## UNDERGRADUATE SEFS SUMMER RESEARCH BURSARIES 2019

### GROUP 1 - FOOD SCIENCE & NUTRITIONAL SCIENCES; ENGINEERING AND COMPUTER SCIENCE

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### GROUP 2 – LIFE SCIENCES AND BIOLOGICAL, EARTH & ENVIRONMENTAL SCIENCE

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**GROUP 3 – MATHEMATICAL SCIENCES; CHEMISTRY AND PHYSICS**

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GROUP 1 - ENGINEERING AND COMPUTER SCIENCE
PROJECT 1 - Investigation of Novel applications for Magnetoresistive Sensors

SEFS Summer Research Bursary linked Position

Magnetoresistive (MR) Sensors are an advanced position sensing technology in the automotive industry, industrial automation and robotics. New Sensor types such as Tunneling MR and Giant MR sensors are emerging with improved accuracy enabling new applications such as contactless sensing, magnetic gesture recognition, non-destructive testing or the bio-analysis sensing.

Microelectronic Circuits Centre Ireland (MCCI) carries out industry-led world-class Analog, Mixed-Signal and RF integrated circuit research. MCCI targets real-life applications with its research and currently has projects in diverse topics such as DNA detection, bio-sensing, imaging for security applications and early cancer detection.

In this project we want to test MR sensors and use them with off the shelf hardware systems such as Arduino and Raspberry Pi etc to prototype new applications. An example of an interesting application is the use of TMR sensors to implement a cuff-less Blood Pressure Monitor [1]. There are opportunities for the student to work at making, 3D printing, programming, analog circuit design, digital design, PCB design etc.

Supervisor: Dr. Daniel O’Hare, Senior Researcher, MCCI, Tyndall National Institute.

UCC Elec Eng endorsers: Dr. Kevin McCarthy, Dr. Padraig Cantillon-Murphy

“I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.”

Any queries relating to this position can be forwarded to Dr. Daniel O’ Hare on email daniel.ohare@mcci.ie.

PROJECT 2 - ‘Post-conflict’ regeneration in Northern Ireland

Orla McKeever MRIAI
Lecturer in Architecture
Cork Centre for Architectural Education
University College Cork
Douglas Street
Cork
email: o.mckeever@ucc.ie
Tel: +353 83 343 6451

“Those who study and learn from the region’s problems can learn from and add to the general body of knowledge concerning cultural diversity and conflict” (Boal, Douglas, and Orr 1982)

Working within the context of ‘post-conflict’ Northern Ireland, (Shirlow 2006) this research will explore the question of whether repressive constraints; relating to the legacy of conflict; exist within the design of civic regeneration projects and if so, how do these manifest within the public realm? In the same way as the Nolli maps of Rome (1736-48) chart the publicly accessible interior space of civic buildings as an extension of the public realm, this question will be explored through the investigation of civic case studies. The threshold condition will be investigated as a key moment in the facilitation or the obstruction of an extension of the public realm while exploring the ‘choreography of daily life.’ (Farrell and McNamara 2017) This research will interrogate immaterial repressive methods and material elements or signals, of specific case studies within the built environment that control, contain and corral the use of regeneration projects, and facilitate the creation of new borders within the ‘post conflict’ environment of Northern Ireland.
“I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.”

**PROJECT 3 - Investigating the patient-centred healthcare model: my health digital assistant**

Throughout the developed world, the population is living longer, resulting in greater demands on the healthcare system. The current expensive and fragmented healthcare model can be replaced by quasi-permanent care whereby the patient has continuous access to doctors and care resources, significantly improving his/her overall experience. ICT can enable this transformation by offering the support and services for a new patient-centred healthcare model. This new model focuses on the patient’s needs, his/her active participation and satisfaction while decreasing operational costs. These goals can be achieved by creating new healthcare services.

This project aims to take advantage of the mobile cloud and leverage the Internet of Things (particularly familiar mobile devices) to render healthcare in a way that is personalised and compassionate, effective and efficient. The system will integrate many forms of patient-centred healthcare. The system will

- provide direct communication channels between patients and healthcare professionals, in contrast to only meetings by appointments;
- support primary care;
- allow to access information from anywhere and at anytime;
- store vast amounts of data at individual, system and population levels.
The summer research project will focus on a tool, called “my health digital assistant” that will work on behalf of the patient by automatically establishing communication with healthcare professionals, collecting, storing and pre-processing vital data (heart rate, blood pressure, blood sugar level, input text, etc.) and sending notifications/alerts.

After the induction phase that will include a review of the state of the art (task 1 – 1 week), the student will analyse and design the software system that will support the “health digital assistant” concept (task 2 – 2 weeks). Task 3 (5 weeks) will consist of programming, tests, evaluation and writing a report. The end result will be a proof of concept system.

I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.

