Mathematics Newsletter

Contents

Page 1-3
Appointments, New MSC Degree.

Pages 4-5
Research in Mathematical Biology.

Page 6-7
News from the MHD Group.

Page 8
The World of Microbes.

Formula for Success

Graduation ceremonies in June saw several years of hard work pay off for the most recent graduates of the Division of Mathematics. Mathematics graduates are well-placed to enter the world of work and so the Division was pleased to welcome another record-breaking intake of students in September. Enrolment in the Level 1 Mathematics course is 15% up on even the record numbers of last year. Also for the first year, the Division is offering an MSc in Mathematical Biology to complement its existing undergraduate degree in the same field. You can find more details the courses offered by the Division on page 3.

In view of the recent expansion and in order to maintain its excellent undergraduate experience, the Division has recently invested in four new members of staff who we are pleased to introduce over the following pages.

New Lecturer in Mathematical Biology

In February Dr. Paul Macklin joined the Division as a lecturer in the mathematical biology research group, a position that was funded under Prof. Mark Chaplain’s recent Advanced Investigator Grant awarded by the European Research Council. Dr. Macklin earned his Ph.D. in mathematics at the University of California at Irvine in 2007, where he developed mathematical and computational techniques to model tumour growth in large, complex tissues. He spent the last few years as an assistant professor at the University of Texas Health Science Center in Houston, where he developed new techniques to calibrate computer models of cancer to individual patients. Part of this work is featured in a new Cambridge University Press book, Multiscale Modeling of Cancer.

Dr. Macklin’s recent arrival to Scotland is not his first – he has already travelled to Dundee and Edinburgh numerous times to collaborate with the group in Dundee and Dr. Steven McDougall at Heriot-Watt University to link a tissue-scale model of tumour growth with a cell-scale model of angiogenesis. You can find details of this work and more of Paul’s research interests on pages 4-5.

Some students from the class of 2010 pictured with staff at their June graduation ceremony.
Meet the new members of the Division of Mathematics

Lecturer in Mathematical Biology

The Division is also pleased to welcome Dr. Hiroko Kamei who joins us for a year as a Lecturer. Dr. Kamei received her PhD from the University of Warwick where she studied objects known as ‘networks’, analysing how the structure of a network influences its dynamics. This was followed by a postdoc position here in the Division working with Dr. Fordyce Davidson on mathematical models of the effects of an anti-cancer drug. In September Dr. Kamei was made a lecturer and, alongside new teaching duties, continues to develop her research interests in the dynamics of coupled cell systems, bifurcation theory and mathematical biology.

Dr. Kamei says “The Division of Mathematics is small and friendly. Students and members of the Division work closely together which gives a comfortable atmosphere. I hope to help students find University mathematics interesting, and broaden their academic curiosity during their student life here in (relatively sunny!) Dundee. Scotland’s winter can be cold, but I like mountain walking and skiing so I’m enjoying living here. I also like badminton and squash so you may see me in the sports centre.”

Lecturer in Magnetohydrodynamics

January saw the appointment of Dr. Antonia Wilmot-Smith as a new lecturer in Magnetohydrodynamics (MHD). She joins Drs. Gunnar Hornig and David Pontin in a research group that was established in 2005. MHD provides a mathematical framework through which to understand the interaction between a plasma (an electrically conducting fluid) and a magnetic field. Studying the MHD equations and their solutions can help us explain phenomena that occur throughout the Universe from the generation of intense magnetic fields in the Sun, to the formation of galaxies.

Dr. Wilmot-Smith is not new to Dundee, having already been working in the Division as an STFC Postdoctoral Fellow since 2007. Her recent work examines the structure and evolution of solar coronal loops, magnetic loops of plasma that form the building blocks of the solar atmosphere. She says “It’s a particularly exciting time to be involved in MHD and solar research. A generation of new satellites are observing the Sun in unprecedented detail while at the same time advances in computing power offer new ways to model the fundamental physics. Our understanding should progress enormously over the coming years.”

The image on the right shows sunspots on the surface of the Sun. Sunspots are regions of intense magnetic field. MHD helps us understand their formation. (Photo: Royal Swedish Academy of Sciences).
Teaching Fellow

The final new face in this edition is new teaching fellow Hannah Coutts. Ms Coutts joins us from St Andrews where she recently submitted a PhD thesis on computational group theory. Group theory studies symmetries as abstract mathematical objects, called groups, while the computational aspect involves developing algorithms to manipulate and investigate these symmetries. For example, certain properties of molecules can be determined by understanding their symmetries. Her PhD research focused on primitive permutation groups and matrix group normalisers and she developed new algorithms for computing these objects.

