

How would you like to use the time for active learning?

- “probably talk about problem sets”, “presenting the most significant problem sets and connect them to modern qbio research if possible”, “I would prefer to present the problem sets”, “Both presenting the problem sets and QnAs are good”

Let's do it!

- “Discussing the issues that the students are interested in or the interesting aspects of your research is also a good idea. In particular, considering that perhaps discussing the topic in a relaxed manner and presenting and discussing your research in a more open way might be more effective than simply waiting for questions from the audience.”

Definitely, please jump in with thoughts or questions whenever!

- “As standard problems can now be explained pretty well by tools like GPT, I would love it if we could use the class time to dive deeper into the underlying principles—especially the history of how these quantitative equations were first proposed.”

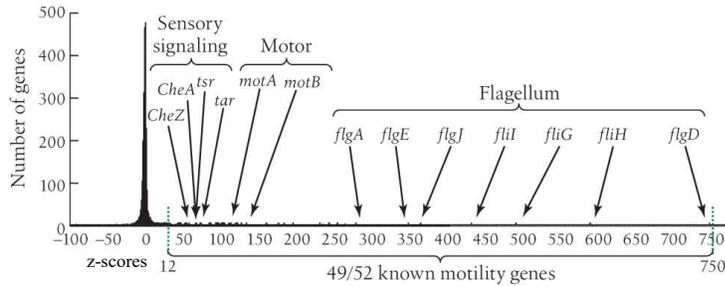
Yes, let's strike a balance.

# Quantitative principles in biological systems

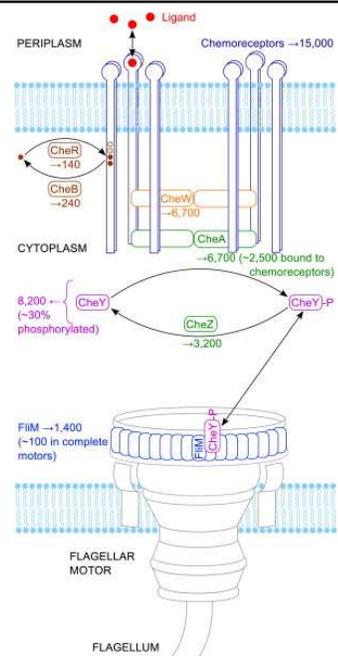
## 2. Chemotaxis and chemical reaction networks

Spring 2026

# Molecular components of chemotaxis

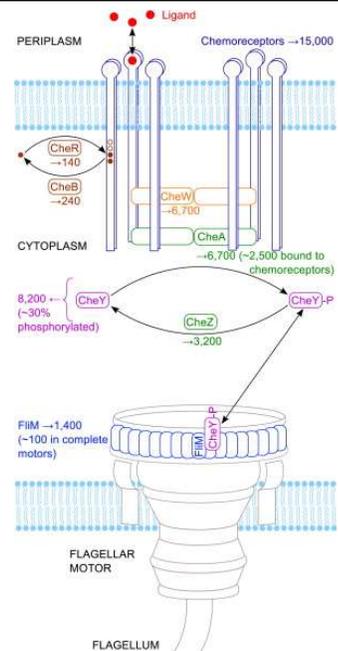
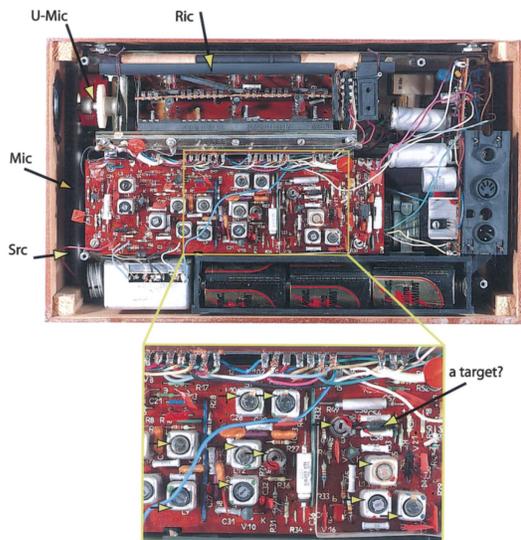


