

Real-time Knowledge-based System and Statistical Process Monitoring, Quality Prediction and Fault Diagnosis for Batch Fermentation Processes

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Outline

- Introduction
 - Statistical process monitoring (SPM)
 - Issues in statistical monitoring of batch processes
 - Batch data organization
 - Adjustment of data lengths and trajectory alignment
- SPM and Quality Prediction:
 - Multiway PLS
 - Integration of SPM with online quality prediction
 - Real-time knowledge-based system integration
- Application to a bioprocess: Fed-batch penicillin fermentation

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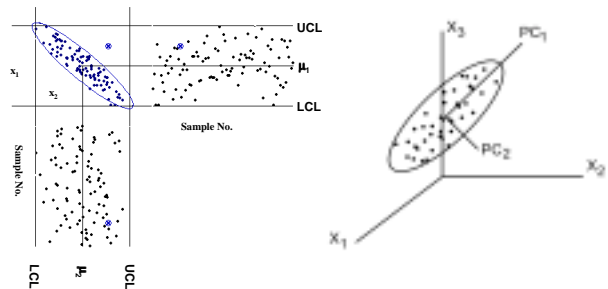
Statistical Process Monitoring

- **Statistical Process Monitoring (SPM)**: Monitor process variables during or at the end of batch to detect abnormal process operation and infer unacceptable quality product
- Goal: Real-time implementation of SPM and quality prediction during batch run with a supervisory knowledge-based system

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Bivariate Control Region



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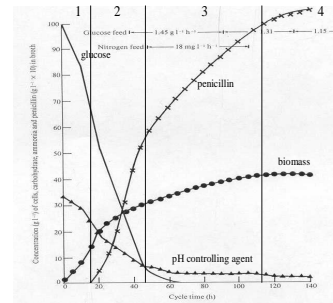
Multivariate Statistical Process Monitoring (MSPM)

- Use of *in-control* runs in the *historical* database
- Development of the statistical model that characterizes normal operation (NOC)
- Computation of control chart limits for use in monitoring future batches

Simulations with and without disturbances were conducted to test the capabilities of MSPM Techniques

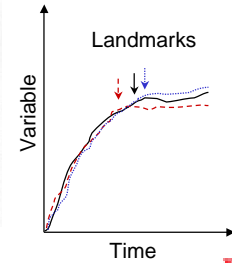
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Batch Process with Several Phases



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*Atkinson and Mavituna, Bioengineering & Biotechnology Handbook

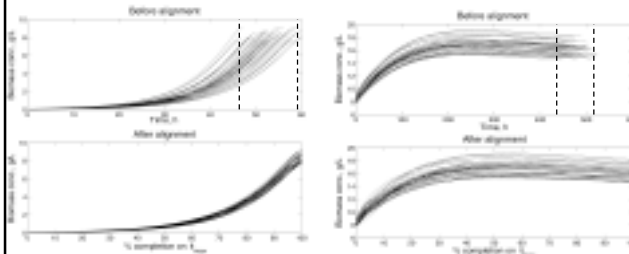


Alignment of Variable Trajectories

Phase 1: Batch

Phase 2: Fed-batch

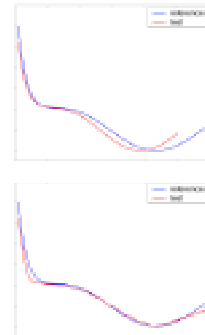
Temporal Variation



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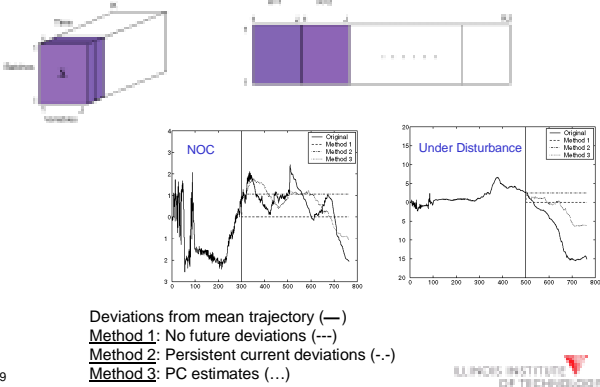
Data Alignment Techniques

- Dynamic Time Warping
 - Nonlinear dynamic programming
- Curve Registration
 - Estimate a smooth warping function by functional data analysis
- Indicator Variable (IV)
 - Re-digitize trajectories with respect to an IV
 - Smooth, monotonically increasing/decreasing, span operation range
 - MPLS for IV generation



