fered by David Green and Trevor Falloon are perhaps the most controversial elements of the book. Mineral physics and its relationship to seismological data, particularly for the lower mantle (the "big" question), are thoroughly treated by Ian Jackson and Sally Rigden. The seismology chapter is perhaps the one disappointment. Given the achievements of its authors, Brian Kennett and Robert van der Hilst, and the remarkable accomplishments in this field in recent decades, one might have expected a more comprehensive treatment of what we have learned and hope to learn from both tomographic (3D maps of seismic velocity anomalies) and regional radial profiles.

The Earth's Mantle fills an important niche. It is not a text, but a source for ideas and current understanding. Although it is a snapshot of a rapidly evolving field, this compilation will be useful for many years. It is well produced, well edited, and up-to-date (with references through at least 1996). It is not quite as coherent as a monograph, but lacks the idiosyncrasies that often arise in books with single authorship. It is much more cohesive than conference proceedings or a set of review papers, and provides frequent cross-referencing. (The authors appear to have read each others' contributions!) I strongly recommend the volume to researchers and students interested in Earth's mantle; others outside the field will also find it a stimulating overview of this exciting area.

NEW MEDIA: SOFTWARE

Virtual Valet

Theo Dreher and Daiki Matsuda

There are a number of excellent software packages on the market that analyze nucleic acid or protein sequences and aid the molecular biologist in experimental design and interpretation. However, these packages do not qualify as a true electronic assistant capable of performing a virtual-reality cloning experiment. Gene Construction Kit 2 (GCK2) is an excellent program that does provide this service. GCK2, which runs on a Macintosh computer, can test the feasibility of cloning manipulations and assist in their design, and also can document and archive the precise sequence rearrangements of a cloning experiment in graphical or sequence format.

Gene Construction Kit 2
by Textco Inc.
West Lebanon, NH. Retail $1399; academic $999.
Phone: (603) 643-1471
www.textco.com

The essence of GCK2 is its ability to present a graphical diagram of DNA segments (for example, plasmid vectors and cloned insertion sequences) for easy interpretation, while maintaining a strict connection between all graphically displayed features and their actual DNA sequences. The view of a particular DNA construct can be readily switched from a graphical diagram to detailed sequence. DNA rearrangements mediated by restriction digestion and ligation can be performed by GCK2 using simple copying and pasting to produce files describing recombinant DNAs; ligations of incompatible termini are disallowed. Comments and descriptions can be attached to particular features of a sequence, and these are automatically retained in subsequent derivatives. All annotations, comments, and actual DNA sequences are searchable by a built-in search engine, so that an accessible archive of the recombinant clones in a laboratory can be assembled. Any clone from that archive can be graphically displayed in a number of ways.

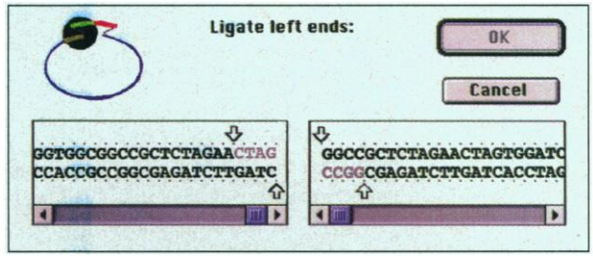

Fig. 1. Ligation Dialog Box. This box appears when ends are not compatible with insertion sites. The OK button remains inactive until the segment ends are made compatible by adjusting arrows above or below the sequences, corresponding to filling in or removing overhanging termini. In this example, one terminus has a 5′ overhang and the other is blunt.

