SFB 1294 Colloquium 13.12.2024

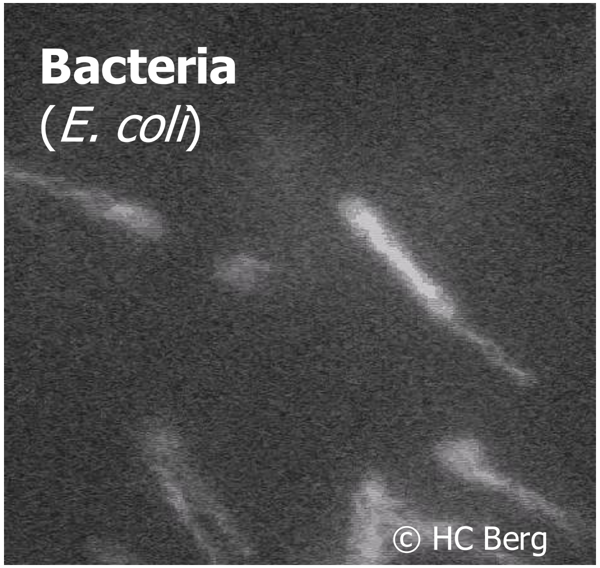
Bayesian Chemotaxis

Information theory of chemotactic agents combining spatial & temporal gradient-sensing

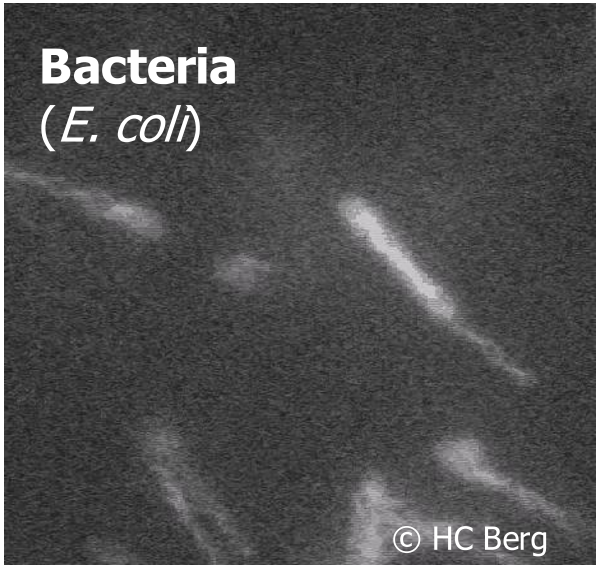
Benjamin Friedrich Biological Algorithms Group
EXC Physics of Life, TU Dresden

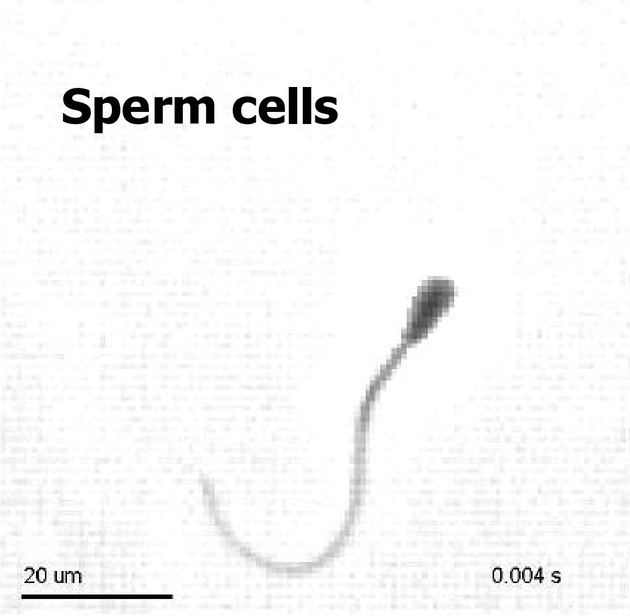
There is a myriad of cells and organisms

… that move actively



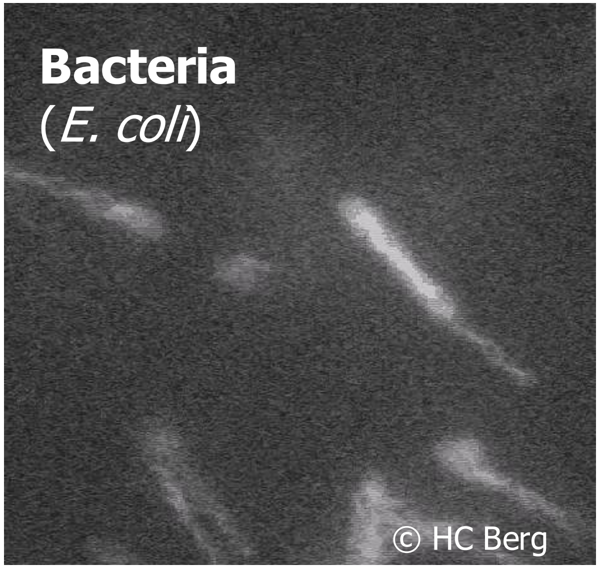
… that move actively

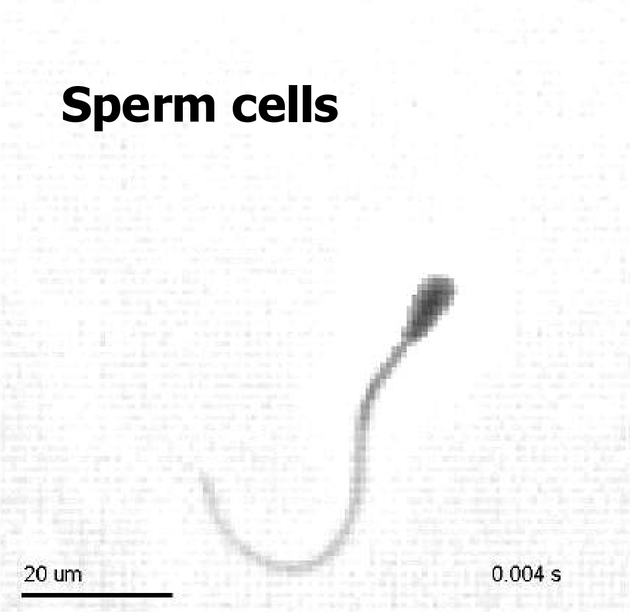


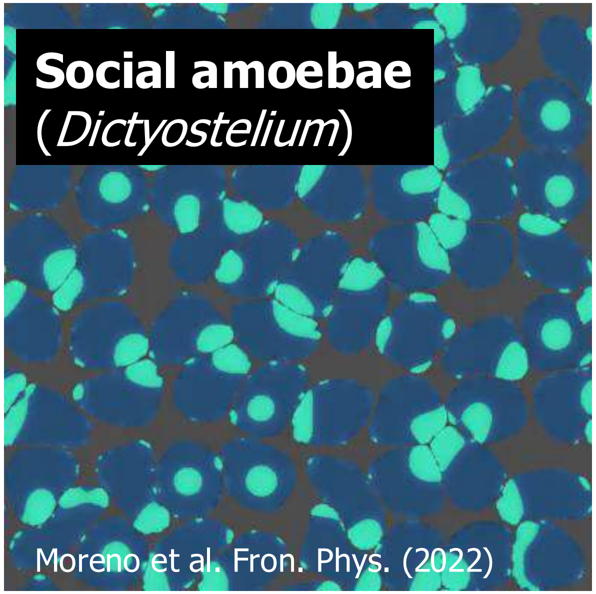


Friedrich et al. JEB (2010)

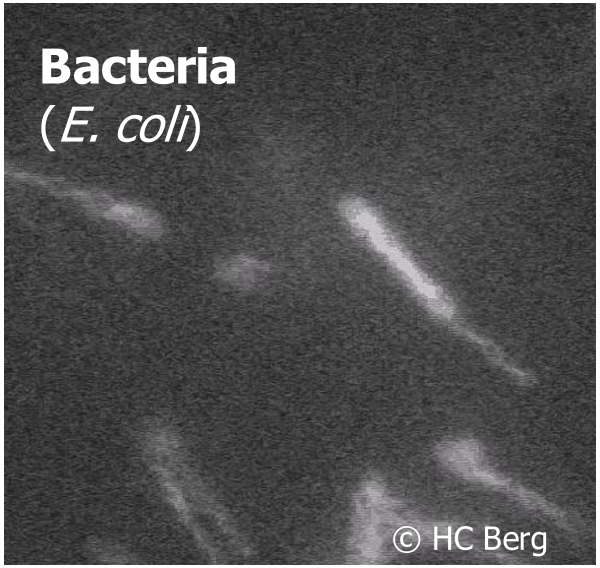
… that move actively

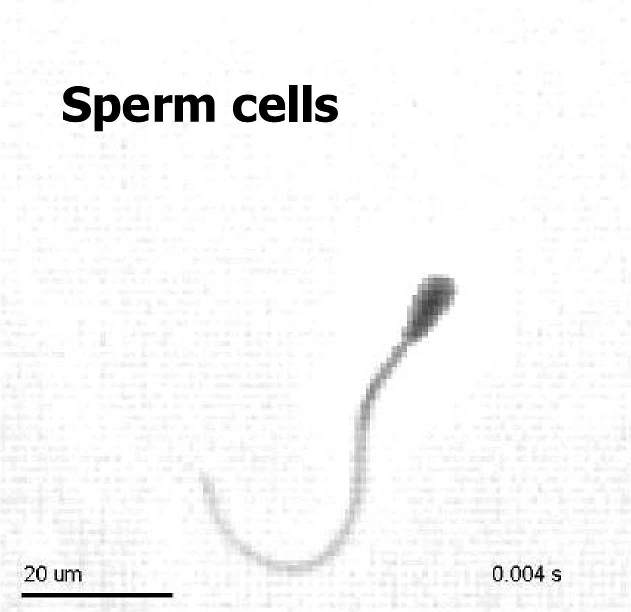


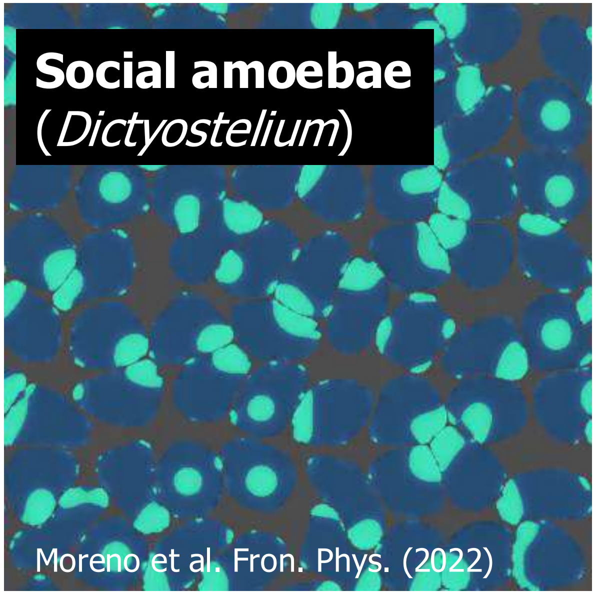




… that move actively

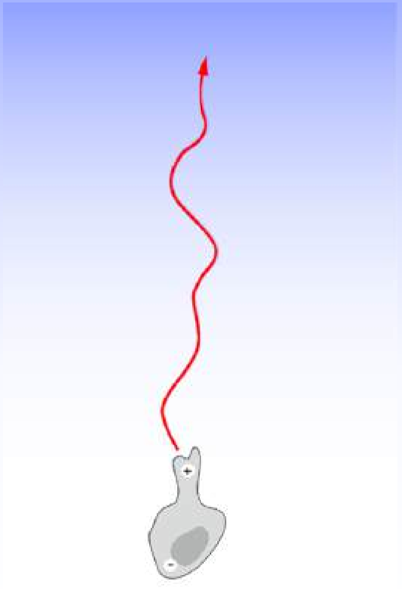






Cells follow **concentration gradients**

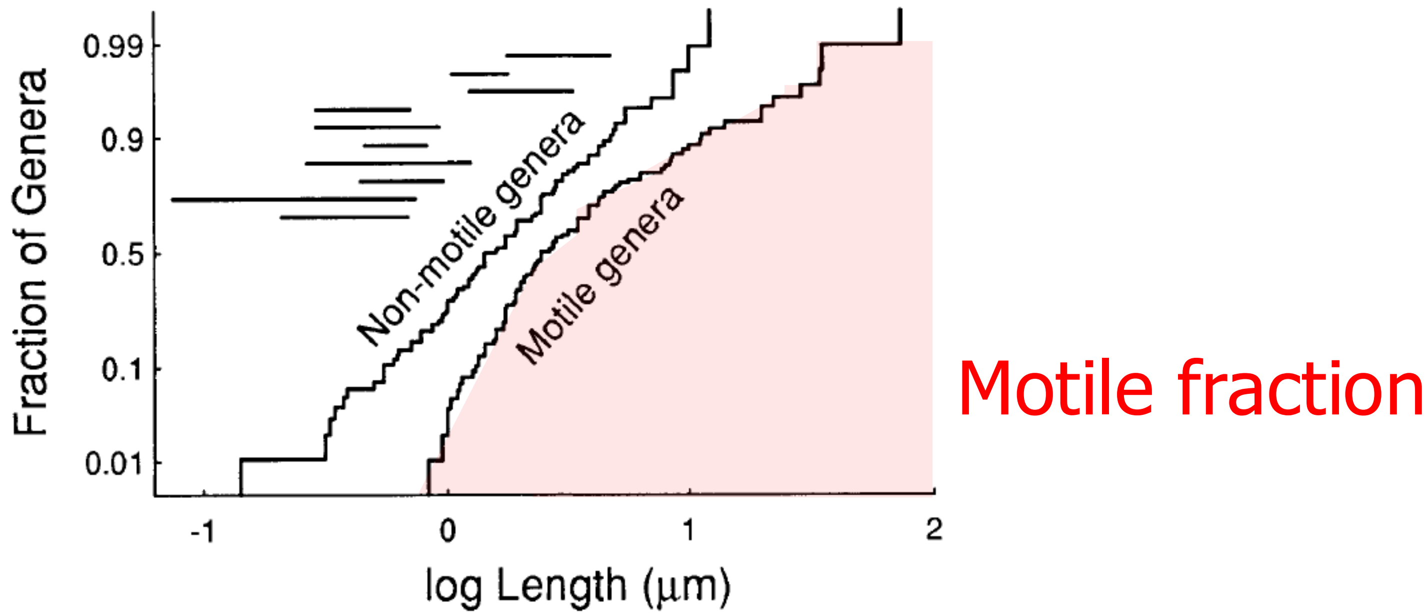
- Bacteria: food
- Sperm cells: egg
- Amoebae: social signals
- Immune cells: pathogens



