MacLogP

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The ability of octanol−water partition coefficients to describe ligand lipophilicity has made the logP parameter a useful tool in classical quantitative structure−activity relationship (QSAR) analyses. The additive fragment-based clogP method has been developed to circumvent the tedious process of analytical determination of logPs.[1] Previously available only on VAX/VMS computers or in UNIX on SGI or SUN workstations, clogP is now operational on Macintosh computers in the form of MacLogP[2] at a cost of approximately $400 for academic institutions.[3]

The software requires a Macintosh System 7 with a 68 020 cpu or better, 1 Mbyte of memory, and 1.9 Mbytes of hard disk space. Installation is straightforward requiring just a few clicks of the mouse to create a *Clogp 1.0* directory containing all of the relevant files—the clogP executable, electronic copies of the installation and user's guides, the library files, etc. The software is equally easy to implement with an on-line help menu available if necessary and several short-cut keys to speed up menu selections. The first time into the program requires the user to enter license information after which MacLogP starts up directly. A tutorial is provided in the user's guide but is not necessary for general use. It primarily points out specific fragment contributions to the hydrophobicity of a compound and outlines the correction factors implemented by clogP due to proximity effects, zwitterionic character, etc. A SMILES[4] tutorial is included as well.

The program consists of three primary windows: Input, Output, and Depict. The Input window accepts both common names (for most drugs and pesticides) and SMILES notation for single or batch mode calculations. The Output window gives the option of terse, detailed, or verbose results. In each case accepted measured values are included if available, and questionable results (due to missing or approximated fragment parameters) are highlighted. The detailed and verbose modes provide an accounting of individual fragment contributions to the calculated logP value. The Depict window displays a 2D illustration of the compound with polar fragments highlighted. Together the Output and Depict windows are very useful for identifying and visualizing individual structural contributions to the calculated logP.

In our analysis of the program we used a separate package to create SMILES notation for approximately 70 compounds and then used the batch mode to calculate logP values. The calculations took less than one minute total. The only immediate problems encountered with MacLogP included the size restriction on the Output text window which allows one to view the detailed results for approximately 25 compounds. When the size limitation is exceeded, earlier calculations are lost. This restriction will be eliminated in the next release of the program. It is often useful to tabulate logP values in a spreadsheet for QSAR analysis, and MacLogP does not provide a direct means to do this. The best alternative is to read the terse output into a spreadsheet program and then edit the file to remove extraneous information. The Depict window shows just one compound at a time. It would be useful to have the ability display two or more compounds concurrently to make direct structural comparisons. Finally, there is a documented bug that indicates some SMILES for compounds with greater than 60 heavy atoms will crash the program. However, this problem was not encountered in our evaluation.

As a whole the program was very easy to implement and provided a large amount of information on the structural contributions to hydrophobicity quickly and in a very user-friendly format. For more information regarding MacLogP and other programs available from BioByte connect to their World-Wide-Web site at http://medchem.claremont.edu.

REFERENCES AND NOTES

(1) Leo, A. J. *Chem. Rev.* **1993**, *93*, 1281.
(2) MacLogP is available from BioByte Corp., P.O. Box 517, Claremont, CA 91711, USA. Fax: (909)624-5509. Email: clogp@medchem.claremont.edu. Evaluation copies are available.
(3) The academic price includes an 800 kbyte disk and a user manual ($600 for government and $998 for commercial users).
(4) Weininger, D. *J. Chem. Inf. Comput. Sci.* **1988**, *28*, 31.

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