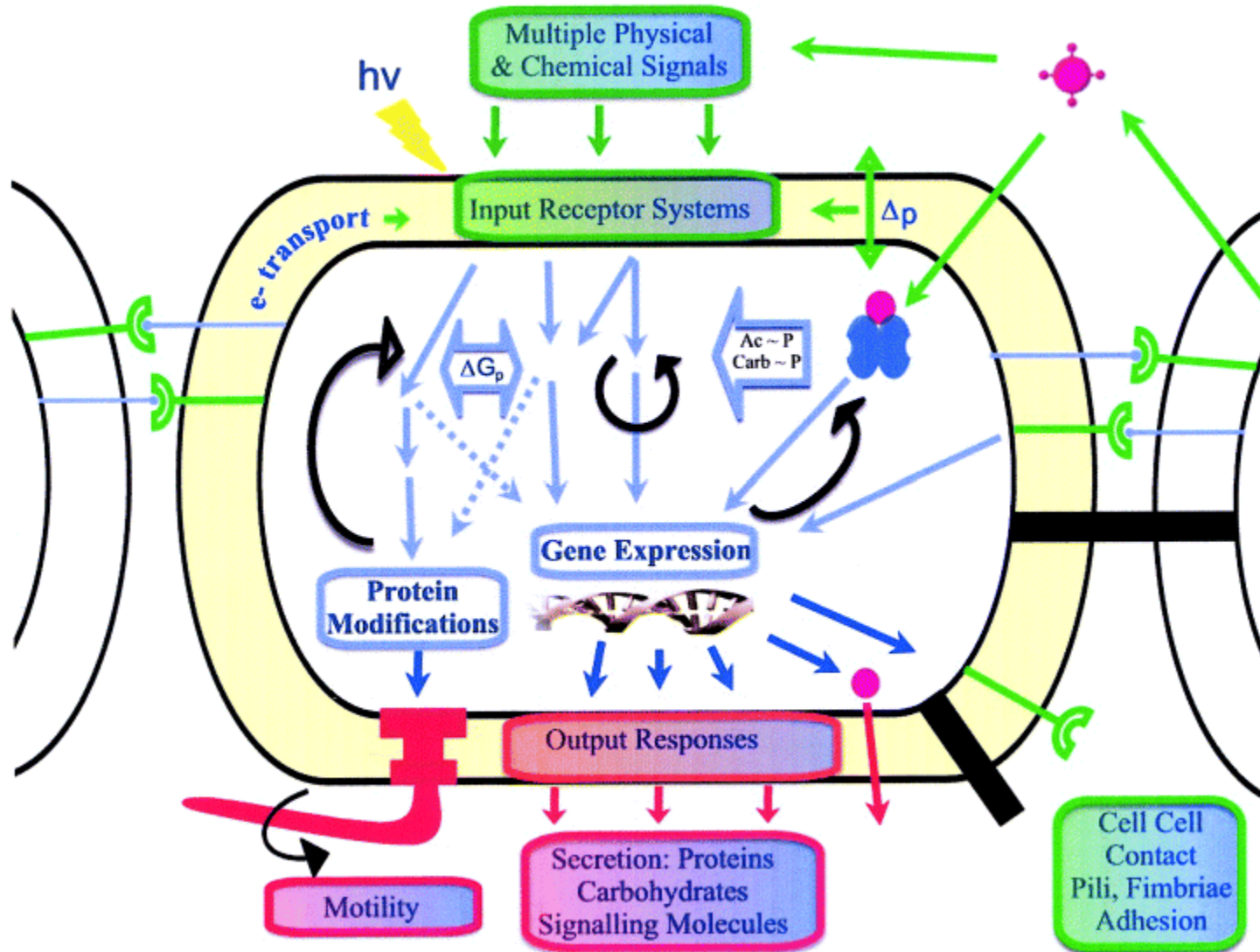
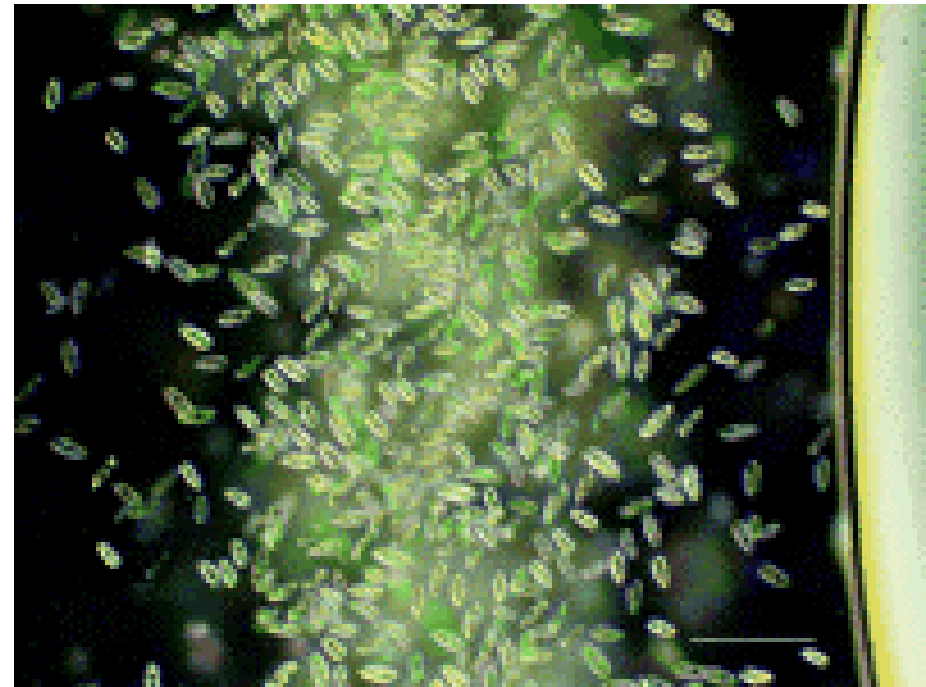
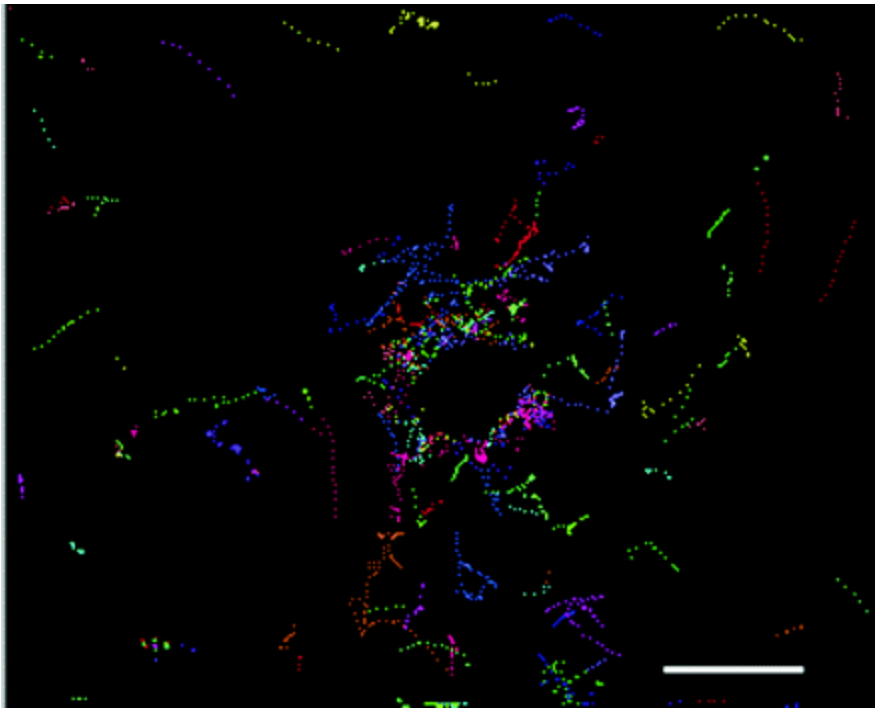


