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Bioreactor design via spreadsheet—a study on the monosodium glutamate (MSG) process

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Abstract

Preliminary design calculation of a unit operation is always necessary to determine an order of magnitude of the proposed chemical plant. This paper describes an application of a spreadsheet in preliminary design of a bioreactor. There are a few steps in bioreactor design which are mass/mole balances and energy balances calculations before carrying out the bioreactor sizing. A spreadsheet was used as a tool to make a quick and accurate calculation. Glutamic acid fermentation is used to describe the overall method in this bioreactor design via spreadsheet. The method presented here is easy to learn and easy for the designer to scale up and to simulate different operating conditions to meet an optimum design from time to time by changing only a few variable such as flow rate and substrate concentration of the feed in the previously constructed spreadsheet.

Keywords: Bioreactor; Spreadsheet; Glutamic acid; Fermentation; Monosodium glutamate

1. Introduction

It is often necessary to develop data for a range of operating conditions, so that the optimum configuration of a bioreactor can be found. There are two conventional methods to perform such a task, either by hand calculation (which is somewhat inaccurate and time consuming) or by any of a number of commercial simulations that are faster but costly to licence. A third alternative is presented here: Insert all the manual calculation equations into any spreadsheet program such as Microsoft Excel. This will eliminate the need for employing expensive simulation software and labouring over hand calculations. Further, the time involved from the programmer's point of view is no more (or considerably less) than that required to learn how to use a commercial simulation package.

Microsoft Excel is a commercial spreadsheet software developed by Microsoft® Corporation, which is widely used today. Microsoft Excel is part of the package Microsoft Office and it is fully developed with statistics, mathematical and engineering applications (Bloch, 2000; Liengme, 1997). One of the engineering applications that is available in Microsoft Excel is a root-finding function such as 'solver' and 'goal seek' which play an important role in process engineering to find a correspondence input with a fixed output. Normally in design, the target output is a fixed variable but the input variable is always very difficult to determine via hand calculation because it requires the designer to run a reversed calculation and work with more than one equation and unknown variable.

The method presented here is easy to learn, and offers a quick way to make preliminary estimates of the bioreactor diameter and height, cooling coil required, diameter of baffle, impeller, and sparger ring. Fig. 1 shows a basic configuration of a typical bioreactor.

2. Spreadsheet calculation procedure

Monosodium glutamate (MSG) is widely used not only by housewives to enhance the taste of dishes but also by professional chefs in restaurants all over the world including Malaysia. It is also added into a variety of processed foods, frozen foods, soups, snacks, instant noodles, etc. The process for producing MSG is a typical bioreaction by applying an enzyme. The first step in

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Nomenclature

C_P	heat capacity, kJ/kg °C
E	energy
$\dot{m}$	mass flow rate, kg/s
P_b	bioreactor bottom pressure, atm
P_{atm}	atmospheric pressure, atm
P_{air}	power absorbed by air flow, W
$P_{Ammonia}$	power absorbed by ammonia, W
P_F	net power generated in fermentation, W
P_e	energy produced within the system
Q_{Gen}	total power generated in fermentation, W
Q_A	power result by agitation heat, W
Q_F	power resultant by micro-organism activity, W
Q_B	power absorbed by broth, W
Q_q	heat flow into system
Q_w	work done by system
R	gas constant m^3 Pa/mole K
T	temperature, °C
T_1	inlet cooling water temperature, °C
T_2	outlet cooling water temperature, °C
T_p	Broth temperature, °C
T_{LMTD}	log mean temperature difference
U	overall heat transfer coefficient, W/m^2 °C
ρ	density, kg/m^3

bioreactor design calculation is a mass/mole and energy balance on the bioreactor. The calculation presented here is based on a glutamic acid fermentation process (Fig. 2).

2.1. Mass/mole balance

First of all, related information on the chemicals utilised (i.e. density, molarity and molecular weight) and the yield of glutamic acid over glucose, $Y_{x/s}$ into the spreadsheet. Subsequently the reaction spreadsheet was developed based on the stoichiometry of glutamic acid fermentation. The full mole/mass balance spreadsheet is

