Integrating Research into the Undergraduate Curriculum – NASA's Microgravity Bioreactor

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Abstract

Currently, there is an emphasis in many funding agencies on integrating research results into the undergraduate curriculum. The basic rationale is that research expenditures will thus be leveraged to improve the quality of undergraduate education by providing students with interesting, real world engineering problems that will motivate, provide opportunities for students to integrate material from different courses, and develop problem solving skills. While there is little disagreement as to the potential benefits of this approach, there is the need for models of how to efficiently perform the research-teaching integration. This paper explores the use of Macromedia Authorware 5 Attain ® to develop an interactive multimedia module that will test the research integration concept and its feasibility.

The module explores the NASA microgravity bioreactor, which was developed in the late 1980's and is significantly impacting the tissue culture research community. The module is structured to interactively lead students through a problem solving strategy that involves problem definition, solution generation, decision analysis, solution implementation, and solution evaluation. Topics covered in the module will include ones that are typically covered in introductory numerical methods and data analysis courses. Initial testing of the module is in a sophomore level introduction to chemical engineering analysis and design course.

I. Introduction

Teaching is most effective and most fun when the student is *properly* motivated. A significant problem in engineering education today can be motivation of students. Given that oftentimes a students M-Q (motivation quotient) is more important to success than their I-Q (intelligence qoutient) (Hendricks, 1987), the importance of finding ways to properly motivate students cannot be underestimated. The goal of the multimedia module under development that is described herein is to help meet this need.

A teacher's motivation toolbox has been described as starting with creating a need (Hendricks, 1987). Experiences create needs. This should be followed by challenging a student. With a need created and a challenge laid down, a student is ready for structuring experiences that consist of telling (both orally and in writing), showing (to provide a model), and doing under a controlled situation where it is ok to make mistakes. Having developed basic skills from structuring experiences, the student is now ready to develop these skills further by attempting real-life problems. Providing recognition and encouragement along the way is also essential. The teacher must possess patience since everyone can be motivated, but not at the same time. This idealized educational process is extremely difficult for an engineering educator to achieve as it requires a considerable investment of time, a resource most engineering educators have in short supply. However, it is undeniable that the greater the investment the greater the interest (Hendricks, 1987).

A 1996 NSF press release stated the idealized education process as follows:

> Picture an ideal university: It has a pervasive culture promoting collaborative research between professors and students; there are internet links between research labs, libraries, and students; and there is an emphasis on discovery-based learning techniques throughout science and engineering curricula. This should be the norm. Often, however, it is not.

NSF is taking steps agency-wide to steer more universities toward this ideal image by encouraging the integration of research and teaching in many of their programs (Marin, 1997). Additionally, the type of open-ended problem-solving skills stressed in ABET 2000 closely resembles the type of skills required to complete the research process.

With limited amounts of time and long lists of responsibilities, faculty members in engineering often feel torn between their teaching and research duties. By incorporating research examples into curricula and collaborating with students on research projects, professors can merge their teaching and research interests, and students can gain important insights into how engineering and science concepts apply to real-life problems (Coppula, 1997). The work underway herein seeks to develop a model for how this integration of research and teaching can most efficiently be achieved.

Multimedia modules can provide some of the key elements of effective teaching that are embodied in research and teaching integration. Well designed modules can quickly create a need through efficient use of text, graphics, and audio to present interesting problems. They can also effectively structure experiences that appeal to a variety of different learning styles. They provide an environment in which modeling of problem solving techniques is possible in a controlled setting that can be made to be non-threatening and encouraging. Multimedia modules have a lot of potential for improving teaching effectiveness and the ability to integrate research and teaching, however, there is the need for models as to how these modules can be efficiently made and kept timely.

II. NASA Bioreactor

Many exciting and important problems in science and engineering research and education are arising at the boundaries between traditional disciplines. One area of chemical engineering research that many feel will have a significant impact on the development of new chemical engineering processes and applications in the future is process technologies in extraterrestrial environments (Frankie and Zubrin, 1999). The NASA rotating wall vessel bioreactor is an example of the benefits of interdisciplinary research. While all the capabilities to design and construct the NASA bioreactor described below have been available for at least twenty years, and the need for such a bioreactor has been around even longer, it was not invented until more recently because the necessary interdisciplinary group of scientists and engineers had not been put together.

