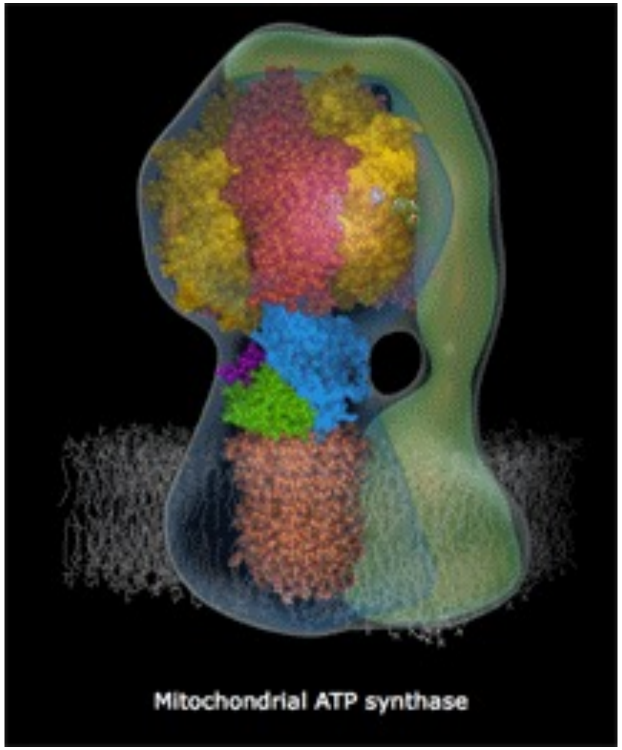
Macromolecular Structures

Sc. in Nanotechnology Engineering
Sapienza University of Rome



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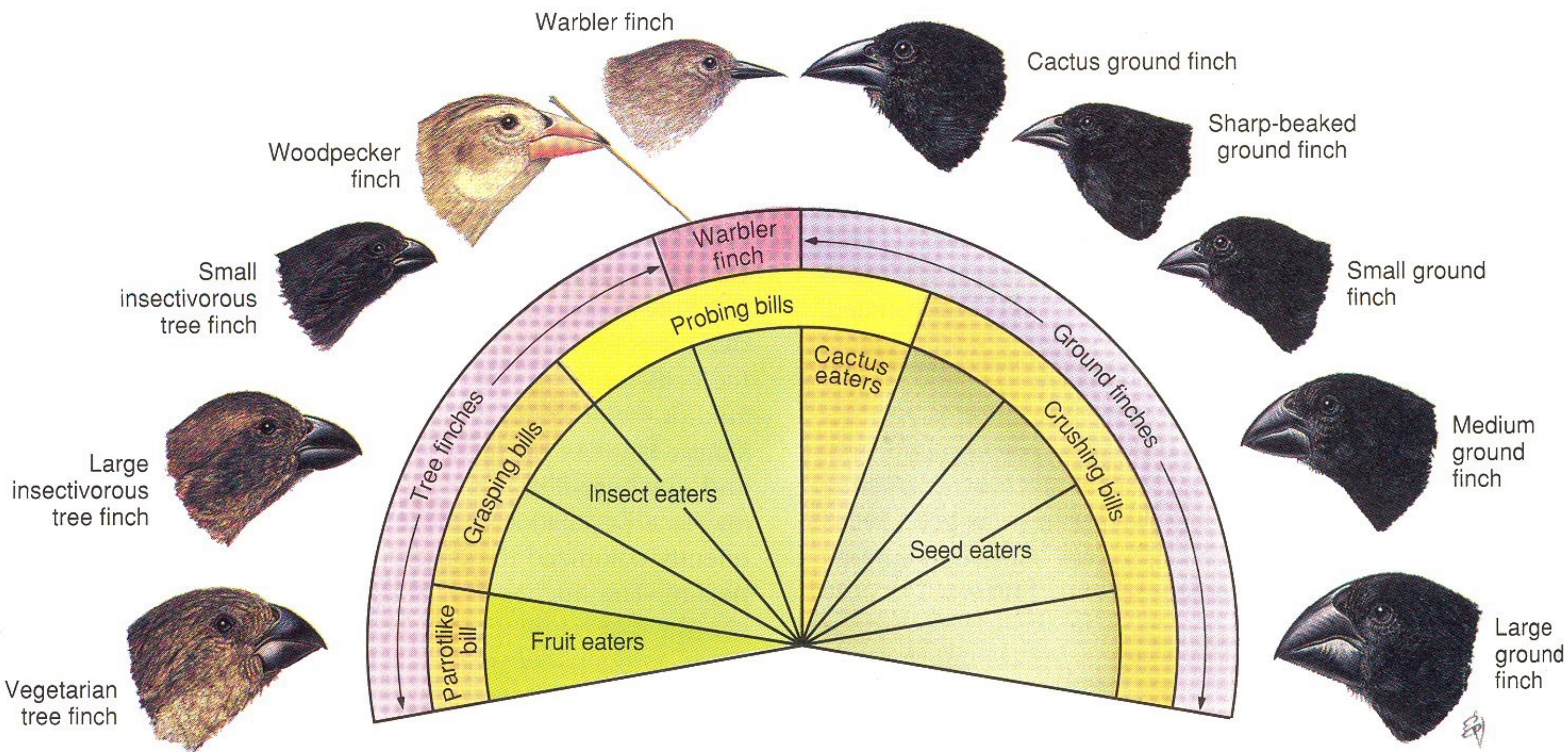
What is evolution?



