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RUGBY SCHOOL

Cover artwork by Leo Aliev (W)

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RUGBY SCHOOL

SEABROKE AND THE TEMPLE OBSERVATORY, THE BIRTH OF SCIENCE AT RUGBY SCHOOL

By Nick Fisher

WITH A FINE DISREGARD FOR THE TEACHING OF CLASSICS, RUGBY SCHOOL RAN WITH SCIENCE TEACHING FROM THE VICTORIAN ERA

Over the past few decades with the growth of the internet, there has also been a growth in the numbers of people interested in searching their family history. Genealogists have never had it so good. Possibly keen to seek out someone famous in their ancestry, people are looking back at census records easily accessed on the web. But George Seabroke (the second) had no such intentions when he embarked on his PhD at Cambridge 15 years ago. He was mapping the Milky Way structure using redshift measurements to help work out the velocities of stars – their speed and direction. A fellow PhD student had been surprised to find George Seabroke's name on the NASA website. Was her tall, young enthusiastic astronomer already famous before completing his research project? Surely not. But no, this NASA reference was to the first George Seabroke. George Mitchell Seabroke. G. M. Seabroke, a Rugby student from Whitelaw House, who took up astronomy with his Housemaster and later founded the British Astronomical Association. And the 21st century Seabroke PhD student had no idea he had such an illustrious ancestor as he embarked on his galactic research.

This discovery has brought the 21st century Seabroke to Rugby twice in the last 15 years. Once, in 2008, three days after submitting his PhD thesis at Cambridge, and this year. On both occasions I had the great pleasure of welcoming him to his ancestor's alma mater and each time George has spoken in the Foxcroft Lecture Theatre. The first time was to talk about his research; the second to give us an update on what has become an impressive European project named *Gaia*. *Gaia* is creating an extraordinarily precise three-dimensional map of more than a thousand million stars throughout our Milky Way galaxy and beyond, mapping their motions, luminosity, temperature, and composition. This huge stellar census will provide the data needed to tackle an enormous range of important questions related to the origin, structure, and evolutionary history of our galaxy.

And each time George Seabroke has visited us he has spent time in the Temple Observatory.

The Temple Observatory at the back of 1 Horton Crescent is representative of the rise of science teaching at Rugby. The advent of science education was marked in 1776 by Adam Walker delivering lectures off timetable. These continued with his son until 1834. The first regular teaching of science began in 1851, with lessons given by the Reverend Berdmore Compton. When Frederick Temple arrived as Head in 1858, he spent 11 energetic


No. 16.] [Price 7s.

SPECTROSCOPIC OBSERVATIONS

ON

THE SUN.

BY

J. NORMAN LOCKYER, F.R.S.

AND

G. M. SEABROKE, F.R.A.S.

LONDON:

years on bold initiatives. The Temple Speech Rooms and Temple Observatory honour his success. He had a lifelong interest in the relationship between science and religion. Temple strengthened the School's academic reputation in the classics, but also instituted scholarships in natural science. Botany was introduced into the curriculum in 1859. In that year, the first science laboratories were built, and chemistry and electricity were taught as an alternative for a select group of students. By 1864, science in the form of chemistry, geology, botany, and physics became compulsory. Then two years later and three years before Temple left to become Bishop of Exeter, two new subterranean laboratories were commissioned on the north side of the New Quad. After Temple left the school, his science legacy flourished. The senior Science Master at the time was the Reverend J. M. Wilson, housemaster of Whitelaw House. In 1871 he was encouraged by a former Rugby pupil to purchase a world-class telescope built by Alvan Clark and Sons and owned by Reverend Rutter Dawes, a distinguished astronomer and observer of double stars. That former Rugby pupil was 23-year-old George Seabroke, now a solicitor in Rugby, but formerly an enthusiastic and talented astronomer whilst a pupil at Whitelaw. A picture of George is below left.

At that time, 1871, the telescope was housed in a wooden observatory building at the back of Whitelaw. The picture above shows the Housemaster, J.M. Wilson, outside with an even larger telescope on a trolley.

1871 was also the year that the Devonshire Commission inspected science education in public schools. Think of this as the Victorian forerunner of modern-day Ofsted and ISI inspections. The Devonshire Commission commended Rugby on being the first school to take up compulsory science teaching in their curriculum. And this plaudit coincided with stellar science observations with the new telescope. Between 1871 and 1876 spectroscopic observations of the Sun were made with Sir Norman Lockyer alongside J.M. Wilson and George Seabroke. This was real observational science being conducted in Horton Crescent. Extraordinary that Sir Norman Lockyer was working with a housemaster and a former Rugby pupil. Lockyer (born in Sheep Street in Rugby) was the Astronomer Royal famed for discovering helium in the Sun using spectroscopic measurements during a solar eclipse!

This success helped to build Rugby's science reputation – not only was science being taught but original science was actually being done. Papers were published in *Monthly Notices of the Royal Astronomical Society* and *Proceedings of The Royal Society*. This success also helped to raise funds and build a new observatory building with its own house at the front.

Both house and observatory were built in 1877. It was fitting that it was named the Temple Observatory after the enthusiastic support for science by the former Head Master. With the new observatory and the telescope purchased in 1871, Seabroke and Rugby pupils continued to publish observations, in particular binary star measurements of Eta Casiopeia. In 1890, George Seabroke founded the British Astronomical Association (BAA). He served as the BAA Double Star Section Director from 1892 to 1915, its Saturn Section Director from 1899 to 1911, and its national president from 1900 to 1902. He also served as Midland Branch President from 1902 to 1903.

The observatory building stands out at the back of 1 Horton Crescent with its Victorian verdigris roof.

But the most precious part is the priceless refractor housed inside. If you want to read more about this scientific instrument, see

The 8¼-inch Clark refractor of the Temple Observatory, Rugby

R. A. Marriott

During the 1850s W. R. Dawes purchased five object glasses from the American opticians Alvan Clark & Sons. The only one to have been in continuous use since then was the last of them, in a complete 8¼-inch refractor.

the publication in the following website: https://articles.adsabs.harvard.edu//full/1991JBAA..101..343M/0000343.000.html

The Clark refracting telescope has seen many astronomical objects in its long history.

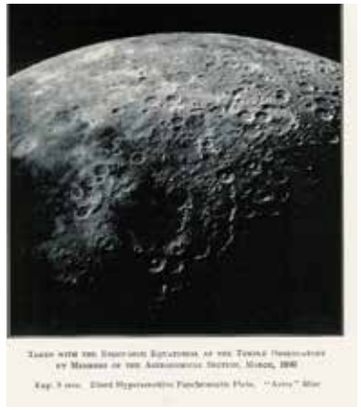
You may think we can only use the telescope at night, but many great observations are made of sunspots during the day. See an example below.

In 1999, we recorded a partial eclipse here in Rugby, 95% obscuration of the Sun (Cornwall had 100%, but it was cloudy). Here in Rugby, Horton Crescent was alive with members of the public visiting the observatory to see a projection of the solar eclipse on a solar screen.

In 2004, we recorded the transit of Venus across the Sun.

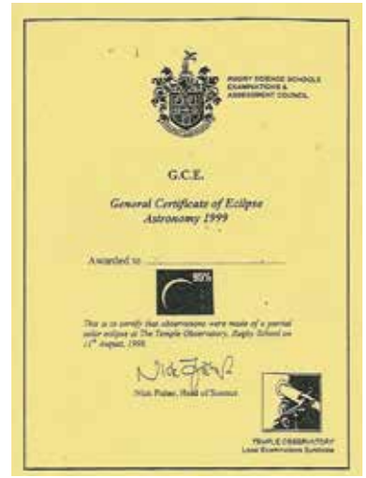
The Seabroke Society was launched quite a while ago. In the late 1990s, we promoted our astronomy heritage through the Seabroke Society, and inviting speakers such as the Astronomer Royal, Prof Sir Arnold Wolfendale, author Dr Simon Singh (author of *Big Bang*) and Manchester particle physicist Brian Cox. The re-launch is led by Beatrice Wynne-Edwards and Charles Swinfen. The society will be hosting an annual Seabroke Lecture, arranging repair to the telescope and putting together observatory activities for the wider community. This year we are also launching a 360 project: Science Archive. Every Wednesday a small group of devoted students will examine school archives from the School Museum and TRR, along with external sources, to establish the facts about the birth of science education and astronomy teaching at Rugby School and the wider area. This will include liaising with the local Rugby and Coventry Astronomical Societies and History Societies. This research will culminate in:

1. An academic report, fully referenced, to be published for the School and local Rugby and Coventry Libraries.
2. An artefact or two that will be curated for local school children to view and study.
3. Guided tours of Rugby science artefacts for local youth groups, science societies and schools.



TAKEN WITH THE 8-INCH EQUATORIAL
AT THE TEMPLE OBSERVATORY
MARCH 23rd, 1949

ILFORD F. P. 2 PLATE. EXP. 10 SECS. FULL O.G. APERTURE
NO FILTER

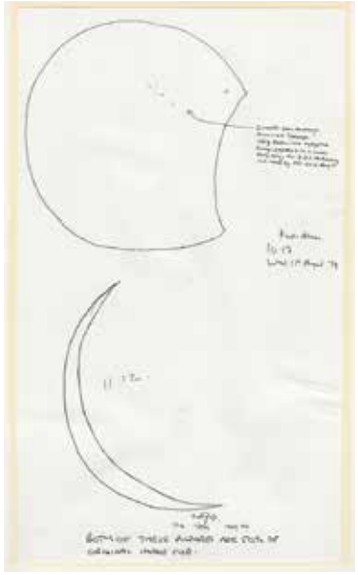


G.C.E.

General Certificate of Eclipse
Astronomy 1999

Awarded to _____

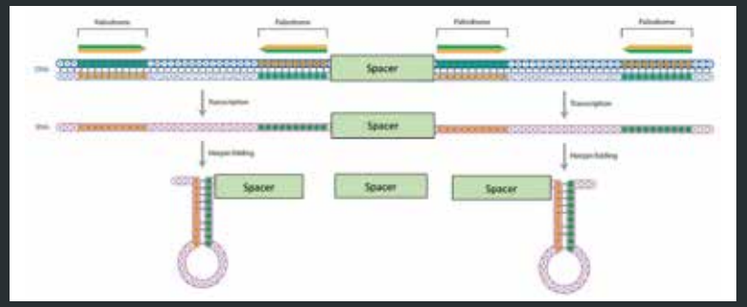
95%



CRISPR- CAS9 – DESIGNER HUMANS

BASED ON: THE CODE BREAKER – WALTER ISAACSON

By James Hon (C)



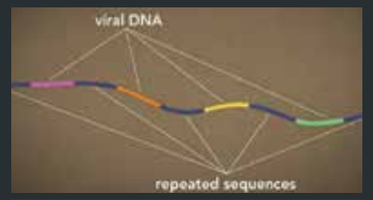
CRISPR

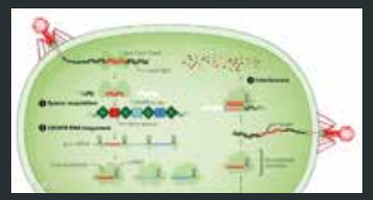
Clustered **R**egularly **I**nterspaced **S**hort **P**alindromic Repeats, aka CRISPR. CRISPR was first discovered by a Japanese scientist, Yoshizumi Ischino, when looking at the bacteria E. Coli. However, its function was only discovered later by Franciso Mojica, who actually came up with the acronym. CRISPRs are parts of DNA containing **repeat**ing sequences which are **palindromic** (the same when read both ways), **interspaced** (separated) by "spacers" **regularly**.

CRISPR- Cas9 in Bacteria

After years of evolution, **bacteria** and **archaea** have developed an immune system, one that is heritable and ever "updating". Their immune system depends on the CRISPR-Cas system, targeting genetic material from **viruses**. Understanding the origin and basis of nature's natural technologies will help us understand how it could help us as humans.

As a virus injects its DNA into a bacteria cell, a small fragment of the viral DNA is integrated into the CRISPR region of the bacteria. The **repeated sequences** in bacteria or archaea are separated by the integrated **viral DNA**, acting as a **"spacer"**. The newly integrated DNA sequence is then transcribed into a complementary **RNA** sequence, a topic briefly covered in GCSE biology. This RNA sequence is then processed into individual units, each containing one derived viral sequence. Let's call these RNA strands **crRNA**. A second RNA molecule, called tracer RNA (**tracrRNA**), binds with the crRNA. This dual RNA complex binds to a Cas9 protein to form a **surveillance complex**.





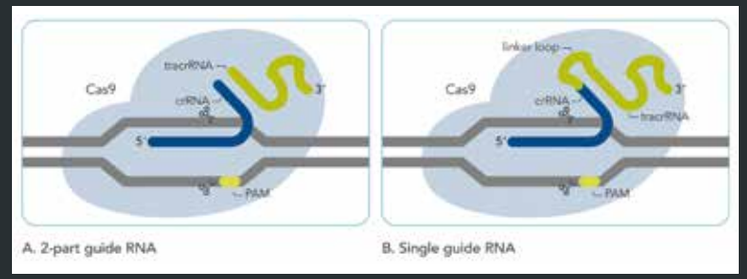
Cas stands for CRISPR associated proteins, which are coded by Cas genes. **crRNA** acts as the guide for the Cas9 protein, whereas the **tracrRNA** acts as the binding handle.

This guide RNA- Cas9 complex acts like the seeker in a hide and seek game, or a Housemaster searching through the House late at night, checking every room. In bacteria the snipping of viral DNA brings about the **destruction** of viral DNA from the cell; this allows survival. The process is slightly different in humans. I will explain what happens when this complex finds the target DNA strands eukaryotic organisms below, and what they do to those strands.

Humans – Animals – Plants

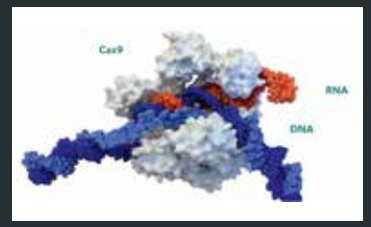
What won American and French scientist Jennifer A. Doudna and Emmanuelle Charpentier their **Nobel Prize** in 2020 was their invention of CRISPR-Cas9 as a gene editing tool. However, their discovery is a double-edged sword, or *"double edged scissors"* to be pedantic. Despite their huge clinical, agricultural or commercial potential, ethical issues arise. However, their invention was a huge step in human evolution, the cost of gene engineering lowered by 99%, experiments take months instead of years, and anyone can easily synthesise a CRISPR/Cas9 in a lab, including you.

In bacteria, the Cas9 enzyme must contain a **crRNA** and a



tracrRNA to function, a crRNA strand alone would render Cas9 useless. In bacteria, a 2-part guide Cas9 is used, so both RNA strands must be used. However, Martin Jinek, one of the collaborators, and Jessica Doudna recognised the great opportunity to **fuse** the tail of one RNA to the head of the other one, successfully engineering a single guide RNA strand that would have the guide information on one end and the binding handle on the other. So in simple terms, they joined **crRNA** and **tracrRNA** together. This would then be named single-guide RNA (**sgRNA**). What was significant was that the discovery of CRISPR/Cas9 technology has now become an invention.

The **crRNA** part is the template region, so in order to target a specific DNA sequence, one could synthesise a **crRNA** sequence strand complementary to the target DNA sequence, fuse it with the **tracrRNA** to produce the synthetic **sgRNA**. The synthetic **sgRNA** can then associate with the Cas9 enzyme, where a structural change occurs. The single guided Cas9 enzyme forms the previously described **"surveillance complex"**, or now named as the **CRISPR/Cas9 technology**.



Circling back to the unanswered question: what does the CRISPR/Cas9 complex, or the synthesised sgRNA-Cas9 complex do when it reaches the target DNA sequence? Well, once the matching DNA sequence has been found, for example a mutation, a second structural change in Cas9 occurs to accommodate the DNA strand. Cas9 then **unwinds** the DNA, and the double strand is held open. The guide sgRNA forms a helix with one strand of the DNA, holding it in place. Then, the **Cas9 cleaver**, a structure within the enzyme, cuts up the targeted sequence precisely, making a double stranded cut – just like a pair of scissors.

(For your interest, the RNA guided Cas9 enzyme finds its target in the vast DNA of a cell by locating then binding to the short PAM (protospacer adjacent motif) sequence, located downstream of the target sequence.)

What does this mean for humans?

There are three ways of cutting DNA:

Disrupt
- Single cut
- Non- homologous end joining
- Addition or deletion of base pairs
- Can cause gene inactivation

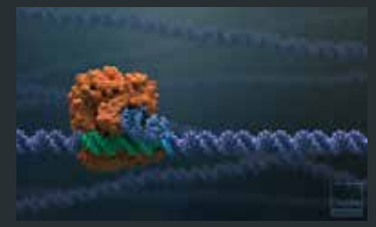
Delete
- Two cuts with two CRISPR/Cas9 used
- Non- homologous end joining
- Middle sequence is "deleted"

Correct or insert
- In Disrupt or Delete
- DNA template added beside the CRISPR/Cas9 unit
- Homology directed repair
- > Correct a gene
- > Insert a gene

The fact that sequences or bases in our DNA can be either **deleted** or **replaced** opens a world full of possibilities. Not only could it cure genetic diseases, CRISPR/Cas9 could be used to customise humans, enhance plants and animals for food; it could even stop or reduce **ageing**…

CRISPR/Cas9 has both commercial and clinical applications.

There are two types of cells CRISPR/Cas9 can be injected into: **Somatic** cells and **Germ** cells. To be clear, **somatic** cells are fully differentiated cells, such as our own red blood cells. This means modifications made in these cells will not be heritable. On the other hand, **germ** cells are



pluripotent, which means it most definitely is heritable; examples will be sperm or egg cells, to even early embryos. If you think about this, there are a lot of embedded ethical implications when put into practice, and we will discuss those at the end.

In terms of clinical applications, diseases that are known to have single genome mutations can likely be tackled by CRISPR/Cas9 in the near future. Such **monogenic** disorders include cystic fibrosis, Huntington's disease and sickle cell anaemia. Jennifer Doudna, the co-creator, predicted CRISPR/Cas9 will be applied to sickle cell anaemia first, due to the technical side of things. Inserting CRISPR/Cas9 into blood cells is a lot easier than solid tissue. However, despite the exciting ongoing trials and experiments, effort must be made to **control** the way DNA is repaired after the "snip", and to limit any **errors** or **unintended** effects CRISPR/Cas9 can commit and cause. In the future, when we have full knowledge and mapping of the human genome and what each region oversees in our bodies, CRISPR/Cas9 could be used to change anything ranging from the susceptibility to diseases to our internal and physical attributes: eye colour, hair colour, bone density, muscle mass, etc.

