

Quantum Ultimum

Bicentenary Edition



Moncrieff-Jones Society
2010-2011

Foreword by Dr Simon Singh

Foreword

Dr Simon Singh MBE is a science writer and author of *Fermat's Last Theorem* and *Trick or Treatment? Alternative Medicine on Trial*. Simon completed a PhD in particle physics from Emmanuel College, Cambridge, and CERN, Geneva. He has also received honorary degrees from Loughborough University, Southampton University, University of the West of England and Royal Holloway; and has received the *Kelvin Medal* from the Institute of Physics. In 2003, Simon was made a Member of the Order of the British Empire (MBE) for services to science, technology and engineering in education and science communication.

“Last year I came to Caterham School to deliver a presentation about how libel law threatens discussion and debate within the scientific community, in particular in relation to alternative medicine. I was very impressed by the students’ insightful and intelligent questions, and their genuine interest in science.

This year I have been invited to write a brief foreword to the Moncrieff-Jones Society’s annual publication, *Quantum Ultimatum*. The society has been very successful in promoting science within Caterham School, and I am delighted to be associated with it. The presentations which took place this year encompass an impressive range of subjects, from *Dark Energy* to *Apoptosis*, and I am delighted by the level of in-depth knowledge the speakers possess, and their interest in and passion for their topic which they convey in their articles.

I offer my congratulations to all the members of the society, and I hope that this fine tradition continues to prosper for many years to come.”



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President's Introduction

“Welcome to the 2011 edition of Quantum Ultimatum: the Moncrieff-Jones Society’s annual publication. This magazine contains a summary of each of this year’s presentations, and will give you a brief insight into the fascinating topics presented by our speakers.

This year the society has been particularly successful. All the presentations have been of phenomenal quality, and I would like to thank all the speakers for their hard work in thoroughly researching their topics and delivering their presentations with confidence and passion. This year has also seen a further increase in the society’s profile within the school, with many more people attending the talks, especially from lower years. I would like to thank everyone who attended for their support and their challenging and insightful questioning. It is very gratifying for the speakers to have their efforts acknowledged, if a little daunting!

I would also like to thank Sally, the Vice-President, for all her help in running the society, and Mr Quinton, whose contributions cannot be overstated. His invaluable guidance, not to mention tireless enthusiasm for the society and science in general, is what has kept the Moncrieff-Jones Society running for many years, as it undoubtedly will for many years to come. I wish the best to those taking over as president and vice-president next year, and I hope you will enjoy it as much as I did!”



Oliver Claydon (President) and Sally Ko (Vice-President) next to the Moncrieff-Jones Society board

Savant Syndrome

Kelvin Tang

Albert Einstein, Mozart, Sigmund Freud, Vincent Van Gogh and Isaac Newton were undoubtedly amongst the most extraordinary people who ever lived in human history. Scientists now speculate that they might have had one thing in common – they were all autistic savants.

Savants, by definition, are rare individuals who, although severely brain impaired, display islands of astonishing excellence in specific areas including drawing, memory, music, calendar calculations, and arithmetic. Normally, all savants have an extraordinary memory of a special type, a memory that is very deep, but exceedingly narrow in area, and they have no idea how they do it.

What is the cause?

The exact cause of savant syndrome is not fully understood. However, scientists, professor Allan Snyder in particular, one the world's most famous expert in savant syndrome, believes that savants' astonishing skills might have been due to a variety of brain impairments, one of which is autism, or rather, a mild form of it, called Asperger Syndrome.

50% of savants are autistic, and the other half have other problems associated with the brain, for example, brain injuries and diseases, mental retardation and developmental disability. By definition, autism is a failure to develop social abilities, language and other communication skills to the usual level. Restricted and repetitive behaviour is one of the signs of autism, and they all began during a child's infancy. Severe cases of autism include a complete inability to communicate with people socially. It is a form of Autism Spectrum Disorder (ASD), and Asperger Syndrome mentioned above is another form of ASD. It has the same signs as autism, except for its relative preservation of linguistic and cognitive development. Even with today's technologies,



there is still no cure for both disorders. So what causes autism? The simple answer is - We don't know yet. However, what we do know is that savant syndrome is often associated with some form of left-brain dysfunction together with right-brain compensation, leading to a predilection for literal and non-symbolic skills, which are what savants are good at.

How good are they?

Stephen Wiltshire, an autistic savant from London, drew a stunningly detailed panoramic view of Tokyo on a 10-meter-long canvas, from memory, only following a short helicopter ride.

Matthew Savage was diagnosed as deeply autistic, incurable. At the age of 6, he discovered the logic of the 88 keys of the piano, and taught himself to play overnight. He's now 18 years old. Jazz legends like Dave Brubeck believe that he is one of this century's most talented pianists.

Kim Peek, the real-life mega-savant (showing astonishing excellence in multiple areas) inspired the creation of the Oscars winning movie Rain Man, in which the character is played superbly by Dustin Hoffman.

Are they creative?

Savants typically adopt a form of mimicry, rather than being authentically creative. What neuroscientists have recently discovered is that creativity is mainly a function of the neuronal networks in the frontal lobe (responsible for idea generation), and that these networks strongly depend on a neurotransmitter called dopamine. The higher the dopamine levels in the networks of the pre-frontal cortex, the more creative people are. However, there are some savants who are creative - here is one.

Rüdiger Gamm is a sudden savant, meaning a normal person who suddenly and unexpectedly acquires savant-like abilities. When he was 21, something extraordinary happened to him. Overnight, he could literally calculate better than a computer. What is special about Rüdiger is that he was able to invent a completely new algorithm immediately after receiving a question that some scientists thought was mathematically impossible, and changed the way he normally calculates. In the 2008 Mental Calculation World Cup in Leipzig, he recited 81^{100} , which took him approximately 2 minutes 30 seconds.

Is there a genius in every single one of us?

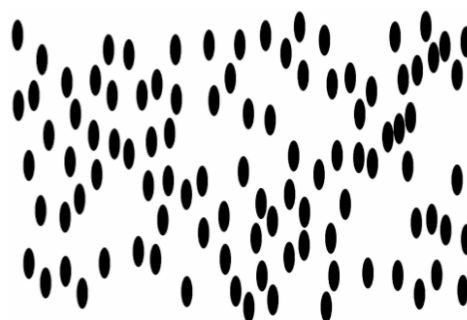
“Savant skills are latent in us all” is suggested by Professor Allan Snyder. His hypothesis is that savants have privileged access to lower level, less processed information, before it is packaged into holistic concepts and meaningful labels. He also suggests that we can acquire savant skills by switching off parts of the brain, allowing areas that are not normally accessible without a rare form of brain impairment present in persons with savant syndrome to become accessible. To test this hypothesis, he carried out this experiment.

He used low-frequency repetitive Transcranial Magnetic Stimulation (rTMS), a noninvasive method to cause depolarisation in the neurones of the brain, to inhibit the left anterior temporal lobe (LATL), a region important for semantic processing, conceptual knowledge, labels and categories. In normal people, conceptual regions dominate over those that process literal detail. In effect, they attempted to inhibit (or reverse) this natural state of inhibition, to shift the balance in favour of greater access to literal detail. How does being literal enhance numerosity? Professor Allan Snyder argues that it removes our unconscious tendency to group discrete elements into meaningful patterns, like grouping stars into constellations, which would normally interfere with accurate estimation. By being literal, a savant sees elements as discrete and disconnected, thus removing this interference.

In the task participants were seated in front of a computer monitor, and informed that they would be shown a series of images, each made up of a number of discrete elements. Each stimulus was presented for 1.5 seconds. There were 20 trials of computer-generated stimuli for each session and there were 3 sessions: before rTMS; immediately after 15 minutes of rTMS; and one hour after rTMS had ceased.

10 out of 12 participants improved their ability to accurately guess the number of discrete elements immediately following magnetic pulse stimulation. Of these 10, 8 became worse 1 hour later, as the effects of the magnetic pulses receded.

In conclusion, the observed improvement in participants' numerosity, following the application of rTMS to the LATL, as predicted by theory, is consistent with the left-brain dysfunction implicated in the savant condition, and accords with contemporary views about hemispheric competition and the disinhibiting influence of rTMS.



Does this really mean savant-like skills are latent in all of us? Possibly, although according to professor Allan Snyder himself, there are technical limitations such as stimulation being less effective in people with thick hair or skulls, and its effectiveness depends on the amount of myelination of neurones. Therefore more studies are needed to improve and refine the theory.

