Bioscience & Bioengineering 101: BB101

Lecture – 12

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Metabolism and Evolution

Outline

- Metabolism
- Evolution

Indian railway network

WHAT IS SHOWN

- Cities and towns of India connected by rail
- **Entities**

WHAT IS NOT SHOWN

- Number of trains in each route
- What determines how many trains operate in a route
- **Flux (dynamic movement)**

https://edugeneral.org/blog/geography/air-transport-in-india/

Mumbai city map

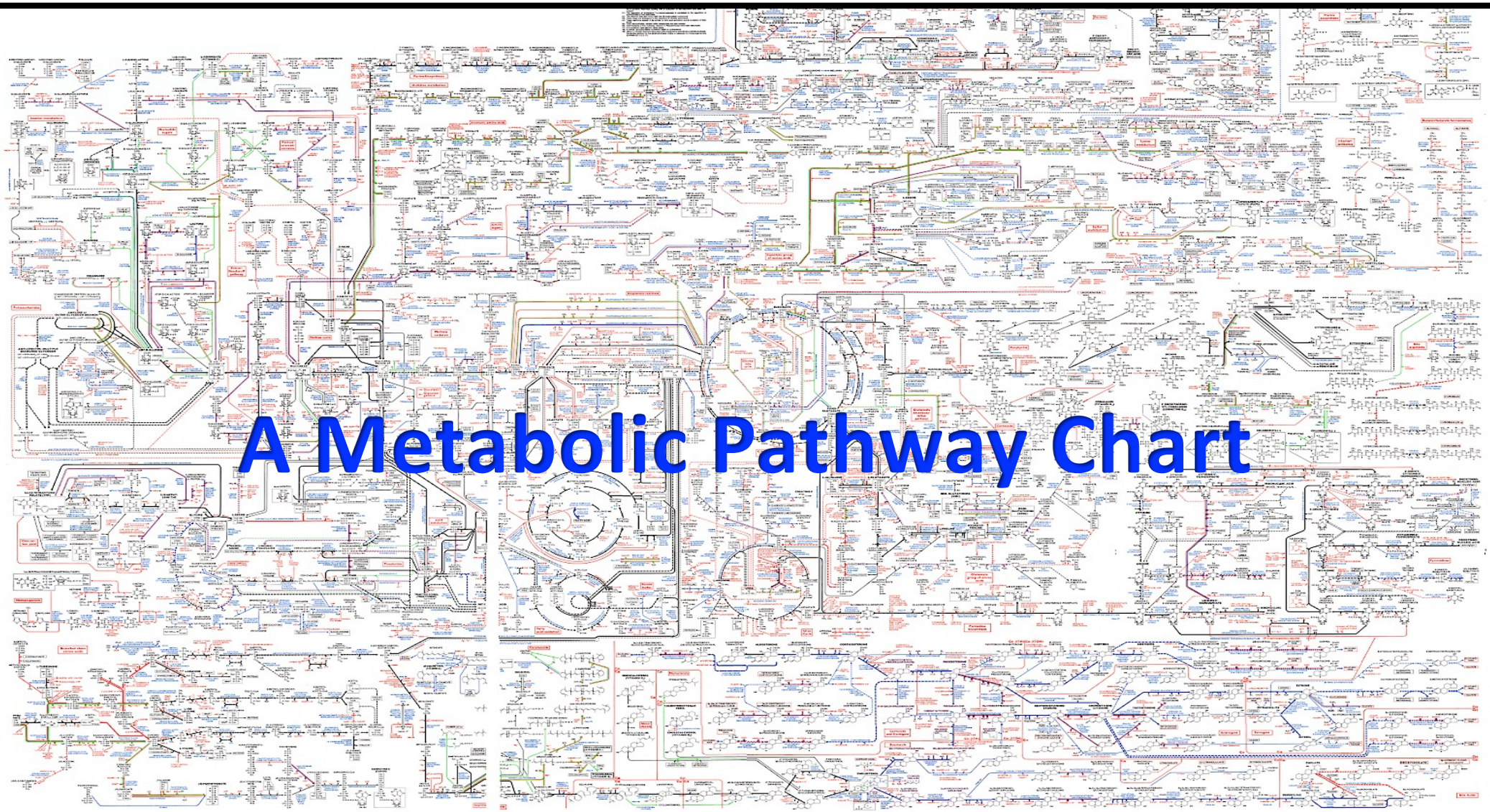
WHAT IS SHOWN

- Various locations connected by road (road network)

WHAT IS NOT SHOWN

- Number of vehicles in each road
- What determines how many vehicles ply on a road
- **Temporal variations**

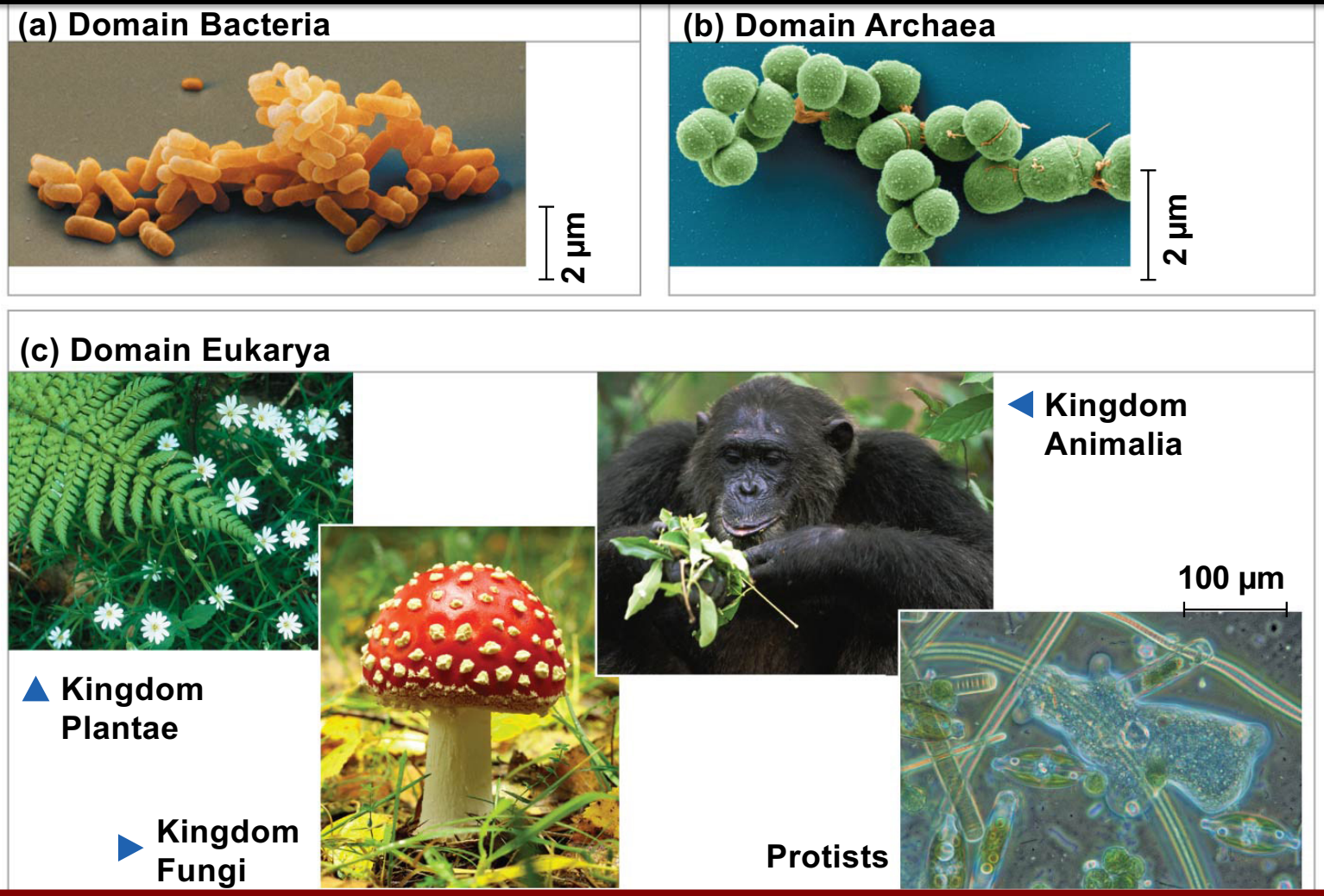
https://edugeneral.org/blog/geography/air-transport-in-india/


A Metabolic Pathway Chart

Metabolic pathway chart

- A metabolic pathway chart is like a rail or road map
  - A dot represents a metabolite i.e., chemical compound
  - A line connects compounds that can be inter-converted
- Metabolism is the totality of an organism's chemical reactions
- Metabolism is an emergent property - that arise from the orderly arrangement and/or interactions of a set of components / parts
  - The parts / components by themselves do not have the "property"

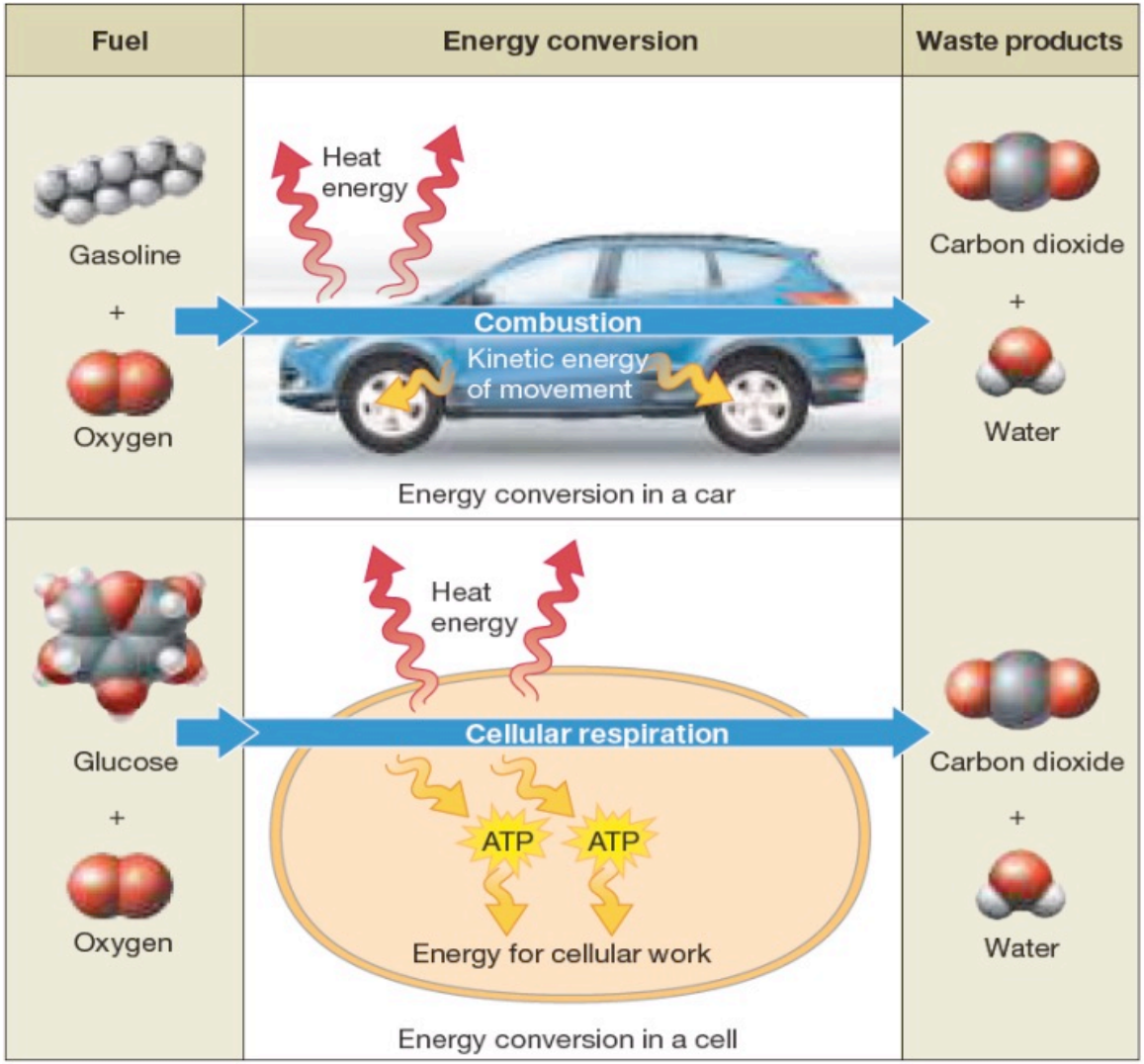
We are discussing metabolism of … all organisms



Cell – a thermodynamic open system

- From the view point of thermodynamics, a cell is an open system
- Cells exchange both heat and matter with the surroundings
- To do this "work", cells need energy
- Cells uptake nutrients, metabolize them, and excrete waste products

Living systems work within the framework of the laws of thermodynamics



▲ **Figure 5.10** An illustration of the two laws of thermodynamics: transformation of energy and increase in entropy

Source of biomolecules?

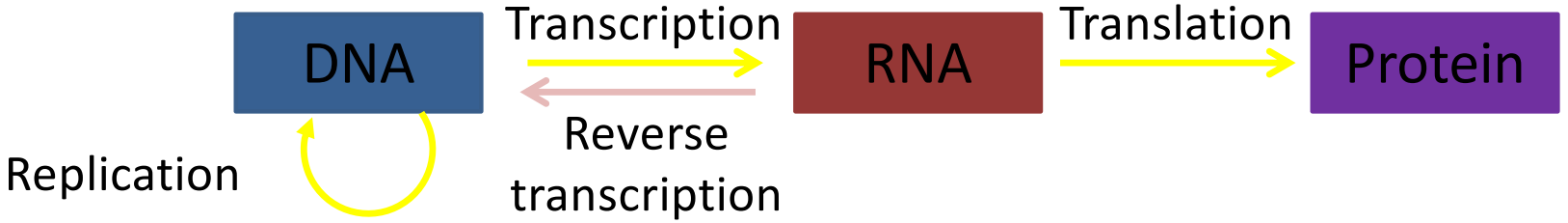
Two of the key characteristics of life:

- Reproduction
- Growth and development

A few key components of a cell

- DNA, protein, carbohydrates, lipids
- Cyclic AMP, GTP, …

From where do organisms get these biomolecules?



