St Benedict's

Journal of Science

including the *History & Philosophy of Science* and

6th FORM CHAPTER

Volume 4 · Special Edition · July 2020

St Benedict's
Catholic School

The Catholic Secondary School for West Suffolk

Published by the Science Department, St Benedict's Catholic School, Bury St Edmunds, Suffolk, UK

Welcome to Volume 4

Volume 4 marks a significant milestone for the *Journal of Science* for two reasons: previously its authors were from Years 7 and 8 at the Lower School Centre, but with the closure of the LSC and the consolidation of all students on the Beetons Way site the Journal now accepts work from all years, including 6th Form.

Secondly, the publication of this edition of the *Journal* has come in extraordinary times for the whole world – COVID-19. Although, like all schools in the UK and around the World, St Benedict's has been closed for a significant period, it has not deterred staff and students from carrying on the education process by setting curriculum work along with the innovative use of streaming video lessons.

All those concerned with the *Journal* were determined to see it published before the end of the academic year. The Editors give their wholehearted thanks and admiration to the students who have worked so hard to provide such excellent pieces of scientific research, writing and poster-making.

Special merit must be afforded to the 6th Form students, prompted by Ms Coogan, who produced some outstanding papers of an extremely high standard, including detailed references that indicated the depth of their research. It is appropriate that they are granted their unique section: the ***6th FORM CHAPTER***.

A MESSAGE FROM Mr W STAFFORD, HEAD OF SCIENCE:

I would like to warmly welcome you to this special edition of the St Benedict's Journal of Science, which staff and students have worked incredibly hard to produce at this unprecedented time.

As the Head of Science it gives me great joy to read this fantastic collection of papers and posters produced by our students, showing us that the passion for the study of the world around us is alive and well. It is a delight to have submissions ranging from those in year 7 and 8 who are in earlier stages of discovery, to those in the 6th form who are continuing along the scientific path at University. The range and scope of the articles produced was enormous, and this is just a fraction of the excellent work submitted. Big thanks must go out to the students, and also Mr Gregory, for his dedication to producing such a wonderful celebration of student work.

I hope you enjoy reading the Journal as much as I did!

Mr Stafford

EDITOR'S NOTE: The papers and posters are in order according to the Year of the students, starting with Year 7 work and progressing up to the 6th FORM CHAPTER.

Volume 4 - Special Edition - 2020

Table of Contents

6TH FORM CHAPTER

Go to pages 78 and 79 for an extract from a popular science book, sent in by Mr WATTS.
You can also have a go at Mr D'MELLO'S *PUZZLE CORNER!*

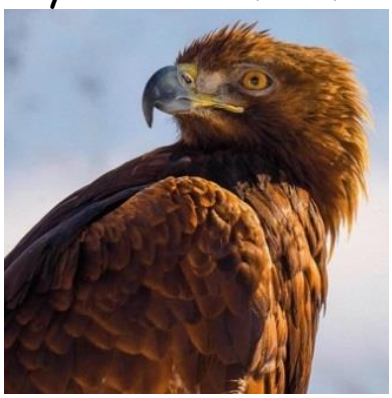
WHAT IS A PREDATOR AND A PREY?

Aideen Redmond (Year 7)

Predator: an animal that naturally preys on others

Prey: an animal that is hunted or killed by another for food.

GOLDEN EAGLE-predator.



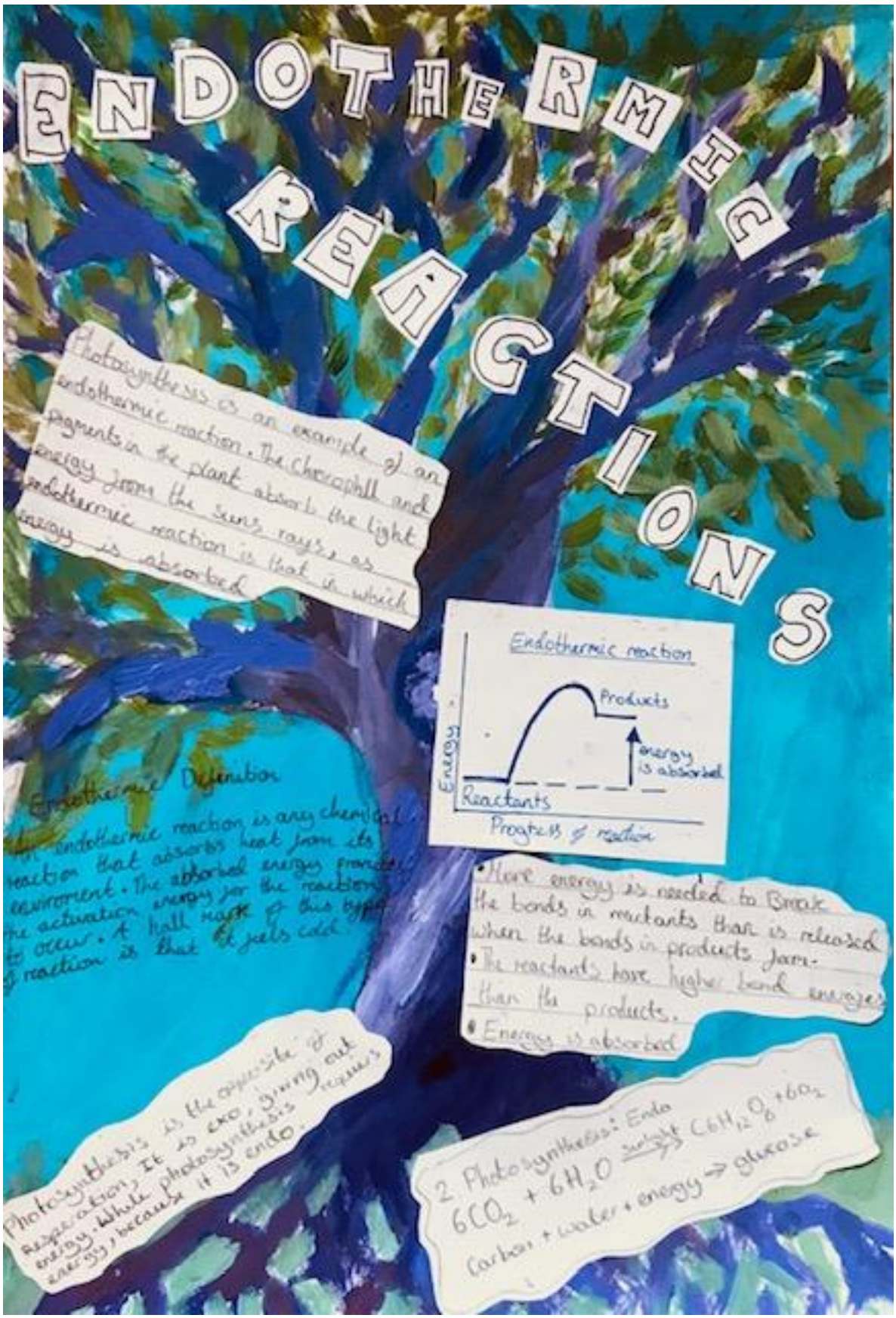
WHERE THEY LIVE:	they live in Scotland!!!
WHAT THEY EAT:	they eat small mammals such as rabbits!
CONSERVATION LEVEL:	least concern
SIZE:	length: 66-100cm
MASS:	female 3-7 kg, male 3.6 kg
WINGSPAN:	1.8-2.3m
ADAPTATIONS:	their sharp eyesight, specially developed feet, sharp beaks and large wings
MATING:	they usually mate for life or for years. They build nest high up.

EUROPEAN RABBIT-PREY.

WHERE THEY LIVE:	they live in Europe
WHAT THEY EAT:	they are herbivores, so they eat grass, flowers, etc.
CONSERVATION LEVEL:	endangered
SIZE:	Length: 34-50cm (Adult, without tail)
MASS:	1-2.5 kg (Adult)
ADAPTATIONS:	Their eyes are set high on their head, their neck is flexible, so they can look out for predators and food. They also have strong legs for running.
MATING:	they can have 5 or more litters in a year, they can start breeding at 4 months old.

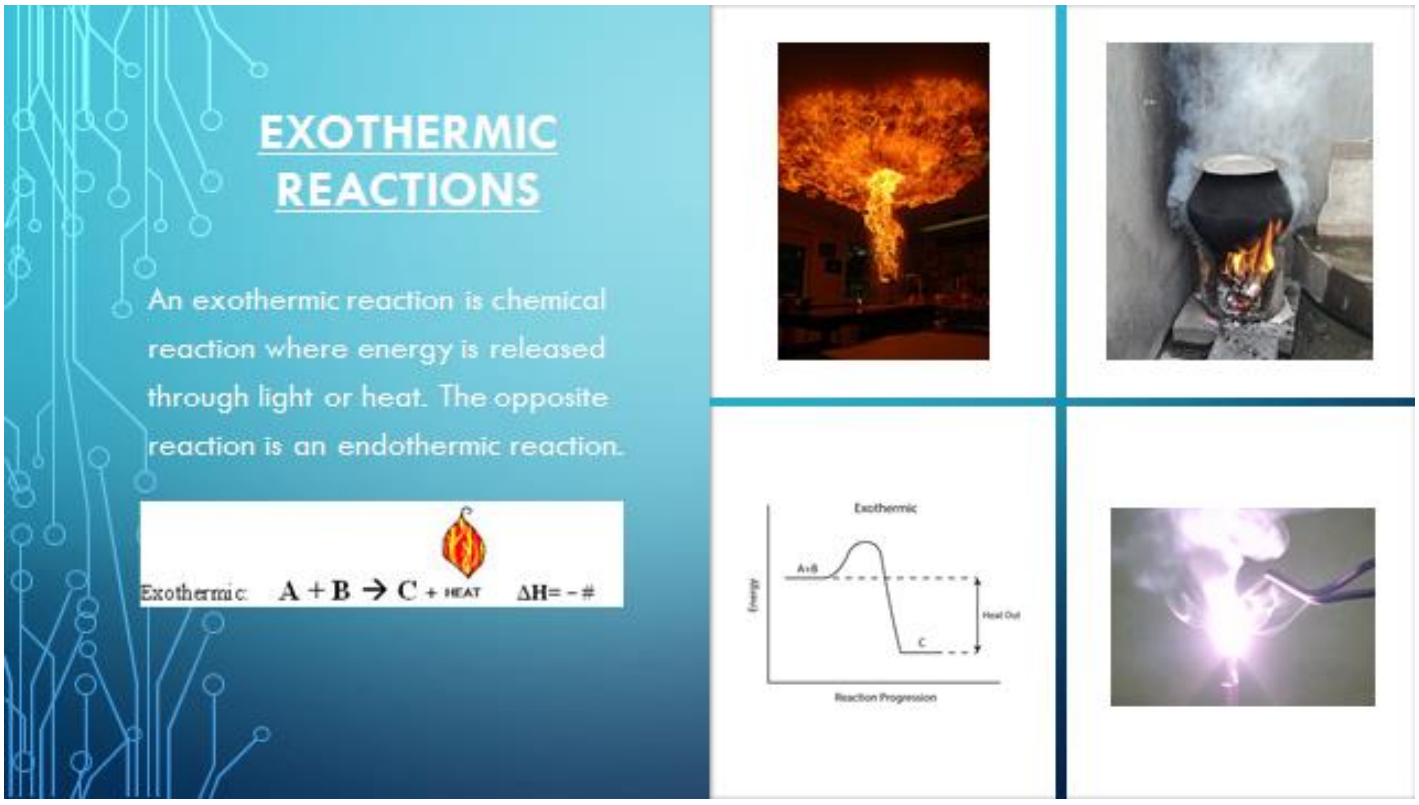
EXOTHERMIC REACTIONS

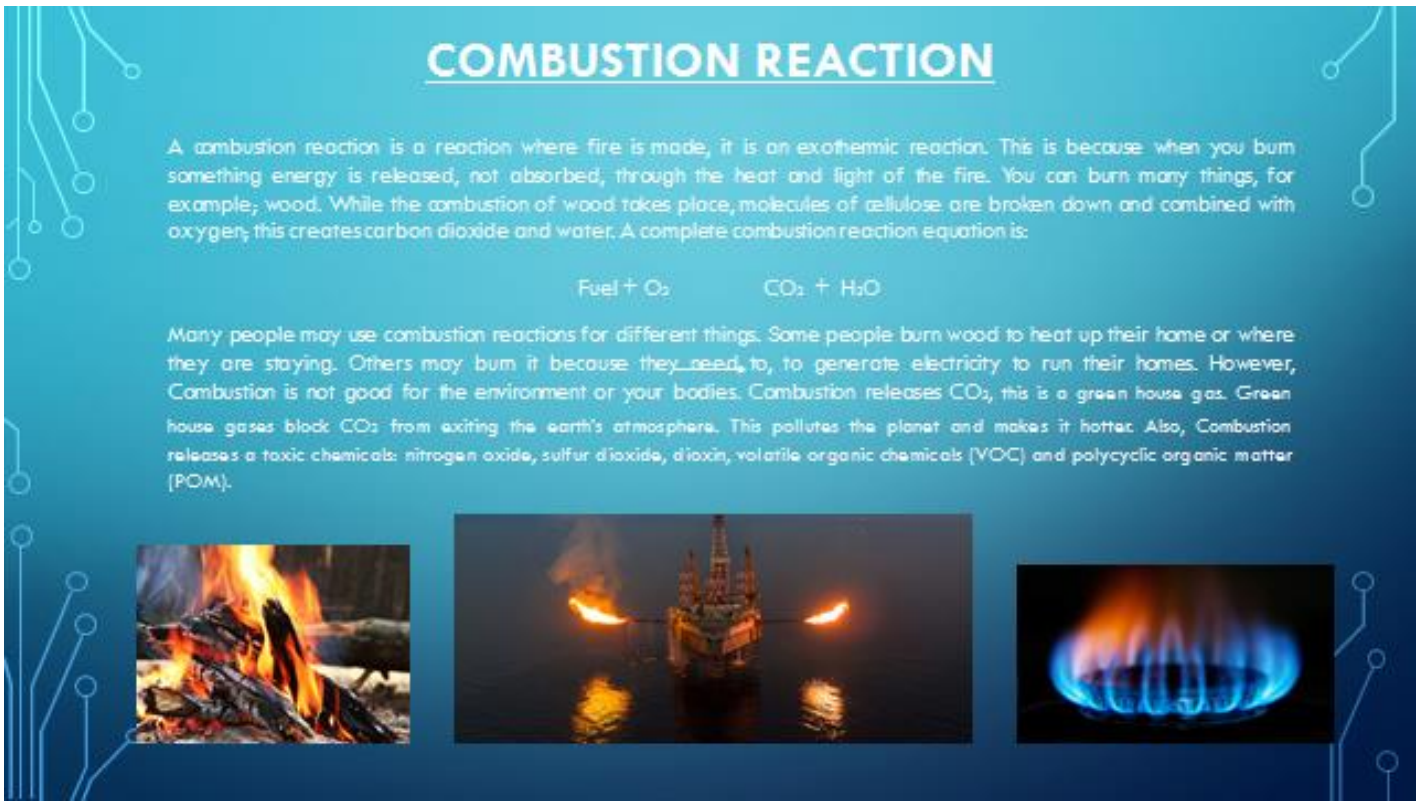
A poster by Ella Chacksfield (Year 8)



EXOTHERMIC REACTIONS

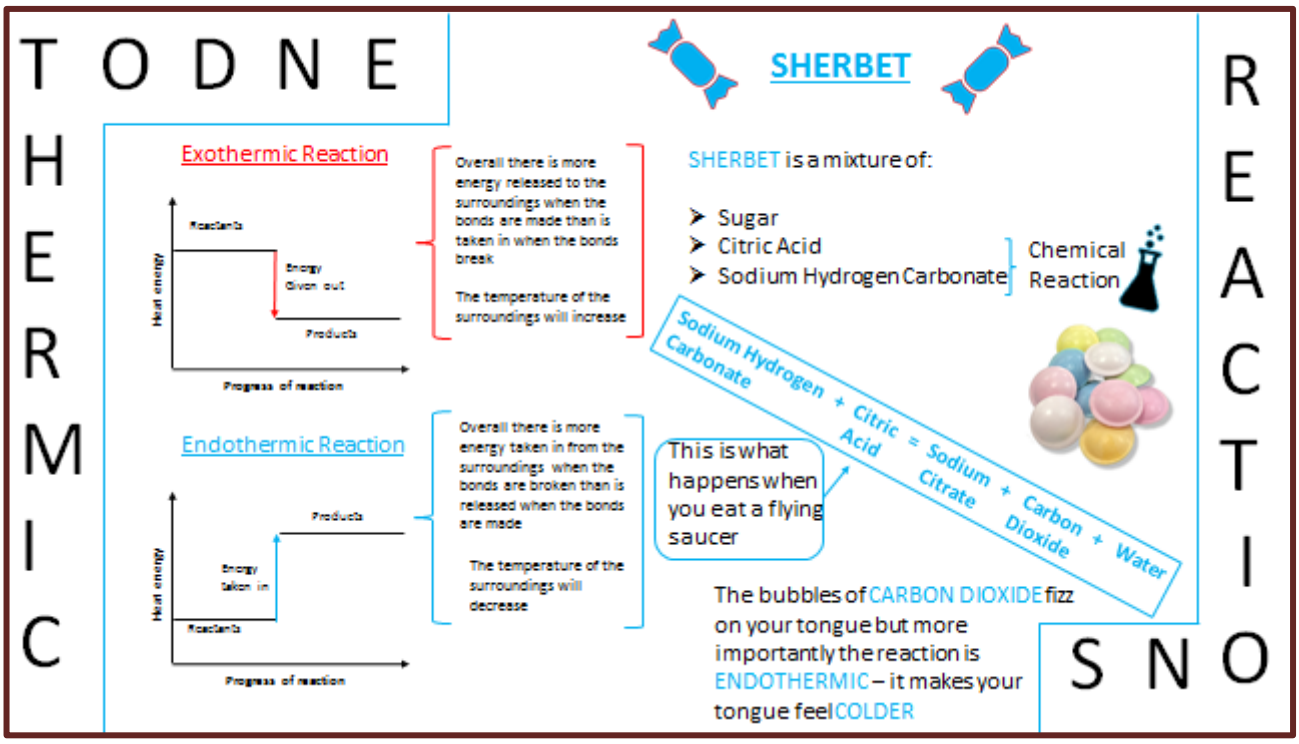
Toby Martin (Year 8)





EXOTHERMIC REACTIONS

Lilia Payne (Year 8)



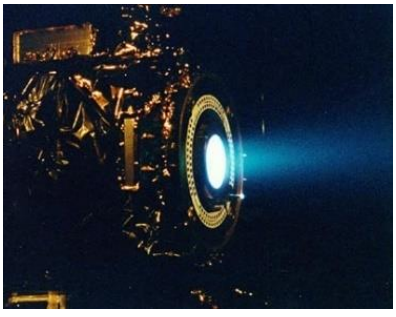
EXOTHERMIC REACTIONS GET US INTO SPACE!

Rockets using **solid fuel** (like firework display rockets) have been around since the Chinese first used them in 1232 in a war against the Mongols. These were tubes filled with gunpowder and are familiar to us every November 5th.

In 1898, a Russian schoolteacher, Konstantin Tsiolkovsky (1857-1935), proposed the idea of space exploration by rocket. In a report he published in 1903, Tsiolkovsky suggested the use of **liquid propellants** for rockets in order to achieve greater range. For his ideas, careful research, and great vision, Tsiolkovsky has been called the father of modern astronautics. However, as far as we know, Tsiolkovsky never experimented with rockets of his own. The development of liquid-fuelled rockets came in the first half of the 20th century with the work of an American, Robert H. Goddard (1882-1945).

In 1926 Goddard achieved the first successful launch of a liquid-fuelled rocket. Fuelled by liquid oxygen and gasoline, the rocket flew for only two and a half seconds, climbed 12.5 meters, and landed 56 meters away in a cabbage patch. By today's standards, the flight was unimpressive, but like the first powered airplane flight by the Wright brothers in 1903, Goddard's gasoline rocket was the forerunner of a whole new era in rocket flight.

Elon Musk's ***Falcon*** rockets use a high-grade kerosene jet fuel (RP-1) with liquid oxygen as the oxidant.



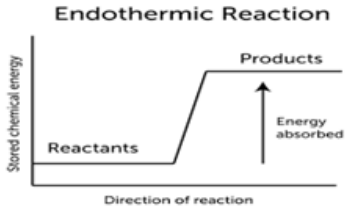
For deep-space missions, the amount of liquid fuel required means that the spacecraft's propulsion system becomes hugely inefficient and uneconomical. However, there are alternatives: for example, **ion propulsion**. NASA has already used ion propulsion on a number of space missions, including the 1998 *Deep Space 1* mission and the 2007 ***DAWN*** mission to flyby the asteroids Ceres and Vesta. In one such rocket engine, atoms of the element Xenon are bombarded with electrons ionising them. This ionised propellant is then focused out the back of the engine, creating an ion jet stream known as an **ion beam**. The movement of the ion beam creates the thrust that moves the spacecraft. The thrust is actually much less than that produced by conventional liquid propellants, but the jet stream can be maintained for much longer periods.

ENDOTHERMIC REACTIONS

John Feely (Year 8)

What is an Endothermic Reaction

- Definition:Endothermic reactions are chemical reactions that absorb heat, respectively.



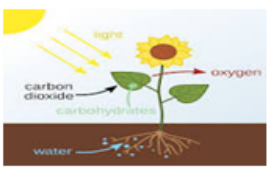
Examples of Endothermic Reactions

- Endothermic Reactions:

Photosynthesis;
Baking Bread;
Evaporation;
Melting Ice Cubes.
I am choosing Photosynthesis

Photosynthesis

- Photosynthesis is an endothermic reaction because in order for it to occur, the plants in which it occurs must absorb energy. The energy they absorb is Light but also absorb Water, Carbon Dioxide and Heat.



ENDOTHERMIC and EXOTHERMIC REACTIONS

Clotilde D'Mello (Year 8)

Endo= absorb

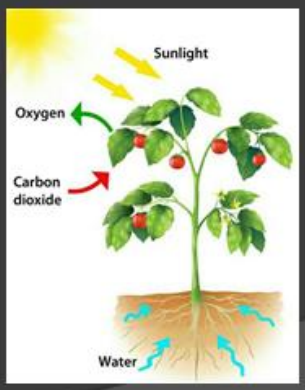
- An endothermic reaction is when the reaction takes heat from its surroundings and its usually transferred as heat energy
- One example of this type of reaction is photosynthesis

Exo= release

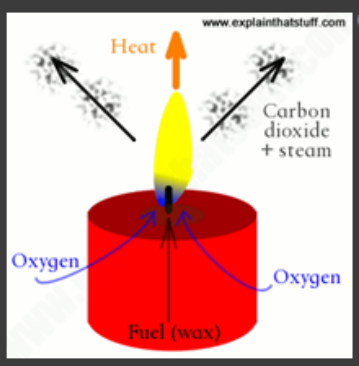
- An exothermic reaction is when the reaction releases heat
- an example of this is burning a matchstick

Endothermic example- photosynthesis

- In this process, plants use the energy from the sun to convert carbon dioxide and water into glucose and oxygen. This reaction requires 15MJ of energy (sunlight) for every kilogram of glucose that is produced:
- sunlight + $6CO_2(g)$ + $H_2O(l)$ = $C_6H_{12}O_6(aq)$ + $6O_2(g)$



Exothermic example- burning a candle

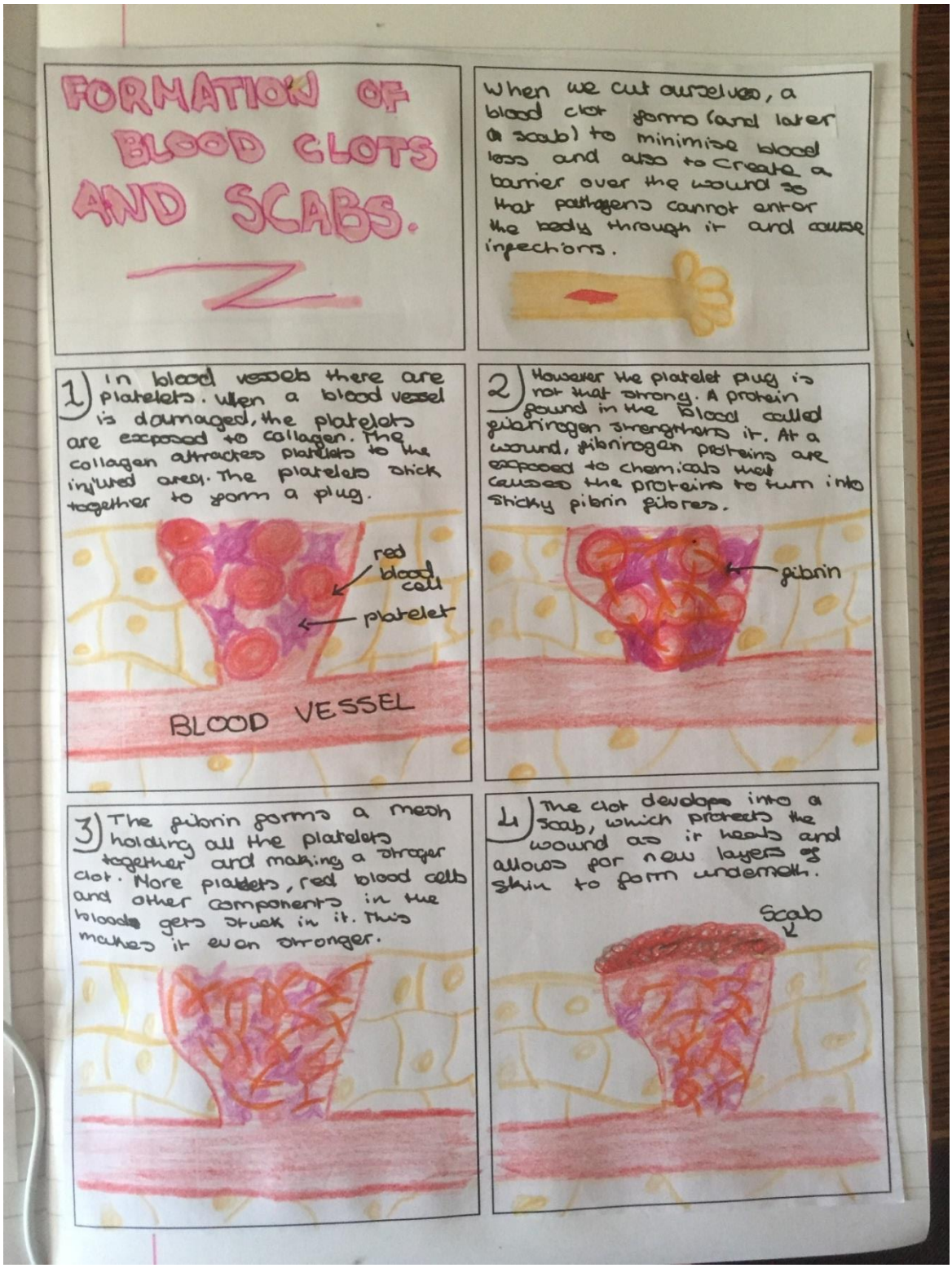


- When a candle burns, it gives off heat rather than taking it in which therefore proves to be an exothermic reaction.

EDITOR'S NOTE: The next section includes examples of posters that some of Mrs Berry's Year 9s made at home. Obviously there was no point in sending them into school, so the students photographed their work and sent them directly to Mrs Berry by email. (Some are difficult to read when reproduced here but their inclusion is merited due to the time and effort that the authors devoted to this homework)

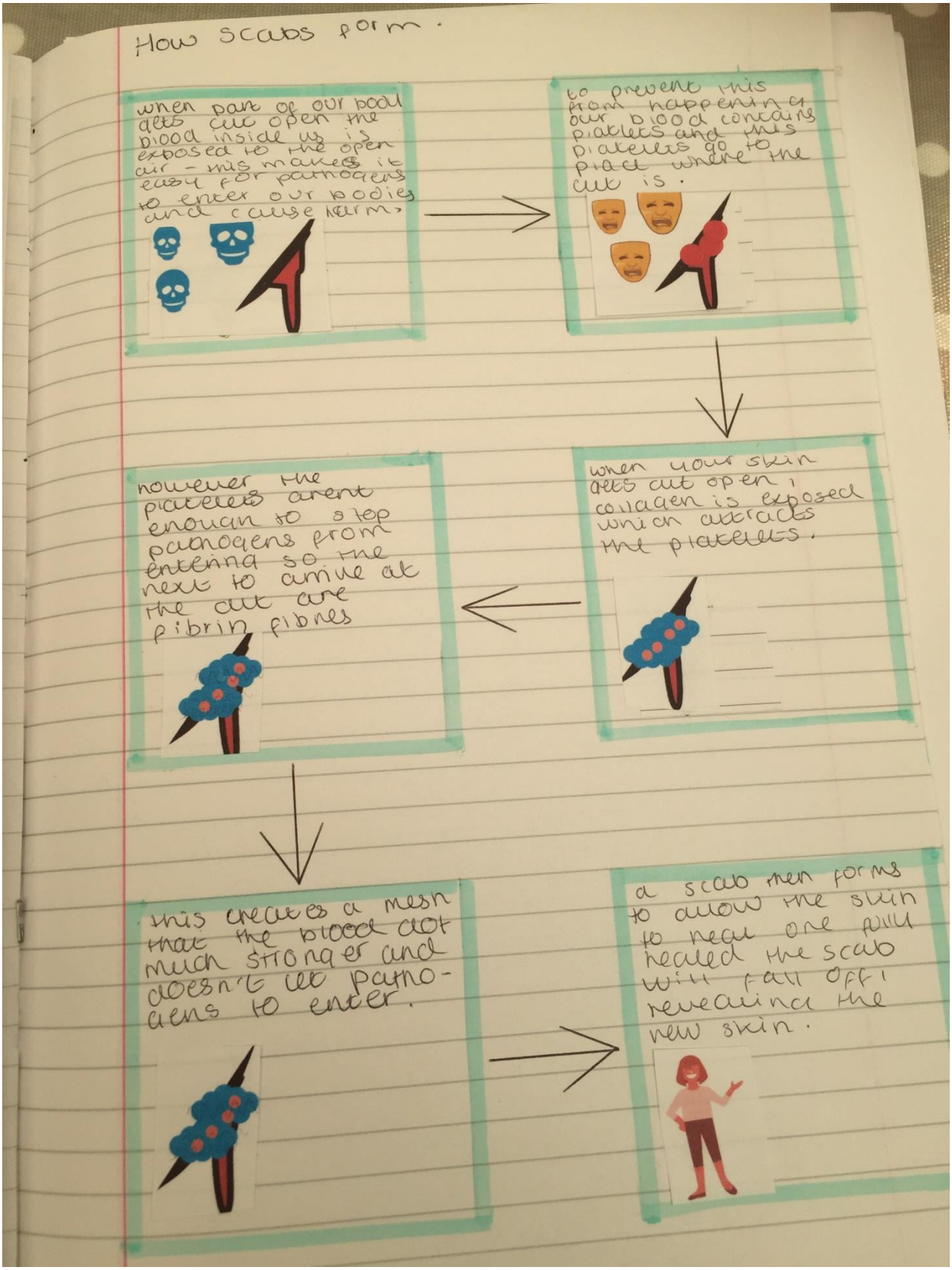
FORMATION OF BLOOD CLOTS AND SCABS

Catherine Dunn (Year 9)