Progress made

One of the earliest studies in 2016 involved a large-scale experiment conducted with **mice** who have HIV by injecting CRISPR technology into mice tails. The study found more than 50% of **HIV** viruses were removed from cells in the whole body. In the same year, October, Chinese scientists decided to treat lung **cancer** patients with CRISPR modified immune cells, during the early days of CRISPR. From the Chinese city of Chengdu, these scientists removed T- cells from patients' blood and used CRISPR/Cas9 to disable the PD-1 gene, which cancer cells use to inhibit T- cells' immune function. Although the participents were not cured, reassurance is provided from the fact that edited T- cells survive and flourish after reinfusion.

In April 2015, researchers in Guangzhou, China, published an article describing their studies. They used CRISPR/Cas9 in 86 non-viable **zygotes** to remove the mutation that causes beta thalassemia; however there was no intention in the implantation of these edited zygotes. This was the very first time where CRISPR/Cas9 is shown to have the potential to cause inheritable changes in the **germline**. This was huge.

In the Second International Summit in Hong Kong in 2018, the world held its breath as we prepared ourselves to step through the doorway of a new era. He Jiankui decided to edit the CCR5 gene in an embryo of a selected **HIV** couple, hoping to free all future generations of HIV infection. This was done in **ex vivo**, then implanted into the mother. The pregnancy and delivery were a success, and "two beautiful little Chinese girls named Lulu and Nana came crying into the world as healthy as any other babies". However, later evidence shows that unwanted off-target modifications were made, and the embryos underwent enough mitosis before CRISPR/Cas9 intervened, resulting in unedited cells in the twins. The first **CRISPR babies** were faced with controversy and backlash, and Doudna and her colleagues had to release a statement. Despite criticising Jiankui and describing his procedure as "irresponsible" and "failed to conform with international norms", there were no calls for a moratorium (ban). Instead, Doudna and her colleagues looked towards the potential of editing germline- it would be acceptable if **risks** are considered, and **criteria** were set. Although He Jiankui's CRISPR babies were not received well internationally, he has kickstarted a new era. There is no turning back.

In July 2019, a 34-year-old mother of four, **sickle cell anaemia** patient Victoria Gray, was injected with stem cells – stem cells extracted from her blood and modified by CRISPR/Cas9. In June 2020, Gray discovered that 81% of her bone marrow cells were producing foetal haemoglobin, freeing her from pain attacks and blood transfusions. This is an example of an **ex vivo** editing of **somatic** cells, where the editing occurs outside the body. The success of this individual story enables us to look into the future, where many more lives of individuals like Victoria Gray could be changed for the better, where we can all live a life free of suffering.

Looking into the future, we could be seeing treatments for retrovirus infections, cystic fibrosis, Huntington's disease, blindness, blood anaemias, **COVID-19** (see "additional areas of research" below) and even cancer. Using CRISPR/Cas9 in **somatic** cells are the main aims of the science world as of now, due to inability to pass on these traits to the next generation. Editing germ cells is what might or might not cross the line; it is what raises the eyebrows of onlooking scientists. The editing of embryos could do good when it eliminates hereditary diseases. However, parent **enhancement** and **customisation** of embryos per se could lead to the theory of **eugenics**, forever changing the human genome, speeding up or intervening with human evolution. The idea of eugenics, the perfecting of humans, equipping everyone with desirable traits, eliminating traits that aren't socially accepted, could arise. Once again, we step into the depths of an ethical debate.

Apart from clinical applications, CRISPR/Cas9 can be used for **enhancing** humans, whether it is changing your eye colour, or having infrared vision. Enhancement usage of CRISPR/Cas9 is generally disapproved of by the scientific community. Due to the differences in legal systems and laws of genetic engineering in countries, any individual could be creating a "superhuman" at any second, or any sort of unofficial and immoral trials involving modifying a human or any organism.

This piece of technology has excited the world of science and

medicine. However, there are many ethical issues to consider. The possibility of the **misuse** of CRISPR/Cas9 could lead to life-threatening new inventions. Yes, it has the potential to **cure** the plethora of genetic diseases that were once incurable, but does the benefits outweigh the dangers? Should CRISPR have been left alone in nature?

Ethical discussions

Say, for example, Huntington's disease, caused by a single gene mutation – is it acceptable for a parent to decide on removing a mutation, despite the risks, if it meant it would prevent next generations from having it?

Should parents have the right to decide on what qualities and attributes their children have and does your view change if it is for disease prevention versus enhancement/ customisation?

Genetic differences give rise to a more diverse society, so should we not cure certain diseases in order to keep the population diverse? Is this diversity important?

Enhancing one individual would give them a huge advantage. However, when everyone has the same procedure, there is no real advantage, so would this simultaneous advance in the human race be beneficial, or just pointless?

People of underprivileged financial backgrounds are at a disadvantage, people who are financially poor cannot compete with those who have resources to edit their offspring's genes. Will the gap between the two increase immensely and how will it affect society? Will the rich rule?

If enhancements or modifications were made to societal norms, will the human race be a one dimensional one?

What effects will the intervention of human evolution have on our race? Who will pay the price for "messing with nature"?

"Beauty standards" are a huge aspect of society, what people perceive as pretty or handsome. Parents might customise their children to "fit in". How will people who had no CRISPR/Cas9 procedures before birth be affected?

Is it right to choose not to remove a Huntington gene from an embryo, knowing right well the suffering the person will experience?

Terrorism could arise where dictators or terrorists effectively "farm" enhanced individuals with superhuman qualities, with their sole purpose of life of being a super soldier. Should CRISPR be stopped due to these possibilities?

Which party will be responsible for mistakes in CRISPR/Cas9 editing?

Additional areas of research

PAC-MAN and CARVER "vaccines"

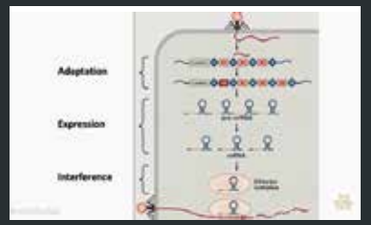


Diagram of how bacteria turn repeated sequence + spacer (viral DNA) into individual crRNA.

Study of mice models where the gene for a black coating is disabled using CRISPR/Cas9.

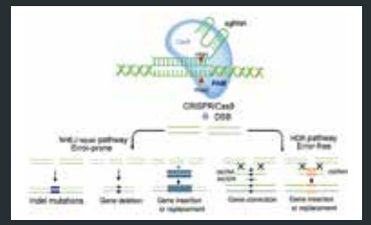
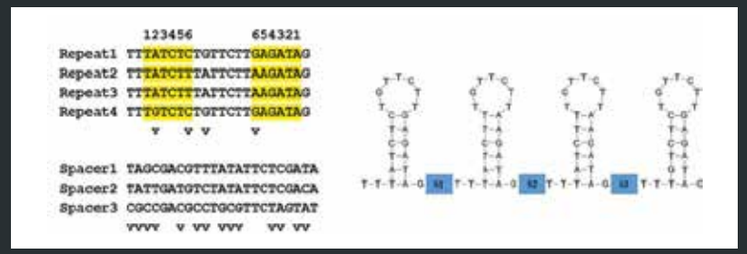


Diagram representing non- homologous end joining and homology directed repair.



Another representation of the CRISPR region, showing the palindromic sequences and the spacers.

Resources

Book: The Code Breaker- Walter Isaacson
https://youtube.com/watch?v=6tw_JVz_lEc&feature=share
https://www.youtube.com/watch?v=KSrSIErIxMQ
https://crisprtx.com/gene-editing/crispr-cas9
https://player.fm/series/crispr-cuts
https://youtube.com/watch?v=TdBAHexVYzc&feature=share
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https://figshare.com/articles/figure/_Sequence_variations_and_possible_secondary_structure_of_CRISPR_clustered_regularly_interspaced_short_palindromic_repeats_RNAs_crRNAs_repeats_of_Candidatus_Liberibacter_asiaticus_strain_A4_/1634773/1
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https://www.science.org/content/article/creator-crispr-babies-nears-release-prison-where-does-embryo-editing-stand#:~:text=He's%20largely%20secret%20use%20of,research%20on%20human%20embryo%20editing.
https://media.npr.org/assets/img/2019/11/01/sickle-cell-crispr-3x-c2fdd5526660277e89d7723e9c753c694fa02a27.jpg?s=600

BIOORTHOGONAL CHEMISTRY AND ITS POTENTIAL IN CANCER

By Kalman Yang (W)

Introduction

Biorthogonal chemistry is a powerful and innovative mechanism which has the potential to revolutionise medicine. In 2022, the Nobel Prize in Chemistry was given to Carolyn Bertozzi, Morten Meldal and K. Barry Sharpless for their work on click chemistry and biorthogonal chemistry. Bioorthogonal chemistry is defined by "a class of high-yielding chemical reactions that proceed rapidly and selectively in biological environments without side reactions towards endogenous functional groups" (1). To put it simply, bioorthogonal reactions are reactions which occur without affecting biological environments. The term 'Bioorthogonal chemistry', coined by Bertozzi in 2003, comes from the concept orthogonality in mathematics, where there is no correlation in one entity when affecting another: 'changing A does not affect changing B'. This therefore allows for the organic synthesis of material to be performed within biological *in vivo* environments rather than *in vitro* laboratory experiments. Bioorthogonal reactions are intended to covalently modify biological molecules with non-native functional groups. This would therefore allow molecules to be tagged for further study. Bioorthogonal reactions, however, must meet certain requirements:

- Bioorthogonal reactions must take place in the same temperatures and pH as found within biological systems and must be non-toxic in these conditions (5) (6)
- The reaction must be selective and produce products in high yields and must not be affected by water or endogenous nucleophiles, electrophiles, reductants, or oxidants found in complex biological environments (5)
- The reaction must be fast even at low temperatures and provide stable products (5)
- The reaction should provide non-native functional groups which are not native to the biological system (5)

Bioorthogonal chemistry can be segmented into two parts: bond formation and bond cleavage. Much of the work around bioorthogonal chemistry has been around bond formation which involves adding a functional group onto a biological molecule. During bond formation, biological handles are first covalently attached to the biological molecule endogenously through processes like metabolic labelling. A probe is then added exogenously by incorporating the molecule from outside the organism. The probe has a reactive function group such as an alkyne which will then react rapidly with the handle to attach the probe with the biological molecule. Bond cleavage involves adapting classic bioorthogonal reactions to be able to relay bond formation. This is a major part of the 'Click to Release' technology which is imperative in drug delivery systems. This click to release strategy was first demonstrated in 2008 by Robillard and his colleagues. They first achieved this with the Staudinger reduction and later with tetrazine ligation.

Bioorthogonal chemistry has wide-ranging applications from imaging to drug delivery systems;

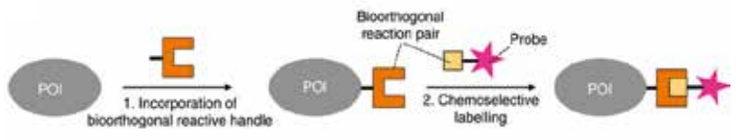

Figure 1: Illustration of the Probe and Handle concept in bioorthogonal ligation

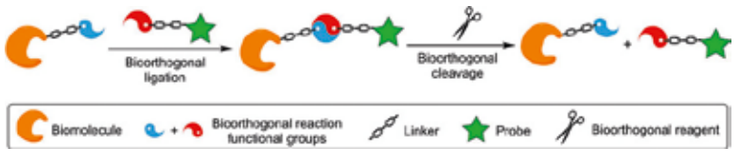

Figure 2 Diagram of Bond Formation and Bond Cleavage

Its chemoselective nature and minimal disruptive features mean that it is able to be applied to both cellular systems and large complex living organisms. Bioorthogonal chemistry is also superior to conventional tagging due to the ability to be able to quickly attach large probes which might not be possible in conventional tagging.

Main types of bioorthogonal reactions

Staudinger Ligation

The first type of bioorthogonal reaction developed was the Staudinger ligation which is based on the Staudinger reaction. The Staudinger reaction forms organic amines and phosphine oxides by reacting azides with phosphines through an iminophosphorane intermediate (iminophosphorane intermediates are versatile synthetic intermediates).

Modifying this reaction, Bertozzi was able to make it useful for attaching two molecules together. She did this by incorporating an electrophilic trap, namely an ester, into the phosphine. This would then give rise to a single ligated product joined together by an amide bond. The electrophilic trap and the iminophosphorane are near to one another meaning that the iminophosphorane is able to react with the trap rather than hydrolysing, enabling the compound to create this amide bond, connecting the two reactants.

Another variation of the Staudinger ligation is the traceless Staudinger ligation. This variation involves the electrophilic trap being connected to the phosphine by a cleavable bond or linker: a cleavable bond is a bond which is able to be broken. The reaction with the iminophosphorane here forms the new amide bond but at the same time breaks the cleavable bond which discards the phosphine oxide moiety. This reaction therefore enables the formation of an amide bond without the incorporation of residual atoms, hence the name 'traceless'.

One advantage of the Staudinger ligation is its biocompatibility. The small azide function group can easily be introduced into biomolecules. The functional group also reacts selectively with phosphines. However, the Staudinger ligation has slow kinetics, leading to inefficient labelling. As mentioned earlier in this article, a bioorthogonal reaction must be fast with high selectivity which is difficult to achieve.

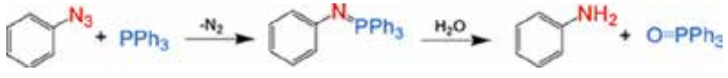

Figure 3 The Staudinger ligation

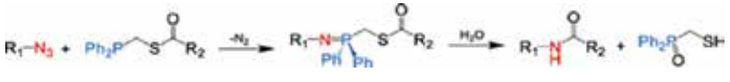

Figure 4: The traceless Staudinger Reaction

Copper Catalysed Azide-Alkyne Cycloaddition (CuAAC)

This reaction was initially proposed by Arthur Michael in 2002. In this reaction the azide reaction with an alkyne to produce 1,2,3, triazole. CuAAC is a type of Huisgen 1,3-dipolar cycloaddition. Huisgen was studying Click Chemistry before it was coined 'Click Chemistry' by Sharpless in 2001. CuAAC is also known as the Click Chemistry reaction. Although uncatalyzed, the reaction is slow in the physiological environment, but at elevated temperatures, it produces a mixture of regioisomers. To combat the slow kinetics at physiological temperatures, Sharpless and Meldal used copper catalysis in azide cycloaddition to dramatically increase its rate and regioselectivity. Regioselectivity is the preference of breaking a bond or forming a bond in one particular area rather than from all directions.

Although the idea of CuAAC seems to be promising, it does come with one substantial downside: the cytotoxity of copper catalysis. Cu (I) can be readily oxidised to Cu (II) which can cause oxidative damage to cells.

To combat this challenge and to make CuAAC suitable for *in vivo* studies, various ligands have been used to stabilise the copper catalysts. Ligands are ions or neutral molecules that can bond to a central metal atom or ion. Ligands donate an electron pair to become a Lewis base and the central atom, by gaining an electron pair, becomes the Lewis acid. In the CuAAC reaction ligands such as tris(triazolylmethyl) amines have shown success in increasing reaction rates whilst reducing the cytotoxicity of the reaction. Furthermore, these ligand modifications have also improved cell permeability for copper catalysts. Through the addition of the ligand, the reaction is therefore viable for *in vivo* studies, and is a commonly used reaction in bioorthogonal chemistry despite its challenges without the ligand.

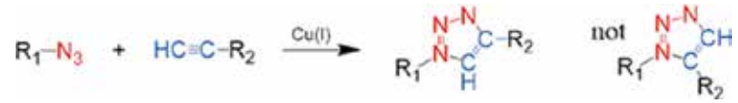

Figure 5 Copper Click Chemistry Reaction (CuAAC)

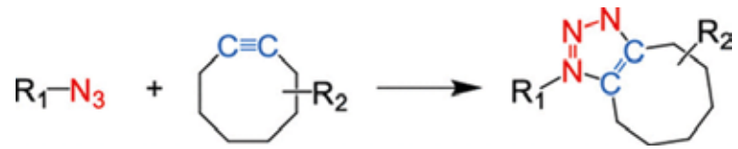

Figure 6 CuAAC

Strain promoted Azide-alkyne cycloaddition (SPAAC)

This type of reaction is also known as Copper-Free Azide-Alkyne Cycloaddition or Cu-free click chemistry as it is similar to CuAAC but without the usage of copper, finding another way to prevent copper oxidative damage to cells. This reaction was first developed by Bertozzi to not only remove the copper catalyst but to also the slow kinetics of current copper-free azide-alkyne cycloaddition reactions. In SPAAC, cyclic alkynes are being used instead of terminal alkynes which increases the rates of reactions. This is because cyclic alkynes are strained due to the bonds which pull back the bonds rather than leave the angles at 180°. High strain in molecules increases the rate of reaction because the strain must be relieved at the alkyne moiety hence greater strain leads to greater kinetics. Some of the most successful improvements to the slow kinetics were achieved using nitrogen containing cyclooctynes (fused rings which produce higher ring strain). Examples of these nitrogen-containing cyclooctynes include 4-dibenzocyclooctynol (DIBO) and aza-dibenzocyclooctynes (DIBAC). Although these molecules react quickly, the size of these molecules makes their *in vivo* incorporation a challenge.

To tackle this issue, bicyclononynes (BCN) combine high reactivity with reduced steric bulk. This means that the molecules still maintain their high kinetics yet in a smaller package, meaning that *in vivo* incorporation into biomolecules such as proteins and glycans is much easier. BCNs therefore improve its viability for SPAAC in bioorthogonal chemistry.

Tetrazine Ligation

The tetrazine ligation was first reported by Blackman et al. and Devaraj et al. It is a fast bioorthogonal reaction that uses the inverse electron demand Diels-Alder reaction (IEDDA) between a tetrazine and dienophile followed by the elimination of nitrogen gas through a retro-Diels-Alder reaction to form a fused dihydropyridine product. (5) The tetrazine reaction is nearly optimal for applications *in vivo* due to its rapid kinetics. However, its major drawback is its varying stabilities in aqueous solution or in the presence in thiols: as reactivity increases the tetrazines become more unstable. A way to improve stability is through disubstituted tetrazines, especially monomethyl tetrazines which maintain stability with high reactivities. Another way is by using 1,2,4-trazines in IEDDA reactions as reported by Prescher et al; the kinetics towards dienophiles have been reported to be satisfactory. These dienophiles can also be optimised to improve stability with reactivity. Trans-cyclooctenes can isomerise to the more stable cis-cyclooctenes which are completely unreactive. By synthesising the molecule, and using dioxolane-fused trans cyclooctenes, the molecule becomes more stable and less prone to this isomerisation.

