Fault-tolerant Control Design and Risk MAP based Resiliency Analysis of Continuous Solid Dose Manufacturing

Presenter: Qinglin Su, Purdue University
Research Participants: Mariana Moreno, Gintaras V. Reklaitis, Zoltan K. Nagy

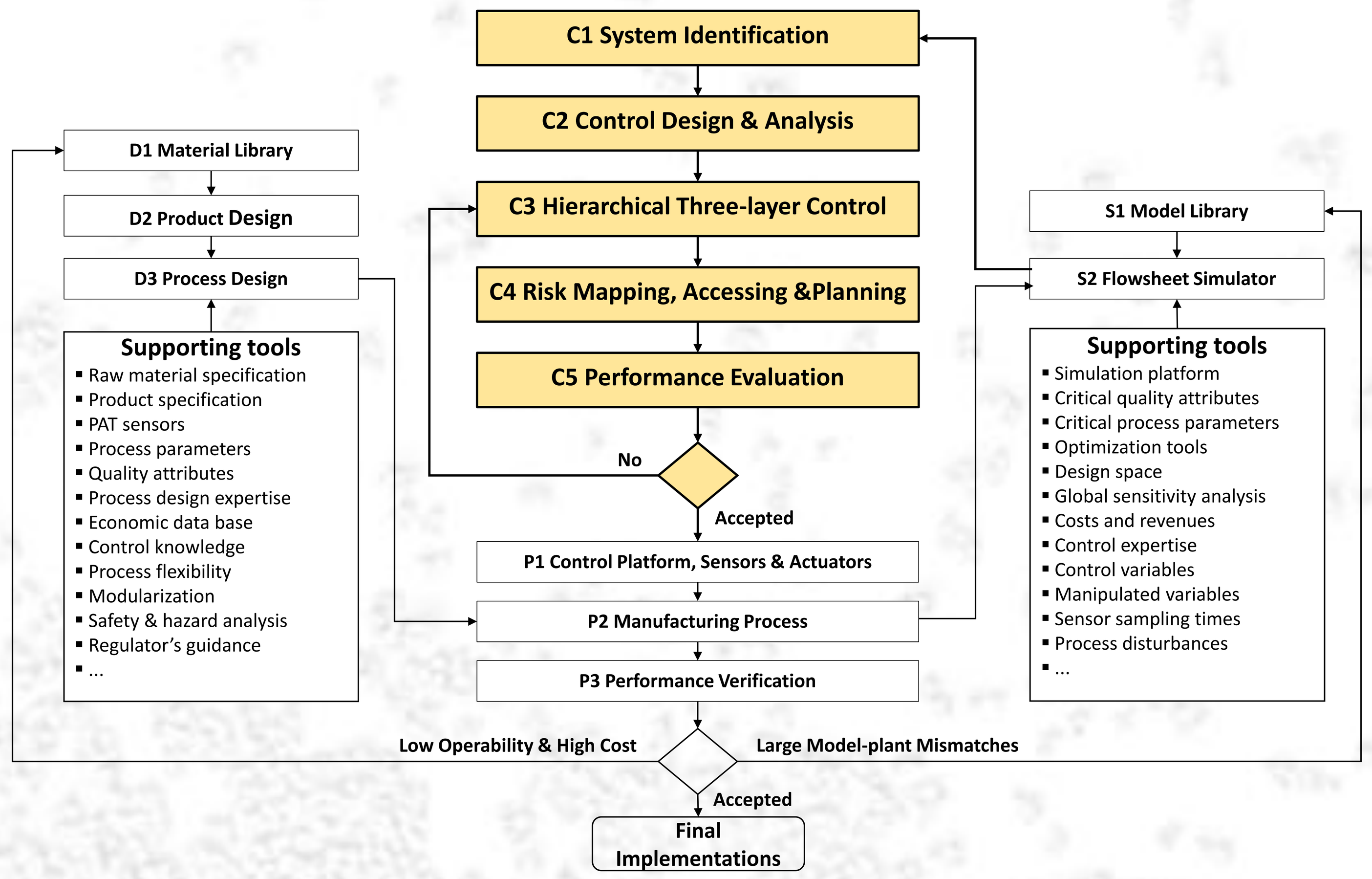
INTRODUCTION

- The paradigm shift in pharmaceutical industry to continuous manufacturing has staged from conceptual demonstration to pilot production, which prompts the strong demands for process systems engineering (PSE) tools for process development.
- A systematic framework for process control design and risk analysis in continuous solid-dosage manufacturing was developed, consisting of system identification, control design and analysis metrics, risk mapping, assessment and planning (Risk MAP) strategies.