Immune cells

Berg, Purcell: Biophys. J. (1977)
Dusenberry: Biophys. J. (1998)
Alvarez, Friedrich, Gompper, Kaupp: Trends Cell Biol. (2014)
Wan, Jekely: Phil. Trans. R. Soc. B (2021)

Only cells larger ½ micron are motile …

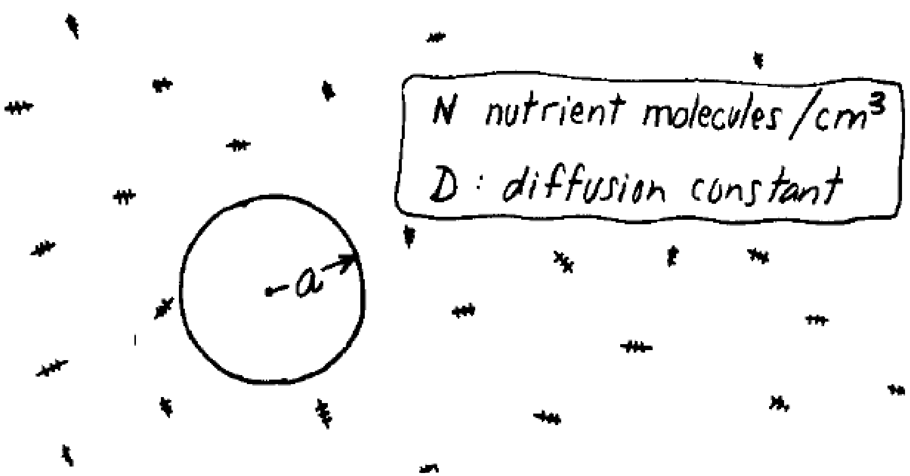


Dusenberry: PNAS (1997): **Minimum size limit for useful locomotion by free-swimming microbes**

… because active motility does not help for "grazing" …

Purcell: Am. J. Phys. (1977):

Life at low Reynolds number



Stirring vs. Diffusion

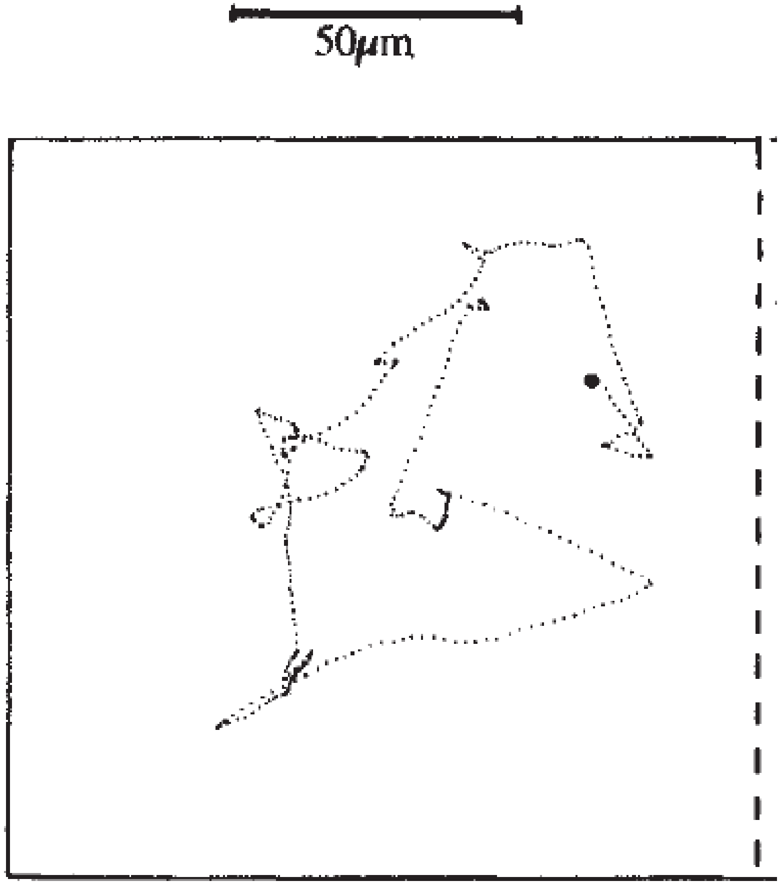
time for transport by stirring: $\frac{\ell}{v}$

time for transport by diffusion: $\frac{\ell^2}{D}$

stirring works if $\frac{\ell v}{D} > 1$

To enhance nutrient uptake
a bacterium would have to swim 1 mm/sec!

… but to find greener pastures

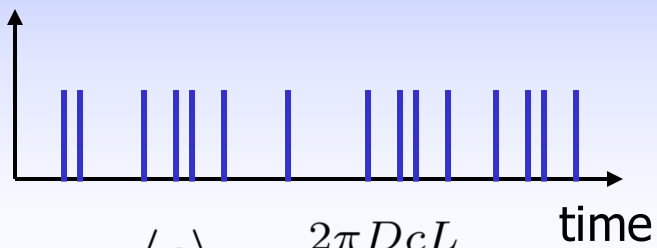


3D-tracking of run-and-tumble chemotaxis of bacterium *E. coli*

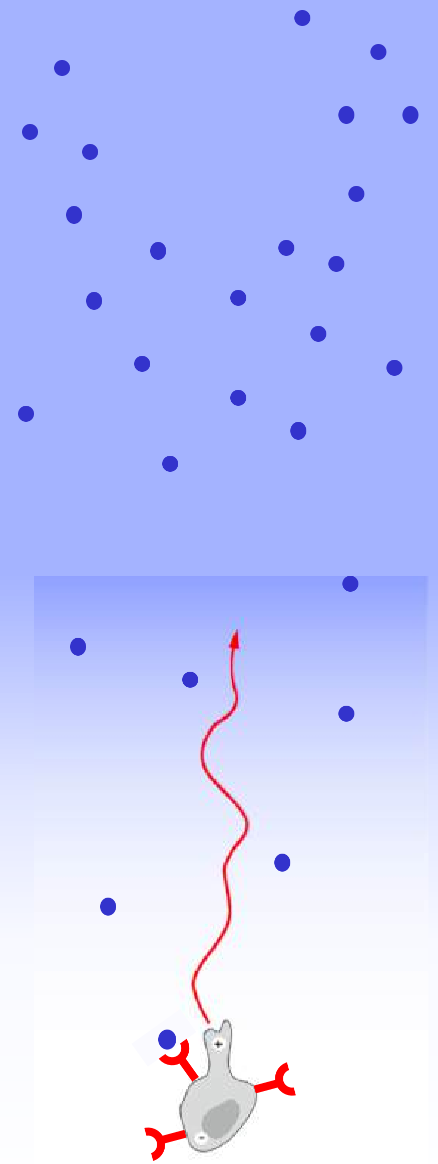
Berg, Brown: Nature (1972)

Molecule counting noise causes **sensing noise**

Detection of chemoattractant molecules



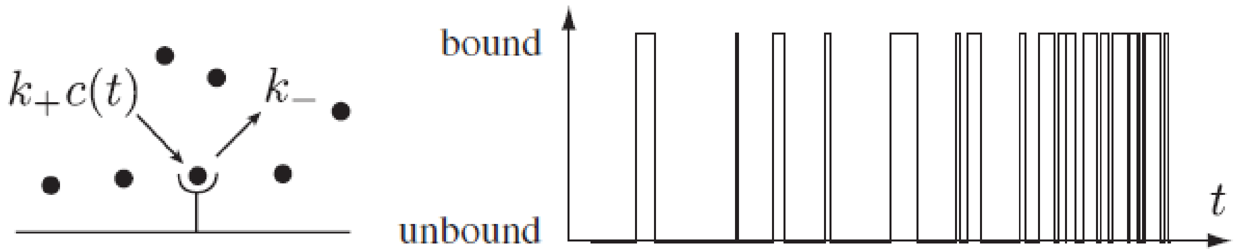
$$\langle s \rangle = \frac{2\pi D c L}{\ln(L/r)}$$



Immune cells

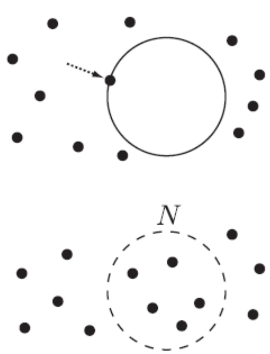
Berg, Purcell: Biophys. J. (1977)
Alvarez, Friedrich, Gompper, Kaupp: Trends Cell Biol. (2014)

How to measure a concentration?



$$\frac{\delta c}{c} \sim \sqrt{DacT}$$

diffusion coefficient | agent size | concen- tration | sensing time



Berg, Purcell: BPJ 1977
Bialek, Setayeshgar. PNAS 2005
Kaizu et al.: BPJ 2014
Mora, Wingreen: PRL 2010, …

