basic education

Department:
Basic Education
REPUBLIC OF SOUTH AFRICA

DNA STRUCTURE AND FUNCTION

PROTEIN SYNTHESIS

SELF STUDY GUIDE

GRADE 12

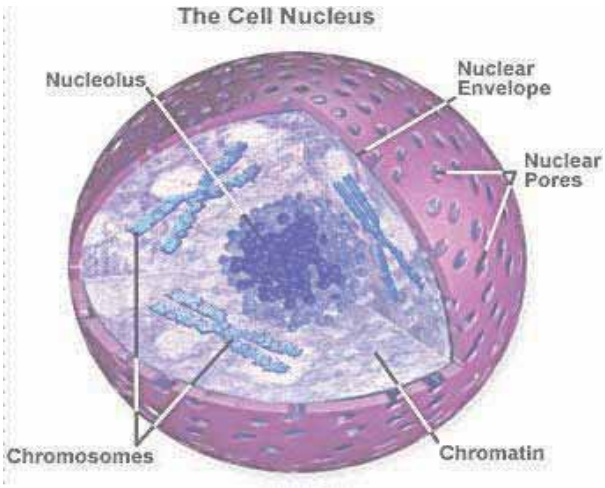
Exploring inside the cell

Before teaching learners about DNA & RNA, revise the structure of a cell (Grade 10 content) and in particular the structure of the nucleus and the position of ribosomes in the cytoplasm. Learners start with a familiar larger structure and then look at progressively smaller structures i.e.

nucleus ⟶ chromosomes ⟶ DNA ⟶ genes

The Nucleus

The nucleus is the most conspicuous organelle in all eukaryotic cells. The nucleus stores all the genetic information in the genes of the chromosomes. It is the CEO of the cell directing all the functions for life and, in addition prepares the cell for growth and replication.



The nucleus
(http://universe-review.ca/I10-04-cellnucleus.jpg)

How is the nucleus constructed?

1. Location and shape in animal cells: rounded and in the centre of the cell

2. Location and shape in plant cells: lens shaped and pushed to the side of the cell by the vacuole.
3. Nuclear membrane or envelope – surrounds the nuclear contents and is a double membrane.
4. Nuclear pores – many and control the passage of molecules and structures into and out of the nucleus.
5. Nucleoplasm – the 'cytoplasm' of the nucleus.
6. Nucleolus – this is an extra dense area of DNA and protein where the ribosomes (rRNA is synthesized) are produced.
7. Chromatin – is made up of DNA (a nucleic acid) and proteins called histones. When the cell is about to divide the chromatin condenses into separate chromosomes.

Points to ponder:

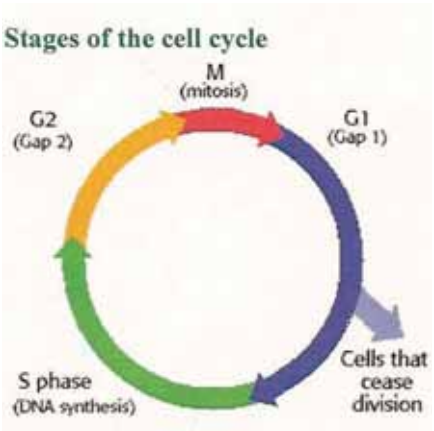
* Suggest how you could model the eukaryotic cell nucleus.

* Consider – Could you draw up a table of the structures related to their function in terms of a factory?

The cell cycle, chromatin, chromosomes and DNA

Cells pass through a cell cycle consisting of mitosis (cell division) and interphase (phase between divisions).

In higher organisms, most actively dividing cells take 18 to 24 hours to complete the cell cycle. During this cell cycle, mitosis is completed in ½ to 2 hours. Most of the time is spent in interphase.



http://www.biology.arizona.edu/cell_BIO/tutorials/cell_cycle/cells2.html

Interphase consists of G1, S and G2 stages.

(It's not necessary for learners to remember these terms but they should understand what is happening to the DNA)

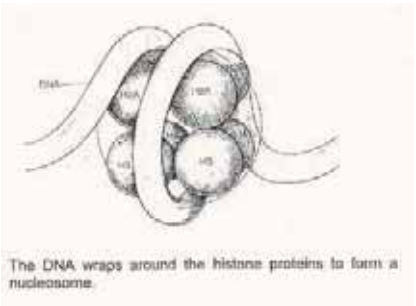
G1 phase: before DNA replication

After mitosis, the cells grow, may differentiate and there is intense metabolic activity. The DNA is active, mRNA is produced and protein synthesis takes place.

- Actively dividing cells e.g. the cells in a developing embryo and meristematic cells in plants, spend hours in this phase before moving to the next phase of DNA replication.
- Some cells mature, specialise and continue to be metabolically active but do not continue with DNA replication, the G2 phase and cell division. As they mature, they lose their ability to divide e.g. red blood cells, muscle cells and nerve cells.
- Some cells, once they mature and specialise, divide only occasionally e.g. cortex cells in plant stems. They may spend years in this phase and only reenter the cell cycle when stimulated.

In all human cells (except the sex cells & rbc's), the chromatin consists of 46 chromosomes. Each chromosome consists of a long ribbon-like structure, the DNA (double helix), wrapped around histone molecules.

(Nucleosome – a group of histone molecules with DNA wrapped around it).



(C. Still; Wits Univ.)

http://www.biology.arizona.edu/cell_BIO/tutorials/cell_cycle/cells1.html

S1 phase: DNA replication

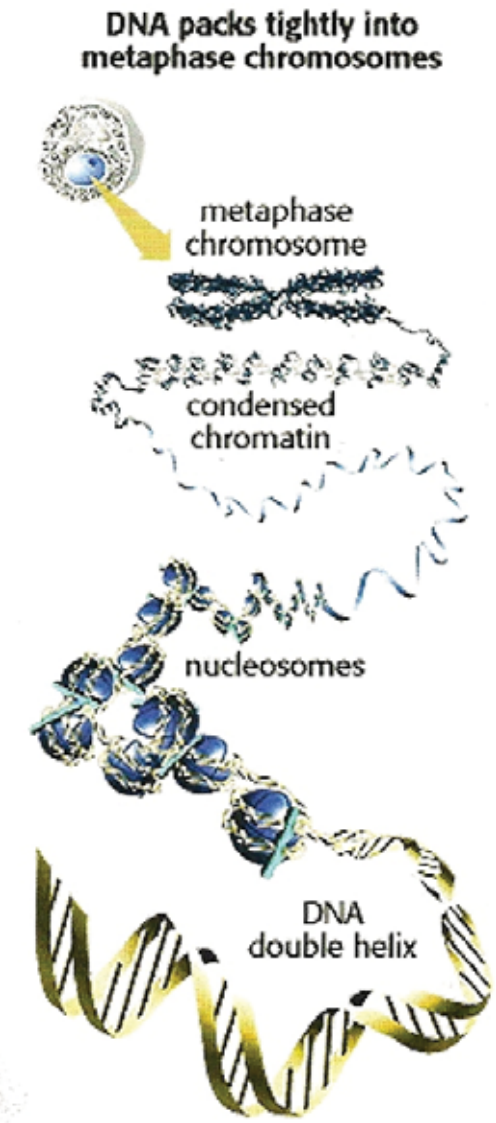
Each of the 46 DNA strands makes a copy of itself, so that there are now two strands of DNA (2 double helices), each wrapped around histones. The two strands are held together at the centromere. The double structure is a chromosome and each strand is called a chromatid.

G2 phase: after DNA replication:

The cells continue to grow, synthesise proteins and undergo other metabolic activity. The cell begins to prepare for mitosis.

At the start of mitosis, the chromatids making up each chromosome prepare for mitosis by condensing and becoming very folded and coiled so that at the start of mitosis the chromosomes look short and thick and one can see the two chromatids held together at the centromere.

If you place the 46 chromosomes end-to-end, the length of the DNA in those chromosomes in one cell is almost 2metres.
Imagine trying to pack this DNA into one microscopic nucleus!



http://www.biology.arizona.edu/cell_BIO/tutorials/cell_cycle/cells1.html

Learners often find it difficult to understand how DNA is packaged inside the chromosome. The following series of diagrams illustrates that packaging. (nm = nanometres).

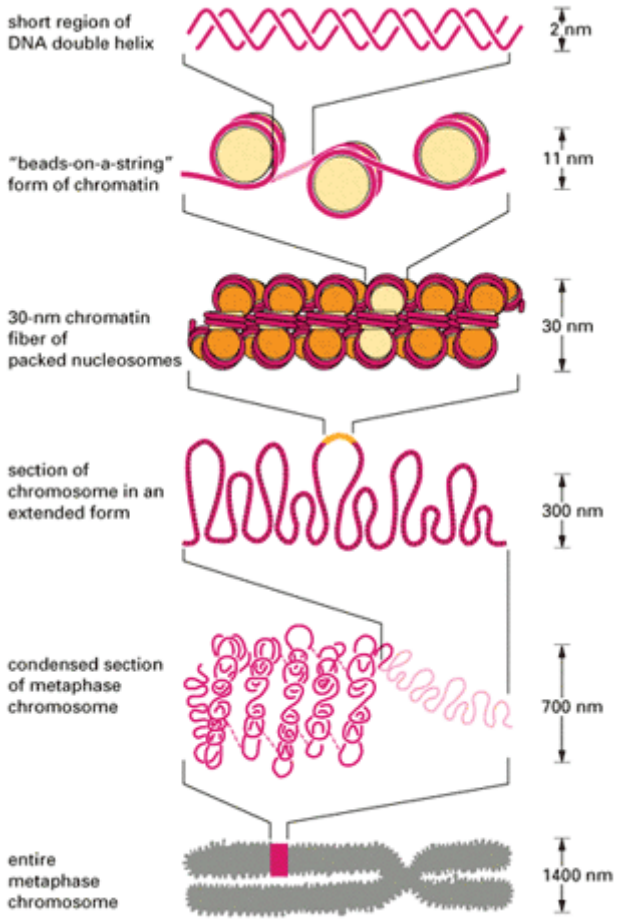


Fig X: Levels of DNA packaging

(http://library.thinkquest.org/C004535/media/chromosome_packing.gif)

Activity 1 A simple model of DNA packaging

Take the material (string and presstick) out of the packet labeled Activity 1.

1. Take the two pieces of string and twist them around one another to represent a DNA double helix (or use two stranded string)

2. Roll the presstick into ten balls of equal size. These are the 'nucleosomes' made up of 'histones'.

3. Now wind your 'DNA' twice around each of the ten 'nucleosomes' .
4. Bend your strand backwards and forwards (2nd diagram from bottom) to create a simplified version of a thick chromatid.
5. Join your chromatid together with another group's chromatid using presstick as the centromere. You now have a 'chromosome'!
(Alternatively, untwist (unzip) and separate your string, add on complementary strings, and join them by a centromere.)

Deciphering the Three Dimensional Structure of DNA – a brief history

Let us begin in 1856:

Gregor Mendel was an Austrian monk. He worked in the small monastery garden with pea plants and did a series of experiments hybridizing pea plants. The results of Mendel's crosses allowed him to conclude from the consistent ratios he obtained that plants transmitted 'elementen' or discrete units. Mendel did not know that his 'elementen' were found on chromosomes and were in fact renamed *genes* in 1909.

1930's – 1940's

It was found by various researchers between these years that DNA, a nucleic acid, is the biochemical responsible for transmitting traits. In 1928 Frederick Griffith contributed to the initial understanding that DNA was the genetic material. He found that genetic information can be transferred from heat-killed bacteria to live bacteria. This process, known as transformation, was the first clue that genetic information is a heat-stable compound. Then in 1944 the Avery and Hershey-Chase Experiments clearly showed that the active principle for transforming a bacterium called *Streptococcus* is DNA. Their evidence confirmed that DNA is the hereditary material. This led to questions regarding the molecular nature of DNA.

