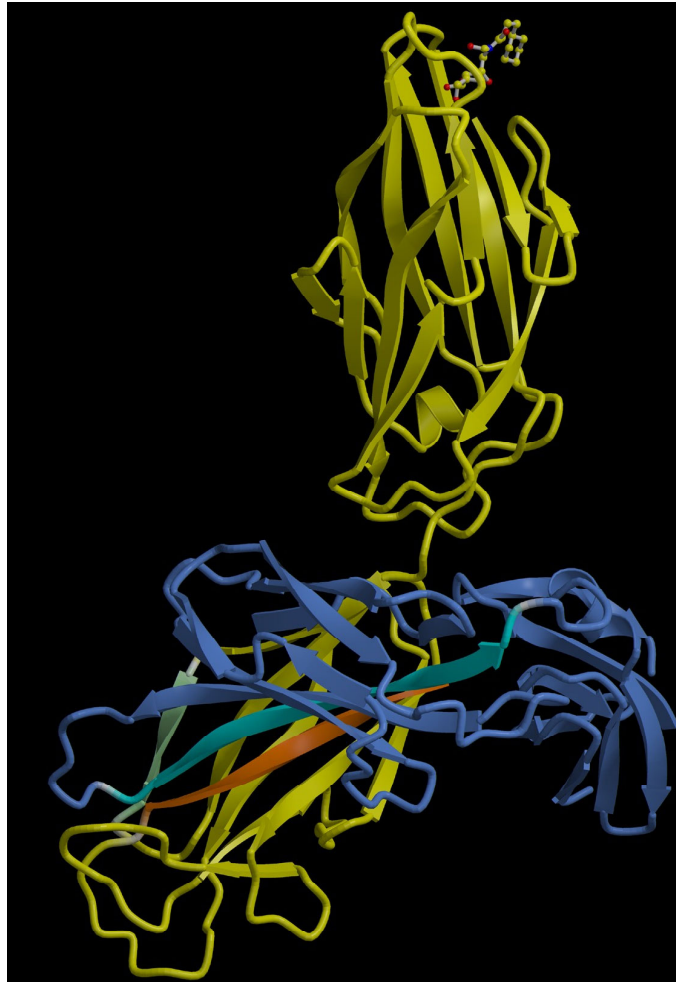


Final report of the Swedish Structural Biology Network (SBNet)



The 3D structure of the virulence-associated bacterial adhesin FimH in a complex with its periplasmic chaperone FimC (Choudhury et al. Science 1999, 285:1061-1066)

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May 2004

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Executive Summary

Structural biology is the area of scientific enterprise that aims to elucidate the three-dimensional structure and dynamic properties of biological macromolecules (proteins, nucleic acids and complexes) at atomic resolution, in order to provide a structural explanation for biological function, role, activity, selectivity, toxicity, etc. Such knowledge is of crucial importance in many different areas, ranging from medical and pharmaceutical science, to forestry and plant technology.

Sweden has long had an outstanding reputation in structural biology, which was reaffirmed by an international evaluation (organised by NFR) in 1999. The international panel of reviewers concluded that “work in Sweden is in the forefront of international efforts to gain structures of important, biologically relevant macromolecules” and that “the Swedish effort has won well-justified respect and admiration within the international community and represents a jewel in the Swedish scientific crown”. Both the importance of the field and the excellence of the Swedish research efforts were appreciated early on by the Foundation for Strategic Research, and a strategic programme in this area was among the first to be funded by the Foundation (in 1996).

As part of this programme, a national network was created (Structural Biology Network, SBN Net) with the aim to improve graduate training and to facilitate knowledge transfer. To this end, SBN Net initiated a large number of activities, including the organisation of an annual national conference, as well as of advanced courses and workshops, a mentor system for PhD students, maintenance of a website and a mailing list through which relevant information is disseminated to the entire Swedish structural biology community, as well as the provision of various forms of travel support. During its seven years of operation, SBN Net has become the hub of Swedish structural biology and:

- contributed to the expansion of the entire area in Sweden in both academia and industry by funding more than two dozen young scientists
- helped improve the quality of graduate training in structural biology in Sweden
- developed a very successful networking component, which has created a genuine structural biology community, covering all areas of structural biology and involving both academia and industry.

0. The objectives of the programme

The main objective of the Programme was to guarantee a continued world-class status for Swedish Structural Biology research. The area had become exponentially more important in the preceding decade, both because of basic scientific interest and curiosity, and because of the many potential industrial applications. Our plan was to strengthen the curiosity-based research in the following strategic areas: membrane proteins, receptor-ligand interaction, protein design, development of computational methods to study enzyme catalysis and drug design. The aims of the programme, as defined in the original proposal, were as follows:

- *"to guarantee a world-class status for Swedish Structural Biology research.*
- *to reinforce excellent research groups.*
- *to carry out academic research of the highest calibre.*
- *to make new efforts to try and remedy perceived current weaknesses. In the first instance, this means establishing a dedicated laboratory for protein expression at Uppsala University.*
- *to strengthen academic research in areas that will be of direct interest to Swedish industry. In particular, we will encourage projects to study integral membrane and receptors proteins, drug design and structures of high medical relevance.*
- *to improve graduate-student training in Structural Biology, to bring it to a world-class level.*
- *to stimulate contacts with industry to facilitate the knowledge transfer that is needed to keep Swedish companies on an equal footing with their foreign competitors.*
- *to improve interactions between the different structural biology groups working in Sweden.*
- *to interact with other programmes supported by the Foundation".*

The following four-tiered approach was proposed in 1994 to strengthen the strategic value of Structural Biology in Sweden:

- **To reinforce excellence;** by supporting new strategic research efforts of the groups that are competing at the highest international level.
- **To remedy current weaknesses;** in particular, by building a protein-expression laboratory in Uppsala.
- **To elevate graduate training to a world-class level;** by organising advanced courses and conferences open to all Nordic students and researchers with an interest in Structural Biology.

- **To facilitate knowledge transfer;** by stimulating contacts between academic groups, contacts with industry, and participation of industrial researchers in the Network.

After the start-up phase of the Network, extra weight was to be given to support projects working in areas of supreme strategic relevance, such as integral membrane proteins, structures of great medical interest, and drug design (both theoretical developments and applications).

1. The history of the Swedish Structural Biology Network (SBN Net)

1.1 Historical overview (up to 1994)

Structural biology is defined here as the area of scientific enterprise that aims to elucidate the three-dimensional (3D) structure and dynamic properties of biological macromolecules (proteins, nucleic acids and complexes) at atomic resolution, in order to provide a structural explanation for biological function, role, activity, toxicity, and selectivity. Such studies are of importance in many different areas, ranging from medical and pharmaceutical science, to forestry and plant technology. In the context of this proposal, structural biology is taken to include:

- biomolecular X-ray crystallography,
- biomolecular NMR spectroscopy,
- near-atomic resolution electron microscopy, crystallography, and tomography,
- modelling of biomacromolecular structure via computational methods.

In addition, some aspects of other disciplines (such as protein engineering, analytical biochemistry, bioinformatics, biopharmaceutical sciences, *etc.*) can be included. The history of structural biology and its development in Sweden between 1960 and 1994 have been described extensively in the original 1994 proposal to SSF for funding of the first tranche of the Structural Biology Network. Briefly, structural biology was born in Cambridge, England in the 1950s where the first macromolecular structures were determined by Crick, Watson, Kendrew, Perutz and co-workers. Since then interest in the 3D structure of biomacromolecules has exploded beyond the wildest imagination of even the most structurally oriented biologist or chemist. Modern structural biology is a merging of different disciplines, which have greatly developed in the past two decades. X-ray crystallography has been the principal source of 3D structural information. The time required to solve the structure of a medium-sized, soluble protein has shrunk in some cases to just a few months or even days. This progress has been made possible by a number of developments relating to the over-expression and purification of protein material, high-throughput crystallisation trials, powerful synchrotron radiation sources and improved detectors, improved phasing methods, accelerated and cheap computer hardware with large memories and advanced graphics capabilities, and the development of novel methods and software (*e.g.*, for automatic phasing and model building).

During the 1980s, multidimensional nuclear magnetic resonance (NMR) spectroscopy developed into an alternative to X-ray crystallography, at least for structure determination of small and medium-sized biomolecules with suitable solubility properties. In addition, NMR allows the study of the dynamic properties of molecules, and the technique is well suited for probing interactions between molecules. In recent years, cryo-electron microscopy (cryo-EM) has become a powerful technique for structural studies of large assemblies, sometimes in synergy with crystallographic studies. Improvements in instrumentation and software have enabled major improvements in the resolution that can be routinely attained in cryo-EM studies. The importance of the field of structural biology is also underscored by the fact that a number of Nobel Prizes have been awarded to structural biologists, including Perutz and Kendrew (1962), Watson and Crick (1962), Hodgkin (1964), Klug (1982), Deisenhofer, Huber and Michel (1988), Ernst (1991), Walker (1997), Wüthrich (2002), and McKinnon (2003).

Protein crystallography has a long tradition in Sweden. Already in the first half of the 1960s two groups started in Uppsala, lead by Bror Strandberg and Carl-Ivar Brändén at Uppsala University (UU) and the Swedish University of Agricultural Sciences (SLU), respectively. Both had previously undertaken post-doctoral studies in Cambridge. For more than two decades, Uppsala remained the sole centre for protein crystallography in Sweden, where Swedish students were trained (Hans Eklund, Ylva Lindqvist, Anders Liljas, Lars Liljas, Inger Andersson), and a number of foreign scientists settled down (Alwyn Jones, Gunter Schneider). With the move of Anders Liljas to Lund University (LU) in 1988, a slow but accelerating transfer of scientists trained in Uppsala to other laboratories in Sweden began. In 1994, when the original proposal to SSF was written, half of the traditional universities in Sweden had at least one protein crystallography group, and also industry had begun to set up structural biology laboratories (often employing crystallographers, NMR spectroscopists and modellers).

High-resolution NMR spectroscopy of biomacromolecules is a much younger discipline, and although NMR facilities had been available in Sweden since 1957, it was not until the 1980s that attention focussed on high-resolution research on biomolecules. An important development was the inauguration of the Swedish NMR Centre (SNC) in 1992 (initially in Stockholm, but later relocated to Gothenburg). The centre provides academic and industrial scientists with access to state-of-the-art equipment and has been an important resource for the entire biologically oriented NMR community in Sweden. By the mid-1990s, most of the traditional universities in Sweden also had at least one biomacromolecular NMR group.

1.2 The conception of SBN Net

In the summer of 1994, a small group of Swedish structural biologists (Alwyn Jones, Sture Forsén, Torleif Härd, and Björn Nilsson; Hans Eklund was co-opted as a further member of this committee, and Gerard Kleywegt acted as scientific secretary) was invited by SSF to formulate a proposal for a strategic research initiative in the area of structural biology. The result of the work carried out by this committee was the programme proposal “Strategic Research in Structural Biology” (a.k.a. “the Blue Book”, available on-line at <http://xray.bmc.uu.se/sbnet/history.html>) that was submitted to SSF in December 1994. The committee suggested that a Structural Biology Network be initiated to address these challenges, with the following objectives:

"The committee feels that the main objective of its proposed programme should be to guarantee a continued world-class status for Swedish Structural Biology research. The area has become exponentially more important in the past decade, both because of basic scientific interest and curiosity, and because of the many potential industrial applications.

The transition of Structural Biology from an area of academic interest to a field with important commercial applications is now far advanced in Europe, Japan, and the USA. Foreign industry has relied almost totally on academia to produce their structural biologists. Many of the new industrial laboratories are competitive at the very highest international levels and are an active part of the Structural Biology community. Swedish industry lags behind most developed countries by at least 5 years in the build-up of their structural groups. Two Swedish companies have invested in setting up their own structural groups to date. Symbicom has a fully equipped X-ray laboratory close to the Biomedical Centre in Uppsala, and there is close interaction with the academic groups. Pharmacia has more recently invested in both an X-ray and an NMR group. A large part of this group was trained in either Uppsala (Lundqvist, Sundström, Kraulis) or Lund (Kördel). We expect this trend to continue with a transfer of educated structural biologists from academia to industry. We will encourage industrial groups to take an active part in the setting up and running of the Network.

We plan to strengthen our curiosity research in the following strategic areas: membrane proteins, receptor-ligand interaction, protein design, development of computational methods to study enzyme catalysis and drug design. This should be of major interest to the pharmaceutical industry and to those involved in the industrial applications of enzymes. "

The original programme proposal had a number of components, including funding of expression laboratories in both Uppsala and Lund, the funding of new positions in the leading structural biology groups (21 PhD students, 12 research assistants, two laboratory

technicians, one research engineer and one Network Lecturer), and the idea of organising a national network within Structural Biology. The projected budget was 100 MSEK.

After a lengthy evaluation procedure (including a review by three foreign experts, Jan Drenth, Guy Dodson and Iain Campbell), this proposal was eventually funded (although slightly modified and to only ~2/3 of the requested level, *i.e.*, 65 MSEK) and took off as one of the very first SSF programmes in 1996 (the revised programme plan is available on-line at http://xray.bmc.uu.se/sbnet/plan_2000.html). The final programme, under the directorship of Alwyn Jones, led to the funding of one expression laboratory located in Uppsala (as per the explicit instructions of SSF), the funding of a considerable number of new positions in the academic structural biology groups in Sweden (20 PhD students, 5 research scientists, two staff in the expression laboratory, and a Network Coordinator), and the organisation of a national network. The aims of the programme were as follows:

- *"to guarantee a world-class status for Swedish Structural Biology research.*
- *to reinforce excellent research groups.*
- *to carry out academic research of the highest calibre.*
- *to make new efforts to try and remedy perceived current weaknesses. In the first instance, this means establishing a dedicated laboratory for protein expression at Uppsala University.*
- *to strengthen academic research in areas that will be of direct interest to Swedish industry. In particular, we will encourage projects to study integral membrane and receptors proteins, drug design and structures of high medical relevance.*
- *to improve graduate-student training in Structural Biology, to bring it to a world-class level.*
- *to stimulate contacts with industry to facilitate the knowledge transfer that is needed to keep Swedish companies on an equal footing with their foreign competitors.*
- *to improve interactions between the different structural biology groups working in Sweden.*
- *to interact with other programmes supported by the Foundation."*

The network, which was named SBN Net (Structural Biology Network), has since then been run by the programme director, Alwyn Jones, and the network coordinator, Gerard Kleywegt. Two of the three international evaluators of the original proposal joined the board of the network, which also included its chair, Björn Nilsson (at the time at Pharmacia, later at Amersham, and presently CEO of KaroBio), the programme director, and a further representative from Swedish industry (initially Uli Hacksell of Astra Draco, who was

succeeded by Jan Hoflack, AstraZeneca and later Martin Norin of Biovitrum). The major task of the board has been to carry responsibility for the budget of the Network and to guarantee the scientific quality and integrity of the programme, a task that included the allocation of the SBN Net-funded positions (after evaluation of scientific proposals). The network part of the program meanwhile grew quickly from humble beginnings (a mailing list and a small website) and has become a highly visible and unifying component of the Swedish structural biology community. In 2002, Henrik Hansson took over the day-to-day running of the Network. It should be noted that, although the programme was originally scheduled to end in December 2000, SBN Net has managed to extend the lifetime of the purely network-oriented activities with a further three years, without additional funding beyond the original SSF allocation.

