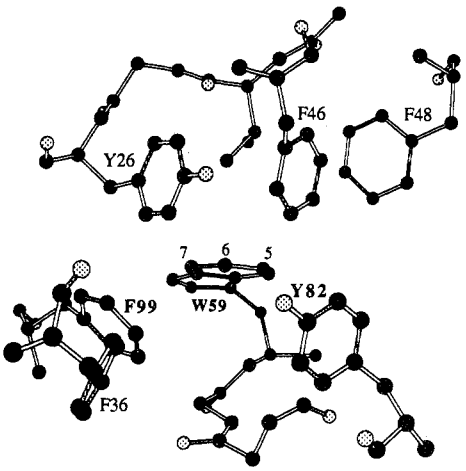

Figure 3. External view of the drug binding site of the unbound protein. The pipecolinyl ring of FK506 is in close proximity to W59 [H(5), H(6), and H(7)] and two additional aromatic residues, possibly F99 and Y82.

preliminary analyses suggest that the additional pipecolinyl–aromatic NOEs may be due to Tyr 82 and Phe 99. The FK506- and rapamycin-binding immunophilins of M_r 13000 and 30000[4] have sequences related to that of FKBP and, like FKBP sequences from other organisms, have high conservation of the aromatic residues that comprise the binding site, including Trp 59, Tyr 82, and Phe 99 (Figure 3).[17] Thus, we expect the structural insights concerning the ligand–receptor complexes reported herein to be relevant to other members of this family of immunophilins.

Acknowledgment. We thank the National Institute of General Medical Sciences (GM-38627, awarded to S.L.S.; GM-30804, awarded to M.K.) for support for this research. National Science Foundation predoctoral fellowships to T.J.W. and M.K.R. are gratefully acknowledged. NMR spectra were obtained through the auspices of the Harvard University Department of Chemistry Instrumentation Center, which was supported by NIH Grant 1-S10-RR04870 and NSF Grant CHE 88-14019.

(17) Galat, A.; Lane, W. S.; Standaert, R. F.; Schreiber, S. L., in preparation.

Computer Software Reviews

Regression. Windows Version. Blackwell Scientific Software, BSP Inc.: 3 Cambridge Center, Cambridge, MA 02142. List price (single installation) $225.00, additional installations $85.00 each, department license (extra) $225.00, academic discount 20%.

Regression is a math-utility program that fits a function to data. Regression can be run on IBM compatibles (with Microsoft Windows version 2.0 or above, at least 512 Kbytes of memory and a mouse) or any Apple Macintosh (with at least 128K of ROM). The use of a hard disk greatly facilitates the use of this software.

The data consist of up to 100 pairs (x,y) and can be input by hand within the windows environment or imported as an ASCII file. The model function used to fit the data is constructed in the Windows environment just as one would write it as a line of computer code. The function ($y = f(x)$) can be of any form (linear or nonlinear) and can include up to 10 parameters to be determined by the program and 10 predefined constants. The model functions can be saved and retrieved. A number of model functions, such as exponential decay, Gaussian distribution, and reaction kinetic equations, are provided. It is very easy to edit both the function and the data in the Windows environment.

The parameters in the model function are determined by minimizing the sum of the squares of the residual errors between the model ($f(x)$) and the data (y). The minimization is accomplished by the Marquardt or simplex algorithm (user's choice). The iterations continue until a specified number of iterations is reached or the errors in the parameters fall below a specified maximum value. The documentation on the algorithms is minimal, but references are given for both algorithms and for the actual programming code.

The program outputs a plot of both the original data with the fitted function and the residuals. The program used in this laboratory gave some problems with the graphics output (the axes and the fitted function were missing). The program also outputs the sum of squares of the residuals and the standard deviation $(SS/df)^{1/2}$ to aid in the interpretation of the goodness-of-fit of the model function.

Regression achieves what it claims to do and is easy to learn to use. The ease of creating and fitting any type of function, especially nonlinear functions, makes Regression a valuable program. However, there are serious limitations to its use that are not readily apparent. The first and most important shortcoming is the limit on the number of data points allowed. While 100 data points may be sufficient in some types of work, much greater amounts of data are generated in most modern computer-oriented laboratories and a maximum input of 100 data points is a serious limitation. Furthermore, the user is only allowed a single independent variable which rules out the use of Regression in any multivariate experiment. These two limitations make Regression unsuitable for many applications.

One further limitation in the software and documentation is that the concept of goodness-of-fit and the significance of a model is given a very cursory treatment. The user needs to have some background in statistics in order to properly use this software. It is all too easy to produce untrustworthy results with any fitting algorithm and it is important for a program to include an indication of the uncertainty in the parameters. Regression does so in a very limited fashion.

