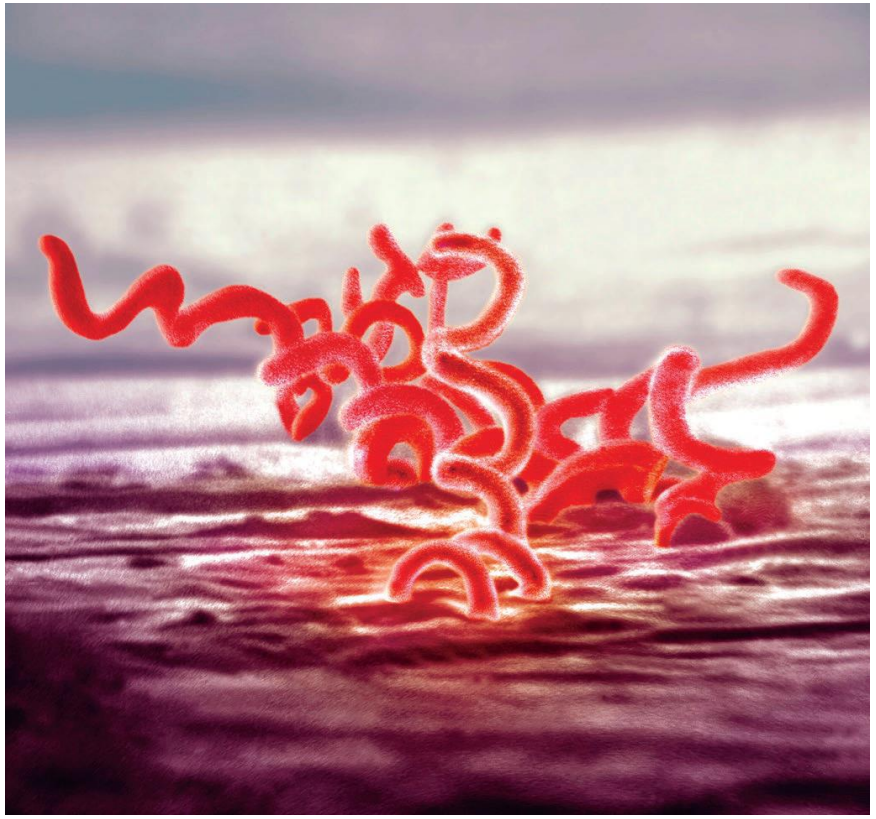


RAJA NARENDRALAL KHAN WOMEN'S COLLEGE (AUTONOMOUS)

MICROBIAL BIOCHEMISTRY

HUMAN PHYSIOLOGY (PG)

4TH SEM

PHY-403, UNIT-37, MODULE II

- Suparna Majumder

Viruses may be small and simple, but they dwarf two other classes of pathogens: viroids and prions.

- **Viroids** are small circular RNA molecules that infect plants. **Viroids** do not encode proteins but can nonetheless replicate in host plant cells, apparently using cellular enzymes.

- These small RNA molecules seem to cause disease by interfering
- with the regulatory systems that control plant growth.

- About a dozen crop diseases have been attributed not to
- viruses but to **viroids,** which are strands of RNA that are naked (not covered by a capsid).

- Like viruses, though, viroids direct the host cell to produce more viroids. Viroids are a concern in agriculture, since they can not only cause the host plant to be unhealthy but also alter the plant's physical characteristics, thus reducing its economic value.

Fig: Viroids infect plants. For example, PSTVd causes potatoes to be become elongated and fibrous compared to normal potatoes.

The extracellular form of a viroid is naked RNA; there is no protein capsid of any kind. Although the viroid RNA is a single-stranded, covalently closed circle, its extensive secondary structure makes it resemble a hairpin-shaped double-stranded molecule with closed ends (Figure). This apparently makes the viroid sufficiently stable to exist outside the host cell. Because it lacks a capsid, a viroid does not use a receptor to enter the host cell. Instead, the viroid enters a plant cell through a wound, as from insect or other mechanical damage. Once inside, viroids move from cell to cell via plasmodesmata, which are the thin strands of cytoplasm that link plant cells.

