大腸菌の走化性は情報に制限される

Escherichia coli chemotaxis is information limited

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Workshop OT 2023 最適輸送とその周辺–機械学習から熱力学的最適化まで

March 16 , 2023

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- 背景：細胞の情報処理動態を可視化する実験技術
- 大腸菌の情報処理効率の評価 Mattingly* and **Kamino*** et al. *Nature Physics* (2021)
- 私の情報処理の効率化 **Kamino** et al. *PNAS in press*

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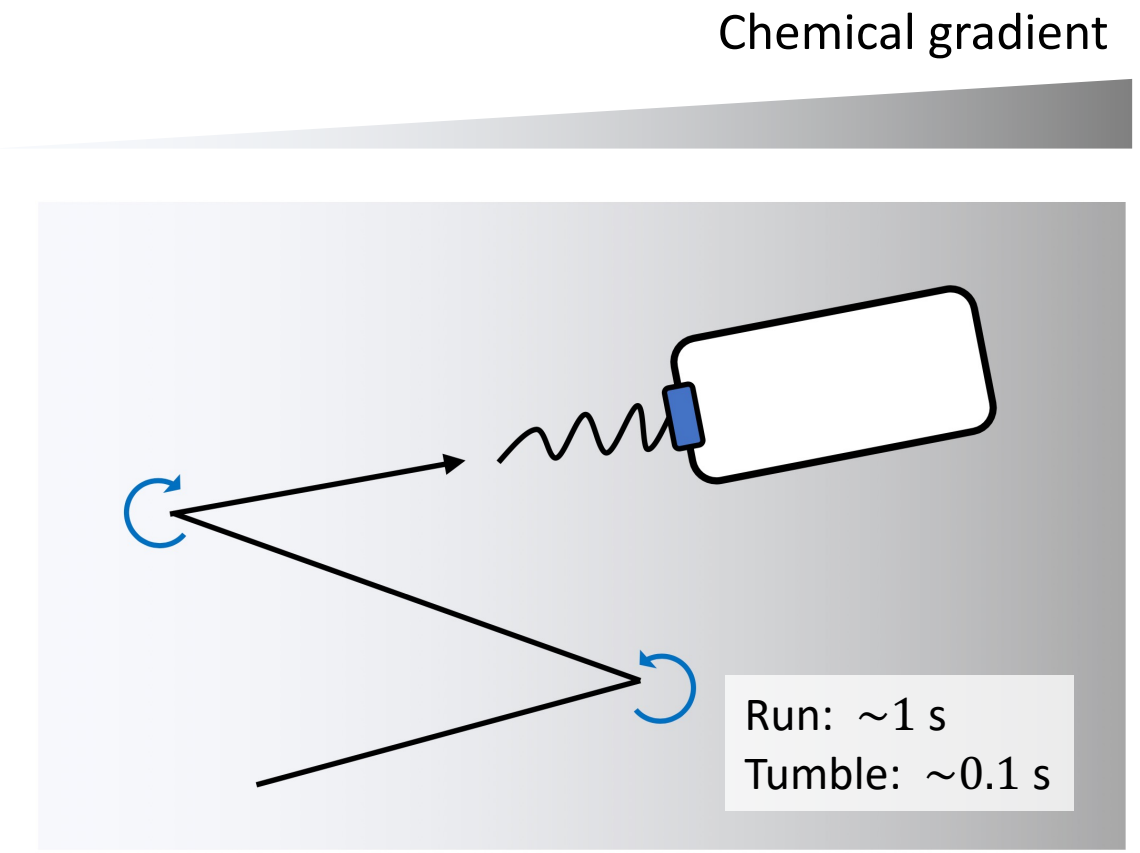
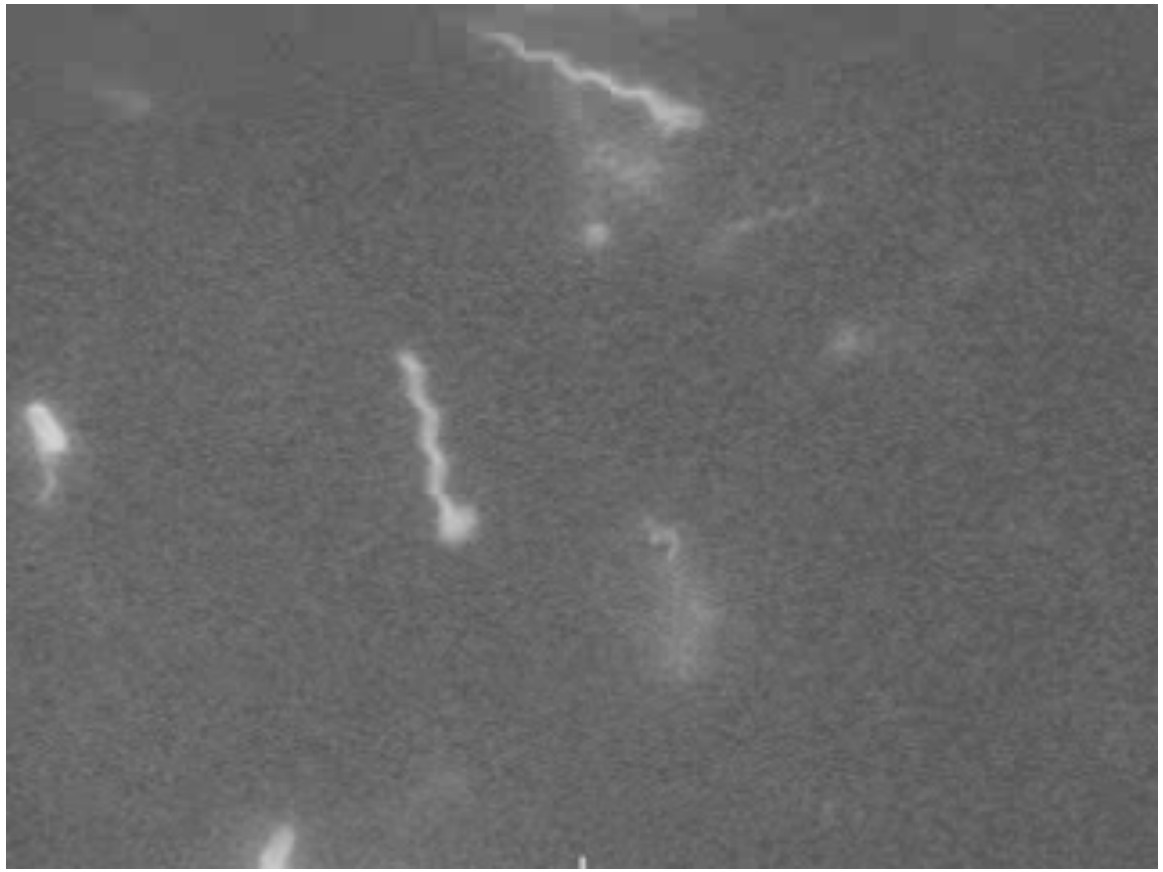
Cells are adaptive **sensorimotor systems**

Goal: to extract principles behind
cellular behavior** and **information processing

***E. coli* chemotaxis** as a minimal model

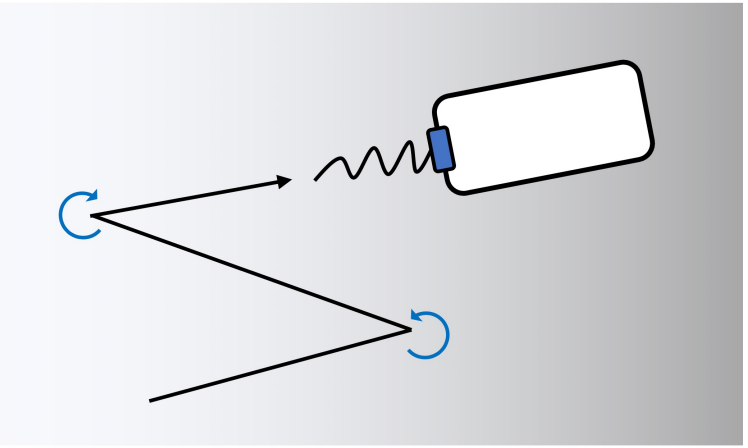


E. coli under a microscope



Turner, Ryu, Berg. (2000) *J. Bacteriol*

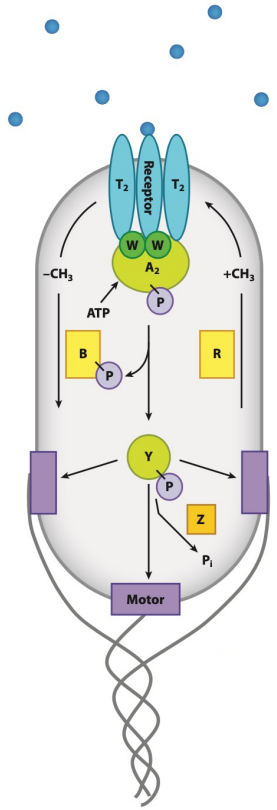
E. coli use **temporal information** of signals to exhibit chemotaxis



