BOTANY HONOURS

SEMESTER IV

CORE COURSE 10
GENETICS
(BOT-A-CC-4-10-TH)

TOPIC NO 6: MUTATION

Dr. Madhuvanti Chatterjee
MAULANA AZAD COLLEGE
KOLKATA
DEPARTMENT OF BOTANY

MUTATION

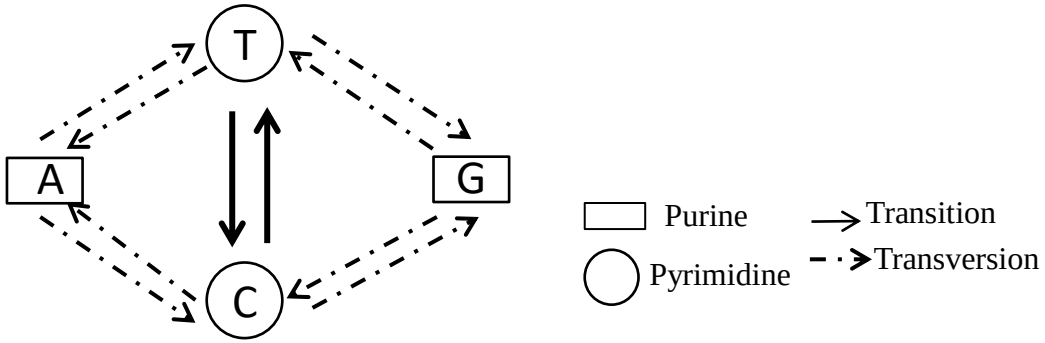
The term *MUTATION* is defined as any sudden heritable change in the genotype of an organism, not explainable by recombination of preexisting genetic variability, and the process by which the change occurs.

Topic no- 6.1. Point mutation-Transition, Transversion and Frame shift mutation

POINT MUTATION: Mutation which involve the deletion /duplication /substitution of SINGLE BASE – PAIRS are known as point mutation.

- Transition : Mutations which involve the replacement of a Purine with a purine (A⇆G) OR pyrimidine with another pyrimidine (T⇆C).

- Transversion : Mutations which involve the replacement of a Purine with a pyrimidine OR Pyrimidine with a purine.



Diagrammatic representation of substitutions possible in DNA

❖ Frame shift mutation : A mutation which involves the addition or deletion of one or a few base and results in the alteration of the reading frame of the codons in the gene (corresponding amino acids of the polypeptide) distal to the mutation.

