VISION PAPER
STRUCTURAL BIOLOGY

medicon valley alliance
Creating Opportunities

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The Medicon Valley Beacons is part of the collaboration project "Medicon Valley—a world class life science cluster"
Between Medicon Valley Alliance and Invest in Skåne. It is partly funded by the EU Interreg IV Programme

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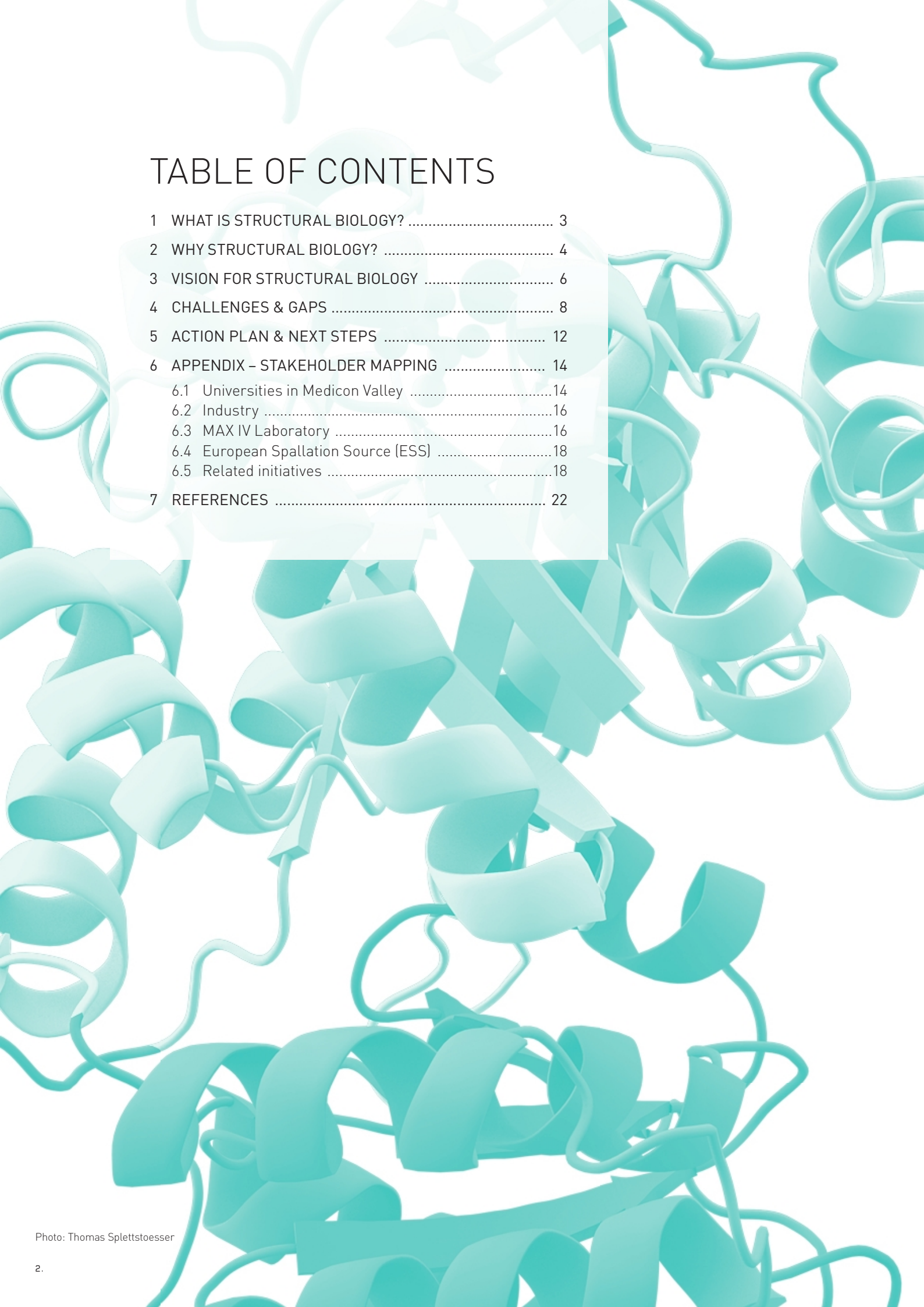

Photo: Thomas Splettstoesser

① WHAT IS STRUCTURAL **BIOLOGY?**

The majority of the life science research done at large-scale synchrotron and neutron facilities, such as the coming MAX IV and ESS facilities, is structural biology.

Structural biology seeks to visualize the three-dimensional atomic structure of biological molecules, such as proteins, in order to understand their functions, properties and interactions. By using various techniques such as X-ray and neutron crystallography, structural biologists can obtain a three-dimensional picture of e.g. a protein involved in a disease that can be the target protein for a pharmaceutical drug. Knowing the structure of the target protein helps in designing drugs that will either inhibit or stimulate it, and in understanding the pharmacological profile of the compounds. Such knowledge will be essential in future drug discovery in order to treat the most complex diseases.

more advanced expression systems, engineering and are difficult to purify. Membrane proteins are important drug targets as they control what substances enter and exit the cells and they impact cell signaling. If more information is revealed about the membrane proteins (i.e. their structure, their function, their interaction, how they can be modified and how they impact the cellular processes), it will give a much better understanding of how drugs actually work in the biological system.
Large-scale facilities such as synchrotrons and neutron sources are essential for many of these structural studies. Synchrotrons generate intense beams of X-rays from an electron storage ring. Synchrotron X-ray crystallography is a mainstay method in structural biology for atomic structure determination. Developments in sources and instrumentation have reduced the size of crystals required for micrometers. Synchrotron X-rays are also increasingly used

Definition of structural biology

"Structural biology seeks to provide a complete and coherent picture of biological phenomena at the molecular and atomic level. The goals of structural biology include developing a comprehensive understanding of the molecular shapes and forms embraced by biological macromolecules and extending this knowledge to under-stand how different molecular architectures are used to perform the chemical reactions that are central to life.
In addition, structural biologists are interested in understanding related processes such as protein folding, protein dynamics, molecular modeling, drug design, and computational biology. Central tools used in this research include X-ray diffraction, NMR, electron microscopy, other spectroscopies and biophysical methods, protein expression, bio-physical and bio-organic chemistry, computer science and bioengineering."
(Source: MIT http://bit.ly/1w3Q2Mr)

Structural biology has grown tremendously as a research field as the structures of more and more proteins have become known. Today, the protein databank contains approx. 90,000 protein structures. In 1990, 500 protein structures were available, while at the end of the 1990s, almost 11,000 structures were deposited in the protein databank. However, the structures of integral membrane proteins which make up 20-30 % of all expressed proteins, are not very well known. This is mainly because it is difficult to produce and isolate membrane proteins in an active form in the amount necessary for structure determination and because it is difficult to obtain crystals of membrane proteins. Several other classes of medically relevant proteins are also under-represented in the protein databank, as they also require

for techniques such as small angle X-ray scattering (SAXS) that yield low-resolution structures of macromolecules in solution. Neutron beams can be generated either by fission in nuclear reactors or in a process known as spallation. In the latter, charged particles such as protons from an accelerator collide with a target at high speed and generate neutrons. Neutrons can be used to study bio-molecular structures in much the same way as X-rays, while they are much more sensitive to hydrogen, an element that plays a key role in many biological processes, but is almost invisible by X-rays. The neutrons also do not cause the same kind of damage to the sample as X-rays do, making neutron and synchrotron sources highly complementary for structural biology studies.