Local concentration increases in time

→ Increase the run length, on average

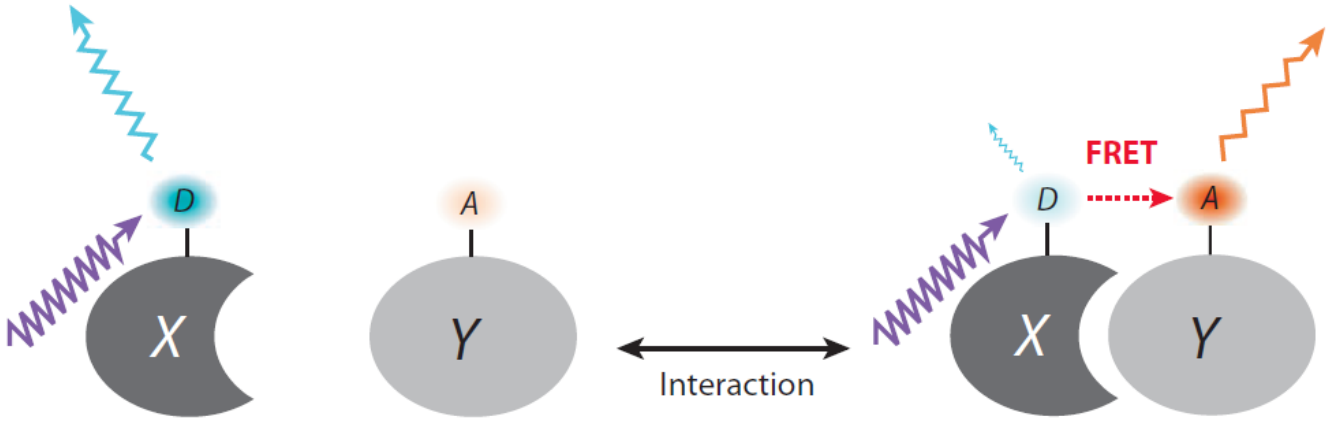
Extracellular signal is processed by
a **biochemical reaction network**



Tu (2013)

*Can we measure **the dynamics of the pathway** inside living cells?*

Molecular interactions inside cells are visualized by **FRET**

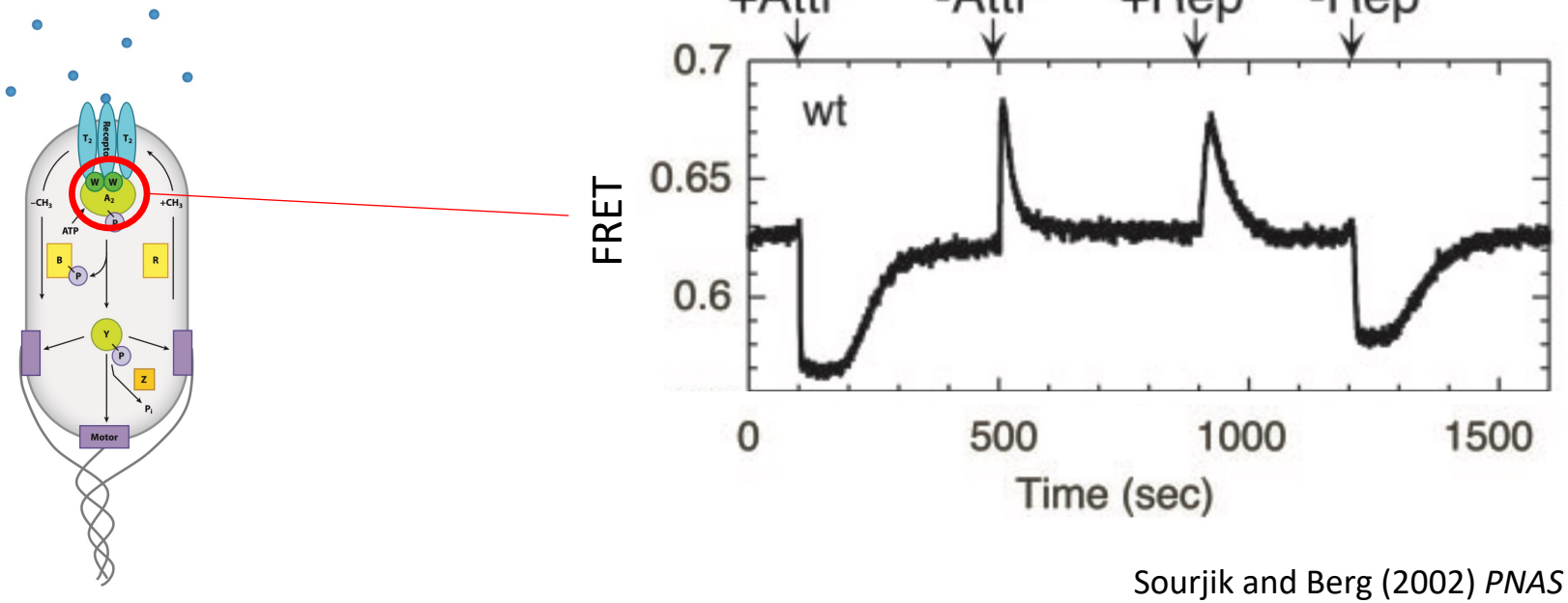


Miyawaki, 2011

FRET also detects:

- Enzyme activities
- Small molecules (e.g., Ca^{2+}, cAMP)

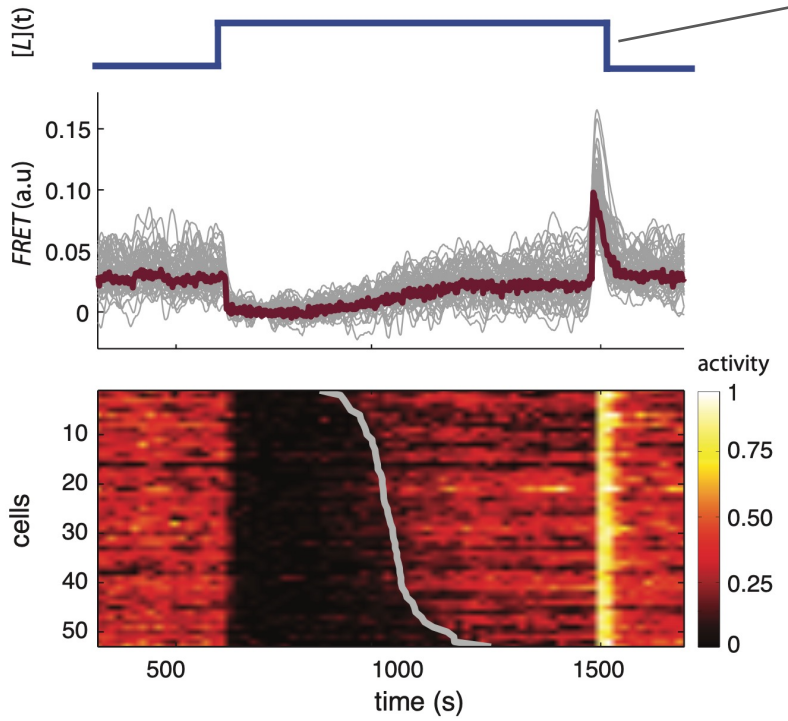
The kinase activity has been studied by
population-level FRET measurements



