From innovation to commercialisation

FSTG Formulation 4.0

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DESIGN OF EXPERIMENT AND MODEL DEVELOPMENT ON THE PROSPECT CL - SCALE UP FACILITY

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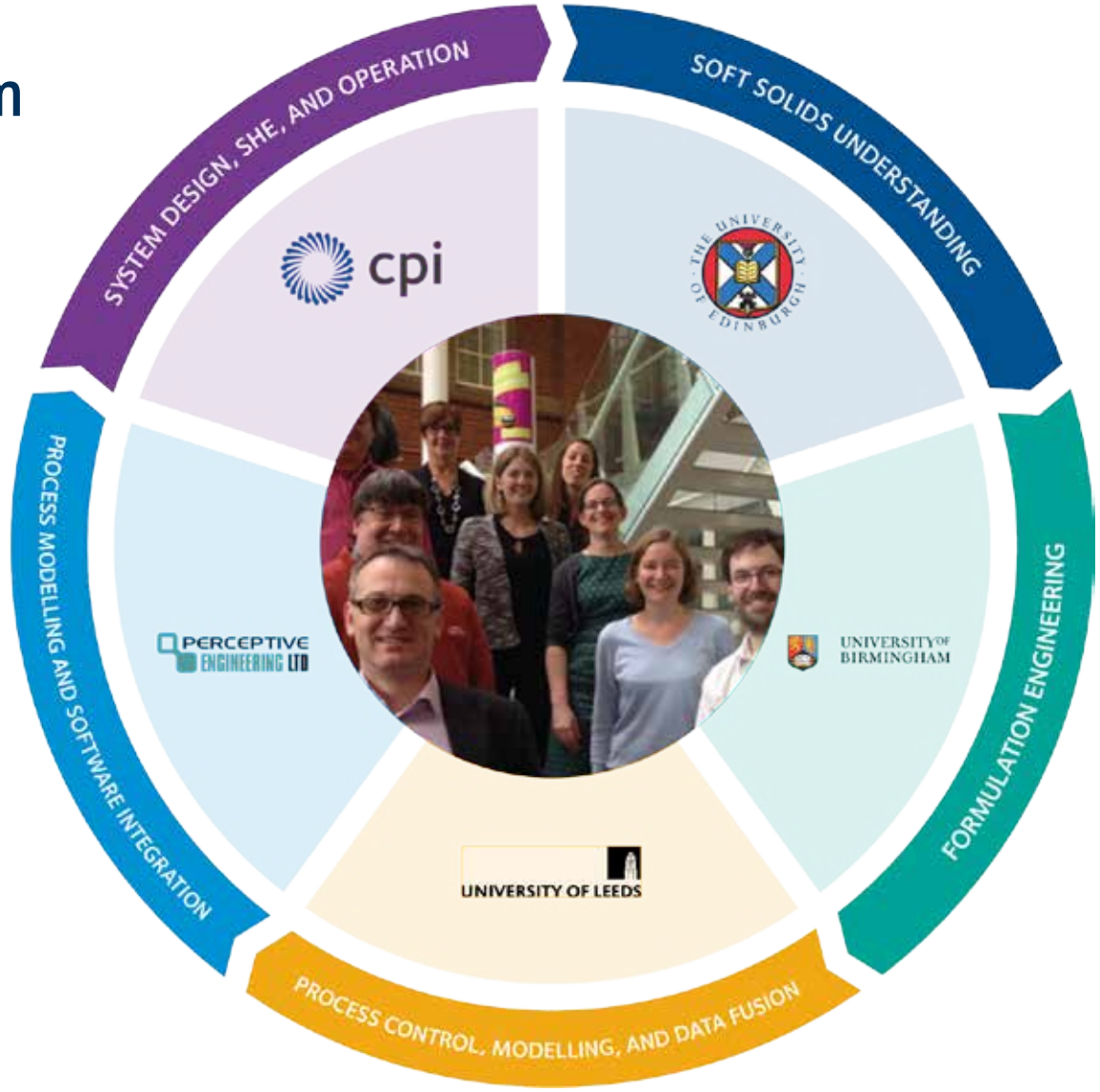