Basic format

GCK2 is built around four window types: Construct, Gel, Illustration, and List. The Construct window, the core of the program, is used to display a DNA molecule (in sequence or diagram form) and to perform actual DNA manipulations—restriction analysis, identification of open reading frames (ORFs), introduction of silent mutations to add or remove a restriction enzyme site, and ligation of DNA segments from various sources to produce recombinant molecules. The Gel window is used for analysis of DNAs from the Construct window by restriction digestion, with output as either a simulated gel electrophoresis run or a table. The Illustration window documents information about recombinant molecules manipulated in the Construct and Gel windows. Diagrams and figures from either of those windows, or elements from other word processing or drawing programs, can be directly copied into the Illustration window. The addition of text, arrows, and other elements is also supported by the drawing features of the Illustration window itself. The most remarkable feature of this window is that elements imported from the Construct or Gel windows retain most of their functionality, permitting immediate changes or adjustments in the format or information. The output from the Illustration window can be used as a description of the steps of a cloning experiment, to be added to a laboratory notebook or included in a publication. The List files contain the information used for finding restriction sites and specifying codon tables. List windows do not need to be accessed during routine work sessions, but they permit lists to be created or modified to customize restriction enzyme lists or compile lists of protein binding sites, promoters, and other features that then can be marked on diagrams of DNA molecules.

Virtual Cloning

Most manipulations in GCK2 are performed in the Construct window. Sequence files of many formats, including GenBank, GCG, and Staden, can be imported into this window, and linear or circular sequences are diagrammed to scale in colors of the user's choice. ORFs can be identified automatically and indicated in both sequence and graphical representations. Features such as ORFs, origins of replication, and promoters can be marked separately, and text annotations and comments (almost unlimited in size) can be attached to such DNA segments. Alternative "generations" or views of a molecule can then be produced (and stored in linked form for ready access) to highlight particular characteristics, and associated comments can be separately retrieved. This feature can provide details such as descriptions of the source of a DNA segment, its intended function, or where the source molecule is stored in the laboratory. In any subsequent manipulations of a particular segment, attached comments are retained.

To begin a virtual cloning experiment, restriction enzyme sites of various cate-

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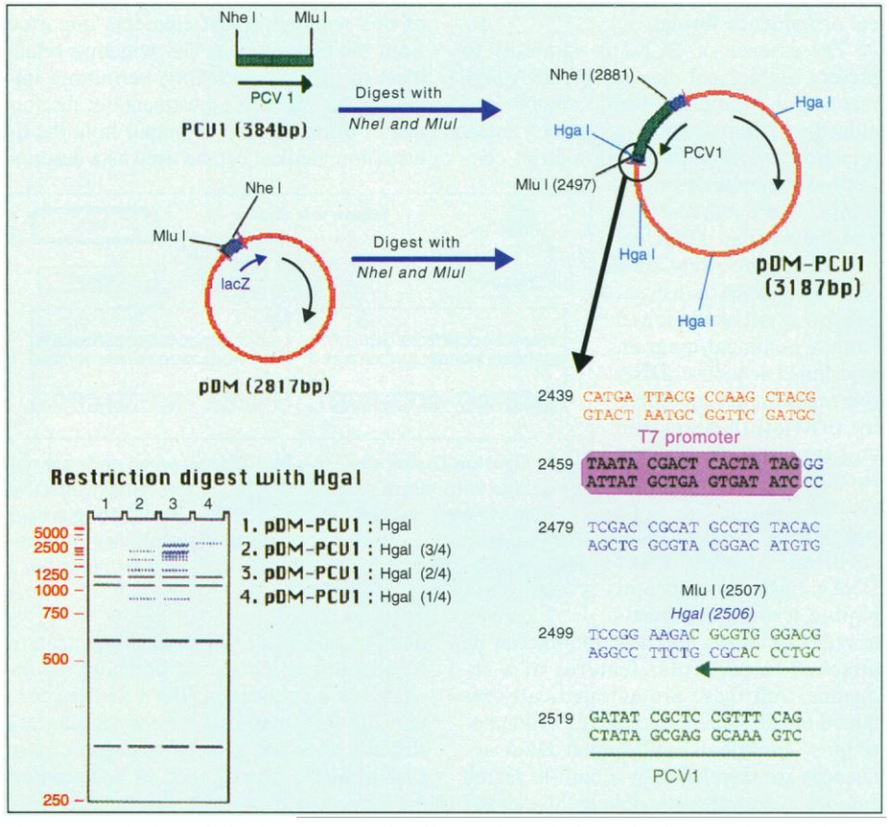

