

Midterm Evaluation of the SSF Program

***Research Infrastructure
Fellows 2014***



SWEDISH FOUNDATION *for*
STRATEGIC RESEARCH

Preface

I wish to express my sincere gratitude to the Evaluation panel members and the Research Infrastructure Fellows for their ambitious work and generous participation, respectively, in preparing the present report.

The Evaluation Report confirms the Foundation's view on the strategic value of research infrastructure. It is further encouraging that all projects are recommended for continued funding for the full 5-year period with specific recommendations for development. The important role of the host institutions in providing adequate settings should not be neglected.

The Foundation will also use the Report as important input for its planning and execution of future related Calls.

With appreciation,



Lars Hultman, Professor
CEO SSF

Mid-term evaluation of infrastructure projects in the programme “Research Infrastructure Fellows”

Introduction

The need of advanced infrastructures offering technology, laboratory practice, data and competence increases steadily as the complexity in technology and specialization increase and as more problem-oriented research activities increases. The problem-oriented research requires typically use of many different techniques, hardly mastered by a single researcher, to cover various aspects of the problem. In a perspective of increased technical complexity and specialization together with the trends of more problem-oriented research put an extra pressure on access to state-of-the-art infrastructures. This means that the infrastructures have to be able to offer not only the most advanced equipment but also advanced competence for user support, guidance and further development. However, the need of such top competences is often overlooked, meaning that the infrastructures with time will degrade in terms of both technology and supporting competence and at worst no longer can meet the requirements from the research communities. Despite the importance of these people for many, often large research communities, there are no career paths supporting infrastructural development and advanced assistance. This is not sustainable in a longer time-perspective and will in many fields affect our ability to stay at the forefront of research.

The Swedish Strategic Research Foundation established in 2015 the first programme ever in Sweden on an alternative career path in the so called “Research Infrastructure Fellow” (RIF) programme. It aimed at strengthening the development and utilisation of research infrastructure at Swedish HEIs (Higher Education Institutions) over SSF’s entire field of activity. These infrastructure projects were supposed to meet the highest international scientific standards and to have a potential to strengthen Swedish industry and society. The project was supposed to focus on infrastructure that supports research within SSF’s priority areas. The call for proposals was directed towards key persons active in the research infrastructure who have a central operative role in developing the activities (see Appendix 1 in the Call for Proposals). The call for proposals resulted in 15 funded projects distributed among the following areas: Life Sciences 5; Materials Sciences & Technologies 7; Biotechnology, Medical Technology and other Life Science Technologies 2; Computational Sciences and Applied Mathematics 1.

In connection with the call for proposals SSF decided that all projects should be evaluated after two and a half years by a specially appointed evaluation committee. This evaluation was to be carried out during on-site visits and the results were to be summarised in a report for each project. The idea is also that the evaluation can influence the funding of the remaining project period and contribute to the formulation of possible related calls for proposals in the future.

Assignment

In January 2018, the Foundation appointed an external evaluation group consisting of four experts:

- Jan-Otto Carlsson (Chairperson), Uppsala University, Professor at the Department of Chemistry – The Ångström Laboratory, Inorganic Chemistry.
- Eva Olsson, Chalmers University of Technology – Professor Experimental Physics at the Department of Physics.
- Bengt Nielsen, Ph.D, CEO at Nielseninnovation AB, formerly Research Manager, EMEA at GE Healthcare, Hospital Physicist at Linköping University Hospital.
- Yngve Sundblad, Royal Institute of Technology (KTH), Professor at the School of Computer Science and Communication (CSC), Department of Media Technology and Interaction Design (MID).

in order to conduct a mid-term evaluation focused on the first phase of the programme covering a period of 5 years.

The evaluation provides a basis for SSF's decision regarding the continuation of the second phase of the projects based on achieved purposes, goals and results.

The purpose of the evaluation assignment is to determine whether the grant is being used to fulfil the purpose of the call for proposals, i.e. whether the projects contribute to improving the research infrastructure itself and making it more accessible, to promoting interdisciplinary collaboration between HEIs and disciplines and to engaging new user groups, including industry. The evaluation is also aimed at providing recommendations containing general and specific assessments as well as brief descriptions of the current state of the projects.

The evaluation highlights lessons that can be of great importance for the second programme phase of the projects and sheds light on what should and can be improved and/or modified.

The following projects were examined by the evaluation committee:

Appl. no	Surname	First name	Area	Gender	Univ	Project title in English
RIF14-0064	Agåker	Marcus	MS	M	UU	The Veritas Beamline @ Max IV
RIF14-0083	Akhtar	Farid	MS	M	LTU	Thermo-Mechanical and Tribology Infrastructure (TMTEST)
RIF14-0078	Andren	Per	LS	M	UU	Mass Spectrometry Imaging Infrastructure
RIF14-0091	Blom	Hans	BE	M	KTH	National infrastructure for super-resolution microscopy
RIF14-0045	Blomberg	Pontus	LS	M	KI	Vecura -an Infrastructure for Clinical Regenerative Medicine
RIF14-0055	Darakchieva	Vanya	MS	F	LiU	Terahertz Materials Analysis Center
RIF14-0081	Dávila López	Marcela	LS	F	GU	Implementing bioinformatic methods in medical research
RIF14-0079	Fernandez-Rodriguez	Julia	LS	F	GU	Research Infrastructure for Advanced Cellular Microscopy
RIF14-0042	Laure	Erwin	AM	M	KTH	Swedish Exascale Computing Initiative
RIF14-0046	Lehtiö	Janne	BE	M	KI	Infrastructure for information-rich proteome analysis
RIF14-0057	Linnarsson	Sten	LS	M	KI	Single-cell analysis
RIF14-0090	Maximov	Ivan	MS	M	LU	Development of Nanoimprint Infrastructure at Lund Nano Lab.
RIF14-0017	Nordell	Nils	MS	M	KTH	Strategic development at Electrum Laboratory - CMPLab
RIF14-0074	Persson	Per	MS	M	LiU	arc- atomic resolution cluster
RIF14-0053	Primetzhofer	Daniel	MS	M	UU	The Swedish Center for Ion-Beam Material Analysis

Overall assessment of the RIF programme

The committee was impressed by the professionalism in the organization and management of the infrastructure and the dedication by the RIF:s to develop and operate the infrastructure at the highest international level to the benefit of usually very large and broad research communities. The age of the evaluated infrastructures was very different from about 30 years to just a few years, which naturally affected in general the number of users and also the profile of the users. For the very young infrastructures many academic users were seen while the older ones attracted relatively more external users, particularly from industry and start-up companies.

Development of instruments and methods at the international top-level was reported and demonstrated at the site visits and some infrastructures were judged to be world-leading in their fields. Considerable efforts have been put in making the infrastructure user-friendly and easily accessible. However, a few infrastructures are suffering from lacking in capacity, mainly due low manning. The 15 key persons supported by the SSF RIF programme are key players in the development of Sweden's Research in Medicine and Science and Technology which will have a long-time impact on the quality of the research. The RIFs play a crucial role not only in the development of the infrastructure but also as a supportive dialogue partner for the users. The dedication of the RIFs is mission critical for the performance and sustainability of infrastructure. The scientific output from all the infrastructures was very impressive in terms of both quality and quantity. The activity plans for the next-coming years were realistic, though in some cases requiring minor corrections.

A variety of organizations, ranging from informal research groups to organizations at the university level, was observed for the infrastructures. In several cases the type of organization hampered an effective long-term planning and clear visibility strategy. The committee was very concerned regarding the lack of overall long-term plans of the infrastructures at several universities. Ten years ago, the universities in Sweden became responsible for the planning and obtaining the research equipment. However, very few universities could communicate solid planning procedures and planning of infrastructures at the site visits even though a few universities seem to recently have initiated such work. The evaluation committee met representatives of the management at both the university and department level. The overall judgement of the RIF programme from these representatives was that it was very valuable and yielded clear career paths for key persons at the infrastructure which purposely contributes to the quality and the long-term development and stability of the infrastructure.

Infrastructures and research equipment are quite expensive to buy and operate. However, the dependency of grants is far too high. After the SSF grant is finished the predominating part of the project needs new grants. Hence, there is a need to bring down the grant dependency below 50% instead of today's level being above 70%. A suggestion might be to start more business oriented, realistic and value-based service fee for service rate seen from an economical standpoint. Very much like companies do as a product or services has to carry its own costs to be a viable business. Another suggestion might be that in cases the infrastructures are about the same at different universities it might be cost-effective and quality-stimulating to merge such infrastructures with a slight individual profiling of them and with a common access system. Good examples of profiling and coordination of advanced infrastructures with joint funding are SNIC for large scale computation and myfab for micro fabrication, respectively.

