

LO3a

Recap L02

Core Concept

01: Evolution, Thermodynamics, Habitat diversity, Ecology, Physiology their integration define Microbiology

02: Unique goal of microbial life: survival, maintenance, generation of ATP, growth of new cells

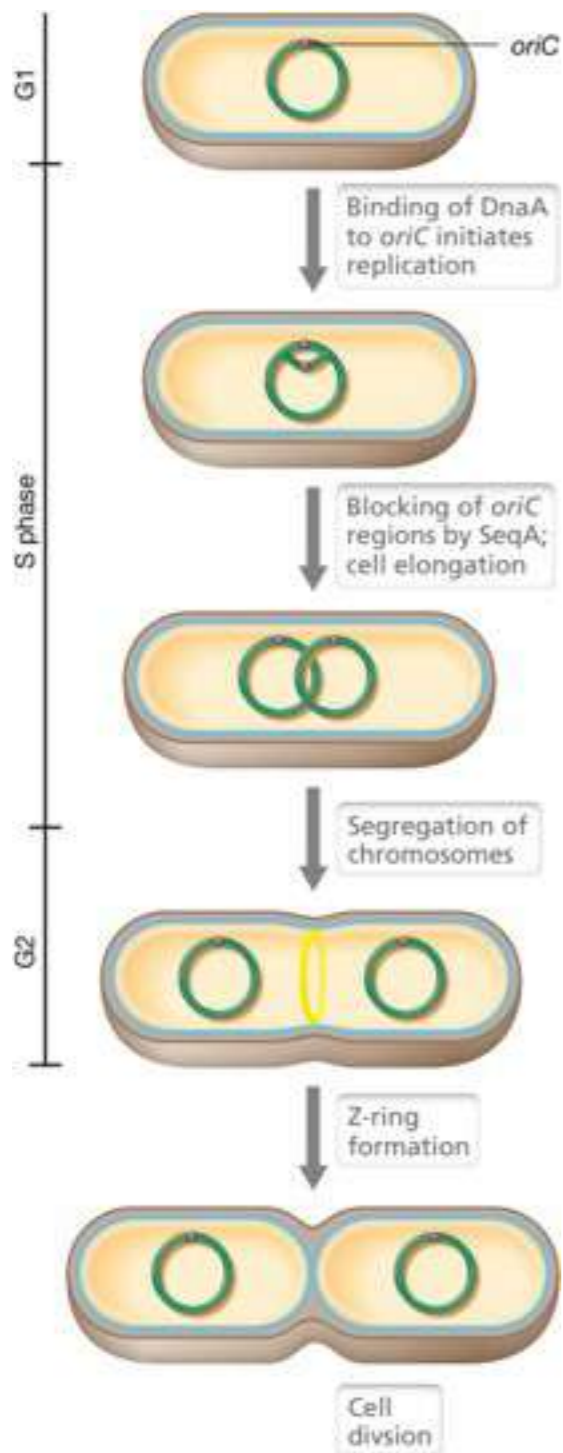
03: Planet's habitat diversity results in genetic, molecular, metabolic and physiological microbial diversity

Key concepts for Microbial Life

- **Metabolic diversity:** cellular processes that support growth
 - ★ **Energy is conserved, reducing power is obtain during catabolic reactions and cells growth by decoupling this power to anabolic-biosynthetic reactions (modularity)**
 - ★ **Electron flow via redox provide energy for ATP synthesis via:**
 1. **Substrate level phosphorylation**
 2. **Oxidative phosphorylation**
 3. **Photophosphorilation**
- **Ecological diversity:** interactions between organisms and their environments
- **Phylogenetic diversity:** evolutionary relationships between organisms

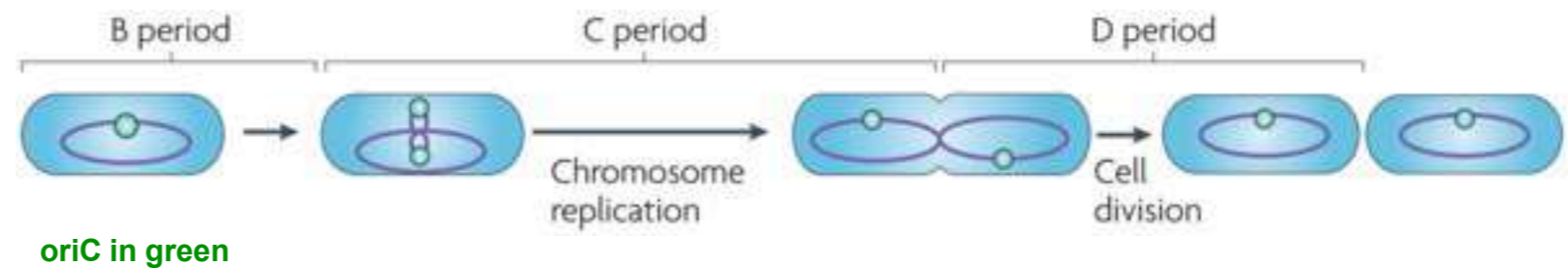
How can microbes grow?
How did microbes invented
biochemistry?

Cellular growth



Growth is intimately connected with nutrient availability and energy status of the cell

Spatial and temporal coordination between the DNA replication and cell elongation, DNA segregation into new cells

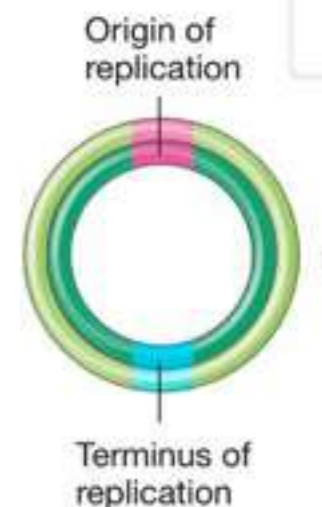


B period: time between division (birth) and the initiation of chromosome replication

C period: time window for chromosome replication

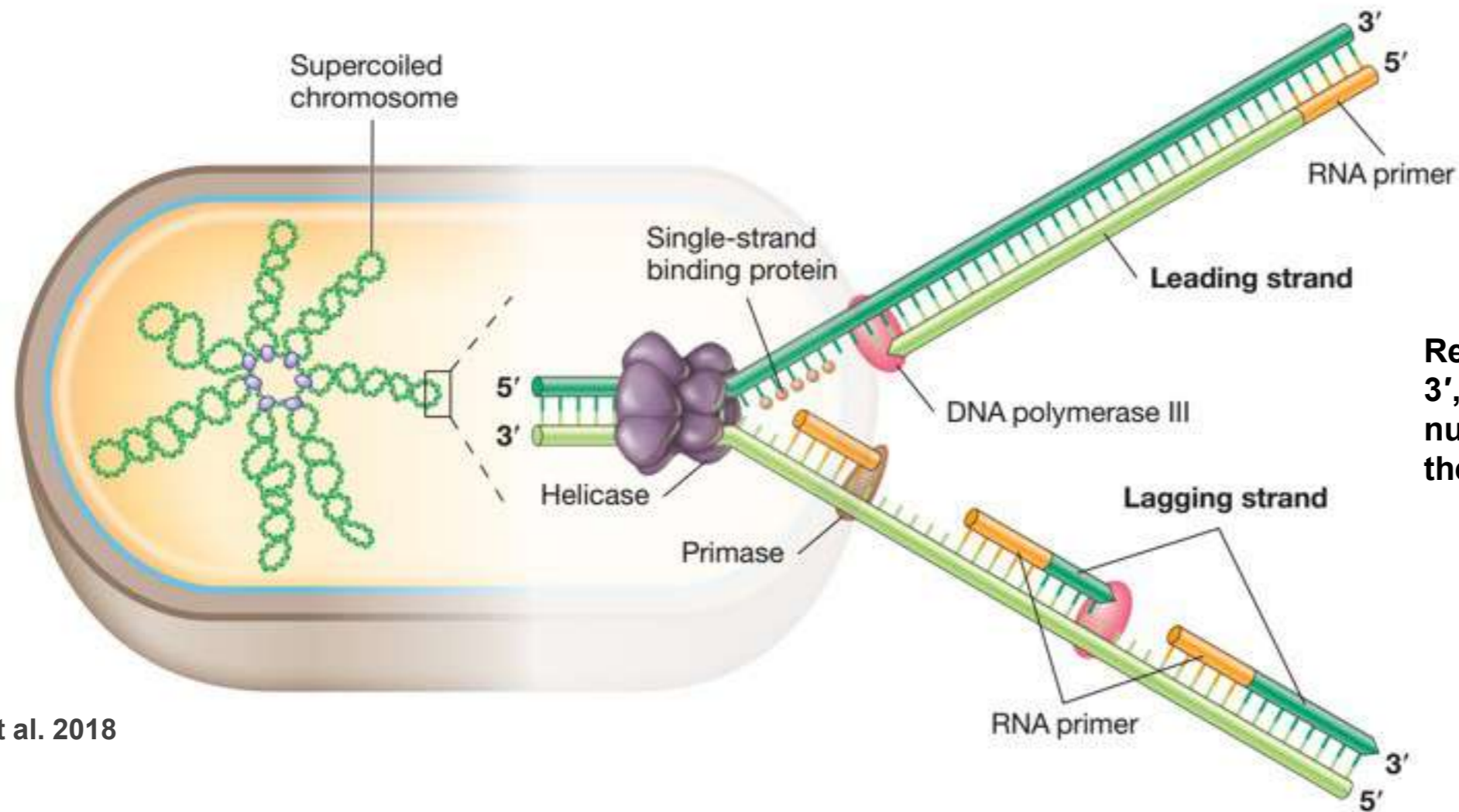
D period: time between the completion of chromosome replication and cell division

Protein Tus binds to terminus site and stop replication



Wang & Levin, 2009

Zooming into DNA replication

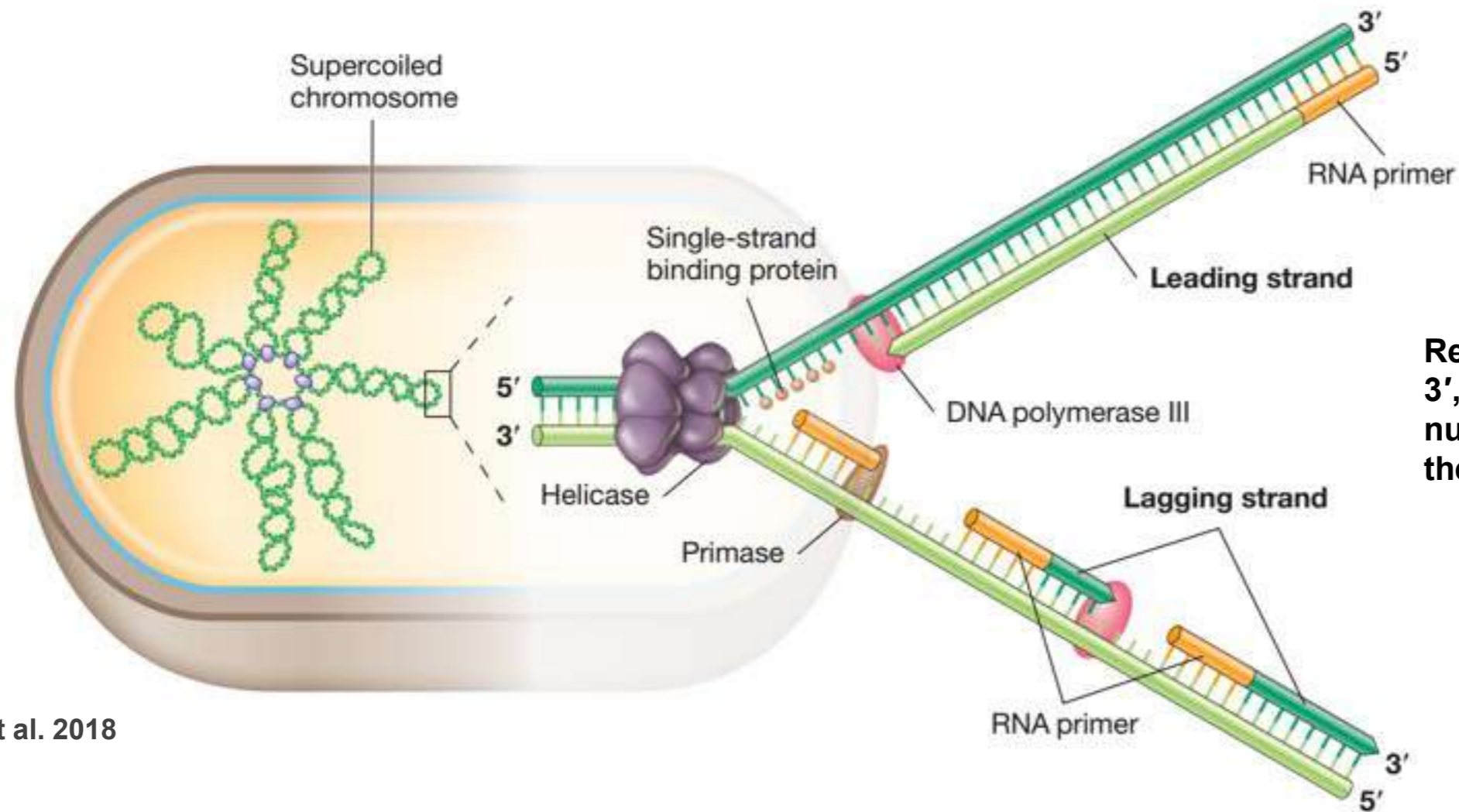


Replication always 5' to 3', adding a new nucleotide to the 3'-OH of the growing chain

Madigan et al. 2018

1. DNA synthesis begins at a single site on chromosome, origin of replication (**oriC**), where DnaA binds and opens up double helix
2. Stabilization of strands by **helicase** (DnaB), and its **helper loader protein** (DnaC). Two helicases are loaded, one onto each strand, facing in opposite directions

Zooming into DNA replication

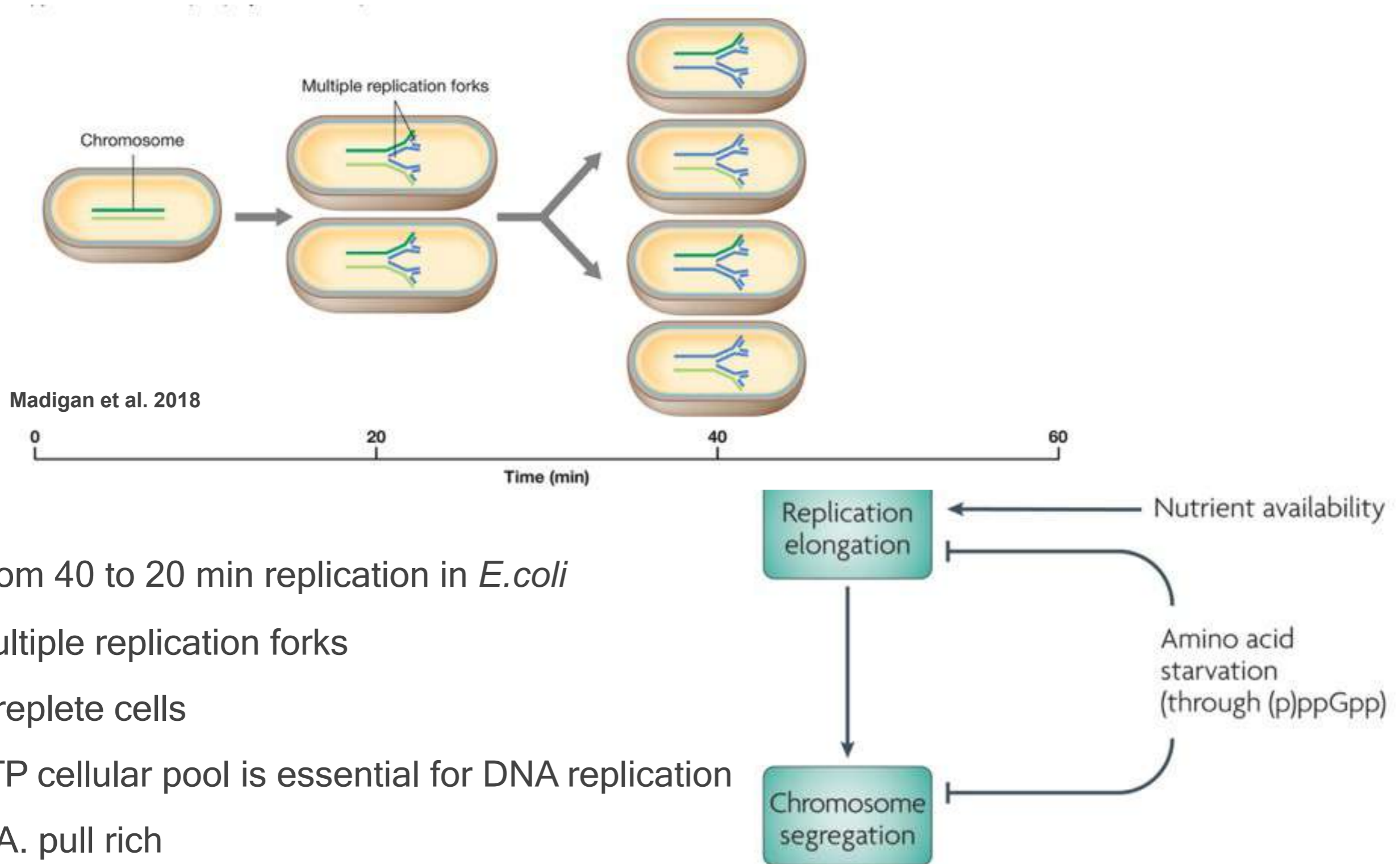


Replication always 5' to 3', adding a new nucleotide to the 3'-OH of the growing chain