*cheA*, *cheB*, *cheR*, *cheW*, *cheY*, *cheZ*, *dnaJ*, *dnaK*, *flgA*, *flgB*, *flgC*, *flgD*, *flgE*, *flgF*, *flgG*, *flgH*, *flgI*, *flgJ*, *flgK*, *flgL*, *flgM*, *flgN*, *flhA*, *flhB*, *flhC*, *flhD*, *fliA*, *fliC*, *fliD*, *fliE*, *fliF*, *fliG*, *fliH*, *fliI*, *fliK*, *fliL*, *fliM*, *fliN*, *fliO*, *fliP*, *fliQ*, *fliR*, *fliS*, *fliZ*, *motA*, *motB*, *tap*, *tar*, *tsr*



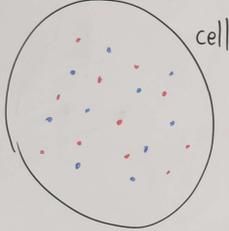
Girgis et al. *PLoS Genet* (2007)  
 Bitbol and Wingreen. *Biophys J* (2015)

# Molecular components of chemotaxis



Lazebnik. "Can a biologist fix a radio?" (2002)  
 Bitbol and Wingreen. *Biophys J* (2015)

## Crash course on chemical reactions



cell

Molecules diffuse around  
+ undergo chemical reactions

Example:  $A + B \xrightleftharpoons[k_{\text{off}}]{k_{\text{on}}} AB$

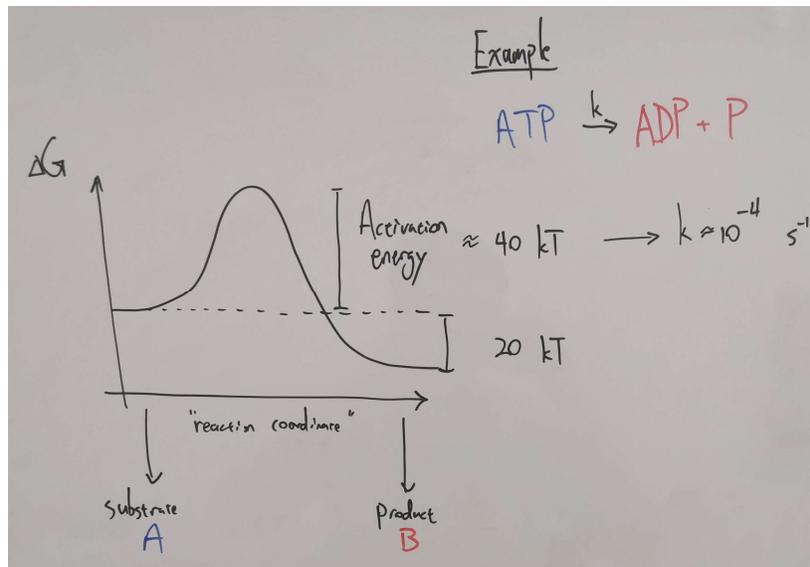
$$\frac{d}{dt} [AB] = k_{\text{on}} [A] [B] - k_{\text{off}} [AB]$$

$$\frac{d}{dt} [A] = -k_{\text{on}} [A] [B] + k_{\text{off}} [AB] = \frac{d}{dt} [B]$$

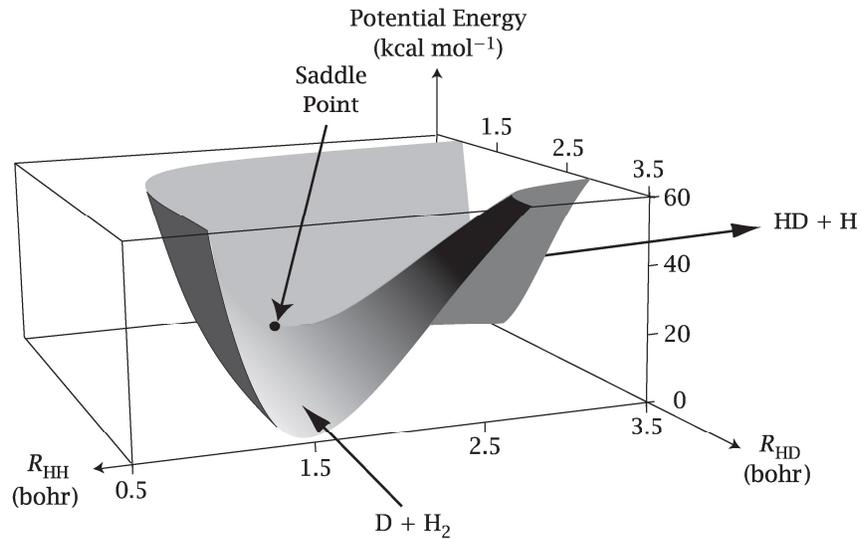
At equilibrium,  $\frac{[AB]}{[A] [B]} = e^{\frac{-\Delta G}{kT}} = \frac{k_{\text{on}}}{k_{\text{off}}}$

