Integration of PI client tools in support of large-scale cell culture manufacturing

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Presentation Outline

- The Nature of Bioprocesses
- Supporting Large-scale cell culture
- PI provides data that enables efficient, responsive support
  - PI BatchView + ProcessBook
  - PI BatchView + DataLink
- Statistical Process Control
- Increased Process understanding

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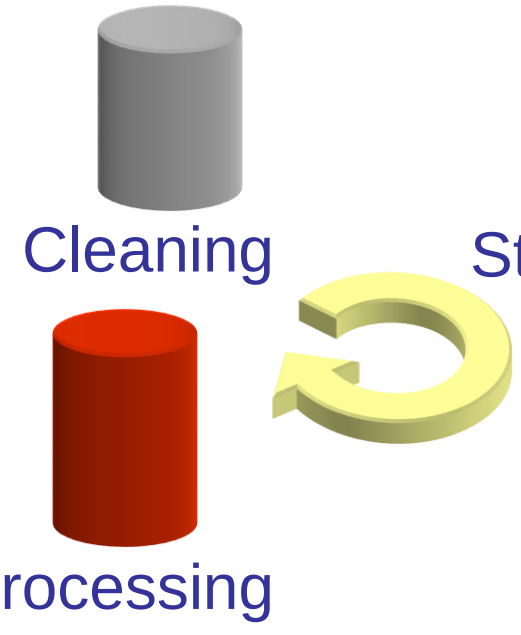
Nature of Bioprocesses

- Batch processes are popular in the world of biotech.
- Well-defined support roles



Process Engineering
Technical Services

Scientific Staff

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Nature of bioprocesses (2)

- Parameters are monitored continuously during the cleaning, sterilizing, preparing and processing.
- Timing of equipment manipulations often depend on other process parameters.
- Each walk in the parameter-space of the bioprocess yields greater process understanding.

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A little bit about cell culture

- Objective: create an environment in the bioreactor that
  - Encourages cell populations to grow exponentially (scale biomass)
  - Allows genetically-engineered cells to produce and secrete protein
- Keep the environment free of all other organisms

A little more about cell culture

- Exponentially growing cell populations deplete the finite nutrients of the bioreactor and must be transferred to a larger environment for further growth.

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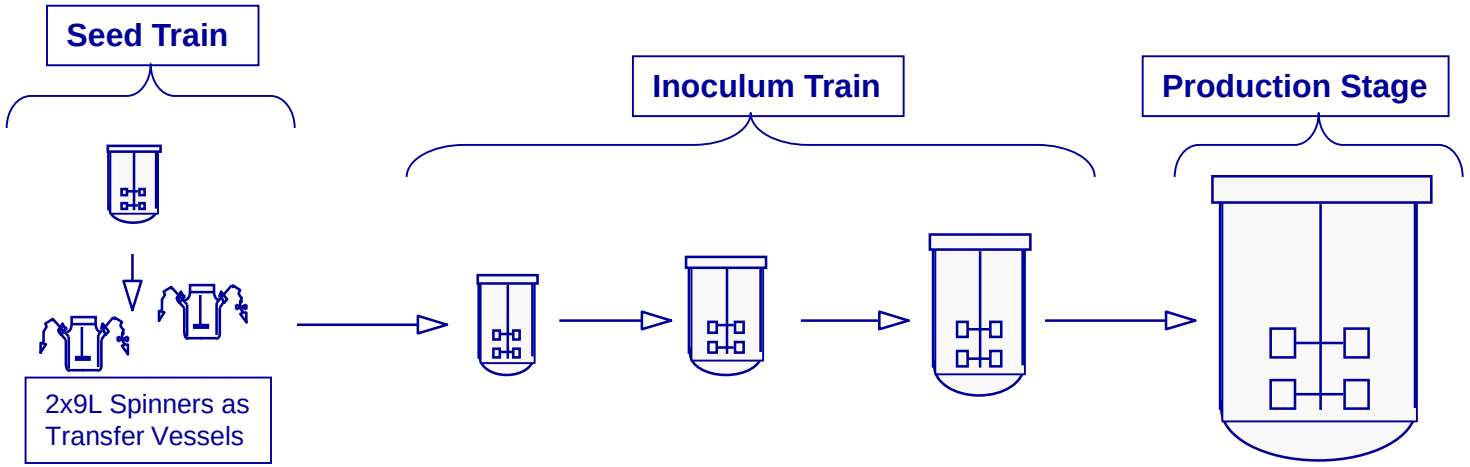
Managing Malthus