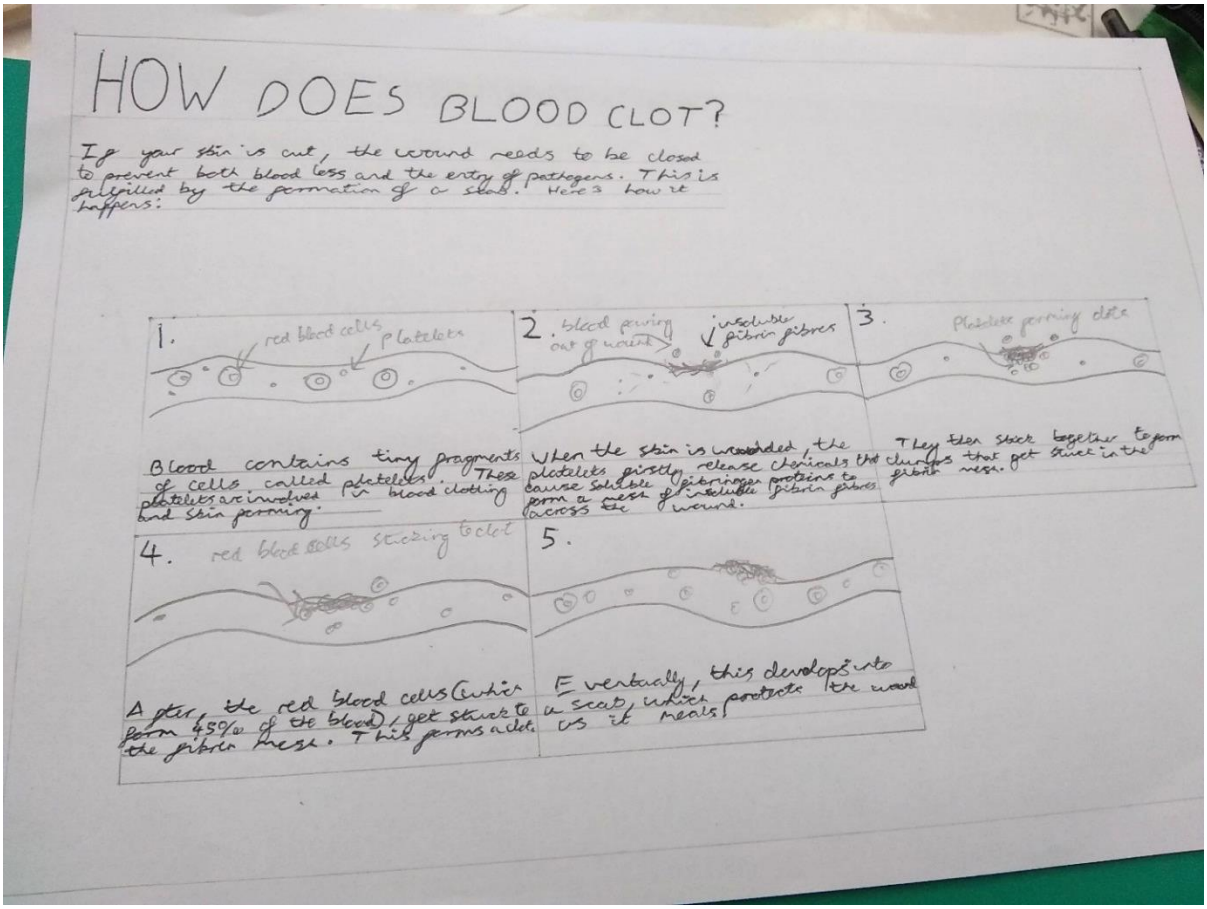
HOW SCABS FORM

Imogen Davy (Year 9)



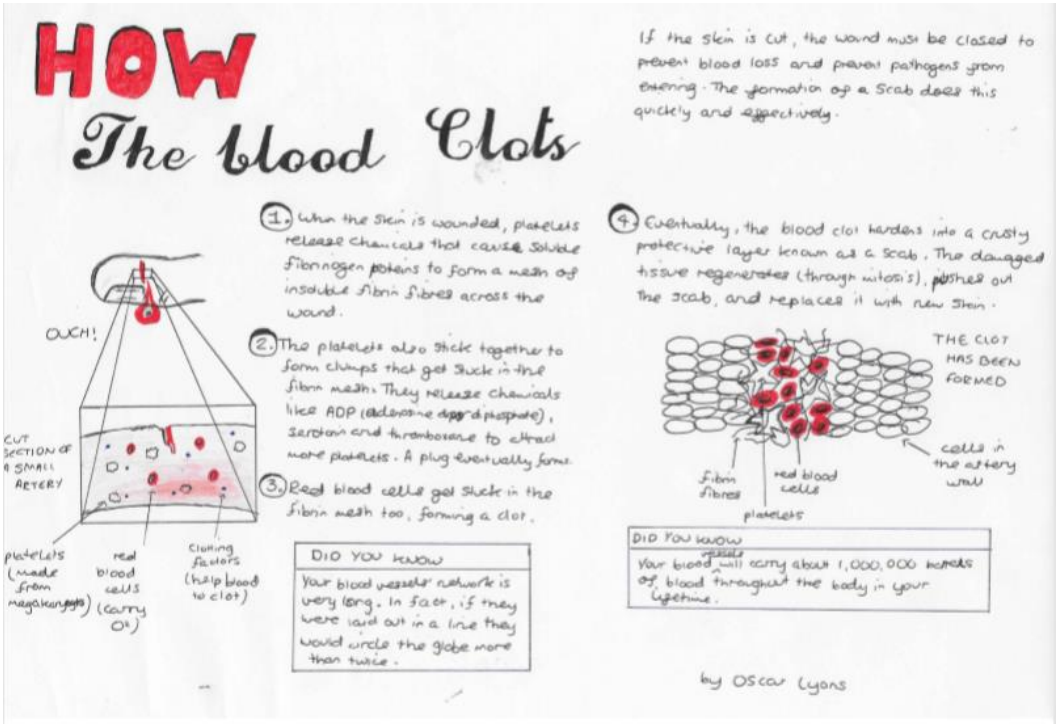
HOW DOES BLOOD CLOT

Luc Wallace (Year 9)



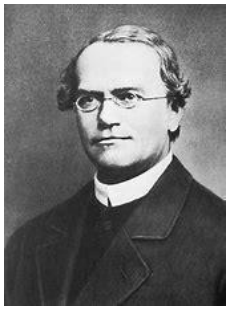
HOW THE BLOOD CLOTS

Oscar Lyons (Year 9)



GREGOR MENDEL – the Father of Genetics?

Bridget Martyn (Year 10)



Gregor Mendel, a Catholic monk born in 1822 Austria-Hungary, is often referred to as the father of genetics: but what did he do to gain this title?

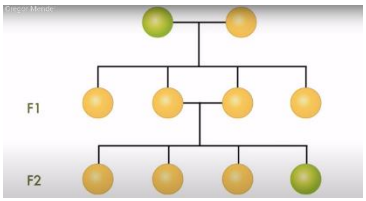
A quick summary is that he discovered the basic principles of heredity, the first person to lay the mathematical foundation of the science of genetics. This sounds a little bit complicated; let me break it down for you…

Try to imagine, it's roughly 1854: the understanding of genetic inheritance at the time is that characteristics from the mother and father kind of 'blend' together to form characteristics. We now understand that this is not actually true … But how did Mendel discover this?

Gregor chose pea plants for his experiment, why you ask? Well, because of the following factors: they have numerous distinct varieties; control of pollination; high proportion of successful germinations.

He bred green peas and yellow peas both from a pure line (inbred line of genetic decent where characteristics are seen in successive generations.)

This diagram may seem shocking at first but when you look at the science it makes total sense:

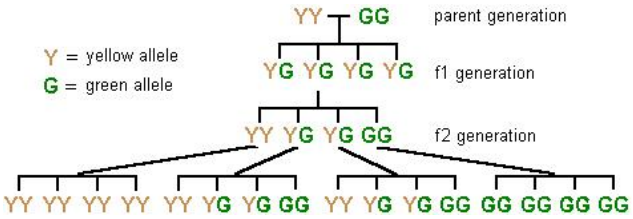


The F1 offspring have both yellow and green colour alleles for the colour gene. The fact that they are yellow proves that yellow is dominant, and green is recessive. In the F2 offspring, 25% are green coloured as they receive a green allele from both parents! Therefore the hypothesis that Mendel produced was that:

-Offspring inherits a version of a gene from each parent

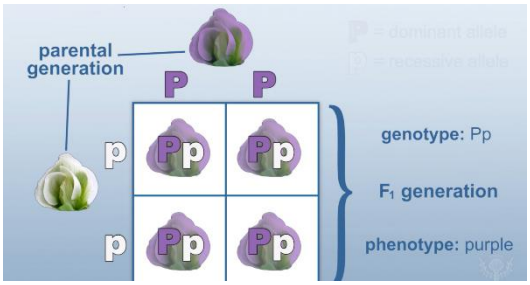
-There are recessive and dominant genes

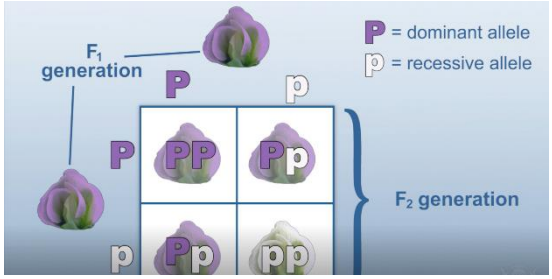
This was a revolutionary discovery!



Let's look at some more tests he did with the pea plants to prove his theory…

White and purple flowers. Same concept, different characteristic… Here you can see the demonstration of what is known as a Punnett square…





From 1854 onwards, Mendel continued to experiment with the pea plant and its many varieties.

He published his experiment in 1866 but it was largely ignored until 1900! Sadly he passed away before it was recognised…

Thank you, Gregor, you truly are the father of genetics!

GREGOR MENDEL

Thomas Prosser (Year 10)

Gregor Johann Mendel was a scientist, Augustinian friar and abbot of St. Thomas' Abbey in Brno, Margraviate of Moravia. Mendel was born in a German-speaking family in the Silesian part of the Austrian Empire he was born on the 20 July 1822 and died of kidney inflammation on the 6th of January 1884.

Some more facts about Mr. Mendel:

- He worked as a gardener and studied beekeeping in his childhood.
- He is an alumnus of what today is known as Palacký University, Olomouc.
- He took the name Gregor upon entering religious life.
- Despite attempting twice, he failed to become a certified teacher.

Mendel's experiment

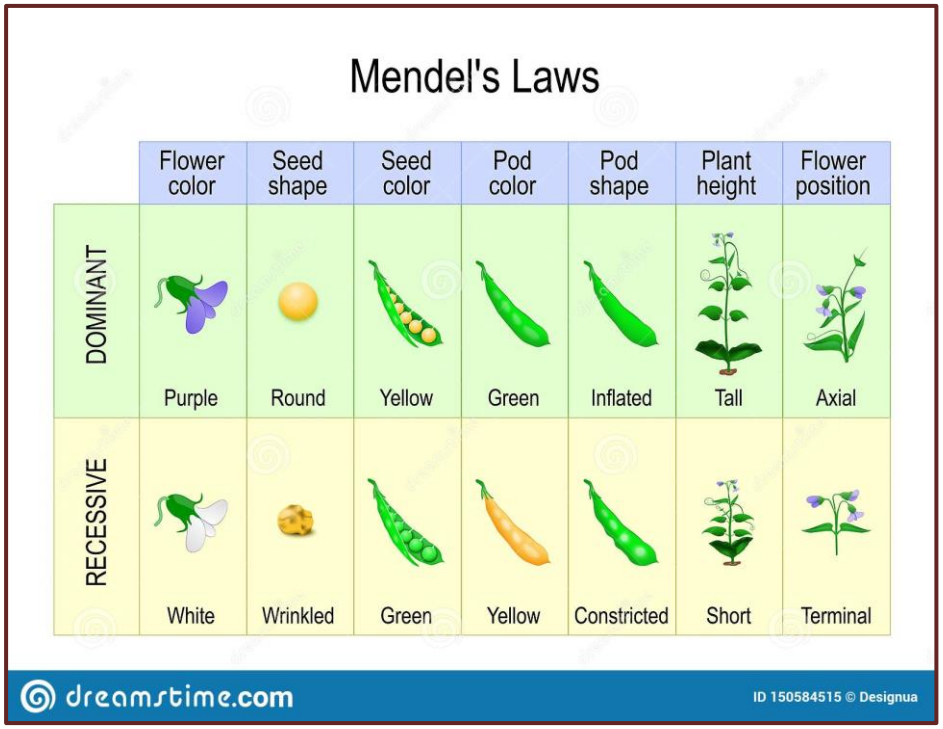
Mendel discovered the basic principles of heredity through experiments in his monastery's garden. His experiments showed that the inheritance of certain traits in pea plants follows particular patterns, subsequently becoming the foundation of modern genetics and leading to the study of heredity.

For his experiments, Mendel selected pea (Pisum sativum) plant because numerous varieties of peas with many different traits (hereditary characteristics) were available. Pea was easy to cultivate, easy to breed and produced new generations within a reasonably short time.

In order to test his hypothesis, Mendel predicted the outcome of a breeding experiment that he had not carried out yet. He crossed heterozygous round peas (Rr) with wrinkled (homozygous, rr) ones. Mendel did not stop there. He went on to cross pea varieties that differed in six other qualitative traits.

In one of his early experiments, Mendel pollinated a purple-flowered plant with pollen from a white-flowered plant. We call the plants from the pure lines the parental generation (P).

The definition of a pure line is a result of inbreeding where animals or plants have certain characteristics that are the same through generations.



GREGOR MENDEL

Rosie Hayes (Year 10)

Who was Mendel and where did he live?

Gregor Mendel was an Austrian monk who discovered the basic principles of genetics through experiments in his garden. His observations became the basis of modern genetics and the study of heredity. Mendel had lived in Brno, Czech Republic.

Why the pea experiment?

Mendel chose to use peas for his experiments because:

- there were many distinct varieties
- offspring could be quickly and easily produced
- it could be experimented with quickly

what happened when he crossed purple flowers with white flowers?

In his first experiment, Mendel cross-pollinated two true-breeding plants of contrasting traits, purple and white flowered plants. The parent plants are referred to as the P generation (parental generation). The offspring of the P generation are called the F1 generation (first filial generation). The offspring of the F1 generation are called the F2 generation (second filial generation). When Mendel did his experiment, the F2 generation was 75% purple-flowered plants and 25% white-flowered plants.

Mendel's hypothesis and outcome

Mendel's hypothesis contained the following:

- There is a pair of factors that controls the appearance of a given characteristic.
- The organism inherits these factors from its parents, one from each.
- A factor is transmitted from generation to generation as a discrete unit.
- When the gametes are formed, the factors separate and are distributed as units to each gamete.

Why was Mendel's work not accepted?

By experimenting with pea plants, Mendel avoided the appearance of unexpected traits in offspring that might occur if the plants were not true breeding. His work was ignored because it was not widely spread, and he didn't make an effort to promote himself.

The fact that Mendel's work failed to receive the attention that it deserved provides an example of how highly original innovators go practically unnoticed until after their death. Only later when their work is rediscovered, or re-evaluated, do they get the credit denied them during their lifetime.

Mendel's seminal paper *"Versuche über Pflanzenhybriden"* ("Experiments on Plant Hybridization") was published in 1866 in *Verhandlungen des naturforschenden Vereines in Brünn* (Proceedings of the Natural History Society of Brünn), hardly a publication that would attract much attention around the rest of Europe.

In 1859 in England Charles Darwin had published his theory of evolution in *"On the Origin of Species"*. Just imagine if he had become aware of Mendel's later work – perhaps the Science of Genetics would have emerged much earlier than it eventually did.

Also in the history of Genetics, there is another person who made a most significant contribution to a completely new discovery and yet received scarce acknowledgment at the time, to the point that some believe that their contribution was deliberately excluded from all publicity. The time was 1953 and the discovery was the 3-D structure of DNA, the biological molecule, present in all cell nuclei, that holds the *genes* that Mendel had predicted would be the 'particles' that carried inheritance from one generation to the next.

The name of that person is **ROSALIND ELSIE FRANKLIN**.

In 1952, at Kings College in London, she produced an X-ray crystallography image (the famous 'Photo 51') of the DNA molecule that proved its structure: a double-helix made of ribose-phosphate units, with pairs of bases (adenine+thymine; cytosine+guanine) strung in between, 10 base pairs per turn of the helix. Unknown to Rosalind at the time, James Watson and Francis Crick, working in Cambridge, acquired her photograph and used its information themselves when they published their work on DNA in 1953. Watson and Crick, along with Maurice Wilkins (Rosalind's boss in London), received the Nobel Prize later, paying hardly any tribute to Rosalind Franklin at all. What is even sadder is that by the time of the Nobel Prize award, 1962, Rosalind had died from ovarian cancer.

At least now, at last, she is receiving the recognition that she deserves.

JOHANN GREGOR MENDEL (1822 – 1884)

Ismail Sanneh (Year 10)

Gregor Mendel, through his work on pea plants, discovered the fundamental laws of inheritance. He deduced that genes come in pairs and are inherited as distinct units, one from each parent. Mendel tracked the segregation of parental genes and their appearance in the offspring as dominant or recessive traits. He recognized the mathematical patterns of inheritance from one generation to the next. Mendel's Laws of Heredity are usually stated as:

1) The Law of Segregation: Each inherited trait is defined by a gene pair. Parental genes are randomly separated to the sex cells so that sex cells contain only one gene of the pair. Offspring therefore inherit one genetic allele from each parent when sex cells unite in fertilization.

2) The Law of Independent Assortment: Genes for different traits are sorted separately from one another so that the inheritance of one trait is not dependent on the inheritance of another.

3) The Law of Dominance: An organism with alternate forms of a gene will express the form that is dominant.

The genetic experiments Mendel did with pea plants took him eight years (1856-1863) and he published his results in 1865. During this time, Mendel grew over 10,000 pea plants, keeping track of progeny number and type. Mendel's work and his Laws of Inheritance were not appreciated in his time. It wasn't until 1900, after the rediscovery of his Laws, that his experimental results were understood.

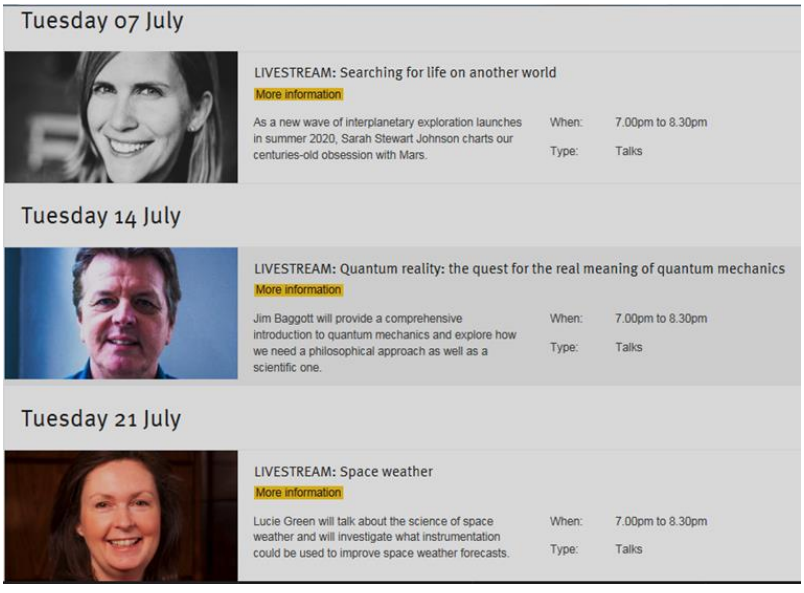
Ri The Royal Institution
Science Lives Here

While we all accepted the need for the 'lockdown' and 'social distancing' in order to combat the threat of COVID-19, it has been a shame that all our Museums have had to close their doors. Many have responded by expanding their output online and via social media.

One excellent example is the world famous **ROYAL INSTITUTION** in London. They are renowned for their programme of weekly, evening lectures in their magnificent auditorium – culminating in the series of Christmas Lectures. Since attending lectures has been impossible, the Ri started scheduling livestreams every Tuesday evening 19:00-20:30.

They are intended for a general audience of all ages and topics have ranged from 'How the Brain Works' to the 'History of the Universe', all delivered by a world-class array of speakers.

Coming up in July:



Watch out for more livestreams throughout the Summer and Autumn at .....

https://www.rigb.org/whats-on/events-2020/livestreams

The Ri has a fantastic history dating back to 1799 when it was founded. Follow the story, including the amazing people that have been involved, such as Humphry Davy and Michael Faraday at the outset, using an interactive timeline at ....

https://www.rigb.org/our-history/timeline-of-the-ri

GREGOR MENDEL

Emil Cheriyan (Year 10)

Who was Mendel?

- Gregor Johann Mendel (20 July 1822[2] – 6 January 1884) was a scientist. Mendel was born in a German-speaking family in a part of the Austrian Empire (today's Czech Republic) and gained recognition as the founder of the modern science of genetics. Though farmers had known for millennia that crossbreeding of animals and plants could favor certain desirable traits, Mendel's pea plant experiments conducted between 1856 and 1863 established many of the rules of heredity, now referred to as the laws of Mendelian inheritance.
- Mendel worked with seven characteristics of pea plants: plant height, pod shape and color, seed shape and color, and flower position and color. Taking seed color as an example, Mendel showed that when a true-breeding yellow pea and a true-breeding green pea were cross-bred their offspring always produced yellow seeds. However, in the next generation, the green peas reappeared at a ratio of 1 green to 3 yellow. To explain this phenomenon, Mendel coined the terms "recessive" and "dominant" in reference to certain traits. (In the preceding example, the green trait, which seems to have vanished in the first filial generation, is recessive and the yellow is dominant.) He published his work in 1866, demonstrating the actions of invisible "factors"—now called genes—in predictably determining the traits of an organism.

Why did Mendel choose pea plants for his investigation?

Mendel selected garden pea plant for his experiments because of the following characteristics:
(i) The flowers of this plant are bisexual.
(ii) They are self-pollinating, and thus, self and cross pollination can easily be performed.
(iii) The different physical characteristics were easy to recognise and study.
(iv) They have a shorter life span and are the plants are easier to maintain.
(b) According to Mendel's law of independent assortment, during the inheritance of two or more characters, the assortment of individual traits takes place independently during gamete formation. Thus each allele of a pair segregates independently and each gamete formed contains one allele of that trait. This law is inapplicable for linked genes.

What is meant by the term 'pure line'?

The definition of a pure line is a result of inbreeding where animals or plants have certain characteristics that are the same through generations. An example of a pure line is the result of inbreeding of a certain flower to help it fight off diseases.

What happened when Mendel crossed pure-breeding purple flowers with white flowers and What hypothesis did Mendel produce?

In his first experiment, Mendel cross-pollinated two true-breeding plants of contrasting traits, such as purple and white flowered plants. The true-breeding parent plants are referred to as the P generation (parental generation). The hybrid offspring of the P generation are called the F1 generation (first filial generation). The hybrid offspring of the F1 generation are called the F2 generation (second filial generation). The F2 generation plants that grew included white-flowered plants. Mendel noted the ratio of white flowered plants to purple-flowered plants was about 3:1. That is, for every three purple-flowered plants, there was one white flowered plant. Figure below shows Mendel's results for the characteristic of flower color.

Mendel carried out identical studies over three generations, (P, F1, and F2), for the other six characteristics and found in each case that one trait "disappeared" in the F1 generation, only to reappear in the F2 generation. Mendel studied a large number of plants, as shown in Table below. His use of statistics to demonstrate the repeated 3:1 ration of traits. Because of the repeatable nature of his findings, Mendel was confident that the ratios of different traits in the F2 generation were representative. As shown in the table, Mendel called the trait that appeared in the F2 75% of the time the dominant trait, and the trait that reappeared in the F2 the recessive trait.

What evidence is there of reproducibility of Mendel's results?

- In 1900 Hugo de Vries, Carl Correns, and Erich Tschermak von Seysenegg, who independently popularized and extended the studies.1900: Rediscovery of Mendel's Work
- Three botanists - Hugo DeVries, Carl Correns and Erich von Tschermak - independently rediscovered Mendel's work in the same year, a generation after Mendel published his papers. They helped expand awareness of the Mendelian laws of inheritance in the scientific world.
- The three Europeans, unknown to each other, were working on different plant hybrids when they each worked out the laws of inheritance. When they reviewed the literature before publishing their own results, they were startled to find Mendel's old papers spelling out those laws in detail. Each man announced Mendel's discoveries and his own work as confirmation of them.
- By 1900, cells and chromosomes were sufficiently understood to give Mendel's abstract ideas a physical context.

GREGOR MENDEL

Elinor Hurry (Year 10)

Gregor Mendel, now known as the "father of modern genetics", was an Austrian Monk who discovered the basic principles of heredity through experiments in his garden. Mendel's observations became the foundation of modern genetics and the study of heredity.

Early Years

Gregor Johann Mendel was born Johann Mendel on the 22nd of July 1822, to Anton and Rosine Mendel, on his family farm, in what was then Heinzendorf, Austria. He spent his early years in that rural setting until a local schoolmaster was impressed by his aptitude for learning at age 11. The schoolmaster recommended Mendel to continue his studies at a secondary school in Troppau. In 1840, he graduated from the school with honours.

Following his graduation Mendel enrolled in a two-year program at the Philosophical Institute of the University of Olmutz. Again Mendel distinguished himself academically, particularly in the subject's physics and maths. In 1843 Mendel graduated from the program despite having suffered from deep bouts of depression that had caused him to abandon his studies more than once.

That same year against his father's wishes, who expected him to take over the family farm, Mendel began to study to be a monk. He joined the Augustinian order at St. Thomas Monastery in Brno, and was given the name Gregor. Mendel was immediately exposed to the research and teaching of its members and also gained access to the monastery's extensive library and experimental facilities as at the time the monastery was a cultural centre for the region.

In 1851, Mendel was sent to the University of Vienna – after his work in the community in Brno exhausted him to the point of illness in 1949 and him failing a teaching-certification exam the following year – to continue his studies in the sciences at the monastery's expense. Mendel studied physics and mathematics under Christian Doppler, after whom the Doppler effect of wave frequency is named. He studied botany under Franz Unger, who had begun using a microscope in his studies.

In 1853, upon completing his studies at the University of Vienna, Mendel was given a teaching position at a secondary school where he would stay for more than a decade. It was during this time that he began the experiments he is best known for.

Experiments and Theories

Around 1854, Mendel began to research the transmission of hereditary traits in plant hybrids. At the tie of Mendel's studies, it was a generally accepted fact that the hereditary traits of the offspring of any species were merely the diluted blending of whatever traits were present in the "parents". It was also commonly accepted that, over generations, a hybrid would revert to its original form, the implication of which suggested that a hybrid could not create new forms. However, the results of such studies were often skewed by the relatively short period of time during which these experiments were conducted, whereas Mendel's research continued over a 7 year period: between 1856 and 1863, and involved tens of thousands of individual plants.

Mendel chose to use peas for his experiments due to their many distinct varieties (7 of which he could manipulate), and because offspring could be quickly and easily produced. He began his experiments on peas with two conditions: 1) possess constant differentiating characteristics and 2) hybrids of such plants, during flowering period, be protected from the influence of all foreign pollen. The second condition was to prevent any accidental impregnations that would cause misleading results.

Mendel planned to selectively cross pollinate the peas with one another to study the traits passed on and the results from each pollination. He acquired about 32 varieties of peas and chose 22 different types to conduct his experiments with which varied in colour and size. He took years of breeding constant family line to perfect the original constant traits.

Mendel used seven pea plant traits in his experiments which included flower colour (purple or white); flower position (axil or terminal); stem length (short or long); seed shape (round or wrinkled), seed colour (yellow or green); pod shape (inflated or constricted) and pod colour (yellow or green). The first generation of the hybrids produced a 3:1 ratio where there were 3 plants showing the dominant traits and 1 showing

the recessive traits. The second generation produces a 2:1:1 ratio. This showed there was one with the recessive trait, two with hybrid trait and one with dominant trait.

When crossing a green pod plant and a yellow pod plant, the first generation (F1) would produce only green plants (given green was the dominant trait colour). But then the second generation (F2) produced a quarter yellow pea pods. These experiments allowed Mendel to conclude on two laws of Inheritance: the Law of Segregation and the Law of Independent Assortment.

What is meant by the term "pure line"?

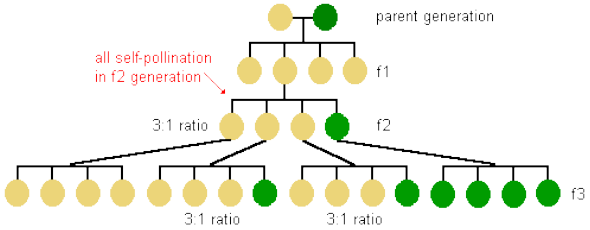
A pure line is a result of inbreeding where animals or plants have certain characteristics that are the same through generations. An example of a pure line is the result of inbreeding of a certain flower to help it fight off diseases.

The Principle/Law of Segregation, Mendel's "First Law"

Mendel concluded on this law after finding when breeding white and purple coloured flowered plants it was not a mix of the two colours, but really one colour was chosen over the other. There are four different parts of the law he included:

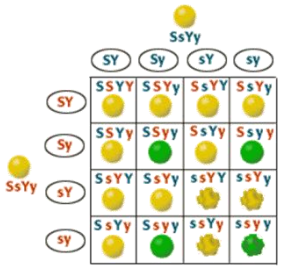
1. There are other forms of genes that can determine the heritable traits, alleles.
2. Each offspring receives one allele from each parent.
3. Either a sperm or egg holds only one allele for each trait and those pair during fertilisation.
4. If the alleles are different one is seen and the other is not as one trait is dominant and the other is recessive.

The law is a direct result from watching the production of the F2 generation and the production of the 2:1:1 ratio. The recessive traits only came when those were the only two being bred with each other.



The Principle/Law of Independent Assortment, Mendel's "Second Law

Mendel decided different pairs of alleles are passed on as individuals and not based upon each other. Mendel saw various combinations, which indicated all of the alleles are segregated from one another. When Mendel began mixing two traits and conducting dihybrid crosses he found a 9:3:3:1 ratio. Unless the traits are linked he concluded various traits are inherited independently and have no relation.



Mendel's Hypothesis:

1. In the organism there is a pair of factors that controls the appearance of a given characteristic. (We call the 'genes')
2. The organism inherits these factors from its parents, one from each.
3. Each is transmitted from generation to generation as a discrete, unchanging unit.
4. When the gametes are formed, the factors separate and are distributed as units to each gamete. This statement is often called 'Mendel's Rule of Segregation.
5. If an organism has two unlike factors (we call the 'alleles') for a characteristic, one may be expressed to the total exclusion of the other (dominant v recessive).

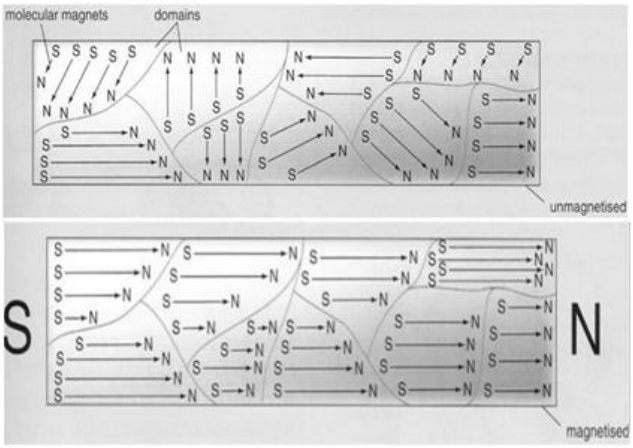
MAGNETISM

Arvin George (Year 10)

OVERVIEW

A magnet is any material that exhibits magnetic properties. This includes their dipolar nature (they have a north and south), attraction to an exclusive group of metals and between opposite poles of separate magnets (north and south) as well as repulsion between opposite poles. A few of the several magnetic metals include Nickel, Cobalt, Iron, Neodymium and Chromium. Materials that can retain their magnetic properties without the need of an external magnetic field are known as ferromagnets (magnetically hard) whereas metals that can only retain magnetic properties while in an external magnetic are known as paramagnetic (magnetically soft). Diamagnetism is a form of magnetism found in all materials. It repels magnetic fields and any magnetic field applied to them creates an induced magnetic field in the opposite direction. An element is only called diamagnetic if there are no other effects on the material unlike in a ferromagnetic or paramagnetic metal where the respective forces overcome the diamagnetic ones.

DOMAIN THEORY

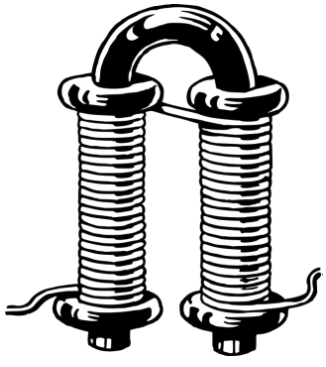


The reason magnetism is exclusive to a set group of materials is explored in domain theory. Domain theory states that within any of the magnetic materials ,whether or not they are currently totally magnetised, there exists small numbers of magnetised atoms aligned with one another in domains or cells within the structure of the elements. In an unmagnetised metal although the domains are aligned within themselves they are not aligned to one another. This causes the overall magnetism to cancel itself out as the magnetic fields are oriented differently. This can change, however, if all domains are aligned and oriented in the same direction; the individual magnetic fields of the domains will sum to a greater field completely magnetising the material. Iron, Nickel, Cobalt and Gadolinium are the only ferromagnets that can become permanent magnets at room temperature due to their unique structure and electronic configuration. Any interference in the alignment of the domains causes a reduction of the capabilities of the magnet. This interference could take the form of thermal energy, where the increased vibrations of the particles misalign the domains (A magnet will completely lose its magnetism at its individual Curie Temperature), or an opposing magnetic field.