THE CENTRE FOR PROCESS INNOVATION

Home to four
NATIONAL CENTRES

CROSS-SECTOR INDUSTRY NEED

PREDICTIVE DESIGN

Faster Innovation

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

MANUFACTURABILITY

Process Innovation

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

4IR CAPABILITY

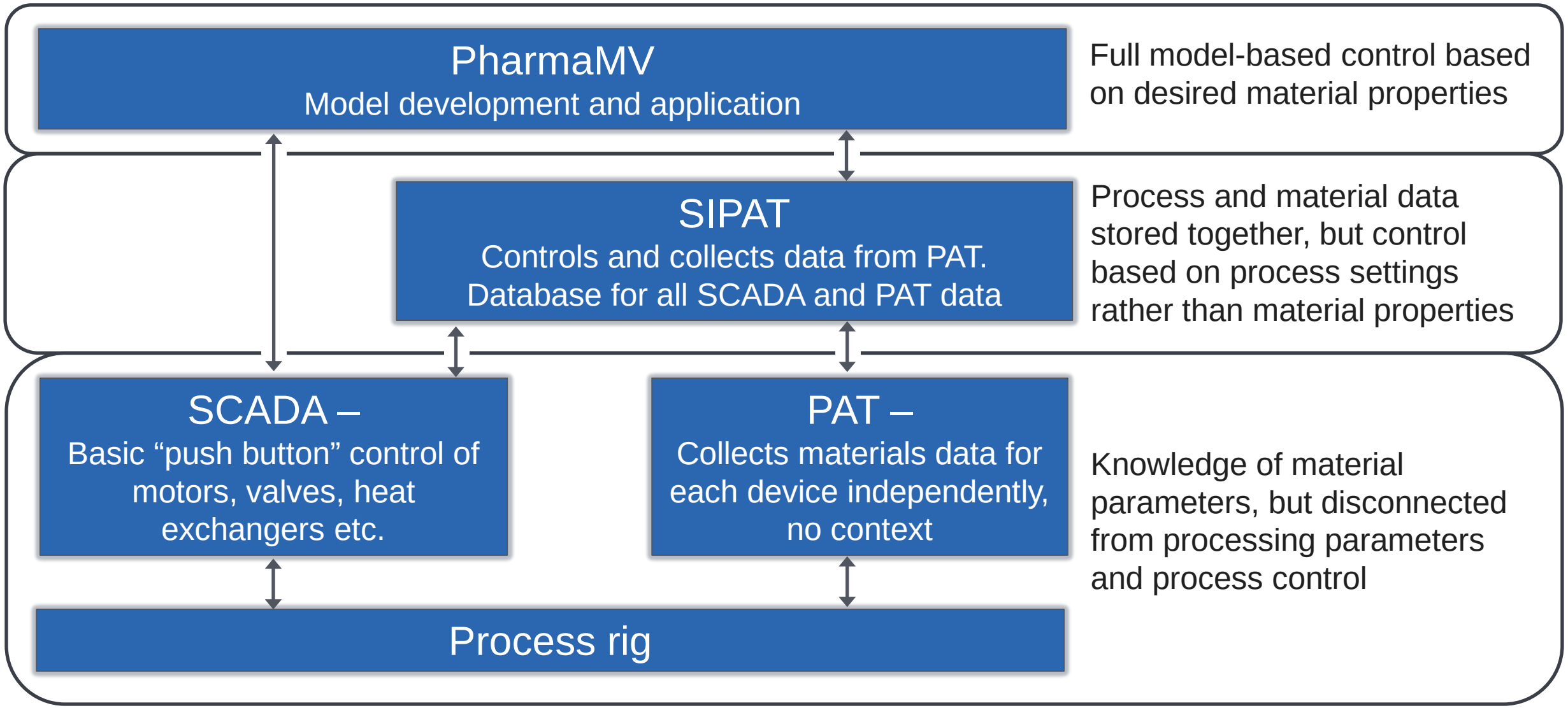
Innovation Enabler

A critical foundational component for knowledge management and problem solving

Need for a better understanding of how to **make and control** complex liquid formulations in manufacturing and scale-up

...to allow for more predictive design thinking and enable the delivery of **faster innovation** and **productivity**

