# Suggested Design Projects – 2002-2003

1. Methyl Methacrylate from Isobutylene (or t-butanol)
2. New Route to Methyl Methacrylate
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4. Diphenyl Carbonate
5. Autothermal Steam Reformer
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7. Antithrombin III Production in Transgenic Goats
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1. Methyl Methacrylate from Isobutylene (or t-butanol)
(recommended by John Wismer, Atochem North America)

Methyl Methacrylate (MMA) monomer is a precursor to acrylic polymers, the most important of which is poly methyl methacrylate (PMMA). Annual worldwide MMA consumption is approximately 4 billion lb/yr, with the U. S. accounting for over 1 billion lb/yr.

You work for one of the major U. S. producers of MMA. Your firm manufactures MMA by the conventional route, which includes the reaction of acetone and hydrogen cyanide (HCN) to form acetone cyanohydrin, followed by hydrolysis, reaarangement to methacrylamide sulfate and esterification to MMA. Although it has high yields, sulfuric acid is used, requiring corrosion-resistant equipment, and producing large amounts of acidic waste sludge. The handling of the highly toxic hydrogen cyanide is also difficult. To your firm's knowledge, all of the MMA made in the U. S. uses the cyanohydrin route.

The improvement of this process has been a focus of worldwide R&D efforts for years. The competitive process route, which has attracted the most attention, produces MMA from isobutylene or t-butanol in three reaction steps:

$$\underset{\text{Isobutylene}}{CH_2{=}C(CH_3)_2} + O_2 \rightarrow \underset{\text{Methacrolein (MA)}}{CH_2{=}C(CH_3)CHO} + H_2O \qquad \text{(R1)}$$

$$\underset{\text{Methacrolein}}{CH_2{=}C(CH_3)CHO} + 1/2\ O_2 \rightarrow \underset{\text{Methacrylic Acid (MAA)}}{CH_2{=}C(CH_3)COOH} \qquad \text{(R2)}$$

$$\underset{\text{Methacrylic Acid (MAA)}}{CH_2{=}C(CH_3)COOH} + \underset{\text{Methanol}}{CH_3OH} \rightarrow \underset{\text{Methyl Methacrylate (MMA)}}{CH_2{=}C(CH_3)COOCH_3} \qquad \text{(R3)}$$

When t-butanol (TBA) is used in R1, the stoichiometry is the same except that a second molecule of water is produced. Selectivity is a key issue in all steps. Side reactions of the oxidation steps create CO and $CO_2$.

The C4 route to MMA has become prominent in Japan in recent years. In the early 1990's, Asahi Kasei Corp. announced a new process that combined steps (2) and (3) using a proprietary catalyst. In 1999, it announced completion of a plant to produce MMA using its DOE (Direct Oxidation-Esterification Process). All indications are that they are very confident that they will be the low cost producers. In October of 1999, they issued a U. S. Patent (US 5,969,178) which elaborates in some detail the conceptual approach to their separation train.. Essentially they recycle excess methanol and unreacted methacrolein to the distillation train between the reactors to help in the separation of MA from water. Their entire separation scheme consists of six columns and a decanter. Given that this process has a variable cost advantage over the cyanohydrin route, a simple process could also give it a capital cost advantage. The patent is conceptual; it does not specify a separation train with a closed material balance. In fact, there appear to be some

options with respect to where the unreacted material is recycled. Much data on the azeotropes of the materials to be separated is included. The patent also includes yields for the two reactor steps. There is mention of some impurities, from which you can deduce some non-selective reactions. Detailed VLE data are available in ASPEN PLUS or in the literature.

Your management asks you to determine how much, if anything, a license to use this technology would be worth to your firm. They need to know the cost difference between building more capacity using the "old" technology, as compared with using the new technology. You are requested to evaluate this technology using the most optimistic data available in the patents. Set the production capacity to 300 million pounds per year.

References:

US Patent 5,969,178

Ishikawa, T., "Vapor-Liquid Equilibriums of the Methanol-Methyl Methacrylate System at 313.15, 323.15, and 333.15K", *Fluid Phase Equilibria*, **3** (1), 23-34 (1979).

