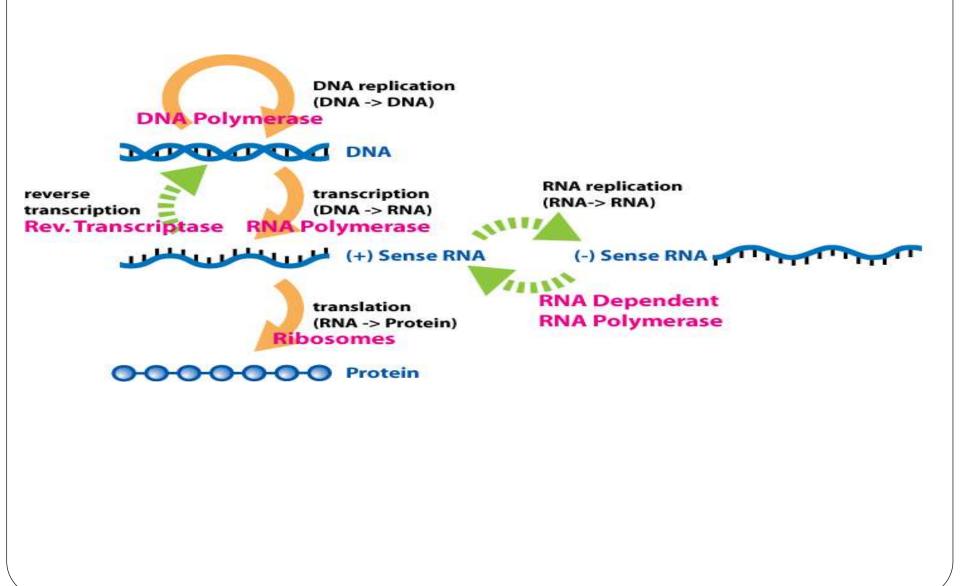


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- 2. Characteristics of the genetic code.
- 3. Wobbles hypothesis.
- 4. Codon bias.

Central dogma of molecular biology



WHAT IS GENETIC CODE?

		<u>.</u>		Secor	nd Letter	ю ,	r		i i	
	_	U		C		A	0	•		_
	U	UUU Ph UUC UUA Let	UCC	Ser	UAU UAC UAA UAG	Tyr Stop Stop	UGU UGC UGA UGG	Cys Stop Trp	U C A G	
st	c	CUU CUC CUA CUG	U CCU CCC CCA CCG	Pro	CAU CAC CAA CAG	His Gln	CGU CGC CGA CGG	Arg	U C A G	31
tter	A	AUU AUC AUA AUG Me	ACA	Thr	AAU AAC AAA AAG	Asn Lys	AGU AGC AGA AGG	Ser Arg	U C A G	le
	G	GUU GUC GUA GUG	GCU GCC GCA GCG	Ala	GAU GAC GAA GAG	Asp Glu	GGU GGC GGA GGG	Gly	UCAG	

- The collection of base sequences(codons) that correspond to each **AMINO ACID** and to TRANSLATION SIGNALS.
- The genetic code is highly similar among all organisms and can be expressed in a simple table with 64 entries.
- The code defines how sequences of nucleotide triplets, called codons, specify which amino acid will be added next during protein synthesis. A threenucleotide codon in a nucleic acid sequence that specifies a single amino acid.

The first CLUE



The Nirenberg and Matthaei experiment was a scientific experiment performed in 1961, by <u>Marshall W. Nirenberg</u> and his post doctoral fellow, <u>J. Heinrich</u> <u>Matthaei</u>. The experiment deciphered the first of the 64 triplet codons in the <u>genetic code</u> by using <u>nucleic</u> <u>acid homopolymers</u> to translate specific <u>amino acids</u>.

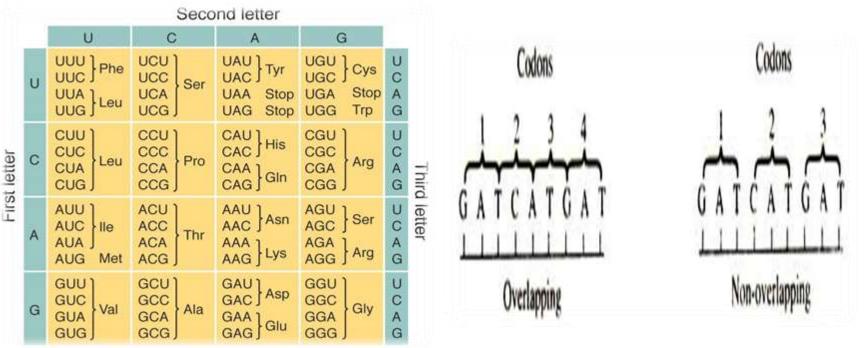
PROPERTIES OF THE GENETIC CODE

<u>1. The code is a triplet codon:</u>

The nucleotides of mRNA are arranged as a linear sequence of codons, each codon consisting of three successive nitrogenous bases, i.e., the code is a triplet codon.

