An Autonomous self-optimizing bioprocess reactor, cyberpunk style – Dall.E-3

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Digital Transformation in Process Development

the drivers for structured and contextualized experimental data

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Objectives of today’s session

- Pharmaceutical Industry progresses towards its Digital Transformation goal
- Investment, commitment, initial results
- Momentum is clear, but is it enough to deliver on the industry expectations

Today’s objectives:

- Share progress of Digital Transformation program for Process Development
- Focus on the efforts needed for Data structuration / contextualization
- Understand Business drivers and Business Value
- Reflect on challenges – focus on Talent attraction: Tech Vs BioTech

Digital Transformation: a business decision

- Pharma Industry is making progress in its Digital Transformation journey
- However, we are still lagging many other industries (Automotive, aeronautics, Supply chain)
- Major issue remains on structuring/ accessing our data at scale to enable advanced analytics
  - ***Running out of excuses…***

- Automotive industry, self driving cars manage much more complex data & infrastructure than our industry
  - Occupancy NN uses 1.4B video frame
  - 30PB of data
  - Deploy NN to 800,000 cars
  - 75,000 NN models trained (2022)
  - Planner decision every 50ms for Autopilot mode

The slow pace of Digital Transformation in our industry is not due to technical limitations: this is a Business Decision

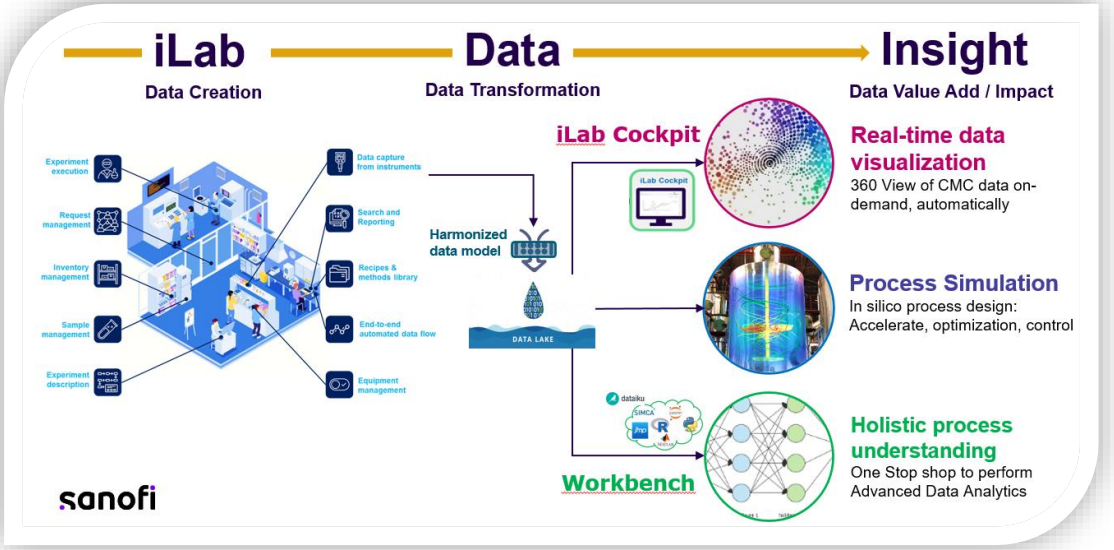
01 A Digital Transformation journey

Sanofi is engaged in a multiyear Digital Transformation program for Process Development activities

*More productive CMC Labs & **faster dev processes** through **data-driven products**, feeding **AI/ML/Modeling** agents, supporting Sanofi launches*

Scope:

- *+2,500 users, ~100 labs, ~20 sites*
- *Process Development in R&D (CMC) and Commercial (MSAT)*
- *All modalities – Biologics/Synthetics*
- *Pharma & Vaccines*
- *GMP and non-GMP*



