Disordered dynamics & complexity of gut microbial communities

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Chaire Modélisation Mathématique et Biodiversité

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Outline

- High-dimensional theoretical ecology: Generalized Lotka-Volterra model
- Random interaction network
- Connections with glassy-like phases and slow-relaxation dynamics
- *Proof of concept* for the applicability to human microbiomes
- Effect of spatial correlations: meta-community approach.
- Conclusions & Perspectives.

Open questions in theoretical ecology

- How does **diversity** affect the evolution of the other species?
- **Response** to external (pulse or probe) **perturbations**?
- **Multiple-attractor regime** likely for the same ecosystem?
- Are **chaotic dynamics** and **cooperative pattern formation** observed and easy to describe?
- **Rare events, cascade of extinctions and tipping points**: how to capture heavy-tailed distributions?

"Diversity - stability debate" (*McCann, Nature (2000)).
What is diversity? Shannon index, species richness?

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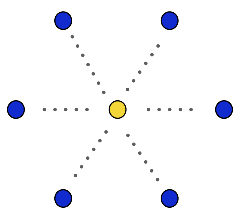
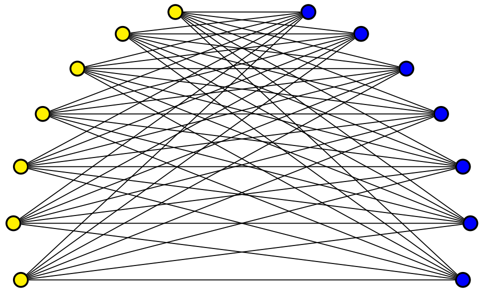
From a few to many interacting components



STATISTICAL MECHANICS



I) Generalized Lokta-Volterra model

The random Lotka-Volterra model for diverse-rich ecosystems

Dynamical equations for the relative species abundances $N_i \geq 0$, with $i = 1, ..., S$

$$\frac{dN_i}{dt} = -N_i \left[V_i'(N_i) + \sum_{j(j \neq i)} \alpha_{ij} N_j \right] + \underbrace{\sqrt{N_i}\eta_i(t)}_{\text{noise}} + \lambda_i$$

immigration rate

$$V_i(N_i) = -\rho_i \left(K_i N_i - \frac{N_i^2}{2} \right)$$

$\rho_i = r_i / K_i$ (growth rate/carrying capacity)

Well-mixed community (no-space dependence)

Demographic fluctuations modelled by Gaussian white noise with $\langle \eta_i(t) \rangle = 0$ and $\langle \eta_i(t) \eta_j(t') \rangle = 2T\delta_{ij}\delta(t - t')$

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?

- **Measuring the effective interactions** in diverse-rich ecosystems: (**open**) **inference problem**.
- **How do correlations among random coefficients affect the species abundance distribution?**

Complex behavior described by random interactions with $\langle \alpha_{ij} \rangle = \mu / S$, $\langle \alpha_{ij}^2 \rangle_c = \sigma^2 / S$, covariance $\langle \alpha_{ij}\alpha_{ji} \rangle_c = \gamma \langle \alpha_{ij}^2 \rangle_c$.

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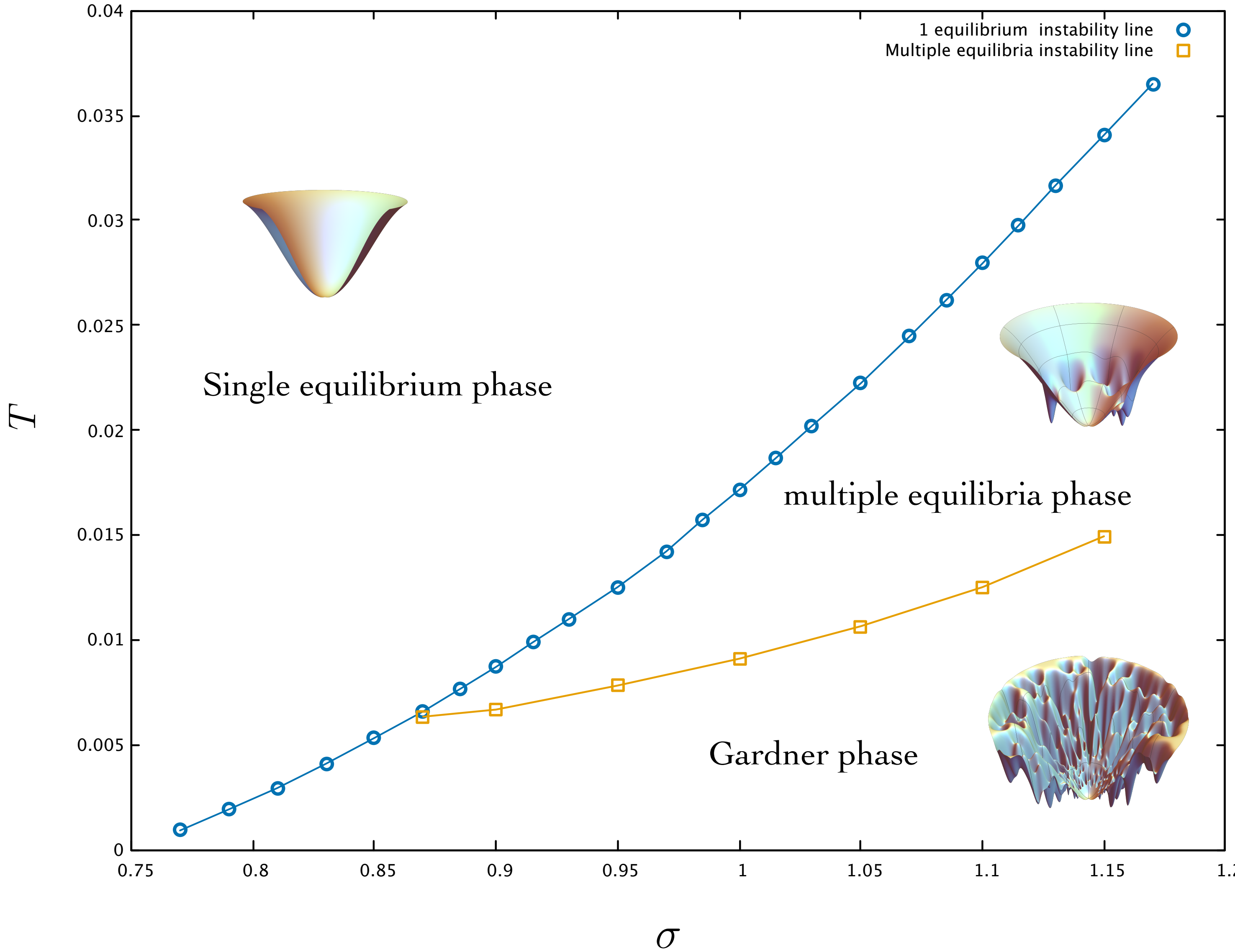
Phase diagram of the random LV with demographic fluctuations

Goal: characterizing emergent collective behaviours in terms of ordered/disordered phases.



- **No sensitive dependence** on the average interaction parameter.

- Exponential number of locally stable states

$$\Sigma(f) \equiv \lim_{S\to\infty} \frac{1}{S} \overline{\log \mathcal{N}(f)} \dashrightarrow \mathcal{N}_{\rm eq} \sim \exp S$$

* Stability landscape:
  Beisner et al., Front Ecol. Environ. (2003);
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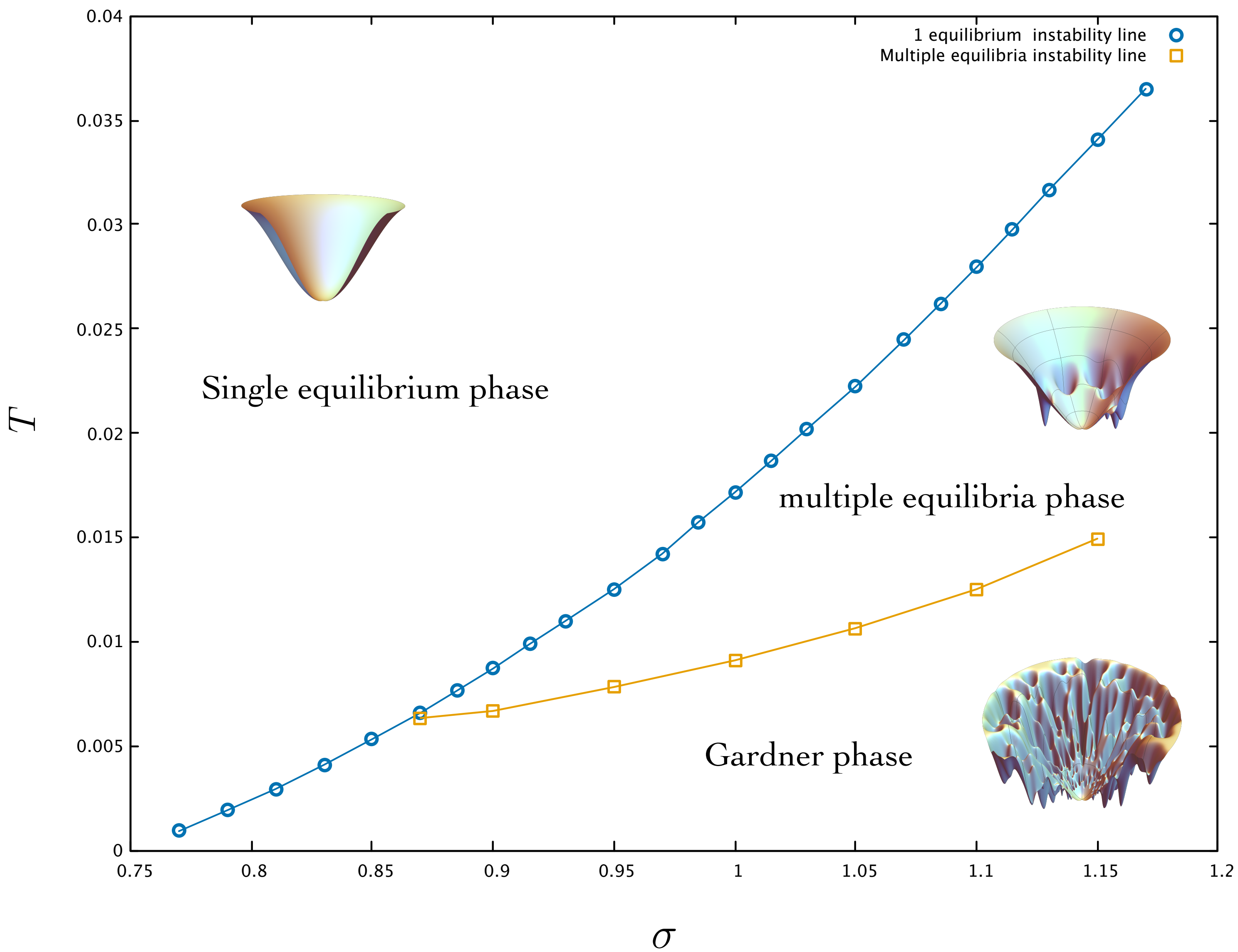

