Introduction to Biology
Origin of Life

Why do we need to know Biology?

- **To find solution to challenges faced by mankind**
- **Sustainability**
- **Design through mimicry – bio-mimicry**
- **Understanding human health and disease, improving the yield of crops, etc.**

Bio-mimicry

Ex-1: **surface of whales do not allow bacteria to stick and grow on them**

- **if we can have such a surface at micro-scale in hospitals, problem of spread of infections can be avoided.**

Ex-2: **beetles can capture water from the air for their requirement**

- **If a similar structure can be made, problems of coastal cities like Chennai can be solved.**

Ex-3: **We are all familiar with solar energy, which uses chemical based solar cells to capture light and generate electricity**

- **Photosynthesis does exactly the same thing, converting light energy into chemical energy, but in a very efficient manner**

Human Health

Second reason for studying biology is to study about us, what happens in the disease state

- **How can we improve our wellness, both physical and mental**
- **Be disease-free and mentally alert, or mentally at peace**
- **It should be possible through a proper understanding of biology, the cell, its processes, the systems as a whole**

- **simple things such as obesity is still not understood properly - it is not a simple calorie counting thing**

Human Health

There are numerous examples of biological problems that are being solved by computer science (or, electrical / mechanical / material) engineers.

- **Developing artificial retina, which allows people with damaged retina to see**
- **Possibility of quadriplegics walking again just by using electrical signals in the brain – researchers working on human-computer interface**
- **Identifying rare disease variants by pattern search – data mining**
- **Organ transplant - In Jan 2022, the world's first pig-heart transplant was successfully achieved in a human patient**
- **etc.**

Scholarly View

The third reason for studying biology is

- **it is there and needs to be understood, e.g., Mendelian genetics, cell morphology, etc.**

  - e.g., to understand inheritance pattern in a family; are bacterial cells different from plant or human cells, cells of different tissues, normal *vs* cancer cells, etc.

- **may not have any immediate application, but may help make a better sustainable life for ourselves/future generations**

- **The 21st century is called the Century of Biology and major advances and breakthroughs are being made with the new biology of genome research – using the complete genetic blueprint of a species.**

- **provides us a complete description of life at the most fundamental level of the genetic code.**

Scholarly View

Compared to Physics wherein we find mostly ‘Universal’ laws,

- **In Biology the rules are generally not ‘Universal’, lot of exceptions are observed, the information available is not complete and understanding is rudimentary**
- **Not to mention, it’s changing as we speak**

Reason for engineers to study biology

Today, Biology has become very quantitative because of large volumes of data generated

- **it's truly Big Data Analytics**

Developing algorithms and databases, addressing storage issues, data mining, applying ML/AI approaches, etc. are now routines tasks in biology

- a new discipline, Bioinformatics and Computational Biology, has emerged for the analysis of large volumes of biological data

Challenge is different types of data – sequences, structures, expression values, image data, clinical data, etc.

In this half-course, we will try to understand some aspects of biology

- **Origin of Life - how life formed, how life evolved, and their relevance**
- **Basic biomolecules of life – DNA, RNA, proteins, etc. and their analysis for knowledge extraction**

  - sequence alignment and sequence database search
- **Can we use molecular sequence data to find the origin of SARS-CoV2 ?**

Origin of Life

First, let us understand what we mean by 'Life'

What are it's features that distinguishes it from non-living things?

- **the ability to replicate and reproduce**

In order to do that, to sustain its survival, and pass on its characters to its progeny

- an organism goes through a whole lot of processes that include its ability to utilize food, it's ability to synthesize food (if required), it's ability to digest food, it's ability to throw out the waste material and keep the machine going

Origin of Life

Life, or any biological system is a highly dynamical system, and its sole purpose is to survive and reproduce.

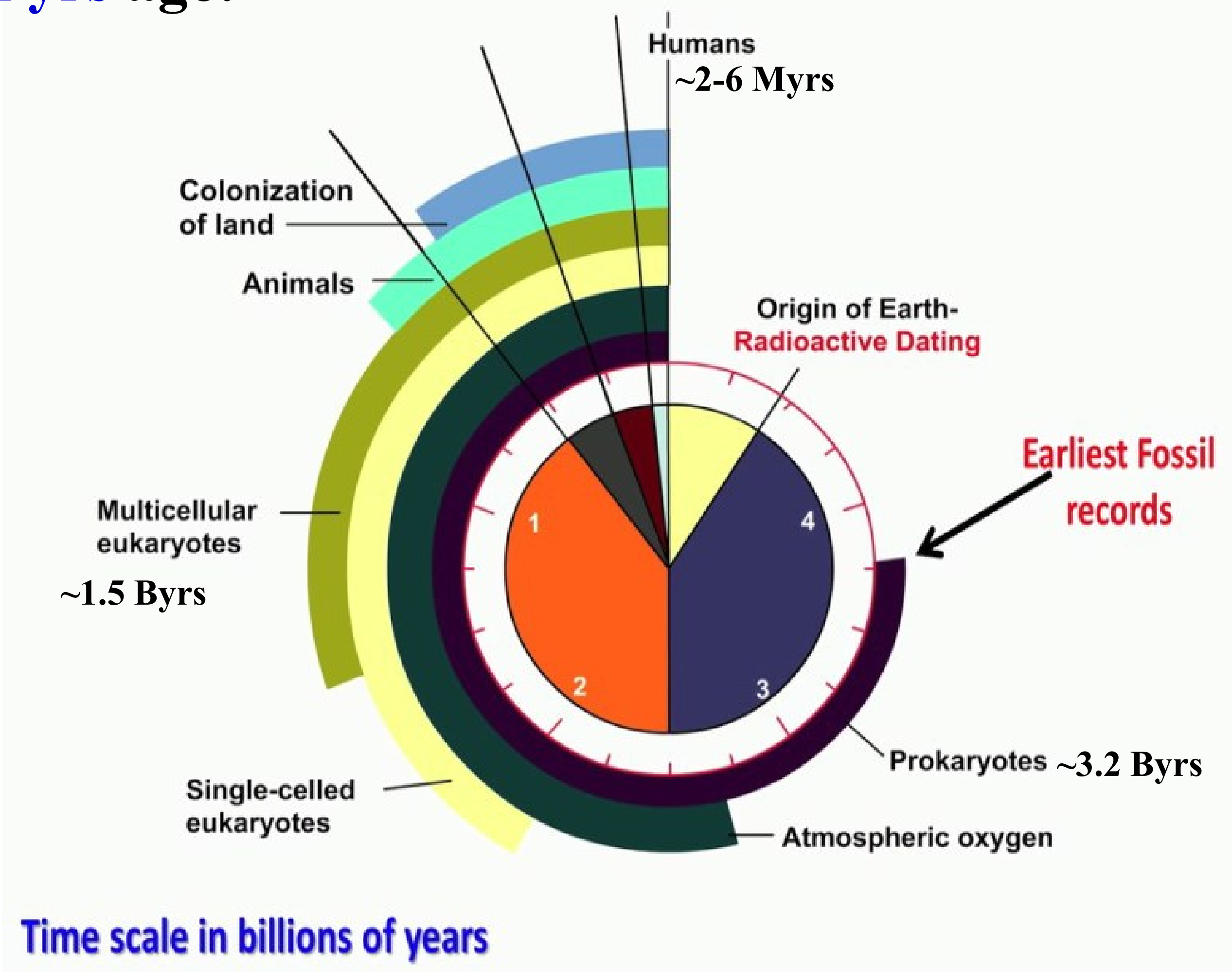
How did life evolve on the earth?

