A Primer on Computers, Information Management, and Internet Access for Cytometry

J. Paul Robinson[1] and Guenter Valet[1]

[1]*Purdue University, West Lafayette, Indiana;* [2]*Max-Planck-Institut Für Biochemie, Martinsried, Germany*

Introduction

Clinical and research laboratories in the field of cytometry are increasingly dependent upon computer technology to collect, analyze, and distribute data. Ongoing developments in computer technology have led to rapid changes in the manner of data manipulation. The impact is being felt in several ways:

1. A more technically proficient user base makes increasing demands.
2. The advanced software for new instruments requires an understanding of many other programs.
3. Operating systems are becoming significantly more complicated, with the goal of making the operation much simpler. This is fine only until the system crashes (which they seem to do regularly), because the complexity of the system far surpasses the capabilities of even advanced users to repair them (examples: Windows 95, OS/2, or Mac operating systems).
4. The trend toward multi-tasked computing requires an appreciation for networking.
5. Active linking of computers for simultaneous data evaluation is now easily achievable and will become more popular.
6. The proliferation of the Web places new demands on cytometry labs as it has on all other aspects of life!
7. Different methods must be employed for data management—particularly if there is a requirement to maintain data for longer periods, or the desire to link multiple types of data as well as historical data sets.
8. Automation of assays will alter our use of cytometric technologies and place increased demands upon data analysis and automated classification systems.
9. New multimedia methods of learning and training will become important.
10. Failure to understand computer technologies will become a significant obstacle as we move into the next century.

This manuscript is designed to be a forum for wide-ranging discussions on all aspects of data collections, evaluations, and manipulation in the cytometry laboratory. Furthermore, we will try to clarify and define both the problems and solutions that face us in light of the information revolution. The material herein will be presented at the Clinical Cytometry meeting in March 1997 and was accurate at the time of writing (January 1997). Obviously this field is changing very rapidly and the user should consider this when using the accompanying information.

In the general discussion we have included the application of computers for the generation of reports, slides, and electronic presentations because cytometry is a highly graphical technology.

Why an Interest in the Internet?

The Internet is as attractive to cytometrists as to anyone else for several reasons. Pri-

0197-1859/97/$0.00 + 17.00

marily, the Internet provides a mechanism for fast international information exchange, e.g., by acting as bulletin boards of scientific societies and user groups for the announcement of meetings, workshops, and courses, by displaying extracts of the scientific literature (abstracts, tables of contents of journals), or by providing collections of laboratory procedures.

An even more important aspect is the interactive potential of the Internet for the conceptual development of science, e.g., by the installation of concept fora by the preparation of consensus processes (see below) and by facilitating the discussion of E-mail groups (e.g., Purdue Cytometry E-mail). Furthermore, the Internet can advance scientific software development for standardization of individual patient disease diagnosis (via databases) and especially disease prognosis from multiparameter cytometric and other data. It also promotes international quality assurance programs, educational offerings (e.g., STEP program) and "remote" learning (see later), and training.

The Internet provides a significant lead time for the early identification of new interest areas in this fast-expanding multidisciplinary research field, thereby dramatically shortening the traditional time lapse between scientific concept, experimental phase, and result publication in journals.

Current Status of Computers in the Laboratory

Operating systems

- IBM PC (Windows 3.1, Windows 95, OS2, DOS)
- Macintosh
- UNIX
- HP

The average cytometrist may feel that operating systems are relatively unimportant. However, incompatibility between operating systems of cytometers and analysis computers or even regular office computers can generate real problems for data presentation. The inability to extract a histogram or dataplot from the cytometry software into a word processor or slide presentation program can be most frustrating. Therefore, some consistency in selection of hardware and software may be desirable to avoid these hassles. With some of the more recent operating systems, interchange of data via networks is easier to achieve, even across operating systems and computer platforms (see Networking).