ADVANCED PROCESS CONTROL



THE PROSPECT CL PROJECT

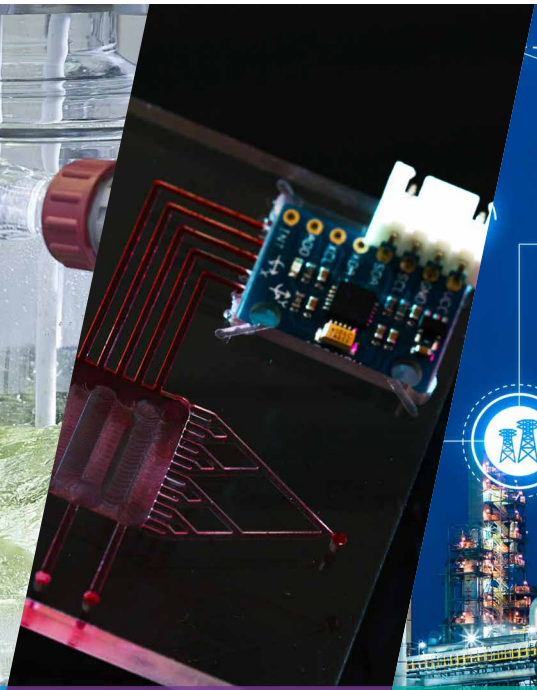
PROSPECT CL

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

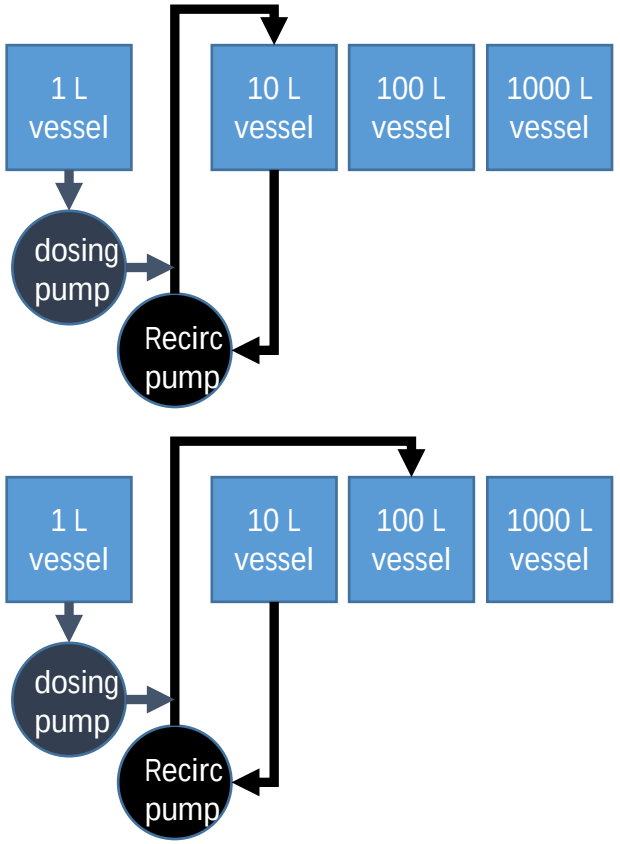
4IR ENABLED CONTROL SOFTWARE

Validate new sensor technologies

Develop process analytical techniques

THE SCALE-UP RIG

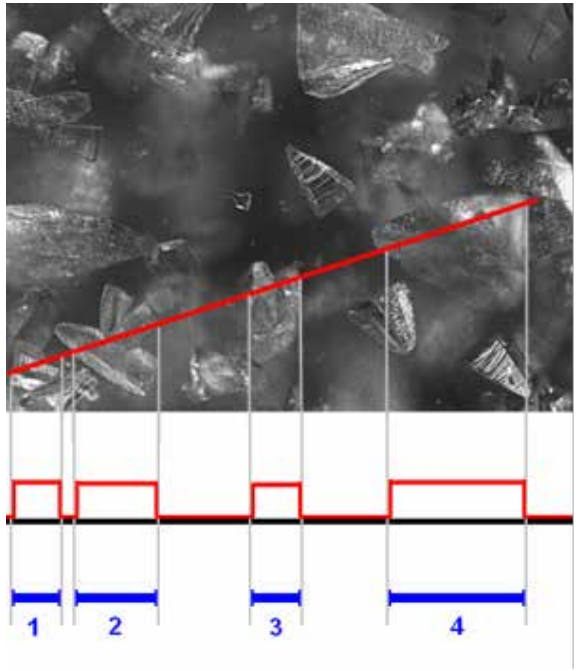
Example configurations:



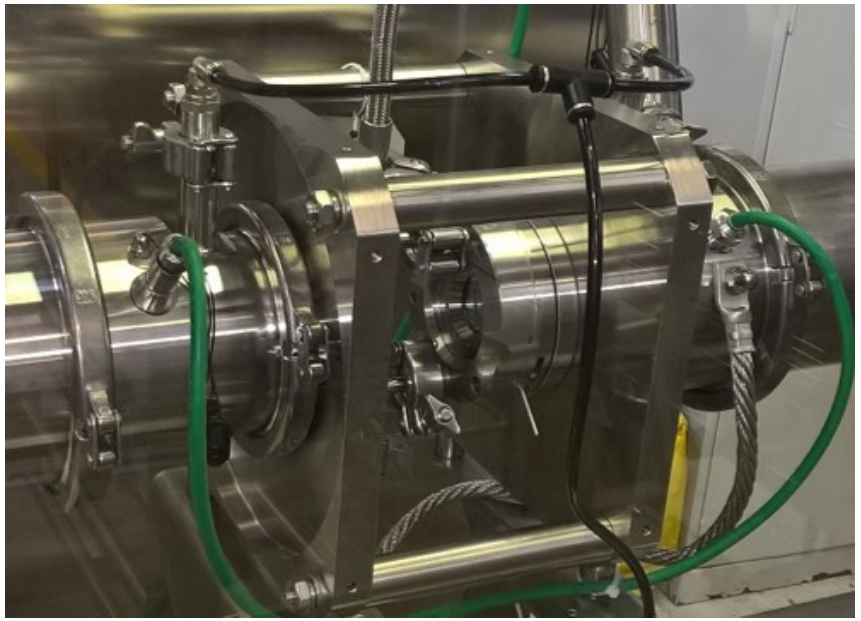
Vessels increasing in size from 1-1000l, flow skid contains pumps and additional sensors (p, T, pH, conductivity, flow)