- **Based on studies done by geologist's, archaeologists, molecular biologists, there is enough evidence to speculate that life on earth evolved from non-living things**

$\Rightarrow$ we have essentially evolved from chemical reactions

Origin of Life

Radioactive dating estimates origin of earth ~4.8 billion yrs ago, and fossil records suggest earliest life forms ~ 3.6-3.8 billion yrs ago.



Origin of Life

Do any of the earliest life forms still exist on earth?

- **yes, bacteria, since over 3 Billion yrs**

Based on various evidences from geological excavations, chemical reactions and biotechniques, biologists divide the process of life and its existence into three phases:

- **Chemical evolution**
- **Acquisition of replicative ability**
- **Biological evolution**

Chemical Evolution

This phase corresponds to very early stages of earth's life:

- **the earth's crust was still very hot,**
- **the oceans and sea were still boiling, and**
- **the atmosphere was highly reducing.**

Chemical Evolution

Any living organism ~ 70% of its body wt is water, and major constituents of dry wt: C, H, O, N, P and S

- **Carbon is most abundant**
- **An interesting property of C is its ability to form covalent bonds with itself & other elements**
- **Another imp thing is highly reducing earth's atmosphere because of presence of H_2S, NH_3, CH_4, CO, and no atmospheric Oxygen**

Geologists, on analyzing early rocks on earth & meteorites, found to be rich in carbon compounds

$\Rightarrow$ the early building blocks were formed with carbon

There are other views as well – early atmosphere was not reducing but had high oxygen.

Chemical Evolution

Hypothesis-1 (A. Oparin & J.B.S. Halden, 1929):

- the very first molecules/biomolecules would have arisen because of abiotic synthesis of small molecules.

- **due to initial reducing environment of earth, any high energy discharge, either in the form of ultra-violet lights, or in the form of lightning would have favoured spontaneous synthesis of simple molecules from existing geological molecules on earth's surface.**
- **In 1953, it was actually demonstrated to be true by Stanley Miller and Harold Urey.**

⇒ first set of sugars or amino acids were formed by a mere abiotic synthesis of these molecules

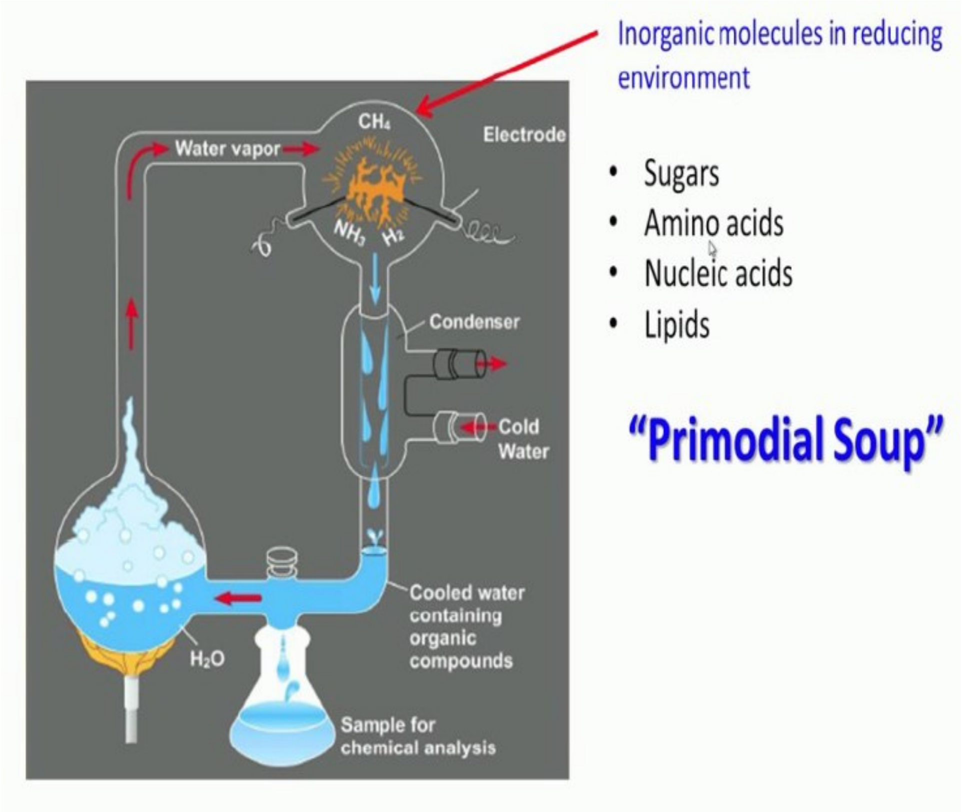
Chemical Evolution

Miller & Urey created the primordial soup in a laboratory setup

- Collected water vapor under a very reduced environment of CH_4, NH_3 & H

- Energy supplied to mimic ultra-violet radiations or lightning through electrodes

- whatever was spontaneously generated was condensed and collected



It consisted of amino-acids such as Alanine & Glycine, sugars, nucleic acid, and nucleic acid bases like Adenine and lipids.

