Bacterial swarming: experiments and modelling

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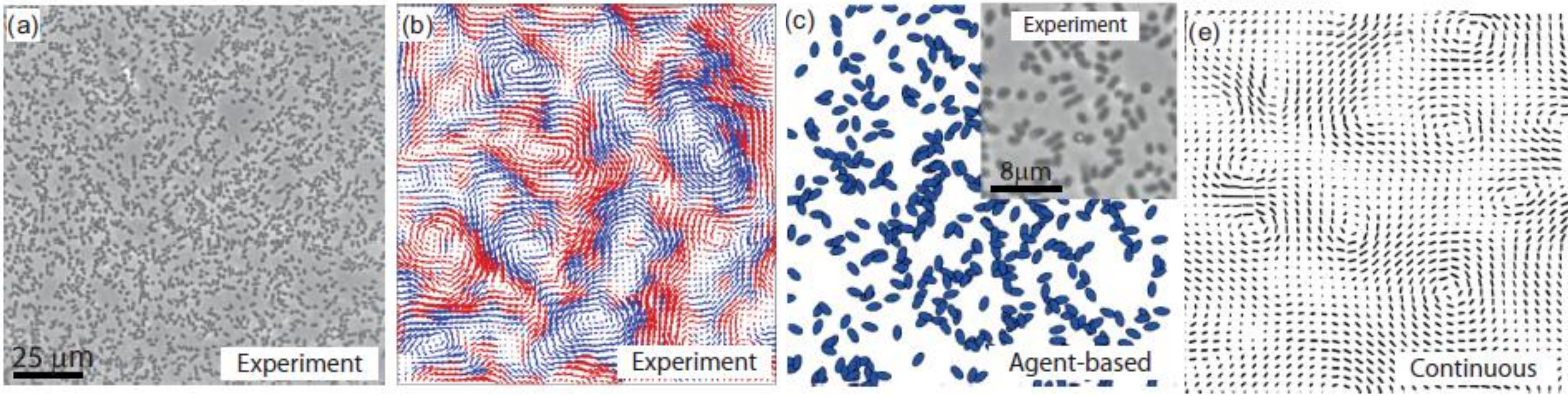
w. Avraham Be'er, BGU



Two sides for bacterial swarming

An example of collective motion in nature

An example of active matter / Self-propelled particles

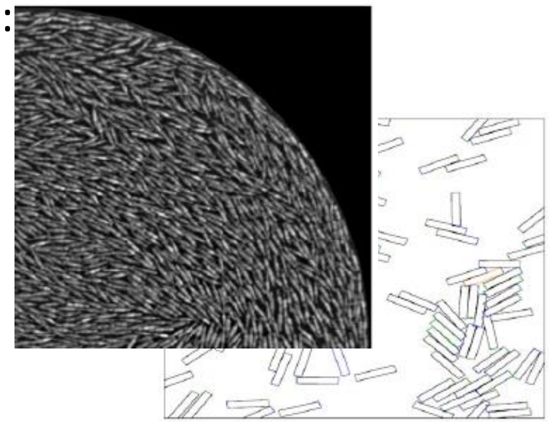
Buhl, 2006
Review: Ariel 2015

Review: Lopez 2012

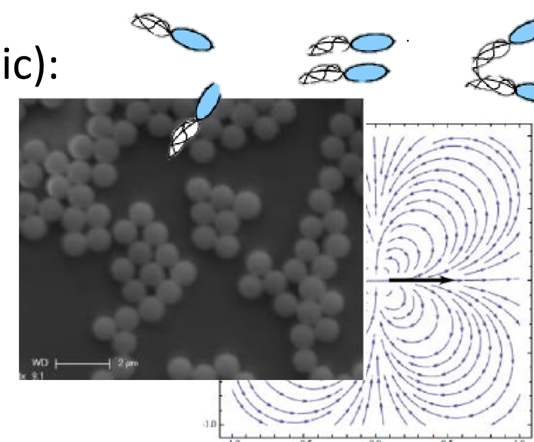
...

Vicsek, Chate

Dry (SPP rods):
Peruani 2006
Narayan 2007



Wet (hydrodynamic):
Zheng 2013
Ryan 2013



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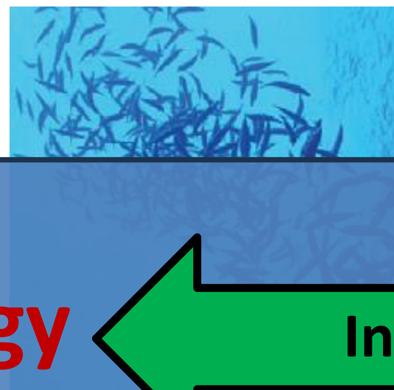

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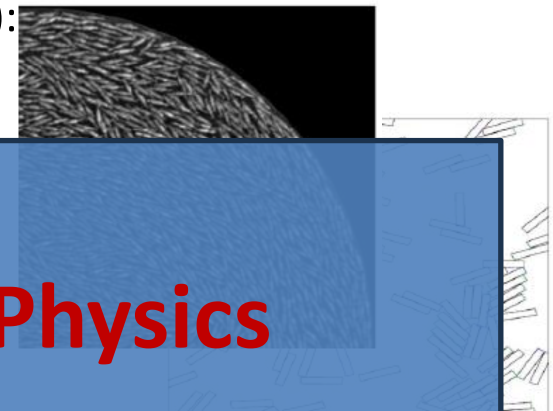

Biology ⟷ **Interaction** ⟷ **Physics**

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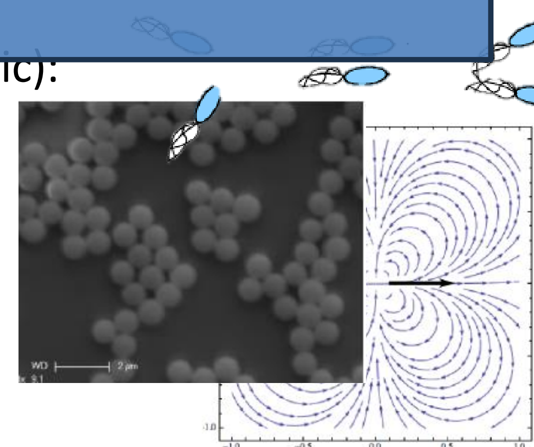

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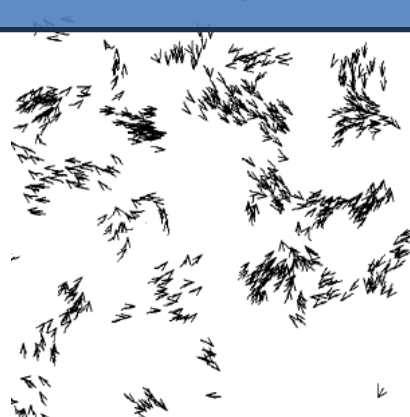
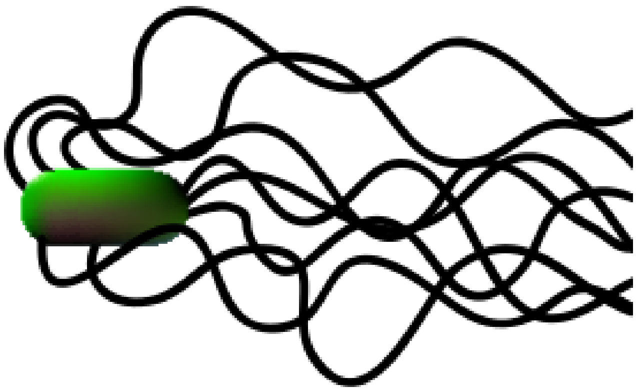


Bacterial swimming

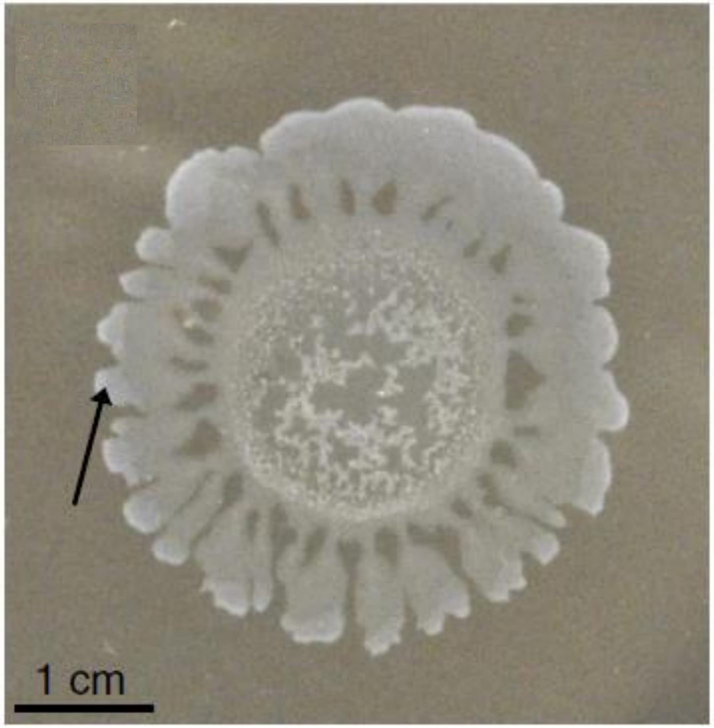


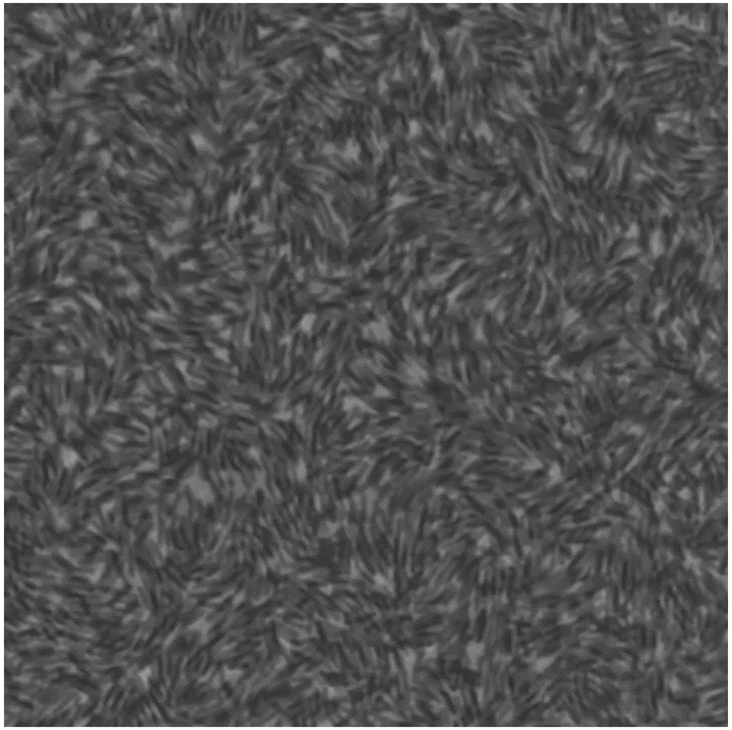
- **Size: a few 1x1x3 µm**
- **Movement using flagella –**
  mechanical motors.
- **Low Reynolds numbers**
- **Run and Tumble**
  Run times have an exponential dist.
  Average run time = 2 secs.
  Tumble: random direction.
- **Chemotaxis: biased random walk**
  Adler ('66): Bacteria adjust the length of runs according to temporal changes in conditions.

Bacterial swarming

Experiments by Avraham Be’er, Ben Gurion University

Bacillus Subtilis

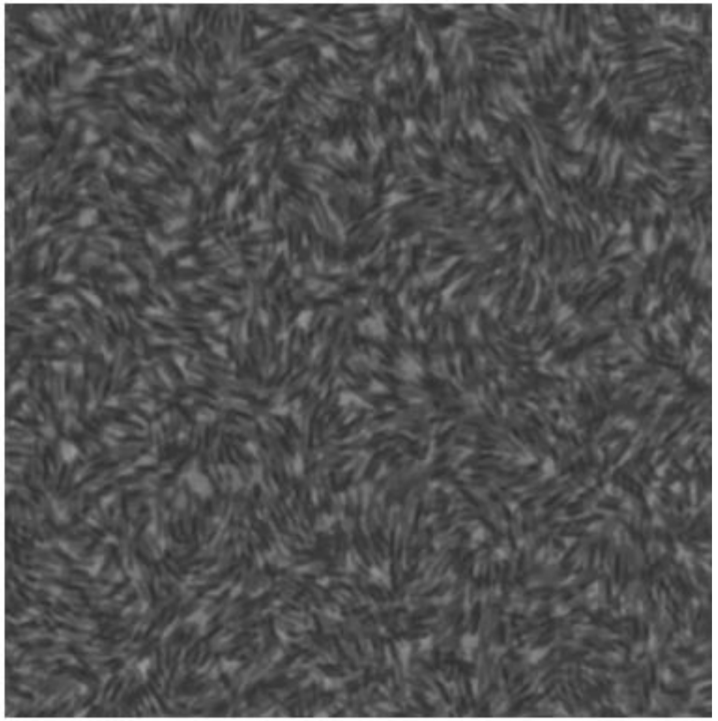




Bacterial swarming

A particular mode of motion

[Kearns 2010]



- Above surfaces - Approximately 2D
- Cells elongate: $\sim 5 \times 1 \times 1\mu\mathrm{m}$.
- Grow extra flagella.
- High density.
- Hydration layer: Surfactants. Highly viscous.
- Chemo-sensors shut down (to some extent) [Harshey 2015].

Higher bacterial conc. $\neq$ higher particle density

Goals

Characterization and quantification

- Collective swarm dynamics

  averages, fluctuations, correlation functions
  topological defects, entropy

- Individuals within a swarm

  random walks

- Phases and Phase transitions

  qualitatively different physical regimes

Understand

- Underlying physics

  particle-particle interactions,
  emergence of collectivity

- Underlying biology

  mutants, coping with stress (e.g., antibiotics)

- Lifestyles and transitions

  biological internal states

- Evolutionary advantages

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Physics ⟷ **Interaction** ⟷ **Biology**

