Information and Fluctuations of Information

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- *ECS129*

The Cell

1. **Quantum of life:**

from 1 cell (bacteria), to 10^{13} in a human

(trivia: there are approx. 10^{14} bacteria in our guts!

- we generate approx. 10^{16} cells during our life time)

2. Cells are "machines":

They can produce chemical or mechanical work. They take energy from their environment.

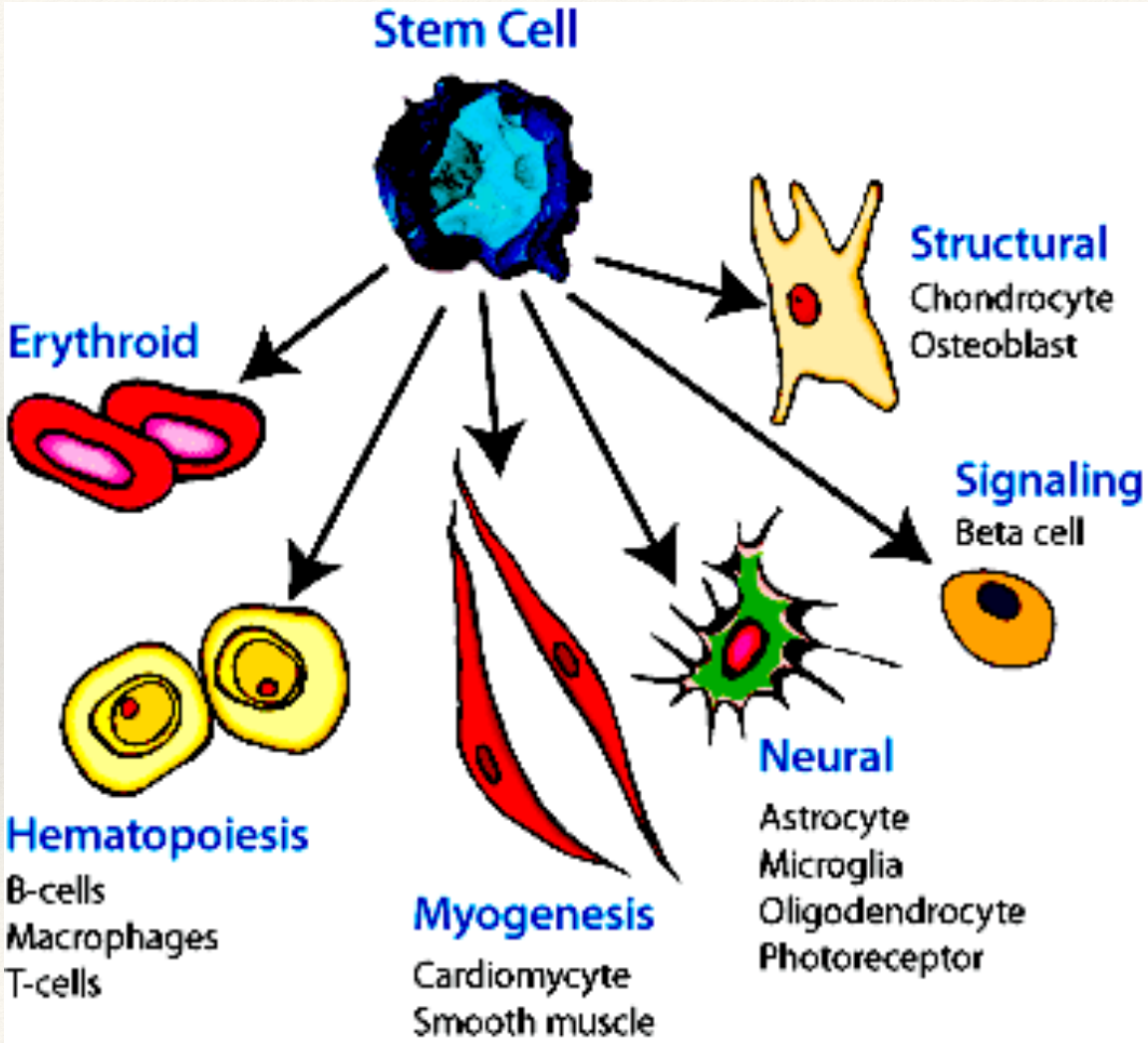
3. Cells self-replicate

4. Their blueprint is the DNA they contain

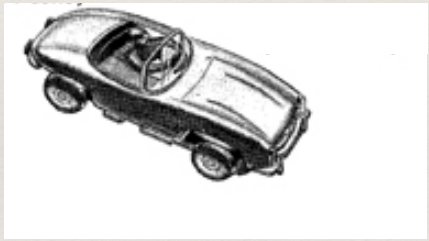
The Cell

All cells of an organism contain the same information…however

They may differ in aspect….and functions.

