A Web-Based Case Study for Chemical Engineering Capstone Course

Dr. Lisa Bullard
Dr. Steven Peretti
Patty Niehues
Shannon White

North Carolina State University

NC STATE UNIVERSITY

Objectives

- Why biotechnology
- What is a case study
- Web-site structure and contents
- Problem statement
- Development of solution
- Exemplary results
- Further development

Why biotechnology?

- Growing job source for engineers
- Non-traditional application of technology
- Novel process challenges
- Unique regulatory environment
- Inherently multidisciplinary
- Availability of local expertise via ISPE

What constitutes a case study

- Purpose
- Problem statement
- Supporting website
- Support information
  - Tutorials
  - Information pages
  - Simulation
- Exemplary solution

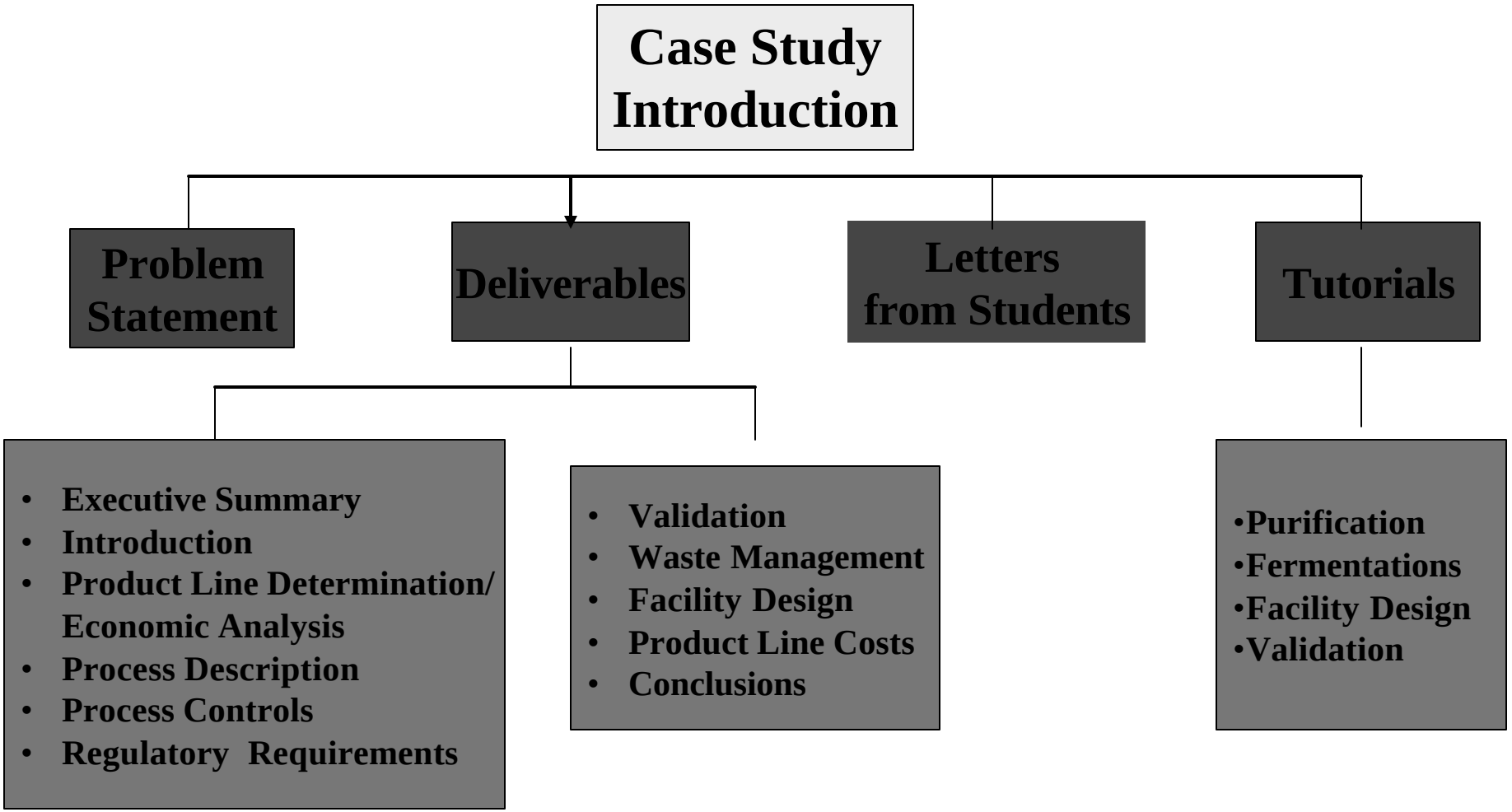
Instructor Materials

- Problem Statement
  - Protein characteristics
  - Facility layout
  - Equipment list
- Website description
- Implementation advice
- Resource material