Central Dogma is not the whole story.
It is integrated with metabolism e.g. where do the precursors for DNA come from?

Nutrient requirements…

Two important requirements: Source of carbon & energy

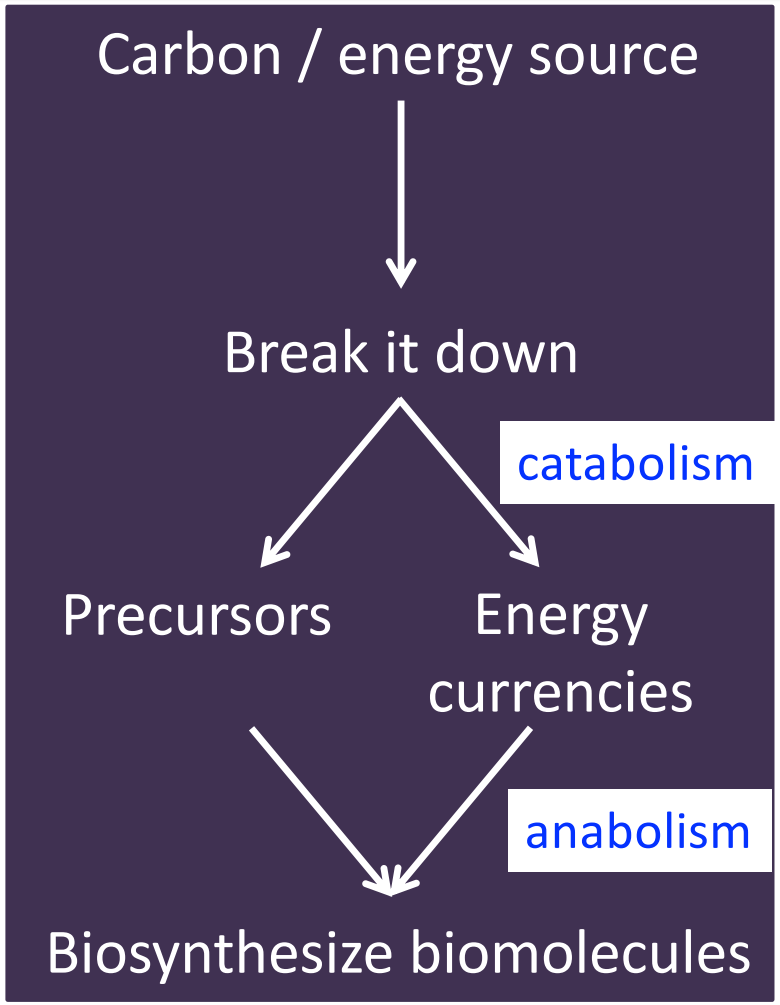
Source of energy: sunlight
Source of carbon: atmospheric CO_2
(auxotrophs; e.g. plants)

Source of energy: glucose
Source of carbon: glucose
(heterotrophs; e.g. animals)

- Many other compounds are known to be used as carbon and energy sources (e.g., lactose, ethanol, glycerol, cholesterol, …)

Extract and biosynthesize

- Metabolism as a whole manages the energy and material resources of a cell
- Catabolism – breaking down energy and/or carbon source to precursors to extract energy
- Anabolism – use energy and precursors to build up required biomolecules

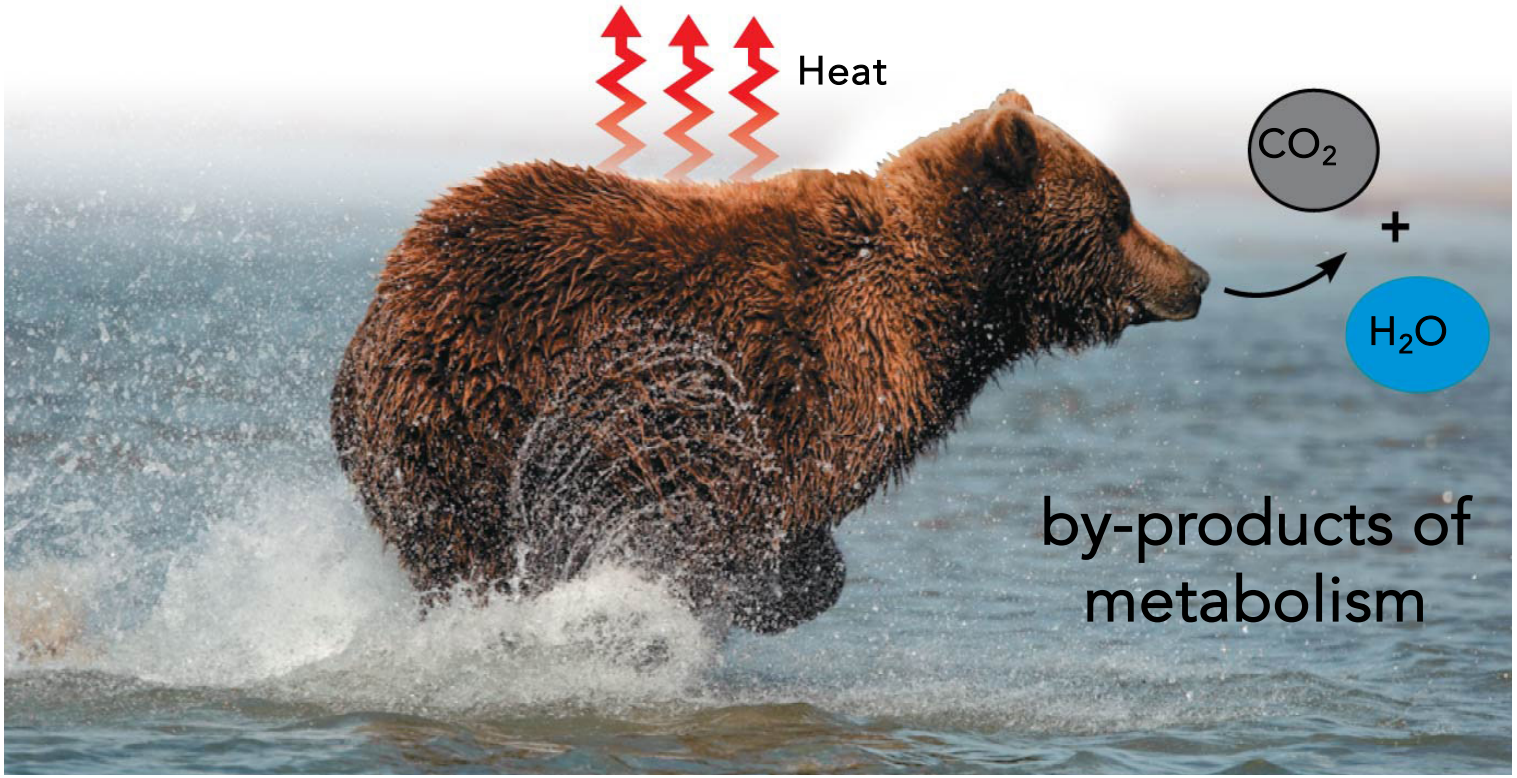


Interconversions of energy forms

The brown bear “metabolizes” the fish it is eating to extract precursors for biomolecules as well as required energy

First law of thermodynamics - Energy can be transferred or transformed, but cannot be created or destroyed

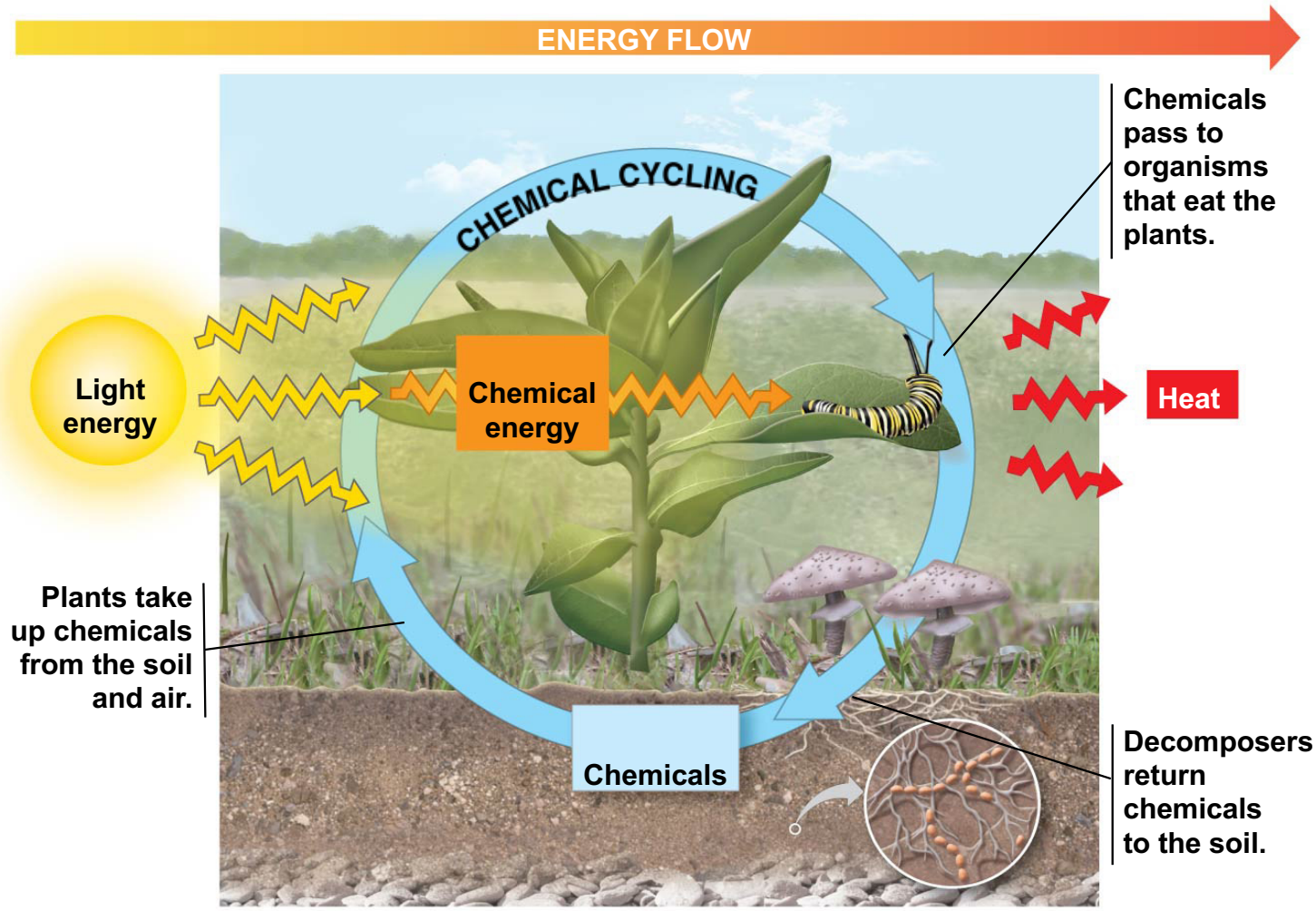
Life and disorder



Second law of thermodynamics: every energy transfer or transformation increases the disorder (entropy) of the universe

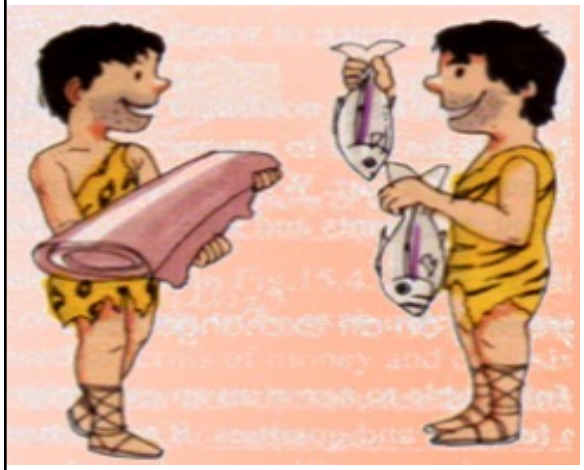
Organisms are "organized" at the cost of the system.