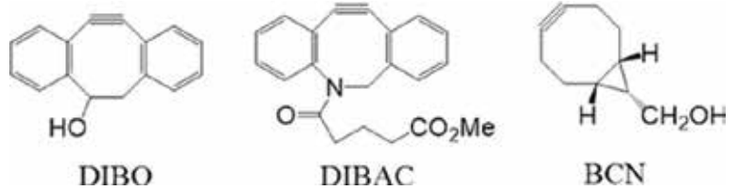

Figure 7 The different nitrogen-containing cyclooctynes

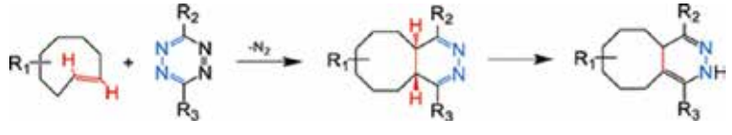

Figure 8 Tetrazine Ligation

Bioorthogonal Reactions	Advantages	Disadvantages
Staudinger Ligation	• Azides and phosphines are biocompatible • The amide bonds which are produced are stable	• Slow kinetics
CuAAC	• Fast reactions • Good regioselectivity	• The toxicity of the copper catalysts is still a concern
SPAAC	• Does not use copper catalysts • Still fast	• Reactions are slower than CuAAC • Steric bulk of molecules which makes it difficult to incorporate into physiological environments
Tetrazine Ligation	• Very fast reactions • Stability is tuneable by modifying the tetrazines of dienophiles	• Its low stability in aqueous environments

What is cancer

Cancer is a disease which can occur in anyone; it is caused by a mutation in genetic materials causing the replication of abnormal cells to occur. The replication of abnormal cells is uncontrollable which also spreads to other parts of the body. Cancer is a dreaded disease which can sometimes lead to the death of the patient. However, through therapies such as chemotherapy, cancer is treatable and occasionally curable. As our population continues to age and grow, the number of new cases of cancer will continue to rise.

Cancer can come about for many different reasons. One reason is because during DNA replication, errors may occur. DNA (Double Nucleic Acid) is a structure which contains genetic material which is wound up in a double helix discovered by James Watson and Francis Crick in the 1950s. The DNA structure also consists of a sugar-phosphate backbone and complementary bases: adenine (A), guanine (G), cytosine (C) and thyine (T). Adenine and guanine are categorised as purine bases due to their distinct two carbon nitrogen rings. Cytosine and thymine are classified as pyrimidines as noted by their one carbon nitrogen ring. Although A-T and C-G are complementary because purines go with pyrimidines, a pairing of A-G and C-T is technically possible. This was discovered by Crick in 1966 and is only possible due to the flexible nature of the double helix which accommodates slightly misshaped pairings.

DNA mutation can also occur through a process called strand slippage where nucleotide bases are added or deleted. If the newly synthesised strand loops out, a new base would be added as it would repeat the sequence on the template strand. However, if the template stand loops out, a base would be deleted also resulting in a mutation.

Although DNA polymerase is good at preventing replication errors, errors still occur every 1 in 100,000 nucleotides which is 0.00001%. This number is seemingly small until you consider that we have

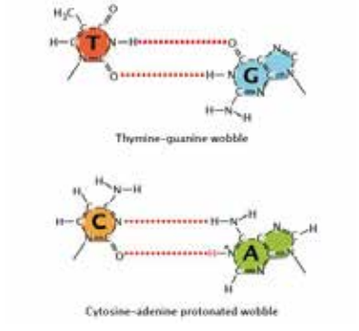

Figure 9 Demonstration of Wobble in DNA

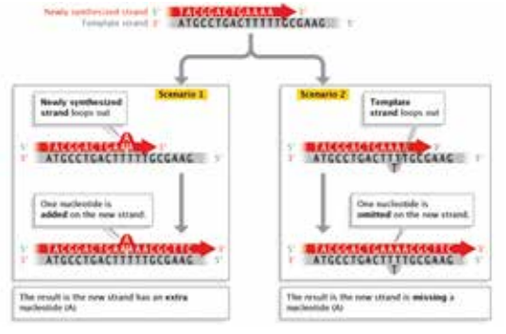

Figure 10 Diagram of strand slippage

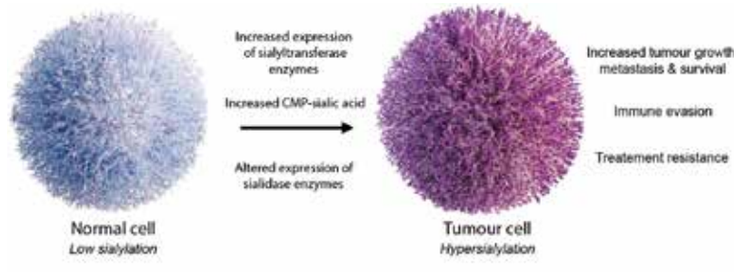

Figure 11 Sialylation in both normal cells and tumour cells

6 billion cells in each diploid cell meaning that every time a cell divides there would be 120,000 errors. Luckily, proofreading occurs during replication meaning that many of these errors are found. The errors are then corrected through a process known as mismatch repair. When the exposed 3'-OH group is seen to be in the 'wrong' position, the process of replication stalls and the error is rectified. This removes about 99% of errors still leaving 12,000 errors in one cell division. As DNA replicates, through hydrogen bonds between molecules, the secondary structure forms and errors in the new synthesised strand will result in deformities in the structure. Through another process called mismatch repair, enzymes find and recognise these deformities and replace the incorrect nucleotide with the right base.

All cells in the human body are coated in a layer of sugars, called glycans. These are glycoproteins which stick out of the phospholipid bilayer. The genome is the complete genetic composition in a cell and the proteome is every protein that a cell can produce, and the glycome is every glycan the cell can produce. However, when looking at cancer cells and normal cells together, there seems to be a specific glycan which is more present in cancer cells – sialic acid. The sialome is comprised of many sialyated structures which play an important role in cell communication. Although, sialic acid has the word 'acid' in its name, it is in fact a sugar. If a child is grumpy and tired normally a slice of cake or two will make them happier. Similarly, if a cell has lots of sialic acid on it, the immune system relaxes, and the cell is able to evade immune detection. This is excellent for our cells as the cell glycoproteins and glycolipids signal to our immune system that they are our cells and do not require an immune response. The lack of this system will lead to autoimmune disease where the immune system attacks healthy cells. The immune system is told to 'never take candy from a stranger'. However, cancer cells have tumour hypersialylation where there is an increase of 60% in sialic acid residues. Sialytransferases are enzymes which produce sialic acids and hypersialylation can occur through the upregulation of these enzymes and results in an excess of sialic acid on the cell surface membrane. Oncogenes such as RAS and c-Myc have led to an increased transcription of sialytransferases which results in the production of more sialic acid.

What does hypersialylation mean for cancer cells? And how does sialic acid really evade the immune system? A tumour has one goal which is to grow and spread around the body (metastasise). This can only be achieved if the tumour avoids detection. For tumour cells, this is a very complicated game of hide and seek. However, our immune systems are trained to play hide and seek and tend to be excellent seekers…probably better than an 8-year-old in primary school. However, the trick that sialic acid has is to supress the immune system when they are caught. Immune cells have membrane proteins called sialic acid -binding immunoglobulin-type lectins (Siglets). You can imagine Siglets to be the eyes of immune cells which are playing hide and seek. The Siglets bind to the sialic acid and an immunosuppressive signal is sent which therefore protects the cancer cell. However, although the hypersialylation evades the immune system, it also becomes a marker for targeted drug delivery for cancer treatment.

Using Bioorthogonal Chemistry to Treat cancer

Due to bioorthogonal chemistry's non-interference with biological processes it has been seen as a way to treat cancer. Currently, many forms of chemotherapy involve attacking the tumour from the outside (radiation) or from the inside using drugs. However, a problem with using drugs to kill cancer cells is that there is also a chance that it could kill normal cells considering that most of its components are almost identical to our cells. On the other hand, if you make a drug which will kill fewer healthy cells, it becomes less effective on cancer cells. Therefore, it is important to think of a method to be able to use drugs of high cytotoxicity without

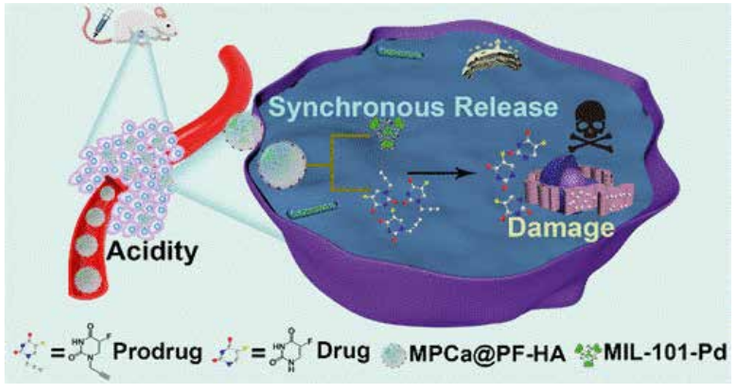

Figure 12 A diagram illustrating the release of prodrugs.

damaging healthy cells. This is where bioorthogonal chemistry exhibits great potential.

How would you send a gift from one person to another across the world? Well, there are a few options. Option 1: Fill a plane with many copies of the same gift and drop a gift off every 2 minutes and hopefully the other person might receive a gift. Option 2: Send it as a package which will be put on a boat to be sailed around the world. When the gift reaches the nearest point to the person a car will pick it up and bring it to their house. Option 3: express delivery – the package will be put on a plane and flown straight to the receiver's house. Option 1 is too general. The possibility that the package would reach the person is near impossible. Many different variables such as the wind speed and direction, the spin on the box and whether the person is even at home will all determine how accurate the drop is. Option 2 is much more precise yet it would take far too long. Maybe the gift was a T-shirt for a baby; by the time the gift is received the baby is too big and the gift is rendered useless. Option 3 is by far the best method. It is fast and precise which is exactly what is needed to treat cancer.

Look back at the reactions discussed earlier. Bioorthogonal reactions have the ability to cleave and join, similar to grabbing an object and releasing it. Researchers are currently finding ways to make this more efficient and effective for treating cancer. A bioorthogonal reaction is completed to join a prodrug (a chemically inactive substance which can be metabolised into a drug) and handle. We can use the tumour characteristic of hypersialylation and determine the cleavage or this bond to release the prodrug. The prodrug will then be released and will be metabolised to a drug which will be able to attack tumour cells.

Conclusion

This form of cellular medicine is very interesting and has the potential to treat many forms of cancer due to bioorthogonal reactions' specificity. However, it is important to note that this technology is very early in its development and could take several years to become a mainstream treatment. We know very little about cancer and even less about how cells interact so it will take much more research to determine whether this is a viable form of treatment or not.

THE FIRST STARS

By Beatrice Wynne-Edwards (St)

Shedding light on the universe's astrological dark age, Dr Emma Chapman's 'out of this world' research into the first billion years after the Big Bang begins to fill in the gaps in humanity's incomplete knowledge of the stars.

Dr Emma Chapman (Royal Society Dorothy Hodgkin Research Fellow and astrophysicist based at Russell-group University of Nottingham) delivered a lecture to the A-level and IB physics students at the 'Physics in Action' event held at Warwick University on the 28 November 2022. Her presentation illustrated the importance and appeal of research into this era and elucidated how natural phenomena and man-made equipment are used in conjunction with theoretical science to paint a picture of the universe over 13 billion years ago.

"I maintain that the cosmic religious feeling is the strongest and noblest motive for scientific research" Albert Einstein – *Ideas and Opinions* (1954)

Dr Chapman, like many, was compelled by the customary tendency of humans to take an interest in where we came from. This interest extends not only to who our ancestors were, but how humans evolved, and even how life came to be on planet Earth. Finally, with modern resources and newly developed technology, we are able to look back even further through time by looking even further through space. To see images from billions of years ago, we now need only look up.

Visible light, which humans see, is only a small part of the electromagnetic spectrum. Not dissimilar to how doctors use X-rays to observe the world around us in a different light, or police use infrared cameras to detect animals and people,; astrophysicists use radio telescopes to detect EM waves with wavelengths too long for our eyes to see. This is particularly useful when looking at ancient stars because as light travels, it loses energy, increasing its wavelength: a process called 'red shift'. Viewing galaxies visible with optical telescopes through radio telescopes can be just as useful, for example the radio lobes emitted from various galaxies in enormous plumes (due to the matter consumed by black holes, as we now know).

The essence of the scientific method is that, in order to diagnose the cause of the observations we make, we must use previously acquired data to make theoretical conclusions that can then be trialled and tested. The missing data in the timeline (from the age of the first stars) could lead to incorrect conclusions in other matters. Therefore, in addition to our natural desire to understand our past, knowledge of this period in the history of the universe is important for other ongoing research too.

The reason we can somewhat easily look back in time through radio and optical telescopes is the useful fact that light speed, although extremely fast compared to everything else, is not infinite. Light photons hurtle across the universe at the incomprehensible speed of 299 792 458 m/s which means that it therefore must take time to travel a distance through space (speed=distance/time). Travelling vast intergalactic distances takes a very long time, even for light. Our closest neighbouring galaxy, Andromeda, is approximately 23,651,830,000,000 km away. Given the speed of light and Andromeda's distance from Earth, light from the Andromeda galaxy takes about 2.5 million years to reach us, meaning that we see the Andromeda galaxy today exactly as it was 2.537 million years ago.

Stars like our sun 'live' for billions of years (approximately 9 billion) until they run out of hydrogen fuel to fuse and 'die' (life cycle of stars). The larger the star, the shorter the lifetime because they consume fuel much more quickly. Using theoretical physics and chemistry, hypotheses have been made about the nature of the first stars. For example, that they were massive, thought to be up to 100 solar masses, and that their lives were

correspondingly short. After about 1 million years, these stars ran out of fuel and gradually became extinct. We also conjecture, by measuring the temperature of light photons once emitted from the first stars, that they were around 1 million°C, much hotter than our sun's 6,000°C. Performing this procedure on even older photons (which tell us the universe used to be very cold) we can conclude the age of the first metal-free stars. The current figure is around 180 million years after the Big Bang.

All stars can be categorised into one of three groups depending on their elemental makeup: metal-rich, metal-poor, and metal-free. Plenty of metal-rich and metal-poor stars can be observed within our galaxy alone but metal-free stars are most probably extinct. This is because the first stars, with such short lifetimes, were the only metal-free stars that ever existed, or ever will exist, and hence the terms are interchangeable. However, if there was one small enough to consume fuel slowly, it could still be present to this day. If indeed still out there, these stars would be camouflaged by the metals surrounding them, so they will be difficult to find and identify. Second-generation stars, however, have already been discovered. BD+44 493 is thought to be the brightest known second-generation star in the sky and at about 600 light years away, it can be seen by the human eye with only a very good pair of binoculars to enhance the image. The metal-free stars were, somewhat ironically, the first sources of metals in the universe. When stars die, they collapse into themselves due to gravity and explode outwards with extremely high energy. The supernovae caused by the deaths of the first stars allowed the first of any elements other than hydrogen and helium to be formed, and these metals polluted the once pristine vacuum of space, meaning that no other metal-free star would ever be created again. Rather more importantly, however, the formation of other elements enabled life to eventually be formed, of this same stardust, 13 billion years later.

"WE ARE MADE OF STAR-STUFF. WE ARE A WAY FOR THE UNIVERSE TO KNOW ITSELF" Carl Sagan – *Contact* (1985)

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SUCCESSES IN SCIENCE 2023

By Sam Robinson, Head of Science

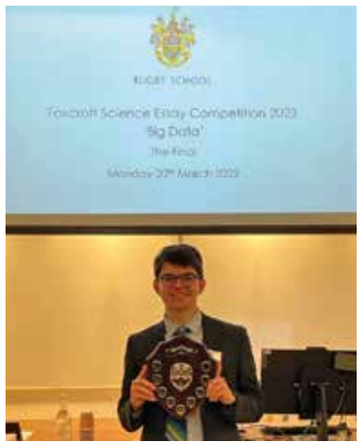
2023 saw some remarkable achievements in extracurricular Science this year. Here are some highlights:

Olympiad results:
Olympiad competitions are open to all LXX and XX scientists. These world-renowned tests seek to challenge the top Science students. Gold awards go to the top 5% in the world. The following were awarded Gold awards this year:

Biology Olympiad: Oliver Butler (T), Yvonne Tang (S) and Laurie Guard (T).

Chemistry Olympiad: Arvin Wang (SF) and Sophia Chen (St).
Special mention to Arvin who was placed in the top 0.3% in the World.

Physics Olympiad: Edgar The (SF), Peter Zhu (M), Sophia Chen (St).



Foxcroft Essay competition:
This year saw a record number of entries to the Foxcroft Science Essay competition. The theme was "Big Data". Six students made the final which took place on 20 March 2023, three from Rugby School and three from local schools. Students were asked to deliver a 10-minute presentation on their essay and answer 10 minutes of questions from the audience. A huge congratulations to Tom Macro (Warwick) for winning the competition. A well done should also go to Beatrice Wynne-Edwards (St), Jemima Barton (St) and Peter Zhu (M) for being awarded Gold Certificates for their essays.

Interschools Chemistry quiz:
In May, the Chemistry Department hosted the annual Inter School Sixth Form Chemistry Quiz – a day of excitement, knowledge-sharing, and camaraderie. Twenty-one enthusiastic teams from surrounding local schools participated, immersing themselves in an intellectually stimulating experience. Rounds ranged from the history of science to intriguing challenges involving boiling points and smelly chemicals; the quiz was a true celebration of chemistry's multifaceted nature. In a close-fought contest, Warwick School's team emerged victorious, earning well-deserved applause. Congratulations to all participants for their dedication and to Warwick School for their triumph.

Bateson Society:
Bateson Society is our Upper School Biology Society, named after OR William Bateson, a leading geneticist. Here are some of the posters from the talks that were given:

WUNDERBAR ECOLOGY: WHY STUDYING LEAVES AND WORMS ISN'T ALL BAD

By Kalman Yang (W)

Dr Thompson (AMT rather than MAT in chemistry) arrived at the Rugby School campus in 2022 coming all the way from South Croydon: a change in scenery from North Face puffers to even more North Face puffers and the School Field E Block. Completing his first year at Rugby, Dr Thompson has introduced the weekly Biology Newsletters for both the Lower and Upper Schools and has attempted to spread his love of Ecology to many students through his enthusiastic attitude and the Ecology Society.

