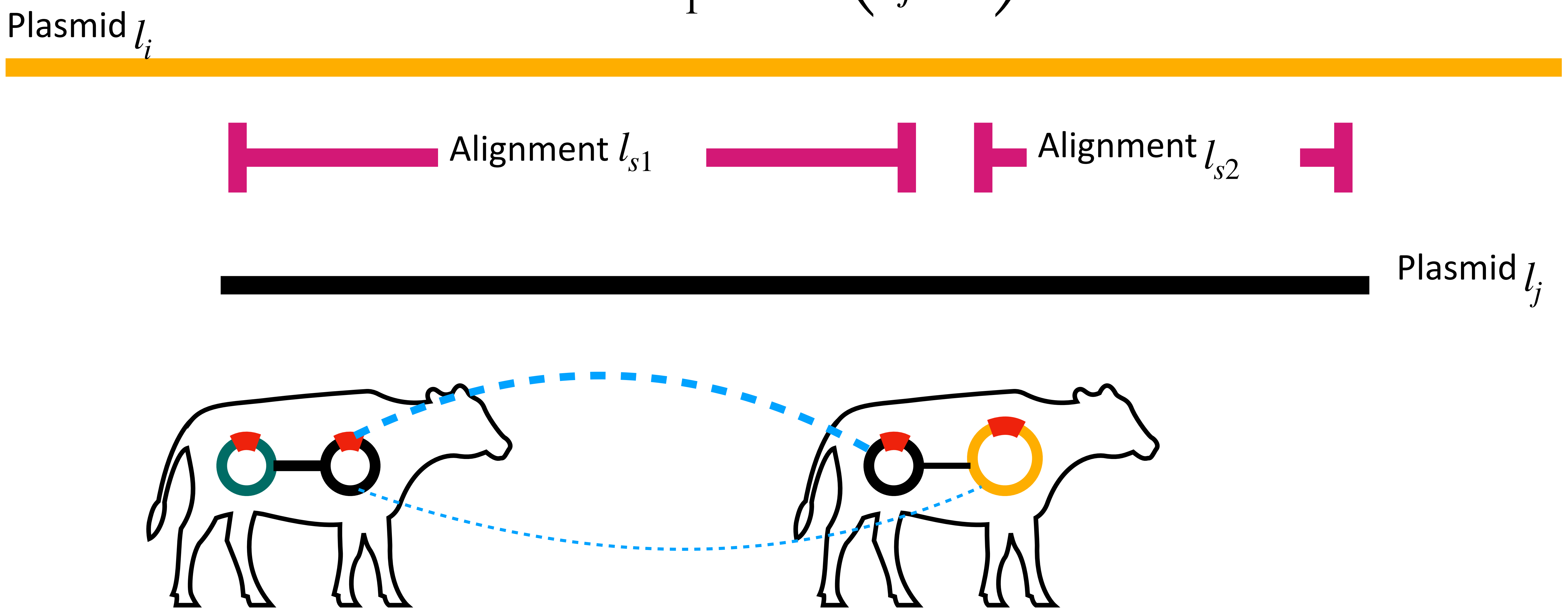




Pilosof et al 2019, 2020

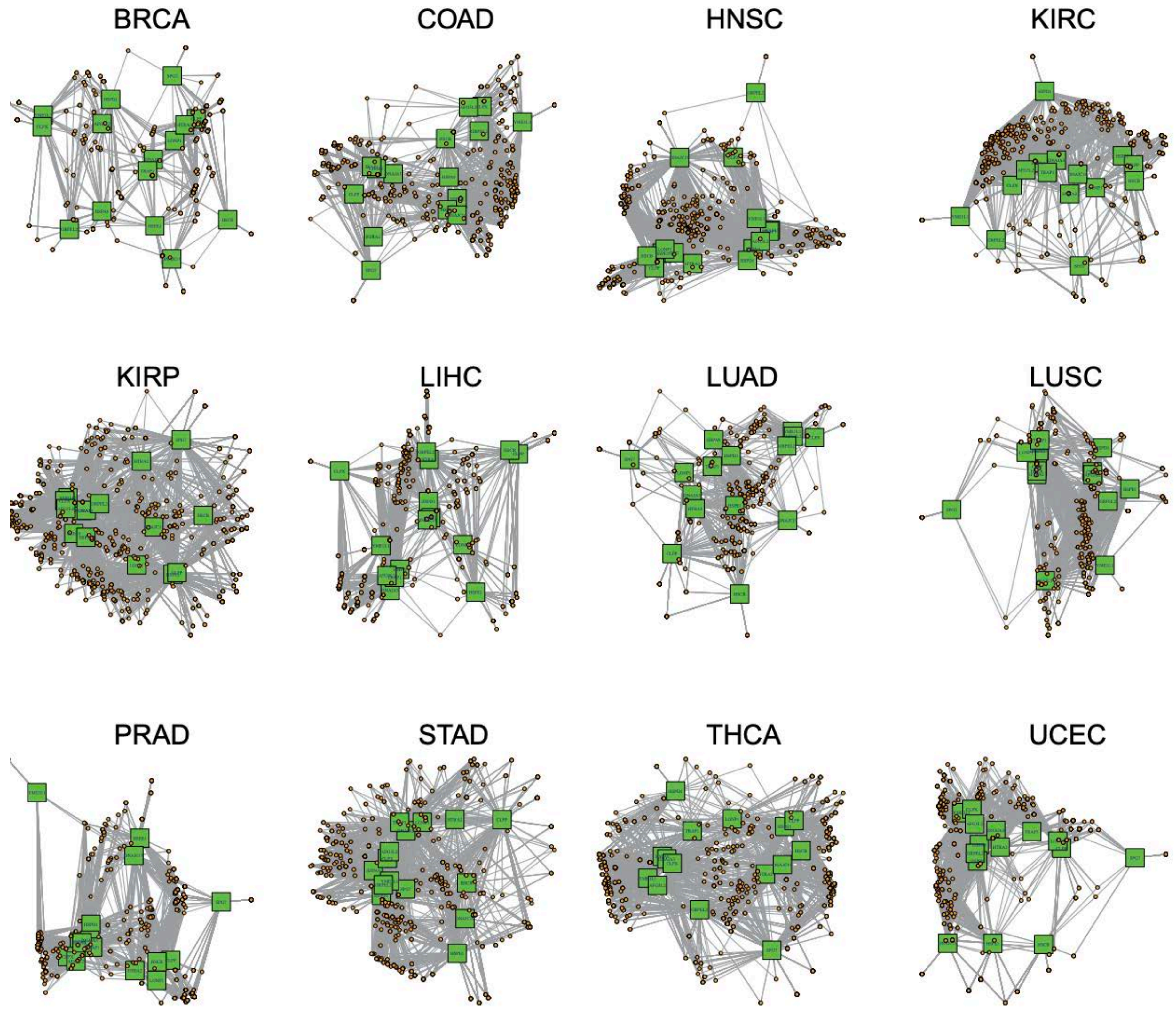
Plasmid similarity

$$w((i,\alpha),(j,\beta)) = \sum_{1}^{k} min\left(\frac{l_s}{l_j}, \frac{l_s}{l_i}\right) \cdot (\%\ \text{identity})$$



Shapiro,…,Pilosof, ISME J 2023

Gene co-expresssion



Galai,…,Pilosof, Nature Communications 2023

Biological systems are complex adaptive systems

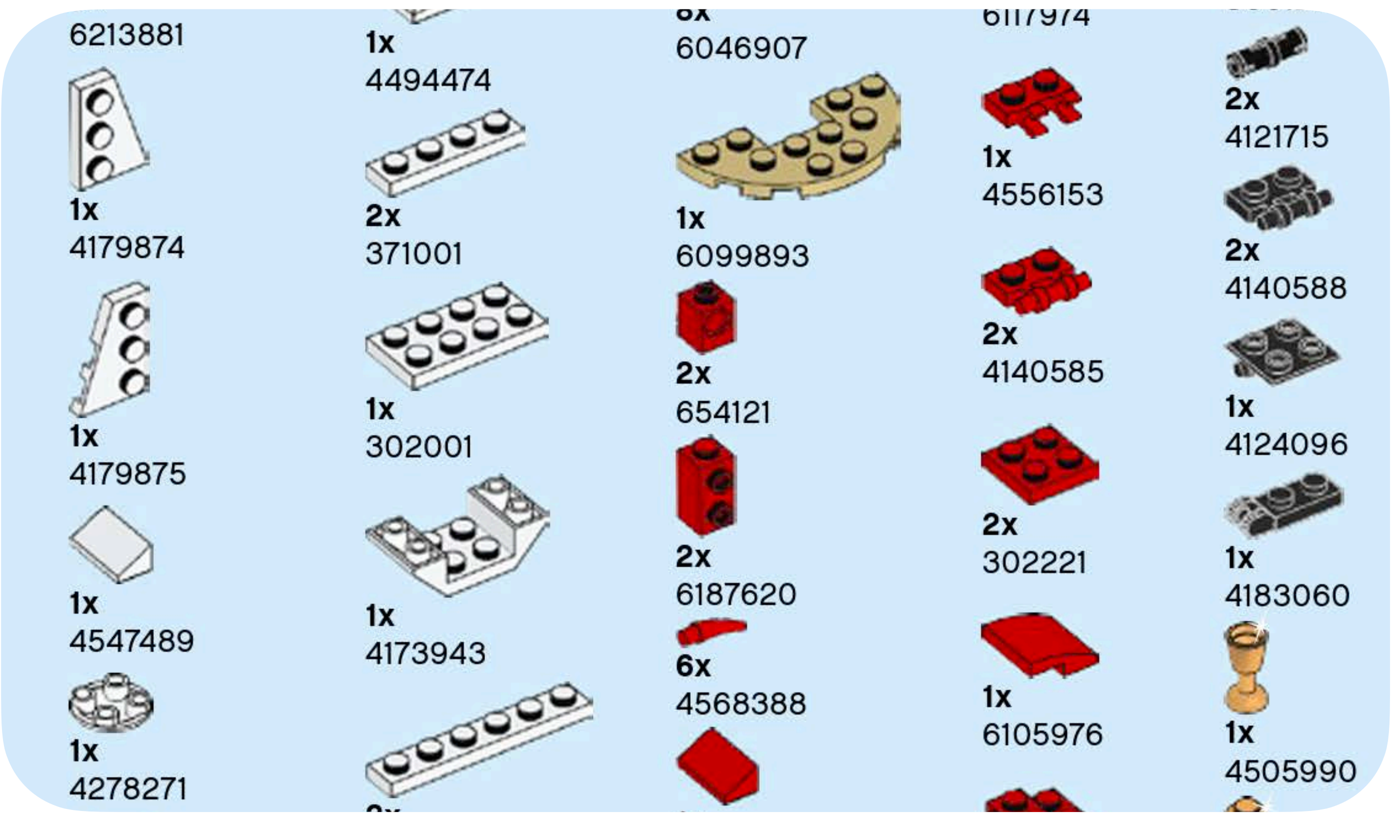
- Components + interactions
- **Emergence of patterns and behaviors**
- Self-organization
- Dynamics
- Adaptation and evolution
- Universality

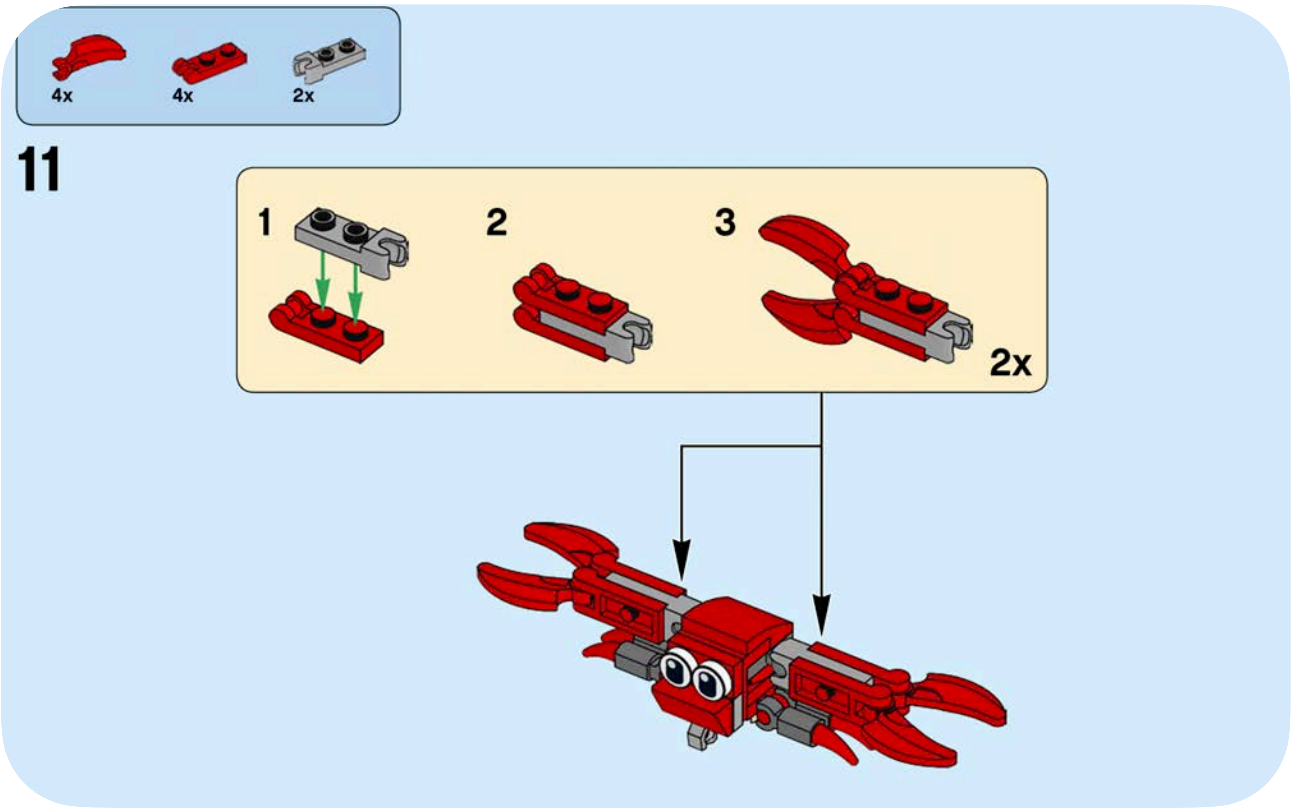
Key concepts: generative processes, microscopic rules, macroscopic patterns

Properties of complex systems as a whole are very different, and often unexpected, from properties of their individual components.

