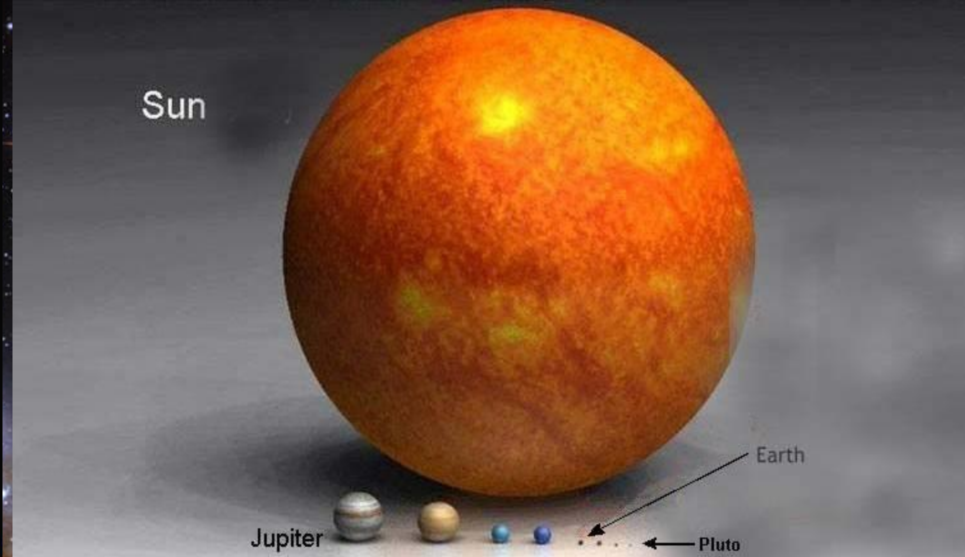
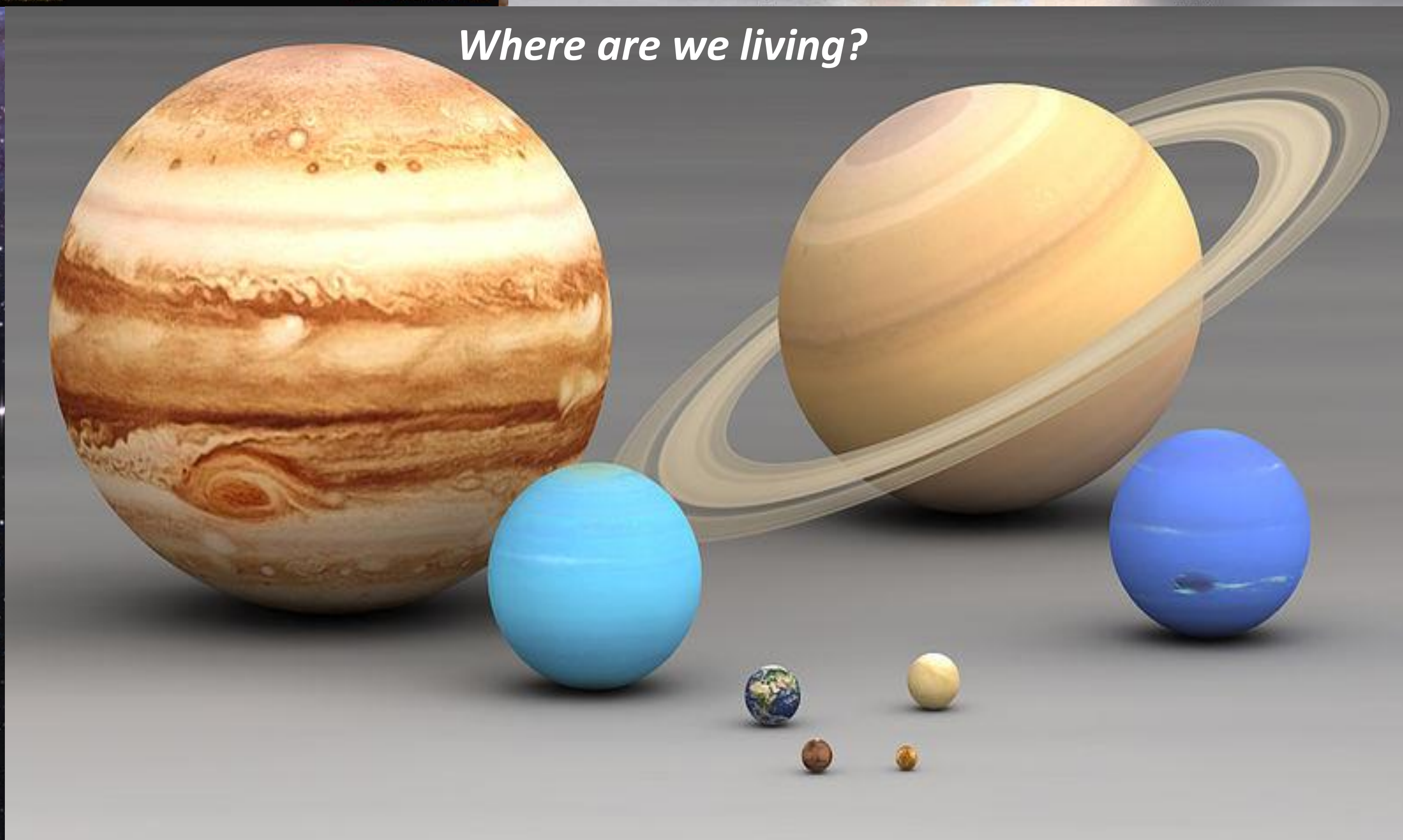
Grammar of Life-a complex adaptive system

Tanmay Mitra, IMSc

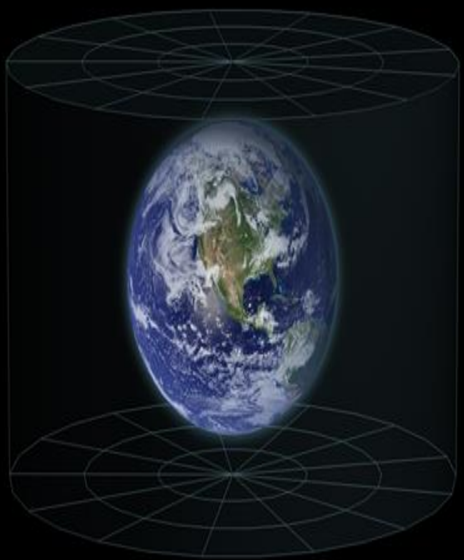


Where are we living?

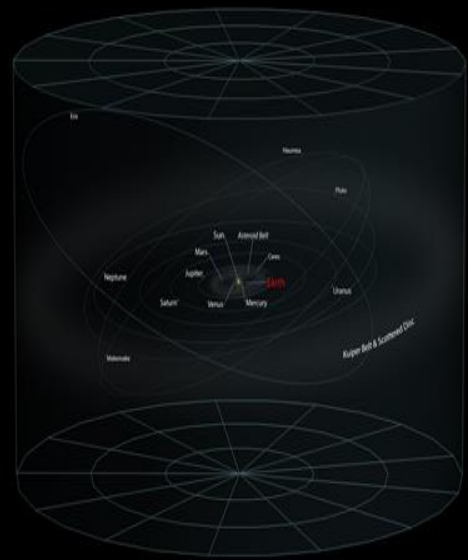


Where is our Solar system in the Milky Way??

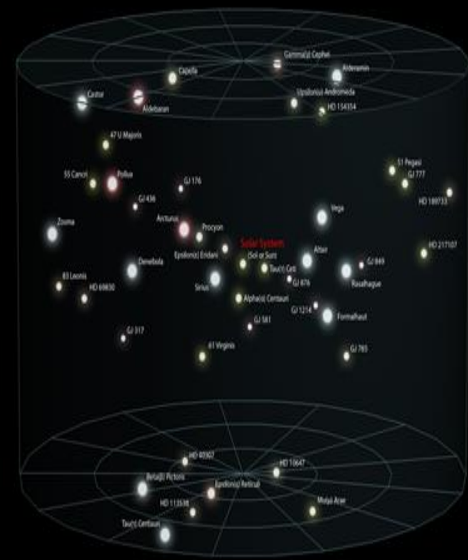
Earth



Solar System



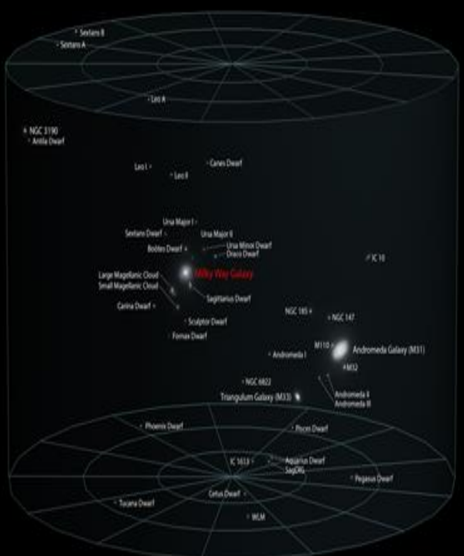
Solar Interstellar Neighborhood



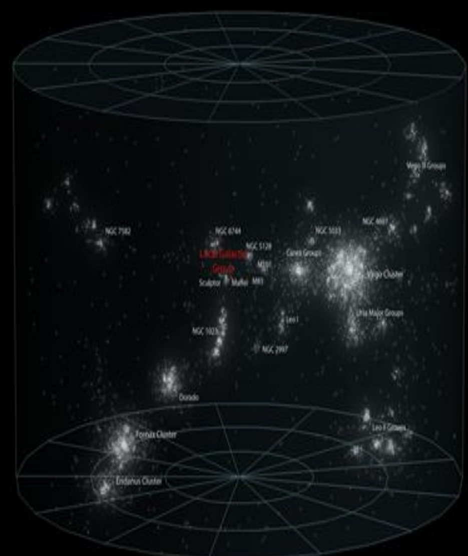
Milky Way Galaxy

Where are we compared to the observable universe?

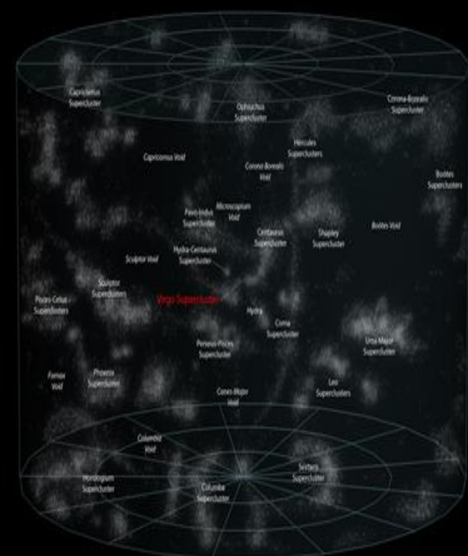
Local Galactic Group



Virgo Supercluster



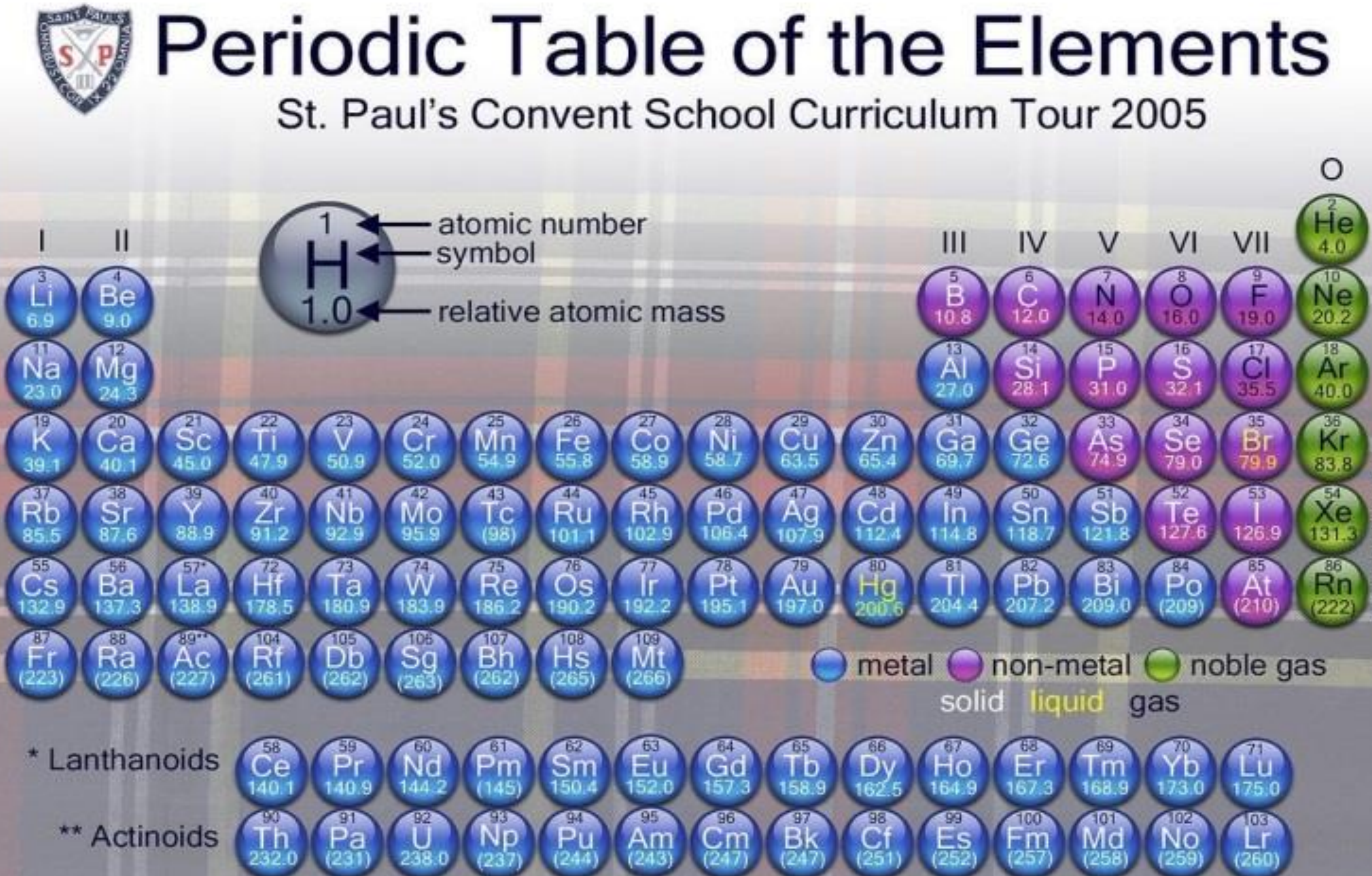
Local Superclusters



Observable Universe

Grammar of the elements : The Periodic Table

Please explore : http://www.ptable.com/#Writeup/Wikipedia



Elements of Life

Elements :

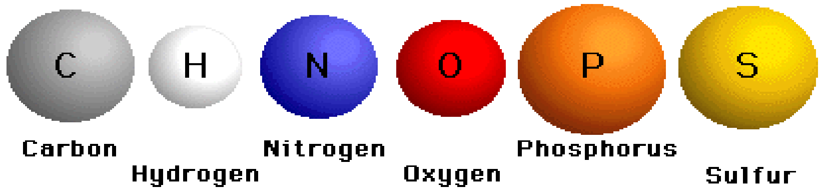
- **59% Hydrogen (H)**
- **24% Oxygen (O)**
- **11% Carbon (C)**
- **4% Nitrogen (N)**
- **2% Others - Phosphorus (P), Sulphur (S) etc.**

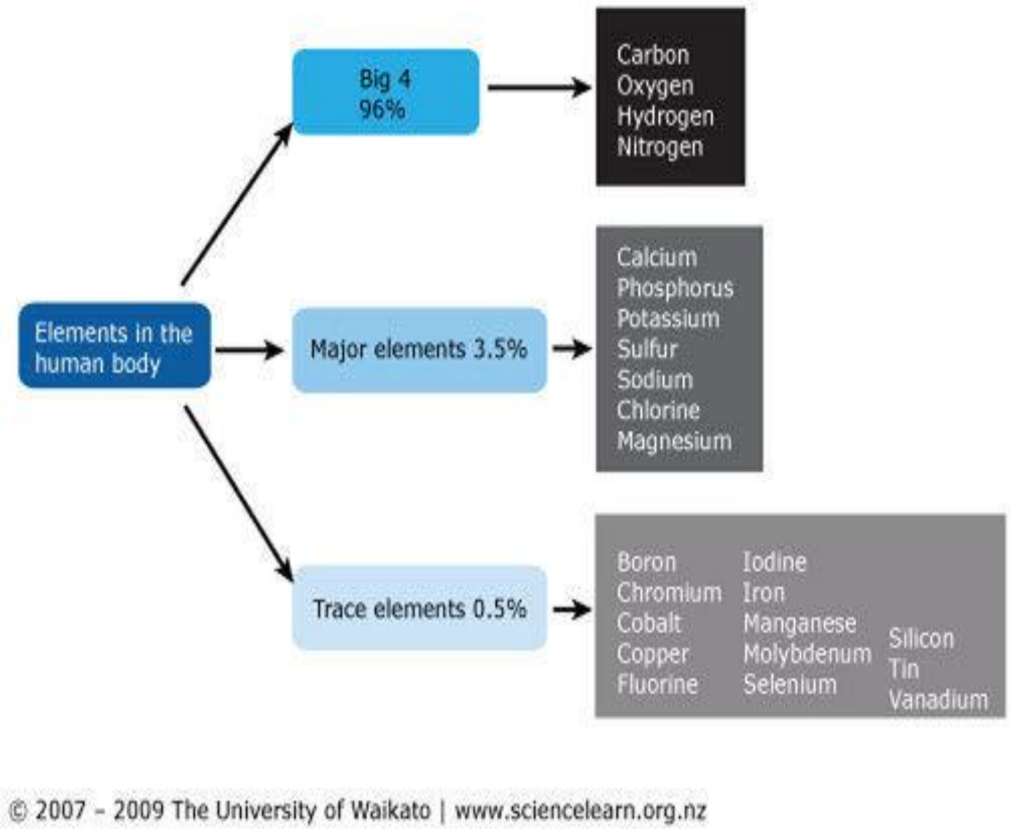
(Na, Ca, Mg, K, I, Fe, Se, Mn, Si, Cl, F, Cr, Zn, Cu are present in less quantity but important for certain biological processes.)

