Energy integration in antibiotic production using heat storage tanks

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Abstract
In this study the problem of reduction of energy consumption in bioreactors system of antibiotics production by means of energy integration is considered. An energy integration scheme with two heat storage tanks ensuring the system operation at different time intervals is proposed. An approach for processes management of energy integration is developed. The problem is formulated in the terms of MINLP. The efficiency of proposed approach is illustrated on the example of the industry.

Key words: Heat integration, Batch reactors, Heat storages, Antibiotics

Introduction
The problem of the reduction of energy consumption in operation of the batch reactors and particularly bioreactors is highly topical nowadays. It refers most directly to the pharmaceutical industry. Many of its production systems use batch reactors in order to perform basic operations. Reduction of energy consumption in such type of production systems can be achieved by conditions of maximal using of internal energy of the system creation. This can be realized by heat integration of the processes. For this purpose it is needed energy integration scheme development and its suitable management. One of the first studies deals with these problems was the work of Vaselenak, J.A. et al. (1986) [1]. It involves different schemes of heat integration which do not consider the problem of their management. Further B. Ivanov et al. (1993) [2] discusses the problem of heat integration in a pair of batch reactors operating simultaneously (at the same time). They propose a method for synthesis of such type of systems taking into account its time characteristics. This is applied to cases where the heat processes carry out in different time intervals by using heat storages B. Ivanov et al. (1993) [3]. The proposed mathematical models of heat exchange processes use for the purpose of optimal synthesis and renovation. However, the problem of the optimal management leading to energy consumption minimization is not discussed in it. In the work of Ch. Boyadjiev et al. (1996) [4] the problem of optimal control of heat integration processes in a pair of reactors is discussed. In this case, it is assumed that the control actions are in the form of time functions which have difficulties in their realization in practice. Recently there have been developed many approaches dealing with the problem of heat integration using two heat storages which involve the environmental impact consideration without processes management, Majozi T. (2006) [6] and Majozi T. (2009) [7]. In the literature are discussed the problems mainly concerned with analysis, modeling and synthesis of heat exchanger networks, giving opportunity for energy savings through heat integration of the processes in the predefined time interval. It has not paid enough attention to cases where the processes are in different time intervals and the style of management. This refers mostly to the real production systems using heat storages.

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**AIM**

The aim of this study is to propose a method for energy saving of antibiotics production in bioreactor system through heat integration of the processes using heat storages and their management style.

**PROBLEM DESCRIPTION**

Let consider a bioreactors system for production of antibiotics. This production consists of the substrate preparation process, sterilization and cooling until operational temperature of the fermentation process is reached. Both, substrate preparation process and subsequent sterilization use the steam as an energy source. The fermentation process is carried out after cooling the sterilized substrate until operating temperature of 30°C.

This process uses technical and cooling water. The idea for reduction of the energy consumption is in the integration of these two processes. If a given reactor is in cooling mode, the energy released can be stored in heat storages in order to be used later in the substrate preparation process in another reactor. This leads to energy savings in the second reactor, and also to reduction of the used for the processes technical water. The realization of this idea needs development of suitable scheme. They should be defined the control actions providing maximum use of internal energy in both reactors.

On Figure 1 is shown such type of scheme for the processes carrying out. Determination of control actions is limited to the parameters of time intervals. Conditions for processes carrying out should ensure a minimum price of used energy from the external systems.

1. **Process description**

Antibiotic production involves processing tasks realized in the batch reactors. According to technical regulation they have the following sequence and parameters:

**Step 1:** Substrate preparation.
1. This processing task implements through water and substrate mixing in an auxiliary reactor with volume of \(5\text{m}^3\).

**Step 2:** Preparation of the components of the fermentation medium.
1. Mixing of \(V_A = 2\text{m}^3\) component of A with \(V_{2.1} = 10\text{m}^3\) of water at 20°C (\(CW20\)) through stirring until production of substrate \(NMA\) with volume of \(V_{2.1}^* = (V_{2.1} + V_A)\).

