The Players

NON-MEMBRANE PROTEINS:

CheA: histidine protein kinase, captures signal from receptor and passes it along
CheW: partner of CheA and receptor (scaffold)
CheY: response regulator, carry signal through cytoplasm
CheZ: activate CheY by dephosphorylation
CheR: methyl transferase, attenuate the passage of signal through regulator (adaptations)
CheB: methyl esterase/amidase, activated by CheA-P, demethylates receptor and makes receptor more sensitive to signals

MEMBRANE PROTEINS:

(MCRs: methyl-accepting chemotaxis proteins; ligand receptors)

Tsr (2600 mol/cell) → serine receptor
Tar (600 mol/cell) → Asp(D), Glu(E), Maltose*

Tig → ribose*, galactose*, glucose
Tap → dipeptides*

Air → O₂

* = there is a partner protein

*CheZ: takes CheY-P → CheY, causes straight (as opposed to tumbling) movement
Chemotaxis: A behavioral response involving the movement of an organism toward an attractant or away from a repellant.

1. The Big Picture — look at core biochemical pathways to understand the chemotaxis ligands
2. Ligands → trans. memb. receptors
3. Signal transduction at cytoplasm small molecule effector interface
4. How signal travels through the cytoplasm.
5. How signal affects a motor
6. Motor mechanics

Strategy nature uses for high sensitivity in high-gain systems

*The length of a small organism isn’t sufficient to detect these changes in concentration.*
Targets:
- serine
- Asp
- Glu
- maltose
- Gal
- G1c (G)
- dipeptides
- O2
- ribose

How the chemotactic targets get put into metabolic pathways... All of them are 0 to 1 step away from a "core" pathway.

3PG = 3 phosphoglycerate

(Why glutamate? The nitrogen in amino acids comes from the air → nitrogen fixation → ammonia, all gets into body via glutamate.)

G → G6P → F6P → F1, 6 BP

What’s the function of the TCA cycle? To put electrons somewhere that can use them (FAD, NADH).

\[ \text{MEMBRANE (mitochondrial or plasma)} \]

\[ \text{ADP + PA} \]

\[ \text{NADH} \]

\[ \text{NAD}^+ \]

\[ \text{2H}^+ + \frac{1}{2} \text{O}_2 \]

\[ \text{H}_2\text{O} \]

\[ \text{NAD}^+ \]

\[ \text{ATP} \]

\[ \text{GPG} \rightarrow \text{3PG} \rightarrow \text{Lipids} \]

\[ \text{DHAP} \]

\[ \text{GAP} \rightarrow \text{1,3 BPG} \rightarrow \text{3PG} \]

\[ \text{CO}_2 \]

\[ \text{AcCoA} \rightarrow \text{lipids} \]

\[ \text{this is} \]

\[ \text{PEP} \]

\[ \text{CO}_2 \]

\[ \text{AcCoA} \]

\[ \text{TCA cycle} \]

\[ \text{C} \]

\[ \text{MA} \]

\[ \text{OA} \]

\[ \text{αKG1} \]

\[ \text{H}_2\text{C} - \text{CO}_2^- \]

\[ \text{H}_2\text{C} \]

\[ \text{O} \]
dipeptides

\[
\begin{align*}
\text{H}_3\text{N} & - \text{N} - \text{C} - \text{CH}_3 \\
\text{H}_2\text{N} & - \text{N} - \text{C} - \text{CH}_3
\end{align*}
\]

\[
\text{tyr} \rightarrow \text{ala} \rightarrow \text{pyruvate}
\]

\[\text{peptoglycan}\]

\[\text{E. coli}\]

sensory array / nanobrain = 10-20 K receptors

\[\text{MCP}\]

flagellum

motor

cytoplasm

periplasm

outer membrane

inner membrane

Attractant

clustering in response to ligand
Case 1: No Attractant

Without a signal, CheA is activated to self-phosphorylate and to phosphorylate Che B.

