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Developing an Advanced Digital Twin for a Pharmaceutical Pilot Plant

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Contents

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What is a digital twin ?

Virtual construct of a physical system

Fully integrated with real-time data exchange

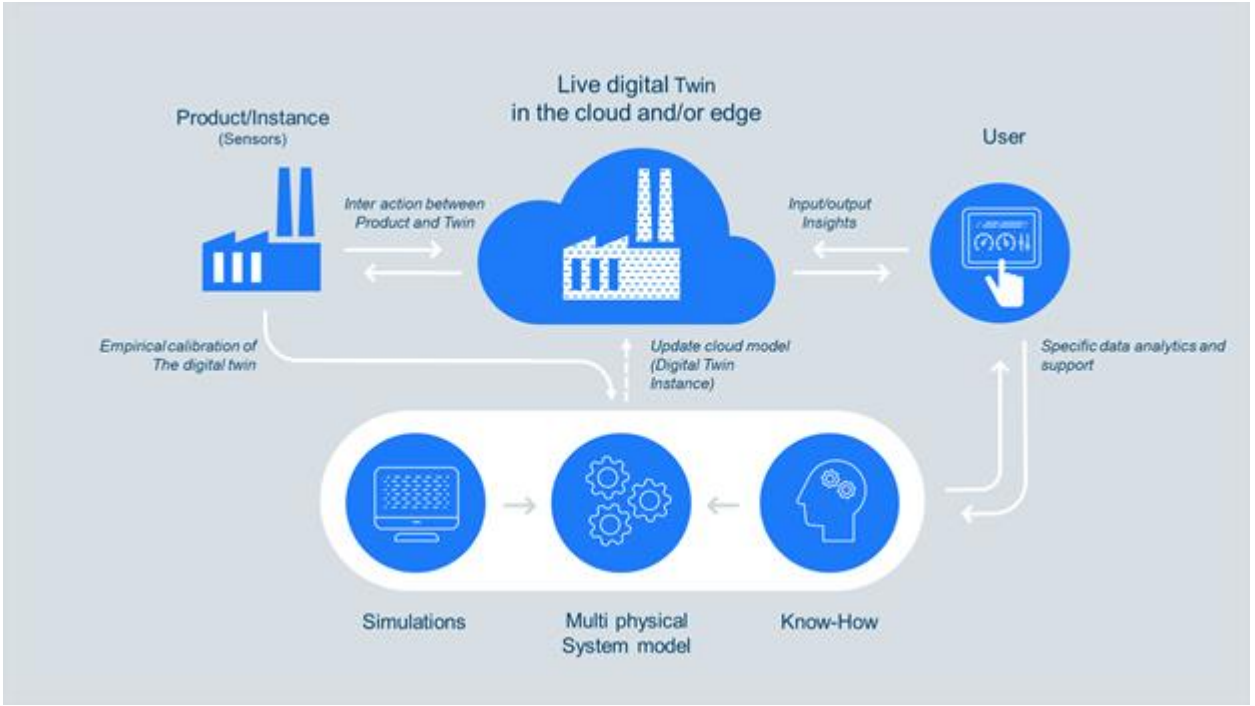

Figure 1. A manufactured product integrated with the Digital Twin through the use of IoT technology.

Forcetechnology.com. 2021. *Digital twins*. [online] Available at: <https://forcetechnology.com/en/services/digital-twins> [Accessed 21 September 2021].

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Project Background

This Project involves working in conjunction with Siemens and Perceptive Engineering on developing an advanced digital twin of a continuous drug manufacturing plant located at the University of Sheffield (DiPP).

The digital twin of the DiPP is constructed by integrating

- advanced mechanistic models;
- advanced control system; &
- cloud technologies.

1: Twin screw granulation **2:** Fluid bed dryer **3:** Cone mill **4:** Blender **5:** Tableting machine

Objectives

Create

Construct an advanced digital twin of the DiPP by integrating advanced mechanistic models, advanced control system and cloud technologies.

Test

Investigation of how different control strategies affect the product properties (e.g dissolution and tensile strength)

Investigation of how small change in humidity and temperature in environment affect product quality

Optimise

Improve the sustainability performance of the DIPP plant using the digital twin

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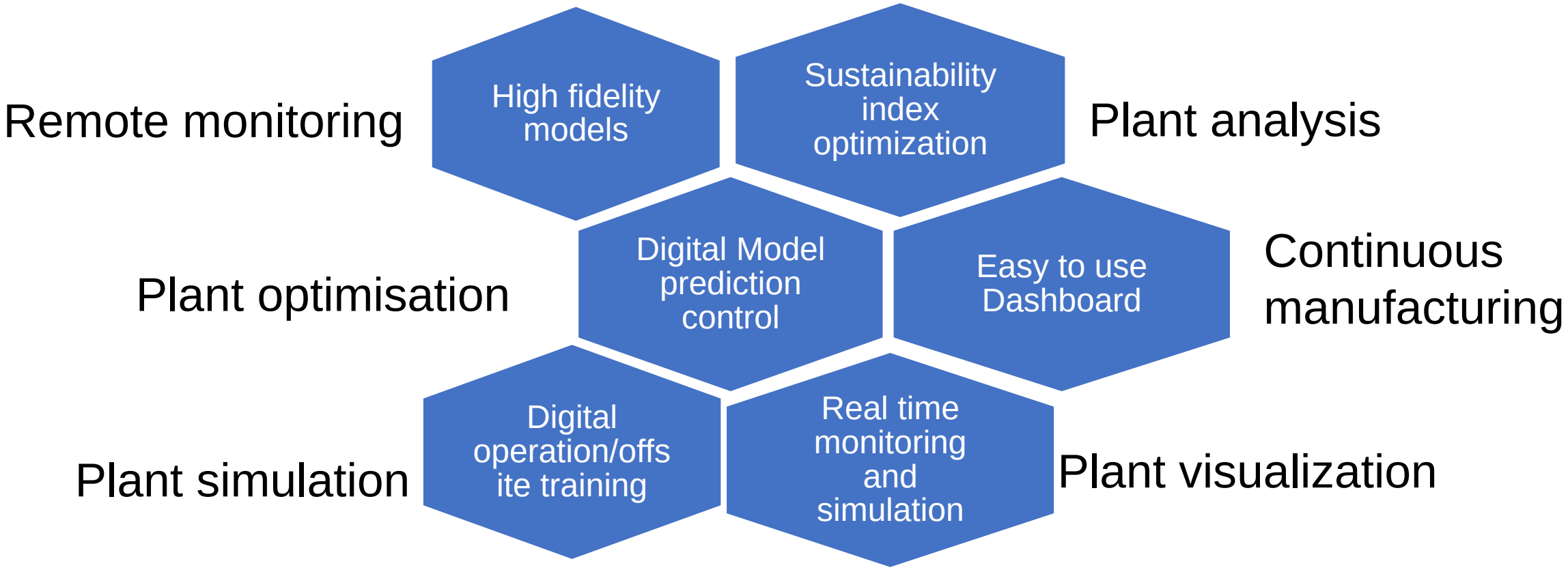
Key features…