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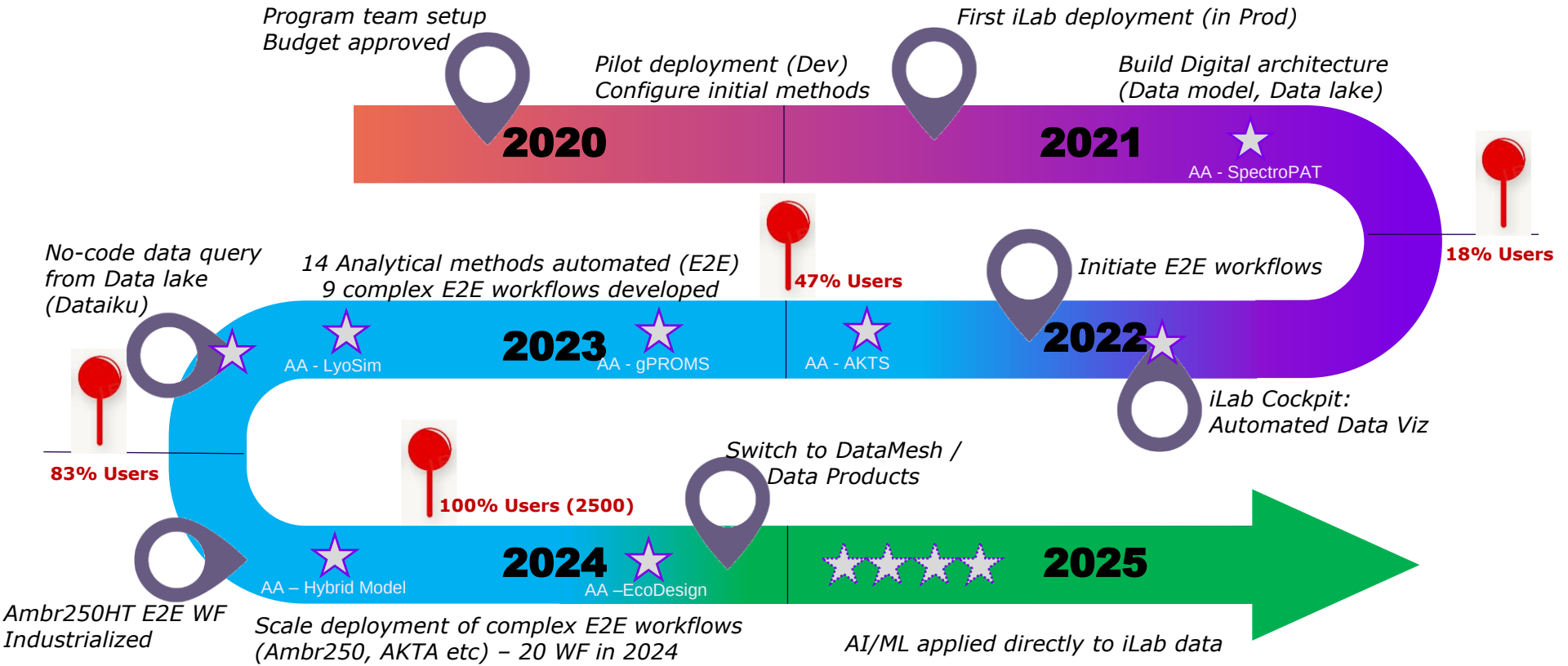
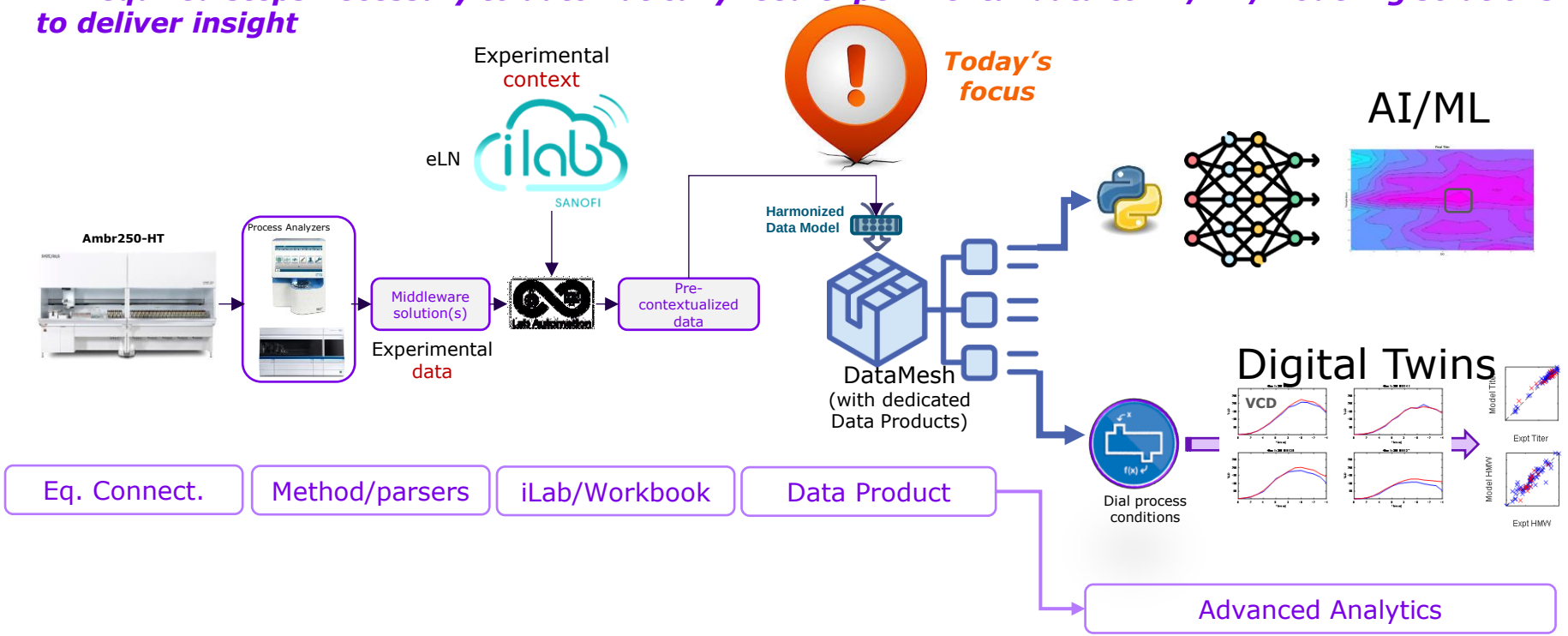
This is a Journey…



