**Switzerland 2013**

**CERN**

The morning of Wednesday 20th November, part of the group went to CERN. It was like a small city, with its own café, post office and social events. And like in any town, you can get lost. We’d been running around in circles for a while until we finally found the restaurant. When we went for lunch there, we heard different languages all around us. CERN recruits people from all over the world. Right now there are about 14000 people working in CERN.

CERN was founded in the cold war in 1952, under the name European Council for Nuclear Research. Their main objective is the experimental and theoretical research of subatomic particles.

Alex told us a little about what CERN is doing, and which questions they’re trying to answer. As the question: What is the universe made of? Democritus, a Greek who lived around 500 BC, already contemplated that matter consisted of atoms, though it wasn’t until the end of the 19th century that this theory was proven. Later we discovered that atoms were made of protons and neutrons in the nucleus, surrounded by an electron cloud. And even these particles are made of yet other particles, called quarks. All these particles are prevented from disassociating by four different forces: Strong force, weak force, electromagnetic force and gravity. But these particles don’t have an intrinsic mass. It’s actually the medium that gives the electrons mass, including in vacuum. Higgs suggested that even vacuum contained something he called a Higgs field and proposed that this field could be turned into a particle when enough energy was added: The Higgs Boson. This particle has recently been discovered and explains the quantity mass. But there are still ways to go. We can actually see only 4% of the mass of the universe; the rest is in the supposedly ‘Dark matter’.

From the 14000 accelerators in the world, the largest is located in Switzerland and partly in France. The Large Hadron Collider, LHC, has a diameter of 27 kilometres. It consists of eight straight parts, eight bending parts, and four detectors. It was built in 2008 and lies about 100 metres underground. It is used to accelerate protons with an energy of around 7 TeV and observe the collisions.

After the talk, we were separated into four smaller groups. Group 4 went with the Physicist Mark to show us around CERN. We went to see LEIR, the first decelerator of CERN. In 1982 they built the LEAR: Low Energy Antiproton Ring. It was used to decelerate and store antiprotons. When antiprotons and protons collide, the particles are destroyed and a large amount of energy is released. In 1996 it was turned into the Low Energy Ion Ring (LEIR) and is now used to accelerate Lead ions before it enters other accelerators and eventually the LHC.

After LEIR, we went to the point where hydrogen enters the system: LINAC2. The Linear accelerator 2 first strips the electrons from the hydrogen ions, leaving only protons. With quadruple magnets, the protons remain in a beam. The protons enter a container with alternately positive and negatively charged Drift-tubes. While one pulls the proton, the other repels them, resulting in acceleration between the tubes.
We also had a quick look at LINAC3, which has the same purpose, but is used to inject lead ions. The lead is stripped from all its protons, giving Pb82+. Since they were kind of secretive about it, we could only peek through the door for a little while.

The Computer Farm, where all the data is stored, was huge. It was once also the main provider of the world wide web, which was invented by Tim-Berners Lee at CERN, but not since it was taken over by commercial providers. They also use ‘The Grid’ to send data all over the world with a speed of 16Gb/s.

CERN was an unbelievable experience. To stand where some of the most intelligent scientist work from all over the globe. They work together with scientist from different disciplines to answer interdisciplinary questions. And we might have stood right above the Large Hadron Collider, though it’s a shame we didn’t get to see it. The reason behind this was that they were doing welding maintenance on the magnets. The seams are then checked with Röntgen radiation. And our guide Mark was really nice. He was smart, and enthusiastically tried to answer all our questions. Like if we’d ever be able to travel to the future, by surpassing the speed of light. Which we certainly can’t with the four dimensions we acknowledge now, but might be possible if we consider a much larger number of dimensions (, or not).