Regression was tested against some software written in this laboratory for doing curve fitting. A spectrum was generated as the sum of three Lorentzian peaks (with no noise), and Regression and the in-house program were used to recover the parameters of the peaks. Both programs used the Marquardt algorithm, but the in-house program was written specifically for Lorentzian curve-fitting, i.e. it included the partial derivatives determined symbolically and not numerically as in Regression. Both programs were successful at fitting quite simple problems (resolved peaks) and both programs failed at fitting extremely ill-conditioned problems (heavily overlapped peaks). There were some cases where the in-house program was able to fit spectra that Regression could not (even when Regression was given a starting guess very close to the true answer). The conclusion is that a program written specifically for the work at hand can perform better than Regression.

One more point that should be noted is that the actual algorithms in Regression are quite simple. Most of the program is probably devoted to the input, editing, and interpretation of the model function. The price of Regression is quite high for the simplicity of the algorithmic work done on the data.

The researcher thinking of purchasing a function fitting program should consider several questions very carefully: how many data points will normally be used; will any multivariate data be used; how ill-conditioned is the problem; and can the necessary programming be done in-house? If the work being envisioned is within the capabilities of Regression then it is a useful program. If not, then one is better served by writing the software in-house specifically suited to the problem.

Jonathan H. Perkins and Peter R. Griffiths, *University of Idaho*

Theorist. Version 1.01. Prescience, Inc.: 814 Castro St., San Francisco, CA 94114. (415) 282-5864.

Theorist is a new WYSIWYG symbolic algebra and graphing program for the Macintosh Plus, Portable, SE, SE/30, II, IIcx, IIci, and IIx computers. This program allows the user to interactively manipulate and graph mathematical expressions and relationships as they appear in books and journals with the ease of a mouse-oriented text editor. Mathematics, graphs (2- and 3-dimensional), and commentary text are all combined in one Theorist document called a "notebook".

The progam is shipped on two 3.5-in. double-sided double-density disks that are not copy protected to allow for personal backup copies only. Disk

one contains a version of Theorist compatible with all Macintosh computers equipped with enhanced 128K ROMs and 1MB memory. Disk two contains a special "souped up" version of Theorist, specifically designed to utilize the high-speed capabilities of the Mac II, IIx, IIcx, IIci, and SE/30. The difference in operation speed between the two versions is quite notable. Both disks contain folders with sample "notebooks" containing graphics, mathematics, and transformations (i.e. Bessel functions, spherical harmonics, γ functions). Color graphics are also supported. The Theorist package also includes spiral bound "Reference" and "Learning Guide" manuals. Due to the extensive features and abilities of Theorist, thorough reading of these manuals is necessary before full application of the program can be realized.

From the first use of Theorist, it is apparent that this is a very powerful and open-ended math program. Equations can be entered to the program either with the mouse or through the keyboard in "Normal" or "Fortranish" mode. "Fortranish" is a very useful feature of Theorist for keyboard entry. With this mode, the user can type in equations on the keyboard in the format used in programming languages. As they are typed, they appear in standard notation on the screen. This feature greatly assists new users in mastering this complex program. Mouse entry is accomplished with the "Equations Palette". This palette contains almost all the symbols, variables, functions, and operators available to Theorist. A bar at the top of this palette gives a continuous display of Theorist's memory consumption (which at times can become quite voracious).

Theorist comes equipped with a wide host of mathematical features including non-commutative algebra, complex numbers and functions of complex variables, integration, differentiation, trigonometry, and matrix and linear algebra. In addition, Theorist allows the user to define and program custom "Transformation Rules" using wildcard variables which are substituted for upon execution of the "Transform", "Expand", or "Simplify" commands. This feature makes Theorist especially powerful and expandable. For instance, by defining a recursion relationship for Legendre polynomials in a "Transformation Rule", the user can generate all the polynomials simply by typing $y = P_n(x)$ (with the appropriate value for n) in the "notebook" and choosing the appropriate command from the menu. The equation then transforms into polynomial form. Trigonometric substitutions can also be programmed with this feature. The folders on the Theorist disks contain whole libraries of these transformations which are in essence entire CRC style math tables containing the proper transformation equations for Chebyshev, Legendre, spherical harmonics, Bessel, γ, erf and other special functions. After performing necessary simplifications and transformations, the "Calculate" command allows for numerical solutions with up to 19-digit precision.