Dr. Dan Grigoras
Senior Lecturer
School of computer Science and Information Technology, Ext 5918, Email grigoras@cs.ucc.ie

**PROJECT 4 - DEVELOPMENT OF AN ULTRASONIC SYSTEM TO DETECT OLIVE OIL FRAUD**

The projected global market for olive oil will be approximately US$11bn (€10bn) by 2020. Extra virgin olive oil (EVOO) is considerably more expensive than other oils, so unscrupulous suppliers dilute EVOO with cheaper oils such as sunflower, soybean, or corn. It has been estimated that nearly 70% of all extra virgin olive oil sold in the USA may be fake. The speed of propagation of an ultrasonic wave may be used to measure certain physical properties of olive oil and vegetable oils, but the speed depends on temperature, and the distance travelled by the wave must be known precisely.

The purpose of this project is to develop a suitable ultrasonic testing apparatus with automated ultrasonic probe positioning, temperature measurement and data acquisition. The ultrasonic probe will be positioned in the oil using a micrometer linear stage using a stepper motor and an Arduino, which must also record the oil’s temperature. Once the probe has been positioned, the ultrasonic signals from a commercial probe unit must be digitised on an oscilloscope and transferred into a PC for signal processing in MATLAB. The system will first be calibrated using water as the test liquid. A series of other tests will then be performed to measure the variation of sound speed with temperature, and thus the possible distinction between EVOO and other vegetable oils, compensating automatically for the oil temperature. This project requires a student interested in instrumentation, measurement, MATLAB programming, signal processing, and practical electronics. Experience of Arduino microcontrollers would be an advantage.

**Supervisor Contact Details:**
I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8 week period during June – September 2019.

GROUP 2 – FOOD SCIENCE & NUTRITIONAL SCIENCES; LIFE SCIENCES AND BIOLOGICAL, EARTH & ENVIRONMENTAL SCIENCE

PROJECT 5 - Investigating fraility and life span using the Caenorhabditis elegans model of aging.

Dr Susan Joyce: School of Biochemistry and Cell Biology and APC Microbiome Ireland and Food Institute UCC email: s.joyce@ucc.ie Tel: 4901343

The hallmarks of aging include altered metabolism and inflammation as well the generation of reactive oxygen species. A range of studies have shown that gut microbial populations are also altered in the process and that this is a function of both senescence and of diet. The nematode C. elegans offers a possibility to examine both frailty and aging in a simple system. This is the model organism in which to study aging. This project will examine the contribution of 3 different short chain fatty acids SCFA, and a number of bacteria that produce them, representative of the gut microbiome, in this context. For any component or bacteria that influence fraility and/or lifespan, the system through which they act will be identified using nematodes isolates genetically modified for these systems. In this way the relative functional contribution of know gut residents that are lost or gained by the elderly populations can be assessed in vivo.

Model and question:
Of Note:
This system and research is active and ongoing in the group
The student will be aligned to myself and to an experienced researcher.

Student General Benefits:
- Students will be integrated into a dynamic experienced work environment as a professional.
- Gain experience of safety, application, planning, execution and analysis of scientific methods and analyses tools in the workplace
- Maintenance of laboratory records and presentation.
- Laboratory informatics and stats.

“I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.”

PROJECT 6 - Functional analysis of alpha-actinin dimerization in cancer

Supervisor: Dr Paul Young

School of Biochemistry and Cell Biology

Email: p.young@ucc.ie
Alpha-actinins are major actin filament cross-linking protein in cells. Their genetics is fascinating. Mutations in all four human genes have now been linked to heritable diseases or traits. Actinin-1 mutations cause macrothrombocytopenia, a platelet disorder characterized by excessive bleeding. Actinin-2 mutations have been linked to a range of cardiomyopathies, and actinin-4 mutations cause a severe kidney condition. Actinin-4 is also overexpressed in many cancers and linked to an aggressive metastatic phenotype. Intriguingly, approximately 16% of people worldwide completely lack actinin-3 and the presence or absence of actinin-3 influences performance in sprint versus endurance sports, with the correct actinin-3 genotype estimated to be worth 0.1 sec in a 100m sprint.

Actinins are dimeric proteins, allowing them to cross-link actin filaments. We have shown that the different actinin isoforms can form heterodimers in several cancer cell lines. Heterodimer formation is important since it will affect the proportion of functional actinin dimers in individuals that are heterozygous for a disease causing actinin mutation or that are overexpressing one isoform in cancer for example.

The project will focus on better understanding actinin heterodimerization. It will explore which factors affect the formation of homo- versus heterodimers – a process that seems to be regulated differentially in a cell type-specific manner.