CREATING MAGNETS

To create magnets all you have to do is align the magnetic domains of the said material throughout the structure, creating a unified magnetic field. There are multiple ways of doing this.

Electricity



There are several ways of creating magnets. This includes running an electric current through a conductor, creating an electromagnet. This occurs because a moving electron creates a magnetic field forcing the domains to align and therefore magnetise them. The magnetic fields of an electric current also explain the existence of naturally 25occurring magnets that do not require contact methods from other magnets. Lodestones, for example are found near the surface but are too strong to be magnetised by the Earth's field; a strong theory is that they were magnetised by lightning bolts and their corresponding magnetic field. A similar story can be applied to Earth's magnetic field as it is generated by electric currents produced in the molten convection currents located in the Earth's outer core.

Contact Methods

There are two main contact methods which include single touch and double touch. Single touch is where a permanent magnet is rubbed over a ferromagnetic material in a single direction to align the domains. This is easily demagnetised and will fade with time as electromagnetic fields and heat interfere with the alignment of the domains. The other contact method is double touch where two magnets are moved along a ferromagnetic material in opposite directions with opposite poles.

Industrial Practices

The industrial process of manufacturing magnets operates on the same principle as standard contact methods but with a greater control over each step of the process and a greater density of material. To begin with appropriate amounts of metal are heated and fused in a vacuum to avoid any reaction with the air that could contaminate the alloy. The metal is then powdered into small pieces and aligned with a magnetic field. It is then pressurised at a typical 10000 psi and heated just below the alloys melting point to allow the particles to fuse. The finished product is then exposed to a magnetic field for a period of time to magnetise it. The magnet is much more densely compacted leading to a greater amount of domains in one area and therefore a greater magnetic field.

DESTROYING MAGNETS

To destroy a magnet all you have to do is create a misalignment in the arrangement of the domains. There are multiple ways you can do this.

AC Current

The alternating nature of AC current forces the magnetic domains to change direction continuously, disrupting their alignment and therefore cancelling out the magnetic field.

Opposing Magnetic field

An opposing magnetic field will force other domains out of position if it is strong enough.

Physical Damage

Hammering and the practice of bending the magnet out of shape can severely weaken the magnetism as it once again allows the domains to break free from their alignment and reduce the effect of the overall magnetism.

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FUN FACT ABOUT MAGNETS: Did you know – the strongest magnet in the whole Universe is a star?

When in a supernova, a star collapses to a **neutron star** and its magnetic field increases dramatically in strength. However, astronomers have observed that a very small number of neutron stars (about 20 in total) appear to generate a monumental magnetic field, many thousands of times stronger than usual – these objects are called **MAGNETARS**.

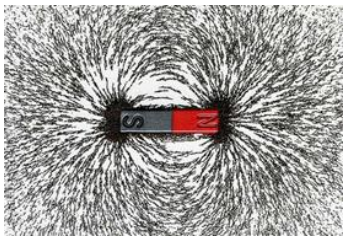
The SI unit of Magnetic Flux Density is the *tesla* (T). Our planet Earth's magnetic field is around 5 microteslas, whereas a Magnetar's field strength is around 100 billion teslas!

https://www.nasa.gov/missions/deepspace/f_magnetars.html

Adrian Smith-Delgado

Magnets

A brief introduction



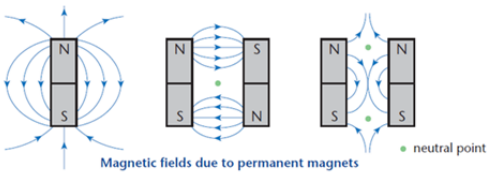
Magnets, are put simply any material/object that has the ability to produce a magnetic field (a region where other magnets or magnetic materials are able to experience a non-contact force), or be attracted to one magnets can either be classified as induced or permanent magnets.

Magnets have two poles, the "north-seeking" [North] pole and the "south-seeking" [South] pole. The magnetic field is always strongest at the polar ends of the magnet.

Permanent magnets are magnets which consist of a material that has previously been magnetized and by itself has the ability to create a continuous and lasting magnetic field.

Iron, nickel and cobalt are examples of pure elements which are ferromagnetic (this means that they are able to form permanent magnets), other ferromagnetic materials include some alloys such as steel and minerals such as lodestone.

The other classification of magnets: induced magnets, include magnetic objects/materials which when placed in the proximity of a magnetic field are able to act in the way a magnet does.



Magnetic fields due to permanent magnets

The force between permanent and induced magnets is always attractive, however when the magnetic field is removed, induced magnets rapidly lose (most, if not all) their magnetism and lost the ability to produce a magnetic field.

If two poles of a magnet are placed in close proximity of one another, the exert forces one each other, either repulsive or attractive. Two like poles repel, while two opposite poles attract.

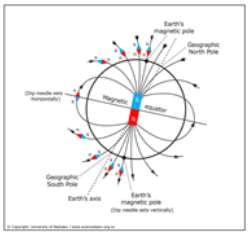
The discovery of magnets… (and the compass)

It would be irrational to state that magnets were invented, instead their qualities were discovered from a naturally occurring mineral called magnetite.

Many sources state that it was the ancient Greeks who discovered magnetite. However, there are alternate sources which states that magnetite was discovered in a region of Macedonia called Magnesia.

The Greeks discovered naturally occurring magnets of magnetite in Turkey. Magnetite forms spontaneously all over the world, but there are relatively large deposits in Scandinavia.

The Vikings patented the first practical magnetic compass and used it extensively in their travels/colonisation and wars. This enabled them to cross oceans to reach the new world and to invade the British isles with relative ease.



The Vikings kept the existence of the magnetic compass a secret, so as not retain the upper hand, but the Chinese also invented the magnetic compass, presumably much earlier than the Vikings. [*Other sources also state records of magnets and their properties from India and Greece dating back around 2500 years]*

After commercial trade with China was established by the Italians, especially after Marco Polo's ventures around the regions, the magnetic compass was introduced to the rest of Europe. This made possible the exploration of the oceans by the Europeans, even though the Scandinavian voyages had enjoyed this technical superiority for upwards of 500 years.

Today all ships large and small use magnetic compasses to navigate, many aircraft from the first world war onwards used compasses for crude and primitive navigation until the GPS rendered them obsolete.

The mineral magnetite is an iron oxide that is easily magnetized when it forms. Magnetite is also known as Lodestone.

How does a compass work?

Modern day compasses have experience relatively little practical change from their predecessors, remaining the primitive, yet robust form of basic navigation.

Inside a compass is a small bar magnet, the north experiences attraction to the south pole of any magnet it is in close proximity of, thus the compass points in the direction of the magnetic field it is in, when not near a magnet, compasses typically point north, due to the fact that the earth is able to generate its own magnetic field, this is what led to the discovery that the Earth's core must be magnetic.

Creation and destruction of magnets/magnetism

Basic Explanation to creating magnets:

To manufacture a magnet, large corporations may melt iron and place it in the close proximity of a strong magnetic field while it cools. Thus, the magnetic field created inside the iron, are able to freely align=n themselves with the outside magnetic field, this process bears the name of: magnetic induction. Magnetic induction can also be conducted outside of the manufacturing environment, it can be done easily in a small-scale form by stroking an iron nail with a bar magnet, which induces a magnetic field in the iron nail: leaving a magnet.

In-depth Explanation (large manufacturing corporation method):

Magnet manufacturing Process

In the manufacturing environment there are numerous processes/methods used to produce magnets, however the typical "powder metallurgy" is the method used. This is where a suitable composition is grounded down into an extremely fine powder, compacted and heated to cause densification (an industrial process that increases the density of something, also referred to as compaction, this is a physical process that can occur naturally whereby sediments are compacted and combined) via "liquid phase sintering". Therefore, these magnets bear the name of sintered magnets. Types of magnet produced using this method include: Ferrite, Samarium Cobalt (SmCo) and neodymium-iron-boron.

How Samarium Cobalt and Neodymium Magnets are made

Materials are melted down in a vacuum or in an inert (unreactive) gas in an induction melting furnace. The molten alloy is either poured into a mould, onto a chill plate, or processed in a strip caster (a machine that produces an extremely thin, continuous metal strip). These cured metal "chunks" are grounded up and fined down to form a fine powder ranging from around 5 micrometres in diameter (a micrometre is around 0.001 millimetres). The product: a fine powder which is highly chemically reactive, capable of spontaneously igniting/combusting in air and therefore protected from exposure to air. This powder is then compressed into large parts. Pressed parts are packaged in moulds ready to be loaded into a vacuum sintering furnace. The particular temperatures and presence of vacuum or inert gas is corresponding to the type and grade of magnet being produced. Both rare earth materials (that makeup both samarium cobalt and neodymium magnets) are heated to a sintering temperature and allowed to densify. During sintering and the process of increasing the density of the magnets, the magnets shrink about 15-20% linearly. Completed magnets have a rough surface and only approximate dimensions, they still do not exhibit an external magnetic field.

Magnetising

After the manufacturing process is finished, the magnet needs to be "charged" in order to be able to produce an external magnetic field. This can be accomplished by the use of a solenoid – a hollow cylinder into which various magnet sizes and shapes can be placed – or instead by employment of fixtures which have the role of imparting unique magnetic patterns.

Magnetic Stabilisation and Calibration

Occasionally, magnets may require stabilization or calibration. Stabilisation is a process of pre-treating the magnets, during and after assembly, in a way that any subsequent use will not result in loss of flux output. Calibration is used to limit down and cap the performance output range of magnets. There are several factors that affect stabilisation and it's vital that this process is regulated with utmost attention to ensure the final product has high-quality performance.

Basic Explanation to destroying magnets:

Magnets can also be destroyed , by removing the magnets magnetic properties. For example: you can heat the magnet up and strike it with a hammer repeatedly, the magnetically aligned atoms easily move out of their arrangements due to the energy provided to the atoms by the thermal energy of the heating process, which once again cancels out the magnetic fields.

Magnetism

In 1820, Hans Christian Ørsted - a Danish physicist born in 1777, during his preparation for a lecture, he discovered that a compass needle would deflect when brought in close proximity of a live electrical wire, people at the time were already aware to the fact that the electric force existed, but any connection between magnetism and electricity seemed revolutionary.

However it took 45 years till James Clerk Maxwell, after producing the electromagnetic theory of light, was able to develop a full explanation of this phenomenon.

Maxwell had shown that a magnetic field is produced by a flowing electrical charge, to put it simply: this occurs due to the fact that an electric current is the movement of electrical charges, this gives us the ability to create electromagnets (or long wires wounded to a coil), this way the magnetic field created by a single wire is amplified and multiplied by the number of turns, electromagnets have the advantage of being able to be switched on and off at will.

However in permanent magnets, which don't possess any electric currents flowing through them, magnetic fields are created (put simply) by:

- The orbit of the nucleus completed by the electron, even though the model that the electron orbits the nucleus has long been proven wrong, it is still a legitimate approximation, and can still be used to explain certain properties/characteristics of the atom, (which is important in the following points)
- The "spin magnetic moment", this a term that states that an electron acts in a way resemble of a magnet, the spin magnetic moment is also a fundamental property of matter, like charge and mass
- Nuclear Spin

The question that subsequently arises, it why don't all object possess magnetic properties, since everything is made up of atoms, and thus orbiting electrons, and these electrons should all have a spin magnetic moment, however it has to be taken into consideration that there are numerous electrons even in the most miniscule of amounts of materials, and the magnetic fields created by these electrons typically cancel out.

Magnetic Field

As previously mentioned magnetic fields are generated by electric currents, which can be macroscopic currents in wires or instead microscopic currents associated with electrons in atomic orbits. The magnetic field B (as shown in the Lorentz Force Law) is defined in terms of force on moving charge in the Lorentz force law. The interaction of a magnetic field with charge leads to numerous extremely useful practical applications. Magnetic field sources are dipolar in nature, consisting of both a north and south magnetic pole. The international-accepted unit for magnetic field is the Tesla, which can be found from the magnetic part of the Lorentz force law $F_{mag} = qvB$.

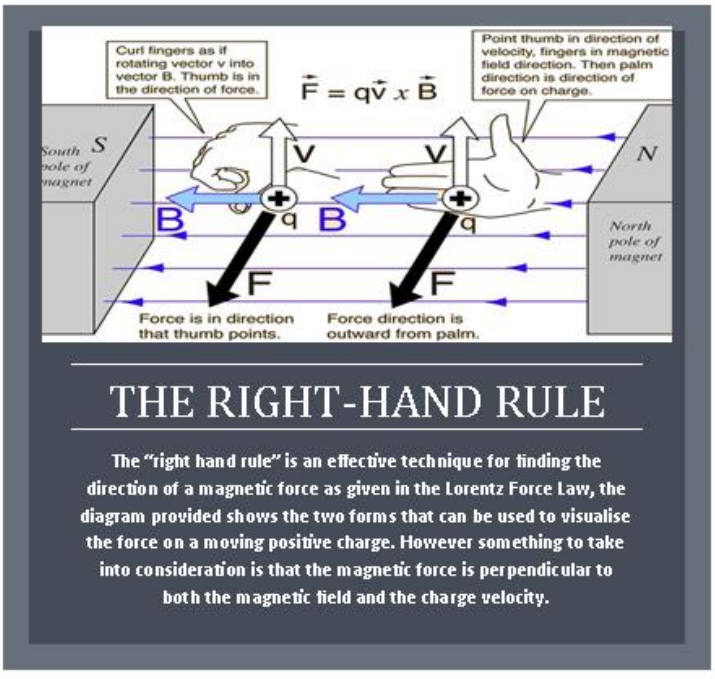
Lorentz Force Law

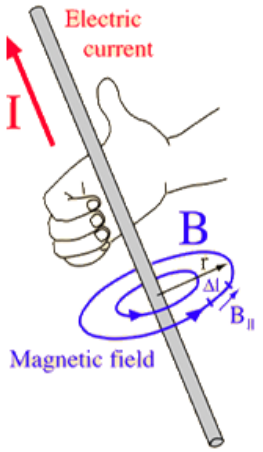
Both the electric field and magnetic field can be defined from the Lorentz force law:

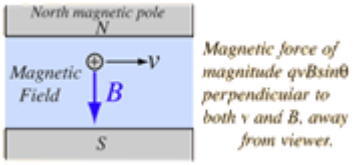
$$\vec{F} = q\vec{E} + q\vec{v} \times \vec{B}$$

Electric force — Magnetic force

The electric force is straightforward, being in the direction of the electric field if the charge q is positive, but the direction of the magnetic part of the force is given by the right hand rule.







The Magnetic Field of Current

The magnetic field lines around a long wire which carries an electric current form concentric circles around the wire, The direction of the magnetic field is perpendicular to the wire and is in the direction the fingers of your right hand would curl if you wrapped them around the wire with your thumb in the direction of the current.

The magnetic field of an infinitely long straight wire can be obtained by applying Ampere's Law.

The expression for the magnetic field is:

$$B = \frac{\mu_0 I}{2\pi r}$$

Ampere's Law takes the form: $\sum B_{||} \Delta l = \mu_0 I$

And for a circular path centred on the wire, the magnetic field is everywhere parallel to the path. The summation then becomes just:

$$\sum B_{||} \Delta l = B 2\pi r$$

$$B = \frac{\mu_0 I}{2\pi r}$$

Bar Magnet

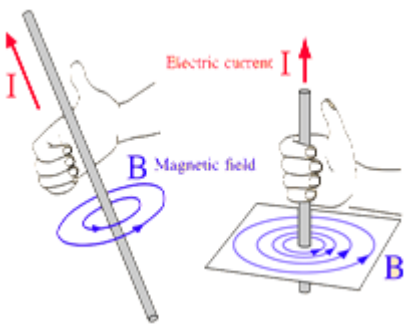
The lines of magnetic fields from a bar magnet form closed lines. By convention, the field direction is taken to be outward from the North pole and in to the South pole of the magnet. Permanent magnets can be made from ferromagnetic materials.

As can be visualized with the magnetic field lines, the magnetic field is strongest inside the magnetic material. The strongest external magnetic fields are near the poles. A magnetic north pole will attract the south pole of another magnet, and repel a north pole.

The magnetic field lines of a bar magnet can be traced out with the use of a compass. The needle of a compass is itself a permanent magnet and the north indicator of the compass is a magnetic north pole. The north pole of a magnet will tend to line up with the magnetic field, so a suspended compass needle will rotate until it lines up with the magnetic field. Unlike magnetic poles attract, so the north indicator of the compass will point toward the south pole of a magnet. In response to the Earth's magnetic field, the compass will point toward the geographic North Pole of the Earth because it is in fact a magnetic south pole. The magnetic field lines of the Earth enter the Earth near the geographic North Pole.

Magnetic Field of the Earth

The Earth's magnetic field similar to that of a bar magnet titled 11 degrees from the spin axis of the Earth. The problem with that picture is that the Curie temperature of iron is about 770 C . The Earth's core is hotter than that and therefore not magnetic.



The Earth's magnetic field is attributed to a dynamo effect of circulating electric current, but it is not constant in direction. Rock specimens of different age in similar locations have different directions of permanent magnetization. Evidence for 171 magnetic field reversals during the past 71 million years has been reported.

Although the details of the dynamo effect are not known in detail, the rotation of the Earth plays a part in generating the currents which are presumed to be the source of the magnetic field. Mariner 2that Venus does not have such a magnetic field although its core iron content must be similar to that of the Earth. Venus's rotation period of 243 Earth days is just too slow to produce the dynamo effect.

Interaction of the terrestrial magnetic field with particles from the solar wind produce the conditions for the aurora phenomenon near the poles.

The north pole of a compass needle is a magnetic north pole. It is attracted to the geographic North Pole, which is a magnetic south pole (opposite magnetic poles attract).

NMR SPECTROSCOPY AND NUCLEAR SPIN

Alex Swarbrick (Year 12)

Introduction to spin

Nuclear Magnetic Resonance or NMR spectroscopy is a technique used in chemical analysis that is able to provide useful information on the chemical environment of certain nuclei by use and measurement of a property called nuclear spin with the use of a strong magnetic field and radiofrequency EM radiation.

Spin is a property present in subatomic particles such as protons, neutrons and electrons that means they have a magnetic moment caused by an intrinsic angular momentum. It is important to note that these particles are not literally 'spinning' in a classical sense. For this to be the case particles would need to be spinning "faster than the speed of light to produce the magnetic moments observed, and furthermore spin is quantised"[3] ; All this combined means that the analogy to 'spin' is a little misleading & a flawed oversimplification of what is actually observed in experiments such as the Stern-Gerlach experiment. We find that subatomic particles adhere to the mathematics of angular momentum, which is the property that gives rise to a nuclei's magnetic moment. As such when referring to 'spin' it is more of a referral to the properties of this intrinsic angular momentum than anything else.

For the purposes of NMR however, we can focus strictly on nuclear spin as a property that gives rise to a proton or neutron having a magnetic moment which correlates to their spin being of values +1/2 or -1/2, or 'spin up' or 'spin down'.

According to Pauli's exclusion principle "two or more identical fermions (particles with half-integer spin) cannot occupy the same quantum state within a quantum system simultaneously". [2] This means that in any given energy level you can have a proton of spin +1/2 and another of spin -1/2, however you cannot have two protons of spin +1/2 within the same energy region. You can however have a proton and neutron of spin +1/2 and another proton and neutron of spin -1/2 in the same energy level.

In NMR we are only interested in nuclei of the likes of C_{13}, N_{15}, F_{19} or P_{31} which have a net spin >0. This table shows the net spins that can arise given the number of **protons(P)** or **neutrons(N)**

Situation	Overall (net) nuclear spin
P+N is **even**	Net spin of ZERO
P+N is **odd**	Nucleus has ½ integer spin (1/2, 3/2, 5/2…)
P+N are **both odd**	Nucleus has integer spin (1, 2, 3…)

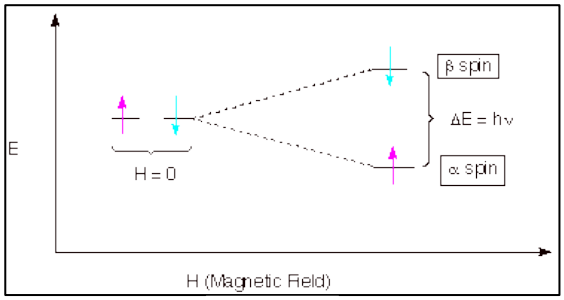
Spin states & energies

A proton with spin generates its own magnetic field & so for our purposes can be thought of as similar to a bar magnet with a magnetic north and south pole. When no magnetic field is applied, the direction of these fields is random and in no fixed direction. Opposite spins exist in states of equal energy and cancel to give a net magnetic field that is virtually zero.

However, if we apply a strong magnetic field B_0, the magnetic moments align in one of two orientations: either with the magnetic field **or** against the magnetic field.

Aligning against the magnetic field requires the proton to be in the higher energy ß spin state (Fig.1).

You can think of it like a compass needle. If a magnet is brought close to a compass, the needle will be attracted to the magnet and point towards it.



(Fig.1)

In order to point the needle away, you need to apply a force from your finger or else the compass needle will swing back towards the magnet.

Due to the energy difference in spin states you will find that there will be slightly more nuclei aligning in the alpha than in the beta spin state. With this we can exploit the fact that we can excite nuclei to the higher energy state through sending either a **sweeping magnetic field** or **pulses of radio frequency (r.f.) radiation**. As excited protons flip back down to the lower energy state, they emit r.f. photons which can be picked up by a receiver and recorded. This process of excitation and relaxation between energy states is known as **resonance**.

The resonance frequency is dependent on the difference in energy between spin states ($\Delta E = hf$) where h is Planck's constant & f is the frequency. ΔE also increases with a stronger magnetic field B_0 and is also dependent on both the magnetic moment of e.g. a proton in ^1H NMR and the chemical environment of the nuclei being observed such as nearby electron withdrawing atoms or groups.

As such $\Delta E = hf = h\gamma B_0/2\pi$, where γ is the magnetic moment of the nuclei being observed. This will be different between ^1H and ^{13}C NMR spectrums and is a number unique to any nucleus.

NMR machines can therefore distinguish between nuclei in two ways:

In the **field sweep method**, the RF signal is held constant and the magnetic field swept. This varies the energy levels between spin states & the magnetic field is found which causes resonance at the fixed frequency. In the **frequency sweep method**, the magnetic field is kept constant & the radio frequencies transmitted are altered to find the frequencies of energy absorption. [4]

In **Fourier transmission (FT) NMR**, which is the more recent & widely used form of NMR, short pulses across a relatively large range of frequencies are sent out followed by a short period of relaxation. This causes excitation to the ß spin state, followed by a release of RF photons which can be picked up by an antenna. The period of relaxation ensures the excess of electrons in the ß spin state is allowed time to relax to their original state. If this time is too short, then the signals picked up would not be as strong.

The use of pulses covering a wide frequency range provides multiple peaks to be detected due to the effect of excitation across a range of nuclei. In order to provide a clear image of the resonant frequency peaks, an NMR spectrum is built up over many pulse & relaxation cycles to create a peak characteristic to certain nuclei.

Building up an image over many pulse & relaxation periods, as opposed to just one reading, ensures noise (e.g. from voltage fluctuations in the receiver) can be greater distinguished from actual resonance peaks. This is because noise is random and evens out, while characteristic peaks are coherent & build-up. [1] This is a significant advantage that FT-NMR has over continuous wave NMR, making it particularly useful for observation of samples where isotopes are in much smaller abundance.

Calculating chemical shift

NMR readings are given on a scale called chemical shift denoted by the Greek letter δ. Chemical shift compares the chemical environments of different nuclei based on their comparative resonance frequencies to a reference compound such as Tetramethyl Silane $(CH_3)_4$ Si

$$\delta = \frac{f_1 - f_{TMS}}{operating\ frequency} \times 10^6\ ppm$$

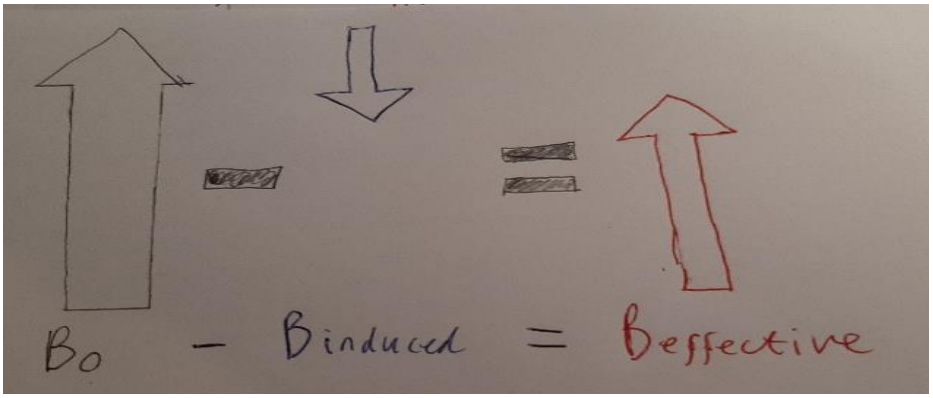
Dividing by the operating frequency ensures that values for δ will be the same **irrespective of the magnetic field strength** of the machine used as frequency is directly proportional to the magnetic field strength. Values for δ are given in ppm as the numerator $f_1 - f_{TMS}$ is in the order of Hz, while the operating frequency is in the order or MHz, thus a value in the order of 10^{-6} is attained & we multiply by 10^6 to give easier numbers to work with.

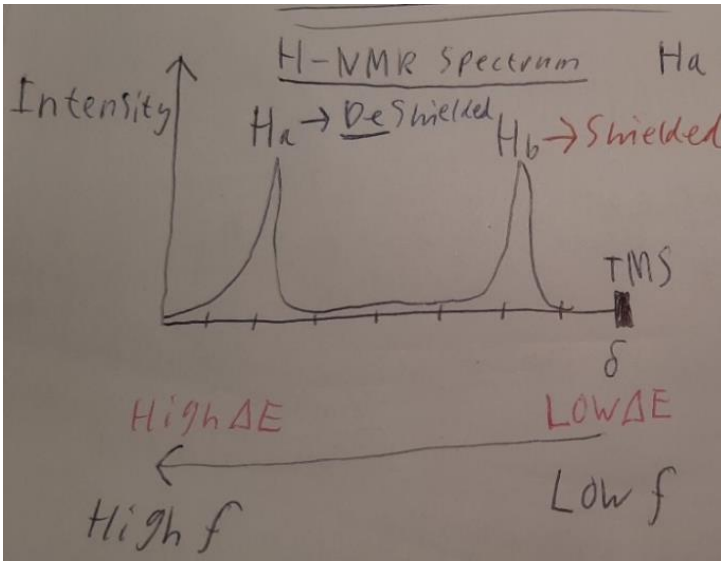
There are differences in values for chemical shift due to slightly different electronic environments around the nucleus that lead to shielding or de-shielding of nuclei from the magnetic field. As such some nuclei experience a greater effective magnetic field and so require a higher energy (and thus a higher frequency) to reach resonance.

Shielding

When a magnetic field is applied, the electrons around a nucleus circulate. This induces a current which in turn induces a magnetic field which is opposed to the applied magnetic field. This means that the effective magnetic field (B_{eff}) on the nucleus itself is reduced and it is said to be shielded. This can be illustrated by magnetic field vectors and the equation:

$$B_{effective} = B_0 - B_{induced}$$



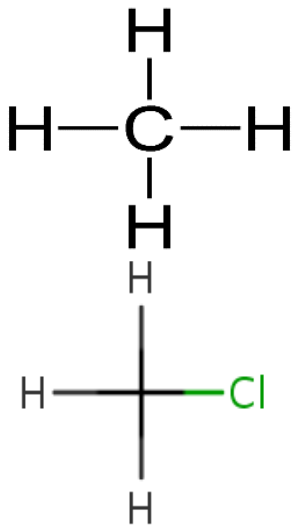


A **more shielded** nucleus will have a **weaker B_{eff}** and so the energy difference between spin states is lower and, as such, resonance will occur at a **lower frequency** and have a **low chemical shift** that is further upfield.

A **less shielded** nucleus will have a **greater B_{eff}** and so a larger energy difference between spin states. This means resonance will occur at a **higher frequency** and you get a **high chemical shift** that is further downfield.

There are two main factors that affect chemical shift patterns and those are electronegative atoms or groups & diamagnetic anisotropy.

Electron withdrawing groups



An electronegative atom or group such as the chlorine in chloromethane pulls electron density towards itself and away from nearby protons. As such, the chlorine has a deshielding effect on nearby protons.

This can be observed by a higher chemical shift in an H-NMR spectrum for the protons in $CClH_3$ than the protons in CH_4. The CH4 protons have no electronegative atom drawing electrons away from them so are more highly shielded & have a lower chemical shift.

Van der Waals' forces can also play a role. E.g. the chemical shift of alcohols is influenced by the hydrogen bonding between molecules. This hydrogen bonding has a de-shielding effect. Variations in factors such as concentration, solvent & temperature will affect the overall amount of hydrogen bonding. It is because of this that we observe a wide range of chemical shift values in alcohols.

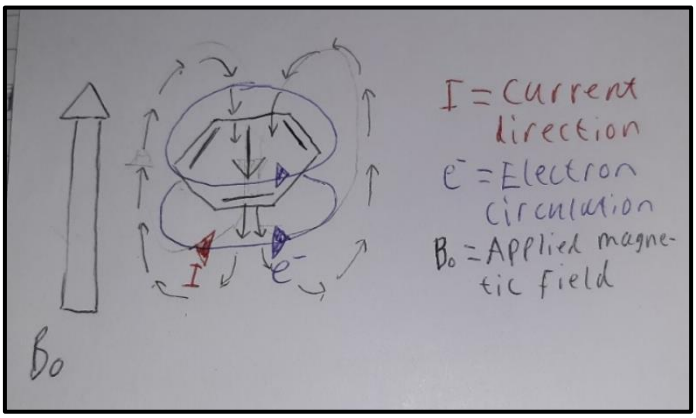
Diamagnetic anisotropy

This is an effect which accounts for the chemical shifts that are observed in **delocalised π systems.** This includes groups such as Alkenes, Alkynes & benzene derivatives, whereby the circulation of electrons is favoured in one plane. This means that a magnetic field may be induced against the applied magnetic field in one position of a molecule and potentially add to it in another.

Diamagnetic anisotropy in Benzene

When benzene is placed in an applied magnetic field a ring current is induced due to the circulation of delocalized p electrons. This current is induced according to Lenz's law, whereby "The direction of an induced current is always such as to oppose the change in the circuit or the magnetic field that produces it." [6]

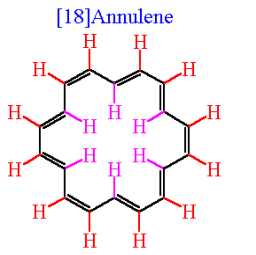
By this definition we know the electrons will circulate in a clockwise manner (see fig.4) such as to induce a magnetic field to oppose B_0 through the benzene ring & add onto the field on the outside.



This can be confirmed with Fleming's right-hand grip rule, whereby your thumb points in the direction of current (opposite to electron flow) and your fingers curl in the direction of the field lines.

Benzene protons lie on the outside of the ring, so they experience the additive effects of both the applied and induced magnetic field, contributing to a high chemical shift in an H-NMR spectrum.

If you were to have a larger pi system, whereby protons could lie inside the ring, then the chemical shift for those protons would be low as the magnetic field vectors of the applied and induced magnetic fields would cancel, leading to a reduced B_{eff}.

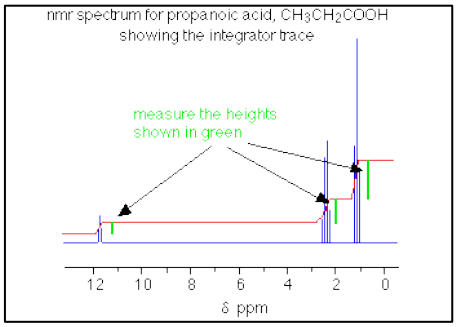


A common example used to demonstrate this effect is annulene. The internal protons experience a reduced $B_{effective}$ as the induced magnetic field opposes the applied magnetic field, thus providing a shielding effect & an exceptionally low resonance frequency, even less than TMS, that gives a low chemical shift.

