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A review of Innovative Chemical Drawing and Spectra Prediction Computer Software

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Abstract: In recent years there has been an increasing research emphasis on complex macromolecular systems. These include polymers and coordination compounds with precise control of structures, multicomponent systems with higher degrees of organization, they involved in confined environments, nanochemistry and nanostructures, biopolymers and bio-inspired chemistry. Successful Spectroscopic studies of these complexes require judicious applications of existing techniques and development of new or improved strategies and methodologies. In this article various Chemical drawing and Spectra prediction computer software are compared and analyzed for their role in research in complex macromolecular systems. We have compared various software like Accelrys (Symyx) Draw, ChemDraw (ChemBioDraw), DrawIt, ChemSketch, ChemDoodle, Chemistry 4-D Draw, MarvinSketch and MestreNova NMR Predict.

Keywords: Chemical drawing, spectral prediction, complex system, coordination compounds, Innovative strategies.

Introduction

The immense development of microelectronics has banished the use of typing machine, drawing pen, Indian ink and templates. Instead, text editors like MS Word, Corel WordPerfect, Lotus WordPro are of general use today. With the aid of these one can create professional looking articles and drawings, and a large amount of time for the rewriting, redrawing and making corrections can be spared as well. The creation of chemical structures with the conventional drawing software applications would be extremely painstaking and practically impossible. Now we have some drawing softwares which have built-in templates, bonds constrained to fixed length and angles, etc. which ensures ease in drawing. These software's also helps in prediction of spectral data and we can even draw 3D structures with help of them.

The presented drawing software applications work on the Windows or McIntosh platforms and some under Linux as well. Under the Windows OS most tasks (printing, screen and printer fonts, resolution or any other system wide parameter) are maintained by the Windows itself and its set-up is the determining factor. Another important point is the user-friendliness of the program. This means that the user interface of the program, which ensures the

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interactive two-way communication between the user and the machine, should be simple but effective. The information sharing with other programs should also be many-sided.

In this review the most popular publication quality chemical drawing software applications on the MS Windows platform are reviewed and a few others are mentioned briefly:

Accelrys (Symyx) Draw 4.1 Academic Edition (Accelrys)[1] (updated January 2013)
ChemBioDraw Ultra 13.0 (ChemDraw), (CambridgeSoft)[2] (updated November 2012)
DrawIt - KnowItAll Academic Edition 2013.1 (Bio-Rad)[3] (updated October 2013)
ACD/ChemSketch 2012 1.04 Free and Commercial (Advanced Chemistry Development)[4] (updated November 2013)
Chemistry 4-D Draw 8.4.6 Pro (ChemInnovation Software)[5] (updated October 2011)
ChemDoodle 6.0.0 (iChemLabs LLC)[6] (updated 1 December 2013)
MestreNova NMR Predict Desktop 9.0.0 (Mesterlab Research)[7] (updated on 27 December 2013)
MarvinSketch 6.2.1 (ChemAxon Ltd)[8] (updated on 28 February 2014)

Installation

The automatic installers of the programs support customized setup. As most of the programs comprise several optional modules, it is advisable to choose the custom setup mode and to select only the modules really necessary. All installation procedures were flawless except ChemBioOffice 13 Ultra[9]: even selecting the custom setup mode, the appropriate dialog window was not initialized and the full package was installed (checked under Windows XP, Vista and 7/64 versions). For some inexplicable reason this bug has slipped through the beta testing or is the side-effect of some last minute modification. This latest ChemBioOffice has other glitches, too: the startup of ChemBioDraw often got stuck at the splash screen, it was necessary to kill the process and to start over several times (WinXP and Win7/64).

Every program has one or more specific, proprietary input/output file formats with unique file name extensions. These associations are always entered into the Windows registry. Most programs are able to deal with several other file formats. During the setup process some programs are quite aggressive and change the file name associations set previously by others.

Fortunately, none of the reviewed chemical software applications behave this way and most of them are polite enough to ask in a dialog box how to handle the foreign file types (if the other program is also installed in your PC, don't allow to alter the corresponding associations).

File operations, data movement

Beyond the basic file input and output operations, the export and import facilities to/from other applications are of high importance. For example, if one has to import a 3D structure from a modelling program or embed an illustration created by another drawing program. Accelrys Draw has a narrow choice of export/import possibilities, mainly molecule and database file filters are available. Chemistry 4-D Draw accepts only MDL molfiles as well. MDL sketch files are supported by ChemDraw and ChemSketch, and vice versa, Accelrys Draw now supports the import of ChemDraw CDX files[10].

ChemDoodle also supports the most important foreign sketch files. However, be prepared for inaccuracies during the import: fine tuning of the imported sketches is usually necessary.