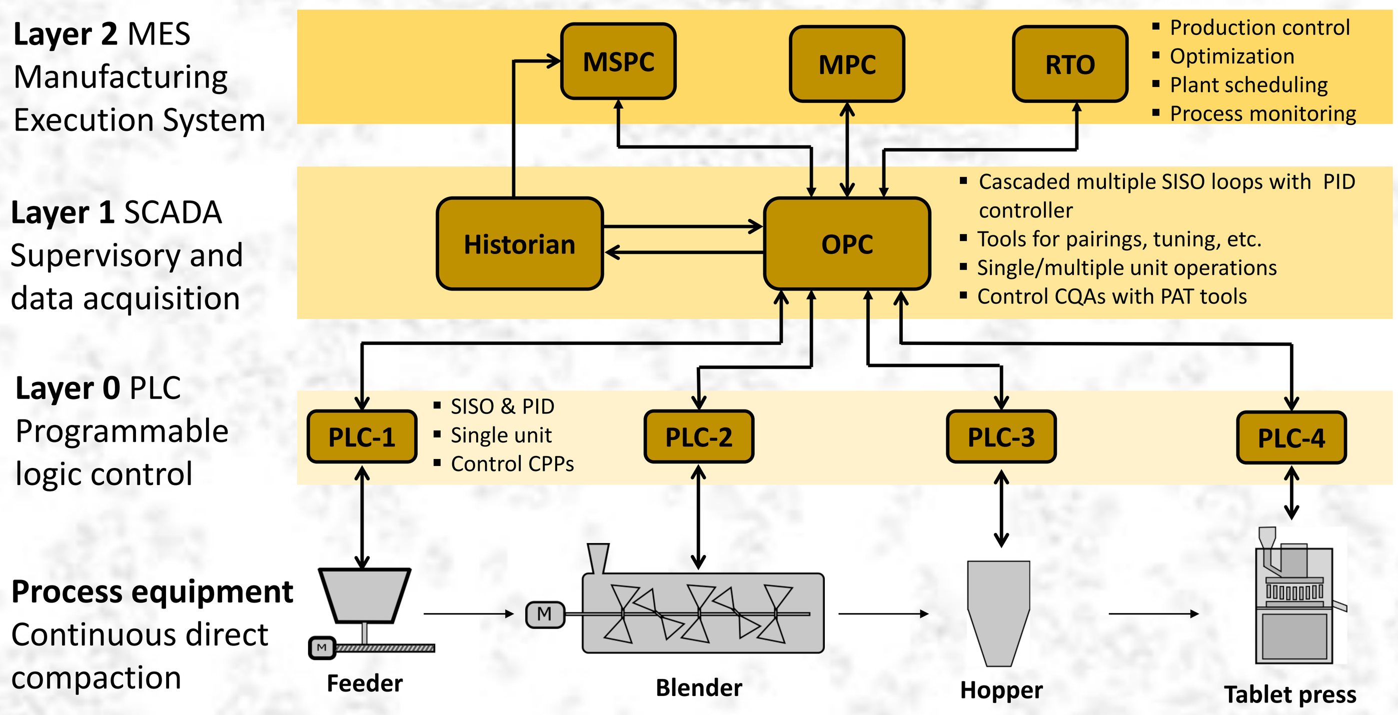
The pilot plant of continuous dry granulation for tablet press in Purdue University

SYSTEMATIC FRAMEWORK FOR CONTROL

- The control framework was integrated with other ongoing research aims in our group, which provide supporting knowledge and tools and make ready the integration of software and hardware for control strategy implementation.

