

## **A Strategic Plan for the Electron Microscope Unit, 2007-2010**

### **Vision**

**The Electron Microscope Unit will be the prime resource for electron microscopy and other selected imaging techniques serving research and teaching in the Western Cape. The Unit will specialize in three-dimensional structure determination.**

### **Objectives**

The Electron Microscope Unit is a resource centre which enables researchers and their students to visualise and analyse microscopic entities arising from diverse fields. The resources it provides are microscopes, preparative equipment, analytical equipment, an infrastructure for image data visualisation, analysis, management and presentation as well as knowledge and experience in a variety of areas of microscopy. The Unit also exists for the promotion of electron microscopy and other forms of microscopic visualisation in research and for the education of users in various aspects of the technology.

A key resource of the Unit are the staff who act as research partners advising on possible microscopy strategies for achieving the required insights and guiding students and researchers in the use of the technology.

The primary areas served are research and postgraduate teaching in Engineering, Health Sciences and Science. The Unit is not structured as a routine diagnostic or quality control facility.

The primary users served by the Unit are from UCT, the neighbouring academic institutions and local industry. Occasional use of the Unit is made by academics from African states and from further afield.

### **Assumptions**

The existence of the Unit as a communal resource provided by the University is justified by the following two assumptions:

1. Microscopy in its various forms is and will remain a key research tool in a wide variety of fields.
2. Sophisticated microscopes and the supporting infrastructure required to make effective use of them are too expensive for individual departments.

### **Governance**

- The Electron Microscope Unit (EMU) is a University facility run by a Director.
- The Dean of the Faculty of Science acts as the line manager for the Director of the EMU.
- The EMU falls into the grants category on the UCT budget and may also make application for granting of capital expenditure, in competition with the rest of the UCT community. The grant base year will be the operational continuing budget for 2005, adjusted for PASS salaries which may be impacted by the remuneration reviews by HR. Post the 2005 year the grant will increase by the target expense rate set by the University Finance Committee, the Director of Finance and the DVC Planning and budgeting as part of the budget process each year.
- The EMU will be serviced and assisted by the Science Faculty. For administrative convenience only, the financial administration of the EMU is handled by the Science Faculty Office.

- The EMU will produce an annual budget for its internal management processes and for the EMU committee. A copy of this budget should also be lodged with the Manager: Financial Information Management and the DVC Research for their information and records. Failure to do so could result in the withholding of the grant for the subsequent years.
- The EMU Committee (EMUC) is established in the research cluster. It advises the UEC and through it the URC on the provision of electron microscopy services to the University's teaching and research community. It receives and reports to the UEC and URC on the annual report, strategic plan and operational plan of the Director of the Electron Microscope Unit. The Chair of the EMUC submits a consolidated annual report to the Chair of the URC. These reports are the vehicles for accounting for the work of the UEC and EMUC respectively and for this reason these reports must indicate what the EMU and EMUC have achieved relative to agreed goals and place the URC chair in a position to judge how well the EMUC has performed.
- The EMUC comprises the Deans of the Faculties of Science, Health Sciences and Engineering and the Built Environment, the Chairman of the URC, the Chairman of the UEC, an academic representative of the user departments in each of the Faculties of Science, Health Sciences and Engineering and the Built Environment and the Director of the EMU.
- The committee meets once a year in order to review the progress made by the Unit and its plans for the following year.

### **Changing Scenarios**

Several important developments in the recent past raise important questions concerning the direction that the Unit should take in the future.

These include:

1. The success of the joint UCT/UWC structural biology programme in establishing the field on the continent of Africa at a high level.
2. The acquisition of a cryo-FEGTEM at UCT.
3. The acquisition of a FEGTEM with EDS, STEM and EELS attachments at UWC
4. The ringfencing by the DST of money for Nanotechnology on the one hand and Structural Biology on the other.
5. The creation of the third component of the ICGEB in Cape Town
6. The availability of funding for a "National Competency Centre" in Structural Biology.
7. The desire of Centre for Catalysis to establish its own resources in Electron Microscopy.

Opportunities will exist in the future to do experiments that could not be contemplated in the past. We need to respond to these changes in a co-ordinated and rational way in order to lever the maximum research and educational advantages.

### **Priorities**

The Unit has two key priorities that will be further elaborated below:

1. The provision of modern microscopes and related equipment which meet the needs of researchers and students at UCT and the surrounding region.
2. The provision of human resources which will enable the equipment to be optimally exploited for research and teaching purposes.