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

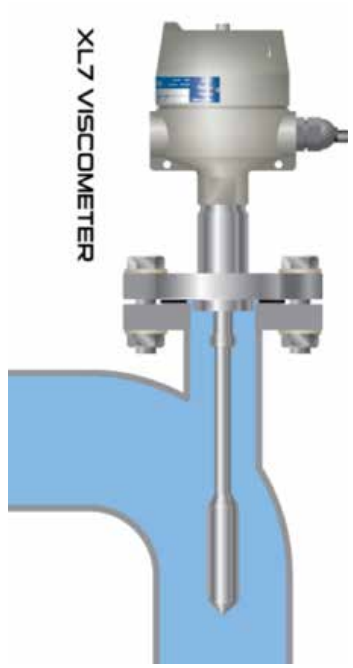
PROCESS ANALYTICAL TECHNOLOGY



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

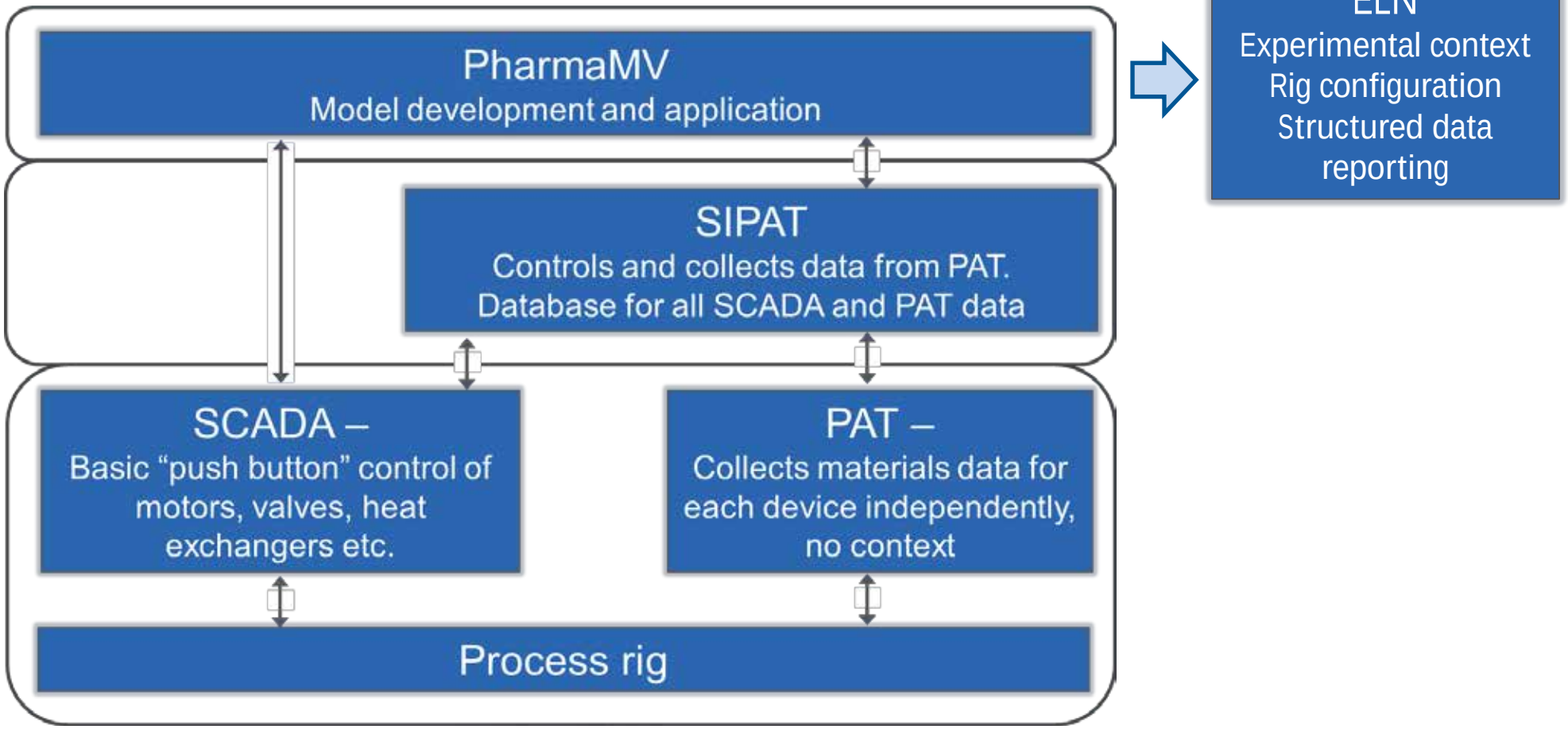


