# How do sperm find the egg?

## Cross-fertilization of theory and experiment

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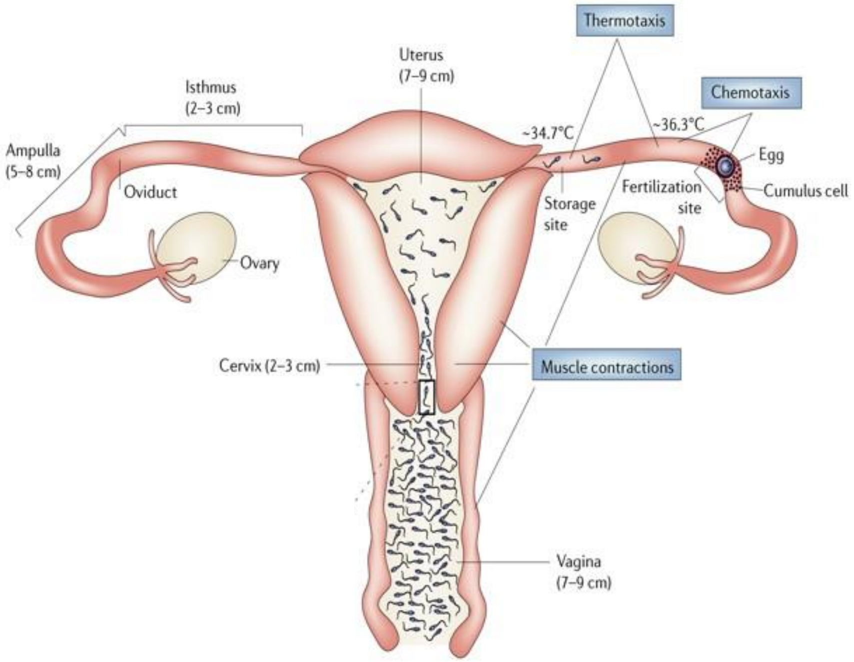
# How do sperm find the egg?

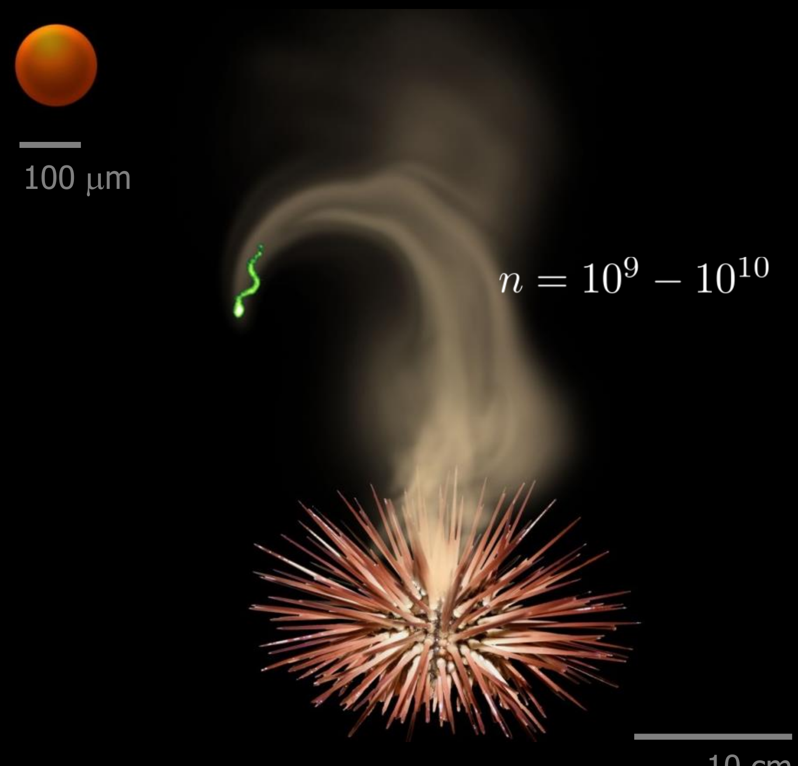
# The search environment matters

# Internal fertilization



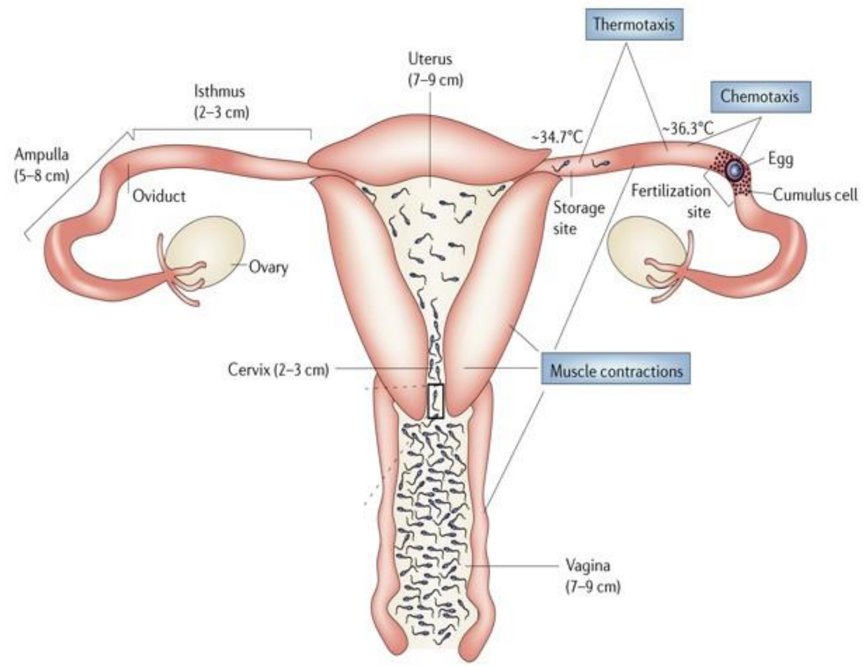
# The search environment matters

## External fertilization



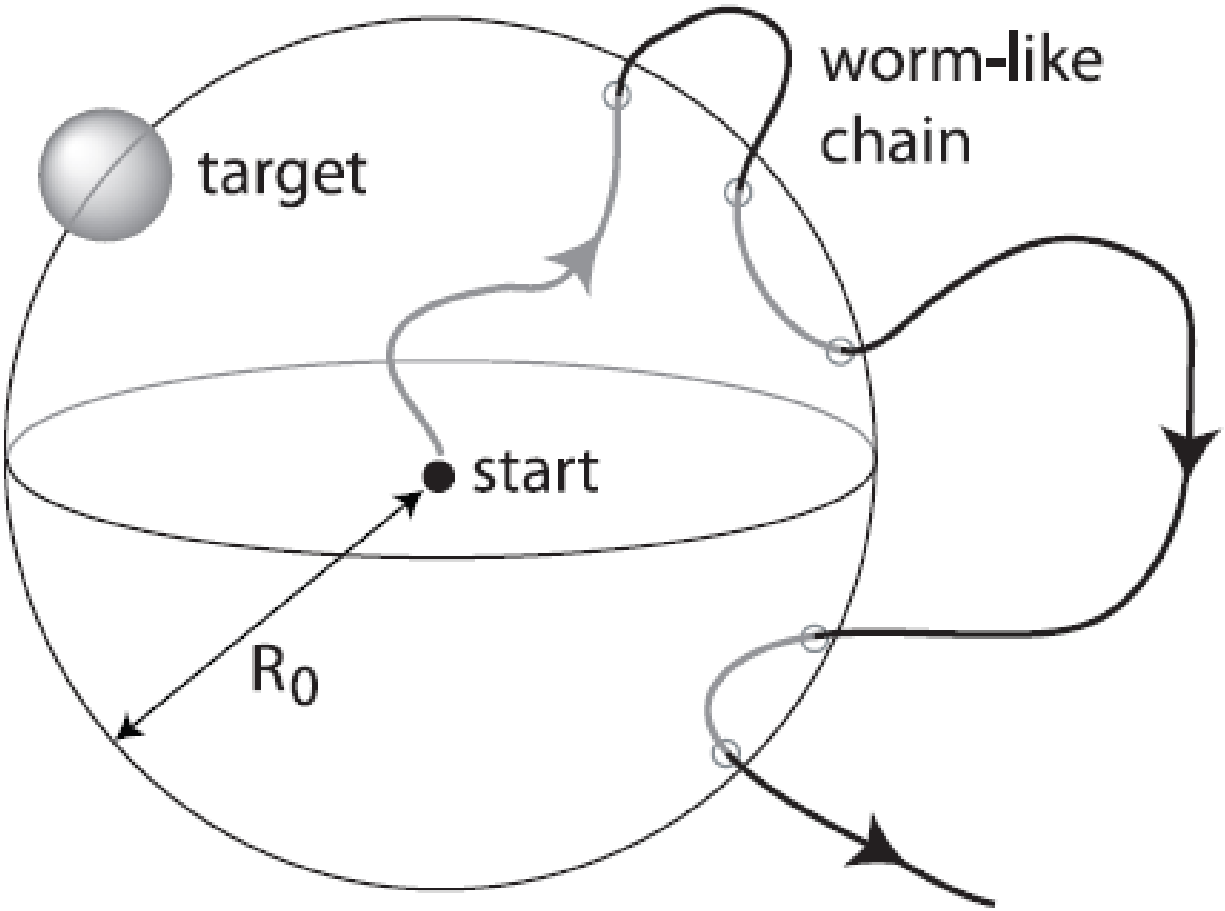



## Internal fertilization




$n = 10^7 - 10^9$

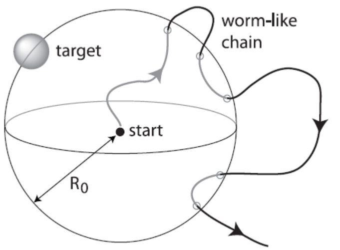
# Idealization: sperm path are persistent random walks



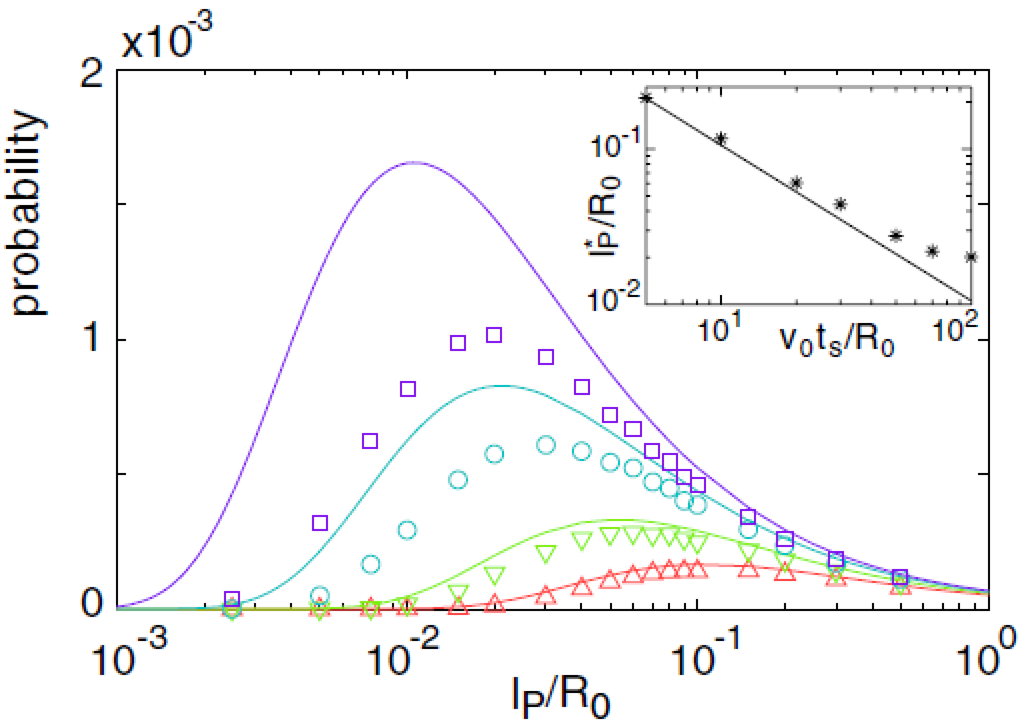

Friedrich et al.: Physical Biology (2008)

# Search along persistent random walks

- Given an initial target distance $R_0$ and finite search time $t_s$, there is an optimal persistence length $l_p$*

