An Operational Plan for the Electron Microscope Unit - 2006 to 2009

Overall strategy

Financial prudence dictates that we are conservative with respect to existing resources and that we maintain them properly and exploit them maximally to leverage advantage from them for out future growth.

The energy which propels a broad range of visualization technologies and techniques arises from within the Unit. Thus the interest of the Unit staff provides a springboard for the users of the Unit and enables them to derive benefit from the technology. The Masters programme in structural biology has produced a number of students whose focus is on the technology and who have the breadth and depth of knowledge to exploit it properly. The intellectual activity centered on biological visualization and EM in particular at the University of Cape Town is now considerable. It is important to exploit this critical mass to create a sustainable environment and to move rapidly to secure equipment which will open new frontiers in African science.

Recurrent activities

- The Unit provides a service in microscopy for between 80 and 120 students and staff members per year.
- The Unit trains between 10 and 20 students in microscopy per year on an individual basis.
- Between 1 and 10 students and staff who are not microscope users make use of the Imaging Centre
- Between 10 and 20 students in total attend the five day course “Introduction to Microscopy for Biologists” which is run once or twice each year depending on demand.
- Participate in the activities of the Microscopy Society of Southern Africa
- Run the Masters Programme in Structural Biology.

Non-recurrent activities

Purchase of a FEGTEM and a FEGSEM

An opportunity to replace our obsolete JEOL200CX with a modern instrument of enhanced capability at a reasonable price has arisen. The British Medical Research Council’s Laboratory for Molecular Biology has decided to dispose of their four year old cryo-FEGTEM, an FEI Tecnai F20 for GBP100k. FEI have offered to refurbish this instrument for us and install it in Cape Town for 100k euros.

An application for approximately R2.5m has passed through the UEC and REEP and is currently under consideration by the NEP. However it is important to inform the LMB in the first week of August 2006 that we wish to proceed with this. UEC has recommended that the University advance the money and that attempts be made to recover it from grants. The DVC has supported this strategy.

A further development is that DST has reserved R25m for funding a national programme in structural biology pending a detailed proposal from me which would contain the following elements:

1. National strategy

2. The setting up of resource centres with equipment, scientific and technical expertise
3. The centres will leverage existing "biotechnology" projects irrespective of their sponsor - specifically in the areas of drug/vaccine design, pesticides/agrochemicals and fine chemical (i.e. drug and drug precursor) manufacture.
4. We would guarantee to train and involve people from HDU's

We should think very carefully about gearing this money optimally.

Also in play at the present time our bid for the ICGEB centre. It would be nice to combine these in a synergistically if this is at all possible. One possible scenario is the following: Site the new microscope as well as a support instrument at Medical school in order to be close to the ICGEB and hire a "senior" scientist at (at least) associate professorial level to run it. A possible business model is that he/she would solicit collaborations nationally and internationally through the ICGEB and would also run training courses (on the scale of the EMBO world programme as well as components of our masters programme) through the centre/facility. We would also set up a lab resource for "work-up" (i.e. preparing proteins, viruses, cells etc for structural studies).

Our previous strategy has proved to be absolutely incapable of raising the funds necessary to replace microscopes or attract staff who have exciting and innovative ideas in microscopy. Faced with a world wide trend in which even minor laboratories have replaced instrumentation in order to do modern experiments it is necessary for us to formulate a viable financial plan or reformulate our research ambitions. Clearly innovative and imaginative leadership are required to break this deadlock.

The following table shows the costs of the four electron microscopes currently in the Unit and shows the replacement year which is consistent with our approved strategic plan.