sanofi ★ ***Industrialization of an Advanced Analytics Capability***

Focus is now on implementation of E2E Workflow

All required steps necessary to automatically feed experimental data to AI/ML/Modeling solutions to deliver insight



All necessary and critical steps implemented by program Factories to deliver Business value

02 Data Structure and contextualization

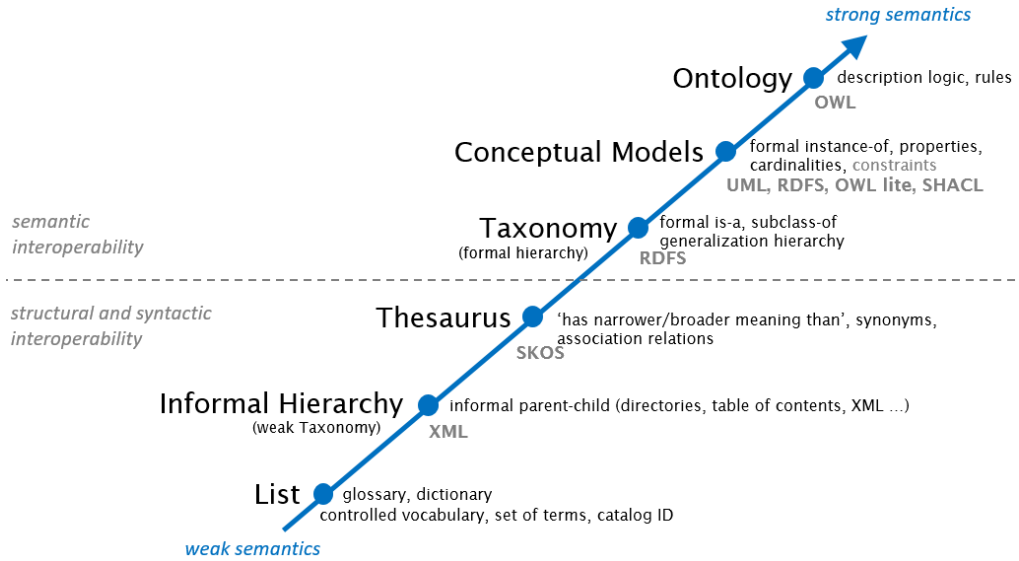
A NON-NEGOTIABLE STEP

Let’s align on some terminology

Ontology

A formal description of knowledge as a set of concepts within a domain, and the relationships that hold between them.

It ensures a common understanding of information and makes explicit domain assumptions thus allowing organizations to make better sense of their data. (NIIMBL consortium)



Sources

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- Michael Uschold and Michael Gruninger “Ontologies and semantics for seamless connectivity” *SIGMOD Rec.* 33, 4 (December 2004), 58-64. DOI=http://dx.doi.org/10.1145/1041410.1041420
- Leo Obrst “The Ontology Spectrum”. Book section in of Roberto Poli, Michael Healy, Achilles Kameas “Theory and Applications of Ontology: Computer Applications”. Springer Netherlands, 17 Sep 2010.
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From Arne Balzer, Mathias Wolf, Olivier Gigonzac