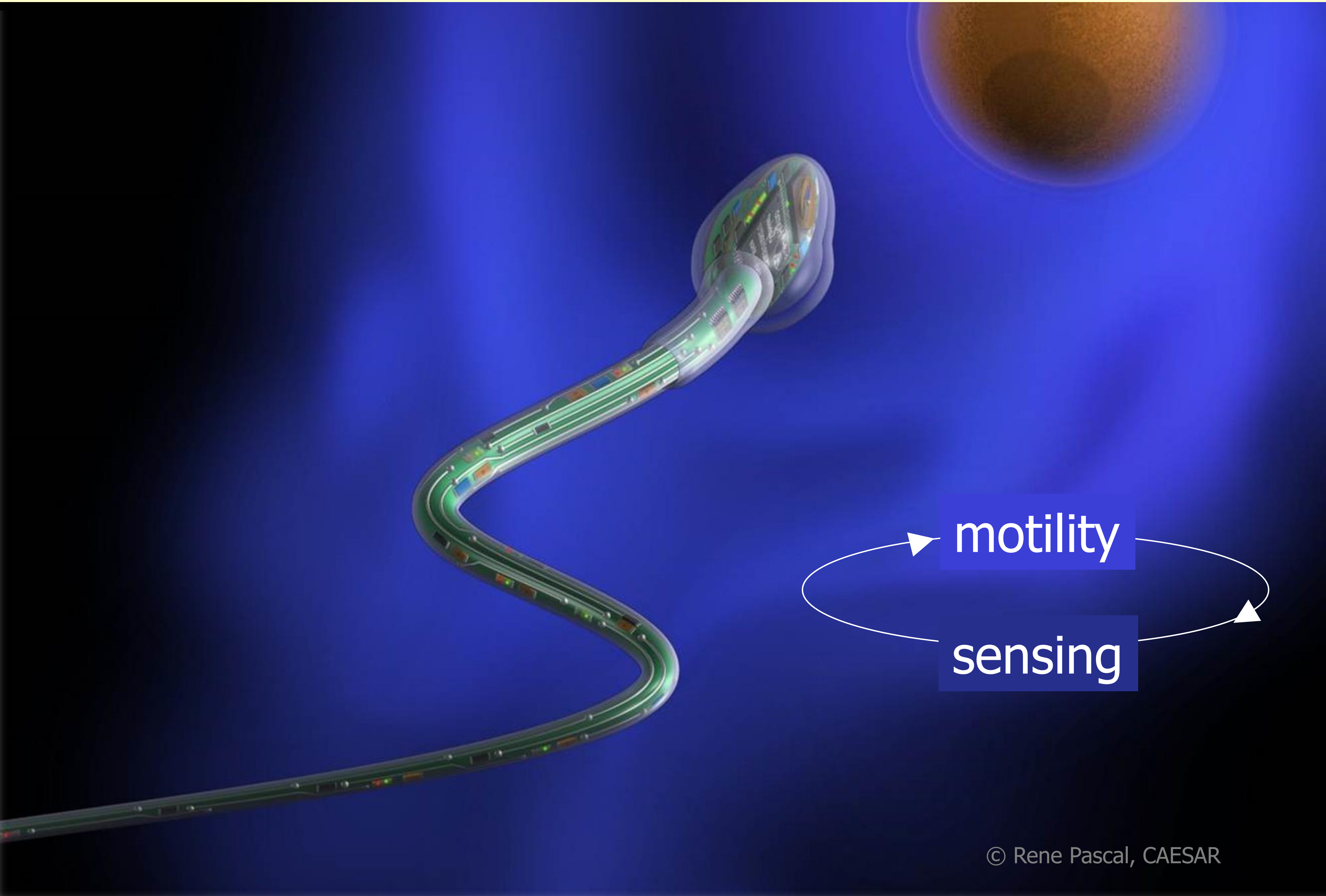



$$D^* = \frac{1}{3} l_P^* v_0 \sim \frac{R_0^2}{t_s}$$



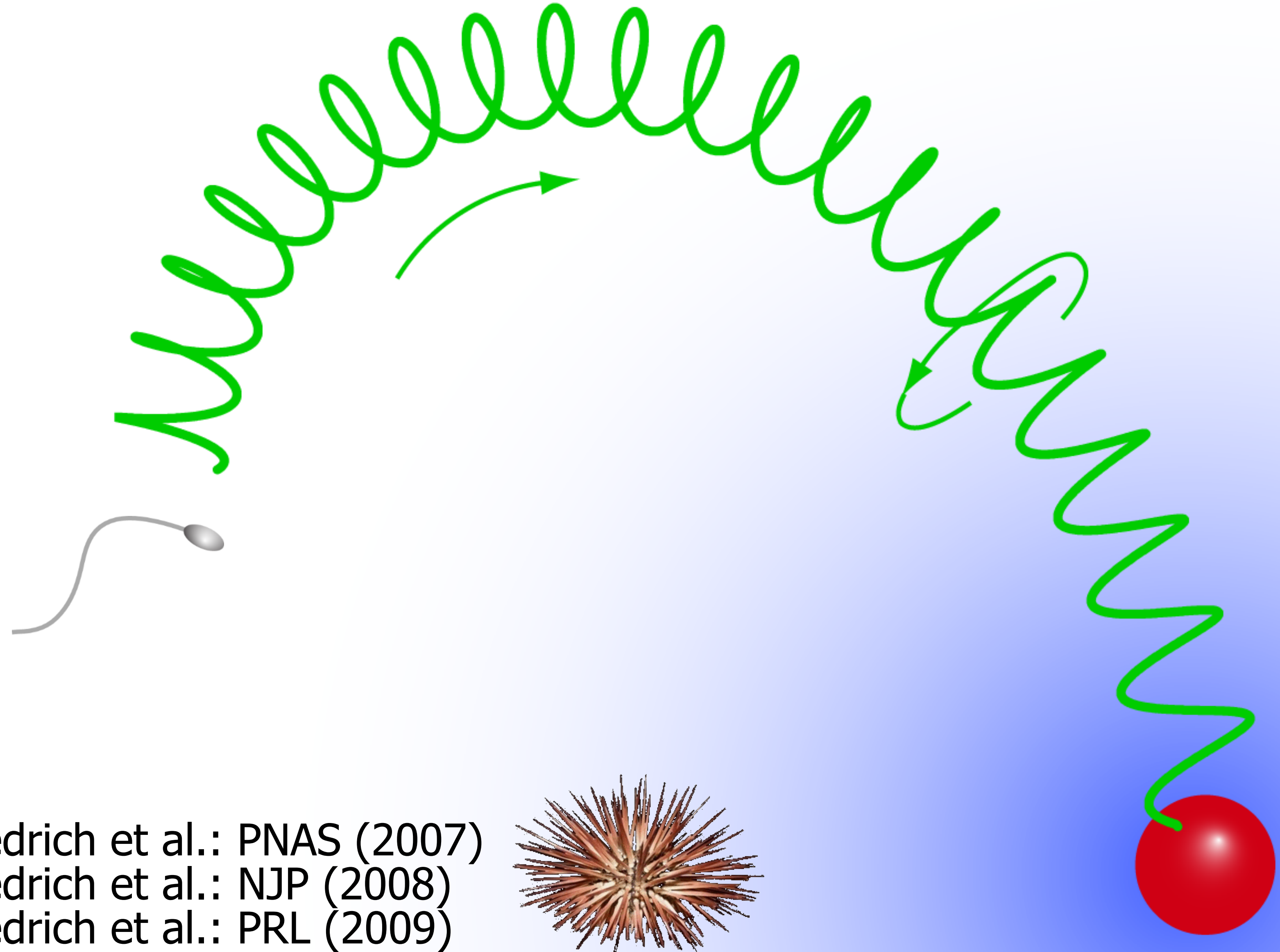

Friedrich et al.: Physical Biology (2008)

# Close to the egg, there is true navigation



# The egg releases chemical guidance cues

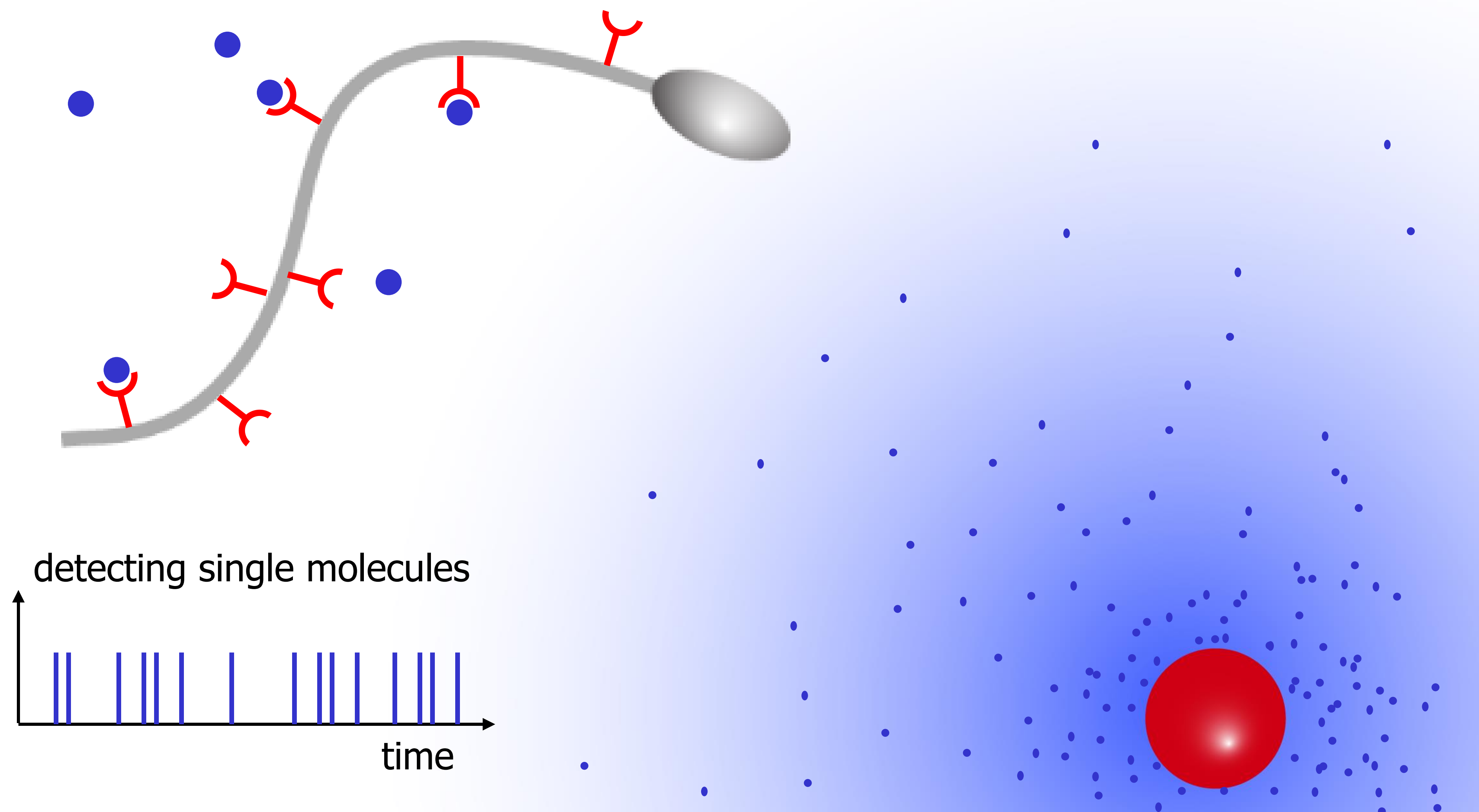
# Theory: Sperm from marine species steer along helical paths



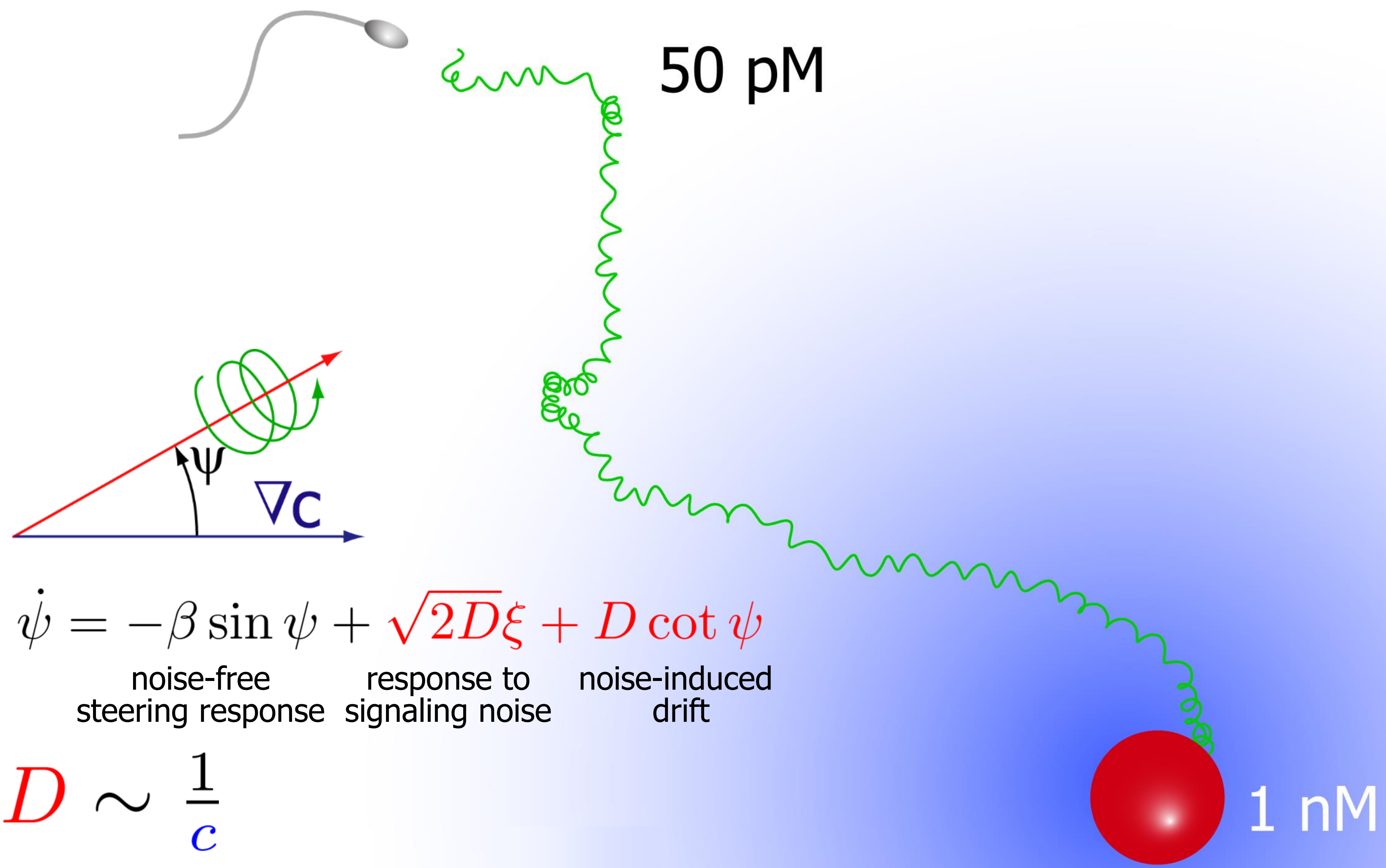
Friedrich et al.: PNAS (2007)
Friedrich et al.: NJP (2008)
Friedrich et al.: PRL (2009)

