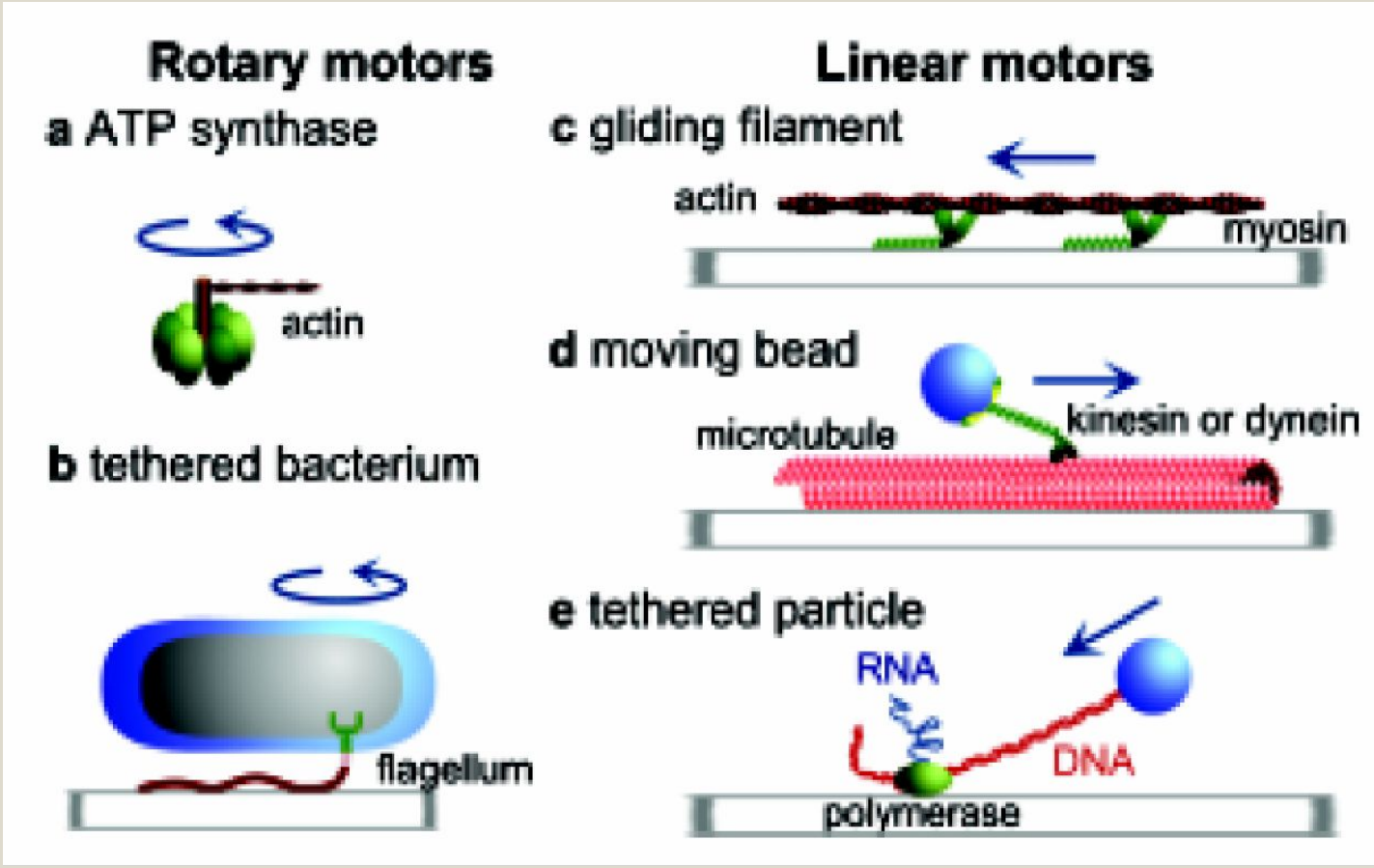
Unit 4 Mechanochemistry

- Molecular Machines/Motors
- Properties of ATP-based Protein Molecular Machines
  - The F0F1-ATP Synthase Motors
  - Coupling and Coordination of Motors
- The Bacterial Flagellar Motor
  - Flagellar motor structure
- Cytoskeleton
- Bioremediation
- Biosensors

Molecular Machines/Motors

- ***Molecular machines can be defined as devices that can produce useful work through the interaction of individual molecules at the molecular scale of length.***
- ***A convenient unit of measurement at the molecular scale would be a nanometer. Hence, molecular machines also fall into the category of nanomachines.***
- ***As our knowledge and understanding of these numerous machines continues to increase, we now see a possibility of using the natural machines, or creating synthetic ones from scratch, by mimicking nature.***

Different types of molecular machines. These machines used by nature for force generation and motion. ***They convert chemical energy into mechanical force via conformational changes.***



- Most of the natural machinery is built from proteins.
- These findings help unravel the mysteries associated with the molecular machinery and pave the way for the production and application of these miniature machines in various fields, including medicine, space exploration, electronics and military.
- *We divide the molecular machines into three broad categories*—**protein based, DNA-based, and chemical molecular motors**.

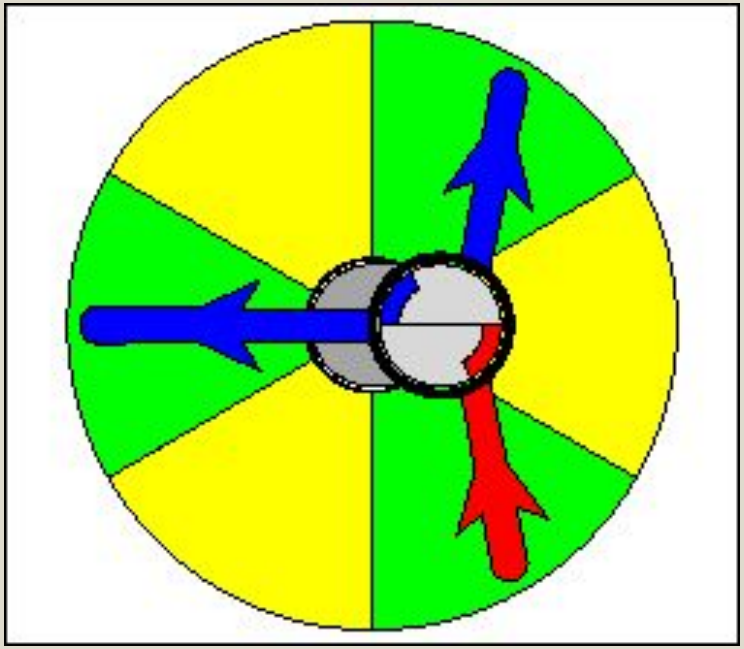
Properties of ATP-based Protein Molecular Machines

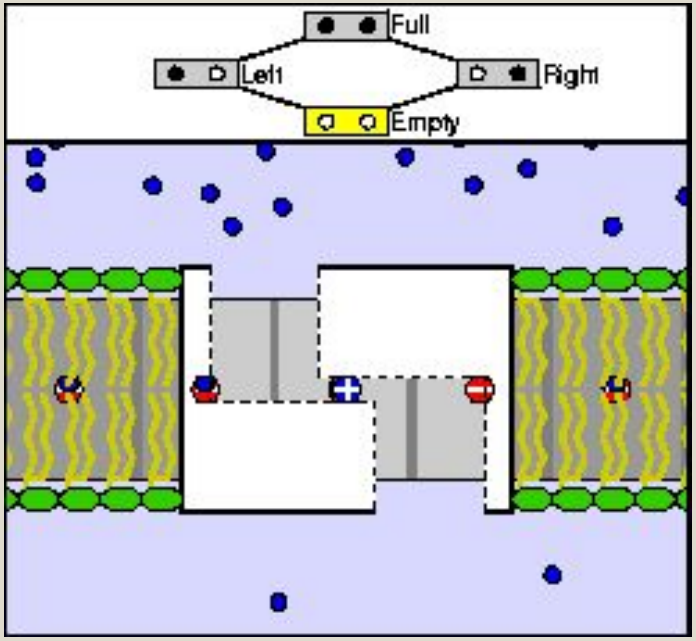
- ***Two form the F0F1-ATP synthase, and the third one is the bacterial flagellar motor.***
- **The protein-based molecular motors rely on an energy-rich molecule known as adenosine triphosphate (ATP),**
- **The machines described in this section, the F0F1-ATPase, the kinesin, myosin, and dynein superfamily of protein molecular machines, and bacteria flagellar motors all depend, directly or indirectly, on ATP for their input energy.**
- **These machines have now been segregated out of their natural environment and are seen as energy conversion devices to obtain forces, torques, and motion.**
- **One disadvantage associated with ATP dependence is that the ATP creation machinery itself could be many times heavier and bulkier than the motors, thereby making it more complex.**
- **These machines perform best in their natural environment, and in the near future it may be possible to have them as a part of biomimetic molecular machinery.**

The F0F1-ATP Synthase Motors

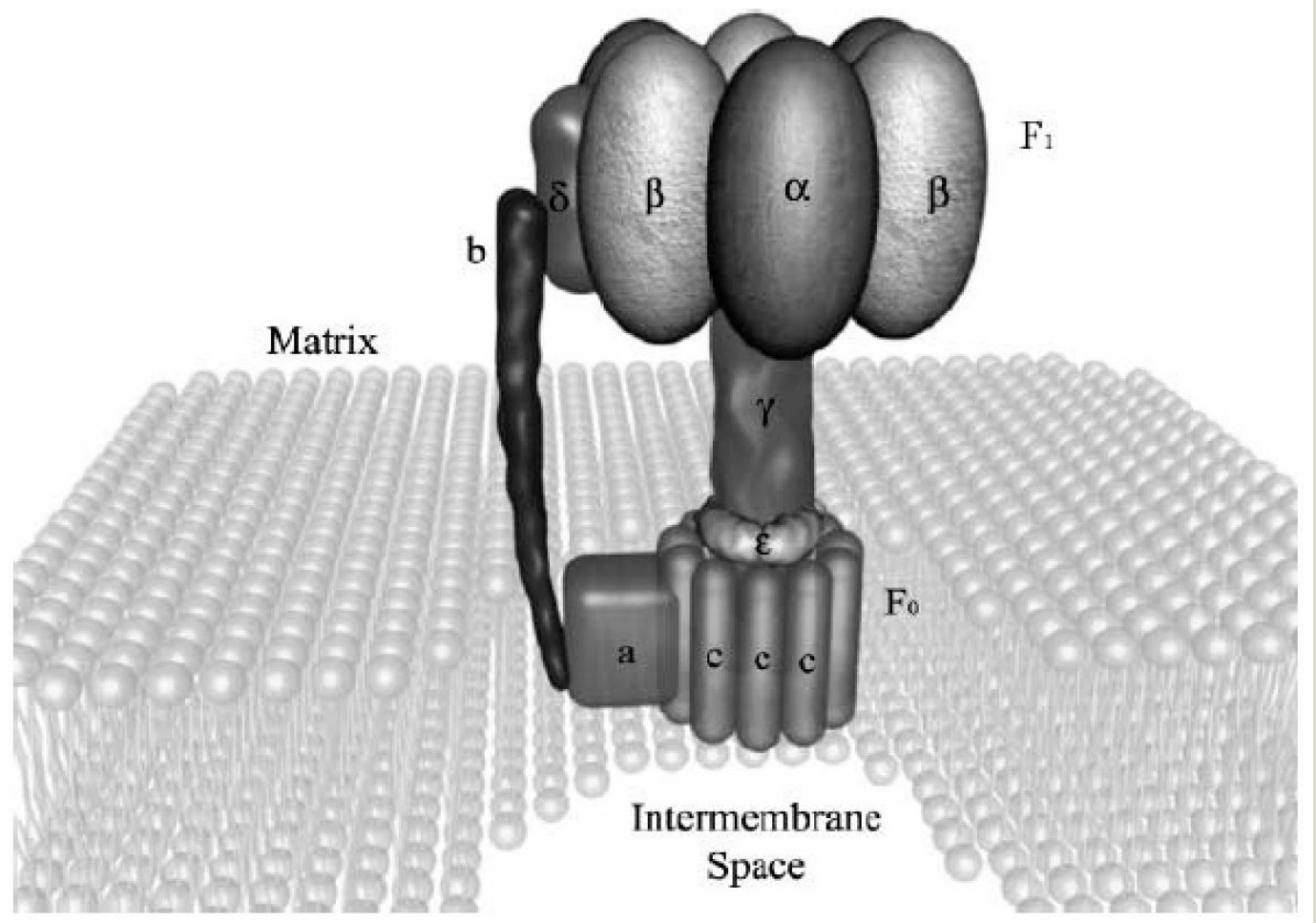
- ATP is regarded as the energy currency of biological systems.
- When this currency is utilized (i.e., the energy of the molecule that is used to drive a biological process), the terminal anhydride bond in the ATP molecule has to be split. This leaves adenosine diphosphate (ADP) and a phosphate ion (Pi) as the products, which are recombined to form ATP by a super efficient enzyme motor assembly called the F0F1-ATP synthase (F0F1-ATPase).
- ATP synthase is present inside the mitochondria of animal cells, in plant chloroplasts, in bacteria, and some other organisms.

- ATP synthase consists of two portions: a membrane-spanning portion, Fo, comprising the ion channel, and a soluble portion, F1, containing three catalytic sites.
- Both Fo and F1 are reversible rotary motors --- perhaps the smallest motors known to science. Fo uses the transmembrane electrochemical gradient to generate a rotary torque to drive ATP synthesis in F1 or, when driven backwards by the torque generated in F1, to pump ions uphill against their transmembrane electrochemical gradient.
- F1 generates a rotary torque by hydrolyzing ATP at its three catalytic sites or, when turned backwards by the torque generated in Fo, as a synthesizer of ATP.