3.5 bln yrs of evolution, but multicellular organisms appeared 1 bln yrs ago. Why? Cell signaling! Secreted molecules --> receptors. Paracrine, endocrine (hormones) systems, neuro/electro-transmitters. Sensitivity, memory, adaptation (desensitization). But first – simplest perception of a signal – how do bacteria look for food?





$$v \sim 30 \frac{\mu m}{\text{sec}}, \tau \sim 1 \text{ sec}, D \sim \frac{(v\tau)^2}{2\tau} \sim \frac{v\tau}{2} \sim 500 \frac{\mu m^2}{\text{sec}}, x \sim \sqrt{Dt}$$

10 sec : $70 \mu m$

1 min : $170 \mu m$

1 hr : 0.15 cm

1 day : 0.7 cm

Not fast enough!

Increase v ? Increase τ ?

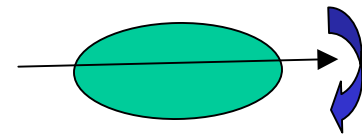
Motor

Brownian

limitation

rotation

(power $\sim v \cdot v$) (20 deg.in 1 sec)

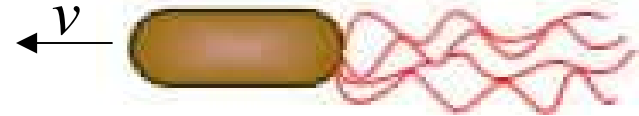


$$(N_+ - N_-) \approx \frac{dC}{dx} \cdot \text{length} \cdot \text{volume} \sim 1 \frac{\mu M}{cm} \cdot 1 \mu m \cdot 1 \mu m^3 \approx$$

$$\frac{10^{-6} \cdot 10^{23} \text{ molecules}}{(10^5 \mu m)^3 \cdot 10^4 \mu m} \cdot 1 \mu m \cdot 1 \mu m^3 \sim 0.01 \text{ molecules}$$

$$N \sim C \cdot \text{volume} \sim 1 \mu M \cdot 1 \mu m^3 \sim \frac{10^{-6} \cdot 10^{23} \text{ molecules}}{(10^5 \mu m)^3} \cdot 1 \mu m^3 \sim 100$$

$$\delta N \sim \sqrt{N} \sim 10$$



$$C(x), x = vt, \quad \frac{dC}{dt} = \frac{dC}{dx} \cdot \frac{dx}{dt} = V \frac{dC}{dx}$$

Two mechanisms for detecting gradients:

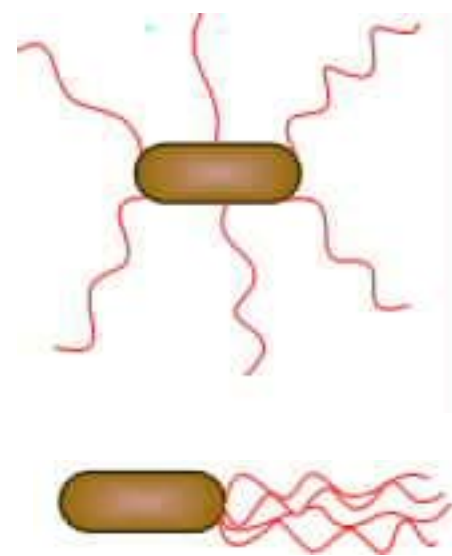
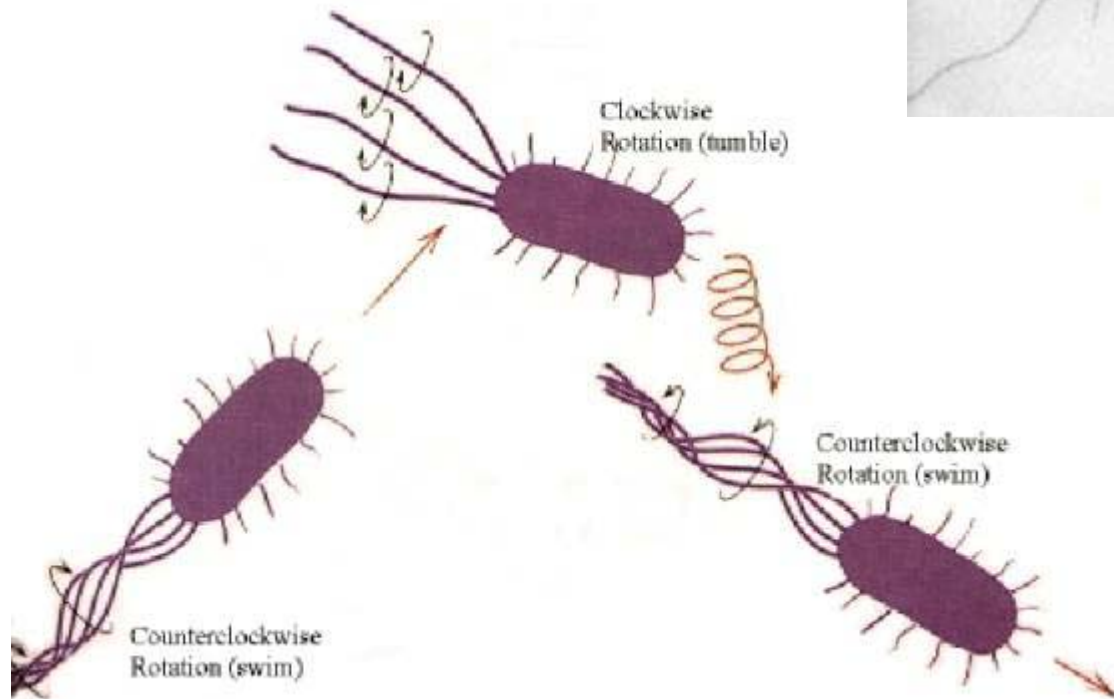
Spatial detection mechanism (simultaneously compare the intensity of stimulation of receptors at different parts of organism) and

