

BIOSTRUCTURAL ACTIVITIES IN MEDICON VALLEY

- a Medicon Valley Academy project

by:

Robert Bywater, Novo Nordisk

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Torbjørn Drakenberg, Fysikalisk kemi, Lund Universitet

Flemming Poulsen, Carlsberg

BIOSTRUCTURAL ACTIVITIES IN MEDICON VALLEY

NATIONAL AND REGIONAL CENTERS

The MAX laboratory

The Swedish national synchrotron laboratory. The laboratory has one experimental station for crystallography.

Contact person:

Anders Svensson, Molecular biophysics, Lund University.

phone: +46 46 222 4512, fax: +46 46 222 4692,

e-mail: Anders.Svensson@mbfys.lu.se

Danish NMR-center

Danish instrument center for NMR studies of biological macromolecules.

Gamle Carlsberg Vej 10, DK-2500 Valby, Denmark

Contact person:

Flemming M. Poulsen, phone: +45 33 27 53 48, fax: +45 33 27 47 08,

e-mail: fmp@crc.dk, <http://www.crc.dk>

Risø National Laboratory

The Danish national laboratory for neutron scattering.

Frederiksborgvej 399, P.O.Box 49, DK-4000 Roskilde, Denmark

Contact person:

Kell Mortensen, phone: +45 46 77 47 10, fax: +45 46 77 47 90

e-mail: Kell.Mortensen@risoe.dk, <http://www.risoe.dk>,

<http://www.nbi.dk/BIOPHYS/>

RESEARCH ACTIVITIES

BIOINFORMATICS

**Center for Biological Sequence Analysis
Department of Biotechnology, Technical University of Denmark,
Building 208,
DK-2800 Lyngby, Danmark**

Contact person:

**Søren Brunak, phone: +45 45 25 24 77, fax: +45 45 93 15 85,
e-mail: brunak@cbs.dtu.dk, <http://www.cbs.dtu.dk>**

Research activities:

The Center for Biological Sequence Analysis conducts basic research in bioinformatics a rapidly growing area in the field of molecular biology. The overall goal of the research is to obtain knowledge of the complex relations between sequence composition - the content and order of the chemical building blocks - and macromolecular structure and function. In addition, the research is aimed at creating entirely new possibilities in the study of evolutionary processes by comparison of sequence patterns across species.

The tremendous growth in the amount of sequence and structure data has brought about a radical change in the possibilities of developing powerful computer methods for classification, prediction and comparison of molecular structure and function. The work of the center is especially focused on novel data driven computational methods, such as artificial neural networks and hidden Markov models. The center is hosting a PhD course, which has been attracting many students from Medicon Valley. The group is interested in establishing new projects with experimental groups. CBS is organised into four smaller groups each headed by an associate professor: (1) DNA/RNA structure and function, (2) Protein 3D structure, (3) Protein function, and (4) Comparative sequence analysis.

Present number of staff:

20-25 (incl. technicians and administrative staff)

Collaborations with groups in Medicon Valley (examples):

S. Buus, University of Copenhagen, Copenhagen, Denmark

A. Fomsgaard, State Serum Institute, Copenhagen, Denmark

J. Hertz, Nordita, Copenhagen, Denmark

I. G. Clausen, Novo Nordisk A/S, Bagsværd, Denmark

P. Warthø, Display Systems A/S, Copenhagen, Denmark

**B. Vabø, Structural Bioinformatics Advanced Technologies A/S,
Hørsholm, Denmark**

J. Bohr, Technical University of Denmark, Lyngby, Denmark

S. Gammeltoft, Glostrup Hospital, Glostrup, Denmark

ASTRA DRACO AB
Astra Draco Bioinformatics
P.O. Box 34, SE-221 00 Lund, Sweden

Contact person:

Bo Servenius, phone: +46 46 337 372, fax: +46 46 337 180
e-mail: bo.servenius@draco.se.astra.com, <http://www.astra.com/draco/>

Research activities:

Within Astra we are establishing a network of bioinformatics center to facilitate the support needed at each research site as well as bringing together a critical mass necessary for the development of bioinformatics. One of the nodes in this network and where most of the bioinformatics work within Astra has hitherto been done, has been established at Astra Draco in Lund since 1996. Our main focus has been to establish a series of databases with sequence and genemapping information and the infrastructure necessary to use these. We have implemented a series of analysis packages and in house developed some tools and interfaces, mostly using Java and C-programming. Most tools can be used with a webinterface. In the near future we plan to integrate functional genomics data from microarrays etc.. We are also interested in integration of biological information from pharmacology studies, toxicology testing and clinical trials by use of database mining techniques, and in general knowledge management techniques. We are actively searching for collaboration in these areas as well as in more strictly bioinformatics techniques.

Astra Draco Bioinformatics has close contacts with bioinformatic activities at Lund university, international bioinformatics efforts such as projects at European Bioinformatics Institute as well as national and international bioinformatics efforts within academia. We are also an industrial mentor for the newly started biocomputing educational program at University of Skövde.

Present number of staff:

3

Collaborations with groups in Medicon Valley (examples):

Anders Liljas, Lund University, Lund, Sweden
Søren Brunak, Technical University of Denmark, Lyngby, Denmark

NOVO NORDISK A/S
Health Care Discovery, Bagsværd

Novo Alle, DK-2880 Bagsværd, Denmark

Contact person:

Henrik Vissing, phone: +45 44 42 69 78

e-mail: hv@novo.dk, <http://www.novo.dk/>

Research activities:

Bioinformatics research at Novo Nordisk is focused on the following main areas:

- Maintaining in-house sequence databases and search tools.
- Genome database mining for new targets.
- Protein sequence alignment in connection with homology modelling and other for structural biology needs.
- Proteomics
- Participation in BioStandards at EBI, Cambridge.

Present number of staff:

10

Collaborations with groups in Medicon Valley : ---

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COMPUTATIONAL BIOCHEMISTRY

Complex Systems Group

Department of Theoretical Physics, Lund University

Sölvegatan 14A, SE-223 62 Lund, Sweden

Contact person:

Anders Irbäck, tel: +46 46 222 3493 fax: +46 46 222 4438

e-mail: irback@thep.lu.se, <http://thep.lu.se/tf2/complex>

Research activities:

The Complex Systems Group, Lund University is engaged in a number of theoretical physics, applied mathematics and algorithm development projects. One major area is protein folding. Our activities in this field have so far been focused on:

- 1. Statistical-mechanical studies of coarse-grained models. Analysis of the folding properties of simple hydrophobic/hydrophilic models. Identification and characterisation of amino-acid sequences with good**

folding properties. Predictions of folding properties given the hydrophobicity pattern, using artificial neural network methods.