Presentations—Slides, overheads and graphics programs

A number of programs can create slides and graphics for presentations and lectures. One such readily available program is MS Powerpoint, which can be used for both Macintosh and PC. Figures can be transferred to 35-mm transparencies using digital slide cameras such as the Lasergraphics Personal LFR. Output devices must be carefully selected to ensure that transfer from the graphics programs is easy and straightforward, for example using a regular printer setup. Color prints have some usefulness in identifying multiple populations, particularly in multicolor immunophenotyping, but high quality output devices such as photographic printers are unnecessary and overly expensive, since most of the figures produced will not be of high resolution. Inexpensive inkjet-type color printers are more than satisfactory for reports and poster presentations. The key concept for the cytometrist is that data presentation is a very graphical phenomenon that increasingly requires the capability of using graphics programs to maximum advantage.

> *The Internet provides a significant lead time for the early identification of new interest areas,…shortening the traditional time lapse between scientific concept, experimental phase, and result publication in journals.*

Information Management

Data collection

Most cytometry data are collected as listmode data on either IBM-type PC or Macintosh computers. For each patient, several files will routinely be collected (despite the inefficiency of this concept), and each file must be individually databased, analyzed, saved, and archived. Almost all cytometry systems manufactured within the past couple of years have the capability of being networked so that data files can be archived to a network data storage facility (see below).

Databases

The use of relational databases in cytometry labs is perhaps considerably less than it should be. Relational databases have several advantages. They can link data from different sources; they can do extended computation and analysis; and they can be used in general lab management for billing, ordering, and project management.

The purpose of this primer is not to discuss the fine details, but to draw attention to the importance of this aspect of computer management in the laboratory. Not only can patient or research data be categorized, but the results can also be sorted later for analyses not considered, or even not yet developed, at the time of data collection. A second area of database use is in maintaining a reference source for the lab. An excellent product for this purpose is Reference Manager (Reference Information Systems), a sortable database originally designed for bibliography generation. Recent versions have allowed extensive variability in the types of data it will accept and manipulate. Using this product we (JPR) have maintained for 13 years a continuous database that now includes more than 12,000 references on flow cytometry, image analysis, and several specific areas of science. This allows us, in essence, to reference automatically all manuscripts, methods, reports, and documents from this lab. References to slides, images, graphs, and figures can also be included. Currently, Reference Manager can save only the location of images but not the images themselves. Future versions, however, are intended to allow that function. Linking references to methods is ap-

0197-1859/97/$0.00 + 17.00

propriate for training and education.

Information Transfer

Networking

Hardware

It is possible to link computers with an inexpensive box simply to print documents on a shared printer. If the only requirement is to print, this is a very satisfactory solution.

However, for exchanging files, it is easier to use a network; or with operating systems such as WIN95, two computers with the same operating system have virtually automatic connection. In this case a network is not required; a network card in each computer is useful but not required for linking the two. Networking, however, has several advantages and is necessary for linking three or more computers. In a networked system, data files can be transferred from one to another and archived on one particular computer if necessary. If a more complex computer system is warranted, as in cases where several instruments and computers (possibly with different operating systems or versions) are present, it may be necessary to install an advanced network, which will require a server computer, i.e., one that manages the network. Examples include Novell, Lantastic, Lanserver (IBM), Windows NT (Lanmanager), NFS.

Linking instruments to servers

Most flow cytometers can be linked to a server computer with little effort. Data are then either collected directly or archived rapidly to the server, keeping the cytometer free for data collection.

Security of data

Password protection is important not just for clinical laboratories but for any laboratory connected to a network. For greater security, passwords should be changed at regular intervals. Once computers have been connected to the outside world, care must be taken for adequate protection of data, particularly with respect to patient information.

Information Storage or Archiving

Backing Up Data

Data backups are best done immediately before a major system crash! Unfortunately, they are usually attempted only after a system crash, with less than comforting results. It has been truly said that it is not IF but WHEN a disk crashes that all the data are lost. Backing up both system files and data is not an optional extra in cytometry. If you need access to data in the future, having a single source is a very dangerous situation. There are several approaches to backing up data. The first is to have a regular total back up every 7 days or so. At worst, only the last week's data are lost if (when!) a major failure occurs and both the system and the previous data are restored to a reasonable facsimile of the operating system. The second approach is to back up the system at the same weekly interval, but do daily backups of data files and files that have been changed. A third possibility is an incremental backup system that simply identifies files that have been changed and backs up only those on a regular basis. One way or another, it is usually possible to restore the system after a major crash.

