



Mutations

Fourth Lecture

March 2008

Molecular and Genetic engineering

Mutations

- Mutations are very common: every cell contains multiple mutations. Also, everyone is genetically different from every other person due to the accumulation of mutations.



Genetic load

- Genetic load: on average, each person has 3 recessive lethal mutations in all cells. We survive because the dominant normal alleles cover up the recessive lethals. Inbreeding—mating with close blood relatives—often causes defective children because the recessive lethals inherited from the common ancestor become **homozygous**.



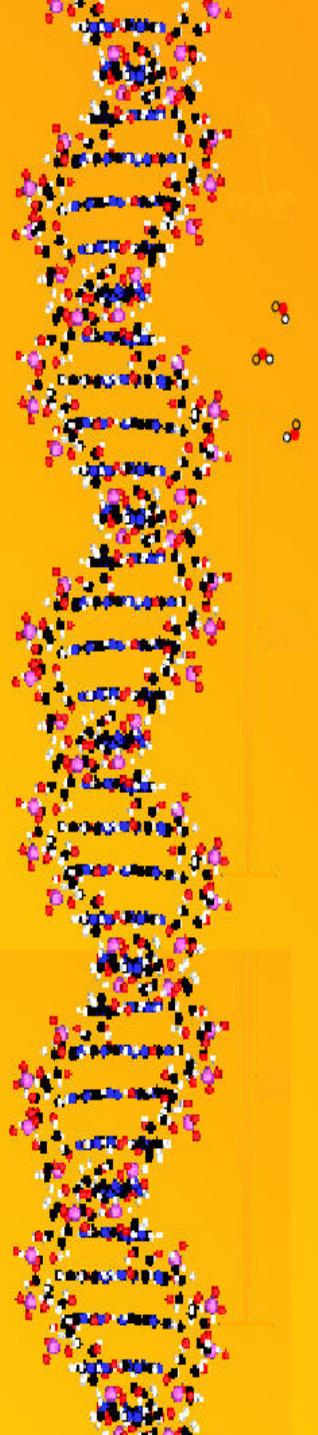
Mutation is a completely random

- Any change in the base sequence of a DNA molecule is a mutation.
- Mutation is a completely **random** process: any DNA base can be mutated, whether it is in a **gene** or **not**.



Basic types:

1. **base substitutions**: convert one base into another, such as changing an A into a G.
2. **Insertions or deletions** of large pieces of DNA.
3. **Combining parts of 2 different genes together.**





introns

- Many mutations occur in regions where they have no effect: between the genes, or in the introns that are spliced out of the messenger RNA. Only mutations within genes can affect the organism.

Base substitution mutations

- **Base substitution mutations** within a gene can alter or destroy the gene's protein product. The protein may not function at all, or it might be less efficient, or it might have an altered pH optimum or temperature optimum. Many of these changes have little or no effect on the organism: these are called "neutral" mutations, because they are neither good nor bad for the organism.





insertions, deletions, and rearrangements

- The larger changes that occur with insertions, deletions, and rearrangements are usually harmful, because they usually destroy at least one gene. However, new useful genes sometimes arise from these rearrangements. One event in particular: attaching the control regions of one gene onto the protein-coding part of another gene. This causes the protein to be synthesized in a new time and place within the organism.



Mutation Causes and Rate

- Rate: for typical genes, base substitutions occur about once in every 10,000 to 1,000,000 cells. Since we have about 6 billion bases of DNA in each cell, this implies that virtually every cell in your body contains several mutations. Clearly, most mutations are neutral: have no effect.



mutations in the germ cells

- **Only mutations in the germ line cells:** cells that become sperm or eggs—are passed on to future generations. Mutations in other body cells only cause trouble when they cause cancer or related diseases.
- **Causes:** The natural replication of DNA produces occasional errors. DNA polymerase has an editing mechanism that decreases the rate, but it still exists.

Radiation and chemical

- Radiation and certain chemical compounds also cause mutations. Chemicals that cause cancer—carcinogens—almost all work by causing mutations.



