

# Modeling microbial diversity

“Deciphering Biology: the Systems Perspective of Health and Disease”

HKBU May 11, 2021

Ned Wingreen (Princeton)

Anna Posfai (CSHL)

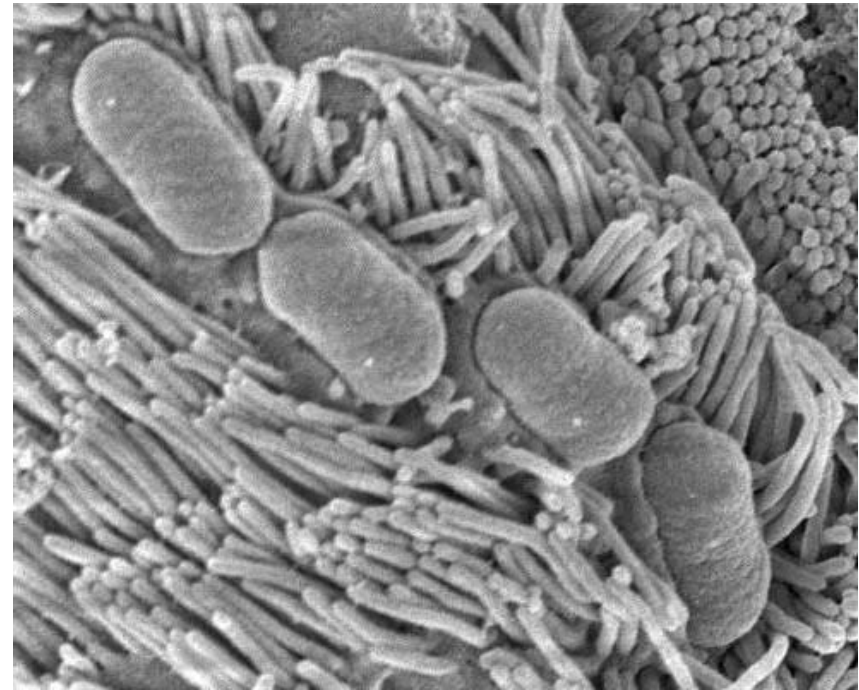
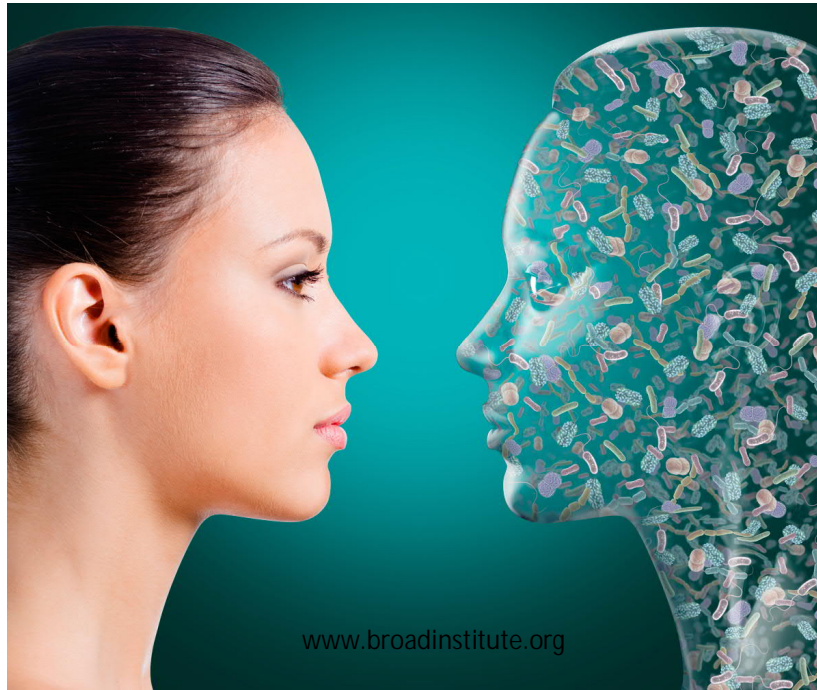
Thibaud Tallefumier (UT Austin)

Yigal Meir (BGU)

Amir Erez (Hebrew University)

Jaime Lopez, Ben Weiner (Princeton)

# The Human Microbiome



Adult human:  $10^{13}$  mammalian cells +  $10^{13}$  microbial cells

>1000 bacterial phylotypes

Human genome: ~ 20,000 genes

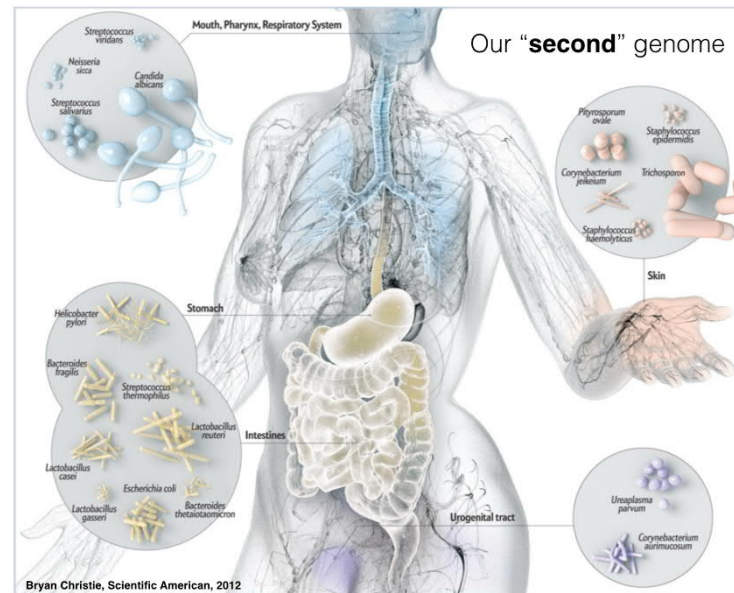
Human microbiome: ~ 100 X human genes (or more...)

# What does our microbiome do?

Food digestion

Mood control

Immune system  
development &  
autoimmunity

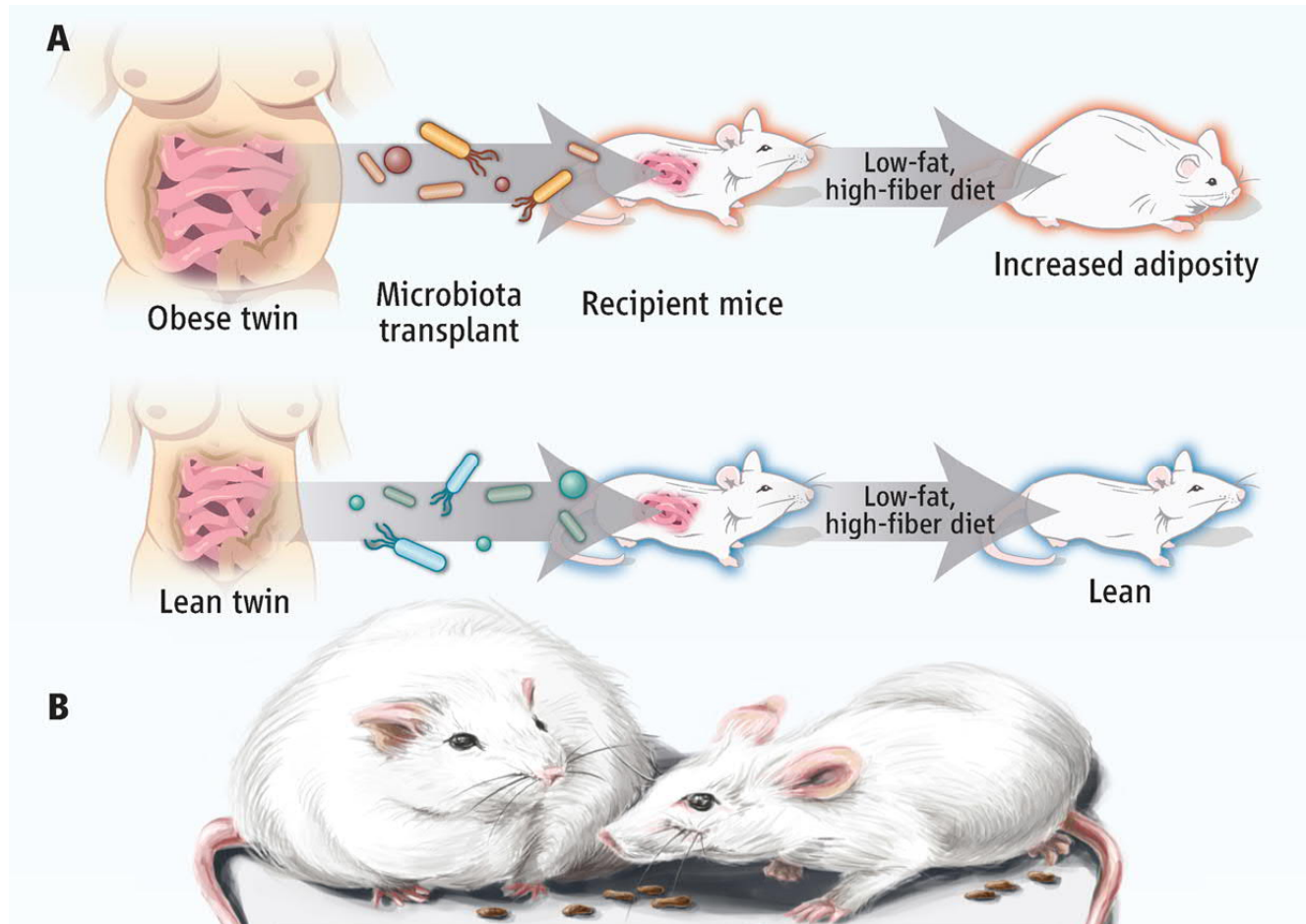


Fighting pathogens

Vitamin synthesis

Bowel function

# Microbiome and Disease



# How can we understand microbiome diversity?

An astonishing characteristic of life is its great variety:

- In tropical rainforests more than 300 tree species may be found on a single hectare.
- In one gram of soil the number of distinct microbial genomes has been estimated at ~ 2000 -- 18,000.

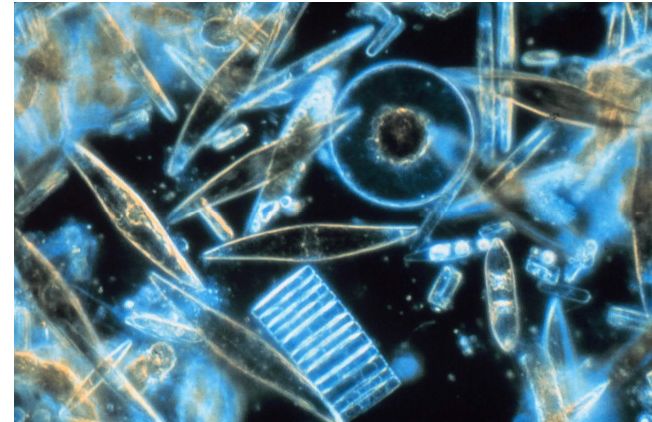
But...the competitive exclusion principle says:

- Two species that compete for the same limiting resource cannot stably coexist.
- In resource competition models, the number of species coexisting in equilibrium cannot exceed the number of resources.

# Paradox of the plankton

Originally described by G. E. Hutchinson in 1961:

"...a limited range of resources supports an unexpectedly wide range of plankton species, apparently flouting the competitive exclusion principle..."





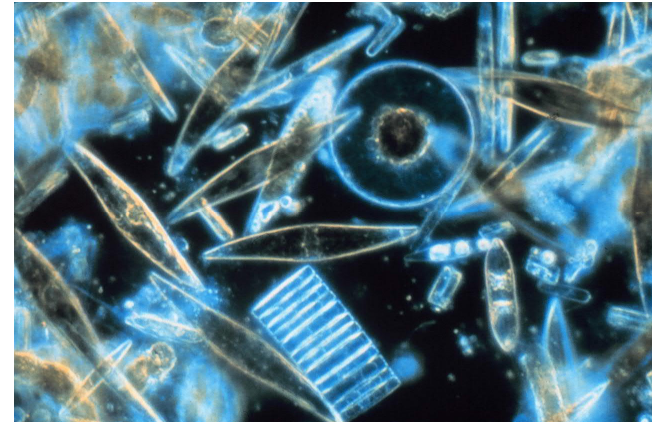
# Paradox of the plankton

Originally described by G. E. Hutchinson in 1961:

"...a limited range of resources supports an unexpectedly wide range of plankton species, apparently flouting the competitive exclusion principle..."

Possible solutions:

- Cross-feeding
- Oscillatory or chaotic population dynamics
- Temporal variation of environment,  
e.g. weather changes, seasonal cycles
- Spatial variation of environment,  
e.g. gradients such as temperature, salinity, exposure to light
- Other limiting factors,  
e.g. predation



EVERYTHING'S A  
TRADEOFF - NOW  
THAT WE CAN DO  
SCIENCE, CAN'T  
WE WIGGLE OUR EARS  
ANY MORE.