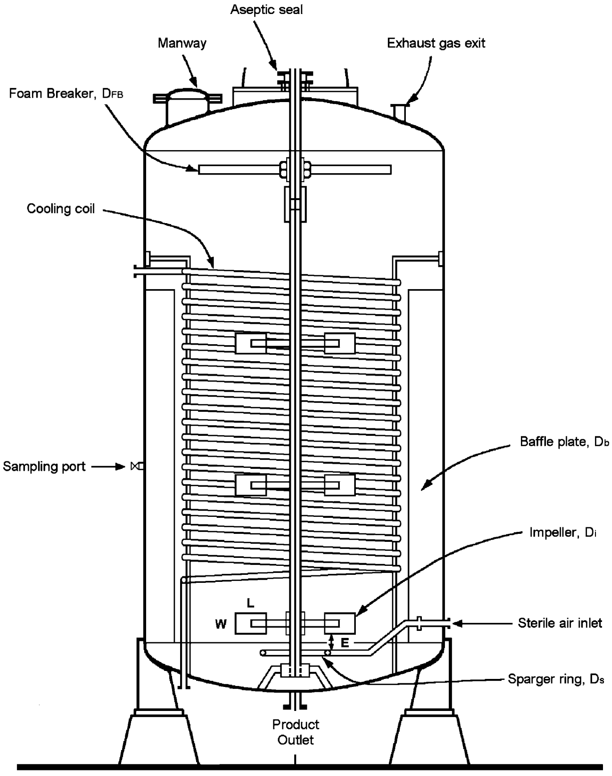


Fig. 1. Typical bioreactor configuration (James & David, 1986).

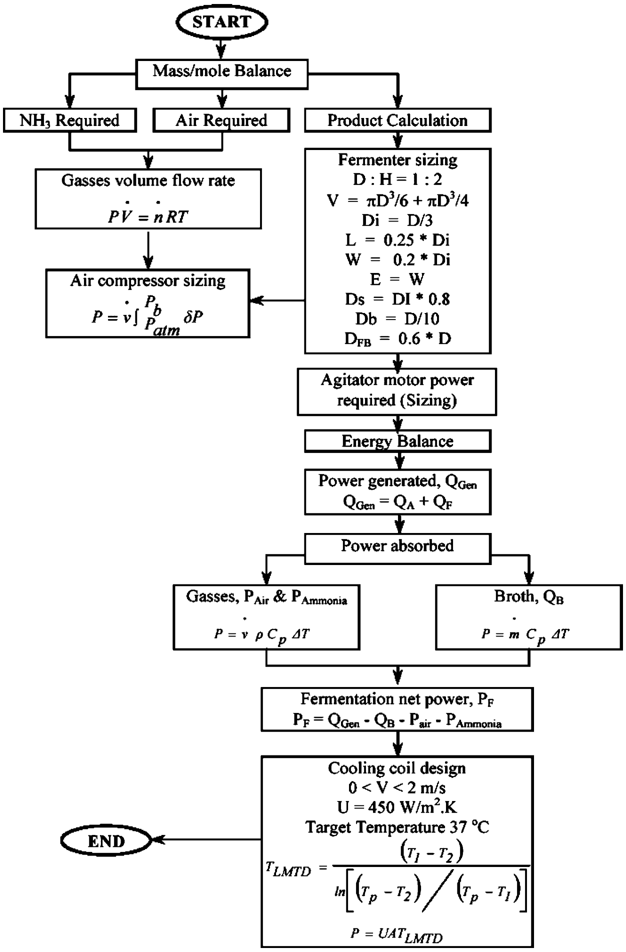


Fig. 2. Bioreactor design calculation procedure.