Mixing of \(V_B = 2\text{m}^3\) component of B with \(V_{2.2} = 10\text{m}^3\) of water \(CW20\) by stirring until substrate \(NMB\) with volume of \(V_{2.2}^* = (V_{2.2} + V_B)\) is produced.

**Step 3:** Fermentation process.
1. Simultaneous transfer of \(NMA\) in the fermentation reactor and its heating by means of steam from temperature \(T_{3.2} = 20^\circ C\) to temperature \(T_{3.2} = 55^\circ C\).
2. Heating of \(NMA\) by steam from \(T_{3.2} = 55^\circ C\) to \(T_{3.2} = 100^\circ C\).
3. Steam sterilization of \(NMA\) at \(T_{st} = 100^\circ C\) approximately within 0.5 hours.
4. \(NMB\) transfer into the fermentation reactor and mixing with \(NMA\) to produce substrate \(AB\).
5. Addition of \(V_{3.5} = 17\text{m}^3 + 18\text{m}^3\) of technical water \(CW20\) with temperature 20°C in order to produce substrate \(NMB\).
6. Steam heating of \(42\text{m}^3\) \(NMB\) until temperature of \(T_{3.6} = 55^\circ C\).
7. Steam heating of \(NMB\) from \(T_{3.6} = 55^\circ C\) to \(T_{3.6} = T_{st}^* = 120^\circ C\) approximately within 2 hours.
8. Sterilization of \(NMB\) by steam \(T_{9}^* = 120^\circ C\) approximately within 0.5 hours.
9. Cooling of \(NMB\) with water \(CW20\) from \(T_{3.9} = T_{st}^* = 120^\circ C\) until \(T_{3.9} = 45^\circ C\).
10. Cooling of \(NMB\) with \(T_{5} = 5^\circ C\) water \(CW5\) from \(T_{3.10} = 45^\circ C\) until \(T_{3.10} = T_{F Work} = 30^\circ C\) approximately within 0.5 hours.
11. Addition of \(IMX\) to \(NMB\) within 0.75 hours to reach the volume of \(47\text{m}^3\) which represents the substrate \(FM\).
12. Fermentation substrate cools until \(T_{F Work} = 30^\circ C\) using \(CW5\) and the fermentation process continues in the same temperature within 120-150 hours until fermentation product \(FB\) is formed.

**Step 4:** Dilution
1. Transfer of \(FB\) to an intermediate tank approximately within 1 hour.
2. Addition of $V_{\text{Waste}} = 23m^3$ of water CW 20 and deactivation approximately within 1 hour to obtain fermentation product $DFB$.

**Step 5:** Filtration
1. Filtration of the diluted product $DFB$ approximately within 12 hours until concentrated raw material $DSC$ is produced.

**Step 6:** Sterilization of the empty fermenter reactor.
1. Rinsing of the empty fermenter reactor using water CW 20.
2. Sterilization of the reactor using steam at $130^\circ C$ approximately within 2 hours.

**2. Description of the processes equipment.**
The process is carried out in a plant which involves the following equipment:
8 (preparatory) reactors (with volume) of $5/8m^3$ for the processes 1.1
3 reactors for substrate with volume of $12/16m^3$ for processes 2.1 and 2.2
14 fermentation reactors with volume of $47/63m^3$ for processes 3.1 to 3.11 and 6.1, 6.2.

They are equipped with 3 coil heat exchangers as each of them have length of $100m$, diameter of $57mm$ and thickness of wall of $3.5mm$.

3 tanks with volume $70/100m^3$ for the processes 4.1 and 4.2.

3 filters press with productivity of $70m^3/h$ for the process 5.1

**3. Scheme for heat integration using heat storage tanks.**
According to the technological regulation there are processes requiring the use of energy from the outside for heating and cooling. Reduction of external energy can be realized through suitable scheme of heat integration. The process of "Cooling" in the reactor after sterilization does not coincide in the time interval with the substrate preparation processes for sterilization of another reactor. For this reason the heat integration scheme proposed in the work of Ch. Boyadjiev et al. (1996) [4] cannot be used. It is proposed the use of heat tanks, storing energy in the hot reactor and its further use for the substrate preparation process into the next reactor. It can be used for the dilution process carrying out after the fermentation process is completed. On Figure 1 it is shown the heat integration scheme using two heat storage tanks.

