CSL Behring Biotherapies for Life™

# A Modelling approach to Increasing Capacity through Plant Optimisation and Cycle Time Reduction in Industrial Scale Bio-Pharmaceutical Manufacturing


James Higgie

CSL Behring, 189 – 209 Camp Road, Broadmeadows, Victoria, Australia 3047

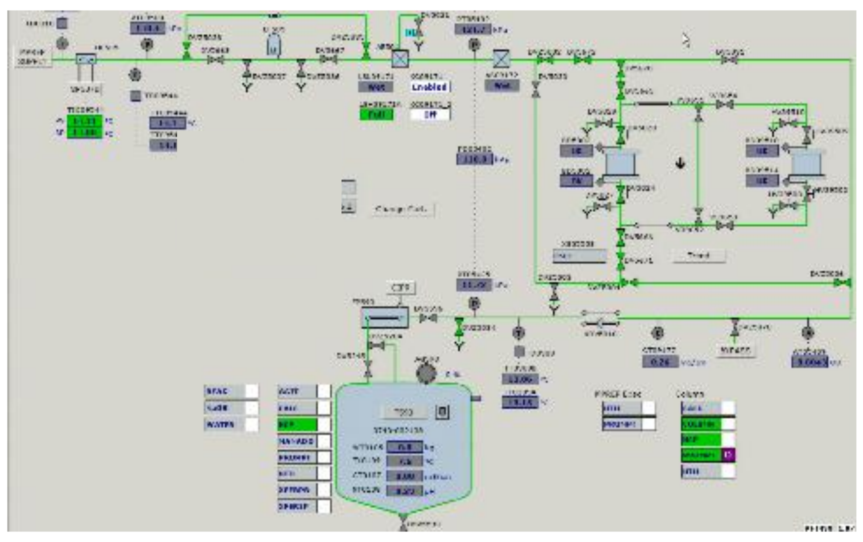

## Introduction

In growing markets, companies undertake manufacturing capacity increases to meet demand, improve manufacturing efficiencies and decrease operating costs. Capacity expansions in existing bioprocess facilities can be achieved by increasing batch size or reducing cycle time. Cycle time reductions can be achieved with little capital investment by streamlining setup times, optimising labour utilisation and batch to batch scheduling. Capital investment to decouple critical path process units, decrease turn around times for in-process testing and introduction of new technologies can also reduce cycle times. CSL Behring's capacity expansion strategy has included a combination of batch size increases and cycle time reduction. This poster will detail how CSL Behring achieved double digit percentage capacity increase with limited capital investment through cycle time reduction at our Broadmeadow plasma fractionation facility.