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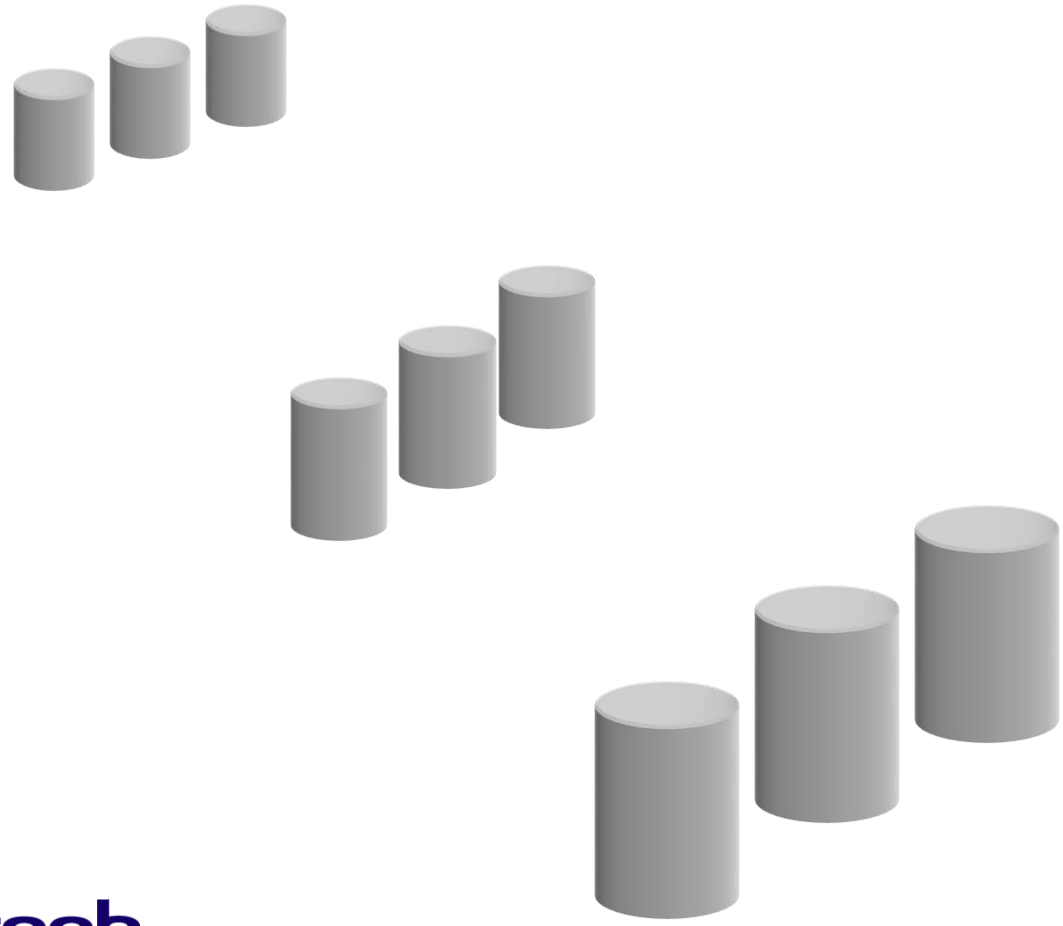
Redundancy



