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Nonlinear Multiple Input Multiple Output Process as a Final Project: Bringing Motivation to the Control Classroom

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Abstract

This paper presents the results of applying a final project in an undergraduate chemical engineering control class. The final project is a nonlinear simulation of a process that has 3 or more inputs and outputs that must be regulated. The simulation includes additional disturbances such as input/output noise and load disturbances such as changes in feed concentration. The purpose is to bring the sometimes-esoteric world of control which is often taught overwhelmingly in the linear Laplace domain back to the reality of actual process applications that are tricky to control. Not only does this provide motivation for the students to learn control but is introduced throughout the course in parts to accentuate this reality prior to each exam in the class. Overall, the students have shown increased efficacy resulting in higher grades for the second and third exams due to the final project being introduced. It also is nice way to introduce something that has similar complexity for regulating actual unit operations in industry.

Introduction

Control Space

The vastness of control theory is summarized in Figure 1. Control is a subject taught to all engineers except for civil, and yet seems like an island of its own. The unique jargon taken from mechanical, electrical, etc. can be daunting to an undergraduate student. Coupled with the often overreliance of dealing with linear systems in the Laplace Domain and control can come across as a very esoteric subject that has little meaning in the real world. Seniors take to and light up when learning and implementing their final design projects. There is a sense that all the courses led to this moment and now it can be applied to building an actual process. And yet control is the subject arguably most critical to a graduating chemical engineer that most likely will have a first industrial job as a process engineer. What does a process engineer do? Well, she is responsible for maintaining a process of unit operation(s) to run at specified conditions 7 days a week, 24 hours a day. Yes, she is essentially doing control. Look again at Figure 1. Realize that those of us that are control engineers, the applied mathematicians of the engineering world, do not cover all the space on the control map of theory. Even after many courses in advanced control or mathematics. Now consider this space of topics. Which of them should be taught to undergraduate students? And to how much depth? Are we preparing students to go into the field of control? Or are we getting them ready to face industrial equipment, seasoned operators, and an intimidating Distributed Control System board containing tens to hundreds of control loops? And that does not include the fact that the processes are often highly nonlinear with little to no fundamental modeling available. Actual disturbances come from either poor control upstream or the fact that the multiple loops on a single unit operation interact with one another leading to effective process gains very different than when all the loops are open, and inputs are manipulated manually. And even though the beauty of a proportional integral and derivative (PID) controller is its simplicity and utility; it is severely hampered by being restricted to single pairs of one input to one output and that it has no idea what the actual input constraints are for the system.

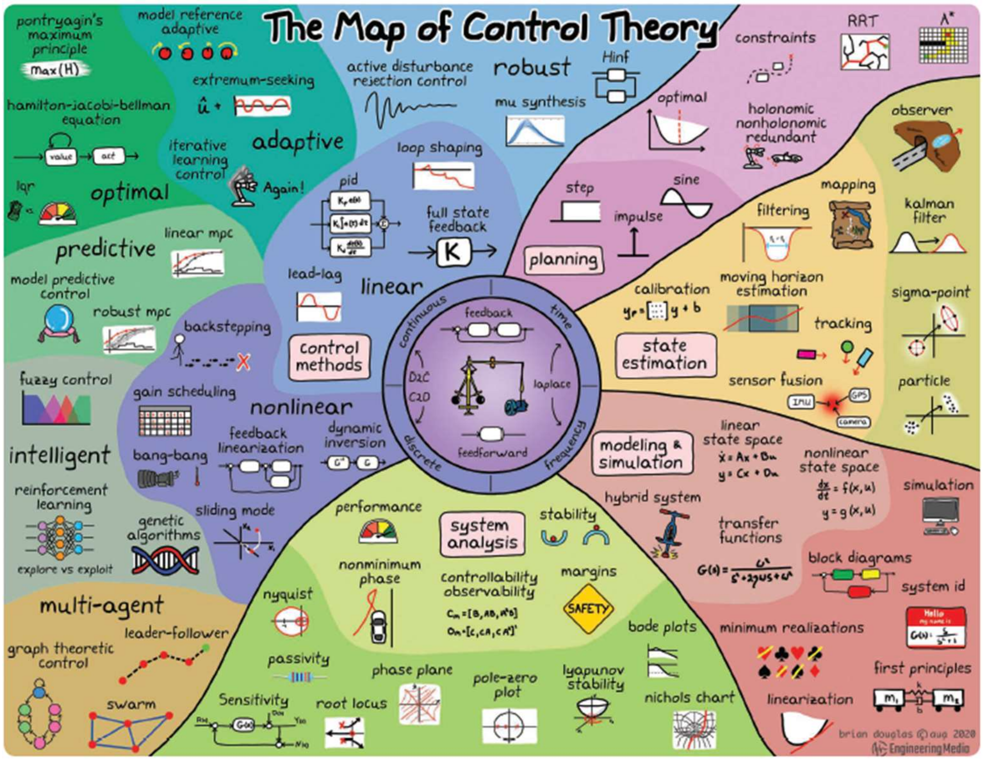


Figure 1. Map of Control Theory [1]

Chemical Engineering Control Classes

There have been discussions as far back as 2006 at various chemical engineering education symposiums where faculty have strongly considered removing process control from the curriculum, that it is a mature field, that it is unlikely to have much future impact on discovery of new technology [2]. And as stated earlier, the primary job of a process engineer is control. The pressure on control as a class increases with the advent of a strong push to reduce curriculums from 130+ credits to 120 credits to increase enrollment into engineering and make in theory retention of students in engineering easier. There have been papers published trying to push major changes in control education methodologies many limiting or removing Laplace Domain usage and increasing use of nonlinear simulations, and yet not happened to large extent [2],[3],[4],[5],[6]. Perhaps best summarized as follows: “Process control is a core course in the chemical engineering undergraduate curriculum, yet it sometimes suffers from an over-emphasis on analytical mathematics without proper motivation from real process challenges”[7].

What Is Industry Looking for?