Energy and matter are connected on the planet



Energy and carbon cycles

Barter system: Utility of currency (money)



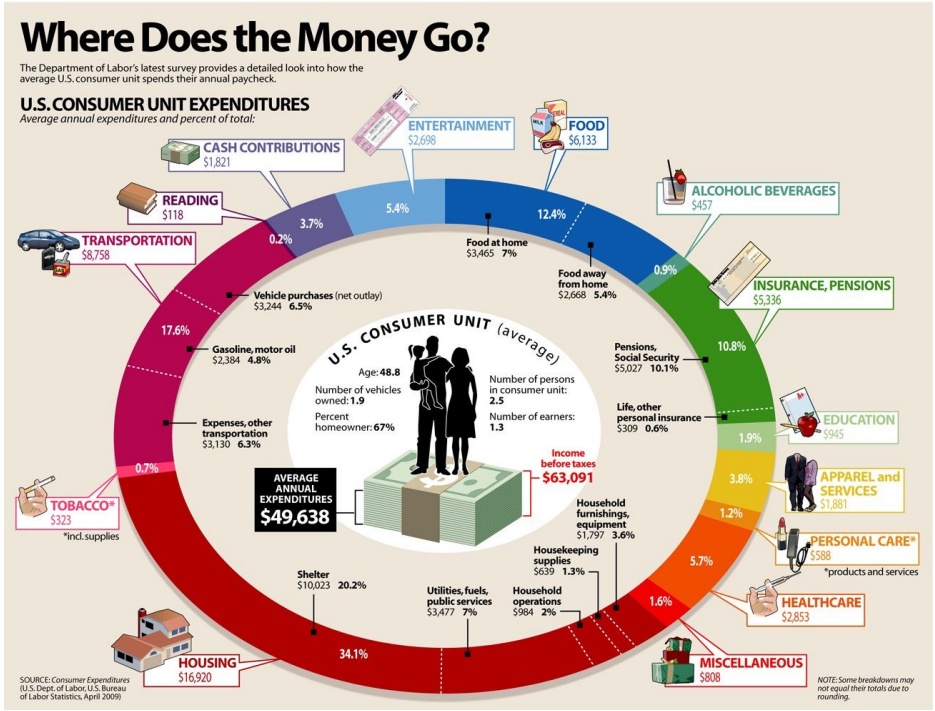
I want your product

I don't want your product

You don't want my product

No barter, only money

Quantify goods and services in terms of “currencies”
Exchange goods and services for “currencies”



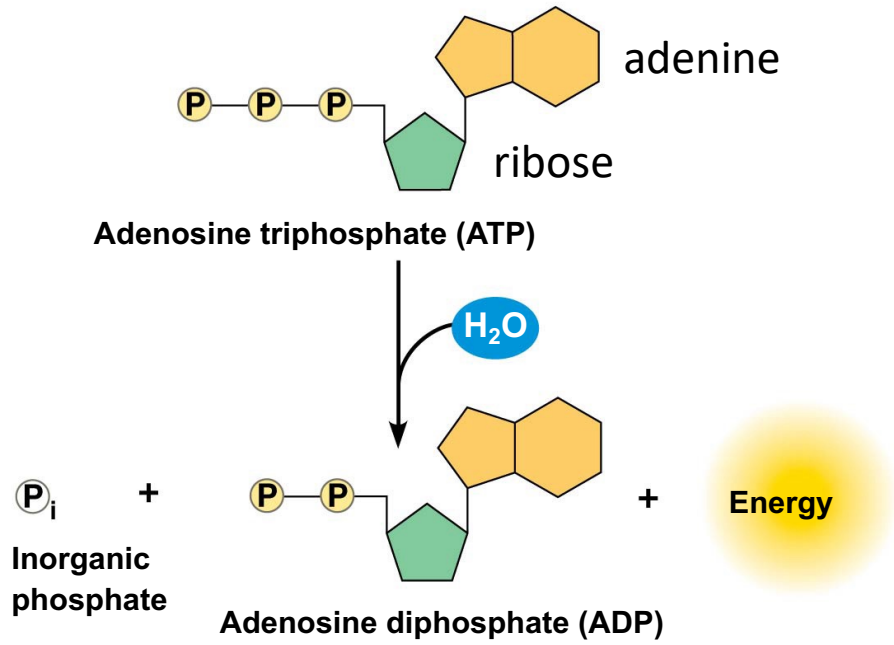
No barter, only money

Organisms metabolize energy source (nutrient) and extract "useful energy" in the form of energy currencies

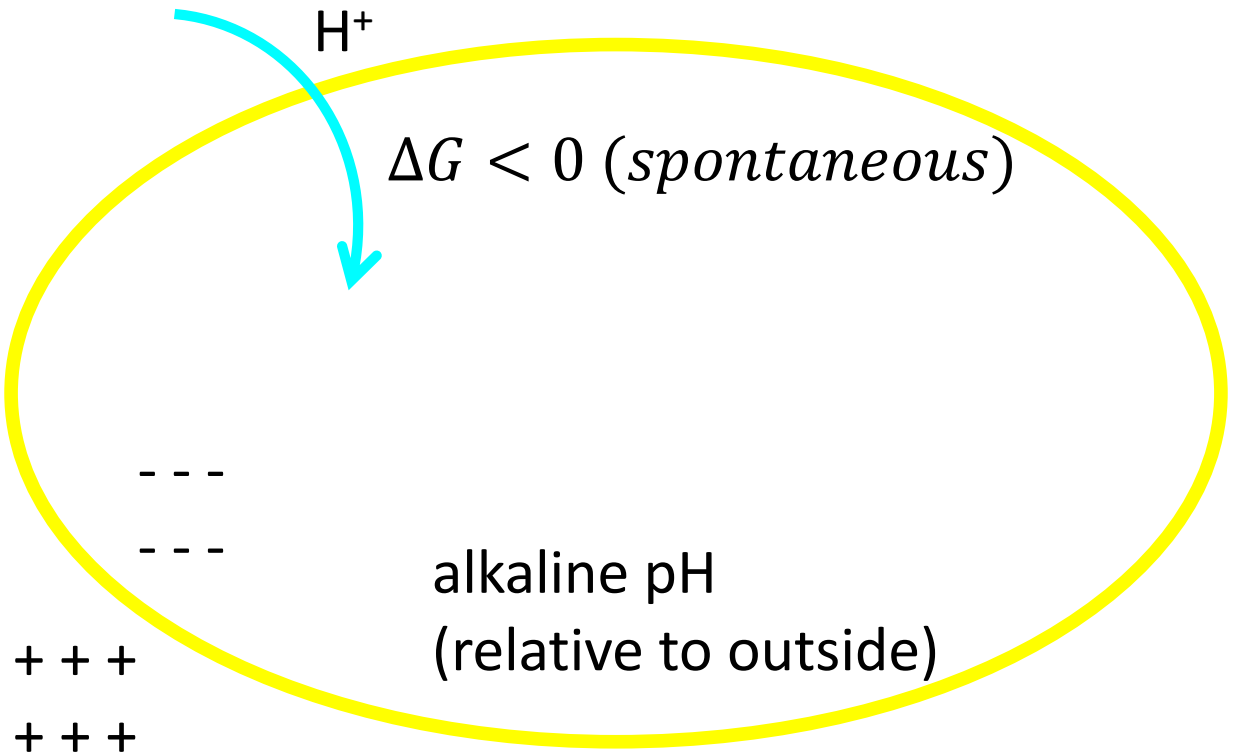
Energy extracted is utilized for performing "work"

(1) Adenylate pool is a widely used energy currency

- ATP: an energy shuttle
- High energy phosphate bonds can be hydrolyzed, energy is released upon hydrolysis
- Energy comes from the chemical change to a state of lower free energy
- Note that Adenylate pool (AMP, ADP, ATP) is the energy currency
- Other high energy bonds: nucleotides, creatine phosphate

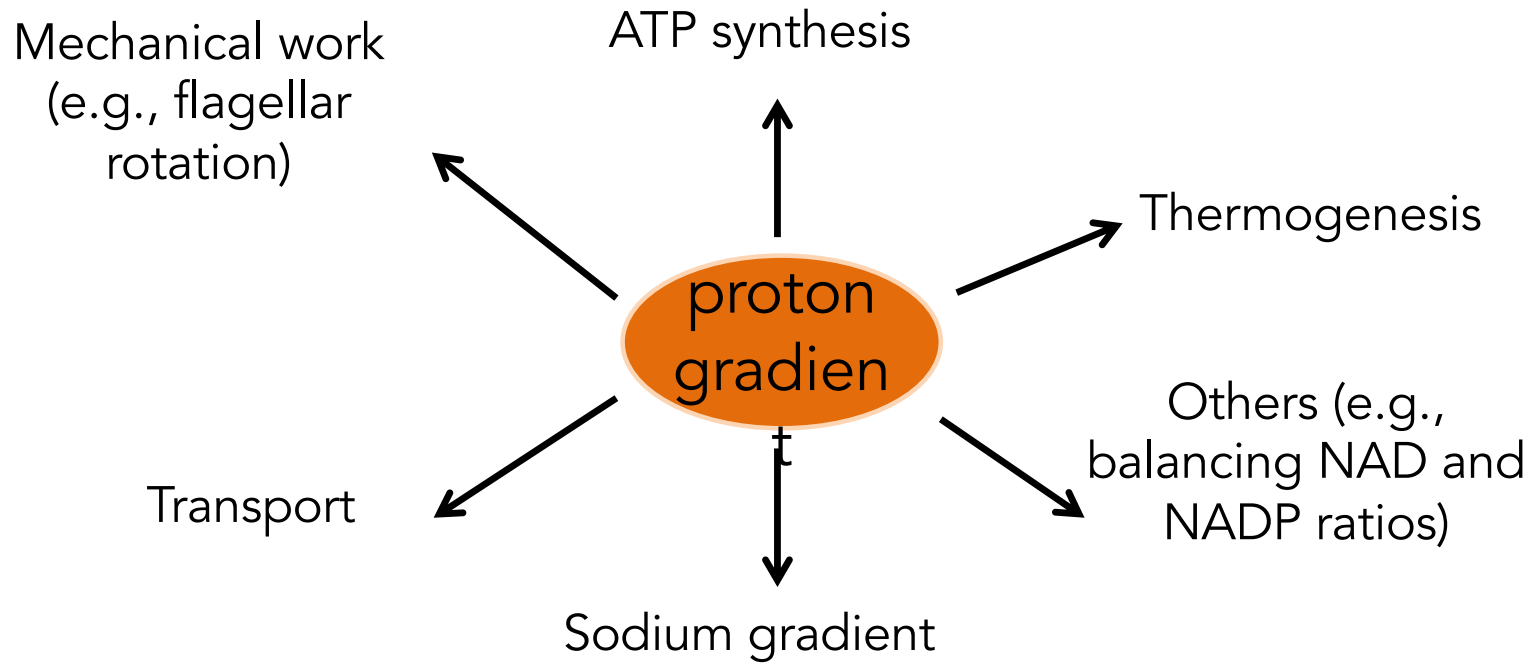


(2) Ion (proton) gradients as energy currencies



G: Gibbs free energy
Amount of energy used for doing work

(2) Ion (proton) gradients as energy currencies



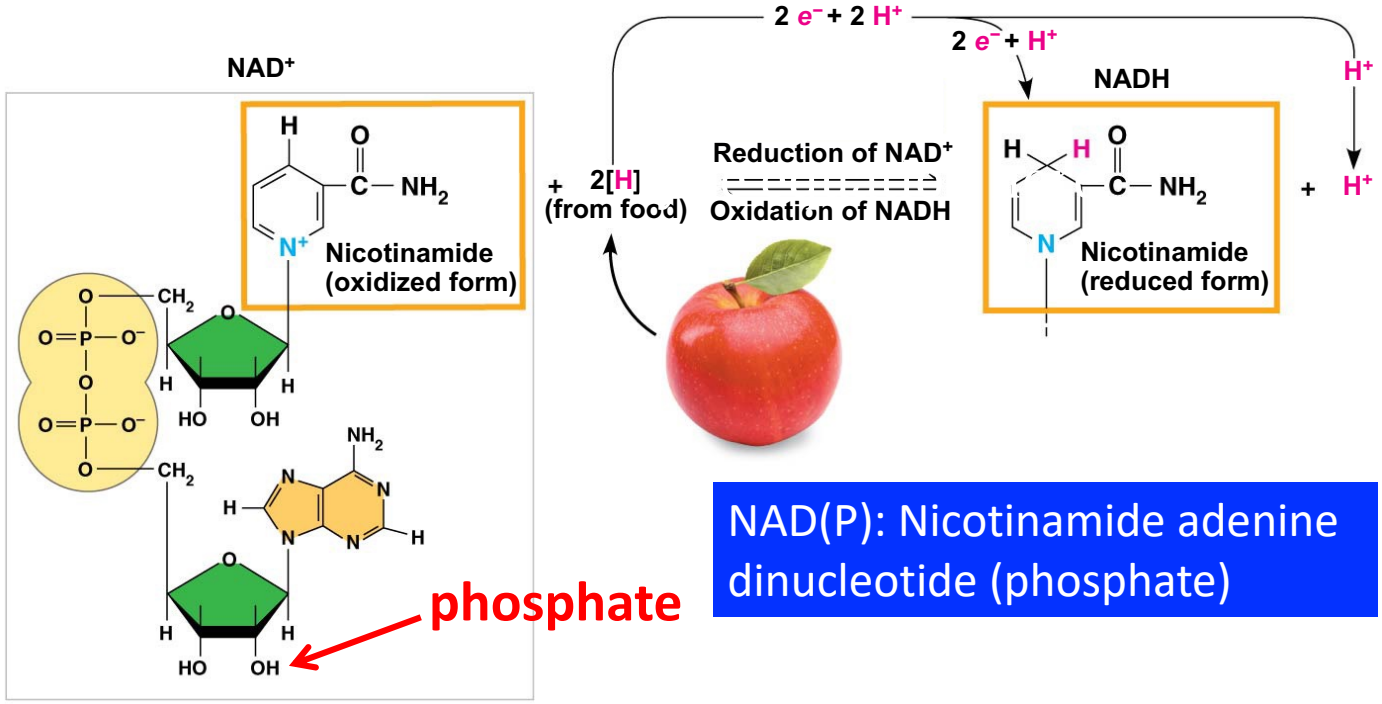
Proton gradients evolved before ATP
Primitive life conditions had pH gradients

A semi-permeable membrane suffices to generate this currency

(3) NAD and NADP: electron shuttles as energy currencies

$$NADP^+ + 2H^+ + 2e^- \rightleftarrows NADPH + H^+$$

$$NAD^+ + 2H^+ + 2e^- \rightleftarrows NADH + H^+$$



NAD(P): Nicotinamide adenine dinucleotide (phosphate)

NAD(P): Nicotinamide adenine dinucleotide (phosphate)

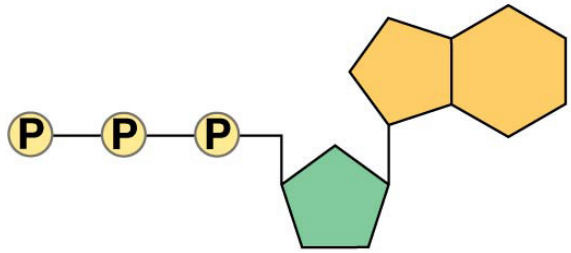
Why 3 currencies? Diversify!

