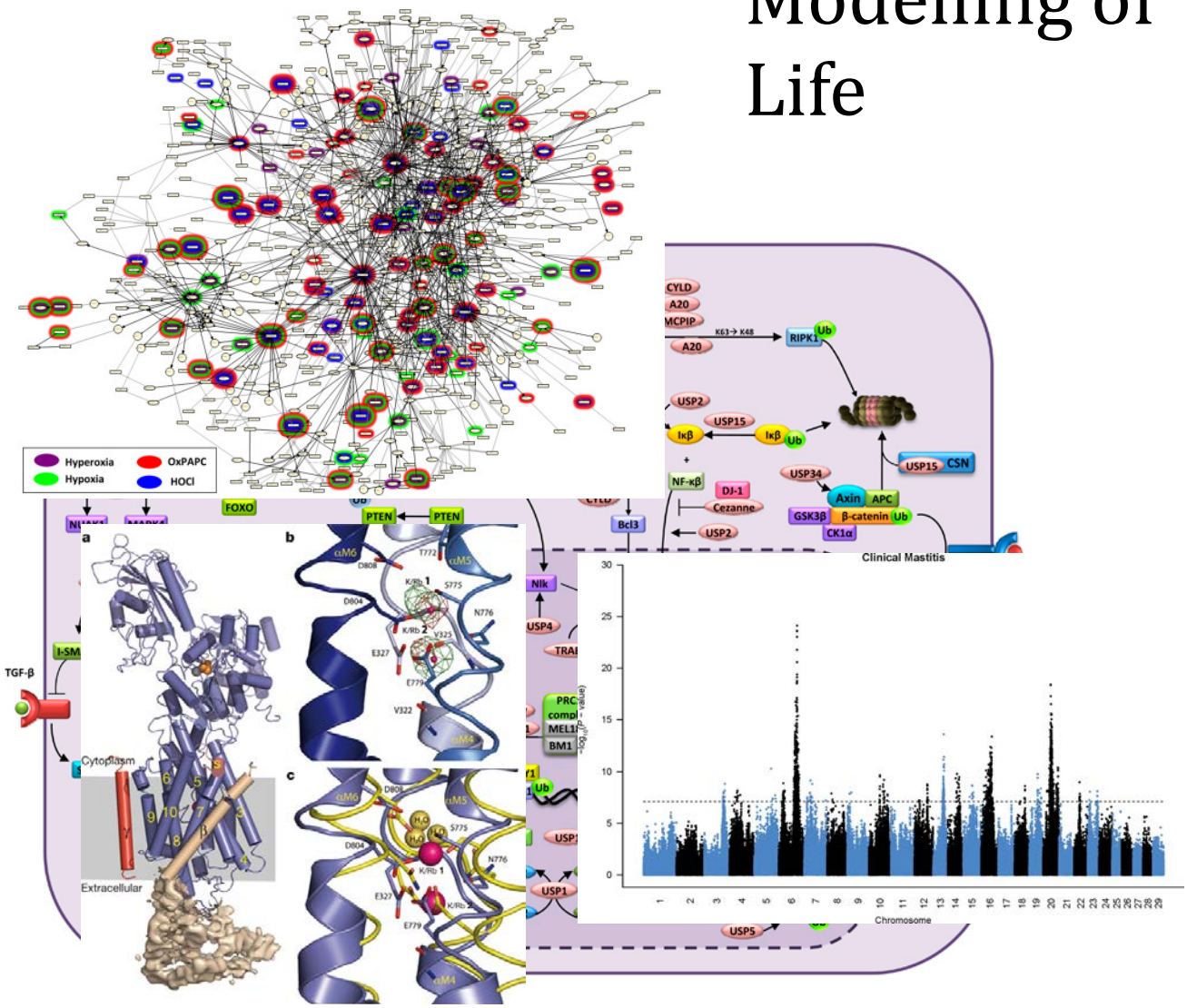
Department of Molecular Biology and Genetics

Strategy 2016-2020

Modelling of Life



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1. Introduction

In 2011, the Department of Molecular Biology and Genetics (MBG) (hereinafter called "the department" or "MBG") was organised in 11 sections, and at that time it was decided to revise the organisational structure after three years. Thus, this spring we initiated a revision of the sections, leading to some modifications of the sections.

The process leading to the proposed strategy was initiated May 2015 by the Departmental Management Group. Each section was asked to fill in a form describing important core values, a SWOT analysis for their section, a strategy for their section and their section's potential contribution to the selected themes. The Public Consultancy and the Business Committees were also asked to provide inputs. Based on the inputs from the sections, the Departmental Management Group had a one-day meeting where they agreed on a vision and mission for the department, the present departmental research strongholds as well as future research themes and focus areas. Following, the sections qualified their contributions to the selected themes and focus areas and the Departmental Management Group met for one day in August 2015 and wrote the first draft of the strategy. In October 2015, co-ordinators for the five themes were appointed and were asked to invite all relevant group leaders to comment on the drafts. Meetings with PhD and undergraduate students were held. The Departmental Management Group met for two days in November and discussed the inputs from the research themes and the students. Finally, the Departmental Management Group met in January and based on the feed-back from the Dean, a final version of the strategy was drafted.

2. Executive summary

The primary focus of this strategy is to outline new research themes, and to align these initiatives with new Master programmes and to thoroughly reorganize existing education programmes.

The future research themes are based on the present strongholds of the department but these strongholds will also be developed as individual disciplines to keep or expand the international competitiveness of these areas.

All of the suggested themes will involve research expertise across the department and we thereby harvest most of the synergy that was outlined for the merger in 2011.

Suggested future research themes:

Modelling of Life (including a new Master programme)
Molecular biology and genetics is in a transition from a focus on single events to studying complex networks. Thus, in many projects ranging from structural and functional biology to quantitative genetics, the handling of large datasets and their mathematical modelling will be increasingly important. A **new Master programme** will educate graduates to cope with these future challenges.

Molecular Medicine (including several Bachelor and Master programmes)
Many groups at MBG already work on aspects of human health and diseases. With this initiative, we will coordinate several of these efforts to lead applications of **external funding** in collaboration with the Faculty of Health. The focus will include a revised education programme with a strong molecular biology footprint and a better integration of aspects from Health.

Molecular Nutrition (including an existing Master programme)
To **match the global challenges** of nutrition, and new opportunities for functional foods and specialised nutrition for well-being, health and disease, we will integrate our present activities and explore new directions.

Centre for Protein Biotechnology *(including a new Master programme)*
The Faculty of Science and Technology (ST) has very strong competences in protein science. We invite to partner our MBG expertise in establishing a centre that will expose the competences of Aarhus University and coordinate contacts to **external funding bodies**. We suggest establishing a **new Master programme** that can educate graduates for new and expanding biotechnological and pharmaceutical markets.

New Breeding Technologies
The breeding of animals and plants to a **global market** requires a high profile research and technology development. By this initiative, we will integrate and expand the present activities to ensure that MBG will be the preferred partner for breeding companies.