https://complexityexplained.github.io

Diversity → Rules → Emergence

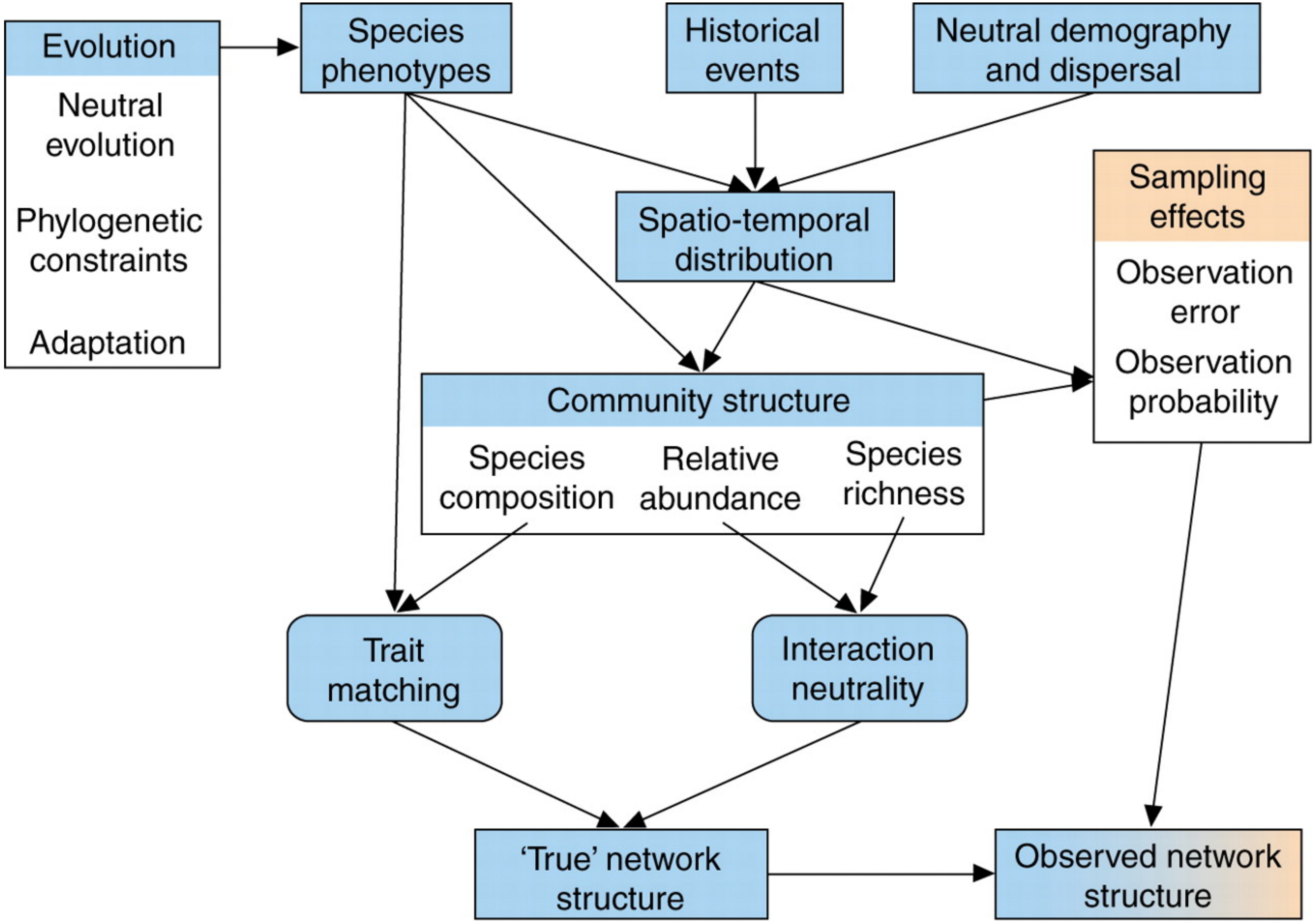




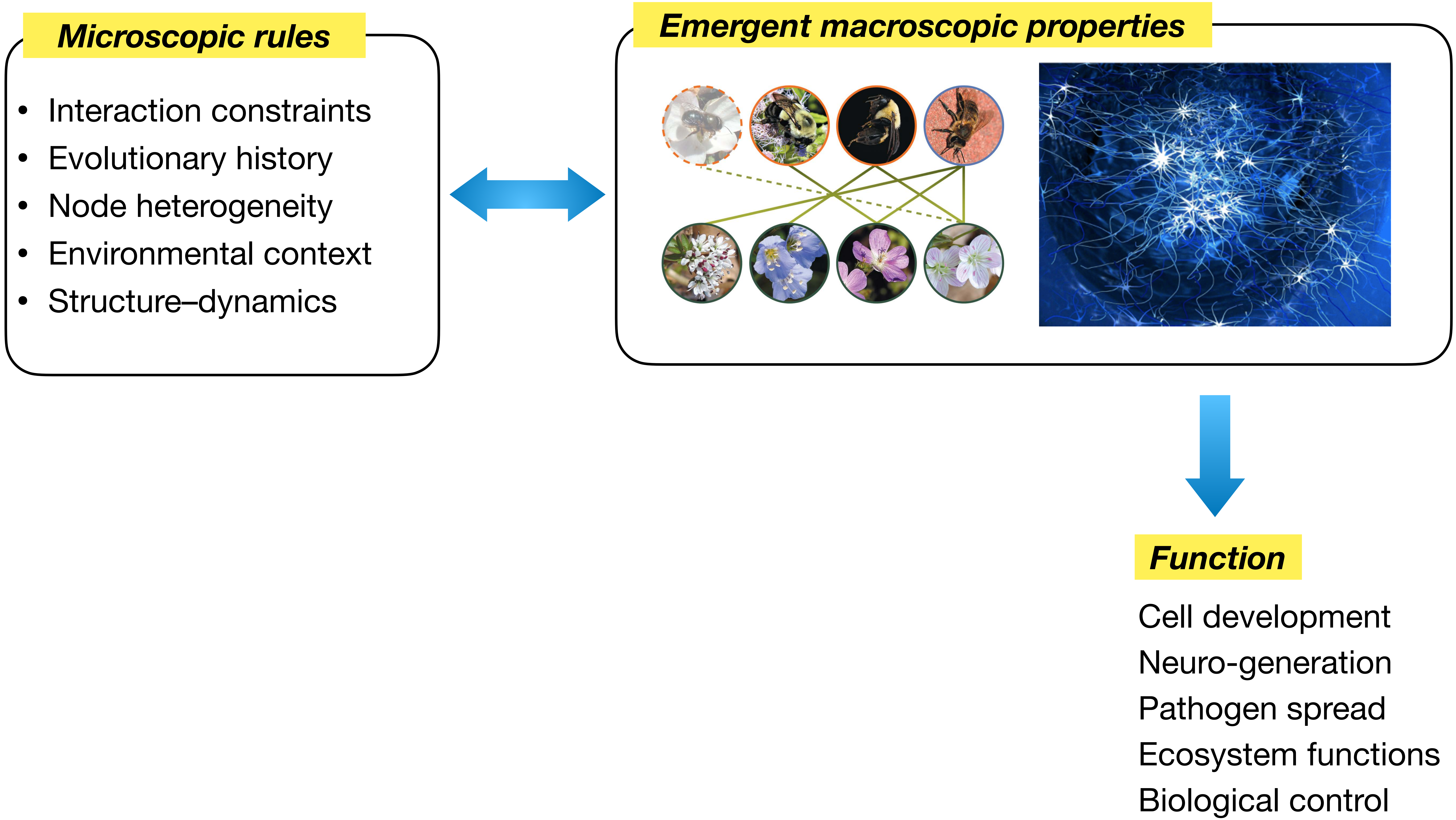
Determinants of structure

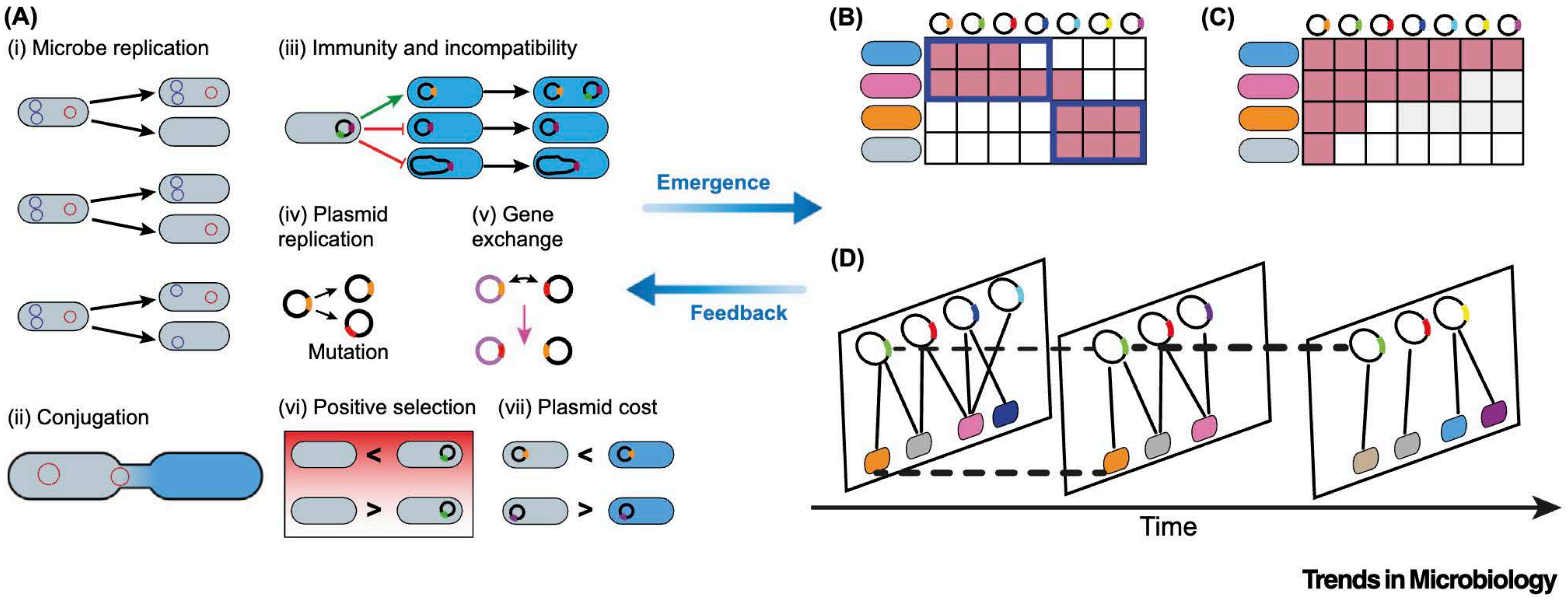
- **Interaction constraints** (physical, chemical, spatial)
  - Protein-Protein Interaction (PPI) Networks: Physical complementarity (lock-and-key)
  - Ecology: spatial distributions
- **Evolutionary history** (assembly, inheritance, coevolution)
  - Gene Regulatory Networks: duplication and divergence
- **Node heterogeneity** (traits, abundance, behavior)
  - Metabolic-networks: metabolite concentration
- **Environmental context** (resources, disturbance, variability)
  - Gene regulatory network: heat shocks that reconfigure the regulation.
- **Structure–dynamics feedbacks** (function shapes structure)
  - Synaptic plasticity: High firing strengthens the synaptic link (long-term Potentiation).

Determinants of structure



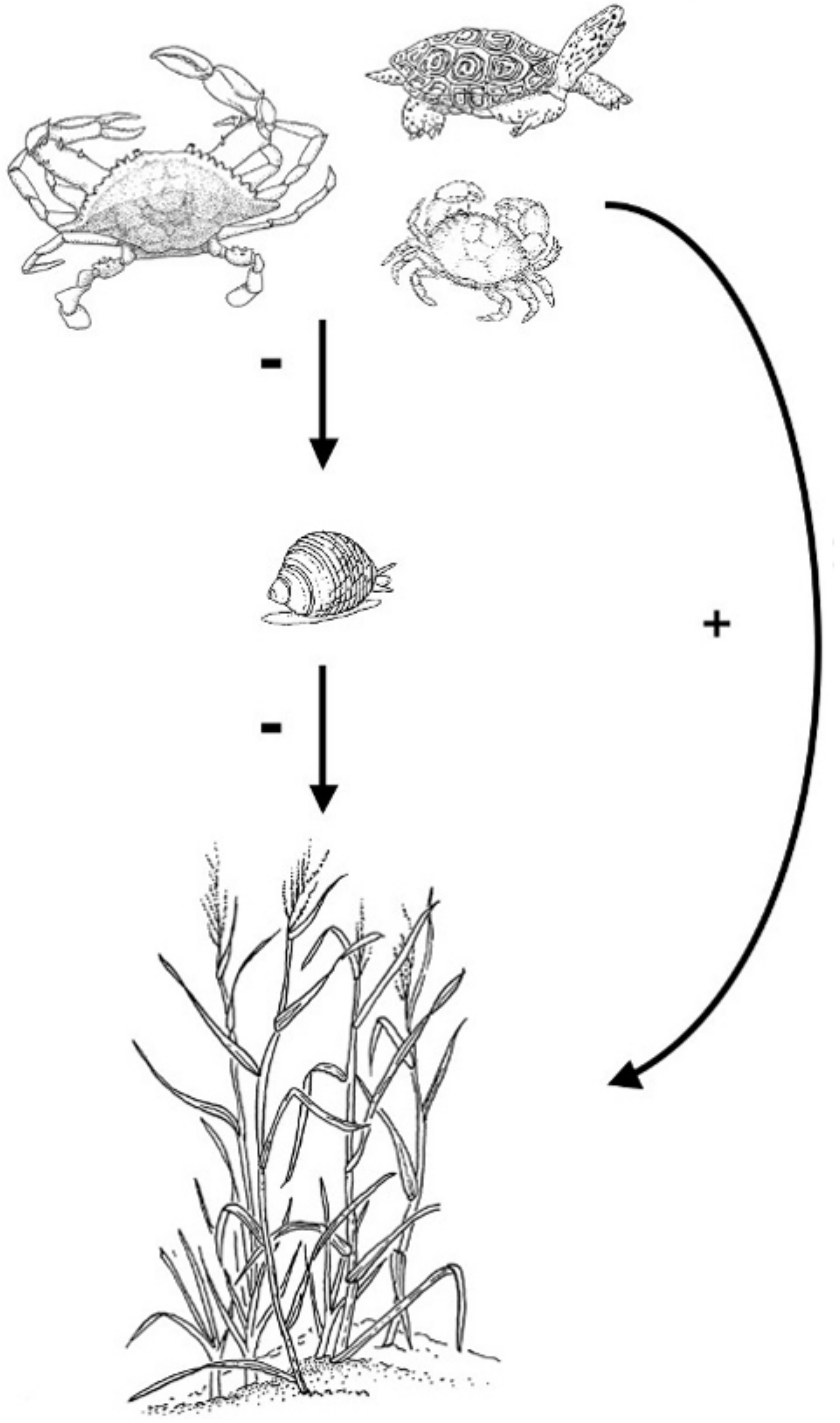
Vázquez et al 2009


Microscopic rules
Interaction constraints
Evolutionary history
Node heterogeneity
Environmental context
Structure–dynamics
Emergent macroscopic properties
Function
Cell development
Neuro-generation
Pathogen spread
Ecosystem functions
Biological control