Methods: cell culture and transfection, western blotting, protein expression and purification, native gel-electrophoresis

References:


“I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.” Paul Young

PROJECT 7 - Targeting the Endosomal Recycling Pathway to Downregulate the Immune-checkpoint protein PD-L1

One of the mechanisms by which tumour cells evade the immune system is to express checkpoint proteins on their surface, which can inactivate invading T cells (part of the immune system). An exciting class of drug are cancer immunotherapies which block the activity of the immune checkpoints. However, some cancers develop resistance to these immunotherapies. In such cases, it would be advantageous to prevent the immune checkpoints from reaching the surface of the cancer cells. I believe this can be achieved by blocking the endosomal recycling pathway.
The endosomal recycling pathway is an intracellular transport pathway that is the main cellular mechanism for controlling the composition of the plasma membrane. Cargo that has been internalised from the plasma membrane is usually sent along the degradative pathway to lysosomes where it is broken down, or it is returned to the plasma membrane via the recycling pathway. Receptor tyrosine kinases, integrins, GPCRs, matrix metalloproteinases, and cadherins are examples of cell surface proteins that are recycled. It is emerging that upregulation of this pathway can lead to the increased aggressiveness of a wide range of cancers. We have published data demonstrating that blocking the recycling of some of these cancer associated proteins can lead to their destruction in lysosomes.

The aim of this project is to determine if endosomal recycling inhibitors can prevent the transport of an immune checkpoint protein called PD-L1 to the cell surface. Various inhibitors will be tested to determine if they can alter the cell surface levels of PD-L1 in the MDA-MB-231 breast cancer cell line. A combination of Western blot and immunofluorescence techniques will be used.

I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.

Dr Andrew Lindsay, School of Biochemistry and Cell Biology, Office 3.09, Biosciences Institute, University College Cork, Cork, Ireland
Phone: +353 21 4901368; Fax: +353 21 4901382
a.lindsay@ucc.ie

PROJECT 8- Generation and biochemical characterisation of an RNA-binding deficient SMAUG1 mutant

RNA-binding proteins (RBPs) impact every cellular process through their interactions with RNAs and other proteins. Not surprisingly many human diseases are linked to alterations in RBP interactions, including muscular dystrophies, neurodegenerative disorders and cancer. Interestingly, many of these diseases are more prevalent or worsen as we age. By examining the molecular interactions and biological roles of RBPs, a better understanding of RBP-RNA networks will provide a wealth of new therapeutic targets, along with clues about ageing.
SMAUG1 is an RBP that has been linked to muscular dystrophies and neurodegeneration\textsuperscript{1–3}. Currently it is not known which RNAs interact with the protein, how SMAUG1 modulates the activity of bound RNAs or how changes in the SMAUG1-RNA interactome influences cell behaviour and disease progression. Therefore, a key step to understanding how SMAUG1 can influence cells is to identify the set of RNAs that bind to SMAUG1.

To identify SMAUG1-bound RNAs in human cells, we will use UV-crosslinking and analysis of cDNAs (CRAC)\textsuperscript{4,5}. For CRAC, we have generated a DNA construct containing a modified version of SMAUG1 with a C-terminal tag of six-histidines, followed by a TEV protease cleavage site and two tandem FLAG tags. As a stringent control for non-specific RNA interactions using CRAC, the aim of the summer research project is to generate an RNA-binding deficient mutant of SMAUG1 using site-directed mutagenesis and verify its reduction in RNA binding using two methods – a dual luciferase reporter system and electromobility shift assays with purified, recombinant SMAUG1 proteins. Overall the summer project will provide an extremely valuable resource to continue our work in identifying the sets of SMAUG1-bound RNAs in normal and disease states.

I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.

Date: 07 February 2019

Kellie Dean, PhD
College Lecturer and Principal Investigator
School of Biochemistry and Cell Biology, 3.91 Western Gateway Building
University College Cork, Cork, Ireland
ph: +353 21 420 5421; e: k.dean@ucc.ie

References:


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**PROJECT 9- Exploring the potential for agroforestry in Ireland**

Supervisor: Dr Markus Eichhorn, School of BEES

Contact: markus.eichhorn@ucc.ie

Agroforestry is a mixed system of cultivation which combines trees with crops or pasture. While widespread throughout Western Europe (Eichhorn et al. 2005) its uptake in Ireland has been limited. With the recent national drives towards decarbonising agriculture, diversifying production and increasing tree cover, agroforestry has the potential to contribute towards addressing these challenges. There have been few attempts though, which limits both the evidence base for its effectiveness and the availability of demonstration plots. A farm near Skibbereen contains one of the small number of trials in the country. Two hectares have been planted with a mixture of broadleaf trees, half of which is silvopastoral (trees plus livestock), the remainder silvoarable (trees plus crops). The former is to be used to shelter poultry, the latter for growing soft fruits and cobnuts between the tree rows, and is at present the only known silvoarable system in Ireland.
In this project the candidate will map the positions of all individual trees and crop plants and measure their current dimensions. These data can be used immediately to examine relative performance of species and test for spatial interactions among plants. Monitoring will be maintained in future years, and therefore this project will provide baseline data for exploring growth and development of the trees and to inform future planting schemes. The student will gain experience in fine-scale mapping of habitats and will be supervised in conducting a preliminary analysis of spatial interactions. Candidates must be able to drive and have access to a vehicle.