3. Mission and Vision

Mission:
Based on a scientific mind-set, the department will offer research-based education and training with focus on: pharma-biotech, food, health & disease, primary production and the environment to meet the challenges of a globalised and knowledge-based society.

The department will carry out excellent basic and strategic research in molecular biology and genetics with increasing emphasis on quantitative biology that will contribute to knowledge-based development in the private and the public sectors both on a short and a long term.

Vision:
To educate independent and highly qualified graduates, PhD's, postdocs and research leaders who will be engaged in the private and public sector and have significant impact on solving important societal challenges.

The department will house at least five basic or strategic research groups belonging to the absolute world elite and create an open and international environment at all levels.

4. Organisation and physical setting

The Department of Molecular Biology and Genetics (MBG) is a large department which houses more than 240 employees, contributing to both research and education within many aspects of molecular biology and genetics. MBG is divided into 12 sections including the EMBL node DANDRITE as an affiliated section (Table 1).

Management: The department is led by a management group consisting of the head of department, the head of secretariat, the 12 section coordinators and the chair of the Research Committee. This organisation ensures a direct link to all employees through the section structure. There are 10 committees at MBG. The chairs of the committees participate in management meetings *ad hoc*, but the chair of the Research Committee is a permanent member of the Management Group since the core tasks of this committee (recruitment and research strategy) are vital to the management of the department.

The department is situated at three different geographical locations: Foulum (by Viborg), Flakkebjerg (by Slagelse) and Aarhus, the latter including staff and students at the following locations: the Science Park, AU campus, iNANO and Biomedicine.

Employee demography (see appendix c for details): At the Department of Molecular Biology and Genetics, there are a total of 85 academic employees (professors, associate professors/senior researchers and assistant professors – tenured and non-tenured), 80 post-doctoral researchers and 118 PhD-students. The technical and administrative personnel comprise 13 administrative staff (academic and non-academic), eight technical academic staff and 55 technical staff (laboratory technicians, cleaning personnel, engineers, greenhouse gardeners).

The age distribution of the academic staff shows a large group above 55 years (32 employees; 38%), but this is balanced by a large group between 35 and 49 years (42 employees; 50%). The female academic staff constitutes a minority (21% of all academics), with the majority being employed at the associate professor level.

Table 1.

Sections and centres at MBG
Centre for Quantitative Genetics and Genomics (**QGG**)
Crop Genetics and Biotechnology (**CGB**)
DANDRITE (EMBL node) (**DAN**)
Genome Stability and Technology (**GST**)
Gene Expression & Gene Medicine (**GEG**)
Molecular Cell and Developmental Biology (**MCD**)
Molecular Genetics and Systems Biology (**MGS**)
Molecular Intervention (**MI**)
Molecular Nutrition (**MN**)
Plant Molecular Biology (**PMB**)
Protein Science (**PS**)
Structural Biology (**SB**)

The age distribution of the technical/administrative staff is quite even, with the exemption of the age category 55 to 59 years which constitutes 31% of all employees in this group. Male employees constitute only 19% of all employees in this group, with the majority being employed as technical staff (22% men in this category).

Education:

The admission grades ("adgangskvotient") are increasing for both *Molecular Biology* and *Molecular Medicine* during 2012 – 2015, and this trend is expected to continue. Around half of the Bachelor students on both educations complete their student within the normal expected time which is very good. However less than 10% complete their Master within the expected time. The same pattern is also observed when comparing the average time spend on the educations. The students exceed with 1.5 and 3.5 month the time set by "fremdriftsreformen 2019" for the Bachelor and Master, respectively.

Remarkably, both study times are within the expected range for 2016 and for the Master a significant decrease has been noted for the last year.

The total number of PhD-students has been reduced by nearly 30% during the years 2011-2015, resulting in a population of 118 in 2015. However, the yearly enrolment of Ph.D.-students shows an overall increasing trend during the years 2011-2015.

Large infrastructure/research platforms:
The department houses three Centres of Excellence funded by the Danish National Research Foundation and act as a partner in two additional Centres of Excellence as well as a Danish-Chinese centre co-funded by the Danish National Research Foundation. MBG houses a large strategic centre funded by the Danish Council for Strategic Research and the EMBL node, DANDRITE which is a joint effort between Department of Molecular Biology and Genetics and the Department of Biomedicine.

5. Employees and culture

The Department of Molecular Biology and Genetics comprises technical, administrative and scientific staff as well as PhD students. The working environment is international, with English being the primary language in all written communication and spoken whenever one or more non-native Danes are present.

The Department of Molecular Biology and Genetics suffers from an uneven gender distribution among the scientific staff, with women constituting only 21%. There are no female professors and only 14 female employed at the associate professor level and four females at the assistant professor level.
A more balanced gender distribution is desirable and achieving this will be of high priority in the coming years. A specific focus will be on the recruitment and career development of women.

The core values listed below have been identified by the Management Group, based on suggestions from all the sections. In contrast to the previous strategy, it was decided to keep it simple and focus on "involvement, communication and collaboration" with the hope that the organisation will take it to heart and act on it.

Core values

- Timely, appropriate, and transparent **involvement** of personnel at all levels in decision processes
- Clear and timely **communication** at all levels
- **Collaboration** and interactions among colleagues based on mutual respect and acknowledgement of the work of others.

6. Overall objective, international position and strongholds (max 2 sider)

The Department of Molecular Biology and Genetics has a strong position in teaching, research, and dissemination of research results to the general public and transfer of knowledge to the industry.

The total publication output by MBG continues to increase, reaching 344 articles and reviews in 2015 with increasingly more citations per publication. Our most recent benchmarking analysis (2012) showed that the output from MBG compares very well to two international high ranking universities (Wageningen and Uppsala) within the three areas "Molecular Biology", "Quantitative and Molecular Genetics" and "Plant Molecular Biology and Crop Genetics" and is well above world average in the parameters analysed. Moreover, the quality of publications (measured by citations and journal impact factor) was increasing. The percentage of papers among the 10% most cited papers in the Web of Science database, for example, was 17% for MBG in total and the Mean Normalized Journal Score (MNJS) is 1,49 meaning that the average "impact factor" of the journals chosen for publication is 1,49 times higher than for the database average. MBG's strong tradition for national and international collaboration is reflected by the fact that 76% and 55% of all publications are the result of national and international collaborations, respectively.

Teaching

The department offers research-based teaching at the undergraduate, graduate and doctoral level in Molecular Biology and Molecular Medicine. Both education programmes attract a large number of students, resulting in a restricted uptake due to "dimensioneringen". This year the threshold grades were 8.8 and 10.9 for Molecular Biology and Molecular Medicine, respectively. On top of these education programmes, the Department of Engineering also offers a Biotechnology education, reaching a total of 210 students who are accepted within biotechnology and molecular biology. Thus, Aarhus University accept more students compared to any other Danish university in that area.