PRIONS:

- Some diseases in humans have been attributed to **prions,** a name coined from the term *proteinaceous infectious* particles.
- The discovery of prions began with the observation that members of a primitive tribe, the Fore, in the highlands of Papua New Guinea died from a disease called kuru (meaning trembling with fear) after participating in the cannibalistic practice of eating a deceased person's brain (**Fig**).
- The causative agent of kuru was smaller than a virus—it was a misshapen protein. It appears that a normal protein changes shape, so that its polypeptide chain is in a different configuration. The result is a prion, capable of causing a fatal infection and a neurodegenerative disorder.
- Prions cause a number of brain diseases in various animal species, including scrapie in sheep and goats, chronic wasting disease in deer and elk, and mad cow disease (formally called bovine spongiform encephalopathy or BSE), which infected over 2 million cattle in the United Kingdom in the 1980s.
- In humans, prions cause an extremely rare disease called Creutzfeldt-Jakob disease. A prion is thought to be a misfolded form of a protein normally present in brain cells. When the prion enters a cell containing the normal form of protein, the prion somehow converts the normal protein molecules to the misfolded prion version.
- To date, there is no known cure for prion diseases, so the only hope for avoiding future illnesses lies in understanding and preventing the process of infection

Fig: Cannibalistic tribesmen in Papua, New Guinea.

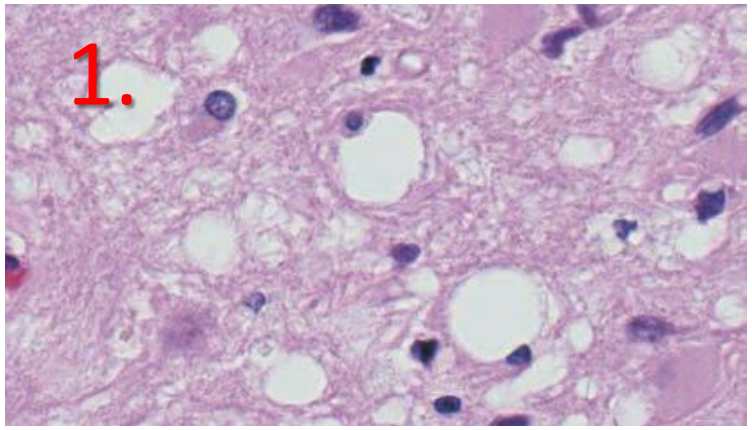
Prion Proteins and the Prion Infectious Cycle

