Biochemistry is a subject that has something to offer those students interested in both the physical sciences and the biomedical sciences. Biochemistry explores the molecules of life and how these molecules and the signalling systems they belong to can lead to disease if they are defective in some way. This magazine, produced by biochemistry students and staff at the University of Bristol, aims to introduce students in schools to biochemistry, and the research and teaching that we do here at Bristol Biochemistry.

Although I trained as a biochemist, as a research scientist I would describe myself as a cell biologist and I am interested in understanding the molecular mechanisms of how and why cancer cells migrate to spread around the body. To study cancer cell behaviour we use a variety of different types of microscope and one of my pastimes is to watch time-lapse videos of cancer cells confronting non-cancer cells. If ever there was a cell ‘bully’ it’s a cancer cell and I want to understand how we might molecularly change that unsociable cell behaviour to perhaps prevent cancer invasion. Hopefully you will get a flavour of the research areas we have here at Bristol Biochemistry; amongst other topics this issue includes an interesting piece on the research and teaching that we do.

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From molecules to organisms – biochemistry under the microscope

Microscope technology is continuously evolving to allow us an ever more detailed look into the workings of biological systems. From tissue structure in living organisms to the atomic organisation of protein complexes, the visualisation of biological processes has never been more striking or enlightening.

Here we explore the way these cutting-edge techniques are applied to the study of biochemistry at the University of Bristol. Scale bars are shown for a sense of, well, scale! Remember 1µm is 1 millionth of a metre.

**Histology** is used to look at the architecture of tissues in organs. Tissue is cut into thin sections and stained so that all the cell layers can be seen. Image 1 is a section showing the organisation of a repairing wound in mouse skin.

**Confocal Scanning Laser Microscopy** is used to detect fluorescent molecules that have been added to cells to label specific proteins. Images are created by scanning a laser across the sample to excite the fluorescent molecules, causing them to emit light which is detected by a camera.

Image 2a is a 3D projection of a zebrafish head in which bones and connective tissues have been labelled in different colours. Image 2b shows a network of neurons grown from stem cells. These images were donated by PhD students Dylan Bergen and Natalia Jimenez-Moreno.

**Multiphoton Microscopes** are used as an alternative to confocal microscopy for thick samples and live cells. Fluorescent molecules are detected by firing two photons at the sample simultaneously. Only the area where the two photons meet is illuminated and so there is no out of focus light and no photodamage at other sites. Image 3 shows a 3D projection of a fly pupal head with the photoreceptor cells of the eye labelled green and fat cells in red. Image was provided by Anna Franz.

**Stimulated Emission Depletion Microscopy (STED)** is a form of super-resolution light microscopy which functions in a similar way to confocal microscopy except that during laser scanning, fluorescent molecules are selectively deactivated to focus the point of illumination. In image 4 you can see a normal confocal image (top) next to a STED image (bottom) which has much more detail. Image from Janine McCaughey.

**Scanning Electron Microscopes** focus a high-energy beam of electrons onto a sample. This interacts with atoms on the sample surface to signal back information about its topography (shape) with up to 1nm resolution, allowing scientists to zoom in on tiny structures which cannot be visualised using photons. Image 5a is a scanning electron micrograph of hair-like structures called cilia in the nose of a zebrafish and image 5b is the surface of the lens of a zebrafish eye. Cilia act as antennae to detect odours. Images were provided by Dylan Bergen.

**Transmission Electron Microscopy** is used to image structures found inside cells and tissues rather than on the surface. Samples are embedded in resin or frozen under high pressure and then sliced into sections that are thin enough to allow electrons to pass through them. Different materials scatter the transmitting electrons differently, creating an image. Image 6 is a section through the middle of a mitochondrion, which provides energy to the cell. Image provided by Nicola Stevenson.