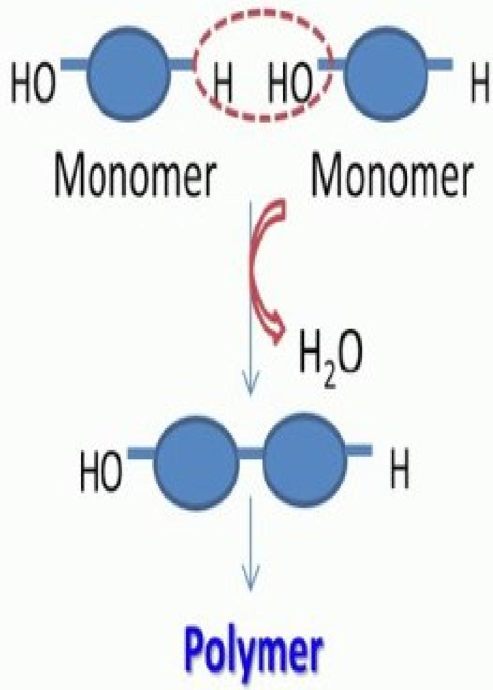
Chemical Evolution

Hypothesis-2: Abiotic Polymerization of Small Molecules

How were macromolecules, such as cellulose (cell wall of plants) formed from small mols?

- **By spontaneous polymerization due to very high rate of dehydration, because of the presence of hot rock, clay or sand which would promote such a chemical reaction.**
- **due to presence of carbonaceous material in the earth's crust, the rate of synthesis was much higher than the rate of hydrolysis.**

Abiotic Polymerization of Small Molecules



- Hot rock, clay or sand
- Dehydration
- Rate of synthesis > Rate of hydrolysis
- Without enzymes

Proof by Sydney Fox (1950s)

- **dripping organic monomers on hot clay (iron pyrite) or sand, which do have these charged sites**
- **monomeric molecules joined together to form polymeric molecules, and in the process, the metal ions facilitate the condensation process.**

Chemical Evolution

Hypothesis-3: Abiotic Replication

When did the replicative ability begin?

- **we do not have clear proof as to how this change happened from a non-replicative to the replicative form and life, but,**
- **we now have sufficient proof that the earliest genetic material, the ideal initiator of this process, must have been RNA.**

The flow of information in the living world:

$$\text{DNA} \longrightarrow \text{RNA} \longrightarrow \text{Protein}$$

Chemical Evolution

What makes RNA the probable candidate as the earliest molecule capable of acquiring the ability to replicate?

RNA is a very versatile molecule. It can

- **Polymerize itself**
- **Cleave itself, i.e., act as an enzyme**

  - this catalytic activity is not dependent on proteins
- **Involved in multiple steps of protein synthesis; even ribosomes are 2/3rd RNA**
- **Even DNA synthesis is dependent on RNA**

Sydney Altman et al, 1980

Chemical Evolution

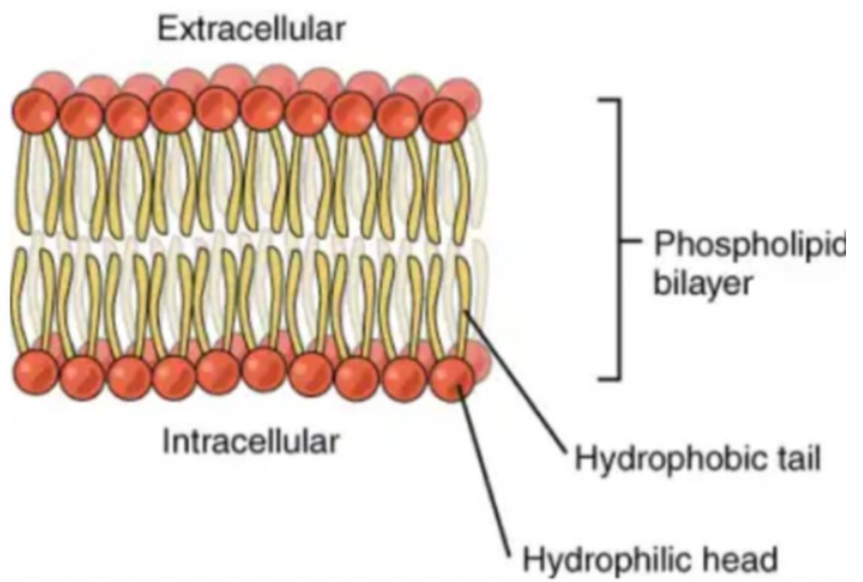
How did cells come into existence?

Hypothesis-4: Protobionts

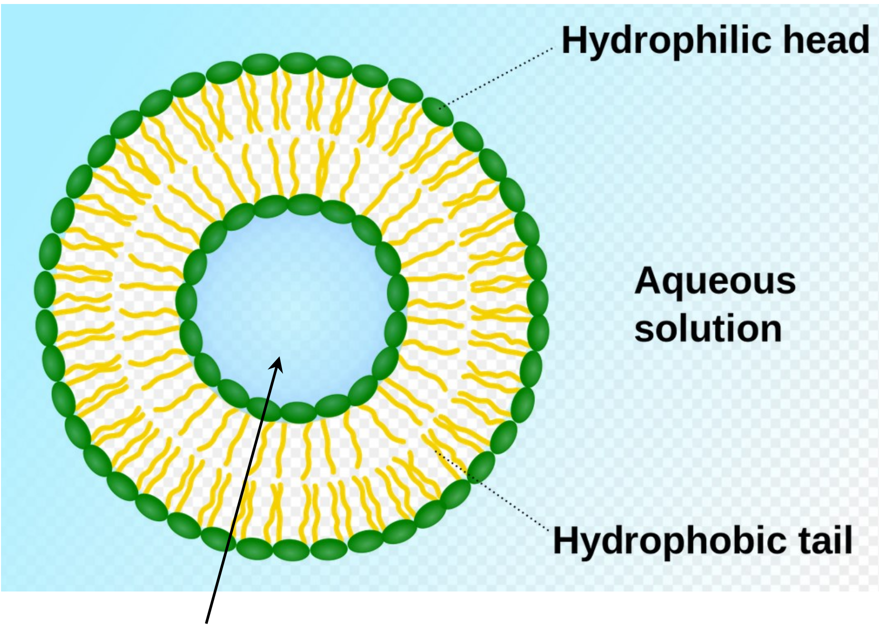
Aggregation of abiotically synthesized molecules for maintenance of internal environment

