Proceedings of the 2006 Winter Simulation Conference
L. F. Perrone, F. P. Wieland, J. Liu, B. G. Lawson, D. M. Nicol, and R. M. Fujimoto, eds.

DISCRETE EVENT SIMULATION FOR BATCH PROCESSING

. Craig W. Alexander

Monsanto
1788 Lovers Lane
Augusta, GA 30901, U.S.A

ABSTRACT

This paper presents the modeling of batch processes using discrete event simulation. Discrete event simulation is often used for transactional-based processes; however, this paper describes an example of representing each batch as a single transaction in order to model process cycle time and utility usage. An example is provided to demonstrate the use of this method for simulating water-for-injection usage in a biopharmaceutical process.

1 INTRODUCTION

Chemical and pharmaceutical manufacturing processes are often simulated to investigate proposed process changes or to better understand process dynamics. This simulation may be performed using rigorous mathematical models to simulate chemical reactions, heat transfer, or fluid flow in the system. However, the plant engineer is usually most concerned with evaluating cycle time and the timing interactions between various phases of the process. This analysis is often performed to consider the effects of proposed process improvements on the overall cycle time of the manufacturing facility. The impact of new changes on utility usage is also of interest.

Manufacturing engineers often investigate cycle time using static methods such as Microsoft® Project or Microsoft® Excel to lay out the batch sequencing and scheduling. This paper considers discrete event simulation as a method of evaluating overall batch cycle time including interactions over time. An example is presented that evaluates the effects of proposed batch sequence improvements on an existing water-for-injection (WFI) system. The simulation allows the user to identify the best path forward for meeting the increased demand on this critical utility.

2 DISCRETE EVENT SIMULATION

Simulation is the process of building a model of a real or proposed system to study the performance of the system under specific conditions. Simulation is especially powerful because it allows the observation of the behavior of the model as time progresses (Ball 2001). Process bottlenecks and delays can be identified so that cost-effective alternatives can be investigated (Hwang 1997). Most importantly, process simulation can be used without affecting the existing production activities (Micrografx 2001).

Manual analysis of batch process cycle time can quickly grow complex as multiple consecutive batches are introduced. There are many variables that affect the process including batch size and resource constraints (Hwang 1997). Discrete event simulation is a method of creating a model that can observe the time-based, dynamic behavior of a system (Ball 2001). Discrete event simulation differs from continuous simulation in that significant changes occur at discrete time intervals (Park and Leemis). This characteristic lends itself to the study of batch processing systems where the batch cycle time sets the discrete intervals.

The major components of a simulation are entities, logical relationships, and the simulation executive (Ball 2001).

Entities represent tangible things found in the production environment such as a vessel or a clean-in-place skid. The iGrafx® software used for the example in this paper refers to these entities as "resources" (Ball 2001). Entities also can represent the transactions in the process. These entities are then the users of the system resources (Schriber and Brunner 2005). The transactions in the example for this paper represent batches of product sequencing through equipment (resources).

Logical relationships define how the entities relate to each other in time. These relationships can be expressed either as constant time or as a mathematical expression. (Ball 2001) Resource capacity constraints can also lead to delays in the process as transactions compete for resource availability (Schriber and Brunner 2005).

The simulation executive is responsible for managing the simulation time. Note that time in the simulation is not necessarily linear. The simulation time will slow down or speed up depending on the computational activity during a time slice (Ball 2001). The simulation executive will perform all operations that take place at a given simulation time before advancing the simulation clock. This simulation time will not correspond to the wall-clock time (Schriber and Brunner 2005).

A simulation does not provide a 100% realistic duplication of the actual process. Computer simulation can generate large amounts of data that can lead to a false sense of security in the numbers (Ball 2001). It is critical to clearly note all assumptions and unknowns that are included in the model development. Since the model starts in an idle state, simulation performance can also be affected by the "run-in" phase as the model "loads up" to approach the steady state phase (Ball 2001). It is very important to calibrate each model to make sure it produces results that are close to reality before running simulation cases to predict future process performance (Domanski 1999).

