From innovation to commercialisation

NEPIC Digitisation and Cyber Security

27th March 2019

"HOW A COMBINED EXPERIMENTAL AND HIGH-THROUGHPUT MODEL-BASED APPROACH CAN DELIVER REDUCED DESIGN & DEVELOPMENT CYCLES, LOWER AND MORE PREDICTABLE CAPEX, LOWER OPEX, HIGHER PRODUCT QUALITY AND IDENTIFICATION OF AREAS TO INVEST IN PROCESS DEVELOPMENT"

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cpi

BREAKDOWN OF TALK

- Overview of CPI
- Case study – PROSPECT CL & link to HTE
- Case study – PROSPECT CP & link to Simulation / Digital Twin
- Summary

CPI is home to four National Centres established to support innovation in their respective industry areas and forms the process element of the High Value Manufacturing Catapult.

NFC CAPABILITY THEMES

Addressing Cross-Sector Industry Needs

PREDICTIVE DESIGN

Faster Innovation

Faster, more reliable approaches to get to an ideal formulation design

RADICAL EFFECTS

Bigger Innovation

Unexpected synergistic effects to deliver bigger or disruptive benefits

MANUFACTURABILITY

Process Innovation

Optimised, reliable system to guarantee the ideal delivery of a formulated product

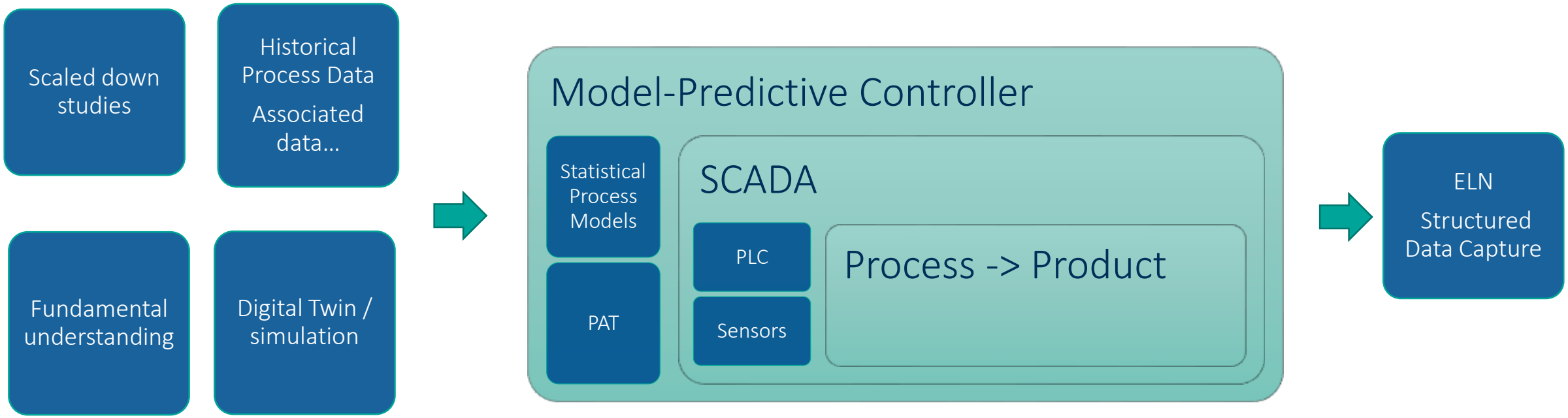
4IR CAPABILITY

Innovation Enabler

A critical foundational component for knowledge management and problem solving

Need for a better understanding of how to make and control formulations in manufacturing and scale-up
…to allow for more predictive design, integrated quality and enable the delivery of faster innovation and greater productivity

A FRAMEWORK FOR PROCESS DIGITALISATION



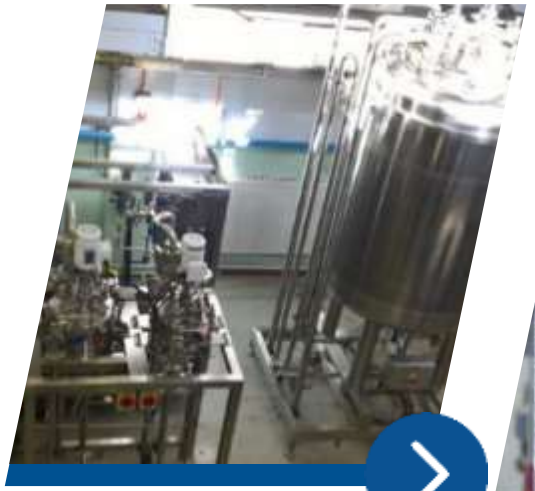
Developing digitalised, innovation-scale process rigs to tackle Manufacturability problems:

- Complex liquid mixing & scale up
- Particles processing, granulation - continuous manufacture

Exemplars of use of digitalisation – PAT, analytics, model-based control, process simulation / digital twin

PROSPECT CL

Proving of real-world, scalable, predictive tools and technologies for complex liquids



The dynamics of manufacture

Enabling predictive scale up

SCALED VESSELS (1-1000L) AND FLOW LOOP

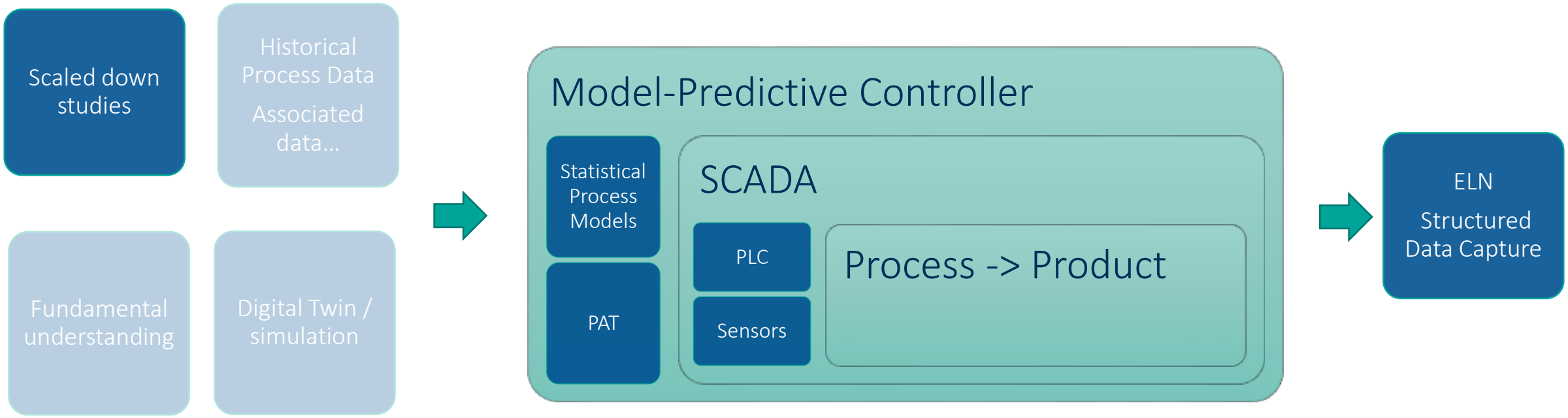
ANALYTICAL INSTRUMENTS AND SENSORS

4IR ENABLED CONTROL SOFTWARE

Validate new sensor technologies

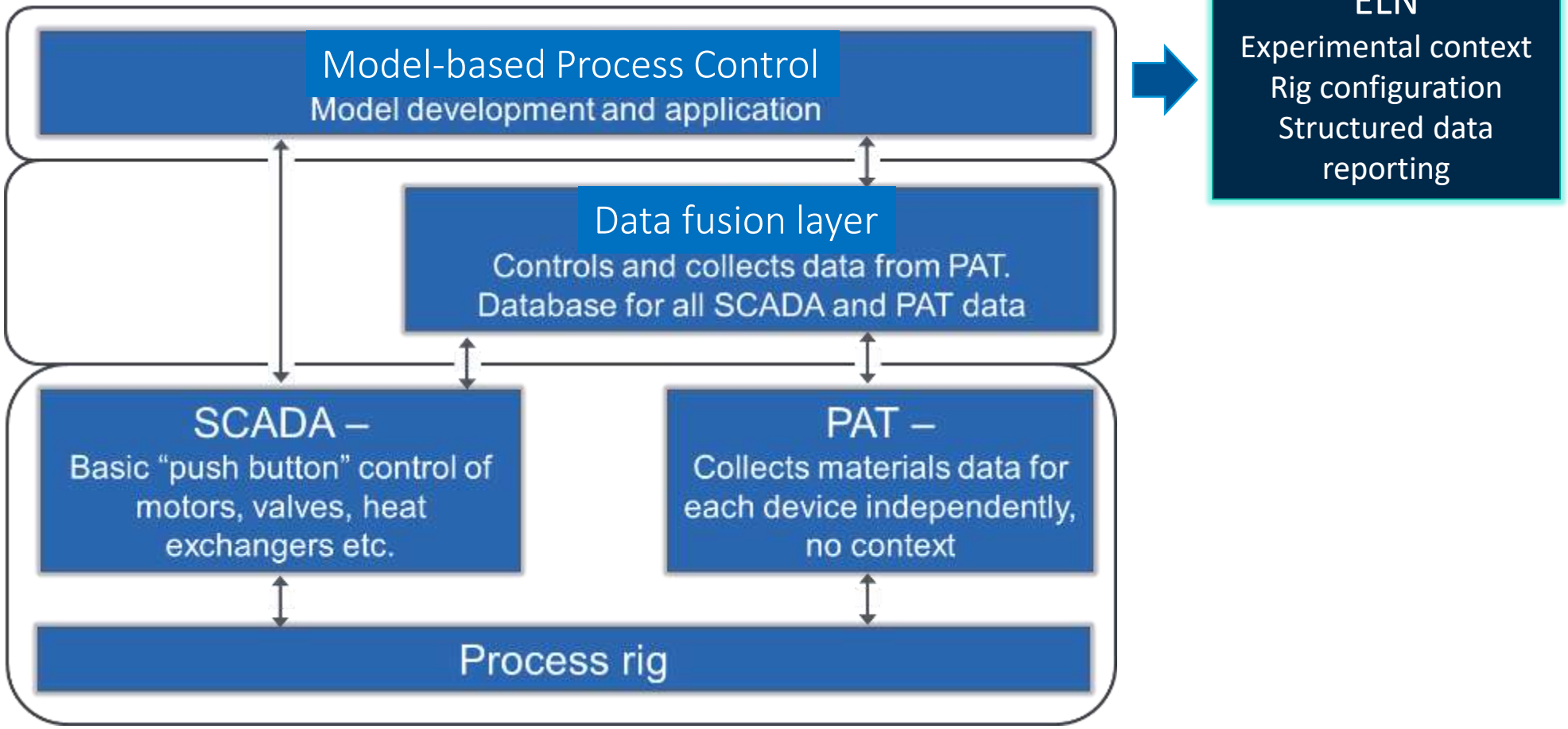
Develop process analytical techniques

