AC 2011-2533: VIRTUAL AND BLENDED LIQUID CHROMATOGRAPHY LABORATORIES FOR CHEMICAL AND BIOLOGICAL ENGINEERING EDUCATION

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Virtual and Blended Liquid Chromatography Laboratories for Chemical and Biological Engineering Education

Abstract

The paper presents a blended educational environment which comprises a traditional hands-on laboratory using a low pressure liquid chromatography system and a virtual version of the low pressure liquid chromatography system and processes, as well as a variety of printed and online learning resources. The blended learning environment for biopharmaceutical production of proteins has been jointly developed by the Northeast Biomanufacturing Center and Collaborative (NBC^2) and the Massachusetts based company ATeL, LLC to address not only the education and training needs of biomanufacturing, but chemical and biological engineering disciplines will benefit as well.

Introduction

To support the development of the infrastructure for biomanufacturing education, training and the workforce, the Northeast Biomanufacturing Center and Collaborative (NBC^2) develops instructional materials and resources, based on harmonized biopharmaceutical manufacturing industry skill standards. These learning and teaching resources, available in printed and online formats form a Global Biomanufacturing Curriculum to support biomanufacturing education and training. As a part of our educational efforts, we designed the first module of a comprehensive interactive virtual learning environment for biomanufacturing – a virtual low pressure liquid chromatography laboratory based on NBC2 equipment and process SOPs utilizing a BioLogic Low Pressure (LP) Chromatography System made by Bio-Rad Laboratories, Inc. This system is a complex piece of equipment that can be difficult for a student to master. For such equipment and processes virtual laboratories can be a very effective teaching tool allowing students to understand the components of the system and prepare them to confidently and successfully perform actual experiments.

Virtual laboratory

A set of interactive simulations forms the core of the Virtual Liquid Chromatography Laboratory (VLCL). The VLCL models the components and processes involved in protein liquid column chromatography. In addition to online lessons, there are on line assessments, a glossary, and supporting materials.

The simulations can be run in three modes. The equipment mode enables students to use animations and 3D images to study the design and functionality of a chromatography system or 'skid', its components and their electrical and plumbing connections, as well as interactions between these components. In this mode, the simulation allows students to zoom-in on a component, rotate it, explore its parts using photo-quality 3D images, and read a description of the component. Fig 1.presents the interface of VLCL running in the equipment mode.