# Measuring concentration = Counting molecules

- Concentration sensing is subject to strong shot noise



# We showed that navigation is adapted to tolerate noise




$$\dot{\psi} = -\beta \sin\psi + \sqrt{2D}\xi + D\cot\psi$$

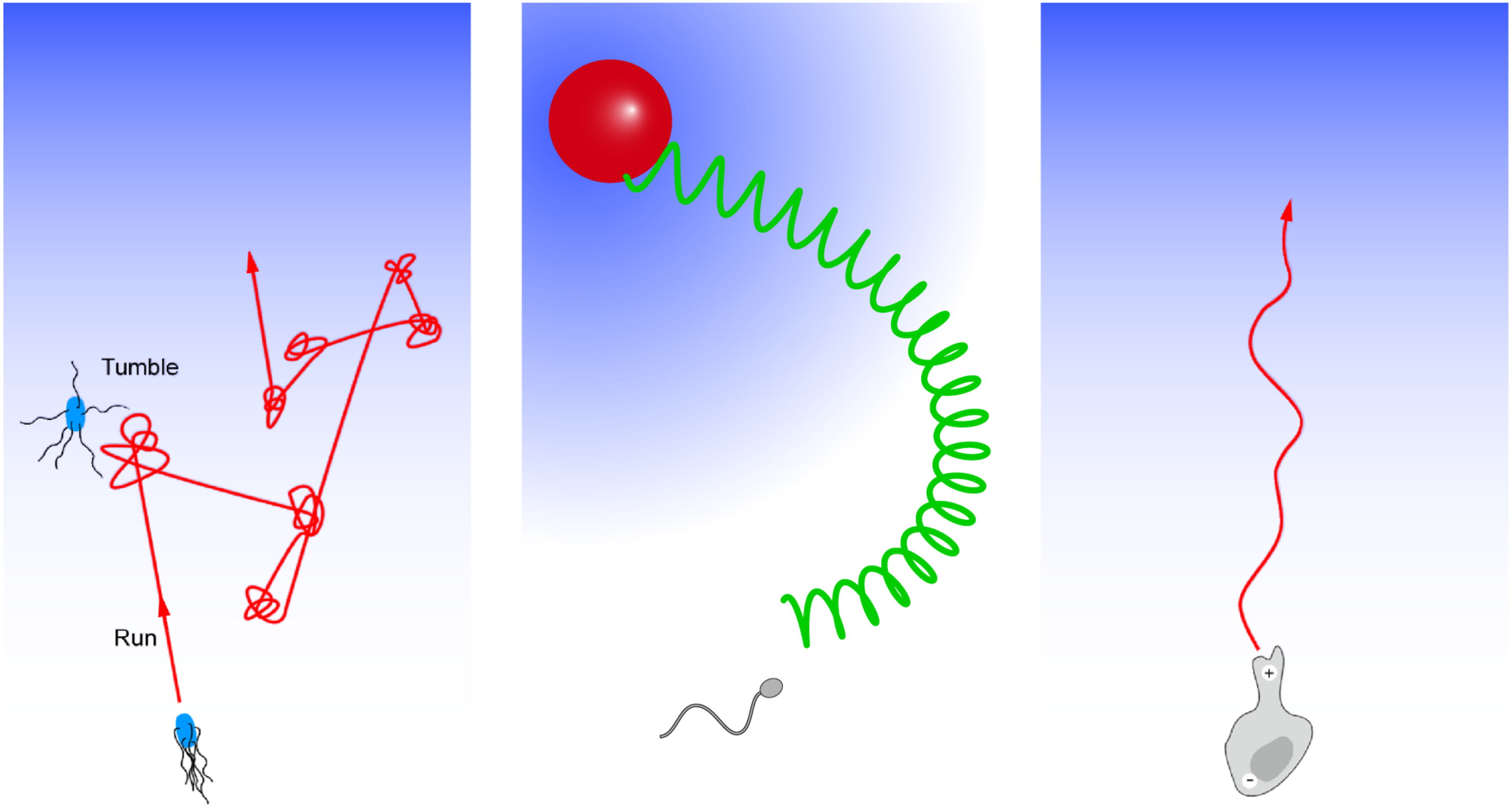
noise-free steering response | response to signaling noise | noise-induced drift

$$D \sim \frac{1}{c}$$

# How to measure a gradient?

exploitation ↔ exploration

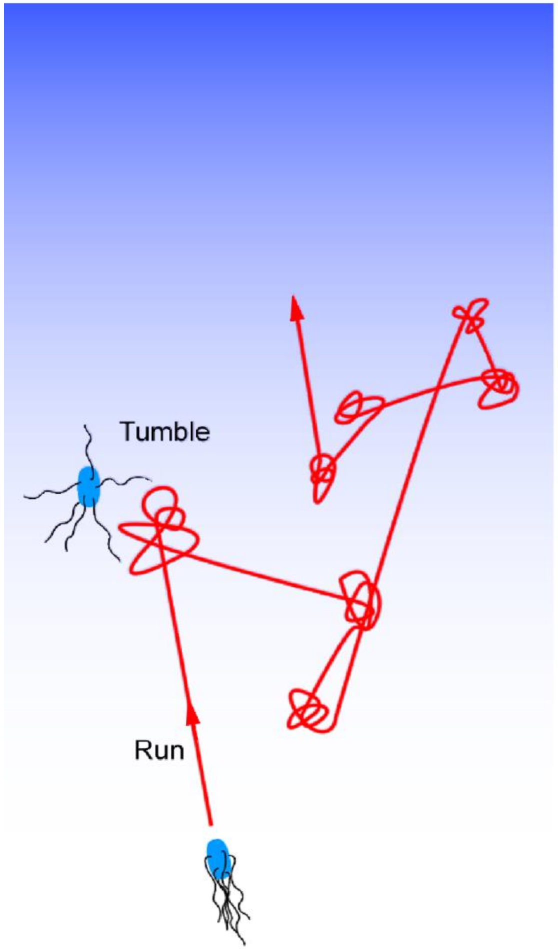
# Gradient sensing strategies are adapted to noise level




Bacterium *E. coli* | Sea urchin sperm | Slime mold *Dictyostelium*

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

# Tiny bacteria can keep their direction only for a few seconds

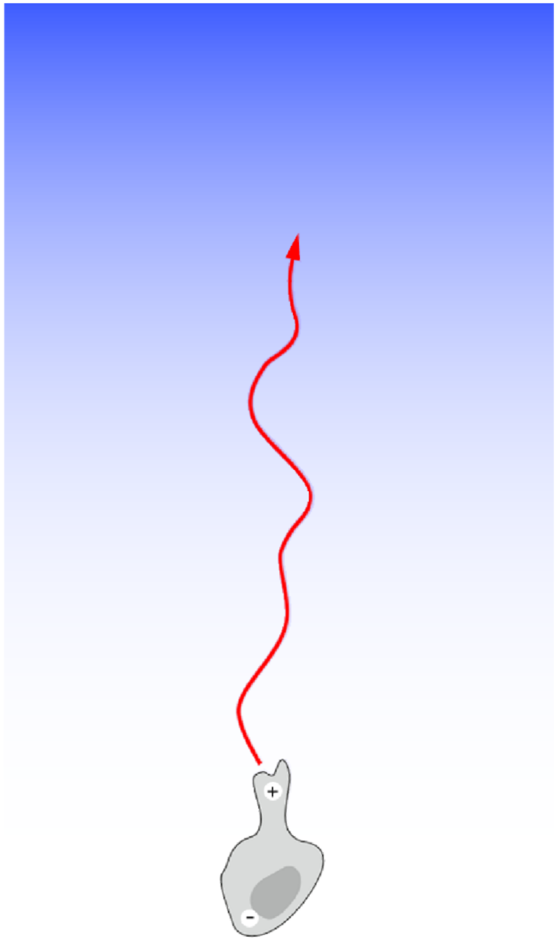



Bacterium *E. coli*

$$D_{\mathrm{rot}} \sim \frac{1}{L^3}$$

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

# Slow slime molds have sufficient time for spatial comparison




Slime mold *Dictyostelium*

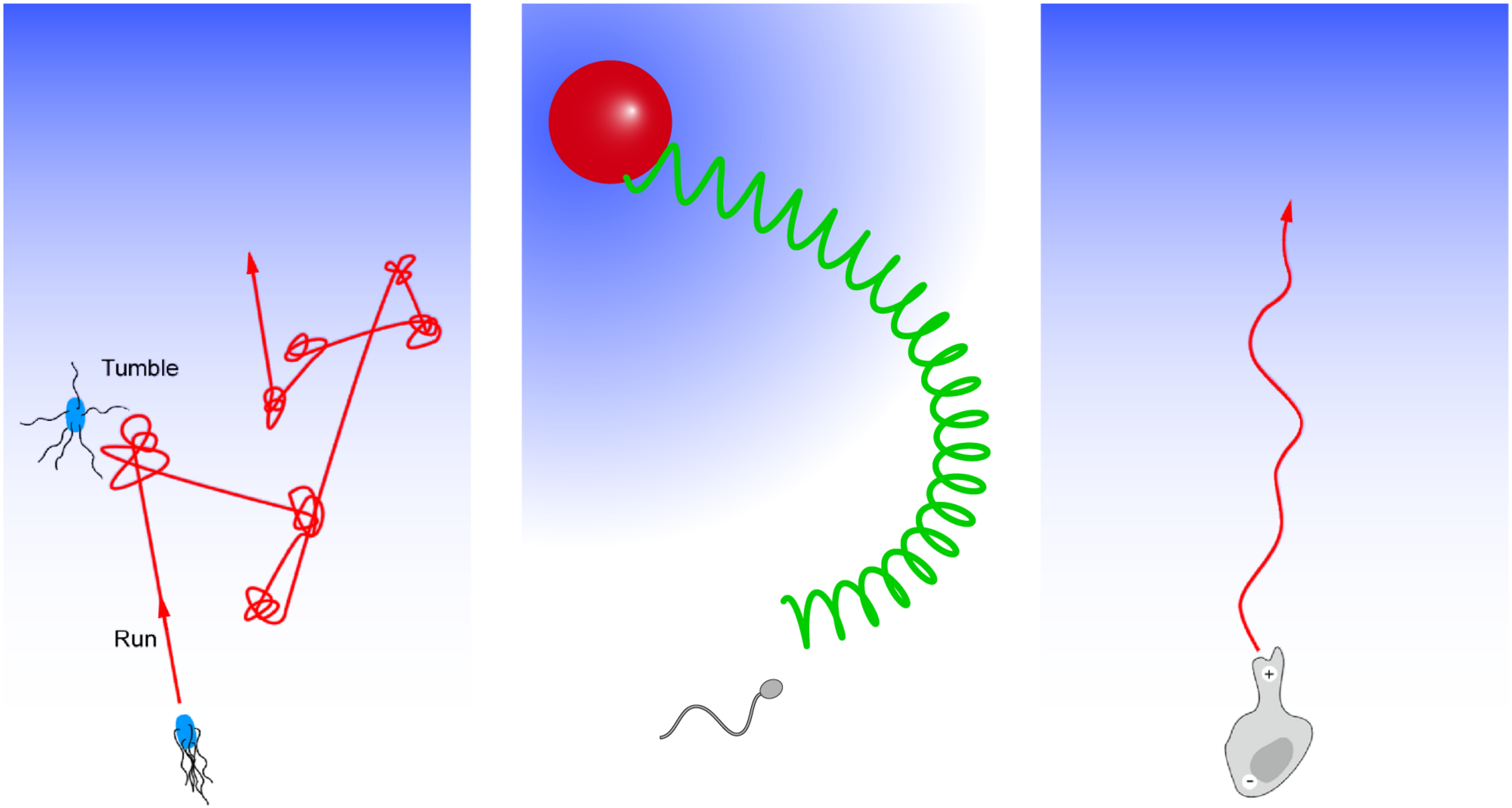
- signal-to-noise ratio

$$\sim \sqrt{Dc} \cdot \frac{\nabla c}{c} \cdot \frac{L^2}{\sqrt{v}}$$

$L \sim 100\,\mu\text{m},\ v \sim 1\,\mu\text{m/min}$

Berg, Purcell: BPJ (1977)

# Navigation strategies of cells are adapted to noise level



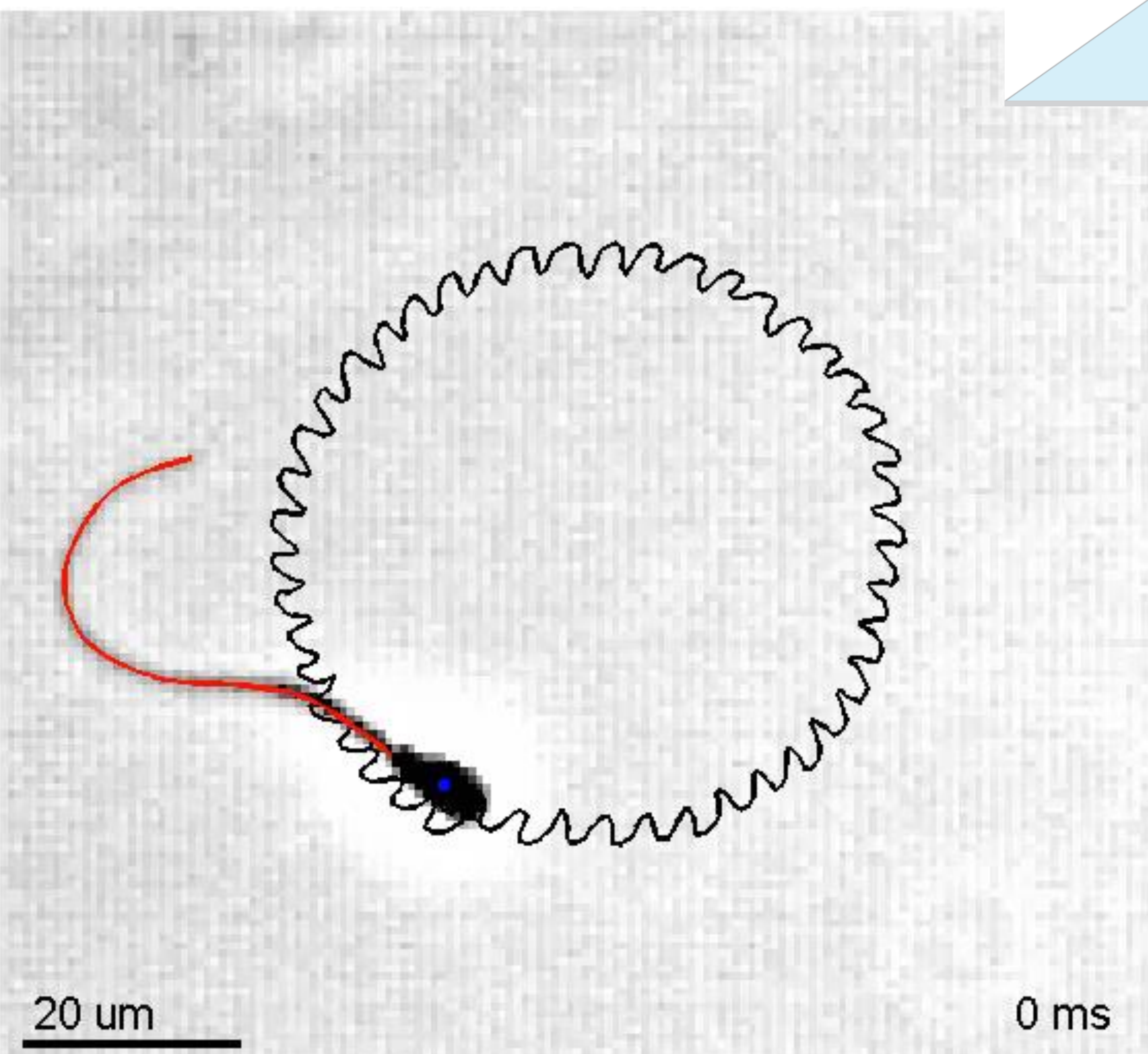

Bacterium *E. coli* | Sea urchin sperm | Slime mold *Dictyostelium*

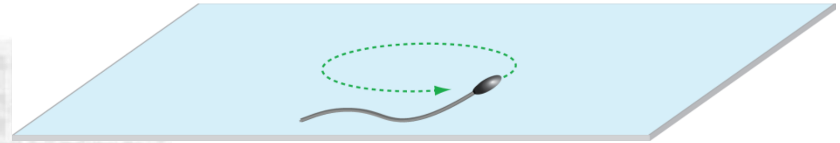
Berg, Purcell: BPJ (1977)
Alvarez, Friedrich, Gompper, Kaupp: Trends Cell Biol. (2014)

