Pharmaceutical Manufacturing Improvement Leverages PI System Data and Analytical Tools

Presented by

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COMPANY and GOAL

Bristol-Myers Squibb discovers, develops and delivers innovative medicines that help patients prevail over serious diseases. We have a goal to apply scientific rigor to produce clinical and economic benefit through medicines that improve patients' lives

Bristol-Myers Squibb

CHALLENGE

Find and utilize data for process understanding, improvement, and efficiency

- Scaleup of clinical manufacturing to commercial manufacturing
- Improve product critical quality attributes
- Improve process efficiency

SOLUTION

Provide Scientists and Engineers with tools to efficiently find the right data

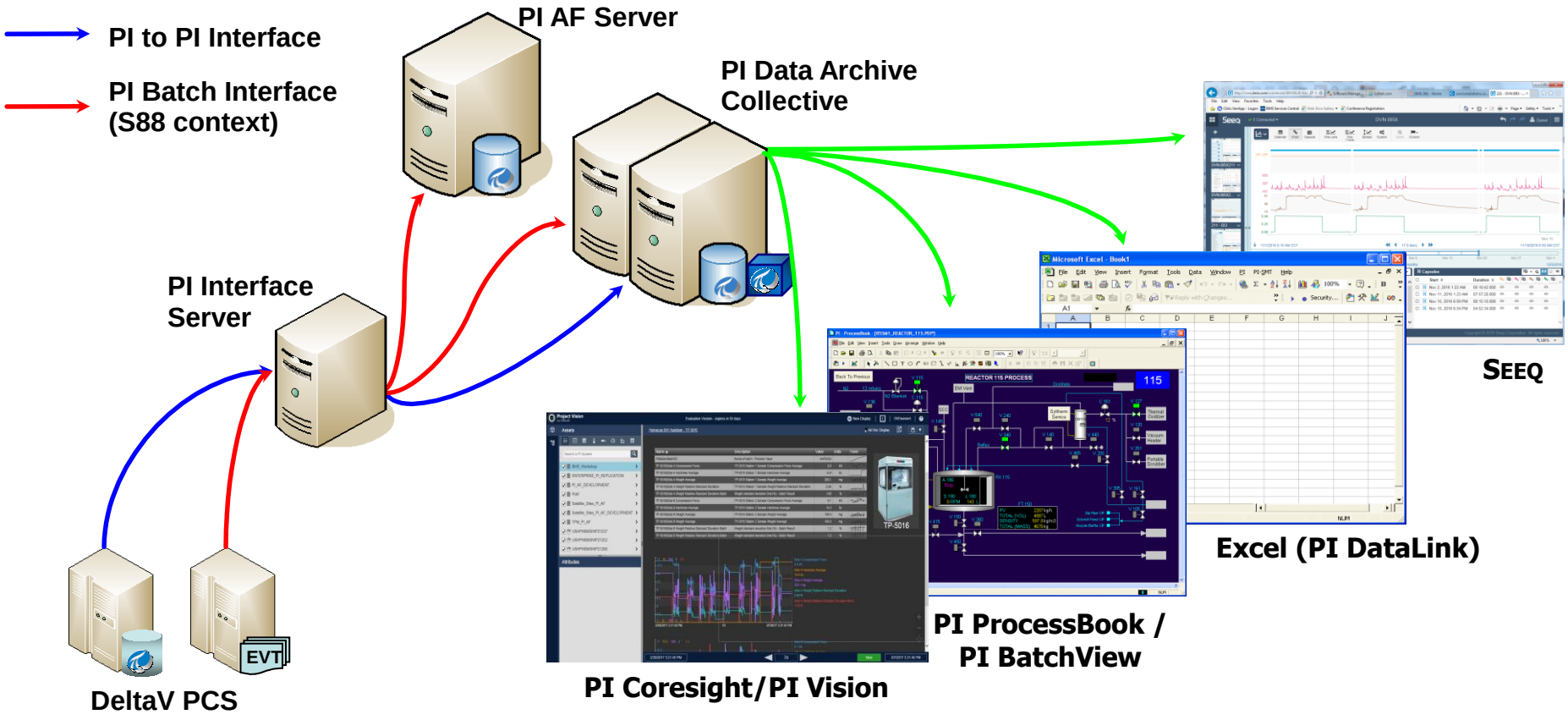
- PI Asset Framework to organize tag data by equipment.
- OSIsoft Partner Seeq for rapid identification of important data through techniques such as condition searches and pattern matching.
- Leverage PI Coresight to "publish" findings and data to a wider audience.

RESULTS

Demonstrated the value of these tools in Process Development and Manufacturing

- Improved productivity of scientists
- Faster scale-up form clinical to commercial manufacturing
- Improved product quality
- Improved manufacturing efficiency

BMS Clinical API Manufacturing Scale-up: PI System Infrastructure



Data collection in pharmaceutical scale-up

- **Goal:**
  - Develop robust and efficient processes to transfer to commercial.
  - Capture and analyze data to support process understanding and support tech transfer and filing.

- **Challenges**
  - Group works with many products. Processes are always changing.
  - Large amounts of data generated during scale-up, but assembling data is time consuming.
  - Sharing and reusing knowledge not always straightforward.

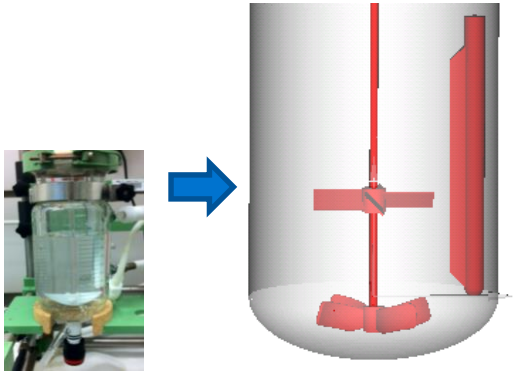


Figure: Development group generates data from lab scale reactors up to large-scale pilot plant vessels.

Use Case:
Drying data collection & analysis

PI Asset Framework combined with Seeq enables fast & easy data collection by:

- Creating searches to quickly find relevant unit operations from raw data.
- Summarizing process parameters (min/max/avg) over search results.
- Allowing visualization and sharing of data from search results.

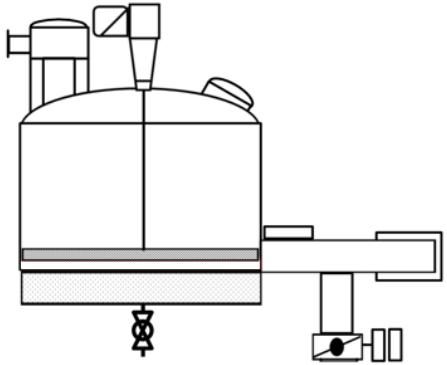


Figure: Schematic of filter dryer

BUSINESS CHALLENGES

- Understand impact of drying parameters on dry time.
- Collecting & summarizing data by hand is tedious and time consuming.

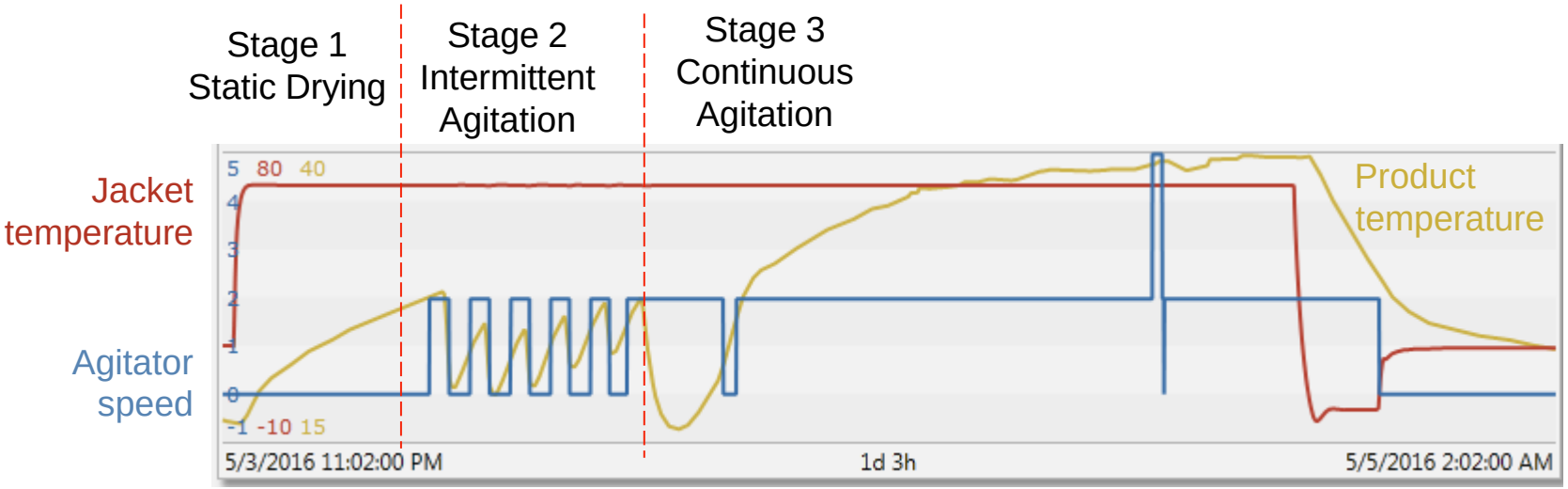
SOLUTION

Utilize PI Asset Framework, PI Batch Database, and Seeq to search PI System continuous data and automatically summarize.

RESULTS AND BENEFITS

- Saves ~1 hr of analysis time per batch.
- Less time spent collecting data, more time spent analyzing data.

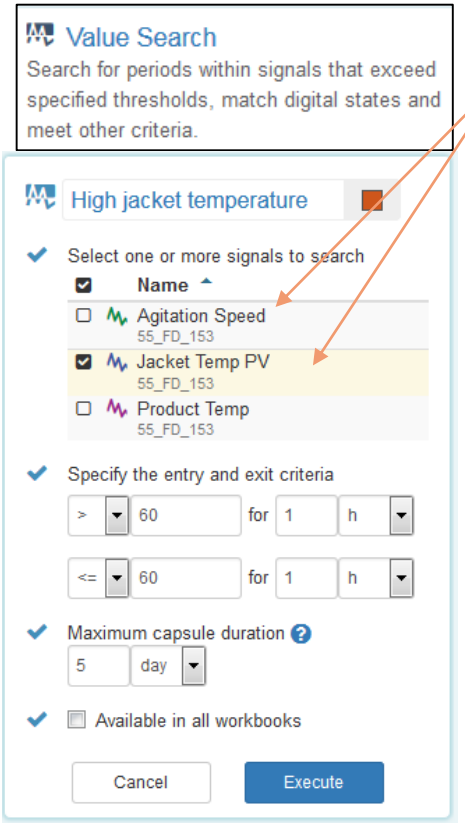
PI Coresight: Visualize Three-stage Drying Process



Parameters of interest for each stage

- Drying time
- Jacket temperature.
- Product temperature min, max, & avg.
- Agitator speed.

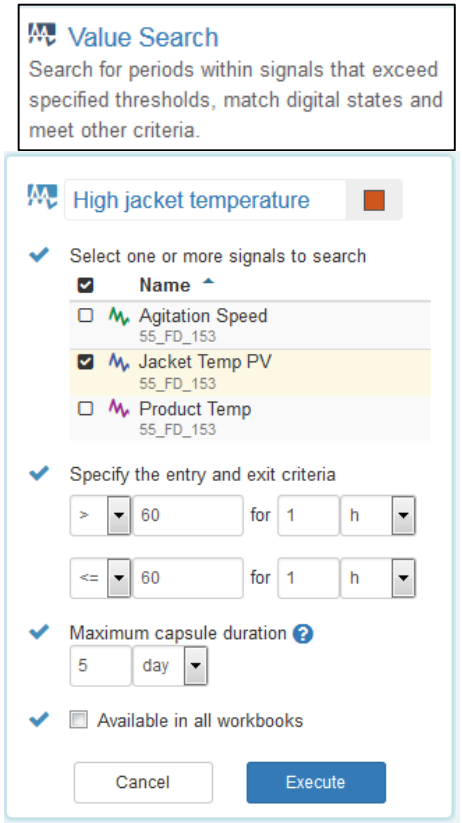
Utilize the Asset Framework and Seeq search to find entire drying operation