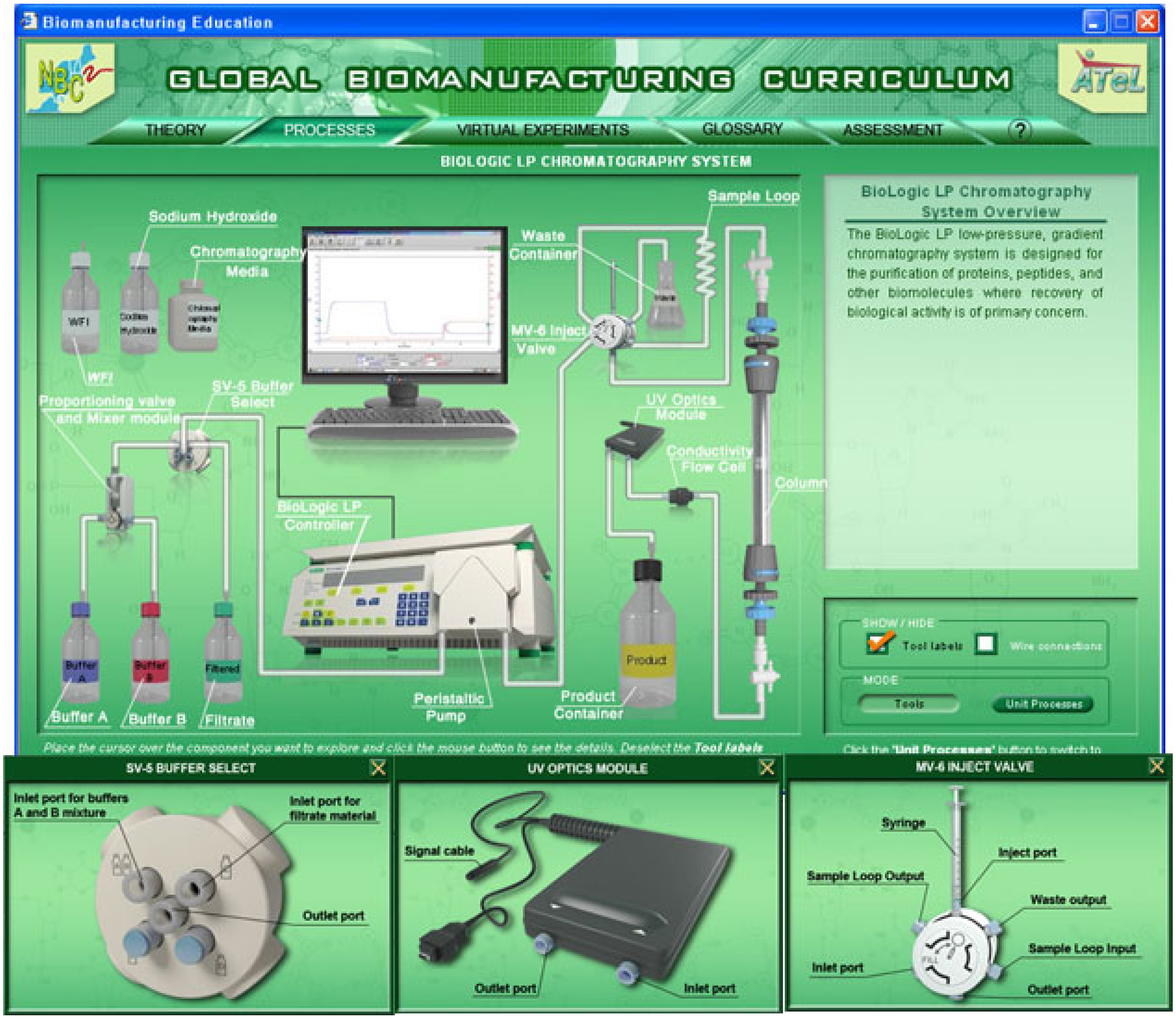

Figure 1. A screenshot of the Virtual Liquid Chromatography Laboratory running in the equipment mode. 3D images of major system components are shown at the bottom.

The process mode (Fig. 2) introduces students to the operation of the system in an interactive and engaging way. Students are able to select either auto or step-by-step mode. In the auto mode the simulation shows students a chain of processes and the computer process control manipulations that occur during protein purification utilizing a computer controlled liquid chromatography system. The step-by-step mode enables students to explore each step, including controller settings and programming, in real-time detail. Students also learn how to use a chromatogram to make calculations, for instance how to calculate the efficiency of column packing, or the resolution of two peaks on a chromatogram. (Fig.3).