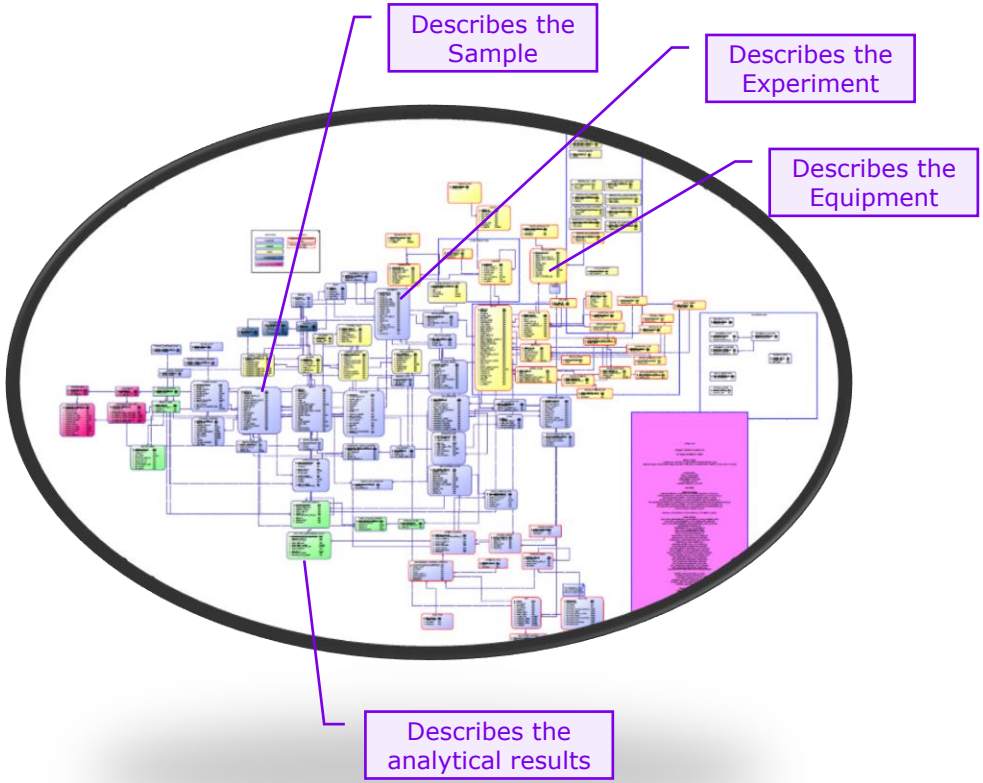
Cornerstone of the Digital Transformation: Data Model

A non-negotiable step

Data model organizes data elements and standardizes how the elements relate to one another. It explicitly determines the structure of data

Ontology: sets the general framework
Logical Data Model provides a visual / conceptual relationship of data entities
Physical Data Model is the translation of the Logical Data Model into the structure of a database

Each data point generated in the lab is mapped in the Data model



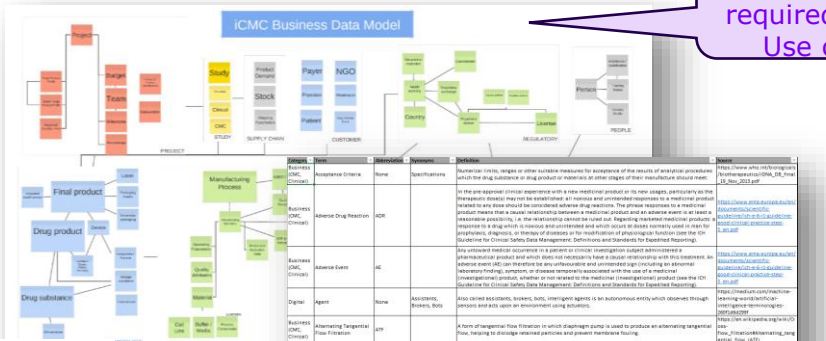
Define Data Model, through Use Cases

*Starts with multiple **Use Cases** defining the Logical data model*

❶ End-users explain what they need to do

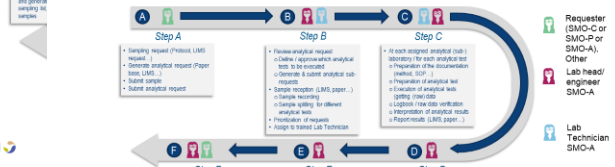
❷ Data mapping / connectivity required by the Use cases

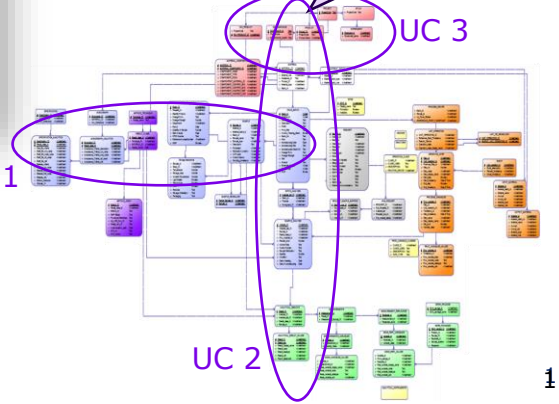
❸ Combination of all use cases builds the full picture



