

Mutations and mutagenesis

Genetics 371B Lecture 14

22 Oct. 1999

What is a mutation?

◆ **Chromosome** mutations

◆ **Point mutations**

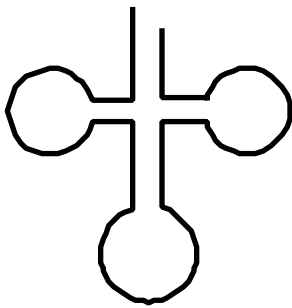
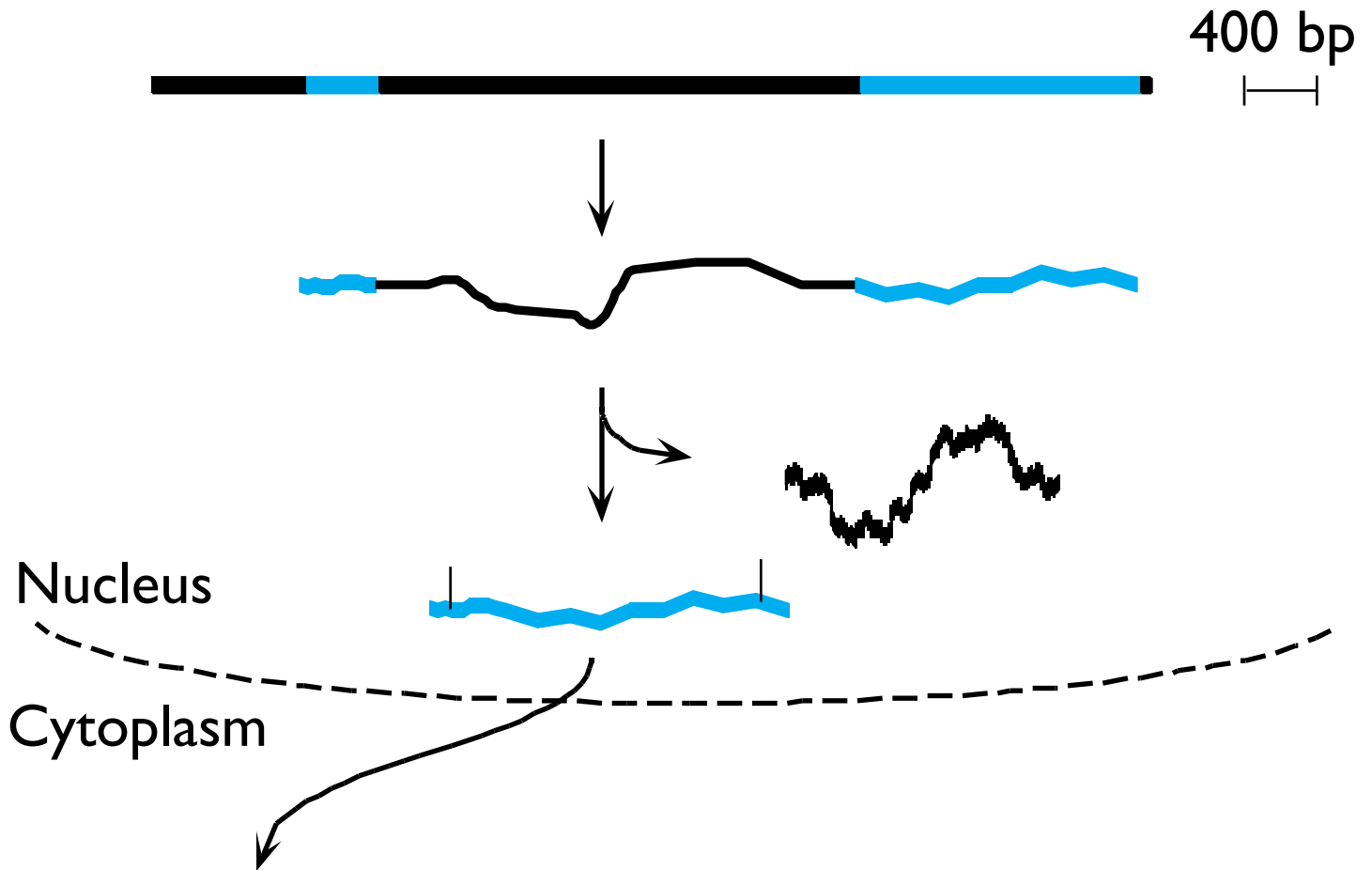
◇ Base substitutions

◇ Insertions/deletions—
frameshift mutations

Is a mutation an allele?