Ms Coutts is joining us for one year as a teaching replacement for Professor Lin who won a prestigious award from the Leverhulme trust to focus solely on his research in numerical analysis. Reflecting on her new teaching duties Ms Coutts told the newsletter “Maths has a bad reputation in Britain, but I believe everyone can enjoy maths as long as it is presented well. I think an enthusiastic lecturer can make all the difference and I try to apply that to my teaching.” We wish Ms Coutts all the best for the final part of her PhD studies, the oral exam.

Mastering Biology

For some years now Dundee has been the only university in the UK to offer a dedicated Mathematical Biology Degree to school-leavers. Following on the success of this degree and the continuing growth of the Mathematical Biology research group, this year the Division rolled out a brand new postgraduate degree: a Masters in Mathematical Biology. Students from Dundee, across the UK and even as far as China, are busy working through courses dedicated to building the research tools needed to probe biological problems. As well as learning advanced mathematical and numerical (computer modelling) techniques, students will also study more specific applications to oncology (the study of cancer), ecology and physiological systems ranging from cell signalling to blood flow. All students will complete their year-long studies by working over the summer on a focused project, where they have an opportunity to "get their hands dirty" applying their new mathematical knowledge to real-life problems.

Studying Mathematics at Dundee

In addition to the new MSc in Mathematical Biology, the Division of Mathematics offers a wide range of undergraduate degrees with options for entry at various levels depending on your existing qualifications. For entry in 2011 into Level 1 we require BBBB at Higher (or equivalent), including a B in Mathematics.

We also offer a Postgraduate Diploma in Mathematics, ideal if you want to upgrade your existing degree, and have a lively PhD programme. Details of all the courses run by the Division of Mathematics can be found on our webpage.
Mathematical Models of Cancer Growth

On his previous visits to Scotland, Dr. Macklin's work focused on linking a tissue-scale model of tumour growth with a cell-scale model of angiogenesis. Here oxygen transport, tissue biomechanics, and tumour morphology (shape) are modelled with a coupled system of nonlinear partial differential equations (PDEs). Oxygen consumption by the rapidly-dividing tumour cells creates regions of hypoxia (low oxygen) within the tumour, a phenomenon that is exacerbated by the destruction of blood vessels by the tumour as it degrades and expands into normal tissue. An important response to hypoxia, both in tumours and normal tissue, is angiogenesis: the creation of new blood vessels to restore oxygen transport. Hypoxic tumour cells secrete angiogenesis-promoting factors that diffuse away from the tumour to nearby blood vessels. Endothelial cells detach from the vessels, migrate towards the tumour, and eventually form a new vasculature that drives additional tumour growth. However, the rapidly-growing tumour generates vessels, causing sustained hypoxia and tumour cell necrosis (death due to hypoxia). The nonlinear interaction between growth, oxygen transport, angiogenesis, and tissue mechanics can lead to tumour shape instabilities, such as fragmentation or invasive fingering (see the figure above left).

Dr. Macklin developed high-accuracy numerical techniques to solve these difficult nonlinear PDEs on moving regions, allowing simulation of tumour growth in complex tissues. For example, Macklin and co-workers simulated glioblastoma multiforme (an aggressive type of brain tumour with a median patient survival time of just 14 months) in virtual tissue including cranium, white and grey matter, cerebrospinal fluid, and membranes (see the right-hand figure). Complex dynamics were observed including a building mechanical pressure between the tumour and cranium, one of the first clinical signs of glioblastoma. While these methods can simulate tumour growth efficiently in relatively large, complex tissues, they have proven difficult to calibrate to patient data. The model parameters tend to lump multiple physical effects (e.g., cell adhesion, cell viscoplasticity (a particular type of biomechanics), and tissue density) into very few parameters. Hence, while they made excellent qualitative predictions, more is necessary to obtain quantitative, predictive models of tumours in individual patients.