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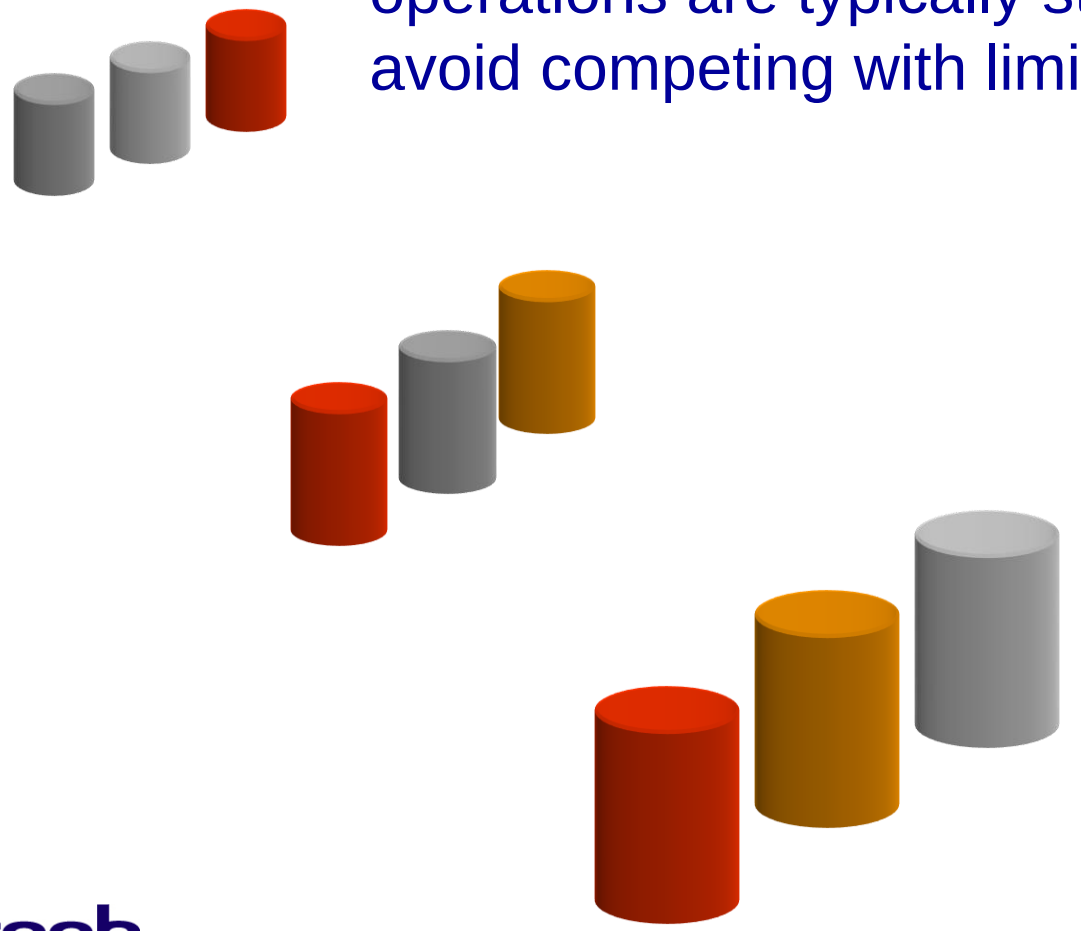
Staggered Operations

Many units go through the same cycle, operations are typically staggered to avoid competing with limited resources



