

## VIRTUAL LABORATORIES AS A WAY TO ENHANCE STUDENTS LEARNING IN BIOSCIENCES

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### Abstract

The rapid development of experimental techniques in biosciences makes it hard for institutions to include practical training for students in those fields. Difficulty often comes from lack of instrumentation in the teaching laboratories, limited economical resources, high student numbers, as well as safety concerns about handling some biological samples. Simulations and virtual laboratories offer a chance to supplement the on-site wet laboratory practicals as well as to offer students some experience with those experiments that are not feasible in the physical setting. It is hence significant for instructors to know about existing resources and to redesign their teaching plans to include virtual laboratories in the education process, in order to enhance students' learning and have them understand modern techniques even if they are not accessible in the physical facilities of the institution. A collection of free resources will be showcased, which means instructors anywhere in the world can access this approach. They are all used inside a web browser, without any requirements for other software, offered under a Creative Commons license. Topics include: chromatography (column chromatography of proteins, thin-layer chromatography for separating amino acids, lipids or pigments); electrophoretic analysis (proteins on cellulose acetate, SDS-polyacrylamide gel electrophoresis of proteins, DNA on agarose gels); UV-VIS spectrophotometric assays; a full-featured molecular biology virtual laboratory (enzyme restriction, polymerase chain reaction and electrophoretic analysis, applied to genetic polymorphisms, forensic analyses, paternity test, foodstuff adulteration, viral infection by SARS-CoV2 or Influenza). These resources are being used over the last decade by numerous instructors with their students, both at high school, professional training and university courses. Groups of students going through the experience of the molecular biology lab range from 6 individuals to 300. Some of the instructors have repeatedly used it for 8 years. Reports from the instructors inform of high satisfaction, particularly in lower-income countries where the teaching institutions have very limited economic resources and cannot have access to advanced techniques and related instrumentation. The presentation is addressed mainly to instructors in science subjects, particularly biological and molecular sciences, at high school or university level, as well as postgraduates with a perspective to become instructors.

**Keywords:** *Virtual laboratories, simulations, biomolecular sciences, experimental techniques.*

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### 1. Introduction

Teaching laboratory techniques in molecular and biological sciences poses a number of challenges depending on the facilities available at the institution. One limitation may be the number of students that can be attended in a laboratory in the available space and time. Another is the requirement for instrumentation that is often expensive, particularly for state-of-the-art technologies. Not negligible is also the possibility to acquire biological samples and the precautions and safety hazards involved in their manipulation. Finally, there is usually little chance in a physical setup ("wet lab") for students to repeat experiments or to explore diverse experimental conditions, due to both space, time and economical constraints. All these difficulties are substantial in lower level educational institutions and in many countries where resources are scarce. However, in all settings it is expected that a graduate will be familiar with modern technology dealing with chemical and biological materials, and be well trained for a world that demands up-to-date professionals.

The continuous progress and affordability of the informatics and communication technologies has increasingly made possible to contemplate that computer simulations may provide a supplement or even an alternative to the real or physical laboratory for the training in experimental techniques in the biomolecular laboratory. Development of such tools may hence be useful to ameliorate the limitations described above.

We could summarize that the "virtual lab" may come handy to be combined with the "wet lab" to provide a more thorough training of the students while mitigating the limitations.

## 2. Objectives

The purpose of this communication is double. On the one hand, to present and share the material we have developed in the form of computer simulations and virtual laboratories, which may be used by both instructors and students to assist in the training process. Those resources are offered for on-line use, with no economical cost, with an open license, from any country, in both English and Spanish versions. Secondly, to put forward some reflections about the most profitable way these tools may be integrated into the teaching and learning process.

## 3. Design and contents

The collection of resources presented here is hosted in one of the university web servers (Herráez, n.d.) and is under continued development. It is hence available for users at any location, provided they have internet access. Most of the time materials, once they have been accessed, run locally in the memory of the user's device (i.e. not in the web server); therefore, there is no need for a strong connection. The Creative Commons license means that, if needed due to difficulty with network, the resources could be duplicated and used in local equipment without internet connection.

All modules are written in HTML, with heavy use of JavaScript and CSS to achieve the simulation effects and respond to the interaction by the user. Therefore, there is no need to install any software other than a standard, modern web browser. Some modules may be used in mobile devices, but due to limitations in screen size and in precision of tactile interaction, it is recommended to use a computer for a better experience.