1.3 Members of the Programme Board

See appendices A1 and A2.

1.4 The development of Structural Biology in Sweden during 1994-2003

Since the submission of the original proposal, a number of significant developments have taken place in Swedish structural biology, in some of which SBN Net has played an active part.

1.4.1. Growth of the academic structural biology groups

Since 1994 Bror Strandberg, Carl-Ivar Brändén, and Sture Forsén have retired. Nevertheless, the number of Principal Investigators (PIs) in Swedish structural biology has more than doubled (from ~20 in 1994 to ~50 in 2003). Moreover, the Swedish structural biology community as a whole has grown by an estimated factor of three during that period. SBN Net has played a direct part in this by funding the positions of 27 structural biologists (of which more than half were female). For the purpose of this report, we define a PI as a person who attracts his/her own funding, who has an independent research program, who has responsibility (scientific and financial) for one or more other people (students, post-docs), and who publishes independently of senior scientists in the same institute. Appendix A13 contains a list of the academic structural biology PIs as of October, 2003.

1.4.2. New and growing industrial research groups

In 1994, Pharmacia (now Biovitrum) in Stockholm and Symbicon in Uppsala had the only operational industrial structural biology facilities in Sweden. Sometime later, Symbicon was incorporated by Astra Draco (now AstraZeneca) and the group was moved to Mölndal near Gothenburg, where AstraZeneca Structural Chemistry Laboratory was built. Since then, both

laboratories have grown and, despite being involved in various mergers, the structural biology groups have remained in Sweden. In addition, a number of other companies have begun to employ structural biologists, and this trend is expected to continue over the next decade. Appendix A14 lists the companies in Sweden that currently have active structural biology departments, or are in the process of setting up activities in this area, or have close collaborations with academic laboratories.

1.4.3. The MAX II synchrotron in Lund

The protein crystallography resources at the MAX II synchrotron in Lund consist of two beamlines. The older, beamline I711, was funded by FRN (10.5 MSEK in 1992) and KAW (5 MSEK in 1998). This beamline has been operational since 1998, and of the approximately 200 days of beam time per year, 65% is allocated to Swedish academia and 10% to Swedish and Danish industrial groups. I711 has had a major impact on Swedish biocrystallography: more than 200 publications using data collected at the beamline have appeared, including many in prestigious scientific journals. With the increasing importance of the MAD technique (Multiple-wavelength Anomalous Dispersion), not in the least for high-throughput and structural genomics research, the need for a dedicated MAD beamline became obvious a few years ago. Grants from KAW (25 MSEK in 1999), the Danish Biotechnology Instrument Centre (14 MDKK in 2000), industrial support from AstraZeneca and Novo Nordisk (12 MSEK), as well as general grants from VR and SSF to MAX Lab have enabled the building of the recently opened beamline I911 (Cassiopeia). Thanks to an innovative beamline design, the beamline will eventually comprise no fewer than five experimental stations. Cassiopeia will have one highly tuneable (0.7–1.8 Å) station suitable for MAD data-collection, and four fixed-wavelength side stations (0.91, 0.97, 1.03 and 1.25 Å), of which two will have a high brilliance beam.

1.4.4. The Swedish NMR Centre in Gothenburg

The Swedish NMR Centre Foundation (SNC) was founded in 1991 through a donation from the Swedish Tobacco Company. Two magnets (500 MHz and 600 MHz) were made available to academic research groups for a five-year period. Following this period, SNC was transferred to Göteborg University. Donations from the Hasselblad Foundation (20 MSEK) and KAW (25 MSEK) enabled the building of the Hasselblad laboratory, and the acquisition of three more magnets of 500, 600 and 800 MHz. The SNC activity in Gothenburg started in 1997 and half of the spectrometer time was made available to researchers at other Swedish universities. When SNC moved to Gothenburg, the university there provided funding for two positions at SNC, and two chairs (one at the natural science faculty and one at the medical

faculty) were focused on NMR research. In 2002, KAW donated a further 30 MSEK, and together with 10 MSEK from the vice-chancellor of Göteborg University, and 5 MSEK jointly from the natural science faculty, the medical science faculty and Chalmers University of Technology, funding became available for a 900 MHz magnet that will be installed during 2004. SNC serves a wide range of scientific activities, including structural biology, surface chemistry, diffusion studies, and studies of dynamics (and thermodynamics) of proteins. All biological NMR groups in Sweden have used the facilities at SNC, and its importance for structural biology in Sweden cannot be overestimated.

1.4.5. National facility for cryo-EM in Lund

As pointed out by the international panel that evaluated structural biology research in Sweden on behalf of NFR in 1999, there has been a need for developing a national facility for high-resolution cryo-EM. This has now been realised at the Chemistry Centre at Lund University, where a Jeol 3000 SFF electron microscope has been installed. It has 300 kV accelerating voltage, a field-emission gun and a liquid-helium-cooled specimen stage. The facility is complemented with auxiliary equipment and two research engineers are employed to take care of the instrumentation. To a large extent the development is financed by SWEGENE, the consortium for functional genomics in the southwestern part of Sweden. The facility is also part of the National Centre for High Resolution Electron Microscopy (nCHREM) that operates several instruments for different types of applications.

1.4.6. The future and impact of structural genomics

Since the late 1990s, efforts are underway to map the entire structural universe of natural proteins. These efforts, typically carried out by very large international consortia, will have an extremely important spin-off effect, in that they stimulate the development of new technologies and methodologies that are of benefit to all structural biologists. Several structural genomics pilot projects, covering some 100-200 genes each, have been initiated by the groups of Härd, Schneider and Nordlund. Nordlund and Härd have developed technology platforms for protein production in *E. coli*, that are among the leading ones in Europe, and Schneider is in the process of developing a platform for insect cell expression. This work has been done within the framework of WCN and SPINE (Nordlund) and a technology development program financed by AstraZeneca (Härd and Nordlund). Present success rates for the process from gene to soluble and purifiable protein for the *E. coli* expression platform are >60 % for bacterial proteins and >30 % for human proteins, and > 50 % of the purified bacterial proteins can be crystallised. Similar technologies have been developed for membrane proteins where > 40 % of some 50 *E. coli* membrane proteins could be

overexpressed and purified. The possible throughput of the *E. coli* platform is 500-2000 genes per year, depending on the level of funding. The newly developed technologies are now being applied on ensembles of genes involved in human diseases, in particular cancer.

In 2001, SWEGENE decided to establish a development centre in Gothenburg focussed on membrane protein structural biology. The membrane protein platform is organised as two closely integrated laboratories: a membrane protein overproduction laboratory, and a structural biology laboratory incorporating both crystallographic and NMR activities. Several scientific collaborations with academic groups in Lund and Gothenburg form the heart of the centre's activities, and they are complemented by a smaller number of interactions with industry and international collaborators. A development objective is to streamline the steps from gene to crystal so that "genome-wide" projects may be tackled on a medium-scale. To this end, a pilot study of 30 membrane proteins from the genome of *Legionella pneumophila* has been initiated, and has driven the introduction of state-of-the-art technologies and methodologies (e.g., nanoliter drop crystallisation robotics) into the platform.

1.4.7. Quality of Swedish structural biology

The Swedish structural biology community has approximately tripled in size since the mid-1990s, but there are several indications that this rapid expansion has not had a negative impact on the quality of the research being done in this country.

First, in 1999 the Chemistry Committee of the Swedish Natural Science Research Council (NFR; now VR) undertook an international evaluation of 31 NFR-funded projects in the area of structural biology (excluding modelling). The international panel concluded that "*work in Sweden is in the forefront of international efforts to gain structures of important, biologically relevant macromolecules*" and that "*the Swedish effort has won well-justified respect and admiration within the international community and represents a jewel in the Swedish scientific crown*". In all, 40% of the projects were given the highest rating (excellent) and a further 30% were judged to be very good.

Second, in the past few years a number of Swedish structural biologists have won important and substantial awards, fellowships and grants from SSF, KVA, KAW, VR, the Gustafsson foundation, EU, etc.

Third, the community as a whole continues to publish papers in some of the most prestigious general and specialised scientific journals.

Fourth, the Swedish structural biology groups continue to attract large numbers of high-potential students as well as foreign post-docs and PIs. Of the PIs listed in Appendix 13, more than 50% was not born in this country, and all but three of these moved to Sweden after 1990.

2. The scientific results

2.1 A description of the research and scientific results

The allocation of funding for the different projects supported by the Network was organised in a series of application rounds ("tranches"). The Programme Director had a non-voting role in the decision making process. In the first tranche, the Board awarded eight PhD student positions in accordance with the aim to "support new strategic research efforts of the groups in Uppsala, Lund and Stockholm that are competing at the highest international level".

Tranche 2 applications were by invitation, involving all PIs in the original Programme Proposal. After scientific evaluation by the Board, 5 student and 4 researcher positions were allocated. In these first two rounds of funding, the allocations were made to Sweden's world-class structural biologists who had been carrying out independent work in Sweden for a number of years. Because of the continued expansion of the field in Sweden, the tranche 2 allocations were restricted to just half of the projects outlined in the original Programme Proposal. This allowed us to broaden our options in the third and fourth tranches. During 1997, the Board allocated the remaining seven student positions (these constituted the "contingency fund" of the original proposal). This process took place in two rounds, for both of which open calls for applications were issued. For tranche 3 (four positions), the Board decided that preference should be given to proposals that were based on a multidisciplinary approach and/or involved a collaboration with industrial or other laboratories. In addition, the Board decided to set priorities in four strategic research areas, namely integral membrane and receptor proteins, drug design, structures of high medical relevance, and methods development (in any of the areas of structural biology). Twenty proposals were received and reviewed by the Board (excluding the Director). For tranche 4 (three positions), the quality of the applications, as determined by their scores in the peer-review process, was the most important overall criterion. In case of equal scores, PIs that were not already funded by the Network were prioritised. Proposals that involved collaboration with another network or programme funded by SSF were viewed upon favourably. A total of 25, often excellent, applications were received, many more than there were positions available.

In retrospect, essentially all seven "contingency fund" positions were awarded to young and talented people who were not operating independently (in Sweden) at the time of writing of the original proposal. It can therefore be concluded that the idea of having a contingency fund was an excellent one, and that it worked extremely well in practice to foster new efforts by young and promising scientists.

The "deliverables" in the programme plan included ~75 publications by the PhD students. The present number (not all of the students have finished their studies) is 90 publications. In addition, ~40 articles have been published by the researchers funded by the programme.

List of all projects that have been (co-)funded by the programme

Names within parentheses denote PhD students that have left the programme prematurely.

Network Coordinator (1996-2002): **Gerard Kleywegt** (UU)

Project: "**Structural Neurobiology/Protein Crystallography/Structural Bioinformatics**"

22 publications in peer-reviewed international scientific journals between 1997 and 2003.

Network Coordinator (June 2002-): **Henrik Hansson** (UU)

Project: "**Structural Bioinformatics: validation of protein structure models**"

No publications 2002-2003.

Project: "**Expression Lab Uppsala**"

Funded personnel: Eva Davey (lab assistant), Petra Franzén (lab engineer)

The "factory" had 11 regular users the last year of financing from SBNet. The equipment and the methodologies, which were developed in the Expression Lab, have also afterward been of much value for the structural biologists at BMC, Uppsala (both SLU and UU).

Tranche 1

Project: "**Structural studies of vesicle-transport proteins**"

PIs: **Gunter Schneider** / **Ylva Lindqvist** (KI)

PhD student: **Louise Kraft** (Stefan Bäckström)

The aim of this project was to express, purify and solve the 3D structure of proteins involved in the neuronal vesicle-transport. By the time this project started, the structures of such proteins were unknown and the mechanisms not fully understood. However, a structure model of such a "SNARE complex" was presented by another research group in *Nature* 1998. Therefore it was decided not to continue with this project.

2 publications in peer-reviewed international scientific journals 1996-2001 and 1 doctoral thesis: "Crystallographic studies of gluconate kinase".

Project: "**Expression and NMR analysis of triply-labelled proteins**"

PI: **Gottfried Otting** (KI):

PhD student: **Patrik Andersson**

5 publications in peer-reviewed international scientific journals 1996-2001 and 1 doctoral thesis: "Development of new NMR techniques and structural characterization of complexes between the N-terminal domain of the *E. coli* arginine repressor and operator DNA".

Project: **"Protein-protein interactions: structural studies of Bruton's Tyrosine Kinase"**

PI: **Torleif Härd** (KI/KTH)

PhD student: **Henrik Hansson**

4 publications in peer-reviewed international scientific journals 1997-2003 and 1 doctoral thesis: "Structure and function of the SH3 domain from Bruton's tyrosine kinase".

Project: **"Ribosomal proteins and factors"**

PI: **Anders Liljas** (LU)

PhD student: **Maria Selmer**

8 publications in peer-reviewed international scientific journals 1996-2002 and 1 doctoral thesis: "Protein-RNA interplay in translation. Structural studies of RRF, SelB and L1".

Project: **"Initiation of blood coagulation: interaction between Factor VII and Tissue Factor and the role of non-catalytic domains"**

PI: **Sture Forsén** (LU)

PhD student: **Andreas Muranyi**

5 publications in peer-reviewed international scientific journals 1996-2000 and 1 doctoral thesis: "EGF-like Modules in Blood Coagulation Proteins. Ca²⁺ binding, module interactions, structure and dynamics as studied by NMR spectroscopy".