Sourjik and Berg (2002) *PNAS*

*How do **individual cells** respond differently from the average?*

Cell-to-cell variations have been revealed by
single-cell FRET measurements

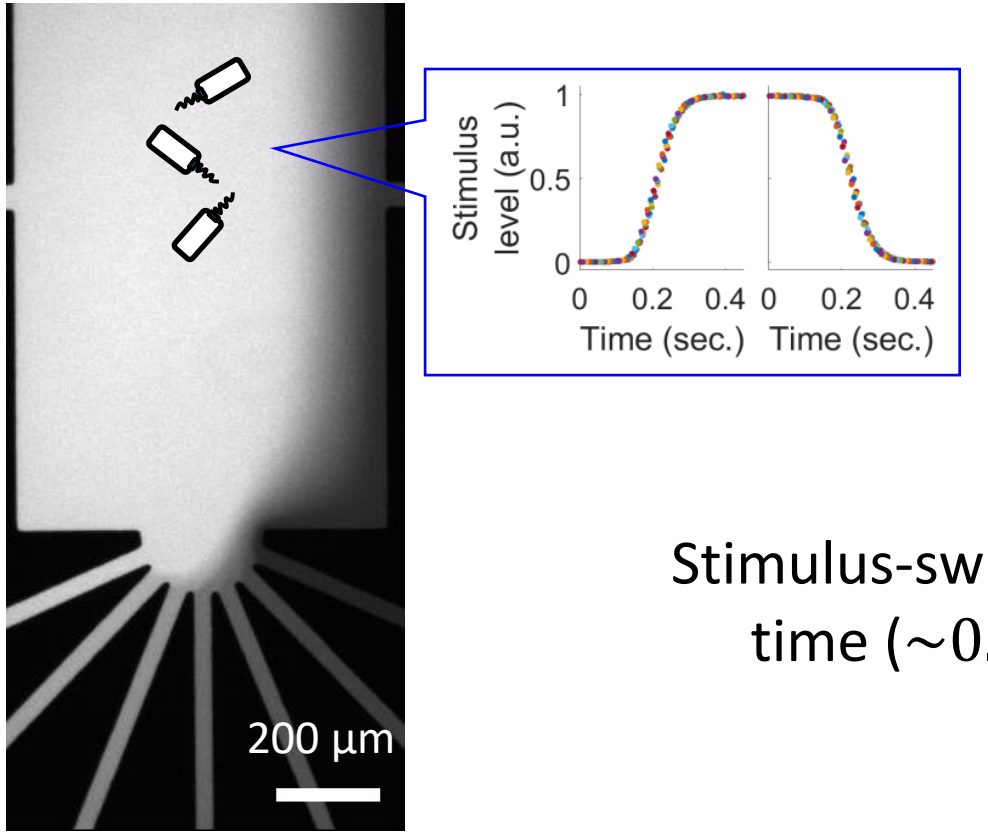


Slow (~10 s) stimulus switching forced us to study slow responses to *supraphysiological doses* of stimuli

*How do individual cells respond in a **faster** and **physiological** regime?*

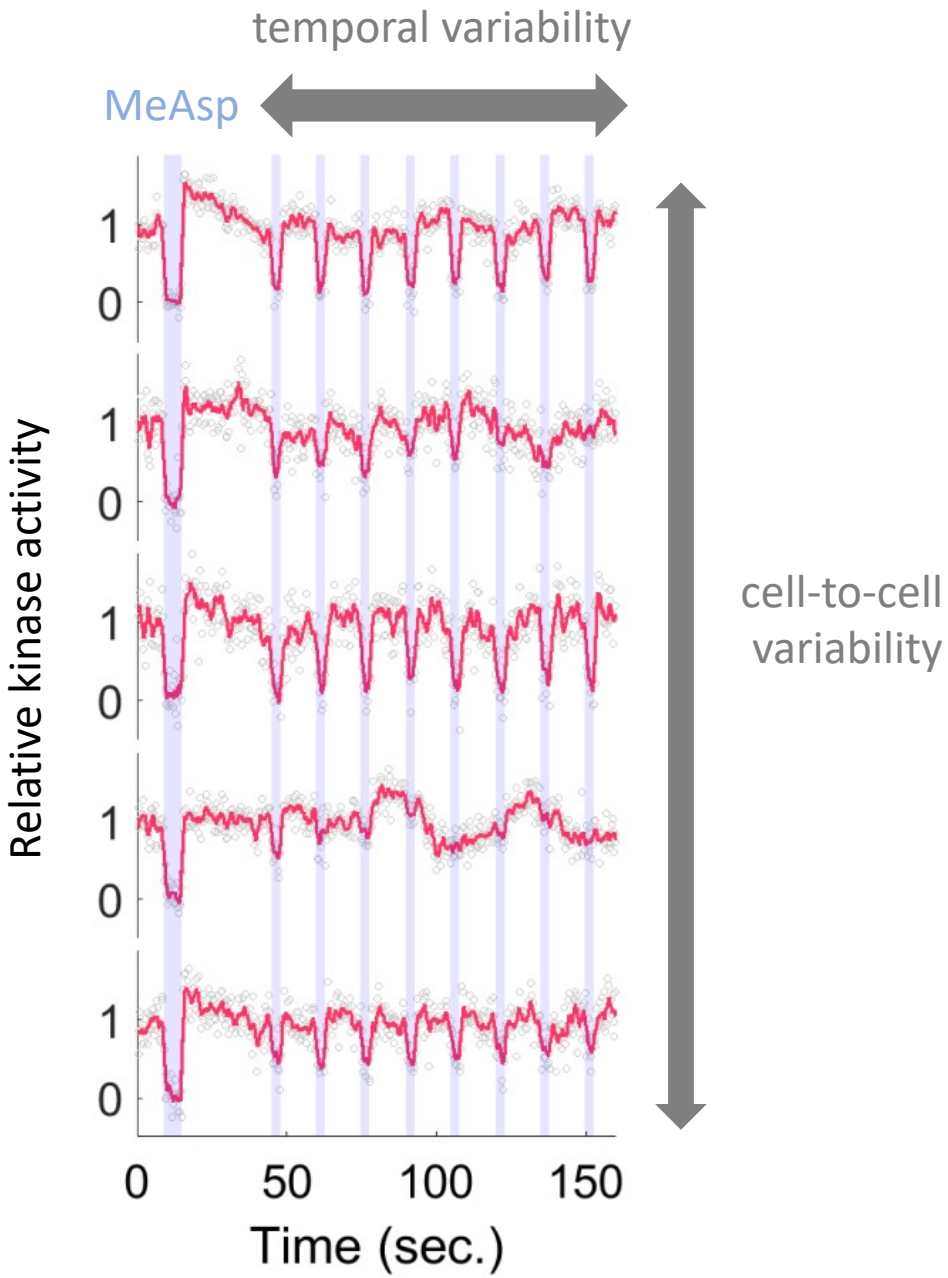
Keegstra, **Kamino** et al. (2017) *ELife*

A computer-controlled microfluidic device has enabled **fast stimulus switching**



Stimulus-switching time (~ 0.1 s) $\ll$ Physiological response time (~ 10 s)

Kamino et al. (2020) *Sci. Adv*



Kamino et al. (2020) *Sci. Adv*

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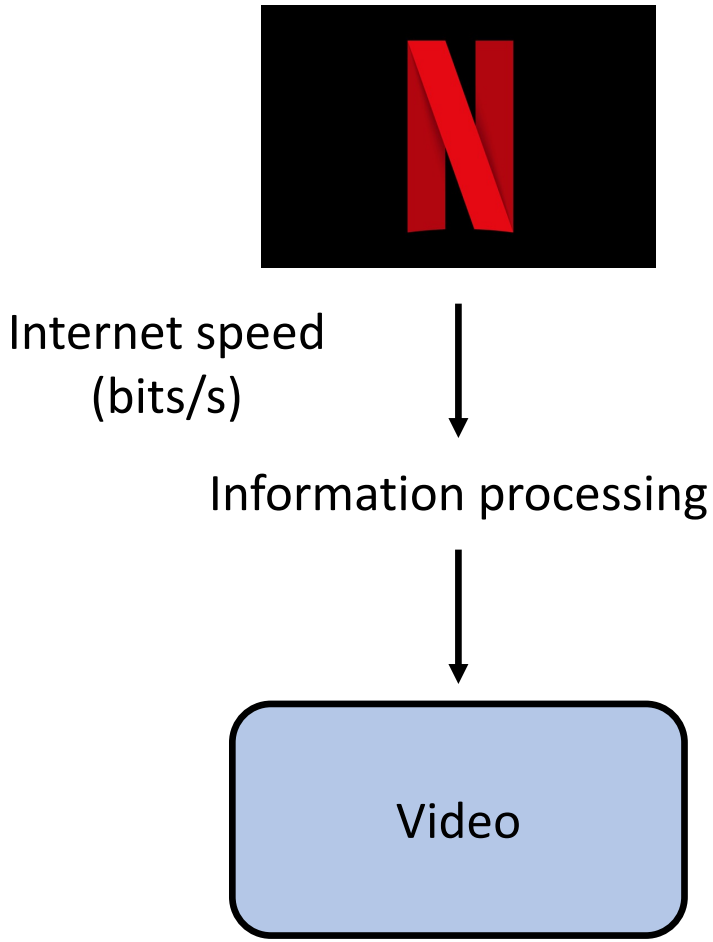
- 技術のブラッシュアップ **Kamino** et al. *PNAS in press*

Questions

- How much information does an *E. coli* cell **acquire** from the environment during chemotaxis?
- To what extent is the performance of chemotaxis **limited** by the amount of acquired information?