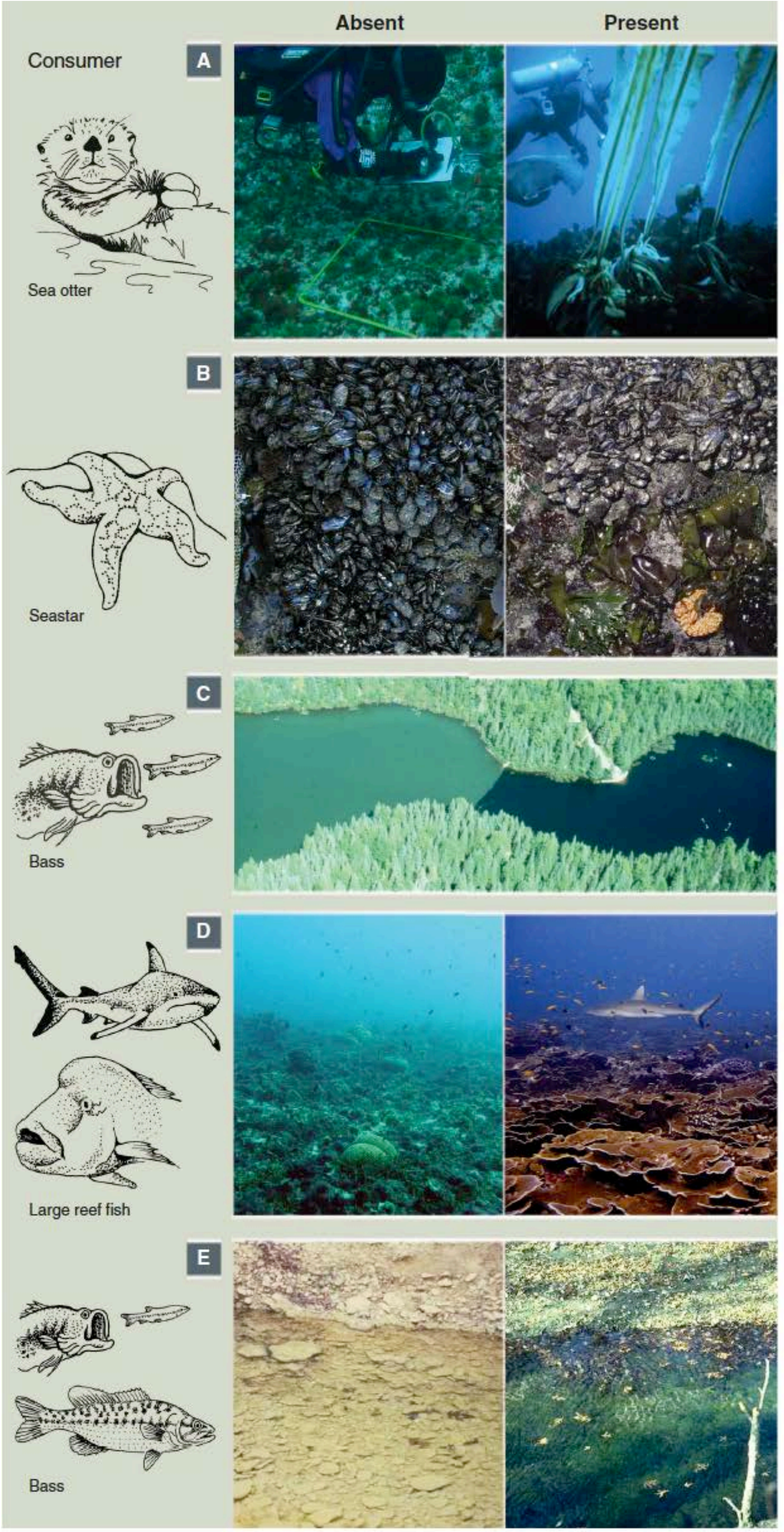
Pilosof, 2023

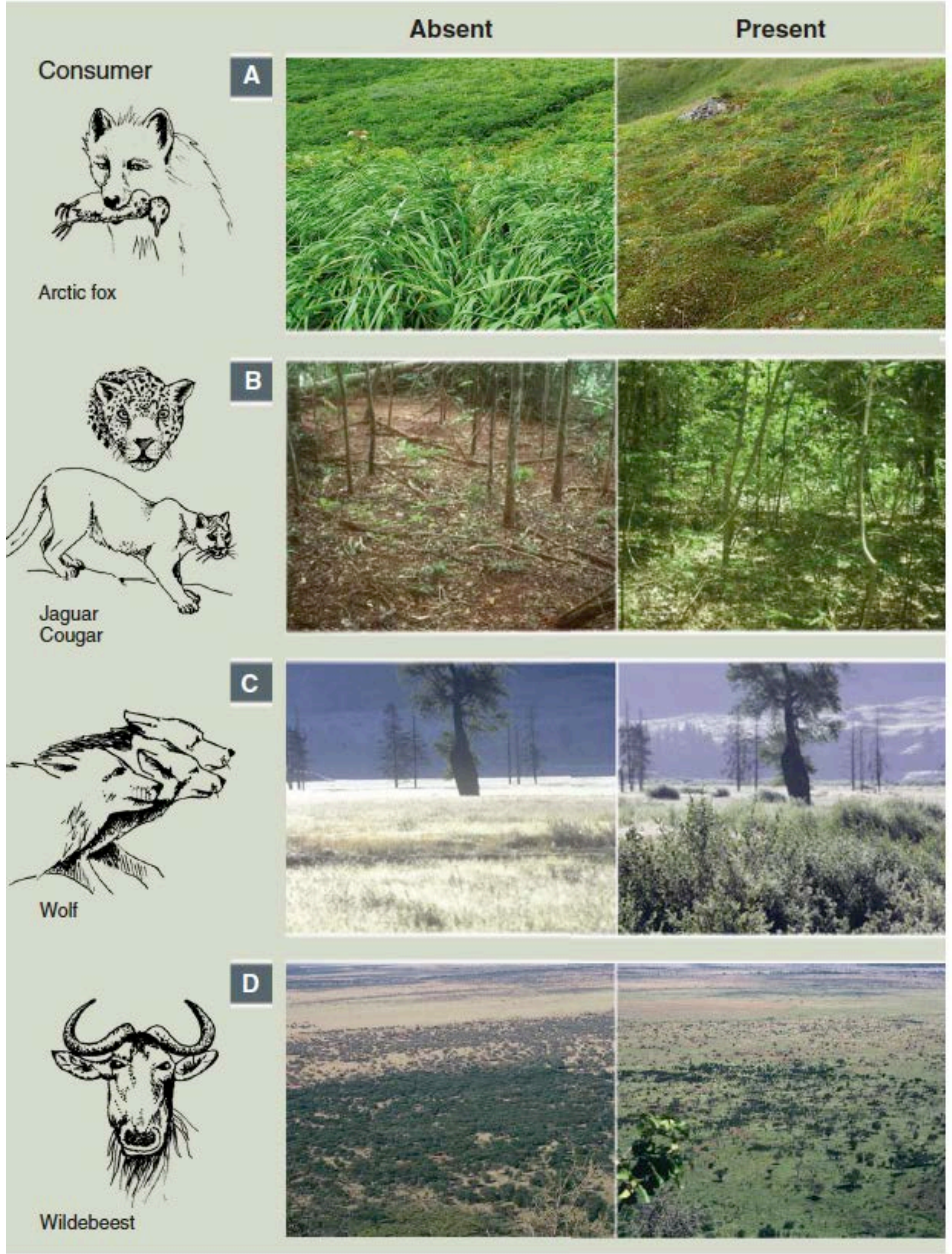
Indirect and cascading effects are a hallmark of networks



Trophic cascades: when the impact of a predator on its prey's ecology trickles down one more feeding level to affect the density and/or behavior of the prey's prey.

Paine 1969, Ecology;
Siliman and Angelini 2012, Nature Education Knowledge Project





Examples for trophic cascades and indirect effects in aquatic and terrestrial environments

https://www.youtube.com/watch?time_continue=60&v=ysa5OBhXz-Q&feature=emb_logo

Estes et al. 2011 Science

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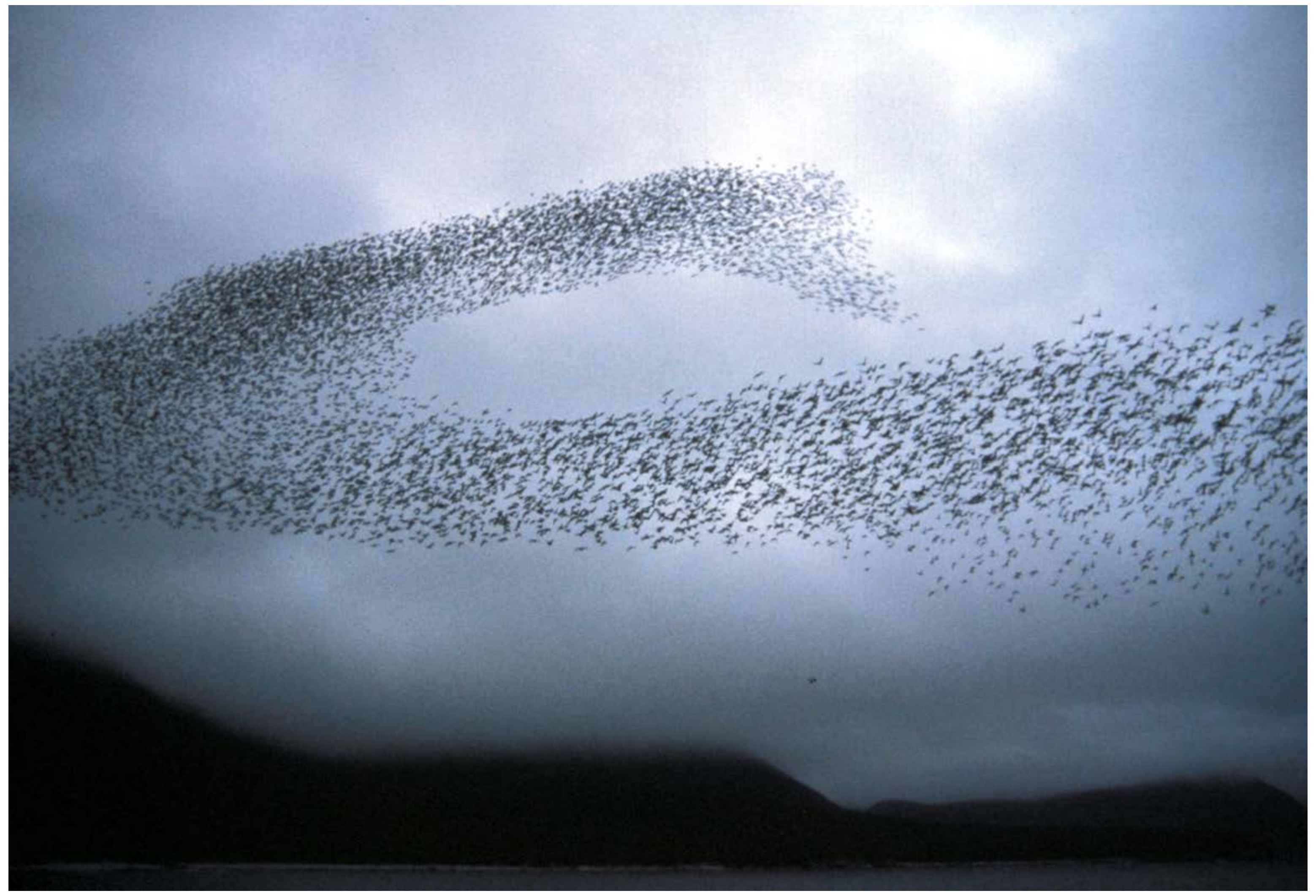
- **Self-organization**
- Dynamics and stability
- Adaptation and evolution
- Universality

Key concepts: collective behavior, pattern formation

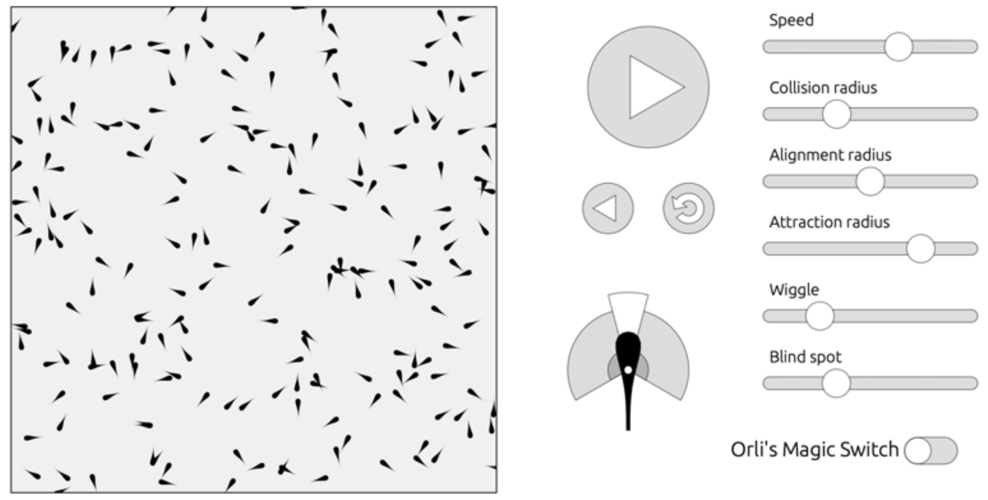
Complex systems may self-organize to produce non-trivial patterns spontaneously without a blueprint. *https://complexityexplained.github.io*

DALLE-4-generated

https://www.nationalgeographic.com/animals/article/140731-termites-mounds-insects-entomology-science