We therefore have no specific interest in intensifying activities towards the student recruitment, but focus should rather be on the quality of the education, progress of the students within the Master programmes and the drop-out rate – especially the relatively low student activity in the Master programmes and on the overall dropout rate in the Bachelor programme of Molecular Medicine.

Research

MBG has five very strong research areas. These "**strongholds"** are described below including important publications from the time period 2010–2015, as well as possibilities for their further development of the strongholds:

Structural Biology

The section for structural biology is a leading community in Northern Europe, and its members are currently engaged in three DG centres, DANDRITE and the MIND neurocentre. An interdisciplinary approach including X-ray crystallography, electron microscopy and small angle X-ray scattering is taken for the characterisation of highly challenging molecular structures of major biological, physiological and biomedical interest. The biological targets include membrane proteins[1-3], giant enzyme complexes[4], ribosomes, viruses and immune system proteins[5]. The section extensively complements its structural analysis with functional biochemical and biophysical experiments. More than 100 people at Aarhus University use the experimental and computational facilities hosted by the section including many researchers at the Department of Biomedicine. The section is a national driving force for establishing state-of-the-art facilities for cryo-EM microscopy at AU and X-ray diffraction at MAX IV in Lund.

Plant Molecular Genetics

Plant molecular genetics at MBG has developed methods and resources in model plants in order to answer fundamental biological questions and establish a foundation for translational research in crops. A consistent effort on genetics and genomic resources in the model legume *Lotus japonicus* has positioned the section as a world leader in plant molecular genetics and in the plant-microbe interaction field. Both the Danish National Research Foundation and ERC have supported the research and promoted interdisciplinary approaches. Biochemistry and structural analysis of proteins and receptor-mediated perception of carbohydrate signal molecules has been developed together with the structural biology section and international/national collaborators in complex carbohydrate chemistry and microbial genetics. New areas of miRNA and phytohormone regulation of plant developmental processes and genome-based analysis of biodiversity have also been established in these projects. More recently, microbiome studies and translational research on white clover and other legume crops have been established and funded by the Danish Council for Independent Research: Technology and Production Sciences (FTP) and the Innovation Fund Denmark. Taking one step further, synthetic biology is employed for the transfer of genes and corresponding traits from legumes into barley and maize in a project funded by and the Bill & Melinda Gates Foundation. The overarching questions addressed in the section are all related to cell differentiation, plant development and plant-microbe interactions.

Quantitative Genetics

The Centre for Quantitative Genetics and Genomics (QGG) has an international leading position in quantitative and statistical genetics applied to animal breeding. The core research addresses the understanding of genetic variation and genetic architecture of complex traits, predicting the genetic potential of individuals and optimisation of breeding programmes and decisions. This requires development and implementation of advanced statistical methods that utilises information from large

complex populations with phenotypes, genome wide genetic markers, whole genome sequence and other OMICS data. The research within QGG is characterised by a very close synergy between method development, basic analyses and application of the developed methods on to practical problems across animal species.
Future developments in the area will include more basic research both in statistical and quantitative genetics. The area has great potential in plant breeding as well as in human genetics. It is the ambition to initiate research and apply models to study the genetic background and be able to predict individual risks of complex human diseases based on genome information.

RNA Biology
Researchers at the Department of Molecular Biology and Genetics at Aarhus University are in the international elite with regard to investigations of the biogenesis, metabolism and regulation of eukaryotic RNA. The topic has been well-funded via the establishment of a Lundbeck centre and a Danish National Research Foundation centre as well as funding from the ERC, Novo Nordisk Foundation, the Danish Cancer Society and all major Danish Research Councils. The research investigates mechanisms that control the biogenesis and turnover of mRNA and non-coding RNA (ncRNA) in the nuclei of both yeast (*S.cerevisiae*) and mammalian (human and mouse) cells[1,2,3]. Moreover, the research uncovers molecular mechanisms occurring in the mammalian cytoplasm to control levels of mRNA/ncRNA as well as microRNA (miRNA)[4,5,6]. Collectively, the aim is to delineate regulatory networks centered around RNA metabolic processes and which causes extensive consequences at the level of cellular transcriptional and translational output. This research has important impact on processes controlling cellular homeostasis, differentiation and disease. Moreover, the results are utilised to develop new RNA-based technologies.

In the future, the department plans to integrate RNA biology into several of its new research themes. RNA biology at the department is largely a quantitative research endeavour and will play a central role in the development of the 'Modelling of Life' action both as a research and as an educational discipline. The many novel ncRNAs discovered in recent years, and which continue to be discovered, promise to change our concept of a 'gene' and dramatically add to the number of functional units within mammalian genomes. Many of these new RNAs, some of which have been discovered by MBG researchers, are linked to disease and already play prominent causal and predictive roles in biomedicine. Moreover, ncRNAs are amply applied as drugs and/or drug vehicles, and thus this research will have a major impact on developing the 'Molecular Medicine' action of MBG. Finally, as RNA and protein often function in complex with each other, RNA biology research will become a major contributor to the 'Protein Research' action. Finally, the department is committed to seek out and support opportunities to position RNA research as an attractive theme for future large funding initiatives. The realisation that genomes of all kingdoms of life are expressing much more RNA than previously thought (80% of the human genome produces RNA and only 2% encode protein!) has made the field of 'non-protein-coding-RNA' extremely attractive as an academic as well as an industrial activity. The latter is mirrored by the fact that major industrial players in Denmark are either actively engaged with, or seriously contemplating to initiate, RNA research and innovation (Chr. Hansen, Novozymes, Roche, Exiqon, Novo Nordisk).

Proteolytic Regulation
Proteolytic enzymes catalyse the hydrolysis of peptide bonds and are involved in most physiological processes, from digestion to blood coagulation. The research area of proteolytic regulation has a long tradition at the Department of Molecular Biology and Genetics, going back to the 1970's, with pioneering primary structure characterisation of proteins in proteolytic enzyme systems in blood coagulation. Also nationally, there is a strong Danish tradition for research on proteolytic regulation. This tradition has been carried on in the department throughout the years. The physiological and pathophysiological

processes, in which the involvement of proteolytic regulation is being studied, are as diverse as cancer, inflammation, growth, autoimmune diseases, and rare hereditary diseases. Methodologically and strategically, the activities involve three-dimensional structure characterisation by X-ray crystal structure analysis, NMR, SAXS, and other biophysical methods; animal disease models; occurrence of proteolytic enzyme systems in different animals, tissues, cells, and in health and disease (proteomics and next generation sequencing); engineering of components of proteolytic enzyme system to produce variants for medical and industrial use; development of principles for pharmacological intervention with pathophysiological functions of proteolytic enzyme systems. The success of the research area is to a large extent based on a multidisciplinary approach, involving not only molecular biologists, but also geneticists, chemists, and physicists. At the department, the research area has been supported by large and prestigious grants, including, in recent years, grants from the Danish national research councils, the Danish Cancer Society, and the Danish National Research Foundation.