- **would have assembled as liposomes**
- **these are amphipathic, i.e., they have a polar head and non-polar tail**

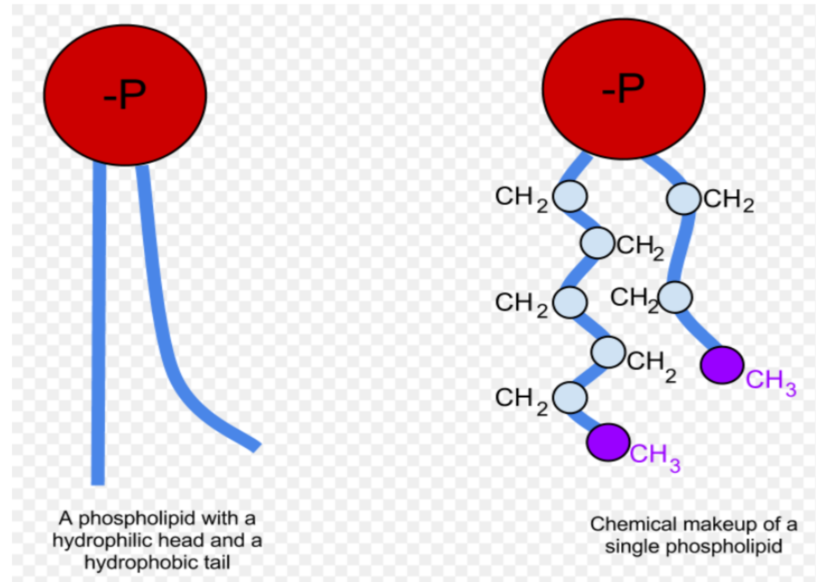
These initial lipid liposomes would have enclosed abiotically synthesized self-replicating biological molecules to form the first and the earliest form of life, called protobionts



Liposomes



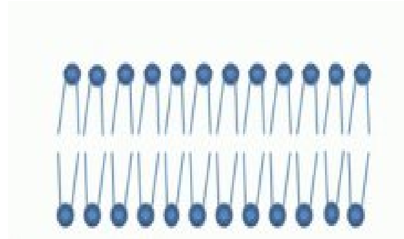
Hydrophilic pocket



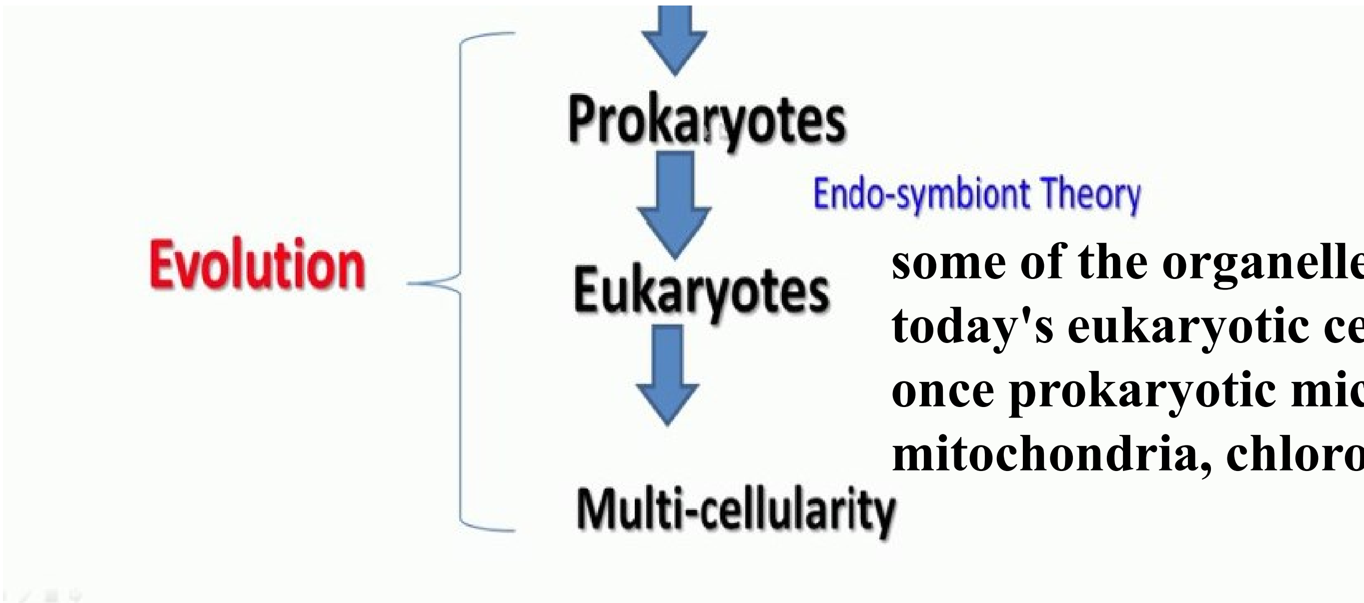
A Liposome is a spherical vesicle made of phospholipids derived from natural or man-made materials