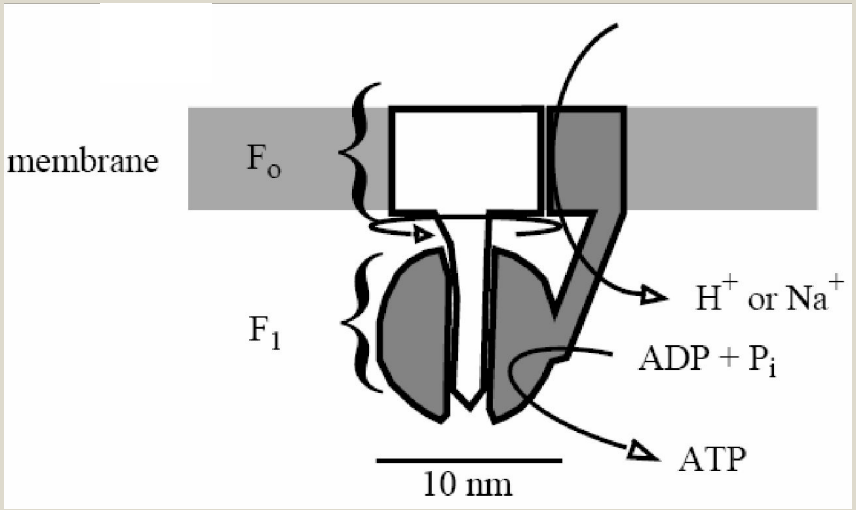

Full
Left
Right
Empty

The F0F1-ATPase motors. The F0 motor is embedded in the inner mitochondrial membrane of the mitochondria. F0 is typically composed of *a*, *b*, and *c* subunits as shown. The F1 motor is the soluble region composed of three *α*-, three *β*-, one each of *γ* -, *δ*- and *ε*-subunits.



Coupling and Coordination of Motors

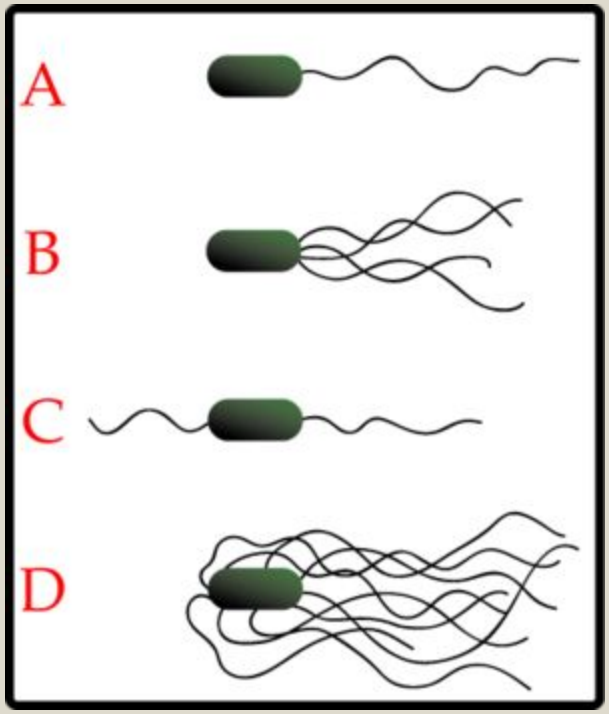
- **The ATP synthase is actually a combination of two motors functioning together, the hydrophobic transmembrane F0-ATPase motor and the globular F1-ATPase motor**



The F0F1-ATPase contains two rotary motors: the membrane –bound F0, driven by the flux of ions across a membrane, and the soluble F1, driven by ATP hydrolysis. These two motors are coupled by sharing a common motor, drawn in white, and a common stator, drawn dark. The figure shows the F0F1-ATPase operating as an ATP-synthase. Rotation of F0 driven by ion flux drives F1 in reverse, causing it to synthesize ATP from ADP and inorganic phosphate.

The Bacterial Flagellar Motor

- **A flagellum (plural: flagella) is a long, slender projection from the cell body, composed of microtubules and surrounded by the plasma membrane.**
- **In small, single-cell organisms they may function to propel the cell by beating in a whip-like motion; in larger animals, they often serve to move fluids along mucous membranes such as the lining of the trachea.**
- **The bacterial flagellar motor is a nanotechnological marvel, no more than 50 nm in diameter, built from about 20 different kinds of parts.**



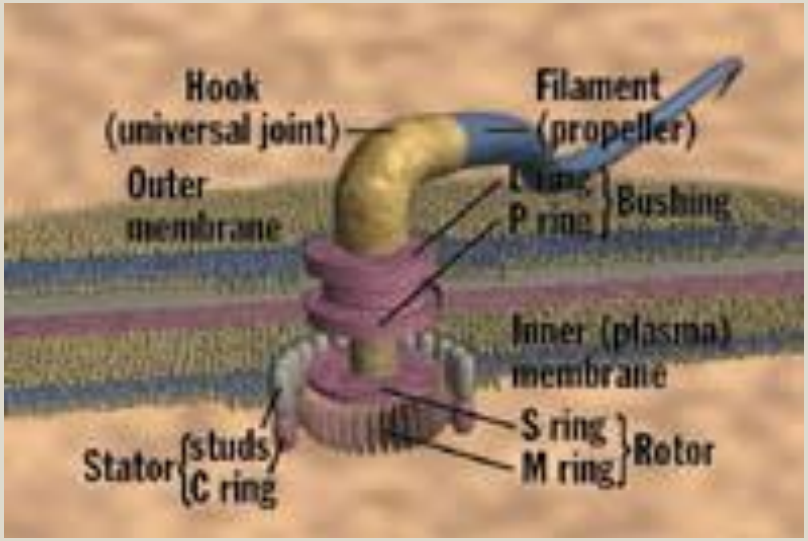
Examples of bacterial flagella arrangement schemes.
A-Monotrichous;
B-Lophotrichous;
C-Amphitrichous; D-Peritrichous

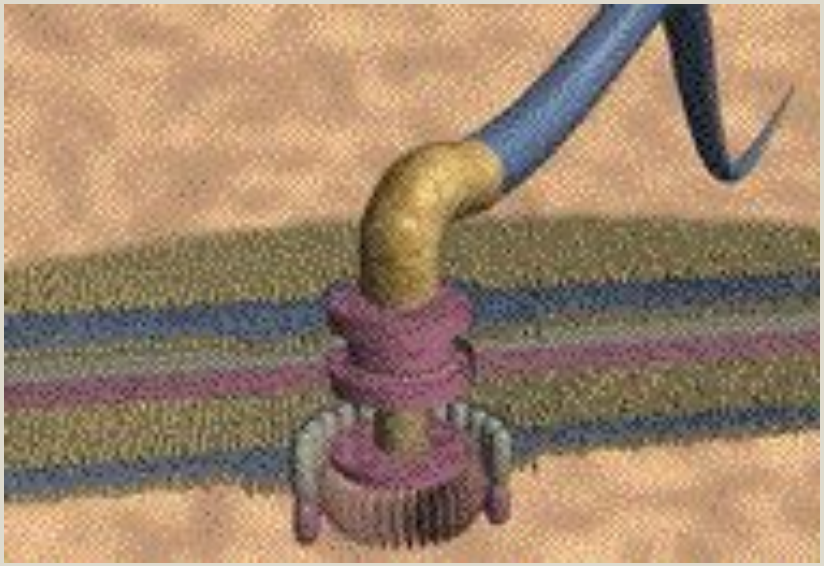
- **It spins clockwise (CW) or counterclockwise (CCW) at speeds on the order of 100 Hz, driving long thin helical filaments that enable cells to swim.**

- **Peritrichously flagellated cells (*peri,* around; *trichos*, hair), such as *Escherichia coli*, execute a random search, moving steadily at about 30 diameters per second, now in one direction, now in another.**

- **Steady motion requires CCW rotation. Receptors near the surface of the cell count molecules of interest (sugars, amino acids, dipeptides) and control the direction of flagellar rotation.**

- **If a leg of the search is deemed favorable, it is extended, i.e., the motors spin CCW longer than they otherwise would. This bias enables cells to actively find regions in their environment where life is better.**





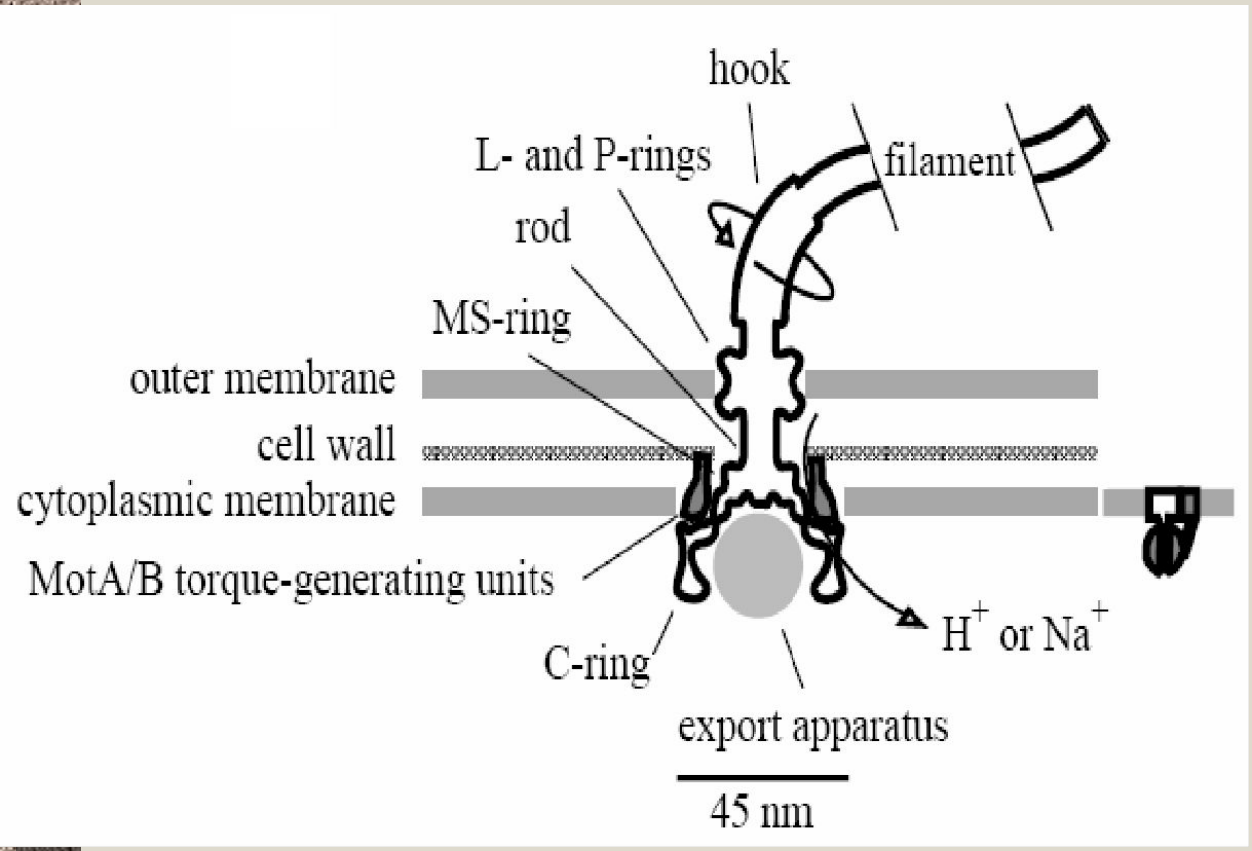
- **Thus, the flagellar motor is the output organelle of a remarkable sensory system, the components of which have been honed to perfection by billions of years of evolution.**

- **A number of bacterial species in addition to *E. coli* depend on flagella motors for motility: e.g., *Salmonella enterica* serovar, Typhimurium (*Salmonella*), *Streptococcus*, *Vibrio* spp., *Caulobacter*, *Leptospira*, *Aquaspirrilum serpens*, and *Bacillus*.**

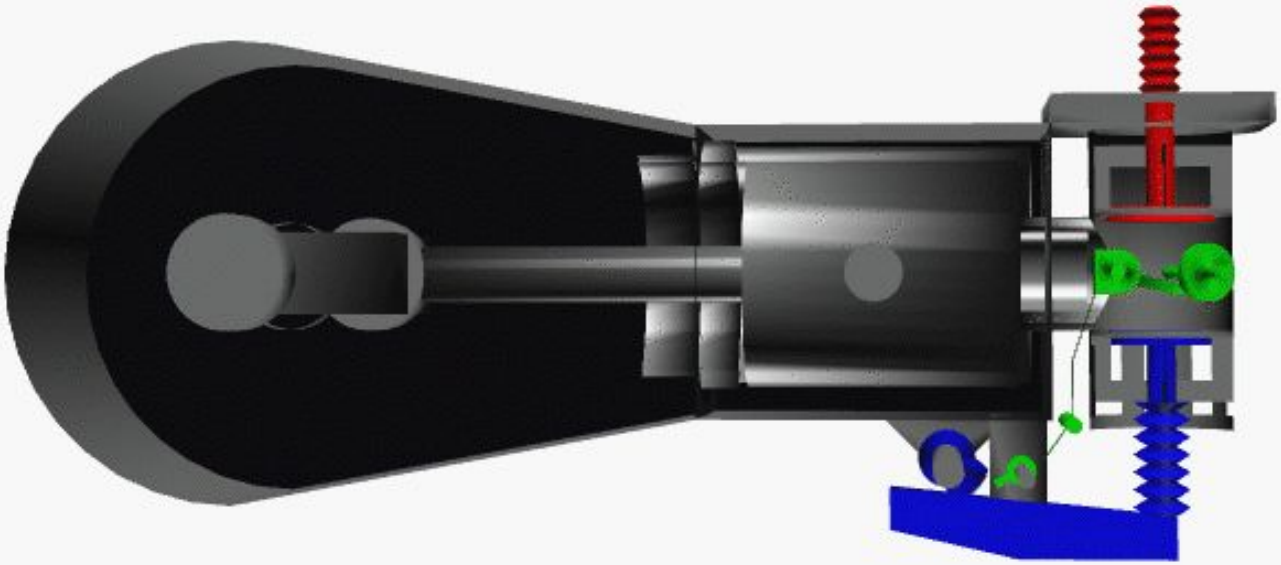
- **The rotation of flagella motors is stimulated by a flow of ions through them, which is a result of a build-up of a transmembrane ion gradient. There is no direct ATP-involvement; however, the proton gradient needed for the functioning of flagella motors can be produced by ATPase.**

Flagellar motor structure

- **Bacterial flagella are the only biological structures known that use rotation for the purpose of locomotion.**
- **Flagella consist of a rotary motor embedded in the cell envelope connected to an extracellular helical propeller. The motor is powered by the flow of ions down an electrochemical gradient across the cytoplasmic membrane into the cell.**
- **The ions are typically H+ (protons), although certain marine and alkalophilic species have motors driven by Na+.**
- **The electrochemical gradient (protonmotive force or sodium motive force) consists of a transmembrane voltage and a concentration difference across the membrane, both of which are maintained by various metabolic processes.**
- **The rotor shown in white (Figure 5), consists of a series of rings spanning the cell envelope and is attached via the flexible hook to the helical propeller or filament. The stator is a ring of particles in the cytoplasmic membrane, containing the proteins MotA and MotB, and anchored to the peptidoglycan cell**



The bacterial flagellar motor. The rotor, drawn in white, consists of a series of rings that span the cell envelope and are attaches to the extracellular hook and filament. The stator consists of a ring of torque-generating units containing the proteins MotA and MotB and anchored to the cell wall. Ions flowing through the motor generate torque by means of unknown interactions between the rotor and stator in the vicinity of the C-ring. The F0F1-ATPase is also shown, to the same scale.



