

From Flint, Charles, Louis, et. al:

"Milch cows and dairy farming; comprising the breeds, breeding, and management, in health and disease, of dairy and other stock; the selection of milch cows, with a full explanation of Guenon's method; the culture of forage plants, and the production of milk, butter, and cheese ... with a treatise upon the dairy husbandry of Holland; to which is added Horsfall's system of dairy management"

Published by Boston, Crosby, Nichols, Lee & co., **1860**

Fig. 109. Churning by Horse-power. — On large farms and inextensive dairies the churning is done by horse-power.

PAT – Process Analytical Technology

An 2004 initiative by the US FDA

- Reducing production cycle times
- Real time release
- Increasing automation
- Preventing rejects, scrap, and re-processing
- Improving energy and material use
- Increasing capacity
- Facilitating continuous processing

Guidance for Industry

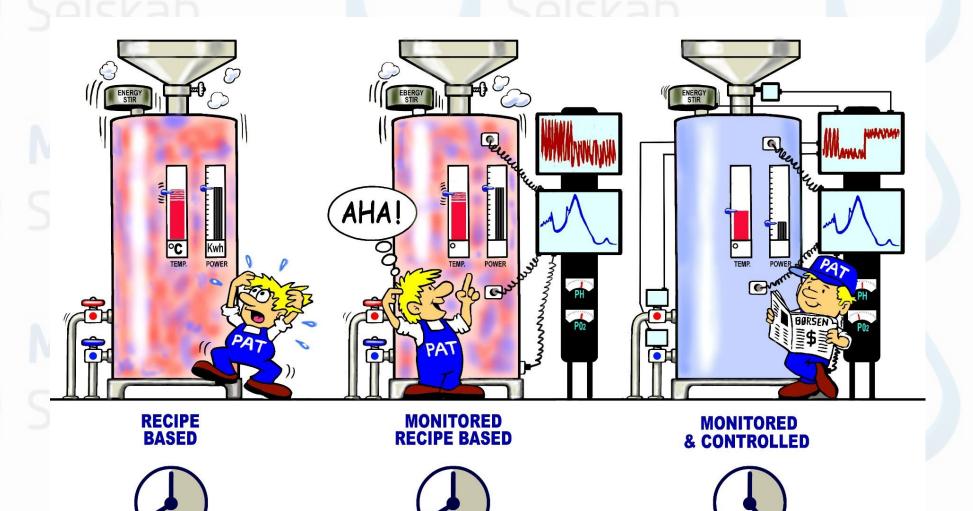
PAT — A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance

U.S. Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER) Center for Veterinary Medicine (CVM) Office of Regulatory Affairs (ORA)

> harmaceutical CGMPs September 2004

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PAT – Process Analytical Technology



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PAT – Process Analytical Technology



The four key PAT Tools

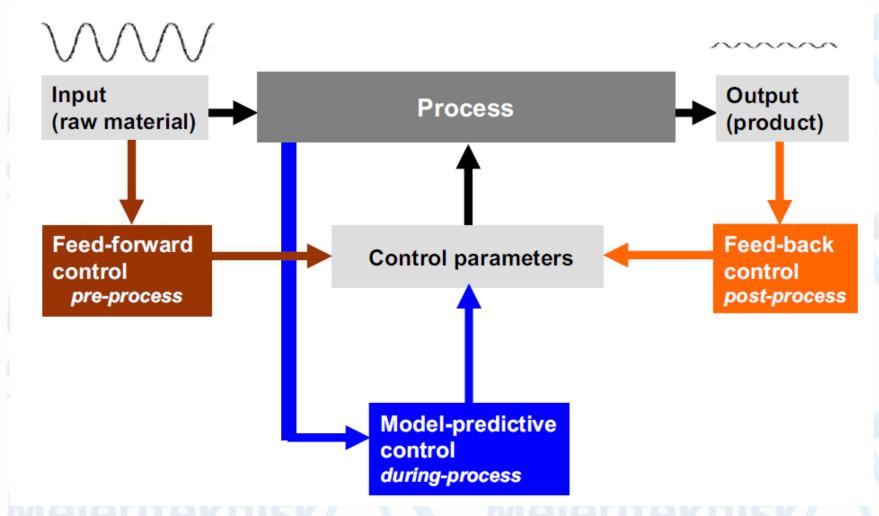
- Process analyzers
- Process control tools
- Multivariate tools for design, data acquisition and analysis
- Continuous improvement and knowledge management tools