It quickly became apparent that Dr Thompson was unlike other Biology teachers who have come to Rugby School: for one, he enjoys his foreign phrases, his favourite being *wunderbar*, meaning wonderful in German. Secondly, his radiating passion for Ecology is not commonly seen in other people interested in Biology. I needed to interview Dr Thompson to fully understand how someone could find leaves and twigs so interesting.

Where did your love for Ecology come from?

Dr Thompson studied Natural Science, specialising in Zoology, at Girton College, Cambridge. He recalls not being particularly interested in zoology when he first started university, as it wasn't really on the curriculum: "Although I didn't take chemistry for A levels, I was really interested in biochemistry. I really enjoyed learning about the chemical reactions that take place in respiration and photosynthesis, and how neatly they mirror each other and flow." However, when taking a course called Behavioral Ecology his perspective quickly shifted. He was enlightened to the world of Ecology, especially after the lectures of William Foster and Nick Davies: what a fall from grace.

A memorable experience at Cambridge for Dr Thompson was when a lecturer asked everyone to draw an elephant. Most people, as you might think, drew a large animal with four legs, large floppy ears, two ivory tusks and a mighty serpentine trunk. Contrasting when people were told to draw a rose, a myriad of different and unique images were drawn. A quick google search of an elephant and a rose shows very similar results to the very quick activity in the lecture.

Why is this? It all comes down to a very simple reason: due to their ways of getting nutrition, plants are static and so have evolved mechanisms of plasticity to reduce being eaten by herbivores, meaning that no two plants really look that much alike as their shape is determined by their environment. A simple answer which shifted Dr Thompson's paradigm. Because of this, plants evolved more complex biochemistry, to produce toxins and even addictive substances to dissuade animals from eating them or to "trick" them into doing their bidding, e.g. pollination or protection of the plant. Animals on the other hand, if they want to evade predators, can run away or hide. This means that the evolutionary pressures, and directions of evolution, are completely different for animals and plants. He was also shown a picture of three elephants walking across the savannah;, the lecturer pointed out the picture actually contained hundreds of species and thousands of individual plants, not just three elephants. This helped him to understand the animalcentric view that most people have of the natural world.

What was your PhD on and what were its conclusions?

Dr Thompson investigated the parent offspring conflict in a

cooperative breeding bird being the pied babbler (*Turdoides bicolor*).

He describes choosing the pied babbler for several reasons:

1. It was habituated.
   a. Humans were able to get close to the bird (as shown by the image above) which makes it ideal for studying, with observation and experimental manipulation being easy.
2. You could put ID tags on it easily, each bird having its own unique set of coloured rings.
   a. This means that you were able to track a single organism throughout its entire life, and easily identify them in their large groups of up to 15 individuals.
3. When Dr Thompson undertook this project, they knew the entire life history of every bird from the 15 years of study at the site. They follow the birds from egg to death.
4. It was cute and charismatic, they are extremely vocal and like to play: chasing each other around trees and causing a great calamity.

Cooperative breeding was one of the main focal points of Dr Thompson's research. In a cooperative breeding environment only one male and one female reproduce. Typically the groups are made up of a breeding pair and their offspring, who help to bring up their brothers and sisters, meaning that it is highly kin structured. The resources which an individual would have used for their own reproduction (primarily food) are instead used to feed the offspring of the breeding pair.

On the face of it, cooperative breeding does not seem to marry up with Darwin's theory of evolution by natural selection. If the "aim" of an individual's life is to pass on its genes to the next generation, why on earth would they forego their own reproduction and actively help out someone else? However, there is a theory proposed by William Hamilton, where inclusive fitness trumps individual survival. Inclusive fitness takes into account how many genes, on average, you share with another individual. If you have a brother or a sister, they are 50% related to you. If you have a child, they are also 50% related to you. If by helping your parents, or other individuals, you can ensure more copies of your genes would pass on to the next generation than if you bred yourself, then this behaviour will be selected. So, if on average you would have two children, and you can help your parents have three more, you will get more copies of your genes into the next generation. This genetic accounting is also used to explain the amazing world of eusocial insects, like bees, wasps, ants and termites, where species have evolved to have whole castes that are completely unable to breed.

By researching parent offspring conflict in a cooperative breeding system, Dr Thompson made some interesting findings. To his surprise, he found that offspring don't try to extort more food for themselves by pretending to be hungrier than they are. Through a series of feeding and playback experiments, he found that how loud they shouted (begged) for food accurately correlated with their level of need. He did, however, find

a very odd behaviour: blackmail. When the chicks are very young, they are almost unable to fly, but will put themselves in dangerous situations to make sure that they are fed faster and receive more food than their adult carers would like. Tricky little birdies.

Why is Ecology so important?
Studying and working in the field of Ecology, Dr Thompson felt that it has allowed him to gain a stronger grasp on how living things function. Ecology is something that flows through living things. Imagine taking a short brisk walk from the Chapel to the Science Department, something many of us Rugby School pupils can recall with relative ease. Most would think of passing Pontines, and School House on the left, followed by the Queens Gate before turning right following the perimeter of The Close. You would then approach the School shop on the right where you would be able to buy the pens which seem to be extortionate. School Field would then appear out of nowhere to the left and finally you would arrive at the Science Department.

On that brisk walk you could have also thought about the elm tree that was planted by the Queen in 1967 or the roots and system that this one tree has formed. There is also the symbiosis of lichen on the towering oak trees and the entire system of producers, consumers, and decomposers to allow life for so many organisms. Even sitting in C4 (a chemistry classroom) looking out the window have you ever thought about how growth rings form on trees or why leaves turn a warmer shade in the autumn? There is also the Rugby School beehive on the roof of the department managed by Mr. Uglow, which illustrates the wonderful mutualism between different living things: bees getting nectar and pollen but the plants being able to reproduce with the aid of the busy little insects.

In GCSE and even A level, there is a massive emphasis on human physiology, inheritance and genetics. This could be explained by the push by the government to have more people working in the medical field or other areas of research that are typically seen as economically more beneficial. Students are made to believe that all Ecology is taxonomy and counting percentage cover using quadrats. However, Ecology encompasses so much more and enriches the meaning of 'life'. Dr Thompson's belief is that without understanding the core principles that underpin the living world, much of life makes far less sense, and that there is a beauty in being part of a dynamic system full of the myriad of organisms that we share the planet with. My personal view on Ecology has slowly shifted from resentment to appreciation. I am sure that with another year, with Dr Thompson barking on about how Ecology links life together, that appreciation might turn into admiration.

THE STRONG BOND SHARED BETWEEN WORLD WAR II AND CHEMISTRY

By Thomas Batchelor

Mr Batchelor investigates the connection between World War II and Chemistry, offering a brief overview of key aspects.
To facilitate your exploration of these intriguing subjects, he provides informative links for further reading.

Introduction

I have always been captivated by how Chemistry and wars have been bound together. The harnessing of chemicals in various forms, including weaponry, medicine, and industry, both on the battlefield and in their home countries, brought about dramatic shifts in the dynamics of wars. World War II was one of the most devastating conflicts in human history and the race to research and development between the Axis and Allies to gain an advantage over the other saw massive progression over this period.

My fascination started as a young boy when talking to my grandfather about his experiences of the war. He recounted stories of watching Spitfires in dog fights with the German Luftwaffe over the rolling hills of Sussex, where he grew up. As an aspiring scientist, he would go hunting in the countryside in search of unexploded incendiary bombs, in order for him to convert them, successfully, into fireworks (with his mum's permission). She would actually facilitate his stupidity, buying him chemicals from the local pharmacy to allow him to produce fireworks of an array of colours.[1]

Since then, I have enjoyed learning stories about how WWII and Chemistry are intertwined. In fact, whilst writing this article, I came across a fascinating story about how a Nazi submarine U-1206, captained by Karl-Adolf Schlitt, was inadvertently flooded by wrongly flushing the toilets with sea water near the battery which produced a lethal amount of chlorine gas. If only he had revised the GCSE topic of electrolysis he might have been able to avert disaster.[2]

Chemicals in Industry

The industrial sector experienced a surge in chemical developments during World War II, as nations sought to enhance their production capabilities and support their war efforts.

As the country had embargoes placed upon it, reducing their access to raw materials, chemists within major German companies, such as Bayer and BASF, became increasingly important to create synthetic materials such as nylon, rubber, and plastics, which all gained prominence due to limited access to traditional resources.

BASF, the global German company within the I.G. Farben group, had a shady role throughout the war. They built a concentration camp next to their factory in Monowitz (near Auschwitz) and forced inmates to conduct labour. Of the approximately 41,000 inmates, 30,000 were killed from poor conditions or, if they were seen as inadequate workers, they would be sent to their death at Auschwitz-Birkenau, for the next to replace them. BASF also had a part to play in Ziklon B (see section on chemical warfare).[3]

For the Allies, the development of synthetic rubber enabled them to overcome the scarcity of natural rubber, which was predominantly controlled by Axis powers. These advancements in materials science bolstered the military-industrial complex, allowing for the production of more sophisticated weaponry, vehicles, and equipment.[4]

The lifeblood of a sustained war advancement is its reliance on fuel to propel the forces forward. With Germany having limited crude oil reserves, limiting its ability to produce fuel, they once again had to rely on their chemists.[5] The German scientists invented and developed two processes that enabled them to synthesise petroleum from their country's abundant coal supplies, establishing the world's first successful synthetic liquid fuel industry. Friedrich Bergius invented a process of high-pressure coal hydrogenation, named the Bergius Process. The process involves the

$$C + H_2 \xrightarrow[\text{heat, high pressure}]{\text{catalyst}} C_nH_{2n+2}$$

hydroliquefaction of brown coal, also known as lignite, into crude oil. The brown coal is ground into a fine powder and heated at 425–480 °C under 200–700 atm. pressure of hydrogen gas in the presence of a catalyst.[6]

The second was the Fischer-Tropsch process, a catalysed chemical reaction in which carbon monoxide and hydrogen are converted into liquid hydrocarbons of various forms.[7,8]

Chemical Warfare

One of the most notable aspects of chemical development in WWII was the use of chemical warfare agents. Both the Axis and Allied powers, very much like WWI, invested substantial resources into researching and manufacturing lethal chemicals that could be used to incapacitate or kill enemy combatants.[9] The most infamous of these chemicals developed by the Germans were the nerve agents, such as sarin, tabun, and soman.[10] These deadly substances presented a new and terrifying dimension to the battlefield, as they could cause rapid and often fatal neurological damage.

Despite dying before the outbreak of WWII, Nobel Prize winning Jewish chemist, Fritz Haber, still had a sinister part to play in the war.[11] To GCSE students, he was prominently known for his invention of the Haber-Bosch process, a way to nourish farmers' fields with nitrogen captured from the air.[12] For others, he is known as the father of chemical warfare, who pioneered mustard gas, unleashing atrocities of chlorine clouds against Allied troops in WWI. Between the wars, Haber's research continued within the field of Germany's secret development of chemical weapons as well as pesticides, Zyklon A. His work was later developed upon, without his direct involvement, to develop Zyklon B, used for the extermination of more than 1 million Jews in gas chambers in the greater context of the Holocaust.[13]

While chemical weapons were employed to a limited extent on the battlefield during the war, the psychological impact they had on both military personnel and civilians cannot be overstated. The fear of chemical attacks influenced military strategies, necessitated the development of protective gear, and diverted resources towards defensive measures. The German chemist Maier said 'I was just working on metal carbonyls', but then added 'metal carbonyls can disable the gas mask filters soldiers used as protection.'[14,15,16]

Image from https://www.history.com/news/world-war-i-gas-chemical-weapons

Medical Advancements

Chemical developments during World War II also played a vital role in the field of medicine. The war brought about significant advancements in antibiotics, blood transfusion techniques, and wound treatment. The mass production of penicillin and so-called "sulfa drugs", for instance, revolutionised the treatment of bacterial infections and significantly reduced mortality rates among wounded soldiers.[17,18] In 1928, Scottish scientist Alexander Fleming accidentally discovered penicillin. Despite Fleming's groundbreaking discovery, progress in harnessing penicillin's therapeutic potential was slow. The challenges lay in producing the compound in sufficient quantities and understanding its properties. In 1938, a team of researchers at Oxford University led by Howard Florey and Ernst Chain decided to investigate Fleming's observation further. They conducted extensive research on penicillin's isolation, purification, and effectiveness against various bacteria, eventually scaling it up to large-scale production.

The availability of penicillin during World War II proved vital for treating wounded soldiers. The antibiotic's effectiveness in combating infections significantly reduced mortality rates among soldiers and civilians alike. Remember that young budding chemist who created fireworks in the war? My grandfather, Dr Frank Ralph Batchelor, went on to work with Ernst Chain in Rome to build upon the advancements of antibiotics of the war. He went on to discover and synthesise new penicillins, such as amoxicillin. I remember him telling me that after the first successful experiment, he had more penicillin G under his fingernail than they would be able to produce in a month.[19,20]

Scientific Collaboration and Post-large-scale

The war served as a catalyst for significant post-war advancements in various fields with knowledge gained during the conflict being repurposed for civilian applications. Controversially, the Allies were keen to profit from sophisticated Nazi military and industrial science and technology and were afraid it might fall into the hands of the Russians. The U.S. military established Operation Paperclip, whitewashing the Nazi affiliations of roughly 1,600 German scientists they deemed useful, awarding them and their families citizenship.[21]

Conclusion

The development of chemicals during World War II had a profound impact on the outcome of the conflict. Chemical warfare agents introduced new levels of terror and influenced military strategies, while advancements in medicine saved countless lives and revolutionised healthcare practices. Chemical developments in industry enabled nations to overcome resource limitations and bolster their war efforts. Moreover, the collaborative nature of scientific research during this period set the stage for subsequent scientific progress.

As we reflect on the legacy of World War II, it becomes clear that the development of chemicals played a crucial role in shaping the course of the war and its aftermath. The lessons learned from this period continue to inform our understanding of chemical warfare, medical advancements and industrial applications, reminding us of the profound and lasting impact of scientific innovations during times of conflict.

Links

1 (The chemistry of fireworks – https://www.youtube.com/watch?v=nPHegSuII_M)
2 The Nazi U-boat sunk by a toilet malfunction https://www.scotsman.com/whats-on/arts-and-entertainment/the-nazi-u-boat-sunk-by-a-toilet-malfunction-1455820)
3 Forced Labor at the I.G. Farben Factory in Auschwitz – https://www.basf.com/global/en/who-we-are/history/chronology/1925-1944/1939-1945/zwangsarbeit-in-auschwitz.html
4 U.S. Synthetic Rubber Program – https://www.acs.org/education/whatischemistry/landmarks/syntheticrubber.html
5 Early Days of Coal Research https://www.energy.gov/fecm/early-days-coal-research
6 100th Anniversary: Bergius Process https://www.chemistryviews.org/details/ezine/5466751/100th_Anniversary_Bergius_Process/
7 German World War II Economics: Raw Materials--Oil https://histclo.com/essay/war/ww2/eco/raw/oil/w2ero-ger.html
8 Fischer-Tropsch Process to Generate Liquid Fuels https://www.e-education.psu.edu/egee439/node/679
9 The chemists' war – https://www.chemistryworld.com/features/the-chemists-war/8837.article
10 The Nazis Developed Sarin Gas During WWII, But Hitler Was Afraid to Use It https://www.history.com/news/the-nazis-developed-sarin-gas-but-hitler-was-afraid-to-use-it
11 Charles, Daniel (2006). Between genius and genocide : the tragedy of Fritz Haber, father of chemical warfare
12 The Nobel Prize in Chemistry 1918 https://www.nobelprize.org/prizes/chemistry/1918/ceremony-speech/
13 Chemical Warfare Agents and Zyklon B https://www.basf.com/global/en/who-we-are/history/chronology/1925-1944/1939-1945/kampfstoffe-und-zyklon-b.html
14 Chemistry In Nazi Germany https://cen.acs.org/articles/91/i37/Chemistry-Nazi-Germany.html
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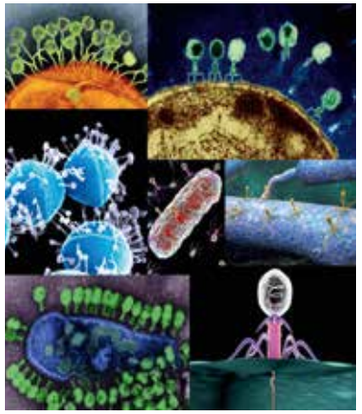
16 Chemistry: The hidden war https://www.nature.com/articles/541154a
17 6 medical innovations that moved from the battlefield to mainstream medicine https://www.statnews.com/2017/11/10/medical-innovations-war/
18 A Brief History of the Antibiotic Era: Lessons Learned and Challenges for the Future https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3109405/
19 Batchelor, F. R.; Doyle, F. P.; Nayler, J. H. C.; Rolinson, G. N. (1959). "Syntheses of penicillin: 6-aminopenicillanic acid in penicillin fermentations". Nature. 183: 257–258.
20 Post penicillin antibiotics: From acceptance to resistance? http://www.histmodbiomed.org/sites/default/files/44828.pdf
21 What Was Operation Paperclip? https://www.history.com/news/what-was-operation-paperclip

BACTERIOPHAGES – ANTIBIOTIC RESISTANCE AND PHAGE THERAPY

By James Hon (C)



We've all heard of antibiotics at some point in our lives. We all know antibiotics treat infections; some of you might even ask for antibiotics whenever you get a bad cold. The problem is that antibiotics only target bacterial infections; they would have no effect on viral infections such as the common cold. This has major implications in our current antibiotic resistance crisis.

Back in the 1900s, even an infection from the smallest paper cut could be fatal. Believing that infections were due to an excess of blood, doctors used to perform bloodletting. Just imagine your reaction if your GP suggested extracting more blood from your forearm to treat your nose bleed! Thankfully, we have moved on now and in today's technologically advanced society, we can all agree that bloodletting is not a viable treatment. In 1928, a Scottish physician and microbiologist decided to take a break from lab work to go on holiday. Upon his return, he discovered a mould on his petri dish that prevented bacteria from growing. Credit to his carelessness, Alexander Fleming had unintentionally discovered penicillin, the world's first antibiotic. He revolutionised medicine and his accidental unearthing has saved millions and continues to do so today.

