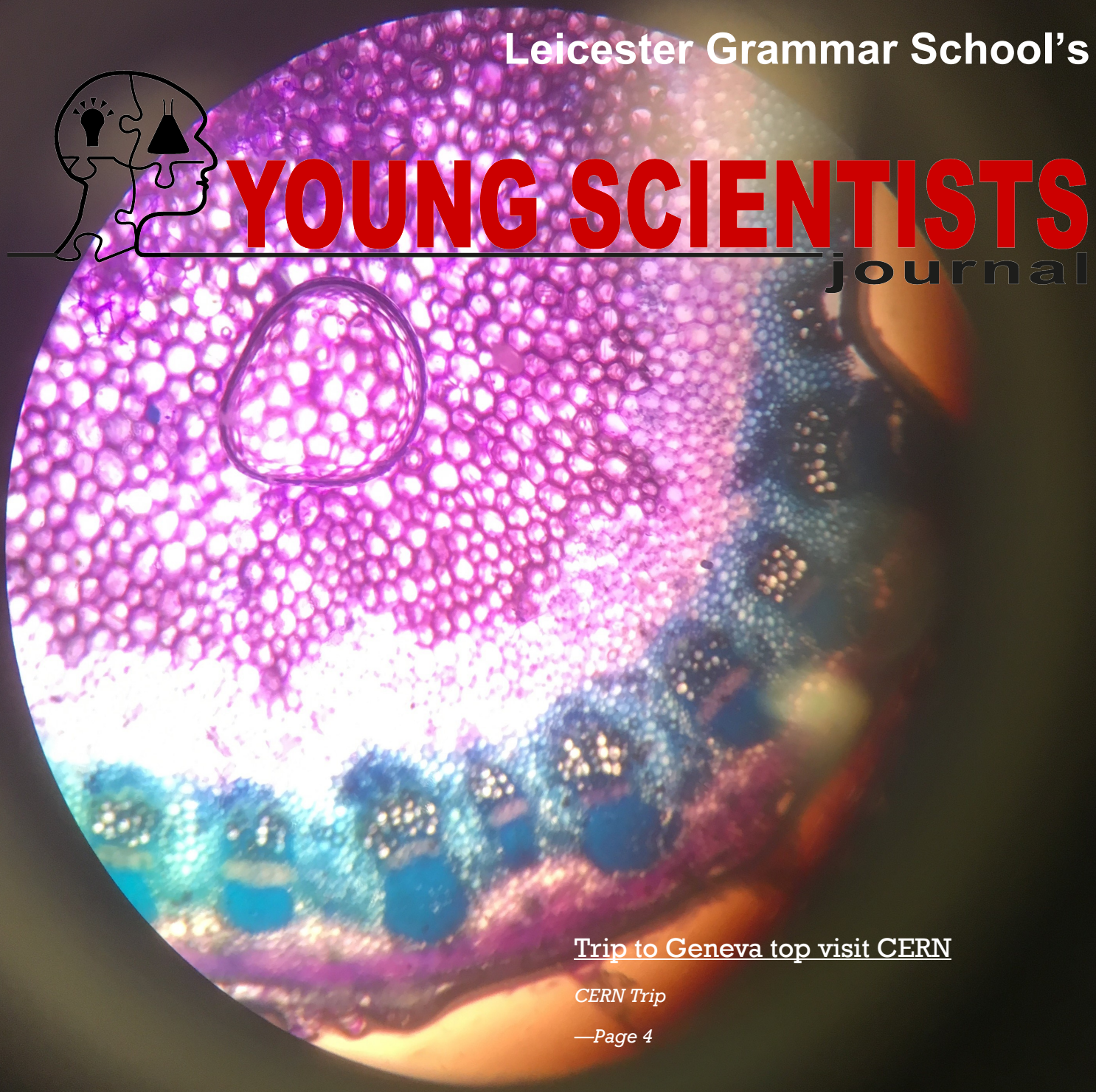
Leicester Grammar School's

YOUNG SCIENTISTS journal



Trip to Geneva top visit CERN

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ISSUE 4 SUMMER TERM 2018

A Message from the Team:

"The student team of the Young Scientists' Journal wish to extend a warm welcome to our second issue. The overwhelming success of the Big Bang Fair, held in March this year, has allowed us to exhibit the project to a rather small audience of 3000 people. Our task was simple - to begin cooking up issues from scratch, with very few ingredients to start with. No pressure!

LGS joined the existing Young Scientist's Journal, as a representative, at the start of 2017. It is the only peer-reviewed publication that is written, edited and run entirely by young people. Through this, any student aged 12-20 from around the world can discover their passion in science through whatever way they wish - be it through building experiments, articles, book reviews, photography or even blogging. Moreover, our team can only flourish with a variety of skills; journalists, technology masters, film-makers and photographers alike are just as valued as our budding scientists.

One of the most prominent questions we are asked is: "but what can I write about?" The scope is boundless. This journal's identity is shaped completely and totally by the people involved. In fact, our philosophy is steadfast - the quirkier the better! Our first issue explored telemetry toasters, black holes, antelopes, full-dive virtual reality and even Cryptozoology - investigating the existence of the Loch Ness Monster!

To think that this all began as a hopeful flicker in a few minds gathered around a table is quite simply extraordinary. From September 2017, we are opening positions of responsibility to younger students, which will involve roles in editing, formatting and photography. We do this in the hope that the Young Scientists' Journal can continue to grow and flourish as the current Year 12 Editorial Team fly the nest at the end of next year. It has been a privilege to see this seedling establish its roots and begin to blossom, and we hope to see it continue a long and fruitful career.

We hold regular meetings, of which you will be informed in the morning Notices; alternatively, feel free to send us an email at lgsyoungscientists@gmail.com."

