Workshop Report

DNA damage is unavoidable. Intrinsic cellular metabolic processes as well as exposure to environmental, physical or chemical agents can lead to DNA damage. The ability to respond to these insults to our genetic material underpins human health and disease. The key details of the major DNA repair pathways have been defined but many aspects of the processes and their regulation require further elucidation and the multi-pathway dynamics connecting cell cycle arrest and DNA repair with phenotypic fate decisions are still inadequately described and poorly understood.

This two-day workshop, sponsored by the Institute of Advanced Studies, MILES (Models and Mathematics in Life and Social Sciences) and the Departments of Mathematics, Nutritional Sciences, Biochemistry and Physiology and Electronic Engineering at the University of Surrey, brought together mathematicians, computational modellers and biologists from the University of Surrey with leading international experts to provide a highly interactive forum to:

- Describe the current status of biological knowledge and modelling approaches in the field.
- Identify gaps in our knowledge and discuss approaches and opportunities for bridging these gaps and stimulating trans-disciplinary research.
- Identify opportunities for new collaborations.
- Provide post-graduate students and post-doctoral researchers with the opportunity to learn more about the field, present their work and interact with international scientists.

The workshop consisted of a series of invited presentations from leading scientists in the field, shorter presentations selected from submitted abstracts and poster sessions with plenty of additional time set aside for discussion throughout the schedule.

DAY 1

Session 1 DNA base damage and breaks

Leona D. Samson, Biological Engineering Department, Centre for Environmental Health, MIT, USA
"The pros and cons of DNA Repair"

Sherif El-Khamisy, MRC Genome Damage and Stability Centre, University of Sussex, UK
"Breaking and sealing the human genome: the consequence of the imbalance"

Philip Aston, Department of Mathematics, University of Surrey, UK
"Mathematical modelling of base excision repair"

Session 2 Modelling repair and stress responses

Kevin Janes, Department of Biomedical Engineering, University of Virginia, USA
"Data-driven modeling of the cellular response to environmental insults"

Peter Svensson, Karolinska Institutet, Department of Biosciences and Nutrition, Sweden
"Combining computational and experimental approaches to model genotoxic and mitotic stress responses"

Simon Reed, Department of Medical Genetics, Haematology and Pathology, School of Medicine, Cardiff University, UK

"How yeast global genome nucleotide excision repair is organized and orchestrated throughout the genome"

Mark Bennett, Institute of Cancer and Genetics, Cardiff University, UK
Novel bioinformatic tools for the analysis of DNA damage and repair processes throughout whole genomes"

Renata Retkute, School of biosciences, University of Nottingham, UK
"DNA replication in cells exposed to DNA-damaging agents"

DAY 2
Session 3 Double Strand Break Repair

Matthew Neale, Genome Damage and Stability Centre, University of Sussex, UK
"Regulation of meiotic recombination by DDR kinases Mec1(ATR) and Tel1(ATM)"

Norman Kirkby, Department of Chemical and Process Engineering, University of Surrey, UK
"Mathematical modelling: From DNA damage and repair to national demand for radiotherapy"

Yeyejide Adeleye, Unilever Safety and Environmental Assurance Centre (SEAC), http://tt21c.org/, UK
"Pathway modelling of DNA damage and its application to risk assessment"

Reza Taleei, Oncology Pathology, Karolinska Institutet, Sweden
"Modelling DSB repair induced by ionizing radiation"

Adam Cole, Department of Chemical Engineering, University of Surrey, UK
"Predicting badly behaved brain tumours with a MiNiMUS of fuss"

Session 4 Repair in the mitochondria

Nadja Souza-Pinto, Department of biochemistry, Chemistry Institute, University of Sao Paolo, SP, Brazil
"The nucleotide excision repair factor XPC modulates mitochondrial bioenergetics in human cells"

Dragony Fu, Institute of Veterinary Biochemistry and molecular biology, University of Zurich, Switzerland
"Human ALKBH7 protein plays a critical role in DNA damage-induced programmed necrosis"

Event themes

Throughout the series of presentations and linked discussions a number of specific themes developed. These included:

- The description and discussion of repair processes for a wide range of different types of DNA lesions.
- Commonalities and differences between repair of nuclear and mitochondrial DNA.
- The impact of DNA damage and its repair on cellular functions and viability.

- Evidence from a number of different sources that, while efficient DNA repair is vital for the maintenance of genomic integrity and long-term health, high levels of repair activity can also be detrimental in certain circumstances, potentially contributing to mutagenesis and/or tissue degeneration.
- Many of the major protein components of the different repair processes have been well characterized but the presentations and discussions made clear that there is still a considerable amount of important on-going research in which the role of new protein components involved in DNA repair is being discovered along with novel subtleties of the repair processes that can have profound impact on repair efficiency and biological outcomes.
- One such example, highlighted in a number of the presentations, was the importance of chromatin structure in the control of DNA repair processes.
- In this context, computational methods are proving their worth in the form of newly developed software tools that permit new methods of data analysis and data visualization at both the chromosomal and whole genome level.
- However, it was evident that the majority of the current research is based on biochemical, genetic and molecular biological methods.
- A range of modelling methods that are already being used in the context of modelling DNA damage and repair where introduced. These included models based on ordinary differential equations, data-driven multi-variate methods and binary decision trees used in conjunction with Monte Carlo sampling routines.
- There was general agreement that there is considerable scope for much more extensive use of modelling provided the most appropriate methods are employed and appropriate data is available or can be generated.

Outcomes

The workshop was attended by 28 delegates, including one from industry, two from the US, four from Europe, two from Brazil, six from other UK universities and 13 from the University of Surrey (representing 6 different departments). The format selected for the workshop:

- Enabled all those present to be brought up to date in a range of different aspects of the research field, which is likely to have been particularly valuable for the post-graduate students and post-doctoral researchers present.
- Gave both biologists and modellers the opportunity to present their work and their personal perspectives.
- Fostered trans-disciplinary discussion.

The workshop was very successful in creating a friendly and collaborative environment in which the delegates were able both to relax and enjoy the meeting as well as taking advantage of the opportunities for in-depth scientific discussion. As a result, we are very hopeful that future collaborations will arise as from this meeting.

In addition, it is our aim is to produce a commentary document describing the key points and themes developed during the meeting for publication in a peer reviewed journal.

Sponsors
Institute of Advanced Studies at the University of Surrey, MILES (Models and Mathematics in Life and Social Sciences) project, Department of Biochemistry and Physiology (FHMS), Department of Nutritional Sciences (FHMS), Department of Mathematics (FEPS), Department of Electronic Engineering (FEPS)

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