Instrument	Year Purchased	Estimated Cost	Replacement Year	Current Replacement Cost	Notes
LEO S440 SEM	1994	R1.2m	2009	R2.5m	
Cambridge S200 SEM	1984	R140k	1999?	R1.35m	Upgraded at a cost of R55k in 1992 and 1994. EBSD added in 1999.
JEOL 200CX TEM	1980	R365k	2000?	R4.5m-R5.5 m	
Zeiss EM109 TEM	1980	R190k	Taken out of service in 2003	R2.5m	Upgraded at a cost of R80k in 1995
JEOL 1200EXII	Acquired			R6m	

	second hand in 2001				
LEO EM912	Acquired second hand in 2003	R3m	2006	R7m	

Part of the complexity of our situation arises due to the need to satisfy both Materials and Biological scientists on one instrument. The fortunate situation, which existed previously, in which most of the projects motivated for the short term could be done on one instrument possibly no longer pertains. Although it is believed that most Materials projects arising from UCT could be done on the Tecnai F20 in the configuration of the Cambridge instrument.

Another equipment replacement issue that will emerge during the time frame of this operational plan is the need to replace the S440 as our front-line SEM. Thought will have to be given to this. The following is clear: Scanning Electron Microscopes are pivotal equipment in surface studies in both materials and biological science. New high resolution equipment (FEGSEM) is both affordable and user friendly and can be configured to meet the needs of both user communities. We would have to contemplate an instrument which would be capable of EDS, EBSD and cryo. An instrument in this category has been motivated by The Department of Chemical Engineering (see attached motivation). They have sought to site the instrument outside of the Unit under their own management. If this were to occur there would seem to be little reason to maintain the SEM capability of the Unit at its current level and the University would presumably need to move the responsibility for providing SEM services away from the Unit. I believe that this is not a satisfactory situation and that rather the needs of Chemical Engineering should be satisfied on the new instrument acquired by the Unit. The benefits of siting the instrument in the EM Unit interms of sharing the running costs, technical and support infrastructure should be made obvious to the Department of Chemical Engineering.

Obviously major users of the EMU will have to play a central role in motivating new equipment and in identifying potential sources of funding. The Director will continue to play a role in co-ordinating these efforts, assembling the applications, and in specifying and sourcing the equipment.

Developing and Sustaining the Infrastructure for Cryo-electron Microscopy
Setting up a centre for cryo-electron microscopy has had substantial cost implications of both a capital an recurrent nature. It is hoped that the major part of the capital funding will be provided by the equipment grant discussed above. The recurrent component which will comprise liquid nitrogen, an increased bill for vacuum component maintenance and an increase in photographic film expenditure will need to be raised from either grants to the Electron Microscope Unit or grants to our users.

Support for a programme on "Advanced Materials in Manufacturing"

Materials science is a key research area which attracts significant worldwide attention and funding. The commitment of the EMU to the establishment of Structural Biology has compromised its support for materials research. This was a choice made by the director. The choice was informed by the decision by the University to disestablish the Department of Materials Engineering on the one hand and to establish the IIDMM on the other. This has left

the remaining members of the Centre for Materials Engineering in a difficult position. Whereas in former times they felt that the director of the EMU was responsive and concerned about their needs they no longer have this perception. The needs that require support are both intellectual and logistical. In the first instance materials students from the Departments of Mechanical Engineering and Chemical Engineering need to be taught the theory and practice of modern microscopy and in the second instance equipment needs to be put in place to support advanced materials research. In many respects the equipment needs of the biological and materials communities are orthogonal at the high end. If we decide to go for funding for a high end machine it will have to be to support one community or the other.

A solution to this conundrum may be to follow the model of the Structural Biology Programme and establish a joint programme in "Advanced Materials in Manufacturing" jointly with neighbouring institutions - notably iThemba and UWC.

In this model UWC or iThemba could take responsibility for raising funds for and maintaining instruments supporting the physical sciences and UCT could do likewise with the biological sciences. No matter what solution is ultimately reached the director will strive to meet the needs of the materials community, but he is of the opinion that a strong case for solving the problems on a regional basis exists.

IIDMM

The EMU is supportive of and is participating actively in developments aimed at providing electron microscopy support to the IIDMM. As plans develop the details of the Unit's involvement and the creation of a new structure encompassing electron microscopy or even all aspects of imaging technology will become clear. At present it appears that the IIDMM researchers will use a consolidated upper campus-based EMU service for their needs, and attention can now be given to developing a Unit capable of supporting diagnostic work located in the Hospital as a component of the NHLS. The Director has organised courses in x-ray crystallography, strucutral bioinformatics and the functional microscopy of host-pathogen interactions in the IIDMM with a view the promoting the use of visualization technology.