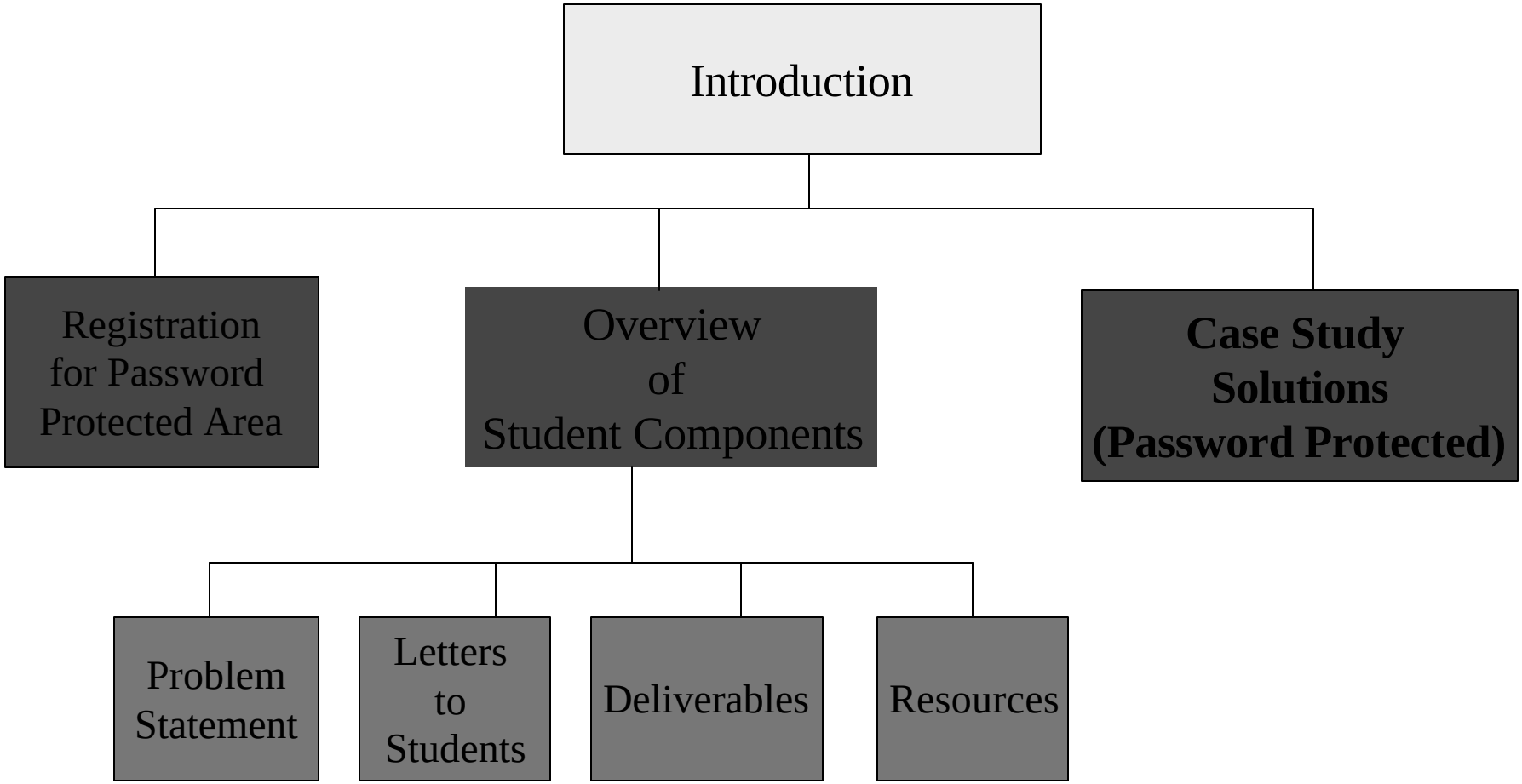
Web-site structure

- Levels of Access
  - Student Access
    - Problem Statement
    - Deliverables
    - Resources
  - Faculty Access
    - Enhanced Problem Information
    - Password Protected Solution
    - Tips
  - Administrator access
    - Full Read and Write Privileges