Cash (liquidity)

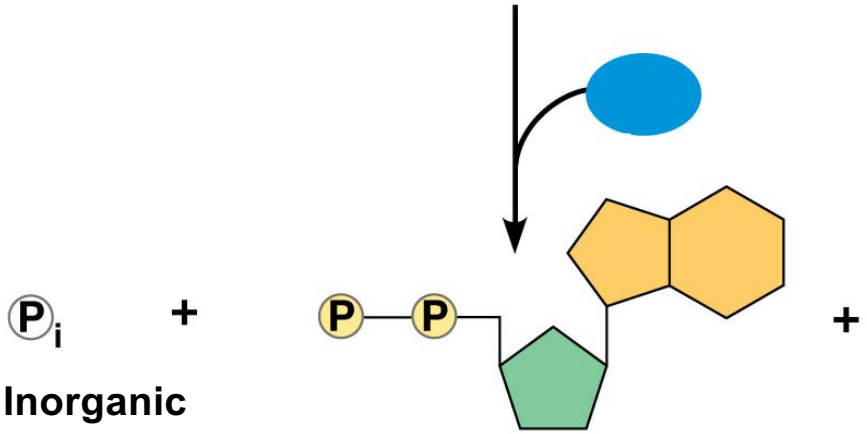
Gold (stability)

Stock market (returns)

ATP hydrolysis releases energy



Adenosine triphosphate (ATP)



Inorganic phosphate

Adenosine diphosphate (ADP)

ATP hydrolysis continues to release energy

IF AND ONLY IF

ATP is continuously replenished

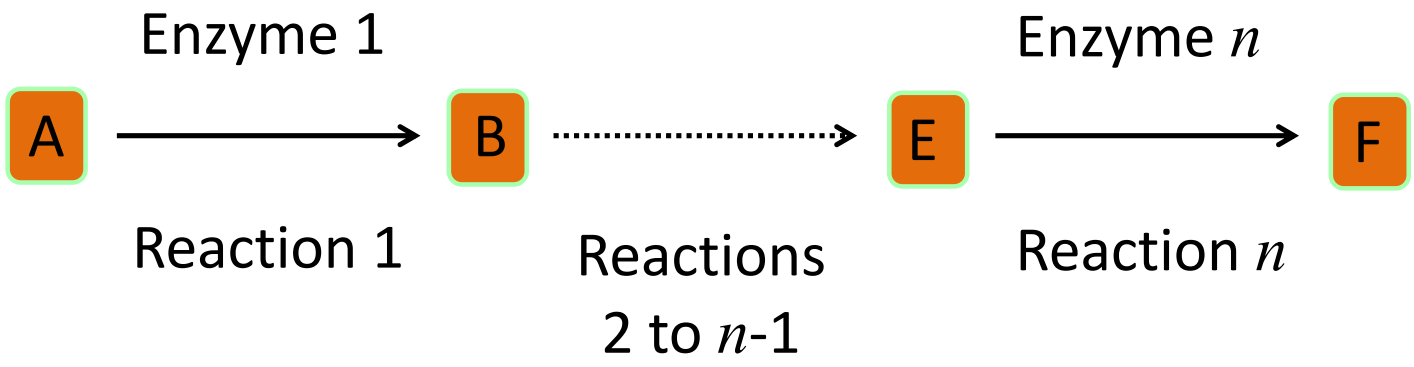
AND

ADP, P_i are continuously depleted

How to do this?
Simple:
Use ADP and P_i to synthesize ATP

Unlike human currency, cells do not store their energy currency, instead make and utilize as required.

Metabolic pathways



A metabolic pathway is a series of steps by which one compound is converted to another

Each step can generate molecules and energy for the cell to utilize

Each step is catalyzed by a specific enzyme

Energy available from oxidation of glucose

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$$

ΔG = -686 kcal/mol

Oxidation of glucose to carbon dioxide

1. In one step
2. In multiple steps

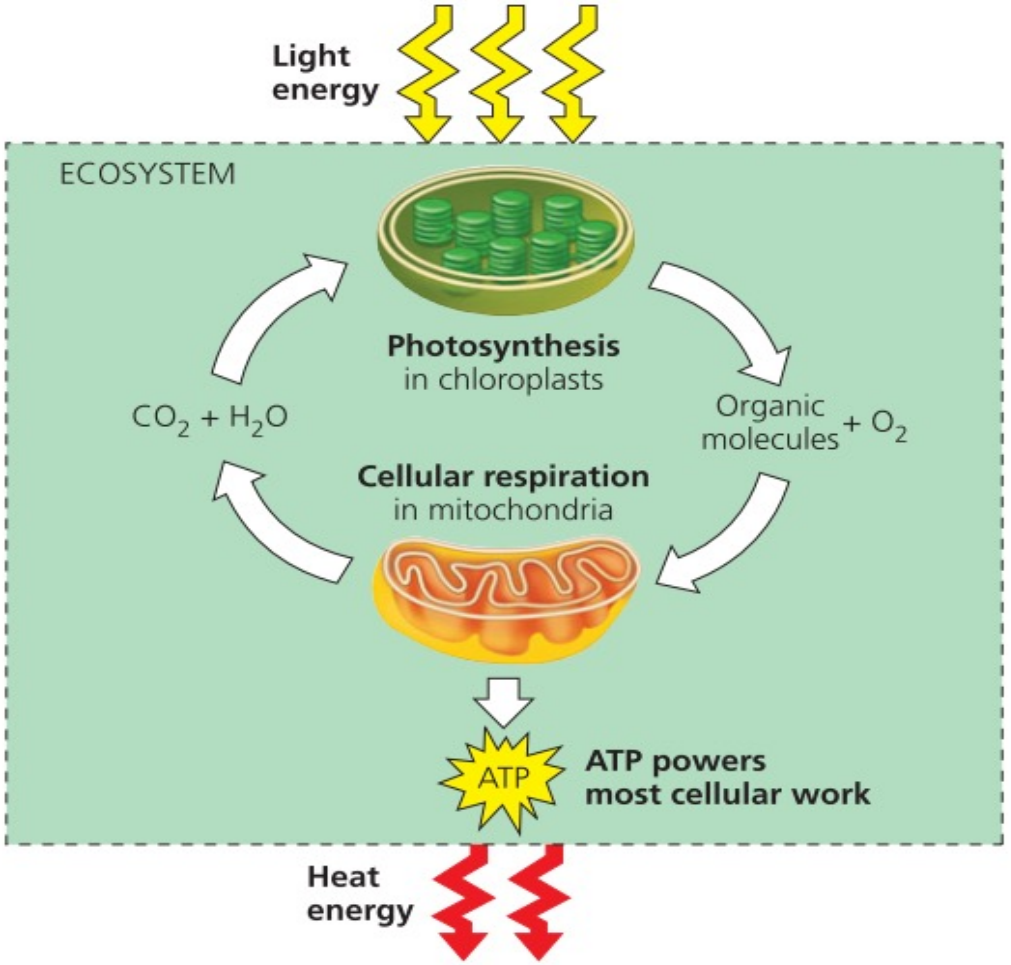
If oxidized in one step:

- Need to use all the available free energy at once
- Lose out on intermediates which can be precursors

Flow of energy to sustain life capable of doing work

How cells harvest the chemical energy stored in organic molecules to generate ATP --- cellular respiration (catabolism)

How plants use waste product of respiration (CO_2 + H_2O) to make organic molecules ---- Photosynthesis (anabolism)



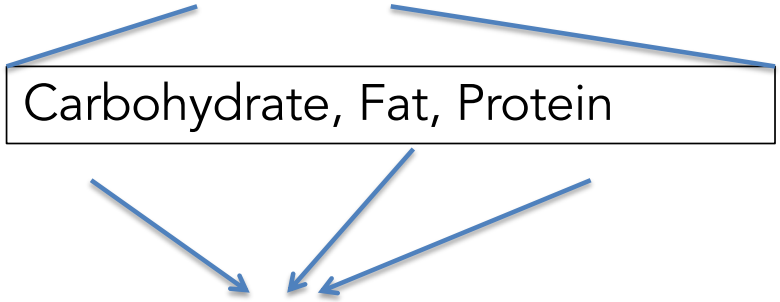
Cellular respiration : Catabolism (destructive)

- Respiration involving O_2 -- Aerobic respiration
- Respiration without O_2 -- Anaerobic respiration

Aerobic respiration

$$\text{Organic compounds} + \text{Oxygen} \rightarrow \text{Carbon dioxide} + \text{Water} + \text{Energy}$$

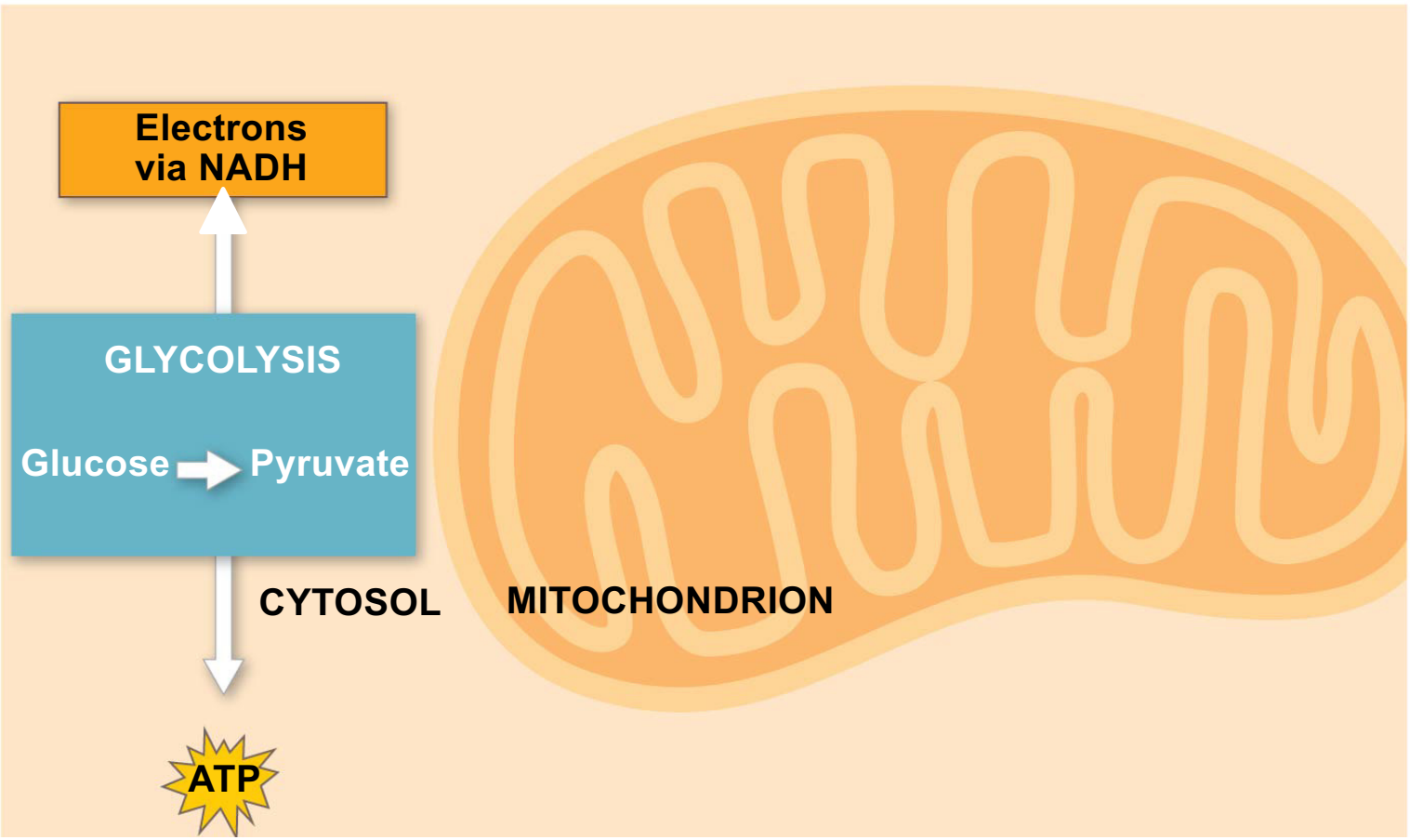
(Food)



Glucose

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O + \text{Energy (ATP + heat)}$$

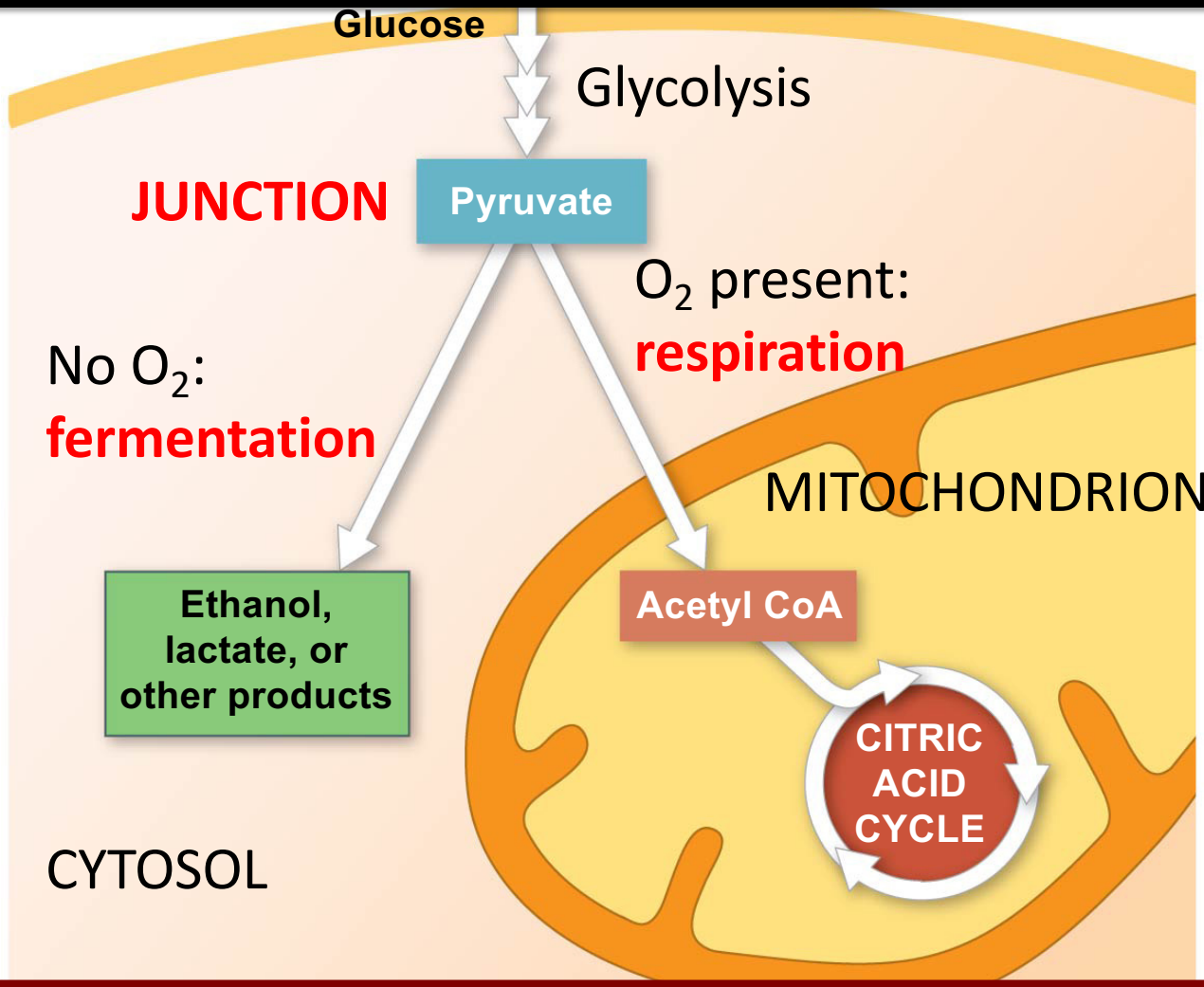
Cellular respiration: stage 1



Glycolysis: breaking down of glucose to pyruvate

Fermentation or respiration?

