New Lecturer in Magneto-Hydrodynamics

The new magnetohydrodynamics (MHD) group in the Maths Division has gained another member this year in the shape of Dr David Pontin. Dr Pontin got his PhD in nearby St Andrews, before spending the last few years doing research overseas, first as a postdoc at the University of Waikato in New Zealand, and most recently as a Research Scientist at the University of New Hampshire in the USA. Dr Pontin says; “I’m really excited to have this opportunity to return to Scotland, and in particular Dundee, and to work again with Gunnar Hornig to develop the new research group in Dundee. Its a great time to be involved in MHD and solar theory, with lots of new satellites just being launched to study our surroundings in the Solar System”.

(continued on page 2)

New Book on Single-Cell-Based Models

Dr. Kasia Rejniak a postdoctoral researcher in mathematical biology has co-edited a new book on “Single-Cell-Based Models in Biology and Medicine.” As the book was very much her project I decided to interview her and find out exactly what it was all about!

Ed: So Kasia tell me what was it that gave you the idea for the book in the first place?

Kasia: It is fascinating to watch live cells under the microscope, to see how they move, divide and interact with one another. As a mathematician I was always interested in making computational models that allow for simulations of cells and cell processes on the computer screen. It turns out I was not the only one. Over the last few years several mathematical biologists have been working on different computational models in which cells are represented as individual entities. (page 3)
Explosive Mathematics by David Pontin

Our group uses mathematical models to describe processes which occur in plasmas, with particular focus on the Sun. Almost all of the matter in the Universe is in the plasma state, from stars and galaxies, to the upper atmosphere of the Earth. A plasma is a liquid or gas that consists of ions and electrons. We use the equations of magnetohydrodynamics (MHD) to describe plasmas. This is a complicated word, but basically what it says is that our plasma must obey the equations of hydrodynamics (being a type of fluid), as well as the equations of electromagnetism. This is because the ions and electrons, which are constantly moving around, generate electric and magnetic fields.

In these plasmas it is very common for the magnetic field to dominate the system. This is because the forces which the magnetic field exerts are so much stronger than other forces such as gravity. The ions and electrons that make up the plasma are trapped on magnetic field lines, and can only move by spiralling around them. For this reason, it is sometimes possible to ‘see’ magnetic field lines in the solar atmosphere, showing up as bright loops (see the figure). In general these field lines are not allowed to break or pass through each other, and so can become very stretched and tangled which builds up a lot of stress and energy. In order to release this energy, a process called ‘magnetic reconnection’ has to take place, which allows the field lines to break, and the topology of the magnetic field to change. It is this magnetic reconnection which is behind energetic and explosive phenomena in all plasmas - this is one of the main focuses of our research in Dundee.

Through studying the Sun, we can learn a lot about the basic processes that go on throughout the cosmos. In addition, of course, all life on Earth depends on the Sun for its source of energy, and so understanding how it is powered and how it might behave in the future is of crucial importance. The Sun also has a certain effect on Earth’s climate, as it goes through its seven year activity cycle. Huge explosions, known as solar flares, are a frequent occurrence in the Sun’s atmosphere (the ‘corona’). Moreover, these solar flares are sometimes associated with an even more fierce phenomenon known as a Coronal Mass Ejection. In each of these events millions of tonnes of plasma erupt outwards from the Sun – and sometimes head in our direction! This can have some nasty effects, such as damage to satellites and power grids as well as danger to astronauts and those onboard high-flying aircraft. However, one more pleasant consequence is the creation of the Northern or Southern Lights (or ‘aurorae’) – brightly coloured curtains sometimes visible in the night sky. They are caused by the radiation and fast particles from the Sun streaming in along the Earth’s magnetic field lines, and hitting particles of the Earth’s atmosphere.

Solving the equations that describe how the plasma behaves allows us to model how these explosive events can occur. In the group here in Dundee, we use a combination of mathematical methods and computer simulations to investigate these processes. Since plasmas are found almost everywhere, the results have many applications in astrophysical systems like stars, galaxies and black holes, as well as in laboratory plasmas, such as those found in nuclear fusion devices.
This brought me to the idea of putting together a collection of papers where different computational models are described by their authors. Together with my colleagues, Dr. Sandy Anderson and Prof. Mark Chaplain from the mathematics division in Dundee, we edited a book that contains 12 chapters from leading authors in the field of single-cell-based computational models.

**Ed:** How do you think mathematical models can help in our understanding of biology?

**Kasia:** Mathematical models will not eliminate biological experiments but may help in determining key factors and key processes by testing first some ideas using computer simulations. To built a mathematical model of a cell, we have to make it much simpler than in reality by taking into account only the most important features, but we also want to represent differences between individual cells as well as their ability to communicate and interact with one another and their surroundings. And the single-cell-based models are ideal for these purposes and allow more realistically to represent biological tissues and multi-cellular organisms and better understand the principles underlying the complex biological processes.

