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Members of industry, faculty, and students have expressed an interest in a cooperative program whereby university students in senior design courses can become more familiar with engineering practice as it relates to the pharmaceutical industry. All participants benefit from the exchange of knowledge and experience. This article presents an actual case study.

Joint Benefits of Industry Sponsored University Design Course

by Steven W. Peretti, PhD, and Daniel B. Dunbar, PE

Introduction

During the Spring semester of 1998, students and faculty in chemical engineering (ChE), electrical and computer engineering (ECE), and computer science (CS) at North Carolina State University in Raleigh, NC participated in a collaborative design effort with industry representatives from ISPE to expand vaccine production facilities for a local pharmaceutical manufacturer. The following description of the efforts made and results obtained is offered as an example of one successful strategy for the development of an industry sponsored multi-disciplinary design project.

Objectives

The primary objective of this project was to establish effective procedures for the development and execution of a realistic, multi-disciplinary design project while providing students the opportunity to learn more about the pharmaceutical industry. As part of this objective, we sought to develop strategies for faculty, student and corporate recruitment, and to identify the support required by the design team. Our experiences and conclusions regarding these issues constitute the majority of what follows.

The senior design project is also an ideal opportunity to use cooperative learning as an effective method of directed self-instruction. Several elements of cooperative learning figured prominently in the design effort:[1]

1. Positive interdependence. Team success depends critically upon each member's contribution;
2. Face-to-face promotive interaction. Some group work must be interactive with members providing feedback, constructive criticism and encouragement;
3. Appropriate use of collaborative skills. Development of communication, decision-making, leadership, and conflict management skills is encouraged;
4. Group processing. The teams set their own goals, assess their performance periodically, and formulate beneficial changes in team function.

The specific objective presented to the students was to execute a preliminary engineering design of a process, automation and controls system, and paperless manufacturing execution system (MES) for the production of a pediatric vaccine. The design was to include process flow diagrams, evaluations of technical and economic feasibility, and development of MES software.

Questions for Vaccine Manufacturer

- Is mixing needed when combining batches? If so, will protein be denatured with intense mixing?
- Is location of pump correct with respect to the sterilization filter? Does it matter? Which vendors are used for peristaltic pump?
- Which vendor do you use for the sterile bottles? Is equipment used for pre-sterilization on site?
- Does flow hood need to be included in conceptual

Figure 1.

Strategy

To provide a realistic multi-disciplinary design project, we sought assistance from the ISPE Carolina Chapter. One of the missions of ISPE is to disseminate information about the pharmaceutical industry. The local chapter officers agreed that exposure of college undergraduates to a design project focused on some aspect of the pharmaceutical industry would further that mission. Representatives of a local manufacturer of

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pediatric vaccines agreed to formulate a project based upon a vaccine production facility.

While preliminary discussions were underway to define the scope of the project, the involvement of disciplines outside of chemical engineering was solicited. Computer science and electrical engineering faculty affiliated with their respective department's design course agreed to participate. This defined the ultimate technical boundaries of the project. The faculty members met several times with the vaccine manufacturer technical liaison to discuss the form and content of the problem statement.

Since open-ended problems offer the most effective learning opportunities, the project statement was kept deliberately simple. Students were presented with a four page document which was used as the basis for a preliminary engineering feasibility study. The document consisted of:

- the following problem statement:

  Best of the Best (BOB) protein has been in development for four years and has shown excellent results in both Phase I and Phase II studies. BOB protein is actually a mixture of complex bacterial proteins with an average molecular weight of 50,000. When injected into infants, it seems to make them resistant to many different bacterial illnesses. Senior management is considering making a capital investment to bring this product to commercialization. Senior management needs engineers to analyze product requirements, develop and define a production process, size equipment/facility, and develop the basic economics and schedule for this project to provide the necessary information to make this critical business decision.