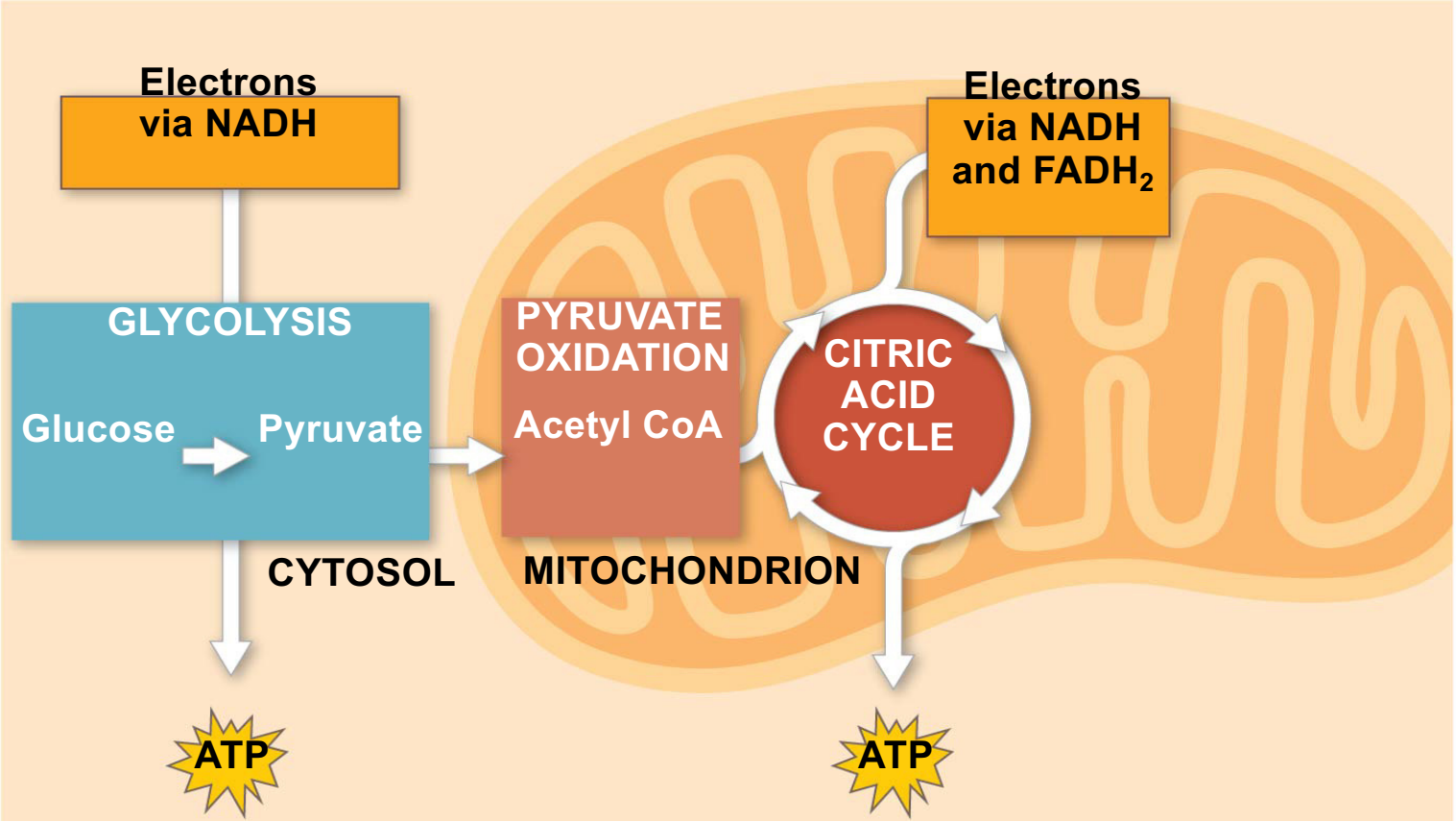
muscle cells (intense exercise)



brain cells – cannot ferment

Figure 9.18

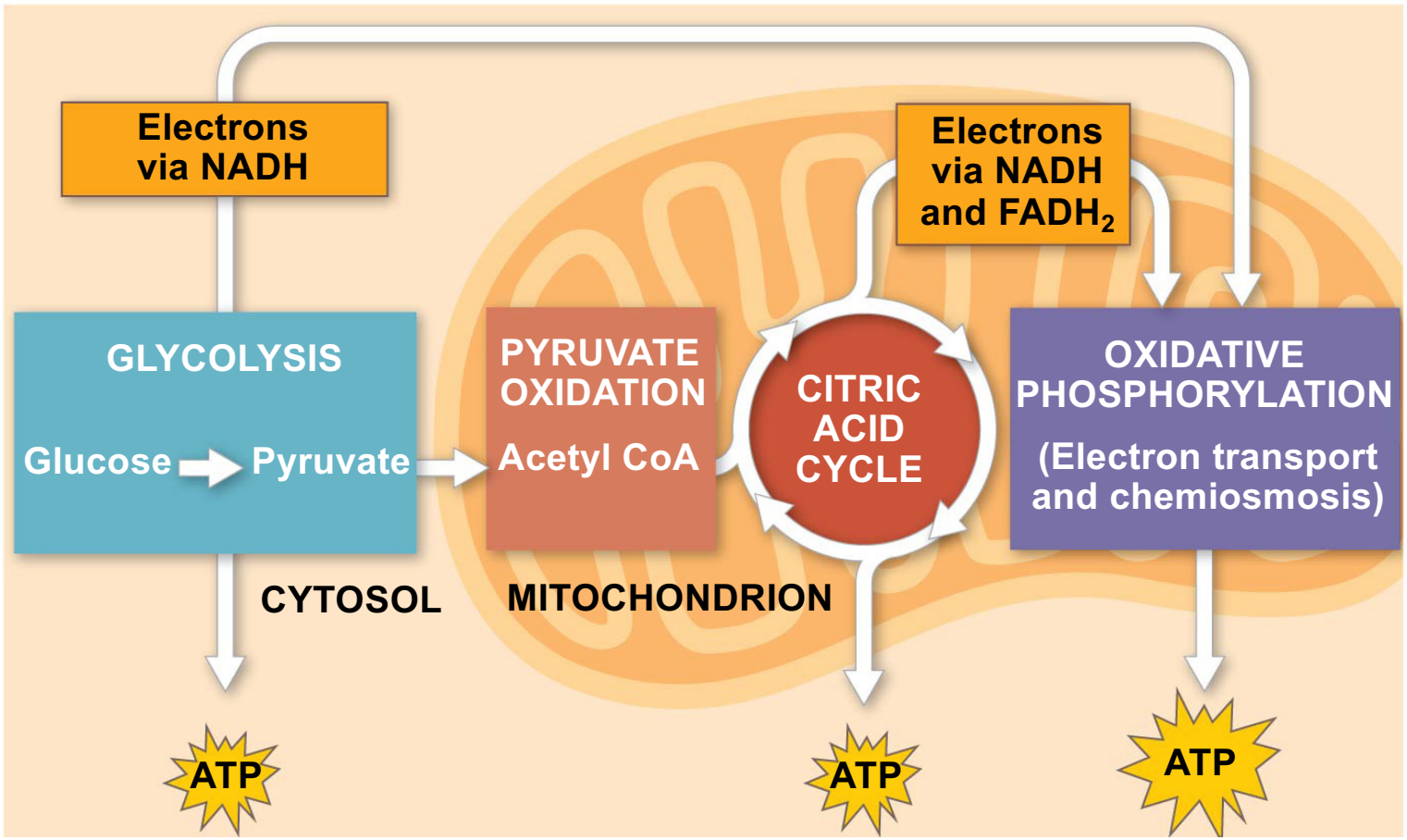
Cellular respiration: stage 2



Nnicotinamide adenine dinucleotide (NAD Flavin adenine dinucleotide hydride (FAD)

Pyruvate to acetyl coenzyme A, then to CO_2 via TCA cycle

Cellular respiration: stage 3



Using NADH to synthesize ATP

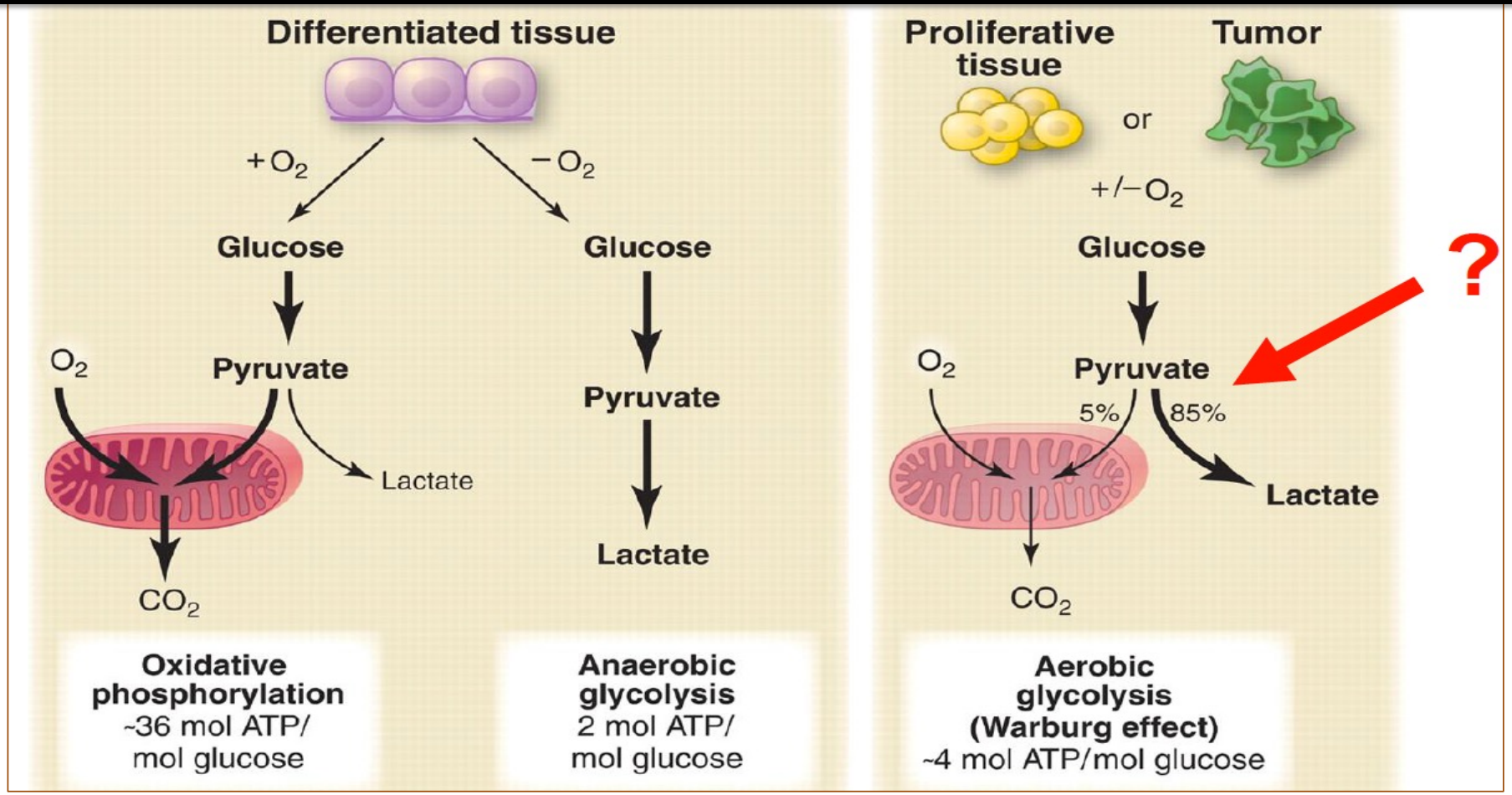
Chemiosmosis

Peter D Mitchell
(1920-1992)

Proposed in early 1960s that NADH oxidation and ADP phosphorylation are linked by a proton gradient