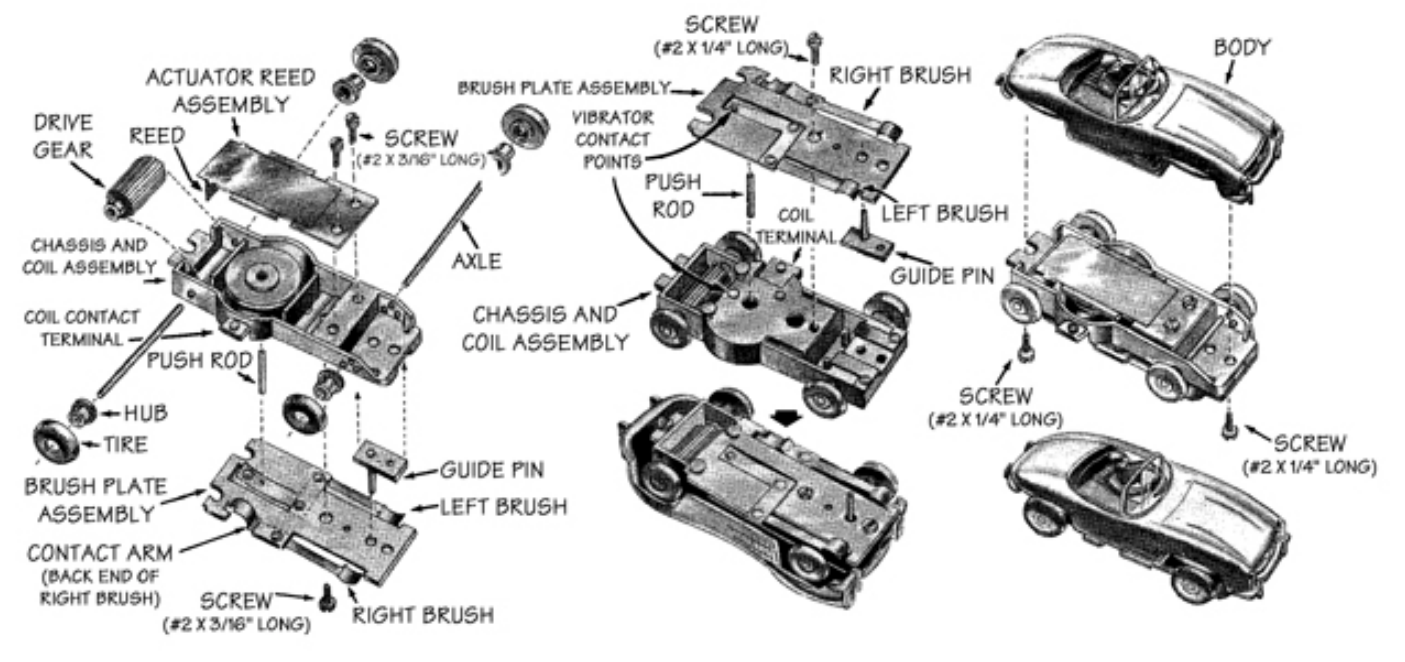


How to replicate a machine?



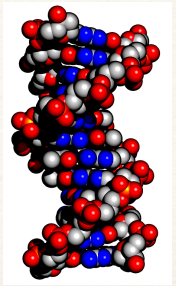
How to replicate a machine?

- List of parts and parts themselves
- A set of instructions on how to put parts together (design)
- An operator
- A manual on how to use the machine

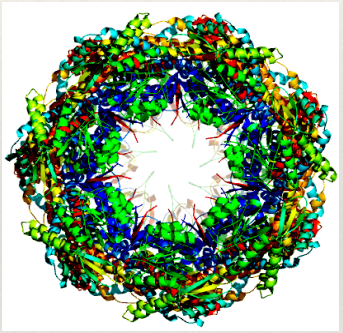


The Cell

Blueprint: parts + design



DNA, genes



Proteins, nanomachines

Assembly

promoter

Processing: logic

Operation “manual”