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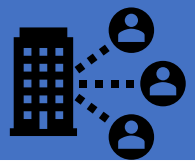
Remote working is more prevalent than ever



Continuous manufacturing in Pharma

Batch vs Continuous

Why now?

Cloud platforms are more secure

Easy and fast access to information

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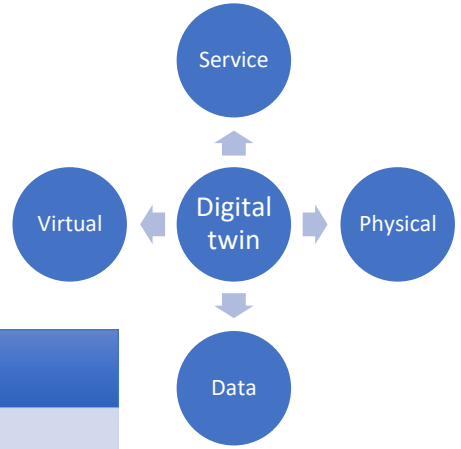
Enabling Digital Technologies



Service

- **Optimization**
  Simulink
  FLEXSIM
  Beacon
  Predix
- **Simulation**
  3dMAX
  Abaqus
  Simulink
- **Diagnosis**
  MATLAB
  Ansys
  3D experience

Data management

- **Data visualization**
  Tableau
  Data V
  FLOT
  Python
- **Data fusion**
  MATLAB
  Predix
  Beacon
- **Data transamination**
  MindSphere
  Predix
  Thingworx
  Aspera

Modeling

- **Geometric modeling**
  AutoCAD
  UG
  SolidWorks
- **Physical modeling tools**
  Simulink
  ANSYS
  Solid works
  PSE
- **Behavioral modeling tools**
  Twin Builder
  ADAMS
  Composer

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Our Approach

1. Model the plant using high fidelity models	2. Build a virtual asset of the plant in MindSphere	3. Design a control strategy in Pharma MV	4. Data Integration design
For simulation and digital model prediction control.	To collect data from the operating physical product Allow historic and real time data insight can be Access by multiple stake holders	Control strategy will be linked to gPROM formulated product to reduce waste and optimise the plant performance	Allow for a full integration with real-time data exchange

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Step 1: Model Development

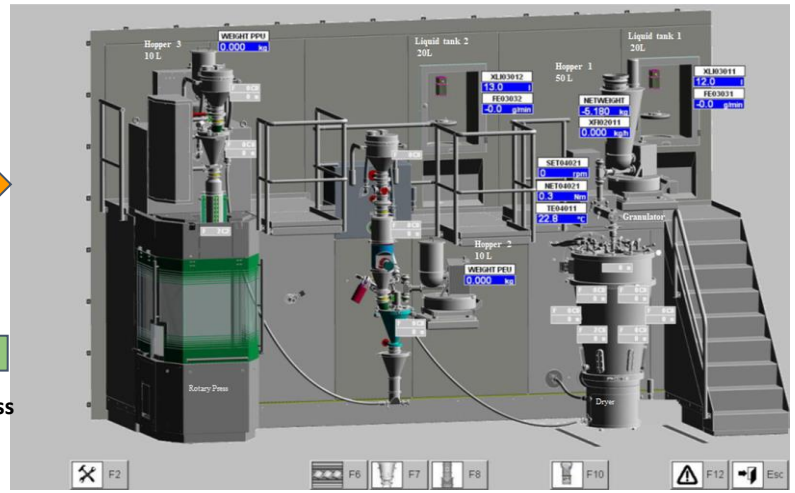
A mechanistic model of the manufacturing line is being developed on PSE's gPROMS Formulated Products to model the Diamond Pilot Plant (DiPP) unit operation using high fidelity model

Physical Process

Process Data

Optimised Process Parameters

Digital Process



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gPROMS FormulatedProducts

Phase 1

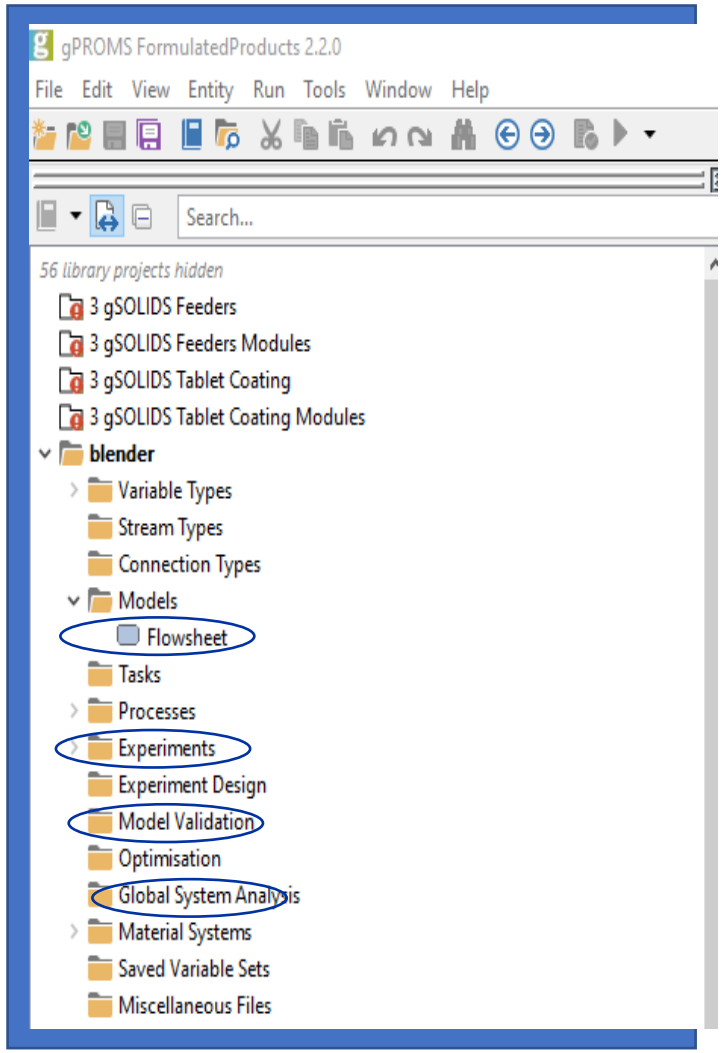
- Build flowsheet model of the DIPP
- Integrate virtual sensors and sustainability models to the flowsheet