In the future

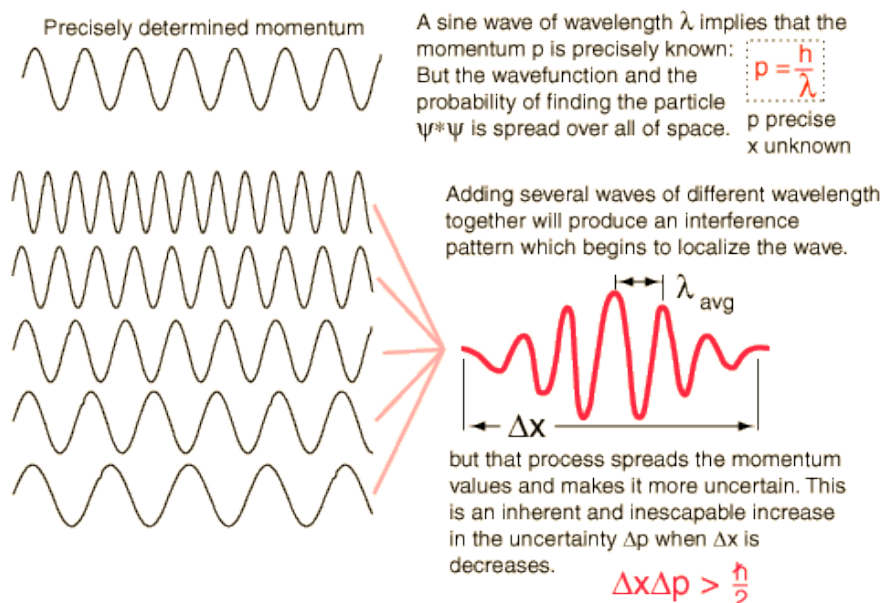
Exploring savant syndrome not only gives us unparalleled possibilities of benefiting ourselves and enhancing our abilities, but also we can help autistic savants to acquire the sociability that all of us already have. By understanding more about how our brains work, we are coming closer than ever before to truly understanding ourselves.

The Uncertainty Principle

Andy Paine

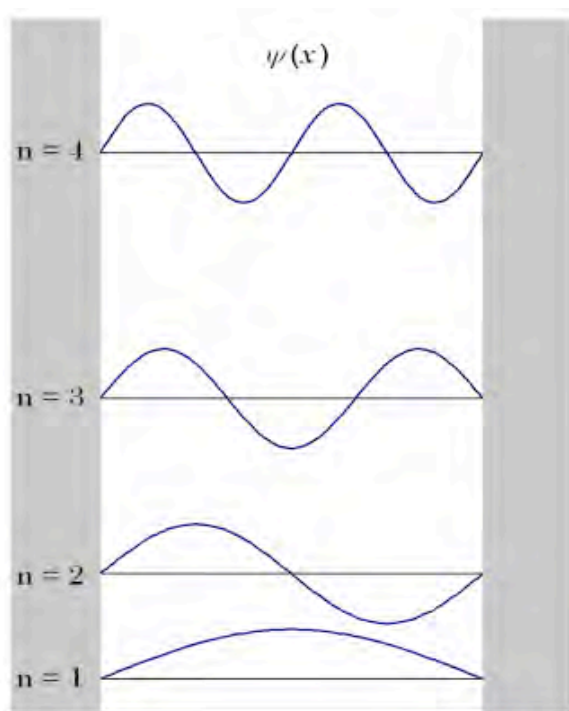
The Uncertainty Principle is defined by: “the precise inequalities of certain pairs of physical properties, such as position and momentum, cannot be simultaneously known to arbitrarily high precision.” To put this in simpler words, when a particle has two properties (e.g. position (denoted by x) and momentum (denoted by p) or energy and time) the Principle prevents us knowing both these features to a given degree of accuracy – there is an uncertainty in their values. This value, conveniently, has a value – the product of the two uncertainties must be greater than or equal to $\hbar/2$ (pictured right). The constant, \hbar is shorthand for $h/2\pi$, with h being the symbol to denote the common constant of the quantum world, named after one of the founding fathers of quantum mechanics – Max Planck. To put some perspective into the equation, \hbar is equal to 1.055×10^{-34} Js, hence why in normal life you don’t find yourself in multiple lanes when you check your speedometer! This also has the interesting side effect of reducing everything in quantum mechanics to a probability, as there MUST be an uncertainty in any values we calculate.

To begin to explain The Principle’s theory, we first have to get our heads around one of the confusing effects of quantum dynamics – wave-particle duality. This states that every particle is also a wave and every wave is a particle. Whilst this has no real world effects, their behaviour on a quantum level becomes very important. Particles can now be diffracted and reflected, whilst waves can be localised at a certain point. The latter of the two lays the foundations for explaining what is happening in the Uncertainty Principle.



The above diagram explains the principle with two different models. Firstly we have the single sine wave (which remember, a particle can be modelled as) which has a precise wavelength (distance between peaks or troughs). Given this knowledge we apply the De Broglie equation which relates momentum and wavelength ($p=h/\lambda$) to find the precise momentum of the particle/

wave. By looking at it this way, we can get a very precise value for the “momentum” of the particle/wave. However, the particle/wave is spread over a large area, thus giving us a very uncertain value for the position of the particle/wave. To solve this issue we use interference patterns of many sine waves together to produce a very localised wave/particle. Whilst this reduces the uncertainty in its position (as the localisation means the wave is spread over a very



small area) the interference pattern nature means that the wave has a number of different wavelengths and so we can only take an average – producing an uncertain value for the momentum (as $p=h/\lambda$).

So what implications does the Principle have, I hear you cry? Well to chemists, quite a lot actually. As electrons are modelled as wave/particles, we must apply the Uncertainty Principle to their characteristics, most notably their position. If we think of each electron as a wave function, so as to say we are modelling it as a wave; this allows us to give it a wavelength, which using the De Broglie equation means we know its momentum. We can also use the interference technique to give it a position. As we know the electron’s energy to a high degree of accuracy, we know its wavelength so we have to say that we do not know its position

particularly accurately. This leads us to the definition of an orbital – “an area of space where there is a high probability of finding an electron.” But how do we know the energy? The diagram above shows a famous experiment called “Particle in a Box.” The diagram shows the resultant interference waves when all wavelengths are projected into the box and allowed to reflect. The experiment shows that only certain wavelengths can remain, as all others destructively interfere to the point where they disappear altogether. From this we can deduce that only waves of a certain energy can remain, thus allowing us to calculate their energy (from knowing which orbital they are in) creating the position uncertainty that leads us to define orbitals as an area of space.

Whilst the Principle may have no “real world” applications, it serves to highlight just how little we can sometimes know about a system and how the natural world remains inherently probabilistic.

Apoptosis

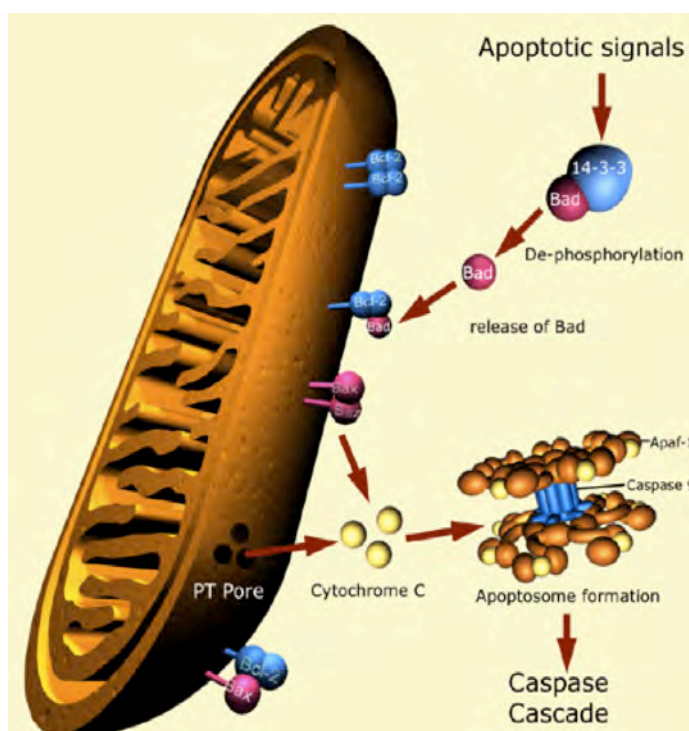
Ashley Goulding

Apoptosis is a process that has developed in multi-cellular organisms and is a mechanism by which a cell can induce it's own death. This has lead to the process being commonly known as "cell suicide". Although this can be misleading, apoptosis actually is essential to the development of multicellular organisms, to the extent that in an average adult human 50-70 billion and in an average human child 20-30 billion cells die each day by apoptosis. In humans apoptosis has a number of vital roles, in embryological development, toe and finger formation is in part due to apoptosis. The digits begin development as part of a webbed hand or foot and then apoptosis removes the cells present in between the fingers or toes leaving the perfectly formed hand or foot. Apoptosis can also act as a final barrier to cells becoming cancerous, after cells have developed a number of mutations the TP-53 gene can produce p53 a protein that induces apoptosis, therefore removing the cells. Unless of course one of the mutations has occurred on the TP-53 gene so therefore apoptosis cannot be induced as a functional p53 protein is no longer produced.

