Report on the 1st Meeting of the

SESAME* Structural Molecular Biology (SMB)

Scientific Subgroup of the

SESAME Scientific Committee

Meeting held in Athens, Greece

April 6 – 7, 2000

Date of this report:

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***SESAME – Synchrotron-light for Experimental Science and Applications in the Middle East**

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Report on the 1st Meeting of the SESAME Structural Molecular Biology (SMB) Scientific Subgroup of the SESAME Scientific Committee;

Athens, Greece, April 6 – 7, 2000

This was the first meeting of any of the Scientific Subgroups for the SESAME project. It was organized to bring together scientists from the Region with a small group of international experts in the field of synchrotron radiation and structural biology to explore SMB opportunities and challenges for the SESAME scientific project in the Middle East and Mediterranean Region and to begin the detailed planning of the SESAME SMB beamlines and associated scientific program. The SESAME Scientific Committee has identified SMB as the premier application for SESAME and the upgrades to the BESSY I machine have been optimized for this application.

The success of the meeting and the impact that this is expected to have on other scientific subgroups shows the great potential for SESAME, its scientific importance to the researchers in the Region and the overall need and importance for the organization of subsequent meetings and workshops in this and other scientific areas to prepare scientists from the Region to exploit the research potential of SESAME.

Background

This first meeting was organized by the chairs of the SESAME Scientific Committee (Ercan Alp and Herman Winick) jointly with the chairs of the Structural Molecular Biology (SMB) Scientific Subgroup (Gitay Kryger and Peter Kuhn) with a total of 19 participants from Cyprus, Greece, Israel, Jordan, Palestine Authority, Turkey, United Kingdom and the USA. Participants from Armenia and Iran were scheduled to attend but unable to receive required Visas in time. Material sent from these countries, as well as material from Morocco, is included in this report. Sixteen of the meeting participants were from SESAME member countries. A list of all registered participants can be found in Appendix A An excellent room at the University of Athens to hold the meeting and local administrative support was arranged by Costas Papanicolas, with help from George Nounesis and Tessi Papathanasiou. Participants from Middle East countries provided their own airfare. Local expenses for participants from Middle East countries were covered by funds from UNESCO. The agenda for the meeting is given in Appendix B.

Executive Summary

The meeting provided the framework for the establishment of close interaction of the participating scientists from the Region, who were charged with the responsibility of planning the SMB program and taking ownership of the project for their countries. The enthusiasm with which the representatives took part in the discussions about the potential of SMB in general and its applicability within the framework of SESAME clearly showed the commitment of the scientists of the Region to take full advantage of this research resource. It has also become clear that significant leadership and scientific support and training from international sources will be required to make full use of this potential. The high level of intellectual support from the international scientific community will play a major role in the success of this project. This support has already become clear through the support form scientists who believe in the peace process in the Middle East, including many scientists with roots in the Region who now work at research institutions around the world.

Representatives from countries in the Middle East Region presented summaries of the present level of research relevant to SMB, with and without the use of synchrotron radiation, in each country. They also gave projections about the increased levels and number of scientists who would be expected to be involved in such

work when SESAME is operational. From these presentations it is estimated that several hundred scientists from the region would pursue SMB research using SESAME.

The requirements for creating a world-class program in SMB were a main topic of discussion. This included beam line characteristics, technical and scientific support personnel, support laboratories and specialized equipment. A special presentation was made on the design of a beam line for SMB research. These discussions led to the unanimous adoption of the following resolution:

"Top priority for the SMB committee is to see a Research Institute established alongside SESAME, for the development of SMB projects and infrastructure in the region. A speedy decision on the site will be helpful."

The members of this advisory group have developed a list of action items charged to individual participants:

1. Develop a full proposal for a Institute for SMB Research at SESAME; Metaxia Vlassi and Pierre Rizkallah
2. Importance of dissemination and start of educational program through the organization of a larger workshop to be held in Cyprus in late 2000; Spyros Skourtis and George Archontis.
3. Publication and dissemination of the results of this workshop and the overall SESAME project in the popular press: Jordan and PA – follow up on those.
4. Summary article for the British Crystallographic Association, Pierre Rizkallah.
5. Establishment of a mailing list/bulletin board; Engin Ozdas
6. Communication to other scientific communities; all
7. Expand the SMB panel to ensure participation of all countries in the Region; all

A draft of the proposal mentioned in Item 1 above is included as Appendix C. In Appendix D we include an earlier write-up on "Opportunities for a Center for SMB at SESAME".

Description of SMB related activities in the Region

The agenda was structured to provide all participants with an overview of the current SMB research programs in the Region and selected talks on current SMB programs at synchrotron light sources in Europe and the USA. These brief presentations provided the basis for extensive discussions about the opportunities and challenges of a world-class SMB program at SESAME.

The representatives of the structural biology (or related) community in the Region presented their views about the status and future prospects for SMB research in each country. These are summarized below:

Armenia (revised 6/17/00)

This is a summary of material sent after the Athens meeting by Ts. M. Avakian, S. G. Gevorkian, V. B. Arakelyan, G. E. Khachatryan and S. Sh. Tatikyan from the Laboratory of Radiation Biophysics and Biosensors, Yerevan Physics Institute, and H. Karapetyan from molecular structure Research Centre of NAS. H. Karapetyan was scheduled to attend the meeting, but did not come because a visa did not arrive in time.

In the Laboratory of Radiation Biophysics and Biosensors at the Yerevan Physics Institute (YerPhI) in Armenia, there is much experience in SR implementation for structural and radiobiological investigations of biological objects using the 4 GeV synchrotron ARUS since 1974. Investigations of different biological objects such as enzymes, amino acids with the use of EXAFS, EPR, and X-Ray structural analysis methods, have been

conducted. The atomic short-range order of Copper-Albumin protein complexes in the freeze-dried form has been investigated by EPR and EXAFS spectroscopy using SR. The superhyperfine structure of EPR spectra of these complexes testifies to the fact that the copper atom is surrounded by four ligand atoms of nitrogen.

Especially interesting results were obtained on the action of SR on tobacco seed virus, allowing us to understand how to study other viruses. Theoretical investigations show that SR can be used for obtaining information about the enzyme's active center structure, which is further used to modify the active centers.

The important aspect of studying enzymes with SR is its effect on fermentative reaction kinetics, namely enzymes' transition from Michaelis-Menten kinetics regime to the cooperative regime. This circumstance may have a wide practical implication in the field of manufacturing and application of bio-sensors. We have also conducted theoretical studies on effects of SR for investigating the binding of ions and ligands with DNA. In particular quite important is the understanding of the binding mechanism of platinum complexes and porphyrin with the DNA. The mentioned ligands possess very important anticancer activity properties. Investigation with the help of SR allows the determination of the exact place of the binding of the above-mentioned ligands with the DNA. These investigations will have a wide practical application in medicine.

The metabolic pathways and intermediate products formed during nitroaromatic compound destroying by aerobic bacteria are in progress at YerPhI in collaboration with other Armenian research centers. Currently the destroying of chemical toxins, particularly nitroaromatic nature ones, are under investigation at YerPhI.