Phase 2

- Estimate parameters and analyse uncertainty using process data
- Carry out experiment and update initial

Phase 3

- Verify the model
- Carry out sensitivity analysis



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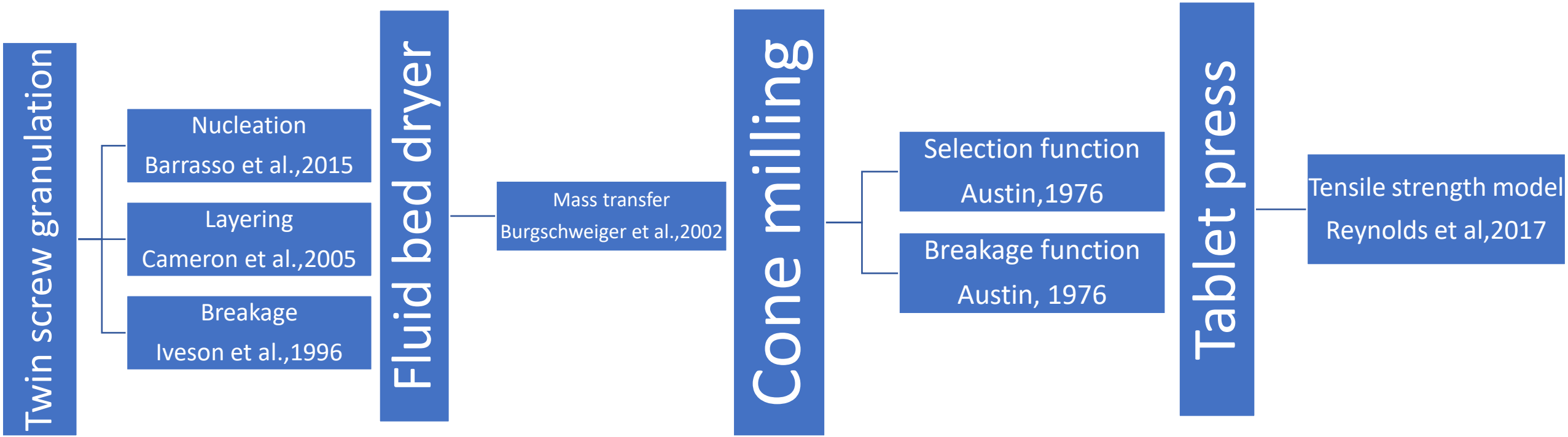
gPROMS FormulatedProducts

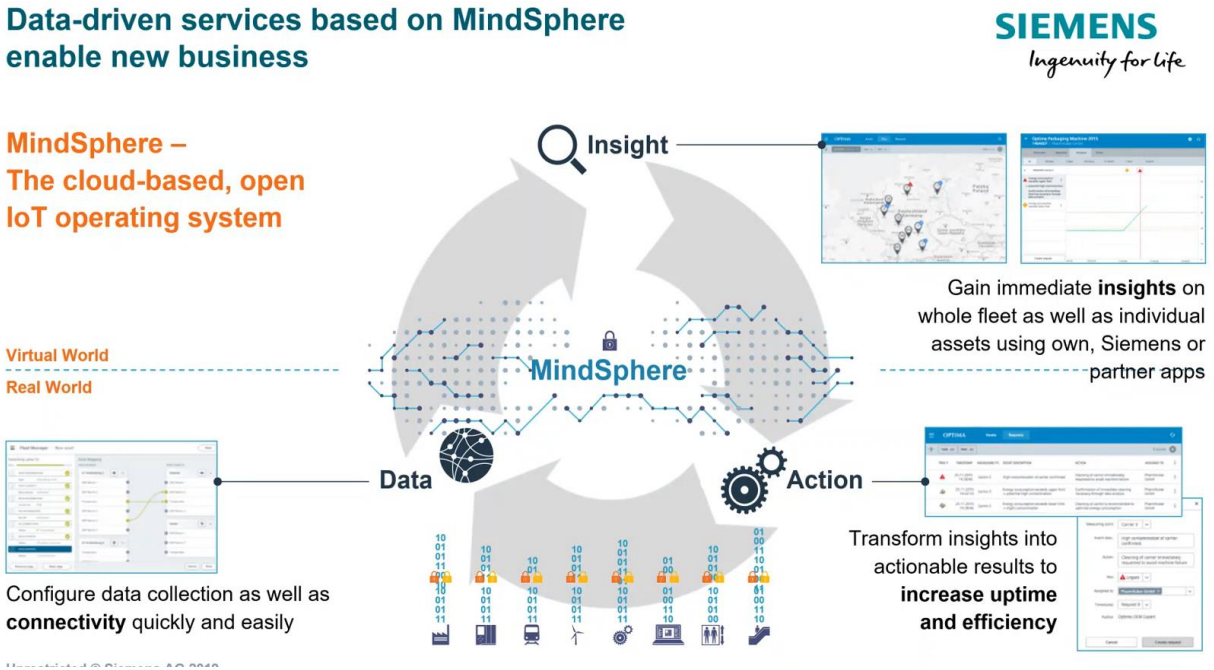
Mechanistic model used in gPROMS for each unit



Step 2: Virtual Asset Development

A virtual asset of the manufacturing line is being developed on MindSphere to allow data transmission of the Diamond Pilot Plant (DiPP) sensors to the cloud.

MindSphere enable users to visualise, analyse and manage both real-time and historical data on cloud servers.



Siemens.sharepoint.com.mcas.ms. 2021. [online] Available at: <https://siemens.sharepoint.com.mcas.ms/teams/Connected_Curriculum/SitePages/MindSphere-Training.aspx> [Accessed 21 September 2021].