The applied & induced field add up on the outside of the ring, so the external protons experience a significant de-shielding effect & thus we observe a very high chemical shift.

Integration Traces in H-NMR

For H-NMR the area under a signal is proportional to the number of protons with the same chemical environment causing that peak. The relative areas of H-NMR peaks correspond to the relative ratios of protons in one environment with respect to another.



By combining the ratio of peak areas & knowledge of the total number of protons you can find which peaks correspond to particular hydrogens.

The relative areas are computer calculated and are given either as an area value underneath each peak, or as an integration trace whereby the area under a peak is proportional to the height gained in the integration trace.

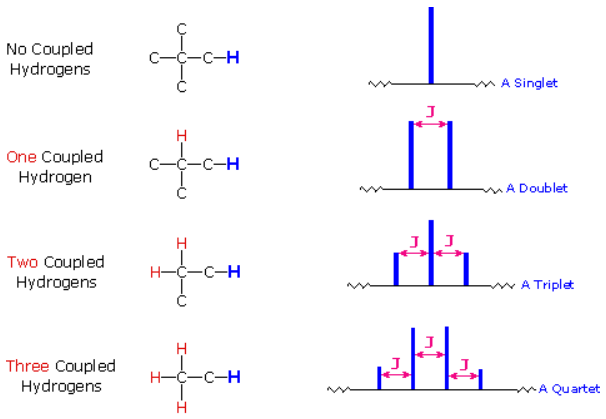
The integration trace is shown in **RED.** The height gained is shown by the green lines & is proportional to areas under each peak. The ratio of these heights corresponds to the ratio of hydrogen atoms sharing the same peak/ environment.

Spin-spin splitting

Spin-spin splitting (or coupling) is a phenomenon observed in NMR spectra due to the interference of the magnetic fields of adjacent nuclei.

Generally speaking, this interaction is only observed with the presence of nearby H-nuclei. For example, the relative abundance of C-13 isotopes in a sample is so small, ~1.1%, that the chance of two C-13 nuclei being adjacent in a structure is very low & so any difference in signal to this effect is strong enough to be observed. It is important to note, however, that coupling is observed in C_{13}-NMR due to the protons adjacent in –CH3, -CH2-, or –CH- groups.

When a magnetic field is applied, nuclei can either align with or against the magnetic field. If they align with the magnetic field then the field vectors of the applied magnetic field & the nuclei's magnetic moment will add up, increasing the effective magnetic field on a nearby nucleus. If a nucleus aligns against the applied magnetic field, its own magnetic moment will detract from the applied magnetic field, leading to a decrease in effective magnetic field experienced by adjacent nuclei.



This interaction results in a splitting of peaks whereby the split end of a peak with the highest chemical shift is due to the enhanced magnetic field when adjacent nuclei align with the magnetic field. Meanwhile the split end of a peak with the lowest chemical shift is caused by adjacent nuclei aligning against the magnetic field.

Splitting patterns

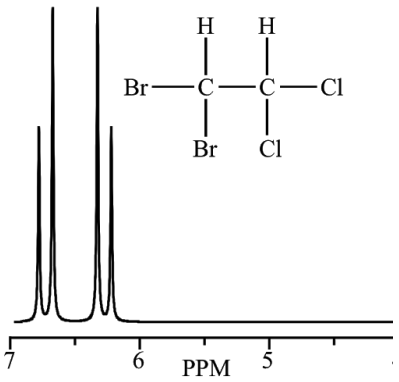
The number of peaks observed in a splitting pattern follows the n+1 rule whereby 'n' is the number of non-equivalent protons that are adjacent to the proton & causing coupling to occur.

The splitting pattern heights follow the ratios of Pascal's triangle, following the binomial theorem. E.g. a signal split into 3 peaks (a triplet) will follow a height ratio of ~1:2:1 and a signal split into 4 peaks (a quartet) will have heights in the ratio of ~1:3:3:1

These heights will not follow a perfect ratio of Pascal's triangle, however…

As can be seen in this splitting pattern that gives us 2 doublets, the doublet of each coupled proton appears to be pointing to a central point. This feature can be used to spot whether two doublets, or any other multiplet for that matter are present.

The two signals are lopsided so as to point to the corresponding signals of proton, say on the left than the right so as to point in the direction of the signal that it is coupled with.



Coupling constant: The distance between peaks, e.g. in a doublet pair or any other coupled multiplet pair is the same in each. This is known as the **coupling constant** which is measured in **Hertz.**

Solvents in NMR

One of the main features of a viable solvent for NMR is for it to provide as little interference as possible to your sample reading.

"The solvent itself will inevitably produce NMR signals which will obscure regions of the spectrum. These 'residual solvent peaks' should not overlap with signals from the sample." [7]

It is for this reason that deuterated solvents are most commonly used. Common deuterated solvents include Benzene (C_6D_6), Chloroform ($CDCl_3$), acetone & more.

The use of solvents containing deuterium ($_2H$) instead of $_1H$ will give a higher chemical shift & not obscure sample readings. Deuterium has both 1 proton & 1 neutron, giving it a net spin of 1. As such deuterated protons resonate at a different frequency, which can help to avoid interference.

Hydroxyl, amino protons and hydrogen bonding

The ability of O-H and N-H groups to form hydrogen bonds leads to their protons showing a broad range of chemical shift values in a spectrum. This is because hydrogen bonding draws electron density from the protons which has a de-shielding effect, moving the chemical shift to the right.

Many factors affect hydrogen-bonding to give OH & NH groups their broad shift ranges:

-Increased temperature → weaker H-bonding → shielding effect

-Concentration → More H-bonding → De-shielding effect

-Polar solvents→ More H-bonding → De-shielding effect

Oftentimes, distinguishing OH/ NH protons requires the use of a technique called **proton exchange** (see below)

Proton Exchange

This technique involves the running of a normal H-NMR spectra followed by one in which the OH or NH containing sample is deuterated before running.

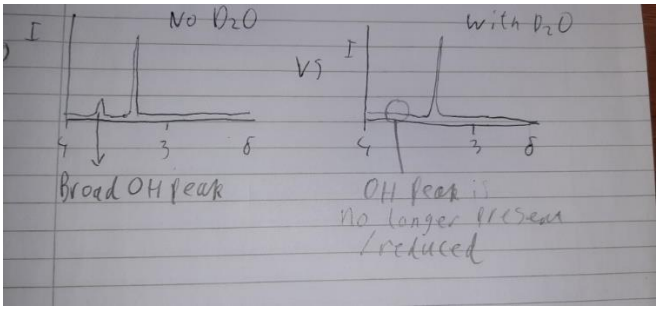
1) H-NMR spectrum run as normal: This captures all peaks in the measured frequency range (including -OH & NH peaks)

2) A small amount of D2O is added to the sample. The sample is well-shaken & the spectrum is rerun.

Once D2O is added deuterium 'exchanges' with the protons attached to the -OH / -NH groups to form an equilibrium. This is given for methanol below:

$$CH_3OH + D2O \quad \leftarrow\!\!-\!\!-\!\!-\!\!\rightarrow \quad CH_3OD + HDO$$

Once the sample is deuterated, we are essentially taking the Spectra for CH_3OD instead of CH_3OH, which results in the displacement of the OH proton peak in the 2nd spectrum with the D2O peak. The absence of this peak can be observed by comparison of spectra.



SOURCES

[1] - Williams & Fleming, (1980), *Spectroscopic methods in organic chemistry, Third edition*

[2] -https://en.wikipedia.org/wiki/Pauli_exclusion_principle
[3] -https://www.scientificamerican.com/article/what-exactly-is-the-spin/
[4] -http://hiq.linde-gas.com/en/analytical_methods/nuclear_magnetic_resonance.html
[5]- http://triton.iqfr.csic.es/guide/man/beginners/chap5-2.htm
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Working sources (not directly referenced but useful nonetheless)

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-Organic chemistry tutor YouTube channel:
https://www.youtube.com/playlist?list=PL0o_zxa4K1BXP7TUO7656wg0uF1xYnwgm
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Images

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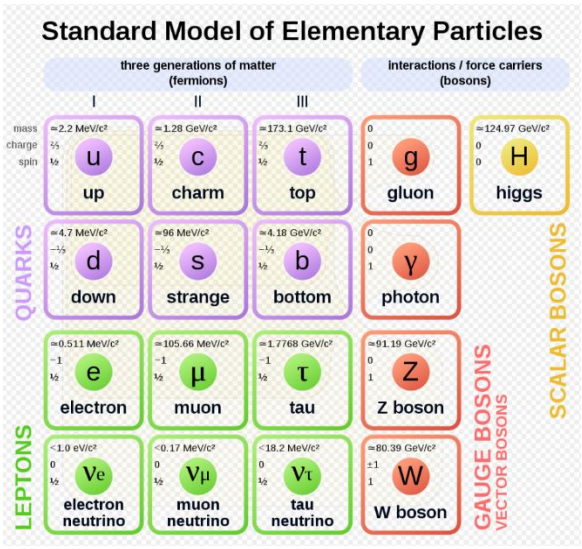
NMR SPECTROSCOPY AND NUCLEAR SPIN

Pierre Hornsblow (Year 12)

WHAT IS SPIN?



Spin is a property of all fundamental particles, all matter particles (fermions) have spin ½ and force carrying particles have spin 0 1 and 2. It is described by Stephen hawking as how a particle looks from different angles, for example a particle spin 0 could look like a sphere as it's the same from every angle, and a particle spin 2 could be like a double headed arrow, which looks the same after a rotation f 180 degrees. And strangely enough a particle f spin ½ would only look the same after two rotations. Of course on this scale nothing "looks" like anything as elementary particles are much too small to be looked at.[1]

Spin was first discovered by the stern Gerlach experiment which involved a beam of silver atoms with a single outer s electron fired into a matching which measures how far up or down a magnetic field is pointing. If you were to fire a beam of subatomic bar magnets though it you would find an even distribution of measured orientations f magnets, but when they fired a silver atoms through they expected the atoms to pass straight through however they found that not only did the outer s electron appear to have a magnetic north and south pole, but that half of the magnetic north poles were pointing exactly up and half exactly down.

This was explained using the concept that if a charge is spinning then it will create a magnetic field in whose direction can found using Flemings right hand rule. However, electrons don't actually "spin" in the traditional sense, they don't even have a well-defined axis to spin about. [1] However if the magnetic north was pointing up it was named spin up, and downward it can be called spin down

Protons, which are made up of two up quarks and one down quarks (up and down doesn't refer to their spin) and have an overall spin ½ which isn't as simple as adding up the spins of the up and down quarks, something which created the "spin crisis" which is still not completely solved.[2]

In 1925 Wolfgang Pauli discovered a property of fermions called the Pauli exclusion theory which states that two similar particles cannot exist in the same state, in other words, the closer together they are, the more their velocities differ so they won't stay close together for very long. [1]

All this leads us up to calculating the spin of a nucleus, which will then lead us to NMR spectroscopy. In order to calculate the spin of a nucleus several physicists came up with the nuclear shell model, similar to the shells in which electrons "orbit" the nucleus.

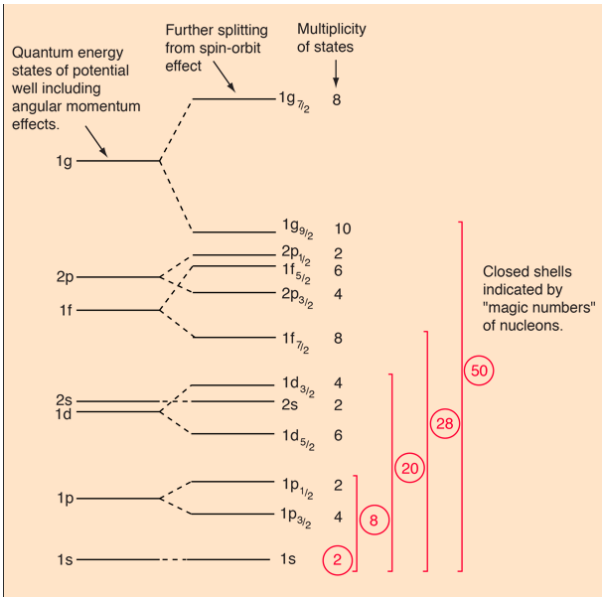
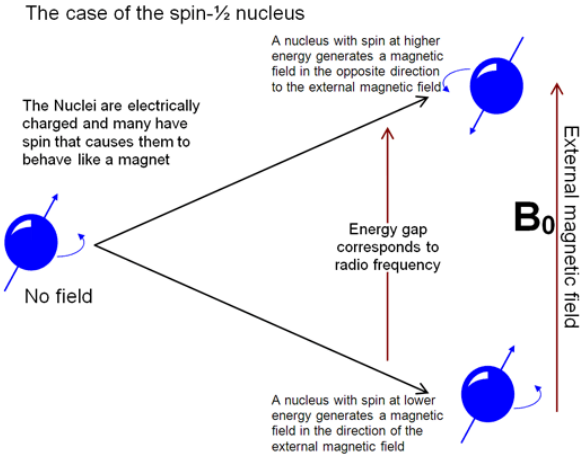


Diagram showing order of filling, and spin number of nuclear shells [3]

It seems absurd that nucleons (protons neutrons) could complete orbits without interacting with each other. However, they behave in was which obey the Pauli Exclusion Principle. Which means that they must exist in discrete energy levels Each energy level is given a spin number and each level (except s) is split into two possible spin numbers where the higher spin number is filled first as it has a lower energy, and the lower spin is number is ½ less than the higher one.



Protons (neutrons are the same but deal with them separately) fill each level with alternating spins so that they obey the exclusion principle and each level can take 2s+1 proton where s is the spin number of that shell. So, for a hydrogen nucleus which only has one proton it has spin of ½ as it has one proton in the 1s orbital. A deuterium ($_1{}^2h$) nucleus has one proton with spin ½ and one nucleus with spin ½ so has a net spin of 1. For larger nuclei like that in $_{17}{}^{35}Cl$ then one spin up proton enters the 1s orbital then one spin down proton enters the 1s orbital to fill it up (2x ½ +1=2) but since one has spin up and the other has spin down then their spins cancel out, this process carries on until the final valence proton in the $1d_{3/2}$ orbital since there is an odd number of protons (17) then it means that the valence proton hasn't been cancelled out by it partner with opposite spin so the protons have spin 3/2. This process is identical for the neutrons except there are 35-17=18 of them so this means the final valence neutron was cancelled out by its partner so the neutrons have a spin of 0. So, the net spin of the nucleus is 3/2. [3]

It is important to remember that this model is incomplete as it can make false predictions for heavier nuclei.

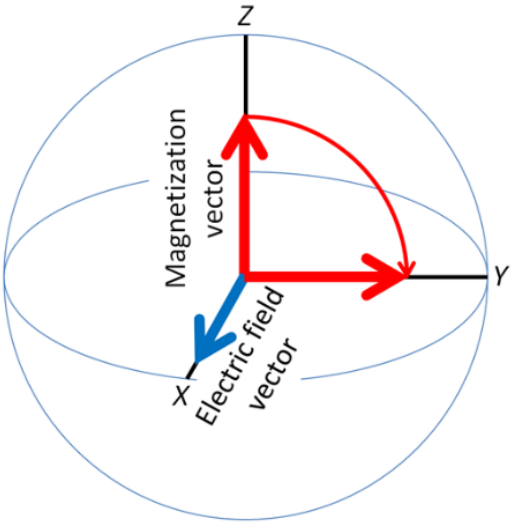
HOW DOES THIS APPLY TO NMR?

Well since all nuclei (except those with spin 0) seem to have magnetic properties it makes sense that they would be affected by a magnetic field, a nucleus can have 2n+1 orientation where n is the spin number of the nucleus. And when a magnetic field is applied there are slightly more in the lower energy orientation but first, what is NMR?

NMR (nuclear magnetic resonance spectroscopy) is an analytical technique used in quality control as well as for finding the molecular structure, purity and contents of a sample. NMR uses the principle described above that nucleuses can have several "orientations", once a magnetic field is applied then there will be slightly more nuclei in the lower energy state, these extra few "target" electrons can be excited up into the higher energy level using a pulse of EM radiation at radio frequencies, when these electrons fall back down into the lower energy state they remit the extra energy as EM radiation at the same frequency, this emission can be detected and used to produce an NMR spectrum. If you increase the strength of the magnetic field then you increase the ΔE. And once a sample has equal amounts of low and high energy state nuclei it is said to be saturated and no more energy states can be filled [4]

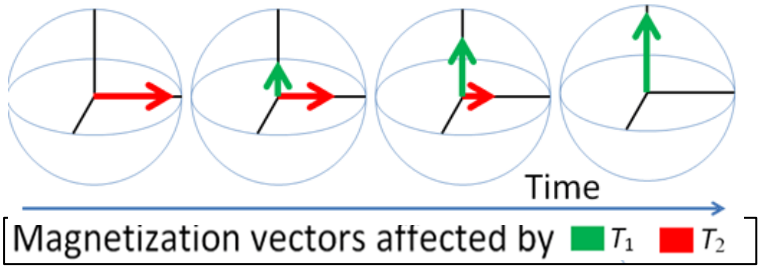
Proton NMR is very common and measures the behavior of spin ½ nuclei in hydrogen, hydrogen nuclei can have 2x ½ +1=2 orientations, as shown in the diagram where the lower energy orientation doesn't oppose the magnetic field. The magnetic field of the nuclei are not perfectly aligned with the magnetic field as they process, the frequency of this precession is equal to the frequency of EM radiation needed to change to higher energy state.

In a sample which is going to be measured, there are more nuclei in the lower energy state than in the higher energy state, so a bulk magnetic moment in the sample is formed. This moment is called the magnetization vector, and it processes around the z axis at a frequency called the Larmor frequency. In order to flip this magnetization vector by 90° a pulse of EM radiation in x-y plane is sent, however it is much weaker than the energy produced by the induced magnetic field, so the x-y plane is made to spin about the z axis at around the Larmor frequency to cause a rotation of 90°. This position is unstable and the magnetization vector will return to z axis by a process known as relaxation. [4]



TYPES OF RELAXATION:

Lattice-spin relaxation. (T_1) This type of relaxation results in the increase of the magnetization vector in the z axis (along the induced magnetic field). This occurs due to some the magnetic frequencies within the sample being equal to the Larmor frequency of the higher energy particles resulting in them returning to the lower energy state.



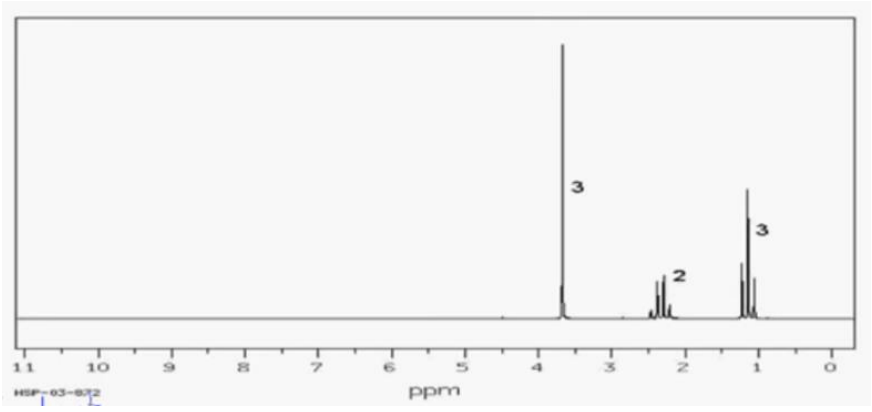
Spin-spin relaxation (T_2) is a decay of the magnetic field in the x-y plane resulting from high energy and low energy state nuclei interacting in such a way that they "swap" energy states, randomly and temporarily. This doesn't decrease the number of high energy state nuclei, but increases the disorder of the magnetic field. [4][5]

CHEMICAL SHIFT

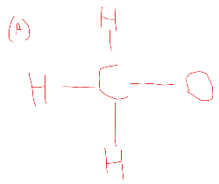
Chemical shift is the difference between the induced magnetic field and the magnetic field felt at the hydrogen nucleus. It is affected by factors such as electron shielding which is in turn affected by electronegativity. I proton NMR the nuclear shift due to magnetic fields created by orbiting s electrons is quite small, in comparison to measuring the chemical shift caused by p electrons which have the effect of increasing the magnetic field at the nucleus due to their orbital shape. Electronegativity causes a chemical shift in compounds such as CH_3X because as X become more electronegative, the electron cloud becomes less dense around the hydrogen nuclei, resulting in a downfield shift because it becomes harder to cause the nucleus to enter a higher energy state, so it releases more energy when it relaxes, so the frequency of the photon emitted is higher. Chemical shift is measured relative to a standard compound, proton NMR this is Si (CH3)4. This compound is used to compare the chemical shift(s) that occur in the sample. It is chosen because it has 12 hydrogens all bonded in the same way producing a very distinct peak, which is at 0 on an NMR spectrum. Also, the electrons are closest to hydrogens here than in any other organic compound, meaning every other peak will be upfield from it. [5][6]

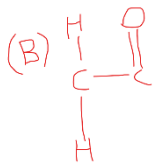
SPIN-SPIN COUPLING

Spin-spin coupling is another example of how the magnetic field at the nucleus is affected. However here it shows the effect from neighboring hydrogens, which makes it very useful to figure out the structure of the compound

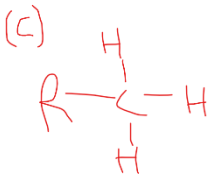


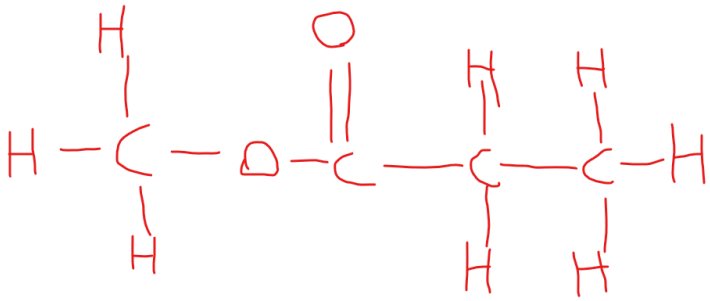
This is a diagram of a substance, you can see three areas where peaks occur in, using a data sheet you would see that the leftmost peak is caused by a hydrogen on a carbon connected to an oxygen atom (H-C-O), the centre peak is caused by a hydrogen on a carbon connected to a carbonyl group (H-C-C=O) the rightmost peak is a hydrogen on a carbon connected to an alkyl group (R-C-H). So far this can all be explained due to the chemical shift. However when you look at the rightmost peak you can see it is made of three peaks (a triplet) this is because the carbon adjacent to it must have 2 hydrogens. This is because the hydrogens could be either both high energy, both low energy or one of each. Is both adjacent nuclei were high energy then they would both oppose the field reducing the field felt at the nucleus of the hydrogen nucleus being measured, resulting in an upfield shift. The opposite goes for if they were both low energy nuclei. And since there are two possibilities of the adjacent nuclei being one high and one low energy, the middle peak is twice as high. Using the same idea for the middle peak (a quartet) we can see that the adjacent group must have 3 hydrogens. [5]





The final piece of information the graph shows is the area under the peaks. This shows the intensity of the energy released so also tells us how many hydrogen atoms which were emitting that frequency there were. So the left most group must look like A as it has 3 hydrogens, the centre group must look like B and the rightmost group must look like C. using this information we can see that the centre peak (B) must be connected to the rightmost peak (C) and the leftmost peak must be connected to the (C=O) group as its peak has no splitting, so must be attached to a group with no hydrogens, meaning the overall compound must look like: (which is methylpropanoate)





SOURCES:

[1] Stephen Hawking, a brief history of time
[2] https://physicsworld.com/a/the-spin-of-a-proton/
[3] http://hyperphysics.phy-astr.gsu.edu/hbase/Nuclear/shell.html
[4] http://chem.ch.huji.ac.il/nmr/techniques/other/t1t2/t1t2.html
[5] https://teaching.shu.ac.uk/hwb/chemistry/tutorials/molspec/nmr1.htm#
[6] https://www.chemguide.co.uk/analysis/nmr/background.html

Our modern understanding of how atoms and their sub-atomic particles behave is very much a product of the 20th century and, in particular, the field of QUANTUM PHYSICS. When it comes to NUCLEAR SPIN and NUCLEAR MAGNETIC RESONANCE, one name stands out above all others: **ISIDOR ISAAC RABI**.

Rabi was born in 1898 into a Jewish family in what was then Austria-Hungary (now Poland). A year later his family emigrated to the United States of America which is where Rabi remained for the rest of his life.

Rabi recognised that protons and neutrons in nuclei act like small, rotating magnets. Atoms and molecules therefore align in a magnetic field. In 1938, he passed a beam of molecules through a magnetic field. When the beam was exposed to radio waves, the direction of rotation could be changed, but only in certain stages, in accordance with quantum mechanics. When the atoms returned to their original positions, they emitted electromagnetic radiation with uniquely characteristic frequencies. This 'resonance' is still known as 'Rabi Resonance' and is fundamental to NMR.

The NOBEL PRIZE IN PHYSICS 1944 was awarded to Isidor Isaac Rabi "**for his resonance method for recording the magnetic properties of atomic nuclei**."

Rabi always appreciated the encouragement his mother had given him when at school in New York. He would have been in his teens at the time and is later famously quoted as follows:

'My mother made me a scientist without ever intending to. Every other Jewish mother in Brooklyn would ask her child after school, So? Did you learn anything today? But not my mother. "Izzy", she would say, "did you ask a good question today?" That difference - asking good questions - made me become a scientist.'

NMR SPECTROSCOPY AND NUCLEAR SPIN

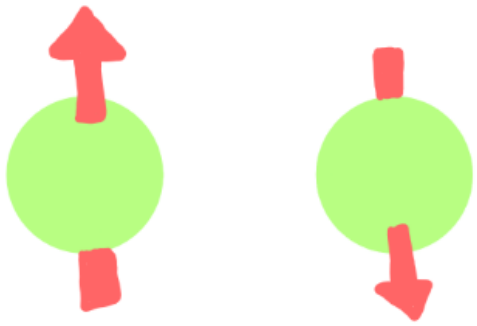
Terri Dodsworth (Year 12)

What is Nuclear magnetic resonance?

Nuclear magnetic resonance, also known as NMR, is a scientific method of determining the shape of a molecule. (Bruker BioSpin , n.d.)This technique relies on the physical phenomenon that atoms that have magnetic nuclei are placed into a magnetic field where they absorb energy and then re-emit the electromagnetic radiation.

Nuclear spin – what is it?

NMR only works with nuclei of atoms that have odd numbers of nucleons (i.e. protons and neutrons); this is because of one of the theoretical principals called nuclear spin. Nuclear spin, also represented by the letter *'I'* represents the net angular momentum of the nucleus. The nucleons do not really spin, it's just a property that they have that has been labelled as 'spinning'. As seen in the image to the left, this 'spinning charge' produces a magnetic field that points up when it spins one direction and in the opposite direction, points down. This is called Spin up and Spin down. These are both given values:

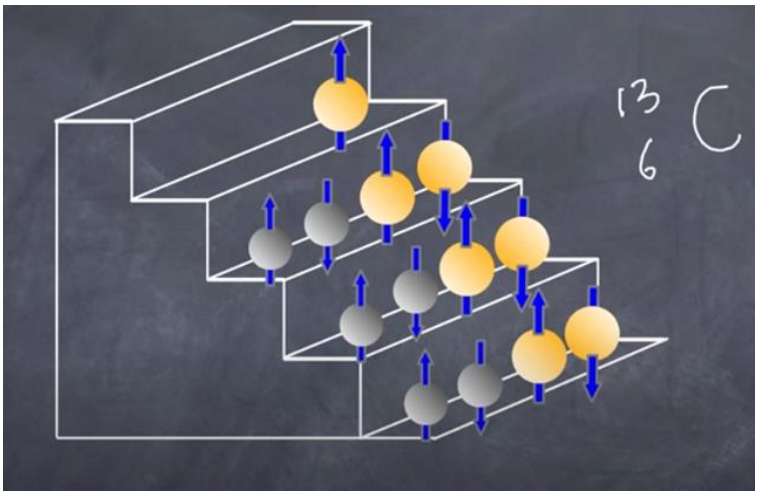


Spin up = ½

Spin down = - ½

(These values are the same for both protons and neutrons.)

Going back to the first point that NMR only works for atoms that have odd numbers of nucleons, we can now have a closer look at why that is so. Another theoretical principal states that you can't have to entities with exactly the same properties on the same energy level. This is why only a spin up proton/neutron can be paired with a spin down proton/neutron once on each energy level. However with an even number of these pairs their values will cancel each other out to give a value of zero unlike odd numbers of nucleons such as in Carbon 13 (seen in the diagram on the right) with 6 protons (three pairs of spin up and spin down on three different energy levels) and seven neutrons. The odd number of neutrons allows there to be a net spin of ½ giving it a small magnetic field (which is needed in NMR spectroscopy). (Explained, 2016) The rules for the overall net spin are as follows:



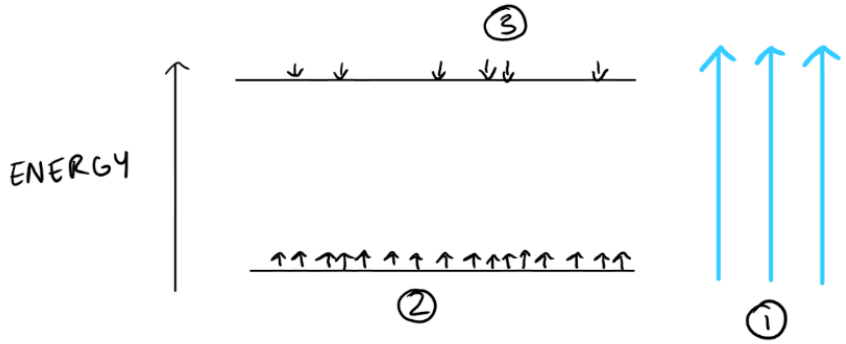
"If the number of neutrons **and** the number of protons are both even, then the nucleus has **NO** spin.

If the number of neutrons **plus** the number of protons is odd, then the nucleus has a half-integer spin (i.e. 1/2, 3/2, 5/2)

If the number of neutrons **and** the number of protons are both odd, then the nucleus has an integer spin (i.e. 1, 2, 3)" (Sheffield Hallam University, n.d.)

How does the NMR spectroscopy work?

Firstly, the sample molecule is placed into the NMR machine and all the nuclei are all spinning in different directions and at different rates. Then a very strong magnet is used to try and align all of these nuclei. This can be described using an image:



On this image 1. Can be seen to represent the direction of the magnetic field that has been applied to the sample molecule. Number 2. Represents the majority of the nuclei in the sample. In the diagram they have been represented by arrows to help demonstrate that they are spinning in the same direction as the magnetic field. You can also see from where they are placed in line with the arrow representing energy that they have a low energy. Moving onto number 3. These arrows represent the minority of the nuclei in the sample that are not following the same direction as the magnetic field and have a slightly higher energy than the rest of the nuclei.

NMR machines use the energy difference between the high and low energy nuclei to determine the structure of the molecule that is present. They do this by firing radio waves at the lower energy nuclei, these nuclei then absorb some of the energy from the waves which causes them to change the direction of their spin and thus move up to the higher energy level (position 3 in the diagram). However, this makes the nuclei unstable and so eventually the nuclei will flip back down to the lower energy level and into the same direction as the magnetic field as it was before. While this is happening, the nuclei will re-emit some of the energy they had previously absorbed; the energy will match how big the gap between the lower and higher energy levels are. (I.e. how big the gap is between position 2 and 3 on the diagram) The energy gap will differ in size depending on what atom nuclei are next to each other in sample molecule being used. The NMR machine then picks this release of energy up and it is recorded. (Chemistry, 2015)

What are proton NMR and Carbon-13 NMR?

The basic difference between these two main types of NMR is that proton NMR detects the type and number of hydrogen atoms in a molecule whereas Carbon-13 detects the type and number of carbon atoms in a molecule. (Madhusha, 2018) Some key words that might come up when dealing with either of these NMR types are:

Chemical shift: In simple terms, the chemical shift just describes the environment that the chosen atom is in which can refer to which atoms are located next to it. It is represented along the x-axis on the NMR graph.