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2. New Route to Methyl Methacrylate
(recommended by Bruce Vrana, DuPont)

Methyl methacrylate (MMA) is a monomer or comonomer in many polymers, most notably Plexiglas (R). The conventional MMA process has many drawbacks, including use of sulfuric acid as a catalyst. Most manufacturers neutralize the sulfuric acid with ammonia, producing byproduct ammonium sulfate, which must be sold or disposed of. HCN is also used in the process, requiring the MMA plant to be linked to a source of highly toxic HCN.

Ineos Acrylics UK Ltd., who bought ICI's acrylics business (who in turn bought DuPont's acrylics business), is commercializing a new route to MMA that eliminates the above problems. Their process carbomethoxylates ethylene to form methyl propionate (MP) using a homogeneous palladium catalyst. MP is then reacted with formaldehyde in the gas phase, giving MMA and water. Both reactions are highly selective. The MMA will then need to be purified to meet normal commercial specifications.

$$CH_2 = CH_2 + CO + CH_3OH \rightarrow \underset{(MP)}{CH_3 - CH_2 - COO - CH_3}$$

$$CH_3 - CH_2 - COO - CH_3 + CH_2O \rightarrow \underset{\underset{(MMA)}{COO - CH_3}}{CH_3 - C = CH_2} + H_2O$$

Your company has asked your group to determine whether this new technology should be used in your Gulf Coast plant. Your job is to design a process and plant to produce 200 MM lb/yr of MMA from ethylene, which is available on the site. Based on past experience, you know that you will have to be able to defend any decisions you have made throughout the design, and the best defense is economic justification.

Your manager has hinted to you that an outstanding report, one that will guarantee your next promotion, will include the effects of the reversible, equilibrium oligomerization of formaldehyde in the plant simulation. If she wanted formaldehyde treated simply, as just a monomer, she would not have assigned your team to the project. Fortunately, ASPEN PLUS provides a simple model to handle formaldehyde (FORMALDEHYDE.BKP, part of the standard installation of ASPEN PLUS) from which you can use the thermodynamic estimation methods. It considers only the equilibrium behavior of the system, not the kinetics of the oligomerization reactions. Assume this is a good approximation. Adding the kinetic effects is well beyond that which can be expected, given the time constraint.

Nonetheless, this model may not be accurate for all process conditions in your flowsheet. A truly outstanding report will recognize this fact, estimate the errors under the range of

conditions in your flowsheet, and include reasonable safety factors. The reference below provides a more detailed thermodynamic model than is used in FORMALDEHYDE.BKP. The model in the paper more accurately represents the data, but adding it to ASPEN PLUS is probably beyond that which can be reasonably accomplished by the project deadline. However, the paper also has experimental data (and references to more data), which can be tested against the ASPEN PLUS thermodynamic model to determine how well the ASPEN PLUS model represents the data for various conditions of your flowsheet.

Assume a U.S. Gulf Coast location on the same site as a large chemical plant. 99.95% pure MMA can be sold for $0.60/lb, according to your marketing organization. Ethylene is available on your site for $0.23/lb. Carbon monoxide can be purchased over the plant fence for $0.12/lb at 100 psig.

Formaldehyde sells for $0.20/lb of contained formaldehyde, and can be bought as a 37% solution in water, with 15% methanol to stabilize the monomer; this solution is called formalin. Alternatively, a neighboring (but high cost) plant produces formaldehyde, which could be purchased over the fence for immediate consumption without the methanol, for $0.22/lb, still as a 37% solution in water. Select whichever formaldehyde source is most economical, considering both the operating cost as well as the capital cost of the plant.

Methanol is estimated by your marketing organization to cost $0.40/gal over the long term. However, if MTBE (one of the largest markets for methanol) is legislated out of gasoline, that price might drop to $0.20/gal, while the price of formaldehyde, made from methanol, might drop to $0.04/lb. Test your economics both with and without the MTBE phase-out prices, and make appropriate recommendations. All prices listed are in 2003 dollars.

The plant design should be as environmentally friendly as possible. Recover and recycle process materials to the maximum economic extent. Also, energy consumption should be minimized, to the extent economically justified. The plant design must also be controllable and safe to operate. Remember that you will be there for the start-up and will have to live with whatever design decisions you have made.

References:

World Patents 99/21820, 99/52628, 99/02480 to ICI

Albert, M., I. Hahnenstein, H. Hasse, and G. Maurer, *AIChE Journal*, **42**, 6, 1741-1752 (1996).

