

Hochschule für Angewandte Wissenschaften Hamburg

Hamburg University of Applied Sciences

# Faculty of Life Sciences

# **Book of Modules**

Degree Programme Pharmaceutical Biotechnology



# Hochschule für Angewandte Wissenschaften Hamburg Hamburg University of Applied Sciences

# **Book of Modules**

# M.Sc. Pharmaceutical Biotechnology

(Examination regulations for first year students from WS 2015/16)

# Faculty of Life Sciences Department of Biotechnology

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#### Aims of the degree programme

The master degree programme Pharmaceutical Biotechnology is a consecutive course of studies, building upon a bachelor degree programme in biotechnology. Aim is a stronger weighting on pharmaceutical products and processes considering the demands of the industry, especially in production and development, to the qualification of the graduates. A broader qualification of graduates of the bachelor course occurs with focus on processes in the pharmaceutical industry whereat the production of active substances by biotechnological processes is central. Great importance attaches to the determination of new active pharmaceutical ingredients as well as pharmacologic aspects; this is in particular the examination of biological activity and the quality control.

The master degree programme should enable for independent identification of possible scopes of duties in a working sphere of the pharmaceutical industry. Problems of different complexity in the everyday working sphere should be recognised and be separated proactively in subtasks, the subtasks distributed in a team and the realisation be controlled. Results of divided duties are brought together and should be interpreted as a whole.

The final degree Master of Science (M.Sc.) leads, after a duration of 1.5 years, to an internationally recognized qualification. Graduates will be able to independently open up new fields of knowledge and to solve complicated problems with scientific methods, also beyond actual borders of knowledge. The provided competences will allow graduates to attain authorisation to a doctorate at German and international colleges and universities.

In the module "Biopharmaceutical of engineering" students will be enabled to understand and to design bioprocesses and to recognise or to estimate complicated circumstances in integrated bioprocesses as well as to develop independently new bioprocesses. The modules "bioprocess of automation" and "process of simulation" provide knowledge of the automation- and technical-based functions of a bioreactor. In these modules, students will learn how to identify model parameters. The students will be enabled to independently analyse bioprocesses and to simulate process guidance strategies with the aim of computer programs.

The modules "Pharmaceutical Technology", "Purification Techniques", "Cell Culture of system" and "Bioanalytics" are provided, following the usual sequence during development of a new active ingredient in the pharmaceutical industry. The students will be enabled to recognise the connections of identification, production and administration of active substances. They know about the meaning of pharmacological parameters and are familiar with quality control and quality assurance of developed products. In practice, they can pronounce recommendations suited for use, realise these recommendations in a team on their own responsibility and indicate developments or improvements in a self-contained way.

The deepening of various key competences is aimed in the module "Biopharmaceutical Research", but also in different lectures. Contributions of students are introduced in lectures individually or as a group and are discussed in the plenary. In addition, project results are reported from research projects that way. In the Research seminar, the atmosphere of a research institution is practiced.

#### **Relation to practice**

If in the preceding study programme no suitable internship was included, such an activity of 20 weeks will be added to the study programme as a so-called practise semester. It is intended to advance these students systematically to common engineer's activities. Besides, students should got aware of the different aspects of the operational decision-making processes and gain a detailed insight into natural scientific, technical, organizational, economic and social interactions of a company. The representative for internships and other placements of the department supports searching for a suitable training place. In addition, the faculty accompanies the training period; every professor can supervise students during their placement. The students may contact these professors any time and will get advice about their settings of tasks and problems, if necessary.

#### Research

The master degree programme is closely interlocked with practically oriented research in the Department Biotechnology. For students, it will offer an insight into up-to-date problems of a modern biotechnology. Seven professors in the Department Biotechnology are involved in two research groups; Prof. Scherer is one of the speakers of the Research Group "Hamburg Biomass Utilization", the Profs. Luttmann (speaker), Andrä, Anspach, Cornelissen, Elsholz and Ullrich, show common research activities in the Research Centre "Bioprocess Engineering and Analytical Techniques". The Master Thesis can be conducted at the university in these research groups and in other working groups. In addition, research is pursued in lab projects (Laboatory Projects). Results of this research continuously flow into the lectures.

#### **Master Thesis**

The master thesis is a theoretical, empiric or experimental investigation with written elaboration. The students should show that they are able to work independently on a problem utilizing scientific methods and knowledge within a given term of half a year. For the successfully completed Master Thesis the students earn 30 CP.

# **Study Overview**

### Start at winter term

|                                  | Biopharmaceutical Engineering Purification Techniques Pharmaceutical Technology Cell Culture Systems Biopharmaceutical Research | 1. Semester |
|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------|-------------|
| 1⁵⁺ Academic year                | Bioanalytics Bioprocess Automation Process Simulation Biopharmaceutical Research                                                | 2. Semester |
| 2 <sup>nd</sup> Academic<br>year | Master Thesis over 26 weeks                                                                                                     | 3. Semester |

#### Start at summer term

| mic year                         | Bioanalytics<br>Bioprocess Automation<br>Process Simulation<br>Biopharmaceutical Research                                       | 1. Semester |
|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------|-------------|
| 1st Academic year                | Biopharmaceutical Engineering Purification Techniques Pharmaceutical Technology Cell Culture Systems Biopharmaceutical Research | 2. Semester |
| 2 <sup>nd</sup> Academic<br>year | Master Thesis over 26 weeks                                                                                                     | 3. Semester |