The site is organized in sections focused on different techniques, namely electrophoresis, chromatography, spectrophotometry, and a molecular biology laboratory for DNA that includes restriction enzyme digestion, PCR, DNA sequencing and electrophoretic analysis.

In all modules, interactivity is a key feature. The user will have to make decisions, choose samples and conditions, prepare mixtures, and act on the elements displayed on the screen in order to perform the experiment. Results obtained will depend on which actions were taken, hence they are not always the same and even failures may be observed, at least in the most elaborate modules.

### 3.1. Electrophoresis

This section includes a simulation of the result of separating serum proteins on cellulose acetate strips, as well as another for lactate dehydrogenase isoenzymes (according to their charge, or their isoelectric point). Both include a choice of samples, like normal and pathological serum, and homogenates from several tissues. For the isoenzymes, there is also a module where the user must gather and apply samples onto the strip, then the separation is simulated and results collected. Another module represents separation of a protein mixture by SDS-PAGE, i.e. in a polyacrylamide gel containing sodium dodecyl sulfate, according to their molecular mass.

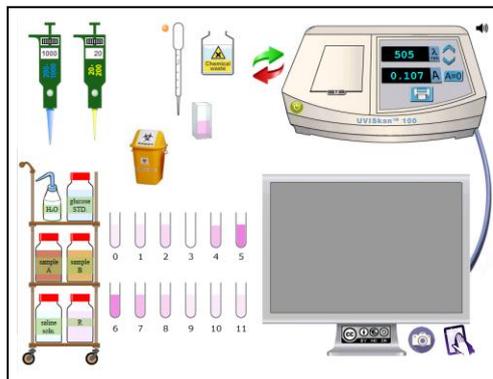
### 3.2. Chromatography

A column is simulated, with a choice of several resins and packings, for animating the separation of diverse protein mixtures. The resulting chromatogram is also displayed in real time. A separate module is used to analyze the content of glycosylated hemoglobin (HbA1c) in a blood sample, which is relevant for diagnosis of diabetes. Finally, thin-layer chromatography may be applied to mixtures of either amino acids, lipids or plant pigments; here the user will manipulate capillaries to apply samples and then run steps for the separation and reveal the result.

### 3.3. Spectrophotometry

A fully-fledged UV-VIS spectrophotometer is depicted, in a simulated laboratory complete with reagents, test tubes, cuvettes and micropipettes. User controls wavelength, introduces and extracts cuvettes with sample, records absorbance values or a spectrum. An assortment of virtual experiments may be run covering several assays: spectra, quantitation against a calibration curve, kinetic determination of enzyme activity, and effect of pH and temperature on the activity of an enzyme.

Figure 1. The spectrophotometry laboratory.

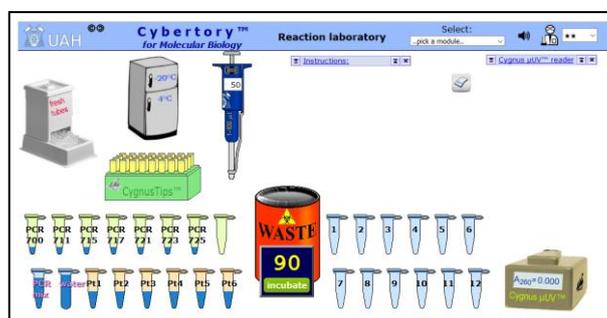


### 3.4. Cybertory: A molecular biology laboratory for genetic analysis

This is an elaborate module, maybe the most similar to real laboratory experiments for its flexibility. It simulates the selection of samples and reagents from a catalog, their acquisition (with order and invoice) and then the work in several modules. The application includes molecular diagnostics with RFLP or PCR of genetic polymorphisms, forensic analysis of DNA, a paternity test using multiplex PCR of polymorphic STR genetic markers, molecular analysis of foodstuff adulteration and mapping of DNA with restriction enzymes.

In the reaction laboratory, users may prepare in test tubes any mixture of the previously acquired samples and reagents, and accordingly run either digestion of DNA with restriction enzymes or PCR amplification with the chosen primers. Then, moving to the electrophoresis laboratory, DNA fragments will separate by size and the resulting pattern revealed and interpreted. There is also a sequencing laboratory where the classical Sanger method is applied, using dideoxynucleotides labeled with 4 fluorochromes.

Figure 2. The reaction laboratory within Cybertory.