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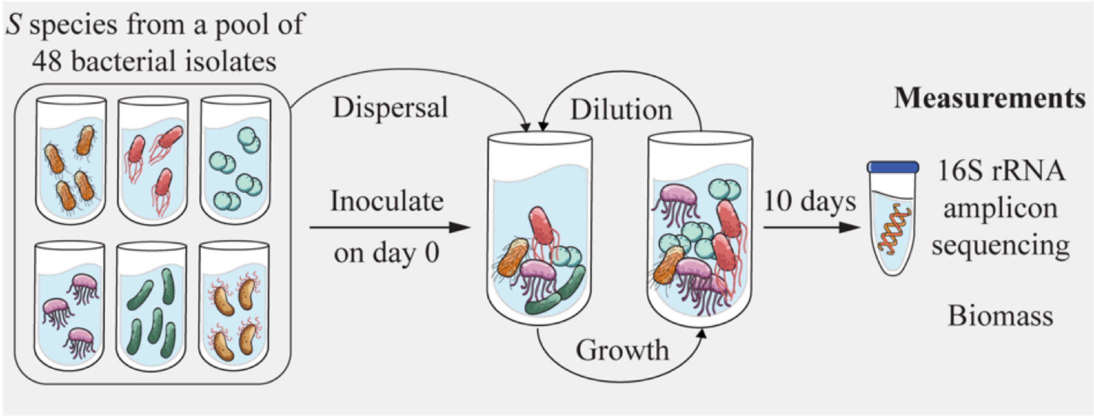

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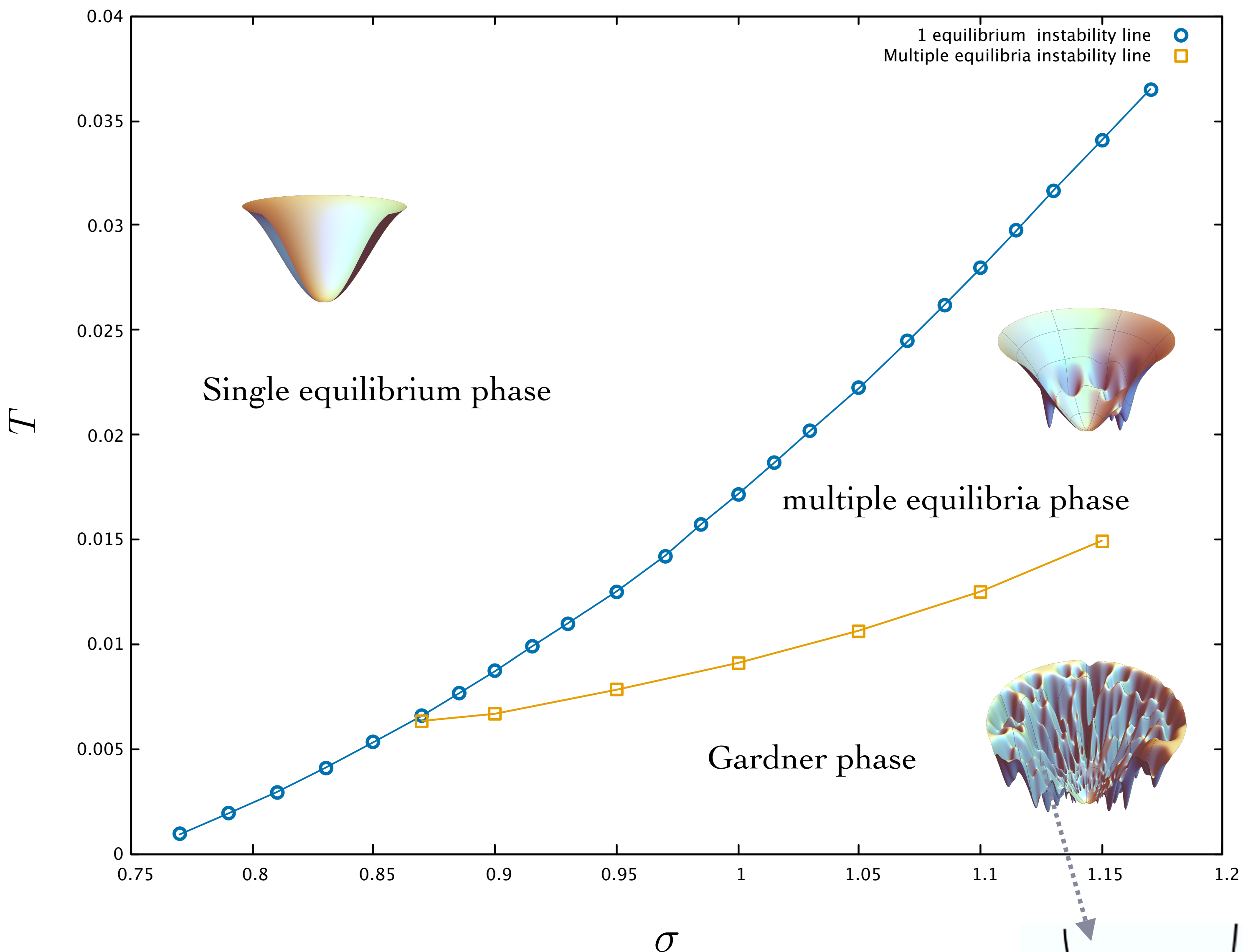

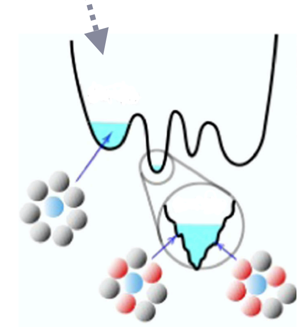

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- At very low demographic noise a **marginally stable amorphous phase:** a Gardner phase.

A. Altieri, F. Roy C. Cammarota, G. Biroli, Phys. Rev. Lett. 126, 258301 (2021)

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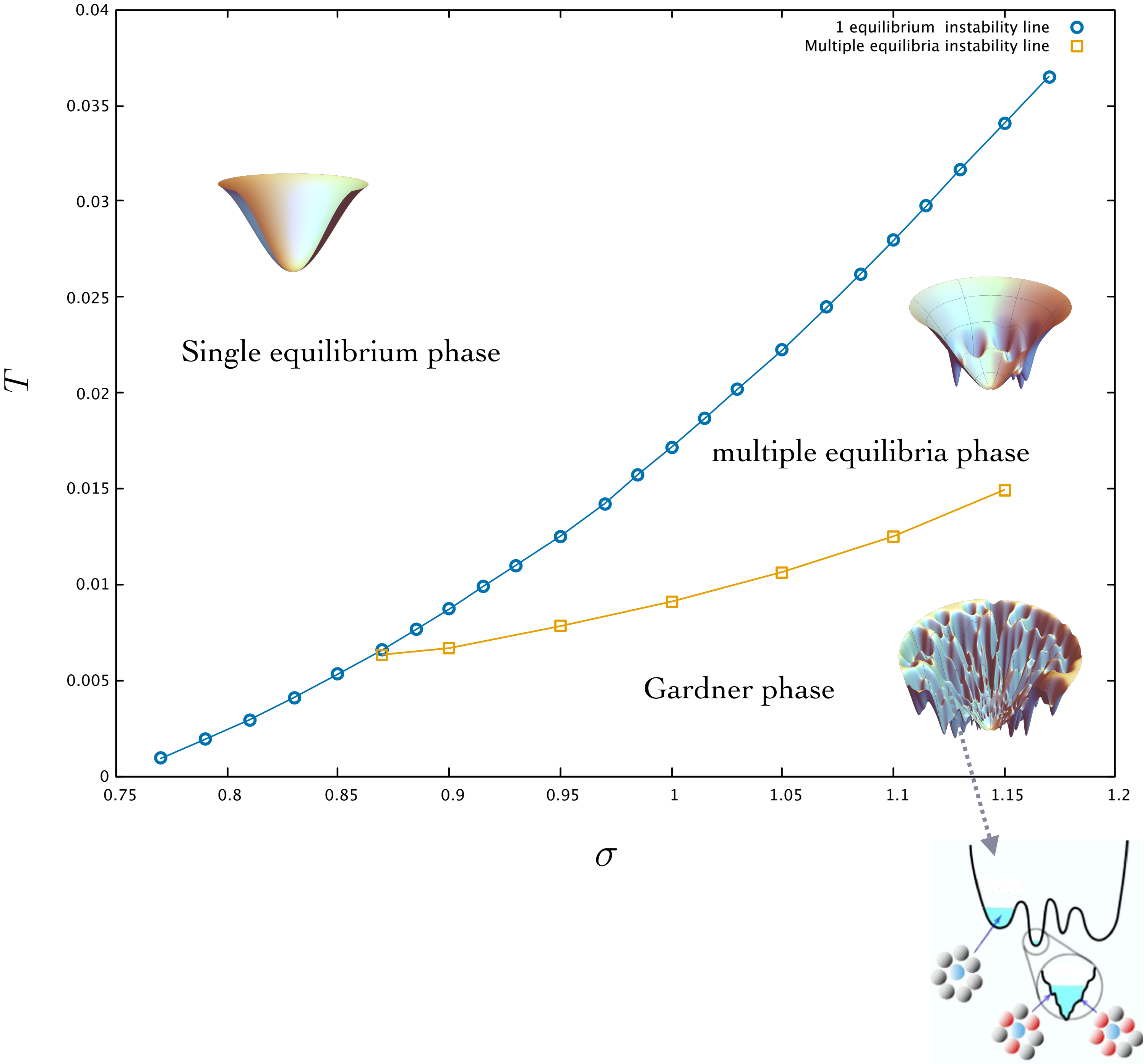