② WHY STRUCTURAL **BIOLOGY?**

The huge infrastructure investments in Medicon Valley in connection with the establishment of the large-scale facilities – MAX IV and European Spallation Source – will provide the region with a competitive advantage. Medicon Valley will host the most brilliant synchrotron X-ray source and the most powerful neutron source in the world. The colocation of the two facilities in Lund and the data management center in Copenhagen will thus offer extraordinary possibilities for conducting groundbreaking research in the public and private sectors.

There is a general expectation that the facilities will drive economic growth and lead to new companies and the creation new jobs in the region. A recent study estimates that between 1,600-2,400 permanent full-time positions will be created because of the new infrastructure. Earlier estimates have been as high as 4,000-5,000. It cannot be expected that the mere existence of the facilities will have positive effects on regional growth and job creation. Experience from other regions with similar facilities (e.g. the ESRF in Grenoble, France) shows that such facilities will not by themselves drive economic development in the region. Few companies choose to relo-cate to a given region for that reason alone. What is important for the relocation to a given region is the critical mass of skilled expertise to recruit from and a pipeline of interesting development projects.

It is therefore necessary to create a vibrant ecosystem with strong scientific competences that surrounds the facilities. The need for excellent universities in close vicinity to the facilities and a large talent pool are very important factors in order to attract companies, investments and top international researchers. If Medicon Valley is able to strengthen the surrounding research environment, the region will have a strong competitive advantage compared to other regions with similar facilities.

The region holds many scientific strongholds within structural biology at the universities and the skill base in the companies in Denmark and Sweden have many complementarities. In addition, Medicon Valley has a high quality of life with the urban environments in Copenhagen and Malmö as well as rural areas close by, which offer many opportunities for leisure activities. In addition, the framework conditions are generally recognized as conducive for doing business and living. Thus, all the building blocks are present in the region and there is much potential for creating a strong internationally recognized research environment.

This vision paper highlights the perspectives for stimulating and strengthening the structural biology research community in Medicon Valley to ensure that the region reaps the full benefit of building the ESS and the MAX IV. It also addresses the challenges and knowledge gaps for reaching the vision as well as suggestions for actions that can be carried out to release the full potential. If Medicon Valley can create a competitive edge within this area in comparison with competing regions, it will be possible to attract talent, business and capital and create jobs in the region.

The vision paper is developed as part of the "Medicon Valley Beacons" project. The paper is based on an extensive dialogue with numerous regional stakeholders over a longer period of time, a 1½ days vision workshop with more than 25 key stakeholders in February 2014 and desk research.

Medicon Valley Beacons: collaborating regionally to compete globally

Medicon Valley Alliance (MVA) exists to make Medicon Valley an attractive destination for the best talent within life science. MVA launches and drives initiatives that put Medicon Valley firmly ahead in the global race for talent. The vision is to release the full potential of Medicon Valley by focusing on the entire life science cluster and spot synergies across borders, disciplines and the public-private divide.

For Medicon Valley to be a serious contender in the highly competitive global life science race, the cluster as a whole needs to strengthen its ability to attract a constant stream of talent and capital. The "Medicon Valley Beacons" was launched by MVA in early 2012 and aims to achieve this by showcasing the region's scientific strongholds and acting as regional landmarks on the global life science map.

The objective is to develop, expand and brand 4-5 research environments that build on Swedish-Danish synergies between existing strongholds – in both the private and public sector – and which span the entire life science value chain from early research all the way to commercialization, in order to drive economic growth and job creation in the region.

Four Beacons – structural biology, immune regulation, systems biology and drug delivery – have been selected following an extensive evaluation of existing life science strongholds in the region based on analysis and input from regional stakeholders. Each Beacon is characterized by being highly cross-disciplinary, building on existing regional strongholds and addressing future demands and medical needs. The individual Beacons focus on areas where there is considerable potential for synergies in Medicon Valley for creating world-leading research environments.

The Medicon Valley Beacons is part of the collaboration project "Medicon Valley – a world-class life science cluster" between Medicon Valley Alliance and Invest in Skåne. It is partly funded by the EU Interreg IV Program.

③ VISION FOR **STRUCTURAL BIOLOGY**

The vision for the structural biology area is difficult to imagine, as it will be very much dependent on the development of MAX IV and the ESS. Especially, the ESS is far away in the future and is not expected to be at full capacity before 2025 at the earliest. It is important to keep in mind that the field of structural biology is much broader than just the MAX IV and the ESS facilities. A number of researchers in the region are already working within this field and use large-scale facilities located in other regions. The interactions between the stakeholders within this research field must be strengthened by building on existing competences and reinforce other competence areas related to structural biology. This is important to ensure that the research community and the industry are well prepared for reaping the full benefits of the unique infrastructure investments.

It could make sense to look not only at techniques applicable to MAX IV and the ESS, but focus on heightening the competence level within the field of "integrated structural biology". "Integrated structural biology combines data obtained by progressive high-resolution methods such as single-crystal X-ray diffraction, small angle X-ray scattering, nuclear magnetic resonance, and cryo-electron microscopy and tomography with modern methods of molecular modelling, theoretical chemistry, and bioinformatics to gain insight into their structure and functions." (http://bit.ly/1sbNoDL). By taking a broader approach to structural biology, it will provide better knowledge of the functionality of biological molecules.

Another suggested focus could be the structure, properties and interactions of membrane proteins, which is e.g. relevant for future target identification and selection. There are numerous regional strongholds within protein research. Medicon Valley is home to one of Europe's largest protein centers, there is a long industrial tradition within development and production of biologics, and naturally the construction of two state-of-the-art facilities, which will make it easier to conduct structural analyses of the membrane proteins. In addition, it will reflect future demand for unveiling the secrets of membrane proteins in connection with future drug development, drug delivery and the individual treatment of patients. There are therefore many existing regional strongholds to build on by focusing on membrane proteins. If Medicon Valley can become a world-leading hub for research within membrane protein structures, this offers huge opportunities for future growth.

Building a strong structural biology community is not an easy task and various actions must be initiated. First of all, strengthening the network between the many stakeholders by bringing them together to exchange knowledge is a first step coupled with communications efforts to highlight the existing competences. At a later stage, activities must be further integrated. This can be done by creating a joint institute/center where academia meets industry in a pre-competitive setting that encourages open innovation.