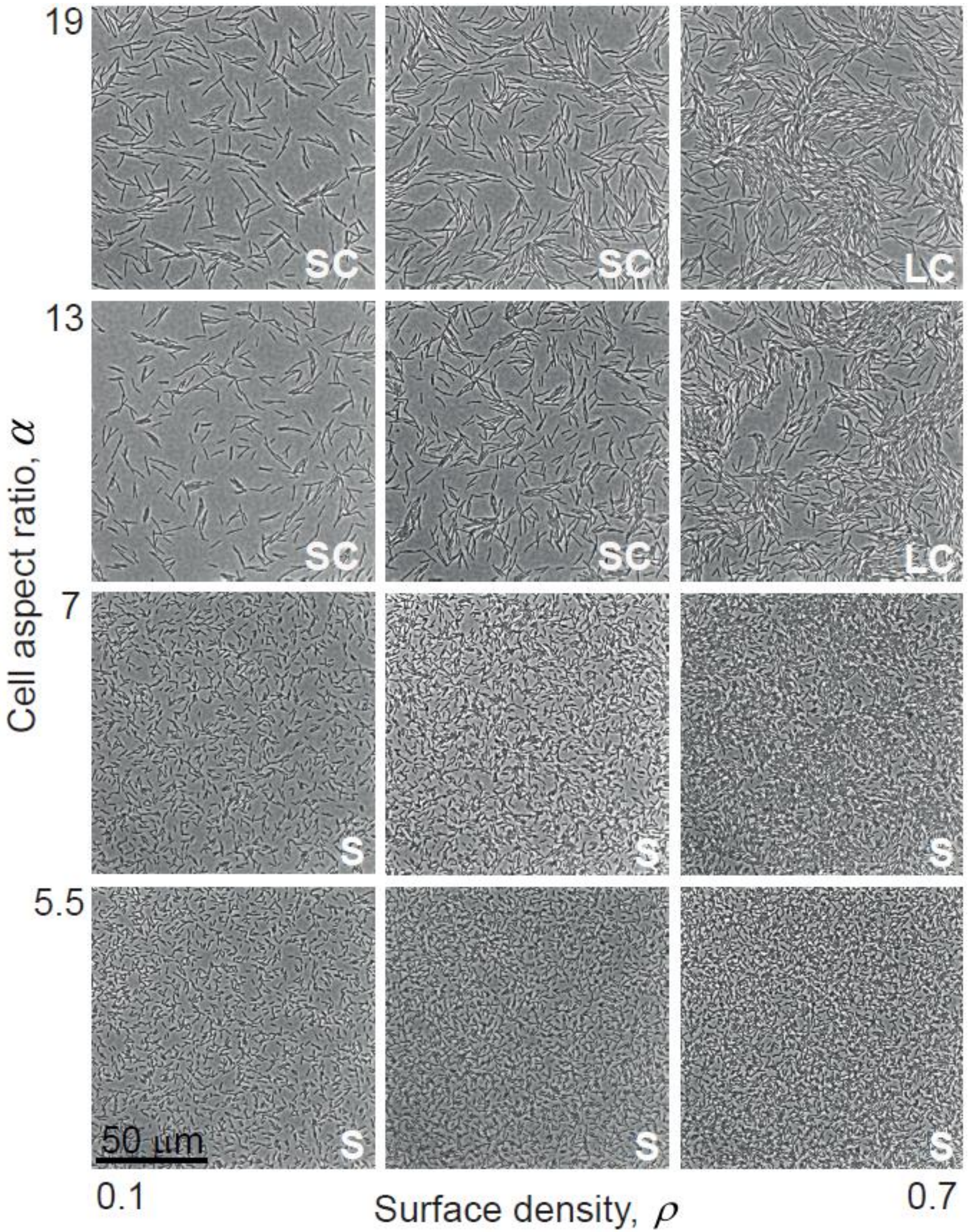
Motivation

Swarming bacteria
(*Bacillus subtilis*)
at different densities
and aspect ratios

Characterize phases

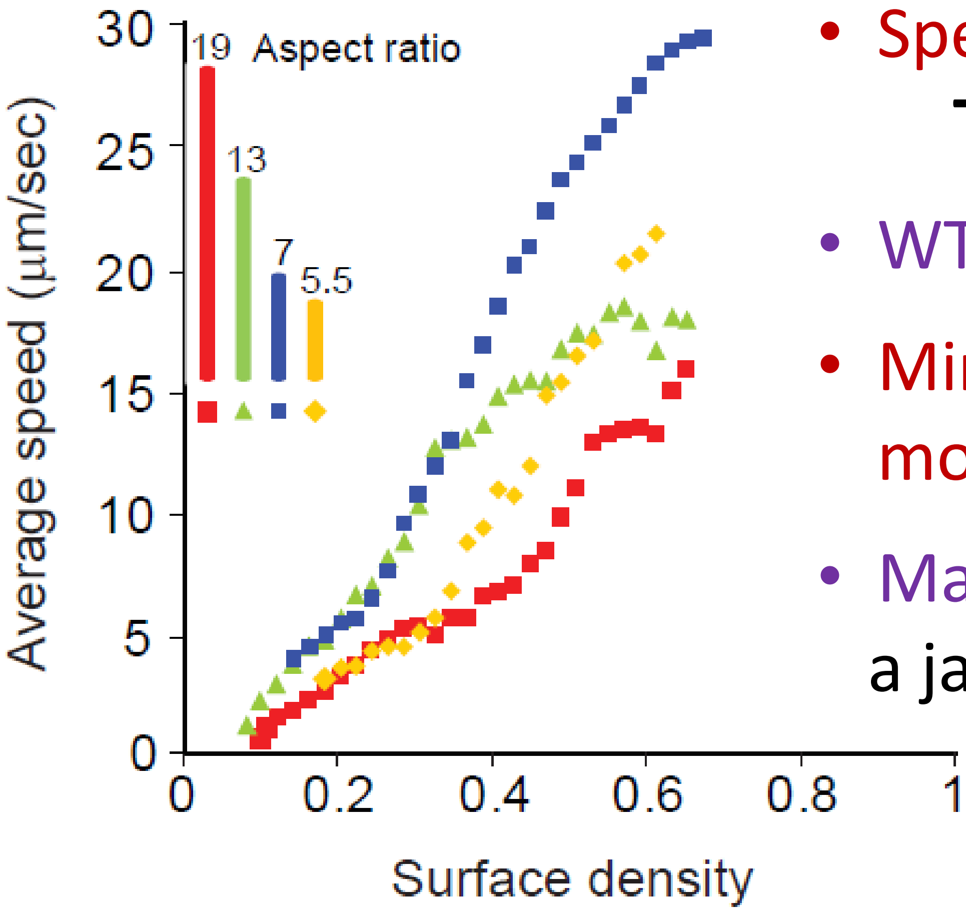
[Be’er et al, 2020]
Track all cells

Compare with
[Jeckel et al, 2019]
for a growing colony



Bacterial collective flow

Average speeds



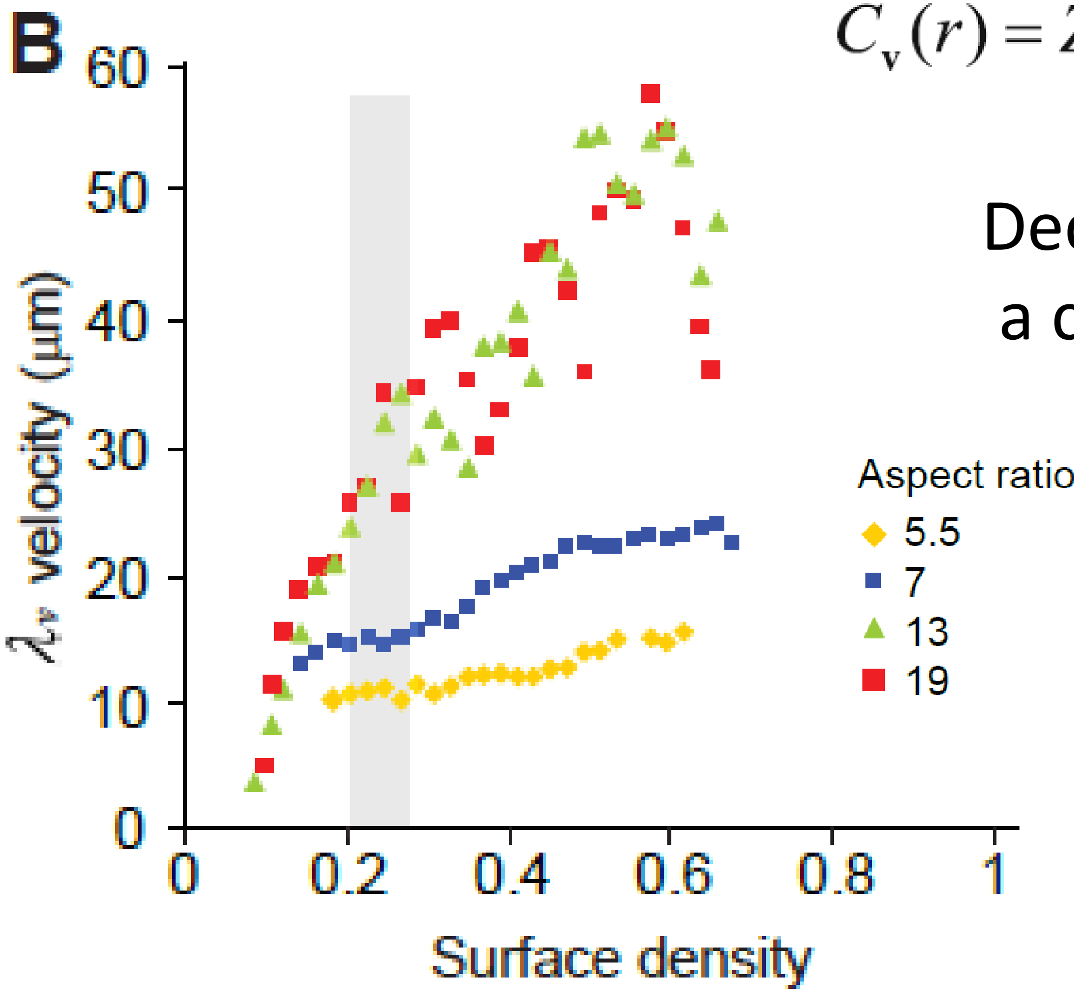
- Speed increases with density
  The hallmark of collectivity
- WT are the fastest
- Minimal concentration for movement – different than SPPs
- Maximal concentration – a jammed phase?

[Be'er et al 2019, 2020]

Correlation functions

Spatial correlations in velocity

$$C_{\mathbf{v}}(r) = Z^{-1}\left\langle \mathbf{v}(\mathbf{x}_1, t)\cdot \mathbf{v}(\mathbf{x}_2, t)\right\rangle_{t,|\mathbf{x}_1-\mathbf{x}_2|=r}$$



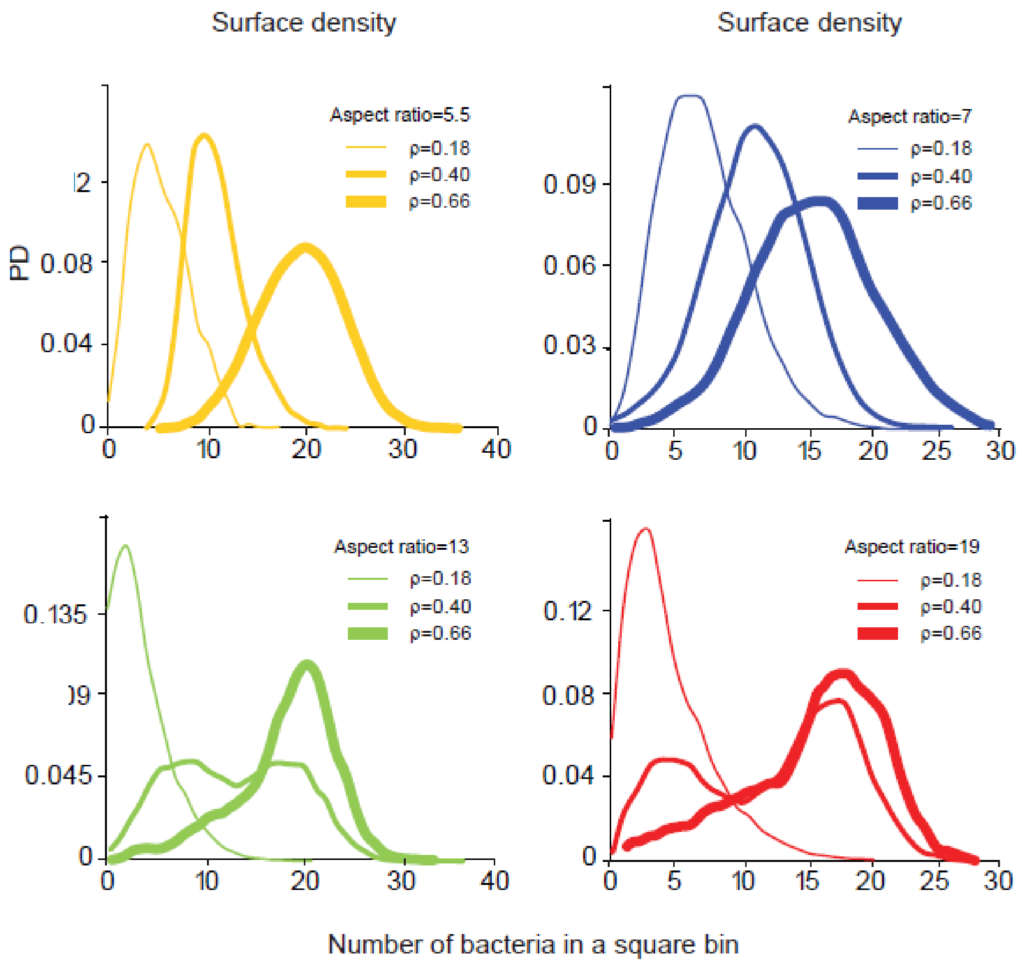
Decay exponentially with
a characteristic length scale

Density distribution

Example: Spatial variation in density

Short cells:
α = 5.5,
7 (WT)

Long cells:
α = 13, 19



Single population

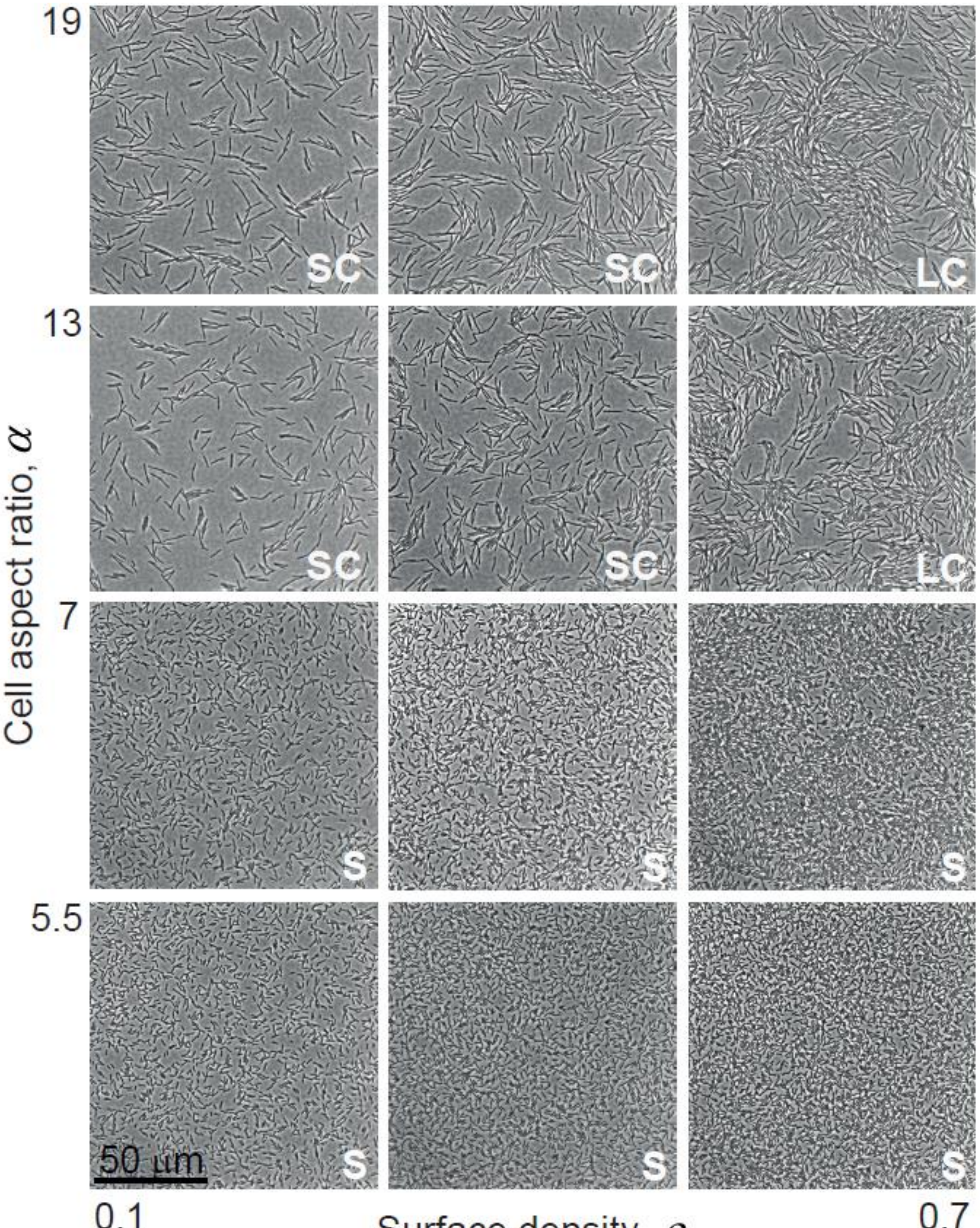
Two populations

Goal

Quantify the (ensemble) distribution of objects (points/rods/other)

Fundamental question in stat-phys:
what information can you get from snapshots (e.g. gas/liquid?)

Use entropy



Thermodynamics

Why entropy?

At equilibrium, entropy has a thermodynamic meaning

$$H = -\int d\mathbf{x} p(\mathbf{x}) \ln p(\mathbf{x})$$

[Carnot 1824, Clausius 1865, Boltzmann 1877, Gibbs, Maxwell]

Plays a key role in phase transitions [Frenkel 1999, Kardar 2007], pattern formation [Cross 1993] and self-assembly [Sciortino 2019].

Computation: e.g. thermodynamic integration.

Out of equilibrium: Shannon entropy is still well defined.

Computationally – a problem.

Entropy and collective motion

Typically assuming a specific model or need dynamics

Theory:

Bialek et al PNAS 2011 , Cavanna et al PRE 2014, Barre JSP 2015, Mann and Garnett Roy Soc Int 2015, Crosato PRE 2018

Estimation:

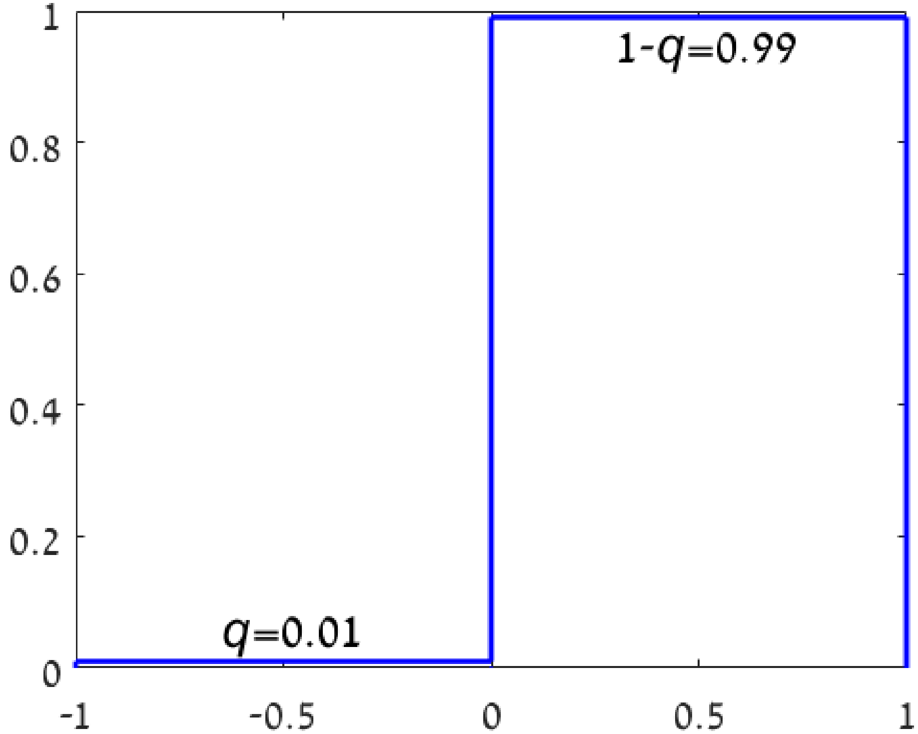
Bialek et al PNAS 2011 , Cavagna PRL 2021

Differential entropy

Estimate continuous entropy. Density $p(x), x \in \mathbb{R}^D$ from samples.

$$H = -\int dx p(x) \ln p(x)$$

Why is it difficult? 1D example



$$H = \underbrace{-\int_{-1}^{0} q \ln q \, dx}_{-q \ln q} \underbrace{-\int_{0}^{1} (1-q) \ln(1-q) \, dx}_{-q+O(q^2)}$$

A well-behaved example

Fine for Monte-Carlo-like methods. It is OK to have fewer samples in regions with a low probability

Differential entropy

Estimate continuous entropy. Density $p(x), x \in \mathbb{R}^D$ from samples.

