Forum Scientium

INFOrum Scientium

Study visits to the London, Cambridge and Oxford 2017

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Editor: Stefan Klintström

The research school Forum Scientium at Linköping University, Sweden, has as one part of its responsibilities to stimulate the PhD students career planning as early as possible. One way that this is done is through study visits to research-intensive companies and to research departments at various universities. During the visits, we try to meet senior persons within research and development, as well as persons who recently made the transition from being a PhD student to becoming a professional. The network of earlier Forum members, the so-called Former Scientium, and the PhD student's supervisors are valuable when arranging the study visits and contributes to the high quality of the visits. 17-19 May 2017, Forum Scientium had an intensive study visit programme in London, Cambridge and Oxford, UK.

"The Forum Scientium pyramid symbolizes the need for a good foundation, the need to receive inputs and have collaborations from more than one side, and the creation of a peak of excellence."

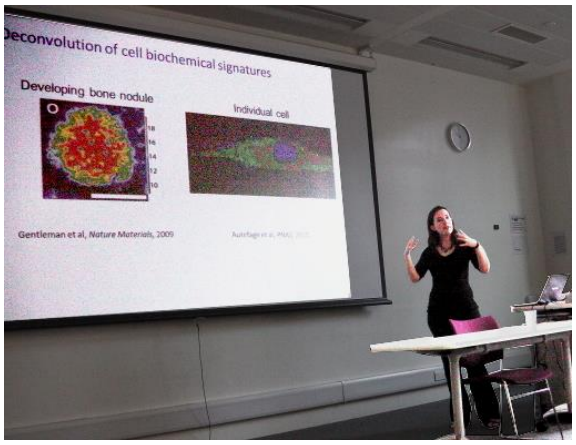
Forum Scientium

LINKÖPING UNIVERSITY

Imperial College, London, Research group of Prof Molly Stevens

The study visit started Wednesday morning with the Imperial College in London and the research group of Professor Molly Stevens. The multidisciplinary interests of Forum Scientium and those of the Steven group intersect over several topics, making it a given choice to start this year's study visit.

When we arrived, we were greeted by former Forum member Abeni Wickham and Research coordinator Benjamin Pierce. After some coffee, we were ready for a seminar packed with science.



The seminar presentations started with an introduction by Prof. Stevens who described some of the research interests and ongoing work in her group. Thereafter presenters from Linköping and the Stevens group took turns presenting their research. Presentations were given by Edwin Jager (LiU) on mechanotransduction and how that affects cells, followed by Amy Gelmi (Steven group, former Forum member) which contrasted with how cell functions are modulated by selected materials. Parmis Blomgran (LiU) described her work on tendon healing, and Abeni Wickham (Steven group, former Forum member) talked about the transition from the applied sciences of Forum via the Max Planck Institute of Colloids and Interfaces, Potsdam, Germany to the Stevens group. Mathias Elgland, Katriann Arja and Linda Lantz (LiU) elaborated on theranostic agents, after which Jenny Peutzer (Stevens group) discussed the generation of collagen fibres. The seminar ended with a presentation by Daniel Aili (LiU, former member of both Forum and the Stevens Group) on peptide folding and hydrogels.

After the seminar, we went for lunch at a nearby pub where the discussions continued in a less formal manner.

More info http://www.stevensgroup.org/

/Anna Södergren & Robert Pilstål

Applied Biomedical Engineering Group at University College London (UCL)

During Wednesday afternoon, part of the group visited the Applied Biomedical Engineering Group at the University College London (UCL). Dr Richard Day welcomed us and gave a short introduction about the group and UCL, highlighting their cross-disciplinary research collaborations with other UCL groups in different faculties but also other universities within London. His research group is strongly focused on the highly porous microspheres produced via thermally induced phase separation (TIPS), and their potential application in cell attachment, tissue integration and drug delivery. The microsphere technology is currently entering into a more commercial phase, initially for non-clinical use, but further pre-clinical trials were planned.