Phospholipids are the main components of biological membranes

Chemical Evolution



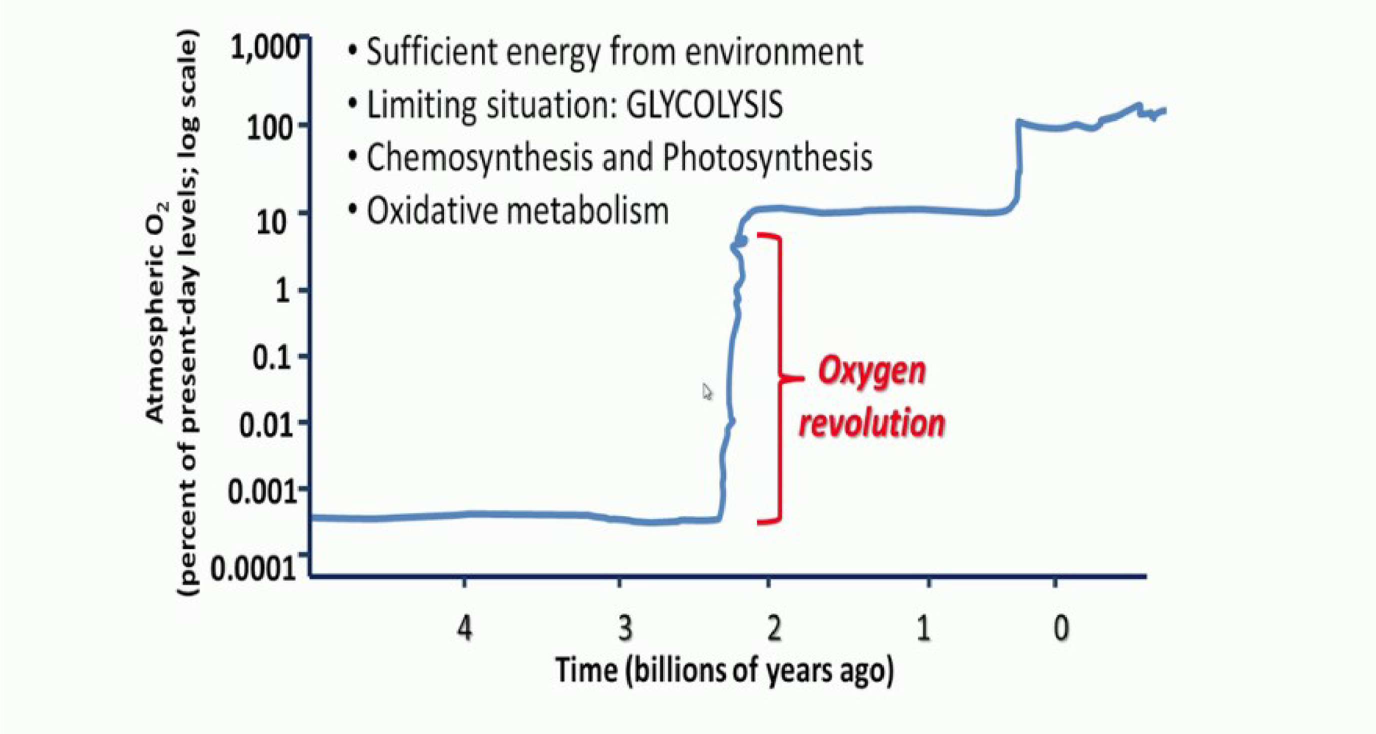
protobionts



some of the organelles in today's eukaryotic cells were once prokaryotic microbes, e.g., mitochondria, chloroplast

And somewhere down the line, the protobionts would have evolved into prokaryotes, time-scale – millions of years

The Oxygen Revolution



Almost for the first 2 ½ billion years, there was hardly any oxygen in the atmosphere.

The Oxygen Revolution

What happened that led to sudden burst from hardly any oxygen to a point where the atmosphere became highly oxidized?

It is believed that it's at this stage, in the earth's life that the plants or the photosynthetic organisms must have evolved.

By the time of 2 ½ billion years, resources must have reduced, the organism would have to find alternate sources of obtaining energy for survival.

One possible way would have been to use the reducing power using hydrogen sulphide.

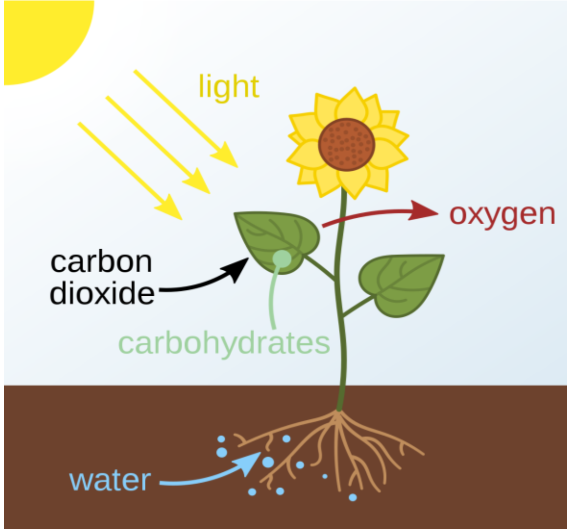
The Oxygen Revolution

After exhausting H_2S, the organism must have developed a much smarter strategy of utilizing the unlimited pool of solar energy and the process of photosynthesis would have evolved.

- oxygen being a by-product, would have resulted in the atmosphere becoming highly oxidized.

New set of chemical reactions would have evolved under oxidizing conditions for breakdown of polymers into monomers and releasing energy

- somewhere at this point probably, the evolution of mitochondria would have happened.



To Summarize

As we understand today, origin of life is divided into 3 stages:

- **First, the stage of chemical evolution - abiotic formation of organic molecules and its polymerization**
- **Second, self-organization, and the ability of these polymers to develop the property of replication and form the early protobionts.**
- **Third, the stage of metabolic evolution, i.e., evolutions in metabolic reactions that happen inside a living organism.**
  - **allow the organism to synthesize food, generate energy from food, and eventually transition from single-cell to multi-cell organism.**

Evolution

An intriguing point in the study of life is that despite the varied forms of life that we see today,

- some of the fundamental metabolic reactions and the way genetic information is coded in our DNA are conserved right all the way from prokaryotes to humans.

Genetic and Biochemical similarity across the living world despite the diversity!

Evolution

Let us now see how from this early form of life, the present-day organisms evolved - a huge array of them.

What is it that caused this variation, this distribution in different life forms, that we call evolution.

What is evolution?

- **Essentially it tries to explain how life must have diversified into multiple forms we see today.**
- **these present forms are believed to be the descendants of a common ancestor**