**Ed:** What different models does the book consider and what makes them different?

**Kasia:** The book contains descriptions of several different models. In some of them cells are represented as points on the lattice, in other as small spheres or ellipsoids, or have deformable shapes and contain elastic boundaries filled with fluid. If one wants to focus on mechanical properties of cells, there are models that incorporate many details of cell structure, if on the other hand one wants to model tumour growth then cells can be represented as points and the model can handle then a few hundred thousands of cells. Very different mathematical and computational techniques are used to define models included in our book, these are cutting edge tools for modern mathematics.

**Ed:** So who is this book really for—who would find it useful?

**Kasia:** We would like to address this book to the students starting their research in the field of mathematical biology to show them a flavour of different techniques that they can use in their studies. Moreover, each chapter contains a review of suitable biological and medical applications to inspire the students to pursue their own research topics.

**Ed:** Unusually the book comes with a DVD what does it contain?

**Kasia:** All models presented in the book are accompanied by simulation movies which are included on the dvd. They show different applications of the models, such as tumour growth, limb development, blood clothing, tissue folding, vascularisation (growth of blood vessels), cell chemotactic movement (movement toward the higher concentration of chemical factors), development of Dictyostelium discoideum or formation of epithelial layers.
Many unicellular organisms live in large colonies that can contain several million individual cells. Normally these colonies grow smoothly with a round morphology, but when the organisms are put under stress by for example low nutrient levels the shape of the colony changes drastically and takes on a branched morphology. This phenomenon can be observed in bacterial growth (fig. 1), fungal colonies and tumour growth (fig. 2). The reason why this occurs in tumours is because the tumour cells have lost their capability to cooperate with other cells and they therefore behave like unicellular organisms. This type of branched growth in tumours can be critical as it is more difficult to surgically remove a branched irregular tumour than one that is round and well defined.

There has been debate within the scientific community why this change in growth dynamics occurs. One explanation is that the organisms have evolved a cooperative behaviour to cope with harsh growth conditions, which means that the entire colony responds to the change in growth conditions by adopting a new growth strategy. The other explanation states that the change in morphology is only due to the basic underlying mechanisms of the growth of the colony and doesn’t invoke any evolutionary explanation but instead relies on the underlying physical laws of growth.

The latter explanation is strengthened by the fact that many inanimate physical growth processes give rise to similar branched patterns. These growth processes are known as diffusion limited because the pattern grows by attachment of particles that move by diffusion. Probably the best example of this type of growth is “Diffusion Limited Aggregation” or DLA. In this growth process one starts with a single particle at the origin and a second particle is released far away from the origin. The second particle moves by diffusion or random walk until it hits the first particle and sticks to it. A new particle is then released and exactly the same process is repeated over and over again. One would expect that this would give rise to a circular pattern growing through the attachment of new particles, but on the contrary the resulting pattern is highly branched and even fractal (see fig. 3 and title image on page 1). This very simple growth process turns out to be very difficult to analyse and very little is known about it from a mathematical perspective. One open problem is the dimension of the pattern, which unlike most other objects is a between 1 and 2.

The work undertaken in the maths division has focused on simulating and explaining the pattern formation from a purely physical perspective and recent results have shown that the nutrient concentration has a direct impact on the colony shape and that the width of the branches is directly related to the abundance of nutrient. An example of cell colonies growing at
**Anti-Cancer Drugs in Scotland** by Hitesh Mistry

Dr. Hitesh Mistry recently arrived in Dundee from Manchester. Working with Dr. Fordyce Davison and Prof. Mark Chaplain he has been developing a mathematical model of new cell-cycle specific drugs. Also, being new to Scotland he has taken the opportunity to visit a few local historic attractions. I asked Hitesh to tell us a little more about his research and his travels.

Mathematics is playing a key role in developing new anti-cancer drugs, with Cyclacel, that are selectively killing cancer cells while leaving other healthy cells unharmed. These new drugs are known as *Aurora Kinase Inhibitors*, which are designed to disrupt the cell cycle to such an extent, that the parent cell will undergo a mitotic arrest and ultimately cell death.

These drugs seem to be selectively killing cancer cells and leaving other fast dividing cells untouched. Mathematics is being used to construct functional networks describing the actions of Aurora Kinase's on the cell cycle. The network is not designed to model every single action of the Kinase's but to construct a description of the key functions these Kinase's are involved in. By doing so we hope to have a deeper understanding of how these drugs are working and maybe provide an insight into why these drugs maybe selective.