What if we mess up one of the nucleotides and change one of the codons? We get a mutation!

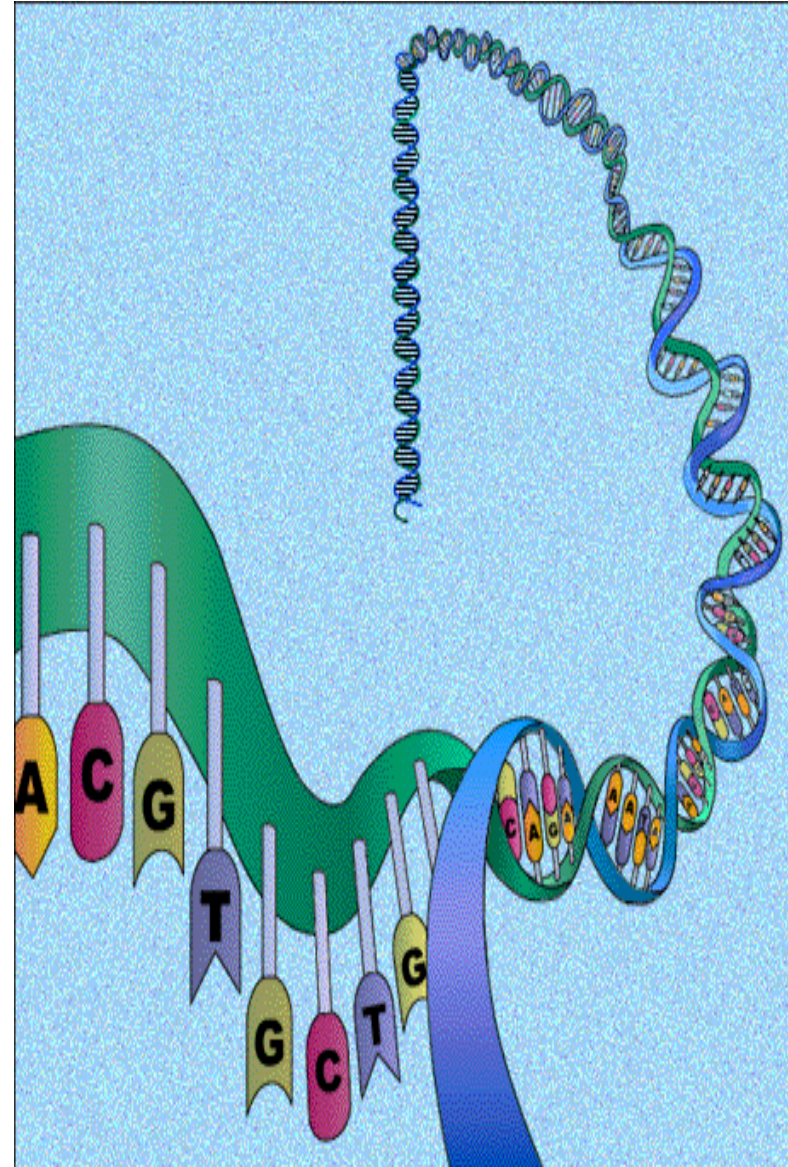
Mutations in DNA sequence

1- Point mutations

2- Frame-shift

3-mutations Insertions
Deletions.

4-Mutations that cannot be
seen in a karyotype



Point Mutation

- A point mutation is a simple change in one base of the gene sequence.
- This is equivalent to changing one letter in a sentence, such as this example, where we change the 'c' in cat to an 'h':
- **Original**
 - The fat cat ate the wee rat.
- **Point Mutation**
 - The fat hat ate the wee rat.



Frame-shift mutation

- In a frame shift mutation, one or more bases are inserted or deleted.
- Because our cells read DNA in three letter "words", adding or removing one letter changes each subsequent word. This type of mutation can make the DNA meaningless and often results in a shortened protein.
- **Original**
 - The fat cat ate the wee rat.
- **Frame Shift – deleted the 't' in 'cat'**
 - The fat caa **tet hew eer at.**



Thymine goes with adenine.

Guanine goes with cytosine.