#### **Module descriptions**

| Master degree programme Pharmaceutical Biotechnology |                                                                                                                                                              |  |
|------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| Module number 1                                      | 1 Biopharmaceutical Engineering                                                                                                                              |  |
| Module coordination/ Person responsible for module   | Prof. Dr. Gesine Cornelissen                                                                                                                                 |  |
| Lecturer(s)                                          | Prof. Dr. Gesine Cornelissen, assistant lecturer                                                                                                             |  |
| Term / Period / Cycle                                | 1 <sup>st</sup> or 2 <sup>nd</sup> term / 1 semester / winter term                                                                                           |  |
| Credits                                              | 6 CP                                                                                                                                                         |  |
| Workload                                             | 180 h: presence 64 h (4 SWS), self-study 116 h                                                                                                               |  |
| Status                                               | Compulsory module                                                                                                                                            |  |
| Attendance conditions/<br>Precognitions              | Corresponding knowledge from professionally associated academic studies with bachelor degree, particularly with regard to cultivation techniques are assumed |  |
| Language                                             | English                                                                                                                                                      |  |

#### **Educational objectives**

#### **Professional and methodical competences**

The students have the ability ...

- to independently address themselves to application-oriented problems after preliminary fundamental lecture contents were imparted, to find approaches and to present them coherently and critically to an audience.
- to understand and conceive biochemical processes for production of recombinant products.
- to reproducibly analyse and characterize these by means of process balances and mathematical operations.
- to perceive and evaluate complex circumstances of integrated processes.
- to independently develop and evaluate experiments of a specific process on the basis of a prevailing solution approach and with the help of present publications or reviews and to present conclusions to an audience.

#### Social and self-competence

The students have the ability ...

- to employ methods and mathematical tools and to use them.
- to generally describe, study and analyse processes which are novel to them.
- to conceive biochemical processes, to divide these processes in sections after evaluating them by technical means and finally characterising them by numerical data processing.
- to address themselves in a team to a confronted field of activity, distribute tasks among each other and to make an agreement about contents after consulting the lecturer.
- to be in the position to frame their own statement for a specific approach and to complete the argument with additional, objective relevant facts.

#### **Contents**

- bioprocesses with different host systems for the production of pharmaceutical products (intra and extra cellular)
- Balancing and analysis of bioreaction processes
- Integrated bioprocess technology
- Optimization of biochemical processes (Design of Experiments)

- Biopharmaceutical Engineering, 100% of module score
- Biopharmaceutical Engineering Practice

| Teaching methods/ Forms of teaching media | Presentation of pharmaceutical processes and their technical assembly with PowerPoint and attendant lecture notes                                                                                                                             |
|-------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                           | Derivation of mathematical backgrounds on the black board                                                                                                                                                                                     |
|                                           | Summary of results in work sheets                                                                                                                                                                                                             |
|                                           | The practical transfer in terms of case studies of real processes is carried out in a separately practice with the help of provided experimental data. Thereby processed problems will be finished as homework and then eventually rectified. |
| Course achievements and performances      | Pharmaceutical Biochemical Engineering lecture and practice: one controlled written examination with performance record                                                                                                                       |
| Literature/ Teaching aids                 | /1/ G. Cornelissen: Lecture notes Pharmaceutical Biochemical Engineering                                                                                                                                                                      |
|                                           | /2/ G. Gellissen: Production of Recombinant Proteins. Novel Microbial and Eukaryotic Expression Systems, 2004.                                                                                                                                |
|                                           | /3/ L. Eriksson: Design of Experiments. Umetrics Academy, Sweden, 2008.                                                                                                                                                                       |
|                                           | /4/ Stannbury and Whitaker: Principles of Fermentation Technology, Pergamon Press, 1986                                                                                                                                                       |
|                                           | /5/ P. M. Doran: Bioprocess Engineering Principles. Academic Press, London<br>New York, 2007                                                                                                                                                  |
|                                           | /6/ B. Kristiansen: Integrated Design of a Fermentation Plant, VCH, 1994                                                                                                                                                                      |
|                                           | /7/ Shuler and Kargi: Bioprocess Engineering, Prentice-Hall International Editions, 1992                                                                                                                                                      |
|                                           | /8/ PowerPoint presentations on E-Learning platform EMIL, including exercises                                                                                                                                                                 |
|                                           |                                                                                                                                                                                                                                               |

| Module number 2                                    | Purification Techniques                                                                                                                                                       |
|----------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Module coordination/ Person responsible for module | Prof. Dr. Birger Anspach                                                                                                                                                      |
| Lecturer(s)                                        | Prof. Dr. Birger Anspach, Prof. Dr. Ernst Sanders                                                                                                                             |
| Term / Period / Cycle                              | 1 <sup>st</sup> or 2 <sup>nd</sup> term / 1 semester / winter term, practical course during semester break                                                                    |
| Credits                                            | 8 CP                                                                                                                                                                          |
| Workload                                           | 240 h: presence 80 h (5 SWS), self-study 160 h                                                                                                                                |
| Status                                             | Compulsory module                                                                                                                                                             |
| Attendance conditions/<br>Precognitions            | Corresponding knowledge from professionally associated academic studies with bachelor degree, particularly with regard to cultivation and purification techniques are assumed |
| Language                                           | English                                                                                                                                                                       |

#### **Professional and methodical competences**

The students have the ability ...