# How does steering along circular paths work?

Let’s consider the simpler 2d case

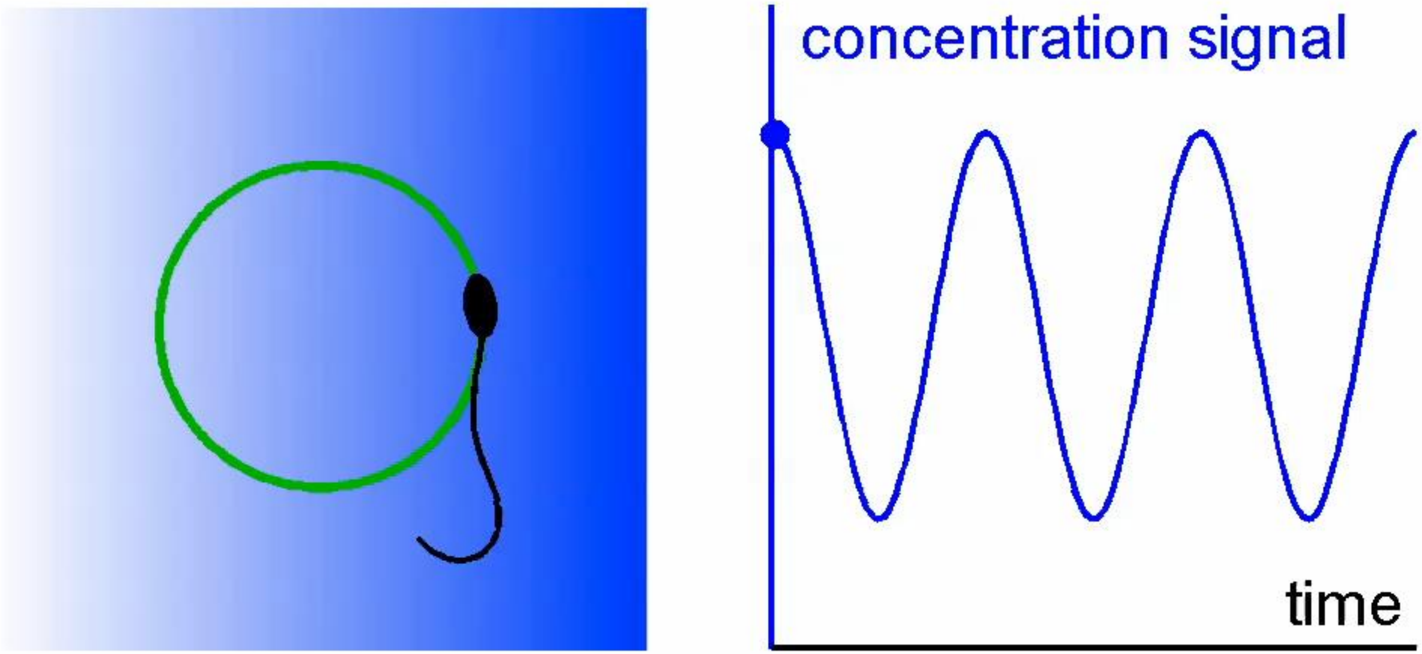
# Sperm swim along circular paths close to boundaries



BMF, I Riedel-Kruse, J Howard, F Jülicher, J exp Biol **213**, 2010

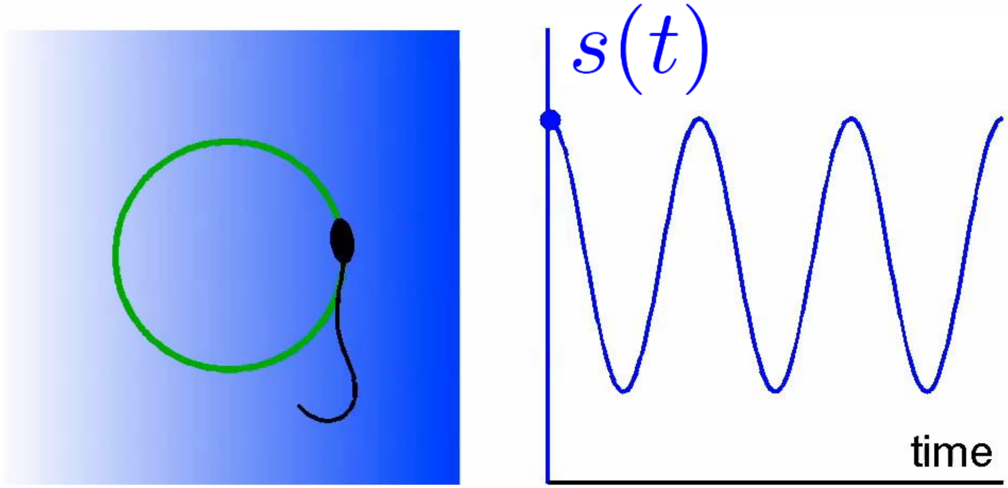
# Theory: Sperm measure concentration along circular paths



# Theory: Sperm measure concentration along circular paths

swimming path $\mathbf{r}(t)$

concentration stimulus $s(t) = c(\mathbf{r}(t))$



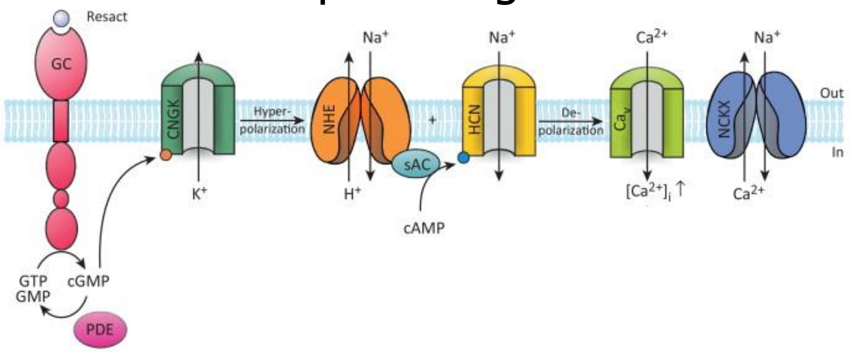
# A signalling system transfers the stimulus into steering

swimming path $\mathbf{r}(t)$

concentration stimulus $s(t)$

path curvature $\kappa(t)$

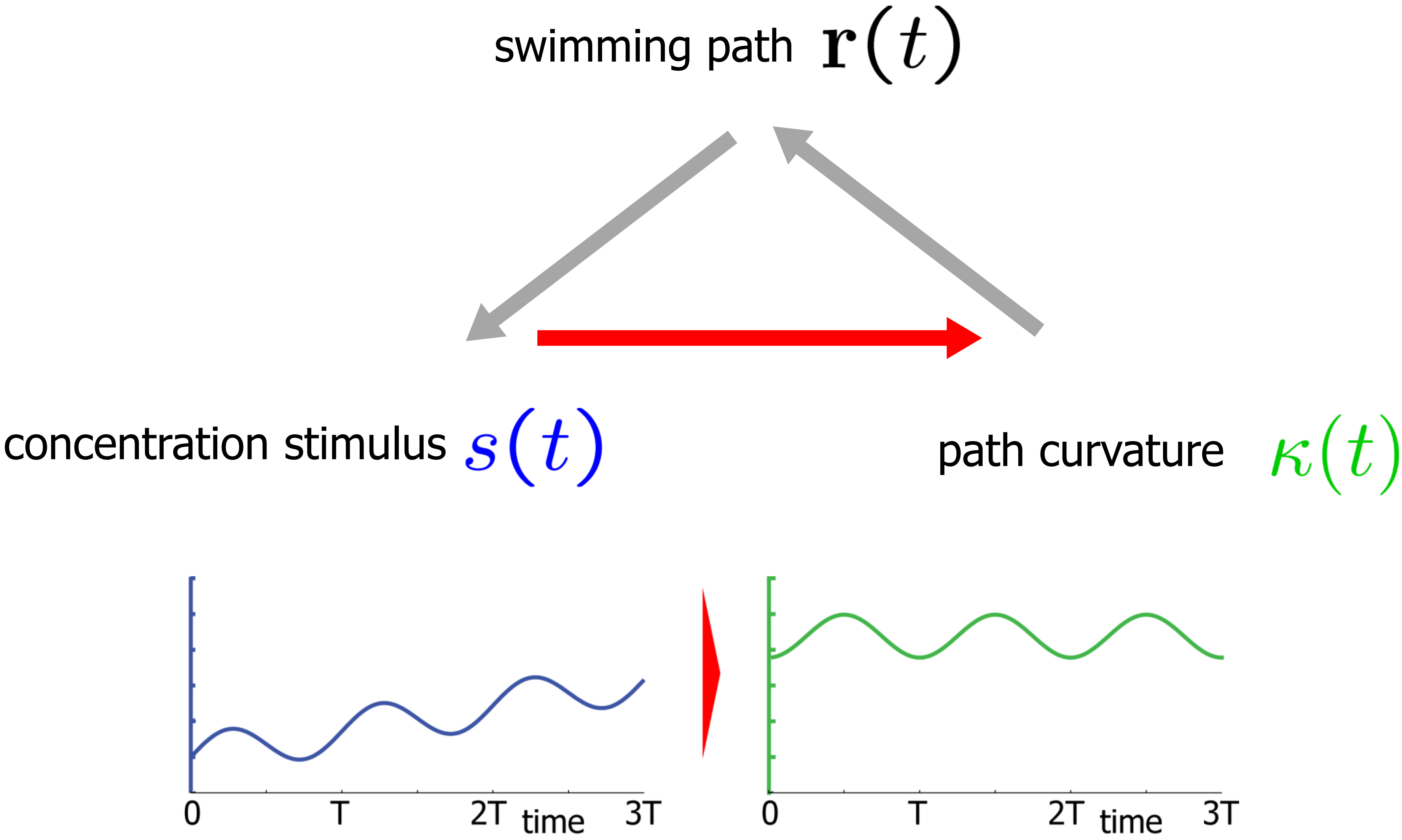
signalling system
inside sperm flagellum



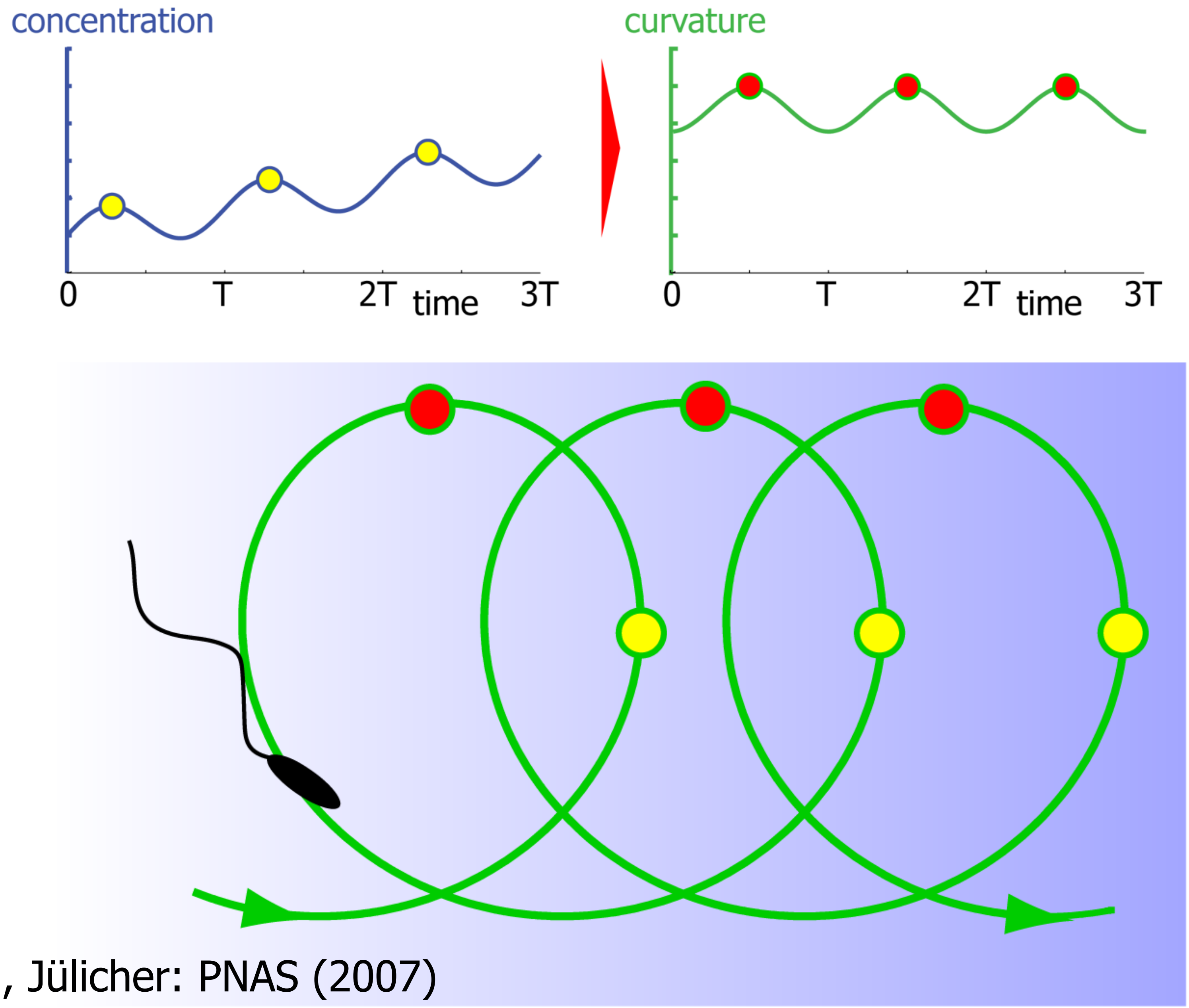

minimal description
as adaptation module

$$\tau_a \dot{a} = ps - a$$
$$\tau_p \dot{p} = p(1-a)$$
$$\kappa = \kappa_0 + \chi(a-1)$$