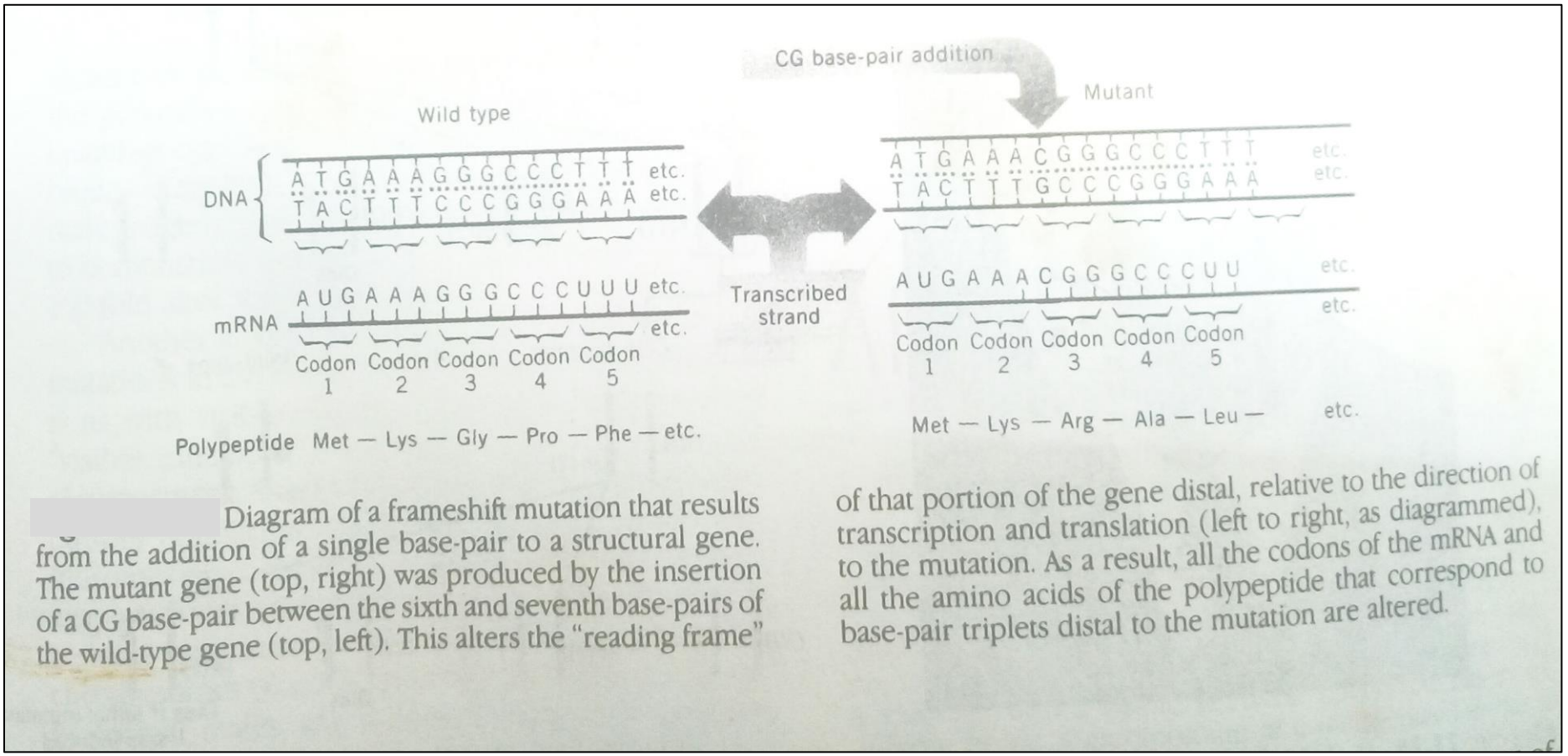


Diagram of a frameshift mutation that results from the addition of a single base-pair to a structural gene. The mutant gene (top, right) was produced by the insertion of a CG base-pair between the sixth and seventh base-pairs of the wild-type gene (top, left). This alters the "reading frame" of that portion of the gene distal, relative to the direction of transcription and translation (left to right, as diagrammed), to the mutation. As a result, all the codons of the mRNA and all the amino acids of the polypeptide that correspond to base-pair triplets distal to the mutation are altered.

Diagram showing the change from the third amino acid in the polypeptide as a result of addition of a single base pair (C/G) in the mutant (Right panel)

MOLECULAR MECHANISMS OF MUTATION

I. TAUTOMERISATION :- The rare forms of the bases which are formed due to the change of the position of the hydrogen atoms from one position to another in the purine or pyrimidine

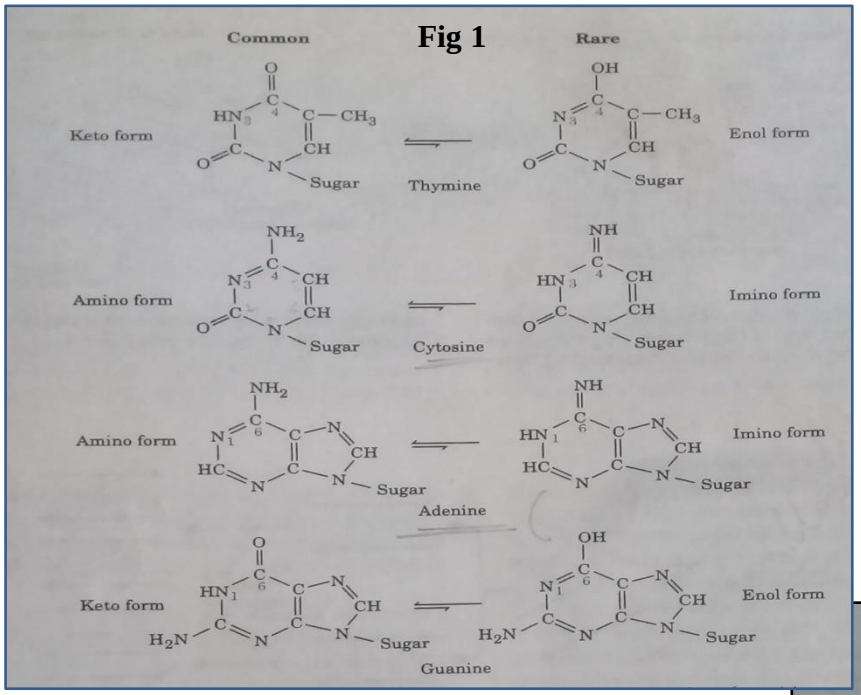


Fig 1

Fig 1: Tautomeric shifts- The more stable keto forms of Thymine and Guanine change to the less stable enol forms AND the stable amino forms of Cytosine and Adenine change to less stable imino forms.

