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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

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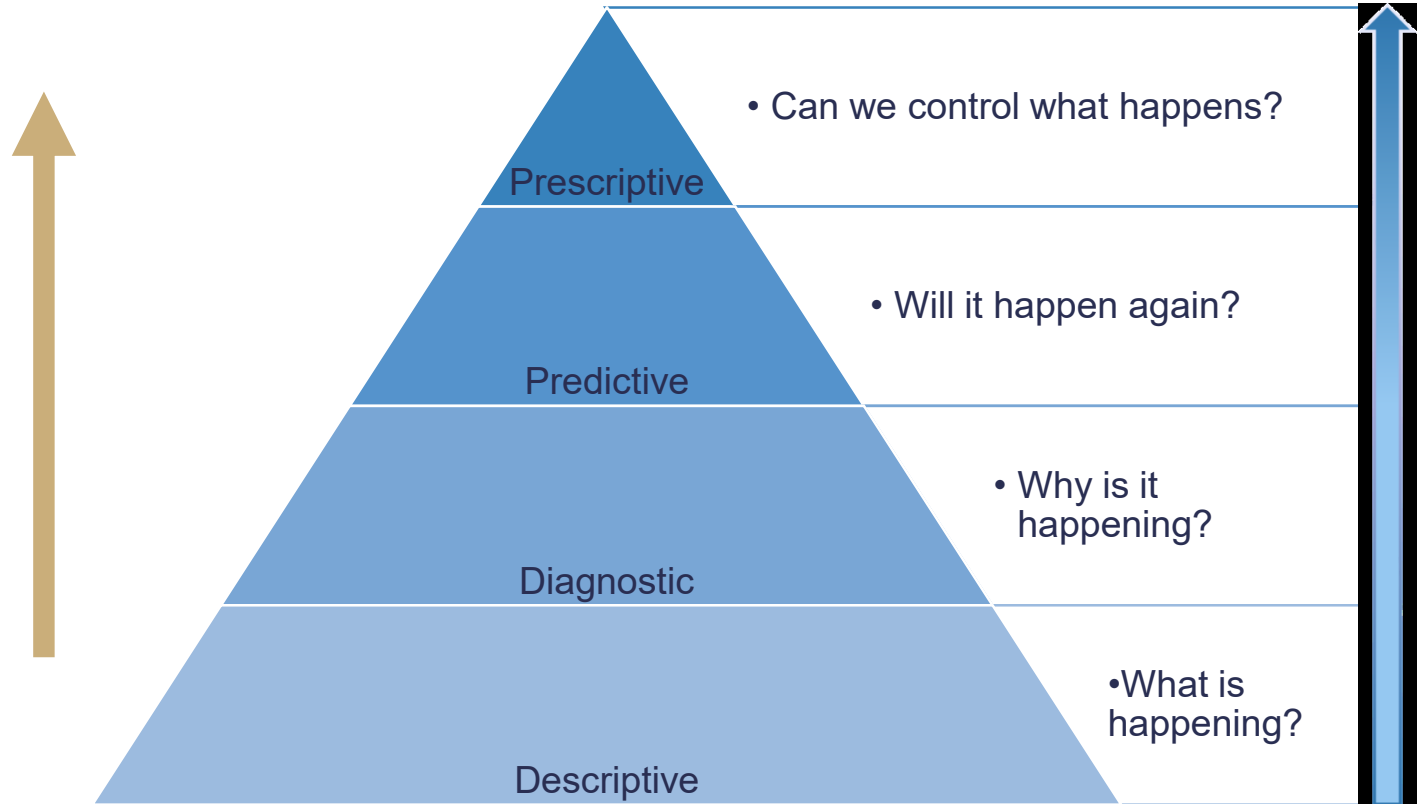
- **Process Data Analytics**