A graph captures the **relationship between information and performance**



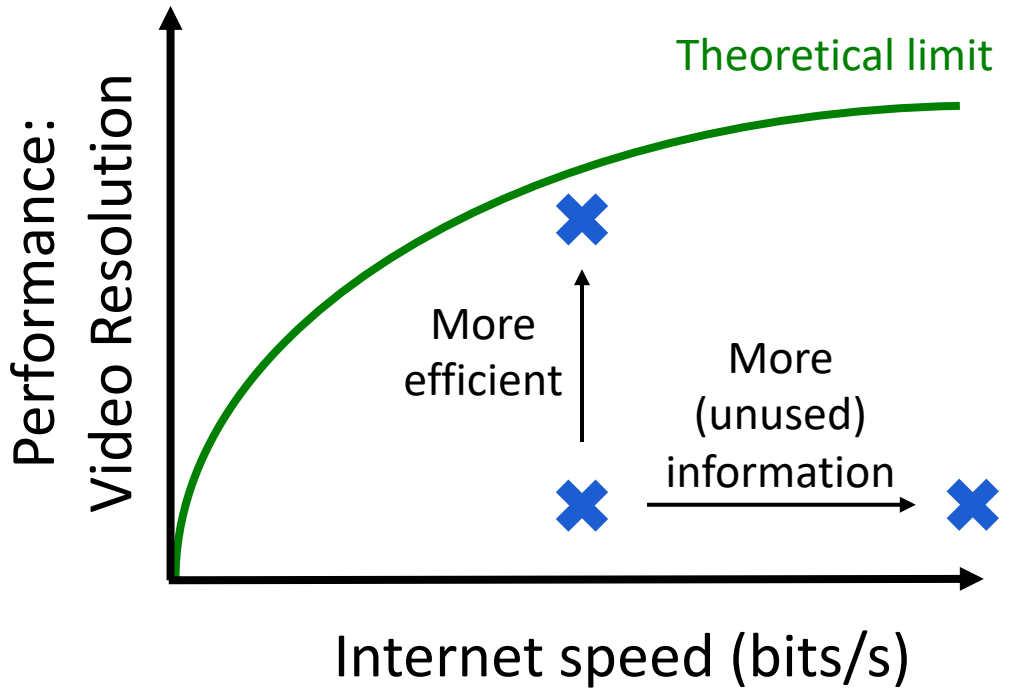
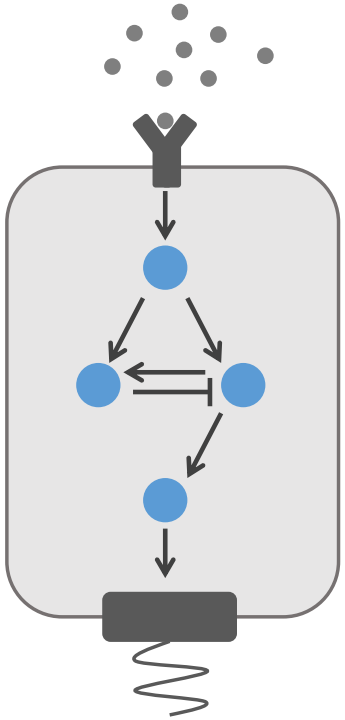
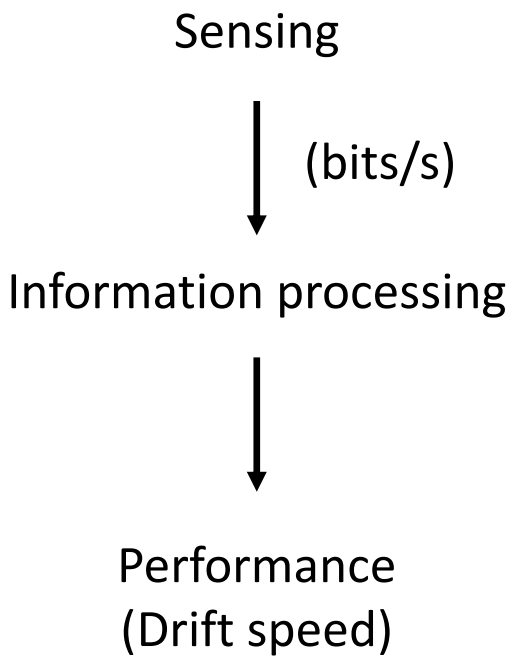


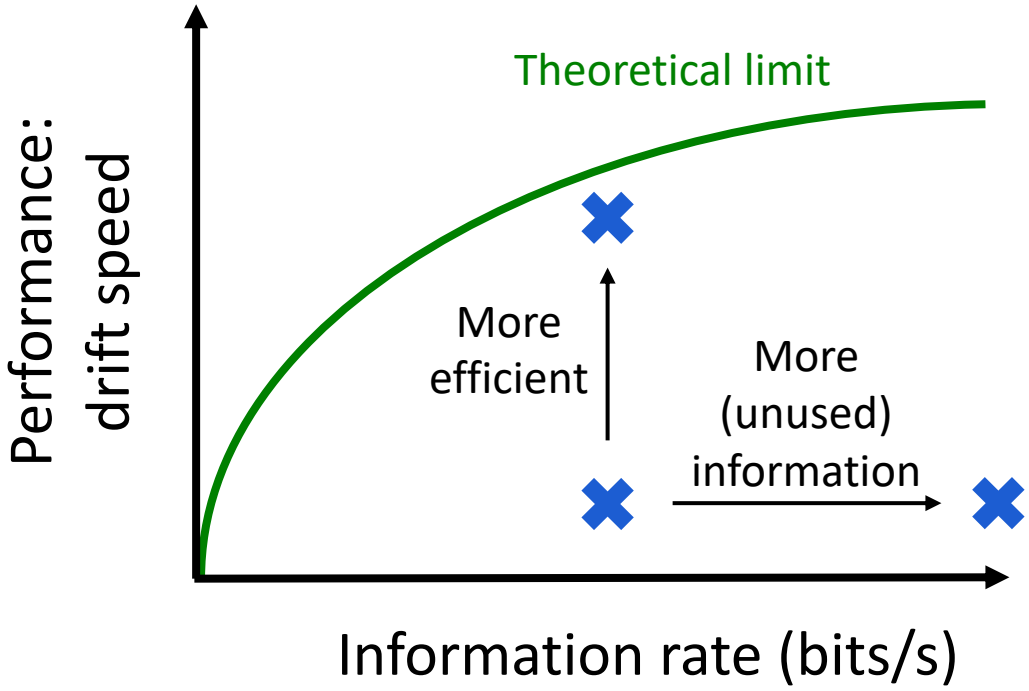
Image: Netflix.com

Tkacik and Bialek (2016) *Annu. Rev. Condens. Matter Phys.*

Direct **analogy** to *E. coli* chemotaxis







In E. coli chemotaxis:

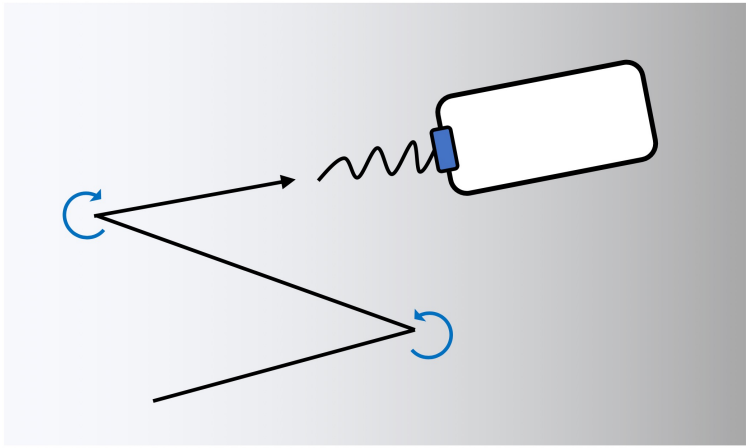
- *What does **the theoretical limit** look like?*
- *Where dose **a real cell** locate in the information-performance plane?*

How much information **do you think** is necessary for chemotaxis?