I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.

PROJECT 10- Investigation into the ability of Th1 Inflammatory and Anti-Tumour Cytokines to Sensitize Resistance Colon Cancer Cell Lines to the EGFR targeted therapy Cetuximab

Abstract

Redundancy between oncogenic receptor tyrosine kinase (RTK) signalling pathways represents a key mechanism of acquired resistance to targeted cancer therapies such as the anti-EGFR biological therapy (cetuximab) in colon cancer. In particular, targeting one RTK may result in compensatory upregulation of bypass RTK genes, which turns otherwise sensitive cells refractory to the initial treatment. The pro-inflammatory Th1 cytokines IFN-\(\gamma\) and TNF-\(\alpha\) are effectors of anti-tumour immunity yet their effect on RTK signalling is unclear. We have shown that IFN-\(\gamma\)/TNF-\(\alpha\) synergise to induce a co-ordinated shutdown of multiple RTK genes in colon cancer cell lines. This transcriptional response is seen across various human cancer cell types and involves up-regulation of EGFR – the target of cetuximab - coupled with repression of a conserved set of RTKs, including HER2/3, FGFR3, INSR and IGF1R. Mechanistically, IFN-\(\gamma\)/TNF-\(\alpha\) mediate RTK shutdown by integrating multiple upstream signalling inputs such as (i) acute transactivation of EGFR, HER2, INSR and IGF1R, which drives activation of PI3K/AKT signalling as well as (ii) RTK-independent induction of p38 and MEK/ERK pathways. Our results suggest that therapies promoting T-cell-mediated antitumour immunity (e.g. immune checkpoint blockers) may produce similar effects as a part of their overall efficacy. This could provide a rationale for combining such immunotherapies with RTK-based targeted therapies in order to overcome acquired resistance to the latter.

Aim
The aim of this project is to test whether IFN-\(\gamma\)/TNF-\(\alpha\)-induced rewiring of RTK signalling pathways sensitizes resistant colon cancer cell lines to the anti-EGFR targeted therapy cetuximab.

References

(1) Resistance to anti-EGFR therapy in colorectal cancer: from heterogeneity to convergent evolution.


(2) Acquired resistance to EGFR-targeted therapies in colorectal cancer.


Supervisor Contact Details:

Ken Nally, Ph.D.
Lecturer in Biochemistry & Principal Investigator
School of Biochemistry & Cell Biology
Host Response and Inflammation Group
Alimentary Pharmabiotic Centre
Rms. 2.10/4.41, Bioscience Institute
University College Cork
Cork City, Ireland

Tel: 353-21-4901302
Email: k.nally@ucc.ie
Web: http://apc.ucc.ie and http://microbemagic.ucc.ie (for children)

Supervisor Declaration:
I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8 week period during June – September 2019.

PROJECT 11 - Regulation of the cytokine expression during Unfolded Protein Response Signalling

Supervisor: Eoin (J.V.) Fleming – j.fleming@ucc.ie

A number of genetic and environmental conditions are characterised by protein misfolding at the endoplasmic reticulum. In the absence of an appropriate cellular response, the accumulation and aggregation of these proteins can result in proteotoxicity and lead to cell death. In eukaryotes therefore, an evolutionarily conserved stress response known as the Unfolded Protein Response (UPR) acts to minimize the detrimental effects on the cell [1]. Our recent studies suggest that the phosphorylation status of an ubiquitin conjugating enzyme Ubc6e may be important in regulating cellular responses to the UPR, with p38 MAPK phosphorylation of Serine residue S184 playing a particularly important role.

Increased expression of the IL-8 cytokine is a feature of UPR signalling, and has been used previously as a marker for increased inflammation under UPR conditions. We wish to use Western blot detection of IL-8 expression as a marker to characterise the role of Ubc6e phosphorylation in the UPR, and have generated a variety of expression constructs expressing phosphorylation deficient and phospho-mimetic forms of the
protein in order to do this. To this end we have purchased a CHO cell line that generates an anti-human IL-8 antibody that can be used for detection purposes. The aim of this proposal for a summer studentship is to optimise the purification of anti-IL8 antibody by affinity chromatography for subsequent use in Western blot analysis. The student will gain experience in a range of laboratory techniques including cell culture, cell transfections, affinity chromatography and western blotting.
I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8 week period during June-September 2019


PROJECT 12 - Assessing the benefits of the UCC tree collection

Trees in the urban environment have a range of benefits including: improving human physical and mental health; increasing biodiversity; sequestering carbon and reducing atmospheric pollution; framing and enhancing historically and culturally important buildings; and encouraging engagement with the natural world by adults and children

The UCC tree collection is made up of c. 2,500 trees of over 120 different species and dates back to the establishment of the University. This project will assess the tree collection across a range of possible benefits. It will also identify a core number of trees for further study and description. The work will build on the previous mapping of the tree collection (2009) and help to demonstrate the value of the collection for research, teaching and civic engagement. In particular, the contribution of the trees towards carbon storage and sequestration will be estimated.