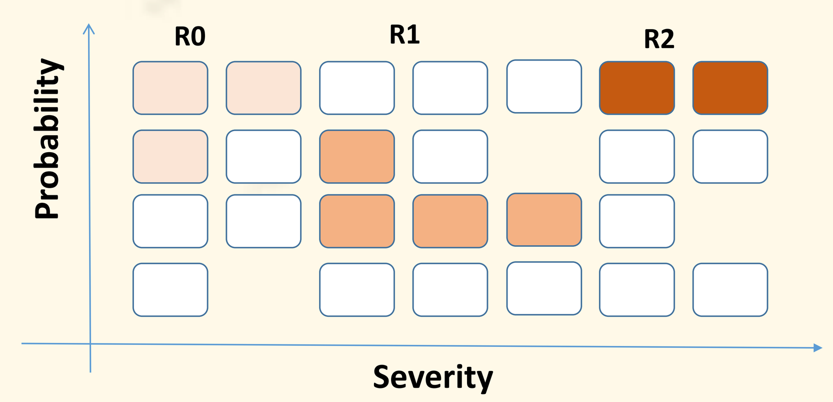


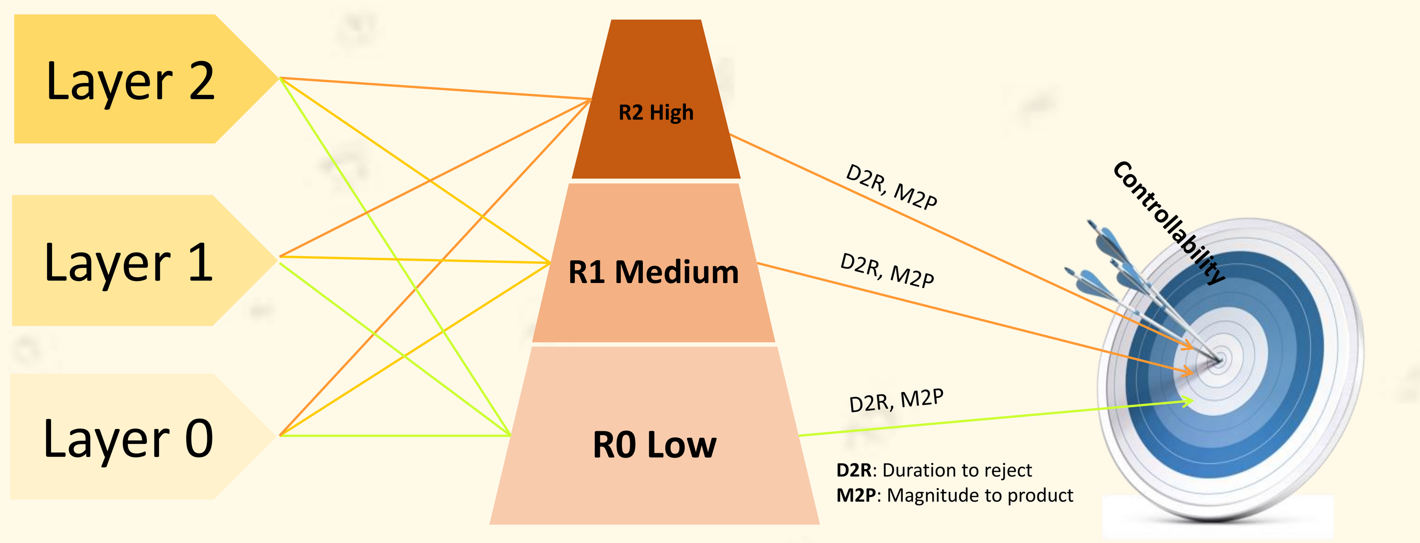
- The hierarchical three-layer control attributed the programmable logic control (PLC) by the equipment vendor as the Layer 0 control, and the supervisory control and data acquisition (SCADA) as the Layer 1 control. The Layer 2 of manufacturing execution system (MES) consisted of advanced model-based control technologies.



RISK MAPPING, ASSESSMENT, AND PLANNING

- The risk management is performed through the risk mapping analysis based on scores of severity and probability.
- Acceptable risks due to common causes or faults are identified from the risk mapping, from the perspective of process control, and are classified as R0, R1, and R2 risk levels.
- The fault-tolerant control strategies at the hierarchical layers are evaluated to give corresponding controllability scores for each risk scenario.





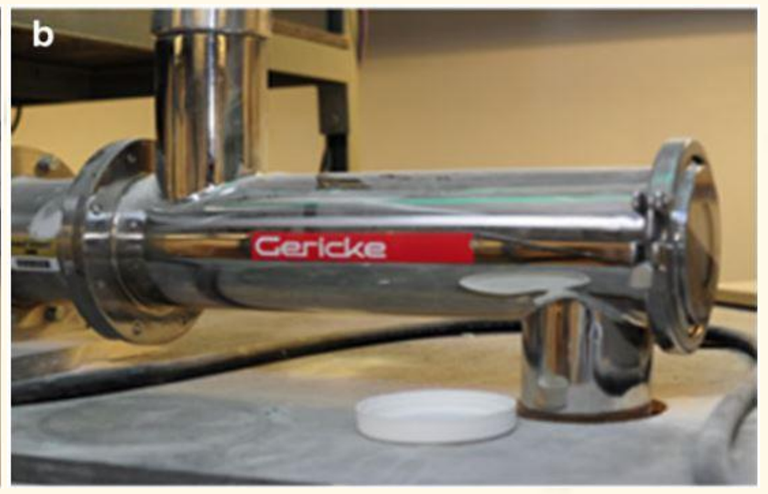
Hierarchical control architecture | Risk levels & fault modes | Evaluation & regulatory filling

APPLICATION: A FEEDING & BLENDING SYSTEM

The framework was applied to a feeding & blending system in Purdue University, in which a flowsheet model for the feeding & blending system was also developed, together with the hierarchical three-layer control design. Common risks due to feeder reloading, sensor fouling and calibration errors, parametric uncertainties were identified in risk MAP.