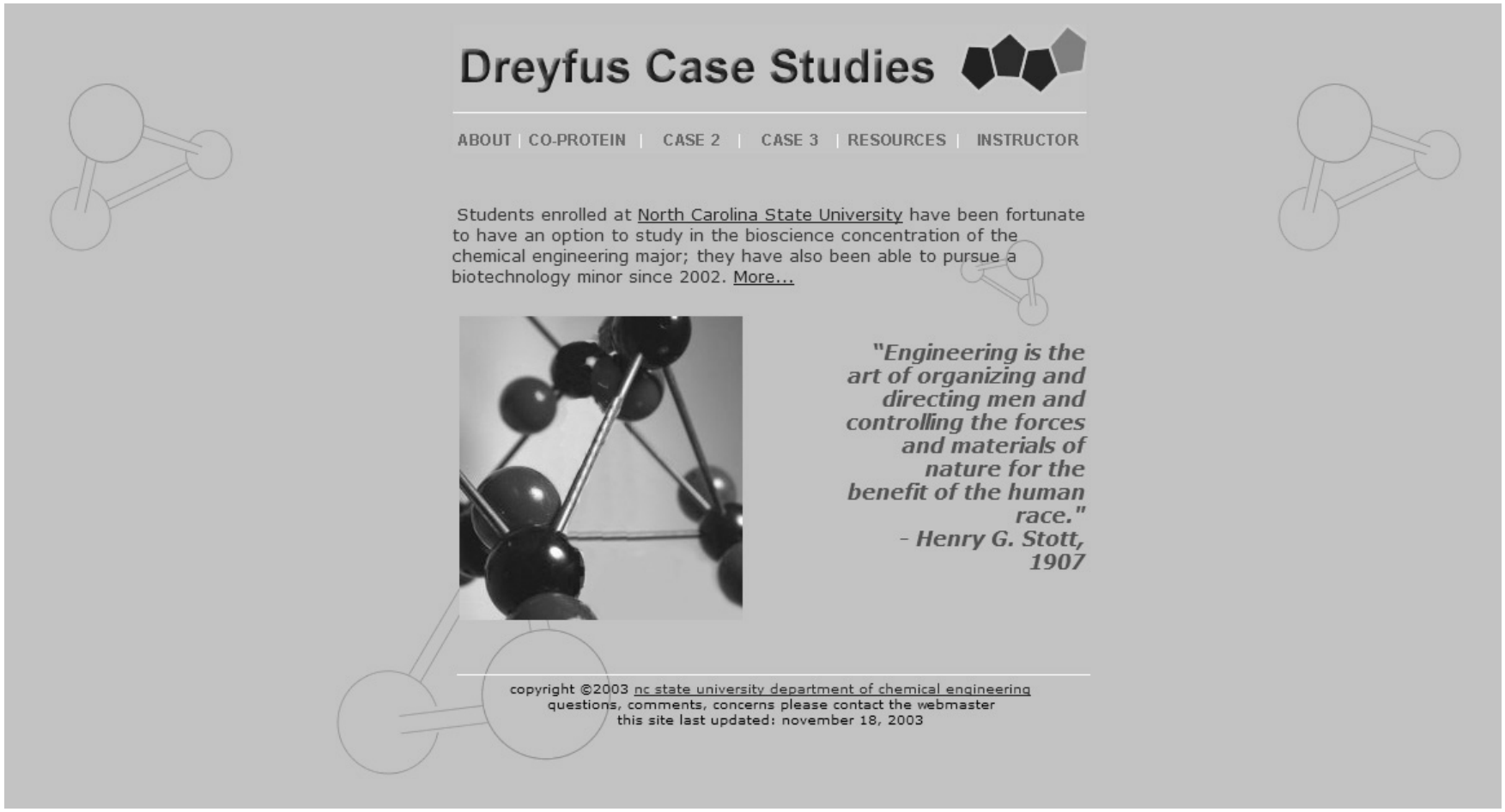
Website
Student Access



Website
Faculty Access



Introductory web page



http://www.ncsu.edu/project/actionagenda/coprotein

Problem Statement

- Retrofit an Existing Biological Facility to Produce Antigenic Co-proteins
  - Potential Candidates:
    - Co-Human Immunodeficiency Virus (HIV)
    - Co-Hepatitis B (Hep C)
    - Co-Hepatitis C (Hep C)
    - Co-Human Papilloma Virus (HPV)
    - Co-Respiratory Syncytial Virus (RSV)
    - Co-Rotavirus