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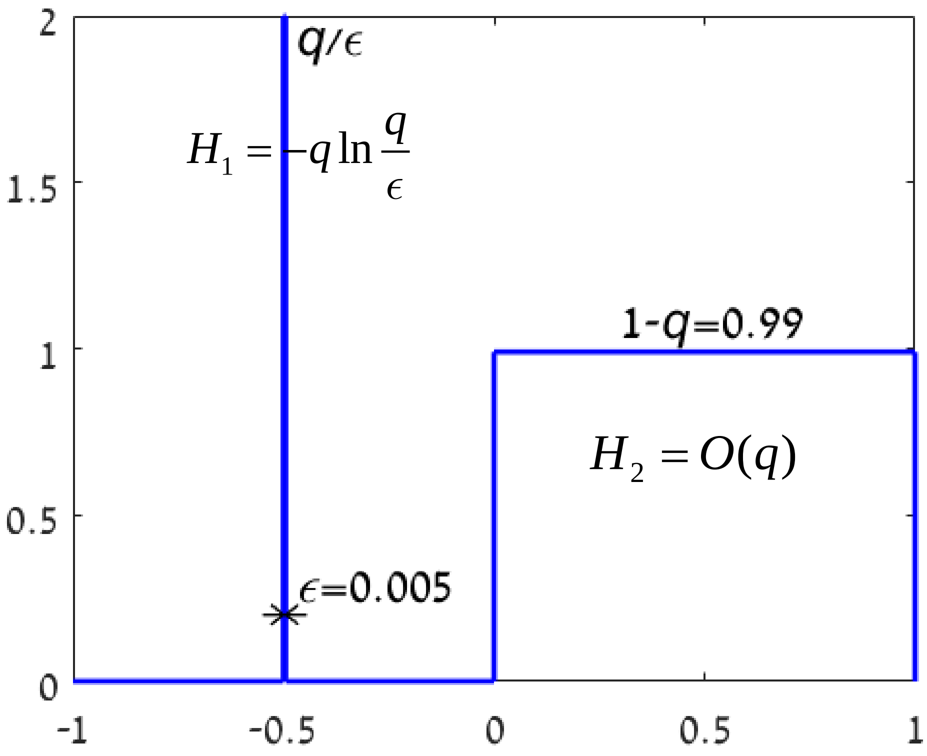
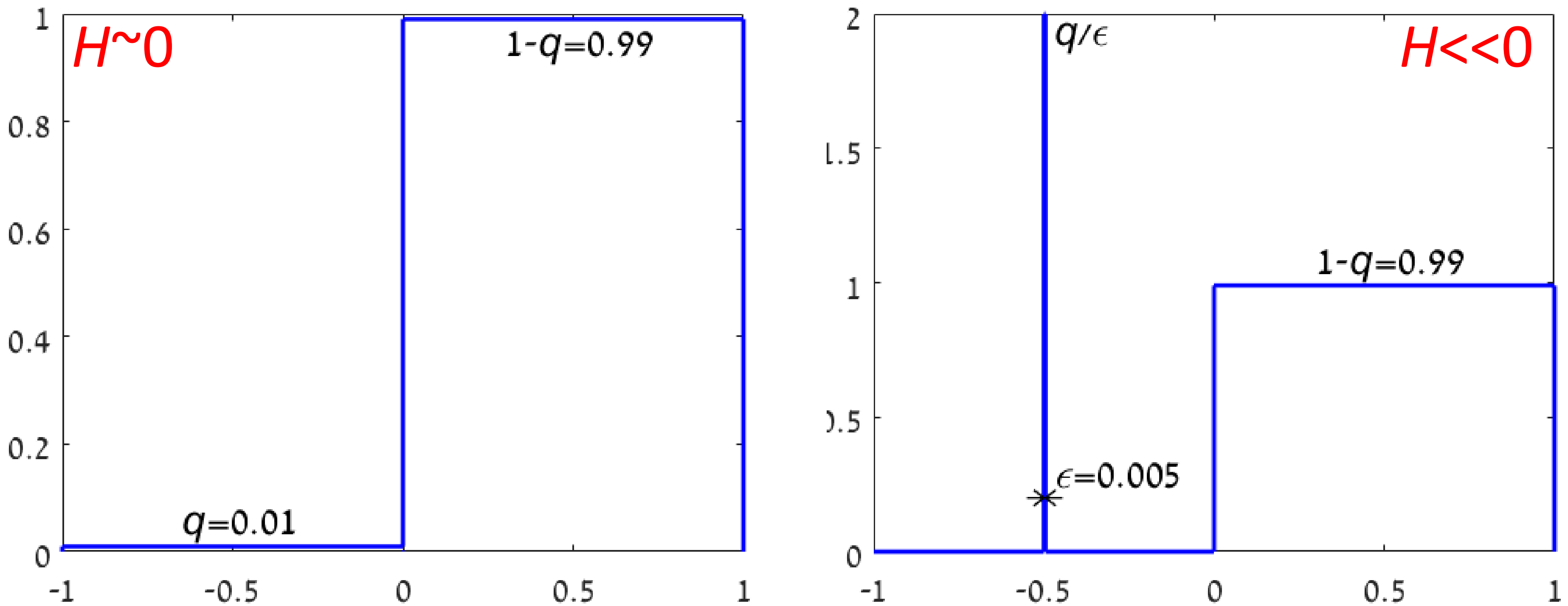


$$H = -q \ln \frac{q}{\epsilon} + O(q)$$

A small fraction q of the samples can be responsible for most of the entropy

Differential entropy



Need a sufficient number of samples ***in each half***
to determine in which case we are facing

Differential entropy

A continuous random variable: density $p(x), x \in \mathbb{R}^D$

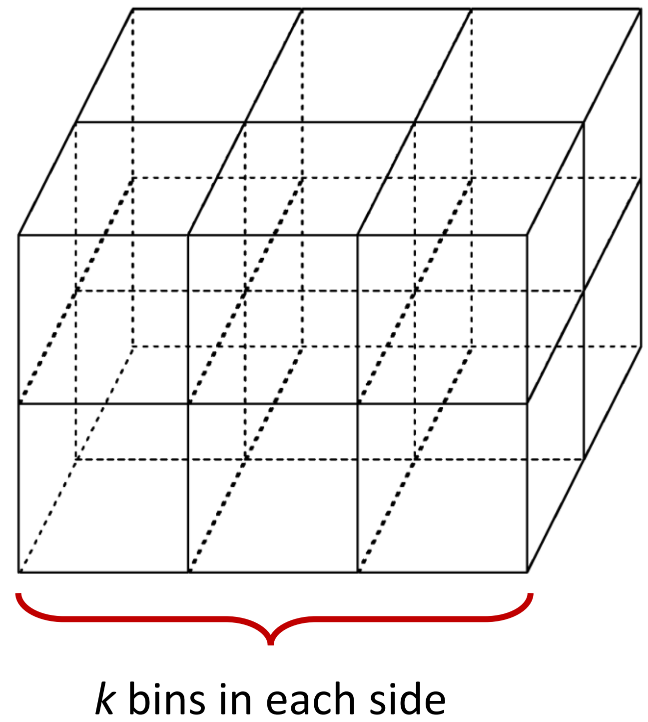
$$H = -\int dx p(x) \ln p(x)$$

Naïve approach: partition into bins

k^D bins

more than k^D samples

Curse of dimensionality



Entropy estimation methods

- Partition trees [Stowell and Plumbley 2009]
- Nearest neighbors: [Kozachenko and Leonenko 1987; Singh et al. 2003; Kraskov et al. 2004; Gao et al. 2017; Lord et al. 2018]
- Lossless compression [dynamical systems/biological sequences: Loewenstern 1977; Ebeling 1997; Grassberger 2002; Stat mech: Feldman and Crutchfied 2003; Melchert and Hartmann 2015; Avinery et al 2019; Martiniani et al 2019]
- Machine learning [Belghazi et al 2018]
- Iterated Gaussianization [Laparra et al 2020]
- Recursive copula splitting [Ariel and Louzoun 2020]

All approaches suffer from the curse of dimensionality

Severe under-sampling of phase space

Entropy estimation

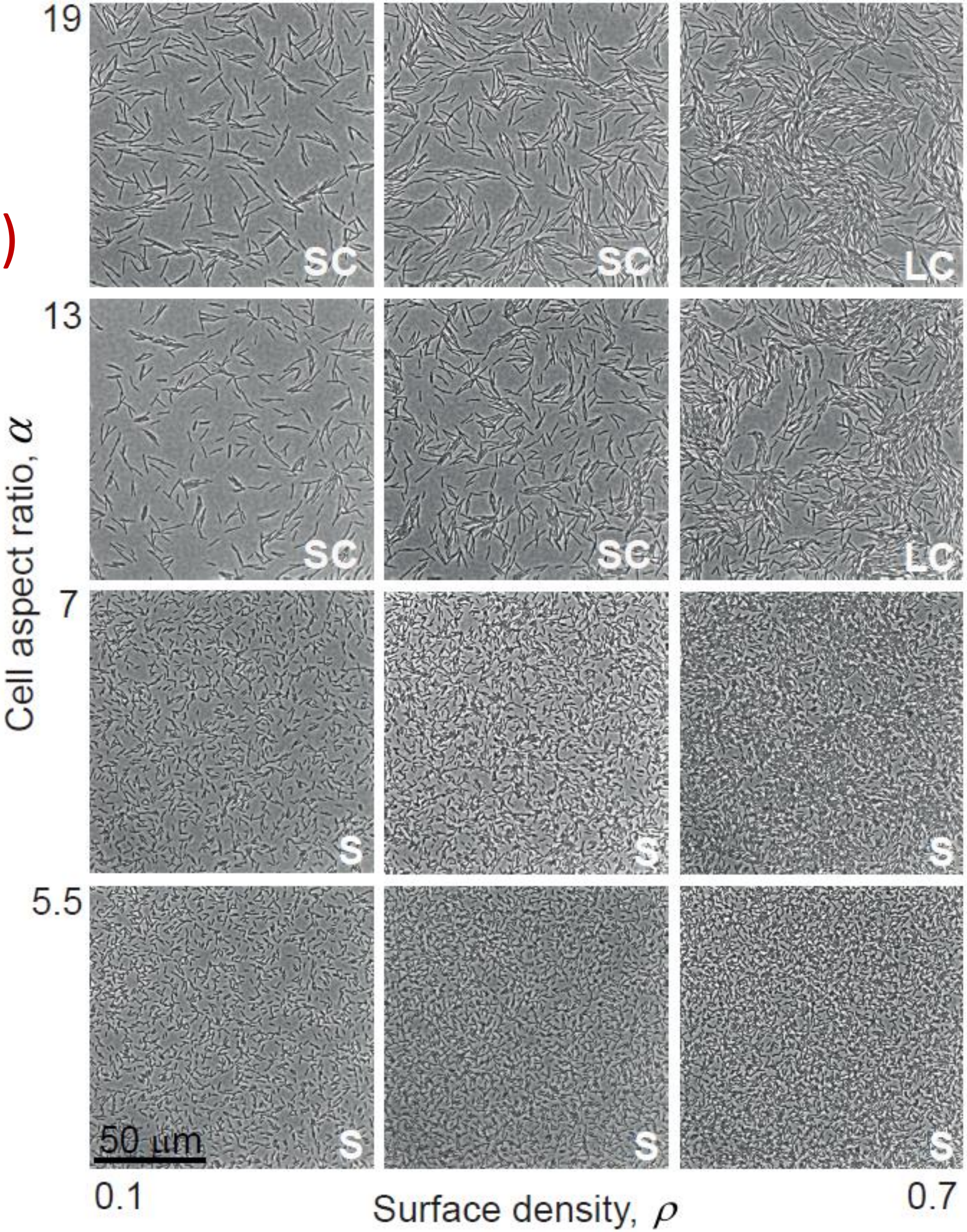
D=100 cells x (*x*, *y*, angle)

bin per dim ≥ 2

samples per bin ≥ 1

10^{90} samples

also,
the number of
particles varies



A more modest goal

What can we measure about the system?

What does it tell us in terms of its entropy?

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What can we measure about the system?

↓

What does it tell us in terms of its entropy?

Answer: an upper bound

(The lower bound is always $-\infty$)

In other words, given a measurement (e.g., correlation function), find the maximal entropy a system can have with the measurement as a constraint.

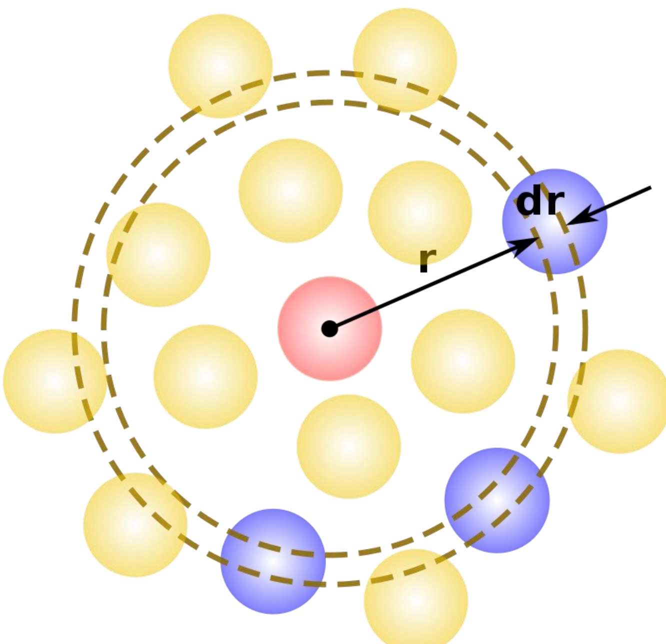
Without assuming knowledge of the microscopic configurations

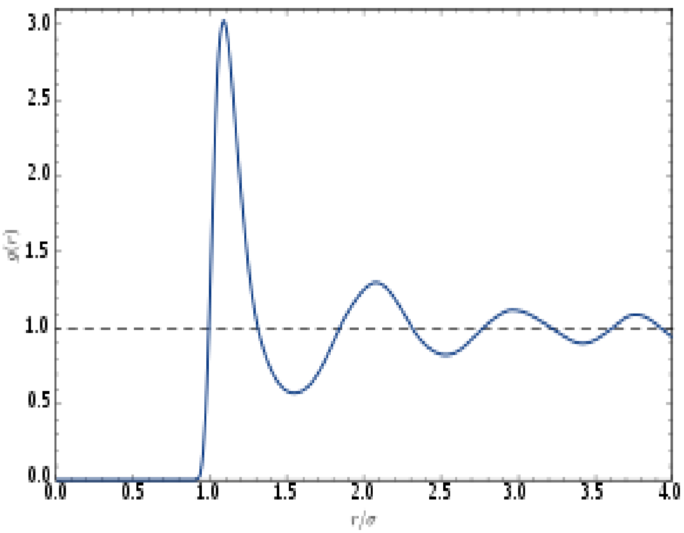
[Schneidman 2003, Shemesh 2013 and more]

Example: the structure factor

The pair correlation function

The average density (divided by $\bar{\rho}$)
at position **r** (or distance *r*) from a focal particle.





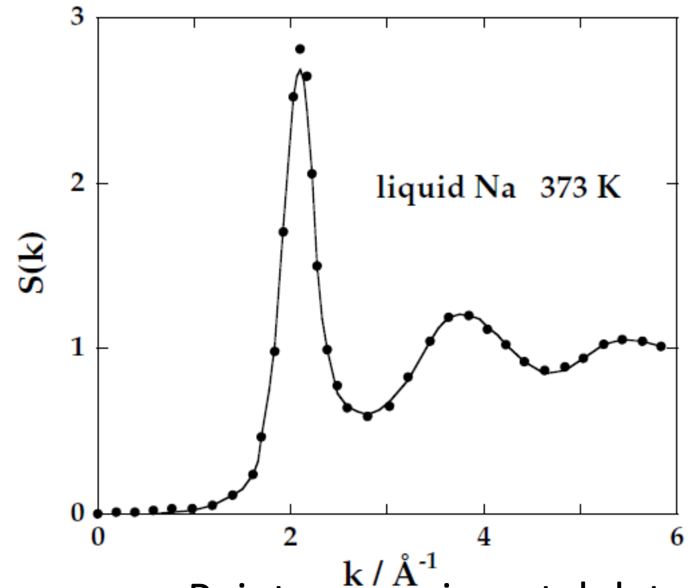
Lennard-Jones fluid. Wikipedia

Example: the structure factor

Essentially the Fourier transform of the pair correlation function (+1)

$$S(\mathbf{q}) = 1 + \bar{\rho} \int g(\mathbf{r}) e^{-i\mathbf{qr}} d\mathbf{r}$$

$$= \frac{1}{N}\langle \rho(\boldsymbol{q})\rho(-\boldsymbol{q})\rangle = \frac{1}{N}\left\langle \sum_{j,k} e^{-i\mathbf{q}(\mathbf{r}_j - \mathbf{r}_k)} \right\rangle$$



Points: experimental data

Line: MC for r^{-4} potential

Theory of Simple Liquids, Hansen

Ideal gas: $S(\mathbf{q}) = N\delta(\mathbf{q}) + 1$

Directly measurable in scattering experiments

Example: the structure factor

Essentially the Fourier transform of the pair correlation function (+1)

$$S(\mathbf{q}) = \frac{1}{N}\langle \rho(\boldsymbol{q})\rho(-\boldsymbol{q})\rangle = \frac{1}{N}\left\langle \sum_{j,k} e^{-i\mathbf{q}(\mathbf{r}_j - \mathbf{r}_k)} \right\rangle$$

The main idea:

Lagrange multipliers to maximize $H = -\int p \ln p dx$

with $S(q)$ as constraints (1 constraint for each **q**).

