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THE MORPHOLOGY AND CYTOSKELETON OF CELLS – A CDIO PROJECT FOR 2ND SEMESTER STUDENTS IN ENGINEERING BIOLOGY

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ABSTRACT

The demand for exact engineering within the life sciences is ever-growing and the Linköping program *Engineering Biology* (270 ECTS credits) thus prepares for a career as an engineer at the interface between engineering, biology, chemistry, mathematics, physics, and medicine. Solid engineering skills are indeed a prerequisite. The CDIO standards were accordingly implemented in 2005 with an introductory project course in which students i) learn to work according to the easy to use interactive project model LIPS, ii) enhance their oral and written communication skills, iii) get a deepened insight in the career role of an engineering biologist, and, iv) apply the project model when dealing with an assigned interdisciplinary task in groups of 5-7 students. The latter is the main part of the course, and we designed one task named *The Morphology and Cytoskeleton of Cells*, located to a pre-clinical setting at the Linköping University Hospital. A senior teacher performs the role of a customer in need of an enhanced method for visualization of certain subcellular structures in cells from patients, and the student group acts as a contractor delivering this product, i.e. a method, that meet 25 carefully specified demands. The novel method should be successfully tested on patient samples before final delivery. Students are given access to a biomedical laboratory and facilities, and have a high quality fluorescence microscope at their disposal. A junior teacher (Ph.D. student) acts as a supervisor for the student group. All students are given specific roles ranging from project leader to various system responsibilities, including documentation. The Customer communicates directly with the project leader and reviews documents, deliverables and milestones/tollgates. Since students are still regarded as laymen, they also have the possibility to limited consultation with two senior teachers experienced in the methodological area. The student group also interacts with two fictitious subcontractors, i.e. *The Clinic* that delivers samples, and *The Chemicals Company* (equaling one of the major actors in the real world) that delivers a full range of chemicals required. Successful delivery demands an extensive literature review in biology and optics/imaging, good laboratory practice, study design, data handling, optimizing of imaging software, as well as ethical considerations. Other concerns are safety issues and economy. The pioneer course was appreciated by the students, and required intensive teacher commitment.

INTRODUCTION

THE LINKÖPING UNIVERSITY ENGINEERING BIOLOGY PROGRAM

It has become evident that physics and engineering are increasingly important for the advancement of biology. The Linköping Engineering Biology Program [1] aims on serious skills in mathematics, physics and engineering, while simultaneously bridging to the emerging new biology and biomedicine. A pioneer class of 30 students was admitted to the Engineering Biology Program in 1994, and since then the annual admission has increased to 60-90 students. Chemistry and biology correspond to approximately one third of the program and the rest is devoted to mathematics, engineering and physics. After seven semesters of general courses in chemistry, biology, physics, mathematics and programming (summarized in **Table 1**), students specialize in one out of seven available profile semesters:

- Bioinformatics
- Biological Production
- Biotechnical Physics - Materials in Medicine
- Biotechnical Physics - Microsystems and Biosensors
- Environmental Science
- Microbial Biotechnology
- Biomedical Engineering
- Protein Chemistry with Protein Engineering

The ninth semester is then devoted to the final M.Sc. thesis. The Engineering Biology Program attracts approximately similar numbers of female and male students.

Table 1: Obligatory and eligible (italics) courses during the first seven semesters of the Linköping University Engineering Biology Program, as of the 2006 curriculum. The introductory project course is bolded.

Semester	Course name	ECTS credits (270 in total)
1-2	Foundation Course in Mathematics	6
	Linear Algebra	6
	General Chemistry	6
	Organic Chemistry	3
	Biochemistry	6
	Algebra	7
	Introduction to Programming	7.5
	Engineering Project for Engineering Biology	6
	Physical Chemistry	7.5
3-4	Calculus, Several Variables	9
	Engineering Mechanics D	4.5
	Electric Circuits	4.5
	Probability and Statistics, First Course	8
	Organic Chemistry	6
	Numerical Methods	7.5
	Biochemistry	7.5
	Physics	6
	Cell Biology	7.5
5-6	*Research at LiTH*	*1.5*
	Molecular Physics	9
	Microbiology and Immunology	9
	Systems Physiology	6
	Molecular Physics	9
	Biological Automatic Control	6
	Databases and Bioinformatics	6

