2.3 The β-Galactosidase Design Case

This example analyzes the production of β–Galactosidase, an intracellular enzyme produced by *E.coli*. This example is recommended for users in the biotech and food industries. In addition, since this example is a batch process, it serves as a medium for discussing several scheduling issues.

At this point, we suggest that you open the β-Galactosidase design case file and examine it briefly. To open this file, simply select the **File: Open...** option from SuperPro Designer's main menu. Then find the file named BGal5_0b in the **Examples\BGal** folder, select it, and click **OK**.

We suggest that you keep the design case flowsheet window open as you read the remainder of Chapter 2.3. However, you should not edit the flowsheet file until after you have finished reading through this chapter.

2.3.1 Process Description

Figure 2.3a shows the entire flowsheet for the β-Galactosidase process (for a better quality printout of Figure 2.3a, please use the printing capabilities of SuperPro).

β-Galactosidase is mainly used in the utilization of cheese whey. More specifically, immobilized reactors with β-Gal have been developed to convert lactose found in cheese whey to glucose and galactose, yielding a sweetened product which can be used as an additive to ice cream, egg-nog, yogurt, and other dairy products. Another application of β-Gal is in the treatment of milk products. A significant number of people are lactose intolerant and cannot digest milk or milk products. Production of lactose-free milk products (using β-Gal reactors) allows those people to digest them.

The β-Galactosidase enzyme is normally produced by *E. coli* up to 1-2% of total cell protein under conditions of induction of the lac operon. Using genetic engineering, the level can go up to 20-25% of total protein. In this example, an easily attainable level of 10% is assumed.

This example analyzes a plant that produces 11,500 kg of β-Gal per year in 134 batches. Several files have been included with this example:

BGal-a: This file represents the process at an early stage of plant design. All equipment is in Design Mode, meaning that all equipment sizes and throughputs are calculated as opposed to being specified by the user.

BGal-b: This file shows the plant after equipment sizes have been specified for key pieces of equipment. In addition, some equipment is reused for multiple unit procedures. The BGal-b file was used to produce the tables and graphs in the rest of Chapter 2.3.

BGal-c: This file is the same as BGal-b, except that final product formulation and packaging unit procedures have been added.

We will focus on the BGal-b file for the rest of our process description.

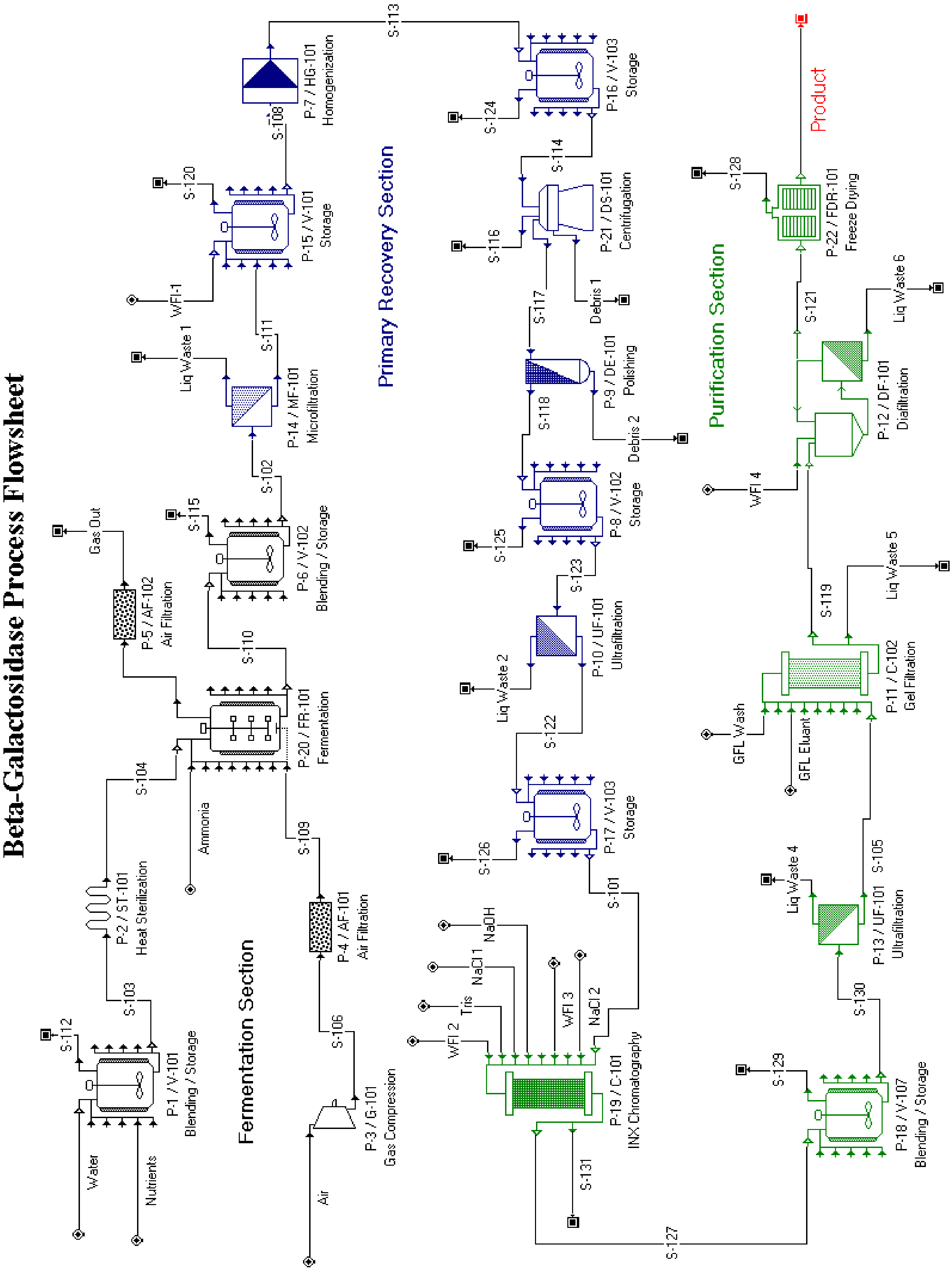
Beta-Galactosidase Process Flowsheet
Fermentation Section
Primary Recovery Section
Purification Section
Product
Water
Nutrients
P-1 / V-101
Blending / Storage
S-112
S-103
P-2 / ST-101
Heat Sterilization
S-104
Ammonia
Air
P-3 / G-101
Gas Compression
S-106
P-4 / AF-101
Air Filtration
S-109
P-20 / FR-101
Fermentation
P-5 / AF-102
Air Filtration
Gas Out
S-110
P-6 / V-102
Blending / Storage
S-115
S-102
P-14 / MF-101
Microfiltration
Liq Waste 1
S-111
P-15 / V-101
Storage
WFI-1
S-120
S-108
P-7 / HG-101
Homogenization
S-113
P-16 / V-103
Storage
S-124
S-114
P-21 / DS-101
Centrifugation
S-116
S-117
Debris 1
P-9 / DE-101
Polishing
S-118
Debris 2
P-8 / V-102
Storage
S-125
S-123
P-10 / UF-101
Ultrafiltration
Liq Waste 2
S-122
P-17 / V-103
Storage
S-126
S-101
P-19 / C-101
INX Chromatography
WFI 2
Tris
NaCl 1
NaOH
WFI 3
NaCl 2
S-131
S-127
P-18 / V-107
Blending / Storage
S-129
S-130
P-13 / UF-101
Ultrafiltration
Liq Waste 4
S-105
P-11 / C-102
Gel Filtration
GFL Wash
GFL Eluant
Liq Waste 5
S-119
WFI 4
P-12 / DF-101
Diafiltration
Liq Waste 6
S-121
P-22 / FDR-101
Freeze Drying
S-128

Figure 2.3a

General note about Flowsheet Sections

The concept of flowsheet sections was introduced as part of release 3.0 to facilitate reporting of results for costing, economic evaluation, raw material requirements, and throughput analysis of integrated processes. A flowsheet section is a group of unit procedures that have something in common. For instance, the ß-galactosidase flowsheet has been divided into three sections: 1) Fermentation, 2) Primary Recovery, and 3) Purification. All the procedure icons of the Fermentation section are displayed in black, while the icons of the Primary Recovery and Purification sections are displayed in blue and green, respectively. If you wish to add unit procedures to a specific section, simply highlight the desired unit procedure icons on the flowsheet, and then click the “Add to Section” icon (the one with two blue triangles on it) on the left end of the **Sections Toolbar**. To specify the default color for icons in a specific section, click the “Edit Section” icon of the **Sections Toolbar** (this icon looks like a small pair of glasses and a piece of paper). This brings up a dialog box which allows you to specify a Starting Material and Active Product for the section. If you click on the “Icon Color” tab of this dialog, you can edit the section’s default unit procedure icon color. These dialogs can also be reached by choosing **Edit: Flowsheet Options: Section: Properties**. For additional information on how to specify flowsheet sections and edit their properties, please see Chapter 13 or consult the Help Facility (look up the keyword “Sections” in the Help index).