Andreas, Joris and Laura

**Centre Universitaire Bioinformatique**

On the second day of our trip to Geneva, we departed to the Centre Universitaire Bioinformatique. Here we had lectures about bioinformatics. There was a general introduction that highlighted that bioinformatics was about analyzing data and that there were several organizations (SIB and CUB) that worked together on this. After the general introduction several lectures followed. Even though I study physics which has not that much to do with bioinformatics, I could understand quite a bit of the lectures. The parts I missed were luckily understood by the pharmacy student Yessir.

The first lecture was about scientific and parallel computing provided by Jean Luc Falcone.He said there were three ways to do research into nature, namely: thinking about it, do experiments or make a simulation. At the university in Geneva they simulate nature, called scientific computing. He proceeded to talk about parallel computing, which is combining multiple computers for more calculating power. In Geneva they had access to around 17.000 cores and 16 Tb of RAM (this is a lot).
At the end of his talk he gave us an example of a project they were currently working on: aneurysms. He showed us a model of how aneurysms slowly fill up with blood and how they eventually rupture. An adequate simulation of this project could map the process of thrombus forming and give new insights on treatment. To make this model they needed scientist of all fields: physics, computer science, biology etc. It was thus a good example of interdisciplinary research.

The next talk was about data analyzing software. More specifically about analyzing data from tandem mass spectrometry. Spectrometry is about analysing different components from a molecule. Usually High Pressure Liquid Chromatography (HPLC) is used prior to mass spectrometry to get more accurate results. The result is a graph, the mass spectrum, with different peaks at certain chemical groups. The speaker said there were several ways of determining what the peaks represented, that is which chemical group. If you have a graph you can compare it to a database with predicted outcomes, compare it with a library of previously found mass spectra or unleash data analyzing software on it. The research group at Geneva was working on such software, and actually created something interesting. Their software would read the found mass spectrum, compare it with the databases and libraries and would find the best fit. The most interesting aspect of their program is that it learns. The more they used it, the better the results.

Anne Estreicher did the next talk, which was about protein databases. She spoke about Uniprot (a universal protein resource), which currently contains about 50 million protein sequences. About ninety percent of these sequences are automatically derived from DNA. Only ten percent was really experimentally found.

She proceeded to explain that Uniprot consisted out of two parts: Trembl and Swissprot. Trembl is an automated database and the results are not reviewed. Swissprot is manually reviewed and contains only about half a million proteins at this moment. The reviewing of data is actually more important than one might think. She told about a certain protein SIRT 5 that was in some aspects wrongly accounted for in the Trembl database. After Swissprot reviewed it they found that it had interesting chemical reactions. The main point was that Swissprot gave reliable experimental data of proteins that could be used in research.

Amos Bairoch gave the next lecture about CALIPHO (Computer and Laboratory Investigation of Proteins of Human Origin). He began with stating that there are about 20.000 protein coding genes and that we know very little about most of the human proteins. More impressive is that these 20.000 genes encode for about 5.000.000 proteins. This is due all the alternative splicing processes and post translational modifications (PTM’s). The goal of CALIPHO is to increase the knowledge of the human proteins. In order to do this, they created Nextprot, a database with lots of information about human proteins. They actually combine the data from Swissprot with other known experimental data about the proteins and thereby create a knowledge rich database. He ended by telling us that the Human Proteome Project (HPP) has as mission to ‘see’ every protein in the Nexprot database.

The following talk was about human orphan proteins by Lydie Lane. She told us that these orphan proteins are proteins you only find in one specific organism and that we know very little about a lot of human orphan proteins. There are about 2500 orphan proteins in the Nextprot database and only about 15 have experimental 3D images.She is also working with the CALIPHO project and her research group looks into these orphan proteins. She showed us an example of fluorescence, where they would look at certain fluorescent proteins to find where the orphan proteins are usually located.At the end she spoke about her current projects. They were doing research into two proteins that might be associated with brain development, and three proteins that are located in mitochondria.