The activities on Proteolytic Regulation will also in the future be a strong research area in the department. It will fit naturally into a future Centre for Protein Biotechnology and also strongly support the activities in Molecular Medicine and Quantitative Biology.

7. Analysis of the department's strengths and weaknesses

Research
The research at MBG is characterised by excellent research originating from Centres of Excellence (funded by the Danish National Research Foundation) and large strategic centres, as well as a number of other strong research groups.

Many projects are multidisciplinary and include industrial partners, which provide an opportunity to participate in strategic projects as well.

Structural biology has access to a world-class infrastructure like state-of-the-art X-ray diffraction in Lund and Hamburg, as well as local SAXS, cryo-EM and NMR.

Many funding bodies do not support small and medium-sized equipment; thus our general infrastructure needs to be upgraded.

The department has a strong funding basis from both strategic and basic programmes expecting to reach DKK 170 million this year, however the forthcoming termination of several Centres of Excellences will be a challenge. Most of the funding originates from public calls, and only limited funding is attracted by direct negotiations with large private funding bodies.

Most of the successful scientists at the department have a PhD-age of +10 years, whereas only a few of the early career scientists can compete nationally and internationally. MBG also has a gender challenge with only 18% female tenures and no female professors.

Fixed-cost burdens to the administration and tax on external funding ("inddækning") give a severe competitive disadvantage as compared to other universities in Denmark.

Education
Two strong and attractive Bachelor and Master programmes (Molecular Medicine and Molecular Biology) are affiliated with MBG. However, limited coherence and content progression in certain parts of the educational programmes together with a sub-optimal prioritisation of topic areas in the curriculum have been identified and are being addressed in the ongoing revision process.
A particular weakness is the lack of quantitative biology in the education, but this shortcoming will be met by the launching of a new honours programme in Quantitative Biology (see description on page 14)

The department's substantial external funding has resulted in the recruitment of a large number of PhD students of which more than 60% are non-Danish; however most of these students leave Denmark again and do not contribute to the Danish labour market.
A major concern is the limited research time for PhD students, especially for students recruited based on a Master's degree, as they only have three years available for research of which a substantial time has to be spend on teaching and taking courses to earn ECTS. The recently enforced "dimensionering" of our Master education programmes leaves *de facto* no alternative opportunities for admission to our PhD programmes for foreign and other external students than a three-year PhD.

8. Strategy 2015-2020

a. Research themes 2015-2020

Building on existing research and expertise, the department wants to promote five research themes in the coming years as well as developing our strongholds even further.

Modelling of Life (theme coordinator: Jens Stougaard)

Molecular biology is currently developing from a scientific discipline with a focus on the qualitative, functional description of individual molecules, proteins and genes towards the quantitative characterisation of the molecular interactions, composing complex cellular or subcellular systems that define macroscopic manifestations. The development of advanced analytical methods and high throughput technologies has changed both the scientific approach and the data analyses required for understanding bio-molecular networks in cells, whole organisms and populations. This often requires handling and analysis of large datasets from multiple experimental sources and the integration of disciplines such as genomics, genetics, proteomics, structural biology, bio-imaging, biophysics, developmental biology, biodiversity studies, bioinformatics and mathematical modelling. A major challenge is to analyse, organise and interpret such "big data" through the development of meaningful mathematical/statistical models as foundations for new hypotheses-driven research. In a parallel effort, a number of amenable model organisms have been established by the scientific community in order to enable fast and efficient testing of hypotheses. This combination of quantitative mathematical/statistical models with massive experimental input and validation from the subcellular to the organism and population level will form a cornerstone for molecular biology of the future, perhaps best described as a change from a descriptive to a predictive science.

The Department of Molecular Biology and Genetics is in a prime position to advance molecular biology in this direction with its broad basis of key molecular disciplines and model systems as well as its experience with quantitative data analysis. To accomplish this goal, the department suggests establishing a Master's Honours programme in Molecular Biology with focus Quantitative Biology and supports this new effort by the recruitment of new scientific personnel, and by a network of the relevant research areas at Aarhus University with, for example, seminar series for the exchange of knowledge, key questions and ideas.

Network activities covering *"Modelling of Life*" will be initiated including a monthly seminar series organised by MBG, which will include both local (AU) and invited speakers. Subsequent network meetings will be organised for the proper and efficient exchange of knowledge. The aim is to integrate all different aspects of quantitative biology wherever relevant, and prepare the department, local collaborations and students for these obvious new challenges ahead.

Molecular Medicine (theme coordinator: Claus Oxvig))

General background: Since the department was founded, research areas of molecular biology with a direct relevance to human disease have been prioritised. It has always been important for MBG to contribute with knowledge that allows a detailed understanding at the molecular level of human disease, although the potential has not been fully exploited. In addition to the benefit of numerous researchers at AU, many methodologies have been developed or first implemented at the department throughout more than three decades.

Education: To meet the increasing demand for people highly educated in the field of molecular medicine, two highly competitive undergraduate (Bachelor and Master) programmes were established in 2007 in collaboration with the Health Faculty.

The Bachelor and Master programmes are now anchored at ST and are currently undergoing revision in close collaboration with Health. The aim is to further integrate specific elements of several courses, and to ensure that complex experimental thinking is stimulated at an early level. New courses, which draw on resources from several different departments, are being developed. In addition, the plan is to further emphasise teaching in bioinformatics at the Bachelor level.

In addition, ST and HE offer a mutual PhD programme in molecular medicine.

Research status and future plans: The development of novel diagnostic, prognostic and predictive methods, including non-invasive imaging or agents suitable for clinical intervention, requires multiple steps. Initial steps focus on understanding pathological mechanisms by describing dysregulated pathways or providing specific molecular details responsible for a given pathological condition. While research groups at MBG traditionally have focused on such early steps, a much broader approach can be taken, aiming at connecting basic biology and mechanistic insight with clinical usefulness. This will not only be to the benefit of society, but is also a fundamental change in research approach which is in agreement with demands of funding agencies of demonstrating the *in vivo* relevance of basic science.

It is important for MBG's research groups to provide novel details of molecular mechanisms relevant to normal and pathological physiology. Many approaches are applied to obtain this information, such as bioinformatics, genetics, proteomics, and protein chemistry. Once a relevant biological target has been identified, novel drug candidates can be suggested by means of structural biology or screening of biological libraries, and prototype drugs can be engineered. Finally, we have started to use relevant animal models of human disease to document preclinical relevance. For the future, we will further strengthen this "pipeline" with the aim of 1) allowing many researchers to drive their projects closer to the clinic, and 2) to bring selected candidate drugs to the level of phase I clinical trial. In this regard, the ability to produce and analyse sufficient quantities of recombinant therapeutic grade protein is obvious and will be facilitated by the establishment of the proposed Centre for Protein Biotechnology, which will be located at AU.