Backup should be made to one of several media. A fast, convenient, but not necessarily foolproof system is to back up to a spare hard disk daily and to a more robust medium weekly. In the event of a crash, restoration of the system is usually relatively easy. Data backup is not a satisfactory substitute for long term archiving. The more sophisticated a system is, the more important the need to organize regular system and data backup. The more you have on a system, the more you lose when it crashes. It is also intelligent to make two copies of each data archive and store one in a location remote from the laboratory, preferably in another building.

Archiving Data

Available data archival technologies

Floppy disk: This is one of the easiest methods for archiving data, but it is limited by restrictions on file size. Data from complex assays may not fit onto a standard floppy disk. Even worse, bad blocks will accumulate on floppies over time. In short, this is not a robust method for archiving data and should be avoided.

Video tape: Video tape was a popular method in the late 1980s because a large volume of data could be stored. However, data reliability was always questionable and the method for retrieval very slow. Video tape for archiving has virtually disappeared.

Standard computer tape: Standard computer tapes are also rare these days. Earlier tapes were capable of storing from 60 to 100 megabytes of data. As with video tape, slow retrieval times and high error rates were common. The inability to randomly access files is a major disadvantage. This method is adequate for small amounts of data, but is not recommended.

Optical disk—WORM: WORM—write once read many—disks were very popular in the late 1980s and early 1990s. However, the cost of the media is very high and no longer competitive. In addition, these systems have the major drawback that each manufacturer created his own proprietary read and write format. WORM disks certainly have the advantage that they cannot easily be erased. Eventually, however, the power of the write-laser diminishes to the point at which the system becomes unreliable.

Optical disk—re-writable: The variety of inexpensive re-writable optical disks currently available makes this a very reasonable system to use for systems with moderate amounts of data to archive. Although not inexpensive on a per byte basis, they are very convenient and will often be the most satisfactory solution for investigators with medium to high data output.

Digital tape: For laboratories with excessive quantities of data and huge systems, digital tape is probably the least expensive option, although tape systems do have a number of disadvantages. The most obvious is that tape systems are not random access, so very often the entire tape must be read to identify and retrieve a selected file, at a cost of many minutes. Another problem is that tapes can "self-erase" some parts of themselves if they are not run through at regular intervals. This is not a particular convenient situation for those without some kind of central computer management in place.

CD ROM: Currently CD-ROMs are probably the least expensive and most convenient technology to use, with a number of advantages. First, the medium is generally readable across all computer systems and operating systems. Consequently, data can be written to the disk with a Macintosh

0197-1859/97/$0.00 + 17.00

computer, for example, but read by an IBM-type PC. Second, the disks currently hold 650 megabytes of data, which is a reasonable amount and likely to be several days' worth of data even for a very large laboratory. Third, the cost is quite reasonable: a recorder is around $500 and the media are less than $7.00 each. It does take around 35 minutes to write 650 megabytes of data to a 2x CD-R (recordable CD), but this time should of course decrease as faster writers become available along with larger digital recording systems (4 gigabytes). The CD has been available for some years and is considered to have a useful lifespan of 15–20 years. The disk itself may last far longer, but reading devices will surely be lacking. We can therefore expect to be able to use CDs in their present form for at least another 5 to 8 years.

"ZIP"-type drives: The brand name "ZIP" has become more or less a generic term for removable disk storage units. Those with experience of previous forms of removable drives such as Bernoulli drives may cringe at the thought of using these. Some early cytometers used 5 or 10 megabyte removable drives that were, at their very best, disastrously unreliable. By contrast, removable disks today represent a mature technology, very reliable and very inexpensive. The major advantage of systems such as Iomega's ZIP drive is that they can plug into the parallel port of a desktop or laptop computer and operate without any installation procedures at all. Although larger and faster drives are available, the increased cost and more difficult methods of operation reduce their desirability. The maximum size of current inexpensive ZIP disks is 100 megabytes at a cost of $14.00 each.