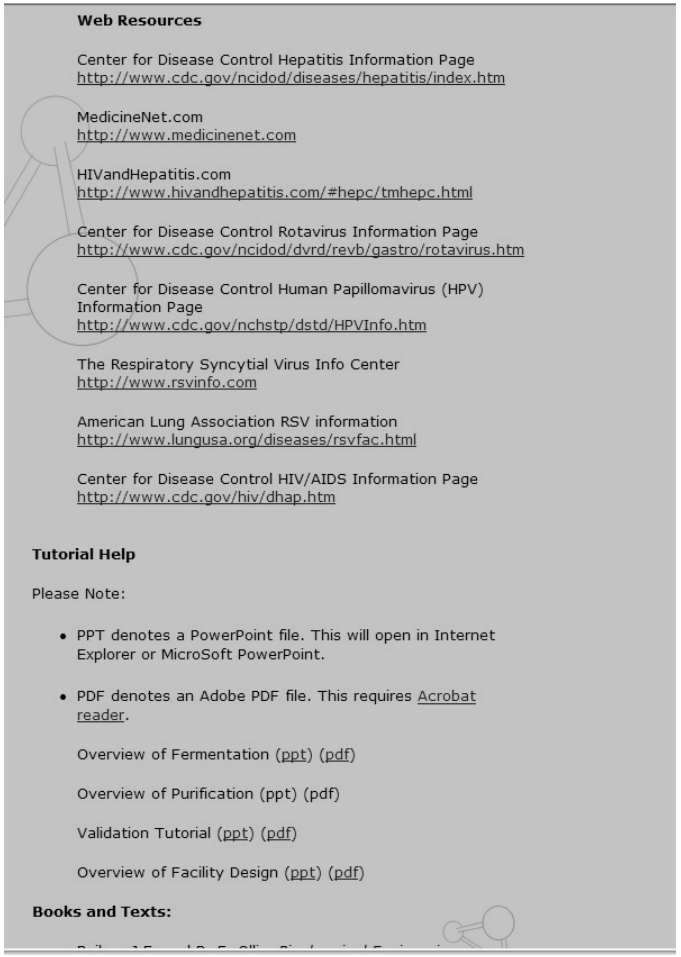
Problem Statement
Objectives

- Learning Objectives
  - Manufacturing process
  - Validation practices and techniques
  - Facility design
  - Regulatory obligations
  - Engineering economics
  - Control/Control systems

Website Resources

Each Case Study has the following resources available to students:

- Web Resources
- Tutorial Help
- Books, Texts, Journals



Web Resources

Center for Disease Control Hepatitis Information Page
http://www.cdc.gov/ncidod/diseases/hepatitis/index.htm

MedicineNet.com
http://www.medicinenet.com

HIVandHepatitis.com
http://www.hivandhepatitis.com/#hepc/tmhepc.html

Center for Disease Control Rotavirus Information Page
http://www.cdc.gov/ncidod/dvrd/revb/gastro/rotavirus.htm

Center for Disease Control Human Papillomavirus (HPV) Information Page
http://www.cdc.gov/nchstp/dstd/HPVInfo.htm

The Respiratory Syncytial Virus Info Center
http://www.rsvinfo.com

American Lung Association RSV information
http://www.lungusa.org/diseases/rsvfac.html

Center for Disease Control HIV/AIDS Information Page
http://www.cdc.gov/hiv/dhap.htm

Tutorial Help

Please Note:

- PPT denotes a PowerPoint file. This will open in Internet Explorer or MicroSoft PowerPoint.
- PDF denotes an Adobe PDF file. This requires Acrobat reader.

Overview of Fermentation (ppt) (pdf)

Overview of Purification (ppt) (pdf)

Validation Tutorial (ppt) (pdf)

Overview of Facility Design (ppt) (pdf)

Books and Texts:

Information pages

Example from a tutorial

Clean in Place (CIP): Used to ensure that the production vessels are free of any contaminants. It is essential to ensuring high quality of all finished drug products. Properly automated CIP systems reduce the need for unsafe manual cleaning efforts and increase the level of consistency and effectiveness of the cleaning process.

All are from Pharmaceutical Engineering, the official journal of the ISPE unless noted otherwise. Links can be found at www.ispe.org.

Adams, Dan G. and Deepak Agarwal, 10, (6), 1990, "CIP System Design and Installation", pp 9-15.

Marks, PE, David M., 19, (2), 1999, "An Integrated Approach to CIP/SIP Design for Bioprocess Equipment", pp 34-45.

Sieberling, Dale, 6, (6), 1986, "Clean-In-Place and Sterilize-In-Place Applications in Parenteral Solutions Process", pp 30-35.