The overall impression of launching the SSF RIF program is a success. Effective planning and operation of infrastructures require specialized personnel. However, without any clear

career path for technical specialists at infrastructures there are obvious risks of losing them which with time will affect the performance of the infrastructure in a negative way. The RIF programme can be regarded as a role model for what initiatives are needed to develop and keep advanced research infrastructures at the absolute forefront of research in a sustainable way, a prerequisite for international top-class research. The alternative career path, opened by this SSF program, is the first recruitment programme of Research Infrastructure Fellows as key persons, developing and supporting users at advanced infrastructures. The RIF programme is strongly encouraged to be followed by new similar initiatives at both research funding agencies and universities.

The evaluation committee recommends that all projects continue with the planned funding and that RIFs work to develop activities according to the proposals stated in the report.

Project evaluation reports

Here are the evaluation committee's assessments and recommendations for all 15 infrastructure projects.

1. Marcus Agåker, RIF 14-0064 Physics and Astronomy Uppsala University Project: The Veritas Beamline @MAX IV

The MAX IV project in Lund includes building up a state-of-the-art synchrotron radiation facility for research and development over a wide range of areas (life science, materials science, energy applications, etc.) The project is technically very complex with, in many cases, development of challenging new technologies all the way from the accelerators to the beamlines. They will enable future experiments to be carried out at purposely designed beamlines. At present there are 16 beamlines at different stages of development in the MAX IV project and there are detailed plans for more beamlines. The VERITAS (Very High Resolution, Intensity and Stability) beamline is designed to employ Resonant Inelastic X-ray Scattering technique (RIXS) for research in many different fields of materials science (communication, optics, electronics, sensors, etc.) and energy related research (solar and fuel cells, batteries). The VERITAS project is a joint project between Uppsala University and the MAX IV Laboratory, hosted by Lund University.

The RIF person Marcus Agåker is the project manager of the whole VERITAS project. His responsibilities are extraordinarily wide and include construction and testing of instrumentation for emission spectroscopy as well as development of software for instrument control and data collection. Moreover, he leads the work in mechanical design of equipment, procurement and production, in many cases with foreign companies. He is also responsible for the VERITAS build-up budget. Agåker's unique competence in the field is further demonstrated by his role as design reviewer for several synchrotron radiation beamlines at the MAX IV Lab as well as abroad. Finally, he is employed as researcher at Uppsala University, 100%, in the division for Molecular and Condensed Matter Physics.

The building-up of VERITAS started in 2015 with planned commissioning two years later. During 2018 the instruments are assembled. The beamline is planned to be in operation in 2019. The project as well as the whole MAX IV project are for several reasons delayed by about two years. The VERITAS project is at present focused on four different areas: magnetism, electrochemistry, molecular data base, and design of an advanced preparation chamber. Considerable progress was reported for the first two areas.

A completely new design concept for handling the samples has been developed for the beamline. It has been presented and well-received at many conferences and other synchrotron radiation facilities in the world. The PhD students involved in the project have a golden opportunity to learn not only the beamline technology but also how to manage large projects with many international aspects. The continued build-up work of the VERITAS beamline follows a revised plan with the beamline in operation in 2019. The work on magnetism and the electrochemistry will continue. The postponed work on establishing a comprehensive molecular data base for fingerprints and interactions of complex molecular systems as well as the development of the advanced sample preparation chamber will now be initiated.

Conclusions and recommendations

- New technologies and a new design concept for sample handling are introduced in the technically demanding VERITAS project. It opens for research in many strategically important areas (communication, energy, materials science). This is a world class project and in the absolute front of the field.
- The RIF Marcus Agåker is a highly qualified researcher and internationally established synchrotron radiation scientist. He has considerable international experience and networks, including research visits to other synchrotron radiation facilities world-wide.
- The pioneering design and build-up of the VERITAS beamline were impressive with excellent management of the whole project.
- Very few infrastructure projects have such complexity as the VERITAS project. It is quite uncommon in Sweden today to uniquely design and build-up new instruments. Based on the achievements in the project, prolonged funding of the project is strongly recommended.

2. Farid Akhtar, RIF 14-0083

Engineering Sciences and Mathematics

Luleå University of Technology

Project: Thermo-Mechanical and Tribology Infrastructure (TMTEST)

There is a lack of fundamental and reliable data for materials operating at extreme conditions. A unique infrastructure for mechanical and tribology characterization of materials at such conditions has systematically been built up at Luleå University of Technology through financial support by international, national and local university resources. The vision is to support research and development on materials mechanical, thermal, tribological behavior in automotive, aerospace, energy and structural applications. The investments in competence and equipment in the TMTEST (Thermo-Mechanical and Tribology) infrastructure are impressive. TMTEST offers access to Academia, institutes and industry and is now used by many different research groups within and outside the university.

Farid Akhtar is an associate professor and Research Infrastructure Fellow; RIF, at Luleå University of Technology. He has been very instrumental for the build-up of the infrastructure and is the engine in developing it in terms of methods, equipment, simulation tools and projects. He was recruited to the university a couple of years ago with the ambition to develop the TMTEST infrastructure. Akhtar's experience of setting-up and managing an infrastructure had been demonstrated earlier by the successful realization of the "National Spark Plasma Facility".

Impressive efforts have been made in building-up the infrastructure in terms of equipment, methods, project structure, access system and management. The infrastructure is considered to be of state-of-the-art. The combination of experimental work for measurements of materials properties at extreme conditions and development of simulation tools was demonstrated and judged to be very successful. The recent investments in the high temperature universal tribometer (1000°C) and the Gleeble 3800 instrument will produce a lot of data for further simulation analysis. The simulations cover various aspects of materials studies (e.g. phase transformations and precipitations), materials testing (e.g. hot ductility/workability) and metallurgical processing (e.g. continuous casting).

The TMTEST infrastructure has developed very well during the first half of the RIF programme. The scientific quality is very high with research covering a wide range of materials properties of relevance to synthesis and use in various applications (tribology, oxidation, energy, sensors, etc.), indicating also the interdisciplinarity of the research. Research results are published in well-known international journals and presented at many different conferences and workshops. Research and development in fields like tribology are extremely important for Swedish industry and a large fraction of the export revenues for Sweden comes from this field making this infrastructure of particular strategic relevance. Partners and users of the infrastructure include LU, SU, KTH, University West, CUMT, UTSB China, Swerea, Sandvik, SSAB, AKZONOBEL to mention a few. Moreover, the research environment is also attractive for partners to put their specialized equipment at the infrastructure. State-of-the-art equipment, competent user support, easy access, organization of informative workshops and management of the infrastructure have been important ingredients in the successful development of the TMTEST infrastructure.

The future development of the infrastructure includes recording of important tribology and thermo-mechanical data for extreme conditions to be used in different simulation tools. The materials systems range from high-temperature alloys to high-temperature energy applications. The research work will continue along plans for

- Establishing robust characterization methods to obtain thermo-physical/mechanical data on the materials behavior for their lifetime used in automotive, aerospace, energy devices and structural applications.
- Introducing and broadening the process simulation methods of materials of industrial interest e.g. light weight alloys, heavy alloys, high temperature and high strength ceramics and composites for aerospace, automotive and fusion energy applications.
- Collecting test data in extreme conditions such as rapid heating and cooling, application of high strain rates, fast dilatometry to produce new and novel materials with superior properties.
- Introducing and broadening the process simulation methods of materials of industrial interest e.g. light weight alloys, heavy alloys, high temperature and high strength ceramics and composites for aerospace, automotive and fusion energy applications.

There are also plans to start working with high-temperature corrosion and energy storage applications.

Conclusions and recommendations

- The evaluation committee was impressed by the achievements of the TMTEST infrastructure. The infrastructure is of high international standard including equipment and all the way to management and support structure.
- The infrastructure covers research fields of extreme importance for Swedish society. The users come from Academia, institutes and from small and large companies.
- The building up of the experimental facilities has been fast. However, the evaluation committee was not sure that important matching scientific and technical competences were available in all cases.
- With the fast build-up of equipment and competence, the evaluation committee recommends a consolidation of the established infrastructure and wait a couple of years before realizing the plans concerning high-temperature corrosion.
- Prolonged funding is recommended.

3. Per Andrén RIF14-0078
Pharmaceutical Biosciences
Uppsala University
Project: Mass Spectrometry Imaging Infrastructure

Mass spectrometry imaging (MSI) is a technique to visualize the spatial distribution of molecules, as biomarkers, metabolites, peptides or proteins by their molecular masses. The pioneering work of Richard Caprioli and colleagues in the late 1990s demonstrated how matrix-assisted laser desorption/ionization (MALDI) could be applied to visualize large bio-molecules (as proteins and lipids) in cells and tissues to reveal the function of these molecules and how function is changed by diseases like cancer. The method is important for researchers in the field of drug development and specifically for the pharmaceutical industry.