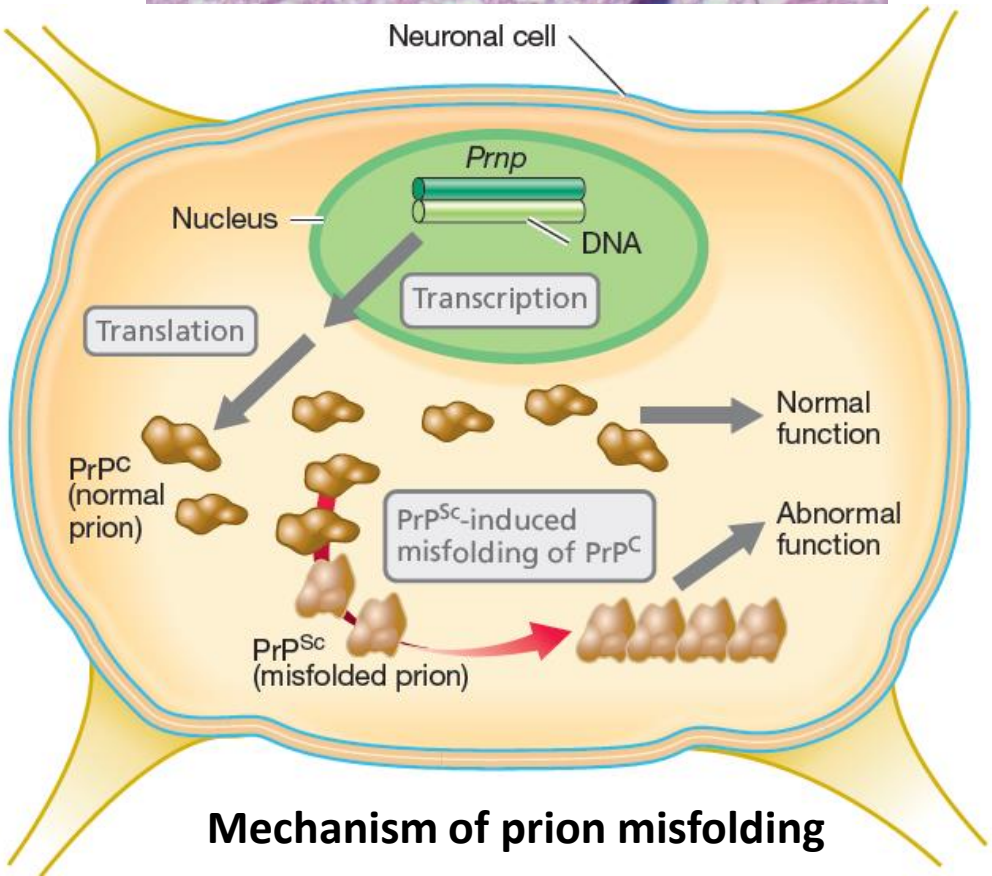
If prions lack nucleic acid, how is prion protein encoded?

- The answer to this conundrum is that the host cell itself encodes the prion. The host contains a gene, *Prnp* ("*Prion protein*"), which encodes the native form of the prion, known as PrP^C (*Pr*ion *P*rotein *C*ellular). This is primarily found in the neurons of healthy animals, especially in the brain. [Fig 1]

- The pathogenic form of the prion protein is designated PrP^{Sc} (prion protein *Sc*rapie), because the first prion disease to be discovered was that of scrapie in sheep.

- When the PrP^{Sc} form enters a host cell that is expressing PrP^C, it promotes the conversion of PrP^C into the pathogenic form. That is, the pathogenic prion "replicates" by converting preexisting native prions into the pathogenic form. As the pathogenic prions accumulate, they form insoluble aggregates in the neural cells. This leads to disease symptoms including the destruction of brain and other nervous tissue.





Mechanism of prion misfolding

All microorganisms must conserve some of the energy released in their energy-yielding reaction(s) in order to grow