This project is informed by the UCC Biodiversity Action Plan (2018-2023) and contributes to a number of its key targets, e.g. Increasing awareness and engagement with biodiversity on campus.

This project will involve:

- Visiting, photographing and measuring key specimen trees in the collection.
• Estimating their carbon sequestration capacity using established model.
• Collection of scientific, historical and cultural information pertaining to the tree collection and specific key trees with the collection.
• The development of outreach tools to engage staff, students and visitors with campus biodiversity.

Contact Details:

Dr Eoin Lettice, School of Biological, Earth and Environmental Sciences, Room 1.17, Butler Building, Distillery Field.
e.lettice@ucc.ie

I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.

PROJECT 13 - Exploiting a platform collection of novel small molecules for behavioural control of key nosocomial pathogens

Supervisor: Dr. F. Jerry Reen, School of Microbiology, UCC. Tel: +353 21 490 1330; email: j.reen@ucc.ie

Background:
Due to the misuse and overuse of antibiotics, the emergence of pathogens that are resistant to virtually all the currently available antibiotics has reached a critical stage. The fast approaching post-antibiotic era has focused efforts of the academic and pharmaceutical communities on the search for new classes of antimicrobial compounds to arrest the increase in mortality levels we currently attribute to microbial infections. Key to this has been the realisation that infections arise from changes in polymicrobial communities, and the interactions between the protagonists within these communities can markedly affect the effectiveness of antibiotic-based challenge. Therefore, understanding the impact of key interactions within these ecosystems is key to priming the effectiveness of drug-based interventions.

Proposed Research Project:
This project will pursue a chemico-biological approach to establishing the anti-infective potential of a suite of novel compounds against model organisms for pathogen control.
The key aims of this project will be:

1. Using an integrated chemico-biological approach, investigate the anti-biofilm and anti-virulence potential of synthetic compounds against model microbial strains for pathogen control.
2. Investigate potential synergistic activity of lead anti-infective compounds with conventional antibiotics.

**Core Skill Development:**
The undergraduate student will be part of a multidisciplinary research initiative interfacing Microbiology, Chemistry, and Technology. Core skills developed through this research will include microbiology, bioinformatics, molecular biology and chemistry.

**Statement:**
I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019

**PROJECT 14 - Enhancing nutrients uptake rate of duckweed in aquaculture wastewater treatment**

Duckweeds are small floating freshwater plants belonging to the family of Lemnaceae. Characterized by high growth rate and high protein content in their biomass, these plants are excellent candidates for the phytoremediation of wastewater and they have been recognised as a potential replacement for imported soy. The project Aquasus, funded by Bord Iascaigh Mhara and developed in the School of Biological, Earth and Environmental Sciences, aims to establish, in Ireland, a circular economy system in which duckweed are used to treat aquaculture wastewater, while the biomass produced in the process can be harvested and used as a protein source in the fish diet. The system will result in a reduction of the impact of aquaculture on natural waters as well as in the production of valuable biomass. The research project proposed focuses on one of the objects of Aquasus, in particular the aim is to maximise the nutrients uptake rate of the plants in order to increase the phytoremediation efficiency of the system and the biomass produced. Previous experiments focused on the determination of the potential uptake rate at different plant densities. During the 8 weeks the student will participate to the design and the execution of short-term experiments in which different potential enhancers of the nutrients uptake rate will be tested. In particular the experiments will focus on strains selection and chemical and/or bacterial stimulation of plant growth.
I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.

Dr. Simona Paolacci (spaolacci@ucc.ie)

Prof. Marcel Jansen (m.jansen@ucc.ie)

School of Biological, Earth and Environmental Sciences

**PROJECT 15- Can bile acids modulate the host peripheral nervous system?**

In addition to trillions of microbial organisms, the gastrointestinal lumen also contains bile acids which have spilled over into the colon. Beyond their role as a lipid detergent, bile acids can act as cross-barrier signalling molecules, communicating between the microbes in the external environment of the gut lumen and the host. Although they are expected to involve endocrine, paracrine and/or immune signalling molecules (Figure 1), the specific mechanisms have not yet been elucidated.
Both intrinsic neural plexi and extrinsic neurons play a key role in regulating gut function. Bile acids may act as the cross-barrier signalling molecule involved in communicating with the host. However, it is unknown if bile acids are transported across the gut barrier to directly activate gut neurons, or if they use an intermediary signalling cell. A good candidate for such a cellular transducer is the glucagon-like peptide 1-secreting L-cell, which is embedded in the epithelium and expresses bile acid receptors.