From Bequette 2019, [7] shows surveys from industry in 2006 to academic coverage in 2015 shown in Figure 2. Fascinating to look at industry needs which cover many advanced topics that are not covered in much depth or at all in academia at the single undergraduate course level. Much of the focus from industry appears to be fundamental modeling leveraged to optimization and advanced control. In Bequette 2019 [7] lists typical chemical engineering control curriculum where modeling, nonlinear dynamics or control optimization get one to two weeks at most. Not sufficient to meet what industry is requiring and another symptom of any control class is back to Figure 1 on control map of theory, does the course suffer scope creep and become more of a survey class than one with depth and real expertise obtained by the students.

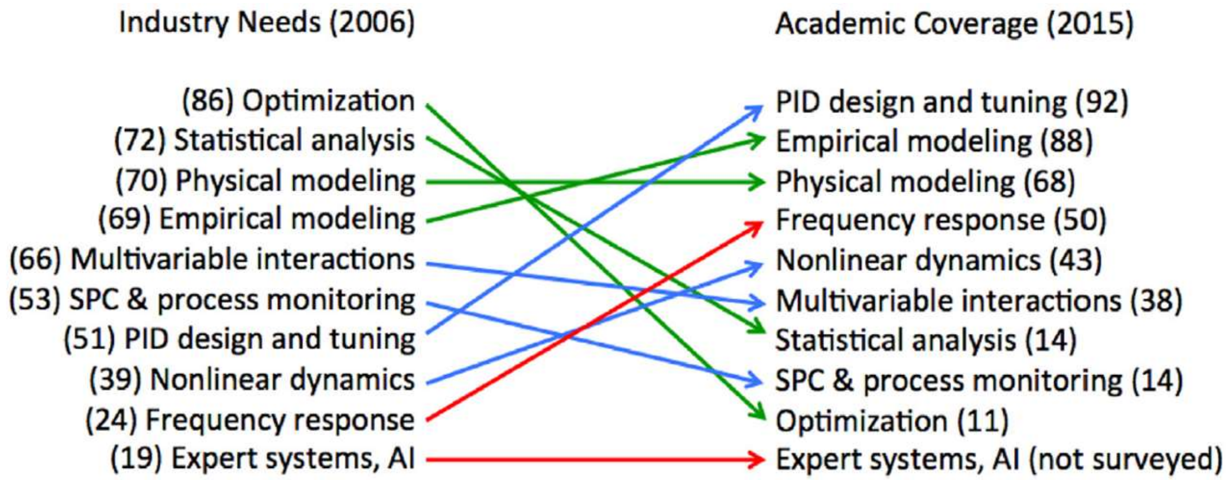


Figure 2. Survey 2006 Industry Mapped to Academia 2015 [7]

Keeping It Real: Need To Teach Operating Regions

There are many reasons to have the students focus and spend time on actual nonlinear systems. The obvious one is to make the simulation they are controlling seem much more relevant and interesting. But the real purpose that is often lost in most control textbooks is that the reliance on the Laplace Domain has robbed the students of understanding the very key point of what an operating region is. There are many control papers in the literature let alone in textbooks that will simply represent this complicated nonlinear process as a matrix of transfer functions. And yes, they will include input constraints. But all these transfer functions do not hold over the range of inputs given for the real process. It is almost comical if it did not have real world repercussions. Students need to understand the key concept that when perturbing the system and fitting it to some reduced transfer function such as a first order plus dead time model that is now going to be used for controller design that this is a linearization of the process and is only accurate within the baseline operating region. And that is true only if the magnitude of the perturbation did not exceed the operating region they are trying to model. Every time a student is taught to use a model for a system in the Laplace Domain only, they lose the fact that the controller designed will not work over the whole range of the input constraints. In fact, that is more a rarity than the norm. Transfer functions for lime kilns, cardiac arrest patients, reactive etchers, etc. do not hold for the range of inputs outlined in final projects given to students[8]. Representing a nonlinear multivariable process by a matrix of transfer functions leads to real repercussions for students that think these are at least close to accurate models that reflect a dynamic range of responses over the input constraints. And instead end up with a system that a single controller can regulate. There are no operating regions. Operating region is not an easy concept to teach. But it is an easy one to show when using proper simulations for the nonlinear system. Use transfer functions for controller design not to simulate the actual process. Make students understand that PID control design is in its essence a linear controller based on a linearization about one operating point. How well that controller will hold at different input values will depend on how nonlinear the system is. When the controller starts to fail the system is in a new operating region, and a new linearized model for new PID tuning will be needed. The straightforward next step to nonlinear control by applying gain scheduling is easily introduced this way. All disturbances to the system can be seen as perturbations to the system that may have moved it to a new operating region.

Proposed Chemical Engineering Curriculum

The authors provided an outline of their chemical engineering curriculum in [9]. It can be summarized as an abbreviated first exam on linear control theory covering Laplace Domain to get to what are process zeros and their importance on dynamic responses and process poles determine process time constants. Then applying controller direct synthesis to see how right half plane zeros cannot be canceled, and that controller affects primarily closed loop poles or eigenvalues. The second exam is on nonlinear control of a single input single output process using internal model based PID controller tuning. Large set point changes and other disturbances are applied. The third exam is on a nonlinear 2 input 2 output multiple input multiple output (2x2 MIMO) system. Students use relative gain analysis for control loop pairing and tuning rules.

The additional work here is inclusion of a final project that has more complexity than can be given in an in-class exam that is motivational for students to use throughout the course to introduce new concepts and have students complete that section prior to when it will be used in an exam. Instead of a final students work on closing all the multivariable single input single output loops make any necessary tuning adjustments and then test the controller on various setpoint changes and disturbances.

Final Project General Framework

Nonlinear MIMO setup with more than 2 inputs by 2 outputs. Not a take home test. Have input/output noise to make it more realistic. Students would submit parts throughout the course to help prepare for the exams too. Each section is then graded and corrected prior to going on to the next stage of the project. Can not work with another student but feel free to ask the instructor questions.

Part 1: Step Responses and Process Gains. (20 pts) Students perturb the process by doing a Step response for each input and then calculate all process gains. Done prior to Nonlinear Single Input Single Output Exam 2.

Part 2: Determine the Relative Gain Array, Input-Output Pairings. (20 pts) Students use the process gains found in Part 1 to calculate the Relative Gain Array then determine the controller input output pairs and their tuning strategies. Done prior to Nonlinear Multiple Input Multiple Output (2x2) Exam 3.