Imagining the structural biology ecosystem in Medicon Valley in 2025

Medicon Valley has cemented its position as an international hub for structural biology and in particular groundbreaking research within membrane protein structures. This position has been secured through a joint effort over the last decade where all elements in the ecosystem have been strengthened to release the full potential.

Fundamental to the success of creating an international hub for structural biology is the excellent academic research community in Medicon Valley. In an effort to bring the research community closer together, the region's universities have actively encouraged cross-border collaboration in the last decade, e.g. by creating a joint M.Sc. in structural biology and a number of Ph.D. programs related to structural biology research as well as specific funding schemes for the research field. As a result, there is a large pool of local talent that possess relevant structural biology competences and they are in high demand by both local and international companies, who have realized that having in-house competences within this field is essential for their future growth.

The MAX IV Laboratory and the ESS are at full capacity with a wide range of beamlines and instruments suited for various types of structural and functional analyses of biologic materials. There is a one-point-of-entry support function for the two facilities in which potential users can approach and be advised on appropriate experiments, procedures for applying for experiment time, data management issues etc. In addition, it has been decided to establish a free electronic laser in Lund to further cement Medicon Valley's position as an international hub for structural biology.

In addition, two research centers have emerged due to the strong focus on structural biology from local stake-holders and the growing importance of structural information in drug discovery. The Medicon Valley Institute for Structural Biology and the Oresund Drug Discovery Center were established in the later part of the 2010s. Both research centers operate in pre-competitive setups and bring researchers together from the public and private sectors in exciting new and temporary constellations. The two organizations are closely integrated into the permanent research environments at the universities and have close collaboration with other excellent research centers in the region, e.g. the NNF Center for Protein Research. The environments of open innovation have already led to innovative and groundbreaking drug discoveries, which are under commercialization in private companies, and new treatment methods, which are currently tested in the clinic. As a direct result of the research conducted in these centers, the Nobel Prize in medicine has been awarded to a Medicon Valley scientist for a groundbreaking discovery within structural biology.

Having a Nobel Laureate in Medicon Valley has greatly boosted the international awareness and attractiveness of the region. It has resulted in a large influx of young talents as well as well-established researchers who relocate to Medicon Valley to be part of this vibrant research community and top-ranked scientists. Global life science companies place significant R&D activities in the region to be close to the large pool of talent, the vi-brant research community and the state-of-the-art research facilities. The venture capitalists have their eyes firmly set on Medicon Valley as profitable investment opportunities are plentiful. Knowledge-intensive jobs have been created, both directly at the various research facilities, but also indirectly in the form of jobs in CROs/consultancies providing services to users of the large-scale facilities, in spinout R&D companies, and in international life science companies that have relocated to the region. In addition, a large number of jobs have also been created in the service sector as a result of a dynamic environment with restaurants, shops, hotels etc. for the incoming researchers.

The Medicon Valley region is often the preferred location for structural biology conferences of high impact, e.g. the International Conference on Biology and Synchrotron Radiation (BSR) and meetings arranged by the International Union of Crystallography. In addition, a recently established structural biology conference has been running with great success for a few years. Since 2017, an annual structural biology summit has taken place in a remote area in Skåne. At this summit, 150-200 top-level scientists and young talents from both aca-demia and industry meet to network, share knowledge and generate new ideas.

The general infrastructure in Medicon Valley is outstanding. The main hotspots in the region are well-connected via an efficient public transportation network and the international airport in Copenhagen has direct flights to all the major life science hubs worldwide. The area in between the large-scale facilities is dynamic with necessary support structures such as utility labs, and temporary accommodation for visiting researchers. Over the years, the governments in both Denmark and Sweden have significantly focused on improving the framework conditions and removing hindrances to the mobility across the Danish-Swedish border. These efforts have stimulated the cross-border collaboration and integration of the Medicon Valley life science cluster.

④ CHALLENGES & GAPS

One of the major challenges in fulfilling the vision of a world-leading research community within structural biology is the financial situation at the ESS. There are still major uncertainties about the ESS construction budget. The total budget is approx. EUR 1.5 billion of which 50 % will be financed by Sweden, Denmark and Norway. The remaining 50 % must be financed by other European countries. These funds have not yet been secured. The Swedish government requires that 80 % of the 50 % financing from other European countries is committed before construction can start. Spain signed a formal letter of intent on February 20, 2014, for 5 % of the costs and on March 11, 2014, it was announced that Great Britain has committed to contribute with approx. 10 %. In May 2014, France committed to eight percent (SEK 1.3 billion), while Italy committed to covering six percent of the construction costs (SEK 999 million) in June 2014 (cf. Life Science Sweden 2014). Negotiations with Germany and other European countries are ongoing.

The construction costs of the instruments at the ESS are included in the total budget, while the different beam-lines at MAX IV have to be financed individually. The decision about the instruments at the ESS is ongoing. Currently, the ESS scientific advisory committee (SAC) is partly focused on physics due to the representation in the committee. A strong external push from stakeholders within life science is therefore necessary to ensure that instruments with life science applications are prioritized. This needs to be done immediately, as it will be decided in 2014 and 2015, which 22 instruments will be built. The construction of MAX IV is well under way with 13 beamlines funded and four more under discussion. In the case of MAX IV, the issue is whether the next beamlines to be decided upon are applicable to life science and how they should be financed (average price per beamline approx. SEK 105 million/EUR 14 million).

The operational costs at ESS are estimated to be approx. EUR 89 million annually. There is still no clear plan for how these costs will be covered. In December 2013, the Swedish Research Council (VR) granted MAX IV SEK 1.39 billion to cover the operational costs from 2013-2018, while Lund University is contributing with SEK 250 million in the same period.

In addition, the access modes for users are not clearly defined. For academic users, it is expected that the access to the facilities, i.e. allocation of experiment time, will be based purely on the scientific excellence of the applications. For the industry, the access modes are important when the companies have to judge the potential of structural biology experiments. For companies to be interested in gaining knowledge about what structural biology can be used for and how it can generate value for their particular company, they will want to know what the costs are and the time horizon before they can judge whether or not to go forward with this research. At MAX IV, the policy for access and industrial use will be discussed later in the spring of 2014. Three different access modes will be implemented for the macromolecular crystallography (MX) beamline: (1) staff doing the data collection, (2) remote access and (3) direct access to beamlines.

Experiences from other facilities show that the policy documents of the facilities are important in proactively encouraging industrial usage. At the neutron facility J-PARC in Japan, a certain amount of the experimental time at the facility is reserved for experiments for commercial purposes. It is interesting to note that life science companies generally occupy most of the beamtime allocated for proprietary research at European synchrotrons and neutron facilities. In the MAX IV strategy plan for 2013-2016, it is stated that the goal is to offer product-oriented service to the industry users either via mediator companies or directly through MAX IV itself. It is expected that the pricing for access to beamtime will be competitive with other synchrotron facilities, e.g. the ESRF charges EUR 3,600/8 hour shift. The ambition

is to generate an additional annual revenue of SEK 10-20 million, equal to approx. 5 % of the user shifts being used for direct commercial exploitation at full operation in 2020.