Information and Fluctuations

Information support: DNA

Information fidelity: copying and proofreading

Fluctuations of information

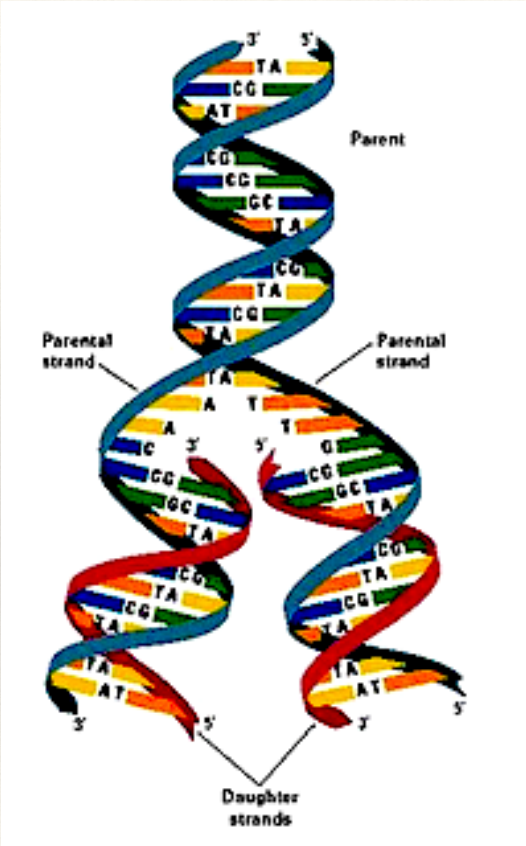
Information and Fluctuations

Information support: DNA

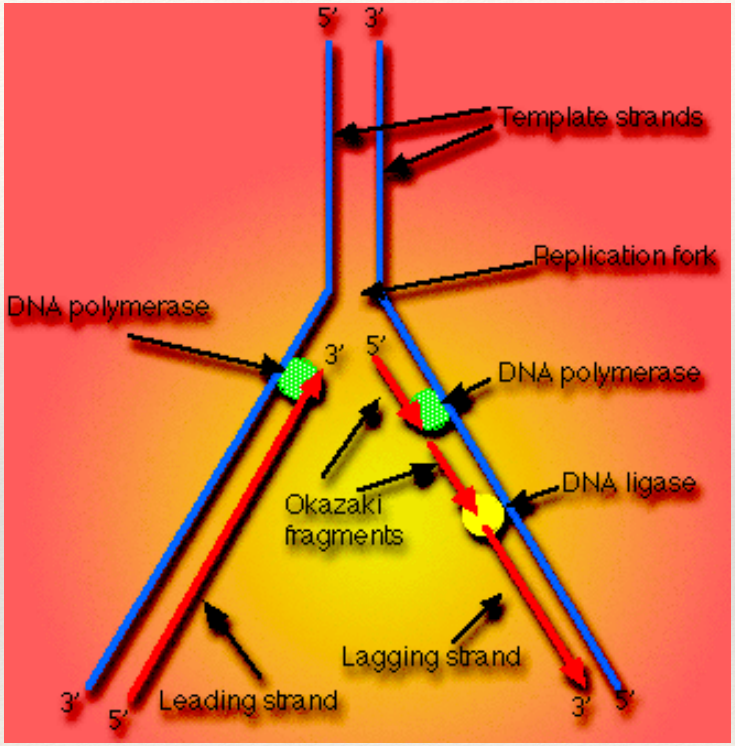
Information fidelity: copying and proofreading

Fluctuations of information

Information: copying mechanism



(replicationdna.blogspot.com)



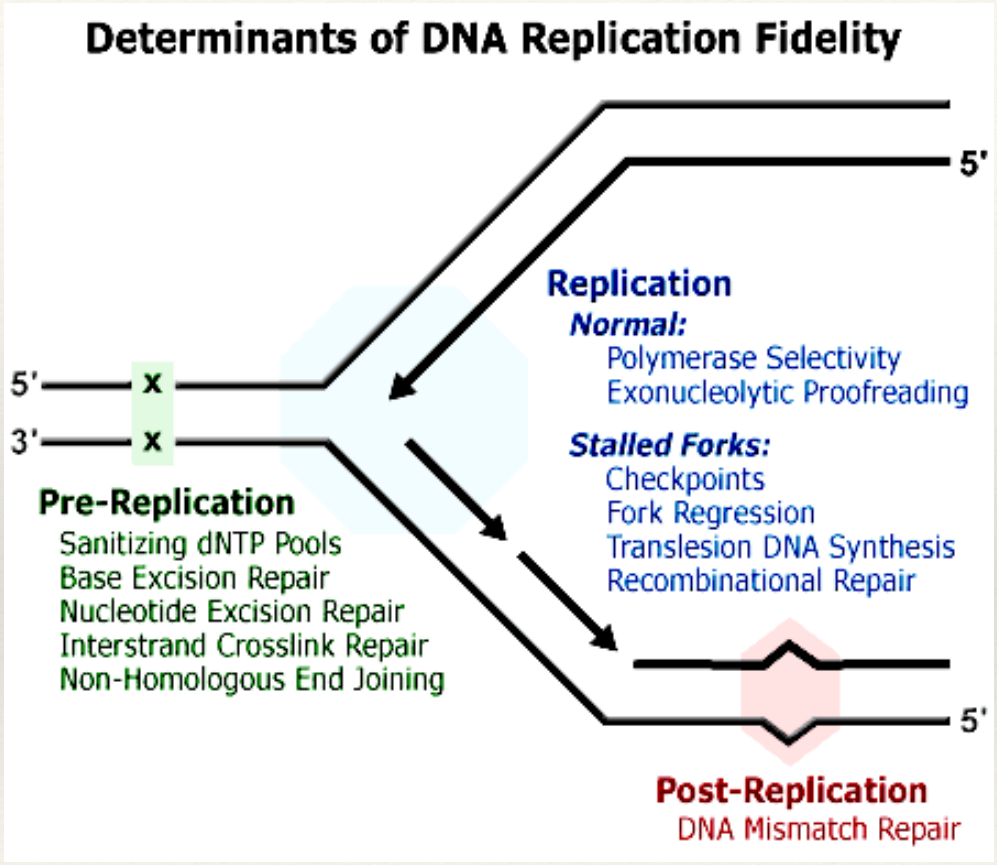
(library.thinkquest.org)

Information: Fidelity

Some facts about DNA replication:

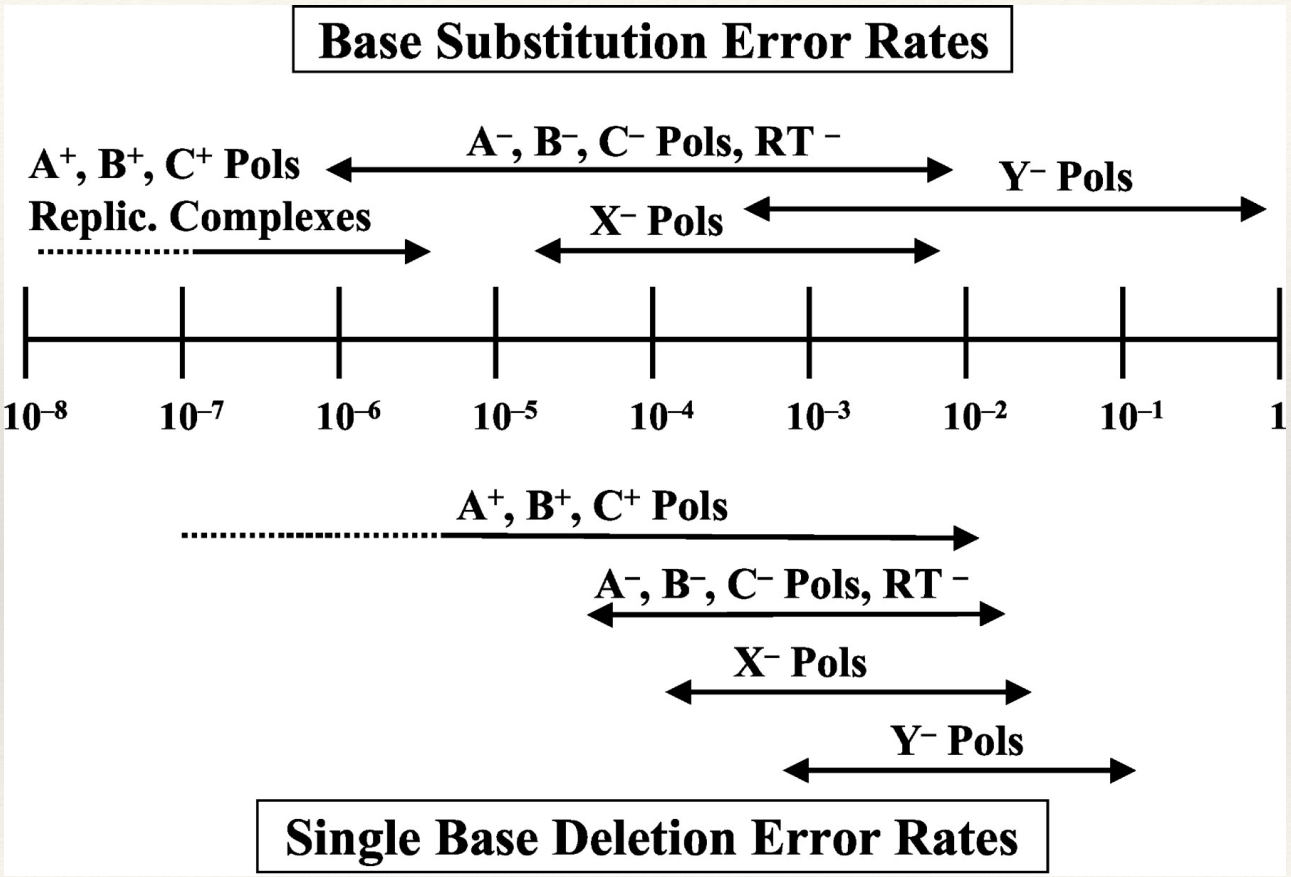
- 6 billion nucleotides of the human genome are replicated in only a few hours (*Remark: DNA polymerase processes ~1000 nucleotides/s*)
- Spontaneous error rate < 1 mutation / genome /cell division
- Where is this accuracy coming from?
  - Specificity
  - Proofreading
  - Post replication repair

Information: Fidelity



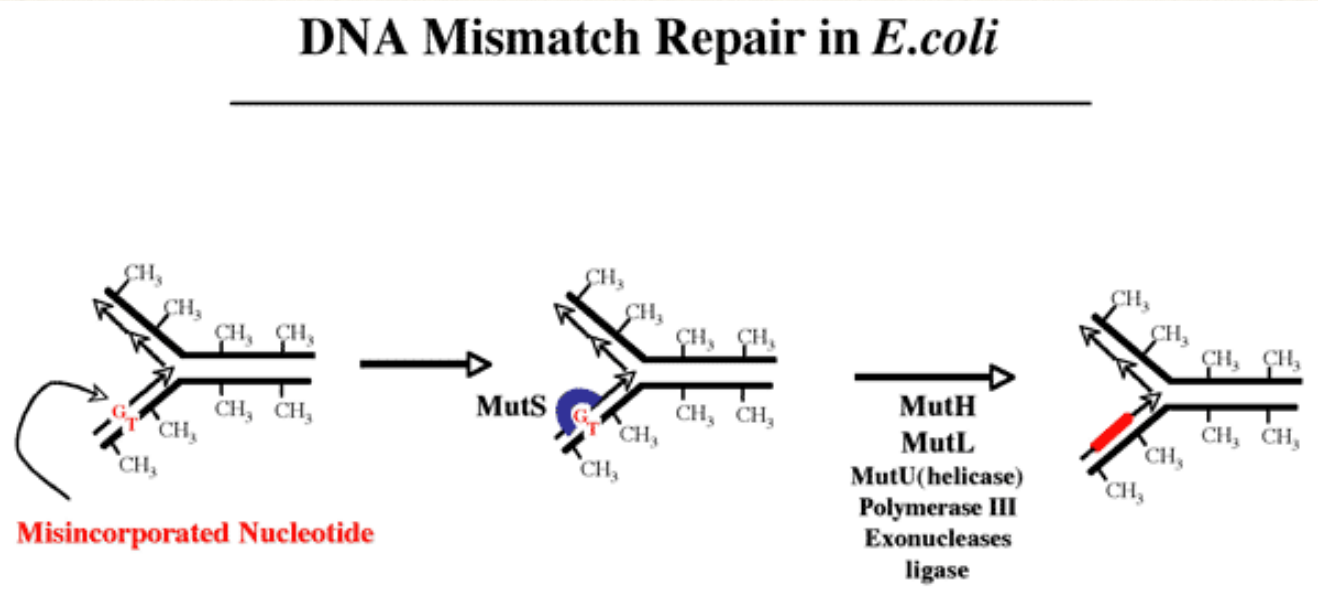
(http://www.niehs.nih.gov/research/atniehs/labs/lmg/dnarf/)