By strengthening our expertise in selected areas, collaboration within MBG will be promoted, and MBG will become an even more attractive collaborative partner for both academic groups and the pharmaceutical industry. We see a large unexploited potential for closer and formalised collaboration with academic research groups outside MBG, in particular groups at Health, potentially aiming at the formation of larger research centres. To promote the latter, we will establish a task force with the aim of initiating a dialogue with relevant research groups.

We have defined four research themes, which all represent both challenges and opportunities

1. Predictive medicine

The systematic use of large datasets generated through rapid advances in large-scale phenotype recording systems (e.g. medical measuring devices, gadgets, wearables), as well as in nucleotide sequencing or mass spectrometric 'omics'-technologies, will dramatically change our healthcare system in the near future. We can use these "Big data" resources to develop novel predictive tools, which combine sophisticated quantitative statistical models with fundamental biological knowledge of molecular mechanisms, to generate novel models, which will accurately predict disease risk or treatment response.

2. Medical Biotechnology
Early discovery combined with enhanced treatment efficacy is essential for future intensified combat against severe human diseases. At MBG, there is a profound expertise on molecular and biochemical mechanisms associated with disease. Focusing on the needs of the future, we will combine these different types of expertise to develop innovative solutions for diagnosis, targeting strategies and drug delivery.

3. Use of animal models to study human disease
Researchers at MBG currently offer the experimental use of three different animal species to the research community, all of which at AU were first implemented at MBG. The models available have different strengths, depending on the specific process to be modelled, and are also associated with different costs and time perspectives. MBG offers the mouse (dagmar.au.dk/mouse) and zebrafish (mbg.au.dk/forskning/corefaciliteter/zebrafish) as vertebrate model organisms, and *C. elegans* (dagmar.au.dk/c-elegans) as an invertebrate model system.

4. Molecular neurobiology
During the past 10 years, several groups at MBG have developed an interest in studying the biology of the central nervous system. This is both based on a gradual development of research in specific molecular mechanisms of the cell in relation to neuroscience and on new recruitments with a specific focus on neuroscience. Recently, some of these efforts have resulted in the establishment of DANDRITE, the Danish node of molecular and translational neuroscience of the Nordic-EMBL Partnership for Molecular Medicine (dandrite.au.dk).

New Breeding Technologies (theme coordinator: Mogens Sandø Lund)
MBG aims at being the preferred scientific partner for developing future breeding technologies for farm animals, aquaculture, cereals, grasses, legumes and honeybees.

This will be achieved by integrating the vast scientific expertise MBG possesses in molecular techniques, basic studies in genetic architecture and regulation of complex traits, developing statistical genetic models, and population genetic models to assess the consequences of application in breeding programmes. In this connection, MBG is in a unique position as it has:

1) a strong centre (QGG) that develops novel statistical genetic models which integrate information from large complex populations with information from whole genome genotyping and sequencing technologies and other new large-scale information sources, as well as

2) groups that excel in molecular genetic studies in farm animals (MGS), cereals and grasses (CGB) and legumes (PMB). This will form the basis for developing the future genomic breeding tools such as genomic selection and genome editing technologies. Genomic selection is successfully adopted by industries in cattle, pig, and grass breeding. We expect that it will further be implemented to improve breeding in aqua cultural species, mink, cereals and legumes, as these industries are expected to benefit greatly from the technology.

Future improvements will be based on more accurate knowledge on the genetic architecture of complex traits and causal variants achieved by integration of whole genome sequence data, epigenomics and transcriptomic data to improve the annotation of functional and regulatory genomic elements. Thus, most agricultural traits are quantitative and subject to environmental influence, and this complexity cannot be deciphered based on the genome sequence information alone. In fact, it is widely acknowledged that the current functional annotations of livestock genomes are insufficient for the discovery of the molecular causes underlying many phenotypes of interest. In order to progress, we aim to identify functional elements underpinning genome function through systematic genome-wide discovery of transcribed loci, both coding and noncoding RNA, and mapping of epigenomic features such as DNA methylation, histone modifications and patterns of chromatin accessibility in livestock.

Only through comprehensive knowledge of functional elements and understanding their role in gene regulation can we fully explore the impact of genetic variation on complex phenotypes in a population. Moreover, integration of the novel biological information in genetic prediction models will enable higher accuracy in the prediction of selection response in breeding programmes for improved animal health and performance.

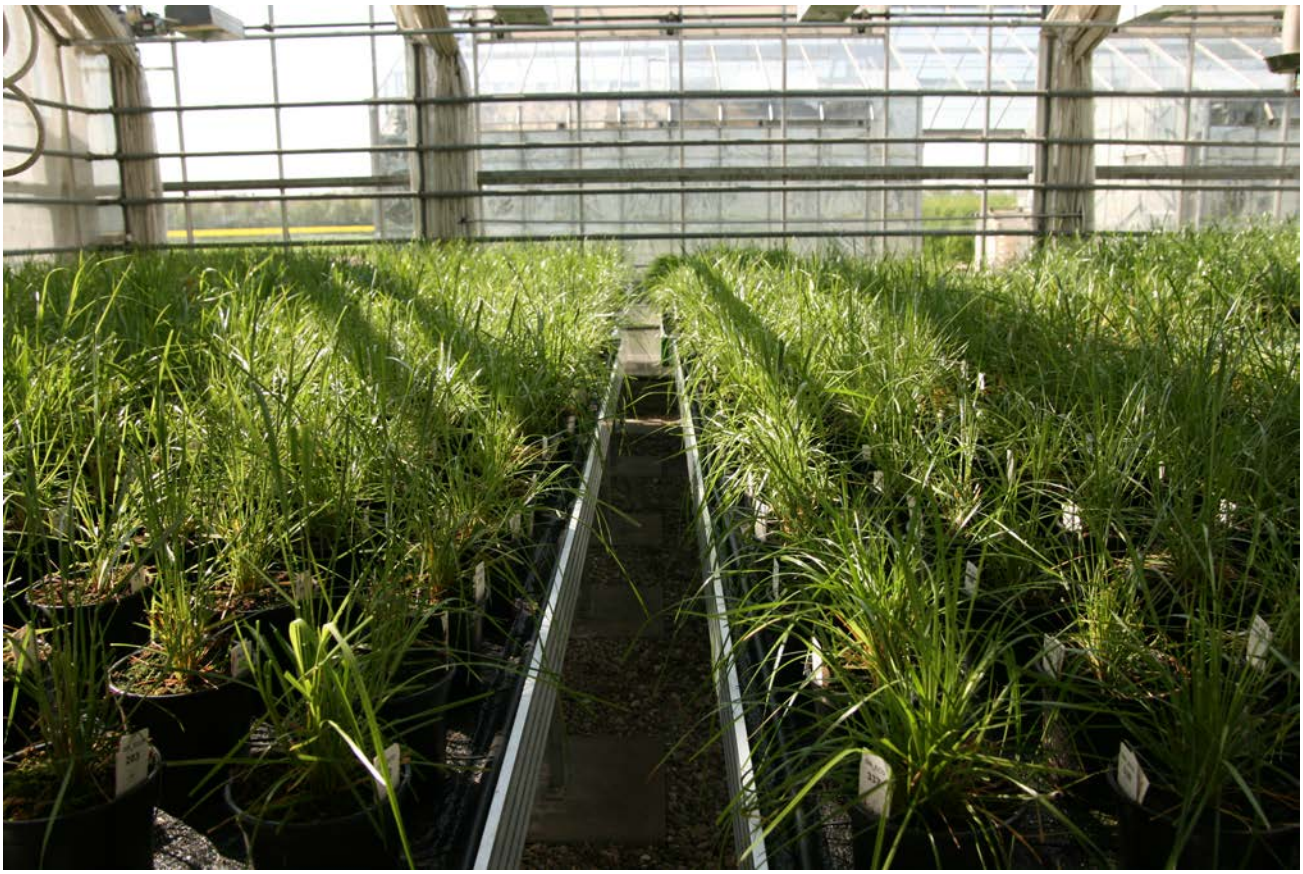
Equally important for future breeding are technologies for automatic and objective measurements of phenotypes of individuals in reference populations or on selection candidates. These may include sensors, cameras, activity measurements, metabolic measurements that record activity or physiology of farm animals, quality of products at slaughter houses, infrared spectra data from millions of milk samples, etc. This creates a big data scenario that needs to integrate breeding technologies in precision livestock farming (PLF).