The talk by Richard Day was followed by Dr. Caroline Pellet-Many, who gave a detailed presentation about her research on VEGF (vascular endothelial growth factor) stimulation of endothelial cell migration, and the role of neuropilins in vascular smooth muscles cells migration.

Finally, Dr Paul Frankel, gave an amazing presentation on how they combine molecular analysis of cell signalling required

for cancer cell motility with 3-D imaging system as a non-invasive approach to accurately monitoring tumour development in adult zebrafish. They are able by using this technique to follow over time how fast the tumour grows and how it generates its own blood vessels.

More info http://www.ucl.ac.uk/day-lab

/Daniel Aili & Judit Randek

Galvani Bioelectronics

A group of nine Forum members arrived to GlaxoSmithKline (GSK) and Galvani Bioelectronics in Stevenage by train from London on 17th May. Daniel Chew (Director of Neuromodulation) welcomed us and treated us very nicely with coffee in the reception building. Kristoffer Famm, the president of Galvani, gave us an overview of Galvani Bioelectronics. Galvani is a new company established in November 2016. It has a perspective view to develop bioelectronics therapies. Based on the global pharmaceutical company GSK and Verily Life Sciences (formerly Google Life Sciences), Galvani applies the expertise of these two parent companies to research and develop the bioelectronics medicine with small implantable devices that will read and modify nerve signals.

Daniel Chew introduced the R&D work streams in Galvani. The perspectives of the research are impressive. With the development of the miniaturized devices many diseases will be possible to treat. After this Jason Miranda (Biology internship lead) and Tariqus Salam (Engineering internship lead) showed the internship system of Galvani and they welcomed the candidates with professional knowledge to join them no matter their background was fit or not. They also provided open and free internship opportunities to the students.

Furthermore, Mark Uden (Head of Biopharm Process Research) presented GSK's research on bioprocesses and gave us the opportunity to visit their laboratories. When new biopharmaceuticals are developed, the new target needs to be identified and a suitable cell line needs to be established for production. Then the process manufacturing conditions have to be optimized and proper analytics need to be established to assure the safety and quality of the biopharmaceutical. Even keeping all those major steps and the variety of research projects in mind, we were still impressed with the sheer size of the research facilities. Especially remarkable was the fully automated disposable microbioreactor ambr® system where the screening and optimization takes place. As well as being able to compare this system with a lab scale 100 L bioreactor while knowing that the full scale would run at 2000 L.

We were very impressed by GSK and Galvani Bioelectronics and highly appreciated their openness. It is rare to get such an insight in companies' research facilities.

More info http://www.galvani.bio/ and http://uk.gsk.com/

/Lianlian Liu, Stefan Klintström and Patricia Roch

Pharmaceutical Biophysics Group, King´s College, London

Professor Jayne Lawrence, head of the Pharmaceutical Biophysics Group at King's College in London, aims to elucidate the physicochemical and biological properties of small- and macro-molecules, lipid membrane systems, macromolecular drugs and drug delivery systems. The methods used in the lab are a combination of advanced analytical techniques, including computer modelling, FT-IR, circular dichroism, Raman spectroscopy, static and dynamic light scattering, rheometry and dilute solution viscometry, atomic force microscopy and X-ray diffraction. But, the most prominent technique being small angle neutron scattering and neutron reflectivity to study drug-membrane interactions.

Despite the busy scientific schedule, Professor Lawrence is also heavily involved in a campaign called Women in Science to encourage women into pursuing and advancing their careers in science, technology, engineering, maths and medicine in higher education and research.

Professor Lawrence stated that she is a bit envious of Sweden for two reasons;

1. Sweden has come a long way when it comes to gender equality in science and in society in general.
2. The world's most powerful neutron source called the European Spallation Source (ESS), a multi-scientific research centre, is currently being built in Lund and will be finished by 2020.

