B3 Group Design Project

Cultured Beef Production

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Contents

MAINLY TALK ABOUT WHY YOUR CHOICE LED TO A BETTER ACHIEVEMENT OF THE DESIGN OBJECTIVES.

The generic structure of a technical report:

1. Introduction: Provide context, motivation, and background information

What is the big-picture problem? Why is it a problem? Who cares?

What have others done to solve the problem? What is still left to do? What did you do?

2. Methods: Explain what you did Provide enough detail for someone else to reproduce your results.

For each aspect, the level of detail should be commensurate with the level of novelty.

3. Results: Show and explain what you found. Provide figures and other qualitative and quantitative evidence for your conclusions.

Explain and interpret what you are showing. Not "What does the data look like?", but "What does the data mean?"

4. Discussion: Consider the implications and limitations of your results

5. Conclusions: Connect your results with the original problem.

What have you actually achieved here? What should be done next?

Tip 1. Emphasise results, interpretation, and discussion.

Tip 2. Technical writing needs to be precise, concise, objective, careful

Tip 3. Every sentence must: (i) make a point (ii) form a logical link between the previous sentence and the next

1 Example

Intro (unnumbered)

Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor **??** incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip ex ea commodo consequat. Duis aute irure dolor in reprehenderit in voluptate velit esse cillum dolore eu fugiat nulla pariatur. Excepteur sint occaecat cupidatat non proident, sunt in culpa qui officia deserunt mollit anim id est laborum.

Figure 1: An example image **E-Cannon2022**

1.1 Example NUMBERED subsection (no * in environment)

Example equation **??**.

$$beef_{moo} = fear^{10} \tag{1}$$

Example list:

- $\boldsymbol{X} \in \mathbb{R}^{n \times p}$, a matrix containing the scrutinised data-points $\boldsymbol{x} \in \mathbb{R}^{p}$ from each sample,
- *regression_targets*, known as $\bar{\boldsymbol{y}} \in \mathbb{R}^{n}$, is a vector containing the regression targets for the samples (individually known as $\bar{y}$), and

- *class_labels* $\in \{1, \ldots, p\}$ which keeps track of which Gaussian each sample came from (a target for classification).

Example table **??**

learning_rate	mse_train	mse_val
1e-05	1.1254	1.1747
0.0001	0.31296	0.3012
0.001	0.095492	0.088045
0.01	0.046835	0.052905
0.1	0.046534	0.052771
1	NaN	NaN

Table 1: Table of Mean Squared Difference from different learning rates.

Example aligned equation:

$$
\begin{aligned}
\mathcal{L}_c &= -ylog(\bar{y}) - (1-y)log(1-\bar{y}) \\
&= ylog(1+e^{-\hat{\boldsymbol{x}}^{\boldsymbol{T}}\boldsymbol{\theta}}) - (1-y)log(\frac{e^{-\hat{\boldsymbol{x}}^{\boldsymbol{T}}\boldsymbol{\theta}}}{1+e^{-\hat{\boldsymbol{x}}^{\boldsymbol{T}}\boldsymbol{\theta}}}) \\
&= (y-y)log(1+e^{-\hat{\boldsymbol{x}}^{\boldsymbol{T}}\boldsymbol{\theta}}) - (1-y)log(e^{-\hat{\boldsymbol{x}}^{\boldsymbol{T}}\boldsymbol{\theta}}) + log(1+e^{-\hat{\boldsymbol{x}}^{\boldsymbol{T}}\boldsymbol{\theta}}) \\
&= (1-y)\hat{\boldsymbol{x}}^{\boldsymbol{T}}\boldsymbol{\theta} + log(1+e^{-\hat{\boldsymbol{x}}^{\boldsymbol{T}}\boldsymbol{\theta}}) \\
\Delta_{\boldsymbol{\theta}}\mathcal{L}_c &= (1-y)\hat{\boldsymbol{x}} - \frac{e^{-\hat{\boldsymbol{x}}^{\boldsymbol{T}}\boldsymbol{\theta}}}{1+e^{-\hat{\boldsymbol{x}}^{\boldsymbol{T}}\boldsymbol{\theta}}}\hat{\boldsymbol{x}} \\
&= (1-y)\hat{\boldsymbol{x}} - (1-\bar{y})\hat{\boldsymbol{x}} \\
&= \hat{\boldsymbol{x}}(\bar{y}-y)
\end{aligned}
$$

END OF TEMPLATE

2 Control systems

2.1 Introduction

Homeostasis, defined as the internal regulatory functions of the body to maintain certain conditions constant (**E-Guyton2006**; **E-Aging2022**), is extremely crucial to living organisms. For example, for humans, the blood pH outside the range between 7.35 and 7.45 can cause death **E-Donaldson2013**. In addition to its significance in maintaining an existing life, homeostasis has great importance in creating a new life: Mammalian cell culture.

