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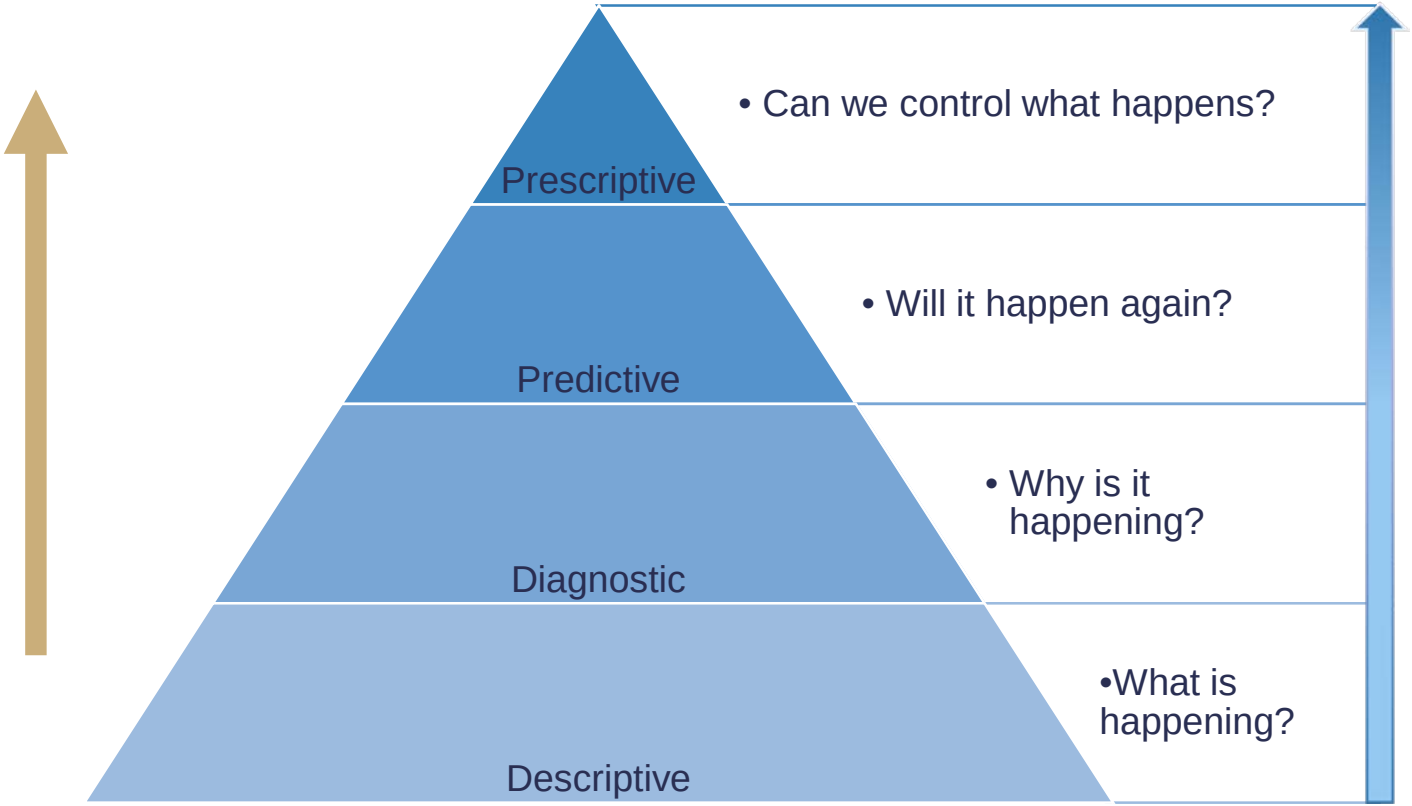
Opportunities and Challenges in Biologics Manufacturing Process Data Analytics Innovation

