THESIS

Sheng Hongfei

2024

MAGYAR AGRÁR- ÉS ÉLETTUDOMÁNYI EGYETEM

HUNGARIAN UNIVERSITY OF AGRICULTURE AND LIFE SCIENCES

Institute of Food Science and Technology

Bachelor's degree in Food Engineering

Studies on Hydrodynamics and Process heat transfer of Bioreactors

Supervisors: Dr.-Habil Arijit Nath

Senior Research Member

Prof. András Koris

Professor

Máté András Molnár

Assistant lecturer

Institute/ Department: Institute of Food Science and Technology/ Department of Food Process Engineering

Prepared by: Sheng Hongfei

Budapest
2024

Content

1 Introduction and Objectives

For long times back, various types of non-fermented and fermented dairy-based food formulas have garnered significant attention across different communities. As time progressed, dairy industries tried their best to improve the quality of dairy-based formulas to fulfil the expectations of consumers (Jang, Lee and Paik, 2024). Among different constituents of milk, proteins, such as α_{S1}-casein, α_{S2}-casein, β-casein, κ-casein, γ-casein, immunoglobulin, bovine serum albumin, lactoferrin, α-lactalbumin and β-lactoglobulin are very important for sustainable health for communities (Bintsis and Papademas, 2022). Milk proteins are popularly used to prepare yogurt, weight management products, protein bars, cultured product, frozen dessert, infant formula, recombined cheese, and sports formulas. Different dairy-based protein concentrates, such as milk protein concentrate, whey protein concentrate, micellar casein concentrate, milk protein isolate, whey protein isolate, micellar casein isolate, whey concentrate, and selectively demineralized whey concentrate are widely used in the food and biopharmaceutical industries (Nath *et al.*, 2020a).

Milk with a standardized amount and quality of protein provides sufficient nutrition to consumers, however, different types of proteins, the milk sensitive community frequently experiences with the symptoms of immunoglobulin-mediated milk protein allergies (de Almeida Kotchetkoff *et al.*, 2022), in some cases. Milk proteins are classified among the “big 8” allergens due to the presence of Immunoglobulin E- and Immunoglobulin G-binding epitopes. These allergens can cause reactions ranging from mild symptoms to life-threatening biochemical outcomes, such as severe enterocolitis, atopic eczema, and immediate immunoglobulin-mediated multisystem reactions (Pratelli *et al.*, 2024). A vast amount of research has explored both thermal and non-thermal processing methods to reduce milk protein allergens (Shriver and Yang, 2011). The reduction of protein allergenicity at the molecular level occurs through the disruption of epitope structures (Dong *et al.*, 2024). Technologies like high pressure, heat treatment and microwave processing have been used to diminish allergenic sequences in milk proteins (Liu, Aimutis and Drake, 2024). Additionally, physical and enzymatic modifications of proteins have been employed for similar purposes. In some instances, the processing of cow’s milk may even result in the formation of new epitopes (neoepitopes) or hidden epitopes (cryptotopes) due to the denaturation of native allergens (El Mecherfi *et al.*, 2019).

Considering the pros and cons of these technologies, enzymatic hydrolysis of allergenic epitopes in protein sequences is viewed as a potentially effective method for reducing milk protein allergens (Calcinai *et al.*, 2022). Beyond reducing allergenicity, enzymatic modifications can also alter the functional properties of milk proteins, as the hydrolysis of peptide bonds produces peptides with unique amino acid sequences at the C- and N-termini. Despite substantial research on enzymatic approaches to reduce allergenic epitopes in milk proteins (Milessi *et al.*, 2022), industrial-scale application remains limited. The key challenges in enzyme-mediated processes include the high cost of enzymes and the need to optimize suitable operating conditions for these processes (Al-Maqdi *et al.*, 2021). It may be felt that understanding the process parameters of unit operations is prerequisite to produce dairy-based protein hydrolysate.

Bioreactors used in food and biotechnological industries are usually designed to meet the requirements of the driving force of enzymatic or microbiological reactions by addressing parameters, such as temperature, oxygen, pH and nutrients. As volume of bioreactor is increased, the efficiency of mixing decreases and microenvironment of bioreactor is modulated compared to smaller scales (Regonesi, 2023a). Parameters of hydrodynamics and process heat transfer, such as the Reynolds number, Power number, Prandtl number, Nusselt number, thermal conductivity and heat transfer coefficient, are associated with mixing and process heat transfer within the bioreactor (Rahimie *et al.*, 2021). These parameters modulate the driving force of the enzymatic reactions during the bioconversion of milk proteins. Therefore, the mentioned parameters are directly affected by the design and geometry of the impellers, and inlet and outlet temperatures of water within the jacket of the bioreactor. Proper stirring ensures a uniform distribution of temperature and solutes (Rong *et al.*, 2021).

In the present research, I paid attention to the mechanical design of bioreactor because it is an important in food and dairy industries. The mechanical design of a lab-scale bioreactor and understanding of process parameters tailored for milk protein hydrolysis were considered. Two main issues, such as geometry of impellers and overall heat transfer coefficient of a bioreactor have been emphasized. The effect of rpm of impeller on hydrodynamics within the bioreactor was investigated. Furthermore, the effect of inlet and outlet temperature of water within the jacket of bioreactor on process heat transfer was studied with special attention on overall heat transfer coefficient. Different dimensionless parameters, such as Reynolds number, Prandtl number and

Nusselt number were studied. By understanding their effects, it is possible to scale up the process for industrial applications, leading to enhanced production efficiency.

Enzymatic hydrolysis of milk proteins is an important aspect in food and dairy industries which is generally performed in a stirred tank bioreactor. Understanding operating parameters, such as temperature and stirrer speed are crucial for enzyme-catalyzed bioreaction. Temperature influences the activation energy (Ea), deactivation energy (Ed) and the constant (A) of the Arrhenius equation of enzyme-catalyzed bioreaction. However, stirrer speed does not play a significant role in small-scale bioreactor (micro-bioreactor) for homogenous catalyst (enzyme)-influenced bioreaction; stirrer speed influences the overall heat transfer coefficient and kinetic parameters of enzymatic reaction in large-scale stirred tank bioreactor.

Papain, a cysteine protease of the peptidase C1 family frequently used in the bioprocess was considered in this investigation. Within the temperature range (60-65 °C), papain exhibits its highest enzymatic activity for breaking down proteins. The exact optimum temperature can vary depending on different factors, such as pH and substrate concentration. At temperatures higher than 70°C, papain activity may start to decline due to denaturation. It needs to be mentioned that however, papain can show highest proteolytic activity at temperature 60-65 °C, its deactivation could be highest in that temperature range. Therefore, in the present investigation, changing the temperature of milk from room temperature (25 °C) to 50 °C (preincubation temperature) and subsequently its alternation to 70 °C were considered.

In the present research, some efforts were made to understand the modulation of inlet temperature of water within the jacket of the bioreactor and stirrer speed within the bioreactor to maintain the desired temperature for biocatalysis reaction. The diameter of the stirred-tank bioreactor was considered 0.6 m. The wall thickness of the bioreactor was considered 0.2 cm and gap between outer diameter and water jacket was considered 1 cm. Impellers with different geometries, such as rushton turbine, marine propeller turbine and pitched-blade turbine were considered. Furthermore, no heat loss from fermenter to environment was considered. The inlet and outlet temperatures of water in bioreactor jacket were evaluated for the change of milk temperature 25 °C → 50 °C within 30 min and subsequently change of milk temperature 70 °C within 20 min. Startup power requirements were evaluated for rotational speed 25 rpm and 50 rpm, and mentioned temperature range considering motor efficiency 75%.

2 Literature review

2.1 Milk

Milk is a white liquid food produced by the mammary glands of female mammals and considered as primary source of nutrition for young mammals including human (St-Onge, Farnworth and Jones, 2000). The Food and Agriculture Organization (FAO) dairy review indicates that around 930 million tons of milk were produced globally in 2022, with an expected annual increase of 1.7% for the next decade. Cows contribute the majority of global milk production (81%), followed by buffaloes (15%). On average, global milk consumption is approximately 112 kg per person per year (Guinee, O'kennedy and Kelly, 2006).

2.1.1 Composition of milk

Milk is comprising with total solid content ~13% (by weight) having macronutrients: proteins (~27%), carbohydrate (~37%) and (~30%), and micronutrients: minerals and vitamins (~6%) (Amatayakul, Sherkat and Shah, 2006). The composition of milk varies depending on the species (cow, goat, sheep), breed, the feeding of animals and the stage of lactation (Schuck *et al.*, 2016). Dairy proteins can be divided into two main categories: (a) casein proteins, which make up 80% of the total protein content by weight and include αs1-casein, αs2-casein, β-casein, and κ-casein, and (b) whey proteins, accounting for 20% of the total protein content, comprising β-lactoglobulin, α-lactalbumin, immunoglobulins (IgG, IgA, IgM), bovine serum albumin, lactoferrin, and lactoperoxidase. In addition, minor proteins such as glycoproteins and lipoproteins, which contribute less than 2% of the overall milk protein content, are produced by distinct genes (Rehman *et al.*, 2003). Milk fats consist of a wide variety of fatty acids, including monounsaturated, trans, polyunsaturated, and saturated fatty acids, each offering distinct nutritional benefits (Shakeel-ur-Rehman *et al.*, 2003). The primary carbohydrate in milk is disaccharide lactose, which contributes to the sweetness of milk and enhances its overall mouthfeel (Nath *et al.*, 2020b). Milk proteins offer significant nutritional benefits and possess unique physicochemical properties that can be altered during processing. As a result, these proteins are a key focus of my investigation (Henriques *et al.*, 2013)

2.1.2 Nutrition from milk proteins:

Milk is regarded as an excellent source of all amino acids, including essential amino acids (EAAs). The protein digestibility-corrected amino acid score (PDCAAS)

and the digestible indispensable amino acid score (DIAAS) of milk proteins are higher compared to most other protein sources (Meena *et al.*, 2017). Casein contains a higher proportion of essential amino acids (EAAs) like histidine (His), methionine (Met), phenylalanine (Phe), and valine (Val) compared to whey proteins. Additionally, casein also has a greater amount of non-essential amino acids (non-EAAs) such as arginine (Arg), glutamic acid (Glu), proline (Pro), serine (Ser), and tyrosine (Tyr). On the other hand, whey proteins are richer in branched-chain amino acids (BCAAs), including leucine (Leu), isoleucine (Ile), and valine (Val), when compared to casein. Both casein and whey proteins contain all EAAs, but they differ in digestion and absorption properties. Whey proteins are highly soluble in food matrices and in vivo, allowing for rapid absorption after gastrointestinal digestion, which results in a short-lived but significant increase in plasma amino acid levels. Conversely, casein tends to clot in the acidic environment of the stomach, delaying gastric emptying and leading to a slow, sustained release of amino acids into the bloodstream (Gorissen *et al.*, 2018). As a result, whey protein is generally regarded as nutritionally superior to casein in terms of biological value, protein efficiency ratio, and net protein utilization. For instance, the biological value of whey proteins is 104, compared to 77 for casein. Similarly, the protein efficiency ratio (PER) is higher for whey proteins at 3.2, while casein has a PER of 2.5. In terms of net protein utilization (NPU), whey proteins score 92, whereas casein scores 76 (Hoffman and Falvo, 2004). Additionally, the amino acid composition and the structure of protein or food may significantly influence the physiological and metabolic effects stimulated by protein intake. For instance, casein may reduce postprandial plasma glucose levels with minimal stimulation of insulin secretion, while whey protein enhances insulin response, resulting in a more substantial decrease in postprandial plasma glucose levels (Chen *et al.*, 2022). Gastrointestinal digestion of milk proteins can exhibit a wide range of biological activities by producing peptides having anti-hypercholesterolemic, anti-angiotensin, antimicrobial, antioxidant, antidiabetic, anti-inflammatory, anticarcinogenic and immunomodulatory activities (Koirala *et al.*, 2023).

2.1.3 Milk protein allergenicity and loss of nutritional value

In addition to the beneficial effects of dairy milk proteins, epitope mapping studies have identified both sequential (linear) and conformational epitopes within these proteins. The presence of immunoglobulin E (IgE)- and immunoglobulin G (IgG)-

binding epitopes in their structure classifies dairy milk proteins as part of the "big 8" allergens. Consequently, dairy milk protein allergy can arise from both IgE-mediated and non-IgE-mediated mechanisms (Abdisa *et al.*, 2024). Individuals allergic to dairy milk proteins can be categorized into different phenotypes based on their reactivity (Tang *et al.*, 2022); However, there is no specific structure or function of dairy milk proteins that accounts for the majority of their allergenic activity. Therefore, it can be inferred that the variability in the human IgE response may be linked to the allergenic potential of any dairy milk protein or its fragments (Koirala *et al.*, 2023). Clinical polysensitization-encompassing cross-sensitization, cross-reactivity, and co-sensitization- to multiple dairy milk proteins is frequently observed (Fiocchi *et al.*, 2010). Various technologies, including high-temperature treatment and high-pressure homogenization are commonly employed in the dairy industry to extend shelf life of milk; however, negative effects have also been documented. Notably, studies have indicated that these technologies may alter the allergenic activity of milk proteins and in many cases, high temperature treatment creates protein precipitation due to denature of proteins (Amador-Espejo *et al.*, 2014).

When milk is heated at a high temperature of more than 60 °C, the tertiary structure of whey protein turns to unfold (Halabi *et al.*, 2020). Heating milk may cause protein deterioration and may reduce its nutritional efficiency. It was found that about one-third of whey protein is denatured when milk is heated at 75 ºC for about 15 minutes and the degree of denaturation is increased with the rises of temperature. For example, Igs denatures when milk is heated at temperature 70 ºC for 30 min, β-lactoglobulin begins to denature above temperature 60 ºC and it is almost denatured above temperature 90 ºC, and α-lactalbumin is completely denatured at temperature 100 ºC (Čurlej *et al.*, 2022). Interestingly, it has been reported that at a temperature higher than 80 °C, denaturation rate of α-lactalbumin is faster than β-lactoglobulin's and denaturation of α-lactalbumin is faster when β-lactoglobulin is present (Wolz and Kulozik, 2015). However, caseins have heat resistance, the disintegration of the casein micelles takes place in a partial way due to dephosphorylation when heating temperature is 80 °C (Sadiq, Gill and Chandrapala, 2021). Subsequently, the broken/denatured whey proteins bind among themselves due to the presence of sulphur containing thiol group (R-SH) by covalent bond (Trivedi, Laurence and Siahaan, no date), or bind with dephosphorylated or disintegrated casein molecules, especially with

κ-casein, which is present in the periphery of the casein micelle by thiol/disulfide interchanges and hydrophobic interactions (Anema, 2021). However, α-lactalbumin does not contain -SH group, it may conjugate with caseins in presence of β-lactoglobulin (Creamer, Loveday and Sawyer, 2011). In addition, heat treatment may promote the formation of isopeptide bond between lysine and glutamine (N-ε-(γ-glutamyl)-lysine) or asparagine (N-ε-(β-aspartyl)-lysine) among different proteins, present in liquid milk protein concentrate (Creamer, Loveday and Sawyer, 2011). Hence, it can be supposed that most of the whey proteins attempt to bind with the casein micelles and among themselves. Therefore, sizes of protein molecules are increased due to heat treatment resulting the protein precipitation and nutritional loss of milk (Čurlej *et al.*, 2022). Furthermore, the amino group of lysine in milk protein bound with lactose causes the Maillard reaction, resulting in browning of milk and reducing the bioavailability of amino acids (Troise *et al.*, 2016). The minerals in milks are also affected by temperature. Different inorganic minerals, such as calcium, magnesium and phosphate in milk are precipitated due to the high-temperature treatment of milk (Aydogdu *et al.*, 2021). However, fat content in milk is not greatly affected by temperature, whey proteins and a small amount of fat globule membrane protein react with sulfhydryl groups and generate hydrogen sulfide when milk is heated at temperature 75 °C (Wang *et al.*, 2024). Fat-soluble vitamins, such as vitamin A, vitamin D, vitamin E and water-soluble vitamins, such as vitamin B2 are not changed due to heating; however, water-soluble vitamins, such as vitamin C, folic acid, vitamin B6 and vitamin B12 are modulated due to the heat treatment of milk (Marriott, 1993). Furthermore, contents of aldehyde and methyl ketone in milk are reduced due to the heating of milk which affects the flavor of milk (Li, Zhang and Wang, 2012).