Another vital role of apoptosis is in the immune system, cytotoxic T-lymphocytes (T-Killer cells) work by releasing granzymes into cells after a perforin protein has punched a whole in the membrane. Granzymes are potent inducers of apoptosis, so the cell then commits suicide via apoptosis. The T-Killer cells can kill virus infected cells like this, but also T-Killer cells induce apoptosis in each other, therefore stopping a build up of T-Killer cells that creates an overactive immune system. If this happens it can lead to auto-immune diseases such as rheumatoid arthritis

During the progression of apoptosis the cell undergoes many changes, the cell shrinks, develops blebs (irregular bulges on the cell membrane) on it's surface, the chromatin in the nucleus condenses and phosphatidylserine, a phospholipid usually displayed on the inside of the membrane, starts to be

expressed on the outer surface. The stages can be brought about via two different pathways, the extrinsic or the intrinsic pathway:



The Intrinsic/ Mitochondrial Pathway

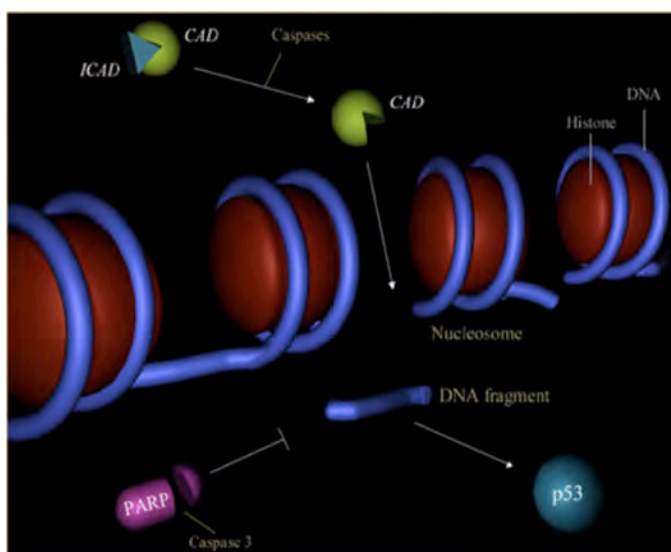
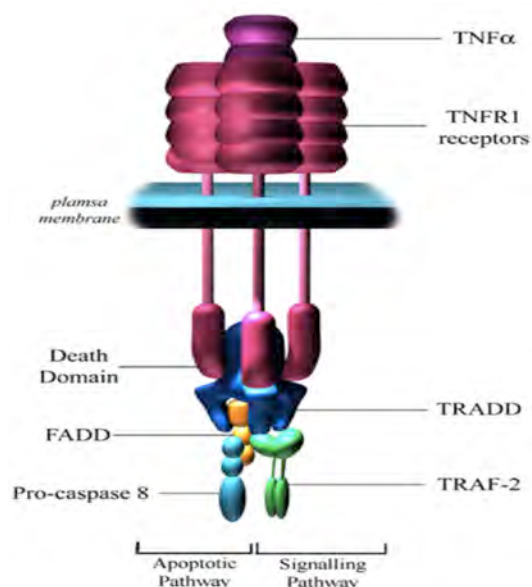
After internal damage or stress to the cell a Bax protein migrates to the outer surface membrane of the mitochondria. The Bax protein causes the release of cytochrome c from the inter membrane space in the mitochondria. How it does this is still unknown. Current theories suggest that the Bax protein directly punches pores into the membrane or that the Bax protein interferes with ion channels. However we do know that this migration of the Bax protein releases cytochrome c. Cytochrome c, which is not normally found in the cytoplasm, combines with apaf-1 (apoptotic protease activating factor) then these complexes

combine to form apoptosomes. This apoptosome activates caspase-9 from it's inactive form,

procaspase-9. The caspases are a family of proteins known for their cleaving ability, normally of each other. So the activated caspase-9 then goes on to cleave and activate both caspase-3 and caspase-7, which then go on to cleave other caspases in what is known as the caspase cascade.

Extrinsic/ Death Receptor Pathway

There are many different receptors included in this group and they all work in a very similar way. In the TNF alpha pathway (as shown in the diagram) TNF alpha binds to the TNF receptor on the outside of the cell. This binding leads to a change in shape of the receptor, which means the death domain, which is part of the receptor located inside the cell, also changes shape. This change in shape means that the SODD, an inhibitory protein usually bound to the death domain, is released. This then allows the TRADD protein to bind to the death domain, which in turn binds to the FADD protein, creating a complex that then recruits pro-caspase-8 and cleaves it, forming an activated caspase-8. This caspase-8 then goes on to cleave and activate other caspases, and so initiating the caspase cascade.



Caspase Cascade Leads To Deformation of the Cell

The characteristic features of apoptotic cells are brought about in two main ways, structural actin filaments are broken down and the chromatin is also broken down. All of this is achieved by caspases that have been activated as a result of the caspase cascade. The actin filaments of the cytoskeleton are cleaved directly by caspases, explaining why the cell shrinks and why blebs develop on the surface.

The breakdown of chromatin is slightly more complicated, there are three main components, activation of DNases, the

inhibition of DNA repair enzymes and the breakdown of structural proteins in the nucleus. Caspases activate DNases (CAD) are normally found in the nucleus as an inactive complex with the inhibitor (ICAD). However caspases, such as caspase-3, cleave the inhibitor so it can no longer bind to the Caspase activated DNase. Therefore caspases activate DNases that go on to cleave the DNA. Caspase-3 also cleaves poly(ADP-ribose) polymerase (PARP), a DNA repair enzyme, removing it's catalytic ability, therefore stopping damaged DNA from being repaired. Caspases also cleave structural lamin filaments in the nuclear envelope. This explains the characteristic condensing of the chromatin.

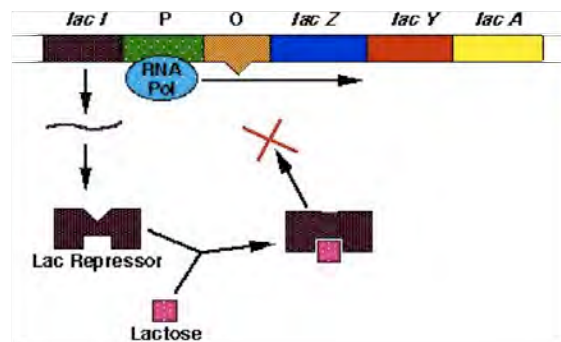
Gene Regulation

Amy Miles

Gene regulation, in broad terms, is the switching on and off of genes. This is needed so energy is not used making proteins that currently are not needed by the cell. New discoveries of the mechanisms of gene regulation are exciting because the understanding of it can lead to new drugs being developed to combat certain genetic diseases. It was not until 1960 that the term 'operon' was first proposed and the first operon to be described was the Lac operon.

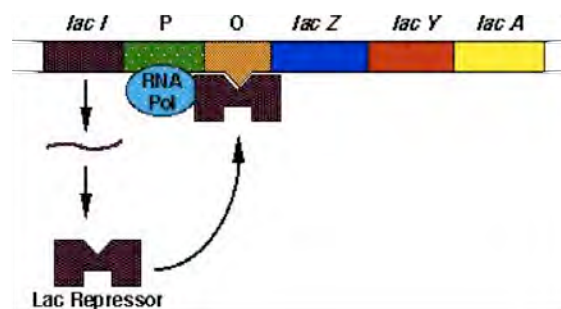
Prokaryotic gene regulation is achieved using operons. An operon consists of a promoter with a group of genes that are transcribed together into mRNA. An example of an operon is the Lac operon encoding lactase. It consists of three genes, a promoter region where RNA polymerase will bind and an operator where a repressor molecule can bind to obstruct RNA polymerase. Further along the DNA is a gene called LacI which encodes a repressor protein.

When there is no lactose in the cell, repressor proteins continually bind to the operator which blocks RNA polymerase from transcribing the genes. However, when lactose is present the lactose binds to the repressor protein at certain binding points and changes the shape of the repressor protein so it can no longer bind to the operator. Without the repressor protein in the way RNA polymerase can continually transcribe the genes into mRNA which can then be translated to form lactase.



When lactose is present in the cell

When glucose accumulates in the cell it inhibits the production of lactase. A nucleotide called cAMP accumulates in a low glucose concentration environment and binds to a protein called CRP. This changes the shape of the CRP so that it can bind to a site near the promoter. This in turn alters the angle of the DNA, which makes it easier for RNA polymerase to bind to the promoter. The opposite is true when glucose is at a high concentration. This reduces the rate of the transcription of the genes and therefore the translation of lactase.

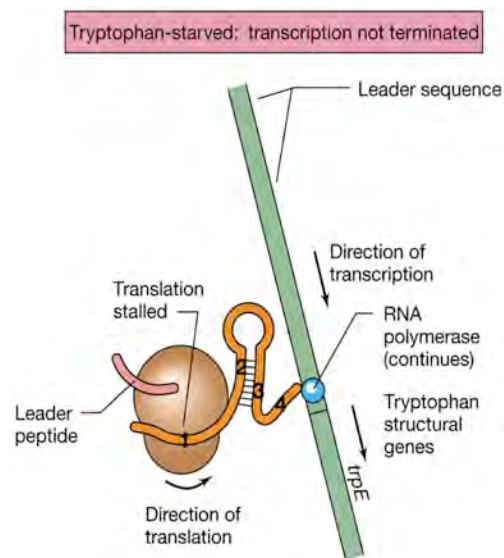


When lactose is not present in the cell

Another operon is the TRP operon. It regulates the production of the tryptophan synthetase, which is an enzyme that catalyses the synthesis of tryptophan, an amino acid. The operon consists of five structural genes, a promoter, an operator and a leader sequence. Further along the DNA there is a gene that encodes a repressor protein, in its inactive state.

When tryptophan levels in the cell are high the repressor protein binds to tryptophan, changing the shape of the repressor to make it active. Therefore the repressor is able to bind to the operator and prevent RNA polymerase from transcribing the gene. As the repressor protein is only bonded to the DNA by hydrogen bonds it can become detached and RNA polymerase can start transcribing the

genes even when the tryptophan levels in the cell are high. To combat this problem there is a second level of regulation, which is attenuation.



