ULg Spectra: an Interactive Software Tool to Improve Undergraduate Students' Structural Analysis Skills

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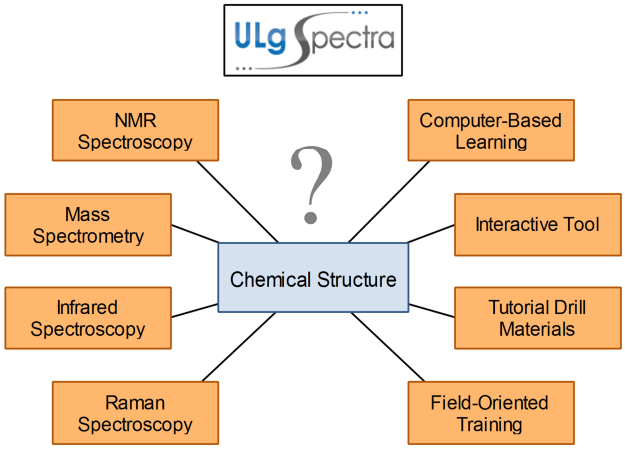
ABSTRACT

The analysis of spectroscopic data to solve chemical structures requires practical skills and drills. In this context, we have developed ULg Spectra, a computer-based tool designed to improve the ability of learners to perform complex reasoning. The identification of organic chemical compounds involves gathering and interpreting complementary information from mass, infrared, Raman and nuclear magnetic resonance spectra. Here, special attention is paid to one-dimensional ^{1}H and ^{13}C NMR spectra and to two-dimensional NMR spectra because these techniques particularly require extensive interactive data manipulation. ULg Spectra offers tutorial-drill materials including spectra that are "authentic" in the sense that they contain solvent and impurity traces rather than being "idealized" spectra often found in textbook examples. A public version is accessible online free of charge. The exam results for two groups of students, one having used ULg Spectra for extra home-based training and the other not, were compared. Statistical data demonstrated higher performance for the "trained" students compared with the control group.

ABSTRACT GRAPHIC



KEYWORDS

First-Year Undergraduate/General, Upper-Division Undergraduate

Analytical Chemistry, Organic Chemistry

Computer-Based Learning, Problem Solving/Decision Making

INTRODUCTION

The determination of chemical structures from spectroscopic data is now included in organic chemistry courses at all universities. In addition to providing students with practical skills in analytical chemistry, this contributes to the development of general competencies associated with the integration of knowledge from various origins. Identification of organic chemical compounds is nowadays mainly taught via textbooks.[1-4] These reference books offer valuable complementary information coming from the combination of mass (MS), infrared (IR) and nuclear magnetic resonance (NMR) spectra. However the rigidity of fixed-image spectra and the need to highlight appropriate details limit the ability of learners to perform the entire reasoning by themselves: i.e. selecting relevant information from each spectrum, handling this information and suggesting a possible chemical structure with an adequate scientific rationale. Various tutorials and drill problems based on fixed images can be found on

the Web.[5–9] Some Web sites explore interactive one-dimensional (1-D) NMR spectra[10-13]. MS and NMR spectra[14] simulations are available but these are not specifically designed to improve structural analysis skills. A large spectral database for organic compounds is available on the Web[15] but it is based on fixed images, does not include any two-dimensional (2-D) NMR spectra, and is not designed for educational purposes.

Here we report the development of ULg Spectra, an interactive computer program (ULg is an abbreviation for the University of Liège). This program is designed to facilitate active learning[16] in real-life structural analysis problem solving. It is a flexible tool that offers many sets of exercises with different difficulty levels, based on the lecturer's requirements and tailored to student needs. This tool can be used in cooperative or collaborative learning[17-19]. Slavin[17] defined cooperative learning as "a set of educational strategies in which students work together in small groups to help each other learn academic content". Cooper et al.[18] showed that even more informal collaborative groups can lead to measurable improvement in student problem-solving ability. Exercises from the database can be solved by collaborative groups of two students with or without the supervision of a lecturer.

Although extensions are planned to fully cover all spectroscopy methods, the current development stage focused on 1-D and 2-D ^{1}H and ^{13}C NMR spectra. ^{13}C NMR spectra were recorded in the **APT** (**A**ttached **P**roton **T**est) mode allowing the observation of all carbons as positive or negative signals depending on the number of protons attached. 2-D NMR is often a requirement for complex molecules, where increased resolution is needed. We have focused on NMR-H**COSY** (**CO**rrelation **S**pectroscop**Y**) which identifies ^{1}H-^{1}H couplings, NMR-**HSQC**-HC (**H**eteronuclear **S**ingle **Q**uantum **C**orrelation) which correlates ^{13}C nuclei with the directly attached protons (one-bond $^{1}J_{CH}$ couplings) and NMR-**HMBC**-HC (**H**eteronuclear **M**ultiple **B**ond **C**oherence) where both two-bond ($^{2}J_{CH}$) and three-bond ($^{3}J_{CH}$) couplings are present.