To solve: use standard expansion methods to 2nd order in conjugate fields (consistent with pair-wide correlations)

[Ariel and Diamant 2020]

Example: the structure factor

Essentially the Fourier transform of the pair correlation function (+1)

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$$\boxed{h_{\text{ex}} = \frac{H - H_{\text{id}}}{N} = \frac{1}{2\langle N\rangle}\sum_{\mathbf{q}\neq 0}\left[\ln S(\mathbf{q}) \ + 1 - S(\mathbf{q})\right]}$$

The excess entropy (compared to ideal gas) per particle.

This is the maximal entropy for all systems with this structure factor.

[Ariel and Diamant 2020], equiv. to 2nd order with [Green 1947, Hernando 1990]

Major generalization

Measure any pair correlation function $\mathbf{\Phi(x)}$ also matrix-valued

Fourier transform to $\mathbf{\Phi(q)}$

$$h_{\text{ex}} = \frac{H - H_{\text{id}}}{N} = \frac{1}{2\langle N \rangle} \sum_{\mathbf{q} \neq 0} \text{tr}[\ln \mathbf{\Phi}(\mathbf{q}) + I - \mathbf{\Phi}(\mathbf{q})]$$

The excess entropy (compared to ideal gas) per particle.

This is the (approximate) maximal entropy for any system with this correlation function

For the structure factor, see [Ariel and Diamant 2020],
General result: [Sorkin et al 2023]

Entropy content of correlations

A functional of correlation functions

$$h_{\mathrm{ex}} = \frac{H - H_{\mathrm{id}}}{N} = \frac{1}{2(2\pi)^{d}\bar{\mathrm{f}}} \mathrm{tr} \int_{\mathbf{q}\neq 0} d\mathbf{q} [\ln \mathbf{\Phi}(\mathbf{q}) + I - \mathbf{\Phi}(\mathbf{q})]$$

CF_1 -> h_{ex1}

CF_2 -> h_{ex2}

CF_3 -> h_{ex3}

- Separate contributions to the entropy
- Classify the degrees of freedom that govern a certain physical regime
- Identify phase transitions

Entropy content of correlations

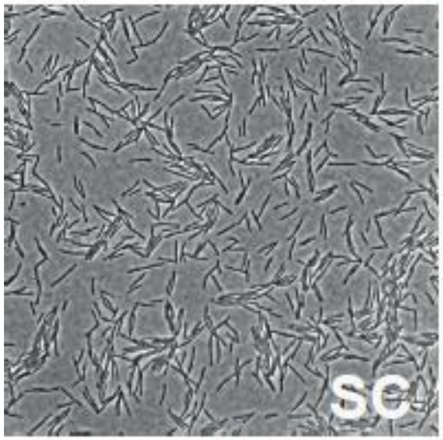
Three correlation functions

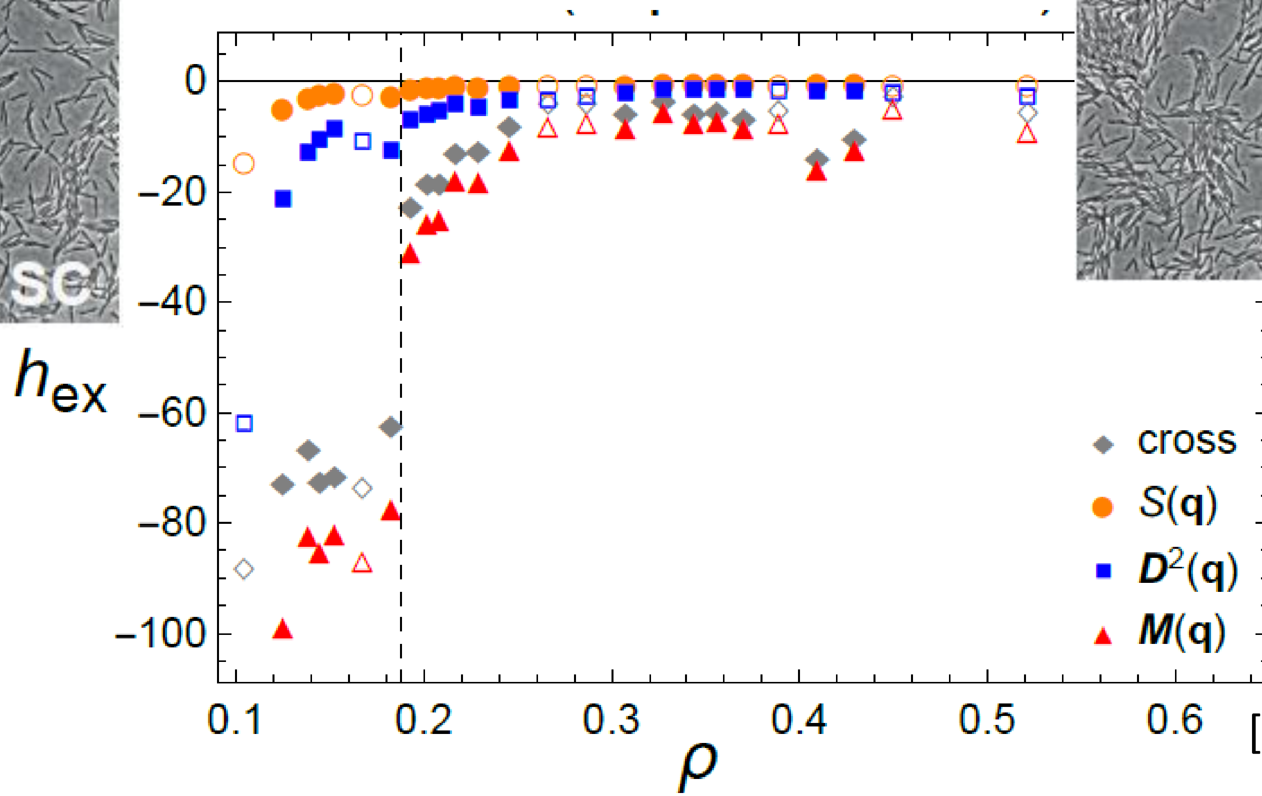
- Positions -> $S(\mathbf{q}) = \frac{1}{N}\left\langle \sum_{j,k} e^{-i\mathbf{q}(\mathbf{r}_j - \mathbf{r}_k)} \right\rangle$
- Orientations -> $D^l(\mathbf{q}) = \frac{2}{N}\left\langle \sum_{j,k} e^{-i\mathbf{q}(\mathbf{r}_j - \mathbf{r}_k)} \begin{pmatrix} \cos l\theta \\ \sin l\theta \end{pmatrix} (\cos l\theta, \sin l\theta) \right\rangle$
- Mixed -> $M^l(\mathbf{q}) = \frac{3}{N}\left\langle \sum_{j,k} e^{-i\mathbf{q}(\mathbf{r}_j - \mathbf{r}_k)} \begin{pmatrix} \cos l\theta \\ \sin l\theta \\ 1 \end{pmatrix} (\cos l\theta, \sin l\theta, 1) \right\rangle$

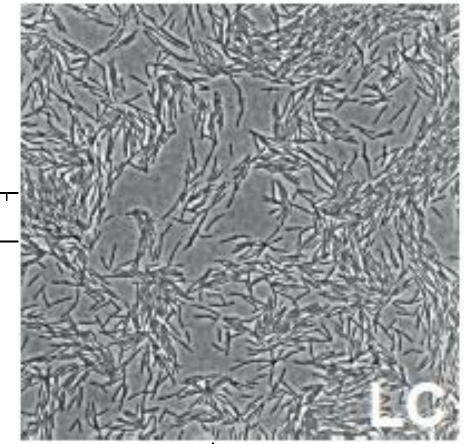
Mixed – Positions - Orientations = entropy of cross-correlations

Results: Swarming bacteria

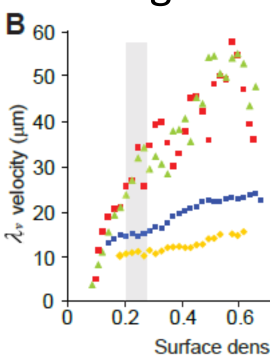
Long cells (aspect ratio 19)







corr length



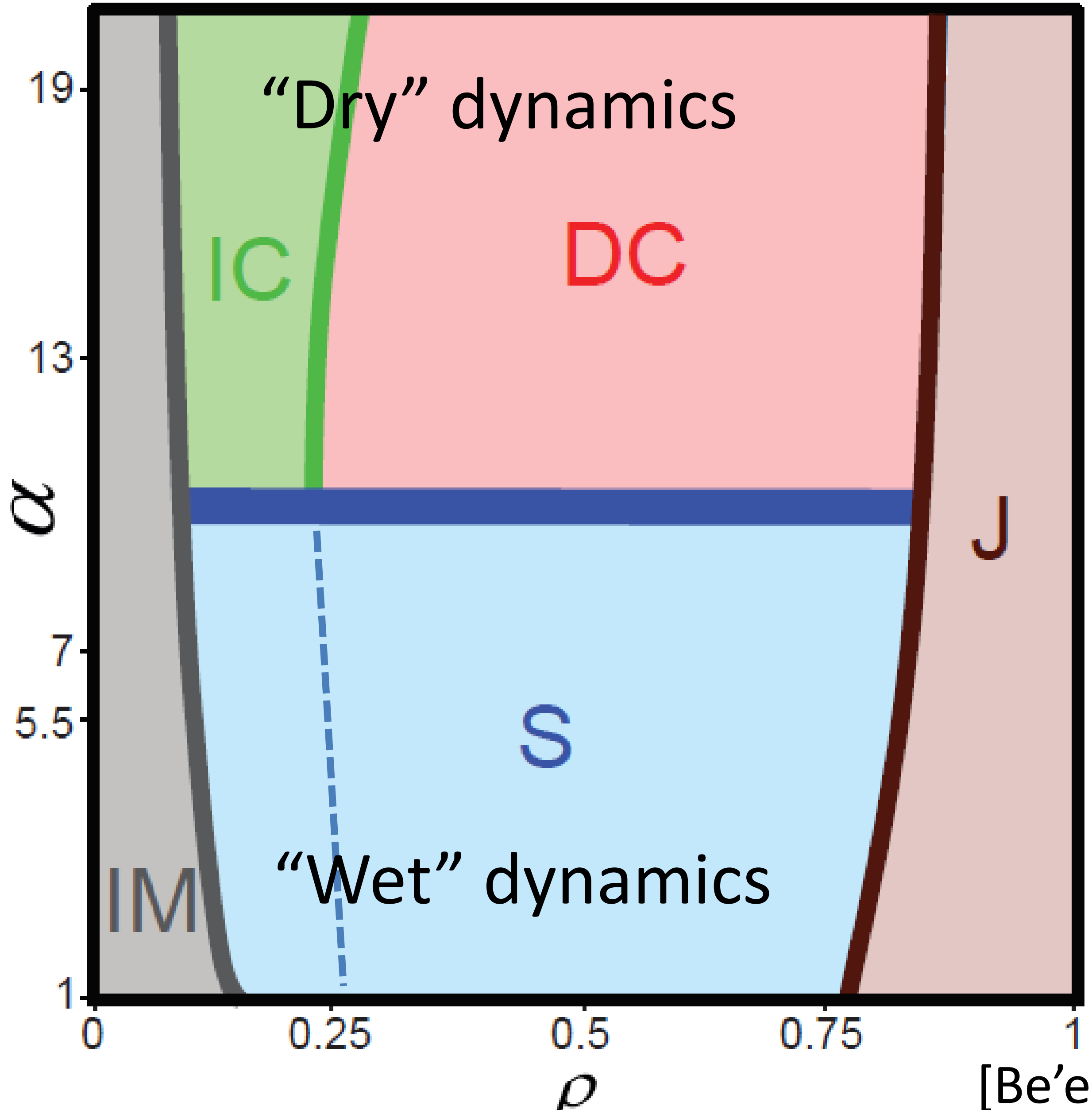
[Sorkin 2023]

Discontinuous jump in entropy -> 1st order transition.

Significant contribution of cross-correlations at low densities.

Two phases: dilute stationary cells and moving clusters ("anti MIPS")

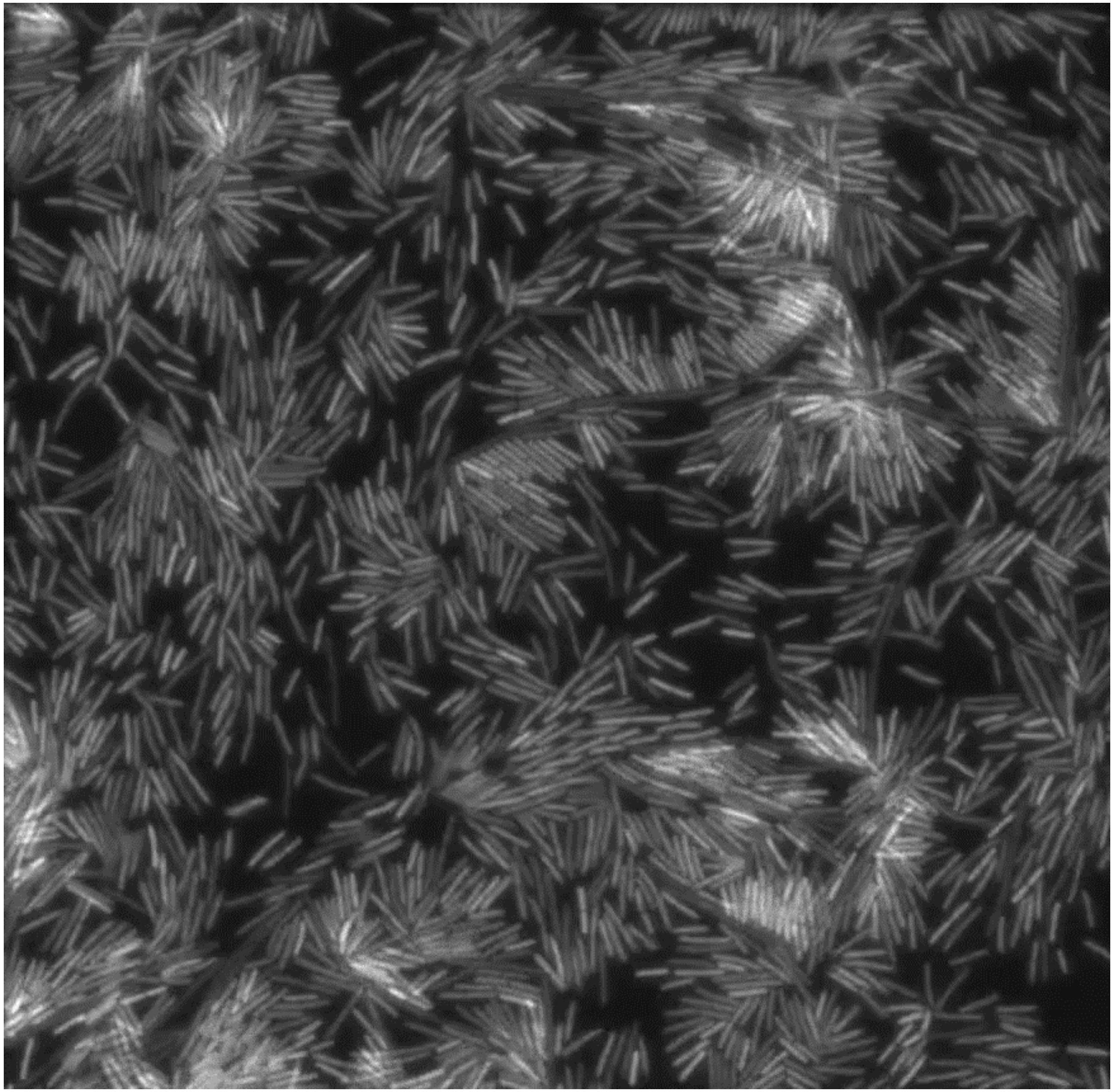
A phase diagram for bacterial swarming



[Be'er et al 2020]

Termination of swarming

In the "jammed" region



[Worlitzer et al,
Science advances 2022]

Termination of swarming

Motivation: Motility induced phase separation
[Cates and Tailleur 2015]

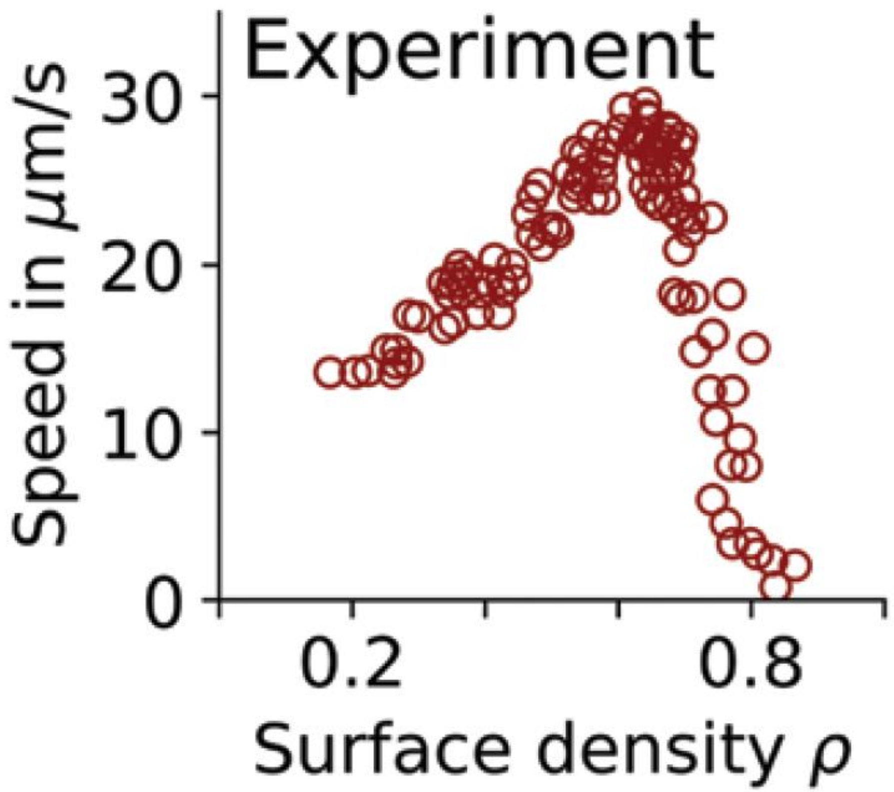
A non-equilibrium effect

Hand-waving explanation:

- When self-propelled particles collide, they slow down.
- Expect that particles at dense regions move slower and accumulate. Positive feed-back.
- Phase separation between dense and dilute fluid phases.
- Will not occur for passive system (hence motility induced).