Information: Fidelity



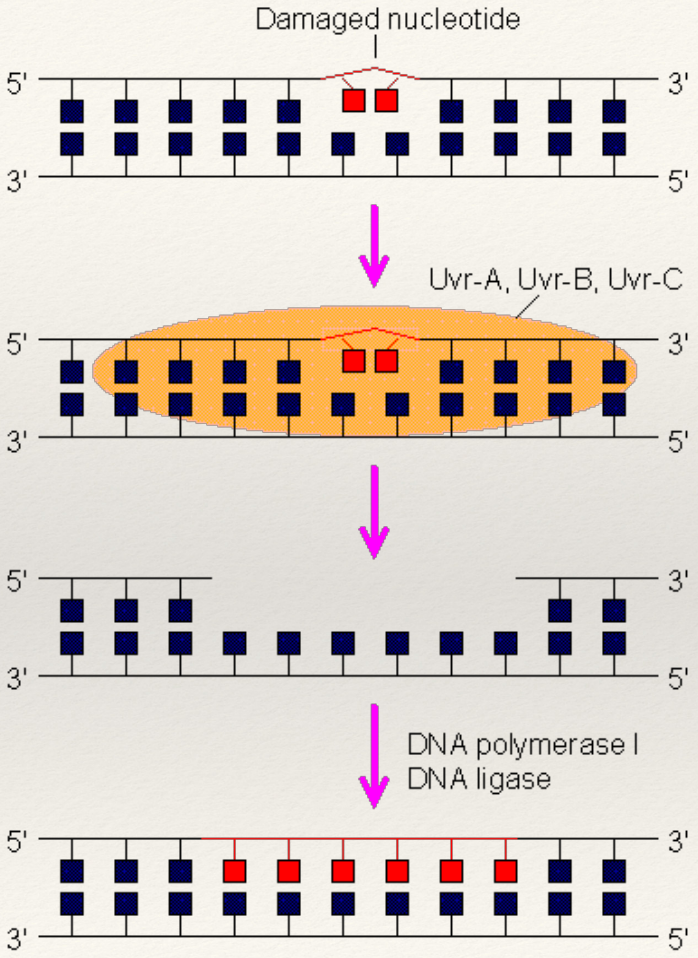
Kunkel T A J. Biol. Chem. 2004;279:16895-16898

Information: Fidelity



(mmr.med.ohio-state.edu)