Integration trace: In simple terms, this refers to how many of the chosen atom you have in the environment. (Chemistry, 2015)

Speaking more specifically about the Carbon-13 NMR only now, as we know from above carbon 13 can be detected because it has an odd number of neutrons in its nucleus. These nuclei will have electrons around them that cause electron shielding, and these 'shields' act almost as a protection device that allows them to be less affected by the magnetic field that is applied to the molecule either through atoms that surround them or by the NMR machine. The more shielding the carbon atom has, the less effect the chemical shift has upon it i.e. the less it will move along the x- axis on the NMR graph (Chemisty, 2015).

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[Accessed 24 04 2020].

NMR spectroscopy is one of the principal techniques used to obtain physical, chemical, electronic and structural information about molecules due to the chemical shift of the resonance frequencies of the nuclear spins in the sample.

It also led directly to the invention of a method that is of immeasurable use in medicine for the non-invasive and safe means of examining the internal structure of living things: MAGNETIC RESONANCE IMAGING.

Many researchers worked on improving and modifying NMR spectroscopy and two in particular, PETER MANSFIELD (University of Nottingham, UK) and PAUL LAUTERBUR (Stony Brook University, USA), in the early 1970s succeeded, independently, in producing cross-sectional images of parts of the body. In Mansfield's case it was the tip of one of the little fingers of one of his secretaries!

During the 1970s a team led by JOHN MALLARD built the first FULL-BODY MRI scanner at the University of Aberdeen. On 28 August 1980 they used this machine to obtain the first clinically useful image of a patient's internal tissues using MRI, which identified a primary tumour in the patient's chest, an abnormal liver, and secondary cancer in his bones.

In 2003 Mansfield and Lauterbur were awarded the NOBEL PRIZE in PHYSIOLOGY OR MEDICINE for their *"discoveries concerning magnetic resonance imaging"*.

The picture on the right shows the two men at the Nobel awards ceremony –

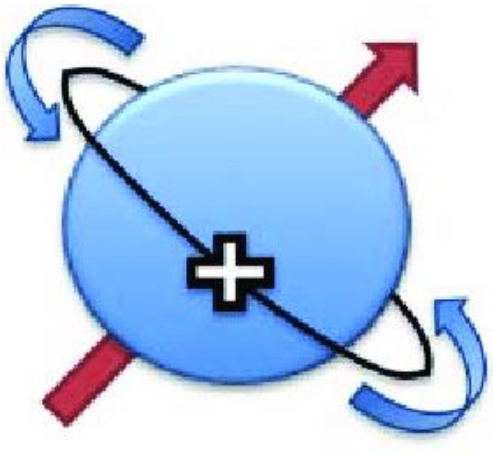
Mansfield on the right and Lauterbur on the left

THE NON-CHEMISTS GUIDE TO NMR SPECTROSCOPY AND NUCLEAR SPIN

Queenie Cestaro (Year 12)

Nuclear Spin

'Spin' is the name given to one of the many properties of certain subatomic particles (protons, neutrons and electrons); it is all to do with the way that particles generate a magnetic field. Let's look at protons for an example:



-Protons carry a **positive** charge

-As we know from physics, all objects with a charge which are spinning, generate a **magnetic field** around them, much like a pole magnet.

-The direction of the magnetic field generated is determined by the direction which the particle spins, for example, in the image to the right, the particle is spinning to the right, generating a magnetic field in the 'up' direction (Fleming's hand rule). In quantum physics, the 'up' spin is given a value of **1/2**

-Now, what if there was a proton which was spinning in the opposite direction (to the left). Using Flemings hand rule, we know that would generate a magnetic field in the 'down' direction – this is given a value of **-1/2** in quantum physics.

-Although neutrons have no charge, they too can generate their own magnetic moment, 'up' or 'down', like that of protons, therefore both protons and neutrons have the property of spin (www.physicshigh.com, 2016)

Combining Protons And Neutrons In A Nucleus

Pairs of protons and pairs of neutrons must have opposite spins in order to co-exist at the same energy level. Essentially, this means they must produce a **net spin of 0** (1/2 + -1/2 = 0). If you were then to add another proton or neutron to this energy level with the same spin as the particle already there, they could not co-exist and thus this particle would have to **move up to the next energy level.**

The same rules do not apply to pairs of different subatomic particles ie., a proton and a neutron in the same energy level – they can have the same spin, however if another proton and neutron were to come along to the same energy level, they would have to have opposite spins to the same particle already in that energy level. (www.physicshigh.com, 2016)

Proton (H+) NMR- Nuclear Magnetic Resonance

Proton NMR spectroscopy is an analytical divide used with the nuclei of atoms. This works for **odd numbered nuclei atoms** (eg., carbon-13) because **they must have a magnetic field, ie., their nuclei have a net spin**.

How it works

The system uses strong magnets to align the nuclei – some of the nuclei will spin in the same direction as the applied magnetic field, and since they follow the magnetic field, they are at a lower energy level. However some nuclei will spin in the opposite direction to the applied magnetic field and will therefore be at a slightly high energy level. (Allery chemistry, 2015)

Imagine it like a fence, where the horizontal beams represent energy levels (the higher beam being the high energy level). The nuclei spinning in the same direction as the applied magnetic field, will be at the lower energy level (lower beam) and the nuclei spinning in the opposite direction to the applied magnetic field will be at a higher energy level (higher beam).

NMR essentially measures this difference in energy levels between the nuclei.

To understand what happens next, we must understand the way that particles with spin react when they absorb radiation. Firstly, remember that the direction they are spinning determines how high their energy level will be when a magnetic field is applied. When these nuclei which are spinning and have their own magnetic moment, absorb radiation, it essentially causes the direction which they're spinning, and hence the direction of their magnetic field, to change – this called the angle of precession. (Sheffield Hallam University). If the direction of their magnetic field changes, it will mean nuclei at lower energy levels will be raised to higher energy levels.

Now we can understand the next step. Radio waves are fired at the aligned nuclei – those at a lower energy level (spinning in same direction as applied magnetic field) will absorb this radiation (become excited), the direction of their magnetic field will change to oppose the applied magnetic field and hence they will move to the higher energy level. These nuclei that had been moved up an energy level, will soon move back down to the lower energy level, but whilst doing so, they will emit the radiation energy they initially absorbed. This emitted radiation is measured by the NMR device and is the difference between the energy levels. (Allery chemistry, 2015)

Chemical Shift

Chemical shift refers to how the hydrogen nuclei that are next to your central H+ nuclei, affect the difference in energy levels. For example, if a hydrogen nucleus is next to a very electronegative nucleus like oxygen or fluorine, there will be a greater difference in energy levels. The more electronegative the nuclei your hydrogen nuclei is next to, the lower the electron density surrounding the hydrogen in (proton), and hence the larger the difference in energy levels. (Sheffield Hallam University)

Spin-spin coupling (splitting)

This refers to how many protons (hydrogen ions) there are next to the hydrogen environment in question. This is seen on a graph produced by NMR. Essentially, on the graph, the number of peaks corresponds to the number of hydrogen environments, For example, in hydrocarbons, your end carbon atom maybe have 3 hydrogens attached, but is also attached to another carbon atom, which itself is attached to two hydrogens, and so on. The central hydrogen forms a large peak; however they split into little peaks which show the hydrogens next to them. The number of smaller peaks is called the splitting number and we work this out using **n + 1,** where n is the number of hydrogens adjacent. This will give the number of peaks that particular hydrogen environment will produce (how many other hydrogen ions it's attached to). So, if there are 0 hydrogens adjacent, 0+1 =1. This is known as a singlet. If there is 1 hydrogen adjacent, 1+1=2 (doublet), and so on. (Allery chemistry, 2015)

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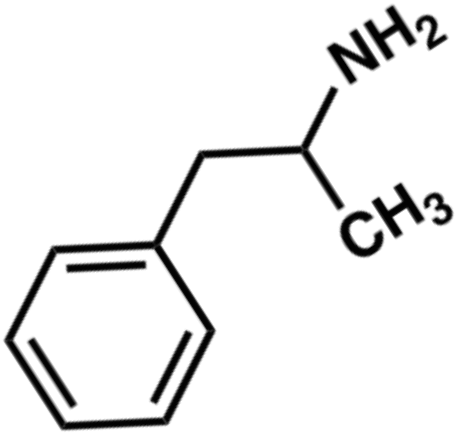
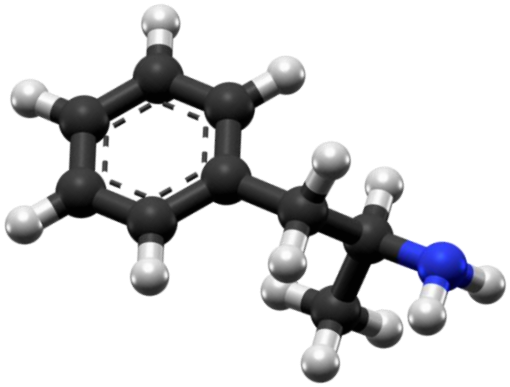
We have learned that understanding the behaviour of protons is important in the development of NMR and has led to the invention of the MRI scanner. The medical use of MRI is in providing an image of the body – it is a diagnostic tool, not a treatment. However, more recently scientists have developed a powerful and effective treatment for cancer that uses protons – PROTON BEAM THERAPY.

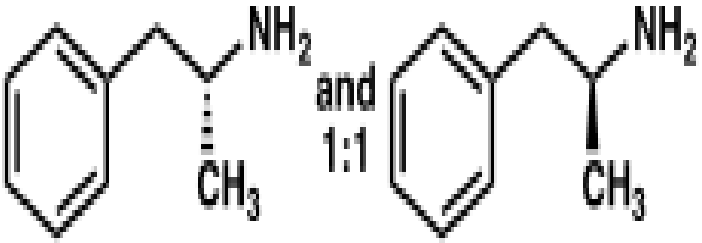
Proton beam therapy (PBT) is an advanced form of radiotherapy, with radiation treatment delivered by accelerated proton beams rather than X-rays. A proton beam delivers some radiation to healthy tissue in reaching the tumour but very little radiation beyond the edge of the tumour being treated. This means PBT is able to treat cancers just as effectively but delivers less radiation to other healthy parts of the body which surround the tumour. It is used particularly in the treatment of tumours in children.

ISOMERS OF AMPHETAMINE

Favio Monteadudo (Year 12)



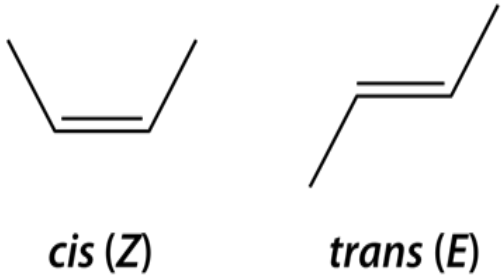




What is a stereoisomer?

Before we discuss amphetamine isomers, we need to know what stereoisomers are. Stereoisomer is defined as a "compound that has the same molecular and structural formula but a different three-dimensional spatial arrangement". (John Older, Mike Smith,2015,283)

One type of stereoisomer is a cis-trans and E/Z isomer, which only occur when there is a double bond like in alkenes where they are unsaturated for example but-2-ene can only be drawn two ways.



These have slightly different properties like Z but-2-ene has a slightly higher boiling point than but-2-ene.

There are some rules for these cis-trans stereoisomer that is called Cahn, Ingold and Prelog (CIP) rules which uses atomic number to determine the Z/E and trans-cis isomer. There are three rules which are.

1. If the two attached atoms with the highest atomic numbers are on the diagonally opposite sides of the double bonds it is an E-isomer. (john older, mike smith, 2015,210)
2. If the two attached atoms with the highest atomic number are not diagonally opposite each other across the double bonds it is a Z-isomer. (john older, mike smith, 2015,210)
3. If the attached atoms have the same atomic number, then the adjacent atoms with the highest atomic number are considered with alkyl group it therefore follows that $CH_3CH_2CH_2 > CH_3CH_2 > CH_3$. (john older, mike smith, 2015,210)

The two with the highest atomic numbers are on diagonally opposite sides of the c=c double bond so this is an e-isomer. The two with the highest atomic number are on the same side of the c=c double bond so this is a Z-isomer.

Optical isomer-enantiomer

Every molecule has a mirror image but some mirror image are different this is what French Physicist Jean-Baptist Biot as he concluded that the change of direction of plane-polarized light when it passed through certain substance was actually a rotation of light, Pasteur observed that there was two crystals in tartaric acid (found in wine). He found out that one set of molecules rotated polarized light clockwise while the other rotated light clockwise while the other rotated light anticlockwise to the same extent.

He observed optical isomer, the two compounds which are asymmetric are called enantiomers and are normally 50/50 mixture which is called a racemic, occur when making these stereoisomers. These optical isomers can polarise light as its light is a form of electromagnetic which travel in all direction but once polarised it goes only one direction. This is how we know how to name them (you use D/L or +/-). The way to tell is (-) enantiomer is anticlockwise rotation, (+) enantiomer is clockwise rotation and a racemic in as no overall effect. (CHEMSHEET, AS 1047)

Amphetamine

Amphetamine is a drug that helps many conditions like ADHD or even narcolepsy and is even a performance enhancing drug. Amphetamine was first synthesized in 1887 in Germany by Romanian chemist Lazăr Edeleanu. Its stimulant effect remained unknown until 1927 where Gordon reported its effects as having sympathomimetic properties. During WWII amphetamine and methamphetamine were used extensively to increase stimulant and performance enhancing effect as it builds up muscle quickly and makes them stronger. In the 1970s the US government made amphetamine illegal for it for its additive effects and to this day it is still illegal. (Wikipedia, 2020)

Medicine

Amphetamine is used to treat ADHD, narcolepsy and obesity as it causes emotion and cognitive effect such as wakefulness and improved cognitive control. The way pharmaceutical amphetamine helps ADHD by helping brain development and nerve growth, there have also been studies that found that long term treatment with amphetamine for people with ADHD decrease abnormalities in the brain structure and function found subject with ADHD and improve function in several parts of the brain so that over time they can concentrate better. (Wikipedia, 2020)

Physical performance

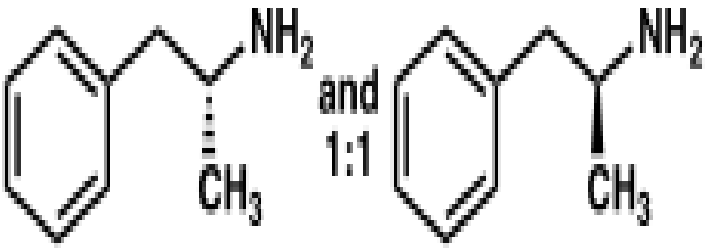
Amphetamine is used as performance enhancing drug which improves an athlete's psychological and physical effect such as increases in endurance and alertness and even helping to build muscle by breaking them down quicker so that they can fatigue less. So, an athlete can be faster and more powerful. Therefore, amphetamine is off limit to athlete and athlete will be banned from events if caught taking this drug. For example, Justin Gatlin (100m, American sprinter) was banned for using amphetamine in 2001 for two years after testing positive for amphetamine but he had attention deficit disorder and the appeal was reinstated by the IAAF .(Wikipedia, 2020)

Stereoisomerism of amphetamine

Amphetamine has a chemical formula of $C_9H_{13}N$ so this means it can be composed of a racemic 1:1 mixture of its two enantiomers, levoamphetamine and dextroamphetamine. Which are both optical isomers, we also see that the chiral centre is at the second carbon after the benzene ring.

Levoamphetamine

Levoamphetamine is one the enantiomer of amphetamine and is known to increase wakefulness and concentration for people with ADHD but is associated with fatigue and decrease of appetite. However, levoamphetamine is no longer manufactured as it takes longer to work than Levoamphetamine is a very dangerous substance when it is pure. (Wikipedia, 2020)



Dextroamphetamine

Dextroamphetamine is the other one of the enantiomers of amphetamine and is known as Dexedrine. We know that it fights fatigue and like levoamphetamine concentration as it can treat ADHD. Dextroamphetamine was also used in many wars to fight fatigue so that the soldiers can fight again in extended combat. Dextroamphetamine is also used for recreational purposes but this is highly illegal as it is very additive, and overdoses is fatal and have caused over 3000 death worldwide due to overdoses .(Wikipedia, 2020)

What is the different between them?

There are many differences but the main one is that in their structure, "levo" means left and "dextro" means right-handed, which shows which side the carbon the methyl group is on. This effects how it bonds and reacts with other compounds for example how potent they both are. Another example is that levoamphetamine is more biased toward promoting Norepinephrine (which activates the sympathic nervous system and regulates the heart and blood vessels.) release than dextroamphetamine, this also increases blood pressure and heart contractility. (quora, 2018)

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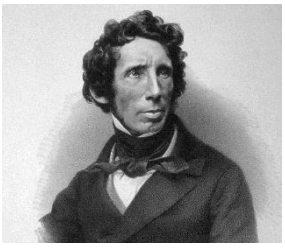
ISOMERS and ISOMERISM The roots of the word *isomer* are in Greek: *isos* plus *meros*, or "equal parts."

It was the German chemist FRIEDRICH WÖHLER who, in 1827, first observed isomerism in a chemical compound. The year before in 1826 another German scientist, Justus von Liebig, had prepared a compound called silver fulminate (AgCNO). Wöhler prepared a compound called silver cyanate which actually had the same elemental composition as silver fulminate (AgCNO), but its properties were different. This finding challenged the prevailing chemical understanding of the time, which held that chemical compounds could be distinct only when their elemental compositions differ.



ISOMERS OF CRYSTAL METH

Alwin Jose (Year 12)

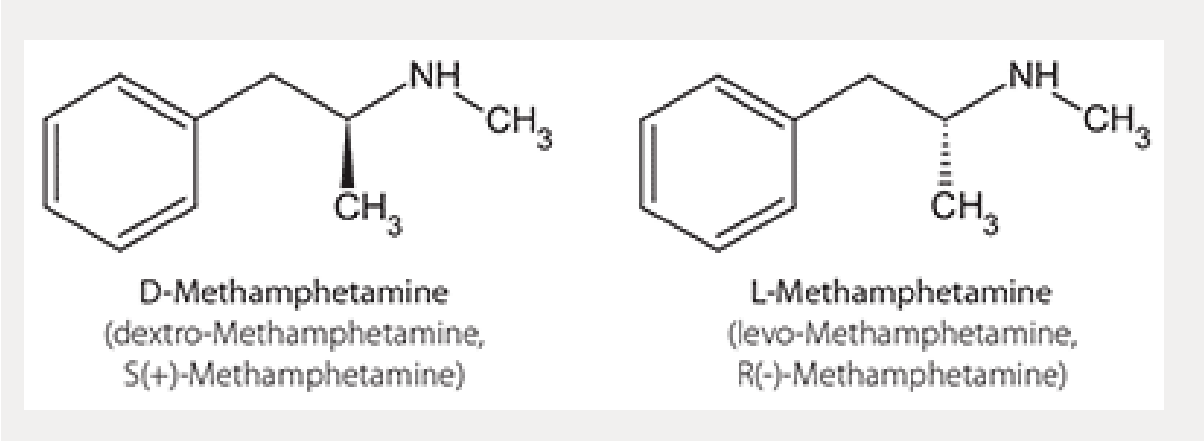
Isomers of crystal meth

Crystal meth is more formally known as methamphetamine but its scientific IUPAC name is N-methyl-1-phenylpropan-2-amine ($C_{10}H_{15}N$) and consists of 2 isomers which are known as levomethamphetamine and dextromethamphetamine more commonly known as l-methamphetamine and d-methamphetamine.

How is it an isomer?

The 2 isomers of Methamphetamine are enantiomers which is a type of optical isomerism and therefore a type of stereoisomerism meaning that the 2 isomers have the same molecular and structural formula but have a different spacial arrangement.

Enantiomers more specifically mean that both the isomers are chiral molecules (molecules that are not super-imposable onto their mirror image). Meaning the two molecules cannot be placed on top of one another to give the same molecule.



From the image above we can tell that the isomers are dependent on the bond angle between the methyl group and a carbon on its chain.

When was it discovered?

Although there are various reports of Methamphetamine first being discovered and created the earliest date goes back to 1893 where a Japanese chemist attempted to find an alternative to a chemical used from the ephedra plant which had previously been used for centuries as a traditional Chinese medicine to help reduce tiredness. Eventually in 1893 they were able to find a manmade alternative now known as crystal meth, and at the time they were able to identify two different sub-groups now represented by the 2 isomers levo and dextromethamphetamine.

At the time of discovery the method of its creation was not very efficient and as a result as time passed more potent methamphetamine was able to be made in a more efficient and time conserving manner. By 1919 it was widely used in Japan as its soluble properties allowed it to be easily injected into patients and after a couple decades it was widely used in WWII by both sides in order to keep their troops awake. But as time passed and the objects side effects began to be discovered the distribution of the item slowly decreased until it reached a point where it was banned by several countries in the 1970's.

What is methamphetamine used for?

The molecule is an amphetamine that acts as a central nervous system (CNS) stimulant which has more than one function depending on its isomer. There are 3 types used which are levomethamphetamine, dextromethamphetamine and Dextro-levomethamphetamine which uses a mix of both isomers. Where L-methamphetamine only affects the CNS both D- methamphetamine and Dextro-levomethamphetamine also affect your sympathetic nervous system (SNS) which also includes your brain as well as spinal cord.,

Levomethamphetamine:

- Levomethamphetamine can be used as a weight loss drug as it provides a mild energy boost increasing the rate of your metabolism as it causes a rise to the normal level of activity in your bodies nerves.
- The L-isomer has no mind-altering effect so is widely used as a non-prescription nasal decongestant.

Dextromethamphetamine:

- This drug affects chemicals in the brain that contribute to hyperactivity and impulse control so can be used to treat narcolepsy ("a chronic sleep disorder characterised by overwhelming daytime drowsiness and sudden attacks of sleep.")
- By being able to change the amount of certain substances in your brain dextromethamphetamine can be used to treat attention deficit hyperactivity disorder (ADHD). This is because it can increase your ability to stay awake and remain focused.
- It is also used as an illegal drug as it has mind-altering effects which causes an increase of dopamine production in the brain and therefore triggers heightened activity in the brains pleasure centre, making it a very addictive substance.

Dextro-levomethamphetamine:

- This is a mix of both the L and D isomer and is therefore known as a racemic mixture so produces the same effects of dextromethamphetamine but in a less extreme form but still has a very toxic side effect meaning it is also banned.

Structure of Methamphetamine:

Both isomers of methamphetamine have the same molecular and structural formula but have a different special arrangement. The 2 isomers can be identified depending on the bond angle at which the methyl group is attached to the carbon atom.

Since this is a case of optical isomerism the two isomers have different effects on plane polarised light and as a result the two isomers can be differentiated. They can be differentiated by seeing the direction in which they polarise the light waves. (-)-methamphetamine will produce an anticlockwise rotation whilst (+)-methamphetamine will produce a clockwise rotation. The racemic mixture of the dextro-levomethamphetamine will produce no rotation as the (+) and (-) will cancel one another out.

IUPAC	(2S)-N-metyl-1-phenyl-propan-2-amine
Formula	$C_{10}H_{15}N$
Molecular Weight (u)	149,223
Form	Oily brown liquid
Acid dissociation constant at 298.15 K	9,9
Fusion Point	170-175°C (443,15 - 448,15 K)
Boiling Point	300-305°C (573,15 - 578,15 K)
LD_{50} (mg/kg)	15

Is it safe to use?

- L-methamphetamine has not impact on the brain so is very safe to use and as a result is available with no prescription needed.
- D-methamphetamine has many side effects such as stomach cramps or muscle tremor as well as the fact that overdoses could be fatal so should only be used if prescribed and under the strict guidelines set by the doctor or carer.

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Although methamphetamine, discovered in 1893, has legitimate uses in treating various medical conditions, its derivative CRYSTAL METH (the hydrochloride salt) has found notoriety in its use as a so-called *recreational drug*. It is, in fact, illegal to possess it in most countries of the world.

Although we may view recreational drug abuse as a comparatively modern social phenomenon, it is almost certain that humans have always experimented in one way or another with psychoactive substances, both natural and man-made. Historically, psychoactive substances have been used by (i) priests in religious ceremonies (eg, amanita muscaria); (ii) healers for medicinal purposes (eg, opium); or (iii) the general population in a socially approved way (eg, alcohol, nicotine, and caffeine).

Pathological use of naturally occurring substances is well told in classical Antiquity. Perhaps the most famous example is *Nepenthes pharmakon* (being a species of the carnivorous pitcher plant) which is mentioned in the 9th century BC in Homer's Odyssey (4, 221). It is written that the beautiful Helen of Troy had received this potion from an Egyptian queen and that she used it to treat the Greek warriors - *“presently she cast a drug into the wine of which they drank to lull all pain and anger and bring forgetfulness of every sorrow”.*

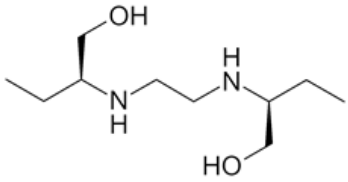
ISOMERS OF ETHAMBUTOL

Alan John (Year 12)

What is Ethambutol?

Ethambutol is an antibiotic primarily used in conjunction with other antitubercular agents to treat tuberculosis. It was first discovered in 1961 at Lederle Laboratories of the pharmaceutical company American Cyanamid. It is a bacteriostatic which halts the reproduction of bacteria by interfering with its metabolism as well as preventing cell walls from forming. It is also effective in the treatment of infections caused by other mycobacterium species such as Mycobacterium avium complex.

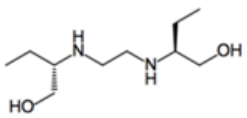
Structure



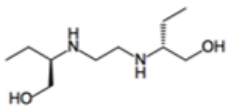
Molecular Formula:
$C_{10}H_{24}N_2O_2$

Ethambutol contains two chiral carbons, which means that it can form stereoisomers. It also contains several functional groups. There are two primary alcohol groups, one at each end of the molecule. There are also two secondary amine groups, each of which are attached to a chiral carbon. Ethambutol also has two ethyl groups which are attached to chiral carbons.

Stereoisomerism



(*S,S*)-(+)-ethambutol



(*R,R*)-(-)-ethambutol

On the left is d-ethambutol, which is used to treat tuberculosis, while on the right is l-ethambutol which can cause blindness. It is an example of an enantiopure drug because it contains only the d enantiomer. Ethambutol also has an (S,R) stereoisomer, but it is optically inactive because the S and R cancel out.

Dangers

Like it's enantiomer, d-ethambutol can have adverse effects on vision, although much less serious. Most are temporary, but in severe cases even the d-enantiomer can cause long lasting or permanent vision impairment. Chills, joint pain, fever, numbness, blurred vision and colour blindness are among the possible side effects, but they are fairly uncommon.

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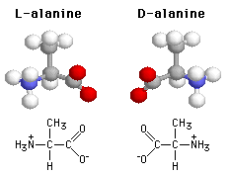
There has been mention in these papers of a form of isomerism known as STEROISOMERISM, in which molecules have the same molecular formula and sequence of bonded atoms (constitution), but differ in the three-dimensional orientations of their atoms in space. Derived from this there are the ENANTIOMERS, also known as *optical isomers*, that are essentially two forms of the same compound that are mirror images of each other.



An optical isomer can be named by the spatial configuration of its atoms. The D/L system (named after Latin *dexter* and *laevus*, right and left), does this by relating the molecule to a reference molecule, glyceraldehyde, which has D- and L- forms, and is basically identifying the right and left handed versions of the molecule.

Now consider this... we all know how essential AMINO ACIDS are in all living organisms, they are effectively the building blocks of all life. All amino acids, except *glycine*, occur as both D- and L- forms – **BUT ONLY THE L-AMINO ACIDS ARE MANUFACTURED IN CELLS AND INCORPORATED INTO PROTEINS!**

(By the way, almost all biologically active sugars are the D-forms!)

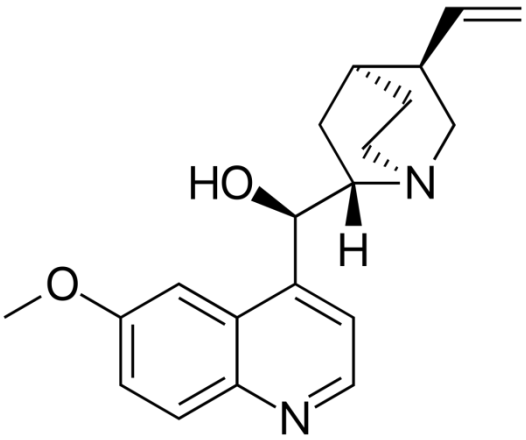
ISOMERS OF QUININE

Abigail Lau (Year 12)

IUPAC name: **(5-ethenyl-1-azabicyclo [2.2.2] octan-2-yl)-(6-methoxyquinolin-4-yl)methanol**

Molecular Formula: **C20H24N2O2**

Skeletal formula of Quinine shown right (Image taken from Wikipedia)



What is it used for?

- Quinine sulfate = Medication to treat malaria when it is resistant to chloroquine (another antimalarial drug) (Anand, Sharma 1997)

Medication can be given orally (tablets) or via intravenous therapy (IV). If IV injections are given too quickly the overdose may cause a sudden heart block, ventricular fibrillation and even death (Anand, Sharma 1997).

How does it treat Malaria?

Quinine has a specific toxicity to the parasite Plasmodium Falciparum. It inhibits the parasite's ability to dissolve and metabolise haemoglobin leading to the parasite's death.
(DrugBank 2017).

- Beverages e.g. Gin and Tonic ,Vodka - quinine is an ingredient in tonic water which gives it its bitter taste. Tonic Water has also been used to treat nigh time leg cramps linked to problems with the circulatory or nervous system.

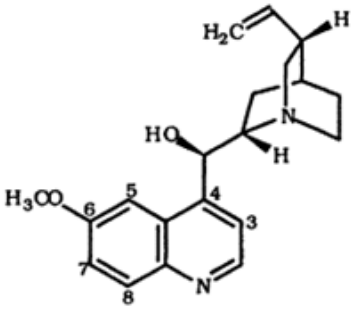
This is not recommended because over consumption of quinine in tonic water can lead to severe side effects such as: bleeding problems associated with platelets, kidney damage, abnormal heart-beat and severe allergic reactions (Roland 2018).

A brief history of quinine

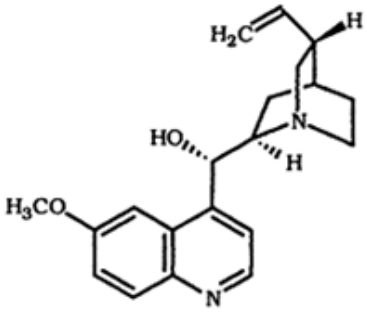
Quinine was found through extraction from the bark of a cinchona tree located in South America by Pelletier and Caventou in 1817. However, it took 150 years from when it was extracted and isolated to be totally synthesised for industrial use. Woodward and Doering synthesised Quinine in 1944. Other malarial drugs e.g. chloroquine are based on the structure of quinine (Kuroda, Izawa 2010).

Isomers of Quinine

Skeletal formulas for quinine and quinidine shown below (Images taken from "Studies in Natural Products Chemistry (2000) www.sciencedirect.com)



quinine **1**



quinidine **2**

Quinine exists as a diastereomer of quinidine which is another drug that can also be used to treat malaria also found from cinchona trees.

What are diastereoisomers?

Diastereomers are optical isomers that are not enantiomers. They are nonsuperimposable, non-mirror images of each other. They have different physical properties as well as different chemical properties. Diastereomers occur when there are two or more chiral centres*.