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MindSphere workflow

Onboarding

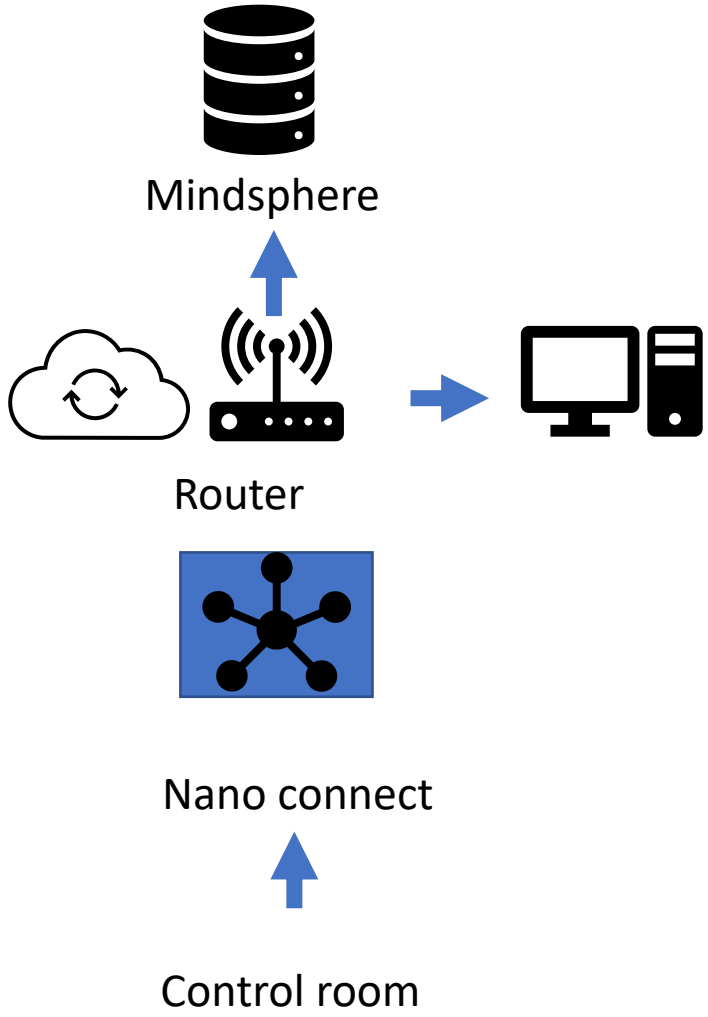
- Connect MindSphere Nano connect hard drive to Pharma MV local pc and to router

Creating a virtual asset

- Create aspect in MindSphere
- Create asset type for templating
- Create the DIPP asset using asset types

Data mapping

- Create a Nano connect asset in the MindSphere
- Map the DIPP asset in MindSphere to the Nano connect asset



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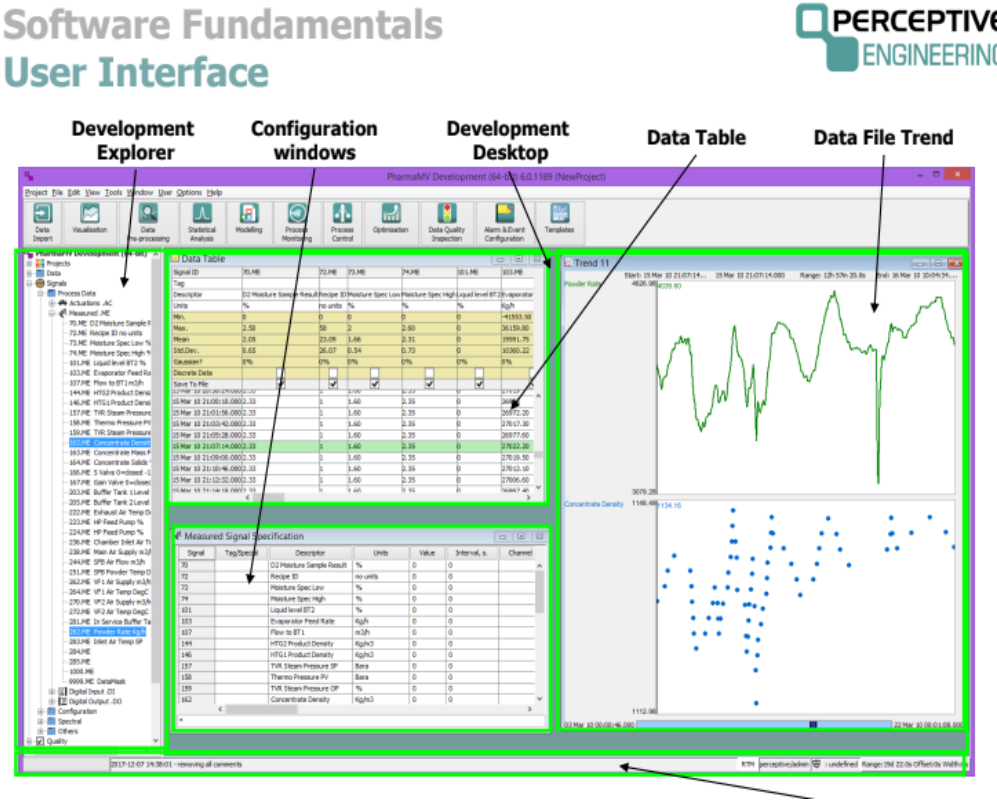
Step 3: Designing Control Strategy

The Pharma MV will be used to integrate process data and PAT data using multivariate analysis and design the control Strategy for the DIPP

The Pharma MV is a suite of software tools employed at the Diamond Pilot Plant that uses multivariate analysis, modelling, data visualization, process monitoring, control and optimization.