Since its discovery, humans have taken antibiotics for granted; we are overusing antibiotics in both livestock production and in the medical field. Antibiotics are mass fed to livestock to ensure maximum yield. A lot of antibiotics are prescribed or taken for viral infections in clinics, as previously mentioned. We are essentially killing the weak (no resistance genes) and selecting for those who are strong (have resistance genes) – an elegant example of natural selection. This results in the creation of "superbugs", those resistant to all antibiotics. The World Health Organisation (WHO) stated that antibiotic resistance is one of the top 10 global public health threats facing humanity, and we have entered an antibiotic resistance crisis. Scientists predict that deaths due to antibiotic resistance in 2050 will surpass the current yearly deaths attributed to cancer. Alarm bells should be ringing and resources should be allocated to neutralise the crisis before it escalates even further. To solve this issue, we shall first gain a stronger understanding of antibiotics.

Antibiotics enter a bacterial cell via simple diffusion through porins, facilitated diffusion through carrier proteins or even by bacterial self-uptake. An important concept to remember is that antibiotics must accumulate to high concentrations to execute their antimicrobial actions. When the minimum concentration is reached, antibiotics have three methods of destruction: inhibiting bacterial cell wall synthesis, protein synthesis and DNA/RNA synthesis. They bind to key sites integral to these processes (e.g. RNA polymerase or ribosomes). You may now wonder, how do bacteria with resistance genes evade antibiotics? There are various ways of achieving resistance. To maintain a low concentration, some bacteria have efficient efflux pumps to remove antibiotics – which ensures a low net concentration of antibiotics. Some bacteria are resistant due to mutations in binding sites of the antibiotic, e.g. ribosomes that carry out protein synthesis. Interestingly, some bacteria are able to directly break down the antibiotic molecule, hydrolysing the bonds, rendering it useless.

With the mechanisms of antibiotic resistance in mind, and its

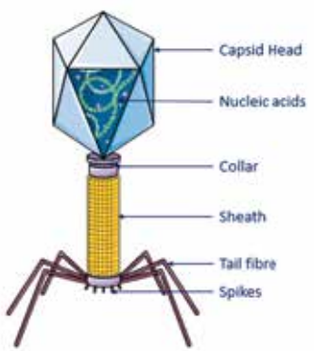
significance in the future of medicine, have a think of how one would approach reversing such a crisis. Here is a hint:
"The enemy of my enemy is my friend"

One way we could approach this is by testing for the pathogen causing an infection before prescribing antibiotics in clinics. Although hugely important, this would just slow down the rate of increase of resistance, not necessarily reverse the crisis. Enter: bacteriophages. Spanning billions of years, there has been an ongoing war between bacteria and bacteriophages (also known as phages – enemies of bacteria); could we befriend our enemies' enemies?

Phages are a type of virus, but look completely different from e.g. COVID-19 because they are classed as a complex virus. The bacteria killing ability of phages was discovered in 1917, by a French microbiologist Felix d'Herelle. This led to the creation of phage therapy, a standard practice used to control and treat infections in Georgia, Poland and Russia in the present day. This was 11 years before the discovery of penicillin. One possible reason it was never really adopted in the West was due to deteriorating relations with the Soviet Union during the World War. However, broad-spectrum antibiotics gained such a large following due to their range, having the ability to kill multiple strains of bacteria at once. Conversely, high specificity could be argued as an advantage. Phages are incredibly specific; they only attack a certain strain of bacteria (never human cells). Broad-spectrum antibiotics often wipe out most bacterial communities, even beneficial bacteria that regulate our bodily processes e.g. our immunity. Phages would leave our beneficial bacteria untouched, preserving an optimum internal environment. You can think of phages as picky eaters, each phage has their favourite dish for dinner every night; each phage only targets a specific strain of bacteria.

There are two types of phages – lytic and lysogenic phages. Having identified a target bacterium, the phage would puncture the bacterial envelope with their spikes, injecting their genetic material, which travels down the sheath. Lysogenic phages incorporate their genetic information into the bacterial genome, remaining passive. Conversely, lytic phages turn bacteria into phage factories, such that the bacteria are creating phage proteins. Eventually, lysis of bacteria occurs, releasing many more phages to carry on their "mission". This process is similar to the mechanism in which HIV viruses replicate. In order for phage therapy to work, only lytic phages are to be used.

Phages are the most abundant beings on planet Earth, there are currently around 1031 phages. To be able to perform phage therapy, a phage specific for an infection must be identified. Where might you find the most phages? The prime location for phage fishing is, disturbingly, sewage water. A sample of sewage water is then poured onto a petri dish with the disease-causing bacterial strain, often multidrug resistant. After incubation, areas where holes appear on the petri dish indicate no bacterial growth – a phage has managed to kill the bacteria. The phage is then sequenced, labelled and stored in a freezer, forming a phage library as more samples are taken.



In practice, patients are given a "phage cocktail", which is essentially a mixture of phages with similar targets, in the hope that if a bacterial species mutate, the other phages would still be able to kill them. Interestingly, it is increasingly common for phages to be coupled with antibiotics. One might ask – I thought these bacteria were resistant to antibiotics, why add antibiotics? I'll explain. If phages fail to kill a certain strain of bacteria, that is because it has developed resistance to phages. Here comes the important part: when resistance to phages develop, the bacteria's resistance to antibiotics is very likely to drop. A simple analogy for this inversely proportional relation is a seesaw: phage resistance goes up and antibiotic resistance goes down.

A famous case study involves the superbug Acinetobacter, also known as the Iraqibacter, ranked first place as the deadliest multi-drug resistant bacteria. Tom Patterson was infected by a strain of Acinetobacter Baumannii, which was in the abscess of a gall stone in his bile duct. Every antibiotic was unsuccessful and Tom had entered a coma. Steffanie Strathdee, his wife, came across phage therapy upon research, which ultimately led to an intravenous administration of a personalised phage cocktail. Three days later, Tom woke up (read the full story below: 11). The funny thing was that it wasn't the phages that killed the Iraqibacter and they developed resistance to the phages. The Iraqibacter "dropped" its slimy capsule to ensure no phage attachment (example of directional selection). As a result of dropping its slimy capsule, antibiotics could easily enter the Iraqibacter cell, accumulating to high concentrations and finally eradicating all Iraqibacter cells present. This is a fantastic example of the relation between phage resistance and antibiotic resistance, further supporting their coupled usage.

Peering into the not-so-distant future, scientists should investigate the possibilities of phage therapy and governments should allocate further funding to bacteriophage research. Although phage therapy has been experimented on generations of eastern Europeans, resources should be distributed for more clinical trials. Due to the specificity of phages, it is crucial for countries to unite in order to create a universal phage bank. This will speed up the identification process of phages, shortening the duration of treatment per patient. Importantly, bacteriophages are the keys to unlock "retired" antibiotics; antibiotics deemed useless due to high resistance could be "made useful" again. Phage therapy was the past and present of eastern European medicine, but also the future of world medicine. Who knew cool-looking viruses found in sewages could save lives!

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11. https://edition.cnn.com/2022/07/08/health/phage-superbug-killer-life-itself-wellness/index.html

Check out recent efforts in combating antibiotic resistance using AI:
https://www.news-medical.net/news/20230525/Scientists-use-AI-to-identify-new-antibiotic-that-could-fight-drug-resistant-infections.aspx#:~:text=by%204%20people-,Scientists%20use%20AI%20to%20identify%20new,could%20fight%20drug%2Dresistant%20infections&text=Using%20an%20artificial%20intelligence%20algorithm,for%20many%20drug%2Dresistant%20infections.

AN INTERVIEW WITH
MRS KATE CARTER, TEACHER OF PHYSICS

By Beatrice Wynne-Edwards (St)

Kate Carter, a recent addition to the Science Department at Rugby School, kindly agreed to an interview in which we discussed her career as an aerospace engineer.

Mrs Carter attended Salford University, which was one of the only universities to offer a course on aerospace engineering at the time, and received a full wage from the Royal Air Force (RAF). This was not only a financial opportunity as it provided a secure career path, for at least the 16 years mandatory return of service. Kate Carter extended this by almost 4 years, serving in the RAF for a total of almost 20 years of her life. Climbing through the ranks, Mrs Carter ended her career in the RAF as a wing commander (equivalent to the rank of a half colonel) and experienced the fighting in Iraq when servicing the squadron of Tornadoes. Despite the many exciting roles she played during her time in the RAF, changing approximately every 18-24 months, Kate Carter found her first tour to be her favourite experience, with the people she worked with being the highlight. Day to day, she prepared the planes for flight and decided which of them were in flying condition, recording damage and ensuring the safety of the pilots. Her favourite type of plane is the VC10, which she worked on during her first tour. Although this type of plane is no longer flown in the RAF, according to Mrs Carter it was the "Queen of the skies" during its time. She also had an interesting experience when working with the Pentagon in Washington DC, USA, developing a defence strategy with Britain's allies.

In school, science and mathematics were Mrs Carter's least favourite subjects, and she actually preferred history and geography. It was only when at university she started to enjoy maths and physics when she saw the useful applications of them in aircraft. She was originally inspired to train in this field after having seen the Red Arrows fly over the Severn Bridge during a family holiday, aged five. Since then, she has always been fascinated in planes and the Royal Air Force. One of only two girls on her course she soon realised that her passion for aerospace engineering wasn't shared by many of her peers. This pattern continued throughout her career, and this meant that Mrs Carter was often the first female figure of authority that many RAF employees met. Instead of letting this intimidate and hold her back, Mrs Carter used the doubt her colleagues had in her to solidify her determination to succeed and prove her ability in her job as an engineer. However, this doesn't mean she didn't feel the pressure of representing her gender in her job. Mrs Carter said that "when my male counterparts made a mistake, it was often put down to lack of experience or training. When I made a mistake, it was because I was a woman". Mrs Carter succeeded in her mission to prove herself and achieve everything she wanted to achieve, regardless of how her colleagues initially perceived her ability as lesser due to her gender.

Before becoming a teacher, Kate Carter worked with the company Lighter than Air, working with the European Union Aviation Safety Agency (EASA) and the Federal Aviation Administration (FAA) when designing and operating surveillance helium balloons (known as aerostats). The balloons are alternatives to imaging satellites and are used around the world, preventing the theft of oil and water from pipes, and aiding in other forms of intelligence-gathering.

Mrs Carter then made the decision to start working as a teacher, as she felt that the shortage of engineers in the UK was a shame and she wanted to encourage students to follow in her footsteps and become an engineer, as she feels it is an "extremely rewarding career" with lots of interesting opportunities. Aside from the appealing holidays, Kate Carter also felt that she wanted to give back and inspire the next generation of science students with encouragement that with specialisation comes increased interest in your field.

KATE CARTER ALSO FELT THAT SHE WANTED TO GIVE BACK AND INSPIRE THE NEXT GENERATION OF SCIENCE STUDENTS WITH ENCOURAGEMENT THAT WITH SPECIALISATION COMES INCREASED INTEREST IN YOUR FIELD.

NANOTECHNOLOGY IN CANCER TREATMENT

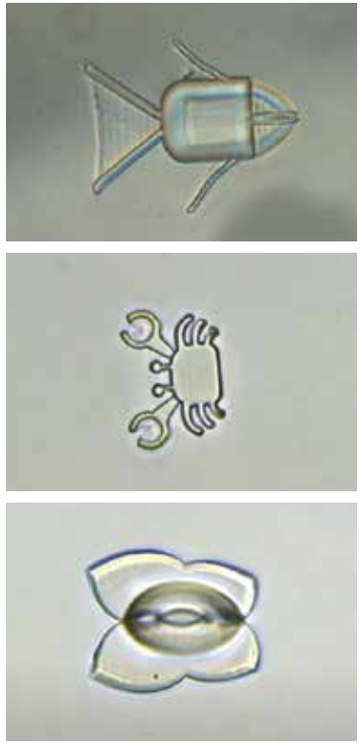
By William Griffiths (T)

Anti-cancer drugs that travel through the blood to cells across the body have been used for many cancer treatments over the last few decades. Due to the severe side effects they can cause, as well as their untargeted nature and killing of nearby tissues, there have been several attempts at using nanomedicines to overcome these issues. However, this targeted delivery remains challenging, so engineering microrobots has become a more popular option, as they would be able to penetrate tissues and reach cancers more efficiently and effectively than nanomedicines solely, to deliver drugs directly into the tumour cells and their microenvironments (ACS, 2021).

Recent years have seen tremendous efforts towards the creation of microrobots, which encapsulate drugs, to overcome the challenges of passive nanomedicines, such as their limited ability to penetrate deep into tumour cores. These are able to move without relying on diffusion, meaning that they have the potential to target cancers more directly, by remaining in close proximity to the cancer cells, through the integration of sensing capabilities to detect the chemical microenvironment of tumours. An example of this has been the approach to package small-molecule drugs, typically below 1 nm in size, into larger nanocarriers up to several 100 nm in size. These microrobots rely upon the acidic microenvironments surrounding cancerous tumours.

The making of new blood vessels around tumours is due to the increased requirement of oxygen of these proliferating, or rapidly growing, tumour cells. However, this leads to the inside of a tumour often having poor vascularisation, leading to it being highly hypoxic (Schmidt, Medina-Sánchez, Edmondson, & Schmidt, 2020). These low oxygen levels force the cancer cells in this area to generate energy via anaerobic respiration, which leads to the production of lactic acid and therefore acidic conditions inside the tumour core. Researchers from the University of Science and Technology of China have developed shape-shifting microrobots 'driven' by magnets, to target a tumour, and then release a drug cargo in response to the acidic local environment surrounding them.

The microrobots are made out of a 3D-printed gel that is pH-responsive. The researchers changed the printing density at specific locations of the robot, so that they would be able to change shape in predictable and useful ways in low pH conditions. Due to this, the scientists nicknamed this process '4D printing', as it adds another 'dimension' to the small structures – movement (Hastings, 2021). Examples of these microrobots,

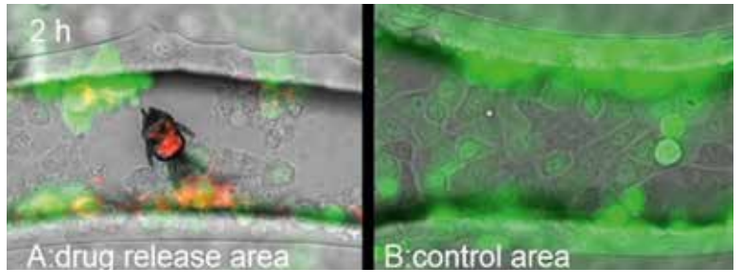


include a fish that opens its mouth, releasing a drug contained in its belly,; a crab that can hold a drug in its claw and release it when it reaches a tumour; and a butterfly than can 'flap' its wings. These are all controlled using magnets to manoeuvre the microrobots to the area they are required. In order to magnetise them, the scientists soaked them in a suspension of iron oxide nanoparticles (American Chemical Society, 2021). This means that the microrobots could be controlled remotely and minimally invasively when they are in the body. So far, the team has tested these microrobots in artificial blood vessels in a petri dish that also contained cancer cells. They successfully manoeuvred the microrobots through the blood vessels and towards the cancer cells, where the pH was reduced to mimic the microenvironment of a tumour. The robots then changed shape and released their drug payload, killing the cells (Irving, 2021).

However, there are still many challenges, both long and short range, that have to be faced when physically targeting cancer, but these depend on cancer location, type and stage. During the long-range targeting stage, where the drugs are only delivered to the specified region in the body, some challenges include:

- Tumours that occur in hard-to-reach locations within the body.
- Drugs smaller than ~5 nm in size (all small-molecule drugs) are prone to renal filtration and then excretion, meaning that the cargo has to have a high concentration of the drug.
- The drugs need to be able to resist the harsh environments of the digestive system, including the acidic conditions of the stomach, as well as the high concentrations of digestive enzymes.
- Intratumoural injections overcome the requirement for long-range targeting, but are often linked to substantial amounts of discomfort, especially when the tumour is situated deep inside the body or when multiple injections are needed (Schmidt, Medina-Sánchez, Edmondson, & Schmidt, 2020).

Once a drug has been delivered to the area surrounding the tumour, short-range targeting takes over, where most anti-cancer drugs need to get to and remain in close proximity with the cancer cells to kill them efficiently. The use of these microrobots, will help to combat this problem.



However, the successful physical targeting of cancers would have significant benefits: absence of the drug from tissues other than the cancer would reduce or even eliminate side effects and lower drug concentrations could be administered less frequently.

In the future, the researchers developing this technology with microrobots, will need to make their testing structures and environments smaller so that they are able to traverse real blood vessels (Irving, 2021), but the technology certainly looks hopeful for targeted drug delivery so far.

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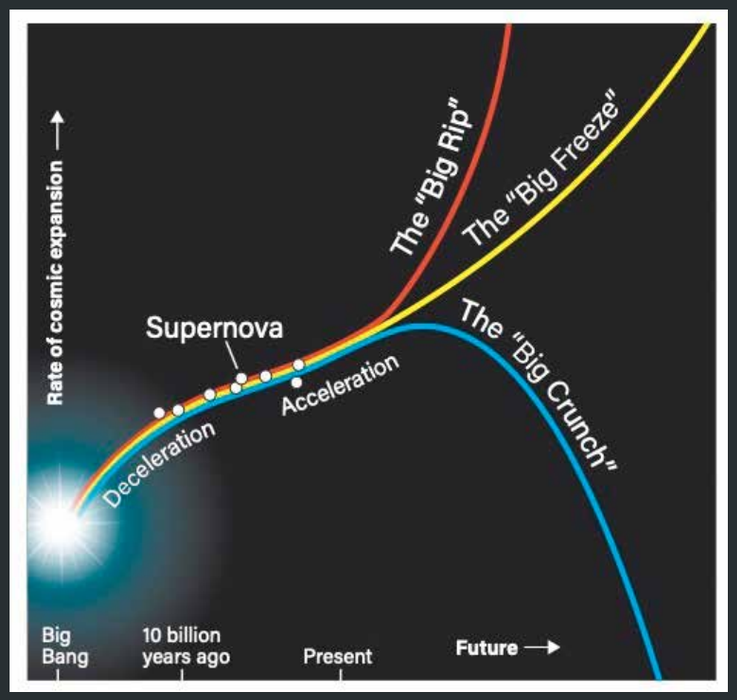
THE EVENTUAL DEATH OF THE UNIVERSE

By Alex Morgan (T)

The James-Webb Telescope, launched on Christmas day 2021, allowed researchers to gain insight into a field of exploration that tells us fundamental laws of the universe. The most impressive achievement that it has set has been the recent infrared "Deep Field" picture which depicts a galaxy cluster, 4.6 billion lightyears away and therefore the telescope depicts what would have been there 4.6 billion years ago. Extreme scales are where fundamental laws of physics start to be made clearer, as can be shown with quantum physics and to an extent the scales that the James-Webb Telescope has allowed us to see. The key concept shown at these distances is the expanding universe theory, which is often associated with a balloon being blown up with various dots moving apart. Assuming this is true, pointing to redshift as our evidence, we can begin to understand the "life-cycle" of our universe. Reason would have it that if a universe is expanding, then at its beginning it must have been expanding from a singularity, a point without time, space or matter. If we can logically find a beginning, then how would we begin to look for an end? Currently, there are three predominantly plausible theories, with some having more flaws than others, and are termed as the "Big Crunch", the "Big Freeze", and the "Big Rip."