Next lecture was about computational evolutionary genomics provided by Evgeny Zdobnov. The talk was a little harder for me to understand. She started to talk about orthology, which was about referring common ancestors. The research group has made a database called orthoDB, which contains orthologous protein coding genes from several fungi and bacteria. They created insect animal models to research the phylogenetic trees of genes and the quality of the genome. Therefore they created the so called “Newick Utilities”.

The last lecture was about genomics of complex traits provided by Alfonso Buil. The research group was led by Emmanouil Dermitzakis. The speaker told that complex traits arise from two components: the environment and genes. They did research into heritability of certain gene combinations. More specifically: into the heritability of diseases. The main problem with this research was that there is an enormous amount of data. This is because not just one combination of genes can create the expression of the disease. The main research is to look which genes give the most expression to a certain disease and map these genes. He told us that they did this by comparing the amount of expression of the disease with the amount of a certain gene that is activated. The other part of complex traits, the environment, is much harder to study. This is because the environment is a dynamic system in contrast to the genome, which is a static system. There is currently not much study of the influence of the environment on complex traits. He ended by saying that there is still a lot of work to be done in his field.

All these talks showed me (and probably others) that interdisciplinary research is quite important. Mainly here with bioinformatics it became clear that this field of research is mostly about tool development. The researchers build vast databases and knowledge libraries for other researchers to get their information. Without these databases other research couldn’t even take place.

**Neuroscience centre**

On Thursday the 21st of November, the group departed to the Neuroscience Centre. Here we received several lectures about the works in neuroscience. The day had begun with an introduction about the different kinds of studies within neuroscience. There are several departments such as basic neurobiology, cognitive neuroscience, developmental neuroscience, computational neuroscience, clinical neuroscience and neuroimaging sciences. Besides the lectures the schools program for the study was explained, it was quite interesting to know how a study like this one is held within the university of Geneva.

One of the spokesmen was biologist Alexander Pouget, who gave a lecture about his work *“Probabilistic inference in neural circuits: From insects to humans”.* Here he spoke about his work within the laboratories and stated that one needs mathematical to understand neurosciences. During the lecture sir Pouget wanted to make clear that the studies in neurosciences, which started over fifteen years ago, are not that advanced as of yet and that in parts of knowledge, there is practically none. The part that stood out of sir Pouget’s lecture was his interaction with the group. He was able to tell his story in such a way, that it was fun and interesting to listen. Both interactive and consisted with jokes. For example, the arithmetic test that the students had to perform. With the test there came the explanation about optimal multisensory integration and perceptual learning. At present day, the studies are to make calculations which neurons are activated within a circumstance. The study in neuroscience cannot proceed because of the little amount of knowledge about this field of science. As a closing statement, sir Pouget said that those whom are not interested in the human brain are crazy.

The next spokesman was Anthony Holtmaat from the Nethterlands. Sir Holtmaat spoke of his work *“From molecules to neurons”.* He presented to the students a research on animals in which he presently is working on. The lecture started with a global explanation about the physiology of the brain. As part of the research fluorescence proteins were used to make neuron activity visible. Here was shown that over time axons and dendrites constantly change. Here was stated that there are more synapses than neurons. If the whiskers of a mouse were to be cut of, the fluorescence proteins could show, that the synapses made changes as result of this event.

The last spokesman was Swann Pichon. He spoke in his lecture about cognitive neuroscience of emotions. Within this research, there is searched to what an emotion is and tried to understand certain emotional dysfunctions. This type of research is, as it has been called, a young and expending field. Sir Pichon explained that emotions are universal with the occasional exceptions. The amygdala in the brain makes it possible to experience fear and so produces amygdala lesion fear blindness. On the other hand there is shown that with anxiety disorder, there is a hyperactive amygdala. Here are studies performed with monkeys and snakes. It was found that a lesion impairs fear recognition, representation and memory. A high level of serotonins makes one susceptible to stress.

At the end of all lectures several master and PhD students came forward. This was a surprising and unexpected turn of events. Here was the possibility to ask these students questions. At the end of the day there was the opportunity to consume a drink with the master and PhD students to exchange each other’s experiences within studies and to network.