There are huge knowledge gaps in terms of knowledge about what structural biology, and in particular ESS and MAX IV, can be used for. There is a general need for educating/informing young as well as experienced scientists and the life science industry. A survey by Analyse Danmark conducted on CEOs of Danish life science companies shows that very few of them have heard about MAX IV and ESS, let alone know what the facilities can be used for and how the methods can be implemented in their R&D activities. It cannot be taken for granted that simply because the facilities are placed nearby, the companies will immediately start to use the facilities. On a general level, the life science industry – apart from the larger life science companies – has not yet grasped the technologies and is unaware of the knowledge that structural biology studies can add to their R&D. To some extent, there is a certain familiarity in using X-ray techniques, but using neutrons for experiments with biological materials is mostly conducted in academic environments. There is a gap in terms of communicating these possibilities between the university researchers and the industry researchers. There is also a gap in the communication between physics researchers, who have traditionally been viewed as users of large-scale facilities, and researchers within biotechnology and pharmacology.

There is a knowledge gap in the skill base in the region. Overall, education in structural biology at the universities should be more widespread to foster the researchers of tomorrow. According to several stakeholders, there is a need for improving the computational/data analysis capabilities to accommodate the increasing demand for analyzing the large amounts of data generated at the large-scale facilities such as the ESS and MAX IV. The competence levels within bioinformatics, computational chemistry, systems biology etc. must be improved.

Another gap that must be addressed is the need for support/service organizations that help potential users by providing information about the types of experiments and what knowledge experiments can provide, prepare samples, perform experiments and assist with data analysis. This is very much related to the above-mentioned gap in knowledge, since many potential users have no idea what type of experiments to carry out, what knowledge can be derived and the actual execution of the experiment. Shared labs close to the facilities will also be needed, as the biological samples are very fragile and cannot be transported for longer periods, e.g. some samples cannot be carried on board planes in the cargo space/room during flights as the low temperatures can compromise the properties of the samples or simply destroy them.

Several regional stakeholders have addressed the need for support organizations, and projects have been initiated on the Danish side with the universities as mediators and with funding from the public sector (e.g. the 3D Imaging Portal at the Technical University of Denmark and the NXus project at the University of Copenhagen). Through these industry portals, companies can gain knowledge on the various types of experiments to perform and what type of valuable information such experiments can disclose. Currently, the services are free-of-charge.

Government-funded initiatives are an excellent way of getting the interest started in terms of generating concrete cases on what structural biology can offer industrial R&D. However, in order to build a sustainable business on a long-term basis, which will truly drive economic growth and job creation, there will be a need for creating a business model where specialized contract research organizations act as mediators between smaller companies and the facilities.

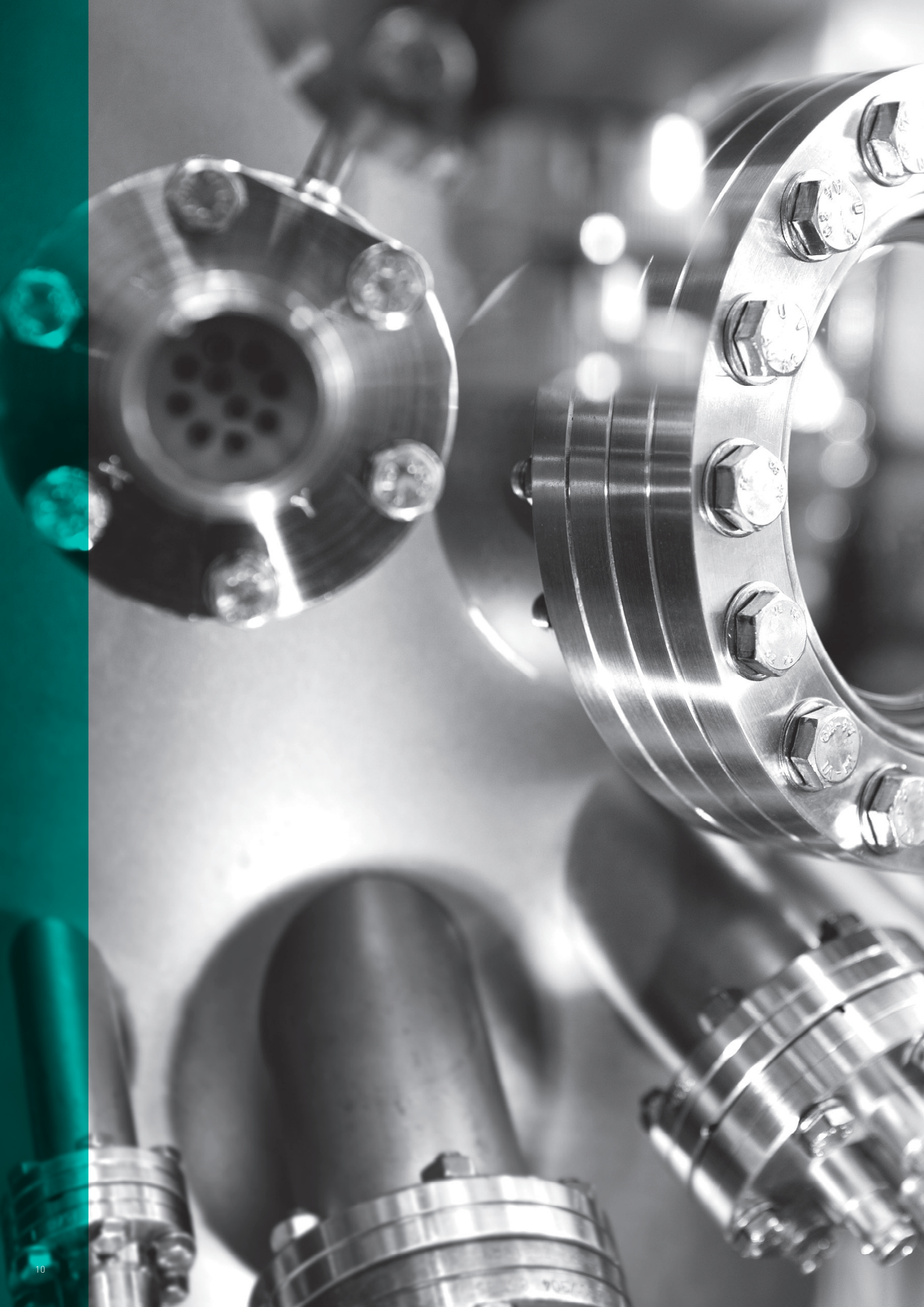

Photo: MAX IV/Johan Persson

This opens up new business opportunities for companies to specialize in competences related to using large-scale facilities.

