



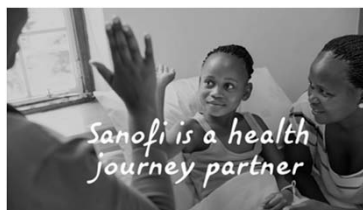
# Implementation of Modeling Platform Approach to \_\_\_\_\_ Accelerate Process Design and Product Launch

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## Sanofi: a global healthcare leader

<https://www.sanofi.com/en/about-us/sanofi-at-a-glance>



- More than 100,000 employees representing 145 nationalities.
- Present in 100 countries with 75 manufacturing sites in 33 countries. Providing healthcare solutions in more than 170 countries around the world.
- €5,894M invested in R&D in 2018 with 35 projects in Phase 3 or submitted for approval.



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## Modeling in Biologics R&D and Manufacturing

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**Rich Portfolio of Models Deployed in Our Industry**  
It takes an ontology approach to fully categorize our models.

### Modeling Applications

Modeling Objects: Molecule, Equipment, Unit Ops, Process, Plant, Warehouse, Supply Chain, Market, ... ..

Supported Areas: Discovery, Process Development, Clinical, Tech Transfer, Commercial Operations, ... ..

### Model Types

Mathematical Models

- First principles, statistical, and hybrid models
- Descriptive and predictive models
- Real-time and offline models

Physical Models

- Scale-down and scale-up models
- In vitro and in vivo models
- Molecular, cell, and animal models
- 3D printed model



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#### Statistical Models

PLS, PCA, Machine Learning, Monte Carlo, ...



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Supervised Learning,  
Unsupervised Learning,  
Reinforcement Learning, ...



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## Modeling by 3D Printing

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### Create Physical Model by 3D Printing

Also known as Additive Manufacturing

#### Fast expanding of 3D printers and 3D printing services

- Lowered price entry point + open-source CAD software
- Thermal plastics → new materials (elastomers, metals, mixed, ...)
- Printer mechanism (fused deposition modeling (FDM) → stereolithography (SLA))
- Prototyping → Industrial scale printing services



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## Practical Applications of 3D Printed Models

- Bioreactor 3D Printed model (100L+) for mixing/settling study to support tech transfer, scale up, CFD model verification
- Flowcells for inline PAT probes (prototypes in plastic, final product 3D printed in SS)
- Custom parts/adaptors supporting everyday activities, e.g., managing single use components in R&D lab and on GMP floor
- Key benefits: quick turn-around and empower scientists/engineers.



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## Modeling Platform

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## An Example of Modeling Platform Approach

### Individual Model

- To answer a key question
  - What agitation rate to use?
  - What size column to use?
  - How long it takes to ...?
  - What would be the success rate?
  - ... ..
- Often carried out by an individual SME

### Modeling Platform

- To systematically support a major activity
  - New product/process development
  - Tech Transfer
  - Scale up
  - Process/facility change
  - ...
- Require a diverse team of SMEs with unique trainings
- May need cross-functional or external consulting support



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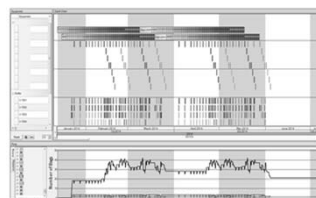
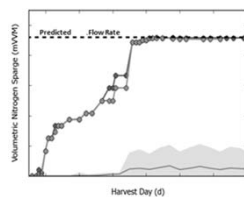
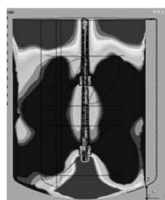
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## An Example of Modeling Platform: Tech Transfer Support

- CFD study between SU and RU → shear, P/V, mixing time
- $K_L a$  → Dynamic Mass Transfer Model → pH and pCO<sub>2</sub> control strategy
- Basic growth/metabolism → cell expansion / feed strategy
- Monte Carlo study → process capability and robustness
- Plant model → capacity analysis / scheduling / logistics
- Model based control
- ... ..