Free energy Rate constants

Enzymes lower activation energies to increase rates.

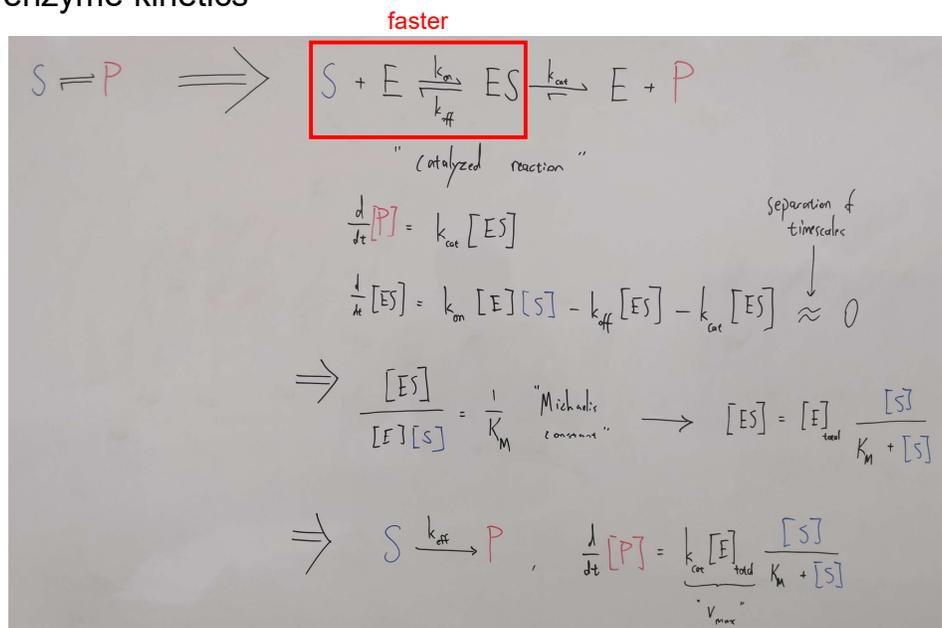


The most probable paths across an energy barrier goes over the saddle point.

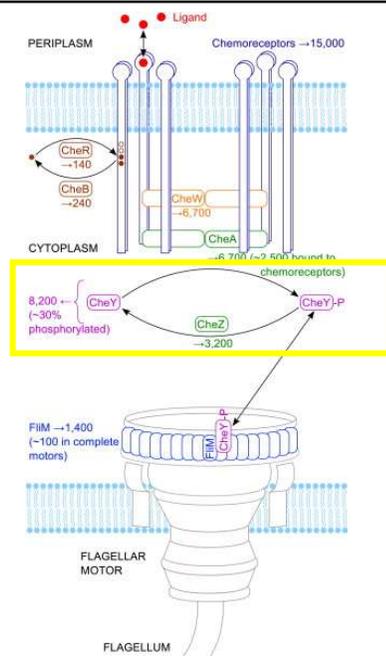
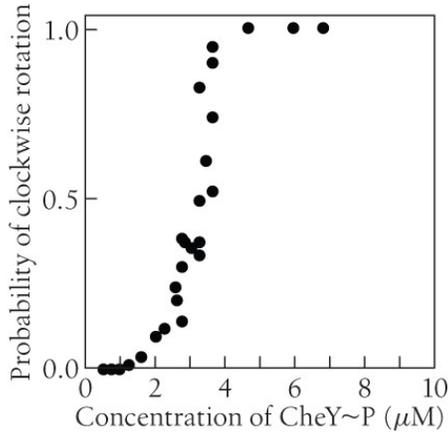