Aside from the necessary support structures, there is also a need for infrastructure in the traditional sense in order to create an all-encompassing ecosystem around the research community, namely improved public transportation, sufficient accommodation, one-point-of-entry to the public administration for foreigners, high quality international schools etc. These things are, however, general prerequisites for creating an attractive world-leading cluster.

Practical feasibility for an MVA initiative

On a more practical level in terms of feasibility for MVA to drive an initiative within structural biology, there are a few things to be aware of, namely the range of other initiatives focusing on ESS and MAX IV (see section 6.6 for a description of the various initiatives/projects). What is different about the MVA initiative is that is does not focus specifically on ESS and MAX IV. Naturally, the two facilities are central to structural biology, but the infrastructure is considered as a means to an end – i.e. to become an international hub for structural biology research by improving the competence level in the region.

MVA is a neutral platform that is able to advocate for collaboration across the Danish-Swedish border and across disciplines. The cross-border perspective is naturally also central to the Interreg pre-project and the future larger project initiated by the Capital Region of Denmark and Region Skåne. Nevertheless, in dialogue with the project management team, it is assessed that the new Interreg project will take a much broader perspective covering many more disciplines and not specifically focus on a research field such as structural biology. The upcoming project will also address framework conditions, which are not central to the Medicon Valley Beacons.

⑤ ACTION PLAN & NEXT STEPS

Numerous ideas for actions have been mentioned in order to create a more cohesive and vibrant ecosystem around structural biology in Medicon Valley. Some of the actions are feasible to do in the short-term and at relatively low costs, while others are only possible at a later stage and with substantial financial means. In addition, some of the activities are out of the scope of this particular initiative and outside the scope of MVA's influence. There are also some actions that are primarily related to the improvement of general framework conditions to create more favorable conditions for cross-border collaboration in general. These conditions cannot directly be changed in the present initiative, but a strong community can actively advocate for these matters on the national level on the Danish and Swedish side, respectively, with MVA as a neutral platform. Some suggestions for actions are outlined below.

Next steps

This paper has outlined the vision for what the structural biology ecosystem in Medicon Valley could be like in 2025. It also highlights some of the challenges and gaps towards getting there. The action plan outlines some of the actions, which can be initiated. Before it is possible to start developing this further, the next-step premise is that additional funds need to be raised by the key stakeholders.

	ACTIVITY	MAIN DRIVER
EDUCATION	Increase collaboration in research and education between DEN-SWE	Universities
	Increase flow/mobility of students., e.g. Ph.D. research school	Universities
	Joint M.Sc. in structural biology	Universities
	Summer school programs within structural biology (e.g. similar to the Niels Bohr International Academy which since 2011 has held an annual graduate Copenhagen Summer School on ESS science with shifting content).	Universities
	Talent management programs, creating role models/ mentors	Universities
SKILLS AND **COMPETENCES**	Data analysis competences, e.g. bioinformatics	Universities
	Computational chemistry – recruitment at universities necessary + involvement of software companies	Universities
NETWORK **ACTIVITIES**	Network activities where experts meet scientists to facilitate knowledge-sharing and create collaboration possibilities (build on existing networks)	MVA
	Annual structural biology "retreat": gather 150-200 top-level researchers (from both aca-demia and industry) and Ph.D. students for 2-3 days with keynote speakers. Should be a scientific program but also lots of time for networking.	MVA
COMMUNI-CATION AND **BRANDING**	Cases on how structural biology can be used in industrial R&D (ongoing)	Universties Public org.
	Web-based community (mapping of academic research and commercial structural biology service companies, information on techniques, calendar with events and courses, coordinating teaching/courses, post events and job openings, inventory of infrastructure)	MVA
	Develop material that promotes what can be done at MAX IV/ESS (Ongoing)	Universties Public org.
	Attract relevant conferences in the region: e.g. Inter-national Union of Crystallography (IUCR) meetings, or International Conference on Biology and Synchrotron Radiation (BSR)	MVA Universities
	Press activities/public affairs activities – list of demands for politicians	MVA
	General branding of the research field and Medicon Valley	MVA
INFRASTRUC-TURE	Support/service organization to facilitate industrial use	Universities Public org.
	Support/service organization for academics that want to create a spin-off	Universities Public org.
	Create shared ESS / MAX IV labs – utility lab	Science Village
	Work towards establishing a structural biology research institute	MVA
FRAMEWORK **CONDITIONS**	Allow public funding to be used across Danish-Swedish borders	
	Provide necessary proof-of-concept funding	
	Long-term funding for developing the research field, e.g. funds earmarked for structural biology/crystallog-raphy research projects, innovation projects etc.	
	Improved transparency in the IPR system, especially in PPP-projects	

⑥ APPENDIX – STAKEHOLDER MAPPING

The following is a non-exhaustive initial mapping of some of the major stakeholders in Medicon Valley, which are relevant to this initiative. The information is derived from the websites of universities, organizations and projects. Naturally, many more could be included in a stakeholder mapping within structural biology and other stakeholders outside the geographic area of Medicon Valley that are also of relevance. Those stakeholders should be included in a more thorough mapping of the area along with a mapping of the core facilities and other relevant infrastructures in the region.

6.1

Universities in Medicon Valley

The following is a non-exhaustive initial listing of departments/groups within the field of structural biology at the universities in Medicon Valley that focus on life science. Obviously, many other scientific fields are relevant to structural biology, which should be included in a more extensive mapping at a later stage.

6.1.1 Lund University

Medical structural biology,
Experimental Medical Science:
The researchers work on proteins that are the essential players of the acquired immune system, thus proteins that can discriminate between foreign and selfantigens. The main defenders in the acquired immune system are the T cells. Hence, understanding the specificity of the T cell receptor is extremely important. The goal is to retrieve a detailed knowledge of the structure and specificity of super-antigens and T cell receptors, which would be an important contribution to understanding human physiology in health and disease.
http://bit.ly/1w5o6cW

Division of Synchrotron Radiation Research (SLF):
The division of synchrotron radiation research focuses on four main areas of research: Catalysis and surface oxidation; low-dimensional semiconductors; high-pressure x-ray photoelectron spectroscopy; and atomic, molecular and cluster spectroscopy. www.sljus.lu.se

Center for Molecular Protein Science:
Research at CMPS covers the molecular properties, structure, function, and interactions of proteins and other biomolecules. www.cmps.lu.se

Dept. of Biophysical Chemistry:
The aim of many of our research projects is to understand the interactions and dynamics of proteins. We use and develop a variety of biophysical tools, in particular nuclear magnetic resonance (NMR) relaxation techniques. www.cmps.lu.se/bpc

Dept. of Biochemistry and Structural Biology:
The focus of our research is within some major areas of modern biochemistry and molecular biology. These include membrane protein structure and function; enzyme structure and function; molecular interactions and molecular assemblies; bio-electrochemistry; RNA, DNA and viruses; structural biology of enzymes and large macromolecular assemblies. www.cmps.lu.se/biostruct