Maria Hancock — Chief Editor

We would like to acknowledge the following for their contribution:

The LGS Editorial Team:

Maria Hancock, Yr 13 — *Chief Editor*

Prabhjot Grewal, Yr 13 — *Design Director*

Charlie Fraser, Yr 13 — *Designer / Writer*

Marcus Teo / Zain Girach, Yr 12 — *Assistant Editors*

Writers:

Keshen Pathmanathan

Harroop Bola

Dil Jobanputra

Riccardo Kyriacou

Benjamin Schwabe

Shashank Bhandari

Teachers:

Mr Reeves

Dr Griffin

Our booth at last year's Big Bang Fair, held at Leicester Grammar School.

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Who are We?

We are a collection of Leicester Grammar School students who have come together to produce a variety of pieces of writing about the world of STEM. As a school, we have become a hub for the Young Scientists Journal, an international peer-review written and edited entirely by young people.

Contact Us

Anyone interested in joining the YSJ to help to write, edit and publish is more than welcome to meet us at our meetings during lunchtimes (specific details will be in the daily notices). We welcome submissions from all year groups on any scientifically-related topic; so come along to a meeting or email us at:

lgsyoungscientists@gmail.com

See more of the Young Scientists Journal at:

ysjournal.com

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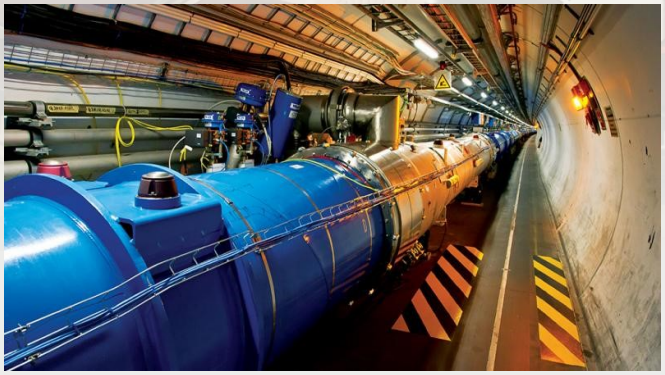
Front Page Photo:

by Marcus Teo

Transverse section of a stem seen through a microscope

CERN Trip

Benjamin Schwabe reviews his sixth form school trip to Geneva



This February half-term a group of about 25 A-level physics students visited Geneva, Switzerland. A nice historic city situated at the end of Lac Léman, we were there to visit CERN, the European Centre for Nuclear Research. This facility is best known for the Large Hadron Collider (LHC) which can accelerate and direct beams of protons and heavy metal ions up to speeds very close to the speed of light. When protons are collided energy is released in the form of particle-antiparticle pairs. Essentially by doing this, the kind of conditions at the very beginning of our universe can be probed, just at a much smaller scale.

They also have some other stuff going on, including a cool outreach programme, which is where we got involved! We spent four days in Switzerland, one of which was actually spent at CERN, one in Bern and the other two in Geneva. Our days in Geneva were fun, we had the opportunity to explore Geneva a little bit, throw snowballs from the Cathedral tower and spend a lot on food! Bern was also interesting, visiting the Albert Einstein museum and getting the chance to wander around. Our day at CERN was obviously the highlight, spending time learning about particle physics, seeing some of the amazing facilities and running some of our own 'experiments'. All in all, it was a really great trip and I would recommend it to all who get the opportunity!

Benjamin Schwabe

Stem Cells

Dil Jobanputra looks into the importance of stem cells

What are Stem Cells?

- Stem cells are unique. They are unspecialised cells that can become different types of cells in the human body (plant equivalent: meristem cells).
- They can stay dormant for a long period of time in the body until being used in growth and repair of the body.
- They can divide and last for a very long time.

2 common types of stem cells

- Embryonic stem cells:
  - ◊ In the first few days after an embryo is formed, these stem cells are present forming all the specialised cells for organs that will be present in the embryo when it is born. These stem cells can become ay type of cell in the body as they are still new.

- Somatic stem cells (adult):
  - ◊ These stem cells are found in the adult's body in different locations (e.g. bone marrow).
  - ◊ They are more limited and cannot become any type of cell but become a specialised cell based on their origin.
  - ◊ Generally used to repair the body.

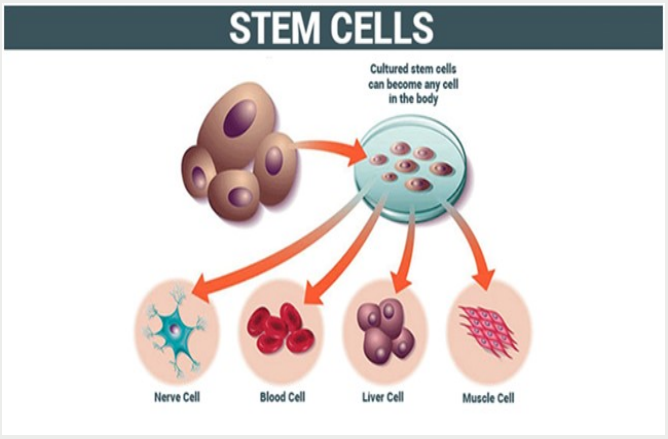
Why are stem cells important?

Scientists have recently discovered that there are more stem cells in the human body than they knew. This was important as it meant that if they could recreate specific conditions, they could induce these cells into becoming tissue cells and therefore recreate entire organs to be used for transplantation.

The reason why this is important is because the human body will reject other organs after a transplant as they are identified as "foreign" to the body. Therefore they will be attacked unless the patient is given drugs to suppress the immune system which can cause multiple other problems as it leaves them open to other diseases. Therefore, if stem cells are used from the patients own body, when the tissue is grown the body may not reject it as the cells still came from the patient so are not foreign. There is proof towards this as bone marrow has been used for years already to create more blood in the body (bone marrow contains the stem cells that are responsible for blood cells).