Sources of Information

Cytometry data

Most flow cytometers routinely collect listmode data for subsequent analysis. Some labs still collect histogram files and ignore the list data. This is clearly a more economical procedure, particularly if no further analysis is required. The advantages and disadvantages of this philosophy are more appropriately discussed elsewhere.

Patient databases

Data files should be linked into some kind of laboratory management system that lists the patient/assay, date, file name, and other pertinent information. Recall of the data should be possible by any known parameter. If both listmode and histograms are stored, these are so designated in the database (see discussion on databases). The final results should also be linked. These could and probably should be automatically entered into the database.

Protocols and methods

A number of books and manuals for flow cytometry methods are available. These materials should be used as reference points for methods specifically developed for a lab. Such documentation is a requirement for clinical labs, but any good research laboratory will have well documented methods.

What is the Internet?

The Internet is a worldwide electronic network physically consisting of wire and glassfiber cables supplemented by terrestrial or satellite radio communication and terrestrial infrared laser links. Data in this network are exchanged between computers by the standardized TCP/IP protocol. The network is mostly accessed from PC, Macintosh, or Unix computers via fast ethernet lines (250 Kbytes/sec or faster), by digital ISDN telephone lines (8 or 24 Kbytes/sec), or by modem connections via slower analog telephone lines (3.6 Kbyte/sec = 28800 baud) using the SLIP or PPP data exchange protocol.

The hardware connection between computer and network is established by computer bus access via a plug-in network card, via external interfaces attached to the parallel printer port, or via telephone modem attached to a serial (RS232) port of the computer.

Appropriate driver software establishes the data communication between computer and network. Telephone modem access to the Internet is achieved through "access provider" companies that operate gateway computers to the Internet. Universities and other larger organizations usually maintain their own high speed ethernet access to the Internet.

Each network computer is identified and accessed by its unique URL (Uniform Resource Locator) address consisting of a mnemonic name (e.g., pcv4.biochem.mpg.de) that is transformed into a unique computer address number (e.g., 141.61.1.64) by a name server computer within the network. Network computers are set up either as clients or as servers. Most computers are client computers, which can demand, display, and download information from server computers and send messages to server and client computers. Name server computers contain address lists and access information required to identify and access each computer in the network.

Gateway computers provide network access from multiclient and server environments of large institutions like universities, hospitals, administrations, access providers, or companies. Routing computers distribute the network traffic within the network in an optimized manner. Network analysis programs permit the individual user to analyze network performance.

Cytometry and the Web

History of the Web

The original Web concept dates back to March 1989 when the inventor, Tim Berners-Lee, circulated a proposal to colleagues at the European Particle Physics Laboratory (CERN). The proposal contained three basic elements: a consistent user interface, an ability to incorporate different computer systems and document types, and an ability to read the documents anywhere on any network. In December 1990, the concept of the World Wide Web (WWW) began to take shape with the creation of the first browser program. The first browser used at CERN appeared in May 1991. By the end of that year, the high energy physics community had general access to the Web. In 1992, CERN made a browser available to the public via FTP, and by January 1993 there were 50 Web servers worldwide. A Mac browser followed in early 1993 along with the first version of MOSAIC for X-windows by the National Center for Supercomputing Applications (NCSA) in Champaign, Illinois.

By October 1993 there were 500 Web servers worldwide, and during 1993 and 1994 a number of browsers that operated on the most common computer systems ap-

0197-1859/97/$0.00 + 17.00

TABLE 1. SOME USEFUL WEB SITES IN CYTOMETRY

Purdue University	http://www.cyto.purdue.edu
Max-Planck	http://www.biochem.mpg.de/valet/cytorel.html
ISAC Homepage	http://nucleus.immunol.washington.edu/ISAC.html
Cytometry Journal	http://marlin.ucsf.edu/dmc-pi/cytometry/cyto.html
Communications in Clinical Cytometry	http://journals.wiley.com/cyt-bin/wilma/com
Clinical Cytometry Society	http://www.cytometry.org
TATIANA[a]	http://www10.uniovi.es/~tatiana/index.htm
Catalog of Free Software	http://www.bio.umass.edu/mcbfacs/flowcat.html