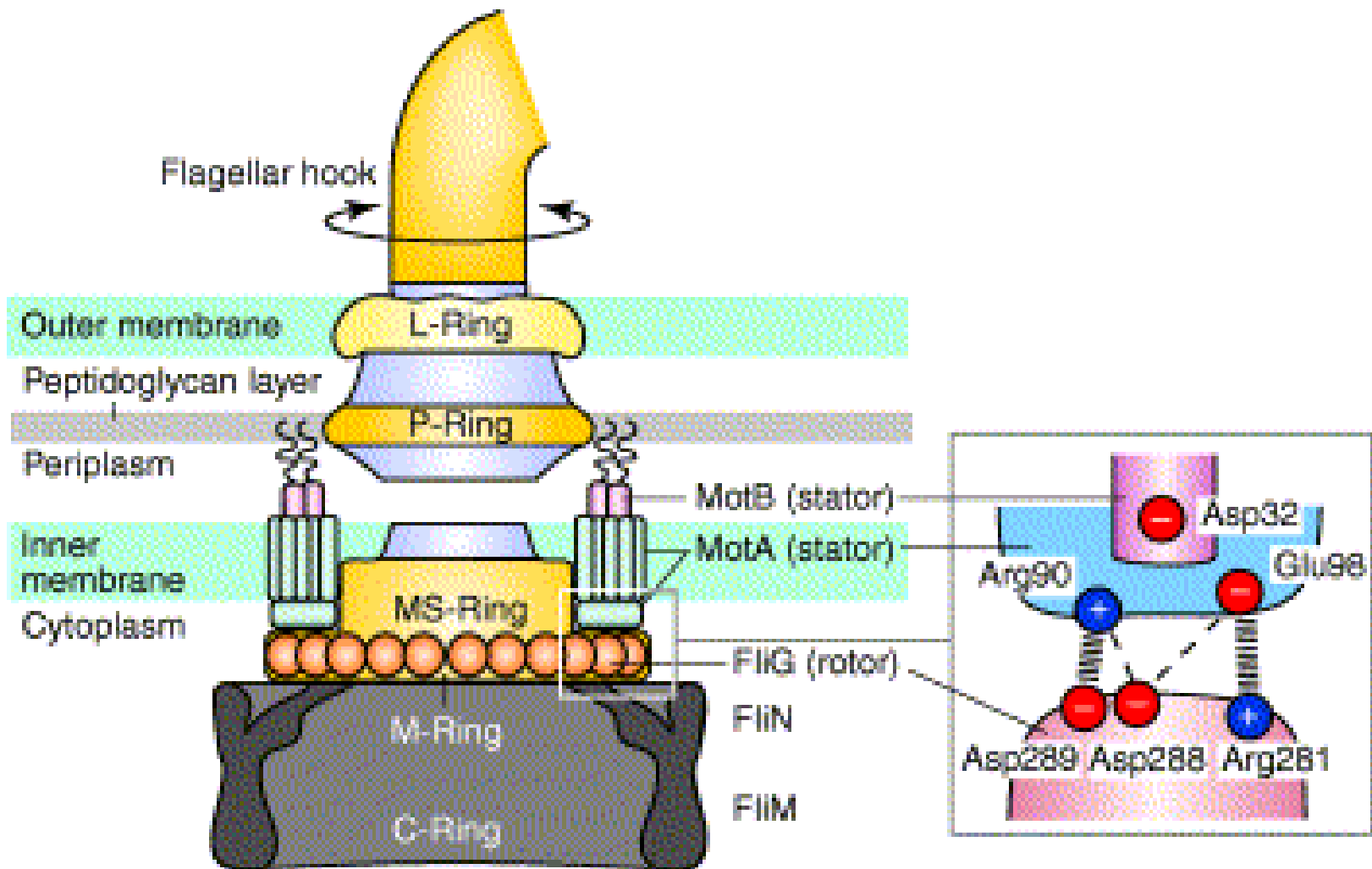
Temporal detection mechanism (sequential compare the intensity of stimulation at different times, between which the organism moves from one location to another).