Exemplary Solution Components

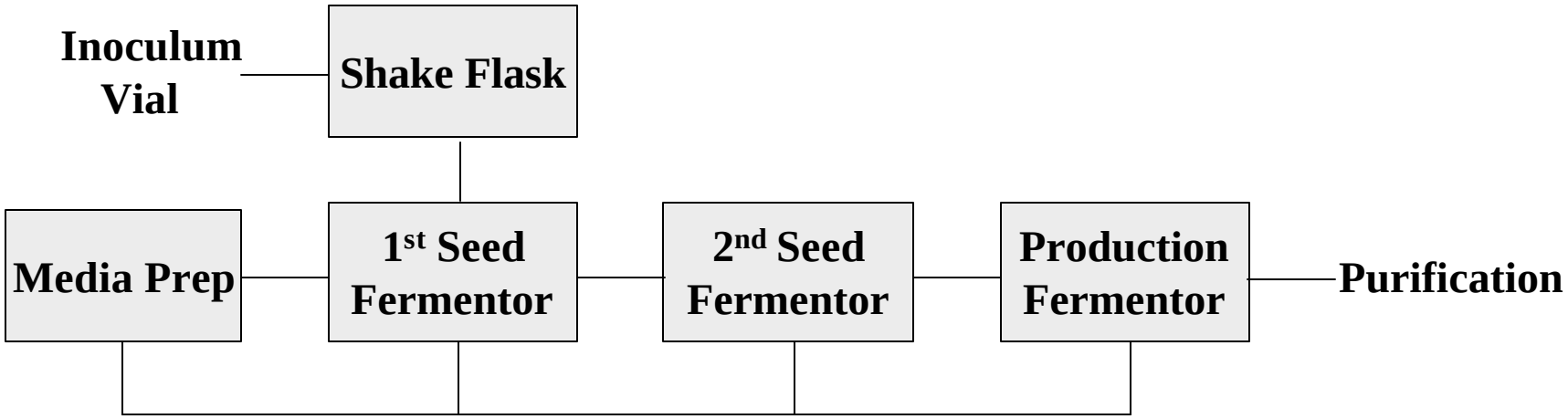
- Executive Summary
- Introduction
- Product Line Determination
- Process Description
- Waste Management
- Regulatory Requirements
- Facility Design
- Validation
- Detailed Manufacturing Costs
- Conclusions

Exemplary solution Recommendations

- Common expression system (*E. coli*)
- Extracellular product
- Analysis restricted to US market
- Market capture grows to 20%
- Subset of potential products selected
  - HIV, HepB, HepC, HPV

Exemplary Solution Production

- Staged Batch Fermentation
  - Shake Flask
  - Seed Fermentors
  - Production Fermentor



Exemplary solution Purification

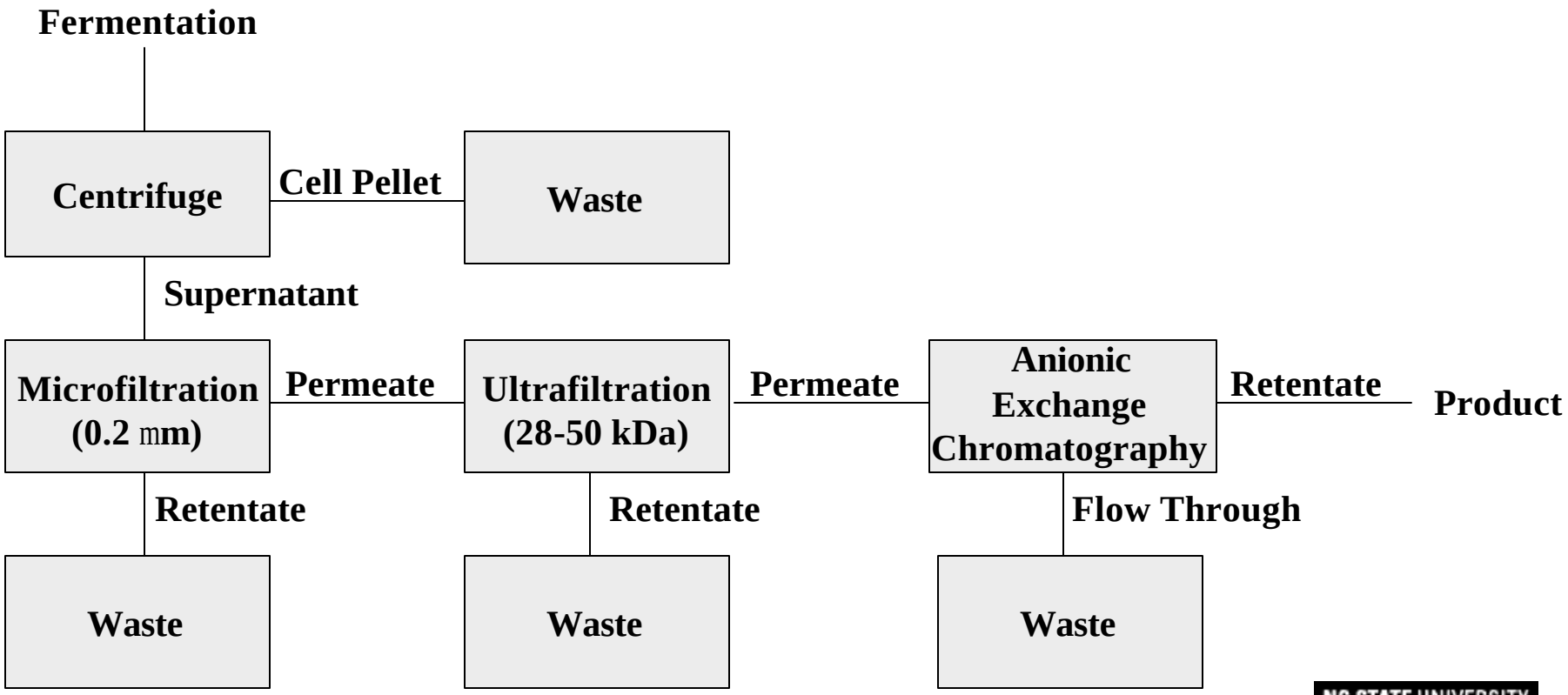
- Similarities
  - Centrifugation
  - 0.2 μm microfiltration
- Differences
  - Ultrafiltration
    - Molecular weight
    - Number of units
  - Chromatography
- Co-HIV is a more complex purification