Protein Structure and Bioinformatics Group:
The Protein Structure and Bioinformatics (LU PSB) develops methods and performs analyses to understand biological and medical phenomena at structural, functional, mechanical and systems level.
http://structure.bmc.lu.se/

Lund Protein Production Platform, LP3:
A cross-faculty facility for protein production and isolation at Lund University. LP3 aims to provide a high quality recombinant protein production service, as close to cost price as possible, primarily to academic research groups based at Lund University. The service facility is integrated with research training and the development of skills in experimental protein science for PhD students and postdocs.
http://bit.ly/1v74Tr2

6.1.2 University of Copenhagen

Biophysical and bioinorganic chemistry, Dept. of Chemistry:
The research interests of the crystallographers in the BBC section span many aspects of crystallography, from method development to studies of inorganic and organic compounds and large biological macromolecules (protein, protein-protein and protein-DNA complexes).
http://bit.ly/1ESsDDM

X-Ray and Neutron Science, Niels Bohr Institute:
The X-Ray and Neutron Science Section is responsible for education and research on structural physics using X-ray and neutron based methods, on materials physics and magnetism, and on biophysics and health-physics using isotope techniques. Large efforts are within instrument design and simulation, related to the ESS project. In this department, the pilot project NXUS is also running. NXUS is searching for cases from the life science industry, where the technique small-angle scattering can contribute to solving a problem by providing valuable knowledge on the structure of e.g. colloids or protein complexes. Experiments and data analysis will be performed at no charge by scientists from the structural biophysics group at the Niels Bohr Institute, KU, who in return, will obtain valuable insight and information for a possible service portal for industry in the future. The NXUS-project runs from September 2013 to May 2015.
http://xns.nbi.ku.dk/ and www.nxus.dk

Biostructural Research, Dept. of Drug Design and Pharmacology:
We determine the three-dimensional structures of biological macromolecules, including membrane proteins and protein complexes, and study the relationship between their structure and function. Our research forms the basis for the design of new drug molecules that are uniquely adapted to the three-dimensional structure of individual receptors, enzymes, transport molecules and other proteins implicated in diseases.
http://bit.ly/1qZU6sN

Copenhagen Small-Molecule NMR Centre:
a national leading facility for advanced bioanalytical NMR spectroscopy of small molecules.
http://bit.ly/ZXEkJB

Protein Biology Group, Dept. of Biology:
The Protein Biology Group (PBG) is part of the Section for Biomolecular Sciences and is composed of four subgroups with a common interest in protein structure-function relationships. Our aim is to bridge quantitative protein chemistry and cell biology by strong research within the fields of protein folding, protein-protein interactions and protein quality control in the cell.
http://bit.ly/1p8dDYh

SBiNLab (Structural Biology and NMR Laboratory):
The research and teaching programs of the laboratory are focused on the structural biology of proteins. Structural Biology of proteins is a discipline of science aiming towards understanding the correlations between the molecular structure and function of proteins, which are the vital engines of the biological cell factory. A wide selection of techniques is implemented at the laboratory including NMR spectroscopy, optical spectroscopy, protein engineering, bioinformatics and molecular biology.
http://bit.ly/1tZcwf3

Novo Nordisk Foundation Center for Protein Research:
The Center comprises a wide range of expertise and skills within its research departments, with activities in the areas of disease systems biology, proteomics, high throughput protein production and characterization, chemical biology, disease biology, and protein therapeutics. The Center will also contribute to the progress of translational research within medicine and provide fundamental insights, which can be used to promote drug discovery and development.
www.cpr.ku.dk

6.1.3 Technical University of Denmark

Physical Chemistry, Dept. of Chemistry:
Understanding the structure and behavior of chemical and biological systems is the main focus of the Physical Chemistry section. The research reaches from the smallest molecules up to large biological systems. Typical tools include scientific computing, X-ray scattering from conventional, synchrotron and free electron laser sources, spectroscopy, and chemical analysis. The section has two main focus areas, which are biophysical chemistry and femtosecond chemistry.
http://bit.ly/1veQKtt

NEXMAP, Dept. of Physics:
The NEutrons and X-rays for MAterials Physics section – NEXMAP – focuses on gaining knowledge on fundamental properties of materials through scattering experiments conducted at Large Scale Neutron and X-ray facilities around the world. Together with advanced modeling and analysis methods this opens unique possibilities for establishing links between the structure, dynamics and functioning of materials.
http://bit.ly/1ESuvfA

Computational Chemical Biology, Center for Biological Sequence Analysis (CBS), Dept. of Systems Biology:
The Computational Chemical Biology group at CBS focuses on the study of the interplay between small molecules and biological systems. The group holds expertise in molecular modeling, machine learning, chemo-informatics and systems chemical biology.
http://bit.ly/1ESuFnl

Enzyme and Protein Chemistry, Dept. of Systems Biology:
EPC applies expertise in protein structure, function, engineering and functional proteomics to unravel the molecular basis for functionality and interactions of components in biological systems and biotechnological processes.
http://bit.ly/1vZun9e

6.1.4 Malmö University

Biointerface, Biofilms
Research Center for Biointerfaces:
The core activity in the group is the interplay between interfaces and biological material and the research hence includes molecular and cellular interactions at interfaces. Examples of application areas are use and development of medical implants, contact lenses, and catheters or analysis, diagnostic and treatment methods that involve surface interactions. Studies of biological interfaces, i.e. molecular structures, interactions with and transport through for example the intestine, skin and artery walls are therefore a central theme.
http://www.mah.se/brcb

6.2

Industry

According to previous mappings of the life science industry and the usage of large-scale facilities, few industry players in the region in fact use structural biology in their R&D (Engmark, n.d.). In fact, only larger pharmaceutical companies utilize structural data in their research and have people employed that work with structural biology, while the smaller companies have not sought information nor discussed the possibilities internally.

There are a few contract research organizations (CROs) which offer services to companies that use structural information in their R&D (e.g. SARomics Biostructures AB, Colloidal Resources AB etc.). There is most likely a huge economic growth potential if CROs, who are experts in designing, executing and analyzing experiments for life science companies, establish themselves in the region.

6.3

MAX IV Laboratory

MAX IV Laboratory is a national laboratory operated jointly by the Swedish Research Council and Lund University. MAX IV Laboratory is a synchrotron radiation facility producing x-rays of high intensity. The facility currently consists of three storage rings: MAX I, MAX II and MAX III. The construction of the next generation, MAX IV, is ongoing and will be open to users in the summer of 2016. MAX IV will be the brightest synchrotron X-ray source in the world.

The MAX IV will consist of two storage rings: (1) a smaller ring with a circumference of 96 meters and an electron energy of 1,500 MeV and (2) a bigger ring with a circumference of 538 meters and an electron energy of 3,000 MeV. The electrons will be accelerated in a linac accelerator (250 meters long, maximum 3,400 MeV). What makes MAX IV different from the current storage rings is that MAX IV will be injected at full energy, which means that the rings can be filled with electrons continuously and thus be at a constant maximum 24/7.