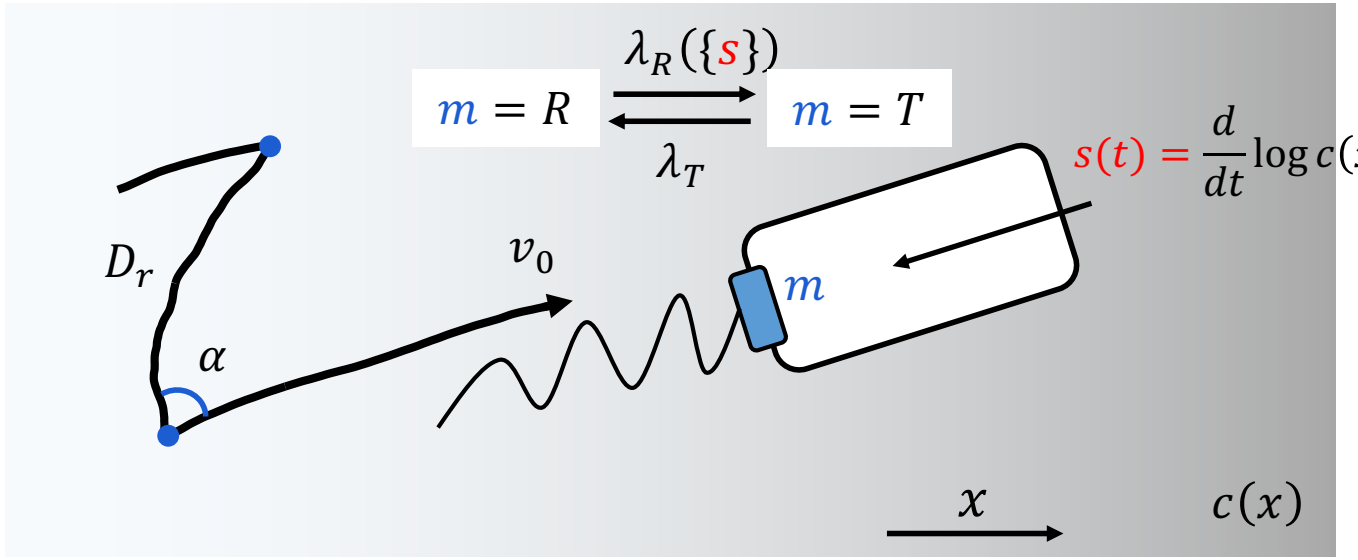
E. coli determine whether a chemical concentration **increases** or **decreases** in a single run

→ **Binary decision** for each run (~1 sec)

→ ~1 bit/sec?



Model of chemotaxing *E. coli*



The model gives drift speed and information rate

Drift speed:

$$v_d\left(\lambda_R(\{s(t)\})\right) = v_0 \frac{(1-\alpha)\lambda_{R0}}{(1-\alpha)\lambda_{R0} + 2D_r} P_{run} \left\langle \left(\frac{\lambda_{R0} - \lambda_R(\{s(t)\})}{\lambda_{R0}} \right) \cos(\theta(t)) \right\rangle$$

Balance between active and passive reorientation

Appropriateness of signaling response

Information (transfer entropy) rate:

$$\dot{I}\left(\lambda_R(\{s(t)\})\right) = \frac{1}{2}\lambda_{R0} P_{run} \left\langle \left(\frac{\lambda_{R0} - \lambda_R(\{s(t)\})}{\lambda_{R0}} \right)^2 \right\rangle$$

Tumble events per sec

signal-induced variation in tumble rate

What is the highest drift speed *with a given information rate*?

Locsei (2007); Mattingly* and **Kamino*** et al. (2021)

E. coli need **very little information** to perform chemotaxis, in principle

Theoretical limit:

$$\frac{v_d}{v_0} \leq \frac{(1-\alpha)\lambda_{R_0}}{(1-\alpha)\lambda_{R_0} + 2D_r}\left(\frac{8\log(2)\, D_r P_{run} \dot{I}}{12\lambda_{R0} D_r}\right)^{1/2}$$

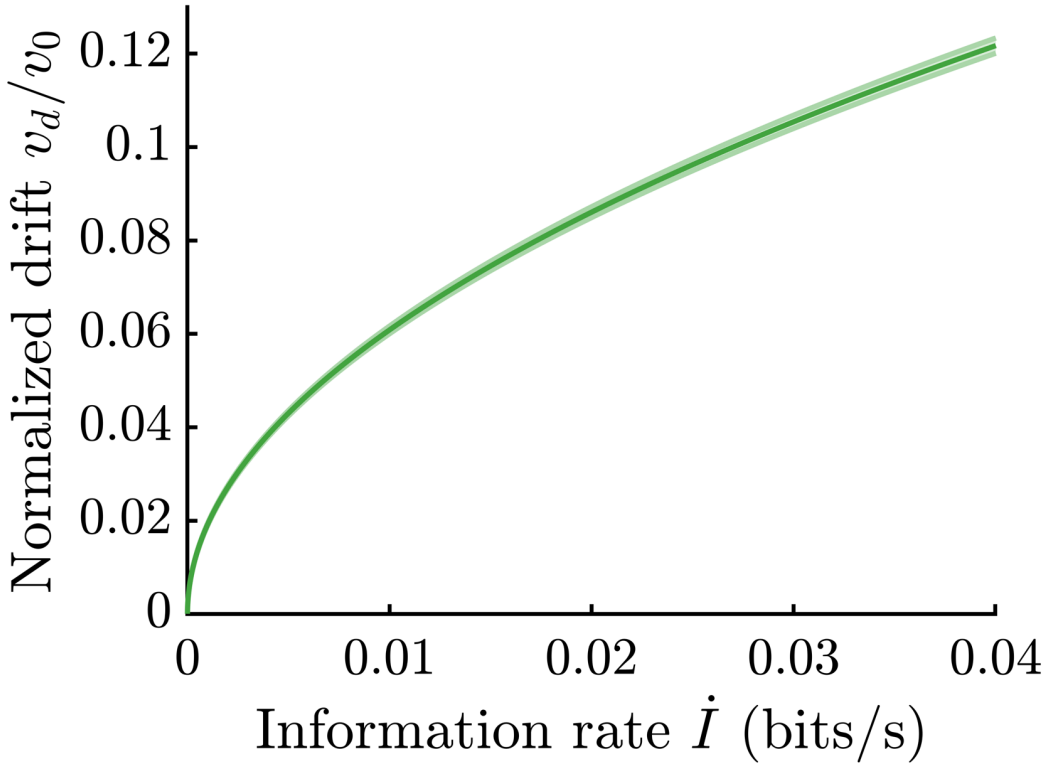
Measurements of behavioral parameters:

$\alpha = 0.06 \pm 0.01$

$\lambda_{R_0} = 0.893 \pm 0.006\ \mathrm{s}^{-1}$

$D_r = 0.0441 \pm 10^{-4}\ \mathrm{rad}^2/\mathrm{s}$

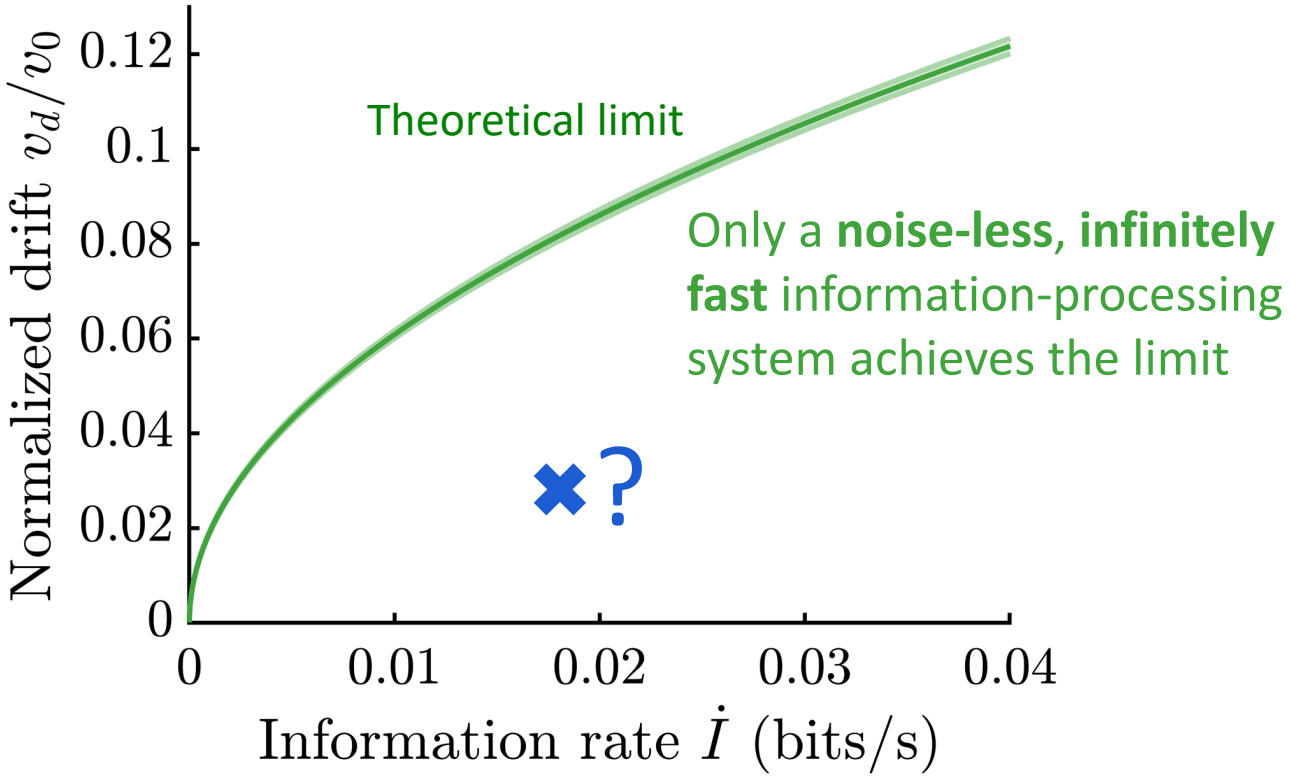
$P_{run} = 0.89 \pm 0.01$



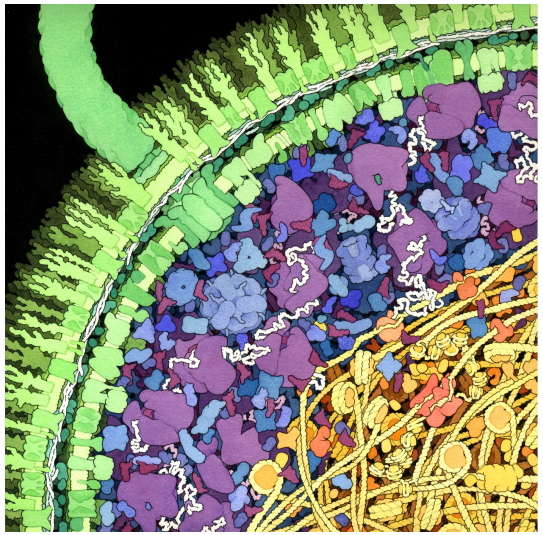
E. coli don't have to answer the binary question perfectly;
*They just need to **slightly increase the chance** of getting the correct answer*

Mattingly* and **Kamino*** et al. (2021)

How far is **a real cell** from the theoretical limit?

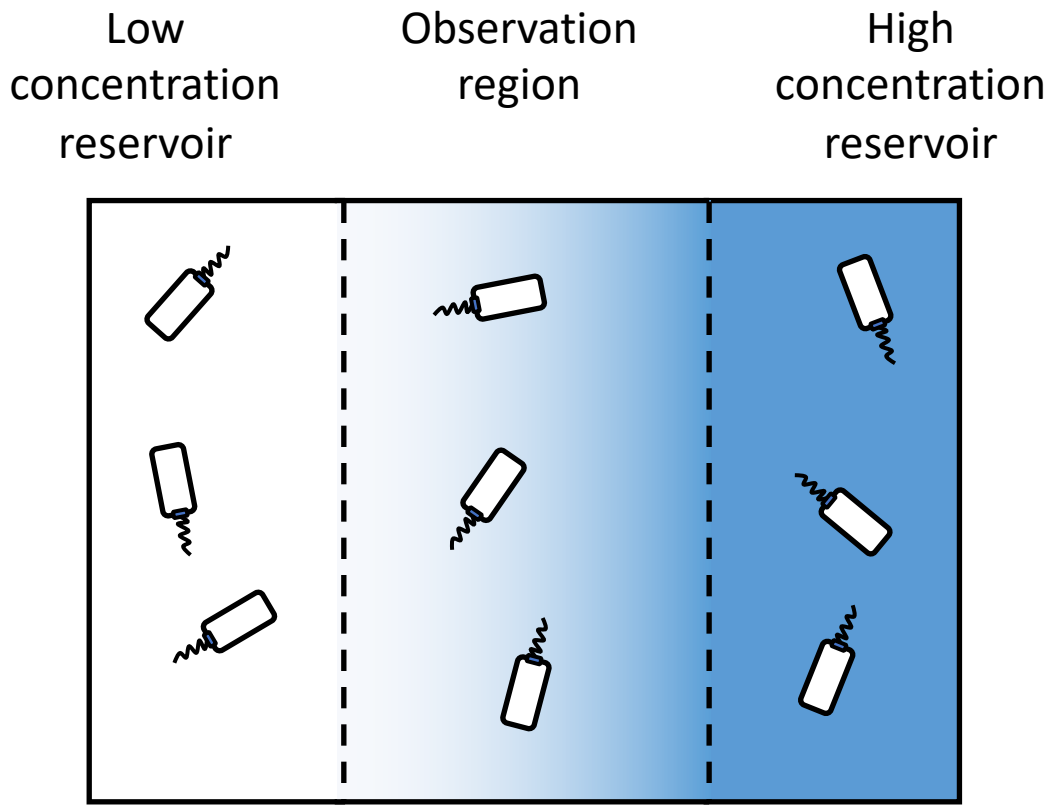


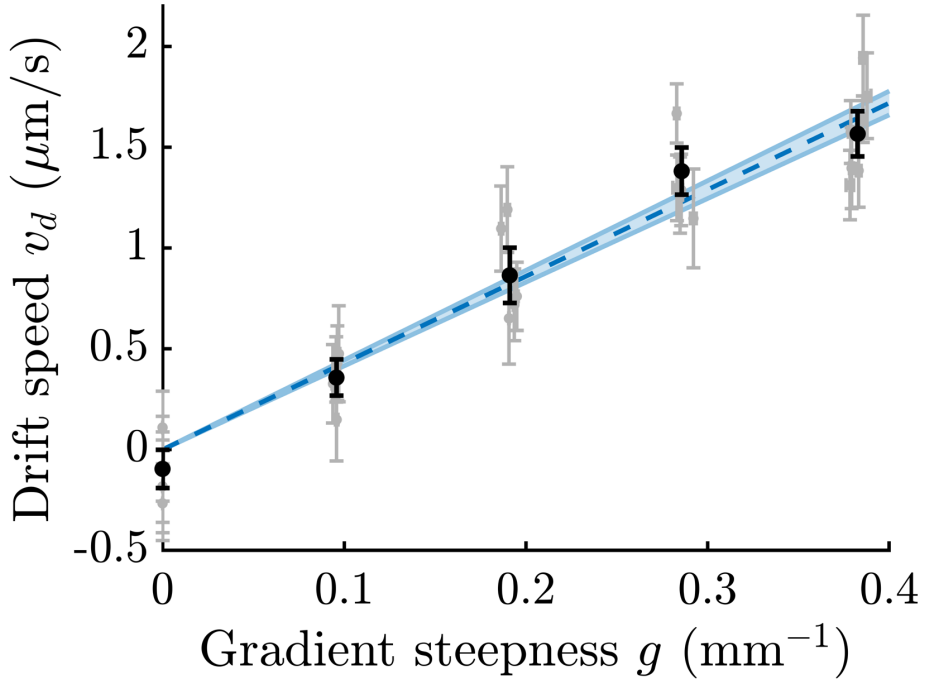
But real cells are **noisy**!