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3. New Route to Propanediol
(recommended by Bruce Vrana, DuPont)

It has been known for many years that a polyester using 1,3-propanediol (PDO) instead of ethylene glycol would have interesting fiber properties in uses such as fabrics and carpets. What has been lacking is an economical way to produce PDO.

In recent years, Shell has patented a new process to produce PDO via hydroformylation of ethylene oxide (EO). DuPont, on the other hand, has purchased technology from Degussa to make acrolein, which can be hydrated and then hydrogenated to PDO. Simultaneously, DuPont is also developing a glucose-based route.

However, sometimes new technology comes from unexpected sources. And it is the job of the chemical engineer to determine what impact it might have. TTC Labs has patented a new route to PDO which goes through acrolein. Acrolein is quite toxic and has a tendency to polymerize, besides being expensive to produce via the Degussa process. This new route potentially produces and consumes the acrolein in the same reactor, or in two closely coupled reactors, thus minimizing the hazards associated with acrolein.

$$HCHO + CH_3 - CHO \rightarrow CH_2 = CH - CHO + H_2O$$

$$CH_2 = CH - CHO + H_2O \rightarrow CH_2OH - CH_2 - CHO$$

$$CH_2OH - CH_2 - CHO + H_2 \rightarrow CH_2OH - CH_2 - CH_2OH$$

The new route uses a classical reaction to produce acrolein from formaldehyde and acetaldehyde, catalyzed by secondary amine salts, either in solution or immobilized. The hydration to 3-hydroxypropanal is acid catalyzed, and can be run either in the same reactor or in a separate reactor. Hydroxypropanal is easily hydrogenated to PDO over a conventional hydrogenation catalyst.

Your company, one of the two industrial giants mentioned above, has asked your group to determine under what circumstances this new technology will be economical to operate, and thus could be a threat to your business. Your job is to determine the optimum reactor configuration and flowsheet, recognizing that you do not have access to all of the data. Design a process and plant to produce 100 MM lb/yr of PDO. Based on past experience, you know that you will have to be able to defend any decisions you have made throughout the design, and the best defense is economic justification.

Your manager has hinted to you that an outstanding report, one that will guarantee your next promotion, will include the effects of the reversible, equilibrium oligomerization of formaldehyde in the plant simulation. If she wanted formaldehyde treated simply, as just a monomer, she would not have assigned your team to the project. Fortunately, Aspen Plus provides a simple model to handle formaldehyde (formaldehyde.bkp, part of the standard installation of Aspen Plus) from which you can use the thermodynamics. It considers only the equilibrium behavior of the system, not the kinetics of the

oligomerization reactions. Assume that this is a good approximation. Adding the kinetic effects is well beyond what can be expected, given the time constraint.

Nonetheless, this model may not be accurate for all process conditions in your flowsheet. A truly outstanding report will recognize this fact, estimate the errors under the range of conditions in your flowsheet, and include reasonable safety factors. The reference below provides a more detailed thermodynamic model than is used in FORMALDE-HYDE.BKP. The model in the paper more accurately represents the data, but adding it to ASPEN PLUS is also probably beyond that which can be reasonably accomplished by the project deadline. However, the paper also has experimental data (and references to more data), which can be tested against the ASPEN PLUS thermodynamic model to determine how well the ASPEN PLUS model represents the data for various conditions in your flowsheet.

Assume a U.S. Gulf Coast location on the same site as a large chemical plant. Acetaldehyde can be purchased for $0.45/lb, according to your marketing organization. Hydrogen can be purchased over the plant fence for $0.50/lb at 200 psig. All prices listed are in 2003 dollars.

Formaldehyde, purchased as formalin (a 37% solution in water with 15% methanol to inhibit polymerization) can be purchased for $0.20/lb (per pound of contained formaldehyde). Alternatively, a neighboring (but high cost) plant produces formaldehyde, which could be purchased over the fence for immediate consumption without the methanol, for $0.22/lb, still as a 37% solution in water. Also, if MTBE (one of the largest markets for methanol, the raw material for formaldehyde) is legislated out of gasoline, the price of both formaldehyde solutions might drop by $0.04/lb. Test your economics both with and without the MTBE phaseout prices, and make appropriate recommendations.