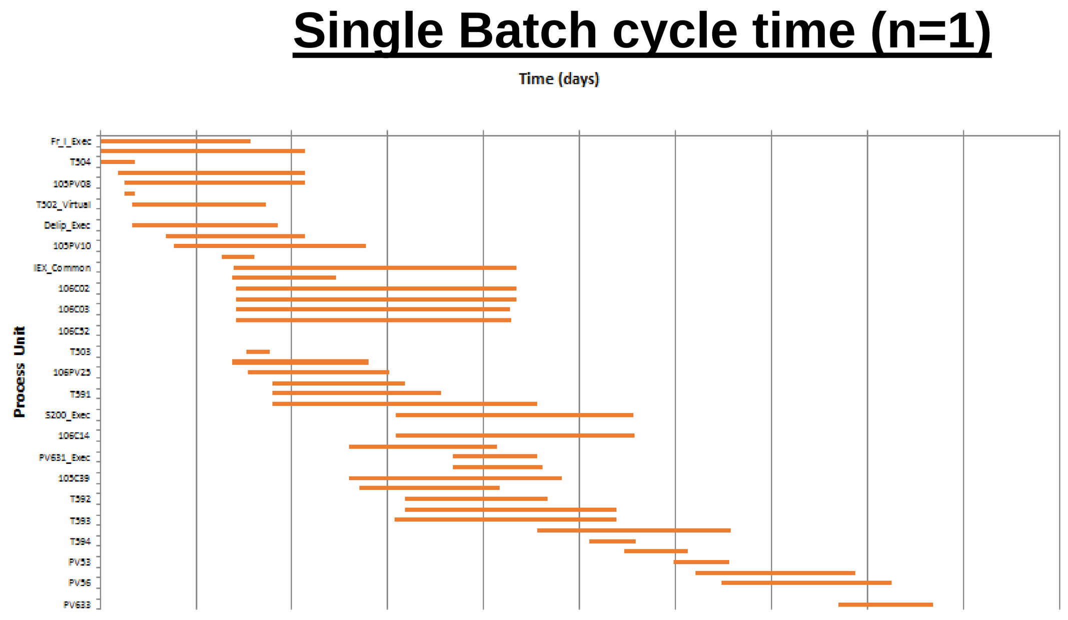
## Data Gathering

Detailed quantitative information was needed to determine the existing performance of the plant with respect to cycle time and individual operation duration, hold and idle times. The data was extracted from our Siemens PMCS 7 SCADA system and gathered from 100 batches worth of data each with 28,000 data points each giving a total of 2.8 million data points. The vast amount of data collected through the execution of processes is referred to as big data and very powerful insights can be gained from its analysis.

