

An Operational Plan for the Electron Microscope Unit - 2007 to 2010

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 our 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 180 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

The FEGTEM is now purchased and will be installed during the remainder of 2007. Fundraising needs to continue however as there is a shortfall of R631,191 and the cost of meeting the pre-installation requirements was R188,691. In order to properly exploit this instrument and make it widely accessible it is important to purchase a digital camera as a very high priority. A proposal to do this in 2007 was rejected by the University Equipment Committee.

It is proposed that this money together with money for a new FEGSEM and other enabling equipment be raised through DAD. A document briefly motivating this is attached.

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.

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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 1200EXII	Acquired second hand in 2001			R6m	
LEO EM912	Acquired second hand in 2003	R3m	2006	R7m	
Tecnai F20	Acquired second hand in 2007	R3m	2017	R10m	

National Structural Biology Strategy

The DST has awarded a grant of R1.1m to the Cape Biotech Trust to (1) enable the existing structural biology programme to continue and (2) to set up a committee to devise a national strategy in Structural Biology. ((1) motivates *inter alia* the continued employment of Ms Amanda Gillespie and Mr Rory Austin.)

A further development is that DST has applied to the treasury for a large amount of funding for 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 Competence Centres with equipment, scientific and technical expertise
3. The Centres will operate within the "Innovation Space" and 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. The programme would guarantee to recruit and train people from historically disadvantaged backgrounds.

We should think very carefully about gearing this money optimally in the interests of UCT.

An important additional element is the establishment of the third component of the ICGEB in Cape Town. Professor Iqbal Parker has been appointed its director. He will need to decide in

collaboration with the DST and with ICGEB what needs to be done in the component. There is pressure that it should contain structural biology. Mr Dhesigen Naidoo of the DST has the responsibility of formulating the government's position and he is in contact with Mr Ben Durham who has formulated the proposals for Structural Biology. It would be nice to combine these in a synergistically if this is at all possible.

One possible scenario is the following: Convert the EMU into a Competence Centre - or a component of a Joint UCT/UWC Competence Centre. A possible business model is that Centre in addition to running its own projects 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 the masters programme) through the Centre. The Centre would also set up a lab resource for "work-up" (i.e. preparing proteins, viruses, cells etc for structural studies).

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 and 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.

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 through 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 has become a fully integrated member of the protein structure research group.
- Dr Varsani will continue with Virus research as well as supporting a wide range of structural work.
- B.T. Sewell will seek further collaborations as well as continuing existing ones.

Signature theme in Drug Discovery

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

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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

Some of the above has already been accomplished. Please note that the director of the CEF seems to want to duplicate the effort that we have put into web-based reporting. This software is largely ready and will go into production in 2008.

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.

Budget

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EMU Charges Proposal	(LAST INCREASE IN 2002)"		
Service	Unit	Old	New
Electron Microscopy (non-FEG)	Per hour	R150.00	R300.00
Electron Microscopy (FEG)	Per hour		R400.00
Ultramicrotome	Per hour	R50.00	R100.00
Operator Charges	Per hour	R150.00	R300.00
Critical Point Drying	Per run	R50.00	R100.00
Sputter coating	Per run	R40.00	R80.00
Carbon coating	Per run	R40.00	R80.00
Scanning negatives	Per hour	R10.00	R20.00
Scanning negatives with operator	Per hour	R50.00	R100.00

EMU budget proposal for 2008

	2006	2007	2008	
Income				
Operating grant	151,116	108,530	112,330	increase of 3.5%
Users (non FEG)	226,021	226,171	250,000	increase of 11%
Users (FEG)			120,000	
Consumables	57,508	53,165	55,000	
From Savings	80,251			
Equipment grant	72,464			
Total	587,360	387,866	537,330	
Expenditure				
Operating	199,784	207,810	239,043	increase of 15%
Equipment	269,000	28,005		
Repair and Maintenance	61,068	96,757	225,787	
Mrs Waldron to EMC 2008			17,500	
Consumables	57,508	55,294	55,000	
Total	587,360	387,866	537,330	
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Actual Running Costs of F20 in Cambridge GBP

	2005	Rand
Maintenance Contract	10942	
Film	4908	
Small parts	3553	
FEG tip replacement	8000	
Bearings	153	
O rings	1674	
Turbo pump	3000	
	2006	
Cryo holder repair	3000	
Maintenance Contract	10942	
Power supply	956	
Camera repair	3000	
Ave per year	25064	350896
	Euros	
Quoted Maintenance Contract	31000	310000
Estimated materials	20000	200000
Budget for 25064-10942 per yr	14122	141220