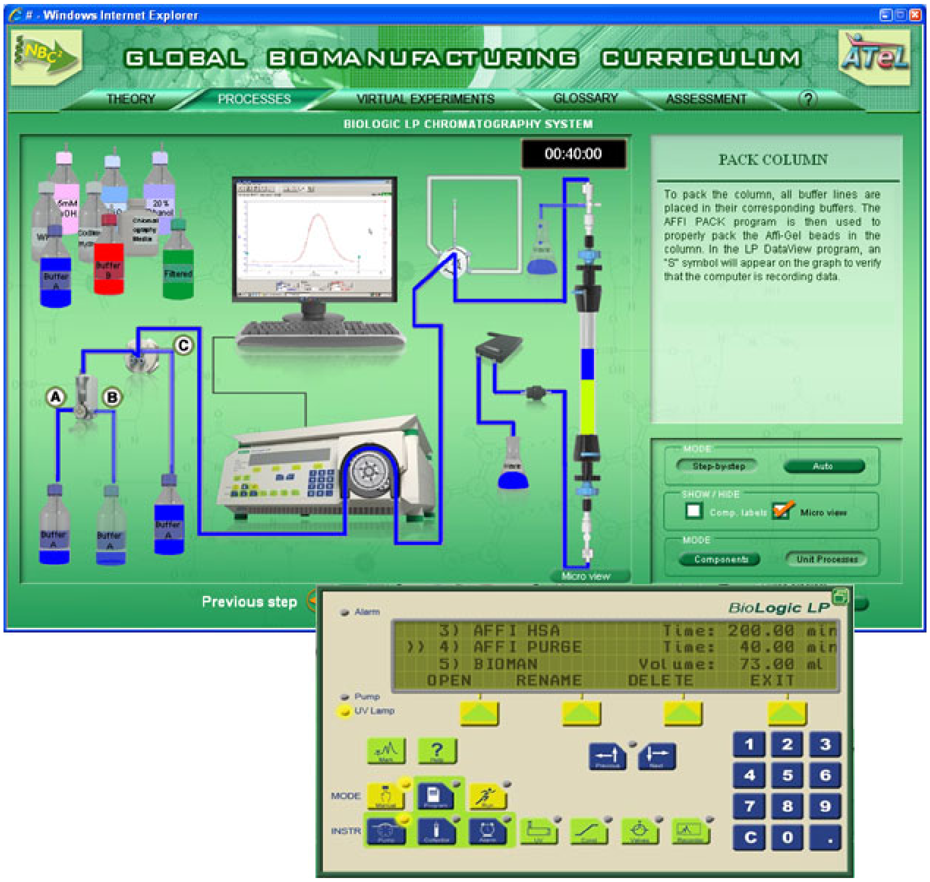

Figure 2. The Virtual Liquid Chromatography Laboratory running in the process mode. An interactive zoomed-in controller enables students to operate the system and set process parameters.

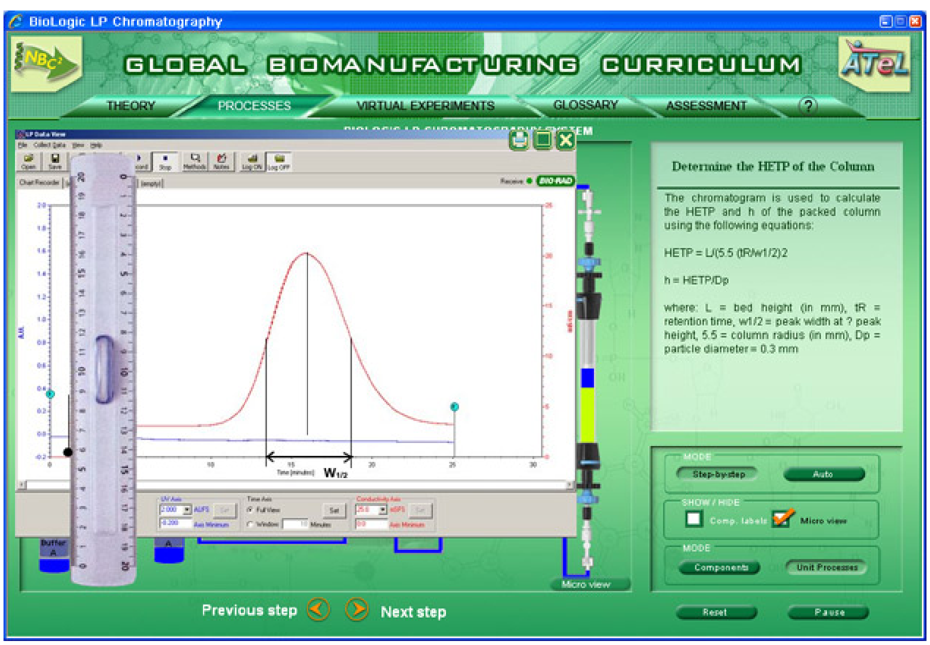

Figure 3. An example of how the Virtual Liquid Chromatography Laboratory teaches students to use a chromatogram to determine the efficiency of column packing.