2. The understanding of the non-randomness of functional protein sequences. Statistical analyses of functional sequences based on existing data bases. In particular, it was shown that hydrophobic amino acids are anticorrelated along the chains for a large group of proteins.

3. Computational methods. Development of algorithms for simulations of systems with a rugged energy landscape. Design of sequences that are thermodynamically stable in a given target structure.

Present number of staff:

10

Collaborations with groups in Medicon Valley: ---

Department of Theoretical Chemistry
Lund University, P.O. Box 124, SE-221 00 Lund, Sweden

Contact person:

Ulf Ryde, Tel: +46 46 222 4502, Fax: +46 46 222 4543

e-mail: teoulf@garm.teokem.lu.se, <http://garm.teokem.lu.se/~teoulf>

Research activities:

The department has in essence four areas of applied research:

1. Spectroscopic applications of the CASPT2 method.

This method has for the first time made it possible to calculate electronic spectra of small and medium-sized molecules to an acceptable and reproducible accuracy. It has been used for over 80 organic and inorganic molecules, including indole, magnesium porphyrin, and retinal.

2. Biochemical applications.

Application of all available theoretical methods (ab initio, density functional, semiempirical, Monte Carlo, molecular dynamics, free energy perturbation, solvation models, etc.) on systems of biological interest. Examples of applications are: determination of the coordination number of the active-site zinc ion in alcohol dehydrogenase, interpretation of PAC experiments on the same enzyme, the relation between structure, function, and of the blue copper proteins, the discrimination between CO and O₂ by myoglobin, and interpretation of mutation studies in lactate dehydrogenase. The applications have also lead to some method developments, e.g. a combined quantum chemical and molecular mechanical geometry optimisation program, routines for estimation of point-charge models, and force-field parameterisations.

3. Theoretical chemistry in solution.

The development of quantum chemical methods in the solvent, using dielectric cavity models and Langevine dipoles, and the construction of accurate intermolecular potentials derived entirely from quantum chemical calculations (NEMO). The potentials are intended to be used in molecular dynamical and Monte Carlo simulations and they give a much higher accuracy than potentials used in standard biochemical applications. Up to now, only smaller molecules has been treated, such as water, urea, and formamide, but now the method is so well developed that it is only a question of time before potentials for all amino acids have been determined.

4. Chemistry of transient species.

Accurate quantum chemical characterisations on unstable or short-lived molecules, e.g. intermediates in the Bergman reaction as a model of enediyne anti-cancer drugs and characterisations of femtosecond reactions.

Present number of staff:

23 (incl. 3 technicians).

Collaborations with groups in Medicon Valley (examples):

R. Bauer & L. Hemmingsen, Dept. Mathematics and Physics, The Royal Veterinary and Agricultural University, Copenhagen, Denmark

K. Mikkelsen, Dept. Chemistry, HC Ørsted Institute, Copenhagen, Denmark

P.-O. Aastrand, Condensed Matter Physics and Chemistry Dept., Risø National Laboratory, Roskilde, Denmark

Statistical Mechanics Group

Physical Chemistry 2, Chemical Center, Lund University, Sweden

Contact person:

Bo Jönsson, phone: +46-46-2228239 fax:+46-46-2224543

e-mail: Bo.Jonsson@fkem2.lth.se, <http://www.fkem2.lth.se/stmech/>

Research activities:

Electrostatic Interactions in Biomolecules

A continuum model has been devised to study salt effects, mutations and pH changes in the binding properties and redox behavior of proteins in solution. The simulations provide a number of free energy derivatives with high precision and generally in good agreement with experiment. The technique has been applied to the calcium binding

proteins calbindin and calmodulin and the copper containing redox proteins azurin and plastocyanin.

Molecular Simulation of Complex Systems

Molecular Dynamics simulations are used for the refinement of conformational information obtained from NMR experiments. Small proteins and oligopeptides are studied and special algorithms have been developed for this purpose. Another project investigates the hydrophobic interaction between two inert surfaces in aqueous solution. We have shown that the traditional Lifshitz expression predicts a too weak attraction at short and intermediate separation.

Algorithms for Numerically Intensive Computations

The research group participates in LUNARC with the aim of developing efficient simulation programs. Special efforts are spent on the parallel use of clustered work stations.

Present number of staff:

6 (4 graduate students)

Computational Chemistry Group

Department of Medicinal Chemistry, Royal Danish School of Pharmacy
Universitetsparken 2, DK-2100 Copenhagen Ø, Denmark

Contact person:

Tommy Liljefors, phone: +45 35 37 67 77 ext 505, +45 35 37 08 50,
fax: +45 35 37 22 09

e-mail: tommy@medchem.dfh.dk, <http://compchem.dfh.dk>

Research activities:

The research activities of the Computational Chemistry group at Department of Medicinal Chemistry, Royal Danish School of Pharmacy include all areas of computational chemistry and computer-aided molecular design. Current focus is on the use of computational methods in studies on molecular recognition and structure-activity relationships, in particular for agonists and antagonists at neurotransmitter receptors. 3D-pharmacophore models for the dopamine D-2 and serotonin 5-HT_{2A} receptors have been developed and successfully used in computer-aided ligand design. Studies towards pharmacophore models for dopamine D-4, AMPA and GABA-A ligands are in progress. Development and validation of 3D-models (including mutation studies) for G-protein coupled receptors from their amino acid sequences are being developed and are currently applied to subtypes of dopamine receptors. Additional areas of activity includes the development of receptor models for ligand binding to Ca²⁺-ATPase and structure-activity studies on insect sex pheromone

components. Intermolecular interactions of high relevance for agonist and antagonist interactions with neurotransmitter receptors are being studied using high-level quantum chemical ab initio calculations and studies towards improved calculations of the free energy of hydration of highly polar compounds are being pursued.

An additional field of high current interest is computational organometallic chemistry, in particular design of catalysts for asymmetric synthesis.