The ESS will allow scientists to study proteins and drugs in an unprecedented manner and it will therefore be of outmost importance for professor Jayne´s research.

More info at
https://www.kcl.ac.uk/lsm/research/divisions/ips/research/pharmabio/index.aspx

/Mathias Elgland & Andrey Höglund

Dinner with hosts Wednesday evening at the Mexican restaurant Wahaca

To give us a possibility to meet our hosts from the first day visits in a more informal way we invited them for a joint dinner at the Mexican restaurant Wahaca.

Cell and Gene Therapy Catapult, London

Catapult is an independent non-profit center of excellence in innovation supported by the UK government. There are many branches of Catapult in different areas of technology, and the one we visited focuses on cell and gene therapy. It was founded in 2012 and has about 130 employees from all over the world.

We were welcomed by Johan Hyllner who is an adjunct professor at the division of Biotechnology at IFM, Linköping. He introduced us to the aim of Catapult that is to provide expertise to small companies and researchers, who otherwise might have great difficulty developing, producing and commercializing their ideas. At Catapult there are more development projects than research as Johan described it. He also introduced us to two employees, Aline Guimaraes and Marcia Mata that both works in the Process Development group. They shared their passion for the mixed workload in the lab and the nice atmosphere among the colleagues.

In the end, we were treated with a tour of the new facilities with an impressive view over London from the lab windows.

Guy´s hospital to the left and the Shard to the right /Camilla Skyttner and Katriann Arja

Wellcome Genome Campus, Hinxton

Early morning at 7 am 18th May 2017 we picked up our to-go breakfasts in the hotel reception and set off with bus from central London heading out towards Hinxton and the Wellcome Genome Campus just south of Cambridge.

Eleven of the Forum Scientium members arrived to the Wellcome Genome Campus, for the day sunny and blooming, around 8:30 am. We walked from the reception to the newly built BioData Innovation Center where we were greeted and welcomed by Joanna Mills and Karen Hunter who lead us to a meeting room where we were served coffee/tea and an interesting introduction. From there we went to the Sanger Institute Sequencing and Data Centres and met Cordelia Langford, Head of Scientific Customer Relations, who explained shortly about the facilities and their usage handling about 10000 samples per month. They are running the sequencing 24/7 for patients in UK.

After this, we got an introduction to the Wellcome Genome Campus from Ross Rounsevell, Business Development Manager at the Wellcome Trust Sanger Institute. Ross explained the vision of the centers on the campus and the view heading forward as well as the general idea for the BioData Innovation Center. Biodata center has a robust backup system not only for sequencing the data but also for all data on the scientists' computers. The importance of the EMBL-EBI and the Wellcome Trust Sanger Institute and their influence on each other was also discussed. The overarching goals of the campus including research, learning, engagement, enterprise and innovation was evident throughout the presentation.

We had presentations from two of the innovative companies that have been part of the BioData Innovation Center from the start, namely Congenica and Eagle Genomics represented by Johan Estellon, Sales and Marketing Manager, Congenica, and Basil Hartzoulakis, Head of Professional Services, Eagle Genomics, respectively. They gave informative presentations talking not only about their research, products and visions but also about the BioData Innovation Centers importance and contribution to the respective companies' success so far. Congencia helps clinicians to make the right decisions for better diagnosis based on information in their database.

Then Joanna Mills, Entrepreneurship and Innovation Centre Manager, Biodata Innovation Centre, gave us a walking tour in the BioData Innovation Centre and a short tour of the Wellcome Genome Campus as we walked to Hinxton Hall opposite of the Wellcome Trust Conference Centre. Where the visit ended with a sandwich buffet lunch together with some of the representatives that we met during the day. After this, we headed further into Cambridge for our afternoon visits.

On behalf of Forum Scientium, we want to thank Joanna Mills for her hospitality and willingness to arrange this visit for us, as well as all others we met during our visit to the Wellcome Genome Campus.

