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INFOrum Scientium

Information from the multidisciplinary doctoral programme Forum Scientium.

Edited by: Stefan Klintström

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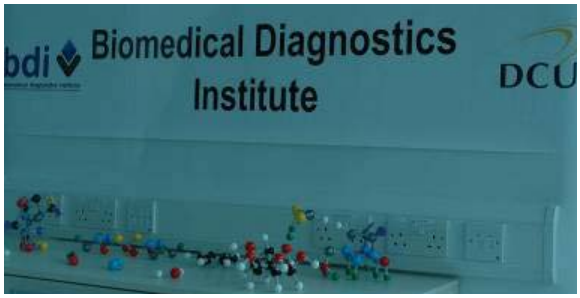
Dublin visit May 20-22, 2009

As part of the PhD-students career planning Forum Scientium makes study visits to research-intensive companies and to research departments at universities. During the visits, we try to meet newly hired PhDs. The network of 76 earlier Forum members, the so called Former Scientium, makes it even easier to have high quality visits. May 20-22, 2009, we visited Dublin.

Biomedical Diagnostics Institute (BDI)

After arrival to the charming city of Dublin in the middle of the night and after having a good night sleep, the first study visit of the trip took place at the Biomedical Diagnostics Institute at the campus of Dublin City University, DCU. At Biomedical Diagnostics Institute (BDI), we met Professor Brian MacCraith, head of the multidisciplinary research institute. The focus of their institute is development of biomedical diagnostic devices. BDI´s vision is to develop diagnostics for early warning of major diseases like cardiac diseases or cancer but also for self-management of health, and

also to link therapeutics with diagnostics. The goal is that BDI´s devices will be able to detect life-threatening events long before a critical level is reached and potentially reducing the necessity for painful treatment. The main focus research areas are breath monitoring for Chronicle Obstructive Pulmonary Disease, cardiac diseases, marker biochip, platelet function studies, coagulation, circulation tumour cells and chemotherapy where the future priority areas are nanomedicine, health monitoring for elderly population and personalized medicine.



The research team consists of 120 researchers with approximately 30 graduate students and 30 Postdocs. The group has collaborations with clinical and pharmaceutical companies where the three keystones of the partnership are; research at the university, patients samples from the hospital and the use of methods development at the companies.

After Professor Brian MacCraith's presentation we were guided around the brand new laboratory where we met Postdoc Lian Leanne who talked about blood clotting and coagulation. We also visited Clorcan Kent who demonstrated microfabrication of chips of different polymers. At the end of the lab tour, we met Postdoc Christy Charlton working on breath monitoring and measurement of carbon dioxide and oxygen in the breathing air.

Paula Linderbäck and Patricia Wennerstrand

Physiology at the University College Dublin (UCD)

The Respiratory, Cardiovascular and Exercise Physiology Research group

After waiting for what seemed to be an eternity, we finally caught the bus to Belfield to go on a visit to the respiratory, cardiovascular and exercise physiology group at UCD. Since the bus was late - so were we and it was a red-faced bunch that came running into the reception in the newly built UCD Health Sciences Centre. Our host, Dr Stuart Bund, came down to meet us and led us to a lecture hall where we started our day by listening to our Forum fellow Isa Lindgren. She gave a general presentation of Forum Scientium and its purpose, followed by a presentation of her own research on adrenergic signalling in the cardiovascular system of chickens. Some members of the UCD physiology group also attended the seminar, several of whom we would meet later during the day.

After the seminar, Dr Bund briefly presented his research and then took us to his lab to show us some of the central equipment of his research. Dr Bund is working on structural, mechanical and contractile abnormalities in hypertension and the regulation of smooth muscle contractile responses of resistance arteries and the ureter. With a pressure myograph system he studies the response of very fine vessels under physiological pressure. Isolated vessels down to less than 100 µm are mounted onto two thin glass cannulas and a buffer is injected in the vessel to obtain a physiological pressure. In contrast to wire myography, one of the more commonly used methods for vascular isolation studies, the pressurized system can be used to study changes in vessel properties in response to different pressures and thereby mimic hypertension. Dr Bund also gave us a tour through their state-of-the-art teaching facilities including the dissection room for human cadavers.