2.2 Design and operation of bioreactors

Bioreactors are an important apparatus used to carry out any kind of upstream bioprocess. Laboratory-scale bioreactors are frequently used in microbiological, biochemical (enzymatic reaction), and tissue culture investigations. According to the requirement, the sizes of bioreactors can vary over several orders of magnitudes (Regonesi, 2023b).

2.2.1 Classification of bioreactors

Bioreactors can be classified as stirred tank bioreactor, fluidized bed bioreactor, fixed bed bioreactor, membrane bioreactor and photobioreactor based on their

architecture. Photobioreactor is exclusively used for the cultivation of photosynthetic microorganisms, whereas other types of bioreactors are used for enzymatic reactions. Architectures of different types of bioreactors are presented in Figure 1 (Wang and Zhong, 2007).

Stirred tank bioreactor: The stirred tank bioreactor is mostly utilized in bioprocess because of its simple geometry. This bioreactor is comprised with a tubular tank with impellers, water jacket and temperature sensor to maintain temperature, and pH controller to maintain pH within the tubular tank. The stirred tank bioreactor produces a homogenous mixture due to constant stirring, which ensures the biocatalytic activity and biochemical process in uniform way within the reactor. Baffles are incorporated into this bioreactor to avoid the formation of vortex (Vikrant *et al.*, 2018).

Fluidized bed bioreactor: A fluidized bed bioreactor is a combination of the two most common configurations, stirred tank bioreactor and packed bed continuous flow bioreactor. It has excellent heat- and mass-transfer characteristics. In the fluidized bed bioreactor (a cylinder column), a fluid (gas or liquid) is passed through a solid granular material (usually a catalyst) at high enough speeds (higher than minimum fluidization velocity) so that granular materials could flow within the bioreactor. Enzymes or microbes are encapsulated within the matrix or those are attached on the surface of matrices and used into the fluidized bed bioreactor (Steynberg *et al.*, 2004; Seong, Dong and Sang, 2006; Gopalakrishnan, Khanna and Das, 2019).

Fixed bed bioreactor: A fixed bed bioreactor consists of a cylindrical column filled with catalysts, also known as catalyst bed (enzyme or microbes in matrix). In the fixed bed bioreactor, a fluid (gas or liquid) is passed through the solid catalyst bed at a speed, however, the position of catalyst bed is fixed. A high pressure drops at two opposite ends of the fixed bed bioreactor can be created due to non-homogeneous void fraction within the catalyst bed. The biocatalytic performance of a fixed bed bioreactor could be modulated by changing the size and shape of catalysts (Krishania *et al.*, 2017).

Membrane bioreactor: Membrane bioreactor is an equipment where combined principles of bioreactor and membrane process are employed. Membrane bioreactors could be classified into different categories, such as enzyme immobilized membrane bioreactor and bioreactor attached with a membrane separation unit. In industrial process, the second choice is mostly used, where free enzyme (non-immobilized) is used in the biocatalytic reaction. In this case, enzymatic reaction takes place within

reactor and lower molecular weight of products are permeated through the membrane pores and enzymes are rejected by the membrane surface. Therefore, products (biomolecules with lower molecular weight) can be obtained in a continuous mode by membrane bioreactor (Iorhemen, Hamza and Tay, 2016).

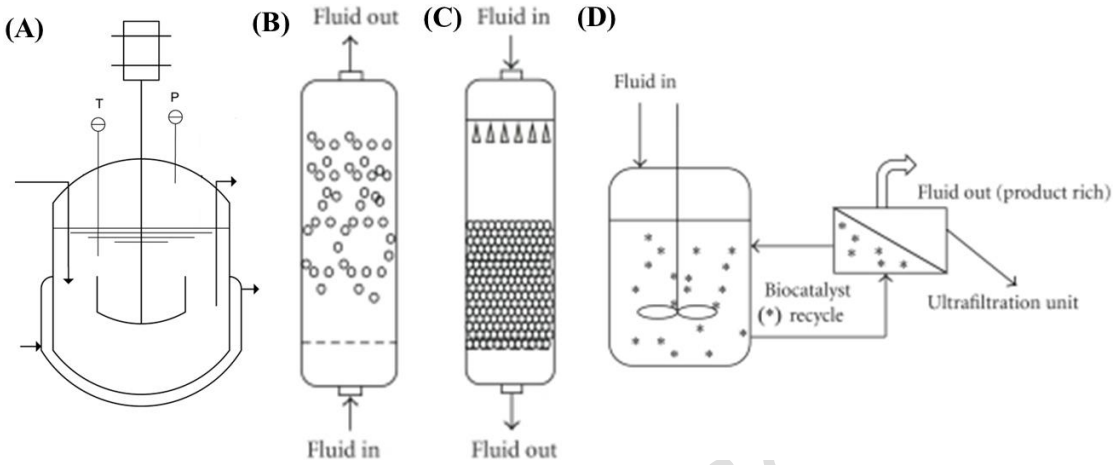


Figure 1. Reactors in bioprocess (A) stirred tank bioreactor, (b) fluidized bed bioreactor, (c) fixed bed bioreactor and (d) membrane bioreactor.

According to requirements of substrate feed, bioreactors could be used for submerged fermentation and solid-state fermentation (Ge, Vasco-Correa and Li, 2017). Submerged fermentation is an operation that involves the growth of microorganisms in a liquid broth or medium, whereas solid state fermentation can be defined as the fermentation process without or near-absence of free water. In figure 2(A) and figure 2(B) these are presented.

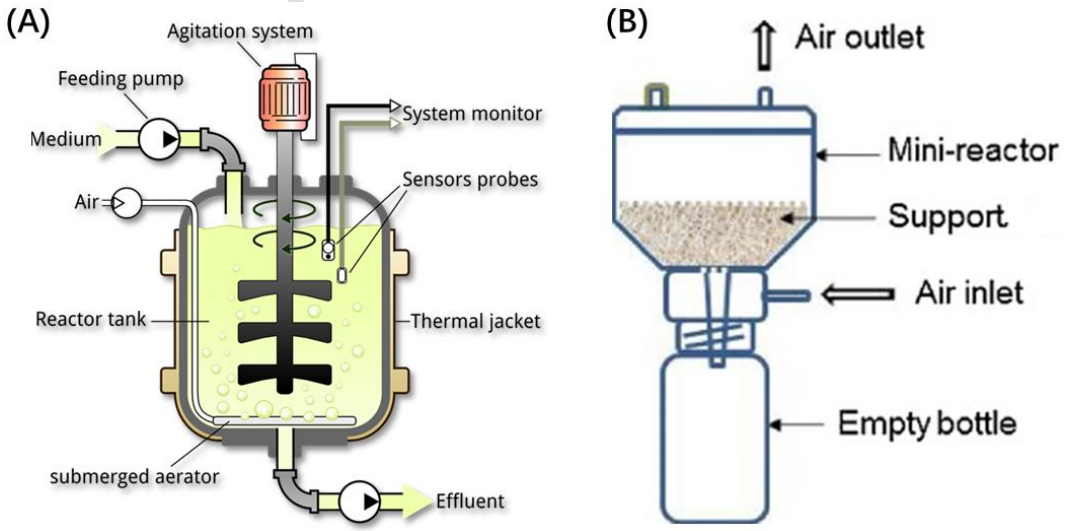


Figure 2. Schematic diagram of bioreactors; (A) submerged fermentation and (B) solid-state fermentation.

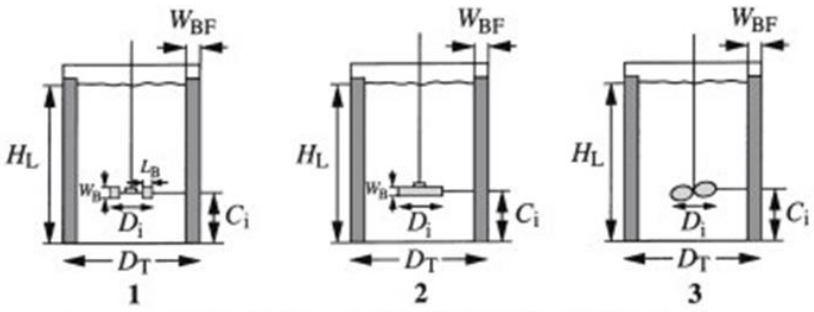
2.2.2 Design of the stirred tank bioreactor

The height, diameter and wall thickness of the reaction tank and the geometry of the impeller are considerable important issues for designing a stirred tank bioreactor. The parameters of hydrodynamic and process heat transfer within a bioreactor significantly influence mixing efficiency, heat transfer and finally overall performance of biocatalytic reaction.

Design of impeller: Typical impeller designs include rushton turbine, pitched-blade turbine and marine propeller. Each of impeller offers distinct advantages for specific applications depending on the viscosity of the reaction medium and the scale of operation (P. Gogate, Beenackers and Pandit, 2000). Different types of impellers are presented in Figure 3.

Figure 3. Schematic diagram of different types of impellers; (A) rushton turbine, (B) marine propeller and (C) pitched-blade turbine.

Various studies have highlighted how the design and shape of the impeller affect fluid flow patterns and shear stress. Impeller's diameter, blade shape, and positioning within the bioreactor influence the formation of vortices, flow regimes (turbulent vs. laminar) and the extent of dead zones (P. R. Gogate, Beenackers and Pandit, 2000; Thangaraj, Nere and Joshi, 2005; Thangaraj and Joshi, 2006). Design parameters of different types of impellers in the bioreactors are presented in Figure 4.



Impeller	D_i/D_T	H_L/D_T	C_i/D_T	Baffles	
				W_{BF}/D_T	Number
1. Rushton turbine $W_B/D_i = 0.2$, $L_B/D_i = 0.25$	0.33	1	0.33	0.1	4
2. Pitched-blade turbine $W_B/D_i = 0.125$, 6 blades, 45°, downward pumping	0.33	1	0.33	0.1	4
3. Marine propeller 3 blades, pitch = D_i	0.33	1	0.33	0.1	4

Figure 4. Design parameters of different types of impellers in the bioreactors.

Impeller Reynolds number (Re_i): The impeller Reynolds number (Re_i) plays a critical role in impeller sizing and design. Conceptually, the Re_i represents the ratio of inertial force to viscous force within the fluid and it is dimensionless. The value of Re_i depends on the geometry of the impeller and stirred tank. Re_i for stirred tank bioreactor can be described according to equation 1 (P. R. Gogate, Beenackers and Pandit, 2000).

$$Re_i = \frac{N \cdot D_i^2 \cdot \rho}{\mu} \qquad equation\ 1$$

Where N_i is the stirrer speed, D_i is the impeller diameter, ρ is the fluid density, and μ is the fluid dynamic viscosity.

It is the ratio that determines whether flow in stirred tank bioreactor remains laminar or transient or turbulent regime. In many stirred tanks laminar regime belongs when Re_i is less than 10, transition region when Re_i is less than 10^3 and turbulent region when Re_i is more than 10^3. Another important dimensionless parameter for mixing within the stirred tank bioreactor is power number (Np).

Power number (Np): The power number (Np) is also known as Newton number, which is related with resistance force to the inertia force. The value of Np depends on several factors including impeller design (geometry and diameter of impeller), impeller rotational speed, number of impellers and its location within the stirred tank. Furthermore, the property of fluids such as density influences the Np. Np for stirred tank bioreactor can be described according to equation 2 (Doran, 2013; Delbridge *et al.*, 2023).

$$N_P = \frac{P}{\rho \cdot N^3 \cdot D_i^5} \qquad \textit{equation 2}$$

Where P is the power, ρ is the fluid density and N is the rotational speed in revolutions per second. Np and Re_i for different types of impellers in the bioreactor are presented in Figure 5.

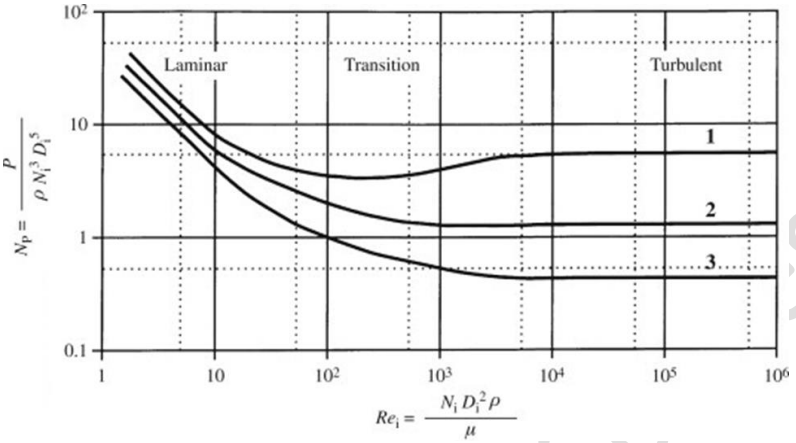


Figure 5. Power number and impeller Reynolds number for different types of impellers in the stirred tank bioreactor.

Wall thickness of stirred tank:

Nusselt number (Nu): The Nusselt number (Nu) is the ratio of total heat transfer (conduction and convection) to conductive heat transfer at a boundary in a fluid. It is a dimensionless number and closely related to the fluid's Rayleigh number. The conductive component is measured under the same conditions as the convective but for a hypothetically motionless fluid. The convection and conduction heat flows are parallel to each other and to the surface normal of the boundary surface and are all perpendicular to the mean fluid flow in the simple case. Nu for can be expressed according to equation 3 (Cheilytko, Schwarzbözl and Broeske, 2024).

$$Nu = \frac{Total\ heat\ transf\ er}{Conductive\ heat\ transf\ er} = \frac{h}{\lambda / L} = \frac{h \cdot L}{\lambda} \qquad \textit{equation 3}$$

Where h is the convective heat transfer coefficient of the flow, L is the characteristic length and λ is the thermal conductivity of the fluid.

The lower value of Nu (1-10) represents heat transfer by pure conduction and the characteristic of slug flow or laminar flow. On the other hand, a larger value of Nu (100–1000) corresponds to more active convection and turbulent flow.