Search: 12261671



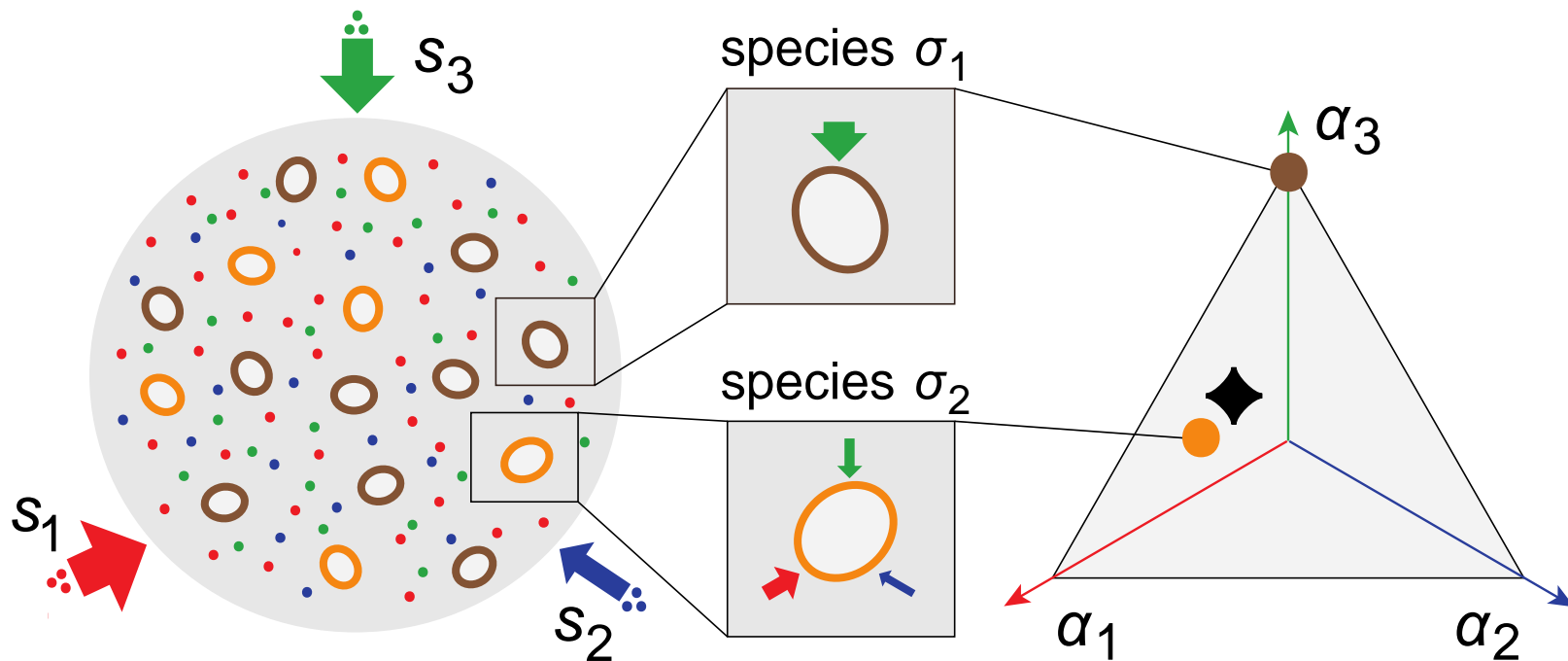
# Resource-competition model with trade-offs

$p$  resources

Species:  $\vec{\alpha}_\sigma = (\alpha_{\sigma 1}, \dots, \alpha_{\sigma p})$

Trade-offs in ability to utilize different resources:

$$\sum_{i=1}^p w_i \alpha_{\sigma i} = E$$



Q & A Break

# Resource-competition model with trade-offs

Nutrient concentrations dynamics:

$$\dot{c}_i = s_i - \sum_{\sigma} n_{\sigma} \alpha_{\sigma i} \frac{c_i}{K_i + c_i} - \mu_i c_i$$

= supply – consumption – loss

Growth rate of species  $\sigma$ :

$$g_{\sigma}(\vec{c}) = \sum_{i=1}^p v_i \alpha_{\sigma i} \frac{c_i}{K_i + c_i}$$

Population dynamics:

$$\dot{n}_{\sigma} = (g_{\sigma}(\vec{c}) - \delta) n_{\sigma}$$

Simplified parameters:

- no nutrient loss:  $\mu_i = 0$
- separation of time scales:  $\dot{c}_i = 0$
- "symmetric" nutrients:  $w_i = K_i = v_i = 1$

# Resource-competition model with trade-offs

Nutrient concentrations dynamics:

$$\dot{c}_i = s_i - \sum_{\sigma} n_{\sigma} \alpha_{\sigma i} \frac{c_i}{K_i + c_i} - \mu_i c_i$$

= supply – consumption – loss

Growth rate of species  $\sigma$ :

$$g_{\sigma}(\vec{c}) = \sum_{i=1}^p v_i \alpha_{\sigma i} \frac{c_i}{K_i + c_i}$$

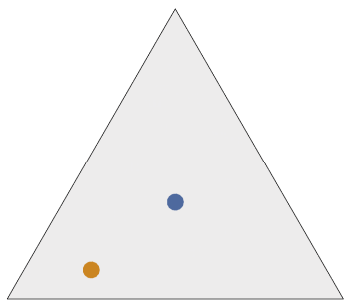
Population dynamics:

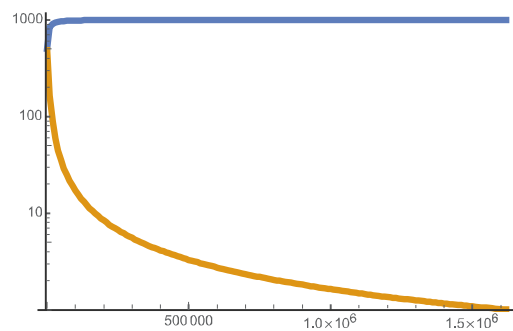
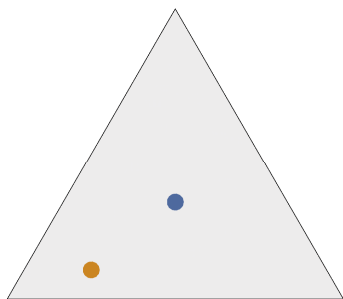
$$\dot{n}_{\sigma} = (g_{\sigma}(\vec{c}) - \delta) n_{\sigma}$$

Simplified parameters:

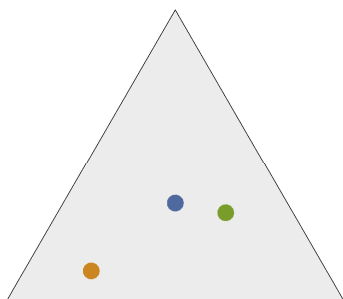
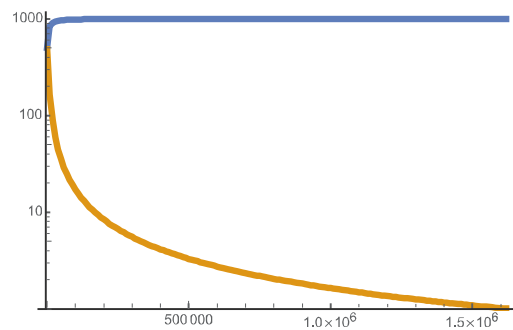
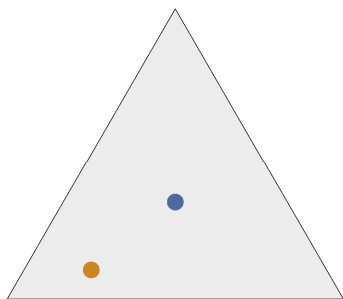
- no nutrient loss:  $\mu_i = 0$
- separation of time scales:  $\dot{c}_i = 0$
- "symmetric" nutrients:  $w_i = K_i = v_i = 1$

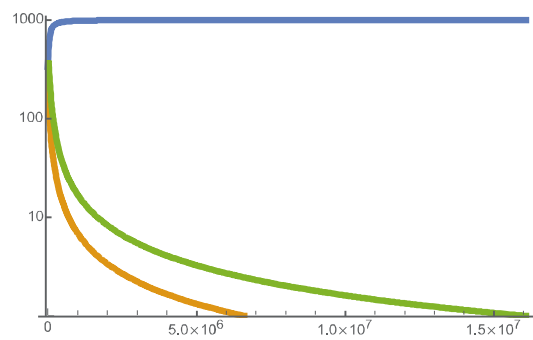
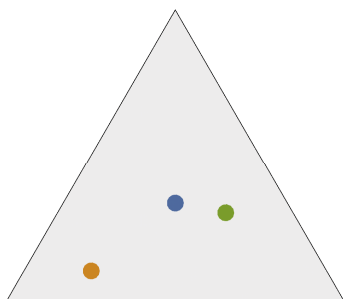
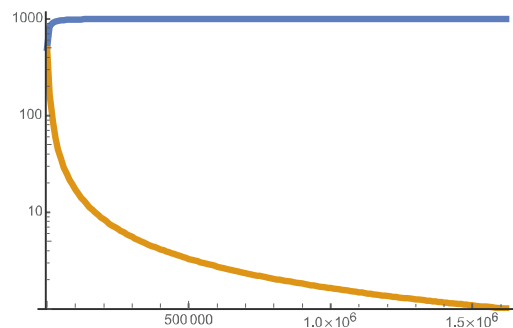
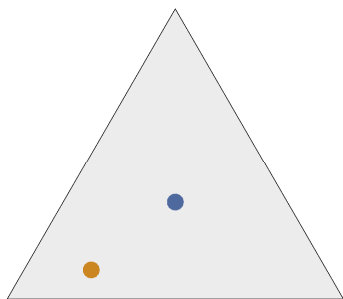
$$\dot{n}_{\sigma} = \left( \sum_{i=1}^p \alpha_{\sigma i} \frac{s_i}{\sum_{\kappa} \alpha_{\kappa i} n_{\kappa}} - \delta \right) n_{\sigma}, \quad \sum_{i=1}^p \alpha_{\sigma i} = E$$

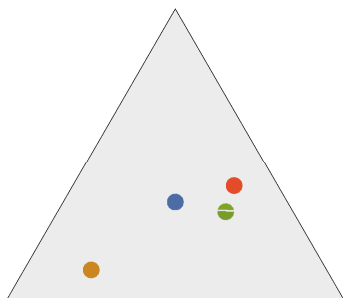
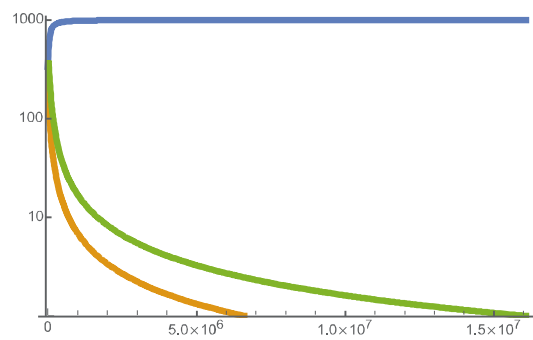
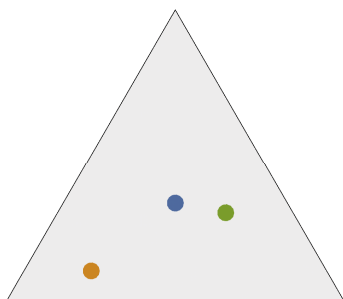
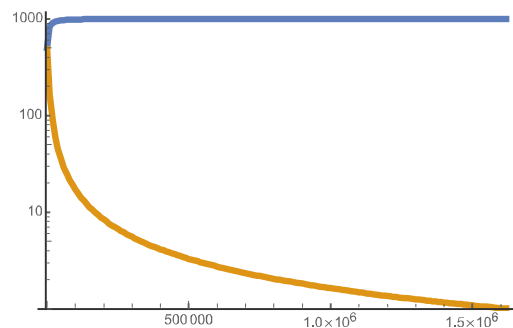
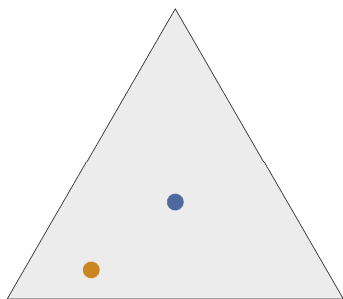


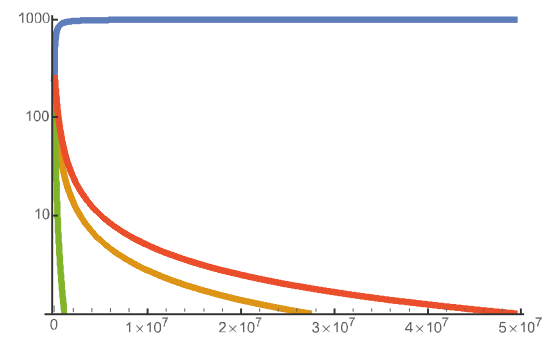
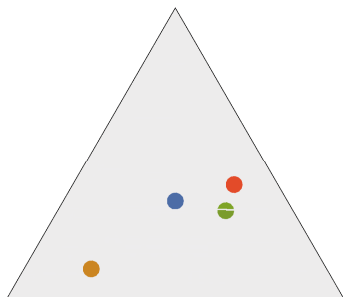
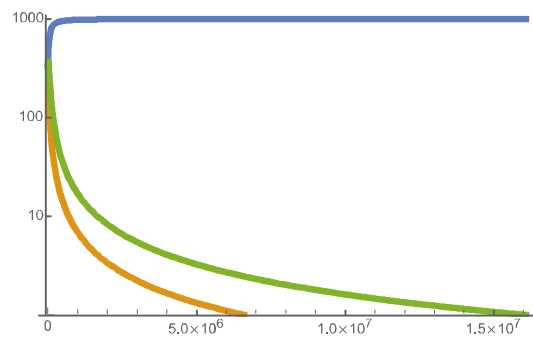
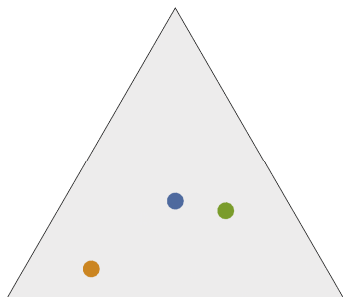
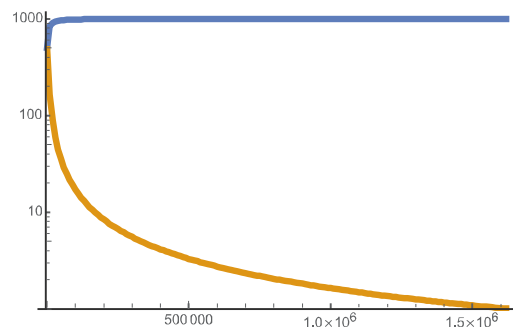
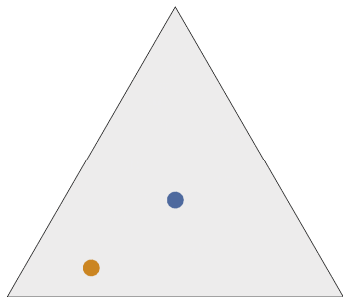