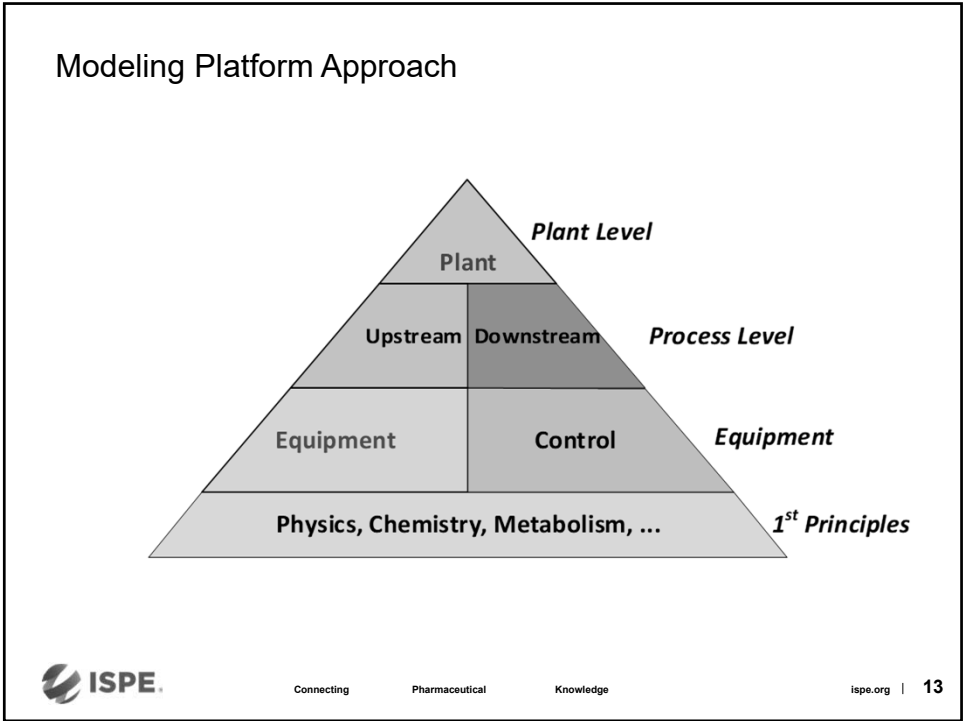
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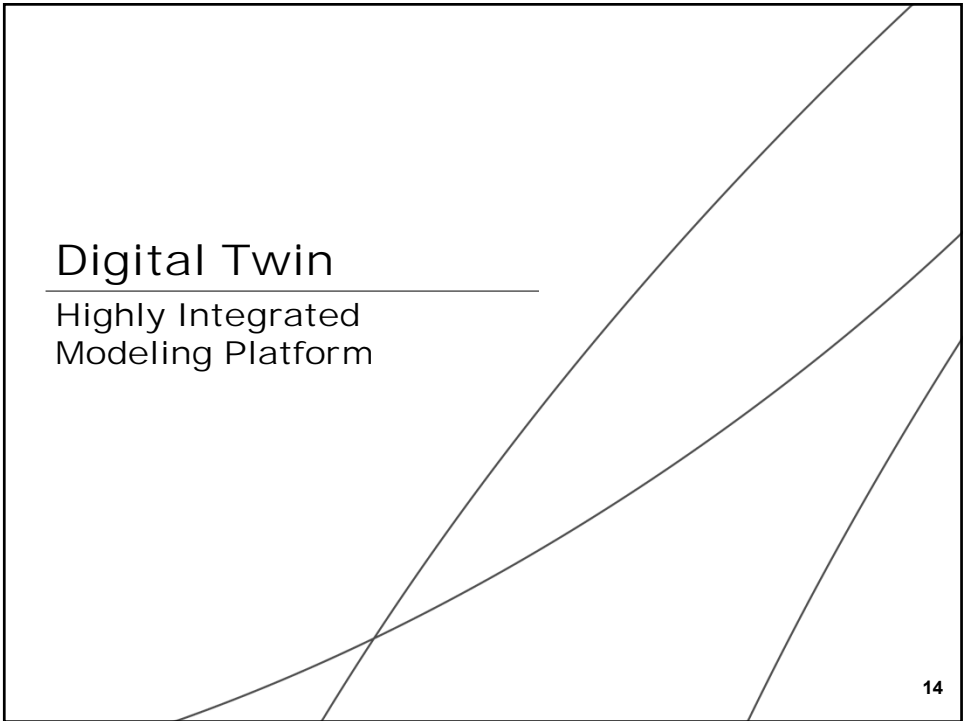
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## Definitions of Digital Twins

Quite simply, a digital twin is a **virtual model of a process, product or service**. This pairing of the virtual and physical worlds allows analysis of data and monitoring of systems to **head off problems before they even occur, prevent downtime, develop new opportunities** and even plan for the future by using simulations. - Forbes

A Digital Twin is an **executable virtual model** of a physical thing or system. – Dassault Systemes

A digital twin is an up-to-date representation, a model, of an actual physical asset in operation. It reflects the current asset condition and includes relevant historical data about the asset. Digital twins can be used to evaluate the current condition of the asset, and more importantly, predict future behavior, refine the control, or optimize operation. - MathWorks

A digital twin is a virtual representation of a physical product or process, used to **understand and predict the physical counterpart's performance characteristics**. Digital twins are used throughout the product lifecycle to simulate, predict, and optimize the product and production system before investing in physical prototypes and assets. - Siemens

A digital twin can be defined, fundamentally, as an **evolving digital profile** of the historical and current behavior of a physical object or process that helps **optimize business performance**. - Deloitte

Gartner defines a digital twin as a software design pattern that represents a physical object with the objective of **understanding the asset's state, responding to changes, improving business operations and adding value**. - Gardner

A digital twin is a virtual model and detailed representation of a system (e.g., product design) or entity (e.g., factory) that can be used to **understand performance, improve processes and create revenue opportunities from services**. - Altran



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## Waze --- An Example of Digital Twin

- Integrated models (geospatial, traffic, ... ..)
- Historical data (statistical model)
- Read-time data feed (user tracking and user inputs)
- Real-time simulation capability
- Ability to predict and assist decision making



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## Digital Twin for Biologics R&D and Manufacturing

Our vision of a Biologics Digital Twin is the application of comprehensive models to support informed decision making by simulating the key characteristics of biologics development and operation.

It represents Integrated Knowledge of product and process technology across the development, manufacturing and business value streams.



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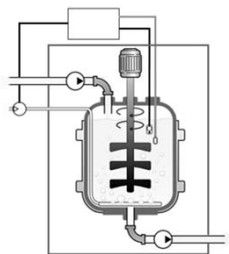
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## Bioreactor Real-Time Digital Twin Models

Real-Time Data from  
Online Sensors

Offline Measurements

Historical Data



Predict Batch Performance

Softsensors

Fault Detection

Model Predictive Control

Mass Balance and Mass Transfer  
Cell Growth and Metabolism  
Chemical Reaction  
Control Algorithm  
Feed, Harvest Vessels  
... ..

All models solved  
simultaneously



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## Summary

In the era of digital transformation of our industry, models are further integrated into platforms that play critical role in process design and product launch.

Investing in modeling capabilities and leveraging external partners will generate net value for programs at all stages.



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## Questions?

Please use the microphone indicated so our recording includes audio of your question

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For further information, please contact  
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