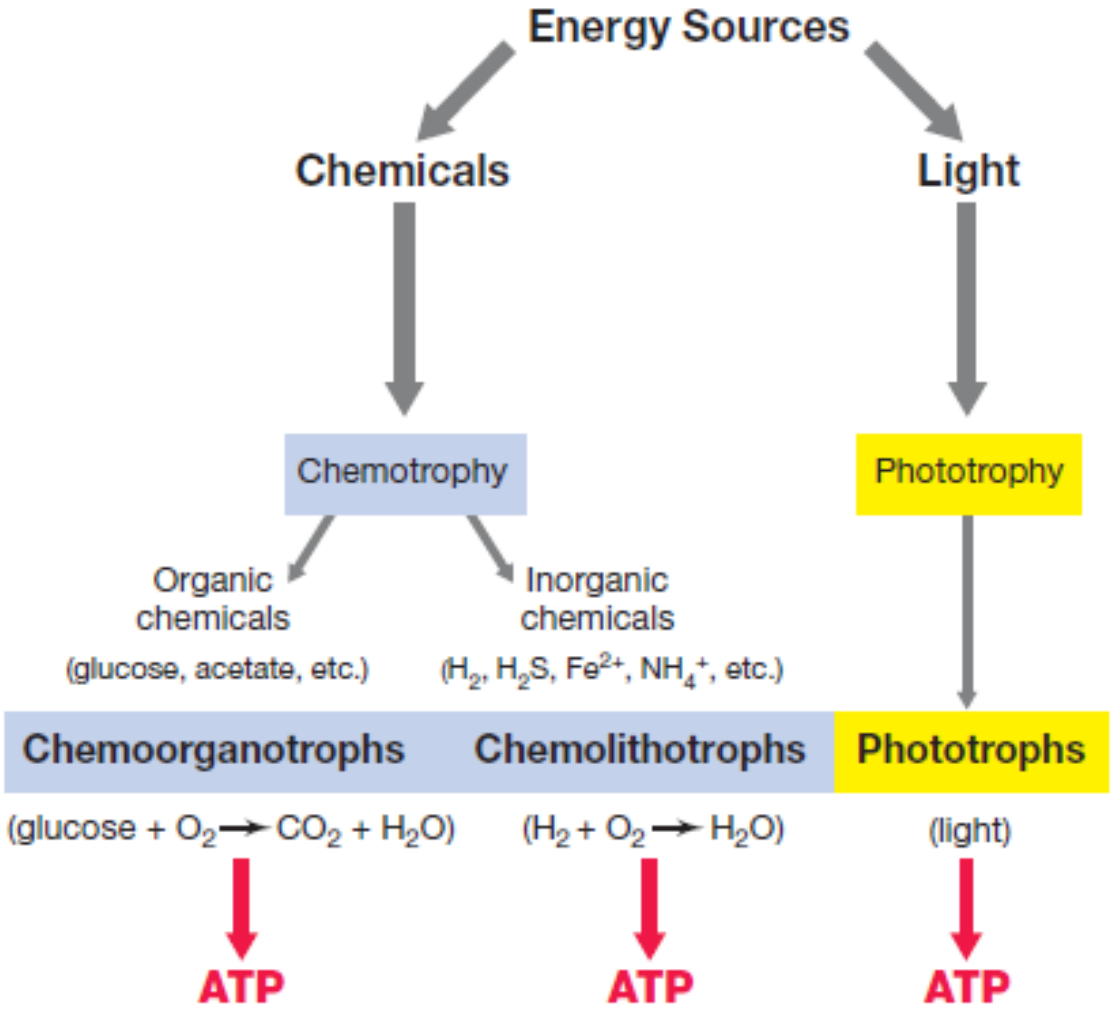