PROCESS DIGITALISATION – PROSPECT CL



Looking to link to lab scales below 1L – lab discovery / High Throughput scale

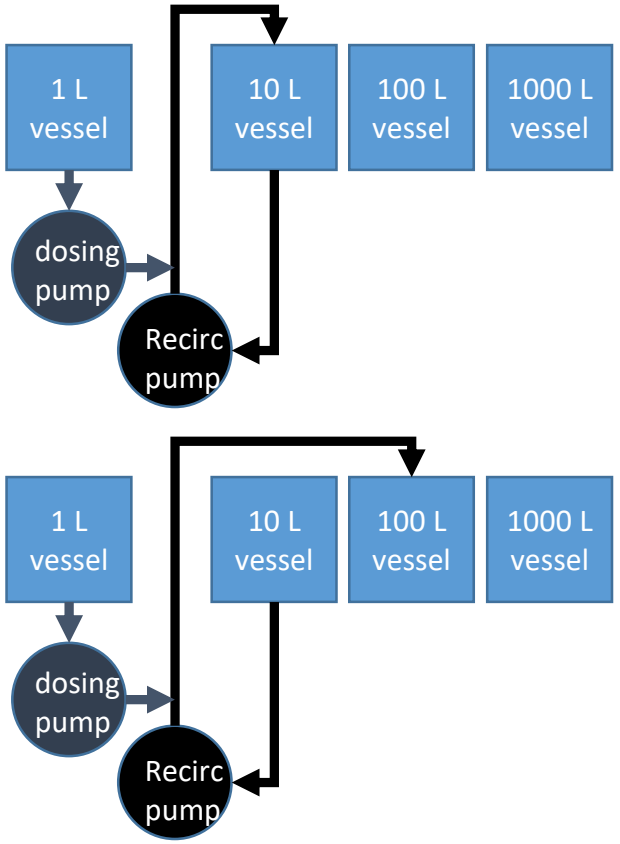
THE DIGITAL INFRASTRUCTURE



- Control system capable of monitoring and controlling product quality attributes
- Smart data fusion for process parameters and PAT output
- Capability to use process models for real time prediction of process parameters
- Capability to detect process abnormalities in "real time" through model based fault detection

THE SCALE-UP RIG

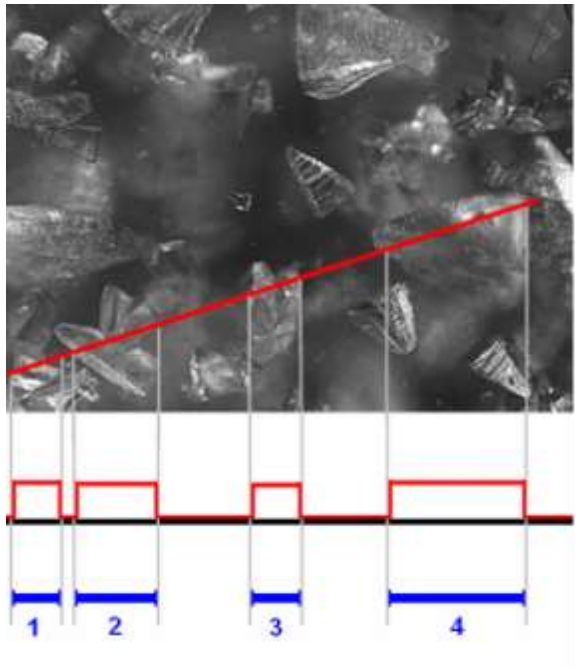
Example configurations:



Vessels increasing in size from 1-1000l, flow skid contains pumps and additional sensors (p, T, pH, conductivity, flow)

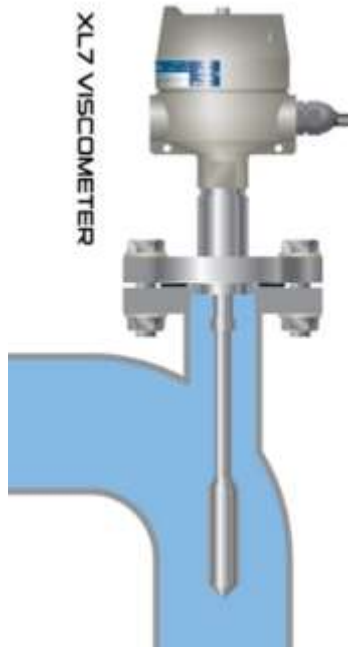
Operating temperature 4 - 50°C in standard mode, future 4-90°C. Operating pressure range 0-6 barg.

PROCESS ANALYTIC TECHNOLOGY



FBRM and Particle Viewer
Chord length distribution and micrographs
FBRM measurement range 0.5 to 2000 um

Insitec
At-line laser diffraction measurement
Measurement range 0.1-2500 um



Hydramotion Rheojet
Operates 250 and 2500 Hz
Measurement range 1-100,000 cP

PREDICTIVE SCALE-UP/SCALE-DOWN APPROACH

DoE

0.1 L

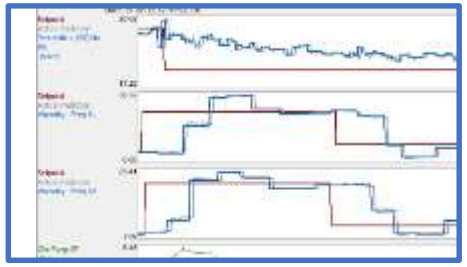
✓ scale-up
scale-down

comparison
of trends ✓

Inform step-change
experiments ✓

Comparison to DoE
predictions ✓

MPC



Automated
process
✓ control

Process data for ✓
MPC development
(e.g. through PRBS)