The study aim is to screen bile acids for their potential neuromodulatory actions on enteric neurons. Calcium imaging will be used to monitor neuronal excitability in the presence of bile acids and to determine if epithelial L-cells are involved in the cross-barrier communication.

The student will gain expertise in dissecting colonic tissue, calcium imaging and data analysis.

“I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.”

Dr Dervla O’Malley, Department of Physiology and APC Microbiome Ireland, Western Gateway Building, University College Cork.

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**PROJECT 16- Base Editing to Correct Cystic Fibrosis Mutations**

Patrick Harrison Ph.D., Physiology

2019 is the 30th anniversary of the identification of mutations which cause Cystic Fibrosis (CF). Drugs are now available for many patients, but approximately 10% of CF individuals have premature stop codon (PTC) mutations. These PTCs do not respond to drugs, and a gene therapy approach is not available for CF (Hart & Harrison (2017), PMID:29107808).
CRISPR gene editing has revolutionised the study of physiology and disease, and is established as a proof-of-concept therapy for many diseases, and human clinical trials are already enrolling patients. However, a concern is that targeted DNA breaks made by CRISPR could lead to long-term DNA damage.

In November 2017, David Liu’s lab at Harvard upgraded CRISPR to bind DNA and deaminate adenine residues thus converting an A:T base pair to a G:C base pair without making a DNA break. This provides a way to correct all three PTC variants (TAA, TAG, TGA) to a tryptophan (W) codon.

The aim of the summer bursary in my lab is to apply the base editing technique to the correction of the W1282X mutation which occurs in about 1% of all CF individuals. Researchers in my group have successfully corrected this mutation with Cas9/gRNA and Cpf1/gRNA by conventional gene editing, and have established a model system to monitor base editing using vectors from the Harvard group. Thus, we have all the necessary reagents, cells and detection systems up and running to test the hypothesis that base editing can correct this mutation and restore normal CFTR function.

I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8 week period during June – September 2019

Patrick Harrison

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PROJECT 17- Improving the biodegradability of whiskey industry by-products through hydrothermal pretreatment

Currently, Irish alcohol industry relies heavily on non-renewable fuels to provide necessary heating for distillation. It is urgent to reduce the use of fossil fuel and GHG emissions to achieve a green whiskey industry. The research question in this project arises from the fact that the biodegradability of typical whiskey industry by-products (such as spent grain) in anaerobic digestion is reported in the range of only 50-70%. This necessitates the development of effective pretreatments to improve the biodegradability and the associated biomethane yield. The recalcitrance of spent grain is largely due to the presence of complex cellulose, hemicellulose and lignin. Pretreatments can be classified into physical, chemical and biological methods, or their combination. The commonly used pretreatments are alkaline and acid pretreatment. However, this will cause some unpleasant problems, such as sodium inhibition and toxic compounds generation. To address these issues, the following research is proposed:

- Hydrolysis of cellulose and hemicellulose in spent grain using hydrothermal pretreatment conducted using a Microwave Digestion System (CEM Mars 6, US)
- Assessment of the biomethane potential of pretreated spent grain in anaerobic digestion (AMPTS Bioprocess, Sweden)

The advantages of hydrothermal pretreatment include: (1) water is used as the only reactant and solvent, and no additional chemicals are needed; (2) water vapor is not generated during hydrothermal condition, which makes it more energy saving; and (3) mild pretreatment condition reduces production of biological inhibitors. In our previous studies, hydrothermal pretreatment has been successfully applied to hydrolyze seaweed, and the subsequent biomethane yield increased by 30%. Overall, this project will deliver an optimised pretreatment method that will significantly improve the biogas production from typical whiskey industry by-products.

“I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.”

Supervisor contact detail: Dr Richen Lin (richen.lin@ucc.ie) and Prof Jerry Murphy (jerry.murphy@ucc.ie)

Environmental Research Institute, School of Engineering, University College Cork
GROUP 3 – MATHEMATICAL SCIENCES; CHEMISTRY AND PHYSICS

PROJECT 18 - THE DESIGN AND SYNTHESIS OF DFS MIMETIC- NEW WEAPONS IN THE BATTLE AGAINST BACTERIAL RESISTANCE

The increasing prevalence of bacterial resistance has been identified by the World Health Organisation as a “global threat” to humanity. As more and more strains of bacteria develop resistance to existing antibiotics, novel approaches are required to tackle this challenge. In this project, we will synthesise molecules which disrupt the bacterial communication system and halt the resistance mechanism.

Over the course of their evolution, bacteria have developed many different strategies for countering the effects of synthetic antibiotics. Some bacteria have evolved a special type of defence where they excrete a chemical messenger on treatment with an antibiotic. These chemical messengers are cis-2-unsaturated fatty acids, with the most important being Diffusible Signal Factor (DSF). We have demonstrated that the presence of DSF leads to increased biofilm formation and resistance to antibiotics, factors that prolong the infection. Effectively, DSF acts a warning signal by behaving as an ‘emergency flare’ to other bacteria, which then produce a biofilm in response. The biofilm works as a shield which protects the bacteria from the effects of the antibiotic.