Pharma MV Workflow

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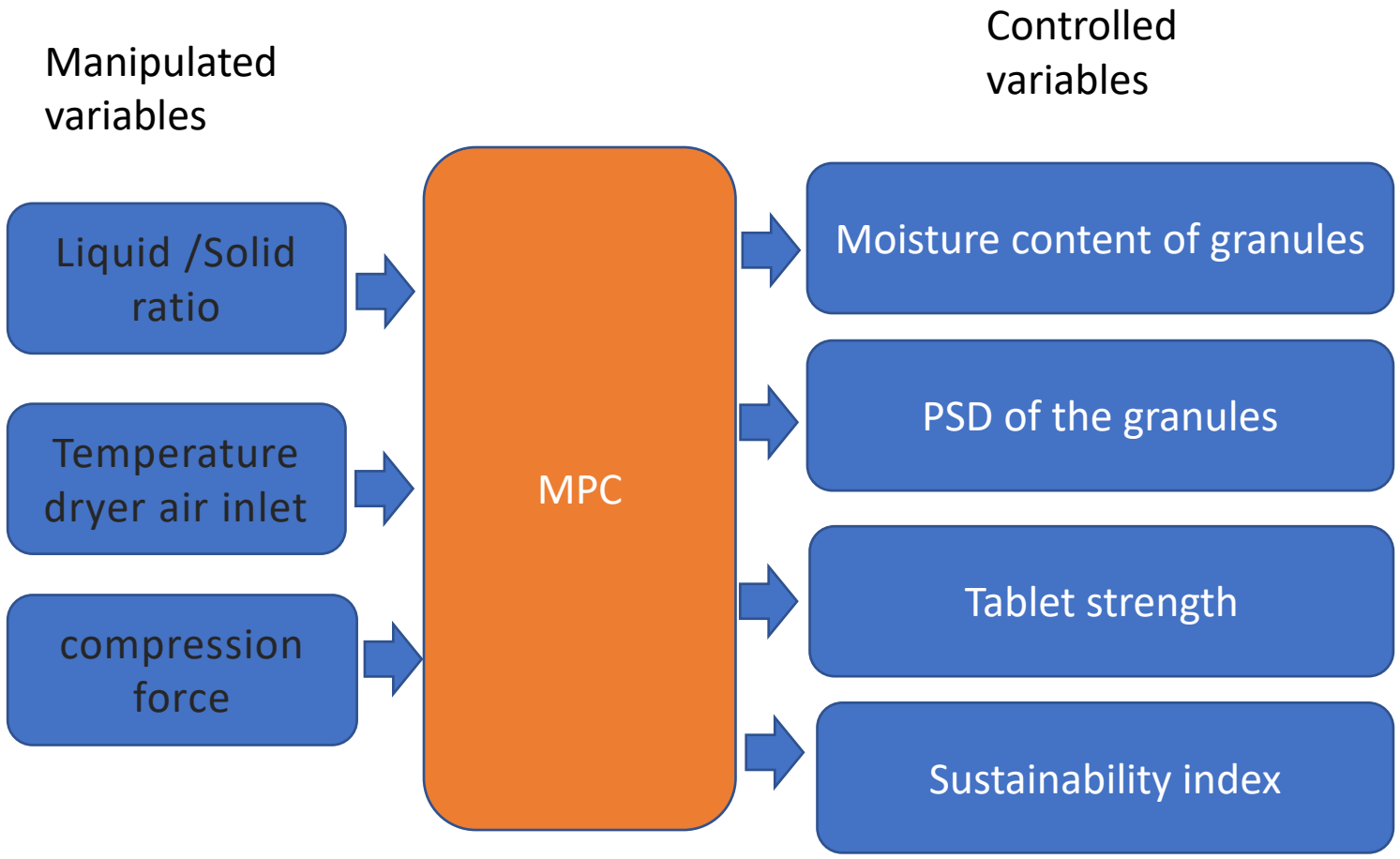
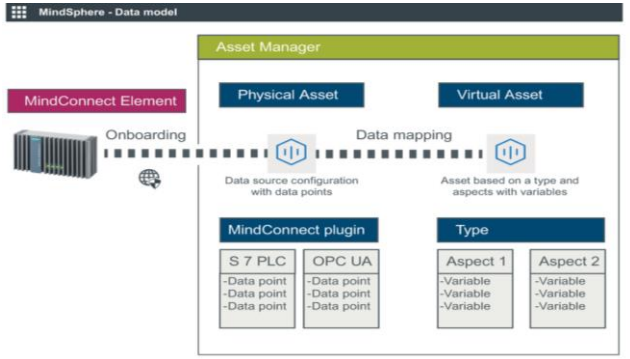
Workflow

- Integrate PAT and Process Data
- Apply Process Response Test
- Structure the controller
- Building a dynamic process model
- Tune and evaluate the controller



Step 4: Data integration design

1	Connect gPROMSFormulated Product to MindSphere to update kinetic parameter using process data
2	Create a digital model predictive control by sending measured variable data to gPROMSFormulated Product and sending back manipulated variable data to Pharma MV
3	Connect WIZ to MindSphere for online visualisation and data analysis
4	Connect gPROMSFormulated Product to MindSphere for digital simulation
5	Connect Mindsphere to Pharma MV to allow remote access to data and allow to multiple connect



Documentation.mindsphere.io. 2021. *Getting Connected to MindSphere*. [online] Available at: <https://documentation.mindsphere.io/resources/html/getting-connected/en-US/115370998027.html> [Accessed 21 September 2021].

```
SCHEDULE
SEQUENCE
PAUSE SIGNALID "2000" STATUS StatFlag # wait for 2 seconds
GET     #Read in the Rstep (Ramp from PharmaMV to synchronize gPROMS solver with PharmaMV interval)
    SIGNALID "GET @30"
    WdogIn;    #receive Watchdog signal from PharmaMV
END
WdogInPrev := WdogIn;
WdogOut := 0; #watchdog readback to be sent to PharmaMV
WHILE TRUE DO
    SEQUENCE
        GET #Read in the Rstep (Ramp from PharmaMV to synchronize gPROMS solver with PharmaMV interval)
            SIGNALID "GET @30"
            WdogIn;
            TempRateIn; #receive the (minutely) Temp rate from PharmaMV
        END
        IF  WdogIn <> WdogInPrev THEN #if the newly read-in ramp value is different from its previous value
            SEQUENCE
            WdogOut := WdogIn;
            REASSIGN Flowsheet1.TC.temp_C_set_point := OLD(Flowsheet1.TC.temp_C_set_point) + TempRateIn/10;END
            Continue for Interval # solve the process differential equation over simulation interval
            TempSPOut := Flowsheet1.TC.temp_C_set_point;
            END
        END
        WdogInPrev := WdogIn;
        SEND
            SIGNALID "SEND"
            STATUS StatFlag
            WdogOut;   # send Watchdog readback to PharmaMV
            TempSPOut;  # send Vessel Temperature SP to PharmaMV (Deg C)
        END
    END
END
END
```