PI Asset Framework

Search results

Seeq creates summary statistics for each search result

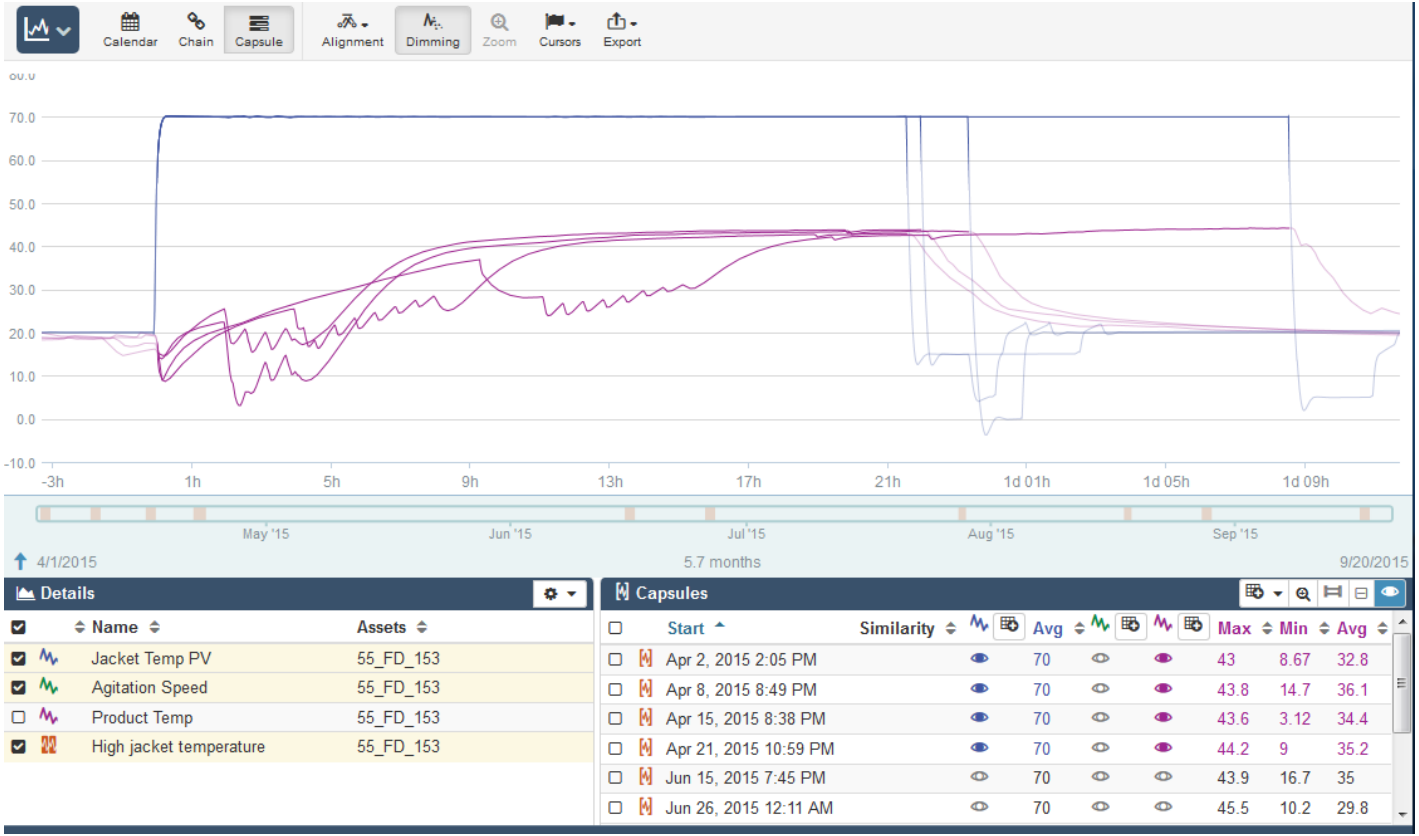


Jacket temperature | Agitator speed | Product temperature

Capsules

Start	Duration	Avg	Avg	Max	Min	Avg
Apr 2, 2015 2:05 PM	21:33:05.892	70	1.36	43	8.67	32.8
Apr 8, 2015 8:49 PM	21:57:49.278	70	1.7	43.8	14.7	36.1
Apr 15, 2015 8:38 PM	23:19:25.516	70	1.77	43.6	3.12	34.4
Apr 21, 2015 10:59 PM	1d 08:32:35.513	70	1.11	44.2	9	35.2
Jun 15, 2015 7:45 PM	22:35:27.096	70	1.34	43.9	16.7	35
Jun 26, 2015 12:11 AM	20:16:35.910	70	1.34	45.5	10.2	29.8
Jul 27, 2015 10:17 PM	20:34:54.566	70	1.2	46	3.34	32.2
Aug 17, 2015 10:24 PM	20:23:58.396	70	1.35	44.9	3.06	33.6
Aug 28, 2015 1:36 AM	19:54:19.880	70	1.28	44.1	14.9	32.2
Sep 17, 2015 1:28 AM	21:11:20.948	70	1.09	39.7	16.3	29.1

Capsule View presents overlaid view of results



Find stage 1 – Search for no agitation

Value Search

Search for periods within signals that exceed specified thresholds, match digital states and meet other criteria.

Agitator off

Select one or more signals to search

Name	
☑	Agitation Speed 55_FD_153
☐	Jacket Temp PV 55_FD_153
☐	Product Temp 55_FD_153

Specify the entry and exit criteria

< 0.1 for 45 min

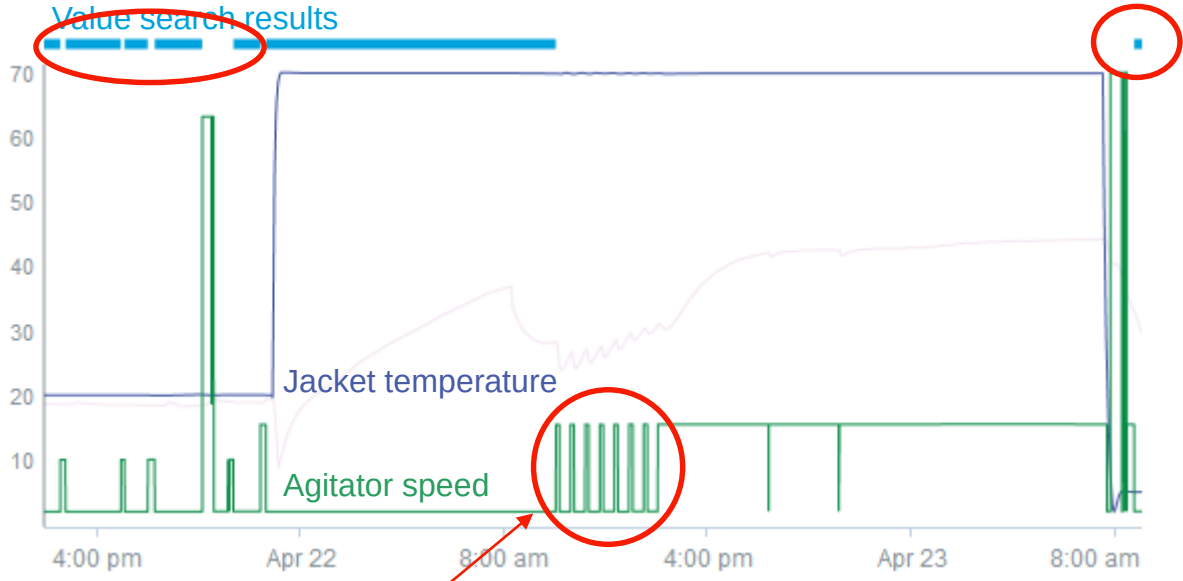
>= 0.1 for 5 min

Maximum capsule duration

1 day

☐ Available in all workbooks

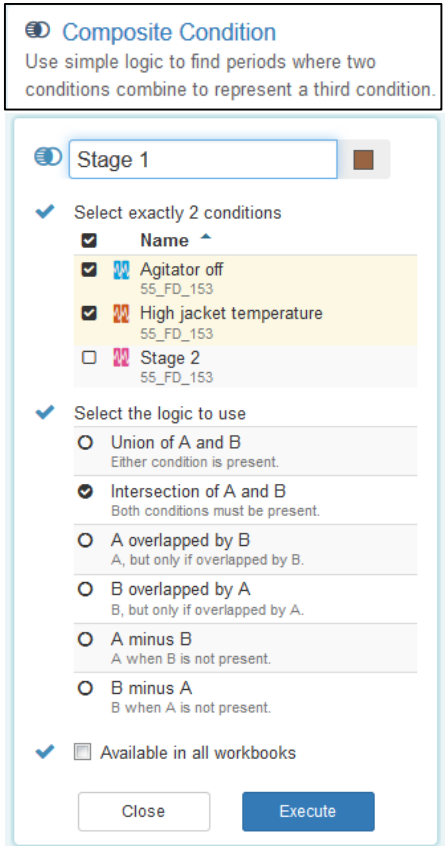
Cancel Execute

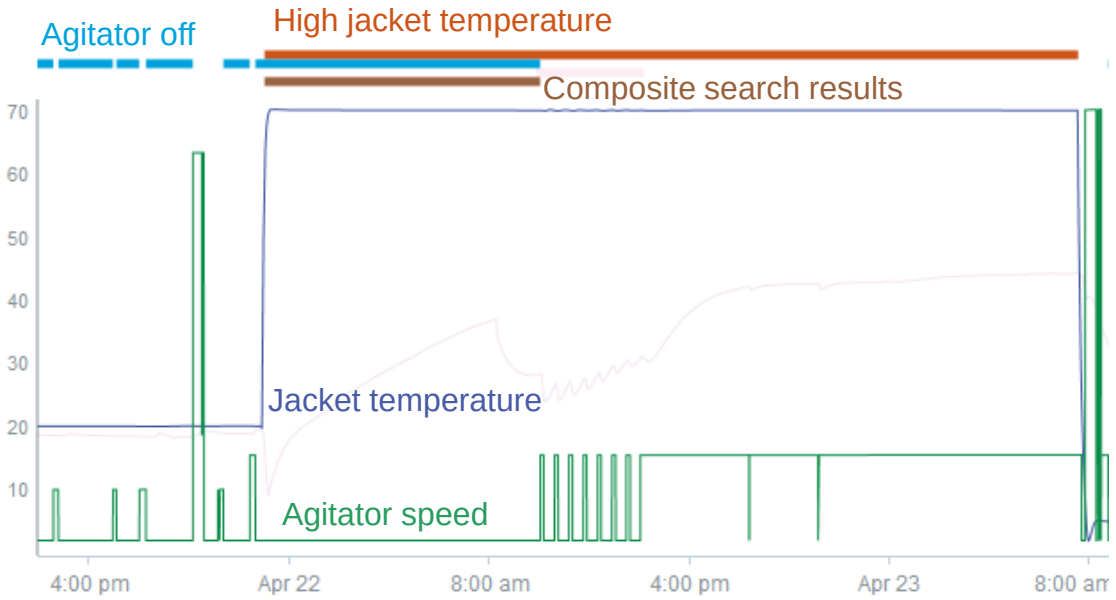


Extended entry condition duration prevents search from finding when agitator is off in stage 2.

Search returns periods where agitator is off but drying is not in progress.

Find stage 1 – Create composite search





A search for stage 3 (continuous agitation) can be created using this same method.

Find stage 2 (on/off agitation) – Create pattern search

Pattern Search

Establish a condition in a visual way by specifying a template pattern and desired similarity.

Stage 2

Select the single signal containing the pattern.

Name

- Agitation Speed — 55_FD_153
- Jacket Temp PV — 55_FD_153
- Product Temp — 55_FD_153

Select the pattern of interest on chart

Select which signal to search.

All signals | Same signal as pattern

Similarity: 98 %

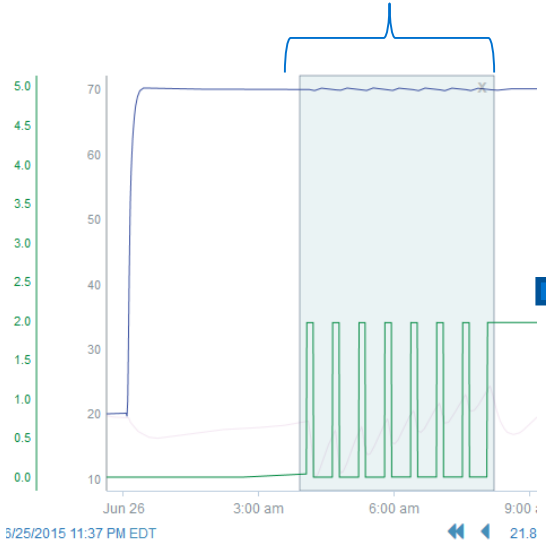
Require similar size

Require similar level

Available in all workbooks

Cancel | Execute

Select pattern of interest



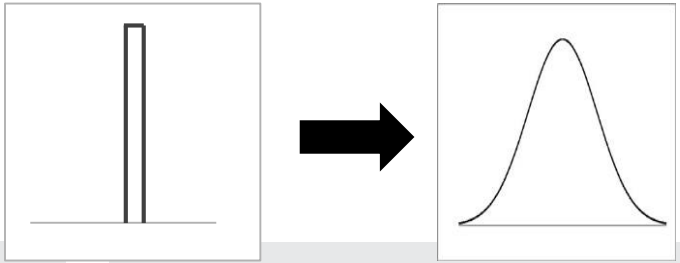
Search results

Capsules

Start	Similarity	Avg	Max	Min	Avg
Apr 22, 2015 9:51 AM	99.03%	70	31.1	23.9	27.4
Jun 15, 2015 11:29 PM	99.16%	70	29.7	22.5	25.9
Jun 26, 2015 3:54 AM	100%	70	24.2	10.2	17.6
Jul 28, 2015 2:01 AM	98.96%	70	27.3	18.4	22.7
Aug 18, 2015 2:08 AM	99%	70	30.4	21.5	25.8
Aug 28, 2015 5:21 AM	98.35%	70	28.6	20.2	24.3
Sep 17, 2015 5:12 AM	98.82%	70	25.4	16.3	20

Similarity describes closeness of match of result to original selected pattern.