There are various ways to implement a process simulation including high-level computer languages, spreadsheets, or simulation software applications. The example in this paper was implemented in *iGrafx® Process™ 2003 for Six Sigma* from the Corel Corporation. This software allows the simulation to be built as a flow chart with each block in the flow chart representing a task or decision. Each block has a series of forms that allow the user to create the logical relationships and enter parameters necessary to define the model. The software includes animation that allows the process to be tracked during the simulation run. Built-in reports are included, and custom reports can be built to track desired parameters. The software package includes a number of interfaces to other programs to assist in analyzing simulation results.

3 EXAMPLE SIMULATION

This paper considers an example simulation that was part of a Six Sigma project to improve WFI availability. During the Measure phase of the project, it was noted that the current WFI availability was demonstrating a high level of performance. Since the current performance was meeting the needs of the present production requirements, the project focus shifted to WFI performance under future manufacturing needs.

Future WFI performance was of concern because the downstream production area of the plant was just coming on-line. This area is a significant user of WFI, and sustained operation had yet to be demonstrated. The second area of concern is that the plant was budgeted for increased production rates over the next few years. WFI demand is expected to increase dramatically as production increases.

Simulation was the obvious choice for evaluating WFI capability to meet future needs. Since part of the manufacturing process was not yet continuously on-line, the increased demand could not be demonstrated in real time. Furthermore, physical and logical changes are required in the existing manufacturing area to realize increased production rates. Simulation is necessary to evaluate the effect on WFI demand since these changes are not yet in place. WFI is critical to current production rates, so experimentation with the existing system is discouraged. Simulation allows experimentation with no risk of negatively impacting production.

4 WFI USAGE MODEL DEVELOPMENT

To be effective, a simulation must be developed and used in a methodical way. One approach to simulation development is:

1. Project Definition
2. Process Mapping (static diagram)
3. Simulation Model (dynamic)
4. Verification
5. Validation
6. Simulation of cases for study
7. Findings, conclusions, and recommendations (Watson 2004).

The first step in creating the simulation is to map out the process in block diagram format. Blocks are created for each major piece of equipment in the manufacturing process. Each unit can then be further broken down into the major activities, e.g. SIP, Operation, and CIP. Each of these blocks can then be split into WFI users or non-WFI users. Fig. 1 shows a portion of the block diagram developed in iGrafx to model the process users of WFI.

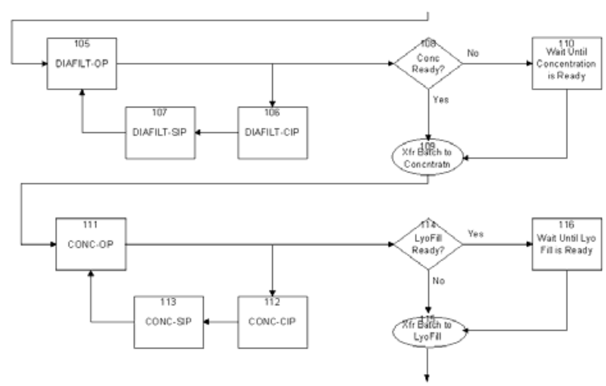

Figure 1: Portion of WFI Block Diagram

iGrafx® simulations are transaction-based. In my example, a batch is represented by a transaction moving through the model. Each non-WFI block is simply a time delay. The batch, or transaction, simply waits for a specified period of simulation time before proceeding to the next block. An attribute was created to set the WFI usage rate and length of usage for each shape that uses WFI.

WFI usage is modeled through the use of Scenario Attributes. A scenario attribute is a dynamic variable that can be updated by defined algorithms as the simulation proceeds. Parameters and storage registers that are to be available to any model block should be set up as scenario attributes. Parameters that are task-specific should be set up as transaction attributes. For example, the WFI storage tank level is stored in a scenario attribute called "WFI_Storage."

A sub-process is set up that is called by each WFI user as shown in Fig. 2. This sub-process calculates the amount of WFI used over a pre-defined period of simulation time. A separate sub-process is used to model the WFI still and generate WFI based on the level in the storage tank (also stored in a scenario attribute). These sub-processes add to or subtract from the scenario attribute WFI_Storage as appropriate to model the WFI system.