In a bioreactor, homeostasis can be achieved by solving the classical problem of tracking the reference signal $r(t)$ in control theory, as shown in Figure **??**. A thoroughly designed bioreactor and its constituent control systems will lead to better achievement of the design objectives, which are: (i) How can one achieve the production rate of 100 kg/month? (ii) How can one produce a better quality of meat?

The design of the control system mainly answers the latter question. The former question is rather answered through the overall process diagram, number and sizes of bioreactors, mass inflows and outflows, so will not be tackled in this chapter. Bioreactor control, however, addresses the formation and maintenance of the optimal environment to produce the best quality of meat. Thus, in this chapter, the design of temperature (T), dissolved oxygen (DO) and acidity (pH) control systems are discussed.

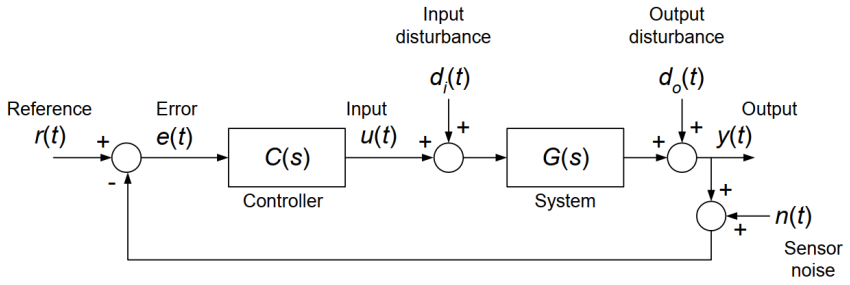

Figure 2: A schematic of a negative feedback control system **E-Cannon2022**

2.2 Temperature control

2.2.1 Introduction

The body temperature of beef cattle should be maintained at $39.6 \pm 0.1^{\circ}C$ **E-Gaughan2014**. To do so, different physical setups of the heat exchanger around the bioreactor will be compared to find the optimal one. Differential equations will be constructed to derive the plant transfer function. Design criteria will be posed with appropriate justification. Dif-

ferent control strategies will be compared to find the optimal one. The design criteria introduced will be used to find control parameters. MATLAB simulations will be used to confirm the validity of the step and impulse responses.

2.2.2 Methods

Various types of heat exchangers used to control the heat in and out of the bioreactor are shown in Figure **??**. The best design choice is (a), the jacketed bioreactor. The logic is as follows: (c) and (d) have the heat exchange inside the bioreactor, causing an intervention in the rotational pathway of the impeller used to stir the meat, and thus adding unnecessary complexity to the design to avoid this; (e) involves taking the meat out of the bioreactor, which firstly may harm the meat cells by pumping and pressurising them above the maximum stress that they they can resist, and secondly has a potential issue of fouling in the pump. One is now left with (a) and (b), but for better heat transfer it is more efficient for the working fluid to cover the entire bioreactor, and for more evenly distributed heat transfer it is better if the inlet and the outlet temperatures of the heat exchanger do not vastly differ. Hence, (a) is the best option.

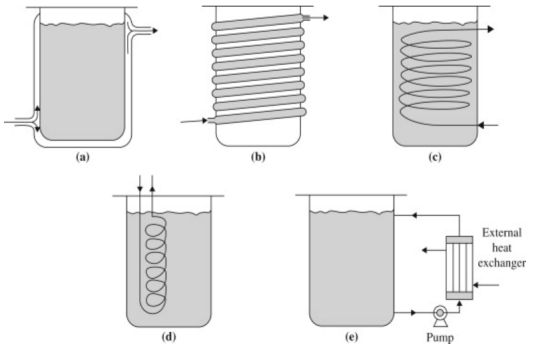

Figure 3: Heat exchanger configurations for a bioreactor **E-Doran2013**

Theoretically, the heat exchanger's working fluid temperature T_{fluid} controls the bioreactor's internal temperature T. Practically, the observer is implemented using a temperature sensor, and the controller is implemented digitally using a computer system, as shown in Figure **??**.