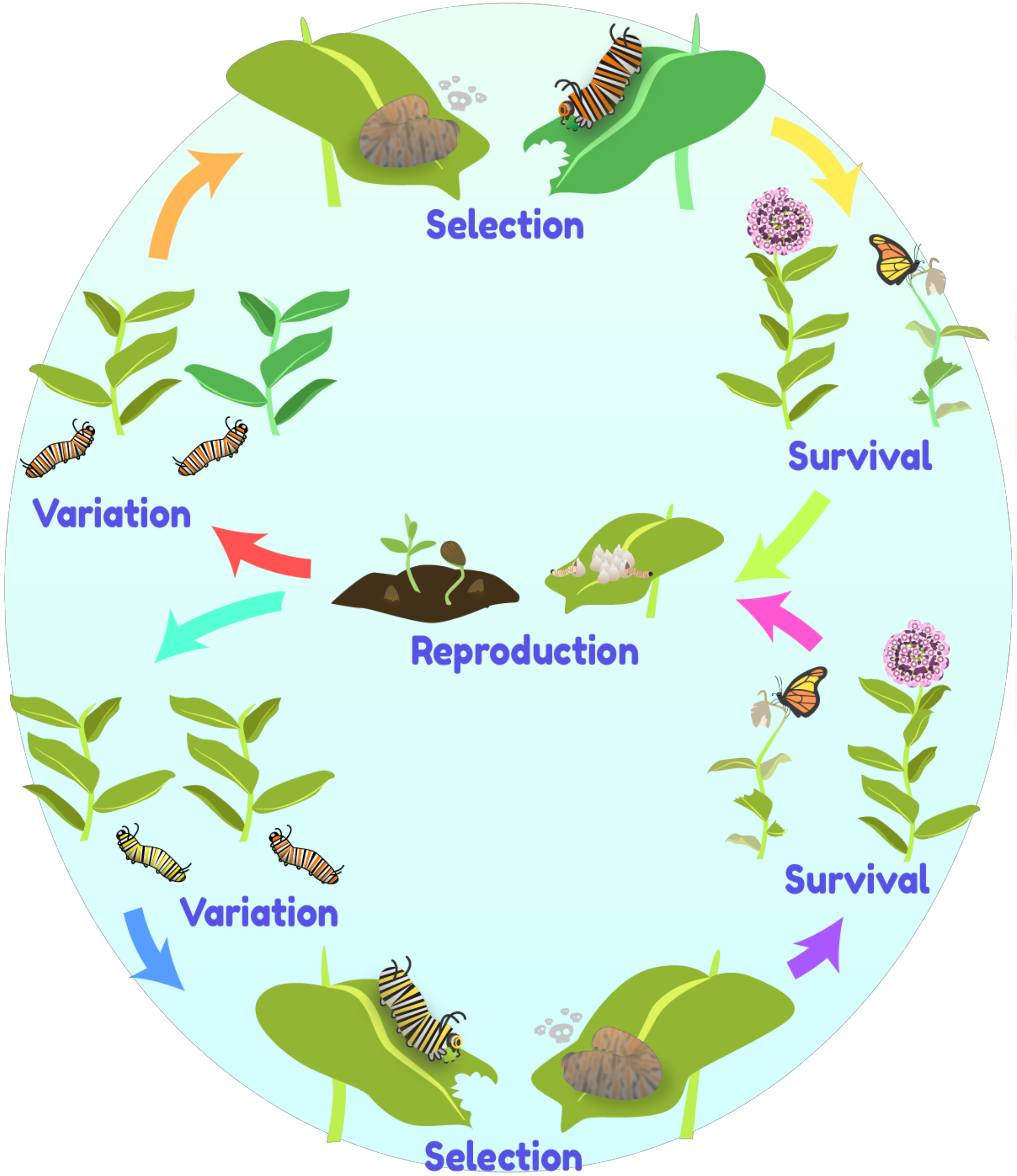
Why Evolution Matters

- Understanding evolution is essential to understand why macromolecules look and function the way they do.
- For engineers, it shows how nature 'designed' systems over billions of years.

What is Evolution?

- Variation
- Heritability
- Natural Selection
- Organism ↔ Environment interactions

Result: adaptive change over time, not random chaos.



WHAT ARE THE ELEMENTS OF EVOLUTION BY NATURAL SELECTION?