Data frame network

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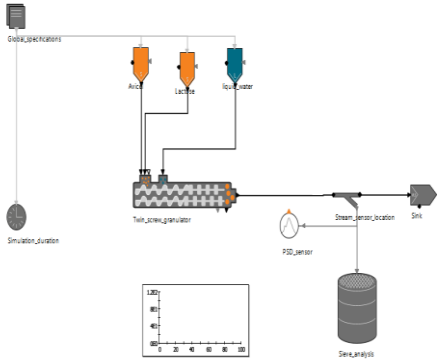
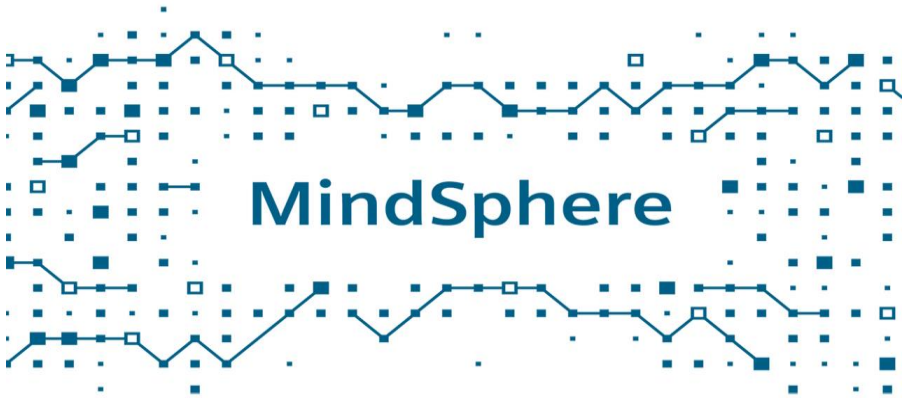


Process simulation models, product models

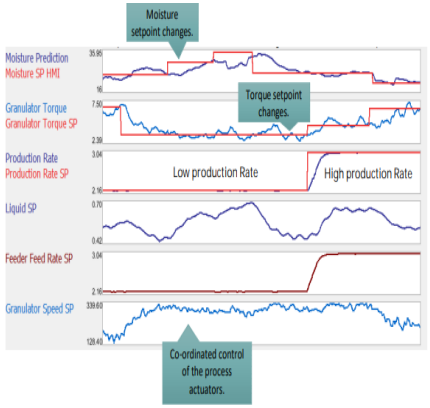
gPROMS Formulated Products

MindSphere

Cloud technology



Digital model predictive control



Pharma MV

Control Platform

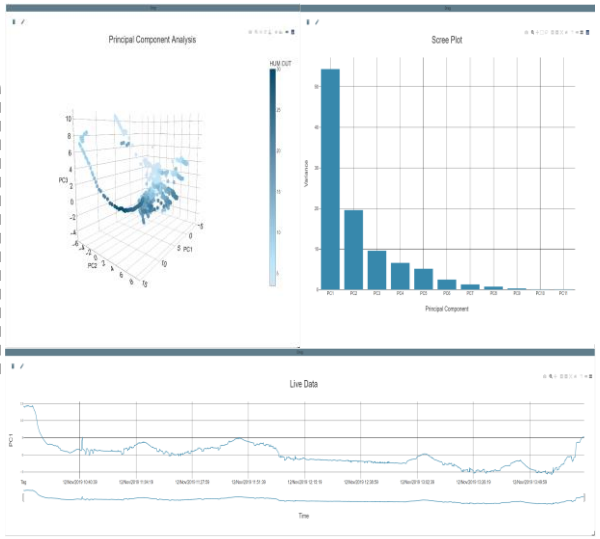
Sensor

NIR

Plant data

WIZ

Dashboard/ Visualisation



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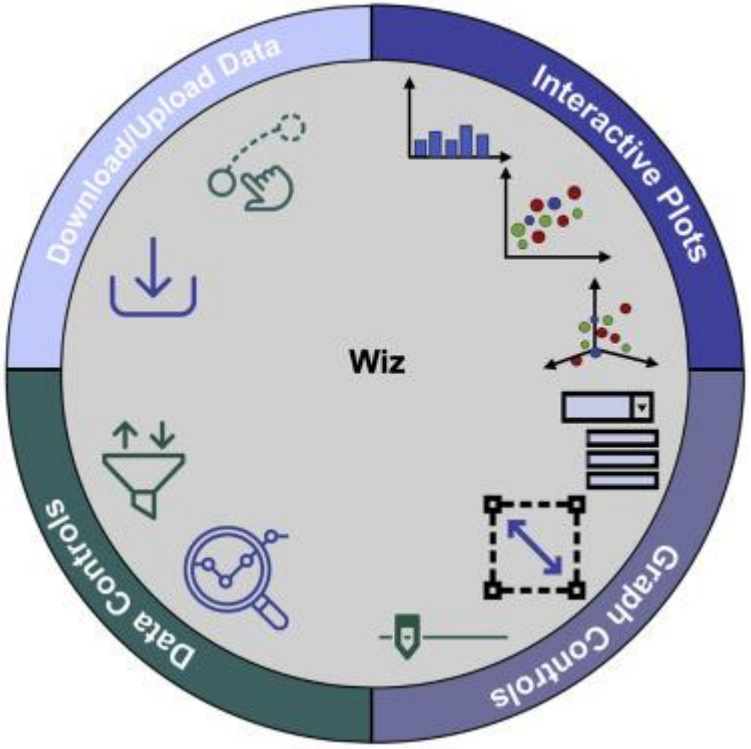
Data Visualisation

Wiz serves as a framework for interactive dashboards that can be utilized by anyone to visualize big data effectively.