Then in 1949 and early 1950's

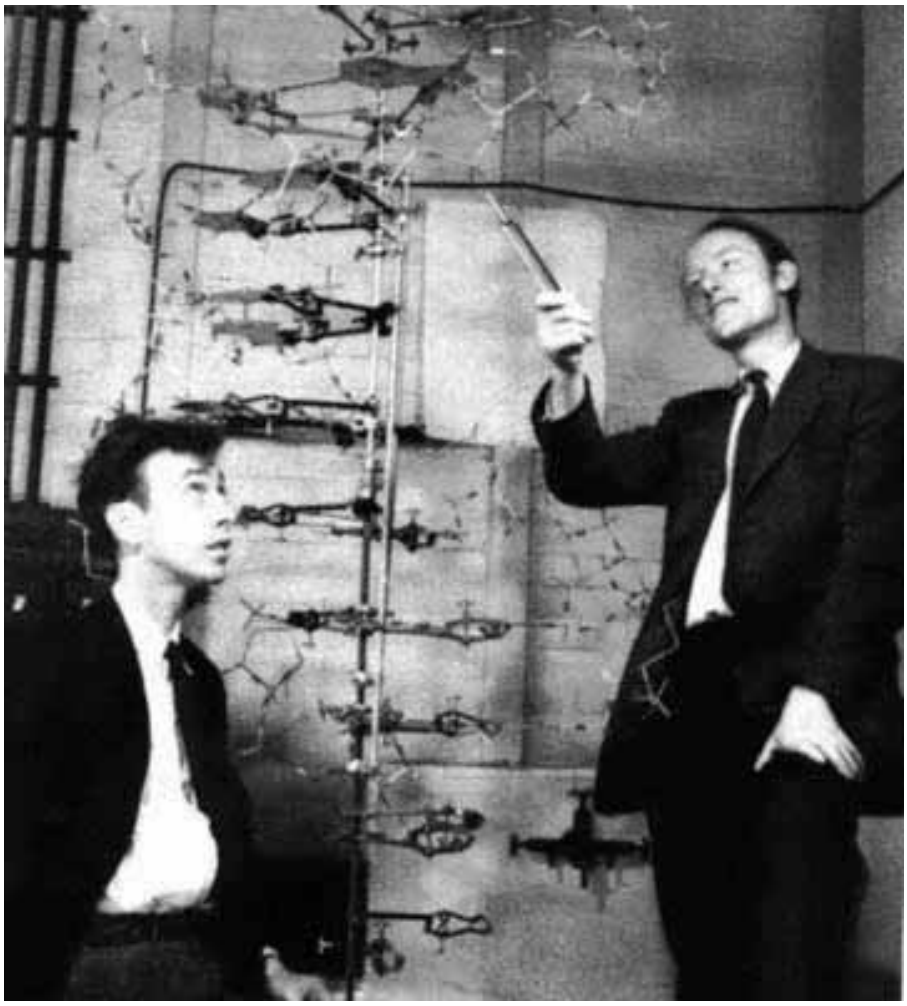
Erwin Chargaff, a biochemist, showed that DNA contains equal amounts of the bases adenine (A) and thymine(T) and equal amounts of the bases cytosine (C) and

guanine(G). He also showed that the DNA composition varies from one species to another, that is, it is species specific.

Morris Wilkins and Rosalind Franklin, a physicist and chemist respectively, showed by using X-ray diffraction a pattern of regularly repeating nucleotides. This was the first clue to the three-dimensional structure of DNA.

Finally in 1953

James Watson, an American biochemist and Francis Crick an English physicist began their collaborative work to try to solve the puzzle of the molecular structure of DNA. Using data provided by Maurice Wilkins and Rosalind Franklin, they made an accurate model of the molecular structure of DNA. This discovery they called 'the secret of life'. In 1962 Crick, Watson and Wilkins received the Nobel Prize for determining the molecular structure of DNA – a double-stranded, helical, complementary, anti-parallel model for deoxyribonucleic acid.



"The Secret of Life"

(http:www.odec.ca/projects/2007/knig7d2/images/WatsonCrick.jpg)

CSStill (2009)

DNA structure

Activity 2

1. Did Watson and Crick use 'the scientific method' to decipher the structure of DNA and construct their model? Justify your answer.

- Discuss in your group.
- Ask one person to give feedback.

2. What did Watson & Crick discover? What do we now know?

a. In pairs, brainstorm the topic 'DNA structure' and in any order write down as many important terms or phrases that you believe relate to the detailed structure of DNA.

You might include some of the following terms in your list:

<u>Structure</u>
Ladder-like
Double helix
Anti-parallel
5′end (containing a phosphate group)
3′end (containing a hydroxyl (-OH) group)

<u>Monomers of DNA</u>
Nucleotides
Sugar = deoxyribose
Phosphate molecule
Nitrogen bases
Purine – adenine & guanine
Pyrimidines – cytosine & thymine

<u>Make-up of DNA helix</u>
2 outer strands
Phosphate sugar link
Backbone
Rungs of ladder
Pairs of bases
Weak hydrogen bonds
Complementary base pairing
A only pairs with T
C only pairs with G

<u>Types of bonds</u>
Covalent bonds, phosphor-diester (sugar-phospate) bonds
Hydrogen bonds
2 hydrogen bonds between A & T
3 hydrogen bonds between C & G

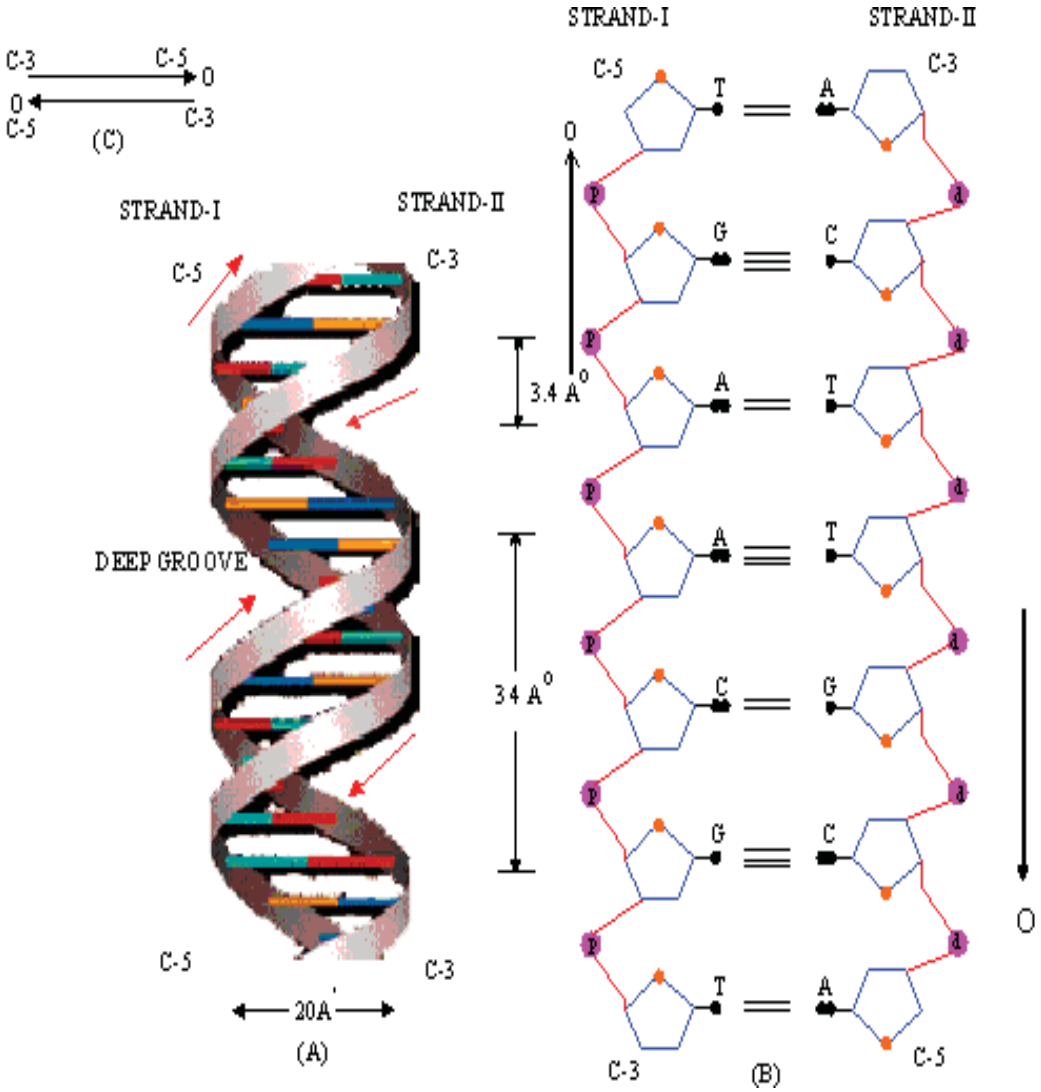


Fig X: The Structure of DNA

(http://pinkmonkey.com/studyguides/subjects/biology-edited/chap8/b0808202.asp)

b. Which terms are essential for matric learners to remember?

DNA, a nucleic acid and nucleotides

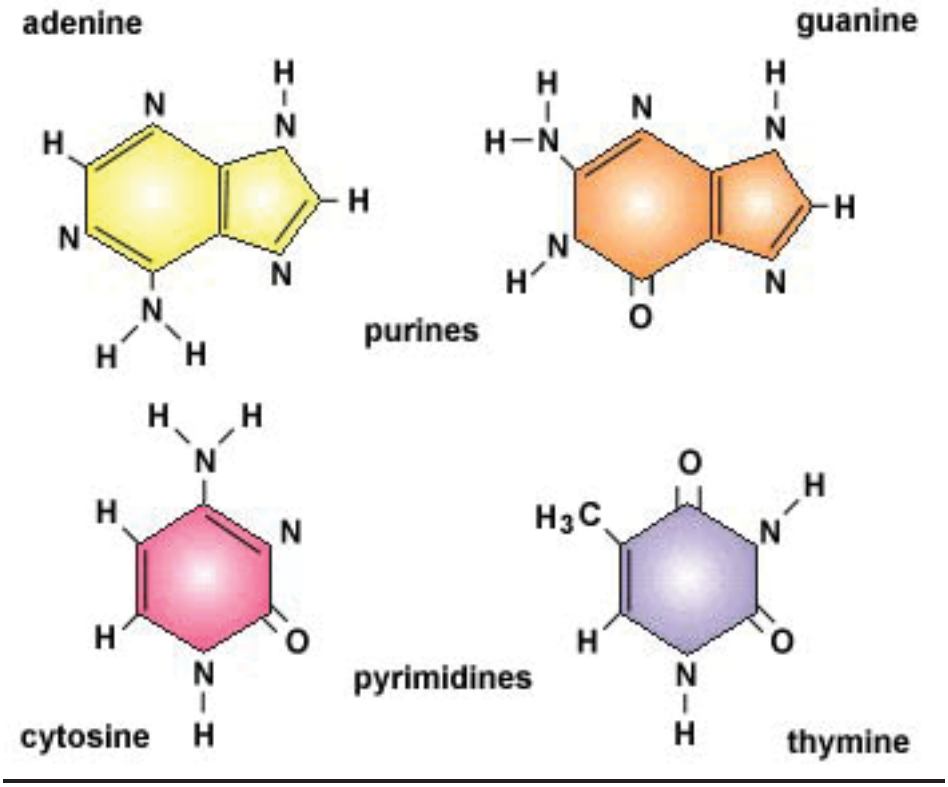
What do learners need to know?

DNA is a nucleic acid made up of two strands, wound around one another to form a double helix. Each DNA strand is made up of nucleotides.

1. Each DNA nucleotide consists of:
    - deoxyribose sugar
    - phosphate
    - nitrogenous base (adenine, thymine, guanine or cytosine)
2. Nucleotides join to each other by **sugar-phosphate bonds** between the **phosphate** of one nucleotide and the **deoxyribose sugar** of the next nucleotide. Many nucleotides join to form a single DNA strand.
3. The two strands are connected by weak **hydrogen bonds** between complementary nitrogenous bases.

    adenine always bonds with **thymine**

    guanine always bonds with **cytosine**



(http://www.uic.edu/classes/bios/bios100/lecturesf04am/nucleotides.jpg)

Learners don't need to know the structures of these molecules but it might be useful to show them diagrams on a chart/ OHT etc so they understand why different shapes are used to represent these nitrogenous bases.
They also don't need to remember how many hydrogen bonds link A to T, & C to G.

Some concepts and statistics:

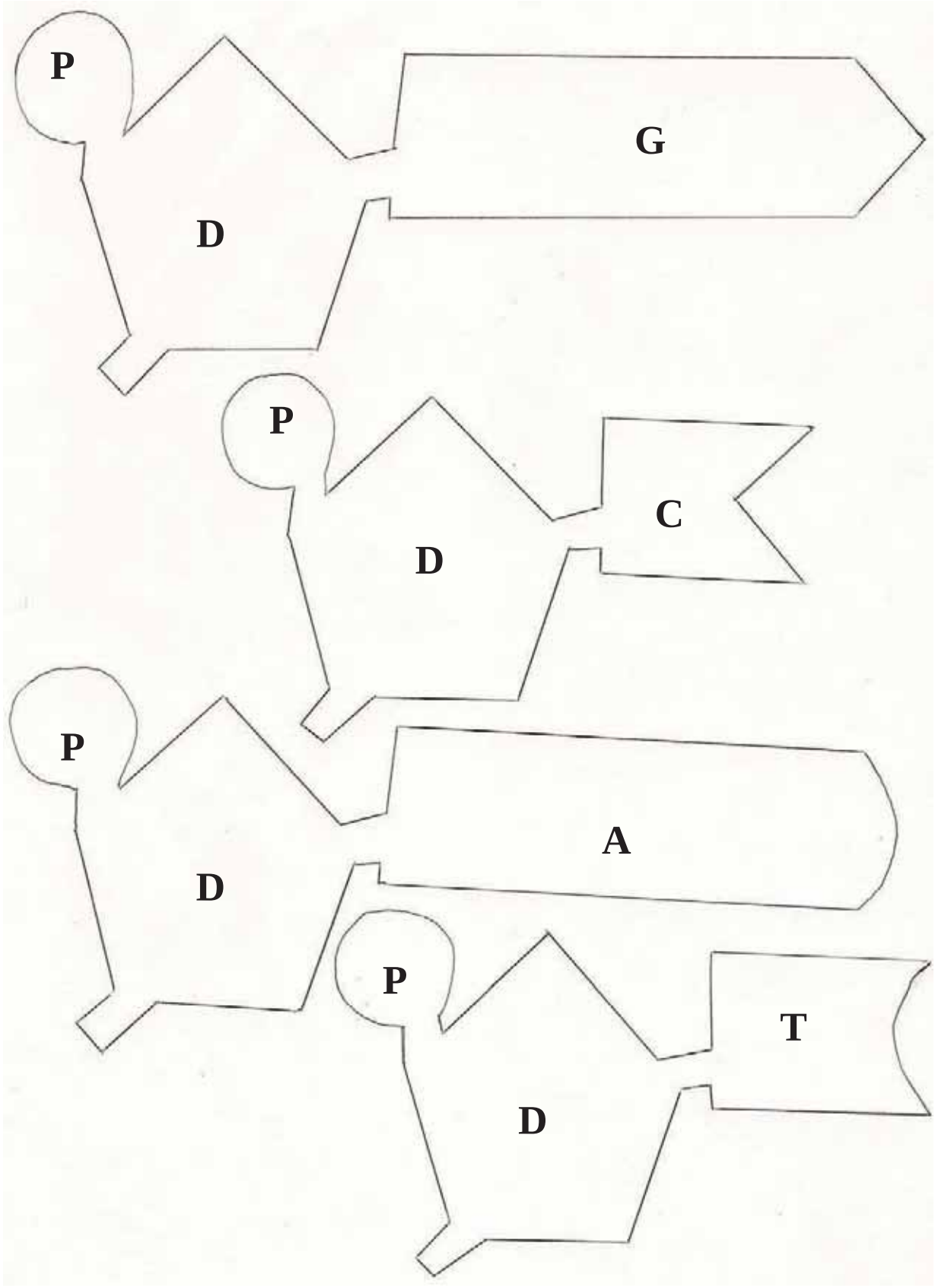
- the human genome is all the DNA in an organism including its genes
- the human genome is made up of just over 3 billion pairs of bases
- each chromosome has 50 million – 250 million base pairs
- each gene is a section of DNA with a specific sequence of bases that acts as the 'instructions' or code for the production of a specific protein.
- the human genome has 20 000-25 000 genes
- the average gene has about 3000 bases
- the genes make up only 2%* of the human genome; the rest of the DNA is made up of non-coding regions, some of which regulate chromosomal structure and where, when and in what quantity proteins are made. The function of 50% of the DNA, made up of repeated sequences and known as 'junk DNA', is not known.
- chromosome 1 has the most genes i.e. 2968, whilst the Y chromosomes has the fewest i.e. 231.