If the plant is not economical under the above circumstances, try to develop another scenario where the technology would be economically competitive with conventional PDO processes. Determine the sensitivity of the economics to the cost of acetaldehyde and formaldehyde, and the selling price of PDO. Assume the competitive price for PDO is $0.75/lb.

The plant design should be as environmentally friendly as possible. Recover and recycle process materials to the maximum economic extent. Also, energy consumption should be minimized, to the extent economically justified. The plant design must also be controllable and safe to operate.

References:

World Patent 02/06393 to TTC Labs

Albert, M., I. Hahnenstein, H. Hasse, and G. Maurer, *AIChE Journal*, **42**, 6, 1741-1752 (1996).

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4. Diphenyl Carbonate
(recommended by Bruce Vrana, DuPont)

Polycarbonates, particularly valued for their optical clarity and impact resistance, have historically been made using highly toxic phosgene. Recently, they have been made via the transesterification of diphenyl carbonate (DPC) with bisphenol A. But the production of DPC has been problematic. The conventional route to DPC also uses phosgene, while another route has troublesome azeotropes.

Mitsubishi Gas Chemical has developed a new route where inexpensive urea reacts with n-butanol, to produce first butyl carbamate (BC) and then dibutyl carbonate (DBC). The DBC must then be purified before it can be reacted with phenol to give phenyl butyl carbonate (PBC). PBC can then be disproportionated to DPC and DBC.

$$NH_2 - CO - NH_2 + BuOH \rightarrow NH_3 + NH_2 - CO - OBu \quad (BC)$$

$$NH_2 - CO - OBu + BuOH \rightarrow NH_3 + BuO - CO - OBu \quad (DBC)$$

$$BuO - CO - OBu + PhOH \rightarrow BuOH + PhO - CO - OBu \quad (PBC)$$

$$2\,PhO - CO - OBu \rightarrow BuO - CO - OBu + PhO - CO - OPh \quad (DPC)$$

At first glance, this process would also appear to have problems, since BC and DBC form an azeotrope which must be broken before the reaction with phenol. However, Mitsubishi found that phenol itself could be used to break the azeotrope. Phenol and DBC distill overhead, leaving BC in the bottoms, which can be recycled. The phenol-DBC stream can then be reacted to form PBC, liberating n-butanol for recycle.

Your company has asked your group to determine whether this new technology should be used in your Gulf Coast polycarbonate plant. Your job is to design a process and plant to produce 100 MM lb/yr of DPC from urea and phenol. Based on past experience, you know that you will have to defend any decisions you have made throughout the design, and the best defense is economic justification.

Assume a U.S. Gulf Coast location on the same site as the polycarbonate plant. This site does not currently produce "chemicals", instead relying on purchased DPC, so you will have to provide all utilities required (boiler, cooling water, etc.). Other outside battery limits investment will be higher than normal also, as well as several elements of operating cost, due to the current lack of chemical manufacturing expertise at the site. In fact, costs are more likely to resemble a totally new plant site than an existing chemical manufacturing site.

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Urea sells for $150/ton, according to your marketing organization. Phenol can be purchased for $0.28/lb. Butanol can be purchased for $0.50/lb. Your company currently purchases its DPC from a polycarbonate competitor for $0.80/lb. Ammonia byproduct can be sold for $200 per ton if it is anhydrous. You may also buy sulfuric acid for $25 per ton to neutralize aqueous ammonia, then crystallize and dry the ammonium sulfate (AS), and sell it for $100 per ton in bulk. You may make and sell anhydrous ammonia or AS or both, or do anything else with the ammonia that is environmentally sound, whichever you decide is most economical. All prices listed are in 2003 dollars.

Your competitor, who wants to keep its plant running at full capacity, is likely to offer you a lower price on the DPC if they believe that you are serious about building your own plant. A quality plant design will indicate that intent to build your own plant. Calculate the DPC price that they would have to offer you for your company to be indifferent between making and buying DPC. In other words, calculate the DPC price that makes the net present value (NPV), discounted at your company's opportunity cost of capital of 25%, of buying DPC equal to the NPV of making DPC yourself. Even if you decide not to build the plant, your company may make some money with this technology by vendor torquing. Calculate the NPV of the technology if it forces your competitor to reduce your DPC price to the indifference point.

The plant design should be as environmentally friendly as possible. Recover and recycle process materials to the maximum economic extent. Also, energy consumption should be minimized, to the extent economically justified. The plant design must also be controllable and safe to operate. Remember that you will be there for the start-up and will have to live with whatever design decisions you have made.