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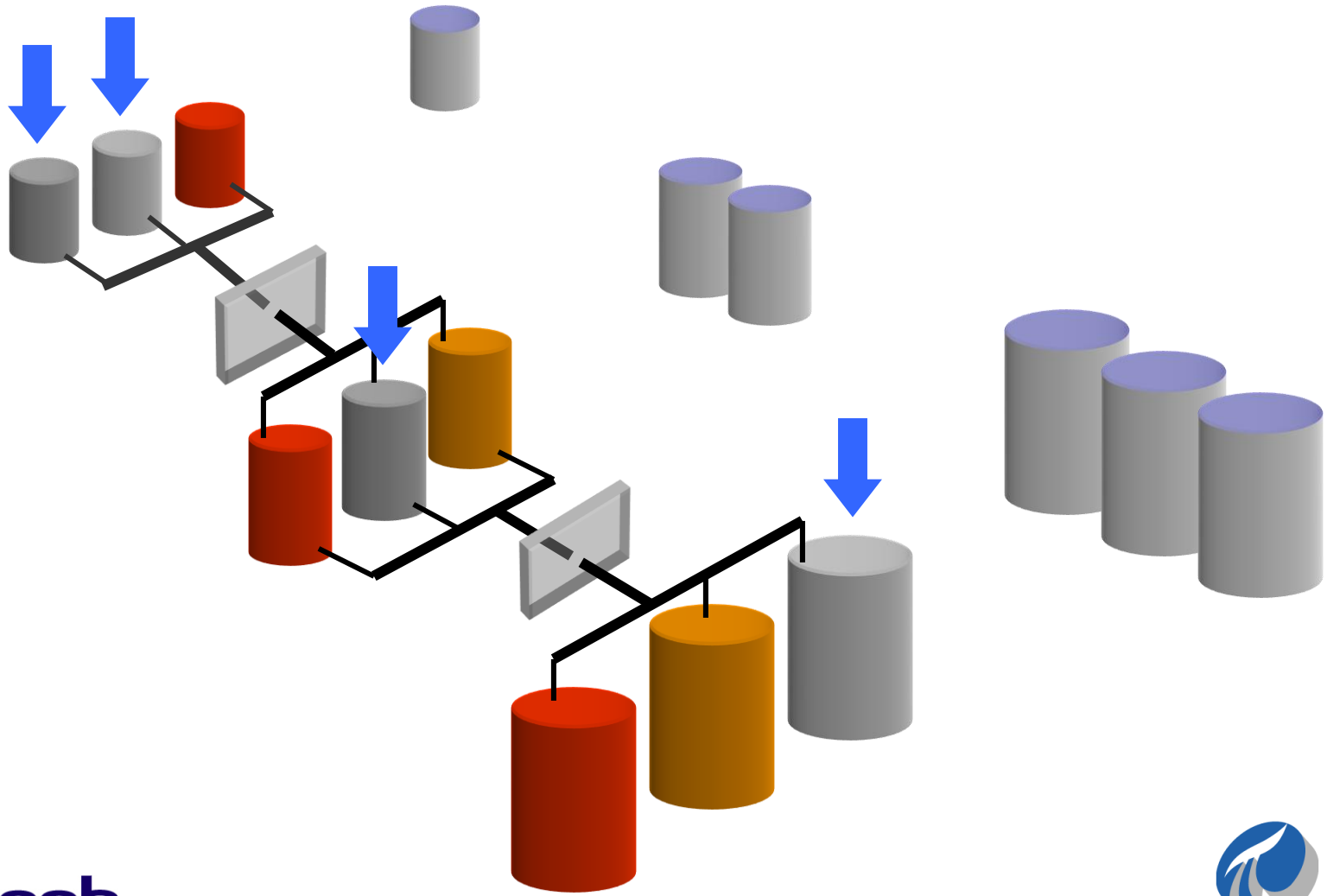
Equipment set-up for cell population expansion



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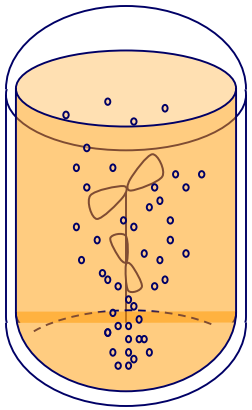
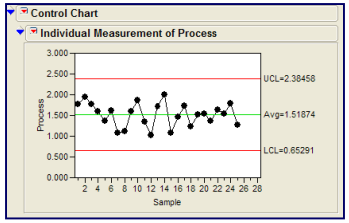
Scientific support large-scale cell culture

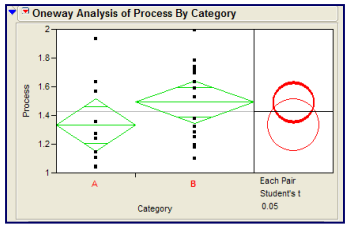


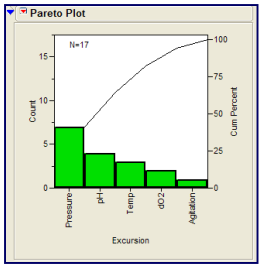
Data/ Obs.