Use Case 2: Biotechnology: Technical Batch Documentation

Uses Case 1: Analytics: Batch Comparision



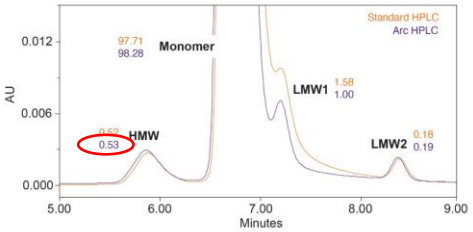


Drivers to build strong data model

The context around "0.53"

Method

- Version
- Analyst
- Date
- Site
- Mobile phase
- Etc…



0.53 %

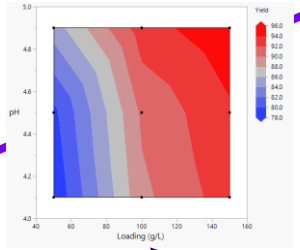
Unit

Downstream process Step

- Project
- Purification step
- Equipment #
- Sample submitted
- Process conditions
- Etc…

Bioprocess step

- Project
- Development Phase
- Ambr250 run
- Vessel #
- Equipment #
- Process conditions
- Etc…



Study associated with experiment (DoE)

- Workpackage
- Objective
- Conclusions
- Model
- Etc…

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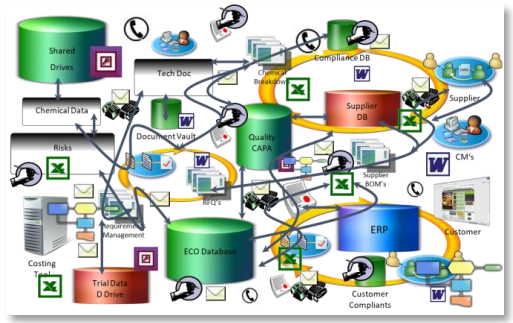
Drivers to build a strong data model

Providing Insight

"Our PPQ run shows an Out of Trend result in HMW: 0.50%. Have we generated such results in the past?"

When your data is not structured:

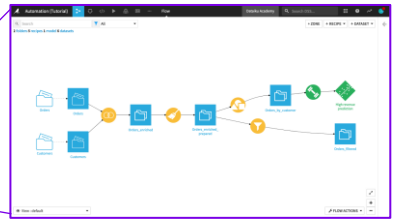


5 scientists, over 2 weeks

- "We could not find an example of such result"
- "What do we do with our PPQ run?"

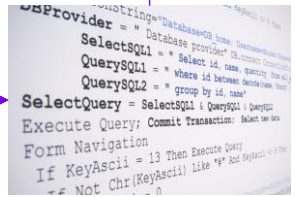
When your data is structured:

Lab Scientist



Self-served data prep.

No-code SQL



- "This project generated 0.53% of HMW during Stretch DoE study in 2022"
- "Can this help justify PPQ Out of Trend results?"

Bioprocess Manufacturing – common Ontology

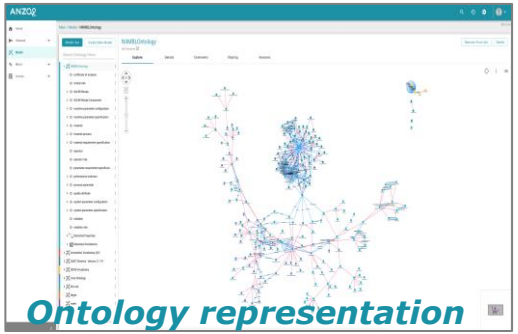
Implemented via NIIMBL – Big Data program

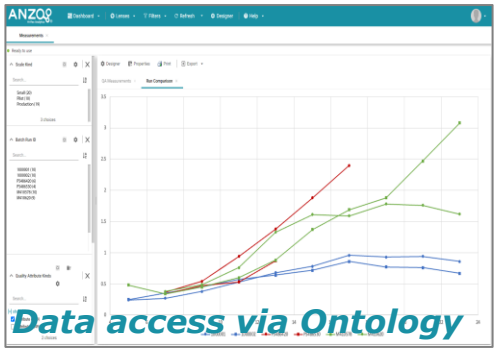
NIIMBL developed a *Bioprocess manufacturing Ontology* using NIIMBL members input.

Ontology ismanaged under Industrial Ontology Foundry (IOF) and "Basic Formal Ontology" (BFO) model

The NIIMBL Ontology for Bioprocess Manufacturing is now Open Source.