The Mass Spectrometry Centre was inaugurated in 2003, then as a part of the Uppsala University Strategic Renewal and collaboration Amersham Biosciences/GE Healthcare. A K&A Wallenberg grant made it possible to invest in two MALDI MASS Spectrometry Instruments. This was the first Mass Spectroscopy Imaging lab in Scandinavia. Until today VR and Uppsala University have invested around 8 million SEK in the facility. Finally, in 2016 SSF awarded the Research Infrastructure Fellow grant worth 15 million SEK.

The applicant and the Director for the NR-MSI is Dr. Per Andrén. His role is to lead the technology research and development as well as driving medical, pharmaceutical and biological projects. Additionally, Per Andrén is engaged in many other center activities: Training, information campaigns, commercialization, establishing protocols and methods, publishing and scientific presentations at national and international meetings.

The technology program proposed will involve significant development of techniques for Mass Spectroscopy Imaging, MSI at high spatial resolutions of as little as a few microns in three dimensions. This will be done together with high sensitivity profiling and imaging based on intelligent on-tissue derivation for monitoring less abundant species. The instrumentation at the center is leading edge from a scientific perspective. The challenge is to create more interest from other researchers and industry for using the facility. This can be a challenge as the technique is not a commodity modality yet.

The scientific output from the center is impressive with 17 peer reviewed papers and 64 oral presentations. Many collaborations with Pharma industry have resulted in more than 100 pharmaceutical compounds from different tissues and have been imaged together with approximately 40 potential drug candidates. The technique is rather new and the center is in the process to establish themselves and grow the number of external users.

The development plans for the second half of the project is to:

- Increase the number of collaboration projects.
- Increase the dissemination, particularly teaching courses of Master and PhD students.
- Increase focus on diagnostic and prognostic collaboration projects (biomarker discovery).

The development of the analysis software MSI-Quant is believed to be a major asset development that could very well become a standard in the field of MSI.

Conclusions and recommendations

- The infrastructure is very well equipped with top notch MSI technology. Due to the fact that the potential and benefit of using Mass Spectrometry Imaging techniques are not so well known to the broad research audience, a type of “marketing activity” will probably be needed in order to get a more broadly use of the infrastructure by outside researchers and industry.
- The very long analysis times needed especially for the very high spatial resolution tasks might be a challenge. At the same time, far from all cases/tasks will benefit from the highest spatial resolution. “New market segments” could be created for new types of applications. The evaluating committee therefore recommend the centre to increase the effort to enhance the infrastructure to become a more broadly accommodating unit for the benefit for Swedish and international researchers as well as industry.
- There is also a need to start charging for the service to outside users. Free service for a top notch facility could be misleading and the value of the technique could be perceived to be low.
- The support for the infrastructure from the University needs to be more clear and specific in order to warrant the sustainability for the infrastructure.
- The infrastructure is state-of-the-art technique where the RIF Per Andrén has contributed significantly to the development. The presented future plans are technically demanding and may open for exciting applications. The broadening of the activities to new application areas was appreciated. Prolonged funding is recommended.

4. Hans Blom, RIF14-0091

SCI - Applied Physics

KTH - Royal Institute of Technology

Project: National Infrastructure for Super-Resolution Microscopy

The Advanced Light Microscope, ALM, was established in 2010 at the SciLife Lab in Stockholm. The investment came from a strategic grant from VR. In 2013 the ALM lab received a national facility grant. With the SSF-RIF grant the ALM-Lab has been able to expand the expert team supporting the external scientists using the equipment. The main application focus is bio imaging and molecular structure.

The aim of the infrastructure is to provide high-quality services to academic researchers, industry and healthcare by using Advanced Light Microscopy, ALM. The infrastructure supports SciLife Lab researchers particularly, but also scientists nationally and internationally are welcome. The infrastructure is also acting as an integral part of the distributed National Microscopy Infrastructure, NMI, in Sweden.

The head of the facility is Dr. Hans Blom, who is very experienced in most of the different microscopy techniques and specifically in the advanced super-resolution fluorescent microscopy technique. It is possible with this technique to obtain nanometer spatial resolution enabling studies of individual molecules. Blom's experience in microscopy instruments and methods is a clear asset in leading of the facility. He is also well connected with international leading microscopy sites. Hence, he is able to rapidly capture and implement new ideas and techniques at the ALM facility.

The infrastructure is very well equipped with a good arsenal of different types of microscopes. The focus of the infrastructure is bio-imaging and molecular structure and the primary technique used is fluorescence microscopy with super-resolution, allowing for studies of both structural details and functional behaviors. The infrastructure will also promote translational implementation of research findings into healthcare and industry. Several instrument and method developments are ongoing within the center. Examples are: Localization microscopy including analysis software, new super-resolution, multi-focus microscopy technique and a new test-protocol in order to make a subject transparent. Maybe the most exciting projects at present are the clinical project on kidney pathology together with a research center in Cologne and the very challenging attempt to recreate the hearing on deaf patients.

The future developments include a broadening of the offerings for the infrastructure to support also light sheet microscopy, that can image living samples in 3D with high speed (10 frames/sec), as well as the fluorescence correlation spectroscopy technique. The collaboration with the microscope manufacturer Leica should also be mentioned as a clear asset for the center.

The infrastructure is a node in the National Microscopy Infrastructure, NMI together with Stockholm University, Gothenburg University, Umeå University, Linköping University and Chalmers. The NMI is a distributed network with a centralized Website where interested users can enter their project requests. Via this project process, NMI will be directing a submitted project to the site with the best fit for a project request, from an equipment and expert point of view.

The infrastructure has been able to hire very experienced staff scientists enabling excellent support of users. However, development plans for these scientists are lacking which is not a

sustainable situation for the infrastructure. This means that after year 2020, when the SSF grant is finished, there is an obvious risk of losing key personal to other similar facilities around Europe. KTH is the host university of the ALM facility and has recently introduced a planning process for all their infrastructures, which is supposed to also include important staff scientists.

The ALM facility has through the years gotten large amount of visibility and publicity. The highly competent staff has certainly contributed to this fact. A key focus within the facility has been the sample preparation techniques that are critical to the results obtained. The spatial resolution of today's microscopes has increased and hence the sample preparation becomes critical.

During the RIF14 grant period 4 major scientific papers has been published. The educational program consists of training of users on different microscopes to be able to operate them by themselves. Courses in the form of Symposia and Workshops, mainly on Super resolution fluorescence microscopy, are scheduled on a yearly basis and the infrastructure also offers a Ph.D. course.

The future development plans for the infrastructure can be hampered by the fact that large equipment investments will be needed continuously. The replacement of older microscopes and introducing new imaging techniques could become a limiting factor for keeping the high profile that Sweden has today in microscopy. Another challenge to manage for the microscopy facilities is the increased data storage and data analysis needs.

The development plans for the second half of the SSF grant are:

- Continued development of the microscopy support, in depth as well as broadening.
- Development of additional educational programs.
- Competence development of the staff.
- Continued integration of the national service through NMI.

Conclusions and recommendations

- The Advanced Light Microscopy infrastructure is well equipped and a competent microscopy center with excellent international track record.
- A long-term solution for the infrastructure in terms of funding will be needed to keep the infrastructure at a sustainable operation level for the future.
- The evaluation committee would recommend the National Infrastructure for Super Resolution Fluorescence Microscopy to look into the user fee at the facility. A too low fee for service will definitely increase the challenges for a sustainable operation in the future.
- The committee was pleased to see the introduction of a strict planning procedure at KTH for their infrastructures.
- The infrastructure is very well-equipped with state-of-the-art microscopes. The competence of the staff is very high with a lot of international connections. The management was judged to be both effective and stimulating. The development of the infrastructure was very positive and the future plans in terms of new application areas were both exciting and demanding. Prolonged funding is recommended.

5. Pontus Blomberg, RIF14-0045

Laboratory Medicine

Karolinska universitetssjukhuset Huddinge

Project: VECURA - An infrastructure for Clinical Regenerative Medicine.

The Good Manufacturing Practice (GMP) facility Vecura was inaugurated at the Karolinska University Hospital already in 1996. In 2008 the first cell based GMP-product for Alzheimer Disease entered into a clinical trial. The Karolinska Center for Cell Therapy, KCC, was established in 2017.

The aim of the facility is to give clinical researchers access to GMP-processed cells and gene therapy vectors for clinical trials and clinical use. The facility has 19 employees and is open for users from academy, healthcare and industry. The facility has approximately 50 % of the funding needed to run the facility through the Karolinska Institutet and Stockholms Läns Landsting, SLL.

