King's College London Neuroscience Society

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Neurosphere

NEUROSOC
KING'S COLLEGE LONDON

Death and Rebirth

Featuring KCL's Multi Award Winning iGEM Team

Neuro-degeneration
The Race against Time

Neuro-regeneration
When Old meets New

Cover Art: Hamaad Khan

Editors' Welcome

No man is an island entire of itself; every man is a piece of the continent, a part of the main;
- John Donne, 1624

As John Donne highlighted almost 500 years ago - everything is interconnected. Indeed, our field of neuroscience is ever moving, and we are increasingly beginning to appreciate that neurons in the brain don't operate in a vacuum. From pre-natal to child, and adult to aged, there exists a constant multi-factorial interplay that ultimately sculpts our brains, and makes us who we are. Perhaps it is this very juxtaposition between our magical perception of existence and the rigidity of our biological underpinnings, that makes neuroscience so appealing to so many.

Our advancing societies bring with them advanced healthcare and standards of living, but now we are faced with a new challenge: the aging population. With age, our brains deteriorate through a multi-factorial process of neurodegeneration, and the race is on to elucidate why, and how we might stop it. However, our advancements in science are also yielding new multi-disciplinary interventions for conditions with critical nervous system damage, specifically by regenerating the neurons, to restore our bodily and mental faculties.

In this second edition of *Neurosphere*, brought to you in collaboration with King's College London's award winning iGEM team, we are taking on the theme of death and rebirth by exploring the current state of research in neurodegeneration and neuro-regenerative medicine. We hope you enjoy it!

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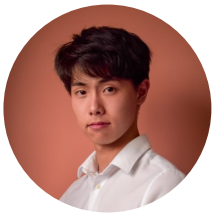

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President's Welcome

Modern neuroscience spans an ever growing number of domains and more than ever calls for collaboration. In the public eye neuroscience is seemingly uncovering secrets to some of the greatest quandaries, but the reality is that we are still many light years away.

The Neuroscience Society of KCL aims to expose these truths and establish a network of thought, discussion and education. This year each member of the committee has worked hard to develop these goals in spite of the limitations. I am grateful to every one of them.

We have also established a digital space to curate contributions from members beyond the committee. Thank you to all those who have submitted their ideas and writings as these generate further thought and progress. This magazine is the spearhead of this initiative, and I hope that future issues will continue to gather work from a wide range of thinkers - neuroscientists, philosophers, medics and beyond..!

Join Us!

If you would like to join the Neuroscience Society, please visit:

www.kclsu.org/groups/activities/join/7254/

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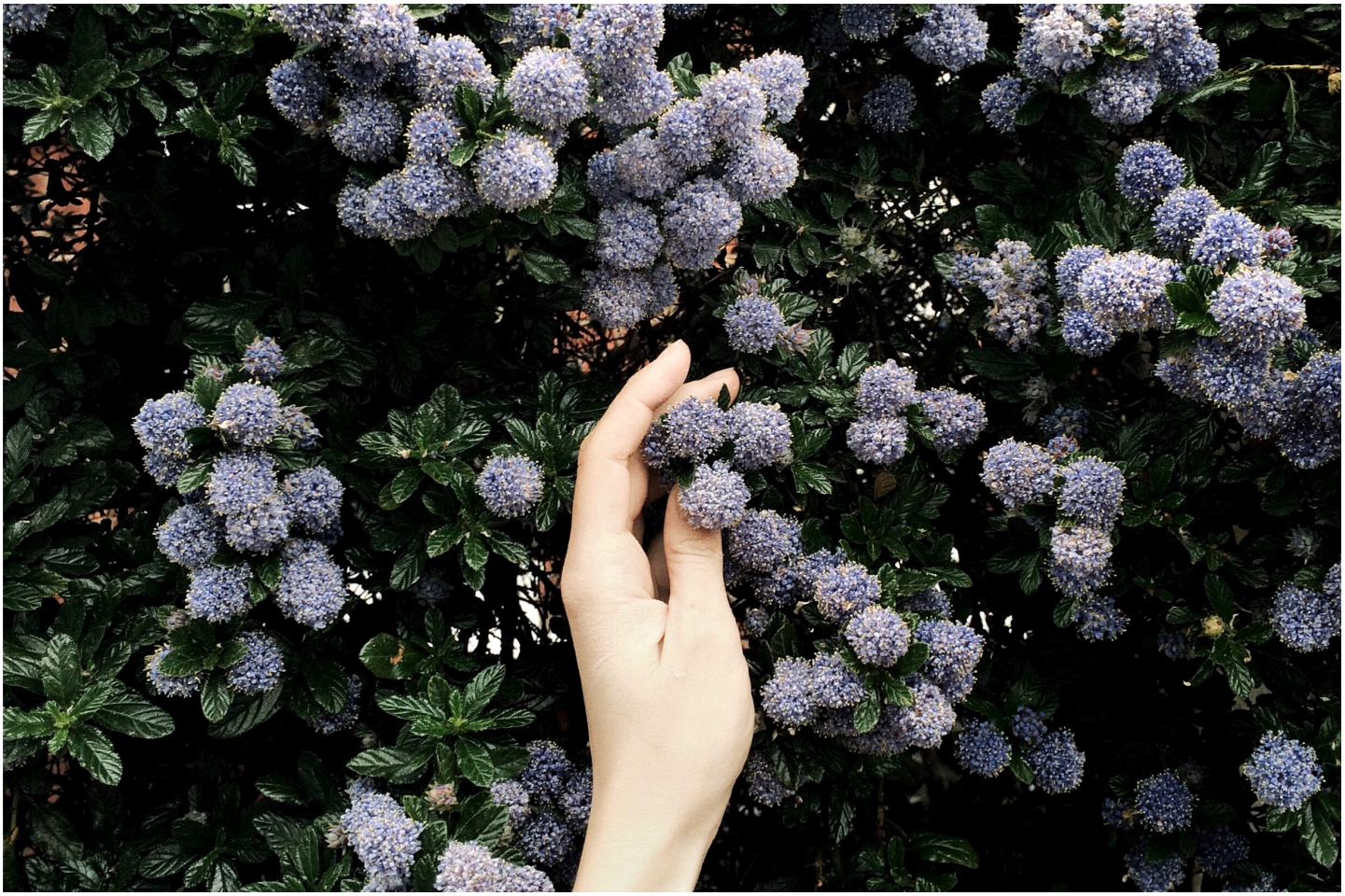
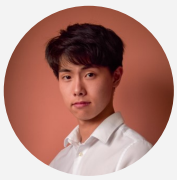
Neurodegeneration



“Microglia-Mediated Synaptic Loss in development and degeneration”



Daniel Shao
MSci Neuroscience

In preparation for a lifetime of the new and unexpected, the brain employs a stratagem of over-production in development, creating double the number of synaptic connections per neuron compared to a matured brain[1]. Yet, only a fraction of these synaptic connections survive through maturation to adulthood[2]. New research has implicated microglia, the brain’s resident phagocytic immune cells, as critical enactors of targeted synaptic elimination in both normal development and aberrant neurodegeneration.