- 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

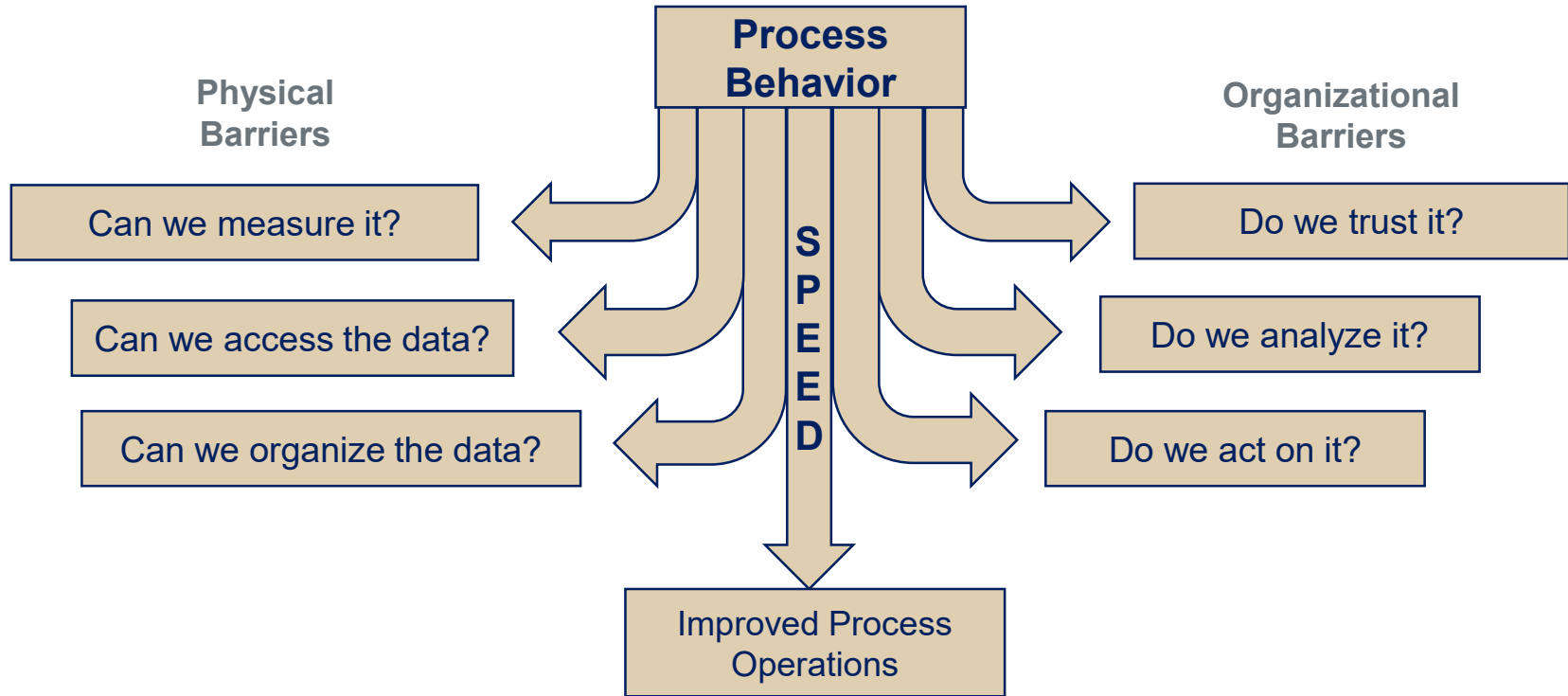
# Evolving Process Data Analytics Focus



# 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 $\neq$ Designed Experiment Data

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

## Biologic Process are Nonlinear and Time Variant

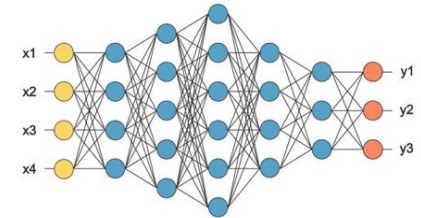
- Linear models often not applicable
- Industry needs to move onward from MVA focus

## 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

① Factor Assignment							
②	Main Effects			③ Interactions			④
	A	B	C	D (A-B)	E (A-C)	F (B-C)	
1	-	-	-	+	+	+	-
2	+	-	-	-	-	+	+
3	-	+	-	-	+	-	+
4	+	+	-	+	-	-	-
5	-	-	+	+	-	-	+
6	+	-	+	-	+	-	-
7	-	+	+	-	-	+	-
8	+	+	+	+	+	+	+

Design Of Experiments (DOE)