The PAT framework

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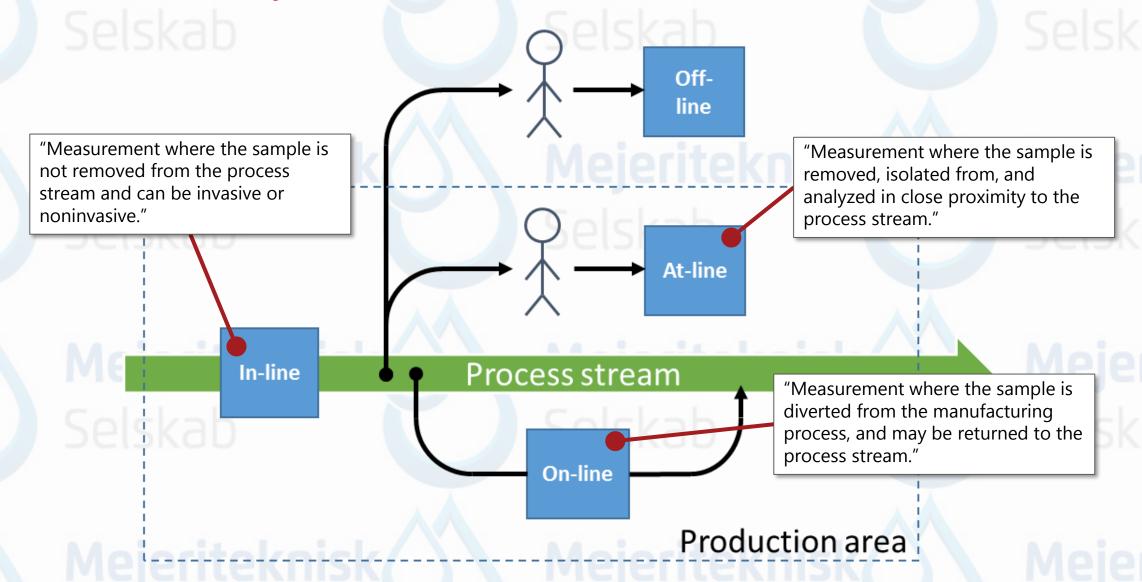


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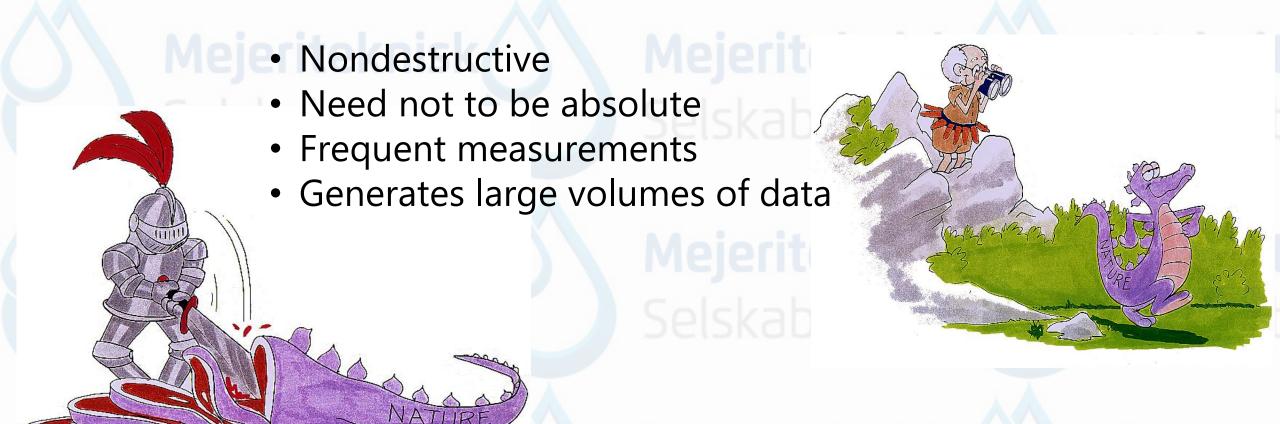
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PAT Process analyzers - methods



PAT Process analyzers - characteristics

"The tools has evolved from univariate process measurements"