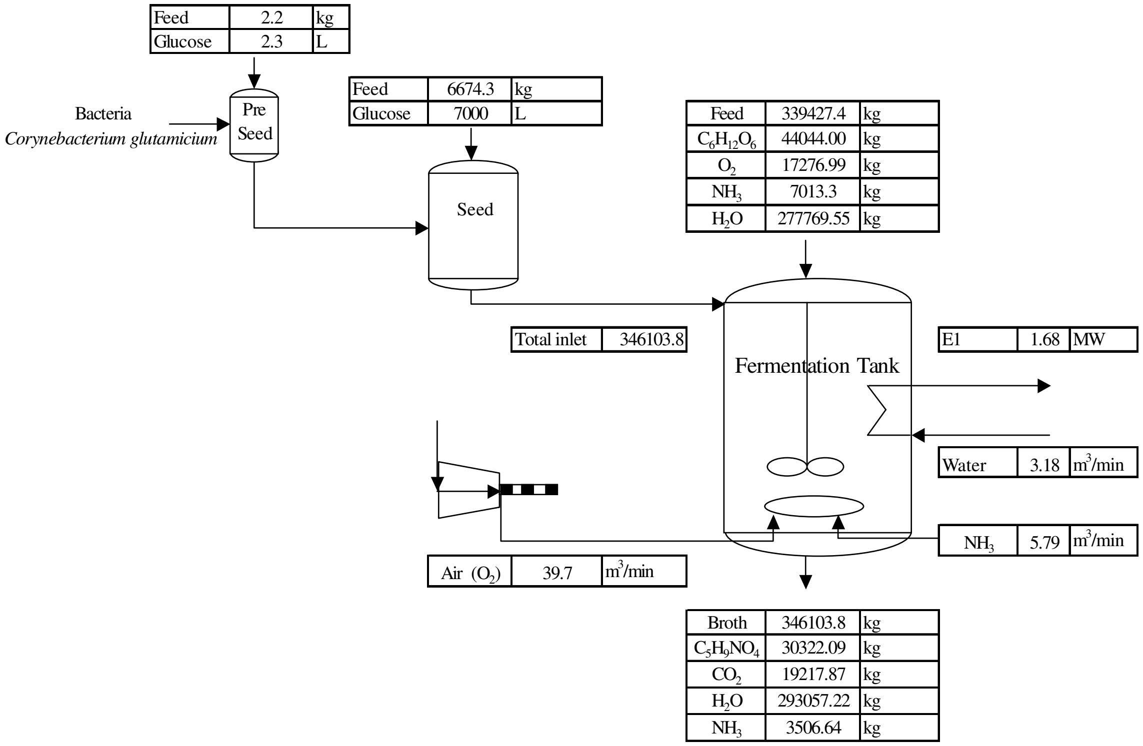


Fig. 3. Summary of mass and heat transfer from MS Excel spreadsheet.

constructed by linking each cell from the reaction spreadsheet to the equation and chemical or physical properties. From this mole/mass balance the amount of substrate (glucose), ammonia, and air (oxygen supply) required can be calculated. The ideal gas law is applied in the spreadsheet for the automatic calculation of air and ammonia flow rate. The ideal gas law is considered applicable since the air pressure is not more than 2 atm. The summary of the mass/mole balance calculated by the Excel spreadsheet is shown in Fig. 3.

The stoichiometric equation of L-glutamic acid fermentation is as follow (Murray, 1985):

$$C_6H_{12}O_6 + 2.21O_2 + 0.84NH_3$$
$$\rightarrow 0.84C_5H_9O_4N + 1.78\,CO + 3.74H_2O$$

The mass balance for the component A in a bioreactor vessel as stated in Biotol (1992) is:

$$V\frac{\delta C_A}{\delta t} = \dot{v}_{\text{in}}C_{A,\text{in}} - \dot{v}_{\text{out}}C_{A,\text{out}} + r_AV \qquad (1)$$

The mole balance of component A of a bioreactor from Biotol (1992) is written as:

$$V\frac{\delta \dot{n}_A}{\delta t} = \dot{v}_{\text{in}}\dot{n}_{A,\text{in}} - \dot{v}_{\text{out}}\dot{n}_{A,\text{out}} + r_AV \qquad (2)$$

The ideal gas law applied to estimates the volume flow rate of gases given as:

$$P\dot{V} = \dot{n}RT \qquad (3)$$

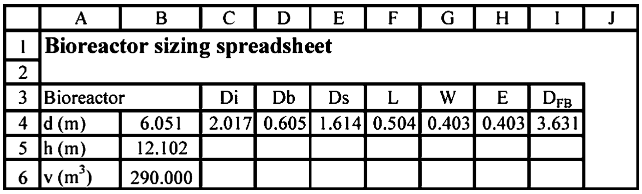
Broth final volume, which is equal to the bioreactor working volume, is estimated as:

$$V = \frac{m}{\rho} \qquad (4)$$

Table 1
Bioreactor design criteria (Hall, Stanbury, & Whitaker, 1999)

Dimension	Ratio
Working volume/bioreactor vessel volume	0.8
Height/vessel diameter (H/D)	2
Vessel diameter/impeller diameter (D/D_i)	3
Sparger ring diameter/impeller diameter (D_s/D_i)	1–1.2
Baffle/vessel diameter (D_b/D)	0.1
Foam breaker diameter/vessel diameter (D_{FB}/D)	0.6
L/D_i	0.25
E/W	1
W/D_i	0.2