Dill

### Modeling enzyme kinetics



# CheY phosphorylation determines tumbling rate.



Cluzel et al. *Science* (2000)  
 Bitbol and Wingreen. *Biophys J* (2015)

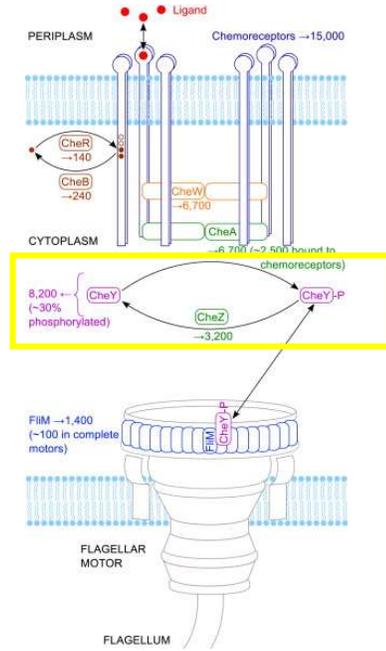
# CheY phosphorylation determines tumbling rate.

$$X_0 \rightleftharpoons X_p$$

$$\frac{d}{dt} X_p = k_p(c) X_0 - k_d X_p$$

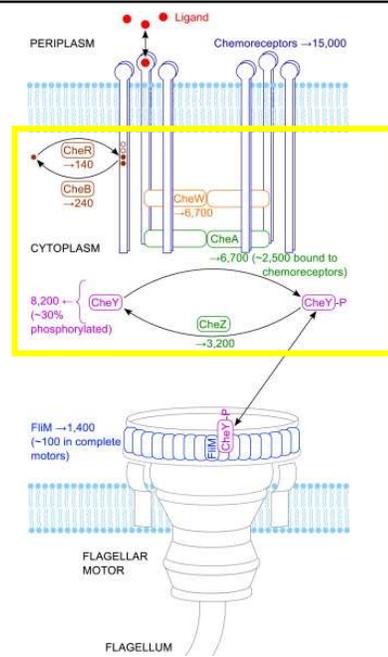
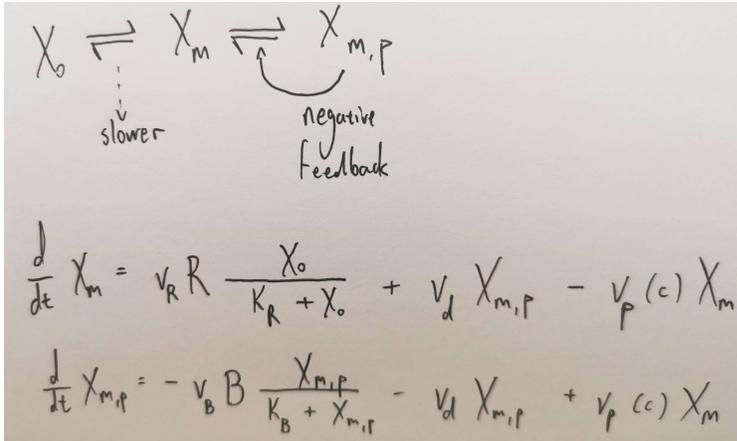
$$\Rightarrow \bar{X}_p = f(c)$$

No adaptation!



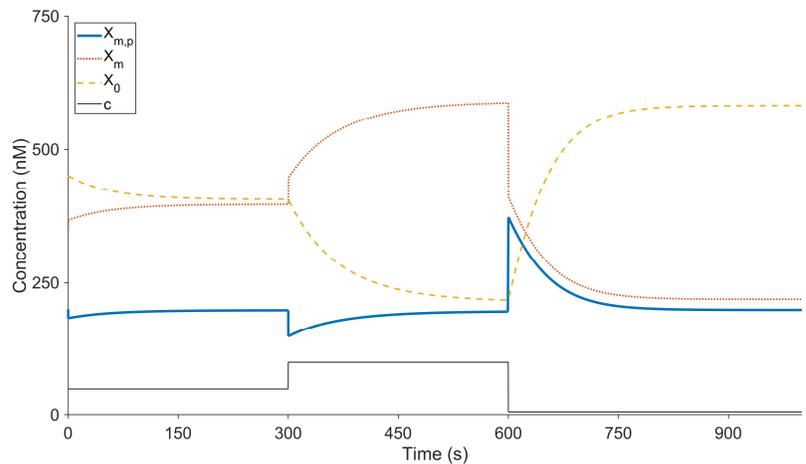
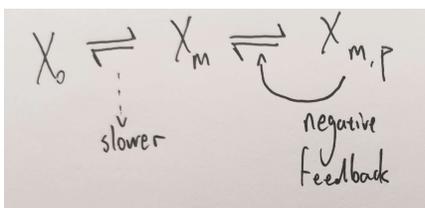
Bitbol and Wingreen. *Biophys J* (2015)