Synaptic pruning is the targeted elimination of supernumerary synaptic structures by microglia during development[3]. This is a critical process in optimising neural wiring and in defining overall brain architecture, with microglia pragmatically removing connections and subsequently apoptosed neurons on a use-it-or-lose-it basis[4]. Thus, microglia act to fundamentally restructure the brain by permanently disconnecting under-utilised circuits, whilst promoting the stabilisation and myelination of high-value circuits. In this way, the brain is specially -tuned based on the environment and experiences that it finds itself in[5]. It is now understood that synaptic pruning is a process that continues throughout childhood and adolescence and may be responsible for the high levels of plasticity in early life[5].

However, this same mechanism of synaptic pruning has been implicated in a plethora of conditions and disorders[6]. Aberrations in synaptic pruning in development are now understood to be linked with autism and schizophrenia – conditions that appear to

manifest during periods of prominent synaptic pruning[7-9]. Conversely, aberrant reactivation of synaptic pruning in later life appears to contribute to the excessive loss of synaptic structures seen in many neurodegenerative conditions – most prominently in Alzheimer's disease[10,11]. Indeed, the presence of microglia around Alzheimer's characteristic amyloid plaques is a noted occurrence[11], and many of the risk genes linked to Alzheimer's are expressed in or depend on microglia for their expression – potentially acting through the immune system's complement pathway to erroneously eliminate healthy connections[10]. This presents microglia and dysfunctional autophagy as a potential key component in a range of disease mechanisms, and further investigation may yield new therapeutic strategies for future remediation[10-12].

In short, microglia and their role in synaptic pruning is critical to the development and maturation of synapses and neuronal networks, and ultimately in defining fundamental brain wiring and overall brain architecture. Although exact mechanisms are yet to be elucidated, aberrant microglial involvement in a multiplicity of conditions presents a novel approach for understanding and potentially treating these conditions.

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"APOE, Astrocytes, and Alzheimer's Disease: The Link of the Century"

Samah Sabreen
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Alzheimer's Disease (AD), a progressive brain disease, is a leading cause of disability and dependency among the elderly with an estimated 28.8 million human years lost to disability[1]. Prior research has primarily focused on the protein hallmarks of AD such as amyloid beta and tau[2], but recently the role of glia in synaptic loss is increasingly gaining attraction. Particularly astrocytes, once thought to be key homeostatic regulators of the brain, are implicated in synaptic loss – a primary correlate of AD. They are now understood to play a critical role in the pathological mechanisms underlying AD, a promising new avenue and non-neuronal approach for AD research.

Astrocytes, named for their stellar appearance, are currently understood to have a role in structural neuronal support and local homeostasis by regulating ion concentrations and neurotransmitters[3-5]. However, emerging evidence reveal astrocytes have a far more involved and invasive role in regulating synaptic health, particularly through phagocytic mechanisms found within the brain's immune response[6]. Phagocytosis is a highly regulated process in which threats such as pathogens and debris are eliminated to maintain neural circuitry development[7]. It is mainly thought to be performed by microglia, the resident macrophages of the brain, but is now known to be also exhibited by astrocytes[8] – particularly when compensating for microglial dysfunction[9]. Certainly, astrocytic phagocytosis naturally becomes impaired with age, however, there is evidence to suggest this impairment becomes accelerated with the influence of risk genes such as the APOE gene[10].

The APOE gene is among the most studied genetic risk factors for AD[11]. The APOE gene codes for apolipoprotein E, a lipid transport protein predominantly produced by astrocytes, and has 3 alleles (epsilon 2 (ε2), epsilon 3 (ε3) and epsilon 4 (ε4)) – with APOE-ε3 being the most common[12]. The APOE

-ε2 genotype, is understood to be protective against AD whilst the ε4 allele is known to increase risk for AD by up to 12-fold in the presence of 2 copies of the ε4 allele[13]. One leading interpretation is that the APOE genotype affects the rate of synaptic pruning by astrocytes[10]. Pruning is a process by which surplus and non-functional synapses are eliminated for efficient functioning of neural networks and overall maintenance of brain architecture[14,15]. Dysregulation of synaptic pruning may provide more insight into studying synaptic loss in AD, potentially serving as a target for intervention.

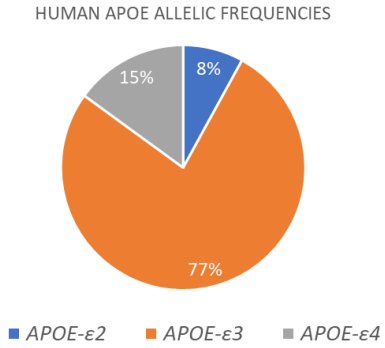

Fig. 1 *Pie Chart of APOE allelic frequencies.*

The link between APOE-ε4 genotype and synaptic loss was previously not explicated. Indeed, now it is known that those with this genotype exhibit reduced astrocytic phagocytic capacity, evidenced by the accumulation of non-functional synapses[10]. Furthermore, it is understood that this accumulation allows for the subsequent aggregation of C1q, a protein that initiates the complement system by opsonising and marking these synapses for elimination through the immune system[16,17]. Once initiated, a cascade of proteins are activated which subsequently induce mast cells, a type of white blood cell, to release proinflammatory molecules and recruit other immune cells[18]. Thus, the combined effects of age and APOE-ε4 genotype hinder astrocytic synaptic pruning, leading to the hyperactivity of the complement system and ultimately facilitating the loss of functional excitatory synapses - imperative for memory circuitry[19,20].

In conclusion, there is a possible link between APOE, astrocytes and AD pathology. Investigating this interaction further, along with other glial-inclusive approaches to AD research, may yield new breakthroughs that may potentially translate into new therapeutic targets and strategies for AD.

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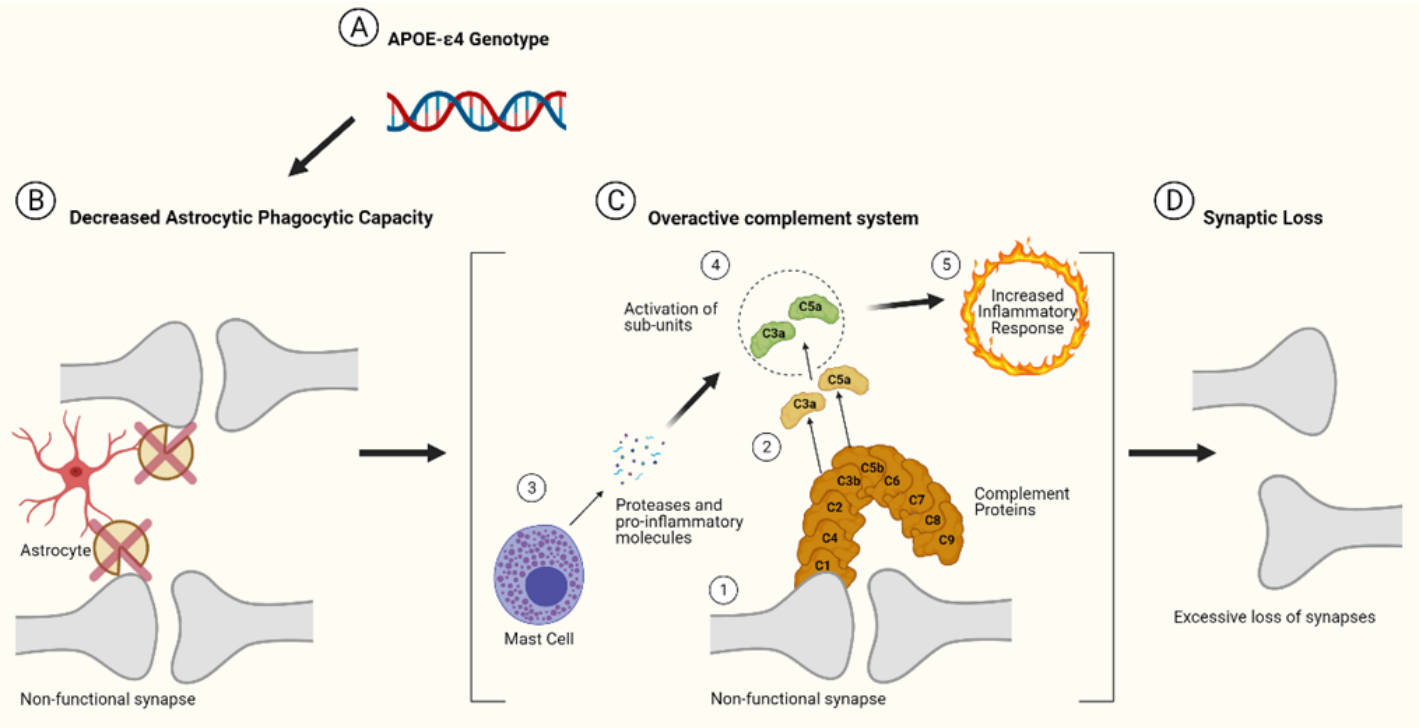