## Attachment C

The Unit currently operates two scanning electron microscopes (SEMs) and three transmission electron microscopes (TEMs). The goal is that one instrument in each category be a front-line research instrument while the other should be a robust, accessible instrument of pedestrian capability. This arrangement which is frequently adopted by leading EM Units throughout the world gives flexibility and robustness to the EM service enabling it to cater for a wide variety of needs including those of experimenters who need to have an instrument maintained in a fixed configuration for an extended period of time. It also increases the availability and accessibility of the microscopy service enabling users to have access to the instruments at short notice at times which are dictated by their research programme. Other models are possible and one in which instruments with differing specialist capabilities are available may need to be considered in the future.

The instruments have a limited lifetime dictated by research trends, advances in technology and the availability of spares. The Unit's experience suggests life expectancies of 15 years for SEM and 20 years for TEM which are longer than the norms at leading universities but are not exceptional. Special circumstances and good fortune may prolong the useful lifetime but equally developments may lead to premature obsolescence. This means that in order to maintain a consistent service UCT must implement a systematic instrument replacement strategy. The consistent instrument profile which will occur as a result of this will significantly enhance the competitiveness of UCT in a number of research areas and will attract and keep researchers that are active in those areas.

Serious consideration needs to be given to the strategic direction of our high end instrumentation. This needs to be driven by two factors: (1) The needs and strategic direction of departments at UCT and (2) The planned development of other sites within South Africa and more particularly in the Western Cape. The current strength of the Unit as a regional centre with a good track record and infrastructure should be maintained in spite of pressure to "level the playing fields". It makes no sense to develop strength in Cape Town but locate equipment in Limpopo! It is therefore crucial that the willingness of potential institutional hosts to bear the costs of, and foster the science associated with, the development of new facilities be properly considered when siting instruments. However the realities of the South African situation are such that the University of Cape Town - which is widely perceived as a Historically Advantaged Institution - should play a leading role in developing other sites and it should therefore be generous in allowing its staff to assist at other sites.

It is a general rule that researchers at UCT delegate many technical issues to the staff of the Electron Microscope Unit. Thus most microscopy related student training is done by the Unit and users turn to the Unit for information and expertise in the latest techniques. To fulfill the expectations of the users it is essential that Unit staff have the opportunity to attend courses that support their line role and that they attend conferences at which work they have done in association with users is presented. The most profitable work results from a synergy between researchers and the staff of the Unit - it is important to foster that synergy by giving Unit staff the opportunity to participate in the development, execution and ultimately the presentation phases of projects. The complexity of modern microscopy, especially in relation to structural biology has not been appropriately addressed in courses currently offered by the University. The director has therefore participated in the establishment of an MSc in Structural Biology which he will coordinate in conjunction with members of the Science and Medical Faculties and staff at UWC.

Electron microscopy in the Western Cape has undergone important developments in the last year with the purchase of field emission TEMs at both UCT and UWC. The configurations purchased by the two universities are essentially complementary. The UWC machine is essentially a materials instrument equipped with an energy dispersive x-ray analyser, STEM and an energy filter. The UCT machine on the other hand is a cryo instrument designed for high resolution biological structure determination. This means that both the bioscience and materials communities in the region will have

local access, for the first time, to the considerable benefits of field emission electron sources presenting the entire EM user community with unprecedented opportunities. In order to fully exploit these opportunities it is necessary that infrastructural development occur at both sites. UCT in particular needs to build and modernize their instrument, especially through the acquisition of a software update and an electronic camera.

There are considerable cost implications in operating instruments at this level and in order to run these instruments the non salary budget of the EMU will have to increase. The extent of this increase is unclear. The real costs of running the F20 in Cambridge were approximately GBP25000 per year over a two year period. However the South African Agents for FEI have proposed an annual maintenance contract price of 51000 euros. We are in a position to minimize our additional costs as we employ a part-time, high-level service technician which would save us the cost of the labour component of the maintenance contract. Nevertheless the costs of running and exploiting the capability of the instrument will be higher than we have previously encountered.

The question is how to achieve an increase in income into the Unit. Funds for the F20 were motivated on the basis of Structural Biology that will be done on the instrument. It will therefore be necessary to raise grants in order to do this work and indeed pay for the maintenance costs of the instrument through grants raised to do structural biology.

Against this background MCB has been given the responsibility to drive the discipline of structural biology by the University. The current head has refused to accept this burden and has instead passed it on to the Director of the EM Unit.

The Director therefore has no option other than to aggressively propose structural biology projects, raise funding, and recruit students. MCB at UCT has further decided to discontinue the structural biology coursework which has enabled students to enter the field. However UWC has not discontinued therefore the only available vehicle for training students in high level microscopy is through another university. A curious but unavoidable situation.

Furthermore the DST has expressed willingness to fund structural biology through its biotechnology initiative and has ring-fenced money for this purpose from 2008. It is conceivable that a new structure could arise out of this DST funding - in which Centres of Competency could be located at participating Universities. Such Centres would maintain instruments and employ people and paid for by the DST. They would also be place where students from any University in the country could do structural biology and do the work for their degrees.