Molecules :

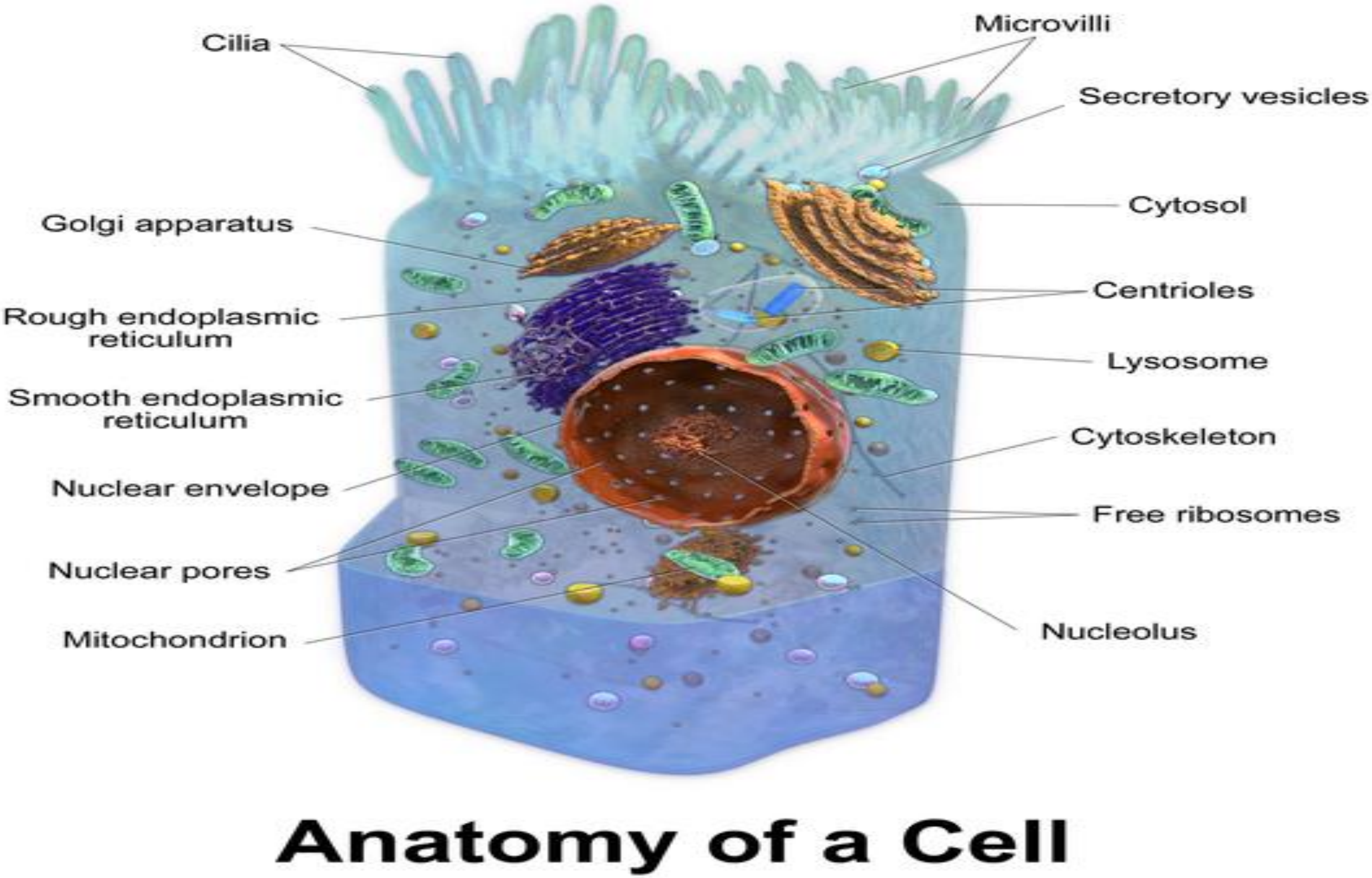
- **50% protein**
- **15% nucleic acid**
- **15% carbohydrates**
- **10% lipids**
- **10% Other**

The Major 6 elements



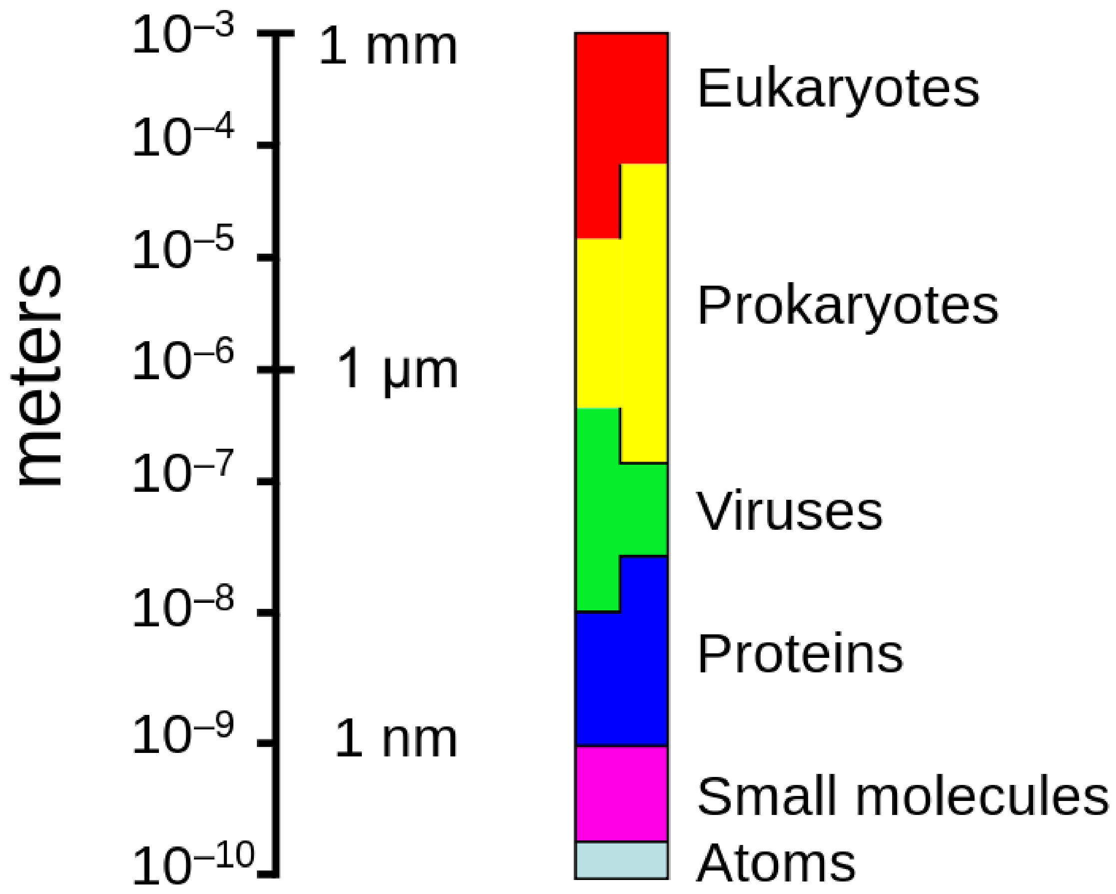


Cell : the building block of life

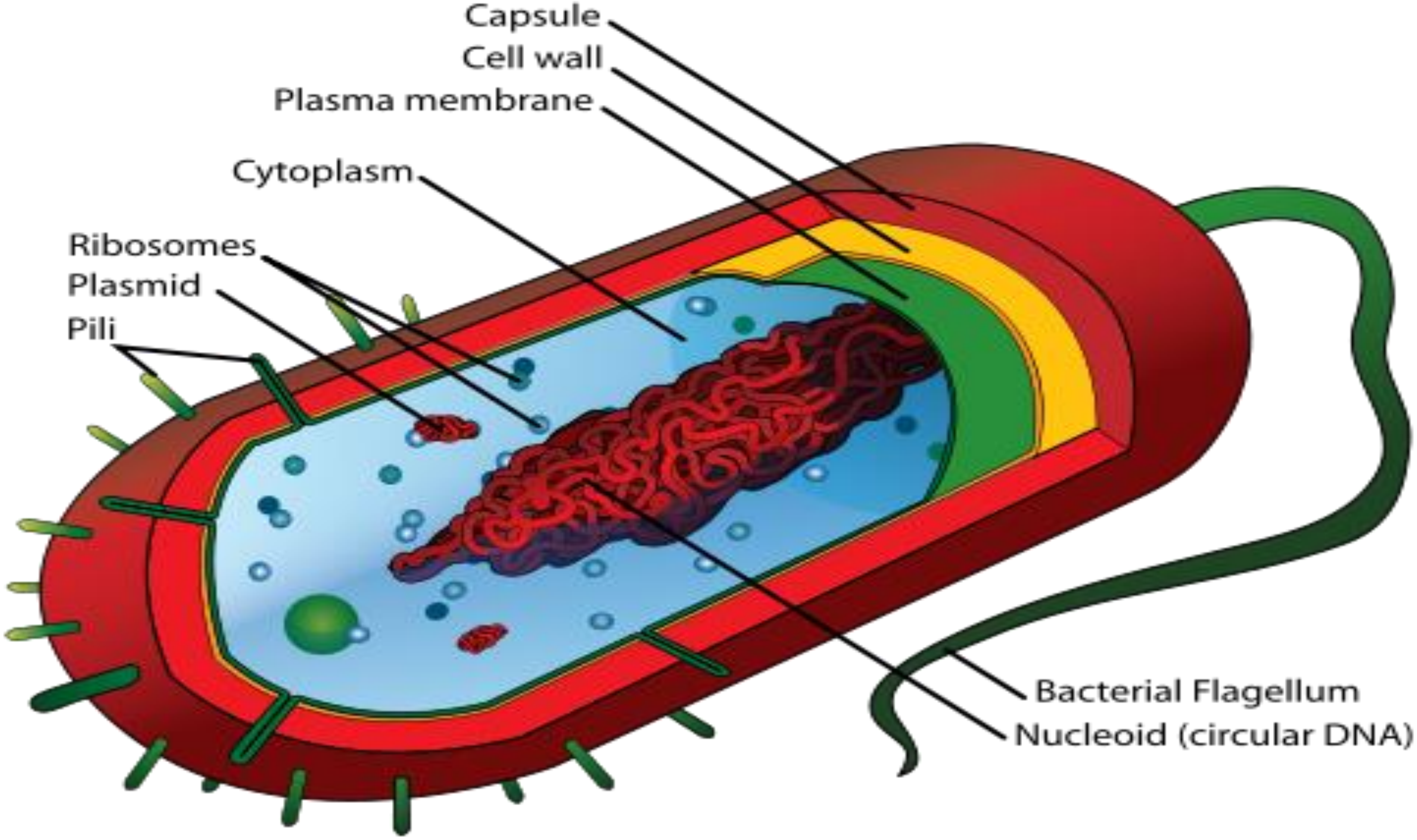


A typical animal cell : Eukaryotic

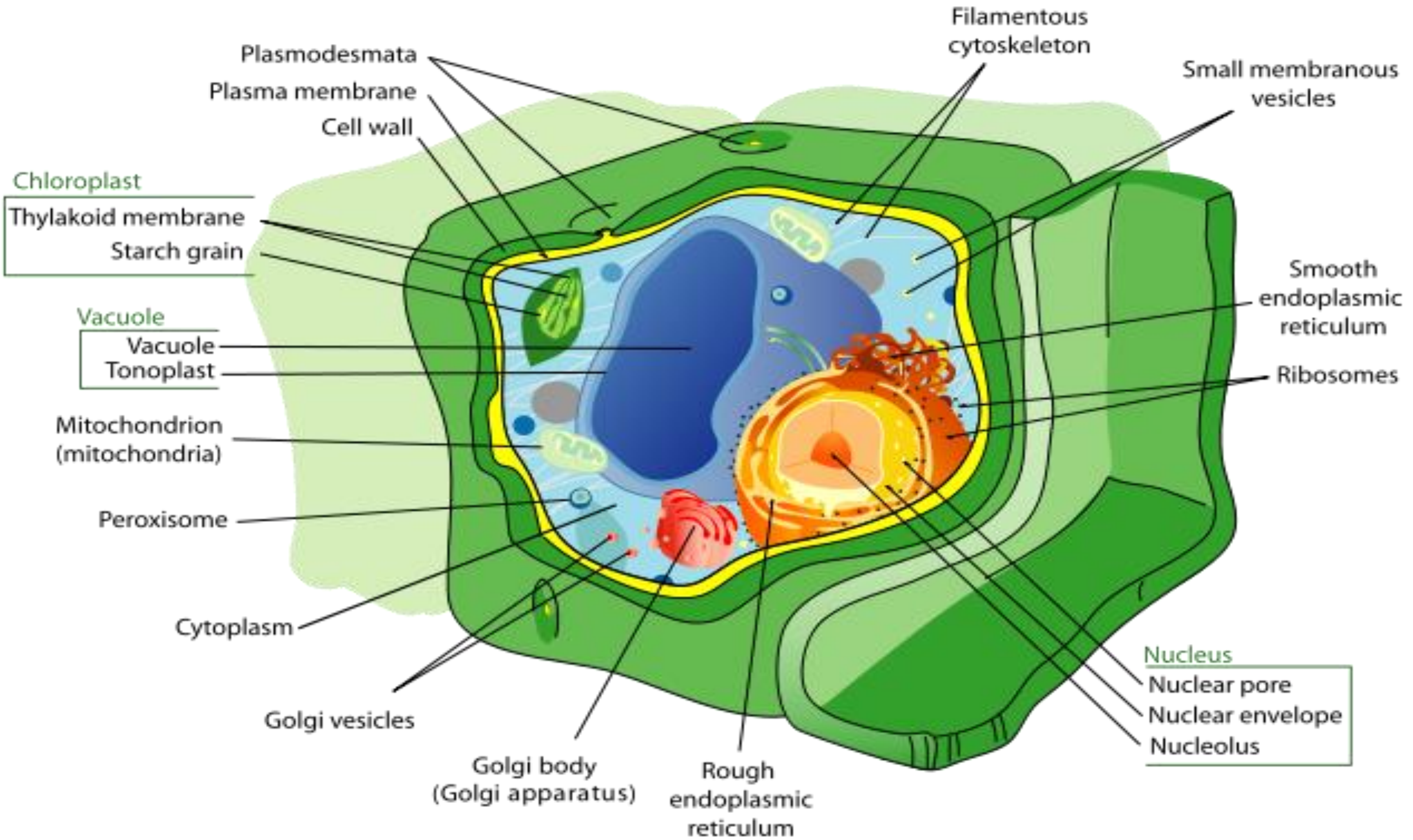
A concept of relative size
(Size of prokaryotes and eukaryotes given in organism level)



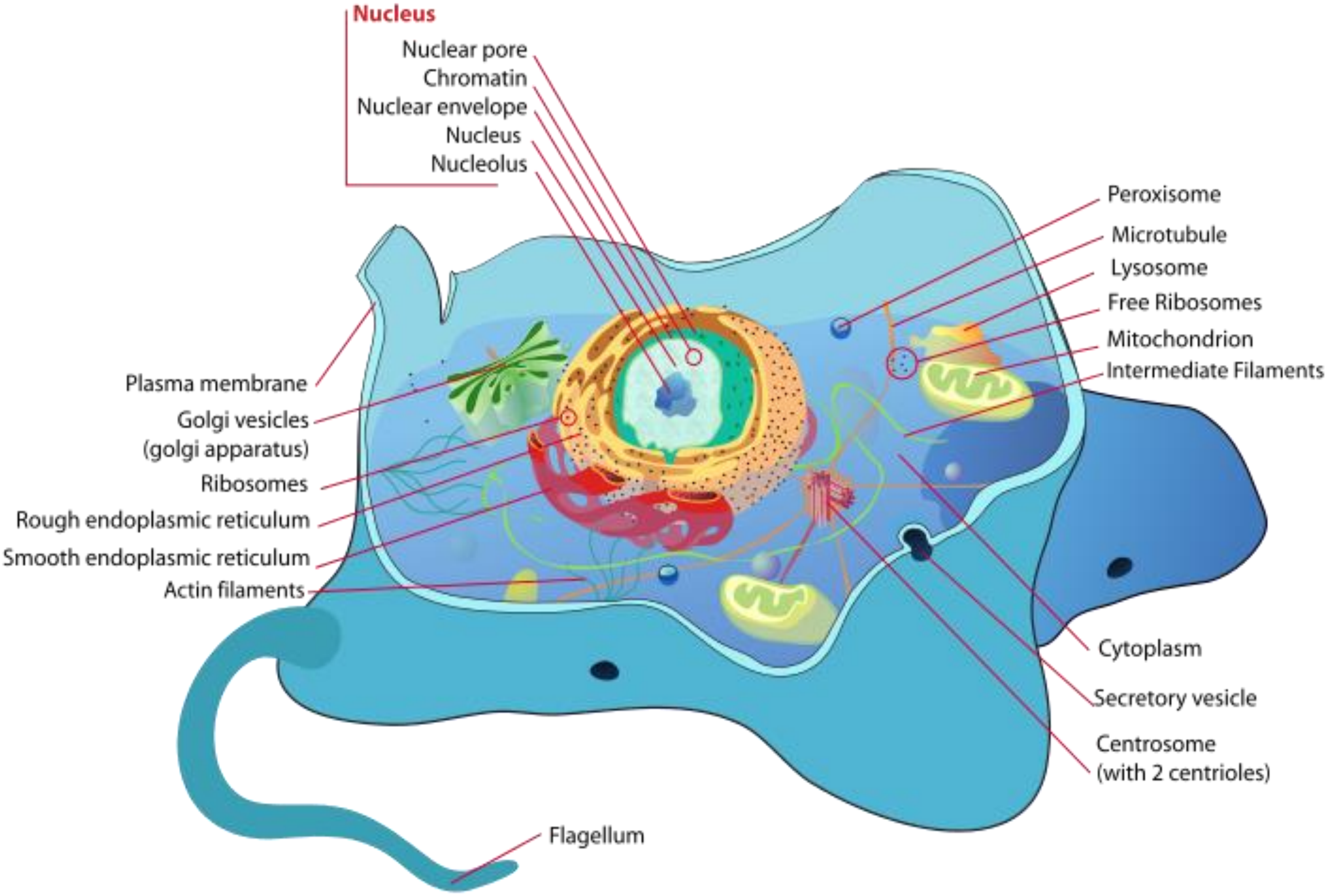
A typical prokaryotic cell



A typical plant cell



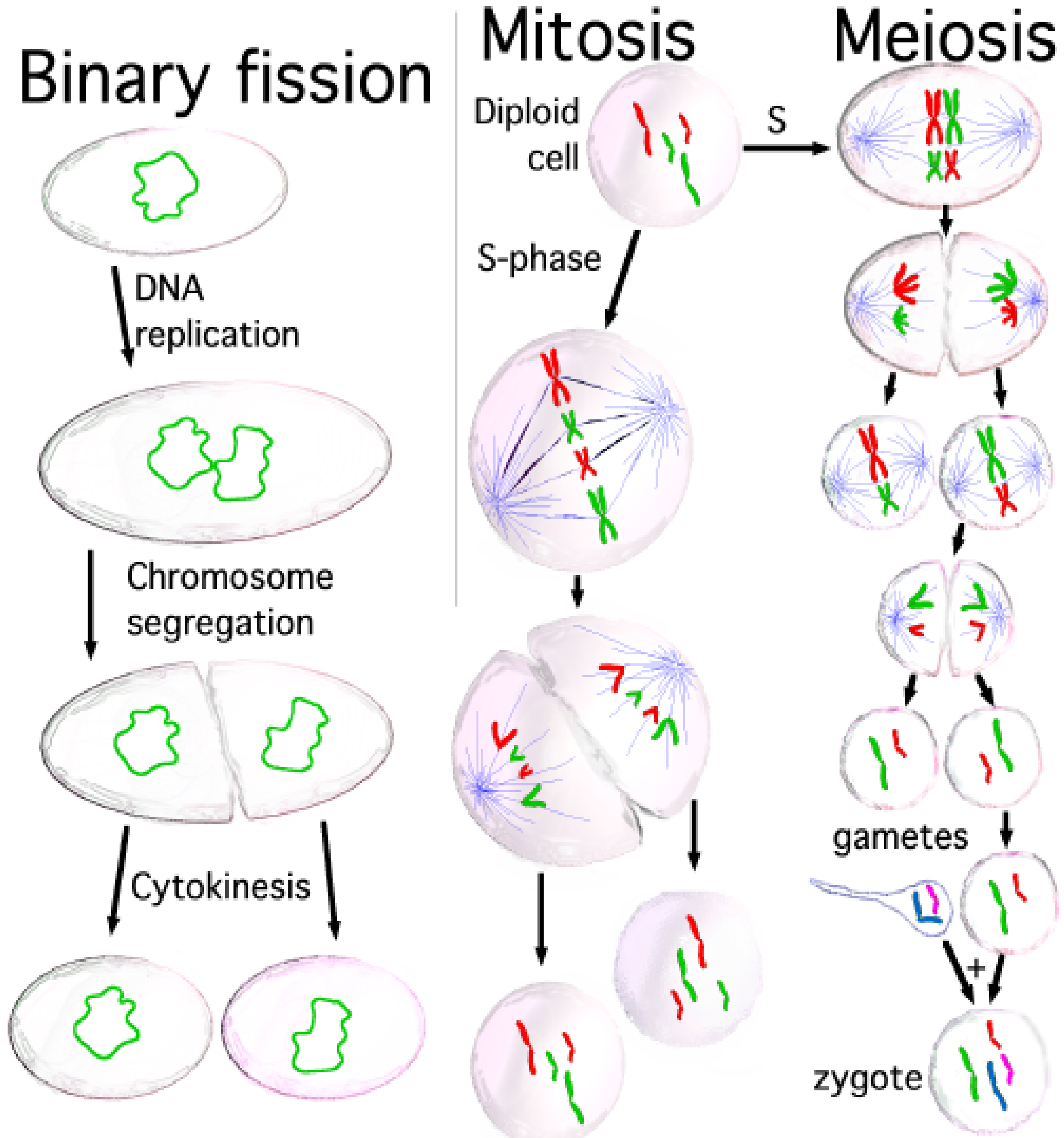
A typical animal cell



Journey from cell to cells : Cell Division

Prokaryotes undergo cell division known as binary fission , where their genetic material is segregated equally into two daughter cells. In eukaryotes, there are two distinct type of cell division: a vegetative division, whereby each daughter cell is genetically identical to the parent cell (mitosis), and a reductive cell division, whereby the number of chromosomes in the daughter cells is reduced by half, to produce haploid gametes (meiosis).