**Cryo Electron Microscopy.** Transmission electron microscopy can be performed at cryogenic temperatures to preserve highly delicate or flexible structures. This has become popular in structural biology as it produces sufficient resolution to visualise protein complexes. Image 7 shows electron micrographs of ribosomes sitting in different orientations. These were then used to computationally model the 3D structure of the ribosome as shown on the far right. This image has been artificially coloured. Ribosomes build proteins according to information encoded in RNA molecules.
Biochemistry and Beyond – Bristol alumni career profiles

A degree in Biochemistry from the University of Bristol opens doors to numerous and diverse career opportunities. We hear from three Bristol graduates from the class of 2008 as they discuss their experiences of Bristol and how it led them to where they are now.

Joshua Savage
Senior clinical trial coordinator

I chose Bristol Biochemistry because of the reputation of the department and I preferred the course structure to that offered by similar institutions. The city of Bristol itself was a big draw to me too, and I have many fond memories of my 7 years there. The most pivotal, inspirational moment of my degree was probably my 3rd year practical project – having the chance to do independent, novel research persuaded me to do a PhD.

I did my PhD in the lab of Prof. Poole at Bristol, studying platelet cell signalling. During this time I was an undergraduate laboratory demonstrator and note taker for a deaf student. I stayed for another year after my PhD as a trial coordinator or subsequently been promoted to a position with greater managerial responsibility.

The best thing about a role as clinical trials coordinator is the feeling that you are actually making a difference to others’ lives by the research you are doing – in practice, this means giving cancer patients access to new and better treatments. My most notable achievements include securing a £2 million grant for a new study and opening new studies to recruitment. All these milestones come as a result of a lot of time and effort put into research funding, there are always many clinical research opportunities in universities across the UK.

Although a biological degree is not a requirement of my current job, my understanding of biochemistry is helpful when developing new studies. I also feel that without my degree, I would never have been appointed as a trial coordinator or subsequently been promoted to a position with greater managerial responsibility.

“The best thing about a role as clinical trials coordinator is the feeling that you are actually making a difference to others’ lives”

Charlotte Colenso
Post-doctoral researcher

After completing my A-levels I had a strong desire to fly the family nest. Flicking through numerous alluring prospectuses at the endless possibilities for learning, I quickly chose to attend the University of Bristol and study Biochemistry.

The Biochemistry course at Bristol was very captivating and highly organized and in the 3rd year we got to undertake a practical project, which I completed in the lab of Dr. Richard Sessions, modelling the hERG ion channel. Dr. Sessions has been an amazing mentor throughout my career and through him I was given the opportunity to do a PhD with Dr. Christopher Dempsey, again at Bristol.

My PhD was challenging at times but I was presented with many wonderful opportunities. For example, I won a Visiting Scholar Award from the Worldwide Universities Network to study Biochemistry. My PhD was challenging at times but I was presented with many wonderful opportunities. For example, I won a Visiting Scholar Award from the Worldwide Universities Network to study Biochemistry in Bergen, Norway for 6 weeks.

This was truly incredible, enabling me to experience science abroad, learn new experimental techniques and to travel to a stunningly beautiful country. I also won International Travel Award funding from the University of Bristol Alumni scheme to present my research at a Gordon Research Conference in the USA. I am extremely grateful for this help as during the conference I met my future research supervisor who offered me a post-doctoral position in Chile researching TRP channels.

During my post in Chile the going was sometimes tough, but as I looked back it was the most incredible three years of my life. I strongly encourage opportunities to travel as part of study/work. I have now gone full circle and am working as a post-doc next door to where I did my practical project all those years ago (2008) working on bacterial resistance.

“I strongly encourage opportunities to travel as part of study/work”

Rebecca Jones
Public engagement manager

I chose Biochemistry at Bristol because I wanted to work at the point where new discoveries are made. I knew starting with Biochemistry would get me within touching distance of that point, and my PhD research and public engagement roles have taken me right up to the edge!