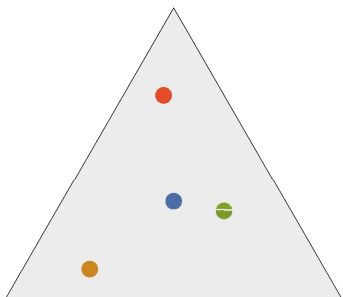
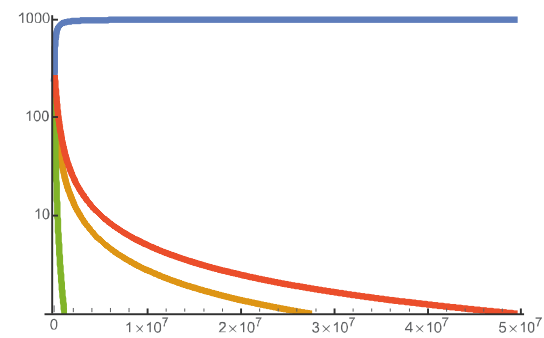
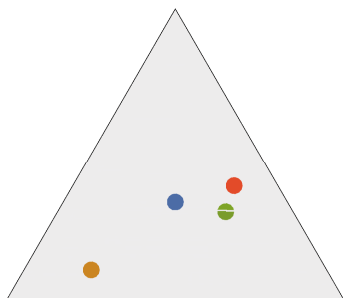
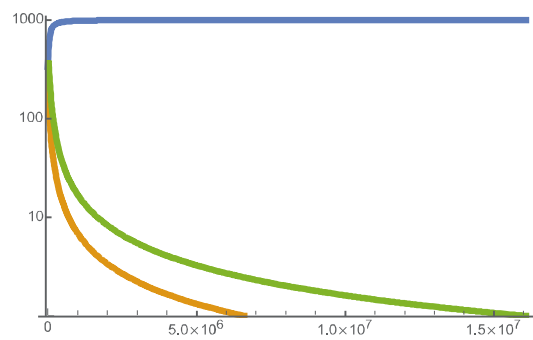
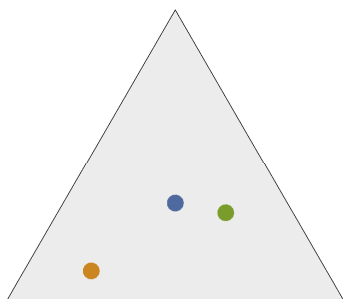
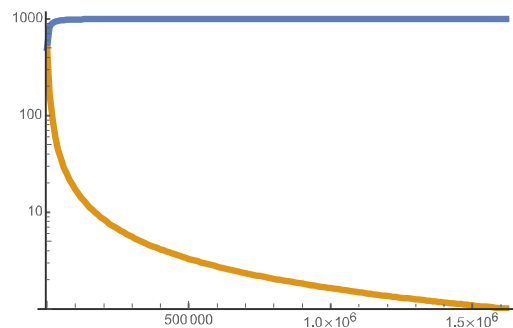
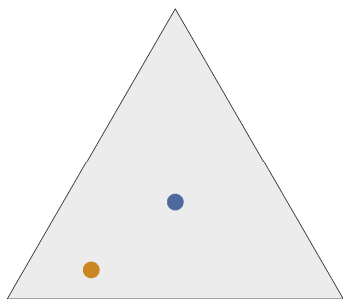


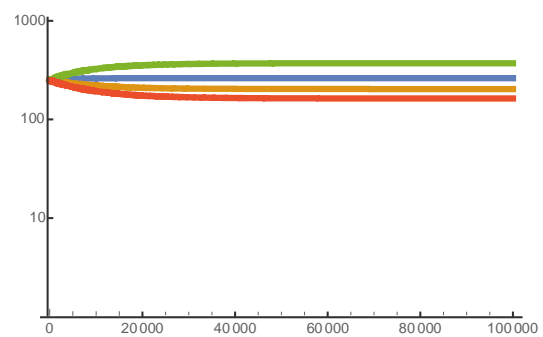
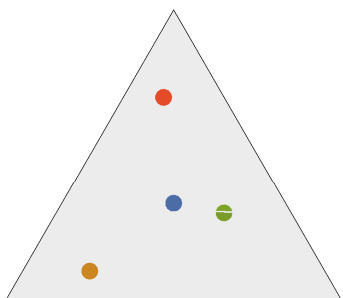
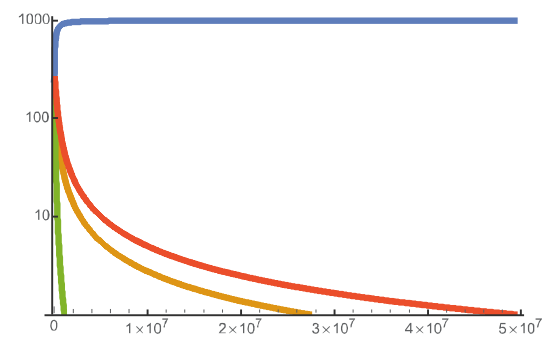
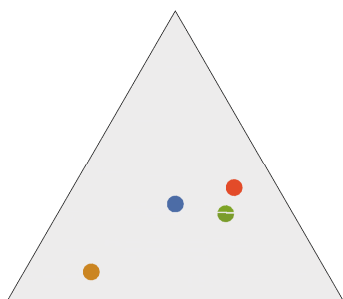
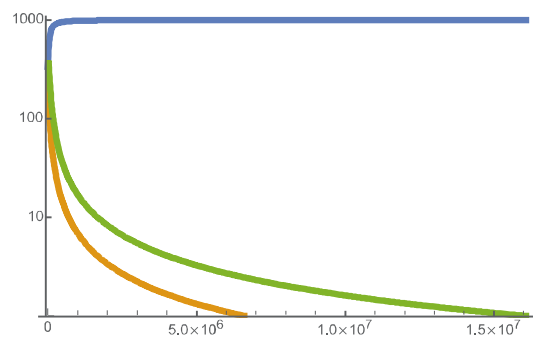
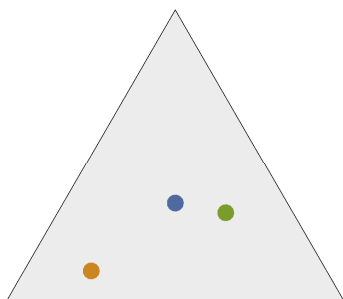
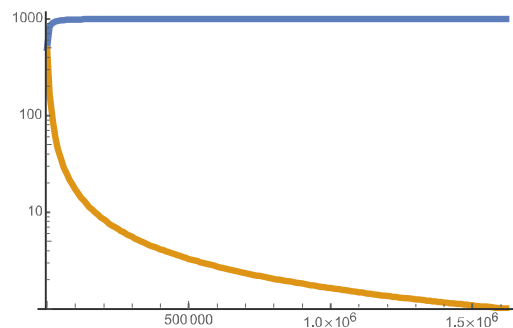
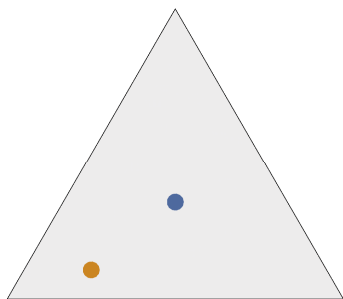




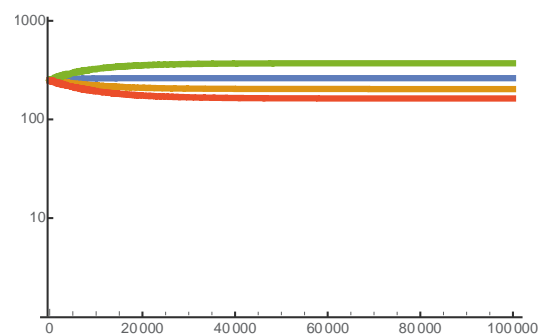
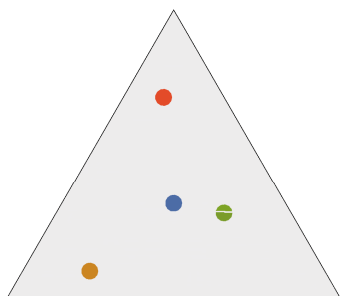
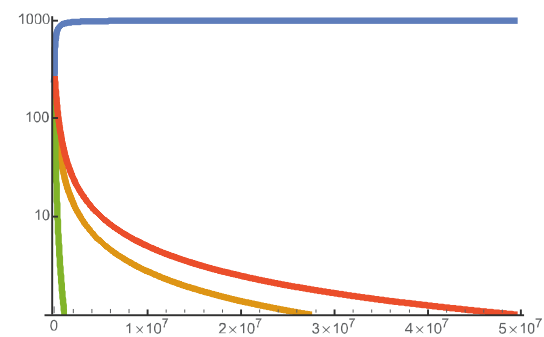
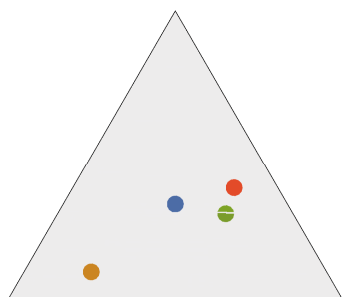
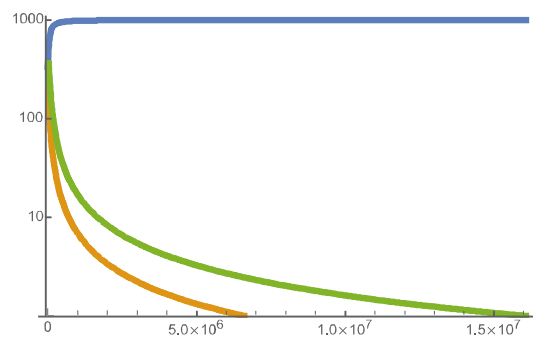
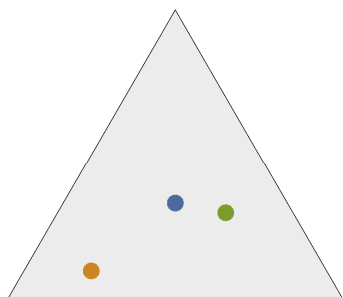
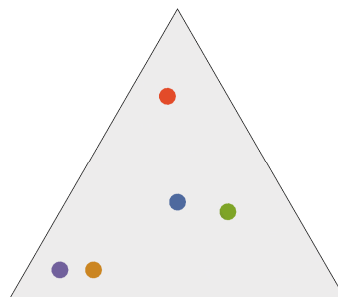
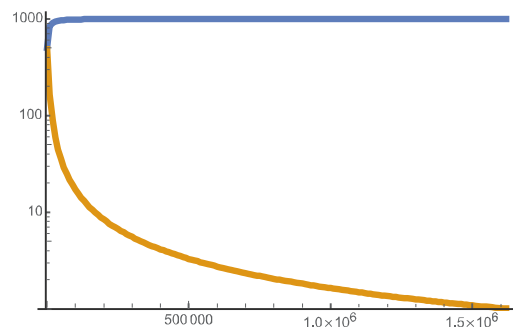
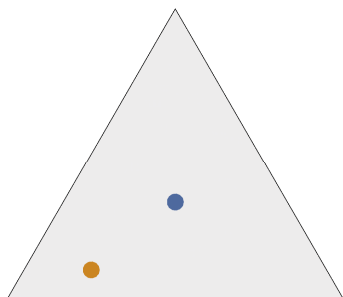