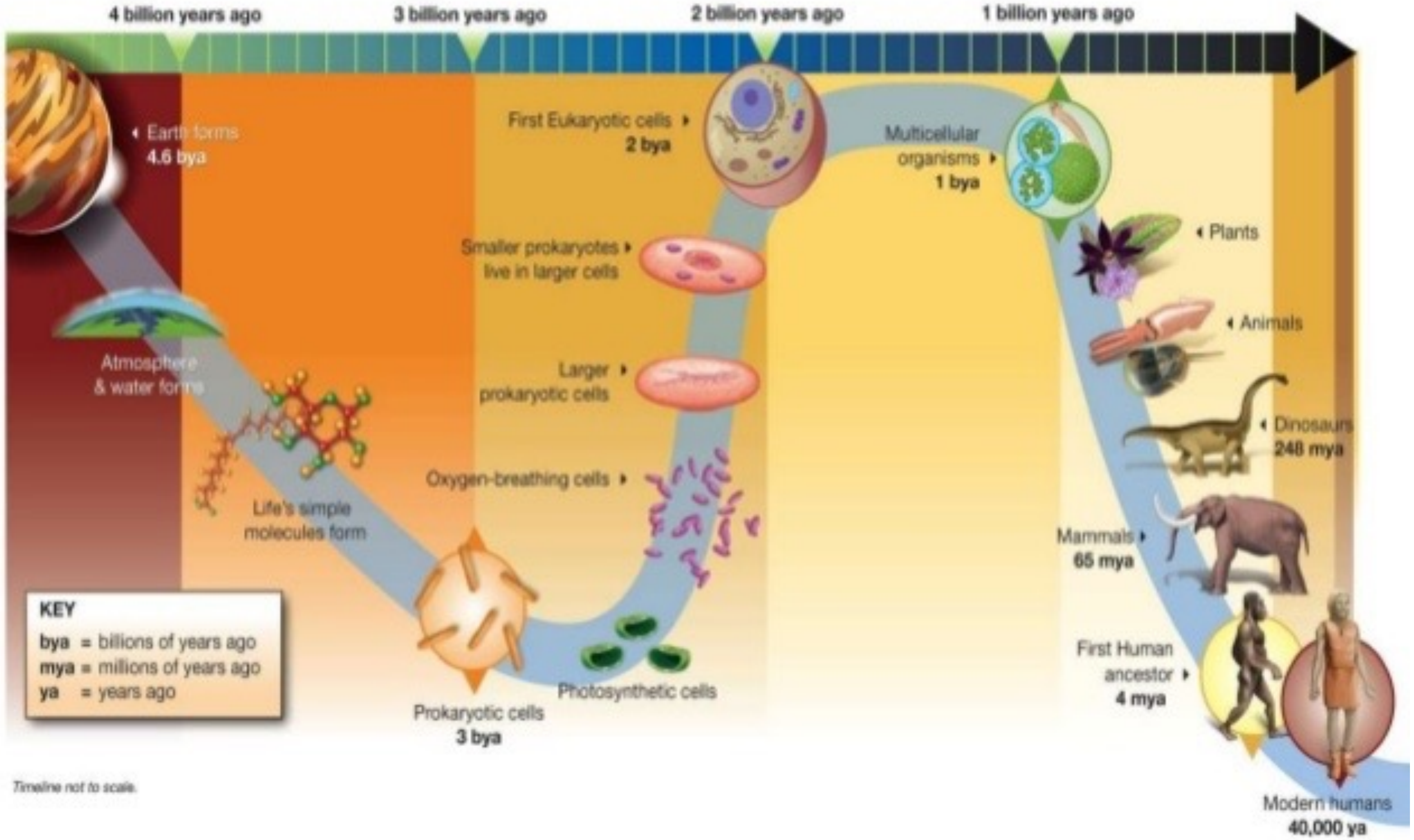
Many more individuals are born than survive (**COMPETITION**).

Individuals vary in traits directly related to their ability to survive and reproduce (**VARIATION**).

These advantageous traits are passed on to offspring (**HERITABILITY**).

This process is repeated generation after generation over long periods of time (**ITERATION**).

Life Timeline



"If the Earth's 4.6-billion-year history is compressed into a single day
… the first life on Earth would appear at 4:00 am …
modern humans would not appear until the last two seconds of 11:59 pm."

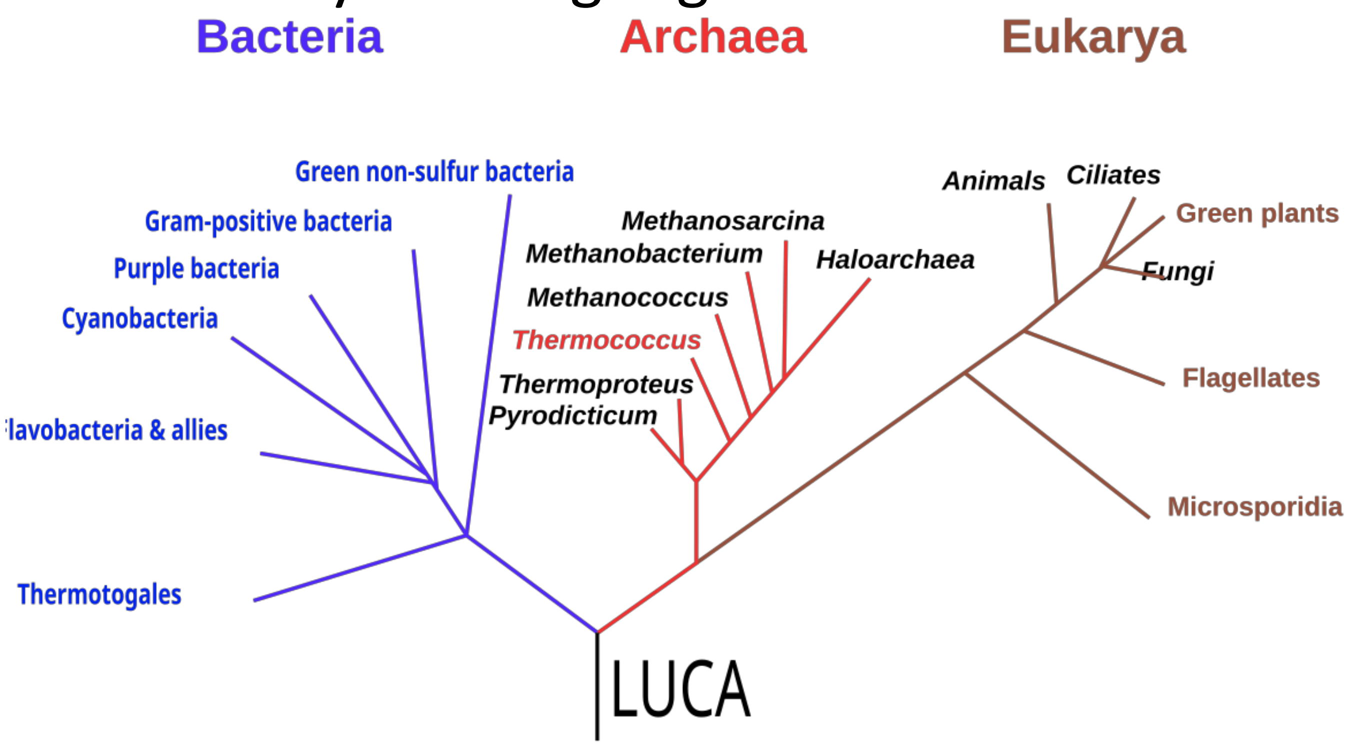
Deep Time: Scale of Evolution

- Origin of life ~3.5–3.8 Ga
- Oxygenic photosynthesis ~2.5 Ga
- Eukaryotes ~1.5 Ga
- Multicellularity ~600 Ma
- Humans <0.3 Ma