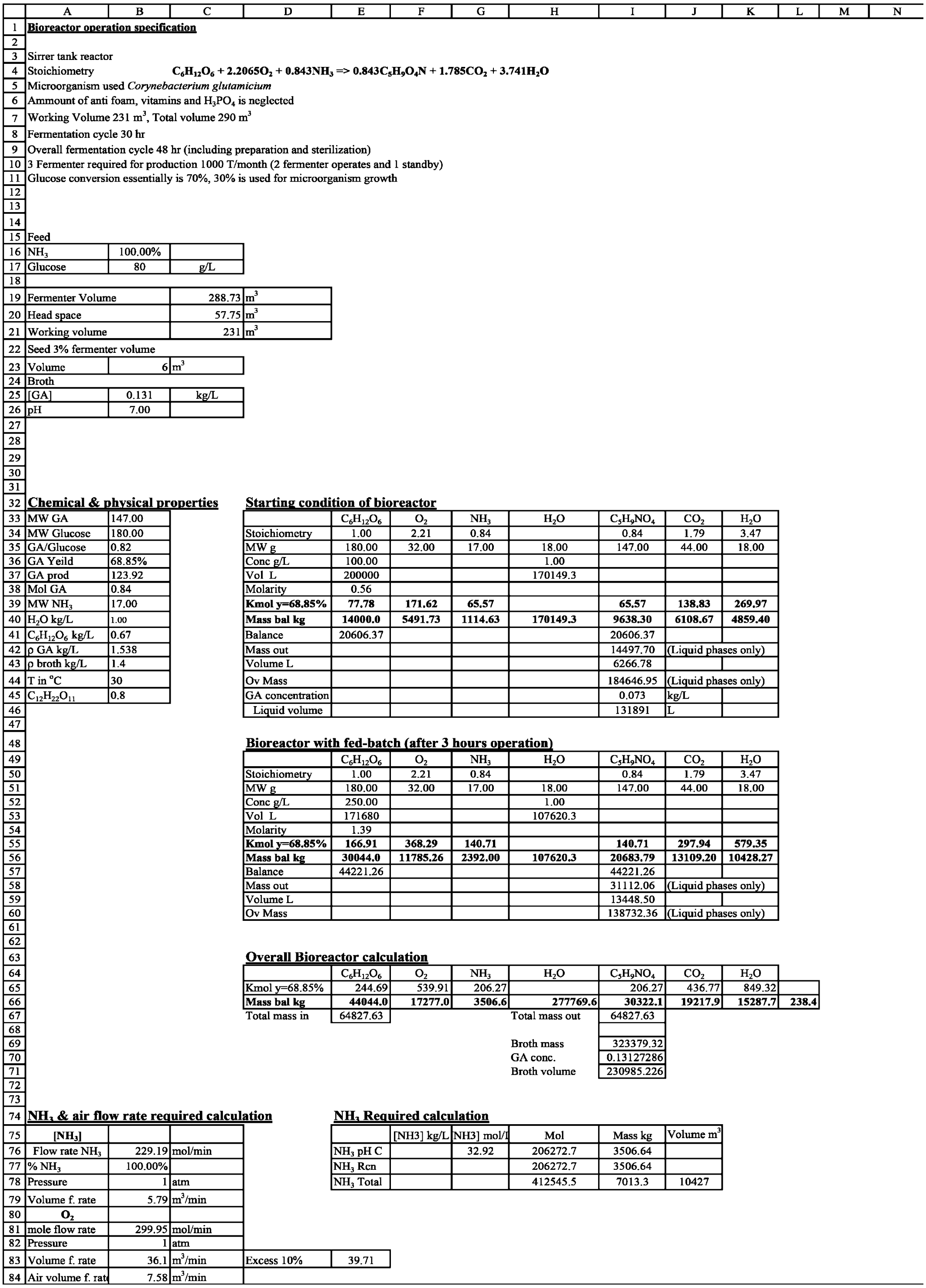
Table 2
Bioreactor sizing spreadsheet



	A	B	C	D	E	F	G	H	I	J
1	**Bioreactor sizing spreadsheet**									
2										
3	Bioreactor		Di	Db	Ds	L	W	E	D_{FB}	
4	d (m)	6.051	2.017	0.605	1.614	0.504	0.403	0.403	3.631	
5	h (m)	12.102								
6	v (m^3)	290.000								

2.2. Bioreactor sizing

After performing the mass/mole balance, the working volume of the bioreactor can be calculated. A typical working volume of a bioreactor is 80% of the total volume as shown in Table 1 (Hall et al., 1999). Based on this information the total volume of a bioreactor can be calculated. A spreadsheet for the bioreactor sizing is constructed by linking the cells of working volume in the mass/mole balance spreadsheet to the bioreactor design criteria as shown in Table 1. Table 2 is an example of the constructed spreadsheet for bioreactor sizing (Fig. 4).