Jack Prior, Workshop on Innovation in Pharmaceutical Manufacturing, 27Feb2020

Opportunities and Challenges in Biologics Manufacturing
Process Data Analytics Innovation

- **Process Data Analytics**
  - Levels of Evolving Process Data Analytics Focus
  - Barriers to Leveraging Process Data
  - Three Realities of Biologics Process Data Analytics
- **Biologics Digital Manufacturing Innovation**
  - 24 Technologies Advancing in Manufacturing Innovation Lifecycle
  - Examples of Innovation Opportunities
  - Forces Restraining Innovation
  - Ways to Accelerate Innovation

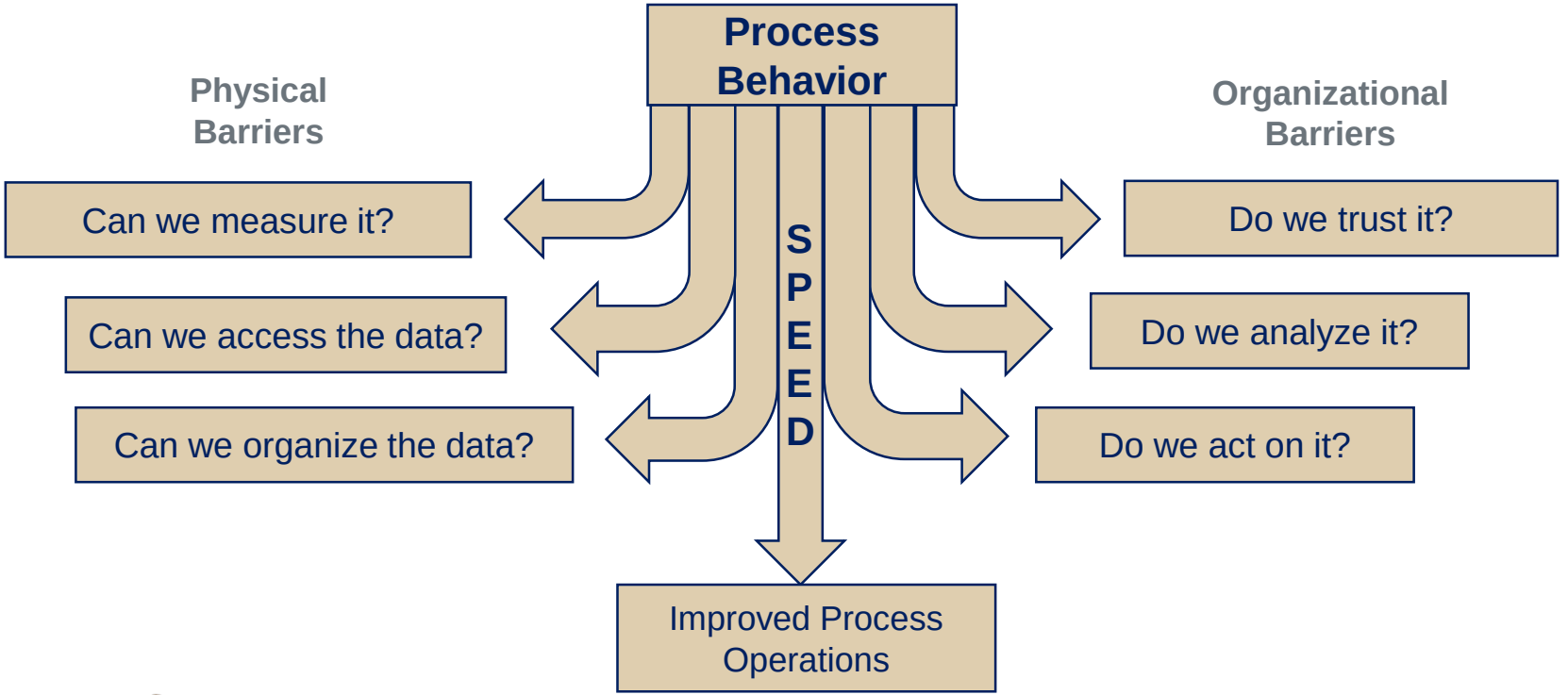
Evolving Process Data Analytics Focus



6 Barriers to Leveraging Process Data

Historically, the industry leverages only 1% of process data generated

- Charles Cooney - MIT



3 Realities of Biologics Process Data Analytics

Manufacturing Data ≠ Designed Experiment Data

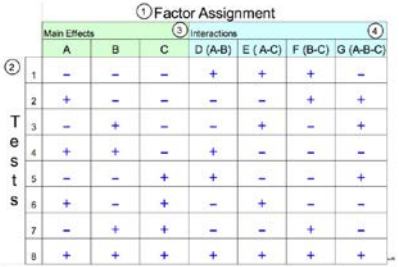
- Correlation ≠ Causality
- Sources of variation typically not in the data
- Operating experience falls in narrow ranges

Biologic Process are Nonlinear and Time Variant

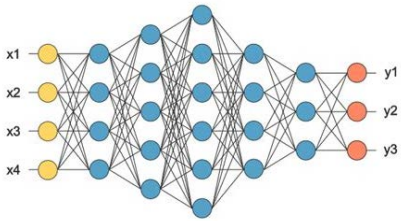
- Linear models often not applicable