### **Infrastructure**

In addition to the electron microscopes mentioned above the Unit has a variety of preparative equipment which has been accumulated in order to serve the needs of users. For many applications the Unit supports all stages of the microscopy process from preparation to publication. .

The Unit strives to differentiate itself from its regional and national competitors by offering excellent resources in focussed areas which are important to both Materials and Life scientists.

A further competitive edge is provided by the synergy which exists between the Unit and its large users, especially the Department of Materials Engineering. The Unit has shown itself to be adept at responding to their needs and developing technology to solve their problems.

With the advent of digital imaging it has become essential to provide computer resources and peripheral equipment to support this. The Unit was an early adopter of this paradigm and desires to maintain its leadership position in this area by continually updating its systems and through

collaboration with those interested in imaging and visualisation in the Departments of Electrical Engineering and the Department of Computer Science.

There are five full-time and one part-time staff members in the Unit. The organisational structure is flat with all staff reporting to the director. Technical staff, have distinct responsibilities, control their own areas and liaise with their own “clients”. Users may interact with one or more technical officers or with the director. This structure has proved to be efficient and effective in providing a high quality service with a minimum of “red tape”.

The primary *modus operandi* of the Unit is that students and researchers are trained to use the equipment and take responsibility for their projects. Technicians are active participants in the planning and training phases of the microscopy and may be called upon for assistance and advice whenever needed. The Unit strives to be highly accessible and available to users by staggering the working hours of staff and by allowing trained users unfettered access to equipment. An alternative *modus operandi* arises because researchers are not able or willing to become users in their own right but wish to exploit the results of microscopy. In these cases work is handed over to a member (or members) of the Unit who does the necessary research in order to achieve the insights required by the researcher.

In most cases responsibility for the microscopy is divided between the user and the Unit, the Unit taking the responsibility for techniques development, training and maintenance of equipment and users taking responsibility for their specimens and scientific results. This approach has been generally effective and enables the Unit with its small number of staff to leverage the productivity of others. However this approach has failed the Unit in that the intellectual property has been exploited by the researcher for his own benefit and as the Unit, which has not claimed ownership of the intellectual property, has not been recognized in quantifiable outputs of the University. The result is that the Unit does not have the record of quantifiable outputs with which to approach potential funders of its own accord. Without this it seems unlikely that that any approach to a science funding organization for new equipment will succeed. A key element in our future strategic plan is to develop an acceptable mechanism of fulfilling our role and still maintaining ownership of the intellectual property we help generate. In particular, at the present time, the Director has an impressive recent history of achievement in Structural Biology which is recognized both nationally and internationally. Furthermore there can be no dispute about the ownership of the intellectual property.

As the needs of users and technology change it will be necessary to accommodate these by changing the utilisation and nature of the physical space occupied by the Unit. Ongoing monitoring and assessment of the situation is necessary.

### **Electron Microscopy Resources outside the EMU**

Recent experience has shown the complexity of planning electron microscopy resources outside of the EMU. It seems unlikely at this stage that external EM resources which are the Unit’s responsibility will ever materialize, although this situation may change. The Unit has no ideological stance on this issue and proposals will be evaluated entirely on pragmatic grounds.

The Unit has by default taken on much of the responsibility of running the X-ray diffraction apparatus housed at UWC. The cost (except for personnel) of this has been covered by the grant from the Carnegie Corporation at present however the long term costs are clearly UWC’s responsibility and some form of service level agreement will ultimately have to be negotiated.

### **Staff development**

Involvement in the application of advanced technology to the solution of problems and the acquisition of insights in all areas is exciting and stimulating on the one hand but challenging and daunting on the other. In order to meet the challenges staff need time and opportunity to keep abreast

of research and development in microscopy. This would include providing opportunities for training for the development of new skills and opportunities for staff to pursue their own interests in microscopy.

Obviously achievement and effort should be acknowledged through just rewards.

## **Teaching**

The academic direction of most students calling on the Unit for services has already been decided as they have been recruited by departments and their projects have been allocated. In many cases consultation between the supervisor and the director or other member of the Unit staff leads to a refinement of the project's goals in terms of available resources.

Teaching in the Unit is usually tailored to individual needs. A standard introductory course for life science students is presented to interested groups by arrangement. The courses are made available to, and are regularly attended by, students from UWC and Stellenbosch. The Unit will continuously assess the need for further courses and create and deliver them when justified by circumstances.

