4
Design and Function of a Light-Microscopy Facility

Kurt I. Anderson, Jeremy Sanderson, and Jan Peychl

Abstract Modern biological research depends on a wide variety of specialized techniques, which collectively are beyond the grasp of a single research group. Research infrastructure, in the form of services and facilities, is therefore an increasingly important foundation for a competitive research institution. A light-microscopy facility is a place of dynamic interaction among users, staff, and equipment. Staff provide the organization, continuity, and expert knowledge required to manage the laser-safe interaction between demanding, selfish, high-performance users and delicate, expensive, high-performance equipment. They introduce novice users to fundamental principles of image acquisition and analysis, often beginning with fluorescence basics, but collaborate with advanced users in the development of new imaging techniques. Intimate knowledge of the experimental needs of the user research groups is required to maximize the effectiveness of equipment purchases, which are also informed by critical evaluation of local sales and support teams. Equipment management encompasses evaluation, purchase, installation, operation, and maintenance, and depends critically on good relations with competent local technical support. Special care should be given to the architectural design of an imaging facility to maximize the utility and comfort of the user environment and the long-term performance stability of the equipment. Finally, we present the details of a web-based equipment scheduling database as an essential organizational tool for running an imaging facility, and outline the important points underlying the estimation of hourly instrument costs in a fee-for-use setting.

4.1 Introduction

Specialization is a hallmark of evolution, both of living organisms and of scientific fields. Modern cell biological research depends on a wide variety of highly evolved techniques, including among many others DNA sequencing, mass spectroscopy, bioinformatics, production of transgenic animals and antibodies, electron microscopy, and light microscopy. This list grows daily, as today's cutting-edge approaches

S.L. Shorte and F. Frischknecht (eds.), *Imaging Cellular and Molecular Biological Functions.*

become essential components of tomorrow's research. Likewise, insight in cell biology often depends on results obtained using multiple techniques. Research infrastructure, in the form of services and facilities, promotes research by allowing all researchers to access important specialized techniques. In simple terms, techniques are "provided" to users by the service in the form of expensive hardware and the expert knowledge required to use it effectively.

The distinction can be made between a service, where staff generate data for the users, and a facility, where staff help users to generate their own data. This distinction has important organizational consequences. In a service environment the equipment can be better maintained and may perform to a higher standard, but higher levels of staff are required. For a large number of systems the service approach may become untenable. In this chapter we will consider implementation of a light-microscopy facility which includes advanced imaging systems such as laser scanning confocal microscopes and has the capacity to cover from a few dozen to a hundred users.

Despite the profusion of core imaging facilities, there is a dearth of literature giving any guidance on how to design, set up and manage these, and the literature written before the turn of the century tends to cover electron microscopy (e.g., Alderson 1975). Judy Murphy has written on facility design, primarily for electron microscopy (Murphy 1993, 2002) and on database selection (Murphy 2001). The most recent article specifically on setting up and running a confocal microscope facility is that of DeMaggio (2002). Another article, by Helm et al. (2001), deals with installing three multimodal microscopes capable of single-photon and multiphoton operation onto one optical table. A usefully illustrated Bio-Rad technical note on setting up a laser scanning microscopy resource was provided by White and Errington (2001) and can be obtained with a request to the confocal microscopy listserver (University at Buffalo 1991). The microscopy (Zaluzec 1993) and confocal (University at Buffalo 1991) listservers both offer a dynamic forum where microscopy-managers exchange views and solutions regarding the practical challenges of running a core imaging facility. The issue of cost management is most often aired. Two recent articles (Humphrey 2004; Sherman 2003) cover policy aspects of managing a core facility, as does the paper by Angeletti et al. (1999), similar to the issues described here.

Light microscopy entails image acquisition, processing (including deconvolution), and analysis. In our view it is best to keep these functions under one roof, as opposed to having separate image acquisition and analysis facilities. The reason for this is that acquisition and analysis are intimately related, and must be closely coordinated for the final outcome to be valid. Separation of these functions creates the potential for conflicting advice from separate acquisition and analysis teams. However, image acquisition, processing, and analysis are each specialities, which can comprise full-time jobs. It is important to remain realistic about the level and type of support which can be offered with a given number of staff positions.

Light microscopy has long been a fundamental technique in cell and developmental biology. The development of genetically encoded fluorophores has revolutionized these fields. Genetic techniques exist to label and manipulate the expression of virtually any gene product. In response to these genetic tools, there have been tremendous technological advances to more accurately visualize fluorescent protein dynamics in living cells, tissues, and organisms. Today there exist an often bewildering multitude of advanced imaging techniques, some of which are broadly useful and some of which are only optimal for a narrow range of applications. It often occurs that molecular biology specialists reach suddenly for advanced imaging equipment at the end of a long genetic experimental procedure, with predictably variable results! This chapter describes approaches we have found successful in setting up, running, and expanding the imaging facilities of the Max Planck Institute for Cell Biology and Genetics (MPI-CBG) in Dresden, the Beatson Cancer Research Institute in Glasgow, and the University of Sheffield. The information contained here is the result of practical experience, which necessarily reflects our preferences and opinions. Others facing similar issues may choose to address them differently.

An imaging facility comprises hardware, people, and organization. “Hardware” refers both to the equipment and to the space in which it resides. “People” refers to both the staff and the users. “Organization” ultimately determines the efficiency with which hardware and people interact. In our view a Web-based database is an essential tool for organizing efficient interactions among hardware and people.

4.2 Users

Users are what it is all about; they can be a blessing and a curse! Good users push staff for assistance with cutting-edge applications, provide valuable feedback about the state of equipment, and are key to recognizing new trends. All users are important for identifying system problems and giving feedback to the staff about the state of equipment. Bad users are selfish monsters who expect the equipment to be in top working condition when they want to use it, but give no thought to the condition in which they leave it. Good luck!