In the stirred tank bioreactor, the Nu number is influenced by Re_i and Prandtl number (Pr). Therefore, Nu is influenced by several factors, such as the impeller's geometry, rotational speed of impeller, thermal conductivity and dynamic viscosity and

specific heat of the reaction medium. Empirical correlation for Nu based on experimental results is mentioned in equation 4 (Wang, Zhou and Chen, 2020).

$$Nu = C \cdot Re^{a} \cdot Pr^{b} \qquad \textit{equation } 4$$

Where C, a and b are constants that depend on the system's specific geometry and flow conditions. These constants must be carefully calibrated based on the size of bioreactor, impeller configuration and operating conditions to ensure accurate prediction of heat transfer performance. Nu for laminar flow and turbulent flow can be expressed according to equation 5 and equation 6, respectively.

$$Nu = 0.023 Re^{0.8} Pr^{0.4} \qquad \textit{equation } 5$$

Where Re is the Reynolds number (dimensionless).

$$Nu = C \cdot Pe^{0.23} \cdot \left(\frac{d_{in}}{L}\right)^{0.5} \qquad \textit{equation } 6$$

Where Pe is Peclet number. It is a dimensionless number.

Reynolds number (Re): Reynolds number (Re) is the ratio of inertial forces to viscous forces within a fluid that is subjected to relative internal movement due to different fluid velocities. Re represents the pattern of fluid flow (laminar, transient and turbulent) in different situations. Re for fluid flow through the channel can be expressed according to equation 7.

$$Re = \frac{u \cdot L}{\mu} = \frac{\rho \cdot v \cdot L}{\mu} \qquad \textit{equation } 7$$

Where v is the flow speed and μ is the kinematic viscosity of the fluid (Holland and Bragg, 1995).

Peclet number (Pe): The Peclet number (Pe) is the ratio of the advection (convection) of thermal energy to the diffusion (conduction) of thermal energy. Pe depends both on the velocity of the flow field and the characteristic length of the system. Pe can be defined according to equation 8.

$$Pe = \frac{u/L}{X/L^2} = \frac{L^2/X}{L/u} \qquad \textit{equation } 8$$

Where L is the characteristic length, u the local flow velocity and X the mass diffusion coefficient (Ollivier-Triquet *et al.*, 2024).

A flow may often have different Pe for heat and mass. This can lead to the phenomenon of double diffusive convection. In the context of heat transfer, Pe can be expressed according to equation 9.

$$Pe = \frac{L \cdot u}{\alpha} = Re \cdot P \qquad \textit{equation } 9$$

Where α is the thermal diffusivity of a material which can be expressed by the thermal conductivity divided by density and specific heat capacity at constant pressure, which is expressed in equation 10.

$$\alpha = \frac{\lambda}{\rho \cdot c_p} \qquad equation\ 10$$

In the context of mass transfer, Pe can be expressed according to equation 11.

$$Pe = \frac{L \cdot u}{X} = Re \cdot Sc \qquad equation\ 11$$

Where Sc is the Schmidt number. It can be defined by the ratio of momentum diffusivity (kinematic viscosity) and mass diffusivity (Du *et al.*, 2025).

Prandtl number (Pr): The Prandtl number (Pr) is a dimensionless number that can be defined by the ratio of momentum diffusivity to thermal diffusivity. Pr can be expressed according to equation 12.

$$Pr = \frac{c_p \cdot \mu}{\lambda} \qquad equation\ 12$$

Where c_p is the specific heat capacity and k is the thermal conductivity(Tutwiler, Shaver and Carasik, 2024).

Pr depends on viscosity and thermal conductivity of fluid. For heat transfer, the Pr is controlled by the relative thickness of the momentum and thermal boundary layers. The small value of Pr (Pr ≪ 1) signifies that the thermal diffusivity dominates compared to the velocity (momentum). On the other hand, large values of Pr (Pr ≫ 1), the momentum diffusivity dominates the behavior (Joo *et al.*, 2025).

Thermal conductivity (λ): Heat conduction is caused by the thermal motion (higher temperature to lower temperature) of microscopic particles, such as molecules, atoms and free electrons inside of an object or between contacting surfaces. According to the second law of thermodynamics, heat flux (q) in any direction is directly proportional to the temperature difference and inversely proportional to the separation distance L. Therefore, it can be expressed according to equation 13.

$$q = -\lambda \cdot \frac{T_2 - T_1}{L} \qquad equation\ 13$$

The constant of proportionality λ is known as thermal conductivity; it is a physical property of the material. Therefore, thermal conductivity of the bioreactor's construction material is a decisive factor. Heat transfer occurs at a lower rate in materials of low thermal conductivity than in materials of high thermal conductivity. Stainless steel having high thermal conductivity is often used to enhance heat transfer

('fundamentals-of-heat-and-mass-transfer-6th-edition', no date). Since $T_2 > T_1$, heat flows in the minus x-direction, q becomes negative, which in turn means that $\lambda > 0$; however, in general, λ is always defined as positive.

The expressions of q with k for multiple solid plates and cylinders, according to Figure 6, are mentioned by equation 14 and equation 15, respectively.

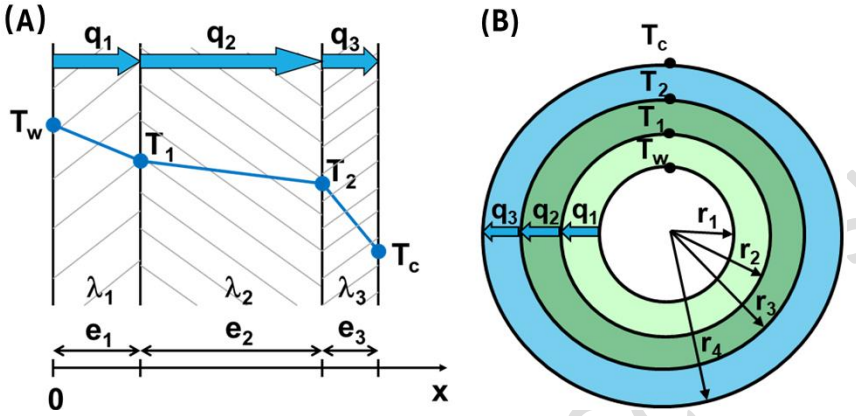


Figure 6. Heat transfer by conduction for different geometries; (A) multiple flat plates and (B) multiple cylinders. T is temperature, q is rate of heat flow, e is thickness of plate, r is radius of cylinder, q is heat flux and λ is thermal conductivity

$$q = \frac{A}{\frac{e_1}{\lambda 1} + \frac{e_2}{\lambda_2} + \frac{e_3}{\lambda_3}}\left(T_W - T_c\right) = \frac{A}{\sum_i \frac{e_i}{\lambda_i}}\left(T_W - T_C\right) \qquad \textit{equation } 14$$

and

$$q = \frac{2 \cdot \pi \cdot L}{\sum_i \frac{1}{\lambda_i} \ln \frac{r_{i+1}}{r_i}}\left(T_W - T_C\right) \qquad \textit{equation } 15$$

Heat transfer coefficient (α): Heat transfer coefficient or film coefficient or film effectiveness (α), is the proportionality constant between the heat flux and the thermodynamic driving force for the flow of heat (i.e., the temperature difference, ΔT). It can be expressed according to equation 16.

$$q = \alpha \cdot A \cdot \left(T_w - T_c\right) \qquad \textit{equation } 16$$

α is used for calculating convective heat transfer or phase transition between a fluid and a solid. It is the reciprocal of thermal insulation. It depends on both the thermal properties of a medium, the hydrodynamic characteristics of its flow, and the hydrodynamic and thermal boundary conditions. There are various methods for calculating the α in different heat transfer modes, fluids, flow regimes and thermohydraulic conditions. Often it can be calculated from the Nu, mentioned in equation 17.

$$Nu = \frac{\alpha \cdot D}{\lambda} \qquad equation\ 17$$

Where, D is geometrical diameter of item.

Overall heat transfer coefficient (U): The overall heat transfer coefficient (U) is usually expressed by combined heat transfer coefficients of individual items. Therefore, in reality, U takes into account the heat transfer coefficients of each stream and the resistance of the pipe material. According to Figure 7, the heat transfer through liquids and solid wall can be expressed according to equation 18.

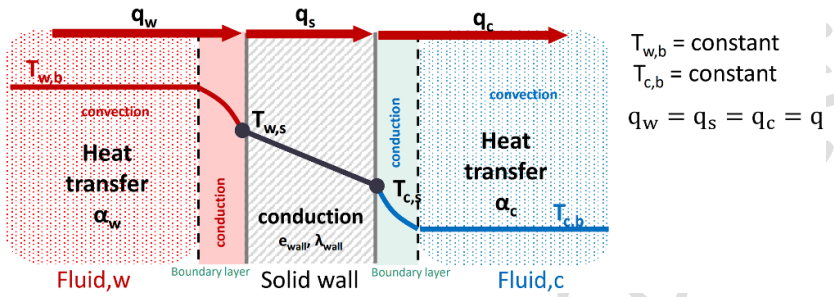


Figure 7. Heat transfers through liquids and solid wall.

$$q = U \cdot A \cdot \left(T_{w,b} - T_{c,b} \right) \qquad equation\ 18$$

Therefore, U can be expressed according to equation 19.

$$U = \frac{1}{\frac{1}{\alpha_m} + \sum_i \frac{e_i}{\lambda_i} + \frac{1}{\alpha_h}} \qquad equation\ 19$$

U is influenced by the thickness (e) and thermal conductivity (λ) of mediums through which heat is transferred.

Logarithmic mean temperature difference: The logarithmic mean temperature difference (LMTD) is a logarithmic average of the temperature difference between the hot and cold fluids at each end of the pipe. LMTD for counter-current and co-current fluid flows is presented in Figure 8.

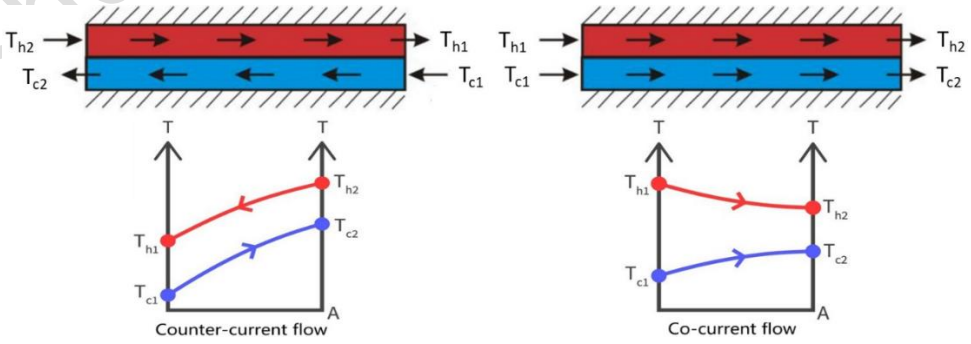


Figure 8. Logarithmic mean temperature difference for counter-current and co-current fluid flows. T_{h1} and T_{h2} are inlet and outlet temperatures of hot fluid. T_{c1} and T_{c2} are inlet and outlet temperatures of cold fluid.

LMTD is used to determine the temperature driving force for heat transfer in fluid flow systems. Accordingly, LMTD can be expressed by equation 20.

$$q = U \cdot A_{total} \cdot \frac{\left(T_{h2} - T_{c2}\right) - \left(T_{h1} - T_{c1}\right)}{\ln \frac{T_{h2} - T_{c2}}{T_{h1} - T_{c1}}} \qquad equation\ 20$$

For a constant area and heat transfer coefficient, the larger value of LMTD signifies the more heat is transferred. The LMTD method is often employed alongside Fourier's law to calculate the heat transfer rate across the bioreactor's jacket. In some cases, the geometric correction factor of LMTD (F, less than 1.0) is applied in the case of counter-current flow (Fakheri, 2003). It can be expressed according to equation 21.

$$q = U \cdot A \cdot F \cdot LMTD \qquad equation\ 21$$

With the above-mentioned definition, the LMTD can be used to find the exchanged heat in the system (Lienhard, 2001), which can be expressed according to equation 22.

$$Q = U \cdot A \cdot LMTD \qquad equation\ 22$$

Where Q is the exchanged heat duty, U is the heat transfer coefficient and A is the exchange area.

Equivalent diameter (d_e): The equivalent diameter (d_e) is defined by the ratio of cross-sectional area and circumference of an item. It is used for the simplification of diameter of an object when the cross-sectional diameter of the object is changed randomly (Zheng and Ji, 2011).

2.2.3 Operation mode of bioreactors

The productivity of bioreactors could be modulated according to the operational mode of bioreactors. Bioreactors could be operated by different modes, such as batch mode, continuous reactor, semi-continuous reactor or fed-batch. Advantages and disadvantages of different operational modes are mentioned in subsequent sections. The different operational modes of bioreactors are presented in Figure 9.

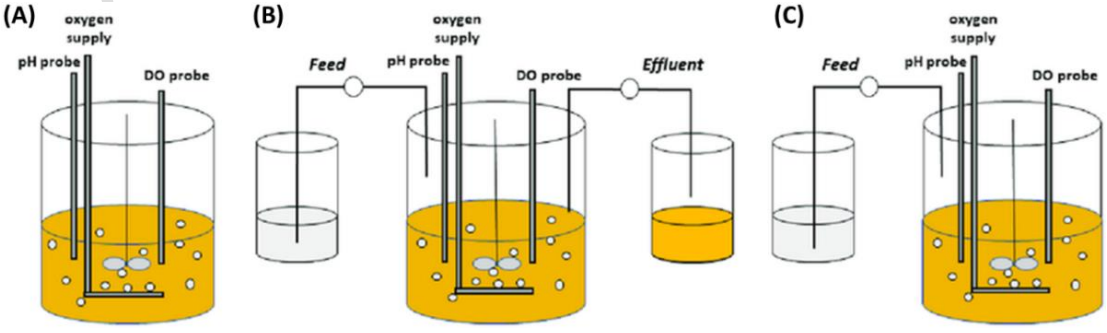


Figure 9. Operational modes of bioreactors; (A) batch mode, (B) continuous mode and (C) semi-continuous reactor or fed-batch.

Batch mode: In a batch process, all substrate or nutrients are provided at the beginning of the process, without adding any more in the subsequent bioprocess. Therefore, it is a closed system. During the entire bioprocess, only gasses, acids and bases are provided to continue the bioprocess. When the bioreaction or bioprocess has finished the bioreactor is emptied for downstream processing. Subsequently, the bioreactor is cleaned and re-filled for the next bioprocess. However, this process is simple and has less chance of contamination, there are risks for substrate or product inhibition (Kumar *et al.*, 2021).

Continuous mode: In a continuous process, fresh media with substrate is added to the bioreactor with a constant flow rate and bioreactor fluid is continuously removed with a similar inlet flowrate. Therefore, it is also known as a steady state process. As a result, enzymes or cells continuously receive fresh substrate and products or cells are continuously removed from the bioreactor. Therefore, bioreactors can be operated for a long period of time without shut down. In many times, continuous bioreactors can be more productive than batch bioreactors. The advantages of this operational mode include reduced substrate or product inhibition and an improved space-time yield, however. the long operational period may increase the risk of contamination within the bioreactor. In addition, enzymes or cells can also be immobilized in continuous bioreactors, to prevent their removal and improve productivity (Nieto-Taype *et al.*, 2020).