Use Case:
Chromatography Column Characterization



BUSINESS CHALLENGES

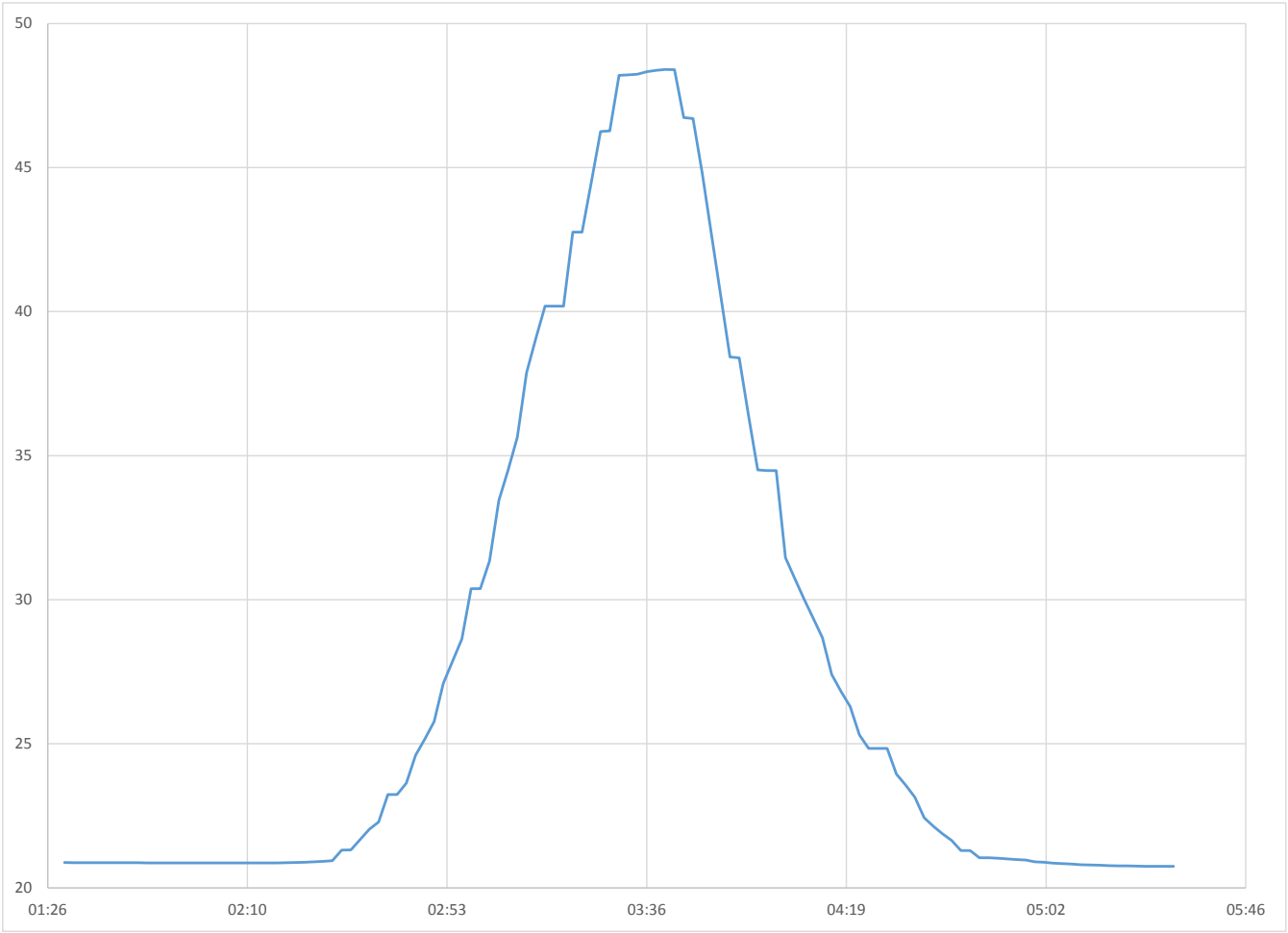
- Homogeneity of packed bed impacts efficiency, yield, and purity
- Proper testing is needed to avoid lost capacity, product losses, or even complete loss of batch.
- Analyzing result of homogeneity test uses a time consuming and variable manual procedure.

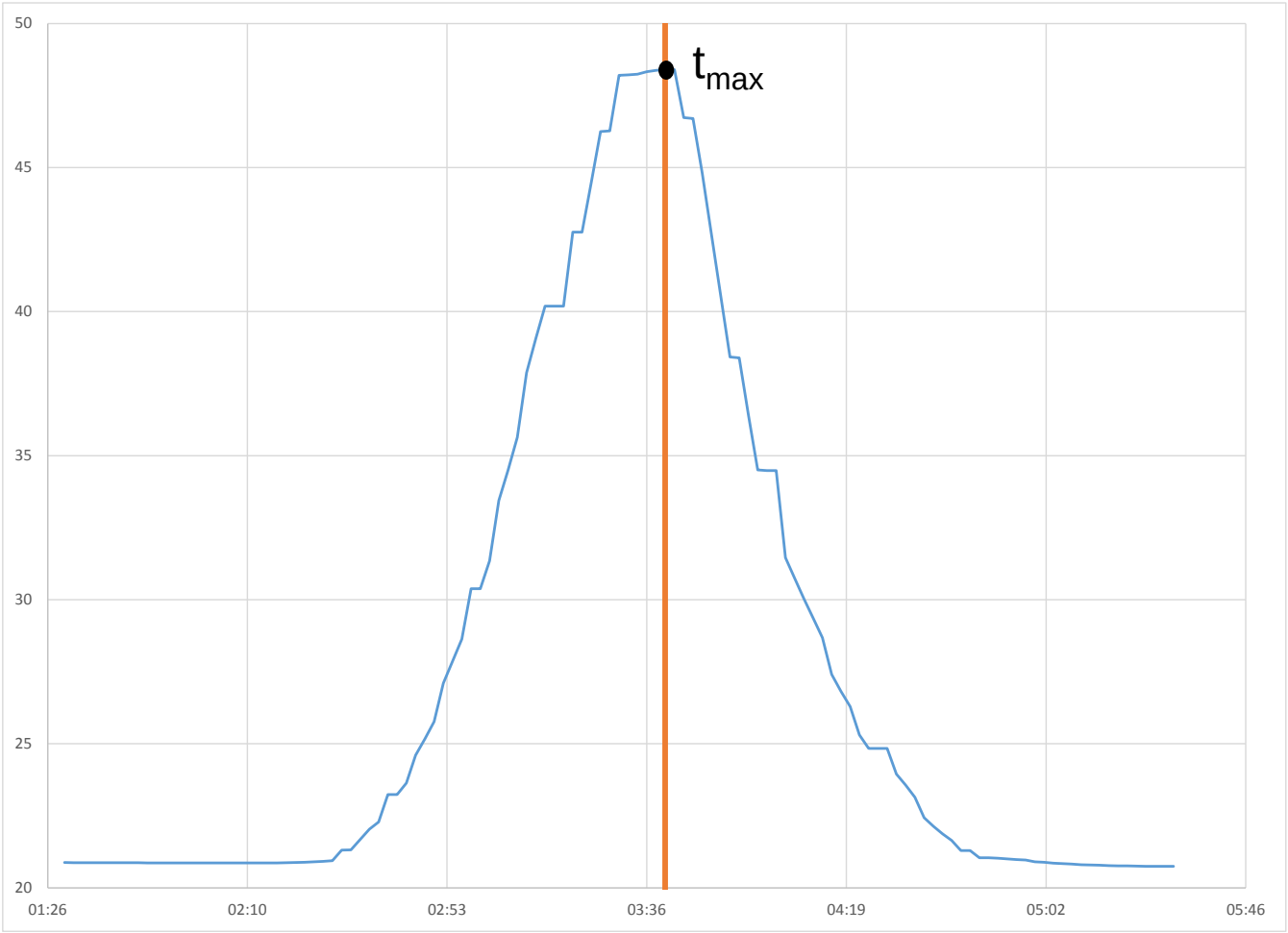
SOLUTION

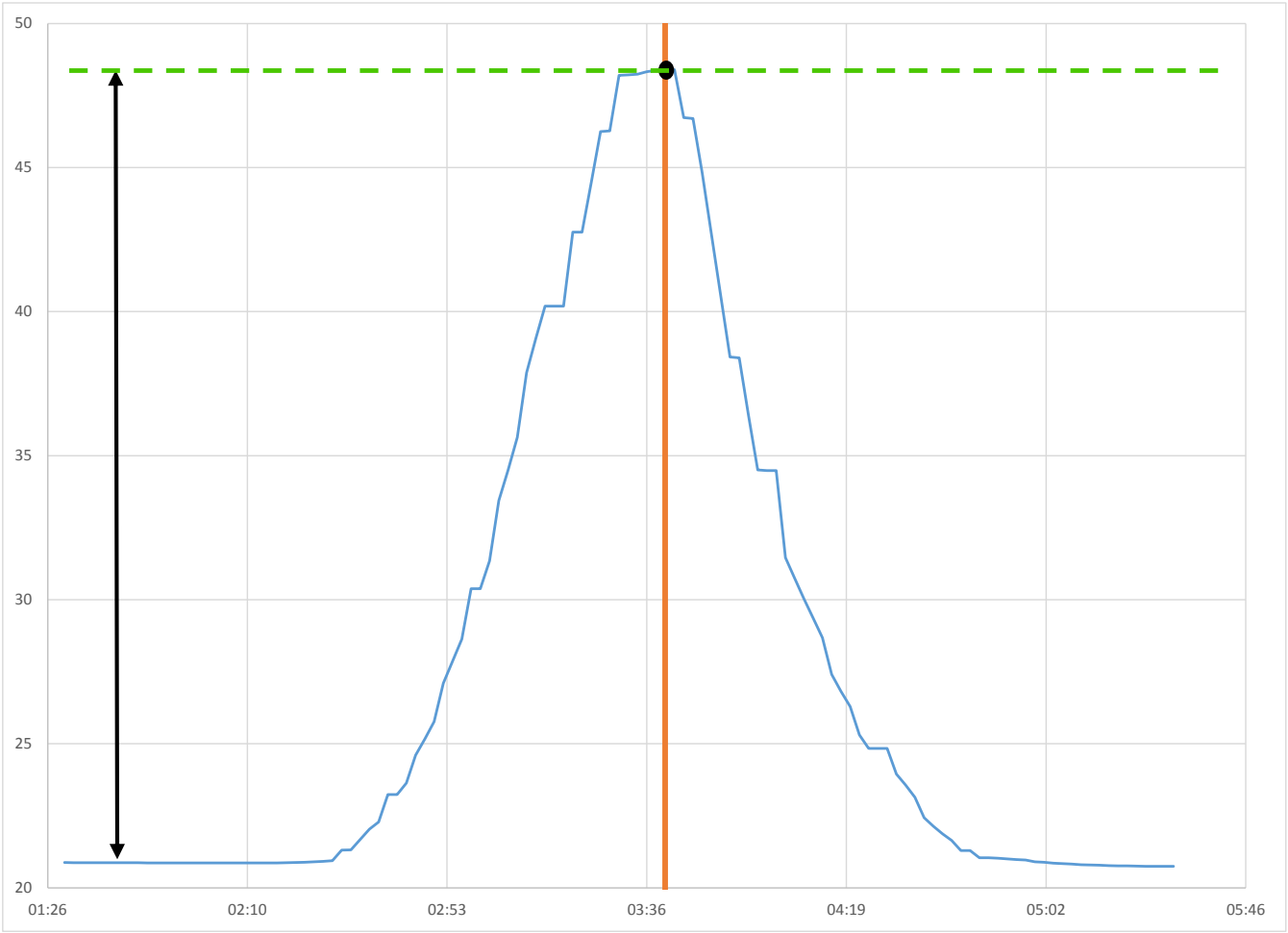
Utilize PI Asset Framework and Seeq to search for PI continuous data and automatically summarize.