Identification/ Elimination of Special Cause Variability

Large-scale







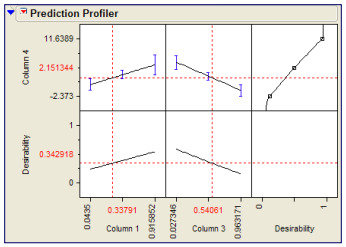
Hypothesis

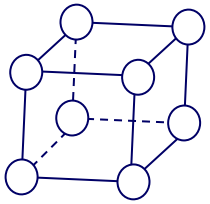
Plant Trials

Data/ Obs.

Experimental Conditions

Laboratory





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Data

It’s better to have it and not need it, than need it and not have it.

- Clarence Worley , *True Romance*

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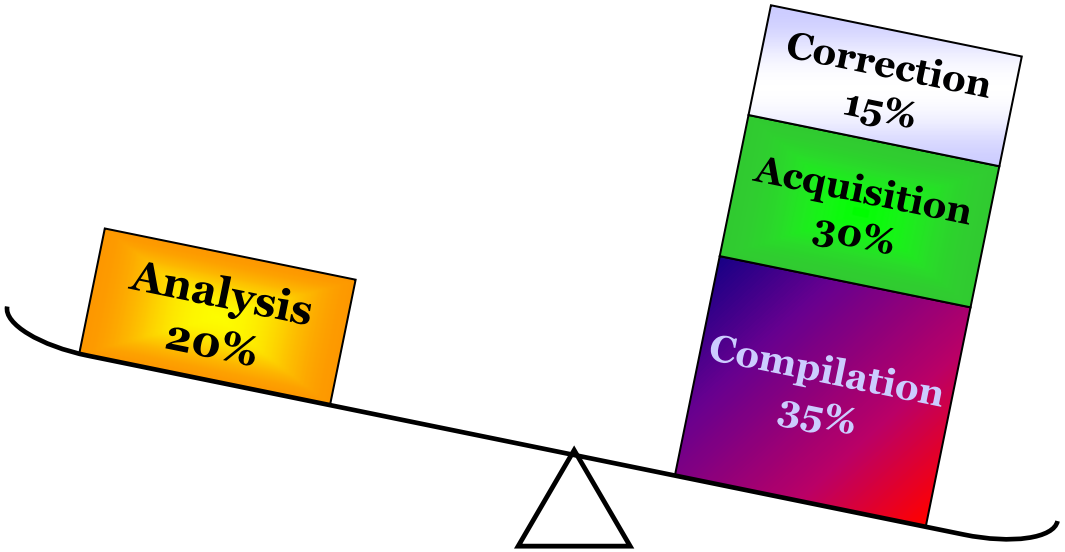
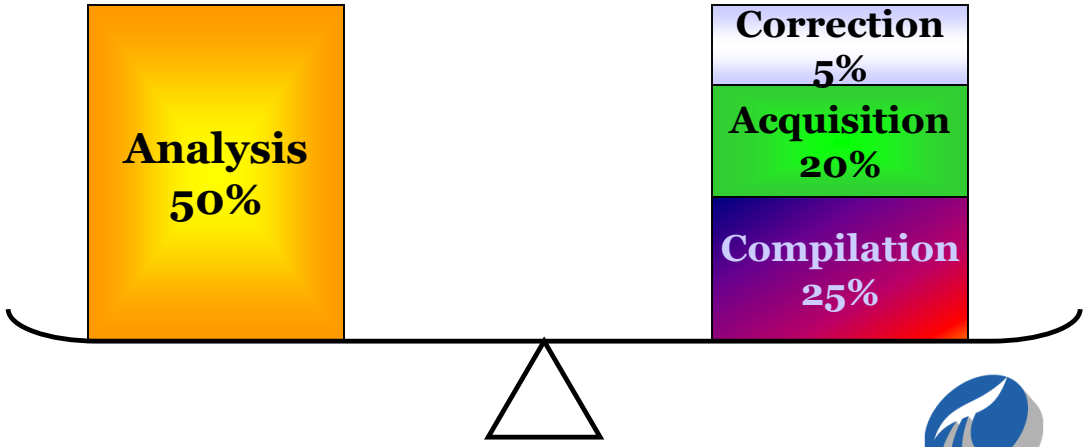
Benefits: Better Process Understanding



Gain more process understanding through analyzing more data and *more thorough* data analysis.