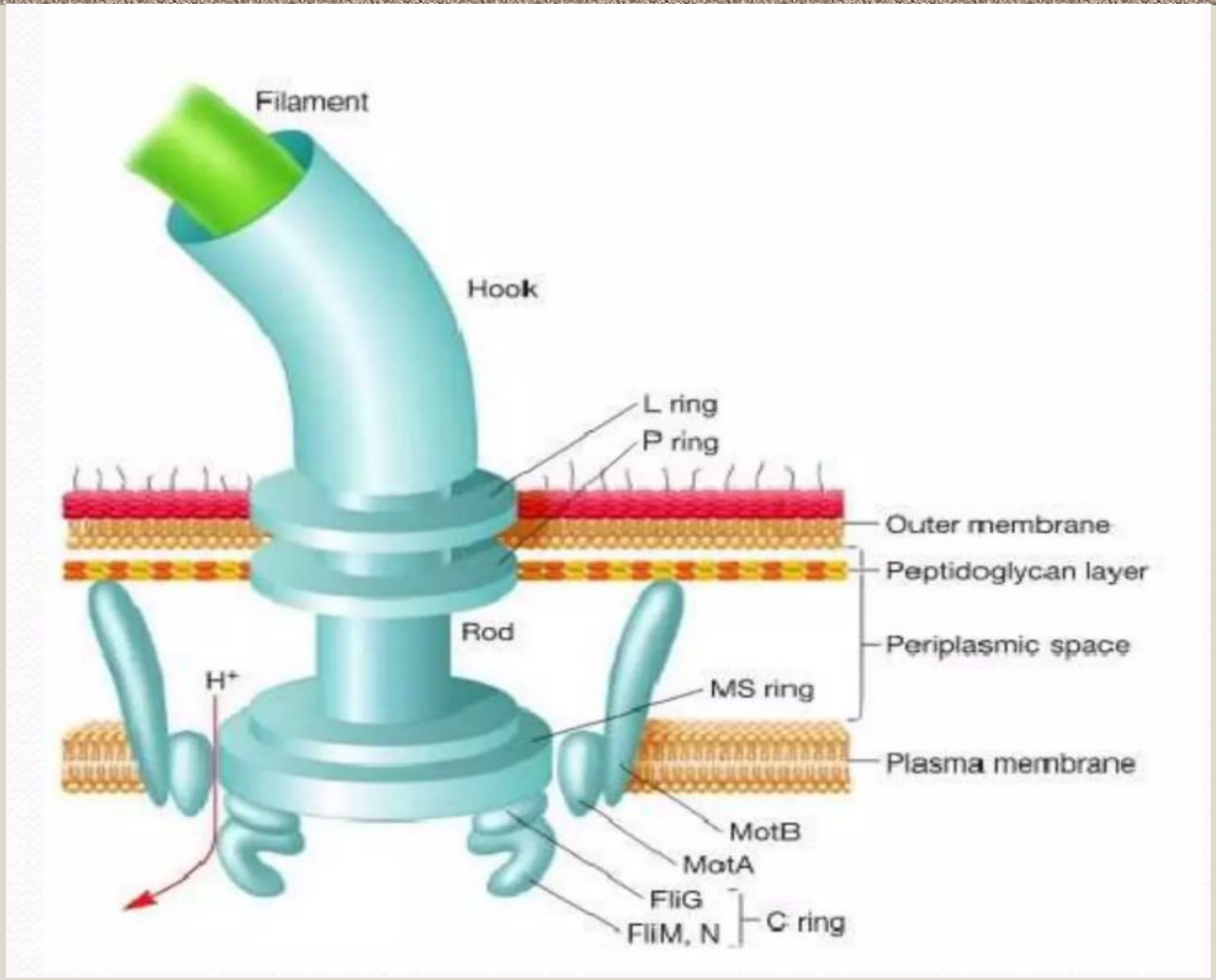
The fuel/air intake system red, the electrical system green, and the exhaust system blue

- The motor is composed of two components:

1) The rotor

2) The stator

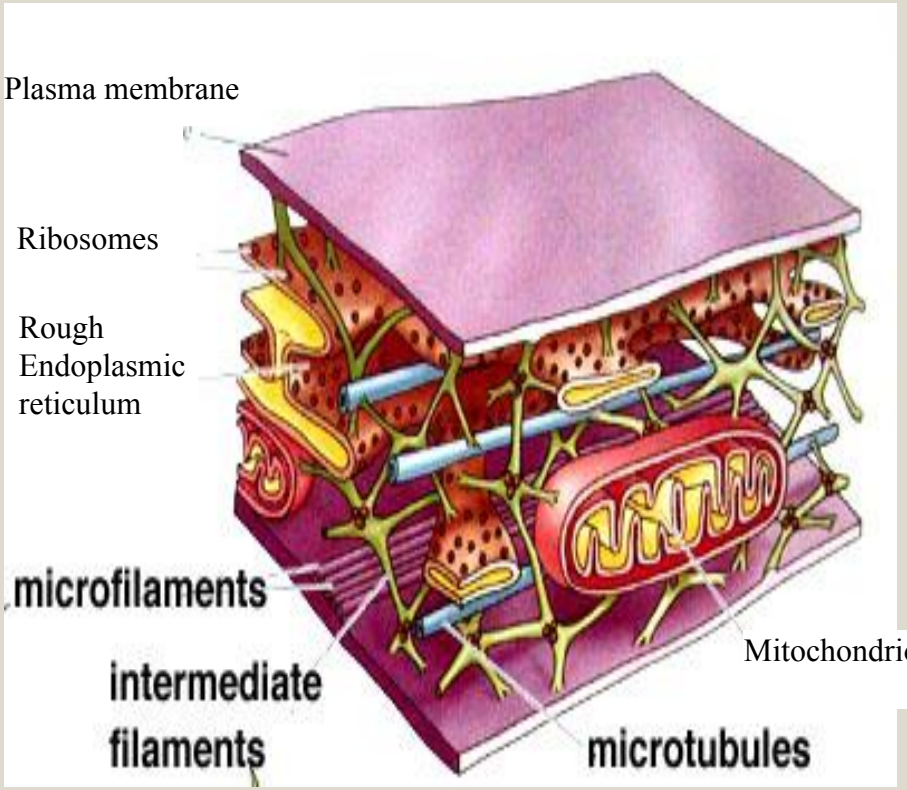
- Gram negative bacteria: rotor is composed of the MS ring & the C ring
- Flagellar protein FliG helps roto& stator interaction
- Stator: composed of proteins MotA & MotB
- Form cahnnel through plasma membrane
- Also anchor MotA to cell peptidoglycan


Filament
Hook
L ring
P ring
Outer membrane
Peptidoglycan layer
Periplasmic space
Rod
H+
MS ring
Plasma membrane
MotB
MotA
FliG
FliM, N
C ring

- Proton motive force generate torque.
- The channel created by MotA &MotB proteins allow protons to move across the plasma membrane from outside to inside.
- They move to the charge and pH gradient
- This movement releases energy which is used by flagellum for rotation

Cytoskeleton: Microtubules, Microfilaments, and Intermediate filaments

- **Cytoskeleton gives the cell shape, structure, and physical organization**
- **Motor proteins can rearrange the structural elements, or move cell components around the cytoskeleton.**
- **The cytoskeleton is in constant state of change depending on the requirements of the cell.**
- **3 major structural elements of the cytoskeleton**
- **<u>Microtubules</u> - hollow, rigid cylindrical tubes made from tubulin subunits**
- **<u>Microfilaments</u> - solid, thinner structures made of actin**
- **<u>Intermediate filaments</u> - tough, ropelike fibers made of a variety of related proteins**



The Myosin Linear Motor

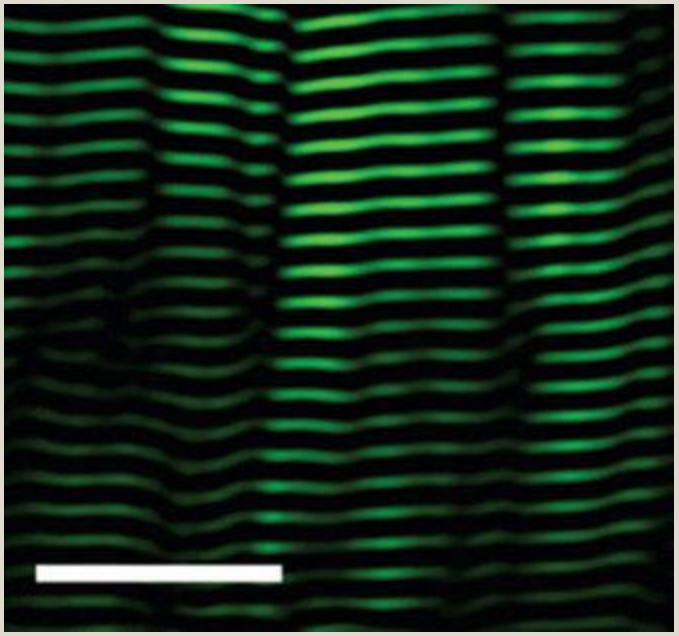
- **Myosin is a diverse superfamily of motor proteins.**
- **Myosin-based molecular machines transport cargoes along actin filaments, the two-stranded helical polymers of the protein actin that are about 5–9 nm in diameter. They do this by hydrolyzing ATP and utilizing the released energy.**

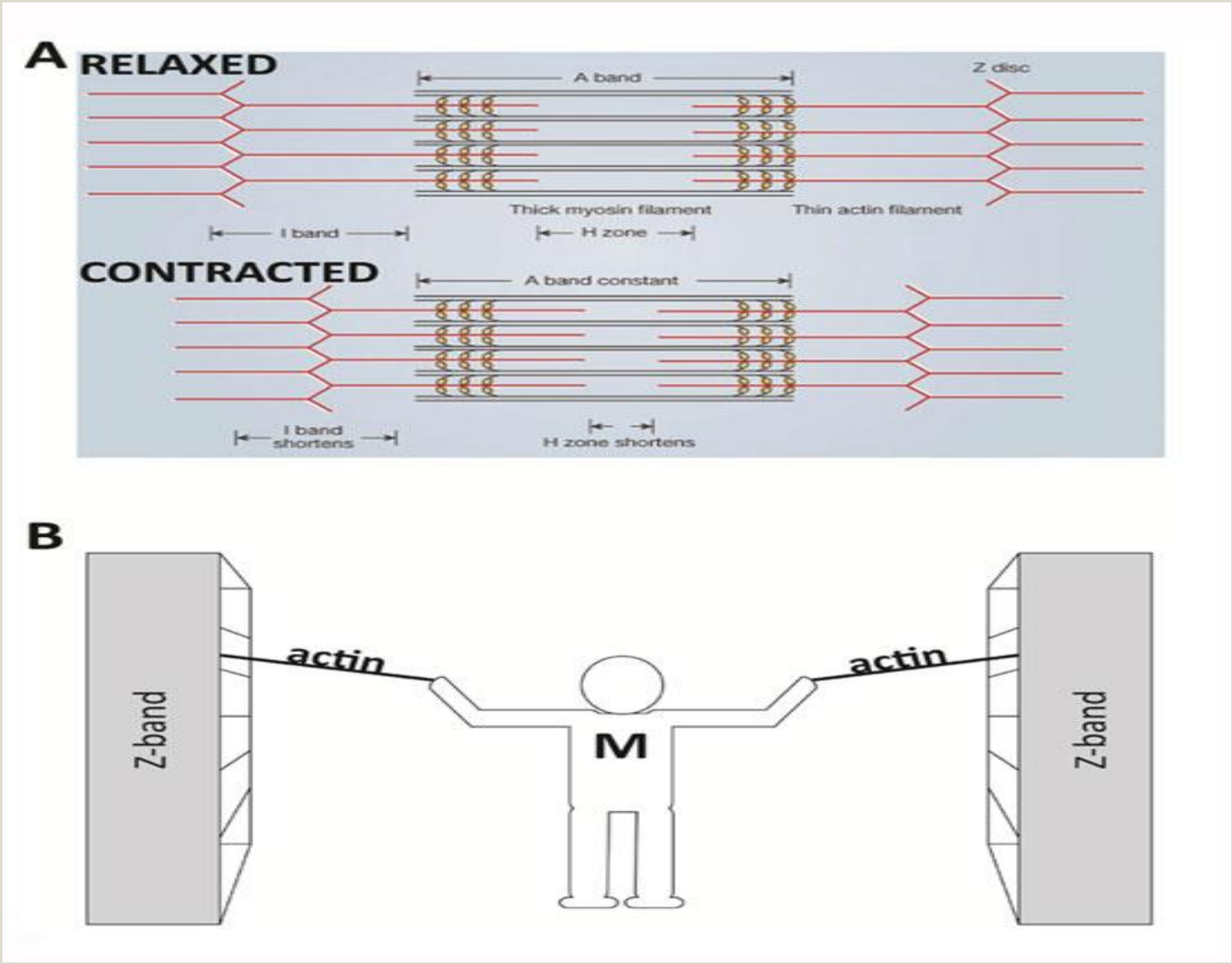
- **In addition to transport, they are also involved in the process of force generation during muscle contraction, wherein thin actin filaments and thick myosin filaments slide past each other.**