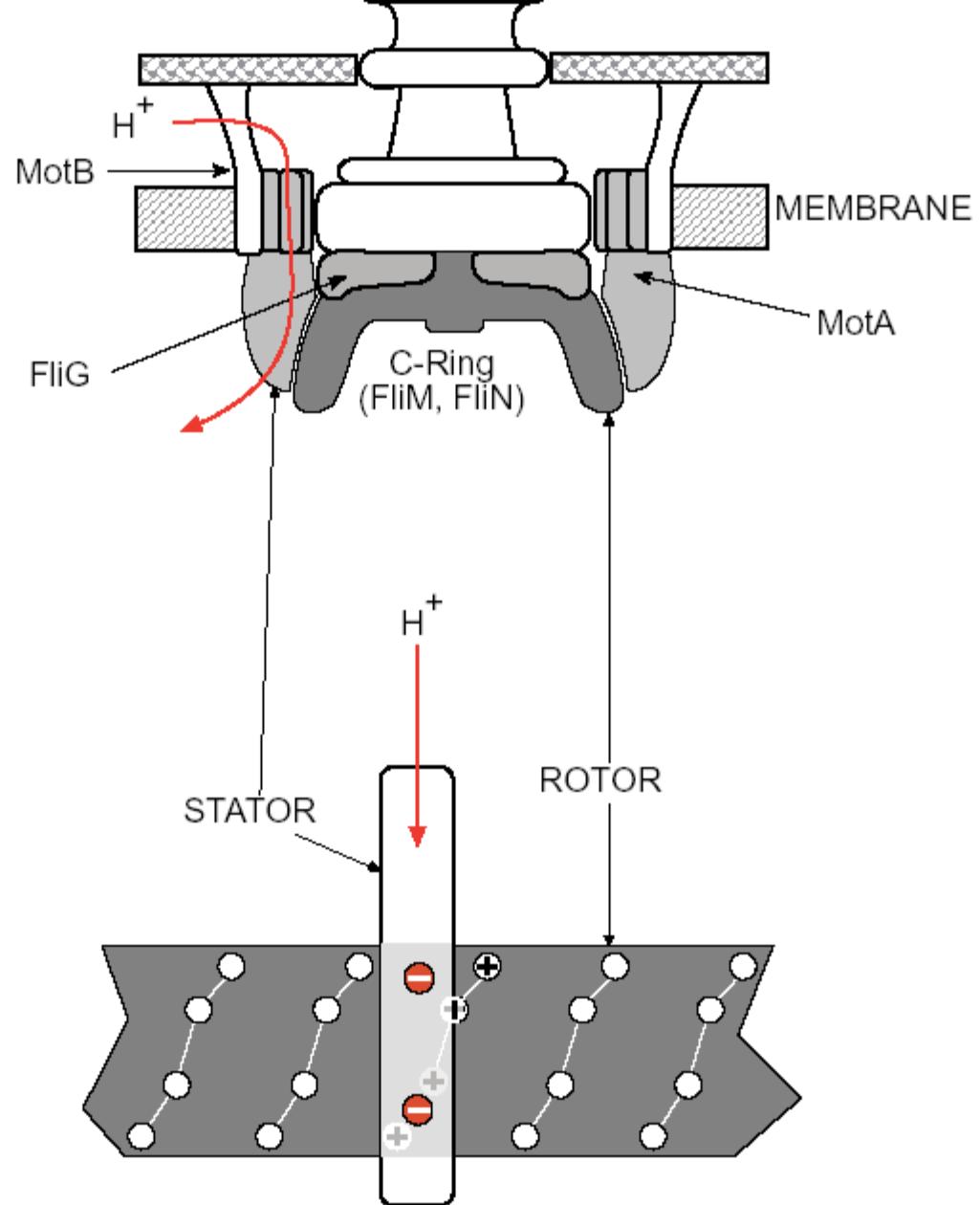
Spatial gradient sensing is impossible. Thus, temporal mechanism.