Our next stop was the lab of Dr. Ken O'Halloran, whose research interest is focused on cardiorespiratory responses to repeated hypoxic exposure. He uses non-invasive methods to study neural regulation of breathing, mainly in rats. Dr O'Halloran also told us a about his research on obstructive sleep apnoea that led us into an interesting discussion about the ethical aspects of animal studies.

We also met Dr. James Jones who is a senior lecturer in physiology and principal investigator in the Conway Institute. He studies central autonomic control of the heart and physiology of the vagus nerve. He showed us some equipment to record the sensing of hypoxia in rat neurons by dissecting out the axons with the cell body still in the rat. It is thus possible to induce hypoxia locally on only the neuron itself and still being able to record the cardiovascular response to the nerve stimuli. Very cool.

Last, but not least, we got the chance to meet Dr. Paul McLoughlin, Professor of physiology, who told us about his research in chronic pulmonary hypertension, hypoxia-induced vascular remodelling, pulmonary hypertension and protective effects of hypercapnia in lung injury.

After a very busy morning, Dr. Bund was kind enough to arrange for us to have lunch together, which also gave us the chance to ask questions about the organization of research at the UCD, the life as a PhD at UCD, funding and salary levels etc. Dr. Bund also got the chance to ask us more about the research situation in Sweden and it all turned out to be a very pleasant ending to a very pleasant day!

Isa Lindgren and Liza Ljungberg

Protein folding, Trinity College

As the field of protein folding continues to expand and diverge, newer and faster methods for observing the intricacies of the folding process are essential for our understanding. As we gain more insight into protein functionality as a result of alternative folding it becomes essential to see at what stages in the folding process these 'choices' are made and what the most influential factors are in directing polypeptides to take their many forms. That is precisely what Dr. Ken Hun Mok is attempting to do at Trinity College in Dublin, Ireland. In order to better understand the process of protein misfolding Ken and his colleges are utilizing an integration of three existing methods. They have constructed a device that allows for rapid mixing within the NMR magnetic and with the assistance of a laser, they can perform a Chemically Induced Dynamic Nuclear Polarization (CIDNP) to enhance NMR signals of the hyperpolarized aromatic side chains. Then using the Nuclear Overhauser Effects (NOEs) from the hyperpolarized aromatic side chains, their neighbouring atoms can be easily detected to distinguish between native and unfolded states. This useful technique allows for the observation of specific folding events with well-resolved spectra on a very short time scale thus helping to refine our existing understanding of many of the smaller stages of protein folding or misfolding.

Dr. Mok also gave us an insight in his interesting collaboration with Prof. Catharina Svanborg at Lund University regarding the HAMLET (Human α-lactalbumin made lethal to tumour cells) complex. HAMLET was discovered by serendipity. Prof. Svanborg and her colleges were actually searching for bactericidal molecules in human milk when they came across a molecule that was able to kill tumour cells while leaving normal healthy cells unaffected. The activity was shown to reside in a complex between the human milk protein α-lactalbumin and the fatty acid oleic acid. By using a wide range of biophysical techniques, including NMR, TEM, AFM and pulse-labelled CIDNP, Dr. Mok and colleges are now trying to determine the structural and chemical properties of the complex. The protein part is not an amyloid formation, but rather a fibril growth that has been arrested in the very early stages. Moreover, the fatty acid seems to be encapsulated by the protein and not vice versa, as would be the case for micelles and vesicles.

We finished the visit and thanked Dr. Mok for an interesting and inspiring presentation of his work. He offered the group an opportunity to pass the line to see the Book of Kelts, Ireland's most precious treasure. Unfortunately, we had to leave in order to catch a bus for the next study visit.