The development of genome editing techniques is a ground-breaking novel field that offers possibilities to make targeted changes to genes in crop plants via genome editing, e.g. by the use of CRISPR/Cas. If, as expected by the end of 2015, some of these techniques will be deregulated at the EU level, a whole new area for targeted mutation strategies is opened, with large potentials to create and exploit genetic variation in crop plants of use for the plant breeding industry. MGB has the ambition to be the

frontrunner in this area when it comes to Danish crop plants. Via Crop Innovation Denmark, projects will be defined together with industrial partners with the aim of improving quality traits such as protein content and starch quality. As important goals of our research activities, the applied projects will strongly support 1) further development of the genome editing technologies in crop plants, and 2) increased basic knowledge on specific genetic determinants of crop traits, which will complement knowledge from functional genomics studies, and which will be highly important for further exploitation of genome-editing technologies for crop improvements.

The development of genome editing will build on top of existing activities where MBG uses synthetic biology and biotech methods to transfer useful genes across genomes. MBG could, for example, work with cis-genesis (transfer of genes between species that can interbreed) in cereals (CGB) and the transfer of legume genes into barley and maize in order to re-establish functional pathways for plant-microbe interactions (PBM).

In terms of education, we will contribute to courses in agro-ecology, offer a range of PhD courses and potentially contribute with courses in MBG's new Master programme in Quantitative Biology. The developing new technologies will be an integrated part of Master and PhD courses in order to educate young scientists in the area.



Molecular Nutrition (theme coordinator: Esben Skipper Sørensen)
"Molecular Nutrition" is the study of molecular and physiological effects of food components on the body conveyed through the gastro-intestinal system. Molecular nutrition research differs from traditional nutrition research by focusing on the physiological effects of bioactive components in the food, whereas traditional nutrition research primarily deals with the food as a source of energy and the macro nutritional building blocks; fat, protein and carbohydrate.

Research in Molecular Nutrition at MBG has primarily focused on structural, functional and biological characterisation of milk components and their application as new functional and bioactive food ingredients. This has been done in close collaboration with the national dairy industry and Arla Foods Ingredients and has led to the filing of several patent applications and development of new protein ingredients, which are now marketed. Likewise, more than 100 scientific articles on milk protein biology have been published. The research in milk molecular biology and the molecular and physiological functions of milk components in nutrition, including the development and tests of specialised milk-based nutrition, will continue to be a highly prioritised research focus theme in molecular nutrition.
Research in minerals and vitamins as food components is a recurring research focus connecting more research groups at MBG, ST in general and HE. Imbalance in intake of minerals and vitamins is linked to developmental problems and are associated with numerous major health challenges. Elucidation of the underlying mechanisms of controlled transport and uptake at the cellular and organism level will be a research focus area in molecular nutrition.
MBG researchers are active within the field of nutritional impact on ageing processes. Nutritional impact on ageing is studied in cellular and animal models, which are used in screening of bioactive food components and to reveal molecular mechanism in the processes. Likewise, the impact of probiotic bacteria on longevity is studied in animal models. Development of cellular and animal models for ageing and longevity and identification of reliable biomarkers for healthy versus unhealthy ageing will be a research theme within molecular nutrition.

The following research themes are prioritised:

Bioactive milk components – high value natural biomolecules for next generation food products. The research in milk bioactives is primarily based on the specific milk components and their potential as advanced food ingredients for promotion and inhibition of specific physiological processes and conditions. Examples are milk proteins and peptides that play a role in the muting or stimulation of the immune response, milk proteins that transport minerals and vitamins and thereby present them in a bioavailable form, and lipids and lipophilic proteins with functions in immunity, inhibition of viral infections and infant brain development. Research focused on the specific bioactive milk components, involving molecular and structural characterisation of the components and characterisation of their biological and physiological activities and hence their potential as new advanced food ingredients will be a highly prioritised focus area in molecular nutritional research at MBG.

Transport and uptake over physiological membranes. A recurring and very central theme in the research in milk bioactives is their interaction with and transport over physiological membranes. To exercise their physiological effect, food components have to interact with surfaces and membranes in the gastro-intestinal tract. To fulfill their function either as caloric fuel, building blocks or as bioactive compounds, the majority of food components also have to cross this membrane. Having crossed the intestinal epithelial membrane and gained access to the blood, some components travel on to interact with and traverse other physiological membranes, such as the blood-brain barrier. Thus, a central theme in molecular nutrition research is interaction with and active/passive transport over physiological membranes. Development, implementation and use of *in vitro, ex-vivo* and *in vivo* models for transport

of food components over physiological membranes will be a prioritised focus area in molecular nutrition research. To be successful in this area, we will engage in collaborations with strong research groups at HE (blood-brain barrier models) and researchers at FOOD and/or HE for the development and implantation of *ex-vivo* and *in vivo* models for the intestinal uptake.