Insitec
At-line laser diffraction measurement
Measurement range 0.1-2500 um



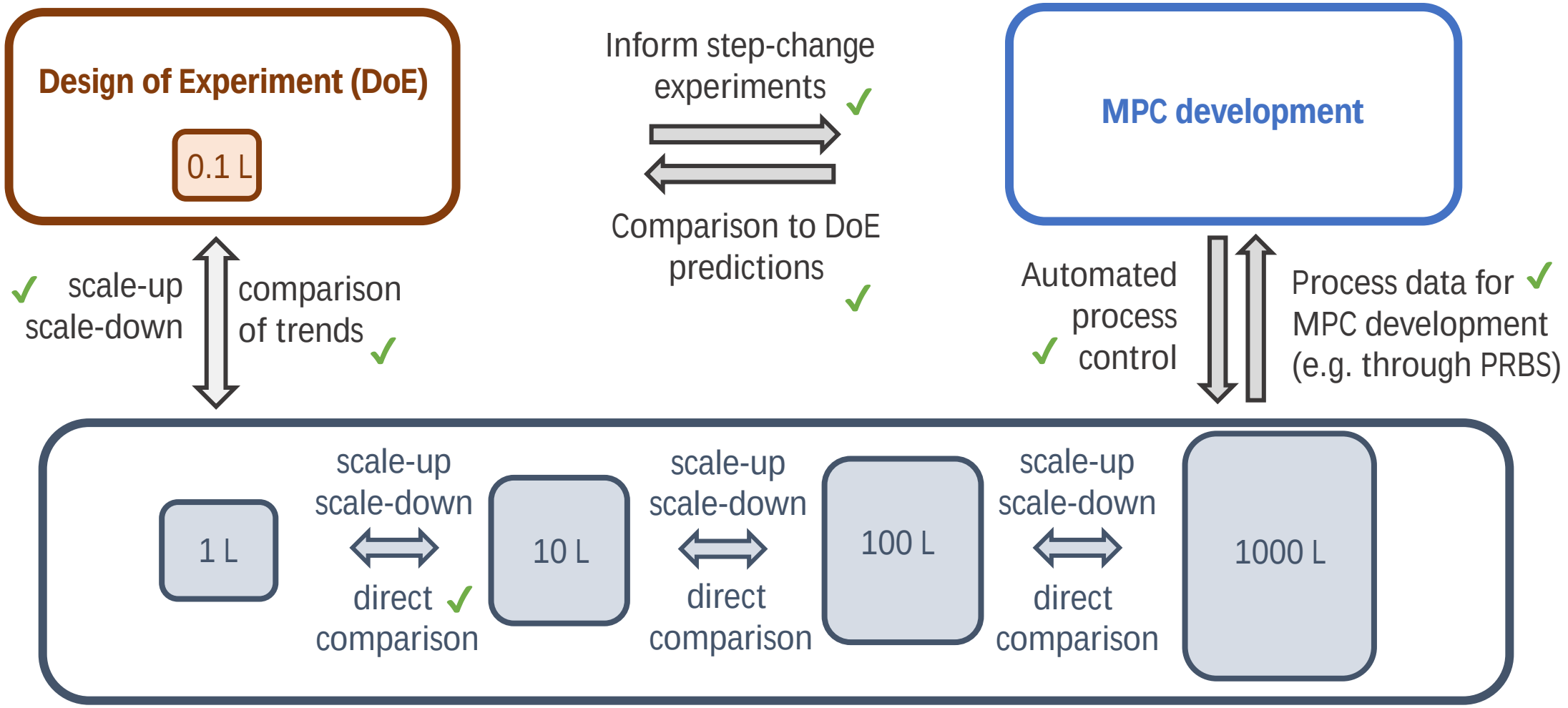
Hydramotion Rheojet
Operates 250 and 2500 Hz
Measurement range 1-100,000 cP