Adaptation requires feedback.

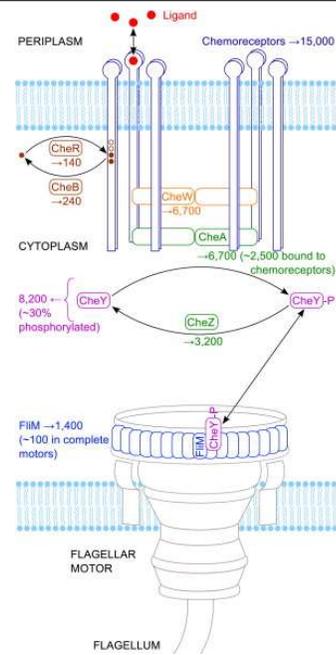
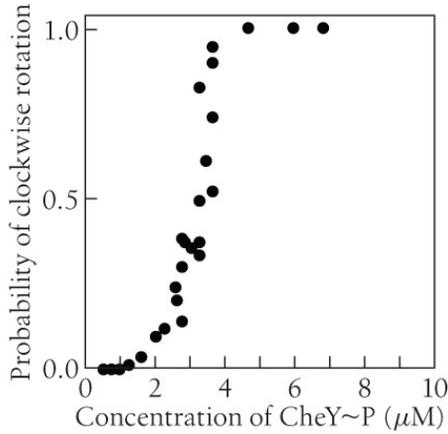


Barkai and Leibler. *Nature* (1997)  
 Bitbol and Wingreen. *Biophys J* (2015)

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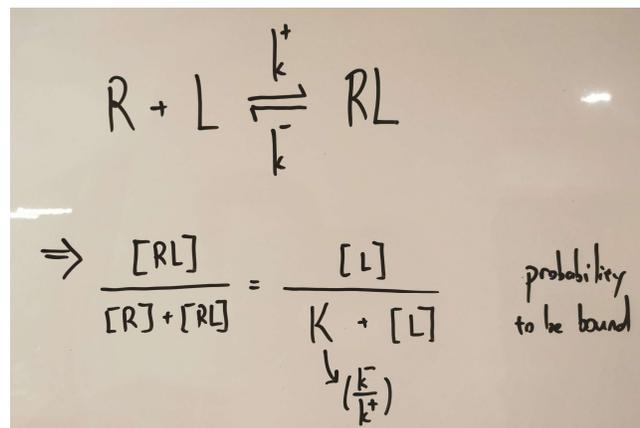
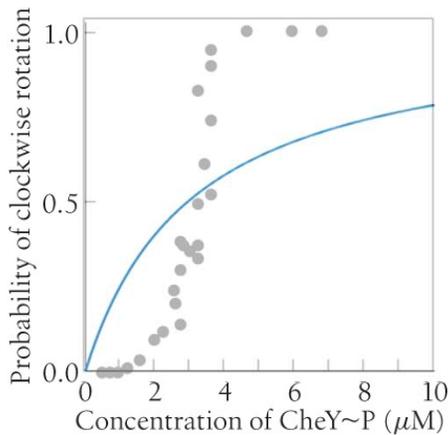


Tumbling rate is **ultrasensitive** to CheY-P.