Part 3: First Order Plus Dead Time Models and Individual Controller Tuning (40 pts) Students use the step responses done in Part 1 along with the calculated controller pairs to find each process time constant and delay. Then using these models and the tuning rules from Part 2 students obtain Multiple Variable Single Input Single Output (MV-SISO controllers). Done prior to Exam 3.

Part 4: MIMO Control. (20 pts) All MV-SISO controllers are now closed at same time (not individually as in Part 3 using the best tuning from Part 3. The control of the complete process is evaluated and any additional tweaking in tuning done at various setpoint combinations and disturbances. This is handed in during the Finals Week.

Wastewater Treatment 3x3 System

The wastewater treatment process has a bioreactor, settler with recycle, and aerator. The process has very different time scales and can exhibit changes in gain sign and inverse responses. A process block diagram of the system see fig. 1. The bioreactor is essentially an aerobic digester.

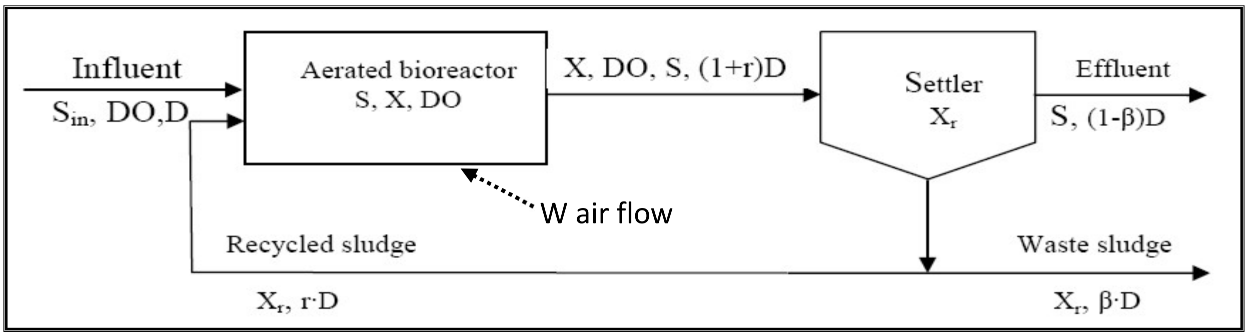


Figure 2. Process Block Diagram Wastewater Treatment Process

The objective is to regulate cell concentration (X), dissolved oxygen level (DO), and substrate concentration (S) by manipulating the dilution rate (flow of feed into the process, D), the gas dilution rate/flow (W), and recycle fraction (r). There is some noise present in the measurements and occasionally there is a disturbance in the feed substrate concentration, Sin.

Table 1 Inputs for Wastewater Treatment

Input	Baseline (initial)	Final Step	Constraints	
Dilution Rate	$D = 0.13\ hr^{-1}$	$D = 0.15\ hr^{-1}$	$Dmin = 0\ hr^{-1}$	$Dmax = 0.4\ hr^{-1}$
Gas Rate	$W = 110\ hr^{-1}$	$W = 100\ hr^{-1}$	$Wmin = 0\ hr^{-1}$	$Wmax = 400\ hr^{-1}$
Recycle %	r=0.6	r=0.7	rmin=0	rmax = 1

Distubance Input

Sin=200 g/L Baseline Sin_dist = 180 g/L (during a disturbance)

Table 2 Outputs for Wastewater Treatment

Output	Baseline (initial)	Final Setpoint
Cell Biomass	X= 400 g cells/L	X = 420 g cells/L
Dissolved Oxygen	$DO = 1.783$ mg O_2/L	$DO=1.65$ mg O_2/L
Substrate	S=280 mg/L	S=260 mg/L

Therapeutic Production Bioreactor 4x4 System

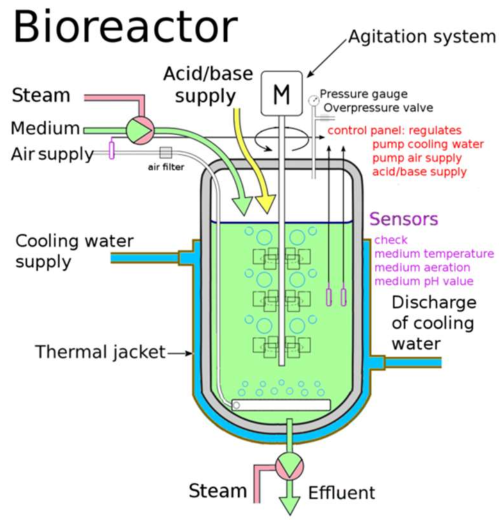


Figure 3. Realistic Bioreactor Setup [10]

Growth Model, Kinetics and Consumption

Growth kinetics in yeast cultures are commonly described by models based on the Monod equation which accounts for substrate inhibition only (Eq. 1) [11]. The maintenance term for substrate consumption (Eq. 3) is the amount of substrate required for the cell to remain alive but not increase in density. The volume in and out of the reactor is equal, thus, is assumed constant.

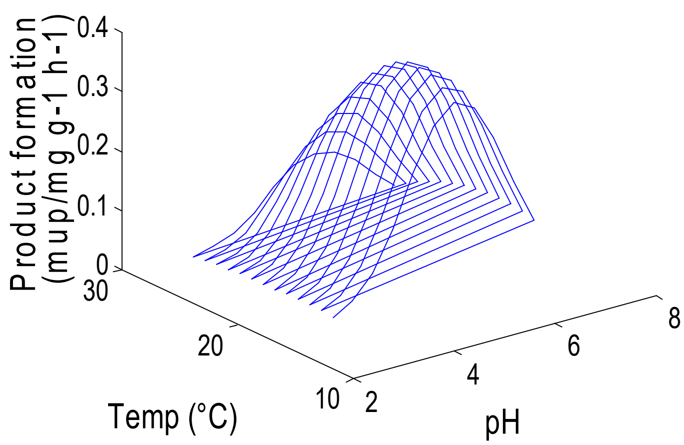


Figure 4. 3-dimensional representation of specific product formation rate [12]

Specific Product Formation Rate

This function (Eq. 6) is the product of three separate terms. The first term μ_{P_0} ,is the characteristic on the given heterologous protein (rHSA). The second term describes the influence of $[H^+]$ on the specific production formation rate and the third term describes the effect of temperature which can either enhance or hinder product formation as shown in Figure 4 [12].