The Big Rip

The expansion of the universe is happening at an accelerating rate in all directions, from every point. So why are we not being torn limb from limb by the universe expanding? Gravity holds matter in place with larger bodies of mass having a stronger force of attraction, and therefore having a greater effect for a larger area. This force is strong enough to attract matter together in large clusters of galaxies, stars and nebulae, and continuing to a smaller scale for planets and organisms. However, as the expansion of the universe accelerates, according to Hubble's constant, there is no limit to the rate of expansion, and therefore it could potentially expand faster than the speed of light. The force of expansion could outweigh gravity, leading to matter being drawn apart. This would start in weaker areas, such as galaxies where the distance is greater and therefore will more readily break apart than in small systems. Following this, stars would explode as pressure built up from nuclear fusion and supported by universal expansion. Planets and other celestial bodies would break apart as gravity would not be strong enough to hold them together. Eventually, the strong nuclear force holding atoms together would be broken by universal expansion, leaving matter as sub-atomic particles and photons. As the universe continues to expand, eventually it would expand faster than the speed of light. When this occurs, particles would no longer be able to interact with each other leaving behind a universe devoid of matter.

The Big Crunch

This theory outlines a point where the universe would expand based on its density, and following this logic, could also contract. Scientist Alexander Friedmann theorised that gravity would eventually halt the expansion of the universe after having been slowed. This steady universe would then start to collapse under gravity, until eventually matter would be condensed to a smaller area, which in turn would increase temperature dramatically, even higher than the surface temperature of stars. Around 100,000 years later, the crunch would occur with matter being torn apart. Supermassive black holes would engulf all matter, and eventually would form one supermassive black hole which would capture the universe until it collapsed under its own gravity into a singularity. Friedmann and others speculated that a collapse such as this could kickstart a new universe, creating a life cycle. While this is an optimistic view that the universe would never end, another contributor to the theory, John Wheeler, stated that it was "partially born from aesthetics" putting these claims into doubt.

The Big Freeze

More commonly known as heat death, this is the theory where, ironically, it would become much colder as energy is dissipated very gradually. In this scenario, gravity would have no effect on the expanding universe and instead would remain constant. Heat death requires the concept of entropy, or the natural tendency towards disorder. Entropy shows that in any system, energy will always be lost, even if unaffected by other forces. For example, the release of energy from radioactive materials would occur even though it received no interaction. Eventually the life cycle of stars would run out of energy to continue, and large clouds of gas and black dwarf stars would be all that remained from main sequence stars. Black holes, however, have a characteristic called Hawking Radiation, which is electromagnetic radiation emitted by a black hole which would cause it to slowly lose mass. Eventually, all energy would be dissipated, and peak entropy would be achieved as the universe is ultimately disordered. This, however, is a lengthy process which would take the unimaginably long duration of $1x10^{100}$ years, which means that we have only lasted $1x10^{-88}$% of the total duration of the universe.

While the idea of an infinitely cycling universe would be appealing, it unfortunately is the least probable of the three ideas. Heat death seems to be the most probable death of the universe, as the universe expanding would not necessarily mean that gravity would be affected. Entropy as a thermodynamic constant creates an end to the universe that means eventually there will be no light, nor heat, nor an excess of energy in any particle and the universe will remain as an unmoving constant. However, humanity will most likely never know the answer, as we are certainly not going to survive to see the end of the universe.

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ALZHEIMER'S AND PARKINSON'S DISEASE: EXPLORING THE DEVASTATING IMPACT OF NEURODEGENERATIVE DISEASES ON THE BRAIN AND BODY

By Tom Zhao (SH)

Neurodegenerative diseases are a group of disorders exhibiting characteristics of a progression in loss of cognitive function and physical structure of neurons in the brain and the central nervous system. These diseases are caused by many factors such as environmental toxins, physical trauma to the brain, or genetic mutations. However, inevitable ageing has been discovered as a common factor in most neurodegenerative diseases. This is because as people get older, it is inevitable for deterioration to accumulate in our cells and the neurons in the brain leading to less efficient function. In addition, different factors interact with each other to increase the risk of developing neurodegenerative diseases. Primarily, neurodegenerative diseases refer to the gradual loss of neurons in the brain and the nervous system through degeneration. As they degenerate, they cannot transmit electrical signals efficiently, therefore, reducing the communication and exchange of information with one another. This normally leads to many problems such as cognitive impairment, uncoordinated movements, and memory loss. In this article, I will be focusing on two main neurodegenerative diseases: Alzheimer's and Parkinson's. I will be looking at their symptoms, pathogenesis, and some preventable treatments available.

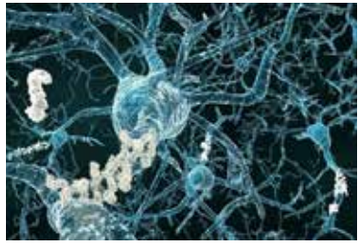
Alzheimer's disease

Symptoms include:
- loss of cognitive function
- difficulties with location finding
- difficulties with decision-making
- lacking new memories
- problems with recalling old memories
- executive dysfunction
- difficulty with language and communication

Alzheimer's disease is ranked as the seventh leading cause of death in the US, and it is the most common type of neurodegenerative disease which causes dementia. Alzheimer's disease was discovered by Dr. Alois Alzheimer when he noticed the abnormal mental illness in a woman in 1906. He examined the patient's brain after death and discovered the abnormal protein clumps and tangles around the neurons which are now known as the amyloid beta plaque and the Tau tangle.

The pathogenesis of Alzheimer's disease

There is a normal protein in the human body called the amyloid protein. The body makes amyloid beta a protein that is secreted from cells. The normal function of amyloid beta protein is still under investigation; it is believed to have essential effects on the normal functioning of the brain by involving the regulation of synaptic plasticity. To prevent the accumulation of this protein, the body's removal system clears this protein away. However, in Alzheimer's disease, the brain starts to aggregate more amyloid beta as we age. Abnormal



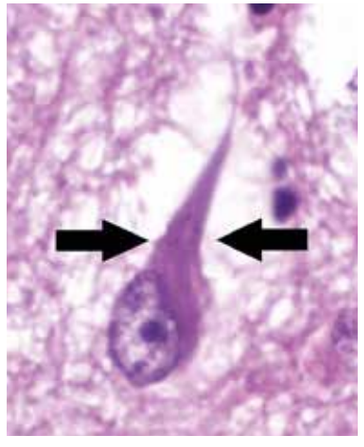
environmental conditions, random genetic mutations, and age-related alterations in protein processing led to the misfolding of this amyloid beta protein. These misfolded amyloid-beta molecules start to aggregate into oligomers which can cause other amyloid beta proteins to misfold forming a chain reaction. As this misfolding cascade forms, this abnormal protein starts to accumulate; this is the primary cause of the loss of neurons and damage to the neurons. Amyloid beta protein can stimulate the generation of reactive oxygen species which are highly reactive free radicals that can damage cells in the body by attacking them. When amyloid beta plaques interact with the metal ions to produce reactive oxygen species in Fenton Reaction. Amyloid beta plaques also disrupt the normal functioning of the mitochondria leading to the production of reactive oxygen species followed by the subsequent oxidative damage to cells and tissues. It also stimulates the immune system to cause inflammation of a region leading to further production of reactive oxygen species. The oxidative stress attack causes damage to the neurons, therefore, exhibiting cognitive impairment and other symptoms of Alzheimer's. As this chain reaction is a self-perpetuating process, it causes lots of nerve damage and neuron loss. This is a permanently irreversible process as the neurons in our brain don't replicate so they can never grow back. The cumulative probability of the formation of this misfold amyloid plaque will increase as people age. Interestingly, about 50% of people with Down Syndrome in their 60s have Alzheimer's disease. Research has discovered that the amyloid precursor gene is on chromosome 21; as the Down Syndrome has trisomy 21 so it is reasonable for this protein to be overexpressed.

Tau

Tau is part of the microtubules which are associated with the stabilisation of the transport system in the brain. In Alzheimer's disease, Tau proteins become abnormally modified and aggregate. They clump together to form Tau tangles; this leads to disruption of the normal functioning of the brain and the nervous system. The tangles do not allow the cytoskeleton to work as efficiently. This is another self-perpetuating process as the formation of one Tau tangle normally leads to many. The destruction of brain cells and neurons lead to cognitive impairment.

Treatments for Alzheimer's disease.

There are currently two medications used to mitigate Alzheimer's disease.
- Cholinesterase inhibitors increase the levels of neurotransmitters known as acetylcholine in the brain. This neurotransmitter is essential for memory and learning. The main cholinesterase inhibitor I had a look at is Donepezil. This drug is fully approved for every stage of Alzheimer's and has moderate side effects.
- The second type of medication is Memantine. Memantine blocks the activity of a neurotransmitter called glutamate. This neurotransmitter is usually harmful to the brain when a high level of them is present. These medications help to improve cognitive function, mitigate cognitive impairment, and reduce the symptoms of Alzheimer's.



Another drug is called Lecanemab. It is still an investigational drug for treating moderate to severe Alzheimer's. It is a form of monoclonal antibody which targets the amyloid beta plaques in the brain. In a more detailed way, Lecanemab binds to the soluble amyloid beta plaques in the brain and it clears this accumulated protein. More clinical trials and investigations are required to fully understand the potential benefits and side effects of Lecanemab.

Here is an interesting paper I found on the effect of Donepezil and Memantine in clinical trial experiments. https://www.nejm.org/doi/10.1056/NEJMoa1106668?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200www.ncbi.nlm.nih.gov

Parkinson's disease

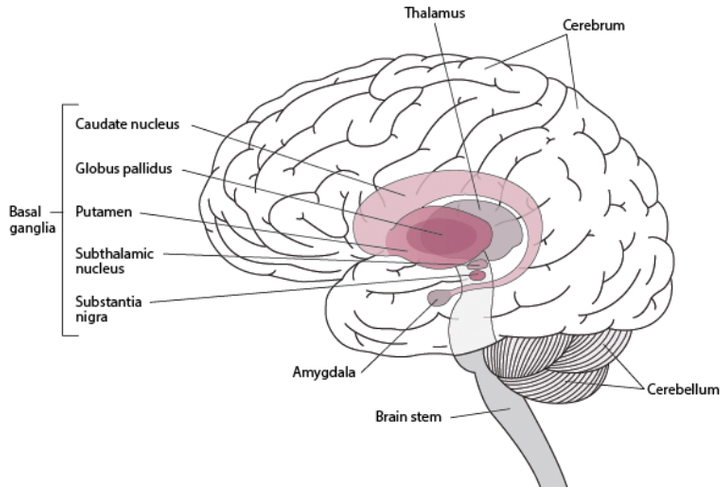
Parkinson's is another neurodegenerative disease characterised by unintended or uncontrollable movements such as shaking, stiffness, and difficulty with balance and coordination. It is shown that only 5-10% of patients experience the disease before the age of 50. Inside

our brain, the cerebellum is responsible for precise movements, automatic movement, muscle memory and coordination. There is a region inside the basal ganglia called the substantial nigra. Those parts are responsible for movement, coordination, automatic movements, muscle memory, and memory attention. The substantial nigra is responsible for the production of dopamine in the brain as it contains nerve cells that produce dopamine. Primarily, dopamine allows signal transmission and thoughts to be passed through between neurons or in the brain as signals. It also acts as a chemical messenger responsible for communication between other parts of the brain for movement regulation. Dopamine deficiency can cause a deregulation in movements as it prevents electrical impulses from being passed through neurons as signals. In Parkinson's, the accumulation of a protein causes the neuron cells in the substantial nigra to die, therefore preventing the production of dopamine. This leads to movement and coordination impairment such as shaking and rigidity. People with Parkinson's disease also lose nerve endings that produce norepinephrine. Norepinephrine is the main chemical messenger involved in the sympathetic nervous system which is responsible for many regulations of non-movement features of the body. The loss of norepinephrine explains the characteristic non-movement symptoms of Parkinson's including irregular blood pressure and heart rate.

The aggregated protein is known as alpha-synuclein: it starts to bundle up much in the same way as amyloid beta does by forming clumps within the neurons called Lewy Bodies. This leads to apoptosis: programmed cell death of the cells in the substantial nigra.

Treatment for Parkinson's disease

Levodopa is the most common medication used to treat Parkinson's disease; however, it can only mitigate the disease. It is converted to dopamine in the brain which can relieve some symptoms of Parkinson's to an extent. Levodopa is converted to dopamine through various chemical reactions. When this drug is taken orally, it is absorbed into the bloodstream which diffuses across the blood brain barrier into the brain. This levodopa is then taken up by dopamine-producing neurons and converted into dopamine by the enzyme L-amino acid decarboxylase and tyrosine hydroxylase. However, the effect of levodopa can be less pronounced over time. This is because the brain becomes less able to use the LDOPA efficiently as the symptoms progress.



Interestingly, scientists have discovered an unexpected trend in the people who have Parkinson's disease: the number of Parkinson's disease sufferers is significantly lower in the smoking population. This was unexpected because we would have thought the mutagens and chemicals in the cigarette would accelerate neuron destruction leading to neurodegenerative diseases, but the reality was the opposite.

Why is this?

There are two theories used to answer this question.

- One theory is that the nicotine in cigarettes may have a neuroprotective effect, so it protects the neurons from being attacked by the reactive oxygen species and abnormal proteins. Nicotine can also bind and activate specific receptors and neurotransmitters in the brain which helps to improve cognitive function and reduce the possibility of getting neurodegenerative diseases.
- Another theory is that, as everyone knows, frequent excessive smoking leads to lung cancer. Coincidentally, Parkinson's disease is more likely to occur at an older age. We can therefore hypothesise that perhaps excessive smoking kills you before you get Parkinson's leading to a low case of Parkinson's in smokers.

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THE VIROSPHERE

By Laurie Guard (T)

As with all other organisms, viruses must be classified via their phenotypes and structure. However, viruses are not typically included in Linnaean taxonomy due to the debate as to whether they should be considered living. As such, they have not historically been considered a living organism and thus need not be classified alongside bacteria, archaea and eukaryotes. Despite this, viruses can be classified in much the same manner as any other 'living' organisms. An early system of classification was developed by Francis Holmes in 1948, which divided viruses into three categories depending on which type of organism they attack – bacteria, animals, or plants. However, this rudimentary system did not refer to the structure or genetics of viruses.

The turning point in classification came in 1972 with the publishing of Baltimore's paper 'Expression of animal virus genomes', typically referred to as the Baltimore Classification. Baltimore's ideas are still considered sound, although they have been developed significantly, with new sub-categorisation of viruses. J. Kuhn writes, in his 2021 paper 'Virus Taxonomy', that 'whereas virus taxonomy has been a niche subspecialty over many decades, the field has recently gained importance'. He attributes this increase in interest to the development of genetic sequencing techniques that have allowed for the discovery and study of viral genetics and new viruses. This article aims to explore and explain the process of virus taxonomy, also considering the future of the field.

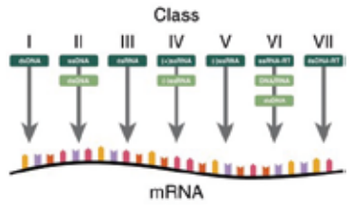
The Baltimore Classification referred to seven major groups of viruses. The first stage of classification is to determine the genetic material of a virus – RNA or DNA – and subdividing these categories into single-stranded and double-stranded (ss and ds). Secondly, the method of transcription in order to produce mRNA is used to further divide the categories. Following these rules, the Baltimore Classification describes viruses as follows:

BCI – Baltimore Classification 1 – is the group containing double-stranded DNA viruses that produce mRNA in the same way as all cells – via polymerase transcription. They use the machinery of the host cell to replicate, relying on host enzymes.

BCII is the classification for single-stranded DNA viruses, which must replicate the single strand and form a double-stranded intermediate in order to undergo standard transcription.

BCIII describes dsRNA viruses, that must undergo transcription before translation in order to obtain a single strand of RNA.

BCIV encompasses ssRNA viruses that can skip transcription as a single strand of RNA is already



Microbiology, Boundless 2013

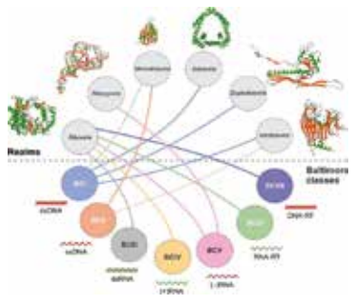
present; their genome can be directly translated. These are described as 'positive-sense', meaning that they can be 'made sense of' by ribosomes without needing to be altered.

BCV viruses contain negative-sense ssRNA, therefore the RNA cannot be directly translated and must be transcribed before it can be processed by ribosomes.

BCVI viruses contain positive-sense ssRNA, but use DNA to replicate – the RNA undergoes reverse transcription, forming DNA which is integrated into the host genome before transcription and translation. This mechanism is well-known as it is how the HIV virus invades cells.

BCVII viruses, which were discovered after Baltimore's original paper was published, are dsDNA viruses. Unlike the similar dsDNA BCI viruses, BCVII viruses can replicate without using the host's enzymes. They produce an ssRNA copy, which is used for translation, before reverse transcribing back to dsDNA to replicate the genome.