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? Effect of introducing **non-symmetric interactions/non-conservative forces**?

II) What about the dynamics?

DMFT: Single species self-consistent stochastic process

1) **Identify the relevant degrees of freedom and treat the rest of the system as a bath.**

2) **The bath is statistically equivalent to singling-out some degrees of freedom.**

Many-body problem replaced by a self-consistent stochastic process for a single degree of freedom.

$$\dot{N} = N\left\{1 - N - \mu\langle N(t)\rangle - \sigma\eta(t) + \gamma\sigma^2 \int_0^t ds\ \langle\chi(t,s)\rangle N(s) + H(t)\right\}$$

The effective noise becomes coloured (accounting for the interaction with the rest of the system).

$$\mathbb{E}[N(t)] = h(t) \qquad \text{Mean abundance}$$

$$\mathbb{E}[N(t)N(s)] = C(t,s) \qquad \text{Correlation function}$$

$$\mathbb{E}\left[\frac{\delta N(t)}{\delta H(s)}\right]_{H=0} = \chi(t,s) \qquad \text{Response function}$$

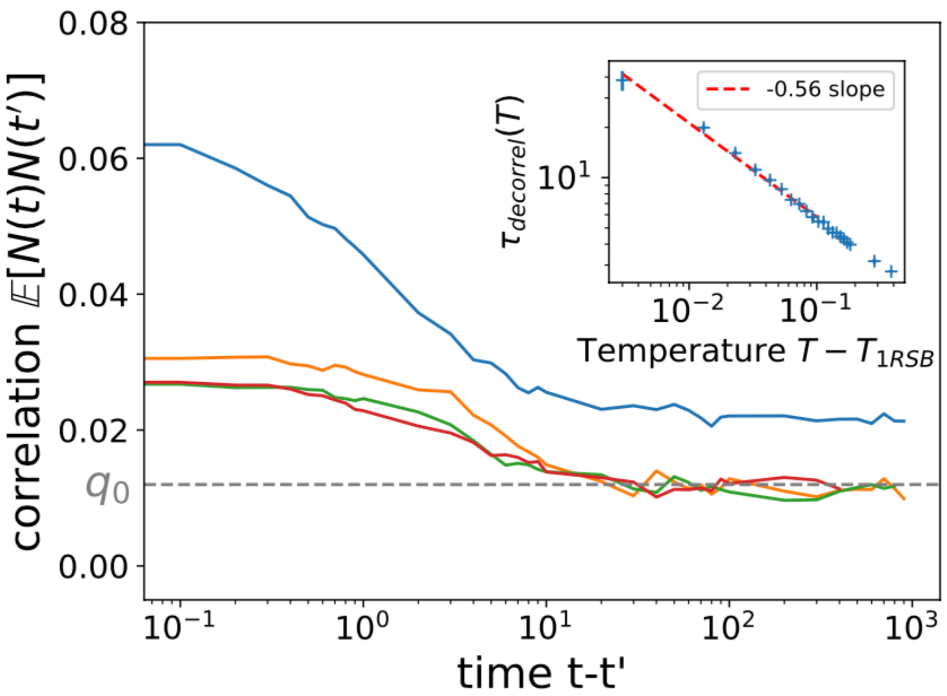
Dynamical correlation functions

- Single equilibrium phase

$$\mathbb{E}[N(t)N(t')] = \frac{1}{SN_{sample}} \sum_{i=1}^{S} \sum_{r=1}^{N_{sample}} N_i^r(t) N_i^r(t')$$

$$\forall t \geq t' > t_{wait} \quad \mathbb{E}[N(t)N(t')] = C(t,t') \simeq C(t-t')$$

Time translationally invariant (TTI) regime



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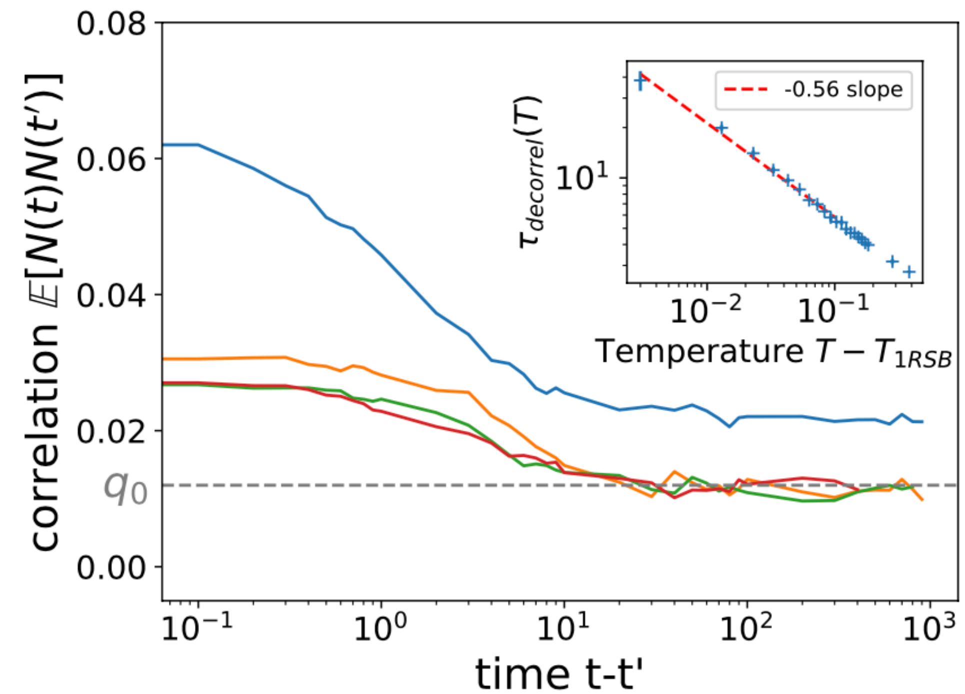


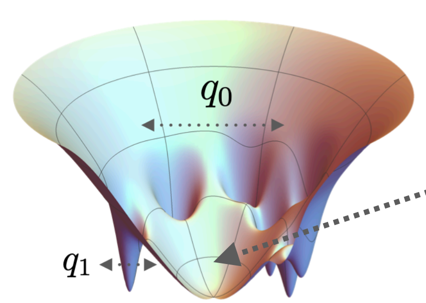
- Multiple equilibria phase

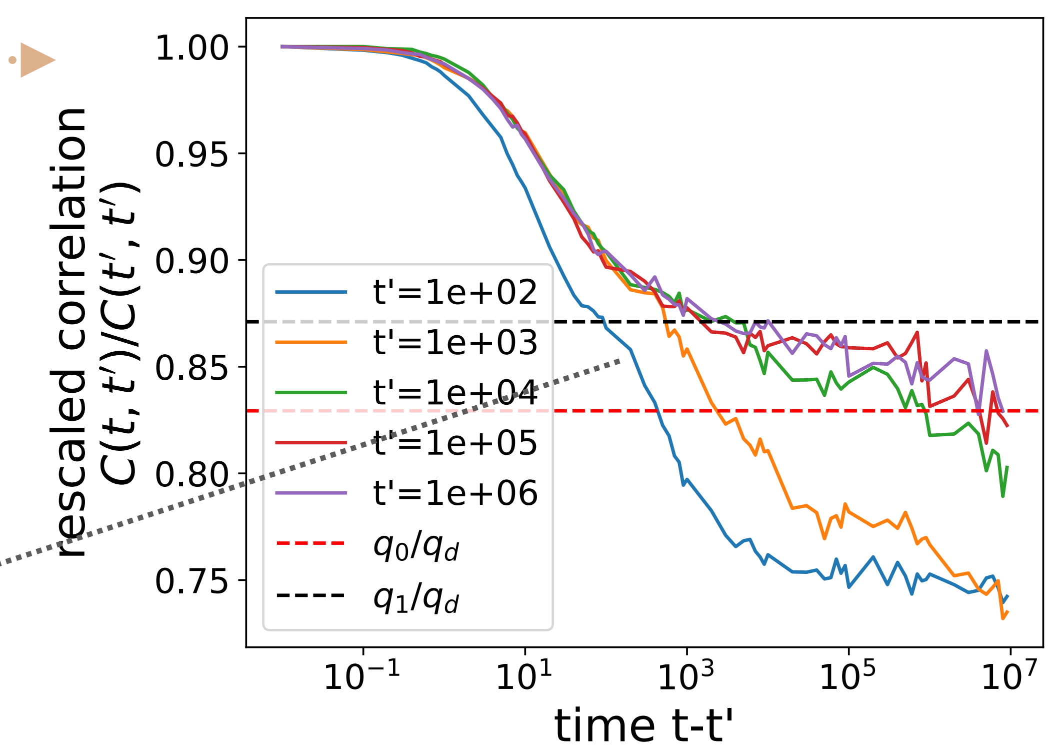
Aging dynamics as in mean-field spin-glasses

L. Cugliandolo, J. Kurchan, PRL (1993)

Dramatic slowing down of the dynamics:

It never sits down in any of these equilibria wandering across the most numerous and marginally stable directions.