Therése Klingstedt and Rozalyn Simon

Clinical Research Centre (CRC) at Beaumont Hospital

The Clinical Research Centre (CRC) at the Royal College of Surgeons in Ireland (RCSI) has a bench-to-bedside approach, which combines clinical and basic research. The research deals with cardiovascular, respiratory, neurologic and rheumatologic diseases and currently there are 40 clinical studies in progress.

When we arrived at CRC Professor Dermot Kenny first gave a short talk, introducing us to platelet biology. He talked about his view on science and their efforts to develop new platelet in vitro assays, in which the in vitro environment mimics physiological conditions. He also presented some of his results regarding GPIb, the platelet receptor that binds von Willebrand factor. The results included both genetic and functional studies of the receptor.

We also got the chance to meet with Gail Plunkett, who is a research nurse at the Clinical Research Centre. Gail spoke about the role of a research nurse working with clinical trials, both in the process of logistic planning as well as the involvement in screening and recruitment of suitable patients. She also told us about current studies in which she was involved, and thanks to Gail we really learned to appreciate the hard work and dedication a research nurse must put into clinical research trials. Getting a single blood sample is not always the easiest thing to do!

Before heading towards UCD Belfield and the next study visit, Gail guided us through the neat facilities of the CRC, including a number of different patient rooms (arrival, consulting, phlebotomy and day suites) and rooms equipped with laboratory instruments (and to the excitement of some of us (guess who..!) a real and alive PFA-100 and VerifyNow!!!).

Hanna Björck and Andreas Eriksson

Centre for BioNano Interactions (CBNI), UCD Belfield

The CBNI is a recently started centre that will focus on nanoparticles and their interactions with biological systems. The centre will provide a link between the university and companies interested in bionano interactions. Professor Kenneth Dawson is the leader of CBNI a research group today consisting of about 30 post-docs and PhD-students. Over the next couple of years, the number of people directly involved in the centre is expected to increase to about 100.

During our visit, we enjoyed a nice lunch with several PhD students and then participated in their group meeting, followed by a quick look at the labs. The group is an international mixture with PhD students and post docs from all over Europe and other continents, which seems to create a nice atmosphere in the group.

Jong-ah Kim, Federico Feneroli, Anna Salvati and Peter Sandin (post doc from Sweden with a Wallenberg scholarship).

Anna Salvati, a post-doc in Professor Dawson's group, gave us a nice introduction to the research at CBNI. Nanoparticles interact with, and can also enter, cells. This can possibly be used for targeted drug delivery but it has also been suggested that the interactions between nanoparticles and living tissue can be dangerous. The research is divided in four areas; synthesis, characterisation, protein interaction and cell applications, short descriptions of each were presented by other post-docs in the group. Many nanoparticles are hard to disperse in biological fluids, as they tend to form aggregates. Dispersion can be enhanced by modifying the surface with adhesion of ions or surfactants. The protein interaction division focuses on the fact that when nanoparticles enter biological fluids they will become covered by proteins. Identifying the proteins surrounding the particles is important as they will in part determine the functionality of the particle. The cell applications have mainly focused on investigating if nanoparticles remain within or exit cells once they have entered. A number of different techniques such as spectroscopy, confocal microscopy and fluorescence are used to track particles within the cell.

As the CBNI is currently undergoing significant expansion, several positions are open. To read more, please visit http://www.cbni.eu/

Emma Ericsson and Kristin Persson

UCD Conway Institute of Biomolecular & Biomedical Research

USD Conway Institute of Biomolecular & Biomedical Research was established in 1999 from public and private funding. The building, comprising an area of 11.200 m^2, opened in September 2003. Today there are approximately 95 Conway fellows and 255 affiliated graduate students. The facilities offers great research opportunities with the access to genome analyzer, PCR-technique, mass spectrometry, proteomics, flow cytometry, histology, confocal microscopy animal facilities and much more. The well-equipped facilities are part of the vision to enable researchers to compete internationally and place Irish bioscience in the global spotlight.