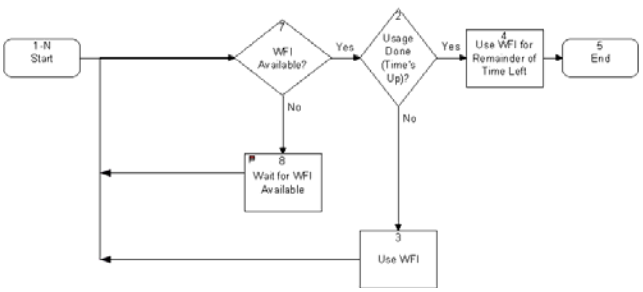

Figure 2: WFI Usage Sub-process Block Diagram

5 MODEL VERIFICATION AND VALIDATION

One of the key steps in simulation development is the verification and validation of the model. This is important both to make sure the model is behaving correctly as well as to increase the credibility of the model as cases are studied (Banks et al. 2005). Verification is concerned with the accuracy of creating a model from the problem specification. That is, "Did you build the model right?" Validation is the process of checking to see if the simulation behaves accurately and consistently to meet the study objectives. That is, "Did you build the right model?" (Ball 2001).

The first step in building a model is to collect data on the real system under consideration (Banks et al. 2005). For the example model being discussed here, we collected data from a number of sources. The upstream manufacturing process has a long run history, and the site electronic data historian has collected detailed data on every batch produced. Automatic reports are generated and archived to summarize the parameters for each batch. We gathered a series of representative batches and collected batch cycle times and WFI usage data from the reports. This data was summarized and statistically evaluated. In most cases, the mean value for each process step was used in the model with consideration given to parameters with large standard deviations as well as data from batches that had extraordinary circumstances that led to exceptionally long or short cycles.

We also collected data on the WFI generation system equipment. Some examples of data collected were modeling the curve for generation rate based on level as well as the maximum generation rate. We also collected storage tank levels for starting and shutting down the WFI still.

An important step in verifying a simulation model is to take advantage of the knowledge of persons most familiar with the real process (Banks et al. 2005). The initial model parameters were reviewed with manufacturing personnel from the upstream production area. These individuals verified that the selected parameters did indeed give a reasonable representation of the manufacturing process. Simulation runs were generated in order to evaluate the cycle times and production rates for this case. Manufacturing personnel carefully reviewed this data and adjustments were made to more closely simulate the real process.

Validation is an iterative process of comparing the model output to the actual system behavior. The discrepancies can then be used to adjust and improve the model (Banks et al. 2005). For the most part, the adjustments to the example model were minor and could be easily accounted for by the randomness seen in the real manufacturing process. The area process engineers were heavily involved in making sure the simulation outputs "looked right" based on their experience with the actual manufacturing process.

Verification of the downstream production process simulation was more challenging because only a limited number of batches have yet been manufactured. Furthermore, many of these batches were run more slowly than expected as personnel moved up the learning curve for the process and operating procedures were verified. Thus, the collection of data and verification of parameters relied more heavily on the subject-matter experts from the area than on historical data.

Once the parameter data was collected, the simulation output was compared to the data from process runs as well as the expectations of the manufacturing engineers. Several iterations were made until the simulation behavior closely resembled actual system performance.

6 ASSUMPTIONS

A number of assumptions were necessary when developing the simulation model and the case data for study.

- The simulation assumed a constant production yield.
- An on-stream time was included to represent the planned shutdown for maintenance activities by limiting the number of days that constituted a simulation year to less than 365.
- The WFI storage tank had the same initial level for each simulation run.

- The WFI generation equipment was assumed to run without an unplanned shutdown.

Another important factor in this simulation analysis is that the simulation was not randomized. All cases were run with fixed task times. The real process has variation due to equipment problems, human factors, and other unexpected delays. Since this simulation was being used in a predictive manner to look at WFI usage rather than predicted cycle times, I did not introduce randomness to the cycle times. We used best estimates for future cycle times and ran the batches back-to-back. This assumption simulates an aggressive demand for WFI.

A number of manufacturing process improvements that are under consideration were included in the model. These improvements will be necessary to achieve the desired production rates. Manufacturing personnel were able to agree on reasonable estimates for the expected cycle times after these changes are implemented. The model took these process changes into account for the simulation runs.

For the example simulation in this paper the effects of run-in are minimized by extending the run time to a full year. As the simulation run-time is extended, the steady-state performance has a larger impact on the statistical results. However, the run-in phase can add to the realism of the model. For example, many sites take one or more process shutdowns each year for maintenance, product changeover, or media fill testing. Since the process will restart from an idle state, the run-in phase for the model can be representative of the real world.