Molecular nutrition and the intestinal immune system. The large and exposed surface of the intestinal mucosa is under constant challenge by ingested foreign antigens, e.g. in micro-organisms, natural or synthetic food products and additives. Hence, the intestine contains the largest concentration of lymphoid tissues in the body, in the form of lymphoid aggregates in Peyer's patches, the lamina propria and as scattered epithelial lymphocyte populations. This high concentration of lymphoid tissues makes the intestine a very important organ in the development of the immune system in the neonate and in the maintenance of a balanced immune response in humans in general. Several immunological diseases are caused by malfunction of the intestinal immune response (e.g. Crohn's disease, Colitis ulcerosa). Also more widespread general intestinal bowel disorders such as diarrhea and constipation can to some extent be ascribed to malfunction in the intestinal immune response or to a malfunctioning intestinal microbiota. Research in ways to affect intestinal immunological development and response by nutritional intervention will be a focus area in molecular nutrition research at MBG. This involves collaborations with research groups at HE, Aarhus University Hospital and other national and international research groups for the development and use of cellular and animal models for screening and testing of milk ingredients. Likewise, participation in a human intervention trial with milk components as potential means of alleviating intestinal bowel disorders and diseases is a realistic goal within the next five years.

Vitamins and minerals: Minerals and vitamins are components of the natural diet. A number of these are also constituents of vitamin supplements, administered as medicine, and/or used as food additives. Imbalance in intake of minerals and/or vitamins – i.e., too much or too little – are linked to developmental problems and are associated with numerous major health challenges as cardiovascular diseases, osteoporosis, and cancer. Moreover, emerging results point at potential roles in obesity, diabetes type 2, psychiatric disorders, and ageing. The broad effects of imbalanced intake of specific minerals and vitamins reflect essential roles in basic cellular functions. Elucidation of the underlying mechanisms of their uptake and functions at the molecular and cellular levels is a focus area. Implementation of existing and new animal models further strengthens this area. An additional strength is the obvious common interests at more levels with numerous other existing research areas/disciplines at MBG – both strongholds and research themes - as well as at ST in general, HE, and Aarhus University Hospital and the consequently mutually potentially beneficial synergisms. Impact of the research on the society will be secured through communication/collaboration with the clinic and by communication to the general public.

Intestinal microbiota-host interaction: It is increasingly clear that the gut microbiota is an important, but so far poorly described, determinant of human health. The gut microbiota affects metabolism and insulin resistance, and is a causal factor in obesity and several types of inflammatory bowel diseases. The bacteria that have a positive effect on health are collectively called probiotic bacteria, and the use of such probiotics as dietary supplements is a growing industry expanding into new areas of application to improve the health of both humans and livestock. However, at the molecular level, little is known about the causal mechanisms of actions of these probiotic bacteria. A better understanding of the microbiota-host interactions will provide a platform for personalised nutrition strategies that can help treat and prevent many diseases. To understand the complexity of host-microbiota and host-pathogen interactions, we face new research challenges. These include adapting and integrating new technologies (e.g. metagenomics, meta-proteomics, and data handling), and we must develop and study new biological model systems and compare molecular mechanisms across different species of model

organisms. We propose a concerted and parallel series of studies of probiotic effects on humans, model organisms and *in vitro* systems, combined with large-scale molecular monitoring (e.g. animal genomics, metagenomics, proteomics, and metabolomics). Such actions could uncover fundamentals of microbiota-host interaction and thereby provide the basis for the validation of specific probiotics for use in human and livestock nutrition.

Healthy ageing: Maintaining health during normal life, or regaining health after a period of sickness and disease, requires a reliable battery of biomarkers for defining health. Optimal stress response profiles of a cell, tissue and organism is one such set of markers that needs to be defined and validated as an indicator of the health status, robustness and resilience of the system at different ages during the lifespan. Irradiation, temperature, microbiota, food restriction, and some specific food components can be tools to elucidate various pathways of stress response during healthy, unhealthy and diseased states.

Centre for Protein (macromolecule) Biotechnology (theme coordinator: Gregers R. Andersen)
Research groups at the Faculty of Science and Technology and the Faculty of Health at Aarhus University (AU) have for more than six decades studied the intimate details of the structure, function and dynamics of proteins and nucleic acids. Examples of internationally acclaimed macromolecular research at AU that have also been extensively developed through centres of excellence include: i) structure determination of proteins and their complexes by X-ray crystallography, NMR, small angle X-ray scattering, and recently cryo-EM; ii) protein folding, protein-nucleic acid and protein-protein interactions through biochemical and biophysical approaches; iii) membrane transport proteins and signal transducing receptors; iv) proteolytic signalling pathways within cancer, inflammation and growth; v) fibrillating proteins and their

role in bacteria and humans. These research activities have been disseminated through more than 30 papers alone in the world-leading journals *Nature* and *Science* over the past 10 years.

With the help of substantial external funding, we propose to establish the Centre for Protein Biotechnology at Aarhus University. The mission of the centre will be to create a world-leading environment not only for fundamental research in functional and structural properties of proteins but also for translating the results of basic research into new protein-based therapeutics, diagnostics and enzymes for green chemistry. Hence, the centre will also have a strong focus on implementing and developing new strategies for protein selection, engineering and production for both therapeutic and industrial use. The centre must recruit outstanding students, the most talented postdocs, and the best junior group leaders worldwide. The centre will likewise establish network activities, ensuring close contacts and collaborations with the Danish biotechnological and pharmaceutical companies, mainly located in the Copenhagen area.

The core of the centre will be formed by AU researchers working within relevant protein biotechnology fields at the Department of Molecular Biology and Genetics, the Department of Engineering, the Interdisciplinary Nanoscience Center (iNano), and the Department of Biomedicine. Examples of biology represented by the participating AU scientists, in which scientific excellence has been demonstrated, are the function of membrane transport proteins, the mechanism of enzymes, receptor mediated signalling and endocytosis in mammals and plants, protein fibrillation, proteolysis as a regulatory and signalling mechanism, innate immunity, protein synthesis, intrinsically disordered proteins and protein-nucleic acid interaction. Within applied science, examples of strongholds are molecular evolution of proteins and aptamers, targeted drug delivery, protein production in plants and dairy relevant protein technology. In terms of existing infrastructure and technology, the participants will contribute to the centre with structural biology (X-ray crystallography, SAXS, single-particle cryoEM and cryoEM tomography, liquid and solid state NMR, molecular dynamics simulations), mass spectrometry, biophysics (spectroscopy, calorimetry, SPR/BLI, kinetic analysis), protein production in pro- and eukarytic hosts (bacteria, yeast, insect cells, mammalian cells, plants), protein purification, protein engineering, protein (antibodies, nanobodies and other protein scaffolds) and aptamer selection, next generation sequencing, animal and plant model organisms (*C. elegans*, zebrafish, mice, *Arabidopsis*).

A Master and a PhD programme in protein biotechnology directly supporting the activities in the centre will be established at AU. The university will offer modern experimental facilities that allow Bachelor, Master and PhD students to obtain first-hand and frequent experience with state-of-the-art equipment and approaches for recombinant protein selection, engineering, production, purification, characterization and usage in, for example, animal models. Making students familiar with the development of therapeutic proteins will also strongly endorse the research theme *Molecular Medicine* at AU.

Access to world-class infrastructure will be a prerequisite for the recruitment of the best young and established scientist and will in addition boost the competiveness of established AU research teams. Examples of infrastructure that might be introduced or significantly improved by the centre include CryoEM, super resolution microscopy, protein production facility, biophysical characterization, mass spectrometry.