Fermentation Section

Fermentation media are prepared in a stainless steel tank (V-101) and sterilized in a continuous sterilizer (ST-101). A compressor (G-101) and an absolute air filter (AF-101) provide sterile air to the fermentor (FR-101). Gaseous ammonia is used as a nitrogen source.

Primary Recovery Section

The first step of the downstream section is cell harvesting to reduce the volume of the broth and remove extracellular impurities; it is carried out by a membrane microfilter (MF-101). Since ß–galactosidase is an intracellular product, the next important step is cell disruption, performed in a high-pressure homogenizer (HG-101). Storage vessels (V-101, 102, 103, and 107) are used at various stages of the process to act as surge capacity for certain unit procedures with restricted throughputs. For instance, upstream of the P-7/HG-101 homogenizer is the P-15/V-101 storage vessel. This vessel is necessary because the time required for homogenization in HG-101 is greater than the time required for microfiltration in MF-101. Since these pieces of equipment do not have storage capacity within them, the difference in flow rates creates a necessity for intermediate storage equipment such as V-101. Notice that some of these vessels are used multiple times within the process (V-101, V-102, and V-103 are each used for two different steps.) After homogenization, a disk–stack centrifuge (DS-101) is used to remove most of the cell debris particles. A dead-end polishing filter (DE-101) removes the remaining cell debris particles. The resulting protein solution is concentrated by an ultrafilter (UF-101), and stored in V-103.

Purification Section

Next the product stream is purified by an ion exchange chromatography column (C-101), further concentrated by a second ultrafiltration step (P-13/UF-101), and polished by a gel filtration column (C-102). Finally, a diafiltration unit (DF-101) exchanges the gel filtration buffer, and the protein solution is lyophilized in a freeze dryer (FDR-101).

Important information about Equipment Sharing

In a batch plant, it is common to utilize the same piece of equipment to carry out multiple unit procedures. As stated above, vessels V-101, V-102, and V-103 are each used for multiple steps within this example process. Similarly, the ultrafilter, UF-101, is used twice. By default, whenever a unit procedure is introduced in the flowsheet, the system assumes that the procedure is carried out in its own piece of equipment. However, you also have the option of selecting one of the existing equipment items that are compatible with this unit procedure through the Equipment Data dialog (right-click on a unit procedure icon and choose the **Equipment Data**… option).

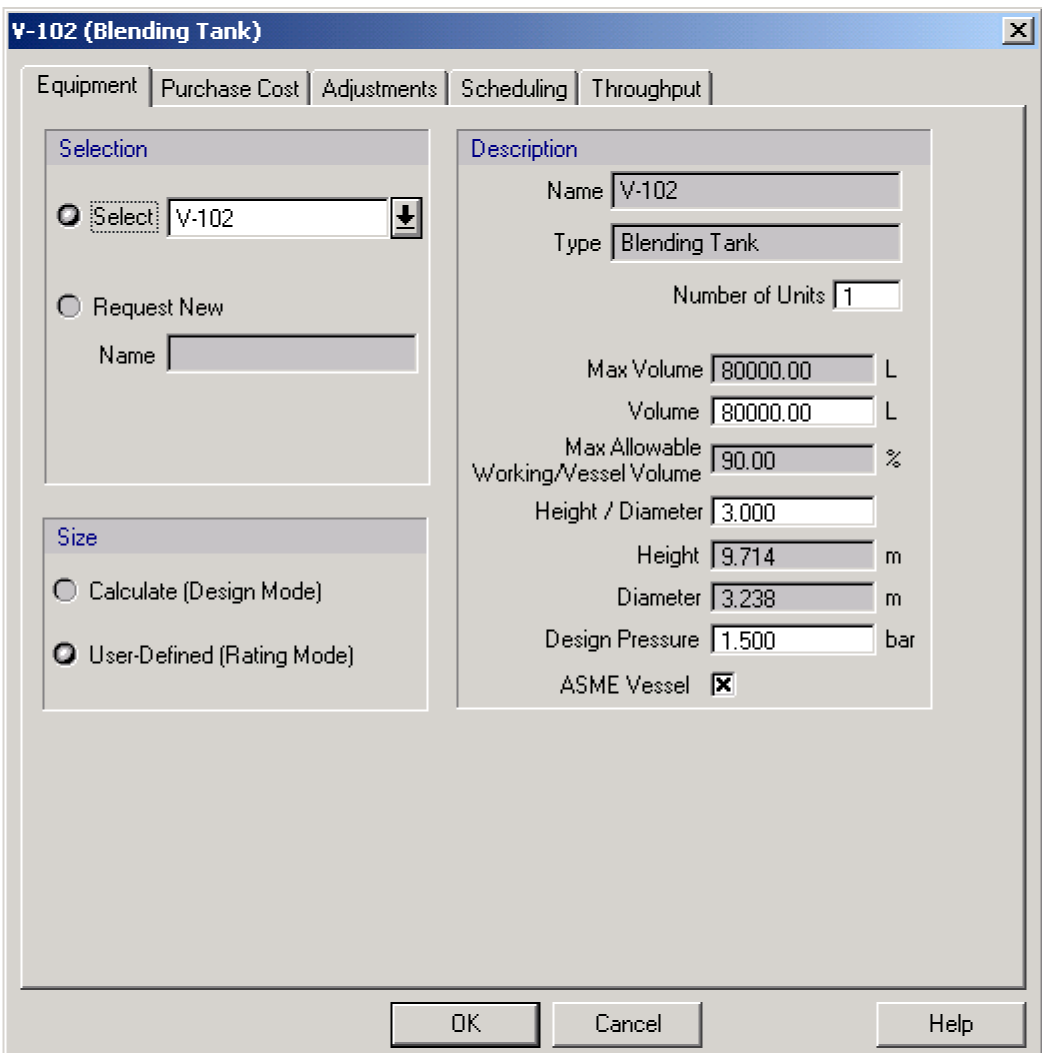

Figure 2.3b: Equipment Data Dialog of a Storage Vessel.

Figure 2.3b displays the equipment data dialog of procedure P-8. Instead of using a unique vessel for this procedure, vessel V-102 (which was first used for procedure P-6) was reused. Equipment sharing is possible in either Design or Rating mode. When multiple procedures share a piece of equipment that is in Design mode (unspecified size), each procedure recommends its own sizing and SuperPro selects the maximum. If the calculated equipment size exceeds the maximum possible value, then SuperPro assumes multiple (identical) equipment items with a total size equal to the calculated total capacity requirement and an individual size that is smaller than or equal to the maximum. For example, if the maximum size of a vessel is 80,000 L, and your process requires 180,000 L of storage capacity, three 60,000 L vessels will be used by SuperPro. In Rating mode, the user specifies the equipment size as well as the number of equipment items employed by a unit procedure. In other words, in SuperPro a single unit procedure icon may correspond to multiple equipment items that operate in parallel, or multiple unit procedure icons may correspond to a single piece of equipment (if the flowsheet is in Batch mode and those procedures share equipment).

Equipment sharing reduces the number of equipment items required for a batch process and consequently saves money in terms of capital expenditures. However, it also introduces scheduling constraints that may reduce the number of batches that can be processed per year. Information on visualization of equipment sharing can be found later in this chapter. For detailed information on the impact of equipment sharing on plant throughput please see Chapter 9 or search for Debottlenecking in the Help Facility.

2.3.2 Initializing Data Specific to Biotech Processes

The Primary Biomass Component and Extra-Cellular Percentage

In bioprocessing, we have formation of intracellular (remain inside the cell) as well as extracellular (released into the solution) products. To capture this as well as the fact that biomass is usually reported on a dry-cell-mass basis, we use the concept of **Extra-Cell %** in streams and fermentation reactions. The “Extra-Cell %” of a component in an input stream (something fed into the system) or a product of a fermentation reaction (something generated in the system) can be specified only if the **Primary Biomass Component** is identified.

This is accomplished through the Pure Component Registration dialog (select **Tasks: Register Components & Mixtures: Pure Components**) shown in Figure 2.3c. The primary biomass component is selected among components whose “Is Biomass ?” flag has been set to true on the ID’s tab of the **Properties** dialog. The Properties dialog is displayed by clicking on a component’s line number (# 3 for Biomass in Figure 2.3c) on the left-most column of the ‘Registered Components’ table and then clicking on the **Properties** button.