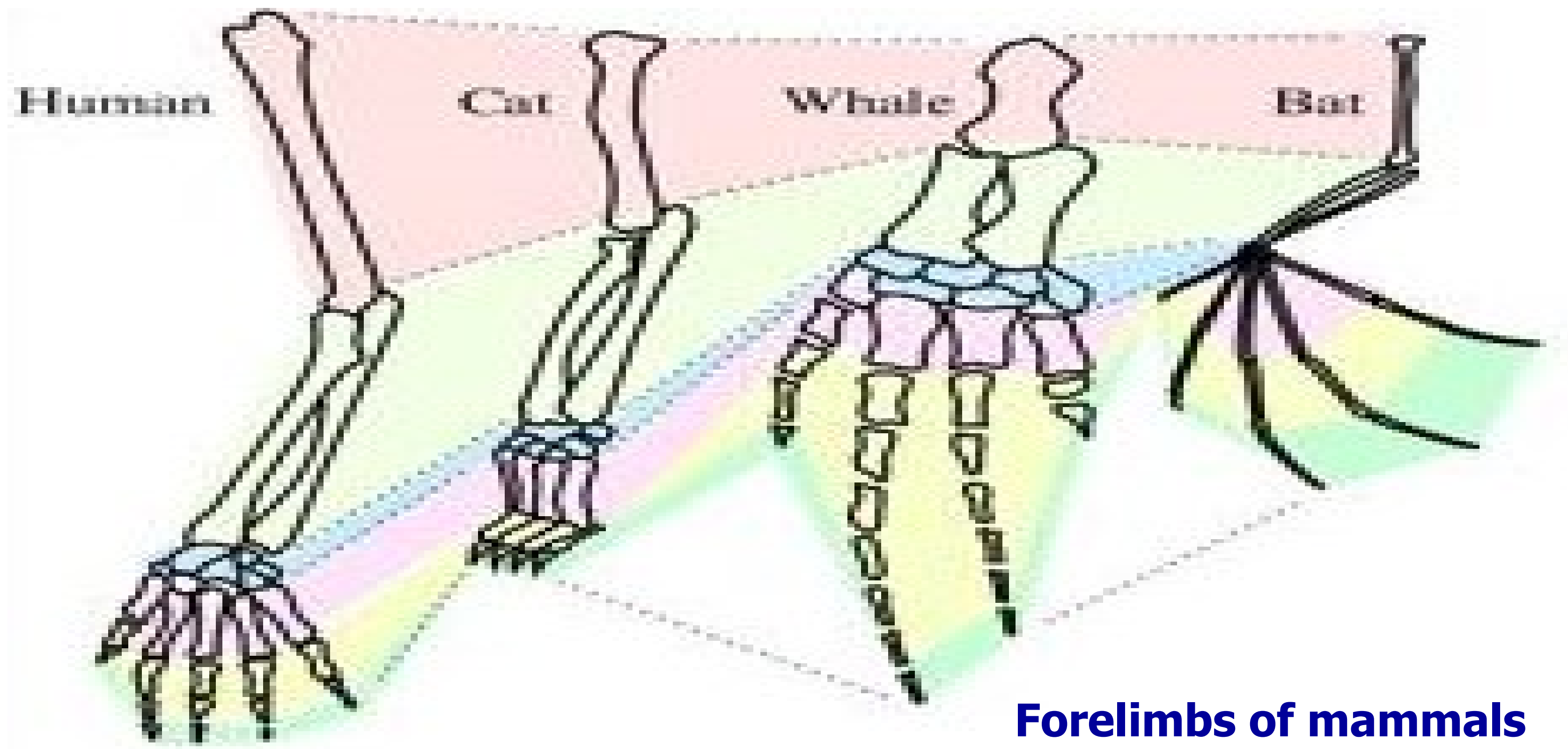
Evolution

During the course of history of earth's life, a lot of changes happened in organisms that were passed on to subsequent generations.

In other words, multiple heritable modifications from one generation to the next occurred, and it is this evolution that accounts for the unity and the diversity of life.

Let's consider an example - the basic skeletal architecture of the wings of Bat and compare it with the forelimbs of Humans/Cats and to the flipper of Whales.

Anatomical Homology

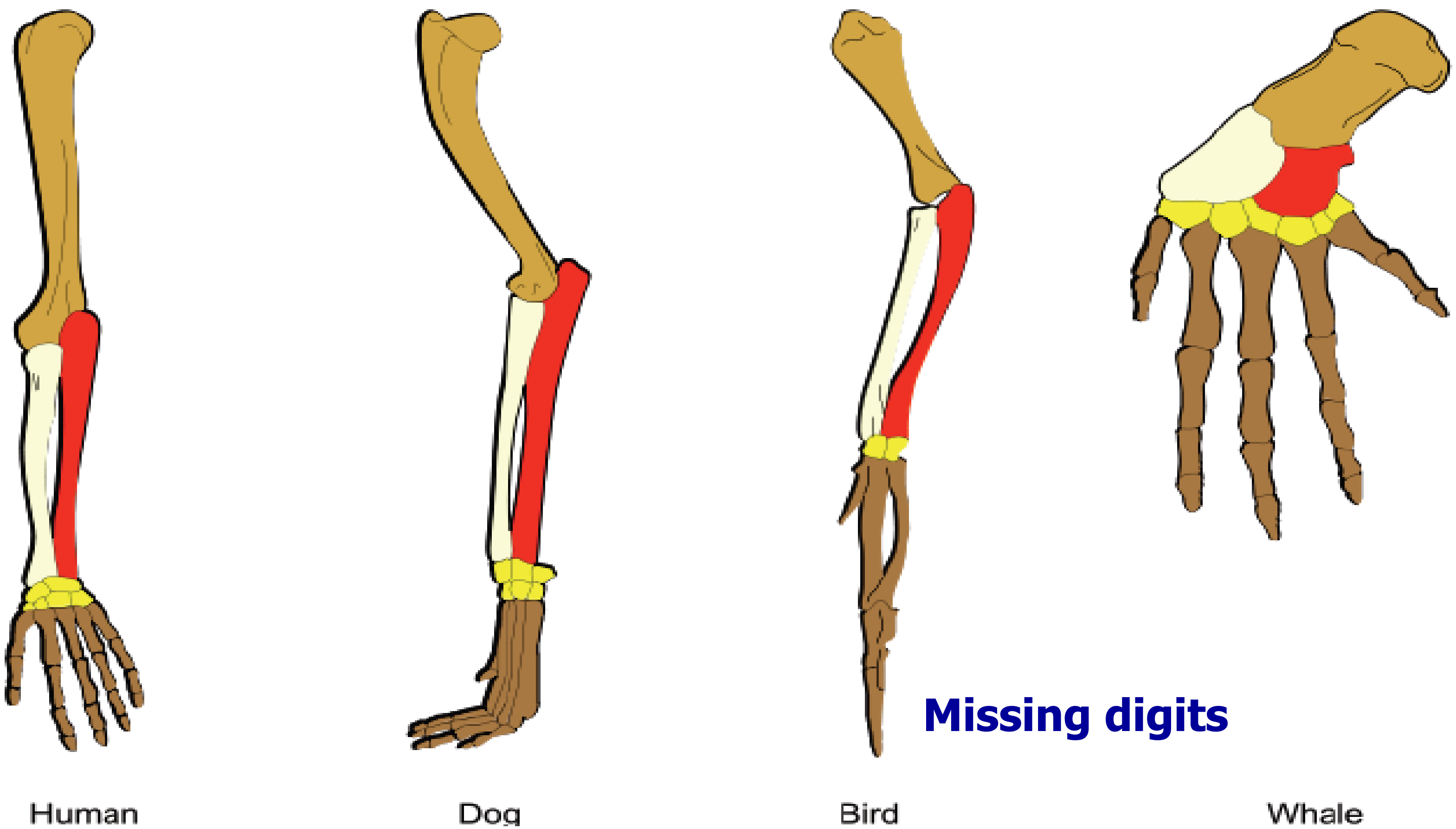


Forelimbs of mammals

Same basic structural plan is evident in all – one can "morph" one into another just by changing the sizes and proportions
- Genetic mutations and changes in the expression patterns of limb-development genes are responsible for these changes