Information: Fidelity



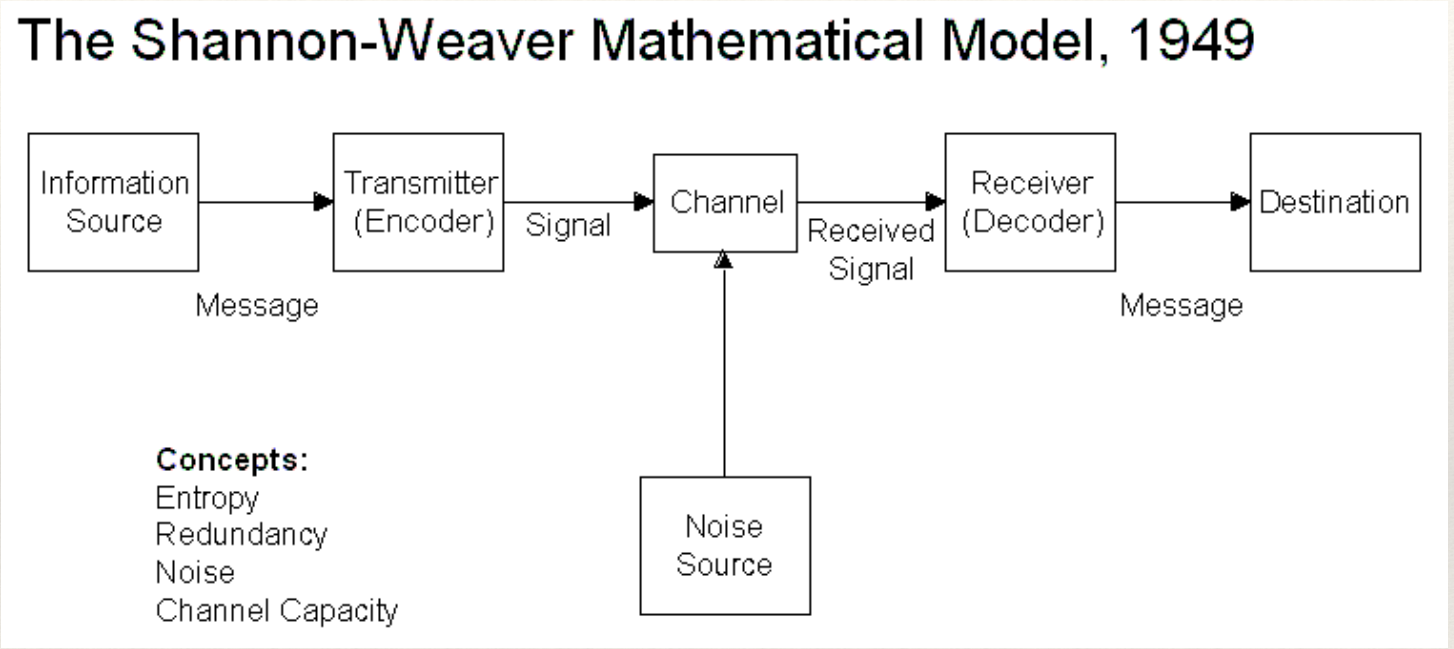
Information and Fluctuations

Information support: DNA

Information fidelity: copying and proofreading

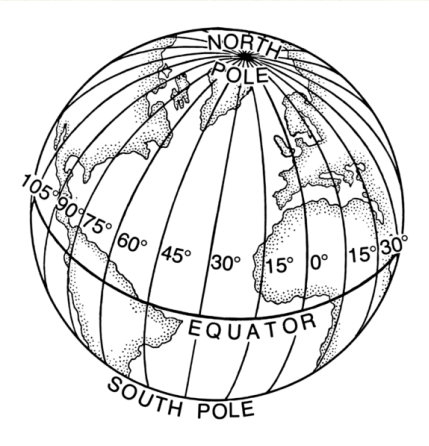
Fluctuations of information

Information and Noise



Noise = unwanted signal

Unwanted noise



How do we measure longitude?

One approach is to look at the time difference between the current position and a Universal time (say at Greenwich).

Sailors would then carry a robust clock (chronometer) to identify Universal time:

- Cook (1772) carried one
- Darwin (1831) carried 22!

Unwanted noise

Computers also encounter noise!

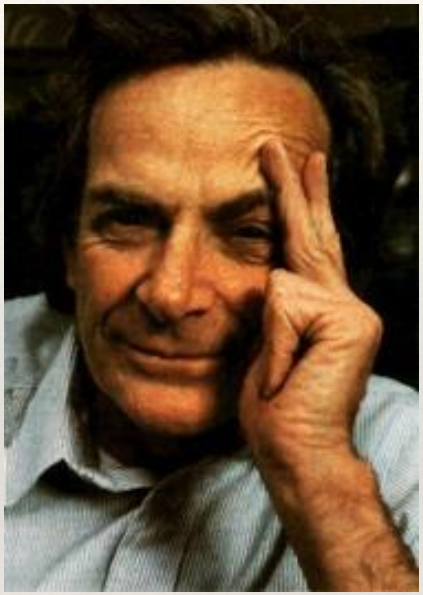
The Ariane 5 tragedy: On June 1996,

The first Ariane 5 was launched…

And exploded after 40 seconds!

The failure of the Ariane 501 was caused by the complete loss of guidance and altitude information 37 seconds after start….due to a numerical error!

Information and Noise



"*Everything that living things do can be understood in terms*

of the jiggling and wiggling of atoms."

Richard Feynman

Altering Information

Darwin's view of mutation plays a central role in his theory of biological evolution:

- **Mutation provides the variation (raw material) upon which natural selection acts.**

- **According to Darwin, the environment does not direct evolution, rather it passively selects among variants.**

Evolution in the laboratory

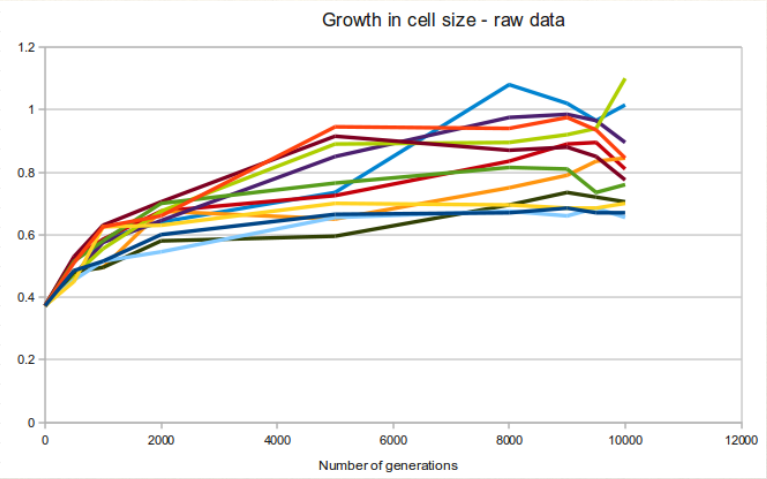
In 1988, Lenski started a long term experiment: he prepared 12 identical flasks of Ecoli cultures on minimal medium, with glucose.

Each day, an aliquote of each flask is used to inoculate a fresh medium.

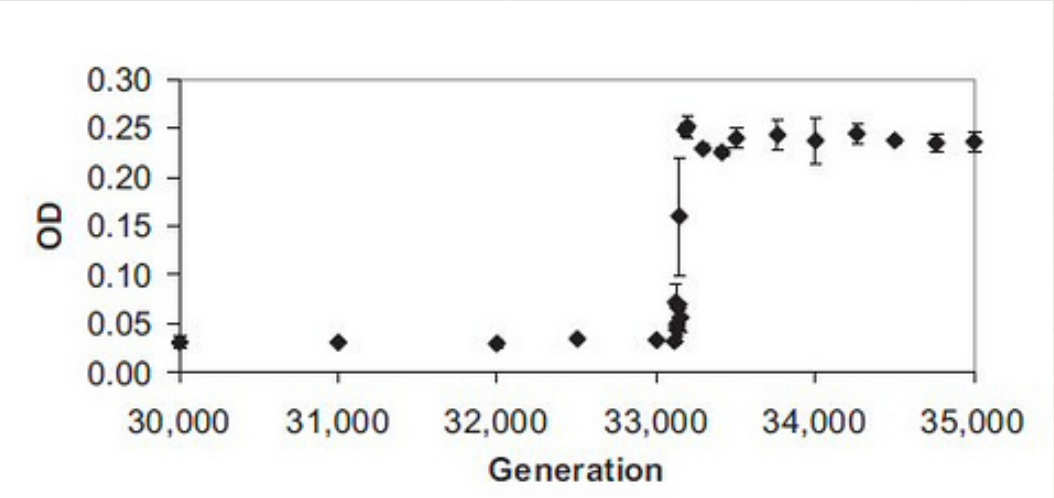
The experiment has been running for more than 35 years, covering more than 80,000 generations.