If the Primary Biomass Component is identified, its **Water Content** is specified (through the same dialog) and there is formation of Primary Biomass (as a fermentation product), the program will automatically associate intracellular water with biomass in order to satisfy its water content as specified during component registration. This is displayed using an “Extra-Cell %” value of less than 100 in the stream dialogs (see Figure 2.3d). This has an impact on material balances in separation procedures (e.g., centrifugation, clarification, filtration, etc.). If a removal percentage is assigned to Primary Biomass, the program will use the same removal percentage for the intracellular portion of all components. This results in solids streams (e.g., retentate, concentrate, etc.) with concentrations closer to reality.

Please note that a fermentation product can be identified as intracellular by specifying an “Extra-Cell %” value of less than 100 in the Stoichiometry tab of a fermentation operation dialog. That component can become extracellular (released into the solution) using a cell disruption procedure (e.g., high pressure homogenization or bead milling).

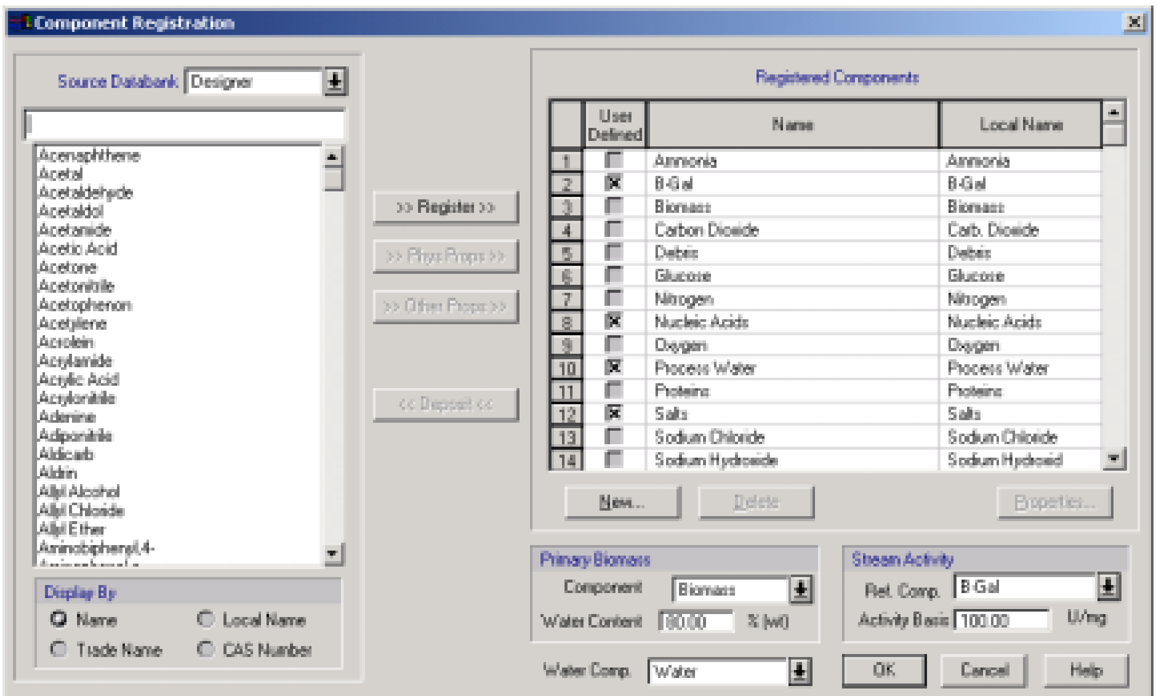

Figure 2.3c: The Pure Component Registration dialog.

The Stream Activity Reference Component

In bioprocessing, the concentration of a product or undesired impurity is often reported as activity measured using a certain assay. In SuperPro this is represented using the **Stream Activity Reference Component** and its **Activity Basis**, expressed in U/mg (see Figure 2.3c). The activity basis represents how many (arbitrary) units of activity (U) correspond to each mg of the reference component present in a stream. This information is used to calculate and report the activity of a stream in U/mL (see Figure 2.3d).

This concept is also applicable to other industries. For instance, in treatment of nuclear waste, the calculated stream activity may represent radioactivity.

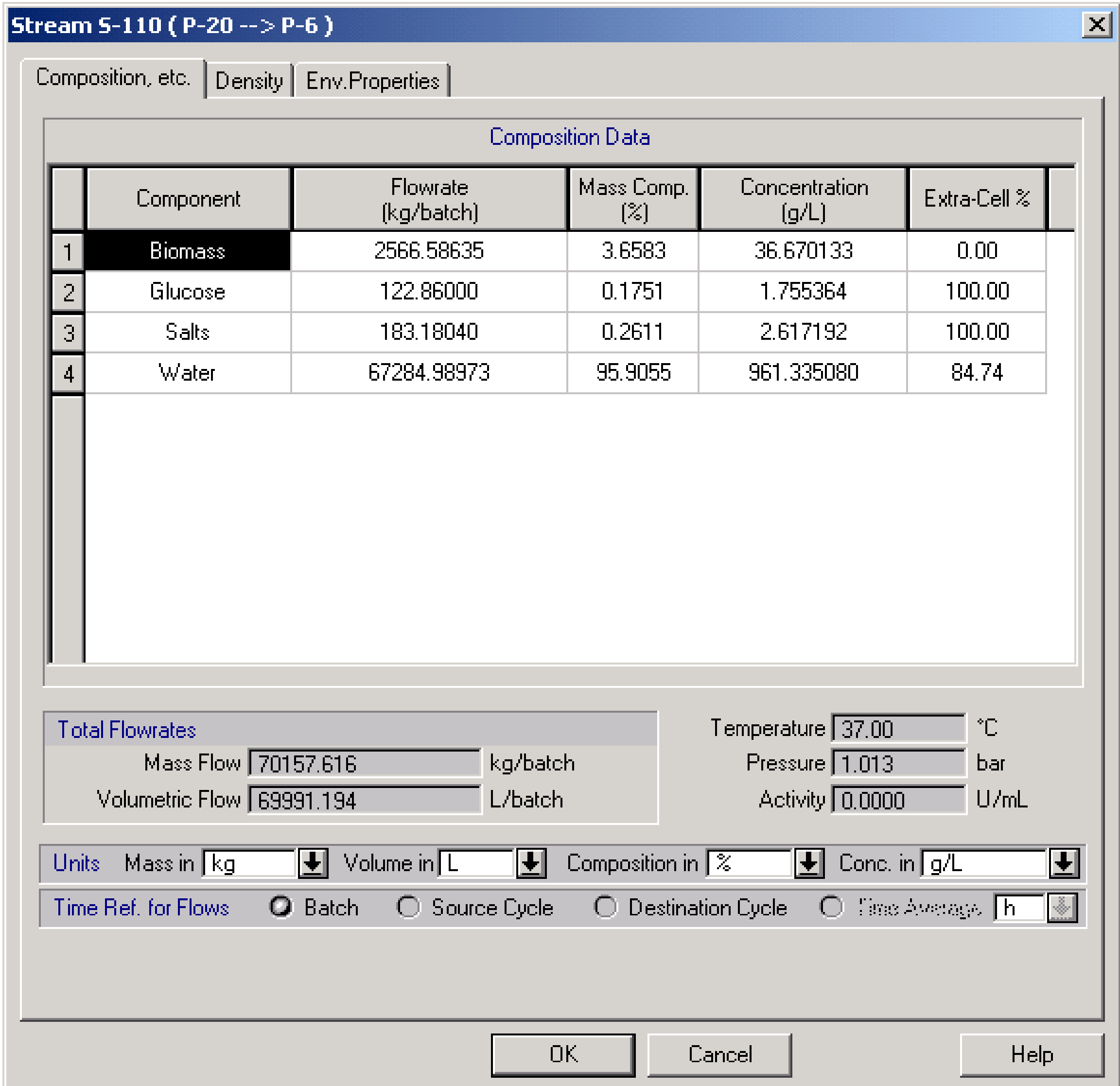

Figure 2.3d: Dialog of stream S-110 (fermentation outlet).