http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml
(*5% according to Dr Carolyn Hancock)

Activity 3: DNA models

Model 1: Cardboard models

Use any simple models of nucleotides such as the ones on the next page to construct a 'DNA molecule'.
You can print the diagrams onto thin cardboard or onto paper which you stick onto cardboard, or you can trace the outline onto different colour cardboard.
Put presstick on the back of each nucleotide and let learners construct the molecule on a wall or the board (or in groups).
Alternatively use cellotape as 'hydrogen' and 'sugar-phosphate' bonds, connecting the nucleotides. Twist your helix and suspend it from the ceiling of your classroom.



Cardboard cutout models: C. Still

Model 2: Cardboard models (more detail, free-standing 3D model)

(C. Still)

Make a model of a DNA molecule using:-

- A stand or base
- A dowel rod/stick
- 2 outer phosphate strands
- Bases that form the rungs of the ladder, A, T, C and G.
- Spacers

Make copies of the next 3 pages. (2 copies each of cytosine- guanine and adenine – thymine; 1 copy of S-P)

1. Remove the pages of base pairs and paste them on a piece of stiff cardboard.
2. Cut each base pair along the dark border. You should have a total of 20 base pairs.
3. Use a crayon or marker pen and colour each of the bases using a suitable colour scheme eg cytosine – red; thymine - blue; adenine – green; guanine – orange.
4. Use a punch or cork borer (or any suitable instrument) to remove the circle in the centre of the base pairs. Stack the base pairs so that all the base names are facing in the same direction.
5. Cut out the nine strips of paper containing the diagrams of the phosphate molecules.
6. Using a razor blade, cut along each dotted line to make a slit in the paper band.
7. Tape each strip to the end of another strip with just enough overlap to keep the slits evenly spaced.

and then.....(PTO)

(Models & activity modified from Montgomery, R.J. and Elliott, W.D. (1994). Investigations in Biology, pp151-171)

1. Obtain a stand consisting of a base and a 60 cm high dowel.

2. Wrap a piece of 2.5 cm wide masking tape around the dowel 2-3 times just above the point where it joins the base.

3. Select a DNA base pair at random and slide it on the dowel through the hole in the base pair until it rests on top of the masking tape.

4. Wrap a second piece of tape above this base pair and add a second base pair on top of this tape (see Fig. 1). Continue this process until all 20 base pairs are assembled on the dowel. The 2.5 cm masking tape will keep the base pairs evenly separated.

5. Starting with the bottom base pair insert one of the tabs of the base pair into the first slot of the side chain (see Fig. 2)

6. Rotate the next base pair above to allow its tab to fit into the next slot of the side chain. Continue until the phosphate strip has been attached to one side of the model. Repeat this process on the other side of the model.

If you have assembled the model properly, it should assume the shape of a double helix.

Fig. 1 Building a model of DNA

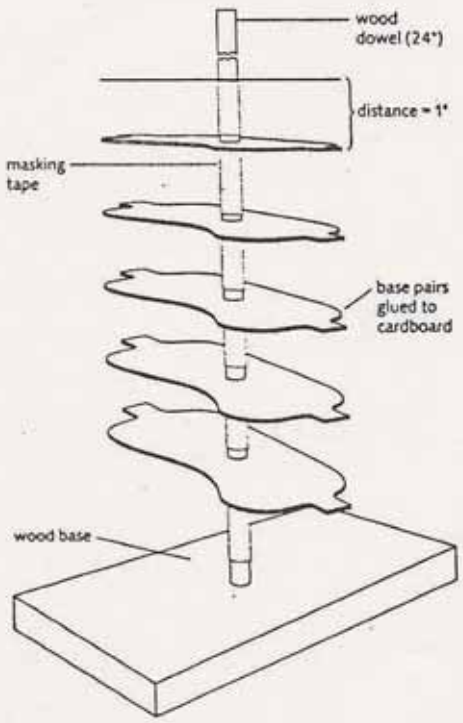
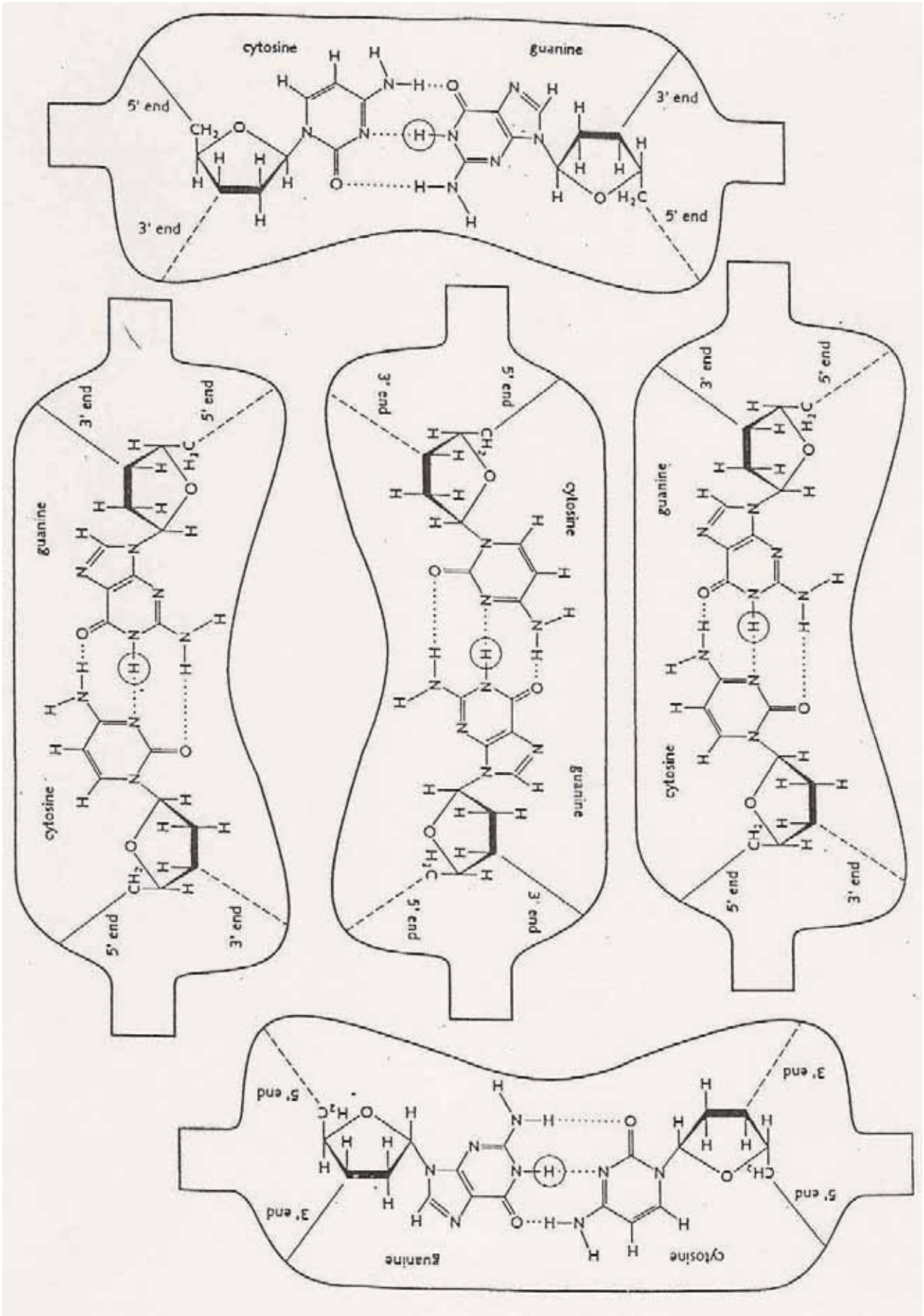


Fig. 2 DNA model close-up


cytosine
guanine
5' end
3' end
3' end
5' end
guanine
cytosine
3' end
5' end
5' end
3' end
cytosine
guanine
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guanine
cytosine
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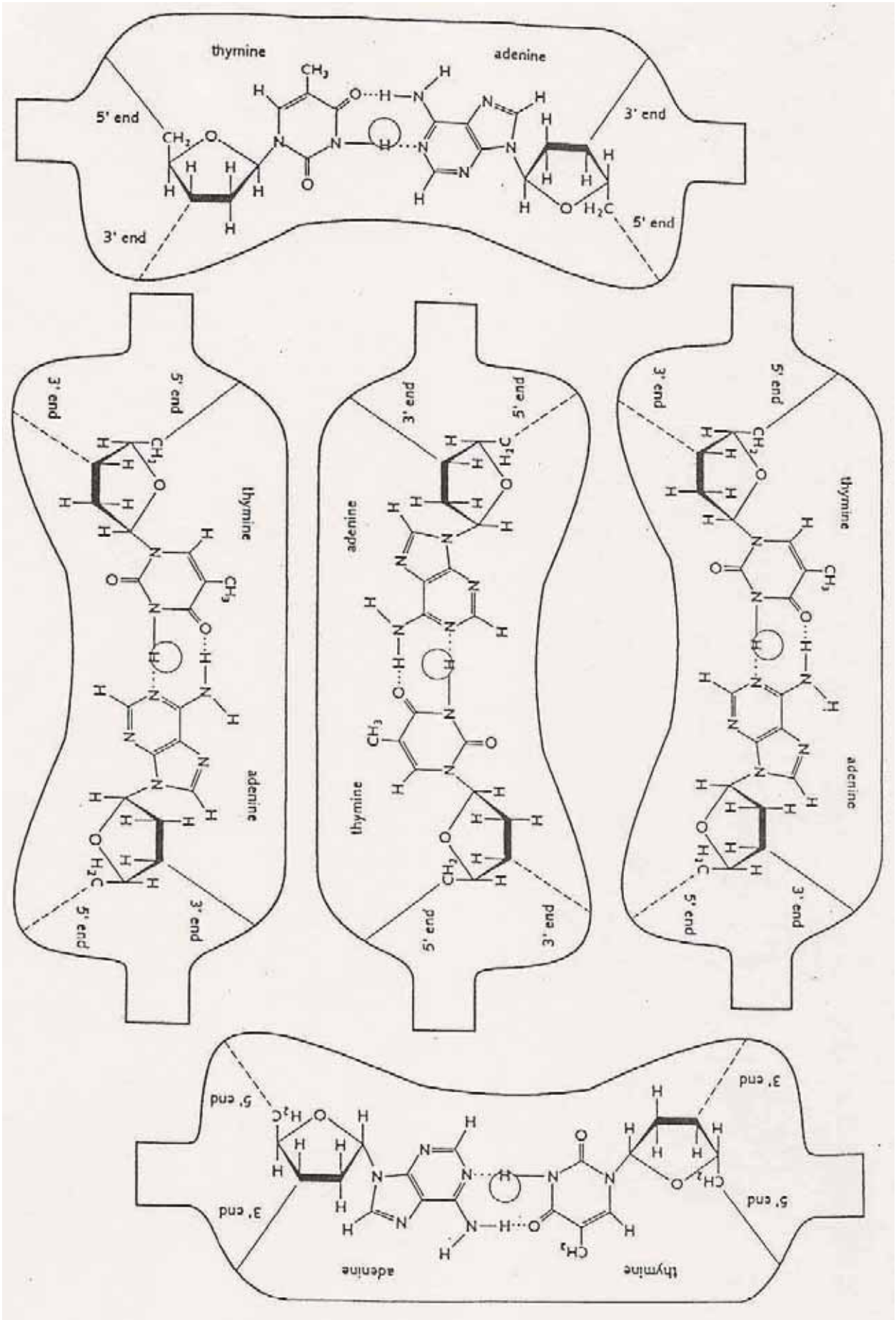
3' end
3' end
5' end
Guanine
Cytosine