Fig. 2 *Diagram depicting the mechanism of synaptic loss through reduced astrocytic phagocytosis and overactive complement system. Subfigures: (a) depicts the risk genotype APOE-ε4, (b) represents reduced astrocytic ability to phagocytose non-functional synapses, (c) capitulates the hyperactivation of the complement system [1, non-functional synapse opsonisation triggering cascade of complement proteins. 2, subunits of complement proteins C3 and C5 leave the complex. 3, mast cells release proteolytic enzymes and pro-inflammatory molecules which 4, subsequently activates the subunits thus 5, leading to increased inflammation in the area.], (d) increased inflammatory environment leads to excess synaptic loss.*

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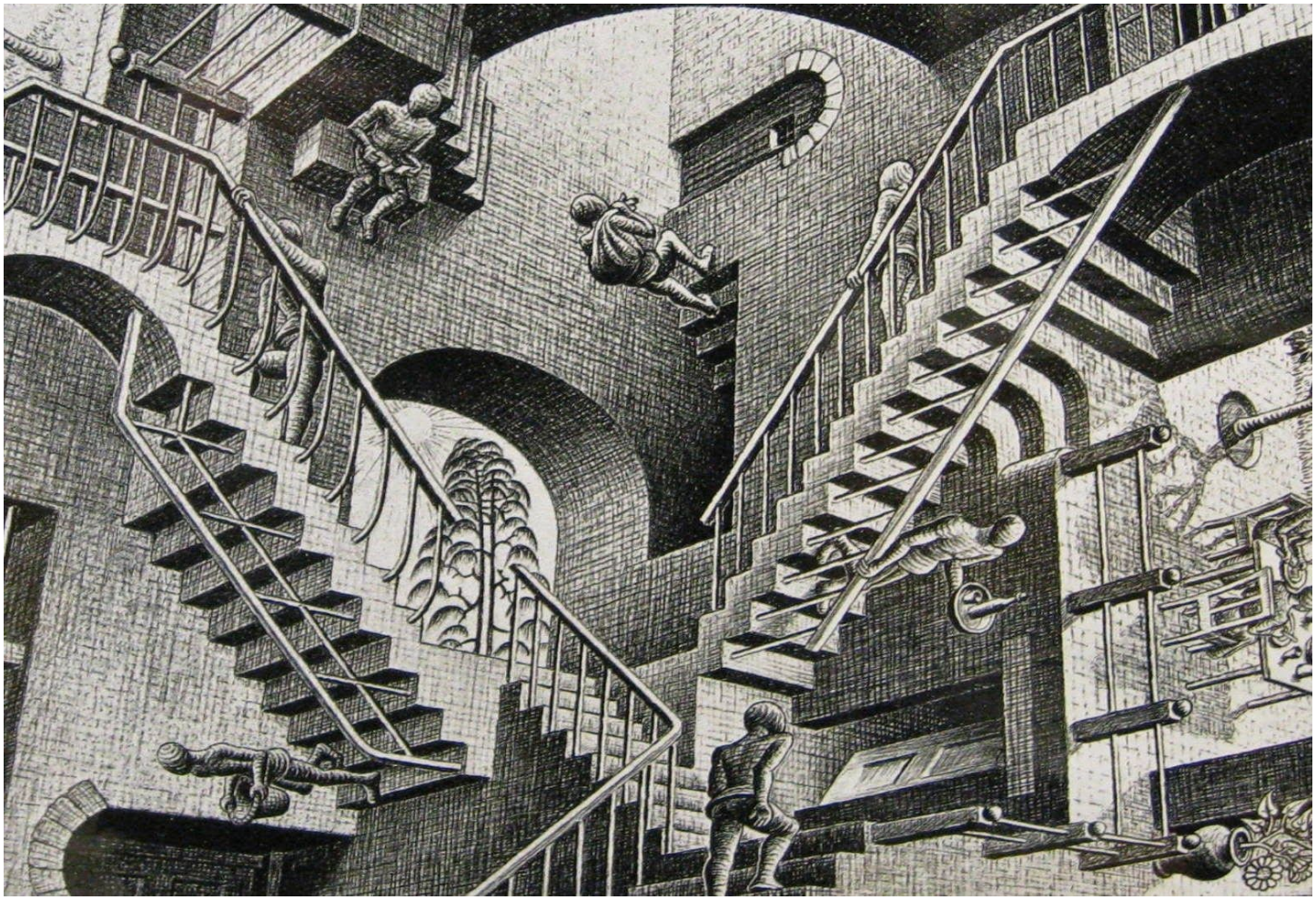
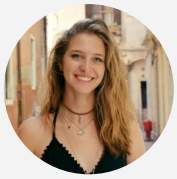


"Multiple Sclerosis: A Case of Chicken Vs Egg"



Vivienne Matthews
BSc Biomedical Sciences

Multiple sclerosis (MS) is a neurodegenerative disease which is characterised by demyelination, which is the breakdown of the protective layer of myelin around axons in the central nervous system (CNS). Additionally, MS is defined by axonal degeneration and activation of the immune system. It is most commonly diagnosed in 20-40 year olds and decreases lifespan by around five to ten years[1]. It is therefore considered to be the neurological condition with the worst life expectancy[2].

This is a multi-factorial disabling neurological disease, and its prevalence as well as the severe effect on patients' quality of life, makes this condition focal in research. However, despite MS being one of the most researched neurological diseases, a key element is still unknown: how MS is initiated.