All users should receive a formal introduction prior to using a piece of equipment, no matter what their experience level. The introductory session is an important chance for facility staff to assess the user’s actual (as opposed to reported) level of experience, and to identify the applications involved. Novice microscopists need to be educated about basics of fluorescence microscopy, such as matching fluorophores to excitation sources and emission filters, choosing fluorophores for use in multiple-label experiments, controlling cross-talk, balancing parameters such as resolution, acquisition speed, sensitivity, and sample longevity, and finally the proper use of equipment so as not to damage it. It is important to separate training from data collection, especially where live samples are concerned. While it may be beneficial to use real samples as training specimens, biological interest may overwhelm the user’s attention span, i.e., the desire to see a certain result may interfere with general learning about the microscope. Users should be encouraged to consult staff at an early stage when embarking on new applications. This ensures that users’ expectations of the capabilities of the existing equipment are realistic, and gives staff time to prepare equipment for new applications. It is also important for users to be aware of the use-load on various systems to have realistic expectations about instrument availability in order to balance this against their experimental needs. Advanced users require help with advanced applications, which forces staff to invest time in learning and preparation in order to provide assistance. This should be encouraged because the expert knowledge of the staff is a crucial asset of the facility, which benefits future users.

4.3 Staff

Staff organize and run the facility by managing users and equipment. Facility staff represent a pool of expert knowledge and experience available for users to consult, who transmit information among users, imaging specialists, and the producers of imaging technology. Their importance and the number of staff required to support an imaging facility are often underestimated. A general overview of staff responsibilities includes safety compliance, especially laser safety, teaching, training, and general user support, equipment maintenance and quality control, and administration. Imaging equipment requires the expert knowledge of competent, motivated staff to deliver maximum performance. In addition, staff maintain an overview of, and serve as a knowledge repository for, the critical imaging applications of the local users. This provides continuity of research results as students and postdocs leave, taking their expert knowledge with them. In this context it may be useful for users to brief staff after important imaging sessions, and for staff to attend research group meetings. Continuing training and education are also essential components of the job, including attending scientific meetings and/or trade exhibits. Staff are able to set unbiased priorities for the resource allocation of a facility based on overall use, not the urgent needs of one vocal group or user. They also provide a vision for future trends by monitoring new developments in the imaging field. The number of staff positions needed to run an imaging facility is determined by the number of imaging systems present, their level of weekly use, the level of support expected by users, and the number of users (Sect. 4.5.3).

4.3.1 Workplace Safety

Staff play an essential role in establishing a safe work environment, especially where laser safety is involved. Very briefly, this first involves identifying hazards and the people likely to be affected by them. Then risk reduction measures are established, including both physical protection measures and organizational measures such as standard operating procedures designed to minimize risk. Users must be made aware of risks and trained in the standard operating procedures designed to protect them. Finally, all of these steps must be documented and periodically reviewed. Laser safety is discussed in Sect. 4.4.4.1.

4.3.2 User Training

User training is an important part of the job, which may not be initially appreciated. Users must first be trained to a level of unassisted competence in equipment use. This can be effectively accomplished during one or two standard, one-on-one training sessions. These sessions last a couple of hours each, and cover fundamental principles such as fluorescence basics, image formation, and confocal detection. Remember that poorly trained users will only be frustrated in their attempts to get good results, and this frustration will ultimately be turned back on the facility. Stomping out the many little fires users encounter on a daily basis dramatically improves the efficiency of equipment use and the level of user happiness. It is also important to follow up on user questions, to have answers by the user's next session. User training may involve courses on specific systems or techniques, which may be taught directly by the staff, or organized by staff in conjunction with company application specialists or recognized experts.

4.3.3 Equipment Management

On the technical side, staff provide assurance to users that the system is performing to a high standard by monitoring and documenting parameters such as the cleanliness of optical components, their mechanical stability, and the power levels of illumination sources such as lamps or lasers. Such quality control may also include regular estimates of system performance, such as resolution and sensitivity, through the use of reliable test samples.

A further crucial function of the staff is to identify problems with equipment and manage solutions. Staff must have the technical competence to handle smaller problems directly. Some manufacturers offer advanced training courses to staff, which allow them to undertake a wide range of adjustments and repairs (for example, laser fiber alignment to recover excitation power in a laser scanning confocal microscope). The cost of such courses should be viewed as an investment, which can be offset quickly by repair bills and wasted user time. When larger problems occur, staff can speed up repairs by performing initial diagnostic tests in close coordination with company service staff. This helps to avoid the situation that the service engineer diagnoses the problem on the first visit but has not brought the necessary parts or tools to finish the job, thus requiring a second visit which may be days to weeks later depending on the engineer's schedule. The goal is to ensure that service engineers bring the necessary parts and knowledge to fix the problem in one visit. Staff then follow up on repairs to ensure they are complete.

Note that the easiest way to keep the equipment in perfect working condition would be to lock the doors and keep the users out! Although seemingly trivial, it is important to ensure that the user does not become the enemy. One way to promote this is for the facility leader to be a facility user as well, i.e., to conduct research which uses the facility as well as managing it. It must be emphasized that a position split between research and running a facility is no longer a full-time research job; however, running a facility does confer research advantages. Leading the facility goes hand in hand with developing an expertise in imaging. This expertise, as well as the facility itself, can be used to attract collaborations with imaging nonspecialists. As a research group leader, the facility leader might develop customized imaging systems for his/her own use, which would then be made available through the facility to benefit the local user community.

4.4 Equipment

The equipment of an imaging facility consists of the imaging systems and their many accessories (i.e., large equipment and small equipment), the space in which they are located, and the tools necessary to keep them running.

4.4.1 Large Equipment

Microscopes, cameras, lasers, and computers are the heart of an imaging facility, and ultimately determine what experiments can be performed. Great care must be taken in purchasing large equipment to ensure that the most benefit is obtained from precious funds. Here are some points to consider with respect to equipment.

You do not just buy a microscope, you also buy the company which supports it. Equipment purchase creates a relationship with sales teams, application specialists, and most importantly service teams. When evaluating equipment for purchase it is crucial to evaluate these company support teams in the context of your own specific facility. How much expert knowledge exists among the users? What is the background of the company application specialists? What is the service procedure when equipment breaks down? How near are the service engineers based? How big an area do they serve? How good are they? A good service engineer is worth his/her weight in gold; a poor engineer will drive you progressively to despondency, despair, and drink – insist on good servicing.