Fig 2: Mismatched pairing-A pairs with C and G pairs with T in their rare tautomeric forms.

The net effect of such an event and the subsequent replication required to segregate the "mismatched" base-pair is an AT to GC or a GC to AT base-pair substitution.

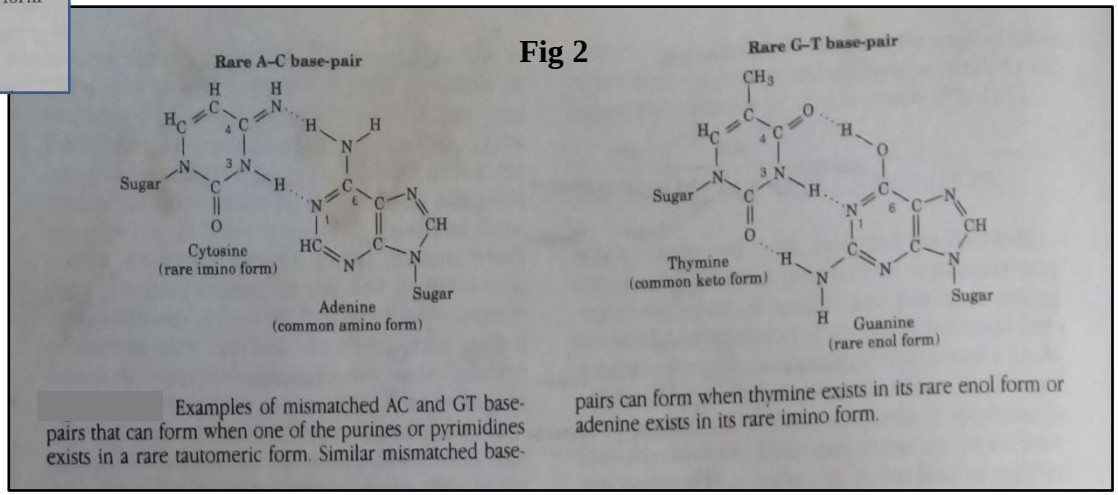


Fig 2

Examples of mismatched AC and GT base-pairs that can form when one of the purines or pyrimidines exists in a rare tautomeric form. Similar mismatched base-pairs can form when thymine exists in its rare enol form or adenine exists in its rare imino form.

MOLECULAR MECHANISMS OF MUTATION

II. ALKYLATION:- The transfer of methyl or ethyl groups to the bases such that their base-pairing potentials are altered

ALKYLATING AGENTS AND THEIR STRUCTURE

CHEMICAL NAME	COMMON NAME OR ABBREVIATION	STRUCTURE
I. Alkylating agents		
Di-(2-chloroethyl) sulfide	Mustard gas or sulfur mustard	$Cl—CH_2—CH_2—S—CH_2—CH_2—Cl$
Di-(2-chloroethyl) methylamine	Nitrogen mustard	$Cl—CH_2—CH_2—\underset{\displaystyle CH_3}{\underset{\vert}{N}}—CH_2—CH_2—Cl$
Ethylmethane sulfonate	EMS	$CH_3—CH_2—O—SO_2—CH_3$
Ethylethane sulfonate	EES	$CH_3—CH_2—O—SO_2—CH_2—CH_3$
N-Methyl-*N'*-nitro-*N*-nitrosoguanidine	NTG	$HN{=}C(\underset{\displaystyle O{=}N—N—CH_3}{\underset{\vert}{\ }})—NH—NO_2$