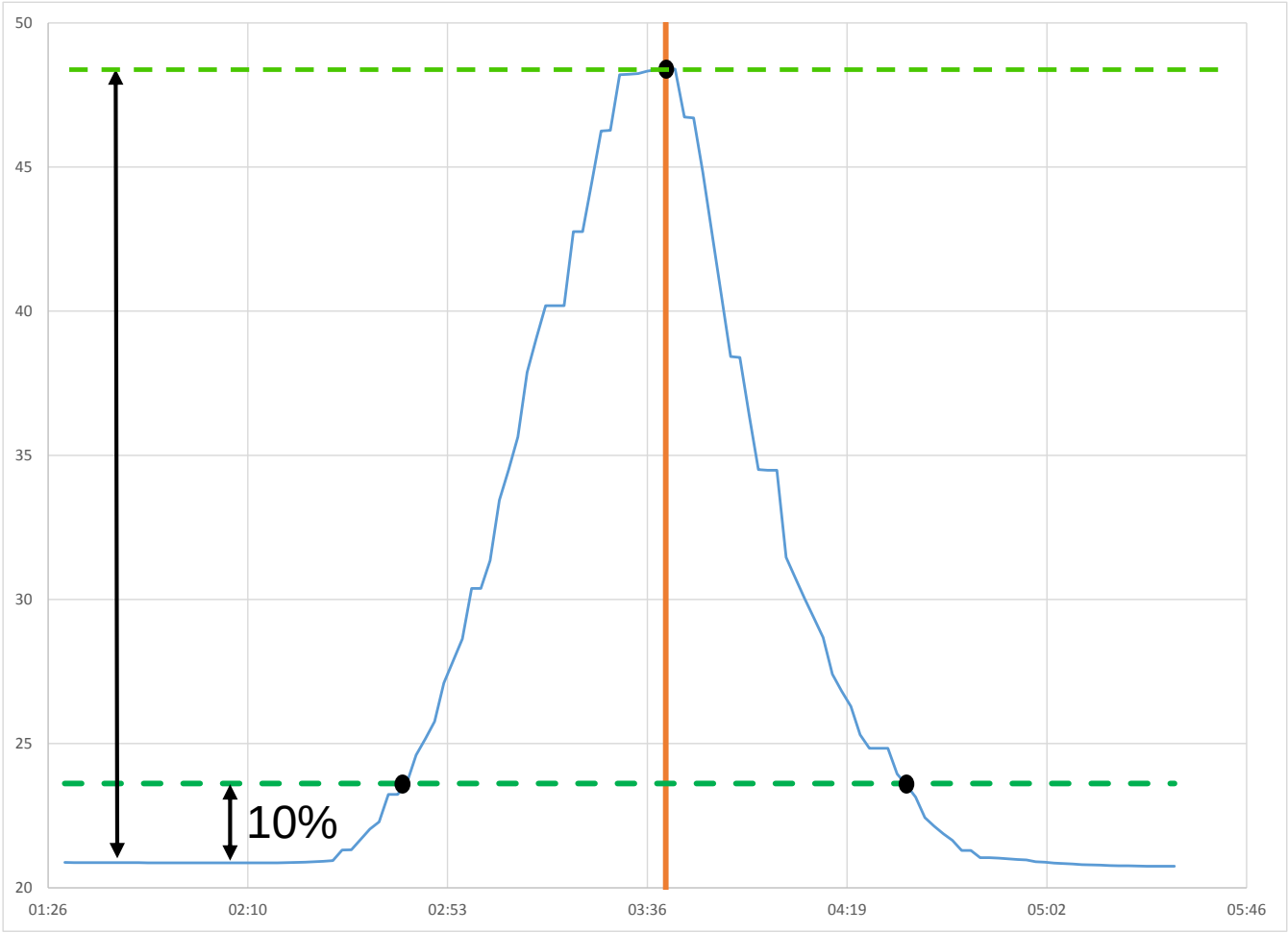
RESULTS AND BENEFITS

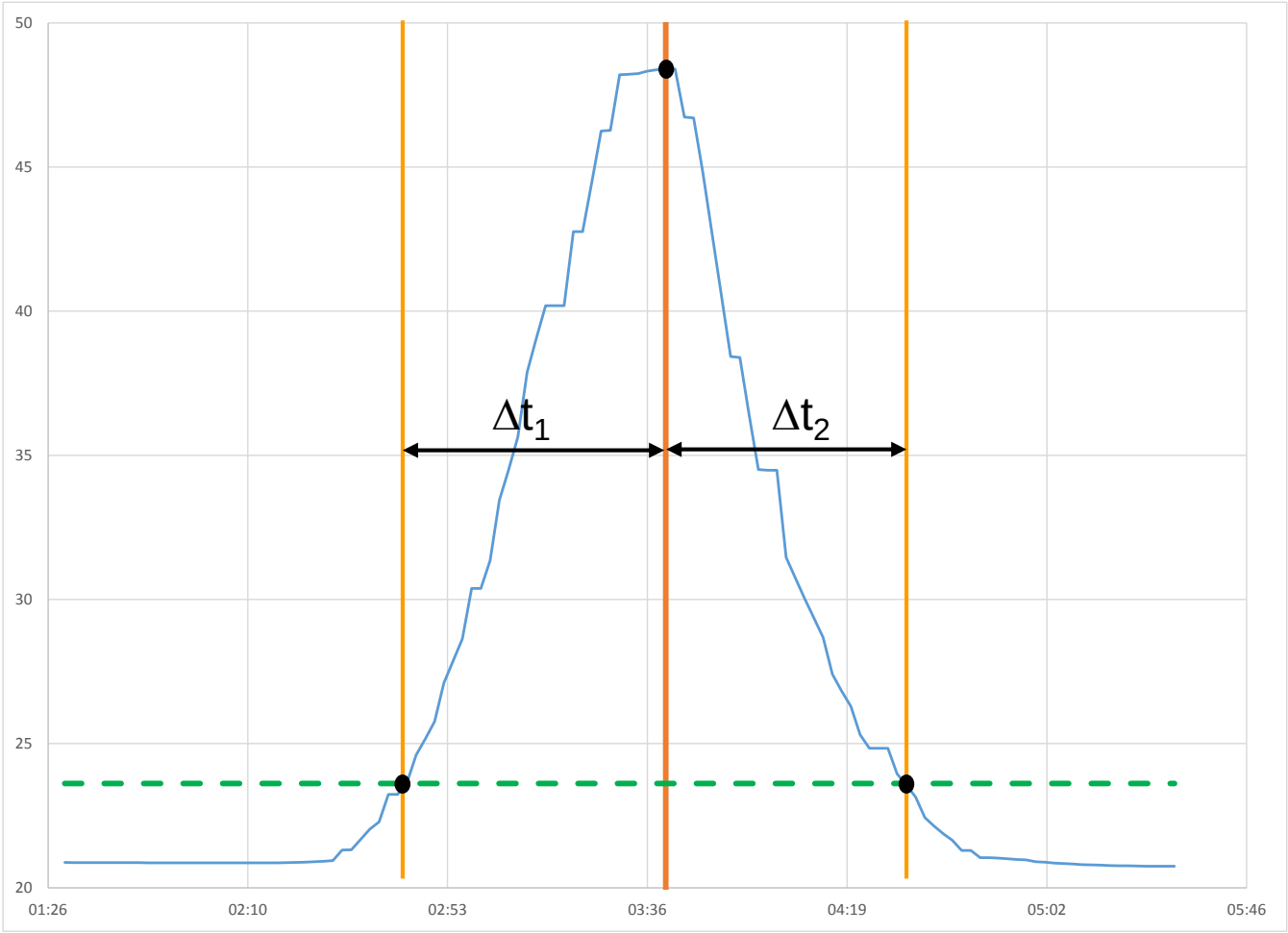
- Saves ~1 hr of analysis time per batch.
- Less time spent collecting data, more time spent analyzing data.