In the same way as a key fits in a lock causing it to open, DSF fits into a biological receptor and “turns on” biofilm formation. This project aims to synthesise molecules which mimic DSF and fit into the same biological receptors but do not “turn on” biofilm formation. These novel molecules will act by jamming the lock closed and shut down the bacteria’s defences.

I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8 week period during June – September 2019.

Dr Tim O’Sullivan, School of Chemistry, tim.osullivan@ucc.ie
It has been recently discovered that bacteria use a communication system known as Quorum Sensing (so bacteria talk!).

Check out our Journal Cover (LEFT) in RSC Journal *Organic and Biomolecular Chemistry*.

Using quorum sensing, the bacteria communicate with each other and coordinate behaviour to the benefit of their colony. For example, in the formation of protective biofilms.

In this way the bacteria *Pseudomonas aeruginosa*, which particularly affects Cystic Fibrosis patients, communicate and cooperate to help defend against the body responses, and antibiotics.

You will make ‘signal molecules’ that are similar but different to that used by *P. aeruginosa*. In this way we will try and interrupt bacteria conversation and take a new look at controlling infection.

This could avoid the acquisition of resistance by the bacteria!

Additionally, you will acquire skills useful for further PhD studies, or for employment within the Pharmaceutical Industry.

**Contact:** Dr Gerard McGlacken  
**Email:** g.mcglacken@ucc.ie

Check out Prof Bonnie Bassler’s lecture on Youtube at:  
[http://www.youtube.com/watch?v=TVfmUfr8VPA](http://www.youtube.com/watch?v=TVfmUfr8VPA)
I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019

PROJECT 20 - Synthesis of Isoquinolinequinone-N-oxides – A Novel Anti-Cancer Scaffold

Dr. Florence O. McCarthy

School of Chemistry, University College Cork. f.mccarthy@ucc.ie; 021 4901695

Synthesis of Isoquinolinequinone-N-oxides – A Novel Anti-Cancer Scaffold

The isoquinoline framework is commonly found in natural products and drugs and is the seed point for much drug discovery. Isoquinolinequinones (IQQ) are a relatively unexplored sub-family although the natural products caulibugulone and mansouramycin incorporate this key IQQ framework and have significant anti-cancer activity.\textsuperscript{1,2} A route to the isoquinolinequinone (IQQ) scaffold has been reported has been developed by our group. This chemistry enables novel C(1), C(6) and C(7) substituted derivatives and selected compounds have good cytotoxic properties against various cancer cell lines including leukaemia and breast.\textsuperscript{3,4}

The N-oxide functionality has acquired a lot of attention in recent years due to its inherent ability to increase/modulate the bioactivity of parent pyridine-type compounds. The N-oxide functionality is thought to act through four major mechanisms depending on the nature of any given compound, of which the
most relevant are acting as a bioisostere of the carbonyl group and their use as hypoxic-selective cytotoxins e.g. tirapazamines. The N-oxide of the isoquinolinequinones is novel and hence is the subject of this project.

This project sets out to optimise the synthesis of the isoquinolinequinone-N-oxide core framework, develop novel chemistry to functionalise the 1-, 2- and 4-positions and generate novel C(6) and C(7) substituted isoquinolinequinone-N-oxides with nucleophiles.

I can confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019. Signed: Florence McCarthy

The centres of Active Galactic Nuclei (AGN) generate huge amounts of energy, whose source is believed to be accretion onto a central supermassive ($\sim 10^9$ solar masses) black hole. These objects sometimes produce oppositely directed “jet” outflows, which emit radio synchrotron radiation, produced by highly energetic electrons accelerated by local magnetic fields. Synchrotron radiation is intrinsically linearly polarized, and the observed polarization can provide information about the orientation of the synchrotron magnetic field. Fine details of the jet structures can be studied using Very Long Baseline Interferometry (VLBI), a technique in which radio telescopes around the world are used together in synchrony to obtain images with extremely high angular resolution.

The Summer project will involve making VLBI images of the compact radio jets of a number of AGN with sensitive, new 6cm+13cm+18cm+22cm data, with the aim of studying the jet magnetic fields and the distribution of material in the immediate vicinity of the jets. The jets of AGN are predicted theoretically to have helical magnetic fields, produced by the combination of the rotation of the central black hole and the jet outflow; the project will focus on analyzing the jet structure in the framework of a model for these helical magnetic fields, in order to estimate fundamental parameters of the jets and their helical fields. Such studies are of considerable importance in the field, and tie in with the fundamental question of how the relativistic jets are generated and launched. The summer project will begin with a brief tutorial in the basics of AGN and radio astronomy.

I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.