PAT Process analyzers : Near-infrared spectroscopic



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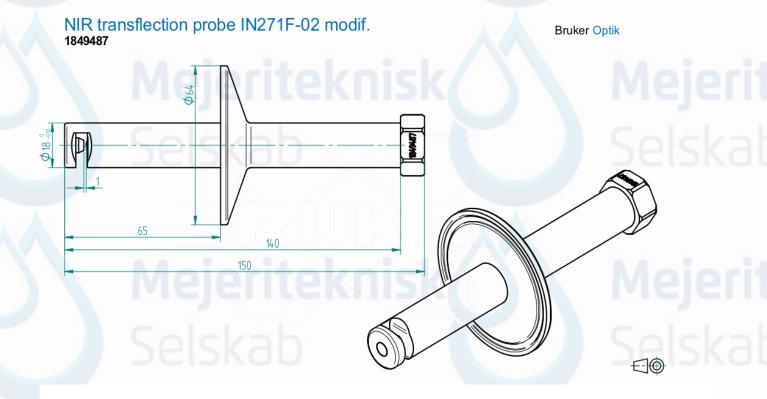
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PAT Process analyzers : NIR In-line





PAT Process control tools

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- Identify and measure critical material and process attributes relating to product quality
- Design a process measurement system to allow real time or near real time (e.g., on-, in-, or atline) monitoring of <u>all</u> critical attributes
- Design process controls that provide adjustments to ensure control of all critical attributes
- Develop mathematical relationships between product quality attributes and measurements of critical material and process attributes

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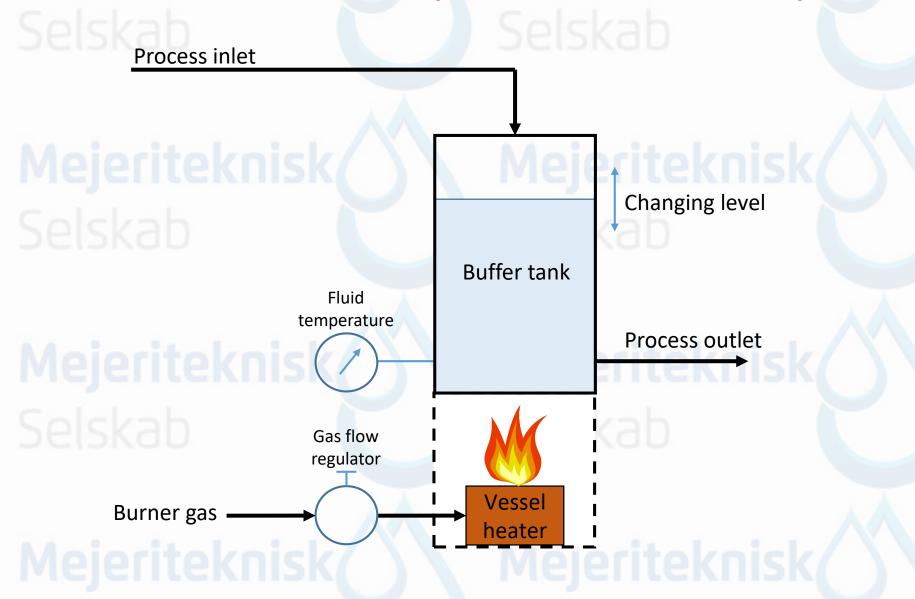
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PAT control tools – it is complex even if it is simple!