- **Myosin molecules were first seen (in the late 1950s) through electron microscope protruding out from thick filaments and interacting with the thin actin filaments. Since that time, ATP has been known to play a role in myosin-related muscle movement along actin; however, the exact mechanism was unknown, until it was explained in 1971.**

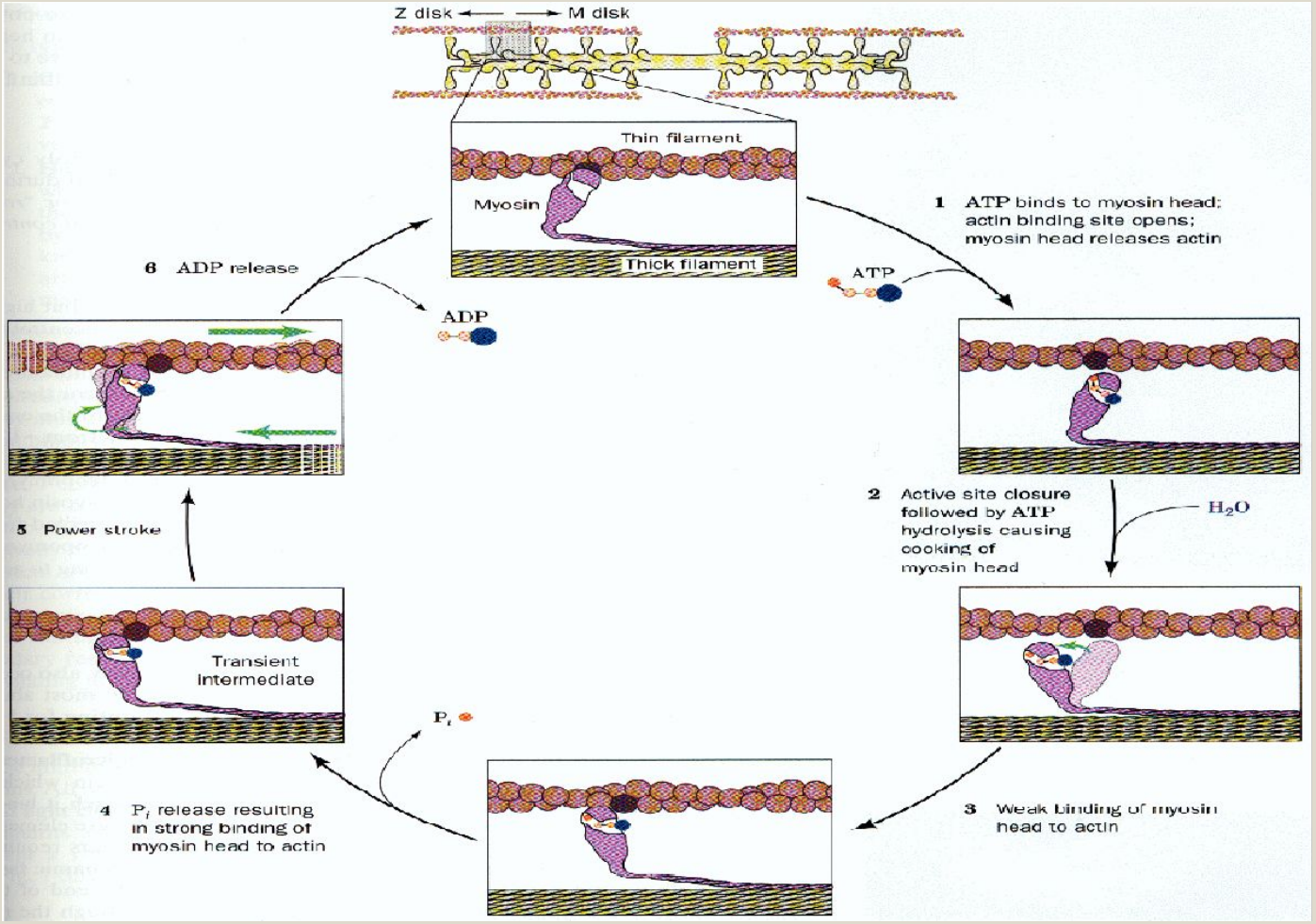
The Myosin Linear Motor

- When muscle cells are viewed under the microscope, one can see that they contain a striped pattern (striations).
- This pattern is formed by a series of basic units called sarcomeres.
- An individual sarcomere contains many parallel actin (thin) and myosin (thick) filaments



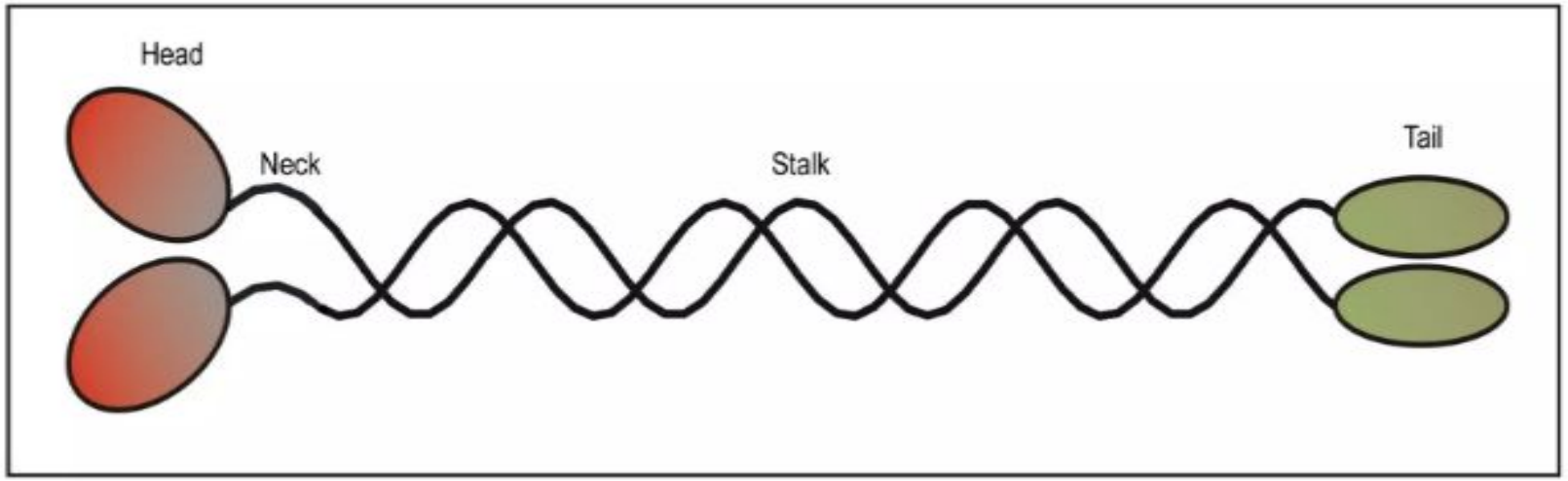

A
RELAXED
A band
Z disc
Thick myosin filament
Thin actin filament
I band
H zone
CONTRACTED
A band constant
I band
shortens
H zone shortens
B
Z-band
actin
M
actin
Z-band

Myosin cross-bridge model of contraction. Myosin uses the energy released from ATP hydrolysis to move along actin.

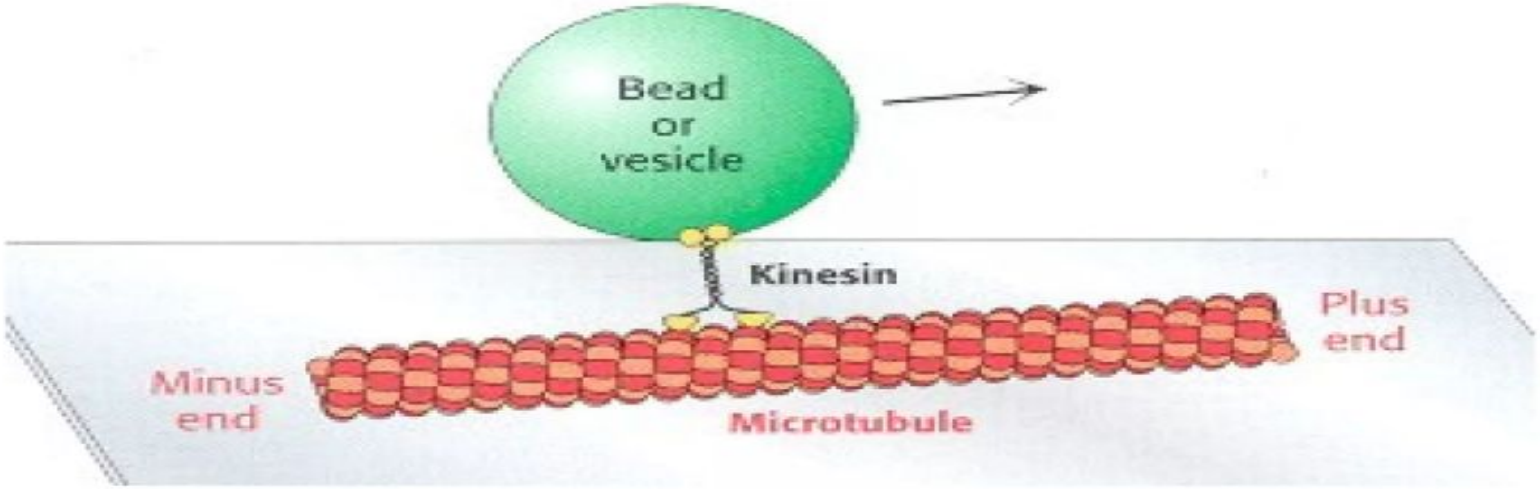


The Kinesin Linear Motor

- The kinesin and dynein families of proteins are involved in cellular cargo transport along microtubules, in contrast to myosin, which transports along actin.
- Microtubules are 25-nm diameter tubes made of protein tubulin and are present in the cells in an organized manner.
- Microtubules have polarity; one end being the plus (fast-growing) end while the other end is the minus (slow-growing) end.
- Kinesins move from the minus end to the plus end of the microtubule, whereas dyneins move from the plus end to the minus end.
- Microtubule arrangement varies in different cell systems. In nerve axons, they are arranged longitudinally such that their plus ends point away from the cell body and into the axon.
- In epithelial cells, their plus ends point toward the basement membrane.
- They extend radially out of the cell center in fibroblasts and macrophages with the plus end protruding outward.
- Similar to myosin, kinesin is also an ATP-driven motor.
- One unique characteristic of the kinesin family proteins is their processivity; they bind to microtubules and literally walk on it for many enzymatic cycles before detaching.



Kinesin 'walks' along the microtubule while carrying its cargo



Kinesin Movement Along Microtubule

- Addition of ATP strongly increases the affinity of kinesin for microtubules
- In a two-headed kinesin molecule in its ADP form, when ATP is bound, the neck linker will bind to the head domain.
- Initial interaction of the head domains with a tubulin molecule on a microtubule stimulates the release of ADP from this head domain & subsequent binding of ATP