1 **Bioreactor operation specification**
2
3 Sirrer tank reactor
4 Stoichiometry $\mathbf{C_6H_{12}O_6 + 2.2065O_2 + 0.843NH_3 => 0.843C_5H_9O_4N + 1.785CO_2 + 3.741H_2O}$
5 Microorganism used *Corynebacterium glutamicium*
6 Ammount of anti foam, vitamins and H_3PO_4 is neglected
7 Working Volume 231 m^3, Total volume 290 m^3
8 Fermentation cycle 30 hr
9 Overall fermentation cycle 48 hr (including preparation and sterilization)
10 3 Fermenter required for production 1000 T/month (2 fermenter operates and 1 standby)
11 Glucose conversion essentially is 70%, 30% is used for microorganism growth
12
13
14
15 Feed

	A	B	C	D
16	NH_3	100.00%		
17	Glucose	80	g/L	
18				
19	Fermenter Volume		288.73	m^3
20	Head space		57.75	m^3
21	Working volume		231	m^3
22	Seed 3% fermenter volume			
23	Volume	6	m^3	
24	Broth			
25	[GA]	0.131	kg/L	
26	pH	7.00		

27
28
29
30
31

	A	B
32	**Chemical & physical properties**	
33	MW GA	147.00
34	MW Glucose	180.00
35	GA/Glucose	0.82
36	GA Yeild	68.85%
37	GA prod	123.92
38	Mol GA	0.84
39	MW NH_3	17.00
40	H_2O kg/L	1.00
41	$C_6H_{12}O_6$ kg/L	0.67
42	ρ GA kg/L	1.538
43	ρ broth kg/L	1.4
44	T in °C	30
45	$C_{12}H_{22}O_{11}$	0.8

32 **Starting condition of bioreactor**

	D	E	F	G	H	I	J	K
33		$C_6H_{12}O_6$	O_2	NH_3	H_2O	$C_5H_9NO_4$	CO_2	H_2O
34	Stoichiometry	1.00	2.21	0.84		0.84	1.79	3.47
35	MW g	180.00	32.00	17.00	18.00	147.00	44.00	18.00
36	Conc g/L	100.00			1.00			
37	Vol L	200000			170149.3			
38	Molarity	0.56						
39	**Kmol y=68.85%**	**77.78**	**171.62**	**65.57**		**65.57**	**138.83**	**269.97**
40	**Mass bal kg**	**14000.0**	**5491.73**	**1114.63**	**170149.3**	**9638.30**	**6108.67**	**4859.40**
41	Balance	20606.37				20606.37		
42	Mass out					14497.70	(Liquid phases only)	
43	Volume L					6266.78		
44	Ov Mass					184646.95	(Liquid phases only)	
45	GA concentration					0.073	kg/L	
46	Liquid volume					131891	L	

47

48 **Bioreactor with fed-batch (after 3 hours operation)**

	D	E	F	G	H	I	J	K
49		$C_6H_{12}O_6$	O_2	NH_3	H_2O	$C_5H_9NO_4$	CO_2	H_2O
50	Stoichiometry	1.00	2.21	0.84		0.84	1.79	3.47
51	MW g	180.00	32.00	17.00	18.00	147.00	44.00	18.00
52	Conc g/L	250.00			1.00			
53	Vol L	171680			107620.3			
54	Molarity	1.39						
55	**Kmol y=68.85%**	**166.91**	**368.29**	**140.71**		**140.71**	**297.94**	**579.35**
56	**Mass bal kg**	**30044.0**	**11785.26**	**2392.00**	**107620.3**	**20683.79**	**13109.20**	**10428.27**
57	Balance	44221.26				44221.26		
58	Mass out					31112.06	(Liquid phases only)	
59	Volume L					13448.50		
60	Ov Mass					138732.36	(Liquid phases only)	

61
62

63 **Overall Bioreactor calculation**

	D	E	F	G	H	I	J	K	L
64		$C_6H_{12}O_6$	O_2	NH_3	H_2O	$C_5H_9NO_4$	CO_2	H_2O	
65	Kmol y=68.85%	244.69	539.91	206.27		206.27	436.77	849.32	
66	**Mass bal kg**	**44044.0**	**17277.0**	**3506.6**	**277769.6**	**30322.1**	**19217.9**	**15287.7**	**238.4**
67	Total mass in	64827.63			Total mass out	64827.63			
68									
69					Broth mass	323379.32			
70					GA conc.	0.13127286			
71					Broth volume	230985.226			