The focus at Conway is to promote knowledge, health and economic advancement through excellence in biomolecular and biomedical research. At the research institute, one strives at fulfilling the goals of interdisciplinary research directed at clinical problems, underpinning by evolving technical platforms and offering structured postgraduate training of basic and clinical scientists.

A lot of effort is made to prepare PhD students and young scientists for a career in research. Postgraduate students receive introduction to core research skills, commercialization and entrepreneurship. A festival of research is arranged at Conway were young scientists present their work orally or as a poster with the chance to be awarded for the best presentation.

One important part of research is to make others understand the research done and this is an important part of the postgraduate training at Conway. Every year the 3:rd year PhD-students compete in explaining their research for a non-scientific audience and the winner is acknowledged for a great achievement.

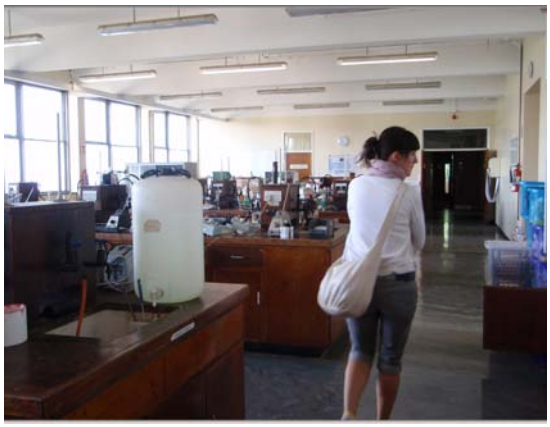
UCD Conway Institute offers a wide range of career opportunities and strives to give a world-class research education for postgraduates and post doctors.

During our visit to the Conway Institute we first got a general introduction by Elaine Quinn and after that postdoc Niamh O´Sullivan presented her research on Schizophrenia in a rat model.

Anna Kivling and Anna Rydén

Synthesis and Chemical Biology UCD Belfield

After the visit at Trinity College, some of us went to visit Prof Stefan Oscarson at the Centre for Synthesis and Chemical Biology, UCD. He met us at the entrance and took us for a tour around the old laboratory building, where they up until a few months ago conducted their research. Recently the group moved to a new laboratory. It is always interesting to see other labs and compare them with ours.



Old lab

Prof. Stefan Oscarson was earlier a professor in Sweden and started his position at UCD, in 2006. His group works with the design and syntheses of different carbohydrates and their conjugates that will function as inhibitors of protein/bacteria interaction (mainly *Escherichia coli* and *Helicobacter pylori*. They have synthesized heptasacharides to investigate the interactions of the *H. pylori* BabA lectin. Lectins are recognition proteins in cells. Bacteria and viruses use lectin to attach themselves to the cells of the host organism during infection. He told us that they have spent around 10 years to develop the synthetic route for these heptasacharides. This gave us a glimpse of how hard it is with synthesis of long chain carbohydrates.

New lab

In collaboration with immunologists and vaccine companies, they are trying to develop a vaccine against diseases caused by bacteria.

Lan Bui and Daniel Kanmert

BiancaMed and NovaUCD

At NovaUCD, The Innovation and Technology Transfer Centre, Ciara Leonard gave a presentation about the ideas and the vision of the centre. We learned that as a part of the university's vision to establish itself among the great European universities, NovaUCD was built with the purpose to offer a supportive environment and incubation facilities to assist innovators and entrepreneurs when commercialising their research. NovaUCD assists the start-up companies with everything from early identification, protection and commercialisation of intellectual property to developing collaborative arrangements and strategic partnerships with industry. Since the start in 2003, 45 companies have used the incubation space, which e.g. has lead to 178 invention disclosures and 125 patent applications. At the moment, 25 companies are located within the NovaUCD, among these Changingworlds (www.changingworlds.com), Lightwave technologies (www.lwavetech.com) and BiancaMed (www.biancamed.com). After the presentation, we got a tour of the facilities, which were very nice :)