Salespeople will generally tell you about the weaknesses of their competitor's products, not their own. Evaluating a system prior to purchase depends on a host of small decisions and factors gleaned from many sources. By all means get the official sales pitch, but also ask for a list of previous purchasers and reference customers. Contact these people for their experiences concerning ease and stability of system use, especially software, and also how they rate after-sales service and support.

It is crucial for facility staff to direct purchasing of the right equipment based on familiarity with the research of the local user community and an overview of products on the market. The latest-greatest imaging technology may not be useful for the applications of the users the facility covers. Software support for a wide variety of hardware components is key, for both versatile use of existing equipment and future system upgrades. Hardware and software flexibility can be maximized through modular system design, for example, though the ability to mount the same optical fiber for epifluorescence illumination on a mercury lamp, xenon lamp, and monochromator. Avoid combining too many features (i.e., total internal reflection fluorescence, spinning disc, and microinjection) on a single imaging system. User access to the system will ultimately become a problem if each separate function is in high demand. Complexity also increases the likelihood of failure. Failure of a system with multiple special functions means that more users will be affected than if TIRF, spinning disc, and microinjection features were on three separate microscopes.

"Many different systems, or many of the same system?" is another basic question. It takes time to become familiar with a system and learn to use it effectively. Having two or more of the same system increases user and staff familiarity with that system (especially its bugs!). The more different systems present, the more time required for a user to get to know them, or conversely the less likely that a user will be an expert user of all of them. User access to "cloned" systems is more flexible, if a clone breaks down, users can work on one of the others. User familiarity with equipment and consistency with previous results are strong inhibitors of trying something new. However, spending precious funds on multiple copies of the same system ultimately limits user access to other, potentially useful technologies. In the case of laser scanning confocal microscopes, each of the major systems has unique advantages over the others. Some experiments may truly work better on one system compared with the others. Company representatives are usually keen to have a monopoly position within an institute, i.e., to see that only microscopes from their company are bought within the whole institute. But in our experience having multiple suppliers in-house generates competition which keeps all the suppliers on their toes.

Technology development must be carefully considered in the context of a user facility. The raison d'être of an imaging facility is to provide access to commercially available, advanced imaging systems. Acquisition of experimental data in an imaging facility requires that system configurations are stable from week to week and month to month. Developmental imaging systems may offer important performance advantages over existing systems, but spend much of their time in configuration flux, i.e., the configuration changes often and the system spends much of its time in pieces on the benchtop. At the point where system parameters stop changing, the system is no longer under development. Advanced users may appreciate the benefits to be had from new technology and therefore be eager to help in development. Other users may be scared away from developmental systems by the extra patience needed to obtain results. It is often useful to "shake down" new systems by first allowing their use only among advanced users, who can identify pitfalls and bugs with facility staff, so they can be corrected or worked around before turning the system over to general use.

4.4.2 Small Equipment

A wide variety of small equipment is required in conjunction with a microscope, especially when live-cell imaging is involved. It is important to budget for this in order to extract maximum value from a microscope system which is already expensive enough. To name but a few bits, microscope accessories include objectives, stages, condensors, lamps, power supplies, and sets of fluorescence filters. For components which occasionally fail, such as power supplies, it is a good idea to keep a backup unit. Having an extra $100 power supply can keep a $100,000 system running; this is where standardization and flexibility of components are important. Small equipment can further encompass computers and monitors, antivibration tables, heating chambers, CO_2 regulators, peristaltic pumps, and microinjection equipment, including needle pullers, micromanipulators, and pressure regulators. All of these bits enable the staff to flexibly cope with shifting user applications, especially the ability to "just try" something out to see if it is worth pursuing.

4.4.3 Tools

As with any undertaking, be it plumbing or molecular biology, good tools are essential for doing a job quickly and correctly. The tools required to support an imaging facility include various screwdrivers (flat, Phillips, and hexagonal heads), spanners, and socket sets with a good selection of small sizes, a razor knife, flashlights, a multimeter, a laser power meter, and an electronic thermometer with a fine probe. Furthermore, compressed air, lens paper, and a variety of cleaning solutions in dropper bottles are essential cleaning aids. Useful solutions include water, ethanol, 1:1 mixture of water and ethanol, and petroleum benzene.

4.4.4 Imaging Facility Layout

There are many considerations in designing the physical space of an imaging facility (Fig. 4.1). These include:

- Laser safety
- User environment
- Equipment environment

4.4.4.1 Laser Safety

For a thorough introduction to laser safety the reader is referred to Winburn (1989). A common example is provided here for discussion. Facility staff must be aware of the wavelengths and power levels associated with each laser built into an imaging system. Imaging systems, such as confocal laser scanning microscopes, generally have lower overall laser classification than the lasers they contain, i.e., a system containing a (hazardous) class 3B Kr–Ar laser may be classified as class 3A (safe) because safety features of the microscope protect the user from the full power of the class 3B laser. Some of these safety features may be defeated by the user, for example, by removing an objective and inserting a mirror into the laser beam path while scanning. Safe operating procedures and user training are important to prevent users from unintentionally exposing themselves to hazardous levels of laser radiation. The full power of the Kr–Ar laser may also be emitted when the system is serviced. For this reason it is important to restrict access to lasers, as discussed below.