	Analytical Chemistry	6
	Signal and Image Processing	7
	Measurement Technology	5
	Signal and Image Processing	7
	Gene Technology and Molecular Genetics	6
7	*Introduction to Operations Research*	*5*
	Mathematical Models in Biology	*6*
	Complex Analysis	*7.5*
	Biomedical Signal Processing	*6*
	Artificial Intelligence and LISP	*7*
	Programming and Data Structures	*9*
	Object-Oriented Programming	*4.5*
	Computer Networks	*5*
	Industrial Economics, Basic Course	*4.5*
	Environmental Measurement Technology	*5*
	English	*6*
	Intercultural Professional Communication –	*6*
	English	*6*
	Communicative French	*6*
	German	*5*
	Image Analysis	*6*
	Cellbiological Methodology	*6*
	Biostatistics	*6*
	Medical Imaging	*7.5*
	Biomechanics	*4.5*
	C++	*7.5*
	Surface and Colloid Chemistry	*4.5*
	Contemporary Sensor Systems	*4.5*
	Bioinformatics-Overview and Practical	*6*
	Applications	*6*
	Industrial Biotechnology	*4.5*
	Leadership	*6*
	Technical Systems and Environment	*4.5*
	Cell Growth and Cell Differentiation	*6*

ENGINEERING BIOLOGY AND THE CDIO INITIATIVE

The CDIO standards are currently mainly implemented in courses and education programs on traditional engineering topics, e.g. mechanics, physics, and others. With a grooving demand of engineering skills within the life sciences, we obviously need to find new approaches of teaching at the bio-technological interface. This of course introduces several challenges, yet also provides new unique opportunities, when implementing the CDIO standards into the program curriculum. In light of successful experiences at the Linköping engineering program in Physics and Electrical Engineering, the board of the Engineering Biology program (270 ECTS credits) took a decision in 2004 to integrate CDIO in a program holistic approach.

INTRODUCTORY COURSE

Accordingly, a first teaching year introductory 6 ECTS credit course was pioneered in 2005 [2], and the course syllabus is found in **Appendix 1**. A major aim of the introductory course is to provide the students with an early opportunity to learn how to master the basics of project work, specifically according to a scalable project model created the educational environment (LIPS [3]) when dealing with an assigned relevant task. A direct transfer of certain projects that may perform well in another engineering education program will of course not always be as rewarding to another group of engineering students. Since the Engineering Biology program students will for instance study cell biology, imaging and programming in higher classes, we hence designed a related project.

Other objectives of the course are to learn formalized project planning/management, administration/documentation, personal communication and oral/written presentation, and an overall responsible contribution as a member of a team. The 2 ECTS credit non-project part of the course consists of lectures regarding the project model, including career example lectures given by alumni students. Other selected topics covered are group dynamics, communication, presentation, and, linguistic and formal aspects of technical documents. The lectures run in parallel with the engagement in the project work, with critical issues often covered in lectures immediately before they become important in the project work.

The early student introduction into project work, accompanied with a deepened insight in the potential future career role of an engineering biologist, will indeed facilitate further adjustments of the program curriculum to meet the requirements of a general integration with the CDIO standards. This work is of high priority and in progress as writing.

The main part (4 ECTS credits) of the introductory course is devoted to a project work. In this paper, we communicate some recent experiences with a novel project task where groups of 6-7 second semester students, with no or very limited previous experience in cell biology or imaging, works as contractors at a pre-clinical department at the Linköping University Hospital. Student groups initially meet a customer that introduces them to some 25 carefully specified technical requirements, and what resources that are available to the group. Students thus enter the present project between tollgates 1 and 2 in the LIPS project model (**Figure 1,** [3]). The LIPS model is then applied throughout the project. Students start-off with a customer-defined task and are given a requirement specification. According to LIPS, the "how to do it" is initially defined in a crude system drawing. The finished product is then the delivery of a working, tested, and applied method that is capable of assaying cellular morphology and subcellular localization of the cytoskeleton in human cells.

THE PROJECT

In brief, the summarized requirements on the product are that it should:

- Allow preservation as well as an extended biological evaluation of human cell samples that are being collected, on request, by the subcontractor "The Clinic" (fictious, **Figure 2**).
- Include a qualified technical and biological protocol for the analysis of cellular morphology and one vaguely specified part of the cellular skeleton, the "cytoskeleton.
- The above with the use of optical methods and cellular imaging. Students are given access to a biomedical laboratory and other facilities, and a high quality fluorescence microscope stand at their disposal (upon request).
- Chemicals and related material are available following ordering from a second subcontractor, "The Chemicals Company" (fictious).
- Image acquisition may be performed with given software, yet all subsequent image analysis must be performed by the use of a stand-alone, free, customizable, scientific imaging software.
- After set-up and optimization, the product should be applied on "patient" samples from The Clinic. The group is asked to support or reject an assumed preliminary diagnosis, and to communicate results to the subcontractor as well as to The Customer.