Meiosis results in four haploid daughter cells by undergoing one round of DNA replication followed by two divisions: homo-logous chromosomes are separated in the first division, and sister chromatids are separated in the second division.

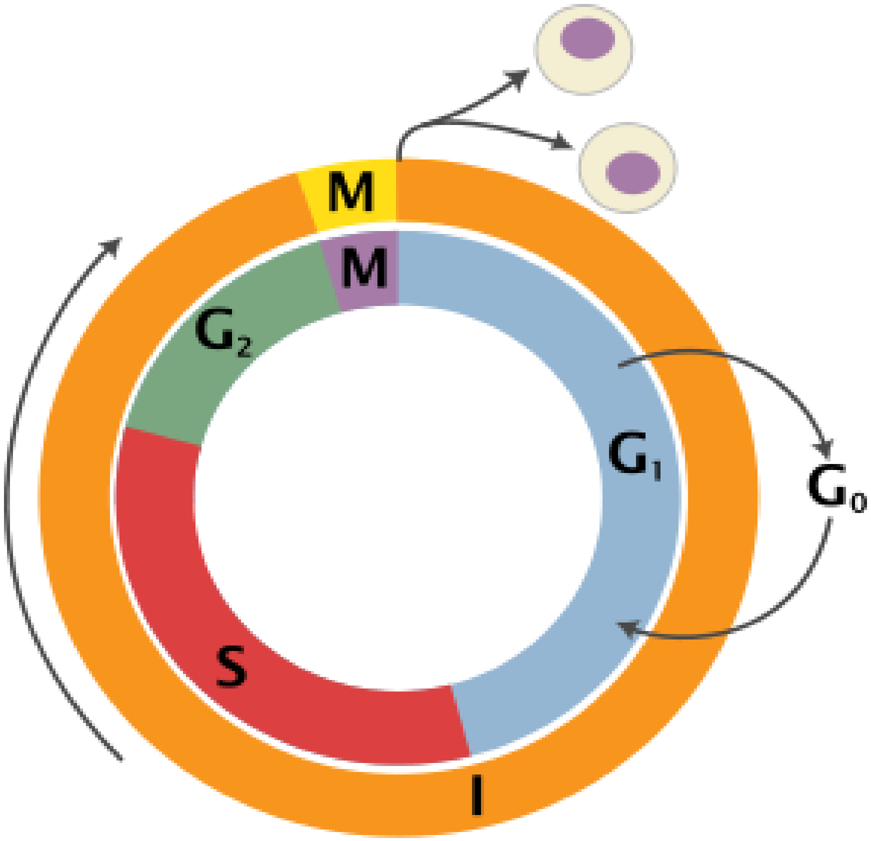


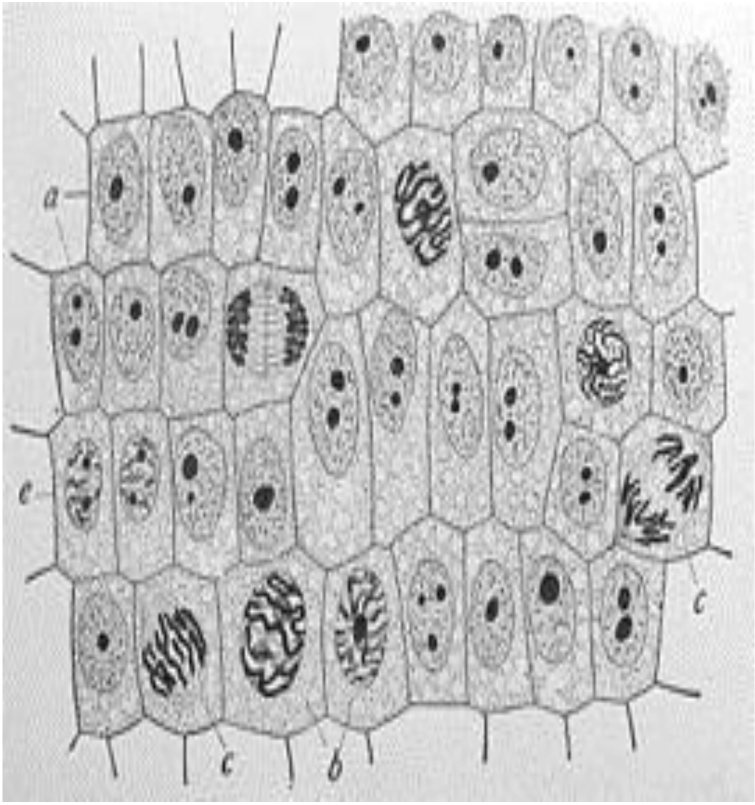
Cell Cycle

- ✓ **The cell cycle, is the series of events that take place in a cell leading to its division and duplication (replication) that produces two daughter cells. In cells without a nucleus (prokaryotic), the cell cycle occurs via a process termed binary fission.**

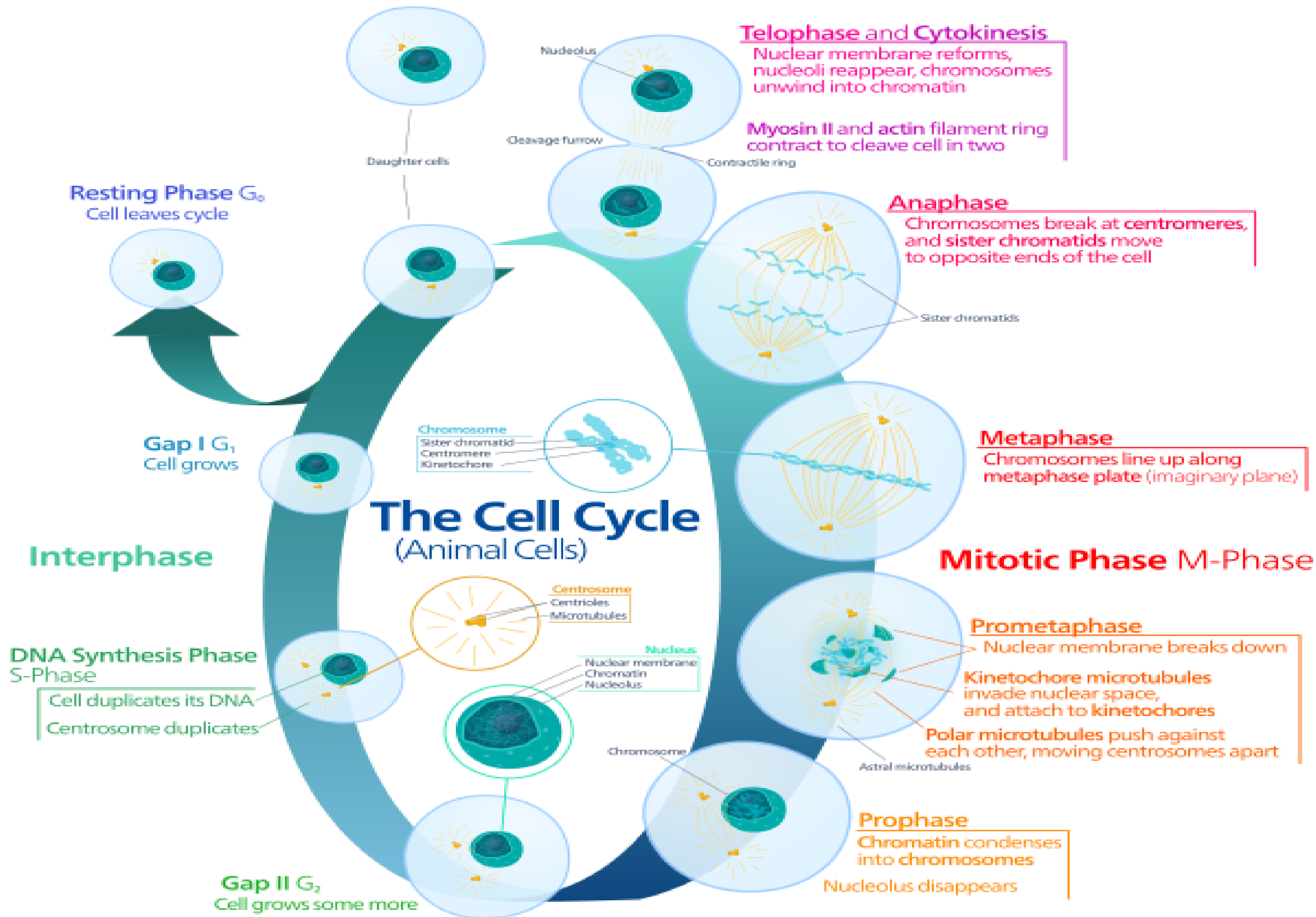
- ✓ **In cells with a nucleus (eukaryotes), the cell cycle can be divided in three periods: interphase—during which the cell grows, accumulating nutrients needed for mitosis preparing it for cell division and duplicating its DNA—and the mitotic (M) phase, during which the cell splits itself into two distinct cells, often called "daughter cells" and the final phase, cytokinesis, where the new cell is completely divided.**

- ✓ **The cell-division cycle is a vital process by which a single-celled fertilized egg develops into a mature organism, as well as the process by which hair, skin, blood cells, and some internal organs are renewed.**


M
M
G_2
G_1
G_0
S
I


a
e
c
c
b

State	Description	Abbreviation	Function
quiescent/ senescent	**Gap 0**	**G0**	A resting phase where the cell has left the cycle and has stopped dividing. A cell can again come back to normal interphase and subsequent mitosis (ex : liver cells) or can stay in G0 for the rest of life (ex : neurons).
Interphase	**Gap 1**	**G1**	Cells increase in size in Gap 1. Some of the cell organelles duplicate their numbers. The *G1 checkpoint* checks for errors and ensures that everything is ready for DNA synthesis. Other metabolic activity and some protein formation.
	Synthesis	**S**	DNA replication occurs during this phase.
	Gap 2	**G2**	During the gap between DNA synthesis and mitosis, the cell will continue to grow. A major portion of mRNA transcription and protein translation takes place. The *G2 checkpoint* control mechanism ensures that everything is ready to enter the M (mitosis) phase and divide.
Cell division	**Mitosis**	**M**	Cell growth stops at this stage and cellular energy is focused on the orderly division into two daughter cells. A checkpoint in the middle of mitosis (*Metaphase Checkpoint*) ensures that the cell is ready to complete cell division.



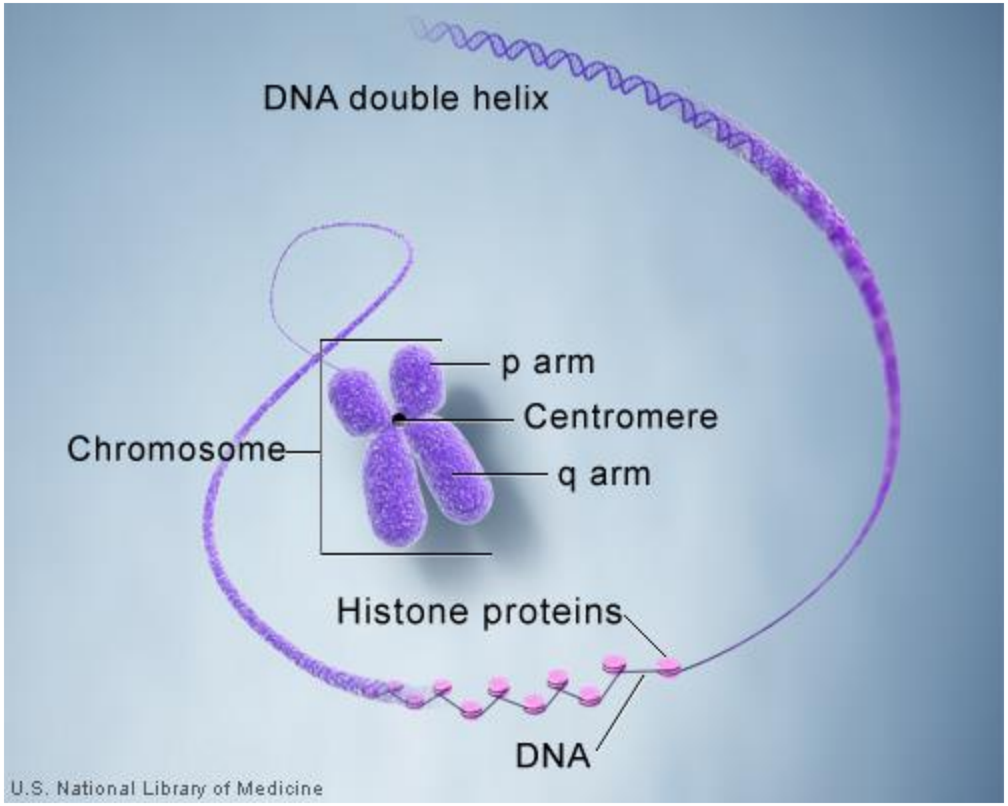
Animation :
http://www.biology.arizona.edu/cell_bio/tutorials/cell_cycle/MitosisFlash.html

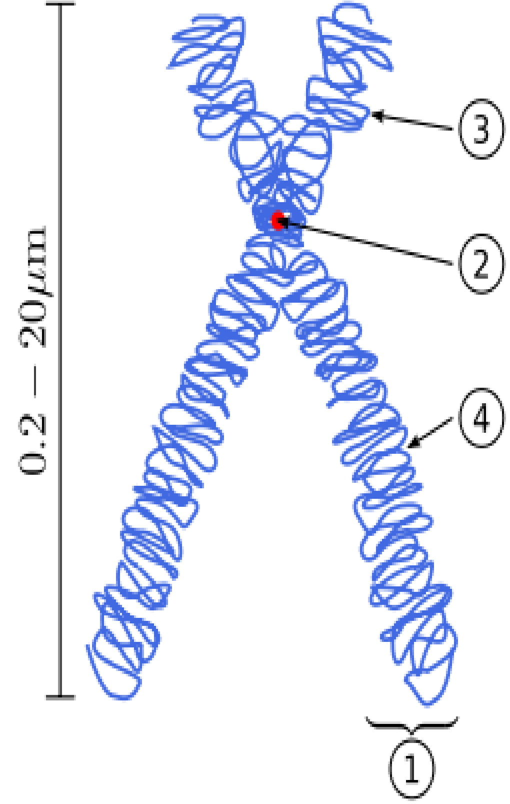
Chromosome

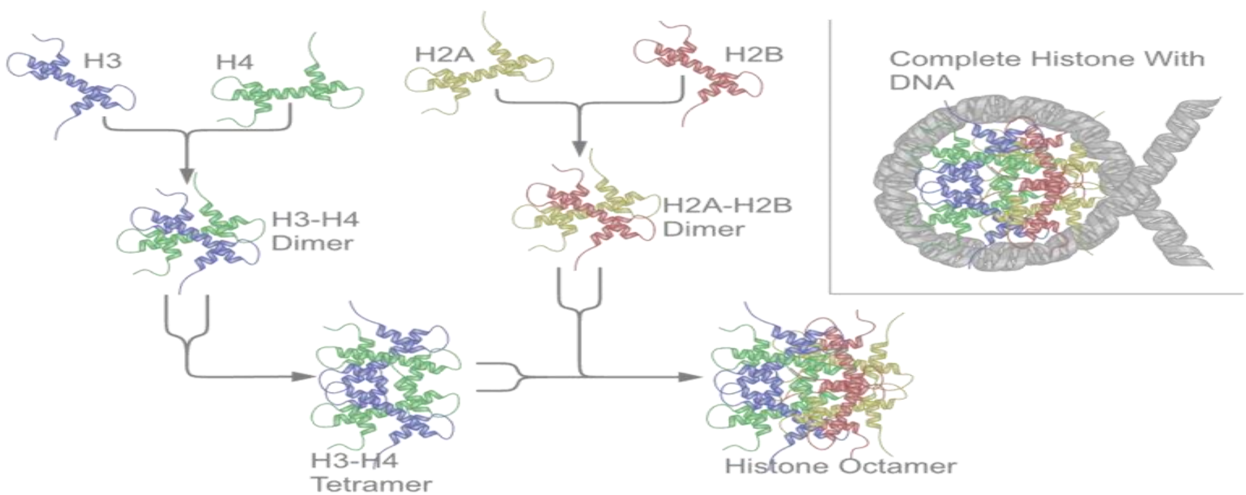
A chromosome is a structure of DNA, protein, and RNA found in cells. It is a single piece of coiled DNA containing many genes, regulatory elements and other nucleotide sequences. Chromosomes also contain DNA-bound proteins, which serve to package the DNA and control its functions. Chromosomal DNA encodes most or all of an organism's genetic information.

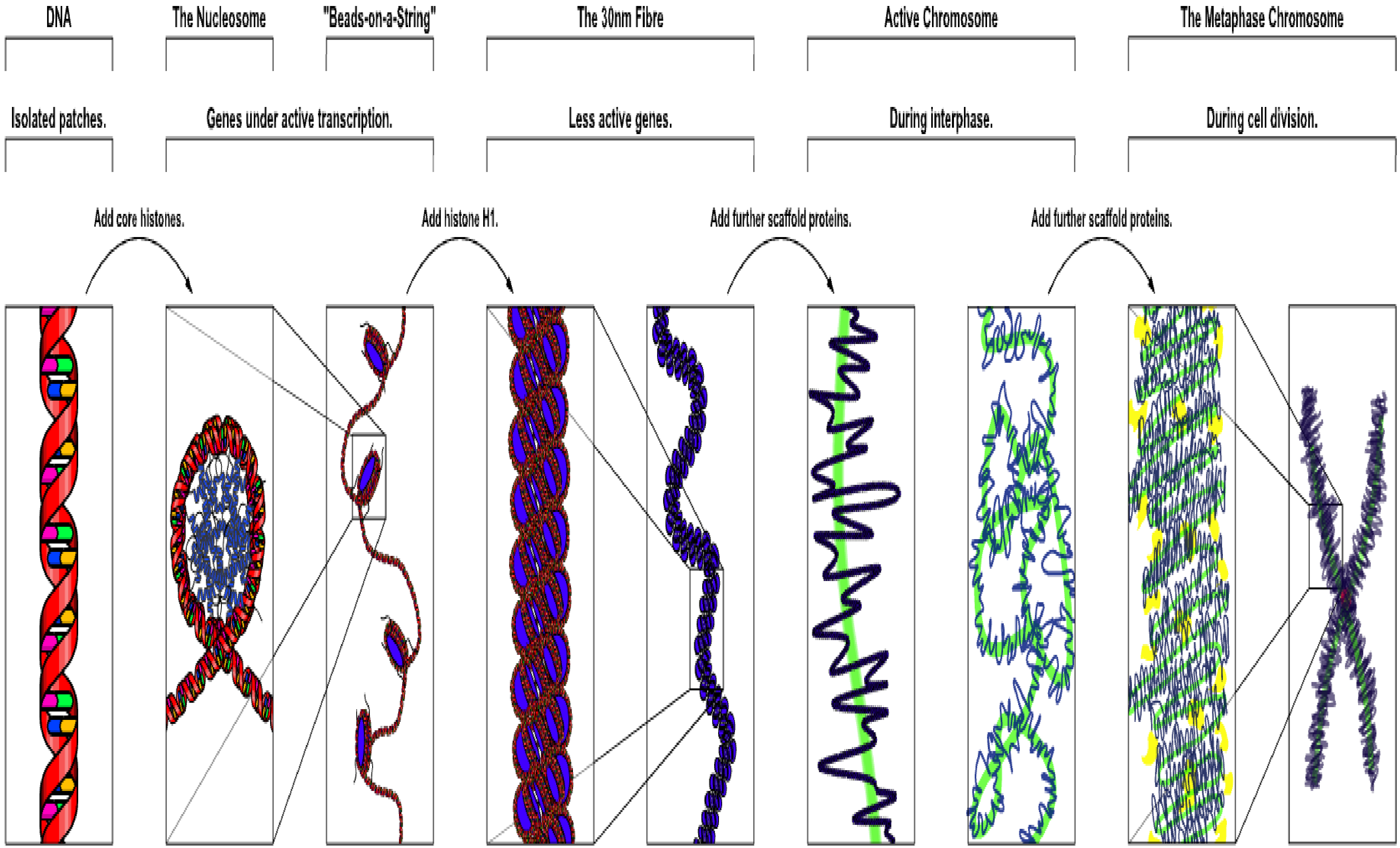
Chromosomes vary widely between different organisms. The DNA molecule may be circular or linear, and can be composed of 100,000 to over 3,750,000,000 nucleotides in a long chain.