Attenuation involves the leader sequence. This includes four short sequences designated one-four. Each section is partially permeable to the sections adjacent to it. When there is a high concentration of tryptophan the ribosome can translate sequence one quickly (as sequence one contains two tryptophan codons and there is plenty of tryptophan to bind to tRNA). Therefore it moves on to translating sequence two quickly as well. This means that when sequence three is transcribed it can not pair with sequence two because there is a ribosome in the way. It therefore pairs with sequence four, forming a stem loop. This binds to RNA polymerase causing it to pause. Sequence four is followed by a series of uracil bases which are held to the DNA template by two hydrogen bonds which are easily broken. The RNA detaches from the DNA and transcription stops.

When the tryptophan levels in the cell are low it takes a long time to translate sequence one so sequence two is free to pair with sequence three. Even though a stem loop is formed the RNA does not become detached as following sequence three is sequence four not A-U pairs. Therefore, transcription and translation of the genes continues.

Gene regulation in eukaryotes is very different and involves transcription factors. Transcription factors are proteins that bind to specific DNA sequences, thereby controlling transcription. This is possible by 2 different methods either by binding to the promoter adjacent to the gene being regulated or by catalysing the acetylation or deacetylation of histone proteins.

Generally the following happens, although all transcription factors vary. The transcription factor binds to the DNA, and a protein called a coactivator binds to the transcription factor. A coactivator acetylates the lysine group of the histones adjacent to where it has bound. This reaction removes the positive charge of the DNA. Usually, the positively charged histones are attracted to the negatively charged DNA. Therefore, without this positive charge the binding between the DNA and the histone will be loosened. Proteins, called bromodomains, recognise and bind to lysineacetylated histone residues and in turn make them targets for remodelling engines. Remodelling engines start stripping away the histones wherever they are bound, which is made easier as the interactions between the histones and the DNA have already been weakened. This makes an opened up region where RNA polymerase can bind and start transcription.

In addition to these coactivators, there are corepressors which act as histone deacetylases, which bind to transcription factors and remove an acetyl group from a lysine, meaning the lysine once again has its positive charge and the histones and DNA are attracted to each other again. This aids the coiling of the DNA around the histones and prevents transcription as RNA polymerase can no longer bind to the DNA.

Time Dilation

Lottie Williams



Einstein's theory of relativity predicts that when an object moves at speeds close to the speed of light, it undergoes 3 relativistic changes.

- 1) An increase in mass
- 2) A contraction in length in the direction of travel and
- 3) A "slowing down" of time.

This slowing down of time is called 'Time Dilation'.

The relative motion between two observers, and the finite speed of light, causes time dilation. To break this statement down, imagine you are in a car and consider your speed. If there were no windows, you wouldn't be able to tell you were even moving since your speed is 0 relative to the car. To someone outside you appear to be moving at the same speed as the car is moving. To someone watching you from the sun, you're moving at the speed which the earth is moving, plus or minus the speed of the car. So this shows us that velocity is not absolute, and in this same way, neither is time. This is part of the theory of relativity, the idea that speed is relative.

However, Maxwell observed that the speed of light is constant, relative to everything. No matter what your speed is relative to the speed of light, the speed of light is always measured to be 180,000 miles per second. However, if classical relativity were right, there would be no absolute velocity and the speed of light would depend on the relative velocity of the person doing the measuring. Einstein came up with a new idea, and said 'every person moving at a constant velocity will observe the same laws of physics that a stationary observer observes, and since the speed of light is a law physics then all observers will measure the same speed of light regardless to their state of motion.'

We all know that speed is just a measure of distance moved in a given time.

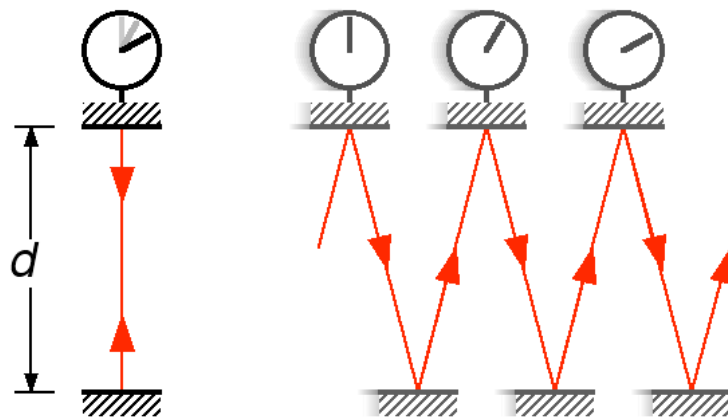
$SPEED = DISTANCE / TIME.$

In order to agree on speed of light (which is always constant) then different observers will have to disagree about distance and time. Therefore, since the speed of light is constant, time cannot be constant.

When two observers are moving at very high, but different, velocities, then the point of view of each person will be that the other's time is running slower. The other person's clock would appear to be ticking at a slower rate than their local clock. Both observers will experience their own time as running normally. The clock obviously is an indication of time. What you've got to realise is that this isn't a statement about clocks but it is time itself that is slowing down. In the universe, time is entirely relative.



Lets construct a clock where light travels from one plate to another. (See diagram). When the light hits the bottom plate the clock advances. Although the clocks are identical, the clock in motion ticks slower than the one at rest. The diagram shows that the clock at rest ticks as the beam of light reflects up and down normally. The beam of light must hit the plates at the same time in both clocks since the speed of light is constant, but it appears the moving clock has a longer time interval because the beam is going further without going any faster. It ticks less often, so less time is recorded. The person who is moving with the moving clock witnesses their own time as normal since their clock appears to look the same as the shown stationary clock.



Although at the speeds we experience there are few noticeable time dilation effects, the phenomenon can still be experimentally observed. Cosmic rays form mesons in the atmosphere which should decay in micro-seconds. However, since they are moving at 99% the speed of light, they actually survive for 6 seconds. This is an experimental way to detect time dilation. The faster something moves through space, the slower they move through time. This can also be visualised using Einstein's space-time continuum. Both are inter-connected and should not be thought about separately.

The Human Papillomavirus

Galina Pekarskaya

What is HPV?

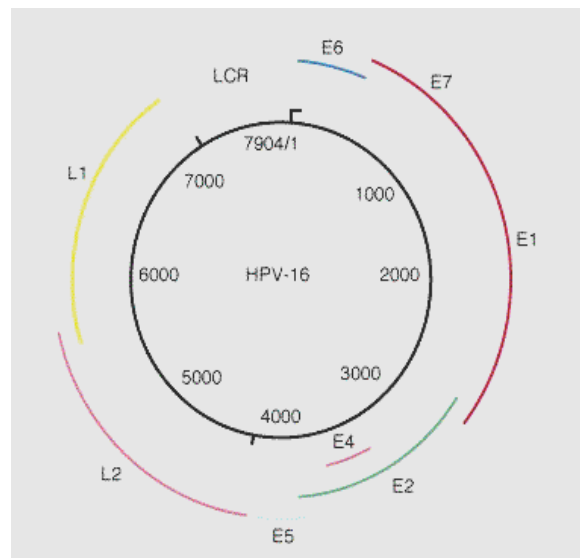
HPV is a virus that causes major and minor neoplasias of the epithelial layers (predominantly in the squamous epithelium) which can lead to a carcinoma. HPV was identified as the cause of cervical and some other epithelial cancers. Research into the virus is extensive as the perfection of a vaccine will potentially lead to prevention of cervical and perhaps other HPV induced cancers.

The structure of the virus

The virus is non enveloped with a capsid made up of 2 viral capsid proteins L1 and L2. The genome of the virus is expressed as a double stranded circular DNA with around 8000 base pairs. The viral proteins are divided into early and late regions according to the order of their expression in the viral lifecycle. E1 – E8 is the early region responsible for plasmid replication, transcription and transformaton. The later region codes for major L1 and minor L2 viral proteins.

HPV lifecycle

In order for the virus to establish itself, damage to the epithelium must be present. The virus infects the basal layer cells, probably targeting stem cells, hence damage is needed to expose the basal cells. These events occur in cells that are differentiating and have not exited the cell cycle as the replication process is almost fully dependent on the cellular DNA synthetic machinery which is only activated in mitotically diving cells. To prevent the cells exiting the cell cycle the viruses encode proteins which reactivate cellular DNA synthesis in non-cycling cells, inhibit apoptosis and delay the differentiation of the infected cell allowing the virus to be reproduced.



Progression of viral gene expression

The virus can bind to 2 different receptors on the cell: HSPG receptor and $\alpha 6$ integrin; both of which are believed to have groups complimentary in shape to the virus. When the receptor are endocytosed (recycled by the cells, for example during movement) the virus enters the cell and uncoats. It is currently unknown how the viral DNA is integrated into the host DNA but the assumption can be made that the host enzymes involved in DNA replication must be involved as the virus has not been shown to have any such enzymes. Once the viral DNA is incorporated its begins to be expressed.