David S. Goodsell

Measuring **drift speed**





***How much information** do E. coli get?*

Mattingly* and **Kamino*** et al. (2021)

Information rate is determined by the statistical properties of the **signal**, **signaling response** and **signaling noise**

Information rate: $\dot{I} \sim \frac{g^2}{4\pi} \int_{-\infty}^{\infty} \frac{V(\omega)|K(\omega)|^2}{N(\omega)} d\omega$

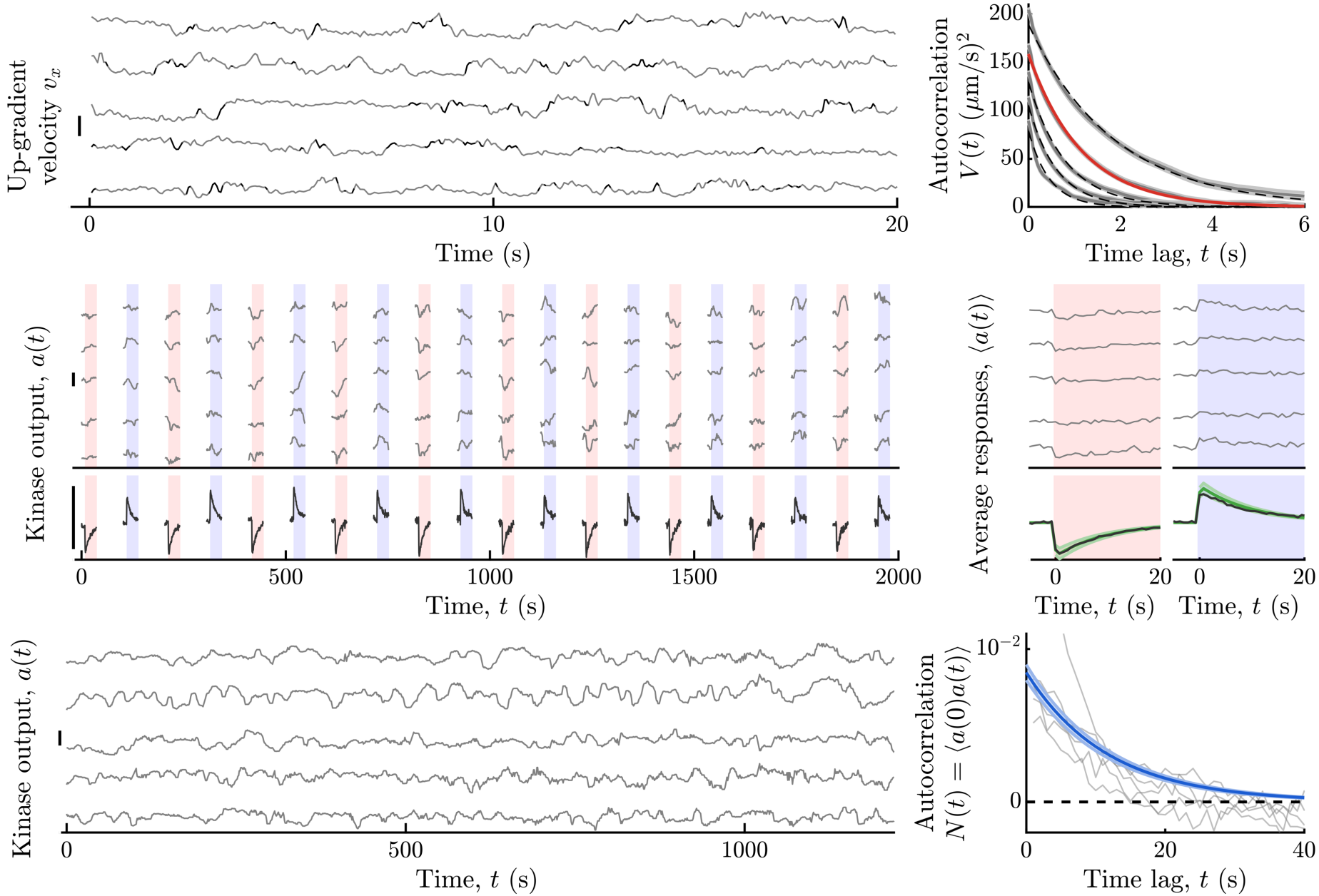
Measuring **signal** = Measuring motion of chemotaxing cells

Tostevin & ten Wolde (2009) *PRL*

Signal

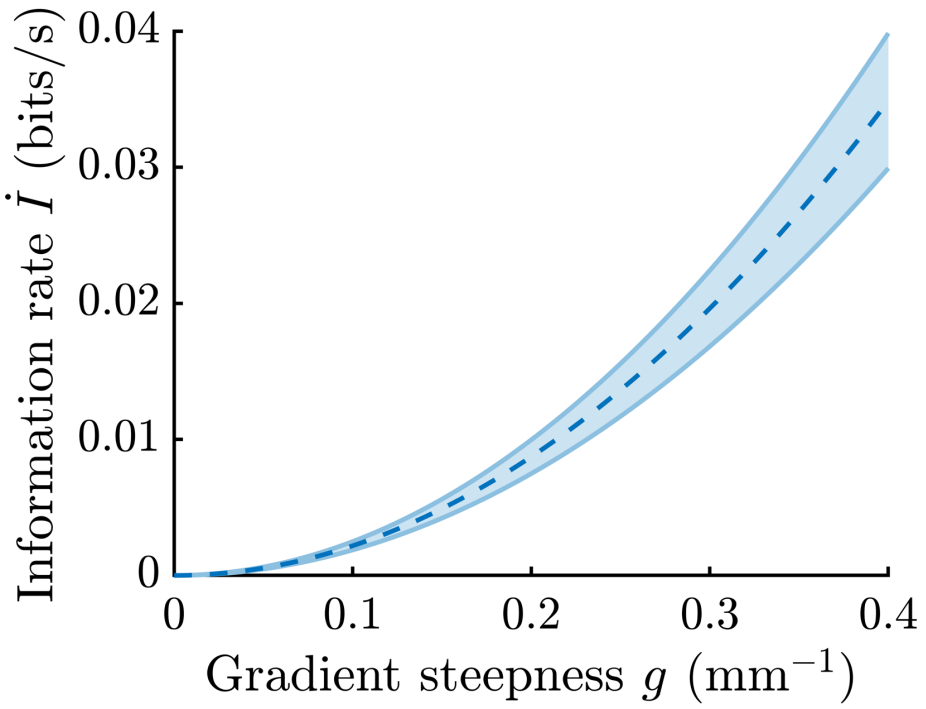
Response

Noise



Mattingly* and **Kamino*** et al. (2021)

Information rate that a single *E. coli* cell acquires from chemical gradients

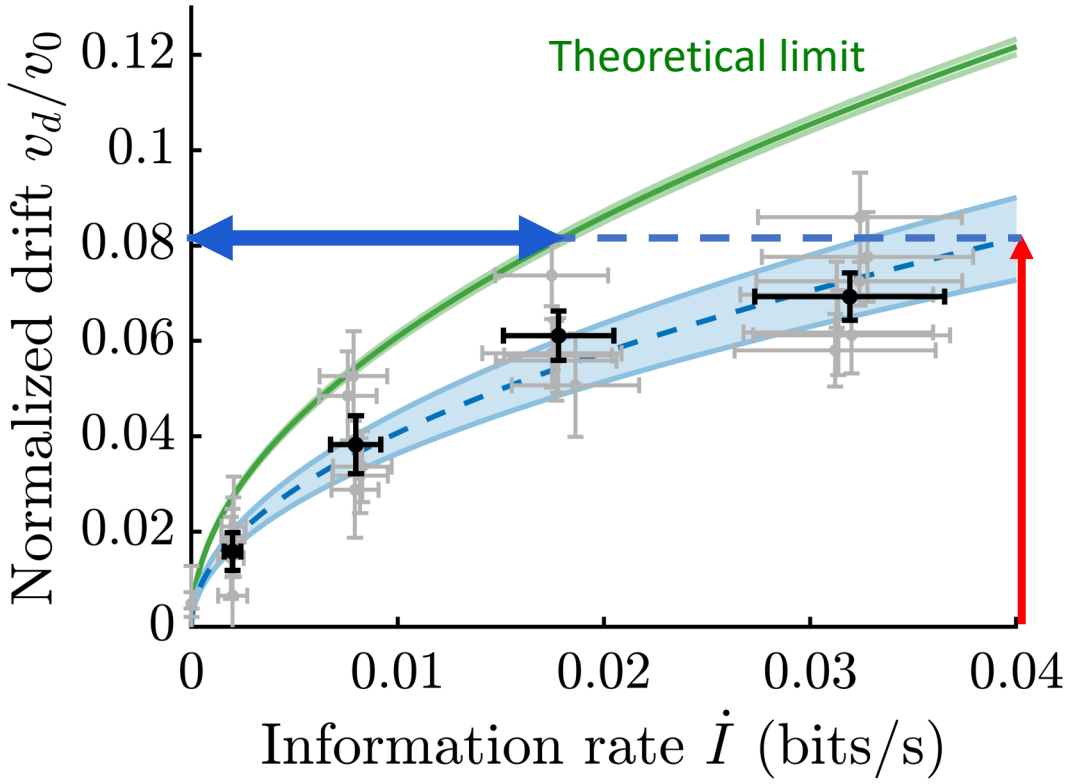


*How well does a **real cell** perform compared to the **theoretically limit**?*

Mattingly* and **Kamino*** et al. (2021)