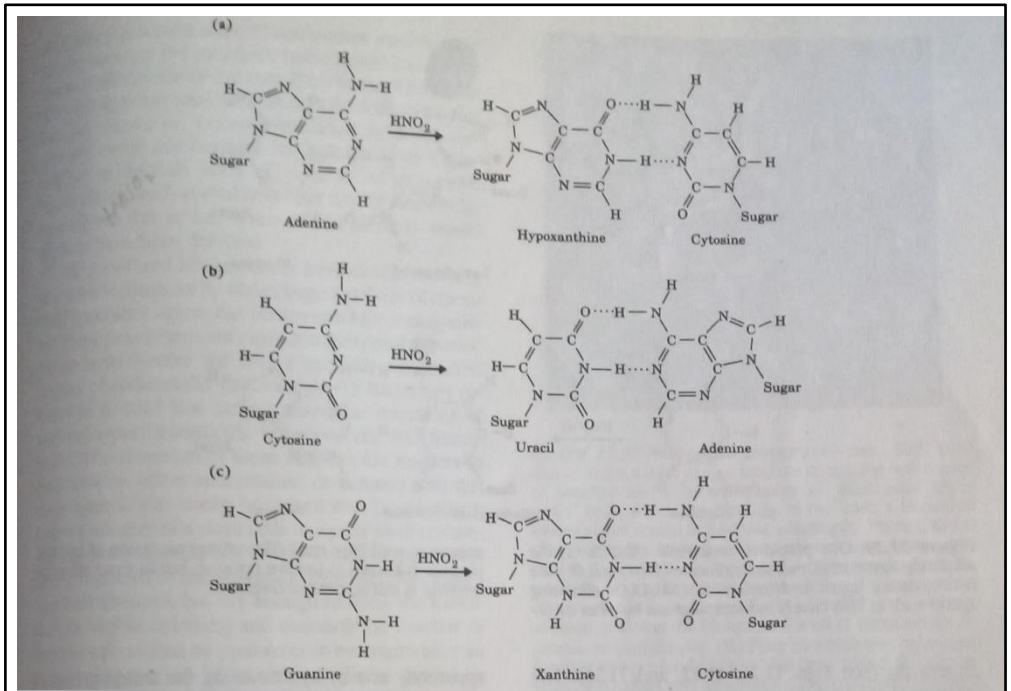
The alkylating agents induce all kinds of mutations like transitions , transversions, frameshift mutations and even chromosome aberrations.

MOLECULAR MECHANISMS OF MUTATION

III. DEAMINATION

Nitrous Acid

Nitrous acid (HNO_2) is a very potent mutagen that acts directly on either replicating or nonreplicating DNA by oxidative deamination of the bases that contain amino groups—adenine, guanine, and cytosine. Conversion of the amino groups to keto groups changes the hydrogen-bonding potential of the bases. Adenine is deaminated to hypoxanthine, which base-pairs with cytosine rather than thymine. Cytosine is converted to uracil, which base-pairs with adenine instead of guanine. Deamination of guanine produces xanthine, but xanthine base-pairs with cytosine just like guanine. Thus, the deamination of guanine is not directly mutagenic like that of adenine and cytosine. Since the deamination of adenine leads to AT ⟶ GC transitions, and the deamination of cytosine results in GC ⟶ AT transitions, nitrous acid induces transitions in both directions, AT ⟷ GC. Nitrous acid-induced mutations can thus also be induced to revert with nitrous acid.