Initializing Fermentation Operations

Correct modeling of fermentation operations is important in biotech processes. SuperPro is equipped with two different types of fermentation models: stoichiometric and kinetic for batch as well as continuous fermentation reactions. The stoichiometric model is used if no kinetic data are available or if simplicity is desired, which is the case in this example. If kinetic data are available, the kinetic model can be used to calculate composition, temperature, and utility profiles as a function of time. Initialization of a stoichiometric fermentation is essentially identical to initialization of a stoichiometric chemical reaction, except that there is an option on the Fermentation Oper. Cond’s tab for fermentor aeration. Please refer to Chapter 2.2.4 for information on initialization of stoichiometric chemical reactions. The same chapter section provides information on initialization of kinetic reactions and generation of profiles as a function of time.

2.3. 3 Process Analysis

At this point, you may want to change the values of certain parameters and redo the calculations (by selecting **Tasks: Solve M&E Balances**). The calculated flowrates and compositions of intermediate and output streams can be viewed by revisiting the input/output dialog windows of each stream (double click on a stream line or click with the right mouse button and select **Simulation Data…).** In addition, a report containing information on raw material requirements, stream compositions and flowrates, as well as an overall material balance, can be generated by selecting the **Tasks: Generate Stream Report (SR)...** option from the main menu. The resulting report can be viewed by selecting the **View: Stream Report** option of the main menu. Tables 2.3a,b, and c display portions of the stream report. These tables were extracted from the spreadsheet version of the Stream Report, which was generated by selecting **File : Export Reports to Excel**. They were then edited in Excel and pasted into SuperPro as a MS Excel worksheet.

Table 2.3a: Overall Process Data

Annual Operating Time	7894.03	h
Annual Throughput	11471.02	kg MP
Batch Throughput	85.60	kg MP
Plant Batch Time	150.61	h
Effective Plant Batch Time	58	h
Number of Batches Per Year	134	

MP = Main Product

Table 2.3b: Starting Material Requirements

Section Name	Starting Material	Active Product	Gross Yield (%)	Amt Needed kg Sin/kg MP
Fermentation Section	Glucose	Biomass	41.78	71.04
Primary Recovery Section	Biomass	B-Gal	4.47	29.68
Purification Section	B-Gal	B-Gal	75.41	1.33

Table 2.3c: Raw Material Requirements – Entire Flowsheet

Raw Material	kg/Year	kg/Batch	kg/kg MP
Water	8,576,000	64,000	747.62
Glucose	823,162	6,143	71.76
Salts	137,484	1,026	11.99
Ammonia	52,930	395	4.61
WFI	31,972,920	238,604	2,787.28
Tris Buffer	25,258,405	188,496	2,201.93
NaCl (0.1 M)	20,692,755	154,424	1,803.92
NaOH (0.5 M)	12,761,902	95,238	1,112.54
NaCl (0.5 M)	1,806,727	13,483	157.50
Flowsheet Total	**102,082,285**	**761,808**	**8,899.15**

Scheduling and Equipment Utilization

SuperPro generates **Operations** and **Equipment Gantt charts** for single and multiple batches. Figure 2.3e displays a portion of the operations Gantt chart for a single batch of this example process.

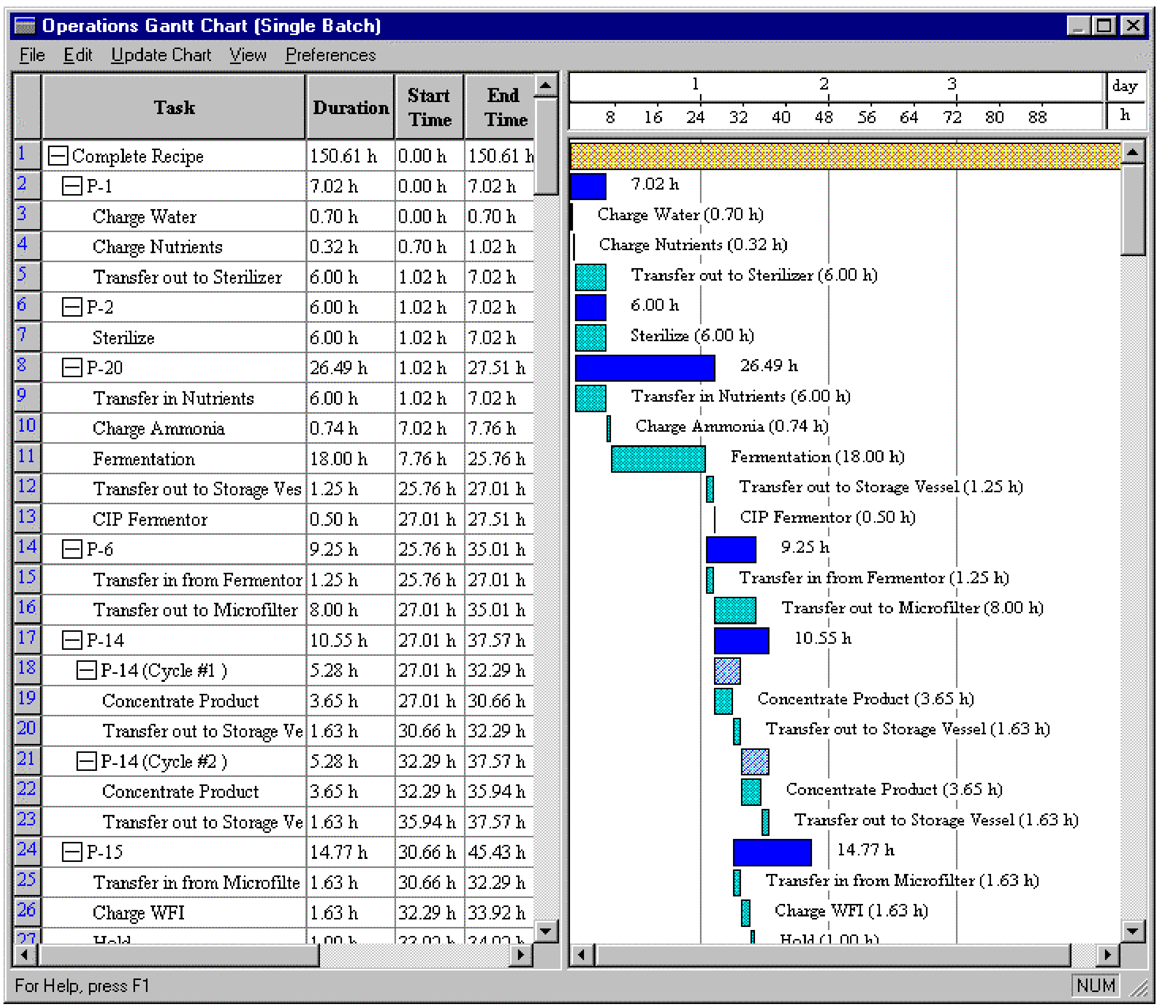

Figure 2.3e: Operations Gantt Chart for a Single Batch.

The left view (spreadsheet view) displays the name, duration, start time, and end time for each activity (e.g. each operation, unit procedure, cycle, batch, etc). You can use the left view to expand or collapse the activity summaries by clicking on the + or – signs in the boxes to the left of the activity names.

The right view (chart view) displays a bar for each activity in the overall process recipe. To edit the scheduling data (or any other data affecting an activity), simply right-click on a bar and a relevant command menu will appear. Selecting the uppermost entry on this menu will bring up a dialog that will allow you to edit the information associated with that particular activity bar. In fact, anything you can accomplish with the other scheduling interfaces, you can also accomplish from the Gantt chart interface. Furthermore, you can redo the M&E balances and have the Gantt Chart updated to reflect the new (calculated) scheduling settings for the recipe by clicking on the Update Chart entry in the main menu of the interface.

Another way of visualizing the execution of a batch process as a function of time is through the Equipment Occupancy chart (select **View : Equipment Occupancy Chart**). Figure 2.3f displays the equipment occupancy chart for two consecutive batches of this example process. Multiple bars on the same line (e.g., for V-101, V-102, V-103, and UF-101) represent reuse (sharing) of equipment by multiple procedures. White space represents idle time. The equipment with the least idle time between consecutive batches is the **time (or scheduling) bottleneck** (C-101 in this case) that determines the maximum number of batches per year. Its occupancy time (approximately 56 hours) is the minimum possible time between consecutive batches (also known as Min. Effective Plant Batch Time). The actual time between consecutive batches (also known as Effective Plant Batch Time) is approximately 58.2 hours. The plant batch time (the time required to complete a single batch) is roughly 150 hours.