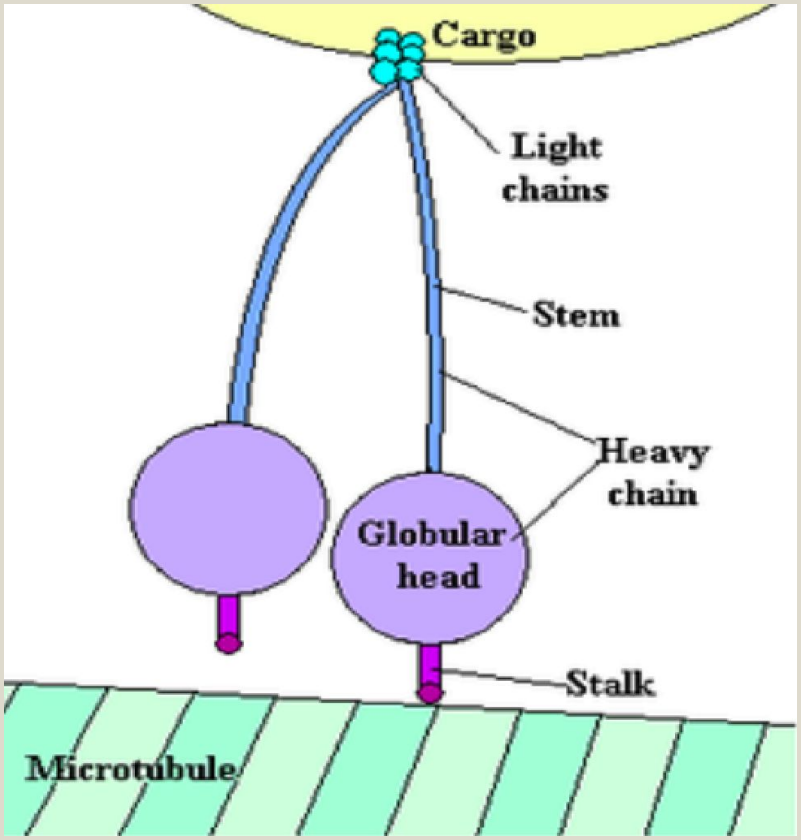
Kinesin Movement Along Microtubule

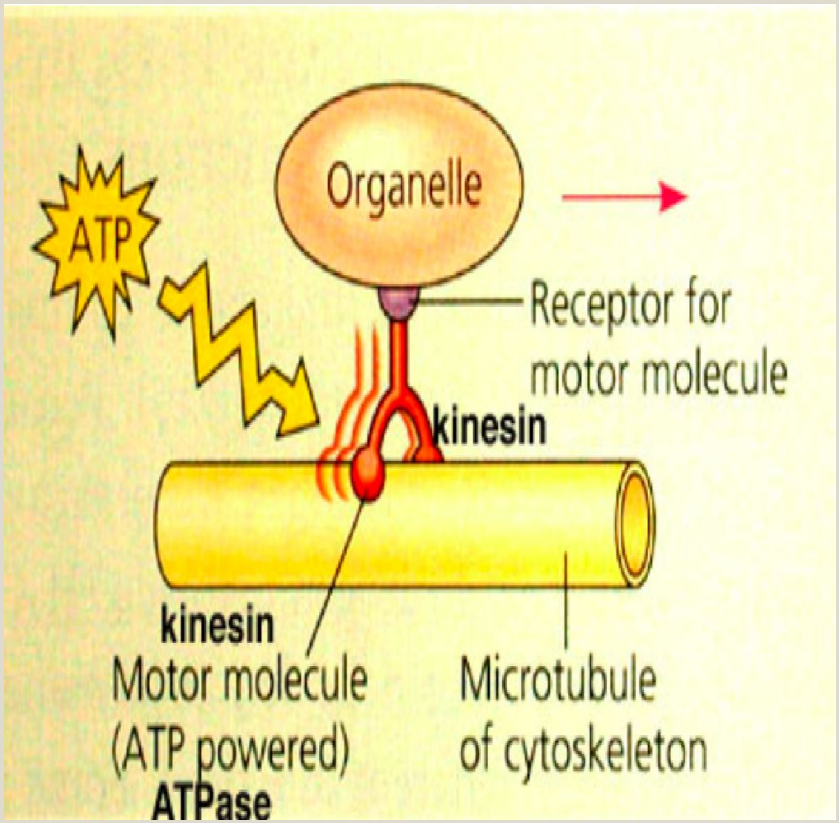
- The ATP binding triggers conformational change in the head domain leading to two events:

1) Affinity of the head domain to microtubule increases
2) Neck linker binds to head domain
3) This will reposition the second head domain.
4) ATPase in the first head domain hydrolyzes ATP to ADP and Pi
5) The second head domain binds to microtubule, the first head domain releases ADP &binds to ATP.

Kinesin Movement Along Microtubule

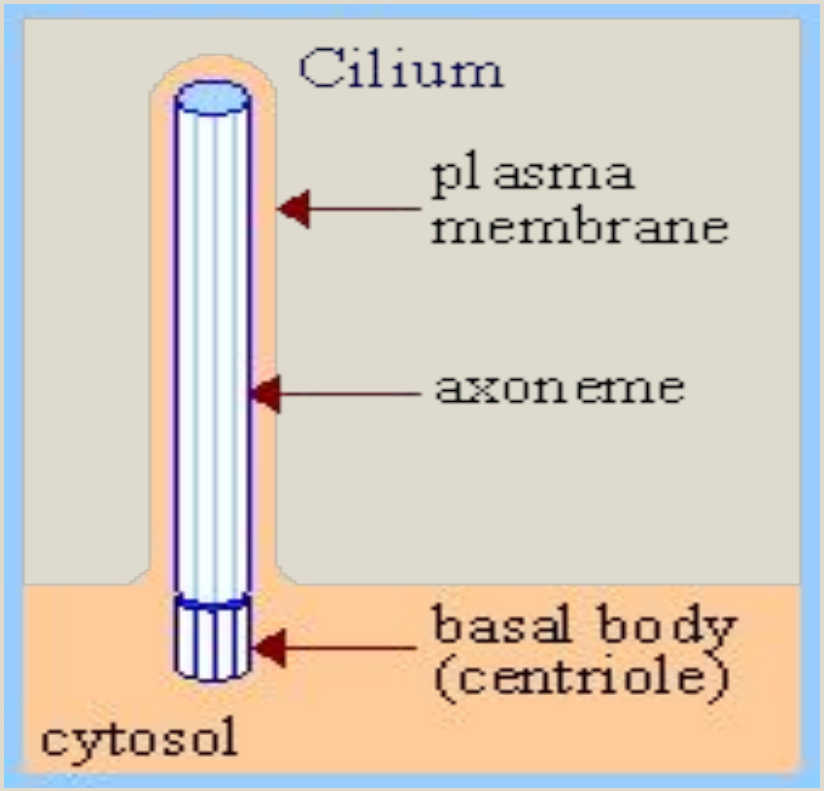
- ATP binding favors a conformational change that pulls the first domain forward.
- The process continues till both head domains are in ADP form simultaneously resulting in the release of kinesin molecule from microtubule.


Cargo
Light chains
Stem
Heavy chain
Globular head
Stalk
Microtubule


ATP
Organelle
Receptor for motor molecule
kinesin
kinesin
Motor molecule (ATP powered) ATPase
Microtubule of cytoskeleton

The Dynein Motor

- **The dynein superfamily of proteins was discovered in 1965.**
- **Dyneins exist in two isoforms: cytoplasmic and axonemal.**
- **Cytoplasmic dyneins are involved in cargo movement, whereas axonemal dyneins are involved in producing bending motions of cilia and flagella.**
- **Because dynein is a larger and more complex structure than other motor proteins, its mode of operation is not as well known. However, electron microscopy and image processing was used to show the structure of a flagellar dynein at the start and end of its power stroke, which gives some insight into its possible mode of force generation.**



Cilia and flagella have a core **axoneme**, a complex of microtubules and associated proteins.

Bioremediation

Definition: Use of living organisms to transform, destroy or immobilize contaminants

Goal: Detoxification of the parent compound(s) and conversion to products that are no longer hazardous to human health and the environment.

Sources of Contamination

- Industrial spills and leaks
- Surface impoundments
- Storage tanks and pipes
- Landfills
- Burial areas and dumps
- Injection wells

Why use Bioremediation?

- No additional disposal costs
- Low maintenance
- Does not create an eyesore
- Capable of impacting source zones and thus, decreasing site clean-up time

Microorganisms

- **Aerobic bacteria:**
  - Examples include: *Pseudomonas*, *Alcaligenes*, *Sphingomonas*, *Rhodococcus*, and *Mycobacterium*
  - Shown to degrade pesticides and hydrocarbons; alkanes and polyaromatics
  - May be able to use the contaminant as sole source of carbon and energy.
- **Methanotrophs:**
  - Aerobic bacteria that utilize methane for carbon and energy
  - Methane monooxygenase has a broad substrate range
    - active against a wide range of compounds (e.g. chlorinated aliphatics such as trichloroethylene and 1,2-dichloroethane)
- **Anaerobic bacteria:**
  - Not used as frequently as aerobic bacteria
  - Can often be applied to bioremediation of polychlorinated biphenyls (PCBs) in river sediments, trichloroethylene (TCE), and chloroform
- **Fungi:**
  - Able to degrade a diverse range of persistent or toxic environmental pollutants

Forms of Bioremediation

- **In situ Bioremediation**
  - Bioventing
  - In situ biodegradation
  - Biostimulation
  - Biosparging
  - Bioaugmentation
  - Natural Attenuation

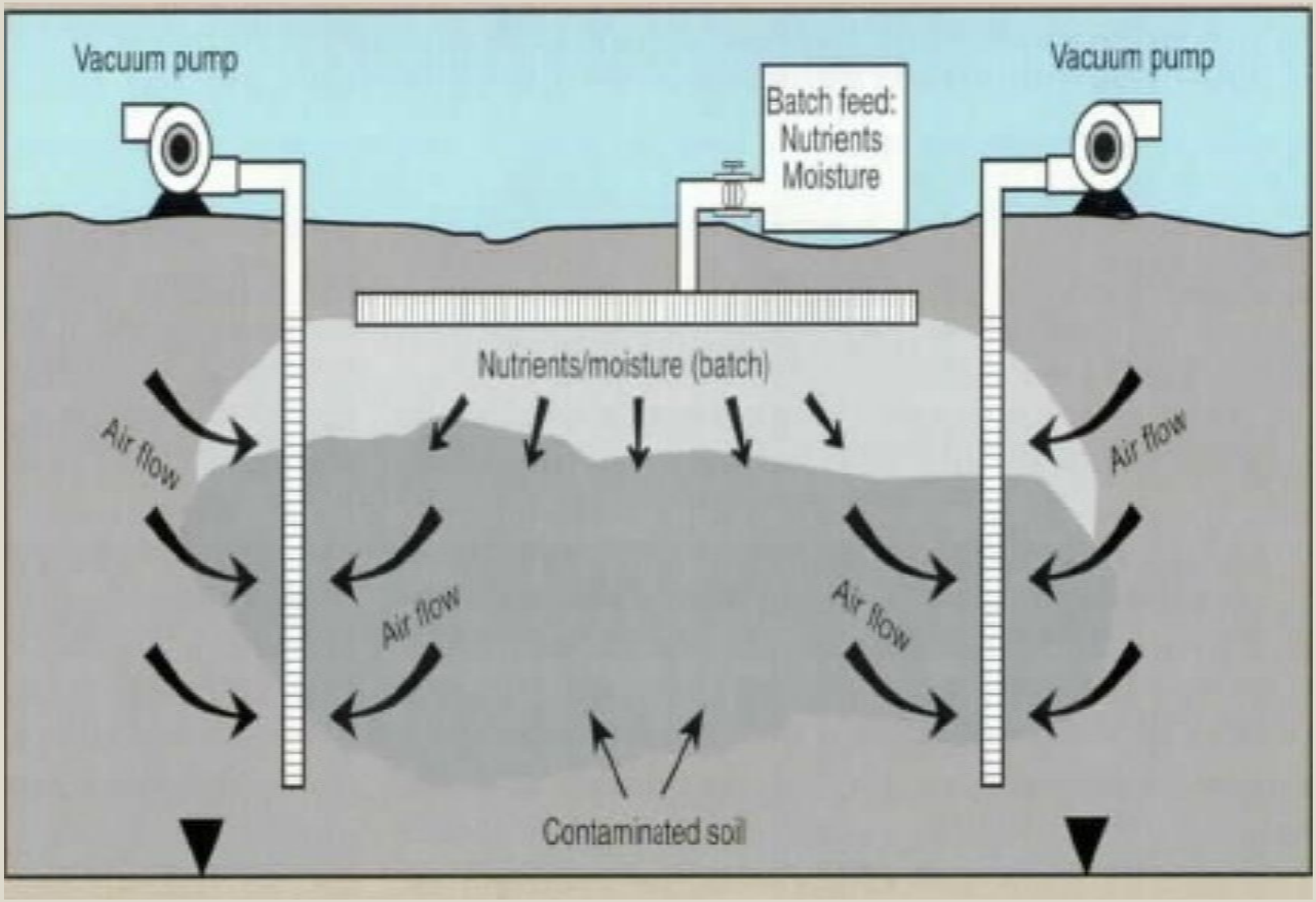
- **Ex situ Bioremediation**
  - Land farming
  - Composting
  - Biopiles
  - Bioreactors

- **Phytoremediation**
  - Phytoextraction or phytoaccumulation
  - Phytodegradation or phytotransformation
  - Phytostabilization
  - Rhizodegradation
  - Rhizofiltration