Look at the bonds between HO and H on both isomers:

Bold wedged line on quinine = bond protruding out from plane of drawing surface

Dashed line on quinidine = bond is extending behind the plane of drawing surface

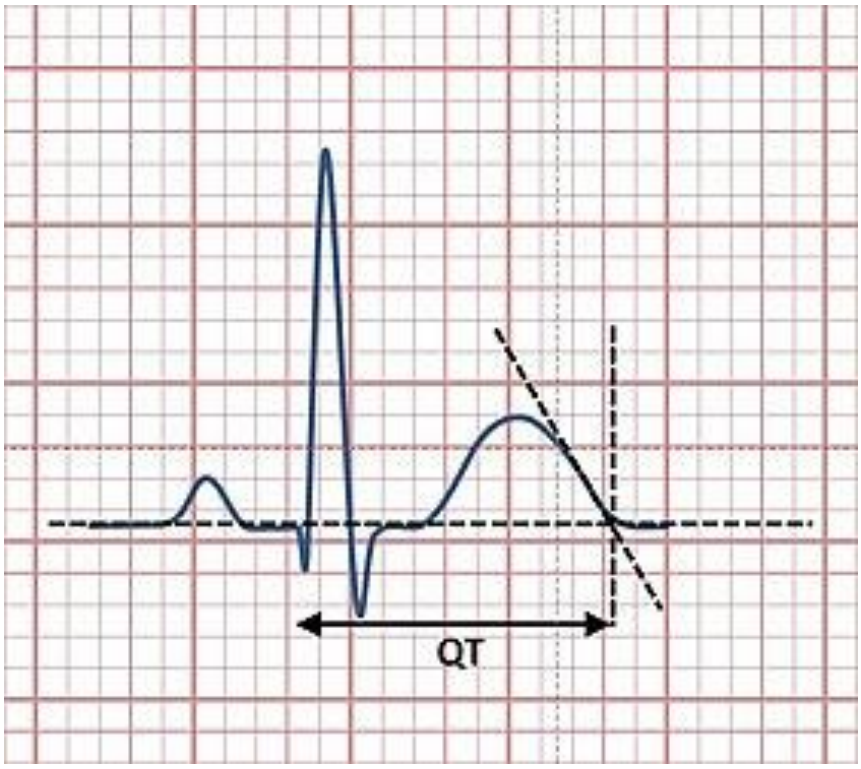
Quinine and quinidine exist as diasteromers of each other because quinine has four chiral centres (which is more than two). If quinine has 4 chiral centres it must have 16 stereoisomers.

- Use 2^n to work out maximum number of stereoisomers where n is the number of chiral centres

**Chiral centre = an atom in a molecule that is bonded to four different chemical species*

The differences between the uses for when quinine and quinidine are used to treat malaria: quinine is used to kill the parasite because of its specific toxicity, quinidine prevents the parasite from growing. Quinidine can also be used to treat and prevent irregular heart rates by prolonging the QT interval (the interval between the contraction/depolarisation of the ventricles to the relaxation/repolarisation of the ventricles). (University of Illinois-Chicago, Drug Information Group 2017)

Image of an ECG below with QT interval annotated (Wikipedia)



IMPORTANT NOTE Quinidine:

- CANNOT help heart blockages (e.g. to help severe side effect from quinidine refer to overdose of quinine in tonic water)
- It treats irregular heart rates but can ALSO CAUSE A FATAL irregular heartbeat called torsade de pointes

(University of Illinois-Chicago, Drug Information Group 2017)

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Ms Lau, in her paper above, has given us a fascinating insight into the discovery of quinine (1817) and its subsequent synthesis for commercial use (1944).

What is less well known is that quinine had been used by the Quechua people of South America about 300 years before its eventual discovery. They didn't know it was quinine, but they had come to realise that the bark of the *Cinchona* tree, when pulped and eaten, would reduce the shivering caused by low temperatures. In fact, because the bark had a really bitter taste, they would mix it with sweetened water to make it taste better.....

They didn't realise it at the time, but they had actually invented TONIC WATER!

Its usefulness in the treatment of *Malaria* also dates back to these early times. Jesuit missionaries visiting South America in the early 1600s brought samples of Cinchona bark back to Europe. Malaria was then rife in and around Rome and the medicinal property of the Cinchona bark was used to treat the disease quite successfully. In fact, towards the end of the 17th century the treatment was used to cure King Charles II who had returned to England with the disease, and Cinchona bark subsequently became popular in London.

19th-century illustration of Cinchona calisaya

ISOMERS OF RETINAL

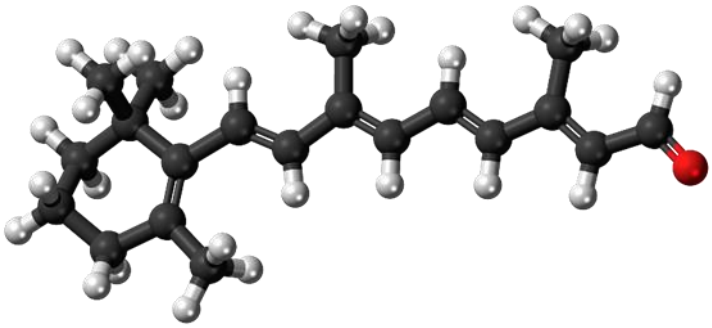
Isobel Browning (Year 12)

Retinal isomers and the vision cycle

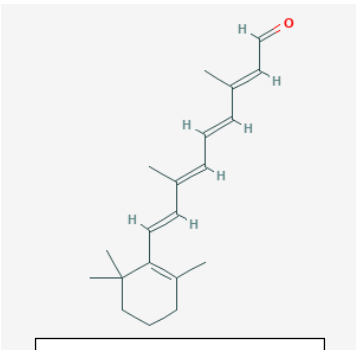
Retinal, also called retinaldehyde is classed as a retinoid, meaning it is a form of vitamin A, a group of unsaturated nutritional organic compounds which include retinol, retinal, and retinoic acid, amongst others. This group of organic compounds has many physiological functions, such as growth and development, the maintenance of the immune system and good vision. The parent molecule of all retinoids is ß-carotene. Animals cannot produce this, so either ingest it from other animals or from the variety of edible plants which produce large quantities of it.

The chemical formula of retinal is C20H28O and its IUPAC name is (2E,4E,6E,8E)-3,7-dimethyl-9-(2,6,6-trimethylcyclohexen-1-yl)nona-2,4,6,8-tetraenal. This paper will focus on two isomers of retinal- 11-cis-retinal and all-trans-retinal- and their crucial role in allowing organisms to convert visual light to metabolic energy, thus allowing vision.

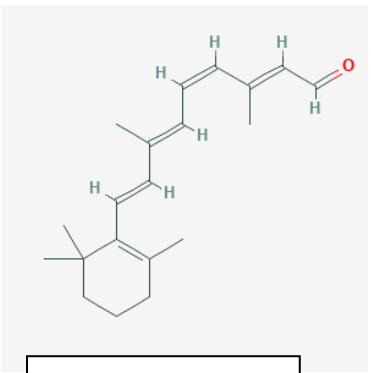
The structure of retinal:



Retinal is a conjugated chromophore. This means the p orbitals of bonded carbon atoms overlap across an intervening sigma bond, connected by delocalised electrons. This conjugation occurs because the retinal molecule is also a polyene; a poly-unsaturated organic compound with three or more alternating double and single carbon bonds. This results in a molecule with overall lower energy and increased stability. Retinal is made up of a ring of 6 carbons, with two methyl groups attached to the 1st carbon, a methyl group attached to carbon 5 and a chain of 9 carbons with alternating double and single bonds, attached to the 6th carbon. Attached to the 15th carbon is a CHO group. The 11-cis-isomer has its largest substituents on the same side of the double carbon bond between the 11th and 12th carbon. The all-trans-isomer, meanwhile, has all 4 exocyclic double bonds in trans geometry, meaning at the 11th carbon the two largest substituents are on opposite sides of the double bond. This results in a difference in shape between the isomers: the cis isomer is bent, whereas the trans form is a more linear molecule, with trigonal planar bonding about the double bonds (a bond angle of about 120 degrees).



All-trans-retinal



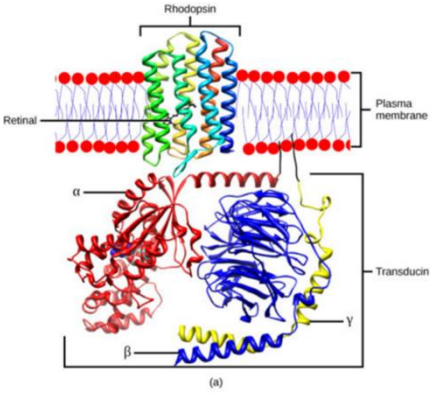
11-cis-retinal

The isomerisation of 11-cis-retinal to all-trans-retinal:

When cis-retinal absorbs a photon, the energy absorbed promotes an electron in the p orbital in the π bond between the 11th and 12th carbon to a higher energy level. This "breaks" the pi component of the bond, allowing for rotation. The molecule swings around this bond 180 degrees and reforms in the trans configuration, before the double bond is reformed. This results in a change of shape, as 11-cis-retinal is bent and the all-trans-isomer is straight.

Role of retinal:

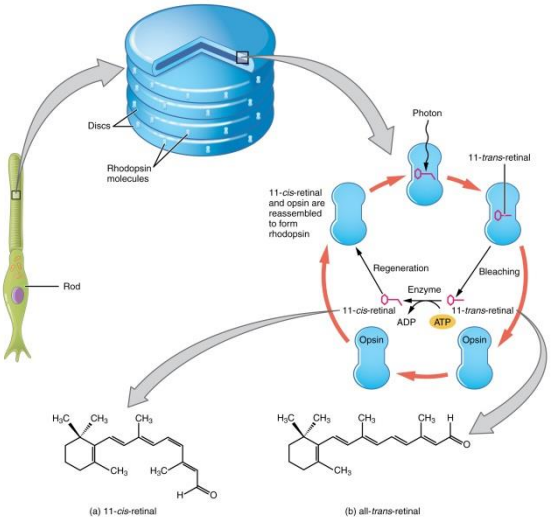
The vision cycle:



The isomerisation of retinal between the cis formation to the trans formation is central to the mechanism of sight utilised by all animals. 11-cis-retinal is found in photoreceptor cells in the retina, bound to proteins called opsins. Together, they form a complex called rhodopsin (or visual purple); an opsin joined to an 11-cis-retinal molecule via a protonated Schiff base (a compound with general structure R2C=NR') on one of its lysine side chains. Opsin alone cannot absorb visible light. However, when it is bonded to 11-cis-retinal in rhodopsin, the molecule can absorb a broad range of visible light, with a peak of absorption around 500nm. When a photon of light reaches the molecule, the 11-cis-retinal molecule isomerises to form all-trans-retinal. Because of the isomerisation, the molecule changes shape. As all-trans-retinal doesn't fit perfectly into the opsin binding point, unlike 11-cis-retinal, the Schiff base linkage becomes unstable and the entire rhodopsin molecule changes shape to compensate. This results in the expulsion of the all-trans-isomer. This rapid movement of the protein causes the membrane attached to straighten out. This membrane forms disc walls making up the photoreceptor cells, and when it straightens out it causes the movement of many discs. Ultimately this results in the closing of Na+ channels in the cell membrane, causing a large potential difference to build across this membrane. This potential difference is then passed to adjoining nerve cells as electrical impulses, which travel up the optic nerve and results in an image in the brain. The all-trans-isomer is then converted back into the cis-isomer by enzyme catalysed reactions, one of which is ATP phosphorylation. It is then attached to another opsin, allowing the cycle to continue.

Animals have three types of visual receptors, which allow us to see colour. In all these the primary molecule is 11-cis-retinal. Variations in sidegroups attached to the opsins mean different wavelengths of light can be absorbed, and therefore colour can be seen.

This mechanism, utilising the isomerisation of retinal from 11-cis to all-trans is found in molluscs, arthropods and vertebrates. This is because it is very sensitive to light and absorbs very strongly, and, in the absence of light is very stable, the isomerisation only taking place in dark once per a thousand years. Moreover, the universal use of 11-cis-retinal as a light receptor is due to the relatively large structural change which occurs, the Schiff base attachment moving 7 angstroms when the molecule isomerises, large enough to generate a nerve impulse.



For decades, scientists have questioned why all known animals have evolved to use 11-cis-retinal in mechanisms allowing them to see, as opposed to 9-cis-retinal or 7-cis-retinal. However, a recent study was able to answer this through building digital models of rhodopsin found in eyes of cows, monkeys and squid, and replaced the 11-cis isomer with that of 7-cis, 9-cis and 13-cis. When looking at the structure, stability and energetics of the resulting molecules, they found that the link between the 11-cis-retinal and opsin has a higher stability than the other isomers and is therefore favourable for photochemical reactions.

Elsewhere in the body:

Evidence suggests retinal may also play a role in adipogenesis in mammals, although the isomer configuration seems to have less effect in this instance. Furthermore, retinal is an immediate metabolic precursor to retinoic acid, which regulates epithelial cell differentiation.

In industry and medicine:

Retinal is relatively common in some skin care products which claim to improve firmness of skin and reduce the appearance of wrinkles, by stimulating collagen production. These features are common to all retinoids. On the skin, enzymes convert the retinoid to retinoic acid, the only active form of vitamin A. The number of steps in this process depends on the retinoid, and as retinal, an aldehyde can be converted to retinoic acid, a carboxylic acid, through just one reaction, retinal is highly effective as a skincare product.

There is also industrial interest due to retinal's potential use as a reactant to produce analogues of retinoic acid, specifically N-(4-hydroxyphenyl)retinamide, which is known to have cancer chemopreventive and chemotherapeutic properties and reduced toxicity.

The discovery of retinal:

The central reactions of the visual cycle were identified by American neurobiologist George Wald, who studied pigments in the retina in the 1940s. He discovered the 11-cis-isomer in its rhodopsin complex, bound to opsin in Schiff base formation as well as proposed the isomerisation of the molecule in the presence of light. As a result, he was awarded the Nobel Prize in Physiology or Medicine in 1967, alongside Haldan Keffer Hartline and Ragnar Granit.

How it is produced:

Vertebrate animals source retinal by ingesting meat or producing their own from carotenoids obtained from photosynthetic organisms.

E.g. ß-carotene + O2 -> 2 retinal.

Retinol is a storage form of Vitamin A. All-trans retinol travels from where it is stored in the liver to the eyes where it is converted to cis retinol by isomerisation ad then oxidised to retinal.

Invertebrates can see through use of hydroxylated forms of retinal. These are produced from xanthophylls.

Synthesis in industry:

There is no clear optimal reaction pathway to produce retinal. It can be obtained through the oxidation of retinol using MnO2 which produces a relatively high yield, with fewer side products. However, retinol is very expensive, costing a similar amount to retinal ($8000- $20 000 per 100g), so this is not economically viable. Alternatively, another common method is to prepare retinal through the hydrolysis and oxidation of retinyl acetate, which is produced on an industrial scale and is therefore much cheaper. But the yield is variable and overoxidation contaminants are common. An ideal pathway is yet to be found.

Toxicity of retinal:

If the retina is exposed to high levels of light, all-trans-retinal molecules accumulate. If too much all-trans-retinal present, it can be toxic and lead to apoptosis and capsase activation. It has also been shown to induce an overproduction of intracellular reactive oxygen species through stimulating NADPH oxidase-mediated reactions. This results in photoreceptor degeneration and abnormal accumulations of all-trans-condensation products have been found in people suffering from age-related macular degeneration, Stargardt disease and some other retinal diseases.

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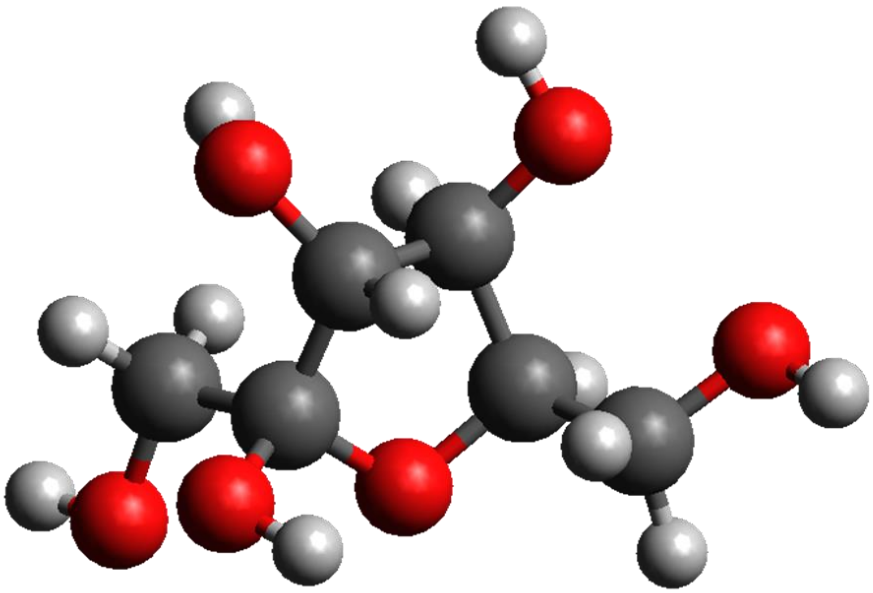
ISOMERS OF THALIDOMIDE

Harriet Green (Year 12)



Thalidomide- C13H10N2O4

TYPES OF ISOMER

Structural Isomers

Structural isomers are compounds with the same molecular formula but different structures. There are 3 types: chain, functional group and positional isomers. Chain isomers have different arrangements of the carbon skeleton. Position isomers have different positions of the functional groups. Functional group isomers have a different arrangement of atoms that changes the functional group.

Stereoisomerism

Stereoisomerism is molecules with the same molecular formula but different spatial arrangements. There are 2 types: E/Z (or geometric) and optical isomers. E/Z isomers often involve a carbon-carbon double bond, this is because there is limited rotation around them. If the two atoms or groups with the highest priorities are on the same side the isomer is the Z isomer. If the highest priority isomers are on opposite sides of the isomer it's the E isomer. Optical isomers have different spatial arrangements of atoms; which have non imposable mirror images.

BACKGROUND OF THALIDOMIDE

Thalidomide was first introduced in West Germany in October 1957, by a company called Chemie Grunenthal GmbH. It was an anticonvulsant which was marketed under the name Contergan as a sedative, and later as a medication for pregnant women experiencing morning sickness. It was claimed at the time as a wonder drug for insomnia, headaches, coughs and colds. It was available over the counter at the time and was widely prescribed across the world to pregnant women.

It was thought to be extremely safe as it had been tested on animals to no ill effect and it had been discovered that it was extremely difficult to achieve a lethal dose- however it had not been tested on pregnant animals and the tests had been conducted on rodents- which metabolise chemicals differently to humans (1).

By 1960 doctors had begun to raise concerns over the potential side effects of the drug. There was evidence to show that a side effect of long term use of the drug was nerve damage. However it still took at least another year until people began to draw connections between use of thalidomide and deformities in babies. By the time thalidomide was identified as the cause of the deformities- roughly 10,000 infants have been born with limb malformation.

The drug has teratogenic effects (it disturbs the development of a foetus, leading to congenital malformations- birth defects) when administered during pregnancy. This occurred in the form of skeletal deformities- the absence of limbs, congenital heart defects, facial palsy, renal and urinary malformations, phocomelia (shortness of limbs) and genital malformations among others. The death rate at and slightly after birth is 40% (Teo Et Al., 2004)

Thalidomide was mainly taken by the pregnant women between 5-9 weeks when the limbs of the infant are still developing (BBC, 2009). It was found that when the drug was administered at the same stage of the chickens pregnancy as the pregnant human mothers who took the drug- limb development was severely affected, but not the main body of the embryo, presumably due to the more advanced development of the blood vessels in the torso and head of the foetus. When the drug was administered in the earlier stages of the pregnancy, when the blood vessels were in earlier stages of their development, the chick embryo died. This was further supported when the drug was administered later in the pregnancy when the embryo's blood vessels were better developed the side effects of limb malformations were less severe (Ledford, 2009). This has led to the conclusion that thalidomide inhibits the development of new blood vessels.

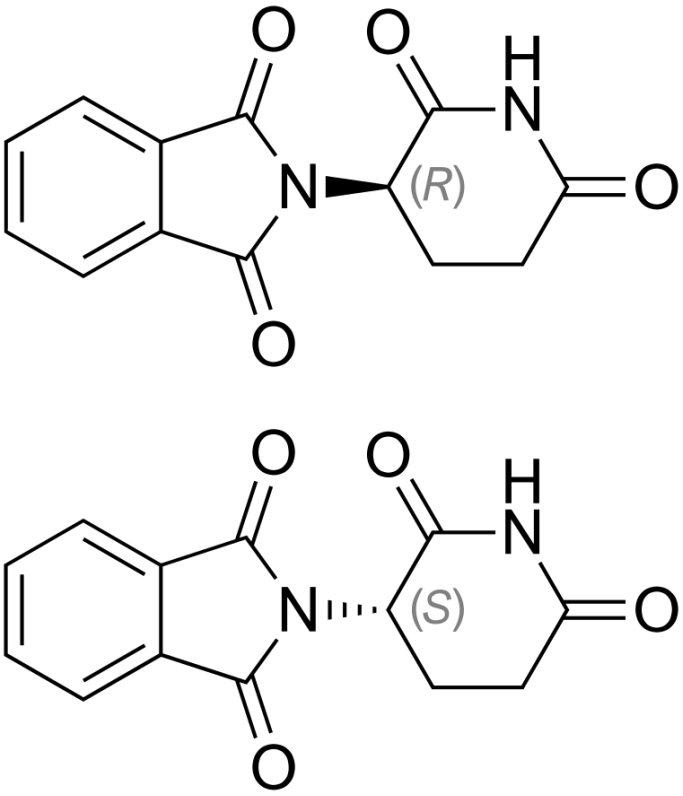
The Positive Uses Of Thalidomide

Thalidomide was later found to be effective in relieving some of the painful symptoms caused by leprosy. It has been used as treatment for leprosy, Kaposi's sarcoma, myelofibrosis (type of bone marrow cancer), RAUs (recurrent aphthous ulcerations) and wasting associated with AIDS or HIV. (Shetty,2007)

Thalidomide as an isomer

Thalidomide has 2 optical isomers due to its chiral centre- the ®- and (S)-enantiomers. The 2 isomers have different uses: the ®-enantiomer is the isomer that helps with morning sickness and has sedative effects. It's the (S)-enantiomer that has the teratogenic effects.

The thalidomide that's available as a drug is a racemic mixture of the 2 isomers. Separating the isomers doesn't help because under biological conditions the isomers interconvert.



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Two papers here, by Ms Green and Mr Lenane, dealing with the isomers of the drug *Thalidomide* also note the fact that its use by pregnant women caused very distressing birth defects, particularly missing and deformed limbs. Introduced in 1957, quite rightly the use of Thalidomide was banned in 1961 as soon as its horrendous side-effects became apparent. One important result of this episode was the adoption of much more stringent regulation, testing and monitoring of new drugs, as well as a greater appreciation of the need to strictly control medication during pregnancy.

However, the Thalidomide story did not end in the 1960s – for many years researchers continued to evaluate the drug, under strictly controlled conditions, for a variety of medical conditions. It is now being used to treat two conditions in particular: leprosy and multiple myeloma (a type of cancer). Furthermore, researchers continue to investigate thalidomide for use in treating a variety of other diseases and conditions. Though more study is needed, thalidomide has shown promise in treating:

- Inflammatory diseases that affect the skin, such as cutaneous lupus and Behcet's disease
- HIV-related mouth and throat ulcers, as well as HIV-related weight loss and body wasting
- Cancer, including blood and bone marrow cancers, such as leukemia and myelofibrosis, as well as cancers found elsewhere in the body

ISOMERS OF THALIDOMIDE

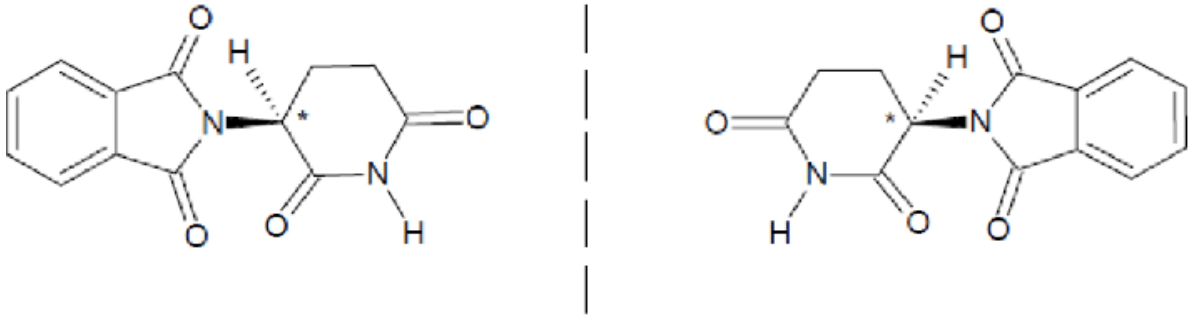
Thomas Lenane (Year 12)

Thalidomide is a molecule with the molecular formula of $C_{13}H_{10}N_2O_4$. It has one chiral atom so it exists as two enantiomers.

Enantiomers are optical isomers which are non-superimposable mirror-image structures. The property of non-superimposability is called chirality. Thalidomide has one chiral carbon atom, which is when four different atoms or functional groups are attached to a carbon atom. Due to there being one chiral carbon the molecular arrangement is tetrahedral and the arrangement of these bonds in space leads to there being two enantiomers.

The two enantiomers of thalidomide are (+)-thalidomide and (-)(S)-thalidomide, the differences between these isomers are denoted by the +/- or R/S. The +/- refers to the ability of each isomer to rotate a beam of plane-polarised light. If the isomer rotates the light in the clockwise direction then it's known as dextrorotatory and this is denoted by the (+), and if the isomer rotates the light in the anticlockwise direction then it's known as levorotary and this is denoted by the (-). The R/S refers to the actual shape of the molecule. In a hierarchy based on the atomic number, where the highest atomic number has the highest priority, if the lowest priority group attached to the chiral carbon is orientated to point away from the viewer and the arc from the second to third priority goes in a clockwise direction then it is an R enantiomer. If the arc goes in an anticlockwise direction then it is an S enantiomer.

The structure of the two isomers of thalidomide are shown below and the chiral carbon is denoted by the * :



(-)(*S*)-thalidomide (+)(*R*)-thalidomide

In 1953 thalidomide was first synthesised by a drug company in West Germany. The drug was made and marketed as a racemic mixture which is a mixture that contains equal amounts of each enantiomer. In 1957 a pharmaceutical company in West Germany introduced thalidomide to the market. The drug was sold in 46 countries under at least 37 different brand names. By 1961 thalidomide was the best selling sleeping pill in West Germany and the UK. It was also found to prevent nausea due to pregnancy.

However in 1960 harmful side effects of thalidomide reported. Patients who took the drugs found that their nerves in their hands and there feet were deteriorating. It was also later found that it caused severe birth defects when taken by pregnant women. Babies were born with severe abnormalities such as hands and feet protruding directly from the torso, others had just a head and a torso, still others had abnormalities with their internal organs such as the heart and the kidneys. Many of these babies died due to the defects and there are estimates of between 8 000 – 80 000 deformed babies born in Europe due to thalidomide. This drug was not banned worldwide until 1962.

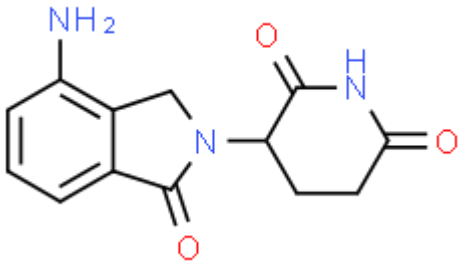
When the drug was synthesised the doctors and pharmacists did not know that the (+)-thalidomide is an effective sedative, whereas the (-)(S)-thalidomide is a teratogen which is a substance that affects foetal development and causes functional and structural disability. The (-)(S)-thalidomide isomer inhibits the growth of new blood vessels which has severe consequences for a foetus. The actual mechanism and reason for the effects of (-)(S)-thalidomide being so different from the effects of (+)-thalidomide is not known. There are many suggested mechanisms to explain the teratogenic action of the (-)(S)-thalidomide isomer. Some of these suggestions propose that (-)(S)-thalidomide might cause its negative effects by blocking the genes coding for some essential proteins. This could be because protein molecules are chiral, so they have different reactions with enantiomers because these are also chiral.

Many people thought that this problem could be solved by purifying the racemic mixture of the two enantiomers to just give the (+)-thalidomide. However, this is not an available solution because the human liver contains an enzyme that can convert the (+)-thalidomide to (-)(S)-thalidomide. Therefore even if a purified solution of thalidomide was administered with only the safe enantiomer this will still result as a racemic mixture after the drug has passed through the liver.

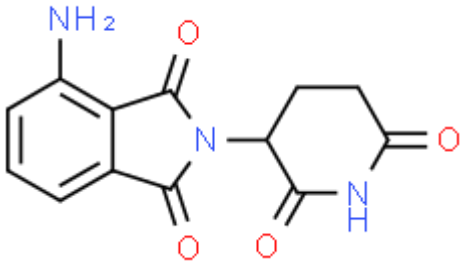
However in 1985 the ban on thalidomide was lifted and in 1998 the USA's food and drug administration approved thalidomide for the treatment of ENL, which is an inflammatory complication of leprosy. The drug doesn't kill the bacteria that causes the leprosy, but it changes the immune response to the bacteria. It's not recommended by the WHO because other drugs can work just as well that don't have the adverse effects. However, thalidomide is easy to produce at a very low cost so this is why it is used to treat ENL in many countries.

In May 2006 the food and drug administration in the USA also granted thalidomide in combination with another drug for the treatment of multiple myeloma which is a bone marrow cancer.

Unsurprisingly the victims of thalidomide are hoping that pharmaceutical companies could discover an analogue with the positive effects of thalidomide but without its harmful side effects. An analogue is a molecule that has a very similar structure to the molecule with the exception of a certain group. One class of thalidomide analogues is called immunomodulatory drugs. Examples are lenalidomide and CC-4047, which are shown below and you can see that they both have a very similar structure to thalidomide:



Lenalidomide



CC-4047

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CENTRAL DOGMA OF MOLECULAR GENETICS

Lily Bawden-Bouche (Year 13)

The central Dogma is a theory which provides an explanation on how genetic information is transferred through generations. The two scientists Francis Crick and James Watson are credited for this explanation and received a Nobel Prize in Physiology and Medicine 'for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material'. However, these two scientists are not completely responsible for this discovery. One man who contributed a considerate amount of research towards Molecular Genetics is Charles Darwin (Charlesworth, 2010). Darwin's work on evolution using many case studies such as with finches in the Galapagos Islands, 'the formation of coral atolls, fossils, 'the voyage of the beagle' and 'The Expression of the Emotions in Man and Animals' (Charles Darwin MA, 1872). This work helped falsify the work done by Crick and Watson.

The work by Francis Crick in 1958 then re-stated in 1970 provided evidence that there were 'three major classes of biopolymers: DNA, RNA and proteins and three classes of direct transfer of information that can occur between these biopolymers', these are 'general transfers, special transfers and unknown transfers' (Heba Sh. Kassem, n.d.). from these three 'general transfers' occur in most cells. General transfers DNA replication, DNA transcription to mRNA and mRNA translation. It is now known that these processes are essential to the replication of DNA and so life. These processes enable the transfer of genetic information and allow growth. Before the process begins the enzymes, DNA Helicase unzips the DNA strand inside the nucleus where it is stored. DNA is held tightly in a double helix which is too large to exit the nucleus. DNA replication and transcription can occur inside the nucleus because the enzymes required to carry out these processes are found in the nucleoplasm. However, translation occurs in the ribosomes in the cytoplasm or on the ribosomes which are attached to the rough endoplasmic reticulum.

Transcription is the first stage in the expression of genes. Performed by the enzyme RNA Polymerases using a DNA strand as a template it links nucleotides together forming RNA strands. Initiation is the first step in Transcription the RNA polymerase binds to a sequence of DNA called the promoter found around the start of the gene. The promoter initiates the transcription of the RNA strand; each gene has its own promoter. RNA polymerase will then separate the DNA strands, providing the single-stranded template needed for transcription. The second stage of Transcription is elongation. In this stage a strand of DNA acts as a template as RNA Polymerase reads it one base at a time, forming an RNA molecule growing from 5' to 3' with complementary nucleotides (Academy, n.d.). The RNA molecule will contain the same information but will replace the base thymine (T) with uracil (U). The final stage of transcription is termination. After this the newly formed strand of RNA leaves the semi-permeable nucleus and goes to a ribosome (Lumen, n.d.). Then translation occurs.

Translation also has three stages: initiation, elongation and termination. Translation is seen as the process where the previously made messenger RNA (mRNA) molecule is 'decoded'. In the first stage, initiation, a tRNA molecule which is also known as the 'initiator' and almost always carries methionine attaches to the small ribosomal unit (a ribosome consists of two units; a small and a large). Together the tRNA and small ribosomal unit bind to the 5' end of the mRNA which contains a 5' GTP cap (Academy, n.d.). They move along the mRNA towards the 3' end stopping when they reach the start codon. The start codon in all mRNA molecules has the sequence AUG and codes for methionine. Next, the large ribosomal subunit binds to from the complete initiation complex.

The following stage is elongation. The ribosomes continue to translate each codon. The triplet code states three nucleotides code for one amino acid. The amino acids are coded for, added to the chain and joined using peptide bonds (Scitable, 2014). This process continues until all codons have been translated. The final stage is termination. This occurs when the ribosome meets a stop codon. The tRNA molecules cannot recognise these codons the translation finishes and the new protein is released. It can occur that a person a has a mutation in their genetic code leading to them possessing a stop codon instead of another codon if one base is simple mistaken meaning the new protein may not have the correct shape and or function. This is called a nonsense mutation. This can be prevented by regulation. It is controlled using cell cycles which contain checkpoints between stages.