Tissue growth is one of the basic tools of medical research. The engineering of tissue requires at least five critical stages of development in cell culture: 1) Assembly of cells in three dimensional arrays; 2) Propagation or growth in three dimensions; 3) Synthesis of the appropriate intercellular 'cement' (matrix) to hold cells together and provide signals to the cells; 4) Diversification and/or specialization of select cell function (differentiation); and 5) The formation of blood vessels to carry nutrients and wastes. Using conventional technology, it is impossible to fully grow human tissue to mature states similar to those found in the human body. NASA's bioreactor, as a precursor to cell culturing in space, has opened the possibility of improving tissue sample growth on Earth outside the human body. Mammalian cells – particularly normal cells – are notoriously sensitive to growth conditions found in standard bioreactors. Gravity-driven fluid flows cause shear forces that can damage cells or prevent them from forming clusters. Thus, conventional bioreactor technology limits the degree to which cell cultures can develop structures and functions similar to tissue found in the human body.

NASA scientists at the Johnson Space Center in Houston have developed a bioreactor that simulates microgravity conditions by using rotation to suspend the cells (see Figure 1; Johnson Space Center, 1999). This low shear culturing environment allows for cell aggregation, differentiation, and growth. In cooperation with the medical community, the NASA bioreactor design is being used to culture mammalian cells into organized tissue. Currently, living cells from human colon, prostate, breast, and ovarian tumors are being successfully cultured in the NASA bioreactor. In the NASA bioreactor, cancer cells grow into a small specimen that resembles the original tumor.

Another use of the NASA bioreactor is to study the effect on cells and tissues of human exposure to microgravity. Musculoskeletal changes such as significant bone and muscle loss occur even when astronauts exercise regularly, but the mechanisms are not yet understood. Tissue

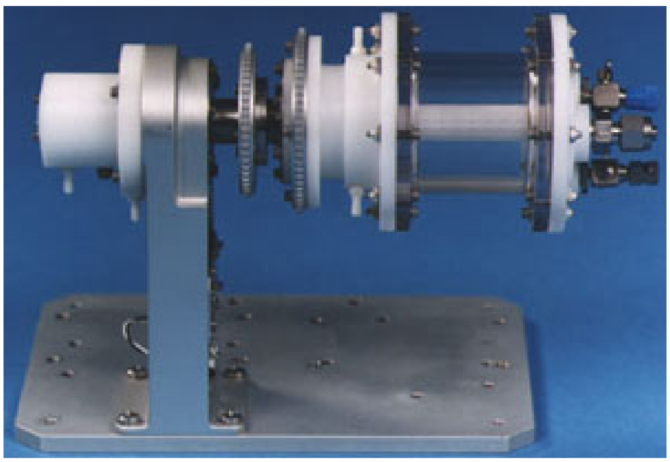

Figure 1: The heart of the bioreactor is the rotating wall vessel, shown without its support equipment (Johnson Space Center, 1999).

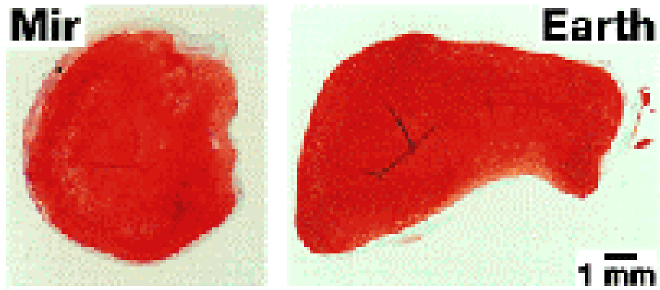

Figure 2: Engineered cartilage samples (Johnson Space Center, 1999).

engineering, a new field that enables tissue equivalents to be created from isolated cells in combination with biomaterials and bioreactor culture vessels, potentially can provide a basis for systematic, controlled *in vitro* studies of tissue growth and function. A method has been developed to create three-dimensional cartilaginous tissue based on cartilage cells, biodegradable polyglycolic acid (PGA) scaffolds, and NASA bioreactors (see Figure 2). The scaffold induces cell differentiation and degrades at a defined rate, whereas the bioreactor maintains controlled *in vitro* culture conditions that permit tissue growth and development (Freed et al., 1997).

