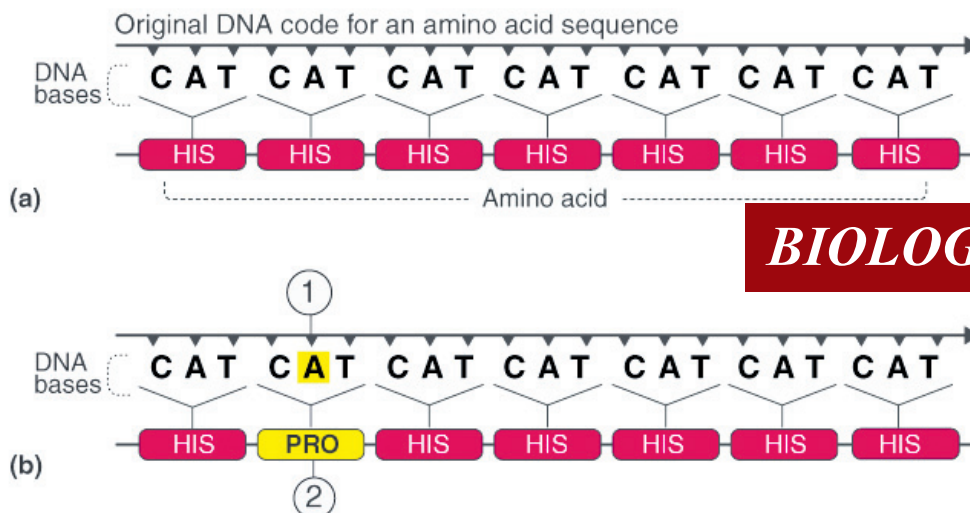


Transfer of Genetic Information.. Nucleotides, Amino acids

GENETIC CODE

During replication and transcription a nucleic acid was copied to form another nucleic acid. Hence, these processes are easy to conceptualise on the basis of complementarity. The process of translation requires transfer of genetic information from a polymer of nucleotides to a polymer of amino acids. Neither does any complementarity exist between nucleotides and amino acids, nor could any be drawn theoretically. There existed ample evidences, though, to support the notion that change in nucleic acids (genetic material) were responsible for change in amino acids in proteins. This led to the proposition of a genetic code that could direct the sequence of amino acids during synthesis of proteins.

If determining the biochemical nature of genetic material and the structure of DNA was very exciting, the proposition and deciphering of genetic code were most challenging. In a very true sense, it required involvement of scientists from several disciplines –



BIOLOGY

- 1 Replacement of a single nucleotide
- 2 Incorrect amino acid, which may produce a malfunctioning protein

acids, the code should be made up of three nucleotides. This was a very bold proposition, because a permutation combination of 43 (4 × 4 × 4) would generate 64 codons; generating many more codons than required. Providing proof that the codon was a triplet, was a more daunting task. The chemical method developed by Har Gobind Khorana was instrumental in synthesising RNA molecules with defined combinations of bases (homopolymers and copoly

Finally a checker-board for genetic code was prepared which is given in Table

The salient features of genetic code are as follows

- The codon is triplet. 61 codons code for amino acids and 3 codons do not code for any amino acids, hence they function as stop codons.
- One codon codes for only one amino acid, hence, it is unambiguous and specific.
- Some amino acids are coded by more than one codon, hence the code is degenerate.
- The codon is read in mRNA in a contiguous fashion. There are no punctuations.
- The code is nearly universal: for example, from bacteria to human UUU would code for Phenylalanine (phe). Some exceptions to this rule have been found in mitochondrial codons, and in some protozoans.
- AUG has dual functions. It codes for Methionine (met), and it also act as initiator codon.

- If following is the sequence of nucleotides in mRNA, predict the sequence of amino acid coded by it (take help of the checkerboard):
-AUG UUU UUC UUC UUU UUU UUC-
- Now try the opposite. Following is the sequence of amino acids coded by an mRNA. Predict the nucleotide sequence in the RNA:
Met-Phe-Phe-Phe-Phe-Phe

Mutations and Genetic Code

- The relationships between genes and DNA are best understood by mutation studies. You have studied about mutation and its effect in Chapter 5. Effects of large deletions and rearrangements in a segment of DNA are easy to comprehend. It may result in loss or gain of a gene and so a function. The effect of point mutations will be explained here. A classical example of point mutation is a change of single base pair

in the gene for beta globin chain that results in the change of amino acid residue glutamate to valine. It results into a diseased condition called as sickle cell anemia. Effect of point mutations that inserts or deletes a base in structural gene can be better understood by following simple example.

- Consider a statement that is made up of the following words each having three letters like genetic code.

RAM HAS RED CAP

- If we insert a letter B in between HAS and RED and rearrange the statement, it would read as follows:

RAM HAS BRE DCA P

- Similarly, if we now insert two letters at the same place, say BI'. Now it would read,

RAM HAS BIR EDC AP

- Now we insert three letters together, say BIG, the statement would read

RAM HAS BIG RED CAP

RAM HAS EDC AP
RAM HAS DCA P
RAM HAS CAP

- The same exercise can be repeated, by deleting the letters R, E and D, one by one and rearranging the statement to make a triplet word.
- The conclusion from the above exercise is very obvious. Insertion or deletion of one or two bases changes the reading frame from the point of insertion or deletion. However, such mutations are referred to as frameshift insertion or deletion mutations. Insertion or deletion of three or its multiple bases insert or delete one or multiple codon hence one or multiple amino acids, and reading frame remains unaltered from that point onwards.

Table 6.1: The Codons for the Various Amino Acids

First position	Second position				Third position
	U	C	A	G	
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
	CUC Leu	CCC Pro	CAC His	CGC Arg	C
	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
	AUG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

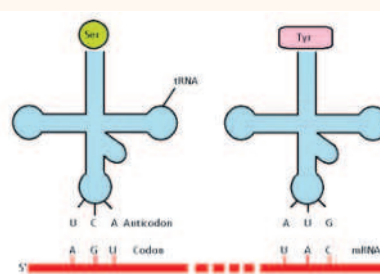
physicists, organic chemists, biochemists and geneticists. It was George Gamow, a physicist, who argued that since there are only 4 bases and if they have to code for 20 amino acids, the code should constitute a combination of bases.

Marshall Nirenberg's cell-free system for protein synthesis finally helped the code to be deciphered.

- Severo Ochoa enzyme (polynucleotide phosphorylase) was also helpful in polymerising RNA with defined sequences in a template independent manner (enzymatic synthesis of RNA).

tRNA – the Adapter Molecule

- From the very beginning of the proposition of code, it was clear to Francis Crick that there has to be a mechanism to read the code and also to link it to the amino acids, because amino acids have no structural specialities to read the code uniquely. He postulated the presence of an adapter molecule that would on one hand read the code and on other hand would bind to specific amino acids. The



- tRNA, then called sRNA (soluble RNA),
- was known before the genetic code was postulated. However, its role as an adapter molecule was assigned much later.
- tRNA has an anticodon loop that has bases complementary

to the code, and it also has an amino acid acceptor end to which it binds to amino acids. tRNAs are specific for each amino acid. For initiation, there is another specific tRNA that is referred to as initiator tRNA. There are no tRNAs for stop codons. In figure the secondary

- structure of tRNA has been depicted that looks like a clover-leaf. In actual structure, the tRNA is a compact molecule which looks like inverted L.