- Available to all in the Biopharmaceutical industry
- Lower the access of Ontology/Data model across the industry
- Provide standardized framework to manage data





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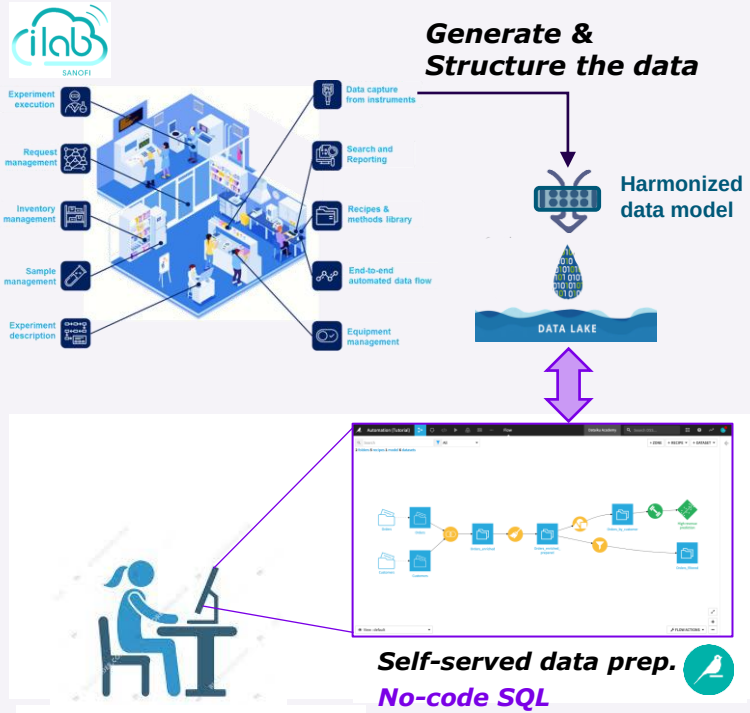
From Boonserm Kulvatunyou, Ph.D.
National Institute of Standards and Technology part of NIIMBL Big Data Team

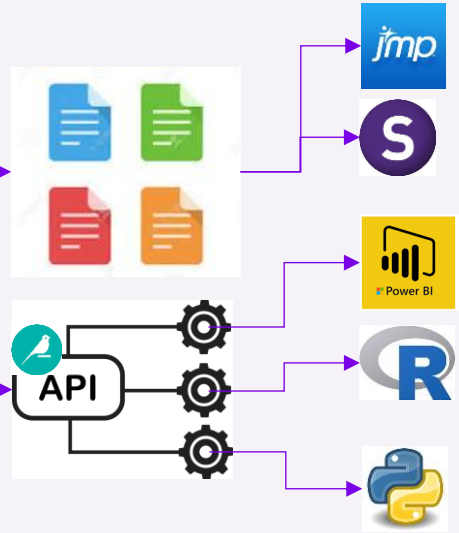
03 Where are we headed

Joining the dots: Generate data / query / analyze



Experimental data automatically structured, contextualized, centralized in Data lake

Direct query by Scientists / Data Scientists to feed into Stats / MVA / Modeling applications



Stats / DoE

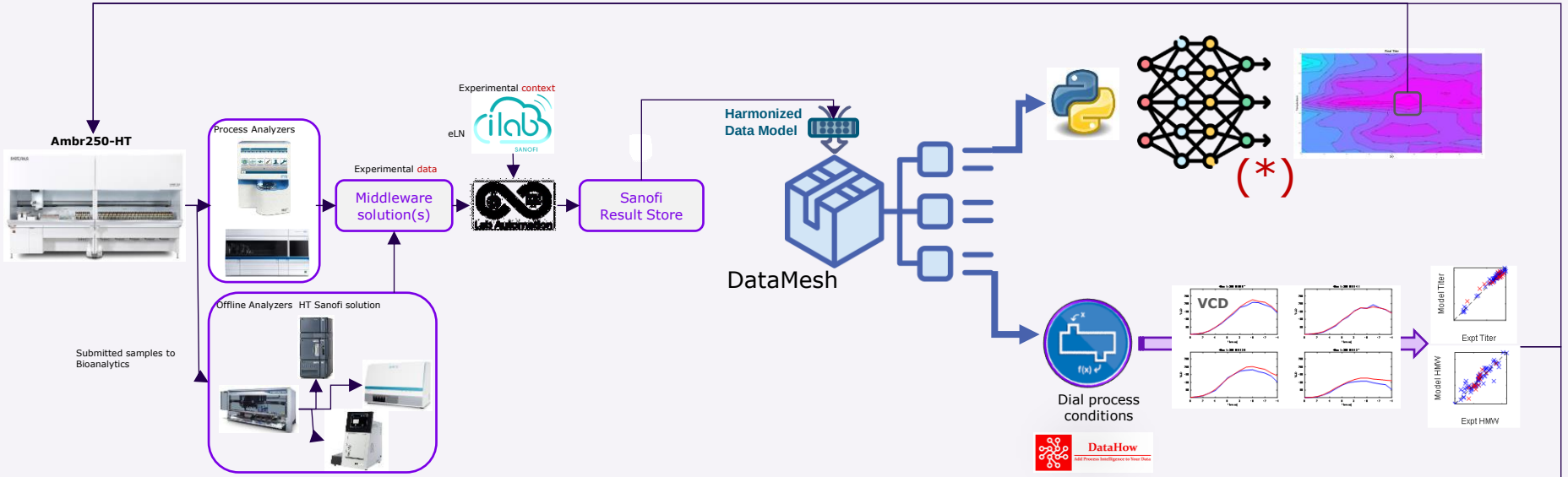
Multivariate analysis

Advanced Analytics
ML

Join the Dots

All cell culture experiments to feed into In-Silico design (Hybrid) and in ML models