thymine
adenine
5' end
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5' end
thymine
adenine
3' end
5' end
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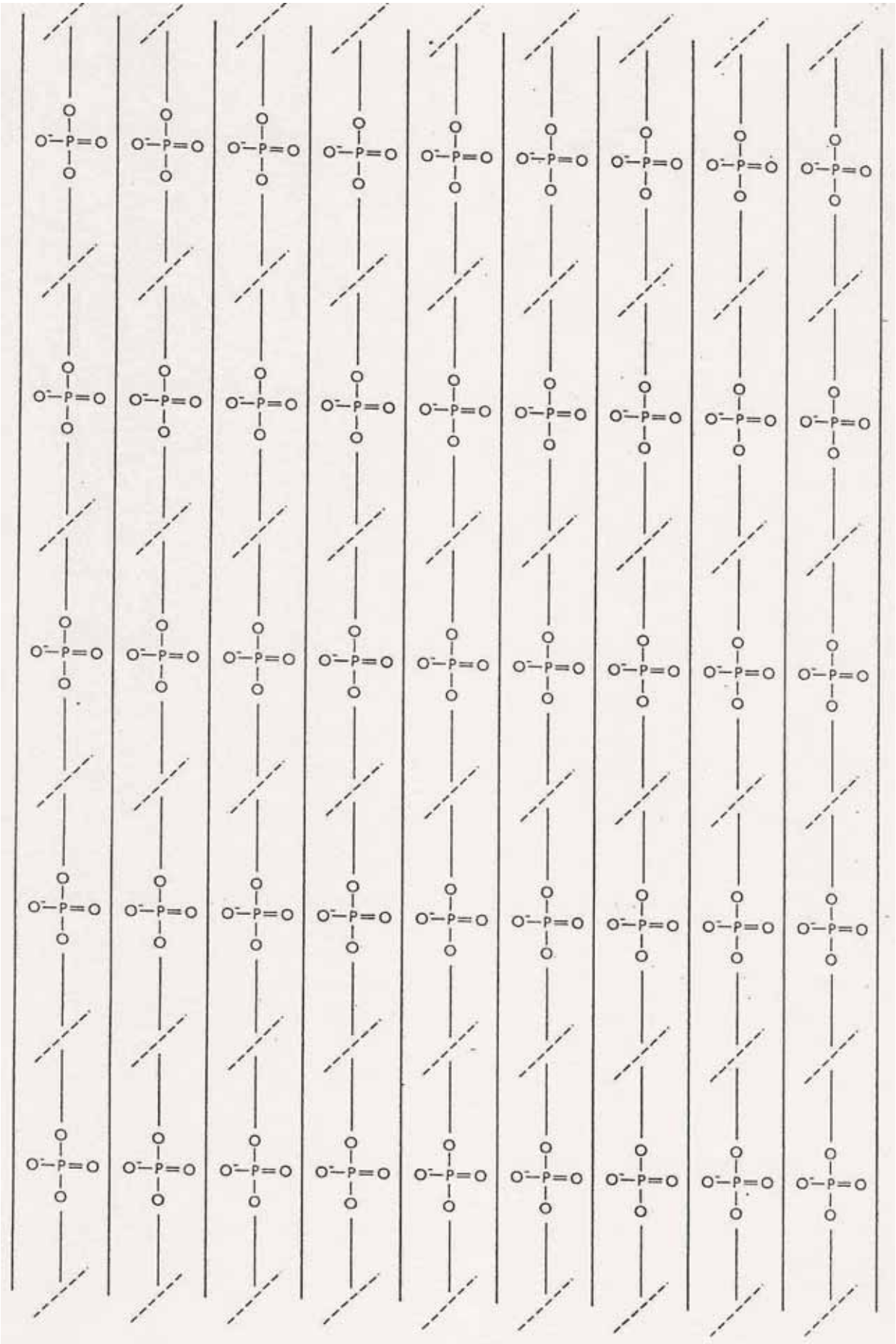
adenine
thymine



DNA Replication or DNA synthesis

When a cell is ready to divide, each DNA molecule duplicates or replicates itself, in a process we call **DNA replication**. In this way each new cell or daughter cell receives an identical DNA copy.

Both strands of DNA in the parent cell acts as a **template** for the formation of two new complementary strands.

Thus the daughter cell receives a DNA double helix, where one strand is from the original DNA and the other strand is newly formed. We term this way of replicating DNA as semi-conservative.

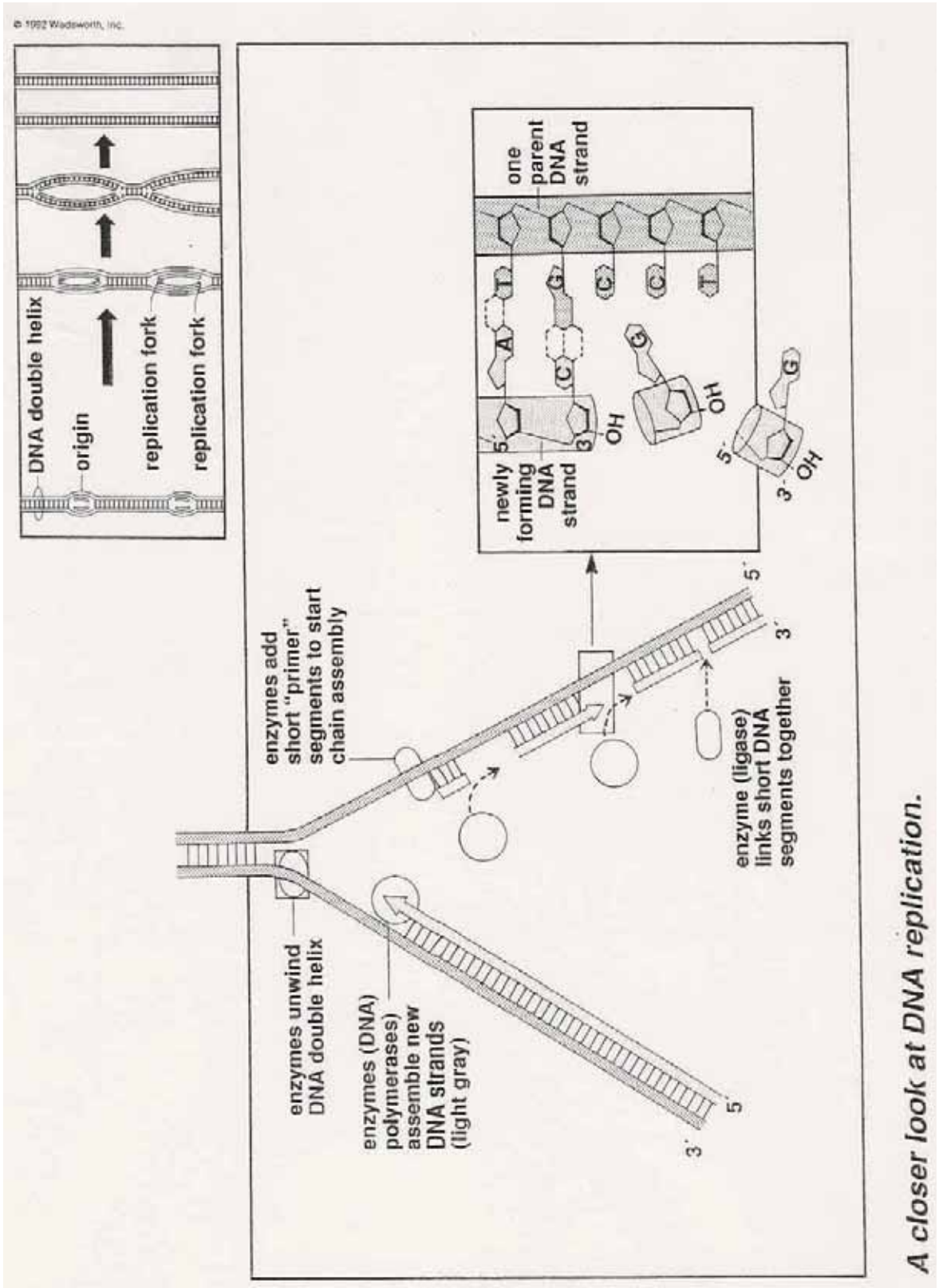
Replication requires:

- Parental double-stranded DNA known as the template
- Complex enzymes and proteins to open up the helix
- An enzyme knows as DNA polymerase
- Free nucleotides with adenine, thymine, cytosine or guanine bases.

The Replication process

1. An enzyme or protein complex opens up the two DNA strands, that is, the DNA helix unwinds.
2. Weak hydrogen bonds between A and T and C and G break, allowing the two strands to part or unzip.
3. This exposes the bases on the template strands.
4. As a result, free nucleotides can be brought in to pair in a complementary way with the template strands.
5. Adenine will pair with thymine by the formation of (two) hydrogen bonds.
6. Guanine will pair with cytosine by the formation of (three) hydrogen bonds.

The next page shows a simplified version of replication. In human chromosomes consisting of 80(-100) million base pairs, replication starts in hundreds of places. These are called replication forks. Nucleotides always attach from the 3' end of the parent nucleotide and so from their 5' end. This means that the nucleotides of one strand attach continuously (the leading strand), whilst the nucleotides in the other strand (the lagging strand) forms in sections which then join together. A series of enzymes control this process. Gradually each replication fork moves towards the next replication fork as the complementary DNA strands form, until they all join forming two separate DNA double helices. (For more detail, refer to tertiary textbooks)



A closer look at DNA replication.

This is still too much information for matric learners (conceptual overload!!!) so keep it simple as shown in this textbook diagram.
(Focus on Life Science, Grade 12, p 47)

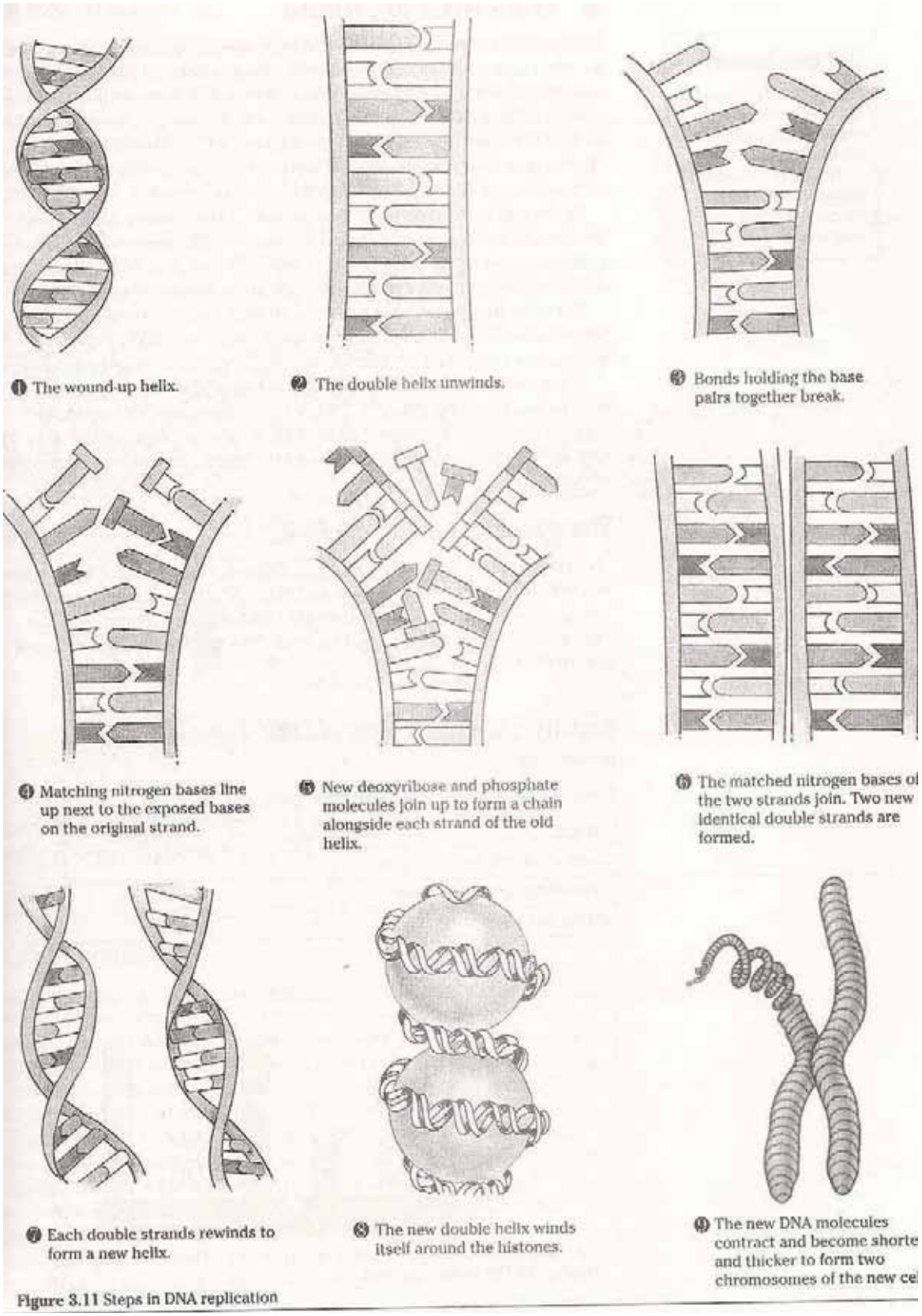


Figure 3.11 Steps in DNA replication

You can use a simple model with different coloured ribbons to illustrate how new complementary DNA strands are formed on the parent strands. (see demonstration)

Completing DNA replication

7. The two molecules twist to form a DNA double helix.
8. The resulting two molecules of DNA will contain the same sequence of bases as the parental DNA.
9. Each new double helix forms winds around groups of histones forming a chromatid. The chromatids are held together by special DNA called the centromere. The entire structure is called the chromosome

Activity 3, Model 1: Cardboard models (continued)

Use the cardboard models that have been stuck on the board or a wall, show how the hydrogen bonds break by pulling apart base pairs. Then ask the learners to bring in complementary nitrogenous bases and match them up forming two DNA double helices. This illustrates replication. Ask the class to identify any differences in the structure of the two double helices. They should be able to show that they are identical.