Present number of staff:

7

Collaborations with groups in Medicon Valley (examples):

K. Gundertofte and K. Bøgesø, H. Lundbeck A/S, Copenhagen, Denmark

M. Nielsen, Sankt Hans Hospital, Roskilde, Denmark

O. Sterner, Organic Chemistry 2, Lund University, Sweden

D. Tanner and T. Rein, Technical University of Denmark, Lyngby, Denmark

B. S. Hansson, Department of Ecology, Lund University, Sweden

M. Treiman, the Panum Institute, Copenhagen, Denmark

F. Björkling, Leo Pharmaceuticals, Copenhagen, Denmark

K. Wärnmark, Organic Chemistry 1, Lund University, Sweden

Molecular Modelling Group

Department of Medicinal Chemistry, Royal Danish School of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen Ø, Denmark

Contact person:

Flemming Steen Jørgensen, phone: +45 35 37 08 50 ext 378, Fax +45 35 37 22 09

e-mail: flemming@medchem.dfh.dk, <http://dfhmac.dfh.dk/mm>

Research activities:

The molecular modelling group was established in 1984 by support from the Danish Technical Research Council. During the following decade the group pioneered the propagation of computer-based methods for studying the relationships between molecular structure and biological activity in Denmark. A considerable number of students have been educated within this area since 1984. Today the research activities focus on studies on interactions between drug related molecules and their biological targets (enzymes and receptors). Considerable expertise has been accumulated on conformational analysis of flexible compounds, homology building of proteins and

calculations on protein-ligand interactions. Together these methods constitute an integrated tool for design of new or improved drugs - Structure-Based Molecular Design.

The methods are applied within projects of pharmaceutical relevance. In order to explain selectivity and resistance three-dimensional models of enzymes related to inflammation (phospholipase A2 and 5-lipoxygenase) and malaria (dihydrofolate reductase from the malaria parasite) have been constructed and studied. New methods for prediction of the passive transport of drug-related molecules across biological membranes are being developed. These methods include effective semi-automatic procedures for conformational analysis and calculation of physico-chemical properties. The group is well equipped with computer facilities and uses a number of state-of-the-art software tools for its activities. Several of the research activities are carried out in collaboration with industrial research groups in the Øresund region.

Present number of staff:

4 (incl. 1 master student).

Collaborations with groups in Medicon Valley (examples):

Astra Draco AB, Lund, Sweden

Novo Nordisk A/S, Måløv, Denmark

ASTRA DRACO AB

Computational Chemistry and Chemometrics, Dep. of Medicinal Chemistry

P.O. Box 34, SE-221 00 Lund, Sweden

Contact persons:

Michael Bodkin (CC), phone: +46 46 336 219, fax: +46 46 337 119

e-mail: michael.bodkin@draco.se.astra.com, <http://www.astra.com/>

Fredrik Lindgren (Chemometrics), phone: +46 46 336 814, fax: +46 46 337 119

e-mail: fredrik.lindgren@draco.se.astra.com, <http://www.astra.com/>

Research activities:

Computational chemistry plays a central role at Astra Draco and is a well integrated function in all pre-clinical research projects. A wide variety of computational techniques are employed to help chemists target novel structures for future synthesis. If the molecular target is known, techniques like homology building, protein-ligand modelling and de novo design are used. Equally important is the close collaboration with combinatorial chemistry on library design and evaluation. In a near future, docking algorithms will allow automatic screening of libraries of

compounds that are either virtually or commercially accessible. Multivariate data analysis is an area of computational chemistry that uses the broad physico-chemical characterisation of drug candidates to rationalise their pharmacokinetic and metabolic properties. QSAR models are developed to understand phenomena such as oral absorption. Other chemometric approaches such as experimental design are used to optimise and validate the biological screening assays before entering a HTS campaign. All software application are running on SGI-machines.

Present number of staff:

2

Collaborations with groups in Medicon Valley (example):

F. Jørgensen, Royal Danish School of Pharmacy, Copenhagen, Denmark

LEO PHARMACEUTICAL PRODUCTS

Industriparken 55, DK-2750 Ballerup, Denmark

Contact person:

Fredrik Björkling, phone: +45 44 94 58 88, fax: +45 44 94 55 10

e-mail: fredrik.bjorkling@leo.dk

Research activities:

The Computational Chemistry at Leo is directed towards the design of novel ligands for pharmaceutical use. Computational methods are used in studies of molecular recognition and structure-activity relationships as well as pharmacophore modelling and studies of ligand-receptor interactions.

Present number of staff:

2

Collaborations with groups in Medicon Valley (example):

P. O. Norrby, Royal Danish School of Pharmacy, Copenhagen, Denmark

LUNDBECK A/S

Ottiliavej 9, DK-2500 Valby, Denmark

Contact person:

Klaus Gundertofte, phone: +45 36 30 13 11, fax: +45 36 30 13 85

e-mail:kgu@lundbeck.com, <http://www.lundbeck.com>

Research activities:

The Department is using state-of-the-art techniques in molecular modelling and tools for the assessment of quantitative structure activity relationships and molecular diversity. The aim of the work is to discover new ligands with high affinity for targets in the central nervous system in collaboration with medicinal and combinatorial chemists.

Present number of staff:

5

Collaborations with groups in Medicon Valley (example):

Tommy Liljefors, Royal Danish School of Pharmacy, Copenhagen, Denmark

NOVO NORDISK A/S

Novo Alle, DK-2880 Bagsværd, Denmark

Modelling (ligand design and engineering)

Health Care Discovery, Måløv, Denmark

Contact person:

Robert Bywater, phone: +45 44 43 45 30

email: byw@novo.dk, <http://www.novo.dk/>

Research activities:

Modelling is carried out in the following areas :

- protein modelling (folding, dynamics)
- structure-based ligand design
- virtual compound libraries

In addition we have the following experimental activities:

- NMR of peptides and synthetic compounds
- Spin label and fluorescence spectroscopy of GPCRs

Present number of staff:

8 (incl. 1 technician)

Collaborations with groups in Medicon Valley (examples):

T. Schwartz, The Panum Institute, Copenhagen, Denmark

P.G. Hansen, Roskilde University Center, Roskilde, Denmark

Modelling (enzyme design and engineering)

Enzyme Business, Enzyme Research, Enzyme Design, Bagsværd, Denmark

Contact person:

Anders Hjelholt Pedersen, phone: +45 44 42 64 84

email: ape@novo.dk, <http://www.novo.dk/>

Research activities:

The modelling group in the department are concerned with design and engineering of enzymes and with structure/function analysis. The main systems are hydrolases. The major targets are altered stability, activity and/or specificity. The computational methods include bioinformatics tools, homology modelling, molecular dynamics and electrostatic calculations. Equipment: State-of-the-art graphics workstations and local servers, access to corporate supercomputers (all SGI).