CONCEPT AND DESIGN FEATURE

Concept

The entire concept is driven by an educational approach, as most of the spectra included in our database have been recorded by students as part of training courses. The ULg Spectra database is designed for students. It contains sets of exercises with different difficulty levels. As the spectra are derived from authentic sources and therefore frequently display solvent and/or impurity signals, they are valuable resources for students to develop meaningful problem-solving strategies[18]. Our software functionalities are totally comparable with those of commercial software packages. Students' training can thus be easily transferred to a professional context. A public version of the database including 50 exercises is accessible online free of charge[20]. Getting started is fast and easy through available video tutorials[21]. The full version, containing about 100 exercises, is available to students at the University of Liège. Both versions will expand further in the future. The full version can be considered as an internal working version and will serve to upgrade the public version afterward.

Features

All of the exercises are numbered, and they are sorted into three categories, namely, A, B and C, of increasing difficulty. An exercise can be searched by its number, difficulty level, molecular formula or molecular weight. Two examples of exercises are displayed in Figure 1 along with the information and spectral data available in each case. To date, mass, IR and Raman spectra are stored as good-quality images. Experimental conditions and various documents or spreadsheets can also be archived for each exercise.

Full nuclear magnetic resonance (NMR) spectral data are stored and include:

- 1-dimensional ^{1}H and ^{13}C NMR spectra,
- 2-dimensional NMR-HCOSY, NMR-HSQC-HC and NMR-HMBC-HC spectra.

The 1-D spectra can be zoomed, and peak integration can be performed as well (Figure 2). 2-D spectra are displayed with the corresponding 1-D projections (top and left). The zoom function is also available for 2-D spectra and automatically applies to both 1-D projections too (Figure 3). As it is useful to overlay NMR-HSQC-HC and NMR-HMBC-HC spectra, this function has also been implemented. Comments can also be added for each experiment if necessary.

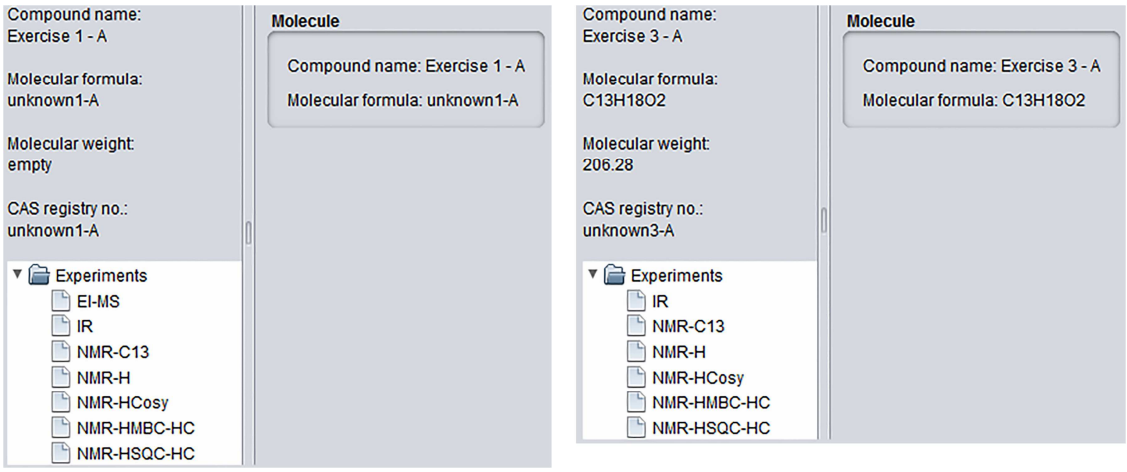


Figure 1. Two examples of information and experiments available for an exercise.