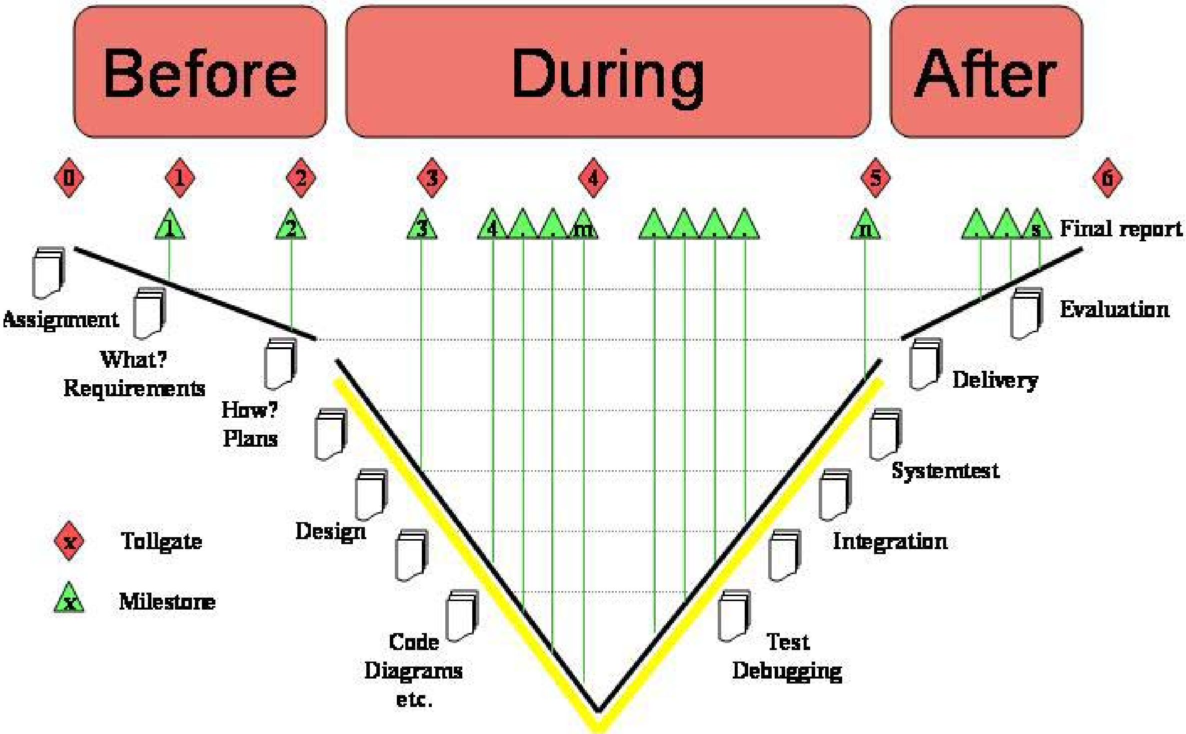

Figure 1: The scalable LIPS project model created by Tomas Svensson and Christian Krysander, Linköping University, Sweden (figure from [3]). It includes the three phases "Before", "During" and "After". The model also includes Word and Excel templates for all formal documents. The project dealt with in this paper start between Tollgate 1 and 2, and end with Tollgate 6. The customer decides on Tollgates 2, 3, 4 and 5.

Each student has 120 hours at her/his disposal to devote to the project work and the working time is carefully regulated in the project model. Because of their limited practical laboratory experience, a senior teacher introduces them to the very basic practical concepts of working in a pre-clinical setting at a real research laboratory specialized in cellular imaging. Obviously, this includes demonstrations on good laboratory practice and serious issues such as safety concerns. Students are also told at the very beginning of the project that safety is always the primary concern, and they are prohibited to work irregular hours or by themselves. A junior teacher (The Supervisor, **Figure 2**) supports the group on a regular basis throughout the project work, and attends weekly group meetings. The Supervisor is not a part of the formal project group organization, and she/he has no official business with The Customer. Yet, for a successful performance of the project, it is vital that The Customer and The Supervisor communicate frequently off the record. Two additional senior teachers are included in the project organization. These are Experts, and they may be consulted for a maximum of 4 hours by the project group.