https://en.wikipedia.org/wiki/Swarm_behaviour



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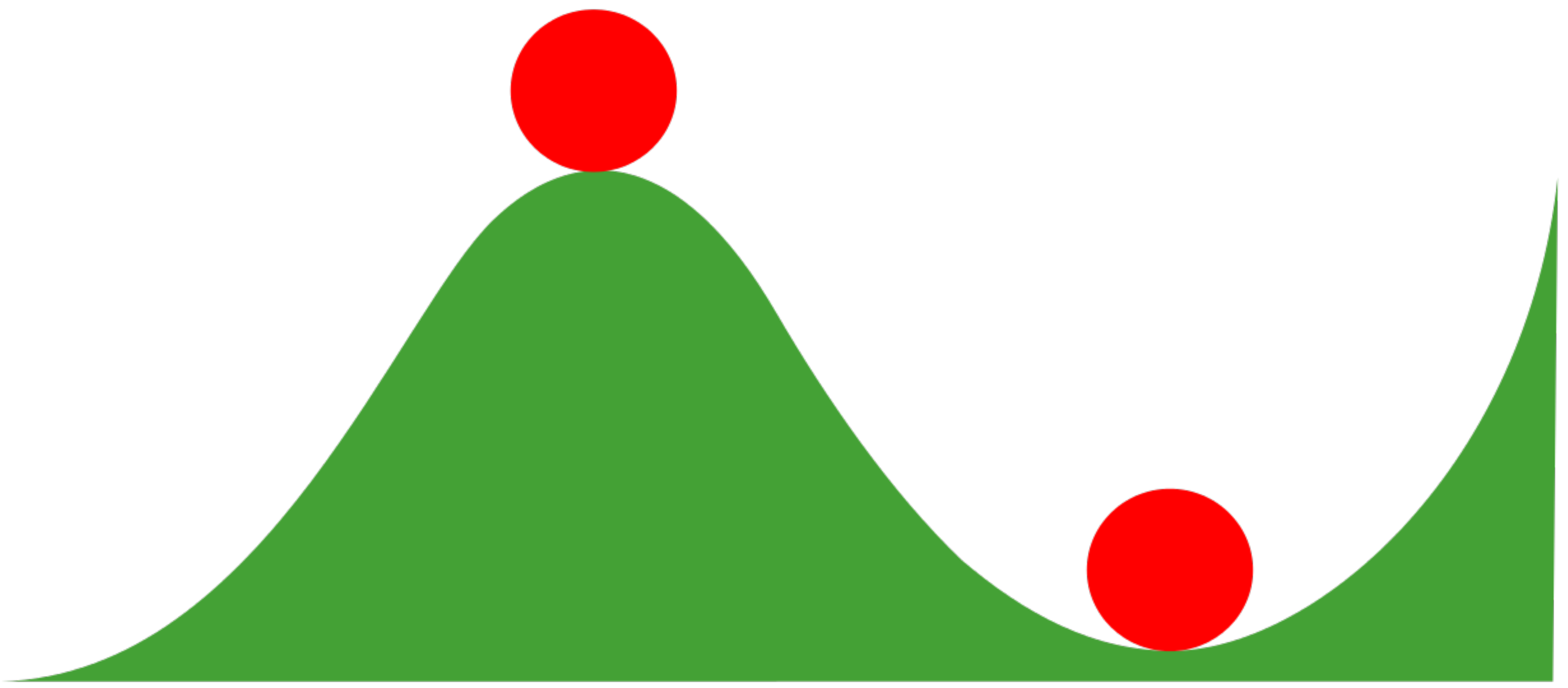
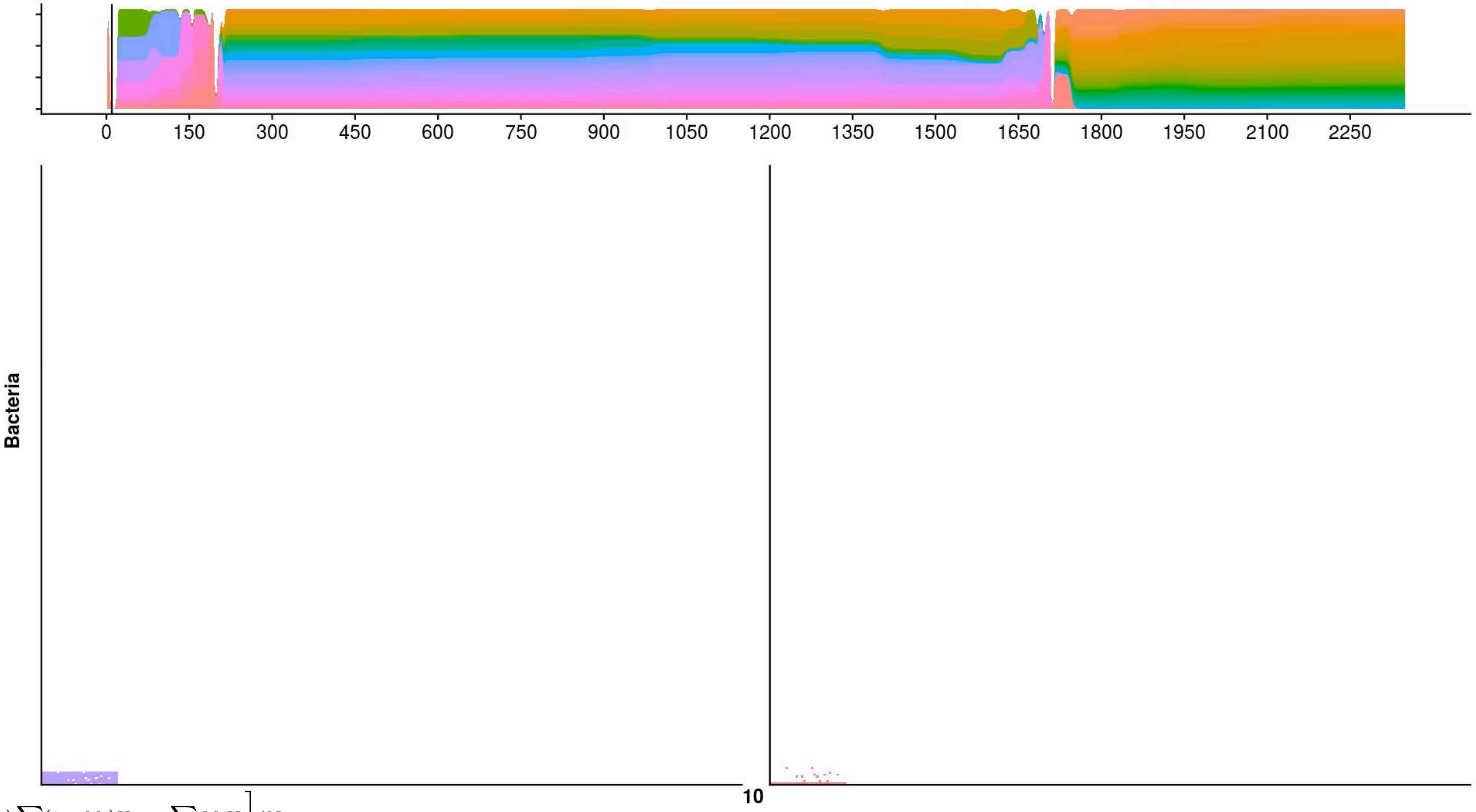


Key concepts: non-linear dynamics, equilibrium

Complex systems tend to change their states dynamically, often showing unpredictable long-term behavior. https://complexityexplained.github.io



$$\frac{\mathrm{d}N_i}{\mathrm{d}t} = rN_i\left(1 - \frac{\sum_i N_i}{K}\right) - \left[(1-q)\sum_j (1-M_{ij})V_j + p\sum_j M_{ij}V_j\right]\phi N_i$$

$$\frac{\mathrm{d}V_j}{\mathrm{d}t} = \beta\phi\left[(1-q)\sum_i (1-M_{ij})N_i + p\sum_i M_{ij}N_i\right]V_j - \left(\phi\sum_i N_i + m\right)V_j$$

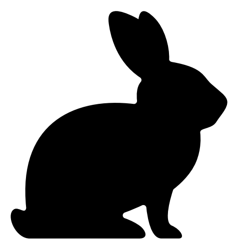
Pilosof et al 2020, Nature Ecology and Evoution

State: set of variables that characterize the system.

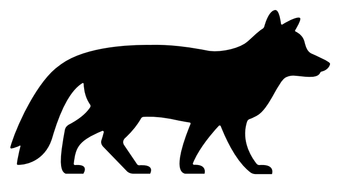
Dynamics: Temporal change in system states.

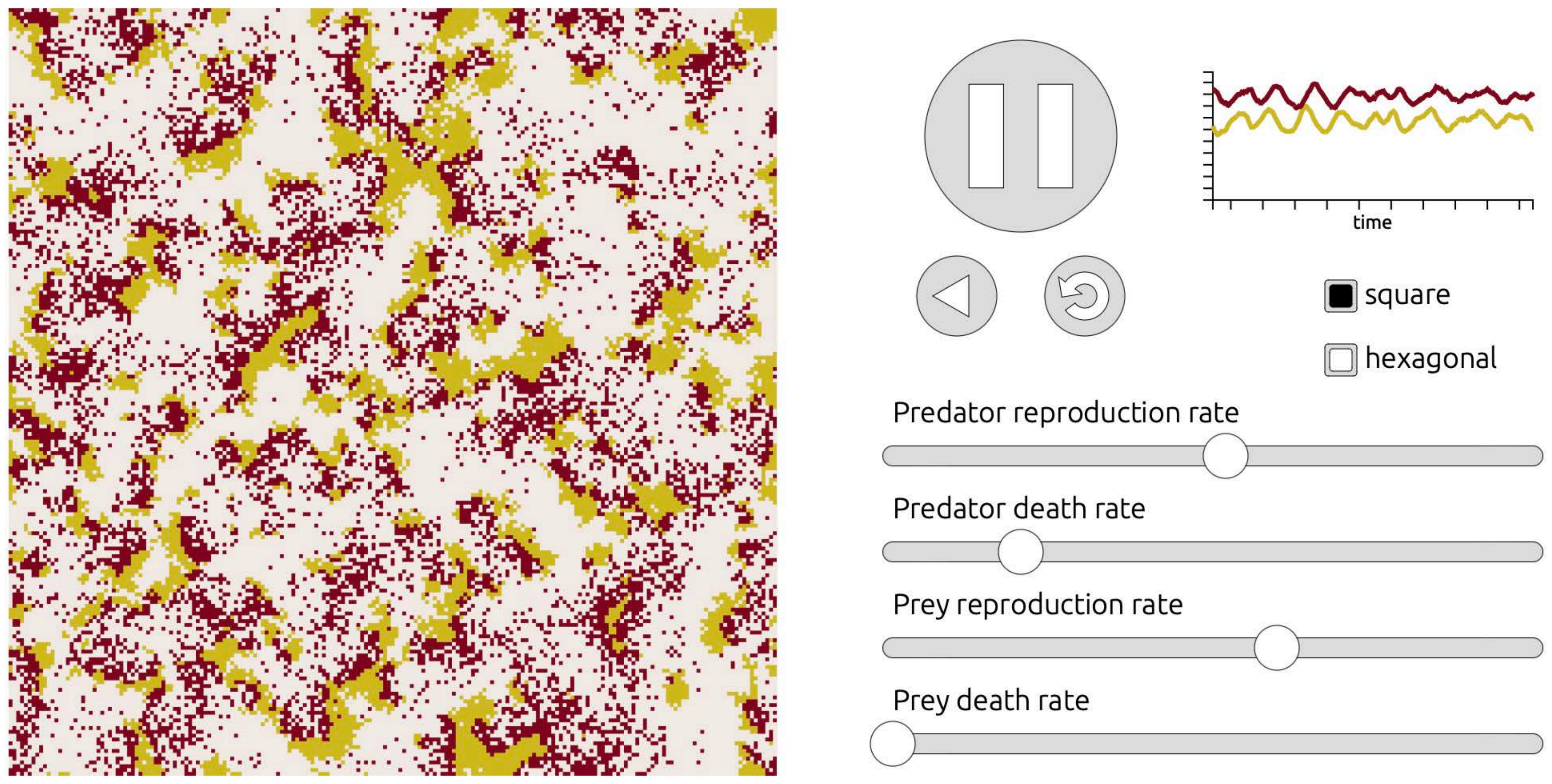
Linear dynamics: states change proportionally to time, current state or change in the environment.

$$\frac{dN}{dt} = rN - aNP$$



$$\frac{dP}{dt} = faNP - qP$$





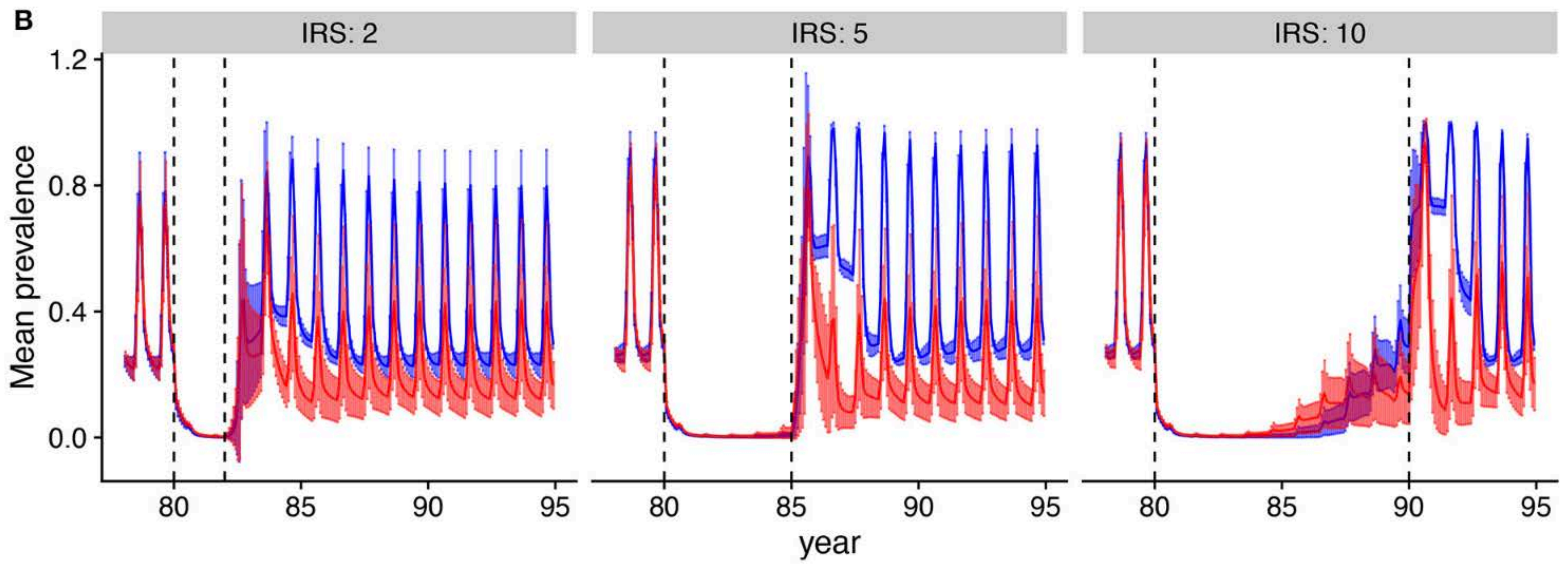
https://complexityexplained.github.io

What is stability?

Many researchers intuitively ask: what happens when I remove a node?
But this is far from being the only way to understand response to perturbations.

Stability depends on:

- Many things (multifaceted concept with multiple definitions).
- Organizational scale.
- The type and scale of perturbation.