By deloying the software in MindSphere one can;

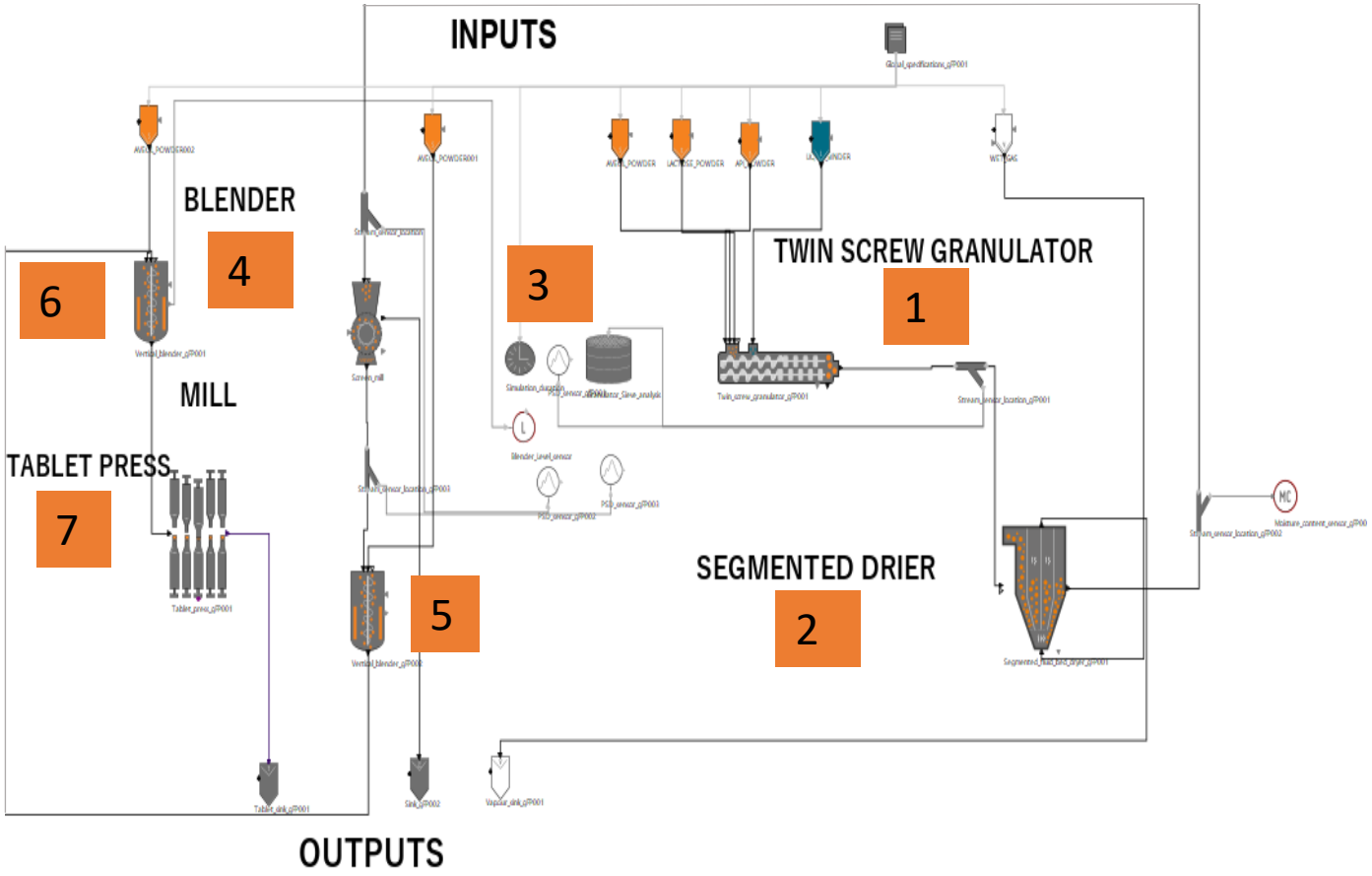
- visualise real-time data from process equipment in multi-dimensions.
- Carry out data analysis for troubleshooting



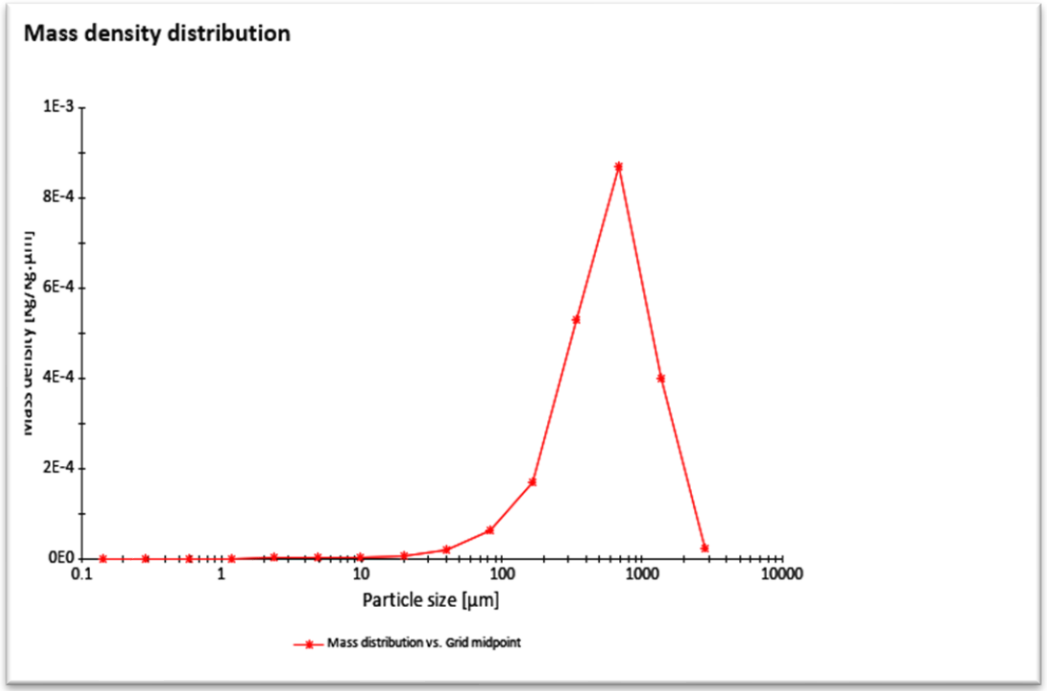
Balzer, C., Octavian, R., Zandi, M., Fairen-Jimenez, D. and Moghadam, P., 2020. Wiz: A Web-Based Tool for Interactive Visualisation of Big-Data. *SSRN Electronic Journal*,.