Initially, the student group must assign an individual responsibility to each member of the group. All communication, including negotiations, with the customer is canalized via a Project Leader. Other obligatory responsibilities are to be in charge of the project documentation, or to manage a subsystem. The current project is divided into three subsystems, all directly and dynamically dependent on each other:

1. **Preparation of biological samples.** This system is both theoretically demanding and hands-on intensive. Common raised questions are: What biological structure is the

product supposed to target? Can this be performed with available resources and the current instrumentation? Can we use specific probes? What are the principles for the detection of probes? What are the limitations? What controls are needed? Where and when?

2. **Microscopy, image acquisition, data handling and export.** The second subsystem is also a mix of hands-on and theoretical challenges. Apart from the above it also introduces further details in questions regarding optics, cell biology and software/programming.
3. **Technological and biological evaluation and feedback systems.** What do we see? How do we quantify data? Artifacts? Do we need to adjust the protocols in subsystem 1? And so on…

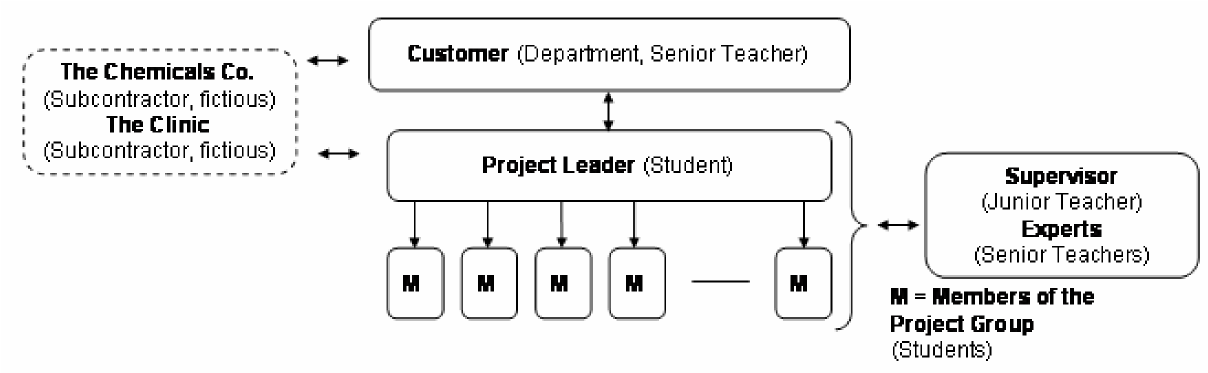

Figure 2: Overview of the project organization. Project group members (M) all have individual responsibilities. The use of fictious subcontractors facilitates experimental planning, and gives teachers some flexibility, i.e. to introduce "unexpected" scenarios.

A major and extremely important feature of the "Before" phase is to identify activities and perform careful planning, including how the resources should be allocated. Before entering the "During" phase, The Customer reviews the detailed plans of the project, summarized in a formal Project Plan (Tollgate 2). It is not until the Project Plan is approved that students are allowed to attack the task with a hands-on approach at the laboratory, i.e., to enter the "During" phase. In the present project we have defined three additional tollgates in the "During" phase in the requirement specification, describing what and when the group must deliver (usually a formal meeting with the customer, starting with a presentation followed by a subsequent discussion). The tollgates are:

- **Project Plan (including Time Plan).** Project week no. 3, Tollgate No. 2.
- **Deliverable No. 1.** Successful pilot test of all individual subsystems (1-3) Project week No. 5, Tollgate No. 3.
- **Deliverable No. 2.** All subsystems (1-3) must be applicable on biological samples. Approval for application on patient samples. Project week No. 7, Tollgate No. 4.
- **Final Deliverable.** The product must meet all 25 specified requirements (unless negotiations have been performed previously). Project week No. 10, Tollgate No. 5.

The application on patient samples is thus a full system test. This way of using pre-defined tollgates has served well in "kick-starting" the project, despite an often encountered state of slight confusion amongst students in the early project weeks. It also provides a convenient opportunity to interact with The Customer that otherwise have to rely solely on formal meeting minutes and the unofficial contacts with The Supervisor.

An additional teacher (that is not a part of the formal project organization) specialized in communication assists during the meeting before Tollgate No. 5, to give constructive criticism on presentations and the technical documentation. When Tollgate No. 5 is passed, the group continues to the "After" phase. This phase includes the important evaluation. Then, the project is closed (Tollgate No. 6).