Kefi et al 2019, Ecol Lett

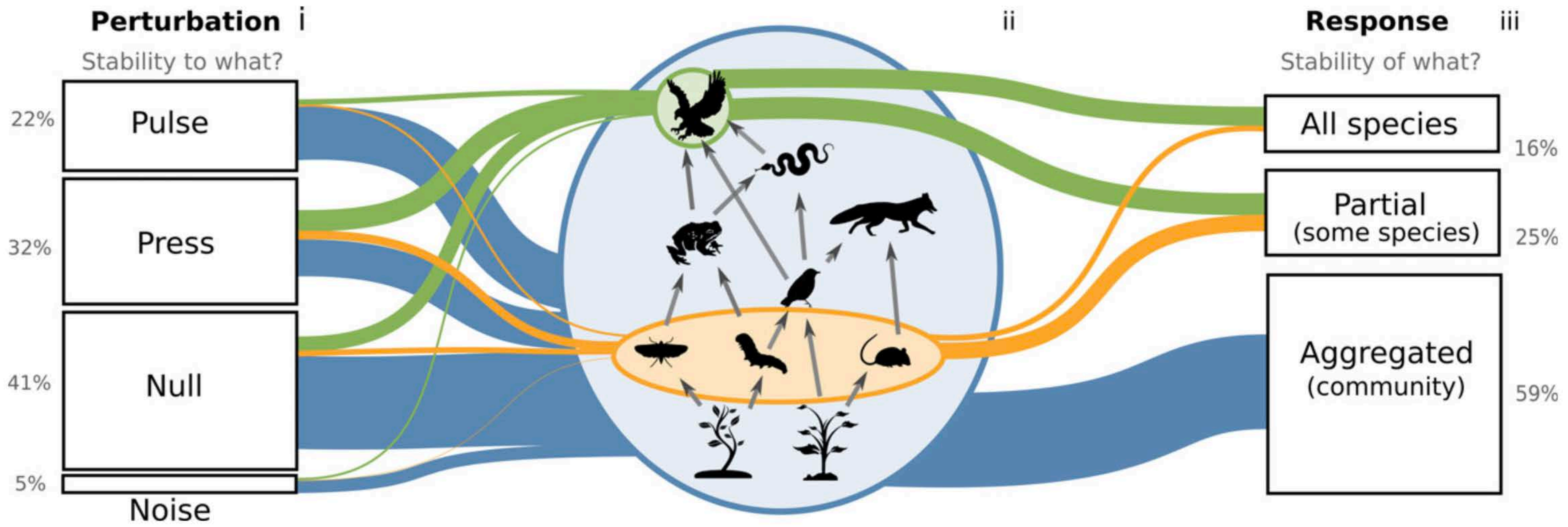
He, Pilosof, et al 2020

Different concepts/definitions of 'stability'

- Local asymptotic stability
- Resilience
- Reactivity
- Qualitative global (asymptotic) stability
- Permanence and persistence
- Invasibility
- Variability
- Robustness

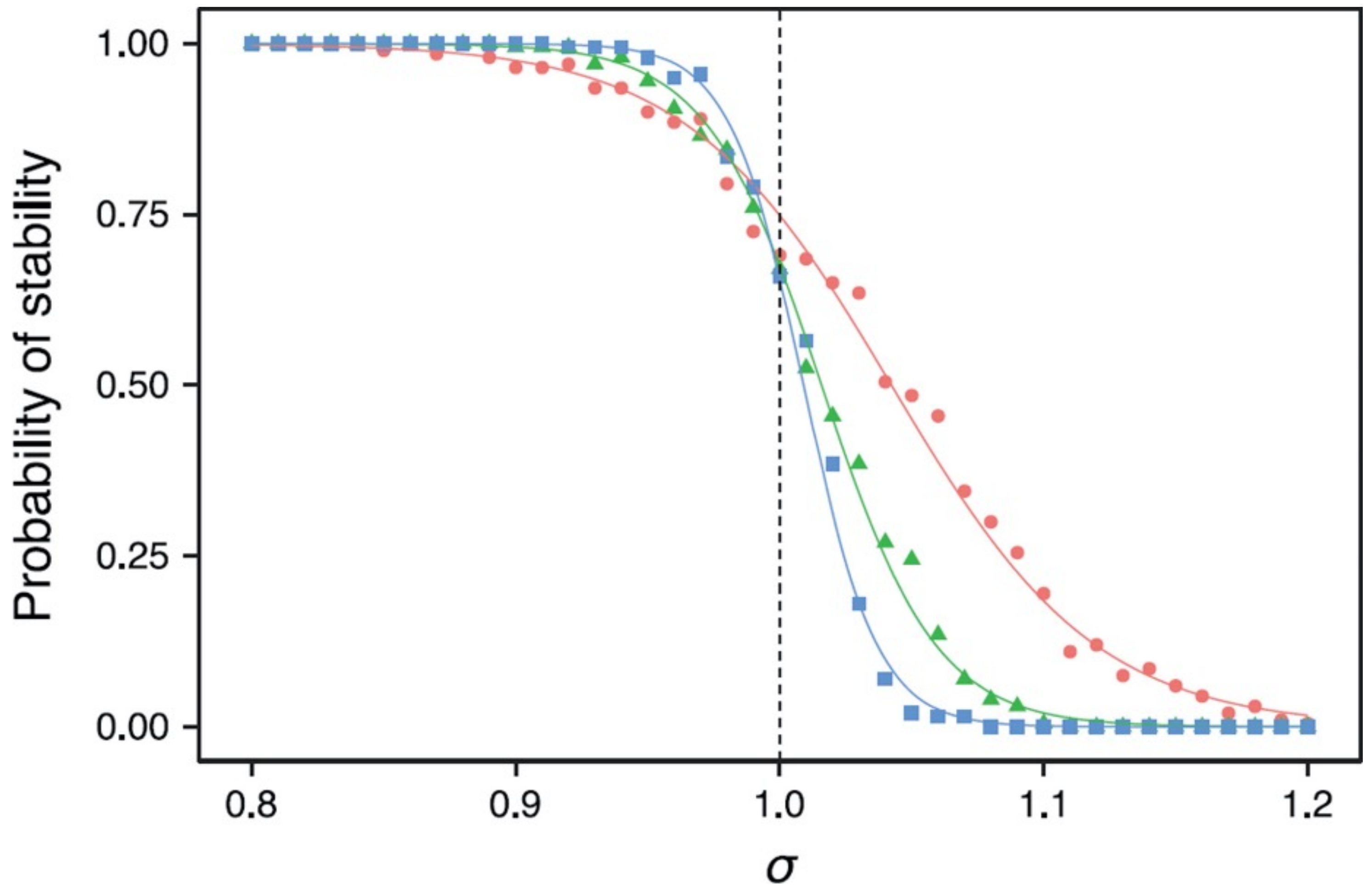
How is stability affected by:

- Number of species?
- Network structure?
- Proportion of mutualistic vs competitive interactions?
- underlying model?



Kefi et al 2019, Ecol Lett

$$\mathbf{A} = \begin{pmatrix} a_{11} & a_{12} & \cdots & \cdots & a_{1N} \\ a_{21} & a_{22} & \cdots & \cdots & a_{2N} \\ \vdots & \cdots & \ddots & \cdots & \vdots \\ \vdots & \cdots & \cdots & \ddots & a_{MN} \\ a_{N1} & a_{N2} & \cdots & a_{NM} & a_{NN} \end{pmatrix}$$



Allesina and Tang, 2015

Hypothesis:
higher diversity
increases stability

Theory:
- Random matrix
- Linear stability analysis

Result:
higher diversity
decreases
stability

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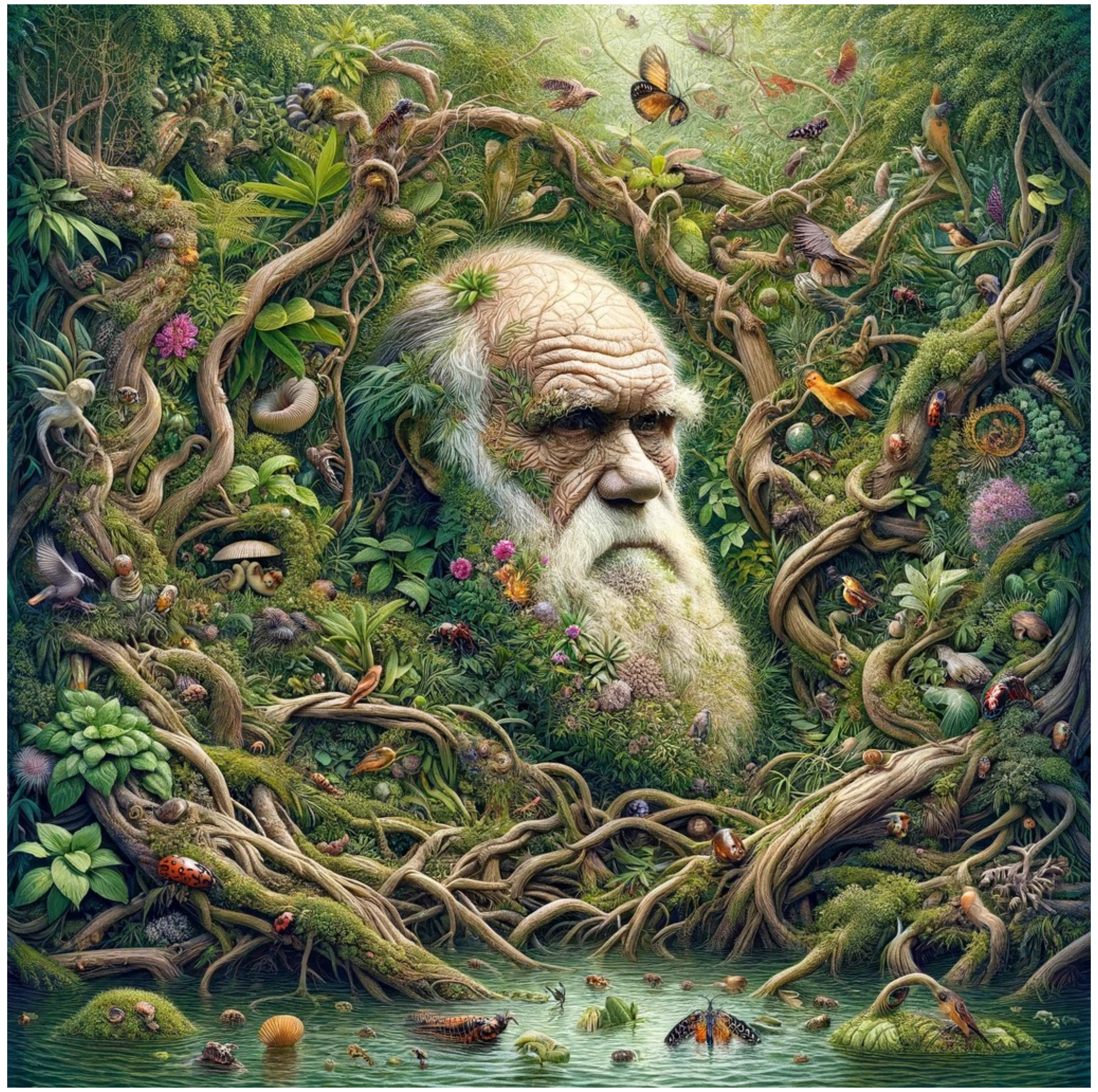
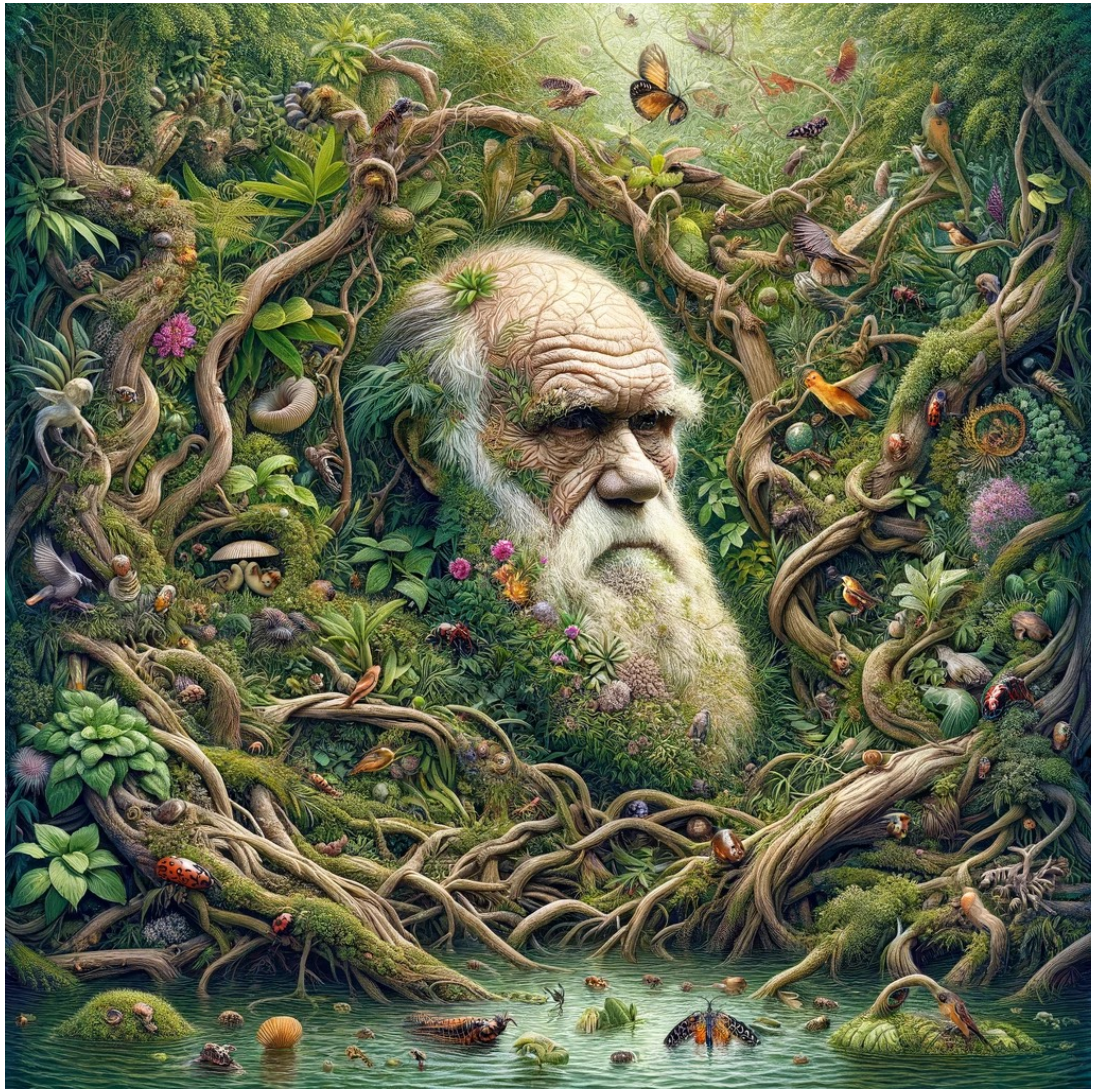


Key concepts: complex adaptive systems



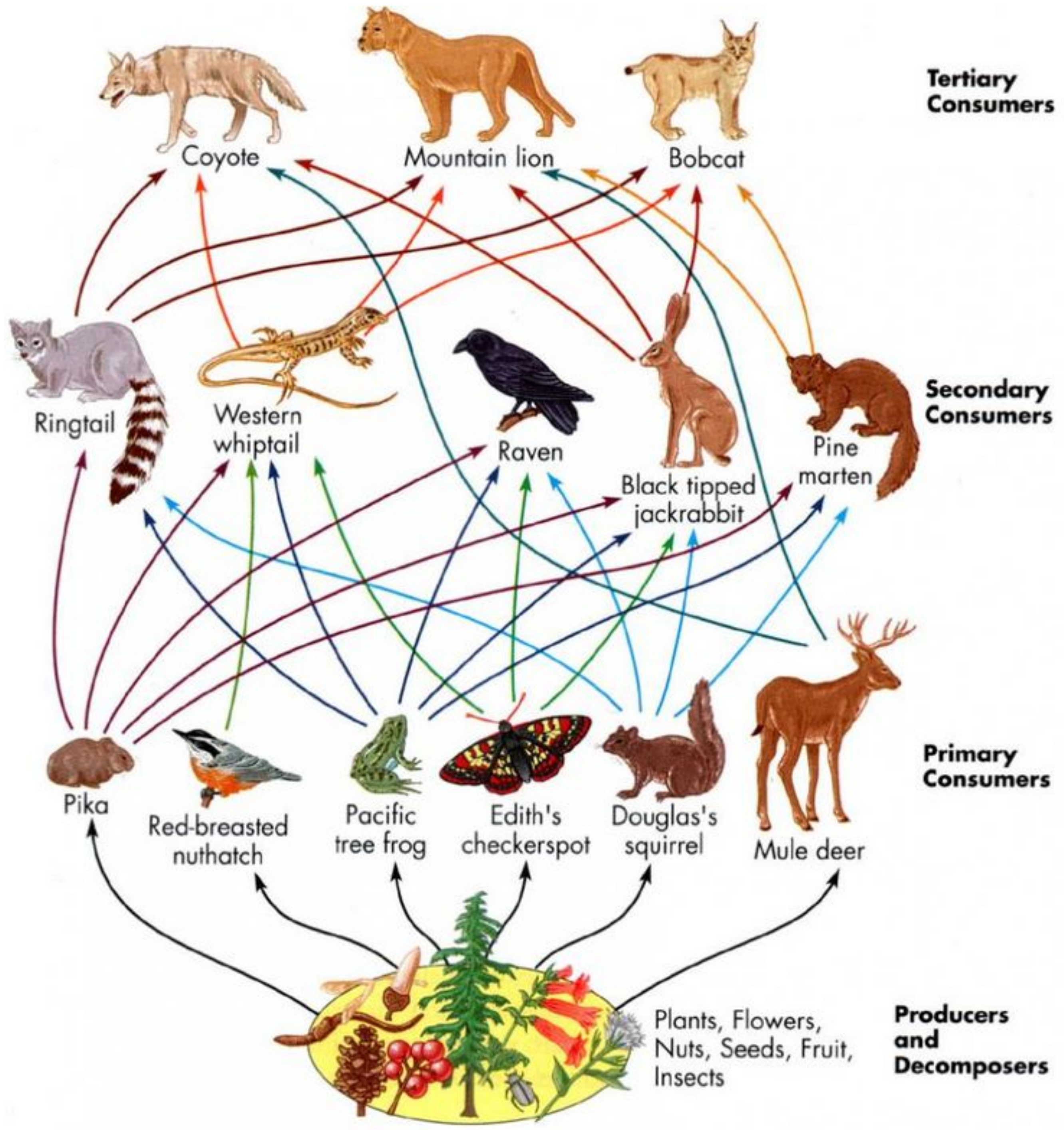
« It is interesting to contemplate an **entangled bank**, clothed with plants of many kinds, with birds singing… **so dependent on each other in so complex a manner**… »