Madigan et al. 2018

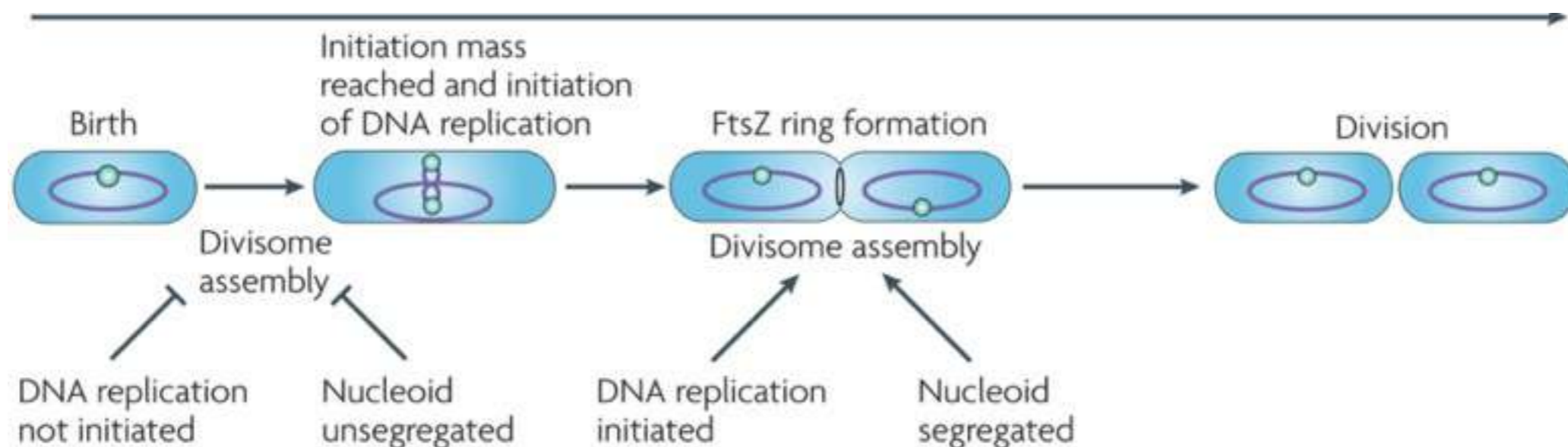
3. Two **primase** and two **DNA polymerase III** enzymes are loaded onto the DNA behind helicases and initiation of DNA replication begins
4. As replication proceeds, replication fork appears to move along the DNA

Nutrient & energy status controls growth rate



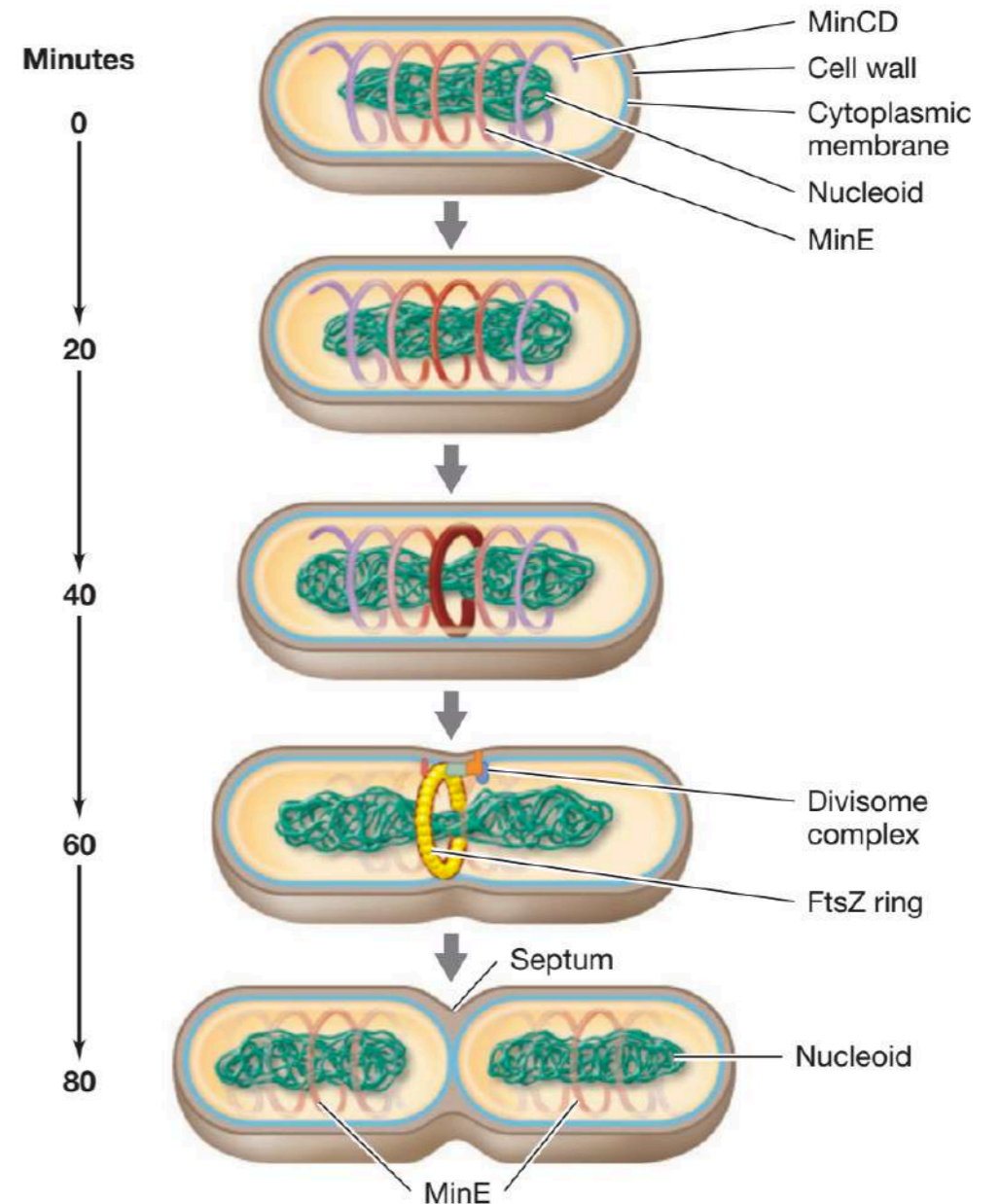
Chromosome segregation and Divisome complex

- *E.coli* daughter chromosomes must still be segregated prior to cell division
- After replication the resulting **circular chromosomes remain interlinked**
- Linkage is broken by the structural maintenance of chromosome complex, which is composed of a **topoisomerase (IV) and MukBEF protein**
- MukBEF proteins move to discrete locations within the nucleoid and recruit a topoisomerase to separate replicated sister chromosomes (a process called **decatenation**) **prior to segregation**
- **Divisome complex: Fts proteins interact in cell to form a division apparatus**
- Precise and temporally coordinate cleavages for growth



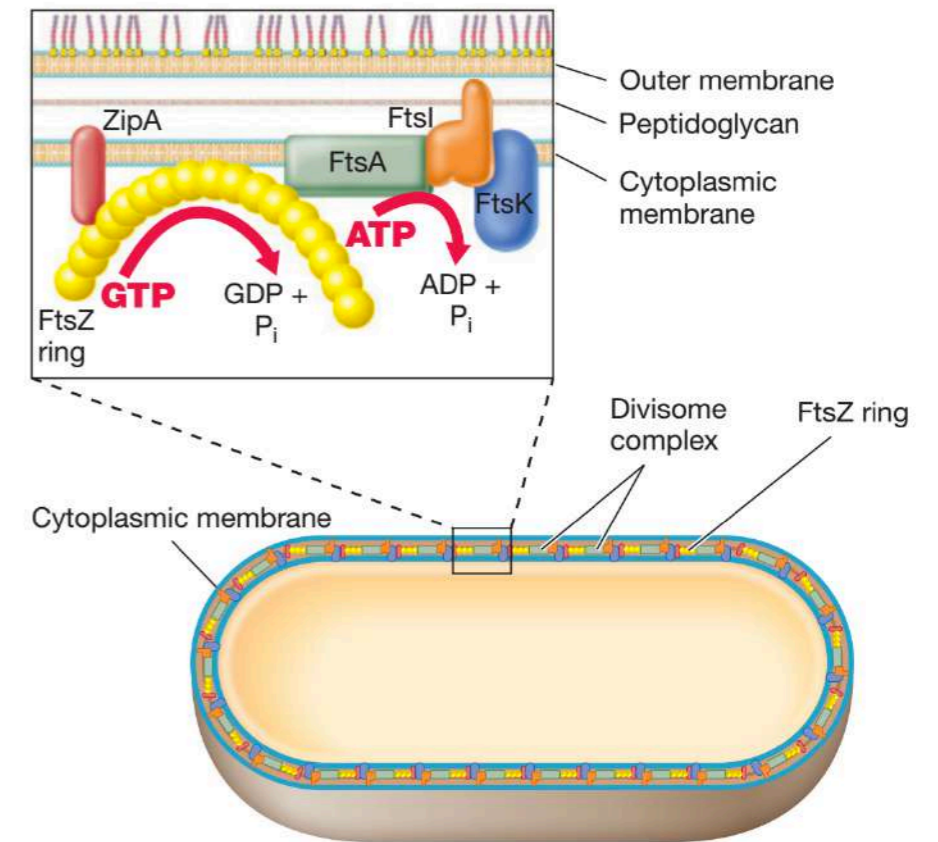
Divisome machinery, I

- Divisome begins with the attachment of molecules of FtsZ in a ring precisely around the cell center — > cell-division plane
- In *E. coli*, about 10,000 FtsZ molecules polymerize to form the ring
- FtsZ ring attracts other divisome proteins, including FtsA and ZipA
- ZipA is an anchor that connects the FtsZ ring to the cytoplasmic membrane and stabilizes it
- Recruitment other divisome proteins for connecting ring to cytoplasmic membrane
- **The divisome forms about 3/4 of the way into the cell-division cycle**
- The divisome also contains Fts proteins needed for peptidoglycan synthesis



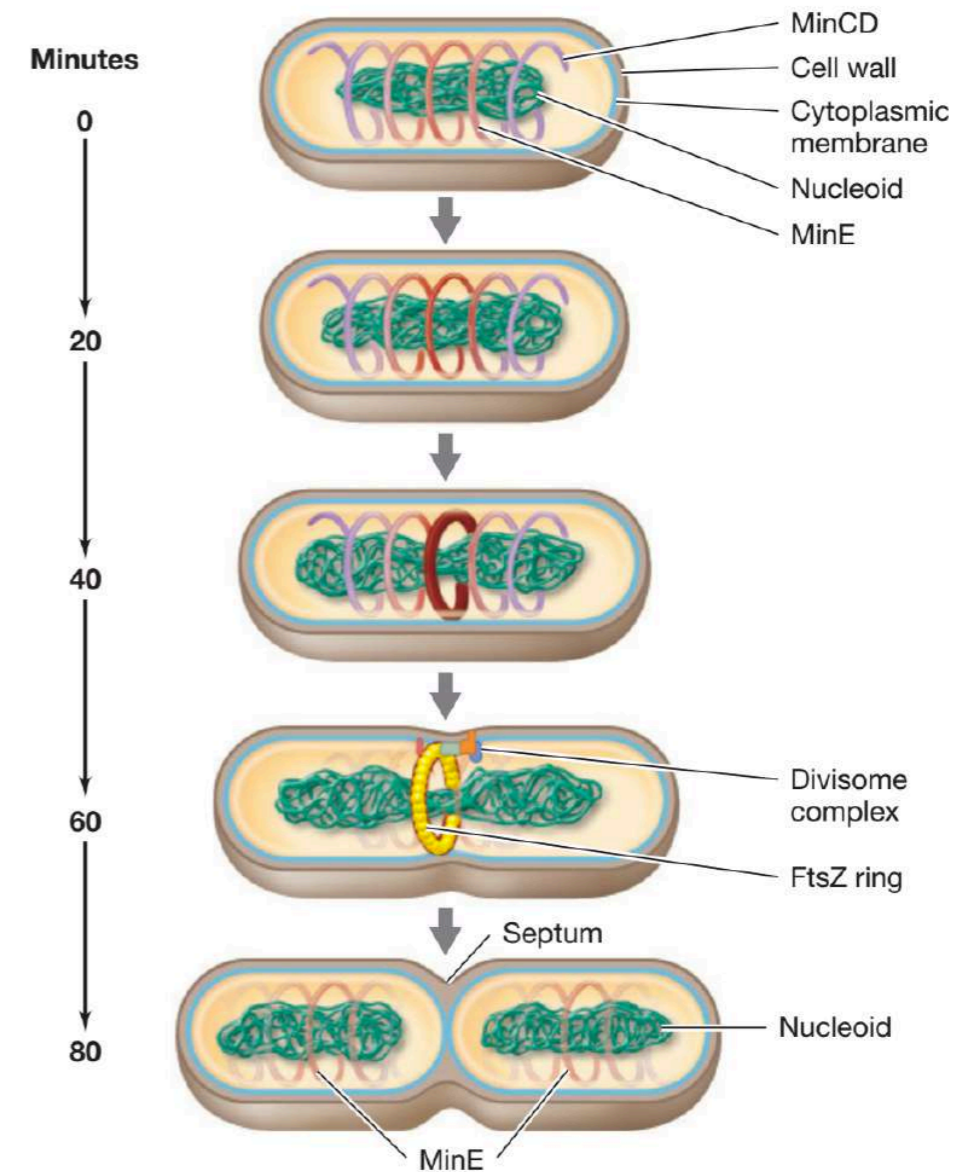
Divisome machinery, II

- FtsI one of several penicillin-binding proteins, inhibited by the antibiotic penicillin
- **Divisome orchestrates synthesis of new cytoplasmic membrane and cell wall material, called the division septum, at the center of a rod-shaped cell until the cell reaches 2x its original length**
- Following elongation, the cell divides, yielding 2 daughter cells
- ATP mediated process



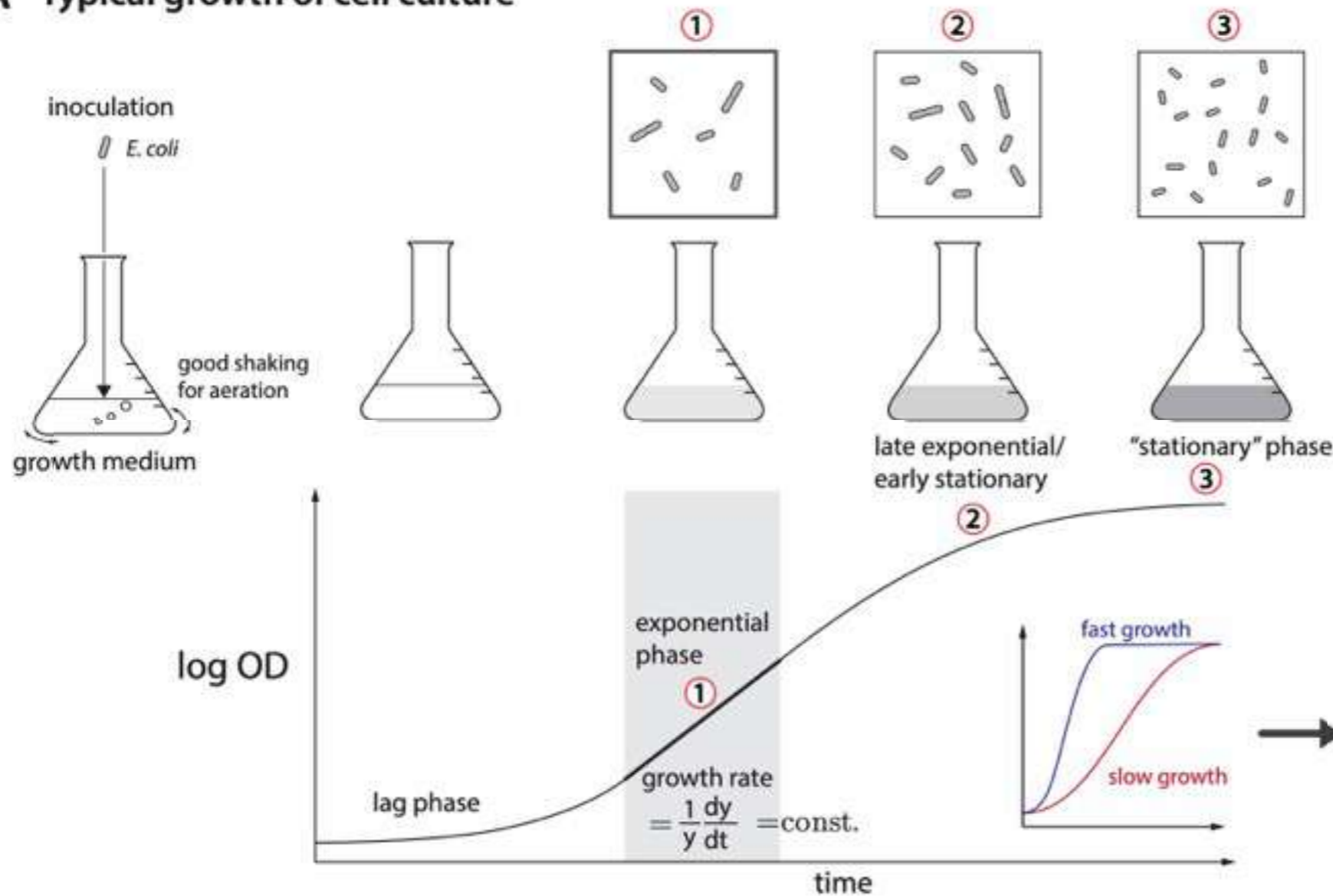
Protein-protein interaction for structural arrangement

- Proteins MinC, MinD, MinE interact to guide FtsZ to the cell midpoint
- **MinD forms a spiral structure** on the inner surface of the cytoplasmic membrane and **localize MinC** to the cytoplasmic membrane
- **MinD spiral oscillates back** and forth along the long axis of the growing cell
- Oscillation inhibits cell division by preventing the FtsZ ring from forming
- Simultaneously, **MinE oscillates from pole to pole to sweep MinC and MinD aside** → MinC and MinD dwell longer at the poles
- As a result, the cell center becomes the most permissive site for FtsZ binding and so the FtsZ ring forms there