Semi-continuous mode: In a semi-continuous process, fresh media with substrate is continuous or sometimes periodically added to the bioreactor but unlike a continuous reactor, there is no continuous removal of bioreactor fluid. The bioreactor is emptied or partially emptied when the bioreactor is full, or bioprocess is finished. Like continuous bioreactor, it is possible to achieve higher productivities. In fed-batch process, a wide ranges of control strategies are required and, in some cases, inhibition of bioreactions through the accumulation of toxic by-products could be happened (Kurniawan *et al.*, 2018). In some cases, bioreactors could be operated with repeated fed-batch mode (Kopp *et al.*, 2020).

2.3 Structure of stirred tank bioreactor

The structure of stirred tank bioreactor is presented in Figure 10. A stirred tank bioreactor is consisted of a cylindrical vessel with water jacket. An agitator is introduced within the cylindrical vessel. The geometry and number of pitches of

impellers can be varied according to necessity. The baffles are attached to the wall of cylindrical vessel. Probes (sensors) for measuring temperature and pH are fitted within the cylindrical vessel. Furthermore, tubes for inoculation and sample collections are introduced within the cylindrical vessel (Prado Barragán *et al.*, 2016).

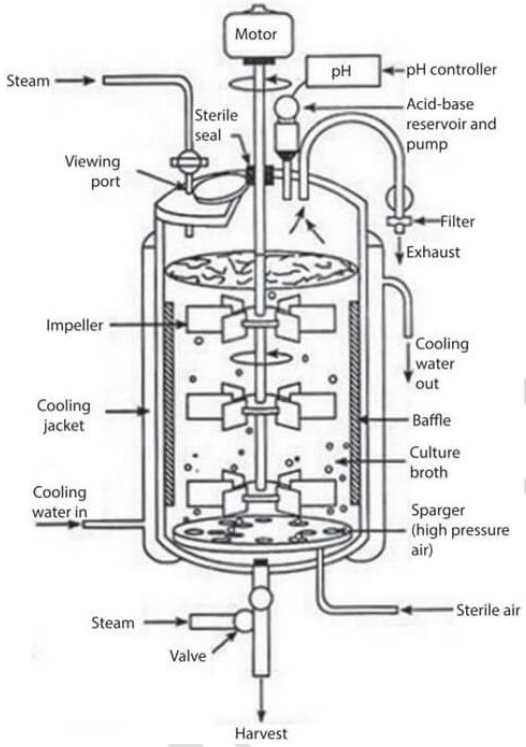


Figure 10. The structure of stirred tank bioreactor.

2.4 The operational steps of stirred tank bioreactor

The operation of a stirred tank bioreactor is followed accordingly: (a) disinfect the bioreactor and tubing with 1% Virkon solution, (b) sterilization of the bioreactor by autoclaving or steam, (c) calibration of temperature and pH sensors, (d) assembled whole bioreactor with tubing, assembles, pumps, and sensors for temperature and pH measurements, (e) supply of substrate or nutrient medium to the bioreactor, (f) adjust temperature and pH of the reaction on medium, (g) inoculation with enzyme or microbes, (h) bioprocess start and continue, (i) collection of reaction mixture or fermentation broth after sufficient time and (j) cleaning of bioreactor, assembles and tubing (Fisher, 2006).

2.5 Cleaning method for the stirred tank bioreactor

In most cases, suspended solids (microbial biomass), proteins, fats and minerals may gradually accumulate on the surfaces of propeller and wall of the bioreactor. Furthermore, different inorganic salts, such as magnesium, calcium and iron might

precipitate on the wall of the jacket (Wang *et al.*, 2014). They may create resistance of heat transfer and hinder the overall process. Therefore, their cleaning after the process is necessary. The wall of the bioreactor is cleaned with 1% Virkon solution and the jacket of the bioreactor is cleaned with 10% acetic acid. Generally, the bioreactor is cleaned after 3-5 batch operations (Brepols *et al.*, 2008).

3 Materials and Methods

Extended shelf-life (ESL) milk having fat content 2.8% was bought from local supermarket in Budapest, Bartók Béla út 47, HU 1114, Hungary.

In the present investigation, hydrolysis of milk proteins in a stirred-tank bioreactor is considered. The modulation of inlet temperature of water within the jacket of the bioreactor and stirrer speed within the bioreactor to maintain the desired temperature for biocatalysis reaction were taken into consideration. To perform the calculation, some assumptions were considered, mentioned below.

- The diameter of the stirred-tank bioreactor was considered 0.6 m. The wall thickness of the bioreactor was considered 0.2 cm and gap between outer diameter and water jacket was considered 1 cm. The front view and top view of the stirred tank bioreactor are mentioned in Figure 11.

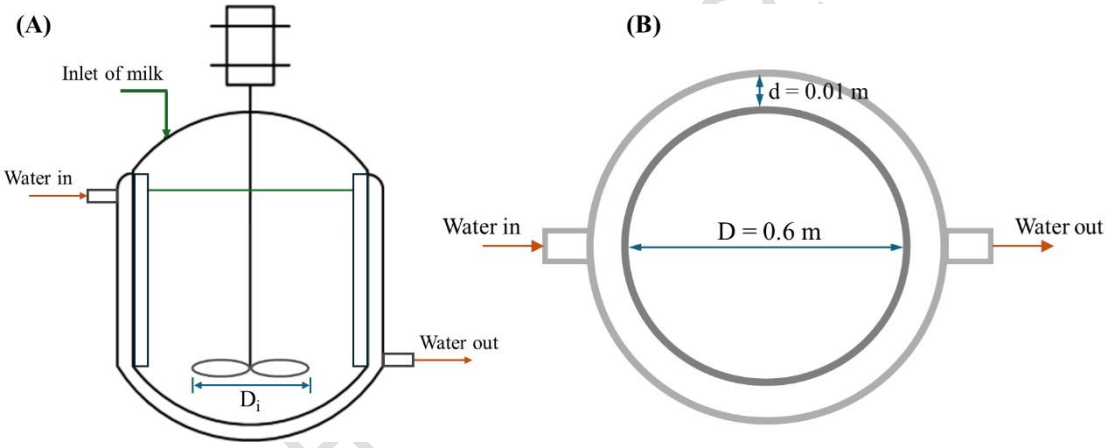


Figure 11. The front view (A) and top view (B) of the stirred tank bioreactor.

- Different rotational speeds of impellers, such as 25 rpm and 50 rpm, and motor efficiency 75% were considered.
- The change of the temperature of milk from room temperature (25 °C) to 50 °C (preincubation temperature) is done by 30 min and subsequently its alternation to 70 °C is done by 20 min.
- Heat transfer is in steady state. No heat loss to environment was considered because the laboratory-scale bioreactor was considered.

Steps for the calculations of hydrodynamic features and process heat transfer according to inlet and outlet temperatures of water in bioreactor jacket for changing the milk temperature 25 °C → 50 °C within 30 min and subsequently change of milk temperature 70 °C within 20 min are mentioned in the subsequent sections. Furthermore, startup

power requirements were evaluated for rotational speed 25 rpm and 50 rpm for different geometry of impellers (rushton turbine, marine propeller and pitched-blade turbine), and mentioned temperature range considering motor efficiency 75%.

3.1 Increase of milk temperature from room temperature (25 ℃) to 50 ℃, followed by 70 ℃.

1. Determination the volume of the milk (V_{milk}) in the bioreactor considering that 90% of bioreactor is filled with milk.

2. Calculation of the mass of milk (m_{milk}) in the bioreactor considering the density of the milk for temperature 37.5 ℃.

3. Calculation of the amount of heat required (Q) to increase the temperature of milk 25 ℃ to 50 ℃ considering the specific heat capacity (C_p) of milk for 37.5 ℃.

4. Calculation of the rate of heat flow (q) for 30 min to increase the temperature of milk 25 ℃ to 50 ℃.

5. With the knowledge of D_T (D_T (m) = D (m) + 2 * Wall thickness of the cylindrical tank (0.002 m), determination of diameters for different types of impellers (Di) according to Figure 4.

6. Determination of the impeller Reynold's number (Re_i), the Prandtl number (Pr) and the Nusselt number (Nu) for different stirrer rotation speeds, such as 25 rpm and 50 rpm. Re_i and Pr were calculated according to equation 1 and equation 12, respectively. Nu was calculated based on the fluid flow characteristics (equation 5 or equation 6).

7. Calculation of heat transfer coefficient (α_{milk}) of milk according to equation 17.

8. Similar calculation steps were followed when the temperature of milk is increased from 50 ℃ to 70 ℃.

9. Calculation of power requirement (P) within the bioreactor according to equation 2 and considering motor efficiency 75%. For that purpose, the power number (Np) was found out according to evaluated Re_i and Figure 5.

Physical characteristics of milk for 37.5 ℃ and 60 ℃ are mentioned in Table 1.

Table 1. Physical characteristics of milk for 37.5 ℃ and 60 ℃.

Temperature (°C)	Density (ρ, kg/m^3)	Dynamic viscosity (μ, Pa*s)	Specific heat capacity (c_p, J/(Kg·°C))	Thermal conductivity (λ, W/(m*K))
37.5	1022	0.0011	3980	0.57
60	1020	0.0008	3850	0.54

10. Calculation of volumetric flow rate of water (W_{water}) within jacket (4000 L/h) was measured experimentally and velocity of water flow (v) within the jacket of bioreactor was measured accordingly considering equivalent diameter (d_e).

11. Re, Nu and Pr for water flow within the jacket of bioreactor for different temperatures of inlet water flow within the jacket of bioreactor. For that purpose, ρ, μ, λ and c_p of water for different temperatures were considered, mentioned in Table 2.

Table 2. Physical characteristics of water for different temperatures.

Temperature (°C)	Density (kg/m^3)	Dynamic viscosity (Pa*s)	Specific heat capacity (J/(Kg·°C))	Thermal conductivity (W/(m*K))
69	976.5	0.000425	4181	0.646
65	979.8	0.000445	4181	0.648
85	970.3	0.000355	4196	0.67
80	972.8	0.000376	4192	0.674

13. Calculation of heat transfer coefficient of water (α_{water}) according to equation 17.

14. Calculation of overall heat transfer coefficient (U) according to equation 19.

15. Calculation of Logarithmic mean temperature difference (LMTD) to increase the milk temperature from 25 °C to 50 °C, followed by 70 °C. Based on this information inlet and outlet temperature of water within the jacket of bioreactor were decided.

16. Calculation of U based on logarithmic value of temperature difference. Equation 20 was used for that purpose. Inlet and outlet temperatures of water within the jacket of bioreactor were decided according to step 15. Subsequently, values of U, evaluated according to step 14 and step 15 were compared. Inlet and outlet temperatures of water were considered acceptable if the error is lower than 5%.

4 Results and Discussion

4.1 Determination of temperatures for inlet and outlet water flow within the jacket of the bioreactor

Volume of milk (Vmilk) could be calculated according to following formula.

$$V_{milk} = \frac{D_T^{\,2} \cdot \pi}{4} \cdot H_L \cdot 90\% = 0.1527\ m^3$$

According to correlation mentioned in Figure 4, Di could be calculated, mentioned below.

$$D_i = D_T \cdot 0.33 = 0.198\ m$$

4.1.1 Calculation when temperature of milk when it is increased from 25 °C to 50 °C.

Temperature of milk was increased from 25 °C to 50 °C. Therefore, average temperature 37.5 °C was considered for calculation. Mass of milk for temperature 37.5 °C could be calculated accordingly.

$$m_{milk-37.5°C} = \varrho_{milk-37.5°C} \cdot V_{milk} = 156.059\ kg$$

Heat requirement to increase the temperature from 25 °C to 50 °C.

$$Q_{milk\ 25°C \to 50\ °C} = m_{milk-37.5°C} \cdot c_{p-milk\ 37.5°C} \cdot \Delta T_{milk\ 25°C \to 50°C} = 15527870.5\ J$$

Heat flow to increase the temperature from 25 °C to 50 °C could be calculated according to following formula.

$$q_{milk\ 25°C \to 50\ °C} = \frac{Q_{milk\ 37.5°C}}{t} = 8626.595\ W$$

Prandtl number for milk in bioreactor to increase the temperature from 25 °C to 50 °C could be calculated according to following formula.

$$Pr_{milk\ 37.5°C} = \frac{c_{p-milk\ 37.5°C} \cdot \mu_{milk\ 37.5°C}}{\lambda_{milk\ 37.5°C}} = 7.68$$

For 25 rpm impeller speed, Re_i, Nu and α could be calculated according to following formulas.

$$Re_{i-25\ rpm,\ 37.5°C} = \frac{\varrho_{milk-37.5°C} \cdot N_{25\ rpm} \cdot D_i^{\,2}}{\mu_{milk-37.5°C}} = 15176.7$$

$$Nu_{25\ °C \to 50\ °C\ milk-25\ rpm} = 0.37 \cdot Re_{i-25\ rpm,\ 37.5°C}^{\ 2/3} \cdot Pr_{milk\ 37.5°C}^{\ 1/3} = 447.494$$

$$\alpha_{25\ °C \to 50\ °C\ milk-25rpm} = \frac{Nu_{25\ °C \to 50\ °C\ milk-25rpm} \cdot \lambda_{37.5°C-milk}}{D_T} = 422.304\ W \cdot m^{-2} \cdot K^{-1}$$

For 50 rpm impeller speed, Re_i, Nu and α could be calculated according to following formulas.

$$Re_{i-50\ rpm,\ 37.5°C} = \frac{\varrho_{milk-37.5°C} \cdot N_{50\ rpm} \cdot D_i^{\ 2}}{\mu_{milk-37.5°C}} = 30353.4$$

$$Nu_{25\ °C \to 50\ °C\ milk-50\ rpm} = 0.37 \cdot Re_{i-50\ rpm,\ 37.5°C}^{\ 2/3} \cdot Pr_{milk\ 37.5°C}^{\ 1/3} = 710.352$$

$$\alpha_{25\ °C \to 50\ °C\ milk-50\ rpm} = \frac{Nu_{25\ °C \to 50\ °C\ milk-50\ rpm} \cdot \lambda_{37.5°C}}{D_T} = 670.365\ W \cdot m^{-2} \cdot K^{-1}$$

4.1.2 Calculation when temperature of milk when it is increased from 50 °C to 70 °C.

Temperature of milk was increased from 50 °C to 70 °C. Therefore, average temperature 60 °C was considered for calculation. Mass of milk for temperature 60 °C could be calculated accordingly.

$$m_{milk-60°C} = \varrho_{milk-60°C} \cdot V_{milk} = 155.754\ kg$$

Heat requirement to increase the temperature from 50 °C to 70 °C.

$$Q_{milk-60°C} = m_{milk-60°C} \cdot c_{p-60°C} \cdot \Delta T_{milk-50°C \to 70°C} = 11993058\ J$$

Heat flow to increase the temperature from 50 °C to 70 °C could be calculated according to following formula.

$$q_{milk-50°C \to 70°C} = \frac{Q_{milk-60°C}}{t} = 9994.215\ W$$

Prandtl number for milk in bioreactor to increase the temperature from 50 °C to 70 °C could be calculated according to following formula.