There are over 500 proteins that can be expressed using *P. pastoris* systems and product formation rates vary greatly. The product to biomass yield, Y_{PX} is usually assumed as constant which is untrue. Zhang et al. [11] provides data for the variation of Y_{PX} with time and substrate concentration respectively (Eq. 7).

Oxygen Consumption and Transfer

Dissolved oxygen concentration in aerobic fermentations is one of the most important parameters and most difficult to accurately model. This varies slightly with most other bioreactor models for oxygen consumption (Eq. 8) as it includes the concentration changes due to dilution with the addition of substrate and ammonium hydroxide. One difficulty with oxygen transfer models is predicting the oxygen solubility in the fermenter media with respect to oxygen solubility in pure water [11]. For oxygen solubility in pure water (Eq. 10), we chose to model this as a function of both temperature and pressure using Henry's law (Eq. 9) as is explained by Doran [13]. Nagy [14] uses a Stechnov type equation to account for decrease in oxygen solubility (Eq.11) due to dissolved salts in the fermentor media. At this point, our model does not have a detailed account for the decrease in solubility of oxygen due to dissolved salts. Predicting the mass transfer coefficient, $k_l a$, accurately presents another problem, this done using the Van't Reit correlation (Eq. 12).

Energy Balance and Temperature Control

Temperature (Eq. 13) is an essential parameter to be monitored in bioprocesses. These equations are very similar to those used by Nagy [14] with the exception of the ammonium hydroxide flow term. The heat generation term uses the heat of reaction as well as the oxygen yield per biomass (g/g). The reactor temperature ODE has a negative sign because heat is usually lost from the reactor to the jacketed fluid (Eq. 14) causing the reaction to be exothermic.

pH Changes and Control

It is assumed that the ammonium hydroxide added to control pH is enough to provide the cells with a nitrogen source. Solving the electron neutrality equation (Eq. 16) determines the concentration of [H^+]. The phosphoric acid (A) is fed at a concentration of A_{in}. The consumption of phosphorous (Eq. 15) is considered negligible to amount present. The concentration of ammonia and phosphoric acid is in units of moles/L and the yield is converted by dividing by mw_{NH3} [11].

The objective is to regulate dissolved oxygen level (DO), substrate concentration (S), temperature (T) and pH. The inputs are the feed flow rate, Fin, the ammonia flow rate, Fnin, the jacket flow rate, Fj, and the volumetric gas flow rate, Vdot.

Table 3 Inputs for Bioreactor

Baseline (initial)	Final Step	Constraints	
Fin = 65 L/hr	Fin = 63 L/hr	Fin_min = 0 L/hr	Fin_max = 150 L/hr
Fnin = 6.2 L/hr	Fnin = 6.3 L/hr	Fnin_min = 0 L/hr	Fnin_max =10 L/hr
Fj= 7000 L/hr	Fj= 6800 L/hr	Fj_min=0 L/hr	Fj_max=10,000 L/hr
Vdot= 0.015 m^3/s	Vdot= 0.017 m^3/s	Vdot_min=0 m^3/s	Vdot_max=0.03 m^3/s

Table 4 Outputs for Bioreactor

Output	Baseline (initial)	Final Setpoint
Dissolved Oxygen	DO = 32.93 %	DO = 25 %
Substrate	S=1.761 g substrate/L	S=1.65 g/L or 2.0 g/L
Temperature	T=22.92 C	T=25 C or 15 C
pH	pH=5.38	pH=6.3

Results & Discussion

Wastewater Treatment 3x3 System

Final Project Part 1: Step Response for Process Gains

For sample results, will show for the wastewater treatment only due to space considerations. For final project part 1 the students each are responsible for one input. She then does a step response in the input and then calculates all the process gains relative to that input. Figure 5 shows a change in the recycle fraction. The process gains by the recycle fraction are quite large with some outputs exceeding the hundreds.