Typically, eukaryotic cells (cells with nuclei) have large linear chromosomes and prokaryotic cells (cells without defined nuclei) have smaller circular chromosomes, although there are many exceptions to this rule. Cells may contain more than one type of chromosome; for example, mitochondria in most eukaryotes and chloroplasts in plants have their own small chromosomes.

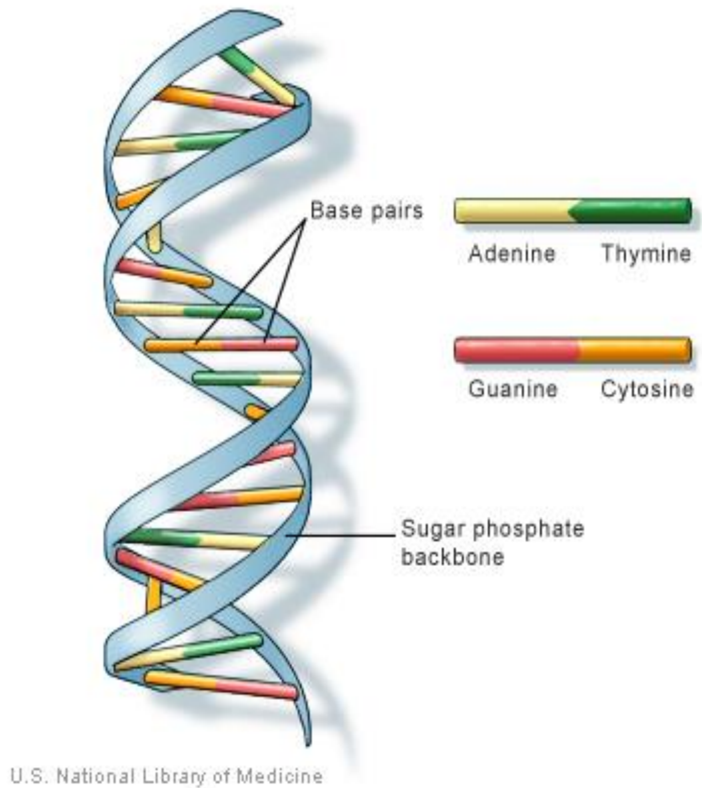

DNA double helix
p arm
Centromere
Chromosome
q arm
Histone proteins
DNA
U.S. National Library of Medicine

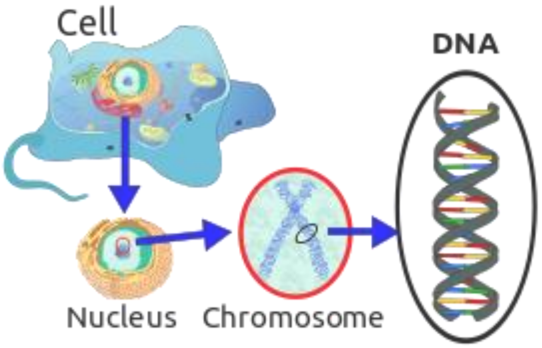

0.2 − 20μm
3
2
4
1

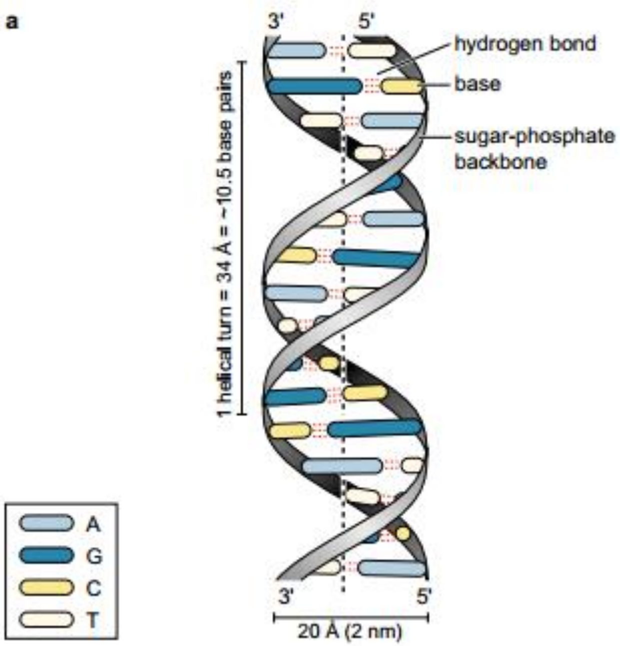

H3
H4
H2A
H2B
Complete Histone With DNA
H3-H4 Dimer
H2A-H2B Dimer
H3-H4 Tetramer
Histone Octamer


DNA
The Nucleosome
"Beads-on-a-String"
The 30nm Fibre
Active Chromosome
The Metaphase Chromosome
Isolated patches.
Genes under active transcription.
Less active genes.
During interphase.
During cell division.
Add core histones.
Add histone H1.
Add further scaffold proteins.
Add further scaffold proteins.

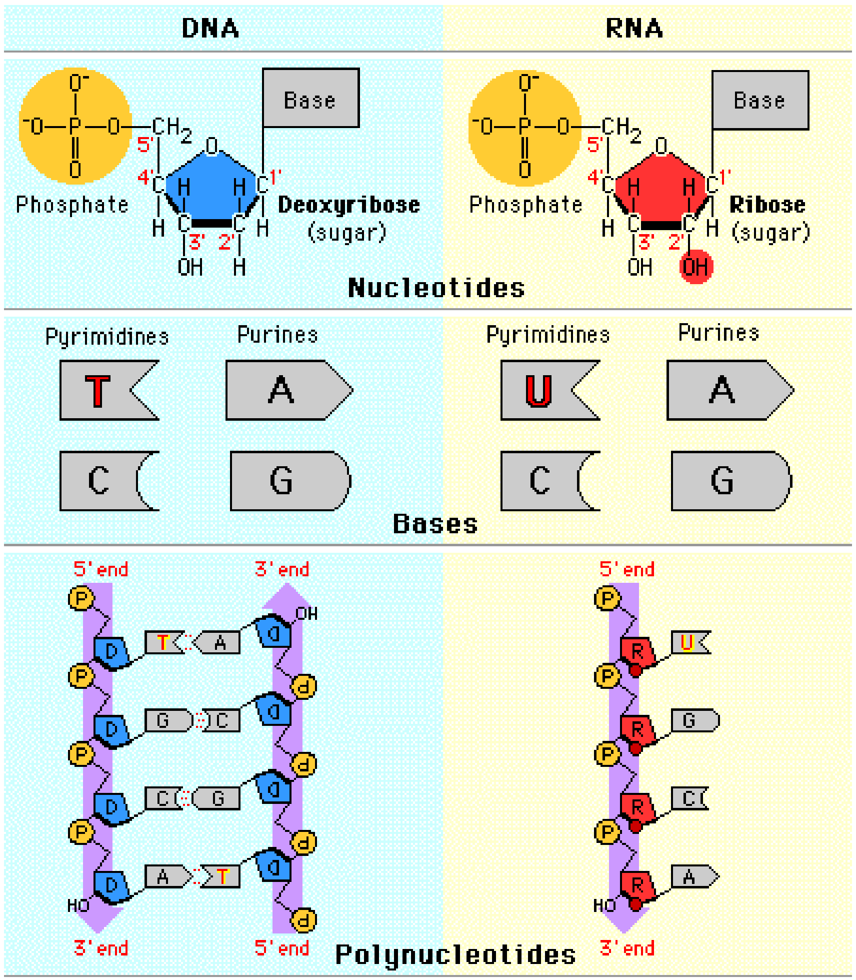
DNA

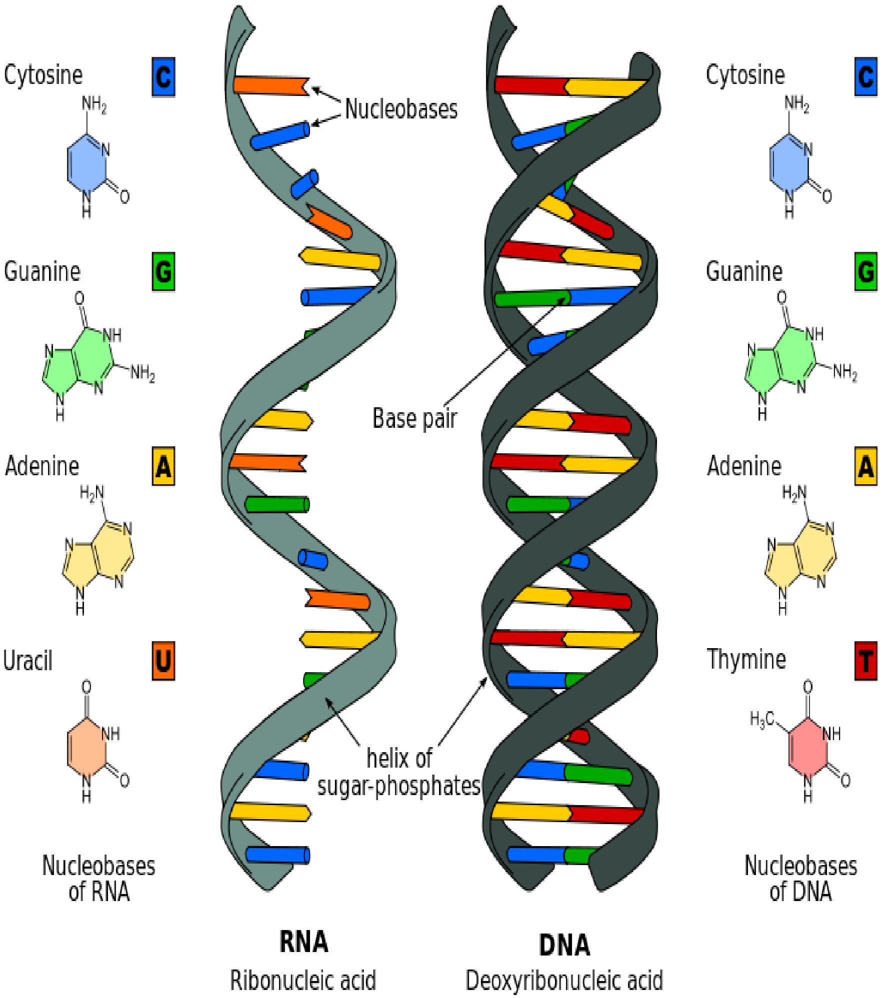

Base pairs
Adenine
Thymine
Guanine
Cytosine
Sugar phosphate backbone
U.S. National Library of Medicine


Cell
DNA
Nucleus
Chromosome


a
3'
5'
hydrogen bond
base
sugar-phosphate backbone
1 helical turn = 34 Å = ~10.5 base pairs
A
G
C
T
3'
5'
20 Å (2 nm)

DNA & RNA

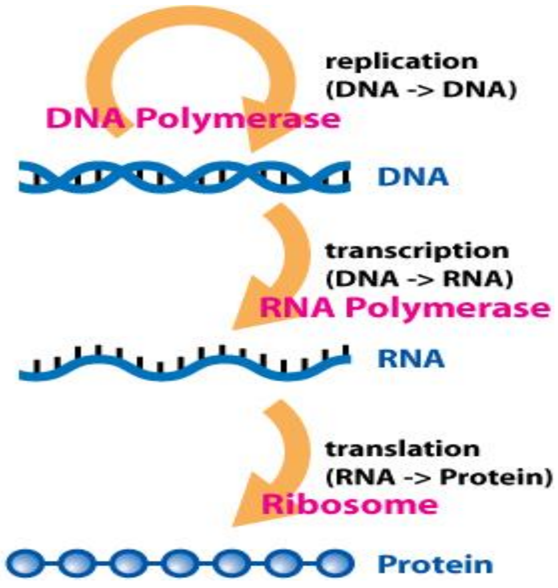

DNA
RNA
Base
Phosphate
Deoxyribose
(sugar)
Ribose
(sugar)
Nucleotides
Pyrimidines
Purines
T
A
U
C
G
Bases
5' end
3' end
Polynucleotides


Cytosine
Guanine
Adenine
Uracil
Thymine
Nucleobases
Base pair
helix of
sugar-phosphates
Nucleobases
of RNA
Nucleobases
of DNA
RNA
Ribonucleic acid
DNA
Deoxyribonucleic acid

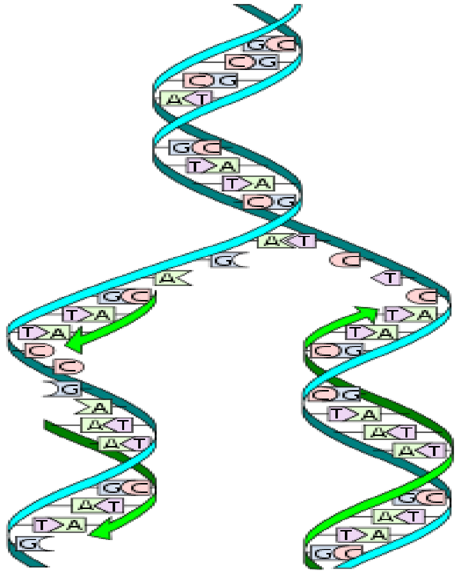
Central Dogma

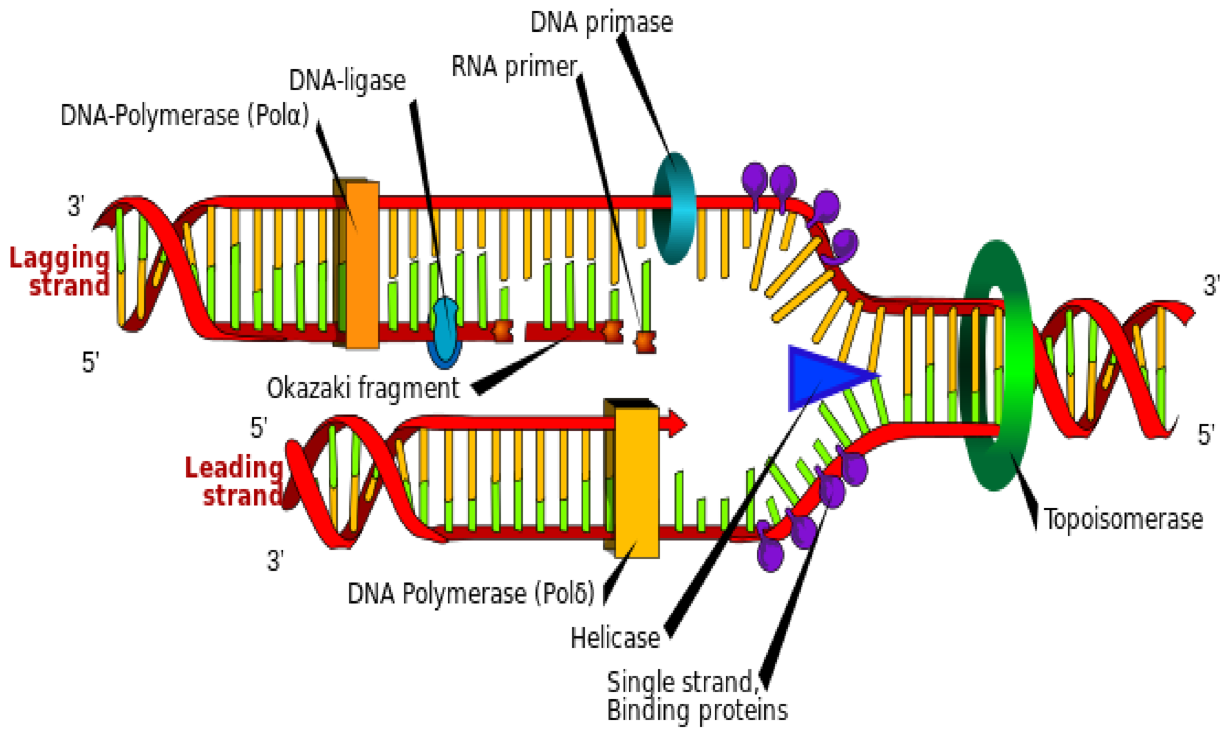
- ✓ The central dogma of molecular biology is an explanation of the flow of genetic information within a biological system. It was first stated by Francis Crick in 1958. It describes the two-step process, transcription and translation, by which the information in genes flows into proteins: DNA → RNA → protein.

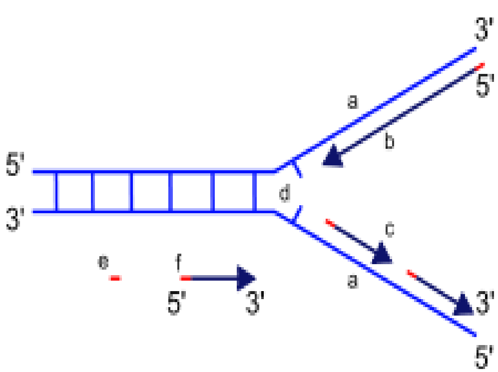
- ✓ *The central dogma of molecular biology deals with the detailed residue-by-residue transfer of sequential information. It states that such information cannot be transferred back from protein to either protein or nucleic acid.*



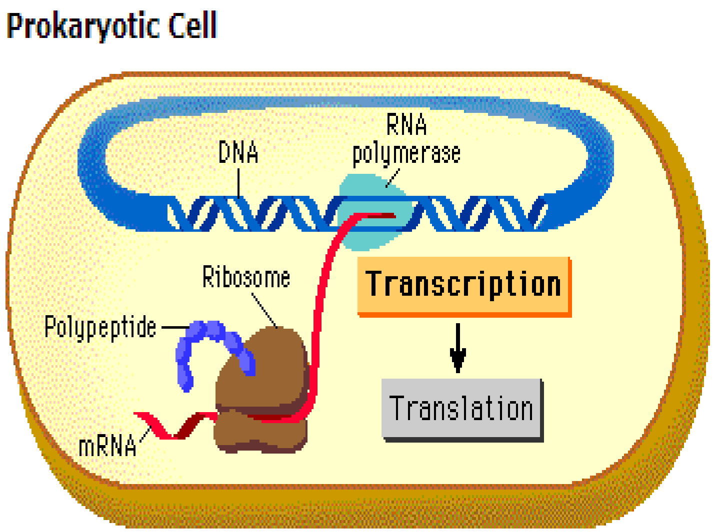
DNA replication : It is the process of producing two identical replicas from one original DNA molecule. This biological process occurs in all living organisms and is the basis for biological inheritance. DNA is made up of two strands and each strand of the original DNA molecule serves as template for the production of the complementary strand, a process referred to as semi-conservative replication.