Concentration sensing as a **Bayesian decision** problem

PRL **104**, 228104 (2010) PHYSICAL REVIEW LETTERS week ending 4 JUNE 2010

Implementation of Dynamic Bayesian Decision Making by Intracellular Kinetics

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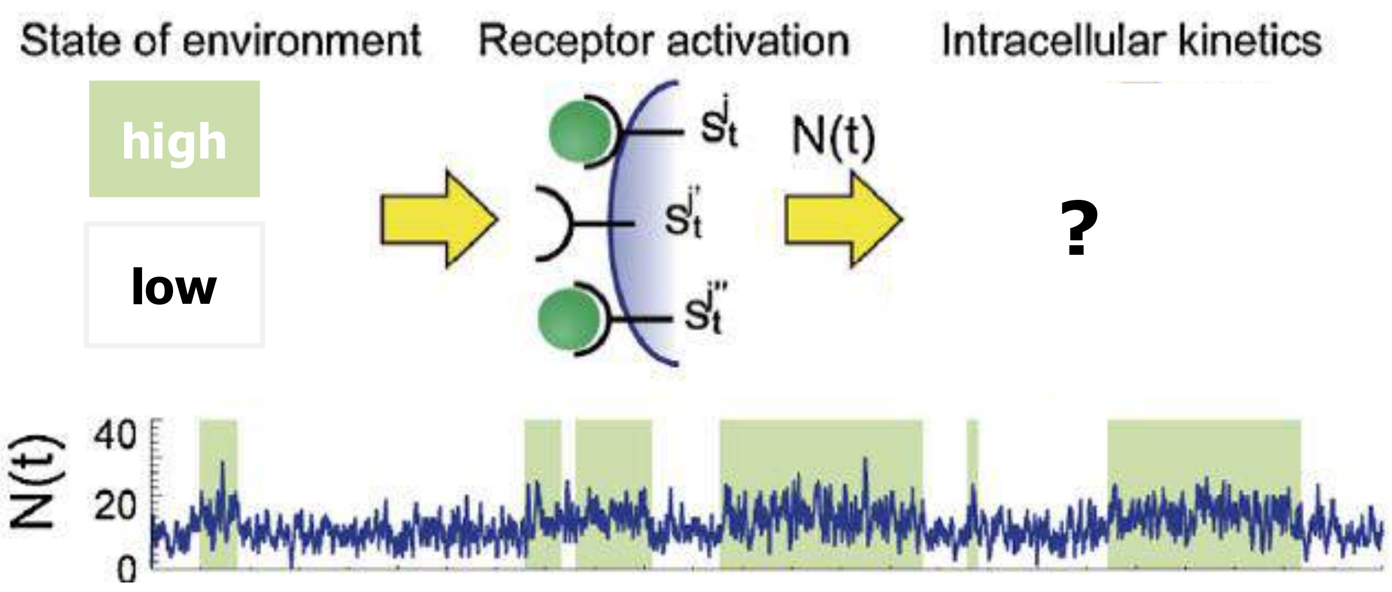
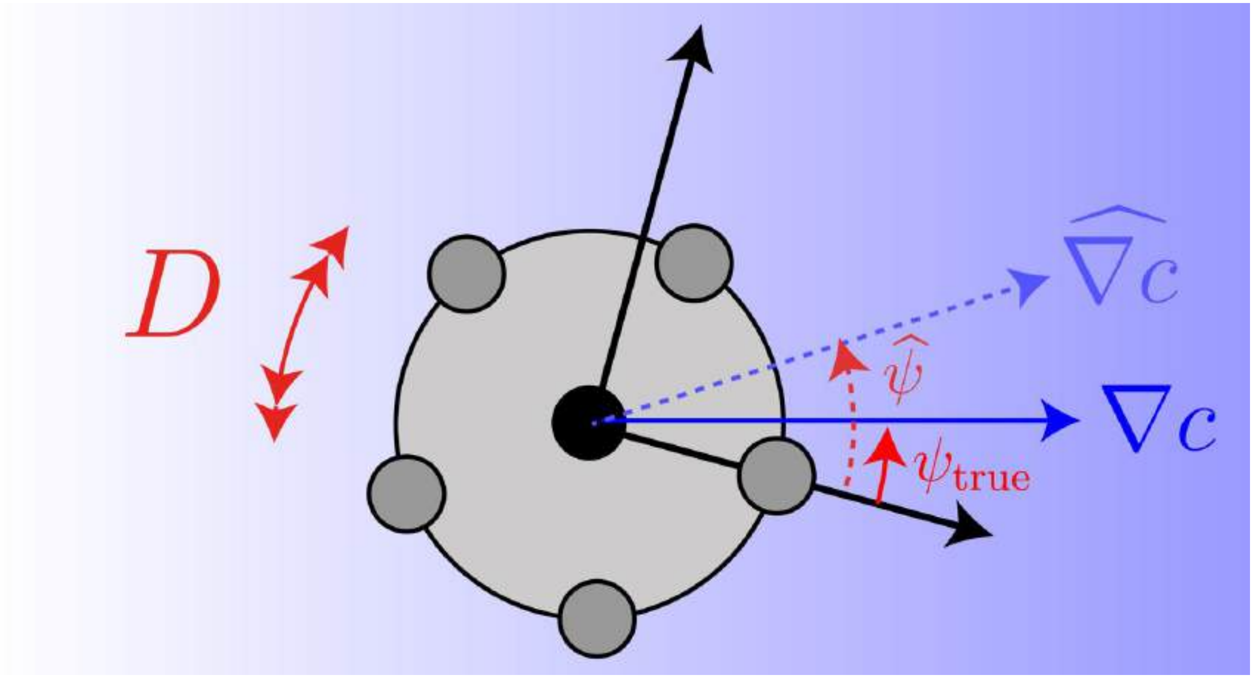
Institute of Industrial Science, The University of Tokyo, 4-6-1 Komaba Meguro-ku, Tokyo 153-8505, Japan

(Received 20 January 2010; published 3 June 2010)

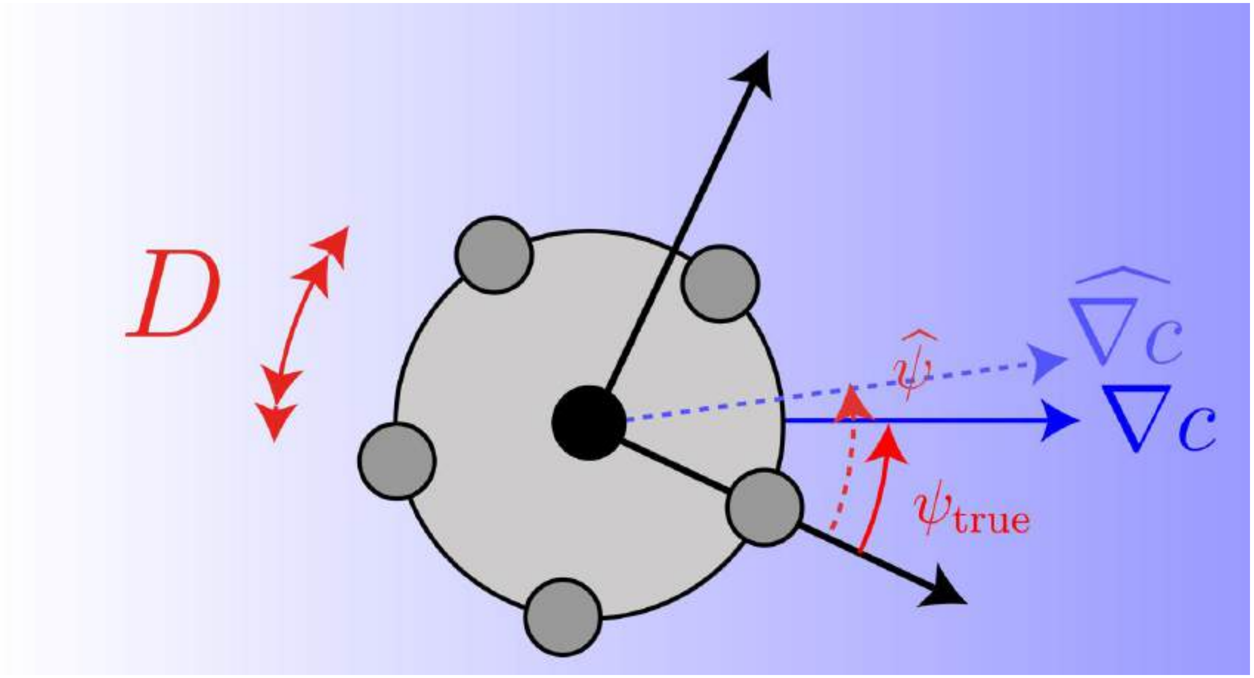


But how to estimate a concentration **gradient?**



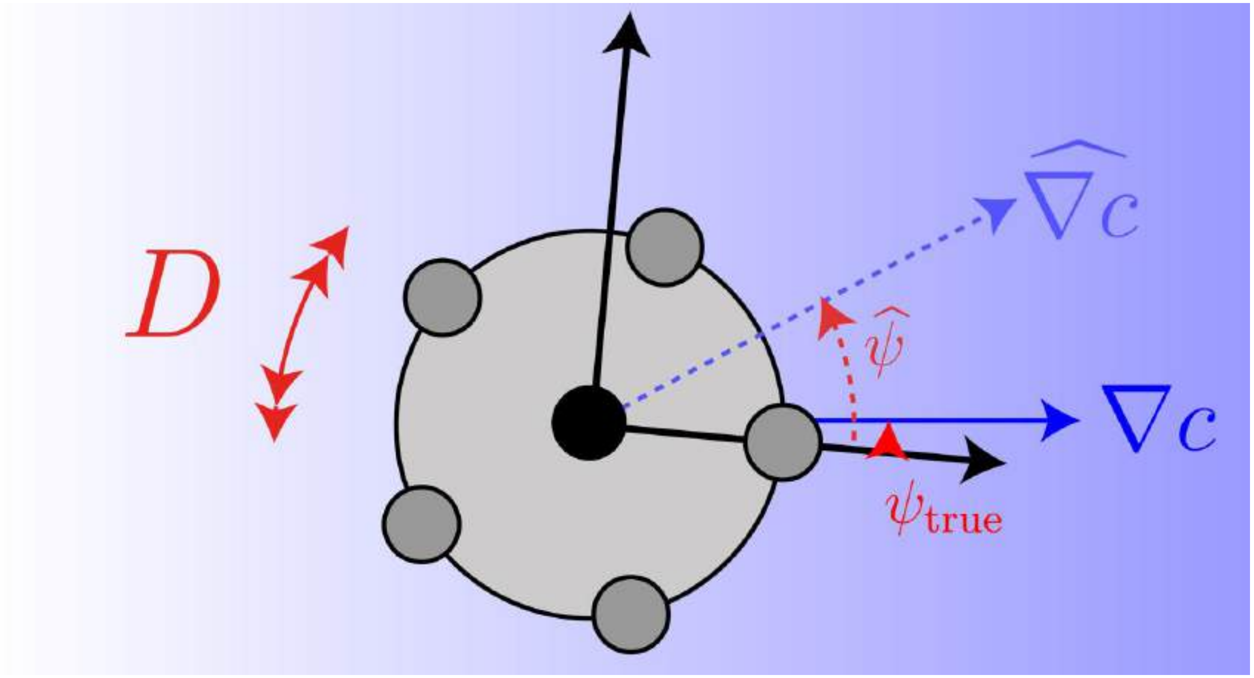
Novak et al. NJP 2021

… in the presence of **sensing** and **motility noise?**



Novak et al. NJP 2021

… in the presence of **sensing** and **motility noise?**

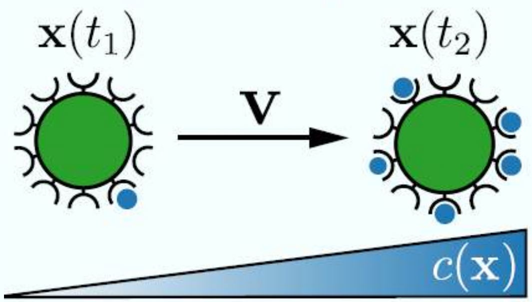


Novak et al. NJP 2021

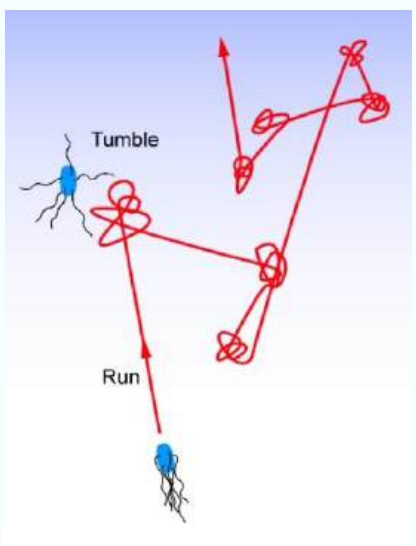
Two fundamental **gradient-sensing** strategies