Present number of staff:

6

Collaborations with groups in Medicon Valley (examples):

O. Mouritsen, Dept. of Chemistry, Technical University of Denmark, Lyngby, Denmark

S. Brunak, Dept. of Biotechnology, Technical University of Denmark, Lyngby, Denmark

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BIOMICROSCOPY

**In situ scanning tunnelling and atomic force microscopy
Department of Chemistry, Building 207, Technical University of
Denmark
DK-2800 Lyngby, Denmark**

Contact person:

Jens Ulstrup, phone: +45 45 25 23 59; fax: +45 45 88 31 36

e-mail: ju@kemi.dtu.dk

This group is engaged in studies of the structure and dynamics of metalloproteins at solid surfaces directly in contact with the natural functional aqueous medium of the proteins. Approaches rest on voltammetry of protein layers, electrochemistry of single-crystal metal

surfaces, and scanning tunnelling and atomic force microscopy in the in situ mode. The latter implies that full double potential control, tip coating etc. are invoked, and is the only Scandinavian facility in this area. These techniques provide unique and complementary information about the properties of surface-bound proteins, denaturation etc. at the molecular level. The data have fundamental perspectives in relation to protein function, tunnelling in protein systems, and protein organisation. Biotechnological perspectives are related to design of biocompatible materials, biosensors, implantates etc.

Activities of the group are presently focused on voltammetry, spectroscopy, fast reaction kinetics, and in situ STM/AFM of a number of redox metalloproteins including cytochrome c, azurin, laccase, and desulphoferredoxin.

Present number of staff:

6 (incl. 1 technician)

Collaborations with groups in Medicon Valley: ---

Electron microscopy
National Center for HREM, Lund University,
P.O.Box 124, SE-221 00 Lund, Sweden

Contact person:

J. O. Bovin, phone: +46 46 222 4769, fax: +46 46 222 4012
e-mail: Jan-Olov.Bovin@oorg2.lth.se, <http://erwitt.oorg2.lth.se>

Research activities:

The group is equipped with a modern transmission electron microscope for cryo-microscopy and electron energy filtered image information and 3D reconstruction of protein crystals. The microscope is capable of reaching resolutions of 0.4 nm. The images are recorded and treated digitally. The group also has preparation facilities for most types of biological experiments. A research engineer is available to assist users. The group has very limited experience in work on 2D protein crystals or reconstructions from single large molecules.

Number of staff

1 (steering group of four professors)

Collaborations with groups in Medicon Valley (example):

C. Holm, Molecular Signalling Group, Department of Cell and Molecular Biology, Lund, Sweden

Electron microscopy

**Electron Microscopy Unit, Lund University, Sölvegatan 25, SE-221 85
Lund , Sweden**

Contact person:

**Eric Carlemalm, phone: +46 46 172 976, fax.: +46 46 172 975
e-mail: Eric.Carlemalm@pat.lu.se, <http://www.emu.lu.se>**

Research activities:

The unit is equipped with classical equipment for lower resolution EM. Thus equipment for TEM, STEM, Energy-dispersive X-ray microanalysis (EDS) and equipment for liquid nitrogen cooling is available. Extensive additional preparative equipment is available. The group is well experienced for classical EM work on biological material.

Present number of staff:

4(include. 2 technicians)

Collaborations with groups in Medicon Valley:

Electron microscopy

**Statens Serum Institute, Artillerivej 5
2300 Copenhagen S**

Contact person:

**Jens Blom, phone: +45 31 95 28 71, fax: +45 31 95 58 22
e-mail: jbl@ssi.dk, <http://www.ssi.dk>**

Research activities:

The transmission electron microscopy laboratory at Statens Serum Institut (TEM-SSI) is associated with the department of Molecular Cell Biology. The objects of the laboratory embrace ultrastructural research within microbiological subjects.

Ongoing projects:

The study of different adhesion patterns in *Helicobacter pylori* (*H. pylori*) in vivo and in vitro. Partners: Leif P. Andersen and Andreas M. Petersen & Karen A. Kroghfelt.

The study of cocoid forms of *H. pylori*. Partners: Torkel Wadström & Hans-Olof Nilsson.

Study of surface-exposed structures of Borrelia organisms by EM-immune-gold labelling. Partners: Michael Theisen.

The ultrastructure of Leishmanial parasites, exposed to licochalcone A, with antileishmanial activity. Partners: Arselan Kharazmi.

Equipment: A Philips EM 201 C from 1981

Present number of staff:

2 (incl. 1 technician)

Collaborations with groups in Medicon Valley (examples):

L. P. Andersen, Department of Microbiology, Rigshospitalet, Copenhagen, Denmark

A. M. Petersen & K. A. Kroghfelt, Department of Gastrointestinal Infection, Statens Serum Institut, Copenhagen, Denmark

T. Wadström & H-O. Nilsson, Department of Microbiology, University of Lund, Lund, Sweden

M. Theisen, Department of Clinical Biochemistry, Statens Serum Institute, Copenhagen, Denmark

A. Kharazmi, Department of Clinical Microbiology, Rigshospitalet, Copenhagen, Denmark

Electron microscopy

Zoological Institute, Lund University, Helgonavägen 3, S-223 62 Lund

Contact person:

E. Hallberg, phone: +46-46-222 46 78, fax: +46-46-222 44 25

e-mail: Eric.Hallberg@zool.lu.se

Research activities:

The group is experienced but has older instruments.

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PROTEIN CRYSTALLOGRAPHY

**Center for Crystallographic Studies
Department of Chemistry, University of Copenhagen
Universitetsparken 5, DK-2100 Copenhagen Ø, Denmark**

Contact person:

Sine Larsen, phone: +45 35 32 02 82, fax: +45 35 32 02 99

e-mail: sine@tovborg.ki.ku.dk, <http://www-ccs.ki.ku.dk>

Research activities:

The majority of the projects focuses on enzymes, that either take part in the nucleotide metabolism or are involved in the degradation or biosynthesis of complex polysaccharides.

Relating to the former group of enzymes we have determined the first three dimensional structures for some bacterial enzymes that are involved in the de novo and the salvage biosynthesis of pyrimidine nucleotides, dihydro orotate dehydrogenase, phosphoribosyl pyrophosphate synthetase and uracil phosphoribosyl-transferase. Our future research aims for a detailed understanding of the catalytic function of enzymes, in addition to structural studies of other enzymes with unknown three dimensional structure belonging to the same biological pathway. These projects are done in close collaboration with the Center for Enzyme Research, University of Copenhagen.