A major new teaching area for the Unit will be the Masters programme in structural biology. This has the potential to alter the direction of structural research at the University and success in projects that are within our capability should be exploited to enhance and renew our equipment creating a sustainable situation. Although the responsibility for planning, content and delivery of the microscopy component arises entirely in the EMU the component will have an MCB course code as the EMU is not a teaching department.

The Unit typically assists up to 160 users per year. The majority use the facilities for a short period of time. Long term users are generally M.Sc. and Ph.D. students whose projects are structured to have a major microscopy component. Certain staff members are also active microscopists. The Unit offers its resources to undergraduate and honours students by arrangement with interested departments.

Our goal is to ensure that students that work with us have a good understanding of the technology that they themselves utilise. However only 10-20 students a year achieve any level of competence or proficiency in electron microscopy.

There is a need to ensure that supervisors are kept up to date with developments in the Unit that may impinge on the projects that they undertake with their students. This is accomplished by personal contact, feedback via the students, updates to the Unit's web site and occasional seminars.

It is the intention of the director of the Unit to put in place a structure which will address the need to develop the shortage in skills in structural biology at the highest level. Even though a number of people that have research interests in, and knowledge of, the field of structural biology exist in the Western Cape there is, outside of the courses offered by the Masters programme, no appropriate vehicle for them to pass this knowledge on. Structural Biology impinges on every field of Biological endeavour and it is entirely appropriate that a degree programme in this area continue to be supported.

## **Markets**

The Unit sees its primary market as being academics who are active researchers and their students. The Unit is therefore structured to support research. In this time of shrinking academic budgets it is important for the Unit to attract additional clients that can be accommodated within the existing paradigm. However it is clear from the foregoing that more use does not necessarily lead to greater sustainability. What is needed is smarter use focussed on projects likely to bring in high rewards.

## Attachment C

Simply turning the wheels just costs money. The selection of high reward projects requires considerable experience, hard work and a good deal of luck. Much time needs to be spent on this and once selected the projects should be pursued to their logical end point.

The issue of collaboration with industry is frequently raised. Some EM work that is done in industry falls into the category of research but a much larger proportion falls into the categories of fault diagnosis or quality control. At this stage accepting fault diagnosis jobs brings in a small amount of “uncommitted” money. Accepting quality control work although potentially profitable, could compromise the Unit’s primary function. I have yet to encounter projects proposed by South African industry in my direct field of interest that are anything less than naive. There is potential to change this and this can potentially be done through the South African Structural Biology Initiative.

### **Fees and costs**

It costs approximately R1500 per hour of electron microscope time to run the Unit. This cost is not affordable by any of the users of the service and thus it remains essential for the University to continue to subsidise electron microscopy. The areas subsidised include staff salaries, funding for major equipment and general infrastructure costs. In order to implement a systematic instrument replacement strategy it is important that the University lay money aside for this purpose at regular intervals. The University has been incapable of doing this.

The Unit has attempted to move towards a situation of partnership with major users in which responsibility for raising funds for instrument replacement is shared. Even though several users have enthusiastically participated in these attempts they have to date not been successful. The majority of users have not accepted responsibility for raising adequate funds to sustain their EM usage.

A fee structure with rates varying from R150 to R1000 per hour of microscope time is in place and was approved in 2002 by the Electron Microscope Unit Committee. The purpose of this fee structure is to make provision for the maintenance of instruments and to cover the cost of consumables used by microscope users.

Any amendment to the fee structure, to cover the cost of the acquisition of new equipment, for example, would be a radical departure from the brief currently given to the Unit and could not be undertaken without wide consultation and ultimately an executive decision.

The fees charged to commercial users cover the full cost of service and exceed those charged by university based EM units throughout the country. Very little revenue is raised from this source.

Insofar as the fees charged for the use of the Unit’s facilities fall far short of their real cost - the Unit is a conduit for research funding. In selected cases the director uses discretionary funds to further subsidise projects in order to allow them to proceed.

### **Risks**

In the undergraduate area the numbers of students are such that in general the demand for resources are predictable. This is not the case when the consumers of a resource are staff members and postgraduate students. Anticipated postgraduate students may not be recruited or may elect to focus their efforts in unpredicted ways. Similar considerations may apply to staff. Indeed researchers whose work depends on EM will not move to UCT unless the resources are perceived as adequate and appropriate. Equally the converse applies - the existence of appropriate and viable EM resources may act as a powerful motivation for certain researchers to join UCT and may influence the research direction of existing staff. In this context it is occasionally necessary for the Unit to be proactive in

the development of capacity. Precise prediction of the EM needs of the community at any time point is probably not possible and therefore the Unit will be faced with occasions on which it has over-capacity in some areas and under-capacity in others.