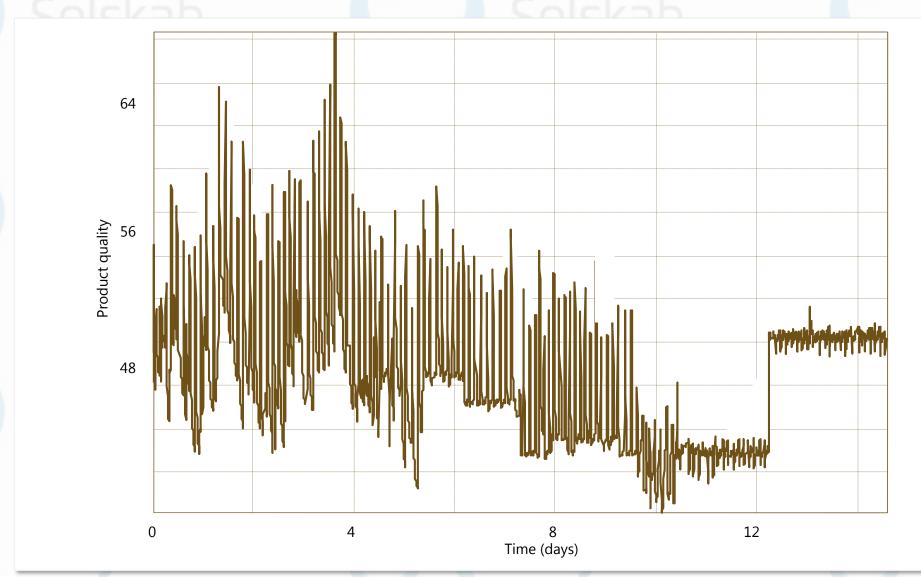


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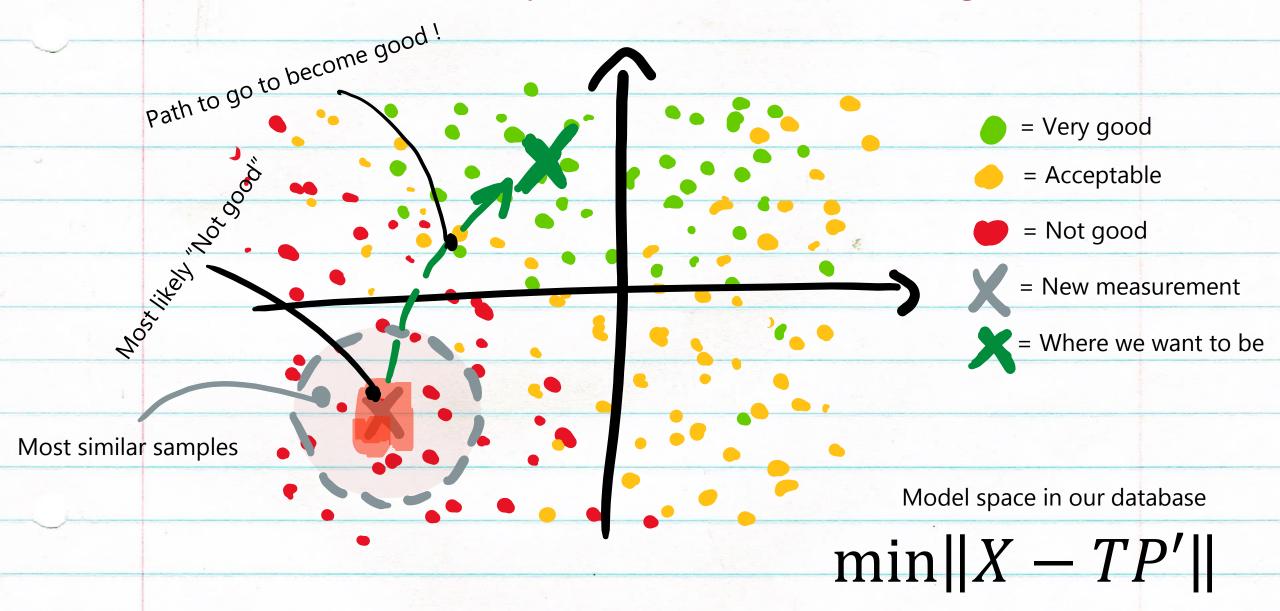
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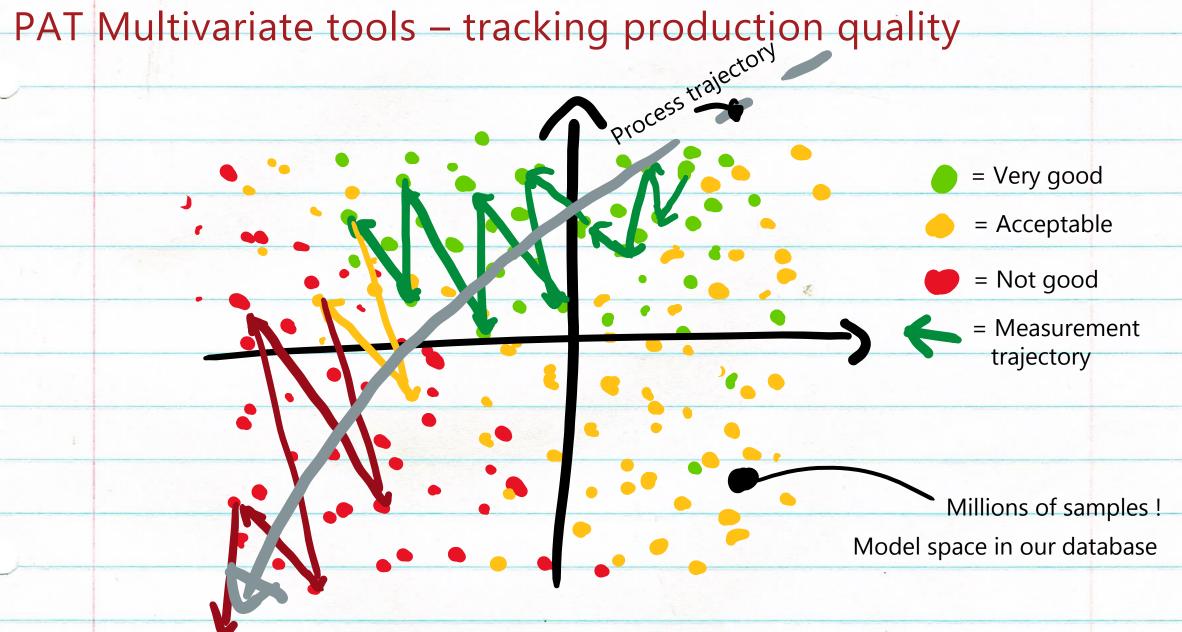
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PAT control tools: frequency and understanding