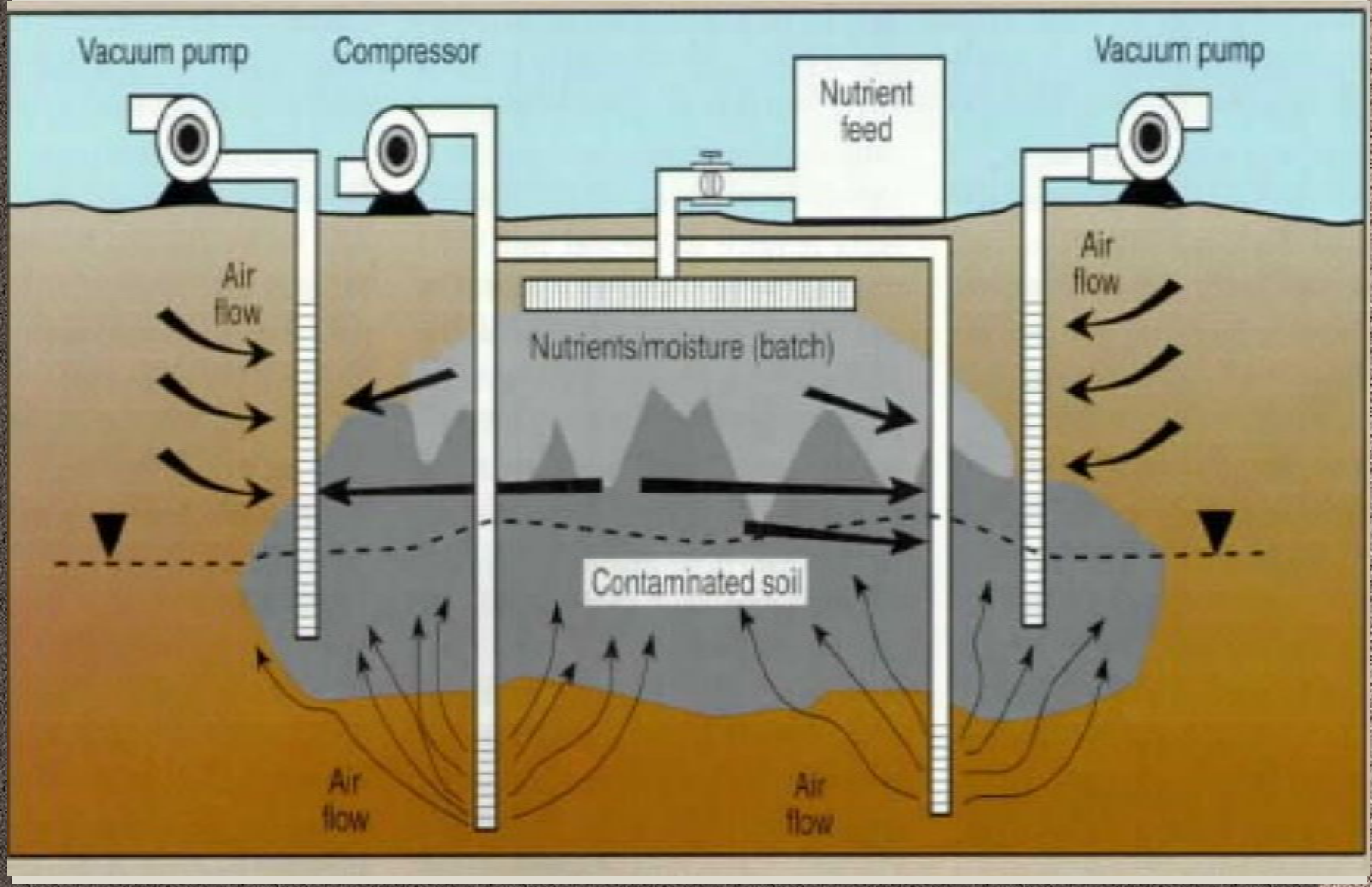
In Situ Bioremediation

- **Bioventing**
  - One of the most common approaches in soil
  - Supply air and nutrients via wells
  - Takes advantage of indigenous microorganisms
- **In situ biodegradation**
  - Supply air and nutrients by circulating aqueous solutions through contaminated soils or groundwater
- **Biosparging**
  - Injection of air below the water table increases groundwater oxygen concentrations and mixing in saturated zone
- **Bioaugmentation**
  - Addition of indigenous or exogenous microorganisms
  - Limits to use: competition and necessity
- **Biostimulation**
- **Natural Attenuation or Intrinsic Bioremediation**

Bioventing


Vacuum pump
Vacuum pump
Batch feed:
Nutrients
Moisture
Nutrients/moisture (batch)
Air flow
Air flow
Air flow
Air flow
Contaminated soil

Biosparging



Five Steps of In Situ Bioremediation

1. Site investigation
2. Treatability studies
3. Recovery of free product and removal of the contamination source
4. Design and implementation of the in situ bioremediation system
5. Monitoring and performance evaluation of the in situ bioremediation system

Ex situ Bioremediation

- **Land farming**
  - Contaminated soil is excavated and spread over land
  - Soil is periodically tilled to improve aeration
  - Remediation due to indigenous microorganisms, as well as chemical and physical processes
  - Generally limited to the superficial 10–35 cm of soil
  - Can reduce monitoring and maintenance costs

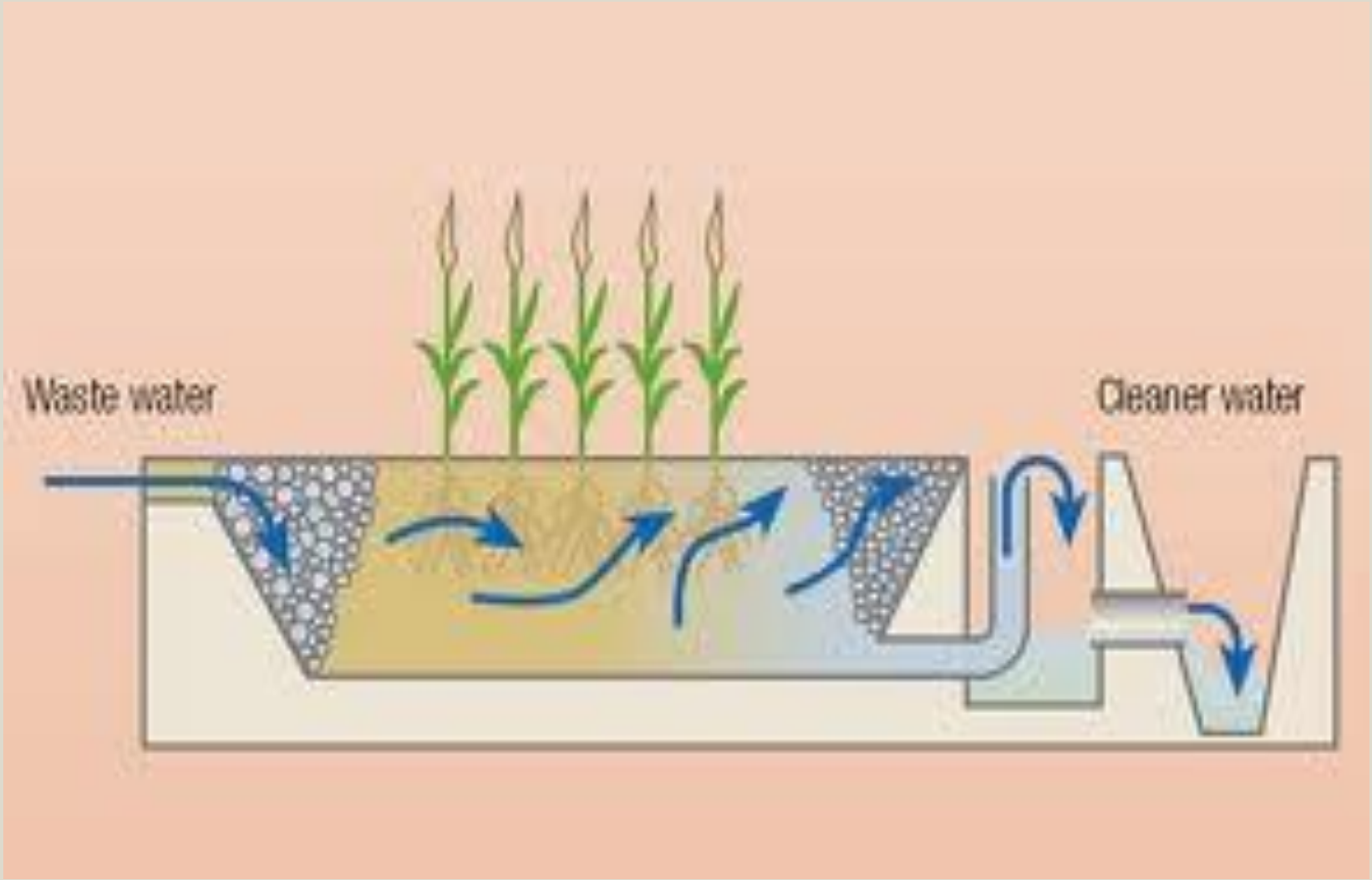
- **Composting**
  - Combines contaminated soil with nonhazardous organic amendants (e.g. manure or agricultural wastes)

- **Biopiles**
  - Combination of landfarming and composting
  - Control physical losses of contaminants

- **Bioreactors**
  - Soil and water pumped up from a contaminated plume and processed through an engineered containment system
  - Degradation in a bioreactor is generally greater than *in situ* because the contained environment is more controllable and predictable

Phytoremediation

- **Phytoextraction or phytoaccumulation**
  - Plants used to accumulate contaminants in the roots and aboveground biomass
  - Can be a relatively low cost option for a large area
  - Results in biomass that must be properly disposed of or reused
- **Phytotransformation or phytodegradation**
  - Uptake of contaminants and transformation to more stable, less toxic, or less mobile forms
  - Eg. metal chromium can be reduced from hexavalent to less mobile (and non-carcinogenic) trivalent chromium
- **Phytostabilization**
  - Mobility and migration of contaminants are reduced through sorption onto or into the plant
- **Rhizodegradation**
  - Breakdown of contaminants through activity of the rhizosphere
- **Rhizofiltration**
  - Water remediation technique
  - Used to reduce contamination in natural wetlands and estuary areas.


Waste water
Cleaner water

Overview of phytoremediation applications.

Technique	Plant mechanism	Surface medium
Phytoextraction	Uptake and concentration of metal via direct uptake into the plant tissue with subsequent removal of the plants	Soils
Phytotransformation	Plant uptake and degradation of organic compounds	Surface water, groundwater
Phytostabilization	Root exudates cause metal to precipitate and become less available	Soils, groundwater, mine tailing
Phytodegradation	Enhances microbial degradation in rhizosphere	Soils, groundwater within rhizosphere
Rhizofiltration	Uptake of metals into plant roots	Surface water and water pumped
Phytovolatilization	Plants evaportranspirate selenium, mercury, and volatile hydrocarbons	Soils and groundwater
Vegetative cap	Rainwater is evaportranspirated by plants to prevent leaching contaminants from disposal sites	Soils

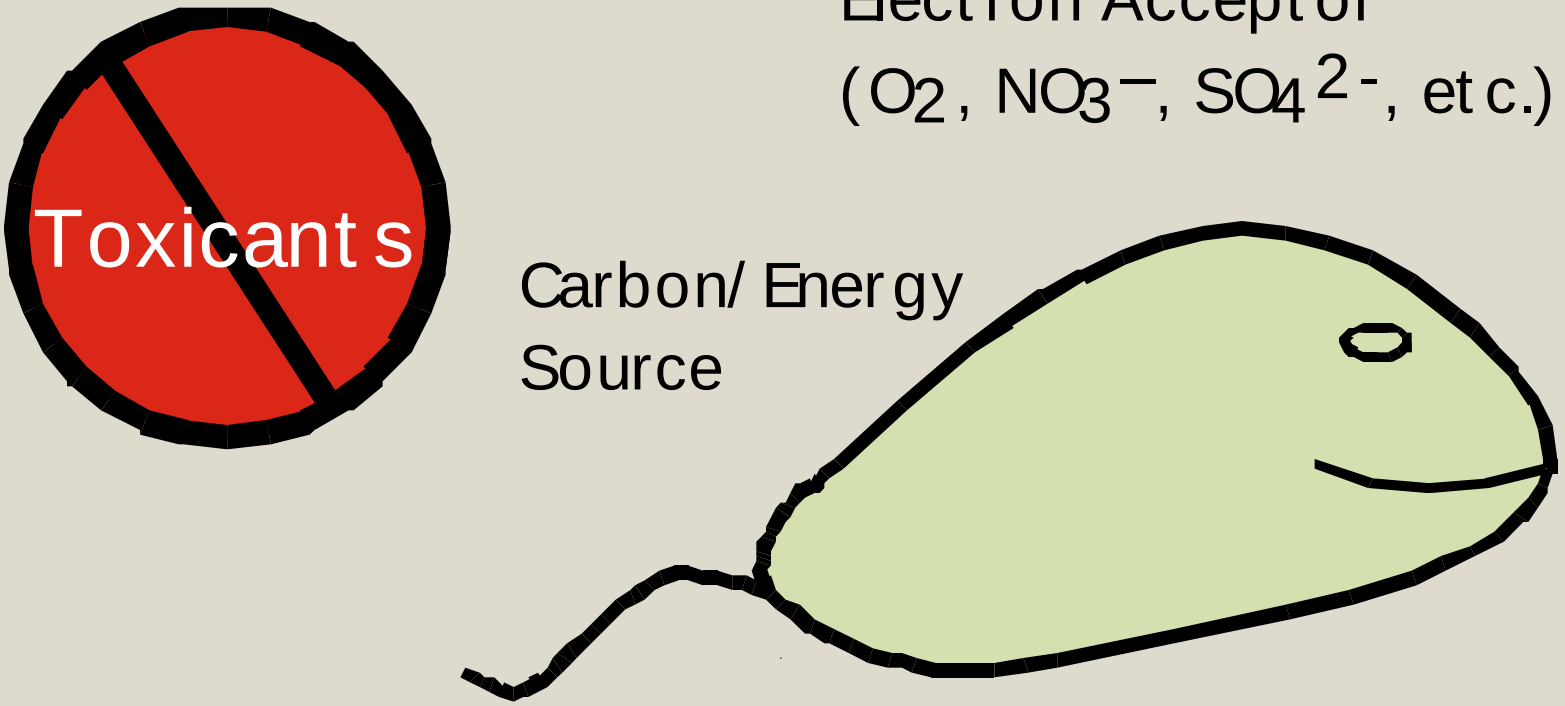
Mechanism of Bioremediation

- Conversion of contaminants to mineralized (e.g. CO_2, H_2O, and salts) end-products via biological mechanisms
- Biotransformation refers to a biological process where the end-products are not minerals.
- Biodegradation involves the process of extracting energy from organic chemicals via oxidation of the organic chemicals