To address this issue, Dr. Macklin developed a model where each individual cell is handled as an object subject to a balance of physical forces. Molecular and cellular biology are expressed through constitutive relations (e.g., as material properties), and each cell is assigned a phenotypic state (proliferating, quiescent, apoptotic, hypoxic, necrotic, or calcified nuclear debris). Transitions between these states are determined by stochastic processes that are tied to the cell’s genetics/proteomics and the microenvironment.
Macklin has collaborated with colleagues in the USA to apply the model to ductal carcinoma in situ (DCIS), a type of breast cancer that is confined to the breast ducts. In current clinical practice, DCIS is typically detected in mammograms as microcalcifications — small calcium deposits that form within the necrotic portions of DCIS. Surgeons typically use these mammograms and limited biopsies to plan their surgeries when selecting tissue for excision. However, the exact relationship between the distribution of the microcalcifications and the actual tumour shape is unknown, and it often takes two or three surgeries to completely eliminate the tumour. A major goal of Macklin’s work has been to understand and quantify the relationship between these microcalcifications and the actual shape and size of the tumour.

By combining mathematical analyses, a search of the biological literature, and image processing techniques, Macklin and co-workers designed a method to calibrate the model to data from individual patients. A typical simulation is shown in the figure above. An interesting feature of the model is that it is sufficiently mechanistic (grounded in basic rules of physics with biologically-justified constitutive relations) that correct tumour behaviour is manifested as emergent phenomena from systems of many cells. For example, necrotic cells in the centre of the duct act as a mechanical stress relief for the growing tumour, which causes a net flux of cells from the outer region (where proliferation is most prevalent) towards the centre of the duct. This slows the rate of tumour advance to a near-constant speed of approximately 1cm per year, a rate consistent with clinical data. Models without this stress relief generally predict exponential growth at unrealistic rates. The model also correctly predicts that the size of calcifications in patient mammograms is linearly correlated with the actual size of the tumour. Moreover, a least-squares linear fit of the simulated DCIS data quantitatively fits clinical data from tumours two orders of magnitude larger than the simulation, suggesting that the model is accurate over spatial scales spanning three orders of magnitude (see right-hand figure). These examples demonstrate the potential of a mechanistic mathematical modelling: the ability to generate testable, quantitative hypotheses that can drive future scientific investigation.

Dr. Macklin hopes that this type of quantitative modelling can have a direct impact on clinical care of patients in the near future by allowing more accurate surgical planning. This will require careful model calibration and validation with close collaboration between teams of mathematicians, biologists, surgeons, pathologists, engineers, and computer scientists. In the coming years, he plans to forge stronger links with experimental biologists and oncologists in order to carry out this work. Indeed, the group has already developed some excellent relationships with the Colleges of Life Sciences and Medicine here at Dundee, and Macklin is pleased to be able to continue his research in this vigorous group!
MHD Group Hosts International Workshop

In August the MHD group joined forces with colleagues from the Solar and Magnetospheric Theory group at the nearby University of St Andrews to host a major international workshop. The seventh “International Cambridge Workshop on Magnetic Reconnection” saw physicists and mathematicians from across the globe descend on Scotland to spend a week discussing recent research on the phenomenon of “Magnetic Reconnection” and exploring new research directions.

Magnetic reconnection is a fundamental process in plasmas which allows a magnetic field to change its topology. Crucially, a change in topology allows for a release of energy stored in the field and that energy release may explain many dynamic events. For example, on the Sun reconnection is thought to be responsible for solar flares, the most explosive events in the solar system, while on the Earth reconnection can cause big problems in the operation of laboratory devices such as fusion reactors.

The workshop series was established after a highly successful meeting at the Isaac Newton Institute in 2004. It aims to bring together leading experts to facilitate progress in this wide-ranging research area. Dr. Gunnar Hornig, Head of the MHD group, said “It was an honour for us to host such a prestigious workshop and we look forward to seeing some of the ideas generated in the many discussions come to fruition over the next few months.”

Topology Unravels Complex Magnetic Fields

by Anthony Yeates, an STFC funded postdoctoral research assistant in the Division.

Recent research in the Magnetohydrodynamics group has uncovered novel ways to predict the behaviour of complex magnetic fields using ideas from the branch of mathematics known as “topology”.

Motivation for the work comes from the magnetic field in the Sun’s atmosphere, which satellite pictures reveal to be highly complex. In fact, the magnetic field lines are braided as they are dragged around by random, turbulent motions inside the Sun. It is the behaviour of the resulting magnetic “spaghetti” that interests solar physicists.

A longstanding puzzle has been: given some initial tangled magnetic field, what kind of relaxed state can it reach through a dynamical evolution? The details of the evolution are likely to be highly complex, with turbulent flows of plasma and intricate patterns of electric currents continually changing the magnetic field. But such an evolution will eventually run out of steam, settling the magnetic field into a relaxed final equilibrium. The precise nature of this final equilibrium is key to understanding the physics of the solar atmosphere, because it determines the amount of energy that the magnetic field can release into heat or explosive events such as solar flares. (Article continues on the following page.)