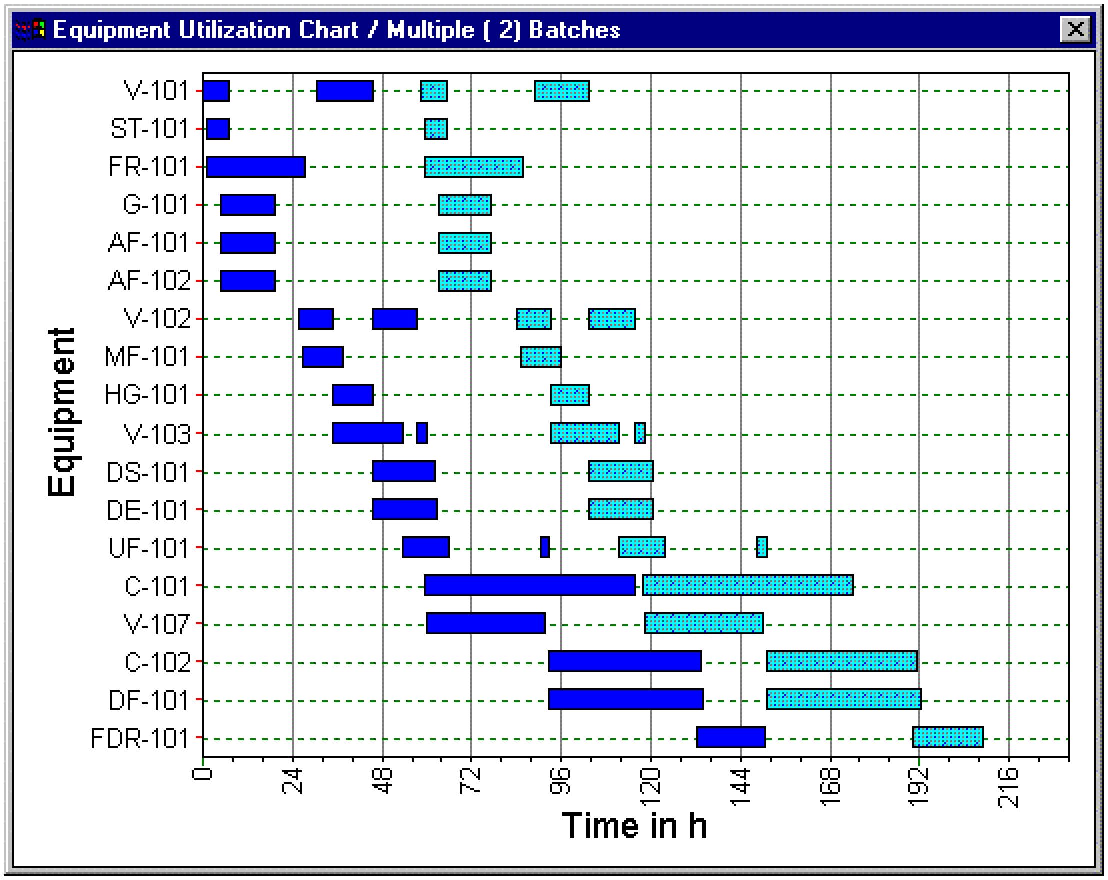

Figure 2.3f: Equipment Occupancy Chart (two consecutive batches).

SuperPro also generates occupancy charts for auxiliary equipment, such as clean-in-place (CIP) and steam-in-place (SIP) skids.

Tracking of Resource Demand and Inventory

SuperPro Designer calculates and displays graphically the demand for resources, such as heating and cooling utilities, power, labor, and raw materials. To view these graphs, select **View: Resource Chart**, and then choose the desired resource from the drop-down menu. Figure 2.3g displays the water for injection (WFI) demand graph for three consecutive batches. The red lines (spikes) represent the instantaneous demand, the blue line represents the averaged demand (averaged over a period of a day), and the green line represents the cumulative demand and corresponds to the y-axis on the right hand side. If you move the cursor close to the peak of a red line, SuperPro displays the operations that create that peak.

Notes:

1) To change the number of batches, right-click on the chart and select **Set Number of Batches**.
2) To change the contents (variables displayed) and the style (e.g., color, thickness, etc.) of the various lines, right-click on the chart and select Edit Style.
3) To print the chart, right-click, select Copy, and then paste the contents of the clipboard into any MS Office application (e.g., Powerpoint, Excel, Word). You may even paste

the clipboard contents into SuperPro itself. To print the chart along with its window frame, press “Alt + PrtSc” when the window is active and then follow the above strategy.

4) The demand data for a resource may also be exported into a file in Excel format with a discretization time interval that can be specified by the user. This is a useful feature if you wish to combine in Excel demand for a certain resource from multiple flowsheets.

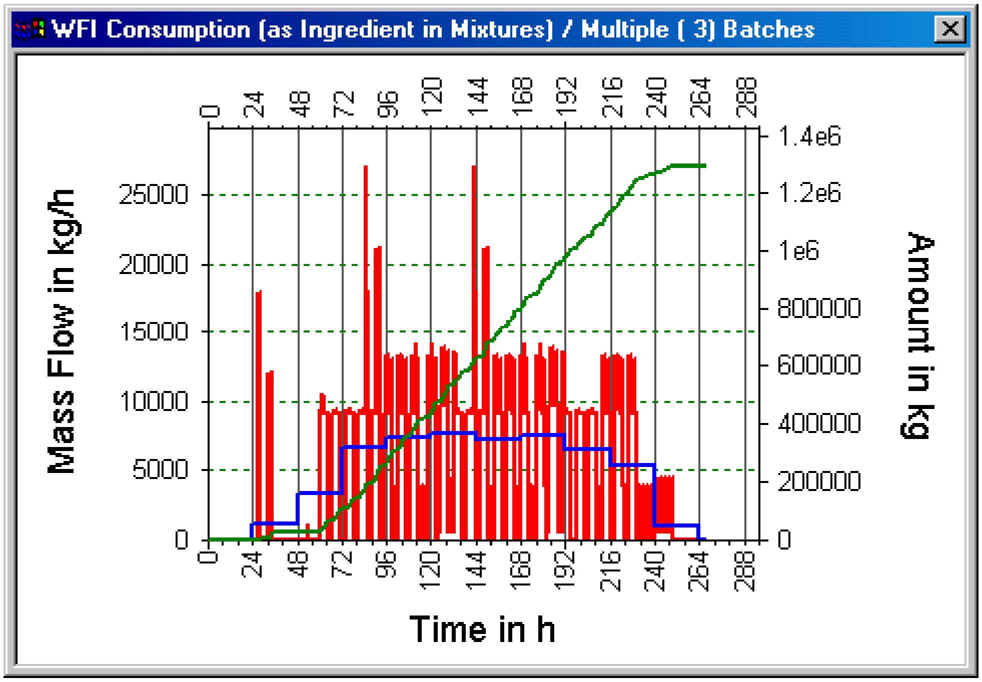

Figure 2.3g: WFI Demand Chart (three consecutive batches).

SuperPro can also analyze and display inventory information for material resources and utilities. Suppose there is a 30,000 kg WFI storage tank. Suppose further that the WFI still has a rate of 15,000 kg/h and it is turned on when the level in the tank drops below 30% and on when it exceeds 85%. To visualize the liquid level in the tank for a single batch, do the following.

Select the menu item **View \ Resource Inventory Chart \ Ingredient**. Select ‘WFI’ and select the **Supply Info** button. Fill out the dialog as shown in Figure 2.3h. Then click OK and on the next dialog click OK again. This will bring up the graph of Figure 2.3i that shows the WFI level in the storage tank. This graph and the associated calculations are very useful in judiciously sizing WFI stills and storage tanks.

Notes:

1) The inventory graph by default displays the inventory level, the rate of supply, and the inventory limit. To change the contents of the graph, right click on the graph and select Edit Style.
2) If you wish to print the chart or export its data in Excel format, please read the notes for resource demand tracking.