**ETH Zurich**

On the fourth day of the excursion in Switzerland, we travelled to Zürich. We visited there the ETH, which stands for the german abbreviation “*Eidgenössische Technische Hochschule”*. The university is part of the French École Polytechnique Fédérale de Lausanne. The ETH Zürich is an international university for technology and natural studies.
We attended different lectures here from different speakers. They gave us information about how the studies are classified and afterwards there were lectures about the latest developments on subjects of physics, chemistry and pharmacotherapy.

First, we attended some lectures about their Material Sciences Department (DMATL). This department has 200 employees. Their goals are to make materials more durable, to create self-healing adaptive materials, to polymerize CO2 (which might solve the greenhouse effect by storing the CO2 in a solid state), or make synthetic fibres with properties similar to spider webs.

The first lecture was from the Materials Theory group. They study the coupling between structure, chemistry, defects and properties: and materials with exotic physical phenomena.
They are using YMnO3 to try to understand the early universe and cosmic strings. Cosmic strings are topological defects which probably formed during a phase transition in the early universe.
YMnO3, when at high temperature, undergoes a phase transition that gives rise to six different domains. They form a whirlpool-like structure with topological properties, similar to what happened in the early universe. By studying this we can get a better understanding how cosmic strings developed in the early universe. They study this by using single-crystals. These crystals have the same orientation everywhere, and can be used to measure certain directional properties like magnetizations.

The second speaker was working in the Laboratory for multifunctional materials. He was making nanobased aerogels. The sample is dried till a wet gel. Afterwards it is super critically dried till you get a highly porous structure. In this particular case they were experimenting with BaTiO3 aerogels. Uses for aerogel are still mostly unknown. Although one chemist that sat next to me said that porous materials could be used as a catalyst of some kind.

The third speaker, Nicholas D. Spencer, was from the Surface Science and Technology Department. They are trying to understand what a surface is, and they modify and characterize surfaces. Their research point is the contact point between two surfaces, the tribologically interacting zone. Tribology is the study of two surfaces that interact (and the friction). He gave an example of their research with gradients, namely that they were looking at the contact of water with hydrophobic and hydrophilic surfaces.

A. Nelson, the fourth speaker, was from the laboratory for interfaces, soft matter and assembly, which was founded in September 2013. They are trying to gain complete control of the microstructure and mechanical properties of 2D materials.
They try to make new materials with nanoscale control on structure and functionality by nanoparticle self-assembly. The nanoparticles get stuck between two liquid interfaces and become a thin sheet. Here they reassemble to the most energetically favourable structure, which is hexagonally close-packed.

They investigated the characteristics of the created materials by applying different kinds of reactions and forces. The results of this group can be used in biomaterials, optics, membranes and energy.

The fifth speaker was from Magnetisation Dynamics in ferromagnetic materials. Magnetism is used in all kinds of things, like hard drives, sensors and also the recently discovered Magnetoresistive Random Access Memory (MRAM). Here, they are trying to make the chips for hard drives and such smaller and faster, but we are reaching the limit as to how dense we can make our hard drives and therefore we need new solutions to do so. In this department they are studying magnetic squares with a vortex core. These are in a magnetic Landau state, a closed magnetic flux, which is energetically most favourable. The vortex core can gyrate, either clockwise of anti-clockwise, depending on polarization.
They can see this gyration with XMCD imaging to reveal the magnetic contrast. They think the difference in polarization of the vortex core can be seen as a binary state (0 or 1), and may be used in data storage.

The sixth speaker worked at Complex Materials. They are interested in bio-inspired compositions. In muscle, the tendons gradually change into the actual muscle. This is far less breakable than when it would abruptly change from tendon tissue to muscle tissue. The department wants to use this in synthetic materials to make connections stronger. They’re also studying self-healing materials. Here they were inspired by bones, in particular osteocytes. They also studied adaptive composite materials.