For years, it has been presumed by scientists that MS is primarily an autoimmune disease, instigated by the inflammatory action on the CNS, which then triggers neurodegenerative cascades. However, evidence for this is conflicting and theories are increasingly opposed as both, neurodegeneration and activation of the immune system, are key aspects of MS and are disease-regulating. An analogy to describe the *'primary neurodegenerative'* argument would be best understood by imagining a superficial cut on a person's skin. In this case there is damage to the tissue, which triggers the immune response, resulting in inflammation, immune cells and protective molecular cascades—a similar inflammatory response is observed in MS. The '*primary immune activation'* argument on the other hand, can be

understood through the example of allergic reactions. The overreaction of the immune system to a foreign substance can, in some severe cases, cause permanent tissue damage — such as in hypersensitivity pneumonitis, which results in permanent lung damage[3].This would be synonymous to the theory that the inflammatory cascade in MS is the primary event, ultimately resulting in neurodegeneration. This example demonstrates the detrimental effect the body's own immune system can cause; with MS being auto-immune this is the assumed pathogenesis accepted by most scientists. However, without clear evidence for either mechanism, the characteristic demyelination of axons in MS is now a topic of controversy as to whether the neurodegeneration triggers an inflammatory effect or vice versa.

Evidence from Genetics

There seems to be a hereditary component to MS as evidenced by twin studies, and higher incidences in Caucasians[4], and women in particular. Research investigating epidemiological data, particularly genetic and environmental risk factors in MS, offers an insight into the potential causes. According to some familial studies, there is insufficient evidence to support a higher frequency of heritable traits linked to immune activation compared to those linked to neurodegeneration exclusively[5]. However, genome-wide association studies (GWAS) have identified an increased risk of MS in gene regulatory networks associated with white blood cells, called CD4+ T-cells[6] which supports the significance of immune activation. The genetic background also makes it a likely causative factor, as the mutation could cause the auto-reactive traits; despite this, it is not conclusive evidence that this is part of the initiation, as it could simply be a contributing factor to this multi-factorial disease.

Evidence from Environmental Factors

Another element of association to MS are the environmental risk factors. Data on environmental influences in MS are more biased, as there have been no well-established links between external factors and direct neurodegeneration exclusively[7]. Whilst not all of the noted environmental risk factors could be explained, some did however, evidence the link to immune activation. The Epstein-Barr Virus (EBV) for example has been associated with increasing risk ins several autoimmune diseases[8] with a potential mimicry mechanism in MS. The theory suggests that foreign EBV-derived peptides could demonstrate some similarity with self-peptides, causing cross-activation of the auto-responsive T-cells. These T-cells could then in turn cascade into the mechanism suggested to initiate MS[9]. A correlation between decreased sunlight exposure or intake of Vitamin D, and increased occurrence of MS has also been evidenced; as deficiency in Vitamin D can increase the risk of relapse in MS[10]. This was a longitudinal cohort-study over 3 years, with 145 relapse-remitting MS participants. Results indicated a strong inverse, linear correlation between 25-hydroxyvitamin-D (25-OH-D) concentrations and the risk of remission. This seems to be a sign that we all need a bit more sunshine in our lives, as it really does help keep us healthy!

Overall, the science behind the primary mechanism of MS remains unresolved. However, it demonstrates how important it is not to become blinded by assumption, as this could lead to a lot of negative results in the future. Most importantly, for the sake of research as scientists and better clinical care for patients, MS is best considered as a multifactorial disease, with many influences from genetics, the environment and its various cascades and phases. Future research should take all of these disease-regulating factors into account and respect that MS is considered a 'snowflake disease', as no two patients are the same.

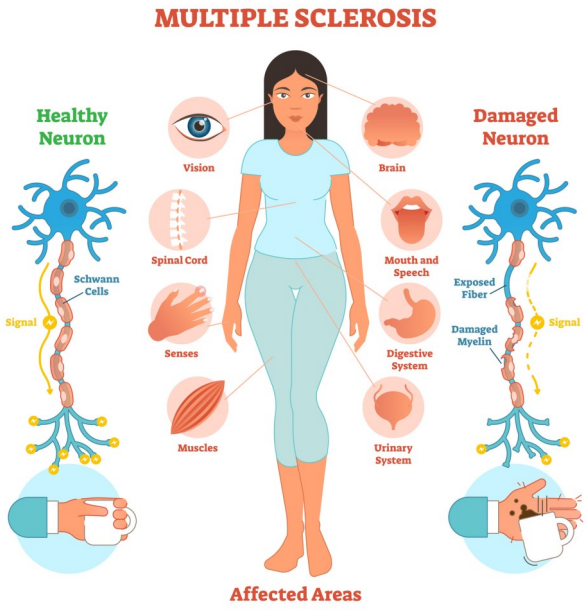


Figure 1: Infographic showing MS symptoms and pathology[10]

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“Kuru: Neurodegeneration by Endocannibalism”

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BSc Psychology

Kuru is a transmissible spongiform encephalopathy (TSE) human prion protein (PrP) disease. Labelled as a ‘slow virus’ and a variant form of Creutzfeldt–Jakob disease (vCJD), kuru is passed on through contamination with, or consumption of, the brain tissue of an infected individual. Typically, this occurs through practices of endocannibalism – a ritualistic mortuary consumption of members of one’s family or community. Interest in kuru was reinvigorated following the outbreak of bovine spongiform encephalopathy (BSE), or ‘Mad cow disease’, in the UK during the early 1990s[3].

Kuru is Fore for ‘trembling’, which is reflected by the shivering tremors that inflict those with the condition. As a PrP disease, kuru causes cerebellar degeneration, which is displayed in infected individuals through impaired motor control, limb weakness, slurred speech, and impaired cognitive function. The condition progresses from this ‘ambulant’ stage into sedentary and terminal stages of the disease within a year of infection[1], and has an incubation period of up to 40 years[3]. The disease has been confined to the Fore people living within mountainous regions of Papua New Guinea. Kuru has predominantly affected women and children, as boys and men older than 6 years of age typically did not partake in the mourning ritual[3]. Cases have been reported from around 160 villages with an approximate population of 40,000 during the height of the disease. From 1957 to 2004, there have been more than 2700 reported instances of kuru, with over 200 deaths per annum occurring in the late 1950s, reducing to less than 5 deaths reported per year during the 21st century.

The Pathogenesis of Kuru

Human prion diseases are associated with abnormal, tangled isoforms of PrP^{3}. Kuru causes vacuolation in

neurons, astrocytes, and oligodendrocytes – creating the characteristic 'moth-eaten' look of TSE-infected brain tissue[1]. However, the presence of the disease does not evoke an inflammatory or immune response in the body, nor does it cause an increase in cerebrospinal fluid protein, as observed in other viruses. Indeed, the tangled PrP isoforms are only present within the brain tissue of infected individuals and have been untraceable in other bodily tissues. PrP diseases are also resistant to ultraviolet and ionising radiation, along with heat[1]. As prion diseases irreversibly denature proteins in the brain, and are thusly resistant to treatment, the main form of prevention is abstention from endocannibalism.

Genetic susceptibilities for kuru have also been identified among people within regions of high prevalence. Previously exposed and surviving individuals tend to be heterozygous for a PrP gene – *PRNP* codon 129, which has been known to affect incubation periods and propensity for developing the disease[3]. However, a variant of the *PRNP* gene, the 127V polymorphism, was found in around 50% of women in a region of historically high kuru incidence – this allele was not present in kuru patients or in people from unexposed populations. There was found to be significantly lower rates of kuru among individuals with the 127V polymorphism, suggesting they have acquired a specialised, protective genetic mechanism against the disease. As prion propagation favours homologous protein-to-protein contact, those who are heterozygous for the gene have resistance to amyloid plaque formation.