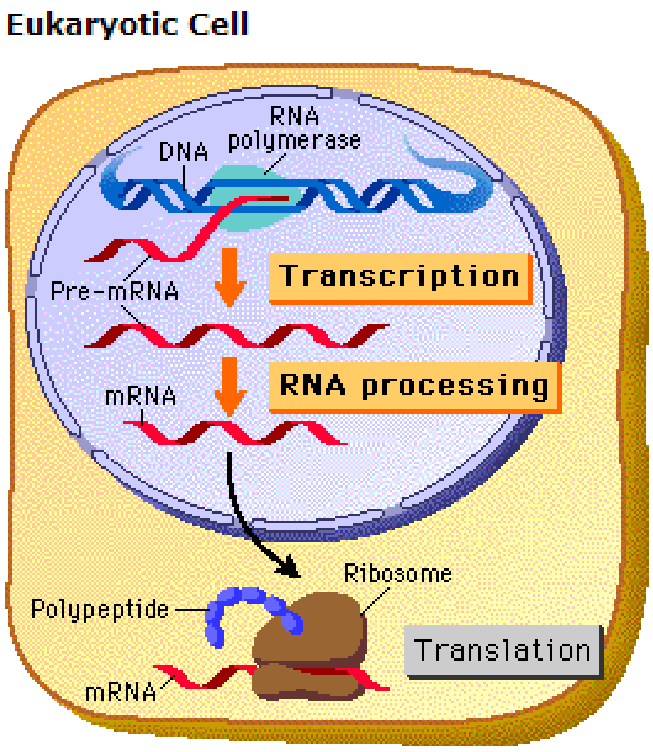




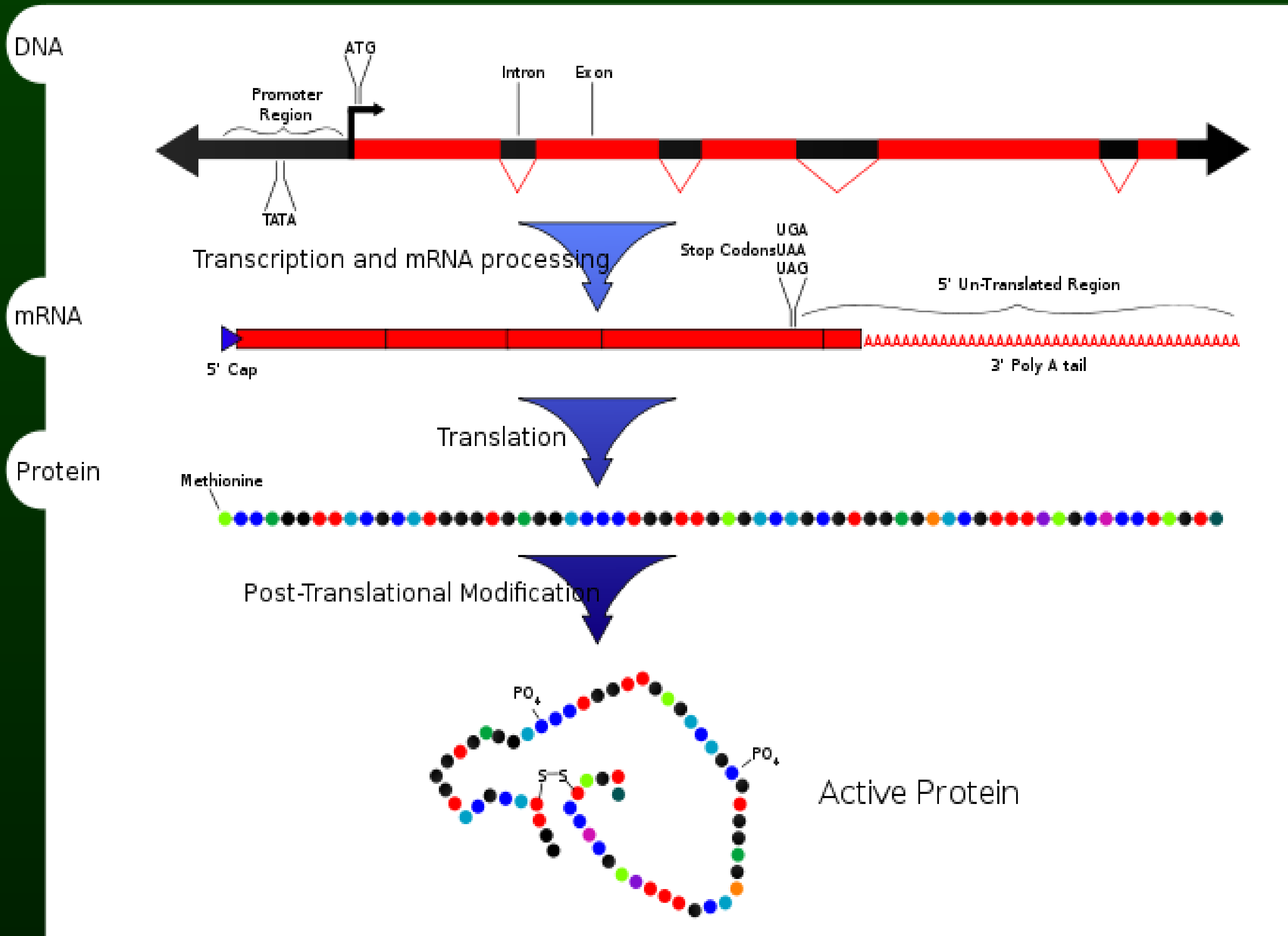


In a prokaryotic cell, transcription and translation are coupled; that is, translation begins while the mRNA is still being synthesized. In a eukaryotic cell, transcription occurs in the nucleus, and translation occurs in the cytoplasm.

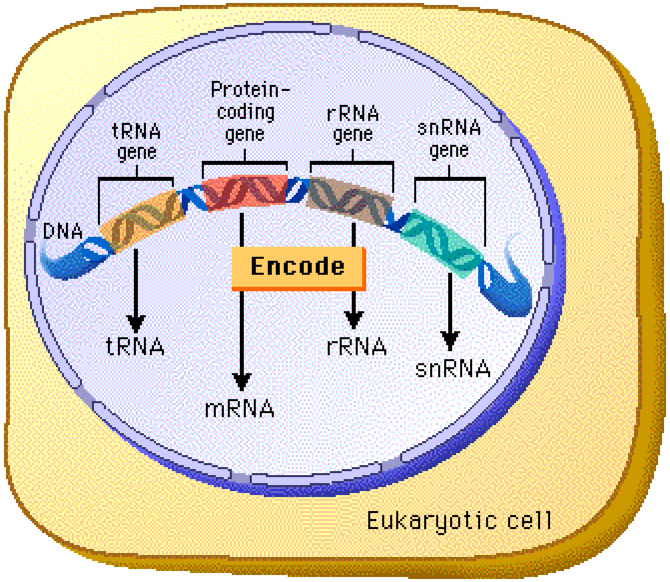


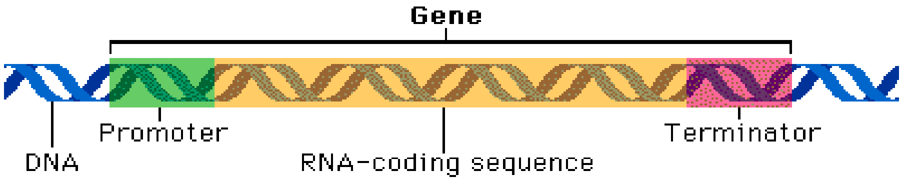


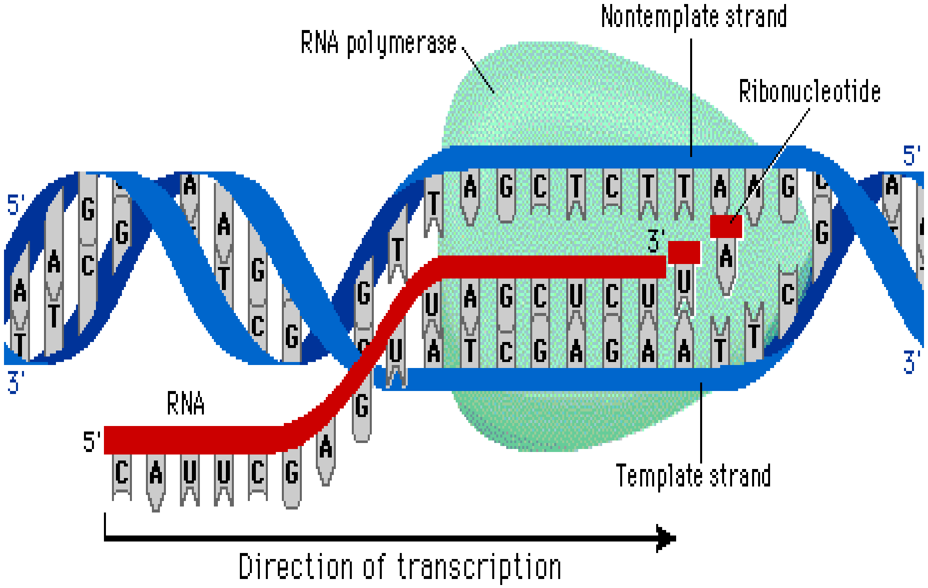
Central Dogma of Molecular Biology : Eukaryotic Model



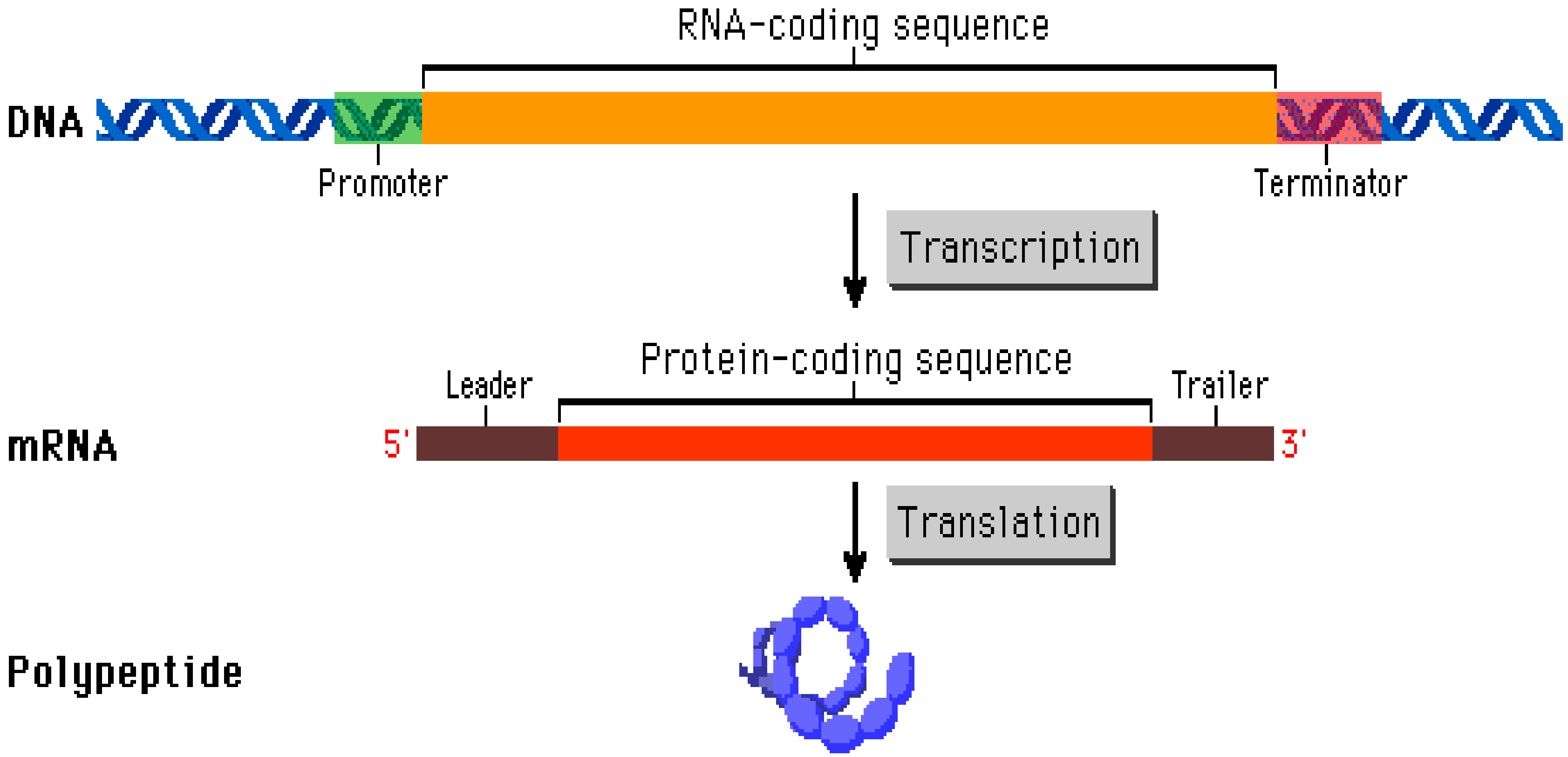
<u>Transcription</u> : ***RNA synthesis involves separation of the DNA strands and synthesis of an RNA molecule in the 5' to 3' direction by RNA polymerase, using one of the DNA strands as a template.***



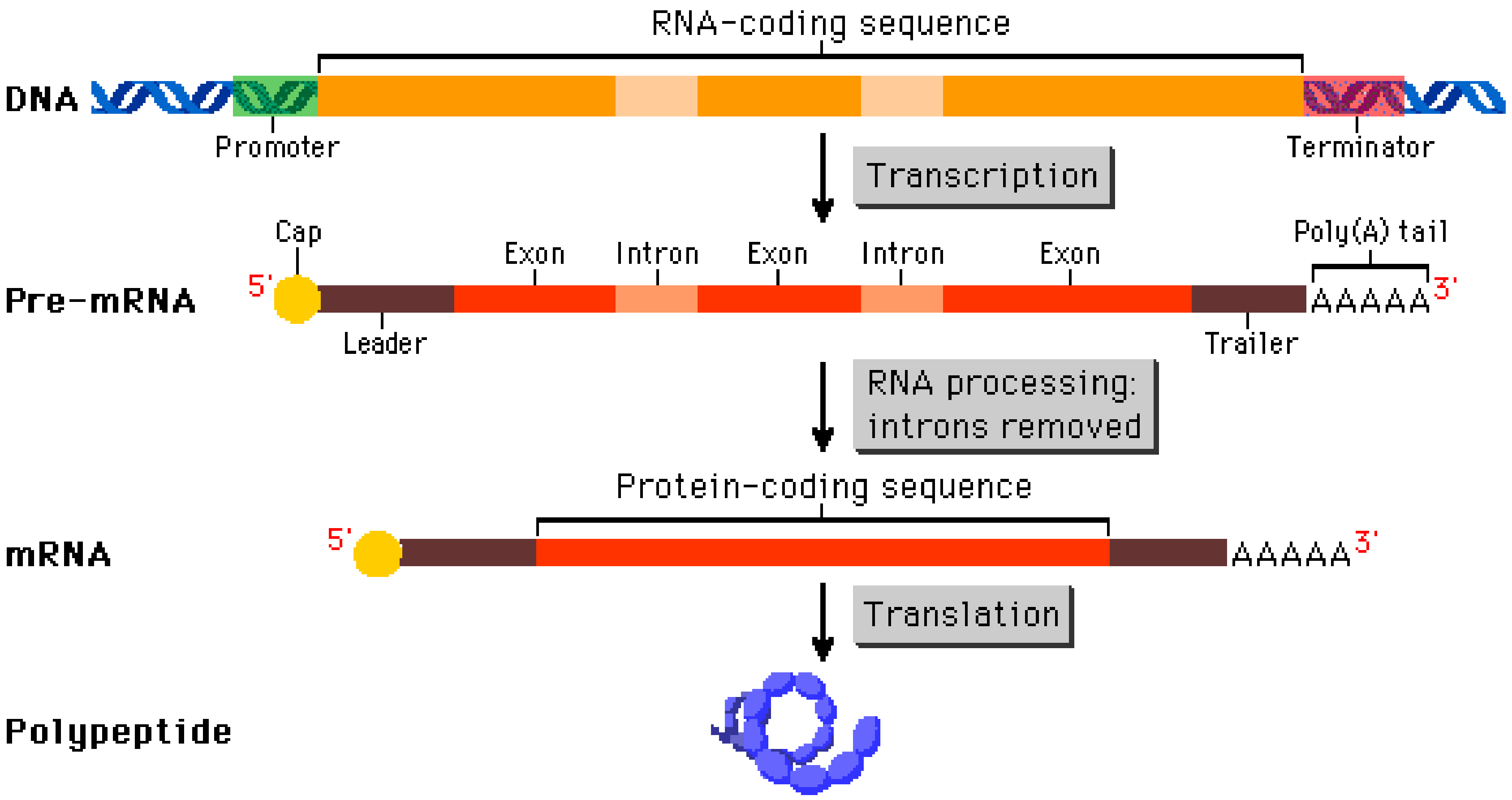




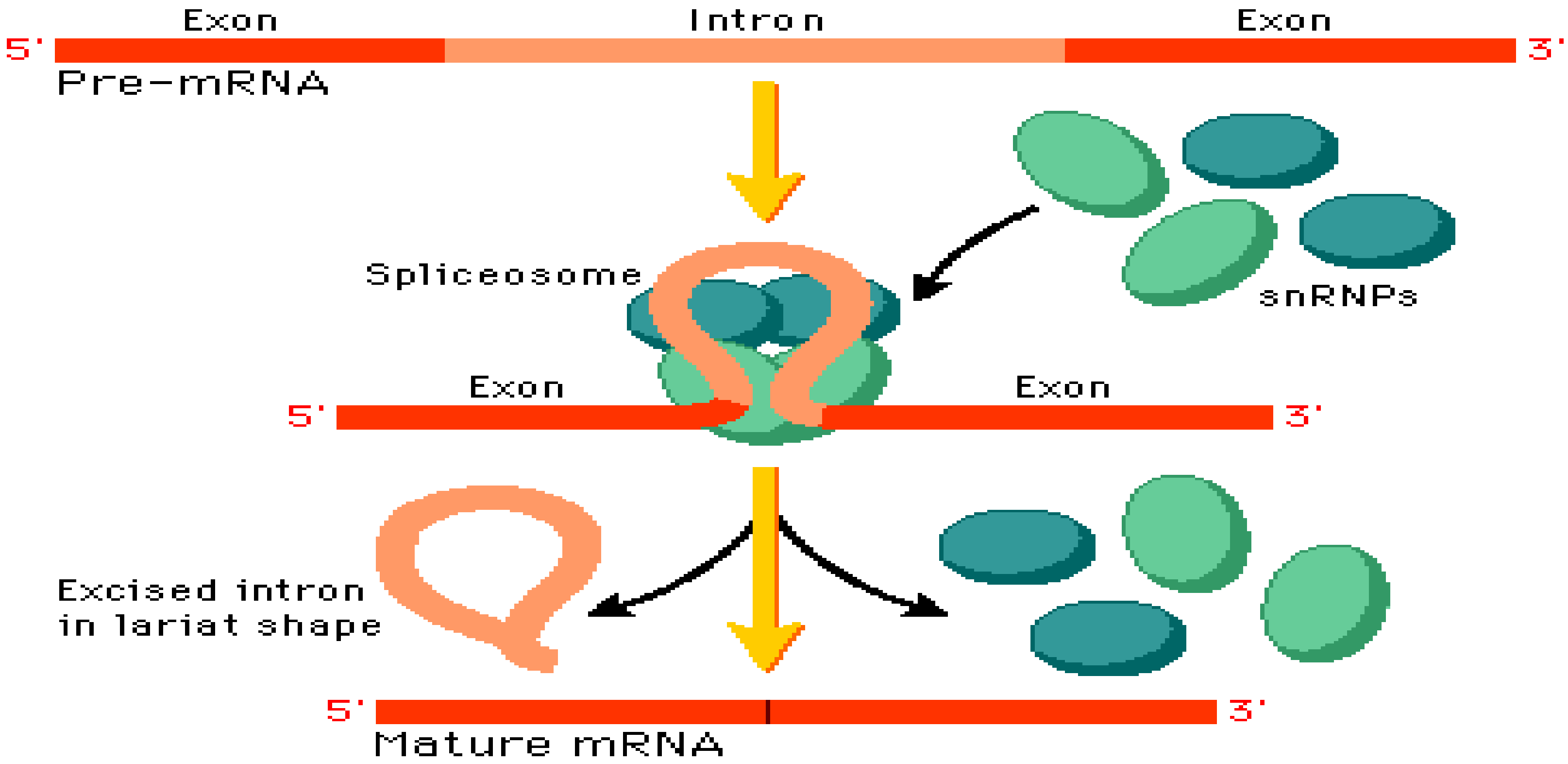
<u>mRNA in Prokaryotes</u> : ***The sequence of a prokaryotic protein-coding gene is co-linear with the translated mRNA; that is, the transcript of the gene is the molecule that is translated into the polypeptide.***



<u>mRNA in Eukaryotes</u> : ***The sequence of a eukaryotic protein-coding gene is typically not co-linear with the translated mRNA; that is, the transcript of the gene is a molecule that must be processed to remove extra sequences (introns) before it is translated into the polypeptide.***

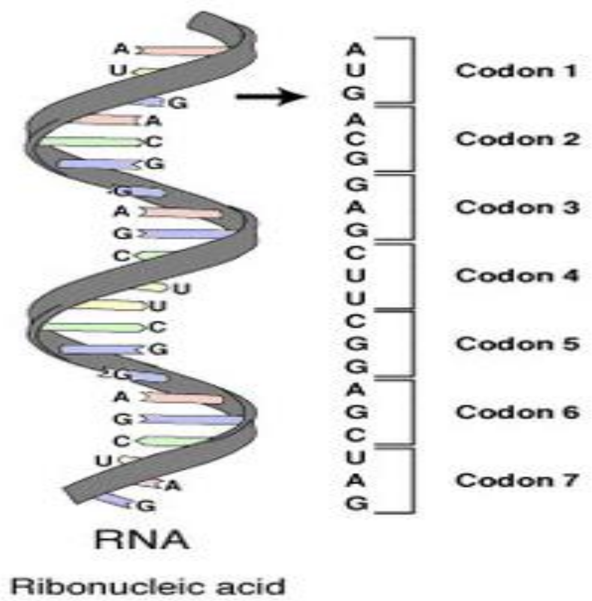


Eukaryotic pre-mRNAs typically include introns. Introns are removed by RNA processing in which the intron is looped out and cut away from the exons by snRNPs, and the exons are spliced together to produce the translatable mRNA.