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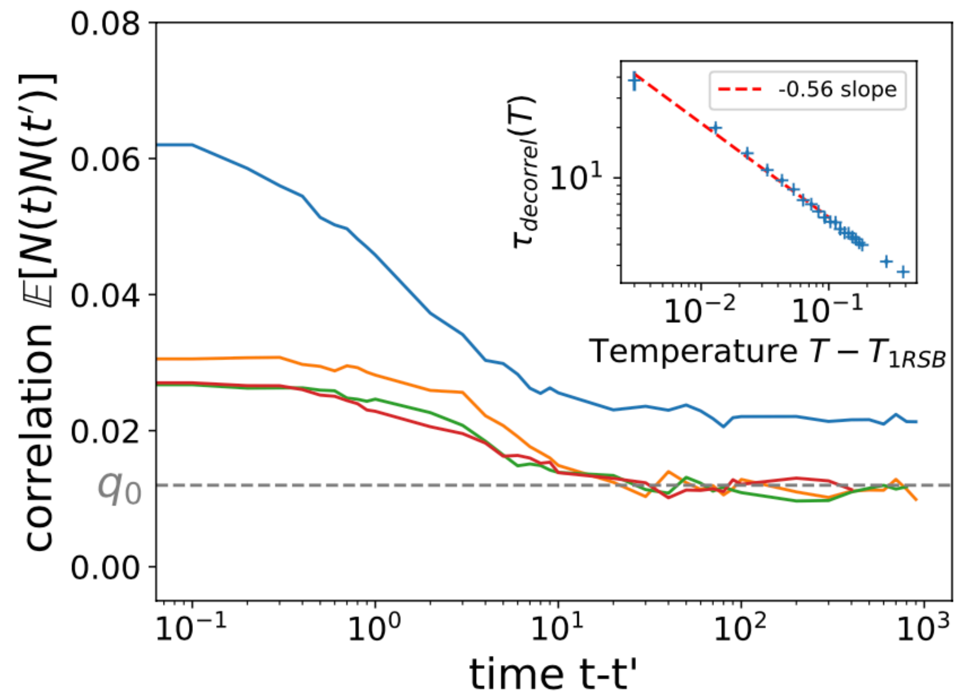

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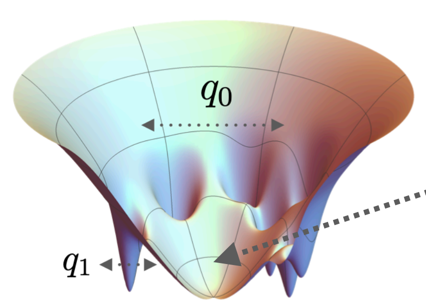
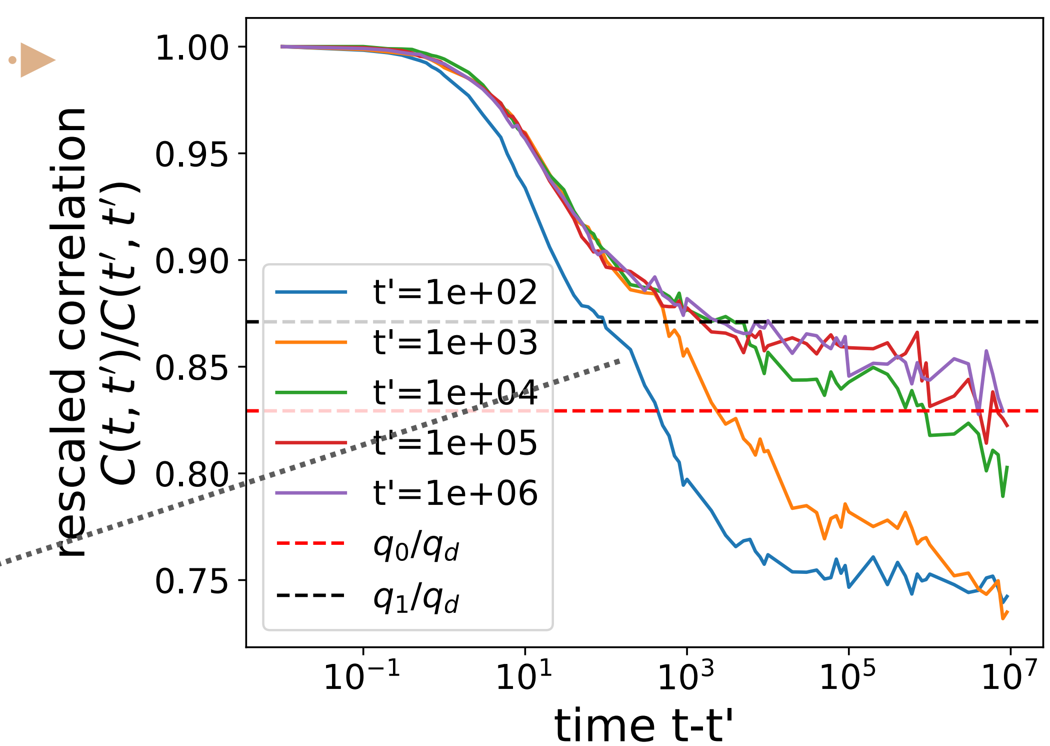
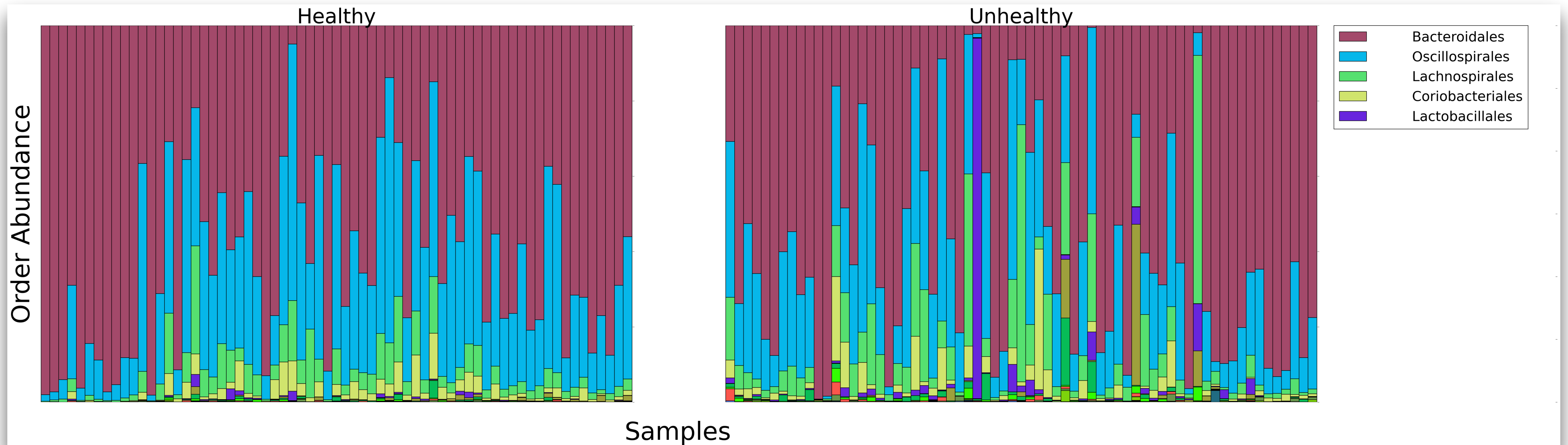




III) Exploring gut microbiome states through GLV model

Taxonomic classification of the gut microbiome

Thanks to sequencing techniques, such as metagenomics, it has been possible to shed light on microbial communities, notably on human and mouse gut composition.



Contrary to most of the studies based on long-time series of individual gut microbiomes, here we stick to single temporal snapshots for the abundances.

Measurable quantities:

mean abundance, inter and intra-state correlations between species abundances

to be compared with theoretically-motivated order parameters (disordered systems approach).