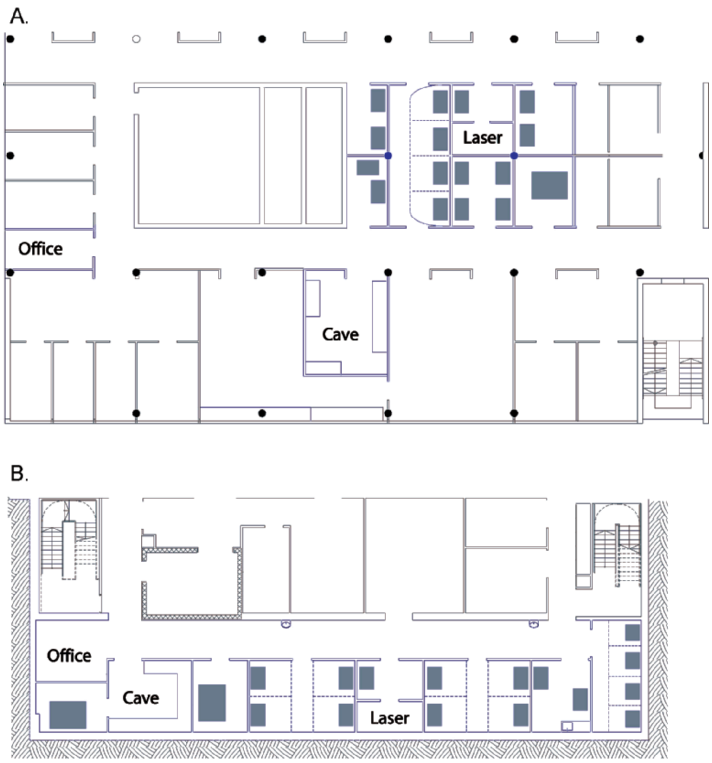

Fig. 4.1 Imaging facility floor plans. **a** Max Planck Institute for Cell Biology and Genetics, **b** Beatson Cancer Research Institute. *Dark lines* indicate space belonging to the imaging facility, *gray lines* delineate other laboratory space. Microscope workstations are indicated by *shaded rectangles*. Bench space for computers for image processing and analysis is indicated by *open rectangles* in the rooms marked *Cave*. Proximity of the cave to the acquisition stations is important for (1) allowing users to quickly check parameters associated with image acquisition and (2) allowing staff to assist with both image processing as well as acquisition. The office has a glass door and a partition overlooking the hallway, allowing staff to monitor events in the facility. Proximity of office to workstations is important for good staff oversight of users and equipment. *Broken lines* indicate sliding curtains used to flexibly partition large rooms into smaller workspaces. *Laser* indicates the laser room, which can accommodate lasers and other loud and/or hazardous equipment associated with microscopes in the adjoining rooms. Note that in **b** access to the imaging facility is controlled via doors with magnetic card locks at either end of the hallway. The facility in **a** is located on the first floor of the building. The facility in **b** is located in the basement, with a light-well providing daylight to the office

The manner and environment in which lasers are used are important aspects of laser safety. For example, it is generally safer to avoid using lasers in "free-space," i.e., open on a benchtop. Fiber-optic coupling at the laser head prevents user interaction with the laser beam. Fiber-optic coupling has an additional advantage, introducing the opportunity to place the laser and the microscope in separate rooms. Additional advantages to user comfort and equipment stability are outlined below. The environment in which lasers are used is important for controlling user access to lasers, especially during the time of equipment servicing. Generally this requires locking all users out of the room in which the system is located while the service staff work on it. Alternatively, if lasers and microscopes can be placed in separate rooms via fiber-optic coupling, service staff can work on hazardous lasers in one room while users remain free to use neighboring systems in the next room.

4.4.4.2 User Environment

Live-cell fluorescence imaging typically requires darkness. For this reason it is important that the ambient lighting level be individually controllable and positionable at each imaging system, for example, by using an architect's desk lamp. The microscope is not only a place for data acquisition, it should also be a place for users to present results to their colleagues and discuss experimental parameters. For this a quiet, private environment where two people can sit comfortably is optimal. The floor space required for an advanced imaging system is around 4–9 m^2 – enough space for a couple of tables and one or two people sitting at the microscope. Alternatively a simple upright microscope may require only 100 cm benchfront alongside other similar systems. Access to system components during installation and maintenance often requires a larger work space. For this reason we have chosen to compartmentalize larger rooms using sliding curtains as dividers. This flexible approach offers many advantages. When the curtains are closed, the user environment is small and private, with good control over ambient lighting. When the curtains are open, access to equipment is enhanced for installation and maintenance. Individual systems can be grouped together for teaching purposes. It is also easier for staff to oversee multiple users and for users to compare results on different systems. This approach is complemented by creation of a central equipment room to house all the lasers and other electronic equipment. This has the significant advantage of removing hot, loud, delicate, hazardous equipment from the user environment.

4.4.4.3 Equipment Environment

Optical components are extremely sensitive to fluctuations in temperature. Zeiss specifies 22 ± 3°C and less than 65% humidity for the operating environment of an LSM 510. Fluctuations of ± 5°C can rapidly lead to misalignment of laser coupling and a drop in excitation power of the instrument, which generally requires a service visit for correction. High humidity, especially in the summertime, can destroy

Table 4.1 Utility considerations. Manufacturer's information on power and cooling requirements for selected instruments

	Power	Heat exhaust (kW)	Water cooling
Zeiss LSM 510 Vis Laser Module	230 VAC (Europe), 3 phase, 16 A per phase 115 VAC (USA), 2 phase, 25 per phase	4	–
Coherent Enterprise II	208–240 VAC, single phase, 29–34 A	–	7.6 l/min, 1.4–4.1 kg/cm^2, 10–60°C inlet temperature
Coherent Innova 70c	208 VAC, 3 phase with ground, 10 A per pulse	–	8.5 l/min, 1.8–4.23 kg/cm^2, 10–35°C inlet temperature
Spectra-Physics Chameleon	220 VAC/6 A 110 VAC/10 A	<2.4	Comes with closed loop chiller

expensive water-cooled lasers by causing condensation inside the laser head and power supply. Dust is an ever-present menace which interferes with the transmission of light through optical components, and in extreme cases can hinder equipment cooling. Control over these environmental parameters is easier to maintain by placing sensitive mechanooptical and electronic equipment in one small room, with restricted user access and a high concentration of utilities, such as heat ventilation, water cooling, special electrical supplies, compressed air, dehumidifier, and dust filter. High-power gas lasers, including the UV lasers used on many confocal microscopes, often have very specific power and cooling requirements, including input and output pressure, input temperature, and flow (Table 4.1). Restricting special utilities to one location can increase their effectiveness and decrease the cost compared with installing them in many rooms. Laser safety advantages with these approaches have already been mentioned. Additional advantages include increased operating stability and protection of sensitive components from user interference.