The Couette-flow NASA bioreactor was designed to provide a uniform low-shear environment with controllable shear levels. This allows the suspension of anchorage-dependent cells to grow in a low-gravity (low-shear), three-dimensional favorable culture environment (adequate nutrient and waste transfer). The vessel consists of two concentric cylinders, both typically 11 cm long, with the outer cylinder typically having a radius of 4.0 cm and rotating at one angular velocity, while the inner cylinder has a radius of 2.86 cm and rotates in the same direction at another angular velocity. The end walls of the vessel are fixed with the outer cylinder and rotate with it. The gap between the cylinders is completely filled with culture medium. The primary rotation of the fluid around the axis of the vessel moves the cells around the vessel so that when a cell is in the upper side of the rotation, it will fall towards the inner wall, and when a cell is in the lower side of the rotation, it will fall towards the outer wall. This motion can keep the cells off the bottom of the vessel, but the centrifugal force imposed by the primary rotation will ultimately force the cells to the outer wall. A secondary rotation is set up by rotating the inner wall at a different angular velocity than the outer wall (Tsao et al., 1997). This secondary flow moves the cells from the outer wall towards the inner wall to assist in suspending the cells. The perfusion flow enters the cylinder through filters on each of the vessel end caps and exits through a filter that forms most of the inner wall. The design provides sufficient circulation for adequate oxygenation and mass transfer of nutrients to the cells. Partially simulating microgravity hydrodynamics, the NASA rotating-wall perfusion vessel has shown excellent performance in earth-based experiments (Tsao et al., 1994). Some experiments have been performed aboard the space shuttle in microgravity. The results of these experiments have been compared to their earth-based analogs.

III. Multimedia Module Structure and Content

The multimedia module under development has a structure that is based upon the premise that its primary function must be to teach students how to think, how to learn, and how to work. It has an emphasis not just on the product of learning, but also the process. This process is aided by showing students the big picture first and then never doing anything for the student that the student can do for themselves because maximum learning is always the result of maximum meaningful involvement. It seeks to build the need before teaching the content. Numerous links to short tutorials are provided because the teaching-learning process is most effective when the student is adequately prepared (Hendricks, 1987).

The specific learning objectives of the module are as follows:

1) Be able to apply basic animal cell culture principles to the design of a bioreactor system.
2) Be able to apply a creative problem solving heuristic to a NASA biological system research challenge.
3) Be able to apply problem definition techniques – Finding out where the problem came from, Present state-Desired state.
4) Be able to apply solution generation techniques - Dunker diagram, K.T. problem analysis, Osborn's Checklist for Adding New Ideas
5) Be able to apply decision analysis techniques to choose good risks to take.
6) Be able to apply solution implementation techniques.
7) Be able to apply solution evaluation techniques.
8) Be able to apply numerical methods to bioreactor data – Roots of Equations, Linear Algebraic Equations, Interpolation, Numerical Differentiation, Numerical Integration.
9) Be able to apply analytical and numerical methods to bioreactor mathematical transport model – Ordinary Differential Equations, Partial Differential Equations.
10) Be able to apply statistical methods to bioreactor data – Mean, Variance, Standard Deviation, Confidence Intervals, Outlier tests, Correlation Coefficient, Linear Regression, Nonlinear Regression, Experimental Design (Factorial design).

As can be seen from the objectives, a significant thrust of the module is to provide students the opportunity to develop creative problem solving skills. The topic area of tissue culture bioreactors particularly lends itself to providing interesting and relevant applications of these skills. The main menu of the module is structured on the five building block problem-solving heuristic of Fogler and LeBlanc (1995), shown in Figure 3.

In defining the problem, students are presented with a concise description of the history and the previous state-of-the-art in tissue culture. They are then challenged to discover whether the real problem (or problems) are related to reactor design, culture biochemical techniques, etc. Along the way they are exposed to some of the common problem definition techniques and given opportunities to develop their skills through tutorials and sample problems.

Having generated a problem definition for tissue culture growth, students are challenged to generate possible solutions. They are provided with common solution generation techniques through tutorials and sample problems. Possible solutions discussed include single-cell co-

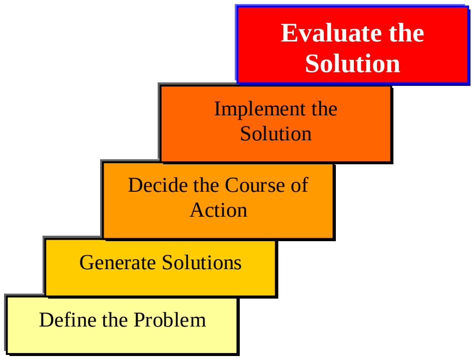

Figure 3: Five Building Block Problem-Solving Heuristic

culture techniques such as bubble-free oxygenation, porous micro-carrier beads, hollow fiber bioreactors, and fluidized bed bioreactors (Duray et al., 1997). These provide excellent mass transfer rates and facilitate high-density cell growth. However, because much of the extracellular matrix in a tissue is laid down during embryogenesis, it is impossible to recreate a normal microenvironment using only collections of well-differentiated cell types.