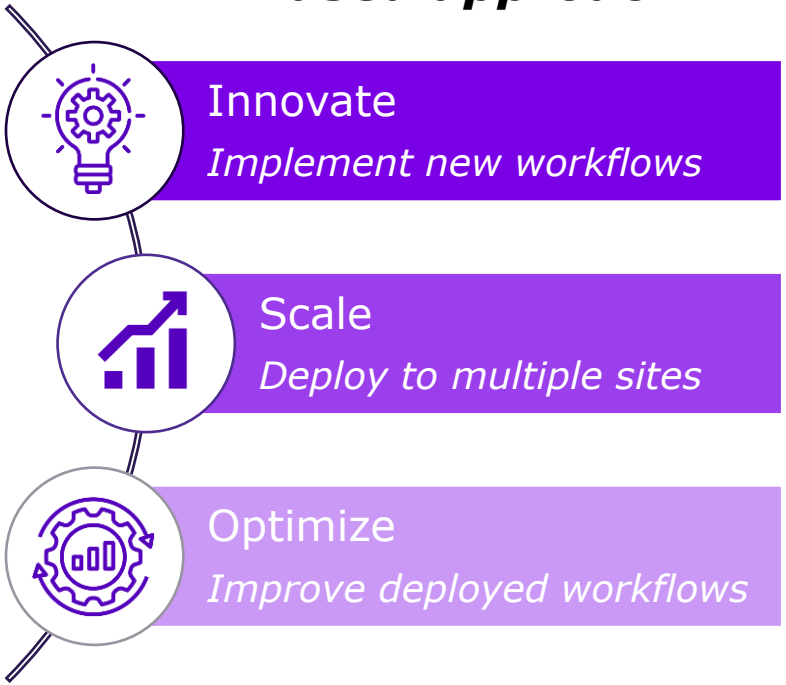
Use proposed new set of experimental conditions to drive to **Process Optimality**



(*) with automated data flows, large numbers of run are becoming available, suitable for ML approaches, specifically intending for Transfer learning across products
- 6 first months of deployment at 1 site: 420 batches / 6700 samples / 175,000 measurements

E2E Data Flow – Moving to full scale

Phased approach



10 new complex workflows per year
- Ambr / AKTA / Chemspeed / Tecan etc

About 20 new analytical methods per year

20 Replicates of workflows / analytical methods
- Copy/paste by first intent (accelerate deployment)
- But heterogenous site-specific equipment connectivity

Continuous improvement - established workflows
- Industrialization, support (Long term Op. model)

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4 areas of focus - Ambition

Become a CMC organization powered by AI at scale

Process Modeling

Physics based Digital Twins

- Reduce wet-lab experiments by dry-lab Digital twins
- Design / Optimize / Control all main Unit Operations in CMC
- Define optimum process conditions, faster and cheaper

AI / GenAI

Optimize processes and increase productivity

- Expert AI agents:
  - *Identify complex process/quality relationships in large datasets*
  - *Drive process productivity*
- GenAI agents for CMC:
  - *Technical reports / dossier generation*
  - *AI-driven knowledge management system - "Digital SME"*

Automation / Robotics

Hyper productive labs

- Automation of low value-added tasks:
  - *Increase project team productivity*
  - *Enable scientists to focus on science*
- Lead the Robotics race:
  - *Integrate complex laboratory tasks*
  - *Assess Humanoid robotics in lab environment*

Digital Transformation

Underpinned by complete access to structured data

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04 Skills and roles

A NON-NEGOTIABLE STEP

Key challenge
Workforce evolution matching Digital Maturity Ambition

- **Strategic investment in our employees:**
  - Structured training in Data Science / Digital
    - *Specific topics: Statistics / MVA / ML / Modeling*
    - *Different levels: Introduction / practitioner / expert*
    - *Community of practice – post training, reinforcement*

- **New skills in Digital / Business organizations**
  - Investment in new skills and new roles

- **Skills:**
  - Data engineers
  - IoT experts (EqCx)
  - Solution Architects
  - Semantic Engineers
  - Data Governance
  - ML
  - Systems modeling

- **Roles:**
  - Data Owners
  - Product Owners
  - Scrum Masters
  - Business System Owners
  - Business Analyst
  - Modelers
  - Data Scientists
  - Digital Training coordinator