Project: **"Structural studies on the Platelet-Derived Growth Factor Receptor and its complex with Platelet-Derived Growth Factor"**

PIs: **Alwyn Jones / Sherry Mowbray** (UU/SLU):

PhD student: **Ulrika Magnusson** (Mary-Rose Hoja)

The primary goal was to study the three-dimensional structure of the human platelet-derived growth factor receptor, with and without the physiologically relevant ligands, as well as a relevant protein tyrosine phosphatase DEP-1. There were problems with aggregation of samples and thus no usable crystals could be produced. Therefore it was decided not to continue with this project.

3 publications in peer-reviewed international scientific journals 1996-2004 and 1 doctoral thesis: "Structural Studies of Binding Proteins: Investigations of Flexibility, Specificity and Stability".

Project: "**Ribonucleotide Reductase holoenzyme complexes**"

PI: **Hans Eklund** (SLU)

PhD student: **Devapriya Choudhury**

6 publications in peer-reviewed international scientific journals 1996-2002 and 1 doctoral thesis: "Functional implications of macromolecular recognition: assembly of adhesive pili and enzyme substrate interactions".

Project: "**Structure of viruses and viral components**"

PI: **Lars Liljas** (UU):

PhD student: **Charlotta Helgstrand (née Axbloom)**

5 publications in peer-reviewed international scientific journals 1996-2002 and 1 doctoral thesis: "Control of Quasi-Equivalence in Virus Capsids".

Tranche 2

Project: "**Time-resolved crystallographic studies of an ATP-dependent carboxylase: dethiobiotin synthetase**"

PIs: **Ylva Lindqvist / Gunter Schneider** (KI)

PhD student: **Jenny Sandmark**

5 publications in peer-reviewed international scientific journals 1996-2002 and 1 doctoral thesis: "Enzymatic mechanisms in biotin synthesis: vitamin B6 catalysis and phosphoryl transfer".

Project: "**Protein-DNA interactions: structural and biophysical studies of runt homology domains**"

PI: **Torleif Härd** (KI/KTH),

PhD student: **Magnus Wolf-Watz**

5 publications in peer-reviewed international scientific journals 1996-2002 and 1 doctoral thesis: "Structure-function relationships of the human Runx1 transcription factor".

Project: "**Structural studies on microsomal glutathione transferase by electron microscopy**"

PI: **Hans Hebert** (KI)

PhD student: **Peter Holm** (Helena Olsson, Marika Joona)

1 publication in a peer-reviewed international scientific journal 2001-2003.

Project: "**Structural studies on protein phosphatases**"

PI: **Pär Nordlund** (SU)

PhD student: **Agnes Rinaldo-Matthis**

2 publications in peer-reviewed international scientific journals 1997-2002 and 1 doctoral thesis: "Crystal structures of human deoxyribonucleotidases".

Project: "**Computational approaches to structure-based drug design and enzyme catalysis**"

PI: **Johan Åqvist** (UU)

PhD student: **Tomas Hansson/Isabella Feierberg**

14 publications in peer-reviewed international scientific journals 1996-2004 and 2 doctoral theses: "Ligand Binding and Enzyme Catalysis Studied by Molecular Dynamics Simulations" (Hansson) and "Computational Studies of Enzymatic Enolization Reactions and Inhibitor Binding to a Malarial Protease" (Feierberg).

Project: "**Crystallography at MAX II**"

PI: **Anders Liljas** (LU)

Independent researcher: **Xiao-Dong Su**

(1) User support for the beam line BL711 at MAX lab until 2002.

(2) Structural studies of cell adhesion molecule L1 and its interaction with integrins:

Cell adhesion molecules (CAMs) play important roles in many biological functions, including cancer progression and metastasis, the three-dimensional structures of CAMs would help to understand the mechanisms of these events and to develop new drugs to inhibit the metastatic processes. L1 CAM is homologous to the insect immune protein hemolin, which crystal structure was determined by me during my post-doc work at CalTech, USA (Su XD et al. 1998 Science 281:991-995). The objectives of this project were to determine the crystal structures of the extracellular domains of L1 family of CAMs, (these CAM proteins include human and mouse L1, Drosophila neuroglian) and to study the structures of integrin domains. Small crystals were obtained on the first 4 domains of neuroglian (Nrg4D) and a two-domain fragment (Ig5-Ig6) of neuroglian.

(3) Deciphering the form and function of LMW PTP homologues in the genomic era

Low-molecular-weight protein tyrosine phosphatase (LMW PTP) is a subfamily of protein tyrosine phosphatase (PTP) superfamily that in concert with protein tyrosine kinases

(PTKs) determine the level of tyrosine phosphorylation in eukaryotic cells. The recent genomic sequencing efforts demonstrated that the LMW PTP homologues are widespread in most organisms including many bacteria, fungi, plants, worms and flies. The structure was determined for one of the LMW PTP homologues in *Bacillus subtilis*, an arsenate reductase.

Collaborative projects:

The structure determination of human cystatin D, an inhibitor of papain-like cysteine proteinases.

The structure determination a beta-glucosidase, Zm-p60.1 from maize.

The structure determination of an extended spectrum beta-lactamase from *K. oxytoca*. 6 publications in peer-reviewed international scientific journals 1998-2002.

Project: "**Experimental studies of biomolecular dynamics by NMR spectroscopy**"

PI: **Sture Forsén** (LU)

Independent researcher: **Brian Finn**

Two main projects have been pursued: [1] High-throughput protein folding and [2] Structure, function and dynamics of a synaptic efficacy modulator.

[1] The first project dealt with investigations of the mechanism by which the protein sequence information in one dimension is converted into the three-dimensional structure of a protein, i.e. the protein folding problem. The goal of the project was to optimise the conditions of protein refolding by varying a large range of conditions in an organised and methodical way, a so-called "high-throughput" approach. Initial investigations of the high-throughput project were promising but the project suffered from a lack of personnel that hindered its successful completion.

[2] The second project involved the determination of the structure of a 190 amino acid protein identified as a regulator of neural efficacy in *Drosophila* and later also isolated from mammals (rat, human). An article on these results was published in early 2000. As with project 1, these studies also suffered from a lack of manpower. In October 2000 and in April 2001, the structures of the homologous proteins from yeast and human were published by two different competing groups. The funding from SBNet ended by the end of the year 2000 and the project was discontinued.

6 publications in peer-reviewed international scientific journals 1997-2000.

Project: "**Structural studies on Membrane Protein Receptors**"

PI: **Sherry Mowbray / Alwyn Jones** (SLU/UU)

Independent researcher: **Jan Saras**

The aim of the project was to determine the 3D structure of a member of the Band 4.1 superfamily, both with and without physiologically relevant ligands. The amino terminal FERM domain (FERM stands for the proteins Band 4.1, Ezrin, Radixin and Moesin) of Ezrin has been shown to be localised at the plasma membrane. During the year 2000 another research group published the structure of the FERM domain of Radixin. The sequence of this protein was almost identical to Ezrin and therefore it was decided not to continue the attempts to solve the structure of the FERM domain of Ezrin.

Project: "Structure/function studies of virulence associated adhesion organelles from pathogenic Gram-negative bacteria"

PI: **Hans Eklund** (SLU)

Independent researcher: **Stefan Knight**

During 1999 we made a major breakthrough in the field of bacterial pathogenesis: we solved the first 3D structure of a virulence-associated bacterial adhesin (FimH) in a complex with its periplasmic chaperone (FimC) (Choudhury *et al.*, Science 1999, 285 :1061-1066; Eisenberg, Science 1999, 285 :1021-1022; Rebbapragada, Trends in Microbiology 1999, 7: 400). This was the first structure ever of a chaperone with a protein substrate bound to it, and the results, in addition to giving detailed information on the assembly and function of adhesive pili, also have profound implications for how we view protein structure and protein folding.

During 2000, a collaboration was established with Dr. Sheila MacIntyre (University of Reading, UK) and Dr. Vladimir Zav'yalov (Institute of Immunological Engineering, Moscow Region, Russia) aimed at elucidating the structure and assembly of the F1 capsular antigen from *Yersinia pesits*. This collaboration later lead to the determination of the 3D structure of the F1 capsular antigen in complex with a chaperone (Zavialov *et al.* Cell. 2003 113(5):587-596).

9 publications in peer-reviewed international scientific journals 1997-2000.

Tranche 3

Project: "Structural Studies on Virus-Host Interactions"

PI: **Holland Cheng** (KI)

PhD student: **Li Xing** (Sevak Markarian)

8 publications in peer-reviewed international scientific journals 1997-2002 and 1 doctoral thesis: "Non-enveloped virus infection probed with host cellular molecules: a structural study".

Project: **"Structural studies of human multidrug resistance protein (MDR) and multidrug resistance-associated protein (MRP)"**

PI: **So Iwata** (UU)

PhD student: **Susanna Törnroth**

6 publications in peer-reviewed international scientific journals 1997-2002 and 1 doctoral thesis: "Structural studies on aerobic and anaerobic respiratory complexes".

Project: **"Crystallographic studies of monoamine oxidase, a drug target in the treatment of clinical depression and Parkinson's disease"**

PI: **Gerard J. Kleywegt** (UU)

PhD student: **Emma Jakobsson**

The aim of the project was to determine the 3D structure of human monoamine oxidase A (MAO A), which is a drug target in the treatment of clinical depression and Parkinson's disease. During the year 2001, another research group published the structure of human monoamine oxidase B and therefore it was decided not to continue with this project. Instead we focussed on determining the 3D structure of another (and related) enzyme of medical interest, namely human semi-carbazide-sensitive amine oxidase (SSAO). This project is an example of collaboration between academia and industry (Biovitrum) that occurred thanks to SBN Net, as one of the student's mentors (Martin Norin) initialised the collaboration.

1 publication in peer-reviewed international scientific journal 2001-2003.

Project: **"Development of Methods for Improved Structure Determination of Larger Systems by means of NMR"**

PI: **Sybren S. Wijmenga** (UmU)

PhD student: **Jenny Cromsigt**

4 publications in peer-reviewed international scientific journals 1997-2002 and 1 doctoral thesis: "New techniques for NMR structural studies on RNA".

Tranche 4

Project: **"Structural studies of cellulases and other enzymes with potential for use in the cellulose industry and bio-organic synthesis"**

PI: **Jerry Ståhlberg** (SLU)

PhD student: **Inés Muñoz**

4 publications in peer-reviewed international scientific journals 1998-2002 and 1 doctoral thesis: "Structural and functional studies of cellobiohydrolase Cel7D from the white-rot fungus *Phanerochaete chrysosporium*".

Project: **"Protein structural dynamics, interactions, and drug design"**

PI: **Mikael Akke** (LU)

PhD student: **Tomas Åkerud**

4 publications in peer-reviewed international scientific journals 1999-2003 and 1 doctoral thesis: "Protein Dynamics Studied by NMR. Kinetics of the Adipocyte Fatty Acid-Binding Protein and Oligomerisation of the Low Molecular Weight Protein Tyrosine Phosphatase".

Project: **"Structure/function studies of virulence associated adhesion organelles from pathogenic Gram negative bacteria"**

PI: **Stefan Knight** (SLU)

PhD student: **Jenny Berglund** (Elinor Eriksson)

4 publications in peer-reviewed international scientific journals 1999-2003 and 1 doctoral thesis: "Structure-function Studies of Organelle Assembly and Receptor Recognition in Organelles Assembled via the Bacterial Chaperone/user Pathway".

2.2 List of participating researchers (senior researchers, post-docs etc.)

See appendix A3.

2.3 Publication list

See appendix A4.

2.4 Important activities and events arranged by SBN Net

An important function of the network has been to bring the Swedish structural biology community together in scientific activities. The annual SBN Net conference is the prime example of this. The meeting has grown into an annual scientific happening and attracts well over 150 participants from academia and industry. The conference is the envy of many a foreign scientist who attends as an invited speaker. It is a meeting place for the PIs to discuss science, science policy, future research directions, the need for big investments, network matters (courses, workshops), *etc.* Industrial scientists have an opportunity not only to meet each other and all the structural biology PIs in one weekend, but also to scout new talent, as most of the students and post-docs present the fruits of their research in talks and posters. Conversely, the meeting provides an excellent opportunity for young scientists to present their work, and to get acquainted with senior scientists (and potential future employers) in academia and industry. Furthermore, students who are involved in the mentor system meet with their mentors during the annual conference to discuss their work, progress, and any

problems or bottlenecks. Last but not least, there is the sheer scientific impact of the meeting. In at least one case, an NMR and a crystallography group discovered that they were working on the same protein and embarked on a successful collaboration. In other cases, contacts between industrial and academic scientists have produced collaborations on systems of mutual interest.

A second important activity concerned the workshops and courses arranged by the Network. These have attracted PhD students and post-docs from all over Sweden as well as from other countries and from both academic and industrial research groups.

A third activity that has been much appreciated and important to the entire community is the “SBN Net Lectureship”. This was an initiative of the SBN Net board and entailed inviting an outstanding structural biologist to come to Sweden, visit all structural biology laboratories, give seminars, and interact with the local students and scientists. The following eminent scientists have received the SBN Net Lectureship:

- Ad Bax (NIH, 1999),
- Michael Rossmann (Purdue, 2000),
- Michael Levitt (Stanford, 2001), and
- John Kuriyan (Berkeley, 2002).

For a full list of events see appendix A5.

Other important activities include:

- The SBN Net web-site, which during the last few years has had more than 40,000 visits annually, serving about 100,000 html-documents (these counts do not include images, visits by robots, *etc.*).
- The mentor system: besides being appreciated both by the students and their mentors, the contacts have led to collaborations between industry and academia.
- Since 1997, SBN Net foreign travel grants have been awarded to 68 PhD students to support lab rotation visits and participation in advanced courses and workshops, enabling these students to acquire skills not readily available in Sweden.
- SBN Net has also supported travel to MAX-lab in Lund and the Swedish NMR Centre to collect data.
- The SBN Net (e-)mailing list, which had approximately 350 subscribers during the last few years, enables a fast and easy contact with the whole structural biology community of Sweden.