You could now join these two double helices or chromatids using any structure to represent a centromere.

DNA and Protein Synthesis

The central dogma of Cell Biology is

DNA makes RNA makes PROTEIN
DNA makes RNA by the process of TRANSCRIPTION
RNA makes PROTEINS in the process of TRANSLATION

DNA —*transcription*→ **RNA** —*translation*→ **protein**

DNA stores the genetic information. The DNA double helix unwinds and one strand is used to make one of the three types of RNA necessary for protein synthesis:-

rRNA – ribosomal RNA (made on DNA in the nucleolus)
mRNA – messenger RNA (made on a section of DNA in the chromosome i.e. a gene)
tRNA – transfer RNA.

This diagram shows mRNA being formed when DNA is transcribed into mRNA

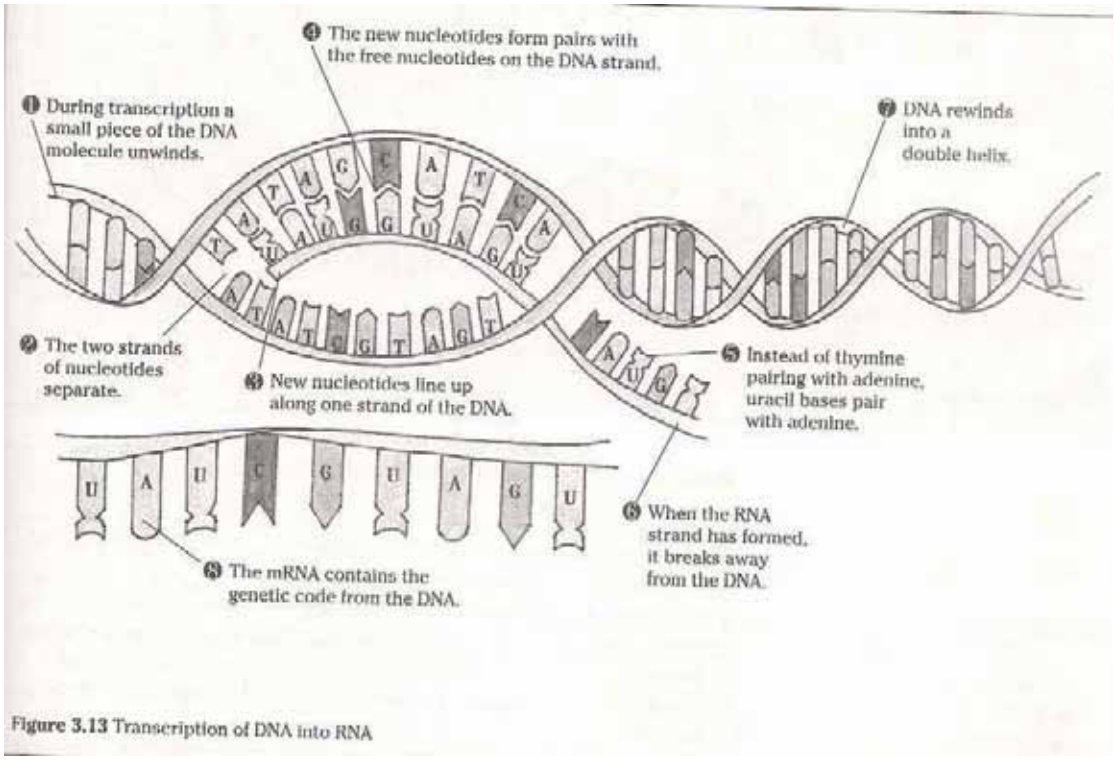


Figure 3.13 Transcription of DNA into RNA

Focus on Life Science, Grade 12, p 49

In transcription, the DNA only partly unwinds, separating along the length of DNA representing the gene. mRNA forms in this region, and then leaves and the DNA strands come together and wind up into a double helix again.

The DNA can never leave the nucleus. It thus requires a messenger to take the message out to the cytoplasm where the mRNA will be read using the ribosomes, both large and small. The message contained in the triplet codons of the mRNA specifies a particular amino acid that is available in the cytoplasm. The transfer RNA brings the amino acid to the ribosome. Here amino acids are linked by peptide bonds and gradually a protein is constructed.

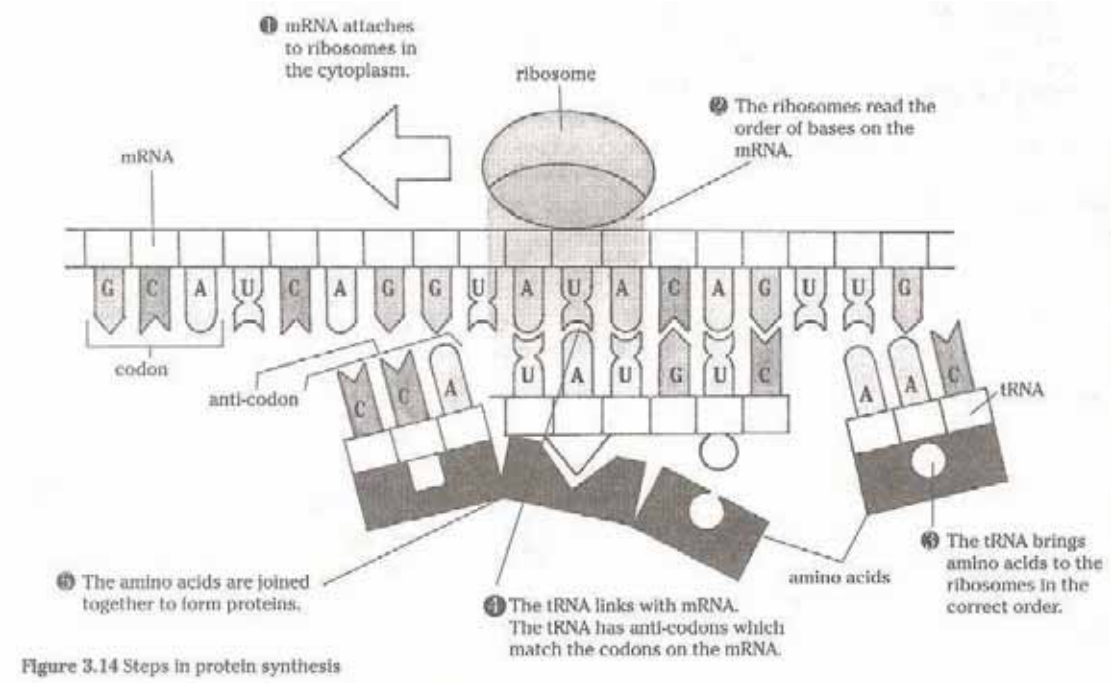
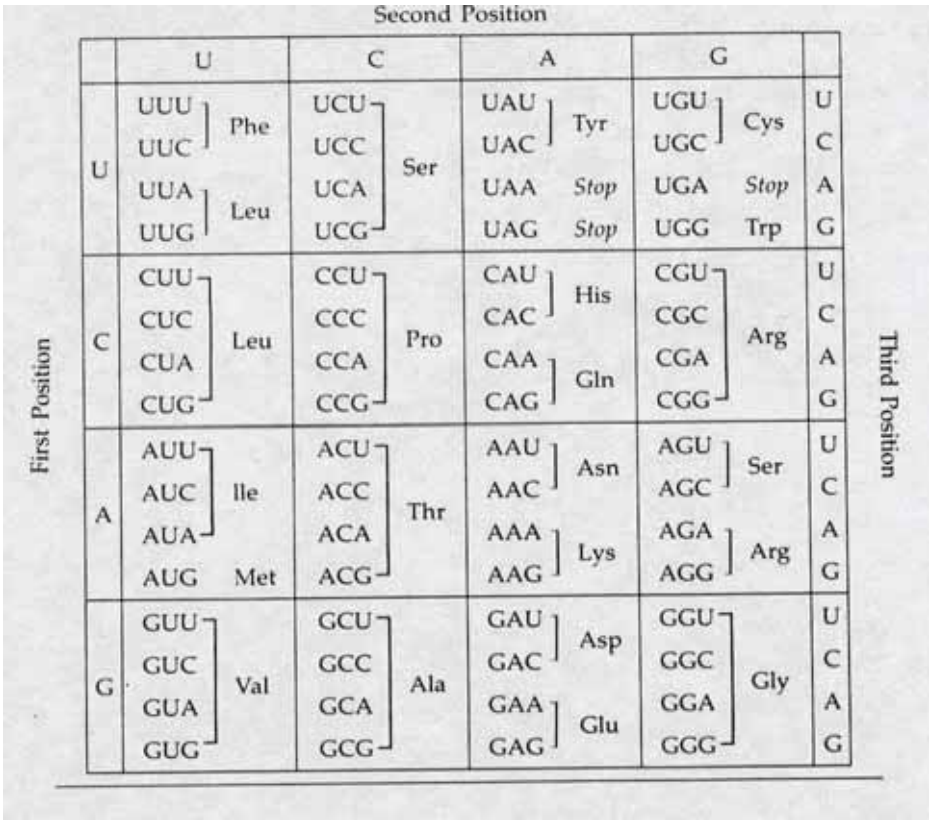


Figure 3.14 Steps in protein synthesis

Focus on Life Sciences Grade 12, p 50

A series of triplet bases specifies the amino acid and this can be ‘read off’ a genetic code chart.

Genetic code chart



First Position	Second Position: U	Second Position: C	Second Position: A	Second Position: G	Third Position
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

(http://www.cs.cmu.edu/~blmt/Seminar/SeminarMaterials/codon_table.jpg)

Activity 4:

1. Let us practice reading the 'words' that specify a particular amino acid.
Using coloured paper, crayons, prestik and scissors set up a simple diagram to show how the information in DNA is translated in a protein.

2. Fill in the corresponding bases and amino acids:

other DNA strand: ….ATGCATGACGTAACCTGA...

template DNA: ….

mRNA: ….

tRNA: ….

order of amino acids:

in protein/polypeptide:

Mutations

Mutations occur when there are changes in the nucleotide sequence of the DNA. If the mutations occur in the body cells, these mutations will not be inherited. Only mutations taking place in the cells that give rise to gametes will be inherited.
There are two types of mutations:

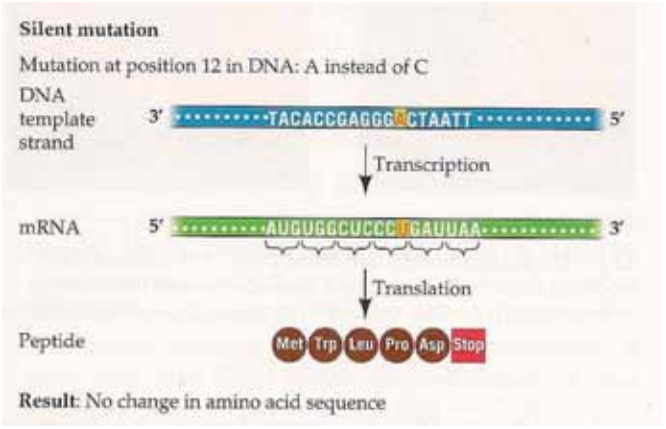
1. **Point mutations**

These are mutations of single base pairs and so affect a single gene. An alteration of a single nucleotide by a gain or loss or substitution can cause one allele (usually dominant) to become another allele (usually recessive).