- a market forecast
- product synthesis information (fermentor yield, reaction conditions and media composition)
- purification information (general performance criteria for ultrafiltration, chromatography, and lyophilization)
- process control and automation requirements
- data collection requirements
- manufacturing execution system requirements

The vaccine manufacturer provided sanitized parameter val-

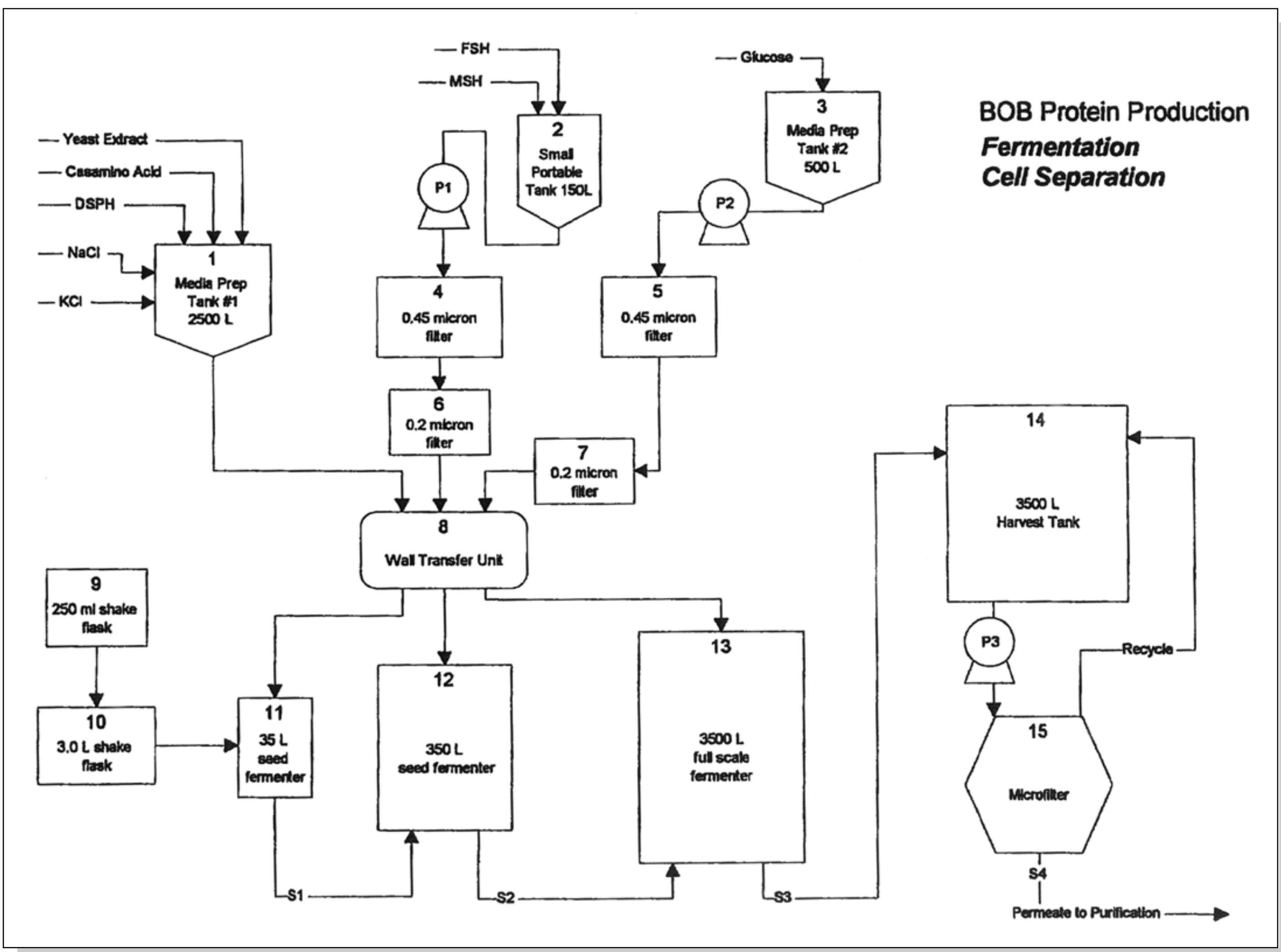

Figure 2. BOB protein production - fermentation, cell separation.