References:

US Patents 6,169,197, 6,031,122, 5,980,445, and 5,714,627 to Mitsubishi Gas Chemical.

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5. Autothermal Steam Reformer
(recommended by William B. Retallick, Consultant)

The Armed Forces need to generate electricity silently and with no tell-tale emissions. Fuel cells are the natural choice, with steam reformers needed to make hydrogen. The hydrocarbons to be steam reformed are the "logistic" fuels, diesel or jet fuel JP8. The reformers must be compact and have light weight. Your company, Catacel.com, has proposed a design wherein the reforming reactor and the heat exchanger are combined into a single module, which is the welded plate exchanger, made by Tranter, Inc. The plates of the exchanger are coated with combustion catalyst on one side and with reforming catalyst on the other side. Vaporized fuel and steam flow through the reforming channels while fuel and air flow through the combustion channels.

The Tranter publication shows the design of their exchanger. Catacel's reformer would comprise of a chain of exchangers connected in series. In each exchanger, the plates are 12 inches long and 4 inches wide. Spacing between the plates is 0.078 inches. Vaporized fuel for combustion is injected at the inlet of each combustor.

The water-gas shift section of the reactor follows the reforming section and is just a continuation of the reforming section. Cooling air instead of fuel plus air flows counter-current to the reformed products. This is shown in the patent application.

Following the shift section there is a membrane that separates pure hydrogen for the fuel cell. The shift output must be delivered to the membrane at a pressure of at least 10 psig. The residue gas that does not go through the membrane is incinerated. The heat release in the incinerator must be no more than 5% of the heating value in the incoming logistic fuel. The membrane and the incinerator are not included in your design. The output of the fuel cell is 100 kw. The efficiency of the fuel cell is about 50%, so that your reactor train must produce hydrogen at a rate of 6 kg/hr.

For the reforming reaction you will need some kinetic data. Herewith are data for reforming methane. You can assume that when the fuel is JP8 or diesel the catalyst will reform the same number of mols of carbon per second when the steam/carbon ratio is increased to 6. For the shift reaction, use the paper by Bunluesin, Gorte, and Graham. Assume that both catalysts and also the combustion catalyst can be coated onto the plates of the Tranter exchanger. For the combustion reaction, assume the limiting case wherein the reaction rate is limited by mass transfer. This is equivalent to assuming that every molecule that hits the geometric surface of the catalyst coating reacts immediately. Assume that the JP8 fuel has the properties of normal $C_{12}H_{26}$.

Your task is to minimize the weight of the chain of exchangers. Here is a way to do this:

1. Assume the number of plates in the exchangers, say 40.

2. Calculate the number of exchangers and the total weight. Also calculate the pressure drop.

3. Repeat with some other number of plates.

In making the calculations you have to keep the heat release on the combustion side of a plate in step with the heat absorbed on the reforming side.

References:

Patent application titled “Autothermal Steam Reformer”.

Plot from the laboratory of Professor Greg Jackson at The University of Maryland, showing the activity of the reforming catalyst.

Paper by Bunlieson, Gorte, and Graham on the water-gas shift reaction.

Literature from Tranterphe, where phe is an abbreviation for plate heat exchangers

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6. Manufacture of Silicon Coated Chips
(recommended by Talid R. Sinno, U. Penn)

In the manufacture of microelectronic chips and devices, it is necessary to deposit a thin film of material (e.g. silicon nitride, silicon dioxide, or amorphous silicon) on a wafer substrate. One way to accomplish this is by using so-called plasma-enhanced chemical vapor-deposition (PECVD), involving parallel electrodes, at low pressure. In this process, the gas-phase reactants are activated by impact with electrons rather than with heat, leading to greatly enhanced reaction rates. On the other hand, a major disadvantage of the PECVD approach is the spatial nonuniformity of the deposited layer, which severely limits the quality of microelectronic devices. The goal of this project is to model, analyze, and optimize a PECVD system in order to maximize the growth rate while maintaining good control over the uniformity of the deposited film.