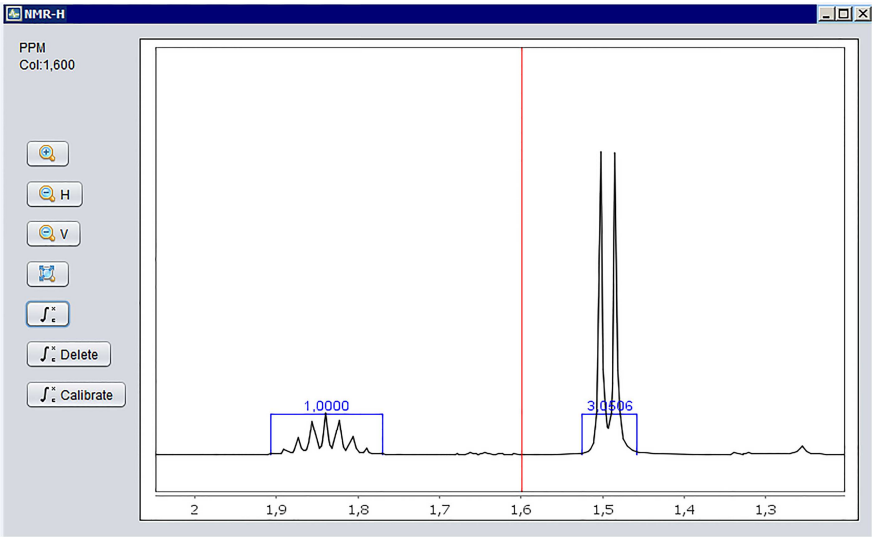


Figure 2. Display of a typical NMR-H spectrum illustrating the zoom, peak integration and calibration functions of the software. The cursor position in ppm is indicated in the top left corner.

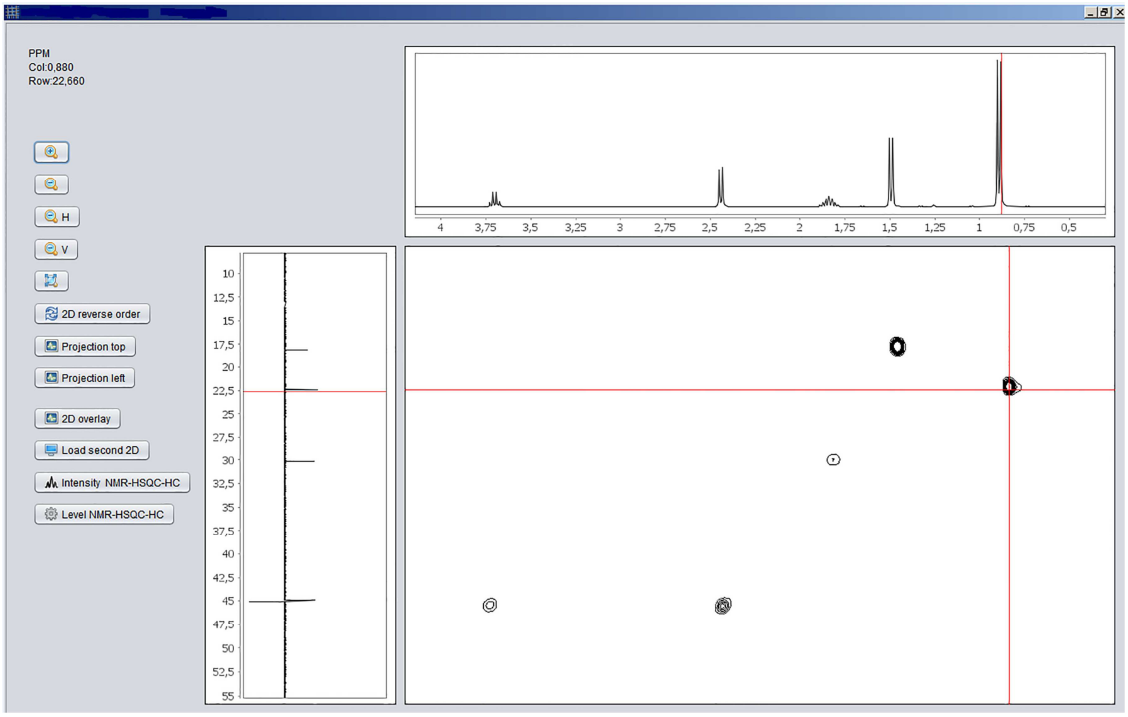


Figure 3. Display of a typical HSQC-HC NMR spectrum with the corresponding 1D-H-NMR (top) and 1D-^{13}C-NMR (left) projections. The cursor position coordinates in ppm are indicated in the top left corner.

Technical considerations

The system relies on a client/server architecture. The data are stored in a PostgreSQL database. The client application is used to visualize and interact with the data. The client/server architecture centralizes all of the data on a server, making data backup and recovery easier. The PostgreSQL database communicates directly with the client in SQL. The NMR data are first processed manually for phase correction and baseline correction and these processed data are then stored in the NMR manufacturer's text format (Bruker). The client is programmed in Java and can run under Windows, Linux and Mac operating system. It is a fat client application so all of the data processing is performed on the end-user machine. The server is used only for data storage so it needs lower requirements: the computational load is supported by the end user machine. This also allows better real-time computation performance.