3. The SBN Net “Graduates”

3.1 The graduate training within the programme.

SBN Net has organised or supported the organisation of 18 workshops and graduate courses. All of these were new and some of them are expected to "outlive" SBN Net. In many of these courses/workshops, top foreign experts were invited to lecture. These experts have been complemented with national and local instructors to ensure the teaching level to be state-of-the-art, in keeping with the original goal of the Network's graduate training programme.

List of courses and work-shops organised or supported by SBN Net:

Number of participants within parenthesis (no records or statistics regarding external and internal participants is kept by SBN Net)

1997

MAD Phasing workshop, Uppsala (~30)

NMR Spectroscopy course, Gothenburg (not known)

1998

Protein Structure & Analysis course, Uppsala (23)

Protein Crystallisation course, Uppsala (40)

1999

Practical Protein Crystallisation course, Uppsala (22)

Cryo-Microscopy & Computer Image Reconstruction Workshop, KI, Huddinge (35)

2000

CNS workshop, Uppsala (92)

NMR structure calculations using ARIA/CNS, Gothenburg (19)

Practical Protein Crystallisation course #1, Uppsala (21)

Practical Protein Crystallisation course #2, Uppsala (20)

Structure-assisted Drug Design, KI, Stockholm (20)

2001

Practical Protein Crystallisation course, Uppsala (20)

Data-processing workshop, Uppsala (44)

2002

Structure-assisted Drug Design, KI Stockholm (19)

Current concepts in structural biology of large molecular assemblies, KI, Huddinge (61)

Expression & Structural Studies of Membrane Proteins, Gothenburg (150)

2003

Practical Protein Crystallisation course, Uppsala (20)

Advanced Course in NMR Spectroscopy, Gothenburg (20)

All courses were primarily intended for PhD students, both SBN Net-funded and others, and post-docs, but undergraduates as well as researchers from the industrial structure biology laboratories also been among the course attendants. The participants have come not only from Sweden but also from all Scandinavian countries and from other countries as well. The pharmaceutical industry has contributed in the arrangement of a few courses, *e.g.*, "Structure-assisted Drug Design" (AstraZeneca and P&U/Biovitrum). The advanced workshops have not generally been directed exclusively towards students, but have been much appreciated by PhD students nevertheless.

For the PhD students who were funded through SBN Net, a mentor system was set up already in 1997. In this mentor system, two mentors were assigned to each student. Student and mentors have been able to meet at least once a year, at the Annual SBN Net Conference, to discuss the student's progress, problems, new ideas, *etc.* Student-mentor meetings outside the annual conference have been encouraged by the opportunity to apply for funding for travel and living expenses from SBN Net. In order to obtain a large enough pool of mentors, all PIs who had been allocated one or more positions were required to act as mentors. In addition, many other PIs, both from industry and academia, volunteered as mentors, which was a very encouraging development, in line with the increased spirit of cooperation and collaboration that the Network has engendered.

There have also been more subtle aspects to the graduate training programme. For instance, during the student-mentor meetings, students had to present their work face-to-face with expert structural biologists. Another subtle training aspect was to get the students who attended the annual SBN Net Meeting to present their research to this forum of both Swedish and international structure biologists. This was achieved by subsidising the conference fee for PhD students and post-docs if they presented a poster or gave a talk on their work. The session organisers for the meetings have, beside the invited prominent foreign researchers, been urged to choose a few "youngsters" to present their research based on their submitted poster abstracts. Through the years, altogether about 90 students/post-docs have orally presented their research this way and the fastidious conference participants have viewed approximately 700 posters.

3.2 Independent researchers

Younger researchers, funded through or by SBN Net, that have established themselves as independent researchers and group leaders:

- Gerard Kleywegt, Research Fellow of the Royal Swedish Academy of Sciences, Uppsala University.
- Stefan Knight, Professor at the Swedish University of Agricultural Sciences in Uppsala.
- Xiao-Dong Su, Professor at the State Key Laboratory of Protein Engineering and Plant Genetic Engineering, Life Science College, Peking University, Beijing, China.
- Devapriya Choudhury, Associate professor, Centre for Biotechnology, Jawaharlal Nehru University, New Delhi, India.
- Mikael Akke, Professor at Lund University
- Jerry Ståhlberg, Associate professor ("lektor") at Swedish University of Agricultural Sciences in Uppsala.
- So Iwata, Professor at Imperial College, London, UK.

4. The impact of SBN Net – on industry and society

4.1 Industrially relevant results of the programme.

One of the four approaches proposed in the programme plan to strengthen the strategic value of structural biology in Sweden was "to stimulate contacts with industry to facilitate the knowledge transfer that is needed to keep Swedish companies on an equal footing with their foreign competitors". Since then, both Biovitrum (previously Pharmacia) and AstraZeneca (Symbicon/Astra Draco) have expanded their research activities in structural biology in Sweden, despite being involved in various mergers. In addition, a number of other companies have begun to employ structural biologists, and this trend is expected to continue over the next decade. SBN Net has achieved its goal of producing highly skilled PhDs, and almost half of these (8 out of 18) have found employment in the Swedish biotechnology and pharmaceutical industries.

The structural biologists of the industrial laboratories at Biovitrum, AstraZeneca, Amersham Biosciences, Karo Bio and Active Biotech Research have been active and valued participants in the Network (*e.g.*, annual conference, mentor system). The Network also involved the industrial participants more closely in its educational activities (*e.g.*, the SBN Net workshops on drug design were organised jointly by academic and industrial scientists). Such initiatives are beneficial to both students (who get to know leading scientists in Swedish industry) and the industrial scientists (who get to know students interested in their area of research).

Before SBN Net, collaborations of structural biology groups, both within academia and between academia and industry, were mainly based on pre-existing personal contacts. The Annual SBN Net Meeting introduced a new forum for making new contacts and has produced several collaborations between industrial and academic scientists on problems of mutual interest. However, since these interactions are on the personal level, *e.g.*, between PIs, SBN Net has no such records or statistics. Some collaboration between academia and industry are mentioned in Appendix 14.

5. The impact of SBNet – to the academic system

5.1 Scientific collaborations between different disciplines and departments.

Essentially all groups that participated in the Network have both national and international collaborations, and many participate in one or more EU-funded programmes. Since these collaborations usually arise from personal networking, merits, and research interests, SBNet has not played a significant role in their establishment and we have no records or statistics regarding this matter. The "Who is Who?" pages on the SBNet website have been intended to help biomedical scientists to identify and contact structural biologists who share some of their research interests.

5.2 Cooperation between the universities involved in the programme.

Not applicable to SBNet.

5.3 Cooperation with other Foundation programmes.

No formal collaborations existed. Some PIs have been involved in other SSF programmes as well as in SBNet.

5.4 International collaboration

No statistics are available.

5.5 The contributions to the mobility of students and researchers.

The SBNet Board allocated funds to support various types of travel for participants in the Network, including:

- Data-collection at SNC and MAX;
- Student-mentor visits;
- Travel and accommodation for SBNet courses;
- Incidental support for travel to other relevant workshops;
- Foreign travel awards for PhD students.

The data-collection support has mainly been utilised by researchers in X-ray crystallography to go to MAX-lab in Lund. Only a few applications for travel to the Swedish NMR Centre in Gothenburg have been received. This might reflect two things: that the NMR structural laboratories elsewhere in Sweden are well-equipped and that there are fewer groups that do research in biomolecular NMR than there are crystallography groups.

The foreign travel awards were intended to fund travel and subsistence for a trip (1-4 weeks) to a foreign centre-of-excellence in any of the areas of (or related to) structural biology, or to a workshop or course with a substantial practical ("hands-on") component. The purpose of the trip had to be to acquire expertise or know-how that was not readily available within Sweden itself. Candidates who received an award had to write a short report of their trip and these have been published on the SBNet web-site. During the last year, 2003, 28 foreign travel grants were awarded (2002:12, 2001: 15, 2000: 4, 1999: 4, 1998: 4, 1997: 1).

5.6 Contributions to the improvement of academic research

By funding innovative young researchers.

5.7 The effect for researchers in the programme.

By bringing the community close together so that their own research can be evaluated against national and international standard.

5.8 Programme relations with the universities.

This has been purely on an administrative level (to handle the transferring of funds).

5.9 The effect for the universities locally.

The improved graduate training via the SBNet courses and workshops.

5.10 The programme contributions to the improvement of handling of immaterial rights.

No.

5.11 Changes in the university system that has been induced by the programme.

Not known.

6. What we have learned

6.1 The most important scientific and non-scientific achievements and shortcomings

- + Major contribution to expansion of the research area in Sweden (27 positions funded) in both academia and industry.
- + A very successful networking component (especially the annual SBNet conference, the web-site and the SBNet mailing list) has created a genuine structural biology community, including all research disciplines and integrating both the academia and industry.
- + Contributed to the improvement of graduate training, not only by arranging dedicated courses and workshops, but also through the annual conferences, SBNet Lecturers, the travel awards to stimulate visit foreign laboratories, and the mentor system.

- The network will disintegrate as the funding ends.

7. The future

7.1 The future of the programme.

The network will disintegrate when the funding ends.

7.2 A long-term perspective of the importance of SBNet

SBNet has created a tightly-knit community with many, many contacts between individual structure biologists at all levels, between academy and industry, between the different research disciplines of structural biology (X-ray crystallography, NMR, EM, Molecular modelling), *etc.*

SBNet allowed a rapid expansion of structural biology at a crucial time by producing a generation of highly skilled young structure biologist.

8. Economic report

Abbreviations

3D, Three-dimensional
EM, Electron Microscopy
EU, European Union
FRN, Forskningsrådsnämnden
GU, Göteborg University
KI, Karolinska Institute
KAW, Knut och Alice Wallenbergs Stiftelse
KTH, Royal Institute of Technology
KVA, Royal Swedish Academy of Sciences
LU, Lund University
MAD, Multiwavelength anomalous diffraction
MSEK, Million Swedish Kronor
NFR, Naturvetenskapliga Forskningsrådet
NMR, Nuclear Magnetic Resonance
PI, Principal Investigator
SBN Net, Structural Biology Network
SLU, Swedish University of Agricultural Sciences
SNC, Swedish NMR Centre
SSF, Swedish Foundation for Strategic Research
SU, Stockholm University
UmU, Umeå University
UU, Uppsala University
VR, Vetenskapsrådet
WCN, Wallenberg Consortium Nord

Appendices

A.1 List of SBNet programme board members

Chair

- Björn O. Nilsson, Karo Bio AB (1996-2004)

Programme Director

- T. Alwyn Jones, FRS, Uppsala University (1996-2004)

Other board members:

- Guy G. Dodson, FRS, University of York (1996-2004)
- Iain D Campbell, FRS, Oxford University (1996-2004)
- Martin Norin, Biovitrum, Structural Chemistry (June 2000-2004)
- Jan Hoflack, AstraZeneca SCL; (Jan. 1997-June 2000)
- Uli Hacksell, Astra Draco; (1996- Jan. 1997)

Network Coordinators:

- Gerard J. Kleywegt, Uppsala University (1996-June 2002)
- Henrik Hansson, Uppsala University (June 2002-2004)

Secretary :

- Ing-Mari Dohlk, Uppsala University (2000-2004)
- Solveig Viring, Uppsala University (1996-1999)

A.2 Activities and responsibilities of the programme board

In the initial stages of SBN Net, the Programme Board had the vital responsibility of allocating funds to groups throughout Sweden. We were fortunate on having world-class structural biologists, Guy, G- Dodson and Iain D. Campbell, on the board to evaluate the applications. The Programme director had no say in these funding decisions.

Later, the main responsibility of the board was to monitor the yearly economy of the Network and to advise on the adjustments that were made during its lifetime. The day-to-day running of SBN Net was managed by the Coordinator and the Programme Director.

A.3 List of the researchers (funded by SBNet)

Name	Type of position	Year of birth	Gender
Bryan Finn, LU	Researcher (FoAss)	?	male
Stefan Knight, SLU	Researcher (FoAss)	?	male
Jan Saras, SLU	Researcher (FoAss)	?	male
Xiao-Dong Su, LU	Researcher (FoAss)	?	male
Gerard Kleywegt, UUNetwork	Coordinator/Researcher	1962	male
Henrik Hansson, UU	Network Coordinator/Researcher	1968	male
Eva Davey, UU	Lab Assistant	?	female
Petra Franzén, UU	Lab Engineer	?	female

A.4 Publication list

I* = Publications with international/industrial co-authors

1. Xing L, Huhtala M, Pietiainen V, Kapyla J, Vuorinen K, Marjomaki V, Heino J, Johnson MS, Hyypia T, Cheng RH. (2004). "Structural and functional analysis of integrin alpha2I domain interaction with echovirus". *J Biol Chem.* **279**(12), 11632-11638. **I***
2. Helgstrand C, Munshi S, Johnson JE, Liljas L (2004). "The refined structure of *Nudaurelia capensis* omega Virus reveals control elements for a T = 4 capsid maturation." *Virology* **318**(1), 192-203. **I***
3. Schafer K, Magnusson U, Scheffel F, Schiefner A, Sandgren MO, Diederichs K, Welte W, Hulsmann A, Schneider E, Mowbray SL (2004). "X-ray structures of the maltose-maltodextrin-binding protein of the thermoacidophilic bacterium *Alicyclobacillus acidocaldarius* provide insight into acid stability of proteins." *J. Mol. Biol.* **335**(1), 261-274. **I*-**
4. Magnusson U, Salopek-Sondi B, Luck LA, Mowbray SL (2004). "X-ray structures of the leucine-binding protein illustrate conformational changes and the basis of ligand specificity." *J. Biol. Chem.* **279**(10), 8747-8752. **I***
5. Sandmark J, Eliot AC, Famm K, Schneider G, Kirsch JF. (2004). "Conserved and nonconserved residues in the substrate binding site of 7,8-diaminopelargonic acid synthase from *Escherichia coli* are essential for catalysis." *Biochemistry.* **43**(5), 1213-1222. **I***
6. Novotny M, Madsen D, Kleywegt GJ (2004). "Evaluation of protein fold comparison servers " *Proteins* **1**(54), 260-270.
7. Feierberg I. (2003) "Computational Studies of Enzymatic Enolization Reactions and Inhibitor Binding to a Malarial Protease Ph. D. Thesis, Uppsala University
8. Magnusson U. (2003) "Structural Studies of Binding Proteins: Investigations of Flexibility, Specificity and Stability " Ph. D. Thesis, Uppsala University
9. Sandmark J. (2003) "Enzymatic mechanisms in biotin synthesis: vitamin B6 catalysis and phosphoryl transfer" Ph. D. Thesis, Karolinska Institute
10. Zavialov A, Berglund J, Knight SD (2003). "Overexpression, purification, crystallization and preliminary X-ray diffraction analysis of the F1 antigen Caf1M-Caf1 chaperone-subunit pre-assembly complex from *Yersinia pestis*." *Acta Crystallogr D Biol Crystallogr* **59**(Pt 2), 359-362.