In one particular process, a 500 Å film of amorphous silicon is deposited on an 8-cm wafer, which sits on top of the lower electrode (Armaou and Christofides, 1999; Christofides, 2001), as shown in Figure 1. The reactor is fed with 10% $SiH_4$ (silane) in He at 1 torr through a showerhead. An RF power source, at 13.56 MHz frequency, is used to generate a plasma (chemically-reactive mixture of ions, electrons, and radicals) at 500 K, which is transported by convection and diffusion to the surface of the wafer where they react and deposit amorphous silicon. In the design of these silicon coated chips, it is an objective to examine this and other configurations for this reactor, to assure that a uniform thin film, containing few impurities, is obtained. These specifications should be adjusted iteratively until satisfactory performance is achieved. The FEMLAB program can be used to prepare simulations of the PECVD process.

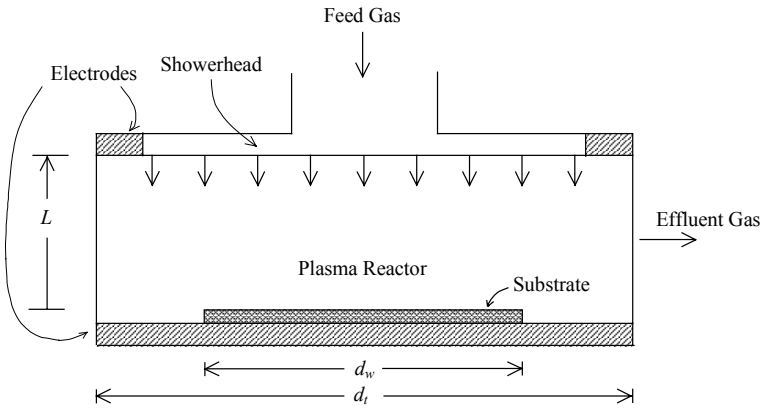


Figure 1 Cylindrical showerhead, electrode, plasma-enhanced, CVD reactor.

In their theoretical analysis, Armaou and Christofides (1999) provide the following kinetic model for the chemical reactions.

Initial Dissociation

Initially, $SiH_4$ dissociates due to electron impact to form silylene radical, $SiH_2$, silyl radical, $SiH_3$, and atomic hydrogen:

$$e^- + SiH_4 \rightarrow SiH_2 + 2H + e^- \quad \text{R1}$$
$$e^- + SiH_4 \rightarrow SiH_3 + H + e^- \quad \text{R2}$$

Then atomic hydrogen reacts with $SiH_4$:

$$H + SiH_4 \rightarrow SiH_3 + H_2 \quad \text{R3}$$

Silyl radicals diffuse toward the wafer surface where recombination reactions occur:

$$2SiH_3 \rightarrow SiH_4 + SiH_2 \quad \text{R4}$$
$$SiH_4 + SiH_2 \rightarrow Si_2H_6 \quad \text{R5}$$

The intrinsic rates of consumption in mol/(cm$^3$min) of the four species are:

$$r_{SiH_4} = -k_1 n_e c_{SiH_4} - k_2 n_e c_{SiH_4} - k_3 c_{SiH_4} c_H + k_4 c_{SiH_3}^2 - k_5 c_{SiH_4} c_{SiH_2} \quad (1)$$
$$r_{SiH_2} = k_1 n_e c_{SiH_4} + k_4 c_{SiH_3}^2 - k_5 c_{SiH_4} c_{SiH_2} \quad (2)$$
$$r_{SiH_3} = k_2 n_e c_{SiH_4} + k_3 c_{SiH_4} c_H - k_4 c_{SiH_3}^2 \quad (3)$$
$$r_H = 2k_1 n_e c_{SiH_4} + k_2 n_e c_{SiH_4} - k_3 c_{SiH_4} c_H \quad (4)$$

where $c$ is the concentration in mol/cm$^3$ and $n_e$ is the electron density given by:

$$n_e\{r,z\} = n_e^{\max} J_0\left\{2.405\frac{r}{r_t}\right\}\sin\left\{\frac{\pi z}{L}\right\} \quad (5)$$