$$Pr_{milk-60°C} = \frac{c_{p-milk\ 60°C} \cdot \mu_{milk\ 60°C}}{\lambda_{milk\ 60°C}} = 5.7$$

For 25 rpm impeller speed, Re_i, Nu and α could be calculated according to following formulas.

$$Re_{i-25\ rpm,\ 60°C} = \frac{\varrho_{milk\ 60°C} \cdot N_{25\ rpm} \cdot D_i^{\ 2}}{\mu_{milk\ 60°C}} = 20827.125$$

$$Nu_{50\ °C \to 70\ °C\ milk-25rpm} = 0.37 \cdot Re_{i-25\ rpm,\ 60°C}^{\ 2/3} \cdot Pr_{60°C-milk}^{\ 1/3} = 500.318$$

$$\alpha_{50\ °C \to 70\ °C\ milk-25\ rpm} = \frac{Nu_{50\ °C \to 70\ °C\ milk-25\ rpm} \cdot \lambda_{60°C-milk}}{D_T} = 447.304\ W \cdot m^{-2} \cdot K^{-1}$$

For 50 rpm impeller speed, Re_i, Nu and α could be calculated according to following formulas.

$$Re_{i-50\ rpm,\ 60°C} = \frac{\varrho_{milk\ 60°C} \cdot N_{50\ rpm} \cdot D_i^{\ 2}}{\mu_{milk\ 60°C}} = 41654.25$$

$$Nu_{50\ °C \to 70\ °C\ milk-50rpm} = 0.37 \cdot Re_{i-50\ rpm,\ 60°C}^{\ 2/3} \cdot Pr_{milk-60°C}^{\ 1/3} = 794.206$$

$$\alpha_{50\ °C \to 70\ °C\ milk-50\ rpm} = \frac{Nu_{50\ °C \to 70\ °C\ milk-50\ rpm} \cdot \lambda_{60°C-milk}}{D_T} = 710.051\ W \cdot m^{-2} \cdot K^{-1}$$

4.1.3 Calculation of temperatures of water inlet and outlet when milk temperature is increased from 25 °C to 50 °C.

Heat transfer area of bioreactor (S) could be calculated according to following formula.

$$S = D_{T_{avg}} \cdot \pi \cdot H_L = 1.1687\ m^2$$

Cross-section area of water flow within the jacket of bioreactor (A) could be calculated according to following formula.

$$A = \frac{\pi \cdot D_{out}^{\ 2}}{4} - \frac{\pi \cdot D_T^{\ 2}}{4} = 0.01928\ m^2$$

Water flow velocity within the jacket of bioreactor

$$v = \frac{W_{volume}}{A} = 0.0576\ m \cdot s^{-1}$$

Equivalent diameter of water flow cross-sectional area within the jacket of bioreactor (de) could be calculated according to following formula.

$$d_e = 4 \cdot \frac{A}{C} = 0.02\ m$$

For 25 rpm impeller speed and temperature 69 °C, Pr, Re, Nu, α and U could be calculated according to following formulas.

$$Pr_{69°C-water} = \frac{c_{p\ water-69°C} \cdot \mu_{water-69°C}}{\lambda_{water-69°C}} = 2.75$$

$$Re_{jacket\ water-69°C} = \frac{\varrho_{water-69°C} \cdot v \cdot D_e}{\mu_{water-69°C}} = 2646.89$$

$$Nu_{jacket\ water-69°C} = 0.21 \cdot Re_{jacket\ water-69°C}^{0.633} \cdot Pr_{69°C-water}^{0.326} = 42.85$$

$$\alpha_{water-69°C} = \frac{Nu_{jacket\ water-69°C} \cdot \lambda_{water-69°C}}{d_e} = 1384.32\ W \cdot m^{-2} \cdot K^{-1}$$

$$\frac{1}{U_{25°C \to 50\ °C\ -25\ rpm}} = \frac{1}{\alpha_{25\ °C \to 50\ °C\ milk-25\ rpm}} + \frac{e}{\lambda_{steel}} + \frac{1}{\alpha_{water-69°C}} = 0.003132\ W^{-1} \cdot m^2 \cdot K$$

$$U_{25°C \to 50\ °C\ -25rpm} = 319.28\ W \cdot m^{-2} \cdot K^{-1}$$

LMTD for heat transfer among water and milk when temperature of milk was increased from 25 °C to 50 °C and impeller speed 25 rpm. The inlet and outlet temperatures of water and milk are described in Figure 12.

$$LMTD_{25° C \to 50\ ° C\ -\ 25\ rpm} = \frac{q_{25° C \to 50\ ° C}}{U_{25° C \to 50\ ° C\ -\ 25\ rpm} \cdot A} = 23.03$$

Error check of the $U_{25°C \to 50°C\ 25rpm}$:

$$U_{25° C \to 50\ ° C\ -\ 25rpm} = \frac{q_{25° C \to 50\ ° C}}{S \cdot LMTD_{25° C \to 50\ ° C\ -\ 25rpm}} = 320.511\ W \cdot m^{-2} \cdot K^{-1}$$

$$Error = 0.384\% < 5\%$$

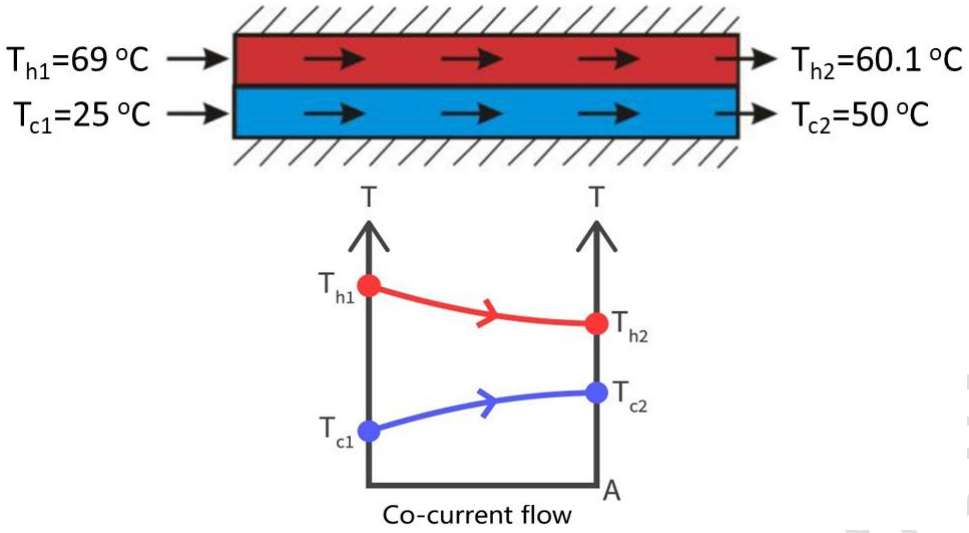


Figure 12. Logarithmic mean temperature difference of milk and water in the jacket of bioreactor when milk temperature is increased from 25 °C to 50 °C and rotational velocity of the impeller is 25 rpm.

For 50 rpm impeller speed and temperature 65 °C, Pr, Re, Nu, α and U could be calculated according to following formulas.

$$Pr_{water-65°C} = \frac{c_{p-water-65°C} \cdot \mu_{water-65°C}}{\lambda_{water-65°C}} = 2.87$$

$$Re_{jacket\ water\ 65°C} = \frac{\varrho_{water-65°C} \cdot v \cdot D_e}{\mu_{water-65°C}} = 2536.47$$

$$Nu_{jacket\ water-65°C} = 0.21 \cdot Re_{jacket\ water-65°C}^{0.633} \cdot Pr_{water-65°C}^{0.326} = 42.3$$

$$\alpha_{water\ 65°C} = \frac{Nu_{jacket\ water-65°C} \cdot \lambda_{65°C}}{D_T} = 1370.52\ W \cdot m^{-2} \cdot K^{-1}$$

$$\frac{1}{U_{25°C \to 50\,°C\ -50rpm}} = \frac{1}{\alpha_{25\,°C \to 50\,°C\ milk-50rpm}} + \frac{e}{\lambda_{steel}} + \frac{1}{\alpha_{water-65°C}} = 0.00226\ W^{-1} \cdot m^2 \cdot K$$

$$U_{25°C \to 50\,°C\ -50rpm} = 441.72\ W \cdot m^{-2} \cdot K^{-1}$$

LMTD for heat transfer among water and milk when temperature of milk was increased from 25 °C to 50 °C and impeller speed 50 rpm. The inlet and outlet temperatures of water and milk are described in Figure 13.

$$LMTD_{25°C \to 50\,°C\ -50rpm} = \frac{q_{milk\ 25°C \to 50\,°C}}{U_{25°C \to 50\,°C\ -50rpm} \cdot A} = 16.6$$

Error check of the U_{50}:

$$U_{25°C \to 50\,°C\ -50rpm} = \frac{q_{milk\ 25°C \to 50\,°C}}{S \cdot LMTD_{25°C \to 50\,°C\ -50rpm}} = 438.55\ W \cdot m^{-2} \cdot K^{-1}$$

$$Error = 0.73\% < 5\%$$

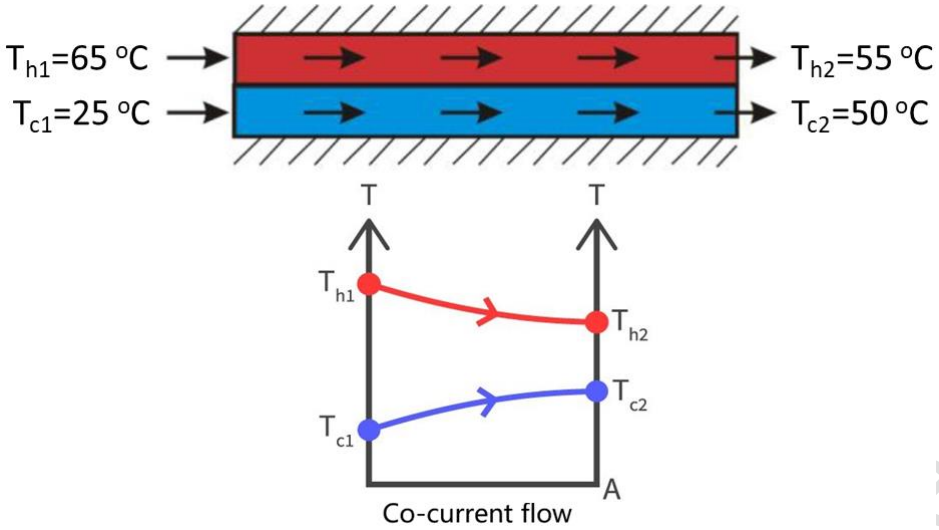


Figure 13. Logarithmic mean temperature difference of milk and water in the jacket of bioreactor when milk temperature is increased from 25 °C to 50 °C and rotational velocity of the impeller is 50 rpm.

4.1.4 Calculation of temperatures of water inlet and outlet when milk temperature is increased from 50 °C to 70 °C.

For 25 rpm impeller speed and temperature 85 °C, Pr, Re, Nu, α and U could be calculated according to following formulas.

$$Pr_{water-85°C} = \frac{c_{p-water-85°C} \cdot \mu_{water-85°C}}{\lambda_{water-85°C}} = 2.223$$

$$Re_{jacket\ water-85°C} = \frac{\varrho_{water-85°C} \cdot v \cdot D_e}{\mu_{water-85°C}} = 3148.69$$

$$Nu_{water-85°C} = 0.21 \cdot Re_{jacket\ water-85°C}^{0.633} \cdot Pr_{water-85°C}^{0.326} = 44.63$$

$$\alpha_{water-85°C} = \frac{Nu_{water-85°C} \cdot \lambda_{water-85°C}}{d_e} = 1495.105 W \cdot m^{-2} \cdot K^{-1}$$

$$\frac{1}{U_{50°C \to 70°C\ -25rpm}} = \frac{1}{\alpha_{50°C \to 70°C\ milk-25rpm}} + \frac{e}{\lambda_{steel}} + \frac{1}{\alpha_{water-85°C}} = 0.002946132 W^{-1} \cdot m^2 \cdot K$$

$$U_{50°C \to 70°C\ -25rpm} = 339.428\ W \cdot m^{-2} \cdot K^{-1}$$

LMTD for heat transfer among water and milk when temperature of milk was increased from 50 °C to 70 °C and impeller speed 25 rpm. The inlet and outlet temperatures of water and milk are described in Figure 14.

$$LMTD_{50° C \to 70° C\ -25rpm} = \frac{q_{milk\ 50° C \to 70° C}}{U_{50° C \to 70° C\ -25rpm} \cdot A} = 21.464$$

Error check of the U_{25}:

$$U_{50^\circ C\rightarrow 70\,^\circ C\,-25rpm}=\frac{q_{milk\,50^\circ C\rightarrow 70\,^\circ C}}{S\cdot LMTD_{50^\circ C\rightarrow 70\,^\circ C\,-25rpm}}=343.53\ W\cdot m^{-2}\cdot K^{-1}$$

$$Error=1.194\%<5\%$$

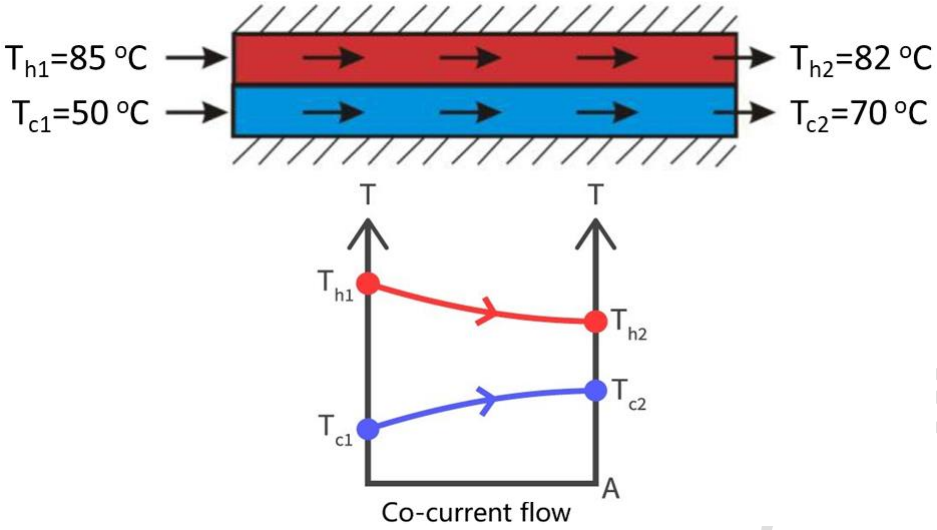


Figure 14. Logarithmic mean temperature difference of milk and water in the jacket of bioreactor when milk temperature is increased from 50 °C to 70 °C and rotational velocity of the impeller is 25 rpm.