TC

Temporal comparison



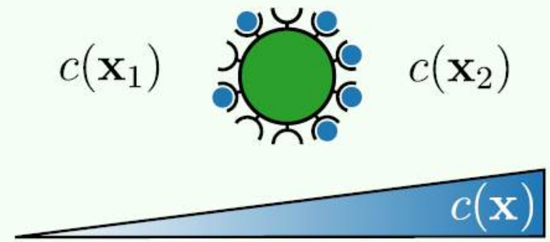
run & tumble

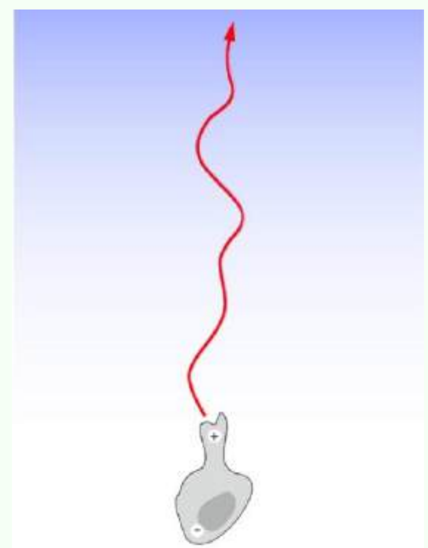


Bacterium *E. coli*

SC

Spatial comparison

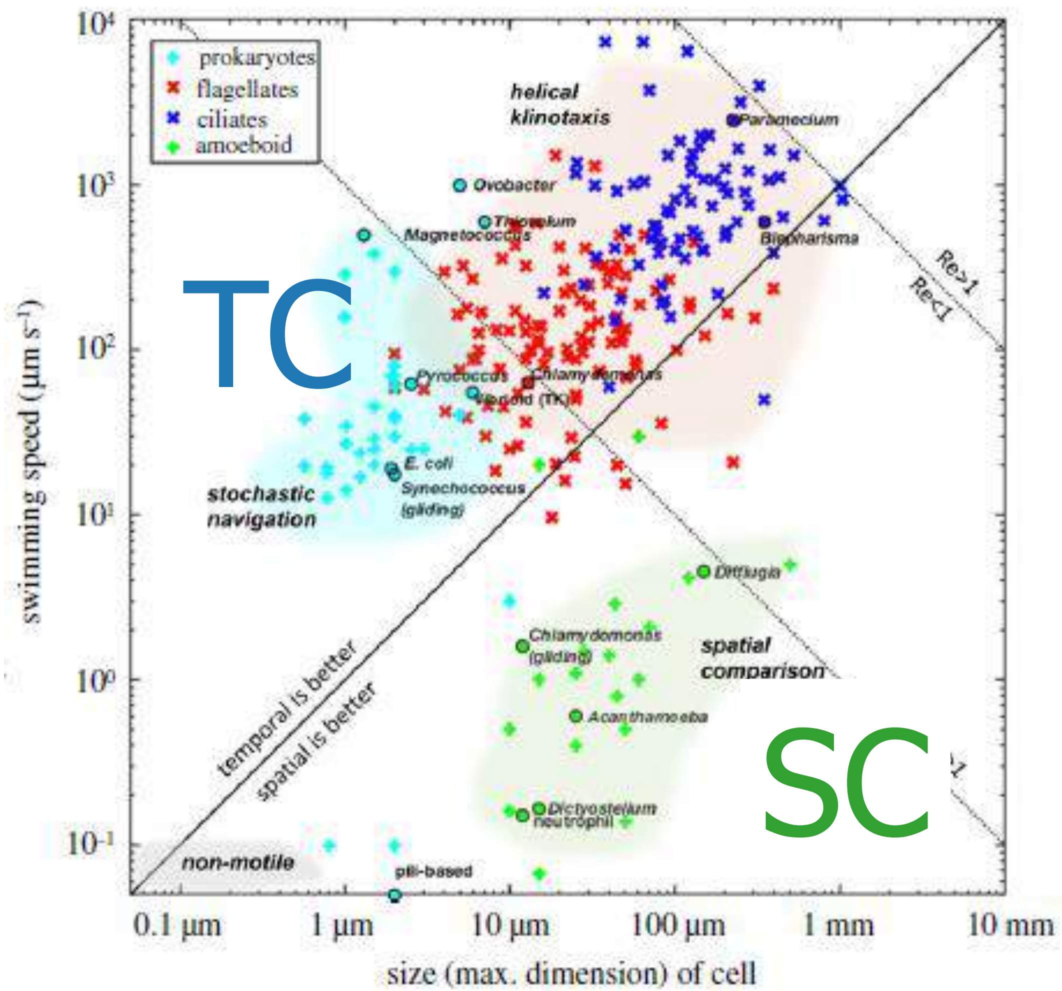


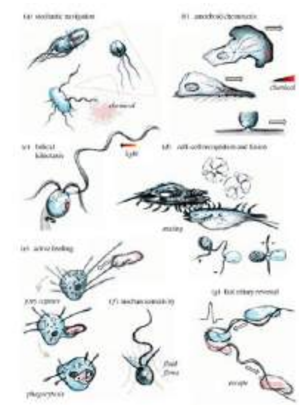


Immune cells

Gradient-sensing strategy depends on **size** & **speed**

speed



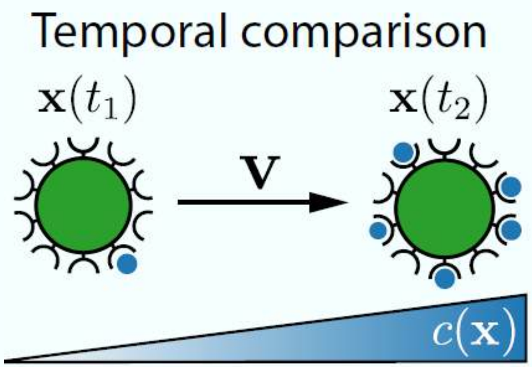


size

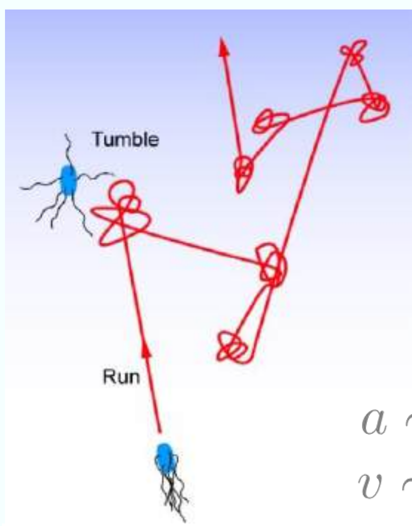
Wan et al.: Phil. Trans. R. Soc. B 2021

Gradient-sensing by **Temporal Comparison**

TC



run & tumble



$a \sim 3\,\mu\mathrm{m}$
$v \sim 10\,\mu\mathrm{m/s}$

Bacterium *E. coli*

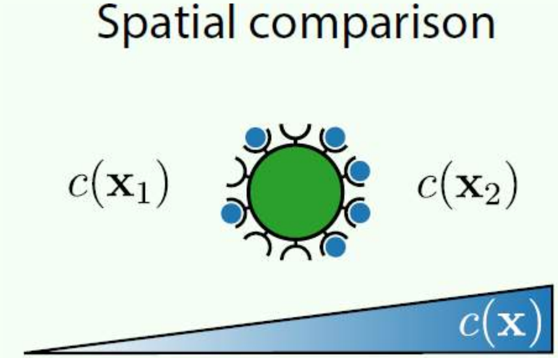
$$\mathrm{SNR}^{\mathrm{TC}} = \frac{v^2 t^3\, \lambda |\nabla c|^2}{c}$$

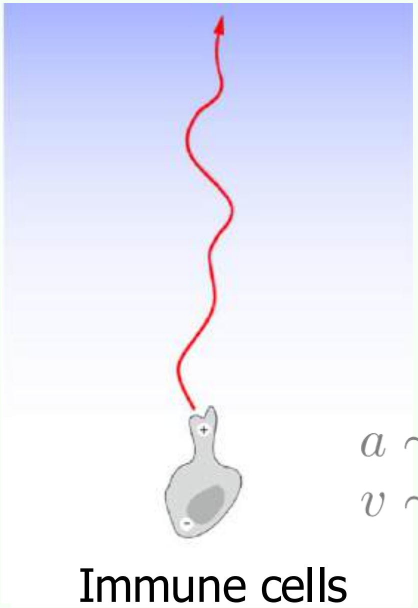
Gradient-sensing by temporal comparison **information-limited** for shallow gradients:

- Brumley et al. PNAS 2019
- Mattingly et al. Nat. Phys. 2021
- Thornton et al. Nat. Commun. 2020
- Nakamura et al. Phys. Rev. Res. 2022

Gradient-sensing by **Spatial Comparison**

SC





$$a \sim 100\ \mu\mathrm{m}$$
$$v \sim 1\ \mu\mathrm{m}/\mathrm{min}$$

$$\mathrm{SNR}^{\mathrm{SC}} = \frac{a^2 t\, \lambda |\nabla c|^2}{c}$$

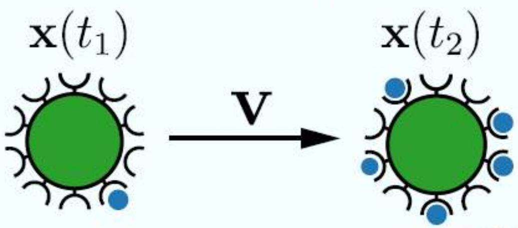
Gradient-sensing by spatial comparison is **information-limited** for shallow gradients:

- Van Haastert et al. BPJ 2007
- Amselem et al. PRL 2012
  Fuller et al. PNAS 2010

Two fundamental **gradient-sensing** strategies

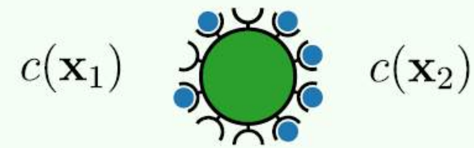
TC

Temporal comparison

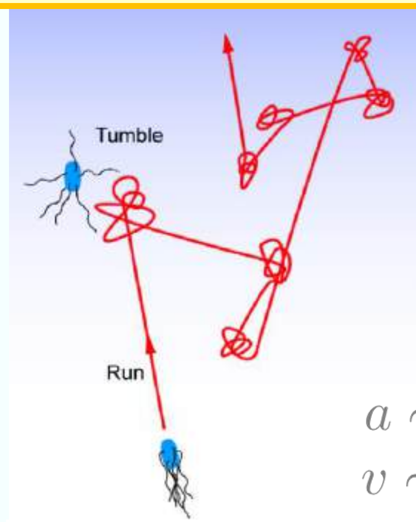


SC

Spatial comparison

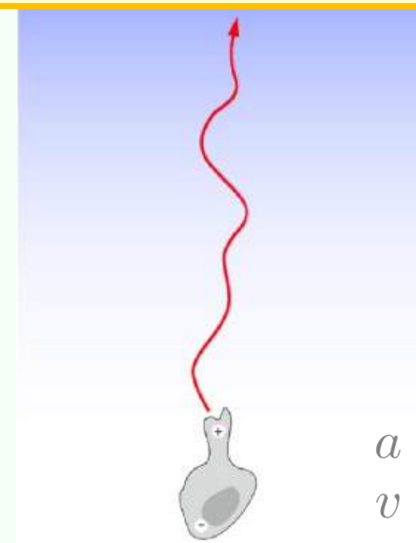


Which strategy works best when?



$a \sim 3\,\mu\mathrm{m}$
$v \sim 10\,\mu\mathrm{m/s}$

Bacterium *E. coli*



$a \sim 100\,\mu\mathrm{m}$
$v \sim 1\,\mu\mathrm{m/min}$

Immune cells

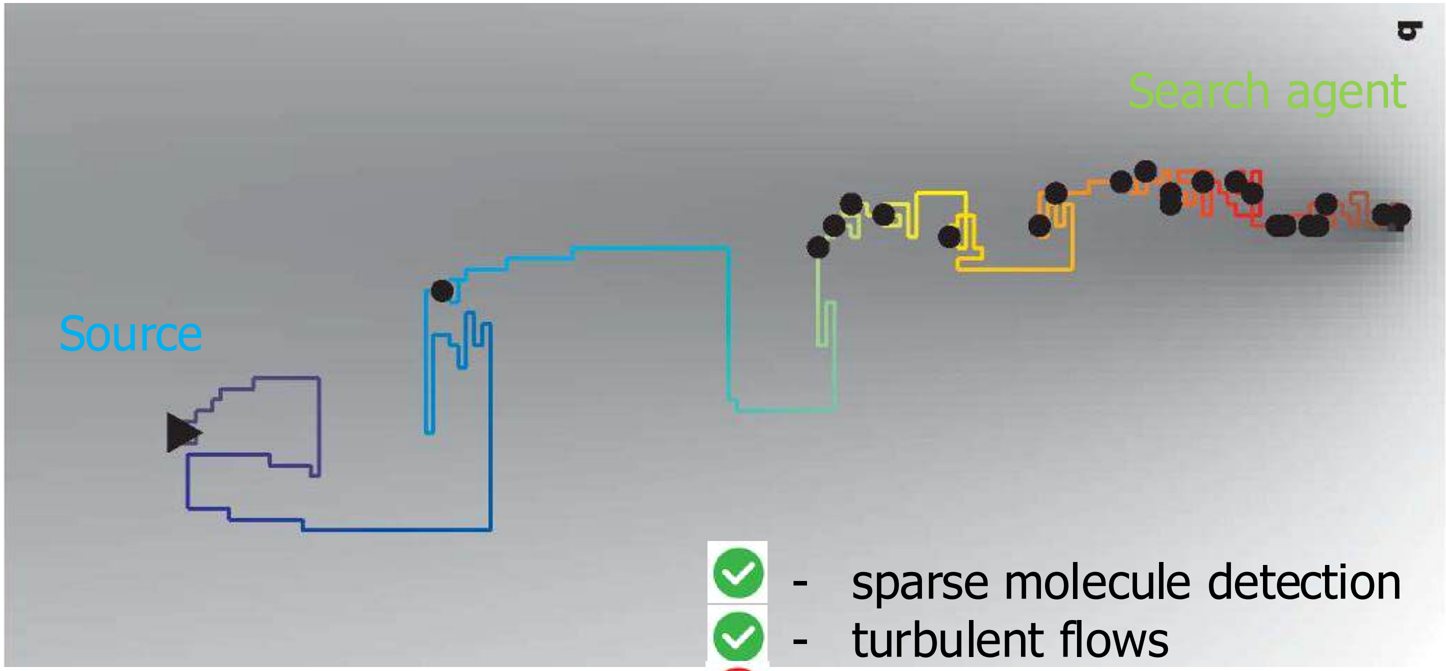
Infotaxis: Update likelihood map of source position

Vergassola et al. Nature 2007:

'Infotaxis' as a strategy for searching without gradients

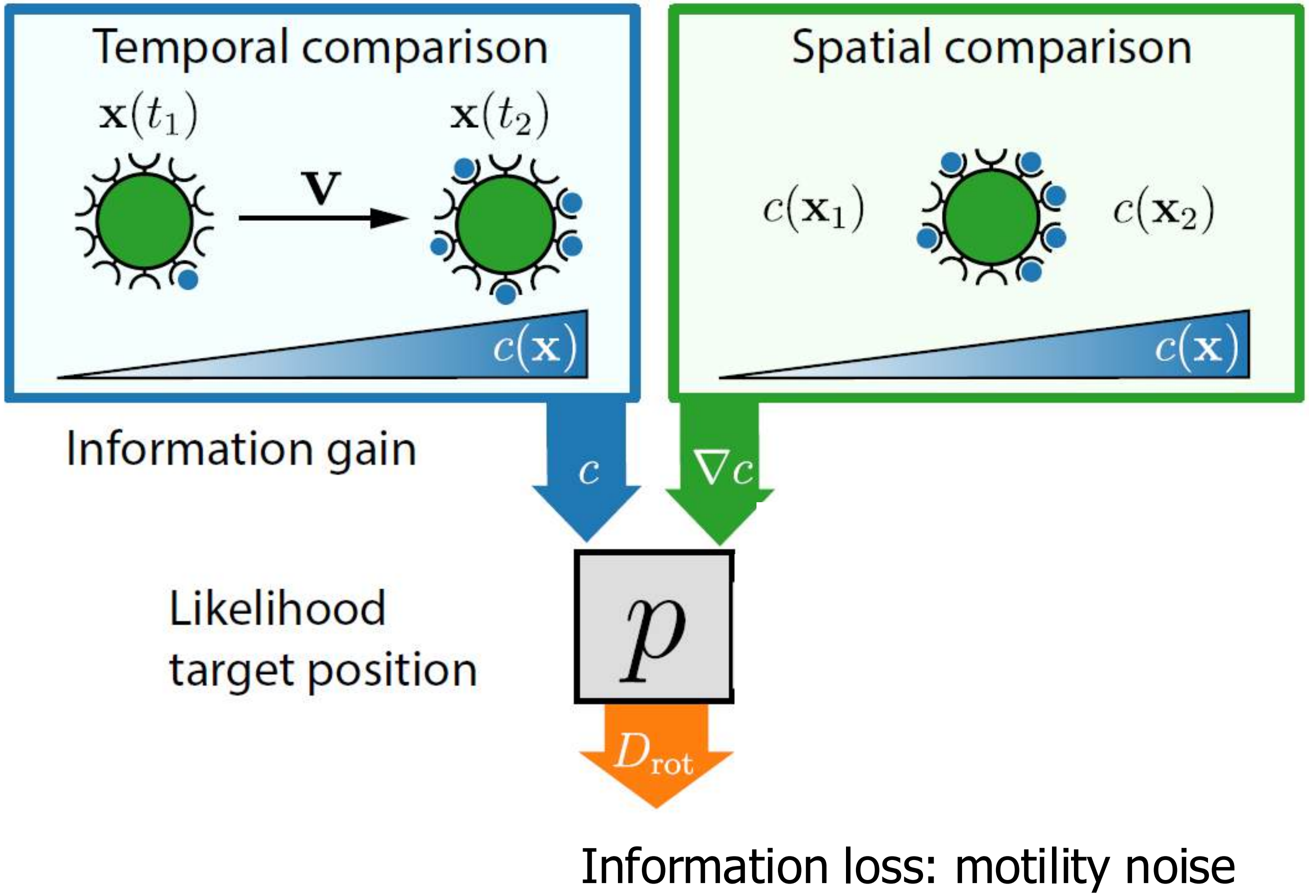
Likelihood of source position $P_t(\mathbf{r}_0) = \frac{\mathcal{L}_{\mathbf{r}_0}(\mathcal{T}_t)}{\int \mathcal{L}_{\mathbf{x}}(\mathcal{T}_t)\mathrm{d}\mathbf{x}}$ Likelihood of past molecule detections

Unlimited information processing capabilities



- sparse molecule detection
- turbulent flows
- no spatial sensing
- no motility noise: allocentric map

An ideal chemotactic agent capable of both **TC** and **SC**



Rode et al. PRX Life 2024

The agent detects both **time and position** of molecules

$\mathbf{s}(t) =$ [redacted]

Vector-val[redacted]
= time & position of molecule detections

Bayesian updating of a likelihood map of target position

Bayes' rule:

new measurement

$$p(\mathbf{x}, t + \Delta t) \sim p(\textstyle\int_{\Delta t} s(t) | \mathbf{x})\, p(\mathbf{x}, t)$$

new likelihood map of target position

cond. prob. of measurement

old likelihood map of target position

Bayesian updating of a likelihood map of target position

Bayes' rule:

new measurement

$$p(\mathbf{x}, t+\Delta t) \sim p\left(\int_{\Delta t} s(t) \middle| \mathbf{x}\right) p(\mathbf{x}, t)$$

new likelihood map of target position

cond. prob. of measurement

old likelihood map of target position

Time-continuous limit:

TC

SC

$$\frac{\partial}{\partial t} p(\mathbf{x},t) = \boxed{\underbrace{(s - \mathbb{E}\, s)\left(\frac{J}{\langle J\rangle} - 1\right) p}_{\mathrm{TC}}} + \boxed{\underbrace{(\mathbf{s} - \mathbb{E}(\mathbf{s}|s>0)) \cdot \left(\frac{a\nabla c}{c} - \frac{\langle a\nabla c\rangle}{\langle c\rangle}\right) \frac{Jp}{\langle J\rangle}}_{\mathrm{SC}}}$$

$$+ \underbrace{\boxed{D_{\mathrm{rot}} \frac{\partial^2 p}{\partial \varphi^2}}}_{\text{motility noise}} + \underbrace{\mathbf{v} \cdot \nabla p}_{\text{co-advection}} + \mathcal{O}(a^2)\,,$$

J … current of hits

Only TC: Barbieri et al. EPL 2011

TC+SC: Auconi et al. EPL 2022

Expected **information gain**

Bayes' rule:

new measurement

$$p(\mathbf{x}, t+\Delta t) \sim p\left(\int_{\Delta t} s(t) \middle| \mathbf{x}\right) p(\mathbf{x}, t)$$

new likelihood map of target position

cond. prob. of measurement

old likelihood map of target position

Expected **information gain:**

TC

SC

$$\mathbb{E}\frac{d}{dt}I = \underbrace{\left\langle J \ln\left(\frac{J}{\langle J\rangle}\right)\right\rangle}_{\mathrm{TC}} + \underbrace{\frac{1}{4}\left\langle J\left|\frac{a\nabla c}{c} - \frac{\langle a\nabla c\rangle}{\langle c\rangle}\right|^2\right\rangle}_{\mathrm{SC}} + \underbrace{D_{\mathrm{rot}}\langle\frac{\partial^2}{\partial\varphi^2}\ln p\rangle}_{\text{motility noise}} + \mathcal{O}(a^3)$$

> 0 > 0 < 0

Auconi et al. EPL 2022

Rode et al. PRX Life 2024

Expected **information gain**

Bay

r

Two decision strategies

Exploration
Maximize expected
information gain
Vergassola et al. Nature 2007

Exploitation
Maximum-likelihood

Expected
information gain:

TC

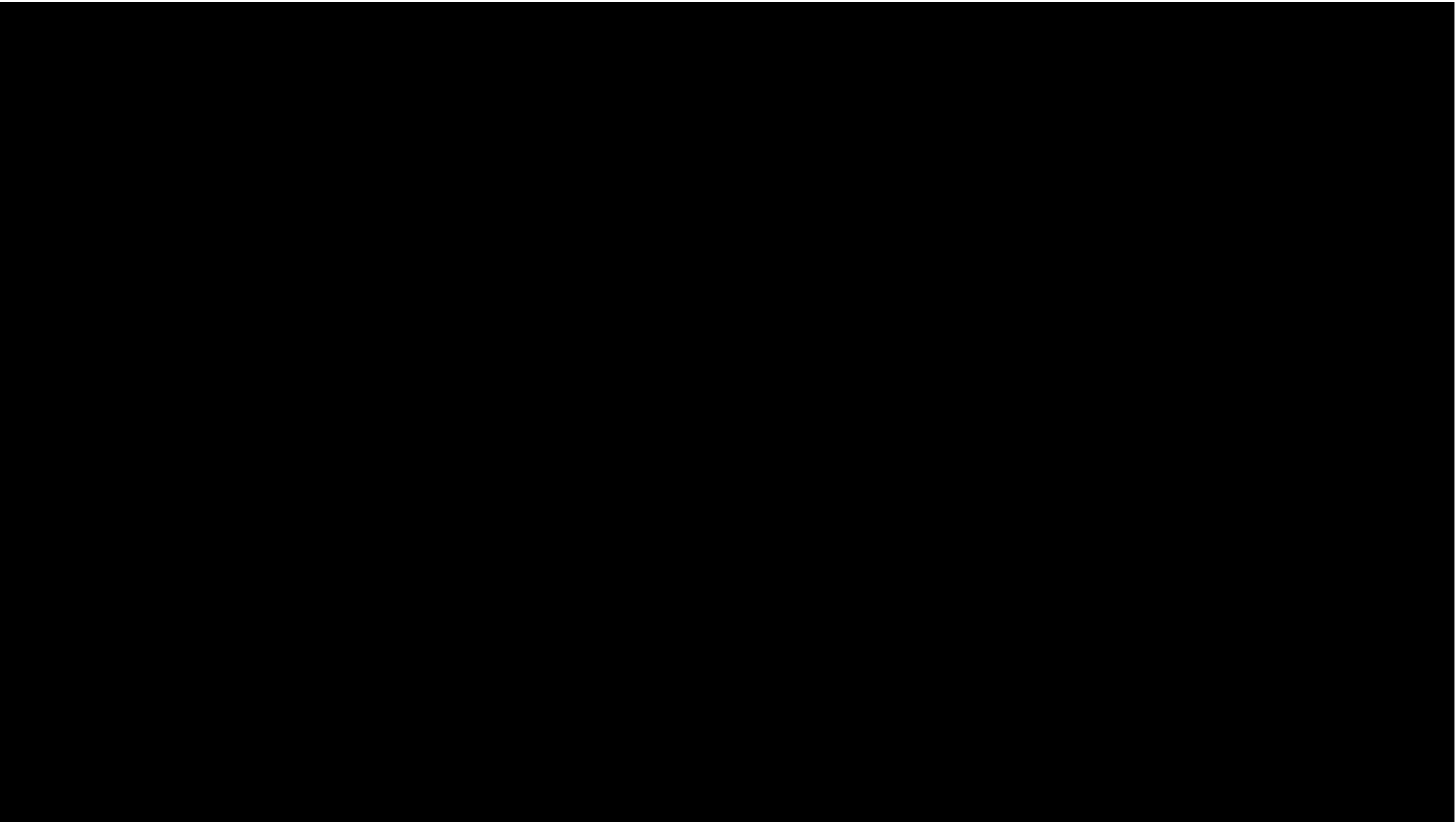
SC

$$\mathbb{E}\frac{d}{dt}I = \boxed{\underbrace{\left\langle J \ln\left(\frac{J}{\langle J\rangle}\right)\right\rangle}_{\mathrm{TC}}} + \boxed{\underbrace{\frac{1}{4}\left\langle J \left|\frac{a\nabla c}{c} - \frac{\langle a\nabla c\rangle}{\langle c\rangle}\right|^2\right\rangle}_{\mathrm{SC}}} + \boxed{\underbrace{D_{\mathrm{rot}}\left\langle\frac{\partial^2}{\partial\varphi^2}\ln p\right\rangle}_{\text{motility noise}}} + \mathcal{O}(a^3)$$