It is planned to isolate highly active mutants from wild types of bacteria. A well known way of producing mutant organisms is the irradiation of cells by diverse types of ionizing radiation. According to previous results, SR is a more powerful and effective tool for mutagenesis than traditional X- and UV-irradiation sources. It is proposed to perform the study of enzymes and enzyme-substrate complexes involved in metabolic processes during SR irradiation from SESAME.

In Armenia the X-ray structural investigations of small molecules was relatively wide spread since 1994 in the Molecular Structure Research Center of the National Academy of Science of the Republic of Armenia (MSRC NAS RA). At present, the molecular structure of biological active compounds, synthesized in Armenia, is mainly investigated at MSRC.

The Institute of Molecular Biology of NAS RA and the Institute of Biochemistry of NAS RA are strongly interested in structural investigations of large molecules. Scientists of the Institute of Biochemistry discovered neurohormones, having proteinal character. According to their hypothesis the interaction brain and heart passes through this neurohormone and they are now working on development of a new mechanism for this interaction. Scientists of the Institute of Biochemistry are also intensively investigating the biochemistry of metal containing proteins acting on the work of the heart.

The results of investigations, carried out in the Laboratory of macromolecular complexes of the Institute of Molecular Biology, show that for different illnesses (diabetes, schizophrenia, stroke and familial Mediterranean fever) the immune complexes in the blood are special and depending on type of illness they differ by composition (by ternary structure).

The main equipment available at the Laboratory for the study of the above mentioned topics are: X-Ray sources (RUM-17), spectrophotometer (Specord M-40), fraction collectors for column-chromatography (LKB), centrifuges (K-24, K-70D). The Laboratory has the complete conditions for carrying out the study in the field of biochemistry and microbiology. The Laboratory of X-ray structural investigations of MSRC is equipped with a difractometer (CAD-4 "Enraf-Nonius") with a low temperature device.

Cyprus - Spyros Skourtis and Georgios Archontis (revised 6/17/00)

In Cyprus, there are currently two institutions that carry out research relevant to SMB. The first one is the University of Cyprus that operates since 1993. The School of Science includes departments of Physics, Chemistry, Mathematics and Computer Science. A department of Biology is also being planned.

The department of Physics has 10 faculty members, with an anticipated doubling of faculty over the next few years. It has a program in theoretical and computational molecular biophysics that focuses on biomolecular structure/dynamics-function studies (biomolecular specificity, protein electron transfer). The Biophysics faculty (Drs. Archontis and Skourtis) has on-going international collaborations with x-ray crystallographers in Oxford, Strasbourg and /or with theoretical groups in the USA (University of Pittsburgh and Harvard University).

The department of Chemistry has nine faculty members, and expects to double its size in the next few years. One faculty member (Dr. Niovi Santama) specializes in Molecular Biology and Biochemistry, and particularly in the study of cellular functions of kinesin-like proteins and motor proteins. Her group participates in a European network (Human Potential RTN Network DG12) and has funding from the US MDA program. The departments of Mathematics and Computer Science include faculty members who specialize in the development of algorithms.

The second main institution is the Institute of Neurology and Genetics (CING) that was established in 1990. It includes 90 scientists, 70 of which are molecular biologists and clinical neurologists. Its personnel provides medical services and conducts research in neurology, genetics and molecular biology (with emphasis on neurogenetic disorders, thalassemia and cancer). The institute has international collaborations with Greece, Turkey, Eastern Europe (Slovenia, Bulgaria, Russia), and the Middle East (Egypt, Tynisia, Lebanon, Jordan).

The clear hope was expressed that the interaction with and participation in SESAME will promote a growth of SMB in Cyprus, with an expansion in its research institutes, and the establishment of many new collaborations and projects.

Greece - Metaxia Vlassi (revised 6/17/00)

Greece already has a well-established program in SMB with approximately 12 research groups, which are mainly funded through EU competitive grants and the Greece Ministry of Development. These research groups cover a diverse program in many aspects of molecular biology and biochemistry. The program is well established with local x-ray sources and expertise in SMB research. The two existing data collection facilities are at the Center of Crystallographic Studies of Macromolecules at the University of Athens and at the Macromolecular Structures Group at Institute of Molecular Biology and Biotechnology, Crete. Greek groups are current users of DESY, Elettra, Daresbury, and ESRF. An urgent need for the overall coordination and implementation of modern techniques in protein expression, purification, and crystallization was expressed in conjunction with the need for training programs for students and scientists in SMB research and the utilization of large research resources like Sesame.

Structural Molecular Biology research groups in Greece are based in various Universities and National Research Institutes:

At the University of Athens, Faculty of Biology, the groups of

1. Prof. E. Moudrianakis (Biology Department of Cell Biology and Biophysics) with research interests covering the structure of chromosome-chromatin assembly, the energetics of the assembly of the nucleosomal components and the mechanism of protein thermostability and enzyme thermoactivity in *Archaea*.

2. Prof. S.J. Hamodrakas (Biology Department of Cell Biology and Biophysics) with research interests focused on the study of fibrous and globular protein structure, folding and assembly, the study of structure and assembly of amyloid-like fibrils and on the prediction of protein structure and function from sequence.
3. Prof. C. Vorgias (Department of Biochemistry & Molecular Biology) with research interests on structure-function studies on chitinolytic enzymes from organisms of biotechnological relevance, protein engineering studies on chitinase A from *Serratia marcesence,* thermostability studies on histone-like protein HU from psychrophilic, mesophilic, thermophilic and extremophilic bacteria, protein-sugar interaction studies, structure-function studies on DNA ligase and DNA polymerase from hyperthermophilic bacteria and protein-protein interaction studies between p53 and rad51.

At the Agricultural University of Athens, Department of Agricultural Biotechnology, the group of

4. Prof. E. Eliopoulos with research interests covering: Structure-function studies on beta-lactoglobulin in native form and in various crystallographic lattices, structure-function studies on Dihydrofolate-Reductase in native form and in various complexes with various inhibitors, calculation and construction of several models of globular proteins and their interaction with membranes and other protein complexes, structural studies on SOD protein from *Drosophila* and the X-ray structure of a monoclonal antibody Fab198 of the heavy muscle distrophy.

At the National Hellenic Research Foundation, Institute of Biological Research and Biotechnology, Department of Cell Biology and Biophysics, the group of

5. Dr. N.G. Oikonomakos with research activities on: Structure-function relationships of allosteric proteins of muscle cell, design of potential hypoglycaemic drugs for the treatment of non-insulin-dependent diabetes mellitus, structure and function of phosphorylase kinase, structural studies of signal-transducing enzymes, crystallographic studies on Fab fragments of monoclonal antibodies against the Main Immunogenic Region of Acetylcholine receptor.

At the National Centre for Scientific Research “DEMOKRITOS” in Athens, the groups of

6. Dr. M. Vlassi (Institute of Biology) with research interests focused on: Crystallographic studies of protein-protein interactions mediated via TPR domains and structure based rational design of ribonuclease inhibitors which can be used as therapeutic agents in pathological conditions associated with ribonuclease homologues.
7. Dr. I. M. Mavridis (Institute of Physical Chemistry) with research interests covering: Molecular structure of supramolecular systems involving cyclodextrins with applications such as (a) CD/pheromone systems for the controlled release and protection of olive pests (b) Enantiomeric separation of optically active compounds (c) Sustained release and stabilisation of drugs and (d) Development of sensors. Interactions of cyclodextrins with glucogen phosphorylase and Structure determination of protein complexes of Prothymosin A.