7 WFI SCENARIOS FOR CASE STUDIES

The purpose of this simulation study is to explore the impact of increased production rates on the ability of the WFI system to meet user demands. Several scenarios for upgrading the WFI system were proposed, but there was little information available to identify the best solution.

The first scenario for modifying the WFI system is to implement control logic changes to override the WFI Still output based on user demand. The WFI Still output flow is adjusted according to a linear algorithm based on level in the WFI storage tank. The proposed demand override algorithm will consider user demand flow in addition to the storage tank level.

Another proposal for upgrading the WFI system is to increase generation capacity. This option would add a second WFI generation system that could fill the existing storage tank. Two options were considered in the simulation study: the addition of a still with about half the output capacity of the existing still and the addition of an identical still to double WFI generation capacity.

The final option under consideration was the addition of a second storage tank for WFI. For this simulation study, the proposed storage tank was considered to be identical to the existing storage tank. For the purposes of simulation, the two tanks are treated as one large tank, which is equivalent to running the two tanks in parallel.

8 SIMULATION RESULTS

The comparison of alternative designs is one of the most important uses of simulation. The analysis of the data generated by the simulation can be used to predict the performance of the system under different conditions (Banks et al. 2005). The WFI Usage simulation was run for each of the WFI scenarios as described in the previous section.

The iGrafx® software used for this simulation can capture the value of a scenario attribute over the run of the simulation. The sampling rate is dependent on transaction activities. It is not a constant sampling frequency, but the number of data points roughly corresponds to one sample every two hours. Box plots of the storage tank level for each of the 5 runs are shown in Fig. 3.

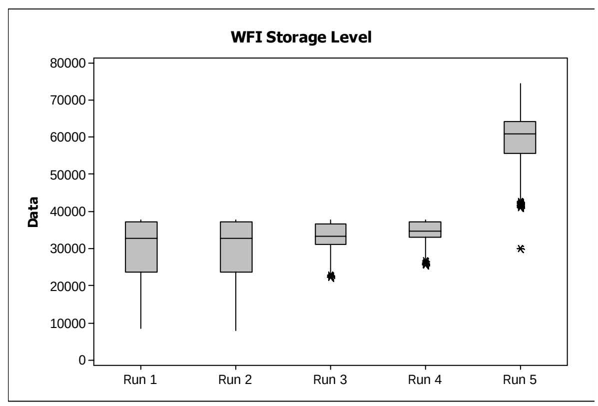

Figure 3: Box plot for WFI Upgrade Scenarios

Box plots are used to show the effects of attribute parameters on continuous data. Box plots show the percentiles of the continuous variable at each level of the discrete parameters. The plot is created by drawing a box with the top at the 75th percentile and the bottom at the 25th percentile. A line indicating the median value is then drawn in the box. Lines called "whiskers" are drawn above and below the box to indicate the extremes of the data (Hoerl and Snee 2002). Outliers are indicated by an asterisk. The formula for a box plot only allows the whiskers to be drawn to 1.5 times the range between the 25th and 75th percentiles (Six Sigma Academy 2002). Points outside this range are considered to be inconsistent with the rest of the data (Hoerl and Snee 2002).

Fig. 3 shows the box plots for each simulation run. Runs 1 & 2 use the existing WFI system with a demand override algorithm added for run 2. Note that each of these runs shows the worst level performance: both actual level measured and the lowest 25th percentile. These runs also show the greatest variation in level. This performance is clearly unacceptable since much of the data is below the alert level that leads to a manufacturing interruption. Further note that there is little difference in the data when the demand algorithm is added.

Runs 3 and 4 show data when additional WFI generation is added to the system. Run 3 represents the addition of a WFI still half the size of the existing still (150% generation capacity), while Run 4 is for the scenario of a second still identical in capacity to the existing still (200% generation capacity). The box plots indicate better performance when compared to the system with only the current WFI generation capacity. The upper end of the data remains the same since we are using the same storage volume. Note that the level never drops to the alert level. Even the outliers remain above this level. The level shows much less variation than for other cases. Interestingly there is no statistical difference between adding 50% or 100% new generation capacity. This validates the ultimate conclusion that more storage capacity is required to accommodate future production rates.