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> ***Students realized that their group's technical solutions would not stand alone, but instead had to fit together smoothly and consistently with those of the group.***

ues to avoid releasing proprietary information. To realize the benefits of cooperative learning methods, the students were required to:

- form focused working groups and function within them
- develop needed technical expertise within the group structure
- formulate group goals in support of the project
- integrate group goals with the project timetable, providing timely support to other groups
- coordinate the activities of the different project groups across technical and disciplinary boundaries
- develop and deliver a consistent (visually and stylistically) presentation of the team's results and conclusions

The project team consisted of 16 students; 10 chemical engineers, four electrical engineers, and two computer scientists. Since NC State does not now have a multidisciplinary design course on the books, each student remained enrolled in their respective design course while working on some aspect of the larger problem.

Faculty participated in this project as advisors and overall organizers, but were not the primary source of technical expertise. They decided to treat the students as technically competent professionals, and interacted with the students in a more collegial than superior manner. The faculty provided resources as needed, and brainstormed with the students on a weekly basis.

Eight industrial advisors provided the bulk of the technical expertise to this project. Employees of the vaccine manufacturer and of four other ISPE-member companies met with the entire project team an average of once every other week. Meetings between working groups and individual industrial mentors occurred after the project team meetings, and at other times as needed. Questions, both written and oral, took the typical form of Figure 1.

1. Available annual manufacture time is 45 weeks, allowing seven weeks for non-production activities such as plant shutdown and semi-annual cleaning.
2. BOB will be manufactured every year for six years from the year 2000 to the year 2006. Concluding in 2006, production will be re-evaluated.
3. Capacity utilization calculations are based on JSB marketing forecast.
4. The product dose level is 0.05 milligrams of BOB protein.
5. Quality control testing support will be available during all manufacturing shifts.
6. An appropriate dust collection apparatus will be owner furnished in Media Prep.
7. The new process suite will be constructed in an existing shell building.
8. All new electrical power, WFI, steam, and compressed air needs will be met by existing sources.

Figure 3. Fermentation design assumptions.

Results

At the start of the semester, faculty gave students a brief description of the project. This was followed by a meeting of the entire project team and industry advisors, where the project was described in more detail. The students immediately requested and received a detailed plant tour, as well as an opportunity to speak at length with mentors in their field. As expected, students then divided the project and themselves into five working groups along discipline lines, with a project manager acting as coordinator of the team effort. It took four weeks of weekly meetings with mentors before each group defined their particular tasks and for the team to develop a process flow diagram around which all future efforts would revolve - *Figure 2*. As the design progressed, students identified the need for assumptions - *Figure 3*. The team developing the paperless manufacturing execution system found it beneficial to produce a mission statement and list of system requirements - *Figure 4*. Despite the fact that little cross-disciplinary interaction occurred during this time, no faculty intervention occurred. The faculty decided that each group was faced with significant technical tasks that needed to be completed before substantive interaction between groups would be fruitful.

This decision proved to be shortsighted. After the initial technical hurdles were overcome, disagreements arose among the different groups, along departmental lines, regarding the scheduling, structure and utility of meetings, the delineation of responsibilities, and the need for cross-disciplinary interaction. The groups had been working in virtual isolation for the better part of two months, and had solidified their opinions about the appropriate direction of the project and the role each group should play. Each group had different needs and expectations, which were not expressed coherently, and therefore, not adequately addressed.

Industry advisors continued to provide input to the students to allow them to model actual engineering practices in resolving the technical issues. However, it became apparent that what was most needed were strong project management skills to bring the project "together." Advisors stressed the importance of an integrated solution in lieu of five individual solutions.

Several mandatory meetings followed, involving group leaders and faculty. During these meetings, students were prompted to identify the technical aspects of the problem that required

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cooperation across disciplines. Faculty also reminded the students that they were expected to give a coordinated audio/visual presentation of their results, and that the evaluation of the project would be based in large part on that presentation. Almost immediately, disagreement was replaced by conversation and collaboration. Students realized that their group's technical solutions would not stand alone, but instead had to fit together smoothly and consistently with those of all the groups. The combination of time pressure imposed by the project deadline and recognition of shared common task (and fate) removed the barriers to cross-disciplinary interaction. The final four weeks of the project were spent in a flurry of working group meetings, assignment of technology transfer liaisons between groups, and coordinated preparation of the final oral presentation. As the importance of scheduling became critically apparent, the project manager produced a completion plan - *Figure 5*. Figures 6 and 7 represent samples of the final deliverable.