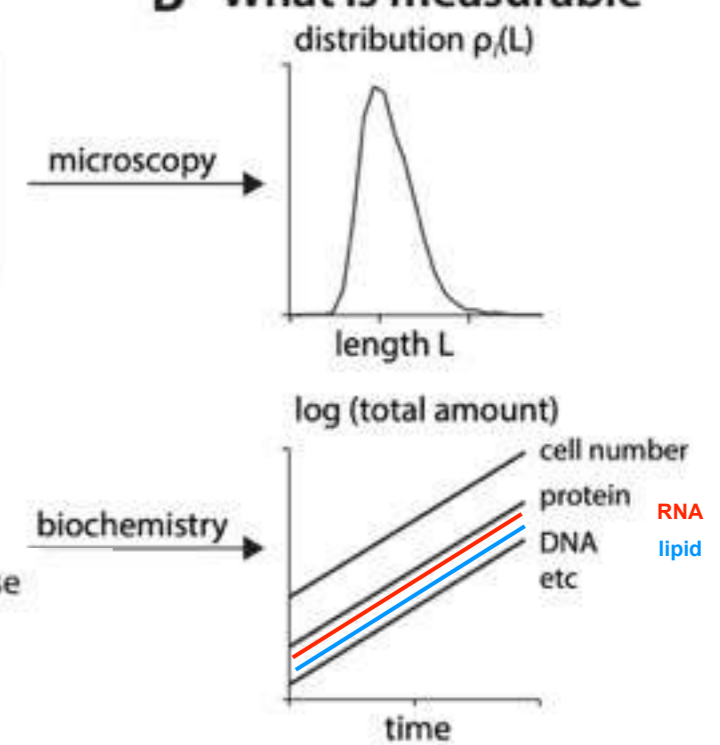


Growth in an homogeneous-predictable-low diversity environment, I

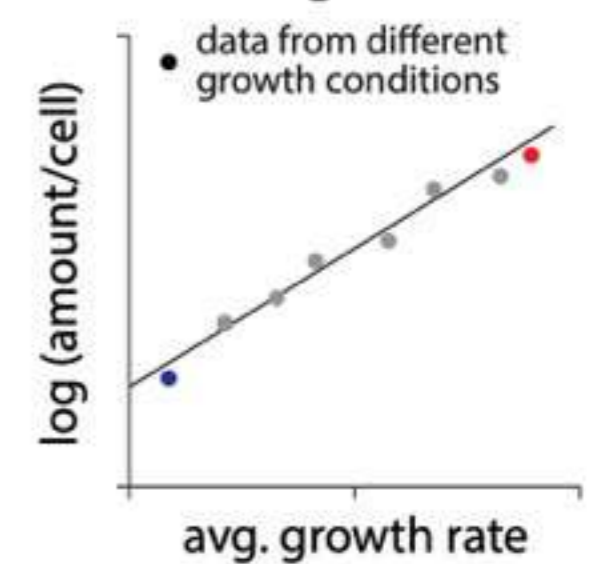
A Typical growth of cell culture



B What is measurable

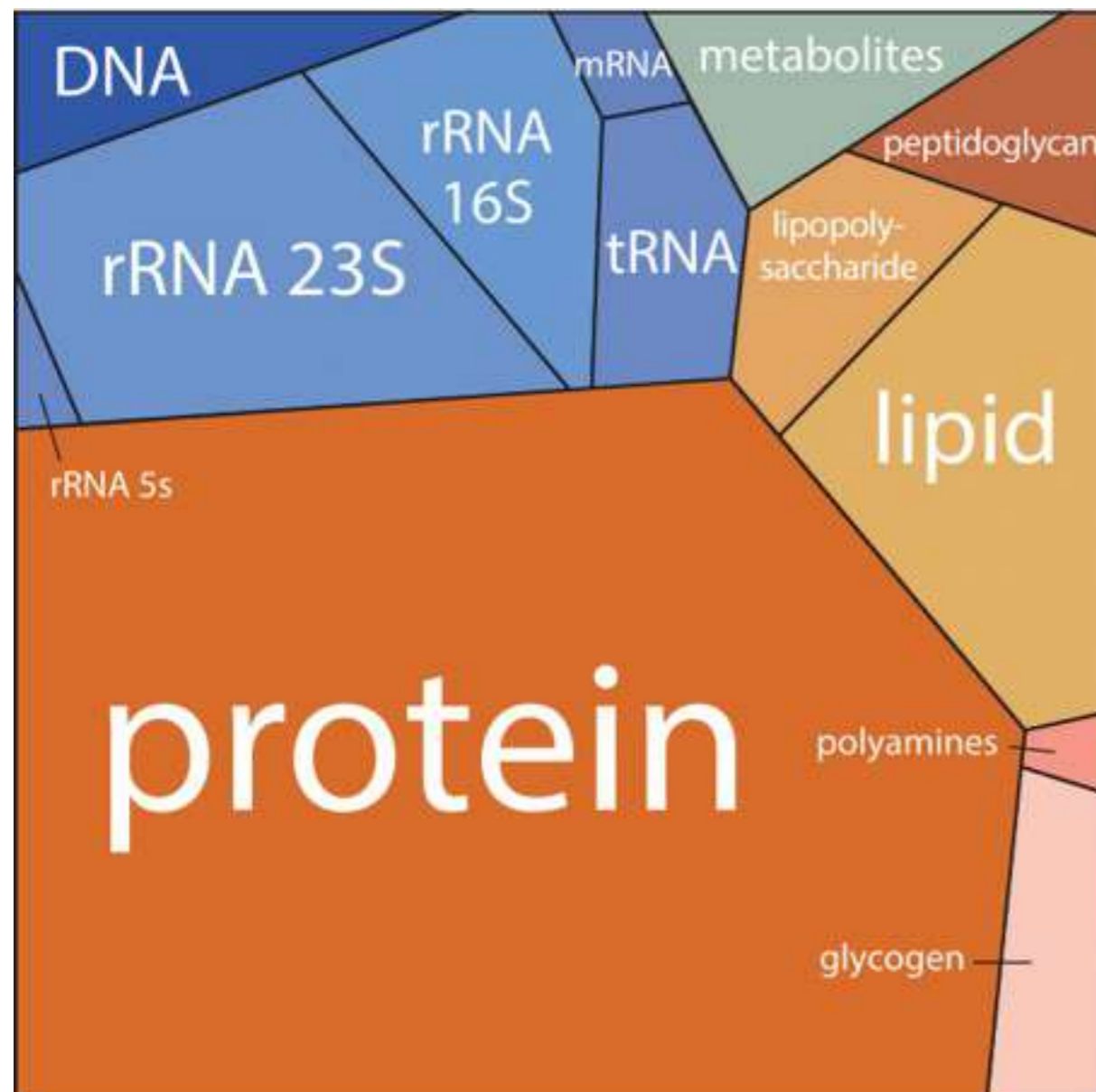


C "(nutrient) growth law"



Growth in an homogeneous-predictable-low diversity environment, II

A Voronoi tree diagram of *E.coli* composition



40 min

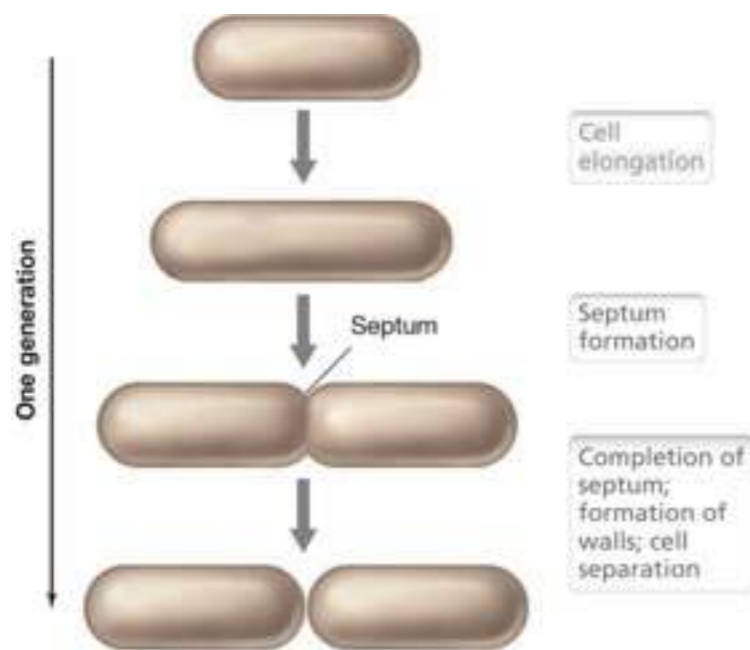
- Each polygon area is the relative fraction of the corresponding cellular constituent (dry mass)
- Similar colors = related functional role
- Steady-state mean cell size (large circles) scales exponentially with nutrient-determined growth rate

Defined growth conditions
What is missing?

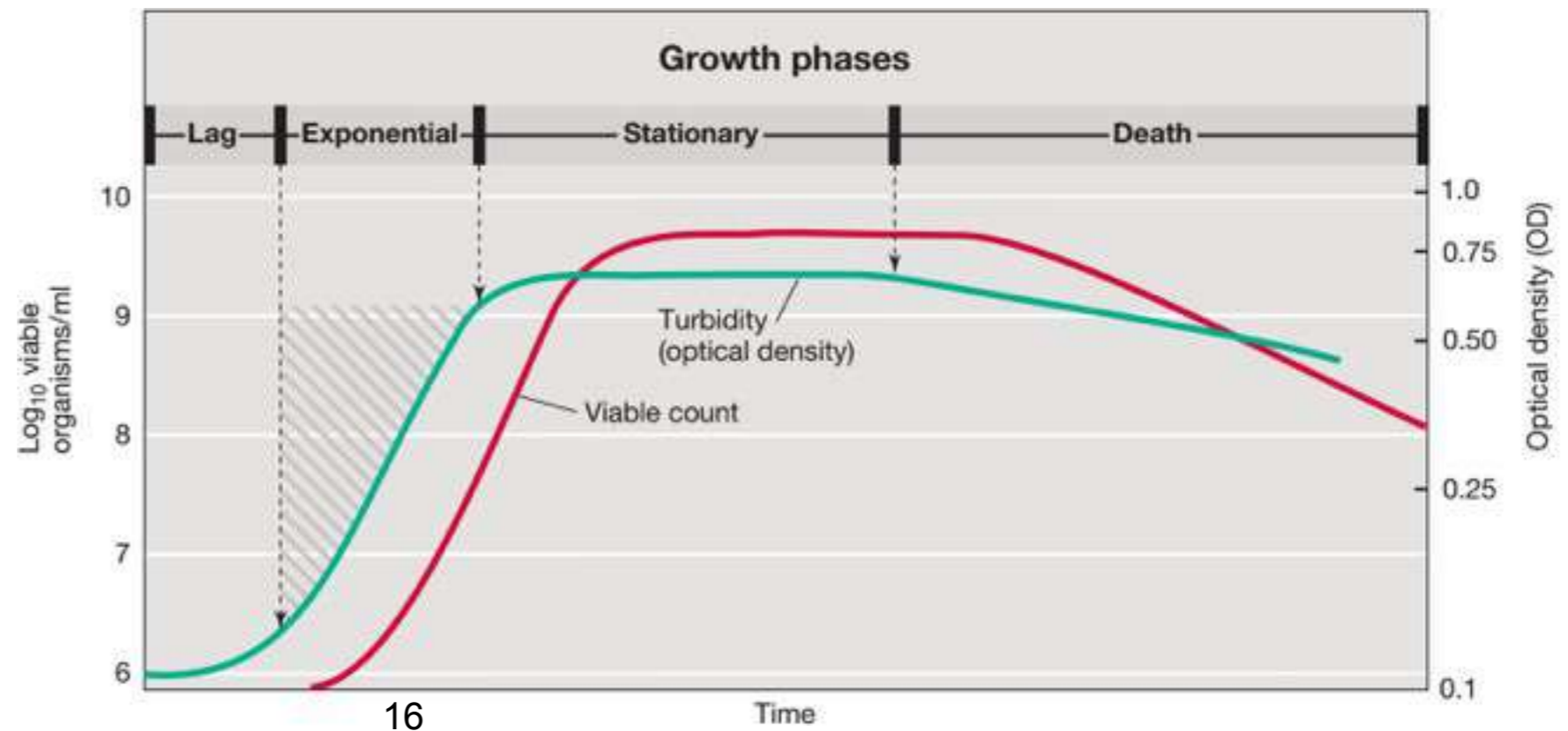
<http://book.bionumbers.org/>

Growth

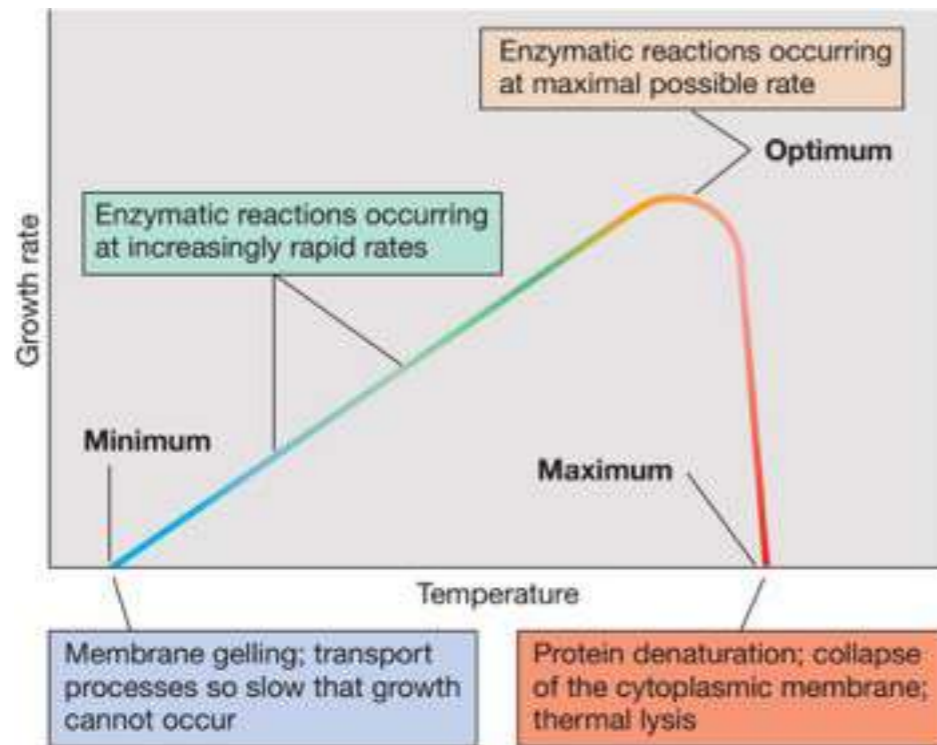
- A fixed relationship exists between initial cell number in a culture and cell number present after a period of exponential growth: $N = N_0 2^n$ where N is final cell #, N_0 is initial cell #, and n # of generations during period of exponential growth
- **Generation time (g)** of the exponentially growing population is t/n , where t is the duration of exponential growth in days, hours, or minutes (**g is the time from 1 cell to 2 cells**)
- Equation $N = N_0 2^n$ can be expressed in terms of n by taking the logarithms of both sides: $n = [3.3(\log N - \log N_0)]$
- **Instantaneous growth rate constant** expresses the rate at which the population is growing at any instant (by contrast, g is the mean time required for the cell population to double); k is expressed in units of reciprocal hours (h^{-1}): $k = 0.693/g$