A further risk is that researchers may choose to do their EM elsewhere in spite of an adequate capability existing in the Unit because of perceived advantages in terms of funding or intellectual input gained through collaboration. Alternatively researchers that are large users of the Unit may motivate and be awarded EM resources of their own, leading to a sudden substantial drop in the use of the Unit.

### **The Future**

Opportunities are being offered to us at the present time that may require us to change our existing structure. These opportunities need to be robustly debated and final policy decisions need to be properly implemented. It is important to have a long term vision when making the necessary decisions.

**I suggest a strategic plan which contains the following elements:**

- 1. Partnership with UWC**
- 2. Partnership with the ICGEB**
- 3. EMU takes responsibility for the discipline of Structural Biology at UCT**
- 4. EMU becomes a national Competence Centre in Structural Biology (or part of it)**

At the present time it is unclear what the details of each of these elements will be. But it is clear that each of them fulfills many of UCT's needs and would be of considerable advantage to the University.

### **Summary of objectives, phrased as deliverables**

- EM services will be provided for 70-100 users per year.
- Non-EM services will be provided for 10-40 users per year.
- 10-20 users per year will be trained to use microscopes on an individual basis.
- 10-20 students per year will attend the course "Introduction to Microscopy for Biologists"
- EM practical sessions will be arranged for undergraduate, honours and masters students or groups.
- New courses will be developed according to demand.
- 5 students per year will complete the MSc programme in Structural Biology
- Existing instrumentation will be maintained.
- Existing instrumentation will be adapted to meet the needs of researchers where possible.
- Unit staff will collaborate in whatever ways are feasible with active researchers in order to further their research goals.
- Unit staff will undergo training as appropriate in order to support the research activities of users.
- New (minor) equipment will be purchased enhance the Unit's capability in focussed areas in support of currently active research projects.
- The IT infrastructure will be improved and modernised.
- Experiments in providing web based services will take place.
- Donors will be sought to provide funding for new electron microscopes.
- Research goals to be supported by the new TEM will be properly formulated in collaboration with our partners.
- The part of the building in which the Unit is housed will be maintained and enhanced to meet current and emerging needs.
- The Unit will communicate its role and capabilities to users and potential users.

## Attachment C

- The Unit will participate in the activities of the Microscopy Society of Southern Africa.
- Members of the Unit will attend international conferences as appropriate.
- The cost and fee structure of the Unit will be reviewed in order to create a workable system which optimises cost recovery.
- Structures to accommodate and support current and future usage of electron microscopes and other related equipment located away from the Unit will be put in place.

### **Conclusion**

Microscopy is a field in which established technique and brilliant innovation lead to ever enhanced insights which benefit science and technology. It is essential that UCT adopt a pre-eminent position in the region and that we seek to excel in certain areas. This is appropriate for a world-class University. It will take significant funding to maintain the position that we have reached and ultimately achieve our vision.

**B.T. Sewell**

**August 2007**

## APPENDIX

### What is Microscopy?

Microscopy is any technique which renders the small visible. There are an enormous number of different techniques which make use inter alia of acoustic pulses, various forms of electromagnetic radiation, electrons and fine probes. The most common form, ordinary light microscopy, is an inexpensive technique of wide applicability. Most other forms are highly specialised techniques practised in a limited way by specialists either in the technology or in the area in which the technology is most appropriately utilised. Electron microscopy on the other hand is of wide applicability but the equipment is so expensive that it is out of the range of most researchers to purchase and maintain. This fact has given rise throughout the world to EM Units in which resources are pooled so that researchers and students have access to the technology.

There are two distinctly different types of electron microscopy: Scanning electron microscopy (SEM) and transmission electron microscopy (TEM). In SEM a fine electron beam is scanned across the sample giving rise to a variety of detectable signals at each point across the scan. Usually a bulk sample is used (as opposed to a thin section) and as the electrons do not penetrate deeply into the specimen, it is surface information that is acquired - the information concerns the shape, elemental composition, crystalline arrangement and defect structure. In the case of TEM thin sections of the sample are illuminated by a wide beam of electrons and electromagnetic lenses are used to form images using those electrons which pass through the material.

Specimen preparation for electron microscopy requires insight, effort, time, skill and involves the use of specialist equipment. Available techniques cover a vast area and are a subject of study in themselves. Sometimes subtle changes in preparative protocols can change the nature of the insights gained using a particular instrumental technique.

### Why is electron microscopy useful to society?

Electron microscopy is the most widely available technique for imaging things which range in size from about 10nm to 1 $\mu$ m - this size range covers biological structures including cells, subcellular components and macromolecules, many structures of geological interest including microfossils and a wide range of phenomena of interest to physicists and materials scientists including dislocations and microcrystals. There are also a number of features of SEM imaging which make it attractive to scientists and engineers examining larger objects. In particular, the enormous depth of field attainable gives objects a natural appearance unobtainable by light microscopy. Furthermore interactions between the electrons and the specimen also give rise to signals which give additional insights. Thus the atomic composition of materials can be fairly easily mapped out with a detail not otherwise obtainable and the crystal and defect structures can also be obtained on both a microscopic and macroscopic scale.