72
73

	A	B	C	D	E
74	**NH_3 & air flow rate required calculation**				
75	**$[NH_3]$**				
76	Flow rate NH_3	229.19	mol/min		
77	% NH_3	100.00%			
78	Pressure	1	atm		
79	Volume f. rate	5.79	m^3/min		
80	**O_2**				
81	mole flow rate	299.95	mol/min		
82	Pressure	1	atm		
83	Volume f. rate	36.1	m^3/min	Excess 10%	39.71
84	Air volume f. rat	7.58	m^3/min		

74 **NH_3 Required calculation**

	E	F	G	H	I	J
75		[NH3] kg/L	NH3] mol/I	Mol	Mass kg	Volume m^3
76	NH_3 pH C		32.92	206272.7	3506.64	
77	NH_3 Rcn			206272.7	3506.64	
78	NH_3 Total			412545.5	7013.3	10427

Fig. 4. Bioreactor mass/mole balance spreadsheet.

The general energy balance equation around the tank is given by Biotol (1992) as:

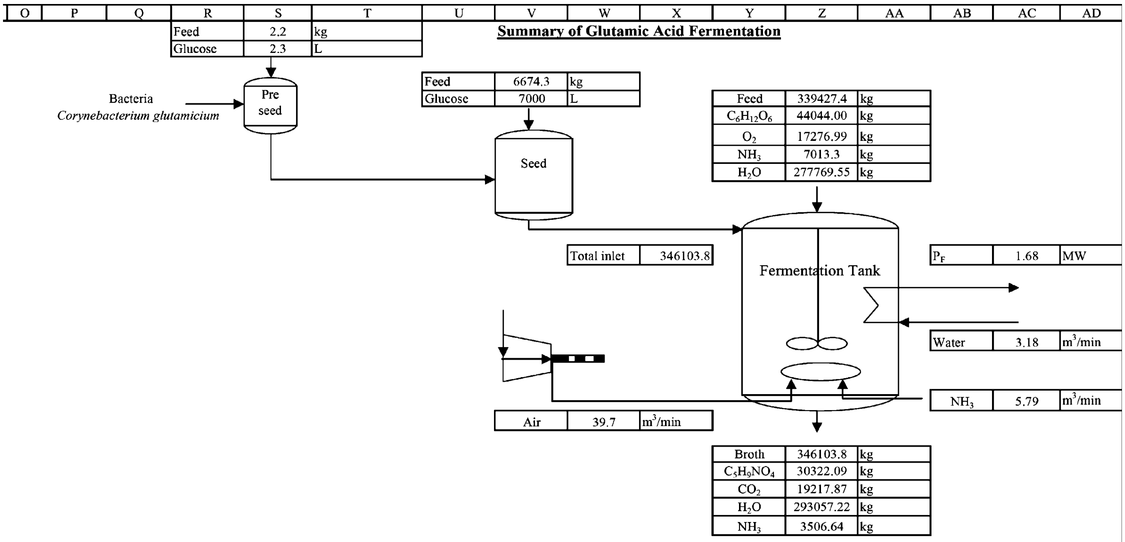
$$\frac{\delta \dot{E}}{\delta t} = \dot{m}_{\text{in}} E_{\text{in}} - \dot{m}_{\text{out}} E_{\text{out}} + Q_{\text{q}} + Q_{\text{w}} + P_{\text{e}} \tag{5}$$

For both hemispherical end and $H = 2D$ shape factor, bioreactor volume is defined as:

$$V = \frac{\pi D^3}{6} + \frac{\pi D^3}{4} \tag{6}$$

2.3. Energy balance and cooling coil design

Since the heat generated by microorganism activity is very hard to predict, we estimate it based on the typical



Pre seed (Lab scale fermenter 2.5 L)