More info
https://www.wellcomegenomecampus.org

/Niclas Björn & Parmis Blomgran

Medical Research Council-Laboratory of Molecular Biology, MRC-LMB, Cambridge

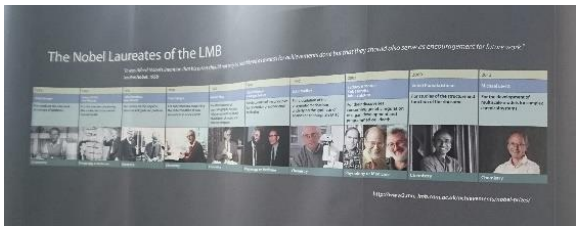
Thursday afternoon 18 May 2017 a group of 14 people from the Forum Scientium Graduate School, Linköping University, went for a study visit to the Medical Research Council –- Laboratory of Molecular Biology (MRC–LMB) in Cambridge. The research institute MRC-LMB conducts research in the field of molecular biology to reveal understanding of fundamental processes from atomic level up to the level of organisms, to improve knowledge of human diseases.

The LMB's research divisions are:

- Cell Biology
- Neurobiology
- Protein and Nucleic Acid Chemistry
- Structural Studies

Nikki Dominguez who arranged our meeting welcomed us in the entrance. The visit was hosted by Dr Madhanagopal Anandapadamanaban, postdoctoral researcher at LMB in the research group of Roger Williams wherein Madhan performs structural studies on mTORC1 protein kinase. Madhan earned his PhD in 2015 at Linköping University within Prof Maria Sunnerhagen's research group.

We had an introduction by LMB's Director; Sir Prof Hugh Pelham. We learned about LMB's history and the background to the research in molecular biology performed there up until today. One important reason for the high quality is the funding system. The absolutely main part of the funding is a shared funding to the MRC-LMB. This makes it important to help each other to be able to keep the high standard. Ten Nobel prizes has, so far, been awarded to MRC-LMB researchers.



Dr Hugh Pelham also told us about long-term projects that have lead, and are intended to make major influence in different areas of research. "There are great opportunities here, people are only limited by themselves", was a nice ending of the presentation!

Dr Madhanagopal Anandapadamanaban gave a talk of his journey to MRC-LMB and how life is as a postdoc at LMB and how to get here; either by talking to group leaders or to come on fellowship. Benefits from being a postdoc here are personal development, funding, advantageous for the CV, networking, and – you get to focus on your research!

Protein and membrane interactions and cellular signalling at structural level was the topic Dr Roger Williams, Fellow of the Royal Society, Group Leader – PNAC division, introduced us to, and how hydrogen deuterium exchange-mass spectrometry (HDX-MS) is highly useful to get insight in these interactions. William's research group focuses on the understanding of phospholipid signalling, currently through phosphoinositide 3-kinases (PI3Ks).

Dr Christopher Russo, Group Leader – Structural Studies, vividly told us everything considering imaging of biomolecules and problems of today's techniques to render atomic resolution. Russo's lab works on improving and developing new methods to enable atomic resolution of biomolecules to achieve understanding of their function,

and how this can be realized by electron cryomicroscopy (cryo-EM).

After these interesting presentations we had a tour at the MRC-LMB facilities, guided by Madhan and his co-worker Alison Inglis. The lab facilities were very open and bright and the open hallway gives you a good connection to the different labs.

Before finalizing with “fika” together with Madhan and Alison in the nice cafeteria, we had a view of the area where the researchers do their yoga during lunchtime.