No one believed him – had to set up lab in a house
Persisted with his idea – designed experiments to prove – culminated in the award of Nobel prize in 1978

Food for thought - Link between Metabolism & Cancer



Vander Heiden, Cantley & Thompson (2009) Science 324:1029-1033

Warburg effect

Otto H. Warburg
(1883-1970)
Image: Wikipedia

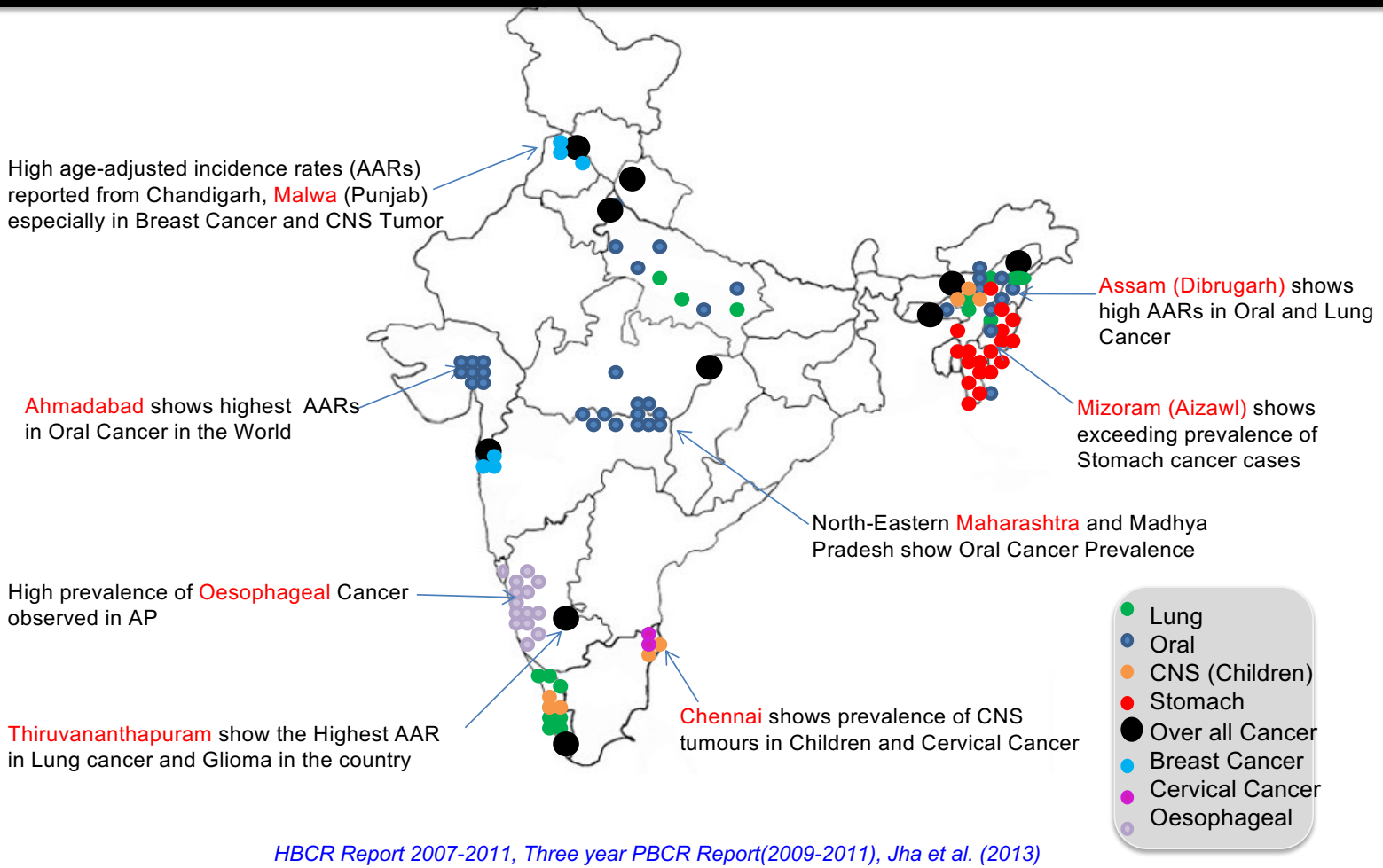
- Cancer cells: high rate of glycolysis
- *Lack of oxygen due to fast cell division*

- Shut down mitochondria
  - Incomplete oxidation – need for precursors
  - Avoid generating reactive oxygen species

- Angiogenesis: formation of blood vessels
- Promoted in cancer – to get more oxygen

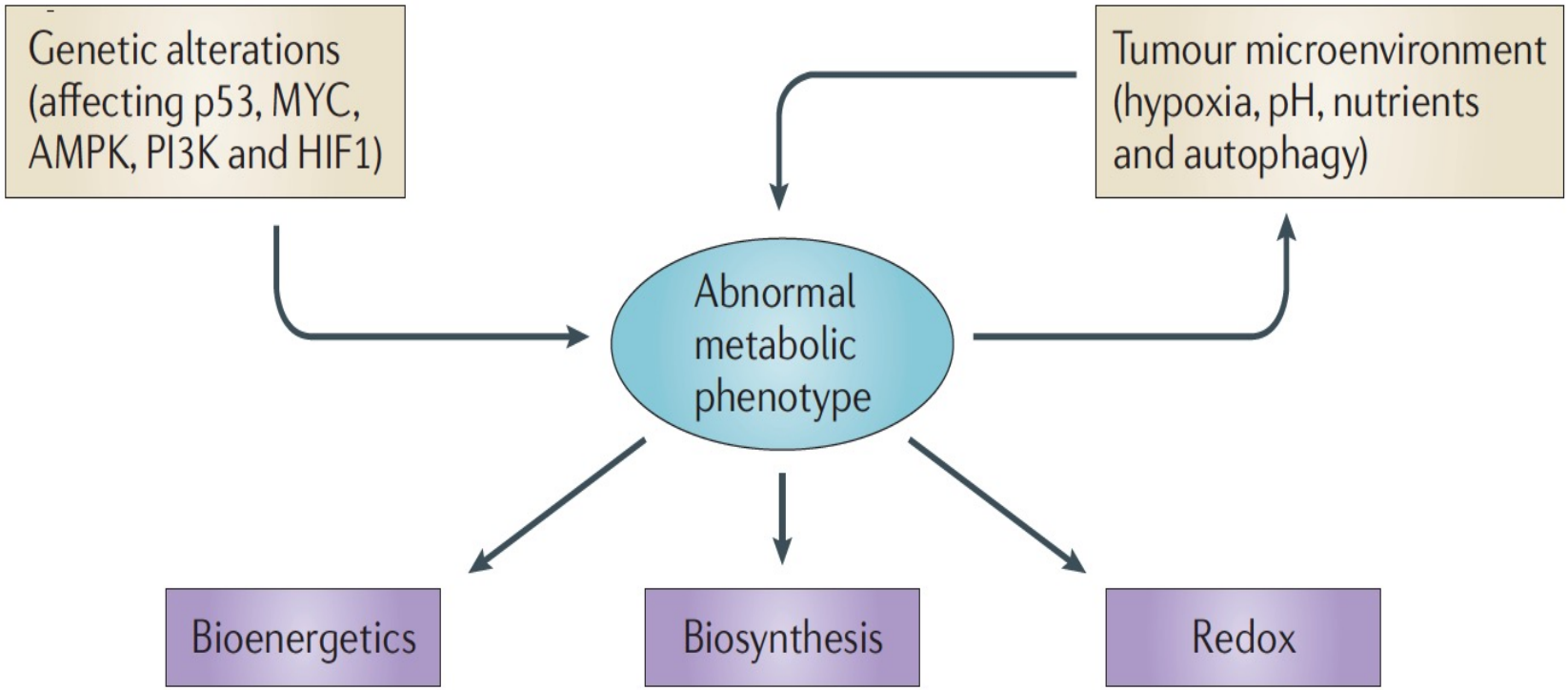
- Cancer cells – heterogeneous
- Some ferment, others respire – depends upon their location relative to blood vessels

Food for thought: Geographic Prevalence of Cancers in India



HBCR Report 2007-2011, Three year PBCR Report(2009-2011), Jha et al. (2013)

Cancer Metabolism



Determinants of the tumour metabolic phenotype?

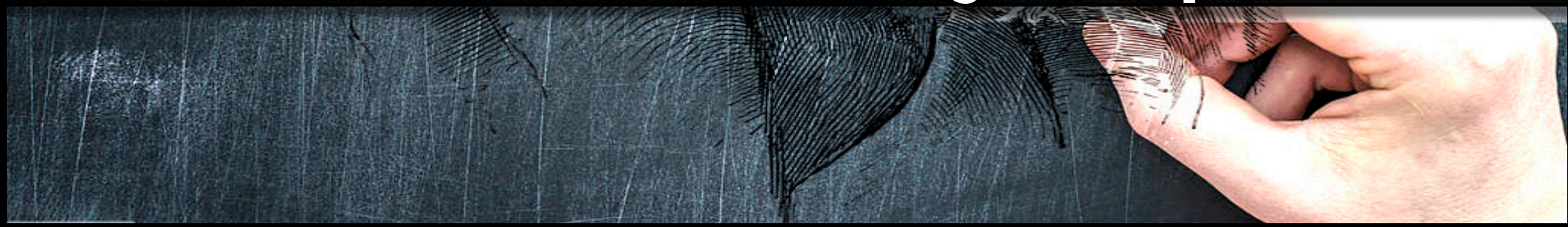
Cairns et al. 2011

PET Scan

- High uptake of glucose observed in many tumours
- Detection and monitoring of human cancers by Fluoro-deoxyglucose Positron Emission Tomography (FDG-PET)

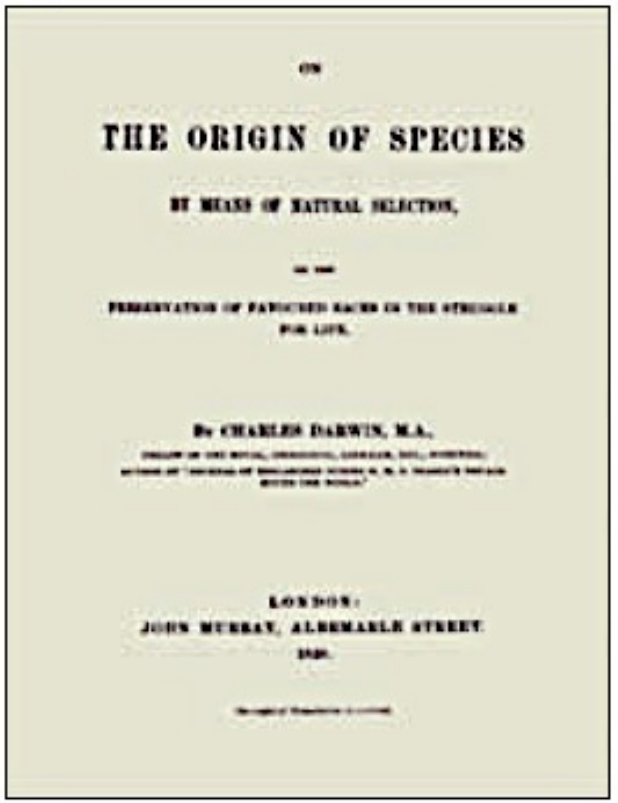
PET scan of a patient with lung carcinoma

Evolution: Darwin and Origin of Species



Darwin and Evolution

- The book that forever changed biology
- On "The Origin of Species" by Means of Natural Selection-1859
- Darwin presented evidence that the today's organisms are descendants of ancestral species
- Darwin proposed a mechanism for the evolutionary process, "natural selection"


ON

THE ORIGIN OF SPECIES

BY MEANS OF NATURAL SELECTION,

OR THE

PRESERVATION OF FAVOURED RACES IN THE STRUGGLE FOR LIFE.

By CHARLES DARWIN, M.A.,

LONDON:
JOHN MURRAY, ALBEMARLE STREET.
1859.