For 50 rpm impeller speed and temperature 80 °C, Pr, Re, Nu, α and U could be calculated according to following formulas.

$$Pr_{water-80\,^\circ C}=\frac{c_{p-water-80\,^\circ C}\cdot\mu_{water-80\,^\circ C}}{\lambda_{water-80\,^\circ C}}=2.339$$

$$Re_{jacket\ water-80^\circ C}=\frac{\varrho_{water-80^\circ C}\cdot v\cdot D_e}{\mu_{water-80^\circ C}}=2980.49$$

$$Nu_{water-80^\circ C}=0.21\cdot Re_{jacket\ water-80^\circ C}^{0.633}\cdot Pr_{water-80^\circ C}^{0.326}=43.83$$

$$\alpha_{water-80\,^\circ C}=\frac{Nu_{water-80^\circ C}\cdot\lambda_{water-80^\circ C}}{d_e}=1477.071 W\cdot m^{-2}\cdot K^{-1}$$

$$\frac{1}{U_{50\,^\circ C\rightarrow 70\,^\circ C\ milk-50rpm}}=\frac{1}{\alpha_{50\,^\circ C\rightarrow 70\,^\circ C\ milk-50rpm}}+\frac{e}{\lambda_{steel}}+\frac{1}{\alpha_{water-80^\circ C}}=0.002127\ W^{-1}\cdot m^2\cdot K$$

$$U_{50\,^\circ C\rightarrow 70\,^\circ C\ milk-50rpm}=470.146\ \ W\cdot m^{-2}\cdot K^{-1}$$

LMTD for heat transfer among water and milk when temperature of milk was increased from 50 °C to 70 °C and impeller speed 50 rpm. The inlet and outlet temperatures of water and milk are described in Figure 15.

$$LMTD_{50\,^\circ C\rightarrow 70\,^\circ C\ milk-50rpm}=\frac{q}{U_{50\,^\circ C\rightarrow 70\,^\circ C\ milk-50rpm}\cdot A}=15.641$$

Error check of the U_{50}:

$$U_{50^\circ C\rightarrow 70\,^\circ C\,-50rpm}=\frac{q}{S\cdot LMTD_{25}}=467.04\ W\cdot m^{-2}\cdot K^{-1}$$

$Error = 0.661\% < 5\%$

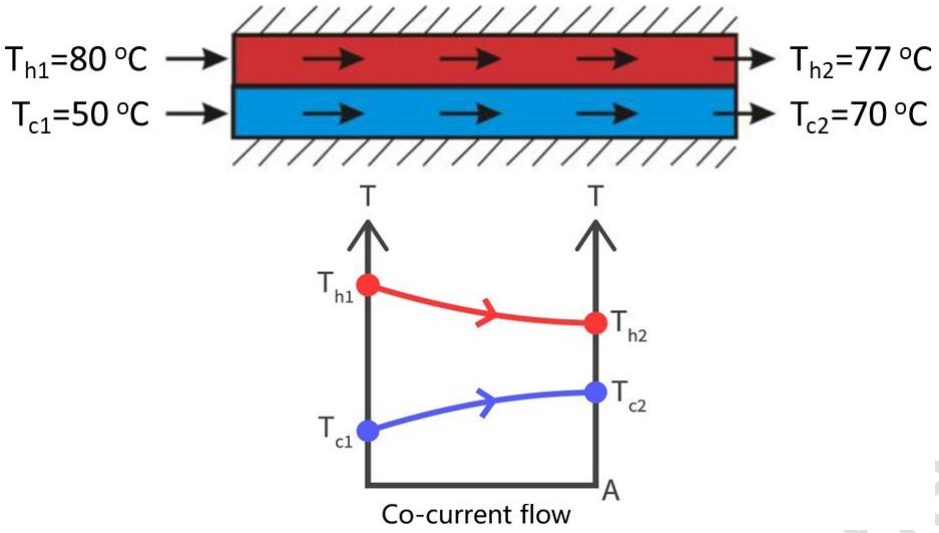


Figure 15. Logarithmic mean temperature difference of milk and water in the jacket of bioreactor when milk temperature is increased from 50 °C to 70 °C and rotational velocity of the impeller is 50 rpm.

4.2 Power consumption for impeller rotation

Calculation the rushton turbine power requirement (We can know $N_p = 7$ from figure 5 of literature view).

At 25 rpm for 37.5°C:

$$P_{25\ rpm-37.5^\circ C} = \frac{\left(N_p \cdot \rho_{milk\ 37.5^\circ C} \cdot {N_{25rpm}}^3 \cdot {D_i}^5\right)}{0.75} = 0.21\ W$$

At 50 rpm for 37.5°C:

$$P_{50rpm-37.5^\circ C} = \frac{\left(N_p \cdot \rho_{milk\ 37.5^\circ C} \cdot {N_{50rpm}}^3 \cdot {D_i}^5\right)}{0.75} = 1.68\ W$$

At 25 rpm for 60°C:

$$P_{25\ rpm-60^\circ C} = \frac{\left(N_p \cdot \rho_{milk\ 60^\circ C} \cdot {N_{25rpm}}^3 \cdot {D_i}^5\right)}{0.75} = 0.21\ W$$

At 50 rpm for 60°C:

$$P_{50rpm-60^\circ C} = \frac{\left(N_p \cdot \rho_{milk\ 60^\circ C} \cdot {N_{50rpm}}^3 \cdot {D_i}^5\right)}{0.75} = 1.68\ W$$

Calculation the pitched-blade turbine power requirement (We can know $N_p = 1.1$ from figure 5 of literature view).

At 25 rpm for 37.5°C:

$$P_{25\ rpm-37.5^\circ C} = \frac{\left(N_p \cdot \rho_{milk\ 37.5^\circ C} \cdot {N_{25rpm}}^3 \cdot {D_i}^5\right)}{0.75} = 0.03\ W$$

At 50 rpm for 37.5°C:

$$P_{50rpm-37.5^\circ C}=\frac{\left(N_p\cdot\rho_{milk\ 37.5^\circ C}\cdot {N_{50rpm}}^3\cdot {D_i}^5\right)}{0.75}=0.26\ W$$

At 25 rpm for 60°C:

$$P_{25\ rpm-60^\circ C}=\frac{\left(N_p\cdot\rho_{milk\ 60^\circ C}\cdot {N_{25rpm}}^3\cdot {D_i}^5\right)}{0.75}=0.03\ W$$

At 50 rpm for 60°C:

$$P_{50rpm-60^\circ C}=\frac{\left(N_p\cdot\rho_{milk\ 60^\circ C}\cdot {N_{50rpm}}^3\cdot {D_i}^5\right)}{0.75}=0.26\ W$$

Calculation of the marine propeller power requirement (We can know $N_p = 0.5$ from figure 5 of literature view).

At 25 rpm for 37.5°C:

$$P_{25\ rpm-37.5^\circ C}=\frac{\left(N_p\cdot\rho_{milk\ 37.5^\circ C}\cdot {N_{25rpm}}^3\cdot {D_i}^5\right)}{0.75}=0.015\ W$$

At 50 rpm for 37.5°C:

$$P_{50rpm-37.5^\circ C}=\frac{\left(N_p\cdot\rho_{milk\ 37.5^\circ C}\cdot {N_{50rpm}}^3\cdot {D_i}^5\right)}{0.75}=0.12\ W$$

At 25 rpm for 60°C:

$$P_{25\ rpm-60^\circ C}=\frac{\left(N_p\cdot\rho_{milk\ 60^\circ C}\cdot {N_{25rpm}}^3\cdot {D_i}^5\right)}{0.75}=0.015\ W$$

At 50 rpm for 60°C:

$$P_{50rpm-60^\circ C}=\frac{\left(N_p\cdot\rho_{milk\ 60^\circ C}\cdot {N_{50rpm}}^3\cdot {D_i}^5\right)}{0.75}=0.12\ W$$

5 Conclusion

In the present investigation, proteolysis of milk proteins by papain within a stirred tank bioreactor has been considered. Papain exhibits its highest proteolysis within the temperature range 60-65°C) and at temperatures higher than 70°C, papain activity may start to decline due to denaturation. Therefore, changing the temperature of milk from room temperature (25 °C) to 50 °C (preincubation temperature) and subsequently its alternation to 70 °C were considered. Efforts were made to understand the modulation of inlet temperature of water within the jacket of the bioreactor and stirrer speed within the bioreactor to maintain the desired temperature for biocatalysis reaction. Conclusions from above mentioned calculation are mentioned below:

1. For heating of milk from 25-50 °C with impeller speed 25 rpm, the water inlet temperature should be 69 °C and outlet temperature should be 60.1 °C.
2. For heating of milk from 25-50 °C with impeller speed 50 rpm, the water inlet temperature should be 65 °C and outlet temperature should be 55 °C.
3. For heating of milk from 50-70 °C with impeller speed 25 rpm, the water inlet temperature should be 85 °C and outlet temperature should be 82 °C.
4. For heating of milk from 25-50 °C with impeller speed 50 rpm, the water inlet temperature should be 80°C and outlet temperature should be 77 °C.

It was found that my choices related to inlet and outlet temperatures of water flow within the jacket of bioreactor are suitable because error values of U were less than 5%. Power requirement for different impellers with different velocities are mentioned in following table.

Table: Power requirement for different impellers rotations with different velocities.

Impeller type	37.5°C		60°C	
	25 rpm	50 rpm	25 rpm	50 rpm
Rushton turbine	0.21 W	1.68 W	0.21 W	1.68 W
Pitched-blade turbine	0.03 W	0.26 W	0.03 W	0.26 W
Marine propeller turbine	0.015 W	0.12 W	0.015 W	0.12 W

However, I emphasized the mechaniical design of a stirred tank bioreactor and modulation of temperature for an enzyme-catalyzed bioreaction, I will do protein hydrolysis by papain within the designed bioreactor and evaluated temperature in the future. Presently, I considered that the diameter of the bioreactor is 0.6 m. In the future, I will design a stirred tank bioreactor for large capacity.

6 Summary

Various types of non-fermented and fermented dairy-based food formulas have garnered significant attention across different communities. As time progressed, dairy industries tried their best to improve the quality of dairy-based formulas to fulfil the expectations of consumers. Enzymatic hydrolysis of allergenic epitopes in protein sequences is viewed as a potentially effective method for reducing milk protein allergens. Furthermore, enzymatic modifications can also alter the functional properties of milk proteins. Enzymatic hydrolysis of milk proteins is generally performed in a stirred tank bioreactor. Understanding operating parameters, such as temperature and stirrer speed are crucial for enzyme-catalyzed bioreaction.

In the present investigation, the mechanical design of a lab-scale bioreactor and understanding of process parameters tailored for milk protein hydrolysis were considered. Two important aspects, such as geometry of impellers and overall heat transfer coefficient of a bioreactor have been emphasized. The effect of rpm of impeller, and inlet and outlet temperatures of water within the jacket of bioreactor on process heat transfer were studied with special attention on overall heat transfer coefficient. Different dimensionless parameters, such as Reynolds number, Prandtl number and Nusselt number were studied. The inlet and outlet temperatures of water in bioreactor jacket were evaluated for the change of milk temperature 25 °C → 50 °C within 30 min and subsequently change of milk temperature 70 °C within 20 min. Startup power requirements were evaluated for rotational speed 25 rpm and 50 rpm, and mentioned temperature range considering motor efficiency 75%. Conclusions from above mentioned operating conditions for enzymatic hydrolysis of proteins in a stirrer tank bioreactor are mentioned below:

1. For heating of milk from 25-50 °C with impeller speed 25 rpm, the water inlet temperature should be 69 °C and outlet temperature should be 60.1 °C.
2. For heating of milk from 25-50 °C with impeller speed 50 rpm, the water inlet temperature should be 65 °C and outlet temperature should be 55 °C.
3. For heating of milk from 50-70 °C with impeller speed 25 rpm, the water inlet temperature should be 85 °C and outlet temperature should be 82 °C.
4. For heating of milk from 25-50 °C with impeller speed 50 rpm, the water inlet temperature should be 80°C and outlet temperature should be 77 °C.

It was found that selection of inlet and outlet temperatures of water flow within the jacket of bioreactor are suitable because error values of U were less than 5%.

7 Nomenclature

Abbreviation	Explanation	unit
A	Jacket cross sectional area	m^2
$\alpha_{25\ ℃→50\ ℃\ milk\ 25rpm}$	Milk heat transfer coefficient at 25 rpm, and the temperature from 25°C increase to 50°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$\alpha_{25\ ℃→50\ ℃\ milk\ 50rpm}$	Milk heat transfer coefficient at 50 rpm, and the temperature from 25°C increase to 50°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$\alpha_{50\ ℃→70\ ℃\ milk\ 25rpm}$	Milk heat transfer coefficient at 25 rpm, and the temperature from 50°C increase to 70°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$\alpha_{50\ ℃→70\ ℃\ milk\ 50rpm}$	Milk heat transfer coefficient at 50 rpm, and the temperature from 50°C increase to 70°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$\alpha_{water\ 65℃}$	Water heat transfer coefficient at 65°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$\alpha_{water\ 69℃}$	Water heat transfer coefficient at 69°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$\alpha_{water\ 80℃}$	Water heat transfer coefficient at 80°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$\alpha_{water\ 85℃}$	Water heat transfer coefficient at 85°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
C	Bioreactor's jacket circumference	m
C_p	Specific heat capacity	$J*kg^{-1}*K^{-1}$ / $J*kg^{-1}*°C^{-1}$
$C_{p\text{-}water\ 65℃}$	65°C water specific heat capacity	$J*kg^{-1}*K^{-1}$ / $J*kg^{-1}*°C^{-1}$

$C_{p\text{-water }69°C}$	69°C water specific heat capacity	$J*kg^{-1}*K^{-1}$ / $J*kg^{-1}*°C^{-1}$
$C_{p\text{-water }80°C}$	80°C water specific heat capacity	$J*kg^{-1}*K^{-1}$ / $J*kg^{-1}*°C^{-1}$
$C_{p\text{-water }85°C}$	85°C water specific heat capacity	$J*kg^{-1}*K^{-1}$ / $J*kg^{-1}*°C^{-1}$
$C_{p\text{-milk }37.5°C}$	Milk average temperature 37.5°C specific heat capacity	$J*kg^{-1}*K^{-1}$ / $J*kg^{-1}*°C^{-1}$
$C_{p\text{-milk }60°C}$	Milk average temperature 60°C specific heat capacity	$J*kg^{-1}*K^{-1}$ / $J*kg^{-1}*°C^{-1}$
D_e	Equivalent diameter	m
D_T	Bioreactor's inner diameter	m
D_i	Impeller diameter	m
e	Steel wall thickness	m
H_L	Bioreactor height	m
L	Characteristic length	m
LMTD	Logarithmic means temperature difference	K / °C
$LMTD_{25\ °C\rightarrow50\ °C\ milk\ 25rpm}$	Logarithmic means temperature difference when the milk temperature from 25°C increase to 50°C, impeller rotation velocity is 25rpm	K / °C
$LMTD_{25\ °C\rightarrow50\ °C\ milk\ 50rpm}$	Logarithmic means temperature difference when the milk temperature from 25°C increase to 50°C, impeller rotation velocity is 50 rpm	K / °C
$LMTD_{50\ °C\rightarrow70\ °C\ milk\ 25rpm}$	Logarithmic means temperature difference when the milk temperature from	K / °C