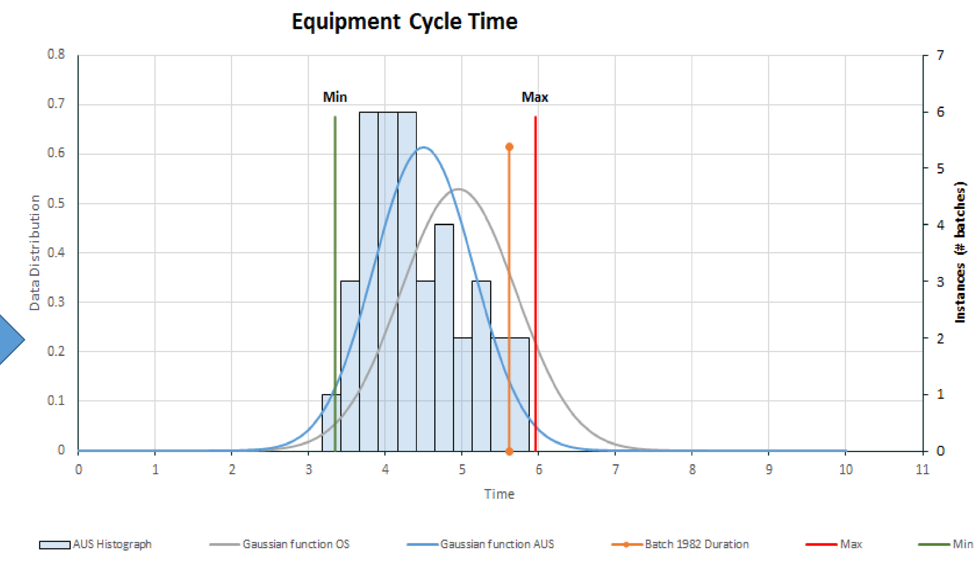
**Siemens PMCS 7 SCADA System**



**Equipment Utilisation graph of a Single Batch cycle time (n=1)**



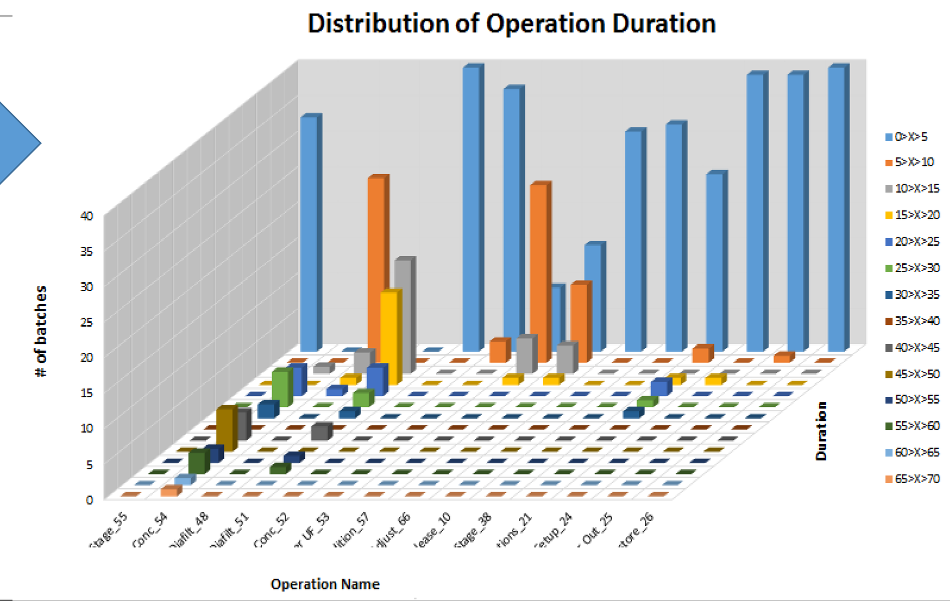

**Example of statistical analyses of a specific process cycle time (n=100 batches)**




**Example of operation steps within a specific process (28,000 data points/batch)**

| Operation | Duration | Hold time |
|---|---|---|
| 3452-001982/Collection Tank._6/Set Proc Stage_55 | 0.000 | 0 |
| 3452-001982/Collection Tank._6/Receive+Conc_54 | 1.754 | 0 |
| 3452-001982/Collection Tank._6/ Diafilt_48 | 0.272 | 0 |
| 3452-001982/Collection Tank._6/ Diafilt_51 | 0.902 | 0 |
| 3452-001982/Collection Tank._6/Further Conc_52 | 0.0487 | 0 |
| 3452-001982/Collection Tank._6/Recover UF_53 | 0.184 | 0 |
| 3452-001982/Collection Tank._6/Addition_57 | 0.228 | 0 |
| 3452-001982/Collection Tank._6/Adjust_66 | 0.074 | 0 |
| 3452-001982/Collection Tank._6/Release_10 | 0.001 | 0 |
| 3451-001982/Transfer PV631 to PV635_31/Set Process Stage_38 | 0.000 | 0.116 |

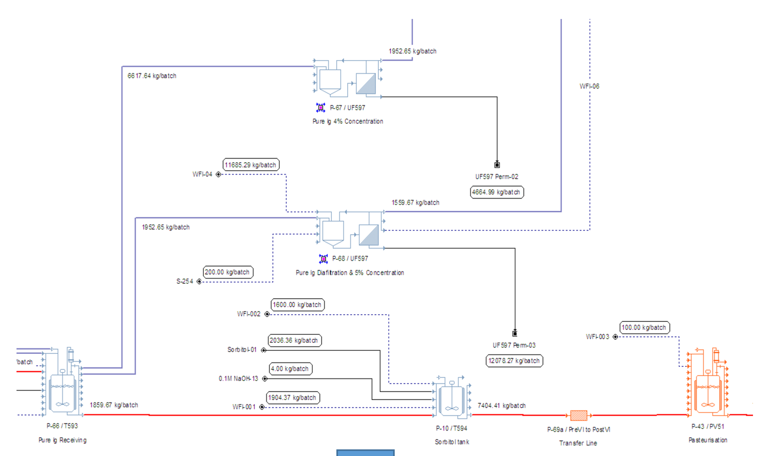
**Example of statistical analyses of operation steps within a specific process (n=100x28,000)**