Of course, the not mutually supported features or objects will not be imported. ChemDoodle has export/import problems with some ISIS sketch files and ChemDraw files[11]. DrawIt often crashed when tried to open ChemDraw files. MarvinSketch has the Document to Structure input mode: it supports the grabbing and opening of embedded structures from common Office document formats: DOC, DOCX, PPT, PPTX, XLS, XLS, ODT in addition to PDF, XML, HTML and TXT[12].

ChemDraw, ChemSketch and DrawIt as these applications are suitable for creating big size posters containing a collection of several data types. If illustrations, charts, diagrams are to be imported from another application, instead of bitmap images (JPG, TIF, GIF, etc.) vector formats (Windows metafiles WMF or EMF, SVG, PDF) should be preferred: the former ones cannot be resized without considerable loss of quality, so the printed images will look ragged, uneven. In some new versions the SVG vector format is also supported. Table 1 summarizes the import possibilities of different files and clipboard objects into the programs:

Table 1. Import possibilities of different files and clipboard objects into the programs

Program	Bitmap images (TIF, GIF, JPG etc)		Windows metafile (WMF or EMF)		MS Word test via the clipboard	From MS Excel via the clipboard		MS Powerpoint slide via the clipboard
	From file	via the clipboard	From file	via the clipboard		table	chart	
ChemSketch 2012 1.04	no	yes but often fails	yes	yes	yes	yes (as OLE object)		
ChemDraw 13	yes	yes	yes	yes	yes (as simple text)		yes (as OLE object)	
Accelrys Draw 4.1	no	as OLE object only	no	no	yes (as OLE object)			
Chemistry 4D Draw 8.4.6	no	yes	no	yes	yes (as simple text or graphics)		yes (as graphics)	
DrawIT 2013.1	no	yes	no	yes	yes (as OLE object)			
MarvinSketch 6.2.1	no	no	no	no	yes (as simple text)		no	no
ChemDoodle 6.0.0	yes	yes	no	no	yes (as simple text)		yes (as bitmap)	yes (as bitmap)

There are no problems in the case of the most important task: the direct transfer of the drawings between these programs and other applications (text editors, Powerpoint, etc).

Drawing of chemical structures

The basic operations, as for example the sprouting or free hand drawing of different bonds, the drawing and joining of rings, the resizing of elements or the whole sketch etc, are handled well by all programs. In Chemistry 4-D Draw the moving of the different objects cannot be constrained to the horizontal or vertical direction.

The figure 1 shows the available different bond types. Some of them are quiery types as well, but can be used well in special circumstances. Mainly by Accelrys Draw, ChemDraw,

ChemSketch and MarvinDraw several database features are supported: query atom and bond types, advanced Markush structures, chemically significant multicenter attachments to resonance delocalized fragments, polymers, reaction features, atom-atom mapping etc., these are not covered here.

In ChemSketch there is a separate handy option button for the direct drawing of bonds with solid or dotted delocalization curves. Of course such structures, as simple drawings, can be assembled manually too.

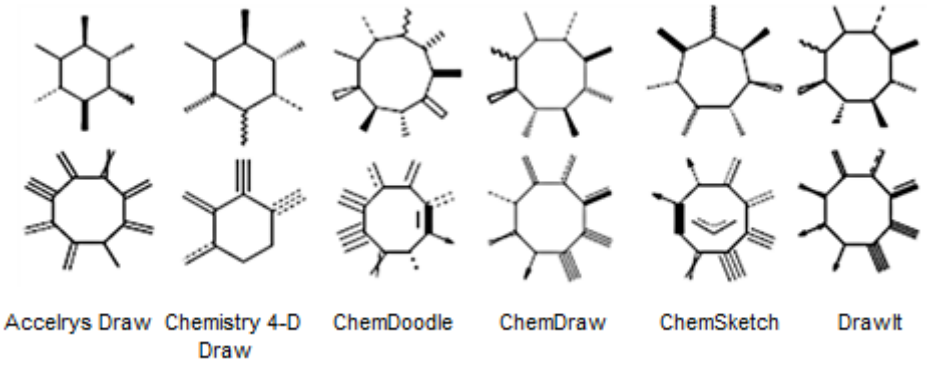

Figure 1. Availability of Different types of bonds in softwares

Chemically interpreted multicenter (coordinative) bonds, such as the ferrocene molecule are available in ChemDraw, ChemSketch and Accelrys Draw. Of course, similar structures can be assembled manually from bits and pieces, when underlying chemistry is unimportant.