- to perceive and evaluate complex circumstances of integrated processes.
- to independently develop and evaluate experiments of a specific process on the basis of a prevailing solution approach and with the help of present publications or reviews and to present conclusions to an audience.
- to understand the unique aspects of biopharmaceutical production in view of qualification of human resources, requirements to the production facility and process safety.

#### Social and self-competence

The students have the ability ...

- to address themselves in a team to a confronted field of activity, distribute tasks among each other and to make an agreement about contents after consulting the lecturers.
- to be in the position to frame their own statement for a specific approach and to complete the argument with additional, objective relevant facts.
- to interpret the EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use and to orientate own tasks towards these regulative guidelines.
- to assume responsibility in a pharmaceutical facility.

#### Contents

- Overview about common downstream unit operations
- Integrated processes: Aqueous 2-Phase-Partitioning, Expanded Bed Adsorption, Extractive Fermentation, Big Beads, Affinity Membranes, Magnetic Beads, Plasmid DNA Purification, Pervaporation
- Quality management for the production of pharmaceuticals: human resources, operation, facility, documentation, quality safety
- Overview about important regularities: national, EU, USA/FDA, WHO

- Purification Techniques, 100% of module score
- Purification Techniques Special Course
- Good Manufacturing Practice

| Presentation of downstream as well as pharmaceutical processes and their technical organisation.                                                                          |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Lectures on E-learning platform EMIL for self-study in case of missing knowledge in downstream processes of Bioproducts.                                                  |
| The students have to independently elaborate sub problems and present them by use of work sheets.                                                                         |
| Independent elaboration of chapters, i.e. of a site master file, as well as summaries in a group of two or individually about special problems.                           |
| Integrated Purification Techniques: written examination with separation problems to be solved and specific questions                                                      |
| IPT Special Course: participation certificate (course achievement)                                                                                                        |
| Good Manufacturing Practice: Case studies                                                                                                                                 |
| /9/ Anspach: Lecture notes about all presentations as PDF                                                                                                                 |
| /10/Presentations on E-Learning platform EMIL, including exercises                                                                                                        |
| /11/Various sorted literature regarding specific problems as PDF                                                                                                          |
| /12/European Commission: EU Guidelines to Good Manufacturing Practice -<br>Medicinal Products for Human and Veterinary Use. 2005 and later                                |
| /13/ PIC/S Secretariat (Eds.): Explanatory Notes for Industry on the Preparation of a Site Master File. 2004                                                              |
| of a site Master File. 2004                                                                                                                                               |
| /14/U.S. Department of Health and Human Services: Guidance for Industry. Sterile Drug Products Produced by Aseptic Processing - Current Good Manufacturing Practice. 2004 |
| t L k T k I s                                                                                                                                                             |

| Module number 3                                    | Pharmaceutical Technology                                                                   |
|----------------------------------------------------|---------------------------------------------------------------------------------------------|
| Module coordination/ Person responsible for module | Prof. Dr. Birger Anspach                                                                    |
| Lecturer(s)                                        | Prof. Dr. Birger Anspach, Prof. Dr. Claus Wacker                                            |
| Term / Period / Cycle                              | 1 <sup>st</sup> or 2 <sup>nd</sup> term / 1 semester / winter term                          |
| Credits                                            | 6 CP                                                                                        |
| Workload                                           | 180 h: presence 64 h (4 SWS), self-study 116 h                                              |
| Status                                             | Compulsory module                                                                           |
| Attendance conditions/<br>Precognitions            | Appropriate knowledge from a professionally associated study programme with Bachelor degree |
| Language                                           | English                                                                                     |

#### **Professional and methodical competences**

The students have the ability ...

- to address themselves towards problems related to applied tasks after being introduced to a topic through basic lecture contents.
- to evaluate solution approaches and to present a critical and comprehensive conclusion in front of an audience.

#### Social and self-competence

The students have the ability ...

- to address themselves to a setting of tasks in a team of students as well as to subdivide tasks and to make arrangements about task contents between students, thereby consulting the lecturer.
- to formulate a statement on their own about a specific approach and to add relevant facts to the arguments.

#### **Contents**

- Biologicals / Drugs / Drug Discovery, Drug Development, Clearance and Metabolism, Protein and Peptide Stability, Preformulation, Formulation, Drug Vehicles, Drug Conjugates
- Pharmacokinetics, Pharmacodynamics, Toxicity Studies, Preclinical Studies, Clinical Trials

- Pharmacology, 50% of module score
- Drug Development & Formulation, 50% of module score

| Teaching methods/ Forms of teaching media | Powerpoint presentations (also students to special topics) If possible, lectures are included from staff of pharmacy companies or excursions are organised to facilities |
|-------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Course achievements and performances      | Drug Development & Formulation: controlled written examination (Klausur) with performance record about case studies und problems                                         |
|                                           | Pharmacology: controlled written examination (Klausur) with performance record                                                                                           |
| Literature/ Teaching aids                 | Anspach: Print-outs and PDFs of all presentations of the lecture                                                                                                         |
|                                           | E-Learning platform Moodle with all presentation from lecturers and students, including exercises                                                                        |
|                                           | Different specialised literature and publications as PDF for introduction in special themes and problems                                                                 |

| Module number 4                                    | Cell Culture Systems                                                                                                                |
|----------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|
| Module coordination/ Person responsible for module | Prof. Dr. Oliver Ullrich                                                                                                            |
| Lecturer(s)                                        | Prof. Dr. Oliver Ullrich                                                                                                            |
| Term / Period / Cycle                              | 1 <sup>st</sup> or 2 <sup>nd</sup> term / 1 semester / summer term, practical course during semester break of summer or winter term |
| Credits                                            | 10                                                                                                                                  |
| Workload                                           | 300 h: presence 112 h (7 SWS), self-study 188 h                                                                                     |
| Status                                             | Compulsory module                                                                                                                   |
| Attendance conditions/<br>Precognitions            | Lecture Cell Culture Techniques is obligatory for attendance of Cell Culture<br>Techniques Special Course                           |
| Language                                           | English                                                                                                                             |

#### **Professional and methodical competences**

Students have the ability to....