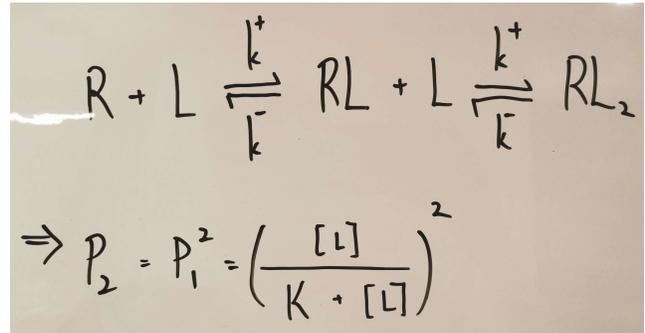
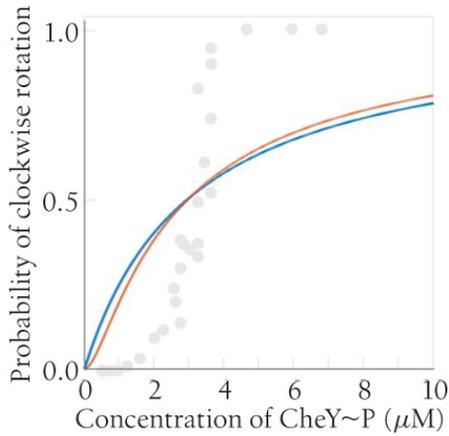
Cluzel et al. *Science* (2000)  
Bitbol and Wingreen. *Biophys J* (2015)

Tumbling rate is **ultrasensitive** to CheY-P, compared to ...



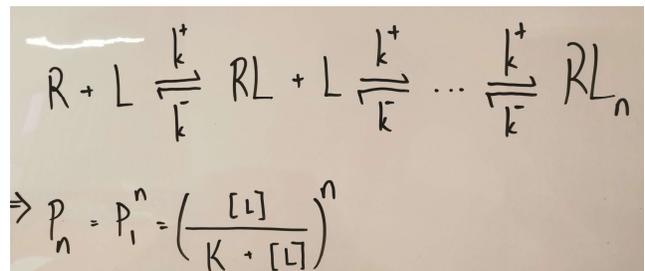
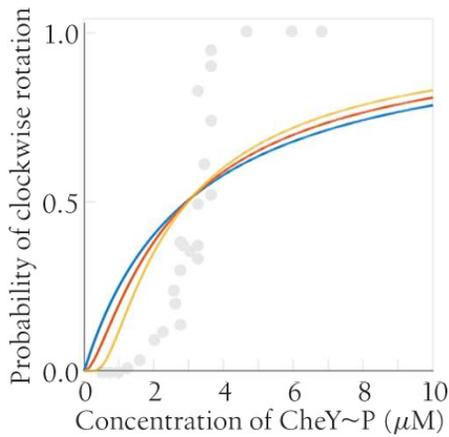
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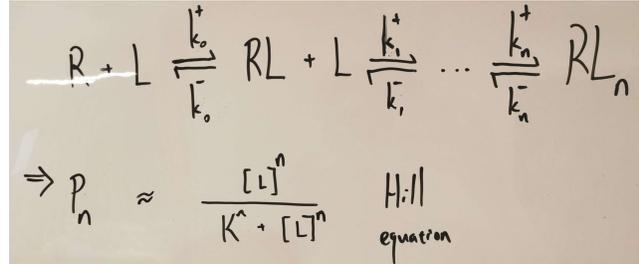
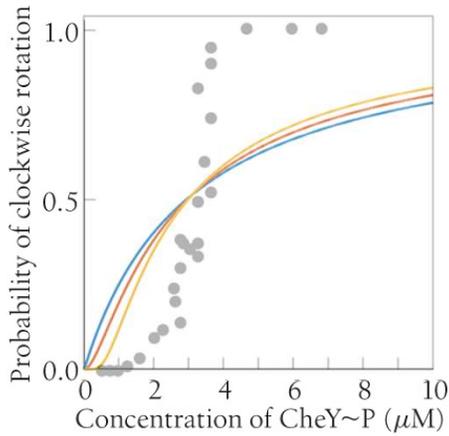
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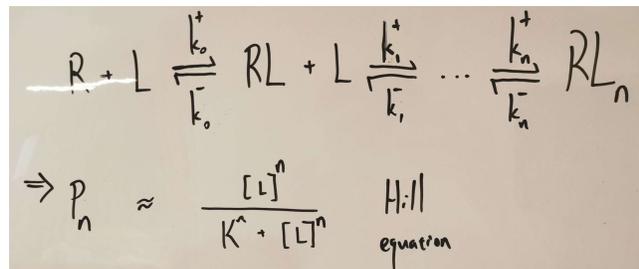
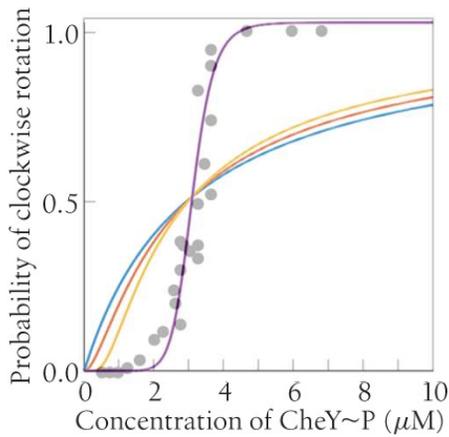
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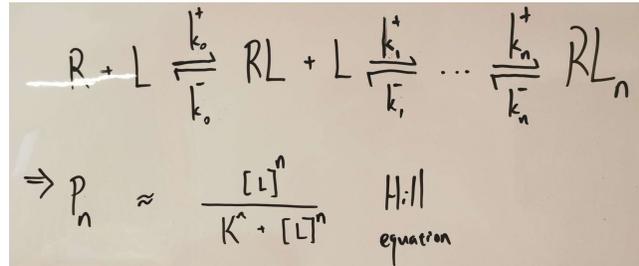
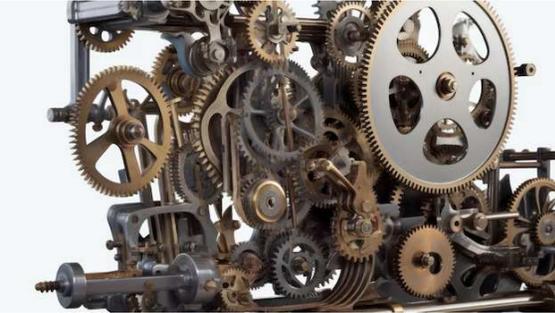
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Tumbling rate is **ultrasensitive** to CheY-P, with a Hill coefficient  $n \approx 10$ .

