Trinity College Science Society

Annual Symposium 11th March 2018
Winstanley Lecture Theatre

Programme

10:00	**Dr Oliver Shorttle**	Geology beyond the solar system
10:45	**Dr Mihkel Kama**	Understanding the Menagerie of Extreme Worlds
11:05	**Silvia Hnatova**	Epigenetic control of neurodevelopmental gene regulatory networks linked to neurodegeneration
11:25	**Dr Barbara Herdy**	Guanine origami in working copies of genes
11:45	**Dr Beñat Gurrutxaga-Lerma**	Multiscale Modelling of Materials
12:30 - 13:30		**Lunch**
13:30	**Dr Mireia Crispin-Ortuzar**	From particle physics to personalized cancer therapy
14:15	**Dr Mary Fortune**	So Your Treatment Doesn't Work: How to Lie with Statistics
14:35	**David Wong**	The Molecular Basis for Circadian Timekeeping in Mammals
14:55	**Adam Prada**	To quantum dynamics from classical mechanics: Feynman Path integrals in disguise
15:15	**Peter Gerlagh**	Solution to the quantum measurement problem
15:35 - 16:15		**Break**
16:15	**Professor Chris Lowe**	Healthcare in the 21st Centrury
17:00	**Krishna Sharma**	Inhibiting protein-protein interactions as an anticancer strategy
17:20	**Solene Rolland**	CRISPR-Cas9 screen: towards the discovery of key players in the cell death pathway triggered by Gram-negative bacteria
17:40	**Herschel Chawdhry**	Major features of tiny creatures - a crash course in particle physics

10:00 **Dr Oliver Shorttle** Geology beyond the solar system

10:45 **Dr Mihkel Kama** Understanding the Menagerie of Extreme Worlds

When it comes to our place in the Universe, we live in an era of discovery, where planets around other stars are being counted and characterised, and the history of our own solar system is being unravelled. I will review some of the typical and the most extreme worlds that have been found, and will discuss what we are learning about the prospects for biologically habitable environments in the cosmos. This will involve some deep diving into work being done in Cambridge on observations and modelling of the composition of planetary material, but also a more general tour of the field. Much of this will be contrasted with our knowledge of Earth and the solar system.

11:05 **Silvia Hnatova** Epigenetic control of neurodevelopmental gene regulatory networks linked to neurodegeneration

Dementia is preceded by a pre-symptomatic that can last for decades. However, recent evidence suggests that in familial forms of dementia, cellular changes are present in early life, during neural development. We propose that individuals with familial forms may compensate the effects of mutation by either buffering through gene regulatory networks or may develop towards a steady-state that makes it more susceptible to disease.

In order to study this, I am using induced pluripotent stem cell-derived neurons from people with familial APP and MAPT mutations. I will consider several levels of regulation of neurodevelopmental networks: RNA, small RNAs and DNA methylation. A combination of experimental and computational approaches, in vivo and in vitro data will help me to address how neural development in familial dementia is affected by changes in dosage of APP and MAPT genes.

11:25 **Dr Barbara Herdy** Guanine origami in working copies of genes

Everybody is well aware of the double helix and Watson and Crick base pairing. Still, there are other non-canonical ways of how nucleotides can interact with each other thereby creating curious structures. For instance, stretches of guanines can assemble in a plane by turning towards each other. When different planes of guanines then stack on top of one another they form a box like structure termed G-quadruplex (G4). G4s are not only found in guanine rich areas in genes but also in their working copies, the messenger ribonucleic acids (mRNAs). mRNAs are transcribed from active genes and then translated by the protein synthesis machinery into the encoded gene product, the protein. It is especially important to control the precise moment when a protein is translated from its mRNA and also where in the cell it is expressed. Therefore, mRNAs need postal codes that tell the protein synthesis machinery where and when proteins have to be made. If the postal code is wrongly read by the protein synthesis machinery or if the codes are flawed by mutations, the proteins may be produced in error or not at all. This is therapeutically relevant as these errors can promote cancer formation. Now, I am interested to know if G-quadruplexes in mRNA are such postal codes and if they have a role in cancer development.

11:45 **Dr Beñat Gurrutxaga-Lerma** Multiscale Modelling of Materials

BREAK

13:30 **Dr Mireia Crispin-Ortuzar** From particle physics to personalized cancer therapy

In this talk I will discuss the intimate relationship between two seemingly separate fields: particle physics and medical imaging for personalized cancer medicine. I will discuss how the techniques that allowed us to discover the Higgs boson at the Large Hadron Collider, and that are now being used to search for new particles that may explain Dark Matter, are very closely related to those that allow us to characterise the phenotypes of tumours using medical images.