Increase productivity of scientific staff by shifting the chore of data acquisition and maintenance to the automated computer systems.



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Benefits (2)

- Real-time process data and trends for troubleshooting (24/7).
- Historical reference that enables
  - rapid assessment of process performance
  - data for training of Mfg. personnel
  - review data for discrepancies
- Ideas for Optimization
- Miscellaneous data analysis

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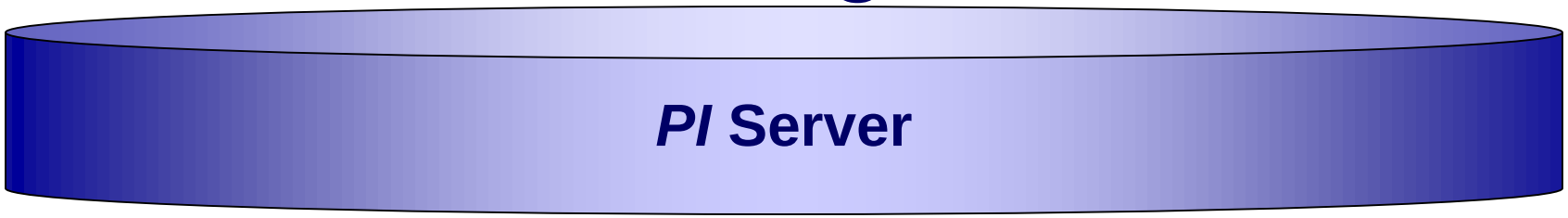
Streaming data



PI Client Tools

BatchView

ProcessBook

DataLink

PI BatchView queries the PI server for batches.

PI ProcessBook plots the data with respect to time.

PI DataLink connects Excel to PI and tabulates data.