The studies of enzymes that take part in the degradation and biosynthesis of complex carbohydrates have until now led to the first structural knowledge of three of the enzymes that are able to degrade the ramified part of the pectic substance in plant cell walls, rhamnogalacturonan acetylerase, rhamnogalacturanase A and a galactanase. These enzymes have been isolated from *Aspergillus aculeatus* and have been cloned and expressed by Novo Nordisk A/S. Future aspects of this research include unravelling of the catalytic function and substrate specificity for these enzymes parallel to the initiation of structural studies of other enzymes acting on related substrates.

The group makes extensive use of the gene technological laboratory and the facilities for protein purification and characterisation that have been built up since 1994. An R-Axis II imaging plate system serves as the device for in house data collections. The group is very well equipped with graphical work stations.

Present number of staff:

14 (incl. 4 technicians)

Collaborations with groups in Medicon Valley (examples):

Center for Enzyme Research, University of Copenhagen, Denmark

Institute for Molecular Biology, University of Copenhagen, Denmark

Novo Nordisk A/S, Copenhagen, Denmark

Danisco Biotechnology, Copenhagen, Denmark

Unizyme, Hørsholm

**PlaCe, Royal Veterinary And Agricultural University, Frederiksberg,
Denmark
Institute of Plant Physiology, Royal Veterinary And Agricultural
University, Frederiksberg, Denmark**

**Protein Structure Group
Department of Chemistry, University of Copenhagen
Universitetsparken 5, DK-2100 Copenhagen Ø, Denmark**

Contact person:

**Michael Gajhede, phone: +45 35 32 02 80, fax: +45 35 32 02 99
e-mail: gajhede@jerne.hi.ku.dk, <http://jerne.ki.ku.dk>**

Research activities:

The group is working in the field of structural investigations of proteins. The activities of the group primarily fall within the following categories:

- 1. The structural basis of allergy and**
 - 2. Structure/function investigations of enzymes.**
- 1. Using crystallography as the primary tool we determine structures of major allergens, e.g. those from birch pollen and from grass. Further complexes between the molecules of the immune system and allergenes are studied, in order to elucidate fundamental properties of the immune response to allergens.**
- 2. The structure/activity relationships between two classes of enzymes, the peroxidases and the glucosyltransferases are being investigated. The group is equipped with a rotating anode based imaging plate system, computing and crystallisation facilities.**

Present number of staff:

8

Collaborations with groups in Medicin Valley (examples):

**M. Spangfort, ALK-ABELLO, Hørsholm, Denmark
L. Thim, Novo-Nordisk A/S, Bagsværd, Denmark
B. Svensson, Carlsberg Research Laboratories, Copenhagen, Denmark**

**Protein Crystallography Group
Department of Medicinal Chemistry, Royal Danish School of Pharmacy
Universitetsparken 2, DK-2100 Copenhagen Ø, Denmark**

Contact person:

Ingrid Kjøller Larsen, phone: +45 35 37 08 50 ext 407, fax: +45 35 37 22 09

e-mail: ingrid@medchem.dfh.dk, <http://www.dfh.dk>

Research activities:

Protein crystallography has been an active research discipline at the department since 1990. Successful crystallisation and structure determination of a number of macromolecules, proteins as well as nucleotides, have been obtained in recent years. The present main topics are:

- a) heparin binding protein, performed in collaboration with Novo Nordisk A/S,
- b) tetranectin, a plasminogen binding protein, in collaboration with H. C. Thøgersen, Univ. of Århus,
- c) PNA (peptide nucleic acid), a project on nucleotide analogs mimicking DNA performed in collaboration with P. E. Nielsen, University of Copenhagen, and
- d) NCAM (neural cell adhesion molecule), a membrane protein involved in e.g. communication between cells. This project includes cloning and expression of separate domains of NCAM and is performed in collaboration with E. Bock, University of Copenhagen. In addition, collaboration has been initiated with J. Egebjerg, University of Århus, on structure determination of the ligand binding part of subunits of the glutamate receptor. Fruitful collaboration with NMR and computational/ modelling groups within the Øresund area exists and is expected to increase.

The group is well equipped with crystallisation and computer facilities and share equipment for data collection with the protein crystallography groups at the university, granted for common use to the groups in 1992. Synchrotron beam time e.g. at MAX lab. is essential for the group.

Present number of staff:

10 (incl. 1 master student and 1 technician)

Collaborations with groups in Medicon Valley (examples):

E. Bock, The Panum Institute, University of Copenhagen, Denmark

L. Iversen, S. Bjørn and H. Flodgaard, Novo Nordisk A/S, Bagsværd, Denmark

P. E. Nielsen, University of Copenhagen, Denmark

Department of Molecular Biophysics
Molecular Biophysics, Center for Chemistry and Chemical Engineering
Lund University, Box 124, SE-221 00 Lund, Sweden

Contact person: Anders Liljas, phone: +46 46 222 4681, fax: +46 46 222 4692

e-mail: anders.liljas@mbfys.lu.se, <http://www.mbfys.lu.se>

Research activities:

The research of the department focuses on a number of systems where experimental structural data are important. The main method is x-ray crystallography. The largest project concerns structural aspects of protein synthesis. Here the ribosomal components (RNA and protein molecules) and the tRNA-molecules and the factor proteins that transiently bind to the ribosome are of prime interest. The work concentrates on procaryotic molecules with an aim to improve and identify new antibiotics. This work is done in large collaborations within and outside the EU. Other projects concern superantigens (collaboration with Active Biotech), molecules related to rheumatoid arthritis (collaboration with Rikard Holmdahl), metal insertion in protoporphyrins (chelataes, collaboration with Departments of Microbiology and Biochemistry, Lund), and calcium binding proteins (collaboration with Sture Forsén and Sara Linse).

The department is responsible for the construction and running of the crystallographic experimental station at the MAX synchrotron.

Present number of staff:

17 (incl. 2 technicians)

Collaborations with groups in Medicon Valley (examples):

F. Björkling, Leo Pharmaceutical Products, Ballerup, Denmark

P. Antonsson, Active Biotech, Lund Research Center, Lund, Sweden

L. Hederstedt and M. Hansson, Departments of Microbiology and Biochemistry, Lund University, Sweden

S. Forsén and S. Linse, Dept. Physical Chemistry 2, Center for Chemistry and Chemical Engineering, Lund University, Sweden

R. Holmdahl, Med. Inflammation Research, Dept. Cell and Molecular Biology, Lund University, Sweden

ALK-ABELLÓ A/S

Research department, Bøge Allé 6-8,
DK-2970 Hørsholm, Denmark

Contact person:

Michael Spangfort, phone: +45 45 74 81 56, fax: +45 45 74 89 42,

e-mail: Michaels@inet.uni2.dk

Research activities:

Develops and manufactures vaccines and in vitro tools for treatment and diagnosis of specific allergy. The Allergen technology research group deals with structure and function of allergens involved in the IgE-mediated immune response.