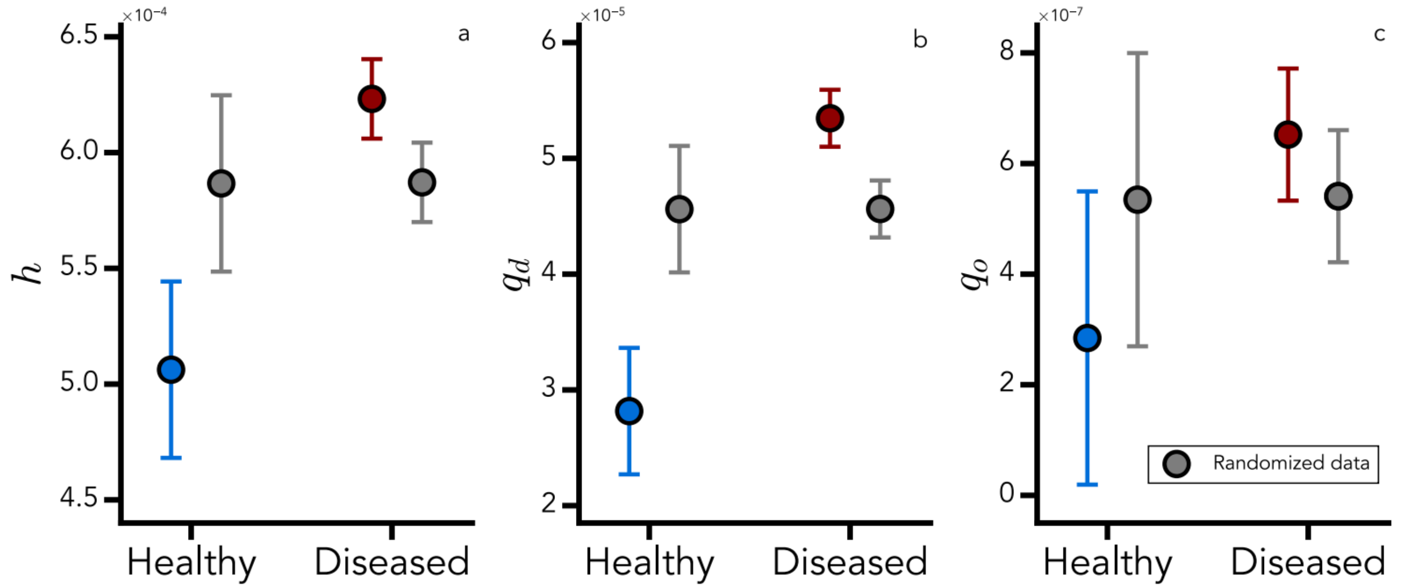
J. Pasqualini, A. Maritan, A. Rinaldo, S. Facchin, E. V. Savarino, **A. Altieri*** & S. Suweis*, arXiv:2406.07465 (2024)

Empirical moment definitions

$$q_d^{Data} = \overline{\langle N^2 \rangle} = \frac{1}{R}\sum_{j=1}^{R}\left(\frac{1}{S}\sum_{i=1}^{S} N_{i,j}^2\right) ,$$

$$q_0^{Data} = \overline{\langle N \rangle^2} = \frac{1}{R}\sum_{j=1}^{R}\left(\frac{1}{S}\sum_{i=1}^{S} N_{i,j}\right)^2 ,$$

$$h^{Data} = \overline{\langle N \rangle} = \frac{1}{R}\sum_{j=1}^{R}\left(\frac{1}{S}\sum_{i=1}^{S} N_{i,j}\right)$$



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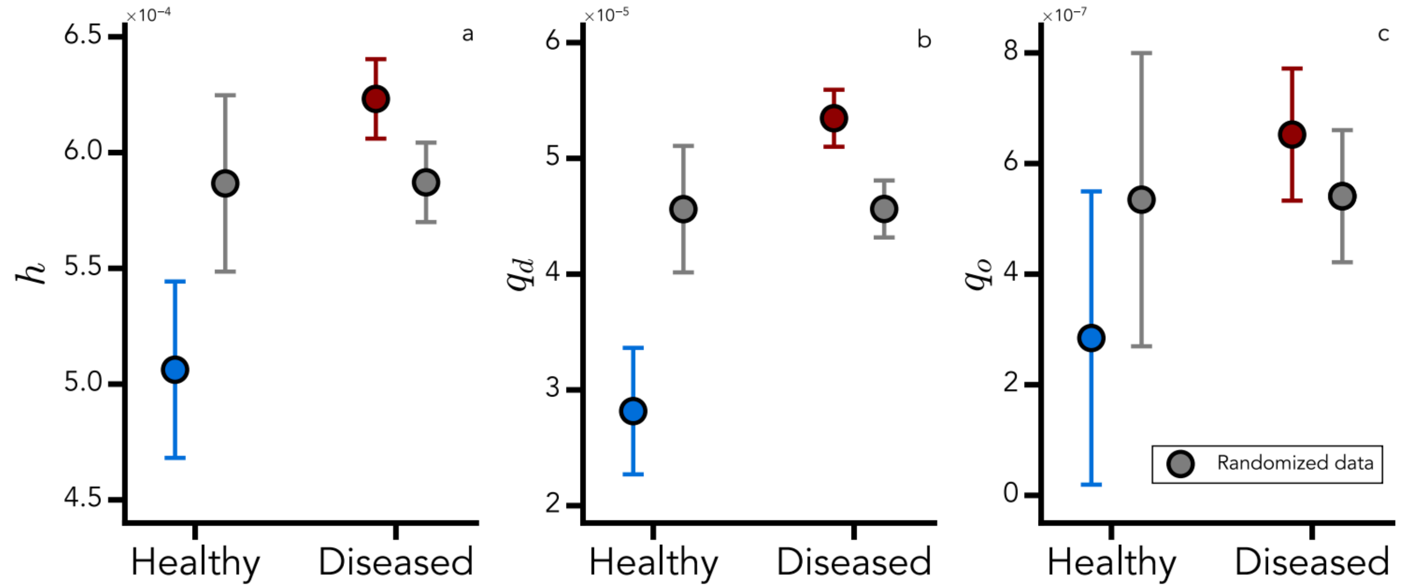


To infer the unknown parameters within a disordered GLV model, let introduce a cost function:

$$\mathcal{C}(\boldsymbol{\theta}|\boldsymbol{\pi}) = \frac{1}{2}\delta H(\boldsymbol{\theta}|\boldsymbol{\pi})^2 + \frac{1}{2}\delta Q_d(\boldsymbol{\theta}|\boldsymbol{\pi})^2 + \frac{1}{2}\delta Q_0^2(\boldsymbol{\theta}|\boldsymbol{\pi}).$$

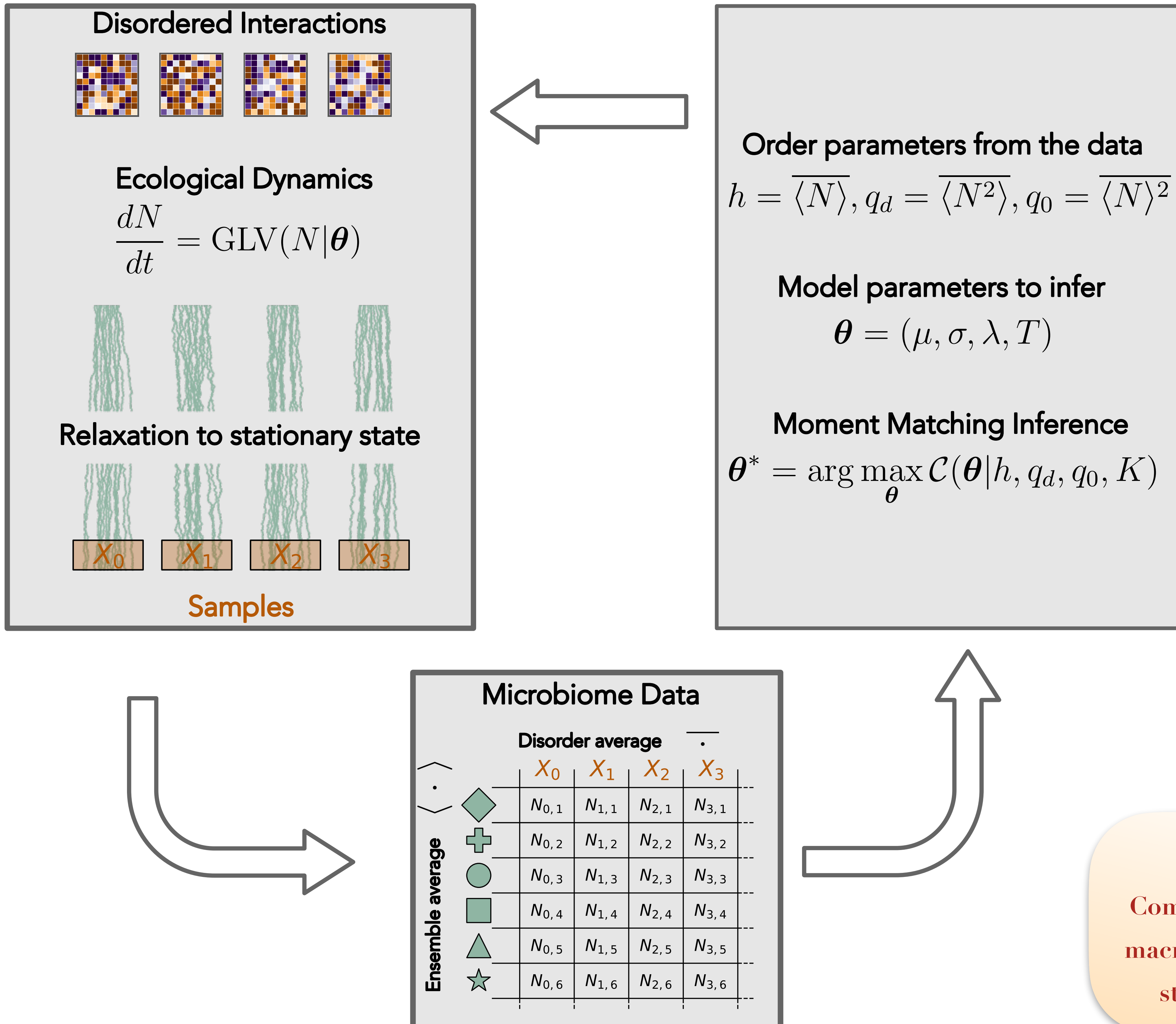
$\boldsymbol{\theta} = \{\mu, \sigma, T, \lambda\}$ Given the information on $\boldsymbol{\pi} = \{h, q_d, q_0, K\}$