The RIF person Pontus Blomberg is the head of the Department. He is a micro-biologist by training and very experienced in the field of cell and gene therapy. He has successively developed and operated the facility from the very first beginning and his leadership is critical also in the future.

The VECURA facility has been very active during the period for the SSF grant and an impressive list of products, projects and activities was presented at the site visit. More than 50 GMP products for clinical tests have been made and more than 700 patients have been treated with products from VECURA. Moreover, Vecura participates also in the Advanced Medicine Product project, CAMP, a national project supported by Vinnova, as well as in the opening of a Pharmacy function for new drug therapies based on biological pharmaceuticals. An indicator of the excellent quality of VECURA is that it attracts international customers from The Netherlands, Denmark, UK, Italy, France, Germany, Austria and Poland. For the remaining half of the SSF grant period the infrastructure will focus on:

- Establishment of a Pre-GMP lab facility is ongoing, in order to increase the availability and capacity at the GMP-facility.
- Development of tools for gene transmission.
- Immunologic therapy.
- Nano-medicine, new EU-grant to be started with Austria, Spain and KI.
- Cell tracking with imaging, a new project under negotiations with industry.

Conclusions and recommendations

- The VECURA infrastructure is a well-established infrastructure since several years. It is well operated and functions excellently with an impressive productivity.
- The VECURA facility will be able to expand its activities both in Sweden and internationally in the future.
- The introduction of the Pre-GMP facility gives a good base for such an expansion.
- The total user fees are today in the span from 2-5 million SEK. This represents 10 to 25 % of the total yearly cost of the infrastructure. An excellent result!
- The VECURA infrastructure is a unique and extremely important infrastructure for many national and international users (Academia, industry, healthcare). The management of the infrastructure was judged to be excellent. The accomplishment of the infrastructure was admirable with well-defined future plans. The RIF person is also judged to play a very important role in the future technical development and management. Prolonged funding is strongly recommended.

6. Vanya Darakchieva, RIF14-0055
IFM (Physics, Chemistry and Biology)
Linköping University
Project: Terahertz Materials Analysis Centre

Electromagnetic radiation with 0.1-10 Terahertz (THz, 10^{12} per sec) is on the border between high frequency end of microwaves, and the low end of infrared radiation. Use of THz radiation is very promising for analysis of materials giving new or complementary information to analysis in other frequency bands.

The RIF, Vanya Darakchieva, has developed and built-up the only THz ellipsometer in Europe and established it as a resource at Linköping University. The goal of the project is now to develop the equipment further and establish THeMPAC (Terahertz Materials Preparation and Analysis Centre). It is an open e-access infrastructure for users in academia and industry, intended to be used in basic and applied research in physics, chemistry, biology and ultra-fast communication.

Dr. Darakchieva, the RIF, leads and initiates the activities with great enthusiasm, concentrating more on the infrastructure than her own research. She is Associate Professor and quite independent from the rest of the university structure. There is a faculty funding for the infrastructure.

Both instrument and methods have been admirably built up. In the original RFI application seven technical goals were specified and five of them have already been reached. Data modelling methodology has also been developed and successfully applied to, e.g., graphene, graphite and thin films.

The THeMPAC infrastructure was inaugurated in March 2016 as a unique resource not only in Sweden but also in Europe. Most of the 11 users so far are from Linköping University but there are also academic users in Lund, Uppsala, Spain, Poland and a Swedish company. At least 14 user groups or research fields have been encouraged. Several THz workshops and courses have been arranged. An obvious strategic output is the establishment of the research centre, THeMPAC with equipment and supporting and a small but very active user community. The scientific output from the infrastructure is reasonable, including at least 8 peer-reviewed publications.

The project is expanding the ellipsometer into an optical Hall effect instrument that can determine in a contactless manner electronic and spin transport properties in materials. This involves frequency calibration, and acquisition of software and hardware, notably a cryostat for superconducting. A specific short-term plan is development and implementation of a data bank of test results. Another improvement of the instrument is a dual rotating compensator that will be developed. There are also concrete plans for collaboration with research groups, e.g. Complex Materials Network at University of Nebraska and the Graphene Research Lab in Linköping. The long-term vision is to develop and employ the unique THz spectroscopy and imaging techniques to address many different needs in basic and applied research, academic and in industry, in Sweden and worldwide.

Conclusions and recommendations

- This unique infrastructure is very promising with impressive results the first two years. The user community is quite small but growing. The academic output is extraordinary.
- The activities depend very much on a few individuals which makes it vulnerable. Recruitment of more research personnel is indispensable.

- More long-term funding must be secured, through more involvement in the university infrastructure.
- It is not clear whether there is an international reference group, otherwise recommended.
- The accomplishments during the first few years are impressive. The experimental technique is new in Europe and is expected to produce a lot of new pioneering knowledge in many different fields of science and technology. The management of the infrastructure was judged to be effective and stimulating. The RIF person will play a very important role in the future technical development and management. Prolonged funding is strongly recommended. The importance and progress of the infrastructure strongly motivate a recommendation for further SSF funding.

7. Marcela Dávila López, RIF14-0081

Bioinformatics Core Facility:

University of Gothenburg,

Project: Implementing bioinformatics methods in medical research

The Bioinformatics Core Infrastructure, BCF, was established in 2006 as one of five Core Facilities at the Gothenburg University. It is a part of the ambition to provide open access to advanced techniques and personnel. The infrastructure develops and implements tools and methods through computer programs and visualization. They are based on statistical and bioinformatics knowledge and developed with the goal to increase user accessibility.

The personnel of the infrastructure is a tight group with 4 bioinformaticians, 4 statisticians and 1 programmer. The leader, the Research Infrastructure Fellow Marcela López, is both operational and managing. She is involved together with the others in most of the activities, from designing the tools, giving PhD courses, finding collaborating medical research groups, applying for grants, external contacts, visibility. The infrastructure belongs to the important and nicely working core facility organization at Gothenburg University from which the BCF infrastructure receives a faculty grant of 8 MSEK per year.

A main goal of the infrastructure is to develop and implement bioinformatic methods for integration and visualization of genomic data from Next Generation Sequencing (NGS). NGS has the potential to revolutionize diagnostics and introduce personalized medicine. The methods are here used in medical research on identification of complex diseases, detection of rarely expressed mutations for early detection of cancer and analysis of amplicon data (RNA or DNA pieces that amplify replication events). The project aims at consolidating the Bioinformatics Core Facility as a national infrastructure. The NGS software and tools are unique in Sweden and intended for specialized users. The focus on user accessibility is important and could be seen, although the development of the tools is not quite finished yet. The development seems to be more or less from scratch.

A central output from the infrastructure is the InVi visual tool for visualization of genomic data. This is fully implemented but more testing is needed. A database for the data has been built. The infrastructure has been involved in a variety of projects, mainly with Sahlgrenska Akademien and Gothenburg University. For the year 2017 nearly 100 projects were reported. 14 scientific papers have been published, also from three collaborating medical research groups, with BCF personnel embedded. Collaboration with the Sahlgrenska hospital works well and has an extensive role in the development of the three strategic areas identified:

- i) data integration from high throughput data with stroke as a case,
- ii) early clinical diagnosis with cancer as a case,
- iii) reliability.

More testing of the of the InVi visual tool is required before it is fully operational. Unfortunately, there is a lack of samples for the testing that will be remedied. An extremely important mission of the BCF platform is workshops and courses in statistics and bioinformatics to meet the needs from the very broad communities. A specific focus will be on development of tools and methods for wet-lab researchers. The external collaborations with universities in Heidelberg and Mallorca will be expanded. Two programmers with bioinformatics competence will be recruited to further strengthen the programming capacity.

Conclusions and recommendations

- The BCF infrastructure is judged to function well in supporting medical and biological research. The close collaboration with hospitals is judged to be both extensive and effective.
- Collaboration with other infrastructures on bioinformatics in the country is strongly recommended, particularly with BILS (Bioinformatics Infrastructure for Life Sciences) and WABI (Wallenberg Advanced Bioinformatics Infrastructure).
- Stronger national and international contacts with similar research and development, in visualization is recommended, e.g., with the strong group in medical visualization in Linköping. From such contacts and surveying similar bioinformatics activities it might be possible to use parts of existing software in the development of the tools from the project, making it more productive. A reference group with such contacts should be formed and trigger a stronger research and development network.
- When recruiting bioinformatics programming personnel, the competition can be met by the attractive medical applications of exciting tools to build. When the tools and methods are reliable offering them to more external users should be considered, also as a possible way for extra funding.
- Gothenburg University has gathered their infrastructures, including BCF, in a common unit, which is a strength particularly in the overall long-term planning.
- The infrastructure has not reached its full strength, due to lack of personnel. The close collaboration with particularly Sahlgrenska Hospital and the dialogue with the users in general to meet their needs was very much appreciated. The smooth and competent management of the infrastructure together with dedicated and skilled personnel make the infrastructure promising. Continued funding from the RIF programme is recommended.