Termination of swarming

In swarming bacteria:

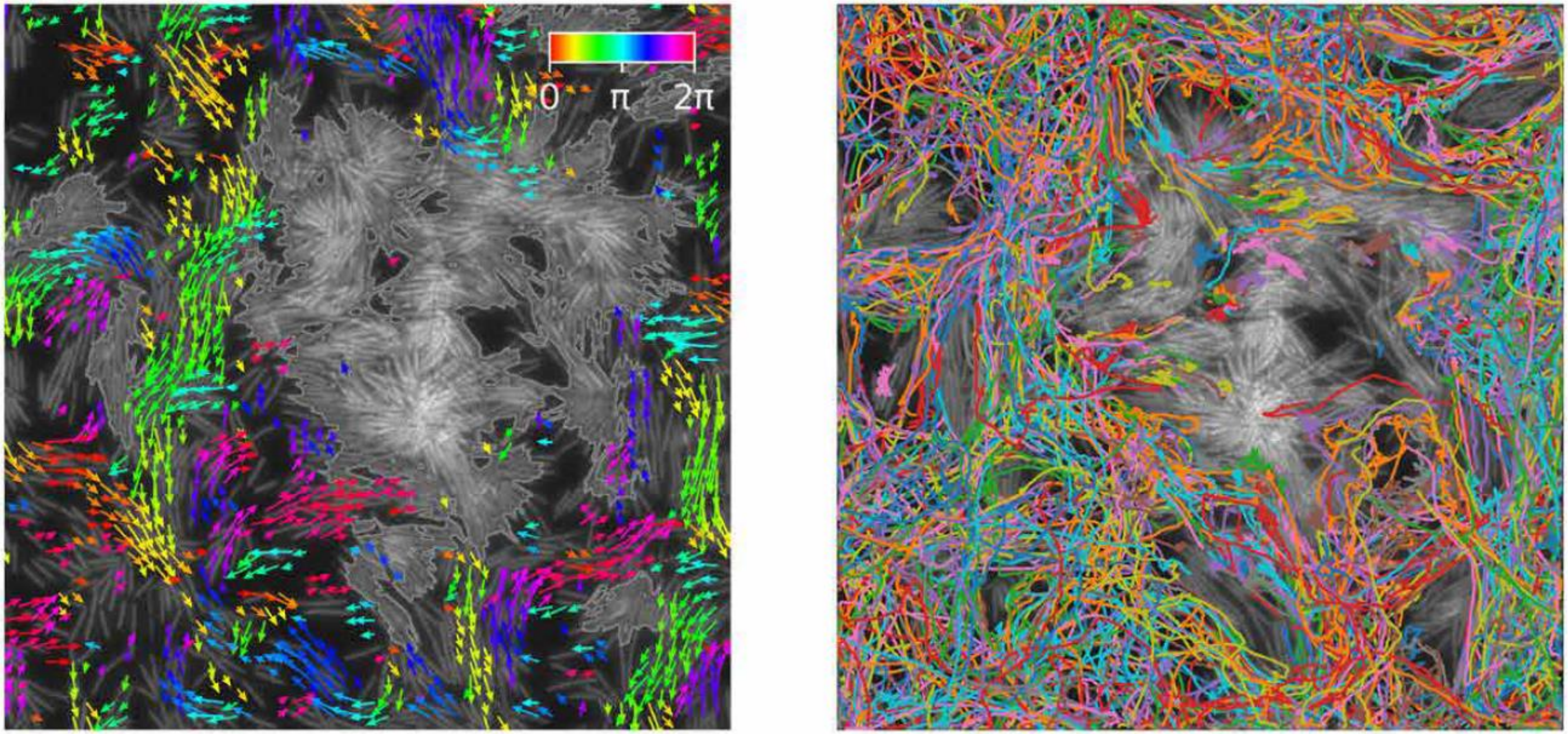


[Ariel et al, PRE 2018]

Termination of swarming = MIPS?

[Grafke et al, PRL 2017; Grobas et al, eLife 2021]

Termination of swarming



[Worlitzer et al, Sci Adv 2022]

Qualitatively consistent with MIPS

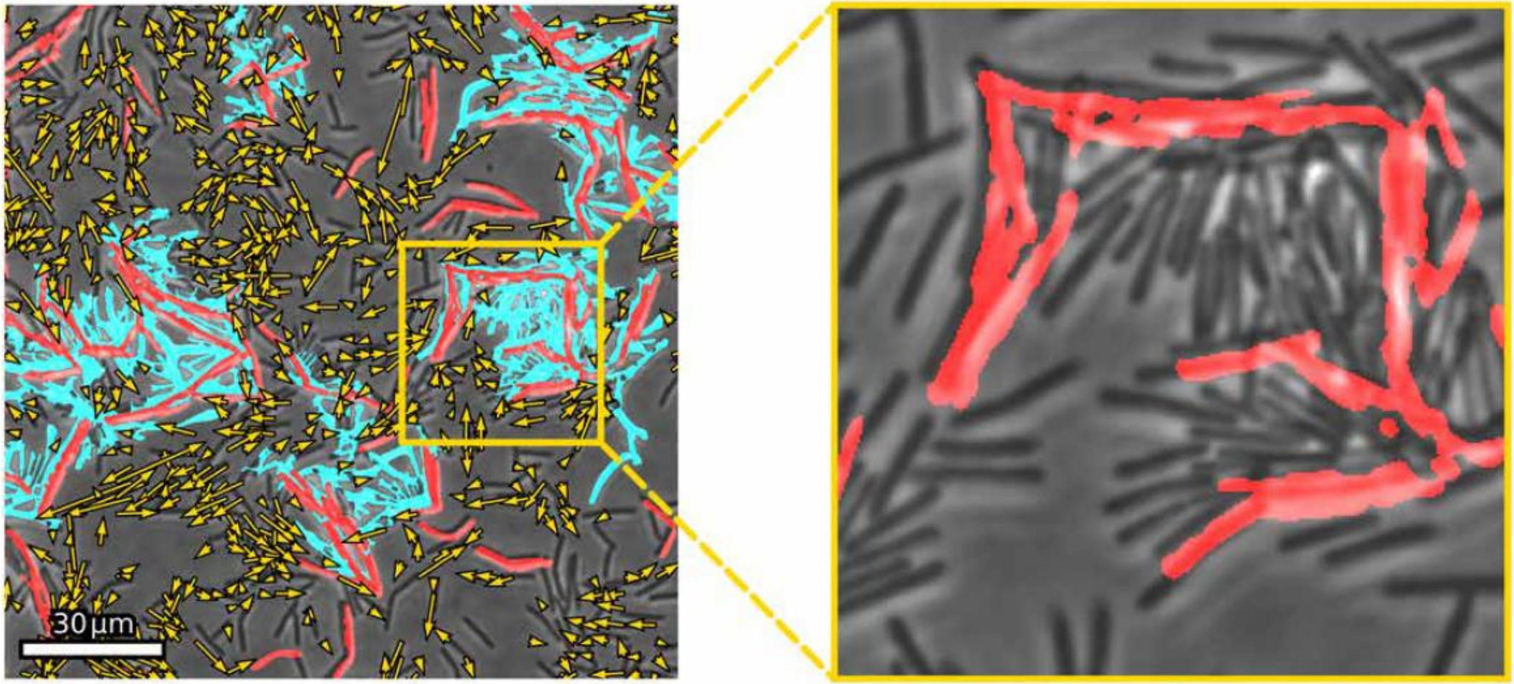
Termination of swarming

But …

Nucleation of stationary aggregates:

We find Extracellular polymeric substance (EPS)

Cells initiate the biofilm program.



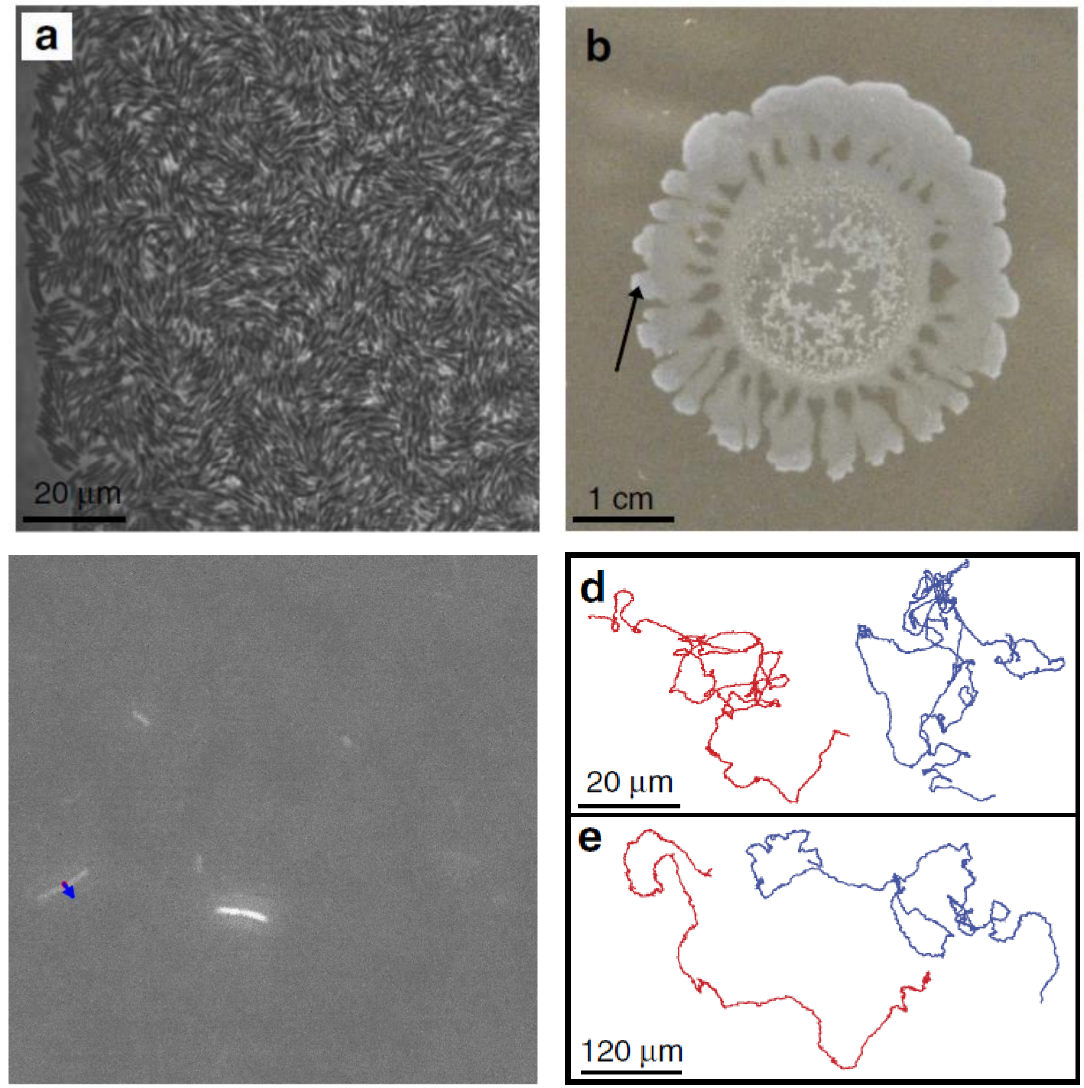
Not purely physics! [Worlitzer et al, Sci Adv 2022]


A single cell within a swarm
We’re all individuals!
- I'm not.
- Shhh.

Individual within a swarm

Ariel et al, Nature Comm. 2015

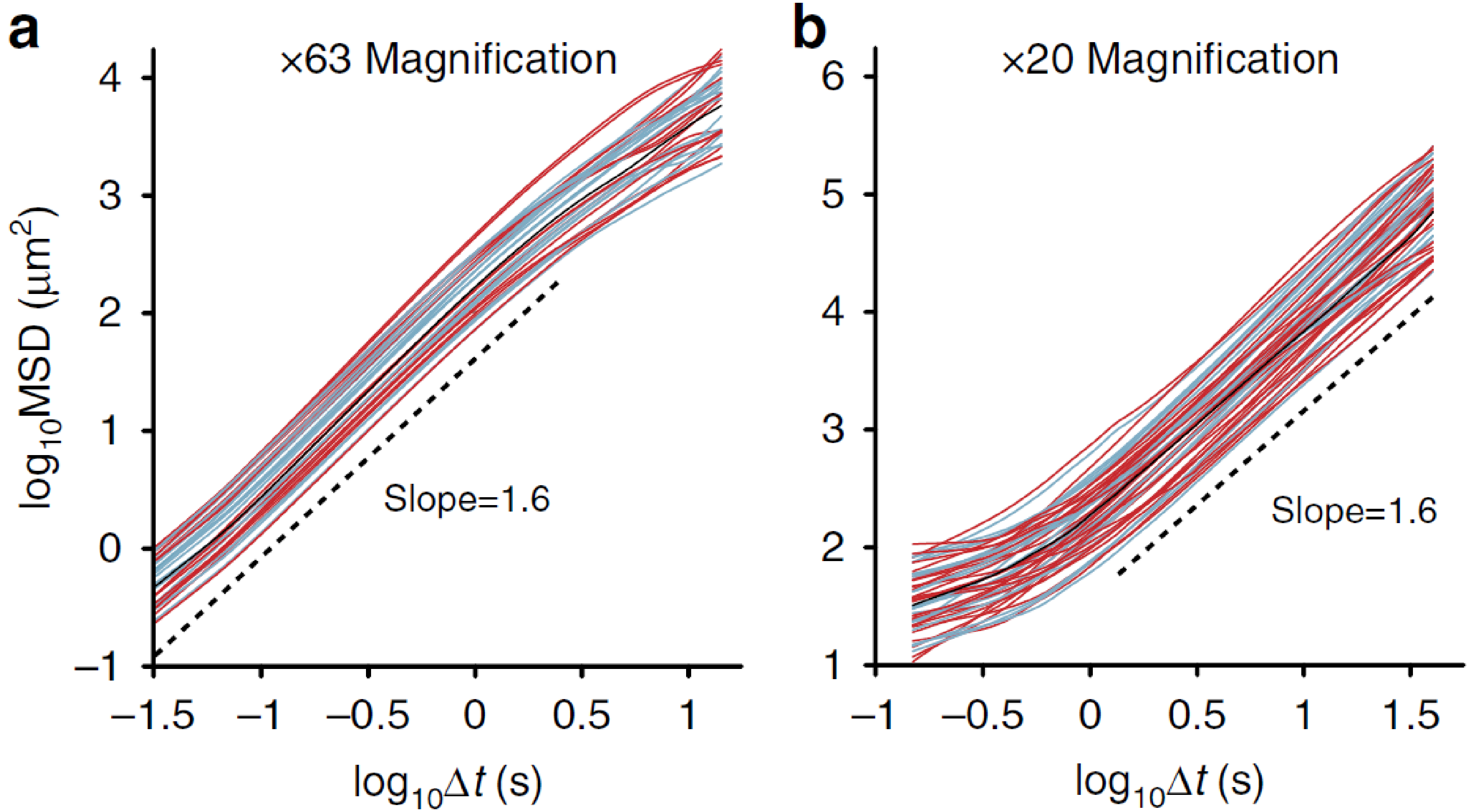
The set-up:



Individual within a swarm

Ariel et al, Nature Comm. 2015

Mean Square Displacement shows super-diffusion

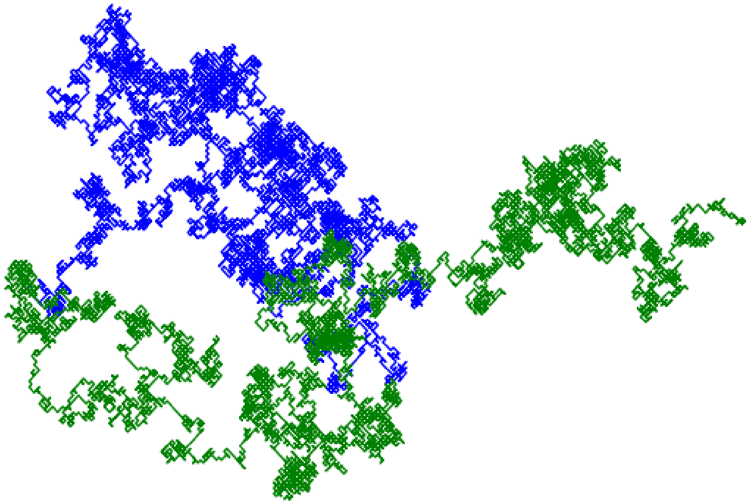


Consistent with a Lévy Walk.