EVALUATION OF ULG SPECTRA

This interactive software has been used since January 2014 by undergraduate students taking structural analysis courses. First-year undergraduate students (a cohort of approximately 300 per year) used the software at home to solve extra drill-exercises. Senior undergraduate students (about 30 per year) used it directly during on-campus tutorial classes in informal collaborative groups[18]. Exercises from the database were solved by collaborative groups of two students supervised by the lecturer.

The impact of the use of ULg Spectra was evaluated by comparing first-year undergraduate exam results achieved by students before it was implemented (i.e. from 2010 to 2013) and after it has been used by the students (i.e. from 2014 to 2017). Since 2010, the determination of chemical structures from spectroscopic data has been included in the second-semester organic chemistry course. Besides 4 hours of formal lecture, five 2-hour "traditional" tutorial sessions of problem solving are organized with explained exercises of increasing difficulty. Since 2014, two additional tutorial sessions focusing on how to install and use ULg Spectra have been scheduled. During the first one, a full description of the software is provided, and key features are emphasized by two demo exercises from the database. Students are invited to get used to the software at home for two weeks. They are expected to install the software, get used to its main functionalities and try to solve a given exercise. The second session is a feedback session where students' questions about the handling of the software are answered and illustrated by two to four additional demo exercises from the database. These tutorial sessions on how to install and use the software could not be considered as spectroscopy training *per se*. Students can then keep on using the software at home to solve extra drill-exercises. This home-based training is not mandatory and students are free to solve as many exercises from the database as they want.

The students were divided into two groups: the control group (before the implementation of ULg Spectra) and the treatment group (after the implementation of ULg Spectra). Instruction time was compared between these two groups. The control group had 14 h of spectroscopy training. Even if we include the feedback session, the treatment group had a maximum of 16 h of spectroscopy training; this additional time did not correspond to more time spent interpreting spectra but was mainly associated with technical considerations. ULg Spectra is a free complementary tool provided by the Department of Chemistry of the University of Liège to students. It could be used during their home study instead of or in addition to books.

Each year, exams were organized in June with a resit in August and were based on the interpretation of MS, IR and NMR spectra to get the chemical structure. A detailed answer with relevant points was graded. Students were required to determine the molecular weight of the unknown compound, explain the main fragmentation pathways from the MS spectrum, identify important peaks in the IR spectrum, interpret ^{1}H NMR, ^{13}C-NMR and HSQC spectra (chemical shift, multiplicity), calculate the index of hydrogen deficiency and finally come up with the chemical structure. Results from 2010 to 2013 and from 2014 to 2017 were pooled into 2 groups (Figure 4): the control group (without ULg Spectra – 1495 exams – mean score: 7.4/20 – median: 7.0/20) and the treatment group (with ULg Spectra – 1390 exams – mean score: 10.0/20 – median: 10.0/20). The Mann-Whitney U test was performed for both groups and a p value <0.001 was obtained indicating a highly significant difference between the two groups ($U = 737987$, $r = 0.25$). The higher scores achieved by students since the implementation of ULg Spectra compared to those obtained by students before its implementation support the beneficial effect of the use of ULg Spectra on student exam performance. The effect size ($r = 0.25$ equivalent to Cohen's $d = 0.52$) represents a 19 % percentile gain for the treatment group over control group[22]. This effect size value also

indicates that 33 % of the distributions of scores do not overlap[23]. Hedges and Hedberg[24] point out that Cohen's d effect sizes around 0.20 are of policy interest when academic competencies are assessed. Furthermore, it was observed that the fraction of students having good and very good results increased with the use of ULg Spectra. Indeed, the fraction of students having a score greater than or equal to 12/20 doubled and the fraction of students having a score greater than or equal to 18/20 was even four times higher. The appearance of a bimodal behavior in the score distribution may result from an additional motivation increase for the best students, linked to the technology-based approach.