[a]Transeuropean Association for Training in Image ANAlysis

peared. In March 1994, the first cytometry Web site was formed at Purdue University (http://www.cyto.purdue.edu) (although the original address was considerably more complex). In 1994 Netscape Communication Corp. was formed by the original authors of Mosaic, and an international conference was held in Geneva to define the future nature of the Web. July 1994 saw the formation of an organization called W3, which became the management organization for further Web development and standardization and eventually was transformed into the World Wide Web Consortium led by the originator of the Web concept, Tim Berners-Lee. The consortium's Web site is http://www.w3.org.

Searching for Information

The Web was rather ineffective until the appearance of the concept of search engines. Interestingly this was a very early development, but one that did not really become available for some years. The original WAIS search engine was implemented on the Web as far back as October 1991; however, the user-friendly search engines such as LYCOS (http://lycos.cs.cmu.edu/), AltaVista (http://www.altavista.com), and Yahoo (http://www.yahoo.com/) have been the ones to make the Web universally accessible. These search engines operate by sending out hundreds of thousands of "robots" that search for and read Web pages, noting every word and then indexing the material into massive databases. Users can nominate a word; the search engines will return the URL and a line of text in which that word is embedded. Unfortunately, the search engines are not well designed for efficient search and retrieval; they often find thousands of instances of a word. What is really needed are programs that do complex searching on keyworded databases, such as occurs with the MEDLINE database. We are likely to see a significant increase in the sophistication of search programs over the next year or two.

Education

Searching medical databases such as MEDLINE is possible in a number of ways. The current system available to most scientists is the OVID search network. Using a Web browser or via a telnet session, data are downloaded to a computer for incorporation into a database or document.

Display of cytometric information in the internet

The variety of media supported on the internet provides good opportunities for exchange of information and for interaction among individuals and groups involved in cytometry throughout the world. Announcements via the internet are instantaneously accessible and WWW-pages can be continually updated if required. Web sites may entertain an E-mail forum to ask questions or exchange comments with colleagues, and to view or discuss results (Table 1; Fig. 1). The future will see the implementation of "electronic" meetings or workshops.

Bulletin board information

Several cytometric groups, both international and national, are currently on-line. These include the Purdue University Cytometry Discussion group, ISAC, and Martinsried (Max-Planck) sites.

Meetings, meeting abstracts, workshops, courses

Some meeting abstracts (ISAC, Deutsche Gesellschaft für Zytometrie (DGZ), European Society for Analytical Cellular Pathology (ESACP)) and notification of upcoming meetings, workshops, and courses are available at regional Web sites (ISAC, Purdue, and Martinsried).

Tables of contents of scientific journals

Journal tables of contents for Cytometry

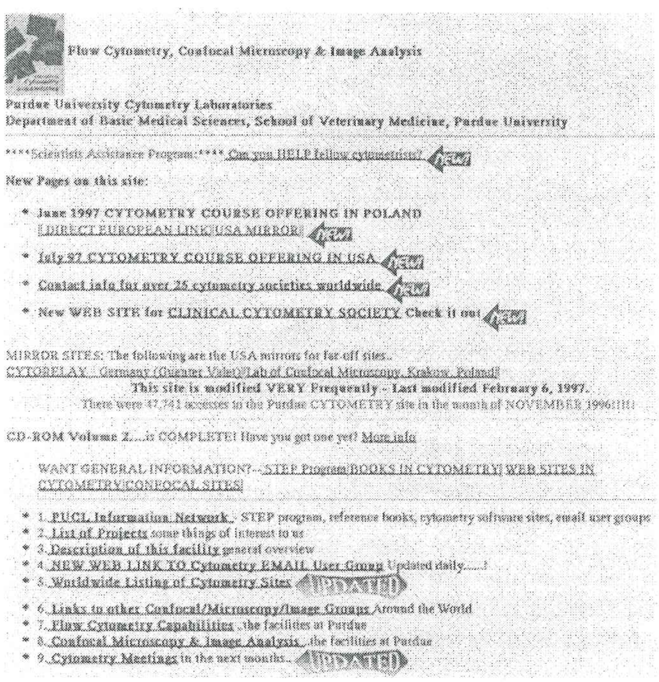

Figure 1. The Purdue University cytometry Web site at http://www.cyto.purdue.edu.