SELECTED EXPERIENCES AND SPECIFIC CHALLENGES

The project has received good rating from the students in course evaluations and during informal discussions. Frequent comments have emphasized that the general topics covered, and the specific project, are all indeed interesting and relevant to their education and potential career roles. The project is a motivator for further studies on the subject. Many students also tend to appreciate the fact that they work at a real research laboratory (the same equipment is regularly being used by the research staff at the department), and the teachers may also take advantage of this when emphasizing the importance of planning. In addition, we have not observed any apparent differences in the contributions and reflections made by male and female students.

The project is important since it facilitates a growing understanding of that the business is not straightforward. Even though the analytical method may be precise, this does not always mean that the biological relevance of the finding is obvious. The task that students are supposed to solve is complex as is biology itself, and interdisciplinary. It is only natural that most students feel a varying sense of confusion at least at some stage during the project, most commonly experienced during the early project weeks. Perhaps this is best illustrated by the *only* question being raised to The Customer on one particular project start-up meeting, immediately after reviewing of the 25 requirements on the product:

"-Are we going to do this, *for real*?"

The sense of initial "despair" is not necessarily restricted to the scientific task. A logical question for each individual is of course: "-What, *specifically*, am *I* supposed to do within this project?" A detailed project planning is of course the only way to overcome such concerns. In concert, students often state that they have learnt at least some important lessons regarding planning, collaboration, communication and group dynamics.

One view is that the project is "tough at some stages, but rewarding". We have maintained a teaching strategy where The Customer set an initial high standard when reviewing the draft of the Project Plan, by giving plenty of feedback and raising concerns regarding details. Also when the Project Plan is accepted on the first submission, a list of remainders is always appended by The Customer. Negotiations are also continuously declined during the early project weeks. As the project progress, The Customer becomes more reasonable once students have put some real effort into the project. Until this date, all projects have delivered good products on schedule, well within the allocated resources (**Figure 3**).

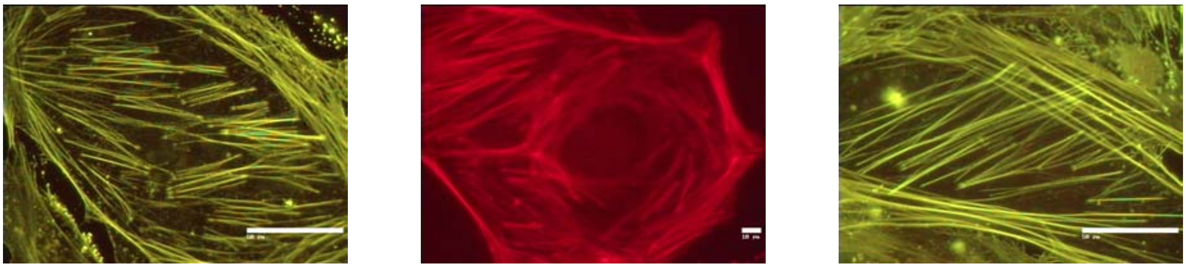

Figure 3: Successful image acquisitions performed by one of the groups during a recent project. Each image is a visualization of the microfilaments in human cartilage cells, obtained by use of three different specific and fluorescent probes. After acquisition, several operations remain, including quantifications.

It is also evident that The Supervisor is of critical importance for a successful outcome of the project. The obvious tasks such as attending at the official group meetings, and performing an active support of the Project Leader, have its fair share of delicate issues. The aim is to support without giving away too much information to the students. Good live improvisational skills are indeed a precious asset in this regard! An equally important role for The Supervisor is to act as the “sensor” in the group. The Customer must also be regularly briefed about the unofficial status of the project. Furthermore, the Experts fill important functions. Students have someone to ask the really tricky questions, and these contacts are somewhat less formal. An additional bonus when fighting for meeting the approaching deadlines is when students realize that not even an expert can answer all questions that are being raised in biology.

But what about if one or several project group member knows too much about the project and how to solve all problems already from the start? This may be the result of attendance in a similar university education, or if the project group has communicated extensively with project groups of the previous year. One potential solution to this would be a creative use of the fictious subcontractors, to introduce the unexpected. For whatever the reason, a certain chemical may become permanently unavailable from the Chemicals Co., or The Clinic may encounter an unfortunate rare sampling error.

This project also provides several opportunities to touch upon ethical concerns. These may range from being critical to literature and software sources, to the ethics in communicating results that are not properly secured in relevant controls, inappropriate image manipulations and handling of patient data.

