During the course of fermentation, heat is produced by cellular metabolism and growth. The heat comes from energy released by chemical reactions within the cells during metabolism, and it increases the temperature of the fermentation broth. Unless the heat of reaction (metabolic heat) is removed, the broth temperature increases beyond optimal reactor conditions for the maintenance of viable cells. Another source of heat into the fermentation broth is mechanical agitation. For successful fermentation, the optimal temperature must be maintained by cooling the reactor contents.

An engineering methodology is introduced here that describes the capacity of a jacketed, stirred bioreactor to remove heat during fermentation. That methodology is then used to quantify the cooling capacity of fermentors with working volumes ranging from 3000 to 15,000 liters.

**Equation 1** provides a starting point for establishing metabolic cooling capacity for a fermentation bioreactor. $Q$ (Btu/h) is the amount of heat that must be removed from the fermentation broth. Typically, $Q$ would include both the heat generated at the peak metabolic rate of the microorganisms and the heat input to the broth by agitation. $U$ is the overall heat transfer coefficient in Btu per ft$^2$ per hour per degree Fahrenheit. It essentially describes the rate at which heat can be removed by the fermentor’s cooling system. $A$ is the heat transfer area in ft$^2$, defining the contact surface area between the fermentation liquid and all heat transfer areas such as the side walls (with a cooling jacket) or internally submerged cooling coils.

$\Delta T$ is the driving force for heat transfer, and it establishes the temperature difference between the fermentation liquid and the cooling fluid inside the jacket or coil. For the metabolic cooling case, a log mean temperature difference (LMTD) is typically used with the fermentation liquid temperature ($T_f$) being held constant. The cooling fluid inlet ($T_{ji}$) and outlet temperatures ($T_{jo}$) are used to determine the difference, as shown in Equation 2.

The overall heat transfer coefficient ($U$) must be determined for each specific heat transfer system used taking into account fluid physical properties, fluid dynamics, and the geometry of the system. For example, a separate $U$ must be calculated for both the jacket and the internal coil because of differences in their geometry and flow rates. Calculation of $U$ is based on the film theory (Figure 1), which

---

**PRODUCT:** LARGE-SCALE FERMENTED PRODUCTS  
**PROCESS FOCUS:** PRODUCTION  
**WHO SHOULD READ:** PROCESS ENGINEERS, MANUFACTURING  
**KEYWORDS:** FERMENTATION, HEAT TRANSFER, PROCESS CONTROL  
**LEVEL:** BASIC
accounts for the various resistances in the heat transfer path.

The film theory assumes that a liquid film exists on both sides of the wall through which heat transfer is occurring and that such liquid films provide a resistance to heat transfer. Fouling or scale deposits on either side of the wall provide additional resistance. Finally, the wall itself provides some resistance to heat transfer. The theory allows calculation of the overall heat transfer coefficient using Equation 3.

In that equation, \( h_f \) and \( h_c \) are the liquid film heat transfer coefficients on the fermentation liquid side and the coolant side, respectively. The variables \( f_f \) and \( f_c \) refer to fouling factors due to scale buildup on the respective sides. \( K \) is the thermal conductivity of the wall and \( l \) is the thickness of the vessel wall (in the case of jacket heat transfer). For an internal coil, \( l \) would be the thickness of the coil wall.

The values for fouling coefficients \( f_f \) and \( f_c \) are typically not calculated. They are instead established based on published data or previous experience. For example, distilled water may have a fouling coefficient of 2000 Btu/ft² h °F, and hard water may have a fouling coefficient of 300 Btu/ft² h °F. Similarly, organic heat transfer media may have a fouling coefficient of 1000 Btu/ft² h °F, and vegetable oil may have a coefficient as low as 300 Btu/ft² h °F.