Function of the viral proteins

E1 protein acts as an enzyme forcing the viral DNA strands apart in order for transcription to take place, hence aids the expression of the virus in the cell. E2 protein ensures that after transcription, the virus is fully expressed in daughter cells produced by cell division. E4 protein aids the release of the

virus once the mature virions are assembled by disturbing the cell membrane. E5 protein stimulates the cells to differentiate faster and remain in the cell cycle (mitotically active for a longer time) hence allowing the virus to remain active in the cell and be produced in greater numbers as cells divide more rapidly. This is done by increasing the number of EGFR's (epidermal growth factor receptors) on the infected cell, hence allowing for more EGF to bind and stimulate cell division.

E6 protein is known as an oncoprotein as it makes the cell more prone to cancer. It allows the virus to remain active in the cell by preventing apoptosis (programmed cell death) which is induced when change to genetic material is identified. This is done by binding to the tumor suppressor protein p53 and stimulating the cell to recycle it via ubiquitination, and as the tumor suppressor is no longer there the virus can reproduce freely within the cell. Therefore the cell becomes more prone to undetectable malignant mutations. E7 protein is also an oncoprotein that inactivates another tumor suppressor in the cell: the retinoblastoma. If a damage to the cells genetic material is detected the retinoblastoma protein prevents the cell from progression along the cell cycle and hence stops the formation of malignant tumors. However the E7 viral protein interacts with the retinoblastoma in a number of complex processes, inactivating it and allowing the cells with damaged DNA to proceed through the cell cycle and mature.

HPV induced cancer diagnosis

HPV induces a neoplasia in the epithelial cells into which the virus is incorporated. This is the effect of the virus brought on by the late differentiation of stem cells of the epithelium and prolonged abnormal growth and division. This neoplasia leads to physical changes in the appearance of the cells of the cervical epithelium and hence when a biopsy is taken of the tissue, HPV infection can be identified by the visible changes in the cell structure. These features are :

- Nuclear enlargement (two to three times larger)
- Elevated amount of chromatin in the nucleus (it simply appears darker on stained slides compared to normal)
- Perinuclear halo (clear area around the nucleus caused by a denser cytoplasm)



Normal cells (left) and infected cells (right)

HPV spread prevention and vaccination

As HPV is a sexually transmitted virus the use of condoms and small range of partners are recommended to prevent the risk of infection. As for more advanced methods of prevention a vaccine has been introduced by the Gardasil pharmaceutical corporation which prevents HPV infection by making the immune system more able to fight the virus by exposing it to the L1 coat protein and allowing it to make antibodies for a faster response in case of a repeated infection. Despite that the vaccine still has many side effects, the research in this area of medicine definitely looks promising as we could potentially vaccinate against cancers caused by viruses and there may well be more that just those induced by HPV.

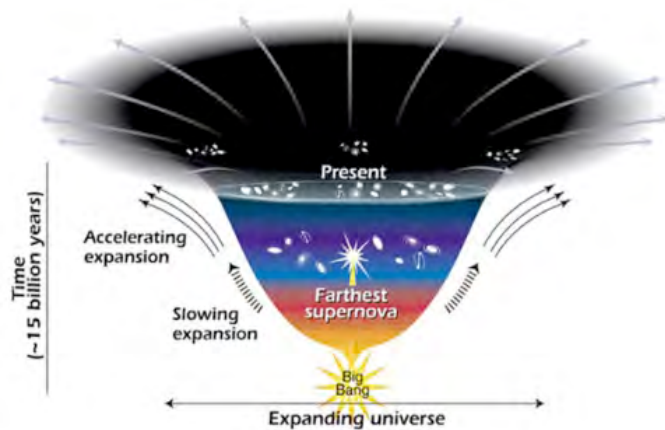
Dark Energy

Kyle Yeung

Dark energy is a hypothetical energy that is inferred to exist because of its effect on the expansion of the universe. It is known to have negative pressure with positive density, causing a repulsion effect on the universe.

The universe has been expanding since the big bang, but acceleration only began about 5 billion years ago out of the universe's current age of about 18 billion years. Before that the expansion was decelerating, because dark matter, matter that can't be observed in the

electromagnetic spectrum, dominated the universe until the amount of dark energy increased to the point where the universe expanded at the accelerating rate that is observed today. To be precise, the concept of dark energy was created to account for the accelerating expansion of the universe, which is included in the models of the universe using Einstein's cosmological constant to represent dark energy.



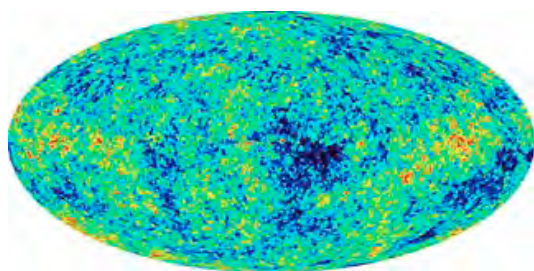
The cosmological constant, Λ , first appeared in Einstein's field equations as a representation of vacuum energy to balance out the force of gravity as his equations predicted an expanding universe. This was before Edwin Hubble had discovered that most galaxies were receding from ours and that the universe was expanding. After that discovery, Einstein abandoned the term. However, in recent years Λ has become the most simple explanation for dark energy, that is energy that is associated with a vacuum, fitting the requirements for dark energy, as it provides negative pressure while having a positive density, as well as being the theory with the most evidence supporting it, and it is the most widely investigated theory today, with Λ used to represent dark energy. Its ratio of observed density over required critical density is expressed as Ω , and for $\Omega = 1$ the universe is thought to be flat, that is, disc-shaped, and expanding infinitely.

The Λ -CDM Model, or Lambda- Cold Dark Matter model of the universe, is currently the most widely accepted model of the universe. It assumes that the universe is flat, and includes a cosmological constant to represent dark energy's influence on the expansion of the universe, counteracting the collapsing effects that gravity provides. This model is currently used as research figures do show that the universe has a shape close to flat, and that its expansion is accelerating. The model suggests that 70 % of the mass-density of the universe is dark energy, while the remaining 30 % is matter, including 25% dark matter. It sets a parameter on the values of Ω as it assumes $\Omega = 1$ thereby allowing us to place restrictions on the possible values of $\Omega \Lambda$.

Like all other forms of energy, we cannot directly measure dark energy in the same way that we cannot measure heat energy or kinetic energy. We can only observe the effects that dark energy has on its surrounding environment, in this case the expansion of the universe. This is similar to measuring heat energy through its effect on the temperature of some water, or the kinetic energy being observed

by through its effect on a block. To measure dark energy's effect on the universe we need to use a standard ruler, or a standard candle. For the standard ruler, we would need to have a known distance capable of measuring distances on a cosmic scale, which could be calibrated over the age of the universe, as well as make precise measurements over the volume of the universe. A standard candle would be an object of known luminosity that could be observed on a cosmic scale, and whose distance from us we could find using its redshift value and maximum brightness. These objects would allow us to measure the history of expansion of the universe and arrive at a range of values of Ω_Λ and Ω_m . As a cosmic ruler we use a technique called baryon acoustic oscillations, and as standard candles we use type Ia supernovae.

Type Ia (One A) supernovae are formed when a white dwarf star explodes. As all white dwarfs are restricted by the Chandrasekhar limit of 1.4 solar masses, their mass and hence luminosity are about the same. The redshift of the supernova allows us to estimate its brightness, while the actual brightness can be observed using telescopes. If the universe were expanding at an accelerating rate, the observed results would be dimmer than they should appear as the supernovae have moved farther from us than we would expect. Thus we can tell if the universe is expanding at an accelerating rate from their luminosity if the observed supernovae at high redshifts are dimmer than they are estimated to be. The original discovery of the expansion rate of the universe was also made through the observation of supernovae. An advantage of this method is that by looking deeper into space we can see light from the distant past, which allows us to analyse the conditions in the more distant past, which also confirm the hypothesis that the universe used to be expanding at a decelerating rate as the observed supernovae are brighter than expected.



The cosmic microwave background (CMB) is another place where we can search for information about dark energy. It is basically the echo of the big bang, and also the most distant phenomenon we can observe with current technology, with a redshift value of over 1000. It is comprised of microwaves which correspond to a temperature of about 2.7 K. Compared with data gathered from baryon acoustic oscillations we can recreate the universe's expansion history.

As standard rulers, cosmological objects can't be uniform enough to serve such purposes. However, by assuming the laws of physics were the same at the start of the universe as they are now, we can use features arising from physical processes in the early universe to set up such a ruler. We can use the large-scale distribution of matter to generate such a ruler. An acoustic wave formed from density fluctuations of matter and photons immediately after the big bang is observed to obtain data.

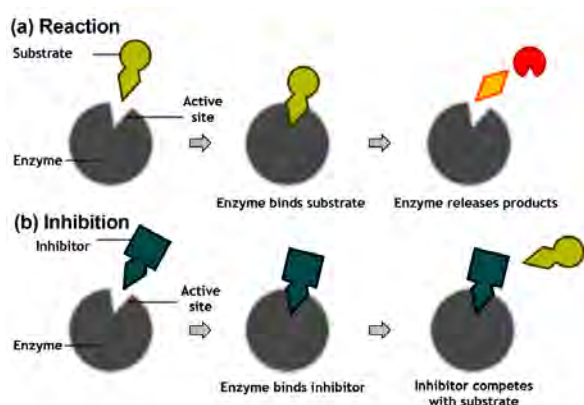
Combining the restrictions of the Λ -CDM Model, data gathered from supernovae, the CMB, and Baryon acoustic oscillations, the current best fit value for Ω is $\Omega_m=0.3$ and $\Omega_\Lambda=0.7$ adding to a total of 1, meaning that the universe is flat and will continue to expand at an accelerating rate. With this expansion, in future galaxies will be redshifted so much that they will not be detectable in the electromagnetic spectrum, so our time for gathering data is limited.