Where can things go wrong?

Drosophila **yellow** gene

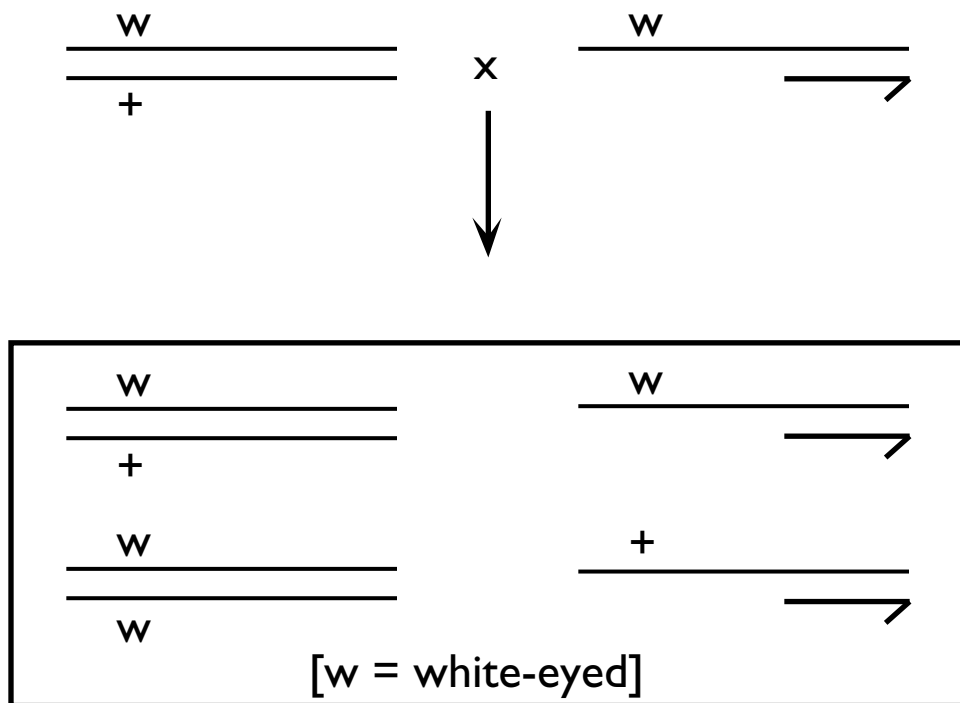


AAGUGCA **AUGUCCAGGACAAAGGGUGGAUCCU...CAAGGUJAA**

CAUA

Mutation frequency

H. J. Muller's assay – **How frequently** does the *Drosophila* X chromosome acquire mutations?



Asked...what fraction of crosses **failed** to give red-eyed male progeny?

Conclusion: ~2 mutations per 1000 X chromosomes

Extrapolating to humans...

Inbreeding, and why it's not a great idea

Some causes of mutations

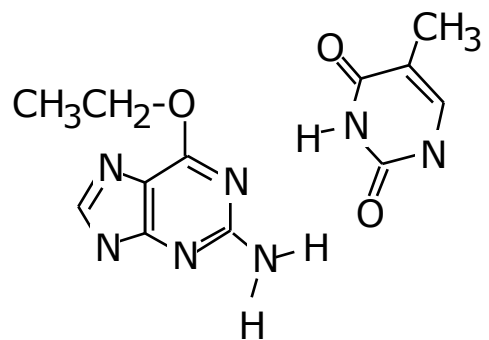
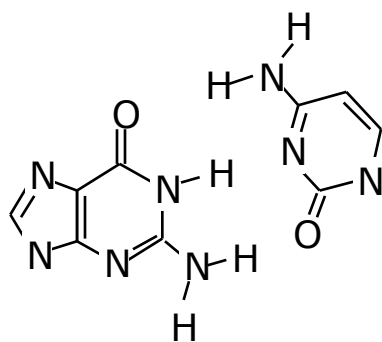
◆ **Misincorporation** during replication

◆ **External causes**

◇ Radiation

◇ Chemical mutagens – e.g.:

○ Alkylating agents



○ Intercalating agents

Damage control

- ◆ **Preventing** misincorporation –
- ◆ Normal activities of polymerase:
 - ◇ Extension of 3' base-paired primer
 - ◇ Removal of 3' unpaired base
- ◆ If incorrect base is put in...

Correcting misincorporation –

Mismatch repair:

1. Identify mismatched bases
2. Identify the original (parental) strand
3. Correct the other strand

Timeout for repair – **Checkpoints**

Lee Hartwell and Ted Weinert, UW (1989)



Phenotype of mutant?