Film heat transfer coefficients \( h_f \) and \( h_c \) are calculated using empirical correlations involving fluid properties and system geometry. Correlations of dimensionless numbers are available for stirred tanks with jackets and stirred tanks with helical coils inside them. For any given system, the correlations take the form seen in Equation 4.

\[
E, a, b, \text{ and } c \text{ are constants from Table 1. } \\
\text{Nu is the Nusselt number. } \\
\text{Re is the Reynolds number and Pr is the Prandtl number. } \\
The \mu \text{ represents the viscosity of the bulk fluid, and }\mu_w \text{ is the viscosity of fluid at the wall. } \\
The Nusselt number includes the film heat transfer coefficient (h), as given in Equation 5.
\]

In that equation, \( K \) represents the thermal conductivity of the fluid (either the fermentation broth or the coolant). For a stirred tank fermentor, \( D \) is the inner diameter of the tank. For a jacketed fermentor, \( D \) represents the equivalent diameter of the coolant flow area. For an internal coil design, \( D \) would be the inner diameter of the coil.

Similarly, \( \text{Re} \) in Equation 4 is separately defined for the tank, the jacket, and the coil. If the tank has an agitator, the amount of mixing (or the level of turbulence) is described by the Reynolds number given by Equation 6.

\[
\text{In that equation, } N \text{ represents the rotational speed of the agitator or impeller, and } d \text{ is the diameter of the impeller. The density of fluid in the vessel is expressed by } \rho, \text{ and the viscosity of the fluid is expressed by } \mu. \text{ For both the jacket and the coil, the Reynolds number is calculated by using Equation 7.}
\]

\[
\text{In that equation, } D \text{ represents the equivalent flow diameter of the jacket or the inner diameter of the coil; and } V \text{ is the fluid (coolant) velocity.}
\]

The \( \text{Pr} \) in Equation 4, comes from Equation 8 and includes the heat capacity \( (C_p) \), viscosity, and thermal conductivity of the fluid.

Table 1 lists the constants for use in Equation 4 for stirred tanks,
jackets on tanks, and helical coils inside tanks. The constants for stirred tanks are appropriate for standard-geometry tanks containing baffles and a flat-blade turbine agitator (six blades). The jacket constants are appropriate for dimpled jackets and helical coils with turbulent flow inside them.

**FERMENTATION EXAMPLES**

For illustration purposes, fermentation with a metabolic heat load of 40 kcal/L per h is evaluated to determine the fermentor volume at which the jacket will provide insufficient cooling capacity by itself. If the jacket cannot provide sufficient cooling, additional cooling capacity must be added through internal elements such as helical coils or cooling baffles. Fermentors were evaluated with working or liquid volumes of 3000 L, 6000 L, 10,000 L and 15,000 L. Results are summarized in Table 2.

The design heat load shown in Table 2 includes metabolic heat generated, heat load due to the agitator and a safety factor of +10%. To maintain the fermentation broth at its optimum temperature of 30 °C, the heat transfer system must be capable of removing the design heat load. The jacket area column shows the available heat transfer area from the bottom of the tank and the sides of the vessel. The overall heat transfer coefficient was calculated using Equation 3. The last column shows the amount of heat the jacket is capable of removing with a jacket inlet temperature of 1 °C and an outlet temperature of 6 °C. The fermentation liquid temperature was held constant at 30 °C, giving a log mean temperature difference of 26 °C (47.6 °F).

At a working volume of 3000 L, the heat removal capacity of the jacket exceeds the design heat load. At larger volumes, however, the heat removal capacity is insufficient to remove the design load. For the 6000-L working volume, the design load and heat removal capacity are close enough to evaluate alternatives such as increasing jacket coolant flow rate and/or decreasing jacket outlet temperatures. Small changes in those parameters may preclude the need for internal heat transfer elements. But the 10,000-L and 15,000-L volumes clearly require additional internal heat transfer area to provide sufficient cooling capacity.