11. Ersmark K, Feierberg I, Bjelic S, Hulten J, Samuelsson B, Åqvist J, Hallberg A (2003). "C2-symmetric inhibitors of *Plasmodium falciparum* plasmepsin II: synthesis and theoretical predictions." *Bioorg Med Chem* **11**(17), 3723-3733.
12. Helgstrand C, Wikoff WR, Duda RL, Hendrix RW, Johnson JE, Liljas L (2003). "The refined structure of a protein catenane: the HK97 bacteriophage capsid at 3.44 Å resolution." *J Mol Biol* **334**(5), 885-899. **I***
13. Jakobsson E, Alvite G, Bergfors T, Esteves A, Kleywegt GJ (2003). "The crystal structure of *Echinococcus granulosus* fatty-acid-binding protein 1." *Biochim Biophys Acta* **1649**(1), 40-50. **I***
14. Davis AM, Teague SJ, Kleywegt GJ (2003). "Application and limitations of X-ray crystallographic data in structure-based ligand and drug design." *Angew Chem Int Ed Engl*. **42**(24), 2718-2736. **I***
15. Kleywegt GJ, Henrick K, Dodson EJ, van Aalten DM (2003). "Pound-wise but penny-foolish: How well do micromolecules fare in macromolecular refinement?" *Structure (Camb)* **11**(9), 1051-1059. **I***
16. Muñoz IG, Mowbray SL, Ståhlberg J (2003). "The catalytic module of Cel7D from *Phanerochaete chrysosporium* as a chiral selector: structural studies of its complex with the beta blocker ®-propranolol." *Acta Crystallogr D Biol Crystallogr* **59**(Pt 4), 637-643.
17. Xing L, Casasnovas JM, Cheng RH (2003). "Structural analysis of human rhinovirus complexed with ICAM-1 reveals the dynamics of receptor-mediated virus uncoating." *J Virol* **77**(11), 6101-6107.
18. Li TC, Takeda N, Kato K, Nilsson J, Xing L, Haag L, Cheng RH, Miyamura T (2003). "Characterization of self-assembled virus-like particles of human polyomavirus BK generated by recombinant baculoviruses." *Virology* **311**(1), 115-124.
19. Benkestock K, Van Pelt CK, Åkerud T, Sterling A, Edlund PO, Roeraade J (2003). "Automated nano-electrospray mass spectrometry for protein-ligand screening by noncovalent interaction applied to human H-FABP and A-FABP." *J Biomol Screen*. **8**(3), 247-256. **I***
20. Bernado P, Åkerud T, Garcia de la Torre J, Akke M, Pons M (2003). "Combined use of NMR relaxation measurements and hydrodynamic calculations to study protein association. Evidence for tetramers of low molecular weight protein tyrosine phosphatase in solution." *J Am Chem Soc*. **125**(4), 916-923. **I***
21. Hansson H (2002). "Structure and function of the SH3 domain from Bruton's tyrosine kinase." Ph. D. Thesis, Royal Institute of Technology.

22. Helgstrand C (2002). "Control of Quasi-Equivalence in Virus Capsids". Ph. D. Thesis, Uppsala University.
23. Muñoz I (2002). "Structural and functional studies of cellobiohydrolase Cel7D from the white-rot fungus *Phanerochaete chrysosporium*". Ph. D. Thesis, Swedish University of Agricultural Sciences.
24. Selmer M (2002). "Protein-RNA interplay in translation. Structural studies of RRF, SelB and L1." Ph. D. Thesis, Lund University.
25. Törnroth S (2002). "Structural studies on aerobic and anaerobic respiratory complexes." Ph. D. Thesis, Uppsala University.
26. Xing L (2002) "Non-enveloped virus infection probed with host cellular molecules: a structural study " Ph. D. Thesis, Karolinska Institute.
27. Kleywegt GJ, Jones TA (2002). "Homo crystallographic—quo vadis?" *Structure (Camb)* **10**(4), 465-472.
28. Koivula A, Ruohonen L, Wohlfahrt G, Reinikainen T, Teeri TT, Piens K, Claeysens M, Weber M, Vasella A, Becker D, Sinnott ML, Zou JY, Kleywegt GJ, Szardenings M, Ståhlberg J, Jones TA. (2002). "The active site of cellobiohydrolase Cel6A from *Trichoderma reesei*: the roles of aspartic acids D221 and D175". *J Am Chem Soc* **124**(34), 10015-10024.
29. Flodell S, Schleucher J, Cromsigt J, Ippel H, Kidd-Ljunggren K, Wijmenga SS (2002). "The apical stem-loop of the hepatitis B virus encapsidation signal folds into a stable tri-loop with two underlying pyrimidine bulges." *Nucleic Acids Res* **30**(21), 4803-4811.
30. Cromsigt J, Schleucher J, Gustafsson T, Kihlberg J, Wijmenga SS (2002). "Preparation of partially 2H/13C-labelled RNA for NMR studies. Stereo-specific deuteration of the H5" in nucleotides." *Nucleic Acids Res* **30**(7), 1639-1645.
31. Flodell S, Cromsigt J, Schleucher J, Kidd-Ljunggren K, Wijmenga SS (2002). "Structure elucidation of the hepatitis B virus encapsidation signal by NMR on selectively labeled RNAs" *J Biomol Struct Dyn* **19**(4), 627-636.
32. Helgstrand C, Grahn E, Moss T, Stonehouse NJ, Tars K, Stockley PG, Liljas L. (2002). "Investigating the structural basis of purine specificity in the structures of MS2 coat protein RNA translational operator hairpins". *Nucleic Acids Res.* **30**(12), 2678-2685. **I***
33. Holm PJ, Morgenstern R, Hebert H.(2002). "The 3-D structure of microsomal glutathione transferase 1 at 6 Å resolution as determined by electron crystallography of p22(1)2(1) crystals." *Biochim Biophys Acta.* **1594**(2), 276-285.
34. Kraft L, Sprenger GA, Lindqvist Y (2002). "Conformational changes during the catalytic cycle of gluconate kinase as revealed by X-ray crystallography" *J Mol Biol* **318**(4), 1057-1069.

35. Magnusson U, Chaudhuri BN, Ko J, Park C, Jones TA, Mowbray SL (2002). "Hinge-bending motion of D-allose-binding protein from *Escherichia coli* : three open conformations." *J. Biol. Chem.* **277**(16), 14077-14084. **I***
36. Xu B, Muñoz IG, Janson JC, Ståhlberg J. (2002). "Crystallization and X-ray analysis of native and selenomethionyl beta-mannanase Man5A from blue mussel, *Mytilus edulis*, expressed in *Pichia pastoris*." *Acta Crystallogr D Biol Crystallogr.* **58**(Pt 3), 542-545.
37. Rinaldo-Matthis A, Rampazzo C, Reichard P, Bianchi V, Nordlund P.(2002). "The crystal structure of an azide complex of the di-ferrous R2 Crystal structure of a human mitochondrial deoxyribonucleotidase." *Nat Struct Biol.* **9**(10), 779-787. **I***
38. Eliot AC, Sandmark J, Schneider G, Kirsch JF (2002). "The dual-specific active site of 7,8-diaminopelargonic acid synthase and the effect of the R391A mutation." *Biochemistry.* **41**(42), 12582-12589. **I***
39. Sandmark J, Mann S, Marquet A, Schneider G (2002). "Structural basis for the inhibition of the biosynthesis of biotin by the antibiotic amcilenomycin." *J. Biol. Chem.* **277**(45), 43352-43358. **I***
40. Kristensen O, Laurberg M, Liljas A, Selmer M (2002). "Is tRNA binding or tRNA mimicry mandatory for translation factors?" *Curr Protein Pept Sci* **3**(1), 133-141.
41. Selmer M, Wilting R, Holmlund D, Su XD. (2002). "Preparation of a crystallizable mRNA-binding fragment of *Moorella thermoacetica* elongation factor SelB." *Acta Crystallogr D Biol Crystallogr.* **58**(Pt 10 Pt 2), 1871-1873.
42. Jormakka M, Törnroth S, Byrne B, Iwata S. (2002). "Molecular basis of proton motive force generation: structure of formate dehydrogenase-N." *Science* **295**(5561), 1863-1868.
43. Törnroth S, Yankovskaya V, Cecchini G, Iwata S. (2002). "Purification, crystallisation and preliminary crystallographic studies of succinate:ubiquinone oxidoreductase from *Escherichia coli*." *Biochim Biophys Acta.* **1553**(1-2), 171-176.
44. Jormakka M, Törnroth S, Abramson J, Byrne B, Iwata S. (2002). "Purification and crystallization of the respiratory complex formate dehydrogenase-N from *Escherichia coli*." *Acta Crystallogr D Biol Crystallogr.* **58**(Pt 1), 160-162.
45. Bäckström S, Wolf-Watz M, Grundström C, Härd T, Grundström T, Sauer UH (2002). "The RUNX1 Runt domain at 1.25Å resolution: a structural switch and specifically bound chloride ions modulate DNA binding." *J Mol Biol* **322**(2), 259-272.
46. Haag L, Garoff H, Xing L, Hammar L, Kan ST, Cheng RH. (2002). "Acid-induced movements in the glycoprotein shell of an alphavirus turn the spikes into membrane fusion mode." *EMBO J.* **21**(17), 4402-4410.

47. Åkerud T, Thulin E, Van Etten RL, Akke M (2002). "Intramolecular dynamics of low molecular weight protein tyrosine phosphatase in monomer-dimer equilibrium studied by NMR: a model for changes in dynamics upon target binding." *J Mol Biol.* **322**(1), 137-152.
48. Choudhury D (2001). "Functional implications of macromolecular recognition: assembly of adhesive pili and enzyme substrate interactions." Ph. D. Thesis, Swedish University of Agricultural Sciences.
49. Cromsigt J (2001). "New techniques for NMR structural studies on RNA." Ph. D. Thesis, Umeå University.
50. Kraft L (2001). "Crystallographic studies of gluconate kinase." Ph. D. Thesis, Karolinska Institute.
51. Wolf-Watz M (2001). "Structure-function relationships of the human Runx1 transcription factor." Ph. D. Thesis, Royal Institute of Technology.
52. Cromsigt JA, Hilbers CW, Wijmenga SS (2001). "Prediction of proton chemical shifts in RNA. Their use in structure refinement and validation." *J Biomol NMR* **21**, 11-29.
53. Cromsigt J, van Buuren B, Schleucher J, Wijmenga S (2001). "Resonance assignment and structure determination for RNA." *Methods Enzymol* **338**, 371-399.
54. Grahn E, Moss T, Helgstrand C, Fridborg K, Sundaram M, Tars K, Lago H, Stonehouse NJ, Davis DR, Stockley PG, Liljas L (2001). "Structural basis of pyrimidine specificity in the MS2 RNA hairpin-coat-protein complex" *RNA* **7**, 1616-1627. **I***
55. Hansson H, Okoh MP, Smith CI, Vihinen M, Härd T (2001). "Intermolecular interactions between the SH3 domain and the proline-rich TH region of Bruton's tyrosine kinase." *FEBS Lett* **489**, 67-70. **I***
56. Hansson H, Smith CI, Härd T (2001). "Both proline-rich sequences in the TH region of Bruton's tyrosine kinase stabilize intermolecular interactions with the SH3 domain." *FEBS Lett* **508**, 11-15.
57. Read RJ, Kleywegt GJ (2001). "Density modification: theory and practice." [In: *Methods in Macromolecular Crystallography* (D Turk & L Johnson, Eds.)], *IOS Press, Amsterdam*, pp. 123-135. **I***
58. van Aalten DM, Milne KG, Zou JY, Kleywegt GJ, Bergfors T, Ferguson MA, Knudsen J, Jones TA (2001). "Binding site differences revealed by crystal structures of *Plasmodium falciparum* and bovine acyl-CoA binding protein." *J Mol Biol* **309**, 181-192. **I***
59. Kleywegt GJ (2001). "Validation of protein crystal structures. [In: *International Tables for Crystallography, Volume F, Crystallography of Biological Macromolecules*

- (Rossmann, M.G. and Arnold, E., Editors)]. *Kluwer Academic Publishers, Dordrecht (The Netherlands)*, Chapter 21.1, pp. 497-506, 526-528.
60. Kleywegt GJ, Zou JY, Kjeldgaard M, Jones TA (2001). "Around O." [In: *International Tables for Crystallography, Volume F, Crystallography of Biological Macromolecules* (Rossmann, M.G. and Arnold, E., Editors)]. *Kluwer Academic Publishers, Dordrecht (The Netherlands)*, Chapter 17.1, pp. 353-356, 366-367.
 61. Kraft L, Sprenger GA, Lindqvist Y (2001). "Crystallization and preliminary X-ray crystallographic studies of recombinant thermoresistant gluconate kinase GntK from *Escherichia coli*." *Acta Crystallogr D Biol Crystallogr* **57**, 1159-1161.
 62. Muñoz IG, Ubhayasekera W, Henriksson H, Szabo I, Pettersson G, Johansson G, Mowbray SL, Ståhlberg J (2001). "Family 7 cellobiohydrolases from *Phanerochaete chrysosporium*: crystal structure of the catalytic module of Cel7D (CBH58) at 1.32 Å resolution and homology models of the isozymes." *J Mol Biol* **314**, 1097-1111.
 63. Bennett MS, Guan Z, Laurberg M, Su XD (2001). "*Bacillus subtilis* arsenate reductase is structurally and functionally similar to low molecular weight protein tyrosine phosphatases." *Proc Natl Acad Sci U S A* **98**, 13577-13582. **I***
 64. Guan Z, Hederstedt L, Li J, Su XD (2001). "Preparation and crystallization of a *Bacillus subtilis* arsenate reductase." *Acta Crystallogr D Biol Crystallogr* **57**, 1718-1721.
 65. Vevodova J, Marek J, Zouhar J, Brzobohaty B, Su XD (2001). "Purification, crystallization and preliminary X-ray analysis of a maize cytokinin glucoside specific beta-glucosidase." *Acta Crystallogr D Biol Crystallogr* **57**, 140-142. **I***
 66. Zouhar J, Vevodova J, Marek J, Damborsky J, Su XD, Brzobohaty B (2001) "Insights into the functional architecture of the catalytic center of a maize beta-glucosidase Zmp60.1." *Plant Physiol* **127**, 973-985. **I***
 67. Wolf-Watz M, Bäckström S, Grundström T, Sauer U, Härd T (2001). "Chloride binding by the AML1/Runx1 transcription factor studied by NMR." *FEBS Lett* **488**, 81-84.
 68. Wolf-Watz M, Grundström T, Härd T (2001). "Structure and backbone dynamics of Apo-CBFbeta in solution." *Biochemistry* **40**, 11423-11432.
 69. Andersson P (2000). "Development of new NMR techniques and Structural characterization of complexes between the N-terminal domain of the *E. coli* arginine repressor and operator DNA." Ph. D. Thesis, Karolinska Institute.
 70. Muranyi A (2000). "EGF-like Modules in Blood Coagulation Proteins. Ca²⁺ binding, module interactions, structure and dynamics as studied by NMR spectroscopy." Ph. D. Thesis, Lund University.