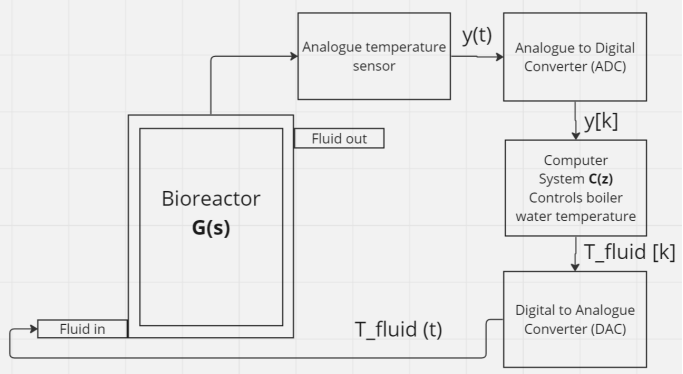

Figure 4: Practical implementation of the control system

The dynamics over time of temperature (T) can be described via the energy balance equation, where ρ is the wet cell density, V is the volume of the bioreactor, c_p is the specific heat capacity, Q_{met} is the metabolic heat generation rate, h is the heat transfer coefficient and A is the area of the bioreactor.

$$\rho V c_p \frac{\partial T}{\partial t} = Q_{met} V - hA(T - T_{fluid}) \tag{2}$$

The change of variables to perturbations $\Delta T = T(t) - T_{ss}$ and $\Delta T_{fluid} = T_{fluid}(t) - T_{fluid,ss}$ leads to Equation **??**. During the entire culturing period ($t > 0$) the steady-state assumption ($\frac{\partial \Delta T}{\partial t} = 0$, $\Delta T \approx \Delta T_{fluid} \approx 0$) can be made because otherwise the cells will die due to the violence of homeostasis. This leads to Equation **??**. Substituting Equation **??** into Equation **??** and taking the Laplace transform leads to the desired transfer function, as shown in Equation **??**.

$$\rho V c_p \frac{\partial \Delta T}{\partial t} = Q_{met} V - hA(T_{ss} - T_{fluid,ss}) - hA(\Delta T - \Delta T_{fluid}) \tag{3}$$

$$Q_{met} V - hA(T_{ss} - T_{fluid,ss}) = 0 \tag{4}$$

$$G(s) = \frac{\Delta T(s)}{\Delta T_{fluid}(s)} = \frac{hA}{\rho V c_p s + hA} \tag{5}$$

2.2.3 Results

The wet cell mass of $3.5 \times 10^{-12}\ kg/cell$ and the cell diameter of $295 \times 10^{-6}\ m$ **E-Furuhashi2021** are used to calculate the density so that $\rho = 0.26\ kg/m^3$. The bioreactor height of $2\ m$ and the bioreactor diameter of $2.1\ m$, are used to calculate the area and the volume of the bioreactor so that $A = 20.12\ m^2$ and $V = 6.93\ m^3$. The yield of the final product

to the wet cell $\eta = 0.5$ is used along with $c_{p,cell} = 3.440\ kJkg^{-1}K^{-1}$ **E-Fellows2009** and $c_{p,water} = 4.180\ kJkg^{-1}K^{-1}$ to linearly interpolate the specific enthalpy as shown in Equation **??**. The heat transfer coefficient is assumed to be $h = 0.5\ kWm^{-2}K^{-1}$. Substituting these values in, the plant transfer function is derived as shown in Equation **??**.

$$c_p = \eta c_{p,cell} + (1-\eta)c_{p,water} = 3.810\ kJkg^{-1}K^{-1} \tag{6}$$

$$G(s) = \frac{10.06}{6.872s + 10.06} \tag{7}$$

The design of the controller is often done by setting the gain margin (GM) or the phase margin (PM) of $C(s)G(s)$ at a chosen frequency. The best design criterion is $PM = 60^\circ$ at $\omega = 4.16\ rad/s$. The logic is as follows: the rise time of the plant's step response, defined as the time taken from 10% to 90% of the steady-state value, is $\Delta t = 1.58 - 0.07 = 1.51\ s$, as it is also visible from Figure **??**. The rise time can be viewed as the mean time taken for the bioreactor to respond to the heat exchanger, and hence the period. The operating frequency is then $\omega = 2\pi/\Delta t = 4.16\ rad/s$.

Practically, there is a higher chance of acceleration or delay in heating and cooling than a sudden overheating or underheating. Thus, one may be more concerned with the phase margin that relates to unexpected phase lags $\angle G(j\omega)$ than the gain margin that relates to unexpected magnitude deviations $|G(j\omega)|$. An acceptable rule of thumb is $PM = 60^\circ$, so one reaches the posed criterion.