> 0 > 0 < 0

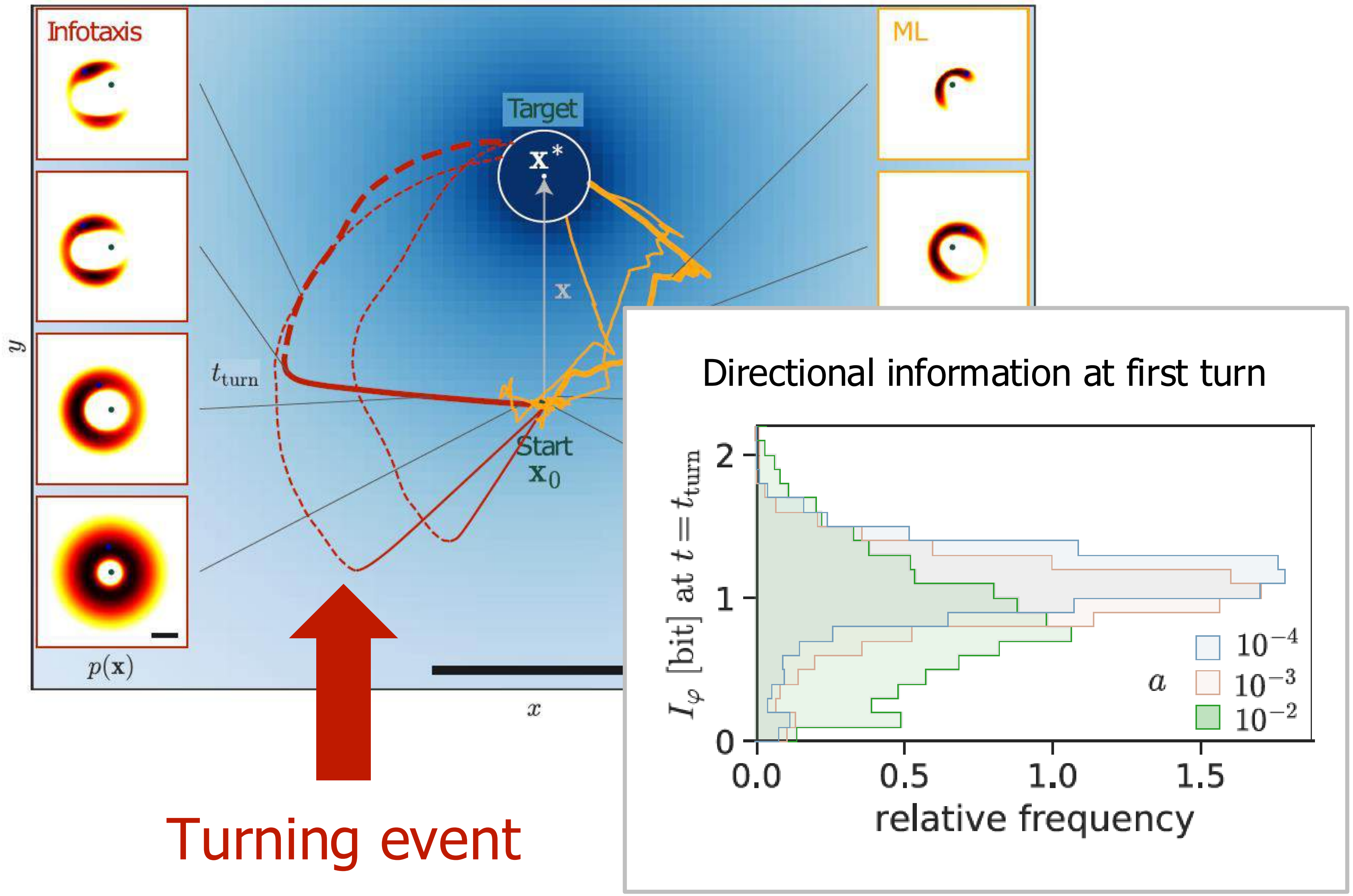
Auconi et al. EPL 2022
Rode et al. PRX Life 2024

Stereotypic navigation in the absence of motility noise

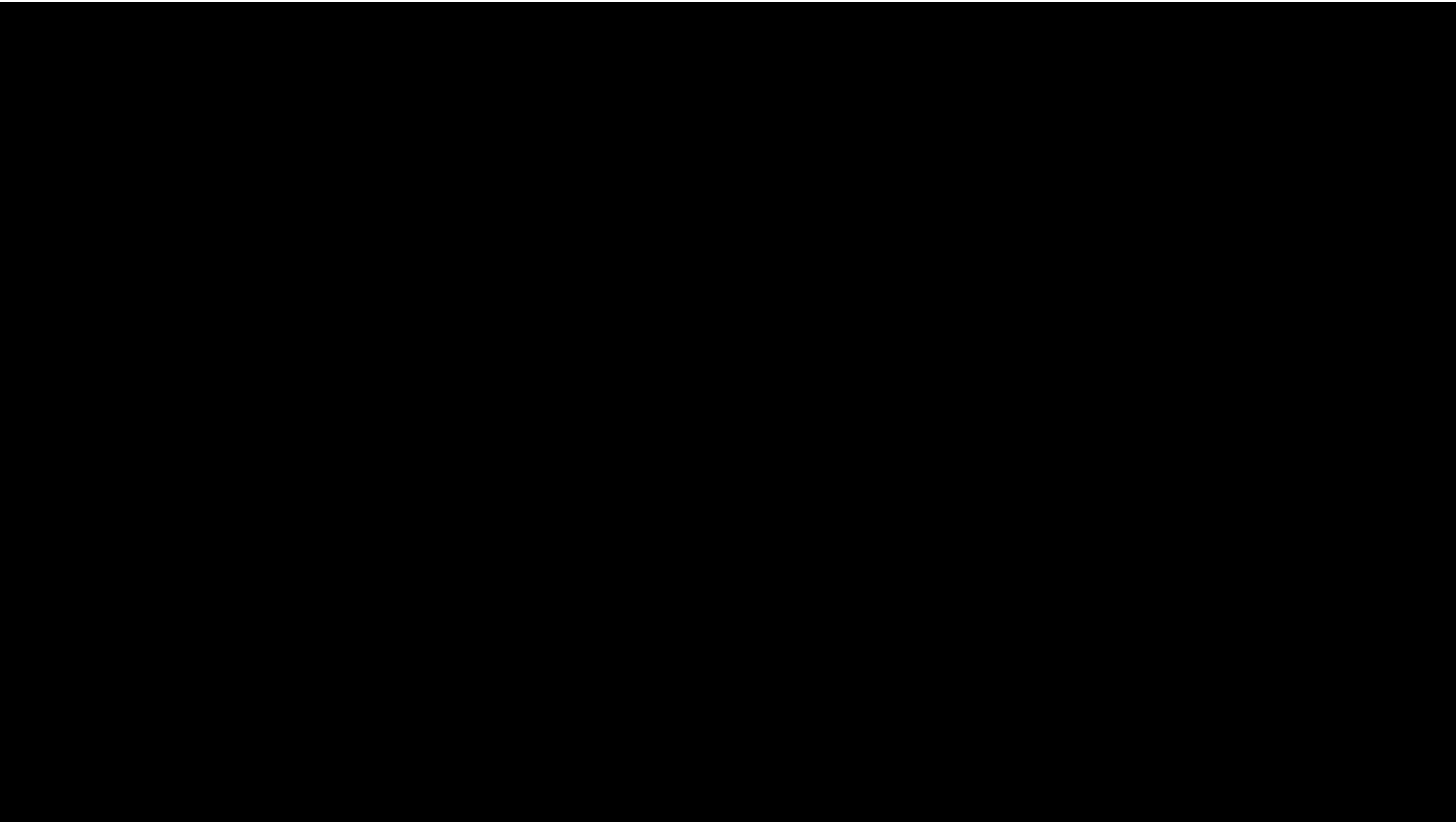


Rode et al. PRX Life 2024

Fun fact: infotaxis agents turn first when they got **1 bit**



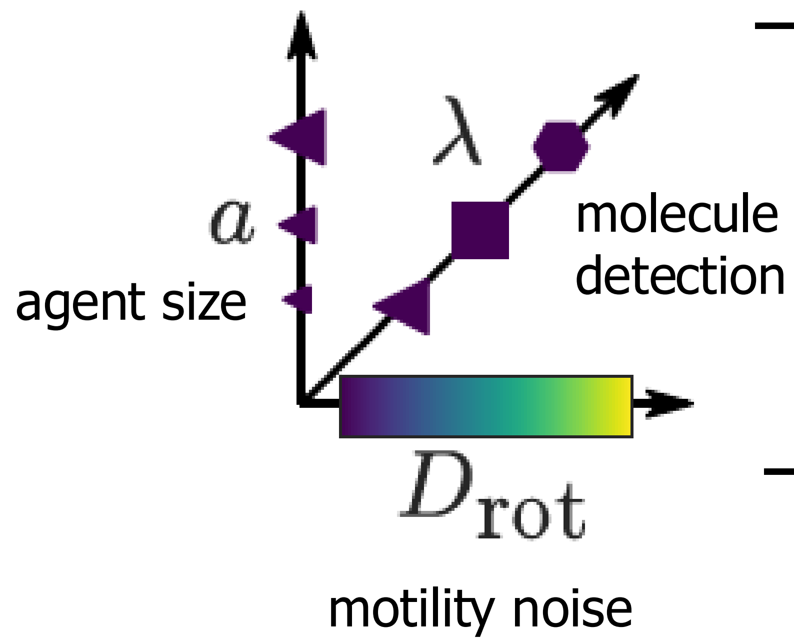
Biased random walk with **motility noise**



Rode et al. PRX Life 2024

Information decomposition as function of noise and size

Three fundamental parameters
(speed can be eliminated)

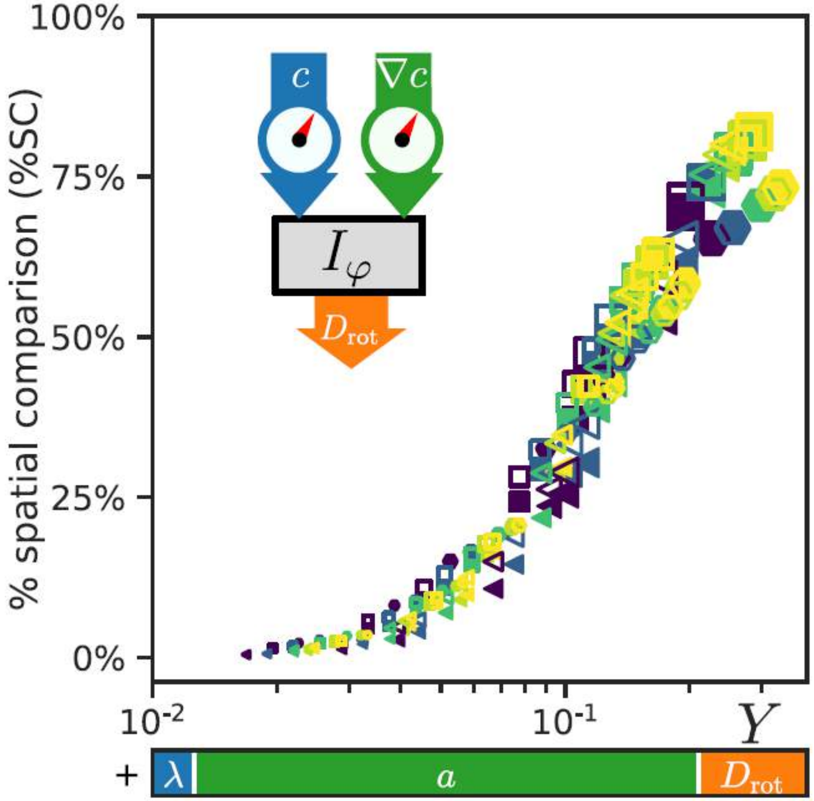


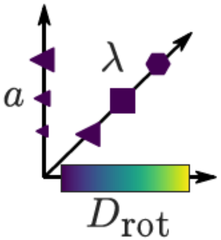
Empirical power-law for
"master" parameter

$$Y \sim \lambda^{\alpha} a^{\beta} D_{\rm rot}^{\gamma}$$

Rode et al. PRX Life 2024

Information decomposition as function of noise and size



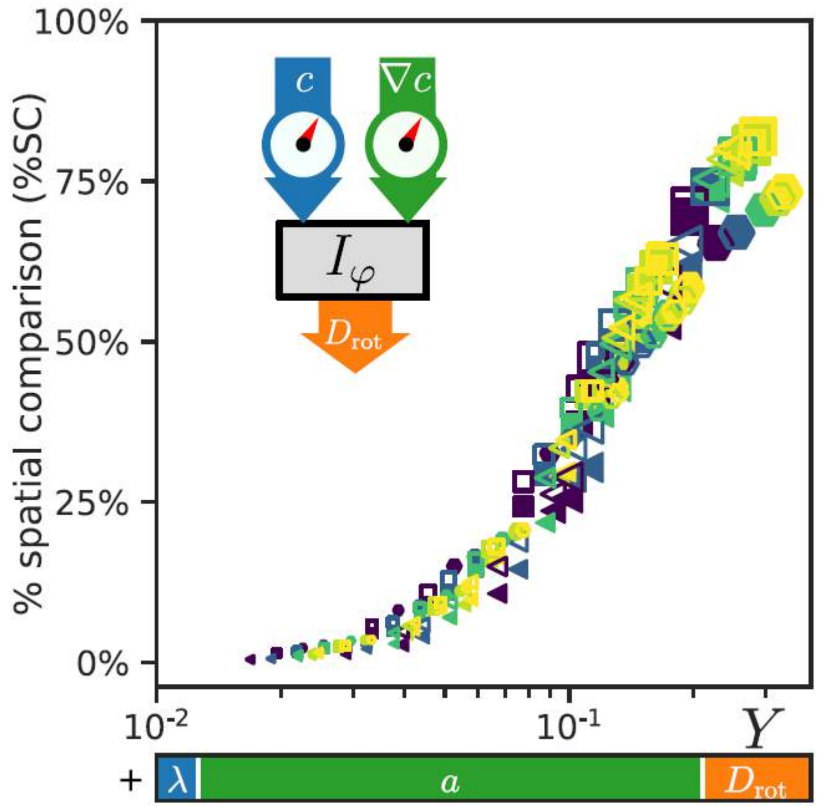


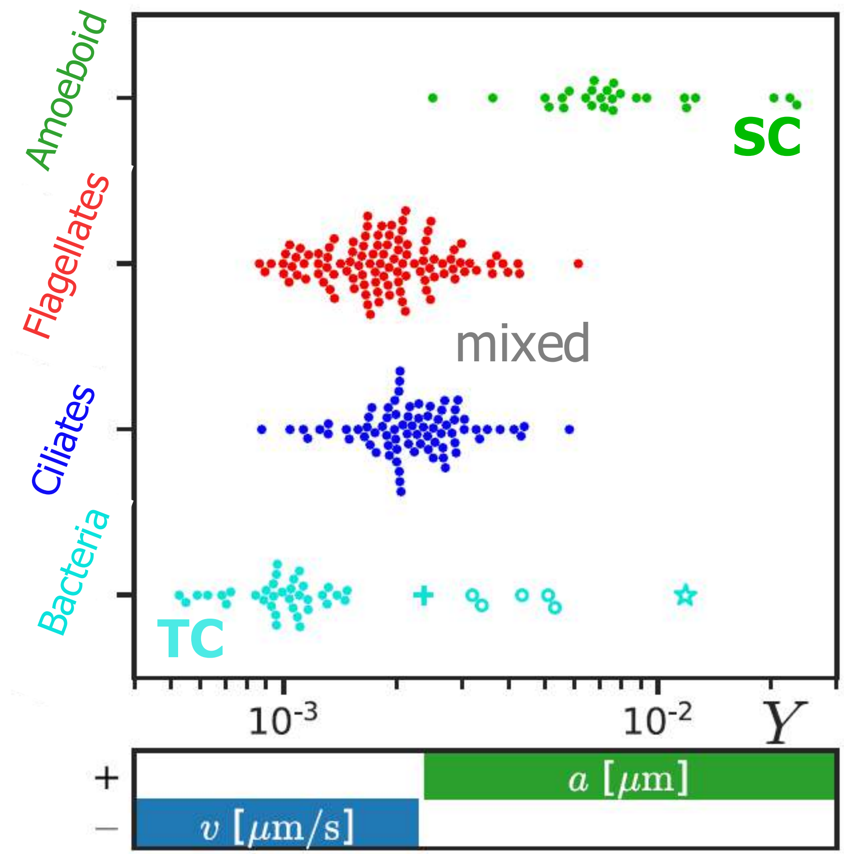
$$Y \sim \lambda^{\alpha} a^{\beta} D_{\mathrm{rot}}^{\gamma}$$