It was during my PhD studies that I discovered public engagement and science communication. My skills naturally lay in talking to people and discussing what I was doing with a broader audience and I soon realised that I wanted to turn things 90° – I wanted to stay connected to cutting edge science, but be the one to take it out to the people who find what we do mesmerising, and to those who don’t think they care.

Public engagement has led me to work at the Royal Society, one of the most esteemed academic institutions in the world, and now to the Cambridge Stem Cell Institute where I run a £500k public engagement programme.

Public engagement is a very rewarding career, but you will be challenged constantly. I like being able to take creative approaches, work with non-scientists, artists, musicians, writers, to convey the things that I had the fortune to be able to see every day. Without Biochemistry I would not be doing what I am now, and I would not have the key skills I need to translate research.

“I wanted to stay connected to cutting-edge science, but be the one to take it out to the wider world”

Article by Dr Nicola Stevenson
Year in industry

Bristol Biochemistry offers its undergraduates the opportunity of a placement year at the end of the second year of their degree. Students spend between 10 and 12 months working full-time for companies and research institutes in the UK and abroad. A placement year provides valuable experience to your studies, providing the confidence and skills to help shape your career after University.

1 Lynden spent his placement at the pharmaceutical company AbbVie in the Medical Affairs Department
What have you learned through your placement?
This experience has taught me so much. I’ve learned a lot about the industry – how big international pharmaceutical companies operate, the balance between medical and commercial, and the inner workings of the NHS, especially on the commissioning side of things. Working in Medical Affairs has taught me a lot, especially as it is quite niche – I hadn’t even heard of it until I started applying for that work. Medical Affairs is a bit of link between R&D and Commercial within pharmaceutical companies. I’ve also learned a lot about myself. I’ve definitely matured, and learned how to handle myself in work-related situations. I’ve learned a lot about effective practice, something which needs to be taught! I’ve also learned how to handle being away from family and friends, something which will be useful in later life.
Do you think it has helped your future career?
Most definitely. Through networking my views on what I want to do have changed. I’m now seriously considering postgraduate medicine – I had never even considered that before. I’ve also realised that I do not want an office job for a very long time – it’s just as useful to know what you don’t want to do!
Would you recommend this to other students – and why?
I would definitely recommend doing a year in industry – in fact, I couldn’t recommend it highly enough. Bristol is a great university, and employers seem to love Bristol students. However, what you can’t put a price on is experience. Employers love that too, maybe even more. Doing a year in industry will not only allow you to expand as a person, it also allows networking, and could possibly be your first step in years to come.

2 Francesca spent her placement at the European Molecular Biology Laboratory in France, working in the laboratory of Marco Marcia
What were the challenges of doing a Year in Industry?
I found it challenging at the beginning. I had learnt lots of concepts from the first two years in Bristol but applying them practically and understanding the lab methods was overwhelming but still exciting at first.
What have you learned through doing it?
Lots about science, but also about the research process and career in general. Every week there were seminars by speakers from all over the world which broadened my awareness of the way international science works.
Would you recommend this to other students – and why?
Definitely. This opportunity to learn in a relatively stress-free environment is really unique and something I expect I will miss in the future.

3 Imogen spent her placement working in the high content imaging team at MedImmuno in Cambridge
What were the challenges of doing a Year in Industry?
It was initially quite daunting being in a new environment where you know very little compared to everyone else. However, everyone was so helpful and friendly, and I very quickly learnt my way around the lab and the technique needed for my project. I have tried to use some really cool technology, how to plan and run my own projects, and that you can never ask too many questions.
Do you think this has helped your future career?
Definitely. This experience has taught me a lot about research, and also about the different roles that are required in a research lab. I have improved my skills in planning and running my own project, and that will be so useful during my final year project, for a PhD, and beyond that. Plus, you get to stay at Uni for a year longer.

