DNA mutation: a change in sequence

THE CAT ATE THE RAT
THE KAT ATE THE RAT

THE CAT ATE THE RAT
THE HAT ATE THE RAT

THE CAT ATE THE RAT
THE CAA TET HER AT

THE CAT ATE THE RAT
THE ECA TAT ETH ERA T

- **Substitution:**
  - Silent – the same meaning.
  - Missense – the meaning is changed.
- **Deletion** – nonsense (the sentence makes no sense)
- **Insertion** – nonsense (the sentence makes no sense)

Substitutions are ***point*** **mutations, while insertions and deletions are *frameshift* mutations.**

DNA Mutations

A mutation is a permanent change in the DNA sequence.

- **Mutations can be:**
  - ***spontaneous*** **(by chance)**
  - ***induced*** **by mutagens (physical, chemical or biological agents)**

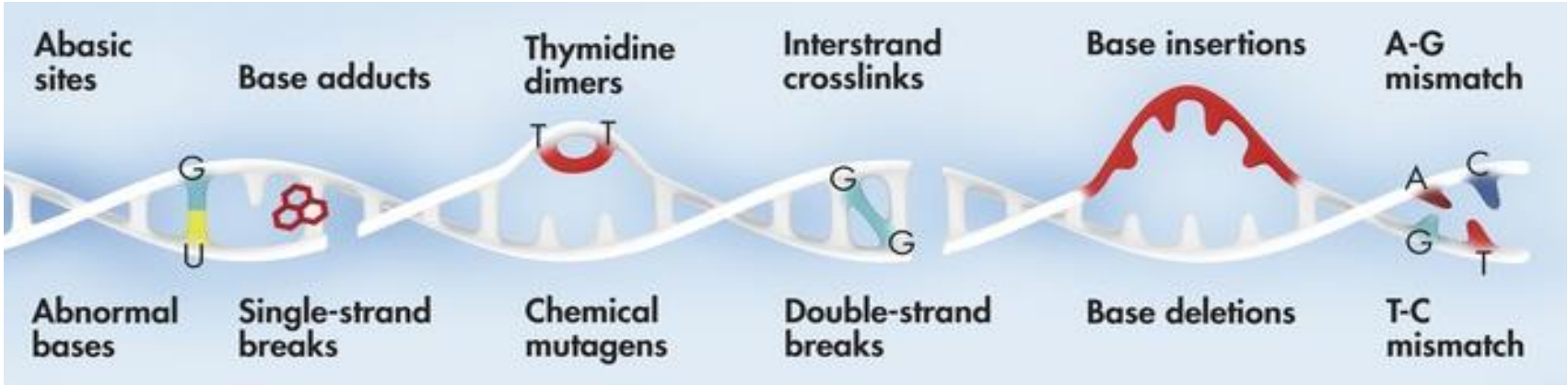
- **Factors that cause mutations:**
  - **external - environmental factors such as sunlight, radiation, and smoking**
  - **native - errors during DNA replication**

- **Mutations can lead to:**
  - **an *evolutionary advantage* of a certain genotype**
  - **disease, developmental delays, structural abnormalities, or other effects.**

Example: Sickle cell anemia is a disorder in which the body makes sickle-shaped red blood cells as a result of DNA mutation.

DNA Damage

DNA is damaged up to 1 million times per cell per day.



- **The cells have an elaborate type-of-damage-specific system of DNA repair that is constantly active.**
- **A cell that has accumulated a large amount of DNA damage, or one that no longer effectively repairs damage incurred to its DNA, can enter one of three possible states:**

1. **an irreversible state of dormancy, known as *senescence***
2. **cell suicide (*apoptosis*) or programmed cell death**
3. **unregulated cell division, which can lead to cancer**