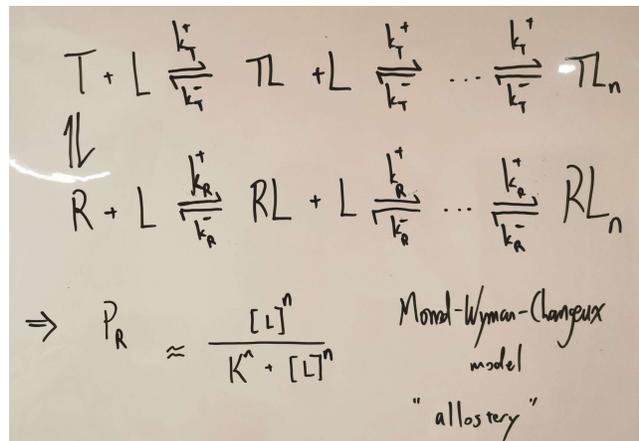
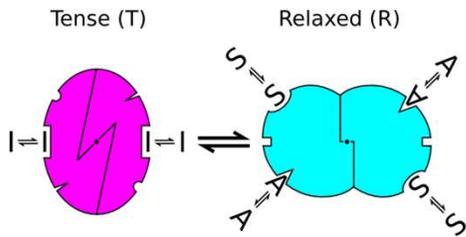


Cluzel et al. *Science* (2000)

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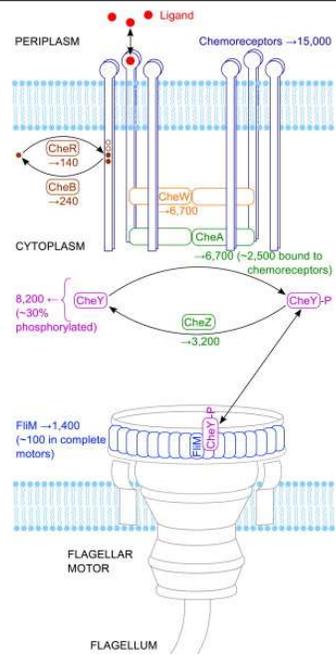
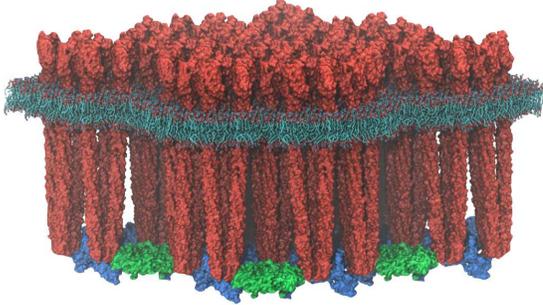