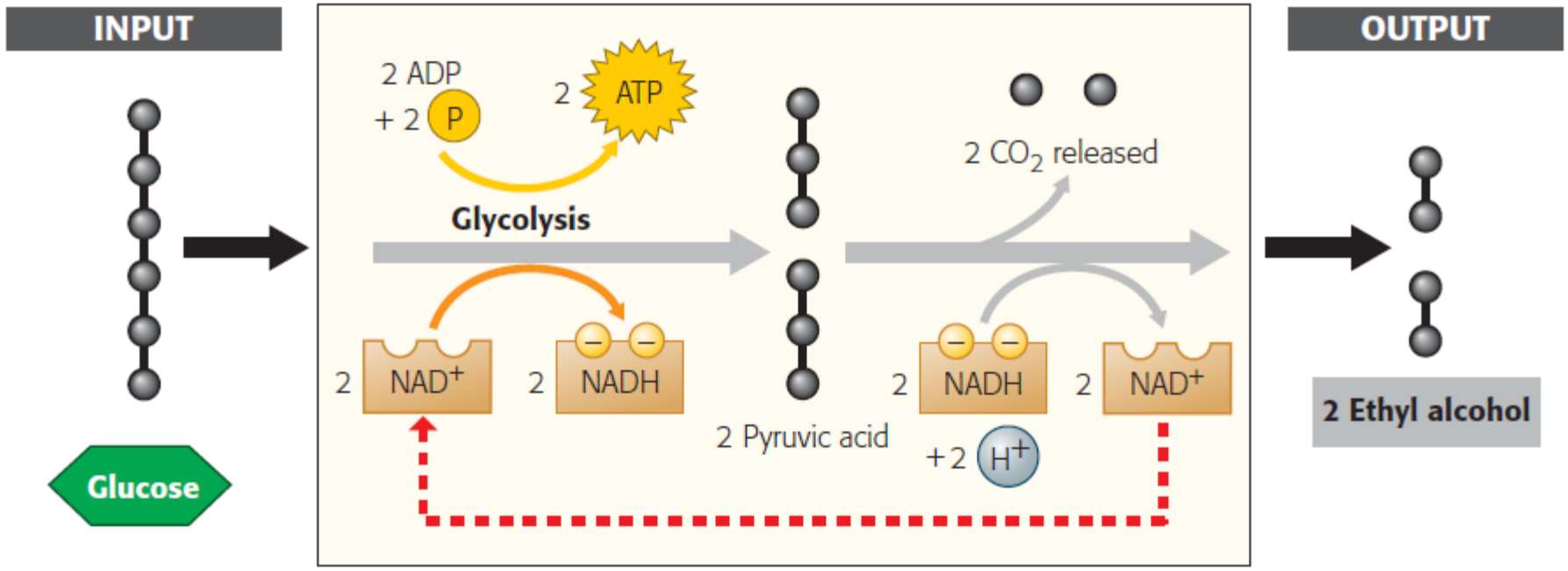