Madigan et al. 2018

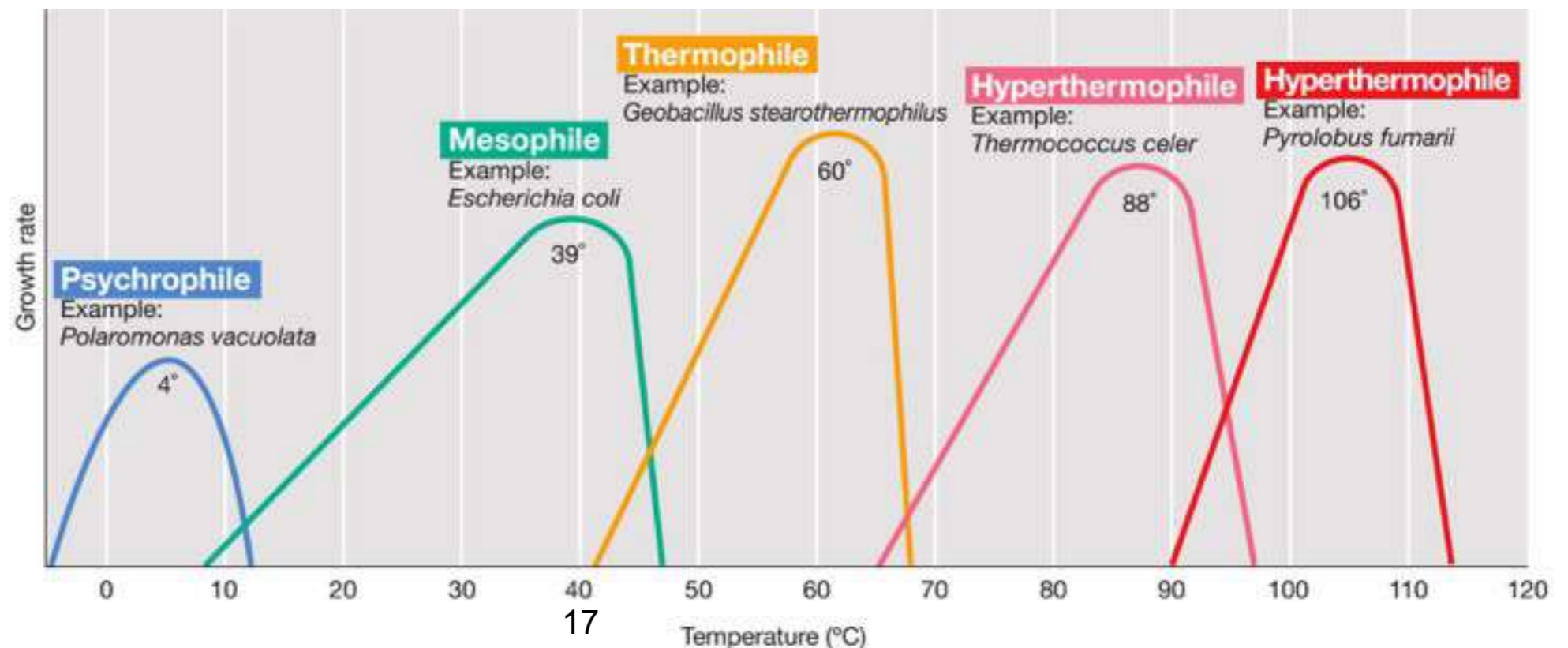


Temperature affects growth



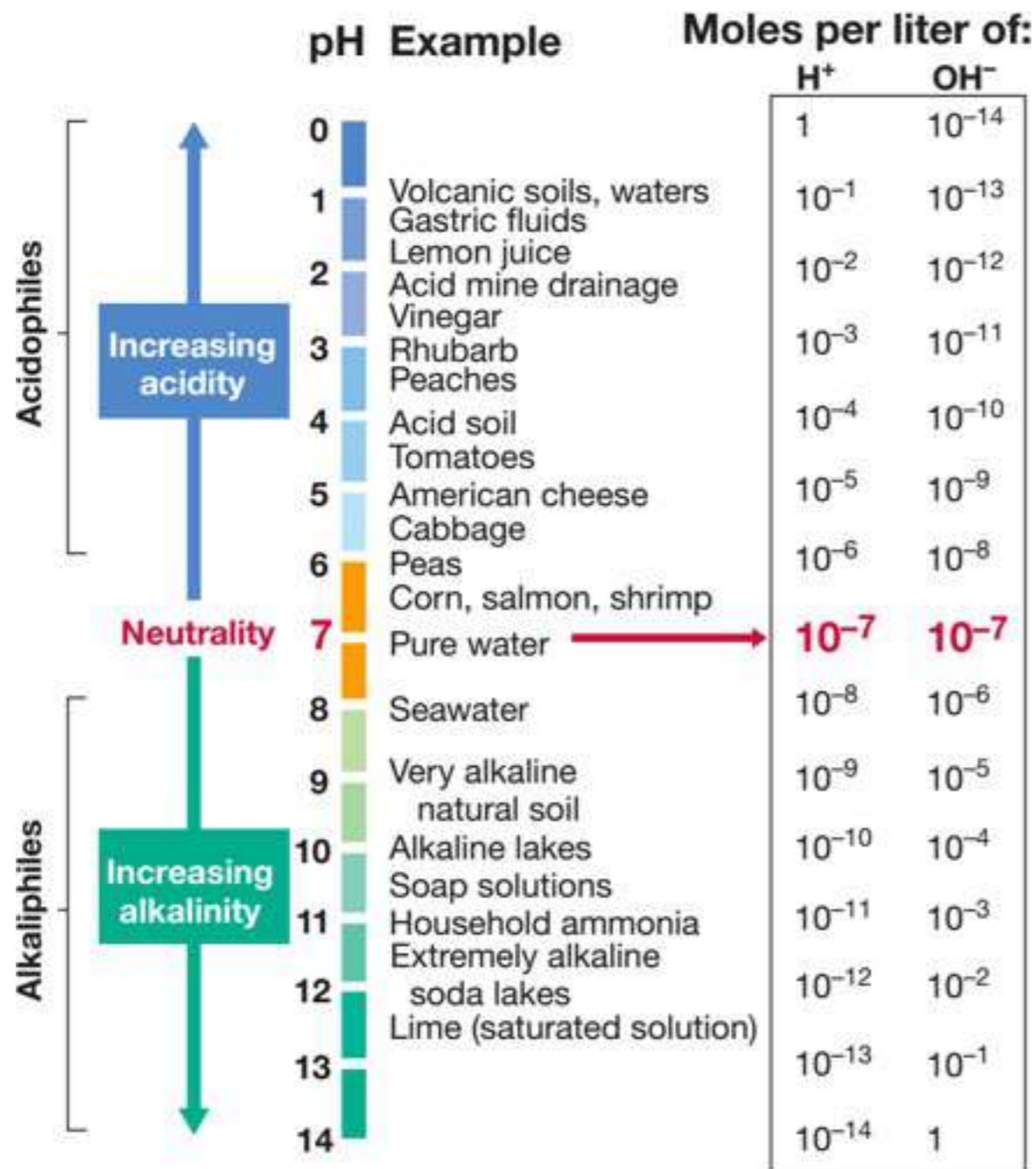
- **Reactions** occur **faster** at warmer temperatures b/c rate of collisions between molecules increases
- If temperature gets too hot the enzyme may denature and fail to function
- **Arrhenius activation energy**, which describes temperature effect on **catalytic rate constant**, k_{cat} , and thermal stability, which describes temperature effect on **thermal inactivation rate constant**, k_{inact}

Peterson et al., 2007



Madigan et al. 2018

pH affects growth



- **Optimal pH for growth refers to extracellular environment only**
- **Intracellular pH** must be maintained in 5 - 9 range
- Extreme acidophiles and alkaliphiles maintain cytoplasmic pH values ~neutrality
- **Extreme pH affects macromolecule structures**
- H-bonds holding together strands of DNA break up at high pH
- Lipids are hydrolyzed by an extremely basic pH
- PMF responsible for production of ATP in cellular respiration depends on concentration gradient of H⁺ across membrane

pH adaptive strategies

Active (proton exclusion, exchange, pumping, consumption and neutralization) and passive (cytoplasmic buffering) mechanisms of pH homeostasis as well as damage mitigation strategies (**DNA repair, synthesis of acid stable proteins**)

Quatrini & Johnson, 2018

- *Lactobacillus plantarum* is an anaerobic bacterium that **produces lactic acid** as metabolic product and thus lowers pH but also prefers low pH values
- *Corynebacterium ammoniagenes* produces **urease that cleaves urea into ammonia** and thus increases pH at the same time, it prefers higher pH values
- *Pseudomonas veronii* also **increases medium pH** but prefers low pH values for growth
- *Serratia marcescens* **strongly lowers pH** but better tolerates comparably higher pH values, with a slight optimum at around pH 8

In summary, we find that microbial growth often leads to dramatic changes in the pH of the environment, and this pH change can promote or inhibit bacterial growth

Ratzke & Gore, 2018

Osmotic pressure affects growth

- **Water availability** is expressed in terms of **water activity** (a_w): vapor pressure of air in equilibrium with a substance or solution / the vapor pressure of pure water
- Values of a_w vary between 0 (no free water) and 1 (pure water)
- **H₂O diffuses** from regions of high water concentration (**low solute concentration**) – > regions of lower water concentration (**higher solute concentration**) in the process of **osmosis**
- Cytoplasm has a higher solute concentration than the environment, so H₂O – > into cell
- Under such conditions, cell is said to be in **positive water balance**, normal cell state

TABLE 5.4 Water activity of several substances

Water activity (a_w)	Material	Example organisms ^a
1.000	Pure water	<i>Caulobacter</i> , <i>Spirillum</i>
0.995	Human blood	<i>Streptococcus</i> , <i>Escherichia</i>
0.980	Seawater	<i>Pseudomonas</i> , <i>Vibrio</i>
0.950	Bread	Most gram-positive rods
0.900	Maple syrup, ham	Gram-positive cocci such as <i>Staphylococcus</i>
0.850	Salami	<i>Saccharomyces rouxii</i> (yeast)
0.800	Fruit cake, jams	<i>Zygosaccharomyces bailii</i> (yeast), <i>Penicillium</i> (fungus)
0.750	Salt lakes, salted fish	<i>Halobacterium</i> , <i>Halococcus</i>
0.700	Cereals, candy, dried fruit	<i>Xeromyces bisporus</i> and other xerophilic fungi

Madigan et al. 2018

Osmotic pressure strategies

Madigan et al. 2018

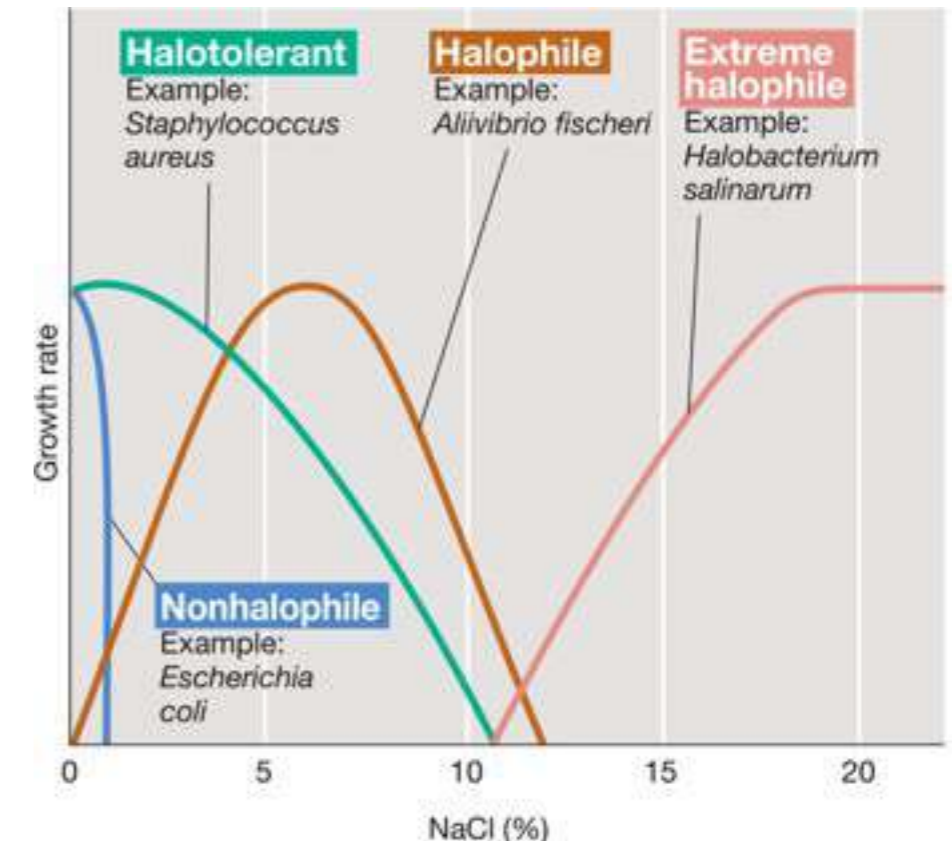
From high a_w → low a_w : cells maintain positive water balance by **increasing its internal solute (compatible not interference with metabolism) concentration**:

1. Pumping solutes into the cell from the environment
2. Synthesizing cytoplasmic solutes

Compatible solutes are highly water-soluble organic molecules & electrolytes: sugars, alcohols, and amino acid derivatives

Glycine betaine, an analog of the amino acid glycine, is widely distributed among halophilic bacteria

Other common compatible solutes include sugars such as sucrose and trehalose, dimethylsulfoniopropionate (produced by marine algae)



H₂O OUT of cells as their medium becomes more concentrated (an osmotic upshift)
H₂O INTO cells as their medium becomes more dilute (an osmotic downshift)

Bacterial membranes have high water permeabilities, so **cellular hydration is altered within seconds** of an osmotic shift

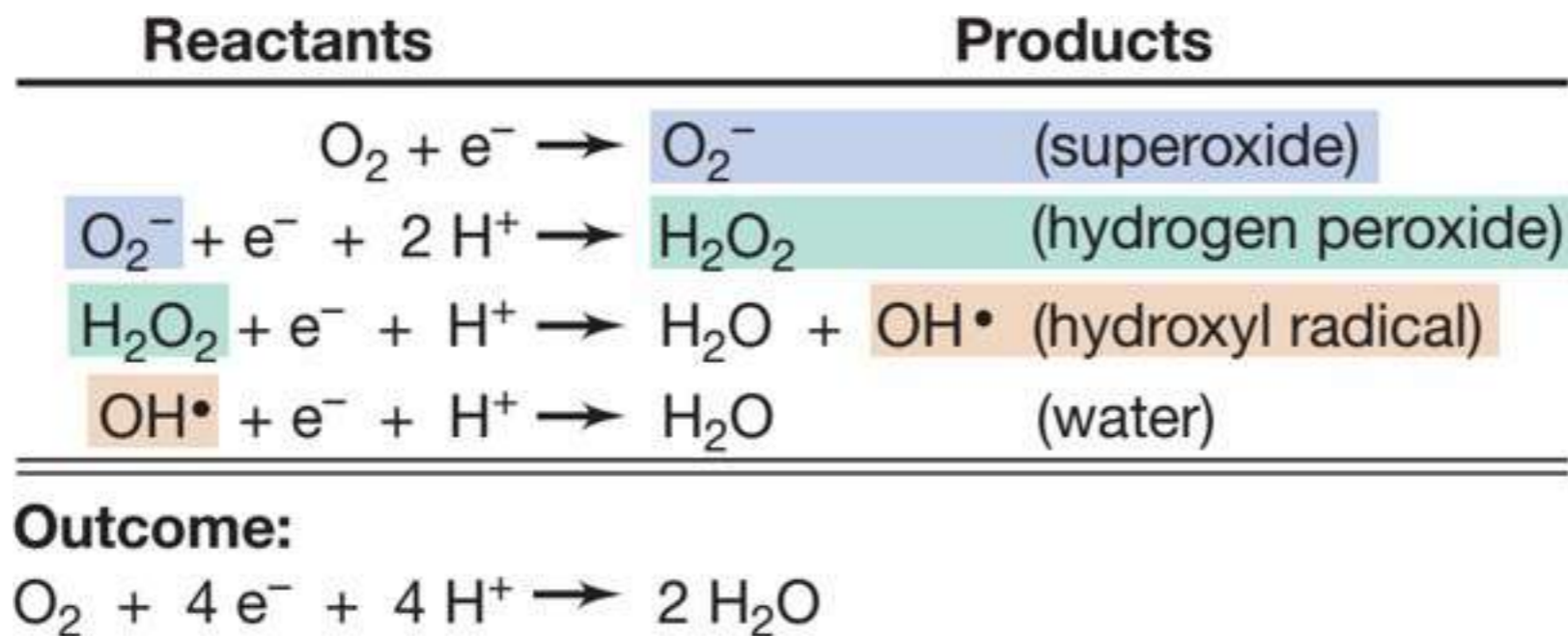
Approximately **0.5 g of water** is bound **per gram of cytoplasmic macromolecules**

At low osmolality, phosphate, the predominant inorganic anion, is present at a concentration of approximately 10 mM. Most metabolites are maintained at comparable or lower concentrations

At high osmolality, the amount of K⁺ exceeds that of nucleic acid phosphate and glutamate accumulates as K⁺ counterion (the concentration of glutamate rising from approximately 0.05 to 0.50 M). The trehalose concentration rises from approximately 0.04 to 0.4 M

O₂ affects growth

- Molecular oxygen (O₂) is not toxic
- O₂ can be converted to toxic oxygen by-products:
 - A. superoxide anion (O₂⁻)
 - B. hydrogen peroxide (H₂O₂) → damage cell components
 - C. hydroxyl radical (OH[•]) → oxidation macromolecules & other organic compounds
- All by-products of the reduction of O₂ to H₂O in respiration
- Flavoproteins, quinones, and iron–sulfur proteins, electron carriers found all cells also catalyze some of these reductions



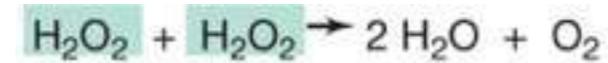
O₂ adaptive strategies

TABLE 5.6 Oxygen relationships of microorganisms

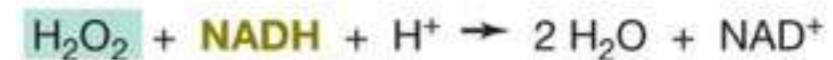
Group	Relationship to O ₂	Type of metabolism
Aerobes		
Obligate	Required	Aerobic respiration
Facultative	Not required, but growth better with O ₂	Aerobic respiration, anaerobic respiration, fermentation
Microaerophilic	Required but at levels lower than atmospheric	Aerobic respiration
Anaerobes		
Aerotolerant	Not required, and growth no better when O ₂ present	Fermentation
Obligate	Harmful or lethal	Fermentation or anaerobic respiration