However, the complex classification of viruses has been developed further from Baltimore's system. While his system is still widely referred to by scientists as an easier, widely understood classification, the ICTV (International Committee on Taxonomy of Viruses) first convened in 1966 in Moscow to develop an official, comprehensive system of classification. Currently, the ICTV states that six 'realms' of viruses exist. A realm is the highest taxonomic rank – a rank that does not exist in Linnaean taxonomy, in which kingdom is the highest rank. Each viral realm can be correlated with one or more Baltimore classifications:



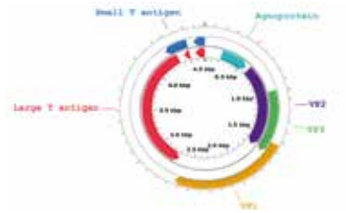
E. Koonin, M. Krupovic, V. Agol 2021

For example, viruses in the realm *Adnaviria* are all double-stranded DNA viruses (BCI), whereas *Riboviria* can be any type of virus except BCI and BCII classifications. Due to the significant volume of viral species, the taxa (levels of structure) are many in number and are subdivided as follows, with the suffix used shown in brackets:
Realm (*-viria*)
Subrealm (*-vira*)
Kingdom (*-virae*)
Subkingdom (*-virites*)
Phylum (*-viricota*)
Subphylum (*-viricotina*)
Class (*-viricetes*)
Subclass (*-viricetidae*)
Order (*-virales*)
Suborder (*-virineae*)
Family (*-viridae*)
Subfamily (*-virinae*)
Genus (*-virus*)
Subgenus (*-virus*)
Species

The ICTV states that 'classification of viruses is based on the collection and comparison of various characters that describe the virus, and can then be used to distinguish one virus from another.' This is to say that viruses are distinguished and therefore classified in taxa via differences in the composition of the genome and the system of gene expression – both distinctions considered in the Baltimore classification – but also by capsid structure, envelope presence, the hosts the virus can target, its effect on a host, and similarity in nucleotide base sequencing. As a result, the ICTV system is significantly more developed, considering a wider range of factors that lead to differences between viruses.

An example route of virus taxonomy would be as follows: (Note that there are such a large number of taxa that some have no unique description).

Realm: *Monodnaviria* – ssDNA viruses with an endonuclease enzyme that carries out rolling circle replication of the genome.
Kingdom: *Shotokuvirae* – Monodnaviria that affect eukaryotes.
Phylum: *Cossaviricota*
Class: *Papovaviricetes*
Order: *Sepolyvirales*
Family: *Polyomaviridae* – the family whose target hosts are mammals and birds.
Genus: *Epsilonpolyomavirus* – polyomaviridae that target cetartiodactyls (hoofed mammals).
Species: *Epsilonpolyomavirus bovis* – the species of this genus that targets cows as a host. The virus causes fatal kidney lesions in cattle.



The Epsilonpolyomavirus bovis genome. F. Giannitti et al., 2022

Since 1966, it has been the sole aim of the ICTV to develop taxa and classify viruses into this system – an enormous task, considering that there are currently over 10,000 unique species classified in the ICTV database. The process of virus classification is extremely difficult, as evidenced by the example provided and by the complex history of virus taxonomy. Unlike other organisms, viruses do not have a common genomic sequence that can be consistently identified, making virus taxonomy inherently different. Viruses are incredibly varying in their composition and function, adding to the challenge of classification. It is hoped that by classifying viruses into realms, kingdoms, phyla and so on, it may become easier for microbiologists to work out and understand the evolution of viruses, and their genetic history. The use of a regulated, specific system of taxonomy also allows for easier classification and study of new viruses, as they can be compared to others of similar taxonomy. While it is an area of study that few scientists ever delve into at more than a surface level, the complexity of virus taxonomy is fascinating and its development is pivotal to future research, just as Linnaean taxonomy has become widespread biological canon. While virus taxonomy is unlikely to ever reach this level of widespread familiarity due to its complexity,

research into phage therapy and new developments in studying viruses mean that virus taxonomy has never been so important. With much of the research into viral structure arising in the last 20 years due to technological improvements in genomic sequencing and computer-rendered protein structuring, the future appears to be bright for this field… and with a 2020 paper finding that there are likely over 100 million unique viral species, there is evidently plenty of scope for research into viruses. It seems that we are only just beginning to explore the inconceivable vastness of the 'virosphere'.

The Virosphere, 2005

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https://dbpedia.org/page/Realm_(virology)
https://www.ncbi.nlm.nih.gov/books/NBK8174/#:~:text=Viruses%20are%20classified%20on%20the,composition%2C%20and%20mode%20of%20replication.

ARE PHOTOVOLTAIC PANELS AS ENVIRONMENTALLY FRIENDLY AS WE THINK?

By Charles Swinfen (T)

As of 2022, just 10% of all solar panels that came to the end of their lifespan were recycled, with the remaining 90% going to landfill. The International Renewable Energy Agency has projected that by 2050, if appropriate PV recycling processes are not implemented, 78 million tonnes of waste will be generated worldwide. With production costs having fallen sharply by 85% since 2010, solar technology has expanded rapidly, with the global combined capacity at 940 gigawatts in 2021. Therefore, although solar panels are playing an integral role in the transition towards renewable energy production, there is a serious waste management issue that must be addressed.

How long do PV panels last?

On average, solar panels can operate for around 30 years before they experience any significant reduction in efficiency. However, even after this 30-year period, they can continue to operate at around 80% of their original generation power. The US Department of Energy conducted a 5-year study, examining the lifespan of 23 different solar panel types. Of these, 13 were concluded to have 'effective lifetimes' over 30 years, meaning many of them can be used for much longer periods of time. Since solar panels only really became popular in the early 2000s, we have not yet had to deal with a significant level of waste disposal. However, solar panel waste is set to increase by more than 4000% over the next decade, so it is essential that waste management systems are established now, in order that we are prepared for the inevitable increase.

Why are so few solar panels recycled?

Solar panels are made up of a wide range of materials, such as glass, aluminium, copper, and silicon. While these substances are widely recycled, panels also contain traces of toxic materials, like lead and cadmium, which require specialist disposal. The general process of disassembling a solar panel is outlined below:

1. The aluminium frame and junction box (which contains all of the electrical components) are removed.
2. The glass cover over the front of the panel is separated and broken into smaller parts.
3. The remaining panel is shredded, and the heat seal components are removed.
4. A machine, using layers of vibrating screens, separates metals, plastics, and silicon into three separate containers.

Both the task of separating the different components and dealing with the toxic substances makes the process of recycling solar panels expensive. This leads many manufacturers to send their panels to landfill instead. Ultimately, it costs companies more to recover the raw materials from an old panel than it does to purchase new components, so from a primarily economic point of view, it makes sense to abandon the old materials. Furthermore, in contrast to the price of recycling the technology, which can be anywhere between $15 and $45 in the US, burying it in landfill usually costs less than a dollar. Hence, many corporations are reluctant to spend large sums on properly disposing of their solar panels. On top of this, the raw materials that are recovered from processing the panels are of relatively low purity, and as a result, cannot be reused to produce new solar panels. An additional challenge in recycling PV panels is that the earlier models had a great deal of variation in their design and chemical makeup. Thus, part of the challenge lies in how to appropriately deal with the different panels that are gradually being retired at the end of their lifespan.

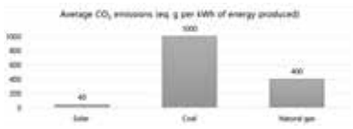
Is there any regulation on the disposal of PV panels?

At present, all countries in the European Union are required to ensure that all PV panels are recycled correctly. Also, in the UK, the Environment Agency requires the disposal of solar panels to fulfil certain legal requirements and standards. For example, all solar panel producers are required to report tonnages introduced to the market, label goods with the correct disposal instructions,

and collect end-of-life products. However, in the US, China, and Australia, three of the largest solar waste producers, there is no formal regulation to control the proper disposal of PV panels. This is the same for many other countries across the world, and hence, a coordinated global response to this problem must be deployed.

Looking at the bigger picture

Although only a small proportion of solar panels are recycled, it is of course important to consider the wider environmental impacts of using solar panels, rather than traditional fossil fuels. In terms of their overall CO2 emissions, the likes of coal and natural gas dwarf the emissions produced by PV panels. Taking into account the processes required to mine the raw materials, manufacture the product, and transport it, the US National Renewable Energy Laboratory produced these statistics:



Important developments and projects

In 2017, *Veolia*, a transnational company involved in waste management, launched a dedicated unit for recycling PV panels in France. At the moment, this is the only commercial-scale plant in the world and is capable of processing a panel in just over a minute. The components of the panels are collected and distributed to various industrial sectors for reuse. This project represents a significant advance towards large-scale solar panel recycling, but between 5 and 10% of the panel is still unable to be reused, and the plant can only process 4000 tonnes of produce per annum. Improving the efficiency of the plant further and replicating it in other locations will be essential for dealing with the increased quantities of solar waste as demand swells. In addition to this, a company called *ReProSolar* is developing a process for recycling end-of-life panels, which will allow for all silicon-based photovoltaic module components to be recovered. These examples of innovation represent a crucial recognition of the need to establish recycling facilities now, with the capacity to deal with future demand.

Conclusion

To summarise, the waste management issues associated with photovoltaic panels must be addressed, with a focus on developing more efficient, and crucially more cost-effective methods of recycling. The current disparity between the cost of sending the panels to landfill and the cost of properly recycling them is huge, and unless recycling becomes either profitable or required by law, companies will continue to dispose of waste improperly. As Sam Vanderhoof, the CEO of Recycle PV Solar, puts it, "We need to face the fact that solar panels do fail over time, and there's a lot of them out there." In my opinion, this is an issue that has been overlooked by the mainstream media, perhaps for fear of a loss of confidence in renewable technology. However, the net environmental impact of solar panels is overwhelmingly positive, and in no way should this problem shadow the huge advances in clean energy production over the last few decades. It is important to remember that the issue is not that solar panels cannot be recycled, but that we do not currently have the technology needed for processing them on a large enough scale. Hence, this is a challenge of high priority that must be tackled over the next decade, particularly as the levels of PV waste are set to increase rapidly over the next 30 years. This will ensure that the impact of solar technology is wholly beneficial for the environment, and that it does not become the very thing it is designed to eliminate: pollution.

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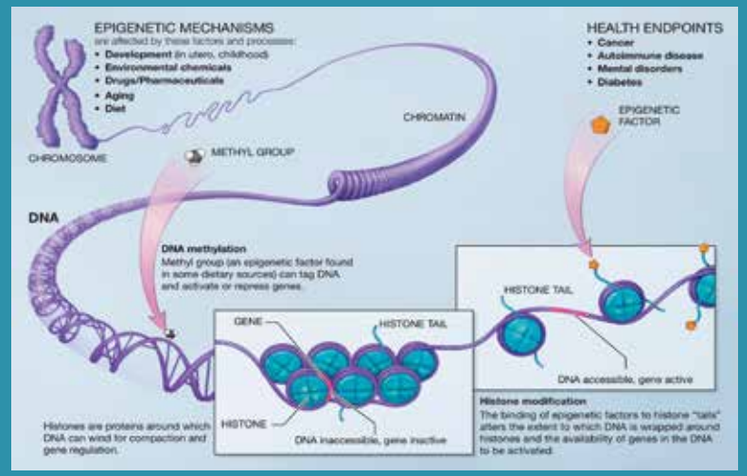
EPIGENETICS:
WHAT IS IT? HOW DOES IT WORK? WHAT CAN WE DO WITH IT?

By Jemima Barton (St)

What is epigenetics?
Epigenetics is the study of how the phenotypic features of an organism can change without modifications to its DNA sequence. In short – epigenetics revolves around gene expression and how it is manipulated. 'Unlike genetic changes, epigenetic changes are reversible and do not change your DNA sequence' (1).

Types of epigenetic changes
DNA METHYLATION
Essentially, methylation turns genes 'off', and demethylation turns them 'on' again. Methylation is the process of adding a methyl group (CH3) to DNA, most commonly to the cytosine (C) base forming 5-methylcytosine. This methyl group 'projects into the major groove of DNA and inhibits transcription' (2) as it prevents RNA polymerase from working during protein synthesis.

HISTONE MODIFICATION
To make chromosomes more compact, DNA wraps around proteins called histones. The more closely packed together histones are, the harder it is for transcription enzymes like RNA polymerase to access the DNA. This means that the gene can't be transcribed or translated, meaning it is not expressed and is turned 'off'. By the same rule, histones that are further apart make it easier for the DNA to be accessed, enabling transcription, so the gene is turned 'on'. Modifying the spaces between histones allows certain genes to be turned 'on' or 'off'.



NON-CODING RNA
During protein synthesis, DNA is used as a template to make RNA, which can then be used to synthesise proteins. Coding RNA is used to make the proteins; however, non-coding RNA is not used. Non-coding RNA can 'attach to coding RNA, along with certain proteins, to break down the coding RNA' (1). This prevents the RNA being translated and turns the gene 'off'. Non-coding DNA can also 'recruit proteins to modify histones to turn genes "on" or "off"' (1).

What are the results of an epigenetic change?
Epigenetic changes can occur throughout our lives and influence many different aspects of it, and they have even been shown to 'occur at a much higher frequency than mutations in the DNA sequence' (4). They can have long-lasting effects, as some epigenetic changes that lead to obesity later in life 'can begin in utero' (6).

One potential result of epigenetic changes is cancer. A tumour results from uncontrollable cell division, which can be stimulated by the inactivation of a tumour suppressor gene. This can be caused by epigenetic changes that turn the gene 'off' without any modification to the genome. Cancer can also be caused by an activated oncogene, which is a proto-oncogene that was turned 'on' by epigenetics, speeding up the cell cycle and cell division.

Epigenetics also have a large role in how we grow. When stem cells differentiate, it is epigenetics that influence which genes they express, hence which characteristics they develop, and which function they have. A new-born would have very different epigenetics to their 20-year-old self, and likewise, their 20-year-old self would have very different epigenetics to their 60-year-old self.

The potential of epigenetics
Because epigenetics plays a role in so many non-communicative diseases, they have the potential to make very effective therapies. Some cancer cells can develop resistance to chemotherapy, and by using epigenetic therapy to 're-sensitise' their faulty 'drug sensitivity genes' (3), chemotherapy has been proven to become more effective. Moreover, as cancer is often caused by reversible epigenetic changes, there is potential for a future therapy that can reactivate the tumour suppressor genes, preventing the growth of tumours. Other diseases that epigenetics could be used to treat include diabetes, heart disease, and many other non-communicative diseases.

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THE STORIES BEHIND THE APOLLO MISSION PATCHES

By Elena Newbould (S)

The Apollo space program was part of the 'Space Race' between the USA and the USSR. USA, specifically NASA, aimed to become the first nation to send man to the moon. It was ambitious. However, after the USSR put the first man in space, the USA would not stop at anything to prove the superiority of their technological innovation. Mission patches were a major part of the Apollo space program, giving flights identity and meaning. The patches originated in the US military where army members created designs to represent significant missions. As all the early astronauts were themselves in the military, they carried this practice into space. The patches that travelled to space are worth up to $20,000. Each patch tells a story and represents the peak of human exploration. The patches had the same aim, yet no two were the same, like how no two Apollo missions were. In this article, I will aim to uncover the stories and meanings behind each Apollo mission and its corresponding emblem.

Apollo 1:

Date: 27 January 1967
Commander: Virgil Grissom
Command pilot: Ed White
Pilot: Roger Chaffee
Aim: Orbit Earth

The first Apollo mission was set to launch on 27 January 1967, from Cape Kennedy in Florida with the aim of orbiting the Earth in 14 days. This is represented in the design as a shuttle is seen in orbit around the planet (over Florida, the launch site) heading towards a moon in the background (representing NASA's ultimate goal). The astronauts' names are displayed in the border. The image is emblazoned on an American flag, which could indicate a sense of the nation's pride and hope for the mission and patriotism from the astronauts and those in charge of the mission. The patch was in fact designed by the crew members. Unfortunately, the mission was not successful, as during a pre-launch training exercise, a fire broke out killing all three astronauts. The men were awarded the Congressional Space Medal of Honour to commemorate their bravery and ambition. Following this, the Apollo program was put on hold.

L to R: Virgil Grissom, Ed White, Roger Chaffee

Apollo 7:

Date: 11-22 October 1968
Commander: Walter Schirra
Command module pilot: Donn Eisele
Lunar module pilot: Walter Cunningham
Aim: Orbit Earth

L to R: Donn Eisele, Walter Schirra, Walter Cunningham

This design is similar to that of Apollo 1. However, there is no American flag, and the rocket is shown to have travelled in a full circle around Earth (which would be a successful mission). Some similarities include the shuttle flying over the Americas, specifically Florida (the launch site). Furthermore, the names of the astronauts border the image. These astronauts were the back-up crew to Apollo 1. Apollo 7 was the first successful manned mission of the Apollo Program and allowed NASA to not only rebuild confidence and reach a goal, but also to test vital life-support and control systems in the modules. The mission also saw the first live television broadcast from space. Overall, the 11-day flight (163 orbits) was a big step forward in the American Space Program.

Apollo 8:

Date: 21-27 December 1968
Commander: Frank Borman
Command module pilot: James Lovell
Lunar module pilot: William Anders
Aim: Orbit moon

This design is unlike the others in a few ways. Firstly, it is triangular instead of circular. Furthermore, the astronauts' names are part of the orbit, rather than the border representing their role played in the mission. The orbit itself is in the shape of the number 8, the mission number, and also represents the translunar and trans earth trajectories. Yet again though, the Americas are forefront, particularly Southeast USA, where the launch site is located in Florida. Apollo 8 was the first ever manned mission to orbit the moon, allowing humans to see the dark side of Earth's natural satellite, as well as witness an Earth rise. William Anders is quoted to have said "We came all this way to explore the Moon and the most important thing is that we discovered the Earth."

L to R: William Anders, Jim Lovell, Frank Borman

Apollo 9:

Date: 3-13 March 1969
Commander: James McDivitt
Command module pilot: David Scott
Lunar module pilot: Russell Schweickhart
Aim: Test lunar module

This design is the first to show neither the Earth nor the moon. This is because, although the mission involved orbiting the moon, the main aim was to test the detaching and redocking of a lunar module after travelling 160km ahead of NASA's goal of landing on the moon. It was proven that the lunar module concept worked, which made the concept of landing on the moon much more realistic. Although the badge does not display Florida, USA is written on the rocket. Once again, the astronauts' and mission's names border the space craft. Other technological advances were tested during that mission: Schweickart performed the first space walk with a backpack life-support system.

L to R: James McDivitt, David Scott, Russell Schweickart

Apollo 10:

Date: 18-26 May 1969
Commander: Thomas Stafford
Command module pilot: John Young
Lunar module pilot: Eugene Cernan
Aim: Test full landing process

This design clearly shows the mission's aim of being a 'dress rehearsal' for Apollo 11. NASA wanted to test the full landing process without actually landing on the moon (the crew were 14.5km from the surface). The spacecraft flies through a roman numeral 10 from the direction of the Earth, specifically North America. The astronauts' names border the image. They were all highly experienced astronauts, and the landing gear test was successful. Although they did not land on the moon, the crew did achieve the highest recorded speed for a manned vehicle at 39,897km/h when returning to Earth.