Lévy walks

Drunk walk:

A drunk walks out of a pub.
He/she moves at a constant speed.
Changes direction at random times.



Time between turns is independent with density $f(t)$.

Let $r(t)$ denote the position of the drunk at time t.

Finite variance -> Central Limit Theorem -> MSD ~ t

$$\left\langle \left| \mathrm{r}(s+t) - \mathrm{r}(s) \right|^2 \right\rangle \sim t$$

Lévy walks

Lévy Walks. Mandelbrot '60s (Lévy flight).
[Shlesinger et al, J. Stat. Phys. 1982]

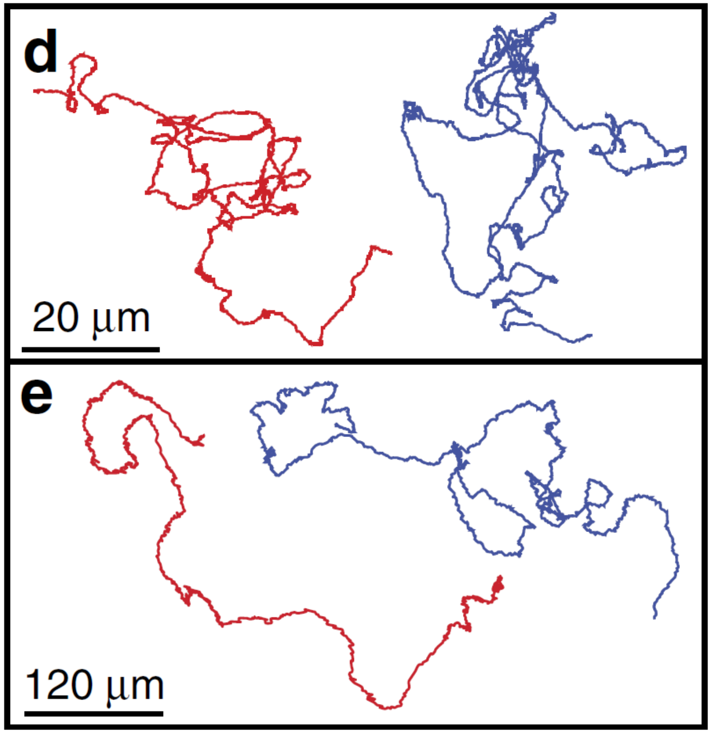
Time between turns has an **infinite** variance, $f(t) \sim 1/t^{1+\mu}$.
Standard CLT does not hold. Obtain Lévy distributions.

$$\left\langle \left| \mathrm{r}(s+t) - \mathrm{r}(s) \right|^2 \right\rangle \sim t^{\alpha}$$

Super-diffusion. $\alpha > 1$

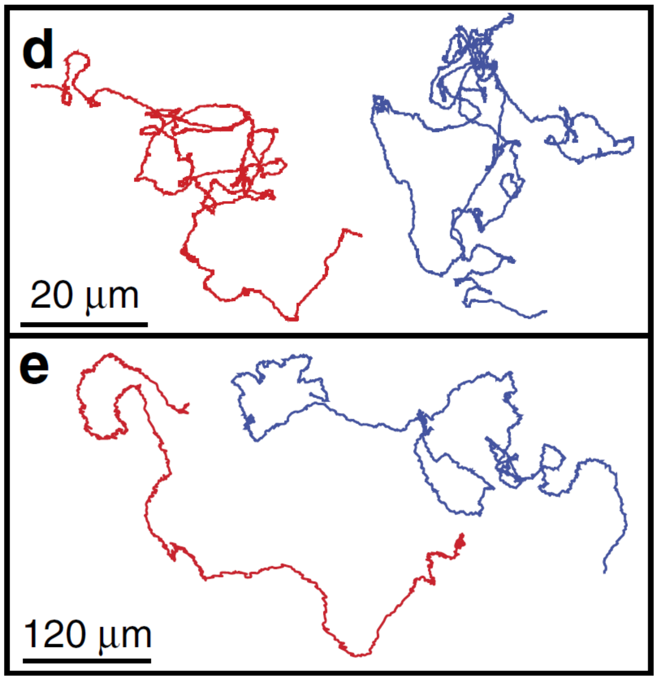
For swarming bacteria we get 1.6

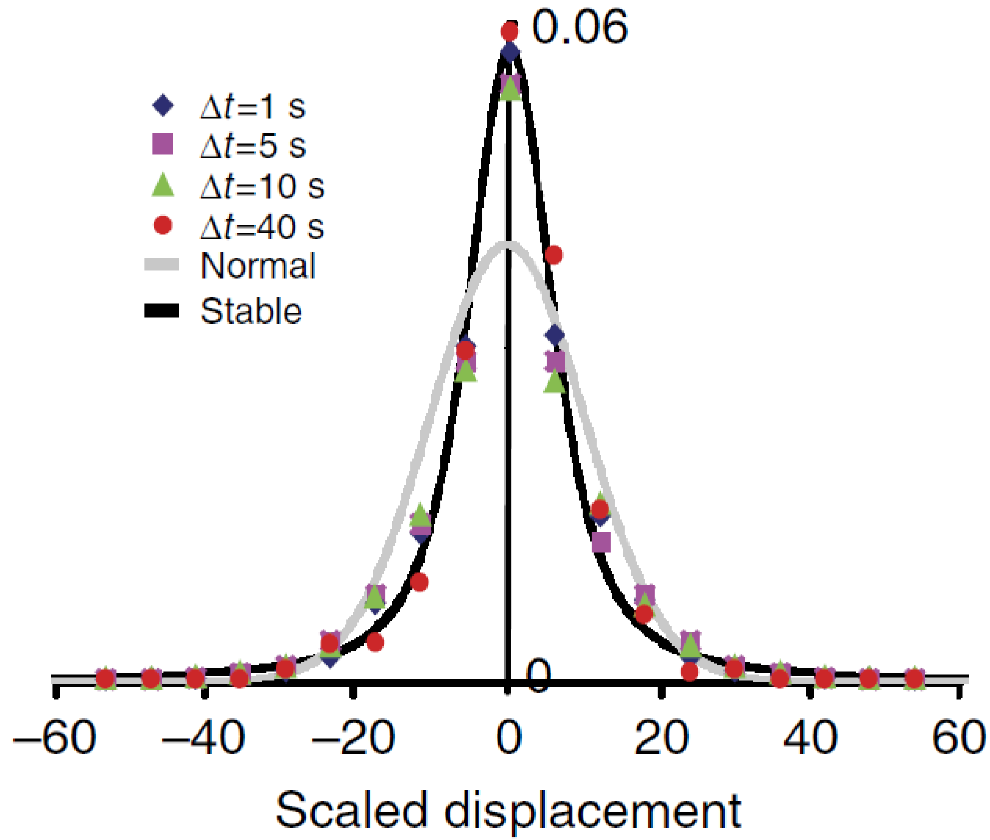
Non-Gaussian statistics.



Swarming bacteria do a Lévy walk

Lévy walks





$P(\Delta x, \Delta t)$

scale: $\Delta t^{1/\beta} P(\Delta x \Delta t^{-1/\beta}, \Delta t)$

α-stable law with parameter β

Swarming bacteria do a Lévy walk

Related models

- Ariel et al, PRL 2017
- Zarfaty et al, PRE 2018
- Ariel and Schiff, Physica D 2020
- Berman and Mitchell, Chaos 2020
- Wagner et al 2022
- Mukherjee et al PRL 2021, 2023
- Padhan and Pandit, PRR 2023
- Singh and Chaudhuri, Nature Comm 2024

Comparing experiments with model

References comparing with swarming bacteria

Agent-based models

Micro-swimmers.

Steric and/or Hydrodynamics interactions

[e.g., Wensink 2012 , Ryan 2016, Ariel 2018]

Continuous models

Effective coarse-grained eq. for the polarization field

[e.g., Wensink 2012, Dunkel 2013, Lushi 2014, Ariel 2018; Jeckel 2018, Worlitzer 2021]

Comparing experiments with model

Agent-based models

Hydrodynamics of micro-swimmers (near a boundary)

[Spagnolie and Lauga, J Fluid Mech 2012]

Stokes equation:

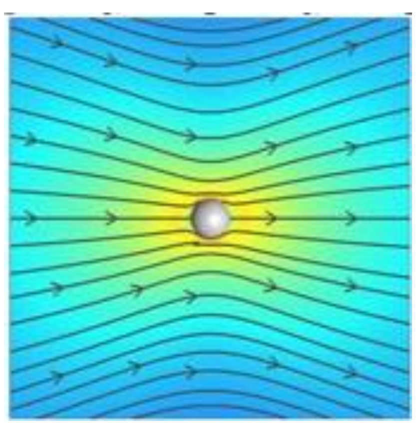
$$-\nabla p + \mu \, \Delta \boldsymbol{u} = 0$$

$$\nabla \cdot \boldsymbol{u} = 0,$$

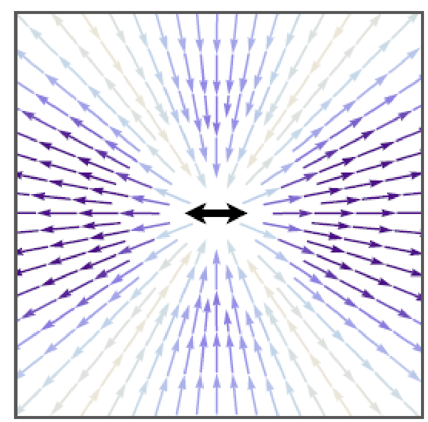
u: velocity
p: pressure
μ: viscosity

Singular solutions:

Force monopole
Stokeslet



Force dipole



Near a wall: image Stokeslets/dipole. Similar to electrostatics.

Continuous models

A PDE for the velocity field/polar order parameter

$$(\partial_t + \mathbf{v}\cdot\nabla)\mathbf{v} = -\nabla p^* - (A + C|\mathbf{v}|^2)\mathbf{v} + \nabla\cdot\mathbf{E}$$

$$\nabla\cdot\mathbf{v} = 0$$

- Material derivative
- Pressure (Lagrange multiplier for incompressibility)
- Self-propulsion
- Stress tensor (short range alignment, long range anti-alignment)

$$\nabla\cdot\mathbf{E} = -\Gamma_0\Delta\mathbf{v} + \Gamma_2\Delta^2\mathbf{v}$$

Linear stability analysis.

Characteristic length scale $\Lambda = 2\pi\sqrt{2\Gamma_2/\Gamma_0}$

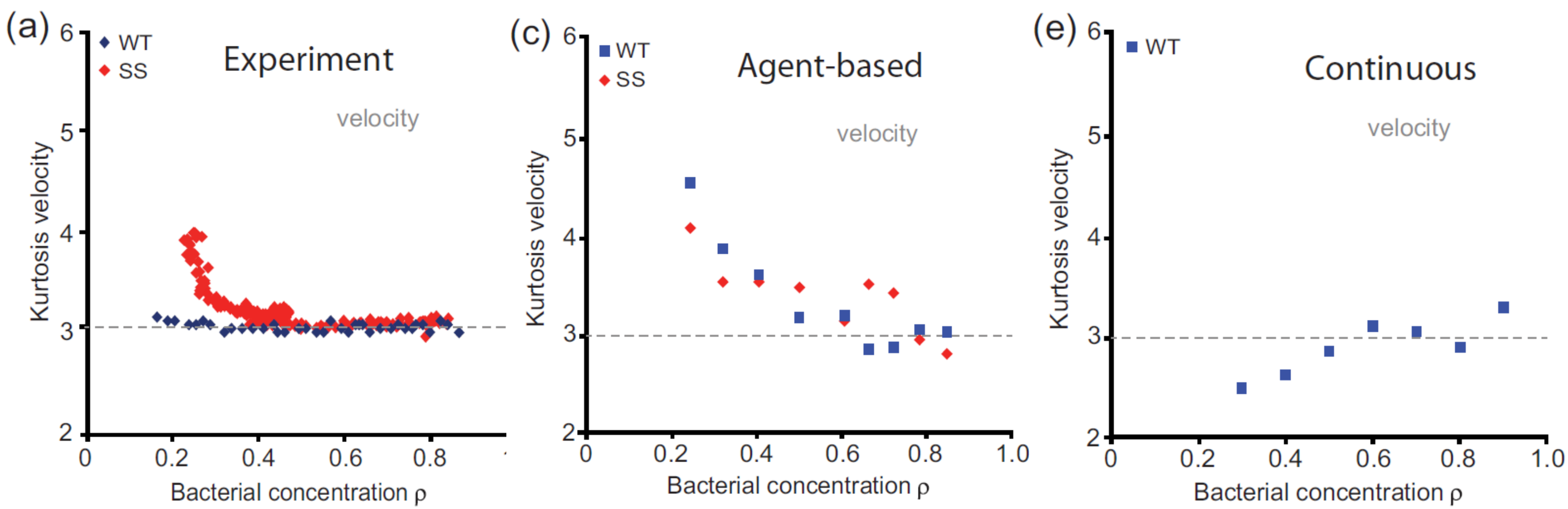
[Dunkel et al, PRL 2013]

Comparing experiments with model

[GA et al PRE 2018]

Velocity – Kurtosis = (Gaussian=3, larger=heavier tail)

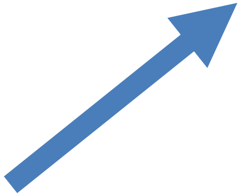
$$\mathrm{Kurt}[X] = \mathrm{E}\left[\left(\frac{X-\mu}{\sigma}\right)^4\right] = \frac{\mathrm{E}\left[(X-\mu)^4\right]}{\left(\mathrm{E}[(X-\mu)^2]\right)^2} = \frac{\mu_4}{\sigma^4}$$



Continuous models: need to add density fluctuations [Worlitzer et al, soft matter 2021]

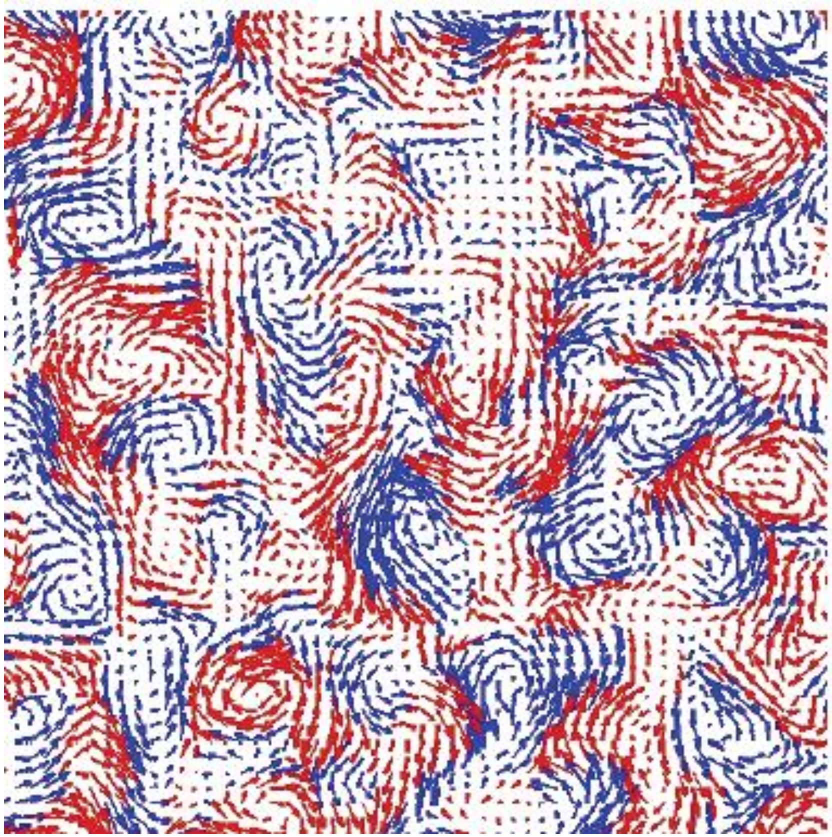
Topological defects in active matter

[recent reviews Giomi, PRX 2013, Bowick et al, PRX 2022]



Polar particles (with head and tail)

Look at a vector field, for example, velocity filed of the swarm



red = counter clockwise
blue = clockwise

Topological defects in active matter

[recent reviews Giomi, PRX 2013, Bowick et al, PRX 2022]

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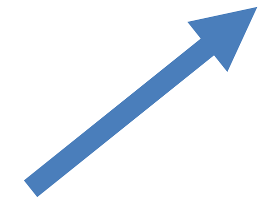