Human DNA

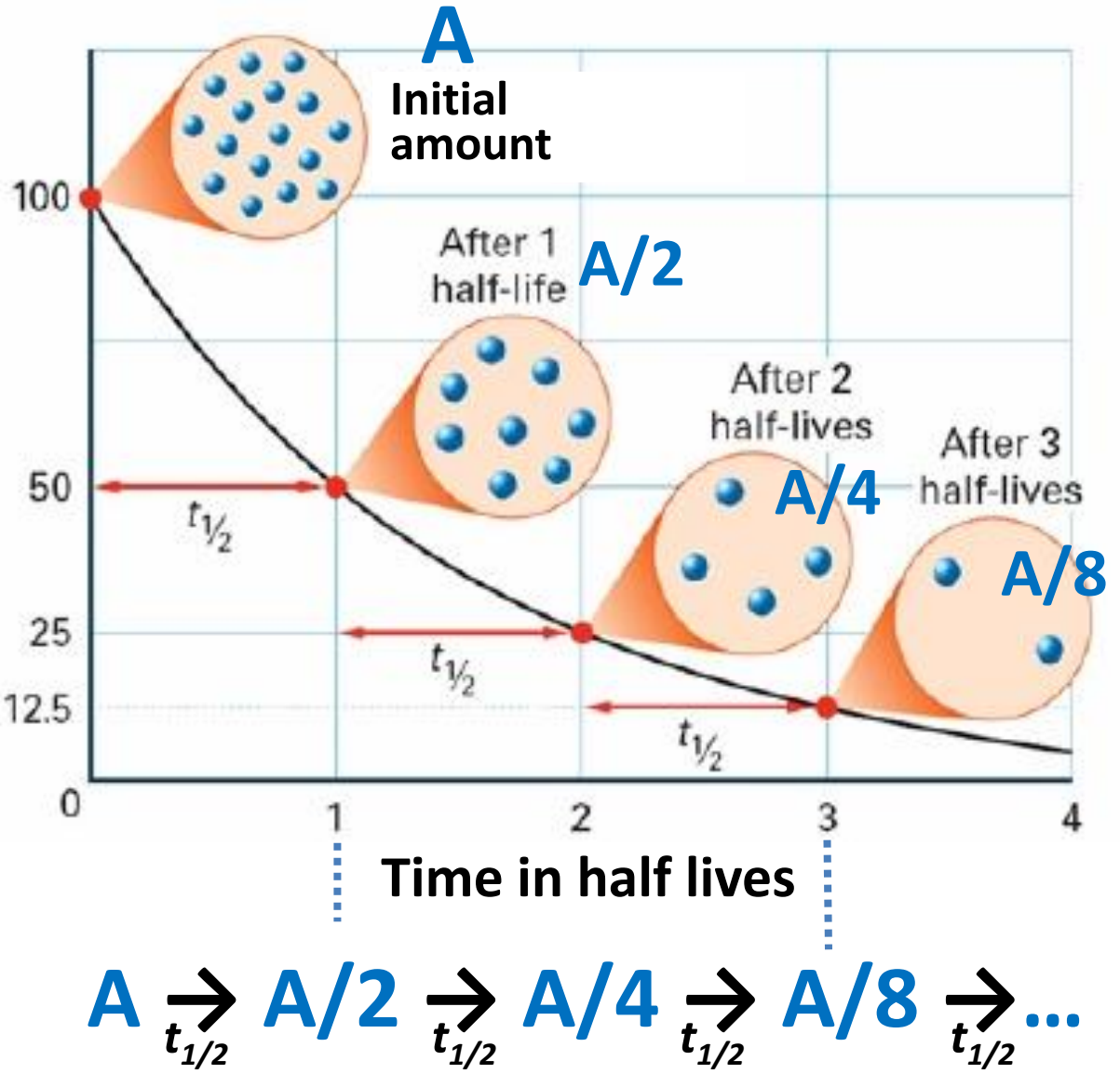
- The Human Genome Project (1990-2003) produced the first complete sequences of individual human genomes.
- Human genome contains ~3 billion bases and ~20,500 genes.
- Over 98% of the human DNA comprises *non-coding repetitive sequences* (the role, functions and descriptions of these sequences are currently being investigated by scientists).

- By 2020, tens of thousands of human genomes have been completely sequenced.
- All humans have the DNA that is 99.9% similar, however the rest 0.01% is enough to identify different individual DNA sequences (*i.e. tell apart which DNA belongs to whom*).
- Primary (and now standard routine!) applications include paternity testing as well as DNA profiling in criminal investigations.

How long does it last?

- **Half life** ($t_{1/2}$) **is a time parameter used in science to describe various random decay processes.**

- **Half life of something is equal to the amount of time it takes for half of this something to degrade, decay or disintegrate.**



$$A \xrightarrow[t_{1/2}]{} A/2 \xrightarrow[t_{1/2}]{} A/4 \xrightarrow[t_{1/2}]{} A/8 \xrightarrow[t_{1/2}]{} \ldots$$

DNA Half-Life

In 2012, researchers have calculated that DNA from bones has a 521 year half-life, which means that the oldest clone-able samples of DNA could be no more than 2 million years old.

This result rules out any possibility of ever replicating dinosaurs, as the youngest dinosaurs were around more than 65 million years ago…

…but we surely can *try* to

bring back the Woolly Mammoth!

Scientists at the US biotechnology company Colossal Biosciences plan to "de-extinct" the prehistoric pachyderms by genetically modifying Asian elephants to give them woolly mammoth traits. They hope the first calf will be born by the end of 2028.

As the first step along the way, they succeeded in creating healthy mice with mammoth-like long and woolly golden hair!