One of the most commonly used controllers in the process control industry is proportional-differentiator-integral (PID). The engineer can use the above criterion along with the condition that "the low-frequency asymptote of the Nyquist on the $M = 1$ line" **E-Cannon2022-2**, which means the unity D.C. gain $\frac{Y(s)}{R(s)} = 1$ and thus zero steady-state error. Through this, one can find the three controller gains in $C(s) = K_p + \frac{K_i}{s} + K_d s$.

2.2.4 Discussion

- (D) discussion of how my choices led to better achievement of the final objectives, compared to other control strategies

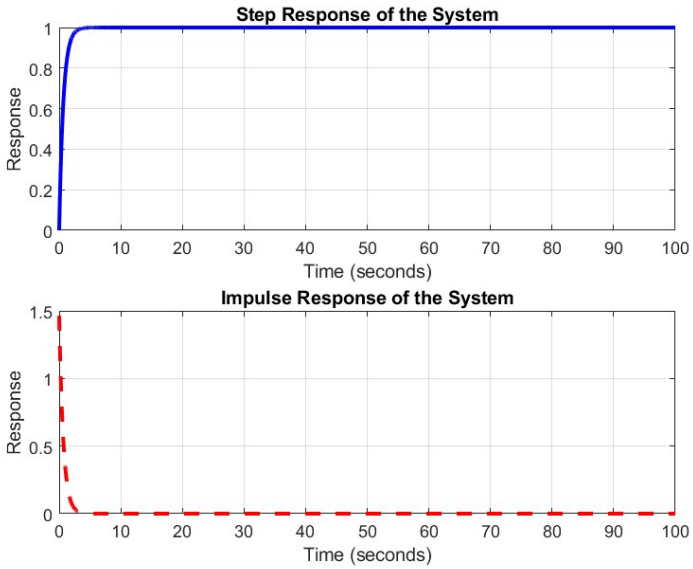

Figure 5: The step and impulse responses of the plant

2.3 Oxygen control

2.4 Acidity control

3 Purification methods

3.1 Lactic acid purification

3.2 Ammonia purification

4 Final product formulation

Item	Process Parameter	Guide Word	Deviation	Potential Causes	Consequences*	Actions Required**
1.1	Temperature	High	Higher Temperature	Metabolic heat buildup [1] Formation of cell lumps in the bioreactor [1] Non-homogeneous heat creation by the cells [1] Controller malfunction Faulty sensor Bioreactor malfunction Medium heater malfunction Temperature wrongly set to cleaning and sterilization temperature (higher than 70 C)	Increased heat stress on the cells Reduced proliferation Activation of the cell heat shock response that alters the DNA and structure of the cells [3] Higher risk of apoptosis (cell death) and development of necrotic tissue Reactor overheat	Add a jacket to the bioreactor to control the temperature Implement alarm systems to alert operators when the temperature is outside of the desired range (36-41 C) [2]*** Have emergency shutdown procedures in place and manual override systems for excessive temperatures Develop cooling mechanisms to reduce the temperature (preferably passive cooling systems to decrease the environmental impact [1]) Use multiple sensors to ensure accurate readings Have emergency shutdown procedures and manual override systems in place
1.2	Temperature	Low	Lower Temperature	Controller malfunction Faulty sensor Bioreactor malfunction	Reduced proliferation Activation of the cell cold shock response, potentially leading to hypothermia	Covered in 1.1

Item	Process Parameter	Guide Word	Deviation	Potential Causes	Consequences*	Actions Required**
1.2	Temperature	Low	Lower Temperature	Medium heater malfunction Bad insulation	Higher risk of apoptosis and development of necrotic tissue Increased viral production for several viruses [3]	Covered in 1.1
2.1	Stirring	No	No stirring	Motor failure Mechanical failure (gearbox, coupling, etc.) Electrical failure (cables, supply, etc.) Power supply failure	Accumulation of cells in cluster Reduced efficiency in nutrient transportation Spatial heterogeneity of the environmental conditions (temperature, pH, etc.) Reduced proliferation	Have space motors available Add sensors to the bioreactor components to monitor the operation and detect malfunctions (e.g. rotation sensor on shaft, current sensor on motor)
				Covered in 2.1 Speed of motor wrongly set		

Notes:

** Poor batch quality may result from any of the mentioned deviations.

*** It is necessary to carry out routine inspections and maintenance checks on bioreactor components (sensors, blades, pipes, etc.). This is essential to ensure optimal performance across all process parameters.

**** In certain cases, apoptosis has been activated at temperatures as low as 30 C and as high as 39 C [3]. Given the wider margin of cell viability at lower temperatures, temperatures exceeding 39 C should be of greater concern to the operator.