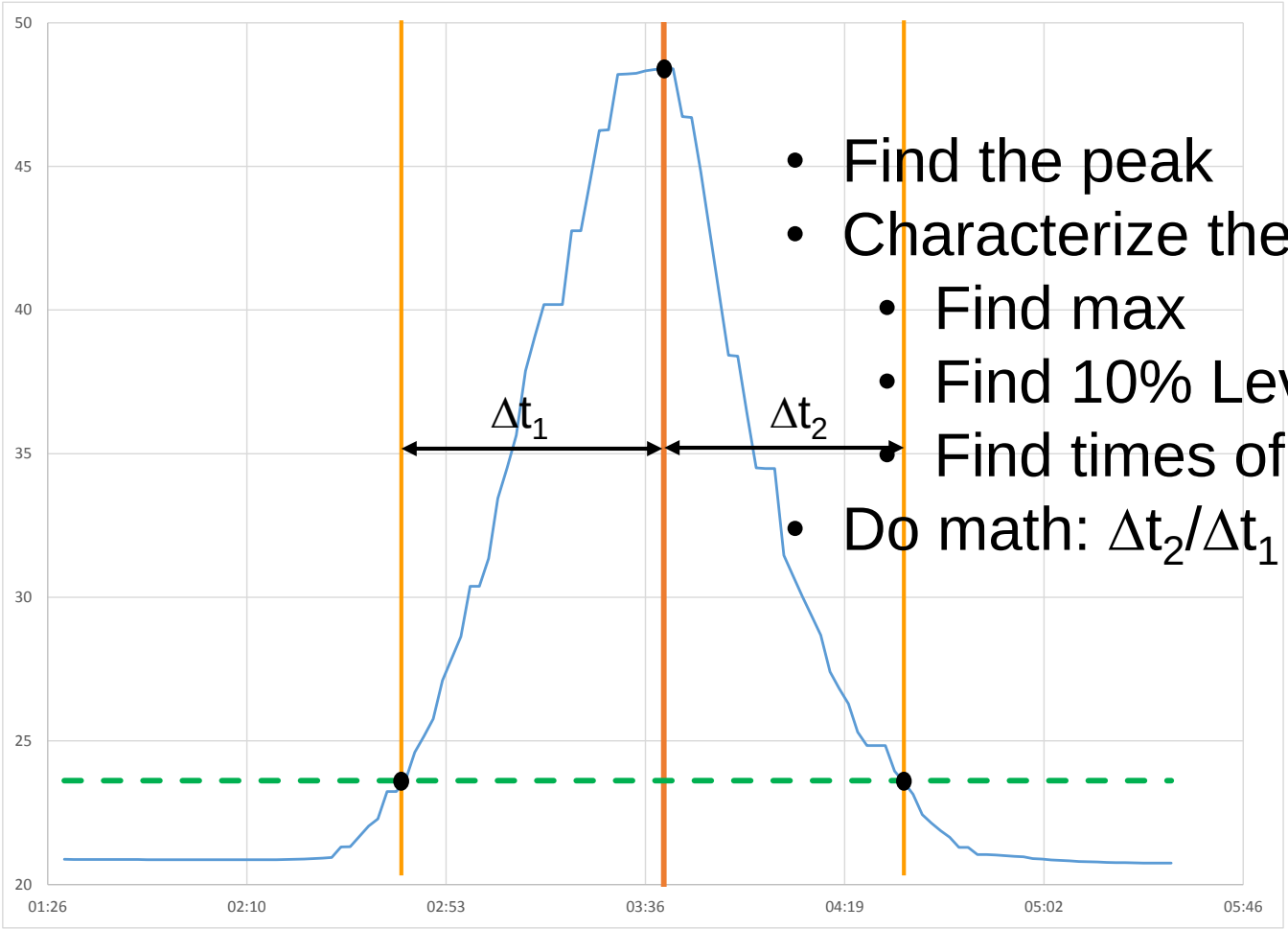






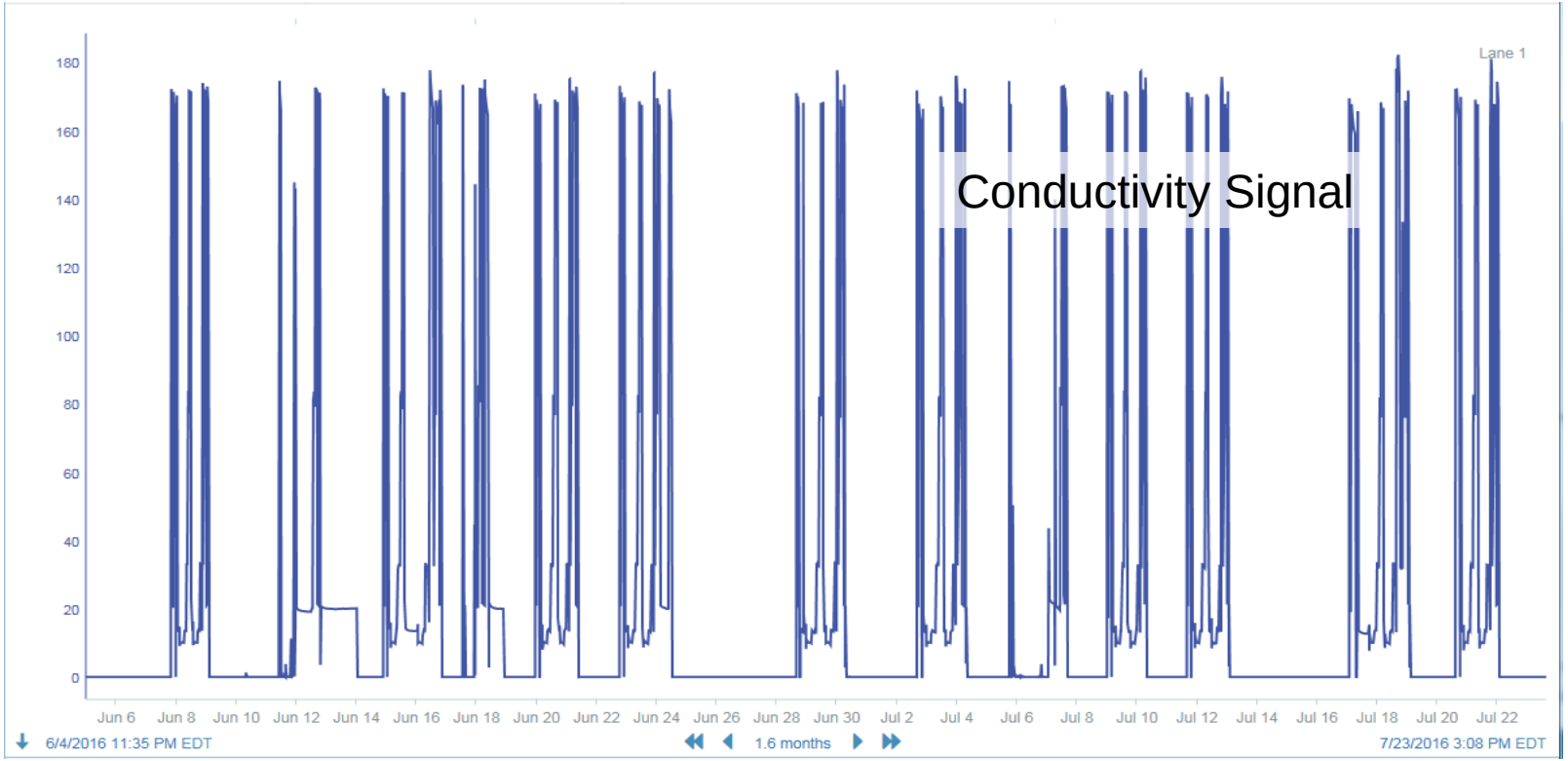




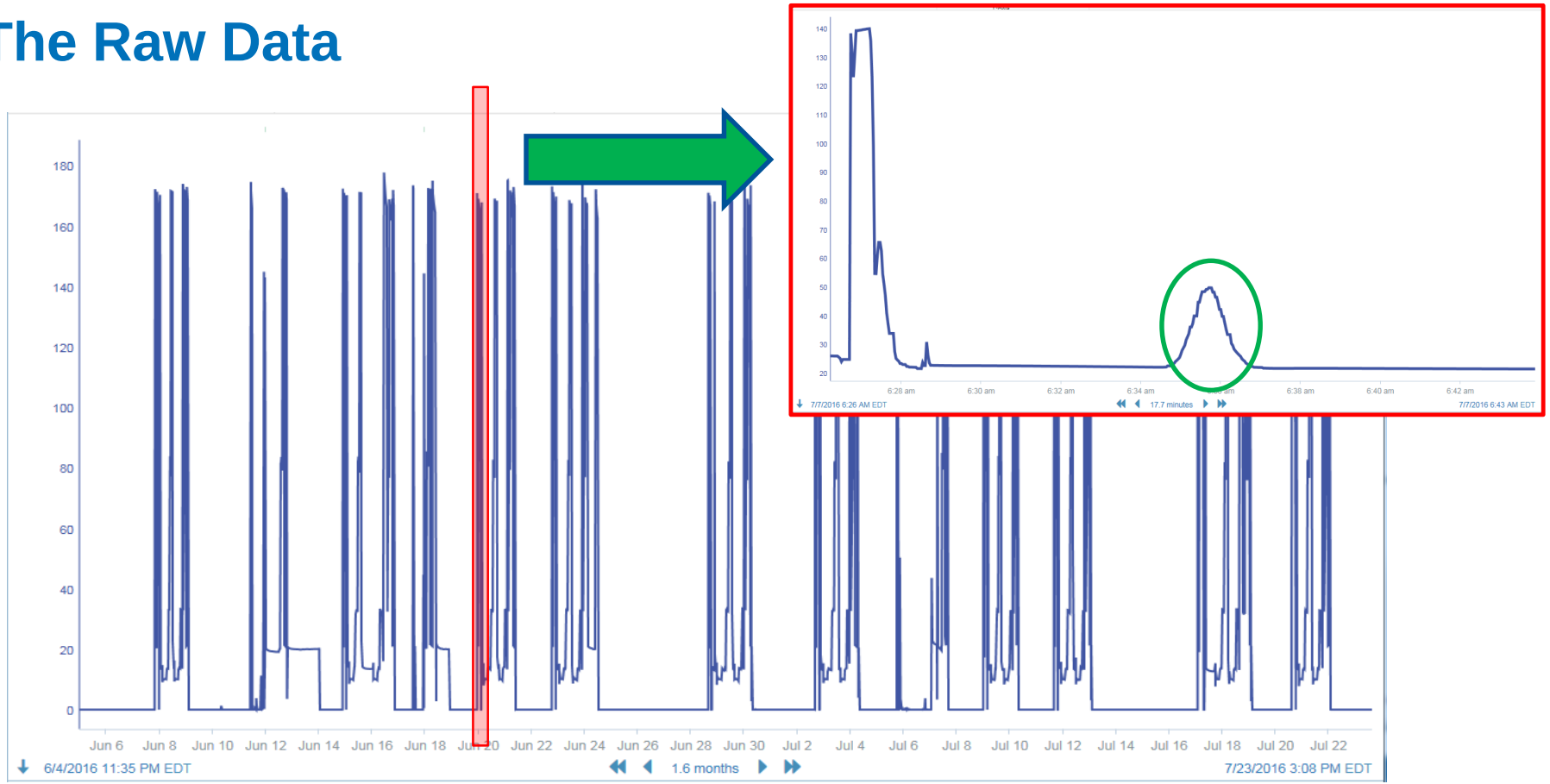


- Find the peak
- Characterize the peak
  - Find max
  - Find 10% Level
  - Find times of interest
- Do math: $\Delta t_2/\Delta t_1$