After the NovaUCD presentation and the tour of the facilities, we returned to the conference room and met Dr. Philip de Chazal and Dr. Redmond Shouldice from BiancaMed. BiancaMed is a very new company being only founded in 2003 however has already tabulated themselves in the field of health monitoring. Dr. de Chazel is one of the founding members of the company and was originally placed at UCD's School of Electrical, Electronic and Mechanical Engineering as a senior researcher. He has extensive experience in the field of health monitoring and is an expert in biomedical software solutions. Dr. Shouldice was a PhD at UCD and when he graduated became part of the BiancaMed group as senior principal engineer.

The BiancaMed company produces products for health monitoring through wireless measurement of breath and heart rate. Their system sends out acoustic waves that will reflect from nearby objects. These reflections will then be detected by the system and through a sophisticated analysis programme can be used to monitor the breath and heart rate of an individual close by. This was first demonstrated in the monitoring of sleep apnea, which causes sufferers to stop breathing while they sleep. The system can monitor a sufferer while they sleep and report on the quality of sleep that the sufferer receives and identify apnea events. This has many advantages over normal methods of apnea measurement, which involve the sufferers being hooked up to numerous machines in special sleep monitoring facilities.

The ingenuity of the BiancaMed device is that it requires no direct connections to the sufferer and they can do it from the comfort of their own home. On top of this, the system can also wirelessly transfer this information, to the Internet, to a patient specific website so that doctors and patients can actively monitor their sleep. BiancaMed is constantly developing new products with the latest system being a wireless monitoring of babies sleep, which can warn if a babies breathing becomes laboured or erratic thus reducing dramatically the possibility of cot death while allowing the baby to sleep normally.

Stephen Macken and Caroline Skoglund

Royal College of Surgeons in Ireland

Former Scientium Sofia Ramström began her career as an upper secondary school teacher in chemistry and biology at Linköping University in 1992. She took her MSc degree in biology in -97 and continued with Biomedical Research School until -98. In 1999, she began her PhD studies as a member of Forum Scientium. She defended her PhD in 2003. The initial name of her PhD project was “Interaction between Platelets and Plasma Coagulation Factors - Development of Global Analysis Methods” with Prof. Tomas L. Lindahl at the division of Clinical Chemistry as supervisor. However, the final name of her thesis was “The role of platelets in whole blood coagulation”. The general aim of her project was to develop a method for the detection of bleeding and clotting tendencies in patients. During this time, she got to work with Flow Cytometry and Free Oscillation Rheometry (FOR).

After her PhD, Sofia had a successful application at Vetenskapsrådet (VR) and continued her employment as doctor (max 2 years) at IBK Clinical Chemistry. She received partial funding from CIRC and FUN. During this time, she had two children and was on maternity leave for two times six months full time then part time. After this, she organized a graduate course in platelet biology at MedBi T6 and was engaged in the Junior Faculty at Linköping University.

After a tip from Former Scientium Jimmy Bakker (se below), she in May 2007 sent an application to the Biomedical Diagnostics Institute (BDI) and started there in August the same year. Her employment as Senior Platelet Biochemist is a link between physics and biology/clinic. She is currently stationed at Molecular and Cellular Therapeutics at the Royal College of Surgeons in Ireland (RCSI).

Linda Andrén and Alma Åslund

Cellix Ltd

On Friday afternoon, we visited Cellix Ltd that is a spin-out company from Trinity College. It was founded in 2004 and formally established in 2006. Since launch, the company has grown and now it has nine full time employees. We met the co-founders of the company Vivienne Williams (CEO) and Dmitry Kashanin. The company has three facilities: R&D and the manufacturing facilities is located in Dublin whilst the sales office is in New York.