![Figure 1. Flow sheet of heat integration based on heat storage tanks.](image-url)
Hot reactor is fermentation reactor \( F_H \) in which the processes of raw materials loading and sterilization are completed (3.1-3.7). It must be cooled until temperature of 30°С for the fermentation process. The cool reactor is a fermentation reactor \( F_C \) in which the processes of the substrate preparation and her sterilization are realized.

In the proposed scheme the hot reactor \( F_H \) is cooled with water \( CW \) through its serpentine. During to it the output of the serpentine water is stored in a heat storage tank 1. Water stored in this tank will be used in the next time interval for realization of the process 4.2. and should be of function to accumulate water needed for the processes. The second heat storage tank has a shouldn’t be more than this one needed for the processes of the substrate preparation and her sterilization are completed (3.1-3.7). It is assumed that during each one of the four processes mathematical modeling

1. Processes mathematical modeling

It is assumed that during each one of the four processing tasks the cooling will be realized in a time dependence of the flow of cooling water. This assumption allows the use of processes models in the form of ordinary differential equations. These equations describe the processes of heat and mass transfer in the following form:

1. The equation describing the change in temperature of the mixture in the reactor \( F_H \) when crossing the flow \( CW \) or \( CW \) and determining debit is described through equation for each one of the time steps:

\[
\frac{dT_H}{dt} = \left( \frac{\phi_W - 1}{\phi_W} \right) F_H C \left( T_i^m - T_F \right)
\]

where \( T_i^m = x_i T_{W}^{20} + \left( 1 - x_i \right) T_{W}^{5} \),

\( x_i = \{ 0 \lor 1 \} \),

\( \phi_W = \frac{T_{F_i} - T_{i^m}}{T_{F_i} - T_i^*} = \exp \left( \frac{UA}{F_W C \rho_W} \right), \)

\( A \) is heat exchanger surface of the serpentine with dimension \([ m^2 ]\), and \( U \) is overall heat transfer coefficient with dimension \([ kWm^{-2}K^{-1} ]\), \( C_F = C_f \rho_f \) with dimension \([ kJm^{-3}K^{-1} ]\), \( C_f \) and according to \([ kg / m^3 ]\), while \( \rho_f \) is with dimension \([ kg / m^3 ]\). Flow of cooling water through the serpentine is \( F_W \) at time of the i-th time interval and it has a dimension \([ m^3 / s ]\).

2. The temperature at the exit of serpentine for each one of the time steps is determined by the equation:

\[
T_i = \left( \frac{\phi_W - 1}{\phi_W} \right) T_{F_i} + \frac{1}{\phi_W} T_i^m, \quad i \in \{1 + 4\}.
\]

The solution of the equation (1) searches at the start conditions \( T_{F_i}(0) \). It should be taking into account that the temperature of the water coming out of the serpentine \( T_i^* \) must be less than the contents in the fermentor \( T_{F_i} \) i.e. \( T_{F_i} \geq T_i^* \).

3. Equation describing the volumes in the heat storages \( S1, S2, SW \) and the temperatures for each time steps as follows

\[
\frac{dV_{S1}^{i}}{dt} = y_{i}^{S1} F_{W_i}, \quad i \in \{1 + 4\},
\]

\[
C_P W V_{S1}^{i} \frac{dT_{S1}^{i}}{dt} = y_{i}^{S1} F_{W_i} C_P W \left( T_{i}^e - T_{S1}^{i} \right), \quad i \in \{1 + 4\},
\]

with start conditions

\[
V_{S1}^{i}(0) = V_{S1}^{i-1}(t_{i-1}), \quad T_{S1}^{i}(0) = T_{S1}^{i-1}(t_{i-1}) \]

and \( i = 1 \) for the first time interval \( V_{S1}^{i}(0) = 0 \), \( T_{S1}^{i}(0) = T_i^{in} \).