4 Annabel spent her placement at the DeDuve Institute in Brussels, working on the regulation of cell energy
What were the challenges of doing a Year in Industry?
I found the main challenge to be learning to work independently and managing my time in the lab. Obviously you have people to guide you, but unlike at university, you don’t have a definite schedule for the day or deadlines to work towards, and after an initial training period I had to plan and write down my experimental protocols for myself. I additionally had to figure out life in another country, which wasn’t always straightforward, especially as not everybody in Brussels speaks English.
What have you learned through doing it?
As well as learning so much more about the control of metabolism, and about how to successfully plan and conduct your experiments, I now have a wealth of knowledge and computer software such as Excel and GraphPad Prism. Year in Industry has also enabled me to develop as a person – I’ve generally become much more independent and willing to take the initiative, and am proud to say that my French has dramatically improved.
Do you think this has helped your future career?
I do, because now I have much more experience of what it is actually like to work in a research laboratory. This has allowed me to make more of an informed decision on what I want to pursue as a career – as a consequence of my positive experience doing a Year in Industry, I think I’d like to continue doing scientific research, and maybe do a PhD. In terms of transferable skills, I have also become much better at presenting and explaining data to others, and at prioritising and organising my time effectively.

Support for finding your placement
Students don’t need to decide about a placement year until the beginning of Year 2. During your first year we give you the information that you need to make your choice, including a chance to talk to students returned from placements, who can give you tips and advice. At the beginning of Year 3 we organise talks from companies, support for CV writing and interviews. Year in Industry has a dedicated member of staff as course organiser and they will work with you individually to help you find your placement.

Not just industry, not just research
Many of our students will take placements in multinational pharmaceutical companies, where they will work on the various aspects of major drug discovery programs. We also place students with smaller biotechnology companies, where students can gain experience of working in a company in the very early stages of research. Importantly, we have expanded the placement year to include other career routes. Several of our students join pharmaceutical companies to learn other key skills, including marketing, clinical trials and intellectual property. Finally, about half of our students will work outside of the commercial sector in a university or research institute. These placements are particularly suited to students who wish to travel abroad.

Career and life benefits
The chance to work in an interesting and challenging work environment offers important opportunities for gaining real-world skills. Students learn about working with others and taking responsibility for projects. A placement will help you develop confidence and communication skills, and learn how to organise your time to meet deadlines for your project. Most students report feeling more confident about careers after university, and this shows up strongly in the destinations of our students after graduation.

Article by Professor Harry Mellor
Don’t be Trapped by (Central) Dogma: Complexes a gogo on B-Floor

It’s a story as old as life itself: genetic information is stored inside cells as DNA which is used to transcribe RNA which is, in turn, translated into a sequence of amino acids that fold to form a protein. This flow of information is the central dogma of biology and was first stated by Francis Crick, co-discoverer of the structure of DNA, in 1958. Does it sound simple? If it does think again because we are still trying to discover why it takes massively complex biological molecules to accomplish this task.

In brand-new labs on B-floor in the School of Biochemistry the teams of Christiane Schaffitzel and Imre Berger are pioneering new scientific techniques to allow them to investigate gigantic protein complexes. Despite advances in genetic engineering and molecular biology, biochemists haven’t yet developed tools to allow them to study proteins made from multiple polypeptide chains, especially when they interact with biological membranes.

Although we can easily synthesise small, individual proteins for study in the lab, when they are particularly large, are designed to live buried inside a hydrophobic membrane lipid bilayer, or when they are meant to be part of a large protein complex, our existing tools stop working.

Transcription

In humans and other eukaryotes it takes more than 100 proteins to transcribe DNA into RNA. Part of this machinery is a complicated and poorly-understood collection of proteins called the preinitiation complex. In Imre and Christiane’s lab they are breaking the problem down into smaller chunks but even this means working on complexes that contain more than 20 polypeptide chains with a combined relative atomic mass of greater than one million Da. Scientists want to know the 3D structure of the proteins in the complex and how they connect to each other but X-ray crystallography, the traditional method for determining the macromolecular structure, won’t work on complexes like this because they won’t form crystals. To get around this problem Christiane has become an expert in cryo-electron microscopy, a technique that is undergoing a revolution in sensitivity and resolution, which has been recognised by the award of the 2017 Nobel prize for chemistry to its developers.