Only in the 1990's it was found that there are stem cells present in the brain and heart which can create nerve cells (neurons) and two other types of cell that support the nerves which opens up the question: Can we use these stem cells to regenerate limbs so that people can regain control parts of their bodies (e.g. regenerating nerve cells and connecting them to prosthetic limbs or even regenerating entire limbs like hands)?

Dil Jobanputra



Phantom pain: A ghost in the machine, or a biological basis?

Keshen Pathmanathan discusses the phantom pain phenomenon

Phantom pain is a pain that feels as if it is coming from a body part that is not there. Its cause is very much up for dispute but the theories can be divided into two overarching categories: a psychological disorder, in which the pain is felt as a result of a person believing that there is pain coming from that region, or the presence of an underlying anatomical issue causing pain to come from that region. These two causes can be succinctly described as a ghost in the machine and a biological basis respectively. It is important to explore both as possible causes in order to reach a conclusion on what the cause of phantom pain is.

The argument for phantom pain being caused by a ghost in the machine is founded on the fact that there must be a psychological reasoning behind the manifestation of physical pain from a non-existent region of the body. This argument considers a range of mental and emotional complications as the possible causes of phantom pain. Sherman says that the possible factors put forward include, 'Unresolved grief (Parkes, 1975), depression (Lindesay, 1985), psychosomatic manifestation of an unstable personality (Gillis, 1969, as quoted by Dawson & Arnold, 1981; Sherman & Sherman, 1983), and psychopathological misinterpretation of ordinary phantom sensations (Schilder, 1935, as quoted by Abt, 1954)' (Sherman, 1997). All these factors are ones that would be expected to alter the normal workings of the mind. Hence, it can be argued that such alterations of the mind would be capable of causing a person to believe that they are in pain from a phantom limb to such an extent that the pain is physically exuded from that limb because of the communication between body and mind that is put forward in the ghost in the machine theory. Moreover, this argument is given weight by the fact that many of the sufferers of phantom pain are, and have been, former soldiers; thus it was reasonable to expect that they are experiencing phantom pain as a result of their post-traumatic stress disorder. It could also be considered that these soldiers were suffering flashbacks to the moment that their limb, which they lost, got injured and these flashbacks in their mind were occurring with such vividness that they felt the pain physically, due to the presence of mind-body dualism.

Surprisingly, it can be argued thanks to recent neuroscience that phantom pain stems from a ghost in the machine. While it may seem oxymoronic to claim that support for a lack of biological basis is provided by a biological basis, the lack of conclusive evidence provided by functional MRI imaging points towards a ghost in the machine. Better imaging of the brain was expected to yield a better understanding of how the mind interacts with the brain, yet in a move which goes against reductionism, it has only served to further complicate our understanding of the mind. Reductionism, which forms the foundation for almost all biological bases, states that by breaking something into smaller fragments and analysing these fragments, one can apply their understanding gained from this analysis to a larger fragment in order to answer a larger question. Thus, it is a common reductionist belief that all emotions and feelings (entities which Descartes would associate with the mind) are simply the result of interactions between brain cells and their affiliated molecules. However, even the latest imaging of the brain fails to explain why we are conscious of much more than our nervous system appears to be transmitting; in the words of Alva Noë, Professor of Philosophy at the University of California, Berkeley, 'We are conscious of both more and less than affects our nervous system' (Noë, 2013). Hence, reductionism's failure to put forward an argument as to why our consciousness exceeds our nervous system promotes the idea that phantom pain, rather than stemming from a biological basis, is a result of some other entity, thus supporting the theory of a ghost in the machine.

The arguments for phantom pain stemming from a biological basis are in stark contrast to those which I have thus far mentioned. Some such arguments centre on the interaction between the central and peripheral nervous systems. One theory suggests that cortical plasticity is the cause of phantom limb pain; the theory claims that when the cortical maps are affected by a stimulus, which in this case is the removal of a limb, a new cortical map is created. The theory puts forward the idea that previous nociceptive input to the region that has lost its sensory input, because of the loss of the limb, coupled with sensory input from the new cortex of the limb creates neuronal

activity that causes a feeling of pain. The reason that this combination of neuronal messages is felt as pain is likely to be due to the fact that the body does not know how to process the fact that it is receiving sensory input from two different areas that are both 'claiming' to be the outer cortex; thus, unable to compute this contradictory information, the brain, in a move which stems from the body's 'fight or flight' instincts, sends out pain signals in order to try and protect you.

There is an alternative train of thought in which it is believed that phantom pain arises from the cortical representation of the limb remaining. Makin et al discovered using MRI scans of the brain that when amputees attempted to move their phantom limb, there was increased neural activity in the area of the sensorimotor cortex that previously corresponded to the amputated limb. Moreover, Makin et al ascertained a positive correlation between activation of the deprived region of sensorimotor cortex and phantom pain. Thus, it is claimed that phantom pain is triggered by strong, long-term sensory experiences, like those caused by top-down inputs because they require a large amount of processing on behalf of the brain. Such sensory experiences are believed to activate the C-fibres in the sensory neurone that previously brought impulses to the central nervous system from the limb, causing pain to be felt. The theory suggests that a lack of inter-regional neuronal communication is the reason behind why the pain is restricted to one specific area; furthermore, it is claimed that the aforementioned maintained cortical representation and interrupted inter-regional communication cause cortical plasticity, rather than the other way.