4.5 Organization

4.5.1 Equipment-Booking Database

The management of a service or facility lies somewhere between running a company and running a laboratory. It is not enough to concentrate on training users and maintaining the microscopes: precious time and effort are required to organize the operation of the facility in such a way as to minimize the administrative burden and maximize the efficiency of equipment and staff. Good organization will exponentially improve the efficiency of operation and contribute significantly to the happiness of users and staff. In our view, an equipment scheduling database is the central tool for managing a multiuser resource such as an imaging facility. It is the central interface with which all users interact in order to book equipment and make appointments with staff members. Paper calendars placed next to the equipment are simply insufficient for all but the smallest of operations.

To begin with, a booking database allows users to book equipment from anywhere on a given computer network, and allows both users and staff to monitor staff availability. This allows users to plan their experiments more conveniently and effectively, eliminating the need to run from one system to the next when checking availability. An online database also allows external users, guests, and collaborators to check equipment availability and confirm bookings ahead of their visit. Similarly, bookings can be cancelled at any time from anywhere. The booking database can also be used to introduce booking restrictions, such as the length of time a booking may last at certain times of the day. We use this feature to keep bookings short during the middle of the day, which increases user access to high-demand systems during peak-use hours. The booking database can also limit the number of days or weeks into the future when use may be booked. This increases the accuracy of user planning and minimizes unexpected cancellations. In the event that users are charged for instrument use, the booking database can automatically generate completely transparent and highly accurate bills to individual users or groups.

A booking database can also promote communication among users and staff. This can take the simple form of a text message appearing on the calendar next to slots which have been blocked or cancelled, explaining why the equipment is unavailable for use and possible effects on future availability. For example, the message "Microscope blocked for 543-nm laser service" has the dual function of informing users why the system is unavailable and reassuring users who had problems with the 543-nm laser that something is being done about it. Communication is further facilitated if the database can automatically generate e-mail to staff and users under appropriate conditions. For example if a system breaks down and staff are forced to cancel bookings, the booking database can automatically send e-mail to all affected users with a short explanation (written by staff) of why the cancellation was necessary. Another important moment for communication is when users book a member of staff for assistance. The database can incorporate a text field on the booking page where users enter comments which will be sent to the requested staff member about exactly what assistance is required (Fig. 4.2). This helps the staff prepare for the booking without having to track down the user and ask why they have been booked. Finally, a booking database can include error-reporting and problem-tracking features which allow users to report equipment problems and staff to record the actions taken to solve them.

Note that in addition to the booking database, mailing lists have an important role in the smooth running of daily events through increased communication among staff and users. For example, all users should belong to a facility users' mailing list, which can be used for important announcements. In addition, we have employed a mailing list for users to swap and fill cancelled bookings. This

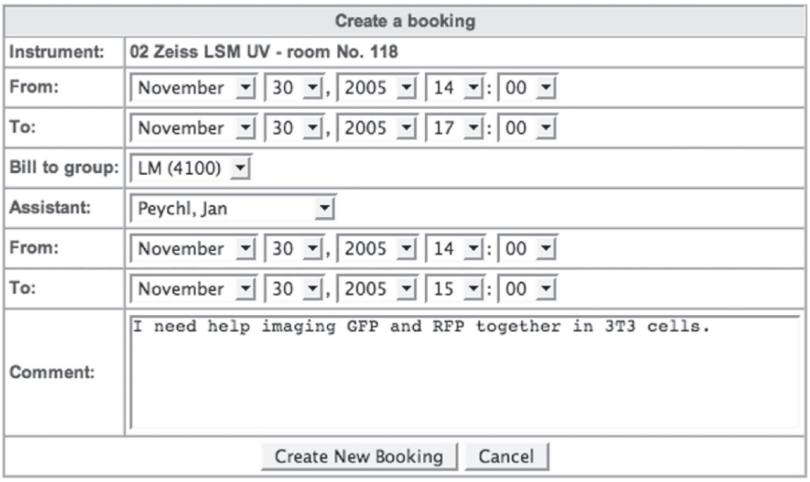

Fig. 4.2 Screenshot of booking database showing booking options. This window allows the user to book a microscope, in this case a 02 Zeiss LSM UV, as well as an assistant, Jan Peychl. The field "*Bill to group*" allows the charges for this booking to be directed to any groups or grants available to the user. Note that the equipment and assistant bookings begin at the same time but the assistant booking is only for 1 h. In this case the user expects assistance for the first hour, but will work independently thereafter. The text in the comment field along with the details of the booking are automatically sent in an e-mail to the assistant to aid in preparation for the booking. The time for which the assistant is booked is also automatically blocked out in the assistant's booking calendar

helps users to make use of last-minute cancellations by other users, and keeps the level of equipment use high.

Aside from scheduling and communication the booking database is an indispensable tool for planning and resource allocation, providing feedback about how the equipment is being used and the use patterns of individual users and groups (Fig. 4.3). Information such as the average number of hours a system is booked per week is essential to prioritize and rationally discuss future equipment purchases. Likewise it is important for staff to identify heavy users and groups, as opposed to vocal users and groups, when allocating resources. Finally, the sum total of all instrument-hours booked gives insight into the number of staff-hours needed to support the facility.

The only way to get a database which does exactly the things you want of it is to develop it in-house. Needless to say this is a costly and time-consuming process. There are a wide variety of free and commercially available calendars to be found on the Internet. Some of these may be adaptable for some purposes. The Institut Pasteur (2007) has developed a scheduling database which is provided free of charge. The database developed at the MPI-CBG light-microscopy facility is available for sale from Scionics.