(all illustrations taken from:
Purves, W., Sadava, D., Orians, G., Heller, C. (2004). Life: the Science of Biology. 7th ed. Gordonsville, VA, Freeman & Co., pp 251-253)

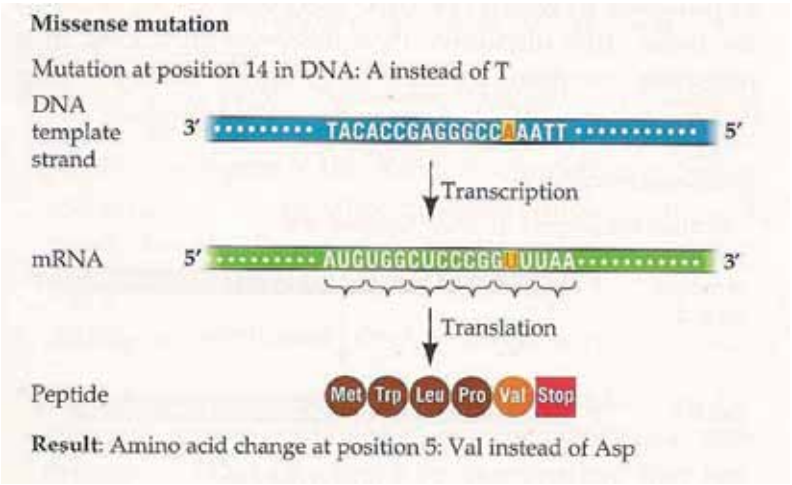
- 'silent mutation'

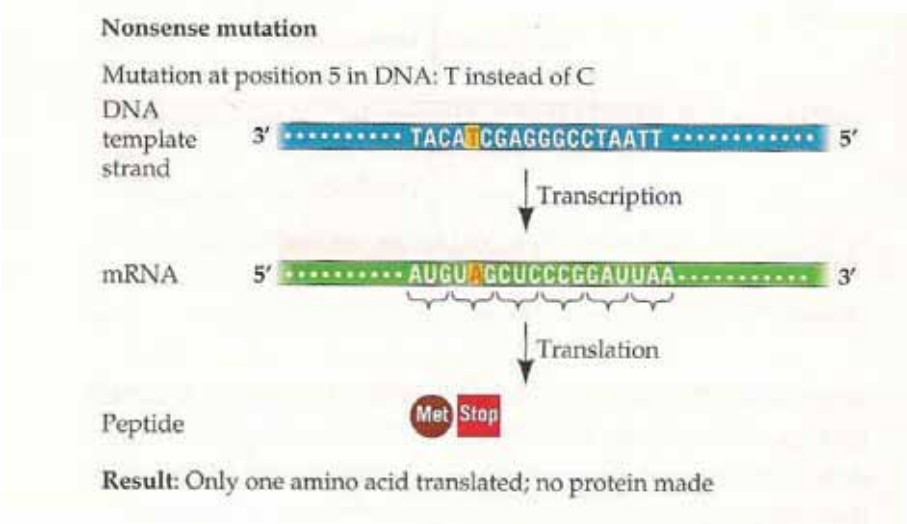
  Sometimes it is a 'silent mutation' because of the redundancy of the genetic code e.g. four mRNA codons code for proline i.e. CCA, CCC, CCU, and CCG. A change in the nucleotide of just one nitrogenous base may result in a change of a codon from CCA to CCC, and tRNA will still carry proline to this codon and there will be no change in the DNA structure.



- substitution:

  Sometimes the mutation can change the genetic message by the substitution of one DNA nucleotide for another.
  A different codon on the mRNA results in a different amino acid being added to the protein eg in sickle cell anaemia, just one amino acid in the haemoglobin has changed, resulting in the lethal sickle cell anaemia allele.



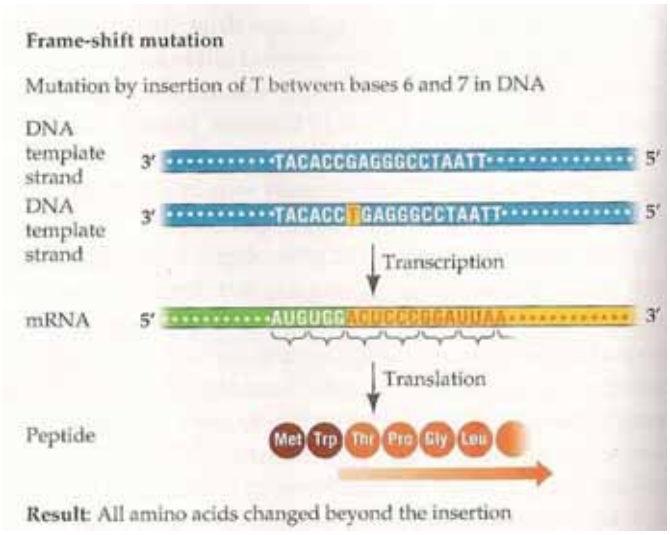


- gain or loss

  The addition or loss of a single DNA base pair changes the message completely e.g.

DNA template strand	... TACACCGAGGGCCTAATT...
mRNA	...AUG-UGG-CUC-CCG-GAU-UAA..
protein	Met---Trp---Leu---Pro---Asp---Stop
addition of T to DNA	... TACACCTGAGGGCCTAATT...
mRNA	...AUG-UGG-ACU-CCC-GGA-UUA-A..
Protein	Met---Trp---Thr—-Pro—Gly---Leu

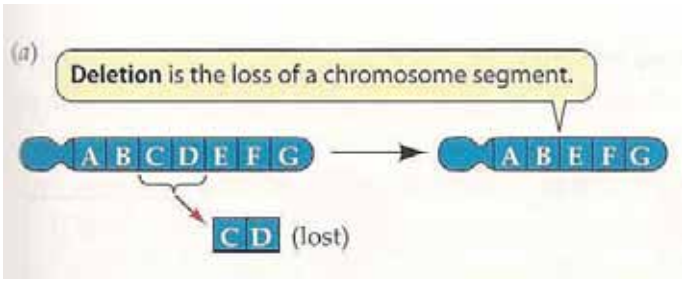
  The new protein is almost always non-functional (and so the gene is recessive).



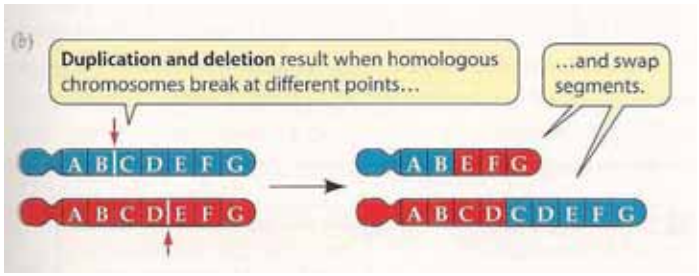
2. Chromosomal mutations

Chromosomal mutations will be dealt with later in more detail. They can occur by deletions, duplications, inversions, and reciprocal translocation.

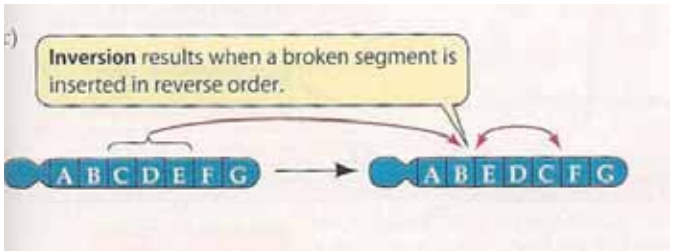
deletions



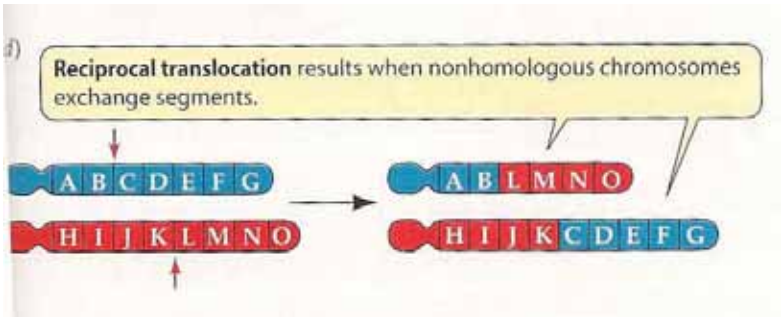
duplications



inversions



translocation.



HOW MUCH DETAIL ON MUTATIONS DO LEARNERS NEED?

Activity 5: Human models- simulating DNA structure, replication and transcription of mRNA

(a revision exercise to link concepts - M. Doidge)

You need:

- star stickers – representing phosphate
- round stickers labelled A, T, G, C and U (use coloured stickers if possible)
- white stickers labelled D or R
-1 label 'enzyme'
- 1 label 'centromere'

(adjust numbers according to workshop/class size),

To make the bangles, take A4 sheets, cut into strips and staple together.

Label the colored bangles or stickers A, T, C, G, U, D or R – use colour coding.

Suggestion: if the class size is more than:

70 – use A-T-G-A-C-C-G-T-T-A-A-C-G-T (1st DNA strand)
i.e. 70P; 16A, 16T, 12G, 12C with 56D stickers; 4A, 4U, 3G, 3C with 14R stickers

60 - use A-T-G-A-C-C-G-T-T-A-C-G
i.e. 60P; 12A, 12T, 12G, 12C with 48D stickers, 3A, 3U, 3G, 3C with 12R stickers

50 - use A-T-G-A-C-C-G-T-T-A
i.e. 50 P; 12A, 12T, 8G, 8C with 40D stickers; 3A, 3U, 2G, 2C with 10R stickers

40 - use A-T-G-A-C-C-G-T
i.e. 40P; 8A, 8T, 8G, 8C with 32D stckers; 2A, 2U, 2G, 2C with 8R stickers

30 - use A-T-A-C-G-T
i.e. 30P; 8A, 8T, 4G, 4C with 24D stickers, 2A, 2U, 1G, 1C with 6R stickers

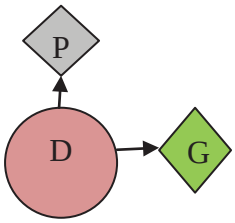
20 - use A-C-T-G
i.e. 20 P; and 4A, 4T, 4G, 4C with 16D stickers; 1A, 1U, 1G, 1C with 4 R stickers

(the order and number of bases on the 1st DNA strand is not important but you need to get the numbers right so the above plan can help you)

Preparing the human model:

- Ask the group to form a large circle. Explain the area within the circle represents the nuclear sap within the nuclear membrane.

- give each person a black sticker to place on the back of their left hand, a white D or R sticker to place on their chest, and a coloured sticker with A,C,G, T or U for the back of their right hand. (make sure the proportions are correct)
  Explain that their chest represents a deoxyribose sugar and they are each a free nucleotide circulating in the nuclear sap.
- additional people – give one person the label 'enzyme' and one person the label 'centromere' and explain that the rest remain on the perimeter of the circle forming the nuclear membrane.
- get all the human 'nucleotides' to move into the 'nuclear sap', the area within the circle
- ask them to hold their left arm forward, and their right hand to the right of their body.



Part 1: DNA structure

- as they circulate, call in free nucleotides and ask them to form a single DNA strand (you can use the code suggested above for the size of your class)
  e.g. A-T-G-A-C-C-G-T-T-A-A-C-G-T
  (i.e. place left hand (P) on left shoulder of the person in front of them (D).)

Questions to group:

- *what bond are they forming with the 'nucleotide' ahead and behind them (sugar-phosphate bonds)?*
- *what does the order of nitrogenous bases represent? (DNA code)*

- now ask complementary free nucleotides to form "hydrogen bonds" with the nucleotides making up the single strand, by holding hands. Then they should link with the nucleotides ahead of them, thus forming the 2nd DNA strand. See if they can work out that in order for them to bond, the 2nd strand now faces in the opposite direction to the 1st strand (antiparallel).
  (the rest of the nucleotides continue to circulate in the nuclear sap)

Questions to group:

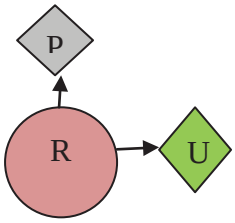
- *at what phase of the cell cycle would one find DNA looking like this.* (anaphase and telophase of mitosis and G1)
- *how many nucleotide pairs should there be in the 46 chromosomes in this 'nucleus' ? (3 billion*)
- *where are the genes – in relation to this human model.*
- *approximately what % of the DNA is made up of genes? (2%)*
- *what is a mutation?*

(can be just one nucleotide nitrogenous base changed eg sickle cell anaemia; several nitrogeneous bases changed; some bases removed – extra people ask one person to act as an ultraviolet ray of light from sun; another an X-ray

Part 2: transcription – mRNA

Questions: at what phase of the cell cycle would transcription and translation occur? (G1 and G2)

- imagine this piece of 'DNA' (represented by the human model) is a gene coding for a specific protein, with the imaginary DNA stretching out on either side.
- tell the 'enzyme' to move in and break the weak hydrogen bonds, by pulling the hands apart – unzipping the DNA. Two strands move apart.
- call in RNA nucleotides to attach to the original chain (template) e.g.



- *question: what is this process called? why does it have that name? (transcription – trans – across; scribe – to write: write the message across onto another molecule*
- call in the enzyme to break the bonds
- lead the mRNA out of the nuclear sap through an opening eg a doorway into the cytoplasm and attach it to any large object – the ribosome.
  (You could extend the game to show translation and protein synthesis)
- tell the two DNA chains to move together again and 'zip up'

Part 3: DNA replication

Now the cell enters the S phase of the cell cycle.