Charles Darwin & Voyage of the Beagle

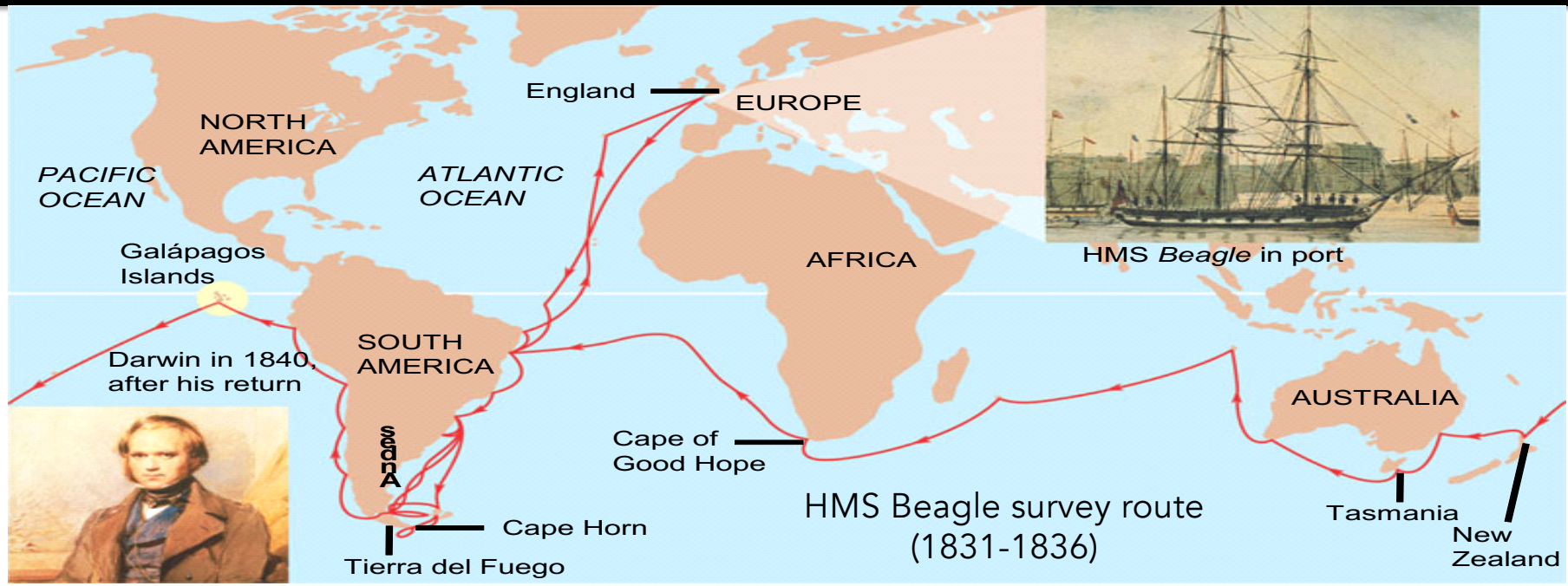
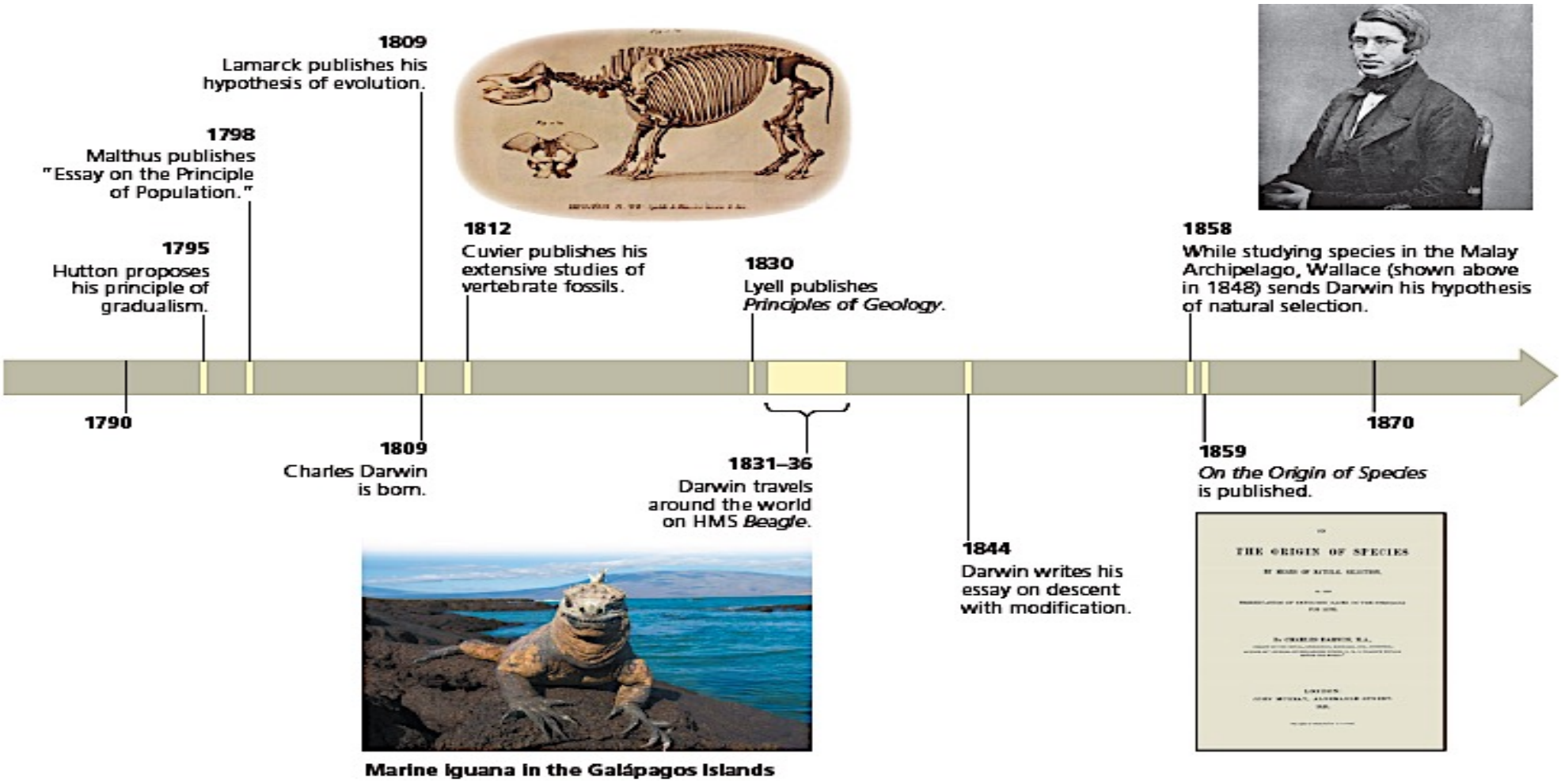


Figure 22.5

- Darwin collected birds, insects, spiders, plants & fossils
- Darwin's experiences during the voyage of Beagle gave him idea that new species originate from ancestral forms through the accumulation of adaptations - Descent with Modification by Natural Selection

Darwin's Journey



Marine iguana in the Galápagos Islands

Beak Variation in Galápagos Finches

Cactus-eater. The long, sharp beak of the cactus ground finch helps it tear and eat cactus flowers and pulp.

Insect-eater. The green warbler finch uses its narrow, pointed beak to grasp insects.

Figure 22.6

Seed-eater. The large ground finch has a large beak adapted for cracking seeds that fall from plants to the ground.

Natural vs. Artificial Selection

Natural Selection

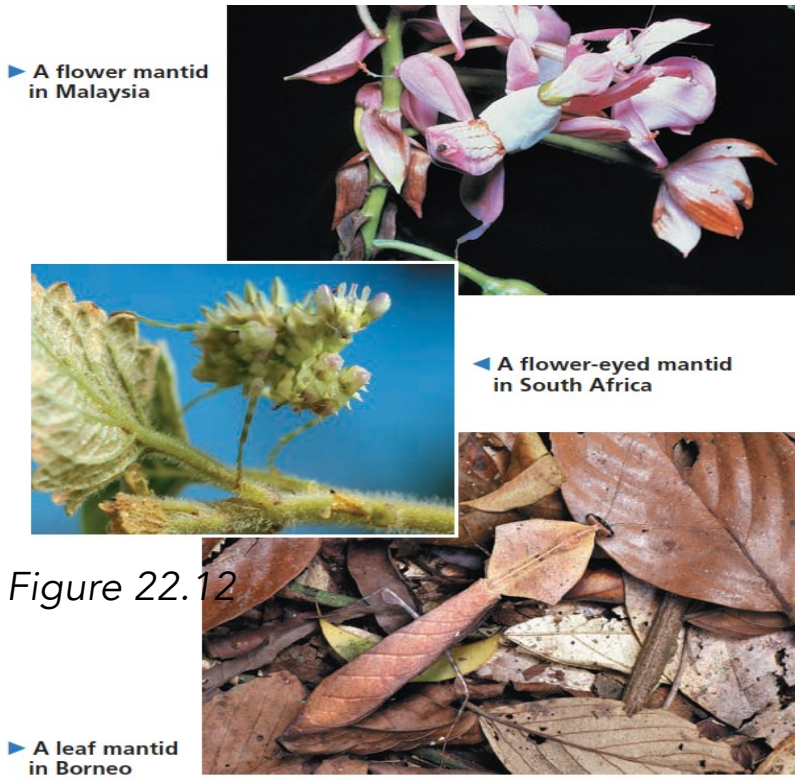


Figure 22.12

Related species of insects "mantids" have diverse shapes and colors evolved in different environments

Artificial Selection

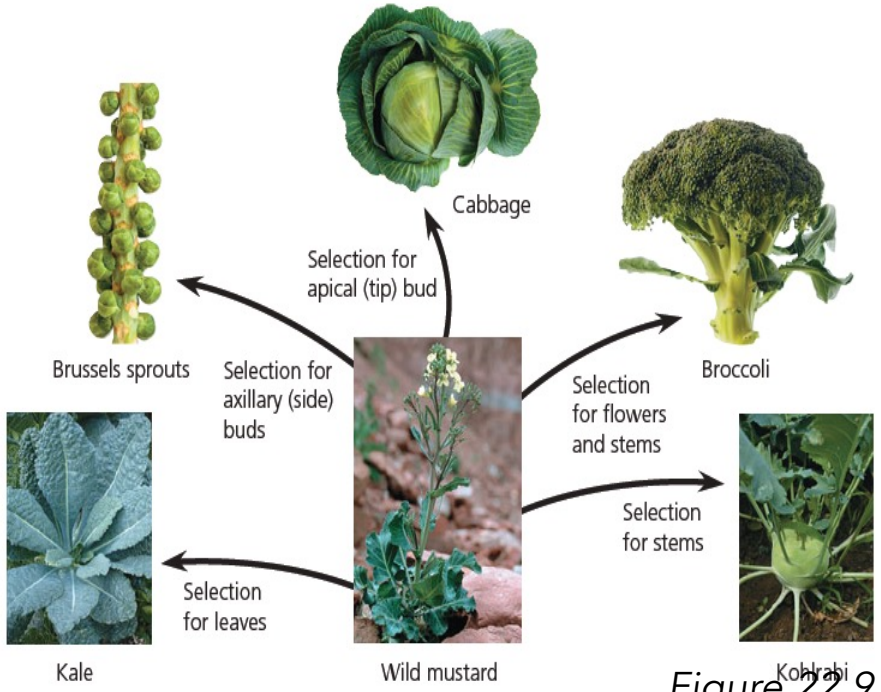


Figure 22.9

Different vegetables have all been selected from one species of wild mustard

To test Whether a Population is Evolving?

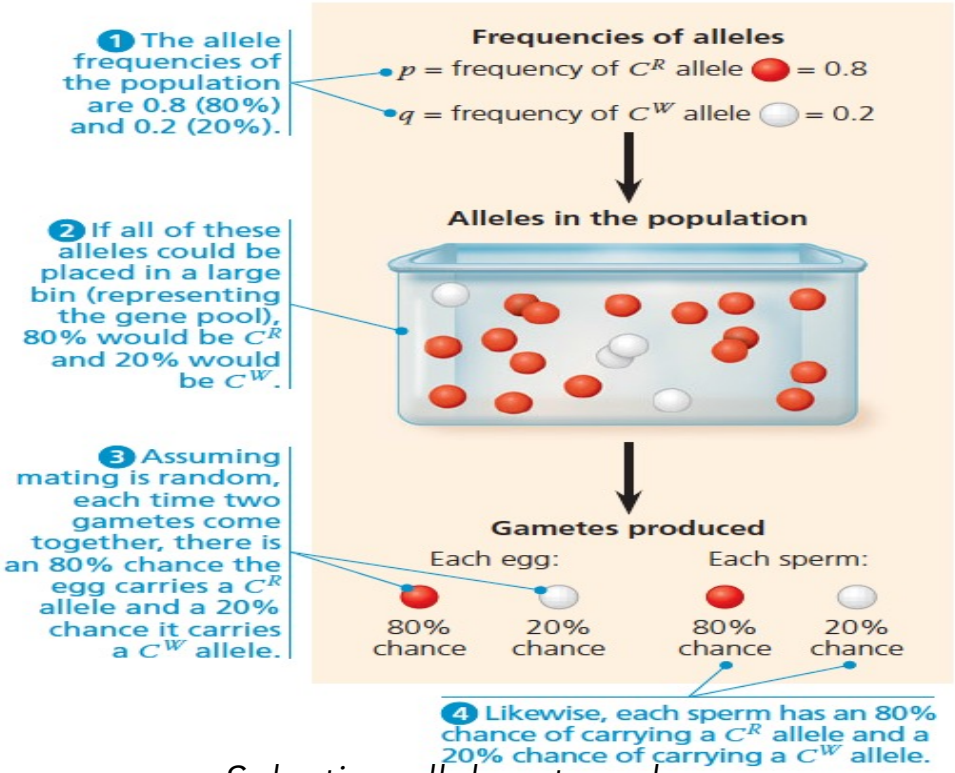
Hardy Weinberg Law

- "**Allele and genotype frequencies of a population will remain constant** *if population is large, mating is random, mutation is negligible, there is no gene flow* and *no natural selection*"

p and **q** represent frequencies of only two possible allele

p² - frequency one homozygote
q² - frequency of other homozygote
2pq - frequency of heterozygous

$$\underset{\text{Expected frequency of genotype}}{p^2} + \underset{\text{Expected frequency of genotype}}{2pq} + \underset{\text{Expected frequency of genotype}}{q^2} = 1$$