# Stimulus oscillations elicit curvature oscillations

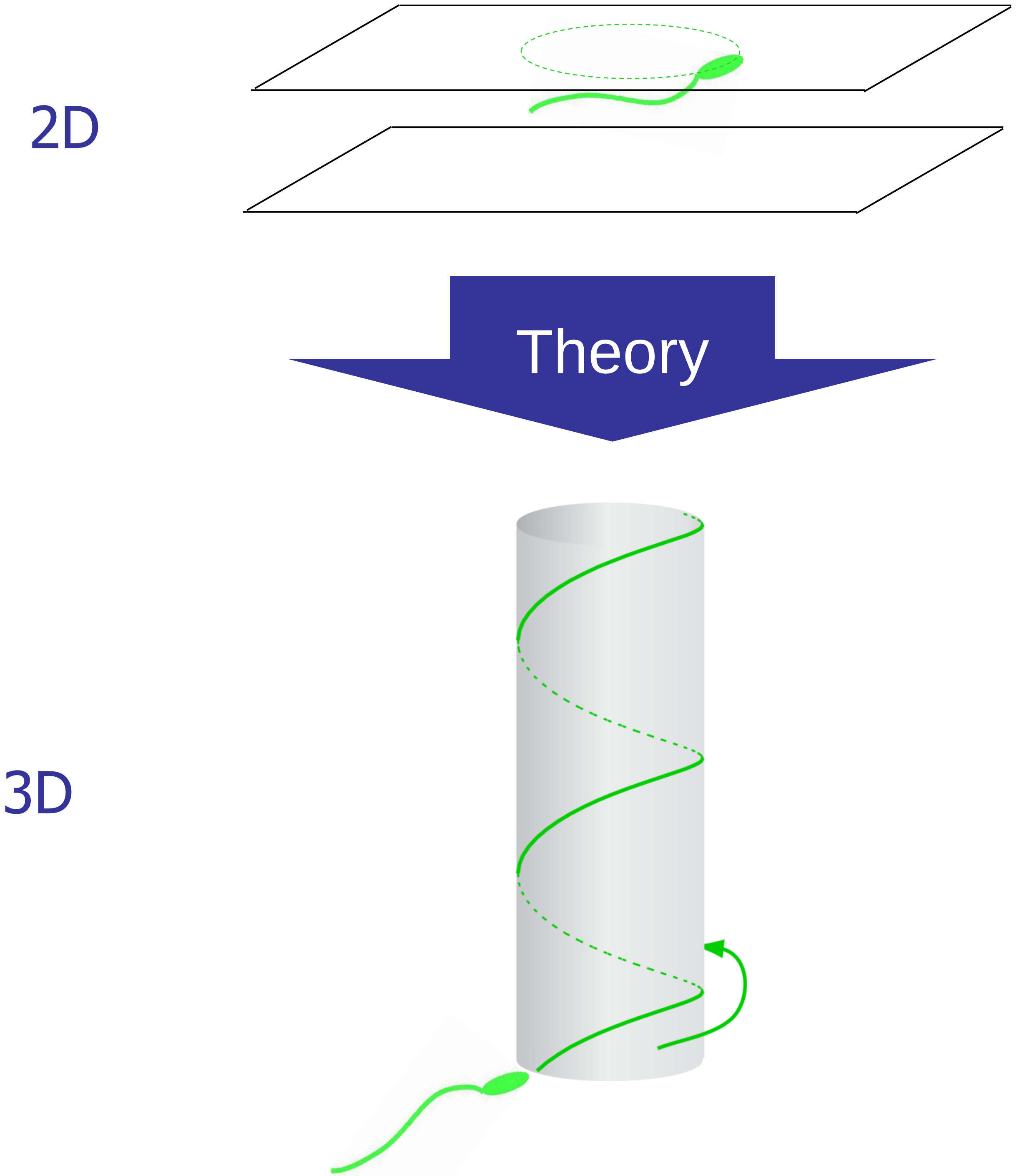


# Theory of sperm chemotaxis

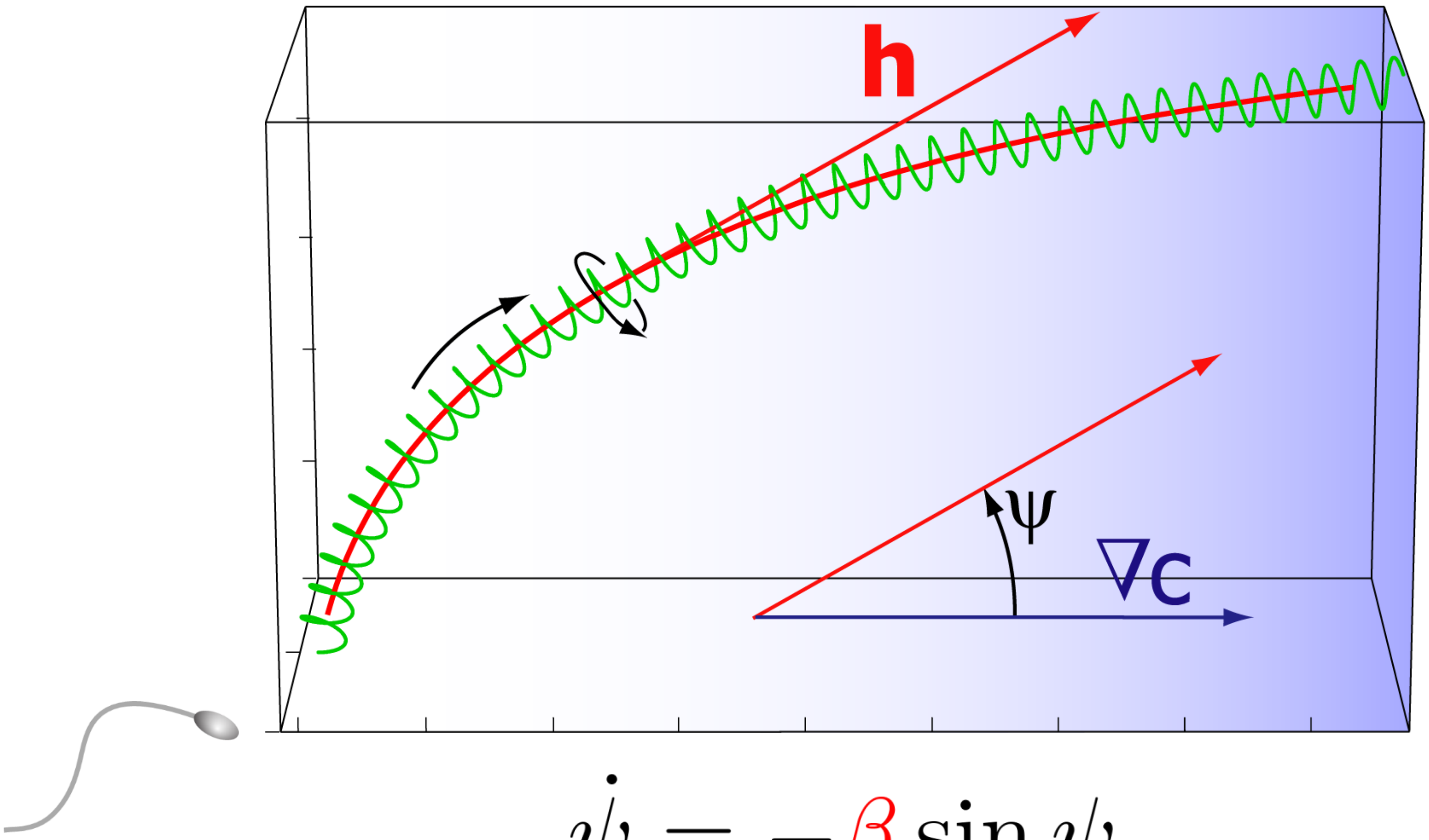



Friedrich, Jülicher: PNAS (2007)

Sperm measure concentration
along circular paths and dynamically
adjust their beat
in a precisely timed manner


2D
Theory
3D

# Steering feedback aligns helical paths with the gradient




$$\dot{\psi} = -\beta \sin \psi$$

$$\beta \sim \frac{\nabla c}{c}$$

Friedrich, Jülicher: PNAS (2007)