The Meselson-Stahl experiment provided proof to the DNA replication process. The theory of DNA replication suggested that it was 'semi-conservative' as that the new strand created was half 'old' and half 'new'. They used three models which used one double helix strand of DNA to produce two new strands. The two new strands consisted of one new and one old strand this was proved by the density of the strands (Matthew Meselson, 1957-1958). Nowadays the semi-conservative nature of DNA replication can be proved using more advanced equipment and the competition of the human genome project.

A peroxisome is 'a small organelle present in the cytoplasm of many cells, which contains the reducing enzyme catalase and usually some oxidase' (John Simpson, 1989). They are small vesicles, single membrane-bound organelles found around eukaryotic cells (BYJUS, n.d.) They are known to absorb nutrients that a cell contains as well as being involved in the digestive process of alcohol in organisms (Rader, n.d.). Peroxisomal membrane and matrix proteins are incorporated in the organelle after translation. For example, catalase folds in the cytosol and is incorporated as a folded protein (Lodish H, 2000).

The term **dogma** is derived from the Greek *dogma* (δόγμα) meaning literally *"that which one thinks is true"* and the verb *dokein*, *"to seem good"*. Its modern meaning can be stated as follows:

"a principle or set of principles laid down by an authority as incontrovertibly true."

Dogma has typically been used to describe principles or doctrines of religions or philosophical schools of thought. However, it can be used to describe *"a principle or set of principles"* in any area, even Science, as we can see from two excellent papers by Ms Bawden-Bouche and Mr Dry.

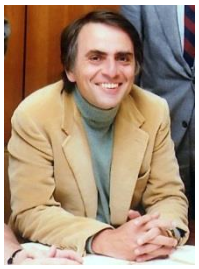
In fact, one might say that everything about Science is dogma according to the strict definition of the word. After all, isn't Science all about 'Laws' and 'Principles' that are deemed to be 'incontrovertibly true'. In education, for example, we teach such laws and principles as though they are definite. This monumentally misses the point!

As a general rule, scientists draw up laws and principles in order to explain events and phenomena: a scientific law is the description of an observed phenomenon. It doesn't explain why the phenomenon exists or what causes it. The explanation of a phenomenon is called a scientific theory. It is a misconception that theories turn into laws with enough research. Furthermore, just because an idea becomes a law, doesn't mean that it can't be changed through scientific research in the future. The use of the word "law" by laymen and scientists differ. When most people talk about a law, they mean something that is absolute. A scientific law is much more flexible. It can have exceptions, be proven wrong or evolve over time.

For example, Newton's Law of Gravity breaks down when looking at the quantum (sub-atomic) level. Mendel's Law of Independent Assortment breaks down when traits are "linked" on the same chromosome.

Two quotes come to mind when considering the role of Science in the search for "incontrovertible truth":

"Science is properly more scrupulous than dogma. Dogma gives a charter to mistake, but the very breath of science is a contest with mistake, and must keep the conscience alive."
George Eliot. Middlemarch: A Study of Provincial Life (1873).



"A central lesson of science is that to understand complex issues (or even simple ones), we must try to free our minds of dogma and to guarantee the freedom to publish, to contradict, and to experiment. Arguments from authority are unacceptable."
Carl Sagan. Billions and Billions: Thoughts on Life and Death at the Brink of the Millenium (1998).

AN INTRODUCTION TO THE CENTRAL DOGMA OF MOLECULAR GENETICS

Alfie Dry (Year 13)

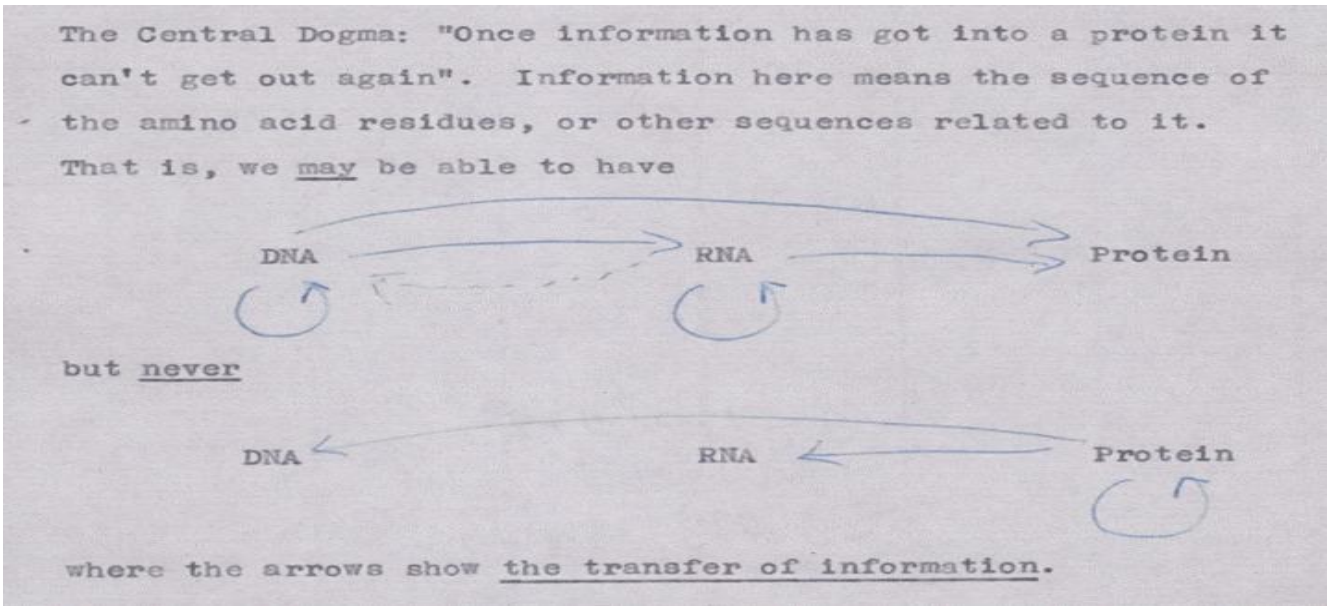
INTRODUCTION

In many modern textbooks, the Central Dogma of Molecular Genetics is stated as a simplistic 'DNA → RNA → Protein' (1) pathway – a theory popularised by James Watson. According to this definition, the Central Dogma describes the processes of transcription and translation which make up the mechanism of protein synthesis by which DNA codes for proteins. However, this definition is one that has strayed from the original theory and in some cases, proves to be refutable. The original Central Dogma proposed in 1957 by Francis Crick states that 'Once information has got into a protein it can't get out again. Information here means the sequence of the amino acid residues, or other sequences related to it' (2). While it may seem like basic knowledge in modern science, Crick's definition was revolutionary and remains valid today (supporting his choice of the word 'dogma') whereas the more modern version does not always hold with so infallibly.

THE PROPOSAL OF THE CENTRAL DOGMA

The first evidence of an understanding of the Central Dogma is in Francis Crick's notes from 1956 (Figure 1). Crick went on to deliver a renowned lecture in 1957 proposing the Central Dogma and stated that "the main function of the genetic material is to control … the synthesis of proteins" and "once information has got into a protein, it can't get out again." (2). Two statements which remain true today and summarise Crick's theory.

Crick had been interested in the relationship between DNA, RNA and proteins for years prior to the lecture and relied on the experimental evidence of the 'RNA Tie Club' – a group of 20 scientists including James Watson and Francis Crick who aimed 'to solve the riddle of the RNA structure and to understand how it built proteins' (3). The access to the experimental results of the group allowed Crick and Watson to build an idea of 'genetic information' (4) in relation to proteins. In the famed 1957 lecture, Crick described this genetic information as 'the determination of a sequence of units', which suggested a link between the sequence of bases in a DNA molecule and the primary structure of a protein. This trailblazing understanding of the nature of genes led Crick to conceptualise the Central Dogma and deliver the theory which remains valid today. This made Crick the first person to propose the idea but all of the 'RNA Tie Club' deserve recognition for their work which led Crick to the theory.



THE FLOW OF GENETIC INFORMATION

DNA is composed of two polymer chains in a double helix made up of monomers called nucleotides. These nucleotides (joined by phosphodiester bonds) comprise of a phosphate linked to a sugar which is linked to a nitrogenous base. Genetic information is stored as the sequence of bases along a nucleic acid chain – as Crick rightly hypothesised. In DNA, the bases are complementary and form hydrogen bonds to hold the two polymer strands together, maintaining the double helix shape. The base Adenine forms two hydrogen bonds with the base Thymine and the base Guanine forms three hydrogen bonds with the base Cytosine. These base pairs provide a mechanism for copying the genetic information in an existing nucleic acid chain to form a new chain as well as using it to synthesise proteins.

It is RNA, rather than DNA, which acts as the direct template in protein synthesis. When the double helix of DNA unwinds around a gene, free floating nucleotides are joined together in an order complementary to the template strand of the DNA. This process is known as transcription. This single stranded RNA is the molecule used at ribosomes to determine the sequence of amino acids used to synthesise a protein – a process known as translation. Each three consecutive bases on the RNA act as a 'codon' (5) which codes for a particular amino acid – the process which validates Crick's assertion that 'the main function of the genetic material is to control … the synthesis of proteins' (2).

Thus, the flow of genetic information can be summarised as:

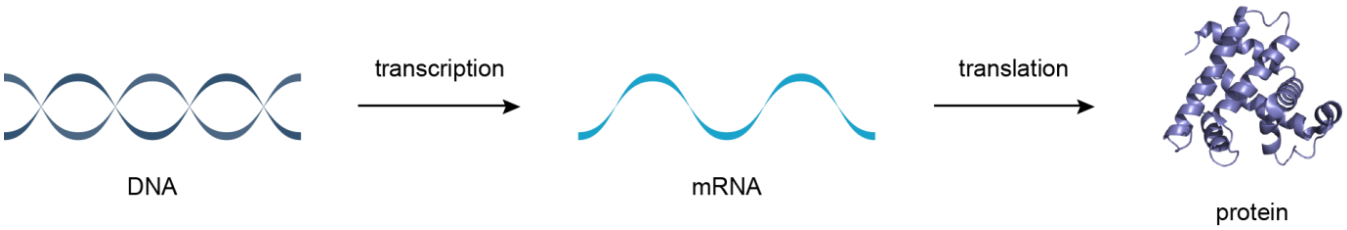


Figure 2

Crick was certain of this flow of genetic information and, perhaps even more importantly, wanted to assert that he considered three flows of information to be impossible due to both lack of evidence and lack of biochemical mechanisms. These were 'protein → protein, protein → RNA, and above all, protein → DNA.'(6) This summarises Crick's meaning when he said that once information had gone from DNA to the protein, it could not get out of the protein and go back into the genetic code. This is the central dogma.

DOES THE CENTRAL DOGMA STILL STAND?

In 1997, 'American biologist Stanley B. Prusiner received the Nobel Prize in medicine' (7) for his discovery of prions - proteins with an altered shape that are capable of transmitting their misfolded structure to other proteins. The distorted protein binds to similar proteins and causes them to change their structure as well, producing a chain reaction 'resulting in many proteins with the altered shape' (8). While prions are the culprits for multiple diseases such as Mad Cow Disease, they are capable of conferring beneficial phenotypes to cells as well, leading some to hypothesise that they may have a role in evolution.

In 2012, a controversial hypothesis stated that 'prion proteins act as epigenetic elements of inheritance' and 'might provide a mechanism for generating heritable phenotypic diversity' (9). A study of the same year suggests that 'combined with genetic variation, prion-mediated inheritance can be channelled into prion-independent genomic inheritance' (10). All of these hypotheses mean that it is possible for prions (which are proteins) to affect the genome of an organism. This directly violates Crick's Central Dogma which states that 'transfer of information from proteins back to nucleic acids does not occur in biological systems' (11). While the exact mechanism of how prions affect the genome and, in the long term, evolution, is uncertain, it is thought that the answer lies in epidemiology. Despite the uncertainties, it is irrefutable that (despite Crick's Central Dogma) a flow of information from protein to DNA through the action of prions is indeed possible.

CONCLUSION

Despite the misquoting of Crick's Central Dogma of Molecular Genetics in many modern textbooks, the basic rule that 'once information has got into a protein it can't get out again' (2) has generally remained undisputed. However, the recent development in the understanding of prions and epidemiology threatens the infallible 'dogma' status of Crick's theory as new pathways for genetic information open up. While this interesting topic does cause a stir with regards to the Central Dogma, it is undisputable that the main flow of genetic information in known cells follows Crick's Central Dogma. Crick jokingly referred to the role of RNA and the use of genetic information in cells as 'the mysteries of life' and in his 1957 lecture proposing the Central Dogma, he took the first step in unravelling those mysteries. Therefore, the importance of the Central Dogma and its enduring relevance cannot be understated.

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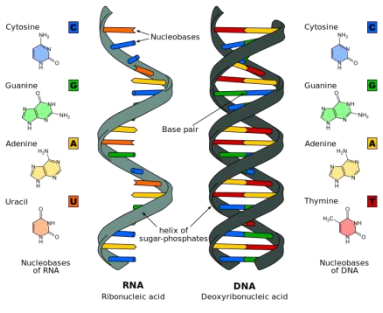
Figure 1: Cobb, M., 2020. *60 Years Ago, Francis Crick Changed The Logic Of Biology*.
Figure 2: Atdbio.com. 2020. *Transcription, Translation And Replication*. [online] Available at: <https://www.atdbio.com/content/14/Transcription-Translation-and-Replication> [Accessed 26 April 2020].

AN RNA WORLD



We have come to accept that DNA is the molecule that defines life – all living things use DNA as their genetic material and there are no exceptions. We might therefore conclude that when it comes to the origin and evolution of life on Earth, it must have started with nature's formation of DNA. However, there is significant evidence that this may not have been the case and that life actually originated using RNA!

Francis Crick himself suggested that RNA, not DNA, could have been the 'primordial molecule'. Throughout the 1970s scientists gathered more evidence of the importance of RNA in biological evolution, based upon the fact that many of the cofactors essential for enzymatic function are either nucleotides or could have been derived from nucleotides very similar to RNA. The phrase "RNA World" was first used by Nobel laureate Walter Gilbert in 1986, in a commentary on how recent observations of the catalytic properties of various forms of RNA fit with this hypothesis.

In November 2019, scientists reported detecting, for the first time, sugar molecules, including ribose, in meteorites, suggesting that chemical processes on asteroids can produce some fundamentally essential bio-ingredients important to life, and supporting the notion of an RNA world prior to DNA-based life on Earth.

STILLE AND SUZUKI COUPLING

Aleena Paul (Year 13)

INTRODUCTION:

A coupling reaction is when two fragments are joined together, in the presence of a metal catalyst. In particular we will be focusing on the Stille and Suzuki coupling where a palladium catalyst is used. Coupling reactions are comprised of several types of reactions, Oxidative Addition, Transmetalation and Reductive Elimination. Stille cross coupling requires tin while Suzuki coupling uses Boron, the two reactions are commonly compared due to similar electronegativity of the 2 elements. (Stille Coupling, 2020)

STILLE COUPLING:

The Stille coupling involves a C-C bond formation between Stannanes and halides. (Stille Coupling, 2020) Stannanes also known as Tin Hydride which is a colourless gas, SnH_4 (Stannane, 2020).Therefore, due to the ablitity to increase the carbon chain length, this reaction is used in the synthesis of many organic polymers, antibiotics and anticancer drugs e.g.Manzamine A

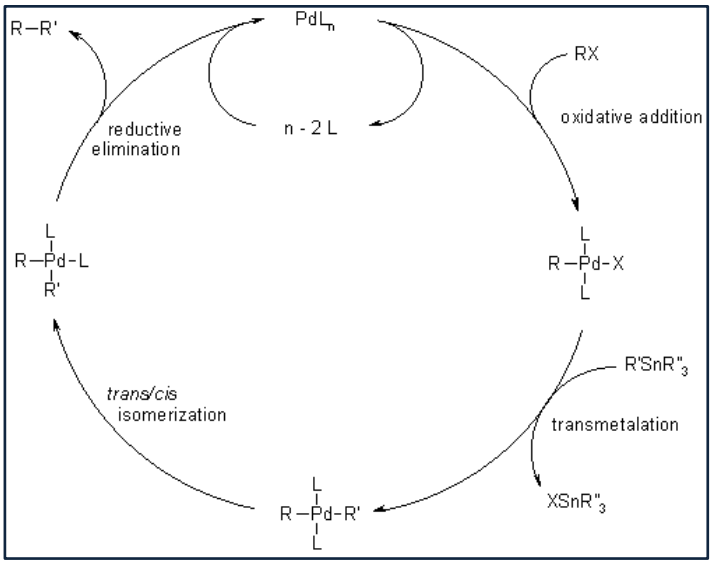
Advantages: Reactants are readily available and there is a wide range of halides to choose from- making this reaction easily accessible for production.

Disadvantages: The tin compounds have low polarity, making them insoluble in water and very toxic.

SUZUKI COUPLING:

In Suzuki Coupling, this occurs between **Organoboronic acid** and Halides.

Organoboronic acid is a derivative of boric acid, where one of its 4 hydroxyl group is replaced by an alkyl group. (Qu and Ramdular, 2020)This reaction is used in the synthesis of anticancer drugs like Epothilone A. Also, Suzuki coupling has been applied to create polymers of aromatic groups e.g.Polyelectrolytes, used in LED lights.



Advantages: Boranes are easy and safe to produce, therefore Suzuki Coupling is cost effective and there's minimal health risks associated with the procedure.

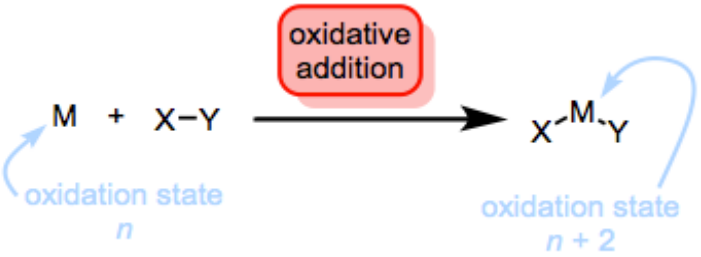
Disadvantages: Chloride substrates react slowly and have low yield. Also, if you don't use a base there will be many side reactions, therefore purification is necessary. (Qu and Ramdular, 2020)

Oxidative Addition:

Oxidative addition involves bond insertion and the addition of two new ligands to the metal; here this is palladium, and thus increasing its oxidation state from 0 to 2 since 2 d sub shell electrons are lost from the metal. For both coupling reactions, this means the addition of the alkyl halide group to the palladium complex. (Evans, 2019)

Transmetalation:

Transmetalation is a type of organometallic reaction that involves the transfer of ligands from one metal to another. In Suzuki coupling ligands are donated from the Organoborane to the Palladium complex. Whereas, in Stille this occurs from Stannane(contains tin) to the Palladium complex.(Transmetalation, 2020)



Reductive Elimination:

This process is the reverse of oxidative addition and causes the oxidation state of the metal centre to decrease, due to formation of a new covalent bond between two ligands,(Qu and Ramdular, 2020).This occurs after transmetalation because the palladium complex gains two new ligands from another metal(mentioned previously).

Grignard Reagents:

These are a group of halides called Organomagnesium halides having a formula of RMgX. (Merck, 2017)Grignard reagents are used in Kumada cross coupling, like the Stille & Suzuki reactions this also generated C-C bonds but differs due to the usage of the grignard reagents with the organic halides.(Kumada Coupling, 2016)

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All of the papers on Stille and Suzuki Coupling mention the use of **Grignard reagents**. Who was 'Grignard'?

VICTOR GRIGNARD, in full François-Auguste-Victor Grignard, (born May 6, 1871, Cherbourg, France—died Dec. 13, 1935, Lyon), French chemist and corecipient, with Paul Sabatier, of the 1912 Nobel Prize for Chemistry for his development of the Grignard reaction. This work in organomagnesium compounds opened a broad area of organic synthesis.

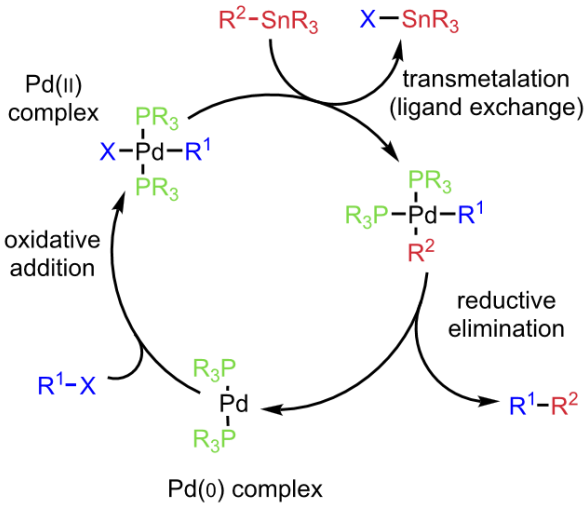
In 1898, while a student under Philippe Barbier at Lyon, Grignard began his prizewinning work with a study of the alkylzinc compounds developed earlier by Sir Edward Frankland. It was Barbier who had Grignard repeat some experiments on the preparation of a tertiary alcohol from a mixture of methyl heptyl ketone, magnesium, and methyl iodide. Grignard hit upon the idea of treating the iodide with the magnesium first and carried out the reaction in ether. This first of the Grignard reagents was a complete success. Grignard's doctoral dissertation (1901) described the preparation of alcohols, acids, and hydrocarbons by means of reactions of organomagnesium compounds. He became a professor of chemistry at Nancy (1910) and at Lyon (1919). At the time of his death, in 1935, some 6,000 papers reporting applications of the Grignard reaction had been published.

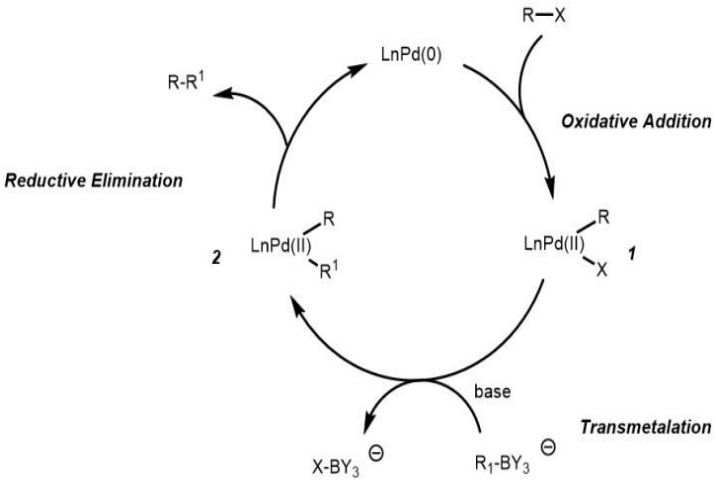
STILLE AND SUZUKI COUPLING

Hannah Conway (Year 13)

Stille Coupling

Stille coupling is the formation of a C-C bond between a stannane (a compound made of tin and hydrogen – SnH_4) and a halide[3]. It is used for the synthesis of natural products e.g. antibiotics and anticancer drugs. The chemistry of organopalladium is extremely valuable due to the exchange between the palladiums 0 and +2 oxidation states[2].





Suzuki Coupling

Suzuki coupling is the cross coupling between organoboronic acid and halides in the presence of a palladium catalyst[6]. It is used to make anticancer drugs and in polymer synthesis[7]. It is compared to Stille coupling due to boron's similar electronegativity to tin, however under conditions where either coupling could take place, Suzuki coupling is the one that will occur[7].

Oxidative Addition

The metal undergoing oxidative addition must have a stable oxidation state which is two units higher than the one it is currently in, e.g. 0 and +2. The metal should be electron rich so that it can easily lose two d electrons to the organic compound which should therefore be electron deficient.[8] For Stille and Suzuki coupling the main product is the trans isomer due to the bulky ligands used on the catalyst which makes the trans more stable than the cis product[5].

STILLE: the oxidative addition is of an alkyl halide to the Pd(0) complex which forms a Pd(II) species[5].	SUZUKI: the oxidative addition is of an aryl halide to the Pd(0) complex which forms a Pd(II) species[7].

Transmetalation

Transmetalation is a reaction/step in a mechanism where one metal which is bonded to an atom is exchanged for another metal[9].

$$M_1\text{-}R + M_2\text{-}X \rightarrow M_1\text{-}X + M_2\text{-}R$$

The X ligand, a halogen, is attracted to electropositive metals, so if M_1 has a greater electropositivity than M_2, It is thermodynamically favourable for the R and X ligands to be exchanged[10].

STILLE: the halogen atom transfers to the more electropositive tin and the organic ligand moves to the Pd.[2]	SUZUKI: first the organoborane is initiated with a base, then the halogen transfers to the boron and the organic ligand moves to the Pd.[7]

Reductive Elimination

Reductive elimination is effectively the reverse of oxidative addition, involving the decrease in the oxidation state of the central metal atom – in this case +2 to 0. A new covalent bond is also formed between the two ligands that have been removed[11]. For both Stille and Suzuki coupling reductive elimination can only occur from the cis complex so the trans product must first be isomerised to the cis product[5,7]. The reductive elimination step gives the desired product and regenerates the Pd(0) species[7].

Limitations

STILLE:	SUZUKI:
● Tin compounds are toxic and have low polarity making them poorly soluble in water[3] ● Very bulky/ heavily substituted reagents - react slowly and often require optimization[5]	● The borane substrates that are commercially available don't include all the R groups needed[7] ● Without the base initiation many byproducts are formed[7]

Advantages

STILLE:

● Tin compounds are air stable, commercially available, and readily synthesised[5]

● A wide variety of electrophiles can be used[5]

SUZUKI:

● Boranes can be synthesised easily at a low cost and with minimal health risks[7]

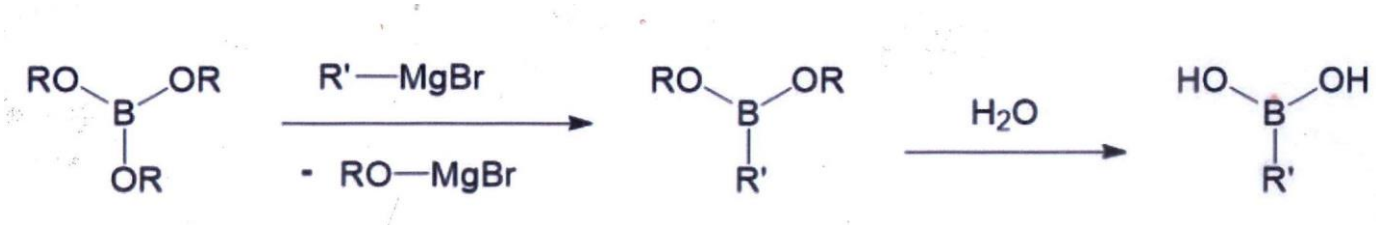
● Can be carried out in heterogeneous or aqueous conditions because organoboranes are water soluble and compatible with water soluble, inorganically supported, ligand-free Pd catalysts[7]

● Boranes are very nucleophilic so don't need extreme conditions for transmetalation to occur meaning its functional group tolerance is increased[7]

● Organoboranes are nontoxic and stable to extreme heating and oxygen & water exposure[7]

Grignard Reagents

A Grignard reagent has the formula RMgX and is made by adding haloalkane to small bits of Mg and ethoxyethane. This is then warmed under reflux for 20-30 mins[1]. One of the ways to synthesise the boronic acid needed for Suzuki coupling is by reacting an Mg Grignard reagent with a borate ester, followed by hydrolysis[7].



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JOHN KENNETH STILLE – a sad story

2010 Nobel Prize award ceremony. From L-R: Suzuki, Negishi and Heck

The Nobel Prize in Chemistry 2010 was awarded jointly to Richard F. Heck, Ei-ichi Negishi and Akira Suzuki *"for palladium-catalyzed cross couplings in organic synthesis."*

The three men are pictured on the right at the award ceremony in Sweden.

What about John Stille, you may ask? Surely he deserved to be awarded the Nobel Prize too!

For the reason, we need to go back to July 1989 and UNITED AIRLINES Flight 232 flying from Denver to Chicago in the US. This flight is particularly famous in the annals of aviation history and has become known as *"The Impossible Landing."*

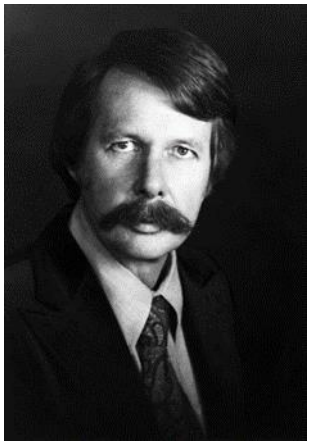
A United Airlines McDonnell Douglas DC-10, carrying 285 passengers and 11 crew members, took off from Denver at 2:09 pm on July 19, 1989. For the first hour, the flight was uneventful. However, at 3:16 pm, a cracked fan blade in the rear engine disintegrated, causing the engine to fail, while flying debris severed all three hydraulic lines and pierced the horizontal stabilizer. This resulted in the loss of all flight controls. The only thing the pilot and co-pilot, Alfred Haynes and William Records, could do was to vary the thrust of the two remaining engines to try and keep the aircraft level and slowly descending. Tt was determined that the plane should attempt to land at the airport at Sioux City, Iowa.

The crew then managed to get the plane lined up with a closed runway, but it was descending too fast and it tilted as it landed. The right wing struck the ground first and broke off. The tail section and the cockpit also broke off as the plane bounced several times. The main portion of the fuselage skidded sideways and rolled onto its back before coming to a stop in a cornfield. Fuel had ignited immediately when the plane hit the ground.

Incredible as it may sound, 184 people survived the crash. Sadly, one of the passengers who did not was... JOHN STILLE. (Note: the Nobel Prize is not awarded posthumously)

STILLE AND SUZUKI COUPLING

Will Harpur-Davies (Year 13)



COUPLING REACTIONS:

Coupling reactions are defined as reactions in which two starting materials are joined together, commonly in the presence of a transition metal catalyst. Each starting material can be described to contain a fragment and a coupling partner, the latter of which is eliminated during the reaction, allowing the formation of a covalent carbon-carbon bond between the remaining fragments. [1], [2] Two classes of coupling reactions arise: homo-coupling (reactions joining two equivalent fragments, and cross-coupling/hetero-coupling (reactions joining two different fragments). [3]

Applications of cross coupling- medicine antitumor drugs etc. Comparable coupling pathways are those of Stille coupling and Suzuki coupling, which both proceed via a similar mechanism and are both Palladium catalysed. The three basic reaction steps in each coupling mechanism are: oxidative addition, transmetalation, and reductive elimination.

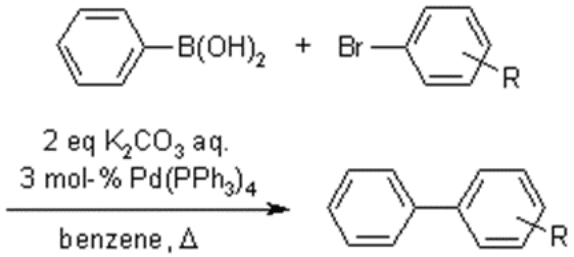


Figure 1 An example of a coupling reaction: The first published Suzuki cross-coupling reaction. [28]

Oxidative Addition:

'The addition of a substrate molecule to a transition metal complex' [4]

The term transition metal is often used to describe the d-block elements (see figure 2). However, more formally the IUPAC defines a transition metal as 'an element whose atom has an incomplete d sub-shell, or which can give rise to cations with an incomplete d sub-shell' (thus excluding elements such as Zinc and Scandium). [5] Regardless, transition metals possess a number of unique, characteristic properties including the ability to form different oxidation states within different compounds, the formation of coloured compounds, and their effective use as catalysts.

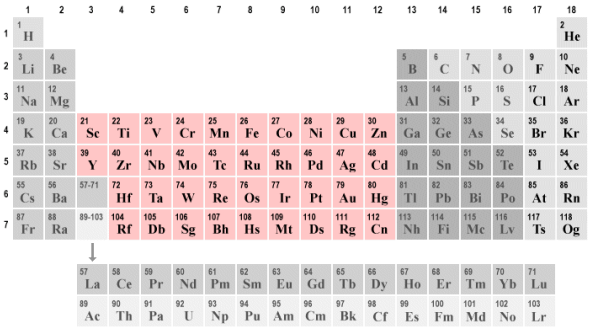


Figure 2

Transition metals are also able to form complex ions whereby ligands (molecules or ions that provide a coordinate bond) donate a pair of electrons to the central transition metal atom, forming coordinate bonds.