Staff Development

In order to continue to provide an excellent service the technical skills of staff need to be upgraded on an ongoing basis. In some cases appropriate courses are held locally but occasionally it is more appropriate to send the technical officers overseas. Such training courses will be partially funded by income arising from fees charged to external users. In particular maintenance and operation of two FEG instruments will certainly raise the bar in terms of the support level necessary.

The Unit has maintained a policy of providing service though an employed staff member. This has advantages for us in terms of both availability and cost of service. It is however not a popular strategy with manufacturers who seek to gain profits from the service of instruments. Indeed electron microscopes have very high costs of development and sales and the only way that the companies can recoup these costs is through service contracts. Typically the cost of a service contract on a Tecnai F20 is USD65k per annum and the cost of maintaining five instruments in the US is around USD200k. We are spending one quarter of that including the salary of our service technician.

To the extent that they are willing existing staff will be trained in both service and applications by a mixture of in-house training and attendance at overseas courses. However the level of commitment required to obtain new knowledge is considered by the staff to be outside of their job description and incentives are required in order to expedite such training events.

Research

The purpose of most of the work done by staff members of the Unit is to further the research of others, however a small amount of time is available for externally funded self initiated research, in particular, it is apparent that we have now assumed international leadership in the study of an important class of industrial enzymes.

- B.T. Sewell intends to continue with the collaboration which has been established with Prof. Michael Benedik at Texas A&M University to solve the three dimensional structure of the nitrilases and will commence a series of projects on other systems as well as collaborative opportunities arise.
- B.T Sewell will continue his collaboration with Dr Muhammed Sayed and Professor Donald Cowan at UWC on the three dimensional structures of industrial enzymes.
- Dr B. Weber will commence research on the malaria parasite.

Signature theme in Medicinal Chemistry

The development of Medicinal Chemistry, which is a primary focus area of the Chemistry Department at UCT, is critically dependent on macromolecular structural insights. At present there is not a single member of the Department with any expertise in macromolecular structure. The Director will support the research of selected people in the Chemistry Department and will offer assistance until they are able to operate independently. The short term goal of the interactions will be the establishment of a signature theme in Medicinal Chemistry, combining the talents of synthetic chemists and chemical pathologists to solve problems related to African diseases, which will attract funding and students into this area.

Improve digital infrastructure

The Unit provides the computer infrastructure necessary for its users to exploit the advantages of digital imaging. The following enhancements are planned and will take place subject to the availability of funds:

- Installation of an image database system
- Introduce web based data management
- Formulate and implement a strategy for digitization of TEM micrographs which is based on users' needs
- Upgrade the digital infrastructure
- Hire somebody to assist with the establishment of a robust, purpose built system.
- Migrate towards a unified computer system for the EMU and the Structural Biology Programme

The director will apply to the Ford Foundation for funding to enable some of the above as well as to enable transparent access from UWC.

Teaching and training

The EMU is without doubt the prime intellectual resource for Biological electron microscopy in South Africa. The Unit offers a very broad range of expertise in relevant modern areas. The Unit offers a one week honours course - “Introduction to Microscopy for Biologists” and a seven week course as part of the Masters in Structural Biology covering cryo-TEM and three dimensional image reconstruction. Significant one-on-one training is also offered by the Unit. The cost of this specialization has been an erosion of expertise in electron microscopy for the physical sciences. Energy will be put into assisting materials users with their teaching and training needs - probably through regional initiatives. The Director will also teach a three week module at third year level in the Department of Molecular and Cell Biology.

Building Maintenance

Rooms 218A and 219 in the R.W. James Building are conveniently located for courses and other teaching activities conducted by the Unit. These rooms are exceptionally hot in the summer and the environment could be substantially improved by the installation of air-conditioning. The offices 215, 216, 217 and 218 also require air-conditioning.