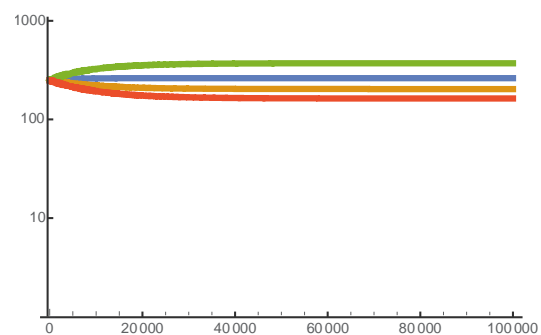
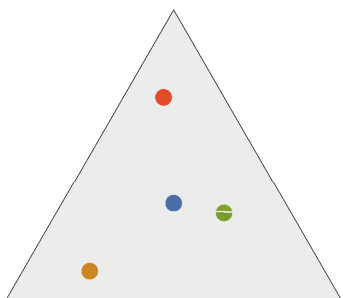
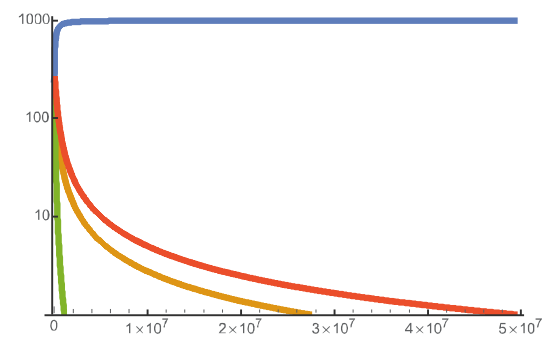
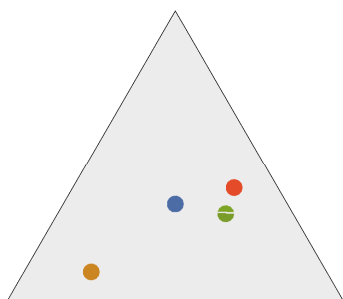
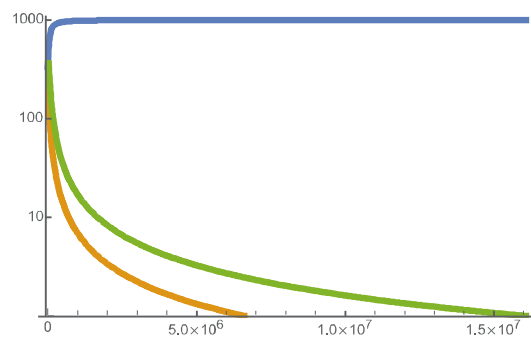
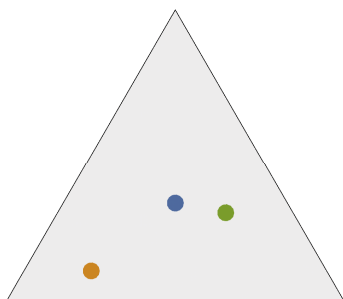
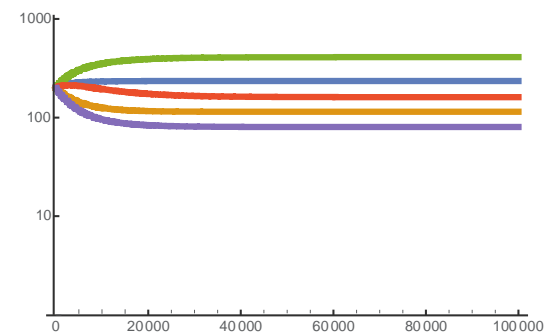
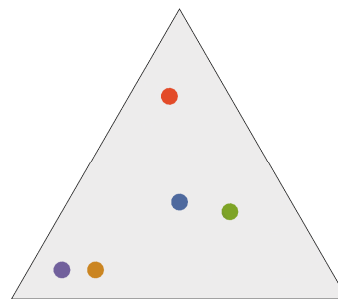
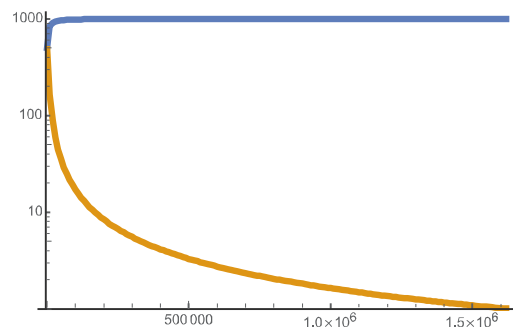
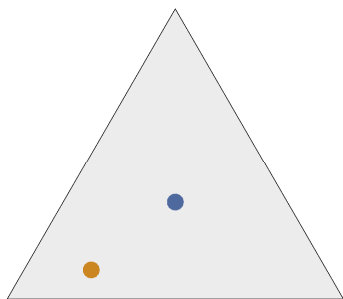


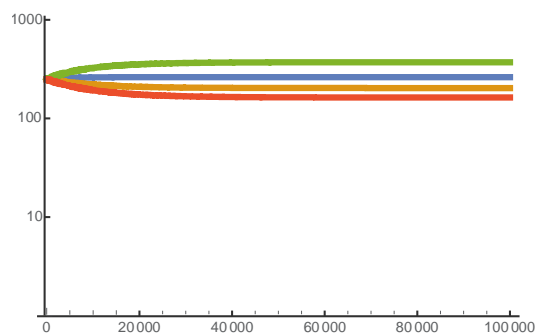
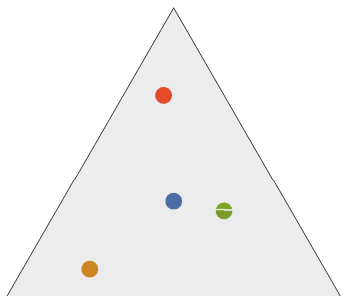
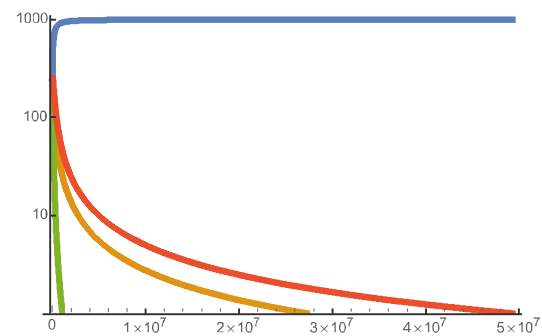
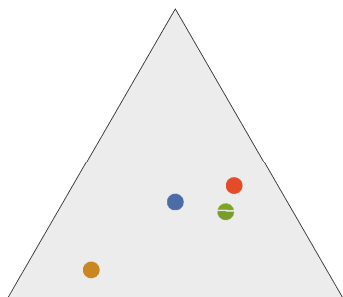
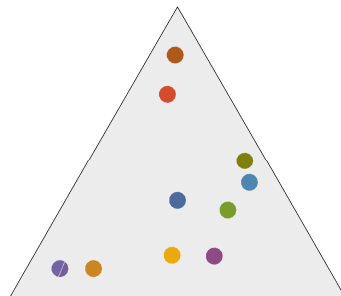
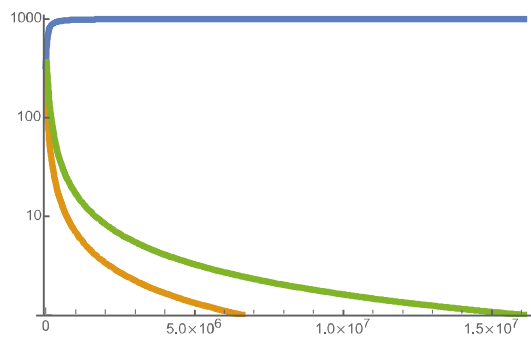
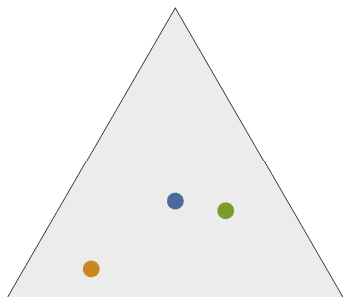
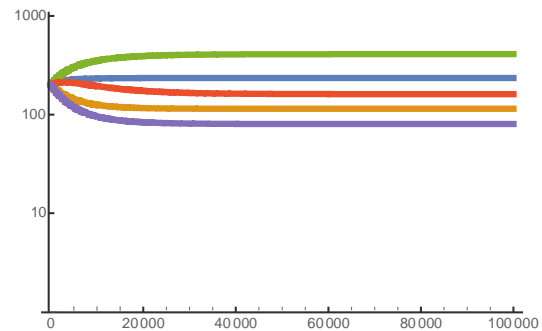
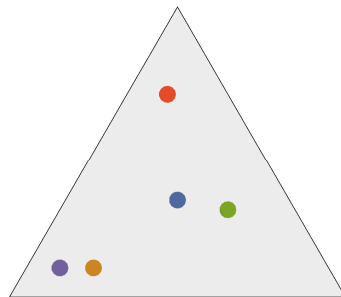
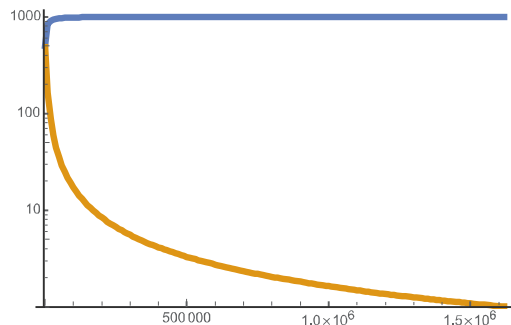
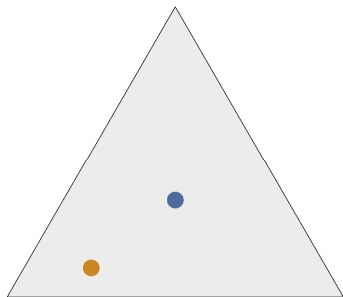


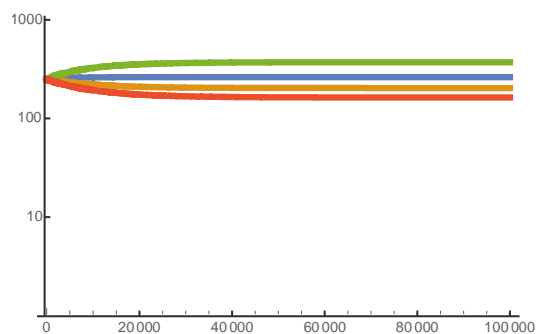
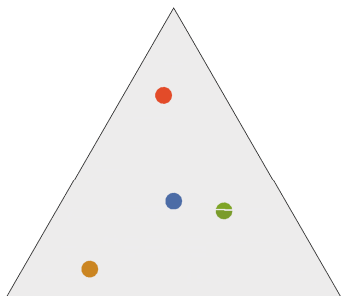
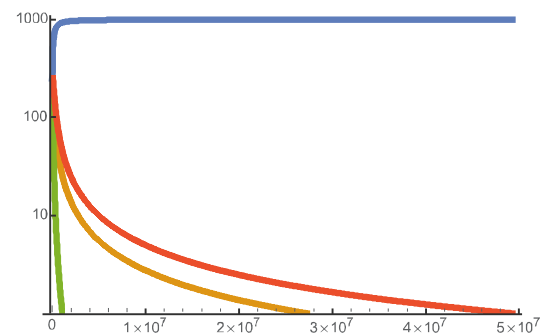
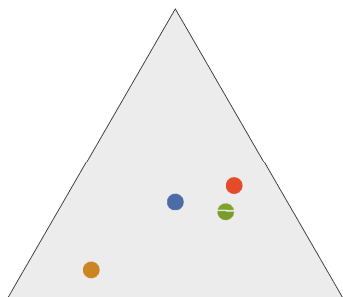
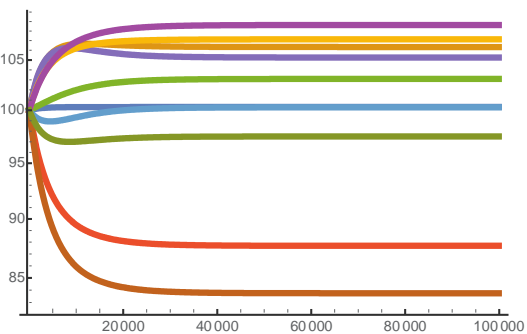
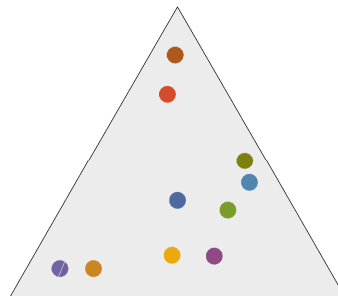
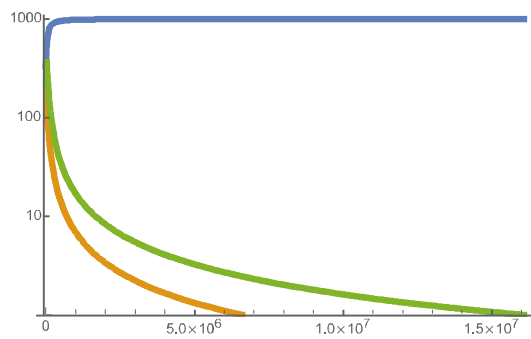
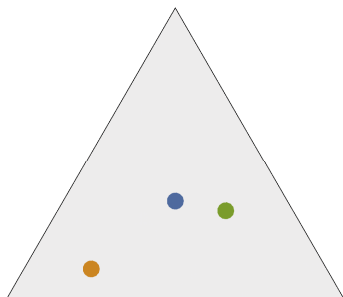
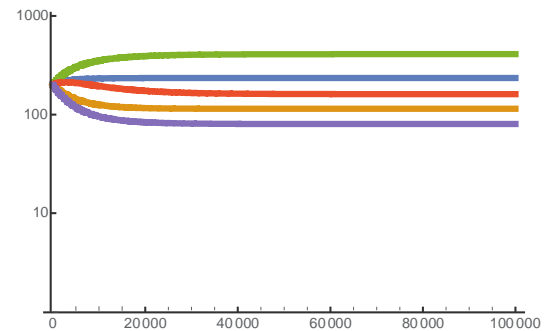
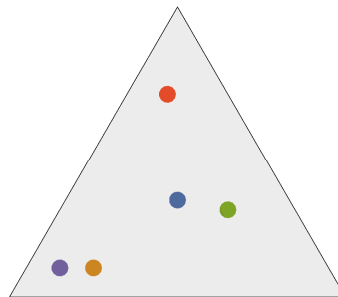
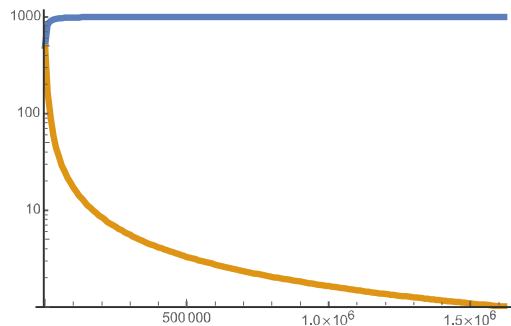
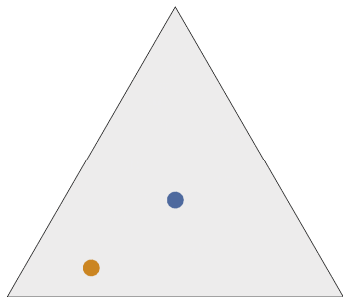