Here, $n_e^{\max}$ is the maximum electron density in the reactor, $r$ is the radial position in the reactor, $r_t$ is the radius of the reactor cylinder, $z$ is the axial coordinate, $L$ is the height of the reactor (distance between the two electrodes), and $J_0$ is the zero-order Bessel function of the first kind. Clearly, the electron density is a maximum at the center of the reactor ($r = 0$, $z = L/2$). The rate constants are:

| Rate Constant | Units |
|---|---|
| $k_1 = 1.870 \times 10^{-11}$ | $s^{-1}cm^3$ |
| $k_2 = 1.590 \times 10^{-10}$ | $s^{-1}cm^3$ |
| $k_3 = 1.325 \times 10^{12}$ | $s^{-1}mol^{-1}cm^3$ |
| $k_4 = 9.033 \times 10^{13}$ | $s^{-1}mol^{-1}cm^3$ |
| $k_5 = 2.830 \times 10^{13}$ | $s^{-1}mol^{-1}cm^3$ |

The deposition rate of amorphous silicon is:

$$r_{dep}\{t,r\} = \frac{1}{\rho_{\mathrm{Si}}}\left[\sum_{i=1}^{4} s_i D_i \frac{\partial c_i}{\partial z}\{t,r,0\}\right] \tag{6}$$

where $\rho_{\mathrm{Si}}$ is the density of amorphous Si, and $s_i$ is the fraction of the flux of species $i$ toward the surface that leads to the deposition of amorphous silicon. These and other physical properties are provided in the references.

Your goal is to implement and solve numerically the model of Armaou and Christofides for the PECVD process and then investigate possible approaches for optimizing the process with respect to film production and uniformity. The model involves the solution of a set of coupled mass transport equations along with an analytical solution for the gas-phase fluid mechanics. Appropriate boundary conditions on the reactor and wafer surfaces also are given. For example, to obtain a uniform thin film of amorphous silicon, it may be desirable to adjust the radial flow rate of silane through the showerhead nozzles. This can be accomplished using simple control algorithms.

In carrying out this design, it is important to set a reasonable production rate and estimate the installation costs and operating costs of the manufacturing train. An estimate of the minimum price per wafer to achieve an investor's rate of return (IRR) of 20% should be determined.

References:

Armaou, A., and P. D. Christofides, "Plasma Enhanced Chemical Vapor Deposition: Modeling and Control," *Chem. Eng. Sci.*, **54**, 3305-3314 (1999).

Christofides, P. D., *Nonlinear and Robust Control of PDE Systems: Methods and Applications to Transport-Reaction Processes*, Birkhauser, Boston, 2001.

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7. Antithrombin III Production in Transgenic Goats
(recommended by Eric T. Boder, U. Penn)

Background

Antithrombin III (ATIII) is a blood plasma protein that helps prevent harmful blood clotting in many serious medical conditions. Approximately 1 in 5,000 individuals are born with hereditary ATIII deficiency leading to reduced plasma levels of this protein. In addition, ATIII deficiency can be acquired as a result of liver diseases, sepsis, shock, burns, multiple trauma, organ transplantation, and various surgical procedures.

Currently, ATIII is marketed in Europe and Japan; this material is derived from donor blood plasma. A recombinant human ATIII (rhATIII) has been developed and evaluated in clinical trials. This product promises to simplify production and is considered safer since it is free of infectious agents potentially present in human donor plasma. The annual worldwide market for human ATIII is $300 million, and availability of the recombinant product could potentially double this demand through expansion of suitable applications.

Product requirements

Pharmaceutical grade rhATIII is to be produced as a sterile, lyophilized powder of ≥99% purity. An initial production run will be required to create 2 kg of material for phase III clinical trials. Due to regulatory constraints, the process used to produce the trial material must be identical to the process used to produce the marketed drug. Therefore, the process should be designed to produce 500 kg/year, which will meet the current worldwide demand. Plans should be evaluated for the possibility of increased demand up to 1,000 kg/yr as well.

Production system

Antithrombin III genes have been cloned and the protein expressed in a number of different systems. Production of ATIII in the milk of engineered transgenic mammals, as described in the listed references, is particularly promising for a product requiring such a high level of production. This method presents the possibility of simplified post-clinical trial scaleup as well. Recombinant human ATIII produced by transgenic goats has recently passed phase II clinical trials; process optimization is limited essentially to the separation methods. Note that one of the patents provides information concerning possible membrane separation modules. Other separation techniques will be considered.