At the Hellenic Pasteur Institute in Athens, Department of Biochemistry, the group of

8. Dr. S. J. Tzartos with research focused on the study of the nicotinic acetylcholine receptors (AChR) of muscle and nerve which are involved in diseases such as the autoimmune disease myasthenia gravis, Alzheimer, Parkinson and Schizophrenia as well as in the addiction of smokers to nicotine. In addition, the structure of Fab antibody fragments able to protect muscle AChR against its pathogenic autoantibodies are been studied. These studies aim to design drugs for the above diseases.

At the Aristotelean University of Thessaloniki, Department of Physics, the group of

9. Prof. C. Kavounis with research interests covering structural studies of proteins such as RAS2 and related mutants, ROP mutant and PK-PKI3 complex as well as of organic and organometallic compounds.

At the Institute of Molecular Biology & Biotechnology, Heraklion Crete, the groups of

10. Dr. K. Petratos with research interests in structure-function studies on bacteria chitinolytic enzymes and various mutants towards the elucidation of the mode of their enzymatic mechanism and their interaction with substrate(s) at molecular level by co-crystallization and X-ray crystallography experiments.
11. Prof. M. Kokkinidis (University of Crete, Department of Biology) with research interests on: The Protein Folding Problem, the stucture determination of type II restriction endonucleases and DNA methyltransferases, novel techniques in protein crystallization, ultrahigh resolution studies of proteins and crystallographic computing.

At the University of Patras, Department of Chemistry, the group of

12. Prof. V. Nastopoulos with research focused on the Crystal structure determination of a DNA polymerase from the thermophilic archaeon *Sulfolobus solfataricus,* of various complement proteins, of a calcium-binding protein as well as of an amidase enzyme *from Sulfolobus solfataricus.* In parallel, crystallography of small molecules has been an area of interest for several years.

Two X-Ray facilities appropriate for Crystallographic studies on Biomolecules exist in Greece:

1. One at the "Center for Crystallographic Studies of Macromolecules" (CCM) located at the Institute of Biology of the National Center for Scientific Research "DEMOKRITOS" in Athens. CCM is equipped with a state-of-the-art X-Ray system for crystallographic studies of macromolecules comprising a Rigaku RU-H3R belt-drive rotating anode generator, R-AXIS IV dual Image Plate detector as well as with a JASCO J-715 Circular Dichroism Spectrometer.
2. The second X-Ray system is located at the Macromolecular Structures Group at the Institute of Molecular Biology and Biotechnology in Heraklion-Crete and consists of a Rigaku RU-H3R belt-drive rotating anode generator and a Mar300 Image Plate detector.

European Community and National grants provide funding for SMB research in Greece.

The Greek SMB groups are current users of European Synchrotron Sources (DESY, Elettra, Daresbury) and are potential users of the SESAME facilities.

Iran - Nasrin Moazami

Dr. Moazami, Director of the Iranian Research Organization for Sciences & Technologies (IROST) in Teheran, was scheduled to attend the Athens meeting, but did not come because a visa did not arrive in time. This is a summary of material sent by her after the meeting. More material is in the Appendix, together with a detailed table giving the statistics of biotechnology research in 17 research institutes related to biotechnology in Iran.

Iran has a population of 64 million and a land area of 1.65 million square kilometers. 170,000 students attend more than 100 universities and colleges. In 1996, the gross national product (GNP) was about $100B.

In 1997 there were more than 83 institutes (including university departments of medical science, pharmacology, biology and biochemistry) involved in research and education related to traditional and modern biotechnology. About 300 research projects have been conducted from 1991 to 1997, of which 258 were in 17 research institutes in four fields;

Basic Science, Agriculture, Industry and Environment, and Medicine. These institutes provide laboratory space for over 364 researchers, of which 96 hold PhD degrees in areas related to biotechnology.

About 40% of biotechnologists and research projects belong to agricultural biotechnology institutes that are mostly involved in plant tissue culture and micropropagation. However, most of the genetic engineering and molecular research is being conducted in production of recombinant proteins (such as medications, vaccines and laboratory enzymes), and gene transfer to plants for conferring tolerance to environmental stress. Persian

Gulf algae plays an important role in production of various vitamins, inorganic material, and bioactive metabolites.

The Iranian plateau, which includes a major part of Iran, Afghanistan and Pakistan, has been a stage to unique events within the spectrum of world transformation over tens of millions of years. During these geographical and climatic changes, plants and animals became widely extinct. Climatic conditions are extremely varied from temperatures of 40 degrees below zero in the Northwest to 53 centigrade in the Persian Gulf region. It is estimated that there are 10,000 plant species, roughly comparable to the number on the European continent, which has about 4 times the area of Iran. Thus there is biological diversity due to these extremes of environment.

Israel - Gitay Kryger

Israel has a very well established SMB research program in four academic institutions: the Hebrew University, the Technion, Tel-Aviv University and the Weizmann Institute. Approximately 10 Investigators at those four institutions are currently involved in SMB research. Each of these groups follows a typical academic program with 2-5 PI's each leading a group of 3-6 students/postdocs and 0-1 technicians working on 1-3 distinct scientific programs. The existing laboratories are all fully equipped with modern rotating anode x-ray sources and modern detectors as well as well established laboratories for molecular biology and biochemistry to prepare the samples. In the future, a new SMB program is planned at Ben-Gurion University and a Proteomics Center at Weizmann Institute. There are also emerging R&D projects in the biotechnology industry that will not depend on academic collaboration.

Outlook for SESAME use: many SR based PX experiments and preliminary tests will be moved from US and Europe facilities to SESAME. Opportunity for new research projects in academia and industry.

Summary: SMB community will benefit from SESAME and may further develop due to its existence. SESAME will benefit from the experience and expertise of Israeli scientists. Limitations: ample access to SR around the world, it is unlikely that researchers in IL will support funds allocation/diversion to SESAME.

Jordan - Khalil Al-Mughrabi

Jordan has currently no direct SMB research program, however basic molecular biology research and university programs are available at a small scale with significant interest in SMB and the desire to expand in that direction. Many universities and scientific institutions are becoming aware of the importance of recent advances in molecular biology in various aspects of biological and environmental sciences and have expressed their immediate interest in SMB developments and opportunities with the availability of Sesame. There are a total of 38 Principal Investigators at six universities and research institute who have research programs in the general arena of biochemistry, genetics and molecular biology to which SMB would be immediately applicable. Sesame will provide the intellectual and operational framework to allow these investigators to explore new research opportunities of regional interest.