Fig: Metabolic processes for conserving energy within microbial world.

MICROBIAL FERMENTATION:

- Our muscles cannot function by lactic acid fermentation for very long. However, the two ATP molecules produced per glucose molecule during fermentation is enough to sustain many microorganisms.
- We have domesticated such microbes to transform milk into cheese, sour cream, and yogurt. These foods owe their sharp or sour flavor mainly to lactic acid. The food industry also uses fermentation to produce soy sauce from soybeans, to pickle cucumbers, olives, and cabbage, and to produce meat products like sausage, pepperoni, and salami.
- Yeast, a microscopic fungus, is capable of both cellular respiration and fermentation. If you keep yeast cells in an anaerobic environment, they are forced to ferment sugars and other foods to stay alive. When yeast ferment, they produce ethyl alcohol as a waste product instead of lactic acid **(Figure)**. This alcoholic fermentation also releases CO_2 .
- For thousands of years, people have put yeast to work producing alcoholic beverages such as beer and wine. And as every baker knows, the CO_2 bubbles from fermenting yeast also cause bread dough to rise.
- (The alcohol produced in fermenting bread is burned off during baking.)



Anaerobic Respiration:

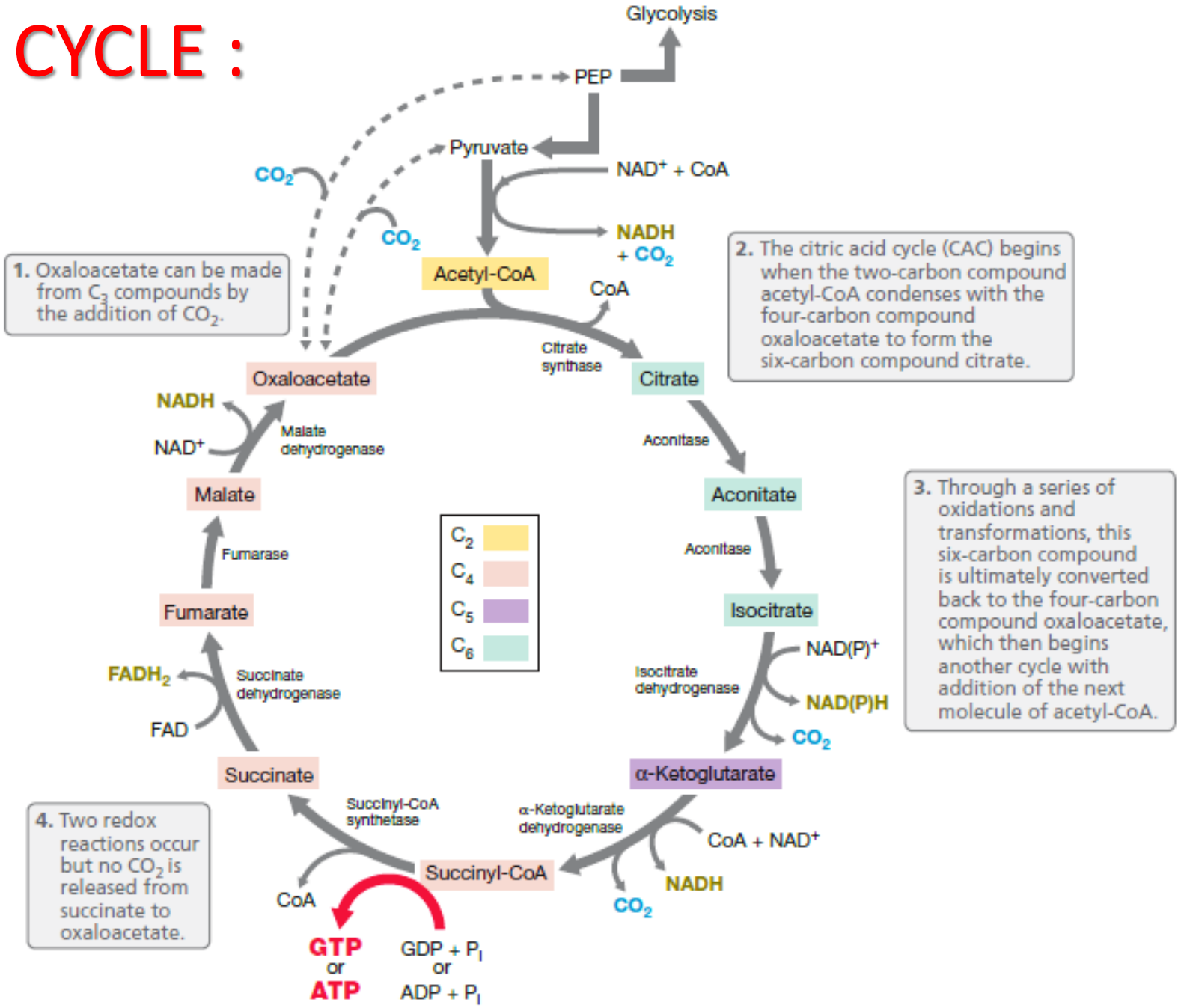
Anaerobic respiration, a process whereby an exogenous terminal electron acceptor other than O_2 is used for electron transport, is carried out by many bacteria and archaea. The most common terminal electron acceptors used during anaerobic respiration are nitrate, sulfate, and CO_2, but metals and a few organic molecules can also be reduced.

Although some bacteria and archaea grow using only anaerobic respiration, many can perform both aerobic and anaerobic respiration, depending on the availability of oxygen. One example is *Paracoccus denitrificans,* a gram-negative, facultative anaerobic soil bacterium that is extremely versatile metabolically. It can degrade a wide variety of organic compounds and can even grow chemolithotrophically. Under anoxic conditions, *P. denitrificans* uses NO_3 as its electron acceptor.