Genetic Code

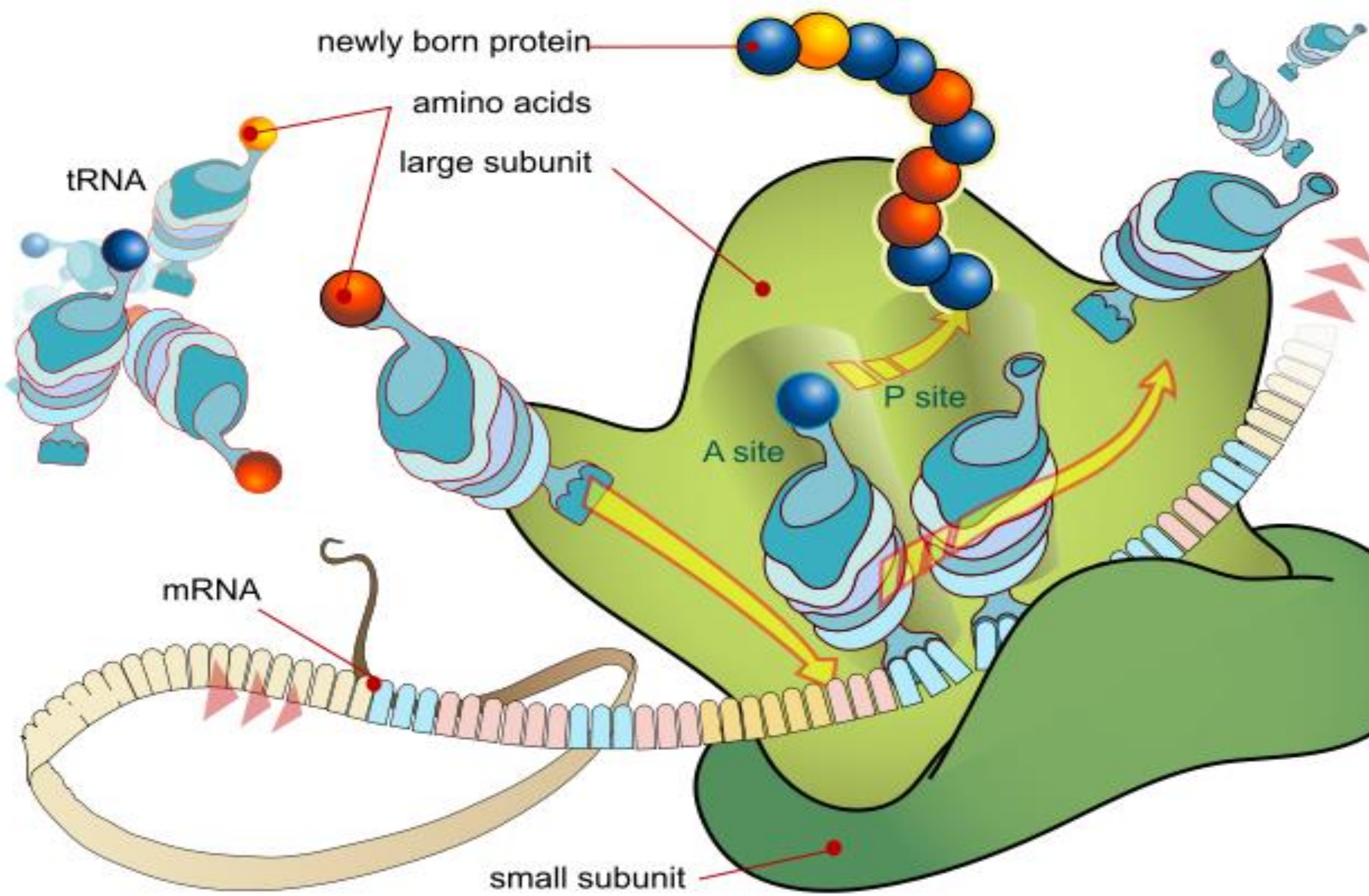
- ✓ *The genetic code is the set of rules by which information encoded within genetic material (DNA or mRNA sequences) is translated into proteins by living cells. Biological decoding is accomplished by the ribosome, which links amino acids in an order specified by mRNA, using transfer RNA(tRNA) molecules to carry amino acids and to read the mRNA three nucleotides at a time.*
- ✓ *The genetic code is highly similar among all organisms and can be expressed in a simple table with 64 entries.*



Second nucleotide

	U	C	A	G	
U	UUU **Phenylalanine** (Phe)	UCU **Serine** (Ser)	UAU **Tyrosine** (Tyr)	UGU **Cysteine** (Cys)	**U**
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	**C**
	UUA **Leucine** (Leu)	UCA Ser	UAA **STOP**	UGA **STOP**	**A**
	UUG Leu	UCG Ser	UAG **STOP**	UGG **Tryptophan** (Trp)	**G**
C	CUU **Leucine** (Leu)	CCU **Proline** (Pro)	CAU **Histidine** (His)	CGU **Arginine** (Arg)	**U**
	CUC Leu	CCC Pro	CAC His	CGC Arg	**C**
	CUA Leu	CCA Pro	CAA **Glutamine** (Gln)	CGA Arg	**A**
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	**G**
A	AUU **Isoleucine** (Ile)	ACU **Threonine** (Thr)	AAU **Asparagine** (Asn)	AGU **Serine** (Ser)	**U**
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	**C**
	AUA Ile	ACA Thr	AAA **Lysine** (Lys)	AGA **Arginine** (Arg)	**A**
	AUG **Methionine** (Met) or **START**	ACG Thr	AAG Lys	AGG Arg	**G**
G	GUU **Valine** Val	GCU **Alanine** (Ala)	GAU **Aspartic acid** (Asp)	GGU **Glycine** (Gly)	**U**
	GUC (Val)	GCC Ala	GAC Asp	GGC Gly	**C**
	GUA Val	GCA Ala	GAA **Glutamic acid** (Glu)	GGA Gly	**A**
	GUG Val	GCG Ala	GAG Glu	GGG Gly	**G**

Translation : mRNA to Protein



Can you address these questions?

- ✓ ***Where does so much diversity come from?***

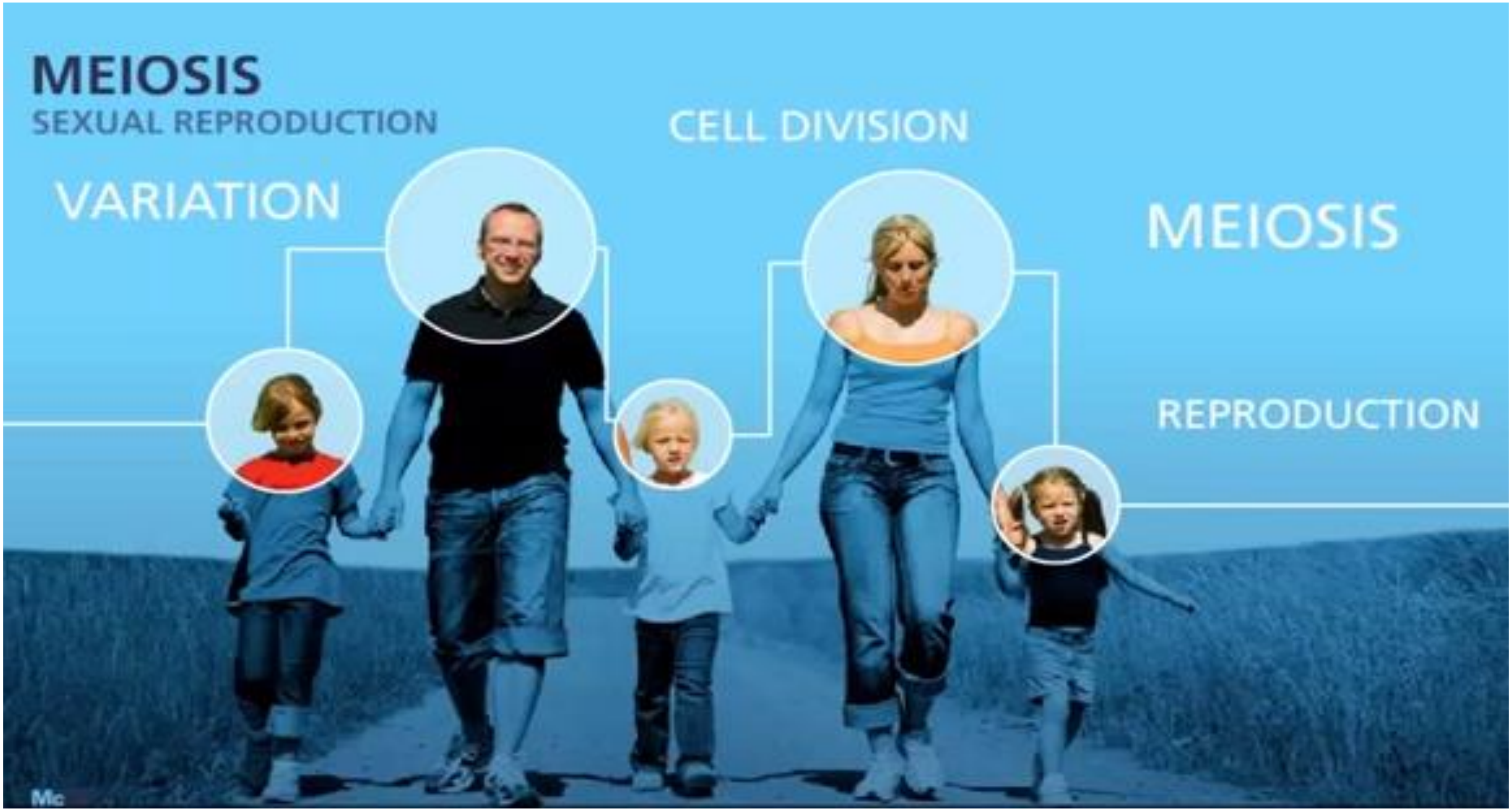
- ✓ ***Is there any need of this diversity?***
  - *More diversity -> More configuration -> Higher chance to find the fittest configuration which will evolve via Natural Selection-> Survival of the fittest-> Evolution -> Survival of the species with efficient members-> Mutations -> Evolution -> Generation of new species!*

- ✓ ***How does information flow from generation to generation?***

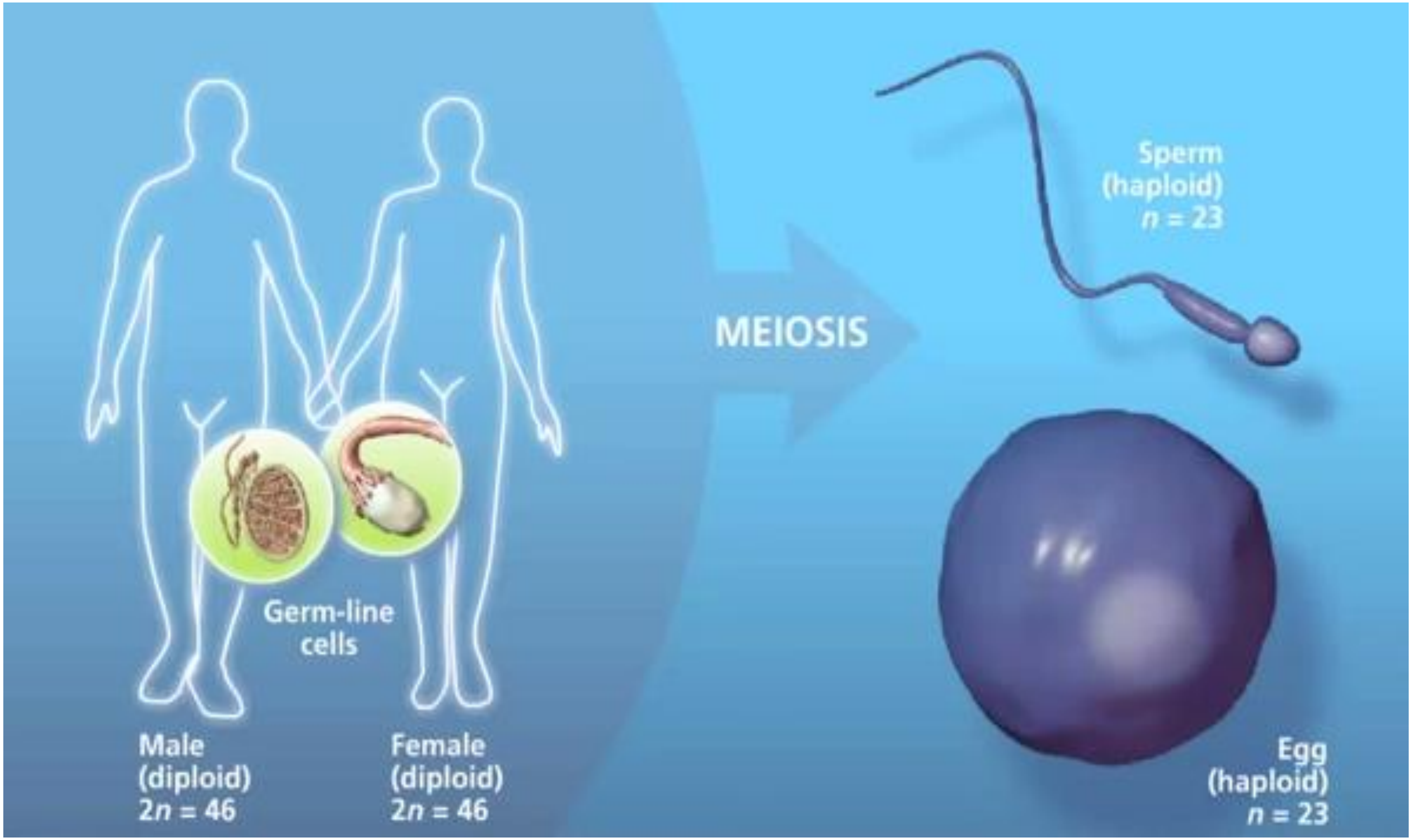
Addressing Diversity : Meiosis

Why do the children differ from their parents?

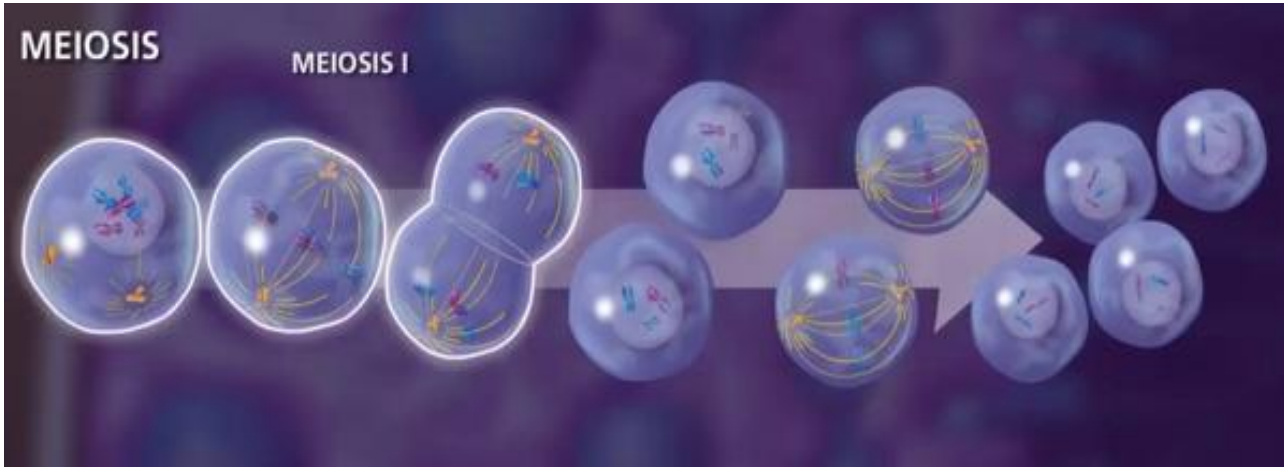
Why do the siblings differ among themselves?