PAT Multivariate tools – qualitative understanding





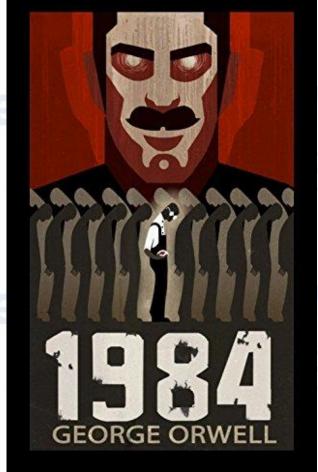
PAT knowledge management tools

Continuous learning through data collection

 A knowledge base can be of most benefit when it consists of scientific understanding of the **relevant multifactorial relationships** (e.g., between formulation, process, and quality attributes) as well as a means to evaluate the applicability of this knowledge in different scenarios (i.e., generalization).

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PAT knowledge management – SCADA and historic data

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Supervision





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Control



Regulation

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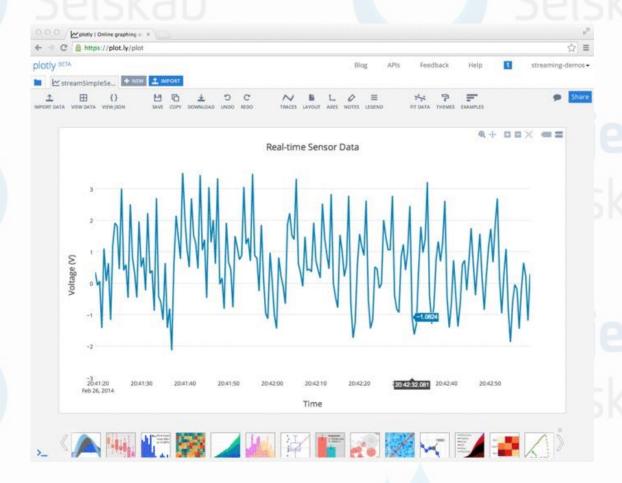