# How to test the theory?

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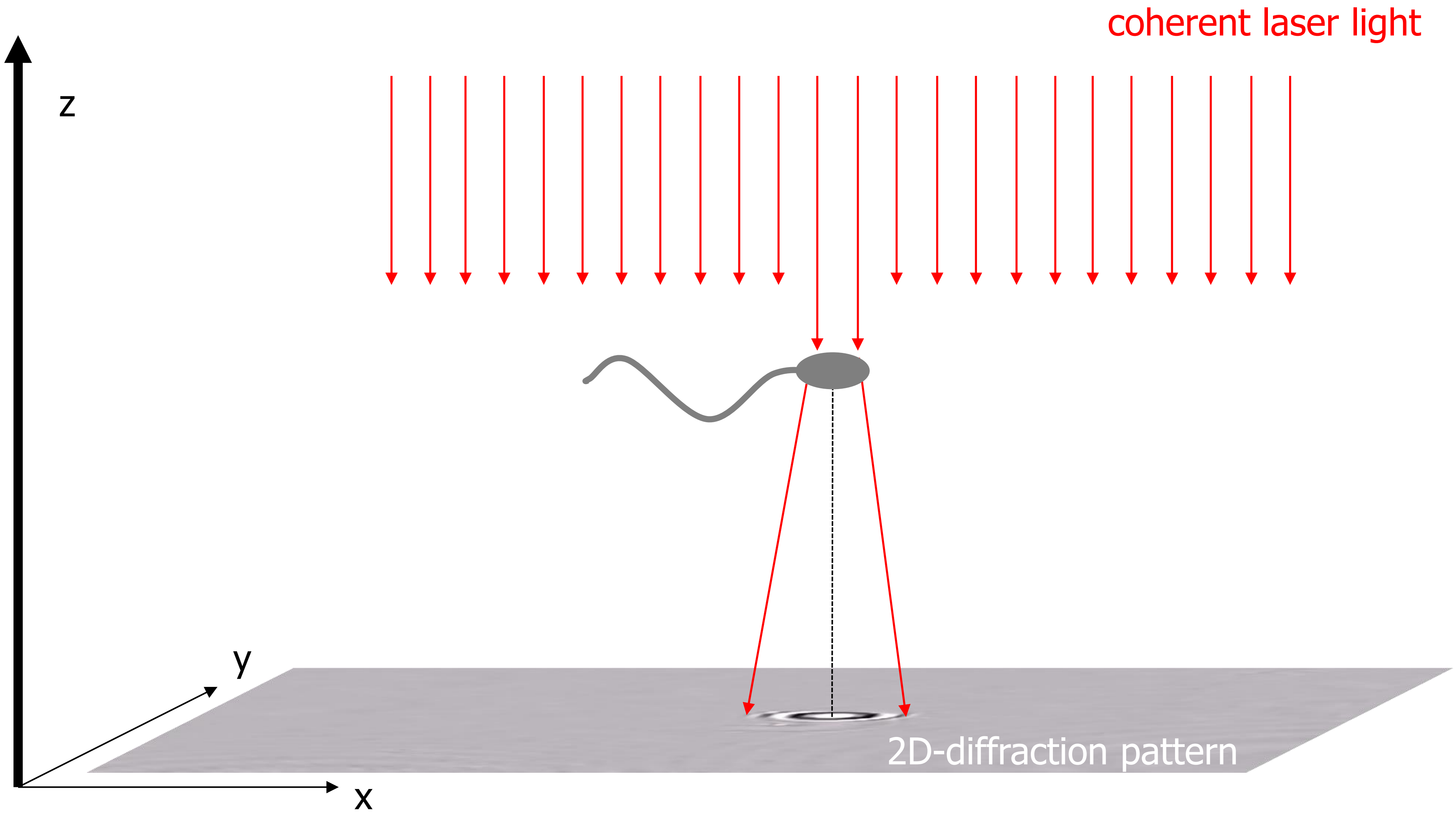
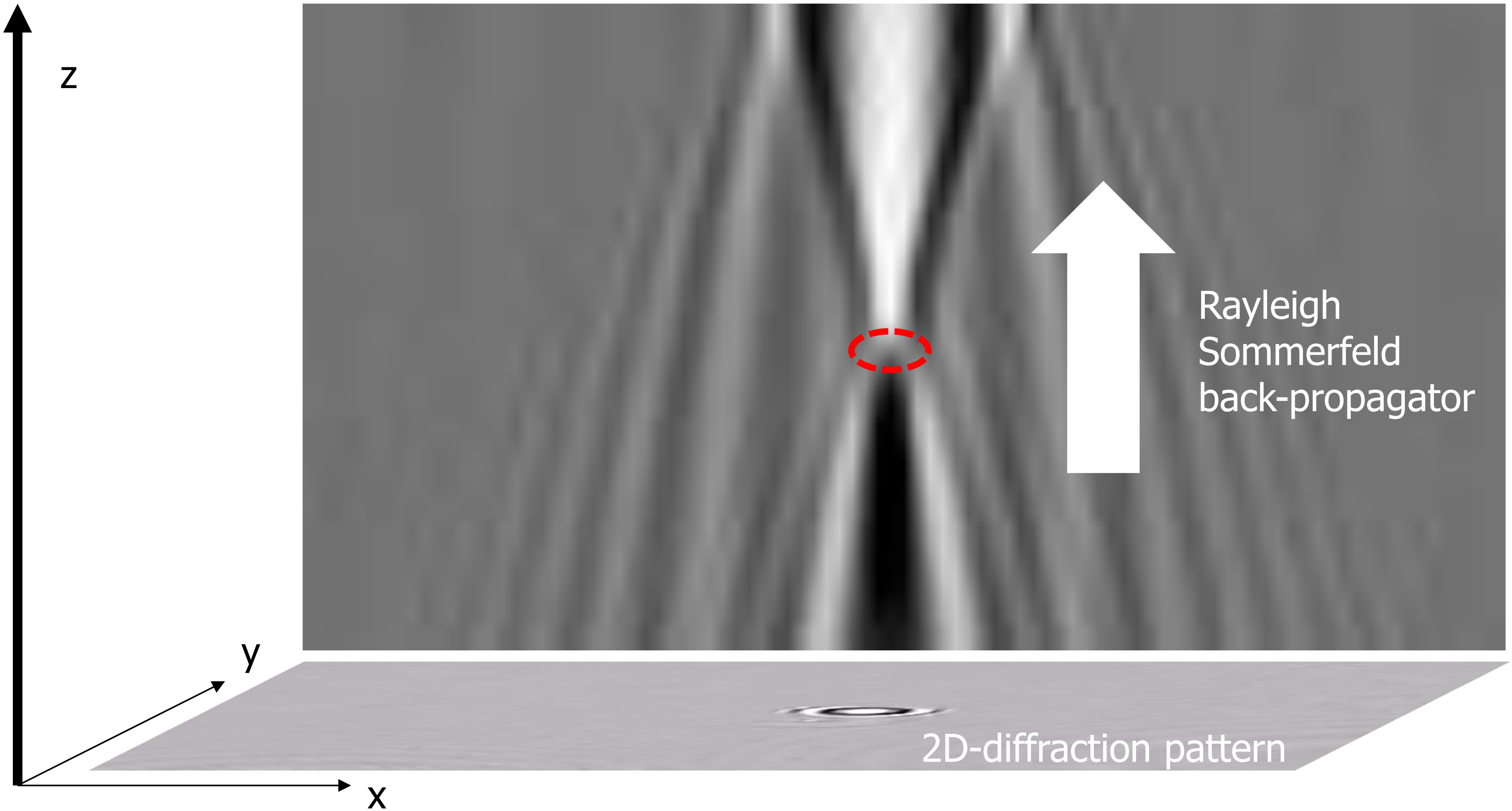
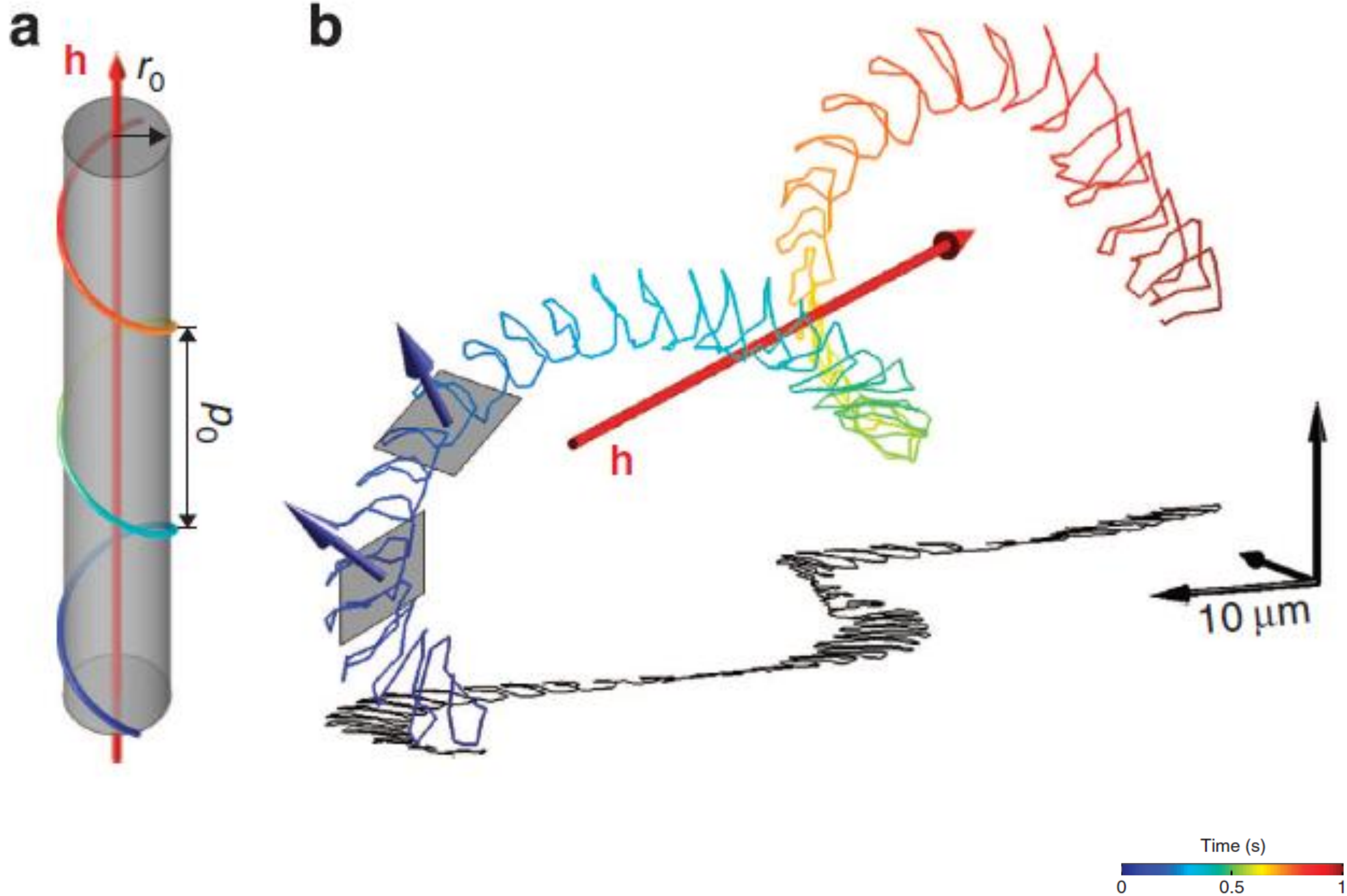
# 3D-tracking from 2D-holographic images



# Numerical reconstruction of 3D-light beam



# Sperm swim along helical paths

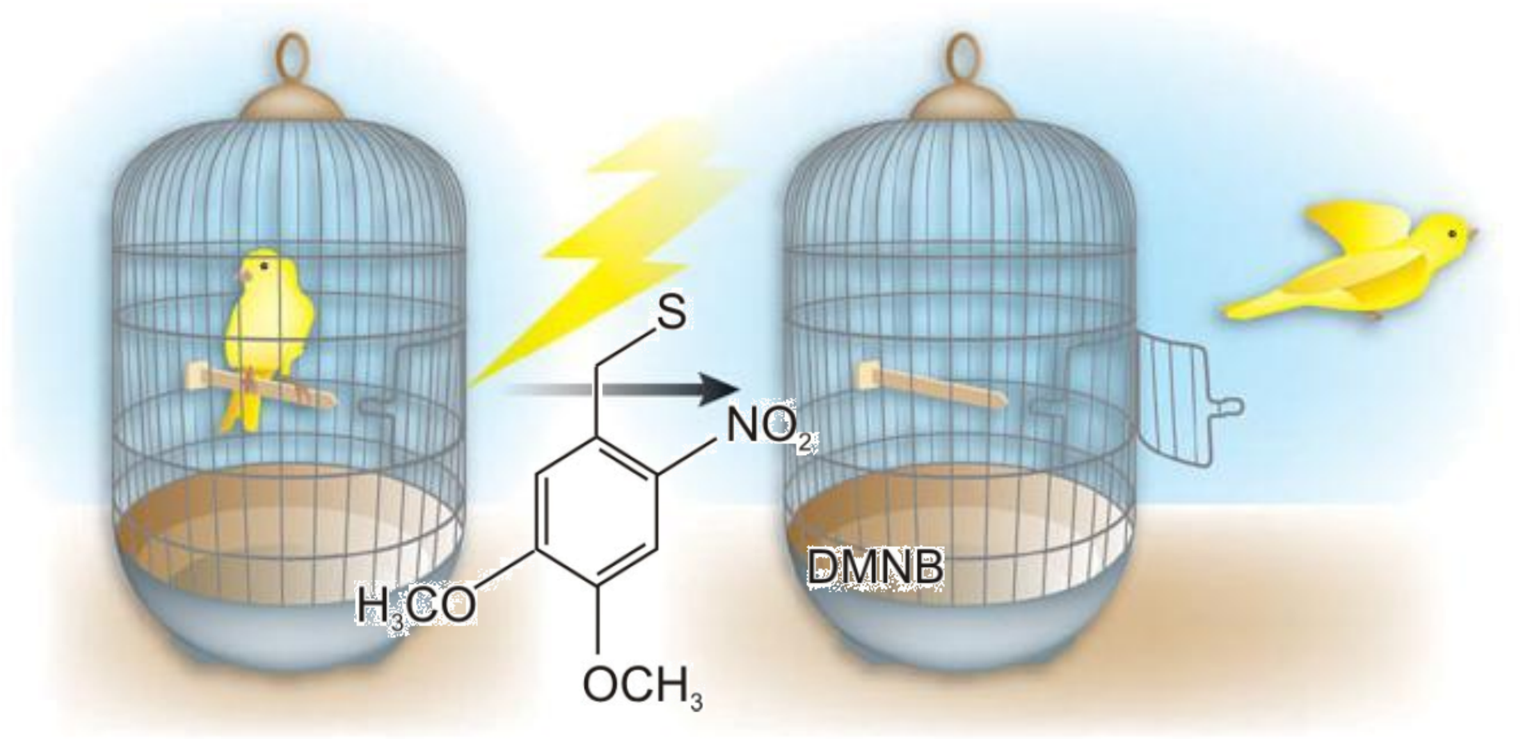



Jikeli*, Alvarez*, Friedrich*, …, Kaupp: Nature Comm **6**, 2015 (*=equal contribution)

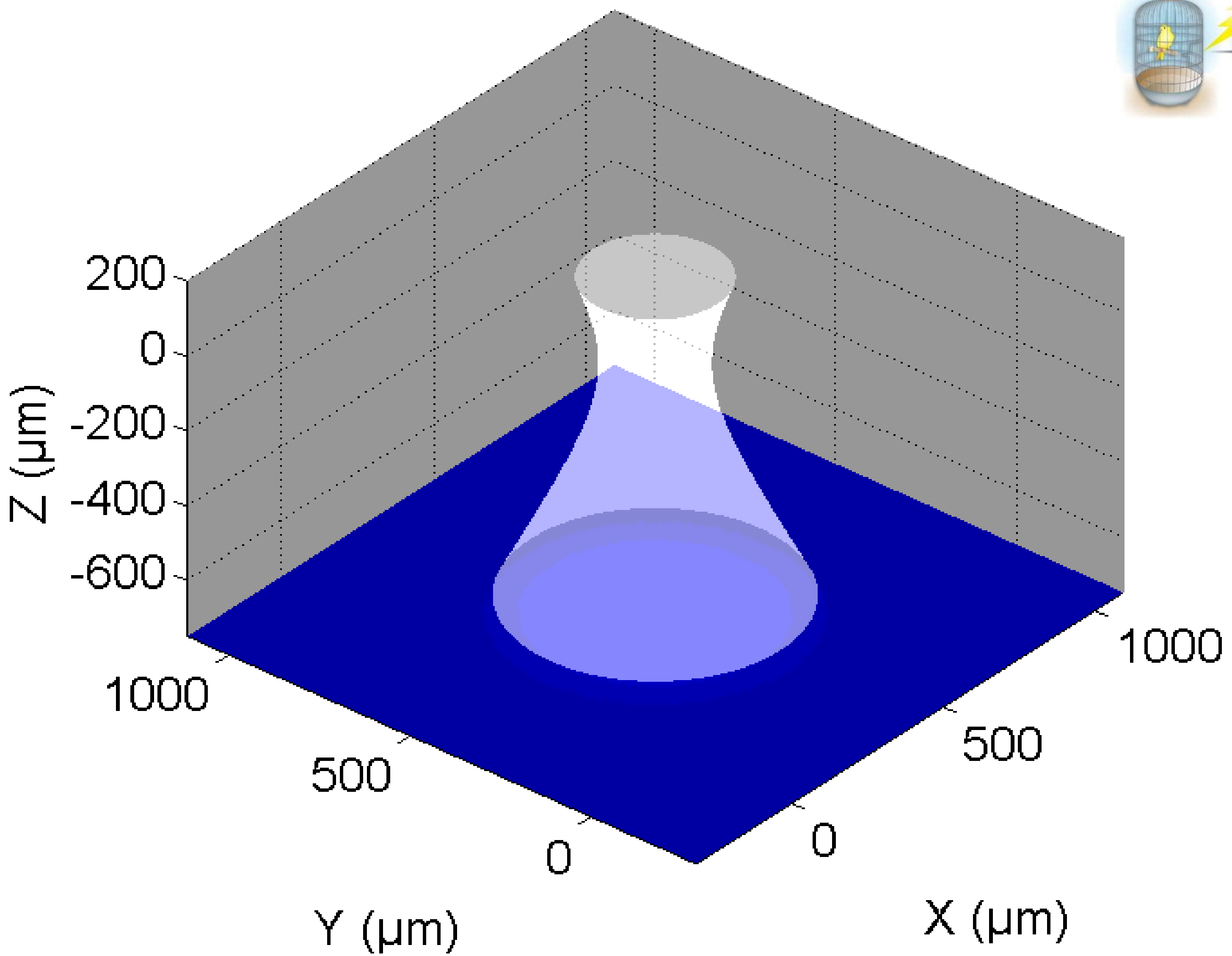
# How do sperm steer along helical paths?