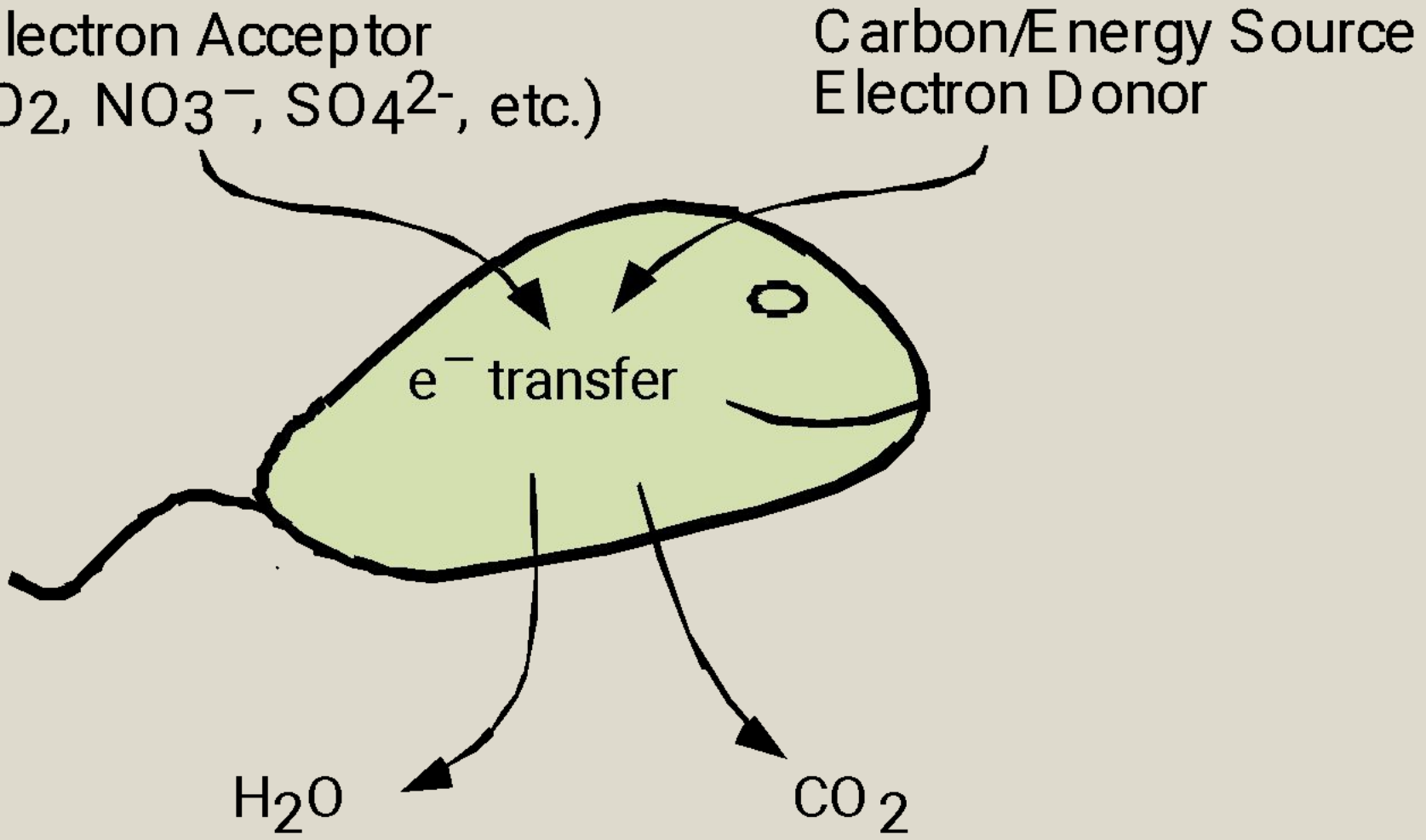
How Microbes Use the Contaminant

- Contaminants may serve as:
  - Primary substrate
    - enough available to be the sole energy source
  - Secondary substrate
    - provides energy, not available in high enough concentration
  - Cometabolic substrate
    - fortuitous transformation of a compound by a microbe relying on some other primary substrate

Requirements for Microbial Growth



Electron Exchange



Aerobic vs Anaerobic biodegradation

Aerobic biodegradation

- If oxygen is the terminal electron acceptor, the process is called aerobic biodegradation

Anaerobic biodegradation

- All other biological degradation processes are classified as anaerobic biodegradation

Environmental Factors

Environmental conditions affecting degradation.

Parameters	Condition required for microbial activity	Optimum value for an oil degradation
Soil moisture	25–28% of water holding capacity	30–90%
Soil pH	5.5–8.8	6.5–8.0
Oxygen content	Aerobic, minimum air-filled pore space of 10%	10–40%
Nutrient content	N and p for microbial growth	C:N:P = 100:10:1
Temperature (°C)	15–45	20–30
Contaminants	Not too toxic	Hydrocarbon 5–10% of dry weight of soil
Heavy metals	Total content 2000 ppm	700 ppm
Type of soil	Low clay or silt content	

Summary

Summary of bioremediation strategies.

Technology	Examples	Benefits	Limitations	Factors to consider
In situ	*In situ* bioremediation Biosparging Bioventing Bioaugmentation	Most cost efficient Noninvasive Relatively passive Natural attenuation processes Treats soil and water	Environmental constraints Extended treatment time Monitoring difficulties	Biodegradative abilities of indigenous microorganisms Presence of metals and other inorganics Environmental parameters Biodegradability of pollutants Chemical solubility Geological factors Distribution of pollutants
Ex situ	Landfarming Composting Biopiles	Cost efficient Low cost Can be done on site	Space requirements Extended treatment time Need to control abiotic loss Mass transfer problem Bioavailability limitation	See above

BIOSENSOR

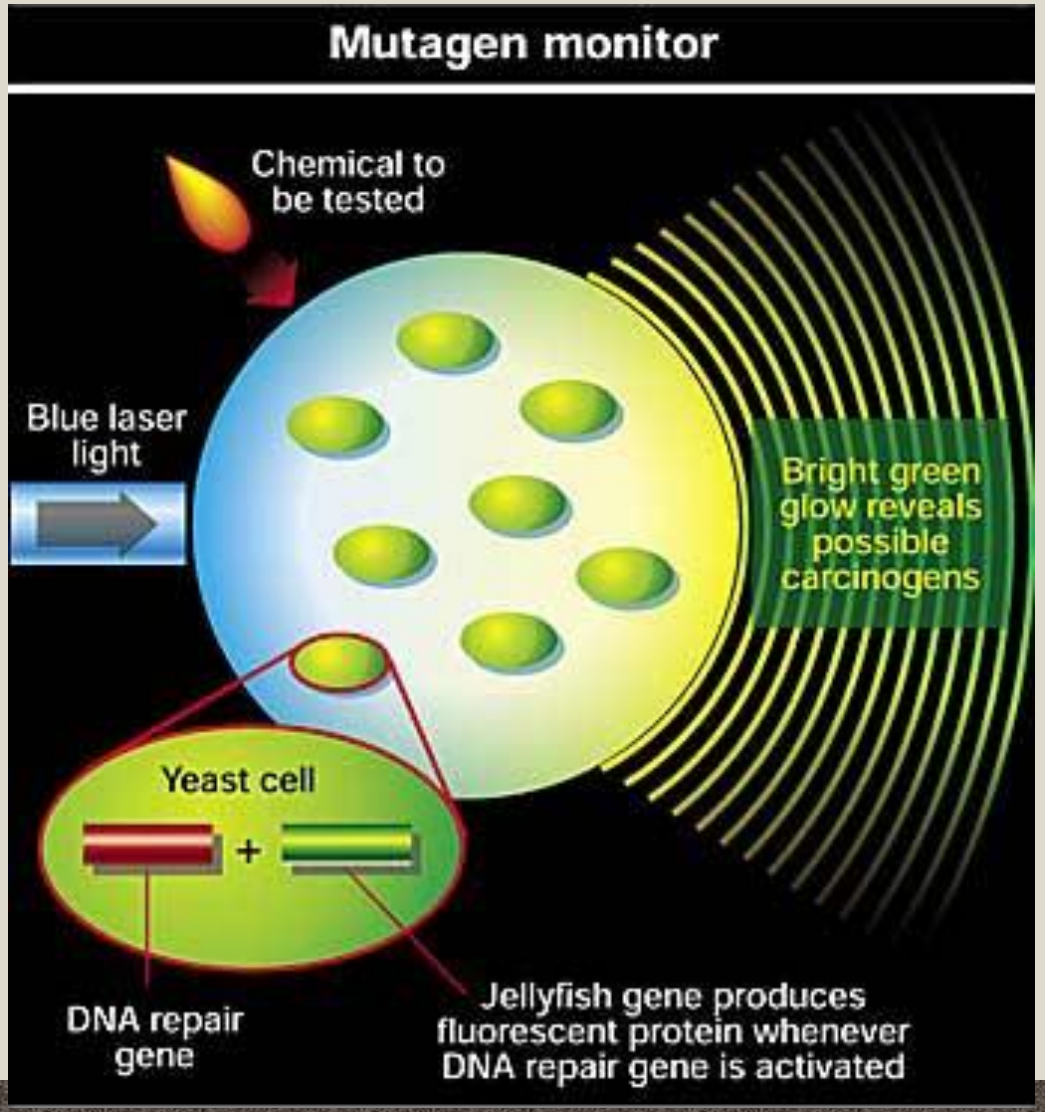
What is a Biosensor?

A biosensor is a self-contained integrated device that is capable of providing specific quantitative or semi-quantitative analytical information using a biological recognition element which is in direct spatial contact with a transduction element (IUPAC, 1996)

1) Biosensor ≠ Bioanalytical system

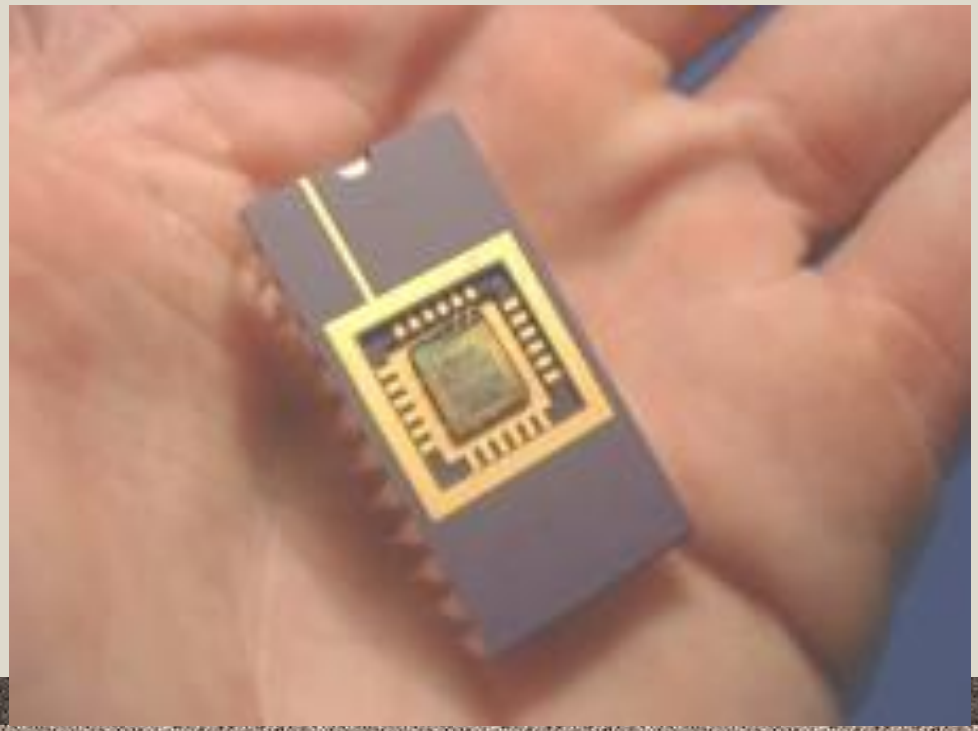
2) An enzyme electrode is a biosensor

"**Biosensor**" – **Any device** that uses specific biochemical reactions to detect chemical compounds **in biological samples**.

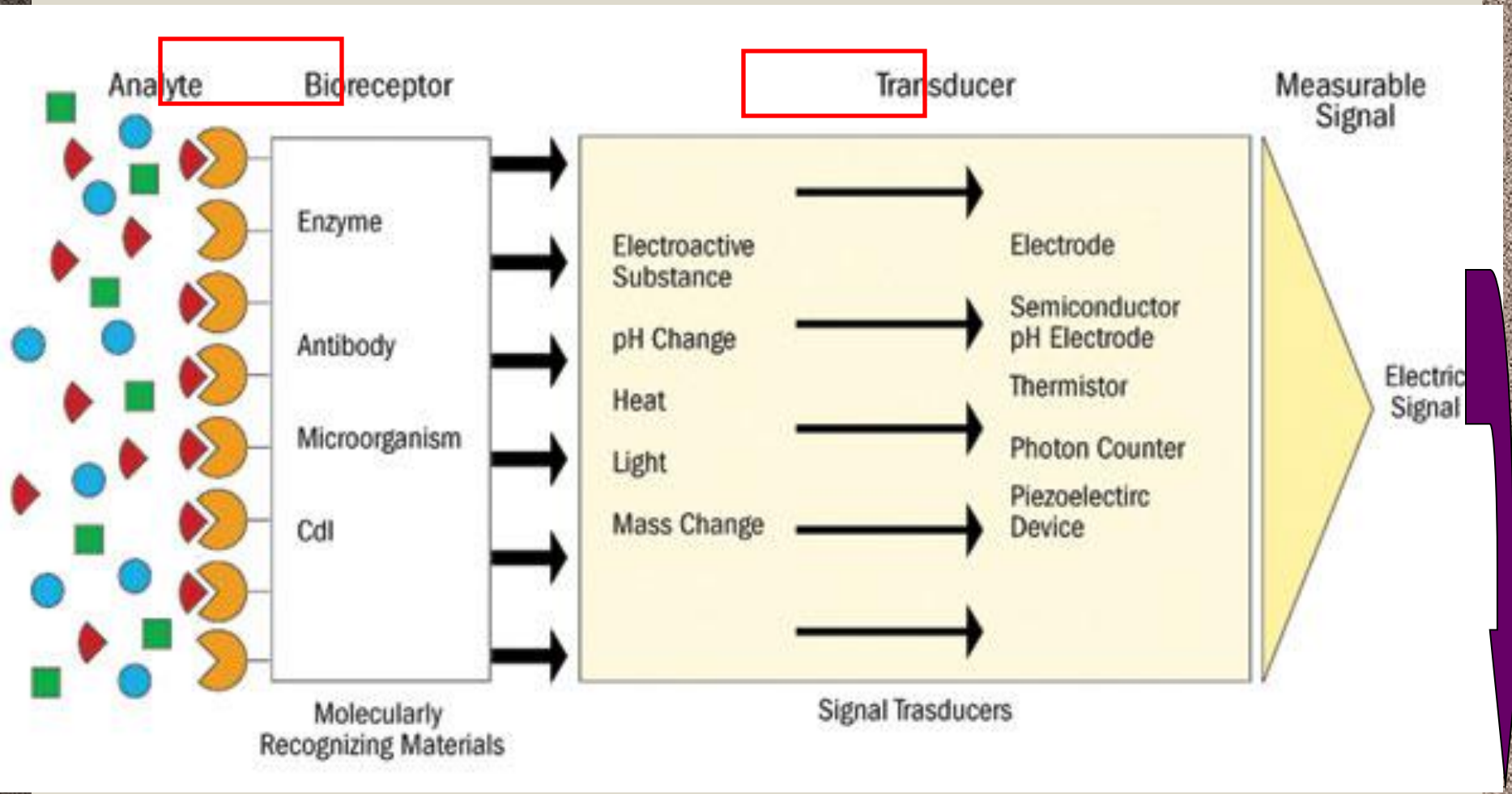


Current Definition

A sensor that integrates a biological element with a physiochemical transduc to produce an electronic signal proportional to a single analyte which is then conveyed to a detector.