Denise C. Gabuzda – Physics Department
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The focal point of this project is the Haber-Bosch process and the using of computational simulations for designing new cheaper and more efficient catalysts.

In the early twentieth century a German chemist Fritz Haber developed the Haber process, along with the help of the German engineer Carl Bosch who developed the process into the required larger industrial scale. Defined as the: “Detonator of the population explosion”, this discovery was a gamechanger and its impact to the human life led to two Nobel Prize: 1918 (Haber) and 1931 (Bosch).

The production of nitrogen fertilizer and ammonia accounts for more than 450 million tonnes per year. The Haber-Bosch process converts atmospheric nitrogen reacting with hydrogen producing ammonia with the use of a catalyst the most widely used being an Iron catalyst promoted with Potassium Oxide. It has been estimated that nearly 50% of the nitrogen found in human tissues is originated from the Haber-Bosch process. The reaction scheme (on the right) $\text{N}_2 + \text{H}_2 \rightarrow \text{NH}_3$ is a reversible exothermic reaction leading to very high temperatures without the use of a catalyst exceeding 3000°C for nitrogen, i.e. the activation energy is too high and consequently the reaction does not occur spontaneously. However, when a heterogeneous Iron catalyst is added to the reaction the energy needed drops off significantly so that the reaction can proceed.

Very recently (January 2018) a new ternary compound, LaCoSi, catalysing ammonia formation in a more efficient way has been synthesised. This important discovery opened new doors that will be addressed in this project:

1) a similar compound LaScSi was previously synthesised but was not catalytically active, why?

2) On the other hand, why does pure Co not promote the reaction?

3) What is the role of Co then?

Using state-of-the-art computational chemistry this proposal will rule the mechanism of LaCoSi in the synthesis of ammonia, elucidating the role of Co and the presence of cooperative effects, the proposal aims to design new catalysts able to overcome the existing ones.

Some References:
Nature 1999, 400, 415  
Nature 2004, 427, 498–499  
Nature Geoscience 2008, 1, 636–639  
Nature Materials 2011, 10, 158–161  
Nature Catalysis 2018, 1, 178–185  

“I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.”

Davide Tiana, School of Chemistry. Email: davide.tiana@ucc.ie
James Bernoulli formulated the following problem in 1691: Assuming a lamina AB of uniform thickness and width and negligible weight of its own, supported on its lower perimeter at A, and with a weight hung from its top at B, the force from the weight along the line BC bends the lamina into a shape known as an elastic curve. What are the possible shapes? Here is Bernoulli’s original figure.

In 1744 Leonhard Euler tackled the problem by solving a variational problem. Euler’s technique gave birth to the method of variational calculus. Nowadays the studies of Bernoulli and Euler are considered the first instances for many areas of modern Mathematics, such as harmonic map theory, nonlinear integrable systems, elliptic function theory, theory of moduli of elliptic curves to name but a few. For example, the studies of the nonlinear integrable partial differential equations, such as soliton equations, began in the 1960’s whereas the modern studies of the extrinsic geometries, considered as extremal points of certain energy functional, began in the 1980’s. Both these areas of research are still very much alive today even though their origin trace back to the theory of elastica. In other words, studies of Bernoulli’s and Euler persist in the twenty-first century, and constitute an ideal entry point into these modern areas of Mathematics.

The variational problem consists of minimizing the bending energy of a thin inextensible wire, which mathematically is modelled by minimizing the integral of the squared curvature for curves of fixed length. The objective of the project is to derive the equations of elastica, and to solve these in terms of elliptic functions. Particular emphasis will be placed on visualizing elastic curves, and proving the uniqueness of the circle and the Euler figure-eight as the only closed planar elastic curves.

Project Supervisor:
Dr Martin Kilian
School of Mathematical Sciences
University College Cork Email: m.kilian@ucc.ie confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8-week period during June – September 2019.
PROJECT 24- Measurements of organic compounds in air by Chemical Ionisation Mass Spectrometry

Supervisor: Prof John Wenger  
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Research Topic:  
Organic compounds are emitted from a wide variety of natural and man-made sources. Although they may only be present at trace (ppb or ppt) levels in air, they have a strong influence on atmospheric composition and can affect human health and Earth’s climate. This project will involve laboratory work involving the use of a new time-of-flight chemical ionisation mass spectrometer to determine the chemicals present in ambient air. Measurements will be made in different environments to determine the species emitted from different sources. Experiments on the atmospheric reactions of the organic compounds will also be performed in a custom-built simulation chamber. The project will involve a lot of data analysis and interpretation to provide a better understanding of the sources, fate and impacts of organic compounds in the atmosphere.

This project is suitable for students of Chemistry, Chemical Physics, Environmental Science and Physics.

Declaration:  
I confirm that all facilities required for the proposed research project are available and that I am available to personally supervise the project during an 8 week period during June – September 2019.

John Wenger