The budget for MAX IV of approx. EUR 330 million excludes the construction of beamlines, which must be financed individually as well as the future operational costs. MAX IV can hold up to 26 beamlines. The financed beamlines are currently:

- BioMAX: multipurpose high throughput beamline for macromolecular crystallography
- VERITAS: soft X-ray Resonant Inelastic X-ray Scattering (RIXS)
- HIPPIE: high pressure X-ray photoelectron spectroscopy (HP-XPS), high pressure X-ray absorption spec-troscopy (HP-XAS) as well as XPS and XAS in ultrahigh vacuum
- NanoMAX: a hard X-ray beamline for micro- and nanobeams
- FemtoMAX: a hard X-ray beamline at the short-pulse facility
- APRES: angle resolved photo electron spectroscopy
- BALDER: in-situ hard X-ray spectroscopy
- FinEstBeaMS: VUV and soft X-ray spectroscopy
- SPECIES: VUV high-pressure photoelectron spectroscopy and RIXS (transfer from MAX III)
- FlexPES: photoelectron spectroscopy and NEXAFS (transfer from MAX III)
- MAXPeem: photo emission electron microscopy (transfer from MAX III)
- CoSAXS: SAXS (small-angle X-ray scattering) to study structure and dynamics on the nanoscale
- SoftiMAX: coherent soft X-ray microscopy and imaging

In addition, there are suggestions for other beamlines, but these are not funded yet:

- MicroMAX: a microfocus beamline for macromolecular crystallography
- MedMAX: a biomedical imaging beamline
- DiffMAX: a beamline for powder diffraction
- iMAX: a nano-to-micro-scale full-field imaging beamline

More information: www.maxlab.lu.se

6.4

European Spallation Source (ESS)

The ESS in close vicinity to the MAX IV in Lund will be a facility for research using neutron scattering techniques, and it will be the world's most powerful source of neutrons for science. The facility is a partnership between 17 European countries. The total budget for the construction of the facility is estimated at EUR 1.8 billion of which 50 % will be financed by Sweden, Denmark and Norway. The remaining 50 % will be financed by other European countries and negotiations are ongoing. The current plan is to break ground during 2014 and to have the first neutrons and the first instruments installed by the end of the decade, with construction continuing until the facility is at full power and a suite of 22 instruments is installed. The construction of the facility is expected to be completed by the year 2025.

The ESS will provide precise structural and dynamic information of molecular structures and their functionalities in hard, soft and biological materials. The facility can be used for a wide range of disciplines such as physics, material sciences, biology, chemistry, pharmacology, nanotechnology and also disciplines such as geology and archeology/cultural heritage studies.

There are many existing neutron facilities around the world (e.g. SNS, Oak Ridge, Tennessee, US; J-PARC, Tokai, Japan; Paul Scherrer Institute, Switzerland; Institute Laue Langevin, Grenoble, France; ISIS, UK), but what will make the ESS unique is that it will be much more powerful measured in the number of neutrons generated. The facilities in Japan and the US have an average accelerator beam power of 1-1.5 megawatt, while the ESS is expected to have a power of 5 megawatt. Furthermore, the ESS will produce long neutron pulses, which creates flexibility in instrument and experiment design. The improved performance of the ESS will entail that experiments can be done much quicker and it will be possible to examine much smaller sample sizes, which favors experiments with biological samples, as the sample quantity if often a problem (Styrelsen for Forskning og Innovation, 2011).

There are 22 instruments in the ESS baseline, and the facility will be constructed with room for more. Currently, three instruments (Broad-Band High Flux SANS; Macromolecular Diffractometer; and Multi-Purpose Imaging) have been approved to commence towards construction, 16 more instruments are currently under consideration, and more proposals are expected in the next few years. In the initial planning phase, a "reference instrument suite" was drafted in which 22 instruments were suggested. Of those 22 instruments, at least 5-7 of the instruments are highly relevant for use in life science and will be able to investigate e.g. protein domain motions, protein complexes, protein-protein interactions, biological membranes, membrane dynamics, enzyme mechanisms, etc.

The ESS data management and software center will be located at the Niels Bohr Institute at the University of Copenhagen. It is expected that the data management center will employ approx. 60 people. Data management will be of great importance for these types of experiments, as they generate large amounts of data that has to be analyzed (this also the case at synchrotrons). Advanced techniques and data management methods must thus be applied to deduce information about the structure of the specific sample.

The center will collect, store and analyze the large amounts of data derived from the experiments at the ESS facility in Lund. In addition, the ESS-DMSC should drive activities such as the simulation of experiments, the development of hypotheses, visualization and analysis of data and develop analysis tools to facilitate the use of the ESS.

More information:
http://www.europeanspallationsource.se
http://www.ess-dmsc.eu

6.5

Related initiatives

A number of initiatives have been funded, primarily by the public sector, in order to ensure that the region reaps the full benefit of heavy investments in infrastructure. The short descriptions below are from the projects' own communication materials and websites.

6.5.1 ESS & MAX IV as growth engines for the Capital Region of Denmark

"ESS and MAX IV as growth engines for the Capital Region of Denmark" is a partnership designed to gear the capital region to exploit the significant growth potential related to the establishment of ESS and MAX IV in Lund and XFEL in Hamburg. The project will utilize the facilities as growth engines to strengthen the research and innovation capacity at universities and companies and to increase the region's ability to attract international labor and development departments. The project budget is DKK 26.6

million and is cofunded by the Capital Region Growth Forum and the European Regional Development Fund. It includes the following partners: the Technical University of Denmark, University of Copenhagen, the Capital Region of Denmark, City of Copenhagen, Lyngby-Taarbæk City of Knowledge & Urban Development, Copenhagen Capacity, Scion DTU, COBIS, and the Confederation of Danish Industry.

The project has five focus areas:

- **Attraction of international labor a nd companies**
- **Identification and preparation of suppliers for ESS and MAX IV**
- **Mappings of applications and best practice**
- **Bridging the gap between business, universities, and the ESS, MAX IV and XFEL**
- **General education, study visit programs, and teaching packages**

Among other things, the activities in the project have led to the creation of a 3D imaging center at DTU. The imaging portal offers consulting, technical support and data analysis related to 3D imaging. Researchers with a specific scientific question will be able to receive free-of-charge test runs at the facilities at the imaging center or at existing large-scale facilities. By offering such test runs, the aim is to prepare the industry for using the future possibilities created by ESS and MAX IV.

A mapping of potential applications has been conducted, including a mapping of applications for the life science industry. Among other things, the mapping report concludes that the larger companies are looking forward to the opportunities that the ESS and MAX IV will offer. On the contrary, the smaller companies have not yet included the facilities in their R&D planning due to the extended time horizon before the facilities (namely the ESS) are in place and a lack of knowledge of the opportunities that the facilities will bring about.