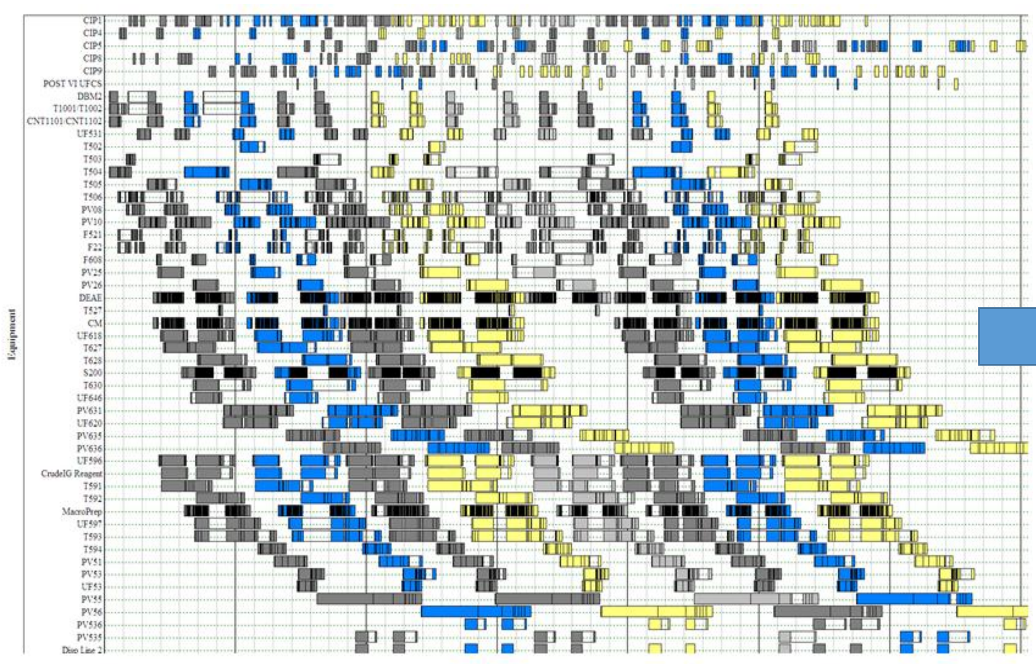

## Process Modelling

High equipment utilisation and complex batch to batch dependencies within the plant made the identification of the overall problem with data alone extremely difficult. Computer models can simplify this complexity and aid in plant debottlenecking. A computer model was produced using Intelligen's Super Pro Designer software package. To ensure the model accurately represented current conditions and staff numbers within the plant the duration of process steps was informed by both original design specifications and the historical data analysed.