- Upskilling
- Reskilling

- ***Increasing Digital Maturity does not happen organically.***
- *It requires time, efforts, investment*
- *This needs to be a key part of the Digital Transformation Strategy*

Biotech Industry challenge

Attract the top tier Data Scientists from tech industry

- **Top Data Science graduates are primarily attracted to tech companies:**
  - Tech companies remain the most competitive salary-wise:
    - *$100,000 – 180,000 for Data Scientists in Tech Vs $85,000 - $150,000 in Healthcare*
  - *Digital maturity / access to state of the art Tech Stack*
    - *Big Pharma have a long way to go to provide the exciting Digital environment to attract Data Scientists*

- **What can Biotech do to attract more talents from tech companies**
  - *Be ready to pay more? Probably, but not only*
  - *Leverage the trend to give meaning to their work – Active external communication*
    - *"Tech for good" or "data science for social impact" are key trends in data science community*
  - *Maturity of typical Big Pharma "TechStack" and access to structured data is a minimum threshold to attract key talents*

Which Sandbox do you want to play in?

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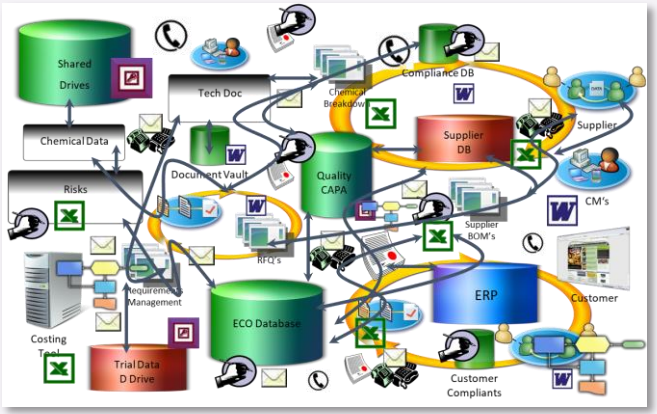
Conclusions

Current versus future state

From where we were …

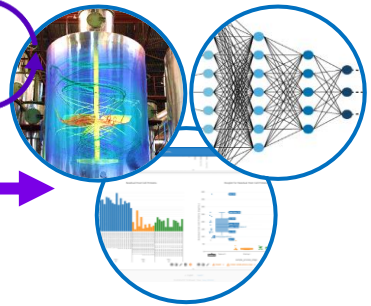


…to where we will be

Hyper efficient labs

FAIR data - structured

GenAI



Digital Twins + ML/AI

Launch Excellence + Fast to patient

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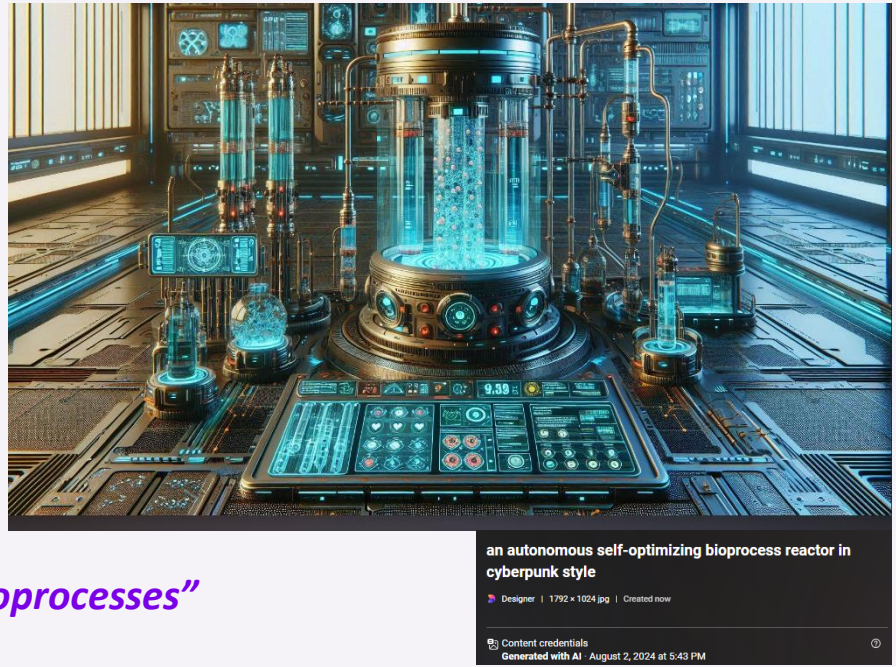
Accelerate the pace

- Industry is moving in the right direction
- We must learn from other industries to catch up on our Data foundation
- Focus and continued investment is required



Moving towards "Autonomous self-driving bioprocesses"

Acknowledgements

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