Empirical power-law for "master parameter" Y

Rode et al. PRX Life 2024

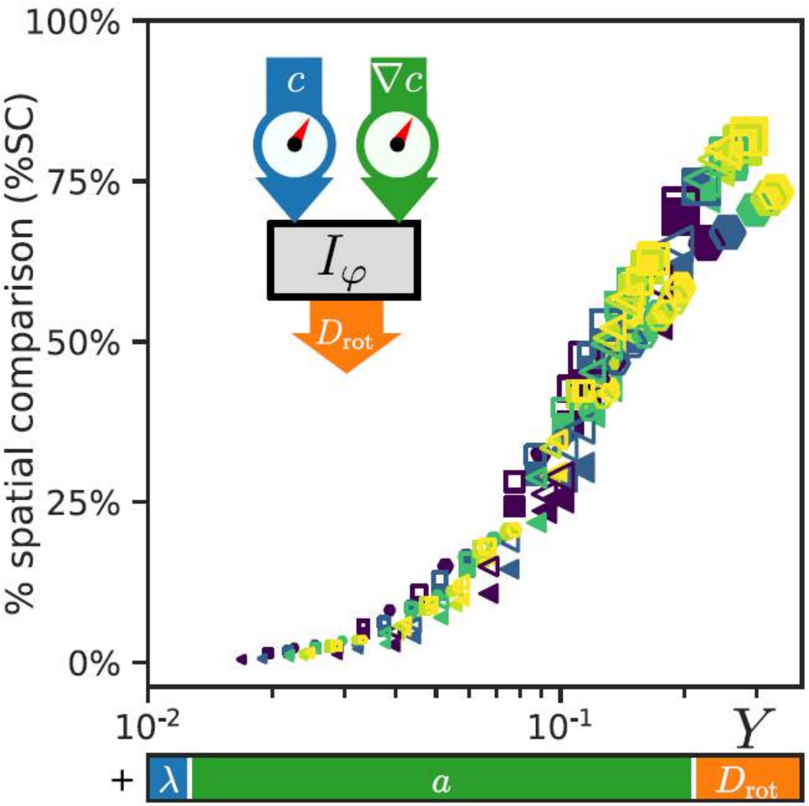
Information decomposition explains strategy of 250 cells