With some possible solutions in hand, the student is challenged to decide which is best using common decision techniques and to decide what actions are going to be needed to implement that solution. In all sections the student is first given the opportunity to present his own ideas and compare those ideas to the considerations involved in the actual development of the NASA bioreactor. The NASA fluid-filled rotating wall vessel bioreactor was originally intended to protect delicate cell cultures from the high shear forces generated during the launch and landing of the space shuttle. When the device was tried for cell-line suspension cultures on the ground, cells were seen to aggregate and form larger structures resembling tissues. This observation offered the exciting possibility that the bioreactor might be used to study the interactions of multiple cell types and their association with proliferation and cellular differentiation during the early steps of tissue formation (Duray et al., 1997).

At this point the student is given additional information on the NASA bioreactor and presented with a number of opportunities to perform numerical analysis and data analysis techniques based on actual ground-based and space-based experiments. The most relevant mathematical model for the bioreactor involves solving the steady-state Navier-Stokes equations in radial and longitudinal directions and taking the solved flow field to calculate the forces on suspended particles and resulting particle trajectories. The forces to be considered are drag from fluid circulation, buoyancy from gravitational fields, and centrifugal forces from the rotation of the vessel. While the complete solution of this problem certainly goes beyond the capabilities of the module target audience of Sophomore engineering students, there are aspects of the mathematical solution that are appropriate and instructive as to the necessity of clearly understanding simpler problems before tackling complicated, real-life problems.

Students are presented with the challenge of what reasonable assumptions can be made to simplify the mathematical problem – Newtonian fluid, constant density, constant viscosity, spherical particles (Hung et al., 1995), noninteracting particles, flow field not affected by particles, laminar flow, axially symmetric flow, etc. Students are asked to determine the forces acting on the particles. They are lead through the solution of the corresponding problem that can be solved exactly – Couette flow viscometer (Bird et al., 1960). The students are then presented with how the solution to the Navier-Stokes equations needs to be changed for the more complicated bioreactor problem. They are also aided in interpreting the graphically presented solutions to these equations.

Videos of particle movements taken aboard space shuttle experiments are explained to allow students to see how trends predicted by modeling are in fact demonstrated in the actual performance of the bioreactor. Comparisons are also made between flight-based (microgravity) and ground-based (1-g) experiments.

IV. Module Development and Testing

The software tool used to develop the interactive multimedia module is Macromedia Authorware 5 Attain ®. Three chemical engineering seniors and one sophomore have used this tool to help develop the module. After going through tutorials available and playing with the package for a couple of weeks to learn its capabilities, the students found Authorware to be a good combination of ease of use and necessary capabilities.

The problems included in the microgravity bioreactor module and sections of its multimedia presentation are being tested for the first time this semester (Spring 1999) in CHEN 220 (Introduction to Chemical Engineering analysis and Design) with 23 students. The typical content for this course is numerical methods for the solution of roots of equations, systems of linear equations, numerical integration, ordinary differential equations, linear regression, nonlinear regression, and statistical analysis of data. After further development during the summer, parts of the multimedia module will be tested next year in Freshman and Sophomore Calculus and Physics courses and Chemical and Mechanical Engineering Numerical Methods courses.

V. Conclusions

The ultimate goal of this work is to develop an efficient and effective model for integrating research results into the undergraduate curriculum. While just being five months into the project has not allowed time for complete development and testing of the proposed model, progress so far has been encouraging. The use of Authorware by undergraduate students to aid the development of course materials has worked well. Both the theoretical and experimental aspects of the NASA bioreactor research project chosen have been conducive to demonstrating the desired learning objectives.

Acknowledgments

This material is based upon work supported by the North Carolina Biotechnology Center under its program for enhancing biotechnology capabilities at North Carolina A&T State University and the National Aeronautics and Space Administration Partnership Award for the Integration of Research into Mathematics, Science, Engineering and Technology Undergraduate Education (NASA PAIR). Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author and do not necessarily reflect the views of the North Carolina

Biotechnology Center nor the National Aeronautics and Space Administration. The help of Damon Campbell, Felicia Martin, and Aisha Robinson (Chemical Engineering students, North Carolina A&T State University) in developing the module presented herein is gratefully acknowledged.

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