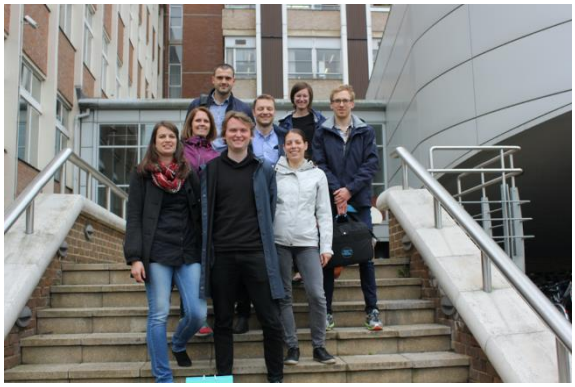
We want to thank all presenters for the interesting and inspired visit that we got at MRC-LMB.

More info at
http://www2.mrc-lmb.cam.ac.uk/

/Malin Hammerman & Linda Lantz

Cambridge Stem Cell Institute

Cambridge Stem Cell Institute is a research centre, located in Cambridge, focusing on the application of stem cells in diagnosis and treatment of many human diseases, especially cancer. We were hosted by Dr David Kent, who has his laboratory at Clifford Allbutt Building, Cambridge Biomedical Campus. During our two-hour visit Dr Kent told us about his group´s research, which concerns problems of the differentiation of stem cells to specialised cells of given tissue and to new stem cells.



Although this decision is made by individual cells, at the level of the tissue process it must be balanced and both types of cells must be produced all times to maintain balance. Dr Kent explained to us that if too many stem cells are produced, it leads to cancer, but if their number of new stem cells is too low, tissues age and degenerate. Understanding the process is a very important step to find new cancer treatments, which can be applied at the early stages of cancer evolution from single cells. After answering our questions concerning the research results presented, we had a discussion about our future prospects of becoming scientists and how we should make our career decisions. Apart from being an excellent scientist, Dr Kent is also involved in The Black Hole project, a website concerning issues related to the education and training of scientists and how science is done. He made us realize that the situation in science and career opportunities has changed during the last years and some of the professors and PhD studies supervisors, working in science for many years, are not aware of this fact. We also discussed the problem of burnout,

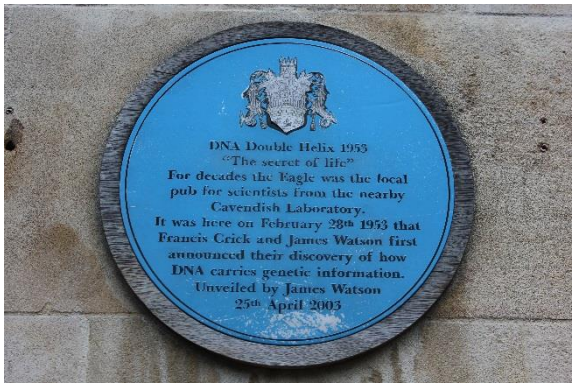
which at some stage affects significant parts of the scientific community.

More info at
http://www.stemcells.cam.ac.uk/

/Maciej Gryszel & Anna Svedberg

Sightseeing- Pub – Punting - Dinner

After ending of our study visits around 5 pm in Cambridge we had some time for sightseeing. As the weather was typically English many of us ended up in the pub Eagle.



This is the pub where Watson and Crick announced their discovery of the DNA double helix in 1953.

Some more brave members of our group tried the typical punting

After this it was enjoyable to sit in at the joint dinner.

Finally at 10 o'clock pm in heavy rain we found our bus waiting for us for the 1,5 hour transport back to London.

MRC Harwell, Oxford

Early Friday morning at seven o'clock, we once again picked up our to-go breakfasts in the hotel reception and set off with bus from central London heading out towards Oxford to visit MRC Harwell.

Helen Ward, the administration manager at MRC Harwell arranged the security passes for entry to all the visitors. Our contact person of the day was Amy Johnson. She welcomed us, offered coffee, and then took us to the seminar room where she introduced us to Mark Gardiner, who is the Facilities Resource and Training Manager at MRC Harwell. Amy gave a short introductory presentation including motto of the Institute, facilities, research, animal

house and their achievements. Harwell is mostly government funded and work with scientists all over the world, but also invites the public to see how the studies are conducted.