THE DIGITAL INFRASTRUCTURE

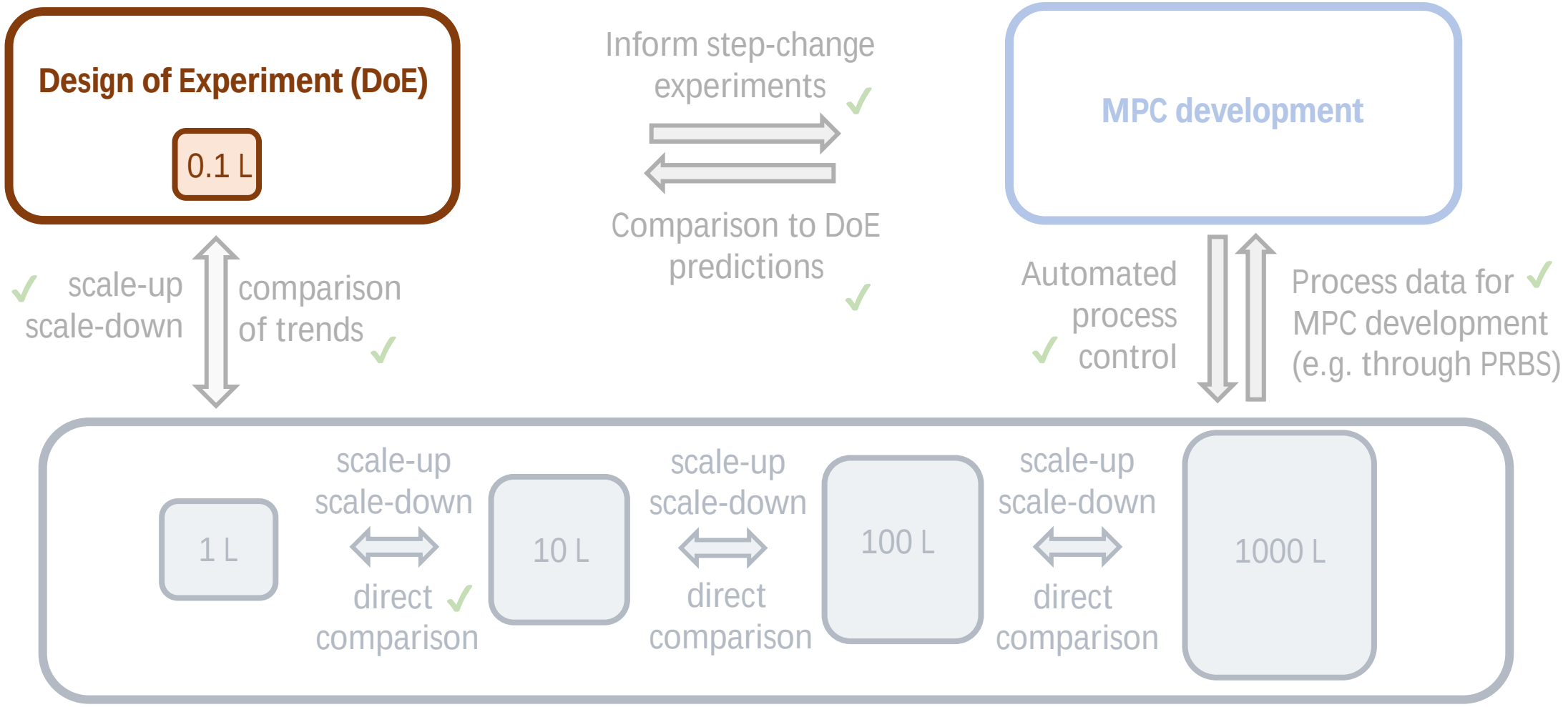


- Control system capable of monitoring and controlling product quality attributes
- Smart data fusion for process parameters and PAT output
- Capability to use process models for real time prediction of process parameters
- Capability to detect process abnormalities in "real time" through model based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

PREDICTIVE SCALE-UP/SCALE-DOWN APPROACH



PREDICTIVE SCALE-UP/SCALE-DOWN APPROACH

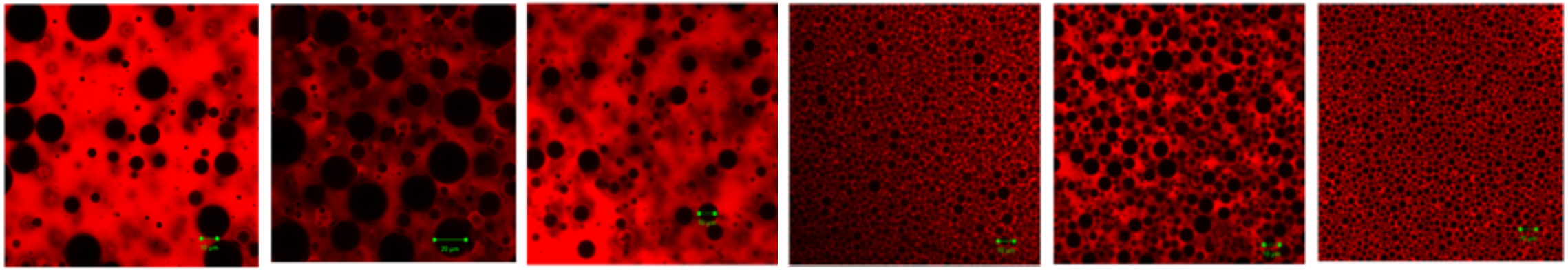


THE MODEL SYSTEM AND DOE PARAMETERS

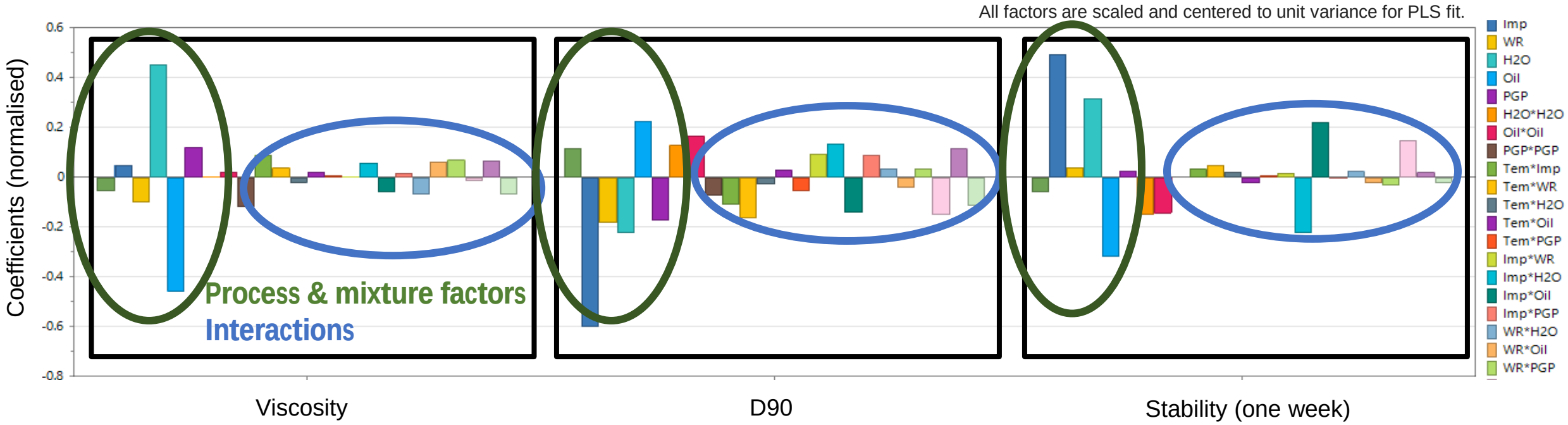
Model system: High internal phase emulsion (HIPE) of water droplets stabilised with polyglyercerol polyricinoleate (PGPR).

