Mutations (2)

Causes of mutations

1. **DNA fails to copy accurately (spontaneous mutations)**

-- Most of the mutations that we think matter to evolution are**“spontaneous (naturally-occurring) ".**

-- Spontaneous mutations occur **even** in a healthy, uncontaminated cell.

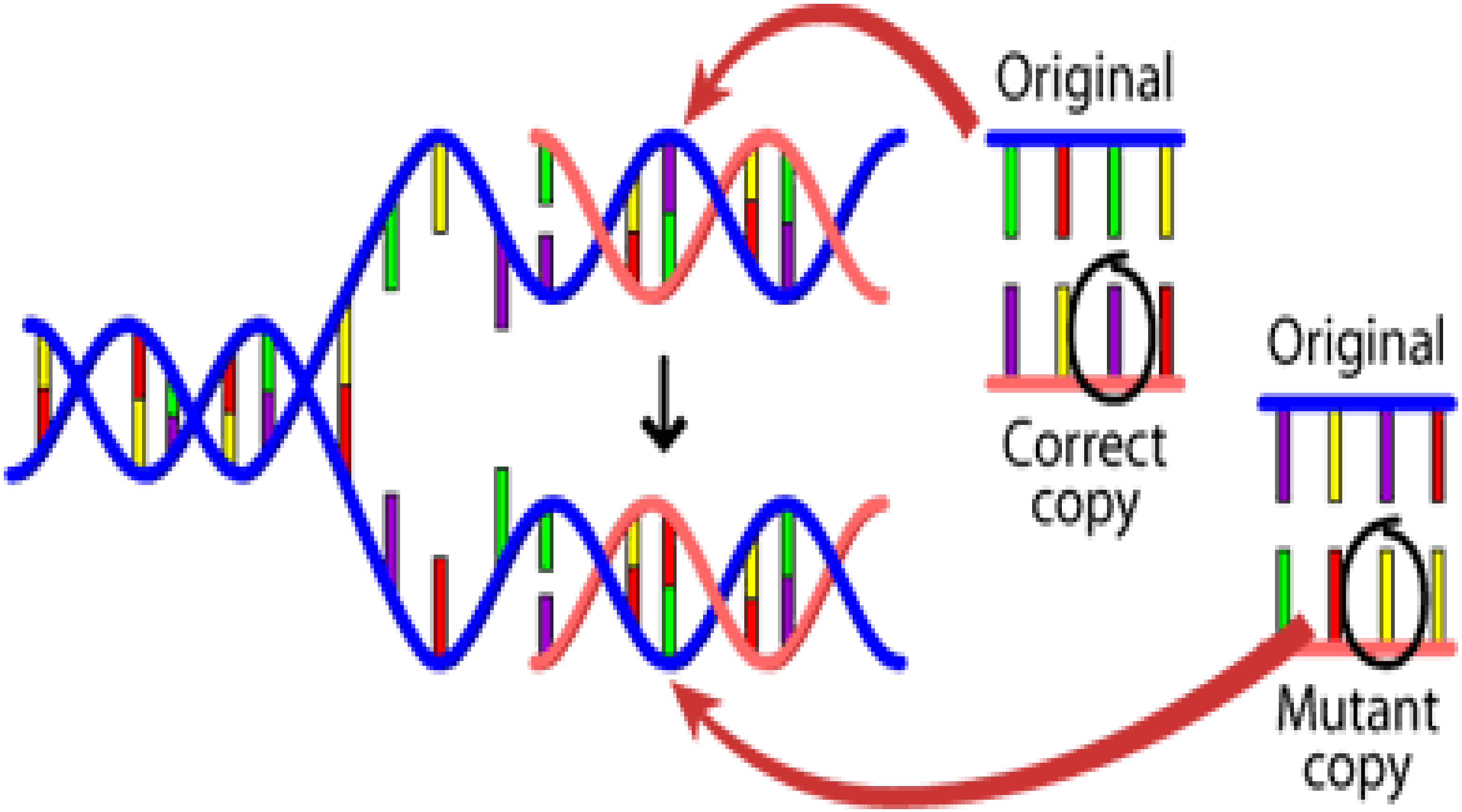
-- The majority of spontaneously arising mutations are due to **error-prone replication** **(translesion synthesis)** after DNA damage in the template strand.