Electron microscopy is widely used to support research in health, life, environmental, archaeological and physical science as well as in several branches of engineering. It is used, for example, by Botanists and Zoologists to assist in classification and by cell biologists to study cellular processes. It is used by chemists to study changes in materials as a result of chemical reactions, physicists and materials engineers to study semiconductors and new materials. Engineers have used our laboratory to study concrete degradation, crack propagation and heat conduction to name but a small subset of projects done in recent years. Archaeologists use electron microscopy both to see small features of

artefacts and to analyse their composition and thus obtain insight into the processes by which the artefacts were made.

Electron Microscopy is also of importance for troubleshooting, product testing and quality control and analysis of competitors products in a number of industries, including but not limited to: Electronics, steel and aluminium, packaging, sewerage and waste disposal, minerals exploration and beneficiation, food processing, drugs, forensics and medical diagnosis. For example, a problem relating to sub-strength nylon fibres was solved when it was realised that microscopic dust particles were becoming embedded in the fibres. In South Africa EM based quality control is done by the steel and aluminium industries, the electronics industry, the chemical industry, the mining industry and the packaging industry.

Electron microscopy (and microanalysis) is routinely used in forensic science. In South Africa, where there is a major problem with gun-crime several microscopes are devoted entirely to the identification of powder residues. Medical diagnosis is less dependent now on EM than it used to be because of the availability of DNA and antibody tests. However there are a number of areas e.g. early identification of certain classes of paediatric tumour in which EM diagnosis remains essential.

### **What are the developing areas?**

This question is not as simple to answer as it is to put. In the biological sciences there can be no doubt that the ability to tag specific types of macromolecule within the cell is leading to previously unobtainable insights in cell biology. Electron microscopic techniques enabling wet specimens to be visualized (“Environmental” SEM) have been developed to the point of being routine and this technology has become crucial to research in numerous fields where chemical reactions involving structural changes in the wet state need to be observed. Performing SEM in the presence of small amounts of air turns out to have desirable effects which make Environmental SEM a technique of wide applicability.

All areas of cryo-microscopy, both in the TEM and SEM are undergoing rapid development. Techniques built around rapid freezing can be used to image structural detail without resorting to the chemical fixation, dehydration and epoxy embedding procedures used previously. This has led to images of biological and other materials which are certainly closer to the truth and has also expanded the range of specimens that can be imaged (e.g. soap bubbles, whipped cream etc). At the high resolution end cryotechniques are being used to obtain images of macromolecules and macromolecular complexes at resolutions that were previously only attainable by x-ray crystallography and leading to insights that are unobtainable by other techniques. New centres have been established in several universities and drug companies (in other parts of the world) to pursue research in this area.

A significant “new” tool is the field emission electron source (FEG). This produces a bright, coherent almost monochromatic beam of electrons. The resolution and contrast achievable with such instruments completely eclipses that obtainable with tungsten or lanthanum hexaboride sources. Whereas previously FEGs were the province of the extremely rich they are now much more affordable and easy to use. There are now two FEGSEMs on the African continent (both in Pretoria) and the first two FEGTEMs are being installed in Cape Town.

Another “new” tool is the Focused Ion Beam. This device uses a beam of gallium ions to abrade the surface of the material. Combined with FEGSEM the technique can be used to produce three dimensional reconstructions of objects by successively abrading and imaging layers of material under computer control and then finally combining the images into a three-dimensional

tomogram. There is one FIBSEM with a thermionic tungsten source at Wits. CSIR is contemplating the purchase of a FIBFEGSEM.

Many electron microscope units have expanded their areas of activity to include a variety of additional imaging modalities. The most common include confocal scanning microscopy (Wits, Pretoria, UFS) and any of the numerous scanning probe microscopies. In confocal scanning microscopy the limitations of light microscopy are overcome by scanning a finely focused point of light across a specimen and measuring the emitted fluorescent signal. The power of the technique lies in its ability to image hydrated, metabolically active tissue and thus obtain insights into the processes occurring inside cells. Exploitation of the technology requires considerable understanding of cell biology and the availability of an infrastructure supporting cell biology which is not present in the Electron Microscope Unit at UCT.

Scanning probe microscopy involves scanning a fine probe, which interacts with the surface in some way, across the specimen. One such technique, scanning tunnelling microscopy, enables atoms in the surface layer to be visualised. Commercial development of scanning probe microscopy has resulted in accessible, easily maintained instruments which would be enabling for a number of experiments especially in Chemistry, Chemical Engineering, Biochemistry and Materials Engineering.