- tell the 'enzyme' to move in and break the weak hydrogen bonds, by pulling the hands apart – unzipping the DNA.
- call in the free nucleotides to form hydrogen bonds along free chains.
- call in the centromere (special area of DNA) to hold the DNA molecules together

Questions – with reference to the structure here:

- *compare the DNA – what similarities and/or differences do you notice in the two chains?* (they are identical)
- *why is this process called replication?* (an exact copy is made)
- *why is this phase in the cell cycle called the S phase?* (new DNA is synthesised/made)
- *if these two DNA double chains are each wound around histones, what would each structure be called?* (chromatids)
- *what would the two DNA double chains held together by a centromere be called?* (chromosome)
- *when would you see this structure in the cell cycle?* (end of S phase, G2 phase, and prophase and metaphase of mitosis)
- *how could mutations occur?*

Activity 6: Extracting DNA from wheat

(Prof V.A. Corfield, Dept of Science and Technology & Public Understanding of Biotechnology)

In this activity, we will extract DNA from ground wheat.

You will need:	
ground wheat (wheat germ)	spice jar
water	wooden stick
dishwashing liquid	teaspoons
methylated spirits	paper towel
	small plastic container

Step 1:

- Place ½ teaspoon of ground wheat (wheat germ) in a spice jar.
  (This ground wheat is from the cells inside the hard outer wheat seed or husk which has been discarded. The ground wheat is very rich in DNA as the endosperm is triploid.)
- Add 10 teaspoon (3 Tblsp/50mls) tap water to the ground wheat and mix non-stop with a wooden stick for 3 minutes.
  (This allows the cells to be suspended and also allows them to be exposed to the other reagents that will be added later.)

Step 2:

- Add ¼ teaspoon of dishwashing liquid to the cells that have been suspended in water in step 1. Mix gently with a wooden stick every ½ minute for 5 minutes.

WARNING

It is important not to let the dishwashing liquid froth and foam too much in the jar, as this may prevent effective extraction of the DNA.

(The dish-washing liquid breaks down fat. The nuclear and cell membranes are made of phospholipids (phosphate + fat) and proteins. The dishwashing liquid destroys the fat and so the DNA is released from the nuclei of the cells.
The DNA is now dissolved in the water.
The DNA threads are fragile and can get broken if stirred too roughly.)

Step 3:

- Remove the wooden stick.
- If there is excessive foam, remove it with a paper towel.
  (This is important as the foam on the top of the mixture may prevent the methylated spirits added in step 4 from reaching the DNA mixture.)

Step 4:

- Tilt the jar and slowly add an estimated equal volume of methylated spirits to the mixture by carefully pouring it down the side of the jar.
  (We use methylated spirits (alcohol) to precipitate the DNA out of the solution. The DNA is dissolved in the water, but can't dissolve in alcohol. When we add methylated spirits to the solution, the DNA precipitates out.
  We pour the methylated spirits slowly so it doesn't mix well with the water. The meths is less dense and will rise to the surface, forming a layer above the water. The DNA precipitate is found in this layer)

WARNING
Methylated spirits is POISONOUS and FLAMMABLE. Teachers should supervise learners carefully at this point.

After adding the methylated spirits to the mixture, some "white, slimey, stringy, gooey threads/ clouds" rise out of the 'mush'.
(Ask the class what these threads are. It's the thousands of DNA strands coming out of solution and sticking together and floating in the meths.)

Step 5:

- Use the wooden sticks to fish the white threads out of the spice jar and transfer them to the small square plastic container., and examine them.

You have found the DNA!

(Are these threads the DNA? No – rather thousands of DNA threads all clumped together.)

DNA fingerprinting

The diagram below, taken from Focus on Life Science, Grade 12, p. 52, illustrates how DNA 'fingerprints' are made in the laboratory.

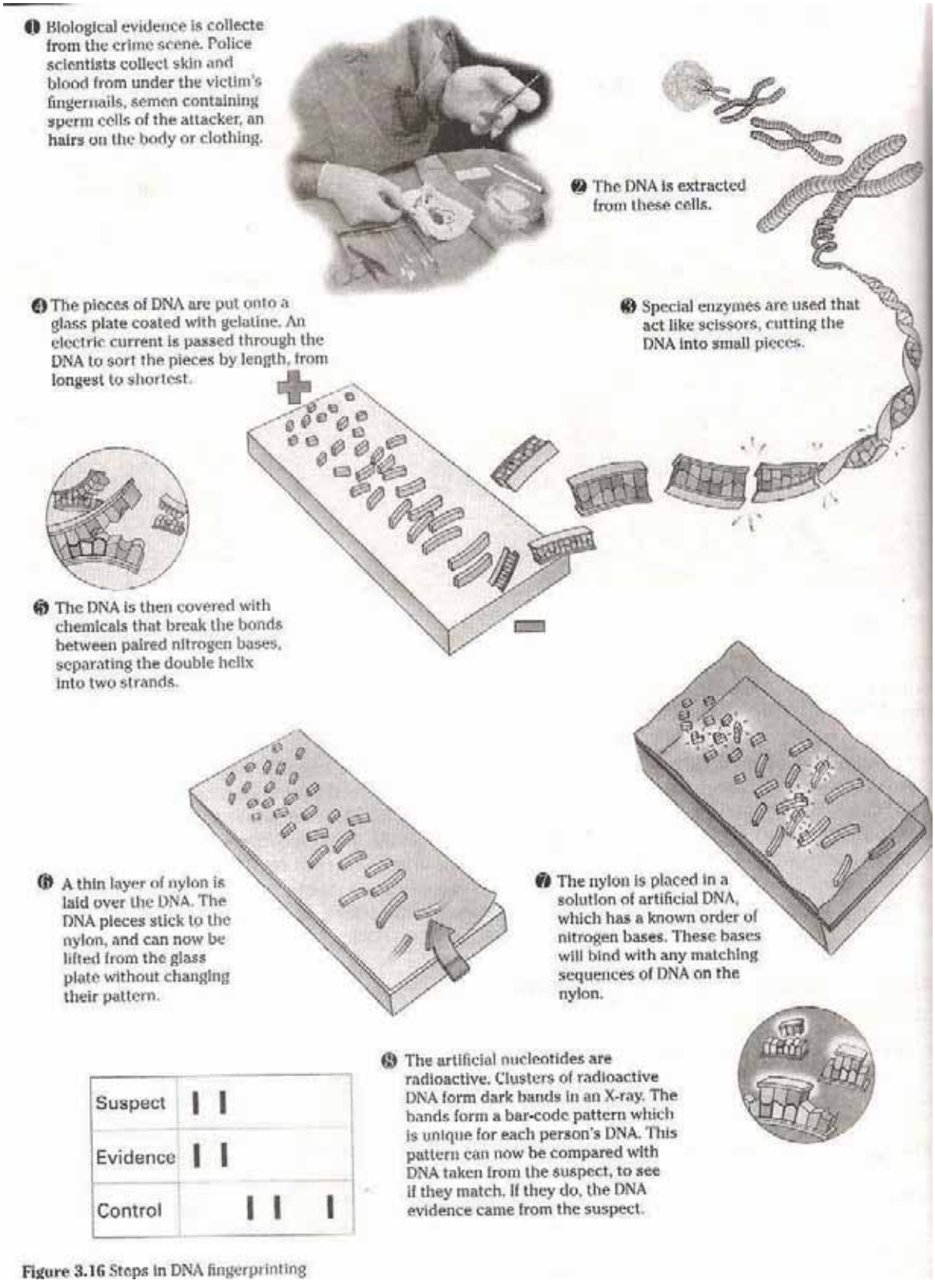


Figure 3.16 Steps in DNA fingerprinting

Can DNA Demand a Verdict?

Since 1987, forensic DNA analysis has made appearances in U.S. courtrooms. Originally known as "DNA fingerprinting," this type of analysis is now called "DNA profiling" or "DNA typing" to distinguish it from traditional skin fingerprinting.

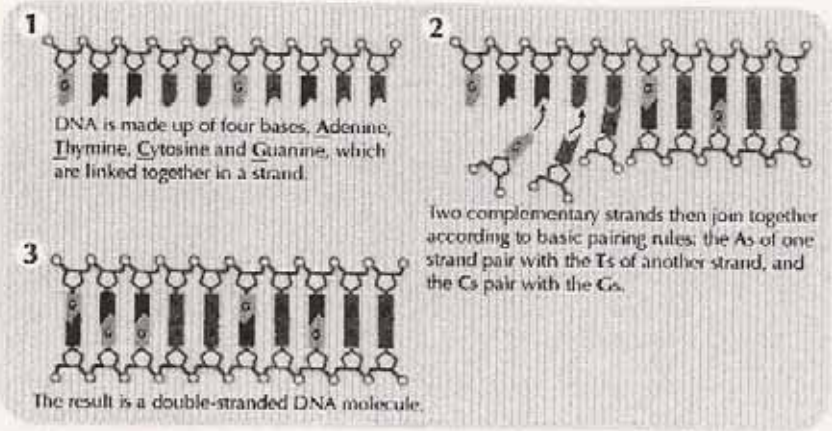
Although used in less than one percent of all criminal cases, DNA profiling has helped to acquit or convict suspects in many of the most violent crimes, including rape and murder.

How can DNA be used to identify an individual?

Every single cell in our bodies contains DNA, the genetic material that programs how cells work. 99.9 percent of human DNA is the same in everyone, meaning that only 0.1 percent of our DNA is unique!

Each human cell contains three billion DNA base pairs. Our unique DNA, 0.1 percent of 3 billion, amounts to 3 million base pairs. This is more than enough to provide profiles that accurately identify a person. The only exception is identical twins, who share 100 percent identical DNA.

At a crime scene, DNA is everywhere. It is present in all kinds of evidence collected at the scene, including blood, hair, skin, saliva and semen. Scientists can analyze the DNA in evidence samples to see if it matches a suspect's DNA.



How is forensic DNA analyzed?

On the right, you can see how DNA evidence is collected and analyzed. In the past, DNA analysis required an evidence sample at least the size of a dime. Today's techniques can multiply the DNA, producing millions of copies from tiny amounts of evidence, such as the saliva from a cigarette butt. This approach is also helpful for analyzing poor-quality

Need to know some DNA basics?

Find the essentials in the Tour of the Basics, and make your own DNA strand online in Build a DNA Molecule.

Can DNA Demand a Verdict?

DNA in evidence samples collected from dirty crime scenes.

If people are blood relatives, is their DNA similar?

Though all people except identical twins have three million bases of unique DNA, blood relatives share more similar DNA than do unrelated individuals. If the DNA profiles from the evidence and a suspect are similar but not identical, blood relatives of the suspect may be investigated further.

What about human error?

Forensic investigators take many precautions to prevent mistakes, but human error can never be reduced to zero. The National Research Council (NRC) recommends that evidence samples be divided into several quantities soon after collection, so that if a mix-up were to occur, there would be backup samples to analyze.

To detect possible contamination of DNA samples during collection or handling, evidence DNA profiles are often compared with those from detectives at the crime scene, the victim, a randomly chosen person or a DNA profile from a database.

The NRC recommends that forensic DNA analysis be conducted by an unbiased outside laboratory that maintains a high level of quality control and a low error rate.

Is DNA evidence alone enough to acquit or convict?

It is easier to exclude a suspect than to convict someone based on a DNA match. The FBI estimates that one-third of initial rape suspects are excluded because DNA samples failed to match.

Forensic DNA is just one of many types of evidence. It is important to examine other clues such as motive, weapon, or additional evidence linking a suspect to the crime scene. The more evidence collected, the less likely it is that samples from a particular suspect were planted, either on purpose or by accident, at the crime scene.

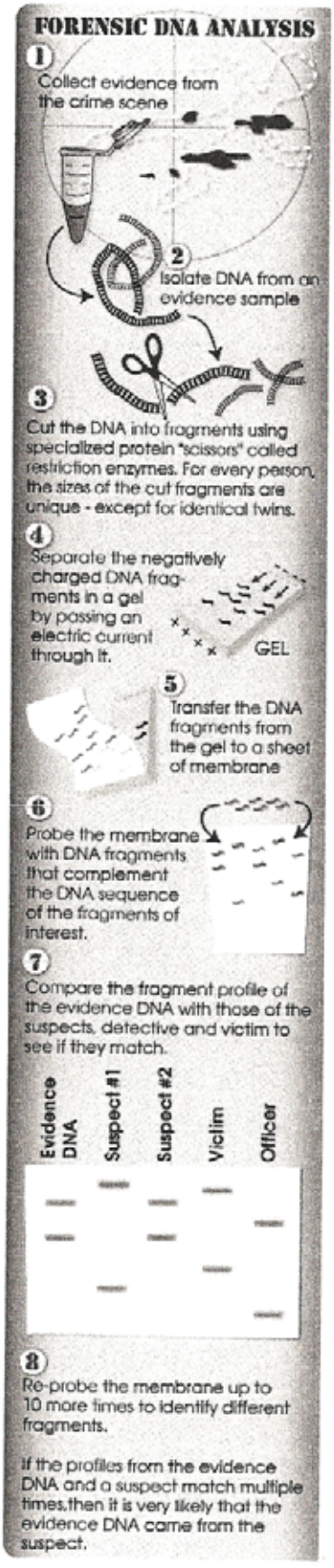
Can DNA evidence exonerate wrongfully convicted prisoners?