	50°C increase to 70°C, impeller rotation velocity is 25 rpm	
$LMTD_{50\ °C \rightarrow 70\ °C\ milk\ 50rpm}$	Logarithmic means temperature difference when the milk temperature from 50°C increase to 70°C, impeller rotation velocity is 50 rpm	K / °C
m_{milk}	Mass of the milk in the bioreactor	kg
$m_{milk\text{-}37.5°C}$	Mass of the milk in the bioreactor when the milk average temperature is 37.5°C	kg
$m_{milk\text{-}60°C}$	Mass of the milk in the bioreactor	kg
N	Impeller rotation velocity	min^{-1} / s^{-1}
N_{25rpm}	Impeller rotation velocity at 25rpm	min^{-1} / s^{-1}
N_{50rpm}	Impeller rotation velocity at 50 rpm	min^{-1} / s^{-1}
Nu	Nusselt number	Dimensionless
$Nu_{25\ °C \rightarrow 50\ °C\ milk-25rpm}$	When the milk temperature from 25°C increase to 50°C, at 25rpm rotation velocity's Nusselt number	Dimensionless
$Nu_{25\ °C \rightarrow 50\ °C\ milk-50rpm}$	When the milk temperature from 25°C increase to 50°C, at 50 rpm rotation velocity's Nusselt number	Dimensionless
$Nu_{50\ °C \rightarrow 70\ °C\ milk-25rpm}$	When the milk temperature from 50°C increase to 70°C,	Dimensionless

	at 25 rpm rotation velocity's Nusselt number	
$Nu_{50\ °C \rightarrow 70\ °C\ milk-50rpm}$	When the milk temperature from 50°C increase to 70°C, at 50 rpm rotation velocity's Nusselt number	Dimensionless
$Nu_{water\ 65°C}$	65°C heating water in the bioreactor's jacket's Nusselt number	Dimensionless
$Nu_{water\ 69°C}$	69°C heating water in the bioreactor's jacket's Nusselt number	Dimensionless
$Nu_{water\ 80°C}$	80°C heating water in the bioreactor's jacket's Nusselt number	Dimensionless
$Nu_{water\ 85°C}$	85°C heating water in the bioreactor's jacket's Nusselt number	Dimensionless
P	Power requirements	W
Pr	Prandtl number	Dimensionless
$Pr_{milk\ 37.5°C}$	Milk average temperature 37.5°C in the bioreactor's Prandtl number	Dimensionless
$Pr_{milk\ 60°C}$	Milk average temperature 60°C in the bioreactor's Prandtl number	Dimensionless
$Pr_{water\ 65°C}$	65°C heating water in the bioreactor's jacket's Prandtl number	Dimensionless
$Pr_{water\ 69°C}$	69°C heating water in the bioreactor's jacket's Prandtl number	Dimensionless
$Pr_{water\ 80°C}$	80°C heating water in the	Dimensionless

	bioreactor's jacket's Prandtl number	
$Pr_{water\ 85°C}$	85°C heating water in the bioreactor's jacket's Prandtl number	Dimensionless
Pe	Peclet number	Dimensionless
ρ	density	Kg/ m^3
$\rho_{milk\ 37.5°C}$	Milk density at average temperature 37.5°C	Kg/ m^3
$\rho_{milk\ 60°C}$	Milk density at average temperature 60°C	Kg/ m^3
$\rho_{water\ 65°C}$	Water density at 65°C	Kg/ m^3
$\rho_{water\ 69°C}$	Water density at 69°C	Kg/ m^3
$\rho_{water\ 80°C}$	Water density at 80°C	Kg/ m^3
$\rho_{water\ 85°C}$	Water density at 85°C	Kg/ m^3
Q	Heat requirement	J
$Q_{25\ °C \rightarrow 50\ °C\ milk}$	Heat requirement of the milk temperature from 25°C increase to 50°C	J
$Q_{50\ °C \rightarrow 70\ °C\ milk}$	Heat requirement of the milk temperature from 50°C increase to 70°C	J
q	Heat flow	W
$q_{25\ °C \rightarrow 50\ °C\ milk}$	Heat flow requirement of the milk temperature from 25°C increase to 50°C	W
$q_{50\ °C \rightarrow 70\ °C\ milk}$	Heat flow requirement of the milk temperature from 50°C increase to 70°C	W
Re	Reynolds number	Dimensionless
Re_i	Impeller Reynolds number	Dimensionless
$Re_{i\ -25rpm\ 37.5°C}$	Impeller Reynolds number	Dimensionless

	when the impeller rotation velocity is 25 rpm, milk average temperature is 37.5°C	
$Re_{i\ -50rpm\ 37.5°C}$	Impeller Reynolds number when the impeller rotation velocity is 50 rpm, milk average temperature is 37.5°C	Dimensionless
$Re_{i\ -25rpm\ 60°C}$	Impeller Reynolds number when the impeller rotation velocity is 25 rpm, milk average temperature is 60°C	Dimensionless
$Re_{i\ -50rpm\ 60°C}$	Impeller Reynolds number when the impeller rotation velocity is 50 rpm, milk average temperature is 60°C	Dimensionless
Re_j	Heating water in the bioreactor's jacket's Reynolds number	Dimensionless
$Re_{jacket\ water\ 65°C}$	65°C heating water in the bioreactor's jacket's Reynolds number	Dimensionless
$Re_{jacket\ water\ 69°C}$	69°C heating water in the bioreactor's jacket's Reynolds number	Dimensionless
$Re_{jacket\ water\ 80°C}$	80°C heating water in the bioreactor's jacket's Reynolds number	Dimensionless
$Re_{jacket\ water\ 85°C}$	85°C heating water in the bioreactor's jacket's Reynolds number	Dimensionless
S	Heat transfer area	m^2

Sc	Schmidt number	Dimensionless
t	Heating time	s
μ	Dynamic viscosity	Pa*s
$\mu_{water\ 65°C}$	65°C water's dynamic viscosity	Pa*s
$\mu_{water\ 69°C}$	69°C water's dynamic viscosity	Pa*s
$\mu_{water\ 80°C}$	80°C water's dynamic viscosity	Pa*s
$\mu_{water\ 85°C}$	85°C water's dynamic viscosity	Pa*s
$\mu_{milk\ 37.5°C}$	Average 37.5°C milk's dynamic viscosity	Pa*s
$\mu_{milk\ 60°C}$	Average 60°C water's dynamic viscosity	Pa*s
U	Overall heat transfer coefficient	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$U_{25\ °C \rightarrow 50\ °C\ 25rpm}$	Overall heat transfer coefficient when impeller rotation velocity is 25 rpm and the milk temperature from 25°C increase to 50°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$U_{25\ °C \rightarrow 50\ °C\ 50rpm}$	Overall heat transfer coefficient when impeller rotation velocity is 50 rpm and the milk temperature from 25°C increase to 50°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$U_{50\ °C \rightarrow 70\ °C\ 25rpm}$	Overall heat transfer coefficient when impeller rotation velocity is 25 rpm and the milk temperature from 50°C increase to 70°C	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-1}$
$U_{50\ °C \rightarrow 70\ °C\ 50rpm}$	Overall heat transfer	$W*m^{-2}*K^{-1}$ / $W*m^{-2}*°C^{-}$

	coefficient when impeller rotation velocity is 50 rpm and the milk temperature from 50°C increase to 70°C	^{1}
V_{milk}	Milk volume in the bioreactor	m^3
X	mass diffusion coefficient	m^2*s^{-1}
λ	Thermal conductivity	$W*m^{-1}*K^{-1}$ / $W*m^{-1}*°C^{-1}$
$\lambda_{water\ 65°C}$	65°C water's thermal conductivity	$W*m^{-1}*K^{-1}$ / $W*m^{-1}*°C^{-1}$
$\lambda_{water\ 69°C}$	69°C water's thermal conductivity	$W*m^{-1}*K^{-1}$ / $W*m^{-1}*°C^{-1}$
$\lambda_{water\ 80°C}$	80°C water's thermal conductivity	$W*m^{-1}*K^{-1}$ / $W*m^{-1}*°C^{-1}$
$\lambda_{water\ 85°C}$	85°C water's thermal conductivity	$W*m^{-1}*K^{-1}$ / $W*m^{-1}*°C^{-1}$
$\lambda_{millk\ 37.5°C}$	Average 37.5°C milk's thermal conductivity	$W*m^{-1}*K^{-1}$ / $W*m^{-1}*°C^{-1}$
$\lambda_{milk60°C}$	Average 60°C milk's thermal conductivity	$W*m^{-1}*K^{-1}$ / $W*m^{-1}*°C^{-1}$
λ_{steel}	Steel thermal conductivity	$W*m^{-1}*K^{-1}$ / $W*m^{-1}*°C^{-1}$

8 References

Abdisa, K.B. *et al.* (2024): Metabolic Syndrome and Biotherapeutic Activity of Dairy (Cow and Buffalo) Milk Proteins and Peptides: Fast Food-Induced Obesity Perspective—A Narrative Review, *Biomolecules*. Multidisciplinary Digital Publishing Institute (MDPI). Available at: https://doi.org/10.3390/biom14040478.

Al-Maqdi, K.A. *et al.* (2021): Challenges and recent advances in enzyme-mediated wastewater remediation—a review, *Nanomaterials*. MDPI. Available at: https://doi.org/10.3390/nano11113124.

de Almeida Kotchetkoff, E.C. *et al.* (2022): Cow's milk allergy immunoglobulin E-mediated: intake of proteins and amino acids, *Revista da Associacao Medica Brasileira*, 68(8), pp. 1027–1032. Available at: https://doi.org/10.1590/1806-9282.20220080.

Amador-Espejo, G.G. *et al.* (2014): Effect of moderate inlet temperatures in ultra-high-pressure homogenization treatments on physicochemical and sensory characteristics of milk, *Journal of Dairy Science*, 97(2), pp. 659–671. Available at: https://doi.org/10.3168/jds.2013-7245.

Amatayakul, T., Sherkat, F. and Shah, N.P. (2006): Syneresis in set yogurt as affected by EPS starter cultures and levels of solids, *International Journal of dairy technology*, 59(3), pp. 216–221.

Anema, S. (2021): Heat-induced changes in caseins and casein micelles, including interactions with denatured whey proteins, *International Dairy Journal*, 122, p. 105136. Available at: https://doi.org/10.1016/j.idairyj.2021.105136.

Aydogdu, T. *et al.* (2021): The influence of milk minerals and lactose on heat stability and age-thickening of milk protein concentrate systems, *International Dairy Journal*, 118, p. 105037. Available at: https://doi.org/https://doi.org/10.1016/j.idairyj.2021.105037.

Bintsis, T. and Papademas, P. (2022): The Evolution of Fermented Milks, from Artisanal to Industrial Products: A Critical Review, *Fermentation*, 8, p. 679. Available at: https://doi.org/10.3390/fermentation8120679.

Brepols, C. *et al.* (2008): Strategies for chemical cleaning in large scale membrane bioreactors, *Water Science and Technology*, 57(3), pp. 457–463.

Calcinai, L. *et al.* (2022): Effectiveness of enzymatic hydrolysis for reducing the allergenic potential of legume by-products, *Scientific Reports*, 12(1). Available at: https://doi.org/10.1038/s41598-022-21296-z.

Cheilytko, A., Schwarzbözl, P. and Broeske, R.T. (2024): Analytical Determination of Nusselt Numbers for Convective Heat Transfer Coefficients in Channel Macroporous Absorbers, *Materials*, 17(11). Available at: https://doi.org/10.3390/ma17112738.

Chen, L. *et al.* (2022): Dairy Milk Casein and Whey Proteins Differentially Alter the Postprandial Lipidome in Persons with Prediabetes: A Comparative Lipidomics Study, *Journal of Agricultural and Food Chemistry*, 70(33), pp. 10209–10220. Available at: https://doi.org/10.1021/acs.jafc.2c03662.

Creamer, L.K., Loveday, S.M. and Sawyer, L. (2011): Milk Proteins | β-Lactoglobulin, in J.W. Fuquay (ed.) *Encyclopedia of Dairy Sciences (Second Edition)*. San Diego: Academic Press, pp. 787–794. Available at: https://doi.org/https://doi.org/10.1016/B978-0-12-374407-4.00433-7.

Čurlej, J. *et al.* (2022): The Effect of Heat Treatment on Cow's Milk Protein Profiles, *Foods*, 11(7). Available at: https://doi.org/10.3390/foods11071023.

Delbridge, J.N. *et al.* (2023): Power, mixing and flow dynamics of the novel Allegro™ stirred tank reactor, *Chemical Engineering Science*, 271, p. 118545. Available at: https://doi.org/10.1016/J.CES.2023.118545.

Dong, G. *et al.* (2024): Non-Thermal Processing Technologies for Allergen Control in Alternative Protein Sources for Food Industry Applications, *Food Engineering Reviews* [Preprint]. Available at: https://doi.org/10.1007/s12393-024-09378-2.

Doran, P.M. (2013): Fluid Flow, *Bioprocess Engineering Principles*, pp. 201–254. Available at: https://doi.org/10.1016/B978-0-12-220851-5.00007-1.

Du, K. *et al.* (2025): Numerical and experimental investigation of film cooling effectiveness distribution predictions that considers the effects of the turbulent Schmidt number, *International Journal of Heat and Mass Transfer*, 236, p. 126294. Available at: https://doi.org/10.1016/J.IJHEATMASSTRANSFER.2024.126294.

Fakheri, A. (2003): A General Expression for the Determination of the Log Mean Temperature Correction Factor for Shell and Tube Heat Exchangers, *Journal of Heat*

Transfer-transactions of The Asme - J HEAT TRANSFER, 125. Available at: https://doi.org/10.1115/1.1571078.

Fiocchi, A. *et al.* (2010): *World Allergy Organization (WAO) Diagnosis and Rationale for Action against Cow's Milk Allergy (DRACMA) Guidelines Revision Panel*.

Fisher, M. (2006): *A Stirred-Tank Bioreactor Delivered in Eight Weeks and One Hour*.

fundamentals-of-heat-and-mass-transfer-6th-edition (no date), pp. 11–33.

Ge, X., Vasco-Correa, J. and Li, Y. (2017): 13 - Solid-State Fermentation Bioreactors and Fundamentals, in C. Larroche et al. (eds) *Current Developments in Biotechnology and Bioengineering*. Elsevier, pp. 381–402. Available at: https://doi.org/https://doi.org/10.1016/B978-0-444-63663-8.00013-6.

Gogate, P., Beenackers, A. and Pandit, A. (2000): Multiple-Impeller Systems With a Special Emphasis on Bioreactors: A Critical Review, *Biochemical Engineering Journal*, 6, pp. 109–144. Available at: https://doi.org/10.1016/S1369-703X(00)00081-4.

Gogate, P.R., Beenackers, A.A.C.M. and Pandit, A.B. (2000): *Multiple-impeller systems with a special emphasis on bioreactors: a critical review*, *Biochemical Engineering Journal*.

Gopalakrishnan, B., Khanna, N. and Das, D. (2019): Dark-Fermentative Biohydrogen Production, *Biomass, Biofuels, Biochemicals: Biohydrogen, Second Edition*, pp. 79–122. Available at: https://doi.org/10.1016/B978-0-444-64203-5.00004-6.

Gorissen, S.H.M. *et al.* (2018: Protein content and amino acid composition of commercially available plant-based protein isolates, *Amino Acids*, 50(12), pp. 1685–1695. Available at: https://doi.org/10.1007/s00726-018-2640-5.

Guinee, T.P., O'kennedy, B.T. and Kelly, P.M. (2006): Effect of milk protein standardization using different methods on the composition and yields of Cheddar cheese, *Journal of Dairy Science*, 89(2), pp. 468–482.