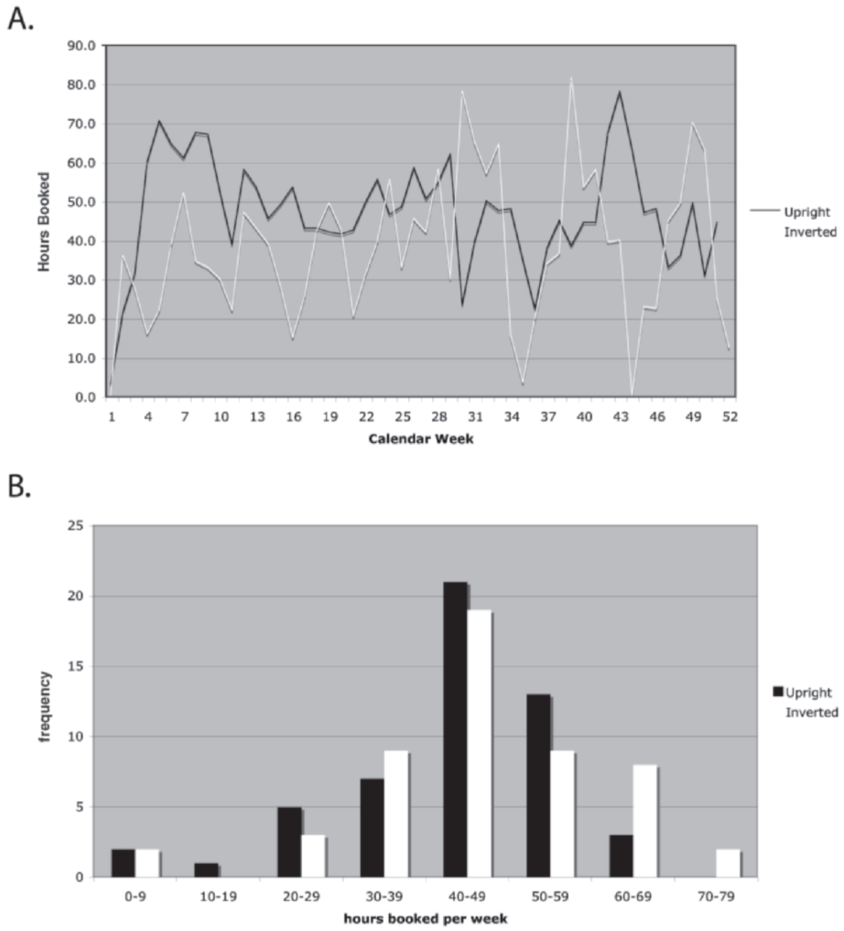

Fig. 4.3 Typical booking database output. Information from the booking database is important for showing that equipment is well used, and to justify purchase decisions. **a** Number of hours booked per week for two confocal microscopes based on upright (*green line*) or inverted (*blue line*) stands. Usage peaks often prompt complaints from users of insufficient microscope capacity (e.g., "The confocals are always booked, we need another one!") However, the average number of hours booked per week for the whole year is 42.7 for the upright microscope and 46.3 for the inverted microscope. Sharp drops in usage are often due to instrument breakdown or repair (inverted microscope, weeks 35 and 44). **b** The number of weeks having a given number of hours booked

4.5.2 Fee for Service

To bill or not to bill? That is the question. There are advantages and disadvantages to both approaches. One of the biggest effects of billing is to minimize frivolous equipment bookings. Frivolous bookings reduce the amount of time available for serious users, and in the extreme case (which we have witnessed) can lead to a hoarding mentality, in which people book instrument time defensively because they fear it is scarce. Assigning a cost to instrument use also raises the awareness of users and group leaders to the costs of running the facility. Billing for equipment time raises user awareness that equipment is expensive and must be treated carefully to promote a long lifetime, and that user mistreatment of equipment raises the cost of running it. In a fee-for-service environment there may be initial displeasure or even hostility on the part of users at having to pay for something they feel they deserve for free. In this context it is important to remember that nothing is free; either users are paying for their own equipment use or someone else is paying for it. In a fee-for-use environment there are no mysterious arrangements conferring preferential access to equipment on some groups; everyone has equal access rights. It can simplify access to facility equipment for outside users, if outside use is desired, and can thereby help to defray the costs for local users.

Alternatively, billing is extra work, requiring additional infrastructure and administration. It requires taking the time to devise and periodically update a cost matrix. This means keeping track of the staff and equipment costs associated with the number of hours of instrument use. It will periodically require explaining the hourly rates to the local group leaders and administrators to show they are getting value for money.

4.5.3 Cost Matrix

Accurate assessment of the hourly cost of running an imaging system requires careful consideration of the many different factors which contribute to cost, such as:

- Capital expenditure: cost of purchasing a system
- Evaluation cost: cost of reaching a purchase decision
- Operating cost: consumables, service contacts, replacement of parts
- Staff support cost: staff time required to keep a system running
- Overheads: building overheads, tools, secretarial support

These costs are summarized in Table 4.2. Operating and staff support costs are frequently underestimated; it costs money not just to buy equipment but also to keep it running. A facility may serve different types of user, as classified by their relationship to the parent or funding institution. For example, users may come from the same university department, different departments of the same university, or from companies outside the university. Depending on where the money to run the facility comes from, a price structure may be needed which reflects different obligations of the parent institution to the various user groups, as well as the ability of different groups to pay for use. For example, the cost matrix might distinguish between internal users, who do not pay the purchase cost or overheads, and external users, who contribute toward the full cost of running the facility.