**DEFINITIONS AND EXAMPLES**

**Coolants:** Chilled water and glycol (or a glycol mixture) are examples of often-used cooling media.

** Fouling:** Occurs when a heat-transfer surface is adversely affected by the build-up of scale or the effects of corrosive fluids, and so on. Fouling causes less heat to be transferred through the wall of a heat exchanger, thus decreasing its efficiency.

**Nusselt number:** Ratio of the convective thermal resistance to the conductive thermal resistance of a fluid; used in dimensionless correlations describing heat transfer. A Nusselt number indicates the relative ease with which heat can be transferred.

**Prandtl number:** A combination of fluid properties that describes the ratio of diffusivity of momentum to diffusivity of heat; used in dimensionless correlations describing heat transfer. A large Prandtl number would imply greater difficulty in transferring heat.

**Scale deposits:** Deposits (e.g., rust or silt) that gradually build up over time on a heat transfer surface and that can cause fouling.

### Table 2: Comparison of heat removed and design heat load

<table>
<thead>
<tr>
<th>Broth Volume (liters)</th>
<th>Design Heat Load (Btu/h)</th>
<th>Jacket Area (ft²)</th>
<th>Overall HT Coefficient (Btu/ft² h °F)</th>
<th>Heat Removed By Jacket (Btu/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3000</td>
<td>590,000</td>
<td>105</td>
<td>129</td>
<td>640,000</td>
</tr>
<tr>
<td>6000</td>
<td>1,160,000</td>
<td>165</td>
<td>126</td>
<td>990,000</td>
</tr>
<tr>
<td>10,000</td>
<td>1,850,000</td>
<td>230</td>
<td>108</td>
<td>1,180,000</td>
</tr>
<tr>
<td>15,000</td>
<td>2,780,000</td>
<td>300</td>
<td>105</td>
<td>1,500,000</td>
</tr>
</tbody>
</table>

### Table 3: Heat transfer resistances and coefficients in overall $U$

<table>
<thead>
<tr>
<th>Broth Volume (liters)</th>
<th>Overall HT Coefficient (Btu/ft² h °F)</th>
<th>Wall Resistance (Btu/ft² h °F)</th>
<th>Fouling Factors Vessel (Btu/ft² h °F)</th>
<th>Fouling Factors Jacket (Btu/ft² h °F)</th>
<th>Vessel HT Coefficient (Btu/ft² h °F)</th>
<th>Jacket HT Coefficient (Btu/ft² h °F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3000</td>
<td>129</td>
<td>285</td>
<td>2000</td>
<td>1000</td>
<td>794</td>
<td>664</td>
</tr>
<tr>
<td>6000</td>
<td>126</td>
<td>285</td>
<td>2000</td>
<td>1000</td>
<td>740</td>
<td>624</td>
</tr>
<tr>
<td>10,000</td>
<td>108</td>
<td>214</td>
<td>2000</td>
<td>1000</td>
<td>698</td>
<td>611</td>
</tr>
<tr>
<td>15,000</td>
<td>105</td>
<td>214</td>
<td>2000</td>
<td>1000</td>
<td>603</td>
<td>600</td>
</tr>
</tbody>
</table>
The overall heat transfer coefficient for the two large volumes is lower than for the 3000-L and 6000-L volumes. The primary cause for that drop is an increase in the thickness of the vessel wall and a resulting increase in heat transfer resistance. The values making up the overall heat transfer coefficient are shown in Table 3. Vessel and jacket fouling resistances were the same in all four cases. The heat transfer coefficients were calculated using correlations previously described.

**Interpreting the Results**

For fermentation with a metabolic heat generation of 40 kCal/L per hour, it was determined that reactors with working volumes greater than 6000 L would be likely to require internal cooling elements. The decrease in cooling capacity as reactor volume increases is exhibited by a decrease in overall heat transfer coefficients. A decrease in overall heat transfer coefficients is due to thicker vessel walls and decreasing heat transfer coefficients in the vessel and the jacket.

**For Further Reading**


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