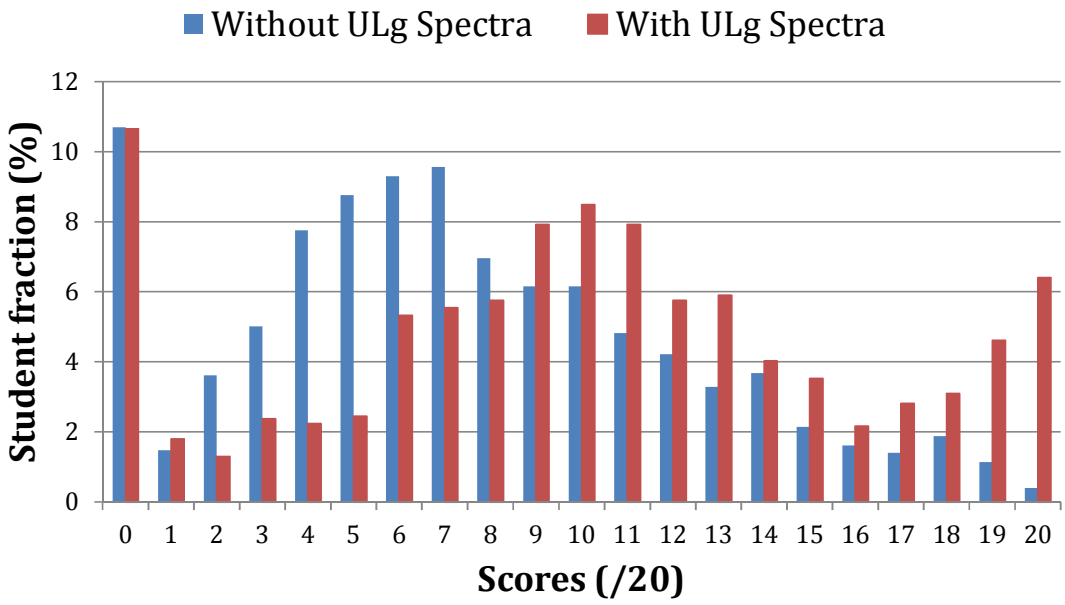


Figure 4. Exam results : correlation of test grades with the implementation of ULg Spectra. The score of 0 was obtained by students who just handed in a blank copy.

STUDENT PERSPECTIVES AND FUTURE DEVELOPMENTS OF ULG SPECTRA

In May 2017 an optional survey of ULg Spectra was sent to the last cohort of first-year undergraduate students. Thirty-eight students (out of the 188 students registered for the June 2017 exam) filled it out. Even though this survey included a limited number of students, results and comments were valuable to evaluate the software. The

analysis of students' answers showed that 90% of the students found ULg Spectra to be helpful or very helpful to gain practical skills. For the majority of the students (76%), the use of ULg Spectra was rather easy (47%), easy (24%) or very easy (5%). After installation of the software, 92% of the students needed 1 or 2 hours to get used to its main functionalities. The response time for 1-D NMR was found to be acceptable by 86% of the students. For 2-D NMR, the response time was considered to be acceptable by 66% of the students. To further improve the response time, processed NMR data size was optimized before being transferred to ULg Spectra. This clearly reduced the response the time for both 1-D and 2-D NMR spectra.

In their comments, students relayed that the installation of ULg Spectra was not always easy (usually because of problems with installing Java). Students mainly complained that the full version of ULg Spectra required a Virtual Private Network (VPN) to access the database. Students suggested some technical improvements for user-friendliness and the development of interactivity for mass spectra and IR spectra.

The results of this survey indicated that ULg Spectra is already useful to students, and their comments have been taken into account to set a timeline for further implementations. The following step will be the development of a multiplatform Web application that will be more user-friendly and faster. Interactivity will also be added for mass, IR and Raman spectra. As the entire concept of ULg Spectra is based on students' skills, these developments will be part of a graduate thesis conducted to obtain a Master's degree in Computer Science and Engineering. Development and testing are expected to be finished by the end of 2018.

CONCLUSION

The structural determination of organic compounds is a relevant pedagogical topic to develop competencies in gathering and using complementary information obtained by various analytical methods. Students' representations constructed during this kind of

problem solving have been used by Domin and Bodner to infer conceptual understanding[25]. Furthermore, a recent study[26] has shown that, when trying to determine a structure, advanced students, in comparison to novices, gaze between NMR pieces of data and chemical structures, or in other words, between spectral information and symbolic representations. This emphasizes the importance of visual effects and confirms how relevant it is to help students to become familiar with interactive spectral data handling.

Current sets of exercises are mainly based on frozen spectral images including the identification of relevant details, a situation that does not foster learners' autonomy. In contrast, ULg Spectra software offers an interactive tool that mimics real field methods using up-to-date analytical experiments to assign the chemical structure of an unknown compound unambiguously. Thanks to tutorial-drill materials, students can improve their ability to perform autonomous complex reasoning.

Statistical data on first-year undergraduate student exam results provide evidence that the use of ULg Spectra effectively contributes to improving their performance. As an example, the fraction of students passing their examination (grade greater than or equal to 12/20) is twice that of the control group.

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