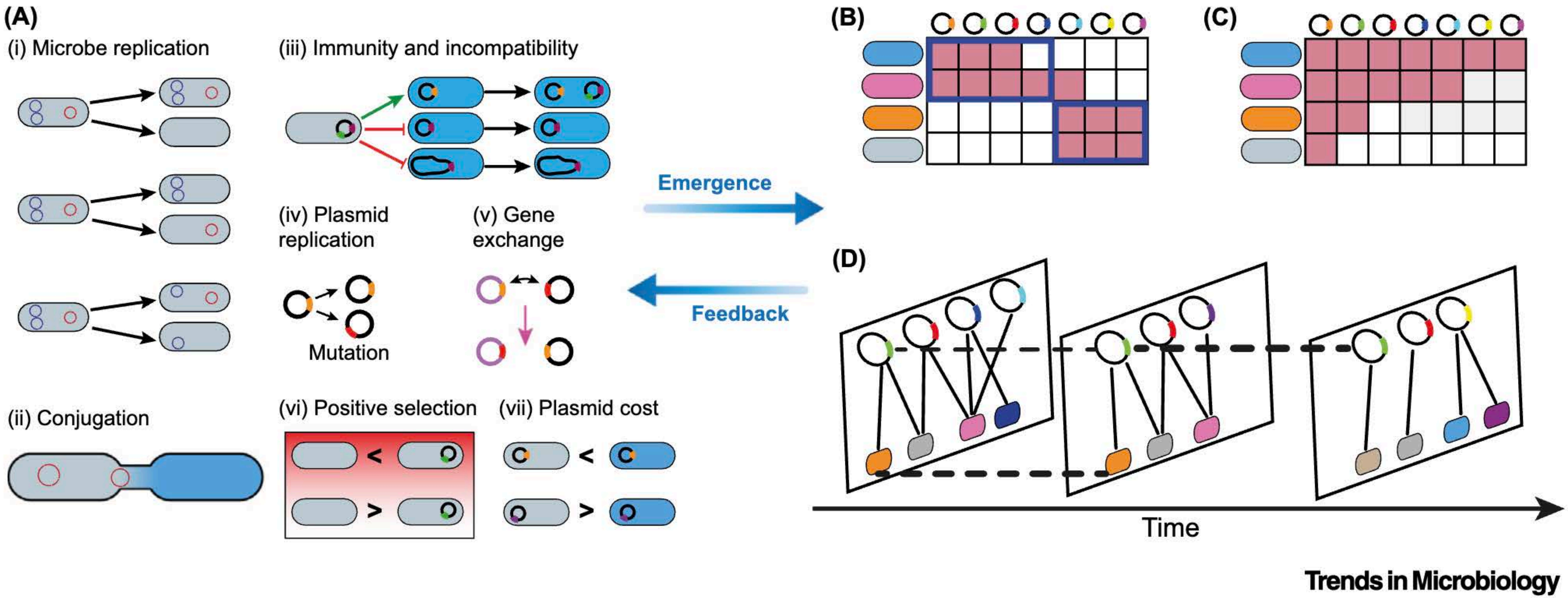
Charles Darwin, 1859

Adaptive

Diversity ⟷ Rules for Interactions ⟷ Emergence

- Evolution
- Ecology
- Stochasticity





Pilosof, 2023

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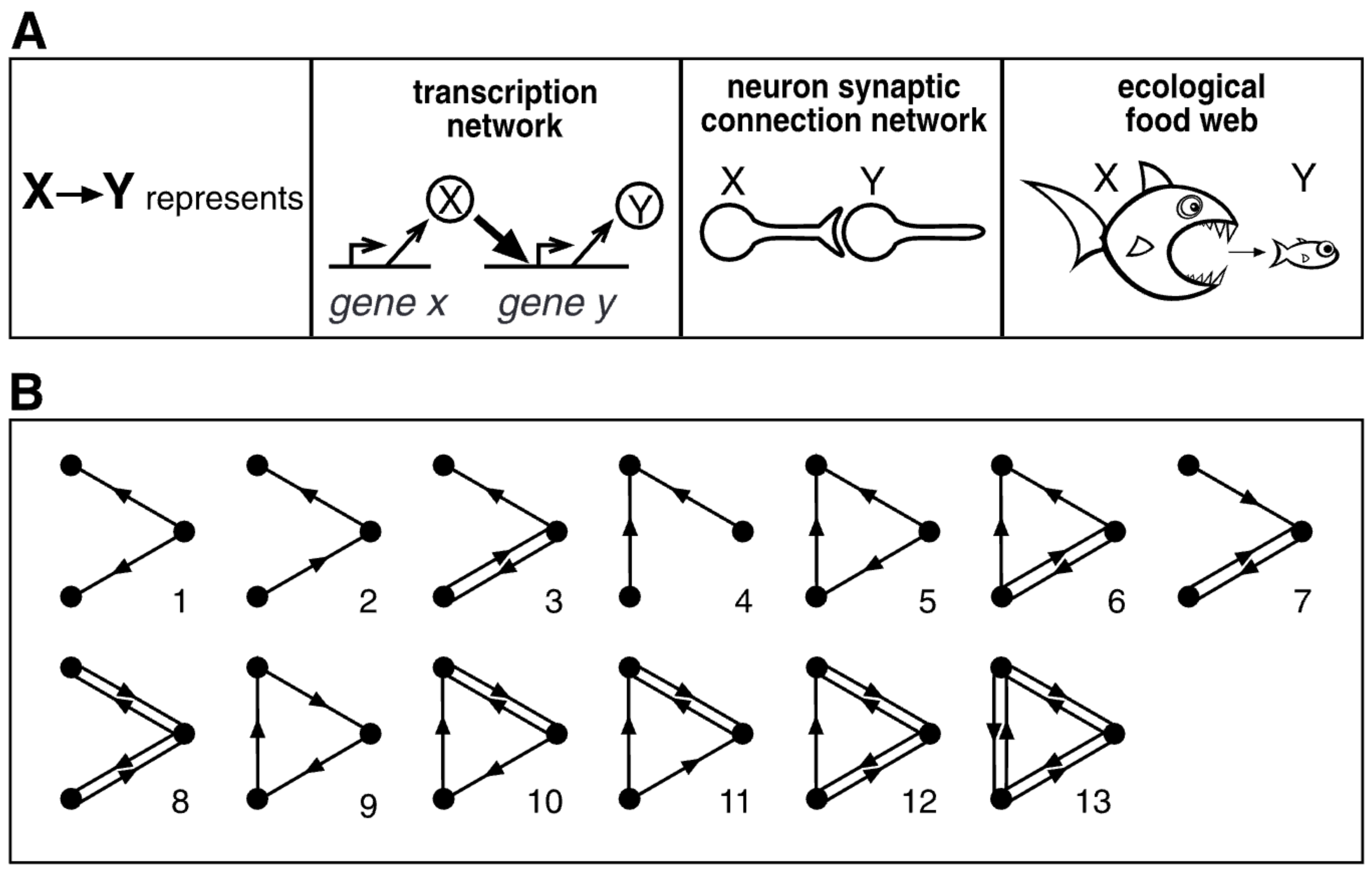


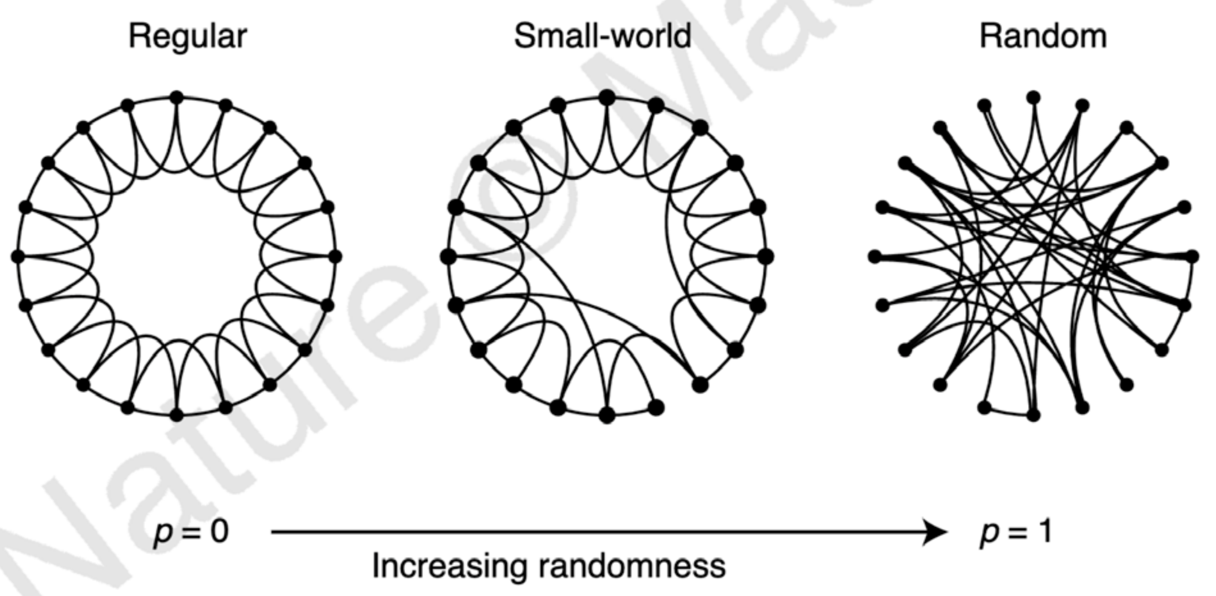
Milo et al. 2000, Science

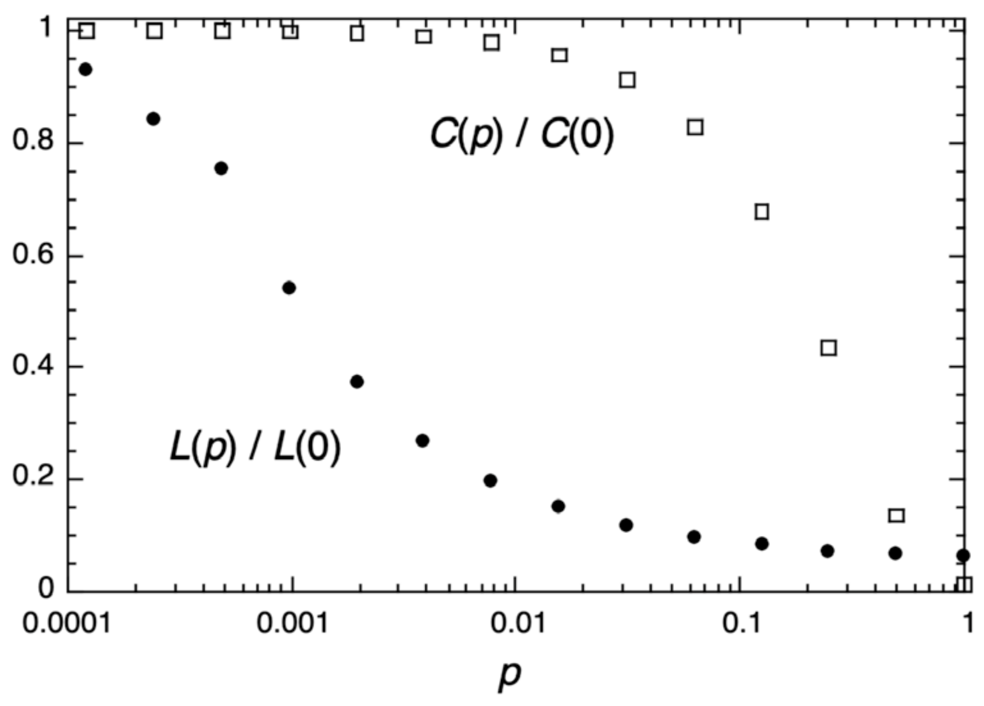
Key concepts: universal patterns, network science

Collective dynamics of 'small-world' networks

Duncan J. Watts* & Steven H. Strogatz

Department of Theoretical and Applied Mechanics, Kimball Hall, Cornell University, Ithaca, New York 14853, USA