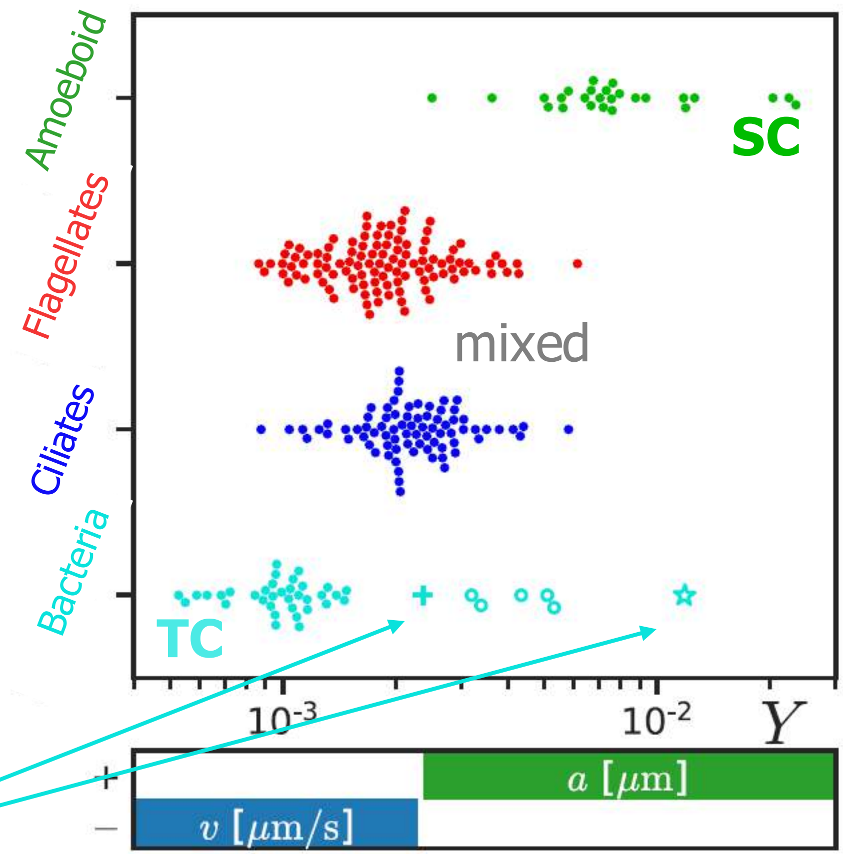




Rode et al. PRX Life 2024

Information decomposition explains strategy of 250 cells





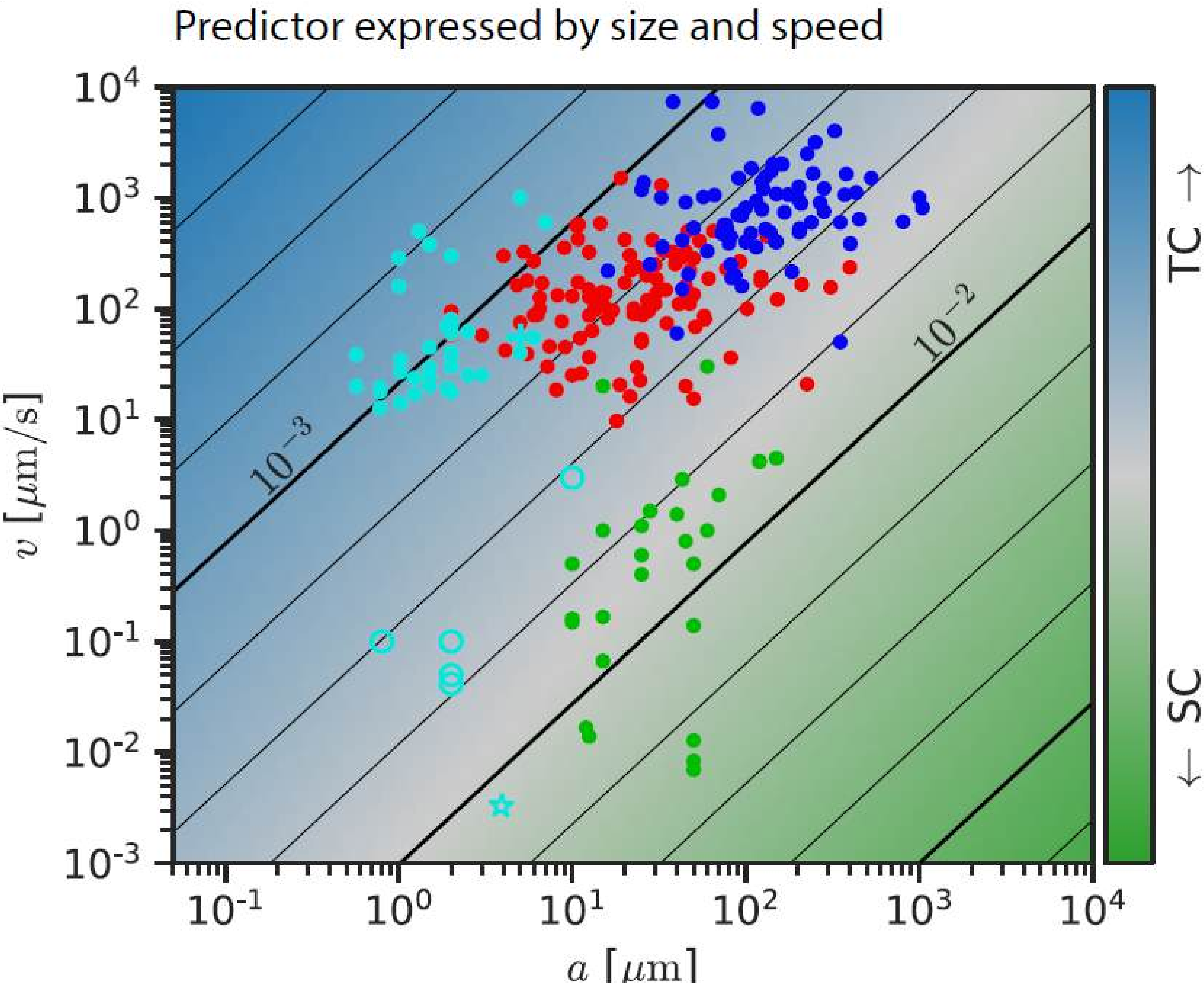
Bacteria using SC

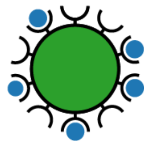
Thar et al. PNAS 2003

Wheeler et al. Nat. Microbiol. 2024

Rode et al. PRX Life 2024

We can rephrase our result in **size *a*** & **speed *v***

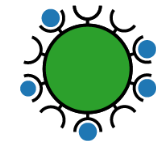


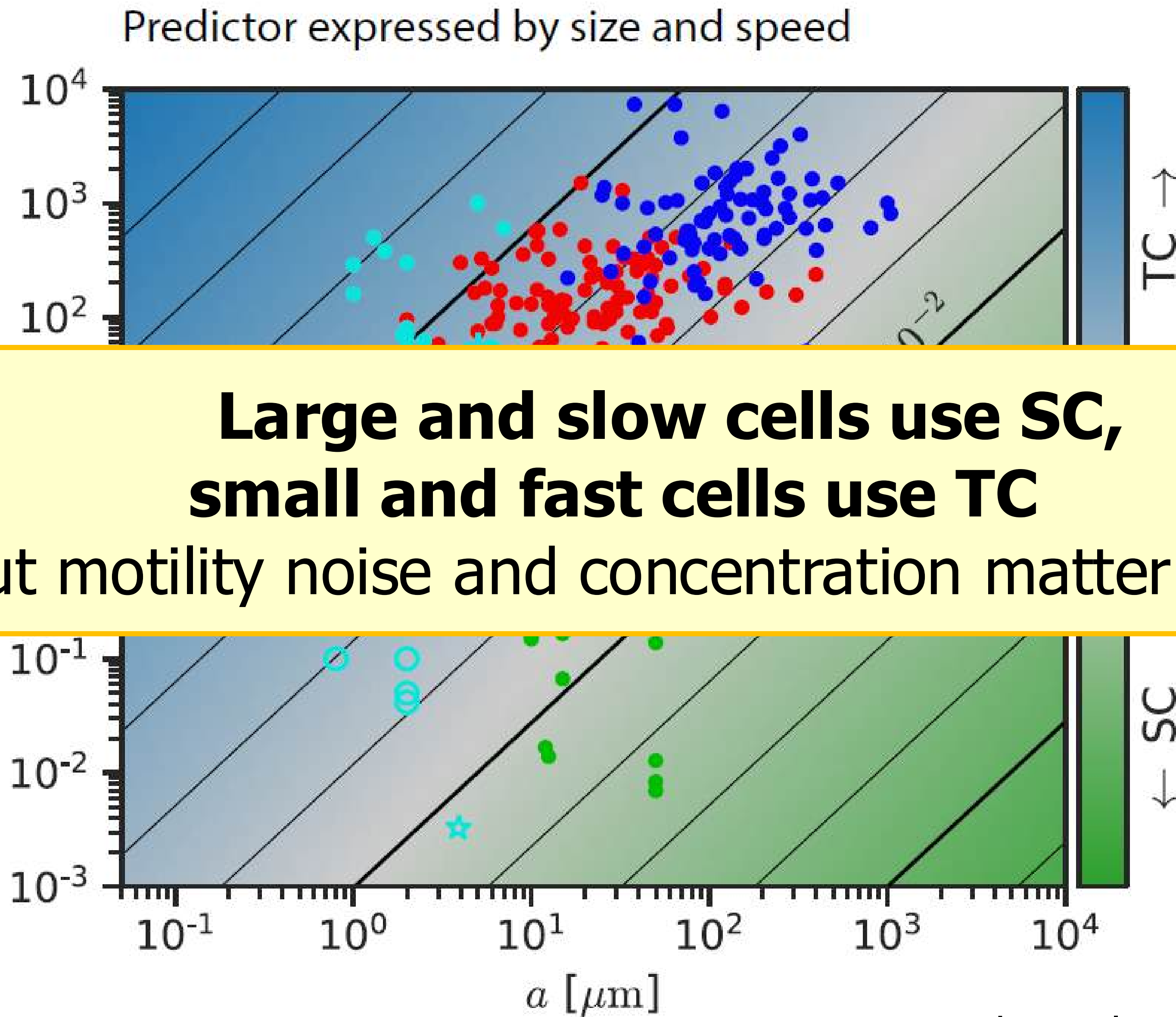


data from Wan et al. 2021

Rode et al. PRX Life 2024

We can rephrase our result in **size a** & **speed v**

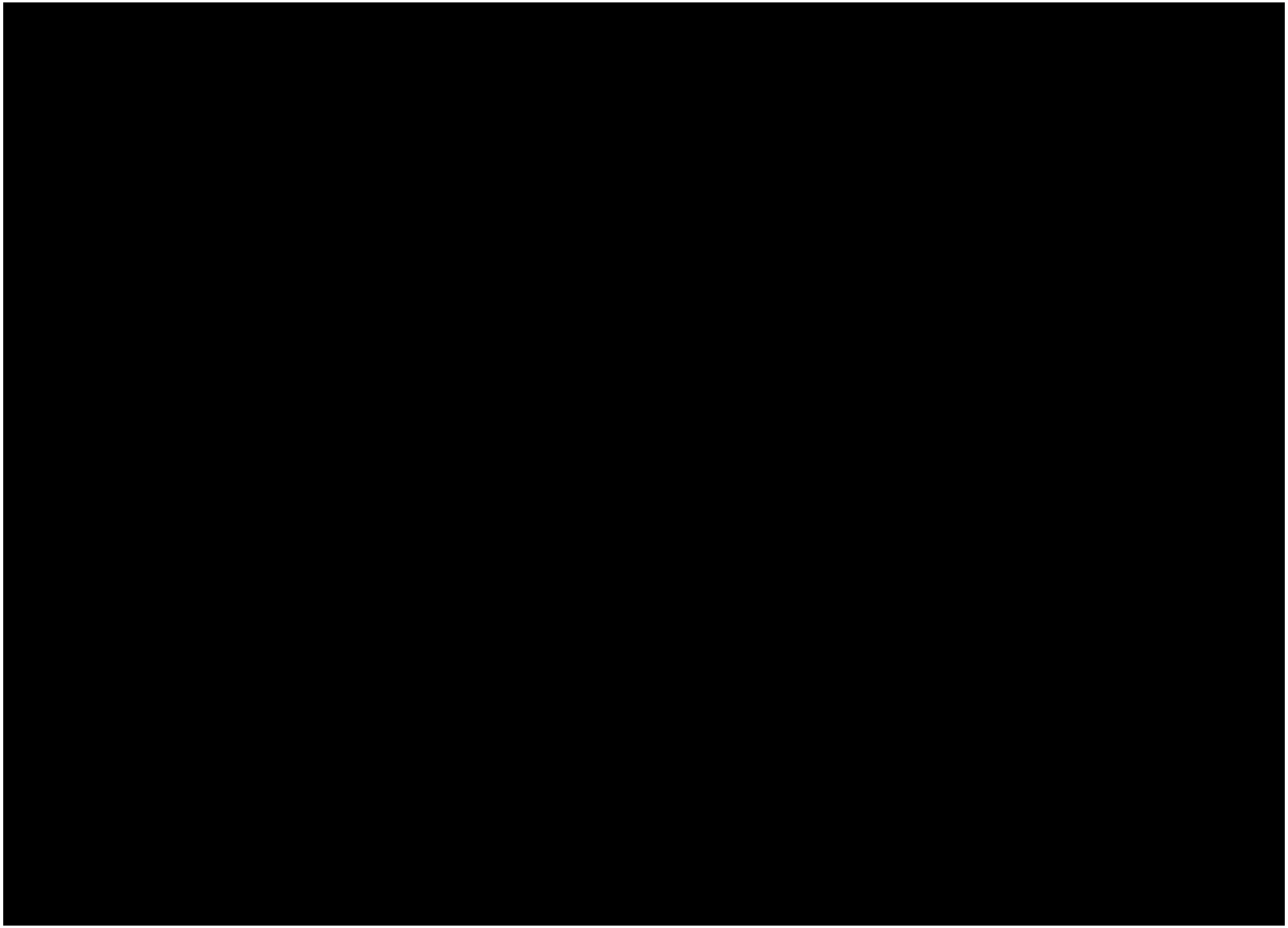




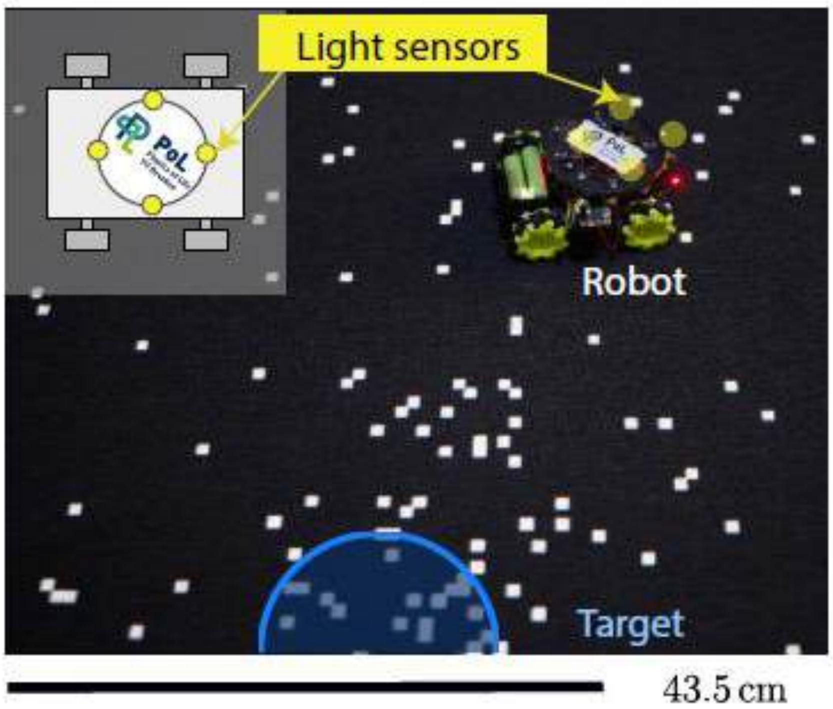
Large and slow cells use SC,
small and fast cells use TC
(but motility noise and concentration matter too)

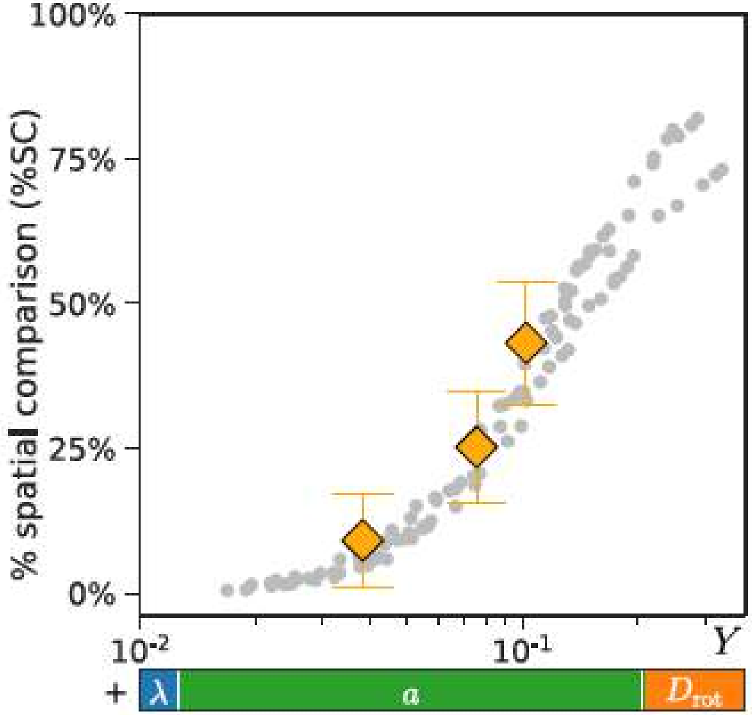
Rode et al. PRX Life 2024

A robotic demonstrator



Robot experiments and simulations agree





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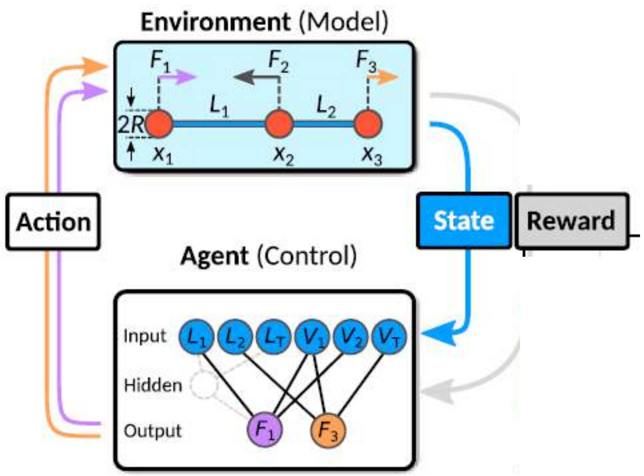
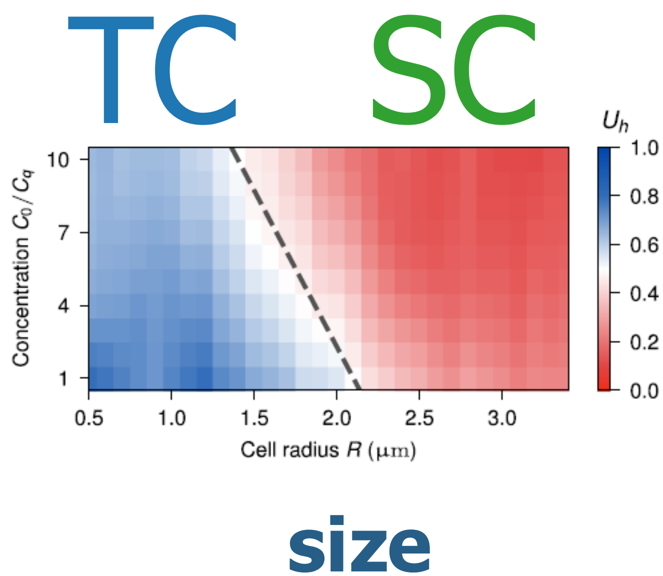
Other: **Limited information processing** capabilities

Learning chemotaxis with **small-scale neuronal networks**:



Hartl et al. PNAS (2021)



Alonso et al. PNAS Nexus (2024)
→ similar finding for **agent size**

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PHYSICS OF LIFE

The Dynamic Organization of Living Matter

Master of Science in Physics of Life

MSc
Physics of Life
CMCB

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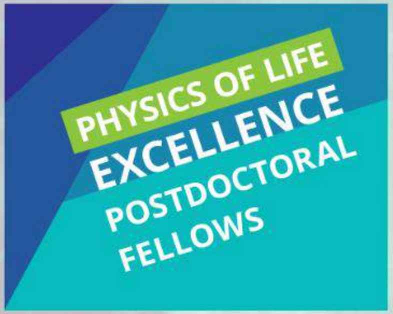
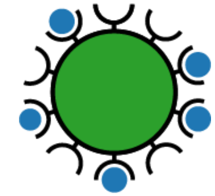
Postdoctoral Fellows



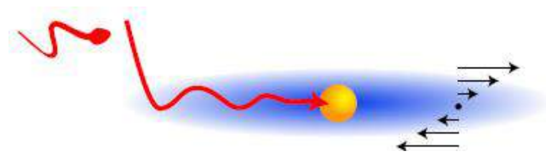
Conclusions & Thank you!

- **Spatial comparison** outweighs **temporal comparison** for ideal agents that are large, slow & persistent



Rode et al. PRX Life (2024)

- **Sperm surf along concentration filaments** in small-scale turbulence



Lange et al. PLoS Comp. Biol. (2021)

Funding:

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