LUCA & Universal Biochemistry

LUCA – Last Universal Common Ancestor

- **What it is:** The hypothetical ancestral organism that lived about **3.5–4.2 billion years ago**, from which bacteria, archaea, and eukaryotes all evolved.
- **What we know:** We infer LUCA's existence by comparing genomes — many essential genes (for replication, translation, core metabolism) are shared by *all* living organisms.



LUCA & Universal Biochemistry

What LUCA had:

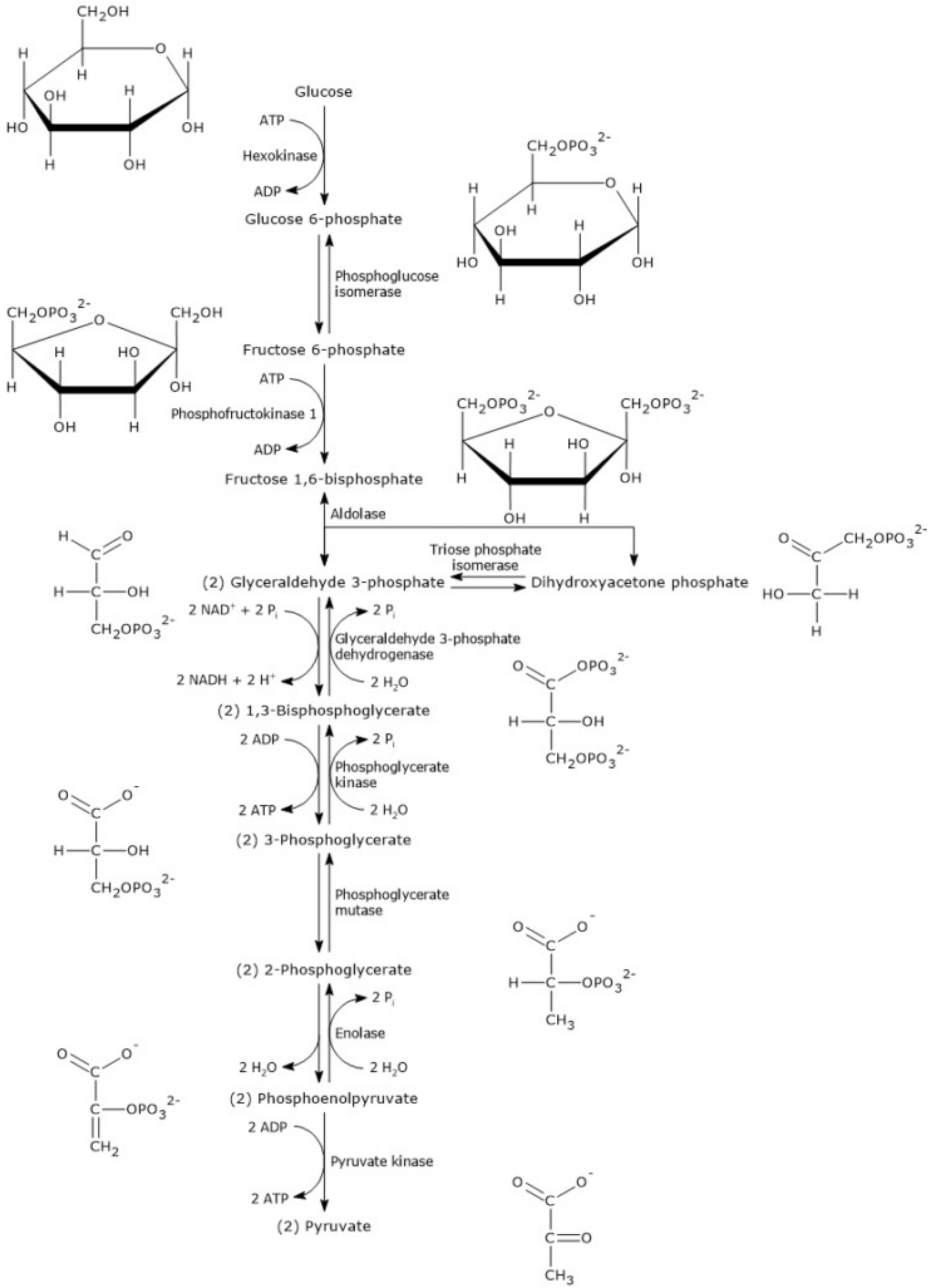
- DNA or RNA genome with a nearly modern genetic code
- Ribosomes for protein synthesis
- Basic metabolic pathways (e.g., glycolysis-like energy generation)
- Cell membrane separating internal chemistry from the environment

Why it matters:

- Explains the **universality of biochemistry** (same 20 amino acids, same genetic code, ATP as energy currency)
- Shows that life had a **single origin**, not multiple independent origins