Homology: Limb Structure

Different functionality despite having similar architecture:



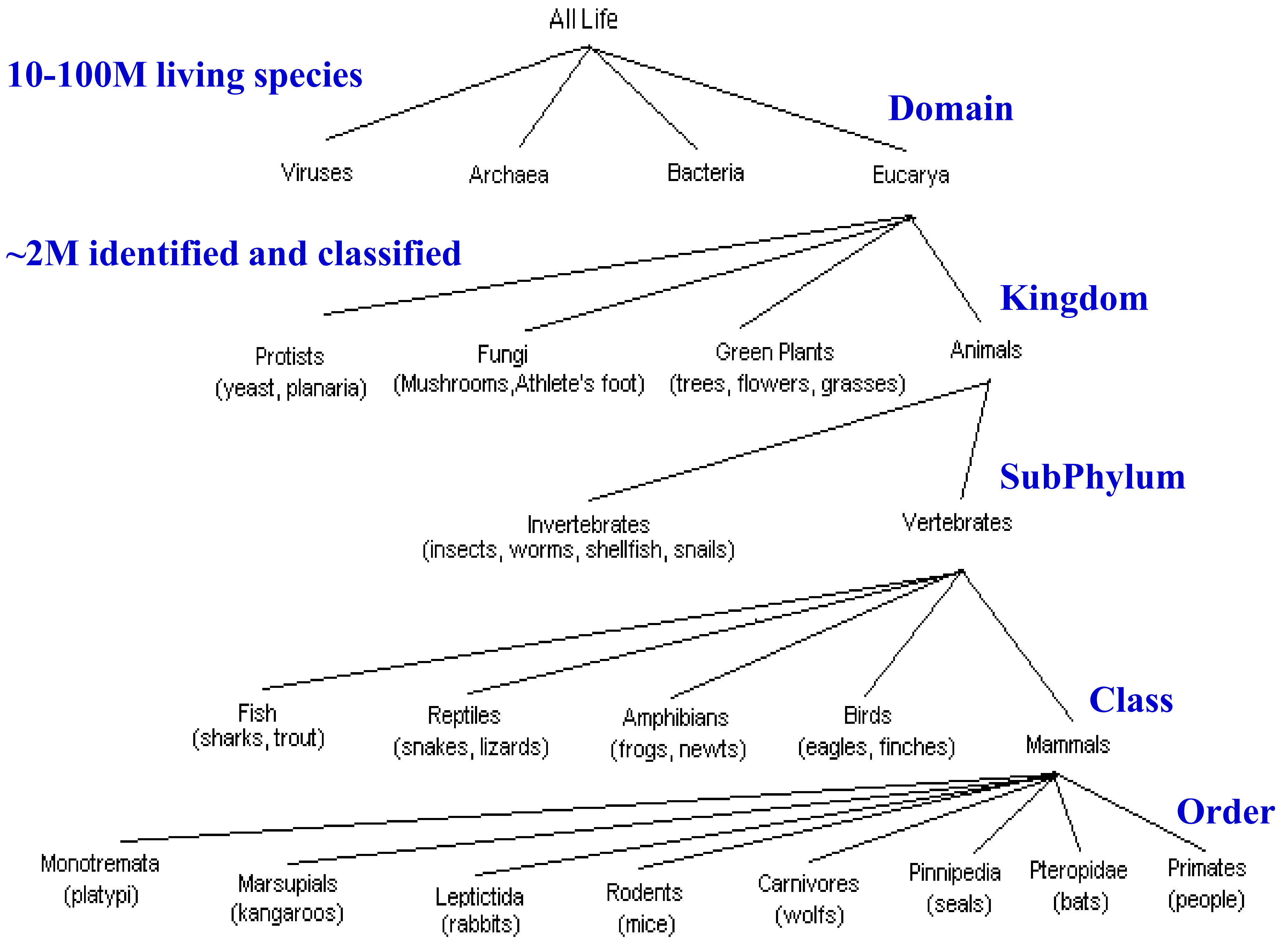
throwing **walking** **flying** **swimming**

Evolution

Similarly, if we look at DNA, the language which codes the information in DNA, has been fairly conserved.

Yet, the DNA found in humans is slightly different from the DNA in earlier organisms, not in terms of its chemical entity, but in terms of further architectural development.

Evolution essentially talks about these changes - acquired by various life processes over the course of earth's history.



10-100M living species
~2M identified and classified
All Life
Domain
Viruses
Archaea
Bacteria
Eucarya
Kingdom
Protists
(yeast, planaria)
Fungi
(Mushrooms,Athlete's foot)
Green Plants
(trees, flowers, grasses)
Animals
SubPhylum
Invertebrates
(insects, worms, shellfish, snails)
Vertebrates
Class
Fish
(sharks, trout)
Reptiles
(snakes, lizards)
Amphibians
(frogs, newts)
Birds
(eagles, finches)
Mammals
Order
Monotremata
(platypi)
Marsupials
(kangaroos)
Leptictida
(rabbits)
Rodents
(mice)
Carnivores
(wolfs)
Pinnipedia
(seals)
Pteropidae
(bats)
Primates
(people)

Evolution

One of the earliest scientist to bring in the concept of evolution was Lamarck.

- **though his theories were disproved later.**

According to him, it is a particular organ, or a particular feature in an organism that develops during the lifetime of the organism based on the usage in that organism.

He reasoned that the organs not being used by organisms eventually become useless, called vestigial organs, e.g., appendix in our body.