In cryo-electron microscopy a beam of electrons is fired through a frozen protein solution before being focussed by a lens onto a detector, traditionally a piece of X-ray film. This detector placed a limit on the resolution that could be achieved but recently direct electron detectors have been developed that are far more sensitive and accurate, allowing them to directly compete with X-ray crystallography for the first time. Imre’s team has been studying a protein complex that was identified in a young man with severe mental retardation. What made this complex unusual was that it was found in the cell cytoplasm whereas the normal version is found in the nucleus. Just why the variant associated with mental retardation had not crossed the nuclear membrane is now being investigated by Imre’s team working with scientists from Stanford and Strasbourg.

Translation and Translocation

After transcription comes translation, carried out by the ribosome – yet another mega-sized complex. These protein-making machines are found both free in the cytoplasm and bound to membranes inside the cell and there’s a reason for this. About one third of all proteins are either inserted into or translocated across membranes. SecYEG is a protein complex that forms a channel through a membrane to allow other proteins to pass from one intracellular compartment to another, but sometimes, when proteins are passing through, it can open to allow the protein to be inserted into the membrane. Together with Ian Colman, another Bristol Biochemist, the lab has determined a structure of the “holo-translocon”, the most complete protein translocation device yet studied.

ACEMBLing protein complexes

It is becoming clearer that most proteins work in concert with others. Many proteins form stable, functional complexes where individual proteins synergise to accomplish essential biological tasks. The easiest way to make a protein in the lab is to engineer E. coli bacteria to make the protein for you. Production of one protein at a time is relatively simple. However, it becomes quickly tricky when you want to study a protein complex with many subunits, because you need to express all of the proteins involved at the same time.

To address this challenge, Imre and Christiane’s teams have invented powerful tool-kits, such as the MultiBac baculovirus/insect cells system (ACEMBL), which allows multiple genes to be made into a single DNA strand optimized to produce many proteins at once. Rather than use bacteria as their protein factories they use insect cells as these are better able to cope with the complex assemblies typically found in higher organisms. PhD students and post-docs in the labs, with help from undergraduate and Masters students, are working towards improving this system using synthetic biology approaches. The vision is to develop novel and powerful tool-kits for multigene delivery into cells, not only to express proteins and complexes, but also to efficiently repair genetic aberrations in cells, tissues and even – maybe – in whole organisms.
The teaching lab... where the magic happens

Our first-year lab has the capacity for more than 100 students. We prepare the lab so it is ready for a science-packed afternoon to ensure that students get the most of the experience.

**Technicians**
Our team of technicians carefully prepare the practicals to an optimum level, so students just need to focus on doing the science when they arrive. They are always ready to fix any piece of equipment or provide extra reagents.

**Demonstrators**
After the morning lectures, a team of enthusiastic demonstrators help students put all that theory into practice. If a student needs any help running an experiment or has any question regarding the practical, all they need is to ask a demonstrator, and they will happily provide answers.

**Practicals**
Students do their first experiments on week one, learning how to use the basic equipment and tools that biochemists use: micropipettes, spectrophotometers, pH meters. Students work in pairs in the lab, improving their teamwork. Every pair has all the necessary equipment to run every practical, allowing them to work independently from other pairs. The practicals gradually increase in theoretical and technical difficulty for students to become proficient at the techniques they will need to use as future biochemists.

**Equipment**
We work to improve our practicals every year, and that involves acquiring new equipment and upgrading older pieces. Our new fluorescence microscopes are the perfect example of this: they allow second-year students to observe the fluorescently-stained cellular skeleton of mammalian cells.

**eBiolabs**
Our students can practice the lab techniques before even coming into the lab. eBiolabs, our award-winning online system, contains all the relevant information for each practical, including interactive animations and videos. Online pre-lab quizzes allow students to test their knowledge before running the experiments, and post-lab assignments assess their understanding after the lab.