Coronal loops outlining the magnetic field in the Sun’s atmosphere, observed in EUV by the TRACE satellite.
**Complex Magnetic Fields**

The remarkable finding is that broad, structural properties of the final magnetic equilibrium can be predicted simply by analysing the initial state, i.e. without knowing the details of the evolution. This is possible due to the presence of so-called topological invariants: properties of the magnetic field that remain unchanged during any continuous evolution. The simplest of these are “fixed points”. A common analogy here is stirring a cup of coffee. However you stir the coffee, there will always be at least one point on the liquid’s surface which ends up precisely where it started. This can be proved mathematically, and is known as the “Brouwer fixed point theorem” - one of the most famous results in topology. But a fundamental advantage of the mathematical approach is that the result is very general, and applies not just to cups of coffee. In particular, it applies to magnetic fields.

Think of magnetic field lines between two boundaries as the “world-lines” of particles of sugar floating on the surface of the coffee. Distance in the vertical direction represents time in the coffee cup, so that the positions of different sugar lumps move around as the stirring proceeds. Their trajectories become tangled (that is the goal of the stirring, after all), just like the magnetic field lines in the Sun’s atmosphere. In the coffee, a fixed point corresponds to a sugar particle that returns to its starting point at the end of the stirring. In the magnetic case, a fixed point corresponds to a magnetic field line that connects the same location on the lower and upper boundaries.

For magnetic fields, the important thing about fixed points is not so much that there has to be at least one (the Brouwer theorem), but that they have to persist during the evolution. They cannot arbitrarily disappear. In particular, if the initial magnetic field has more than one fixed point, it is not necessarily possible for the additional ones to disappear. The topological theory on which the Brouwer theorem is based implies that there is a minimum number of fixed points that have to be present in the final relaxed magnetic field, depending purely on the initial state. In Dundee we have exploited these powerful ideas to predict the minimum amount of structure that relaxed magnetic fields must contain. This is a great example of how fundamental mathematical laws underpin the physical world around us.

The figure shows a computer model of a braided magnetic field in its initial state. The six cross-sections visualise its topology. In the coffee analogy, the cross sections show how an initial pattern of cream on the surface would be swirled up over time (from bottom to top). Fixed points of the overall magnetic field, or equivalently of the complete stirring operation, are places in the topmost cross-section where all four colours meet.
Mathematical Summer

Fourth year Mathematics (BSc) undergraduate Aysem Zorlu spent several weeks over the summer studying in the Nesin Mathematical Village, Turkey. Here Aysem reports on her experience.

“The Nesin Mathematical Village is a small village in Sirince set in the beautiful mountains in the west of Turkey. Over the summer, around 100 university and high school students from across the world gather for a summer school in mathematics. With many courses on offer, I chose to take two a day, allowing free time for individual study and, of course, to enjoy the scenery and activities such as hiking and horse riding! Classes came in the form of seminars and discussions, led by a number of visiting professors and covering a huge range of topics, from Relativity to Ring Theory to Combinatorics. In fact, the school was so enjoyable that I ended up staying for four weeks, double the length of my booked stay! Overall I gained a much better understanding of how our University studies fit into the wider mathematical world and an idea of which research areas might interest me as I continue with further study.”

Hopping into the World of Microbes

Dr. Fordyce Davidson, Reader in Mathematics within the Division, has been awarded a "Discipline Hopping" grant from the Medical Research Council to allow him to work more closely with colleagues in Life Sciences. The focus of his project will be on the formation of "biofilms". Fordyce explains: A biofilm contains billions of individual bacteria encased in a self-produced polymer glue. Despite each bacterial cell being genetically identical, the community soon differentiates into sub-populations, each carrying out a different role.

Just how this complex multi-cellular decision making process occurs is far from understood. This is really important as almost all bacteria that occur in the natural environment exist in these closely-knit biofilms where they affect almost every aspect of our lives: they are the base of most infections, are crucial for the effective treatment of sewage, are used in the industrial production of enzymes for washing powder and even impact on our daily dental care: plaque is a bacterial biofilm! It is well-known that identical living cells within complex multi-cellular organisms (like humans) can respond to environmental signals and perform different, but co-ordinated roles. One of the most striking examples of this is in embryo development. This process is due to “cell differentiation”. Only recently was it discovered that simple single-celled organisms such as bacteria, also display cell differentiation and so to some extent can behave as "super -organisms". Hopefully, the application of mathematical modelling will shed new light onto this important and fascinating problem.