One of objectives that we wanted to achieve was to connect technical, hands-on skills training with an understanding of the basic scientific concepts underlying liquid column chromatography. With this in mind, we have developed an animation detailing the interactions on a molecular (nano) scale between the beads in the packed column and the proteins in the filtrate during liquid column chromatography (Fig.4).

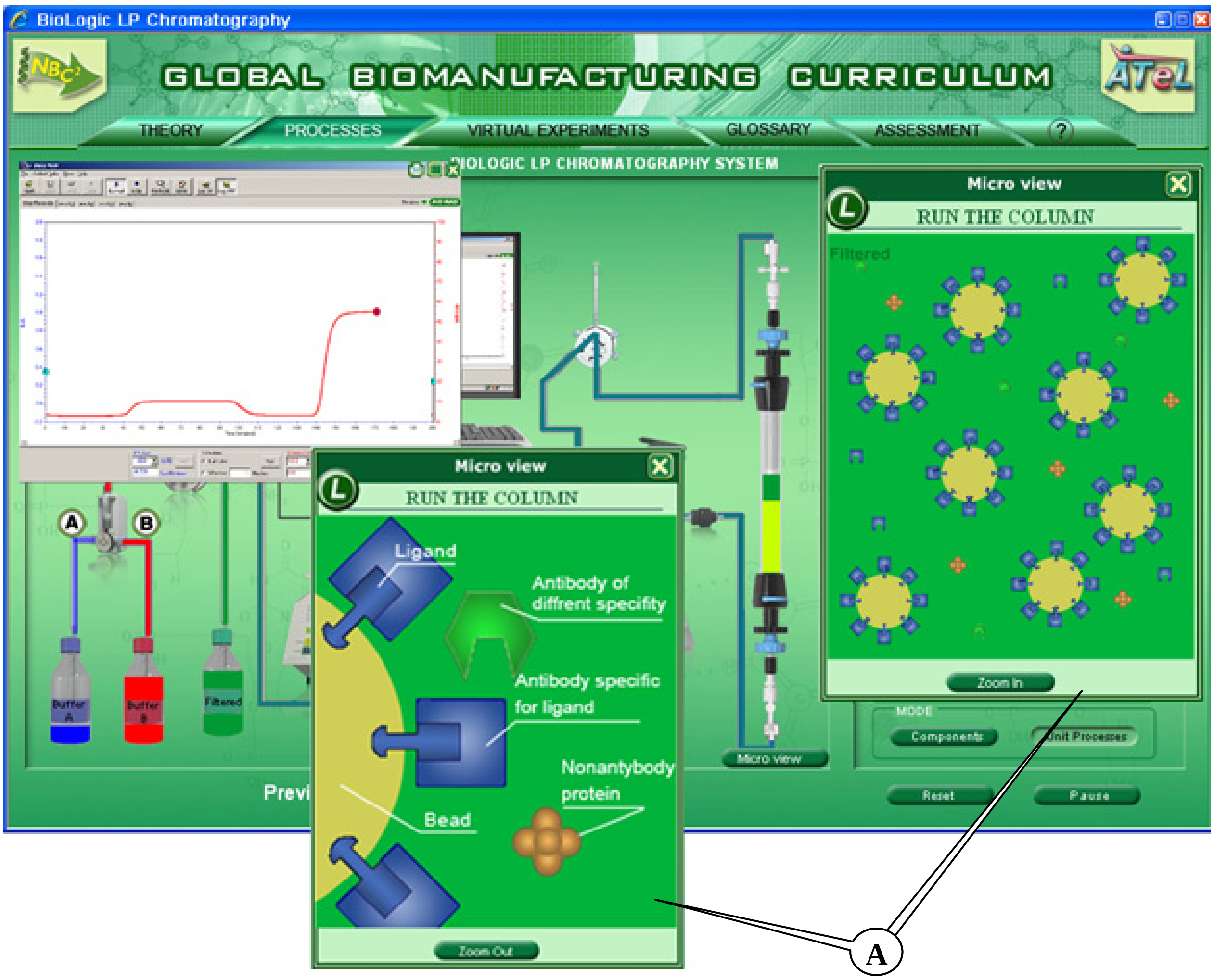

Figure 4. A screenshot of the chromatogram during the "Load" phase of the liquid column chromatography process, with a plateau representing the flow through on the left and on the right images of what is occurring at the molecular level between the packed beads in the column and the proteins in the filtrate (the protein of interest attachés to the beads, while unwanted proteins appear in the flow through. Using the Zoom-In/Zoom-Out button, students can observe the processes at two levels of magnification (A).