\[
\frac{dV_{S2}^{i}}{dt} = y_{i}^{S2} F_{W_i}, \quad i \in \{1 + 4\},
\]

\[
C_P W V_{S2}^{i} \frac{dT_{S2}^{i}}{dt} = y_{i}^{S2} F_{W_i} C_P W \left( T_{i}^e - T_{S2}^{i} \right), \quad i \in \{1 + 4\},
\]

with start conditions

\[
V_{S2}^{i}(0) = V_{S2}^{i-1}(t_{i-1}), \quad T_{S2}^{i}(0) = T_{S2}^{i-1}(t_{i-1}) \]

and \( i = 1 \) for the first time interval \( V_{S2}^{i}(0) = 0 \), \( T_{S2}^{i}(0) = T_i^{in} \).
\[ \frac{dV_{SW}^i}{dt} = y_{i,SW}^i F_{Wi}, \quad i \in \{1 + 4\}, \]  
\[ C_{Wi} \frac{dV_{SW}^i}{dt} = y_{i,SW}^i F_{Wi} C_{Wi} (T_{SW}^i - T_{SW}^i) \]

with start conditions 
\[ V_{SW}^i(0) = V_{SW}^{i,0}(t_{i-1}), \quad T_{SW}^i(0) = T_{SW}^{i,0}(t_{i-1}) \]

and \( i = 1 \) for the first time interval 
\[ V_{SW}^i(0) = 0, \quad T_{SW}^i(0) = T_{SW}^{i,0}, \quad C_{Wi} = C_{Wi} \] 

with dimension \([k \text{J/m}^{-1} \text{K}^{-1}]\), and \( C_{Wi} \) according to \([k \text{g/m}^{-3}]\), \( y_{i,SW}^1 = \{0 \lor 1\} \), \( y_{i,SW}^2 = \{0 \lor 1\} \), \( y_{i,SW}^3 = \{0 \lor 1\} \) depending on whether the filling in the appropriate heat storage tank in the given time interval is done or not.

4. Equation describing the change in the values of the cooling flow \( F_{Wi} \) with the time.

In the most general case flow through the cooling serpentine can be described by the expression:
\[ F_{Wi} = A_i + (B_i - A_i) \exp(-C_i t), \]

where the values of the coefficients \( A_i, B_i, C_i \) should be determined

At the end of the fourth time interval at the end of the process the parameters in heat storage tanks \( V_{SW}^{s1}, V_{SW}^{s2}, V_{SW}^{s3} \) and \( T_{SW}^{s1}, T_{SW}^{s2}, T_{SW}^{s3} \) are reached.

2. Aims of the heat integration

The purpose of heat integration is using a minimum quantity of resource (steam and cooling water) for carrying out of the processes in both reactors. This can be achieved by providing conditions of the maximum quantity of heat recovery from the cooling reactor. This heat is stored in heat storage and further used in the substrate preparation process in another reactor, and contents \( S2 \) for Stage 4. It should be taken into account the energy used in cooling with water \( CW5 \) too.

The purpose of heat integration can be described by the expression:
\[ Cost_{INT} = \min \{Cost_{\text{steam}}^* + Cost_{\text{WS2}}^* + Cost_{\text{Water}}^*\} \]

where \( Cost_{\text{Water}}^* \) is the price of steam, \( Cost_{\text{WS2}}^* \) is the price of energy \( CW5 \) cooling and \( Cost_{\text{Water}}^* \) price of water used for carrying out the processes in case of heat storage tanks.

These components are determined according to the expressions:
\[ Cost_{\text{steam}}^* = C_{\text{Steam}} \left( CP_{Wi} V_{SW}^{s1} \left( T_{SW}^{s1} - T_{SW}^{s1}\right) \right) \]
\[ Cost_{\text{WS2}}^* = C_{\text{Steam}} \left( CP_{Wi} V_{SW}^{s2} \left( T_{SW}^{s2} - T_{SW}^{s2}\right) \right) \]
\[ Cost_{\text{Water}}^* = C_{\text{Water}} \left( V_{Water}^{s1} - V_{Water}^{s1}\right) + \left( V_{Water}^{s2} - V_{Water}^{s2}\right) + V_{SW}^i \]