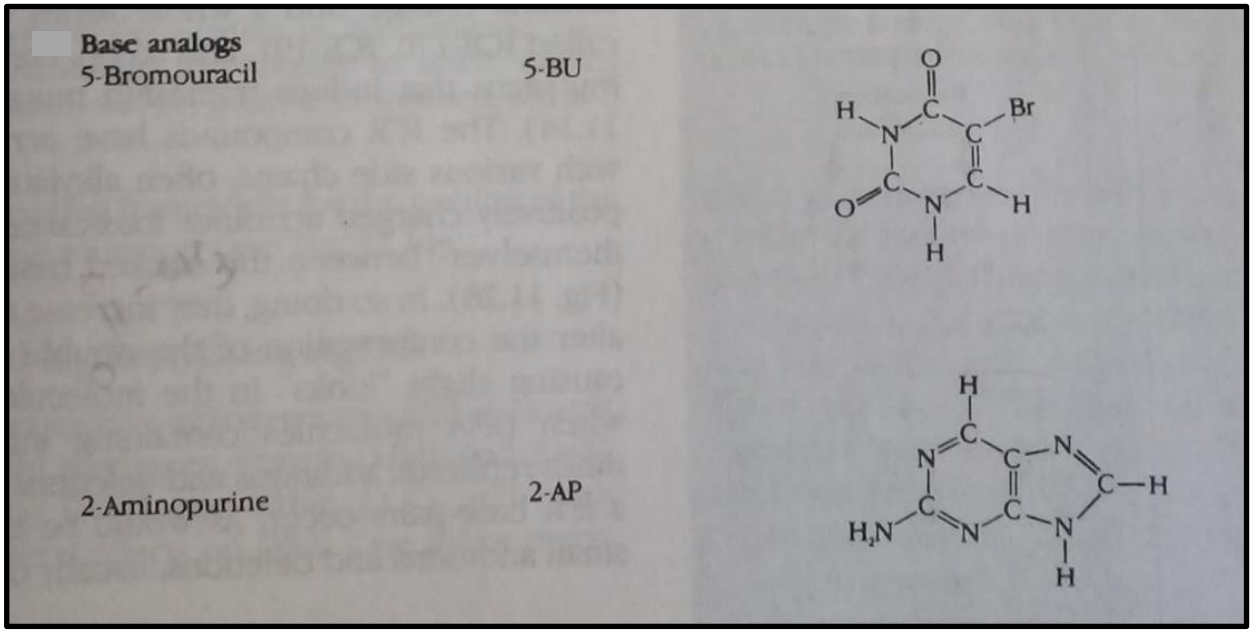


Mutagenic action of nitrous acid. Oxidative deamination converts (a) adenine to hypoxanthine, causing AT⟶GC transitions; (b) cytosine to uracil, causing GC⟶AT transitions; and (c) guanine to xanthine, which is not directly mutagenic. The combined effects of nitrous acid on adenine and cytosine explain its ability to induce transitions in both directions, AT⟷GC.

The combined effect of nitrous acid on adenine and cytosine causes bidirectional AT↔GC transition

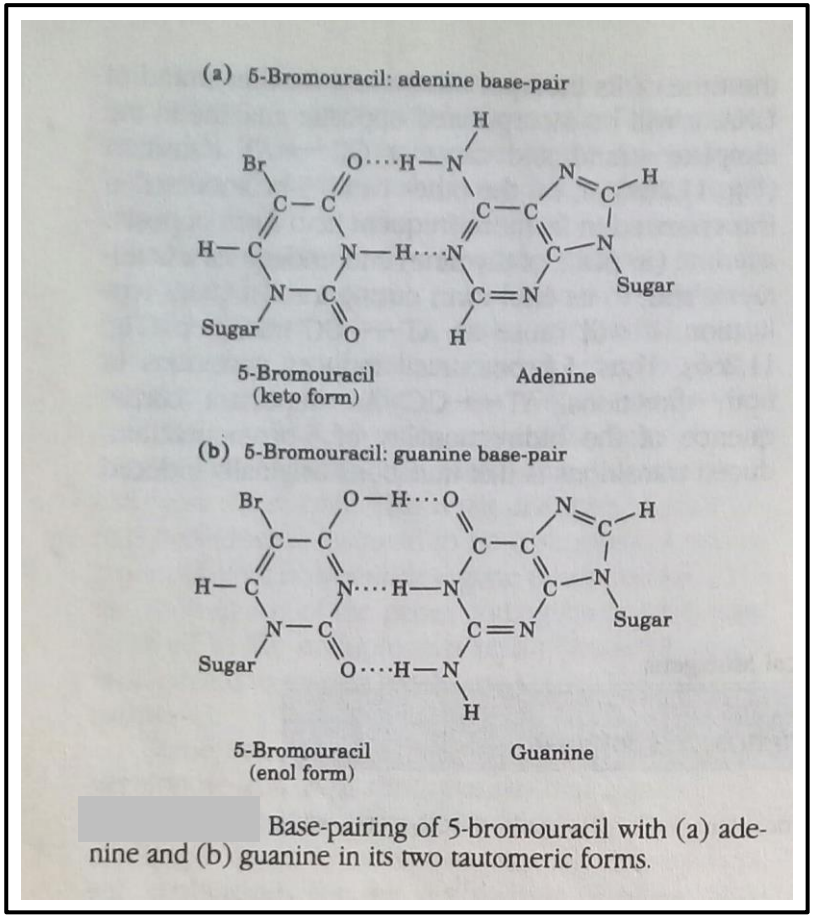
MOLECULAR MECHANISMS OF MUTATION

IV. BASE ANALOGUE INCORPORATION



TWO MOST COMMONLY USED BASE ANALOGS: 5-bromouracil which is a thymine analog AND 2-aminopurine is a purine analog

IV. BASE ANALOGUE INCORPORATION



Base-pairing of 5-bromouracil with (a) adenine and (b) guanine in its two tautomeric forms.

In its more stable keto form, 5BU pairs with adenine. After a tautomeric shift to its enol form 5BU pairs with guanine