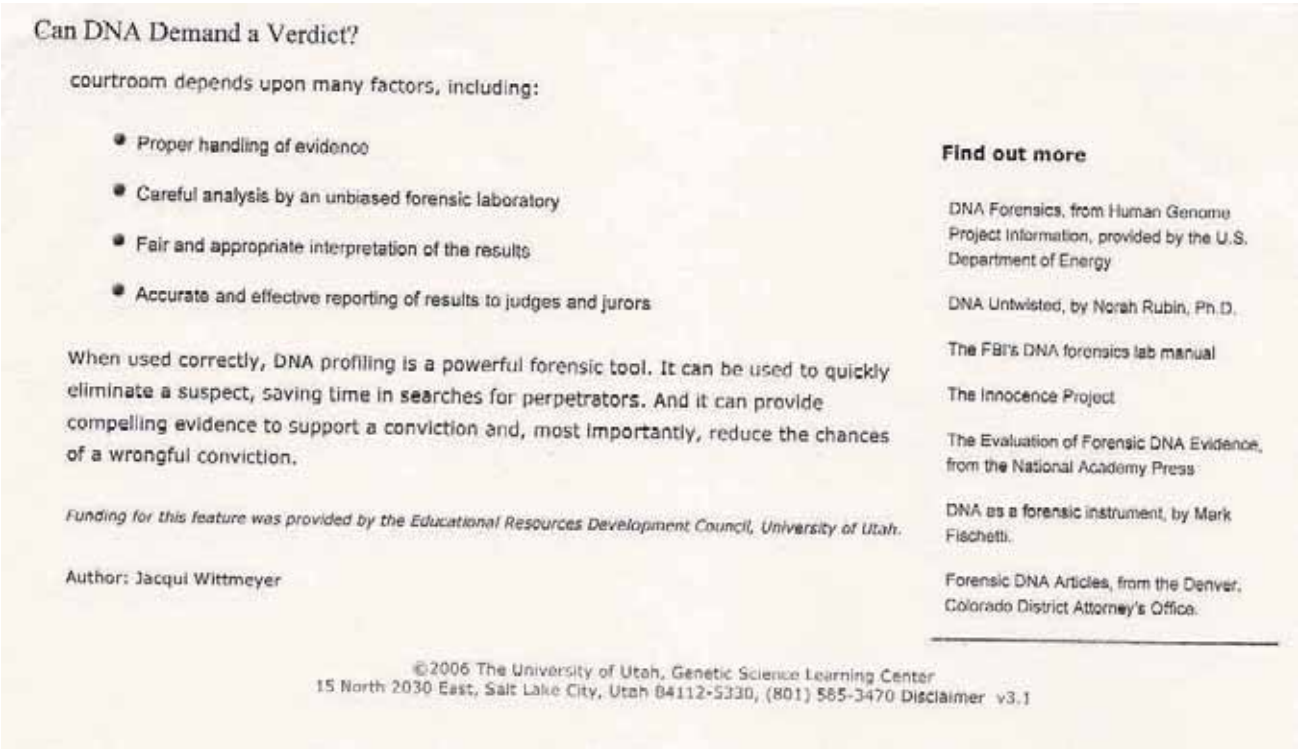
The Innocence Project at New York's Benjamin N. Cardozo School of Law aims to exonerate prisoners wrongfully convicted of crimes. The project uses DNA profiling evidence to support the re-evaluation of criminal cases. But DNA evidence alone is not enough to get a person out of jail: the case must be re-examined by a judge, along with lawyers representing both sides of the case. Since 1992, the Innocence Project has exonerated over 100 prisoners, including eight who were on death row - one of whom was only five days from execution.

Thirty-three states restrict the time for post-trial submission of DNA evidence to six months or less. New York and Illinois, on the other hand, will reconsider cases with compelling DNA evidence regardless of when the trial ended. Unfortunately, the evidence from some cases has been lost or destroyed, making DNA analysis impossible.

Is this technology used appropriately for justice?

DNA profiling can be a powerful tool in criminal investigations. Its success in the





Can DNA Demand a Verdict?

courtroom depends upon many factors, including:

- Proper handling of evidence
- Careful analysis by an unbiased forensic laboratory
- Fair and appropriate interpretation of the results
- Accurate and effective reporting of results to judges and jurors

When used correctly, DNA profiling is a powerful forensic tool. It can be used to quickly eliminate a suspect, saving time in searches for perpetrators. And it can provide compelling evidence to support a conviction and, most importantly, reduce the chances of a wrongful conviction.

Funding for this feature was provided by the Educational Resources Development Council, University of Utah.

Author: Jacqui Wittmeyer

Find out more

DNA Forensics, from Human Genome Project Information, provided by the U.S. Department of Energy

DNA Untwisted, by Norah Rubin, Ph.D.

The FBI's DNA forensics lab manual

The Innocence Project

The Evaluation of Forensic DNA Evidence, from the National Academy Press

DNA as a forensic instrument, by Mark Fischetti.

Forensic DNA Articles, from the Denver, Colorado District Attorney's Office.

In analysing DNA profiles, if you are trying to match a suspect with DNA collected from a crime site, the DNA profile (fingerprint) for both the suspect and the evidence should be the same.

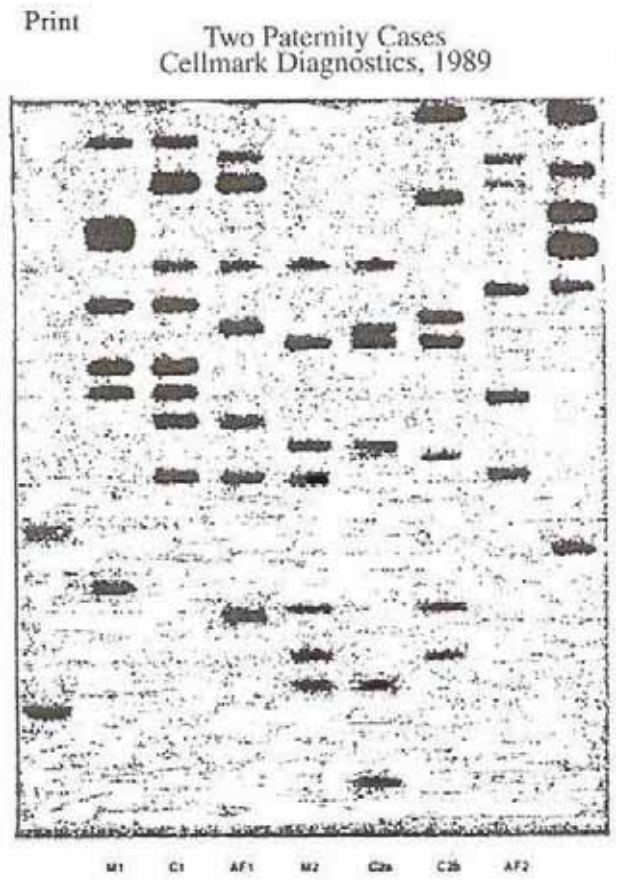
If you are trying to determine the parents of a child, then the bands on the DNA profile of the child have to match either the mother or the father (or both) since the child has inherited DNA from both parents.

Activity 7: Analysing DNA profiles

Case 1: Paternity case

http://www.woodrow.org/teachers/bi/1992/DNA_printing.html

This print from two paternity cases shows the DNA fingerprints of two different mothers, their children and the alleged fathers.



Use the following key:

M1 – 1st mother

C1 – 1st child

AF 1 – alleged father of 1st child

M2 – 2nd mother

C2a – 2nd child

C2b – 3rd child

AF2 – alleged father 2

Is AF 1 the father of C1? .....

Is AF2 the father of C2a? ..... C2b? .....

Explain your answers: .....

.....

.....

Do you think the quality of these prints is good enough for court evidence?

.....

.....

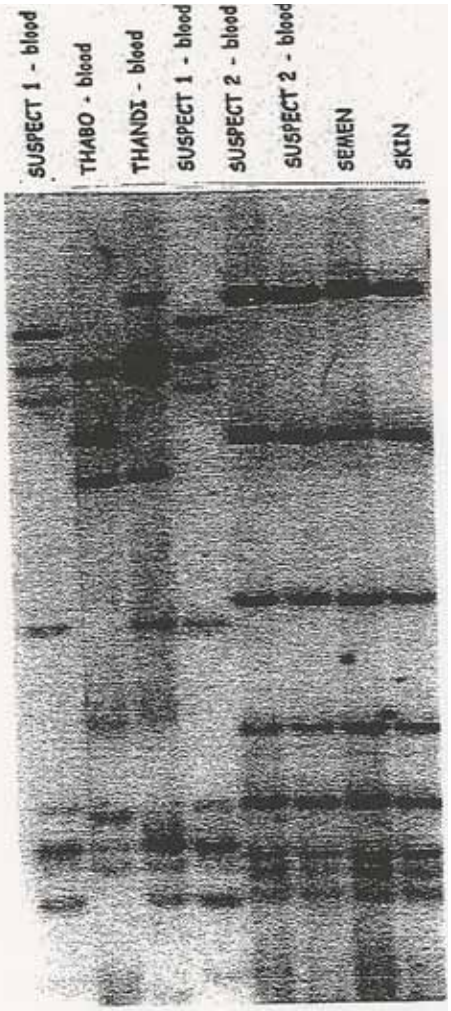
Case 2 – finding the rapist

(adapted from Nel, E., Page, J., Moshoeshoe, M. and Moremi, S. (2000). Rainbow Biology Project; Genetics for Today, Centre for Science Education, University of Pretoria)

Thabo and Thandi, a young couple, were returning home from a movie one evening when they were attacked by thugs. Thabo was knocked to the ground and stabbed and Thandi was raped by one of the men. Thandi fought hard and scratched her rapist. The police heard their screams and came to their help. They took them to the hospital and since Thandi had been raped, semen samples were taken from her vagina and pieces of the attacker's skin from under her fingernails for DNA analysis. Blood samples were also taken from Thandi and Thabo for DNA fingerprinting.
The police also started a search for Thandi's attackers and arrested two suspicious looking individuals found running down a street. Samples of their blood was also taken for DNA fingerprinting.
However were either of these men the rapist?

You have been supplied with the DNA fingerprints produced by the forensic laboratory from the blood, semen and skin samples. Use them to answer the following questions.

1. Do either of the two suspects have a DNA fingerprint which matches the fingerprint of the DNA from the semen or skin samples? If so, which suspect?
2. Why was a DNA fingerprint created for Thabo and Thandi as well?
3. Is there a possibility that this evidence would not stand up in a court of law? Explain your answer.
4. Suggest why two fingerprints were made for each suspect.



Activity 8 Modelling the making of a DNA fingerprint

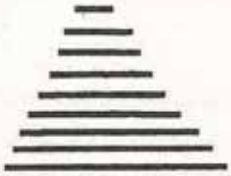
(Nel, E., Page, J., Moshoeshoe, M. and Moremi, S. (2000). Rainbow Biology Project; Genetics for Today, Centre for Science Education, University of Pretoria, pp 27-29)

You have been given two paragraphs typed without spaces between the words. Use them to carry out the following steps.

1. Cut out the separate lines of words in the **first** paragraph. Keeping them in the same sequence, join them all together in one long line with sticky tape. Make sure that there are no gaps between the letters. (Pretend that this is DNA that you have isolated from one sample).

2. Lets pretend that you add a restriction enzyme to this DNA which cuts the DNA at any place where the letter A is followed by the letter T. Look along the length of your 'DNA' and find all the spots where there is AT.

3. Using scissors (restriction enzyme), cut up the 'DNA' after the T at each of these spots so that you have a whole lot of shorter lengths of 'DNA'.



4. Arrange these short lengths of 'DNA' on the desk from shortest to longest as shown in the diagram. (You are now acting as the electrical current that separates the DNA segments out on the gel according to size).

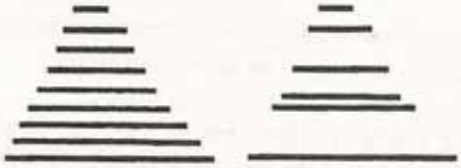
5. You now have a 'DNA fingerprint' (a pattern of bands) from the first sample.

6. Now cut out the separate lines of words in the **second** paragraph and join them all together in one long line with sticky tape. (Pretend that this is DNA that you have isolated from a different sample)

7. You add the **same** restriction enzyme to this DNA so that it will cut at the same spot - AT. This is important because you want to compare the two DNA fingerprints to find out how many (if any) segments they have in common.

8. Once you have cut up the 'DNA', sort the segments from shortest to longest.

10. Remember that during the process of electrophoresis, the shorter a segment of DNA, the faster it moves. Therefore two pieces of the same length will move the same distance. Arrange the second set of 'DNA segments' next to the first set, taking care to put pieces of the same length next to each other and fitting the other pieces in between, in a place appropriate to their length. See the diagram below.



Now answer these questions:

1. Which segments or bands do both samples have in common?
2. Is it possible that the 'DNA' came from the same organism? Explain your answer.
3. Name three uses for this technique of DNA fingerprinting in our society.

A fingerprint taken from the scene of a crime has no value on its own. The police must either:

- catch a suspect, take his / her fingerprint and see if it matches the one at the scene of the crime, or
- they must be able to match the fingerprint to one that they already have in their files.

In the same way, having a DNA fingerprint from a crime scene does not automatically identify the criminal. It has to be matched to that of a suspect. The police would like to have a record of everyone's DNA fingerprint. Because each person's DNA fingerprint is unique, the police would then be able to match the crime scene's DNA to a specific person.

Acknowledgements:

Ms C Still and Ms M Doidge of Witwatersrand University for assisting in the compilation of this guideline