Unit operation	Process output (y)	Process input (u)	Control Layer	Controller type
API feeder	API flowrate	Screw rotation speed	L0	PID
Exp. feeder	Exp. flowrate	Screw rotation speed	L0	PID
Blender	API composition	API flowrate	L1/2	PID, Ratio, MPC
	Powder flowrate	Excipient flowrate	L1/2	PID, MPC
	API mixing RSD	Rotation speed	L1/2	PID, MPC
	Rotation speed	Motor current	L0	PID

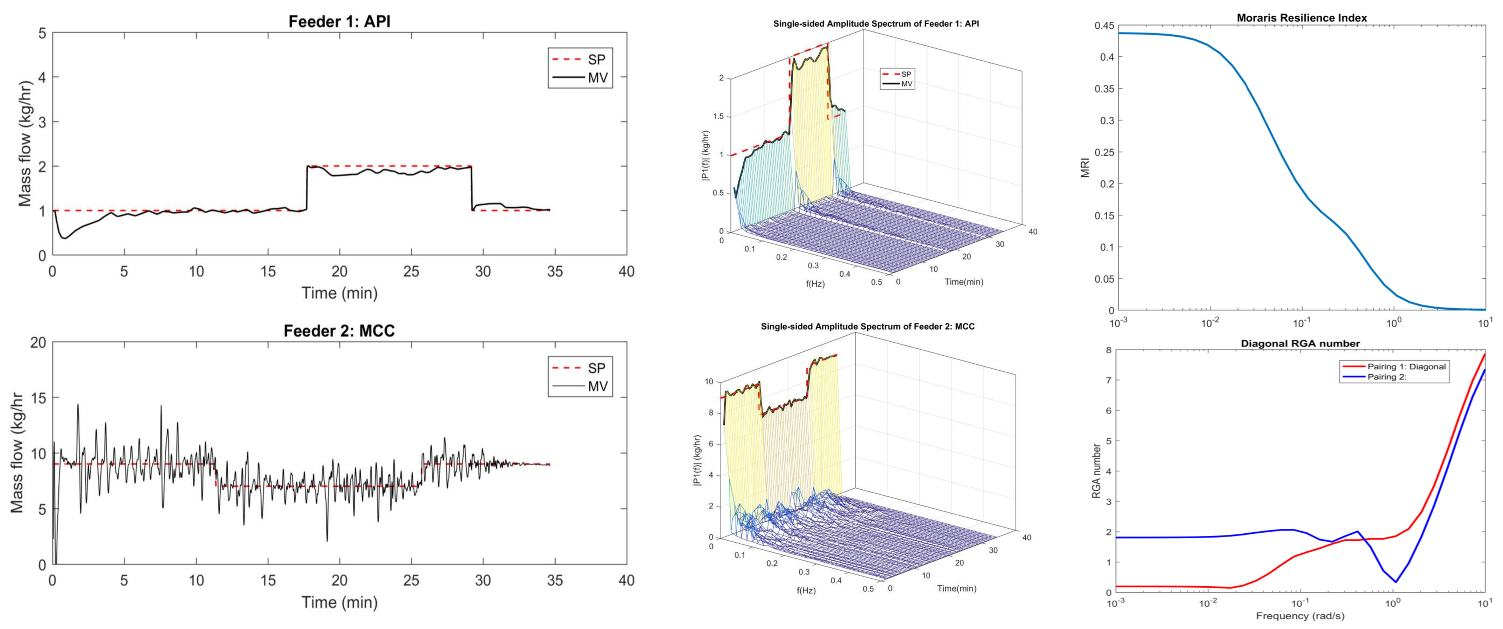
Two Schenck AccuRate PureFeed AP-300 feeders