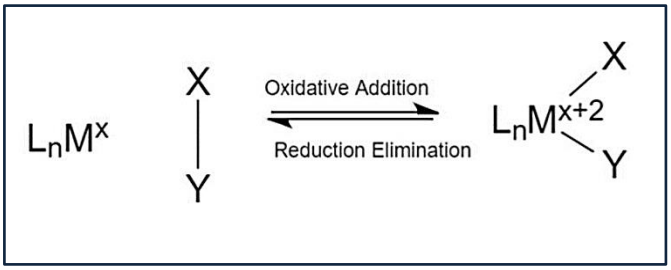
Oxidative addition occurs when ligands are added to a central metal, and the oxidation state is of the central metal ion is increased (it is oxidised). Typically, during **mononuclear** (single metal ion) addition, the oxidation state of the central metal ion increases by +2 due to the addition of 2 anionic (more electronegative than metal) ligands to the complex. [6] The general scheme for an oxidative addition reaction is shown in equation 1, where Mx denotes the central metal 'M' with initial oxidation state 'x' and Ln represents the 'n' ligands already co-ordinately bonded to the metal.

In this general (forward) reaction:

(i) that the oxidation state of the metal increase by 2

(ii) the co-ordination number of the metal (the number of co-ordinate bonds) increases by 2; it becomes co-ordinately saturated.

(iii) 2 new ligands are added to the molecule 'X' and 'Y'. [7]



Equation 1 General oxidative addition reaction

Strictly speaking, the increase in oxidation state of a metal centre by addition of a group (an electrophile) does not represent oxidative addition, even though the process is an oxidation and a species is being added. Instead, this is known as oxidative ligation [8]. For oxidative addition the electrophile must introduce two new ligands.

It is often also important to consider the spatial arrangement of the added ligands, distinguishing them as either cis or trans (though rearrangement can occur).

In complex ions of square planar or tetrahedral configuration geometrical isomerism can arise, as shown in the following figures:

In the cis orientation, attached groups arrange adjacent to each other, whereas in the trans orientation they arrange opposite to each other. In a similar way, octahedral complexes also show this from of isomerism.

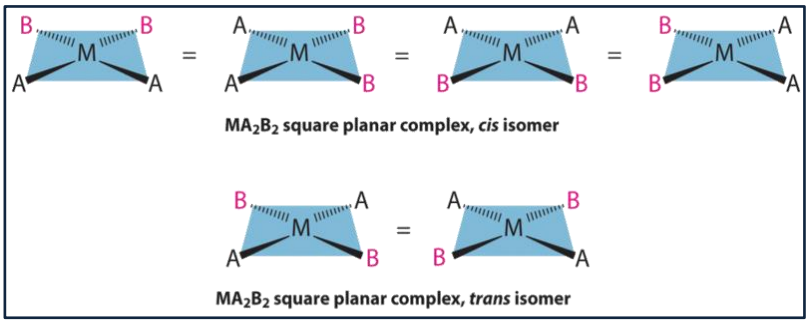


Figure 3 Cis/Trans isomerism arising in square planar complexes [29]

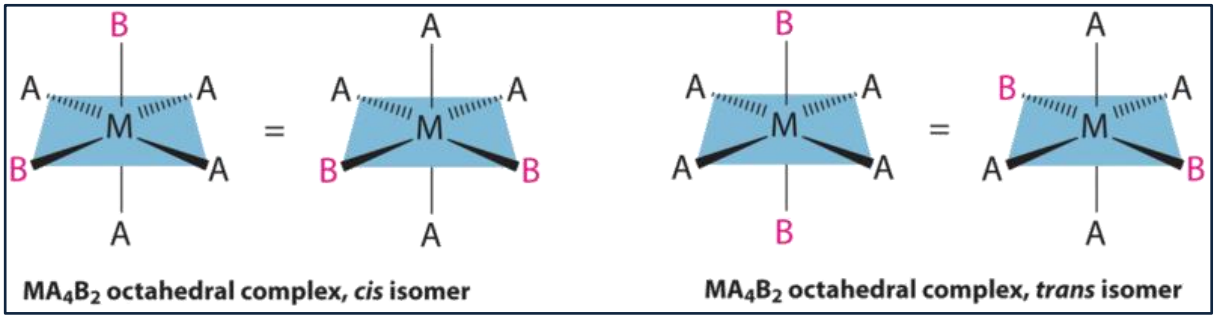


Figure 4 Cis/Trans isomerism arising in octahedral complexes [29]

Reductive Elimination:

As equation 1 illustrates, oxidative addition reactions exist in an equilibrium with the reverse process, reductive elimination. In this reverse process ligands leave the metal, decreasing (reducing) its oxidation state.

In the general (reverse) reaction:

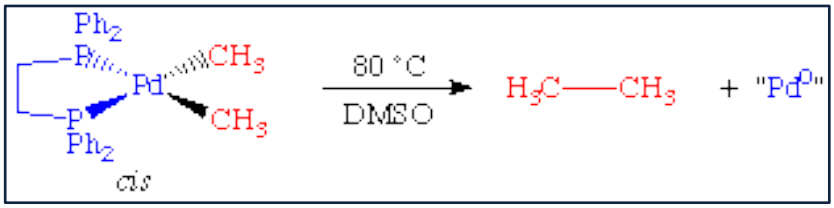
The oxidation state of the central metal decreases by 2

The co-ordination number of the metal decreases by 2; it becomes co-ordinately unsaturated

Two cis oriented ligands form a sigma-covalent bond and leave the complex

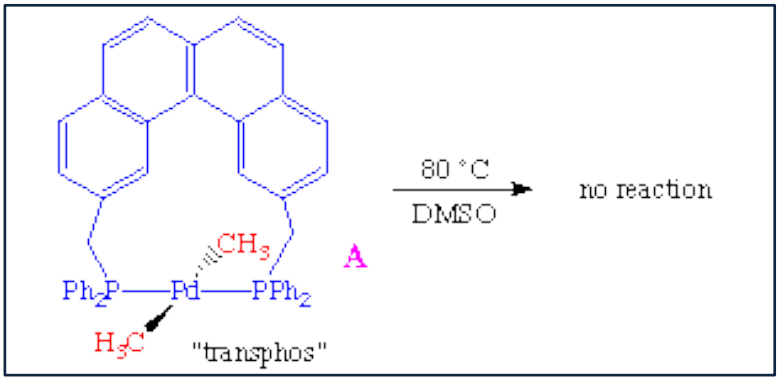
Perhaps the most important point here is the necessity of the mutual cis orientation of the leaving groups, though this does appear intuitive; any leaving groups must be arranged next to each other for a bond to form between them. Therefore, when devising a catalytic pathway using metal complexes, it is important that the leaving product has ligand fragments attached next to each other.

In fact, this principle was shown by chemists Gillie and Stille in 1980 who investigated a known reductive elimination reaction (equation 2):



Equation 2 [30]

They then synthesised an alternate group attached to the diphenyl phosphine (PPh2) ligands that forced the complex ion arrangement to be trans. Subsequently, no reaction was seen and the two alkyl (-CH3) groups did not reductively eliminate (equation 3). After carrying out other control experiments to check, they were able to conclude that ligands in the mutually trans arrangement could not reductively eliminate.



Equation 3 [30]

Often, oxidative addition and reductive elimination are key steps in industrial catalytic cycles; reactants add to a transition metal complex, rearrange, and then leave by elimination. However, not all compounds can undergo these reactions. Chemical reactions are generally concerned with finding the lowest possible energy arrangement for a system of particles and thus it is natural to accept that for oxidative addition to occur the central metal must have oxidation states that are energetically accessible, stable and are separated by two units (so that a catalyst is stable enough to be produced, then used, and oxidative addition is able to occur). Moreover, the reacting metal or complex must have 2 available co-ordination sites; the central species is co-ordinately unsaturated. As an extension to this, large groups already attached reduce the ability of oxidative addition to occur as there is less space for incoming ligands to bond (an effect known as steric hindrance). Finally, since the central metal formally loses two valence electrons, oxidative addition is favoured if the metal is electron rich and the incoming organic compound is electron poor (an electrophile). [8]

The reverse of this, for reductive elimination, favours a relative high formal charge on the central metal (such that it resists the transfer of its electrons to the ligands), is increased by the steric hindrance of larger groups on the metal, and requires a stable leaving group to from in a cis orientation.

Transmetalation:

Transmetalation is an organometallic (organic compounds bonded with at least one metal) reaction in which ligands are transferred from one metal to another [9], or more simply 'the transfer of a metal atom from one substrate to another' [10]. Although little is understood about the process, transmetalation forms metal-carbon bonds and can alter the reactivity of intermediates or rearrange fragments in synthetic routes. Common occurrences of transmetalation include in cross-coupling reactions (specifically Stille, Suzuki, Sonogashira, and Negishi reactions) [9].

The general form of a transmetalation step can be seen below (equation 4):

$$RM^1 + M^2X \rightleftharpoons RM^2 + M^1X$$

Equation 4 Transmetalation equilibrium [11]

The reaction procedure depends on the relative electronegativities of the ligands on each metal. In the general reaction above, the halogen (X) thermodynamically favours bonding with a more electropositive metal (i.e. less electronegative) due to the relatively high electronegativity of halogens. Therefore, for the reaction to be favourable it is required that M1 be more electropositive than M2, though the reaction exists in equilibrium so ensuing reactions that are irreversible (so do not allow the products of the equilibrium to exist for very long) can prevent the reverse process occurring. Usually in transition metal catalysed processes, transmetalation is the rate-determining step. [11]

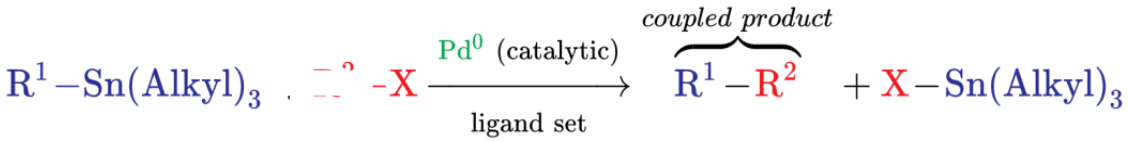
Specifically, in cross-coupling reactions the general form of the transmetalation step is (equation 5) with various metals (M) being used for different reactions:

$$R^1X + MR^2 \rightleftharpoons R^1R^2 + MX$$

Equation 5

THE STILLE REACTION

The RSC Name Reaction Ontology (RXNO) defines Stille coupling as 'a cross-coupling reaction where a stannane (an organotin compound) reacts with an organohalide or organotriflate' [12].



Equation 5 The general equation of the Stille reaction [31]

The reaction is palladium-catalysed and is often used in synthetic procedures due to its wide scope (the reaction has a large range of potential reactants). For example, each of the organotin and organic electrophile reagents can be a variety of compound types:

Organotin reagent:

R^1 – Aryl, alkyl, vinyl, allyl or even heterocyclic groups are all known to work [13]

Electrophile reagent:

R^2 – Aryl, vinyl, allyl, acyl halides or pseudo halides. Heterocylic compounds can also work [13]

Organotin compounds (stannanes) are compounds that contain a covalent Sn-C bond [14]; an organic group attached to tin. Classified by their oxidation states, tin compounds can for 4 main groups depending on the number of substituent groups (1 – 4). Tin(IV), which would have 4 attached groups, is the most common [15] [16]. The formation of organotins became more ordinary after the discovery of the Gringard reaction, which made producing Sn-C bond much easier.

Organohalides, similarly, are organic compounds with a substituted halide (e.g. haloalkanes are a form of organohalide). They are widely used as the electrophile in cross-coupling reactions (though 'high cost, environmental toxicity, and sluggish preparation' have motivated research into altenatives [17]).

Triflates, often represented by –Otf, have systematic names of trifluoromethanesulfonates and are groups with the molecular formula CF3SO3−, displayed formula:

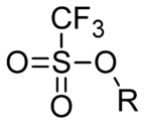


Figure 3 Triflate group [32]

Interestingly, triflic acid (CF3SO3H) is a superacid, one of the strongest known with a pKa ~ -15 [18] (this is mostly due to the stability of the CF3SO3 1- ion, the molecule is able to dissociate very easily and release H+ ions in aqueous solution). Triflates can act as the electrophile in the reaction due to them being pseudohalogens – they have similar chemical properties to the halogens.

The aryl functional group consists of molecules that are derived from an aromatic (benzene) ring.

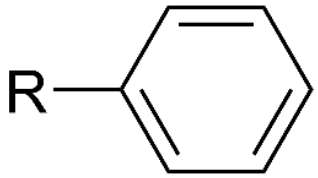


Figure 4 Simplest aryl group [19]

Alkyls are organic molecules that are derived from an alkane molecule (with substituted hydrogen).

Vinyl functional groups contain fragments with the formula –CH=CH2.

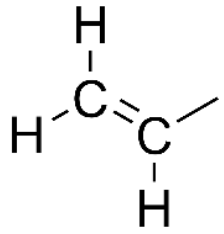


Figure 5 Vinyl group [20]

Allyl groups are a subset of vinyl groups and require an extra –CH2, giving the functional group a formula RCH2−CH=CH2.

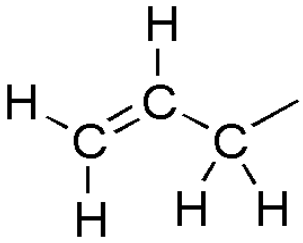


Figure 6 Allyl group [21]

Acyl halides are derivatives of carboxylic acids and contain the carboxyl group (C=O) and a halide. A common example is an acyl chloride (where the halide is chlorine, -Cl).

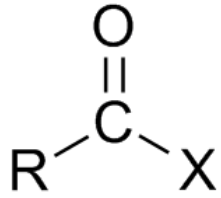


Figure 7 Acyl group [22]

Mechanism

It should be noted that, as with all mechanisms, the pathways are only proposed theories that model the mechanism, rather than defining what is "actually" happening absolutely. Here I will present the most widely accepted mechanism for the Stille reaction.

The catalytic cycle:

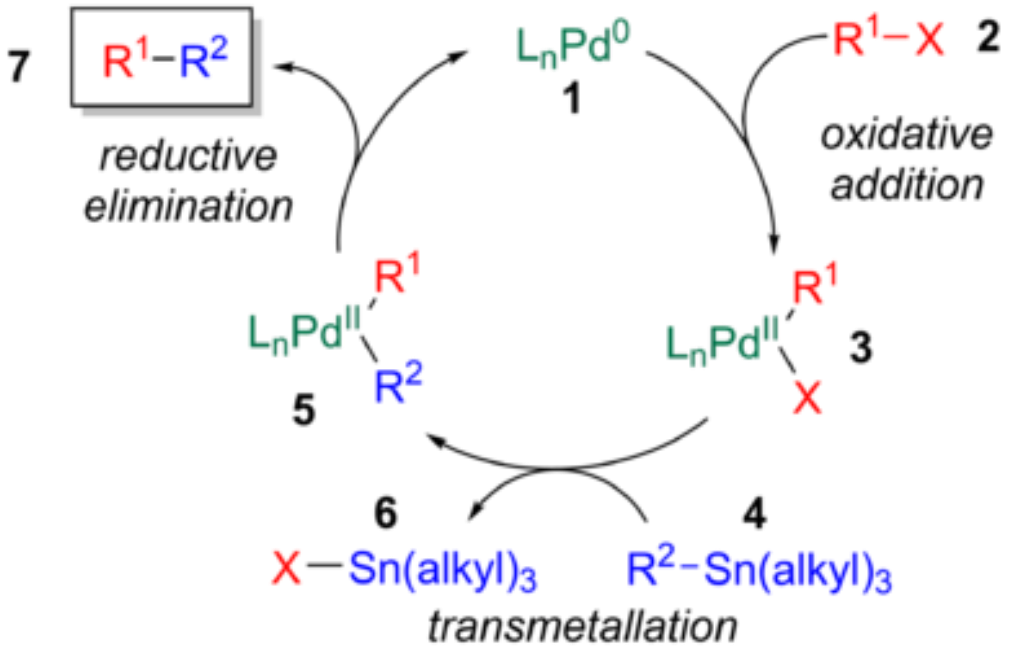


Figure 8 Catalytic cycle of the Stille Reaction [23]

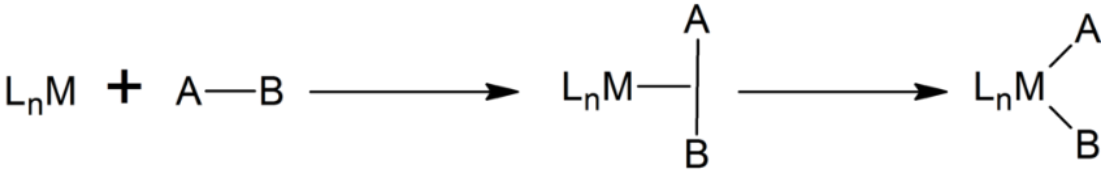
As is common with cross-coupling reactions a palladium (Pd) catalyst is present.

APPENDIX:

Oxidative addition mechanisms:

The mechanisms by which oxidative addition proceed depend on the reactant substrates involved. The two most common pathways are the 'Concerted' pathway and 'SN2-type'.

Concerted pathway:



Equation 7 Concerted Oxidative Addition pathway [24]

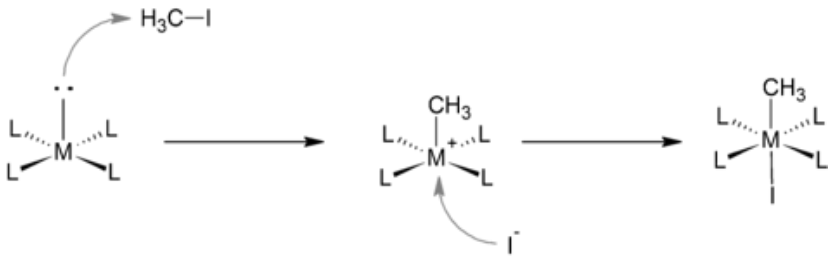
When nonpolar substrates are involved, oxidative addition usually proceeds via a concerted mechanism. As the metal approaches the A-B molecule, a 3-centered σ-complex is formed (making the 'T-shaped' bond in the centre step above) where ligands bind to each other through their σ-electrons [25]. If the metal is nucleophilic enough (is electron rich), the bond can then be cleaved by a process known as back donation/back bonding. Evidently, the ligands will initially be in a cis arrangement, though isomerisation may occur.

To understand back bonding, it is important to consider another type of molecular orbital (MO) known as an anti-bonding orbital. When considering the arrangement of electrons (the basis of all chemistry) which are quantum particles, quantum laws must be used. One such law is the Pauli Exclusion Principle which states that no two fermions (of which an electron is one) can have the same quantum state. In other words, this means that at a quantum level, electrons can never be 'identical' (same orbital, same spin, etc). When atoms come together to bond, as their orbitals overlap there is an ability for more than one electron to be in the same quantum state which violates the Exclusion Principle and instead, an anti-bonding orbital (denoted by an asterisk *) is formed. Anti-bonding orbitals are at higher energy levels than their counterpart bonding orbitals [26].

In ligand complexes, back donation involves the release of electrons from the nd orbital of the metal to the empty π*-antibonding orbital of the ligand [27]. If the metal is electron rich, this relieves the excess negative charge around the metal, making the M-L bond stronger (more stable).

SN2-type

If the substrate ligands are polar, a different pathway can occur. In this the nucleophilic metal attacks the less electronegative (more positive) ligand substrate, eliminating the more electronegative fragment of the molecule as an anion. The anion then rapidly co-ordinately bonds with the metal.



Equation 8 SN2-type mechanism [24]

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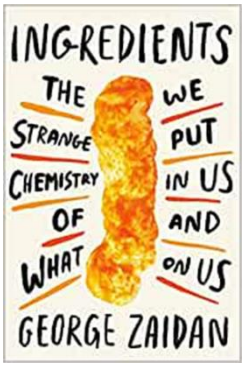
A SPECIAL FEATURE from

Mr A WATTS

Mr Watts is an avid reader, particularly of authors who take a somewhat 'sideways look' at Life and Science!

One such author is GEORGE ZAIDAN, an American science communicator, television and web host producer, and a chemist at MIT. He is currently executive producer at the American Chemical Society. His first book, 'INGREDIENTS', has attracted Mr Watts' attention and to give you a flavour of Zaidan's writing (no pun intended!), Mr Watts has offered up the following passage describing how incredible plants and aphids are.....



Remember that plants are constantly pumping what is essentially syrup from the leaves to the rest of the plant via sieve tubes buried deep within their tissue. If you want access to this sugar rush, you cannot just take a bite of a plant. Leaves, shoots, stems—in other words, the parts of the plant that house most of the sugar superhighway—are not sweet. (Think celery stalks.) That's because when humans take a bite of plant with our gigantic gnashing teeth, we're not just getting the sieve tubes; we're getting all the other parts of the plant that don't have a constant stream of sugar whizzing through them, and that tends to cancel out the sappy parts. We're also getting bitter chemicals the plant makes specifically so they don't taste good. Unfortunately, we just don't have the delicate machinery required to dip into a plant's sugar superhighway. But there is a creature that does: the humble little aphid.

Aphids, also known as plant lice, are quite small, usually green, and absolutely terrible for plants. We'll start our story with a single lady aphid—let's call her Mabel—landing on a plant. Mabel is about 5 millimeters long, but she's big for an aphid. Most species are about 2 to 3 millimeters long. Once Mabel finds a spot she likes, she spits out a small bead of saliva that quickly hardens to the consistency of peanut butter. As it's hardening, Mabel unfurls her "stylet," which is kind of like a hypodermic needle, except it's flexible and has two channels instead of just one.

The stylet is basically Mabel's mouth: her face just sort of stops being a face and starts being a long, flexible needle.

Mabel penetrates the gel saliva that she's just spit out with her hypodermic needle–face, and soon the tip of her stylet arrives at the surface of the plant. Unlike the metal needles that doctors jab you with, Mabel's stylet doesn't punch through plant cells; it worms its way between them. Mabel pushes her stylet into the plant in gentle pulses: before each pulse, she spits out a small glob of gel saliva, then penetrates it, and when the tip of her stylet pokes out the other side of the glob, she spits out another glob, penetrates that one until her stylet tip comes out the other side, and so on. These globs of gel saliva harden, creating a sheath that protects (and lubricates) her stylet as she pushes it between plant cells, farther into the plant.

Every so often, Mabel needs to get her bearings. Her stylet doesn't have eyes—it has no way to know where it is inside the plant—so she pokes the tip of her stylet into a nearby cell. Once inside, she takes a "sip" of the cell's contents. In other words, she sucks up some of the cell's guts into one of the two channels in her hypodermic needle–face and "tastes." We don't really know what "tasting" is like for Mabel, but we think she's checking to see how sweet or sour it is. If it's not sweet enough and/or too sour, she retracts her stylet, changes direction, and moves on, deeper into the plant. Eventually she penetrates the holy grail of plant anatomy, the sugar superhighway that is a sieve tube.

As you might guess, plants do not want to be penetrated. Especially not in the sieve tube, because they know what's coming next: large-scale theft of the sugar they've worked so hard to create. Plants are not ungenerous. They have no problem making a fair trade with an insect or an animal, something along the lines of:

HEY! YOU, THING THAT CAN MOVE! I'M STUCK HERE, BUT I NEED YOU TO TAKE ALL THESE FERTILIZED EMBRYOS I'VE MADE FAR AWAY FROM HERE SO THEY CAN GO FORTH YONDER UNTO THIS WORLD. (IN CONSIDERATION OF SAID SERVICES, YOU MAY DRINK NECTAR FROM MY SWEET FLOWER OR EAT MY SUGAR-SWEET FRUIT.) SOUND GOOD? GREAT, DONE DEAL.

But when something tries to take sugar without giving anything in return, the gloves come off. When a caterpillar, for example, chews, rips, and tears plant tissue, plants do a bunch of things in response. Electrical and chemical signals travel to the rest of the plant, alerting it to damage. Long, thin proteins inside the sieve tube called forisomes double or triple in width, partially blocking the tube. The cell starts producing a sugar called callose that also helps to plug up the tube.

But Mabel knows that this defensive dance is coming. So as soon as she confirms that the cell she's penetrated is a sieve tube, she spits out a different kind of saliva that pretty much stops the plant's defensive response in its tracks. Now she's basically set. She's suppressed the plant's sieve tube defense system, and because the tube is under pressure, she doesn't even have suck up the sap. She just opens or closes a valve in her head to control the flow.

But there is one more plant sap defense Mabel has to deal with: sugar. Specifically, the can-of-Coke–high or sometimes even Aunt Jemima–high concentration of sugar in sieve tube sap. As this incredibly concentrated syrup travels through Mabel's digestive tract, it encourages water out of her cells,* so much so that other cells, deeper in Mabel's gut, have to send their water to the front lines to replenish their fellow troops. Unfortunately, Mabel's gotta eat, so she keeps gulping, and this water loss continues. The more sap passes through Mabel and out her butt, the more water is "sucked" out of her body. Eventually, if she doesn't stop feeding on this plant syrup, Mabel will lose so much water to the sap that she'll dry out, shrivel up, and die.

Or at least she would . . . if she didn't have two elegant methods to deal with this water-loss problem.

To be continued!

Mr D'MELLO'S

Mr D'Mello has set us 3 puzzles, 2 for the Physicists and one for the Mathematicians:

1. **Imagine you are up in the International Space Station orbiting the Earth. Are you weightless? Why not?**
2. **Imagine you are in a lift. You feel heavier when it moves up, and lighter when it starts to move down. Does your weight actually change in the lift? Why not?**
3. **What is 0^0 (zero to the power zero)?**

ANSWERS ON A POSTCARD, PLEASE…

Or you can email Mr D'Mello at jdmello@st-benedicts.suffolk.sch.uk

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JULY

JOCELYN BELL BURNELL

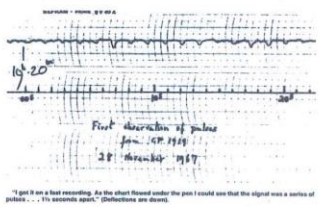
BORN: 15th July 1943
BIRTHPLACE: Lurgan, NORTHERN IRELAND

Jocelyn's birthplace, Lurgan, is in County Armagh, Northern Ireland, and it must be significant that Jocelyn's father, an architect, helped design the ARMAGH PLANETARIUM. It is said that when she found her father's books on ASTRONOMY, this sparked her interest in the subject, even as a young girl.

When she failed her 11+ exam (!) her parents sent her to a boarding school in York (England) where she was hugely impressed by her PHYSICS teacher, Mr Tillot. His enthusiasm made her even more determined to become a scientist.

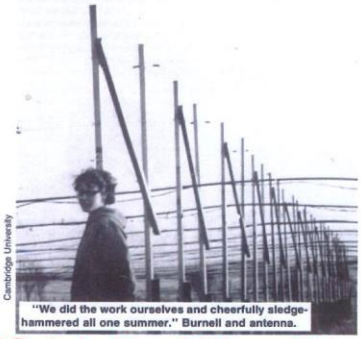
After gaining a degree in PHYSICS at Glasgow University in 1965, she moved to CAMBRIDGE UNIVERSITY where she completed a PhD with a thesis titled: *THE MEASUREMENT OF RADIO SOURCE DIAMETERS USING A DIFFRACTION METHOD.*

When she arrived at Cambridge in 1966 she helped build a special type of RADIO TELESCOPE and it was her work with this that was to make her famous.



"I got it on a fast recording. As the chart flowed under the pen I could see that the signal was a series of pulses . . . 1½ seconds apart." (Deflections are down).

She used the radio telescope to study signals coming from distant radio sources, known as QUASARS: however, in 1967, while ploughing through miles of chart recordings, she found a remarkable pattern of signals from a single source.



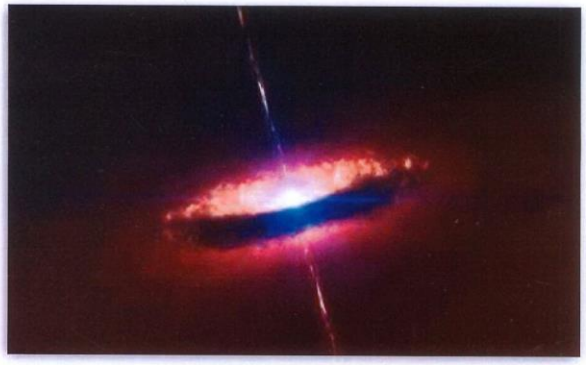
Cambridge University

"We did the work ourselves and cheerfully sledge-hammered all one summer." Burnell and antenna.

She detected regular PULSE SIGNALS at a constant rate of one every 1⅓ seconds. At first she thought they might have been signals from a distant, alien civilisation; however, after further study, the true explanation was found –

JOCELYN HAD DISCOVERED THE FIRST PULSAR!

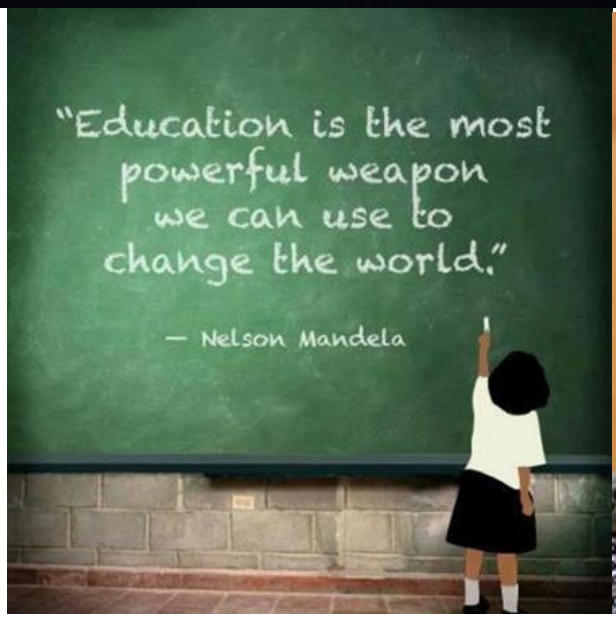
When some stars come to the end of their life they explode in what we call a *SUPERNOVA*. The remaining core of the star collapses into a small but unbelievably dense sphere of matter called a *NEUTRON STAR*. Neutron stars often spin very rapidly while emitting a beam of electromagnetic radiation, rather like a STELLAR LIGHTHOUSE, which we detect as rapid pulses.



Many scientists consider that Jocelyn's discovery of the first pulsar was the greatest scientific discovery of the 20th Century

"The fact is that no species has ever had such wholesale control over everything on earth, living or dead, as we now have. That lays upon us, whether we like it or not, an awesome responsibility. In our hands now lies not only our own future, but that of all other living creatures with whom we share the earth."

David Attenborough, Life on Earth



Society for Popular Astronomy
STARGAZING FOR EVERYONE

St Benedict's is a member of the Society for Popular Astronomy.

The Society for Popular Astronomy was set up way back in 1953 (as the Junior Astronomical Society) to promote an interest in astronomy and help beginners of all ages to get started in this fascinating hobby. It's a role we are still performing today!

Everyone is welcome to join the SPA, whether a novice or a more experienced enthusiast, and whether old or young. We believe we offer something for everyone.

However, we are particularly focused on helping the beginner to this, the oldest of sciences which still makes an enjoyable hobby in our modern day. Most of all, we aim to make stargazing fun!

A CAREER IN ASTRONOMY?

If you are thinking about studying for a career in Astronomy, the SPA is a very good source of information to get you started – What GCSEs are best? Find local Astronomy Clubs. Get links to the Royal Astronomical Society's career advice section…and much more. There are a huge number of 'space careers', so there really is something for everyone.

CAREER PATH OUTLINE
Academic route

- GCSEs (or equivalent) in English, Maths, Physics, Chemistry, Biology, MFL, Computer Science, DT
- A-levels (or equivalent) in Physics and Maths; also subjects like Further Maths, Chemistry, Geography, Biology, Languages, Computer Science, DT.
- Undergraduate degree in Physics, with focus on Astronomy or Geophysics topics, Astrophysics, Geology, Geoscience, Space Science, Planetary Science, Engineering.
- Masters – either MPhys or MSc.
- A PhD in a specialist area

(GCSEs and A-levels in Astronomy or Geology are not required but can be taken for interest)

https://www.popastro.com/main_spa1/

https://ras.ac.uk/education-and-careers/careers