The theory of dark energy has its flaws, and other alternate theories exist, but to find out more about dark energy, more accurate data from improved instruments will be needed. NASA has launched the Joint Dark Energy Mission to make more observations, and the successor to the Hubble Space Telescope will be able to observe supernovae with redshifts 5 times the current limit. Until we have better data, dark energy remains one of the most perplexing conundrums in the universe.

Enzyme Inhibition

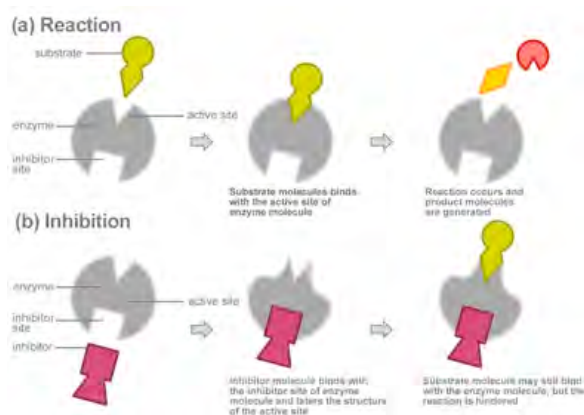
Ohis Ojo

Enzymes Inhibitors are small molecules prevent enzymes from catalysing reactions, reducing the rate of enzyme controlled reactions. They do so by binding to specific parts of the enzyme, preventing the active site from accepting the substrate or preventing it from breaking down (or building up) the substrate. There are 2 Types of Inhibitor. Reversible inhibitors bind to enzymes with non-covalent interactions such as hydrogen bonds and ionic bonds. These multiple weak bonds between the inhibitor and the active site combine to produce strong and specific binding – preventing the enzyme from forming any enzyme-substrate complexes; therefore it is unable to catalyse reactions.



Competitive inhibition is a form of reversible inhibition. This form of inhibitor binds to the active site of an enzyme non-covalently due to the fact that the shape of the inhibitor is structurally similar to the substrate. However when an enzyme enters the active site, it doesn't react with the enzyme – therefore the enzyme is unable to catalyse reactions – reducing the rate of reaction. However, the enzyme-inhibitor complex formed is unstable – hence it is reversible. This form of inhibition can be reduced by increasing the substrate concentration because the substrate competes with the inhibitor for the active site. One enzyme affected by is competitive inhibition is Succinate dehydrogenase, an enzyme present in all mammalian mitochondria. This enzyme catalyses the

8th step of the Citric acid cycle, also known as the Krebs cycle. The citric acid cycle which is involved in the chemical conversion of carbohydrates, fats and proteins to produce usable energy. It is also involved in the electron transfer chain is basically the process that cells produce ATP. The specific step that succinate dehydrogenase catalyses is the oxidation of succinate to fumarate and reduction of ubiquone to ubiquinol. However this enzyme, central in inhibited by the malonate ions, because the chemical shape of the inhibitor is very similar to that of the succinate. The only difference between the Malonate ion and succinate is the, lack of a double CH₂ bond in the centre of the ion. Therefore the inhibitor can enter the active site of the enzyme however; no chemical reaction will take place. The enzyme is just held in the active site by ionic and hydrogen bonds. However this inhibition is only temporary it can be out competed by the succinate ions for the active. Therefore increasing the substrate concentration reduces the effect of enzyme inhibition.



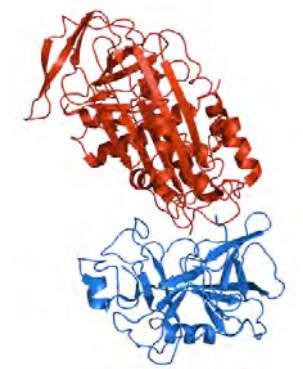
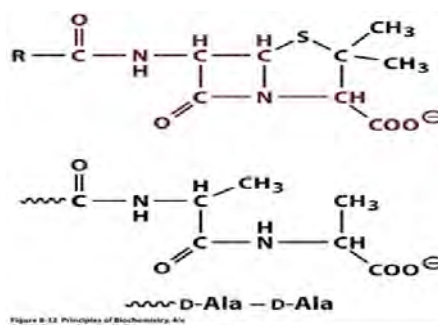
Another form of reversible inhibition is non-competitive inhibition. This is a special form of Mixed Inhibition because the inhibitor can bind to free enzyme or an enzyme-substrate complex. Normally they do not bind to the active site of the enzyme. Non competitive inhibition alters the globular structure of the enzyme (by binding to the polypeptide chain, disrupting the hydrogen and ionic bonds that hold the tertiary structure of the enzyme together) or binding to the prosthetic group (a non protein group associated with an enzyme required for it to catalyse reactions). The effect of inhibition cannot be decreased by increasing substrate concentration because the inhibitor is not competing with substrate for active site; therefore the enzyme is

unable to catalyse the reaction. This type of inhibition reduces the maximum rate of an enzyme controlled reaction without altering the affinity of an enzyme to a substrate. Cytochrome c Oxidase is an enzyme that is

affected by non-competitive inhibitors. This enzyme is involved in the final stage of the electron transfer chain. One of the prosthetic groups crucial to the enzyme is one of its 2 heme groups called heme a₃ and the Cu B centre. Cyanide has a high affinity for certain metallic complexes such as those present in the copper and heme groups. The cyanide ion can rapidly combine with the heme group a₃ or the copper prosthetic group, forming an ionic bond with the prosthetic group – therefore the group is prevented from transferring the electrons to the binuclear centre. Inhibiting this enzyme prevents intracellular oxygen operation. Therefore they respire anaerobically, leading to lactic acid build up which is toxic to cells.

Another form of Enzyme Inhibitor is irreversible inhibition. This form of inhibitor covalently changes an enzyme. When they bind to the enzyme they do not destroy the structure of the enzyme, they specifically alter the shape of the active site, therefore enzyme substrate complexes cannot be formed. They usually do so by reacting with the –OH and –SH groups. However, the effects of Irreversible Inhibition are decreased by increasing substrate concentration. Suicide Inhibition is a type of Irreversible Inhibition.

This form enters the active site of an enzyme, initially forming a non-covalent enzyme-inhibitor complex. It is then modified by enzyme to produce a reactive intermediate group that reacts irreversibly to form a stable enzyme-inhibitor complex, leaving the enzyme covalently inactive. Penicillin is a famous example of a suicide inhibitor. The enzyme it inhibits is serine type d-ala-d-ala carboxypeptidase. This enzyme is involved in the synthesis of the peptidoglycan cell wall – it cross linking of different peptidoglycan strands in order to make the new peptidoglycan layer strong enough to prevent osmotic lysis. Penicillin enters the active site because it is of similar shape to the d-ala-d-ala end of the peptide the enzyme binds to. In the active site it is converted it into an intermediate which irreversibly binds covalently to the Ser₄₀₃ residue of the active site. This irreversible inhibition prevents the final cross linking of the nascent peptidoglycan layer, disrupting cell wall synthesis, because the d-ala-d-ala substrate is unable to enter the enzyme active site. This means that, not only is the bacterium unable to divide and it is also suspect to osmotic lysis.



Alpha 1-antitrypsin (A1AT) is glycoprotein produced in the liver. One of its functions is to protect the lungs from the neutrophil elastase enzyme (a serine protease), which can disrupt connective tissue by breaking down the protein elastin. The reactive centre loop of alpha-1 antitrypsin extends out from the body of the protein and directs binding to the target protease. The protease cleaves the serpin at the reactive site, establishing a covalent linkage between the carboxyl group of the serpin reactive site and the serine hydroxyl of the protease. The resulting inactive serpin-protease complex is highly stable. Although A1AT is a protein, it avoids being hydrolyzed as a substrate by the protease by excluding water from active site and destabilizing the transition state and forming a stable enzyme inhibitor complex. Alpha-1-Antitrypsin deficiency is a genetic disorder caused by defective production of alpha 1-antitrypsin. Symptoms of alpha-1 antitrypsin deficiency include shortness of breath and wheezing. A1AD also

causes impaired liver function in some patients and may lead to liver failure. It is treated by avoidance of damaging inhalants, by intravenous infusions of the A1AT protein, by transplantation of the liver or lungs.