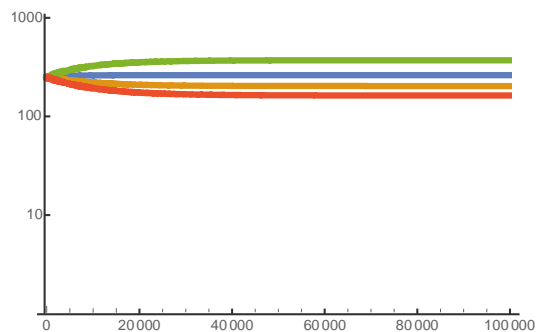
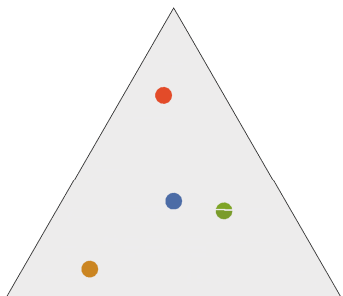
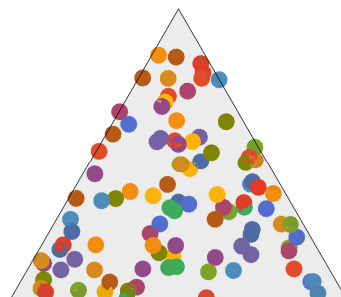
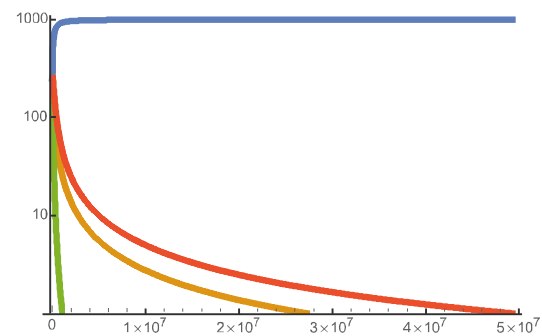
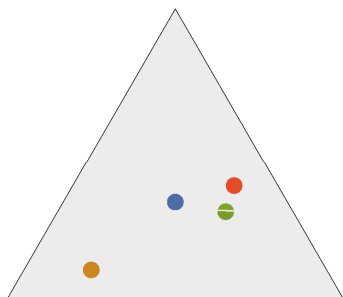
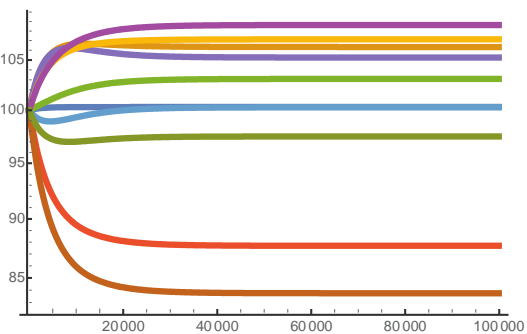
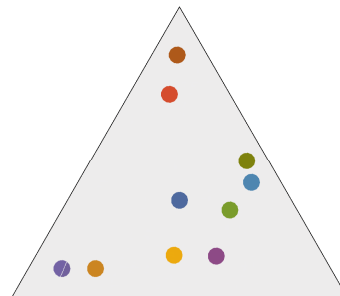
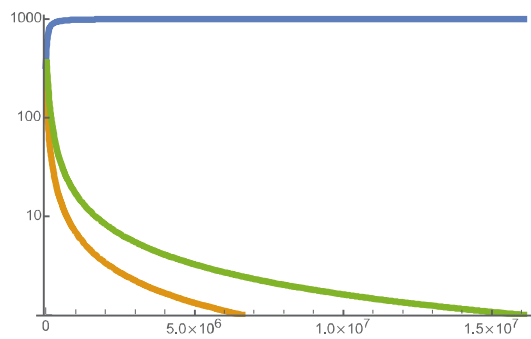
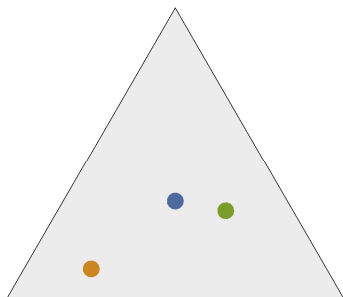
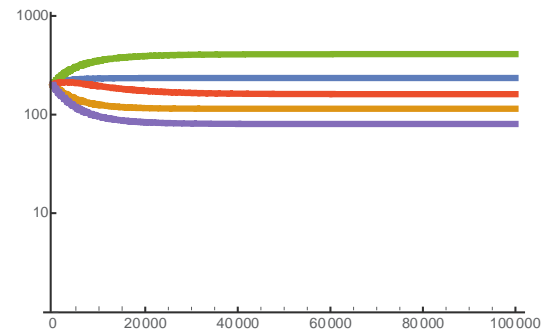
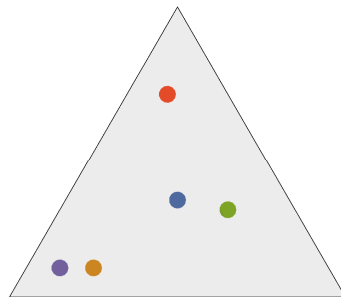
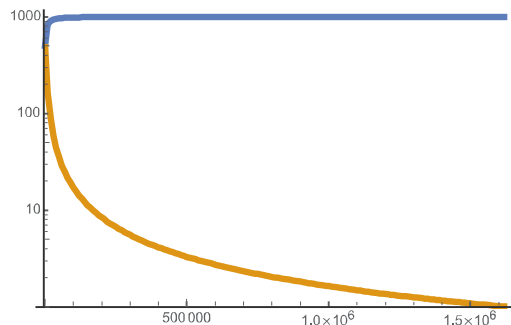
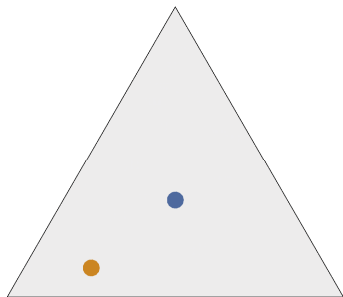


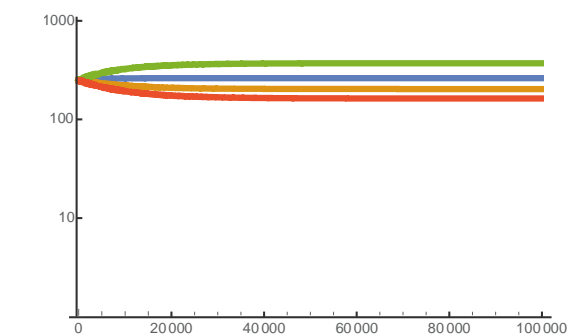
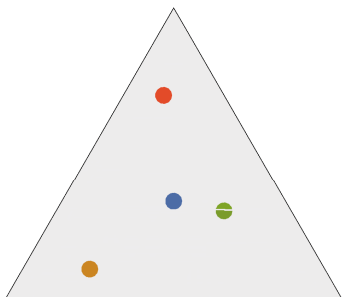
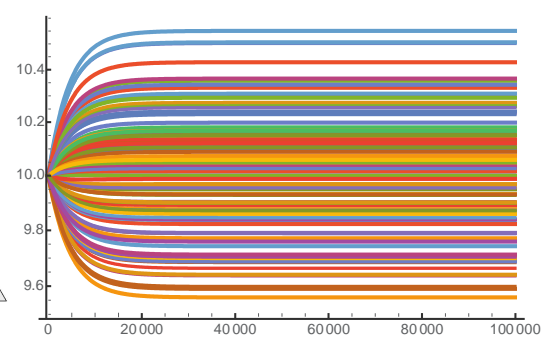
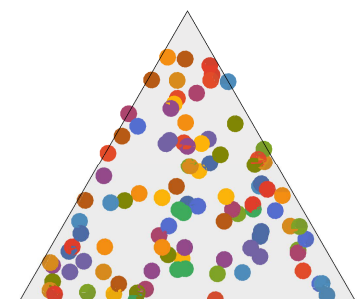
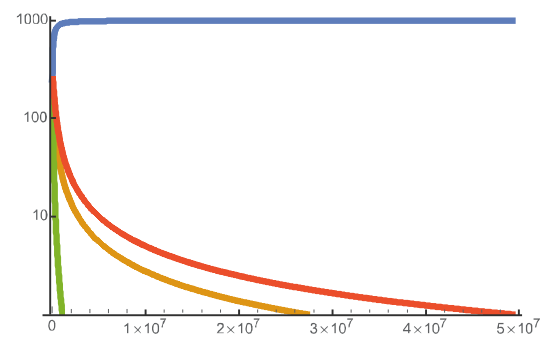
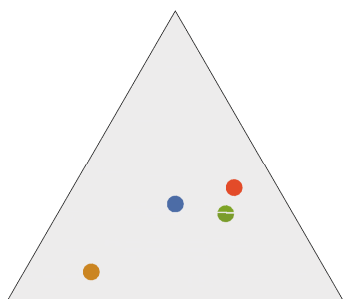
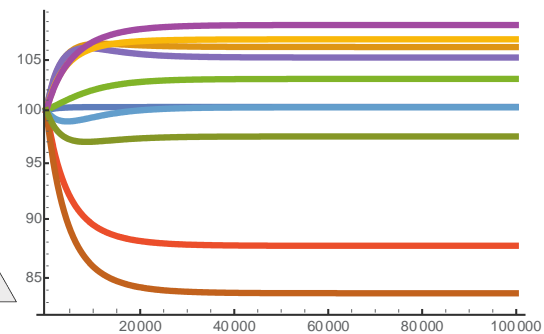
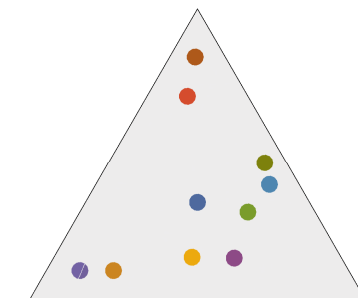
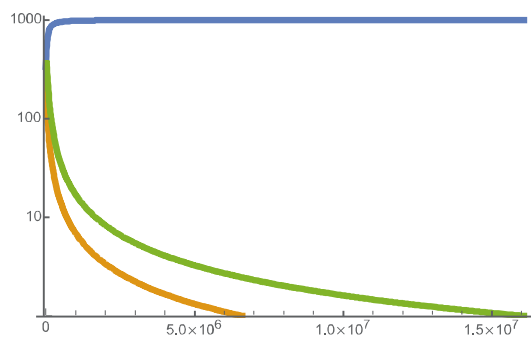
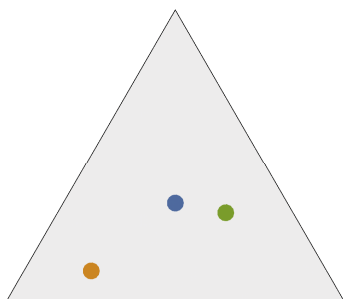
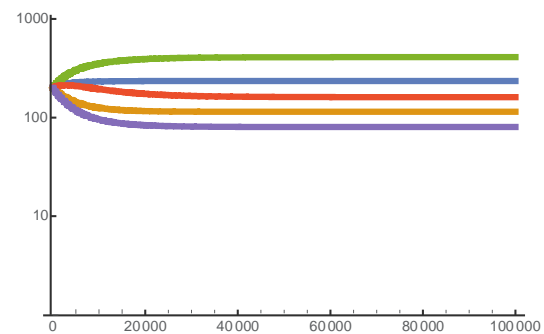
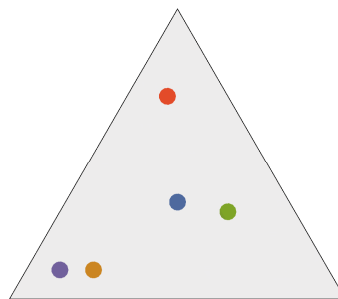
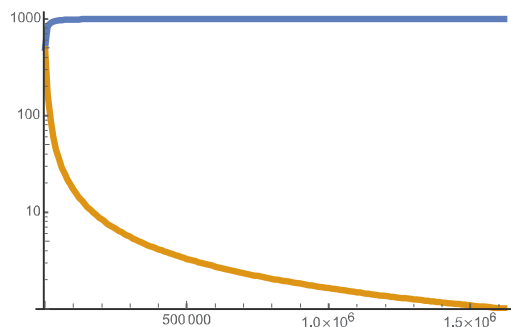
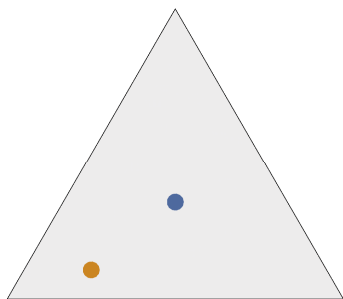