For example, when a cell divides, it makes a copy of its DNA — and sometimes the **copy is not quite perfect**.

-- Naturally occurring DNA damage is estimated to occur **10,000 times** per cell per day in **humans** and **100,000** times per cell per day in **rats**.

-- In mice, the **majority of all mutations** are caused by **translesion synthesis**.

-- Likewise, in yeast, **more than 60%** of the spontaneous single base pair substitutions and deletions are caused by **translesion synthesis**.


Original
Correct
copy
Original
Mutant
copy

2. External influences can create mutations

-- Mutations can also be caused by **exposure to specific chemicals or radiation.**

-- These agents are called **mutagens.**

-- Mutagens cause the **DNA to break down**.

-- This is **not necessarily unnatural** — even in the most isolated environments, DNA breaks down.

3. Errors introduced during DNA repair

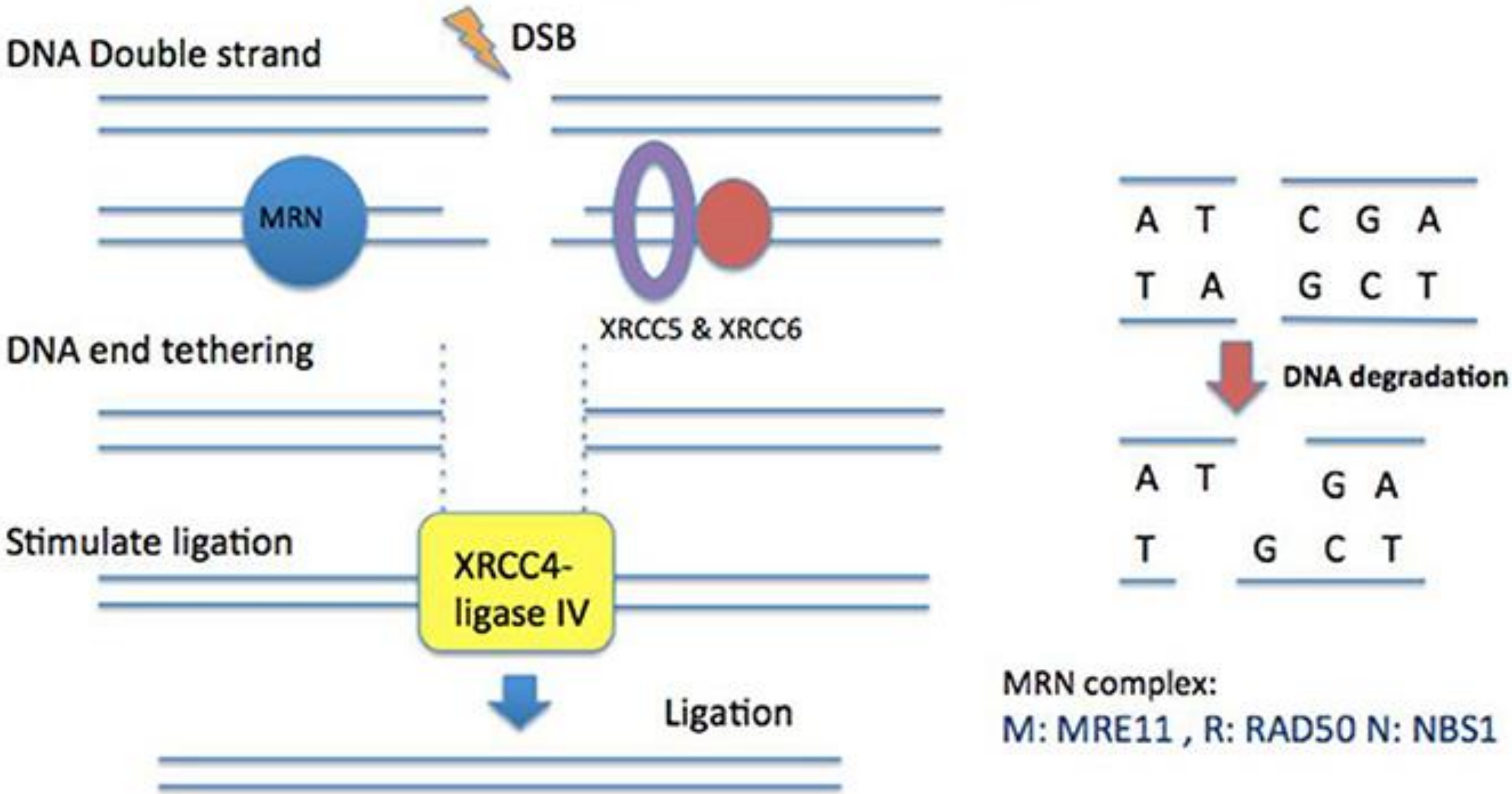
-- Although naturally occurring double-strand breaks occur at a relatively low frequency in DNA, their repair often causes mutation.