Case Study: Glycolysis

- Present in bacteria, archaea, eukaryotes
- Highly conserved enzymes
- Likely one of the earliest metabolic pathways
- Evidence of strong evolutionary constraint



Molecular Similarity: Orthologs & Homologs

- Example: GAPDH structure conserved from E. coli to humans
- Sequence and 3D structure homology
- Evolution uses duplication + divergence to innovate

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E.coli GAPDH                                                  TIKV GINGFGRIGR IVFRAAQKRS
His-GAPDS      MGSSHHHHHH SSGLVPRGSH MASMTGGQQM GRGSEFMVKV GINGFGRIGR LVLRVCMEKG

E.coli GAPDH   DIEIVAIND- LLDADYMAYM LKYDSTHGRF DGTVEVKDGH LIVNGKKIRV TAERDPANLK
His-GAPDS      -VRVVAVNDP FIDPEYMVYM FKYDSTHGRY KGTVEHKNGR LVVDNLEINV FQCKEPKEIP

E.coli GAPDH   WDEVGVDVVA EATGLFLTDE TARKHITAGA KKVVMTGPSK DNTPMFVKGA NFDKYAG—-Q
His-GAPDS      WSSVGNPYVV EATGVYLSIE AASGHISSGA RRVIVTAPSP D-APMLVMGV NEKDYNPGSM

E.coli GAPDH   DIVSNASCTT NCLAPLAKVI NDNFGIIEGL MTTVHATTAT QKTVDGPSHK DWRGGRGASQ
His-GAPDS      TVVSNASCTT NCLAPLAKVI HERFGIVEGL MTTVHAYTAT QKTVDGPSKK DWRGGRGAHQ

E.coli GAPDH   NIIPSSTGAA KAVGKVLPEL NGKLTGMAFR VPTPNVSVVD LTVRLEKAAT YEQIKAAVKA
His-GAPDS      NIIPSSTGAA KAVGKVIPEL NGKLTGMAFR VPTPNVSVVD LTCRLAQPAS YTAIKEAVKA

E.coli GAPDH   AAEGEMKGVL GYTEDDVVST DFNGEVCTSV FDAKAGIALN DNFVKLVSWY DNETGYSNKV
His-GAPDS      AAKGPMAGIL AYTEDQVVST DFNGDSHSSI FDAKAGIALN DNFVKLVSWY DNEYGYSHRV

E.coli GAPDH   LDLIAHISK- --
His-GAPDS      VDLLRYMFSR EK
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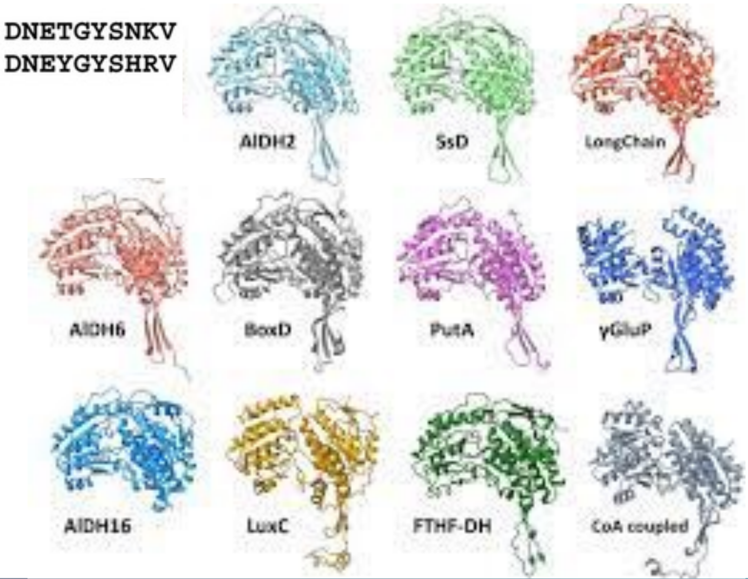