- understand the structure and function of eukaryotic cells at the levels of macromolecules and cell organelles. They know the significance of cell culture techniques for applications like protein expression, tissue engineering, primary cell culture, stem cell culture and cell-based bioassays (lecture Cell Culture Techniques).
- cultivate and subcultivate isolated cells under sterile conditions. They have the knowledge to select and use
  appropriate cell types for very different biotechnological applications. Students know sources of information
  for media and growth conditions in order to expand cells and keeping their cellular characteristics unchanged
  (Cell Culture Techniques Special Course).
- understand the large variety of prokaryotic and especially eukaryotic expression systems and how to make use of them. They can define the characteristics of various cell types and their corresponding vectors as well as strategies for cloning and expression (lecture Hosts and Expression Systems).

#### Social and self-competence

Students have the ability to....

- achieve educational objectives by teamwork as well as independently.
- acquire the knowledge by creative learning / time management and to cope with stress.
- work team-oriented and based on the division of labour as well as presenting and documenting the data scientifically.

#### Contents

Lecture Cell Culture Techniques: **introduction to cell biology**: structure and cellular components of pro- and eukaryotic cells; microscopic methods; biosynthesis and transport of secretory proteins; cell motility and shape: microfilaments, microtubules and intermediate filaments; integration of cells in tissues; **cell culture methods**: design and equipment of a cell culture laboratory, cell culture containers, sterile techniques, contaminations, media and supplements, cultivation of cells, tissue and organ culture; **applications**: tissue engineering (cell therapy, tissue constructs, organ modules, stem cells, perfusion culture, quality control); mass cultivation in bioreactors for production of therapeutic and diagnostic proteins; transgenic animals and gene pharming; production of monoclonal antibodies; methods for isolation specific cell types; plant cell culture

Cell Culture Techniques Special Course: **baculovirus expression system**: propagation, infection and harvest of Sf9 cells; colorimetric Trypan blue viability test; sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and western blot analysis to determine the expression rate; **transfection of CHO cells with His**<sub>6</sub>-**GFP-Rab11**: estimation of the transfection rate using the fluorescence microscope; **immunofluorescence analysis of organelles in mammalian cells**: seeding CHO cells; immunofluorescence analysis using organelle specific antibodies; effects of cytoskeleton binding drugs like nocodazole and taxol; **primary culture of cardiomyocytes:** preparation of heart tissue; mechanical dissociation and by trypsin; seeding and microscopic analysis of primary cells; **toxicity test using animal cell culture replacing animal tests:** testing dilution series of toxic reagents for determining cytotoxicity using

#### neutral red uptake assay

Lecture Hosts and Expression Systems: pros and cons of existing expression systems; comparison of costs, product yields and appropriate posttranslational modifications; selected examples taking in consideration vectors as well as strategies for cloning and expression: e.g. bacteria Escherichia coli, yeast Pichia pastoris, insect cells Spodoptera frugiperda and baculovirus, mammalian Chinese Hamster Ovary (CHO) cells, hybridoma cells, plant cells

- Cell Culture Techniques, 100% of module score
- Cell Culture Techniques Special Course
- Hosts and Expression Systems

| Teaching methods/ Forms of teaching media | Seminaristic lectures with beamer presentation or using overhead projector; lecture scripts; practical course in groups of two students, script                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Course achievements and performances      | CCT lecture: written examination with performance record CCT practical course: final report HES: Seminar paper including presentation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Literature/ Teaching aids                 | Lectures Cell Culture Techniques and Hosts and Expression Systems: "Molecular Cell Biology", Harvey Lodish, Arnold Berk, Chris A. Kaiser, Monty Krieger, Matthew P. Scott, Anthony Bretscher, 6 <sup>th</sup> ed., 2007, Verlag Palgrave Macmillan "Zell- und Gewebekultur", Toni Lindl, Gerhard Gstraunthaler, 6th ed. 2008, Spektrum Akademischer Verlag, Heidelberg "Culture of Animal Cells", R. Ian Freshney. 5 <sup>th</sup> ed. 2005, Wiley & Sons "Tissue Engineering: Essentials for Daily Laboratory Work: From Cell Biology to Artificial Organs", W. W. Minuth, R. Strehl, K. Schumacher, 1. ed. 2005, Wiley-VCH "Gentechnik. Biotechnik", T. Dingermann, 1999, Wissenschaftliche Verlagsgesellschaft Cell Culture Techniques Special Course: Script for practical course |

| Module number 5                                    | Bioanalytics                                                                                             |
|----------------------------------------------------|----------------------------------------------------------------------------------------------------------|
| Module coordination/ Person responsible for module | Prof. Dr. Jörg Andrä                                                                                     |
| Lecturer(s)                                        | Prof. Dr. Jörg Andrä, Prof. Dr. Olaf Elsholz                                                             |
| Term / Period / Cycle                              | 1 <sup>st</sup> or 2 <sup>nd</sup> term / 1 semester / summer term                                       |
| Credits                                            | 9 CP                                                                                                     |
| Workload                                           | 270 h: presence 72 h (6 SWS), self-study 198 h                                                           |
| Status                                             | Compulsory module                                                                                        |
| Attendance conditions/<br>Precognitions            | The successful completion of a module in "Instrumental Analysis" in a Bachelor programme is recommended. |
| Language                                           | English                                                                                                  |

#### **Professional and methodical competences**

The students have the ability ...