Sample protocols are provided so that any user can perform a successful experiment on their own. Apart from that, it is expected that instructors will customize the procedure according to the context and abilities of their student groups.

## 4. Assessment on the use of a virtual laboratory

As already mentioned, the virtual laboratories are openly available in the web for anyone to use. We do not have a reliable estimate about their use, other than ranking in web searches and visit counters in a few sections. Only the Cybertory has access restricted by username and password, meant precisely to gain some knowledge about its use. Interested persons, either instructors or individual students, may get access just by email request, and this access must be renewed when a new year arrives. Some instructors have repeatedly used the resource with their groups of students over several years since 2017.

A survey was designed to assess how the Cybertory virtual laboratory has been used and how the experience has been. It was distributed by email to ca. 600 instructors worldwide (totaling 45 countries) that had requested access to the resource and used it with their students at some moments along the period 2017 to 2024. The online questionnaire, anonymous, with 11 items (table 1), received 170 responses from 21 countries.

Table 1. Questionnaire distributed as a survey of instructors' experience and assessment.

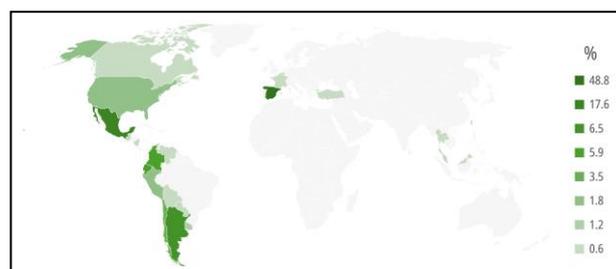
Q1	Which country are you in?
Q2	Educational level of your students. (If you use it in several, please fill a survey for each)
Q3	Number of students in each group using the Cybertory. (You can check more than one)
Q4	Total number of students using the Cybertory in an academic year. (You can check more than one)
Q5	Which experiments in Cybertory do your students work on? (You can check more than one)
Q6	In which stage do you use the Cybertory, within your teaching strategy? (You can check more than one)
Q7	Motivation for using the virtual laboratory.
Q8	Your perception of how much your students value these aspects: (1= little or no value; 3= neutral; 5= much valued)
Q9	Your own evaluation, as instructor, of these aspects: (1= little or no value; 3= neutral; 5= much valued)
Q10	Please value your overall satisfaction with the tool, as an instructor.
Q11	Please value how you perceive your students' overall satisfaction with the tool.

The extension of this short article does not allow for a detailed report of this survey, which will be provided in the oral presentation at the congress. As a brief summary, see table 2.

Table 2. Summary of results of the survey.

Q1	<b>21</b> countries (see fig. 3)
Q2	<b>18%</b> Secondary education / High school; <b>25%</b> Professional training degree / Technical degree; <b>52%</b> University (college, BSc); <b>4%</b> Master / Postgraduate degree
Q3	<b>13%</b> up to 10; <b>68%</b> 11 to 30; <b>18%</b> 31 to 50; <b>3%</b> 51-100; <b>4%</b> over 100 students per group
Q4	<b>7%</b> up to 10; <b>37%</b> 11 to 30; <b>25%</b> 31 to 50; <b>21%</b> 51 to 100; <b>10%</b> over 100 students per year
Q5	<b>58%</b> Forensic analysis PCR. <b>51%</b> Paternity test PCR. <b>46%</b> Forensic analysis RFLP. <b>36%</b> DNA sequencing. <b>32%</b> Beta-S globin (sickle cell anemia). <b>29%</b> Viral infection (COVID). <b>21%</b> Dairy products adulteration. <b>15%</b> Celiac disease. <b>10%</b> Cytochrome P450 polymorphism. <b>9%</b> Vegetable oil adulteration. <b>7%</b> Resistance in plants. <b>2%</b> RET protooncogene (MEN2A neoplasia)
Q6	<b>79%</b> Instead of the real laboratory, which is not feasible. <b>20%</b> After the real laboratory, as reinforcement, review or to expand the experiments. <b>39%</b> Previous to the real laboratory (wet lab), as preparation or training.
Q7	<b>28%</b> Don't have the equipment and techniques available in real laboratory. <b>20%</b> Have the equipment but economically not affordable. <b>52%</b> As a complement to the real laboratory.
Q8	(Mean   Median, max. 5 points) <b>4.6   5</b> Accessibility. <b>4.4   5</b> Ease of use. <b>4.6   5</b> Contribution to understanding of techniques and to learning. <b>4.3   4</b> Degree of realism (not just visual, but functional) compared to a real experiment. <b>4.6   5</b> Attractive character of the theme of the experiment.
Q9	(Mean   Median, max. 5 points) <b>4.8   5</b> Accessibility. <b>4.6   5</b> Ease of use. <b>4.8   5</b> Contribution to understanding of techniques and to learning. <b>4.5   5</b> Degree of realism (not just visual, but functional) as compared to a real experiment. <b>4.9   5</b> Economical considerations (against similar commercial products more sophisticated)
Q10	(Mean   Median, max. 10 points) <b>9.4   10</b>
Q11	(Mean   Median, max. 10 points) <b>8.6   9</b>