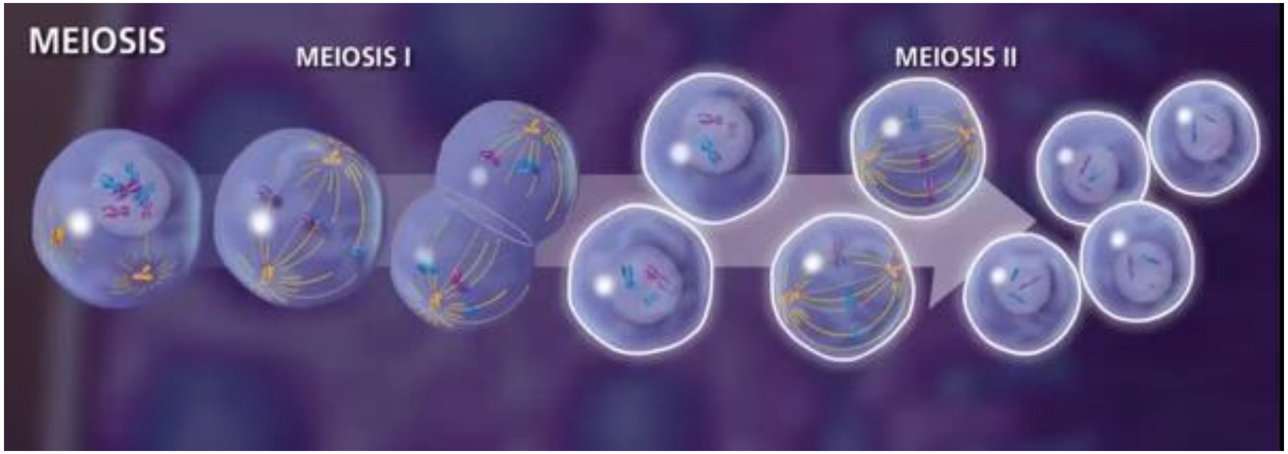


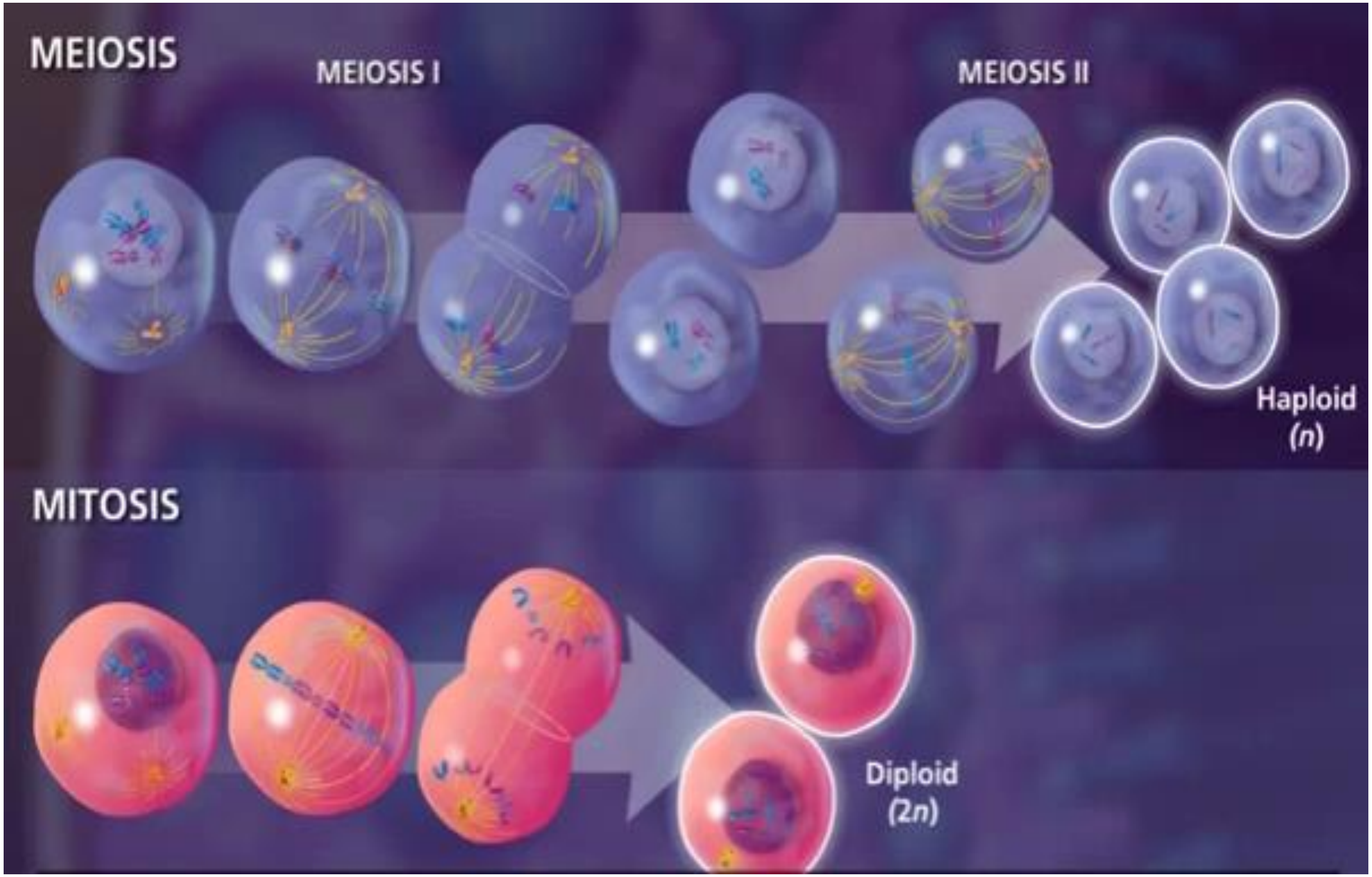
Why does we need meiosis? : Conserve chromosome no. Diploid to Haploid



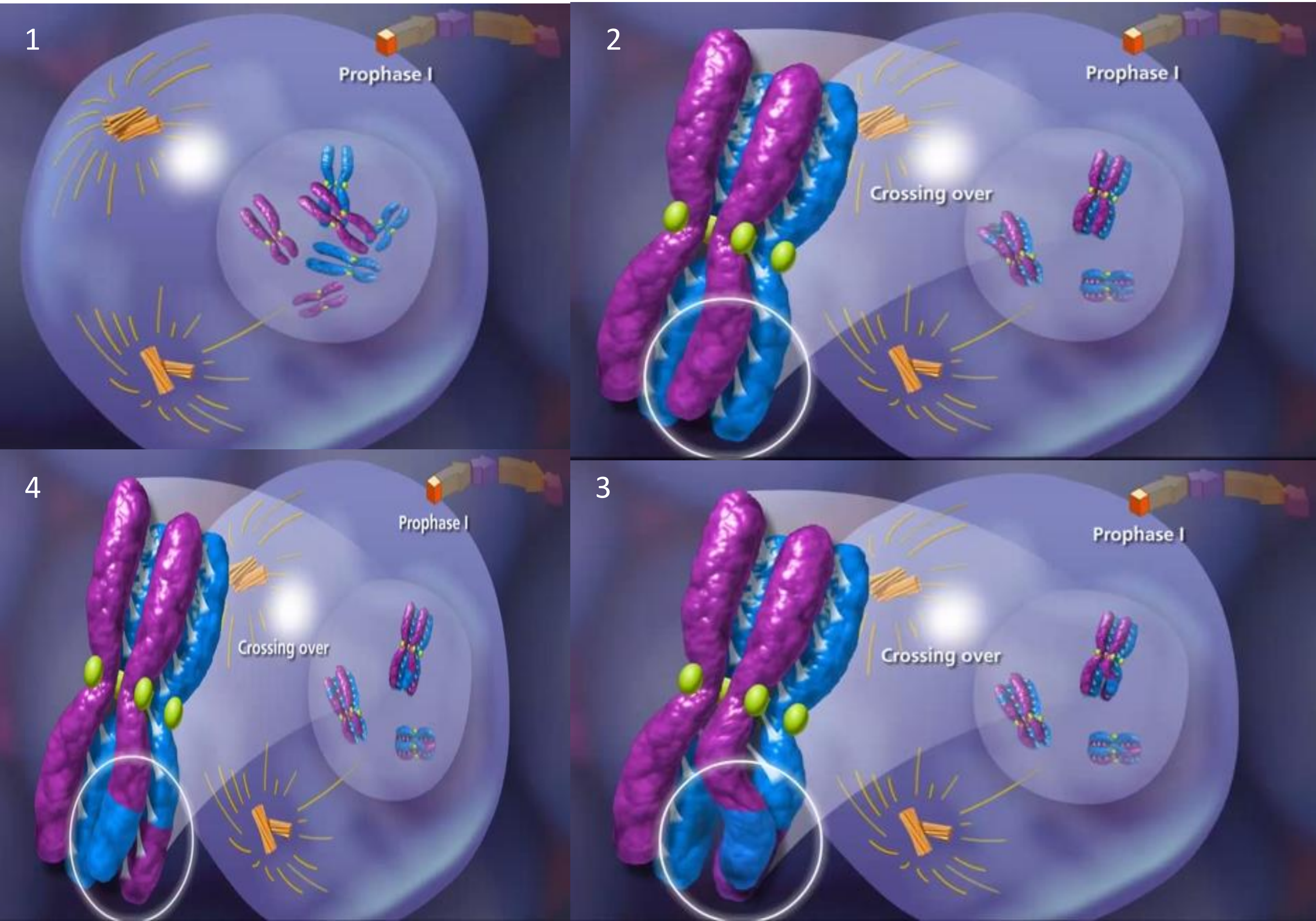
Meiosis I and Meiosis II

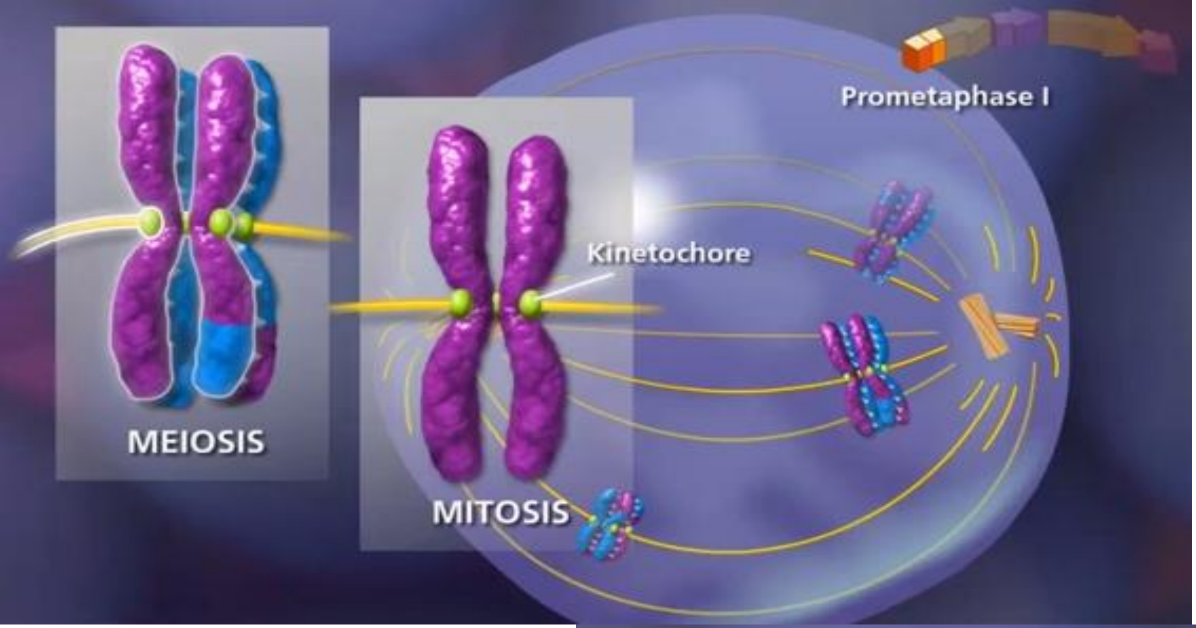





MEIOSIS
MEIOSIS I
MEIOSIS II
Haploid
(n)
MITOSIS
Diploid
(2n)

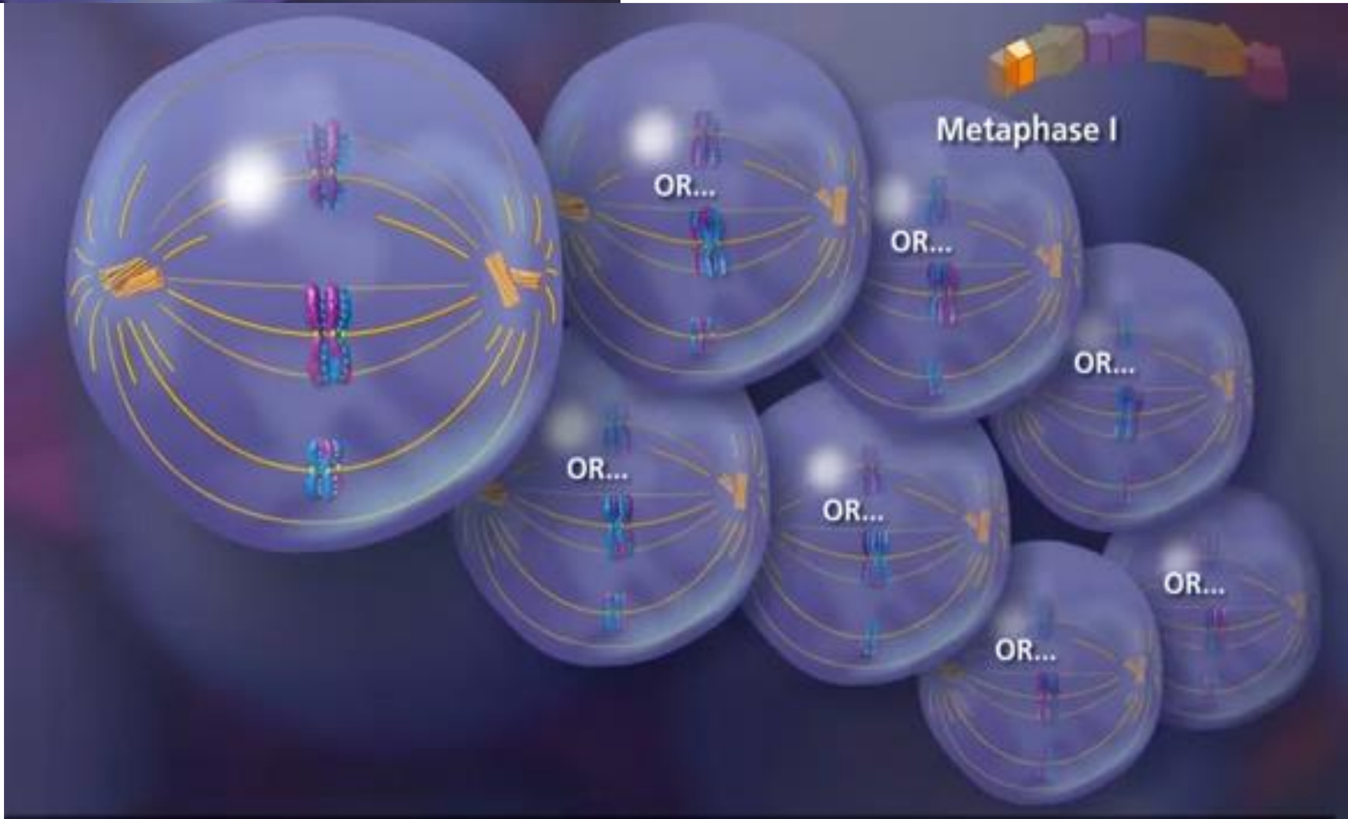
The Crossing-over between non-sister chromatids

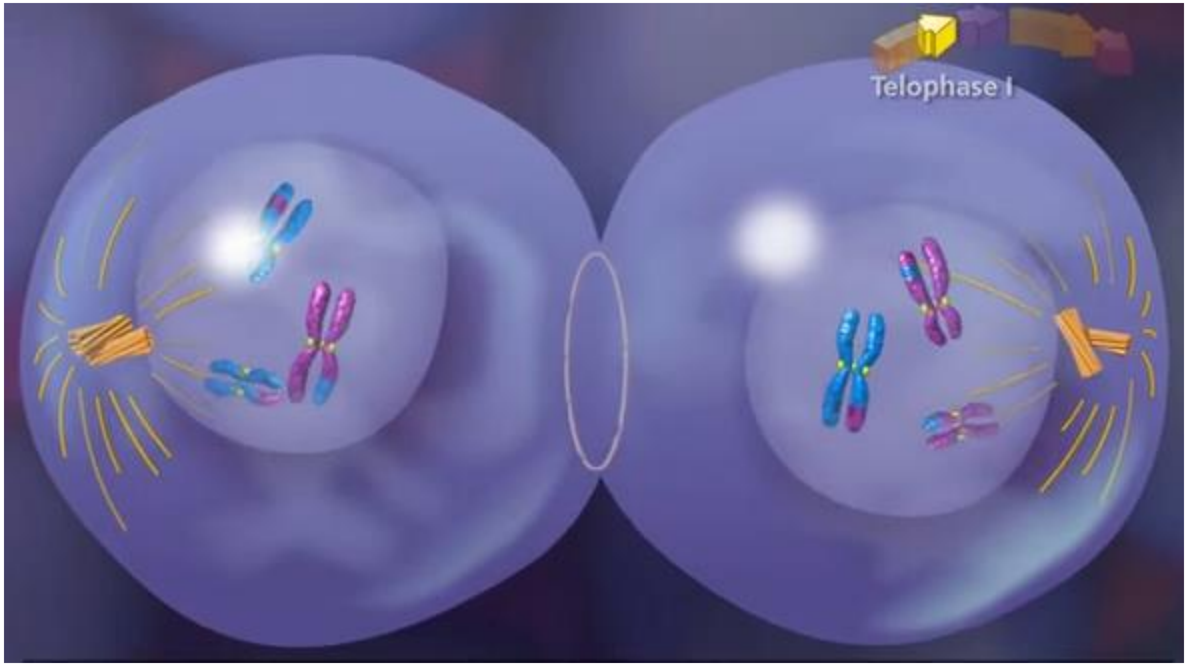




In Meiosis : **Sister chromatids of homologous chromosome are attached to only one pole by the kinetochore microtubules.**
In Mitosis : **Sister chromatids are pulled by the two opposite poles.**

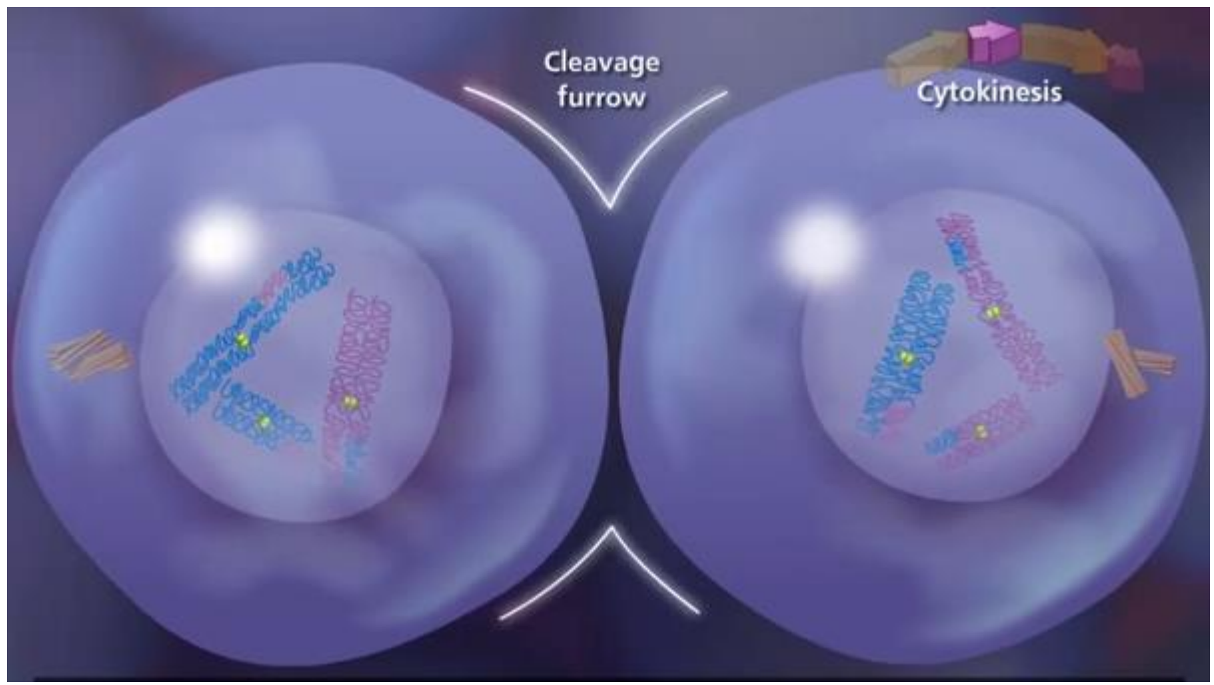
***Independent assortment* with respect to the micro-tubules of opposite poles : Random alignment of the tetrad in metaphase plate : Increased diversity.**