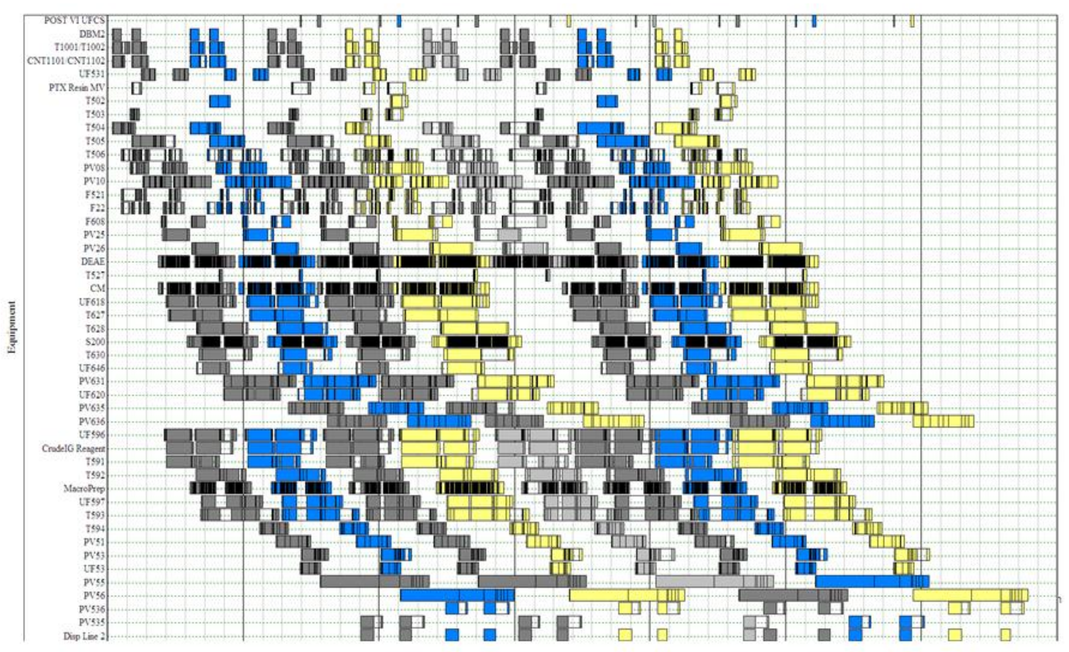
**Super Pro Designer model**



**Schedule Pro Equipment Utilisation Current**



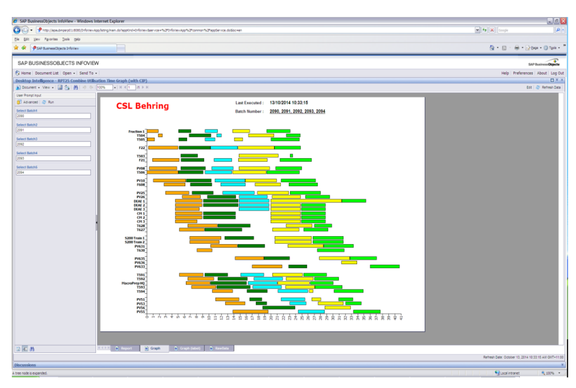
**Optimal Design solution**

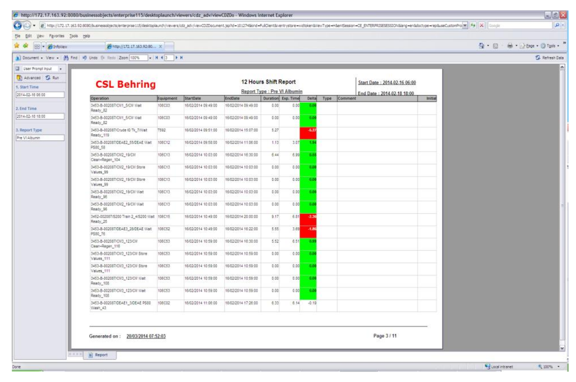


Exporting the model to Intelligen's Schedule Pro software allowed an overall visualisation of operating conditions in the plant. This lead to the discovery of significant non-value adding gaps between process stages and batches. In addition it allowed the identification of bottlenecks caused by established operation decisions made at process steps up stream. Selecting the right combination of batches types and side products and optimal application of labour to a dynamic critical path lead to our final design solution with reduced cycle time

## Implementation

Implementation involved communication of a clear vision to staff and detailed requirements for which they would be held accountable. This was achieve with daily meetings to review hits and misses and plan for the day ahead. The meeting included Manufacturing, Engineering Services, Engineering Projects, QC and operational planning. The Schedule Pro model was adjusted every day to reflect current conditions and subsequently calculate new critical path priorities to guide shopfloor decision making. To assist with effectiveness reviews, CSL Behring developed various reporting tools, a cycle time reporter and a shift reporter. Supervisors use the shift reporter to review the operation durations achieved during their shift compared against expected durations, comments are added to explain and record delays. The cycle time was slowly reduced over time as operational staff adjusted to a new work day pattern. The target cycle time was achieve after four months of implementation.





## Lessons Learnt

The philosophy of big data is to move away from anecdotal and small data sets to obtain a more statistically meaningful information.

Process modelling based on statistically meaningful data allowed the visualisation of complex problems, which is critical for creative design thinking and problem solving.

This approach allows the appropriate amount and type of resources to be applied to the areas of highest return.

The implementation of cycle time reduction in bio-process facilitates requires teamwork, education, and tools that empower staff to make informed real time decisions.