8. Julia Fernandez-Rodriguez, RIF14-0079
Centre for Cellular Imaging Core Facility
University of Gothenburg
Project: Research Infrastructure for Advanced Cellular Microscopy

In 2006 an open access center for Life science was established at Gothenburg University. Gradually the Centre for Cellular Imaging, CCI was formed and step by step the CCI has gained national and international recognition. The goal of the Centre for Cellular Imaging, CCI, is to develop and implement new preparative methods and workflows for innovative imaging technologies like: Correlative Light/ Electron microscopy, super-resolution and functional microscopy. The key applications are all within life sciences. One of the strengths of the infrastructure is to obtain further knowledge about cell structure and function. Another key driver for the infrastructure is to make these methodologies broadly available to the life science community, academia and industry, as well as the healthcare organizations.

The director for the Centre for Cellular Imaging, CCI is Dr. Julia Fernandez-Rodrigues. She is very experienced in the field of super resolution microscopy and a clear and articulated leader for the CCI. Her extensive national and international networks give the centre visibility as well as easy and natural access to new developments in the field of microscopy. Within the National Infrastructure for Microscopy, NMI, CCI has a strong position and Julia Fernandez-Rodrigues is also very active within the NMI. (NMI consists of Umeå University, Stockholm University, KTH and Linköping University).

The CCI is very well equipped with a state of the art equipment base and tools for cellular imaging. The staff are experts in the fields of biology, cell biology, chemistry, physics and image processing & image analysis. The whole staff is focused on giving support for their customer base on their different research topics. The number of external users is large and increasing. During 2017 they were more than 200! The bottleneck for being able to accept more users is the availability of experts to support the increasing number of users. The development of new methods in connection with new research applications is seen to be increasing and also shifting into more clinical oriented methodologies. One such new application is the ongoing "Skin Regeneration and Wound-Healing" project supported by SSF.

The scientific output from CCI in terms of publications is always together with external users and the focus of the centre is method development in dialogue with users. This means that newly developed methods can be offered within both the Centre and the NMI.

The major challenge for the CCI centre, as for all infrastructures in general, is to be able to keep the experts who are vital for the survival of the infrastructures.

The immediate development plans for the CCI are:

- International Networking.
- Intensive and expanded collaboration with industry partners.

Conclusions and recommendations

- The evaluation committee sees the CCI-centre as a good role-model for an infrastructure with a clear role for the centre with method developments as a focus, not own research.
- The evaluation committee recommends that an international advisory board is established in order to keep the leading position that the facility has reached.
- The suggested development plans were judged to be very relevant and realistic.
- The CCI has a laudable support from Gothenburg University.
- The close dialogues between the infrastructure and the users pave the way for important development of the whole infrastructure. The management was very competent and welcoming with a profound ambition to provide research service at different levels. Prolonged funding is strongly recommended.

9. Erwin Laure, RIF14-0042
Parallel Computer Centre
KTH - Royal Institute of Technology
Project: Swedish Exascale Computing Initiative

The Parallel Computer Centre (PDC) was established at KTH in 1990 and is one of the two large high-performance computer centres in Sweden. The goal of the SECI (Swedish Exascale Computing Initiative) is to explore hardware and algorithms for many-core computer architectures and reduced needs of input/output operations increasing the performance of the current systems and preparing for the next generation supercomputers. SECI is a co-design effort with collaboration on hardware, algorithms, programming environments and applications.

The RIF, Erwin Laure, is a key person as director of PDC at KTH since 2010 and initiator of many of its current activities. He is responsible for the strategic and daily operation. He is also strongly connected to international cooperations in supercomputing such as PRACE, the Partnership for Advanced Computing in Europe. The SECI team is embedded in user groups and in the PDC team of experts.

The main "instruments" in PDC have been competitive new supercomputers in new generations, typically every 5-7 years. The current main supercomputer "BESKOW" was installed in 2014 and performs up to 2.5 PF (petaflops, 10^{15} floating point operations per second). It is the largest high-performance computation resource in the Nordic countries. The infrastructure also consists of the pre- and post- processing system TEGNÉR, also used for less demanding computational processing, and several mass storage units. Methods developed are mainly computational algorithms taking advantage of the parallel computing and visualisation methods for presenting resulting data. Specifically, three co-design projects have been initiated in different fields: Life sciences (molecular dynamics), engineering (fluid dynamics) and computational chemistry.

A national perspective is the close cooperation between academic supercomputer installations in Sweden through SNIC, Swedish National Infrastructure for Computing, which together with universities gives basic funding to the infrastructures. There are about 600 active users of PDC, about 150 simultaneously. Main user areas are physics, life science and molecular dynamics and there is also considerable industrial collaboration in use and training. Scania has invested more than 50 MSEK in equipment. The team of experts at PDC supports the users and gives courses and workshops on aspects and applications of supercomputing.

A strategic focus for the RIF is software and methods for future high-performance computing architectures, which is essential for keeping Sweden competitive in research and development. A knowledge pool is built for new domains such as artificial intelligence and image analysis.

Preparations have already started for the acquisition in 2020 of a next generation supercomputer with performance in the EF (exaflops, 10^{18} floating point operations per second) magnitude. Results from SECI will be a key factor in this procurement process. Efforts in the three co-design projects will continue and be expanded to other domains, e.g. climate.

Conclusions and recommendations

- The strategic focus for the RIF is on software and methods for future high-performance computing architectures. This is essential for keeping Sweden competitive in research and development.
- The SECI project allows focus on the hard infrastructure problems in supercomputing.
- The joint funding of the supercomputer infrastructure in Sweden through SNIC (Swedish National Infrastructure for Computing) with its own responsibility to distribute resources. It should be a pattern also for other infrastructure areas.
- The overall strategic planning procedures of the infrastructures at KTH, where PDC and SECI are included, was appreciated.
- Software and methods for future high-performance computing as well as international co-operations are key issues for the RIF person. The value for the future supercomputing in Sweden of SECI and its first results highly motivate a strong recommendation for continued funding from the RIF programme.

10. Janne Lehtiö, RIF14-0046

**Oncology-Pathology
Karolinska Institutet**

Project: Infrastructure for information-rich proteome analysis

The infrastructure “*National facility for biological mass spectrometry*” started as a core facility at Karolinska University Hospital in 2005. In 2009 the facility was moved to SciLife Lab as a regional organization financed by SLL and SciLife Lab. VR funded a national initiative called BioMS in 2016 in collaboration with Lund and Gothenburg. In 2018 SciLife Lab became a national facility. The infrastructure is part of a distributed network in Sweden, BioMS, where each facility has their special competence and technology matching their different competences.

- SciLife Lab: Mass Spectroscopy, biology and proteomics.
- Lund: Mass Spectroscopy mainly specific proteomes.
- Gothenburg: Informatics.

By the natural individual profiling and focus of the different sites within BioMS the resources can be used more efficiently and competences can be kept at a high scientific level.

The goals for the “*National facility for clinical proteomics mass spectrometry*”, include development of novel methods and services for proteomics/genomics, sub-cellular analysis and protein-small molecular binding analysis. The infrastructure provides information-rich data for proteomics on the molecular level (phenotype).

Professor Janne Lehtiö has purposely and successfully developed and built-up the infrastructure from the beginning, starting as a post doc, to what it is today where he now is Node director for the national facility. He has also several other duties on the research management level, Hospital FoU director and Head of the Oncology Pathology Department. His own research team consists of 20 persons with a focus on: Technology development, application development and cancer research. There is no doubt that Janne Lehtiö has been and will continue to be a key player within the infrastructure.

Development of instruments and methods has been the key focus within the infrastructure. The number of external users, outside SciLife Lab, is growing. The fee for service has grown from 1.6 million SEK in 2016 to 1.8 million SEK in 2017 and for 2018 it is expected to grow further. The trend now is that there will be more projects and the projects are becoming broader and more demanding.

The users are researchers within the Life-Science field and primarily SciLife Lab researchers are using the infrastructure today. Life Science industry and international users are today representing a large fraction of the user population. The strategic relevance includes biological and biochemical research. Other topics are applied oriented research like translational research and drug development.

The output of the infrastructure, scientifically and strategically has been strong over the period of the SSF RIF14 grant. The team has published 5 papers with major impact. Two of them is in Nature and Science journals, respectively. The group is one of the leading sites within their field of science in the world.

Several new technologies and applications have been initiated that will have a profound impact on the future research:

- How does genomics variants influence protein levels?

- Cancer genome aberration can cause cancer specific proteins to be released. These proteins can be recognized by the immune system.
- Liquid chromatography-mass spectrometry for Peptide ID and relative quantification.
- Protein clustering and cluster annotation.
- Classification prediction of sub-cellular localization.
- In depth plasma analysis – plasma proteomics.