\[ \text{ATP} \xrightarrow{\text{CheA}} \text{CheA}^\text{P} \xrightarrow{\text{CheY}} \text{CheY}^\text{P} \]

migrate to motor

\[ \land \]

causes clockwise rotation = tumble

NB: clockwise/clockwise is defined as looking from flagellum to bacterium, i.e.

\[ \text{CheA} \]

\[ \text{CheA}^\text{P} \]

\[ \text{CheY}^\text{P} \]

\[ \text{CHE comp'd} \]

phospho-

swimming in a run, all going CCW

cheY^P = tumble

STOP
Case 2: Sensing an Attractant / Repellant

1. When $A \rightarrow AP$, you cannot make $YP$.
2. Che $Y \rightarrow$ t½ 0.1-0.2 sec
   Reason: $CheY(P) \xrightarrow{H_{2}O_{P}} CheY$
3. Lack of Che $Y(P) \rightarrow$ no interaction w/ flagellum motor

→ Bacterium will go m longer runs as it moves up the concentration gradient. Direction is completely random, runs are just longer in the direction of the attractant.

→ The number of MCPs in a cell indicate how desirable that receptor's target is to the cell. More receptors, more desirable. This is how bacteria make "decisions" between different attractors.

Case 3: Sustained Stimulus

1. Lots of attractant (signal) causes methylation of $MH1$ and $MH2$.
3. Weaker inhibition of $A$ HPK (histidine protein kinase) activity

→ $AP \rightarrow YP \rightarrow$ flag. motor $\rightarrow$ CW rotation $\rightarrow$ tumble
Aron & Luebner (1999):

E. coli ± 1 mM Asp (D)

**Exact Adaptation:** system resetting

$T_{self} = 6$ minutes for system to adapt & turn off

$\Rightarrow$ During period of adaptation, CheR (methyl transferase) is working.

CheR makes methyl ester of MH2.
CheB undoes what was done by CheR; also deaminates glutaminines

\[ \text{Glu} \xrightarrow{\text{CheB}} \text{Glu} \xrightarrow{\text{H}_2\text{O}} \text{NH}_3 \]

\[ \text{Glu} \xrightarrow{\text{CheB}} \text{Glu} \xrightarrow{\text{New substrate for CheR}} \]

Keep in mind that there's a repellant system working in parallel with this...

**Bacterial Flagellar Motor.**

- chemical energy from metabolism → make something spin
- electrostatic interactions
- create gradient of protons; release of gradient drives motor

**N.B.**: Flagella don't actually move around; through the membrane:

- CheY\(\oplus\) effects vast conformational changes in the protein
How do you generate a proton gradient?

\[ \text{fuel} \xrightarrow{} \text{NAD}^+ \xrightarrow{} \text{NADH} \xrightarrow{\text{H}^+} \text{H}_2\text{O} \xrightarrow{\frac{1}{2} \text{O}_2} \text{H}^+ \]

\( \Delta G \) (free energy) can be used to generate \( \text{H}^+ \) gradient.

What is \( \text{H}^+ \) gradient used for?

1. \( \text{ADP} + \text{Ri} \rightleftharpoons \text{ATP} \)
   \[ \Delta G = 34 \text{ KJ/mol} \]

2. flagellar rotation
3. ion transporters

Outside

Inside

For each \( \text{NADH} \) oxidized, you transfer 8 to 10 \( \text{H}^+ \)s.
How do pumps work?

Coenzyme Q

Q ubiquinone  \(\text{QH}^+\) semiquinone  \(\text{QH}_2\) hydroquinone

代谢 \(\rightarrow e^-\) 生物膜 \(\rightarrow e^-\) 氧化

\[2H^+ \leftrightarrow e^- \quad 2H^+\]

- One \(e^-\) flows across membrane
- Two protons get pumped
- \(e^-\) loses energy in the process

第二泵模型：光驱动质子泵

\(\text{Fe}^{3+} + e^- \rightarrow \text{Fe}^{2+}\) 伴随构象改变

\(e^- \rightarrow \text{Fe}^{2+}\) 伴随蛋白复合体

His (normal PK, V6)

PK (unusually high, n7)