All teachers involved in the project must understand and apply the LIPS model. Another concern is that you must suppress a common instinct and rather ask questions than give answers. Other challenges with this specific project are that it is time-consuming for the involved teachers, and you can never leave students alone at a biomedical laboratory because of safety issues. In addition, you need access to suitable cellular imaging equipment, i.e. at least one good fluorescence microscope with a digital camera. Furthermore, most chemicals and consumables are relatively expensive, fluorescent probes and cell-culture perhaps in particular. The good news is that there are several useable open source code imaging softwares available [4], of which some are being supported by the US National Institute of Health (NIH). Apart from traditional literature sources, e.g. textbooks and databases, some companies also gladly provides students with handbooks on the use of chemicals and probes.

CONCLUSION

The LIPS project model is indeed applicable for teaching also within the non-traditional engineering settings, such as cellular imaging. The transfer to the bio-technological interface presents tedious challenges, but is rewarding for both students and teachers.

ACKNOWLEDGEMENTS

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ABOUT THE AUTHORS

Jonas Wetterö is a cell biologist by training, equipped with a Ph.D. in applied physics (biomaterials). He is specialized in inflammation, biomaterials, and biosensor sciences. *Sofia Pettersson* is a Ph.D. student currently engaged in research concerning tissue engineering. Her basic training was within the Linköping Engineering Biology program. *Kajsa Holmgren Peterson* is a senior university lecturer specialized in cellular imaging, celiac disease and related disorders. She has a M.Sc. in physics and electrical engineering, as well as a Ph.D. in medical microbiology (cellular imaging).

REFERENCES

[1] http://www.liu.se/education/ug/TCTBI

[2] Kindgren A, Järrendahl K, Uvdal K, Tengvall. CDIO based course in Engineering Biology. 1st Annual CDIO Conference; 2005; Queen's University, Kingston, Ontario, Canada; 2005.
[3] Svensson T, Krysander C. Introduction to Lips. http://www.liu.se/cul/resurser/lips?l=en
[4] Escott EJ, Rubinstein D. Free DICOM image viewing and processing software for your desktop computer: what's available and what it can do for you. Radiographics 2003;23(5):1341-57.
[5) www.cdio.org

APPENDIX 1 – COURSE SYLLABUS

studiehandboken@lith

Linköping Institute of Technology | Search

Valid for
year : **2006**

TFYY98 **Engineering project for Engineering Biology, 6 ECTS credits.**
/Ingenjörsprojekt för teknisk biologi/

For: TB

Prel. scheduled hours: 32
Rec. self-study hours: 128

Area of Education: Technology
Subject: Others

Advancement level: B

Aim:
Learning objectives: - Relate basic concepts in physics and electronics to engineering work. - Develop an understanding of what engineering is all about and how the work is performed. - Administration, planning, communication, documentation, and presentation of project work. - Contribute as a member of a team.

Prerequisites:

Organisation:
Organisation: lectures and project work

Course contents:
Lectures - Introductory lecture, CDIO, project descriptions, situating the engineering profession, Group dynamics when working together, Model for project work at LiTH, Communication. Industry related guest lectures. The engineers role as a communicator. Analysis of and adaptation to receivers. Written presentation. Linguistic and formal aspects of technical documents: instructions, reports and descriptions. How to prepare and execute an oral presentation. Project work - The projects are aimed at presenting the engineering working situation and in addition give the students training in team work and communication. The project work is performed in groups of 5-6 students. Each project takes 2-3 groups. The groups are put together by the course management, which also assigns a project to each group. -All projects are described in brief on the course homepage. The person responsible for the project presents a more detailed introduction during the first meeting with the students. During the work the students have a given maximum time for supervision. In addition, some help to use information search tools will be provided. - The projects have in common that they follow the Model for project work at LiTH, which is introduced during the lectures and also presented in a compendium. Also the examination follows a common pattern for all groups and projects. -The project work should be documented during the work, and at the end presented in the form of a demonstration and a written report. Both the demonstration and the report is a part of the examination.

Course literature:
Compendia in Model for Project work at LiTH. Each project is described in a short report, which contains a list of relevant reference literature.

Examination:

UPG1	Active participation at lectures, exercises and conference.	1 p.
UPG2	Project work	3 p.

To pass UPG1 attendens to a minimum of 75% of the lectures and to the project conference is required. Grades are given as 'Fail' or 'Pass'.