The technology and method developments are in a phase where the techniques are starting to move into clinical use. The first applications are mainly within the oncology field.

Future projections:

- Proteomics is still on the steep development curve.
- Next big wave in omics: proteomics and multi-layer analysis.
- Clinical proteomics.
- Experimental omics and big data mining.

Risks:

- Sustainable level of funding to allow large-scale proteomics will be critical. Infrastructure financing is fragmented and short term today.
- Career path for technical experts in academia is missing.

For the future there is a financial need of the centre of approximately 15 million SEK per year for staying on the top level in terms of instrumentation. This is a major challenge for a very fast-moving discipline. The expectation is that there will be an increase in speed and sensitivity of approximately 20 % per year for the type of instruments needed for this type of research.

Conclusions and recommendations

- The National facility for biological mass spectrometry at SciLife Lab is functioning very well and the unit offers leading edge knowledge and technologies for the exciting field proteome-genomics in Sweden as well as internationally. The techniques developed hitherto offer outstanding research opportunities but also very interesting and important capabilities that eventually will become clinically important applications starting in the field of oncology.
- Due to the very fast technology turnover within the field, the future financing needs must be thought through by the universities in order to make the efforts and investments hitherto sustainable.
- To continue to primarily be dependent on new grants is not a sustainable method for the future.
- The key players of the facility have a profound value to the centre and their long-term continuation or replacements needs to be considered.
- The evaluating committee sees a risk for Janne Lehtiö to be overloaded due to his many engagements and duties.
- The evaluation committee was impressed by the achievements and management of the infrastructure and strongly recommends prolonged funding.

11. Sten Linnarsson, RIF 14-0057
Medical Biochemistry and Biophysics, MBB
Karolinska Institutet
Project: Single-cell analysis

Fifteen years ago basically the whole human genome (the so called HUGO project) had been sequenced from bulk cell populations, i.e., an averaged picture of the genome had been obtained. However, bulk sequencing could not reveal heterogeneities in cell populations – of highest importance in basically all biological processes – and it was obvious that sequencing of individual cells was needed to be able to study the most fundamental cell processes. In 2009 the first single-cell RNA sequencing (scRNA seq) method was published. Since then there has been an impressive methodological development in isolation and lysis of single cells, reverse transcription, and cell DNA amplification as well as sequencing library preparation. In 2014 the National Eukaryotic Single-cell Genomics Facility at SciLifeLab in Stockholm, founded by Sten Linnarsson (RFI) and Rickard Sandberg, was started with a focus on eukaryotic single-cell genomics and transcriptomics.

The RFI Sten Linnarsson is the natural leader and key person of the infrastructure. He is now leading and managing a group at KI. Before that he founded the company Global Genomics AB and has been both CEO and CTO of the company. He has developed both instruments and methodology of significant importance for the operation of the infrastructure. The cutting-edge technologies provided by the infrastructure are mainly developed by the founders of the infrastructure. The infrastructure is hosted within the SciLife Lab, KI Solna.

The development of the facility has been directed towards higher throughput, improved computational tools, and acquisition of organism single cell RNA sequencing datasets for healthy adult mouse and human. The platform has developed both instruments and methods for large-scale single cell RNA sequencing, where Linnarsson is a pioneer in the field and has made significant contributions in both cellomics spatial omics. At present users come with cells and get raw expression data back after analysis at the facility. More than 320000 cells have now been sequenced in 137 projects on 9 different species. The predominating user of the infrastructure is KI. Other users include the universities in Lund, Stockholm and Uppsala, respectively. However, there is a lack of manpower hampering a faster development with the specific goal of developing methods for single cell RNA sequencing allowing for analysis of at least 10000 cells/day for less than \$1/cell.

The infrastructure has contributed significantly to the development of the whole field. It has produced a lot of data for many users and many different application areas and formed the basis for extensive international publishing. The strategic relevance of the project is mainly in Academia but is expected to expand into clinical settings in a medium-term perspective. A lot of publications have been produced on the basis of the data produced by the infrastructure. A recently published breakthrough in Nature is the development of a technique for capturing dynamic processes in individual cells, which means that both disease and embryonic development processes can be studied.

The plans for the future are ambitious and include both small and large projects. The RFI is one out of five principal investigators in the very demanding Human Cell Atlas (HCA) initiative. It is a global collaboration for 3-D mapping of all cells in the human body and how they interplay with each other to form tissues as well as how changes in the cell system may influence health and disease. Linnarsson is both on the board of the HCA project and coordinator in it.

Conclusions and recommendations

- The Eukariotic single cell RNA sequencing facility is a young and world-leading infrastructure within SciLife Lab and hosted by KI. The RIF is one of the pioneers in the field.
- The infrastructure has significantly contributed to the development of the single cell sequencing technology by designing both instruments and methodology.
- Future plans are ambitious and include further development of techniques to produce large sequencing data. The international Human Cell Atlas project is very exciting and demanding and of strategic importance for society as a whole.
- The manning of the infrastructure (staff only 6 persons), though very competent, is very limited and cannot fully meet users' needs depending on financial constraints.
- KI is in a stage of developing a system for long-term planning of infrastructures which should give the single cell RNA sequencing a more solid future planning.
- On the basis of the impressive achievements in terms of development of instruments and methodology as well as the scientific output and the future plans prolonged funding is strongly recommended.

12. Ivan Maximov, RIF 14-0090

Physics

Lund University

Project: Development of Nanoimprint Infrastructure at Lund Nano Lab

Lund Nano Lab (LNL) is part of Myfab (the distributed Swedish national infrastructure for micro- and nanotechnology) which is a national research infrastructure for both fundamental and high-tech company-related research and development. The LNL offers service all the way from materials synthesis and structuring to property measurements and device fabrication. Nanoimprint lithography (NIL) has been identified as a next generation lithography technique that is relatively fast and inexpensive compared to electron beam lithography. NIL transfers a lithographic pattern by a direct mechanical contact between a hard stamp and a substrate with a deposited polymer. It can be used for large scale fabrication of high resolution nanostructures, e.g. nanowires, with a very high throughput.

The RIF person Maximov is a pioneer in the NIL field. He has had different positions within LNL, many of them coordinating. He has published many papers in international journals in the area and demonstrated excellent scientific and technical achievements. He has good international experience with well-established networks and has managed research infrastructure teams since 1998.

NIL means that a variety of different process techniques have to be applied. Several groups in Europe are involved in development of the NIL technology. However, the NIL technology developed at LNL is unique and includes both nanowires and large area processing. The substantial progress in the development of ultra-high resolution nanoimprint technology, based on IPS OrmoStamp material, is impressive with demonstration of a sub-20 nm OrmoStamp imprint process as well as sub-10nm replicas. The development of reactive ion etching (RIE) methods for stamp technology is in progress.

This infrastructure is very important for many research fields as well as for many different companies and quite a few users are coming from companies (mostly small). The proposed direction of the development will be very important in the scaling up of many nanotechnological applications and hence also very relevant for many different companies. Three new user groups have started to use the NIL facility recently. New research areas are represented by single molecule spectroscopy and bio-computation. The nanoimprint infrastructure is an open-access infrastructure available to all users in Sweden via LNL and Myfab.

The future plans include development of specific protocols, e.g. reactive ion etching of stamps with high resolution, optimization of nanoimprint methods and introduction of new materials in the technology. Of highest priority is the development of a process flow based on Si-master stamps and OrmoStamp material with testing of all process steps, from stamp fabrication to growth of NWs. Another exciting new area is to combine the Nano Imprint Lithography with the block copolymer technology for further development of the stamp technology and directed self-assembly of BCP steered by NIL patterning. The predominating application areas are biophysics, medical devices, and sensors.

Conclusions and recommendations

- The NIL technology has been further developed and substantial progress in the ultra-high-resolution nanoimprint technology has been made.
- The new APEX ICP-RIE etch tool has been installed and is in operation.
- RIE methods for stamp technology are in progress.

- An observation is that stronger interaction with polymer research groups addressing crucial aspects could promote the progress in improvement of the spatial resolution.
- New user groups have started to use the NIL.
- The infrastructure is available through LNL and Myfab with well-established routines for open access.
- It was obvious that there is strong support and long-term planning for NIL within LNL.
- The development plans are regarded to be very relevant and realistic.
- Prolonged funding is highly recommended.