Evolution in Lenski's cultures

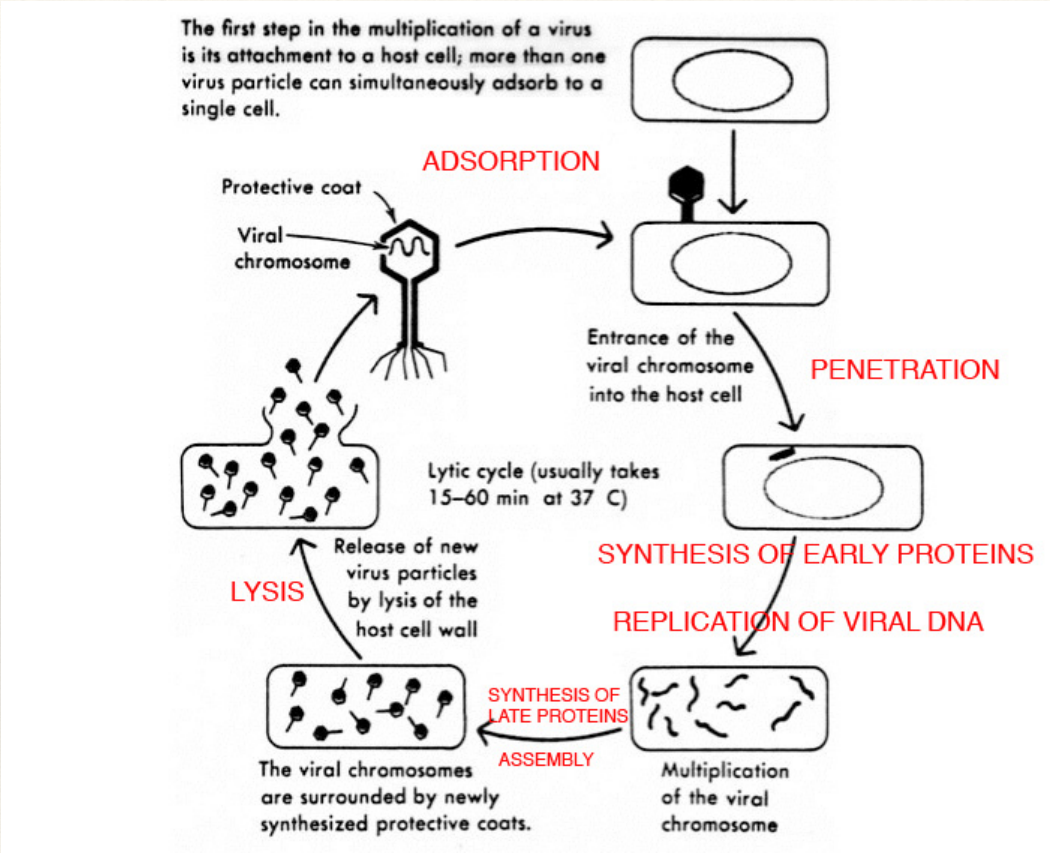
All 12 cultures lead to cells with larger volumes (better adapted to minimal medium)



Some bacteria in one of the 12 cultures started using citrate as a food source.



Luria and Delbruck experiments



(http://textbookofbacteriology.net/phage.html)

Luria and Delbruck experiments

After infection with a phage, a culture of E.Coli will clear up…to grow back again after a few hours: some resistant bacteria survived, leading to a new resistant colony.

How did these variants come to be? Two hypotheses:

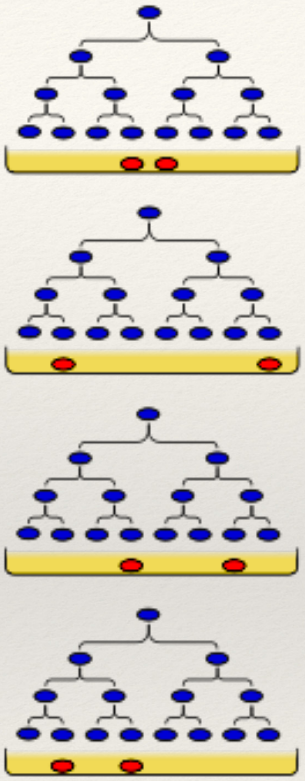
-Hypothesis of acquired immunity

The variants were exposed to the phage, but survived the attacks; their progeny maintained the immunity

-Hypothesis of mutation to immunity

Immunity comes from mutations that occurred independently of the presence of the virus.

Hypothesis 1: Induced mutation



(A) Induced mutation

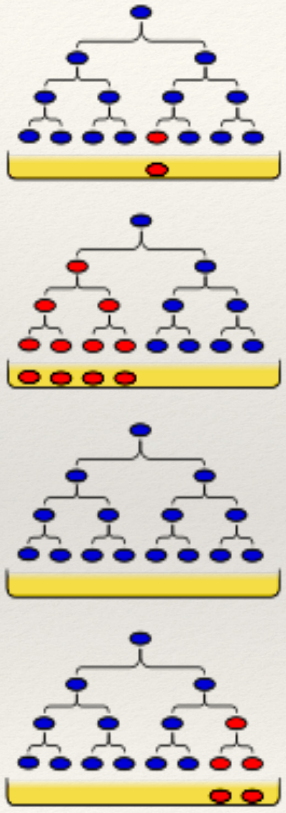
Resistant mutants ***arise in response*** to the bacteriophage. All progeny from the survivors are also resistant.