Dmitry Kashanin and Vivienne Wlliams

The R&D team has together with different universities and industries validated Cellix's platform for a number of research areas such as bacteriology, cardiovascular, oncology and respiratory. They have developed a microfluidic drug screening tool that is now used by large companies like i.e. Astra Zeneca and Pfizer.

Their technology offer, in a physiological micro-environment, cell-based flow assays mimicking blood capillaries. In this manner, possibilities for interaction-studies between a variety of cells and proteins arise in a fast and reliable way. The platform developed by Cellix provides the pharmaceutical- and biotech-researchers with a unique solution that enhances their drug discovery programs and eliminate false leads.

Venaflux is the name of the Cellix's most popular product. It is a semi-automated microfluidic system capable of measurements of cell adhesion to i.e. antibody-coated microcapillaries. This is done together with special biochips and user-friendly analysis software, everything developed by Cellix. The two different biochips offered by the company are the Vena8 and VenaEC. The Vena8 is built up with eight enclosed microcapillaries in parallel, each which may be coated with a different adhesion molecule. The VenaEC biochip enables seeding and culturing of endothelial cells due to a tissue culture treated surface.

The VenaFlux platform

After a presentation by Vivienne Williams, who mainly talked about things to consider when starting up a company, we had a tour in the lab and met Dmitry who showed us some of their technique. It was a very nice Friday afternoon.

Sara Nilsson and John Olsson

Trinity Centre of Bioengineering (TCBE)

The final day for study visit, a few of us went to the Trinity Centre of Bioengineering (TCBE). Just a short walk from the century old buildings that forms the original Trinity College, lays TCBE, which is multidisciplinary and integrates engineering and medicine. Research conducted here regards orthopaedic implants, cardiovascular biomechanics, impact biomechanics, bone mechanics, biomaterials, cell mechanics, tissue engineering and neural engineering. The Trinity centre for Bioengineering was established in 2002 and integrates the bioengineering research activities of four schools and three faculties of Trinity College. Dr. Matthew Haugh and Dr Bruce Murphy welcomed us in the reception and we were guided to a lecture hall were some of the research from the different departments were shortly introduced. The session started with Dr Haugh who showed how mechanical stimulation inside a bioreactor could be used to differentiate mesenchymal stem cells into chondrocytes. These cells could then be used together with a scaffold in cartilage repair. Next, Dr Kevin O´Kelly presented data on the mechanics of ceramic materials used in orthopaedic implants. Dr O´Kellys showed how crack propagation could be investigated in these materials using nano indentation technique. The last talk was held by Dr Bruce Murphy. He talked about his research position where he develops and evaluates ideas for different clinical purposes. He is for example involved in a project with a new method for angioplasty as well as developing a

bioreactor, to simulate a blood vessel, where flow and shear stress can be tested. After the presentations, we were guided around the laboratories where MSc cell culture was performed in scaffolds and bioreactors and we were also guided through the biomechanical testing site.

Fredrik Agholme and Pernilla T Eliasson

An Evening of Food, Folklore and Fairies

Friday evening we experienced an enchanting evening of Irish folklore and storytelling while enjoying a candlelit traditional Irish dinner in Dublin's oldest pub, The Brazen Head. The renowned storyteller Johnny Daly took us back into a world of the imagination with wonderful insights and magical stories about Irish life in times past. E.g. why the humble potato so influenced Irelands history, and the peoples beliefs and superstitions surrounding the otherworld of the fairies.

www.irishfolktours.com

Stefan Klintström

Former Scientium Jimmy Bakker

Networking pays off

If you want to get somewhere in science, you have to present yourself at conferences and network with other scientists. Or at least that's what people say. I guess that was one of the reasons I sent in a contribution for the last conference during my PhD education within Forum Scientium. This conference turned out to be about four weeks before the deadline of my thesis and I hardly had anything written yet. So you may understand I didn't really feel like going. Fortunately, I did go anyway, because on the way to the conference, I met our very own Professor Bo Liedberg, on the way to the same conference, who brought me in contact with a professor from Dublin and later with Åmic AB in Uppsala and a few weeks later, I had a Post-Doc position at Dublin City University.