- to evaluate qualitative and quantitative characteristics of a sample, especially considering accuracy, plausibility and traceability.
- to evaluate and classify analytical problems and to independently elaborate approaches in view of quality assurance.
- to effectively automate wet-chemical analytical methods especially for off-line and at-line analytics as well as to adequately employ chemo- and biosensors.
- to employ biochemical analytical methods for the search about new active pharmaceutical ingredients and to define measuring parameters particularly with regard to quality assurance.
- to introduce bioinformatics as a tool to ascertain proteins and polynucleotides.
- to apply *in vitro* bioassays in the various phases of drug development on a reasonable basis.
- to apply bioassays with special microorganisms to determine drug absorption and availability.
- to differentiate various detections techniques concerning accuracy and sensitivity and to employ these accordingly.
- to evaluate potential targets.
- to differentiate advantages and disadvantages of high throughput screening methods and high content screening methods for drug discovery.

#### Social and self-competence

After successful completion of the module, students will have the ability to evaluate, independently or in a team, a strategy concerning a specific analytic problem. In projects, i.e. the lab project, they are able to distribute work about themselves and to consolidate results in a meaningful manner. They are able to identify meaningful methods in view of a specific analytical problem and to substantiate the significance of the results. The will learn to critically reflect their own results – in view of the data itself as well as the evidence of the method employed – and to defend the conclusion in front of an audience.

#### **Contents**

The module communicates basic knowledge to gain quantitative analytical characteristics of a sample and to substantiate qualitative analytical characteristics as well as special knowledge in view of novel analytical techniques to find and to confirm the biological activity of new drug:

- Analytical characteristics (detection limit, limit of quantification)
- Evaluation of strategies (applications in the field of soil, water, air and bioreactor analytics with special consideration of the sampling technique
- Off-line und at-line analytics as well automation (FIA, dispersion coefficient, comparison of CFA / FIA / SIA, apparatus (pumping systems, injection systems, tubings, manifolds, detectors), application examples of

FIA, SIA, MSFIA)

- Introduction to biostatistics
- Special biochemical analysis techniques (ELISA, sequence and structure analysis, proteomics, mass spectrometry, bioinformatics, molecular interactions)
- Chemo- and biosensors
- Functional assays for the determination of biological activity
- In vitro assays (cell-based and without cells)
- Detection methods (radioactivity, fluorescence, luminescence, label-free detection)
- Atomic force microscopy, nanoscopy
- In vivo Imaging

- Off-line and At-line Analytics, 50% of module score
- Biochemical Analytics, 50% of module score
- Bioassays

| Teaching methods/ Forms of teaching media | Seminaristic lectures, presentations with Powerpoint, short presentations of students, reports and group work about specific problems as well as concepts about new developments, short video sequences                                                                                                                                                                                                                                                                                                           |
|-------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Course achievements and performances      | <ul><li> 2 written examinations (graded)</li><li> Bioassays: seminar paper including presentation (not graded)</li></ul>                                                                                                                                                                                                                                                                                                                                                                                          |
| Literature/ Teaching aids                 | <ul> <li>Current editions of:</li> <li>Harris, Quantitative Chemical Analysis</li> <li>K. Cammann, Instrumentelle Analytik</li> <li>Trojanowicz, Flow Injection Analysis</li> <li>Gey, Instrumentelle Analytik und Bioanalytik</li> <li>Lottspeich/Engels, Bioanalytik</li> <li>Alberts, Molecular Biology of the Cell</li> <li>Choudary, Bioassay Techniques for Drug Development</li> <li>Summaries and work sheets related to the lectures as well as specific method manuals and scientific papers</li> </ul> |

| Module number 6                                    | Bioprocess Automation                                                                                                                                                  |  |
|----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| Module coordination/ Person responsible for module | Prof. DrIng. Reiner Luttmann                                                                                                                                           |  |
| Lectures                                           | Prof. DrIng. Reiner Luttmann, DiplIng. Ulrich Scheffler                                                                                                                |  |
| Term / Period / Cycle                              | 1st or 2nd term, 1 semester, summer term                                                                                                                               |  |
| Credits                                            | 7 CP                                                                                                                                                                   |  |
| Workload                                           | 210 h: presence 80 h (5 SWS), self-study 130 h                                                                                                                         |  |
| Status                                             | Compulsory module                                                                                                                                                      |  |
| Attendance conditions/<br>Precognitions            | Knowledge in Basics of Electrical Engineering Measuring Techniques, Automatic Control, Heat and Mass transfer, Bioreactor and Fermentation Technology are precondition |  |
| Language                                           | English                                                                                                                                                                |  |

#### **Professional and methodical competences**

The students have the ability ...

- to understand basic functions of bioreactors.
- to evaluate classical measurement techniques and extended atline analysis system.
- to describe exclusive functional units and control loops of bioreactors based on energy and mass balances.
- to transform mathematical system approaches in normalized control theory form.
- to benchmark dynamic behavior of bioprocess control loops and to find appropriate control parameters.
- to develop open-loop and closed-loop control procedures for media components and cell physiological parameters.