If correct, we expect:

•A large # of small cultures will have a nearly constant proportion of resistant cells.

•Mutant cells arise only after selection begins with the addition of phage, not before.

Hypothesis 2: Spontaneous mutation



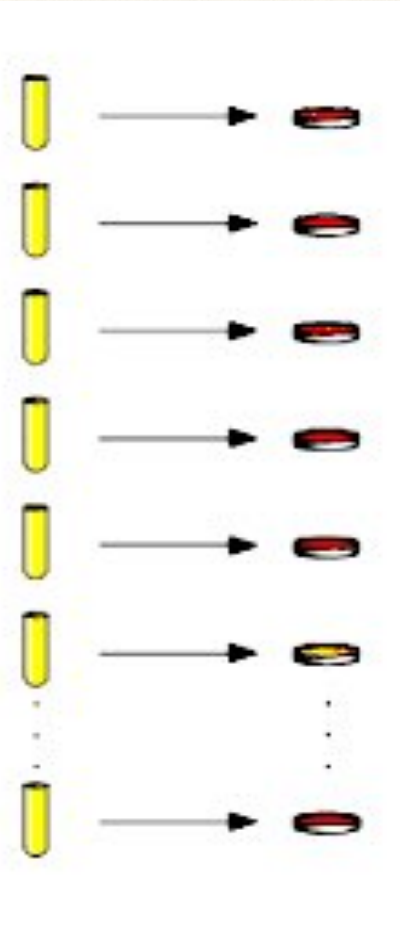
(B) Spontaneous mutation

Mutations ***arise by chance*** at a constant rate and at any point in time; the mutation is subsequently selected for.

If correct, we expect:

- The number of resistant cells will be determined by how early in a culture the mutation event occurred.
- A large # of small cultures will have the proportion of resistant cells fluctuate.

Luria and Delbruck experiments

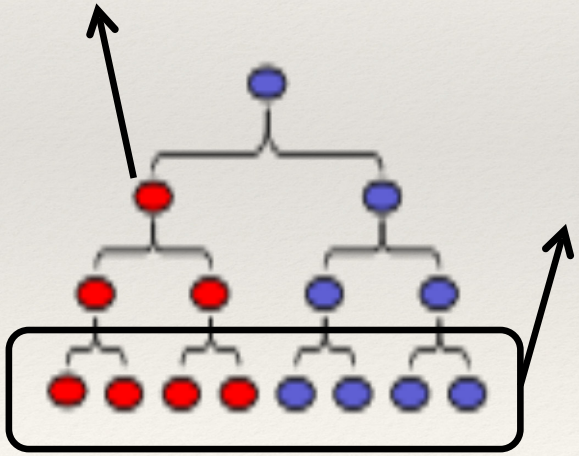


	Separate cultures	
	Culture number	# $T1^R$ mutants
	1	1
	2	0
	3	3
	4	0
	5	0
	6	5
	7	0
	8	5
	9	0
	10	6
	11	107
	12	0
	13	0
	14	0
	15	1
	16	0
	17	0
	18	64
	19	0
	20	35
mean		**11.3**
variance		**694**
$\frac{\text{variance}}{\text{mean}}$		**60.8**

Altering information

The **mutation frequency** is the frequency or proportion at which a specific kind of mutation is found in a population of cells or individuals.

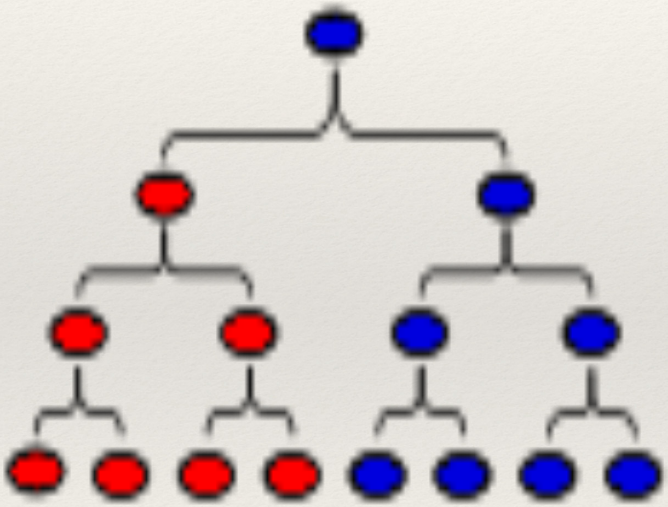
one mutation event



4 mutants out of 8 cells total
mutation frequency = ½

Altering information

The **mutation rate** is a measure of the basic tendency of a gene to mutate



1 in the total # of cell divisions (7 total)

= **1/7 (1 mutation per seven cell divisions)**

References

DNA replication fidelity. Kunkel, T.A. *J. Bio. Chem.* (2004). **279**:16895

Dynamics of adaptation and diversification: a 10,000-generation experiment with bacterial populations. Lenski, R.E. & Travisano, M. **PNAS (USA) (1994), 91:6808.**

Mutations of bacteria from virus sensitivity to virus resistance. Luria, S.E. & Delbrück, M. *Genetics* (1943), **28**:491