Facilities for protein/immuno chemistry, crystallisation, molecular biology. Equipment for structural biology: relying on external collaboration with Carlsberg Research Center (NMR) and Protein Crystallography Group, University of Copenhagen (X-ray crystallography).

Present number of staff:

4 (incl. 1 technician)

Collaborations with groups in Medicon Valley (example):

Carlsberg Research Center (NMR spectroscopy group) and Protein Crystallography Group, Chemical institute, University of Copenhagen .

NOVO NORDISK A/S
Health Care Discovery
Novo Alle, DK-2880 Bagsværd, Denmark

Contact person:

Lars Iversen, phone: +45 44 42 61 20
e-mail: lfiv@novo.dk, <http://www.novo.dk/>

Research activities:

Crystallisation and structure determination of proteins and protein-ligand complexes. Proteins as drug targets and therapeutic protein are investigated. Projects running under Novo Nordisk A/S core business areas are pursued. Equipment: Presently relying on external equipment. A mar345 imaging plate detector system will be fully implemented at Novo Nordisk A/S by the end of 1998.

Present number of staff:

4 (incl. 2 technicians)

Collaborations with groups in Medicon Valley (examples):

Protein Crystallography Group, Dept. Medicinal Chemistry, Royal Danish School of Pharmacy, Copenhagen, Denmark.
Protein Structure Group, Dept. of Chemistry, Lab. IV, University of Copenhagen, Copenhagen, Denmark.

Dept. Molecular Biophysics (MAX-lab), Center for Chemistry and
Chemical Engineering, Lund University, Lund, Sweden.

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NEUTRON SCATTERING

Biophysics

Department for Condensed Matter Physics and Chemistry Department
Risø National Laboratory
DK-4000 Roskilde, Denmark

Contact person:

Kell Mortensen, phone: +45 46 77 47 10, fax: +45 46 77 47 90
e-mail: Kell.Mortensen@risoe.dk, <http://www.risoe.dk>,
<http://www.nbi.dk/BIOPHYS/>

Research activities:

The biophysics related research at Risø addresses to a large extend questions related to the structure of bio-molecules, as well as their organisation. Theory and computer simulations provides new understanding of protein folding. Neutron and x-ray scattering is, for example, used to investigate aqueous suspensions of proteins and protein complexes, DNA-strands and their complexes with other molecules, RNA-protein complexes in ribosome's, etc. A variety of studies are related to the self association of amphiphilic molecules, including model systems of phospholipids and surfactants, as well as complex systems like that of natural humic acids, and the association between lipid monolayers and proteins. Bio-related molecules like peptides are synthesised with a main aim of new technological applications.

Present number of staff:

10

Collaborations with groups in Medicon Valley (examples):

R. Bauer, Inst. Mathematics and Physics, Agricultural University,
Frederiksberg, Denmark

O. Mouritsen, Phys. Chem., Technical University of Denmark, Lyngby,
Denmark

D. Posselt, IMFUFA, Roskilde University Center, Roskilde, Denmark

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NMR SPECTROSCOPY

Center for Studies of Macromolecular Structure and Dynamics
Division of Phys. Chem. 2, Chemical Center, Lund University
P.O.Box 124, SE-221 00 Lund, Sweden

Contact person:

Torbjörn Drakenberg, phone: +46 46 222 4470, fax: +46 46 222 4543,
e-mail: trbjrn bor.fkem2.lth.se, <http://www.fkem2.lth.se>

Research activities:

The group has for more than two decades been involved in studies of biological macromolecules. The main theme in the research of the group has been studies of the relations between the structure, dynamics and functional properties of intracellular proteins involved in the Ca^{2+} -dependent signalling, with an emphasis on calbindin $\text{D}_{9\text{K}}$ and calmodulin. Calbindin has been used as a model system for developments of the NMR techniques as well as for mutational studies. More recently structures of domains from proteins in the blood coagulation system have been determined. This work is currently focused on pairs of EGF-domain with an unusually high affinity for Ca^{2+} -ions. To understand why some EGF-pairs have high Ca^{2+} - affinity the three-dimensional structure is needed and presently NMR appears to be the sole alternative. The third general project deals with bacterial cell surface proteins. The solution structure of the plasma protein binding domains are determined as well as the dynamics of the isolated domains and their interaction with the plasma protein, IgG or albumin.

In the above studies not only mutant proteins but also proteins labelled with ^{15}N and/or ^{13}C are produced. The group has now a good experience in production of recombinant proteins and site directed mutagenesis using E. coli.

The available NMR equipment includes spectrometers at three frequencies: 360, 500 and 600 MHz. This combination is of great advantage in studies of biomolecular dynamics. Furthermore, the group will have access to an 800 MHz NMR instrument that will be installed at the Swedish NMR Center in Gothenburg during 1998.

Present number of staff:

13 (incl. technicians)

Collaborations with groups in Medicon Valley (examples):

U. Hedner, Novo Nordisk A/S, Bagsværd, Denmark

J. Stenflo, Dept. of Clinical Chemistry, Malmö General Hospital, Sweden

L. Björck, Dept. of Cell and Molecular Biology, Lund University, Sweden

B. Kragelund, Carlsberg Research Center, Denmark

The Danish Instrument Center for NMR studies of Biological Macromolecules.

Gamle Carlsberg Vej 10, DK-2500 Valby, Denmark

Contact person:

Flemming M. Poulsen, phone: +45 33 27 53 48, fax: +45 33 27 47 08,

e-mail: fmp@crc.dk, <http://www.crc.dk>

It is the purpose of the centre to provide access for Danish scientists to a 750, a 600 and a 500 MHz NMR spectrometer. The Instrument Centre was established by the Danish Natural Science Research Council for NMR studies of biological macromolecules.

The Carlsberg Laboratory, Department of Chemistry, headed by Professor Klaus Bock, is in charge of the management, administration and maintenance of the centre.

The major users are:

The NMR Groups of the Department of Chemistry of University of Copenhagen, Docent Jens Jørgen Led.

The NMR Group of the Department of Chemistry of University of Odense, Docent Jens Peter Jacobsen.

The NMR Groups of the Department of Biology and Chemistry of University of Roskilde, Professor Poul Erik Hansen.