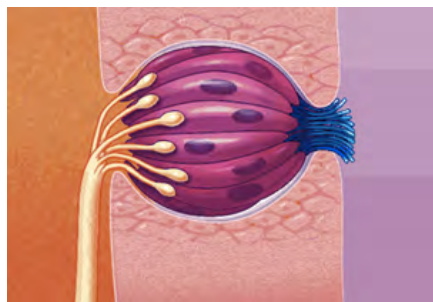
Animals and plants have evolved to synthesise a vast array of poisonous products including peptides and proteins that can act as inhibitors. Natural toxins are usually small organic molecules and are so diverse that there are probably natural inhibitors for most metabolic processes. These natural toxins include α -Amanitin which is found in several members of the *Amanita* genus of mushrooms. RNA polymerase II is the enzyme affected by α -Amanitin. It found in eukaryotic cells and it catalyses the transcription of DNA to synthesize precursors of mRNA which is a template for the synthesis of proteins by ribosomes and microRNA which is involved in gene silencing. Alpha amanitin interacts with the bridge helix in RNA polymerase II forming a strong hydrogen bond. This interaction interferes with the translocation of RNA and DNA needed to empty the site for the next round of RNA synthesis. Diarrhoea and cramps are the first symptoms. Typically, on the 4th to 5th day has severe effects on the liver and kidneys, leading to total system failure in both. Death usually takes place around a week from ingestion.

The Biochemistry of Taste

Glen Gowers

Taste is perhaps the most important sense of all. Warning us of potential poisons and guiding us towards foods we need most. Thus we can expect the mechanisms for taste to be complex and intricate. There are two components to our perception of flavour, olfaction and gustation (more colloquially smell and taste).

The gustatory and olfactory receptors seem very similar at first glance as they both recognize the concentration and type of dissolved molecule in the extracellular fluid. After recognition they both communicate this information to the Central Nervous System (CNS). However, when looking closer the receptors are very different. Olfactory receptors are simply neurons, while gustatory receptors are modified epithelial cells that synapse onto sensory neurons.



Taste Receptor Cells

Taste receptor cells, in clusters known as taste buds, are mainly located on the upper surface of our tongue, however they are also found numerous further down the throat, on the roof of the mouth and even in the trachea which holds new possibilities on asthma treatment (as a bitter stimulus relaxes muscles lining the trachea). The buds are located on projections, much like villi, called papillae. There are three different shaped papillae called Foliate, Circumvallate and Fungiform. Each papillae holds many clusters of taste receptor cells, within each cluster there are between 50-150 taste cells, many basal cells and supporting cells, in addition each taste bud has a set of afferent sensory axons to transmit information about the stimuli. The chemically sensitive part of the taste receptor cell is a small apical-membrane region near the surface

of the tongue. Tastants are categorized into 5 separate categories, each contributing to the foundation of each flavour.

Olfactory Receptor Cells

A thin epithelial layer of cells contains the olfactory receptor cells. When we breathe in, or indeed in the case of this talk have food in the mouth, odorants waft between layers in the nasal cavity. However for transduction to occur they first dissolve in the nasal mucus. The mucus contains glycosaminoglycans, proteins (including antibodies which prevent the entrance of viruses or bacteria who seek a direct link to the brain), odorant binding proteins (to facilitate the diffusion of odorants through the mucus) and enzymes (which clear the mucus of odorants, speeding recovery of receptors from transient odors). Each odorant stimulates a unique pattern of neurons. In contrast all tastants stimulate the same neuron. Thus we perceive 'bitter' without the ability to discriminate between cyclohexamide and quinine (by this analysis, if we had no olfactory mechanisms, an apple would be undistinguishable from an onion if bitten into!).

Olfaction receptors

The odorant binds to a specific olfactory receptor protein in the cell membrane of a cilium of a receptor cell. The receptor activation stimulates a heterotrimeric G protein called G(olf). The alpha subunit of the G(olf) protein in turn activates adenylyl cyclase which produces cAMP. The cAMP binds to a cAMP-gated cation channel. Opening the channel increases the cells permeability to Na⁺, K⁺ and Ca²⁺ ions. The influx of these ions causes an inward current leading to membrane depolarization (which opens Ca²⁺-activated Cl⁻ channels). The inward current of the Cl⁻ ions further depolarizes the cell membrane as Cl⁻ ions move down their electrochemical gradient out of the cell. If the receptor potential exceeds the threshold an action potential is triggered in the soma, which travels down the axon directly to the brain. It is the pattern of the receptor cell activity that signals the identity of specific smells.

Salt Tastant mechanism for Transduction

The mechanism for the transduction of the salt tastant (Na⁺) is the simplest of the mechanisms. Salt sensitive taste cells have an Na⁺ selective channel called ENaC. This receptor is common to many epithelial cells and is blocked by the widely used drug Amiloride. Unlike voltage gated sodium ion channels involved in axon potential propagation these channels are unaffected by depolarization of the cell membrane. When we ingest food the concentration of Na⁺ ions outside the cell increases, Na⁺ diffuses down its electro-chemical gradient. This resultant inwards current causes a membrane depolarization to a new voltage (from -60mV to about +40mV!). The new polarization of the taste cell is defined as its receptor potential. As well as cations affecting saltiness, evidence suggests the cation's paired anion does too. For example NaCl taste saltier than sodium acetate. Suggesting the larger anion is the greater its inhibition to the ENaC receptor.

Sour Tastant mechanism for Transduction

Sourness is the measure of acidity and by definition the concentration of H⁺ ions. Sourness is evoked by these protons in two ways. Firstly the ion can penetrate the ENaC channel involved in the transduction of Na⁺ ions. The H⁺ influx is an inward current and subsequently has the same depolarizing effect as previously mentioned in Na⁺ transduction. Secondly the protons can block a K⁺ ion channel. The fall in K⁺ permeability results in a membrane depolarization. In addition to this, if the sourness is great enough the concentration of H⁺ ions causes a significant drop in the

extracellular pH causing conformational changes to ion channels, which changes the permeability of the cell to ions thus depolarizing the cell.

Sweet Tastant mechanism for Transduction

A tastant (e.g. Sugar molecule) binds to a 7-transmembrane receptor of the taste cell membrane. This activates heterotrimeric G protein, stimulating adenylyl cyclase, which increases the amount of cAMP (cyclic adenosine monophosphate), and activates PKA (Protein Kinase A) which subsequently phosphorylates (closes) a K⁺ ion channel. The resulting depolarization opens voltage gated Ca²⁺ channels increasing concentration of Ca²⁺ ions, leading to transmitter release.

Bitter Tastant mechanism for Transduction

Bitterness has an evolutionary stance in warning of poisons. Perhaps because poisons are so diverse there are several mechanisms for the transduction of bitter tastants (e.g. Calcium or quinine). The first mechanism involves a bitter compound directly inhibiting K⁺ ion channels, as in previous mechanisms, this causes a membrane depolarization. Leading to a transmitter release. The second mechanism involves a ligand binding to the 7-transmembrane receptor and activates a G protein "Gustducin" which stimulates phosphodiesterase, this forms AMP from cAMP. The reduction in cAMP leads to the depolarization of the membrane. The third mechanism involves another ligand binding to a receptor linked to a G protein, activating phospholipase C. The resultant increase in IP₃ (inositol 1,4,5-triphosphate) releases Ca²⁺ ions from the stores in the endoplasmic reticulum, raising the internal concentration of Ca²⁺ which leads to the transmitter release.



Umami/Savory Tastants mechanism for Transduction

The savory taste is generated when glutamate (or other similar amino acids) binds to a glutamate-gated nonselective cation channel and opens it. The resultant depolarization opens voltage gated ion Ca²⁺ channels. This stimulates transmitter release. Glutamate may also activate a particular subtype of metabotropic receptor and thus lead to a decrease in cAMP concentration. Other amino acids do taste bitter though (leucine for example) and they trigger either cAMP or IP₃ mediated messenger systems.

Release of neurotransmitters leading to an action potential in the afferent sensory neuron

The above mechanisms were all temporarily left hanging in description with the release of neurotransmitters. Now all the described mechanisms coalesce for the uniform ending that is the action potential propagation to the brain. With the depolarization of the taste cell which stimulates the release of neurotransmitters the action potential must now cross the synaptic cleft to the afferent neuron. The influx of Ca²⁺ ions trigger the exocytosis of neurotransmitter-filled vesicles. Experimental support for this has come from studies using aequorin, a protein that emits light when exposed to Ca²⁺. If aequorin is introduced into the taste cell, light is emitted at the synaptic cleft each time the cell transmits a nerve impulse, indicating an increase in cytosolic Ca²⁺ concentration. There are two pools of neurotransmitter vesicles, the first is the releasable pool bound to the inner surface of the plasma membrane, the other is the reserve pool attached to the cytoskeleton by the protein synapsin. The entry of Ca²⁺ ions stimulates a Ca²⁺ calmodulin-dependent protein kinase which catalyzes the phosphorylation of synapsin. This disrupts its ability to link vesicles to the cytoskeleton so more join the releasable pool hence the number of discharging vesicles increases and so making synaptic transmission more efficient.

The Neurotransmitters are expelled from the pre-synaptic cell (stimulated by the increase in Ca²⁺ permeability) they diffuse across the synaptic cleft and bind. It has been researched and found that, primarily, serotonin is used as the main neurotransmitter in chinese mice taste cells, suggesting its use in human taste cells. The influx of Ca²⁺ ions cause a conformational change in the tertiary structure of a temporary protein linking synaptic vesicles to the plasma membrane. The conformational change opens the protein channel and releases serotonin. The vesicle and plasma membranes then fuse. Serotonin diffuses across the synaptic cleft and binds to 5-HT receptors (5-hydroxytryptamine) which are ligand gated ion channels. The channels open and allow Na⁺ ions to flood into the post synaptic cell. This depolarization opens voltage gated ion channels to open, further flooding the neuron with ions. This influx surpasses the threshold and triggers an action potential. After the action potential the Ligand (serotonin) dissociated from the ion channel and is taken up by the presynaptic cell by active transport and is re-used as a neurotransmitter.