13. Nils Nordell, RIF14-0017

EECS - Electrumlaboratoriet, ELAB

KTH - Royal Institute of Technology

Project: Strategic development at Electrum Laboratory - CMPLab

The Electrum Laboratory was inaugurated in 1987 as an environment for innovation common to education, research, development and small-scale production. It maintains several laboratories covering most aspects of micro- and nano-technology, including processes, material and device characterization and simulation tools. It belongs to the Swedish Nano and Microfabrication Infrastructure, Myfab, which is a distributed infrastructure coordinating the major cleanroom facilities on microfabrication in Sweden. It provides access to all processes and equipment in the network for both academia and industry and works very well with about 250 users at the Electrum node. In the frontline of the micro- and nanofabrication is the integration of components in three dimensions. By developing and using a Chemical Mechanical Polishing (CMP) technology, the Electrum Laboratory has successfully demonstrated how extremely smooth layers can be produced in different materials, which is a prerequisite for 3D integration. It will attract many new users nationally and internationally since both the technology and competence at Electrum is judged to be both unique and high.

The RIF, Nils Nordell, is a key person as director of Electrum Laboratory and initiator of many of its current activities. He is responsible for the strategic and daily operation. He devotes 40% of his time to the important CMP project and has established important international networks.

The infrastructure develops very well with particularly important methods for 3D integration. The methods include development of sequences of process steps for metallization, 3D integration of CMOS nanoelectronics, silicon carbide planarization after epitaxy for 3D device structures, and heterogeneous integration for systems on chip. The tool box created for integration in three dimensions is impressive where the Chemical Mechanical Polishing (CMP) technology is of utmost importance.

A lot of users from academia and industry were seen. The infrastructure is easily accessible via the Myfab booking system. There are incubator facilities where users can get access to the whole lab, and to production and business services. Since 2003 at least ten companies have used these facilities. Specifically for the CMP project there are established user groups at KTH, Chalmers and three companies. Seminars and user meetings are arranged on a regular basis.

3D microfabrication is important for a variety of application areas. Many strategically important process steps and sequences have been successfully developed and applied, making also the Lab very attractive as a collaboration partner on the European market. The Horizon 2020 project CAMART - an excellence centre of advanced materials research and technology - together with the Institute of Solid State Physics, University of Latvia and RISE Acreo. At least six papers have been published. A direct result in innovation is the development of a silicon carbide power device with a company.

The future plans include upgrading of the laboratory for CMP with better temperature and humidity control, reduction of contamination and water saving installation. CMP will be used particularly to realize the sensitive and critical sub 50 nm metal contacts, representing a demanding state-of-the-art technology.

Conclusions and recommendations

- Integration of components in three dimensions at a nanoscale is a technically demanding field, requiring deep insights in various process technologies. The RIF has demonstrated that he is able stretch many process steps. The progress in the chemical, mechanical process technology is impressive.
- The close cooperation with many different users and the easy access to the infrastructure was appreciated.
- The infrastructure is strategically important for many areas (electronics, sensors, optics, medicine, etc) and was judged to be of state-of-the-art.
- The cooperation of the nano- and microfabrication infrastructure in Sweden through Myfab and the participating four universities is commendable. It should be a pattern also for other infrastructure areas.
- The overall strategic planning procedures of the infrastructures at KTH, where Electrum is a heavy part, was appreciated.
- The evaluation committee was very pleased with the accomplishments made of the Nano-and Microfabrication infrastructure at KTH. The management of the whole infrastructure as well as of the individual subprojects is impressive. The value of the CMP project for the future development of nano technology in Sweden and its first results highly motivate a recommendation for continued funding from the RIF programme.

14. Per Persson, RIF14-0074
Physics, Chemistry and Biology (IFM)
Linköping University
Project: Atomic Resolution Cluster, ARC

The Atomic Resolution Cluster, ARC, is a joint initiative in atomically resolved electron microscopy between the universities in Linköping and Lund and can be regarded as a distributed infrastructure. The heavy investments in recent years in equipment at both universities and long research traditions in relevant research areas make ARC to a state-of-the-art infrastructure.

The key persons in the infrastructure play an important role in the development of the infrastructure as a whole all the way from planning, technical development, meeting new users, the managing on the day to day basis, outreach in general, etc. Basically there are two directors – one at each node – acting as CEOs but also connecting the nodes to each other very well. The collaboration between the two nodes was judged to be very informal. It was noticed that the two nodes (LiU and LU, respectively) didn't have the same organization and not even a common advisory board. The LiU node is hosted by the Department of Physics and Materials where the LiU director is employed. The LU node is hosted by an umbrella organization, the Chemical Center at LU, formally a status close to a department which makes the infrastructure more independent.

The infrastructure has developed clear routines to judge and assist in projects proposed by external users. Users with no or limited experience need a lot of support all the way from the important sample preparation to the interpretation of data. For the more advanced applications, access to the facility can be gained after discussion with experienced researchers at the facility. For ordinary routine work the users can get license to operate microscopes themselves after adequate training. However, for the latter case there is a lack of capacity at the infrastructure. The complexity of the technique in the high-resolution applications requires usually long-term commitments and partnerships between users and the infrastructure. Unfortunately, very few large companies are among the users of the infrastructure up to now. However, the infrastructure has attracted quite a few smaller companies which may have a recent experience of the technique from their education. Finally, there is an increasing use of the ARC infrastructure from other universities. On the national arena the infrastructure together with other electron microscopy facilities are pushing VR for recognition of a national infrastructure in advanced electron microscopy. The overall scientific level of the research at the infrastructure is judged to be very high with frequent publishing in international journals. There are few external users of the high-resolution capacity while use of the low-end capacity is much higher and probably requiring investments in microscopes.

The plans for the future includes a variety of different issues like efforts to establish an electron microscopy lab recognized as outreach at LiU, consolidate the recent development of the infrastructure (e.g. cryo TEM and ETEM) as well advising on acquisition of an electron beamline (cryo-TEM) for MAX IV. Different outreach activities towards particularly various companies are planned. For some companies long-term partnerships with the infrastructure is probably preferred. Concerning method development in-situ heating in the microscope up to 1300°C as well as in-situ preparation in the ETEM are planned.

Conclusions and recommendations

- The ARC infrastructure is a recently formed advanced infrastructure in an area of large interest and high importance for research groups from both industry and academia.
- The ARC infrastructure is distributed to two nodes (LiU and LU). It is a very advanced state-of-the-art infrastructure operated by highly competent researchers.
- The two nodes in Linköping and Lund, respectively are organized in different ways and without a common scientific board. It is recommended to form an international scientific advisory for the overall long-term strategic development of the infrastructure.
- It was not obvious from the site visit in Linköping which status the ARC infrastructure has in the universities' long-term planning of infrastructures. The impression was though that the infrastructure was regarded positively by the vice-chancellor. For keeping the ARC infrastructure at a high international level a more solid long-term planning at the university level is required.
- The key person(s) have extremely important roles in both the nodes with their activities and involvement in all the development steps for the facilities. The hosting universities are encouraged to take further steps to establish a long-term stability in terms of equipment and personnel for the facility.
- Future strategy of attracting researchers from industry should be refined and initiatives of workshops, courses, webcasting should be encouraged.
- The development plans were regarded to be very relevant and realistic.
- On the basis of the presented accomplishments, future plans, and management prolonged funding is recommended.

15. Daniel Primetzhofer, RIF14-0053

Physics and Astronomy

Uppsala University

Project: The Swedish Center for Ion-Beam Material Analysis

The Tandem Laboratory (TL) at Uppsala University is a Swedish national center for ion-beam material analysis. The center provides capabilities for non-destructive characterization at the nanoscale, ion-beam induced modification of material properties and ultra-sensitive accelerator mass-spectrometry. The TL has both national and international collaboration partners. The users include academia, industry, museums and society. The TL has a board with internal and external board members representing research and industry that regularly monitors the activities. The TL is a national research infrastructure placed as a special unit within the Faculty of Science and Engineering. It is the only laboratory in Sweden for ion implantation. The applications range from electronics and solar cells to medicine and life science in general and even archeology. The facility is among the most interdisciplinary research infrastructures in Sweden. The main goal of the RIF project is to sustain and advance the capabilities of the TL infrastructure for ion beam analysis.

The RIF person Daniel Primetzhofer is an Associate Professor at Uppsala University, Director of the TL and Head of the Ion Physics Research Group. In the role of Director for TL he plans and participates in the upgrade projects. He also coordinates and supports a PhD/Postdoc user group from different divisions and departments at Uppsala University employing the available instrumentation and performing data evaluation. He establishes contacts to new users within the academic sector and industry. This engagement has in particular lead to increased research activities in collaboration with Linköping University and a working agreement to grant LiU regular access to the infrastructure with technical and scientific consulting. He is well established in the field of ion-beam analysis with a deep knowledge and wide-spread national and international collaboration networks.