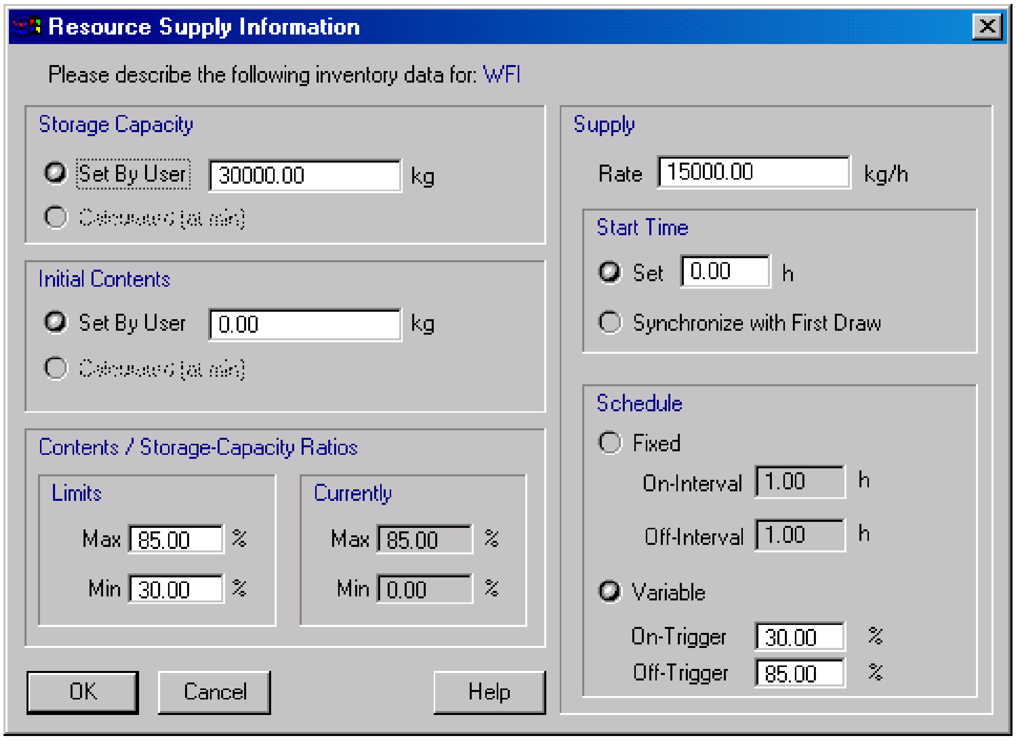

Figure 2.3h: The resource supply info dialog.

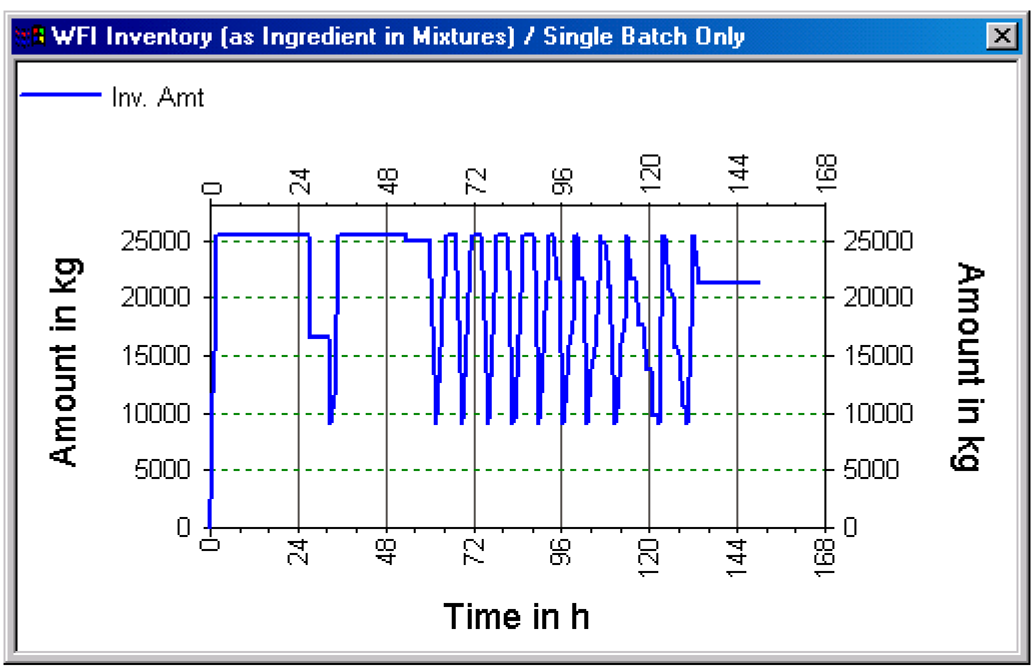

Figure 2.3i: WFI liquid level in its storage tank during a single batch.

Throughput Analysis and Debottlenecking

SuperPro is equipped with powerful throughput analysis and debottlenecking capabilities. The objective of these features is to allow the user to quickly and easily analyze the capacity and time utilization of each piece of equipment, and to identify opportunities for increasing throughput with the minimum possible capital investment. For a detailed throughput analysis example, please see Chapter 9 or search for Debottlenecking in the Help Facility.

Select **View: Throughput Analysis Charts** to view the utilization and throughput potential charts. Both charts indicate that procedure 19 in chromatography column C-101 is the bottleneck. It has the highest combined utilization and the lowest throughput potential.

2.3.4 Cost Analysis and Economic Evaluation

Several different economic reports can be generated from SuperPro Designer. To view the essential economic evaluation results for the whole process, please select **View: Executive Summary**. You will need to generate the **Economic Evaluation Report** (EER) and the **Itemized Cost Report** (ICR) if you wish to view the detailed results. Portions of the EER and ICR appear on the following pages. For more information on the economic evaluation calculations, please consult Chapter 8.

The Economic Evaluation Report (EER)

This report provides information on the capital investment and operating costs for the entire flowsheet. It also includes profitability and cash-flow analysis tables. Additional cost data, broken down per section, is available in the Itemized Cost Report (which follows the EER tables).

To generate the EER, select **Tasks: Generate Economic Evaluation Report**. To view it, select **View: Economic Evaluation Report**. Like the stream report, the economic evaluation report is a text file which may be read by a variety of text editors and word processors. The same report (like any other report) can also be generated in spreadsheet format by selecting **File: Export Reports to Excel.** The EER for the β-Galactosidase design case begins on the next page.

Economic Evaluation Report (EER) for the "BGal4_7b" Design File

The EER provides summaries and detailed breakdowns of various factors which affect the overall capital investment and the operating cost. Additional cost data, broken down per section, are available in the Itemized Cost Report (which follows the EER tables).

```
EXECUTIVE SUMMARY (1999 prices)
=============================================================================
 TOTAL CAPITAL INVESTMENT                      63386000  $
 CAPITAL INV. CHARGED TO THIS PROJECT          63386000  $
 OPERATING COST                                34922000  $/year

 PRODUCTION RATE                                  11538  kg/year of B-Gal (in Product)

 UNIT PRODUCTION COST                              3027  $/kg of B-Gal (in Product)

 TOTAL REVENUES                                63462000  $/year

 GROSS MARGIN                                     44.97  %
 RETURN ON INVESTMENT                             35.84  %
 PAYBACK TIME                                      2.79  years
 IRR AFTER TAXES                                  24.14  %

 NPV (at 7.0 % interest)                       79127000  $
=============================================================================


MAJOR EQUIPMENT SPECIFICATION AND FOB COST (1999 prices)
===========================================================================
 Quantity/        Description                          Unit Cost      Cost
 Stand-by                                                ( $ )       ( $ )
---------------------------------------------------------------------------

   1/0  ST-101    Heat Sterilizer                        361000      361000
                  Diameter = 7.50 m
                  Length   = 5.55 m

   1/0  V-101     Blending Tank                          287000      287000
                  Volume   = 80000.00 L
                  Diameter = 3.24 m

   1/0  G-101     CF Compressor                          188000      188000
                  Power = 235.52 kW

   1/0  AF-101    Air Filter                               4000        4000
                  Rated Throughput = 0.13 m^3/s
```

***** To keep this manual concise, most of the equipment listed in the EER was deleted from this table. If you wish to see the entire table, please open the BGal4_0b.spf example and generate the EER. *****

```
   2/0  FDR-101   Freeze Dryer                          1491000     2982000
                  Tray Area = 6.01 m2
                  Capacity  = 453.08 kg H2O/cycle

                  Cost of Unlisted Equipment                        1989000

===========================================================================
 TOTAL EQUIPMENT PURCHASE COST                                      9946000
===========================================================================
```

Economic Evaluation Report (continued)

```
FIXED CAPITAL ESTIMATE SUMMARY (1999 prices)
=================================================================

 A. TOTAL PLANT DIRECT COST (TPDC)  (physical cost)

  1. Equipment Purchase Cost               $        9946000
  2. Installation                                   3347000
  3. Process Piping                                 3481000
  4. Instrumentation                                3978000
  5. Insulation                                      298000
  6. Electricals                                     995000
  7. Buildings                                      4476000
  8. Yard Improvement                               1492000
  9. Auxiliary Facilities                           3978000
                                   ------------------------
                                       TPDC =      31992000

 B. TOTAL PLANT INDIRECT COST (TPIC)

  10. Engineering                                   7998000
  11. Construction                                 11197000
                                   ------------------------
                                       TPIC =      19195000

 C. TOTAL PLANT COST (TPDC+TPIC)        TPC =      51186000

  12. Contractor's fee                              2559000
  13. Contingency                                   5119000
                                   ------------------------
                                    (12+13) =       7678000

=================================================================
 D. DIRECT FIXED CAPITAL (DFC)     TPC+12+13 =      58864000
=================================================================
```