interaction parameters, noise and immigration

order parameters and carrying capacity

J. Pasqualini, A. Maritan, A. Rinaldo, S. Facchin, E. V. Savarino, **A. Altieri*** & S. Suweis*, arXiv:2406.07465 (2024)

From the multi-species dynamics to inference



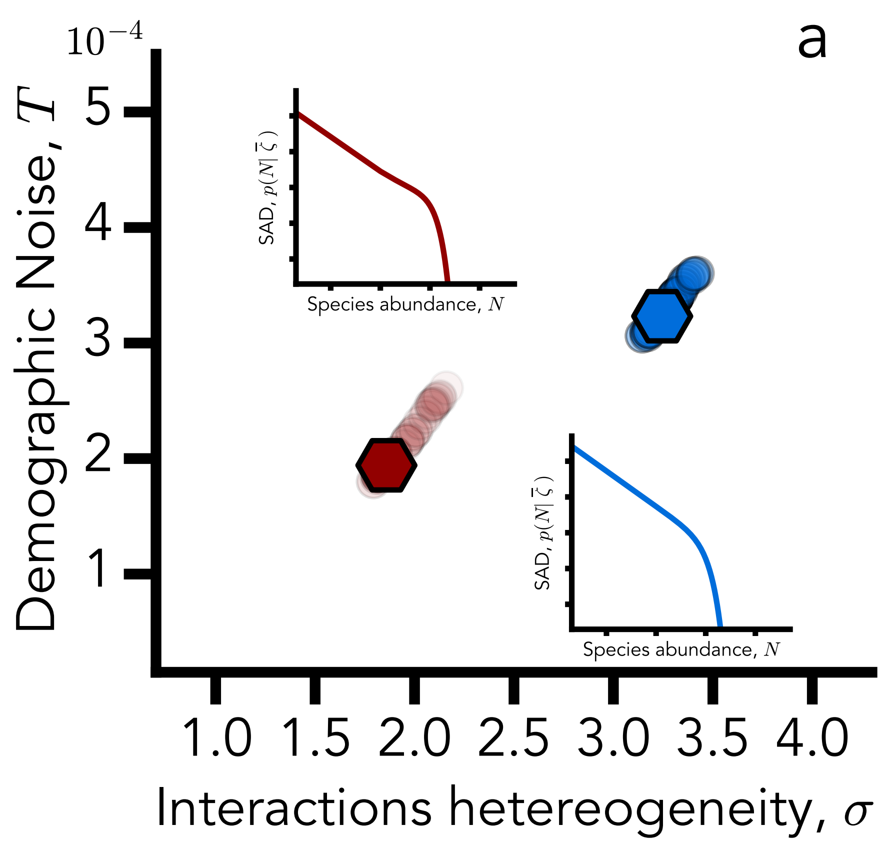
Hp:

Communities in the same macrostate share the same statistical properties

Two distinct noise-driven regimes

Promising outcomes to distinguish healthy and diseased samples, within a statistical physics perspective.

Healthy samples well described by a finite demographic noise picture.
Unhealthy samples — instead — by a low-noise scenario.



Panel a: inferred parameters.
Hexagons correspond to the two solutions with the lowest cost function value.

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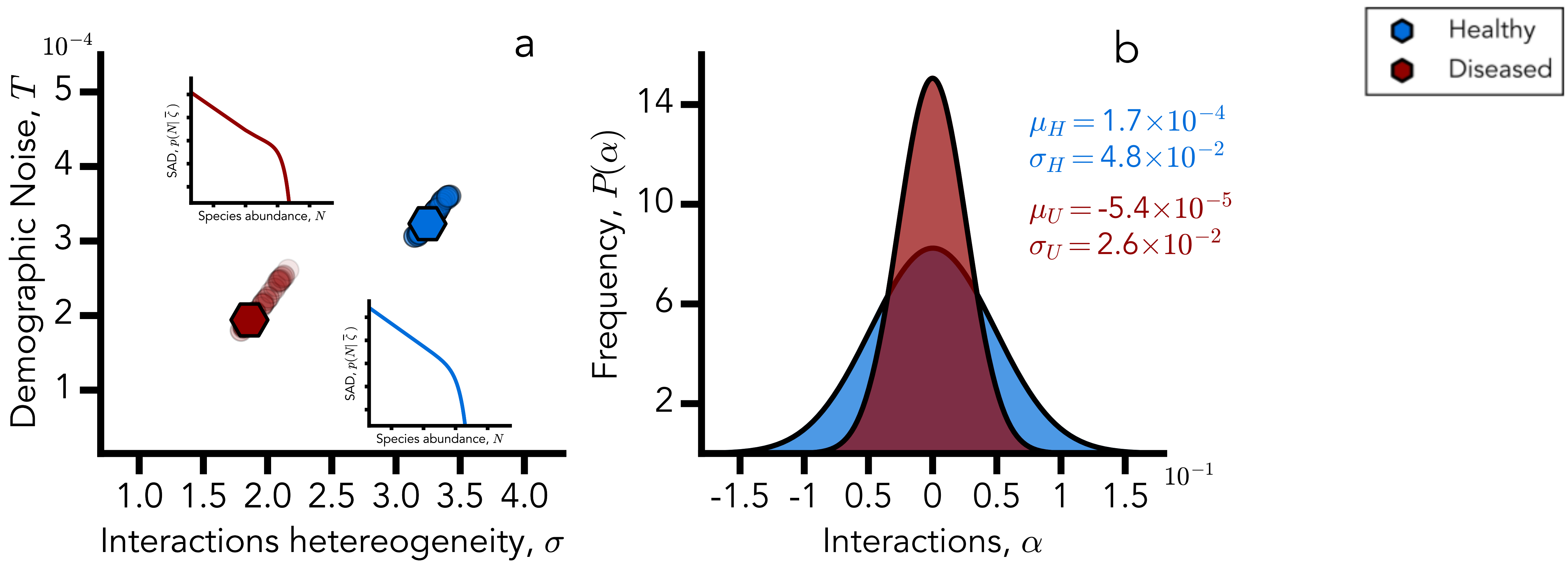

Panel a: inferred parameters.
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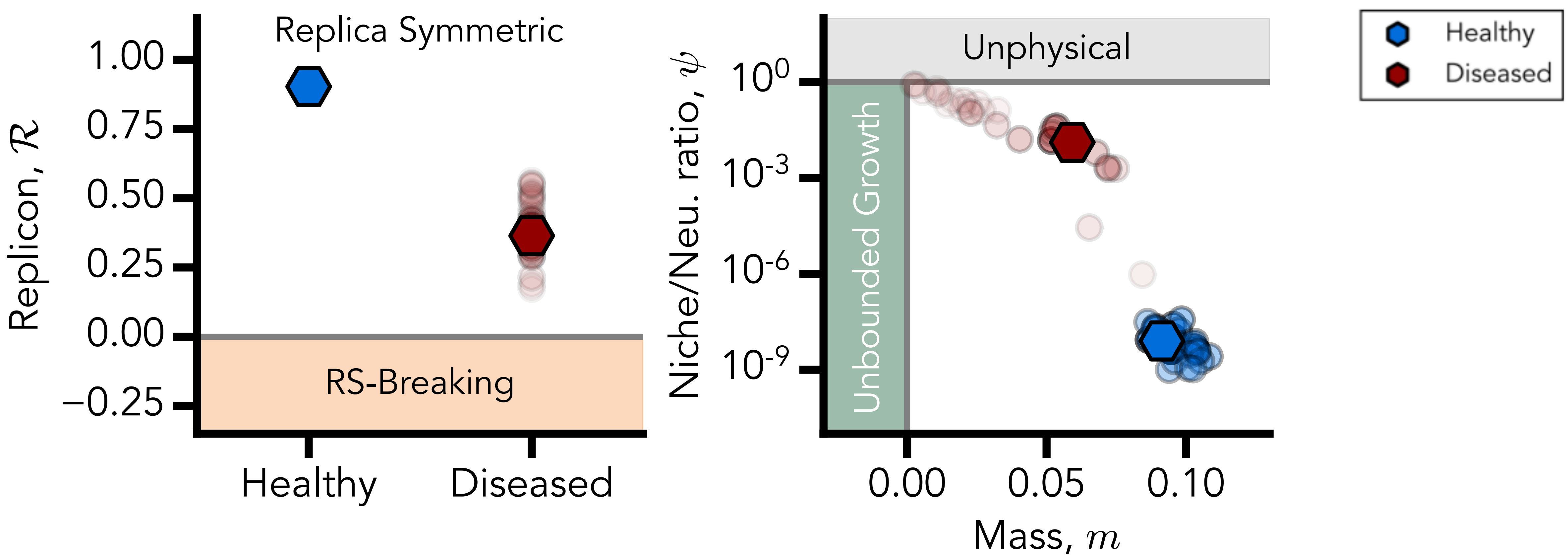
Panel b:
Probability density for healthy (blue) and diseased (red) microbiomes versus interaction strength.

Dysbiosis reduces the heterogeneity of the interactions.

What about stability?