Members of the Mathematical Biology Group have been roaming the rolling hills of Scotland on many a weekend. Travelling to fairytale castles in the heart of Perthshire to Abbeys on eerie gloomy lakes. During the Historic Scotland weekend visits were made to Doune Castle, Stirling Castle and Inchmahome Priory. Doune Castle is famous for the setting of Monty Pythons Holy Grail and indeed one can sample a bottle of Holy Gr-Ale while enjoying the splendid views offered by the Castles tower! Inchmahome Priory is much more of a gloomy place set on an island in the middle of Lake Menteith it is a monastery dating back to the 13th century. The island is also the location of one very strange tree, which has never had to compete for light and so the branches droop to the ground in a rather sad manner. Finally a visit to central Scotland is never complete without taking in the breathtaking views at Queens view.
New research has shown that the aggressiveness of cancer tumours may be determined by the tissue environment in which they grow. The finding has the potential to impact on how certain cancers are treated. Dr Sandy Anderson, of the Division of Mathematics, has developed a mathematical model which predicts how tumours grow and invade tissue. The results produced by the model have given startling insights into how cancerous tumours develop in the body.

"What this model predicts is that the more barren and harsh the tissue environment surrounding it is, the more aggressive the tumour becomes," said Dr Anderson. The combination of maths and laboratory research to develop such models has been hailed as a "new era in cancer research" by Professor Vito Quaranta, a leading American cancer biologist who is collaborating on the project.

Dr Anderson's research was published in the scientific journal Cell and is one of the few purely mathematical modelling papers to appear in the history of this prestigious biological journal. "What our research shows is that the micro-environment in which the tumour grows acts like a Darwinian selective force upon how the tumour evolves," said Dr Anderson.

"Much of current biomedical research being carried out on cancer is done in isolation of the real environment in which the tumour naturally grows, but these results show that this environment could be the crucial determining factor in the tumours development." The model developed by Dr Anderson also shows a clear relationship between the shape of a cancer tumour and how aggressive it is. Aggressive tumours tend to assume a spidery shape in the model, while more benign growths are a generally more spherical in shape.

"One interesting prediction is that if you make the environment the tumour is growing in more harsh or barren, then the more likely it is that any surviving cancer cells will be the most aggressive and hardest ones. This clearly has a potential to impact on how certain cancers are treated, since most of the current treatment strategies are focused on making the tissue environment as harsh as possible for the tumour in the hope of destroying it." Dr Anderson is collaborating on his work with experts in cancer biology at Vanderbilt University in the United States, led by Prof. Vito Quaranta and Dr Alissa Weaver, who are in the process of carrying out the physical validation of the results produced by the mathematical model.

Prof. Quaranta hailed the combination of mathematics and laboratory research as a major development in how we approach cancer. "A new era in cancer research has begun," said Prof. Quaranta. "Mathematicians are bringing entirely new vistas to our field, cancer is no longer an ugly beast to defeat, but rather it is a complex process that can be described rationally and conquered perhaps slowly, but surely."

The figure shows a mathematical model (represented by equations swirling in the ocean) predicting that the tumour structure is largely dependent on its environment. A smooth-margined non-invasive tumour (bottom left) grows in a mild nutrient-rich environment (symbolized by the calm ocean); the invasive finger-like tumour (top left) represents a tumour growing in a harsh, nutrient-poor environment (symbolized by the turbulent hurricane). A second prediction is that, in mild microenvironments, many phenotypes of a heterogeneous tumour-cell population coexist (represented by the phenotype mountains).
Bumper Final Year

Mathematics at Dundee had a bumper crop of final year students graduating—some of whom can be seen in this photo accompanied by a subset of their lecturers. Dundee appears to be bucking the UK trend which shows a general decrease in the numbers of mathematics students. This positive trend is also seen in our undergraduate numbers that are at an all time high compared with previous years.

Class of 2007- Front (left to right): Alistair Taylor, Dawn Rosie, Fiona Wilson, Kate Adams, Ren Lee, Gemma Bancroft, Fiona Roberts. Middle: Callum Stewart, Steven Oram, Shelly Smith, Jennifer Loudon, Emma Stewart. Back: Dr. David Thomas, Dr. Gunar Hornig, Prof. Alistair Watson, Dr. Fordyce Davidson, Dr. Giles Thomas.