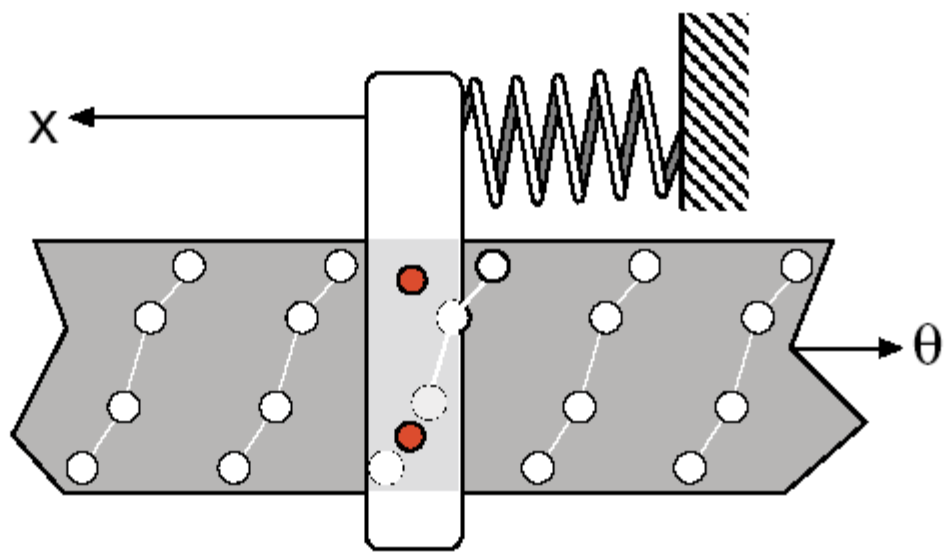


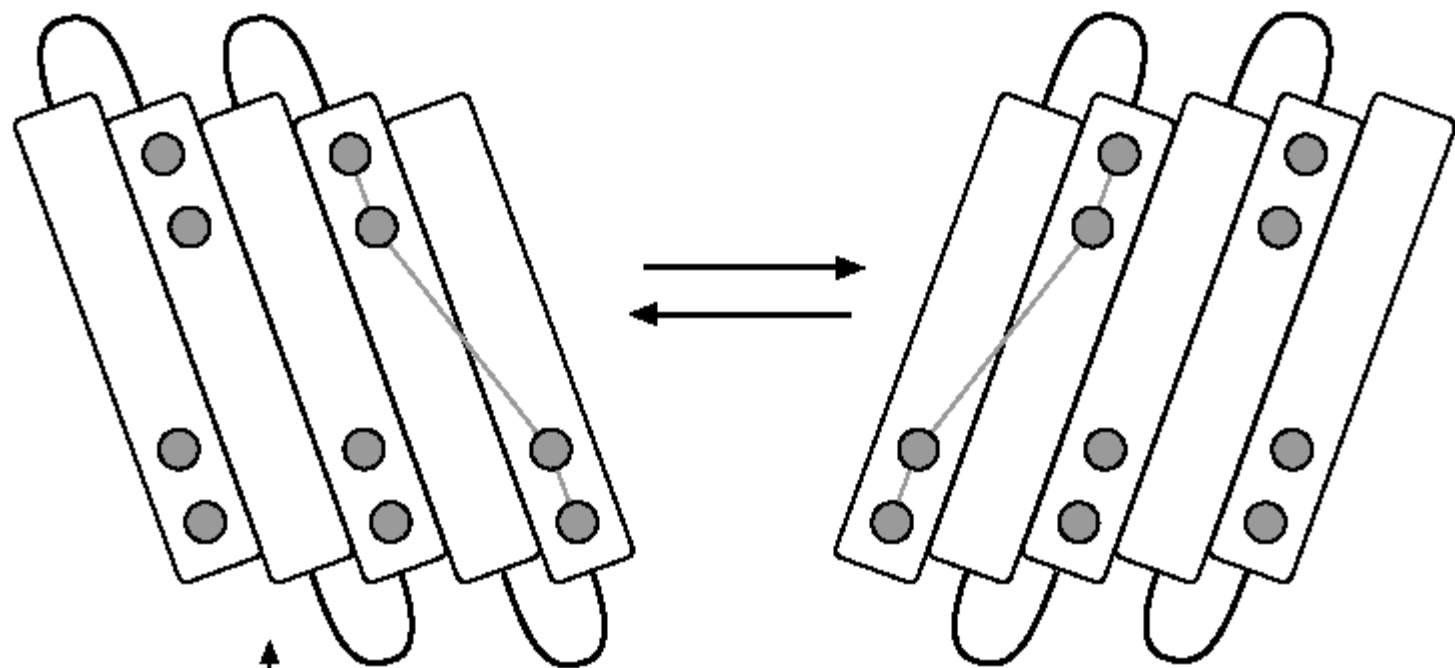
flagella:
left-
handed
helices











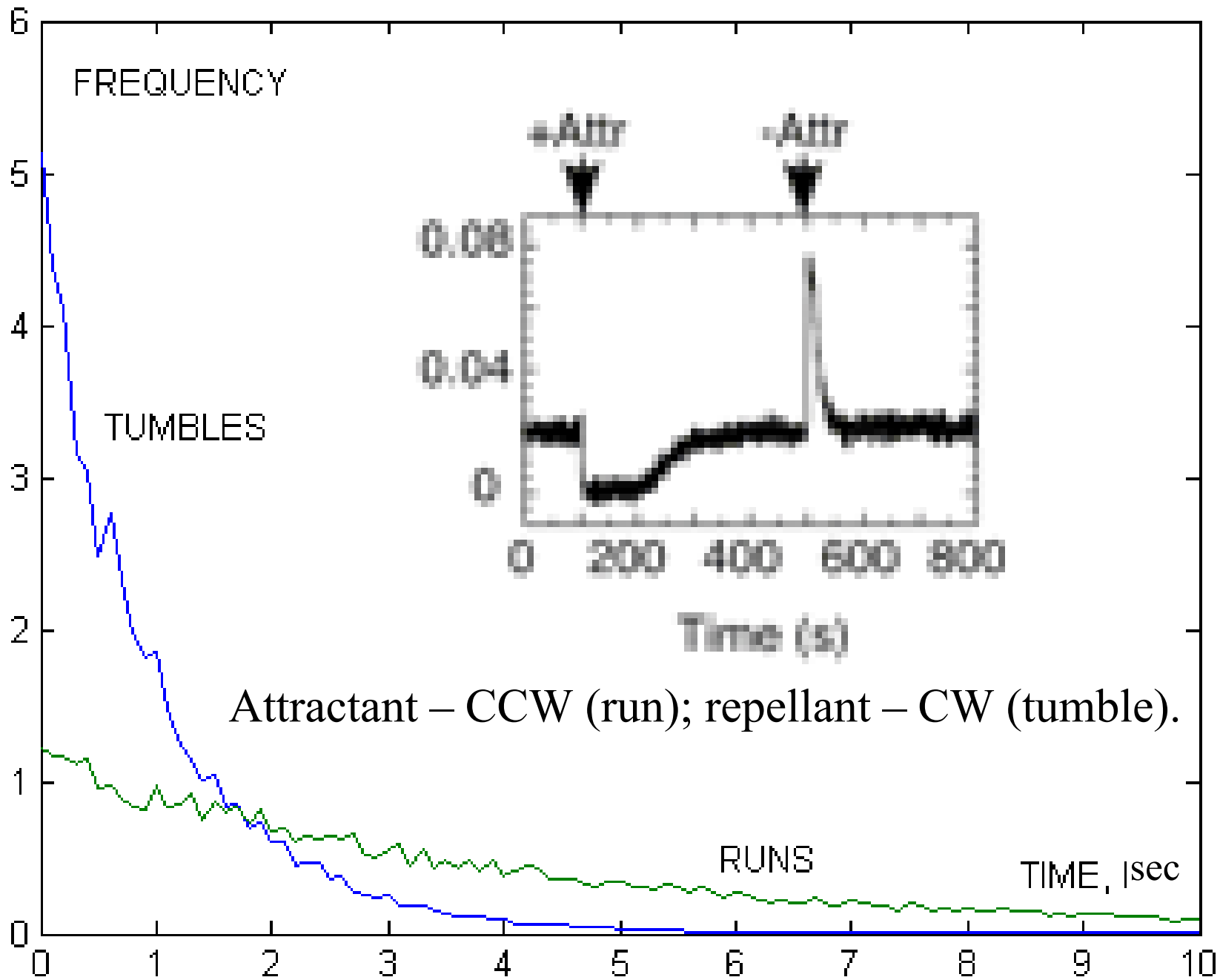
CCW

CW

$$\frac{V}{k_B T}$$

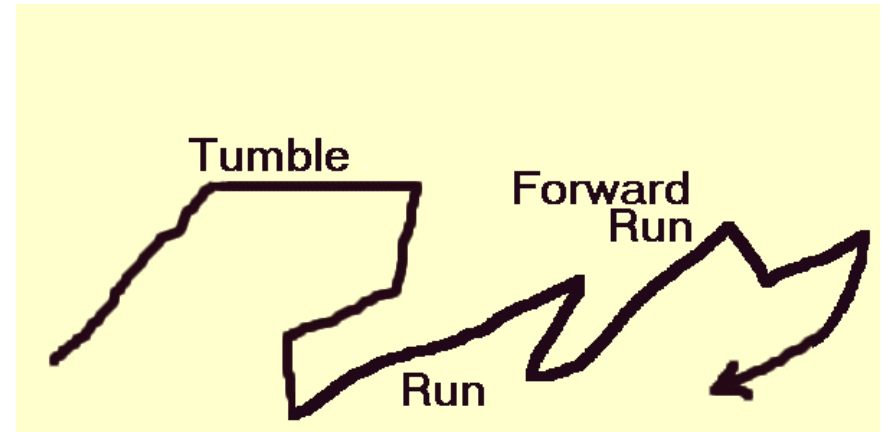
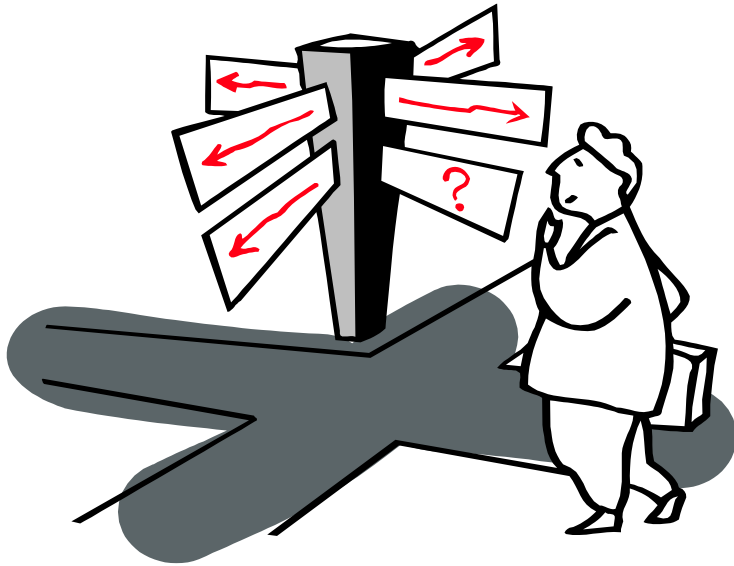
Binding of CheY-P

Reaction