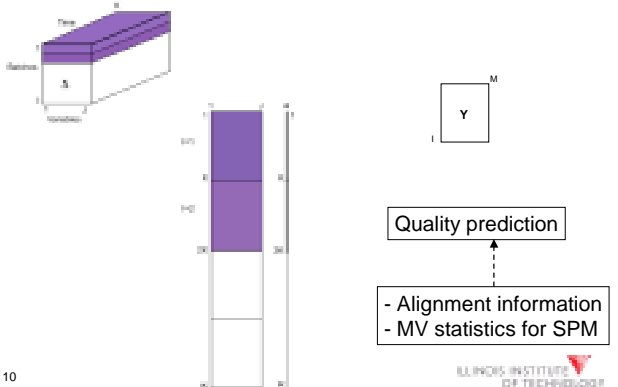
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Alternatives for Unfolding a Batch Data Array



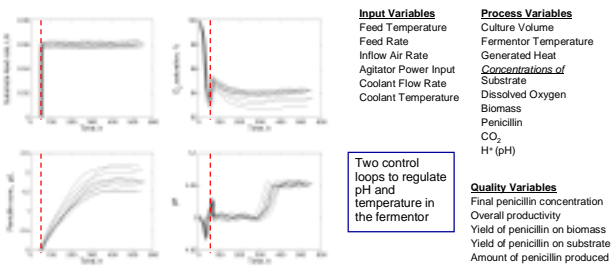
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Alternatives for Unfolding a Batch Data Array



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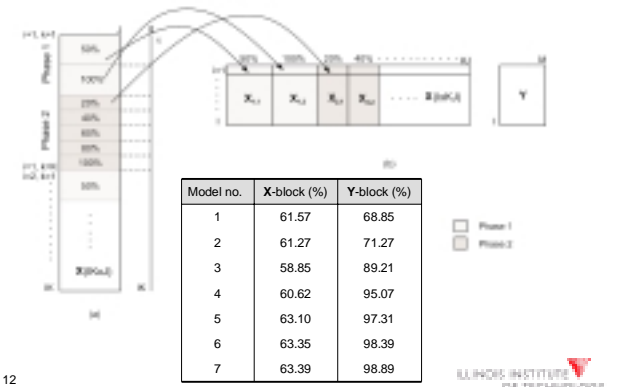
Fed-batch Penicillin Fermentation



G. Birol, C. Undey and A. Cinar, A Modular Simulation Package for Fed-batch Fermentation: Penicillin Production, Computers and Chemical Engineering, 26(11), 1553-1565, 2002.

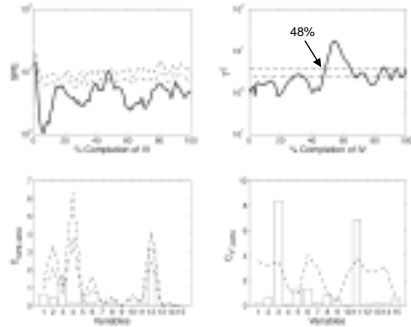
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Integrated Framework: MSPM & Quality Prediction



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Case: Drift disturbance

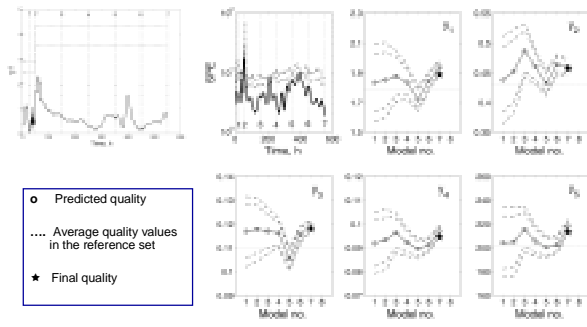


Session: 263b, 2:20pm, Friday, Nov. 8
 Room: 205, Indianapolis Convention Center



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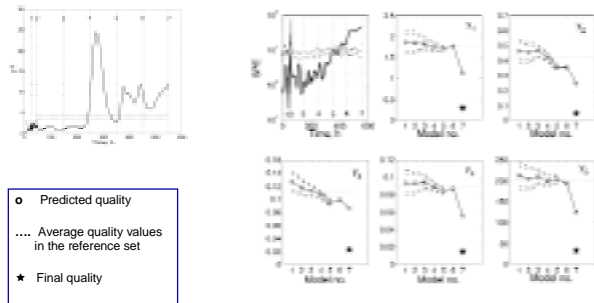
Quality Prediction: Good Batch (NOC)