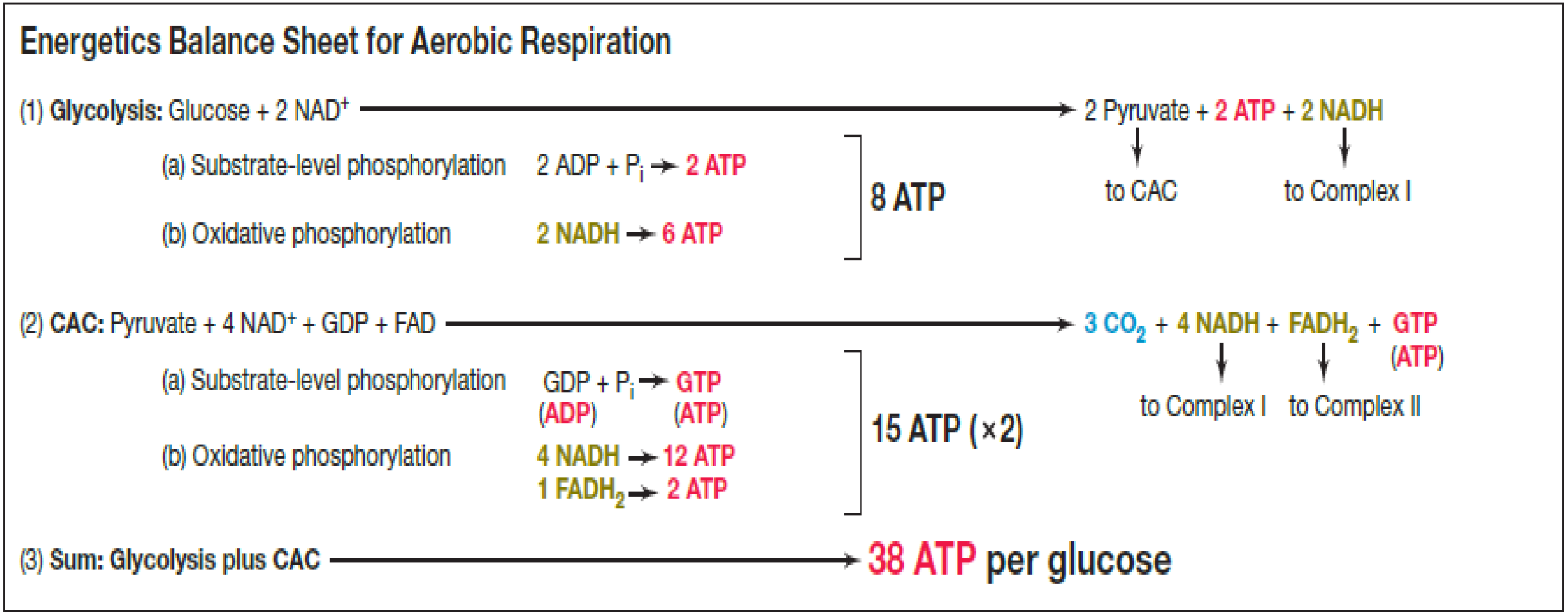
Table Some Electron Acceptors Used in Respiration

	Electron Acceptor	Reduced Products	Examples of Microorganisms
Aerobic	O_2	H_2O	All aerobic bacteria, fungi, and protists
Anaerobic	NO_3^-	NO_2^-	Enteric bacteria
	NO_3^-	NO_2^-, N_2O, N_2	*Pseudomonas*, *Bacillus*, and *Paracoccus*
	SO_4^{2-}	H_2S	*Desulfovibrio* and *Desulfotomaculum*
	CO_2	CH_4	All methanogens and acetogens
	S^0	H_2S	*Desulfuromonas* and *Thermoproteus*
	Fe^{3+}	Fe^{2+}	*Pseudomonas*, *Bacillus*, and *Geobacter*
	$HAsO_4^{2-}$	$HAsO_2$	*Bacillus*, *Desulfotomaculum*, *Sulfurospirillum*
	SeO_4^{2-}	Se, $HSeO_3^-$	*Aeromonas*, *Bacillus*, *Thauera*
	Fumarate	Succinate	*Wolinella*

Citric Acid CYCLE :



Energy Yield from Citric Acid CYCLE :



Glyoxylate pathway:

- Citrate, malate, fumarate, and succinate are common natural products, and organisms that use these C_4 or C_6 compounds as energy sources use the citric acid cycle for their catabolism.
- By contrast, two-carbon compounds such as acetate cannot be used as growth substrates by the citric acid cycle alone. This is because the citric acid cycle can continue to operate only if oxaloacetate is regenerated at each turn of the cycle; any siphoning off of oxaloacetate (or any other citric acid cycle intermediates) for biosynthesis would starve the cycle of what it needs to continue functioning.
- Thus, when acetate is used as an electron donor, a variation on the citric acid cycle called the **glyoxylate cycle** (Figure) is employed, so named because the C_2 compound glyoxylate is a key intermediate.