The Disappearance of Kuru

In light of BSE, modern research into kuru has demonstrated that neurodegenerative disorders can result from infectious agents and terminally progress as a 'slow virus'[5]. Moreover, findings drawn from kuru research have facilitated further understanding of neurodegenerative conditions such as CJD and Alzheimer's disease (AD); amyloidoses share common pathogenic mechanisms - PrP plaques in kuru form similarly to amyloid plaques and neurofibrillary tangles in AD[5].

Fortunately, the prevalence of kuru has rapidly declined since the banning of endocannibal mourning practices by the Australian government in 1954[3], especially in cases among children and adolescents[1]. However, questions still remain over the origins of this unique and novel disease; was an initial transmission of CJD to Papua New Guinea responsible for the kuru epidemic? Did the disease change into its current form as a result of practices of endocannibalism[1]? Not only could these questions be answered through further research into kuru, but findings from such research may lead to major breakthroughs within the field of neurodegeneration more broadly.

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“Lumbar Puncture: Diagnostic Testing in Neurology”

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MBBS Medicine

A lumbar puncture is a medical procedure in which a sample of cerebrospinal fluid (CSF) is obtained from a patient’s back in order to be analysed[1]. It has been a diagnostic tool for over a century now and is vital in detecting signs of various central nervous infections and neurological conditions. However, despite its old age, the lumbar puncture still proves to have a lot of tricks up its sleeves as recent findings suggest it can be an extremely useful tool in detecting early signs of even more neurological diseases.

Also known as a “spinal tap”, the procedure requires the patient to lay in a foetal position[2] (see Figure 1). After the application of a local anaesthetic, a fine needle is inserted in between two lumber vertebrae of the patients back (usually L3/4 or L4/5) so that it pierces to the subarachnoid space in the back. Once this is achieved, a sample of CSF is drawn out via an aseptic non-touch technique. There are many purposes for removing CSF including measuring its pressure, sending a sample to a laboratory for further analysis, or simply for therapeutic use to relieve an increase in pressure in the head or spine (in a subdural haemorrhage, for instance)[1]. The procedure is usually commented as being uncomfortable, albeit not painful, and the patient is to lay on their back for an hour afterwards for post-operative monitoring and is advised not to drive themselves back home[3].

Figure 1 – Position of a patient during a lumbar puncture[6]

A lumbar puncture can be performed on both children and adults and is currently used to determine a variety of neurological diseases in the brain – most commonly meningitis. Meningitis is a condition where the meninges (membranes lining the brain and spinal cord) become inflamed due to a pathogenic infection[4]. Signs of a bacterial or viral infection can be detected by analysing the clarity and colour of the CSF drawn out of along with a high proportion of white blood cells, protein, and antibody response and a low glucose level being found in its contents. The same method can also be used to identify other brain disorders such as encephalitis as well as immune conditions such as Guillain-Barré Syndrome.

Whilst the use of this technique has been successful in establishing conditions of an immune origin, lumbar punctures are now being understood as having the potential to diagnose more complex neurological conditions. Most recently, researchers at Quebec's "Institut national de la recherche scientifique" identified plasma markers obtained via lumbar punctures that can help diagnose Alzheimer's in a patient, up to five years before its onset[5]. Alzheimer's (a form of dementia) is a difficult disease to identify at such an early stage, with the main diagnostic tools still being performing cognitive tests on patients as well as brain imaging. Both of these are not as reliable or as good at identifying Alzheimer's early on as the plasma markers identified. However, there has been a steady increase in the testing of CSF to diagnose Alzheimer's and with further positive outcomes such as this, the number will only rise.

Lumbar punctures do not only need to be used to draw out CSF either. While this is the commonest reason for performing a spinal tap, the method can also be utilized for injecting medication into patients too. Most commonly these are antibiotics, chemotherapy medication or pre-operative anaesthetics (known as an epidural)[6]. However, with time, the list of illnesses that can be possibly treated via giving medication through a lumbar puncture has been slowly growing too. In 2019, the American Academy of Neurology, conducted a preliminary trial for a drug aimed at slowing the progression of amyotrophic lateral sclerosis (ALS) in people with a mutation of the superoxide dismutase 1 (SOD1) gene[7]. Spinal taps were already used to diagnose ALS but the fact that the same procedure can help treat the same illness is incredibly big news.

To conclude, although being an age-old technique, the story of the lumbar puncture is not yet over. The benefits of spinal taps seem to be getting stronger and stronger and this procedure may prove to be one of the defining features of both diagnosing and possibly treating complex neurological conditions.

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2

Neuroregeneration

“Understanding Spinal Injuries: King’s College London iGEM ”

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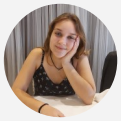

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Kate Flanagan
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Every year 200-500 thousand people are affected by Spinal Cord Injuries (SCI)[1]. The symptoms range from chronic pain to complete loss of sensation and motor and autonomic functions below the injury site, where the neural pathways are completely damaged[2]. SCI involves primary and secondary mechanisms of injury; the primary injury is caused by the initial traumatic event, and are often caused by accidents such as road accidents and falls, especially among the elder population. The secondary injury is caused by a series of biological and functional changes which usually lead to nerve degeneration, growth inhibition and inflammation in the injury site[3]. Depending on the injury location and socio-economic constraints, individuals affected by SCI have different survival rates and are more vulnerable to adverse outcomes in particular in low and middle-income countries or when the injury site is in the cervical section of the spinal cord.”[1].

Rehabilitation can help, in some cases, to regain control of autonomic functions and is important for multiple reasons such as maintaining stable bone and muscle density. Usually, rehabilitation is planned and carried out by a multitude of professionals ranging from clinicians to psychologists and dietitians - an interdisciplinary approach to ensure a safe mental and physical adaptation to living with SCI[4]. Over 60% of individuals affected by SCI suffer from chronic pain, which has a very strong negative impact on the persons’ quality of life, and so pain management is an extremely important component when designing treatment plans[5]. However,

rehabilitation alone will usually not lead to extensive functional recovery, and therefore there is a need for alternative neuroregenerative approaches capable of restoring total functional capacities and decreasing the impact of secondary injuries and neuro-degeneration[4].

SCI progresses over 3 stages: acute, sub-acute and chronic[3]. The acute phase comprises of the pathophysiological events that occur directly after the initial primary injury, which may include, ionic imbalance, free radical formation, and necrotic cell death[3]. This is followed by the sub-acute phase, during which surviving axons demyelinate, cells die via apoptosis , and a glial scar forms around the lesion site. The chronic phase commences after neurorecovery plateaus, where the glial scar extends and enlarges as it matures, causing axonal retraction[3].