71. Abola EE, A Bairoch, W C Barker, S Beck, D A Benson, H Berman, C Cantor, S Doubet, T J P Hubbard, T A Jones, G J Kleywegt, A S Kolaskar, A van Kuik, A M Lesk, H W Mewes, D Neuhaus, F Pfeiffer, L F Ten Eyck, R J Simpson, G Stoesser, J L Sussman, Y Tateno, A Tsugita, E L Ulrich, J F G Vliegthart (2000). "Quality control in databanks for molecular biology." *BioEssays* **22**, 1024-1034. **I***
72. Andersson P, Otting G (2000). "Time-Shared X(w1)-Half-Filter for Improved Sensitivity in Subspectral Editing." *J. Magn. Reson.* **144**, 168-170.
73. Carredano E, Karlsson A, Kauppi B, Choudhury D, Parales RE, Parales JV, Lee K, Gibson DT, Eklund H, Ramaswamy S (2000). "Substrate binding site of naphthalene 1,2-dioxygenase: functional implications of indole binding." *J. Mol. Biol.* **296**, 701-712. **I***
74. Chen YW, Dodson EJ, Kleywegt GJ (2000). "Does NMR Mean "Not for Molecular Replacement"? Using NMR-Based Search Models to Solve Protein Crystal Structures." *Structure Fold Des* **8**, R213-R220. **I***
75. Cromsigt JAMTC, Schleucher J, Kidd-Ljunggren K, Wijmenga SS (2000). "Synthesis of specifically deuterated nucleotides for NMR studies on RNA." *Proceedings of the 11th conversation on Biomolecular Structure & Dynamics* **2**, 210.
76. Feierberg I, Luzhkov V, Åqvist J (2000). "Computer simulation of primary kinetic isotope effects in the proposed rate-limiting step of the glyoxalase I catalyzed reaction." *J. Biol. Chem.* **275**, 22657-22662.
77. Forsell K, Xing L, Kozlovskaya T, Cheng RH, Garoff H (2000). "Membrane proteins organize a symmetrical virus." *EMBO J.* **19**, 5081-5091.
78. H. Hansson, C.I.E. Smith & T. Härd, (2000). "The SH3 domain from Bruton's tyrosine kinase is likely to be involved in forming a homodimer". *Biophys. J.* **78**(1)69A.
79. Henriksson H, Muñoz IG, Isaksson R, Pettersson G, Johansson G (2000). "Cellobiohydrolase 58 (P. c. Cel7D) is complementary to the homologous CBH I (T. r. Cel 7A) in enantio-separations." *J. Chromatogr. A* **898**, 63-74.
80. Kleywegt GJ (2000). "Validation of protein crystal structures." *Acta Crystallogr D Biol Crystallogr* **56**, 249-265.
81. Knight SD (2000). "RSPS version 4.0: a semi-interactive vector-search program for solving heavy-atom derivatives." *Acta Crystallogr D Biol Crystallogr* **56**, 42-47.
82. Knight SD, Berglund J, Choudhury D (2000). "Bacterial adhesins: structural studies reveal chaperone function and pilus biogenesis." *Curr Opin Chem Biol* **4**, 653-660.
83. Kragelund BB, Hauenschild A, Carlström G, Pongs O, Finn BE (2000). "1H, 13C, and 15N assignments of un-myristoylated Ca²⁺-frequentin, a synaptic efficacy modulator." *J Biomol NMR* **16**, 85-96.

84. Muranyi A, Evenas J, Stenberg Y, Stenflo J, Drakenberg T (2000). "1H, 15N and (13)C assignments and secondary structure of the EGF-like module pair 3-4 from vitamin K-dependent protein S." *FEBS Lett.* **475**, 135-138.
85. Muranyi A, Evenas J, Stenberg Y, Stenflo J, Drakenberg T (2000). "Characterization of the EGF-like module pair 3-4 from vitamin K-dependent protein S using NMR spectroscopy reveals dynamics on three separate time scales and extensive effects from calcium binding." *Biochemistry* **39**, 15742-15756.
86. Sauer FG, Barnhart M, Choudhury D, Knight SD, Waksman G, Hultgren SJ (2000). "Chaperone-assisted pilus assembly and bacterial attachment." *Curr Opin Struct Biol* **10**, 548-556. **I***
87. Sauer FG, Knight SD, Waksman G, Hultgren SJ (2000). "PapD-like chaperones and pilus biogenesis." *Semin Cell Dev Biol* **11**, 27-34. **I***
88. Wu B, Hammar L, Xing L, Markarian S, Yan J, Iwasaki K, Fujiyoshi Y, Omura T, Cheng RH (2000). "Phytoreovirus T = 1 core plays critical roles in organizing the outer capsid of T = 13 quasi-equivalence." *Virology* **271**, 18-25.
89. Xing L, Casanovas J, Cheng H (2000). "Distinct binding mode of cellular receptor to human poliovirus and rhinovirus." *J. Clin. Virol.* **18**, 63-64.
90. Xing L, Tjärnlund K, Lindqvist B, Kaplan GG, Feigelstock D, Cheng RH, Casanovas JM (2000). "Distinct cellular receptor interactions in poliovirus and rhinoviruses." *EMBO J.* **19**, 1207-1216.
91. Anderson M, Högbom M, Rinaldo-Matthis A, Andersson K, Sjöberg BM, Nordlund P (1999). "The crystal structure of an azide complex of the di-ferrous R2 Subunit of Ribonucleotide Reductase reveals a novel carboxylate shift with important implications for di-iron catalysed oxygen activation." *JACS* **121**, 2346-2352.
92. Chaudhuri BN, Kleywegt GJ, Björkman J, Lehman-McKeeman LD, Oliver JD, Jones TA (1999). "The crystal structures of alpha 2u-globulin and its complex with a hyaline droplet inducer." *Acta Cryst D Biol Crystallogr.* **55**, 753-762. **I***
93. Chaudhuri BN, Kleywegt GJ, Broutin-L'Hermite I, Bergfors T, Senn H, Le Motte P, Partouche O, Jones TA (1999). "Structures of cellular retinoic acid binding proteins I and II in complex with synthetic retinoids." *Acta Cryst D Biol Crystallogr* **55**, 1850-1857. **I***
94. Choudhury D, Thompson A, Stojanoff V, Langermann S, Pinkner J, Hultgren SJ, Knight SD (1999). "X-ray structure of the FimC-FimH chaperone-adhesin complex from uropathogenic *Escherichia coli*." *Science* **285**, 1061-1066. **I***
95. Feierberg I, Cameron AD, Åqvist J (1999). "Energetics of the proposed rate-determining step of the glyoxalase I reaction." *FEBS Lett.* **453**, 90-94.

96. Finn BE, Drakenberg T (1999). "Calcium binding proteins." *Adv. Inorg. Chem.* **46**, 441-494.
97. Hung DL, Knight SD, Hultgren SJ (1999). "Probing conserved surfaces on PapD." *Mol Microbiol* **31**, 773-783.
98. Hung DL, Pinkner JS, Knight SD, Hultgren SJ (1999). "Structural basis of chaperone self-capping in P pilus biogenesis." *Proc Natl Acad Sci U S A* **96**, 8178-8183.
99. Jones TA, Kleywegt GJ (1999). "CASP3 comparative modeling evaluation." *Proteins: Struct. Funct. Genet.* **Suppl. 3**, 30-46.
100. Käck H, Sandmark J, Gibson K, Schneider G, Lindqvist Y (1999). "Crystal structure of diaminopeptidyl transferase: evolutionary relationships between pyridoxal-5'-phosphate-dependent enzymes." *J. Mol. Biol.* **291**, 857-876. **I***
101. Kleywegt GJ (1999). "Recognition of spatial motifs in protein structures." *J. Mol. Biol.* **285**, 1187-1197.
102. Kleywegt GJ (1999). "Experimental assessment of differences between related protein crystal structures." *Acta Cryst D Biol Crystallogr* **55**, 1878-1884.
103. Kleywegt GJ, Jones TA (1999). "Software for handling macromolecular envelopes." *Acta Cryst D Biol Crystallogr.* **55**, 941-944.
104. Marelis J, Kolmodin K, Feierberg I, Åqvist J (1999). "Q: a molecular dynamics program for free energy calculations and empirical valence bond simulations in biomolecular systems." *J Mol Graph Model* **16**, 213-225, 261.
105. Selmer M, Al-Karadaghi S, Hirokawa G, Kaji A, Liljas A (1999). "Crystallization and preliminary X-ray analysis of *Thermotoga maritima* ribosome recycling factor." *Acta Cryst D Biol Crystallogr* **55**, 2049-2050.
106. Selmer M, Al-Karadaghi S, Hirokawa G, Kaji A, Liljas A (1999). "Crystal structure of *Thermotoga maritima* ribosome recycling factor: a tRNA mimic." *Science* **286**, 2349-2352.
107. Stenberg Y, Muranyi A, Steen C, Thulin E, Drakenberg T, Stenflo J (1999). "EGF-like module pair 3-4 in vitamin K-dependent protein S: modulation of calcium affinity of module 4 by module 3, and interaction with factor X." *J. Mol. Biol.* **293**, 653-665.
108. Wang J, Choudhury D, Chattopadhyaya J, Eriksson S (1999). "Stereoisomeric selectivity of human deoxyribonucleoside kinases." *Biochemistry* **38**, 16993-16999.
109. Wolf-Watz M, Xie XQ, Holm M, Grundström T, Härd T (1999). "Solution properties of the free and DNA-bound Runt domain of AML1." *Eur J Biochem* **261**, 251-260.
110. Xing L, Kato K, Li T, Takeda N, Miyamura T, Hammar L, Cheng RH (1999). "Recombinant hepatitis E capsid protein self-assembles into a dual-domain T = 1 particle presenting native virus epitopes." *Virology* **265**, 35-45.

111. Zou JY, Kleywegt GJ, Ståhlberg J, Driguez H, Nerinckx W, Claeysens M, Koivula A, Teeri TT, Jones TA (1999). "Crystallographic evidence for substrate ring distortion and protein conformational changes during catalysis in cellobiohydrolase Ce16A from *Trichoderma reesei*" *Structure Fold. Des.* **7**, 1035-1045. **I***
112. Hansson T (1998). "Ligand Binding and Enzyme Catalysis Studied by Molecular Dynamics Simulations." Ph. D. Thesis, Uppsala University.
113. Andersson P, Gsell B, Wipf B, Senn H, and Otting G (1998). "HMQC and HSQC experiments with water flip-back optimized for large proteins." *J. Biomol. NMR* **11**, 279-288. **I***
114. Andersson P, Nordstrand K, Sunnerhagen M, Liepinsh E, Turovskis I, and Otting G (1998). "Heteronuclear correlation experiments for the determination of one-bond coupling constants." *J. Biomol. NMR* **11**, 445-450. **I***
115. Andersson P, Weigelt J, and Otting G (1998). "Spin-state selection filters for the measurement of heteronuclear one-bond coupling constants." *J. Biomol. NMR* **12**, 435-441.
116. Andersson P, Annala A, and Otting G (1998). "An alpha/beta-HSQC-alpha/beta experiment for spin-state selective editing of IS cross peaks." *J. Magn. Reson.* **133**, 364-367.
117. Axblom C, Tars K, Fridborg K, Orna L, Bundule M, and Liljas L (1998). "Structure of phage fr capsids with a deletion in the FG loop: implications for viral assembly." *Virology* **249**, 80-88. **I***
118. Cromsigt JAMTC, van Buuren BNM, Zdunek J, Schleucher J, Hilbers CW, and Wijmenga SS (1998). NMR Studies of RNA and DNA. Improved Structure Determination via Incorporation of Chemical Shift Restraints and Global Structure Information." [In: *Magnetic resonance and Related Phenomena* (Eds: D.Ziessow, W.Lubitz, F.Lenzian)] *Proc. 29th Ampere-13th ISMAR; Berlin*, August 2-7, 1998, 132-133.
119. Groves P, Finn BE, Kuznicki J, and Forsen S (1998). "A model for target protein binding to calcium-activated S100 dimers." *FEBS Lett.* **421**, 175-179.
120. Julenius K, Thulin E, Linse S, Finn BE (1998). "Hydrophobic core substitutions in calbindin D9k: effects on stability and structure." *Biochemistry* **37**, 8915-8925.
121. Hansson H, Mattsson PT, Allard P, Haapaniemi P, Vihinen M, Smith CI, and Härd T (1998). "Solution structure of the SH3 domain from Bruton's tyrosine kinase." *Biochemistry* **37**, 2912-2924. **I***
122. Hansson T, Marelus J, and Åqvist J (1998). "Ligand binding affinity prediction by linear interaction energy methods." *J. Comput.-Aided Mol. Des.* **12**, 27-35.

