Bio-Rad MacReader ELISA Reader Software

ELIOT M. HERMAN

Plant Molecular Genetics Laboratory, Agricultural Research Service, United States Department of Agriculture, Beltsville, Maryland 20705

Received September 16, 1987

INTRODUCTION

Enzyme-linked immunosorbent assays (ELISA) are currently the method of choice in the detection and quantitation of low concentrations of specific antigens by specific antibodies. The assay is widely used in basic science, in monoclonal antibody selection, and in serological detection of viral infections. For example, the method currently used for the initial screening of patients infected with HIV, the causative agent of AIDS, is a very sensitive ELISA assay. ELISA assays are most often accomplished by adsorbing the material to be tested (the antigen) to plastic microtiter plates that consist of a grid of small wells in an 8 × 12 format [96 wells/plate]. The plate is then incubated with the specific antibody that binds to the antigen and then with a second antibody that binds to the first antibody, which is coupled to an enzyme that produces a colorimetric reaction. The formation of enzyme product is proportional to the amount of antibody bound. As a consequence, the total concentration of the antigen can be calculated by comparison with a set of standards. The ELISA plates are read in a specialized spectrophotometer called an ELISA reader. Each plate generates 96 separate readings, but since a given experiment may easily use 20 or more plates, some method of computer-mediated data management is very desirable.

SETUP

The equipment used is a Macintosh Plus computer with dual disk drives. The software occupies about 330 kB with an unmodified system file. The software requires the following hardware: a Bio-Rad 2550 ELISA reader connected to the Macintosh serial connector by an RS-232 interface. The total cost of the hardware is $8000 for the ELISA reader, $500 for the RS-232 interface, and an excessive $125 for the cable to connect the Macintosh serial connector to the RS-232. Installation is simply a matter of connecting all of the cables into the appropriate outlets.

SOFTWARE USE

The documentation is complete and straightfoward. The widespread use of ELISA in medical laboratories where the assays are primarily run by medical assistants was apparently taken into account when the documentation was prepared. The software documentation describes the stepwise use of the software in increasingly more sophisticated uses. Every menu command is described. In the few places where an individual menu command may result in the irreversible loss or modification of the data, an appropriate warning is present in the manual.

The software setup requires a stepwise analysis of the experiment used to set up the ELISA assay. The format of the plate is specified by mouse clicking an 8 × 12 format displayed on the Macintosh screen. The wells that contain blanks, standards, positive controls, and negative controls can be specified as shown in Figure 1. Alternately, one of four different commonly used formats specified in the software may be used. As many as three different plate assay chemistries

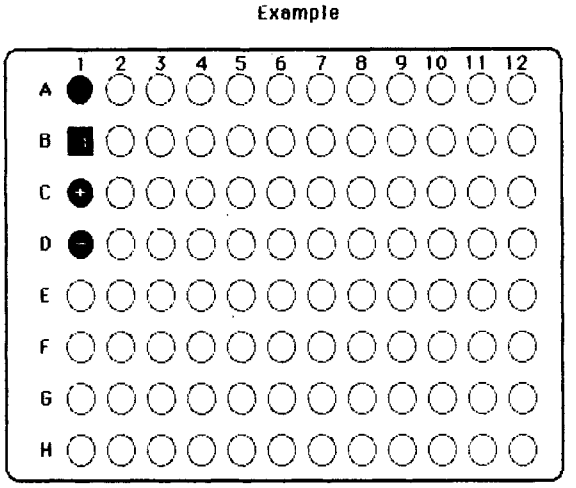

Figure 1. Setup for format of an 8 × 12 96-well ELISA plate. In this example the well A1 is shown as blank, B1 is a standard, C1 is a positive control, and D1 is a negative control. The graphic display of the ELISA plate and the ability to easily specify which wells contain various types of controls is one of the best aspects of the basic mode of the software.

can be defined, although most commonly only a single chemistry is used per plate. After the plate conditions are defined, the plate is read by menu command. The software does not ask for experimental information until the command to read is activated. The program then asks for *assay number*, *plate number*, *patient*, *chemistry*, and *name of analyst* and offers a small note pad for four lines of specific notes. After this information is recorded, the computer proceeds to read the plate. The orientation toward medical tasks is clearly shown by the pattern. If the information was inserted during the plate definition phase, it could result in a mixup between patients with possible adverse consequences. However, for basic science uses it would be better to record the information during the setup phase. It is unfortunate that the program is not offered in either basic science or medical formats. The differences in the lines of code required to be written would be quite small.

Although the setup and the design of the software do have some faults for basic science uses, when the software is used in the advanced modes, it really proves its usefulness. Full menu options are available to permit analysis, quantitation, and graphing of the ELISA results. For example, the software offers canned commands for analysis of serial dilutions of specific antigens that are used to quantitate concentration of an unknown. The standards can be graphed out by menu selection, and the concentration of the unknown may be readily determined. Options permit other dilution factors to be used to customize the analysis. Obviously incorrect data can be flagged on the 8 × 12 format, and these outliers can be removed prior to analysis and graphing. Other menu commands permit rejection of data outside specified lower or upper limits.