With the aim of creating a strong environment for the development of therapeutic proteins but also to provide easy and affordable access for the centre investigators to mouse models, it becomes essential that access to a stable and smoothly operating mouse facility is secured. The AU department of Biomedicine is currently constructing a new animal facility in a building expected to be inaugurated in 2017. This will

provide an excellent framework for in vivo studies, but it is essential that AU ensures its functionality in terms of management and a reasonable pricing policy throughout the centre life time.

AU has excellent new teaching laboratories for training master and PhD students in experimental work. However, to obtain full synergy with the external funding to the centre AU must make significant investments in equipment for teaching such that the students enrolled in the master and PhD programmes directly associated with the Centre for Protein Biotechnology will obtain first-hand and frequent experience with modern equipment and approaches for protein engineering, production, purification and biophysical characterization.

b. Talent

The Ph.D.-education: The Department of Molecular Biology and Genetics will continue to strive to attract and educate the best qualified candidates within the field. One concern is the substantial teaching load on the PhD students, as well as course activities, which minimises the time available for research. This is particularly a problem for students enrolled based on a Master's degree, i.e. as "5+3".

We propose to increase the number of PhD students enrolled based on a Bachelor's degree, i.e. "4+4" or ("3+5"), but see earlier comments on the results of "dimensioneringen" (p. 12).

The PhD teaching load could be reduced by increasing the involvement of postdocs in teaching and by a commitment of the lectures to take part in theoretical exercises.

The PhD study is primarily focusing on an academic carrier, despite the fact that only a minority of the students will take that route. During the PhD study, more attention should be given to job possibilities in the private and public sectors in general.

Due to the widespread location of the department, the PhD students very rarely meet and exchange experiences. To facilitate the interactions between the students, annual PhD meetings will be established as well as social events in connection with the departmental seminars.

Although the supervision of PhD students already to a large extend is working fine, focus will be on optimising the use of biannual meetings with the advisory groups.

During the past decade, focus has been on attracting international PhD students, and we now have a ratio between Danish and international students of 40:60.

If it is possible to attract more strong Danish students, we could provide more PhD's for the Danish labour market and we could also get more "4+4" students.

Postdoc-level: There is a gap between the PhD education and the further career, especially for foreign students. Earlier recruitment of foreign students (3+5) would create a closer connection to the Danish society. Closer contact to the industry would create career possibilities.

c. Research and recruitment

The recruitment of the right staff is the single event that will have most impact on the future of the department. To qualify for the future calls and subsequent selection of strong candidates, the department has launched a thorough procedure actively involving the local research committee and relevant sections making sure that all decisions are supported by the organisation.

During the past 10 years, the department has established a number of Centres of Excellences and other large centres that have been promised an embedment of their activities. Thus, we will open a number of these positions the coming years, and they complement well the future needs to support our strategy. In addition to the embedded positions, we have suggested additional positions, which all have been accounted for in our four-year budget.

d. Education

The department is responsible for two Bachelor programmes in Molecular Biology and Molecular Medicine, two Master programmes in Molecular Biology and Molecular Medicine and contributes significantly to a Master programme in Molecular Nutrition and Food Technology.

There is a restricted uptake in both Bachelor programmes. In 2015, 90 students were accepted for Molecular Biology and 60 students for Molecular Medicine, resulting in cut-off grades of 8.8 and 10.9 in 2015, respectively.

Education of students is the most important task among our activities, and it is very important to make sure that our educations match the future needs.
The strategy for 2010-2015 suggested a major revision of both education programmes, and this work is in progress. During this process, we identified limited coherence and content progression in certain parts of the educational programmes together with a sub-optimal prioritisation of topic areas in the curriculum. A further focus area in the revision will be on new teaching methods and tools that to a higher degree activate the students and thereby stimulate the learning process.

The present status of the revision process points towards the following focus areas:

Bachelor in Molecular Biology:
Introductory course providing improved basic quantitative skills (calculations, etc.)
Better alignment and progression of basic and advanced courses
Integration of all individual practical courses into one consecutive event
Upgrade and expansion of bioinformatics

Establishment of a special basic course in molecular biology and biochemistry targeted students from other Bachelor programmes.

Bachelor in Molecular Medicine:
Integration of disciplines from both MBG and Health in newly designed courses
Upgrade and expansion of bioinformatics

Master in Molecular Medicine:
More experimental courses
Possibility of including courses from both MBG and Health of own choice

To reduce the number of students drop-outs, more focus will be given on career tracks advice already from year one.

New teaching initiatives:
To ensure that the knowledge from the research activities of the proposed research themes is transferred to the next generation, we propose to establish two new Master programmes:
Master programme in Protein Research associated with the Centre for Protein Biotechnology and a Honours programme in Quantitative Biology.

The time students spend on completing their education appears to be within the required time frame for a Bachelor's degree. However, the students do not finish their Master's degree fast enough, which needs to be addressed, although not a major issue as the average for the Master Students is within the expected range for 2016

e. Public sector consultancy

All competences at MBG must come into play regarding the Ministry of Food and the industry. This should result in new projects in the collaboration agreement with the Ministry of Food, as well as industrial collaborations.
The agricultural research and related expertise in the former governmental sections must be maintained and made visible towards Danish Centre for Food and Agriculture (DCA) and relevant ministries.

f. Business collaboration

Business collaborations at MBG take place in the areas of agriculture and food as well as pharmacology and biotechnology and include both large and small companies. There are mainly three types of business partnerships: 1) collaboration with a start-up / spin-off company, often originating from AU, 2) contract research, where researchers at MBG undertake tasks defined by the company and 3) strategic project involving company partners and typically supported by strategic funding bodies.
In the spring of 2015, a Business Committee was established at MBG, with the aim of increasing the dialogue and cooperation with the industry. MBG's Business Committee has five members representing the different areas of the MBG's business interests. The chair acts as the committees contact person and represents the department at the Faculty's Business Committee.

The involvement of companies at both undergraduate and postgraduate levels can pave the way for subsequent research activities between the teachers and companies.

g. Physical setting

The lack of physical co-localisation of the research groups and the physical distance to the students are clear drawbacks for the development of the department's research and teaching activities.

Physical co-localisation of staff and students is an imperative factor for the future of the department.
As soon as Aarhus University has decided to allocate part of the University Hospital to the department, we will initiate a thorough process involving all staff categories and students to design the optimal housing plan for the department. We have already appointed a committee to initiate and follow the process, and it is very important that we are involved at earliest stage of the planning process.
While waiting for the master plan to be executed, space will be freed in buildings 1130 and 1131 by redesigning the laboratories during the renovation process. The freed space will be made available to the section of Molecular Genetics and Systems Biology presently situated in Foulum. The Centre of Quantitative Genetics and Genomics will remain in Foulum until the final merger of the department at the University Hospital location