We might look at the condition for stability/marginal stability of the two datasets.

$$\mathcal{R} = (\beta\sigma)^2 \left(1 - \sigma^2 \overline{\langle \left(\frac{\partial N}{\partial \xi}\right)^2 \rangle}\right) = (\beta\sigma)^2 \left(1 - (\beta\sigma)^2 \overline{(\langle N^2 \rangle - \langle N \rangle^2)^2}\right)$$



$$\psi = \mathbb{P}\left[\zeta > \zeta^*\right] + \mathbb{P}\left[\zeta < -\zeta^*\right] = \frac{1}{2}\mathrm{Erfc}\left(\frac{\zeta^* + \bar{\zeta}}{\sqrt{2}\sigma_\zeta}\right) + \frac{1}{2}\mathrm{Erfc}\left(\frac{\zeta^* - \bar{\zeta}}{\sqrt{2}\sigma_\zeta}\right)$$

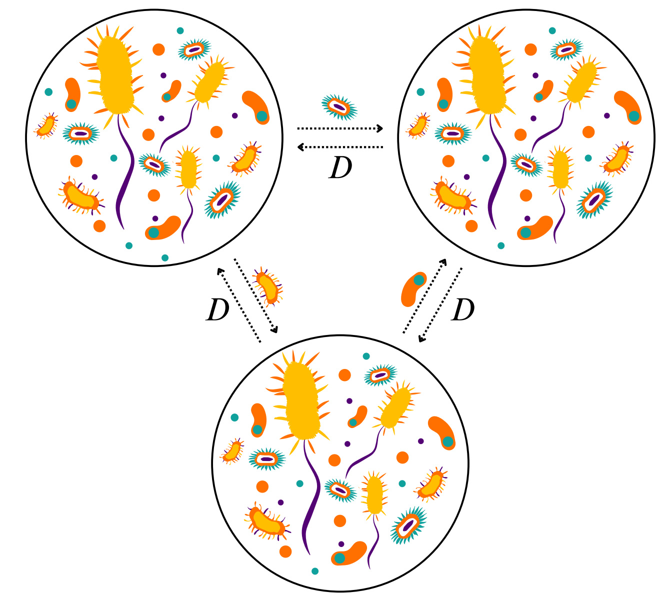
$$\zeta^* = \sqrt{4\frac{m(1-\nu)}{\beta}} \qquad \bar{\zeta} = K - \mu h \qquad \sigma_\zeta = \sqrt{q_0}\sigma$$

How to incorporate spatial dependence?

Metacommunity model with diffusion

Network of ecological communities coupled by (passive) dispersal:

$$\dot{N}_i^u = N_i^u \left(1 - N_i^u - \sum_j \alpha_{ij} N_j^u\right) + \eta_i^u \sqrt{N_i^u} + \underbrace{\frac{D}{L} \sum_v (N_i^v - N_i^u)}_{\text{insurance effect}}$$



$S \to \infty$ Number of species

$L \to \infty$ Number of patches

J. Denk, O. Hallatschek, PNAS 119 (2022)

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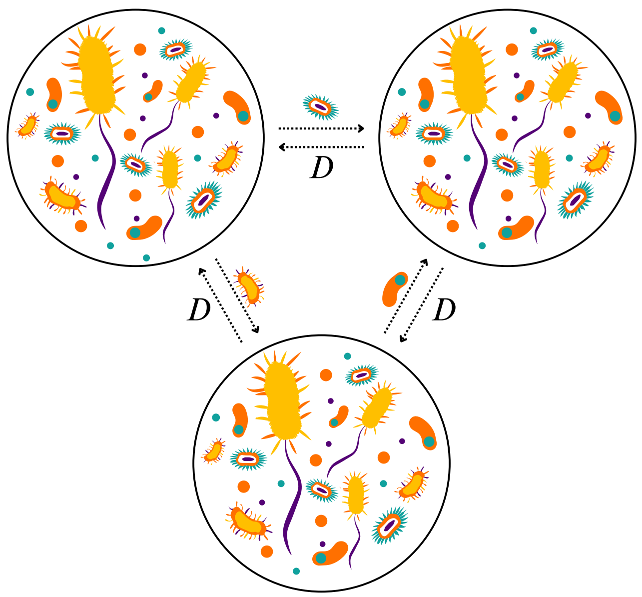
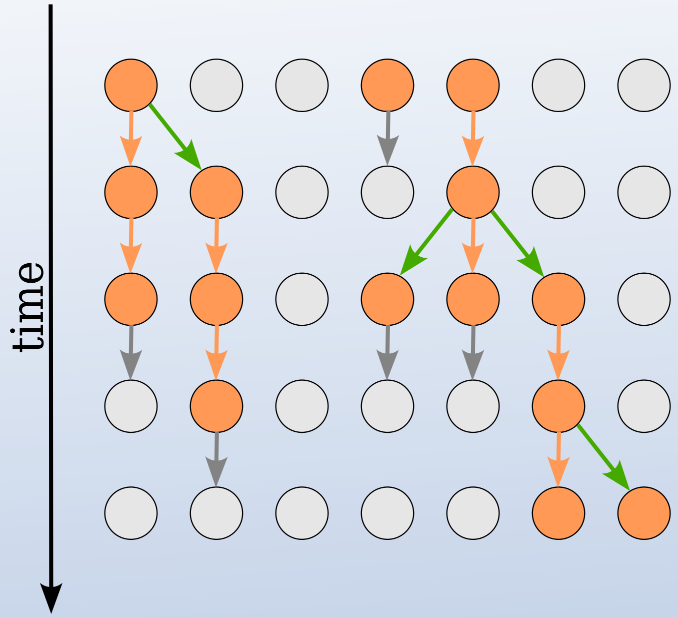


$S \to \infty$ Number of species

$L \to \infty$ Number of patches

? What kind of emergent behaviour without interactions?

$$\dot{N}^u = N^u (1 - N^u) + \eta^u \sqrt{N^u} + \frac{D}{L} \sum_v (N^v - N^u)$$



2nd-order phase transition belonging to **Directed Percolation** universality class.

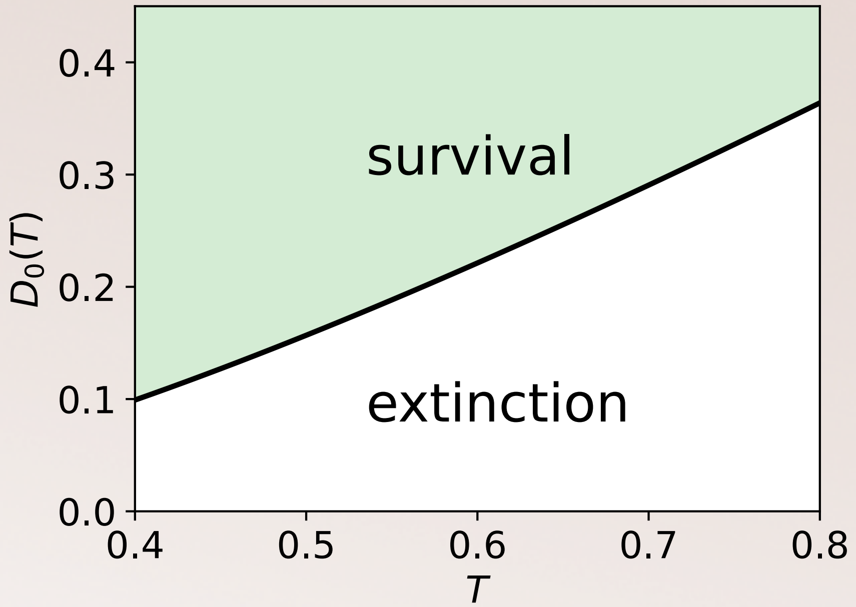
Main Mechanism due to the interplay between migration and death/birth rates.

Directed Percolation transition: active/inactive phases

$$\dot{N}_i^u = N_i^u\left(1 - N_i^u - \cancel{\sum_j \alpha_{ij} N_j^u}\right) + \eta_i^u\sqrt{N_i^u} + \frac{D}{L}\sum_v (N_i^v - N_i^u)$$

Without interactions, each equation corresponds to a Directed Percolation process.

- Self-sustained (active) phase, driven by finite migration;
- Extinction (inactive) phase, due to small or zero diffusion.



? What happens with (strictly) competitive couplings? $\alpha_{ij} = \mu > 0$ $\longrightarrow$ **No qualitative change**

Upon increasing the # of species and heterogeneity: many (**coupled**) **Directed Percolation processes**

OPEN PROBLEM!