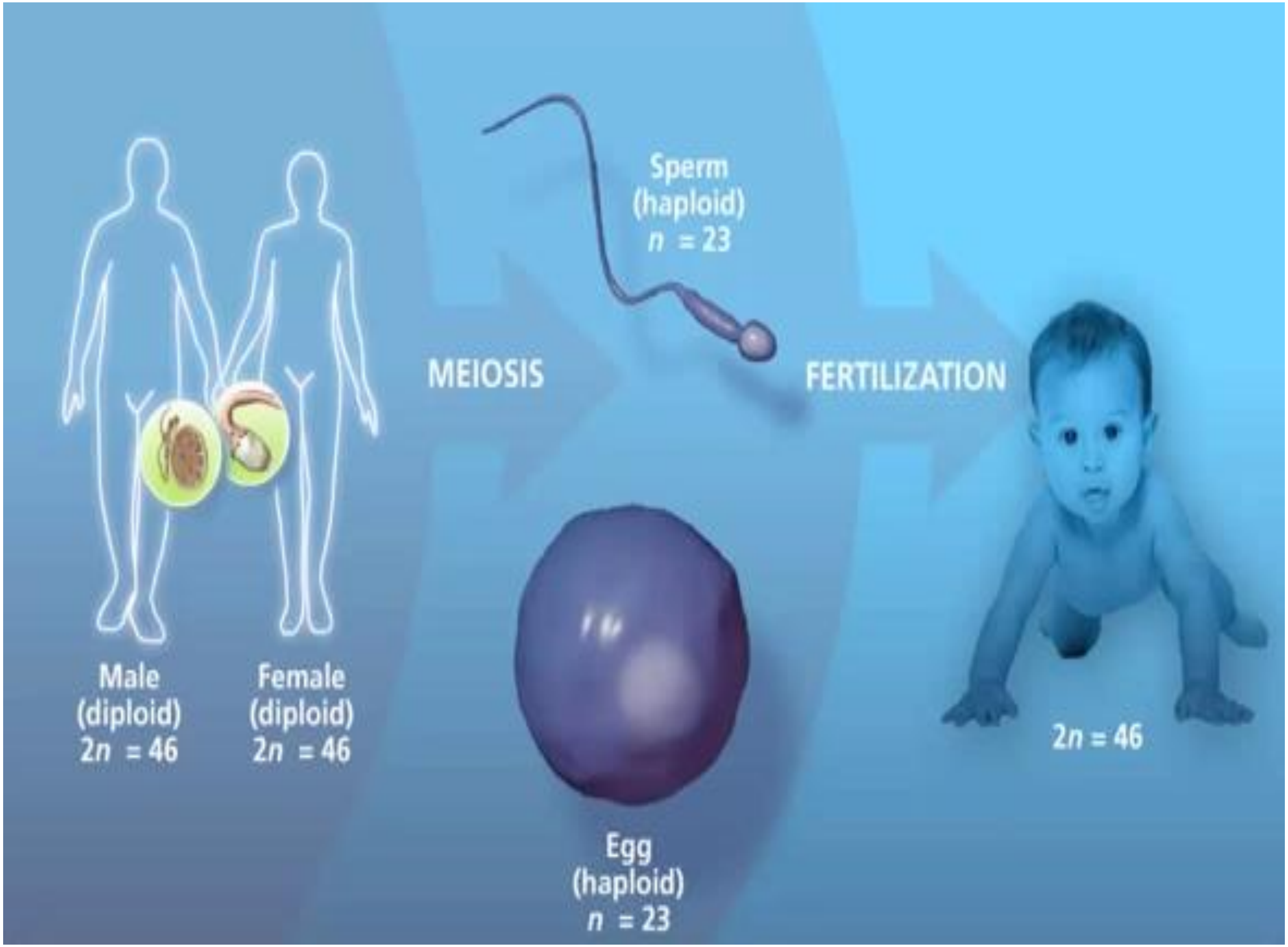




Telophase I

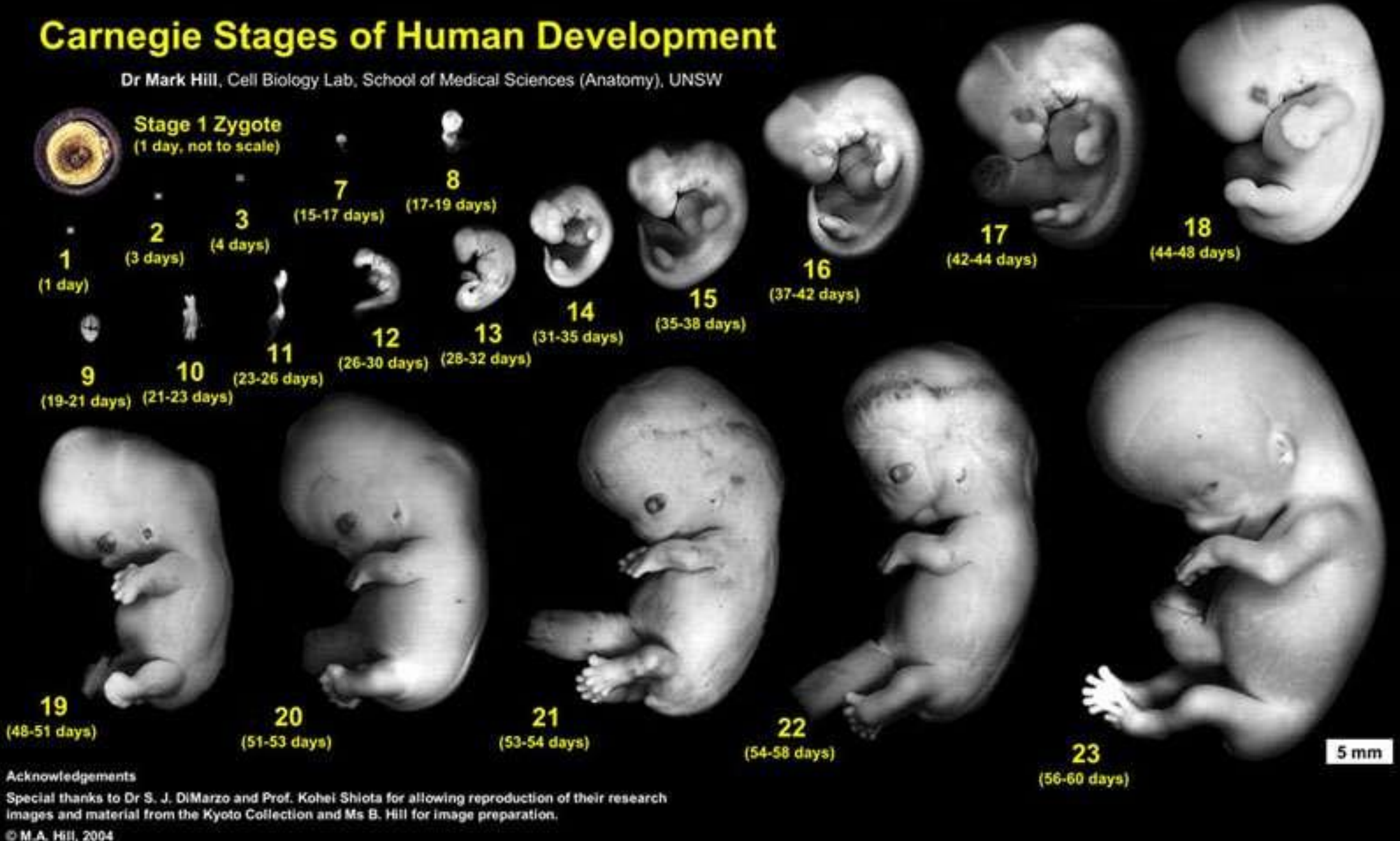
Cytokinesis after Meiosis I




Sperm
(haploid)
n = 23
MEIOSIS
FERTILIZATION
Male
(diploid)
2n = 46
Female
(diploid)
2n = 46
2n = 46
Egg
(haploid)
n = 23

Why are siblings different from each other?

1. *The cross-over*
2. *Independent Assortment*
3. *Approach to some probabilistic calculation*


Carnegie Stages of Human Development
Dr Mark Hill, Cell Biology Lab, School of Medical Sciences (Anatomy), UNSW
Stage 1 Zygote
(1 day, not to scale)
1
(1 day)
2
(3 days)
3
(4 days)
7
(15-17 days)
8
(17-19 days)
9
(19-21 days)
10
(21-23 days)
11
(23-26 days)
12
(26-30 days)
13
(28-32 days)
14
(31-35 days)
15
(35-38 days)
16
(37-42 days)
17
(42-44 days)
18
(44-48 days)
19
(48-51 days)
20
(51-53 days)
21
(53-54 days)
22
(54-58 days)
23
(56-60 days)
5 mm
Acknowledgements
Special thanks to Dr S. J. DiMarzo and Prof. Kohei Shiota for allowing reproduction of their research images and material from the Kyoto Collection and Ms B. Hill for image preparation.
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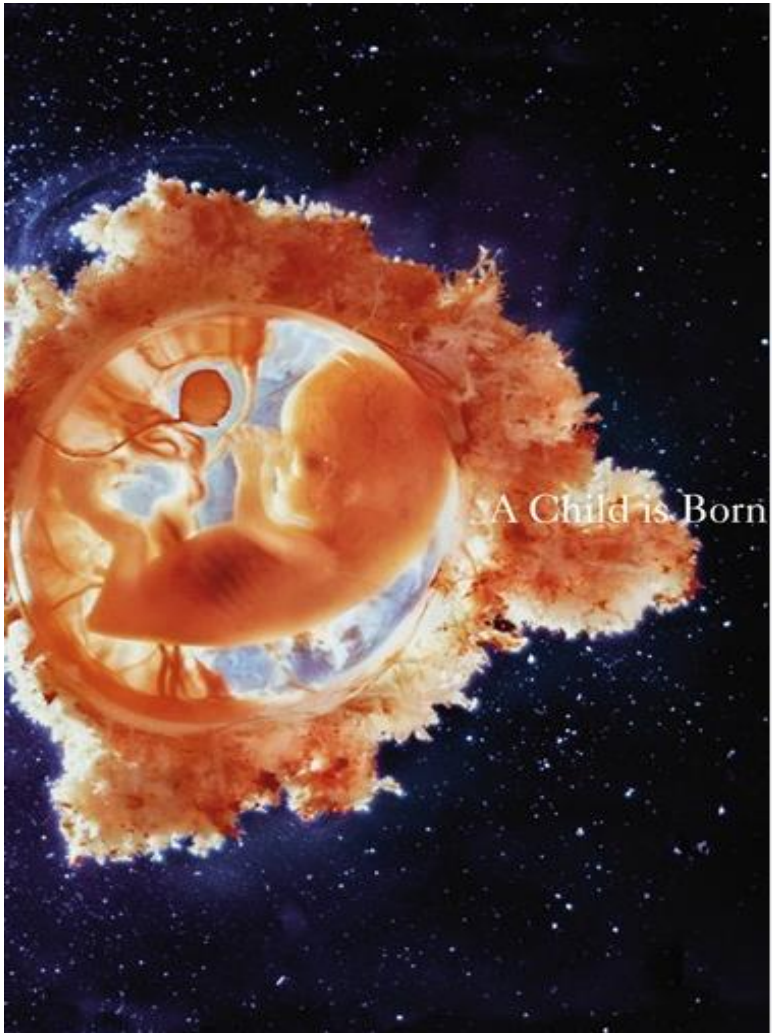
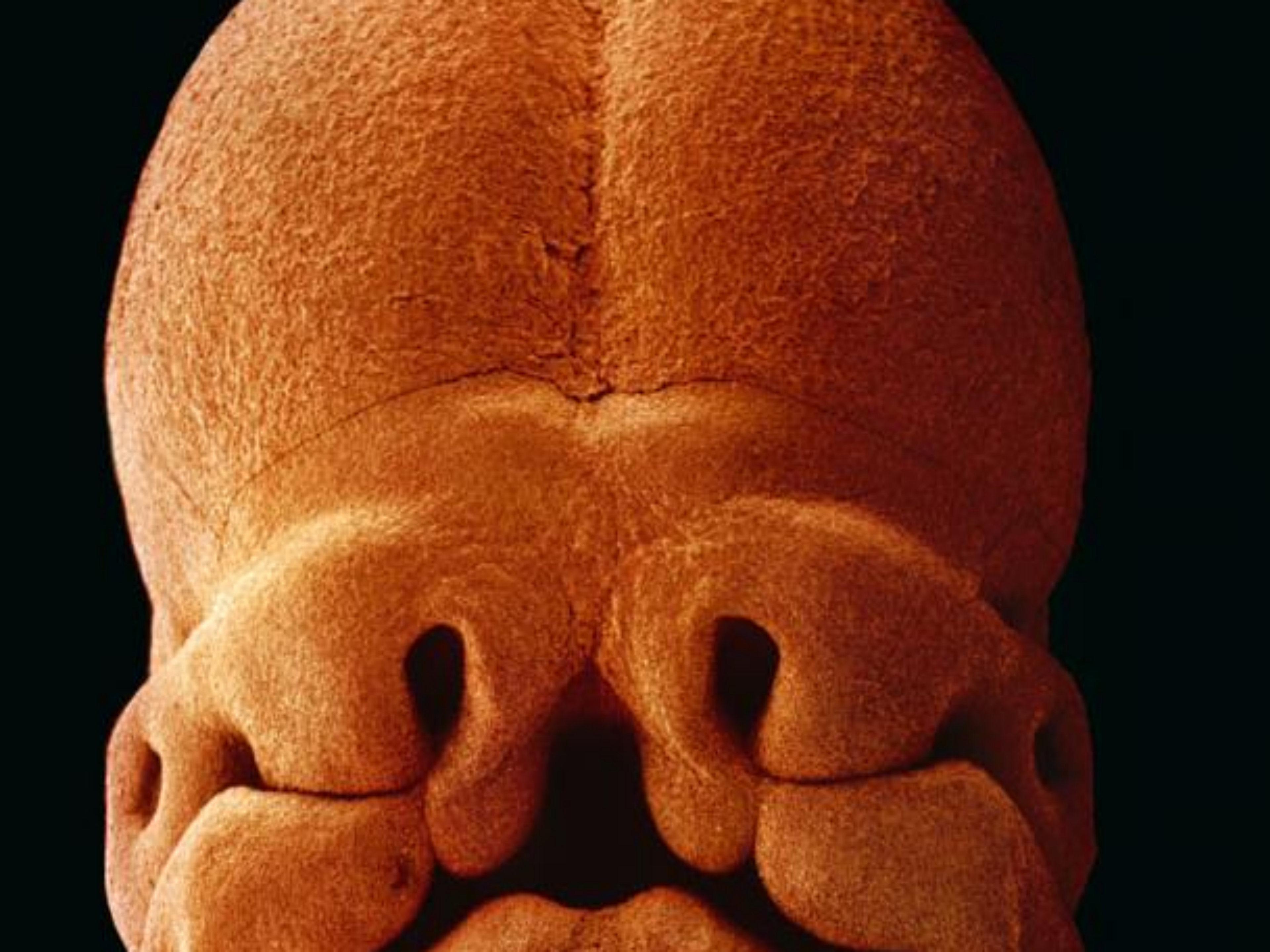
A Child is Born: Photographs of the foetus developing in the womb, by Lennart Nilsson





Phenotype & Genotype

- ✓ ***"The <u>phenotype</u> is the composite of an organism's observable characteristics or traits, such as its morphology, development, biochemical or physiological properties, phenology, behaviour, and products of behaviour (such as a bird's nest)."***

- ✓ ***"The <u>genotype</u> of an organism is the inherited instructions it carries within its genetic code. Not all organisms with the same genotype look or act the same way because appearance and behaviour are modified by environmental and developmental conditions. Likewise, not all organisms that look alike necessarily have the same genotype."***

- ✓ *Suppose, you have 2 pens of same model but of different colours : Green & Red.*

- ✓ *Colour = Observable characteristic or trait = one component of phenotype.*

- ✓ *Green & Red = Forms of colour = Forms of the component which belongs to phenotype.*

- ✓ *What determines the colour of the pen?*

  Ans : Some chemicals which are being used by the company to provide a particular colour to a pen.

- ✓ *Chemicals are as important as the interaction among them.*

- ✓ *Can you tell : what determines a particular colour without knowing all the chemicals and chemical reactions?*

  Ans : No!

- ✓ **Say, Green is the outcome of : A + B + C + D. Also, suppose if you change D with E or F, the outcome is still Green. So, Green can be a result of any of these 3 combinations : A + B + C + D or A + B + C + E or A + B + C + F.**

- ✓ **Red is the outcome of : P + Q + A + B. If you change A with K or R or J, the outcome is still Red. So, Red can be a result of any of these 4 combinations : P + Q + A + B or P + Q + K + B or P + Q + R + B or P + Q + J + B.**

- ✓ **Without knowing the precise details, you can not tell what the combination is, even if the colour is a particular one. This "information" of combination is like : *"Genotype"*.**

- ✓ **The combination : [_ + _ + _ + _] determines the character-colour and the combination can produce different effects (in this case, either Green or Red).**

- ✓ **This combination is equivalent to : *Gene*.**

- ✓ **How many alternative forms of the combinations are there to determine the colour?**

  Ans : 7 (4 for Red, 3 for Green)

- ✓ ***Allele* is one of the alternative forms of the same gene (combination of 4 having the form : [_ + _ + _ + _]). In a population, multiple alleles are possible. But, in a particular organism, there will be 2 copy of the same gene.**

- ***Genotype (G) + Environment (E) + Genotype & Environment interactions (GE) → Phenotype (P)***

- **Environment includes food-habits, lifestyle, chemical/radiation exposure, weather, stress of work, other stresses, pathogens and all other outside factors.**

- **Broad version of Phenotype = Combination of characteristics or traits including any behavioural /physiological changes → Genesis of Diseases.**

- **Genetic disorders → Directly controlled by the Genotype.**

- **Genetically linked disorders → Mostly controlled by the Genotype but to arise in a state of disorders, Genotype needs several bad changes (mutations which can lead to bad outcome) imposed by the Environment.**

- **Other disorders (mostly) → Due to Genotype & Environment interactions.**

- **Infectious Diseases : Mostly controlled by Environment (E) [pathogens] but outcome or defense is the result of Genotype & Environment interactions.**

Life as a complex adaptive system

- ✓ **Complexity of the biological processes!**
- ✓ **Many processes are simultaneous. There are enormous amount of molecules in our body. Even if you know, what each of them is doing, it is not fully possible to determine the outcome as a whole!**
- ✓ **Bio-molecules and their individual functions : Microscopic details.**
- ✓ **Whatever we act, we decide, we do, we think, we conceive, we memorize, we feel, we adjust, we learn, we adopt, we recognize : we do these in system level (as a whole)..**
- ✓ **Is individual molecule or cell, able to decide/think/memorize/feel on its own? No!!**
- ✓ **Where do these macroscopic phenomenon or system level properties emerge from?**

- **Disorders come in *"System Level".***

- **The laws of interaction, and which interacts with whom and with what logic- these information are necessary to form the basic understanding of the complexity.**

- ***The study of complex systems represents a new approach to science that investigates how relationships between parts give rise to the collective behaviors of a system and how the system interacts and forms relationships with its environment*.**

- **You all have some experience of lining up during prayer. How do you self-organize, even if no body is actually controlling the process from outside?**

- **How do heart, liver, lungs, kidneys … these organs self-organize their cells?**

- **"*Self-organization* is a process where some form of global order or coordination arises out of the local interactions between the components of an initially disordered system. This process is spontaneous: it is not directed or controlled by any agent or subsystem inside or outside of the system. "**

- ✓ **A person tends to adjust with situation (outside/inside) and fairly maintains the system property. This is called *robustness* under perturbations (changes)!**

- ✓ ***Where do learning, conscience, adaptation, recognition, memory, aging emerge from? Property of emergence! Examples : Immune System, Nervous System, Humans themselves!***

Towards research in complex systems

- ***Research in complex systems*** **: to determine the fundamental physical laws of the complexity, robustness, emergence and self-organization.**

- ***Complex network*** **: consider the components as the nodes and the interactions as the links.**

- **Complex network can be found in cellular level, organ level, among the components of a particular system, even within us, within society!**

- **What are the *governing laws*? Is there anything common (*universality*) among all these networks? Goal of research is along that direction.**

- **Need of *statistical physics, mathematical modeling, non-linear dynamics, computer science, programming and of course fair knowledge of chemistry and biology.***

Feel the beauty of nature!
See the colour, the diversity of nature!
Hear the "sound" of the soundless flow of evolution!
Sense and respect the uniqueness among us and among the organisms!

Thank you !!

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