In order to draw a definite conclusion on this matter, more information about the nature and workings of both the mind and brain are required than what is currently available. I have put forward a number of theories as to the cause of phantom pain, yet those claiming phantom pain as a ghost in the machine rely on assumptions that the mind is able to interact with the body, while those offering a biological basis attempt to extract a causation from a correlation. The issue of phantom pain may be neither one of a ghost in the machine nor a biological basis, but instead one of consciousness as proposed by Megan Erickson: 'Contemporary neuroscience follows Descartes in conceptualizing [sic] consciousness as something that occurs internally. The difference is that for Descartes, the soul was the ghost in the machine, while for neuroscientists, the ghost is the machine.' We are conscious of much more than our senses inform us; perhaps understanding the root of this consciousness is at the heart of understanding phantom pain.

Keshen Pathmanathan

BIBLIOGRAPHY

Andoh J et al. Cortical Plasticity as a basis of phantom limb pain. Fact or fiction? Neuroscience (2017)

Descartes, Rene. 1637. Discourse on the Method of Rightly Conducting the Reason, and Seeking Truth in the Sciences. pp. 19–20

Makin, T. R. et al. Phantom pain is associated with preserved structure and function in the former hand area. Nat. Commun. (2013)

Sherman R.A. (1997) Psychological Factors Influencing Phantom Pain. In: Phantom Pain. The Springer Series in Behavioral Psychophysiology and Medicine. Springer, Boston, MA

http://bigthink.com/think-tank/the-ghost-in-the-machine-unraveling-the-mystery-of-consciousness

https://www.amputee-coalition.org/limb-loss-resource-center/resources-for-pain-management/managing-phantom-pain/

https://www.britannica.com/science/C-fiber

https://www.everydayhealth.com/pain-management/how-pain-works.aspx

https://www.goodtherapy.org/learn-about-therapy/issues/somatization

https://www.mayoclinic.org/diseases-conditions/phantom-pain/symptoms-causes/syc-20376272

https://www.ncbi.nlm.nih.gov/pubmed/11336780

http://newlearningonline.com/new-learning/chapter-7/descartes-i-think-therefore-i-am

http://www.nytimes.com/2003/04/19/books/i-feel-therefore-i-am.html

http://www.science20.com/ars_scientifica/ghost_machine-81494

https://www.sciencedirect.com/topics/neuroscience/neuronal-activity

https://www.philosophybasics.com/branch_reductionism.html

https://www.psychologytoday.com/blog/body-sense/201204/emotional-and-physical-pain-activate-similar-brain-regions

https://www.psychologytoday.com/blog/pathological-relationships/201203/emotional-phantom-limb-pain

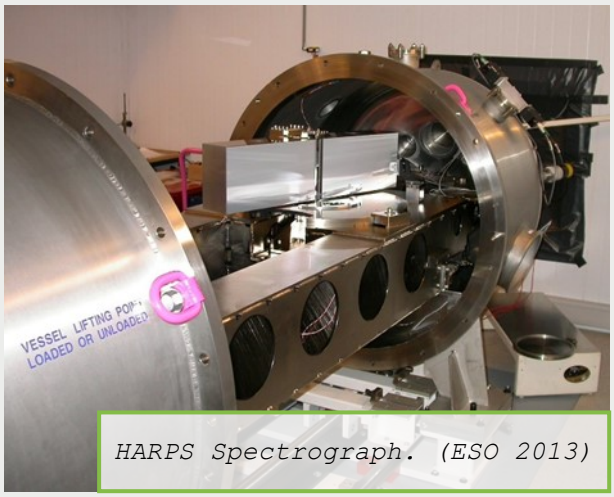
https://www.youtube.com/watch?v=9TrbOoirkhM

This Earth-like exoplanet could sustain alien life

Shashank Bhandari contemplates the possibility of alien life

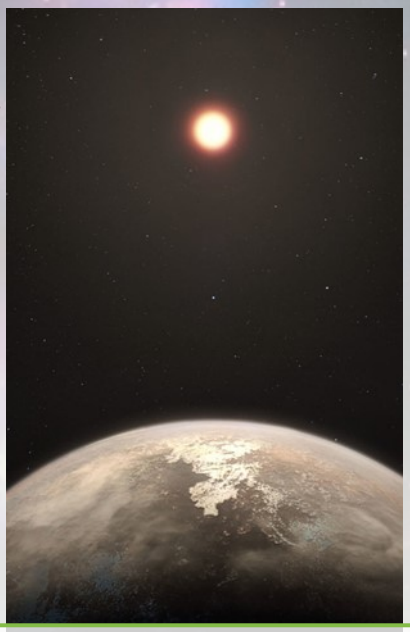
On the 15th of November 2017, Ross 128 b was discovered. The rocky exoplanet, which lays on the inner edge of the habitable zone of Ross 128 - a red dwarf star, could potentially sustain alien life. With a relatively temperate climate, and a mass at least 1.35 times larger than Earth, Ross 128 b could end our search for extra-terrestrial Intelligence.

Ross 128 b was discovered on the 15th of November 2017 by ESO's HARPS spectrograph (High Accuracy **Radial Velocity** Planet Searcher), which is located in the La Silla Observatory, Chile. In Astrophysics, Radial Velocity is a process of finding exoplanets whereby the parent star's light spectrum is shifted slightly because of a potential exoplanet's gravitational pull on the parent star. The spectrum goes blue when the star is moving towards the observer, and red when the star is further away. If this spectrum is altered in regular intervals, then it is safe to assume that an exoplanet is present – an exoplanet is an object that orbits a star, omitting those in our solar system.