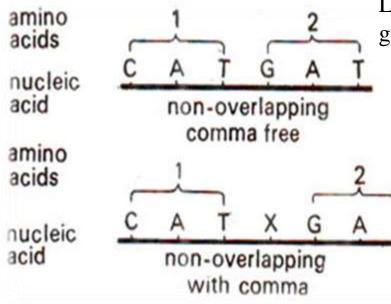
2. The code is non-overlapping:

In translating mRNA molecules the codons do not overlap but are "read" sequentially. Thus, a non-overlapping code means that a base in a mRNA is not used for different codons.



<u>3. The Genetic Code is</u> <u>'commaless':</u>

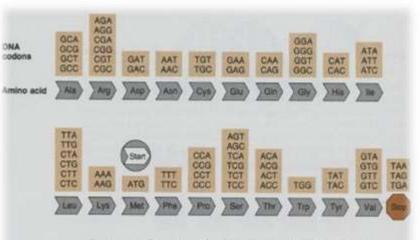
It means that after one amino acid is coded, the second amino acid will be automatically, coded by the next three letters and that no letters are wasted as punctuation marks.

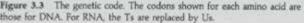


4. The code is non-ambiguous:

Non-ambiguous code means that a particular codon will always code for the same amino acid. Generally, as a rule, the same codon shall never code for two different amino acids.

However, there are some reported exceptions to this rule: the codons AUG and GUG both may code for methionine as initiating or starting codon, although GUG is meant for valine. Likewise, GGA codon codes for two amino acids glycine and glutamic acid.





5. The code has polarity:

The code is always read in a fixed direction, i.e., in the 5' \rightarrow 3' direction. In other words, the codon has a polarity. If the code is read in opposite directions, it would specify two different proteins, since the codon would have reversed base sequence.

Codon :	UUG	AUC	GUC	UCG	CCA	ACA	AGG
Polypeptid	e:→Leu	lle	Val	Ser	Prof	Thr	Arg
	Val	Leu	Leu	Ala	Thr	Thr	Gly←

	U	Second No C	A A	G
U	UUU Phenylalanine	UCU Serine	UAU Tyrosine	UGU Cysteine
	UUC Phenylalanine	UCC Serine	UAC Tyrosine	UGC Cysteine
Ŭ	UUA Leucine	UCA Serine	UAA STOP	UGA STOP
	UUG Leucine	UCG Serine	UAG STOP	UGG Tryptophan
c	CUU Leucine	CCU Proline	CAU Histidine	CGU Arginine
	CUC Leucine	CCC Proline	CAC Histidine	CGC Arginine
	CUA Leucine	CCA Proline	CAA Glutamine	CGA Arginine
	CUG Leucine	CCG Proline	CAG Glutamine	CGG Arginine
A	AUU Isoleucine	ACU Threonine	AAU Asparagine	AGU Serine
	AUC Isoleucine	ACC Threonine	AAC Asparagine	AGC Serine
	AUA Isoleucine	ACA Threonine	AAA Lysine	AGA Arginine
	AUG Methionine	ACG Threonine	AAG Lysine	AGG Arginine
G	GUU Valine	GCU Alanine	GAU Aspartate	GGU Glycine
	GUC Valine	GCC Alanine	GAC Aspartate	GGC Glycine
	GUA Valine	GCA Alanine	GAA Glutamate	GGA Glycine
	GUG Valine	GCG Alanine	GAG Glutamate	GGG Glycine

6. The code is degenerate:

More than one codon may specify the same amino acid; this is called degeneracy of the code.

• The amino acids Tryptophan and Methionine have one codon each coding for them (UGG & AUG).

• Nine amino acids namely, Phenylalanine, Tyrosine, Histidine, Glutamine, Asparagine, Lysine, Aspartic acid, Glutamic acid and Cysteine and 2 codons each coding for them.

• Isoleucine has 3 codons coding for it.

• Five amino acids namely Valine, Proline, Threonine, Alanine and Glycine have 4 codons each coding for them.

• Three amino acids, namely Leucine, Arginine and Serine, have 6 codons each.