3. Control variables

The idea of management of the cooling process consists of determination of the control variables, which provide for minimum quantity of resource for realization of the processes in both the reactors. These variables are:
\[ A_i, B_i, C_i, t_i \], \( \forall i \in \{1, 4\} \).

\[ x_i = \{0 \lor 1\}, \quad y_{i,SW}^{s1} = \{0 \lor 1\}, \quad y_{i,SW}^{s2} = \{0 \lor 1\}, \quad y_{i,SW}^i = \{0 \lor 1\} \]

4. Constraints

Constraints are related to the requirements of the technology for processes duration and the technical constraints of the cooling equipments (serpentine).
\[ \sum_{i=1}^{4} t_i \leq t_f \]
\[ B_i \leq F_{MAX}, \quad \forall i \in \{1, 4\} \]
\[ V_{SW}^{s1} \leq V_{2,1} + V_{2,2} + V_{3,5} \]
\[ V_{SW}^{s2} \leq V_{Water} \]
\[ \sum \left( y_{i,SW}^{s1} + y_{i,SW}^{s2} + y_{i,SW}^i \right) \leq 1 \]
\[ \left( y_{i,SW}^{s1} + y_{i,SW}^{s2} + y_{i,SW}^i \right) = x_i \]
\[ Cost_{\text{INT}} < Cost_{\text{NOINT}} \]

where \( Cost_{\text{NOINT}} \) are the energy costs and water for process realization without heat integration.

5. Formulation of the problem of heat integration management

Management problem consists of determination of variables (12, 13) in which the objective function has a minimum (10) subject to the constraints (14).
Thus formulated problem is in the terms of mixed integer nonlinear programming (MINLP), as for its solution known methods and tools such as, e.g. *GAMS* [5] *Brooke A. et al. (1998)* can be applied.

**MOTIVATING EXAMPLE**

An example in supporting of the procedure. The efficiency of proposed method of heat integration of the processes is illustrated on the example of antibiotics production. This production realizes in batch reactors in the processes sequence described in 2.1.

The processes data are the following:

\[
\begin{align*}
C_{P_{F}} &= C_{P_{W_{5}}} = C_{P_{W_{20}}} = C_{P_{1}} = C_{P_{2}} = \ldots \\
T_{1}(0) &= T_{2}(0) = T_{NBA}(0) = T_{W_{20}} = 20^\circ C, \\
T_{F}(t_f) &= T_{fer} = 30^\circ C, T_{W_{5}} = 5^\circ C, \\
T_{w} &= 100^\circ C, T_{3.1} = 55^\circ C, \\
V_{P} &= V_{N MBA} = 42 m^3, \\
V_{1}(0) &= V_{2}(0) = V_{NBA}(0) = V_{NBB}(0) = 2 m^3, \\
V_{21} &= V_{22} = 10 m^3, V_{3.5} = 18 m^3,
\end{align*}
\]

\[\begin{align*}
F_{5}^{MAX} &= F_{20}^{MAX} = 0.04 m^3/s, V_{N MBA} = 42 m^3, \\
t_f &= 6000 s, U = 1.2 kWm^{-2}K^{-1}, A = 56.55 m^2 \\
C_{Steam} &= (CG_{steam} / 4.184) lv/ GJ, \\
CG_{Steam} &= 277.00 lv/ GCal, \\
C_{W_{5}} &= (CG_{W_{5}} / 4.184) lv/ GJ, \\
CG_{W_{5}} &= 681.00 lv/ GCal.
\end{align*}\]

The scheme of heat integration of the processes is applied and the optimal control parameters are obtained by using FMINCON of MATLAB 6.50.

On Table 1 are listed the optimal values of control variables obtained through optimization procedure application according to the model described in 3.