Mark Gardiner then took us on a tour of the Mary Lyon Centre, which houses over 50,000 mice with different genetic mutations. Scientists worldwide are studying these mice to gain insight into human diseases like diabetes and deafness. They take many measures to ensure hygienic conditions and to prevent any contamination or infection of their mice. We were informed in advance about all the rules and regulations, the most important being not to be in contact with any rodent 48 hours before of the visit to their facility. Before entering the animal facility, we had to change all clothes except underwear, put on an overall and pass through the air shower. Mark showed us how the mice are grown, maintained and used for experiments. They have developed different disease models, necessary instruments like measuring hearing, heart rate, movement, behaviour and morphological symptoms. The centre is also an expert in producing genetically modified strains using CRISPR/Cas9 technology and they store all their strains as an embryo in liquid nitrogen that upon demand can be transported to various locations in different countries. The extensive tour lasted for two hours and our host was more than happy to answer questions and show us specific instruments that we found interesting. We thank Amy and Mark for a very interesting and nice study visit. More information can be found at https://www.har.mrc.ac.uk/

/Kalle Bunnfors and Ankit Macwan

Advanced Bioprocessing Center at Brunel University, London

One group began Friday morning with a long and hearty English breakfast before going underground from King's Cross and westward towards Uxbridge. At Brunel University, we were greeted by Dr. Svetlana Ignatova, Dr. Peter Hewitson and Dr. Jonathan Huddleston from the Advanced Bioprocessing Centre (ABC). Their group is specialized in two types of liquid-liquid separation techniques known as Counter-Current Chromatography (CCC) and Centrifugal Partition Chromatography (CPC). These methods use immiscible solvents to separate a target molecule by alternately mixing and settling the solvents in a dynamic centrifugal system. One of the solvents acts as a stationary phase and is held in place by centrifugal force. The other solvent is pumped through either a tubing (CCC) or through a network of cells (CPC) as a mobile phase. In CCC, the solvents are flowing inside a tubing that is wound up on bobbins that rotate around their own axis and at the same time around a second axis (kind of like how the moon rotates around the earth that rotates around the sun) (Figure 1).

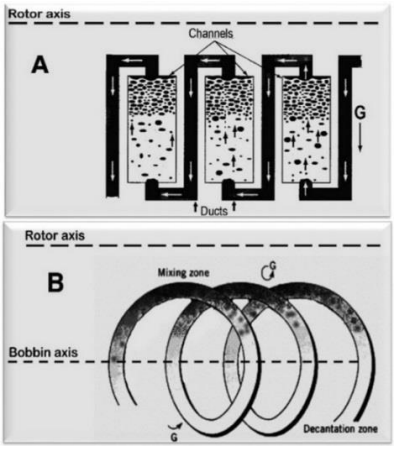


Figure 1. Principles of (A) Centrifugal Partition Chromatography (CPC) and (B) Counter-Current Chromatography (CCC).

This way, some parts of the tubing contain mixing zones between the solvents. In the other parts of the tubing, the solvents settle and separate, leaving the molecules in a phase depending on their partition coefficient. These techniques have the advantage of being very suitable for scaling up. ABC conduct both academic research and are actively involved in various industrial projects to solve difficult separation matters. After an interesting and descriptive talk about the techniques by Dr. Ignatova we first got a look of their millilitre scale prototype of a CCC (Figure 2) and, during the tour of their labs, a slightly larger version of 18 litres (Figure 3) operating at volumes more appropriate for industrial use.

Figure 2. Dr. Svetlana Ignatova demonstrates a small-scale CCC designed in a student project.