	$C_6H_{12}O_6$	O_2	NH_3	H_2O	$C_5H_9NO_4$	CO_2	H_2O
Stoichiometry	1.00	2.21	0.84		0.84	1.79	3.47
MW g	180.00	32.00	17.00	18.00	147.00	44.00	18.00
Conc g/L	100.00			1.00			
Vol L	2.3			2.0			
Molarity	1.80						
kmol y=68.85%	**0.0009**	**0.0020**	**0.0008**		**0.0008**	**0.0016**	**0.0031**
Mass bal kg	**0.2**	**0.06**	**0.01**	**2.0**	**0.11**	**0.07**	**0.06**
Balance	0.24				0.24		
Mass out					0.17	(Liquid phases only)	
Volume L					0.07		
Ov Mass					2.12	(Liquid phases only)	
GA concentration					0.073	kg/L	
Liquid volume					1.5	L	

Seed (mini fermenter 8 m³)

	$C_6H_{12}O_6$	O_2	NH_3	H_2O	$C_5H_9NO_4$	CO_2	H_2O
Stoichiometry	1.00	2.21	0.84		0.84	1.79	3.47
MW g	180.00	32.00	17.00	18.00	147.00	44.00	18.00
Conc g/L	100.00			1.00			
Vol L	7000			5955.2			
Molarity	1.80						
Kmol y=68.85%	**2.72**	**6.01**	**2.29**		**2.29**	**4.86**	**9.45**
Mass bal kg	**490.0**	**192.21**	**39.01**	**5955.2**	**337.34**	**213.80**	**170.08**
Balance	721.22				721.22		
Mass out					507.42	(Liquid phases only)	
Volume L					219.34		
Ov Mass					6462.64	(Liquid phases only)	
GA concentration					0.073	kg/L	
Liquid volume					4616.2	L	

Fig. 4 (*continued*)

Table 3
Data for typical glutamic acid fermentation from Atkinson and Mavituna (1992)

Agitator power required	15 hp $(1000\ \mathrm{gal})^{-1}$
Heat of fermentation	100 Btu (h)$(\mathrm{gal})^{-1}$
Agitation heat	38 Btu (h)$(\mathrm{gal})^{-1}$
Broth temperature	37–38 °C
Inlet cooling water	10 °C

operation data for fermentation as shown in Table 3 (Atkinson & Mavituna, 1992). The energy balance spreadsheet constructed by linking this design data to the cells of the bioreactor working volume, air and ammonia flow rate and the substrate flow rate. This spreadsheet will calculate the net fermentation heat generated per unit time (power), which is equal to the cooling coil duty that is yet, to be designed. Water is chosen as the coolant

Table 4
Energy balance and cooling coil design spreadsheet

	A	B	C	D	E	F	G	H	I	J	K
1	**Detailed energy balance on bioreactor**										
2											
3	**Bio-Chemical Engineering method (Design Data)**										
4	Working volume					230.97	m^3				
5	Agitator	15	hp/1000gal	42342.74	W/m^3	9.78E+06	W				
6	Ferm Heat	100	Btu/h.gal	7735.7	W/m^3	1.79E+06	W				
7	Agitation Heat	38	Btu/h.gal	2939.6	W/m^3	6.79E+05	W				
8	Total power generated	2.47E+06	W								
9											
10											
11	**Power absorbed by broth**				**Power absorbed by gasses**						
12	Cp	4200	J/kg.C		Tout gas	37					
13	mass	346103.8	kg		**Air**				**NH_3**		
14	δT	9	C		Tin air	28			Tin gas	-33.5	
15	Tin	28	C		Cp	1007	kJ/kg.K		Cp	2158	kJ/kg.K
16	Tsteady	37	C		Density	0.1614	kg/m3		Density	0.6894	kg/m3
17	Heat abs	1.31E+10	J		VFR	39.71	m3/s		VFR	5.79	m3/s
18	Power abs	1.21E+05	W		MFR	6.409194	kg/s		MFR	3.991626	kg/s
19					Power abs	5.81E+04	W		Power abs	6.07E+05	W
20											
21	Net Power of Fermentation, P_F	1.68E+06	W								
22											
23	**Cooling coil design**										
24	Water										
25	T °C	10									
26	F.rate Qf (kg/s)	20.0									
27	Heat Q (W)	1.68E+06									
28	T_{mean}	20									
29	Cp (water) J/kg.C	4200									
30	Density (kg/m^3)	999									
31											
32	From figure 12.1 and Table 12.1 (Chemical engineering vol. 6)										
33	U Overall coefficient	400	550	700	W/m^2 .°C						
34	LMTD	14.8	C								
35	A required	206.1	m^2								
36											
37	Layout and tube size										
38	Outside diameter	73.152	mm		2.88	in					
39	Inside diameter	62.7126	mm		2.469	in					
40	Coil diameter	4.532	m								
41											
42	Numbers of tubes										
43	Area of one coil	3.27	m^2	neglecting tube thickness							
44	Number of coil	63	say	64							
45	Tube per passes	4	16 passes								
46	Heat transfer area	209.41	m^2	Base on outside diameter							
47	Check reasonable										
48	Tube cross sectional area	0.00309	m^2								
49	Area per pass	0.01	m^2								
50	Volumetric flow	0.02	m^3/s								
51	Tube side velocity Ut	1.62	m/s	Satisfactory between 1 to 2							
52											
53	**Summary of cooling coil design**										
54	Heat Load	1679.5	kW								
55	Volumetric f. rate (water)	0.02	m^3/s								
56	Heat transfer area (required)	206.11	m^2								
57	Heat transfer area (design)	209.41	m^2								
58	OD coil	73.152	mm								
59	ID coil	62.71	mm								
60	Length/coil	3.27	m								
61	Number of coil	64									
62	V (Tube side velocity)	1.62	m/s								
63	U (Overall HTR coef)	550	W/m^2 .°C								