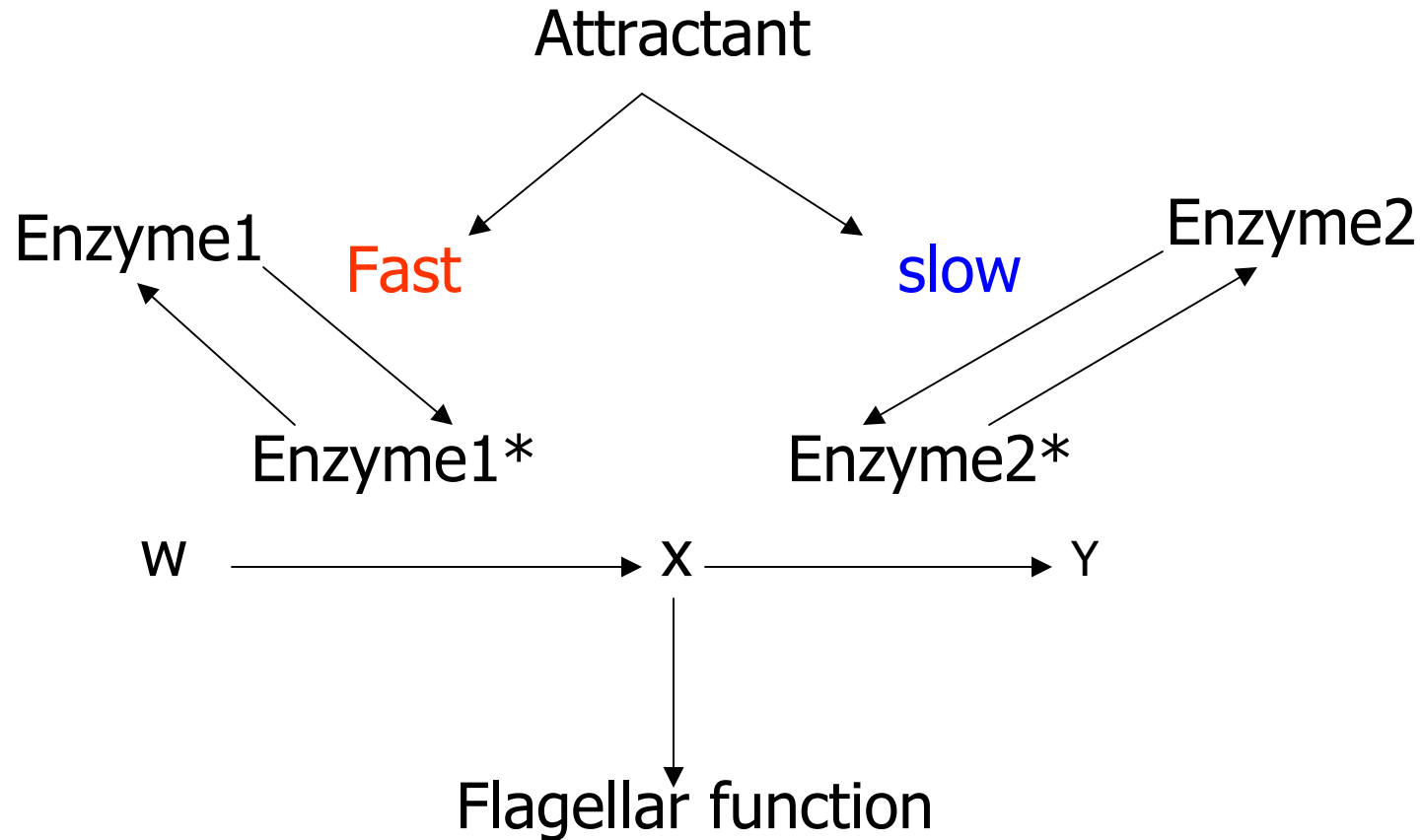
Bacteria are not so simple. They can detect very small changes in chemical concentrations in the range from $10^{-3} \mu M$ to $10^3 \mu M$

But they are not so complicated, either. In the presence of positive or negative gradient, the cells achieve chemotaxis by varying tumbling frequency.