TABLE 2

Site	FTP Address	Contains
PURDUE	ftp.cyto.purdue.edu	Utility programs, sample data images, software
CYTORELAY	ftp.biochem.mpg.de	Sample data, Web Sites

(since 1995) and Communications in Clinical Cytometry are available from the Wiley Cytometry Website. Tables of contents for Analytical Cellular Pathology (ACP) are available at Martinsried, and recent volumes at the Web site of the publisher, Elsevier Scientific. In addition, tables of contents for other journals are available at the Elsevier Science Tables of Contents service.

Book reviews

Information on most cytometry-related books and reviews are available on the Purdue home page (as well as on the Purdue CD-ROMs). Web site reviews can be published very rapidly. Currently, the Purdue site contains reviews on some 25 books in cytometry, confocal microscopy, and image analysis.

Exchanging data

Data exchange can take place via FTP through a number of sites around the world. A few of these sites are listed in Table 2. Much of the contents listed is also available on the Purdue CD-ROMs (see later).

Exchanging software

The most comprehensive site for cytometry software is that of Eric Martz at the University of Massachusetts (http://www.bio.umass.edu/mcbfacs/flowcat.html), which maintains all of the free and shareware software available worldwide. Software can be downloaded at any time. The entire site is replicated on the Purdue CD-ROM series and any program can be copied directly to one's own computer.

Mirror sites around the world

Mirrors at several sites duplicate the contents of other Web sites. Examples include mirrors for the ISAC WWW site in Germany, Spain, and the UK. For Europe, the CYTORELAY node at the Max Planck Institute, Martinsried, Web site has mirrors of ISAC, Purdue University, Scripps Research Institute, and JCSMR (Australia). For North America, the Purdue site has mirrors for the CYTORELAY site in Germany and the Laboratory of Confocal Microscopy center at Jagiellonian University in Krakow, Poland. These mirrors enable a user to link to a nearby computer system to download data much faster than possible from the original site, which may be halfway around the world.

Using the Web for Consensus Documents and Ring Trials

One of the most difficult aspects of generating consensus documents is the need for public distribution for review and comment. Journals are cautious about publishing these materials, since they are almost always subject to significant change and the reader cannot easily determine how far out of date the material is, particularly if he is not aware of the most recent publications. For this reason, we propose the use of the Web for consensus and ring trial data as the most appropriate and desirable for the following reasons.

1. Data can be published on the Web without lengthy delays

   The protocol design complete with all details can be easily reproduced on the Web. Figure 2 shows a printout from the CYTORELAY ring trial Web page (http://www.biochem.mpg.de/valet/consens1.html) as an example. The participating laboratories can be identified and the nature of the required samples described.

2. Appropriate caveats reflecting the very latest information can be placed beside the data

   As the information is updated, it is possible to place caveats and comments on the data. This changing database can stimulate an ongoing discussion of the data. All of this information can be placed in the Web site so that observers are fully aware of the status of the trial.

3. Data can be graphically presented and updated on a regular basis

   Not only can data tables be presented, but figures representing the data can also be displayed. These can be graphics such as line charts, in 2D or 3D, as best represent the data. It is now possible to link these to a database that is automatically updated without intervention by the site manager.

4. All documents can carry running dates so that the reader is aware of the current status

   The reader can always know the current status, including the last update and the degree of completeness of the trial. This ensures that the reader has adequate information to evaluate the data presented. It also places pressure on the webmaster to ensure that the site is regularly maintained and updated.

When final data are in, the full report can be appropriately published in a journal in a complete manner

After completion of the trial, when data analysis and protocol evaluation are finished, the consensus will normally be reported in a regular journal. We propose that the Web is the most appropriate medium for reporting the progress of ring trials as the data are continually changing and updated.