#### Social and self-competence

The students have the ability ...

- to evaluate the automation functionality of bioreactors and to complete available equipment meaningfully.
- to describe mathematically functionalities of bioreaction processes and to adapt bioreactor control parameters appropriately.
- to scrutinize controlled fed batch processes and to configure the essential instrumental engineering.

#### **Contents**

- Automation structures of bioreactors
- Classical inline- and online-measuring techniques at the bioreactor such as temperature, pH, pO<sub>2</sub>, etc.
- Extended physical and (bio)chemical analysis for atline measurement of cell density, substrates and products
- Commercial available data acquisition- and data processing systems for bioreactors
- System theoretical description of functional units (aeration, agitation, mass transfer, off gas, feed and harvest) as well as exclusive control loops (temperature, pH, pO<sub>2</sub> and level)
- Development of adaptive pO<sub>2</sub>/feed- and pO<sub>2</sub>/agitation control
- Development of control procedures for cell specific growth rate

- Bioprocess Automation
- Bioprocess Automation Special Course

| Teaching methods/ Forms of           | Presentation of practical applications and technical details with                                                                                                                                  |  |
|--------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| teaching media                       | PowerPoint and attendant lecture notes                                                                                                                                                             |  |
|                                      | <ul> <li>Derivation of mathematical background at the panel</li> </ul>                                                                                                                             |  |
|                                      | <ul> <li>Deepening of knowledge with accompanying tutorials and mathematical exercises</li> </ul>                                                                                                  |  |
|                                      | <ul> <li>Experimental work for determination of mass transfer and reaction<br/>parameters as well as for continuous culture level control and<br/>temperature control</li> </ul>                   |  |
|                                      | <ul> <li>Independent preparation of intermediate and final reports of investigated experiments</li> </ul>                                                                                          |  |
| Course achievements and performances | The course will be finished with a controlled written examination with performance record and is accompanied by intermediate check-ups of knowledge.                                               |  |
|                                      | For participation of the special course check-ups of the theoretical background must be completed. A successful attendance is to be demonstrated by protocols and a colloquium in a timely manner. |  |
| Literature/ Teaching aids            | /16/P. F. Stanbury, A. Whitaker and S. J. Hall: Principles of Fermentation<br>Technology, Pergamon Press, Oxford New York, 1999                                                                    |  |
|                                      | /17/K. G. Carr-Brion: Measurement and Control in Bioprocessing, Elsevier<br>Applied Science, London and New York, 1991                                                                             |  |
|                                      | /18/MN. Pons: Bioprocess Monitoring and Control, Hanser Publishers,<br>Munich Viena New York, 1991                                                                                                 |  |
|                                      | /19/G. Stephanopoulos: Chemical Process Control - An Introduction to Theory and Practice, Prentice Hall International Editions, 1984                                                               |  |
|                                      | /20/B. A. Ogunnaike, W. H. Ray: Process Dynamics, Modeling and Control,<br>Oxford University Press, New York Oxford, 1994                                                                          |  |
|                                      | /21/R. Luttmann: Lectures notes Introduction to system theory and control engineering                                                                                                              |  |
|                                      | /22/R. Luttmann: Lectures notes Selective chapters of Bioprocess Automation                                                                                                                        |  |
|                                      | /23/R. Luttmann und U. Scheffler: Theoretical elaboration and experimental guidance for the special course Bioprocess Automation                                                                   |  |

| Module number 7                                                                                                                                                                                                 | Process Simulation                             |  |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|--|
| Module coordination/ Person responsible for module                                                                                                                                                              | Prof. DrIng. Reiner Luttmann                   |  |
| Lectures                                                                                                                                                                                                        | Prof. DrIng. Reiner Luttmann and co-workers    |  |
| Term / Period / Cycle                                                                                                                                                                                           | 1st or 2nd term, 1 semester, summer term       |  |
| Credits                                                                                                                                                                                                         | 7 CP                                           |  |
| Workload                                                                                                                                                                                                        | 210 h: presence 64 h (4 SWS), self-study 146 h |  |
| Status                                                                                                                                                                                                          | Compulsory module                              |  |
| Attendance conditions/ Precognitions  Basic knowledge in Measuring Techniques, Automatic Control, Heat and transfer, Upstream and Downstream Process Engineering, Matrix Algebra solving differential equations |                                                |  |
| Language                                                                                                                                                                                                        | English                                        |  |

#### **Professional and methodical competences**

The students have the ability ...

- to develop mathematical models of dynamical processes in biochemical engineering, based on mass and energy balances, on mass transfer correlations and reaction kinetics approaches.
- to use this models for determination of global process parameters with numerical procedures and least square methods.
- to simulate the dynamic equations using MATLAB.
- to identify unknown parameters by fitting simulation results to experimental data with heuristic optimization procedures.

#### Social and self-competence

The students have the ability ...

- to apply methods and mathematical tools which allow them.
- to simulate and proof mathematical models found in literature.
- to describe own experimental results with given models or
- to change given models for a better description of own problems.
- to design biochemical process strategies and test these ideas with simulation.
- to analyze biochemical processes by use of numerical mathematical tools.