Halabi, A. *et al.* (2020): Structural characterization of heat-induced protein aggregates in model infant milk formulas, *Food Hydrocolloids*, 107, p. 105928. Available at: https://doi.org/https://doi.org/10.1016/j.foodhyd.2020.105928.

Henriques, M.H.F. *et al.* (2013): Effects of liquid whey protein concentrate on

functional and sensorial properties of set yogurts and fresh cheese, *Food and Bioprocess Technology*, 6, pp. 952–963.

Hoffman, J.R. and Falvo, M.J. (2004): *PROTEIN-WHICH IS BEST?*, ©*Journal of Sports Science and Medicine*. Las. Available at: http://www.jssm.org.

Holland, F.A. and Bragg, R. (1995): Flow of incompressible Newtonian fluids in pipes and channels, *Fluid Flow for Chemical Engineers*, pp. 70–95. Available at: https://doi.org/10.1016/B978-034061058-9.50004-9.

Iorhemen, O.T., Hamza, R.A. and Tay, J.H. (2016): Membrane bioreactor (Mbr) technology for wastewater treatment and reclamation: Membrane fouling, *Membranes*. MDPI AG. Available at: https://doi.org/10.3390/membranes6020033.

Jang, H.J., Lee, N.K. and Paik, H.D. (2024): Overview of Dairy-based Products with Probiotics: Fermented or Non-fermented Milk Drink, *Food Science of Animal Resources*. Korean Society for Food Science of Animal Resources, pp. 255–268. Available at: https://doi.org/10.5851/KOSFA.2023.E83.

Joo, D.S. *et al.* (2025): Numerical study on Prandtl number dependence of thermal convection in an internally heated pool, *International Journal of Heat and Mass Transfer*, 236, p. 126251. Available at: https://doi.org/10.1016/J.IJHEATMASSTRANSFER.2024.126251.

Koirala, P. *et al.* (2023): Dairy Milk Protein–Derived Bioactive Peptides: Avengers Against Metabolic Syndrome, *Current Nutrition Reports*. Springer, pp. 308–326. Available at: https://doi.org/10.1007/s13668-023-00472-1.

Kopp, J. *et al.* (2020): Repetitive Fed-Batch: A Promising Process Mode for Biomanufacturing With E. coli, *Frontiers in Bioengineering and Biotechnology*, 8, p. 573607. Available at: https://doi.org/10.3389/fbioe.2020.573607.

Krishania, M. *et al.* (2017): Design of Bioreactors in Solid-State Fermentation, *Current Developments in Biotechnology and Bioengineering: Current Advances in Solid-State Fermentation*, pp. 83–96. Available at: https://doi.org/10.1016/B978-0-444-63990-5.00005-0.

Kumar, V. *et al.* (2021): Recent developments on solid-state fermentation for production of microbial secondary metabolites: Challenges and solutions, *Bioresource Technology*,

323. Available at: https://doi.org/10.1016/j.biortech.2020.124566.

Kurniawan, T. *et al.* (2018): Semi-continuous reverse membrane bioreactor in two-stage anaerobic digestion of citruswaste, *Materials*, 11(8). Available at: https://doi.org/10.3390/ma11081341.

Li, Y., Zhang, L. and Wang, W. (2012): Formation of aldehyde and ketone compounds during production and storage of milk powder, *Molecules*, 17(8), pp. 9900–9911. Available at: https://doi.org/10.3390/molecules17089900.

Lienhard, J.H.. (2001): *A heat transfer textbook*. Phlogiston Press.

Liu, Y., Aimutis, W.R. and Drake, M.A. (2024): Dairy, Plant, and Novel Proteins: Scientific and Technological Aspects, *Foods*. Multidisciplinary Digital Publishing Institute (MDPI). Available at: https://doi.org/10.3390/foods13071010.

Marriott, B.M.. (1993): *Nutritional needs in hot environments : applications for military personnel in field operations*. National Academy Press.

El Mecherfi, K.E. *et al.* (2019): Combined microwave processing and enzymatic proteolysis of bovine whey proteins: the impact on bovine β-lactoglobulin allergenicity, *Journal of Food Science and Technology*, 56(1), pp. 177–186. Available at: https://doi.org/10.1007/s13197-018-3471-9.

Meena, G.S. *et al.* (2017): Milk protein concentrates: opportunities and challenges, *Journal of food science and technology*, 54, pp. 3010–3024.

Milessi, T.S. *et al.* (2022): Improvement of functional properties of cow's milk peptides through partial proteins hydrolysis, *Journal of Food Science and Technology*, 59(11), pp. 4520–4529. Available at: https://doi.org/10.1007/s13197-022-05533-x.

Nath, A. *et al.* (2020a): Production of liquid milk protein concentrate with antioxidant capacity, angiotensin converting enzyme inhibitory activity, antibacterial activity, and hypoallergenic property by membrane filtration and enzymatic modification of proteins, *Processes*, 8(7). Available at: https://doi.org/10.3390/PR8070871.

Nath, A. *et al.* (2020b): Production of liquid milk protein concentrate with antioxidant capacity, angiotensin converting enzyme inhibitory activity, antibacterial activity, and hypoallergenic property by membrane filtration and enzymatic modification of proteins,

Processes, 8(7). Available at: https://doi.org/10.3390/PR8070871.

Nieto-Taype, M.A. *et al.* (2020): Continuous Cultivation as a Tool Toward the Rational Bioprocess Development With Pichia Pastoris Cell Factory, *Frontiers in Bioengineering and Biotechnology*. Frontiers Media S.A. Available at: https://doi.org/10.3389/fbioe.2020.00632.

Ollivier-Triquet, E. *et al.* (2024): Flow and transport in the vadose zone: On the impact of partial saturation and Peclet number on non-Fickian, pre-asymptotic dispersion, *Advances in Water Resources*, 191, p. 104774. Available at: https://doi.org/10.1016/J.ADVWATRES.2024.104774.

Prado Barragán, L.A. *et al.* (2016): Fermentative Production Methods, *Biotransformation of Agricultural Waste and By-Products: The Food, Feed, Fibre, Fuel (4F) Economy*, pp. 189–217. Available at: https://doi.org/10.1016/B978-0-12-803622-8.00007-0.

Pratelli, G. *et al.* (2024): Cow's Milk: A Benefit for Human Health? Omics Tools and Precision Nutrition for Lactose Intolerance Management, *Nutrients*. Multidisciplinary Digital Publishing Institute (MDPI). Available at: https://doi.org/10.3390/nu16020320.

Rahimie, M. *et al.* (2021): *Graphing Behaviour of Heat Transfer In Terms of Nusselt and Reynolds*, *Journal of Computing Research and Innovation (JCRINN)*. Available at: https://jcrinn.com:eISSN:2600-8793.

Raies, M. *et al.* (2014): *IgE and IgG cross reactivity between cow and buffalo milk proteins in Swiss albino mice model*. Available at: https://www.researchgate.net/publication/239526593.

Regonesi, G. (2023a): *BIOREACTORS : A Complete Review*. Available at: https://doi.org/10.13140/RG.2.2.11630.79685.

Regonesi, G. (2023b): *BIOREACTORS : A Complete Review*. Available at: https://doi.org/10.13140/RG.2.2.11630.79685.

Rehman, S.U. *et al.* (2003): Effects of standardization of whole milk with dry milk protein concentrate on the yield and ripening of reduced-fat Cheddar cheese, *Journal of dairy science*, 86(5), pp. 1608–1615.

Rong, S. *et al.* (2021): Effects of impeller geometry on the 11α-hydroxylation of canrenone in rushton turbine-stirred tanks, *Journal of Microbiology and Biotechnology*, 31(6), pp. 890–901. Available at: https://doi.org/10.4014/jmb.2104.04002.

Sadiq, U., Gill, H. and Chandrapala, J. (2021): Casein micelles as an emerging delivery system for bioactive food components, *Foods*. MDPI AG. Available at: https://doi.org/10.3390/foods10081965.

Schuck, P. *et al.* (2016): Recent advances in spray drying relevant to the dairy industry: A comprehensive critical review, *Drying Technology*, 34(15), pp. 1773–1790.

Seong, Y.S., Dong, H.L. and Sang, D.K. (2006): Effect of uniformity of gas distribution on fluidization characteristics in conical gas fluidized beds, *Studies in Surface Science and Catalysis*, 159, pp. 557–559. Available at: https://doi.org/10.1016/S0167-2991(06)81657-5.

Shakeel-ur-Rehman, S.-R. *et al.* (2003): Effects of standardization of whole milk with dry milk protein concentrate on the yield and ripening of reduced-fat cheddar cheese.

Shriver, S. and Yang, W. (2011): Thermal and Nonthermal Methods for Food Allergen Control, *Food Eng. Rev.*, 3, pp. 26–43. Available at: https://doi.org/10.1007/s12393-011-9033-9.

Steynberg, A.P. *et al.* (2004): Fischer-Tropsch reactors, *Studies in Surface Science and Catalysis*, 152, pp. 64–195. Available at: https://doi.org/10.1016/s0167-2991(04)80459-2.

St-Onge, M.-P., Farnworth, E.R. and Jones, P.J.H. (2000): Consumption of fermented and nonfermented dairy products: effects on cholesterol concentrations and metabolism, *The American journal of clinical nutrition*, 71(3), pp. 674–681.

Tang, R. *et al.* (2022): Four clinical phenotypes of cow's milk protein allergy based on dairy product specific IgE antibody types in North China, *Frontiers in Immunology*, 13. Available at: https://doi.org/10.3389/fimmu.2022.949629.

Thangaraj, K. and Joshi, J. (2006): Effect of Impeller Design on Flow Pattern and Mixing in Stirred Tanks, *Chemical Engineering Journal*, 115, pp. 173–193. Available at: https://doi.org/10.1016/j.cej.2005.10.002.

Thangaraj, K., Nere, N. and Joshi, J. (2005): Effect of Internals on Flow Pattern and Mixing in Stirred Tanks, *Industrial & Engineering Chemistry Research - IND ENG CHEM RES*, 44. Available at: https://doi.org/10.1021/ie0503848.

Trivedi, M. V, Laurence, J.S. and Siahaan, T.J. (no date) *The role of thiols and disulfides in protein chemical and physical stability*.

Troise, A.D. *et al.* (2016): Evolution of protein bound Maillard reaction end-products and free Amadori compounds in low lactose milk in presence of fructosamine oxidase I, *Food Chemistry*, 212, pp. 722–729. Available at: https://doi.org/https://doi.org/10.1016/j.foodchem.2016.06.037.

Tutwiler, S.A., Shaver, D.R. and Carasik, L.B. (2024): Influence of cross-sectional aspect ratio and Prandtl numbers on pressure drop and heat transfer characteristics in twisted elliptical tube bundles, *International Journal of Heat and Fluid Flow*, 109, p. 109494. Available at: https://doi.org/10.1016/J.IJHEATFLUIDFLOW.2024.109494.

Vikrant, K. *et al.* (2018): Recent advancements in bioremediation of dye: Current status and challenges, *Bioresource Technology*, 253, pp. 355–367. Available at: https://doi.org/https://doi.org/10.1016/j.biortech.2018.01.029.

Wang, L., Zhou, Y. and Chen, Z. (2020): Investigation of Heat Transfer Efficiency of Improved Intermig Impellers in a Stirred Tank Equipped with Vertical Tubes, *International Journal of Chemical Reactor Engineering*, 18. Available at: https://doi.org/10.1515/ijcre-2019-0196.

Wang, S.-J. and Zhong, J.-J. (2007): Chapter 6 - Bioreactor Engineering, in S.-T. Yang (ed.) *Bioprocessing for Value-Added Products from Renewable Resources*. Amsterdam: Elsevier, pp. 131–161. Available at: https://doi.org/https://doi.org/10.1016/B978-044452114-9/50007-4.

Wang, Y. *et al.* (2024): The Impact of Thermal Treatment Intensity on Proteins, Fatty Acids, Macro/Micro-Nutrients, Flavor, and Heating Markers of Milk—A Comprehensive Review, *International Journal of Molecular Sciences*. Multidisciplinary Digital Publishing Institute (MDPI). Available at: https://doi.org/10.3390/ijms25168670.

Wang, Z. *et al.* (2014): Membrane cleaning in membrane bioreactors: A review, *Journal*

of Membrane Science, 468, pp. 276–307. Available at: https://doi.org/10.1016/J.MEMSCI.2014.05.060.

Wolz, M. and Kulozik, U. (2015): Thermal denaturation kinetics of whey proteins at high protein concentrations, *International Dairy Journal*, 49, pp. 95–101. Available at: https://doi.org/https://doi.org/10.1016/j.idairyj.2015.05.008.

Zheng, T. and Ji, T. (2011): Equivalent representations of beams with periodically variable cross-sections, *Engineering Structures*, 33(3), pp. 706–719. Available at: https://doi.org/https://doi.org/10.1016/j.engstruct.2010.11.007.

9 List of Tables and Figures

Tables

Figures

Acknowledgment

I would like to express my heartfelt gratitude to my BSc thesis supervisors, Dr.-Habil Arijit Nath (Senior Research Member), Prof. András Koris (Professor), and Máté András Molnár (Assistant lecturer) for their invaluable support and guidance. My sincere appreciation goes to the faculty members of the Department of Animal Product and Food Preservation Technology at the Institute of Food Science and Technology, Budai Campus, Hungary, for their encouragement and assistance. I would like to extend my warmest thanks to my parents, whose unwavering support, love, and encouragement have been my foundation throughout my studies. My appreciation also goes to my classmates and friends, who have been wonderful companions on this academic journey. Additionally, I would like to acknowledge the administrative staffs who have been immensely helpful in providing technical supports.

DECLARATION

on authenticity and public assess of final thesis

Student's name:	Sheng Hongfei
Student's Neptun ID:	Y3B5XE
Title of the document:	Studies on hydrodynamics and process heat transfer of bioreactors
Year of publication:	2024
Department:	Food Process Engineering

I declare that the submitted final thesis is my own, original individual creation. Any parts taken from an another author's work are clearly marked, and listed in the table of contents.

If the statements above are not true, I acknowledge that the Final examination board excludes me from participation in the final exam, and I am only allowed to take final exam if I submit another final thesis.

Viewing and printing my submitted work in a PDF format is permitted. However, the modification of my submitted work shall not be permitted.

I acknowledge that the rules on Intellectual Property Management of Hungarian University of Agriculture and Life Sciences shall apply to my work as an intellectulal property.

I acknowledge that the electric version of my work is uploaded to the repository sytem of the Hungarian University of Agriculture and Life Sciences.

Place and date: 2024 November 5th

Sheng Hongfei

Student's signature

DECLARATION

Sheng Hongfei (student Neptun code: Y3B5XE) as a consultant, I declare that I have reviewed the final thesis and that I have informed the student of the requirements, legal and ethical rules for the correct handling of literary sources.

I **recommend / do not recommend** the final thesis to be defended in the final examination.

The thesis contains a state or official secret: yes no

Date: Budapest, 2024. November 5th

Dr. habil. Arijit Nath
Internal supervisor

Molnár Máté András
Internal supervisor

Dr. habil. Koris András
Internal supervisor