Co-Protein Characteristic Table

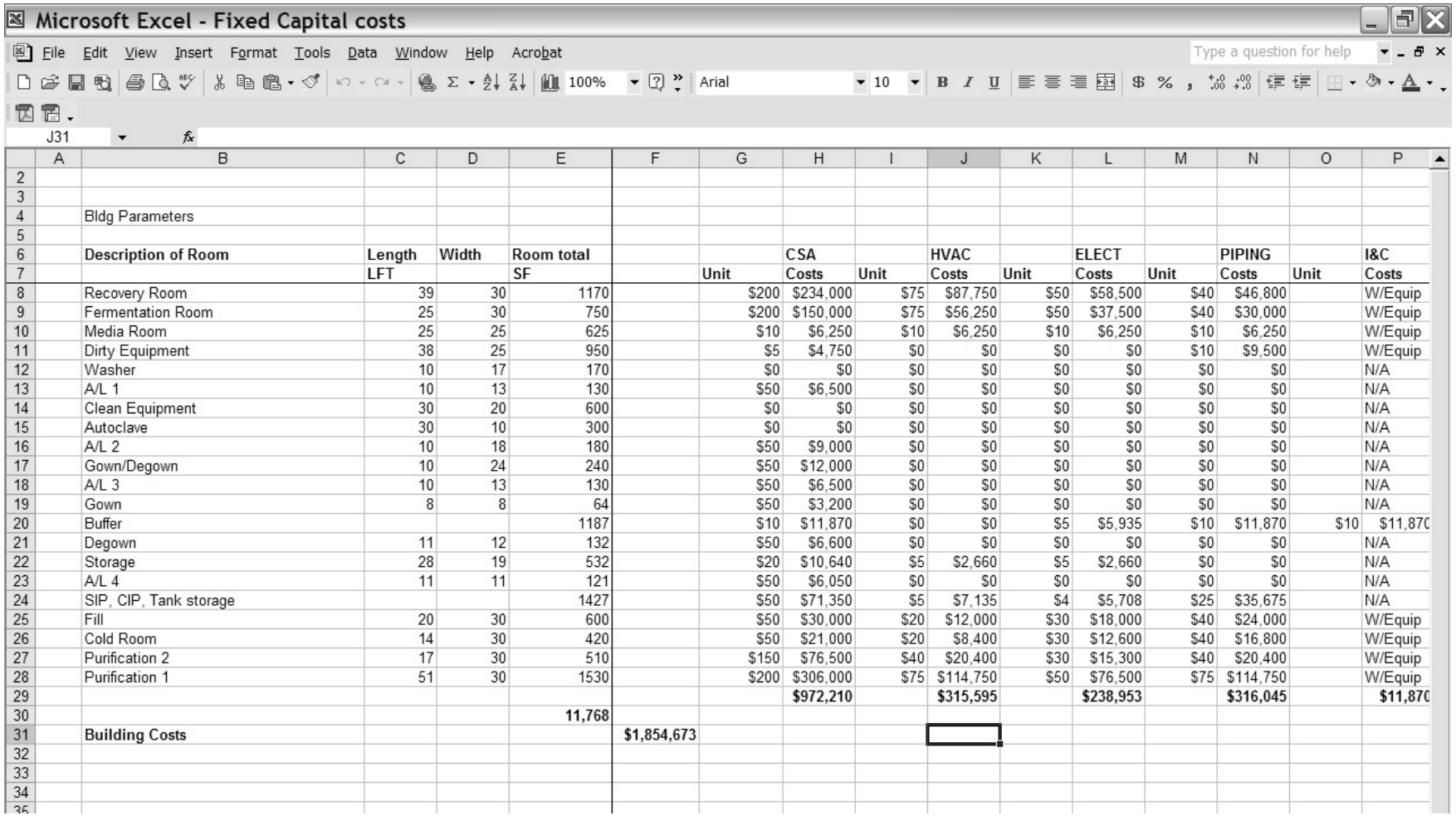
Protein	Molecular Weight (+/- 2 kDa)	Overall Charge	Known Contaminants Co-produced (+/- 2 kDa)
co-HCV	6	Neutral	< 3 > 10
co-HPV	10	Neutral	> 50
co-Rv	30	Positive	28 (-charge) > 50
co-HIV	10	Negative	10 (+ charge) < 50