Lebanon - Pierre Rizkallah

Because of its political and economical situation, Lebanon at the present time has no focus on in research oriented higher education but mostly teaches first degree courses and only few masters courses. A few disciplines mostly in the Humanities cater for PhD level education. The basic matrix for research exists at the Lebanese American University, which is starting a scientific program and its Principal Investigators have expressed interest in SMB research. In the future, research will be most likely oriented towards local human health problems such as Thalassemia, infections agents (TB, Typhoid) and also veterinary related work and agricultural applications. Lebanon does have highly skilled graduates in all fields but a high incidence of brain

drain to the developed countries further complicates the establishment of regional research activities. The top priority appears the investment in motivation and Sesame could be the start to this effect and encourage young scientists to stay in Lebanon and established scientists around the world to interact with their colleagues in Lebanon. Sesame would also help in establishing collaborations amongst scientists from different countries in the Region and foster the intellectual exchange.

Morocco - Information supplied by Abdeslam Hoummada and Abdelaziz Soukri.

A group doing research in biological dynamics and molecular protein engineering is headed by Professor Soukri in the Biology department of the University HASSAN II of Casablanca. The work is done in close collaboration with two Universities in Spain (Sevilla and Saragossa).

The main fields of this group are:

* Understanding the mechanism of enzyme action, stability and gene structure using directed mutagenesis and molecular modeling.

* Study of the conformational change during the regulatory process.

* Study of the interaction of enzymes with some metals.

* Looking for a new and strong inhibitor of enzyme activity.

For more details concerning these subjects please contact Prof. Soukriat the e-mail address: a_soukri@hotmail.com.

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There are currently 11 universities with 65 biochemists and biologists on staff who have mostly teaching responsibilities. The establishment of an international research center in the Region could enable the interaction with scientists of member countries and encourage local research programs to be started.

Turkey - Engin Kendi (revised 6/17/00)

The Molecular Biology studies in Turkey have been carried out mostly at the larger Universities located in Ankara and Istanbul. They are either private or public Universities. Some of these studies are, peptide-lipid, drug – lipid interactions in model and biological membranes, protein structure and stability, genetic manipulations to improve the potential of bacteria to degrade toxic chemicals, molecular mechanisms and genetic regulation of antibiotic resistance in bacteria, transcription from ribosomal RNA genes and so on.

X-ray structural investigations of small molecules in Turkey have been studying since 1970. Small Molecule Crystallography Research Group at the Hacettepe University is equipped with a CAD-4 Enraf Nonius diffractometer and interested in biologically active compounds as well as metal-organic compounds, metal complexes of Schiff bases and so on.. synthesized in Turkey. The small molecule community is operating very

successfully a service center for about 50 principal investigators. Among the research areas of these groups there are, crystal structure studies, magnetic properties of homo and hetero nucleus metal complexes, magnetic properties of $R_x R'_{1-x} Mn_2Ge_2$ systems (R, R' = rare earth metal), molecular modelling, molecular mechanics calculations, studies on metal intercalated Fullerides, high T_cSuperconducting thin films and negative thermal expansion materials.

As a result; molecular biology and Crystallography Research Groups are well organized and are very competitive intellectually at the international level. Though the importance of SMB research is well recognized, lack of the experimental facilities prevents any axperimental research in Turkey.

The Turkish research community is well prepared for Sesame and has currently approximately 70 potential users of synchrotron radiation in SMB and materials research. Any opportunity in a SR center will certainly open up a new research area for all Turkish Scientist in each disciplines.

Appendix A – List of Participants

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Appendix B – Agenda

AGENDA FOR FIRST MEETING OF THE SESAME STRUCTURAL MOLECULAR BIOLOGY (SMB) SCIENTIFIC SUBGROUP

Administration Building of the University of Athens Panepisttimiou 30, Athens.

Thursday, April 6, 2000

8:00 am *Informal get together (coffee, etc.)*

8:30 Welcome - Costas Papanicolas (University of Athens)

8:45 SESAME - Herman Winick (SSRL/SLAC/Stanford University)

a - Status of the project
b - SESAME as a source for SMB research

10 minute talks (+5 minutes for discussion) by representatives of Middle East Countries on the status of SMB research in their country and potential use of SESAME by scientists from their countries.

9:30 Armenia; Harutyun Karapetyan (Yerphi)

9:45 Cyprus; Spyros Skourtis & Georgios Archontis (Cyprus University)

10:00 Greece; Constantinos Vorgias (University of Athens)
Metaxia Vlassi (Demokritos Research Center)

10:15 *Coffee break*

10:45 Iran; Nasrin Moazami (Biotechnology Institute)

11:00 Israel; Gitay Kryger (Weizmann Institute)

11:15 Jordan; Khalil Al-Mughrabi (Al Balqa' University)

11:30 Lebanon; Pierre Rizkallah (Daresbury/Lebanon)

11:45 Palestinian Authority; Said Assaf (Arafat Scientific Center)

12:00 Turkey; Engin Kendi & Engin Ozdas (Hacattepe Univ.)

12:15 *Group Lunch*

Overview of SMB with synchrotron radiation

13:30 Current capabilities of synchrotron radiation based SMB
Peter Kuhn (SSRL/SLAC/Stanford University)

14:15 Molecular biology, biochemistry & crystallization requirements
Gitay Kryger (Weizmann Institute)

15:00 Coffee followed by informal discussions at a social event at the Museum of the University of Athens

19:00 *Group Dinner*

Friday, April 7, 2000

8:00 am *Informal get together (coffee, etc.)*

8:30 Beam Lines for SMB - Ercan Alp (APS/Argonne National Lab.)

9:15 Experience with, and facilities for, biological macromolecular crystallography
Bob Batterman (CHESS/Cornell Univ.)
Anastassis Perrakis (EMBL)

Possible other presentations (to be decided at the meeting)

10:00 Round table discussion - topics include:

- Support facilities for SMB users
- Technical staff requirements for SMB research Detectors
- Suggestions for members of an External Advisory Comm.
- Plans for future SMB group meetings
- Activities at the next IUCR meeting
- Exchange programs between ME countries and others

12:00 *Group Lunch*

13:30 Drafting of meeting report

16:00 Summary and final discussions

17:00 Close of meeting

Appendix C
Draft Proposal for a SESAME SMB Program and Associated SMB Institute
Pierre Rizkallah, Metaxia Vlassi
July, 2000

SMB Science Sub-committee
Inaugural Meeting, Athens, 6/7 April 2000

Preamble:
The Structural Molecular Biology (SMB) Science Sub-committee was drawn from the interested community of Structural Molecular Biology researchers from the region served by SESAME, some of whom are currently based elsewhere. They share the desire to establish research projects, within the SMB interest area, based in the region. The meeting discussed all the different aspects that would influence this outcome, and agreed on a set of requirements that form the immediate objectives, when SESAME becomes operational.

Scientific Background

Current Status:
At present, Structural Molecular Biology research is small and fragmented in the region served by SESAME. High levels of skilled staff are available, but only limited resources are available to address important region specific problems: Health care, agricultural, veterinary and biotechnological development. Economic ability is the main limitation, but other limitations in academic education and access to enabling technology exist. Many of these will be overcome by collaboration within the SESAME framework.