LABOR REQUIREMENT AND COST SUMMARY

Section Name	Labor Hours Per Year	Labor Cost $/year	%
Fermentation Secti	12689	759000	18.86
Primary Recovery S	24521	1466000	36.44
Purification Secti	30085	1799000	44.71
TOTAL	67295	4024000	100.00

Economic Evaluation Report (continued)

RAW MATERIALS COST SUMMARY

Raw Material	Unit Cost ($/kg)	Annual Amount (kg)	Cost ($/yr)	%
Process Water	0.010	8576000.00	85760	0.67
Glucose	1.000	823162.00	823162	6.48
Salts	1.600	137484.00	219974	1.73
Ammonia	0.500	52930.00	26465	0.21
WFI	0.100	31972978.25	3197298	25.16
Tris Buffer	0.150	25258404.94	3788761	29.82
NaCl (0.1 M)	0.130	20692755.04	2690058	21.17
NaOH (0.5 M)	0.120	12761902.29	1531428	12.05
NaCI (0.5 M)	0.190	1806726.64	343278	2.70
TOTAL		102082343.16	12706000	100.00

VARIOUS CONSUMABLES (1999 prices)

MEMBRANE or FILTER CLOTH

Procedure Name	Equipment Name	Unit Cost ($/m^2)	Annual Amount (m^2)	Cost ($/yr)
P-9	DE-101	12.00	26800.00	322000
P-10	UF-101	200.00	133.64	27000
P-12	DF-101	250.00	41.51	10000
P-13	UF-101	200.00	26.37	5000
P-14	MF-101	200.00	169.68	34000
SUBTOTAL				398000

CHROMATOGRAPHY RESINS

Procedure Name	Equipment Name	Unit Cost ($/L)	Annual Amount (L)	Cost ($/yr)
P-11	C-102	200.00	17540.56	3508000
P-19	C-101	200.00	8419.47	1684000
SUBTOTAL				5192000
TOTAL				5590000

Economic Evaluation Report (continued)

WASTE TREATMENT / DISPOSAL (1999 prices)

a. SOLID WASTE

Stream Name	Unit Cost ($/kg)	Annual Amount (kg)	Cost ($/yr)
	a. Subtotal (Solid Waste)		0

b. LIQUID WASTE

Stream Name	Unit Cost ($/kg)	Annual Amount (kg)	Cost ($/yr)
Debris 2	1.000e-002	202075.82	2000
Liq Waste 2	1.000e-002	3392864.25	34000
Liq Waste 6	1.000e-002	1337718.30	13000
Liq Waste 5	1.000e-002	20538100.51	205000
Liq Waste 1	1.000e-002	4692478.85	47000
Debris 1	1.000e-002	68857.43	1000
Liq Waste 4	1.000e-002	519741.94	5000
	b. Subtotal (Liquid Waste)		307000

c. EMISSIONS

Stream Name	Unit Cost ($/kg)	Annual Amount (kg)	Cost ($/yr)
	c. Subtotal (Emissions)		0

WASTE TREATMENT/DISPOSAL TOTAL COST (a+b+c)	308000

Economic Evaluation Report (continued)

UTILITY REQUIREMENTS (1999 prices)

ELECTRICITY

Procedure Name	Equipment Name	Annual Amount (kWh)	Cost ($/yr)
P-3	G-101	441838	44184
P-7	HG-101	313002	31300
P-10	UF-101	33905	3391
P-12	DF-101	23370	2337
P-13	UF-101	10338	1034
P-14	MF-101	46894	4689
P-20	FR-101	498986	49899
P-21	DS-101	40512	4051
P-22	FDR-101	25750	2575
Unlisted Equipment		89662	8966
General Load		268987	26899
SUBTOTAL			179324

HEAT TRANSFER AGENT : Steam (0.2800 $/1000 kg)

Procedure Name	Equipment Name	Annual Amount (kg)	Cost ($/yr)
P-2	ST-101	748680	210
P-22	FDR-101	259044	73
SUBTOTAL			282

HEAT TRANSFER AGENT : Cooling Water (0.0250 $/1000 kg)

Procedure Name	Equipment Name	Annual Amount (kg)	Cost ($/yr)
P-2	ST-101	52970262	1324
SUBTOTAL			1324

HEAT TRANSFER AGENT : Chilled Water (0.1750 $/1000 kg)

Procedure Name	Equipment Name	Annual Amount (kg)	Cost ($/yr)
P-3	G-101	38722304	6776
P-7	HG-101	67628398	11835
P-10	UF-101	621337	109
P-12	DF-101	377116	66
P-13	UF-101	1681399	294
P-14	MF-101	23112113	4045
P-20	FR-101	394140398	68975
P-21	DS-101	6973328	1220
SUBTOTAL			93320

TOTAL	272644

Economic Evaluation Report (continued)

ANNUAL OPERATING COST - SUMMARY (1999 prices)

Cost Item	$/Year	%
Raw Materials	12706000	36.38
Labor-Dependent	4024000	11.52
Equipment-Dependent	11097000	31.78
Laboratory/QC/QA	925000	2.65
Consumables	5590000	16.01
Waste Treatment/Disposal	308000	0.88
Utilities	273000	0.78
Transportation	0	0.00
Miscellaneous	0	0.00
Advertising and Selling	0	0.00
Running Royalties	0	0.00
Failed Product Disposal	0	0.00
TOTAL	34922000	100.00

PROFITABILITY ANALYSIS (1999 prices)

A. DIRECT FIXED CAPITAL	$ 58864000
B. WORKING CAPITAL	1578000
C. STARTUP COST	2943000
D. UP-FRONT R&D	0
E. UP-FRONT ROYALTIES	0
F. TOTAL INVESTMENT (A+B+C+D+E)	63386000
G. INVESTMENT CHARGED TO THIS PROJECT	63386000
H. REVENUE STREAM FLOWRATES	
kg/year of B-Gal (in Product)	11538
I. PRODUCTION (UNIT) COST	
$/kg of B-Gal (in Product)	3026.576
J. SELLING/PROCESSING PRICE	
$/kg of B-Gal (in Product)	5555.556
K. REVENUES ($/year)	
Product	63462000
L. ANNUAL OPERATING COST	34922000
M. GROSS PROFIT (K-L)	28540000
N. TAXES (40 %)	11416000
O. NET PROFIT (M-N + Depreciation)	22716000
GROSS MARGIN	44.97 %
RETURN ON INVESTMENT	35.84 %
PAYBACK TIME (years)	2.79

Economic Evaluation Report for the Design File "BGal4_7b" (cont.)

CASH FLOW ANALYSIS (thousand US $)

YR	CAPITAL INVESTM	DEBT FINANCE	SALES	OPERAT. COST	GROSS PROFIT	LOAN PAYMENT	DEPREC	TAXABLE INCOME	TAXES	NET PROFIT	NET CASH FLOW
1	-17659	0	0	0	0	0	0	0	0	0	-17659
2	-23546	0	0	0	0	0	0	0	0	0	-23546
3	-19238	0	23798	22444	1354	0	5592	0	0	1354	-17884
4	0	0	63462	34649	28812	0	5592	23220	9288	19524	19524
5	0	0	63462	34649	28812	0	5592	23220	9288	19524	19524
6	0	0	63462	34649	28812	0	5592	23220	9288	19524	19524
7	0	0	63462	34649	28812	0	5592	23220	9288	19524	19524
8	0	0	63462	34649	28812	0	5592	23220	9288	19524	19524
9	0	0	63462	34649	28812	0	5592	23220	9288	19524	19524
10	0	0	63462	34649	28812	0	5592	23220	9288	19524	19524
11	0	0	63462	34649	28812	0	5592	23220	9288	19524	19524
12	0	0	63462	34649	28812	0	5592	23220	9288	19524	19524
13	0	0	63462	34649	28812	0	0	28812	11525	17287	17287
14	0	0	63462	34649	28812	0	0	28812	11525	17287	17287
15	4521	0	63462	34649	28812	0	0	28812	11525	17287	21809

IRR BEFORE TAXES	34.453	%	INTEREST	7.00%	9.00%	11.00%
IRR AFTER TAXES	24.141	%	NPV	79127	62518	48808

Depreciation Method: Straight-Line

DFC Salvage Factor 0.05

Itemized Cost Report (ICR) for the "BGal4_7b" Design File

The Itemized Cost Report (ICR) provides detailed operating cost data, broken down per flowsheet section and cost item. It enables the user to readily identify the cost sensitive sections of a process – the economic hot-spots. For instance, a quick look at the following tables reveals that the Purification section is the most expensive part of this process. In particular, raw materials and equipment contribute large amounts to the overall expense of the project. Thus it would be wise to allocate resources to optimize this section, as opposed to using those same resources elsewhere where optimization would have little effect on the overall project cost. A look back at the Economic Evaluation Report reveals the cost of each individual piece of equipment, as well as the costs for installation, piping, instrumentation, etc. The user should look at each of these expenses to ensure they are accurate for their particular application. For instance, if no auxiliary facilities need to be constructed, or if the required freeze dryers can be shared with another process, the overall cost will be significantly reduced. Another potential "economic hotspot" is the high cost of raw materials, notably the WFI and buffer solutions. Perhaps the quantities of these materials could be reduced.