During the RIF project a chamber for in-situ materials characterization has been designed, built and taken into test operation during 2017. An effort to spread information about the new capabilities has also been started. The micro-beam facility of the TL has been improved by the purchase of new power supplies and an improvement of the scanning system. The gas detector system for Heavy Ion Time-Of-Flight (TOF) Elastic Recoil detection analysis installed in 2016 has been improved throughout 2017 and a series of interlock systems protecting the sensitive electronics have been installed. The sample holder design has been changed to allow a higher sample throughput and higher flexibility in sample shape. A new detector has been installed at the TOF-MEIS (medium energy ion spectroscopy) facility. The new detector complements the already existing large solid angle detector. An improved depth of resolution has been confirmed for the new detector. The system for the large solid angle detector has been modified to permit detection of secondary electrons originating from the ion impact. The beam has been realigned and the beam trimming system has been optimized.

The number of users of the facility is continuously increasing and expands to new fields. The easy access to the facility and the competent service and support facilitate for particularly new users. There is a continuous need of upgrading the Tandem Laboratory in Uppsala, which has been met by using fees.

The overall activity at the Laboratory results in more than 150 publications per year with many of them in high impact journals. In total about 30 different academic and non-academic users have used the infrastructure for ion beam analysis and ion beam materials

modification. Finally, the unique accelerator mass spectrometry attracts several hundreds of museums and national authorities and radiocarbon dating was carried out for more than 150 costumers.

The future plans include further work to allow analysis with lower doses and higher spatial resolution. The number of users is to be increased and this further emphasizes the need for the hardware to drift stability and capacity of the TL.

Conclusions and recommendations

- The TL is a well-established infrastructure with national and international users from academia, industry, museums and society.
- The infrastructure has excellent equipment and is well organized.
- The RIF project has developed very well with important expansion of the capabilities of the TL, maintaining a position in the forefront of ion-beam material analysis.
- The booking of the infrastructure is performed manually. This is time consuming and the plans to introduce a web base booking system like the LIMS that also is used by the distributed Swedish national infrastructure for micro- and nanotechnology, Myfab, would further promote the work to increase the number of users.
- The idea of establishing a National School on different complementary analysis methods is interesting and should be further explored.
- The TL is a separate unit within the Faculty of Science and Technology. However, there are no long-term plans or guarantees from the Faculty or the University. Considering the importance of the TL, the hosting university is encouraged to take further steps to establish a long-term stability in terms of equipment and personnel for the facility.
- The plans for further development within the RIF project are regarded to be very relevant and realistic.
- The output, development and management of the infrastructure were appreciated and motivate strongly prolonged funding.



SWEDISH FOUNDATION *for*
STRATEGIC RESEARCH

The Swedish Foundation for Strategic Research announces grants for

Research Infrastructure Fellows

The Swedish Foundation for Strategic Research announces the availability of a total of SEK 240 million in grants in a national call for proposals directed towards research infrastructure that meet the highest international scientific standards and strengthen present or future Swedish-based industry and society. This initiative has a focus on infrastructure supporting research within the SSF's priority areas.

SSF:s selected Research Infrastructure Fellows will be supported by grants of SEK 15 million for a period of 5 years (incl. overheads) to be used for salary, research infrastructure tools, and running costs. After two and a half years, a programme committee will make site visits to follow up the implementation of the grant, which may affect funding for the remaining period.

Background

Research infrastructure resources such as large research facilities, centres for expensive equipment and instruments, coordinated labs, test-beds, and knowledge collections (such as data banks) have ever ever-increasing importance for research and are a prerequisite for top-notch performance in many fields. Research infrastructure resources are tending to get larger and more complex, and are inherently beyond the sole control of a single research group or even a university department. Long-term and large investments as well as demanding operations are usually a characteristic feature of many infrastructures. Sweden has an impressive research infrastructure, where easy access and efficient use are vital to national competitiveness in research and development. Key persons of different kinds – often outside a classic academic path – play an extremely important role for the successful development and use of research infrastructures. The present five-year SSF programme is intended to contribute to the development of research infrastructures and to its support and user-accessibility, as well as to enhance career paths for specialists within academia.

Scope of the present call

The objective of this call is to promote key persons committed to research infrastructures. These persons are essential to the operation and methodological development of the infrastructures, but also to the training and supervision of users at the infrastructures. The call is thus typically aimed at persons who have chosen another career path than the classic academic tenure track and are instrumental for the research community and the future development of important new research tools, such as machine directors, beam-line scientists, laboratory or centre directors.

According to the statutes of the Foundation, research infrastructure of concern for the present call should support the natural sciences, engineering and medicine, promote the development of strong research environments of the highest international standards, and enhance Sweden's future competitiveness.

Furthermore, the Foundation prioritises research within the following areas:

- Bioengineering
- Computational Sciences and Applied Mathematics
- Information, Communication and Systems Technology
- Life Sciences
- Materials Science and Technology

which means that these areas will be given priority over infrastructure supporting other areas.

Eligibility

The research infrastructure must be hosted by a Swedish university and must be prioritised by the vice-chancellor of the university, involving long-term scientific goals, funding and use. It must be of broad national interest and provide a basis for world-leading research. It is a requirement that the infrastructure is or will become an open-access facility, i.e. open to scientists from all universities and research institutes, and preferably also be accessible to users from industry and other countries. This open access may, however, be limited by quality screening of user project proposals. It is regarded as a merit if the infrastructure offers e-access to users. The price charged for user access should be limited to actual cost.

The proposal must be submitted by a main applicant who is the key person for the infrastructure in question. The Research Infrastructure Fellow must be employed by a Swedish university or a university college.

Each application must be co-signed by the vice-chancellor of the university and by the head of the host's infrastructure unit/department/centre/facility who underwrites the applicant's employment. Each university may only be represented in a maximum of three (3) applications, as a host university, in this call. Furthermore, each key person may only be represented in one (1) application as main applicant.

Applications that fail to comply with these conditions will not be considered. It is the responsibility of the main applicant to check the proposal for compliance with the rules before submission.

Proposal and submission

A complete application must contain, among other data specified in the portal:

- Description of the research infrastructure and its national (and, where applicable, international) role and competitiveness
- Description of the state of the art within the area concerned

- Description of technical and/or method development that the applicant will be engaged with at the infrastructure during the SSF grant period
- Details of the relevant expertise of the main applicant (and CV)
- Description of how the infrastructure fits in with the host university's strategy for research infrastructure and how/if it relates to the Swedish Research Council's "Guide to research infrastructures", or equivalent
- Description of the organisation of the infrastructure and the intended role and competence development plan of the applicant within the infrastructure, beyond the support period of SSF
- Description of the accessibility of the infrastructure and the number of potential users from different sectors and areas, including e-access
- A budget section including as primary items the salary cost of the applicant (up to 100%), running costs and instrument/module add-ons, refurbishing or method development related to the project
- Detailed account of the expected strategic significance of the project, presenting a vision of utilisation or commercial exploitation of the results in Sweden during the project's lifetime and/or up to 10 years after completion of the SSF project
- A Letter of Intent (LoI) signed by the vice chancellor of the university and by the head of the infrastructure unit/department/center/facility. Additional LoIs may be required if the key person is employed by a different organisation (deployment for work off-site at the infrastructure - "secondment").

The proposal must be written in English and submitted via the web portal of the Foundation at: <http://apply.stratresearch.se>. Note that it is necessary to consult the portal in order to get a complete picture of all particulars required for submission. Please log on to the portal well in advance of the deadline. Please also submit the application in good time before the deadline. When the application has been submitted, the system will indicate whether any data fields are missing. As long as this is done before the application deadline, it is possible to submit and re-submit as many times as necessary.

All applications must be submitted by **14:00 hours (2:00 pm CET) on 29 January 2015**. No additional material will be considered after this deadline.

Please note that the Foundation is subject to the Principle of Public Access to Official Records (Offentlighetsprincipen). Thus, applicants should avoid submitting material that they do not wish to be made public, for example information that could prevent patenting.

Evaluation

Applications will be assessed by an evaluation committee including experts from academia, industry, and from international research infrastructure resources.

The applications will be reviewed according to the following criteria:

- Conformity to scope and eligibility as outlined above, including: definition of infrastructure, university priorities, accessibility (by different type of users), and e-access
- Scientific quality: originality, strengths, weaknesses, level of technical advancement and method development, degree of interdisciplinarity, and feasibility of the research infrastructure project
- Strategic relevance to Swedish academia, industry and/or society, and impact of the proposed project
- Qualifications of the applicant (key person), previous technical or scientific achievements, international experience and networks, and leadership/management of research infrastructure teams.

Proposals that offer coordination of research infrastructure in given fields are prioritised over competing local ones.

Time schedule

October 2014	Programme announcement
29 January 2015, 2:00 pm CET	Deadline for submission of full proposal
November 2015	Final decision by Governing Board
January 2016	Project start

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