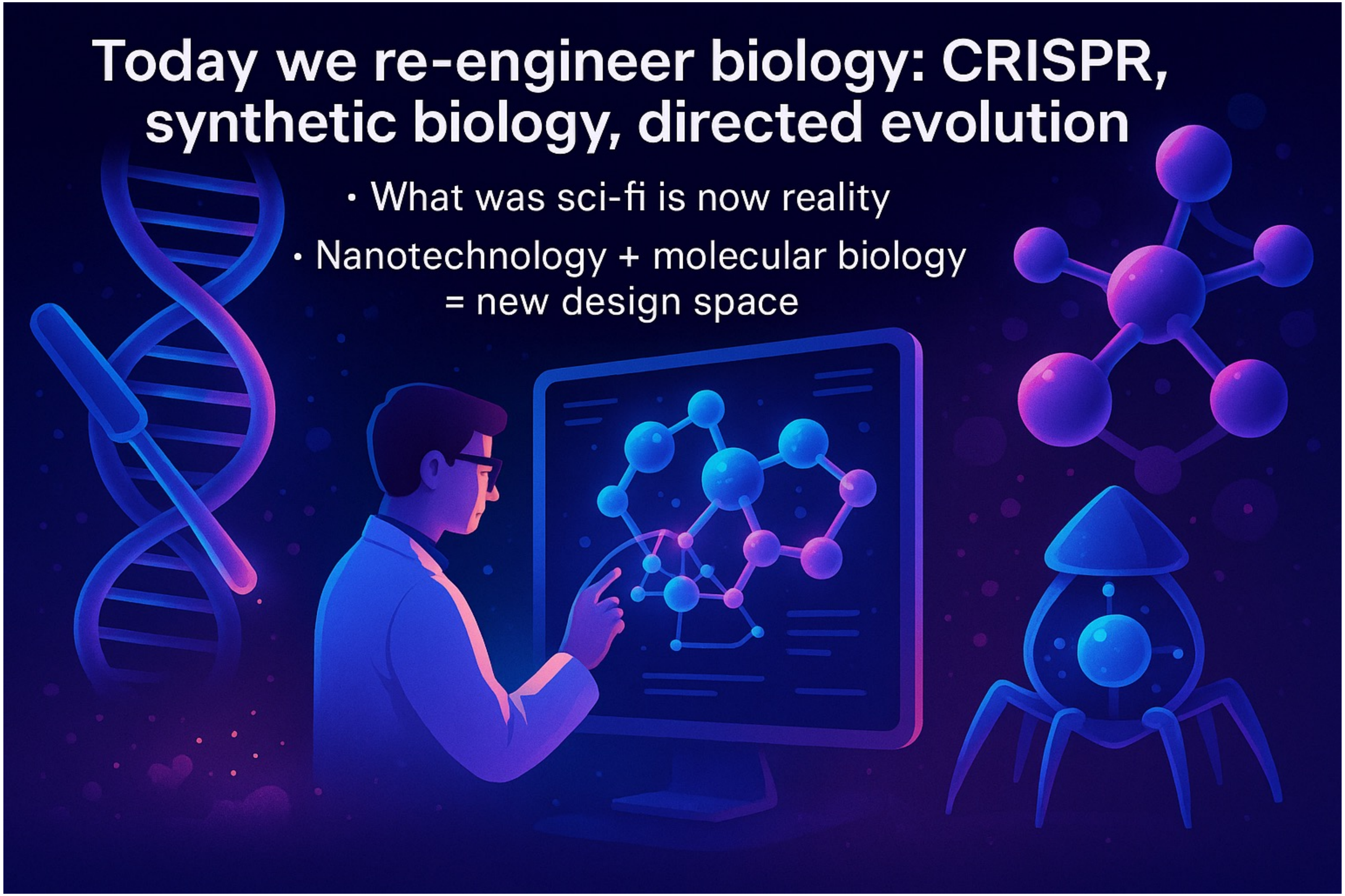
Universal Evidence

- Genetic code, metabolic pathways, ribosome structure all conserved
- Hard evidence that life shares common origin
- Not just Darwin's finches — it's molecular and measurable