1 L

scale-up
scale-down
direct ✓
comparison

10 L

scale-up
scale-down
direct
comparison

100 L

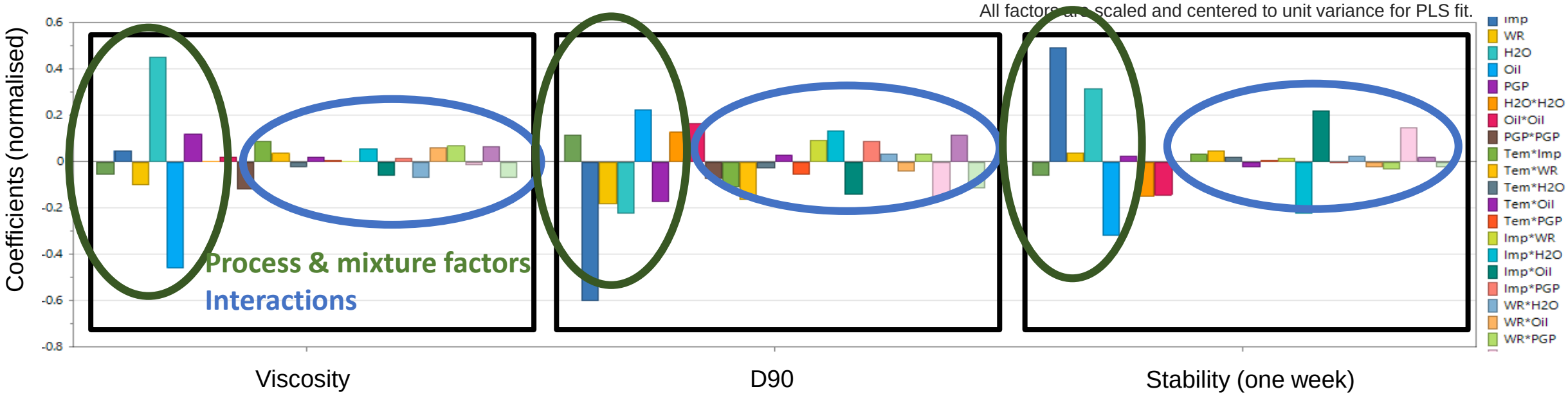
scale-up
scale-down
direct
comparison

1000 L

THE MODEL SYSTEM AND DOE PARAMETERS

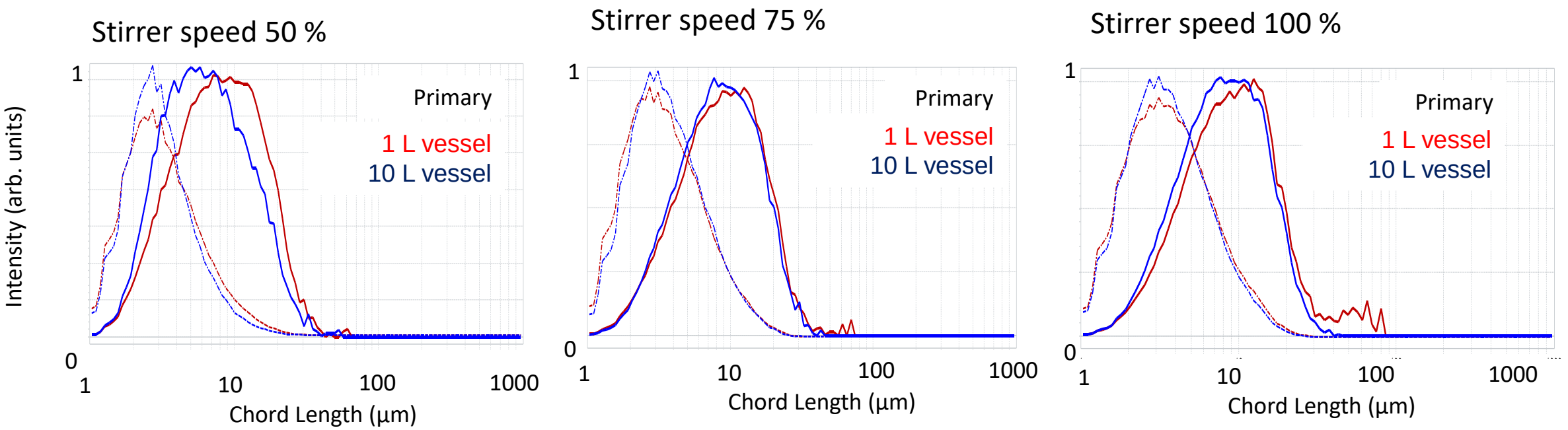
Model system: High internal phase emulsion (HIPE) of water droplets stabilised with polyglycerol polyricinoleate (PGPR).

DoE: Combined mixture-process design considering oil/water ratio, PGPR content, stirrer speed, temperature and water injection rate.



- Main factors stirrer speed, water addition rate, temperature and mixture
- Significant impact of combined factors, e.g. interaction of stirrer speed and oil
  - **This is confirmed by PRBS experiments and model predictive controller (MPC)**
- **Scale-up shows that DOE model seems to be predictive of behaviour on pilot plant scale**