Theorist also makes extensive use of the mouse's "point and click" ability for performing mathematical manipulations. With the mouse, the user is able to isolate a single variable in a polynomial thus "solving" for it. Entire expressions can be moved and substituted into other expressions with the mouse as well. Solving a system of linear equations is fast and easy with these mouse-oriented substitutions. Furthermore, Theorist's menu contains commands (with keyboard equivalents) for all the available features.

In the "notebook" document. text, comments, definitions, equations, derivations, and graphs are automatically outlined, placing derivations and graphs as subcategories of the original equations. In the case of multiple solutions to an equation (i.e. a quadratic), Theorist automatically establishes "Case Theories" each containing a possible solution. All this is accomplished with no effort on the part of the user. Although the equations appear in standard notation on the screen, they are bitmapped upon printing. A separate program called Expressionist is recommended by the designers of Theorist for publication quality printouts of these expressions.

The most attractive and impressive feature of Theorist is its interactive graphing utility. Theorist comes equipped to produce stunning plots in two or three dimensions. Two-dimensional plots can be generated for equations in rectangular or polar coordinates. Contour maps of density functions in two dimensions can also be generated. Three-dimensional graphs support rectangular, spherical, and cylindrical coordinates. In addition, through the use of a user-defined transformation rule, other coordinate systems can be supported as well. Graphs in Theorist are interactively related to their parent equations. If a change is made in the original equation, the graph immediately and automatically adjusts to compensate. Every feature of the graph can be completely controlled and manipulated by mouse-selection. Three-dimensional surface plots appear as illuminated (shadowed) opaque surfaces on black and white monitors, while additional options of transparent and translucent plots exist for color monitors. One impressive feature for color plotting is the ability to directly map the color scheme to some function of the coordinates. For example, the amount of yellow at a point on a spherical surface plot could be mapped directly to represent the value of θ at that point, or the saturation and hue could be mapped to represent the real and complex parts of the value of a complex function. With the mouse, the user can rotate a 3-d graph, or shift the point of view on a 2-d graph. Effects of "zooming in" and "zooming out" are also supported as well as the ability to alter the resolution of the graph. A "graph details" window gives extensive control over every remaining aspect of the graph, including the range of each variable, position and labeling of axes, texture and color of the surface, appearance of a "wireframe" on a surface, cropping, and through what type of "lens" a three-dimensional graph is seen.

In addition to the graphing features listed above, Theorist also features built-in graphic animation. An animation parameter is added to the original equation and serves as the time-dependent factor in that equation. Selecting "Animate" from the "Graph" menu generates a series of sequential plots with progressive values for the animation parameter. The graphs then form a "movie" allowing the user to see the evolution of the expression with the changing parameter.

Although Theorist offers no specific chemistry-related features (except perhaps for the "Electron Orbital" graphics example included on the program disk), it is a versatile and powerful mathematical tool, useful in both scientific and educational applications.

John P. Feagins, *The University of Texas at Austin*

Chemintosh II. SoftShell International Ltd.: 2754 Compass Drive, Suite 375, Grand Junction, CO 81506. List price $595.00; academic discount directly from vendor $395.00; student price $95.00; free demo.

Chemintosh is a drawing tool for the Macintosh that incorporates many of the useful features of both MacDraw (see review, *J. Am. Chem. Soc.* **1985**, *107*, 6140) and ChemDraw (see review, *J. Am. Chem. Soc.* **1988**, *110*, 7260). It is extraordinarily easy to use for anyone who has had drawing experience with either ChemDraw or MacDraw as well as for the beginner.

Most of the drawing tools are specialized for organic structures and include polygons from 3- to 8-sided, a benzene ring, and both a chair and a boat cyclohexane. Predefined bold and dashed lines are also included both with parallel sides and as wedges. There are reaction, equilibrium, and resonance arrows predefined as well. In addition, there is a single bond drawing tool as well as one that permits the creation of "regular zigzag" acyclic chains. When this tool is used, the number of bonds involved can be changed merely by dragging the mouse from the origin point and this number is displayed as well. Bonds and rings can be added to previously drawn structures and will lock in precisely to previously defined atom positions. Pieces added to an existing structure are automatically grouped and this grouping cannot be undone. However, there is a very convenient erasing tool that allows either bond or atom deletion. In the case of atom deletion, all bonds to that atom are deleted as well.

When rings are added to pre-existing structures, the user has full control as to whether they are joined in a spiral, fused, or bridged fashion. When new lines are added on top of structures so that they cross existing lines, the bond behind is broken to give a three-dimensional perspective. Once created, the horizontal, vertical (or both) dimensions of the drawings can be modified. This allows the user to readily construct figures that represent depth. In addition, there is a tool which allows rotation of defined objects as well as flipping objects both in the vertical and horizontal sense. Text is unaffected by these operations. Also included is a collection of s, sp-hybrid, and d orbitals as well as predefined electron pairs, radical cation, anion symbols, and simple charges.