Selecting alleles at random from a gene pool

Figure 23.7

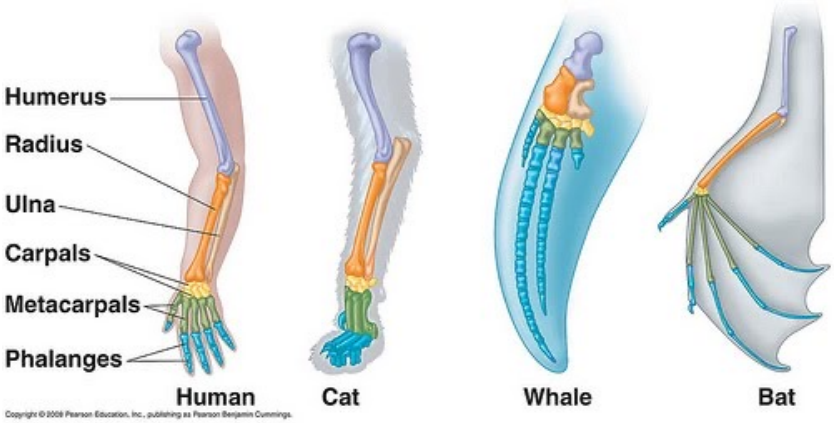
Convergent vs. Divergent Evolution

Convergent Evolution

Similar traits in independent species

which species that are not closely related to each other

Divergent Evolution



A trait retained by common ancestor evolves into different variation

Figure 22.15

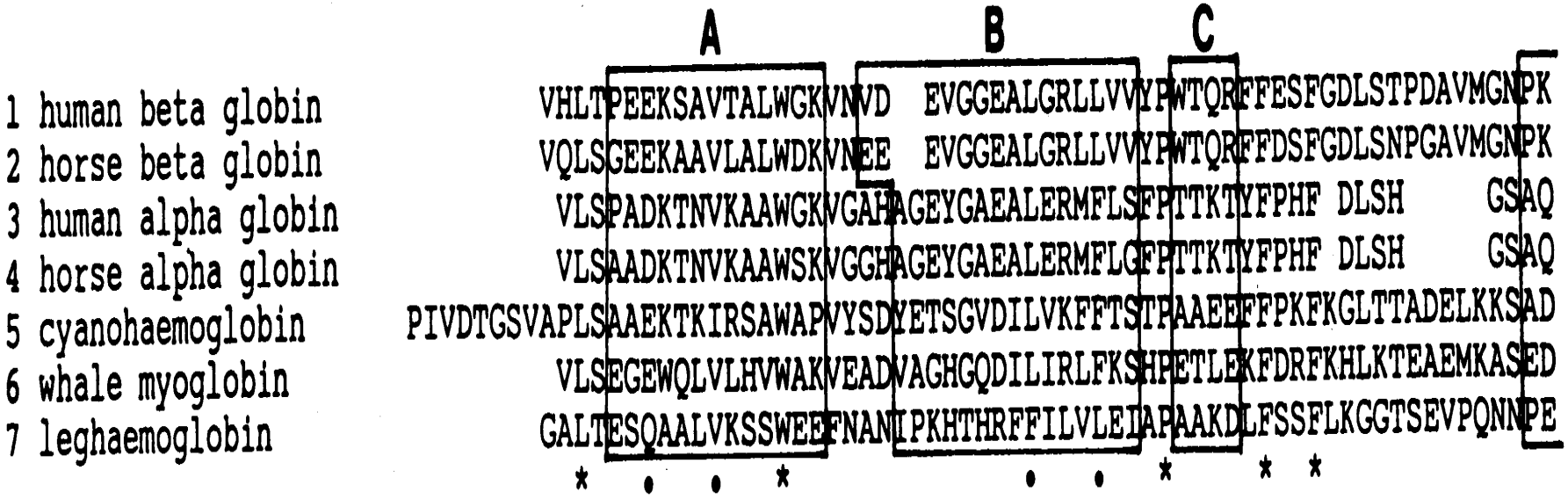
Evolution is Supported by Scientific Evidence

- Organisms share characteristics because of common descent (homology) or because natural selection affects independently evolving species in similar environments in similar ways

- Evolution of Drug-Resistant Bacteria - In bacteria and viruses because resistant strains of these pathogens can proliferate very quickly

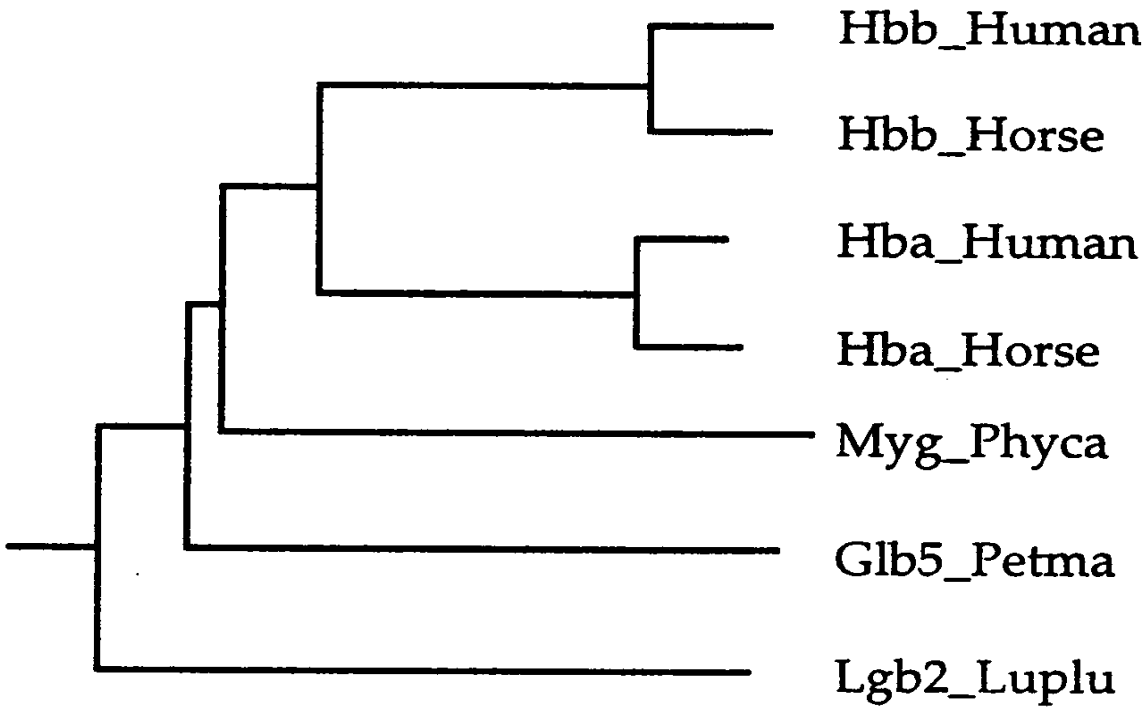
Bioinformatics and Sequence Alignment

Multiple sequence alignment of 7 Globin sequences

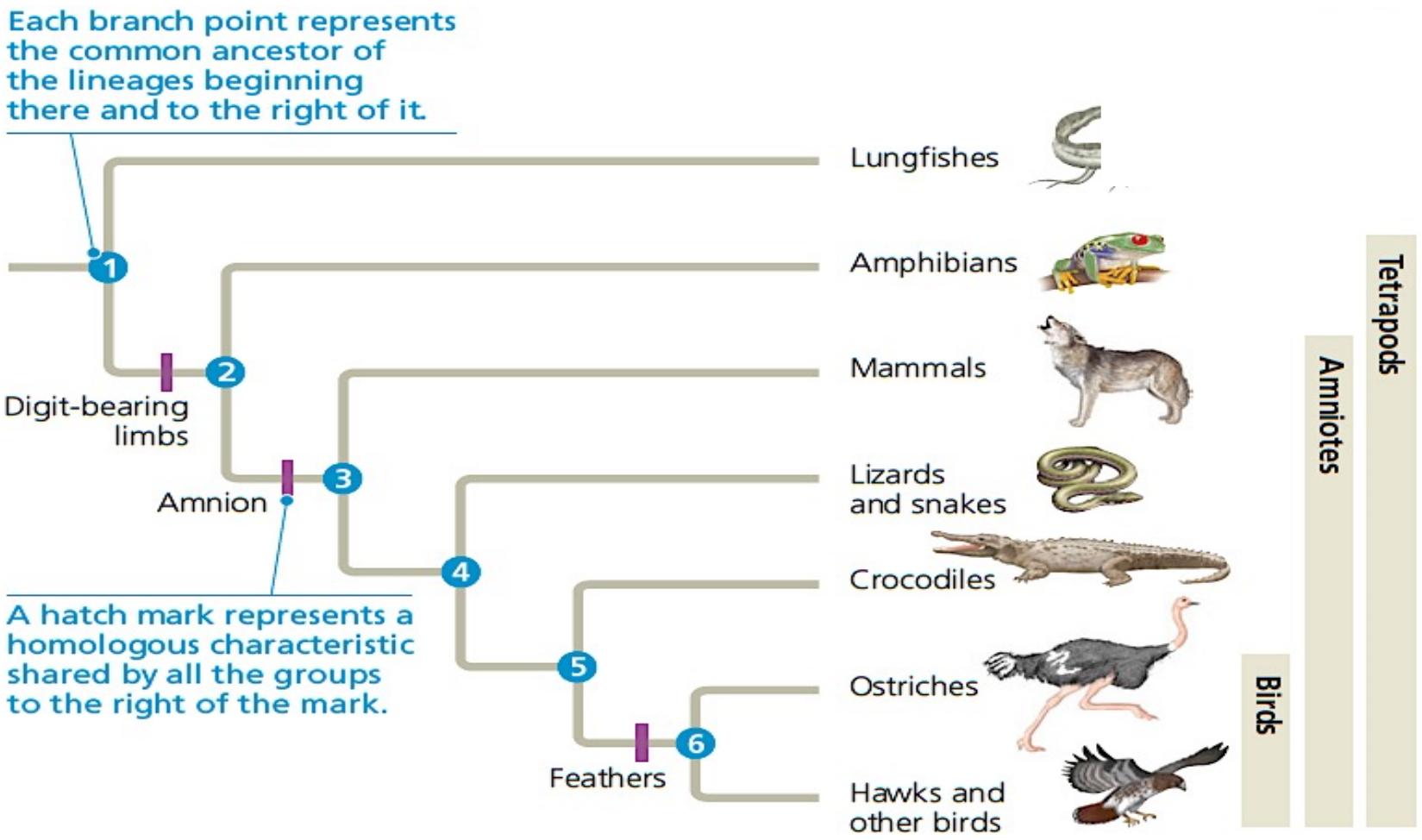


Bioinformatics and Sequence Alignment

Multiple sequence alignment of 7 Globin sequences



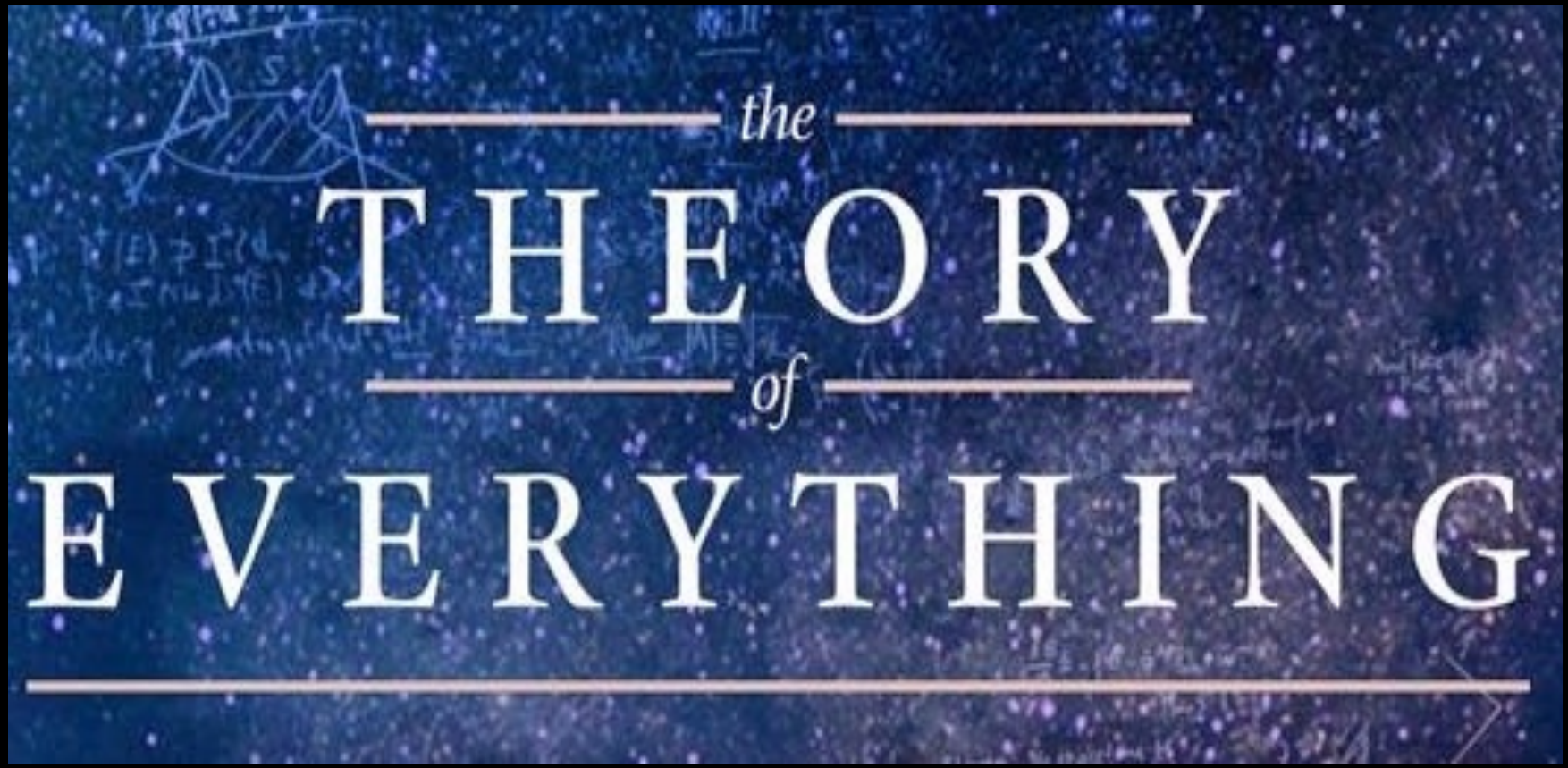
Evolutionary Tree



Summary

- Metabolic pathways, cellular respiration & Warburg effect
- Darwinian revolution changed traditional views of evolution
- Adaptations of organisms and the unity and diversity of life explained by "Descent with modification by natural selection"

Take Home Messages



- There should be no boundary to human endeavor. However bad things may seem there is always something you can do and succeed at. While there is life there is hope. STEPHEN HAWKING, THE THEORY OF EVERYTHING
- Need for ethics and integrity in science research and publication.
- Natural selection weeds out the un-adapted and the best-adapted survive

References

- Campbell Biology - Reece, Urry, Cain, Wasserman, Minorsky, Jackson 9th Edition, Cummings
- The Origin of Species by Means of Natural Selection – Charles Darwin
- *Video contents*
  - Tree of Life
  - Charles Darwin (the man that changed the world)
  - Modern genetics confirms evolution