SCALE-UP ON THE PROSPECT CL RIG

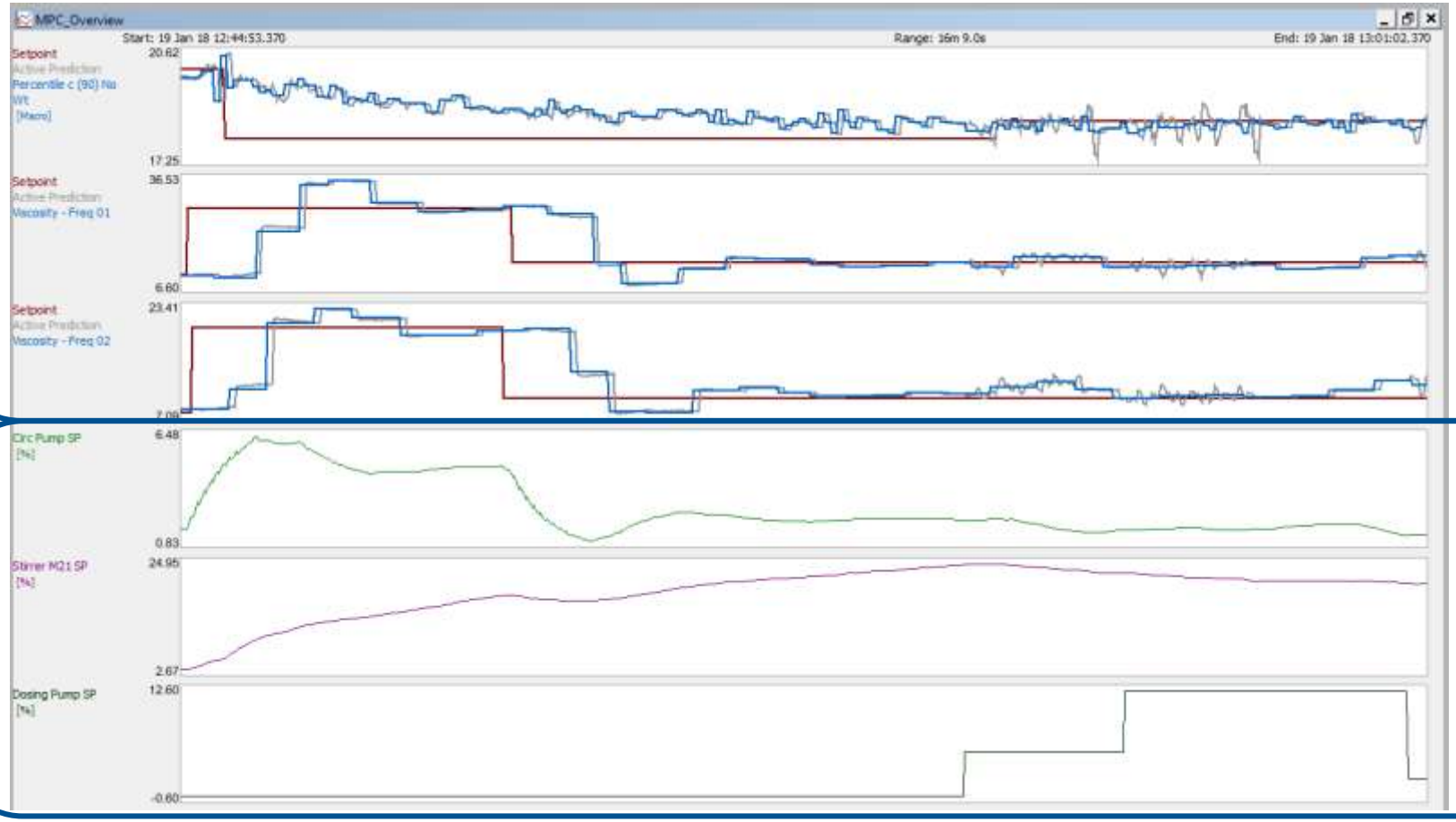


Successful scale-up from bench-top DOE model to 10 L

- Control of particle size, viscosity and stability when scaling up/down
- DOE trends can be confirmed on larger scales – more validation experiments to follow

MPC DEVELOPMENT AND VALIDATION

- Pseudo-random binary sequence (PRBS) experiments for MPC development
- Control of particle size and viscosity and one step ahead real-time predictions of MPC model
- **Same trends as observed in the DoE model – DOE is predictive of scale-up process**



Controlled variables

(D90, viscosity)

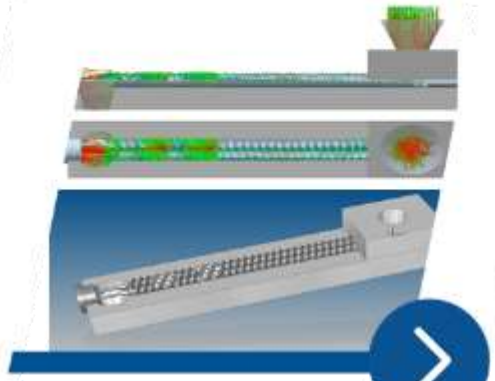
ARX 1st order model

Manipulated variables

(stirrer speed, dosing rate,…)

PROSPECT CP (COMPLEX PARTICLES)

Proving of real-world, scalable, predictive tools and technologies for particulate formulations