- Industry needs to move onward from MVA focus

Big Data Requires Big Effort

- Very small N available vs. big “consumer” data sets
- Data integration and wrangling requires investment
- Data limited early when need is greatest



Design Of Experiments (DOE)

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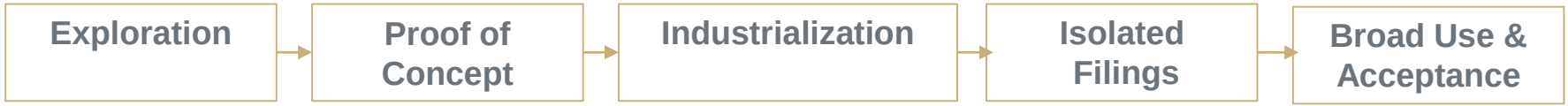
24 Technologies Advancing in Manufacturing Innovation Lifecycle*



Sensing	Multi-Attribute Methods	Real-Time Release Testing	Soft Sensors	Raman Probes	Cell Density Probes	pCO2 Probes	
Quality	Augmented Reality on Floor	Imaging Systems	Digital Release	CFD Mixing Validation	Video SOPs	Review by Exception	MES Systems
Control	Raw Material Adaptive Control	Multivariate Control	Digital Twins	Data Lake Systems	MVA-based Monitoring		
Operations	Lights-Out Manufacturing	Continuous Downstream Ops	Continuous Capture	Inline Mixing	Continuous Harvesting	Single-Use Technology	

**Rough Placement For Discussion*

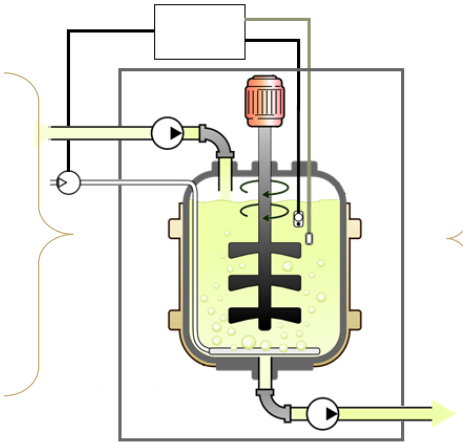
Opportunity: Bioreactor Real-Time Simulation “Digital Twin” Models

Can we encapsulate accumulated process understanding in a real-time “twin” that monitors and predicts process behavior?