Table 4.2 Hourly cost of instrument use. The total cost associated with 1 h of instrument use can be estimated by summing the different types of cost listed here. The internal price is the sum of the evaluation, operating, and support costs, which reflects only the cost of running the equipment. The external price reflects all costs associated with instrument use, including the purchase price and building/administrative overhead

	Upright system	Inverted system
Purchase cost	18.01	18.99
Evaluation cost	0.15	0.20
Operating cost	7.89	11.34
Support cost	5	6
Overhead cost	50	50
Internal price	13.05	17.54
External price	81.06	86.53

Table 4.3 Time basis for cost recovery. This is the number of hours (per week or year) which the system is used. The time basis for cost recovery must be estimated for a new system, but later may be set according to the actual number of hours a system has been booked

	Estimate	Upright system	Inverted system
Hours/day	10	–	–
Days/week	5	–	–
Hours/week	50	–	–
Less 10% downtime	45	42.7	46.3
Hours/year	2,340	2,220.4	2,407.6

4.5.3.1 Time Basis of Cost Recovery

The first point to consider in the design of a cost matrix is the time basis for cost recovery. Each cost must be recovered over a fixed length of time. For example, the purchase cost is recovered over the lifetime of the instrument, whereas service contracts run on yearly time intervals. Some repairs, such as the replacement of objective front lenses and cleaning of immersion oil from inside the objective, may be required every 2 years. The number of hours per year available for recovering these costs is essentially the number of hours per year the instrument is in use (Table 4.3). For a new instrument this number must be an estimate, but after the instrument has been used for a while the time basis for cost recovery can be set according to actual instrument use. If the time basis for cost recovery is set too high, the hourly cost to the user will be lower, but it will be impossible to completely recover costs. If the time basis for cost recovery is set too low, hourly costs to the user will be higher and more money will be recovered from the users than required to run the equipment. Increased use lowers the hourly cost by increasing the time basis of cost recovery, providing that increased use is not associated with increased *abuse*, which in turn increases the cost of repairs.

4.5.3.2 Purchase Cost

The purchase cost may or may not be passed on to the user depending on how the equipment was purchased, for example, through grants or directly through the budget of the parent institution. The time basis for recovery of the purchase cost is simply the lifetime of the instrument in years multiplied by the number of hours per year the instrument is used (Table 4.4). The anticipated lifetime of the instrument therefore has considerable impact on the hourly rate which must be charged to recover the purchase cost of the instrument. A longer lifetime results in a lower hourly rate to recover the purchase cost, but remember that an older system will become more expensive to run as time goes on owing to higher repair costs.

4.5.3.3 Evaluation Cost

The evaluation cost is the cost of making a purchase decision. This cost results primarily from the number of staff-hours spent on such tasks as instrument demonstrations and comparisons, discussions with users and company representatives, as well as time spent on equipment installation and testing (Table 4.5). This cost is generally small over the lifetime of an instrument; however, reaching a purchase decision can take up a substantial amount of staff time.

Table 4.4 Purchase cost. Recovery of the instrument purchase price (in arbitrary units) for two different systems over 5-, 7-, or 10-year time periods. Time basis refers to the number of hours per year the system is used, i.e., the number of hours per year available for cost recovery

	Upright system	Inverted system
Purchase price	280,000	320,000
Time basis	2,220.4	2,407.6
5-year recovery time	25.22/h	26.58/h
7-year recovery time	18.01/h	18.98/h
10-year recovery time	12.61/h	13.29/h

Table 4.5 Evaluation cost. The evaluation cost consists primarily of the staff time required to reach a purchase decision. Other costs, such as travel and accommodation for company or laboratory visits, might also be included

	Staff man-days required	
	Upright system	Inverted system
Company meetings	3	2
User meetings	2	2
Demonstrations	5	3
Installation	4	3
Total days	14	10
Staff cost per hour	30	30
Total cost	3,360	2,400
7-year recovery	0.22/h	0.14/h

4.5.3.4 Operating Cost

The operating cost includes the repair and replacement of parts, consumables, and service contracts (Table 4.6). Each repair or part replacement should have a length of time over which its cost must be recovered. Some repairs will be one-offs but others (such as laser tube replacement or objective lens repairs) can be expected to occur at regular intervals. Note that the estimation of operating costs for a new system will be very rough approximations at first, but will become more accurate as actual expenses accumulate. The operating cost requires periodic updating when costs have been completely recovered or new costs arise.

4.5.3.5 Staff Support Cost

The cost of staff support is determined by the desired level of staff support. How much help do the users expect to receive from staff? In our estimation this cost is time-consuming and difficult to objectively and accurately measure. One advantage of a booking database is that users can book staff directly for assistance and the cost can be accurately assigned back to the user who "consumed" it. However, much of

Table 4.6 Operating cost. The operating cost includes consumables, the repair and replacement of parts, and service contracts. The cost of each item is recovered according to its frequency of occurrence. Many events (replacement of lasers, repair of objectives) may be expected to occur at regular intervals

	Cost	Months to recover	Cost per hour
Upright system			
Mercury bulb	116	1	0.682
×40 objective repair	673.2	24	0.165
Service Contract	3,256.8	12	1.596
Maintenance visit	1,643.1	12	0.805
×60 objective repair	800	24	0.196
×100 objective repair	1,064	24	0.261
Scan-head overhaul	19,000	36	3.105
Argon laser	6,626	36	1.083
Total	–	–	7.89
Inverted system			
Mercury bulb	116	1	0.682
Service contract	3,727.12	12	1.827
Objective repair	633.27	24	0.155
Repair	6,948	24	1.703
Maintenance visit	1,891.25	12	0.927
Objective repair	809	24	0.198
Scan-head overhaul	15,375.1	36	2.512
Argon laser	6,626	24	1.624
UV laser	14,000	48	1.716
Total	–	–	11.34

Table 4.7 Cost of system support. The support ratio is the number of hours of system use requiring one general hour of staff support. The higher value (6) indicates the upright system requires less support that the inverted system. Staff cost is 30/h. Dividing the number of hours the system is used each week by the support ratio gives the number of staff-hours required to support each system. On the basis of the values in this example, general support for four confocal microscopes would require approximately 35.6 h (=2 × 17.8) of staff support, or one full-time staff position. This is exclusive of the staff-hours needed to support direct booking by users for training and application assistance

System	Support ratio	Cost per hour	System-hours/week	Staff-hours/week
Upright	6	5	42.7	8.5
Inverted	5	6	46.3	9.3
Total	–	–	–	17.8

the staff's time is consumed by tasks which cannot be directly related back to any one user. General system support includes random trouble-shooting, sudden requests for user support, software maintenance, hardware maintenance, performance monitoring, and, of course, managing system repairs. The sudden user request deserves special mention. Such requests are typically associated with people using equipment who need help right there and then to be able to proceed with their day's experiment. Ten to 15 min of staff time can make the difference between a successfully used or a wasted booking. However, a series of sudden requests can easily consume the entire day. And because of their rapid-fire nature, it is extremely difficult to record how much time was spent with each user, and if the need for assistance was due to a fault in the system (for which all users should pay) or of the user (for which each user should pay). A simple and general estimation of the cost of staff support can be made by estimating the number of hours of equipment use which require 1 h of staff support (Table 4.7). This number will be lower for sophisticated systems requiring more support, and higher for robust systems requiring less support. These values can be adjusted according to the level of support desired by the local user community. Note than a partial estimation of the total number of staff-hours required to support the facility (i.e., the required number of staff positions) can be derived by dividing the number of system-hours booked by the support ratio.