Early results

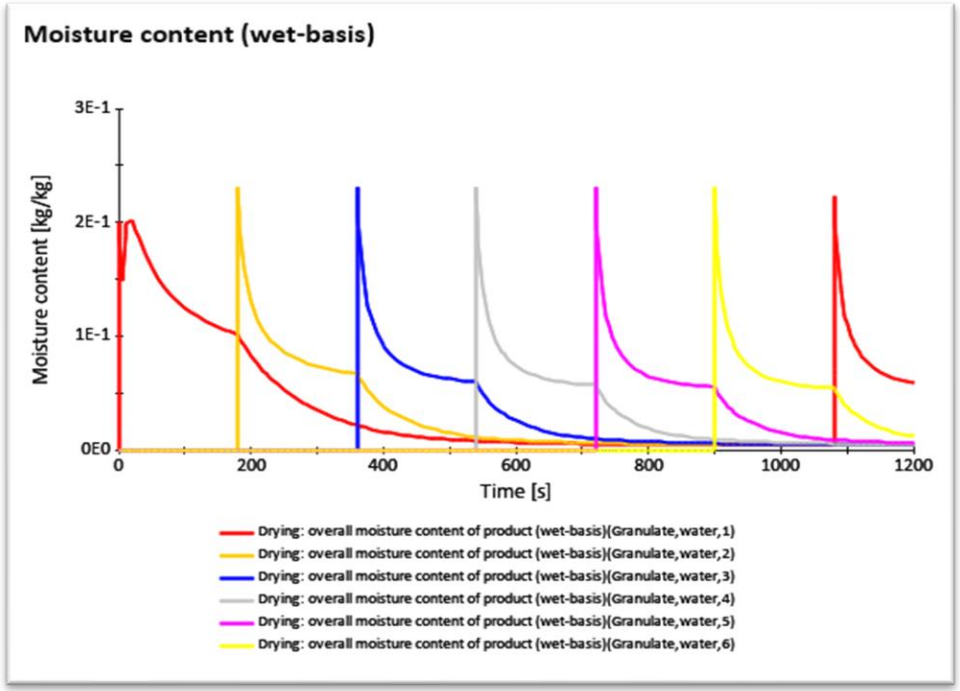
Integrated flowsheet of on the DiPP on gPROMS Formulated Product



Early results



PSD OF the granules existing the granulator



Moisture content of the granules existing the segmented drier

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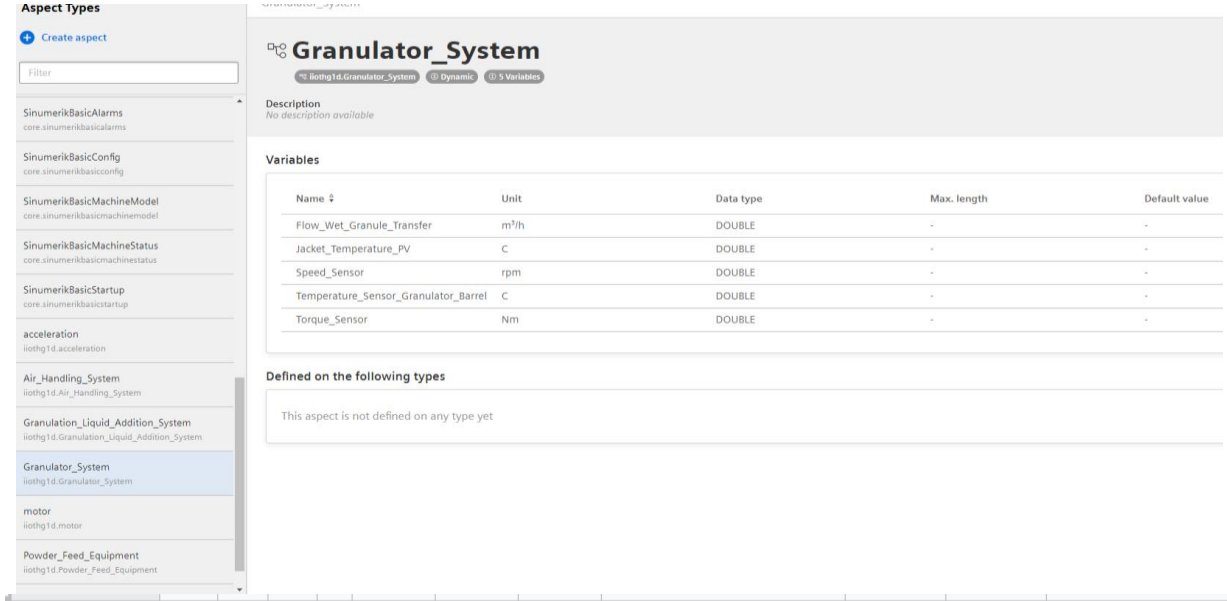
Early results

MindSphere aspects and asset for the DiPP

Data mapping

DiPP sensor tagging list



Signal ID	Tag				Description	Machine Output	Units	System	Location	
	WE	02	01	1	Weight Sensor-Powder Dosing Unit 1			Powder Feed Equipment	D3	
	WT	02	01	1	Weight Transmitter-Powder Dosing Unit 1				D3	
	XFI	02	01	1	Calculated Mass Flow Indicator-Powder Dosing Unit 1				D3	
1176.ME	X	02	01	1	Speed Motor Powder Dosing 1		rpm		C3	
1178.ME	X	02	01	1	Weight Powder Dosing 1(Net)		kg		C3	
1180.ME	X	02	01	1	Weight Powder Dosing 1(Net) SP		kg		C3	
1182.ME	X	02	01	1	Weight Powder Dosing 1(Net) SP H_Limit		kg		C3	
1184.ME	X	02	01	1	Weight Powder Dosing 1(Net) SP L_Limit		kg		C3	
1174.ME	XFIC	02	01	1	Mass Flow Indicator Controller-Powder Dosing Unit 1		kg/h		E3	
	LET	03	01	1	Level Sensor - Granulation Liquid Tank 1			Granulation Liquid Addition System	B3	
1170.ME	XLI	03	01	1	Content Indication - Granulation Liquid Tank 1		L		B4	
	FE	03	03	1	Mass Flow Sensor - Granulation Liquid		g/min		E2	
	FT	03	03	1	Mass Flow Transmitter - Granulation Liquid				E2	
1244.ME	XFI	03	03	1	Mass Flow Granulation Liquid		g/min			
1022.ME	FC	03	03	1	Flow Controller (Variable Voltage Controller)		rpm		D3	

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Challenges

- Patent information
- Multidisciplinary hence support required
- Covid-19 pandemic delaying projects by months
- No systematic way of designing a digital twin
- Deferent formats makes integration difficult

Acknowledgments

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Thank You!