Once the action potential has been triggered the signal must be propagated along the axon. A local flow of electric current is induced that alters the membrane potential in surrounding areas of the membrane. This opens voltage gated ion channels causing an influx of Na⁺ ions. The influx of ions then causes the channels to close and the K⁺ voltage sensitive channels to open. K⁺ now flows out of the neuron, bringing the membrane potential back to its resting state. The cycle is repeated along the neuron. The refractory period. During this period Na⁺-K⁺ pump uses ATP to fully restore the resting potential. This period lasts about 10 milliseconds which results in a limit to the frequency with which neurons can transmit impulses.

Regeneration

Ross Hendron

Regeneration is the ability to re-grow lost or destroyed tissues in an organism. The benefits of this talent are colossal; regenerated tissues show no scarring, so the regenerating individual can repair itself to full former health and this may be crucial for the future survival of the organism. Radically different animals boast such ability, and through observing their methods of regeneration it is possible to study this unusual process in detail.

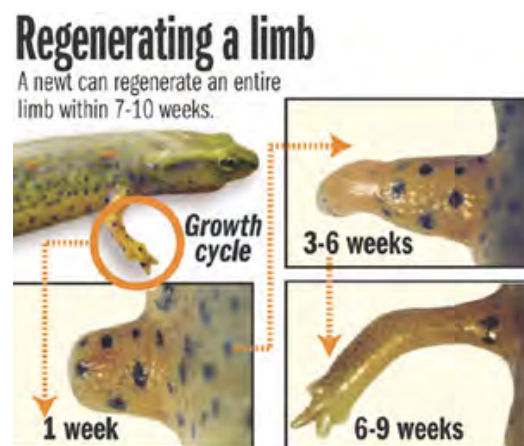
The concept of regeneration may remind some people of rumours and suspicions they had as children that if a worm is cut in half two more would grow back from the pieces. This is in fact false; however some species of earthworm for example will grow back the entirety of their body if just a small section of the head containing the vital organs remains intact. Jellyfish too, are renowned for the ability to regenerate their bodies back from devastating damage, however both annelids (segmented worms) and cnidarians (jellyfish) are invertebrates and therefore their unspecialised structure is hard to relate to humans, which is why it is more intriguing to look at vertebrates that are capable of regenerating the mess of muscles, organs, blood, fat, bone and nerves that together can make a healthy animal.



One of the most popular animal classes studied for their regeneration secrets are the amphibians. One particular species, *Ambystoma Mexicanum* – otherwise known as the Axolotl, draws particular interest. As if having large exposed red gills and a cheeky looking face wasn't enough, the Axolotl possesses extraordinary regeneration powers too.

For example, losing a limb at its base would usually be enough to doom an organism; however amputation is only the start for the axolotl. Nerve deviation triggers cells such as dermal fibroblasts surrounding the damaged site to dedifferentiate, meaning that they revert back to a stage of pluripotency, observed in stem cells last seen in that limb at the foetal stage when the appendage was first generated. The result is a blastema, a bump of stem cells, which rapidly covers the wound. The cells of the blastema then divide and differentiate into muscles, skin, bone, nerves and blood vessels as required, and a new functioning limb can be grown in a matter of weeks from the proximal base to the fingertips using only the remaining cells of the old limb. This final stage of redevelopment is identical to the one observed in embryonic development.

This type of regeneration is important for quickly allowing an organism such as a lizard or salamander to recover from predator attacks. In fact it is necessary for some who use transvertebral autotomy to escape their larger foes: When gripped by the tail some organisms can contract muscles which are designed to snap the weak tail bones they surround, thus breaking off their own tail. The separated tail will continue to writhe around, temporarily disorientating the predator enough to allow for the organism to escape. Regeneration begins immediately afterwards; a blastema forms to seal the wound preventing blood loss and ensures survival for the organism. Meanwhile the predator enjoys a consolation snack for its efforts.



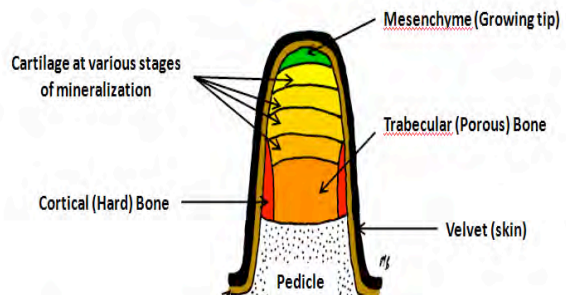


The Irish Elk (Megaloceros Giganteus) is now extinct but its antlers are to this day unmatched in size - together reaching 3.6m wide.

Of course we are not amphibians. We mammals seem to have evolved without the need to regenerate - though there are of course exceptions. Every spring, deer also take part in a ritual of re-growth. Antlers serve as an iconic symbol of the stag. Larger antlers can intimidate weaker stags and will deliver more damage if a fight must determine the dominant male. The size of the antlers usually indicates how healthy the stag is, and large antlers are used to help attract a mate. Following the mating season these structures are shed, only to be re-grown for the next mating season. Taking the fallow deer as our model, the mass of the antlers can average at 2kg, were we to take the now-extinct Irish Elk instead this mass would be closer to 40kg, truly a staggering amount of tissue to regenerate every year - especially when you appreciate that these bone antlers are organs filled with intricate blood vessels. Every year a stag will regenerate larger antlers than before with more branches signalling its experience and maturity.

Following the mating season, as the day length increases, testosterone levels in the stag decrease. This hormonal change serves as a chemical signal to prepare the body to shed the antlers. When the antlers are cast from the head at the pedicles, which is where the head meets the root of the antler, the surrounding skin is raised to form a wound epithelium. This covering shows similarities to the blastema previously described, but we must be careful not to confuse axolotl limb regeneration with antler regeneration. The key difference is that no cells dedifferentiate in antler re-growth; instead the blastema is formed of mesenchymal cells already present in the deer's tissues. These cells are also known as multipotent stem cells and are simply undifferentiated cells. They will develop to form distinct growth zones as the antlers enlarge and split into separate tips.

A large volume of oxygen must be supplied to the growing organs to meet the high metabolic demands of rapidly regenerating tissues as they require lots of energy and therefore must respire more. This is why antlers have a need for many blood vessels rapidly growing alongside the bone and cartilage.



As the diagram shows, the mesenchyme layer remains on the antler tip where growth occurs as stem cells continue to differentiate and divide. From the base to the tip cartilage mineralises to form strong bone. As with all fully-formed bones, a dense cortical layer surrounds the porous trabecular centre. The velvet that grows with the antler will be cast off when re-growth is complete revealing the finished bone underneath.

This dramatic seasonal cycle has given rise to the need for deer to grow back their antlers quickly, just as how being vulnerable to predators has induced a selective pressure for salamanders to evolve a regeneration process. Humans lack both of these selective pressures and therefore have not needed to evolve to be able to regenerate, despite the wealth of opportunities human regeneration poses.

In recent experiments with mice, some strains have under certain conditions been able to regenerate ear cartilage. Such promising results spark hope that one day regenerative medicine for humans will be advanced enough to regenerate entire organs or amputated limbs. Until then, we are left to marvel at the lowly earthworm beneath our feet, and envy the power of regeneration.

Past Moncrieff-Jones Society Presidents and Vice-Presidents

2007 - 2008

President Luke Bashford
Vice-President Edd Simpson

2008 - 2009

President Tonya Semyachkova
Vice-President Raphael Zimmermann

2009 - 2010

President Alex Hinkson
Vice-President Alex Clark

2010 - 2011

President Oliver Claydon
Vice-President Sally Ko

Past Moncrieff-Jones Society Endorsers

Dr Jan Schnupp, lecturer in Department of Physiology, Anatomy and Genetics at Oxford University.

Dr Bruce Griffin, professor at Surrey University, specialising in lipid metabolism, nutritional biochemistry and cardiovascular disease.

Dr Simon Singh, author and science writer.

The Moncrieff-Jones Society

“The Moncrieff Society was founded by John Jones in 1967, as a ‘liberal science society’ - its mission to address a gap in the range of 6th Form societies. Sir Alan Moncrieff was an eminent Old Caterhamian in the medical field and John Jones was a Head of Chemistry at Caterham School for many years. The Society was renamed the Moncrieff-Jones Society in the year that John Jones retired, as a way of recognising the massive contribution John made to Science at Caterham School.

True to the liberal spirit in which the Moncrieff Society was formed, meetings over the years have included the reading of scenes from Brecht’s *‘Life of Galileo’*, an exploration of the works of Leonardo da Vinci and even an entertainment based on scientific themes. Individuals have spoken on interests as diverse as cell biology and thermodynamics, and intellectual *tours de force* have ranged from the quantum world of the very small to the vast sphere of astrophysics.

We live in an age of Science. There has never been a greater time to study Science and with the massive problems the world faces, it is through science that we look for solutions. It is a testimony to the input of so many generations of Caterhamians that the society survives and thrives some 44 years on.”

Dan Quinton is Head of Science at Caterham School





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