HARPS Spectrograph. (ESO 2013)

As mentioned above, Ross 128 b has a mass that is only marginally higher than Earth's mass. Obviously, this would result in an extremely similar gravity, which would be only 1.12 times higher (10.95 N/kg compared to Earth's 9.8 N/kg). In addition, the surface temperature on Ross 128 b is almost homogeneous to what is needed for Abiogenesis – the development of life. It can range from 213.15 K (-60°C) to approximately 294.15 K (21°C). Also, despite being **20** times closer to its parent star than Earth is, Ross 128 b receives only 1.38 times the amount of irradiation that Earth receives. This is because Ross 128, the star around which Ross 128 b orbits, is a Red Dwarf star - which are quite faint. Ross 128 b is situated in the perfect area - the planet is estimated to lie within the habitable zone, in which liquid water, an imperative element for survival, can exist.



An artist's impression of the planet Ross 128 b. Ross 128 lies in the background. (ESO/M. Kornmesser)

At this point, you may be considering other Earth-like exoplanets, such as TRAPPIST-1 E/F/G or Proxima Centauri b (these all lay in the habitable zone of their stars). In fact, Proxima Centauri b is another Earth-size planet which is only 4.25 light years away from Earth (in comparison, Ross 128 b is around 11 light years from Earth). Understandably, you may be wondering what makes Ross 128 b any more superior than Proxima Centauri b or TRAPPIST-1 E/F/G? Well, here's where it gets interesting: Ross

128 (Ross 128 b's parent star) is a remarkably quiet star, unlike TRAPPIST-1 and Proxima Centauri (and most other Red Dwarfs) - which are prone to releasing fatal solar flares. These solar flares have the potential for atmospheric erosion and they also produce a plethora of radiation. The lack of violent flares from Ross 128 is a distinguishing factor for habitability on Ross 128 b.

As well as that, Ross 128 b is heading right toward us. In 79,000 years (which is merely a blink of an eye in cosmic terms), the exoplanet will be the closest star to Earth.

Evidently, Ross 128 b is a pre-eminent target for the search of life outside Earth. However, there is one major drawback; we are currently unaware whether Ross 128 b has an atmosphere. Forthcoming projects like the *James Webb Space Telescope* and the *European Extremely Large Telescope* could detect biomarkers, such as oxygen, to determine whether Ross 128 b has an atmosphere. If we take the notion where Ross 128 b **does** have an atmosphere thick enough to nourish water, a contingency is plausible where the human species could potentially encounter some form of extra-terrestrials. Or, of course, in the predicament where Earth is cataclysmically destroyed, Ross 128 b could be our future refuge.

Shashank Bhandari

BIBLIOGRAPHY

https://en.wikipedia.org/wiki/Ross_128_b

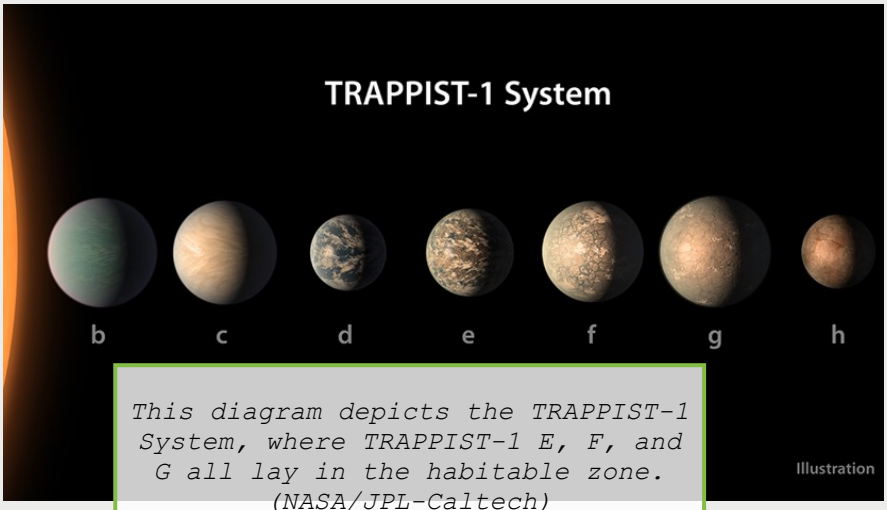
https://www.eso.org/public/unitedkingdom/news/eso1736/

https://www.nytimes.com/2017/11/15/science/planet-ross-128.html

http://www.planetary.org/explore/space-topics/exoplanets/radial-velocity.html

https://www.theguardian.com/science/across-the-universe/2017/nov/15/potentially-habitable-world-found-just-11-light-years-away-ross-128-b

https://www.theregister.co.uk/2017/11/15/ross_128_b_exoplanet_is_the_new_proxima_centauri_b/



This diagram depicts the TRAPPIST-1 System, where TRAPPIST-1 E, F, and G all lay in the habitable zone. (NASA/JPL-Caltech)

Absolute Zero and Absolute Hot

Riccardo Kyriacou investigates the limits to the universe's temperature

One of the most interesting concepts in physics is the idea that there are certain values which cannot be exceeded. Famous examples such as the speed of light are known to be fundamental limits in physics and are vital in our understanding of the universe. Indeed, another well-known example of these values is 0K (−273.15°), or absolute zero, corresponding to the lowest possible temperature in the universe where the fundamental particles have no kinetic energy. However, does an upper limit to the temperature scale exist? Is there an "absolute hot"? Is it even possible to reach absolute zero or "absolute hot"? These are the questions I hope to answer during my article.

Absolute zero, is it even possible?

Let's just get this out of the way, it is currently understood that it is impossible to reach absolute zero, and, although scientists have been very close, there are underlying rules in quantum physics that forbid this temperature from existing in the universe. First, let's briefly discuss the practical difficulties in reaching a temperature of absolute zero before diving into the theory. Experimentally, the difficulty with getting a material to reach 0K is that a cooling agent is required that is already at absolute zero in order to decrease the object's temperature. For obvious reasons, no such coolant exists at this temperature. Furthermore, the object will never cool down to the exact temperature of its cooling agent because it approaches the cooling agent's temperature asymptotically due to the laws of thermodynamics. But rather than thinking about something being cooled to this temperature, which as far as we know is impossible, let's imagine the deepest, darkest and coldest corner of the universe. Could a lone particle at this point in space, or any hypothetical point in space, reach absolute zero?