Specific niche

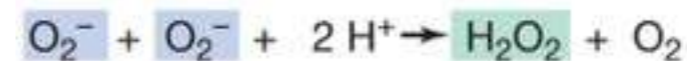
Metabolic machinery to detoxify



(a) **Catalase**



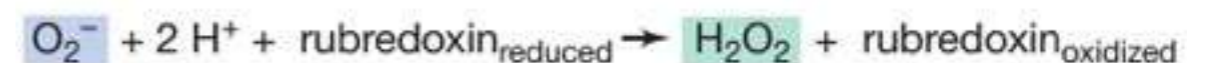
(b) **Peroxidase**



(c) **Superoxide dismutase**



(d) **Superoxide dismutase/catalase in combination**

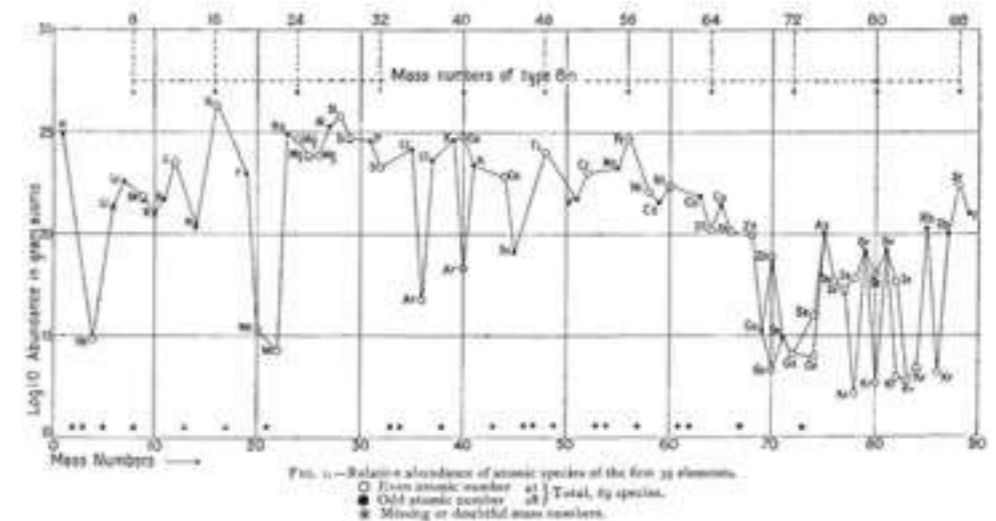


(e) **Superoxide reductase**

Elemental composition of Earth and microbes

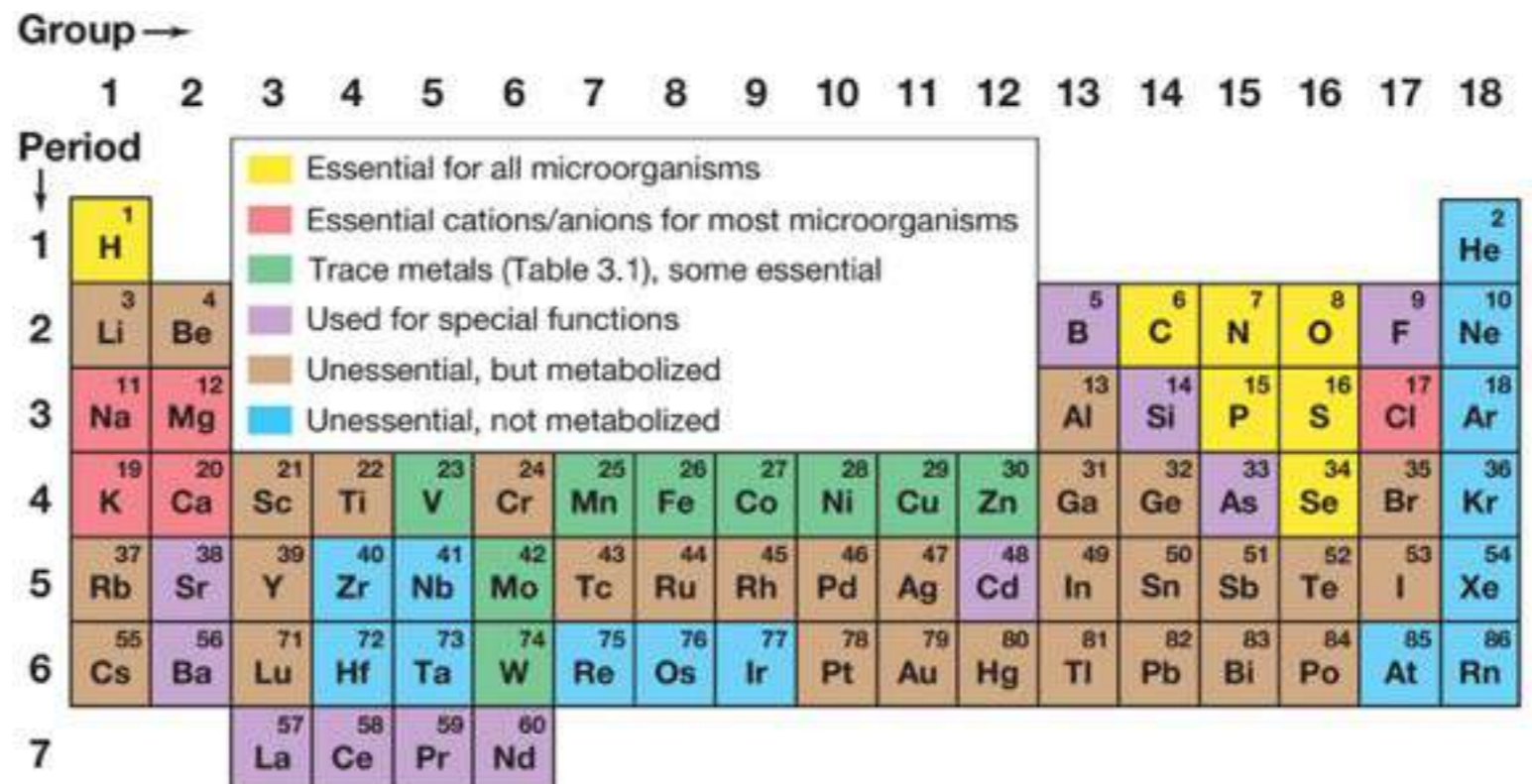
Aston, 1924

- Universe, Earth, Life share important elements
- Majority of Universe is H and He and some others
- The essence of Life is the other elements



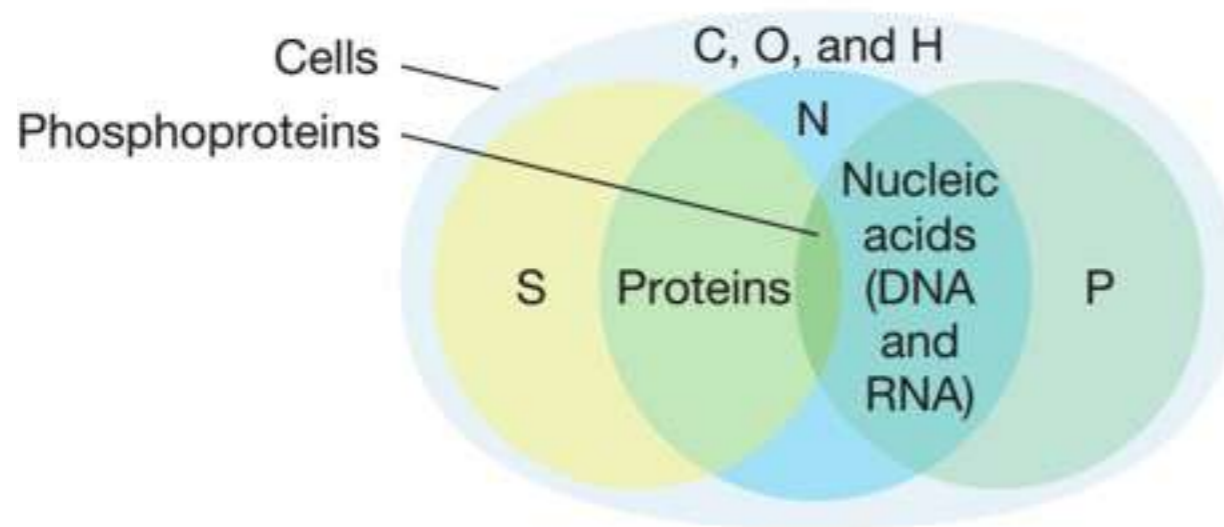
The Elemental Composition of *E. coli*

Element	% dry	Substrate Source	Cellular Components
C	55	DOC, CO ₂	Main constituent of cellular material
O	20	O ₂ , DOM, CO ₂	Constituent of cell material and cell water; O ₂ primary electron acceptor in aerobic respiration
N	10	NH ₃ , NO ₃ ⁻ , NO ₂ ⁻ , DON, N ₂	Constituent of amino acids, nucleic acids, nucleotides, and coenzymes
H	8	DOM, H ₂	Main constituent of organic compounds and cell water
P	3	PO ₄ ³⁻ , DOP	Constituent of nucleic acids, nucleotides, phospholipids, LPS, teichoic acids in gram positives
S	1	SO ₄ ²⁻ , H ₂ S, HS, DOM	Constituent of cysteine, methionine, glutathione, several coenzymes
K	1	Potassium salts	Main cellular inorganic cation and cofactor for certain enzymes
Mg	0.5	Magnesium salts	Inorganic cellular cation, cofactor for certain enzymatic reactions
Ca	0.5	Calcium salts	Inorganic cellular cation, cofactor for certain enzymes
Fe	0.002	Iron salts, DOM	Component of cytochromes and Fe-proteins; cofactor for many enzymes



From macromolecules to cell

Elemental composition of informational macromolecules



(b)

Macromolecular composition of a cell

Macromolecule	Percent of dry weight
Protein	55
Lipid	9.1
Polysaccharide	5.0
Lipopolysaccharide	3.4
DNA	3.1
RNA	20.5

(c)

- About 75% of microbial cell wet weight (a single cell of *Escherichia coli* weighs just 10⁻¹² g) is water
- The remainder ~ 25% is primarily macromolecules—proteins, nucleic acids, lipids, and polysaccharides
- The building blocks of these macromolecules are the amino acids, nucleotides, fatty acids, and sugars, respectively

Basic Cellular Metabolism

1. Energy source to generate ATP

2. Carbon source of assembling cellular building blocks

3. For maintenance of existing cells/ for growth of new cells

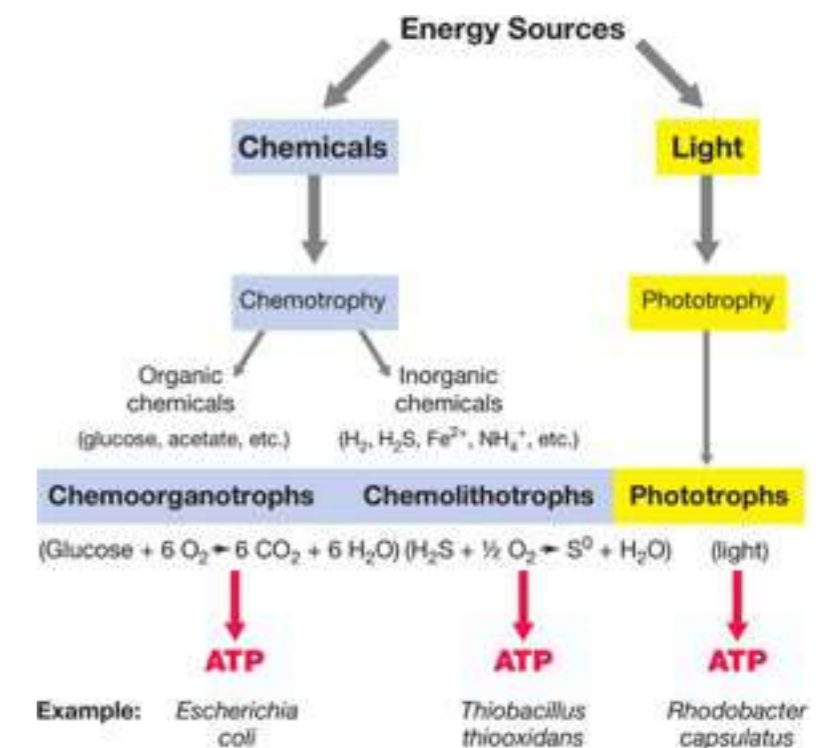
- > Successful exploitation well-defined energy and carbon source
- > Physical, biological and chemical properties vary in space and time

Carbon source	Energy source		
	Chemical, organic	Chemical, inorganic	Light
Fixed organic	Chemosynthetic organoheterotroph (Example: humans, fungi, <i>Pseudomonas</i>)	Chemosynthetic lithoheterotroph (Example: <i>Beggiatoa</i> sp.)	Photosynthetic heterotroph (Example: purple and green bacteria; <i>Rhodospirillum</i>)
Gaseous CO ₂		Chemosynthetic lithoautotroph (Example: ammonia-, hydrogen-, and sulfur-oxidizing bacteria; <i>Nitrosomonas</i> , <i>Aquifex</i>)	Photosynthetic autotroph (Example: plants, algae, <i>Prochlorococcus</i>)

Terminology:

- Autotroph: carbon from CO₂ fixation
- Heterotroph: carbon assimilated from (fixed) organic compounds
- Photosynthetic: energy from light
- Chemosynthetic: energy from oxidizing reduced chemicals
- Chemolitho: energy from oxidizing inorganic reduced chemicals
- Chemoorgano: energy from oxidizing organic reduced chemicals.

Madsen, 2016



LIVING vs NON living

You are alive if you have:

1. A membrane subsystem for compartmentalizing the functional network components
2. An autocatalytic metabolic subsystem that functions out-of-equilibrium by capturing energy and material resources
3. An information-based subsystem for processing and transferring genetic information to the progeny via self-replication

Ganti, T. in The Principles of Life (ed. Szathmary, E. and Griesemer, J.) Ch. 3(Oxford Univ. Press, Oxford 2003).

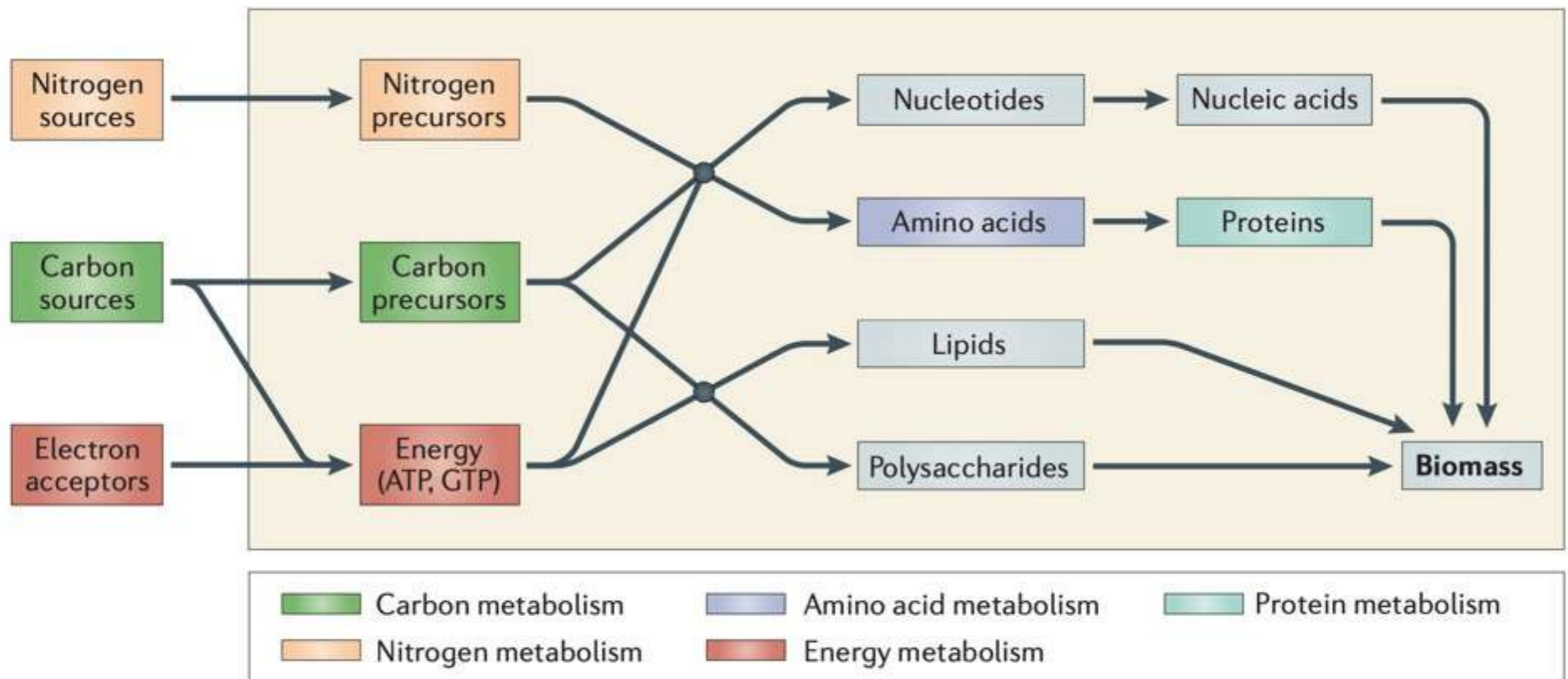
Metabolism & Growth in a limited environment

Habitat characteristics and nutrient limitations faced by three physiological classes of microorganisms			
Habitat type	Photoautotroph	Chemolithotroph	Chemoorganoheterotroph
Ocean water	Daily light cycle, light penetration depth; scarce iron	Flux of reduced inorganic compounds, especially NH_3 , H_2S , H_2 , or CH_4 from nutrient turnover and hydrothermal vents	Carbon flux from phototrophs, dead biomass, and influent waters
Lake water	Daily light cycle, light penetration depth; scarce phosphorus	Flux of reduced inorganic materials, especially NH_3 , H_2 , and CH_4 from nutrient turnover	Carbon flux from phototrophs, dead biomass and influent waters
Sediment (freshwater and oceanic)	Daily light cycle, light penetration depth	Flux of reduced inorganic materials, especially NH_3 and H_2 from nutrient turnover or H_2 , H_2S , or CH_4 from hydrothermal vents	Flux of organic carbon from phototrophs and dead biomass; flux of final electron acceptors to carbon-rich anaerobic strata
Soil	Daily light cycle, light penetration depth	Flux of reduced gaseous substrates, especially methane from nutrient turnover by anaerobes	Slow turnover of soil humus, dead biomass, plant root exudates; leaf fall from vegetation
Subsurface sediment	No light	Flux of reduced inorganic materials, especially H_2 and CH_4 from geothermal origin	Carbon flux from nutrient turnover