The Raw Data



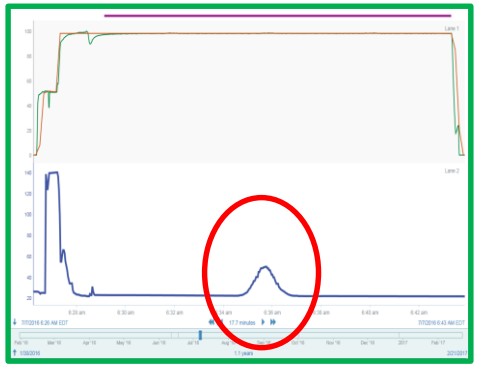
The Raw Data



Find data of interest based on process conditions

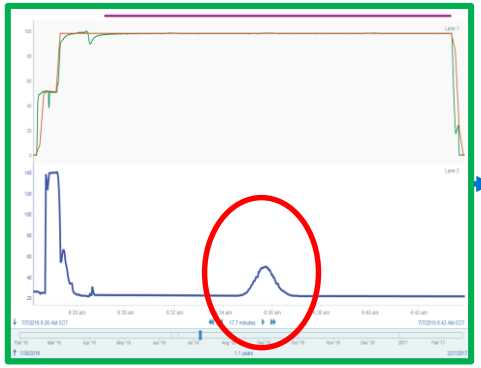
= Signal Logic

= Capsule Logic



= Signal Logic

= Capsule Logic

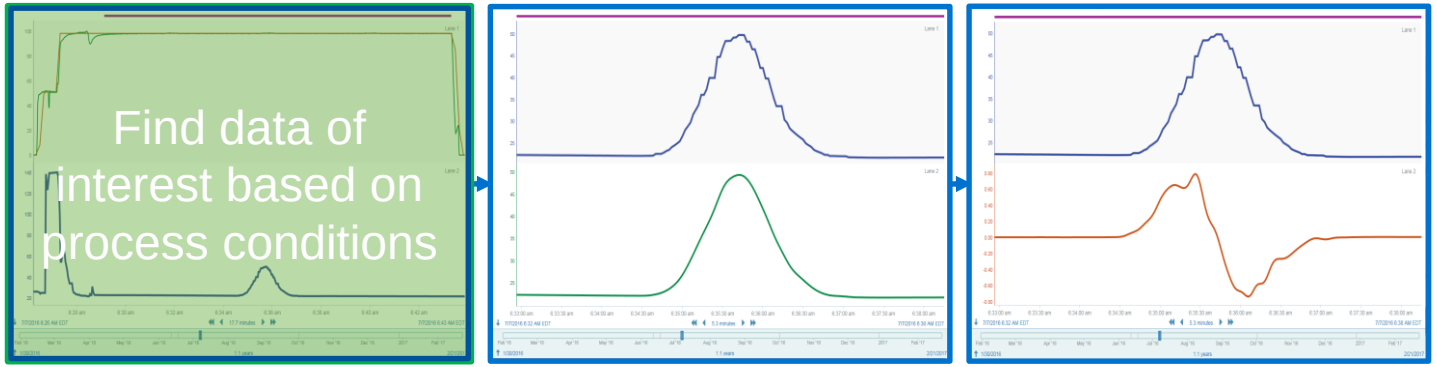


Smooth Data

1st Derivative

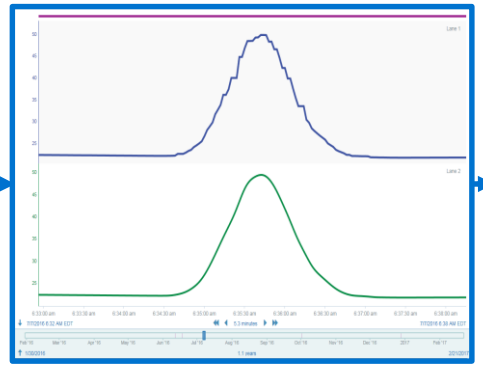
= Signal Logic

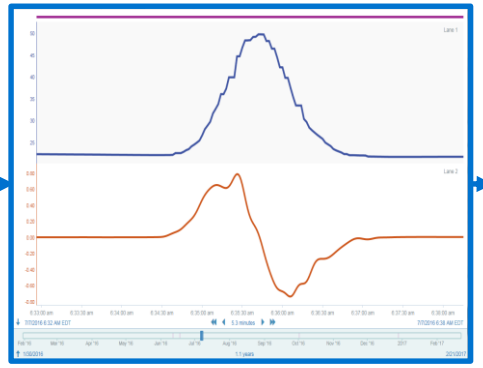
= Capsule Logic



= Signal Logic

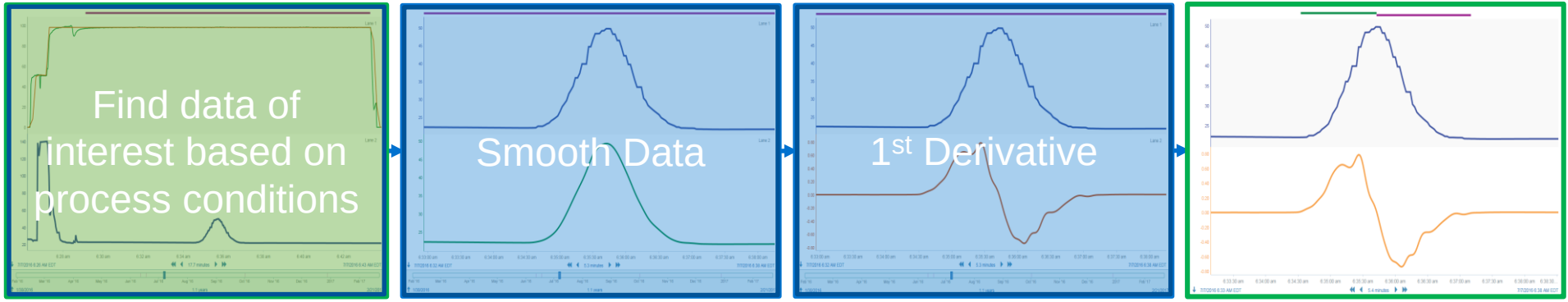
= Capsule Logic





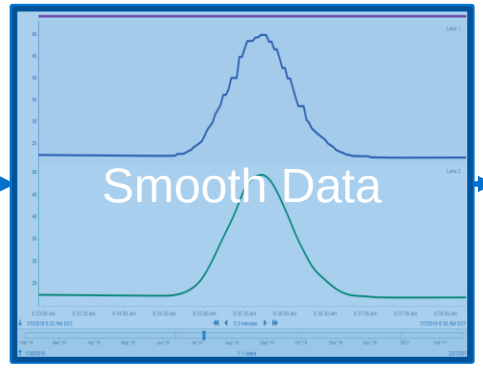
= Signal Logic

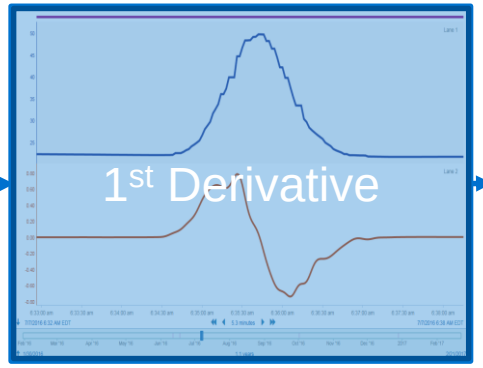
= Capsule Logic

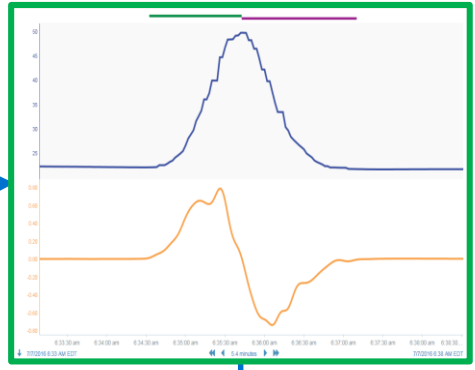


= Signal Logic

= Capsule Logic



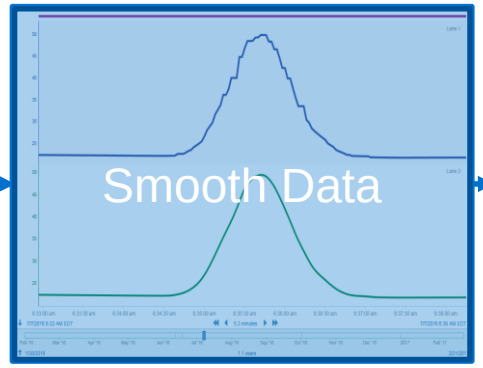


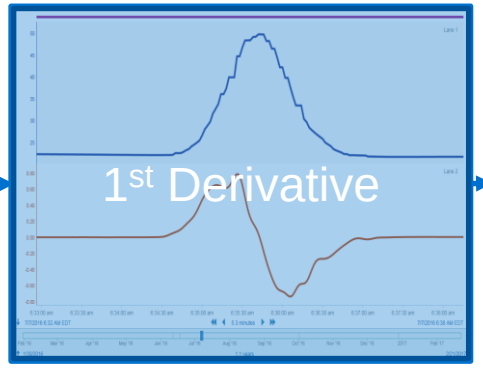


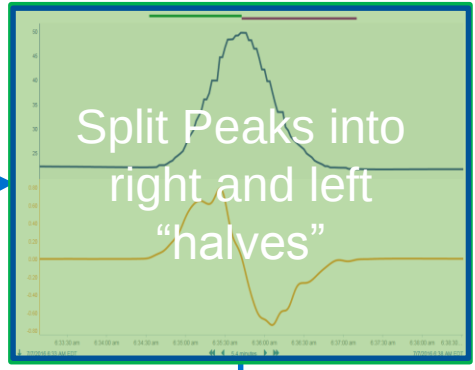
10% Threshold

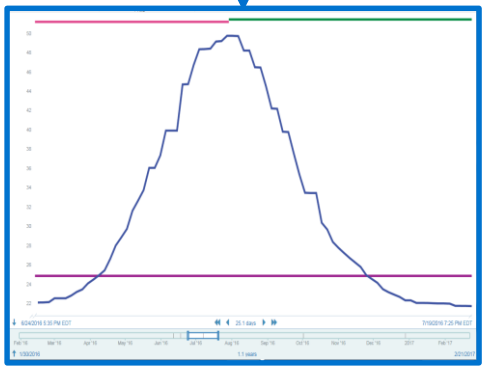
= Signal Logic

= Capsule Logic



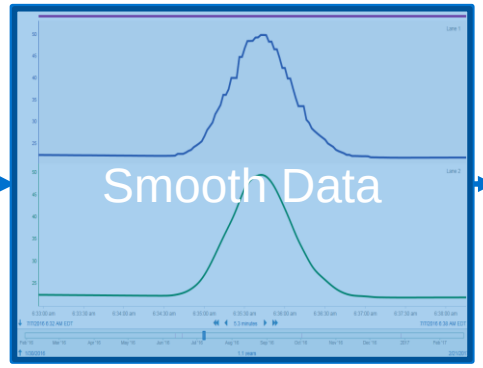


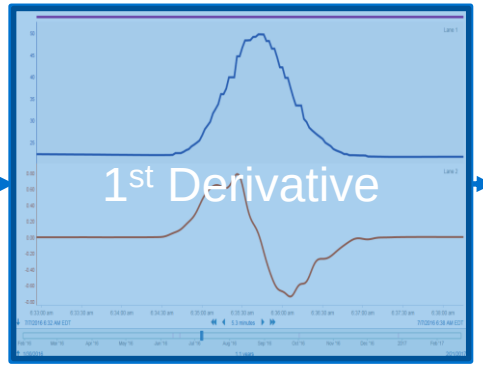


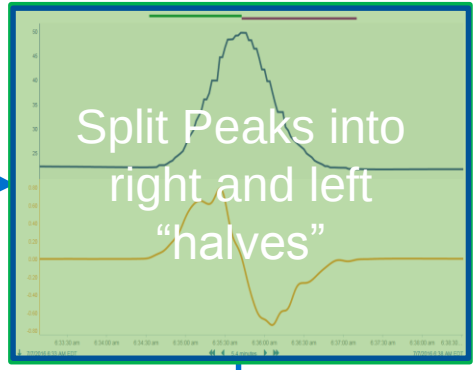


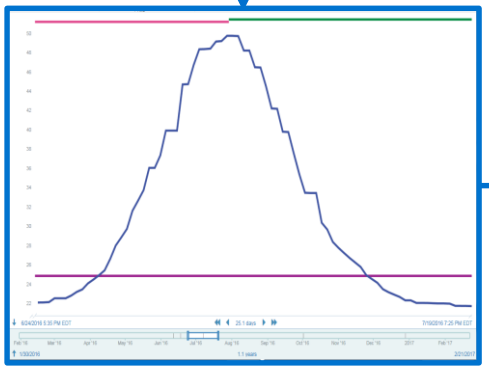
= Signal Logic

= Capsule Logic





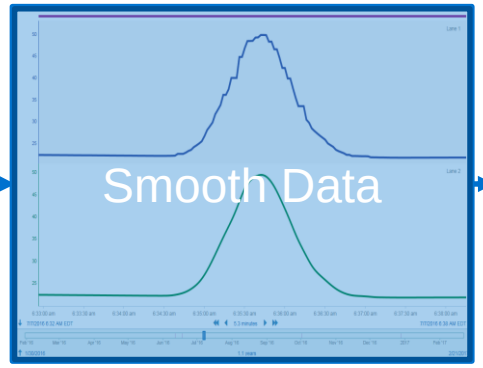


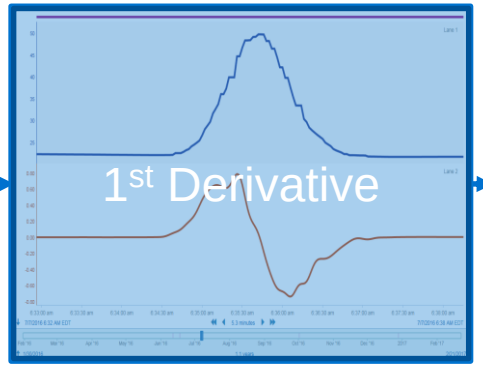


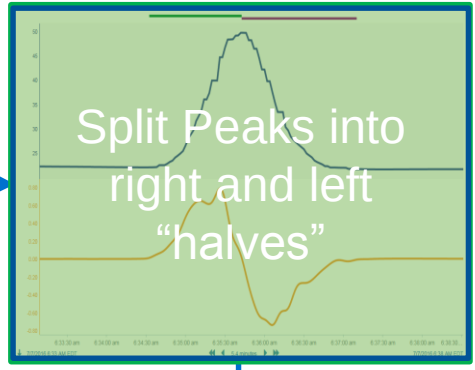
Segment Portion Above Threshold

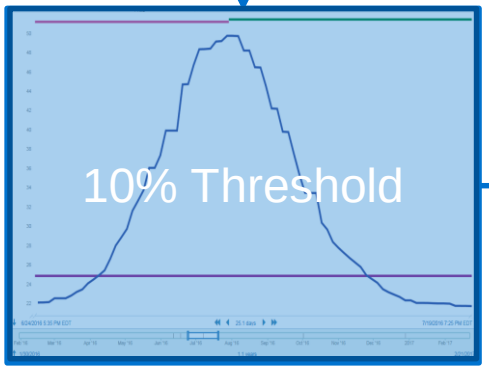
= Signal Logic

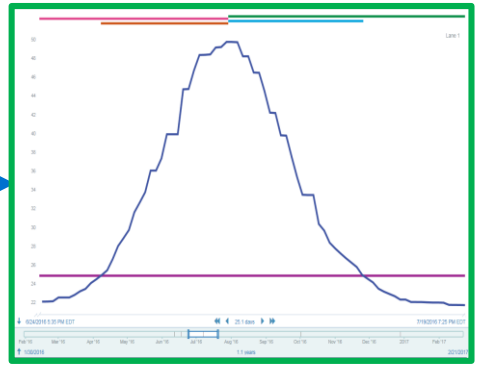
= Capsule Logic





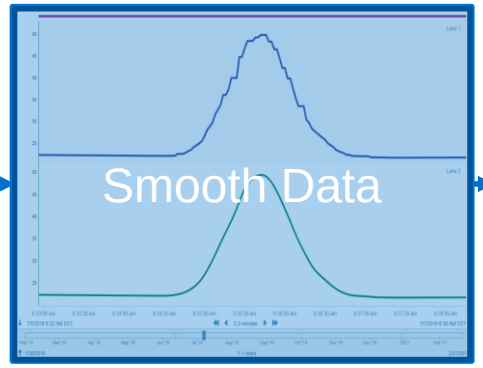


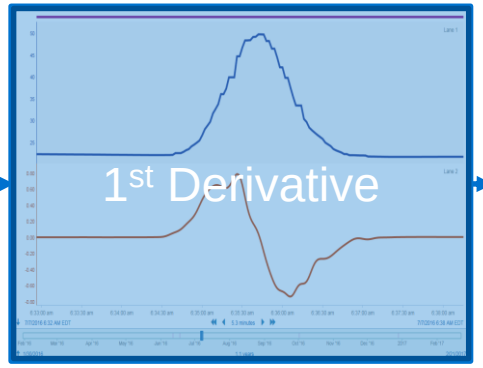


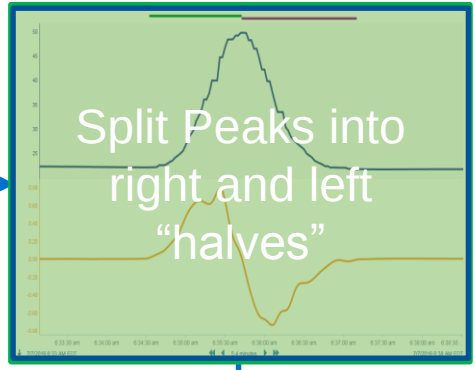


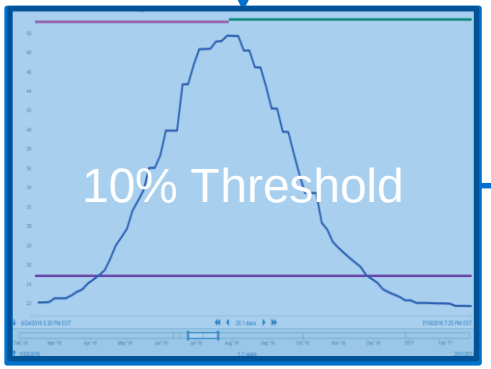
= Signal Logic

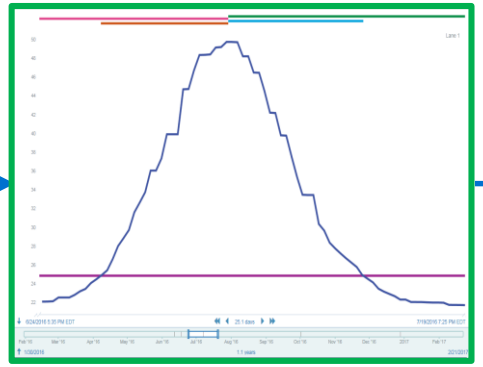
= Capsule Logic







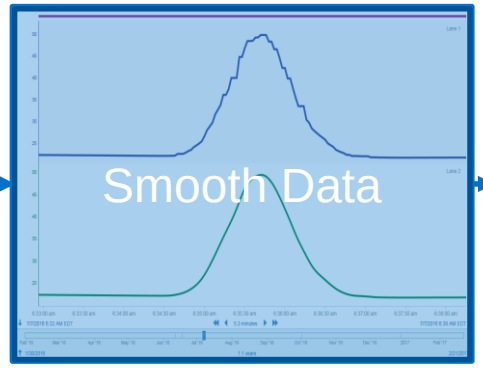


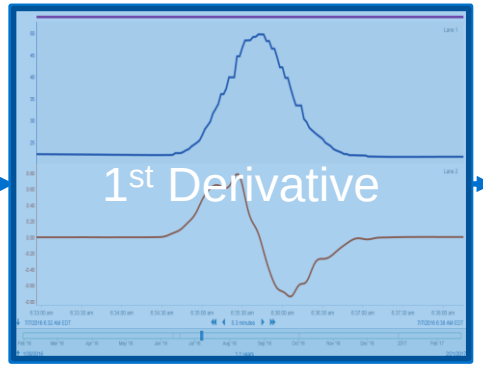


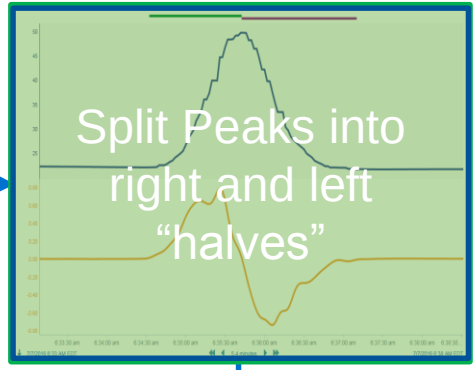