E. coli are **efficient in information usage**

~ 42% of acquired information used



Cell signaling systems have evolved to efficiently use information

Mattingly* and **Kamino*** et al. (2021)

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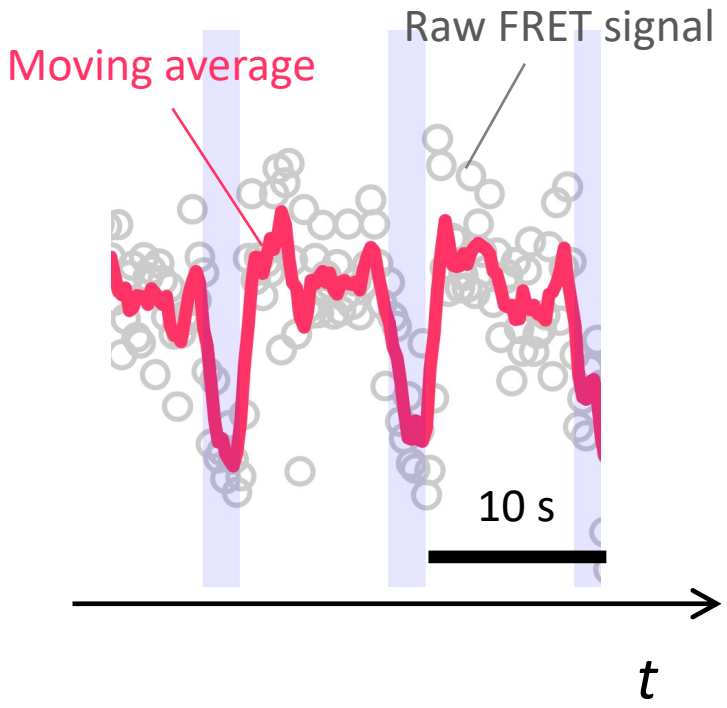
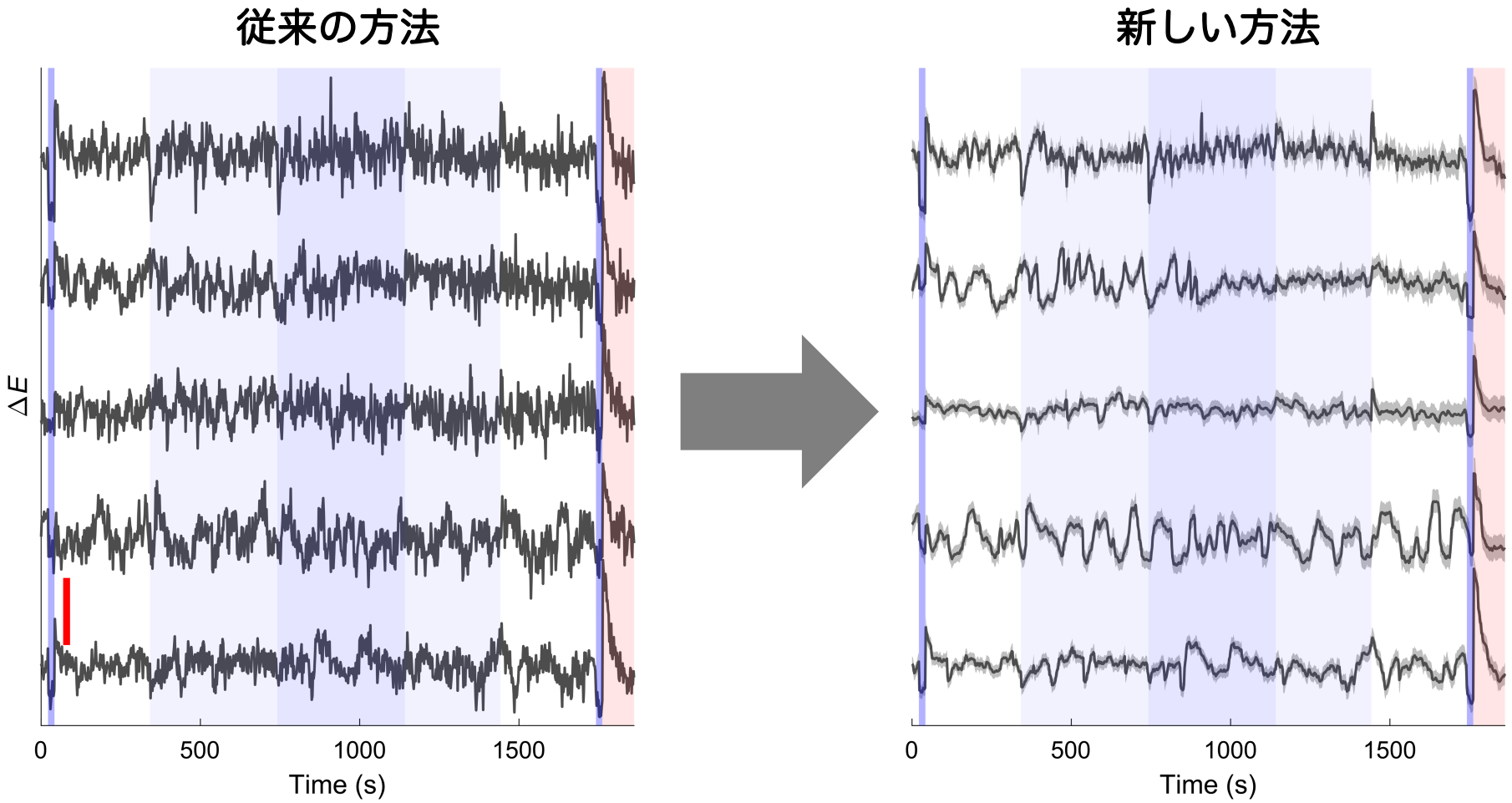
FRET signals from single bacteria are **VERY noisy**



Could we improve the SNR?

ベイズフィルタを用いたFRETデータ解析法の最適化 Kamino et al., *PNAS in press*



まとめ

- 生物学において細胞を一種の情報処理機関と見る視点は広く共有されているが、それを定量的に捉える試みは少ない。
- 大腸菌の走化性においては、系の単純さゆえに理論的進展は比較的速かった。しかし細胞が小さいために一細胞レベルの実験が難しく、それが律速となっていた。
- 近年、FRETを用いて、大腸菌一細胞の内部状態が高い精度で測定可能になった。
  - Keegstra and **Kamino** et al. *Elife* (2017)
  - **Kamino** et al. *Sci Adv* (2020)
  - **Kamino** et al. *PNAS,* in press
  - Moore* and **Kamino*** et al. *bioRxiv,* under review
- 一細胞FRET測定を応用し、細胞が処理する情報レート（~10^{-2} bits/s）とその利用効率（~10^{0}）を評価した。
  - Mattingly* and **Kamino*** et al. *Nat Phys* (2021)

Acknowledgement

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@Yale

Mattingly*, H. H., **Kamino***, K., Machta, B. B., & Emonet, T. (2021). Escherichia coli chemotaxis is information limited. *Nature physics*, (*Equal contribution)

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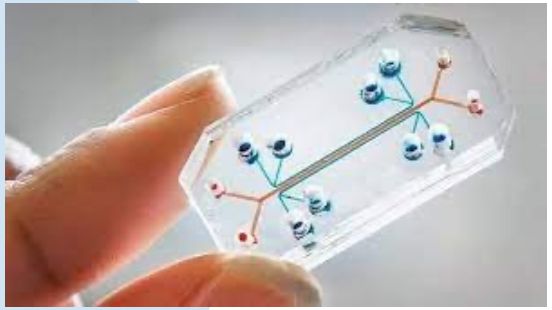
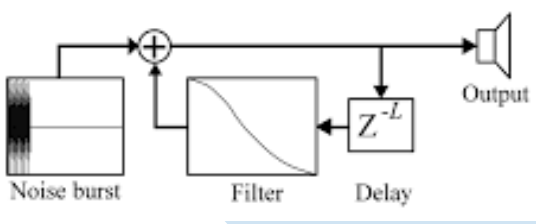
Microfluidics

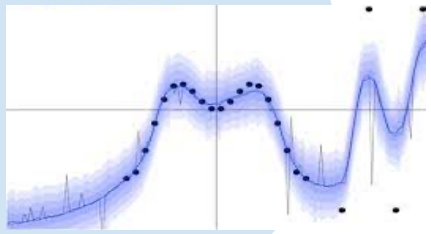


Live-cell imaging

Mathematical modeling



Machine learning



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