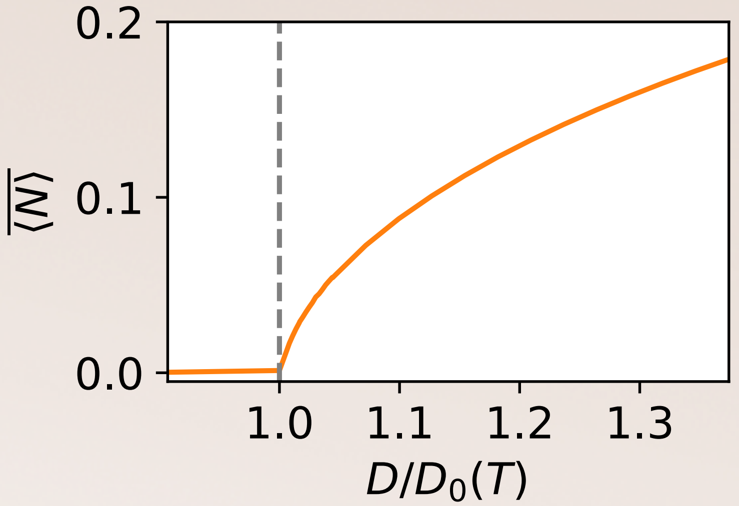
Dynamical Mean-Field Theory: mapping to a single DP process

$$\dot{N} = N\left[1 - N - \mu h - \sigma\xi(t) + \sigma^2\gamma\left(\int_0^t R_d(t-s)N(s)ds + \int_0^t R_0(t-s)N^*(s)ds\right)\right] +$$

coloured noise

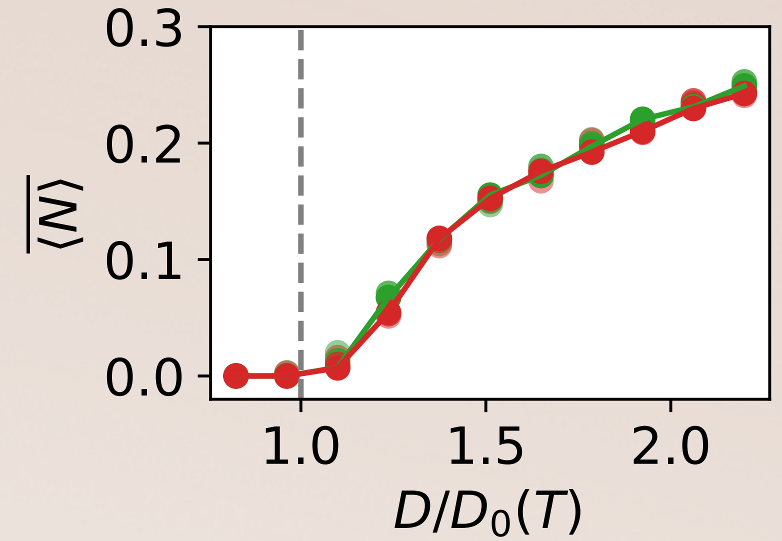
memory kernel

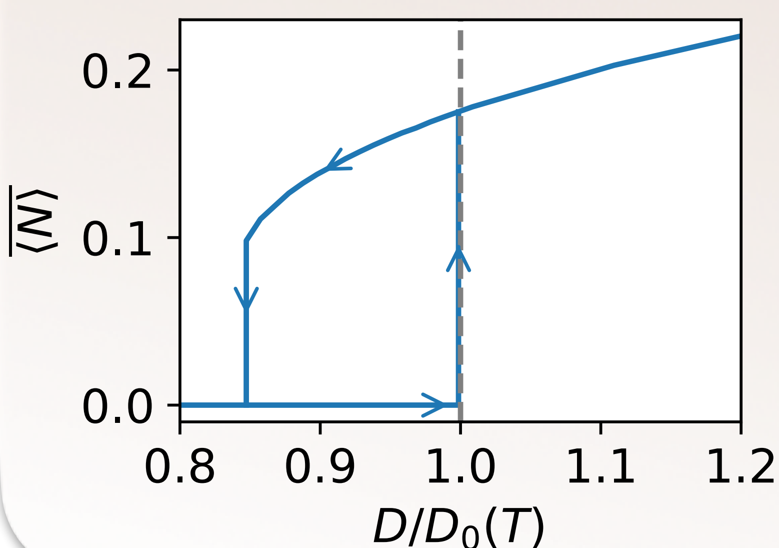
$$+\eta(t)\sqrt{N} + D(N^* - N)$$



HIGH NOISE

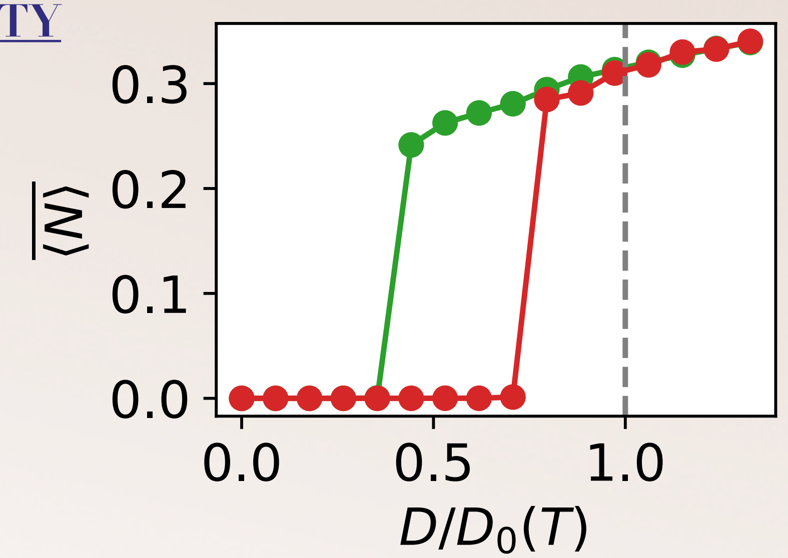
- Continuous transition
- Irrelevant quenched disorder



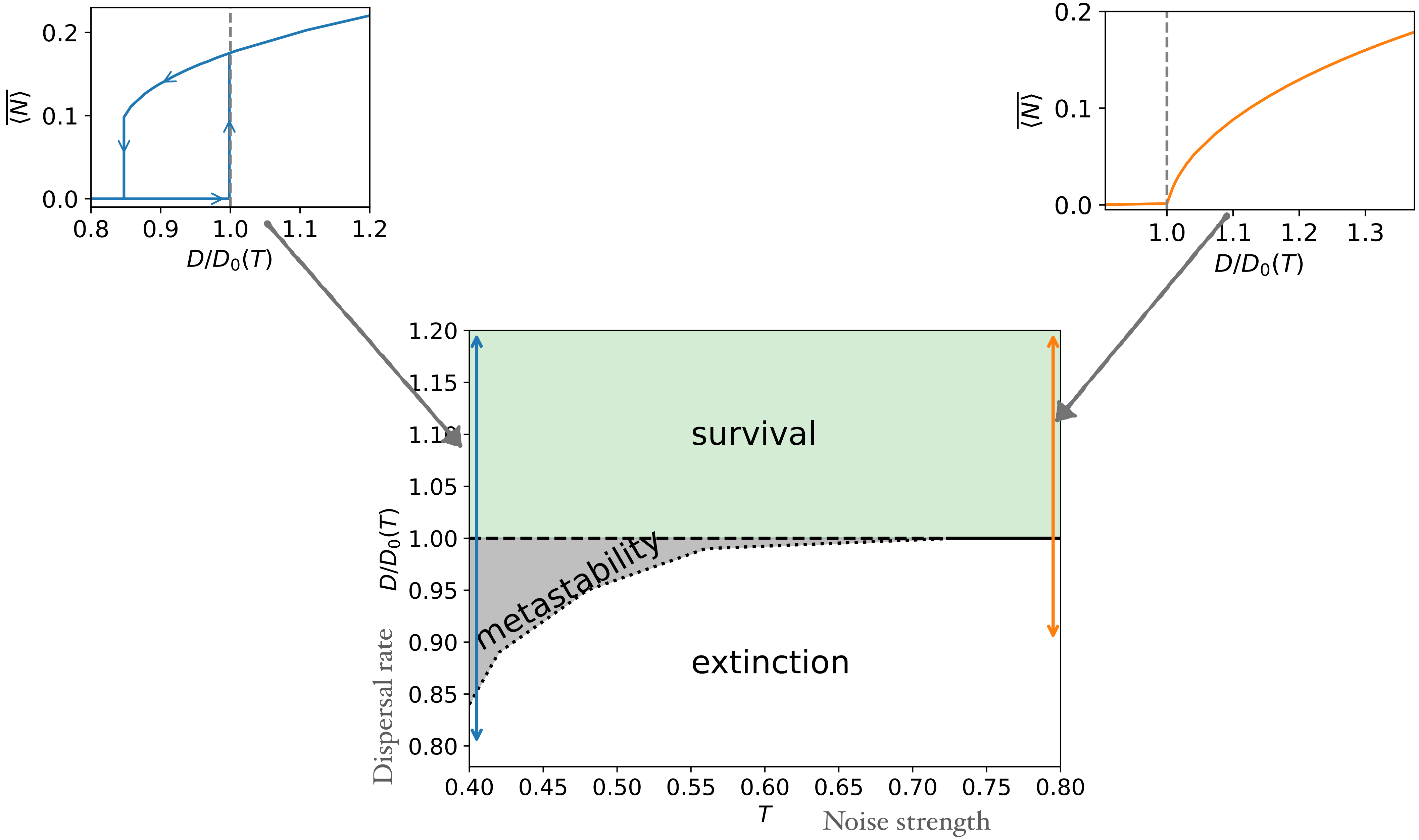


LOW NOISE + HETEROGENEITY

- Discontinuous transition
- Hysteresis/Bistability
- Survival due to disorder



Full phase diagrams in the heterogeneous case



Constant interactions across patches.

The **continuous line**: continuous phase transition (ordinary **DP**).

Dashed lines: the limits of the **metastability** region, beyond which discontinuous behaviour.

Conclusions

- Well-mixed Generalized Lotka-Volterra model incorporating **demographic noise** and **heterogenous interactions;**

- Detection of three distinct phases: single equilibrium; **multiple equilibria phase; amorphous Gardner phase** (marginally stable). The latter associated with extremely **slow relaxation dynamics**.

- **Data-driven inference protocol** for classifying healthy and inflammatory bowel diseased samples.

- **Metacommunity scenario**: continuous versus discontinuous phase transition (hysteresis and metastability).

Ongoing work @ MSC and future perspectives

- In-depth investigation of multiple equilibria phases for microbial communities (numerics & tailored experiments);

- Analysis of entangled resource-species dynamics with non-logistic functions;

- Multi-layer approaches for spatial models.

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Thank you for your kind attention!