123. Hultgren SJ, Hung DL, Jones CH, and Knight S (1998). "Periplasmic PapD-Like Chaperones in Bacteria: Structure and Function." [In: *Molecular Biology of Chaperones* (edt Bernd Bukau)], *Harwood Academic Publishers, Chur*, ??-??.
124. Kleywegt GJ, and Jones TA (1998). "Databases in protein crystallography." *Acta Crystallogr D Biol Crystallogr* **54**, 1119-1131.
125. Kolmodin K, Hansson T, Danielsson J, and Åqvist J (1998). "Molecular Dynamics Simulations of Substrate Dephosphorylation by Low Molecular Weight Protein Tyrosine Phosphatase." *ACS Symp. Ser.* 721, ??-??.
126. Käck H, Gibson KJ, Lindqvist Y, and Schneider G (1998). "Snapshot of a phosphorylated substrate intermediate by kinetic crystallography." *Proc. Natl. Acad. Sci. USA* **95**, 5495-5500.
127. Käck H, Sandmark J, Gibson KJ, Schneider G, and Lindqvist Y (1998). "Crystal structure of two quaternary complexes of dethiobiotin synthetase, enzyme-MgADP-AlF₃-diaminopelargonic acid and enzyme-MgADP-dethiobiotin-phosphate; implications for catalysis." *Protein Sci.* **7**(12), 2560-2566.
128. Marelus J, Graffner-Nordberg M, Hansson T, Hallberg A, and Åqvist J (1998). "Computation of affinity and selectivity: binding of 2,4-diaminopteridine and 2,4-diaminoquinazoline inhibitors to dihydrofolate reductases." *J. Comput.-Aided Mol. Des.* **12**, 119-131.
129. Marelus J, Hansson T, and Åqvist, J (1998). "Calculation of Ligand Binding Free Energies from Molecular Dynamics Simulations." *Int. J. Quantum Chem.* **69**, 77-
130. Muranyi A, Finn BE, Gippert GP, Forsen S, Stenflo J, and Drakenberg T (1998). "Solution structure of the N-terminal EGF-like domain from human factor VII." *Biochemistry* **37**, 10605-10615.
131. Otte K, Choudhury D, Charalambous M, Engström W, and Rozell B (1998). "A conserved structural element in horse and mouse IGF2 genes binds a methylation sensitive factor." *Nucleic Acids Res.* **26**, 1605-1612.
132. Soto GE, Dodson KW, Ogg D, Liu C, Heuser J, Knight S, Kihlberg J, Jones CH, and Hultgren SJ (1998). "Periplasmic chaperone recognition motif of subunits mediates quaternary interactions in the pilus." *EMBO J.* **17**, 6155-6167. **I***
133. Åqvist J, and Hansson T (1998). "Analysis of Electrostatic Potential Truncation Schemes in Simulations of Polar Solvents." *J. Phys. Chem.* **102**, 3837-
134. Kleywegt GJ, and Read RJ (1997). "Not your average density." *Structure* **5**, 1557-1569. **I***

A.5 Events organised or supported by SBN Net

- "The first annual meeting of Swedish Structural Biology Network", Åkerblads Hotel, Tällberg, June, 1997
- "The second annual meeting of Swedish Structural Biology Network", Åkerblads Hotel, Tällberg, 8-11 May, 1998
- Course: "Practical Course in Protein Crystallisation", Uppsala University, May 1998
- Course: "Protein Structure & Analysis" 22-26 June, 1998, Uppsala University.
- Course: "Practical Course in Protein Crystallisation", Uppsala University, May 1999
- "The third annual meeting of Swedish Structural Biology Network", Åkerblads Hotel, Tällberg, 11-14 June, 1999
- Course: "Cryo-EM" 22-25 October 1999, Karolinska Institute, Huddinge (supported by SBN Net).
- SBN Net Lecturer 1999: 22 November -2 December 1999 Dr. Ad Bax (NIDDK/NIH, Bethesda) visited Sweden receiving the first "SBN Net Lectureship". This included a tour around Sweden arranged by the SBN Net coordinator.
- Workshop: "CNS work shop" 7-8 February 2000, Uppsala.
- Workshop: "NMR structure calculations using ARIA/CNS" 29-30 March 2000, Swedish NMR Centre, Gothenburg.
- Course: "Practical Course in Protein Crystallisation", Uppsala University, May 2000 • "The fourth annual meeting of Swedish Structural Biology Network", Åkerblads Hotel, Tällberg, 9-12 June, 2000
- Course: "Structure-assisted Drug Design", 13-16 June, 2000, Karolinska Institute, Stockholm (SBN Net in collaboration with Karolinska Institute, AstraZeneca SCL and Pharmacia & Upjohn)
- SBN Net Lecturer 2000: 8-18 January 2001 Prof. Michael Rossmann (Purdue University) visited Sweden as "SBN Net Lecturer".
- Course: "Practical Course in Protein Crystallisation", Uppsala University, May 2001 • "The fifth annual meeting of Swedish Structural Biology Network", Åkerblads Hotel, Tällberg, 15-18 June, 2001
- SBN Net Lecturer 2001: 10-20 September 2001, Prof. Michael Levitt (Stanford University) visited Sweden as "SBN Net Lecturer".
- Course: "X-ray Data-processing", Uppsala University, 27-28 September 2001
- Course: "Practical Course in Protein Crystallisation", Uppsala University, 2-6 June 2003.

- "The sixth annual meeting of Swedish Structural Biology Network", Åkerblads Hotel, Tällberg, 31 maj-3 June, 2002
- Course: "Structure-assisted Drug Design", 11-14 juni, 2002, Karolinska Institute, Stockholm (SBNet in collaboration with Karolinska Institute and Biovitrum)
- Workshop / conference: "Structural Forum 2002", 28 August - 1 September, 2002, Karolinska Institute, Huddinge (supported by SBNet)
- Workshop / course: "Expression & structural studies of membrane proteins" 28-29 October 2002, Göteborg University and Chalmers University of Technology (supported by SBNet).
- SBNet Lecturer 2002-2003: 20-27 March, 2003 Prof. John Kuriyan (University of California, Berkeley) visited Sweden as "SBNet Lecturer" ..
- "The seventh annual meeting of Swedish Structural Biology Network", Åkerblads Hotel, Tällberg, 12-16 June, 2003
- Course: "NMR course at the Swedish NMR Centre", Gothenburg, 17-21 November 2003. (SBNet in collaboration with the Swedish NMR Centre)

A.6 PhD exams

Tomas Åkerud

Gender: Male

Year of birth: 1974

University of basic academic training: Uppsala University

Affiliation: Biophysical Chemistry, LU

Supervisor: Mikael Akke (LU)

Project title: Protein structural dynamics, interactions and drug design

Mentors: Pär Kraulis (SU), Anders Åberg (AZ)

Actual starting date: 1 January, 1999

Administrative starting date: 1 January, 1999

Funding ended: 31 December, 2002

Continued career: AstraZeneca SCL, Mölndal

PhD awarded: 16 April, 2004

Thesis title: Protein Dynamics Studied by NMR. Kinetics of the Adipocyte Fatty Acid-Binding Protein and Oligomerisation of the Low Molecular Weight Protein Tyrosine Phosphatase

Jenny Berglund

Gender: Female

Year of birth: 1973

University of basic academic training: Uppsala University

Affiliation: Molecular Biology, SLU

Supervisor: Stefan Knight (SLU)

Project title: Structure/function studies of virulence associated adhesion organelles from pathogenic Gram-negative bacteria

Mentors: Jerry Ståhlberg (SLU), Derek Ogg (Biovitrum)

Actual starting date: 1 September 1998,

Administrative starting date: 1 July, 1997

Funding ended: 30 June, 2002

PhD awarded: 16 April, 2004

Thesis title: Structure-function Studies of Organelle Assembly and Receptor Recognition in Organelles Assembled via the Bacterial Chaperone/user Pathway

Ulrika Magnusson

Gender: Female

Year of birth: 1974

University of basic academic training: Uppsala University

Affiliation: Dept. of Cell- & Molecular Biology

Supervisors: Alwyn Jones (UU)/Sherry Mowbray (SLU)

Project title: Structural studies of the platelet-derived growth-factor receptors

Mentors: Ylva Lindqvist (KI), Hans Hebert (KI & LU)

Actual starting date: 1 July, 1996

Administrative starting date: 1 July, 1996

Funding ended: 30 June, 2001

PhD awarded: 21 November, 2003

Continued career: AstraZeneca, Södertälje

Thesis title: Structural Studies of Binding Proteins: Investigations of Flexibility, Specificity and Stability

Jenny Sandmark

Gender: Female

Year of birth: 1973

University of basic academic training:

Affiliation: Medical Biochemistry and Biophysics, KI

Supervisor: Schneider

Project title: Time-resolved crystallographic studies of an ATP-dependent carboxylase: dethiobiotin synthetase

Mentors: Sherry Mowbray (SLU), Inger Andersson (SLU)

Actual starting date: 1 July, 1996

Administrative starting date: 1 July, 1996

Funding ended: 30 June, 2000

PhD awarded: 5 September, 2003

Continued career: AstraZeneca, Lund

Thesis title: Enzymatic mechanisms in biotin synthesis: vitamin B6 catalysis and phosphoryl transfer

Isabella Feierberg

Gender: Female

Year of birth: 1972

University of basic academic training: Uppsala University

Affiliation: Dept. of Cell- & Molecular Biology

Supervisor: Johan Åqvist (UU)

Project title: Computer modelling of enzyme catalysis

Mentors: Lennart Nilsson (KI), Gunter Schneider (KI)

Actual starting date: 1 July, 1998

Administrative starting date: 1 July, 1996 (Tomas Hansson)

Funding ended: 30 June, 2000

PhD awarded: 4 April, 2003

Continued career: AstraZeneca, Mölndal

Thesis title: Computational Studies of Enzymatic Enolization Reactions and Inhibitor Binding to a Malarial Protease

Charlotte Helgstrand (née Axlom)

Gender: Female

Year of birth: 1972

University of basic academic training: Uppsala University

Affiliation: dept. of Cell- & Molecular Biology, UU

Supervisor: Lars Liljas (UU)

Project title: Structure of viruses and viral components

Mentors: Gunter Schneider (KI), Hans Hebert (KI & LU)

Actual starting date: 1 March, 1997

Administrative starting date: 1 January, 1997

Funding ended: 31 December, 2000

PhD awarded: 15 November, 2002

Continued career: ?

Thesis title: Control of Quasi-Equivalence in Virus Capsids

Susanna Törnroth

Gender: Female

Year of birth: 1973

University of basic academic training: Uppsala University

Affiliation: Department of Biochemistry, UU

Supervisor: So Iwata (UU/Imperial College, UK), Janos Hajdu (UU)

Project title: Structural studies of human multidrug resistance protein (MDR) and multidrug resistance-associated protein (MRP)

Mentors: Holland Cheng (KI), Medina

Actual starting date: 1 September, 1997

Administrative starting date: ?

Funding ended: 30 June, 2001

PhD awarded: 4 October, 2002

Continued career: Research engineer within the SweGene project at Chalmers University

Thesis title: Structural studies on aerobic and anaerobic respiratory complexes

Li Xing

Gender: Female

Year of birth: ?

University of basic academic training: Beijing University

Affiliation: Dept. of Biosciences, KI

Supervisor: Holland Cheng (KI)

Project title: Structural studies on virus-host interactions

Mentors: So Iwata (UU), Elisabeth Sauer-Eriksson (UmU)

Actual starting date: 1 January, 1998

Administrative starting date: 1 January, 1998

Funding ended: 31 December, 2001

PhD awarded: 2 Sept, 2002

Continued career: PostDoc in the same lab, *i.e.* KI

Thesis title: Non-enveloped virus infection probed with host cellular molecules: a structural study

Inés Muñoz

Gender: Female

Year of birth: 1970

University of basic academic training: Alcala de Henares, Madrid, Spain

Affiliation: Molecular Biology, SLU

Supervisor: Jerry Ståhlberg (SLU)

Project title: Structural studies of cellulases and other enzymes with potential for use in the cellulose industry and bio-organic synthesis

Mentors: Gerard Kleywegt (UU), Uwe Sauer (UmU)

Actual starting date: 1 October, 1997

Administrative starting date: 1 January, 1998

Funding ended: 31 December, 2001

PhD awarded: 17 May, 2002

Continued career: Researcher within the Structural Biology and Biocomputing Programme at the Spanish National Cancer Centre (CNIO)

Thesis title: Structural and functional studies of cellobiohydrolase Cel7D from the white-rot fungus *Phanerochaete chrysosporium*.

Maria Selmer

Gender: Female

Year of birth: 1970

University of basic academic training: Lund University

Affiliation: Molecular Biophysics, LU

Supervisor: Anders Liljas (LU)

Project title: Structural studies on ribosomal proteins and RNA and their complexes

Gender: Female

Mentors: Pär Nordlund (SU), Torsten Unge (UU)

Actual starting date: 1 July, 1996

Administrative starting date: 1 July, 1996

Funding ended: 30 June, 2000

PhD awarded: 22 February, 2002

Continued career: Post-doc with Venki Ramakrishnan at the MRC Laboratory of Molecular Biology, Cambridge, England.

Thesis title: Protein-RNA interplay in translation. Structural studies of RRF, SelB and L1.

Henrik Hansson

Gender: Male

Year of birth: 1968

University of basic academic training: Stockholm University

Affiliation: Dept. of Biotechnology, KTH

Supervisor: Torleif Hård (KI/KTH/GU)

Project title: Protein-protein interactions

Mentors: Sybren Wijmenga (UmU), Karl Hård (AZ)

Actual starting date: 1 December, 1996

Administrative starting date: 1 January, 1997

Funding ended: 31 December, 2000

PhD awarded: 25 January, 2002

Continued career: SBN Net Coordinator

Thesis title: Structure and function of the SH3 domain from Bruton's tyrosine kinase.

Louise Kraft

Gender: Female

Year of birth: 1972

University of basic academic training: Göteborg University

Affiliation: Medical Biochemistry and Biophysics, KI

Supervisor: Ylva Lindqvist (KI)

Project title: Structural studies of vesicle-transport proteins

Mentors: Lars Liljas (UU), Johan Åqvist (UU)

Actual starting date: 1 October, 1996

Administrative starting date: 1 July, 1996

Funding ended: 30 June, 2000

PhD awarded: 14 December, 2001

Continued career: AstraZeneca SCL, Mölndal

Thesis title: Crystallographic studies of gluconate kinase.