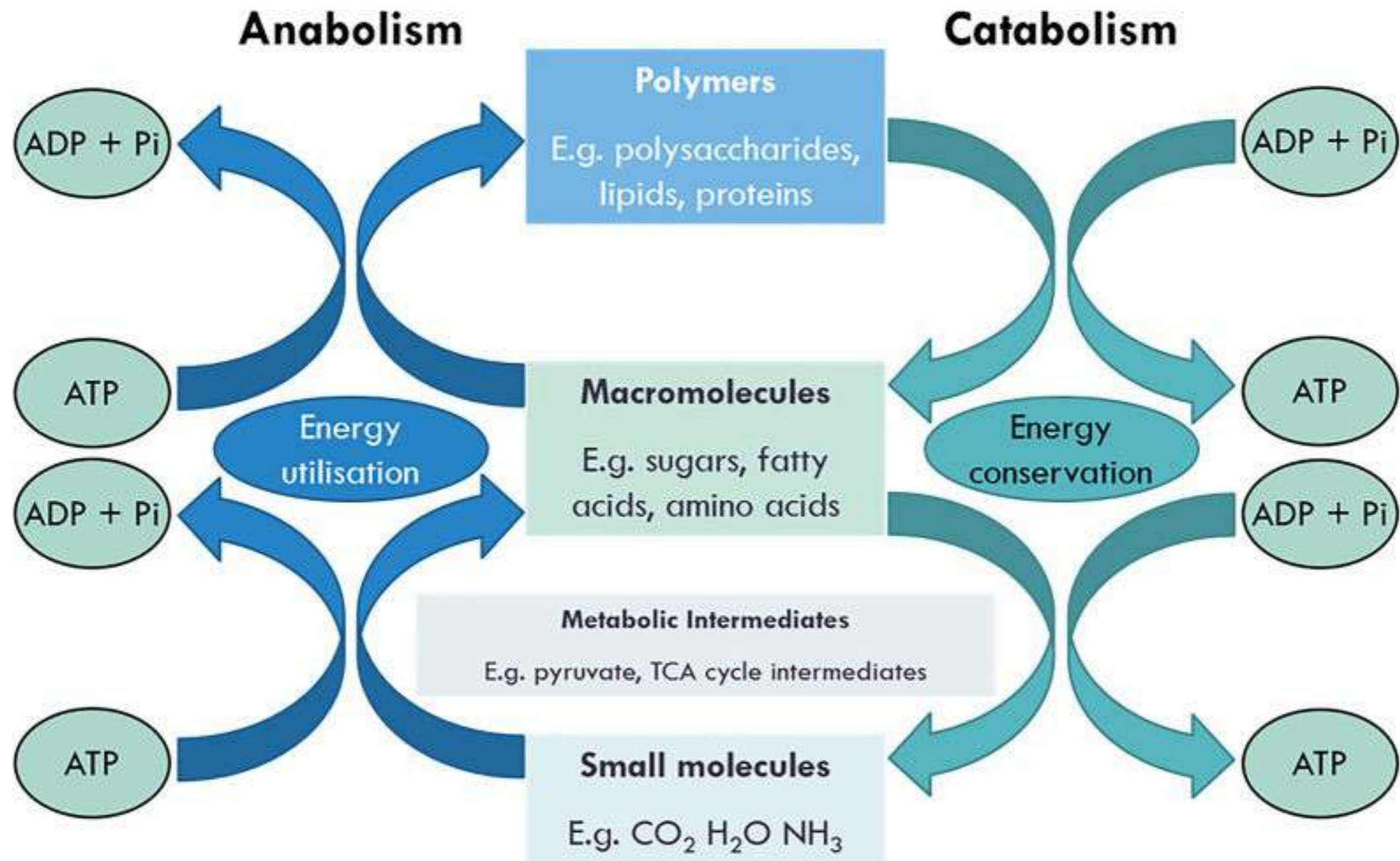
Coordinated Metabolism

Beyond fuelling cellular activities with building blocks and energy, metabolism also integrates environmental conditions into intracellular signals

Metabolisms underlying regulatory network is complex and multifaceted



Anabolism and Catabolism

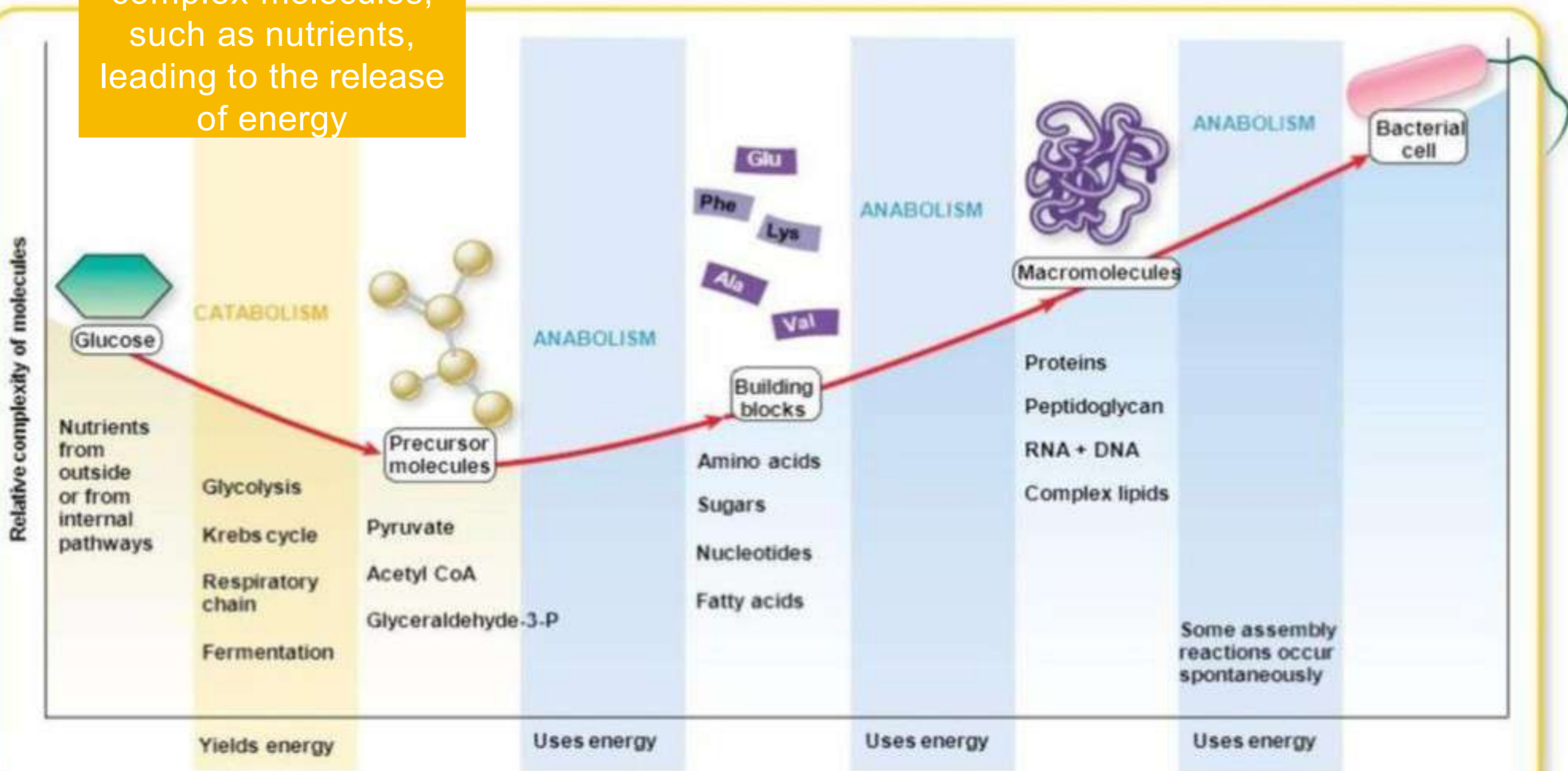


(Judge and Dodd, 2020)

Metabolism

Catabolism: The degradation of complex molecules, such as nutrients, leading to the release of energy

Anabolism: The energy-dependent formation of building blocks and macromolecules in a cell



Real Growth in a limited environment

Rapid exponential growth is not real in the environment

In 48 h assuming that *E.coli* that doubles every 20 min, given its weight 10⁻¹² g, there will be 2.2x10³¹ g

In the environment:

- Sporadic rapid growth
- Slow growth
- Sporadic slow growth
- Dormancy

Estimates of microbial growth rate, dormancy, or survival time (ST)

Habitat	Organism	Doubling time (DT) or survival time (ST)	References
Growth rate			
Laboratory medium	<i>E. coli</i>	20 min DT	Koch, 1971
Human intestine	<i>E. coli</i>	12 h DT	Koch, 1971
Mouse	<i>Salmonella typhimurium</i>	10–24 h DT	Brock, 1971
Rumen	Heterotrophic bacteria	~12 h DT	Brock, 1971
Pond	Heterotrophic bacteria	2–10 h DT	Brock, 1971
Lake water	Heterotrophic bacteria	10–280 h DT	Jannasch, 1969
Ocean	Heterotrophic bacteria	20–200 h DT	Vaulot et al., 1995
Ocean	Autotroph, <i>Prochlorococcus</i>	~24 h DT	Gray and Williams, 1971
Soil	Heterotrophs: α Proteobacteria, rhizobia	100 days DT	Mailloux and Fuller, 2003
Shallow groundwater	Heterotrophs: <i>Acidovorax</i> , <i>Comamonas</i>	15 days DT	Hoehler and Jorgensen, 2013
Marine surface sediments	Sulfate reducers	1 year DT	Holmes et al., 2013
Shallow subsurface	<i>Geobacter</i>	46 h DT	Phelps et al., 1994;
Deep subsurface	Heterotrophs	100 years DT	Fredrickson and Onstott, 2001
Deep marine sediments	Sulfate reducers, heterotrophs	200–3000 year DT	Hoehler and Jorgensen, 2013

Principle of Bioenergetics

Energy flows (radiation—>chemical—> heat)

Matter cycles (uptake—>growth—> death—>recycle)

Energy is defined as the **ability to do work**, kilojoules (kJ), a unit of heat energy

All chemical reactions in a cell are accompanied by **changes in energy**, energy being either required or released as a reaction proceeds

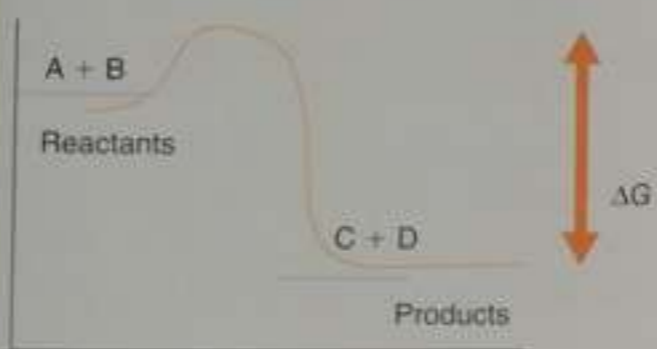
$\Delta G^{0'} < 0$, reaction will proceed with release of free energy- exergonic

$\Delta G^{0'} > 0$, reaction requires energy in order to proceed- endergonic

Thermodynamics: the branch of chemistry that predicts what can happen based on the energy state of reactants and products

In 1877, the American mathematician, Josiah Gibbs, sought to quantify the amount of "useful work" that can be harnessed during completion of chemical (or other) reactions:

$A + B \rightleftharpoons C + D$



Types of reactions:
Changes in state
Dissolution/precipitation
Complexation
Acid/base
Sorption/desorption
Oxidation/reduction (key for biological systems to generate ATP)

Products - reactants = $-\Delta G$ (free energy)

$$\Delta G = \Delta G^{\circ} + RT \ln \frac{[C][D]}{[A][B]}$$

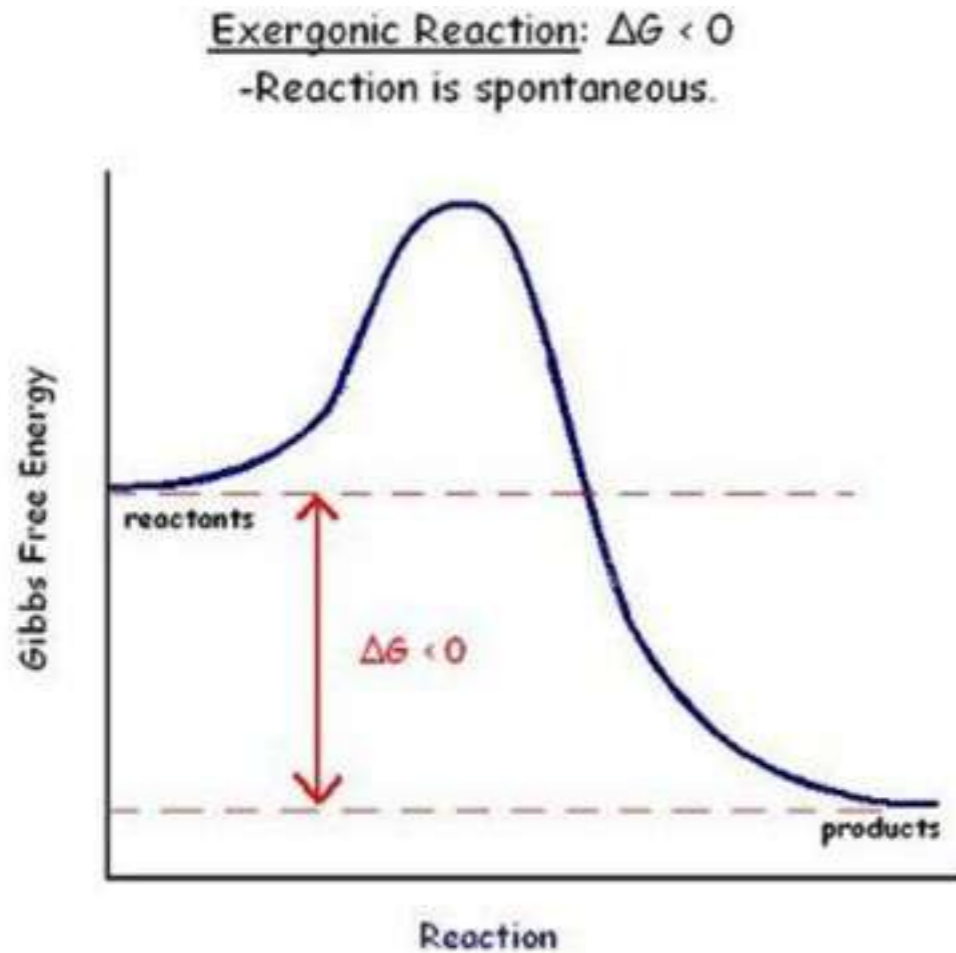
ΔG = free-energy change under conditions specified
 ΔG° = free-energy change under standard conditions of 1 atm pressure and 1 M concentration
 T = temperature (degrees K)
 R = universal gas constant (8.29 J/mol/K)

Madsen, 2016

A $\Delta G^{0'} > 0$ reaction under standard conditions can become exergonic $\Delta G^{0'} < 0$ under the actual conditions present in the microbial habitat