### **What factors should influence our major equipment strategy?**

Planning the equipment needs of the Unit is extraordinarily complex and requires factoring in the available technology, the interests and capabilities of the Unit staff, the interests of the current pool of potential users, the prevailing fashions in research, potential future trends and so on. The trend at UCT has been to replace electron microscopes and associated equipment on a 20 year cycle driven not by planning but by crisis - this period is too long. The advance of technology is dictating obsolescence norms of less than ten years in the case of SEM and about fifteen years in the case of TEM. Leading universities elsewhere in the world replace their electron microscopes on a two to ten year cycle. Near the end of its lifetime the equipment is increasingly unreliable and maintenance becomes a major factor as does the unavailability of the equipment. Users lose interest in the old equipment (and the techniques possible with them) and adopt a range of different strategies from changing their field of activity to leaving the University. The consequence of this is that when new equipment is purchased it takes time to build up a new user base. This is wasteful as the best opportunities for cutting edge research are when the equipment is new.

A shorter and less stochastic replacement cycle would have important consequences:

Staff members would be able to plan research careers centred on microscopy rather than on the occasional availability of cutting edge equipment. Staff of the Unit could be deployed in supporting and researching current and interesting technology rather than fixing obsolete technology. UCT could have a consistent profile with respect to microscopy.

The question of the sort of equipment that is required in the Unit is an important one to answer. Pedestrian microscopy is less expensive, widely used, is reliable, appropriate to teach to students at a variety of levels in a number of subject areas and is easy to maintain - even in Africa. Obsolescence of this class of equipment occurs over time because the manufacturers devise ever more accessible instruments which match the prevailing technological paradigm and users become disinclined to invest time in acquiring skills needed to operate old equipment which they perceive as unnecessary. This level of equipment can be maintained with mediocre staff requiring a moderate level of training. If only pedestrian microscopy were provided it would be impossible to proceed with most investigations beyond a fixed point and an extraordinary number of real insights would be missed. This vision is incompatible with that of a world class University. It is therefore essential that UCT

purchase instruments that have the potential to make a real difference - this was the mindset adopted in purchasing the S440 and accessories, the cryo-ultramicrotome and the digital camera for the TEM and in setting up the Imaging Centre. The director believes that overall the strategy has been an unequivocal success. However it is expensive in both money and staff time, involves increased risk and it is essential that users be supported by Unit staff that have had the opportunity to undergo appropriate training. Careful choices must be made in the specialities chosen taking account of current academic focus of the users and human resources in the Unit. .

South Africa is pitifully far behind as far as its pursuit of the top end of EM is concerned. The problem relates not only to the availability of instrumentation but also to the availability of expertise. Because better instruments and incentives were available elsewhere a large proportion of people with expertise have left the country. A widely perceived problem is lack of commitment to the provision of resources. This has led to a climate of uncertainty in which electron microscopy seems to have been especially vulnerable and a number of facilities have contracted or closed down altogether. However simply buying the best instruments will not suddenly put SA at the forefront - it will take years of sustained commitment to the funding of projects and to the training of people before the results are visible.

### **How best are the Unit's instruments maintained?**

One of the key roles of the Unit is the maintenance of the equipment in its custody. We have opted to employ a maintenance technician in a half time post rather than to rely on service contracts with suppliers. The equipment complement of the Unit is such that on purely economic grounds it is difficult to decide unequivocally between these two maintenance models. Employing a maintenance technician makes long term instrument monitoring possible and ensures that faults are properly fixed and that catastrophic faults occur infrequently. It also makes it feasible to operate old instruments and ensures a high availability of these instruments. An additional advantage is that it gives the Unit the capability of designing modifications to equipment to meet changing user needs. Our past experience with maintenance contracts has also highlighted the difficulty Johannesburg based suppliers encounter in servicing instruments located in Cape Town.

### **Where has the Unit's money come from in the past?**

The University has provided the entire staffing budget of the Unit, most of the IT and related budget, the entire budget for new minor equipment and much of the running budget of the Unit. The University has also funded travel to conferences and training courses. The Unit attempts to recover (and is generally successful at recovering) the costs of consumables and instrument maintenance by charging user fees. Some of the user fees paid by external clients has been used to supplement staff travel expenses and the Unit's IT needs. The Director has had access to FRD research funding which has largely been spent on funding and maintaining computer hardware and software and in funding his own projects. Although provided for research these funds have had a substantial positive impact on the viability of services to users.

Major equipment has been funded entirely by the University or partly by the University and by the NRF. A second hand cryo-TEM was acquired from the Wellcome Trust as a result of a collaboration between the Director and Professor Helen Saibil at Birkbeck college.