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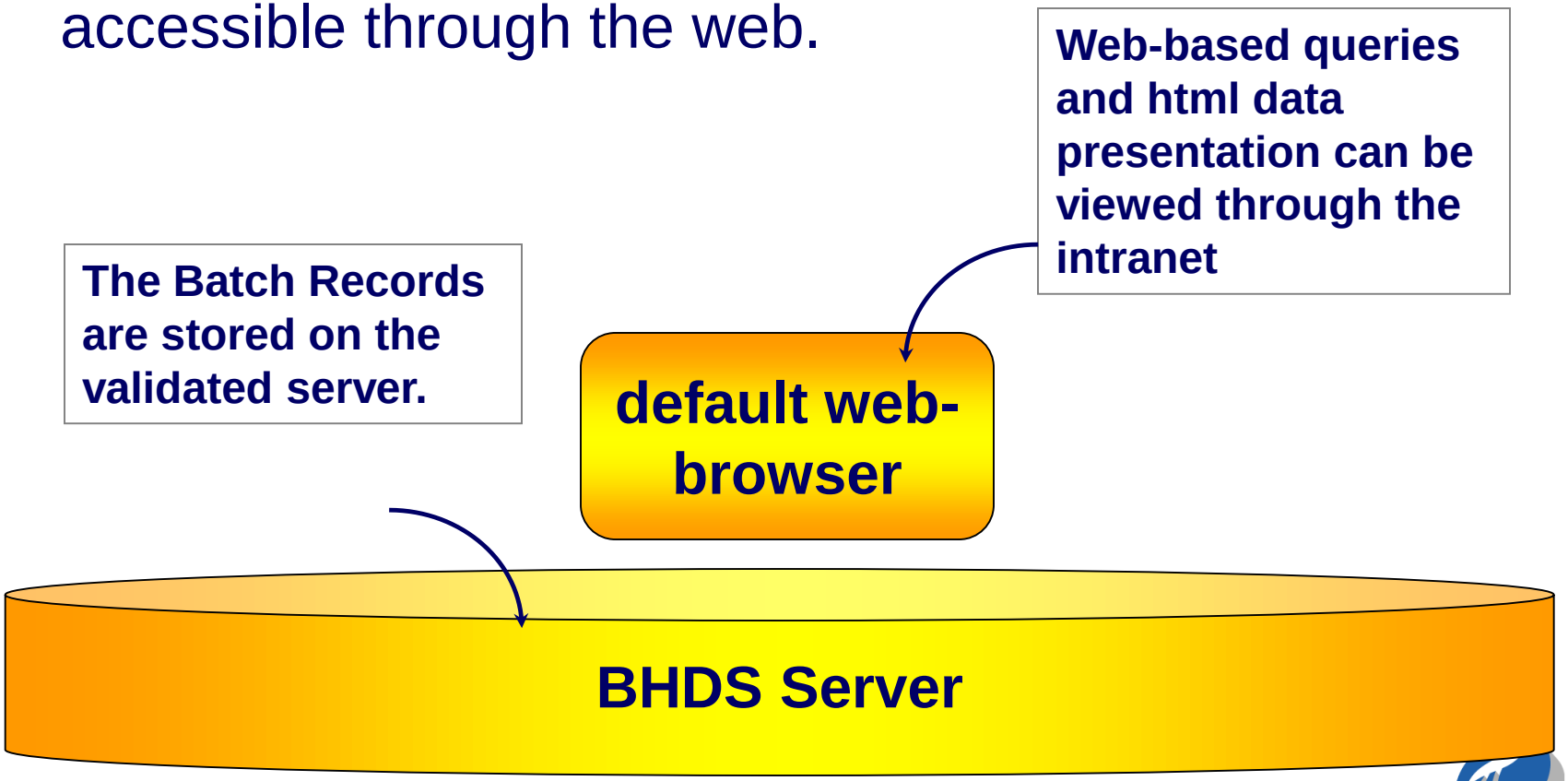
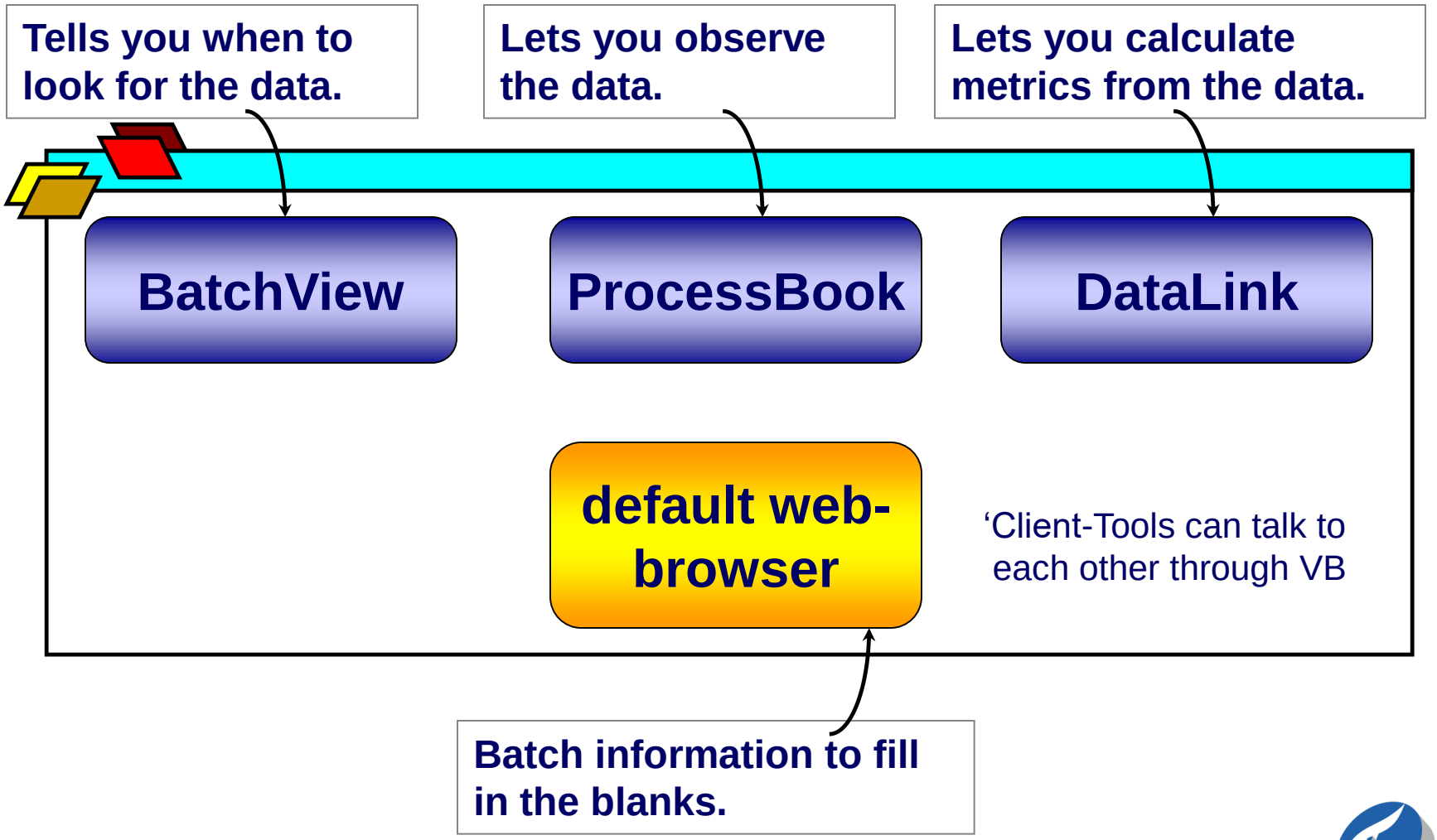
Batch Records