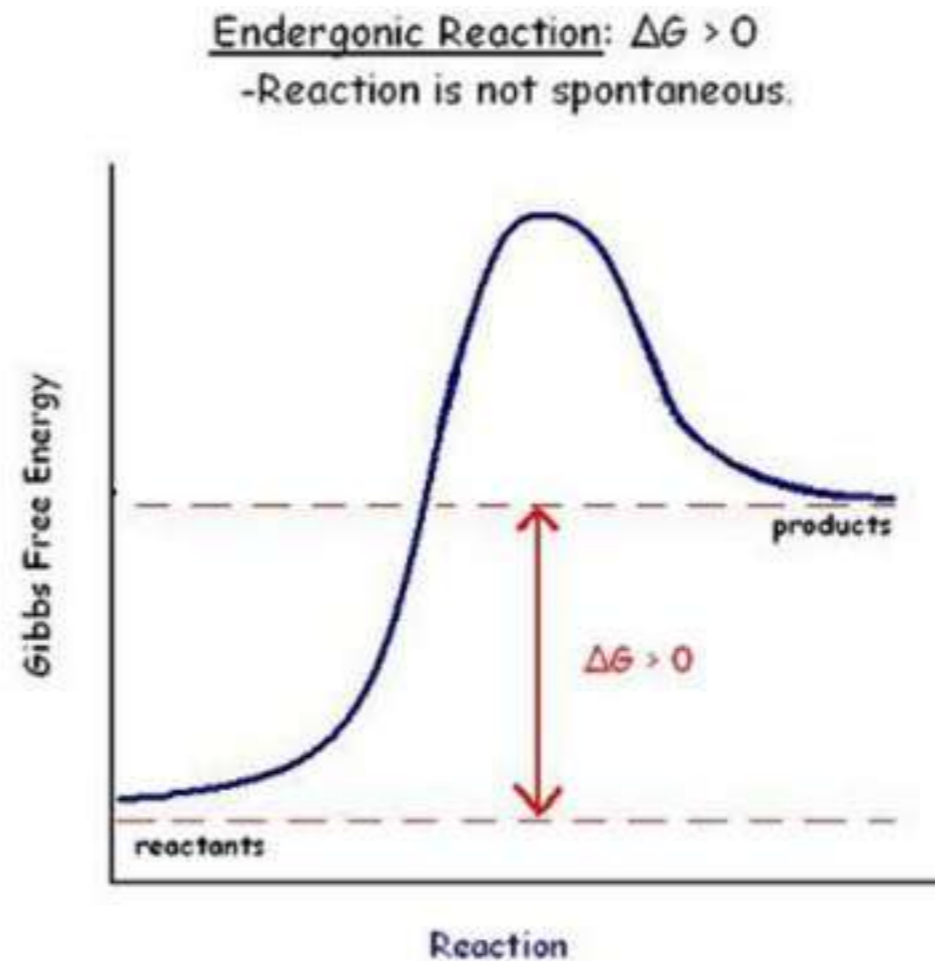
Spontaneous

$\Delta G^0' < 0$, reaction will proceed with release of free energy- EXERgonic



Not Spontaneous

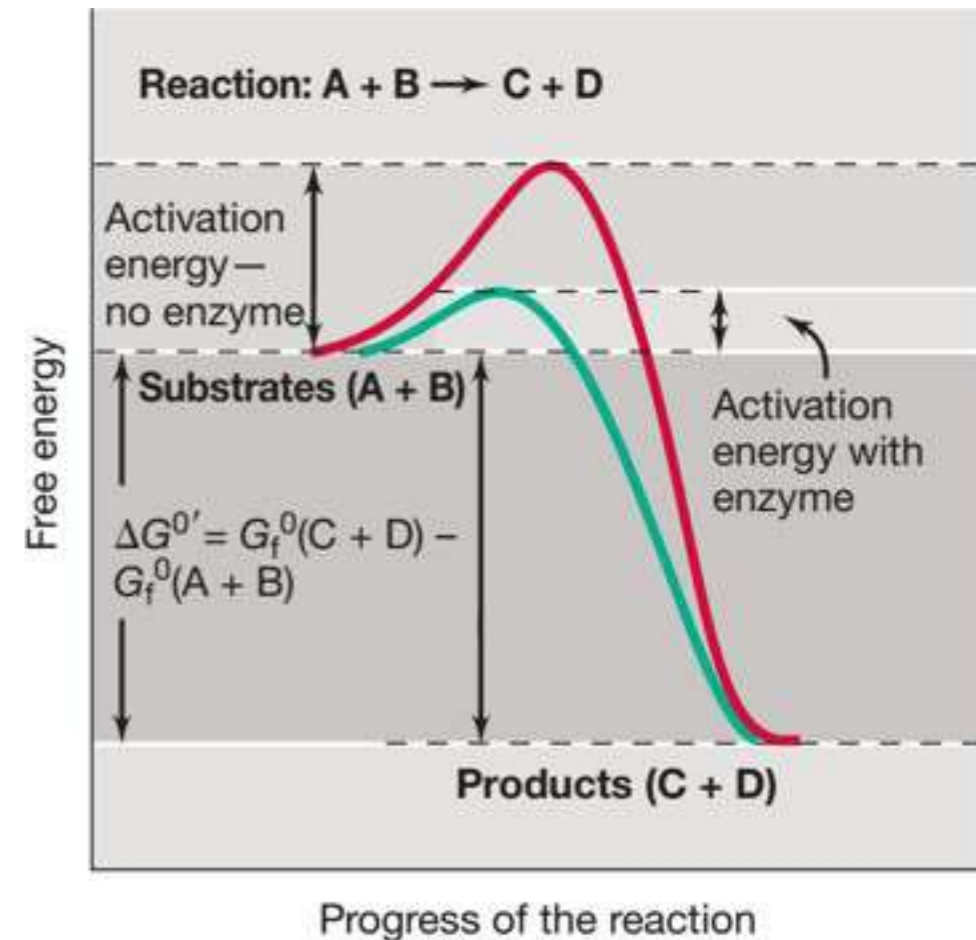
$\Delta G^0' > 0$, reaction requires energy in order to proceed- ENDERgonic



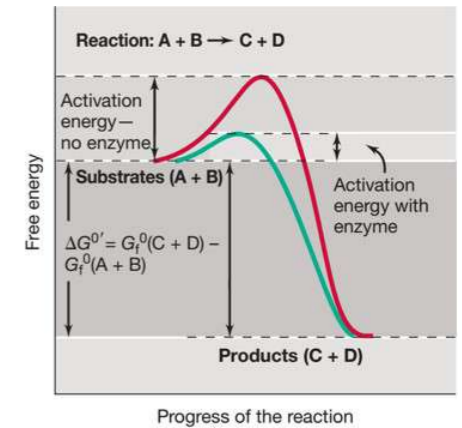
1. Libretexts. "11.5: Spontaneous Reactions and Free Energy." Chemistry LibreTexts, Libretexts, 13 July 2018
2. Science, Ck12. "Spontaneous and Nonspontaneous Reactions." CK-12 Foundation, CK-12 Foundation, 28 Mar. 2017

Enzyme, I

- Free-energy calculations reveal only whether energy is released or required in a given reaction
- $\Delta G^{0'}$ says nothing about the rate of the reaction
- **Activation energy** can be viewed as the **minimum energy required** for a chemical reaction to begin
- **Catalysts function by lowering the activation energy** of a reaction thereby increasing the reaction rate



Enzyme, II



- **Catalysts** have no effect on the energetics or the equilibrium of a reaction but **affect the rate at which a reaction proceeds**
- **Most cellular reactions will not proceed at significant rates without catalysis**
- The **major** catalysts in cells are enzymes, **proteins** (or in a few cases, **RNAs**) that are **highly specific**
- This **specificity** is a function of the precise **3D structure** of the enzyme.
- In an enzyme-catalyzed reaction, the enzyme combines with the reactant, called a substrate, forming an enzyme-substrate complex. Then, as the reaction proceeds, the product is released and the enzyme is returned to its original state, ready to catalyze a new round of the reaction
- **Prosthetic** groups bind **tightly** to their enzymes, usually covalently and permanently (e.g. heme group present in cytochromes such as cytochrome c)
- **Coenzymes**, with a few exceptions, **are loosely and often transiently** bound to enzymes
- Single coenzyme molecule may associate with a number of different enzymes (e.g. vitamins)

Speed and specificity of a reaction

If the enzyme has more than one possible substrate, the k_{cat}/K_m values determine the specificity of the enzyme for each

The higher this value the more specific the enzyme is for that substrate

This is because a high value of k_{cat} and a low value of K_m are expected for the best substrates

If k_{cat}/K_m – which is the apparent second-order rate constant for the enzyme-catalyzed reaction – approaches the diffusion limit ($\sim 10^8$ – $10^9 \text{ M}^{-1} \text{ s}^{-1}$), the enzyme cannot catalyze the reaction any better and is said to have reached ‘**catalytic perfection**’

—> second-order rate constants that approach their rates of encounter ($\sim 10^9 \text{ s}^{-1} \text{ M}^{-1}$) with the substrate in solution

Triosphosphate isomerase, superoxide dismutase and carbonic anhydrase are examples of perfect enzymes

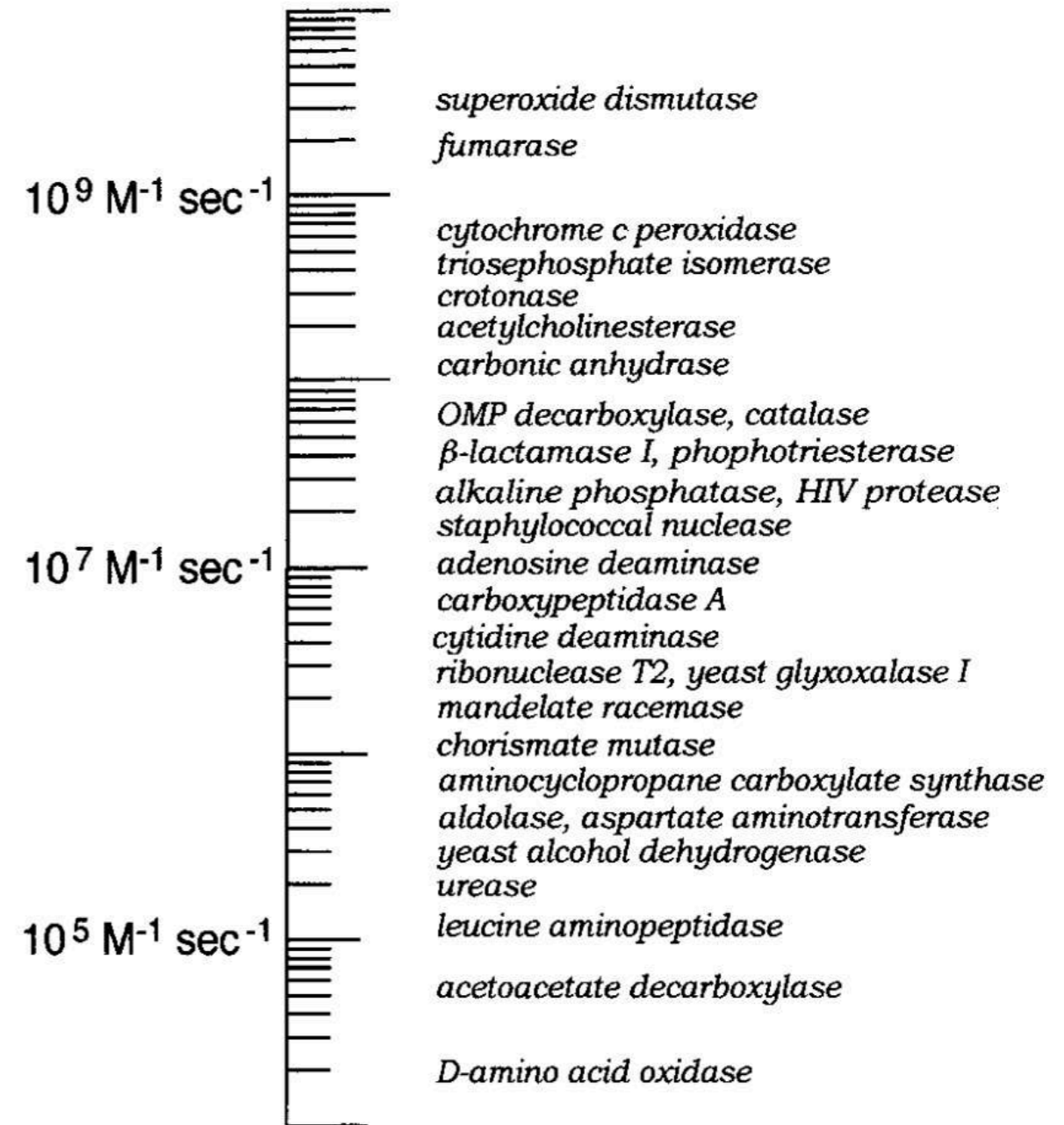


FIGURE 1. Representative values of k_{cat}/K_m at 25 °C compiled from the literature.

Evolution in action !

The **half-life** of a reaction: amount of time needed for a reactant concentration to decrease by half compared to its initial concentration

Enzymes allow organisms to **channel the flow of matter to their own advantage**, allowing some reactions to proceed rapidly compared with other reactions that offer no selective advantage

After a substrate is bound at an enzyme's active site, its half-life is usually a small fraction of 1 s

Rapid turnover is necessary if any enzyme is to produce a significant rate of reaction at the **limited concentration** ($<10^{-5}$ M) at which enzymes are present within the cell

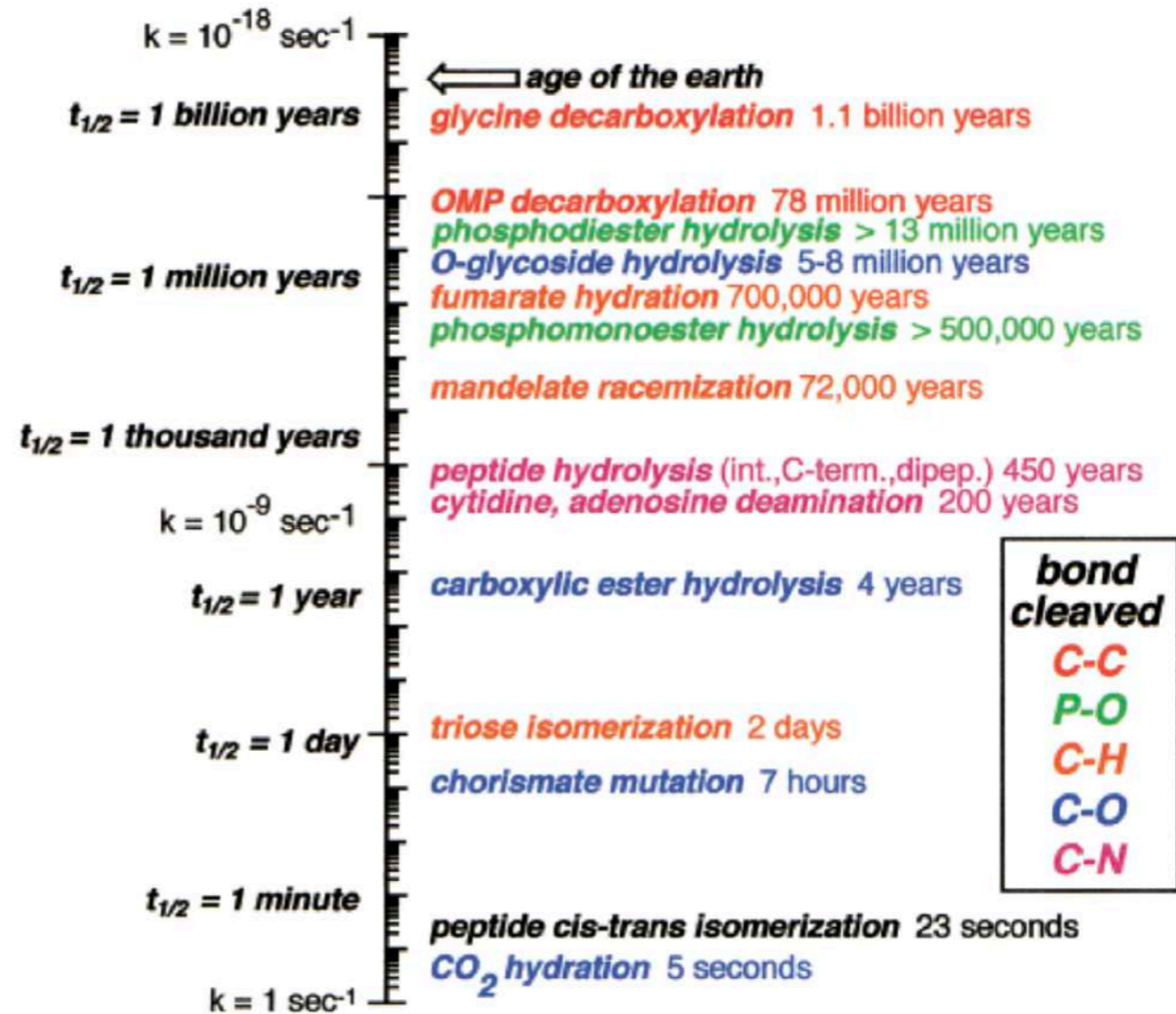


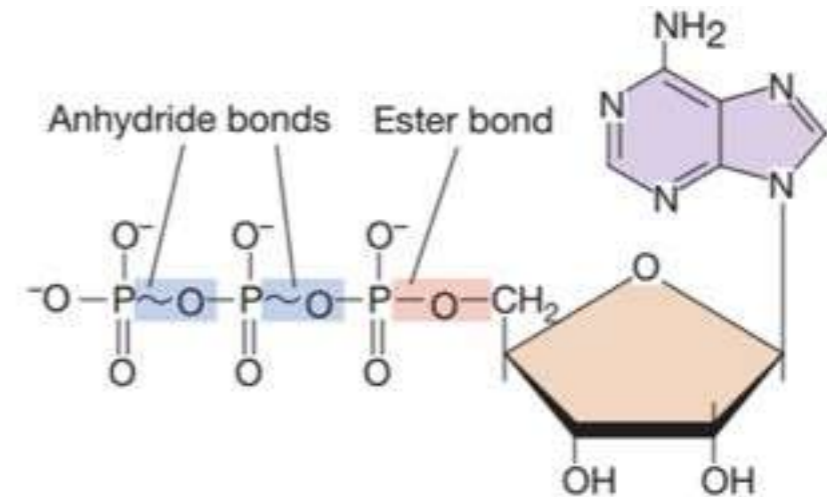
FIGURE 4. Natural half-times of some biological reactions in neutral solution at 25 °C.