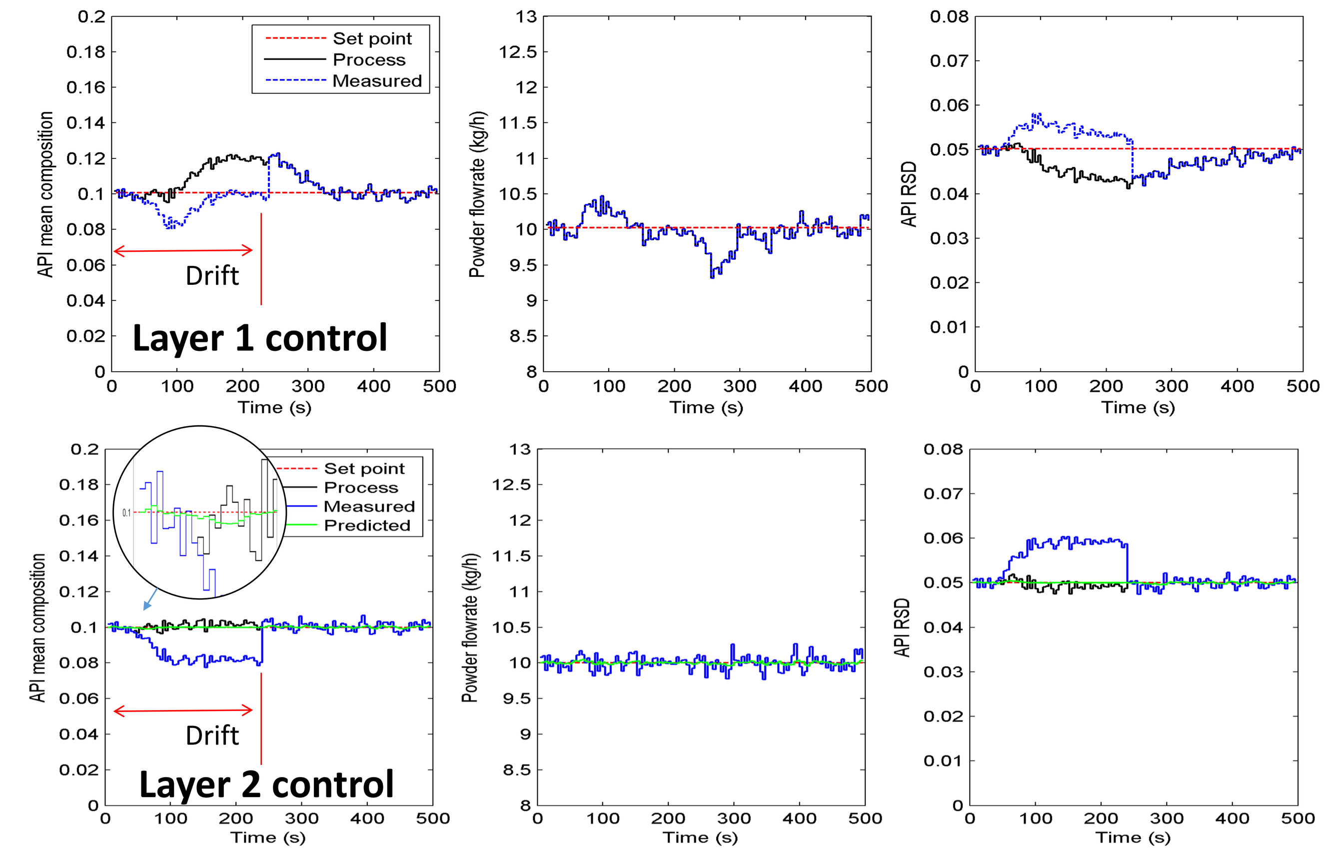
Gericke GCM-500 continuous blender

RESULTS AND DISCUSSION

- Process variance not only affects the product quality, but also has an adverse effect on the process control. When the process operates at high frequency, the control system may be uncontrollable or less resilient, e.g., as shown by the decreasing Morari's resilience index (MRI) and the change of control pairing by relative gain array (GRA) with the increase of varying frequency.



- For a risk scenario of R2 level, e.g., the PAT sensor drift in the API composition measurement by Near Infrared spectroscopy (simulated), the control strategy developed at the Layer 1 can not maintain the API composition at the set point. While the Layer 2 control with advanced estimator-based model predictive control can detect the measurement gross error and maintain the API composition at the set point until the drift was corrected.



CONCLUSION AND FUTURE WORK

- Based on the risk MAP design, potential risks under which the control performance deteriorates were taken into account for evaluating the three-layer control design. These have demonstrated the importance of a systematic control evaluation system to the quality assurance in continuous manufacturing processes.
- The future work would consider the downward integration of PAT tools with the L0 control panel in the field with an attempt to ensure consistent quality attributes at each unit operation step and minimum intervention propagating from upstream to downstream.

NSF Engineering Research Center for Structured Organic Particulate Systems (C-SOPS)

www.ercforsops.org

RUTGERS THE STATE UNIVERSITY OF NEW JERSEY
PURDUE UNIVERSITY
NJIT New Jersey's Science & Technology University