Calculate Asymmetry Ratio

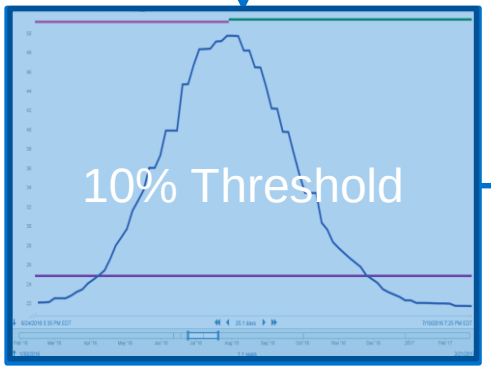
= Signal Logic

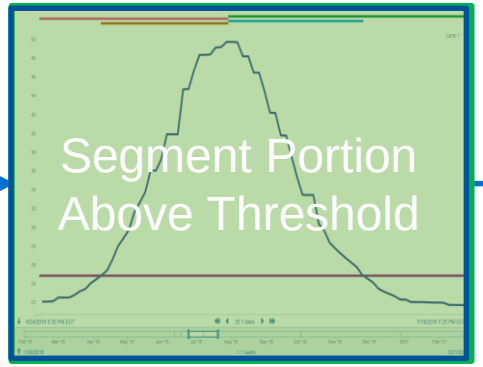
= Capsule Logic

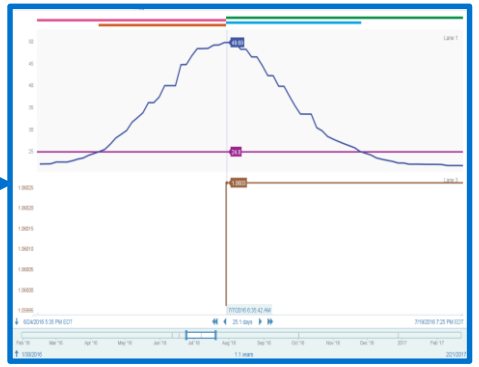






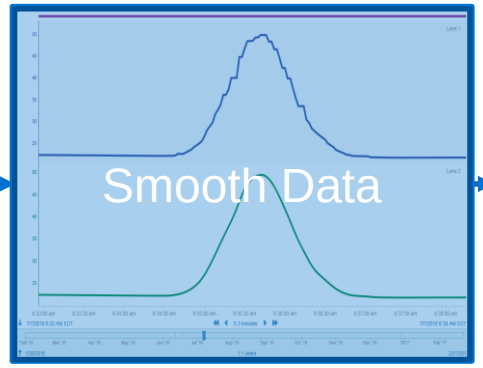


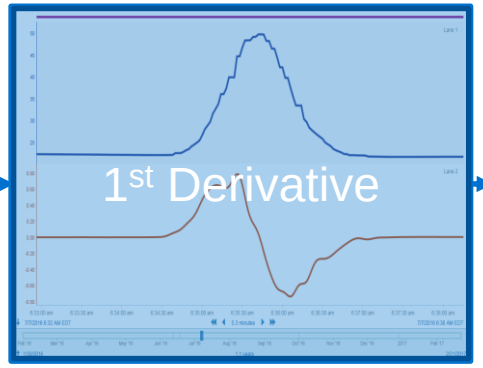


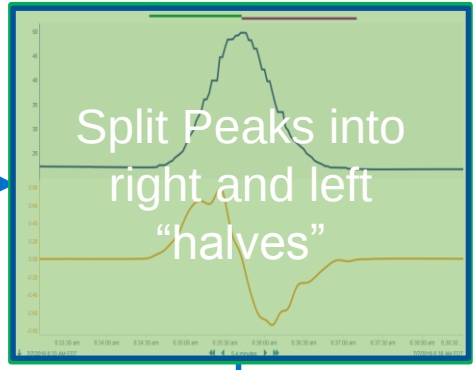


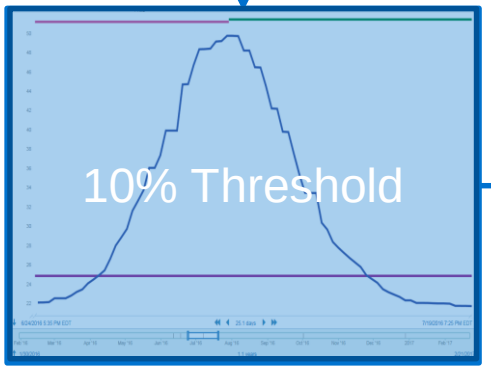
= Signal Logic

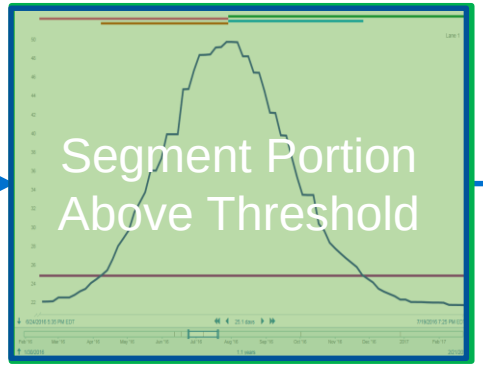
= Capsule Logic

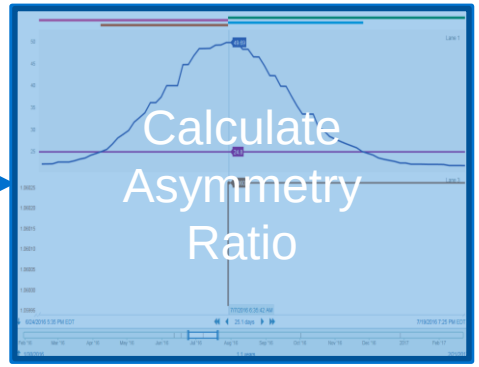








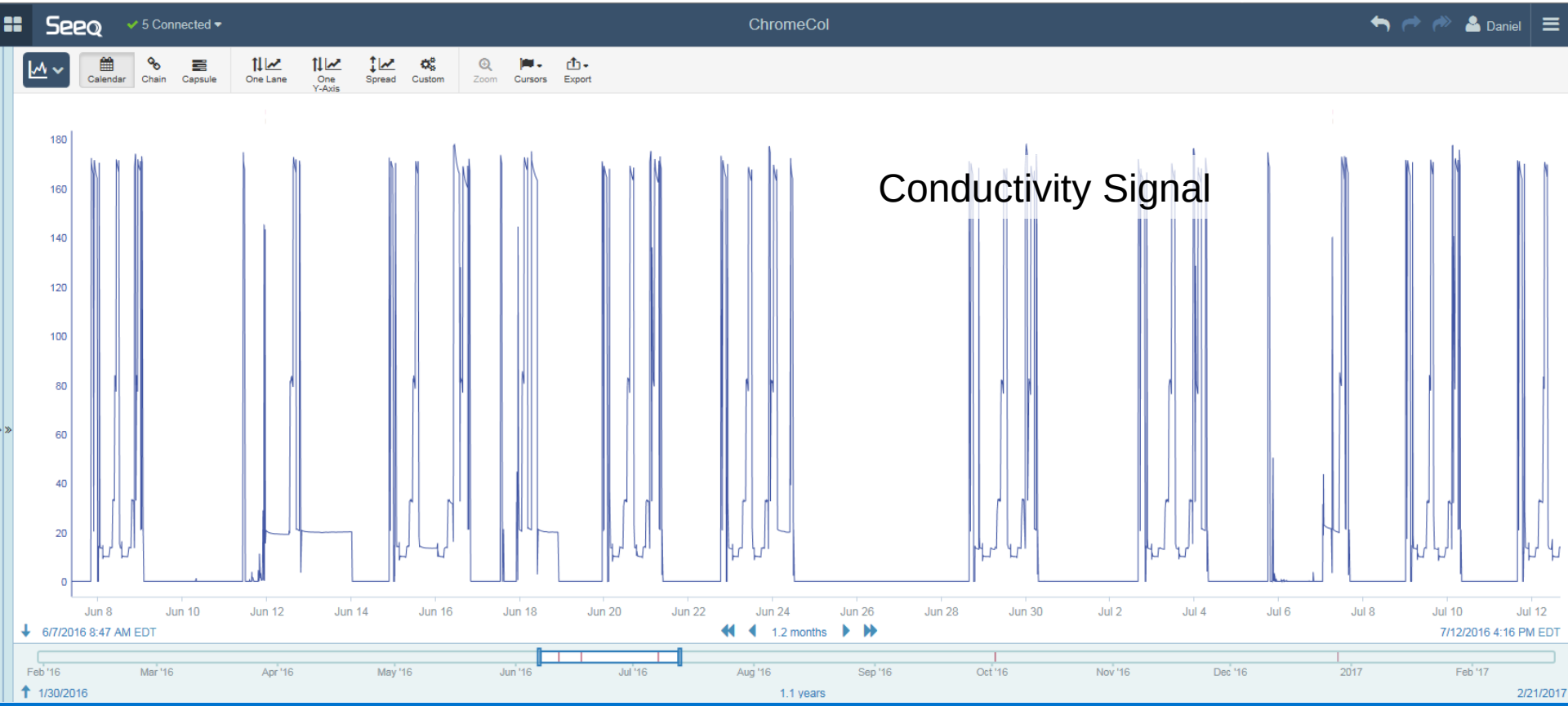




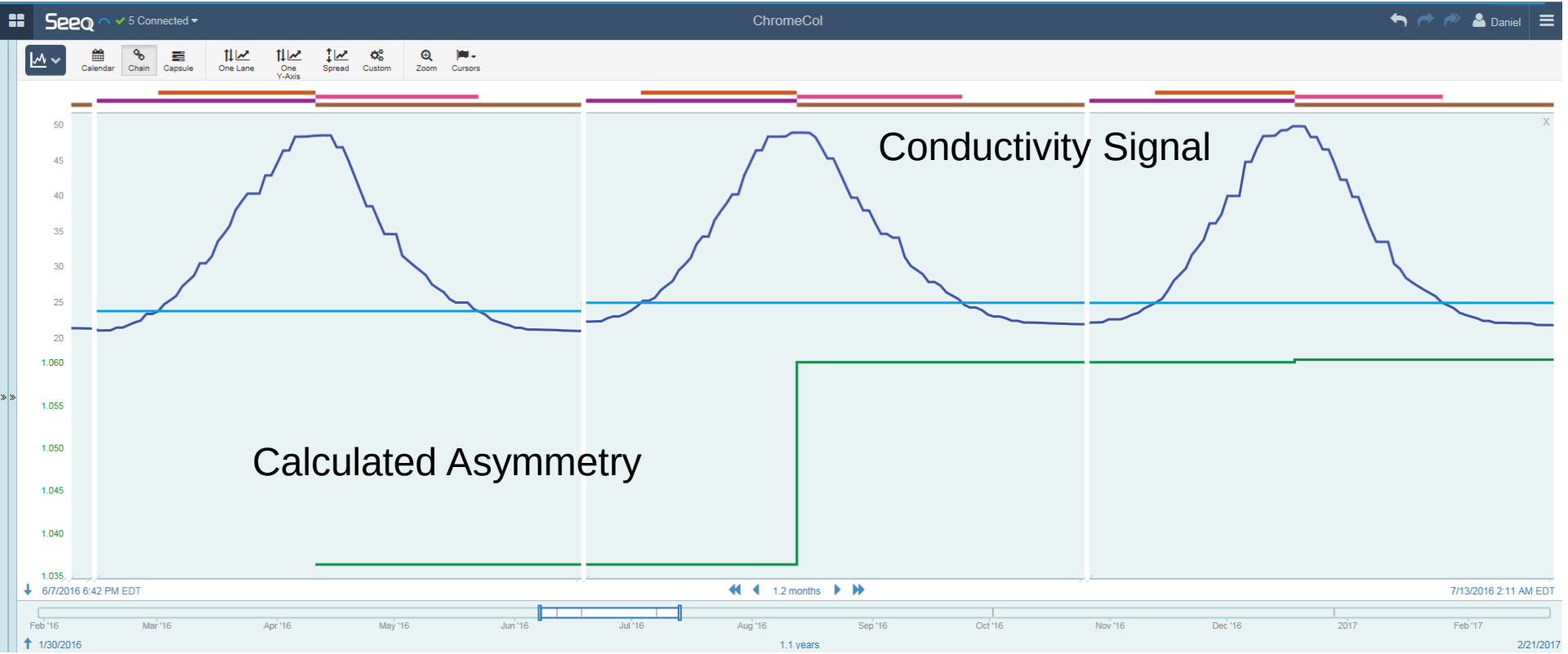
= Signal Logic

= Capsule Logic

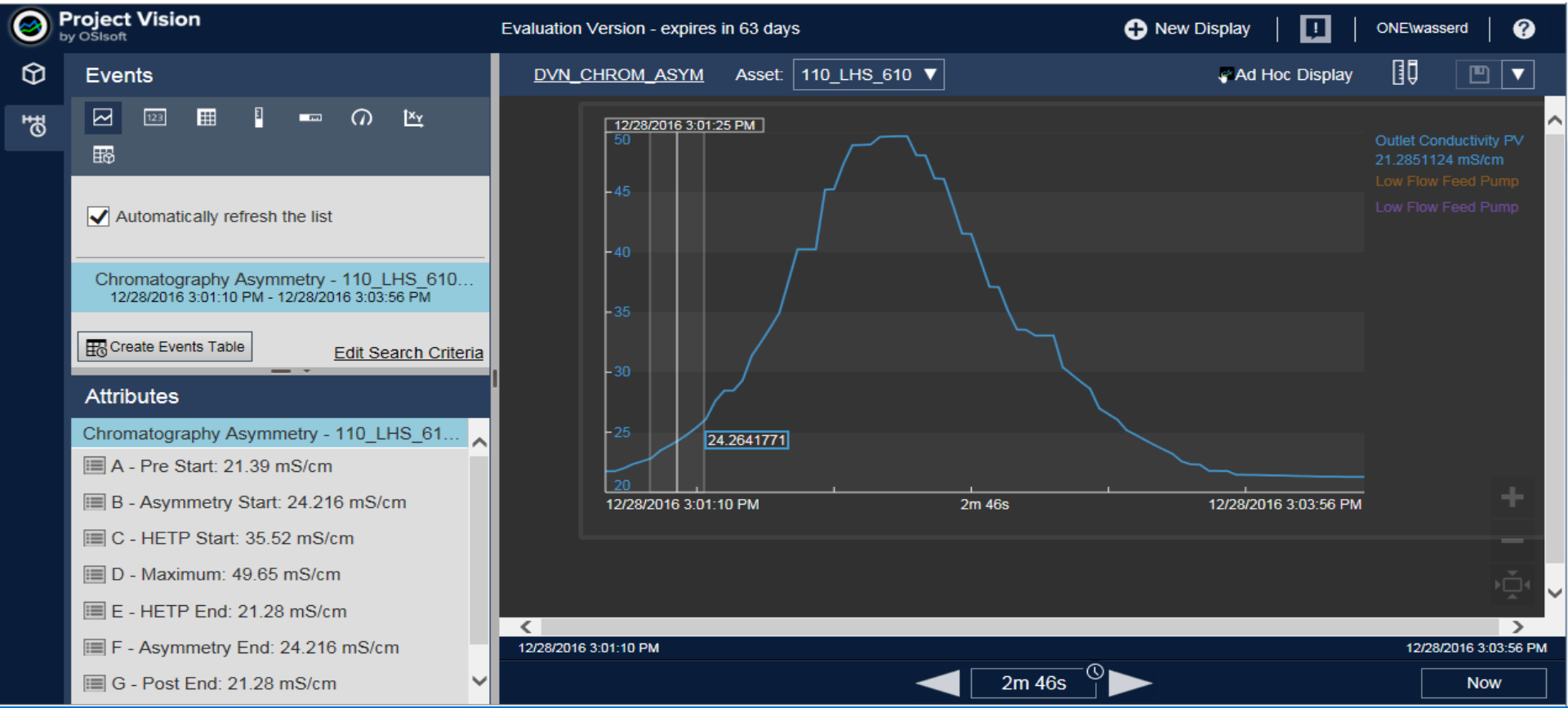
Result: Automatically go from this….



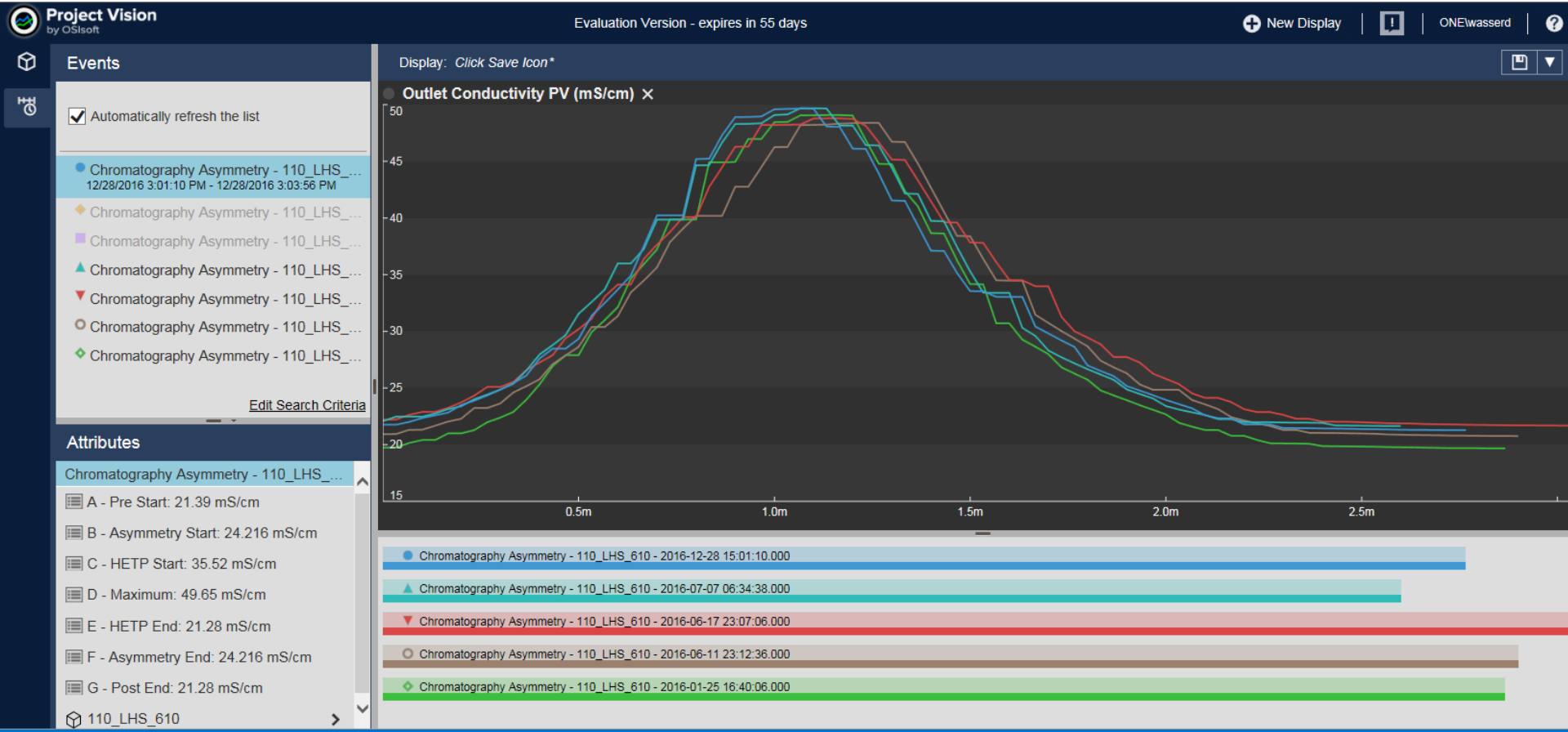
…to this:



Translate logic to PI AF/EF and PI Vision for GMP use:



Easily evaluate and compare (overlay) peaks in PI Vision:



Summary of Automation of Chromatography Column Characterization

Bristol-Myers Squibb

CHALLENGE

Replace manual confirmation of correct column packing with an automated process

- Improper packing can cause low yield, poor quality of product or even complete product loss. Confirmation of correct packing is very important!
- Requires specialized knowledge to find data
- Requires specialized knowledge to confirm packing is correct

SOLUTION

Capture knowledge for confirming packing using Seeq and data in the PI System

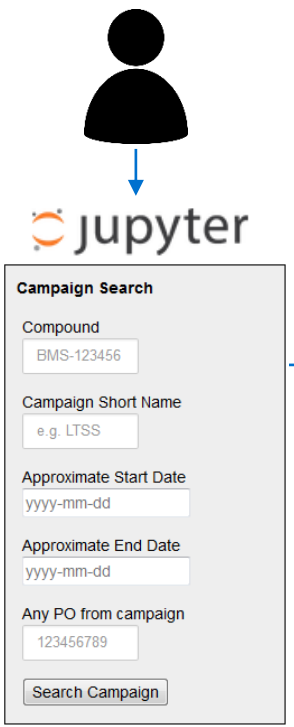
- Seeq provided flexible tools for finding conditions (capsules) and manipulating data (signals)
- Developed and tested automation of confirmation of correct packing

RESULTS

Fully automated column packing confirmation deployed using PI AF/EF and Project Vision

- Automated packing homogeneity test deployed to GMP environment reduces time and improver consistency