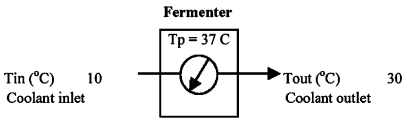


Table 5
Summary of calculated results

Parameter	Value
Total volume	290 m^3
Liquid volume (working volume)	231 m^3
Tank OD	6 m
Total height/diameter	2
Percentage fill	80
Pressure (liquid surface)	1 atm
Pressure (bottom)	1.64 atm
Air flow rate	36.1 m^3/min
Oxygen flow rate	7.6 m^3/min
Ammonia flow rate	5.8 m^3/min
Sparger diameter	2.22 m
Sparger hole diameter	6 mm
Sparger pipe diameter	0.1 m
Off segmented baffle (total) d_b	0.6 m
Baffle ratio d_b/d_t	1/10
Baffle plate d'_b	0.5 m
No. of turbine	3
Impeller diameter	2.12 m
Impeller d_i/d_t ratio	0.3
Motor power required	9.8 MW
Heat load	1.7 MW
U	550 W/m^2 °C
Coolant inlet temperature (water)	10 °C
Coolant flow	3.2 m^3/min
Coil side velocity	1.62 m/s
Coil area required	206.1 m^2
Coil pipe diameter OD	73 mm
Coil pipe diameter ID	63 mm
Coil diameter	4.53 m
Coil spacing	0.06 m
No. of coil	64
Area provided	209.4 m^2

because it is cheap and available. A spreadsheet to calculate heat transfer area required is then constructed by linking Eqs. (7)–(10). The design parameter such as cooling pipe diameter and size of coolant inlet are fixed by the designer. The heat transfer area, pipe diameter and size of inlet value are used to determine the coolant side velocity. The purpose of coolant side velocity or coil inner velocity calculation is to check whether the design is applicable or not. If the coolant side velocity is larger than 2 m/s mean then the designed cooling coil is not applicable because of lack in heat transfer. The way to overcome such a problem is to design a larger coolant. A larger coolant inlet will reduce the flow rate of coolant without reducing the total heat transfer area so that the tendency will be to reduce the coolant side velocity into the correct operating range. Table 4 shows an example of the constructed spreadsheet for the energy balance and design of the cooling coil.

The energy contained in the liquid is given by Kern (1965) as:

$$P = \dot{m}C_P\Delta T \tag{7}$$

By substituting $m = \dot{v}\rho$ the energy contained in the gasses phase is written as:

$$P = \dot{v}\rho C_P\Delta T \tag{8}$$

the log mean temperature difference, T_{LMTD} is defined as:

$$T_{\mathrm{LMTD}} = \frac{(T_1 - T_1)}{\ln[(T_P - T_2)/(T_P - T_1)]} \tag{9}$$

Duty of a cooling coil with heat transfer coefficient U is given by Sinnott (1996) as:

$$P = UAT_{\mathrm{LMTD}} \tag{10}$$

Table 5 shows the summary results of the bioreactor design, carried out MS Excel.

3. Conclusions

A bioreactor design spreadsheet is easy to learn, and offers a quicker way for preliminary calculation of the bioreactor design. A spreadsheet also eliminates human error in doing the iteration calculation, which is commonly used in design calculation. This method also offers an easy way for the designer to scale up and optimise the process. By using this method the designer also escapes the costly simulation software license. The spreadsheet method also provides a cheaper alternative to the designer compared to costly commercial software.

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