What We Learned

The most important lesson that the faculty and students learned through this effort was that the most significant challenge to team success is interpersonal dynamics, not technical difficulty. The ChE students had no background in fermentation or protein purification; the EE students had not dealt with programmable logic controller networks before; and the CS students had no experience with manufacturing execution systems. Good manufacturing practice and FDA regulations regarding sterility and material handling were new to everyone. Yet none of these issues proved to be a serious impediment to project completion. Cross-disciplinary communication was **the** impediment to success.

Furthermore, intermediate presentations at large team meetings do not overcome the communication barrier, even when groups identify, intellectually, the need for information exchange. Lacking familiarity with concepts and technology presented by other disciplines breeds hesitance to interact across disciplines. The groups that shared a common background (fermentation, purification, and lyophilization) interacted extensively from the beginning despite having little shared knowledge regarding the particular processes they sought to design. It was not until faced with the imminent disaster of a botched presentation that groups made serious efforts to communicate.

Extensive involvement of an industrial partner lent a degree of reality to the project that is difficult for faculty to simulate independently. Plant visits gave students and faculty an understanding of the physical aspects of the facility that greatly clarified their subsequent thought about process design and implementation. In fact, several students commented that "if we could have been an equipment operator for a day, we would have understood the process even better and design would have been much easier." Also, regular attendance of professionals at team meetings, and communications via phone and e-mail gave students tremendous technical guidance and feedback.

Active and interested sponsorship by a professional society was invaluable because it dramatically increased the resources available for student consultation. In our case, sponsorship by an energetic local ISPE chapter meant that students could approach any chapter member (out of nearly 100), regardless of corporate affiliation. This contributed significantly to the success of the project because students gained the cooperation of local consulting professionals and equipment vendors who possessed expertise different from that of the vaccine manufacturer's employees. This was most helpful in areas such as project management, process validation, and cost estimation. These advisors also attended team meetings regularly.

Working on a realistic problem in collaboration with practicing professionals offered the students opportunities and resources beyond the typical design experience. Since faculty were tionship was redefined from sage-disciple to a collegial one. As a result, the students took more personal responsibility for their technical education. That independence, and subsequent success, fostered confidence in their technical prowess. One student thought that this was probably exactly what her first job was going to involve, so she felt very well prepared and anxious to get started. Another noted that "there is no way I thought we would get as much done as we did."

Treatment as a colleague by faculty and other professionals also inspired a level of self-motivation and effort that is beyond

April

1998

Sun	Mon	Tue	Wed	Thu	Fri	Sat
			1 Team Status Meeting	2	3 ——Complete Equipment	4
5 Specification, Start Cost Estimate—	6	7	8 Team Status Meeting	9	10 —Complete Cost Estimate—	11
12	13	14	15 Team Status Meeting	16	17 —Format Report—	18
19	20	21	22 Team Status Meeting	23	24 —Organize Presentation—	25
26	27	28 Dry Run	29 Final Presentation	30		

Figure 5. Completion plan.

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MES Mission Statement

This system is to present operating instructions to operations personnel; collect data from manual inputs, automated instrumentation, and/or process control devices; collect "performed by"/"checked by" signatures; track material and equipment usages; and enforce workplace rules.

System Requirements

The system shall:

- Maintain a master production record. This record holds step-by-step instructions used to generate individual production runs that are uniquely identified by a control/batch number.
- Print out the master production records with blanks to show where data inputs occur.
- Print a completed or in process production run.
- Allow qualified personnel to update or change the master production record.
- Enforce that only the latest "approved" master production record is used in generating production runs.
- Provide a scaleable function to allow for future growth both in users and in numbers of master records in use.
- Collect "performed by" and "checked by" signatures for each production step. Each signature must be date/time stamped by the system. The "checked by" signatures are to be collected after the production step is complete. The "performed by" signatures are to be collected at the time of step execution.
- Receive inputs from keyboard, barcode scanner or electronic interface to a "smart device". A smart device is one that will allow two way communications through a data port.

Figure 4.