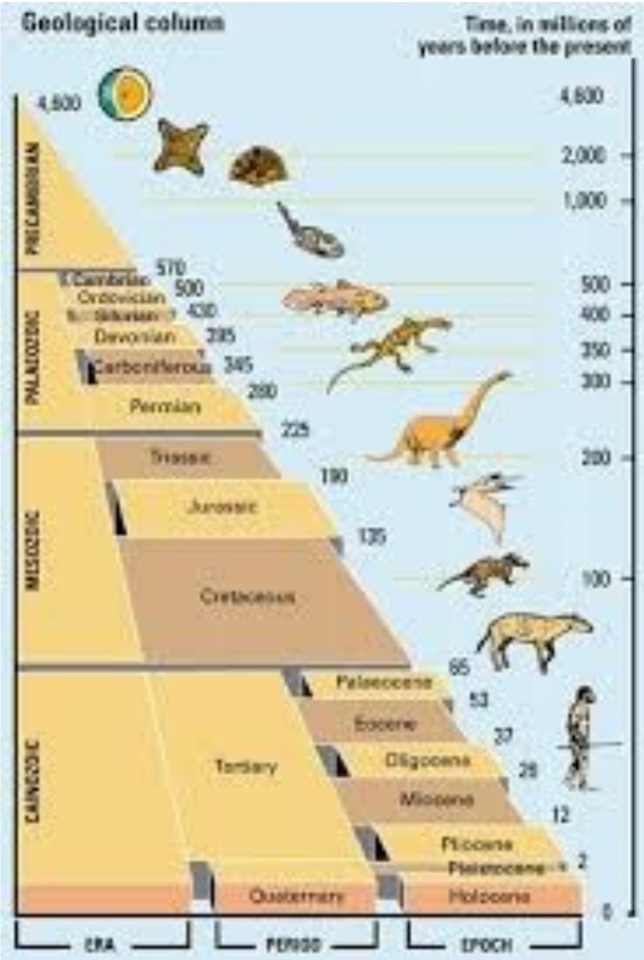
Evolution as Nature's Engineering

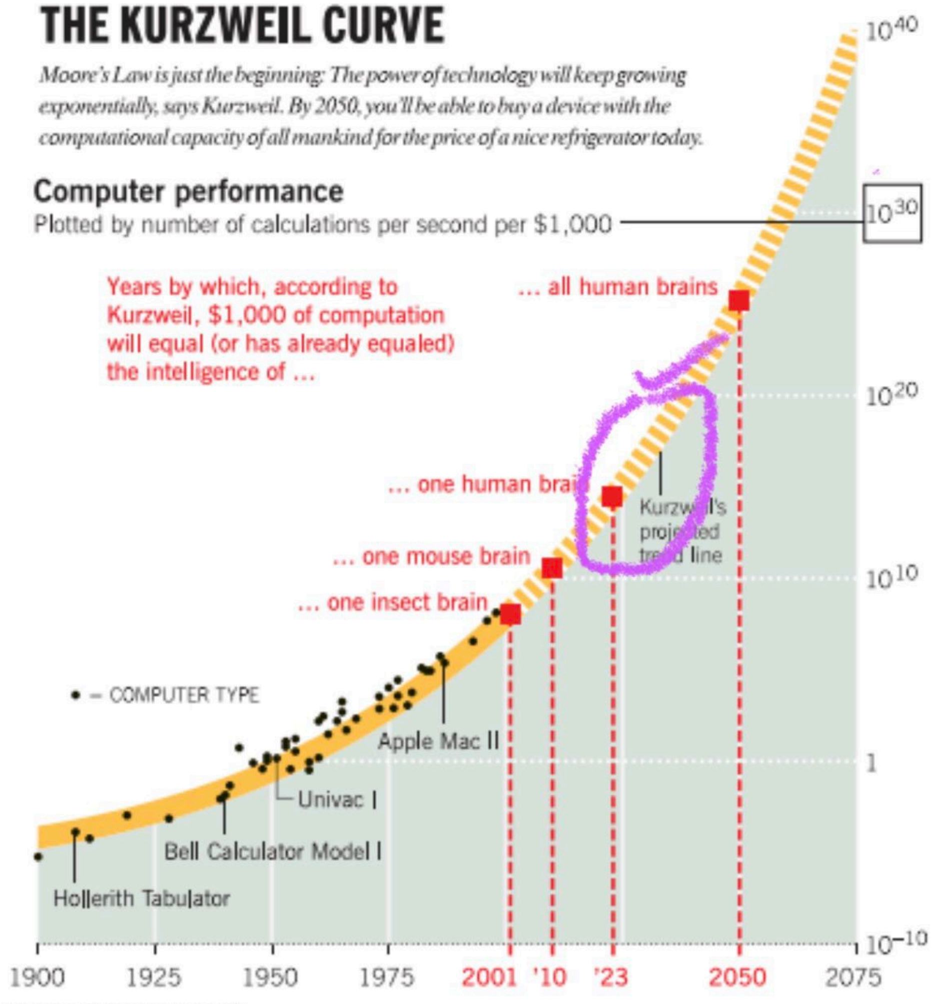
- Incremental prototyping across billions of years
- Gene duplication, recruitment, optimization
- Compare with iterative design cycles in engineering