Real-Time Data from Online Sensors (IoT)

Offline Measurements

Historical Data



Predict Batch Performance

Enable Soft sensors

Detect Fault and Failures

Model Predictive Control

Hybrid Models

Mass Balance and Mass Transfer
Cell Growth and Metabolism
Chemical Reactions
Control Algorithms
Feed, Harvest Vessel Levels

+

MVA/Machine Learning fit of model residuals

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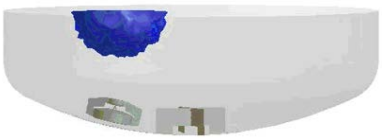
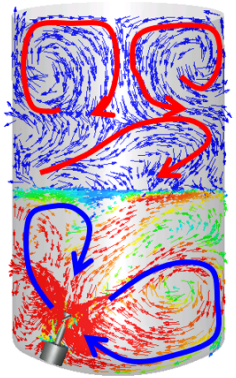
Opportunity: Mixing Validation using Computational Fluid Dynamics

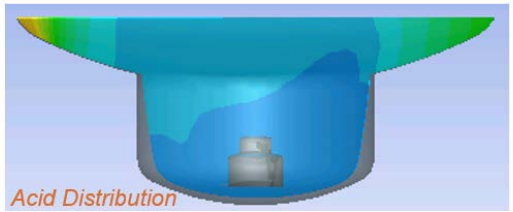
- Conventional sensors/sampling may not capture worst case locations
- CFD examines entire vessel -- no blind spots
- With right expertise, CFD can surpass conventional mixing assessments
- CFD ready to serve the primary role in primary mixing validation in many circumstances



Bolus addition



Mixing viscous fluid



Viral Inactivation –

Opportunity: Modern Data Lake Architecture

Digital Products

Exploratory Applications

Business Applications

cGMP Applications

Data Repository

Data Lake

Data Sources

MES

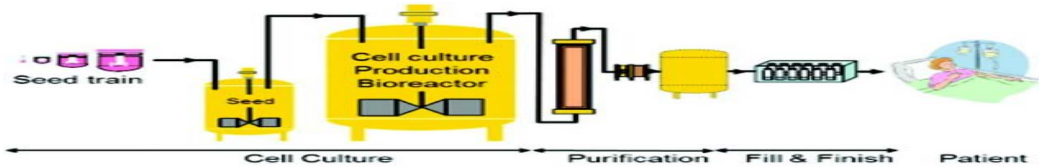
LIMS

Events, CAPA & CCR

Regulatory

ERP

Raw Materials



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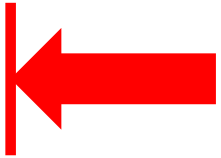
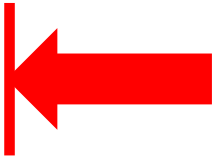
12 Forces Restraining Biologics Digital Innovation

Exploration



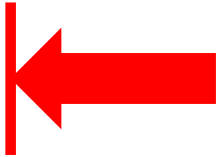
- Data Engineer/Modeler/Science Skills
- Access to Large Quantities of Right Data
- Matching Right Solution to the Right Problem

Industrialization



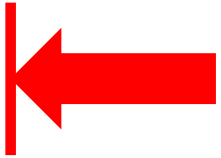
- Critical-Mass Market for Vendor Commercialization
- Digital Infrastructure Integration / Validation*
- Consistency with Flawed Legacy Methods*

Initial Filings



- Right Fit to Critical Product/Process Need
- Lead Time to Build into Early Process Development*
- Fear of Being First Mover=Risk of Approval Delays*

Broad Use



- Legacy Platforms Investments
- Full Regulatory Acceptance (US, ROW)*
- Worldwide Filing Timing & Complexity*

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*Regulator Influenced

5 Ways to Accelerate Digital Innovation

Industry

- Investment in Digital Infrastructure & Integration
- Sr. Management Encouragement & Risk Tolerance

Joint

- Innovation in Agile Software Validation – Software CPV?

Regulators

- Continued FDA Innovation Promotion Programs
- Continued Global Regulatory Harmonization