Novo-Nordisk, Senior Scientist Svend Ludvigsen

The Carbohydrate Structure Group of Carlsberg Laboratory, Department of Chemistry, Professor Klaus Bock, and senior scientist Jens Duus.

The NMR Technology Group of Carlsberg Laboratory, Department of Chemistry, Professor Ole W. Sørensen.

The Protein Structure Group of Carlsberg Laboratory, Department of Chemistry, Professor Flemming M. Poulsen.

Contact person: Jens Duus

e-mail [_ HYPERLINK mailto:jd@crc.dk __jd@crc.dk_](mailto:jd@crc.dk)

Roskilde University Center

Department of Life Sciences and Chemistry, Roskilde University Center,
P.O.Box 260, DK-4000 Roskilde, Denmark

Contact person:

Poul Erik Hansen, phone: +45 46 74 24 32, fax: +45 46 74 30 11

e-mail: poulerik@virgil.ruc.dk, <http://www.ruc.dk>

In Roskilde there are three groups working in the area of biomolecular NMR:

1. A group led by Erik Tuchsén works with protein dynamics based on amide proton exchange and with electrostatic calculations.

2. A group led by Pauli Kofod studies binding of d⁶-metal complexes with oligonucleotides. The structure of the adducts are studied by means of multinuclear NMR involving also the metal nuclei. Potential cancerogene activity of the adducts are also studied.

3. A group led by Poul Erik Hansen is involved in structural determination of proteins using NMR. For example in a collaboration with Mark Hinds and Ray Norton from Melbourne and Georg Anderlüh, Ljubljana, on the structure of equinotoxins. Furthermore there are studies on the use of isotope effects on the NMR parameters as a tool in studies of proteins and a study on the C-H coupling constants in collaboration with David Neuhaus, Cambridge.

Present number of staff:

8

Collaborations with groups in Medicon Valley (examples):

O. H. Olsen, Novo Nordisk A/S, Bagsværd, Denmark

J. T. Pedersen, Acadia (in a planning stage), Denmark

Protein structure group

Carlsberg Laboratorium, Kemisk afdeling

Gamle Carlsberg Vej 10, DK-2500 Valby, Denmark

Contact person:

Flemming M. Poulsen, phone: +45 33 27 53 48, fax: +45 33 27 47 08,

e-mail: fmp@crc.dk, <http://www.crc.dk>

Research activities:

The Protein Structure Group of the Carlsberg Laboratory is engaged in studies of proteins by NMR spectroscopy. Presently (May 1998) members of the group studying the molecular mechanism of cell adhesion. For this purpose we are determining the three dimensional structure of modules of the neural cell adhesion molecule, a modular build protein that is present on the surface of nerve cells. This protein is an important component for the morphogenesis of the neural system, and it is also relevant for the processes of learning. The group is also studying the mechanisms of interactions in protein folding. For these studies we are using the four helix bundle protein, acyl coenzyme A binding protein (ACBP), as a model system. We have recently identified the residues which are important for the formation of the rate limiting step of the apparent two-state folding process. These residues have been conserved in all the species of known ACBPs both in yeast and in the plant and animal worlds.

The group has determined the structures of the following proteins: acyl coenzyme A binding protein, the complex of acyl coenzyme A binding protein with palmitoyl Coenzyme A, barnase, barwin, birch pollen allergen bet v 1, a chymotrypsin inhibitor 2, chymotrypsin inhibitor derivative, lipid transfer protein, the lipid transfer protein in complex with the ligand palmitoyl-coenzyme A, lipid transfer protein in complex with the ligand palmitate, NCAM Ig-module 1, NCAM Ig-module 2, NCAM module-1 in complex with a peptide that stimulates neurite outgrowth, NCAM fibronectin type III module 2, the N-terminal module of alpha-2-macroglobulin receptor associated molecule.

Present number of staff:

11 (incl. 1 technician)

Collaborations with groups in Medicon Valley (example):

E. Bock, The Panum Institute, University of Copenhagen, Denmark

The Protein NMR Group
Department of Chemistry, University of Copenhagen.
Universitetsparken 5, DK-2100 Copenhagen Ø

Contact person: Jens Jørgen Led, phone: 45 35 32 03 02, fax: 45 31 35 06 09

e-mail: led@kl5axp.ki.ku.dk

Research activities:

NMR spectroscopic studies of the structure and dynamics of a series of biologically important proteins, in order to obtain specific and detailed information at the molecular level about the function and activity of the proteins. The group has a considerable expertise both in NMR studies of the structure and function of proteins, and in the development of computational methods for the extraction of quantitative information from the complicated NMR spectra of proteins, as mentioned above. Most recently the group has determined the solution structure of the human insulin hexamer - the largest protein structure (36 kD) so far to be determined by NMR.

Development of new computational and NMR spectroscopic methods for the extraction of detailed biological information from NMR spectra. The overall aim of this activity is to improve the quality and quantity of biological information obtained from NMR spectra, through a more direct extraction of the information from the spectra. This includes the application of advanced mathematical methods such as the Linear Prediction and the Least Squares methods in the analysis of multi-dimensional NMR spectra. The group has been among the pioneers in the implementation of the linear prediction methodology in the analysis of NMR data. Most of the groups research is carried out in collaboration with other research groups.

The group has a state-of-the-art 500 MHz Varian Unity INOVA spectrometer, and shares, together with three other Biomolecular NMR research groups in Denmark, a similar 800 MHz spectrometer at the Danish national NMR facility, located at the Carlsberg Research Center.

Present number of staff:

9 (incl. 2 master students and 1 technician)

Collaborations with groups in Medicon Valley (examples):

J. Ulstrup, Department of Chemistry. Technical University of Denmark, Lyngby, Denmark

A. Holm, Department of Chemistry, The Danish Agricultural and Veterinarian University, Denmark

K. Josefsen, The Batholin Institute, University of Copenhagen, Copenhagen, Denmark

Novo Nordisk, Bagsværd, Denmark.

**ASTRA-DRACO AB
Dep. of Medicinal Chemistry
P.O. Box 34
SE-221 00 Lund, Sweden**

Contact person:

Göran Carlström, phone: +46 46 337 844, fax: +46 46 337 119
e-mail: goran.carlstrom@draco.se, <http://www.astra.com/>
Gunnar Grönberg, phone: +46 46 337 065, fax: +46 46 337 119,
e-mail: gunnar.gronberg@draco.se, <http://www.astra.com/>

Research activities:

At the department of Medicinal chemistry, NMR is used as a tool for characterisation of chemical structure and conformation of synthesised compounds, using one- and two-dimensional proton and heteronuclear NMR techniques. We are also studying drug:target interactions, focusing on identification of structural entities with high binding affinity, as well as determination of the three-dimensional conformation of the bound compound. Access to identified target molecules, enable us to perform three-dimensional structure determinations of proteins, using inverse-detected triple resonance experiments on doubly labelled (^{13}C and ^{15}N) material.