- The Official Batch records are stored on another server accessible through the web.



Data Access Tools by Function



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CIP Support (Cleaning)

- Technical staff reviews CIP trends
- Many cleaning procedures, many different units
  - 3 CIP Units
  - 25 reactors, 10 media preparation vessels to clean
  - Innumerable Flow paths
  - 19 different cleaning recipes

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Media Preparation Support

- Manufacturing and Technical Staff review MP Trends for real-time troubleshooting
- Product-specific MP procedures, few units
  - 25 bioreactors (4 sizes)
  - 7 media preparation vessels (4 sizes)
  - 3 media specialized vessels (2 sizes)
  - 5 media treatment units

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Cell Culture Support

- Scientific Staff reviews and scores every culture (4 per run) and every media prep
- Scientific Staff comments on forward-process-ability of all cultures and product impact of excursions (which can originate in CIP/SIP)

Embedding PI BatchView ActiveX into PI ProcessBook

- CIPByRun
  - Allows user to move from Batch ID quickly to time window on multiple units for multiple recipes.
- MediaPrepByRun
  - Allows user to move from Batch ID to each
- FermByRun
  - Allows user to move from Batch ID of any procedure to all the scientific data related to the run.

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Engineering Computation and Statistical Process Control

- In all areas of cell culture manufacturing, there is opportunity to reduce variability through applying principles of SPC

- Data-based decision-making capability to perform corrective/preventative actions and identification and elimination of special cause variability

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Embedding PI BatchView into Excel to use DataLink

- Collect summary or Individual Metrics from a batch
- Throw data into Statistical Analysis Software (JMP) for analysis
- Use for routine or ad hoc analysis

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Manufacturing Uses PI

- Routine Monitoring
- Shift Changes
- Mass Balance
- Sample Labeling

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Increased Process Understanding

- Re-targeting parameters
- Analysis of valve sequencing versus sterility risk.
- Key correlations leading to increased productivity/yields
- Troubleshooting/understanding instrument influences on process variability.

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Acknowledgements

- Edwin Legaspi - piadmin
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