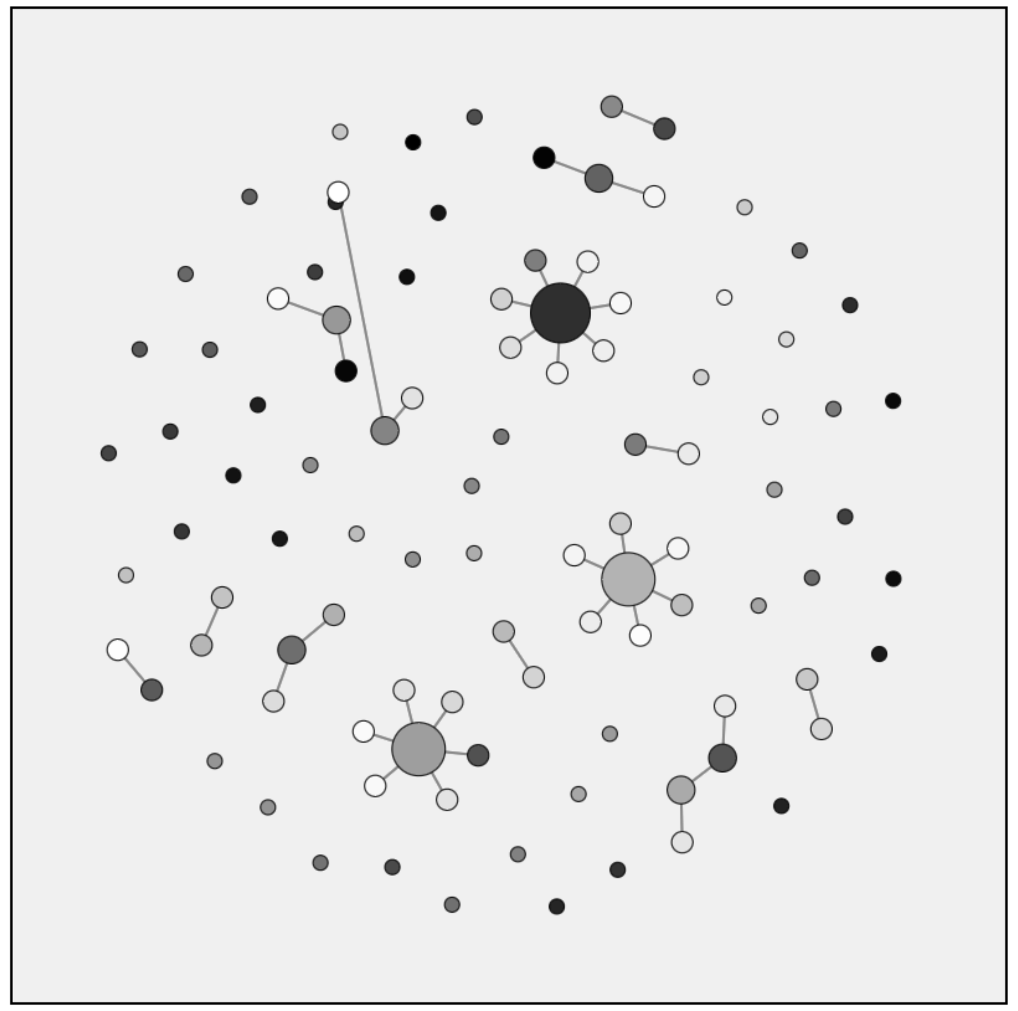


https://ecomplab.shinyapps.io/network_generation/

Emergence of Scaling in Random Networks

Albert-László Barabási* and Réka Albert

Systems as diverse as genetic networks or the World Wide Web are best described as networks with complex topology. A common property of many large networks is that the vertex connectivities follow a scale-free power-law distribution. This feature was found to be a consequence of two generic mechanisms: (i) networks expand continuously by the addition of new vertices, and (ii) new vertices attach preferentially to sites that are already well connected. A model based on these two ingredients reproduces the observed stationary scale-free distributions, which indicates that the development of large networks is governed by robust self-organizing phenomena that go beyond the particulars of the individual systems.



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Complex small-world regulatory networks emerge from the 3D organisation of the human genome

C. A. Brackley, N. Gilbert, D. Michieletto, A. Papantonis, M. C. F. Pereira, P. R. Cook & D. Marenduzzo

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Published: April 2004

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Journal of Theoretical Biology

Volume 214, Issue 3, 7 February 2002, Pages 405-412

Regular Article

Small World Patterns in Food Webs

JOSE M. MONTOYA [a b 1], RICARD V. SOLÉ [a c]

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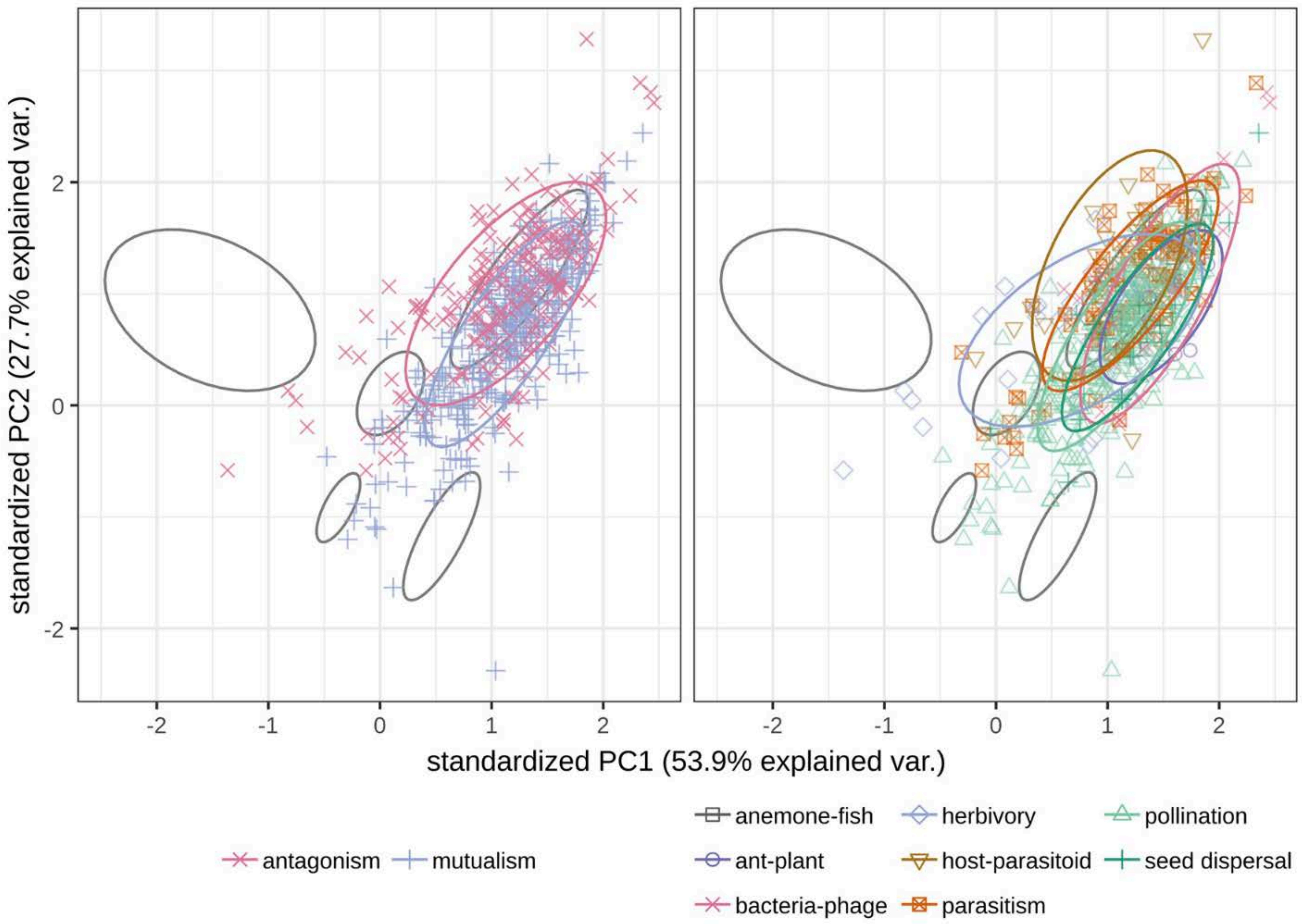
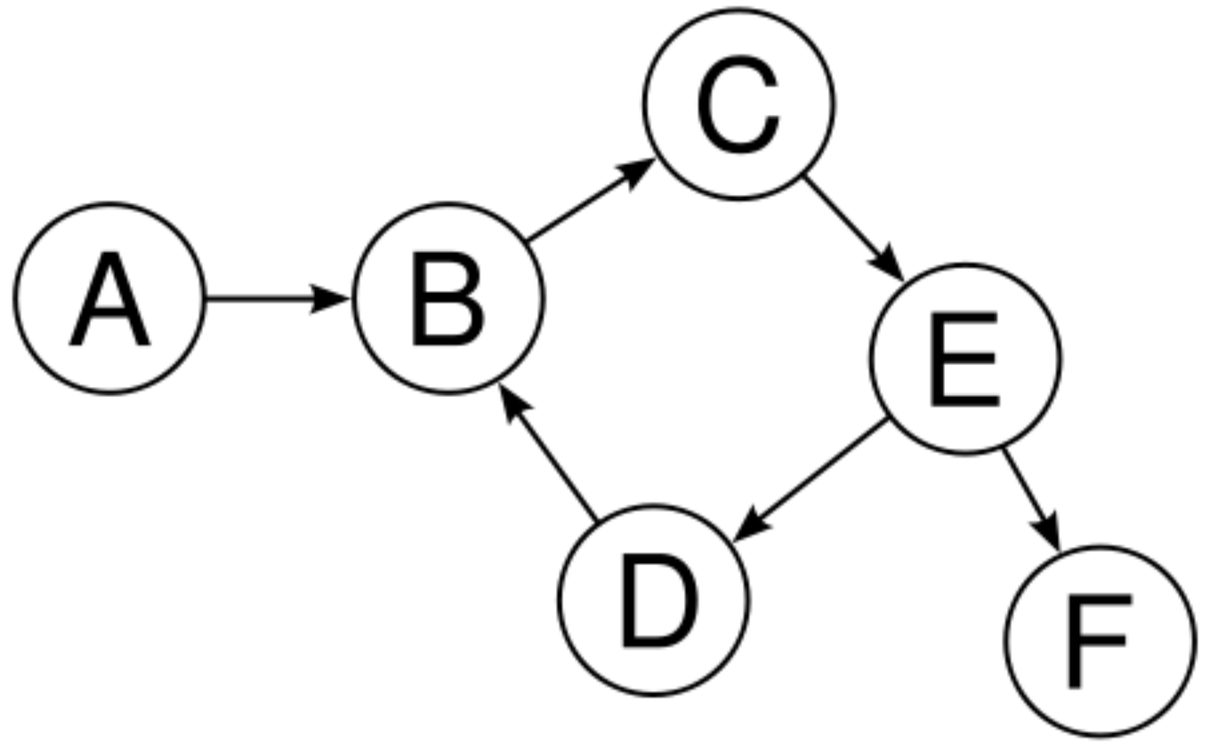


Michalska-Smith et al 2019

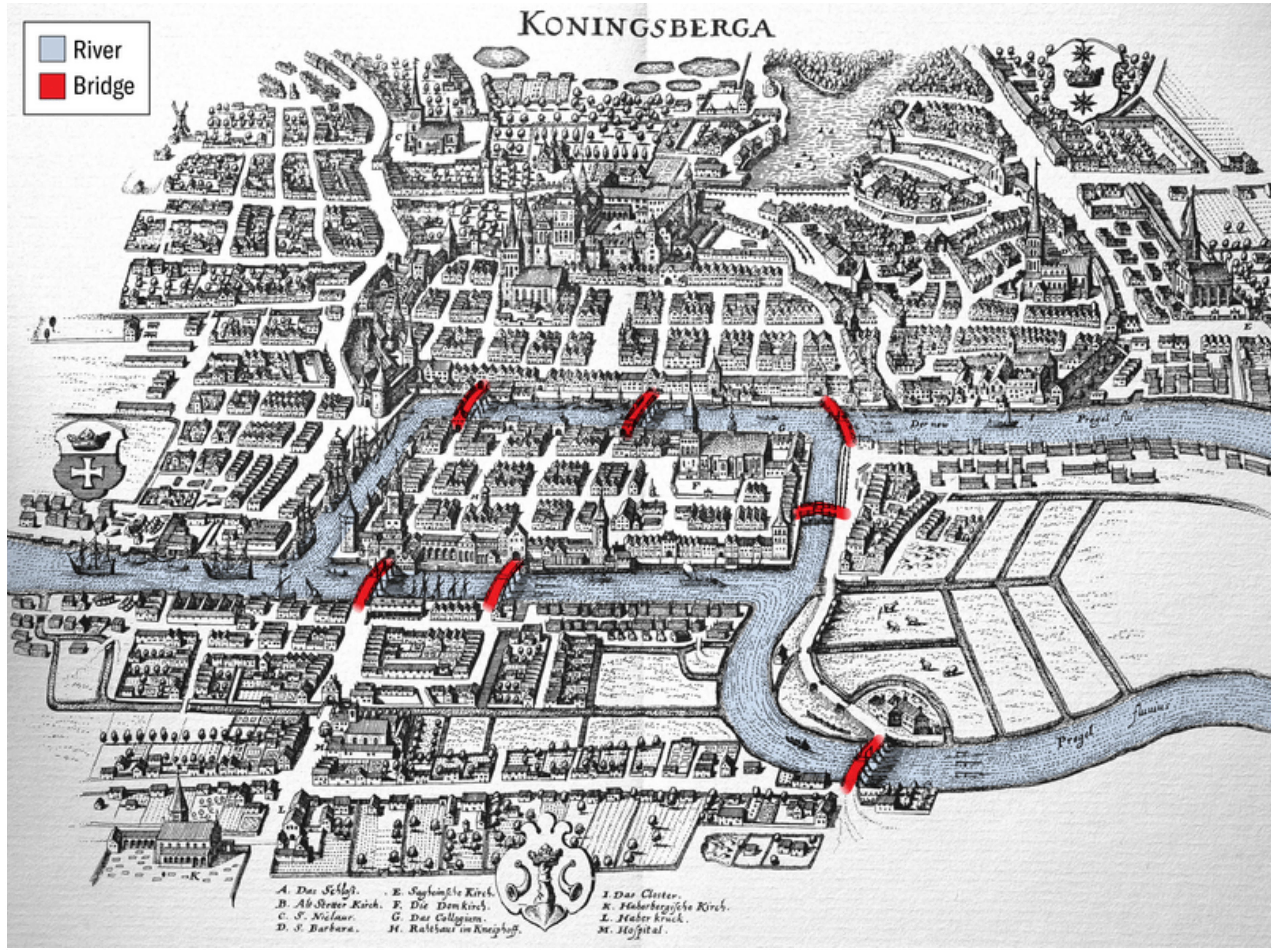
Complex systems can be represented by graphs

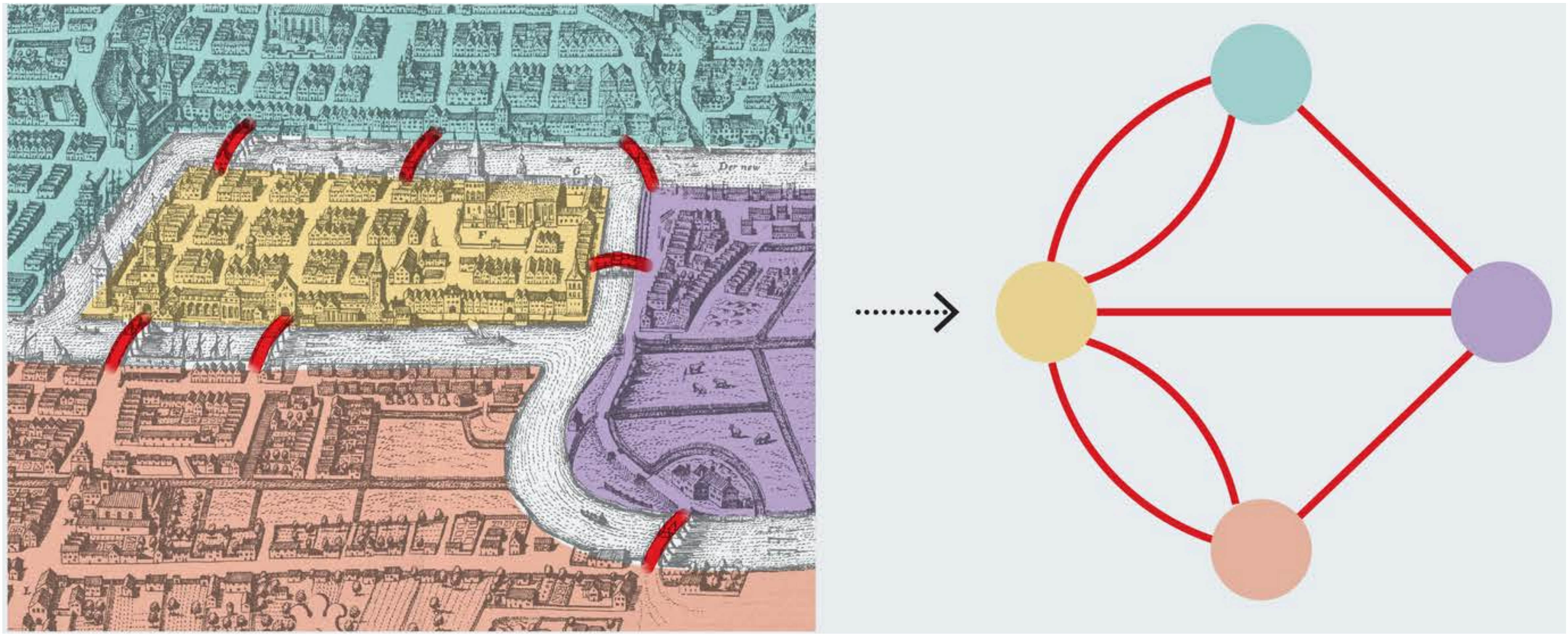
- Graphs represent multiple interactions between multiple components.
- Graph properties can be analyzed at the node, meso-scale and network levels.
- Theory exists for many types of graphs (e.g., DAC)



Euler’s 7-bridges problem

Is it possible to take a walk through the city that crosses each of the seven bridges exactly once and returns to the starting point?