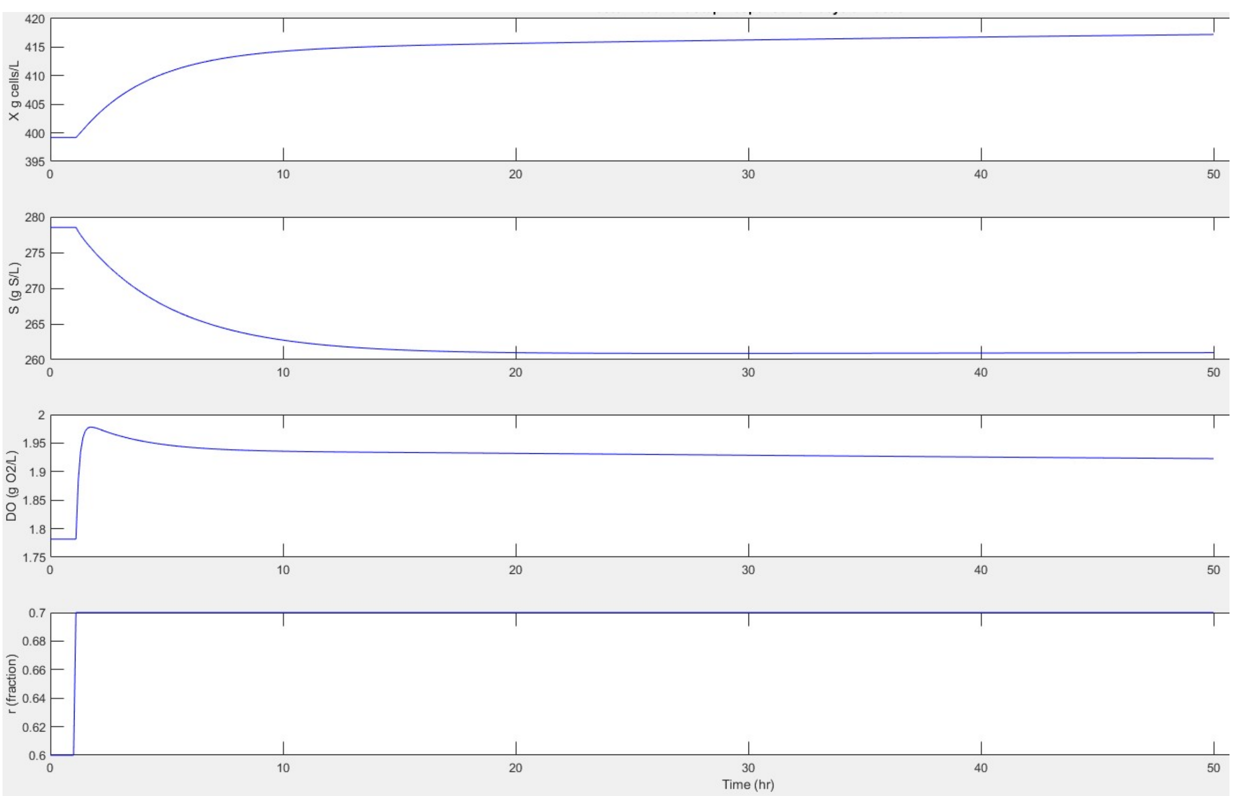


Figure 5. Step Response due to recycle fraction, r, in wastewater treatment.

Final Project Part 2: Relative Gain Array

For the students to obtain the best set of controller pairings, they use the relative gain array. The relative gain array is the open loop (manual) process gain between an input and output over the process gain for the same pairing when all the other inputs and outputs are perfectly regulated [8]. If the value is a fraction the system is considered amping since interactions make the process gain effectively larger than when the system is completely open. If the value is greater than one the system is crunching. The interactions due to the other controlled or closed loops actually make the effective process gain less. The objective is to choose the pairings so that the relative gain array is closest to one where system acts as if it is decoupled e.g. no interactions from the other loops. The relative gain array also helps in tuning the individual controllers cause one can plan for the interactions when all loops will be closed. The overall objective is that when all loops are closed each loop is slightly underdamped (small overshoot past change in setpoint) or slightly overdamped (approaching the setpoint quickly but not crossing over it). Table 5 has the process gain matrix and shows why this is such a difficult system since process gains go from single digits to thousands. Process time constants also change dramatically from different input/output combinations. This part is done as a group.

Table 5 Process Gain Matrix

	Inputs		
Outputs	Dilution Rate D	Gas Rate W	Recycle Fraction r
Cell Biomass X	-4.6E+3	4.00	205.5
Substrate S	-1.8E+3	1.52	-150.0
Dissolved Oxygen DO	39.8	-0.005	-0.82

Table 6 shows the calculated relative gains for all the input and output combinations. Highlighted in yellow in Table 6 is the best set of controller pairings (closest relative gain value to 1.0).

Table 6 Relative Gain Array

	Inputs		
Outputs	Dilution Rate D	Gas Rate W	Recycle Fraction r
Cell Biomass X	-0.29	0.95	0.34
Substrate S	0.13	0.21	0.66
Dissolved Oxygen DO	1.16	-0.16	0.00

Table 7 shows the tuning rules for each individual pairing when done individually prior to closing all the loops for the process.

Table 7 Tuning Pairs and Rules

Pairing	**System Type**	**Tuning Rule Individually**
X vs W	Slightly Amping	Tune for slightly overdamped.
S vs r	Somewhat Amping	Tune for fairly to somewhat overdamped.
DO vs D	Slightly Crunching	Tune for slightly underdamped.

Final Project Part 3: Individual Controller Tuning

In part 3, each student is individually responsible to design a single PID controller for a specific input/output pair that follows the tuning rules determined in Table 7. Initial controller tuning is obtained by fitting a first order plus dead time model for the step response for that input/output pair. The students use the resulting model with internal model based PID control tuning where the only tuning parameter is a desired closed loop time constant that is typically chosen (if no inverse response present) from the dead time plus one third to one half the process time constant calculated for the simplified first order plus dead time approximation [8]. The student then tweaks controller gain, integral or derivative time constant tuning parameters to get the desired control response from Table 7. Control performance statistics such as percent overshoot, rise time, and settling time are calculated, and brief description of control response performance and robustness provided. Figure 6 shows the controller for recycle fraction, r, regulating substrate, S. The tuning rules in Table 7 is to design this loop so its control response is fairly to somewhat overdamped.