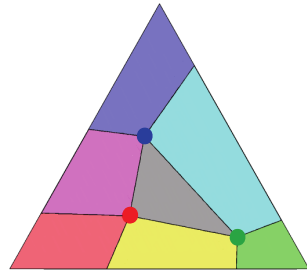




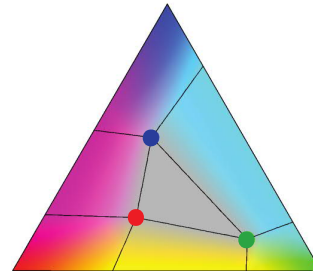




# species = # resources:



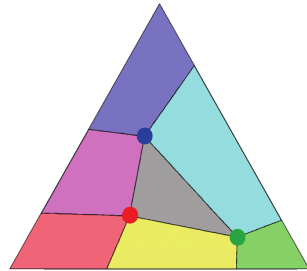
Surviving species



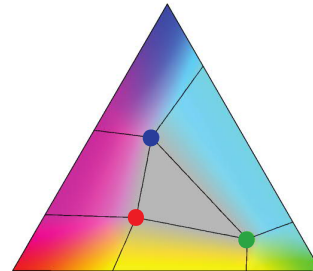
Nutrient concentrations

$$g_{\sigma}(\vec{c}) = \sum_i \alpha_{\sigma i} \frac{c_i}{1 + c_i}$$

# species = # resources:



Surviving species

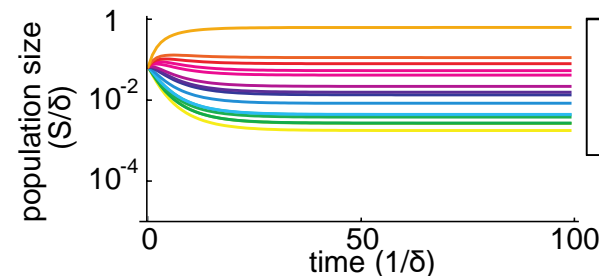
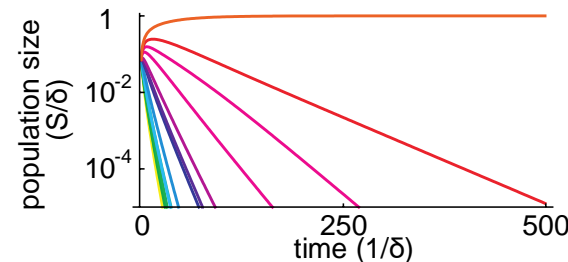
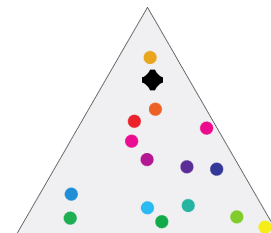
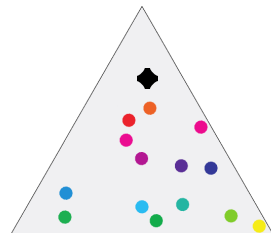


Nutrient concentrations

$$g_{\sigma}(\vec{c}) = \sum_i \alpha_{\sigma i} \frac{c_i}{1 + c_i}$$

# species  $\geq$  # resources:

A collection of  $\{\vec{\alpha}_{\sigma}\}$  species coexist in steady state  $\Leftrightarrow$  the supply  $\vec{s}$  lies within the convex hull of the species  $\{\vec{\alpha}_{\sigma}\}$ .



Gold species acts as "keystone species".

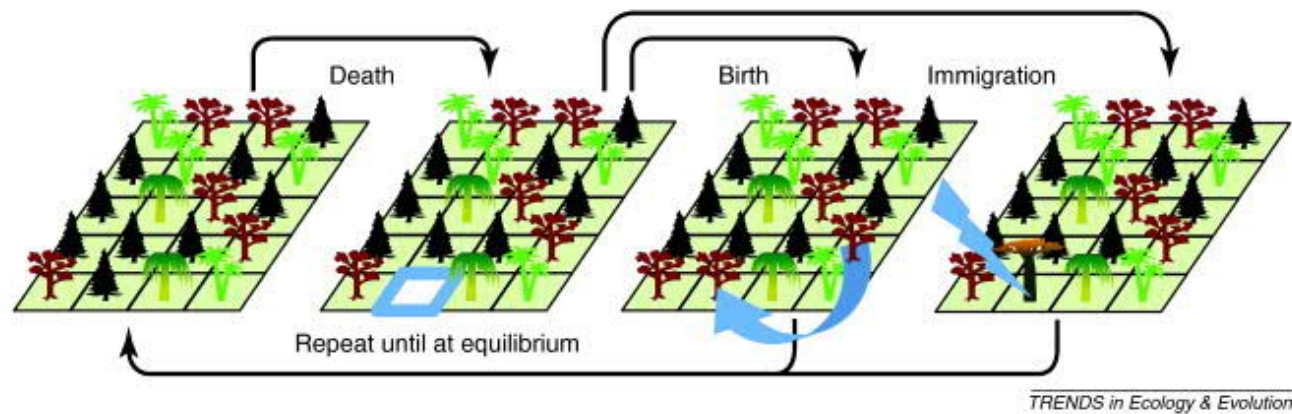
Competition  $\rightarrow$  nutrient concentrations too low for certain species to survive  $\rightarrow$  at most #resources-1 species survive.

Neutrality  $\rightarrow$  balanced nutrient concentrations  $\rightarrow$  all species equally fit  $\rightarrow$  all species survive!

Q & A Break

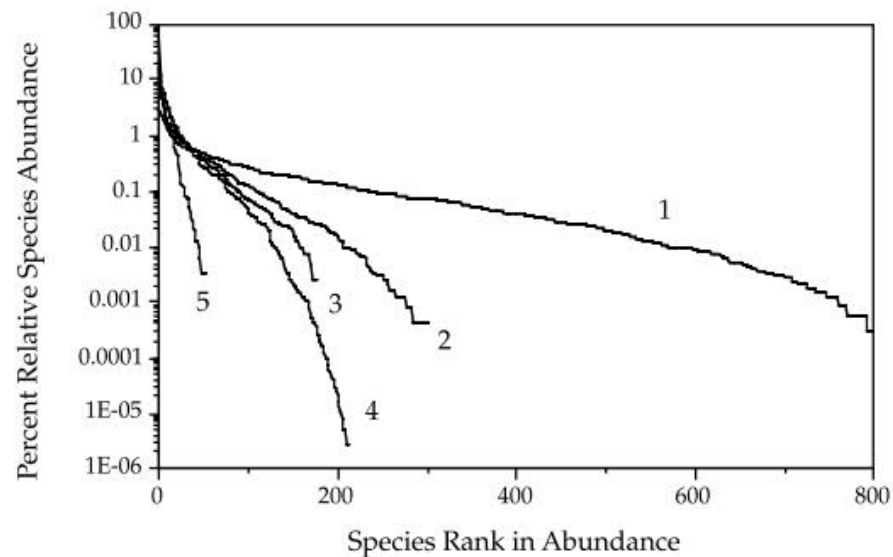
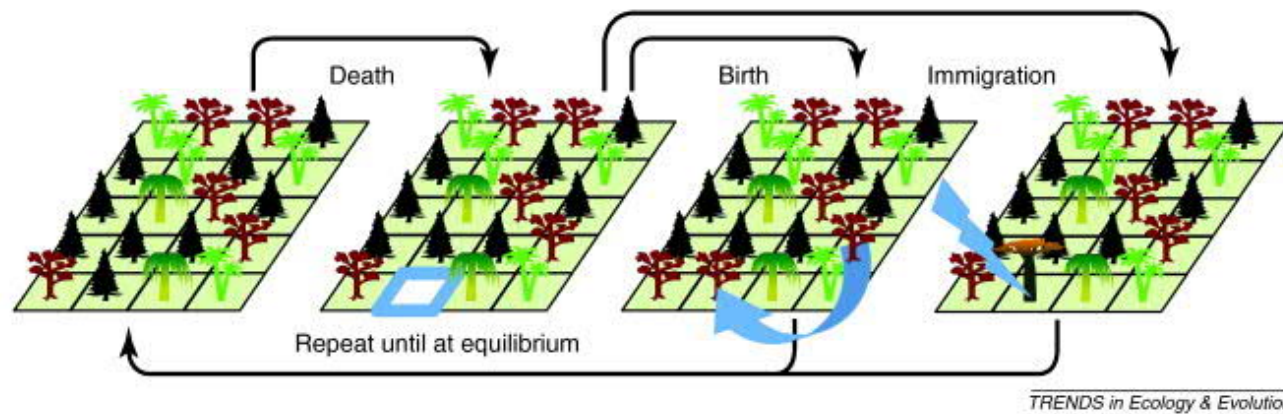
# The neutral theory of biodiversity

Neutral theory: species are ecologically equivalent, and diversity emerges from ecological drift.



# The neutral theory of biodiversity

Neutral theory: species are ecologically equivalent, and diversity emerges from ecological drift.



1. Tropical wet forest in Amazonia
2. Tropical dry deciduous forest in Costa Rica
3. Marine planktonic copepod community from the North Pacific gyre
4. Terrestrial breeding birds of Britain
5. Tropical bat community from Panama

# Connection to the neutral theory of biodiversity

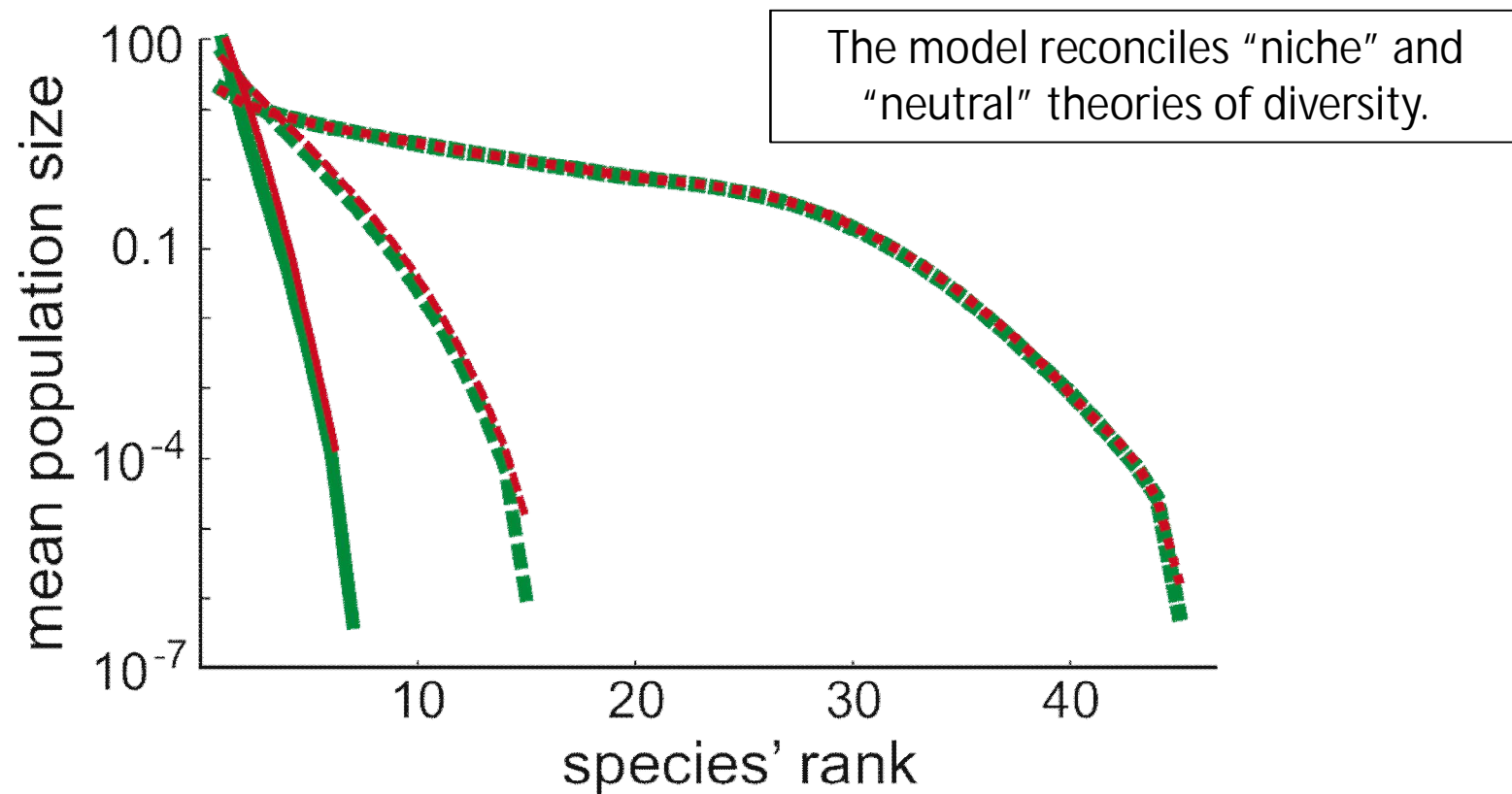
Rank-abundance curves

red – resource-competition model

green – neutral model

total population:  $N_{\text{tot}} = 100$

immigration probabilities:  $\nu = 0.001, 0.01, 0.1$



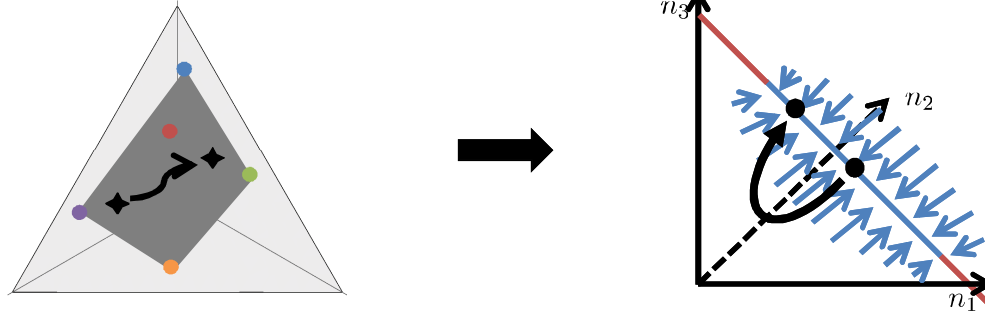
# Robustness of coexistence

- I. Against population disturbances
- II. Against fluctuations in nutrient availability
- III. Against variability in species' budgets and death rates

# Robustness of coexistence

## II. Against fluctuations in nutrient availability:

If nutrient supply changes, but remains in the convex hull of the species, the populations find a new equilibrium of coexistence.