**eBiolabs supports many different subjects within the biosciences. All students in the Faculty of Biomedical Sciences use it to help them carry out successful experiments in the laboratory.**

Explore: bristol.ac.uk/ebiolabs/biochem

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Article by Alejandro Lorente Pons
Graduating in Biochemistry

The University of Bristol summer degree ceremonies take place in July each year in the formal setting of the Great Hall, Wills Memorial Building. The School of Biochemistry celebrates this event with a graduation lunch for our new graduates and their families and friends.

This year the party preceded the formal graduation that took place at 4pm on 17th July 2017. Graduation day in the university calendar is a special day for staff because we are very proud to share the successes of our students. It is a day when we can catch up on what our students have been doing since we last saw them, which this year was at a very memorable pizza party in Royal Fort Gardens on a sunny day, when we all celebrated their final exam, and it is the last opportunity to wish our graduating students the very best for the future.

The photographs on this page capture the spirit of the celebrations that took place at Biochemistry’s graduation lunch. The students are dressed in their graduation gowns and are joking with their tutors and lecturers. As Head of School, I particularly enjoy meeting the parents of our students at this event and discovering things about my tutees that I didn’t know.

Following the lunch, we all walked down the hill to the Wills Memorial Building for the formal graduation ceremony. The ceremony began, as always, with a procession of staff into the Great Hall. Each student was then presented to the Pro Vice-Chancellor by the Dean of the Faculty and received the applause of the huge audience of students from a number of disciplines and their families.

Science and Society
Science, and scientists, do not stand apart from the rest of society. Instead, they play a central role in our modern world. This unit will explore the relationship between science and the society we live in. What does the general public think of science (and scientists), and how can scientists themselves shape that opinion? Who funds UK science – and why? And how is ‘doing science’ influenced by the wider culture?

Research Training
Training our students to be researchers is one of the most important things we do. Research skills such as problem solving, gathering and synthesising information and data analysis, are essential to a wide range of careers. In this course, students will learn to think and act like a scientist, designing their own experiments to solve a genuine research question and presenting their findings in a scientific format. Some may end up publishing their results in the latest scientific journals.

For more information on the new MSci degree: bristol.ac.uk/study/undergraduate/2018/biochemistry/msci-biochemistry

Course structure of MSci in Biochemistry

Year 1 & 2
- Lectures, tutorials, practicals

Year 3
- More advanced lectures
- Literary project
- Research project (BSc only)
- Research Training (MSci) [see left]

Year 4 (MSci only)
- Science and Society [see left]
- Extended Research project (16 weeks)

Optional units – choose 2 from:
- Synthetic Biology
- Cell Biology of Development and Disease
- Protein Assemblies and Molecular Machines

11% of people in the UK aged 26-60 have a postgraduate qualification*

Masters graduates earn £5,500 per year more – £200,000 over a working lifetime*

MSci in Biochemistry

Bristol has run a BSc in Biochemistry for over 50 years, but from 2017 we are expanding our undergraduate programmes to include a 4-year Master of Science (MSci) degree. This will allow students to get deeper into the subject, develop a broader range of skills and become highly proficient researchers, thinkers and creators of the future.

Science and Society
Science, and scientists, do not stand apart from the rest of society. Instead, they play a central role in our modern world. This unit will explore the relationship between science and the society we live in. What does the general public think of science (and scientists), and how can scientists themselves shape that opinion? Who funds UK science – and why? And how is ‘doing science’ influenced by the wider culture?

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Article by Dr Alice Robson

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*Sutton Trust LSE study 2013

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96% of students studying a BSc in Biochemistry at the University of Bristol reported overall satisfaction with the biochemistry programme
(Results of the 2016-17 National Student Survey)

2018 Open Days
Friday 15 June
Saturday 16 June
Saturday 8 September

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