There are two text tools, one for adding captions and the other for adding atom labels to structures. The latter automatically positions the label on top of the atoms and hides the bonds behind. The appropriate label is typed into a small window at the top of the screen where the program automatically assumes that numbers are to be subscripted. Clicking, then, on any atom will incorporate the predefined label. The text incorporation mode also permits all of the stylistic changes that one has available in Microsoft Word (italicizing, super- and subscripting, etc.).

In addition to the above, the user has the option of loading, as easily accessed sets, structures previously created in Chemintosh documents. A large collection of predefined structures is provided, including, for example, all the common amino acids and carbohydrates.

One cute feature of the program is the ability to display optional help screens which dynamically change as the user moves through drawing operations. The help window displays text as well as pictures that show how each individual tool is used once it is selected. There is also an optional help pane that explains what options are available as the cursor is moved around the screen. The reviewer found this help feature extraordinarily annoying as it constantly changed as the cursor was moved. However, the user is under no obligation to display this help pane.

All of the drawing object sizes can be changed to match the user's individual preferences. Line lengths and widths are definable in pictal increments and the font and style for each text tool can be set individually. Several preference files can be established and switching from one to the other is quite straightforward.

Overall, the program is simple to use and comes highly recommended. The reviewers have used MacDraw (in preference to ChemDraw) for many years but switched to Chemintosh II ten minutes after the package was first examined.

Susie Pruett and James K. Whitesell, *University of Texas*

Book Reviews

Chiral Liquid Chromatography. Edited by W. J. Lough (Sunderland Polytechnic, UK). Routledge, Chapman & Hall: New York. 1989. ix + 276 pp. $112.00. ISBN 0-412-01741-5.

This book is a review of the various aspects of the development and applications of chiral liquid chromatography. It is organized in five parts with a total of 16 chapters plus an appendix and an index. The titles of the five parts are the following: (1) Introduction, 3 chapters; (2) Chiral Derivatization, 1 chapter; (3) Direct Chiral Resolution, 8 chapters; (4) Strategy for Development of LC Enantiomeric Determination Methods, 3 chapters; and (5) Future Trends and Requirements, 1 chapter. Each of the chapters includes summary tables of useful information. Extensive references to the scientific literature are accumulated at the end of each chapter. The introductory chapters on Molecular Asymmetry; The Importance of Enantiomer Separations; and Chiral Liquid Chromatography: Past and Present give an important perspective to the book. Chapter 4 on Chiral Derivatization is particularly well done with an extensive table of derivatization reagents. Part 3 includes chapters on Chiral Ligand Exchange Chromatography; Synthetic Multiple-interaction Chiral Bonded Phases; Immobilized Proteins As HPLC Chiral Stationary Phases; Cyclodextrin Inclusion Complexation; Binding To Cellulose Derivatives; Binding To Synthetic Polymers; Ion-Pairing; and Other Direct Chiral Resolution Methods. Each of these chapters gives a good introduction and overview to the particular technique and examples of applications. Part 4 includes chapters on Consideration Of Other Techniques; Choice Of Chiral LC Systems; and Optimization. Chapter 13 discusses what other techniques, including spectroscopic and chromatographic, have to offer for enantiomeric determinations. Chapters 14 and 15 then deal with the development and optimization of the separation in actual problems.

This reference book has done an excellent job of organizing and summarizing the development of techniques and separation methodologies for the separation and analysis of enantiomeric mixtures. The organizational approach taken of presenting the information according to the chiral recognition mechanism was an excellent and appropriate choice on the part of the editor in recognition of the rapid developments in this field and also the volume of the contributions to the literature. The recently adopted regulations by the Food and Drug Administration regarding chiral purity and pharmacology of individual enantiomers focus increased attention on the methods discussed in this book.

This book is to be highly recommended to a wide range of research personnel that use liquid chromatography techniques particularly those in biochemistry and the pharmaceutical sciences. It is a very complete and a useful and timely reference book.

Bruce L. Currie, *University of Illinois at Chicago*

Enzyme Chemistry: Impact and Applications, Second Edition. Edited by Colin J. Suckling (University of Strathclyde, UK). Chapman and Hall: London. 1990. xii + 383 pp. $79.95. ISBN 0-412-34970-1.