DARPA

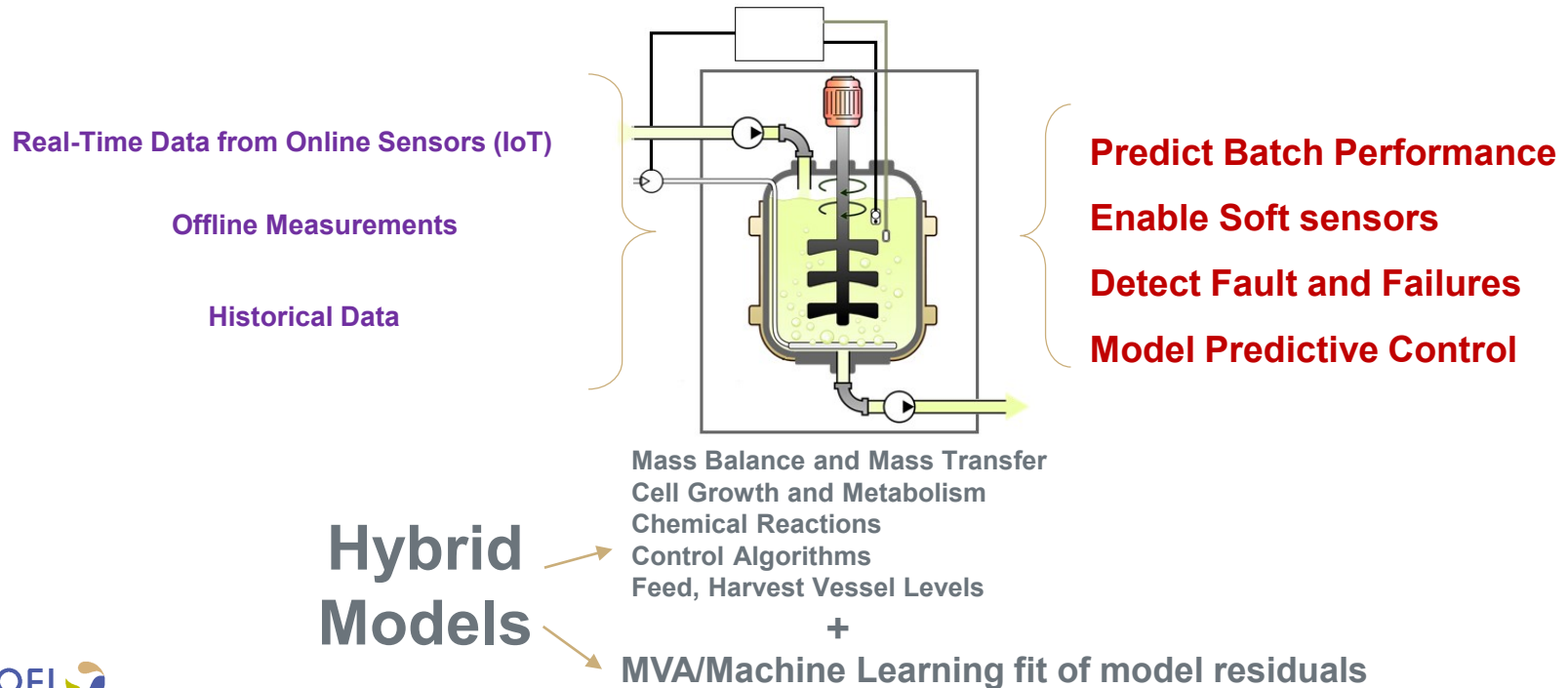
# 24 Technologies Advancing in Manufacturing Innovation Lifecycle\*



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

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

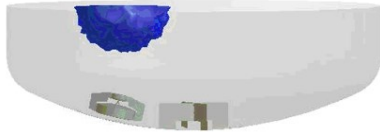
*Can we encapsulate accumulated process understanding in a real-time “twin” that monitors and predicts process behavior?*



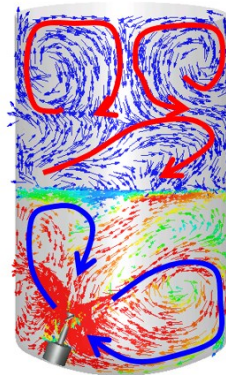
# Opportunity: Mixing Validation using Computational Fluid Dynamics

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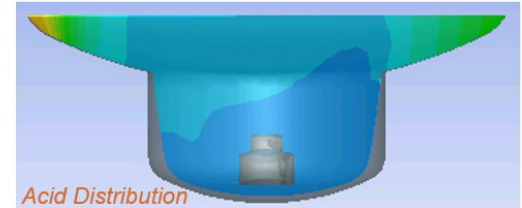
- Conventional sensors/sampling may not capture worst case locations
- CFD examines entire vessel -- no blind spots
- With right expertise, CFD can surpass conventional mixing assessments
- CFD ready to serve the primary role in primary mixing validation in many circumstances