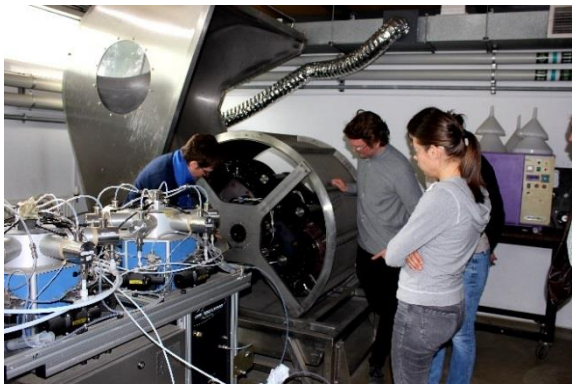


Figure 3. Demonstration of a large-scale CCC.

We also were shown some of their work on electrospinning, 3D printing and a very interesting talk with Dr. Ruth Mackay and their prototypes of microfluidic devices for point-of-care diagnosis. After an interesting and pleasant visit we were guided by our hosts to the bus stop where some of us headed for the airport.

More info at
http://www.brunel.ac.uk/bib/bioprocess-engineering/abc

/Jonas Christoffersson & Charlotte Immerstrand

Oxford Nanopore Technologies

The last day of our study visit tour, a group of ten members took a bus early morning at seven o'clock from London to the company Oxford Nanopore Technologies Ltd. We were warmly greeted by Senior Director of Research James Clarke, Senior Scientist Ioana Pera and Senior Scientist Jonathan McKendry. We had a presentation of the company and the Nanopore DNA Sequencing Technique, including a review of the current trends of the DNA detection technologies.

The MinION, which is the world's first and only nanopore DNA and RNA sequencer, and the description of the development of the technique was very impressive. It is a portable, real time, long-read, low cost device that has been designed to bring easy biological analyses to anyone. We also learned about other developments within the company, eg PromethION for large volumes of samples, and SmidgION that only needs a smart phone. After the presentation and discussion, we were offered a tour to the laboratory facilities. We got the opportunity to visit the labs where the products are fabricated and tested, and also the fundamental research of new technologies is done. Altogether approximately 190 persons are working within the company, and very many of them have a PhD exam. Finally, we were invited to a lunch pizza meeting together with our hosts and some of their colleagues. They gave us a brief intro about their background and how, and why, they transferred from the academia to industry, specially.

We were very happy to have visited the Oxford Nanopore Technologies and

especially impressed by the positive and very open atmosphere, and the proudness the employees expressed.

More info at https://nanoporetech.com/

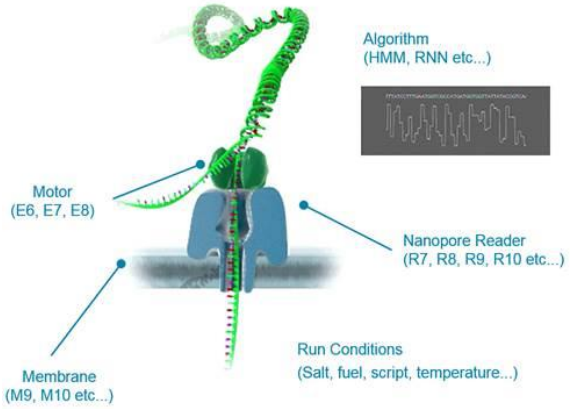


Illustration of the nanopore technique. A helicase is added to the sample, but will not become active until it connects to the membrane pore protein. As the nucleic acid chain is transported through the pore the current changes are measured. With the developed algorithms the sequence of bases is given as a real-time output. (With kind permission from Oxford Nanopore Technologies)

Illustration of the handheld MinION. (With kind permission from Oxford Nanopore Technologies)

/Lingyin Meng and Lei Wang

Finally

After a the very condensed three-day schedule with lots of very fruitful visits to impressive research departments and research intensive companies most of the participants were exhausted, but happy to have learned more about possibilities for their future careers.

Most of the members returned directly by air to Linköping, but some first made a short sightseeing in Oxford before returning to London for a nice weekend.