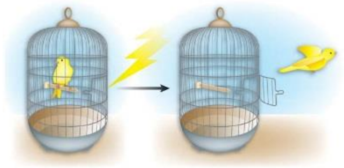
# Using light to "print" 3D concentration gradients

- Chemoattractant with chemical cage
- UV light removes cage



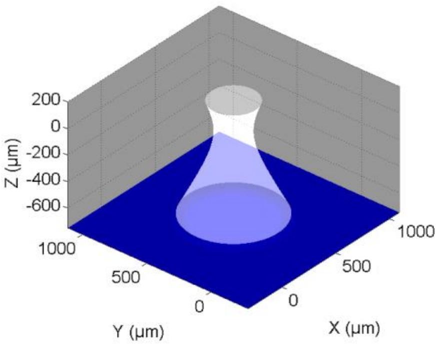
# Using light to "print" 3D concentration profiles

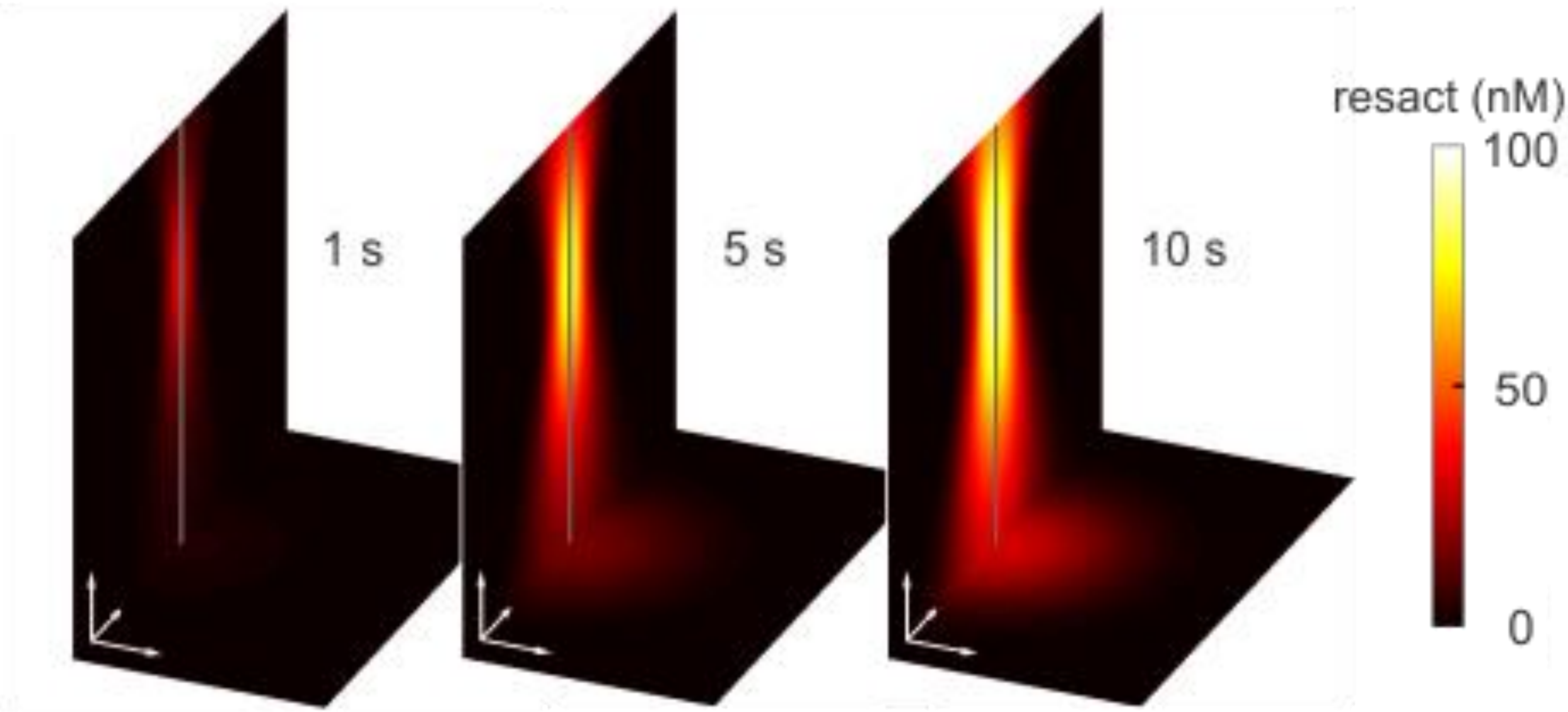


# We compute how the concentration evolves in time

- calibrated light intensity
- quantum yield
- diffusion coefficient



# Tracking a sperm cell in a 3D concentration profiles

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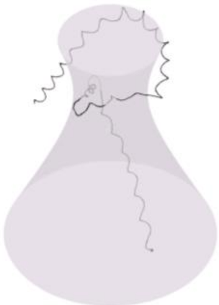
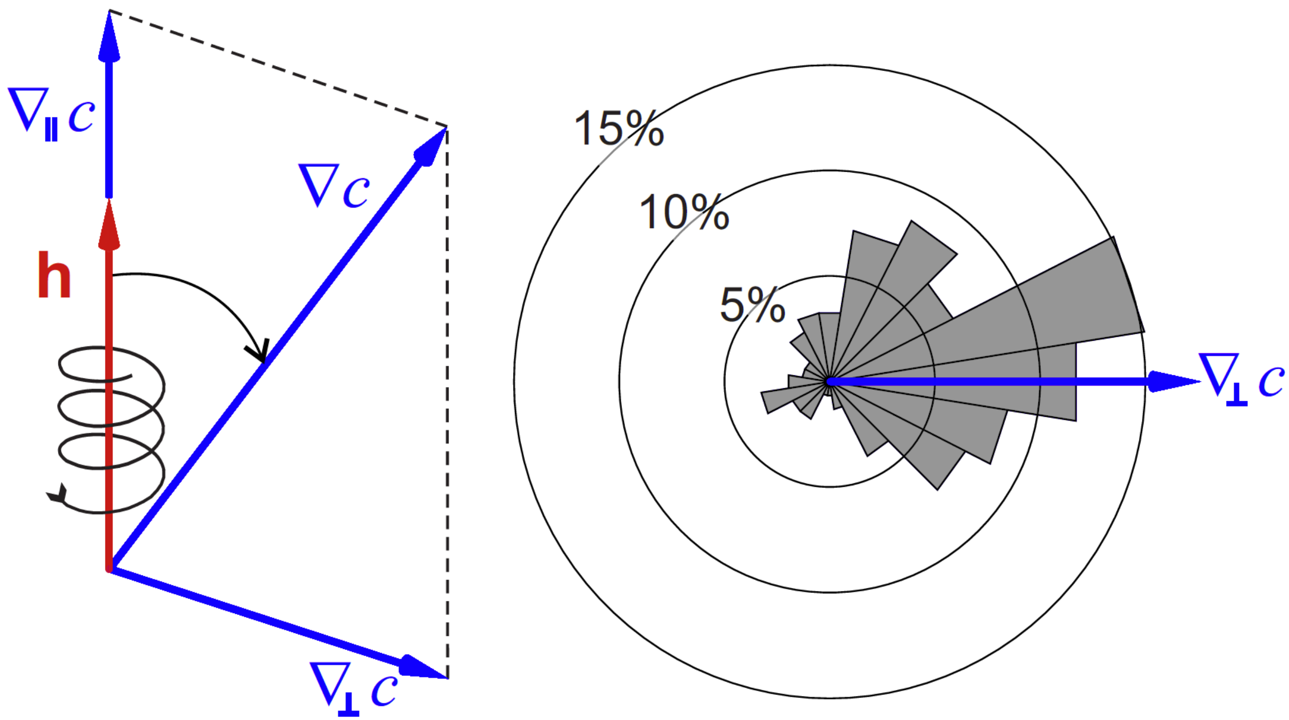
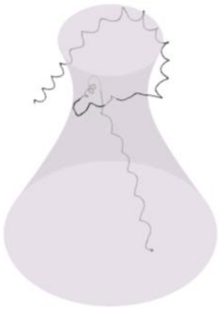
# Helical paths bend in the direction of the local gradient

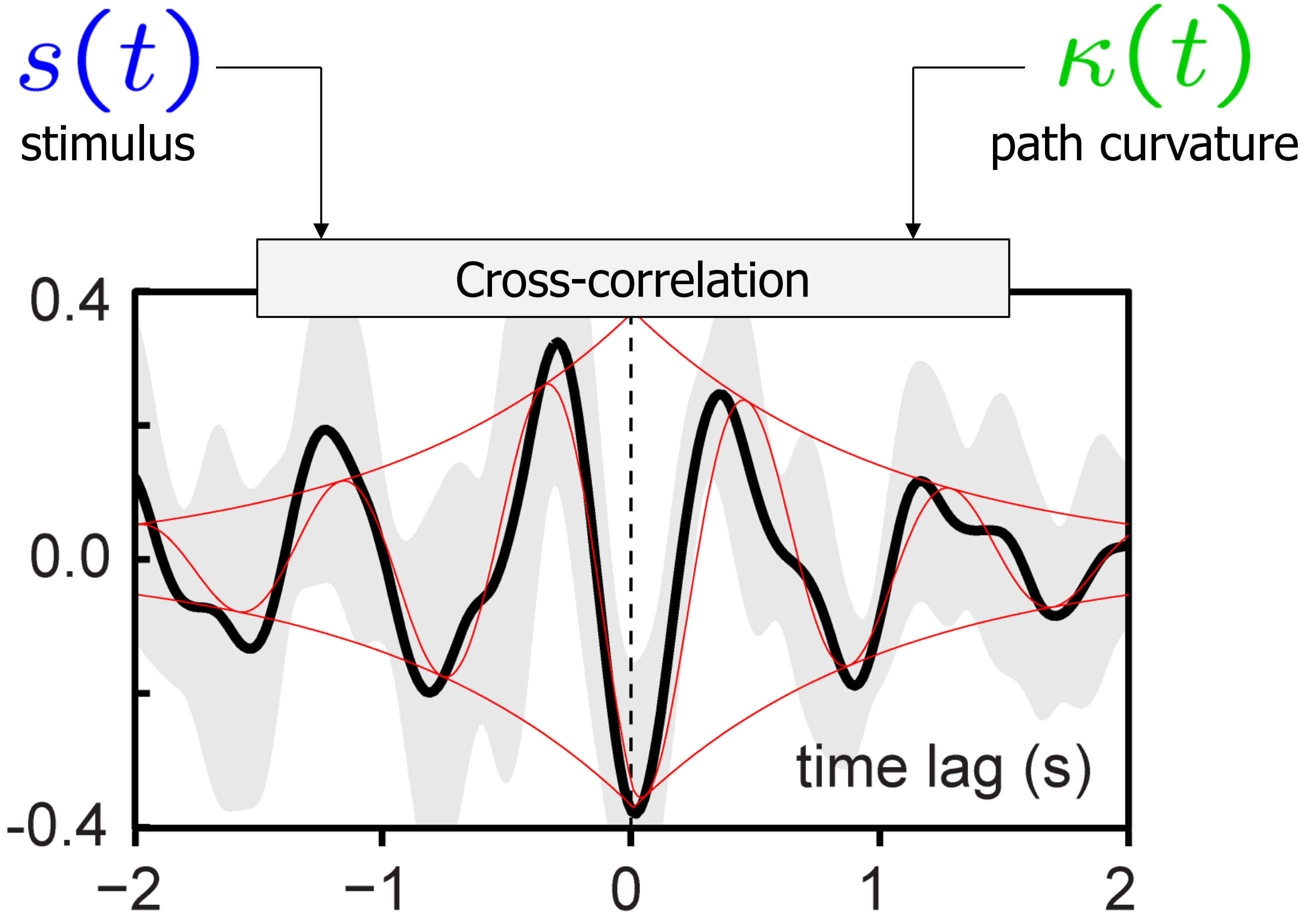





Jikeli*, Alvarez*, Friedrich*, …, Kaupp: Nature Comm **6**, 2015

# We can extract the sensory-motor transfer function

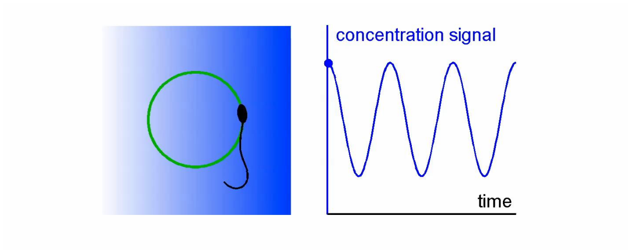


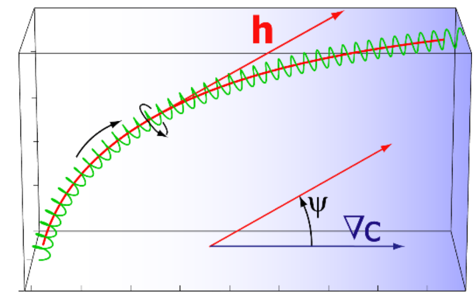



Phase-locked oscillations with phase-lag of 167°±35°, close to the optimum value 180°