-- **Non-homologous end joining (NHEJ)** is a major pathway for repairing double-strand breaks.

-- NHEJ involves **removal of a few nucleotides** to allow somewhat inaccurate alignment of the two ends for rejoining followed by addition of nucleotides to fill in gaps.

-- As a consequence, NHEJ often introduces mutations.

Non-Homologous End Joining



Mutation rate

-- Mutation rates **vary substantially** across species.

-- We still do not know why it is so.

-- In **humans**, the mutation rate is about **50-90 de novo mutations per genome per generation.**

It means that each human accumulates about 50-90 novel mutations that **were not present** in his or her parents.

-- This number has been established by sequencing thousands of **human trios**, that is, two parents and at least one child.

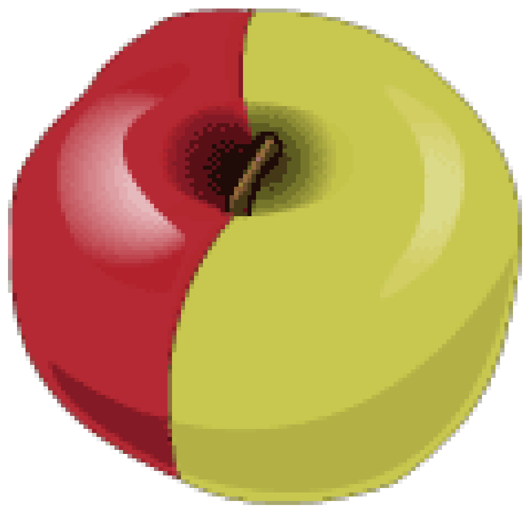
Effects of mutations

1. Somatic mutations

- Since all cells in our body contain DNA, there are lots of places for mutations to occur.
- However, some mutations **cannot be passed** on to offspring and do not matter for evolution.
- These are called **somatic mutations.**
- Somatic mutations occur in **non-reproductive cells** and won't be passed onto offspring.

For example, the golden color on half of this red apple was caused by a **somatic mutation**.

Its seeds **will not carry** the mutation.



2. Germ line mutations

- The only mutations that matter to **large-scale evolution** are those that can be **passed on to offspring**.

- These occur in reproductive cells like **eggs and sperm** and are called **germ line mutations**.

Effects of germ line mutations:

A single germ line mutation can have a range of effects:

1. No change occurs in phenotype:

- Some mutations **don't have any noticeable effect** on the phenotype of an organism.
- Perhaps the mutation occurs in a stretch of **DNA with no function.**
- Or perhaps the mutation occurs in a protein-coding region, but **ends up not affecting the amino acid sequence** of the protein.

2. Small change may occur in phenotype

For example, a single mutation caused this cat's ears to curl backwards slightly.

3. Big changes occur in phenotype

- Some really **important phenotypic changes**, like DDT resistance in insects are sometimes caused by single mutations.

- A single mutation can also have **strong negative effects** for the organism, even leading to death.

- Mutations that cause the death of an organism are called **lethal mutations**.