Future Outlook:
The human genome is yielding its secrets after a heroic effort by many scientists across the world. The first fruits of this success will be most eagerly awaited by SMB researchers, to learn ever more about disease mechanisms and to devise new therapies. Also, many other organism genomes are becoming available, with a possibility of routine genome sequencing over the next generation. While many gene products (proteins) are important individually, macromolecular assemblies are becoming more important, particularly where a number of macromolecules work in tandem, e.g. the ribosome. This is the area where SESAME will be able to make a significant contribution:

1- Macromolecular Crystallography is the premier tool in SMB research today. It reveals the 3-dimensional structures of proteins at the atomic level, thereby, giving insights into the structure-function relationships of these proteins.
2- The full range of properties is not always explained by a macromolecule's 3D structure. The quaternary structure is often needed to complete the picture. Such information is possible with single crystal x-ray diffraction (macromolecular crystallography), while aggregation states and molecular shapes can be studied with small angle x-ray solution scattering (SAXS).
3- A large number of enzymes depend on a metal element for their function. Extended x-ray fine structure (EXAFS) is an important tool in probing the metal environment, for mechanistic studies that complement the 3D structure.
4- Ligand binding and reaction dynamics can be studied with spectroscopic methods. The bench top instruments are not as intense as a synchrotron light source, and the accessible band pass is not as wide as necessary for techniques such as circular dichroism. Speed up results in the ability to study short-lived species and proteins that are stable only for a short time.
5- Studies of protein stability are often reliant on folding pathways. Time resolved fluorescence spectroscopy, one tool that can provide answers, is an area well suited for exploitation with SESAME.
6- Elemental or chemical mapping in biological specimens will benefit from SESAME, in the study of disease processes or the efficacy of therapies.

7- Experimental results are knowledge quanta, which have to be used in theoretical calculations to generate intelligence. Computer modeling will be an important element in the exploitation of results to devise input for scientific and economic applications and development in the region.

Objectives

The Overall Objective:

The Committee agreed that the top priority is the establishment of a Structural Molecular Biology Institute, at the same site as SESAME, whose remit would be **'the development of the skills and infrastructure needed for SMB research in the region'**. It will act as a catalyst to shorten the relatively long lead-up time for projects, making some of them ready to receive the first SESAME synchrotron light to be produced. The Institute will also act as a seed for increased quantity and improved quality of SMB projects disseminated around the region, to make them World competitive. It will be the hub of a network of SMB researchers, sharing ideas and experiences, and providing necessary training for young scientists. **The mature SMB Institute, 3 to 5 years after the start, may be expected to cater for some 50 projects, with around 500 or more researchers involved.**

Institute Specific Objectives:

Molecular Biology and cell culture facilities, at Containment Levels 1 & 2, for:

1- Gene cloning, sequencing and expression facilities
2- Protein Purification facility
3- Biochemical characterisation facility
4- Reaction dynamics / kinetics measurement facility
5- Crystallization facility

Synchrotron Specific Objectives:

Ultimately, a fully established program in SMB will require a number of stations equipped for specific activities within the standard disciplines:

Stations for Macromolecular Crystallography:

a) High intensity, fully tunable x-ray diffraction station, operating range from 0.6 to 1.8Å, for MAD (Multiple wavelength Anomalous Dispersion) data collection.
b) High-intensity, semi-tunable wiggler side-station centered at the Se absorption edge, around 0.98Å for SAD (Single wavelength Anomalous Dispersion) and SIRAS (Single Isomorphous Replacement with Anomalous Signal) data collection.
c) Long wavelength diffraction station on a bending magnet beam line, operating between 2 and 2.5Å.

Stations for Extended x-ray Absorption Fine Structure, EXAFS:

a) Lower energy x-ray station operating between 4 and 10 KeV.
b) Higher energy x-ray station, operating between 8 KeV and the highest energy available from a MPW.

Station for small angle solution scattering:

a) X-ray station operating at 1.5 Å.

Station for Circular Dichroism:

a) Station on a bending magnet beam line, operating between 100 and 1000 nm.

Station for UV/Vis Fluorescence Spectroscopy:

a) Station on a bending magnet beam line, operating between 100 and 1000 nm

Station for Vacuum UV spectroscopy and imaging:

a) Station on a bending magnet beam line

Station for Infra-red Spectroscopy:
a) Station on a bending magnet beam line, to be shared with the above Vac/UV facility.

SMB Institute Implementations for above Objectives:

The statement of objectives above assumes a fully developed facility. Initially required will be the SMB Institute with capability for sample preparation and training and a subset of beamlines (some of which could be shared with other disciplines) to enable the core research to develop.

1- Molecular Biology Institute providing user laboratories and scientific/technical staff support for the Biochemical preparatory work.
2- Fully tunable, high energy resolution, diffraction wiggler x-ray beam line, operating from 0.6 to 1.8 Å for MAD experiments and other high intensity applications.
3- Semi-tunable (lower energy resolution) wiggler diffraction x-ray beam line centered at around 0.98 Å for Se-Met enhanced anomalous (SAD, SIRAS) and high-intensity data collection.
4- Solution Scattering bending magnet or wiggler beam line, shared with a Materials Science small molecule diffraction facility, operating at 1.5Å.
5- Wiggler hard x-ray EXAFS beam line, shared with Materials Science users, operating in the wavelength range 1.8Å to 0.7Å.

Requirements and Costs

All costs are estimated based on current pricing of instrumentation and their availability. The estimates do not include general infrastructure of the Institute, which will include wet-lab setups, administrative support, high-speed internet and intranet connectivity, and computational setup and support. The estimates for the synchrotron beamlines are for capital equipment only and do not include staff costs, overhead or contingency. The development and construction of the beamlines will heavily utilize the SESAME machine shops, designer groups and technical pool.

Hardware Requirements: Institute

1- **Molecular Biology laboratory**:

- Tabletop centrifuges x 2 (15K US$)
- Centrifuge for bacterial culture (50K US$)
- Incubators, many types and sizes are necessary (35K US$)
- DNA/RNA/protein electrophoresis and transfer systems, including: electrophoresis apparatus, power supplies, gel dryers, speed vac, transfer systems (westerns, southerns, northerns) (total 35K US$)
- Ultracentrifuge (65K US$)
- Hot room (37°C) (50K US$)
- beta and gamma counters (28K US$)
- PCR X 2 (16K US$)
- -70°C (10K US$) and other freezers (3.5K US$)
- UV spectrophotometer (16K US$)
- Sequencer (100K US$)
- gel documentation system (16K US$)

Total capital cost: 450K US$

Glassware, fine chemicals and other consumables: 10K US$ per year, for each project/group. On average, ten different projects are envisaged each year.
Total recurrent cost: 100K US$ per year.

2- Biochemistry laboratory:

- Homogenisers (10K US$)
- HPLC FPLC (100K US$)
- Cold room (4°C) (50K US$)

- Centrifuges (65K US$)

Total capital cost: 225K US$

Chemicals and other consumables: 5K US$ per year, for each project/group, 10 projects each year.
Total recurrent cost: 50K US$ per year.

3- Biochemical Characterisation and Reaction Dynamics:

- Spectroscopy suite with UV/Vis (20K US$)
- IR (20K US$)
- Dynamic light scattering (30K US$)
- Fluorescence and electro-spray mass spectrometers (200K US$)
- micro-spectrophotometer system(100K US$)
- Stop-flow system, isothermal titration and differential scanning calorimeters (130K US$)
- Surface plasmon resonance (200K-300K US$)

Total capital cost: up to 800K US$

Chemicals and other consumables: 5K US$ per year, for each project/group, 10 projects each year.
Total recurrent cost: 50K US$ per year.