Bolus addition



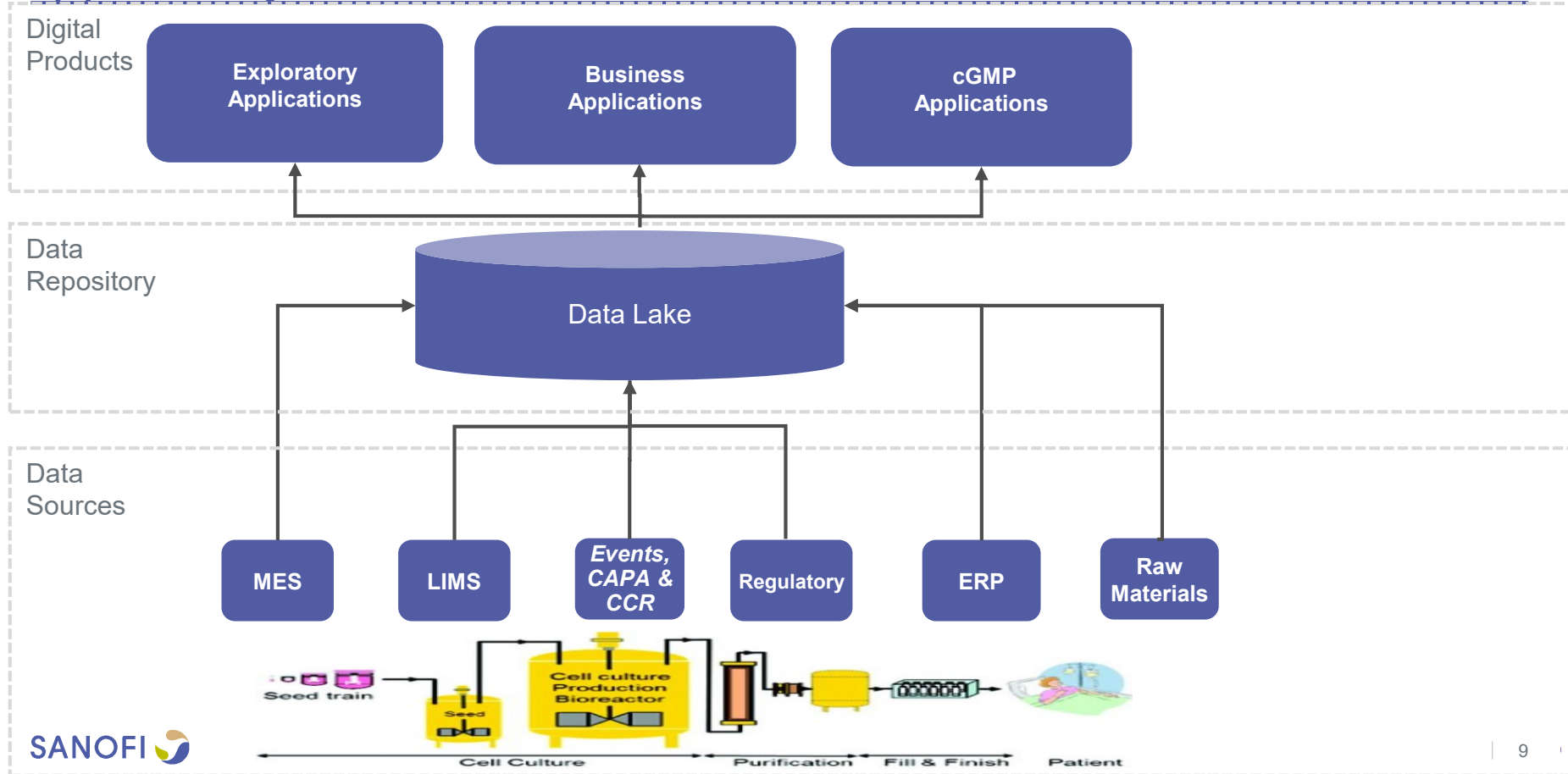
Mixing viscous fluid



Viral Inactivation –



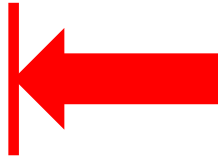
# Opportunity: Modern Data Lake Architecture



# 12 Forces Restraining Biologics Digital Innovation

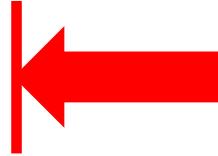
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## Exploration



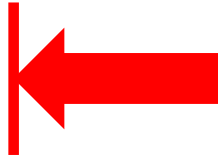
- Data Engineer/Modeler/Science Skills
- Access to Large Quantities of Right Data
- Matching Right Solution to the Right Problem

## Industrialization



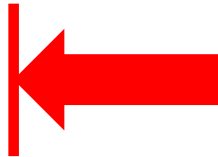
- Critical-Mass Market for Vendor Commercialization
- Digital Infrastructure Integration / Validation\*
- Consistency with Flawed Legacy Methods\*

## 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\*

# 5 Ways to Accelerate Digital Innovation

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## 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