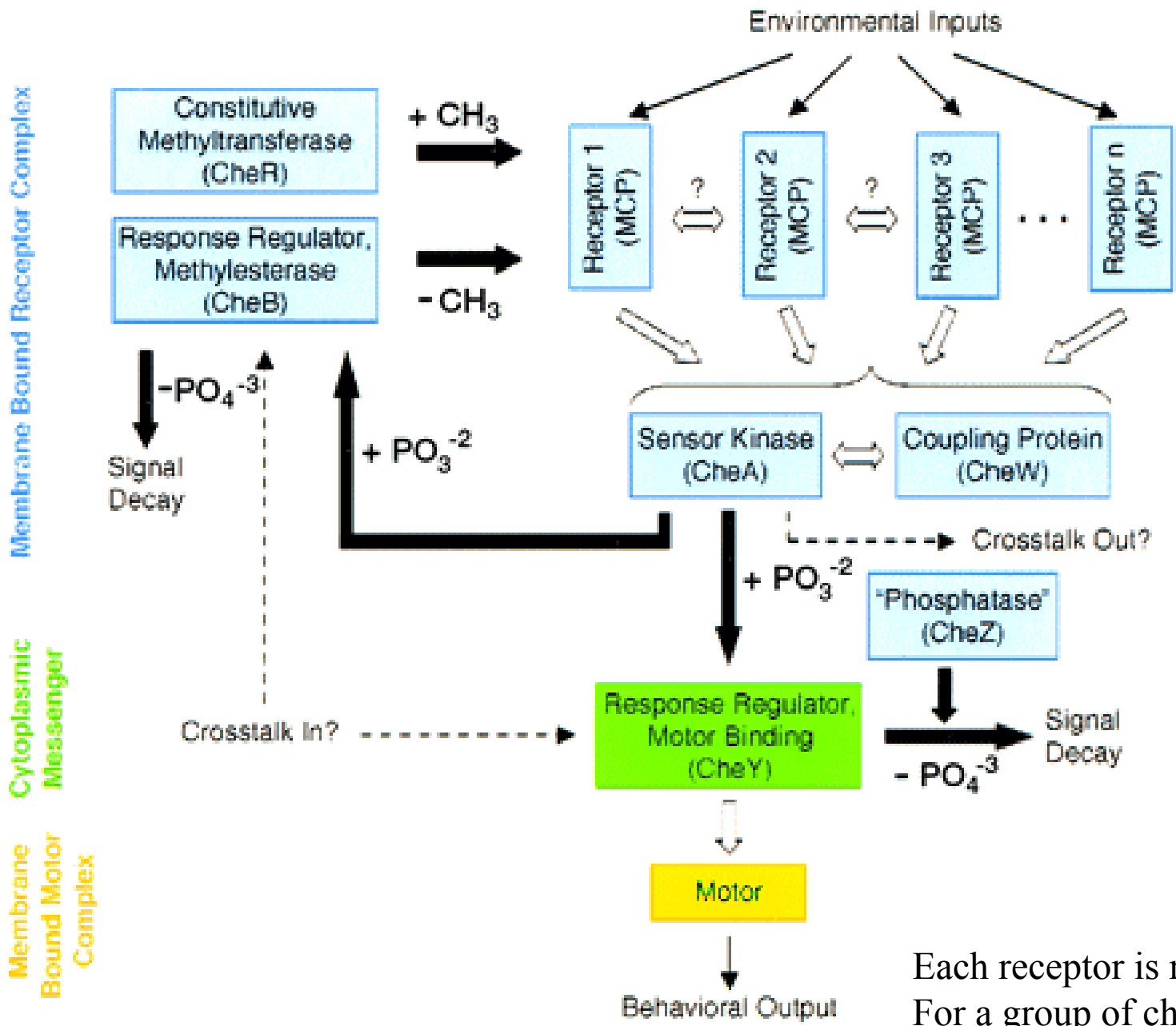


The main question is: what is the molecular mechanism?

How does the temporal sensing mechanism works?

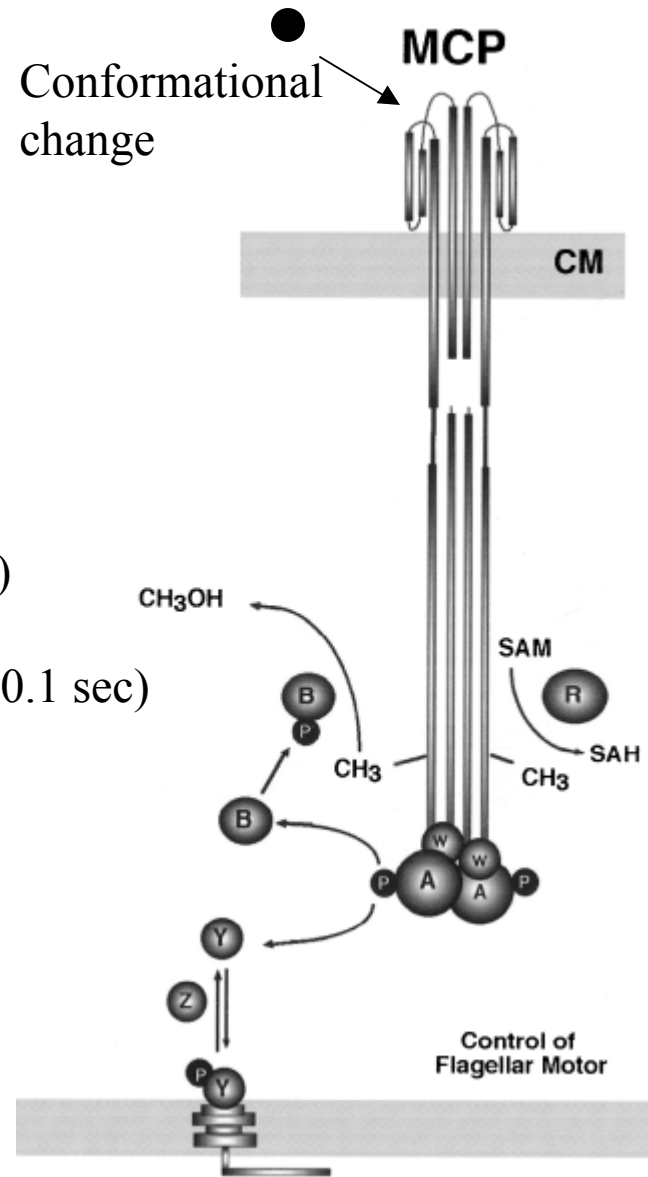
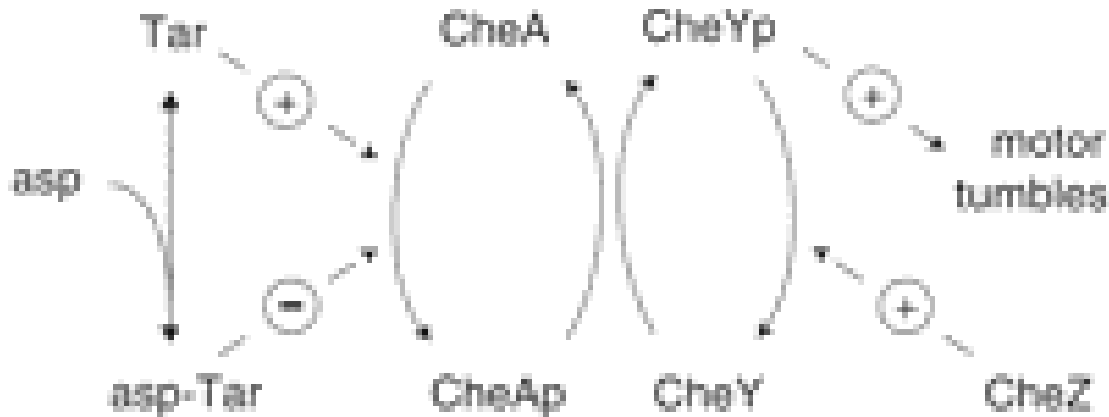


First, how does bacterium swim?