#### Contents

- Description of dynamic processes and system approaches, mass and energy balances, mass transfer and reaction kinetics
- Systems with lumped parameters and distributed parameters
- Linear and non linear systems
- Introduction in MATLAB
- Numerical differentiation and integration
- Stationary and dynamic processes
- Least square and parameter identification
- Applications in Biochemical Engineering
  - growth processes
  - inducible reaction process

- o production of recombinant proteins
- o high cell density process

#### Courses

• Analysis, Modeling and Simulation of Bioprocesses

| <ul> <li>Analysis, Modeling and Simulation of Bioprocesses</li> <li>Analysis, Modeling and Simulation of Bioprocesses</li> </ul> |                                                                                                                                                                                                                                                                                                                                                                              |  |
|----------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| Teaching methods/ Forms of teaching media                                                                                        | <ul> <li>Presentation of technical details, practical applications and mathematical background with PowerPoint and attended lecture notes</li> <li>Derivation of mathematical background at the panel</li> <li>Computer exercises with practical applications of simulation and numerical analysis of real processes were carried out with real experimental data</li> </ul> |  |
| Course achievements and performances                                                                                             | The courses will be finished with one controlled examination with performance record and are accompanied by an intermediate check up of knowledge                                                                                                                                                                                                                            |  |
| Literature/ Teaching aids                                                                                                        | /24/R. Luttmann: Lecture note Analysis, Modeling and Simulation of Bioprocesses /25/R. Luttmann: Lecture note Advanced Biochemical Engineering                                                                                                                                                                                                                               |  |
|                                                                                                                                  | /26/ Mathworks: MATLAB® - The language of Technical Computing. Prentice Hall, New York 1997                                                                                                                                                                                                                                                                                  |  |
|                                                                                                                                  | /27/ G. Lindfield and J. Penny: Numerical Methods Using MATLAB <sup>®</sup> . Elis Horwood, London Toronto, 2000                                                                                                                                                                                                                                                             |  |
|                                                                                                                                  | /28/S Adam: MATLAB® und Mathematik kompetent einsetzen. Wiley-VCH, Weinheim, 2006                                                                                                                                                                                                                                                                                            |  |
|                                                                                                                                  | /29/ J. Kahlert: Simulation technischer Systeme. Vieweg Wiesbaden, 2004                                                                                                                                                                                                                                                                                                      |  |
|                                                                                                                                  | /30/I. J. Dunn, E. Heinzle, J. Ingham, J. E. Prenosil: Biological Reaction<br>Engineering – Dynamic Modelling Fundamentals with Simulation Examples,<br>Wiley-VCH, 2003                                                                                                                                                                                                      |  |
|                                                                                                                                  | /31/Bioreaction Engineering Modeling and Control (Eds. K. Schügerl, K. H. Bellgardt), Springer, Berlin, Heidelberg, New York, 2000                                                                                                                                                                                                                                           |  |
|                                                                                                                                  | /32/P. Arbenz: Kurze Einführung in MATLAB1, Institut für Computational Science, ETH Zürich, November 2005/Januar 2006                                                                                                                                                                                                                                                        |  |
|                                                                                                                                  | http://people.inf.ethz.ch/arbenz/MatlabKurs/matlabintro.pdf                                                                                                                                                                                                                                                                                                                  |  |
|                                                                                                                                  | /33/L. K. Nielsen, R. B. Newell, I. T. Cameron, T. Howes: MATLAB PROGRAMMING, A Primer for the Process Engineer, Department of Chemical Engineering, The University of Queensland, 2001                                                                                                                                                                                      |  |
|                                                                                                                                  | http://www.nt.ntnu.no/users/thz/matlab/Quensland_matlab_tutorial.pdf                                                                                                                                                                                                                                                                                                         |  |
|                                                                                                                                  | /34/ L. Voges: Skript zur Vorlesung/Übung Modellierung von Bioprozessen des<br>Lehrstuhls für Bioprozesstechnik der Otto-von-Guericke-Universität<br>Magdeburg (Fakultät für Verfahrens- und Systemtechnik, Institut für<br>Verfahrenstechnik), 2008                                                                                                                         |  |
|                                                                                                                                  | http://www-ian.math.uni-<br>magdeburg.de/home/risch/NUM2005/Einfuehrung_in_MATLAB.doc                                                                                                                                                                                                                                                                                        |  |

| Module number 8                                    | Biopharmaceutical Research                                                                  |  |
|----------------------------------------------------|---------------------------------------------------------------------------------------------|--|
| Module coordination/ Person responsible for module | Prof. Dr. Gesine Cornelissen                                                                |  |
| Lecterur(s)                                        | All Professors of the department biotechnology                                              |  |
| Term / Period / Cycle                              | 1 <sup>st</sup> or 2 <sup>nd</sup> term / 2 semesters / summer and winter term              |  |
| Credits                                            | 7 CP                                                                                        |  |
| Workload                                           | 210 h                                                                                       |  |
| Status                                             | Compulsory module                                                                           |  |
| Attendance conditions/<br>Precognitions            | Appropriate knowledge from a professionally associated study programme with Bachelor degree |  |
| Language                                           | English                                                                                     |  |

#### **Professional and methodical competences**

Students shall gain theoretical knowledge and experimental experience within central topics of pharmaceutical biotechnology.

Students have the ability to....

- understand even complex tasks in the frame of experimental plants, set-ups, instructions and data and to transfer these information to their own lab project.
- work with literature data bases, to obtain current qualified technical literature, to critically interpret and incorporate additional facts into their own projects.
- to independently plan laboratory experiments inclusively procurement of materials, to accomplish, to interpret and present these experiments.