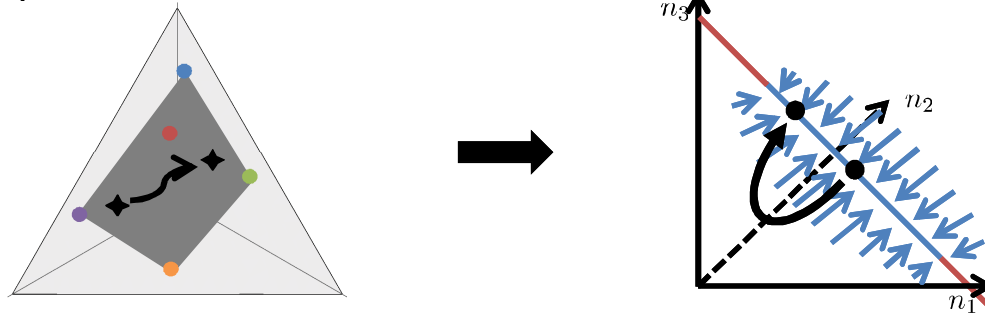




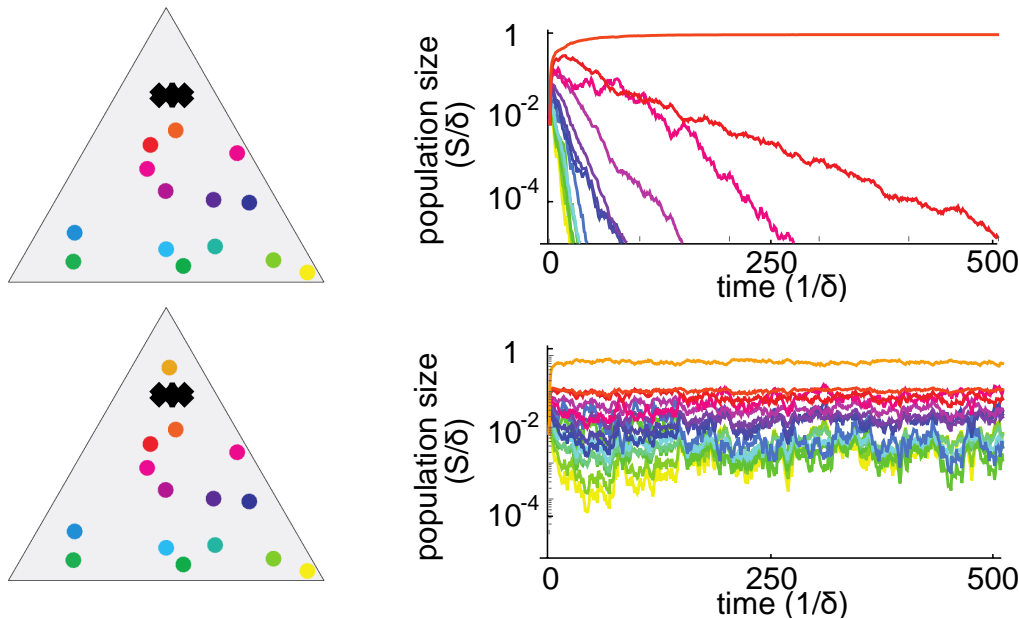
# Robustness of coexistence

## II. Against fluctuations in nutrient availability:

If nutrient supply changes, but remains in the convex hull of the species, the populations find a new equilibrium of coexistence.



Time-dependent nutrient supply: The supply regularly changes, at a fixed time interval  $T$ , to a new randomly selected supply, while the total supply is fixed:



Mean supply hypothesis:  
A collection of species  
 $\{\vec{\alpha}_\sigma\}$  coexist.

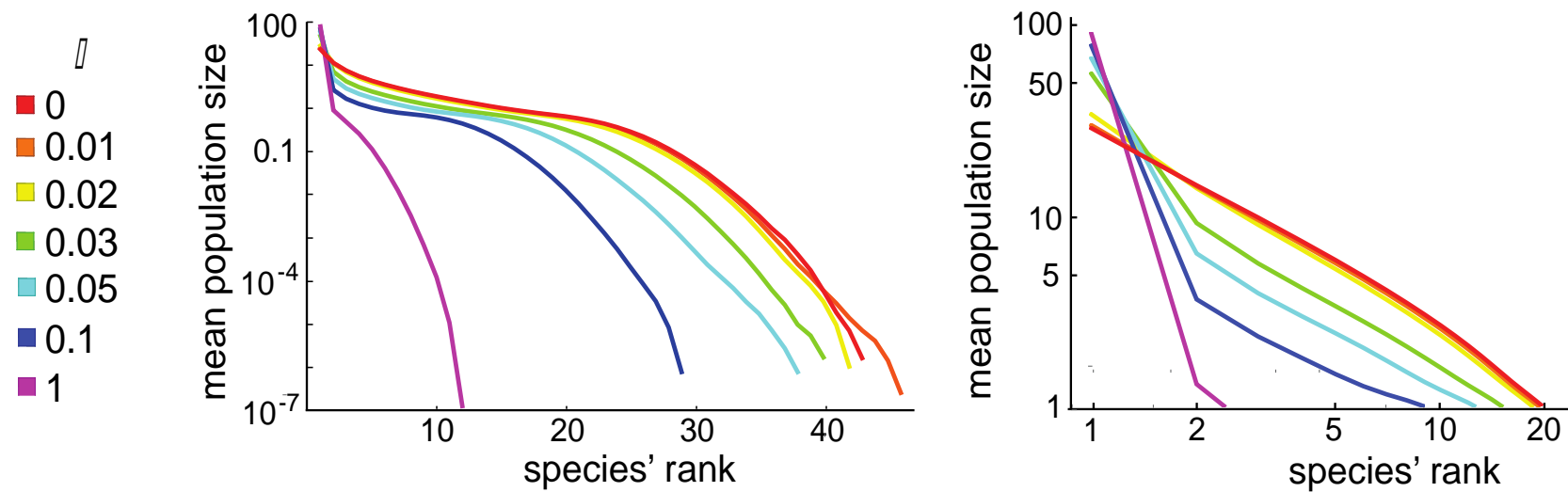


The mean supply  $\langle \vec{s} \rangle$  lies  
within the convex hull of  
the species  $\{\vec{\alpha}_\sigma\}$ .

# Robustness of coexistence

## III. Against variability in species' budgets and death rates:

In the deterministic version of the model, diversity is lost. However, in the stochastic version, diversity can be maintained:



$\Sigma \leq 0.02 \quad \Rightarrow \quad \text{High diversity}$   
 $\Sigma \geq 0.03 \quad \Rightarrow \quad \text{Low diversity}$

# Conclusions

- Features of model that allow for coexistence:
  - Organisms take part in shaping their environment.
  - All species are subject to the same trade-offs.

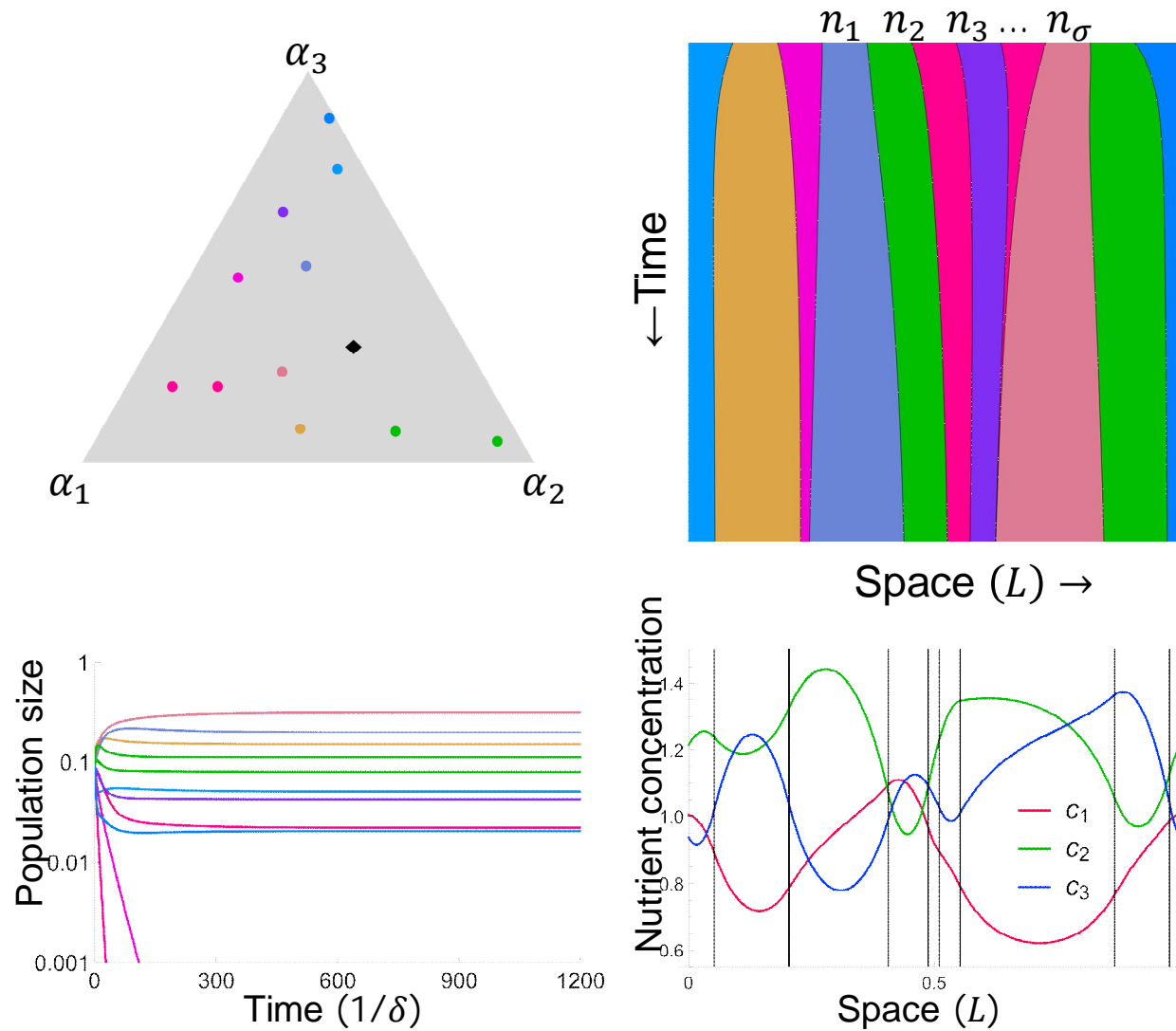
# Conclusions

- Features of model that allow for coexistence:
  - Organisms take part in shaping their environment.
  - All species are subject to the same trade-offs.
  
- Similarities with natural ecosystems:
  - Keystone species
  - Species' abundance patterns replicate neutral theory

# Conclusions

- Features of model that allow for coexistence:
  - Organisms take part in shaping their environment.
  - All species are subject to the same trade-offs.
  
- Similarities with natural ecosystems:
  - Keystone species
  - Species' abundance patterns replicate neutral theory
  
- Beyond the chemostat:
  - Spatial structure

# Spatial structure



Weiner, Posfai, & NSW, PNAS (2019)

# Conclusions

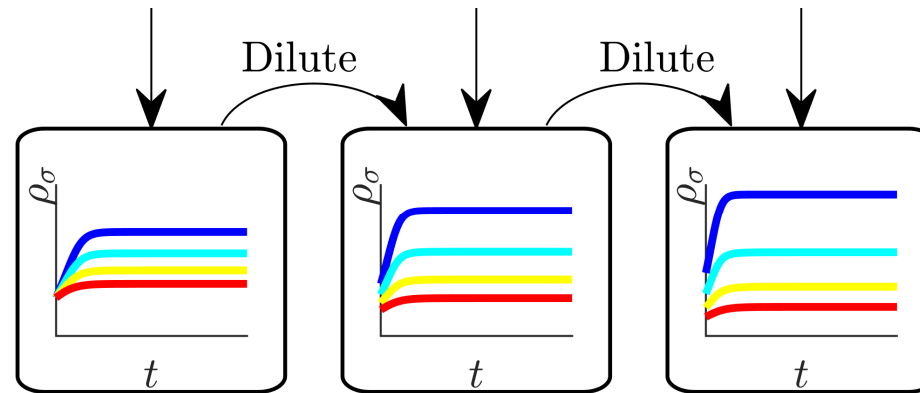
- Features of model that allow for coexistence:
  - Organisms take part in shaping their environment.
  - All species are subject to the same trade-offs.
  