Dundee Hosts Three International Workshops

The Division of Mathematics in Dundee hosted no less than three international workshops on cancer modelling in 2007. Two of the workshops were as part of the Marie Curie research training network, “Modelling, Mathematical Methods and Computer Simulation of Tumour Growth and Therapy” that promotes collaboration between 12 different European groups working on the mathematical modelling of different aspects of cancer. A core goal of the network is in training a new generation of mathematicians that specialise in Cancer modelling. This is done via a series of summer schools, where students who are part of the network are taught the techniques that will allow them to develop and analyse such models, and workshops, that allow the students to present their work in the company of more experienced senior scientists.

The third workshop was somewhat different as it was funded by the ICMS (International Centre for Mathematical Sciences, based in Edinburgh) and was a truly international meeting, that saw some of top researchers in the world converge on Dundee to talk about their work on mathematical models of cancer growth and progression. Plenary talks were given by Nicola Bellomo (Turin), Miroslaw Lachowicz (Warsaw), Yannis Kevrekidis (Princeton), Angela Stevens (Heidelberg), Thomas Hillen (Alberta), Hans Othmer (Minnesota), Sandy Anderson (Dundee), Vito Quaranta (Nashville), Avner Friedman (Ohio), Robert Gatenby (Arizona), Philip Maini (Oxford), Helen Byrne (Nottingham), John Lowengrub (California), Luigi Preziosi (Turin), Jonathan Sherratt (Heriot-Watt).

Of course it wasn’t all work, as some of the photos below can testify. The end of workshop dinner was held in Jimmy Chungs delicious Chinese buffet, where not only was the food free for all participants but so was the beer!
Letter From the Head of Division

I am very happy to contribute an article for this Newsletter in my capacity as the current Head of Division. First of all I would like to thank my predecessor, Prof. Alistair Watson, for all his hard work and efforts during his period of tenure and in expertly steering and guiding the Division through to where we are now.

My first year (or so) as Head has already seen several major changes. At the Division "Night Out" in June 2007, we all marked the “retiral” of Dr. David Thomas and Prof. Alistair Watson, with over 80 years of service between them. Thanks to them both for their years of service and dedication to the Division/University over all these years, and continued thanks to Alistair who has been helping out this academic year with tutorials.

The Division was sad to hear of the news that Professor Ron Mitchell died in late November. Ron came to Dundee in the late 1960s to a Chair in Numerical Analysis and was responsible for laying the foundations of and then building up the Division’s research excellence in this area which continues to this day. Those who knew Ron either as a colleague or as students will remember him fondly for his warmth and wit as well as his many contributions over many years to the life of the Division.

However, we are also pleased to welcome this year two new members of staff – Professor Ping Lin and Dr. David Pontin. Ping joined us in October 2007 from the National University of Singapore as the new Chair of Numerical Analysis and Computational Mathematics, while David arrived in January 2007 as a second member of the MHD Group. It is also a great pleasure to welcome Dr. Antonia Wilmot-Smith as a Research Fellow to the MHD group.

Much of this year has been taken up by preparing our RAE submission which was sent off in late November 2007 (results will not be known until December 2008). Thanks to all who helped out. The final document was very positive and the Division is moving from strength to strength in its research. We now have four very active and dynamic Research Groups: Mathematical Biology, Numerical Analysis, Applied Analysis and MHD, all undertaking internationally excellent research. The future holds many new and challenging problems for us all in these areas and it is an exciting time to be involved in applied mathematics. In the still relevant words of David Hilbert:

"Who of us would not be glad to lift the veil behind which the future lies hidden; to cast a glance at the next advances of our science and at the secrets of its development during future centuries? What particular goals will there be toward which the leading mathematical spirits of coming generations will strive? What new methods and new facts in the wide and rich field of mathematical thought will the new centuries disclose?“ (D. Hilbert, opening speech to the 1900 Mathematics Congress in Paris)

At an institutional level, we have all undergone much change due to the re-structuring of the University. However, we are all benefiting from the synergy and value-addedness of our new College and are now well-placed to face the challenges that the future will no doubt bring. Here in the Division we are all looking forward to our long-awaited move to our new premises next to Life Sciences.

In looking to the future, it is perhaps fitting to end with some words of wisdom from a “local” mathematical hero, Sir D’Arcy Wentworth Thompson, who notes the timelessness and inherent lasting value of mathematics:

"I know that in the study of material things, number, order and position are the threefold clues to exact knowledge; that these three, in the mathematician’s hands, furnish the ‘first outlines for a sketch of the Universe’."

Final Word from the Editor

As always I would very much like to thank the respective authors (both staff and students) for their contributions to the newsletter as they capture the true spirit of what has been happening at Dundee. This issue hopefully highlights the fact that there is a great deal diversity in mathematics with the formation of new groups (MHD) and the publication of great books we move optimistically into 2008!

Sandy Anderson (Editor)

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