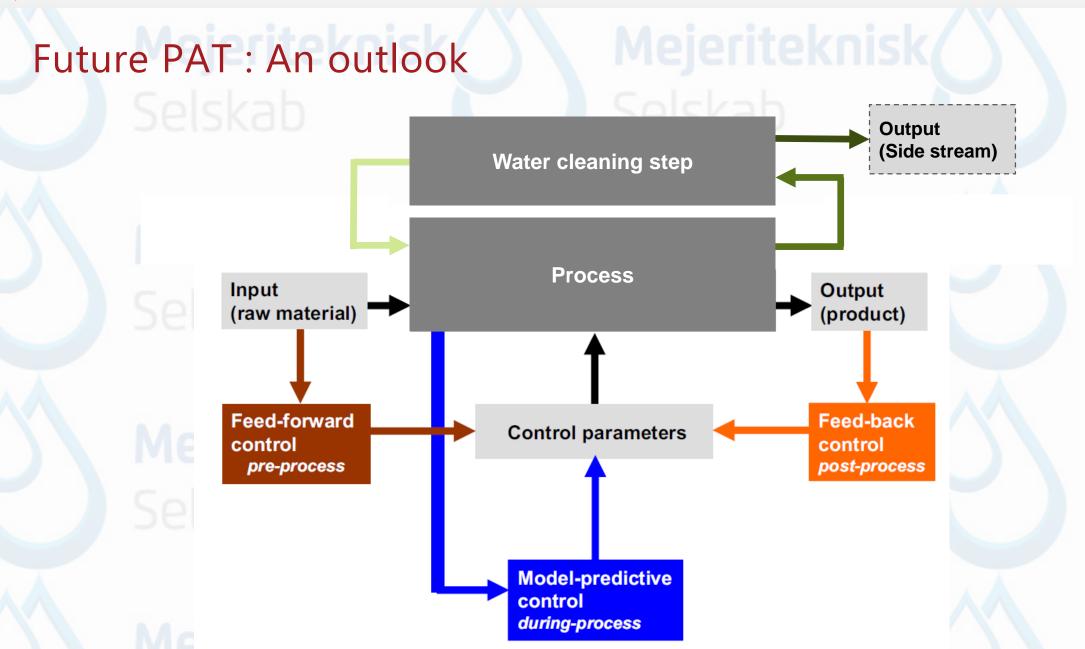
Storage

PAT knowledge management – SCADA and historic data

Data needs to be available

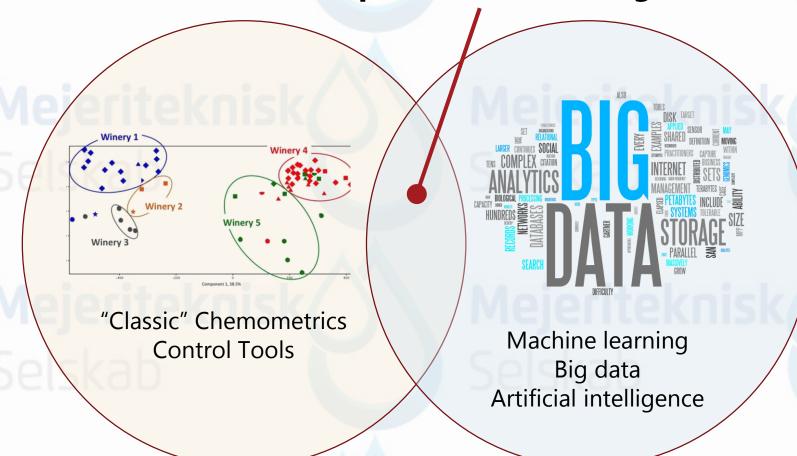
- In most companies I visit, massive and multifactorial data extraction is surprisingly difficult
- Low data retention should be a pre-2019 problem
- We call them data graveyards!





Future PAT : An outlook

Deep Process Learning



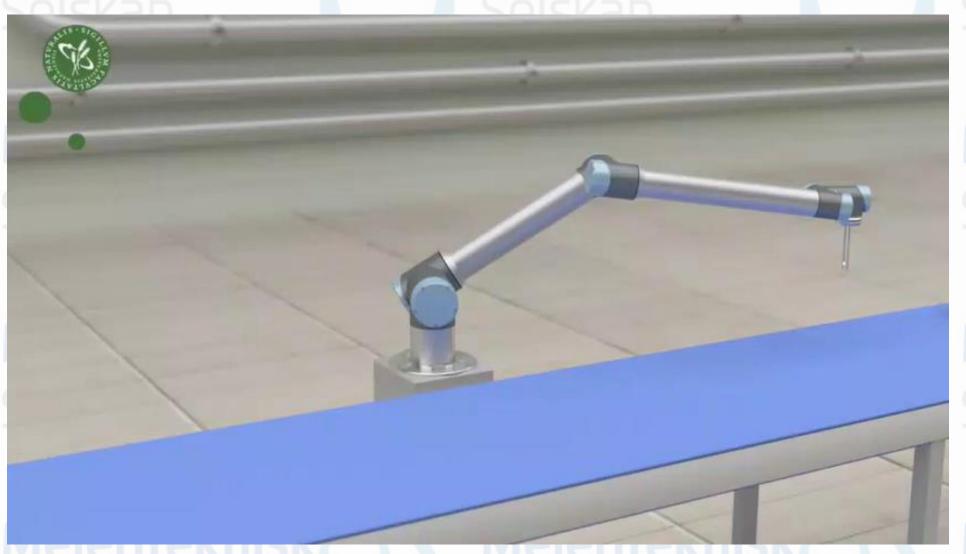
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SayCheese: Automated on-line measurement of cheese



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"Measurement is the first step that leads to control and eventually to improvement. If you can't measure something, you can't understand it. If you can't understand it, you can't control it. If you can't control it, you can't improve it"

— H. James Harrington

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