Once again, we end up at the familiar answer of 'no'. However, this raises a more interesting problem, one that lies within the actual mathematics of quantum theory. In fact, the specific concept that forbids absolute zero is Heisenberg's infamous uncertainty principle. Heisenberg's principle states that the knowledge of two related variables, such as position and momentum, is limited. It can be expressed as:

$$\Delta x \Delta p \geq \frac{\hbar}{2}$$

Here, Δx represents the uncertainty in position and Δp represents the uncertainty in momentum, with ħ/2 (the reduced Plank constant over 2) acting as a limit. What does this actually mean though? Well, let's look at what the equation tells us. The limit (ħ/2 which is equal to h/2π, where h is Plank's constant) is just a very small number, and from the equation we can see that the product of the two uncertainties (Δx and Δp) must be greater than or equal to this limit. In other words, the uncertainties are inversely proportional to each other; if you increase one of these uncertainties, the other must decrease so that the equation is satisfied and the product of ΔxΔp is less than the limit ħ/2. This translates to the fact that, in quantum mechanics, the position and the momentum of a particle are not strictly defined. The more you know about the position, the less defined the momentum becomes and *vice-versa.* Of course, this is a simplification of the Heisenberg uncertainty principle, an extremely complex area of quantum mechanics, but the implication still stands.

Let's now apply this to the particle in space. If the particle is at absolute zero (-273.15 °C), then it implies that it will not move at all. Thus, according to the uncertainty principle, the "perfect stillness" of the particle at 0K implies that the position, x, is perfectly defined, as its position is fixed, and thus its momentum is zero. However, from the relationship above, we can see that this is forbidden, and when the position is perfectly defined, the momentum of the particle becomes perfectly undefined, not zero. Consequently, the particle enters a state of quantum fluctuation, in which its momentum can be a range of values, due to the fact that this momentum is not, and cannot, be defined. This creates a problem for our particle.

Momentum requires the particle to have energy, and, if the particle has a completely undefined momentum, and thus a possible range of momentums, it must have a very real minimum average in kinetic energy. This is known as the zero -point energy of a particle and translates to a very real minimum in average energy, and to a minimum temperature, that a particle can have when cooled to absolute zero. Thus it is impossible, by the very mathematics of quantum mechanics, to have particles with no energy, and absolute zero cannot be reached. Taking our example of the particle, it means that even if cooled to absolute zero, the particle will still vibrate with some certain energy

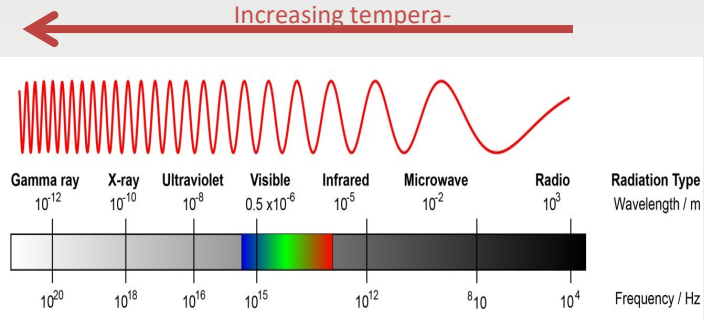
and thus, it has a minimum temperature slightly above absolute zero.

Absolute hot?

So absolute zero may be impossible but is there an absolute hot, a highest possible temperature? Well, the answer is complicated. Wien's displacement law can be used to find the maximum wavelength of electromagnetic radiation emitted by an object (specifically a black-body radiator) at a certain temperature:

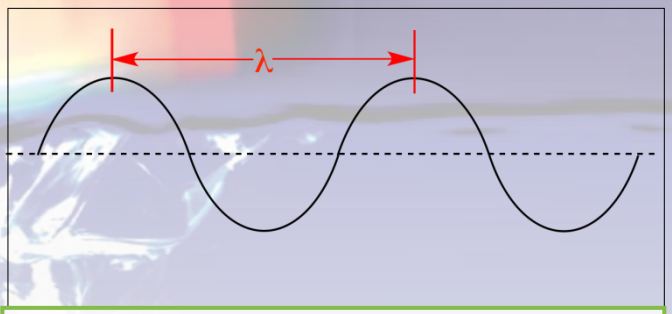
$$\lambda_{max} = \frac{b}{T}$$

In this equation λ_{max}, is the maximum wavelength of the thermal radiation, T is the absolute temperature in Kelvins and b is a constant of proportionality called Wien's displacement constant, equal to about 2.9 10^{-3} mK. So, what does this equation show us? Well, since b is a constant, the wavelength of black body radiation (thermal radiation emitted by a perfectly black absorber of radiation) is inversely proportional to the max wavelength of the electromagnetic radiation emitted. In practice, this means that as you increase the temperature on an object, the wavelength of the electromagnetic radiation that it emits will decrease. Thus, the electromagnetic radiation emitted will go from radio waves, to microwaves and all the way to gamma rays as the temperature increases. This diagram may help you to visualise this:



So, going forward with our quest to find "absolute hot", surely there is no maximum temperature, as theoretically we can just keep adding temperature? Well, not exactly. You see, if a black body is heated to an absurdly high temperature of 1.417×10^{32} kelvin, the resulting wavelength will be 1.616×10^{-35} m (shown in the diagram below). This incredibly small wavelength is a very special distance in quantum physics known as the Planck length. The Planck length (denoted as ℓP), as we understand so far, is the smallest possible distance in the universe and, as a result, a wavelength of 1.616×10^{-35} m could not get any smaller. Just like with absolute zero, we run into a problem. If at this temperature (known as the Planck temperature, denoted as T_p), the wavelength emitted is the smallest it can possibly be, what would happen if we added a bit more energy to the system. The somewhat unsatisfying answer is that we just don't know. Our understanding of physics breaks down at this point and, until we develop a theory of quantum gravity, this answer will remain a mystery. Theoretically, we can just keep adding energy, but at this temperature, we cannot predict what will happen. So, as it stands, "absolute hot" would be a temperature of 1.417×10^{32} K, as after this temperature, physics itself will break down.