- Similarities with natural ecosystems:
  - Keystone species
  - Species' abundance patterns replicate neutral theory
  
- Beyond the chemostat:
  - Spatial structure

# Conclusions

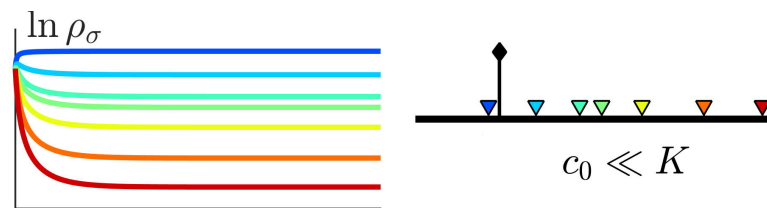
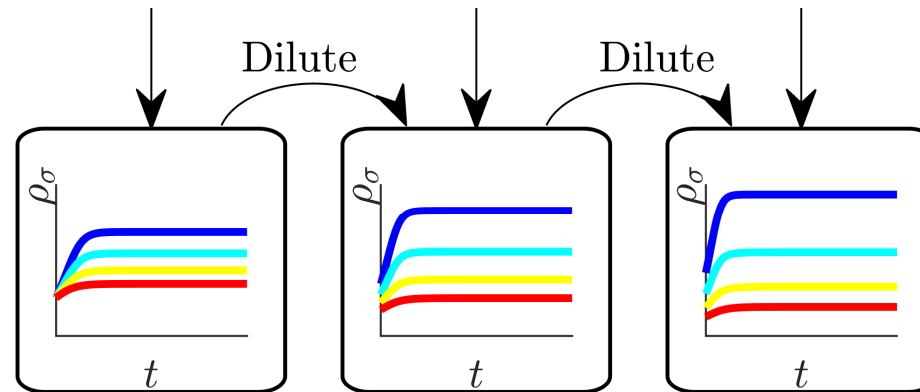
- Features of model that allow for coexistence:
  - Organisms take part in shaping their environment.
  - All species are subject to the same trade-offs.
  
- Similarities with natural ecosystems:
  - Keystone species
  - Species' abundance patterns replicate neutral theory
  
- Beyond the chemostat:
  - Spatial structure
  - "Seasonal" ecosystem



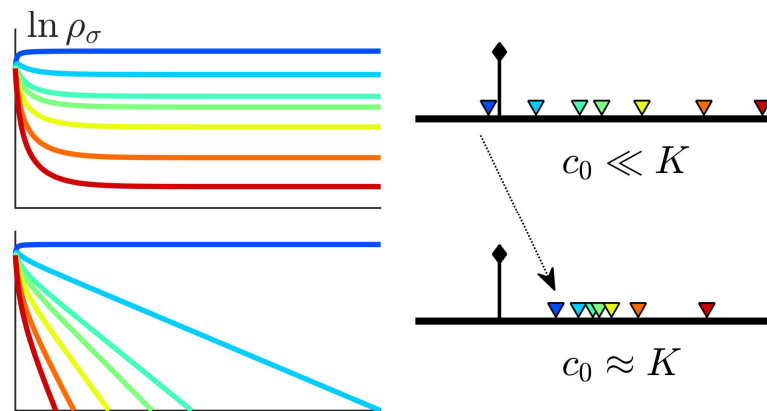
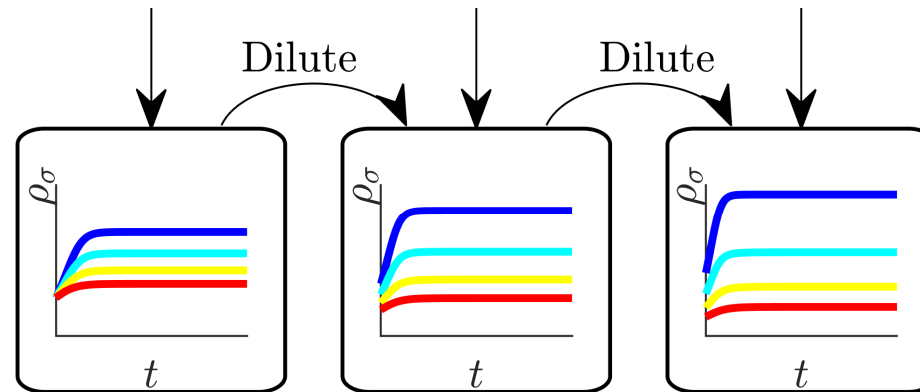
# "Seasonal" ecosystem (serial dilution)



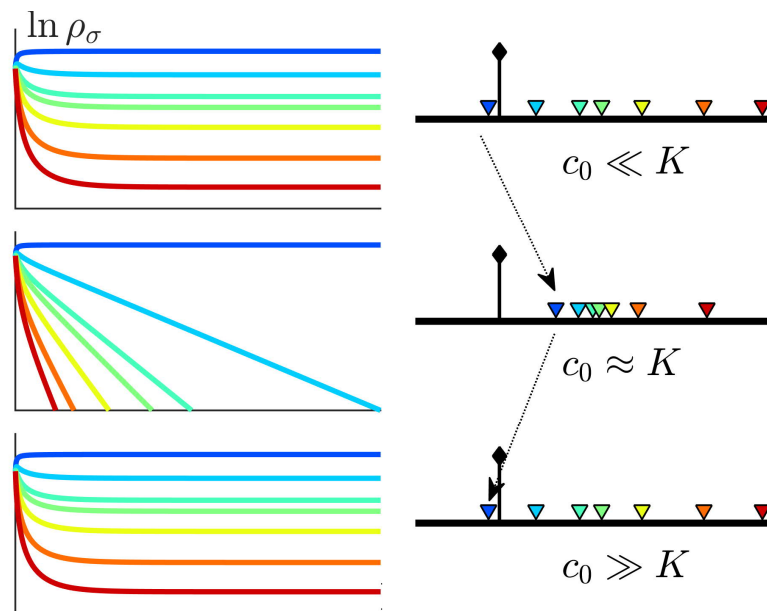
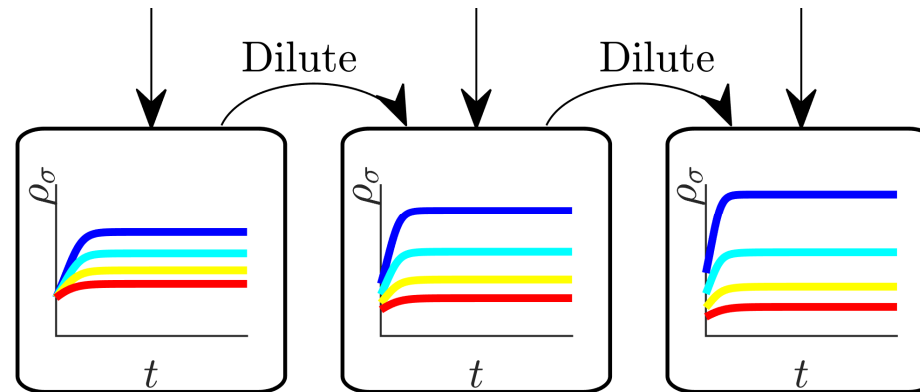
# "Seasonal" ecosystem (serial dilution)



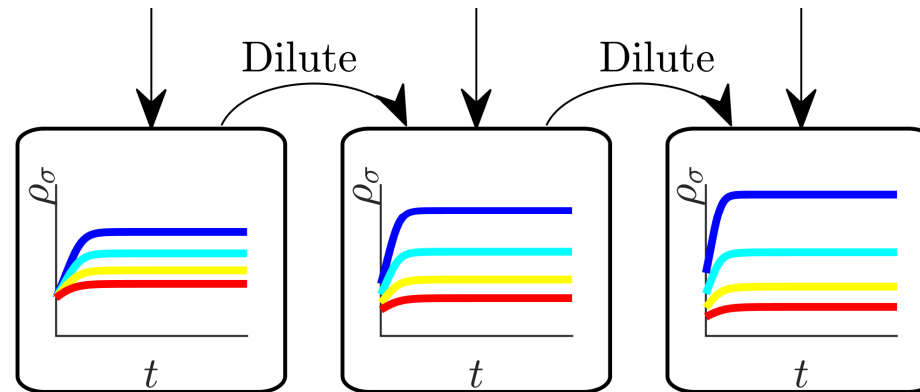
# "Seasonal" ecosystem (serial dilution)



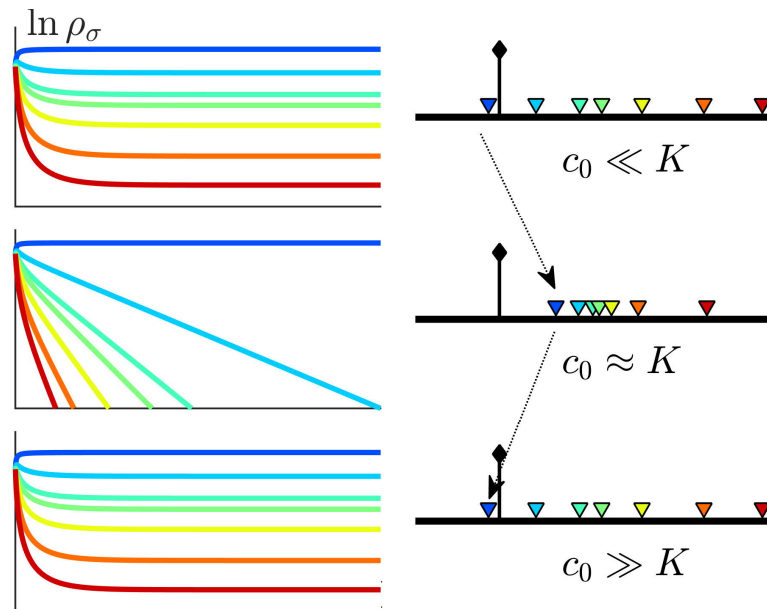
# "Seasonal" ecosystem (serial dilution)



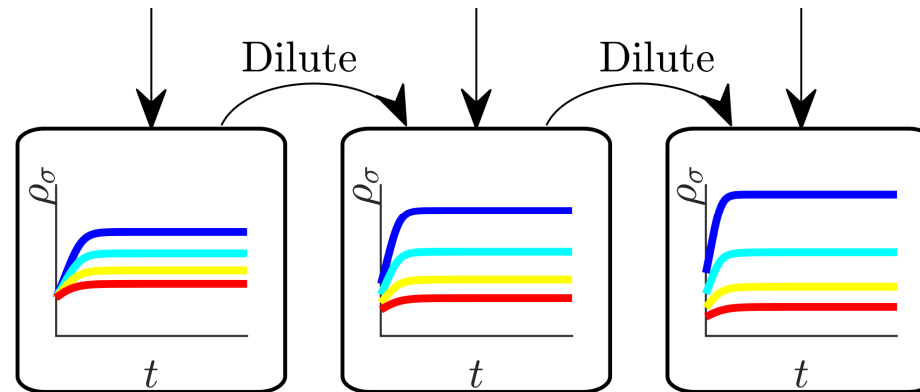
# "Seasonal" ecosystem (serial dilution)



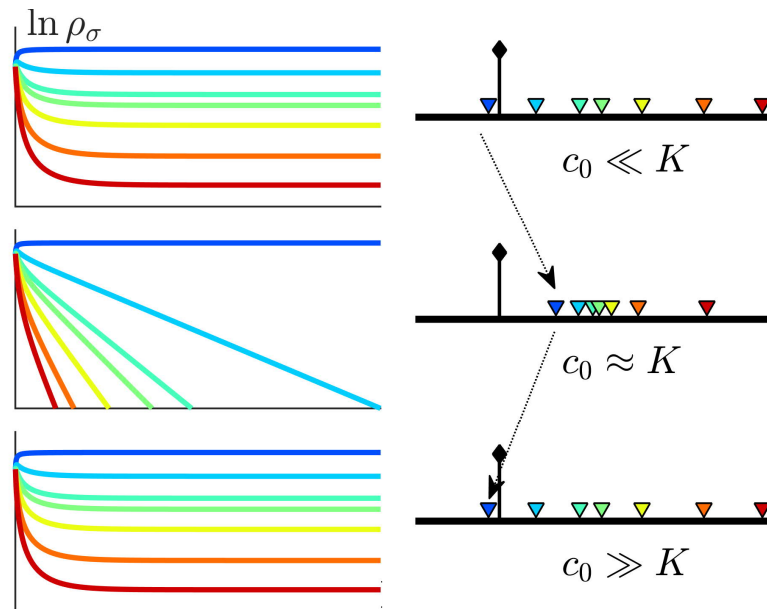
"Early-bird"  
effect



# "Seasonal" ecosystem (serial dilution)



"Early-bird"  
effect



# Summary

- Features of model that allow for coexistence:
  - Organisms take part in shaping their environment.
  - All species are subject to the same trade-offs.
- Similarities with natural ecosystems:
  - Keystone species
  - Species' abundance patterns replicate neutral theory
- Beyond the chemostat:
  - Spatial structure
  - "Seasonal" ecosystem



Center for the Physics  
of Biological Function

Thank you!

Posfai, Taillefumier, & NSW, Phys Rev Lett (2017)

Weiner, Posfai, & NSW, PNAS (2019)

Erez, Lopez, Weiner, Meir, & NSW, eLife (2020)