PROBLEMS

Reading the plate is a far more complicated process than it should be with a computer of the capability of the Macin-

tosh. To read a plate, the *read plate* command is pulled down from the menu; a plate identification format appears that includes information such as *patient*, which, while it can be ignored, indicates that the software assumes a medical testing laboratory. This can be by passed by clicking the mouse; a dialogue box then appears instructing to press *start* on the ELISA reader. It is necessary to click *OK* on the Macintosh and then to press *start* on the ELISA reader, which is very cumbersome. This process is repeated for reading several plates, which requires a number of mouse clicks and repeated physical movement from the ELISA reader to the Macintosh and back again. This type of user interaction will help ensure against errors by slowing down the process and by making every step in the analysis deliberate. This may be necessary in a medical testing environment where the technical staff may not understand the underlying basis of the equipment use and there is the ever-present possibility of litigation for errors. A more streamlined version that is completely controlled from the Macintosh, which deletes the *patient* designation for the samples, would be useful for basic science laboratories.

The results are saved in an 8 × 12 spreadsheet format that may be exported by menu selection to ASCII text format (for MACWRITE use) or more usefully as Microsoft EXCEL format. The ability to directly transfer several thousand data points into a powerful spreadsheet program is of great potential use. However, it must be noted that if data are exported in either ASCII or EXCEL format, only the actual data are transferred and all identification with regard to format or data manipulation done in MACREADER is lost. If the data are not saved in MACREADER format first and then transfered to ASCII/EXCEL as a SAVE AS command, then essential information that cannot be retrieved is lost.

The software is written in Microsoft Basic, and as a consequence of being written in a higher level language, the software can be much slower than is usually expected from a program running on a Macintosh Plus. If multiple screens are opened, the program greatly slows down and runs at an irritating snail's pace.

CONCLUDING COMMENTS

The MACREADER software provides a valuable interaction between the Macintosh computer and the Bio-Rad 2550 ELISA reader. In the basic mode the software can be irritating to use due to its orientation toward the medical testing laboratory. However, the ability to easily record, manage, and manipulate several thousand data points still makes the software useful. In the advanced modes the software is more oriented toward basic science uses and has many features, including the ability to analyze and quantitate unknown samples. Perhaps Bio-Rad will consider providing future versions of the software programmed in assembly language to speed up the processing and to offer a basic science version.

BOOK REVIEWS

How to Find Chemical Information. A Guide for Practicing Chemists, Educators, and Students. Second Edition. By Robert E. Maizell (Technology Information Consultants). Wiley-Interscience, New York, 1987. xvii + 402 pp. $44.95.

The strength of this book lies in its organization. Infrequent users of chemical information resources can quickly and easily locate the tools that exist, determine how they are used, and select the appropriate pathway for solving a given problem. In addition, the comprehensive treatment of many topics allows it to serve equally as a text for the student of chemical information. Updated and expanded from the 1979 edition, it has over 50% more pages; because of reformating, there is more information per page. This edition has 19 chapters, 4 more than the earlier, and the material in 3 chapters has more than doubled. There is an unusual amount of history about Chemical Abstracts Service, which those interested in the topic will find very informative and useful.

The first three chapters are very brief: basic principles, communication of chemical information, and formulation of search strategies are surveyed. Chapter 4 discusses current awareness programs and includes, at the end, a list of addresses and telephone numbers of organizations that are referenced. Similar listings are found in other chapters throughout the book. Chapter 5 focuses on obtaining source documents. Abstract and indexing services are covered in the next three chapters with the chief emphasis on Chemical Abstracts Service: its history, development, organization of the abstract issues, and use of the indexes and support publications. Governmental technical information centers are detailed in Chapter 9.

Online databases is the one area of chemical information that has changed most significantly in the years between editions of this book. Maizell allots one-eighth of the present text to the content of online databases, textual and chemical structure search strategies, suppliers, and costs. The descriptions of databases in this chapter allow users to determine which vendors and files would be most useful for a given search.

Chapters 11 and 12 discuss the roles and uses of reviews, encyclopedias, handbooks, and other reference works. The patent literature is covered in Chapter 13: why patents are important, the unique function they serve, and patent information services. To locate sources of patents, readers must also consult Chapter 5, which lists over 60 libraries that maintain numerical sets of U.S. patents.

Reflecting the author's long-term industrial background, the next five chapters deal with locating and using information on safety, chemical marketing, process information, chemical analysis, and physical property data. These are especially useful since source documents on some of these topics are difficult to locate. The references included in the chapter on numeric data are comprehensive and complete.

The concluding chapter summarizes briefly the highlights of the text and points to future trends. Maizell emphasizes the delivery of chemical information as the area where significant changes will occur in the next few years.

Finally, a principal strength of any reference book is its index. A new Name Index has been added and the Subject Index more than doubled. Index entries in this volume allow readers to locate needed material easily and directly.

David F. Zaye, *Chemical Abstracts Service*