Riccardo Kyriacou



This diagram shows the wavelength of an electromagnetic wave. If λ is smaller than a distance of 1.616×10−35 m our understanding of physics breaks down.

BIBLIOGRAPHY

http://hyperphysics.phy-astr.gsu.edu/hbase/wien.html

https://physics.nist.gov/cgi-bin/cuu/Value?plktmp

http://www.bbc.com/future/story/20131218-absolute-zero-to-absolute-hot

http://www.pbs.org/wgbh/nova/physics/absolute-hot.html

https://www.youtube.com/watch?v=OvgZqGxF3eo

https://www.youtube.com/watch?v=UzLDkMfR_60

https://www.youtube.com/watch?v=4fuHzC9aTik

Images:

https://www.google.co.uk/search?q=em+spectrum&safe=strict&source=lnms&tbm=isch&sa=X&ved=0ahUKEwjQqL7WlvvaAhVkAcAKHRw1A5QQ_AUICigB&biw=1600&bih=794#imgdii=Q80abQ7drb_7wM:&imgrc=Xn7z1afZBDAPQM

https://johnbunniv.wordpress.com/2017/02/16/blog-3-electromagnetic-spectrum/

CRISPR: The Future of Medicine

Harroop Bola discusses the importance of CRISPR and the effects this type of genetic modification can have on medicine

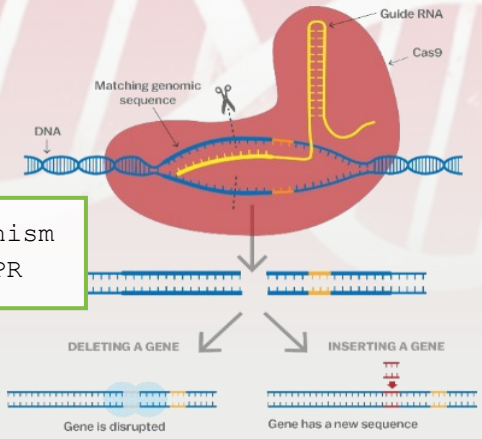
A new dawn of gene therapy has emerged on the horizon, CRISPR. Imagine the significance of genetic modification, possessing the power to modify and facilitate specific changes to human DNA. Revolutionising genetic engineering, CRISPR (Clustered Regularly Interspaced Short Palindromic Repeat) provides an efficient and effective method of genetic modification.

What is CRISPR?

CRISPR is fundamentally important to the survival to prokaryotic life, specifically bacteria. The segment of DNA containing short repetitions of base sequence, in addition to the Cas9 protein, accentuates its cardinal value as a core weapon in the defensive armada against viruses. This phenomenal weapon has evolved into genetic engineering, providing the main mechanisms for the treatment of genetic diseases such as the papillomavirus. The ability to edit a genes function and control the processes of genetics have led to many ethical issues, in addition to its highlighting potential, in being a key player in medicine.

CRISPR technology was inspired by the protective defences of prokaryotic life, possessed by archaea and bacteria. These organisms use CRISPR derived-RNA and various Cas proteins, including Cas9 to slice the DNA of viruses, incorporating viral DNA into spaces. CRISPR is a specialised region located in the DNA of prokaryotes, it has two distinct characteristics; the presence of nucleotide repeats and spacers. Repeated sequences of nucleotides are distributed throughout the CRISPR region, spaces being inter-spread within these repeated sequences. What are spacers? Spacers are sections of DNA that derive from viral phage DNA, being present as short sections within a palindromic repeat (sequence of nucleotide is same in both directions). Unlike the repeated sections of nucleotides, each spacer DNA is individually unique, but like phage DNA.

Cas (Crispr associated) genes code for cas proteins, including helicases and nucleases; these enzymes are responsible for unzipping and cutting of DNA, respectively. This indicates the importance cas proteins are for the destruction of viruses.



The mechanism of CRISPR

How does CRISPR work?

Bacteriophages infect bacteria, such as Escherichia coli. Phage particles consist of an icosahedral head and a tail section involving a helical sheath and tail fibres. The double stranded linear DNA is contained within the head of the λ phage. Infection begins when the phage particle recognises and binds onto the host, injecting viral DNA through the tail into the cytoplasm of the bacterial host. Following infection, the phage DNA can enter the lytic cycle, where λ DNA is replicated and new phage particles are produced. Cas genes transcribe and translate proteins, in addition to transcribing spacers into cr-RNA. This

system attaches onto viral DNA, where enzymes slice and break phage DNA apart. However, in the situation where the viral infection occurs because of an unrecognised λ bacteriophage, a different system occurs.

CRISPR system for unrecognised and new bacteriophage:

Cas genes code for different classes of cas proteins, the cas proteins attach and "ingest" the phage DNA, using helicases and nucleases to slice the viral DNA. The viral DNA is then transported and incorporated into the palindromic repeats of bacterial DNA, as a spacer; behaving as a memory bank against future bacteriophages.

What is the CRISPR Cas9 system?