From Evolution to Engineering

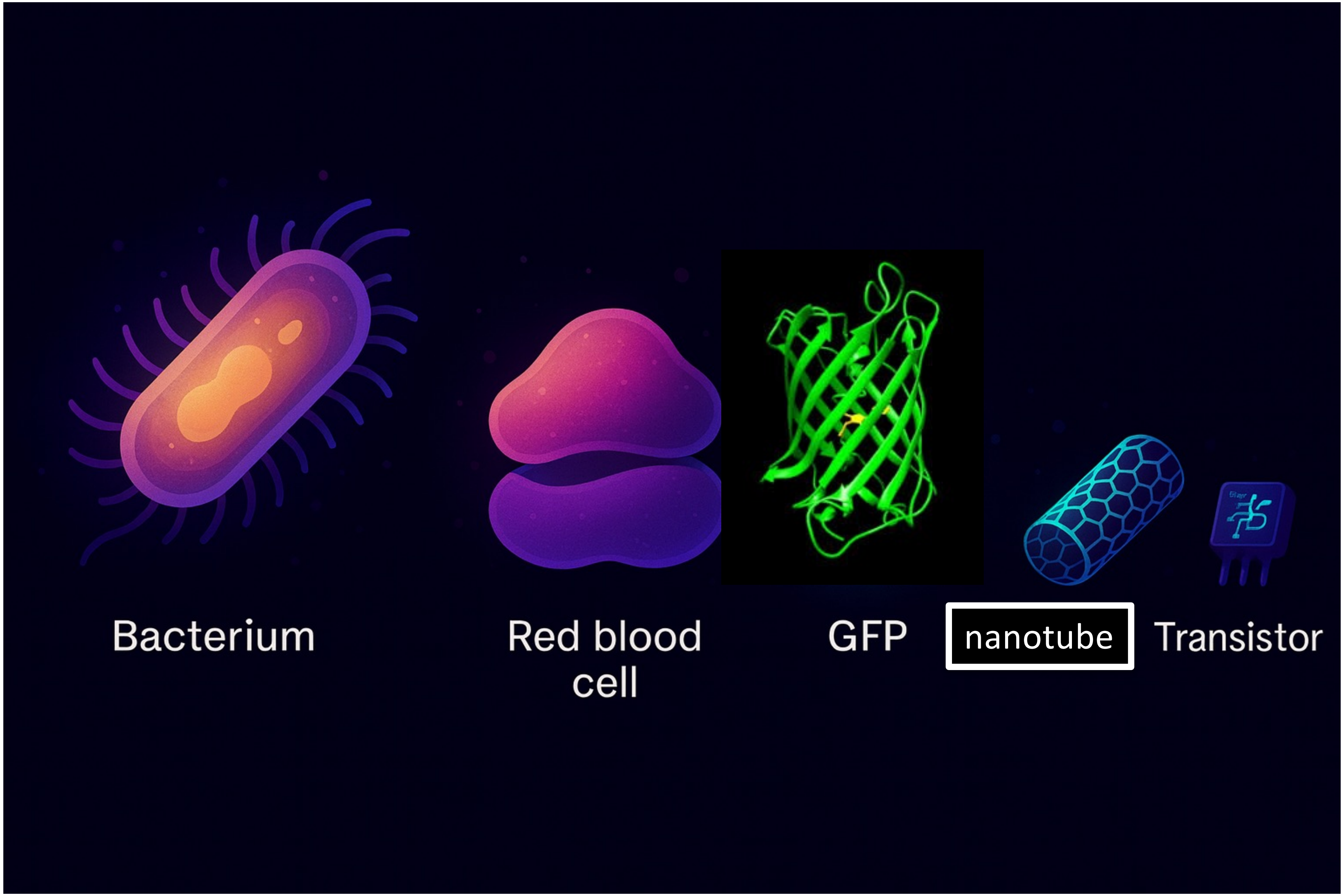


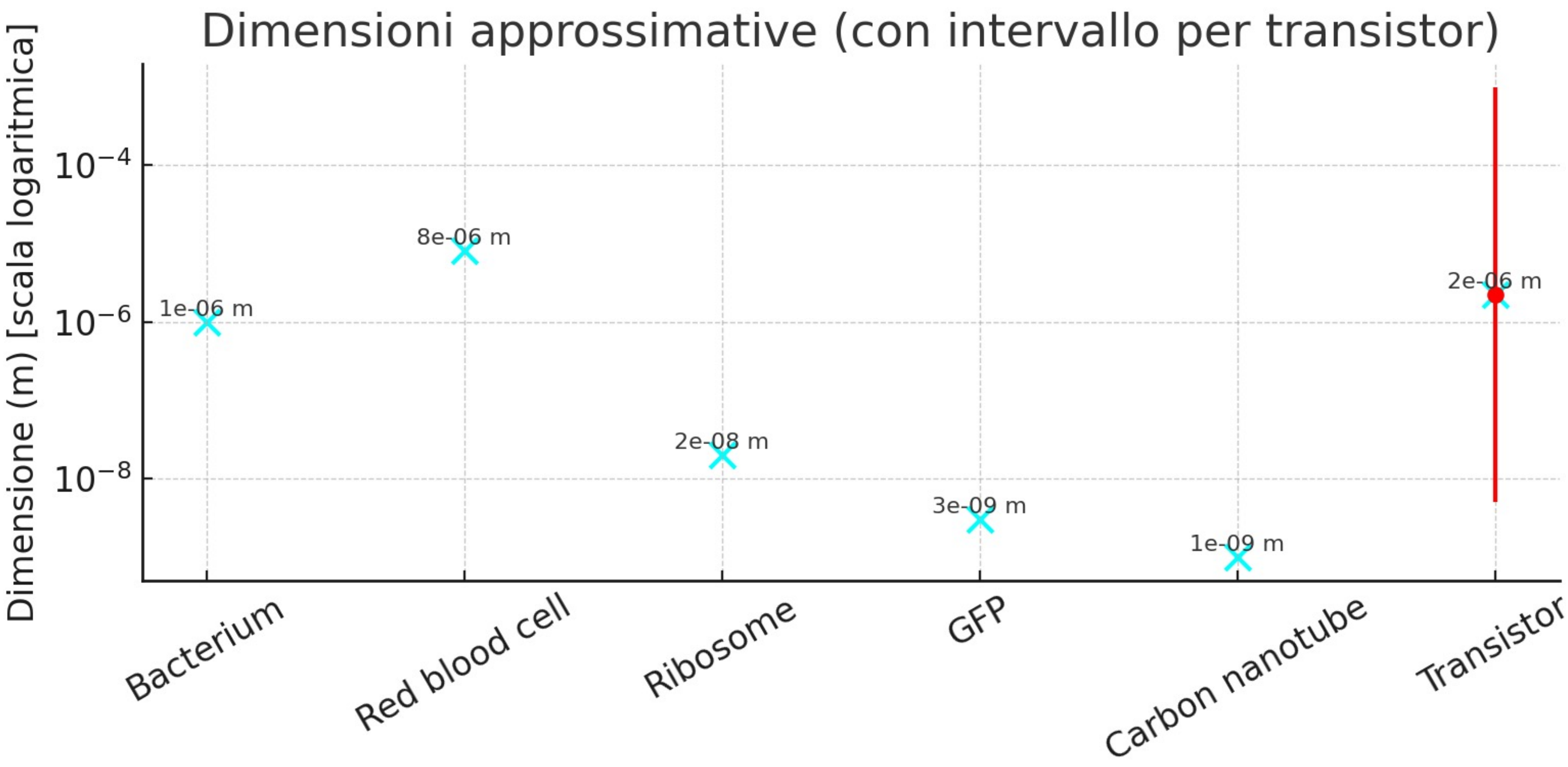
Deep Time vs Human Technology





- billions of years vs decades of human tech
- nature as the ultimate R&D lab with infinite parallel experiments.


Bacterium
Red blood cell
GFP
nanotube
Transistor


Dimensioni approssimative (con intervallo per transistor)
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10^{-4}
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2e-08 m
3e-09 m
1e-09 m
2e-06 m
Bacterium
Red blood cell
Ribosome
GFP
Carbon nanotube
Transistor

Implications for This Course

- Macromolecular structures shaped by evolutionary constraints
- Learning from nature's solutions helps design better nanodevices
- We stand at the beginning of a new engineering revolution

Summary & Challenge

Summary:

- Evolution explains molecular complexity
- Life is deeply engineered by selection
- We can now re-engineer life

Challenge:

Pick a molecular machine and think: how might it have evolved?

Further Reading – Evolution & Universal Biochemistry

- NR Pace (2001), 'The universal nature of biochemistry', PNAS — [Open link]
- Moody et al. (2024), 'The nature of the last universal common ancestor', Nature E&E — [Open link]
- SJ Kierans (2024), 'Glycolysis: multifaceted metabolic pathway', JBC — [Open link]
- MJ Harms et al. (2013), 'Evolutionary biochemistry', PNAS — [Open link]
- Court, Waclaw & Allen (2014), 'Lower glycolysis carries a higher flux...', arXiv — [Open link]