4.5.4 Advisory Committees

Internal and external advisory committees can provide useful feedback and support for running a facility. An internal advisory committee composed of users can serve to keep relations with users smooth and give them insight into what it takes to keep the facility running. It provides an official conduit for user input on big issues such as new equipment purchases and the manner in which the facility is run, and a forum to air the many smaller issues which also arise. An external advisory committee, comprising other facility leaders and imaging specialists, provides an important reference point for the state of an imaging facility with respect to the status quo. An external advisory committee can provide proactive facility managers with crucial support for important "big picture" decisions, such as identifying trends and planning future spending.

4.6 Summary

An imaging facility integrates many functions within a research institute (Fig. 4.4) Many imaging facilities have evolved from a few microscopes to fill the available space in their local environment. In the future we expect that imaging facilities will be considered from the beginning as important components in the design of research buildings. This will allow imaging specialists to ensure that maximum utility is obtained from precious research funds through efficient planning of space, staff, and equipment. Staff play an important role in providing continuity and expertise above and beyond equipment maintenance. The flexibility of space use is of primary importance. We have emphasized that a laser room can improve laser safety while increasing the stability of equipment performance and comfort of equipment use. An equipment-scheduling database is vital for experiment planning, facilitating communication among users and staff, and establishing accountability.

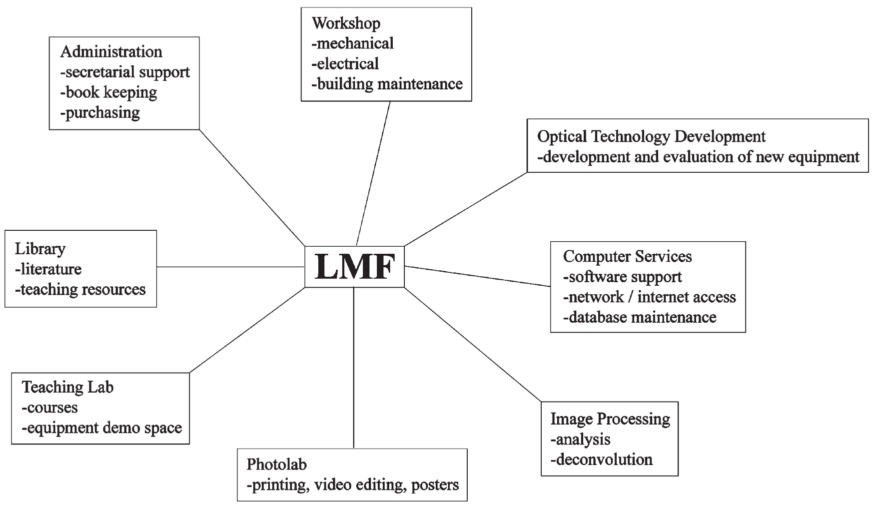

Fig. 4.4 Relationship of a light-microscopy facility (*LMF*) to other services. A variety of other support services are required to keep an LMF running. Depending on the local environment, these services may be completely external to the LMF or partly contained within it. For example, some imaging facilities also cover photolaboratory functions. Or image processing may exist as a separate facility if there are local specialists

References

Alderson RH (1975) Design of the electron microscope laboratory. Practical methods in electron microscopy, vol 4. Elsevier, New York

Angeletti RN, Bonewald LF, de Jongh K, Niece R, Rush J, Stults J (1999) Research technologies: fulfilling the promise. FASEB J 13:595–601

DeMaggio S (2002) Running and setting up a confocal microscope core facility. Methods Cell Biol 70:475–485

Helm JP, Haug F, Mogens S, Storm JF, Ottersen OP (2001) Design and installation of a multimode microscopy system. Proc SPIE 4262:396-406. http://www.math.uio.no/~atlej/LOV/files/HelmetalProcSPIE4262.pdf

Humphrey E (2004) How to promote a facility in order to increase use, acquire new equipment and, as a result, increase revenue. Microsc Today 12:32–36

Institut Pasteur (2007) PPMS: Pasteur platform management system for the PFID facility. http://www.pfid.org/html/ppms_agree/?fr. Cited 2 May 2007

Murphy JA (1993) Designing a microscopy facility: step by step procedure. In: Robards AW, Wilson AJ (eds) Procedures in electron microscopy, vol 7. Wiley, Chichester, pp 1:1.1–1:1.23, 1:2.1–1:2.2

Murphy JA (2001) Image management for a multi-instrument, multi-platform microscopy facility. Scanning May

Murphy JA (2002) Designing a microscopy/analytical instrumentation facility: step by step procedure. Microsc Today 10:36–39

Sherman D (2003) Core facility management session: maintaining major equipment in the core microscopy facility. Microsc Today 11:40–45

University at Buffalo (1991) Confocal@listserv.buffalo.edu – archives. http://listserv.acsu.buffalo.edu/archives/confocal.html. Cited 5 Dec 2006

White N, Errington R (2001) Setting up and managing a biological laser scanning microscope resource. Bio-Rad technical note 12 (reference no 9MRC50TN26). http://microscopy.bio-rad.com/reference/technical/Tech12.pdf

Winburn DC (1990). Practical laser safety. Dekker, New York

Zaluzec NT (1993) The Microscopy ListServer. http://www.microscopy.com/. Cited 5 Dec 2006