### **What are the quantifiable outputs of the Unit?**

The main output of the Unit is postgraduate students who have had experience with and exposure to microscopy. Between five and ten papers per year and a much larger number of conference

proceedings are published by users of the Unit. There is no correlation between the amount of use made by users of the Unit's facilities and their academic output.

### **What limits the "samples in - results out" service?**

There is pressure on the Unit from certain users to provide a comprehensive service in the sense that the staff of the Unit take full responsibility for all aspects of the microscopy and return to the investigator with a result. The Unit has resisted operating in this way for the following reasons: 1) The Unit has insufficient staff to service the needs of every investigator who requests this service. 2) Unit staff do not generally have the training and insight into the field of expertise of the investigator and insights into problems generally arise as a result of synergy between the investigator and the microscopist. 3) The standard fees charged by the Unit are absurdly low when viewed against the cost of employing a technician. This cost structure encourages researchers to exploit this service for their selfish ends. 4) Microscopy often results in substantial research grants and consultancies for our users - there have only been two cases where these financial rewards have been invested in expansion of the Unit. 5) The contribution of the microscopy is consistently undervalued by researchers using the Unit in this way.

Consideration has been given to employing technicians on an ad hoc basis to service the needs of researchers requiring such comprehensive service, however difficulty has been encountered in identifying people willing and able to fulfill this role.

In other cases supervisors have stated that their students do not have the time to get involved in the microscopy but they nevertheless need the insights provided by it. Therefore they would like to download the microscopy. The Director strongly believes UCT students should not be deprived of the opportunity of being trained in microscopy in this way and that the involvement of the students in all aspects of gaining the insights that they need is a key component of their research training.

### **What opportunities for regional co-operation exist?**

In the early eighties the Western Cape was well endowed with EM capability with new microscopes in 6 departments at UCT, a new unit at the MRC in Parow equipped with top of the range instrumentation, new SEMs in Wood Science and at the FFTRI in Stellenbosch, an new TEM and SEM in the Physics and Anatomy Departments at UWC, a new SEM at the Museum, a new TEM and SEM at the Cape Technikon and three well equipped EM labs run by the Provincial Health Services.

Most of this infrastructure disappeared leaving the EMU at UCT as the survivor. However much is now being reinstated. The Department of Cardiothoracic Surgery at UCT has two TEMs and two SEMs, one of which is a high end machine with unique capability in the region. The NHLS has established new EM centres at Groote Schuur and Tygerberg and has re-established the centre at Red Cross hospital by acquiring the EM109 from UCT.

Both UWC and Stellenbosch have moved existing departmental microscopes to a single location and reorganised posts in order to create EM units. Both institutions have adopted the view that in order for EM to survive, resources must be pooled. Furthermore a new SEM was purchased in Stellenbosch and a major new FEGTEM aimed at nanotechnology is being installed at UWC. The university units have displayed a willingness to share resources but the better developed infrastructure at UCT makes it easier for their students to use our facilities than vice-versa at present.

It would be nice to site complementary equipment at the various regional centres. This would require a common vision and willingness to share. This has been achieved in the past with the siting of the confocal scanning microscope at the Medical Research Council laboratories in Parow. The MRC has also contributed to the rationalisation of regional resources recently by moving their TEM to the Department of Cardiothoracic Surgery and the confocal scanning microscope to the University of Stellenbosch.

A problem for microscopy in the region is that too little came from too much. Essentially the work arising from the region was too little to justify the cost of maintaining so many machines and the infrastructure to support them. It would be a mistake to purchase new instrumentation at every location simply because a University (or museum or technikon or hospital) “Must have an Electron Microscope” and indeed the costs are so high that this is unlikely. It would equally be a mistake to abandon electron microscopy completely because of the perceived history of failure. The solution is to create strong regional centres in which complementary capabilities are allowed to flourish while duplicated services are eliminated as much as possible.

The practicality of regional centres is greatly enhanced by the existence of the Internet. In its simplest form this involves the distribution of digital images by e-mail and ftp. Enhanced functionality including interactive operation of instruments using web protocols is possible if not immediately practical because of slow network links. Because of its strong digital infrastructure UCT’s EM Unit is well positioned to provide such services.

### **What about Equity?**

The Electron Microscope Unit has 1 academic, 3.5 technical and 1 departmental assistant posts funded by the University. In addition the lecturer in Structural Biology currently funded by the Carnegie corporation of New York is located in the Unit. We have 1.5 white males, four brown males (two coloured, two Indian) and one white female filling these posts. The oldest white male is fifty-four years old at present.

The Unit has contributed significantly to the achievement of the University’s equity goals by training non-white and female students.