The experimental mode allows the students to practice what they will do in the actual liquid column chromatography laboratory. Using a computer mouse and keyboard students can manipulate virtual labware and materials (e.g. move and replace buffers, filtrate, cleaning solutions and such), connect system components, and set up and program the system controller. The system corrects them when they are wrong. In addition, students can collect and handle data from the virtual process. Detailed step-by-step on-screen instructions guide students through the experiment. Students are able to print out a simulated chromatogram and make calculations.

At any time during the process students can access embedded NBC2 PowerPoint presentations, Standard Operating Procedures (SOPs), a glossary and other online resources which facilitate "just-in-time" learning. After completing the virtual experiment, students are asked to answer assessment questions.

VLCL allows students to study subjects and practice technical hands-on skills at their own pace, when and where they choose. The Virtual Liquid Chromatography Laboratory employs technologies design and a framework developed by ATeL for STEM education and corporate training [3-5]

Hybrid Laboratory

VLCL is linked with a traditional hands-on laboratory using a BioLogic LP Chromatography System produced by Bio-Rad Laboratories (Fig. 5). This combination forms the Hybrid analytical and production Liquid Chromatography Laboratory (HLCL) which is designed to facilitate a blended learning mode.

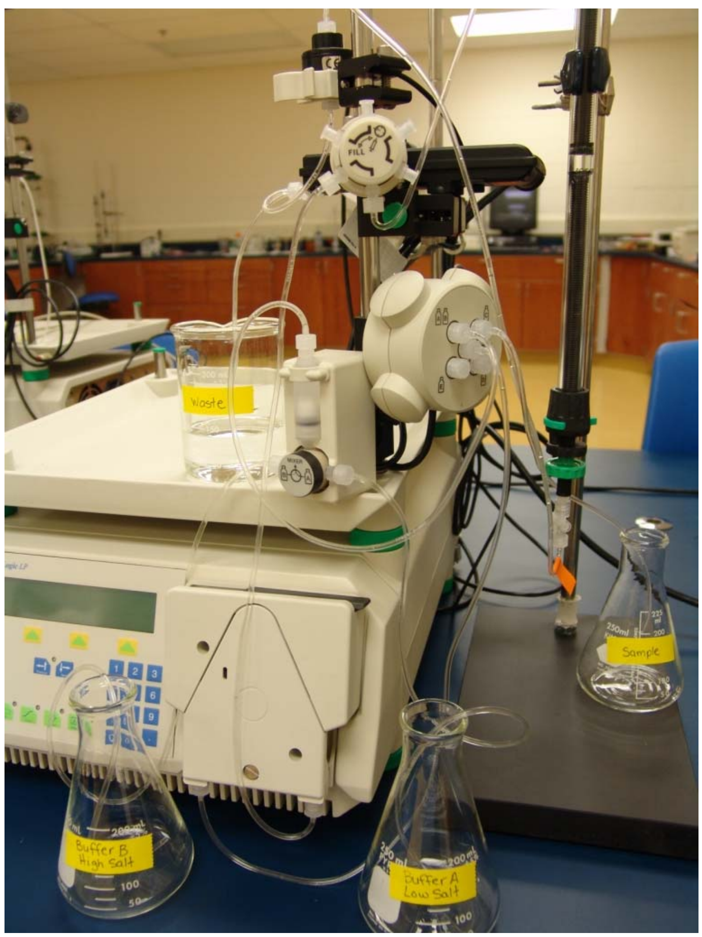

Figure 5: Actual LP Biologic Chromatography System

Learning cycles

The proposed blended learning cycle recommends a five-step approach to student learning:

1. use simulations and online materials to learn the theory and basic principles underlying protein purification;
2. use simulations to become familiar with a liquid column chromatography system, its components and their function;
3. perform virtual experiment(s);
4. evaluate knowledge and virtual skills, using a built-in assessment tool, before granting access to the real chromatography system;
5. use the real BioLogic LP Chromatography System to purify proteins.