WOLFENDEN and SNIDER, 2001

Table 1. Cleavage of Polymers at 25 and 100 °C

reaction	bond $t_{1/2}$		no. of bonds per polymer	$t_{1/2}$ per cleavage event	
	25 °C	100 °C		25 °C	100 °C
protein hydrolysis	400 years	5.5 weeks	123 (RNase A)	4 years	7 hours
polysaccharide hydrolysis	4.7×10^6 years	160 years	10^5 residues (glycogen)	50 years	12 hours
RNA hydrolysis	4 years	9 days	70 residues (tRNA)	20 days	3 hours
DNA hydrolysis	140 000 years	22 years	10^9 residues (human DNA)	1 month	2 hours

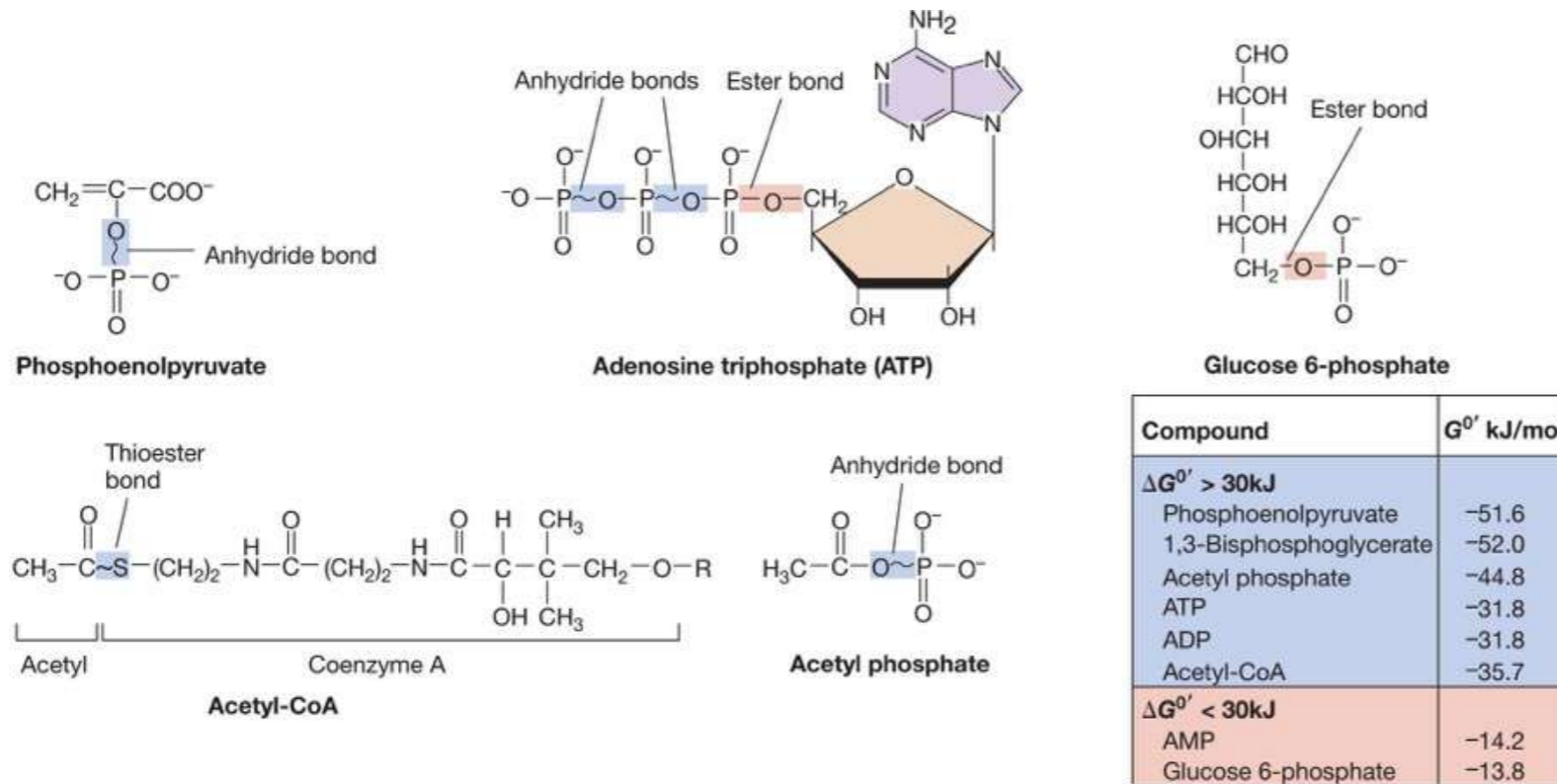
Energy conservation



- ATP generation, adenosine triphosphate
- **ATP the energy currency of the cell** – > cell motility, biosynthetic reactions, replication, cell growth and heredity, its generation relays:
 - 1. **Substrate-level phosphorylation**
 - 2. **Membrane-bound e- transport chain** – > create **H⁺ motive force** that drives ATP synthetase embedded in cytoplasmic membrane
- Earth including biota are a very heterogeneous and complex environment – > thermodynamics (prediction of reactions that are energetically favorable)

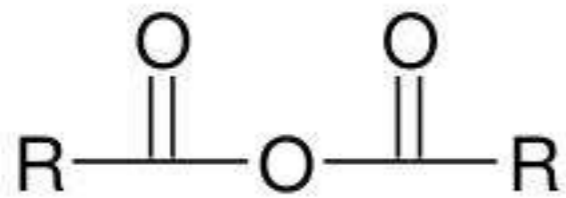
Energy-rich compounds

Madigan et al. 2018

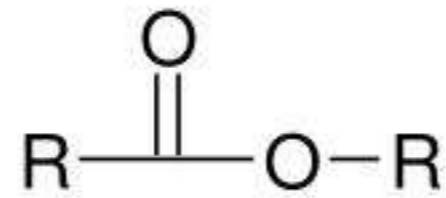


- The energy released from **redox** reactions **fuels energy-requiring cell functions**
- Free energy released in the coupled **exergonic redox** reaction **must first be trapped** by the cell and conserved
- Energy conservation in cells is accomplished through the formation of a set of compounds containing **energy-rich phosphate or sulfur bonds**
- The biosynthesis of these compounds functions as the **free-energy trap**, and their hydrolysis releases this energy **to drive endergonic reactions** ($\Delta G^{0'} > 0$)

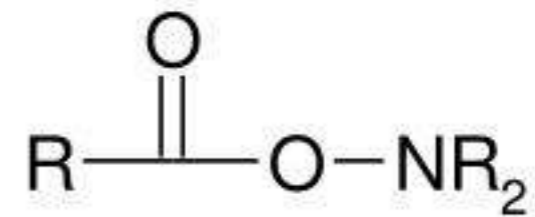
C and P: Anhydrides and Esters



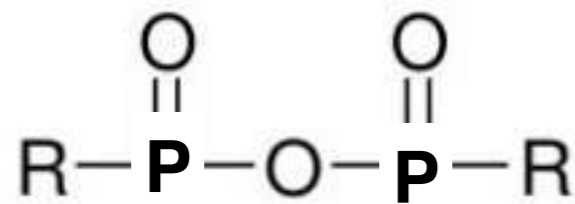
Anhydride



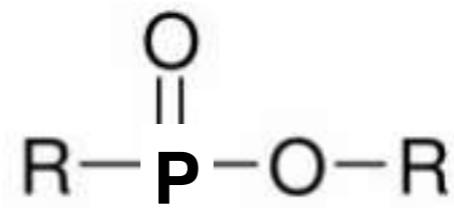
Ester



Amide



Anhydride



Ester

ATP

Electron Donors and Electron Acceptors

- Cells conserve energy released from **exergonic reactions** by **coupling** the reaction to the **biosynthesis of energy-rich compounds**, such as ATP
- Reactions that **release** sufficient **energy to form ATP** require **oxidation–reduction** biochemistry
- An **oxidation** is the **removal of an electron** (or electrons) from a substance, and a **reduction is the addition of an electron** (or electrons) to a substance: [OILRIG](#)
- In redox reactions, we refer to the **substance oxidized** as the **electron donor**, and the **substance reduced** as the **electron acceptor**
- By convention, in writing a redox couple, the **oxidized** form of the couple is always placed on the **left** (before the forward slash) followed by the **reduced** form **after** the forward slash

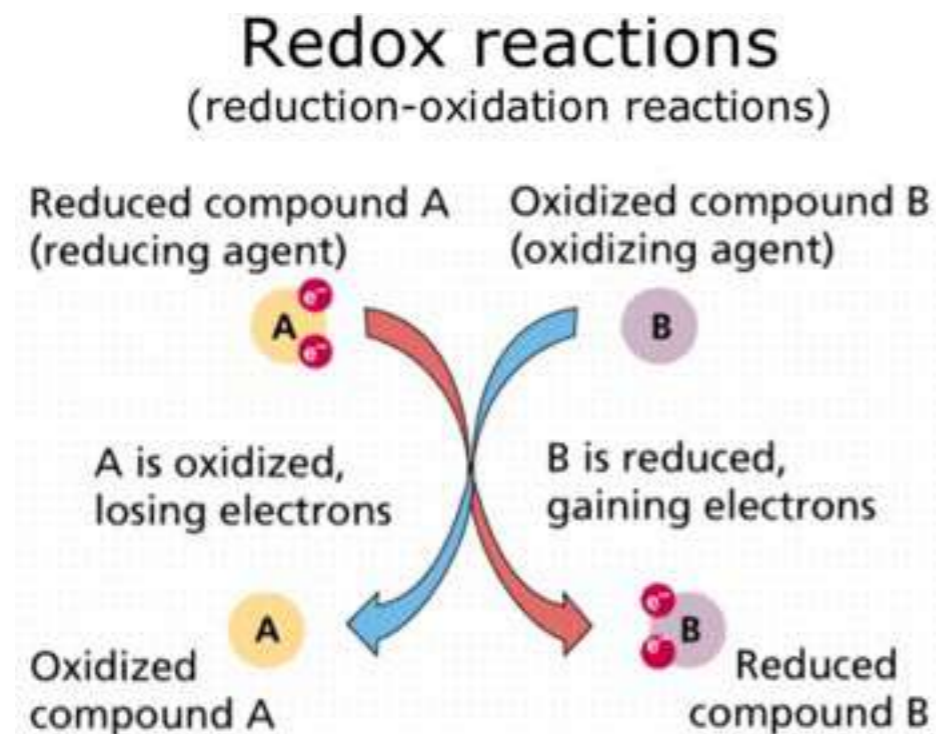
Electron Donors and Electron Acceptors

- **Substances differ** in their tendency to donate or accept electrons
- This **tendency is expressed as their reduction potential** (E° , standard conditions), a value measured in volts (V) compared with that of a reference substance, H_2
- When two redox couples react, the **reduced substance** of the couple (E° is < 0 , negative) **donates electrons** to the **oxidized substance** ($E^{\circ} > 0$, positive)
- The half reaction with the more negative E° proceeds as an oxidation and is therefore written in the opposite direction
- **Redox reactions: reactions consisting of the movement of electrons between substrates constituting reduction (addition of electrons) and oxidation (removal of electrons) reactions**

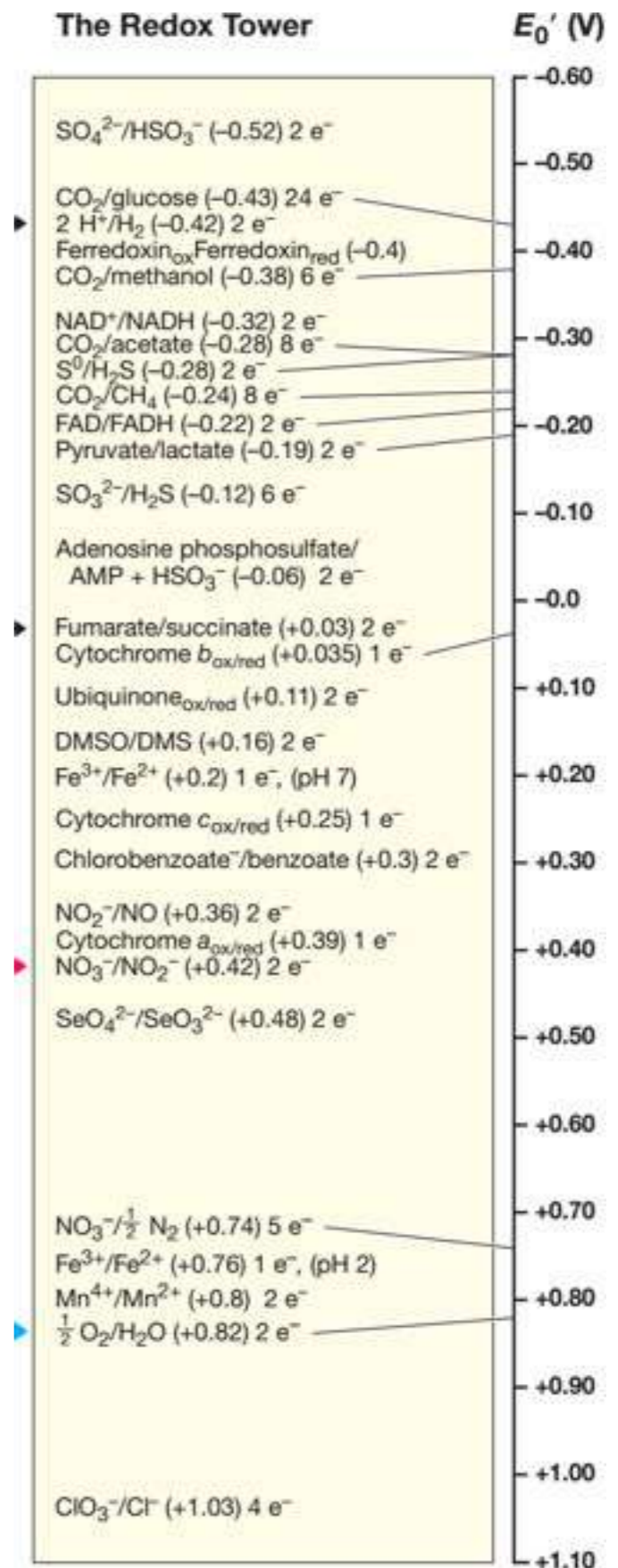
Redox Tower

Reduced

- Redox couples are arranged from the **strongest donors at the top ($E_0' < 0$)** to the **strongest acceptors at the bottom ($E_0' > 0$)**
- The larger the difference in reduction potential between electron donor and electron acceptor, the **more free energy is released** ($\Delta G^0'$ can be computed via Nerst equation from reduction potential)

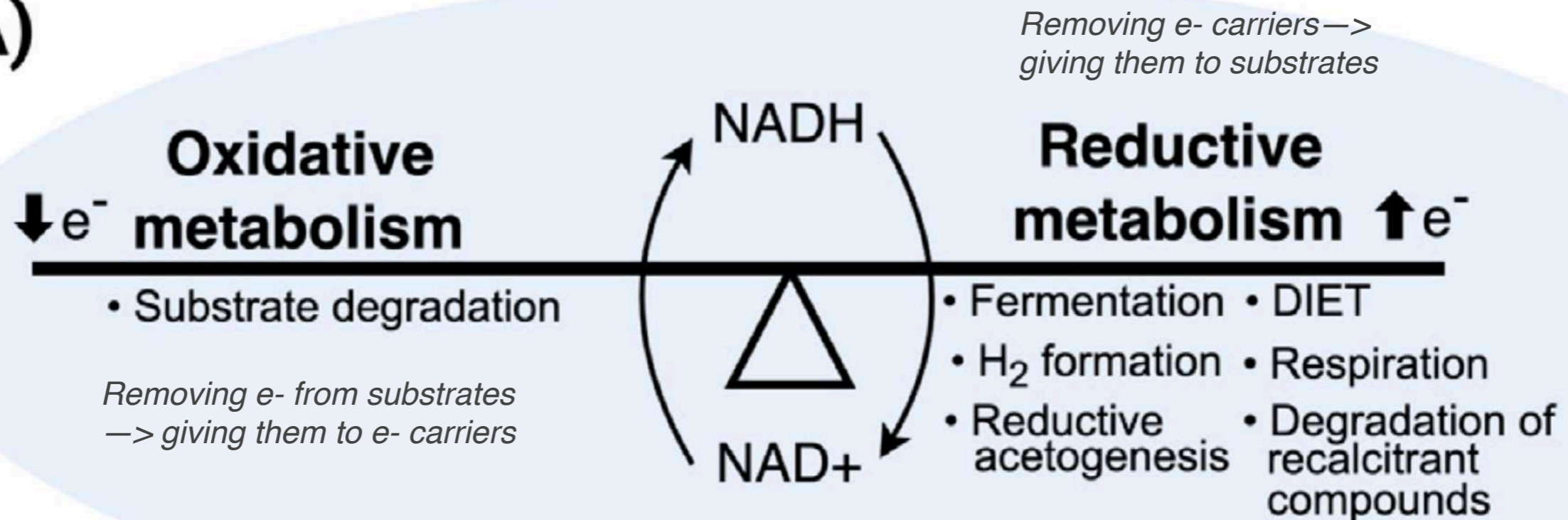


Oxidized



Redox Tower for electron carriers molecules

(A)



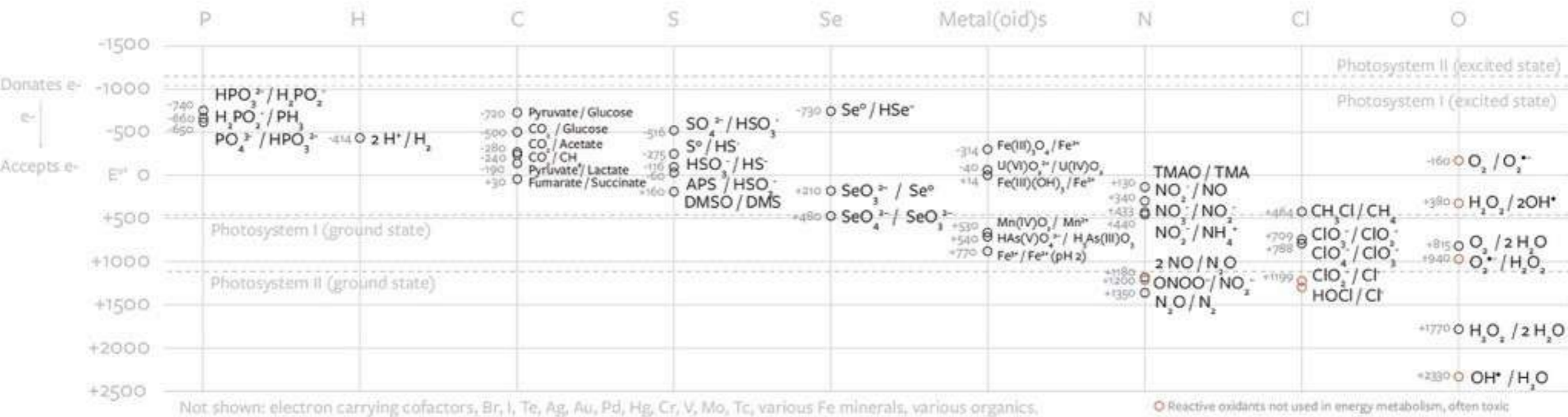
NAD⁺ and NADH balance in microbial communities: microbial processes constantly balance NAD⁺ (oxidized) and NADH (reduced) levels

Substrate breakdown (oxidation) generates NADH, while various pathways (respiration, fermentation) reoxidize NADH

Redox couples in the environment

Redox couples and potentials (mV) for elements common in biology at pH 7 and temperature 25 C *

Redox potential indicates the propensity for a compound to transfer electrons to another compound. A more-negative redox potential means a compound is more likely to donate electrons (e⁻). All of life gets its energy by capturing the change in potential energy from the transfer of electrons from the reducing compound to the oxidizing compound.



Across periodic table

High diversity of key molecules in the Electron Transport Chain