The Post-Doc was at the Biomedical Diagnostics Institute, a multidisciplinary institute working on future diagnostics. The institute is situated at Dublin City University (DCU) in Ireland, but cooperates with several institutes and companies worldwide. One of those companies is Åmic, my actual employer. Åmic and DCU applied for a Marie Curie TOK (transfer of knowledge) scholarship and received funding to send two Post-Docs to Ireland. And I was one of them.

As you may know, Åmic is developing a diagnostic platform based on capillary flow driven by micropillars on low cost plastic chips, produced by CD injection moulding technology. At DCU, there is a lot of expertise on optical detection and fluorescence amplification techniques. It was our job to integrate those two technologies together into a platform to predict cardiovascular disease. Of course, my multidisciplinary Forum Scientium background fit this project very well.

Now I am back in Sweden and have a permanent contract at Åmic in Uppsala. And all that because of a conference I did not want to go to…

Jimmy Bakker

Former Scientium Sofia Ramström

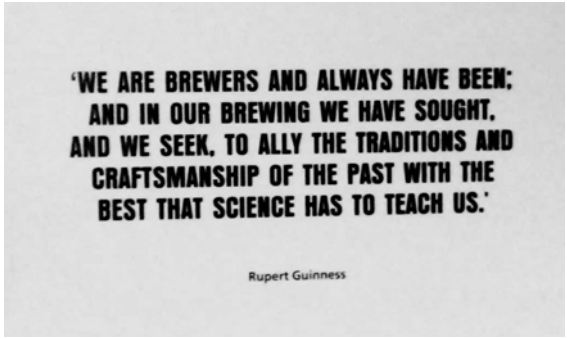
In 2007, my 2 years of "postdoktorsanställning" at the lab for Clinical Chemistry at Linköping University Hospital were ending up (thanks to the Swedish parental leave allowance, I managed to make these 2 years stretch from 2003 to 2007…). Therefore, I had to move on, and found a postdoctoral position at the Biomedical Diagnostics Institute (BDI) in Dublin, Ireland. I am now employed by BDI, which has its base at Dublin City University (DCU), but my position is as a Senior Platelet Biochemist based at the Royal College of Surgeons. I moved here in November 2007, to get started and try to sort everything out, before the family arrived in January 2008. Moving two chil-

dren, then 2 and 4, and a husband who had a job in Linköping but nothing set here felt as a huge decision, but actually, it all went very well. Within 9 months, the kids spoke English (although with a Dublin accent…!) and the eldest had started school, my husband found a position here and my tasks had become a bit clearer. My position is not a "normal" 2 years postdoc-position with a pre-defined project plan, instead my role is to provide clinical/biological expertise and to work together with the BDI researchers at DCU with focus on development of medical devices. In this position, my past within Forum Scientium has proven to be very useful, as I am already used to work within projects spanning between disciplines and also have a basic knowledge about the methods used at DCU. For the moment, I try to keep two different research focuses, one with more basic platelet research and one with a more commercial device development focus. It is fun, although sometimes hard to find enough time, but in the end, I hope it gives insights and merits that might be of use both within the academia and within industry. This time has been a great experience to all of us, and the time here has passed really quickly. For the moment we don't know when we will be moving back, but our long-term plan is to return to Sweden, as there are many things there you appreciate much more after living abroad for a while... In the meantime, anyone with thoughts of going to Dublin is very welcome to give us a call!

Sofia Ramström

Finally

We visited some nice pubs



And some of us visited the Guinness brewery