According to the procedure described in paragraph 5, calculations have been carried out to determine the optimum operating effects \((F_{W_{20}}, F_{W_{5}}, t_{W_{20}}, t_{W_{5}})\) in the case without heat integration of the processes. The task of mathematical programming was performed using MATLAB 6.50. The optimal values of the variables for case without heat integration processes are given in Table 1.

| Table 1. Optimal control variables values of system with two heat storages |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| i | \(t_{in} [\text{sec.}]\) | \(A_i\) | \(B_i\) | \(C_i\) | \(x_i\) | \(y_{S1}^{x}\) | \(y_{S2}^{x}\) | \(y_{SW}^{x}\) | \(T_{S1}^{x}\) | \(T_{F1}(t_i)\) |
| 1 | 1784.8 | 0.0152 | 0.0219 | 1.0686e-4 | 1 | 1 | 0 | 0 | 62.2 | 81.8 |
| 2 | 575.7 | 0.0383 | 0.0400 | 1.0000e-4 | 1 | 0 | 1 | 0 | 62.2 | 71.5 |
| 3 | 1902.3 | 0.0400 | 0.0204 | 0.0100 | 1 | 0 | 0 | 1 | 62.2 | 48.3 |
| 4 | 1737.2 | 0.0400 | 0.0399 | 0.0100 | 0 | 0 | 0 | 0 | 62.2 | 30.0 |

On the Figure 2 are shown the temperatures variation in the reactor and output of the serpentine at different time intervals for the case of heat integration and continuous control variables.

\[V_{NBA} = V_{NBB} = 12 m^3, V_{5}(0) = V_{AB} = 24 m^3,\]

\[F_{5}^{MAX} = F_{20}^{MAX} = 0.04 m^3/s, V_{N MBA} = 42 m^3,\]

\[t_f = 6000 s, U = 1.2 kWm^{-2}K^{-1}, A = 56.55 m^2\]

\[C_{Steam} = (CG_{steam} / 4.184) lv/ GJ,\]

\[CG_{Steam} = 277.00 lv/ GCal,\]

\[C_{W_{5}} = (CG_{W_{5}} / 4.184) lv/ GJ,\]

\[CG_{W_{5}} = 681.00 lv/ GCal.\]
Figure 2. Temperatures variation in the reactor in the case of heat integration system and continuous control variables.

Figure 3. Volumes variation of the heat storage tanks in the time.

In the Figure 3 are shown the volumes of the heat storage tanks over the time.

Figure 4 shows the optimal values of mass rate functions of cooling flow in the time ensuring minimum energy costs during processes "cooling-heating" realization.
Figure 4. Variation the mass rates of cooling liquid media through the serpentine, ensuring minimum energy costs.

The prices of the resources used for heating and cooling processes for the proposed system with two heat storage tanks in optimal management and those ones in system without heat integration are presented in Table 2.

Table 2. Energy costs of system with and without heat integration

<table>
<thead>
<tr>
<th>Type of costs</th>
<th>Costs for the case without heat integration [lv.]</th>
<th>Costs for the case with heat integration [lv.]</th>
<th>Saving %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost_{STEAM}</td>
<td>1168.40</td>
<td>720.84</td>
<td>38.30%</td>
</tr>
<tr>
<td>Cost_{W20}</td>
<td>377.15</td>
<td>161.24</td>
<td>57.24%</td>
</tr>
<tr>
<td>Cost_{W5}</td>
<td>389.89</td>
<td>527.95</td>
<td>-35.40%</td>
</tr>
<tr>
<td>Cost_{SUM}</td>
<td>1935.50</td>
<td>1410.00</td>
<td>27.15%</td>
</tr>
</tbody>
</table>

It is obviously that the optimal management of the heat integration process leads to significant reduction of about 57.24% of water used CW20 of cooling and coolly water CW5 increase by -35.40% respectively. At the same time the steam needed for the processes is reduced of about 38.30%. Use of heat storage tanks doesn’t require a schedule of processes in all reactors to be developed and total energy saving (cooling water and steam) comes to 27.15%.

CONCLUSION
On the base of the obtained results, can be done the following conclusions:
1. A scheme for heat integration with two heat storage tanks is proposed and the problem of optimal management of processes is formulated.
2. The problem of its management is described in terms of the mixed non-linear mathematical programming with optimal criterion of minimal cost of the used resources.
3. Applying heat integration of the processes in system with heat storage tanks and their optimal management on the example of the industry shows that the energy cost can be reduced by 27.15%.

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