Allostery for cooperativity



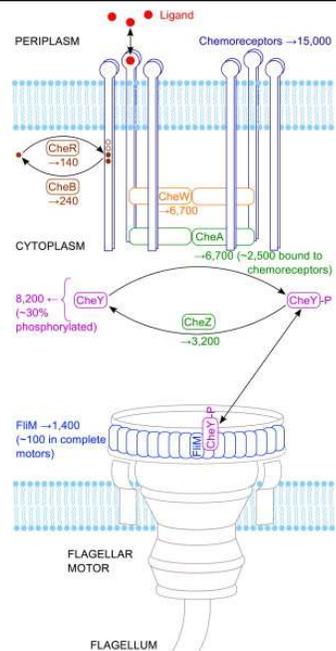
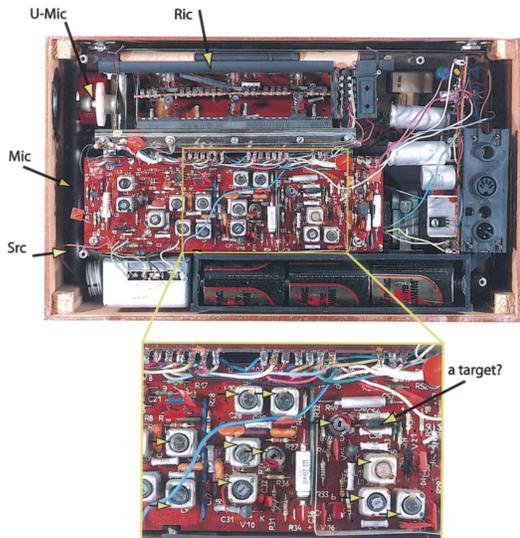
# Counting molecules in chemotaxis

$\sim 10^0$  ligands  $\rightarrow$  CheA  $\rightarrow$   $\sim 10^3$  CheY within 1 sec



Bitbol and Wingreen. *Biophys J* (2015)

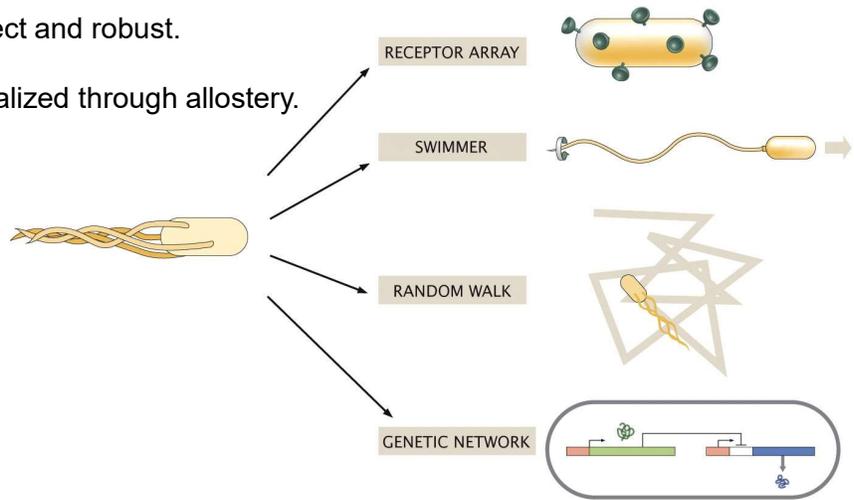
# Molecular components solve life's problems.



Lazebnik. "Can a biologist fix a radio?" (2002)  
 Bitbol and Wingreen. *Biophys J* (2015)

## Summary

- Biology implements molecular mechanisms to solve life's problems, many of which are physical.
- Adaptation can be perfect and robust.
- Cooperativity can be realized through allostery.



Phillips et al