7. Some codes act as start codons:

In most organisms, AUG codon is the start or initiation codon, i.e., the polypeptide chain starts either with methionine (eukaryotes) or Nformylmethionine (prokaryotes). Methionyl or N-formylmethionyltRNA specifically binds to the initiation site of mRNA containing the AUG initiation codon. In rare cases, GUG also serves as the initiation codon, e.g., bacterial protein synthesis. Normally, GUG codes for valine, but when normal AUG codon is lost by deletion, only then GUG is used as initiation codon

Start RNA Stop ACCA AUG-AUA-GCC-GAU-GGG UCA-GGAG Met -Ile -Ala-Asp-Gly protein

The start codon is AUG and it also codes for Methionine There are three stop codons UGA, UAA, UAG



8. Some codes act as stop codons:

• Three codons UAG(amber), UAA(ochre) and UGA(opal) are the chain stop or termination codons. They do not code for any of the amino acids.

These codons are not read by any tRNA molecules (via their anticodons), but are read by some specific proteins, called release factors (e.g., RF-1, RF-2, RF-3 in prokaryotes and RF in eukaryotes). These codons are also called nonsense codons, since they do not specify any amino acid.
The UAG was the first termination codon to be discovered by Sidney Brenner (1965).

9. The code is universal:

• Same genetic code is found valid for all organisms ranging from bacteria to man.

• But recently, some differences have been discovered between the universal genetic code and mitochondrial genetic code.

Codon	Usual Use	Alternate Use	Where Alternate Use Occurs
AGA	Arg	Stop, Ser	Some animal mitochondria, some
AGG			ptorozoans
AUA	Ile	Met	Mitochondria
CGG	Arg	Trp	Plant mitochondria
CUU	Leu	Thr	Yeast mitochondria
CUC			
CUA			
CUG			
AUU	Ile	Start(N-f Met)	Some prokaryotes ^a
CUG	Val		5 X2
UUG	Leu		
UAA	Stop	Glu	Some protozoans
UAG	100000		
UGA	Stop	Trp	Mitochondria, mycoplasmas
		Selenocysteine	E.coli*

Wobbles Hypothesis

- In 1965, Dr. F.H.C. Crick proposed a hypothesis called wobbles hypothesis to explain the phenomenon of the same transfer-RNA recognizing more than one codons.
- The third base of the codon is not so specific in its base pairing and may wooble(loosly pair).
- He discovered that if U is present at the first position of the anticodon, it can pair with either A or G, respectively, in the third position of the codon .similarly G at the 1st position of the anticodon could pair with C or U.
- Inosine can pair with either A,U or C.

ANTICODON-CODON BASE-PAIRING RULES

Base at first position (5' end) of tRNA	Base at third position (3' end) of mRNA	
A	U	
A C G	G	
G	C or U	
U	A or G	
1	A, U, or C	
5'	3 2 1 tRNA 3'	

1. Codon usage bias refers to differences in the frequency of occurrence

of <u>synonymous</u> <u>codons</u> in coding DNA. A codon is a series of three <u>nucleotides</u> (a triplet) that <u>encodes</u> a specific <u>amino acid</u> residue in a <u>polypeptide</u> chain or for the termination of translation (<u>stop</u> <u>codons</u>).

2. There are 64 different codons (61 codons encoding for amino acids plus 3 stop codons) but only 20 different translated amino acids. The overabundance in the number of codons allows many amino acids to be encoded by more than one codon. Because of such redundancy it is said that the genetic code is degenerate. The genetic codes of different organisms are often biased towards using one of the several codons that encode the same amino acid over the others-that is, a greater frequency of one will be found than expected by chance.

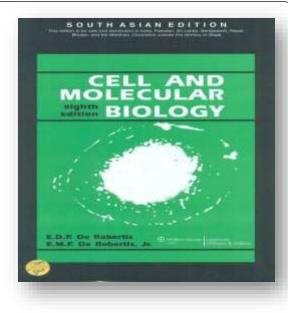
CODON BIAS

Codon for	E. coli	Yeast	Euglena chloroplas	
Arginine (6)*	CGC	AGA	CGU/CGC/AGA	
Leucine (6)	CUG	UUG	UUA/UUG/CUU	
Serine (6)	UCU/UCC/AGC	UCU/UCC	UCU/UCA/AGU	
Proline (4)	CCG	CCA	CCU/CCA	
Tyrosine (4)	UAC	UAC	UAU/UAC	
Lysine (2)	AAA	AAG	AAA	



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