Linking Laboratories Electronically

The ABCs of FTPs for PhDs and MDs

The best known medium for transmission of electronic information today is the display of WWW-pages with text, graphic, audio, and video information. In addition, E-mail messages can be exchanged between WWW-clients, files downloaded by FTP (file transfer protocol), and downloaded WWW-pages displayed off-line. The Gopher information system and a multitude of newsgroups and companies display continuously updated information. The Internet contains a variety of commercial TCP/IP intranets, like Compuserve, America On-Line, Europe On-Line, and T-OnLine, from which the individual user has access to the general Internet. FTP and Telnet are slightly more difficult to deal with than Web browsers, so less experienced users avoid these communications

0197-1859/97/$0.00 + 17.00

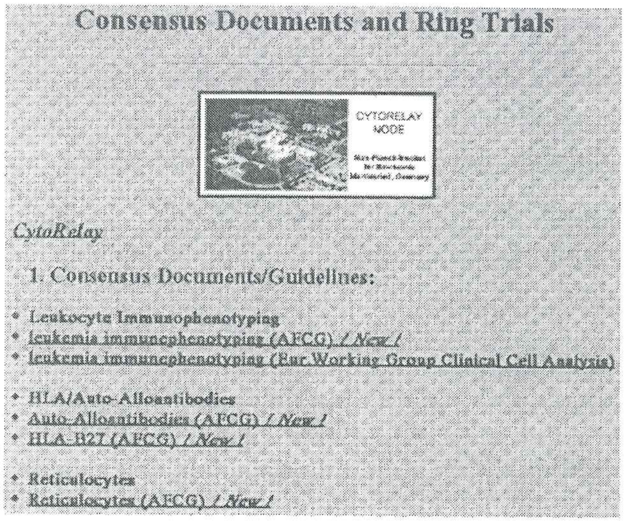

Figure 2. An active ring trial shown from the CYTORELAY Web site at http://www.biochem.mpg.de/valet/cytorel.html.

protocols, even though Web browsers are actually using them transparently to the user.

Off-line Internet by FTP-download

Because CD-ROM updating is limited for practical reasons to 6-month or 1-year periods, we have proposed a system for regular updates to a user's site[1] (e.g., for meeting and course announcements, consensus updates). Such updates can be achieved automatically if cytometric WWW-page providers store their pages in compressed form on FTP server computers from which they can be collected by suitable programs (such as provided on all Martinsried WWW-pages) daily, weekly, or monthly according to the interest of the individual user. Following decompression, the received files can be inspected off-line with the network browser from a hard disk in the same way as CD-ROM files.[2] This system is available on the CYTORELAY site and is now a method employed by several software manufacturers to bring updated information to some Web sites.

Multimedia Cytometry

The Purdue Cytometry CD-ROM

The first volume[3] of the Purdue Cytometry CD-ROM was published in April 1996. Subsequent volumes are produced approximately every 6 months, with the second volume[4] appearing in December 1996. These disks are essentially a "Web-on-disk": the entire disk operates as if the user were on the Web. The disks contain large amounts of data covering many facets of cytometry. For instance, Volume 2 contained in excess of 14,000 files all organized via a series of indexes.

These CDs were produced to solve a specific problem for the cytometry community—sorting through the vast quantity of information on the internet and identifying the "cytometry-related" subset. Further, because of the graphical nature of cytometry, the CD-ROM provides appropriate storage for large graphic files. Finally, by using a Web browser as the interface to the disk and its content, the user can navigate his way effortlessly through the information. More can be learned about these CD-ROMS by sending an E-mail message to cdrom@flowcyt.cyto.purdue.edu.

The CD-ROMs provide solutions to several problems facing scientists today:

1. Coping with too much information
2. Sharing information
3. Maintaining the information in an organized manner
4. Educating graduate students and staff
5. Providing information for those without access to the Internet

Conclusion: Cytometry, A World Leader in Use of Computers and the "Net"

Cytometry groups were among the leaders in creating user E-mail groups or "listserves." The first such was the Purdue E-mail group started in 1989 by Steven Kelley and J. Paul Robinson. This group now serves on a daily basis over 1,600 scientists interested in cytometry. The service is also placed on the Web where it is accessed by a large number of people every day. Purdue University established the first cytometry Web site in early 1994, providing the cytometry community with a large amount of information as well as linking to sites all over the world. The cytometry site at Martinsried, Germany, known as CYTORELAY, was one of the first to establish mirrors and internet checking facilities and the first to place consensus protocols and results on line for immediate comment.