Modelling the dynamics of material and process

Enabling predictive scale up

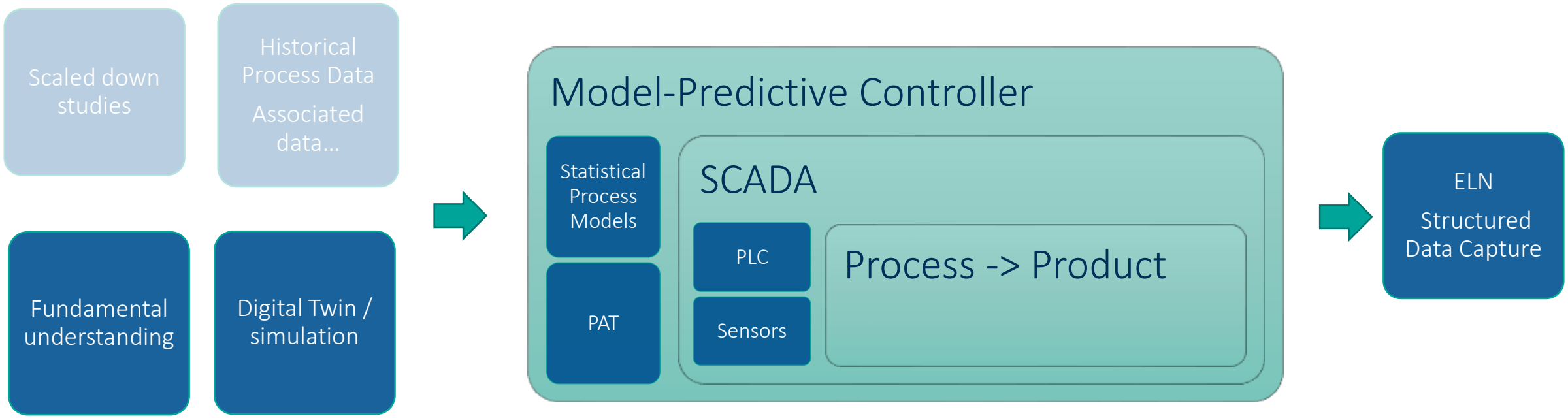
Validate new sensor technologies

Develop process analytical techniques

Project reaching conclusion

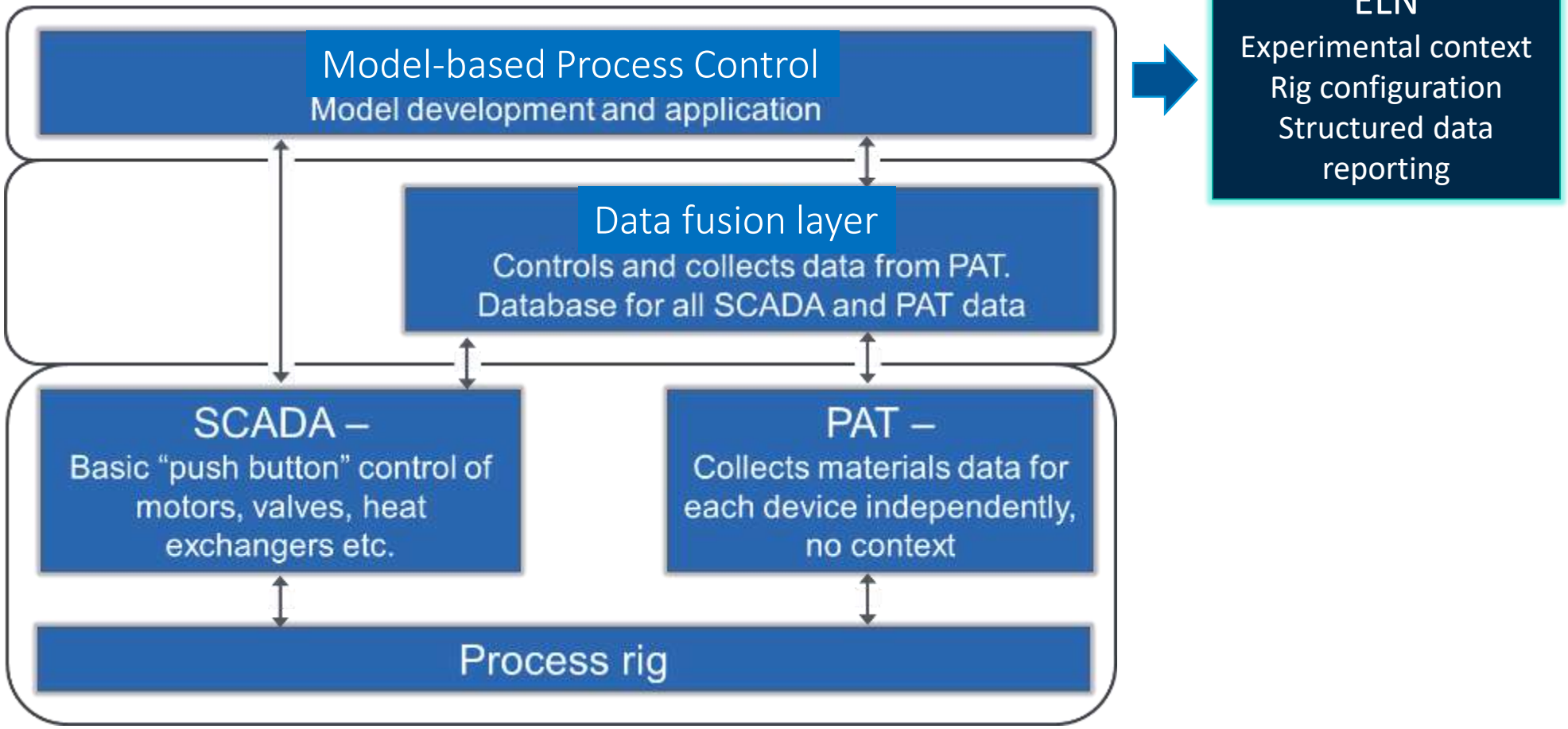
Two year project just beginning

PROCESS DIGITALISATION – PROSPECT CP



Linking to combined Discrete Element / Population Balance models – “Digital Twin”