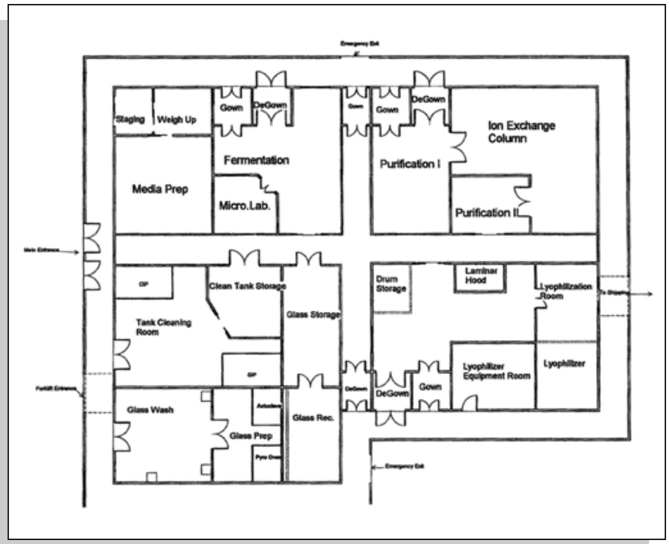

Figure 6. BOB protein manufacturing facility.

that encountered elsewhere in the curriculum. One student remarked that "I worked harder on this course than any two I have ever taken, and it was great. We are so lucky to have worked on this project." Another offered that "even though it was hard because we didn't know anything about fermentation at the start, it was fun learning how it all worked." This is the type of comment we'd all like to hear at the end of a course.

From an industry perspective, this type of project brings working professionals back into the classroom. We witness the difficulties students from various technical disciplines have in really communicating with each other. We realize that many of the problems we encounter in our daily work lives because "he just doesn't speak the same language" have their origins in the very disciplines we profess to be expert in and practice. In seeing students struggle to overcome these barriers with each other, it focuses the importance of acquiring project team skills that are most effective in stimulating cross-disciplinary communication.

Conclusions

Over the course of this project, the faculty and industrial partners often discussed how the course might be better structured and organized. Toward that end, we have developed several recommendations.

1. Begin faculty and student recruitment during the semester preceding the course offering. Meeting with corporate sponsors, developing the problem statement, and organizing the logistics of the course should begin about three months prior to the start of the semester.
2. Select students with a high interest level in the field represented by the project.
3. Seek corporate partners who are willing to provide a high level of interaction with the students in the form of contact time.
4. Solicit the involvement of an active professional society. ISPE involvement was a tremendous asset in company

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recruitment, particularly beyond the primary partner. Without such support, the overall quality of the final product would have been greatly reduced, and the students' experience would have been substantially lessened in quality.

5. Provide a structured environment in which cross-disciplinary communication is encouraged from the beginning. We recommend that one aspect of this consist of a series of tutorials, given by students, that describe each discipline to the others as a means to "break the ice." Also, appoint a project management team with representatives from each discipline involved. And, whenever possible, constitute cross-disciplinary working groups.

As faculty, we have a responsibility to provide our students the most complete opportunity possible to develop the skills they will require in the working world, whether technical or interpersonal. The senior design project offers a unique opportunity for faculty to facilitate the transition from student to practicing professional in a cooperative, supportive environment.

As an industry, we have a responsibility to form these types of partnerships with academia. Providing the opportunity for students to work collaboratively across disciplines on actual bio/pharmaceutical projects improves team organizational, communication, and problem solving skills. And everyone wins! Students get to experience some real world challenges. Faculty broaden knowledge base and have the opportunity to expand industry contacts. The university's curriculum is advanced. ISPE's role of improving education is fulfilled and the Society is introduced to the future generation of engineering professionals. Sponsoring companies have the ability to interact with potential future employees and forge stronger ties with the university. Industry advisors have the opportunity to share their knowledge and experience. A technical problem gets the benefit of energetic and innovative attention and everyone has a good time in the process.

Looking Ahead

Faculty and industry advisors see the value of hands on unit operations lab work with actual pharmaceutical equipment to supplement course study. NC State with its ISPE Carolina Chapter sponsor will be starting up and operating a bench scale fermentor, the results of which will be the subject of a future article. A special note of thanks to Wyeth-Lederle, Sanford NC for its continued support.

References

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