References: Levy, J. H., et al. *Sem. Thromb. Hemostasis* 27: 405 - 416 (2001)
Pollock, D. P., et al. *J. Immunol. Meth.* 231: 147 – 157 (1999)
U.S. Patent 6,441,145
U.S. Patent 6,268,487
GTC Biotherapeutics website (http://www.transgenics.com)

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8. Edible Protein from Cheese Whey by Ultrafiltration
(recommended by Leonard A. Fabiano, U. Penn)

A cheese plant produces cheddar cheese from whole milk and has a current whey stream of 1,000,000 lb/day. The plant operates 7 day/wk. The operating day is 20 hr and plant cleaning takes place in the remaining 4 hr. The whey is currently subjected to evaporation and spray drying to produce a dried product, which is sold as animal food for $0.15/lb, with just marginal profits. The drying operation, however, eliminates cheese whey as a waste stream from the plant. Company management would like to investigate the use of ultrafiltration to produce a whey protein concentrate to be sold as food additives for human consumption. Your group has been asked to propose a design.

Your design should produce three dry powder products containing: (1) 35% protein (based upon the sum of true protein, TP, and non-protein nitrogen, NPN), (2) 75% protein, and (3) 85% protein. In the first year of operation, market forecasts anticipate sales at 14,000 lb 35%/day, 4,000 lb 75%/day, and 400 lb 85%/day. Price forecasts are $0.65/lb, $1.25/lb, and $2.50/lb of dried powder, respectively. Over the next 10 years, it is anticipated that cheese production will increase by 4% annually.

When manufacturing whey protein concentrates, ultrafiltration will increase the concentration of protein while selectively removing the low molecular weight solutes-ash (salt) and lactose. For the 35 and 75% products, continuous processing will be advantageous because spoilage will not occur in residence times of less than 4 hr. For the 85% product, a carefully designed batch process may be preferable, with batch times less than 4 hr. Note that the maximum protein concentration that can be achieved with ultrafiltration is about 55%, on a dry solids basis. To reach 75 and 85%, diafiltration must be utilized, as discussed in the reference materials.

Your design must account for cleaning and sanitizing the equipment. A strategy is suggested in the reference materials.

<u>Design Basis</u>

Feed composition (weight basis)

| | |
|---|---|
| True protein, TP | 0.6% |
| Non-protein nitrogen, NPN | 0.3 |
| Lactose | 4.9 |
| Ash | 0.8 |
| Butter fat | 0.05 |
| Remainder is water | |
| Density is 8.5 lb/gal | |

Membrane rejection coefficients (fraction of solute that does permeate through)

| | |
|---|---|
| True protein | 0.97 |
| Non-protein nitrogen | 0.32 |

| | |
|---|---|
| Lactose | 0.085 |
| Ash | 0.115 |
| Butter fat | 1.00 |

Membrane cartridge ($PM_{10}$ from Koch Membrane Systems)

| | |
|---|---|
| Cost of 26.5 $ft^2$ hollow-fiber cartridge | $200 each |
| Cost of cartridge clamps, gaskets, adapters | $15 per cartridge |
| Membrane life | 1 yr |
| 3 in diameter, 40 in long | |
| Manifold spacing | 7 in centers |

Optimum cartridge operating conditions

| | |
|---|---|
| Inlet pressure | 30 psig |
| Cross-flow pressure drop | 15 psi |
| Permeate pressure | 5 psig |
| Recirculation rate per cartridge | 23 gpm |

Equation for membrane flux rate

$$J = 27.9 - 5.3 \ln\{CF\}$$

where J is the flux rate in gal/($ft^2$ membrane-day) and CF is the concentration factor (feed volume/retained volume). This equation was developed using $PM_{10}$ cartridges in the laboratory.

Cost of concentrates to formulate cleaning solutions

| | |
|---|---|
| CIP acid from Ecolab | $9.09/gal |
| Ultrasil 22 from Ecolab | $11.86/gal |
| Sodium hypochlorite (5.25 wt%) | $0.90/gal |

Municipal waste treatment*

$1.00/1,000 gal of hydraulic load
$0.12/lb of BOD** above 300 mg/L
$0.10/lb of TSS (total suspended solids)

* Given these high costs, alternate strategies for waste treatment may be considered, as suggested in the reference materials.

** Estimate the BOD load based upon BOD being 60% of the theoretical COD for the complete oxidation of organics, primarily lactose.

References:

Notes are provided that describe the kinds of microfiltration processes (batch, multistage feed-and-blend, diafiltration, etc.). Some assistance is provided in formulating the design models.

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