In all recent versions of these applications but Chemistry 4-D Draw nearly every parameter of every object and their elements can be independently restyled and trimmed, a very useful feature in advanced hands. In the case of Chemistry 4-D Draw the parameters of a full object can be modified, but not part of the object. When three-dimensional structures are imported, the recent versions of all programs are already capable of 3D rotation. Each program is able to the automatic addition of hydrogens, although these are only implicit hydrogens, and the saved file will not contain them. ChemSketch, ChemDoodle and MarvinSketch has an option to convert and add implicit hydrogens as explicit, physical ones. Chemistry 4-D Draw Pro, when using its intelligent NamExpert feature, can create structures from chemical names.

The drawing of laboratory glassware or process flow diagrams is very handy in DrawIt: the library files contain a vast amount of drawings and chemical engineering symbols. ChemSketch, ChemDraw and ChemDoodle also contain templates for glassware; additional templates are downloadable. A very useful feature in ChemDraw and ChemDoodle is the TLC plate tool, especially for the users of laboratory e-notebooks. It allows the user to create and depict easily TLC plates with origin line, solvent front, and one or more lanes. The lanes can be populated with spots of different Rf, size, shape, or colour, and with option for automatic display of Rf values. A similar TLC tool is available in ChemSketch, too, as an installable extension, but compared to the direct graphical editing of the former two it is quite clumsy (data has to be entered into a dialog table).

A new gel electrophoresis tool has been added to ChemDraw 13. In terms of biochemical sketches ChemDraw and ChemSketch are the best: they contain more graphical objects than the other programs, on the other hand, these can be filled with simple or shaded colours and/or patterns. With ChemSketch a shaded double DNA helix can be created in five minutes. However, the new BioDraw templates of ChemDraw make the creation of DNA even easier.

2D→3D and 3D→2D conversion of structures:

Most of these applications have modules or bundled programs, which are capable of 2D → 3D conversion:

- Accelrys Draw: Convert 2D to 3D (add-in)
- ChemDraw: must have Chem3D sister program installed
- ChemSketch: 2D to 3D conversion included
- Chemistry 4-D Draw: sister program ChemSite
- DrawIt: bundled program 3DViewIt
- ChemDoodle: MarvinSketch: built-in 2D → 3D module or bundled program MarvinSpace

Except Chem3D all of these modules are free or come with the basic versions. The automatic conversion of 3D structures to the usual 2D shorthand drawings using standard bond lengths and angles has always been problematic. Nice drawings are usually produced only in the case of small molecules.

Chemical Name and Nomenclature

These programs are capable of parsing the linearized forms of substituents and convert them into structures. With the exception of ChemDoodle all programs are able to assign systematic names to structures according to IUPAC rules, and vice versa. Therefore, these are very convenient when you are generating chemical names. Summary of IUPAC module in different versions is given in table 2.

Table 2. Summary of IUPAC module in different versions

Program	Structure to name	Name to structure
ChemSketch 2012 1.04	upto 50 atoms/3 rings	no
ChemDraw 13	Ultra Version Only	Ultra Version Only
Accelrys Draw 4.1	yes	yes
Chemistry 4D Draw 8.4.6	yes	yes
DrawIT 2013.1	upto 10 atoms in free and all in academic	upto 10 atoms in free and all in academic version
MarvinSketch 6.2.1	yes	yes
ChemDoodle 6.0.0	not supported	yes (without stereochemistry)

All of the programs are able to assign the stereochemistry to all asymmetric tetrahedral atoms and double bonds according to Cahn-Ingold-Prelog (CIP) priority rules. All but ChemSketch do this on-the-fly while editing the structure. The method used in ChemSketch is quite clumsy: when editing the structure, you have to delete manully the previous R and S markers and ask for re-assignement of stereochemistry.

Spectroscopic Prediction

Some novelties in these programs are the spectral data publishing features, spectrum interpretation and database management tools. UV, IR, NMR, MS spectra and chromatograms can be imported and embedded into the documents and join with structures etc.

The most versatile are DrawIt and ChemSketch when purchasing the appropriate add-ons. The curves can be resized, zoomed, scaled, corrected, annotated, and peak list and tables are easy to create. Finally, they can be embedded into the final document. Basic spectrum manipulations, such as Fourier transformation of the FID signals are not possible.

All of these applications enable the user to assign structures to spectra. Before making any decision, it is highly recommended to check that what spectrum and database formats are supported by the current versions.

Molecular weight, and constitution %: All of the programs.

NMR: **^{1}H and ^{13}C**: KnowItAll, ChemDraw (with ChemNMR module in the Ultra version), ChemDoodle, ChemSketch (to be purchased), Accelrys Draw (with ACD/Labs Add-ins, only for versions 3.x), MarvinSketch (NMR Prediction, requires licence, free for academics), MestReNova NMR Predict (available in Demo Version)

^{19}F, ^{31}P and ^{15}N NMR: ChemSketch (to be purchased), MestReNova NMR Predict

The chemical shifts are not calculated, but determined with the aid of the applied databases; therefore, the precision of the results is a function of the included molecules.