Control genes

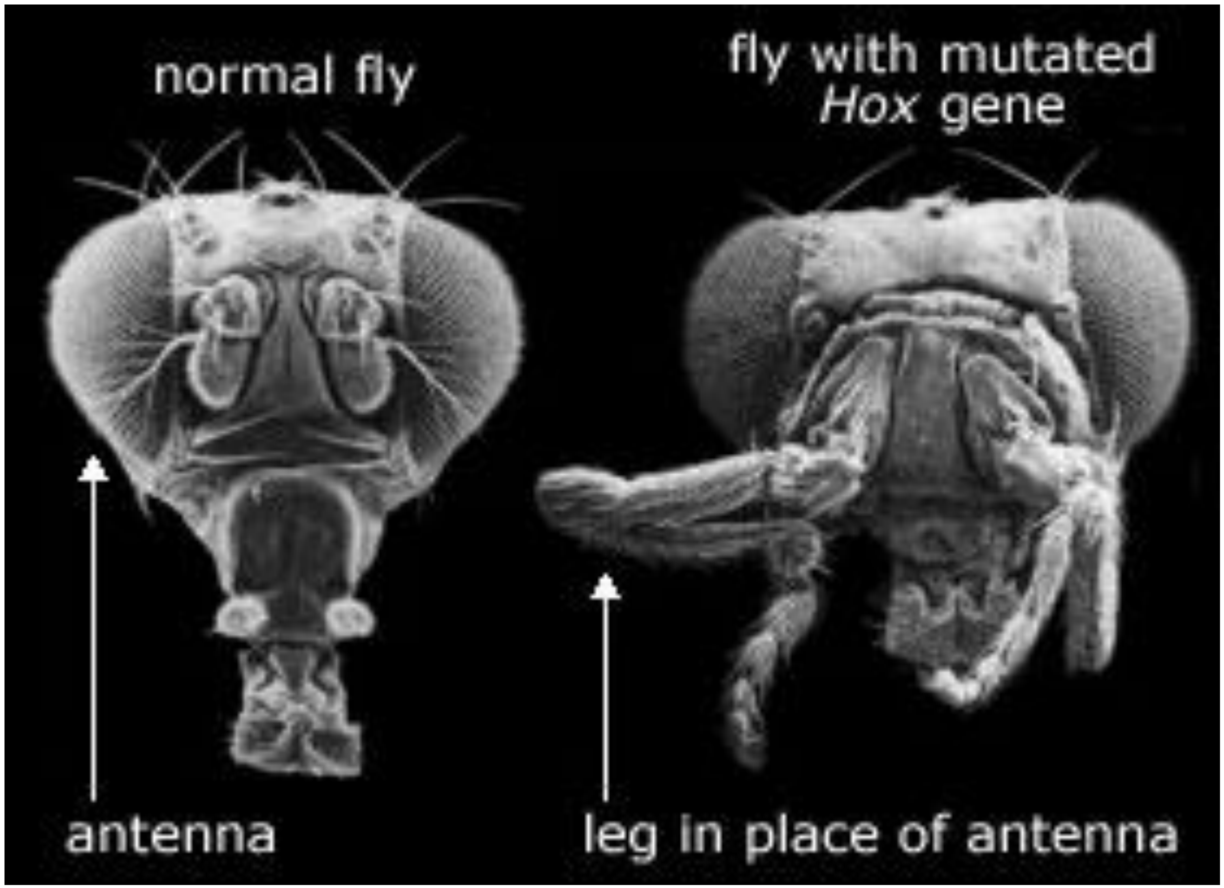
- Some regions of DNA **control other genes**, determining when and where other genes are turned "on".
- Mutations in these parts of the genome can **substantially change** the way the organism is built.
- Many organisms have **powerful control genes** that determine how the **body is laid out**.

- For example, ***Hox* or *Homeobox* genes** (nearly 300) control the formation of **body parts** and **designate where the head goes and which regions of the body grow appendages.**

- Such **master control genes** therefore direct the building of body "units," such as segments, limbs, and eyes.

- Mutations in these control genes can **transform one body part into another.**

Scientists have studied flies carrying *Hox* mutations that **sprout legs on their foreheads instead of antennae!**



Mutations are random

- Mutations can be **beneficial, neutral**, or **harmful** for the organism, but **mutations do not "try" to supply what the organism "needs."**
- Factors in the environment may influence the rate of mutation but are **not generally thought to influence the direction of mutation.**

- For example, exposure to **harmful chemicals** may **increase the mutation rate**, but will **not cause** more mutations that make the organism **resistant** to those chemicals.

- In this respect, mutations are **random** — whether a particular mutation happens or not is unrelated to how useful that mutation would be.


Thank You!