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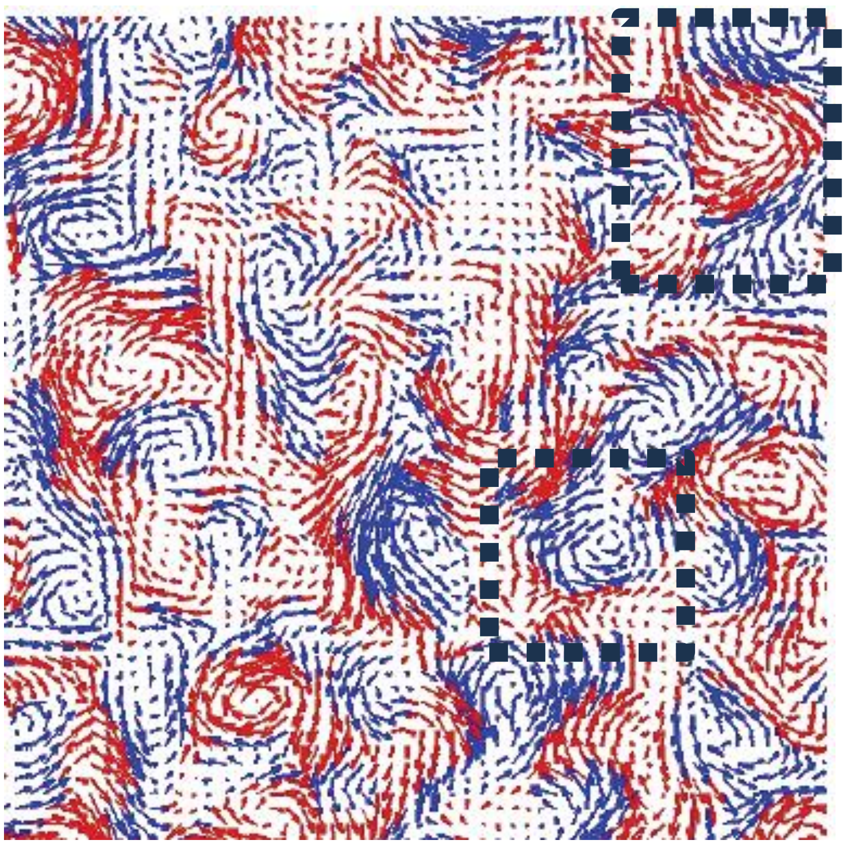
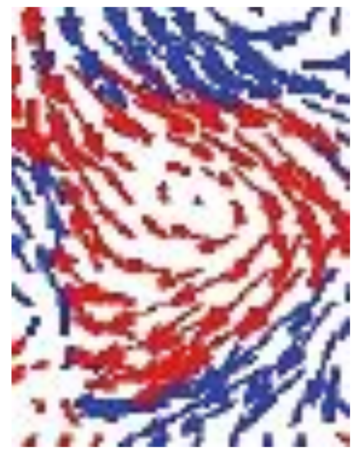
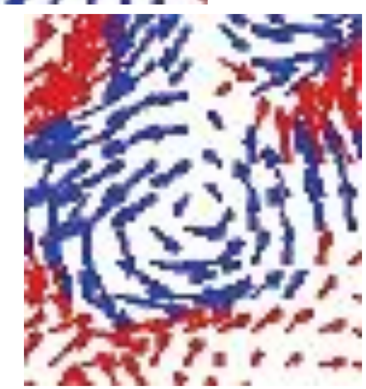




look only on the direction

Why? Maybe we don’t know the speed



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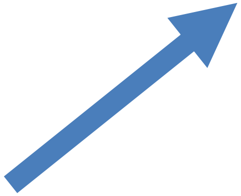

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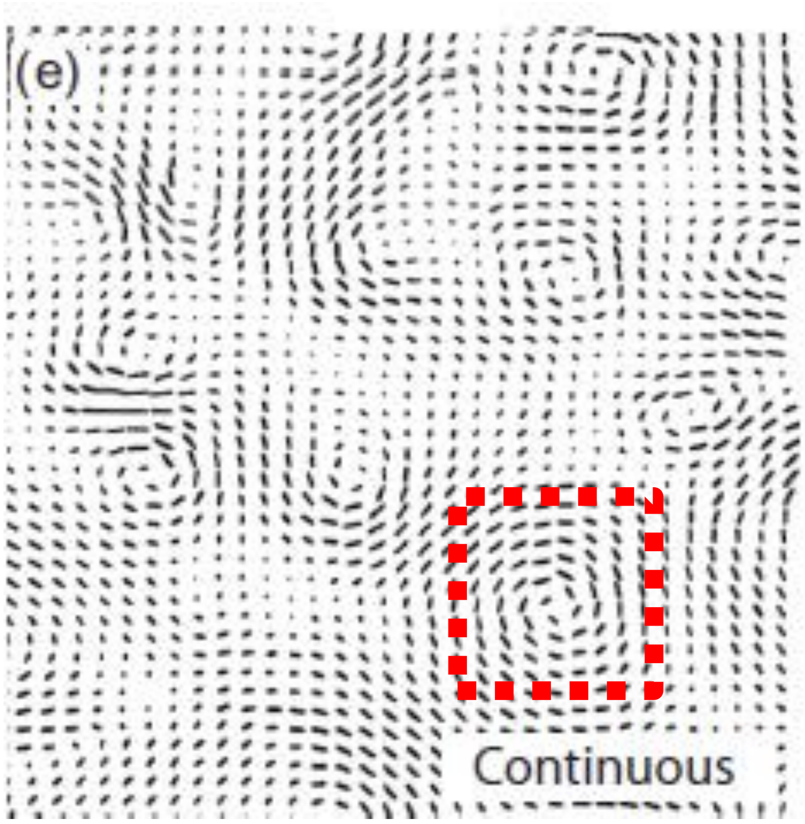
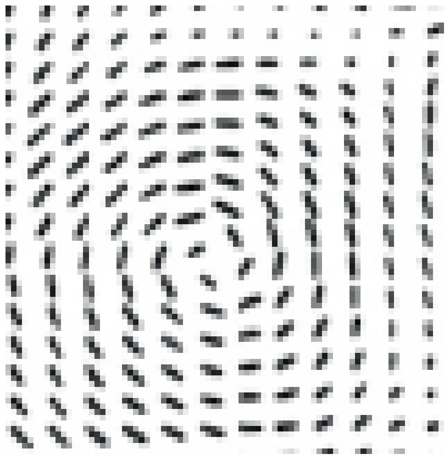
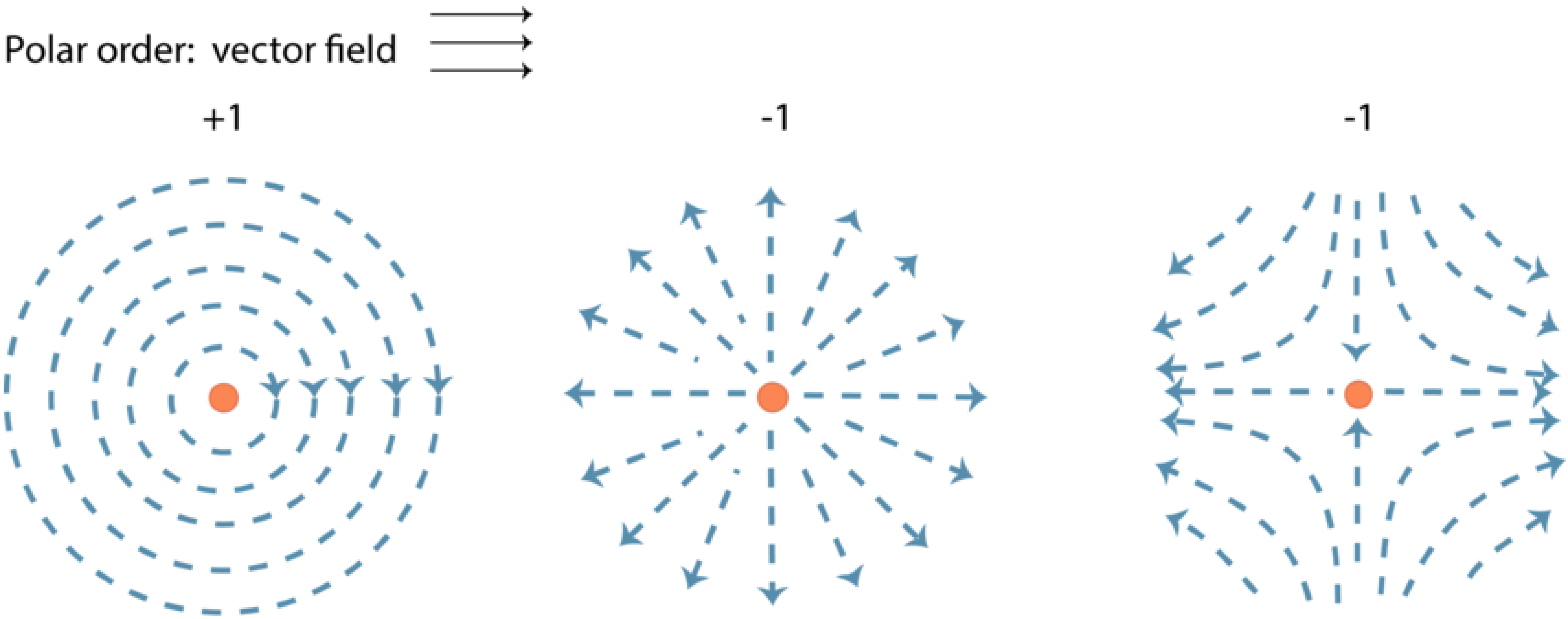


singular points in which the direction is not defined



Defects in vector fields



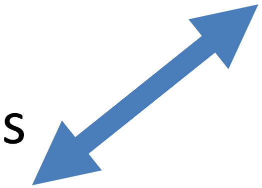
Only integer charges!

Comes from the fact that the field is continuous

(except @ singularities)

Defects in nematic fields

[recent reviews Giomi, PRX 2013, Bowick et al, PRX 2022]



Nematic particles (head-tail symmetry) Liquid crystals

Look at a nematic field, for example, cell orientation

+1/2 -1/2

singular points in which the direction is not defined

Only integer and half-integer charges!

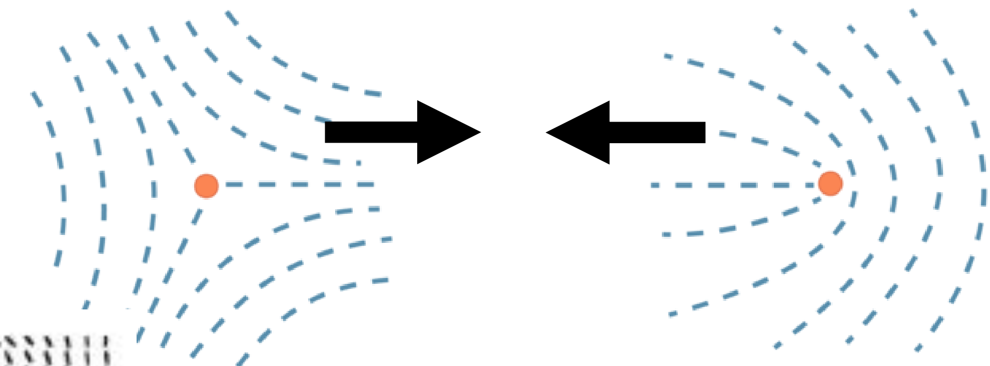
Comes from the fact that the field is continuous

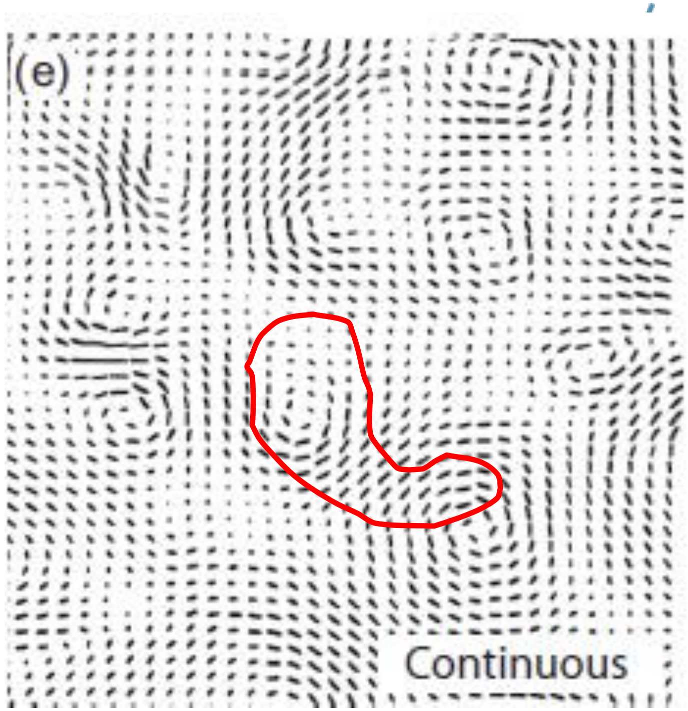
(except @ singularities)

Topological defects

If the orientation field changes in time

1. Defects can move
2. Annihilate
3. Created





Conservation of charge

In any close region, the total charge can
Change if defect come in or go out

Topological defects

Add physics (a shallow exposition)
[recent reviews Giomi, PRX 2013, Bowick et al, PRX 2022]

Defects cost elastic energy that increases with |charge|

Interaction – coulomb to leading order

Relaxation to equilibrium -> defects annihilate and vanish

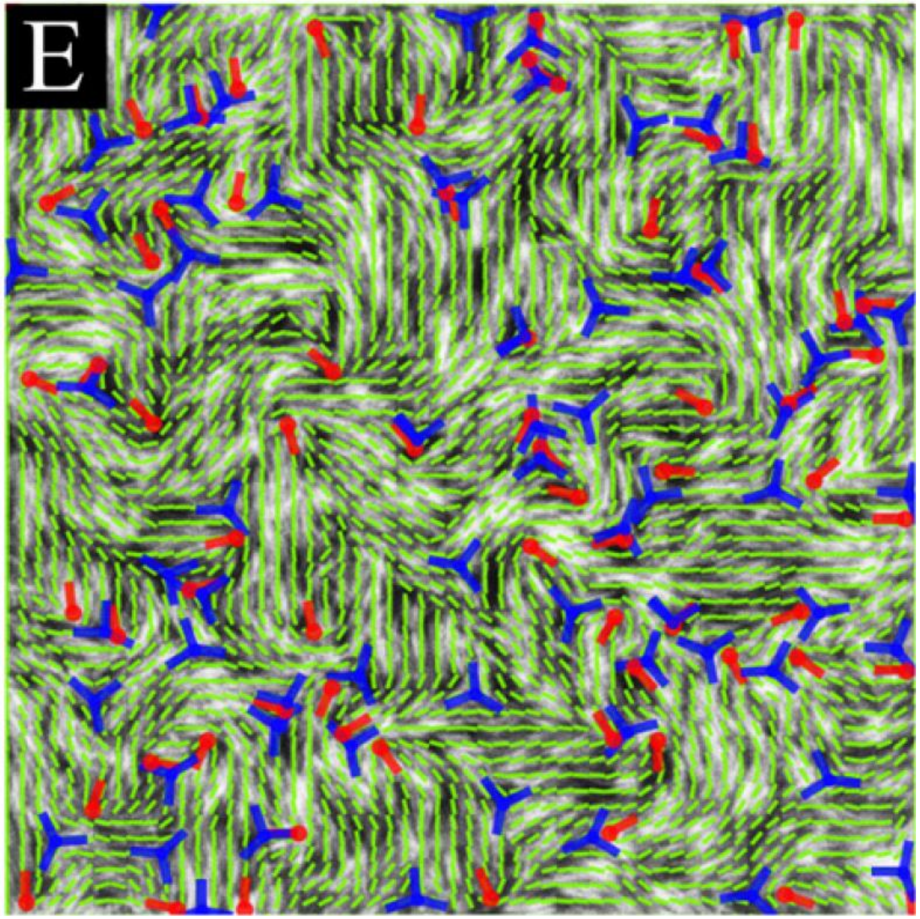
Add activity -> spontaneous creation -> steady state

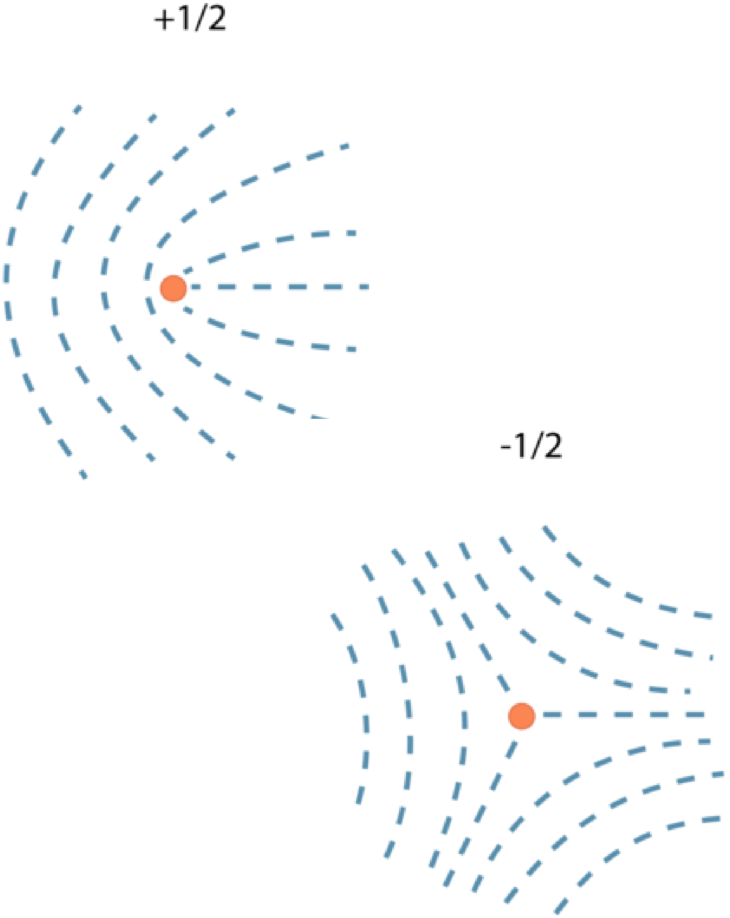
Examples:
Microtubules [Keber et al, Science 2014]
Epithelial cells [Blanch-Mercader at al, PRL 2018]
Cytoskeletal reconstitutions [Guillamat et al, Nat. Commun. 2017]
Baceria: gliding *Myxococcus xanthus* [Copenhagen et al, Nat. Phys. 2021]
Bacillus subtilis biofilms [Nijjer et al, Nat. Phys. 2023]