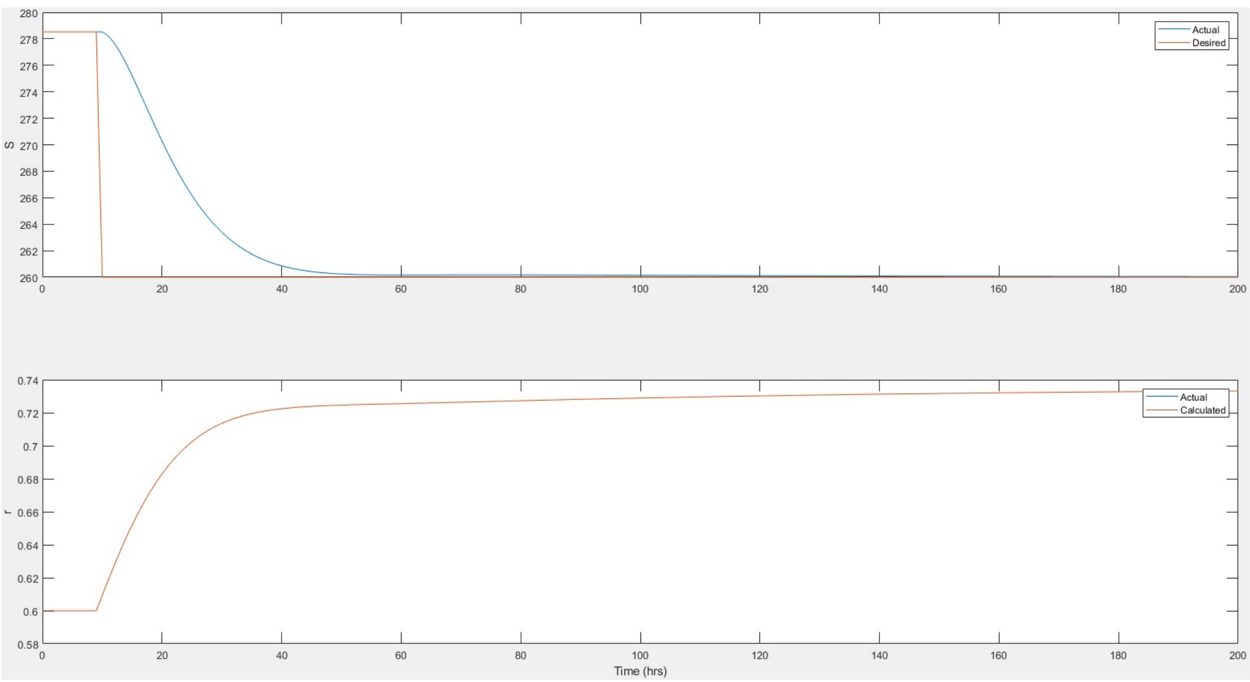
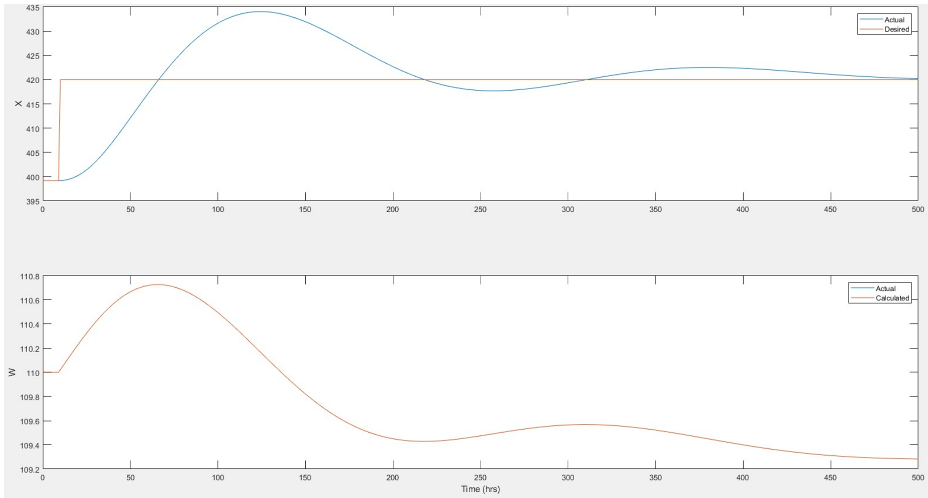


Figure 6. Control response of recycle fraction, r, to substrate, S

Final Project Part 4: MIMO Control

As a group, the students take the tuning parameters for each individual controller done in Part 3 as the starting tuning for the complete system to be regulated. The expectation is that by following the tuning rules in Table 7 the interactions between control loops can be mitigated somewhat so that each loop is slightly underdamped to overdamped in response to a setpoint change. Given that the system is nonlinear there still may be quite a lot of tweaking of control parameters for one or more of the control loops. There are trade offs in performance versus magnitude of disturbances that may be caused in the other control loops. It is important for the students to realize that there is no single set of ideal tuning parameters. Always there will be trade offs between performance and robustness and how large a magnitude interactions between loops is acceptable. For some processes product may still be of good quality even though a setpoint has not been quite reached

A.



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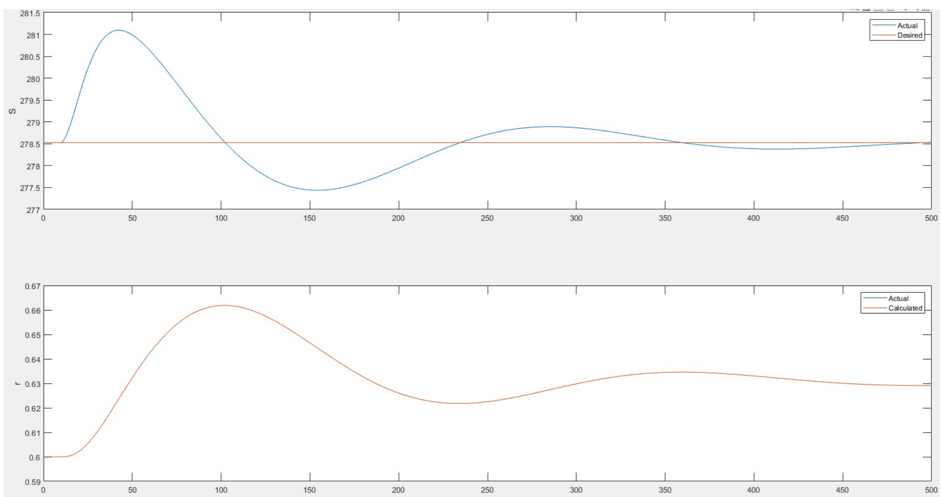

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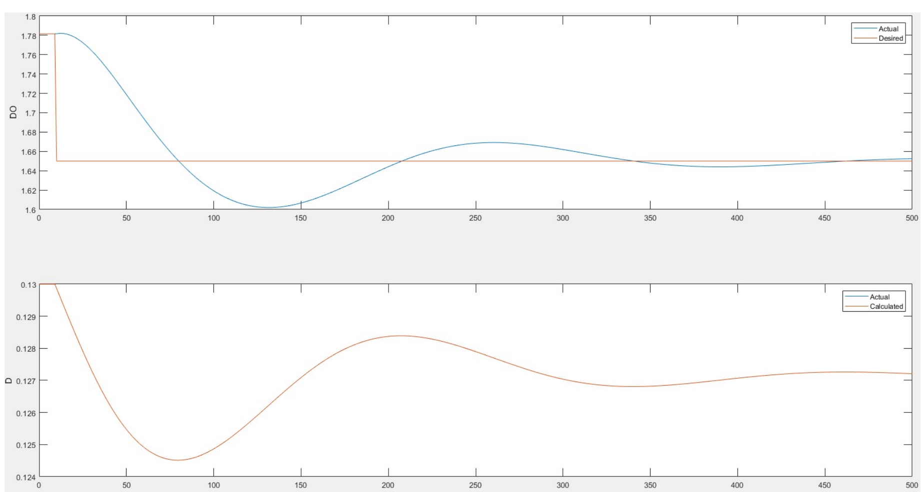