Components of a Biosensor



History of Biosensors

- **1916 First report on immobilization of proteins : adsorption of invertase on activated charcoal**
- **1922 First glass pH electrode**
- **1956 Clark published his definitive paper on the oxygen electrode.**
- **1962 First description of a biosensor: an amperometric enzyme electrodre for glucose (Clark)**
- **1969 Guilbault and Montalvo – First potentiometric biosensor:urease immobilized on an ammonia electrode to detect urea**

History of Biosensors

- **1970** Bergveld – ion selective Field Effect Transistor (ISFET)
- **1975** Lubbers and Opitz described a fibre-optic sensor with immobilised indicator to measure carbon dioxide or oxygen.
- **1975** First commercial biosensor (Yellow springs Instruments glucose biosensor)
- **1975** First microbe based biosensor, First immunosensor
- **1976** First bedside artificial pancreas (Miles)
- **1980** First fibre optic pH sensor for in vivo blood gases (Peterson)
- **1982** First fibre optic-based biosensor for glucose
- **1983** First surface plasmon resonance (SPR) immunosensor
- **1984** First mediated amperometric biosensor: ferrocene used with glucose oxidase for glucose detection

History of Biosensors

- 1987 Blood-glucose biosensor launched by MediSense ExacTech
- 1990 SPR based biosensor by Pharmacia BIACore
- 1992 Hand held blood biosensor by i-STAT
- 1996 Launching of Glucocard
- 1998 Blood glucose biosensor launch by LifeScan FastTake
- 1998 Roche Diagnostics by Merger of Roche and Boehringer mannheim
- Current Quantom dots, nanoparicles, nanowire, nanotube, etc

Basic Characteristics of a Biosensor

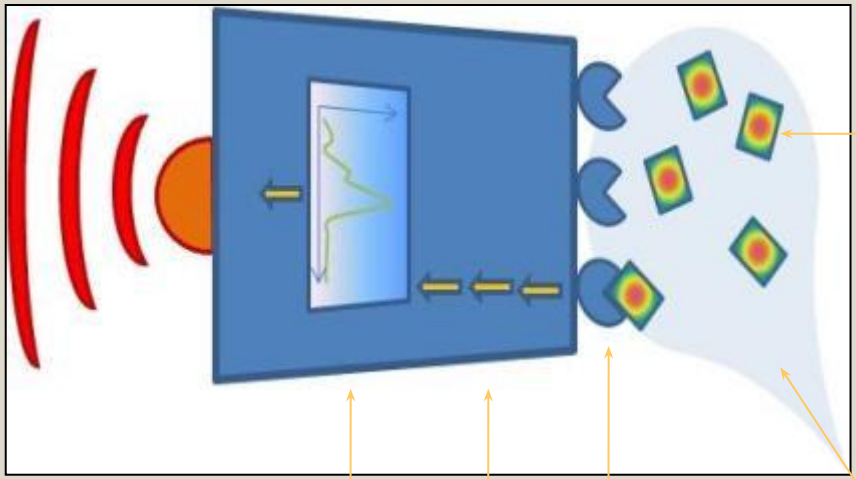
1. LINEARITY Linearity of the sensor should be high for the detection of high substrate concentration.

2. SENSITIVITY Value of the electrode response per substrate concentration.

3. SELECTIVITY Chemicals Interference must be minimised for obtaining the correct result.

4.RESPONSE TIME Time necessary for having 95% of the response.

Biosensor


Response
Analyte
Analysis
Signal
Detection
Sample handling/ preparation

Biosensor

1. The Analyte *(*What do you want to detect)

Molecule - Protein, toxin, peptide, vitamin, sugar, metal ion

2. Sample handling *(*How to deliver the analyte to the sensitive region?)

(Micro) fluidics - Concentration increase/decrease), Filtration/selection

Biosensor

- **3. Detection/Recognition**

  (How do you specifically recognize the analyte?)

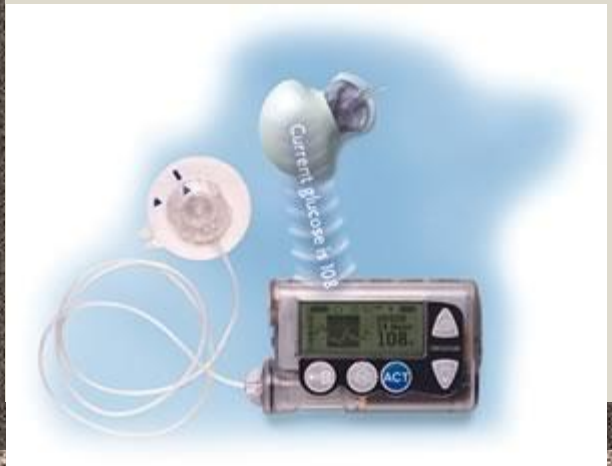
4. Signal

(How do you know there was a detection)

Example of biosensors

Pregnancy test

Detects the human choriogonadotrophin (hCG) protein in urine.



Glucose monitoring device (for diabetes patients)

Monitors the glucose level in the blood.

Example of biosensors

Infectous disease biosensor from RBS

Old time coal miners' biosensor

Research Biosensors

Biacore Biosensor platform

Typical Sensing Techniques for Biosensors

- ✔Fluorescence
- ✔DNA Microarray
- ✔SPR Surface plasmon resonance
- ✔Impedance spectroscopy
- ✔SPM (Scanning probe microscopy, AFM, STM)
- ✔QCM (Quartz crystal microbalance)
- ✔SERS (Surface Enhanced Raman Spectroscopy)
- ✔Electrochemical

Types of Biosensors

1. **Calorimetric Biosensor**
2. **Potentiometric Biosensor**
3. **Amperometric Biosensor**
4. **Optical Biosensor**
5. **Piezo-electric Biosensor**

Piezo-Electric Biosensors

Piezo-electric devices use gold to detect the specific angle at which electron waves are emitted when the substance is exposed to laser light or crystals, such as quartz, which vibrate under the influence of an electric field.

Measure changes in pressure, acceleration, temperature and strain by converting them to an electrical charge.

The change in frequency is proportional to the mass of absorbed material.

Electrochemical Biosensors

- Sense out changes in the electrical properties of a solution due to production/consumption of ions/electrons.
- Classified into :

1)Conductimetric

2)Amperometric

3)Potentiometric

Potentiometric Biosensor

- **Used to determine the analytical concentration of some components of the analyte gas/solution.**
- **Signal is measured as the potential difference (voltage) between the working electrode & reference electrode when there is no current flow.**
- **Working electrode's potential depends on the analyte in the gas /solution phase.**
- **The measured potential can be used to determine the analytical quantity of interest.**

Optical Biosensors

- **Colorimetric for color**
  Detects a color change associated with a specific chemical reaction between the sample and the sensing materials.
- **Photometric for light intensity**
  Photon output for a luminescent or fluorescent process can be detected with photomultiplier tubes or photodiode systems.

Calorimetric Biosensors

If the enzyme catalyzed reaction is exothermic, two thermistors may be used to measure the difference in resistance between reactant and product and, hence, the analyte concentration.

Electrochemical DNA Biosensor

- **Steps involved in electrochemical DNA hybridization biosensors:**
  - **Formation of the DNA recognition layer**
  - **Actual hybridization event**
  - **Transformation of the hybridization event into an electrical signal**
  - **Quercetin : electroactive indicator for hybridization detection**

DNA biosensor

Motivated by the application to clinical diagnosis and genome mutation detection

Types DNA Biosensors

- Electrodes
- Chips
- Crystals

Wearable Biosensors

Ring Sensor

Smart Shirt

Biosensors on the Nanoscale

- **Molecular sheaths around the nanotube are developed that respond to a particular chemical and modulate the nanotube's optical properties.**

- **A layer of olfactory proteins on a nanoelectrode react with low-concentration odorants (SPOT-NOSED Project). Doctors can use to diagnose diseases at earlier stages.**

- **Nanosphere lithography (NSL) derived triangular Ag nanoparticles are used to detect streptavidin down to one picomolar concentrations.**

- **The School of Biomedical Engineering has developed an anti- body based piezoelectric nanobiosensor to be used for anthrax HIV hepatitis detection**

Potential Applications

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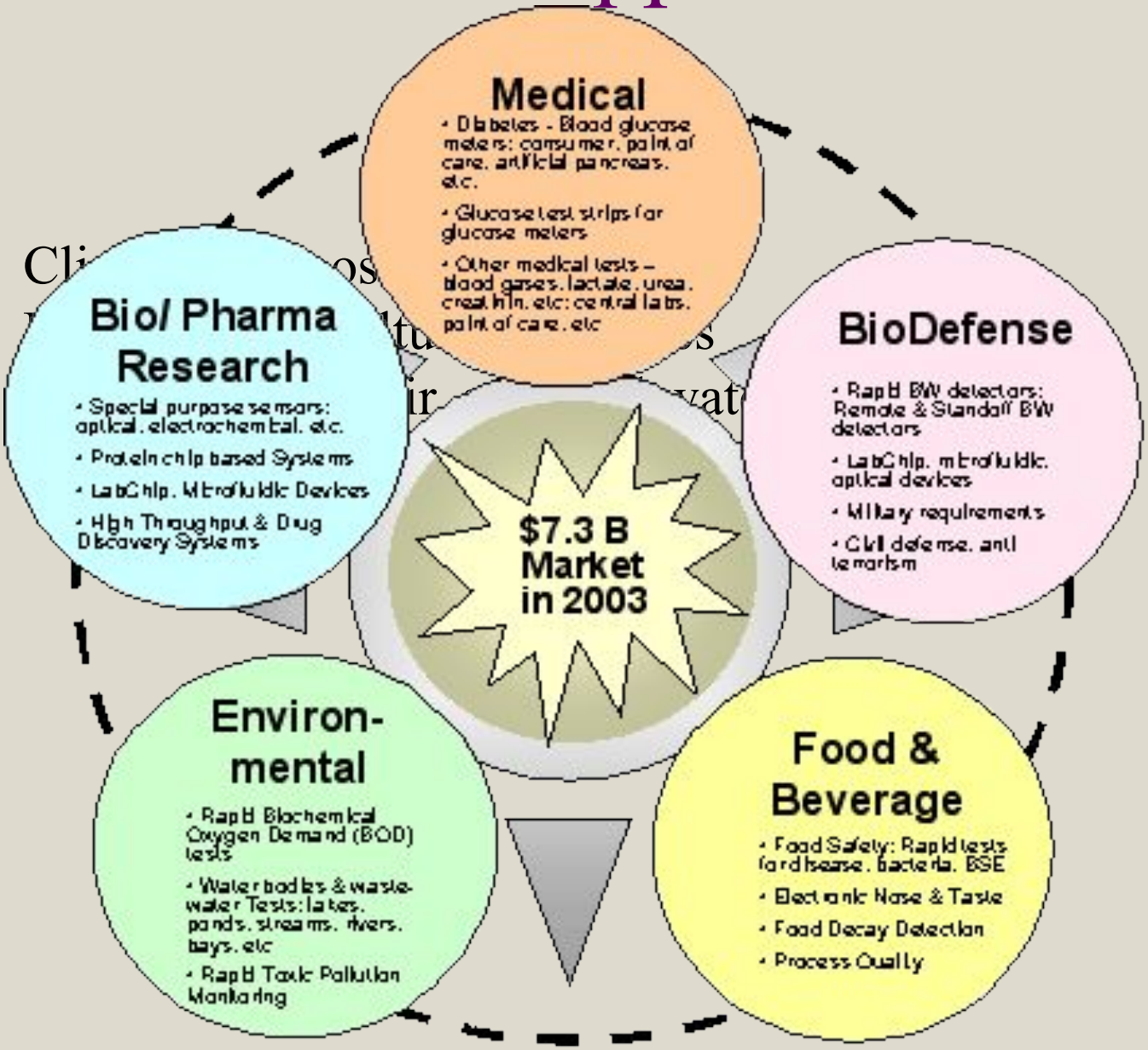

Source: Takeda Partners

Application of Biosensor

- Food Analysis
- Study of biomolecules and their interaction
- Drug Development
- Crime detection
- Medical diagnosis (both clinical and laboratory use)
- Environmental field monitoring
- Quality control
- Industrial Process Control
- Detection systems for biological warfare agents
- Manufacturing of pharmaceuticals and replacement organs

- **Biosensors play a part in the field of environmental quality, medicine and industry mainly by identifying material and the degree of concentration present**