The ^{13}C NMR module of the DrawIt/KnowItAll (if the full suite is installed) and ACD/CNMR can show molecules possessing analogue chemical environment similar to those of the carbons in question. ChemSketch has also developed this scheme into their NMR prediction modules through their "calculation protocol" environments. MestReNova NMR Predict is only capable to give NMR spectral prediction but it is very quick and best results were obtained.

IR: KnowItAll, ChemSketch (with UV-IR Manager add-on)

These softwares can also predict other physical properties:

ChemDraw: logP, CLogP, critical pressure, temperature and volume, Henry's constant, Gibbs energy, heat of formation, MP, BP, molrefraction. Some of these are available in the Ultra version only.

ChemSketch: logP (free version). With ACD/PhysChem Suite: molar refractivity and volume, parachor, surface tension, index of refraction, density, polarizability, logP, logD, pKa, Hammett σ etc. For the time being, earlier direct interaction of I-Lab from within ChemSketch is not supported.

DrawIt/KnowItAll: logP, logD, pKa, Rule of Five (depending on licence).

Accelrys Draw: Rule of Five, isotopomer distribution, enumerate stereoisomers and Markush structures as well as ACD Lab's Physicochemical and NMR predictors (only for versions 3.x)

ChemDoodle: Several topological indices, structural and analytical data, Rule of Five, H-bond donor/acceptor number, molar refractivity and volume, polar surface area, XlogP, many thermodynamic and physicochemical properties, isotopic distribution, etc.

MarvinSketch: protonation and pKa, logP and logD, charge and polarizabiltiy, generation of tautomers, conformation and molecular dynamics (using the Dreiding force field), 3D alignement, topology, surface area, Hückel analysis (HOMO, LUMO, localization energy, etc.), H-bond donor/acceptor properties. The results of several of these calculations are shown graphically as isosurfaces as well. All of these are available in the basic/free version. Table 3 gives pricing and trial information of discussed programs.

Table 3. Pricing, Trial and available platform information of the programs

Program	Working Platform	Free Trial	Commercial Pricing	Academic Pricing
Accelrys (Symyx) Draw 4.1	Windows/Macnitos	N/A		Free
ChemBioDraw Ultra 13.0	Windows/Macnitos/ipad	Yes (2 weeks)	USD 9.99 (ipad), USD2,690.00 (Mac/Win)	
DrawIt - KnowItAll Academic Edition 2013.1	Windows 8, 7, Vista, or XP	N/A		Free
ACD/ChemSketch 2012 1.04 Free	Windows/Macnitos/Linux	N/A		Free
ACD/ChemSketch 2012 1.04 Commercial	Windows/Macnitos /Linux	Yes	USD 1,620.00 (Mac), USD 570.00 (Mac/win one Year)	USD 370.00 (Mac), USD 150.00 (Mac/win one year),
Chemistry 4-D Draw 8.4.6 Pro	Windows 7/Vista/XP, Macintosh OS X	Yes	USD 499	USD 299 (Edu. & Govt.), USD 149 (students)
ChemDoodle 6.0.0	Windows/Macnitos /Linux	Yes	USD 5400 (one Year)	USD 75 (No Expiration)
MestreNova NMR Predict Desktop 9.0.0	Windows/Macnitos	Yes (45 Days)	USD 1528 (one year)	USD 390 (one year)
MarvinSketch 6.2.1	Windows/Macnitos/Linux	Yes	USD 1960 (annual), USD 4470 (no expiration)	USD 420 (annual), USD 959 (no expiration)

Conclusion

Apart from small corrections, no new features can already be added to the drawing functions of pure chemistry. For the time being, ChemDraw and ChemSketch are the most powerful chemical drawing applications. ChemDraw and ChemSketch are about neck and neck. When creating complex drawings from the available graphical objects ChemSketch is perhaps a hair's breadth ahead. ChemDraw or especially adventage when assembling from templates.

Apart from ChemBioDraw has the Chemistry 4-D Draw, these applications contain several ready template pages of different ring systems, amino acids, carbohydrates, etc. and these can be pasted quickly into the document. Other templates, for example laboratory glassware, are also available (except in Accelrys Draw). The programs allow the user to create custom templates. Of course, the technique of the creation and use of the templates are different in each program; perhaps the solution and organization used by ChemSketch is the most advanced one. A large amount of additional chemical, biochemical, biological,

manufacturing, etc. templates for ChemDraw are available as downloadable support from the CambridgeSoft's site.

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5- Chemistry 4-D Draw 8.4.6; ChemInnovation Software Inc., San Diego, USA; URL: http://www.cheminnovation.com
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