Sum: Isocitrate + Acetate ⟶ Succinate + Malate

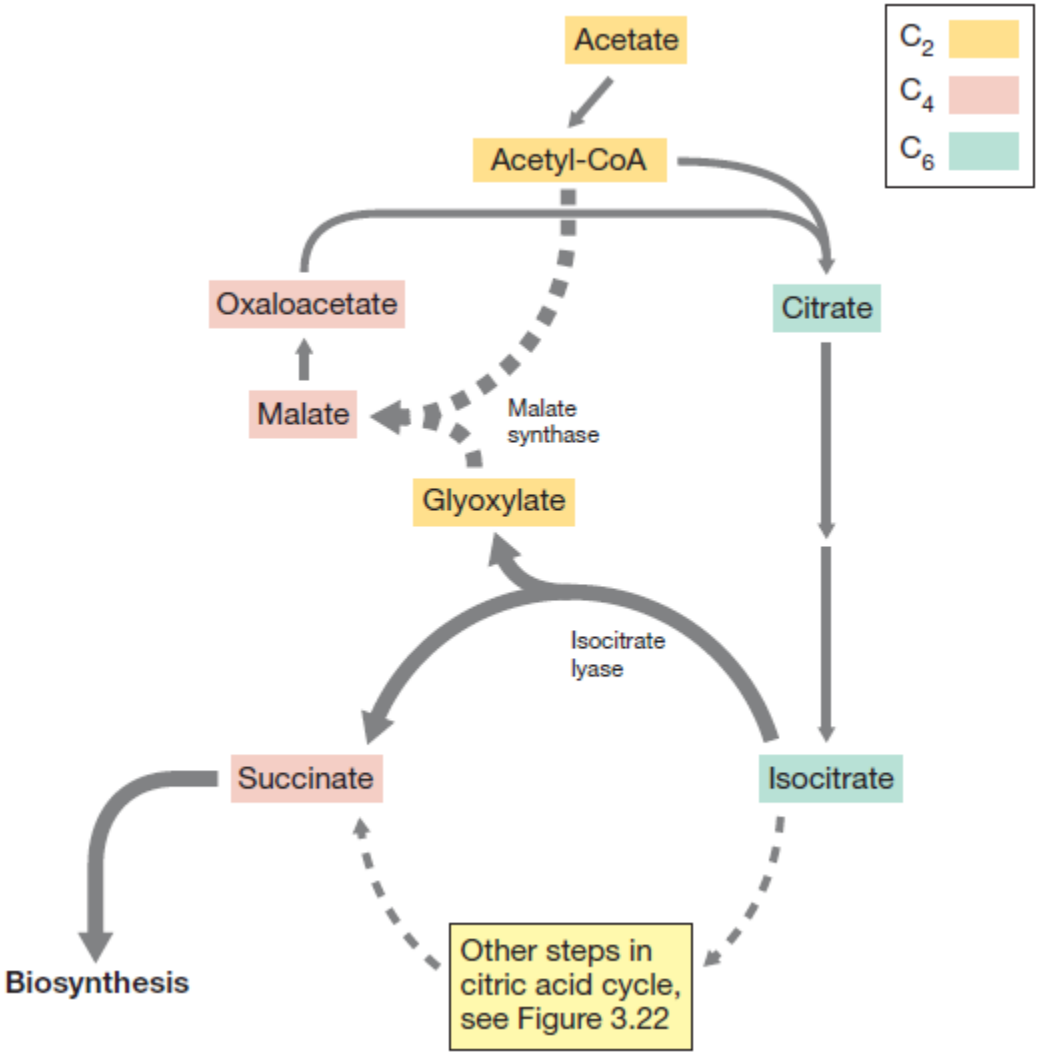


Fig: The Glyoxylate pathway