After this lectures, four PhD students from the department of Chemistry and Applied Biosciences came to talk about their research, mainly focussed on chemistry and pharmacotherapy.
Oliver Horlacher was studying Pyridomycin as a lead for new anti-tuberculosis agents. Pyridomycin is a natural product of a certain bacterial strain, which inhibits InhA, which in its place inhibits mycolic acid synthesis in *Mycobacterium tuberculosis*. Mycolic acid is part of the bacterial cell wall, by losing this long fatty acid, the bacteria loses his structure.
Some *M.tuberculosis* strains have evolved so they are resistant to some or all antibiotics. The goal of their project is to simplify the structure of pyridomycin and characterize the binding with the InhA receptor.

The second lecture, given by Nikolaus Krall, was mainly about working on targeted drug delivery for cancer therapy. Current anti-cancer therapy, like chemo, is very nonspecific and also harms the rest of the body. The lecturer spoke about making those anti-cancer agents more specific to the tumour itself. Tumours show overexpression of certain proteins on the surface of the cell. By raising an antibody against these proteins, you could target the tumour cells more specific. To do this you would have to combine an antibody with an anticancer agent. But antibodies are fairly large, consisting of two heavy, and two light chains, and a large amount of antibody never reaches the tumour cell. Small ligands work better and the researchers are trying to make those small ligands specific for the tumour cells on basis of the overexpressed proteins. The research results show that no longer the entire body is affected by the drug, but the build-up is mainly around the tumour area.

Filip Roudnicky tries to identify therapeutic targets and biomarkers for invasive bladder cancer by the profiling of the tumour vasculose. Tumours stimulate the rapid growth of blood vessels to get more blood. These vessels are less neat and leakier in comparison to normal blood vessels.
They found out that the protein Endocan is upregulated in invasive bladder cancer. This protein interacts with certain growth factors to stimulate blood vessel creation. Inhibition of this interaction could offer a new strategy to inhibit tumour angiogenesis (forming of new blood vessels).

The fourth and last lecture was given by Martina Roos. She is trying to make a RNA drug to target miRNA for tumour suppression. This technique relies on the specific binding capacity of nucleotides. miRNA are small molecules (oligonucleotides) which can specifically bind to its complementary sequence, inhibiting the target mRNA. They identify coding and non-coding RNA that play a role in disease-associated pathways.
They are currently working with Let-7 microRNA, a noncoding RNA molecule. It is recruited by the RNA induced Silencing Complex (RISC) and represses translation of complementary sequences. With Let-7 it leads to the repression of oncogenes. Lin-28 blocks modification of pre-Let-7 into Let-7. They found out that protecting the loop in the pre-RNA molecule with an anti-sense oligonucleotide prevents the activity of Lin-28 on Let-7.

After the lectures we were split into four groups. Group B went to a Vascular Imaging department. They were mapping the lymph system of a mouse by using low IR-radiation after inserting a dye that absorbs at around 800nm. This made the lymph system light up on the images.

Someone else showed us obese mice, which lacked the Lep gene, meaning they didn’t get the ‘I’m full’-signal, and couldn’t stop eating. Obesity triggers a response in your body that stimulates obesity even further, making it a vicious circle. The reseacher was trying to find a way to cure this.She also showed us how they imaged blood vessels in certain organs. They had worked a kidney till it was transparent, and then injected a DII dye into the blood vessels to colour them. They used a ultra-microscope to make lots of pictures of different depth by making a light sheet, and photograph them. The pictures can then be combined into a 3-dimensional representation.

The ETH lectures covered a large variety of subjects. The first few lectures about subjects related to physics of course interested me the most as I’m a physicist. I really like the research being done with material sciences. The other lectures were really interesting too and showed a large variety of research subjects that are currently looked into. All in all it was a great experience for me and I am even considering doing a master’s degree in Zürich.