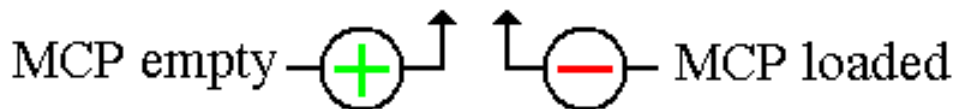
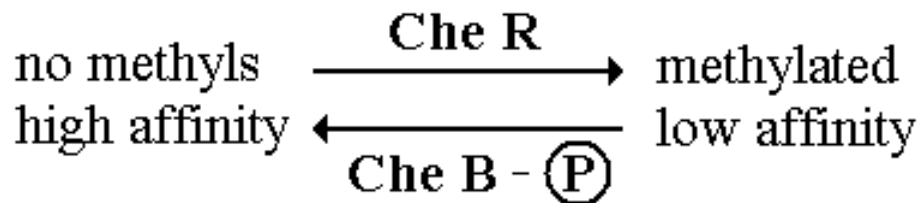


Each receptor is responsible For a group of chemicals

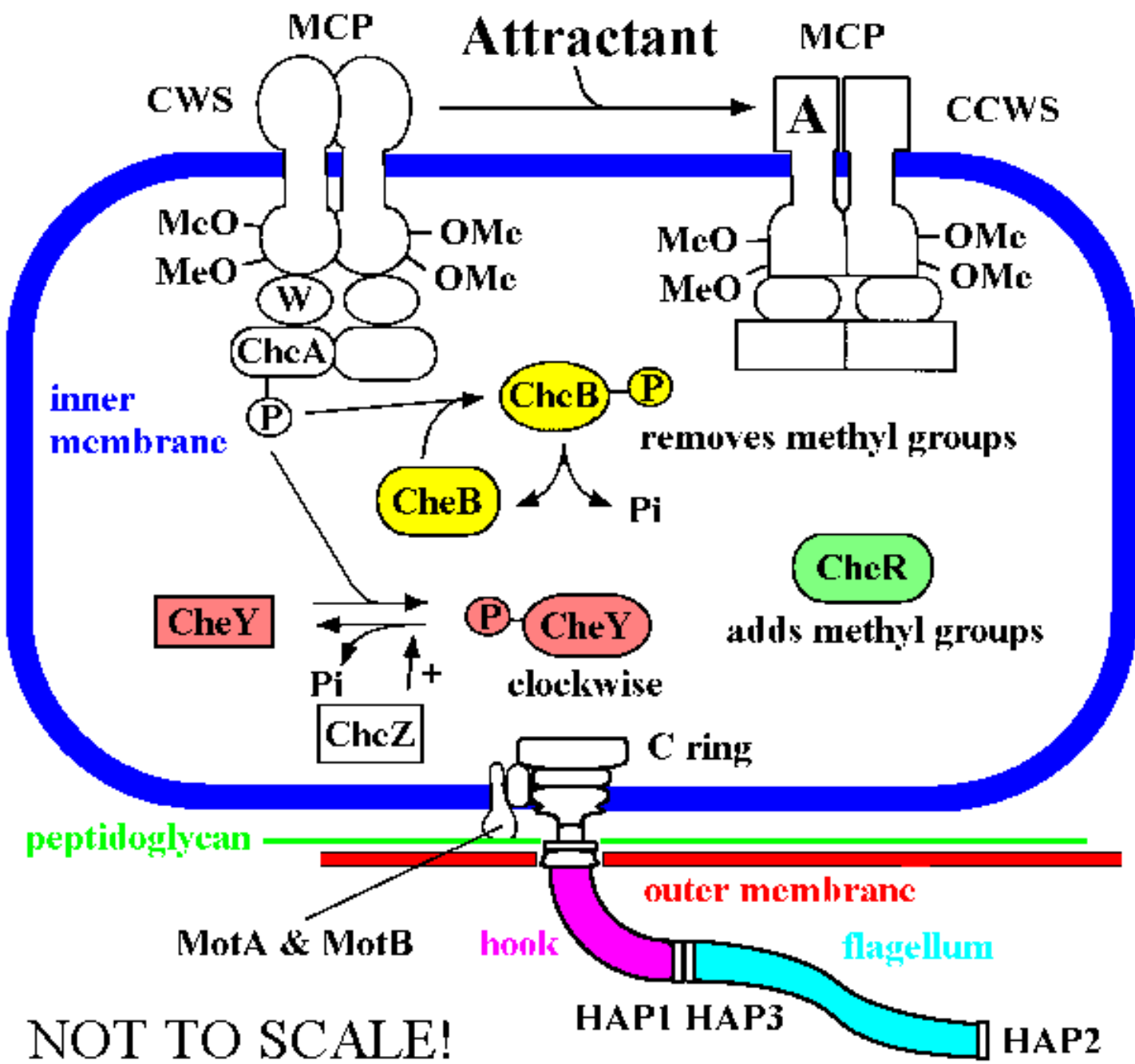
MCP = methyl-accepting chemotactic protein



- 1) CheW is a docking protein
- 2) CheA is an autophosphorylating kinase (wasteful cycle)
- 3) CheA-P passes P to CheY and CheB
- 4) CheY-P diffuses, binds to the motor, CCW \rightarrow CW. (~ 0.1 sec)
- 5) CheZ dephosphorylates CheY-P
- 6) Methylation increases ability to phosphorylate CheA
- 7) CheR transfers methyl groups to the receptor
- 8) CheB-P demethylates the receptor (~ 10 sec – 10 min)



4 methylation sites at each α -helix; 8 - total



NOT TO SCALE!