Exemplary solution
Purification

Co-HIV Purification Block Flow Diagram



Economic Analysis
Fixed Capital Costs


Microsoft Excel - Fixed Capital costs

File Edit View Insert Format Tools Data Window Help Acrobat

Type a question for help

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	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
2																
3																
4		Bldg Parameters														
5																
6		**Description of Room**	**Length**	**Width**	**Room total**			**CSA**		**HVAC**		**ELECT**		**PIPING**		**I&C**
7			**LFT**		**SF**		**Unit**	**Costs**	**Unit**	**Costs**	**Unit**	**Costs**	**Unit**	**Costs**	**Unit**	**Costs**
8		Recovery Room	39	30	1170		$200	$234,000	$75	$87,750	$50	$58,500	$40	$46,800		W/Equip
9		Fermentation Room	25	30	750		$200	$150,000	$75	$56,250	$50	$37,500	$40	$30,000		W/Equip
10		Media Room	25	25	625		$10	$6,250	$10	$6,250	$10	$6,250	$10	$6,250		W/Equip
11		Dirty Equipment	38	25	950		$5	$4,750	$0	$0	$0	$0	$10	$9,500		W/Equip
12		Washer	10	17	170		$0	$0	$0	$0	$0	$0	$0	$0		N/A
13		A/L 1	10	13	130		$50	$6,500	$0	$0	$0	$0	$0	$0		N/A
14		Clean Equipment	30	20	600		$0	$0	$0	$0	$0	$0	$0	$0		N/A
15		Autoclave	30	10	300		$0	$0	$0	$0	$0	$0	$0	$0		N/A
16		A/L 2	10	18	180		$50	$9,000	$0	$0	$0	$0	$0	$0		N/A
17		Gown/Degown	10	24	240		$50	$12,000	$0	$0	$0	$0	$0	$0		N/A
18		A/L 3	10	13	130		$50	$6,500	$0	$0	$0	$0	$0	$0		N/A
19		Gown	8	8	64		$50	$3,200	$0	$0	$0	$0	$0	$0		N/A
20		Buffer			1187		$10	$11,870	$0	$0	$5	$5,935	$10	$11,870	$10	$11,870
21		Degown	11	12	132		$50	$6,600	$0	$0	$0	$0	$0	$0		N/A
22		Storage	28	19	532		$20	$10,640	$5	$2,660	$5	$2,660	$0	$0		N/A
23		A/L 4	11	11	121		$50	$6,050	$0	$0	$0	$0	$0	$0		N/A
24		SIP, CIP, Tank storage			1427		$50	$71,350	$5	$7,135	$4	$5,708	$25	$35,675		N/A
25		Fill	20	30	600		$50	$30,000	$20	$12,000	$30	$18,000	$40	$24,000		W/Equip
26		Cold Room	14	30	420		$50	$21,000	$20	$8,400	$30	$12,600	$40	$16,800		W/Equip
27		Purification 2	17	30	510		$150	$76,500	$40	$20,400	$30	$15,300	$40	$20,400		W/Equip
28		Purification 1	51	30	1530		$200	$306,000	$75	$114,750	$50	$76,500	$75	$114,750		W/Equip
29								**$972,210**		**$315,595**		**$238,953**		**$316,045**		**$11,870**
30					**11,768**											
31		**Building Costs**				**$1,854,673**										
32																
33																
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Economic Analysis
Projected Sales Revenue