More information:
http://www.imaging.dtu.dk/Industriportal.aspx
Project period: 2012-2014

6.5.2 ESS & MAX IV as growth engines for the Oresund region and the ÖKS-area

Region Skåne and the Capital Region of Denmark have received financing from the Interreg Program to conduct the pre-project "ESS and MAX IV as growth engines for the Oresund region and the ÖKS-area". An important aspect of the project is to include all relevant actors as stakeholders and/or as actual project partners in a future Inter-reg project. The activities in the pre-project will primarily take the form of a number of process activities, which are intended to ensure a shared overview and status in terms of themes to focus on and the partners to include. An important part of the pre-project will be to support the process of formulating new cross-border efforts by including various stakeholders (universities, public administration, organizations and companies). The overall aim of the project is to prepare a joint and coordinated effort across the Oresund region with the purpose of exploiting ESS and MAX IV as growth engines for the Oresund region. The concrete goal of the project is to hand in an Interreg project application in late 2014.

The preliminary indications are that the coming project will have a broad scope with four work packages:

- **Academia-industry collaboration (i.e. industrial use of the facilities and suppliers of products and services during construction)**
- **Research and education within regional strongholds**
- **Reception of international labor and cross-border obstacles**
- **International attractiveness**

The project team is aiming for a large project with many partners and has a broad scope with focus on all the disciplines related to industries applied at the Max IV and the ESS (e.g. construction, materials, life science, food etc.).

More information:
http://bit.ly/1w3Twi6
Project period: Nov. 2012-Sep. 2014

6.5.3 ESS MAX IV in Southern Sweden – TITA

ESS MAX IV in Southern Sweden – TITA. TITA is the acronym for the Swedish words for growth, innovation, accessibility and attractiveness. The purpose of the project is to use the establishment of the research facilities to stimulate growth, strengthen the innovation structure and promote accessibility and attractiveness in the region.

The project was launched in January 2010 and completed in December 2012. The TITA project was a Swedish project that included Region Skåne, the municipalities in Skåne, Lund University, Invest in Skåne, ESS AB, Malmö University, the County Administrative Board of Skåne, Kristianstad University, Region Blekinge, Swedish University of Agricultural Science and Blekinge Institute of Technology. The TITA project had a budget of approx. EUR 5.3 million.

Five strategies were developed in order to guide, mobilize and inspire stakeholders to continue the work of regional mobilization around the upcoming research facilities:

- **Build a region which is strong in education**
- **Create dynamic research environments**
- **Increase accessibility throughout the region**
- **Develop the international attractiveness of the region**
- **Enhance the competitiveness and innovative capacity of the business sector**

These strategies are to be developed further in various future projects, e.g. in the Interreg pre-project mentioned above.

6.5.4 Øresund Materials Innovation Community (ØMIC)

The Øresund Materials Innovation Community (ØMIC) is an EU Interreg IV project, aimed at developing a strong and dynamic innovation environment within material sciences (hard, soft and biological materials) in the Øresund region. The project included the following seven work packages:

- **Community building and communication**
- **Education planning**
- **Early business planning**
- **Knowledge sharing in science parks**
- **Regional branding**
- **Bibliographical investigation**
- **Future planning**

According to the EU Interreg website, the project did not reach its goal of a strategic coordination of the region's activities, mainly because of the abandonment of the joint Oresund University. Instead, the project focused on creating closer collaboration between stakeholders that had specific interests within topics related to ESS and MAX IV. Thus, the main activities were meetings, seminars and training for scientists, students and companies.

More information:
www.oresund.org/materials
Project period: Oct. 2009-Jul. 2010 (Phase 1) / May 2010-Dec. 2012 (Phase 2)

6.5.5 Science Village Scandinavia

Lund University, City of Lund and Region Skåne have formed Science Village Scandinavia AB. The vision is to develop Science Village Scandinavia into an infrastructure supporting the new facilities ESS and MAX IV in the area between the locations where the two facilities are under construction. Together they shall form an exciting and creative world-class research and innovation village, as well as an international area for sustainable urban development. Construction is scheduled to begin during 2014.

Science Village Scandinavia will consist of buildings aimed at research facilities, research institutes, research institutes for Lund University and other universities, companies related to innovation and research, a Science Centre and Business Centre, premises for laboratories, administration, service and accommodation. There will also be service functions such as restaurants, cafes, shops, gyms and other spaces for recreation and culture, and furthermore a variety of various creative venues.

More information:
www.sciencevillage.com

6.5.6 Science Link

Science Link is a network between leading research facilities of photon and neutron sources and their users. The project aims to support and encourage innovation and entrepreneurship in the Baltic Sea Region. Apart from the research facilities, the network also includes scientific institutes, universities and regional organizations that serve as service and promoting units. Science Link is partfinanced by the European Union (Baltic Sea Region Program) and involves 17 partners from eight countries.

More information:
www.science-link.eu
Project period: 2012-2014

6.5.7 Cluster for Accelerator Technology (CATE)

CATE will offer companies in the region a competence development program within accelerator technology, which in the long run will give the companies better opportunities to get contracts for the construction and maintenance of research facilities demanding advanced accelerator technology equipment. The purpose of the competence program is to offer companies free, tailor-made courses. Some companies in the project will also get the opportunity to build an accelerator module in collaboration with other companies, universities and CERN experts. The cue will be learning by doing. A project objective is also to spread the knowledge of business opportunities within the accelerator technology industry.
The project is cofinanced by the EU Interreg IV and the following project partners: Aarhus University, Roskilde University, Chalmers University of Technology, Business Development Centre Central Denmark (Væksthus Midtjylland), Region Västra Götaland, Region Skåne, Region Sjælland, Force Technology, DTU/Risö.

More information:
www.cateproject.se
Project period: Jan. 2011-Jun. 2014

6.5.8 Danish Centre for the use of Synchrotron X-ray and Neutron facilities (DanScatt)

The Danish Centre for the use of Synchrotron X-ray and Neutron facilities (DanScatt) is a Danish Research Council center with the aim to support Danish scientists and students performing research involving X-ray and neutron scattering.
http://bit.ly/1v79r0E

6.5.9 CoNEXT (University of Copenhagen)

The project will strongly intensify neutron and x-ray based research at the university through several interfaculty collaborations that will lead to a great increase in the number of users of large facilities coming from the University of Copenhagen. The majority of the project will be used for financing the education of young scientists (PhD students and postdocs in the use of neutron and x-ray sources).

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MEDICON VALLEY
BEACONS

The Medicon Valley Beacons is an initiative to create a handful of world-class research environments, known as Beacons, in the Danish-Swedish life science cluster, Medicon Valley.
The Medicon Valley Beacons cover the following areas: Immune regulation – Structural biology – Systems biology – Drug delivery – Independent living