Jenny Cromsigt

Gender: Female

Year of birth: 1972

University of basic academic training: University of Nijmegen, The Netherlands

Affiliation: Dept of Medical Biosciences, UmU

Supervisor: Sybren Wijmenga (UmU)

Project title: Development of methods for improved structure determination of larger systems by means of NMR

Mentors: Mikael Akke (LU), Mats Wikström (Biovitrum)

Actual starting date: 1 July, 1997

Administrative starting date: 1 July, 1997

Funding ended: 30 June, 2001

PhD awarded: 27 September, 2001

Continued career: IP Manager, Galapagos Genomics BV, Leiden, The Netherlands

Thesis title: New techniques for NMR structural studies on RNA.

Devapriya Choudhury

Gender: Male

Year of birth: 1964

University of basic academic training: North Eastern Hill University, Shillong, India

Affiliation: Molecular Biology, SLU

Supervisor: Hans Eklund (SLU)

Project title: Ribonucleotide reductase holoenzyme complexes

Mentors: Anders Liljas (LU), Tomas Lundqvist (AZ)

Actual starting date: 1 March, 1997

Administrative starting date: 1 January, 1997

Funding ended: 31 December, 2000

PhD awarded: 18 May, 2001

Continued career: AstraZeneca SCL, Mölndal (2001); Associate professor, Centre for Biotechnology, Jawaharlal Nehru University, New Delhi, India (2002)

Thesis title: Functional implications of macromolecular recognition: assembly of adhesive pili and enzyme substrate interactions.

Magnus Wolf-Watz

Gender: Male

Year of birth: 1971

University of basic academic training: KTH

Affiliation: Dept. of Biotechnology, KTH

Supervisor: Torleif Härd (KI/KTH/GU))

Project title: Structure and dynamics of proteins in solution

Mentors: Sture Forsén (LU), Johan Kördel (Biovitrum)

Actual starting date: 1 February, 1997

Administrative starting date: 1 January, 1997

Funding ended: 31 December, 2000

PhD awarded: 1 June, 2001

Continued career: Post-doctoral fellow in Dr. Dorothee Kern's lab, Brandeis University

Thesis title: Structure-function relationships of the human Runx1 transcription factor.

Patrik Andersson

Gender: Male

Year of birth: 1967

University of basic academic training: Umeå University

Affiliation: Medical Biochemistry and Biophysics, KI

Supervisor: Gottfried Otting (KI/Univ. of Canberra, Australia)

Project title: NMR spectroscopy of large proteins

Mentors: Torleif Härd (KI/KTH/GU)), Bryan Finn (LU)

Actual starting date: 15 April, 1996

Administrative starting date: 1 July, 1996

Funding ended: 30 June, 2000

PhD awarded: October, 2000

Continued career: Ericsson Radio Systems in Kista (near Stockholm)

Thesis title: Development of new NMR techniques and Structural characterization of complexes between the N-terminal domain of the *E. coli* arginine repressor and operator DNA.

Andreas Muranyi

Gender: Male

Year of birth: 1966

University of basic academic training: Lund University

Affiliation: Biophysical Chemistry, LU

Supervisor: Torbjörn Drakenberg (LU), Sture Forsén (LU)

Project title: Solution structures of blood coagulation protein domains

Mentors: Gottfried Otting (KI), Torleif Härd (KI/KTH/GU))

Actual starting date: 1 July, 1996

Administrative starting date: 1 July, 1996

Funding ended: 30 June, 2000

PhD awarded: 19 May, 2000

Continued career: Post-doc with Kristy Downing at the Oxford Centre for Molecular Sciences (2000) Amersham Biosciences in Uppsala (2002)

Thesis title: EGF-like Modules in Blood Coagulation Proteins. Ca²⁺ binding, module interactions, structure and dynamics as studied by NMR spectroscopy.

Tomas Hansson

Gender: Male

Year of birth: ?

University of basic academic training: ?

Affiliation: Dept. of Cell- & Molecular Biology

Supervisor: Johan Åqvist (UU)

Project title: Computational approaches to ligand design and enzyme catalysis

Mentors: Lennart Nilsson (KI), Gunter Schneider (KI)

Actual starting date: 1 July, 1996

Administrative starting date: 1 July, 1996

Funding ended: n/a (continued by Feierberg)

PhD awarded: 16 May, 1998

Continued career: post-doc with Wilfred van Gunsteren at the ETH in Zürich. Researcher at KaroBio, Stockholm (2003).

Thesis title: Ligand Binding and Enzyme Catalysis Studied by Molecular Dynamics Simulations.

A.7 Lic exams

Peter Holm

Gender: Male

Year of birth: 1974

University of basic academic training: Linköping University

Affiliation: Dept. of Biosciences, KI

Supervisor: Hans Hebert (KI & LU)

Project title: Electron crystallography of microsomal glutathione transferase

Mentors: Alwyn Jones (UU), Hans Eklund (SLU)

Actual starting date: 1 August, 1999

Administrative starting date: 1 January, 1997

Funding ended: 30 June, 2002

Licentiate exam: 2000

Continued career: PhD student (see Appendix A8)

Li Xing

Gender: Female

Year of birth: ?

University of basic academic training: Beijing University

Affiliation: Dept. of Biosciences, KI

Supervisor: Holland Cheng (KI)

Project title: Structural studies on virus-host interactions

Mentors: So Iwata (UU), Elisabeth Sauer-Eriksson (UmU)

Actual starting date: 1 January, 1998

Administrative starting date: 1 January, 1998

Funding ended: 31 December, 2001

Licentiate exam: 1999

Continued career: PhD awarded during 2002 (see Appendix A6)

A.8 Future exams.

Agnes Rinaldo-Matthis

Gender: Female

Year of birth: 1971

University of basic academic training: Stockholm University

Affiliation: Dept. of Biochemistry & Biophysics, SU

Supervisor: Pär Nordlund (SU)

Project title: Structural studies on protein phosphatases

Mentors: Anders Liljas (LU), Ladenstein

Actual starting date: 1 February, 1997

Administrative starting date: 1 January, 1997

Funding ended: 31 December, 2000

PhD degree anticipated: 28 May 2004

Peter Holm

Gender: Male

Year of birth: 1974

University of basic academic training: Linköping University

Affiliation: Dept. of Biosciences, KI

Supervisor: Hans Hebert (KI & LU)

Project title: Electron crystallography of microsomal glutathione transferase

Mentors: Alwyn Jones (UU), Hans Eklund (SLU)

Actual starting date: 1 August, 1999

Administrative starting date: 1 January, 1997

Funding ended: 30 June, 2002

PhD degree anticipated: 2004

Emma Jakobsson

Gender: Female

Year of birth: 1974

University of basic academic training: Uppsala University

Affiliation: Dept. of Cell- & Molecular Biology, UU

Supervisor: Gerard Kleywegt

Project title: Crystallographic studies of monoamine oxidase, a drug target in the treatment of clinical depression and Parkinson's disease

Mentors: Stefan Knight (SLU), Martin Norin (Biovitrum)

Actual starting date: 1 January, 1999

Administrative starting date: 1 January, 1999

Funding ended: 31 December, 2002

PhD degree anticipated: 2004

A.9 No exams.

Sevak Markarian (PI: Holland Cheng)	Left position. Reasons unknown.
Marika Joonas (PI: Hans Hebert)	Left for employment in industry (Statoil).
Helena Olsson (PI: Hans Hebert)	Left for employment in not known medical company.

A.10 The SBNet innovation list

[A list of innovations and prototypes that have been produced, spin-off companies founded or being contemplated, etc]

No records or statistics kept by SBNet.

A.11 The patents lists

[A list of patents awarded or pending. Specify any exploitations or plans for exploitation, *etc.*]

No records or statistics kept by SBNet.

A.12 A list of awards to SBNet funded researchers

[A list of awards to participating researchers, *etc.*]

No records or statistics kept by SBNet.

A.13 Swedish structural biology PIs in academia

PIs with an asterisk behind their name were included in the 1999 “International Evaluation of Structural Biology” carried out by NFR (now VR; note that this evaluation did not include modelling). PIs whose name is bold text were suggested participants in the original 1994 proposal to SSF. Nearly all of the listed PIs, or members of their respective research groups, have participated in activities arranged by the SBNet (*i.e.* annual conference, network courses or workshops).

<u>PI:</u>	<u>Institute:</u>	<u>Research area:</u>
Alwyn Jones *	UU	Crystallography
Lars Liljas *	UU	Crystallography
Torsten Unge *	UU	Crystallography
Janos Hajdu *	UU	Crystallography
Robert Robinson	UU	Crystallography
Suparna Sanyal	UU	Crystallography
Gerard Kleywegt *	UU	Crystallography, Structural Bioinformatics
Johan Åqvist	UU	Computational biology and simulation
David van der Spoel	UU	Computational biology and simulation
Hans Eklund *	SLU	Crystallography
Sherry Mowbray *	SLU	Crystallography
Inger Andersson *	SLU	Crystallography
Stefan Knight *	SLU	Crystallography
Jerry Ståhlberg	SLU	Crystallography
Anders Liljas *	LU	Crystallography
Salam Al-Karadaghi *	LU	Crystallography
Marjolein Thunnissen	LU	Crystallography
Derek Logan	LU	Crystallography
Mikael Akke *	LU	NMR
Torbjörn Drakenberg *	LU	NMR
Sara Linse *	LU	NMR
Hans Hebert *	LU	EM
Guoguang Lu	LU	Bioinformatics
Gunter Schneider *	KI	Crystallography
Ylva Lindqvist *	KI	Crystallography

Appendix A.13 Continued

<u>PI:</u>	<u>Institute:</u>	<u>Research area:</u>
Rudolf Ladenstein *	KI	Crystallography
Doreen Dobritzsch	KI	Crystallography
Kurt Berndt	KI	NMR
Philip Koeck	KI	EM
Holland Cheng *	KI	EM
Ulf Skoglund *	KI	Tomography
Oleg Shupliakov	KI	Tomography
Lennart Nilsson	KI	Computational biology and simulation
Andrey Karshikoff	KI	Computational biology and simulation
Pär Nordlund *	SU	Crystallography
Darcy Birse	SU	Crystallography
Christina Divne	KTH	Crystallography
Helena Berglund	KTH	NMR
Elisabeth Sauer-Eriksson *	UmU	Crystallography
Uwe Sauer	UmU	Crystallography
Jürgen Schleucher	UmU	NMR
Lennart Sjölin *	GU	Crystallography
Torleif Härd *	GU	NMR
Martin Billeter *	GU	NMR
Göran Karlsson	GU/CUT	NMR
Vladislav Orekhov	GU	NMR
Ute Kregel	CUT	Crystallography
Richard Neutze	CUT	Crystallography
Bengt Persson	KU	NMR, Bioinformatics

A.14 Swedish companies with structural biology research activities.

Listed are the name of the company, the head of (structural biology) research, the number of PhDs involved in structural biology research, and the disciplines covered by the laboratory.

<u>Company:</u>	<u>Head:</u>	<u>PhDs:</u>	<u>Disciplines:</u>
Biovitrum	Martin Norin	27	Structural Biochemistry & Biophysics Computational Chemistry Protein Expression & Purification Research Informatics
AstraZeneca	Anders Åberg	25	Crystallography NMR Modelling Protein Engineering
KaroBio	Mats Carlquist	11	Crystallography & Modelling
Active Biotech Research	Björn Walse	3	Crystallography (active collaboration with Anders Liljas, Marjolein Thunnissen and Salam Al-Karadaghi, LU) NMR (active collaboration with Mikael Akke, LU) Computational biology and simulation
Amersham Biosciences	Annika Bergensträhle	2	Computational biology and simulation
Medivir	Christer Sahlberg	1	Crystallography (active collaboration with Torsten Unge, UU)
SidecTechnologies	Ulf Skoglund	8	Cryo-electron tomography

B. Questions for the Programme Director

B.1 If the programme had been set up today, what changes would you have made to it given everything that you now know?

It is now 10 years since I was asked by SSF to prepare a Programme Proposal. I was asked to chair the views of a group of people, which limited the possibilities for defining a programme. Today, I would recommend something different but if I had the same people to argue with in the planning stage it would not have been accepted. I would now prefer SSF to support two (three would be better) Structural Biology Centres at the level of ~30M Skr over 5 years, plus Network funding to arrange a yearly meeting, and advanced graduate courses. The latter would be at the level of 1M Skr/year and would be have been organized by one of the Centres

B.2 What – if anything – will ultimately be the main impact of the programme on society and academy?

The lasting benefit of SBN Net, at least for a few years, will be the Networking aspects of the Programme. For the first time, all structural biologists in Sweden (academic and industrialists alike) had a yearly forum to meet and discuss science. Only a few senior people ignored this opportunity.

B.3 What do you expect will happen [What has happened...] to the activities within the programme after the Foundation funding has expired?

We have applied for continuing funding for the Network aspects of SBN Net. Even if we get funding, this will be for only a short time. We will, therefore, lose what we have built up. Structural Biology in Sweden will not have died at the end of SBN Net, but funding such meetings is not possible from other sources.

B.4 What was the problem of the programme?

We were one of the first to get started so we were guinea pigs. Within the Network, things worked very well. We had a fantastic Coordinator in Gerard Kleywegt, and world-class researchers on the Board in Guy Dodson and Iain Campbell. Guy and Iain's presence made the scientific evaluation process fair and more insightful than is usual.

It was not always easy to organize courses outside Uppsala, but with some notable exceptions

One or two senior scientists were notable only by their absence.

B.5 What was the most fun with the programme?

The success of our SBN Net conference.

B.6 Your main complaints and appreciations of the Foundation?

I have no serious complaints. As I said, we were guinea pigs at the start but that was understandable. The paperwork was not overwhelming. Swedish Structural Biology is in SSF's debt.

B.7 Your view of the programme board and its role?

The most active period for the Board was when we had to make funding decisions. It did its job professionally, as I expected.

The British members were not always able to come to the Conference but I have been glad to see their continued involvement. We made good choices. Björn Nilsson played an important role as Chairman, especially when we were allocating resources to different groups.

SBN Net took a good deal of my time, but it was worth it. I would like to thank SSF for their support over the last 10 years.