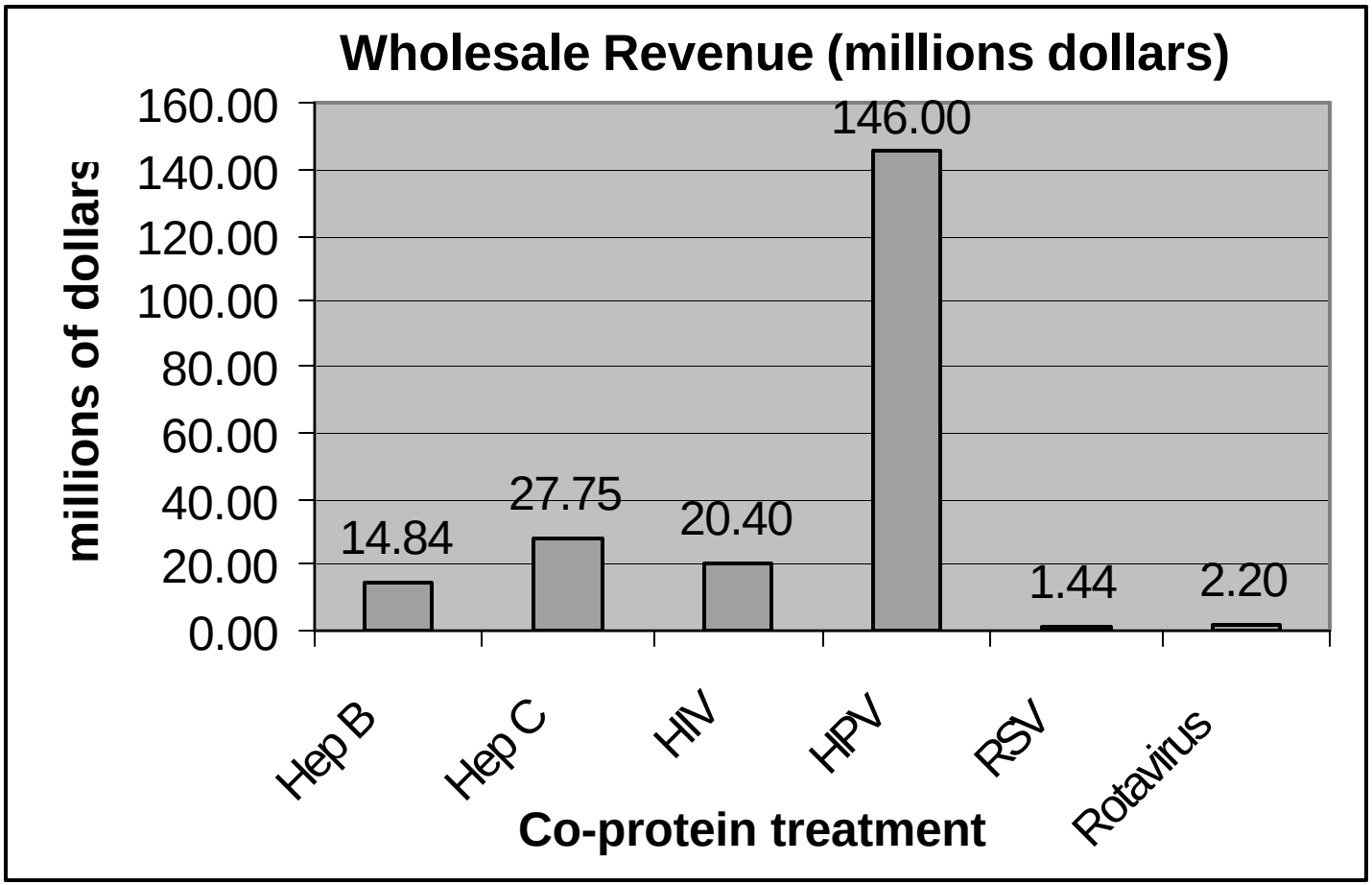

Figure 7. Sales Revenue for year 2006.

What's next?

- Completion of co-protein case study
  - Implementation advice
  - Expand tutorials
  - Develop SuperPro Designer simulation
  - Testing this year - looking for volunteers

What's next?

- Ammonia synthesis plant
  - Available Online in February 2004
- Citric acid retrofit/expansion project
  - Expand tutorials
  - Add mechanical engineering component to solution
  - Develop instructor's manual
  - Testing next spring
  - Available Online May 2004

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Contact Information

- Website Location:
  http://www.ncsu.edu/project/actionagenda/coprotein
- NC State Chemical Engineering Department
  http://www.che.ncsu.edu
  - Dr. Lisa Bullard
    (Lisa_Bullard@ncsu.edu)
  - Dr. Steven Peretti
    (peretti@eos.ncsu.edu)
  - Patty Niehues
    (pniehues@nc.rr.com)
  - Shannon White
    (Shannon_White@ncsu.edu)

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