Although the formation of a glial scar re-establishes CNS integrity after injury, it prevents repair and re-growth of axons. Chemical inhibitory molecules, particularly chondroitin sulfate proteoglycans (CSPGs) in the reactive extracellular matrix of the glial scar, are found to inhibit neuronal growth and axon regeneration. CSPG readily interacts with negatively charged proteins in the extracellular matrix and disrupts the balance of the spinal cord microenvironment[6]. At the molecular level, this is characterised by the down-regulation of regeneration-promoting factors such as neurotrophic factors, and up-regulation of harmful factors, including cytokines, and chemokines. At the cellular level, endogenous neural stem cells differentiate mainly into astrocytes instead of functional neurons. At the tissue level, despite glial scar formation, haemorrhage and ischemia, death of oligodendrocytes as part of the disease progression lead to demyelination of most lesioned axons, causing impaired signal transduction in the presence of axonal regrowth inhibiting molecules[6].

In the acute and subacute phases, neurons and glial cell shrinkage and death combined with axonal dieback, hinders patients' sensory and locomotive function below the lesion[7]. The secondary injury mechanisms involve necrosis— cell death due to schema and accumulation of toxic substances; and apoptosis— programmed cell death of surviving cells. Despite sensory and motor impairment below the injury site previously mentioned, structural and functional alterations also occur above the level of injury. These may include grey, white matter, cord atrophy and a decrease in axonal myelination can prolong functional recovery in the chronic phase of SCI[7]. Progressive demyelination in the spinal cord is correlated with worsened sensory impairment and increased neuropathic pain, adding complications to functional recovery of patients in the chronic phase. In conclusion, trauma-induced SCI strongly correlates with neurodegeneration in the CNS, and together with the complex pathophysiology of SCI, need to be taken into clinical consideration for patients' functional recovery[7].

Regenerative therapies are the most promising in terms of functional recovery and combating the inhibitory microenvironment of SCI. Treating spinal cord injury requires localised approaches to ensure the therapy is acting at the lesion site and mechanical support to bridge the cyst. There are both regenerative drugs and surgeries which have shown positive preliminary results in restoring spinal cord function.

Regenerative drugs are a promising treatment for SCI as they specifically target the molecules in the lesion site that make the environment unfavourable for axon regeneration such as the aforementioned CSPGs, inhibitory cytokines and chemokines. Chondroitinase ABC (ChABC) is one such regenerative drug that degrades the glycosaminoglycan chains of CSPGs, releasing the growth factors that have bound it and downregulating the inhibitory actions of the CSPGs. As such, ChABC is an anti-inhibitory drug that promotes neurite sprouting in the glial scar. These neurites can reconnect across the scar or form synapses with axons that run parallel to the scar to create a new pathway for signals to be transmitted across the lesion site. Extensive trials in rats provide evidence for functional recovery following treatment of a spinal cord injury with ChABC. Other pharmacological strategies, such as that used by anti-NOGO-A, use antibodies that target proteins that inhibit neurite growth. Anti-NOGO-A is also anti-inhibitory and has shown increased neurite regeneration, formation of synapses and functional recovery in various model organisms and in humans. Combinatorial treatment of both drugs provides better results than using either in isolation because the drugs target two different inhibitory molecules and as such using both in combination increases the anti-inhibitory effects[10]. Regenerative drugs are useful in that they permit axonal regrowth, however they lack the structural support to guide the growth they promote. Therapies that provide mechanical support and the possibility for localised drug delivery are the perfect treatment to combine the benefits of regenerative drugs with a scaffold that bridges their deficiencies.

Our project, founded through the International Genetically Engineered Machine Competition (iGEM), consists of a holistic view and approach to SCIs, we plan to use a biocompatible and biodegradable Polycaprolactone (PCL) scaffold, coated in a mussel foot protein bioadhesive, to facilitate axonal regrowth and regeneration. The mechanical strength of PCL, degradation properties and residuals make this scaffold a compatible candidate to the spinal cord environment. We have also considered the use of a hydrogel using lipid microtubules loaded with thermostabilized ChABC for localized and continuous drug delivery. Spreading awareness about SCI and making our product as accessible and inclusive as possible are also essential objectives to our project development. SCI and post-injury neurodegeneration not only affect the patient's motor function but also their quality of life, particularly their mental health. We hope to collaborate with more organisations and professionals that are passionate about understanding SCI in order to design an appropriate approach capable of alleviating the burden of neurodegeneration. Lastly, we are hoping that in the process of developing and presenting our project through the iGEM competition we can engage with the public and make neurodegeneration a more easily understandable concept.

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If you would like to learn more about our work towards spinal cord injuries, reach out to us via our social media links below!

KCL iGEM 2021

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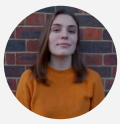
“Student Perspectives: King’s College London iGEM ”

King’s College London has been participating in the International Genetically Engineered Machine (iGEM) competition since 2018. iGEM is a renowned synthetic biology and genetic engineering competition started by MIT and takes place annually. Students at high school, undergraduate and overgraduate levels work throughout the summer to produce a project involving Synthetic Biology to solve a global issue. This culminates in the Giant Jamboree in November, where all teams converge and present their projects. However, iGEM is not limited to scientific research. The competition emphasises an entrepreneurial spirit, and more than 150 start-ups have arisen from iGEM projects. Additionally, a crucial element of iGEM is ensuring your project affects the world only in a beneficial way and necessitates engaging with both the ethics and stakeholders of your research.



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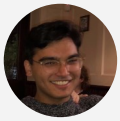
Alya Masoud Abdelhafid
BSc Nutrition



Harsh Bumia
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Luke Bateman
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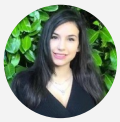

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The multidisciplinary nature of the competition, combined with the scientific rigour and prestige makes this a learning experience like no other for King's students.

At KCL, the iGEM cycle begins in February where students are recruited to join the team. In previous years, we held in-person interviews, where applicants were tasked to present a mock iGEM project in front of the Team Leaders. This year, due to the pandemic, we conducted a week-long virtual hackathon and students presented their projects over Zoom. The application and interview process is highly competitive and rigorous due to the high number of applicants and intensity of the iGEM competition.

Once recruitment is completed and the team has been chosen, the team works from March-May (with a break for exams of course!) towards brainstorming and designing their project. In summer, the team conducts their experiments in the lab and works on the deliverables of the competition. Deliverables include a poster, a promotional video and a website. Students are encouraged to get involved with the Synthetic Biology community through collaborations with other iGEM teams, engaging with stakeholders and developing outreach programmes.

The first iGEM team at King's, 3' Suspects, was focused on combating antibiotic resistance by engineering a library of small RNAs as new tools to regulate gene expression[1]. They achieved a Silver Medal and built a foundation for future teams. In 2019, KCL students founded Capacity, which developed two software tools to regulate the ratio of viral capsid proteins to advance novel gene therapy applications[2], which also received a Silver Medal.

Last year we developed our project, Renervate, which focused on improving treatment for spinal cord injury through the design and modelling of a 3D-bioprinted polycaprolactone based scaffolding, coated in a mussel-foot protein-based bioadhesive[3]. Our team was the first KCL iGEM team to have won both a Gold Medal and the prize for Best Therapeutics Project in the Overgraduate Division! We were also nominated for Best Model and Supporting Entrepreneurship, the best result for a team at KCL thus far. We are grateful for the support of our PI's Anatoliy Markiv and Alison Snape and supervisors Professor Annalisa Pastore and Dr Caterina Alfano. Without their help we would not be able to take part in the iGEM competition and owe our success to them.