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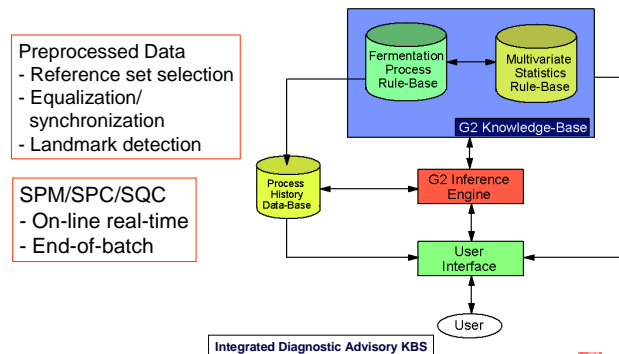
Quality Prediction: Faulty Batch (Drift)



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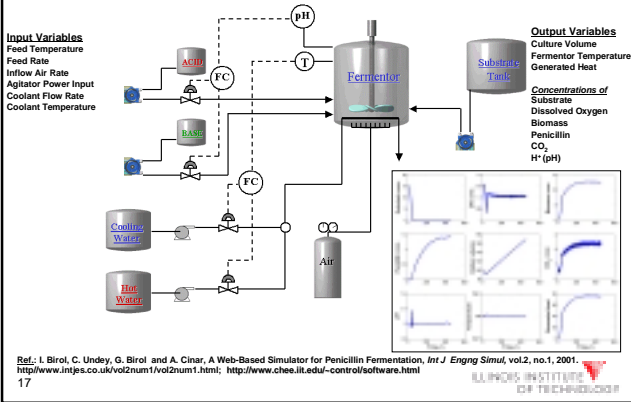
Integration of the Techniques in RTKBS



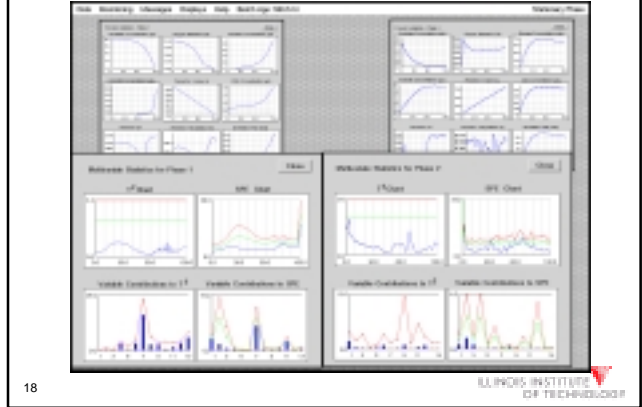
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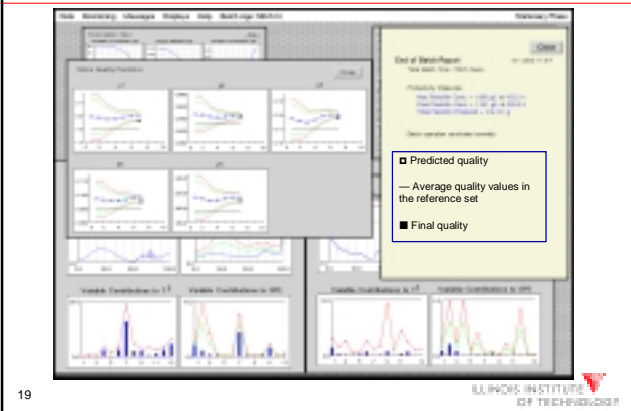
Fed-batch Penicillin Process Flow Sheet in G2



RTKBS Case 1: NOC batch



RTKBS Case 1: NOC batch (end-of-batch)



RTKBS Case 2: Faulty batch (drift)



RTKBS Case 2: Faulty batch (drift) (end-of-batch)



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Conclusions

- Real-time SPM provides opportunity for timely intervention saving a batch that may lead to deteriorated product quality
- SPM based on variable direction provides an alternative monitoring method
 - Preserving variable direction in unfolding is advantageous:
 - ▶ No future value estimation required
 - ▶ Data alignment performed simultaneously
 - Care should be taken for discontinuities in IVs
 - Divide progress of the batch into phases
 - ▶ Divide data as batch/fed-batch phases

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Conclusions

- Online quality prediction allows early assessment
- Enhanced multivariate charting: **faster fault detection/diagnosis**
 - Detailed trend analysis and diagnosis using contribution plots with limits
- Framework suitable for integrating into a real-time supervisory knowledge-based system
- MV Chart Interpretation Automated via RTKBS

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