The CD-ROM series is also an advanced concept since it uses HTML language, rather than more complex systems, as an "authoring" system. The major advantage of the "Web-on-a-disk" system is that it is universally readable on all computer platforms.

In summary, the cytometry community is fortunate in having a number of groups that are leaders in the information age. The community is thereby provided with state-of-the-art technologies for dissemination of vast data resources, rapid means to seek consensus, and ability to share data worldwide. These concepts will help to shape the cytometry community over the next several years as many people come to grips with the "information superhighway."

References

1. Valet G, Valet M, Robinson JP: Off-Line Internet: A Timesaver for slow WWW-Sessions. Cytometry Suppl. 8:105, 1996.
2. Robinson JP, Kelley S, Valet G: CD-ROM Electronic Distribution for Cytometry. Cytometry Suppl. 8:106, 1996.
3. Purdue Cytometry CD-ROM, Volume 1. J. Paul Robinson, Purdue University, 1996.
4. Purdue Cytometry CD-ROM, Volume 2. ISSN 1091-2037. J. Paul Robinson, Purdue University, 1996.

0197-1859/97/$0.00 + 17.00

TISSUE ENGINEERING
Volume 4, Number 2, 1998
Mary Ann Liebert, Inc.

Small Intestinal Submucosa: A Tissue-Derived Extracellular Matrix That Promotes Tissue-Specific Growth and Differentiation of Cells *in Vitro*

SHERRY L. VOYTIK-HARBIN, M.S.E.E., Ph.D.,[1] ANDREW O. BRIGHTMAN, Ph.D.,[1] BEVERLY Z. WAISNER, B.S.,[2] J. PAUL ROBINSON, Ph.D.,[2] and CARLTON H. LAMAR, D.V.M., Ph.D.[2]

ABSTRACT

The importance of understanding cell–extracellular matrix (ECM) interaction is now evident as scientists, engineers, and physicians search for novel scaffolds that support and maintain tissue-specific cellular growth and function both *in vivo* and *in vitro*. Small intestinal submucosa (SIS) represents an ECM that has been derived from porcine intestine while preserving its natural composition and architecture. More recently, an extract of this physiologic ECM, which forms a three-dimensional gel *in vitro*, has been developed. When compared to routinely used culture substrata (e.g., plastic, Vitrogen, and Matrigel), intact SIS and SIS-derived gel possess unique compositional and architectural features. Simple squamous epithelial (pulmonary artery), fibroblastic (Swiss 3T3), glandular epithelial (adenocarcinoma), and smooth muscle-like (urinary bladder) cells were seeded upon intact SIS and SIS-derived gel and their morphologic response evaluated. For each of the four cell types studied, intact SIS and SIS-derived gel were equivalent or superior in their ability to support and maintain expression of tissue-specific phenotype when compared to the routinely used substrata, plastic, Vitrogen, and Matrigel. Therefore, SIS may provide a novel biologically derived scaffold for the growth and study of a variety of cell types *in vitro*. Such information regarding the influence of substrate structure and function on cell behavior will be useful in the development of successful tissue engineering strategies.

INTRODUCTION

INTERACTION OF CELLS WITH THEIR EXTRACELLULAR MATRIX (ECM) plays a crucial role in the organization, homeostasis, and function of all tissues and organs. It is the continuous cross-talk between cells and the surrounding matrix environment that orchestrates critical processes such as the acquisition and maintenance of differentiated phenotypes during embryogenesis, the development of form (morphogenesis), angiogene-

[1]Hillenbrand Biomedical Engineering Center and [2]Department of Basic Medical Science, School of Veterinary Medicine, Purdue University, West Lafayette, Indiana 47907.

This work was presented in part at the Inaugral Meeting of the Tissue Engineering Society, held in Orlando, Florida, December 13–15, 1996.