Our project was inspired heavily by iGEM Leiden 2019 and iGEM SCIE Great Bay 2019, who focused on using protein-based hydrogels to treat burn wounds, and applications of mussel foot proteins (MFPs) respectively. After watching their presentations at the 2019 Jamboree, we decided to combine their initiatives to work towards a solution for spinal cord injury. Our project design was set in motion by our discovery of the mussel protein, Perna viridis foot protein 5-Beta (Pvfp-5β) which is highly adhesive and shows great promise in the creation of bioadhesives. We reached out to Professor Pastore who pioneered research into this protein and is based at King's. Professor Pastore and her collaborator Dr Alfano soon became our supervisors and were key in the development of our project. We also gained invaluable help from academics and industry professionals during the design of our 3D-bioprintable scaffold. Although the field of central nervous system reconstruction and regeneration is still in its infancy, we are proud to have built upon previous research and contribute to the development of regenerative therapeutics. If you'd like to learn more about our project and spinal cord injuries, some of our 2021 team members from KCL iGEM - Sichun (Angela) Yao, Beatriz Laureano and Kate Flanagan - have written an article in this magazine. Be sure to check it out!

The advantages of participating in iGEM are endless. Each team member develops invaluable skills that will benefit them in their future careers - whether this is in academia or industry, or in a field outside of STEM. The chance to work in an interdisciplinary group allows one to develop an understanding of the importance of different perspectives and

backgrounds in a research group. iGEM strongly encourages and rewards collaboration across teams and disciplines as well as Science Communication, allowing one to improve their interpersonal and professional skills. iGEM necessitates professionalism and strong communication as the need to reach out to academic and industry experts is essential in designing a scientifically and ethically sound project. This, alongside outreach to local communities, ensures that you gain communication skills which are required in any field of work. Consistently working alongside team members provides the opportunity to develop your ability to work as a team and communicate effectively. Working as a group of students, we set our own deadlines and organise and allocate tasks between ourselves, with little intervention from staff. This serves as a catalyst to ensuring such skills develop to the fullest, mirroring the real working environment. iGEM forces you out of your comfort zone, enabling you to build on your ability to communicate with unknown faces, as we must actively interact with other iGEM teams and professionals and presenting our project in front of large crowds!

As the principal iGEM deliverable is the creation of a website, or 'Wiki', most team members are required to learn HTML, CSS and Javascript. Teams are primarily judged upon the content of their Wiki, resulting in students gaining a strong foundation in these languages to best present themselves and their project. A basic understanding of programming has become a fundamental skill required by several occupations in the STEM industry. Beyond this, students learn to use graphic design and animation softwares such as Adobe Illustrator, Adobe Premiere Pro, Canva, and OpenToonz to produce content for the Wiki, social media accounts, and SciComm initiatives. Video editing, website design, social media marketing, are only some of the lucrative, non-scientific skills that can be obtained through participating in iGEM and are necessary in an increasingly more online world.

In 2020 specifically, our team worked towards developing their coding skills and learning how to work with computer aided design (CAD) software to model our scaffold. We also utilised bioinformatics and Molecular Dynamics software to research and model Pvfp-5β. Beyond this, we looked into the creation of genetic algorithms that can predict which mutations will improve the properties of our protein. As SnapGene graciously provided us with full software licenses for the summer, we were able to design a gene expression system that facilitated the production of our bioadhesive protein in bacterial cells. With regards to the scaffold system, we also used MATLAB to investigate and model the properties of our material. These are only some of the dry lab skills we obtained throughout the summer. We also learnt how to apply for grants and network with professionals. In particular, we successfully applied for and received a competitive grant from the Promega Corporation, which ensured our participation in the competition. Scientifically, the iGEM competition is a gift that keeps on giving; you never know what you're going to learn next. Our team went from developing novel software, such as our very own degradation simulation program, to learning how to write systematic reviews.

The most desirable aspect of participating in an iGEM team is the extent to which you work and contribute to the scientific community. iGEM allows students to experience the 'full-science' cycle. This ranges from developing a project idea and proposal, all the way to applying for streams of funding, conducting community outreach on Synthetic Biology and your project, as well as considering the societal impacts of your own project. iGEM projects can further be developed into start-ups due to the strong entrepreneurial presence within the competition - students are encouraged to explore the process of filing a patent and also developing prospective business plans. These are the sort of experiences that are not typical of a summer internship or an Extra-Mural Year, allowing you to mature not only as a scientist, but as a well-rounded individual.

The COVID-19 pandemic hit the UK just as we were about to enter the lab, scattering us across the world and forcing us to adapt our project to a virtual setting. Despite residing in a total of 16 different time zones, we successfully managed our project through frequent Zoom calls, weekly team meetings and online socials. We retained our team dynamic by ensuring consistent contact and collaboration

between team members and subgroups. Furthermore, we made sure to take frequent breaks and host socials to keep up our spirits and have some laughs as we preserved through all of the deadlines. Google Drive was a life-saver in ensuring all team members could see what each sub-group was working on. Many of our team members persevered through very early morning starts and/or midnight meetings - we are very proud of what our team accomplished in 2020!

The demanding nature of iGEM requires adaptation and time-management, particularly for students in their final and penultimate years of study. Strong organisational skills and effective communication are of the utmost importance to ensure optimum execution of the proposed project. The final stretches of the iGEM season result in a high-stress environment for all teams, especially as the Wiki deadline approaches.

All of the hard work and dedication that teams devote into the projects across the globe transpires into the Giant Jamboree, the largest Synthetic Biology conference in the world. In November, teams travel to this event, which provides fantastic opportunities to meet and discuss with other teams, as well as network with prominent members in the field of Synthetic Biology across the globe. Here, you can fully appreciate the potential of synthetic biology as a solution for issues currently facing many different communities. The event lasts for a whole week, beginning with teams presenting their posters on multiple floors, and ending with the awards ceremony. Last year, we attended the Virtual Giant Jamboree alternative, which was still a fantastic event to have attended despite it being online. Lastly, throughout the event, there are multiple workshops and events to attend - there's something for everyone, from Women in STEM initiatives to Minecraft events!

If you would like to get involved with the growing Synthetic Biology community at KCL or are keen to join the iGEM team next year, join the KCL Synthetic Biology and Biotechnology societ Last year, the society was founded to connect students from interdisciplinary backgrounds through Synthetic Biology. The society also provides a platform for iGEM team members to connect with the King's community and encourages members to get involved in similar initiatives.

Don't forget to keep up with us throughout our 2021 adventures and follow us on our social media, linked below! This summer we will complete the second phase of our 2020 project Renervate, as we plan to validate our project design and computational work in the lab. If the Giant Jamboree is held in person, we will present in Paris this November and plan to make the King's community proud!