Investigations by Jennifer Doudna and Emmanuelle Charpentier on the mechanisms of cas9 in Streptococcus pyogenes, led to the importance and understanding of cas9 proteins in the CRISPR system. Cas9 consists of two structures containing nucleases, these nucleases are enzymes that are responsible for the catalysis of the cleaving of phosphodiester bonds between mononucleotides, cleaving the chains into smaller units. Cas 9 acts as a "pair of molecular scissors", being able to cut the two strands of DNA at a specific location in the genome, therefore the sections can be added or removed. Furthermore, another fundamental molecule involved in the CRISPR-Cas9 system is guide-RNA (gRNA). gRNA consist of a small piece of a pre-designated RNA sequence, located within a longer RNA scaffold. The scaffold section binds to DNA and the pre-designated sequence guides Cas9 to the correct section of the genome. Consequently, ensuring that Cas9 enzymes cut the right point within the genome. The guide RNA is designed to locate and specifically bind onto a precise sequence of DNA, through RNA-DNA base complementary base pairing. Therefore, this means that the guide RNA will only bind onto the target sequence of the DNA, without binding onto unnecessary regions of the genome. The Cas9 guided by the guide RNA, cuts both strands of DNA at the target sequence. At this stage, the cell recognises the damaged DNA and attempts to repair it. This method can be manipulated by geneticists, by introducing selected genes into the genome, ultimately promoting a mutation; a mutation which may provide an advantage to the cell of interest.

What are the medical applications for the CRISPR Cas9 System?

CRISPR can potentially reduce the acceleration of antibiotic resistance; a devastating development that limits the effectiveness of antibiotics. As a society which is reliant on consuming antibiotics to treat minor infections, including sore throats, the excessive and negligent over-use of antibiotics has seen dire consequences, consequences as explained by Sir Alexander Fleming during his Nobel Prize speech that "there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant". Therefore, it is fundamentally important that alternative treatments to bacterial infections must be sought after, a potential development is CRISPR. The CRISPR Cas system can destroy plasmids; plasmids are transferred to other bacterium through horizontal transfer, spreading the antibiotic resistant gene. If the CRISPR-Cas system specifically targets resistant genes within the plasmids, then horizontal transfer will not occur.

Genetic Modification & Engineering:

Another prospective medical application includes the treatment of genetic diseases, a prominent highlight of CRISPR gene therapy. Diseases which involve a genetic element

such as hepatitis B, cancer and even high cholesterol can be treated by modifying germline or somatic cells. Germline cells are reproductive cells, therefore by removing the specific gene responsible for the inherent disorder and replacing it with another, it prevents the transfer of the gene across generations. Researchers have conducted experiments using CRISPR technology on mice, whom were suffering muscular dystrophy. Using gene editing tools, they managed to remove the individual defective gene from the genome of the mice, enabling further generations of mice to inherit a genome with the absence of the defective gene. In addition to this, a more promising development of CRISPR gene editing is the possible treatment of HIV. Researchers at McGill University AIDs centre used the CRISPR technique to successfully remove the viral DNA from the host cell; following cleaving, the natural mechanisms of repair took place. The removal of viral DNA from the host genome disrupts the lysogenic cycle of viruses, henceforth preventing the entrance of HIV into the lytic cycle and from causing harm. Furthermore, there are endless possibilities with the CRISPR-Cas9 system in treating a plethora of genetic disorders, and so plays a crucial role in medicine.

It is evident that emergence of precise gene editing technology would revolutionise medicine, introducing modern methods towards the treatment of genetic disorders. A new sector of medicine would not only improve the quality of life or enhance life expectancies but would form a new generation of social attitudes. Genetic engineering using the CRISPR-Cas9 system would open new opportunities for exploitation by editing specific defective genes and replacing them with more ideal ones in embryonic cells, effectively creating designer babies. There are many ethical issues involved with germline editing, although it is cardinal to recognise that for humanity to advance, genetic editing is the next step.

“Genetic engineering in a pill”

Harroop Bola

BIBLIOGRAPHY

Kagele, D., (2015). A CRISPR approach to precision medicine. The Jackson Laboratory. Available from [Online]: https://www.jax.org/news-and-insights/jax-blog/2015/august/a-crispr-approach-to-precision-medicine (Accessed 4th March 2018)

Harvey, P., (2014). CRISPR: A game-changing genetic engineering technique. Harvard University, The Graduate School of Arts and Sciences. Available from [Online]: http://sitn.hms.harvard.edu/flash/2014/crispr-a-game-changing-genetic-engineering-technique (Accessed 4th March 2018)

Farnoosh, G., et al., (2017). CRISPR genome editing and its medical applications. Biotechnology and Biotechnological equipment. Available from [Online]: https://www.tandfonline.com/doi/full/10.1080/13102818.2017.1406823 (Accessed 4th March 2018)

Fan, S., (2017). CRISPR pill may be key in fight against antibiotic resistance. Singularity Hub. Available from [Online]: https://www.tandfonline.com/doi/full/10.1080/13102818.2017.1406823 (Accessed 4th March 2018)

Hsu, P.D., et al., (2014). Development and applications of CRISPR-Cas9 for genome engineering. Cell. Available from [Online]: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4343198/ (Accessed 4th March 2018).

Doudna, J., (2015). How CRISPR lets us edit our DNA. TED. Available from [Online video]: https://www.youtube.com/watch?v=TdBAHexVYzc (Accessed 4th March 2018)

Bozeman Science, (2016). What is CRISPR? Available from [Online video]: https://www.youtube.com/watch?v=MnYppmstxIs (Accessed 4th March 2018)

“What is CRISPR-Cas9”, (2016). Your Genome. Available from [Online]: https://www.yourgenome.org/facts/what-is-crispr-cas9 (Accessed 4th March 2018)