Fig. 2. Description of cloning steps in the Illustration window. The figure at lower left represents a simulated electrophoretic analysis of full Hga I digestion in lane 1 and partial digestion in lanes 2 to 4, where the partially digested fragments are shown in dotted blue lines. The extent of partial digestion can be selected, with three, two, and one cuts per molecule specified in lanes 2 to 4.

gories can be identified. When marked on the diagram of a DNA molecule, these sites act as boundaries for specifying DNA fragments that can be selected and copied to the clipboard and then deposited at a target restriction site in another molecule in a different Construct window by simply pasting; pasting can be an insertion at a single restriction site or a replacement of material between two sites. When DNA termini are incompatible, a very workable Ligation Dialog Box (Fig. 1) permits the user to fill in or remove overhangs before ligation is possible. The effect of these manipulations on protein coding regions can readily be assessed from the sequence view of the Construct window. A useful feature assists in adding or removing a restriction site by silent mutation.

Restriction sites selected from the Construct window can be pasted into a Gel window to readily produce a simulated electrophoretic analysis, including the simulation of a partial digestion (see Fig. 2). The pattern produced from gels of different concentrations can be approximated by choosing appropriate separation ranges (with a threshold setting defining the fragment size at the bottom of the gel). This is a powerful tool in selecting the best diagnostic restriction cleavages for verifying experimental constructs.

Multiple Constructs

The Illustration window is functionally very flexible; contents of the Construct and Gel windows can be copied into it, allowing a coherent description of a sequence of cloning steps to be assembled (see Fig. 2). Multiple views of a single construct, each emphasizing different features to prevent cluttering, or related constructs joined by arrows and text can be assembled in the Illustration window. Tabulated fragment sizes or simulated gel electrophoresis separations of chosen restriction digestions can be added to the Illustration. After assembly of the various elements into the Illustration window, last-minute adjustments are a simple matter, because Construct and Gel elements retain their activity.

A limited set of drawing functions are active when an Illustration window is open; text can be readily added in several styles, with multiple fonts supported. To overcome most deficiencies of the drawing functions, elements can be imported from other programs using the clipboard.

As with the other windows, printing is very well supported, producing a faithful high-quality representation of the active window. The contents of an Illustration window can also be exported as PICT files to other programs for production of slides or incorporation into a word processor file, although small format changes appeared during several trials.

Summary and Assessment

Gene Construction Kit 2 is a well-written program, well supported by the manual and by online help. Because it can show DNA molecules either in diagram form for overall clarity or in nucleotide sequence form for detailed analysis of junction sequences, it provides excellent assistance in planning cloning experiments. The graphical representations are flexible and of high quality, and the linkage to actual sequence functions reliably. Basic sequence interpretations that are important for planning cloning experiments—such as restriction mapping, translation, and presentation of protein sequence alongside its coding nucleotide sequence—are performed simply and flexibly. Graphics were loaded and refreshed extremely quickly in our tests with a Macintosh G3 computer.

Overall performance would be greatly enhanced by a set of buttons for easy access of common features that now are activated by mouse access to submenus or by triple-key typing; this is in most cases also true of zooming in and out. The current design may make it difficult for the more occasional user to effectively make use of the program because many of the most-used features are submenu items that are not visible on the screen until the parent menu is selected. In addition, the graphical and sequence versions of a Construct window, and the gel and tabular forms of a Gel window, cannot be viewed simultaneously.

In summary, GCK2 is an excellent program that can greatly assist the design and documentation of recombinant DNA experiments. The output is flexible enough to provide full information about a particular construct for a laboratory notebook, and its quality is high enough for publishing. The program can archive constructs along with extensive comments. The ability of GCK2 to search these comments, as well as the nucleotide sequences themselves, permits easy retrieval of information about long-forgotten clones that clutter the freezers of many molecular biology laboratories. The assistance of this well-designed electronic valet makes molecular biology more productive and fun, while keeping it neat and tidy.