14:15 **Dr Mary Fortune** So Your Treatment Doesn't Work: How to Lie with Statistics

Medicine can be so hard sometimes. Is your discovery that Magical Unicorn Sparkles (patent pending, available from your website for the low low price of only $199 a bottle) can cure cancer being prevented from seeing the light of the day by science's unreasonable demand for evidence? Well, worry no more! With a few simple errors in clinical trial design, you too can quickly produce significant results

14:35 **David Wong** The Molecular Basis for Circadian Timekeeping in Mammals

Most organisms have evolved behavioural and physiological rhythms to anticipate the regular changes in the environment caused by the rotation of the Earth. These roughly 24-hour oscillations are known as circadian rhythms, and they function at the cellular level as well as the organismal level.

Mammalian cell-autonomous circadian rhythms involve a core transcriptional-translational feedback loop (TTFL) composed of activating elements (CLOCK, BMAL1) and repressive elements (PER, CRY). CRY proteins are thought to be essential for circadian transcriptional feedback repression, and so CRY-deficient mutants are often used as arrhythmic animal and cellular models.

However, under certain conditions, circadian rhythms of the PER2::LUC reporter continue to be expressed in CRY-deficient cells and tissues ex vivo. Here we show that these CRY-less rhythms are temperature compensated and generated post-transcriptionally, without detectable cycling of clock gene transcript levels. We find that CRY-less oscillations are less robust compared with wild-type cells, being highly susceptible to environmental perturbation.

Using live cell imaging, biochemical and pharmacological approaches we find that CRY-deficient cells exhibit a significant dysregulation of normal protein homeostasis suggesting that differential sensitivity to cellular stress may account for the sensitivity of CRY-less oscillations to exogenous stimuli.

Our findings suggest that the principal utility of the TTFL in cellular clock function is to confer robustness upon post-transcriptional timekeeping mechanisms.

14:55 **Adam Prada** To quantum dynamics from classical mechanics: Feynman Path integrals in disguise

Particles behaving like waves; that is the usual picture in quantum mechanics. Schrodinger's equation is a wave equation after all. This applies well to electrons, which are light, but for atomic nuclei, this is not a useful approach. Living on the edge of quantum and classical dynamics, the method of choice for nuclei are the Feynman path integrals. In this lecture, I will explain, how one can use a cheap classical simulation to obtain quantum results using a useful isomorphism in the path integral formulation of quantum mechanics.

15:15 **Peter Gerlagh** Solution to the quantum measurement problem

One of the classic problems in physics is the quantum measurement/collapse problem. This is the question, WHY the quantum state (wavefunction) collapses WHEN it is measured. Although we still don't know why the quantum state collapses, it has been discovered why the quantum state appears to collapse when a quantum system is measured. It turns out that so long as the quantum state collapses onto states which roughly correspond to classical world states, it looks as if measurement coincides with collapse. I will show this by comparing the Copenhagen Convention to a theory in which the wavefunction collapses once every Christmas.

BREAK

16:15 **Professor Chris Lowe** Healthcare in the 21st Centrury

17:00 **Krishna Sharma** Inhibiting protein-protein interactions as an anticancer strategy

Proteins form an integral part of the cellular machinery and are responsible for carrying out a diverse range of important functions within living organisms, such as cell growth, DNA replication. Each of these functions is regulated by a complex network of proteins consisting of interactions between various proteins. Molecules which can selectively modulate aberrant protein-protein interactions (PPIs) are novel therapeutic candidates for treating human diseases. Whilst PPIs have traditionally been considered as "undruggable", research in this area has led to the emergence of several effective methodologies for inhibiting PPIs. Our research work involves synthesis of macrocyclic organic molecules to target the p53-MDM2 interaction as an anti-cancer therapy

17:20 **Solene Rolland** CRISPR-Cas9 screen: towards the discovery of key players in the cell death pathway triggered by Gram-negative bacteria

The body has several layers of defence against foreign organisms. When it comes to bacteria, the immune system is, of course, deployed to help fight against the infection. In addition to this large scale army, cells themselves can restrict bacterial spread and infection. Intracellular immunity comprises several pathways and varied modes of actions. Among these scenarii, cell death is an important one but little is known about how this mechanism is triggered and regulated.

What a better way of studying this, than taking advantage of a bacterial adaptative immunity system (namely CAS-9) to perform a genetic screen and exploring the steps leading from the intake of the bacterium within the cell to its death.

17:40 **Herschel Chawdhry** Major features of tiny creatures - a crash course in particle physics

What are the fundamental laws of Nature? How does the Universe work? What is matter made of? Particle physics seeks to answer these most fundamental of questions; progress in this field during the last 50 years has led to the most precisely-tested predictions in the history of science. In this talk, I will discuss the history of the field, the current state of research and my own work on predicting results from experiments at the Large Hadron Collider - the biggest machine in the world.