Run 5 represents the system with a 100% increase in storage tank capacity. The box plots for these runs clearly indicate a statistically significant advantage to this scenario. The outlier levels are due to the tanks filling from the initialization value. The level never approaches the alert level, so there is no danger of a process interruption. Note, also, that there is an improvement in variation over the existing situation. Doubling the storage tank capacity is clearly the most advantageous upgrade to the WFI system.

9 CONCLUSION

Discrete event simulation has been shown to be a useful tool for analyzing batch manufacturing processes. Cycle time analysis, interaction between phases, and even utility usage can be successfully modeled using a transaction-based approach.

This paper has discussed the development of a simulation of WFI usage along with the results. The details of the simulation development were presented along with the assumptions made to account for future performance enhancements to the actual process. Performance was investigated several proposed WFI system scenarios.

The analysis of the simulation results clearly showed that the most desirable WFI system performance would be gained if the storage capacity is increased. Doubling the storage capacity by the addition of a new tank, or the conversion of another storage tank to WFI service, demonstrated the best ride-through capability for large surges in WFI demand.

The WFI simulation demonstrated the capability of providing a reasonable approximation of the performance of the WFI system as well as the manufacturing systems. This model has a number of potential applications for the future, including modeling usage of other utilities, adding other manufacturing areas to understand interactions across the process and the potential of proposed changes to the process, addition of randomization to allow statistical modeling, and confirmation and verification of manufacturing forecasts for production.

REFERENCES

Ball, P. 2001. Introduction to discrete event simulation. *Originally presented at the 2nd DYCOMANS workshop on Management and Control: Tools in Action*, Algarve, Portugal, 15-17 May 1996, 367-376. <http://www.dmem.strath.ac.uk/~pball/simulation/simulate.html>. [accessed March 13, 2006]

Banks, J., J. S. Carson II, B. L. Nelson, and D. M. Nicol. 2005. *Discrete-Event System Simulation*. 4th ed. Upper Saddle River, New Jersey: Pearson Prentice Hall.

Domanski, B. 1999. Simulation versus analytic modeling in large computing environments. White paper, Responsive Systems Company. <http://www.responsivesystems.com/papers/misc/Simulation.pdf>. [accessed March 13, 2006]

Hoerl, R. and R. D. Snee. 2002. *Statistical Thinking: Improving Business Performance*. Pacific Grove, California: Duxbury.

Hwang, F. 1997. Batch pharmaceutical process design via simulation. *Pharmaceutical Engineering*, January/February. <http://www.ispe.org//Template.cfm?Section=Referece&Template=/MembersOnly.cfm&ContentID=13019&CFID=2610699&CFTOKEN=46656408>. [accessed March 13, 2006]

Micrografx. 2001. The role of process modeling and management within six sigma. White paper. Dallas, Texas. <http://courses.washington.edu/outfox/IgrafxProcessMgtandSix%20Sigma.pdf>. [accessed March 13, 2006]

Park, S., and L. Leemis. Discrete-event simulation: A first course. *Presentation, College of William and Mary*. <http://www.cs.wm.edu/~esmirni/Teaching/cs526/DESAFC-1.1.ppt>. [accessed March 13, 2006]

Schriber, T. J., and Brunner, D. T., Inside discrete-event simulation software: How it works and why it matters. In *Proceedings of the 2005 Winter Simulation Conference*, ed. M. E. Kuhl, N. M. Steiger, F.B. Armstrong, and J. A. Joines, 167-177. Piscataway, New Jersey: Institute of Electrical and Electronics Engineers.

Six Sigma Academy. 2002. *The Black Belt Memory Jogger*. 1st ed. Salem, New Hampshire: GOAL/QPC.

Watson, G. 2004. Simulation Analysis. *Monsanto Six Sigma Black Belt Training 2004, St. Louis*. Business Systems Solutions International, Inc.

AUTHOR BIOGRAPHY

CRAIG W. ALEXANDER is a Plant Improvement Engineer with Monsanto in Augusta, Georgia. He holds a Bachelor of Electrical Engineering degree from Auburn University and a Master of Science in Engineering degree from the University of New Orleans. He is certified as a Six Sigma Black Belt by Monsanto and is a registered Professional Engineer in Georgia and Louisiana. His e-mail address is <craig.w.alexander@monsanto.com>.