# Theory and experiment of helical steering

swimming path $\mathbf{r}(t)$



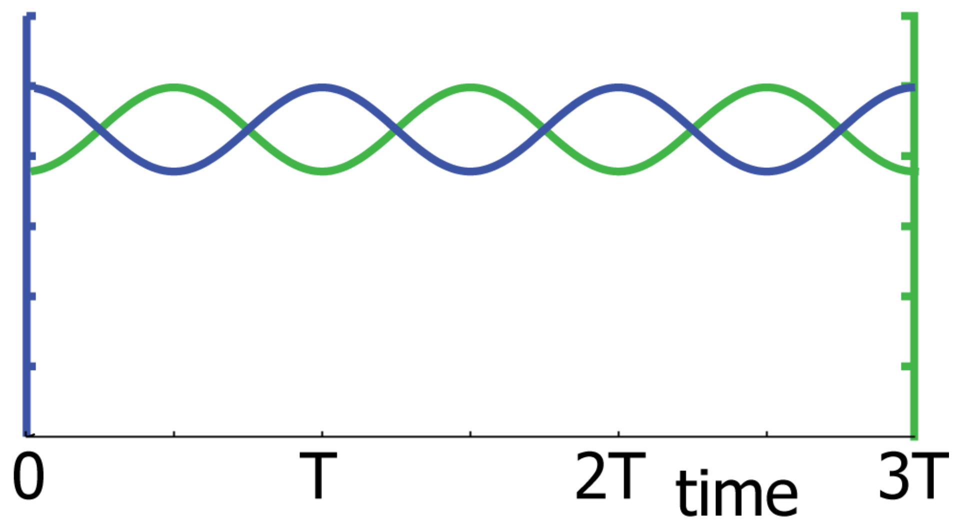




concentration stimulus $s(t)$

path curvature $\kappa(t)$

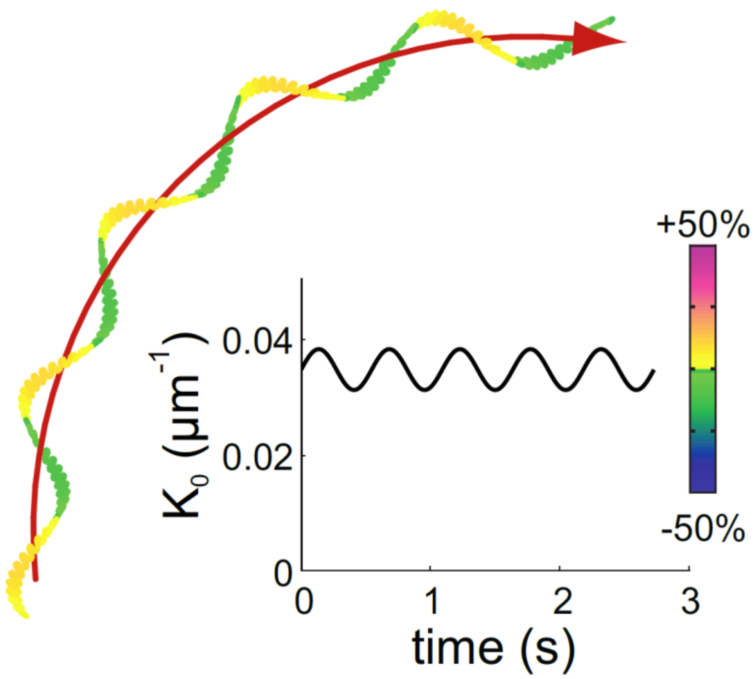
concentration

curvature



# Experiments prompt an extension of the theory

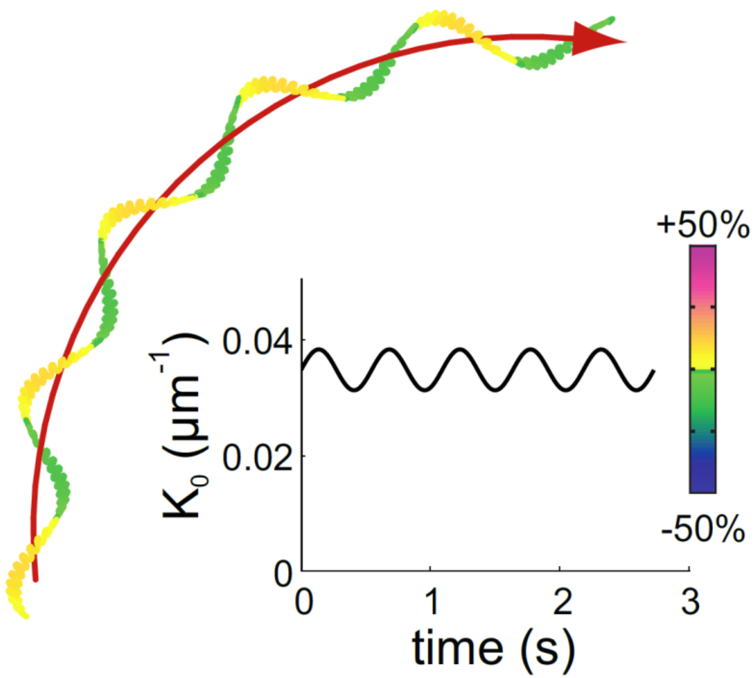
Small-amplitude oscillations of flagellar asymmetry
↓
gradual helix alignment

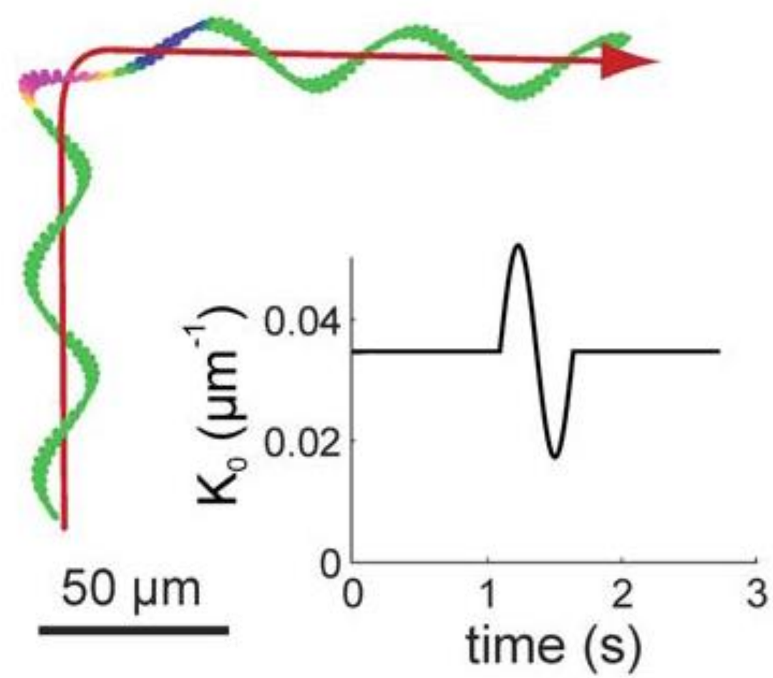


# Experiments prompt an extension of the theory

Small-amplitude oscillations of flagellar asymmetry
↓
gradual helix alignment

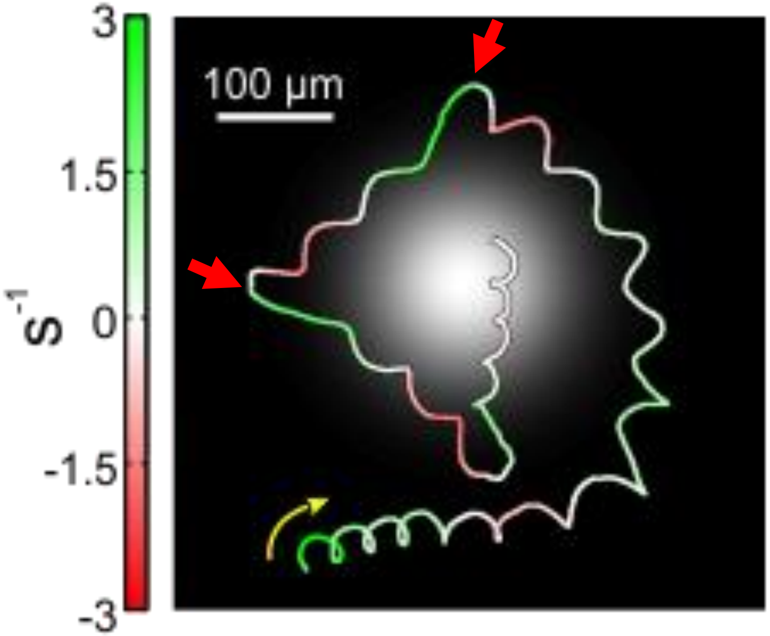
Large amplitude modulations of flagellar asymmetry
↓
sharp turns

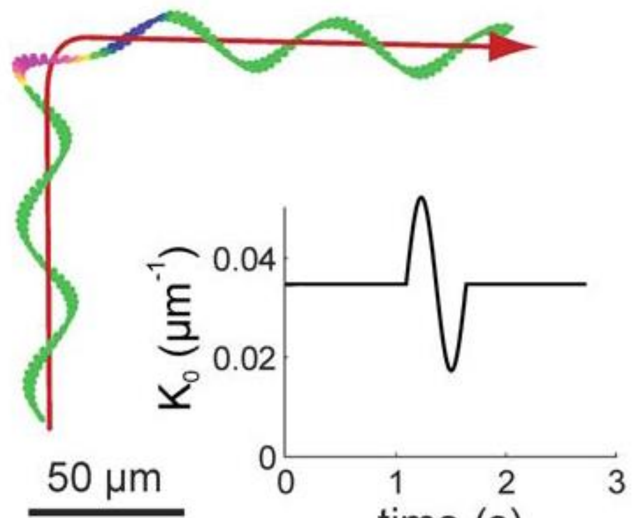


# Sharp turns are used in emergencies

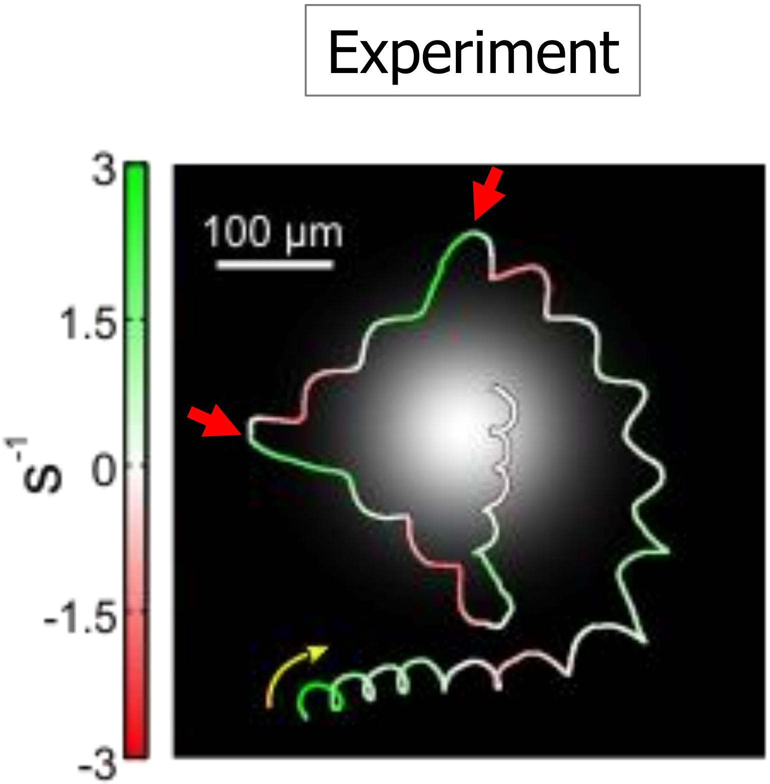
Experiment

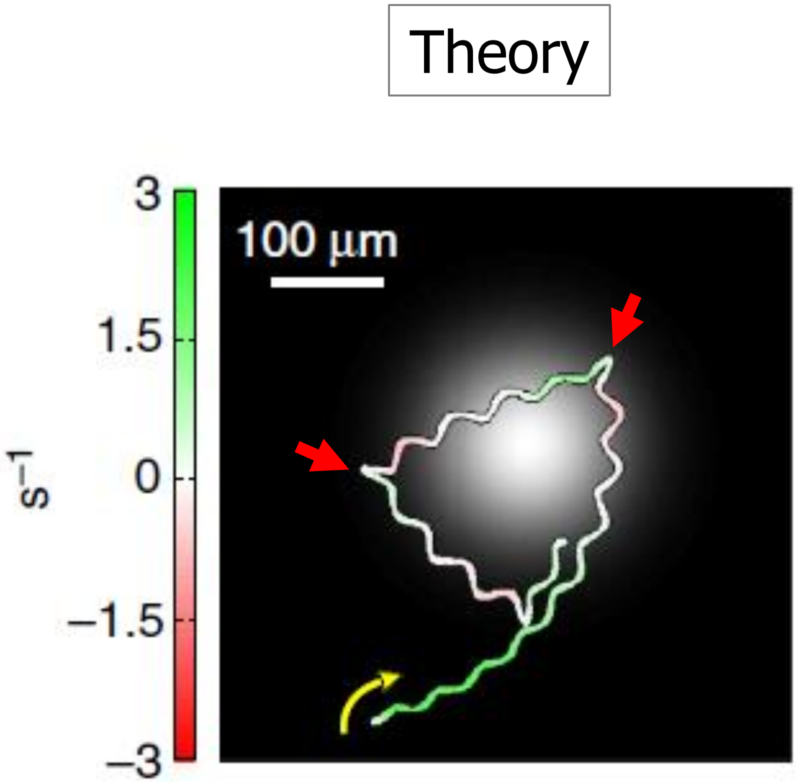



Jikeli*, Alvarez*, Friedrich*, …, Kaupp: Nature Comm **6**, 2015

# Experiment and theory of adaptive feedback




**"If life gets worse, respond strongly."**

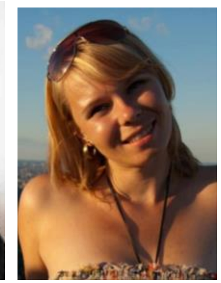
# Thank you for your attention !

- The experimental team
  - Jan Jikely
  - Luis Alvarez
  - Laurence Wilson



  - René Pascal
  - Rèmy Colin
  - Magdalena Pichlo
  - Andreas Rennhack
  - Christopher Brenker





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