4- Crystallization:

- Crystallization Robot (48K US$)
- pH meters with appropriate electrodes x 5 (10K US$)
- Stereoscopes x 3 (30K US$)
- CCD camera (1.5K US$)
- Steady temperature rooms (20°C) (50K US$)
- Cryo-cooler (30K US$)
- Goniometer heads for capillary- and cryo-mounting x 10 (5K US$)
- Crystal mounting tools x 3 sets (1K US$)

Total capital cost: 176K US$

Crystallization reagents and various consumables such as micro-pipettes, crystallization screens, plates, sample holders, cryo-crystallography tools (crystal caps, micro-tubes, cryo-loops, magnetic bases, *etc*.)
Total recurrent cost: 20K US$ per year

Hardware Requirements: Synchrotron

The cost estimate is based on the figures in 'SESAME A Proposal for a Synchrotron Radiation Source in the Middle East' (the green book). Most items already feature in the green book. This restatement accounts for the SMB part of the costs, although it should be remembered that some of the beamlines, and their costs, will be shared with Materials Science users.

1- X-ray Beamlines and optics x 4 (1,600K US$)
2- X-ray hutches x 4 (1,000K US$)
3- CCD detector systems for PX x 2 (1,500K US$)
4- EXAFS detector (350K US$)
5- Hardware for data acquisition x 4 (600K US$)
6- Computers for data analysis x 4 (400K US$)
7- Computers for graphics applications, model building, refinement etc. (250K US$)
8- Computers for computational Chemistry and modeling (250K US$)
9- Internet and local area networks (400K US$)

Total capital cost: 6,350K US$

1- Maintenance and spares for the above (500K US$)
2- Amortisation of aging capital items, to be replaced, on average, every 3 years (500K US$)
Total recurrent cost: 1,000K US$ per year

Software Requirements:
License agreements with appropriate providers of software.
Total recurrent cost: 50K US$ per year

Ancillary Requirements:
Biological samples holding area / laboratory / storage / cooled compartments are needed close to the stations within the synchrotron building, separate from the Institute. Their capital costs is assumed in the synchrotron hardware requirements above.
Total recurrent cost: 50K US$ per year

Staff Requirements:
Staff costs will depend significantly on the local conditions, tax laws and standard of living, for which reason they will not be addressed here.
1- Institute staff x 5 (additional staff, on secondment, to be sought. See below)
2- Station staff (see below) x 8
3- Electrical/Electronic engineers x 3
4- Mechanical engineers and technicians x 3
5- Software engineers, systems managers, network support x 5

Summary of estimated costs, not including staff

	CAPITAL	RECURRENT
Molecular Biology	450	100
Biochemistry	225	50
Characterisation	800	50
Crystallization	176	20
Beamlines	6,350	1,000
Software	-	50
Ancillary	-	50
Staff	-	-
Total	**8,001**	**1,320**

Operation

Time Scale:
The SMB Institute infrastructure, in terms of the biochemical laboratories, could be made ready within 2 years of a positive outcome for the proposal. SESAME is envisaged to have its first stored beam 3 years after the start. Some beamlines and stations construction can be run in parallel. Station commissioning can start only after the first stored beam, and would take between 1 and 2 years for fully developed facilities ready for production. The intervening time between the completion of the Molecular Biology/Biochemistry facility and the first user beam, will be used for readying appropriate SMB projects, i.e. the Institute will have been productive well ahead of SESAME.

Scheduling and accounting systems:
1- Quota definitions and project priority setting will be made on a national basis.
2- Continuous acceptance of research and beamtime proposals will be possible.
3- Accounting will be based on delivered time units of access.

4- Preference will be given to researchers from the Region and their collaborators with a certain percentage set aside for researchers from the international community

Mode of operation:

Access to the Institute will assume the 'Collaborative model':
Institute staff will have joint ownership, by agreement, of projects under development that require significant input from Institute staff.

The 'Associate model' will apply to other projects, nominated by the stakeholder countries, which require access to the facilities at the Institute, where the operators have already acquired the necessary skills:
The various facilities will be accessible with minor technical support from Institute staff.

Access to the synchrotron will be under the 'medium support model':
An operational station is made available, with a manual of technical instructions, assistance at the start of the experiment and when problems arise, and scientific support during working hours. Higher involvement of station staff in the research and joint ownership, by agreement, are also possible. This level of support requires 2 members of staff per station, at the user interface.

Staffing:

The level of support staff requirement indicated above maybe subdivided into 2 categories:
1- Permanent members of SMB staff, resident on site and dedicated to the services offered.
2- Seconded staff from partner countries, who will learn 'on-the-job' and assist with the operations, over periods of 1 to 3 years.

Other training will be carried out through a combination of workshops on site, training periods at other synchrotron centres across the world and joint appointments with universities and research institutes of the region.

Conclusion

Benefits to the Region:

The proposal aims at providing an enormous boost to the infrastructure of the SESAME region, since it brings World-class Structural Molecular Biology within grasp. Biotechnology will flourish in an atmosphere suited to the region, which addresses its topical concerns and ambitions. It provides a framework for the expansion of high technology applications in a part of the world that always lacked cutting edge facilities.

Additional benefits are expected at the scientific, social, economic and political levels:
- Stimulating one area of science will stimulate all other areas indirectly.
- The International profile will make SMB research attractive and will contribute towards the reversal of the chronic brain drain.
- Local suppliers will need to tool up to the level required for a synchrotron, bringing general benefits to the region.
- Cross border collaborations will bring about a higher level of cooperation across the region, not currently known. The notion of a 'Laboratory without walls' will deepen the sense of mutual destiny and interest among the partner nations.

Cost Effectiveness:

The evolution of similar sized facilities across the world, e.g. BESSY I profiled in the green book, shows a linear growth of the number of user groups and actual researchers over the course of a facility's lifetime. A mature facility often caters for around 200 user groups, comprising some 2000 researchers (Principal investigators, postdoctoral assistants and students). The areas of activity often are equally shared between the physical and the life sciences. Therefore, an overall capital spend of 8M US$, and a recurrent spend of just

over 1M US$ per year, represent good value for money to be spent on supporting the scientific needs of the developing SMB community of the Region. This activity will not be diverted from other facilities in the world. It is brand new activity, which otherwise would be not done, and its benefits would never be discovered.

Recommendation:

The SMB Scientific Sub-committee recommend the acceptance of this proposal, which matches the purposes and aims of UNESCO, the leading partner in the SESAME project.

Appendix D
Opportunity for a Center for Structural Molecular Biology at SESAME
Peter Kuhn, Stanford University
October, 1999

This document is intended for those who are interested in the opportunities for the development of a world-class scientific program in Structural Molecular Biology (SMB) at SESAME. The goal of this document is to layout the targets, requirements, and milestones for the establishment and successful operation of a SMB Center within the larger organization of the SESAME facility. The elements required for a successful synchrotron radiation program include a capable source of x-radiation, technical and experimental expertise, scientific innovation and support, and an integrated off-line research resource to enhance effectiveness and efficiency of the scientific experiments carried out by researchers from the region.