The above analysis shows how the economic reports can be used not only for estimation of the total cost of a process, but also as a tool to optimize the process through "what-if" scenarios. Would it make economic sense to use a less expensive chromatography resin if it required more cycles to be run and more buffer solution to be used? It depends on how many more cycles are needed, and how much cheaper the new resin is. Would a radically modified purification scheme be better than the current scheme? It depends on what equipment, reagents, etc. would be required for the modified purification, and what the overall yield of the product would be. This type of what-if analysis is quick and easy to perform using SuperPro Designer.

To generate the Itemized Cost Report, select **Tasks: Generate Itemized Cost Report (ICR)**. To view the report, select **View: Itemized Cost Report**. A portion of the Itemized Cost Report for the β-galactosidase case follows.

Itemized Cost Report (continued)

```
FLOWSHEET PARAMETERS
=======================================================
 Operating Time             =       7897 (h/yr)
 Main Product Rate          =      11538 (kg/yr)
 Plant Batch Time           =        151 (h)
 Effective Plant Batch Time =         58 (h)
 Number of Batches Per Year =        134
=====================================================================
```

```
COST PER FLOWSHEET SECTION (1999 prices)
=====================================================================

 SECTIONS IN:       Main Branch

 Fermentation Section   Sin = Glucose           Aout = Biomass
----------------------------------------------------------------------
 Cost Item              $/kg MP      $/Batch       $/Year      %
----------------------------------------------------------------------
 Raw Materials          100.131         8622      1155361    26.78
 Equipment              170.935        14719      1972330    45.72
 Labor                   65.761         5663       758781    17.59
 Consumables              0.000            0            0     0.00
 Lab/QC/QA               20.323         1750       234500     5.44
 Waste Trtm/Disp          0.000            0            0     0.00
 Utilities               16.757         1443       193354     4.48
 Transportation           0.000            0            0     0.00
 Miscellaneous            0.000            0            0     0.00
----------------------------------------------------------------------
 Section Total          373.908        32196      4314326   100.00
----------------------------------------------------------------------

 Primary Recovery Section   Sin = Biomass           Aout = B-Gal
----------------------------------------------------------------------
 Cost Item              $/kg MP      $/Batch       $/Year      %
----------------------------------------------------------------------
 Raw Materials           20.394         1756       235313     4.85
 Equipment              198.141        17062      2286242    47.17
 Labor                  127.086        10943      1466384    30.25
 Consumables             33.130         2853       382265     7.89
 Lab/QC/QA               27.872         2400       321600     6.64
 Waste Trtm/Disp          7.242          624        83563     1.72
 Utilities                6.196          534        71498     1.48
 Transportation           0.000            0            0     0.00
 Miscellaneous            0.000            0            0     0.00
----------------------------------------------------------------------
 Section Total          420.061        36171      4846864   100.00
----------------------------------------------------------------------

 Purification Section   Sin = B-Gal             Aout = B-Gal
----------------------------------------------------------------------
 Cost Item              $/kg MP      $/Batch       $/Year      %
----------------------------------------------------------------------
 Raw Materials          980.676        84444     11315510    43.93
 Equipment              592.659        51033      6838385    26.55
 Labor                  155.921        13426      1799086     6.98
 Consumables            451.330        38863      5207657    20.22
 Lab/QC/QA               31.937         2750       368500     1.43
 Waste Trtm/Disp         19.409         1671       223956     0.87
 Utilities                0.675           58         7793     0.03
 Transportation           0.000            0            0     0.00
 Miscellaneous            0.000            0            0     0.00
----------------------------------------------------------------------
 Section Total         2232.607       192245     25760886   100.00
----------------------------------------------------------------------
```

Itemized Cost Report (continued)

SUMMARY (Entire Flowsheet)

Cost Item	$/kg MP	$/Batch	$/Year	%
Raw Materials	1101.201	94822	12706184	36.38
Equipment	961.735	82813	11096956	31.78
Labor	348.768	30032	4024251	11.52
Consumables	484.459	41716	5589922	16.01
Lab/QC/QA	80.132	6900	924600	2.65
Waste Trtm/Disp	26.652	2295	307518	0.88
Utilities	23.629	2035	272644	0.78
Transportation	0.000	0	0	0.00
Miscellaneous	0.000	0	0	0.00
Flowsheet Total	3026.576	260613	34922076	100.00

Sin = Section Starting Material
Aout = Section Active Product
MP = Main Product (of the entire flowsheet)

BREAKDOWN PER COST ITEM AND SECTION

Cost Item	Fermentatio $/year	Primary Rec $/year	Purificatio $/year	Subtotal $/year	%
Raw Materials	1155361	235313	11315510	12706184	36.38
Equipment	1972330	2286242	6838385	11096956	31.78
Labor	758781	1466384	1799086	4024251	11.52
Consumables	0	382265	5207657	5589922	16.01
Lab/QC/QA	234500	321600	368500	924600	2.65
Waste Trt/Dsp	0	83563	223956	307518	0.88
Utilities	193354	71498	7793	272644	0.78
Transportation	0	0	0	0	0.00
Miscellaneous	0	0	0	0	0.00
Subtotal	4314326	4846864	25760886	34922076	100.00
Contribution (%)	12.35	13.88	73.77	100.00	

RAW MATERIALS COST BREAKDOWN (Values in $/year)

Raw Material	Fermentation	Primary Recov	Purification	Subtotal	%
Process Water	85760	0	0	85760	0.67
Glucose	823162	0	0	823162	6.48
Salts	219974	0	0	219974	1.73
Ammonia	26465	0	0	26465	0.21
WFI	0	235313	2961984	3197298	25.16
Tris Buffer	0	0	3788761	3788761	29.82
NaCl (0.1 M)	0	0	2690058	2690058	21.17
NaOH (0.5 M)	0	0	1531428	1531428	12.05
NaCI (0.5 M)	0	0	343278	343278	2.70
TOTAL	1155361	235313	11315510	12706184	100.00
Contribution (%)	9.09	1.85	89.06	100.00	

2.3.5 The Environmental Impact Report (EIR)

The Environmental Impact Report provides information on the amount and type of waste generated by a manufacturing or waste treatment facility. It also provides information on the fate of a compound that enters an integrated manufacturing or waste treatment facility. To create the environmental impact report select **Tasks: Generate Environmental**

Impact Report (EIR). To view this report, select **View: Environmental Impact Report**.

2.3.6 Product Formulation and Packaging

SuperPro Designer contains a variety of formulation, packaging, and transportation unit procedures in order to capture the cost associated with such processes.

Entities

Most material flows in SuperPro designer are *bulk material* flows. Discrete parts (e.g. bottles or boxes) are termed entities. A discrete operation converts a bulk stream into and entity stream (e.g. bulk liquid product to filled bottles) or one entity stream to another (e.g. unlabeled bottles to labeled bottles). Discrete procedures may be placed on the flowsheet and connected like any other procedure. Connection points for entity streams are indicated by an open connection point.

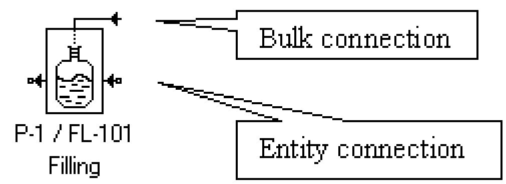

Figure 2.3f Bulk and Entity Connections

To familiarize yourself with the formulation and packaging models and the concepts of discrete streams and entities, please open the **BGal5_0c.spf** design case in the EXAMPLES\BGAL folder and visit the simulation data dialog windows of those operations. As usual, you can open these dialogs by right clicking on the various packaging unit procedure icons and their corresponding streams. Notice the different interface of discrete streams, which display the flow of discrete entities as well as the equivalent bulk flow (based on the bulk ingredients that compose the discrete entities). For more information on discrete streams and entities, please consult the Help Facility.

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