The NMR group at Astra Draco is primarily involved in preclinical research, but also serve other departments within the company with NMR investigations on specific problems, e.g. identification of metabolites and impurities, and characterisation of pharmaceutical preparations. Some of the problems require detection of very small quantities of material.

Available instrumentation include a Varian VXR 300 MHz and a two channel Inova 400 MHz spectrometer, used mainly for routine applications, and a Varian Inova 500 MHz spectrometer for research applications. The 500 MHz instrument is a two channel instrument equipped with waveform generators and several probeheads, including 3 and 5 mm inverse detection probes with z-gradient coils, a nano-probe, 5 and 10 mm broadband probes, and a 5 mm dual probe for ^1H and ^3H for radiolabelled compounds. Presently, we are investigating the acquisition of a LC-NMR system. Astra Draco has access to both 600 and 800 MHz spectrometers at Astra Structural Chemistry Laboratory (ASCL) in Mölndal south of Gothenburg. The group consists of two members with expertise on both the application of NMR on small molecules and carbohydrates, and on biomolecular NMR for structural studies of peptides, proteins and DNA.

Present number of staff:

2

Collaborations with groups in Medicon Valley: ---

NOVO NORDISK A/S
Health Care Discovery
Novo Alle, DK-2880 Bagsværd, Denmark

Contact person:

Svend Ludvigsen, phone: +45 44 42 61 69
e-mail: svl@novo.dk

Research activities:

Activities: Structure, dynamics, ligand interaction, and general characterisation of hormones, receptors, enzymes, inhibitors, and other relevant proteins using NMR spectroscopy.

Equipment: 600 MHz Varian Unity spectrometer allocated 100%(almost) for biomolecular NMR, access to several in house instruments in the range 200-400 MHz instruments, and access to instruments at "the Danish Instrument Center for NMR Studies of Biological Macromolecules".

Present number of staff:

3 (and a variable number of part time NMR users)

Collaborations with groups in Medicon Valley (examples):

Danish Instrument Center for NMR Studies of Biological Macromolecules, Carlsberg Laboratorium, Valby, Denmark

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MASS SPECTROSCOPY

ASTRA DRACO AB
P.O. Box 34, SE-221 00 Lund, Sweden

Contact persons:

Mats Berglund, Dept. of Analytical Chemistry; phone: +46 46 336 196, fax: +46 46 337 168, e-mail: mats.berglund@draco.se.astra.com, <http://www.astra.com/>
Lars-Erik Edholm, Dept. of Bioanalytical Chemistry, phone: +46 46 336 349, fax: +46 46 337 144 e-mail: lars-erik.edholm@draco.se.astra.com/, <http://www.astra.com/>

Research activities:

Mass spectrometry is today used throughout the whole process of research and development. Today, we have 26 instruments, where the majority is concentrated at the department of Analysis - Substance and at the department of Bioanalytical Chemistry. Biomolecules are studied using ionisation techniques like electrospray, nano-electrospray and MALDI in combination with MS and MS/MS. Characterisation of both the covalently bound structure as well as the 3D structure is possible.

For the characterisation of chemical structures of biomolecules, we use molecular weight determinations of intact proteins and of oligonucleotides (antisense or PCR products), sequencing of peptides and short oligonucleotides. Characterisation of post-translational modifications (phosphorylation, glycosylation etc.), and degradation products are also performed. In screening studies, such as Proteomics, identification of unknown proteins are today best performed by means of mass spectrometry.

The different types of instrumentation we use are; tandem mass spectrometers, double focusing magnetic sector instruments, time of flight instruments, ion traps, quadrupoles, and hybrids of these. The majority of the instruments are hyphenated with different separation technologies like HPLC and capillary electrophoresis, for on-line purification and/or separation. Other separation systems like gel electrophoresis are also interfaced with mass spectrometers.

Present number of staff: ---

Collaborations with groups in Medicon Valley: ---

NOVO NORDISK A/S
Health Care Discovery
Novo Alle, DK-2880 Bagsværd, Denmark

Contact person:

Per Franklin Nielsen, phone: +45 44 42 62 76
email: pfn@novo.dk

Activities: Purification and structural determination of bio-molecules by mass spectrometry. Mapping of post-translational modifications. In-vitro estimation of enzymatic stability of peptides.

Equipment: Sciex Perkin-Elmer API III triple quadrupole LC/MS/MS instrument equipped with electrospray and heated nebulizer ionisation inlet. Perceptive Voyager RP MALDI-MS instrument equipped

with reflector and delayed extraction. Bio-Ion 20K PDMS-TOF instrument.

Present number of staff:

2

Collaborations with groups in Medicon Valley: ---

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MEMBRANE BIOPHYSICS

**MEMPHYS - Membrane and Statistical Physics Group
Department of Chemistry, Building 206, Technical University of
Denmark
DK-2800 Lyngby, Denmark.**

Contact persons:

**Ole G. Mouritsen and Thomas H. Callisen, phone: +45 45 25 24 63, fax:
+45 45 93 48 08
e-mails: ogm@kemi.dtu.dk and hoenger@kemi.dtu.dk,
<http://www.fki.dtu.dk>**

Principal areas of research within biophysics:

**biomembranes and proteins, fluctuating surfaces and interfaces,
statistical mechanics, microscopic models, computer simulation
techniques (MC, MD), micro-calorimetry, fluorescence spectroscopy,
electron spin resonance spectroscopy.**

Specific biophysical research topics:

**phase transitions and cooperativity in lipid bilayers and biological
membranes, membrane lateral organisation, nano-scale domains,
polypeptides, channels, proteins, enzymes (lipase's), cholesterol,
lysolipids, drugs, insecticides, membrane permeability, non-
equilibrium phenomena: driven-diffusive systems, structured
interfaces, inter-layer forces, wetting, bending elasticity,
supramolecular aggregates, self-assembly, polymers, liquid crystals.**

Equipment:

**workstation cluster for large-scale computer simulations, high
sensitivity differential scanning calorimeters, fluorescence
spectrometer, electron spin resonance spectrometer, high performance
liquid chromatography system.**