The technical studies (see for example Rabedeau *et al*.) have shown that SESAME will produce very intense focused x-ray beams that are ideally suited for diffraction studies on biological macromolecules. This opens the scientific opportunity for researchers to perform worldwide competitive scientific experiments at SESAME. In summary, a user facility will be developed at SESAME to establish and further foster SMB research in the Region by providing access to state of the art beam lines and ancillary facilities for SMB research to be conducted by current and future SMB scientists in the Region. The synchrotron SMB Resource at the Stanford Synchrotron Radiation Laboratory (SSRL) and experiences from the user community are used throughout this document as the basis for the recommendations and ideas.

The SESAME SMB Center can be developed to be fully competitive with the most modern state-of-the-art beam lines at SSRL and most other synchrotron sources around the world. It will provide for world class science to be conducted using this resource if implemented carefully as a true user facility. It has been shown in the design report that a beam line on SESAME is highly competitive to some of the best beam lines currently available for SMB research. The sample acceptance phase space calculations show that a crystallographic beam line on SESAME will produce diffraction similar to SSRL BL9-2 (before SPEAR3), DESY BW6 and NSLS BM4. The explanation for these calculations are given on the poster and abbreviated in the following: While flux (number of photons per unit band width produced by the source) and brightness (flux per unit source phase space) are the most widely quoted source metrics, the majority of macromolecular crystallography applications do not fall neatly into flux or brightness limited measurements. Perhaps the best alternative merit function to flux or brightness maps the source phase space into the sample acceptance phase space assuming appropriate optics are utilized in the transformation from source to sample phase space. This sample-based approach provides the flexibility to accurately relate the demands of macromolecular crystallography to the source properties. For example, a typical protein sample with 0.1-0.3 mm transverse dimensions and 0.2degree (3.5 mrad) or larger mosaicity has approximately a $(0.5\ \text{mm-mrad})^2$ sample acceptance phase space. The overlap integrals of this sample acceptance phase space with the phase space of the sources are shown on the poster.

1. Overall Layout of the Center

The success of the Center should be built upon three basic premises - i) intellectual excellence leading to forefront research; ii) developing and providing forefront synchrotron-based technologies; and iii) providing effective support to the user community. Through leadership provided by the Center's management and scientific staff, advisory committees, and the faculty and users, the Center has to develop and maintain a strategic plan that guides its overall development.

The staff of the Center has to develop a research and operations program around the needs and requirements of the Center and its users. The Center should allow its users to conduct a complete crystallographic experiment from handling samples to collecting high quality diffraction data to solving structures. The special

environment of the Region requires special attention to be given to the needs of the users and the Center should foster young investigators to perform high-quality science utilizing the resources of the Center.

SMB Advisory Committee (SMBAC): The SMB Center should be advised by an advisory committee established by the SESAME Council as soon as possible. It should consist of scientists from the Region, from worldwide SMB user facilities at other synchrotrons and scientists who are highly experienced synchrotron users. The key responsibility of the SMBAC is to advice on the most suitable ways to construct and operate the Center. A timely success of the Center could be further maximized by cross-training scientists and engineers at other synchrotrons and utilization of engineering designs of optical elements and other hardware from already successful SMB beam lines. The SMBAC would be responsible for establishing the appropriate exchange programs and evaluation of suitable options for the SESAME beam line configurations. The establishment of a larger virtual center for SMB research involving a sister center like SSRL's SMB Resource could be established with the help of the SMBAC.

Scientific and support staff: The Center should have an initial core of three to five scientific staff members supported by a similar number of engineers and technicians. The expertise of the staff must be spread over the full spectrum of required skills to successfully develop and operate the Center. This should include expertise in synchrotron instrumentation, advanced hardware and optics, electronics and software development, MAD, single-wavelength and other crystallographic methods. Scientific staff also develop and organize workshops and extended user training sessions on a regular basis. The Center should establish close ties with one or multiple international synchrotrons to train its staff initially and for a continuous exchange of information and training. If feasible, the exchange with one successful center for SMB research at one other synchrotron should provide the main lead for beam line concepts.

The operations staff is responsible for preparing the beam line for each user group and maintaining the experimental equipment. This is a critical component for preventing delays or experimental compromises due to missing or broken instrumentation. User groups are met by the responsible staff member and are given an orientation of the beam line. New users are trained in data collection, as well as in data processing. Staff also help users with their data collection strategies as well as with the processing of difficult data. Staff members are normally accessible during working hours to respond to unanticipated problems (*i.e.* mechanical, electrical or software) and by phone at night and on weekends.

2. Background on SSRL

Below we give some detail on the SSRL SMB operations to put the specification and success indicators for SESAME into context. Even though the magnitude of a SMB Center at SESAME would be initially smaller, the SSRL concept of a fully integrated program, which has developed over many years in collaboration with an extremely supportive and inspirational user community, can serve as one possible model. The SSRL SMB group currently operates 8 beam lines of which 5 are dedicated to macromolecular crystallography, 2 to biological XAS and 1 to SAXS. A total of about 800 users utilize the SMB Resource annually to conduct their experiments. All stations are continuously improved and efficiently operated by the technical and scientific support staff. Each scientific staff member at SSRL pursues a vigorous research program to conduct forefront structural science typically directed towards new technical and methodological developments in structural biology related to advanced experimentation at the synchrotron.

An integrated resource - mode of operation and unique features: The SSRL SMB Resource operates within the overall framework of the SSRL laboratory, but specifically focuses its activities on the eight beam lines and their associated instrumentation that are dedicated primarily to SMB research covering the three technological focus areas. All SSRL general users gain access via a centrally managed, fully integrated proposal review system. SSRL also manages all major beam line construction and beam line improvements. Where relevant and applicable, standards can be (and are) established either lab-wide or over appropriate

clusters of beam lines to cover areas like instrumentation control, software user interfaces and data reduction and analysis tools, data archival and storage, training and documentation, *etc*. Benefits of this fully integrated mode of operation include more efficient utilization and sharing of staff, reduction in the amount of documentation and effort needed to maintain the complex and large enterprise, ready propagation of enhancements in hardware and software across all relevant beam lines, and enabling the users to more easily move from one beam line to the other without need for a significant amount of retraining.

High level of user satisfaction and support: SSRL and the SMB Resource put a high priority on obtaining user feedback, addressing issues and improving performance and service. Within the framework of the Resource, the fully integrated technical and scientific staff provides the basis for much of SSRL's character. All users can be given a high level of support and are generally very pleased with the quality of beam and their overall experience. The integrated model enables all SSRL users to easily access and apply for beam time on any of the beam lines, hence using combinations of techniques to address problems (e.g., active site electronic and metrical structure using XAS simultaneous with high resolution crystallography or low resolution and high resolution diffraction experiments on a system with a large unit cell). This emphasizes a feature of SSRL and the SMB program; that is, its commitment to users and providing the best possible beam, state-of-the-art instrumentation, and a very high level of scientific and technical support.