⇒ His theory based on use or disuse of a particular part was not the reason for evolution

Evolution

Remarkable observations made by Charles Darwin

Most interesting observations that he made were in the Galapagos Islands

- **in each island, there were unique birds, species and tortoises and no two islands had exactly the same kind of species, though similar to those found in the nearest island.**

Another observation he made during his voyage across the coastlines of Africa, Southern America, and Australia, was that the distribution of the species mirrored how the continental drift actually happened in the earth's history, e.g.,

- Giant flightless birds: Rhea (S. America), Ostrich (Africa), Emu (Australia)

Evolution

Darwin Qs:

- **Why are there so many species of living things?**
- **How do new species arise?**
- **How does the population of an organism evolve?**
- **How do organism adapt to their environment?**
- **How is one species related to another?**

He observed that, in a given population of a species, e.g., humans, there are individuals with different features (height, colour of hair/eyes/skin)

- these differences within a species, called variations, are heritable.

Evolution

The other observation he made in the Galapagos Islands was:

- **though the species were different in different islands, based on the environment which was being provided by the island, the species could adapt to that environment.**
- **e.g., in the islands where vegetations were found at a much lower level, the neck of the tortoises were smaller, while in those islands where vegetations were slightly at a higher level, the tortoises had a longer neck.**

$\Rightarrow$ the species can adapt to the changing environment.

Evolution

The third observation he made was that

- **as a population grows in size, eventually, the resources become limited.**
- **this would result in a competition among the individuals of a population for the resource**
- **Lead to '*the survival of the fittest*'.**

⇒ Individuals with traits, or variations which allow them to *best adapt* to the environment are most likely to survive and reproduce, and also pass on these favourable characters to the next generation.

Evolution

To summarize Darwin's observations:

- **Individuals in a population exhibit variable traits: Variations**
- **Many traits are heritable**
- **Species adapt to their environment**
- **Limited resources lead to competition for survival as a consequence of growing population**

⇒ Individuals with traits which allow them to best adapt to the environment will most likely survive and reproduce.

Natural Selection

In 1859 Darwin along with another naturalist, Alfred Russell Wallace, presented their ideas to the London Philosophical Society, and he published his most famous work, called ‘The origin of species by means of natural selection’.

- **every species shows an evidence of descent from a previous species with modifications $\Rightarrow$ they all have a common ancestor**
- **the pressure which brings about these modifications, or variations, is the environment in which the organism lives.**
- **This pressure, provided by the environment is what is called the ‘natural selection’.**

Natural Selection

A classic example of natural selection has been around the time of industrial revolution, giving rise to a species of peppered Moth (J.W. Tutt,)

1811 - most moths in England were light-colored

1848 - when industrial revolution was taking place in Manchester, a lot of peppered and black coloured moths were observed

- **by the end of 19th century, in a period of ~90yrs, light-coloured moths were totally outnumbered by dry, dark-coloured moths.**

1896 - J.W. Tutt presented it a case of natural selection

⇒ Change in the colour was a favourable trait, giving the moths survival advantage

Types of Natural Selection

How do organisms adapt to the environment?

- **Stabilizing**
- **Directional**
- **Diversifying**

Assume you have a population trait exhibiting normal distribution and that the environment is conducive and the conditions are fine

- **In such a case there is no need for the outer extreme of the organisms to grow**
- **such kind of a selection where the central most acquired characters are retained is a stabilizing selection.**

Types of Natural Selection

If we have a situation where suddenly the environmental conditions force in such a fashion that it is this set of extreme outliers that have a survival advantage

- **this is an example of directional selection**

If a population, which because of a continental drift, or some other kind of catastrophe, gets split into two populations with different characteristics

- **this is called as the diversifying selection.**

Two common & unifying features across all three situations – it is the environment that provides the selection pressure, and it is the ability of certain individuals in a population to adapt to that change. How?

Mendelian Genetics

Darwin did not know

- **what is the molecular mechanism which causes this variation.**
- **how are these variations passed on to successive generations?**
- **Why do certain species go extinct?**

Mendelian Genetics

How are the variations caused?

- **There are multiple ways, and the most classic way is the process of mutation.**
- **During DNA replication, an error gets incorporated in a gene and this mutation is favourable (or neutral) to the organism – it get's fixed in the population**
- **During sexual reproduction - we get a certain set of genes from our father, and a certain set of genes from our mother**
- **this has been one of the major reasons for variation and is one of the major reasons for success of survival in higher organisms.**

Mendelian Genetics

What are the causes of extinction?

- **It is speculated that if a species fails to adapt itself to a changing environment, it will go extinct, or**
- **if it specializes to such a point that it cannot re-adapt itself, then also it can undergo extinction.**
- **Catastrophic event, e.g., either a huge meteorite hit the earth or volcanic fury led to extinction of dinosaurs.**

Mendelian Genetics

How do we try to understand evolution?

- **through fossil records,**
- **through geological excavations;**
- **by comparing the anatomical structures, or**
- **by comparative embryology**
- **Molecular phylogeny – look at similarities in DNA, RNA and proteins sequences/structures,**

e.g., DNA that codes for enzymes involved in basic metabolic reactions are highly similar across evolution.

Evolution is a continuous process!

the evolutionary changes accumulate over generations and then diversify into a newer species – but this happens over the scale of thousands of years

- In molecular phylogeny we try to analyze these variations at the DNA level to understand evolution, and also to understand the function of various genes/proteins.

Syllabus of the Second Half of Sci-II

Unit 1: Introduction: Classification of Living Organisms, Origin of Life and Evolution, Biomolecules – Nucleotides, Amino Acids, and Macromolecules – DNA, RNA and Proteins

Unit 2: Cell Biology: Structure and Function - Prokaryotic and Eukaryotic Cells, DNA Replication, Transcription, Translation – Central dogma, DNA sequencing - amplification, cloning, restriction enzymes, PCR sequencing

Unit 3: Biological data analysis: Types of biological data, Gene structure in prokaryotes and Eukaryotes, Pattern search in sequence data analysis (k-mer analysis) and applications.

Syllabus of the Second Half of Sci-II

Unit 4: Sequence Alignment – algorithms for pairwise comparison of sequences and database search, resources for biological data – how to search and extract relevant data and biological information.

Unit 5: Multiple sequence alignment and Phylogeny with applications

Assessment:

Assignments – (10%),

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Final exam (30%)

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