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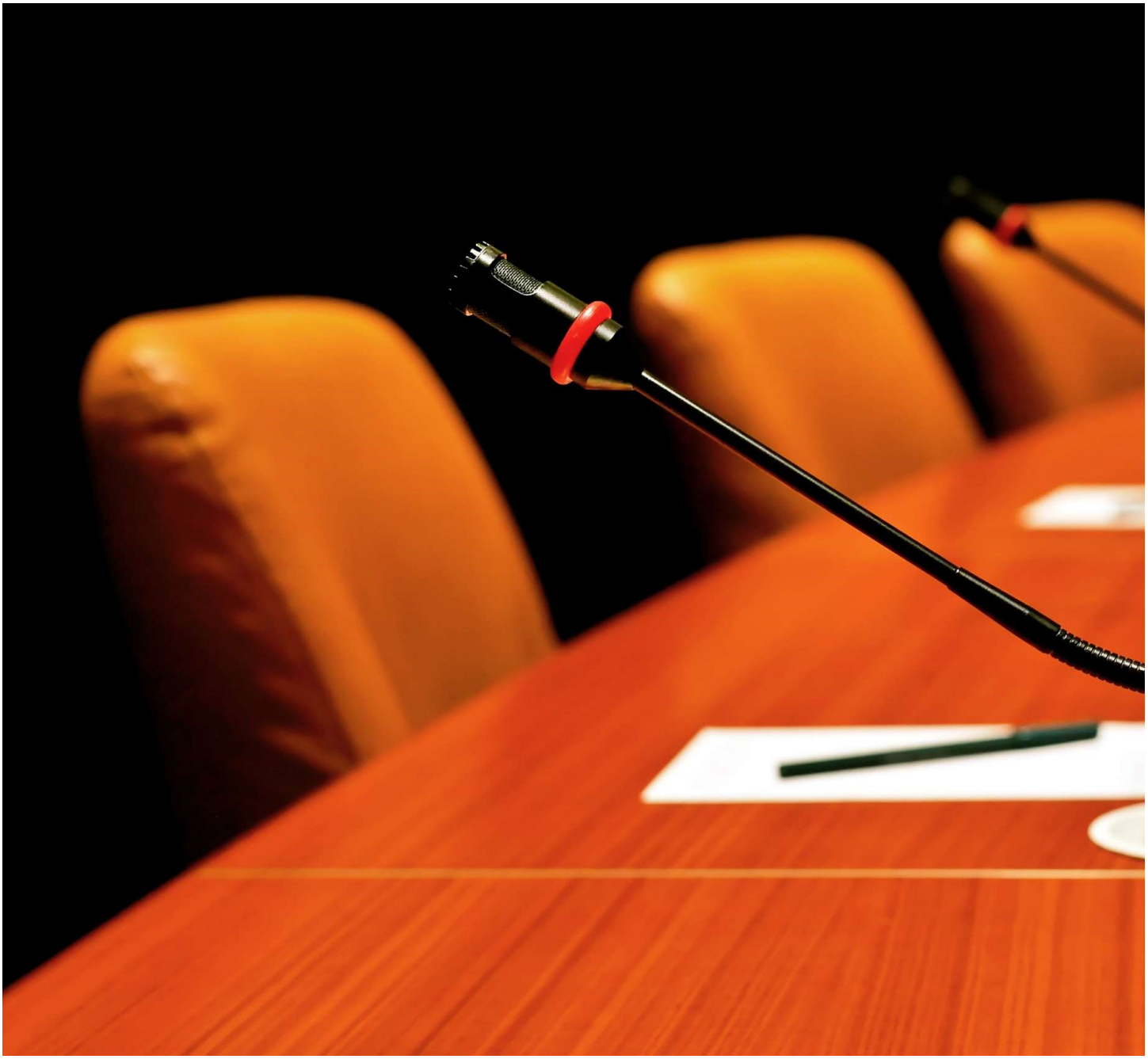
Annual General Meeting



King's College London Neuroscience Society

"AGM Elections"

Thursday 15th April 2021

Core Committee Roles

The following positions are available for election

President

Responsible for all society activities and events, and manages the various aspects of day-to-day running of the society through working with the VPs and other committee members.

Essential

- Current committee member
- Management and leadership experience

Preferred

- Current senior member of any society

Vice President (x2)

Responsible for all society activities and events, and manages the various aspects of day-to-day running of the society through working with the VPs and other committee members.

Essential

- Current committee member
- Management and leadership experience

Preferred

- Current senior member of any society

Secretary

Works closely with the President to ensure the success and general organisation of the society. Prioritises and delegates tasks, and ensures activities comply with KCLSU regulations.

Essential

- Current committee member
- Management and leadership experience

Preferred

- Current senior member of any society

Treasurer

Responsible for society finances, budgets, and memberships. This includes reimbursing society -related costs. Assists in financial aspects of charity events and our annual conference

Preferred

- Financial experience

King's College London Neuroscience Society

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General Committee Roles

The following positions are available for election

Events Officer

Responsible for planning the society's various events throughout the year, overseeing all events and assisting where required.

Preferred

- Event management experience
- Logistical acumen

Publicity Officer

Responsible for all aspects of marketing and communications relating to the society, which includes social media accounts and newsletters. Creates posters for key events.

Essential

- Social media literacy
- Experience with graphic design

Website Manager

Responsible for maintaining and continuously improving the society website. Works closely with the Publicity officer to update site with events and opportunities. Also manages the website blog.

Essential

- Web design skills (preferably Wixsite)

Editor-in-Chief

Responsible for leading a (non-committee) editorial team; setting out specifications for student-submitted articles, editing and guiding students through the publication process. Ultimately designing, compositing, and delivering our society magazine "Neurosphere".

Essential

- Scientific writing experience
- Editing experience

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General Committee Roles

The following positions are available for election

Charity Officer

Responsible for organising fundraising events for the charity of choice, liasing between the charity and KCLSU. Works with the Treasurer to oversee the charity account. Also assists the University Challenge Lead in organising the University Challenge event.

Essential

- Interests and experience in fundraising

University Challenge Lead

Responsible for organising the inter-university University Challenge event; coordinating with representatives from other universities' Neuroscience Societies, organising logistics and overseeing the running of the event.

Essential

- Event management experience

Conference Lead

Responsible for selecting the theme of the annual society conference; contacting speakers, organising logistics and overseeing the running of the event,

Essential

- Previous attendance of at least 1 academic conference or symposium
- Experience organising academic events

Neuroscience Rep

Responsible for liaising with their course's students; sharing events and opportunities. A flexible role; includes assisting as needed within the committee (event organising, publicity, blog writing, society collaborations, etc).

Essential

- Must be on the Neuroscience course (UG)

Preferred

- Links with other societies

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General Committee Roles

The following positions are available for election

Medicine Rep

Responsible for liaising with their course's students; sharing events and opportunities. A flexible role; includes assisting as needed within the committee (event organising, publicity, blog writing, society collaborations, etc).

Essential

- Must be on the Medicine course (MBBS)

Preferred

- Links with other societies

Psychology Rep

Responsible for liaising with their course's students; sharing events and opportunities. A flexible role; includes assisting as needed within the committee (event organising, publicity, blog writing, society collaborations, etc).

Essential

- Must be on the Psychology course (UG)

Preferred

- Links with other societies

Post-Graduate Rep

Responsible for liaising with their course's students; sharing events and opportunities. A flexible role; includes assisting as needed within the committee (event organising, publicity, blog writing, society collaborations, etc).

Essential

- Must be on a Post-graduate course

Preferred

- Strong links to IoPPN departments

Applying for AGM

The deadline for applications is
11.59pm on Wednesday 14th April.

Apply by scanning the QR code:

Committee Icon designs by Ruby Morton

www.kclneurosoc.org