At Montgomery County Community College, the Virtual Liquid Chromatography Laboratory was used to teach student interns working on an industry- college collaboration project that involved testing chromatography resins for their potential application in the biomanufacturing industry. Prior to performing experiments students used the virtual learning module in all three modes. First, they became familiar with the system components running the simulation in the equipment mode. The process mode was extremely helpful in teaching the students the correct order of events for successfully performing the experiment and gave them confidence in their ability to properly prepare the column for the experiments. Finally the experiment mode allowed the students to run-through the experiment without the risk of losing valuable starting material. The students were confident and capable of performing the experiment independently. The VLCL will be used in a classroom setting this semester during a Biomanufacturing class, the effectiveness of the virtual lab as a teaching tool will be further evaluated.

In the fall 2009 Biomanufacturing Course at Great Bay Community College (GBCC), students used the Virtual Liquid Chromatography Laboratory to assemble the actual Bio-Rad LP Chromatography System and to use the system to purify Human Serum Albumin by affinity liquid column chromatography. Students had less trouble understanding the pathway of fluids (or how the system is plumbed and how to operate the valves that manage the flow of fluids). They also more readily understood the relationship between the chromatogram and what was happening in the column during the pack, equilibrate, load, wash and elute cycles using this truly hybrid mode.

Currently the VLCL is being formally evaluated at Finger Lakes Community College. Fifteen students using the virtual laboratory as part of a Biomanufacturing class will complete a 20 question evaluation that will focus on the usability of the module and it's value in the blended teaching approach. The instructor will also complete an evaluation of the module and report on student outcomes.

Presentation, discussion and evaluation of the VLCL at the annual national BIOMAN workshop for biomanufacturing faculty at Ivy Tech Community College (Bloomington, IN, July 12-15, 2010) has generated very positive and enthusiastic response. Several attendees requested access to the VCL module to potentially incorporate it into their Biomanufacturing curriculum. In addition, faculty were excited by the prospect of future virtual laboratories to teach upstream processing skills such as the use of large scale bioreactors.

Conclusion

It is apparent that the VCL can guide students in the use of a complex system such as a liquid column chromatography system and can educate them on the relationship between what is happening in the system and the column and the resultant chromatogram. Students report that using the virtual chromatography system with the real chromatography system equipment and process SOPs allows them to quickly assemble and accurately use the real chromatography system to purify biopharmaceutical proteins. They understand the process.

We believe that the combination of online and hands-on learning ensures integration of theoretical knowledge and practical skills and enhances students' understanding and workplace performance. Our plans include thorough testing to evaluate and compare the impact on student learning of hybrid labs versus the separate use of hands-on or virtual labs, as well as to develop virtual labs for the upstream processes.

The suggested approach can be applied to various areas of advanced technological education and corporate training.

References:

1. NBC2, *Pichia pastoris* – HSA Core Production System, 2010, www.lulu.com
2. ATeL, LLC, *e-Learning Tools*, http://atelearning.com
3. Y. E. Cherner, A. Karim, A. Khan, *Using Simulation-based Hybrid and Multilevel Virtual Labs for Fiber Optics, Photonics, and Telecom Education,* in Proc. ASEE Annual Conference, 2008, Pittsburg (PA).
4. Y. E. Cherner, A. O. Lotring, G. Graebner, *Training Tomorrow's Submariners Today - An Innovative Approach and Simulation-based e-Learning System*, I/ITSEC, 2004, Orlando, FL.
5. Y. E. Cherner, D. V. Davis, *Use Of Interactive Virtual Labs for Teaching Introductory and Engineering Physics*, in Proc. ASEE Annual Conference, 2006, Chicago (IL).

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