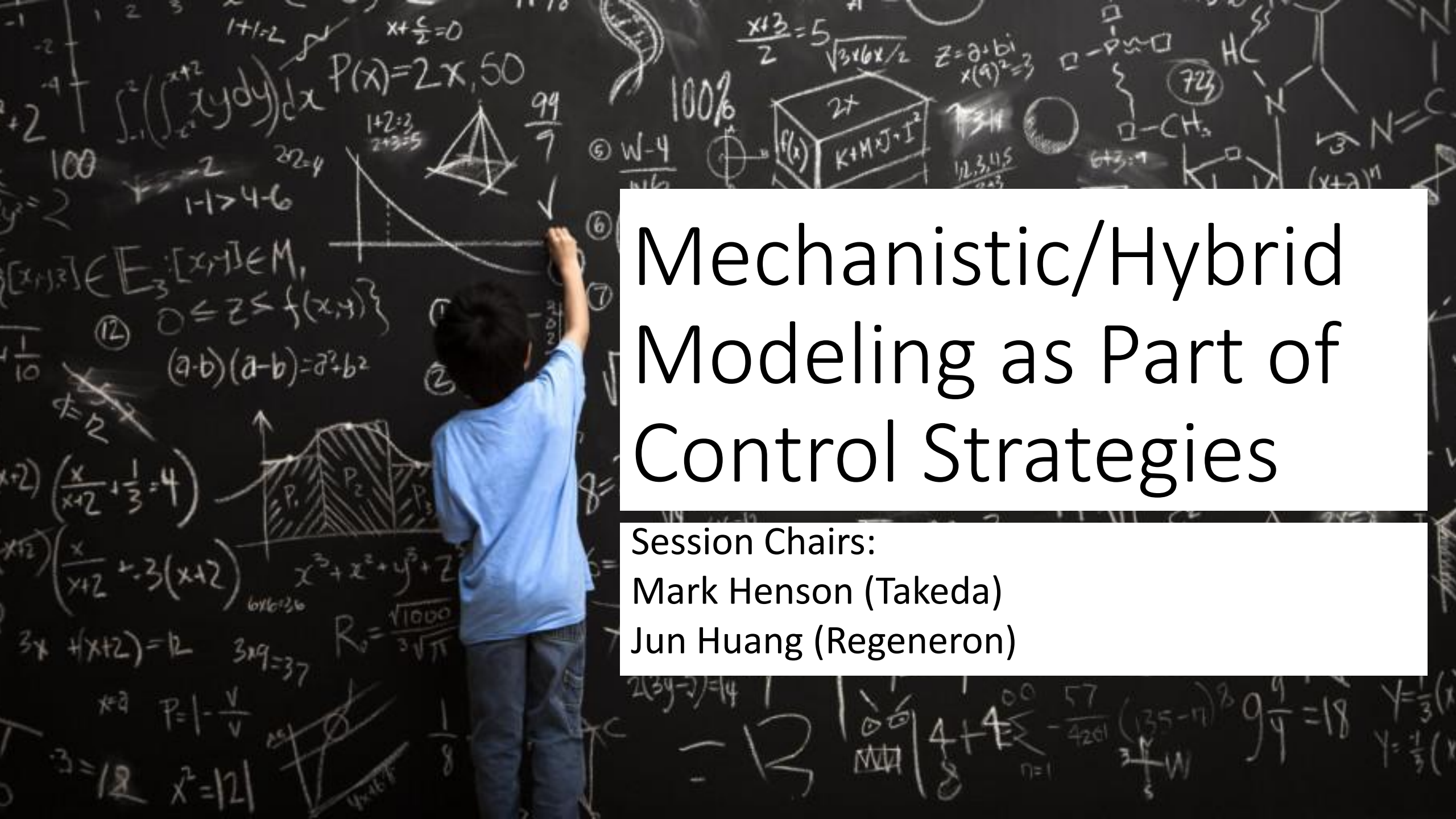


A young boy in a blue shirt is seen from behind, writing on a large chalkboard. The board is densely covered with various mathematical and scientific notations, including algebraic equations, calculus integrals, geometric diagrams of a pyramid and a cube, and chemical structures. The boy is pointing at a graph on the board with his right hand.

Mechanistic/Hybrid Modeling as Part of Control Strategies

Session Chairs:

Mark Henson (Takeda)

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Session Introduction

- Mechanistic and First-Principles (“knowledge-driven”) models represent objective counterparts to **data-driven/empirical models (chemometric, machine learning etc)** which are inherently subjective
- Based on established mathematical descriptions of systems and/or components, these models offer potential advantages (interpretability, **robustness**, scalability, transferability) over empirical models
- Accuracy/bias issues when compared to “reality” can potentially be mitigated via calibration (“hybridization”) with data
 - **Hybrid models combine the best of both worlds of mechanistic and empirical modeling – harnessing the known and unknown rules**
- In recent years, there has been increasing interest in use of hybrid models for process control strategies

Potential Topics

- Process vs. overall control strategy uses?
- Anecdotes and/or Lessons Learned
 - Development & Deployment
 - Quality/Validation
 - Regulatory
- Other Topics / Parking Lot

Process vs Overall Control Strategy Uses?

- *Small molecule use cases:*
 - *DP continuous blending RTD model based on mixing/flow math hybridized w/ empirical monitoring of tracer pulse trials*
 - *API drying using hybrid model –based soft sensor (Pfizer)*
 - *...??*
- *Bioprocess Use cases:*
 - *Cell culture modeling (Biogen etc)*
 - *Downstream purification modeling*
 - *...?*

Lessons Learned: Development & Deployment

- *Relatively smaller datasets needed for mechanistic/hybrid vs. data-driven modeling*
- *Ability to extrapolate outside calibration range*
- Xx
- Xx

Lessons Learned: Quality/Validation

- *Any different risk tolerance or requests from internal QA for mech/hybrid models?*
- *Any different validation experiences vs. empirical models?*
- Xx
- Xx

Lessons Learned: Regulatory

- *Pre-submission discussion learnings?*
- *Submission/query observations?*
- Xx

Other Topics / Parking Lot