#### Social and self-competence

Students have the ability to ...

- to handle their projects with responsibility, cost-consciously, and with a high degree of autonomy.
- to contact experts it necessary, to discuss experimental designs and additional technical preparations with colleagues and the project manager and to defend these preparations against critical arguments.

#### Contents

- The contents are dependent on the choice of projects and cannot be named globally.
- Conceivable are tasks related to research programmes and projects in biochemistry, molecular biology, microbiology, biochemical engineering, bioprocess engineering, downstream processing and related fields.

- Lab Project, CP fraction
- Research Seminar

| Teaching methods/ Forms of teaching media | Typically an experimental task is bound to the lab project, which is prepared in any laboratory at the faculty Life Sciences of the HAW Hamburg. The project report is typically completed with technically and project oriented as well as office software. |
|-------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

| Course achievements and performances | The project is completed with a score (oral presentation and/or project report), the seminar by attending at least 80% of the seminar dates offered in one year and a presentation (usually regarding the lab project). |
|--------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Literature/ Teaching aids            | Up to date technical literature                                                                                                                                                                                         |

| Module number 9                                    | Master Thesis                                                                        |  |
|----------------------------------------------------|--------------------------------------------------------------------------------------|--|
| Module coordination/ Person responsible for module | Prof. Dr. Birger Anspach                                                             |  |
| Lecturer(s)                                        | All Professors of the Department Biotechnologie                                      |  |
| Term / Period / Cycle                              | 3 <sup>rd</sup> term / 1 semester / summer or winter term                            |  |
| Credits                                            | 30                                                                                   |  |
| Workload                                           | 900 h                                                                                |  |
| Status                                             | Compulsory module                                                                    |  |
| Attendance conditions/<br>Precognitions            | It must be verified that 45 credit points of the first study year have been reached. |  |
| Language                                           | English                                                                              |  |

#### **Professional and methodical competences**

Students have the ability to....

- analyse and systemise complex engineering and scientific tasks in biotechnology and neighbouring disciplines, based on a deepened methodological expertise as placed in the master programme and also to define their own relevant tasks.
- familiarise themselves with the state of scientific and technical knowledge of a specific task utilizing learnt knowledge as well as national and international technical literature and databases.
- in case of an experimentally orientated task: to familiarise themselves with the scientific and technical basics of the technical requirements of experiments, to elaborate a reasonable programme of succeeding experiments, to accomplish these experiments, to critically appraise the results on the basis of theoretical knowledge, and further to elaborate follow-up tasks.
- in case of a theoretically orientated task: to critically discuss the state of scientific and technical knowledge from literature and to compare with learnt fundamentals, to find conjunctions between similar fields of knowledge, and to elaborate conclusions and directives.
- to complete a task in a preset time frame by means of an efficient problem-oriented workflow, to critically scrutinise the task and to elaborate follow-up tasks.

#### Social and self-competence

Students have the ability to....

- act independently in a team solving a scientific task, thereby organising the team when indicated, and delegating subtasks in case of complex projects.
- guide and coordinate a team working on a specific task, to identify conflicting tasks and to raise a professional solution.
- identify and define relevant interfaces in interdisciplinary projects.
- conclude results of a project in a scientific report and to present these results in front of an audience.

#### Contents

Specific tasks of actual research projects in working groups of the faculty life science or companies working in the field of biotechnology or neighbouring disciplines.

#### Courses

Master- Thesis

| Teaching methods/ Forms of teaching media | Individual discussions between mentoring professor and student by means of reports and experimental results  Discussions in presentations of intermediate or final results |
|-------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Course achievements and performances      | Final report (Master – Thesis) with performance record based on a numerical grading scale                                                                                  |
| Literature/ Teaching aids                 | Necessary teaching aids depend on the research subject.                                                                                                                    |

## Curriculum

| No. | Module                        | Course                                               | SWS |
|-----|-------------------------------|------------------------------------------------------|-----|
| 1   | Biopharmaceutical Engineering | Biopharmaceutical Engineering                        | 2   |
|     |                               | Biopharmaceutical Engineering Practice               | 2   |
| 2   | Purification Techniques       | Purification Techniques                              | 2   |
|     |                               | Purification Techniques - Special Course             | 1   |
|     |                               | Good Manufacturing Practice                          | 2   |
| 3   | Pharmaceutical Technology     | Pharmacology                                         | 2   |
|     |                               | Drug Development and Formulation                     | 2   |
| 4   | Cell Culture Systems          | Cell Culture Techniques                              | 3   |
|     |                               | Cell Culture Techniques - Special Course             | 2   |
|     |                               | Hosts and Expression Systems                         | 2   |
| 5   | Bioanalytics                  | Off-line and At-line Analytics                       | 2   |
|     |                               | Biochemical Analytics                                | 2   |
|     |                               | Bioassays                                            | 2   |
| 6   | Bioprocess Automation         | Bioprocess Automation                                | 2   |
|     |                               | Bioprocess Automation - Special Course               | 3   |
| 7   | Process Simulation            | Analysis, Modelling and Simulation of Bioprocesses   | 2   |
|     |                               | Analysis, Modelling and Simulation of Biopr Practice | 2   |
| 8   | Biopharmaceutical Research    | Laboratory Project                                   | 4   |
|     |                               | Research Seminar                                     | 1   |
| 9   | Master Thesis                 | Master Thesis                                        |     |