Figure 7. Control responses all loops closed. A. W vs X B. r vs S C. D vs DO

yet. Or it is possible that some disturbance could result in product that is off specification. Each process has its unique challenges, and it is critical to have students run different ones to gain greater exposure. Figure 7 shows the hardest combination for the system with a fairly large setpoint change in biomass, X, while maintaining both substrate concentration and dissolved oxygen at baseline levels. Results of the interactions are fairly to somewhat underdamped even after some detuning from the individual tunings in Part 3. Any more detuning hurts the performance for the other setpoint combinations. It is important for students to gain an appreciation for what is good control or not is dependent on the system being regulated. Some systems are much more challenging and expectations cannot be as high. Here have a system with process gains of a thousandfold different and time constants that are three to five fold different as well.

Student Performance on Nonlinear 2x2 Control Exam

The culmination of the control course is to have the students successfully be able to determine proper pairing of two inputs to two outputs for a nonlinear process and design a set of controllers that takes into account the interactions present between the control loops. The exam is given timed with three hours. In Table 8, can see how the students performed with no final project (as outlined in this paper) versus when they had a final project to motivate the students and to provide more graded practice. As seen the results are impressive. Not only is the average score higher (91.6 to 84.7) but has much less variation with a standard deviation of 7.3 as compared to 11.8.

Table 8 Student Performance on Nonlinear Multiple Input Multiple Output Exam

	No Final Project	Final Project
Years Taught	4	3
Mean	84.7	91.6
Standard Deviation	11.8	7.3

Future Work and Conclusion

In the future, the goal is to add more nonlinear systems with three or more inputs and outputs. Initial work has been done on a distillation column with condenser and partial reboiler, and simulation of a tabletop experiment [15] where a tank is heated, and fluid level is measured that has a feed stream and salt stream entering with gravity flow exiting the tank to conductivity and temperature sensors. The long-term objective is to design sufficient unit operations so that the whole class can participate in plant-wide control project. The simulated nonlinear processes are also ideal for students to use for learning gain scheduling where control parameters change with input or output values. The models presented here have been used with dynamic matrix control and multiple model predictive controllers by the authors. The simulated systems could be readily used to teach design of experiments as well as different post and online parameter/output estimation.

The key point is that students have a straightforward methodology to handle nonlinear multiple input multiple output systems and feel comfortable applying this knowledge on a real industrial process. Two students have gone on to industry (one as a process engineer and the other on a research internship) where within the first month of work they re-tuned all the PID controllers for their respective processes. One did so for a Campbell Soup production process and the other for a research pilot plant. Neither student was the top student in his class getting grades of B+ and A- in the control course. Yet both due to the number and quality of nonlinear process simulations felt completely comfortable to seize the opportunity to use what they had learned in an industrial setting receiving praise and in the Campbell Soup case placement on more advanced projects. It is critical to have our students work on as realistic case studies as possible to not only learn the nuances and downfalls of applying controllers in different operating regions, but to gain critical confidence in their abilities to succeed in the real world. This simply cannot be done adequately using linear transfer functions as system models.

Acknowledgments

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Appendix

Wastewater Treatment Modeling Equations and Baseline Conditions

The system is governed by the following set of non-linear differential equations:

$$\frac{dX}{dt} = \mu X - D(1+r)X + rDX_r$$

$$\frac{dS}{dt} = \frac{\mu}{Y}X - D(1+r)S + DS_{in}$$

$$\frac{dDO}{dt} = -K_0\frac{\mu}{Y}X - D(1+r)DO + DDO_{in} + \alpha W[DO_{max} - DO]$$

$$\frac{dX_r}{dt} = D(1+r)X - D(\beta+r)X_r$$

Growth rate depends on both substrate (*S*) and dissolved oxygen (*DO*): $\mu = \mu_{max} \times \frac{S}{K_S+S} \times \frac{DO}{K_{DO}+DO}$

TABLE 2: BASELINE CONDITIONS

Variable	Large set point change	Feed disturbance	Units
X	186.9028	399.1684	g cells/l
S	196.8017	278.5263	g substrate/l
DO	1.9471	1.7817	mg O_2 /l
Xr	373.6888	798.3367	g cells/l
D	0.1227	0.13	hr^{-1}
W	50.88	110	hr^{-1}

r	0.6005	0.6	-
S_{in}	200	200	g cells/g substrate
μ_{max}	0.15	0.15	g substrate/l
Y	0.65	0.65	mg O_2 /l
K_S	100	100	mg O_2 / g substrate
K_{DO}	2	2	hr^{-1}
K0	0.5	0.5	-
α	0.018	0.018	-
β	0.2	0.2	mg O_2 /l
DO_{in}	0.5	0.5	mg O_2 /l
DO_{max}	10	10	g cells/l