C. J. Suckling has assembled eight interesting reviews in the general area of enzyme chemistry. These articles cover a broad spectrum of subjects within enzymology and enzyme chemistry and are specifically written from the point of view of the chemist. The book opens with a set of three general reviews which introduce and discuss "The mechanistic basis of enzyme catalysis", "Chemical models of selected coenzyme catalyses", and "Selectivity in synthesis-chemicals or enzymes". The focus then shifts, and specific topics are discussed in more detail. This includes chapters on "Enzymes as targets for drug design", "The impact of metal ion chemistry on our understanding of enzymes", "The enzymology of the biosynthesis of natural products", and "Enzymes in the food industry". Finally, this second edition of *Enzyme Chemistry* concludes with an article that strays away from the chemical focus of the book and touches on the current application of molecular biology to enzymology.

The objective of *Enzyme Chemistry* is to introduce the chemist to enzymology. As a result, the articles are written to address a chemical audience, and a good foundation in basic chemistry is required to appreciate this book. Furthermore, since a number of chapters focus on the enzymatic catalysis of organic reactions, *Enzyme Chemistry* should be of particular interest to the organic chemist.

Overall, the articles are well-written and well-edited. Each provides a thorough and scholarly account of the topics that are reviewed, and each emphasizes the basic chemistry involved in the study of enzymes and enzyme mechanisms. *Enzyme Chemistry* succeeds in illustrating that fundamental chemical problems are interwoven into biological systems and shows the necessary intermingling of chemistry with enzymology. Although the articles are written to introduce the chemist to enzymology, the articles are presented at a sophisticated level; consequently, *Enzyme Chemistry* is an excellent compendium of reviews that can be appreciated by both chemists and enzymologists.

Richard A. Ikeda, *Georgia Institute of Technology*

Rings, Clusters, and Polymers of Main Group and Transition Elements. Edited by H. W. Roesky (Universität Göttingen). Elsevier: Amsterdam. 1989. xii + 548 pp. $170.75/Dfl. 350.00. ISBN 0-444-88172-7.

The chemistry of rings, clusters, and polymers is becoming an important branch of inorganic and organometallic chemistry. Such compounds are of interest because of their unusual properties and their potential for applications in the areas of catalysis, electronics, and ceramics.

This book is divided into the following eleven chapters: (1) Boron, Aluminum, Gallium, and Indium with Oxygen and Sulfur (Bowser and Fehlner), which emphasizes mainly boron; (2) Boron Hydride Clusters (Greenwood), which includes the deltahedral boranes and which is organized according to the number of boron atoms; (3) Polysilanes (Hengge and Stüger); (4) Germanium–Carbon Rings (Mazerolles); (5) Rings with Phosphorus–Carbon Multiple Bonds (Fluck and Neumüller); (6) Azaphospholes (Schmidpeter and Karaghiosoff); (7) Multiple Bonds Between Transition Metals and Main Group Element Atoms (Herrmann); (8) Unsaturated Four-, Six-, and Eight-membered Metallaheterocycles and Metal-Containing Polymers (Roesky); (9) Organometallic π-Systems (Huttner and Lang); (10) Polynuclear Transition Metal Complexes with Sulfur Ligands (Krebs and Henkel); and (11) Clusters of Metals and Nonmetals (Whitmire). The authors of all of these chapters are authorities in their fields and the coverage is excellent with numerous literature references at the ends of the chapters. There is also a short (6 pages) subject index.

This book covers many areas of descriptive chemistry that are important in modern inorganic chemistry, particularly the chemistry of the non-transition elements. However, there are also some notable omissions. Boron–carbon and silicon–carbon rings are not covered in the book even though the less important germanium–carbon rings are covered. The inclusion of "polymers" in the title may mislead some readers to expect much more inorganic polymer chemistry than is actually present in the book. Despite these omissions this book is an essential addition to any library collection in inorganic chemistry.

R. Bruce King, *University of Georgia*

A Computational Approach to Chemistry. By David M. Hirst (University of Warwick, England). Blackwell Scientific Publishers: Cambridge, MA. 1990. viii + 444 pp. Paperback: $39.95. ISBN 0-632-02743-6. Hardback: $78.95. ISBN 0-632-02431-3.

In this book Hirst surveys a number of commonly used computational chemistry methods: molecular electronic structure, molecular mechanics and dynamics, chemical reaction models, and statistical mechanics of liquids. For each topic, the background of each method, basic theory, and examples of calculations are given. Many subtle features are covered, without complicating the picture with detailed references to specific software packages. Each chapter also contains an extensive list of current literature references for further reading. A logical companion to a course based on this book would be a laboratory sequence using actual programs