Strong intellectual development through scientific staff and faculty: SSRL is in itself a Stanford University Department with its own faculty. The regular SSRL faculty has 12 active members and there are also affiliated faculty and consulting faculty (scientists outside Stanford who provide advice and expertise in diverse scientific fields). Faculty involvement in all areas of synchrotron research, including molecular environmental sciences, materials sciences, applied physics and chemistry greatly enriches the intellectual environment at and contributes significantly to new funding initiatives and planning for the future. SSRL also has a strong scientific staff who invest about 50% of their time in research and 50% in facility development and user support. There are nine Ph.D. scientific staff members in the SMB area, of which five are involved in macromolecular crystallography (in addition to the three faculty members).

3. The Beam Lines for the Center

It will be critical for the overall success and worldwide competitiveness of the Center that the beam line(s) are dedicated to their purpose and that shared beam lines are being avoided (single purpose beam lines instead of shared amongst multiple disciplines).

The Center's core responsibility is providing high-intensity synchrotron beams for forefront experiments in SMB. The concept of SSRL's beam line 9 is used as one possible arrangement for implementation. This beam line receives its radiation from a 16-pole permanent magnet wiggler insertion device that produces a fan of 15 mrad of synchrotron radiation. This fan of radiation is split amongst 3 beam lines.

Beam line 9-1 is -5.2 mrad off center with an acceptance of 3.0 mrad. K.B. type optics are employed to achieve a 6:1 demagnification in the horizontal (final focus of 1.3 mm) and a 2:1 demagnification in the vertical (final focus of 0.15 mm). It is optimized for monochromatic and ultra-high resolution data collection with an accessible wavelength range of 1.0 to 0.7 Å. Diffraction data are recorded on a fast MAR345 image plate detector. The standard beam collimation and conditioning system and detector positioning system first developed on BL9-2 will be installed during the 1999 shutdown period. In 2000, a 2x2 CCD detector will be implemented on this line as an alternative detector.

Beam line 9-2 is -0.4 mrad off center and collects 2.0 mrad of radiation. It has been optimized as a state-of-the-art MAD beam line and is now fully operational. This high intensity wiggler beam line is equipped with a pre-collimating mirror for high-energy resolution, benefiting MAD experiments (wavelength range of 0.56 Å to 4.4 Å). A Huber Kappa diffractometer and a Quantum-4 CCD detector mounted on a high-precision positioning

table are currently provided for data collection. A 3x3 matrix CCD detector (31.5 x 31.5 cm^2) is on order from ADSC and will be installed on BL9-2 in the spring of 2000.

Beam line 9-3 is +5.0 mrad off center and receives 2.5 mrad radiation. It is a side station with end station like physical access configured with a vertically collimating pre-monochromator mirror, moveable-exit double crystal Si(220) monochromator, and post-monochromator toroidal focusing mirror covering the energy range 4600-40000 eV. It is dedicated for biological XAS and equipment includes a 30-element Ge fluorescence detector array, a LHe cryostat, optical alignment rails and the same computer/software environment as BL7-3. Capabilities under development include polarized protein single crystal XAS, and XAS-imaging and XAS-tomography.

The SESAME beam lines could be configured similarly with state-of-the-art optical configuration to achieve maximum efficiency for the particular experiment. The experimental station should be equipped with all the standard devices, tools and equipment so that visiting scientists can conduct complete crystallographic experiments while at the beam line. This includes a precision table that carries all the experimental equipment and allows alignment of the experiment to the x-ray beam. The experimental equipment consists of a remote controlled beam conditioning system with filters, slits and shutter, a fluorescence detector to measure the XAS signal for MAD experiments, a multi-circle diffractometer (*e.g.* Huber Kappa diffractometer with motorized sample stage), an advanced detector positioning system with variable sample-detector distance from ~50mm to ~1000mm and an advanced x-ray detector (see below). The equipment should also include 3D graphics workstations for instrument control and data analysis, microscopes, cryo-cooling systems (cryostat, dewars, tools), and a spacious user area. The experimental enclosure should be large enough in size to accommodate all routine and most specialized equipment such as additional liquid helium cryostats, laser and other optical systems. A detailed list of instrumentation can be provided upon request.

Currently a wide variety of detector options for macromolecular crystallography are available for a new beam line. The most commonly used detectors on synchrotron beam lines are fast imaging plate systems (such as the MAR345 detector, 34.5cm diameter) and matrix CCD based detectors (such as the ADSC Quantum-4, 18.8cm x 18.8cm). New technology allows to overcome the problems of small size of the CCD based detectors and available on the market now are large 3x3 and 4x4 matrix detectors with an active surface of 31.5cm x 31.5cm and 42.0cm x 42.0cm, respectively. The new detectors have a readout time of approximately 1 second and are, therefore, significantly faster than the previous generation of CCD detectors (~9 seconds) and far outperform imaging plate detectors (~90 seconds). The large matrix CCD detectors also require very significant computing power to handle, analyze and store the data in real time. A 4x4 CCD detector will, for example, require a large multiprocessor server with at least 3TB of storage and advanced data backup devices. The price range for the detectors is spread from less than $200k (MAR345) to $2.5M (4x4 ADSC Quantum-420), which does not include the computing systems and service contracts. The most suitable detector would be chosen in consultation with the SMBAC at the time of purchase approximately 9 months before completion of the beam line. The computer systems must be specified to support i) the data flow from the detector and provide ii) real-time data analysis capability and iii) on-line data storage for about one week of full running schedule. Based on the experiences of limitations with the current 18 cm x 18 cm CCD detector on BL9-2, the larger 3x3 or 4x4 CCD detectors would provide an excellent match to the capabilities of the SESAME beam line(s).

4. Capabilities:

With the availability of a dedicated high-power wiggler ID beam line equipped with advanced instrumentation for SMB research, investigators from the Region could perform cutting edge experiments in a very timely fashion. One can anticipate that on such a resource many experiments that are currently considered 'specialized' would become standard, such as ultra-high resolution data collection, collecting complete data to the crystals resolution limit for large unit cells, high-resolution MAD phasing, high and low energy MAD data collection and micro-crystals. The advanced optical configuration will ensure outstanding performance

characteristics for MAD data collection with an energy resolution of 0.017% $\Delta E/E$. This very narrow energy bandpass will allow detection of very weak anomalous signals providing the required phasing information to solve the structure.

Full remote control of all beam line hardware and a user-friendly interface for data collection and analysis will allow of effective and efficient use of the beam time. An advanced computational environment should be established that allows the visiting scientists to easily analyze diffraction data in real time. In addition, off-line resources should be provided to be used by scientists for a limited time after the experiment because it must be anticipated that many research groups in the Region do not have access to powerful computing resources in their home laboratories.

5. Other support equipment

The Center should provide additional support equipment including incubators for storing samples at the beam line, short and long term cryo-sample storage, two sample preparation laboratories, cold-rooms, additional microscopes with video capability, cryo-tools, xenon derivatization systems, offline EPR spectrometer, glove-boxes, a machine shop, a storeroom and a wet-laboratory and user lounge in close proximity to the beam line.

Participants in the SESAME SMB meeting, Athens, Greece, April 7, 2000.