

Utrecht Summer School "Exploring Nature's Molecular Machines" **August 15-26, 2011, Utrecht University**

This course focuses on the chemical principles underlying protein structure and function and how proteins form an assembly of "molecular machines" that work together to sustain the living state. We will explore how proteins "know" what shape they should fold up into following their synthesis, how they cluster into dynamic macromolecular complexes, and how these complexes communicate to form "social" networks that enable cells to move, replicate, signal, and execute other vital processes. The students will be introduced to advanced methods in structural and molecular biology for decoding the cellular protein machinery at atomic resolution, and examine how malfunction of specific components can lead to systemic failure and disease. The school will combine theory (lectures, tutorials) with experiment, laboratory tours and a visit to a leading Biotech company.

Course Director

Dr. J. Holthuis
H.R. Kruytgebouw, room N605
Padualaan 8, 3584 CH Utrecht, NL
E-mail: j.c.holthuis@uu.nl
Phone: +31 (0)30 253 6630

Course Coordinator

Mrs. Cecile Lemette
H.R. Kruytgebouw, room N606
Padualaan 8, 3584 CH Utrecht, NL
E-mail: c.lemette@uu.nl
Phone: +31 (0)30 253 3966

Lecturers

Prof. dr. M. Baldus, Prof. dr. A. Bonvin, Prof. dr. I. Braakman, Dr. E. Breukink, Prof. dr. R. Boelens, Prof. dr. P. Gros, Prof. dr. A. Heck, Dr. J. Holthuis, Dr. E. Huizinga, Prof. dr. G. van Meer, Dr. S. Mohammed, Dr. S. Rüdiger, Prof. dr. J. Tommassen, Dr. P. van Bergen en Henegouwen, and others.

Target Group

Advanced bachelors / beginning masters in the early stage of their study with a background in chemistry, molecular biology or biophysics as well as proficiency in English. Applicants go through a selection procedure.

Course Aim

To introduce the student to technology for decoding nature's molecular machines, and how the acquired knowledge provides a rationale for novel therapeutic interventions and applications in nano- and synthetic biology.

Period

15-08-2011 - 26-08-2011 (2 weeks)

Credits

3.0 ECTS credits + Certificate of Attendance

Website

<http://www.utrechtsummerschool.nl/>

Program outline

Date	Location	Time	Topic
Week 1			
Monday, August 15	Kruyt building O622	09.00-09.30	Registration, coffee
		09.30-09.45	Opening and Welcome
		09.45-11.00 11.00-12.30	General introduction to summer school and Bijvoet Centre - Program outline - Bijvoet graduate school for biomolecular research Biomolecular NMR spectroscopy I - Introduction to solution NMR
	Minnaert building	12.30-14.00	Welcome lunch
	Bloembergen building, seminar room	14.00-17.00	Biomolecular NMR spectroscopy I (continued) - Exploring gene transcription by solution NMR - Site visit NMR facilities
	Kruytbuilding 6 th floor Noord	17.00	Welcome drinks
Tuesday, August 16	Kruyt building O123	09.00-12.15	Biomolecular NMR spectroscopy II - Introduction to solid-state NMR - Membrane proteins studied by solid-state NMR
	Kruyt building O123 & O126	13.00-17.00	Modelling biomolecular interactions - Computational methods to model & dissect biomolecular interactions - Computer practicum
Wednesday, August 17	Kruyt building O126	09.00-12.15	Protein folding & molecular chaperones I - Mechanisms of protein folding & chaperoning - Protein folding and chaperoning in intact cells
	Kruyt building 7 th floor Oost	13.15-17.30	Protein folding & molecular chaperones II - Practicum
Thursday, August 18	Kruyt building O126	09.00-12.00	Biomolecular mass spectrometry I - Deducing composition & assembly of molecular machines by mass spectrometry
	Kruyt building 6 th floor Oost	13.00-17.30	Biomolecular mass spectrometry II - Site visit BMS facilities - Practicum
	Minnaert Building	17.00	Summer School Drink (offered by the Faculty of Science)
Friday, August 19		09.00-17.00 19.00	Excursion to Merck-Sharp & Dohme, Oss (meeting point: Utrecht Central Station ticket office) Summer School Diner in down town Utrecht (offered by the Bijvoet graduate school)
Saturday, August 20		09.30-17.00	Discover Holland Day (meeting point: Moreelsepark)
Sunday, August 21		09.30-17.00	Outing to Kröller-Müller Museum & National Park (meeting point: Moreelsepark)

Date	Location	Time	Topic
Week 2			
Monday, August 22	Kruyt building O622	09.00-12.15	Immunology made crystal clear I - Crystal-structure determination of large protein complexes - Molecular dissection of the immune response
	Kruyt building 8 th floor Noord	13.00-17.30	Immunology made crystal clear II - Practicum
Tuesday, August 23	Kruyt building O123	09.00-12.15	Mechanisms of membrane homeostasis I - Lipid sensor & flippase machinery - Bifunctional lipids as tools for elucidating membrane homeostatic machinery
	Kruyt building 6 th floor Noord	13.00-17.30	Mechanisms of membrane homeostasis II - Practicum
Wednesday, August 24	Kruyt building O123	09.00-12.15	Bacterial cell envelope synthetic machinery I - Structure, function & biogenesis of the bacterial cell envelope - The bacterial cell envelope as target for antibiotic drug development
	Kruyt building 4 th & 8 th floor West	13.00-17.30	Bacterial cell envelope synthetic machinery II - Practicum
Thursday, August 25	Kruyt building O123	09.00-12.30	Growth factors, cancer & therapeutic nanobodies I - Mechanisms of growth factor receptor signalling & down regulation - Llama antibodies (nanobodies) as diagnostic and therapeutic agents
	Kruyt building 5 th floor Noord	13:30-15:00	Growth factors, cancer & therapeutic nanobodies II - Site visit microscopy facilities
	Utrecht University Library	15.00-18.00	Preparation for MiniSymposium
Friday, August 26	Kruyt building W726	09.00-12.30	MiniSymposium & Wrapup
	Kruyt building 6 th floor Noord	12.30-13.30	Farewell Lunch