- Test results can be trended and correlated with process performance to further optimize efficiency and cycle time.

Use Case: Leverage Asset and Batch Context
Automate Campaign Summaries in Seeq



Jupyter notebook hosted on BMS intranet.

Campaign info from user

PI Batch

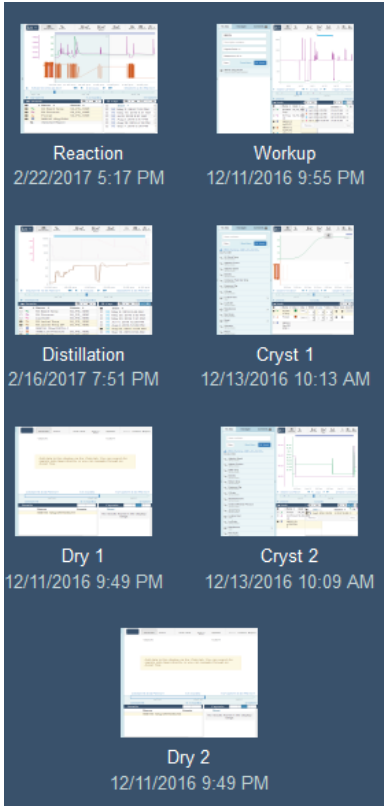
PI SDK: Grab S88 names for each unit operation.

PI System

Python

Seeq

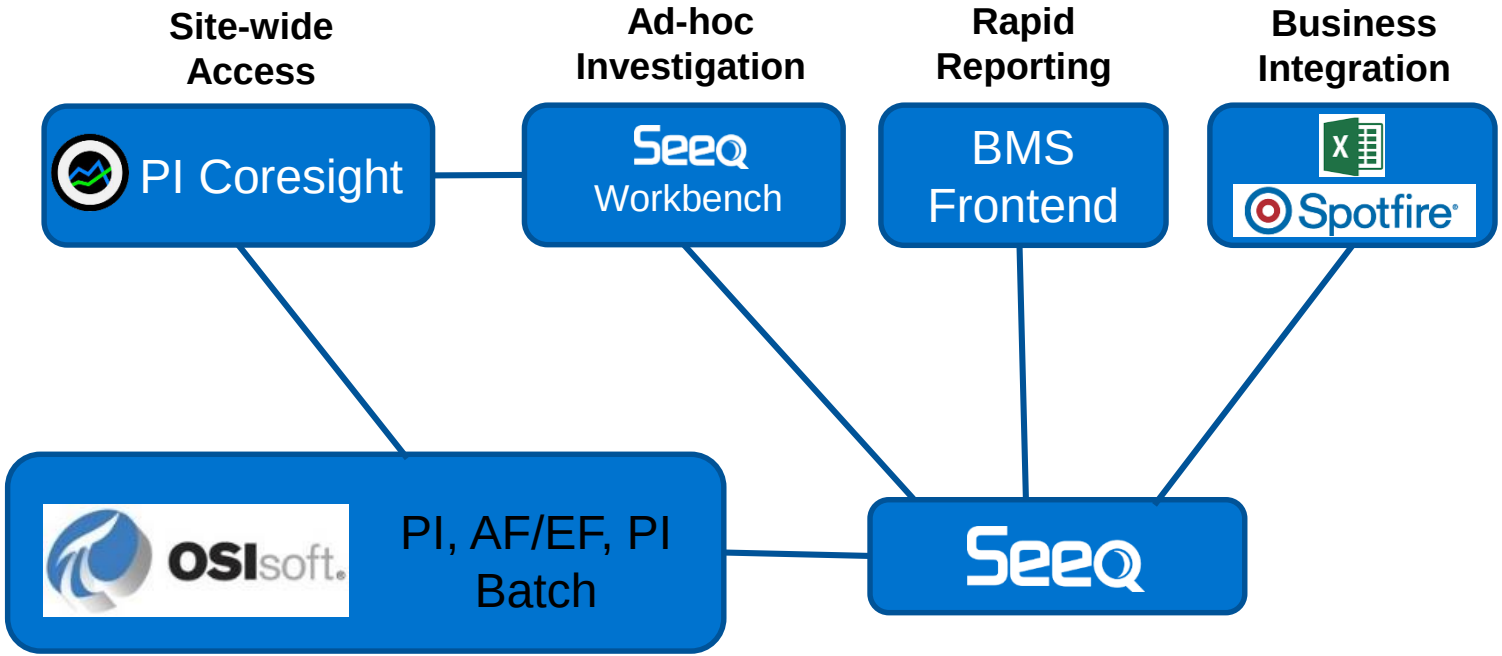
Seeq REST API: Automatically create Seeq searches on string tags using S88 names.



Sheet for each unit operation. Searches find data from each batch in search range.

Benefits

- Open architectures let you get most value from your data.
- Use the best tool for the task.



Summary: Complimentary Tools Meet Needs Across the Organization

- Use PI AF/EF, PI Coresight/PI Vision and Seeq to explore PI System data, discover events, and find data of interest
- Use Seeq to develop logic to capture, share, and automate generation of process knowledge
- Further automation of knowledge generation facilitated by open architecture of the PI System environment
- Knowledge can be deployed to the plant floor and GMP environments using AF, EF, and PI Coresight/PI Vision.

Continue the Discussion

- Seeq – Booth 16
- OSIsoft Visualization – Booth 51
- Asset Framework and Event Frames – Booth 50

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Seeq

Questions

Please wait for the **microphone** before asking your questions

State your **name & company**

Please remember to…

Complete the Online Survey for this session

http://bit.ly/uc2017-app

감사합니다

谢谢

Danke

Merci

Gracias

Thank You

ありがとう

Спасибо

Obrigado

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