An Operational Plan for the Electron Microscope Unit - 2005 to 2007

Review of accomplishments based on the previous plan

The two papers on the cyanide degrading nitrilases have been published. A paper on the structure of an interesting GroEL mutant has been submitted to Nature Structural and Molecular Biology, the Wellcome Grant enabling this work has now terminated. The NRF awarded us grants to determine the EM structure of a glutamine synthetase and to determine the X-ray crystal structure of a nitrile hydratase. Both of these goals have been accomplished. In addition the EM structure of a cyanide hydratase has been completed. An unprecedented number of students at all 3 Western Cape universities submitted theses which utilised EM which was done in the Unit (MSc 13, PhD 7).

The Leo 912 was installed and its digital camera has proved extremely popular with users. The EM 109 has been decommissioned and is being stored.

Dr Price, Mr Duncan and Mrs Waldron were all rewarded with pay increases.

Dr Arvind Varsani was appointed as a lecturer in structural biology. Mr Sean Karrien was appointed as departmental assistant and has proved capable in assisting with a number of computer based tasks.

Unforeseen circumstances

The Leica S440 suffered a major and expensive breakdown which was caused (at least in part) by a power cut-off. No grants were obtained by Dr Arvind Varsani - the URC rejected his application because he was appointed on a T2 contract and the NRF rejected his application because he is not eligible for permanent residence because he has a T2 contract.

Overall strategy

The overall Unit strategy has elements of conservatism and boldness. 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.

But we must be bold to create new opportunities using the srpingboard provided by the grant from the Carnegie Corporation of New York to fund a Masters programme in structural biology. This programme has provided an academic staff member in the area of EM based structural biology. Projects motivated by this person could drive the acquisition of the new equipment desperately needed and enable the evisaged work of the IIDMM.

Recurrent activities

- The Unit provides a service in microscopy for between 70 and 100 students and staff members per year.
- The Unit trains between 10 and 20 students in microscopy per year on an individual basis.
- Between 30 and 60 students and staff who are not microscope users make use of the Imaging Centre
- Between 20 and 30 students in total attend the five day course “Introduction to Microscopy for Biologists” which is run between 2 and four times depending on demand.

- Participate in the activities of the Microscopy Society of Southern Africa
- Run the Masters Programme in Structural Biology.

Non-recurrent activities

An important facet of our non-recurrent activities will be to realize the potential of the Leo 912. This will have a determining effect on the success or failure of our application to replace the 200CX TEM. Our need is to raise the additional R3m to exploit the offer made to us by Leo.

Our previous strategy has proved to be absolutely incapable of raising the funds necessary to 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.

Replacement of Major Instrumentation

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	2010?	R2.5m	Upgraded at a cost of R80k in 1995
JEOL 1200EXII	Acquired second hand in 2001			R6m	
LEO EM912	Acquired second hand in 2003	R3m	2006	R6m	

The need to replace the JEOL 200CX TEM remains pressing although the capabilities of the LEO EM912 remain to be explored. The issue is the 200kV capability of the 200CX. This is

the minimum accelerating voltage appropriate for studies on metals and has substantial advantages over 120kV for biological studies as well - notably lower heating effects. We have been offered the possibility of upgrading the 912 to a 200kV 922 with cryo at a cost of R3m.

Strong support from Prof. Dirk Knoessen at UWC remains and support has been forthcoming from Prof. Jan Coetzee at University of Pretoria which is contingent on us obtaining funding to set up a National Centre for Cryo-microscopy however we have not adequately exploited this idea to date.

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 in that most of the projects motivated for the short term (see appendix to Annual Report) could be done on one instrument possibly no longer pertains.

Undoubtedly our best strategy is to capitalize on our success in setting up the structural biology programme.

Developing and Sustaining the Infrastructure for Cryo-electron Microscopy
Setting up a centre for cryo-electron microscopy will have 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.

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.

Upgrade to S440

The S440 scanning electron microscope, purchased in 1994, was at the time the leading digital instrument on the market. Rapid developments in technology have made it difficult to maintain integration with the network and have made it impossible for the manufacturers to deliver on their promise of a resolution enhancement based on the technology which we have. Furthermore the one real weakness in our instrument at the time of purchase was the stage design. This has now been substantially improved and the latest design coupled with enhanced computer hardware and software would enable automatic particle analysis which would be of real benefit in many engineering, biological and environmental studies. It was hoped that the funds necessary to implement these upgrades would be found by 2003 this has not happened and motivation for the improvement of this instrument will have to be backed up by strong projects before this can occur. The Unit will help users, especially in the Centre

for Materials Engineering, to formulate motivations to grant holders for the upgrade and maintenance of this instrument.

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. The following overseas training is planned:

- Mr J. Duncan will attend training at The Woodlands in Texas on the maintenance of Rigaku equipment.

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:

- 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. Significant funding for this work has not yet been found but is being actively sought. At present a large number of local collaborations are active and work on each of these will continue.
- M.A. Jaffer will continue with work on the three dimensional structure of the chromatin fibre.
- M.E. Waldron will continue to study fish ageing. Work in collaboration with the SFRI has commenced.
- Dr Brendon Price will pursue several areas relating to the structure and function of nitrilase enzymes in bacteria and fungi in collaboration with B.T. Sewell. A grant application in this area will be prepared and submitted to the NRF.

Improve digital infrastructure

The Unit provides the computer infrastructure necessary for its users to exploit the advantages of digital imaging. Enhancement of the system will be paid for in part by fees charged to external users. The following enhancements are planned and will take place subject to the availability of funds provided by the University:

- Installation of an image database system
- Allow interactive access to the S440 using web protocols
- Introduce web based instrument booking
- 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.

Teaching and training

There is a need to promote electron microscopy in South Africa especially as a tool for Structural Biology. The determination of the three dimensional structures of subcellular objects and immuno-localization are the two key areas of EM application in modern biology.

The Cape Town area has the highest concentration of talent in structural biology in the country and people who have experience in NMR, X-ray crystallography, bioinformatics, molecular modeling and the other disciplines required by Structural Biology. It is our intention to exploit our advantage in this area by recruiting students and running the MSc in Structural Biology. Course notes and reference material for our existing course, “Introduction to Microscopy for Biologists” will be made available on the Web. Workshops will be conducted in the Unit by local and foreign microscopists on a self-funding basis when the opportunity is presented.

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.