Topological defects

[Li et al 2019, Yashunsky et al 2024]

The bacteria are polar – but the dominating interactions are nematic





Orientation field and ±½ defects [Yashunsky et al, soft matter 2024]

Topological defects

[Li et al 2019, Yashunsky et al 2024]

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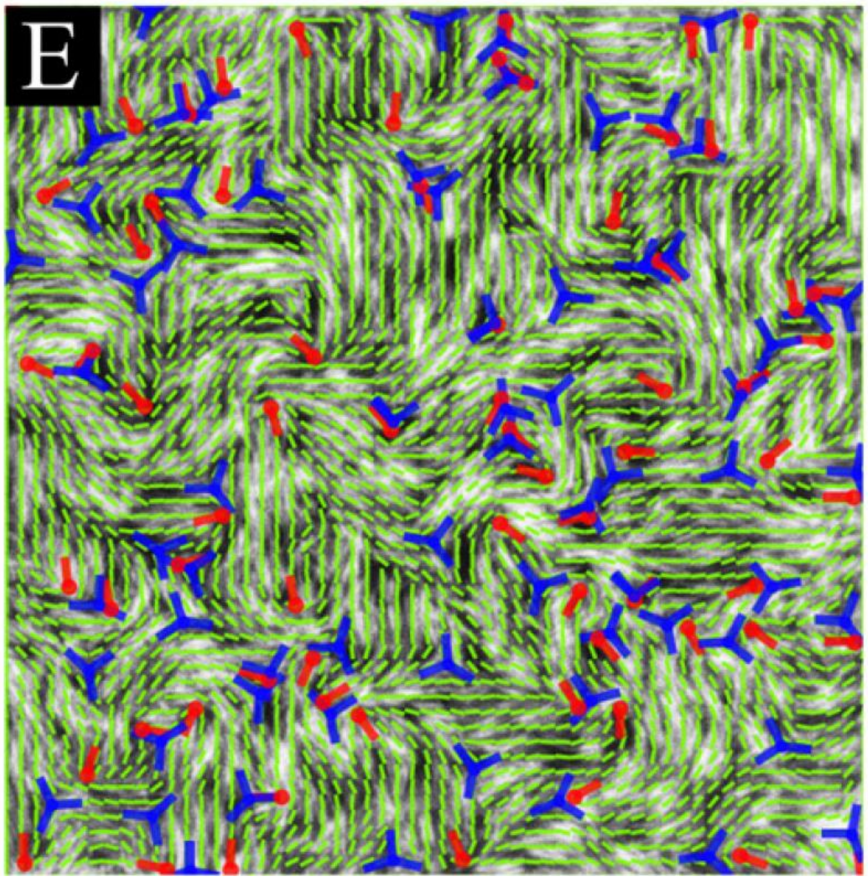

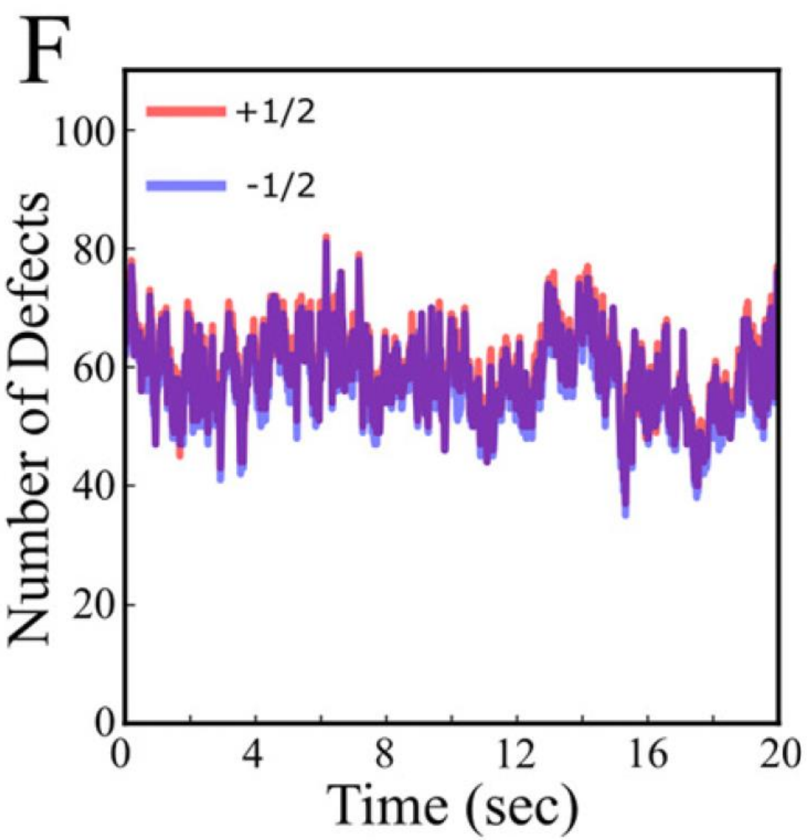

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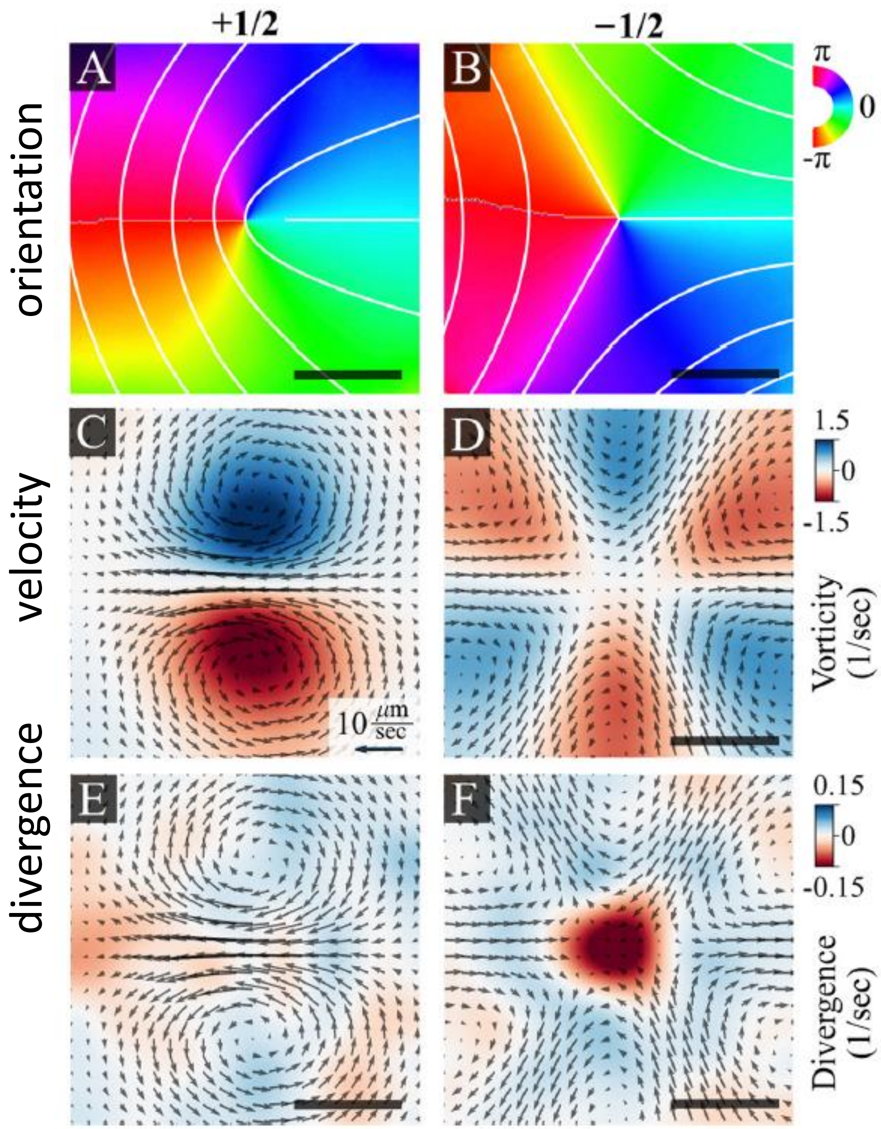
Topological defects



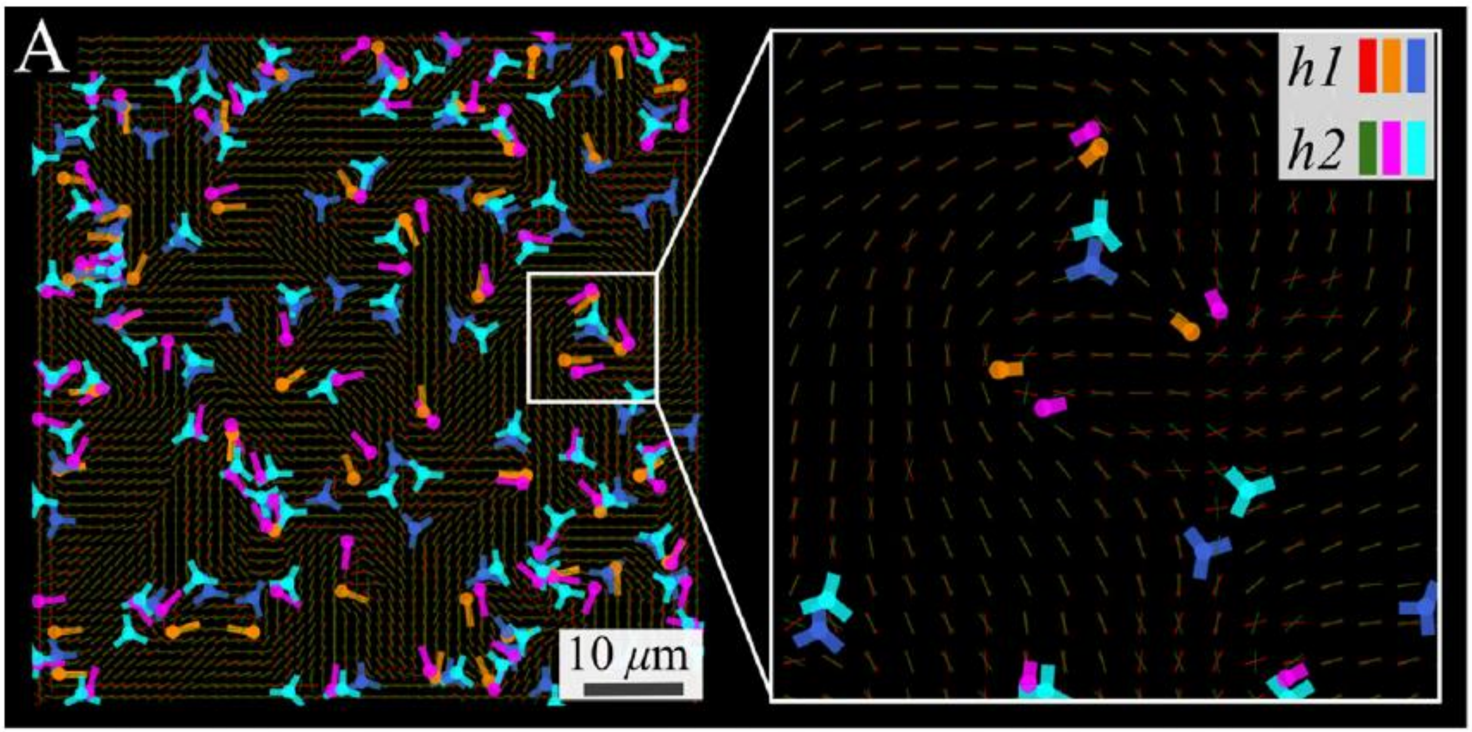
Orientation and Flow around defects agree with the theory of active nematic

Divergence field does not.
accumulation at -1/2

[Yashunsky et al, soft matter 2024]

Topological defects

3D structure – thin layer (7um)



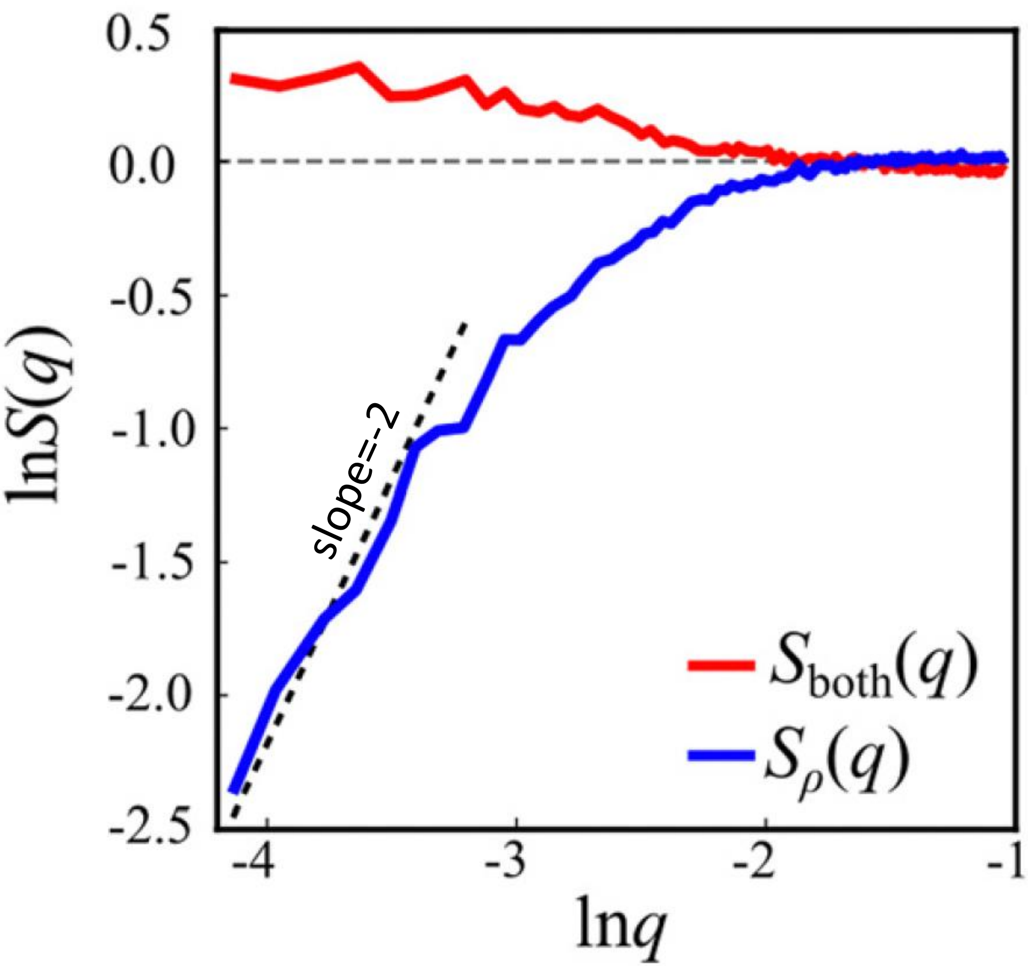
Correlations between layers – defect lines

The quasi-2D picture holds [Shendruk et al 2018]

[Yashunsky et al, soft matter 2024]

Topological defects

Structure factors – **evidence of hyperuniformity**



$$S(\mathbf{q}) = \left\langle \frac{1}{N} \left| \sum_{i=1}^{N} e^{-i\mathbf{q}\cdot\mathbf{r}_i} \right|^2 \right\rangle$$

$$S_2(\mathbf{q}) = \left\langle \frac{1}{N} \left| \sum_{i=1}^{N} \sum_{j=1}^{M} e^{-i\mathbf{q}\cdot(\mathbf{r}_i - \mathbf{R}_j)} \right|^2 \right\rangle$$

$$S_\rho(\mathbf{q}) = S_{+1/2}(\mathbf{q}) S_{-1/2}(q)/2 - S_{\pm 1/2}(\mathbf{q})$$

Slope=-2 agrees with ionic solutions at equilibrium

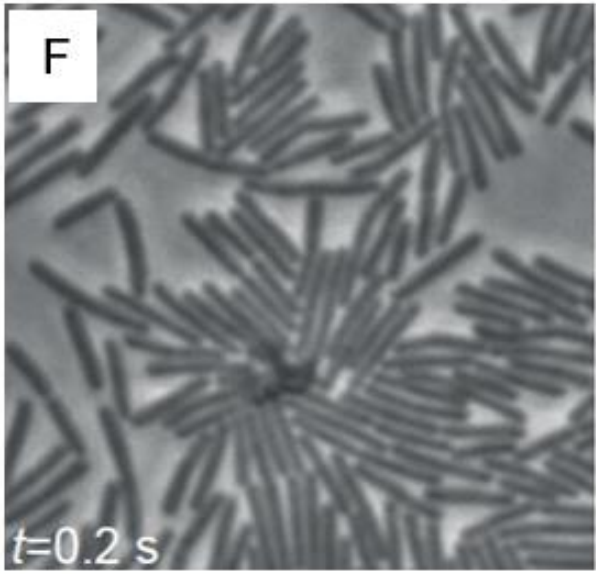
[Yashunsky et al, soft matter 2024]

Topological defects

Why defects?

Coarse-grained property – encode physical information of the microscale

- Easier to detect than single cells – allow a wider field of view
- Comparison to theory
- Study spatial distribution (entropy)
- Study creation and annihilation
- Mutants
- Coupling to biology



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Movement Ecology

REVIEW Open Access

A statistical physics view of swarming bacteria

Check for updates

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