Figure 3. Location of users that responded to the survey.



## 5. Discussion

As we have presented in the introduction, computer simulations may provide alternatives to overcome limitations that affect teaching laboratories. Even where the real experience is available, there is

still benefit in using virtual laboratories so that students come more prepared to the physical setup, that they can review their work, repeat, try different conditions, explore both the techniques and the outcome of results from experiments that allow variations. This may bring a training more similar to real life research, using the scientific method, exploring freely, practicing interpretation of results, both predicted and unexpected. It is most important that the simulations and virtual laboratories have not a closed design with respect to both the options and the results, but are open to changing parameters and provide results strictly according to what was done. For example, although samples must be programmed in the software, it is preferable that they can be assigned randomly, in a way that the output will be different for each student at each attempt. In this way, the experience is richer than what may be provided by, for instance, slide shows and videos, which necessarily follow one single path and bring always the same result.

Several high-quality products are in the market, undoubtedly excellent solutions to complement students' training, but the cost makes them not a choice for many educational institutions. Open access and cost-free resources are a strong value for what we are presenting here, together with the possibility of dynamically expanding the virtual experiments available, through collaboration with interested instructors and scientists, as it has indeed happened in our case. Apart from this, we believe that the flexibility that some of our modules offer in terms of experimental design by the student, with coherent, variable, positive or negative results, is not present in many products and means a remarkable advantage for a solid training of our students, moreover when provided free to be used from any location in the world.

The survey conducted among instructors that use Cybertory reports use from secondary up to tertiary education, with stronger involvement in university and technical degrees. Most popular topics were genetic identity tests (forensic and paternity). A majority of users (79% in Q6) resorted to it as a replacement for some experiments they could not run physically; however, this does not mean they had no facilities at all, since the most frequent response (52%) on Q7 was that virtual complemented the real laboratory. Since we could not poll the students, we rely on what their instructors perceived about their interests and experiences. The score in all aspects was very high, averages above 4.4 over 5. In turn, instructors' appreciation was slightly higher and the economical issue was particularly valued (this question was not addressed to the students). The overall satisfaction with the Cybertory was valued 8.6 by students and 9.4 by instructors, with median values of 9 and 10 respectively.

To finish, here is a quote from the feedback received recently from a professor in a technological institute, who has been a user along the last five years:

*I take this opportunity to express my gratitude for allowing us access to this powerful teaching-learning tool. Without a doubt, since I began using it in my classes, my students have lost their fear of not being able to understand and have become much more adventurous in trying it in real life. In the lab I lead, I don't have the tools to run all the analyses that I can perform thanks to the Cybertory. My students are surprised to see that in real-life situations, the same results are obtained, and I am delighted that each one can experience the importance of being thorough in the development of their experiments. Obtaining different results is fantastic because it motivates them to continue until they obtain their own results and compare them with their classmates. Without a doubt, the Cybertory has helped many young people at my institution change their perspective on the difficulty of performing this type of testing and has redirected the paths of several of them, inspiring vocations toward the field of molecular biology and its applications. I hope you allow us to continue using this tool, which has become indispensable for me and my students.*

### Acknowledgments

The initial idea and part of the inner coding that runs the simulations in Cybertory are due to Robert M. Horton, Ph.D. (Horton & Tait, 1999), who offered it for the Netscape browser; in 2006 he released the code under GNU GPL license, which allowed us to convert to modern browsers syntax and to expand it for PCR assays and many new types of experiment.

The SDS-PAGE simulation adapted an original design by David Mix and Dr. Paul Craig (Rochester Institute of Technology), with valuable help from Prof. Robert M. Hanson (St. Olaf College).

Much code has been developed thanks to advice and examples openly shared in the web.

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