Topic descriptions

	Subject (approximately one day each)	Lecturers
1	<p>Biomolecular NMR Spectroscopy NMR is an invaluable spectroscopic tool to study molecular machines and protein interaction networks at an atomic level. NMR can give the structure, but also the dynamical picture, of proteins and protein complexes in solution, membranes or even cells, in conditions close to their native environment. We will introduce modern biomolecular solution and solid-state NMR spectroscopy, and treat various experimental and computational methods to analyze structure and dynamics. The course, a combination of tutorials and exercises, will present examples of recent research. A site visit to the NMR Research Infrastructure is planned. http://www.nmr.chem.uu.nl/Main/index.php</p>	Prof. dr. Rolf Boelens Prof. dr. Marc Baldus Prof. dr. Alexandre Bonvin Dr. Klaartje Houben Dr. Marie Renault
2	<p>Protein folding & molecular chaperones DNA makes RNA makes protein – this is the central dogma as formulated by Francis Crick in 1958. The most enigmatic step in this fundamental sequence of life is at its end: how do proteins fold into their active three-dimensional structure? A particular set of molecular machines, molecular chaperones, are organizing protein folding inside the cell. Understanding of their mechanism of action is of crucial importance to understand the last step of the central dogma. http://www.bijvoet-center.nl/cpc</p>	Prof. dr. Ineke Braakman Dr. Stefan Rüdiger Dr. Jürgen Gent
3	<p>Biomolecular Mass Spectrometry The structural and functional characterization of protein complexes is essential to understand biological processes at the molecular level. An essential aspect of deducing structure is detailed knowledge of the protein sequence. The exact termini and post-translational modifications can have serious repercussions on protein structure. In order to obtain these details a proteomics characterization is required. The use of different enzymes, nanoflow chromatography and various fragmentation techniques for tandem mass spectrometry will be discussed. Native mass spectrometry is used to analyze intact protein complexes. To study the topology of the assembly often the complex is dissociated. Next, the identification of the generated subcomplexes reveals the structural composition of the protein complexes. http://bioms.chem.uu.nl/</p>	Prof. dr. Albert Heck Dr. Shabaz Mohammed Dr. Reinout Raijmakers Dr. Esther van Duijn
4	<p>Immunology made crystal clear The human body is capable of recognizing and clearing bacteria and viruses. One arm of the innate immunity is represented by the so-called complement system that acts in blood and tissue fluids. It consists of ~30 large multi-domain proteins that together mount an attack on the pathogens, while protecting the host tissue. In this session we will discuss the structural techniques, expression of mammalian secreted proteins and crystal-structure determinations of large multi-domain protein complexes, needed to elucidate the molecular mechanisms underlying this immune response. http://www.uu.nl/EN/faculties/science/organisation/depts/chemistry/research/csc/Pages/default.aspx</p>	Prof. dr. Piet Gros Dr. Eric Huizinga Dr. Pramod Madoori
5	<p>Mechanisms of membrane homeostasis After the quest for the Holy Grail of the genome, it has become painstakingly clear that a sequenced genome does not permit meaningful predictions on the properties of the non-equilibrium membrane systems of a cell. In this session, we will focus on: the physicochemical properties of membrane lipids in relation to their cellular functions; how cells maintain lipid diversity and non-random lipid distributions; the underlying protein machinery of lipid converters, sensors and flippases; how dysfunction of this machinery disrupts key cellular processes, resulting in disease.</p>	Prof. dr. Gerrit van Meer Dr. Joost Holthuis Dr. Per Haberkant

	<p>We will also discuss the development of unique experimental tools for tracking down lipid homeostatic machinery and for visualizing lipid-protein interactions in live cells.</p> <p>http://www.me.chem.uu.nl/</p>	
6	<p>Bacterial cell envelope synthetic machinery</p> <p>The cell envelope of bacteria consists of a cytoplasmic membrane, a cell wall and, in the case of Gram-negative bacteria, of an additional membrane, the outer membrane. The cell wall is responsible for the shape and the rigidity of the bacteria and is an ideal target for antibiotic development. The outer membrane is a semi-permeable barrier that is responsible for the intrinsic resistance of Gram-negative bacteria against antibiotics. We will discuss the structures of these layers and the mechanisms by which their constituents are synthesized, transported and assembled in the cell envelope.</p> <p>http://www.bio.uu.nl/microbiology/(Tommassen) http://www.uu.nl/EN/faculties/science/organisation/depts/chemistry/research/cboc/research/rescb/Pages/default.aspx (Breukink)</p>	<p>Prof. dr. Jan Tommassen Dr. Eefjan Breukink</p>
7	<p>Growth factors, cancer & therapeutic nanobodies</p> <p>Growth factor receptors are multiply implicated in human cancer: they protect the cells from apoptosis and induce cell proliferation. Receptor down regulation is nature's most important mechanism for negative feedback of signaling. We investigate the signals and mechanisms that are involved in the regulation of internalization and intracellular transport using advance microscopical techniques like homo- and hetero-FRET. We are furthermore specialized in the development of antibody fragments from Llama (VHH) that we can be used in the imaging of solid tumors in mice and man (diagnosis) and for the targeting of therapeutics to the tumor.</p> <p>http://web.science.uu.nl/cad/</p>	<p>Dr. Paul van Bergen en Henegouwen Dr. Rob Roovers Ing. Jarno Voortman</p>