L to R: Eugene Cernan, Thomas Stafford, John Young

Apollo 11:

Date: 16-24 July 1969
Commander: Neil Armstrong
Command module pilot: Michael Collins
Lunar module pilot: Edwin "Buzz" Aldrin
Aim: Land on the moon

This patch was designed by the crew members then silk-screened by professional artists onto non-flammable beta cloth. The eagle (an idea originated from Jim Lovell, the commander of Apollo 13) was inspiration for the name of the lunar landing module. It also resulted in the now famous phrase from Neil Armstrong "The Eagle has landed" which immortalised this momentous mission. The olive branch held in the eagle's talons was Collins' attempt to show that the exploration of the moon would be peaceful as it had previously been suggested that the eagle looked menacing, dangerous and predatory. The crew chose not to have their names on the badge as this was an accomplishment of all American people. This mission's success was a huge milestone and turning point of the space race against the USSR (who put the first man, Yuri Gagarin, in space) and raised questions such as "What else is possible?". During the mission, the famous words "One small step for man, one giant leap for mankind" were spoken and the first steps on Earth's natural satellite were taken. Additional objectives such as scientific exploration, deployment of a television camera, and deployment of a solar wind experiment, seismic experiment package and a laser ranging retroreflector (allowing scientists to calculate the distance between the Earth and moon by emitting pulses of light and recording the time taken for them to be reflected back to Earth). Overall, this extremely successful mission commenced the beginning of the golden era of space exploration, as seen by the golden lettering on the mission patch.

L to R: Neil Armstrong, Michael Collins, Buzz Aldrin

Apollo 12:

Date: 14-24 November 1969
Commander: Charles Conrad
Command module pilot: Richard Gordon
Lunar module pilot: Alan Bean
Aim: Land a module on rough terrain

This design shows a traditional ship orbiting the moon bearing an American flag. This ship signifies that the astronauts, whose names border the image, were all in the Navy. It also connects the American War of Independence with the Cold War and represents the clipper ship which brought foreign land close to the US. This mission may be under the radar due to its predecessor's great success; however NASA still had further to go. This mission's aim was to see if lunar modules could be landed on rougher areas, specifically spots that had particular geographical interest. The crew landed on the Ocean of Storms, roughly 1,500km west of the Apollo 11 landing site. The crew then proceeded to carry out a selenological inspection, surveys, and sampling land.

L to R: Charles Conrad, Richard Gordan, Alan Bean

Apollo 13:

Date: 11-17 April 1970
Commander: Jim Lovell
Command module pilot: John "Jack" Swigert
Lunar module pilot: Fred Haise
Aim: Land a module on rough terrain

This design shows art on a more abstract scale, displaying three Pegasus flying from the Earth (with a trail behind them) towards the moon with the Sun (representing the Greek God of Sun, Apollo, after whom the mission is named) blazing behind them. The three mythical creatures represent the three astronauts. As with Apollo 11, this mission patch does not display the astronauts' names. Instead, written in Latin are three words: 'ex Luna Scientia', which translates as 'from the moon, knowledge'. This is what was hoped to be gained from this mission – more knowledge of geology, topography, chemical makeup, and weather conditions. However, this mission of discovery soon turned into one of survival after an oxygen tank exploded in the command service module. The crew were forced to shut down the command module to conserve power and oxygen. They sheltered in the lunar module while the mission was aborted, and the spacecraft headed for re-entry. The crew suffered with freezing temperatures, a lack of water and asphyxiation from the carbon dioxide they were breathing out. Mission control's engineering team designed an air filtration out of simple materials from the lunar module's cleaning facility and instructed the crew on how to construct it. Ultimately, the crew returned to Earth safely and NASA deemed the mission to be a 'successful failure'. However, the Apollo program was put on hold for several months to ensure this would not happen again.

L to R: Jim Lovell, Jack Swigert, Fred Haise

Apollo 14:

Date: 21 January – 9 February 1971
Commander: Alan Shepard Jr
Command module pilot: Stuart Roosa
Lunar module pilot: Edgar Mitchell
Aim: Complete Apollo 13 mission successfully

L to R: Stuart Roosa, Alan Shepard, Edgar Mitchell

For this design, rather than a spacecraft or rocket, a star is shown with its trajectory towards the moon. The star represents the rocket which could indicate good fortune and hope. The three trails from the rocket represent the three astronauts. Apollo 14's main aim was to complete the Apollo 13 mission successfully, and it was set to land on the Fra Mauro hill formation (Apollo 13's landing site). The crew collected 42kg of rocks that would be analysed by scientists and surface studies were carried out with the hope of learning more about Earth's natural satellite. Aside from scientific achievements, the mission was significant in other ways: the first coloured television images were broadcast from the moon; Apollo 14 once again proved lunar modules capable of landing on rough, uneven surfaces; and Alan Shepard became the first man to hit a golf ball on the moon while celebrating his overcoming Ménière's Disease.

Apollo 15:

Date: 26 July – 7 August 1971
Commander: David Scott
Command module pilot: Alfred Worden
Lunar module pilot: James Irwin

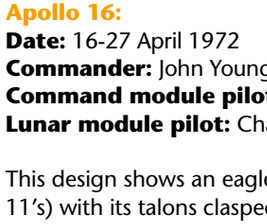
This design simply shows the moon as NASA's new aim was to stay on the moon. For the next few missions, NASA designed their lunar modules for longer stays. The astronauts, represented by three stylised birds (perhaps eagles, referencing the patch of Apollo 11) to symbolise flight, stayed on the moon's surface for three days (this could also be implied by the number of birds). The mission also saw a lunar vehicle used for the first time to collect rock samples further from the landing site. These would allow for more detailed scientific studies in the hope of discovering more about the moon. While Scott and Irwin explored the moon's surface, Alfred Worden used a scientific instrument module to study the moon while in orbit. This equipment included a panoramic camera and a satellite to measure the moon's gravitational field and solar particles. NASA concluded that Apollo 15 was the most successful manned flight ever, even more so than Apollo 11.

L to R: David Scott, Alfred Worden, James Irwin

Apollo 16:

Date: 16-27 April 1972
Commander: John Young
Command module pilot: Thomas Mattingly
Lunar module pilot: Charles Duke

This design shows an eagle (identical to that of Apollo 11's) with its talons clasped on a badge bearing the mission's name. The badge's colours are dedicated to the American people as they are the same colours as the nation's flag. A gold NASA vector crosses in front of it. As with the previous mission, only the moon is displayed, which symbolises NASA's newfound aim on staying on the moon for longer periods of time. The astronauts' names as well as 16 stars (mission number) border the image. This mission, although vigorously rehearsed, almost ended with failure, as before the lunar module detached from the main command module, NASA aborted the landing due to technical malfunctions. Fortunately, it was resolved four hours later, and the crew were able to continue the mission. During the now shorter mission, following a successful landing in the Descartes Highlands, Duke and Young deployed a lunar rover and a low-lunar orbit satellite, as well as carrying out 26 experiments. While in orbit, Mattingly mapped the lunar equator and completed a spacewalk to collect the data from the SIM (satellite information module) bay.



L to R: Thomas Mattingly, John Young, Charles Duke

Apollo 17:

Date: 7-19 December 1972
Commander:: Eugene Cernan
Command module pilot: Ronald Evans
Lunar module pilot: Harrison Schmitt
Aim: Final lunar landing

This design is very busy and incorporates a lot of messages and symbolism. The insignia is dominated by an image of the statue of Apollo, the Greek God of the Sun after whom this space program was named. As Apollo was the God of the Sun, it also symbolises the importance of this mission for mankind. Behind this statue is the outline of an eagle in flight, relating back to the patches of earlier missions such as Apollo 11. The red bars inside the eagle represent the American flag, displaying patriotism and pride, whilst the three stars are dedicated to the three astronauts. In the background the moon, Saturn and a galaxy are drawn which symbolises the future aims of NASA to explore the entirety of the Universe. The eagle overlays the moon, showing this has already been conquered. This emblem with such meaning was designed by artist Robert McCall in collaboration with the astronauts, whose names border the picture. The final lunar landing occurred over 50 years ago in December 1972 and broke many records. It was the first night launch of an American manned spaceflight, at 00:33am on 7 December 1972. As well as this it set the record for the longest manned lunar landing flight (12 days), the furthest distance travelled by a lunar vehicle (35km), the biggest collection of lunar samples (110.4kg) and the longest lunar orbit. This mission was one of extreme significance, particularly for the crew members. Harrison Schmitt became the only scientist to ever land on the moon and Eugene Cernan left the last ever set of footprints on the lunar surface. The crew left a plaque signed by them and the then President Nixon which said: "Here man completed his first explorations of the Moon. December 1972 AD. May the spirit of peace in which we came be reflected in the lives of all mankind."

L to R: Harrison Schmitt, Eugene Cernan, Ronald Evans

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HAZARDS, RISKS, AND THE APPEAL TO NATURE FALLACY

By Leo Aliev (W)

In recent years, consumers have had to face a seemingly endlessly increasing range of so called "natural" products. The food and personal care industries have been bombarded with "non-toxic", "non-GMO" and "clean" claims. It has become so commonplace that many consumers have become heavily guided by these labels without even knowing their meaning or rather, the lack thereof.

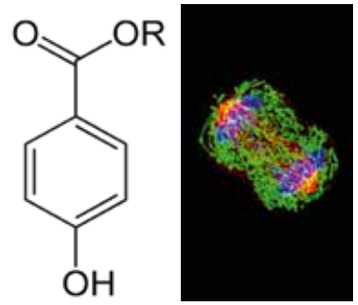
In the age of misinformation, fearmongering is something so accepted that it has become exponentially more difficult to debunk false claims. This is colloquially referred to as "Brandolini's law". It states that the amount of energy to refute misinformation is in order of magnitude larger than to produce it. This is especially true of the "clean" label that has been plaguing our personal care products from shower gels to sun creams. With no clear definition, this method of marketing products, based on how pure and "natural" they are, is primarily an example of an entirely misguided and potentially dangerous view of one of the most important principles of toxicology: the difference between hazard and risk.

Hazards vs Risks

Risk is the product of hazard and exposure. In other words, there is no risk to us if an ingredient is at a low enough concentration in a product or drug, even if it is hazardous. You may have heard of this as "the dose makes the poison". This statement is so well known yet so selectively overlooked that many of our buying decisions totally fail to consider our exposure to so called "unsafe" ingredients. "Clean beauty" is a term popularised by a branch of the personal care industry in the last few years that follows this exact misleadingly simple principle of ignoring dose when it comes to chemical compounds. Its basic idea is that ingredients can be divided into a class of good and bad, natural and chemical, or clean and dirty. This approach of course has no scientific or even commonsensical basis as if we only consider hazards, then every ingredient can be considered hazardous. Take salt – we must consume some to stay healthy, yet if we consume a bucket of it, we will most probably die.

"Clean" Marketing

This new "clean" industry started to spread disregard and mistrust of already existing regulations in various governing bodies, especially the FDA (Food and Drug Administration) in the United States. At the head of this fearmongering is the Environmental Working Group, more commonly known as the EWG. The company is widely known for its support of organic foods and for their "SkinDeep" database, which is a website where you can find a personal care product and check for how "safe" it is. If a product does not have any "nasty" ingredients (or if a brand pays enough money to the EWG) it will get the clean stamp of approval. This method of marketing has become so widespread that publications like *Vogue*, *Allure* and *Cosmopolitan* have all adopted and now facilitate this alarmist language of the notion that products in your bathroom may be a cause of concern and you should switch to a clean alternative.



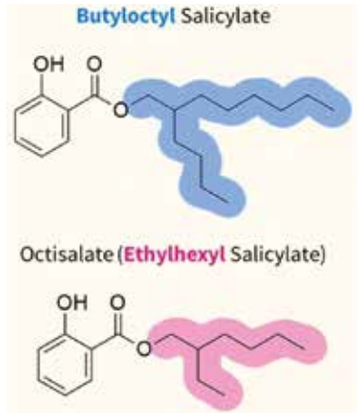
Do parabens give you cancer?

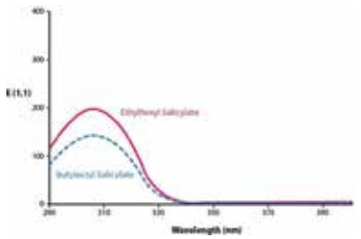
Perhaps the most heavily demonised class of ingredients are parabens. These are preservatives added to drugs and personal care products to extend their shelf life and make them remain safe and effective for prolonged periods of time. However, you might notice that effectively no products on the shelf today in a local pharmacy will have these ingredients. This is because parabens have been linked to breast cancer in a particularly famously misinterpreted study(1). This may look alarming at first. After all, the general conclusion that newspapers drew from the study was that parabens may cause breast cancer due to their weak estrogen-mimicking properties, increasing the transcription of protooncogenes in breast cancer tissue when used in personal care products, leading to a possible tumour development. However, this study has since been heavily criticised since it only looked at breast cancer tissue and measured the concentration of parabens there and did not compare it with healthy tissue. Additionally, even if parabens were only found in breast cancer tissue, that alone would not prove that they caused the cancer as many other factors may be at play. For example, breast cancer tissue might be more prone to collecting parabens or the equipment used to extract the tissue could have been washed with detergents containing parabens, introducing more of them into the sample. Moreover, the blank samples with no tissue at all were still found to contain parabens.

Nonetheless, the study was widely referred to as proof that our products, albeit with insignificant concentrations of parabens, are responsible for breast cancer, of course selectively overlooking the fact that the estrogen found in oral contraceptive pills is 2 million times more potent than butylparaben and only associated with a minute increase in the risk of cancer(2). Yet this eruption in the press made it unfavourable for brands to use parabens in their products as companies like the EWG called for a ban on the use of parabens in drugs and personal care products. This resulted in companies effectively being forced to use less studied preservatives like phenoxyethanol which, although safe, have less data to back their efficacy.

Maybe we should just avoid all risk?

It may be argued that this is simply an overabundance of caution from a brand's perspective. After all, we do not want even the slightest of risks when it comes to what we put on our skin or in our body. Except it is impossible to simply avoid all risk. Any ingredient substitution, especially a less studied or more "natural" one is more likely to result in adverse effects like allergies, irritation, or inflammation. That argument is just another inconsistency of this green- washed marketing strategy.





Unregulated organic sunscreen ingredients

A notable example of this hypocrisy is in sun protection creams. To grossly oversimplify, they use ultraviolet-absorbing ingredients to convert ultraviolet light into infrared light, which is heat, thereby protecting our skin from sunburn and skin cancer. These ingredients are split into two categories: organic and inorganic (mineral). There are two inorganic sunscreen ingredients: zinc oxide and titanium dioxide. On the contrary, organic sunscreens have many more variations including avobenzone, oxybenzone and octisalate. New filters are constantly being developed. This is because of the uniqueness of carbon's bonding. Often these ingredients are also demonised by "clean" brands due to their synthetic origin and more misinterpreted studies blown out of proportion. Due to the constant evolving nature of

UV protective ingredients, it takes a long time and a lot of data to approve new substances as safe and effective for use. However unregulated sunscreen ingredients can be used in products as so called “sun protection factor boosters”. These unregulated ingredients are not officially approved as sunscreen ingredients as not enough research has been conducted for manufacturers to be selling them as drugs. Sunscreens are a form of medical therapy in Australia, the US and Canada. As a result they are labelled as “inactive” ingredients on the packaging while acting exactly like another organic filter. An example of this is butyl-octyl salicylate. This compound has a very similar ultraviolet absorbance spectrum as octisalate. This is because it has an identical functional group to octisalate, a common sunscreen ingredient. This is the group that converts UV to infrared (Salicylate functional group). The only difference between the ingredients is that butyl-octyl salicylate has a longer carbon skeleton and a butyl group instead of an ethyl. However, as it is unregulated, brands do not have to disclose it as an active ingredient.

What countless natural brands do is market their sun creams as “all mineral” and “inorganic” claiming to only use zinc oxide and titanium dioxide as their UV filters whilst using unregulated organic filters like butyl-octyl salicylate to make the product more cosmetically elegant as inorganic filters leave a heavy white cast. This is done while scrutinising other organic filters like octisalate which is effectively identical to the ingredient that the brand uses itself. Misleading marketing and abuse of what is essentially a legal loophole, creates two problems at once: people resort to avoiding organic sun protection products while desperately trying to get their mineral sun creams to work often underapplying and thereby putting themselves at more risk due to their white cast. A survey in Australia, the skin cancer capital of the world, has found that between 2013 and 2017 there was a 7% decrease in the opinion that sunscreen can be used safely daily. Moreover 17% of adults agree that sunscreen ingredients are bad for health if used regularly. This decrease in public trust of what is an essential product can be linked to the rise of such preposterous advertising and misleading claims.

Yet, why are we so susceptible to this type of marketing? Why do we want to pick the “natural” option? This is called the appeal to nature bias. It is when someone claims that just because something is natural, it is good for you, especially compared to synthetics. This is a common label put onto food and cosmetic products, often where a brand claims that X percentage of the product is from natural origin. However, this is a logical fallacy. We are naturally inclined to believe that something is better for us if it’s of natural origin only because nature is sometimes used as an authoritative reference point. People may invoke nature to lend credibility to their arguments, as if it represents an indisputable and universal truth. The idea is that nature existed long before human constructs and should be revered as a guide or arbiter of what is right or desirable. However, many of us fail to consider that nature is often trying to kill us. Poisonous plants, animals, harsh climates, and disease are all natural too. That is exactly why we have shaped our environment to fit our needs. Synthetically made ingredients are often better for us in the right context as they are made to complete a specific task and are synthesised in sterile conditions. Yet our food and personal care industries have managed to exploit our appeal to nature bias for nothing but an outward appearance of sustainability and health simply covering monetary gain at the expense of public trust in scientific institutions.

The truth is science is messy, confusing, and impossible for any one person to fully understand, let alone someone just shopping for new shampoo. This is why expertise is specific. At some point, we must trust what expert scientists’ consensus on a topic is. More often than not, that consensus is blurred. Hence, when toxicologists assess the safety of given ingredients, their primary task is to contextualise the use of the chemical. This involves considering all use cases and even accidental exposures of a product or drug, including the frequency of application or ingestion, accidental inhalation, and the interactions of the ingredient with other substances in the product. (This includes aggregate exposure).
It is so easy to create a façade of simplicity for an uninformed consumer simply trying to buy safe and healthy products by ignoring the toxicological nuances of ingredients and merely labelling them as good or bad based on scanning an ingredients list and finding a word that feels too unfamiliar. It is important for the average consumer to recognise that the products on the shelves of rebuttable retailers are safe to use as instructed. This is key as, without this trust, toxicologists and biochemists must pour resources into disproving claims that have been disproven decades prior, wasting money instead of investing it in research that is still to be done.

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