“This question is so banal, but seemed to me worthy of attention in that neither geometry, nor algebra, nor even the art of counting was sufficient to solve it.”

The rise of network science

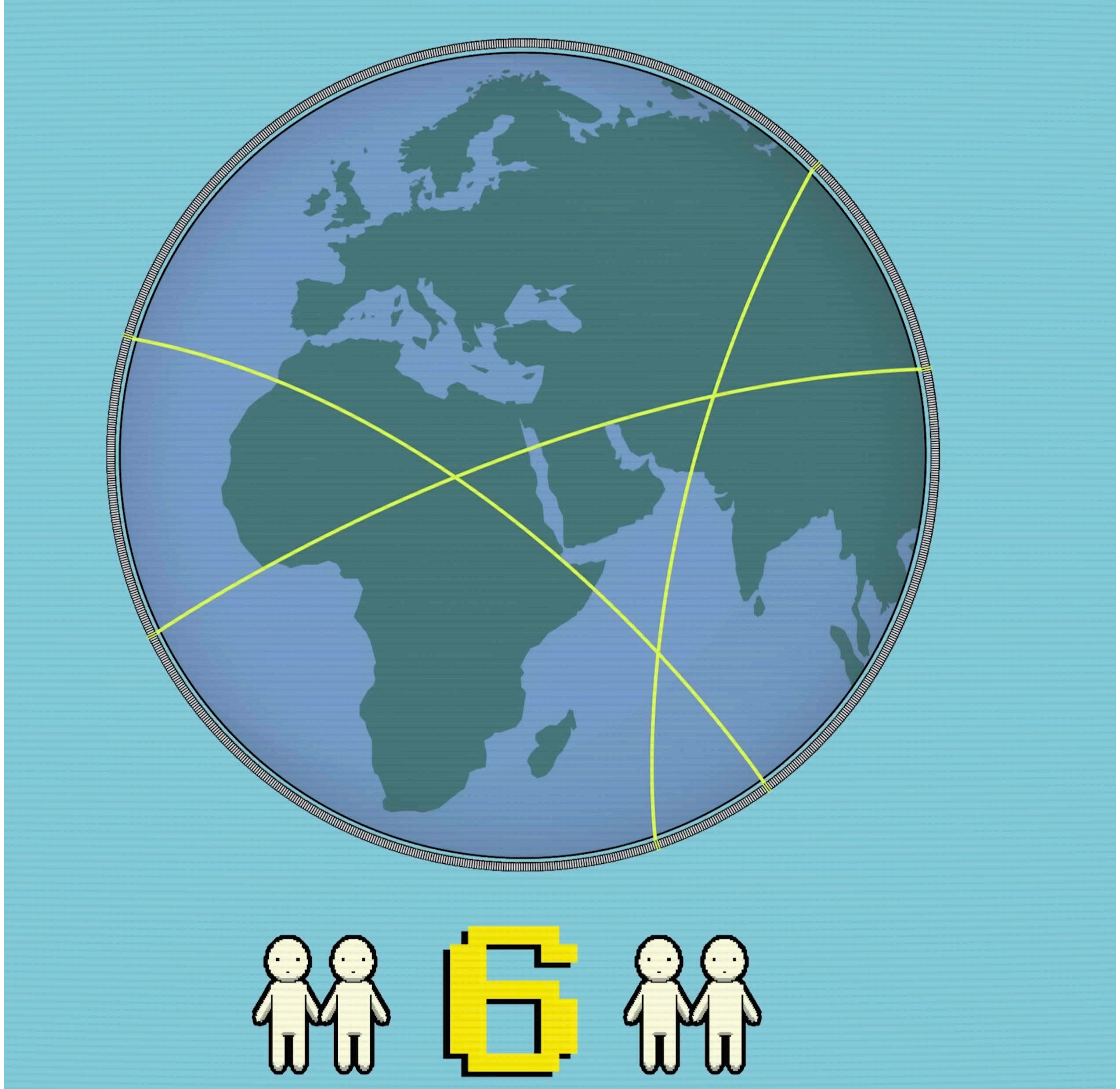
- **Graph theory** is old and many disciplines have dealt with their own networks.

- Network science exploded at the dawn of the 21 century for two reasons:
  - Better data collection for building lists and maps (e.g., a list of metabolic pathways).

  - Key discovery: although the **processes** behind network generation are different, the **architecture** of networks emerging in various domains are similar to each other. **Emergence is governed by the same organizing principles.**

- Consequently we can use a common set of mathematical tools to explore these systems.

Network Science Book, Barabasi 2021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Network science is…

- Interdiscpilinary
- Empirical and data driven: focus on systems function, prediction, control.
- Theoretical:
  - Graph theory: mathematical foundations.
  - Statistical physics: stochasticity, universality, emergence.
  - Discipline-specific therory, particualry in regard to generative processes.
- Computational.

https://www.ted.com/talks/eric_berlow_simplifying_complexity

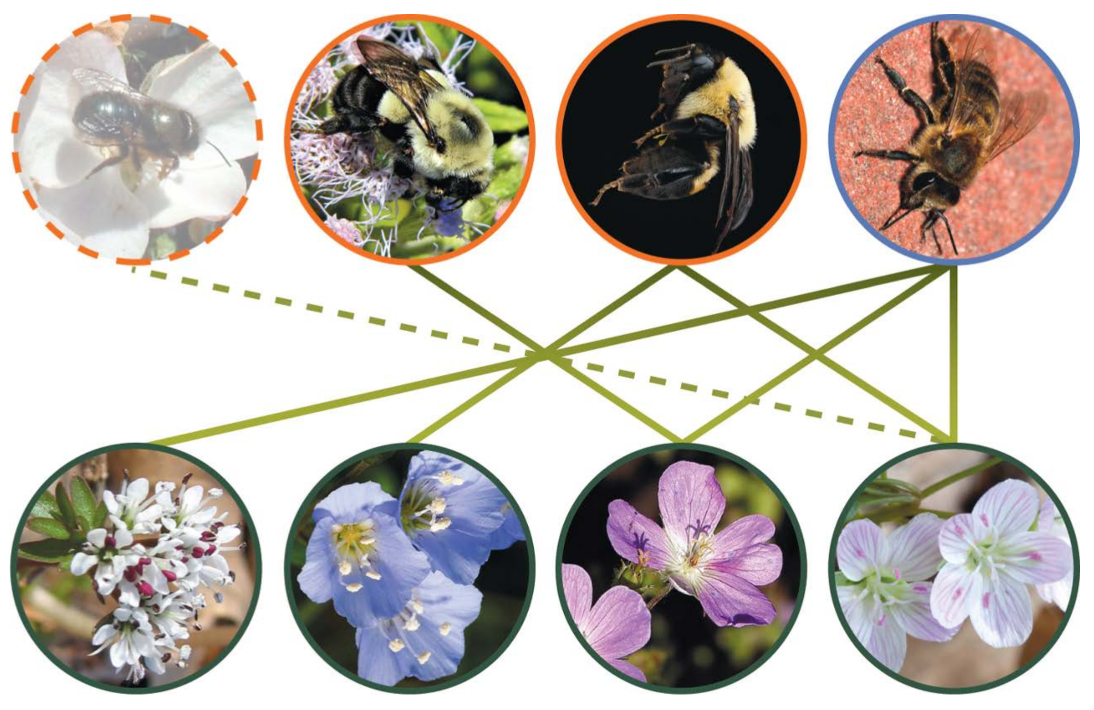
This will follow us throughout the course.

1. Quantify the ***structures*** of biological networks.
2. Relate these structures to ***dynamics, stability*** and ***function***.
3. Understand how and why these structures were formed (***generative processes***).

Microscopic rules

- Interaction constraints
- Evolutionary history
- Node heterogeneity
- Environmental context
- Structure–dynamics

Emergent properties



Function

Cell development
Neuro-generation
Pathogen spread
Ecosystem functions
Biological control

Stability

1. Quantify the structures of biological networks.

- Is the network clustered?
- Are there central nodes?

2. Relate these structures to dynamics, stability and function.

- Is the network resilient to perturbations?
- Will a novel species invade the network?

3. Understand how and why these structures were formed.

- Is there a phylogenetic signal?
- How does co-evolution affect structure?
- What is the role of spatial dynamics?

Research effort

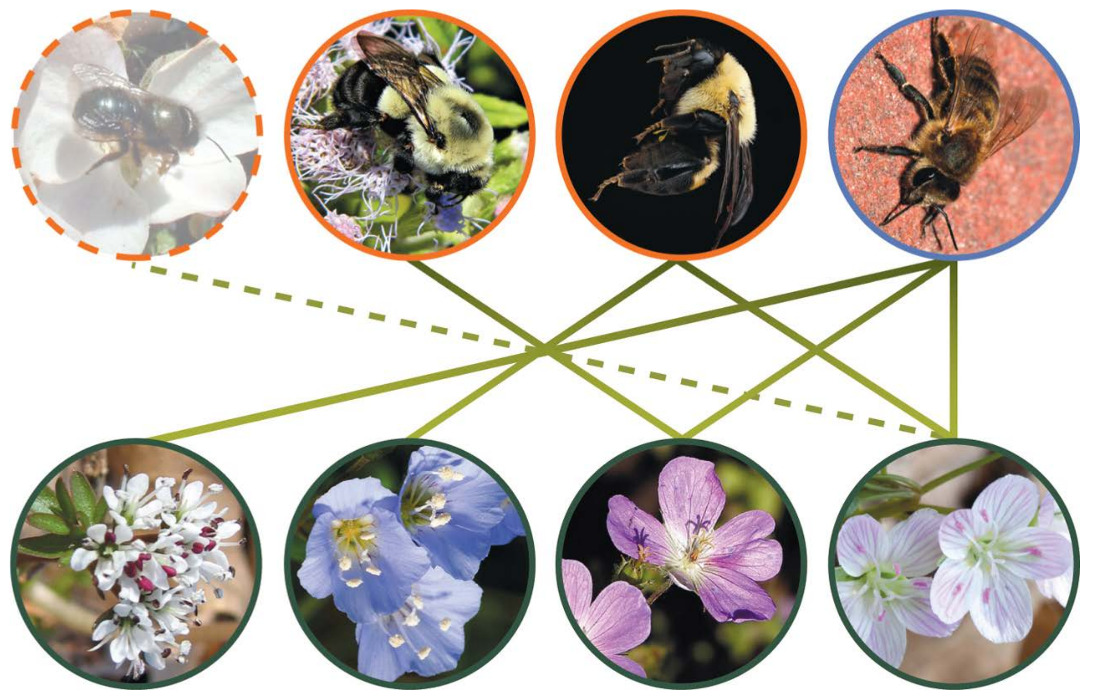
Microscopic rules

- Interaction constraints
- Evolutionary history
- Node heterogeneity
- Environmental context
- Structure–dynamics

Low

Very high

Emergent properties



Low

High

Function

Cell development
Neuro-generation
Pathogen spread
Ecosystem functions
Biological control

Stability


Network structure influences biological processes that affect our lives

Summary

1. Biological systems are diverse, complex and adaptive.

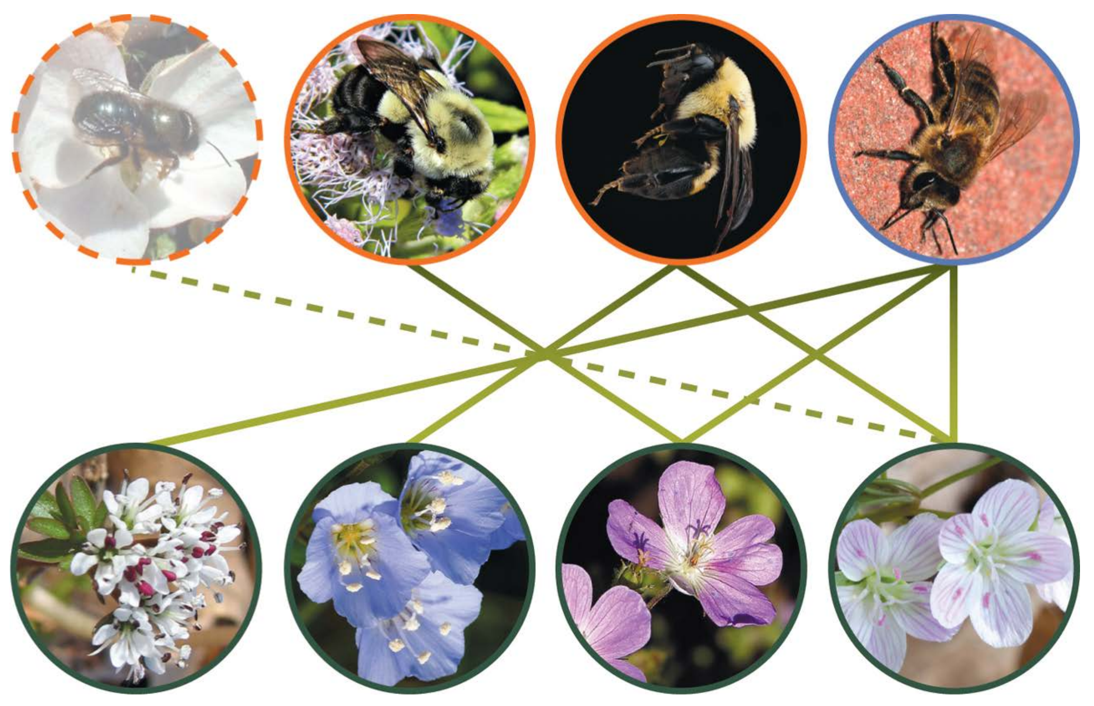
2. Complex systems can be described using networks.

3. Structure affects system stability and function.

Microscopic rules

- Interaction constraints
- Evolutionary history
- Node heterogeneity
- Environmental context
- Structure–dynamics

Emergent properties



Function

Cell development
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Stability