Pichia pastoris Bioreactor Modeling Equations and Baseline Conditions

1	Growth kinetics (Monod equation)	$\mu = \begin{cases} \dfrac{\mu_{max} S}{K + S + \left(\dfrac{S^2}{K_i}\right)} & S > S_{crit} \\ 0 & 0 \leq S < S_{crit} \end{cases}$ $S_{crit} = m_s X$
2	Cell growth	$\dfrac{dX}{dt} = -\dfrac{F_{in} + F_{Nin}}{V} X + \mu X$
3	Substrate consumption	$\dfrac{dS}{dt} = \dfrac{F_{in}}{V} S_{in} - \dfrac{F_{in} + F_{Nin}}{V} S - (Y_{SX}\mu + m_s) X$
4	Substrate inhibition	$\mu = \dfrac{\mu_{max}}{\left(K + S + \dfrac{S^2}{K_i}\right)} S$
5	Nitrogen consumption	$\dfrac{dN}{dt} = -\dfrac{F_{Nin}}{V} N_{in} - \dfrac{F_{in} + F_{Nin}}{V} N - Y_{NX}\mu X$
6	Specific product formation rate	$\mu_P = \mu_{P_0} \cdot \dfrac{K_1 \cdot [H^+]}{K_1 \cdot K_2 + K_1 \cdot [H^+] + [H^+]^2} \cdot \left\{ a \cdot exp\left(\dfrac{-\Delta G_1}{RT}\right) - b \cdot exp\left(\dfrac{-\Delta G_2}{RT}\right) \right\}$
7	Protein production	$\dfrac{dP}{dt} = -\dfrac{F_{in} + F_{Nin}}{V} + k_{dw} \cdot \mu_P \cdot X$
8	Oxygen consumption	$\dfrac{dO}{dt} = -\dfrac{F_{in}}{V} O_{in} - \dfrac{F_{in} + F_{Nin}}{V} O - Y_{OX}\mu X + k_L a(O^* - O)$
9	Henry's law	$H = H_{ref} e^{\left(-C\left(\frac{1}{T_{abs}} - \frac{1}{T_{ref}}\right)\right)}$
10	Oxygen solubility in pure water	$O^*_{pureH_2O} = \dfrac{P_T Y_{OG}}{H}$
11	oxygen solubility in the fermentor media	$O^*_{media} = O^*_{pureH_2O} k_{salt}$
12	Van't Reit (mass transfer) correlation	$k_L a = \left(2.6\ x\ 10^{-2} \left(\dfrac{P_G}{V_L}\right)^{0.4} V_S^{0.5}\right) 3600$
13	Reactor temperature	$\dfrac{dT}{dt} = \dfrac{1}{V}(F_{in} + F_{Nin})(T_{in} + T) + \dfrac{(-\Delta H_{rxn})}{28\rho C_P}\mu X - \dfrac{UA_h}{V\rho C_P}(T + T_J)$
14	Jacket reactor temperature	$\dfrac{dT_J}{dt} = \dfrac{F_J}{V}(T_{J,in} - T_J) + \dfrac{UA_h}{V\rho_j c_{P_j}}(T + T_J)$
15	Phosphoric acid consumption	$\dfrac{dA}{dt} = -\dfrac{F_{in}}{V} A_{in} - \dfrac{F_{in} + F_{Nin}}{V} A$
16	Electron Neutrality	$(10K_w + K_b[NH_3])[H^+]^4 - (2K_w^2 + K_w K_{a1}[H_2PO_4])[H^+]^2 - K_w K_{a2} K_{a1}[H_2PO_4][H^+] - K_w K_{a3} K_{a2} K_{a1}[H_2PO_4] = 0$

Parameters		Value	Parameters		Value
Max. specific growth rate(h^{-1})	μ_{max}	0.146	Oxygen conc. in inlet stream (g/L)	O_{in}	*0*

Const. growth rate (MeOH/L)	K	1.5	Nitrogen conc. (g/L)	N_{in}	*14.7678*
Growth Rate: s inhibit (MeOH/L)	K_i	8.86	H_2PO_4 conc. (g/L)	A_{in}	*0*
Maintenance term (MeOH/g)	m_s	0.0071	Substrate inlet temp. (°C)	T_{in}	*20*
Yield coeff. (s/cell) (MeOH/g)	Y_{SX}	0.84	Inlet temp. jacketed fluid (°C)	T_{jin}	*6.779*
Yield coeff.(NH_3/cell) (NH_3/g)	Y_{NX}	0.14	Heat transfer coeff. (J/hm^{2}K)	U	*3.6E5*
Protein production (mg g^{-1} h^{-1})	μ_{P_0}	6.4417	Volume of jacket (g/L)	V_j	*200*
Michaelis pH function (mol L^{-1})	K_1	2.1195E-5	Heat transfer area (m^2)	A_h	*20*
	K_2	2.39E-7	Density: reactor media (g/L)	ρ	*1080*
Parameters of Arehenius eqn.	a	1.4858	Specific heat capacity media (J/gK)	C_P	*4.18*
	b	3.6512	Density: jacket fluid (J/gK)	ρ_j	*1113*
Regnault const.(J mol^{-1} K^{-1})	R^2	0.9178	Specific heat capacity of fluid (J/gK)	c_{P_j}	*2.2*
Apparent Gibbs energy (J mol^{-1})	ΔG_1	42.1682	Heat of rxn (kJ/mol O_2 const.)	ΔH_{rxn}	*300000*
	ΔG_2	69.1584	1st step of H_3PO_4 diss. (mol/L)	K_{a1}	*7.25E-3*
DCW to WCW ratio	k_{dw}	3.3	2ndstep of H_3PO_4 diss. (mol/L)	K_{a2}	*6.31E-8*
Solubility of media vs. pure H_2O	k_{salt}	*0.702*	3rd step of H_3PO_4 diss.(mol/L)	K_{a3}	*3.98E-13*
Gram substrate per gram cells	Y_{SX}	*0.84*	Equilibrium constant for water	K_W	*1E-14*
Gram oxygen per gram cells	Y_{OX}	*1.452*	Dissociation constant for NH_3	K_b	*1.8E-8*
Gram nitrogen per gram cells	Y_{NX}	*0.14*	System pressure (atm)	P_T	*1*
Cell conc. inlet stream (g/L)	X_{in}	*0*	Mole fraction of O_2 in gas	Y_{OG}	*1*
Product conc. (g/L)	P_{in}	*0*			

Inputs	Symbol	Baseline Value	Min	Max	Outputs	Symbol	Initial Value
Substrate conc. (g/L)	S_{in}	*160*	-	-	Reactor temp(°C)	*T*	*22.92*
Flow into the Jacket (L/hr)	F_j	7000	*0*	*25000*	O_2 (%)	DO	32.93
Volumetric gas flow (m^3/s)	V_{dot}	0.015	0	0.025	*pH in reactor*	pH	5.386
Flowrate in (L/hr)	F_{in}	55	0	150	Product conc. (mg/L)	P	2266
Flowrate of NH_3(L/hr)	F_{nin}	6.2	0	15	Substrate conc. (g/L)	S	1.761
					Cell conc.(g/L)	X	153.6