THE DIGITAL INFRASTRUCTURE



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PHYSICAL PAT SENSOR INTEGRATION FOR PROSPECT CP

Prospect CP

Connection to ConsiGma (replacing fluid bed drier)

Multieye

NIR probe from Innopharma

Kaiser Phat Raman probe

6 mm spot size and 785 nm laser

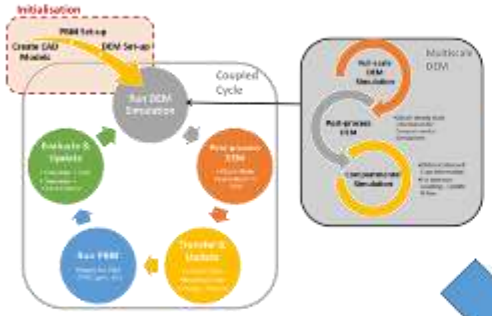
N.B. The attachment has been fully specified with interlocks/locking screws for laser safety

Eyecon 2

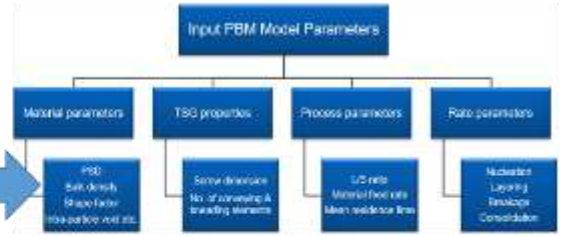
Particle Size Distribution and shape analysis from Innopharma

DIGITAL TWIN OF TWIN SCREW WET GRANULATION PROCESS

Discrete elements model (smaller scale)



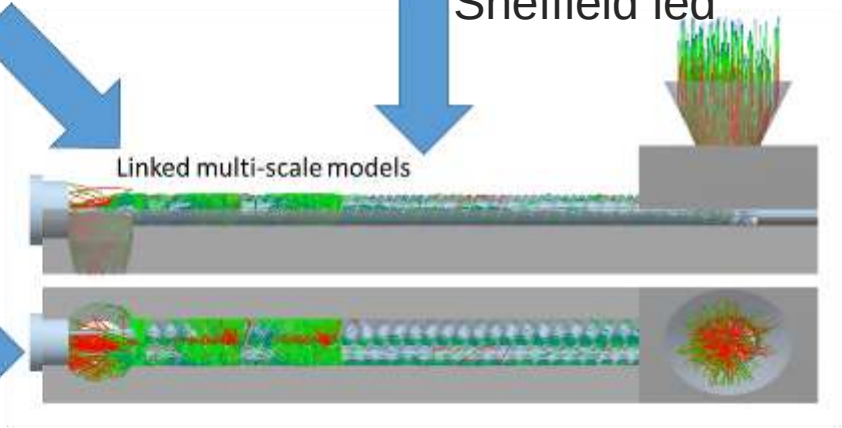
Population Balance model (larger scale)



Edinburgh led

Sheffield led

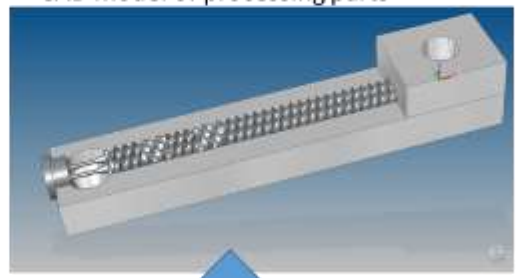
Linked multi-scale models



ConsiGma 1 model developed as part of broader project to utilise academic models in industry

Output= Prediction of product parameters and more agile determination of high quality products in the real world with less materials waste

CAD model of processing parts



Equipment- GEA Consigma 1 Twin Screw Granulator

Models for Particulate Processing (MPP)

SUMMARY

- Have created a digitalised innovation-scale rigs for studying complex liquids and powder processing
- Through implementation of model predictive control have demonstrated capability to connect bench / HTE scale to larger scales
- Through a ‘digital twin’ and models predictive control project we have enabled predictive design of manufacturability within a powders laboratory

THANK YOU

for more information

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