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

Confocal images show the variability of the system:

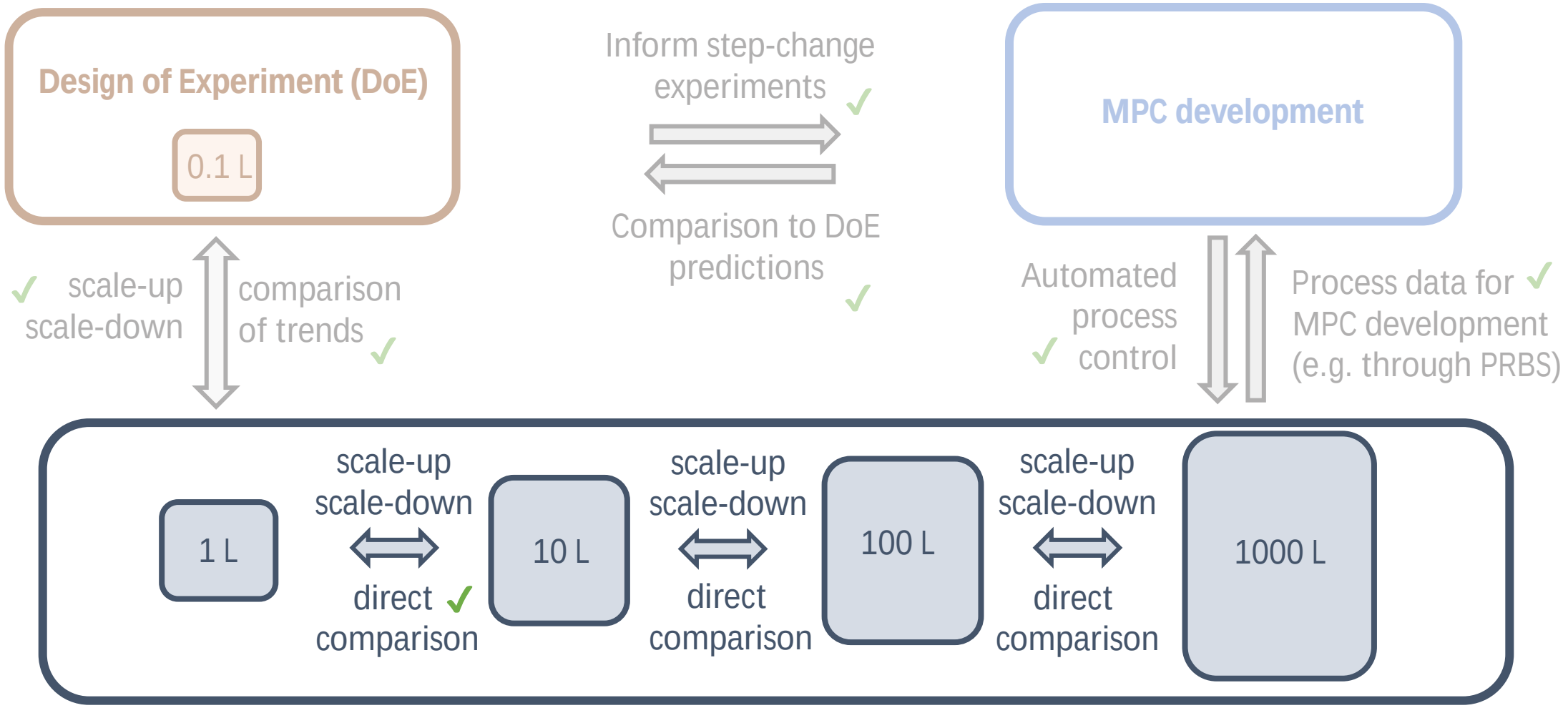


DESIGN OF EXPERIMENT RESULTS

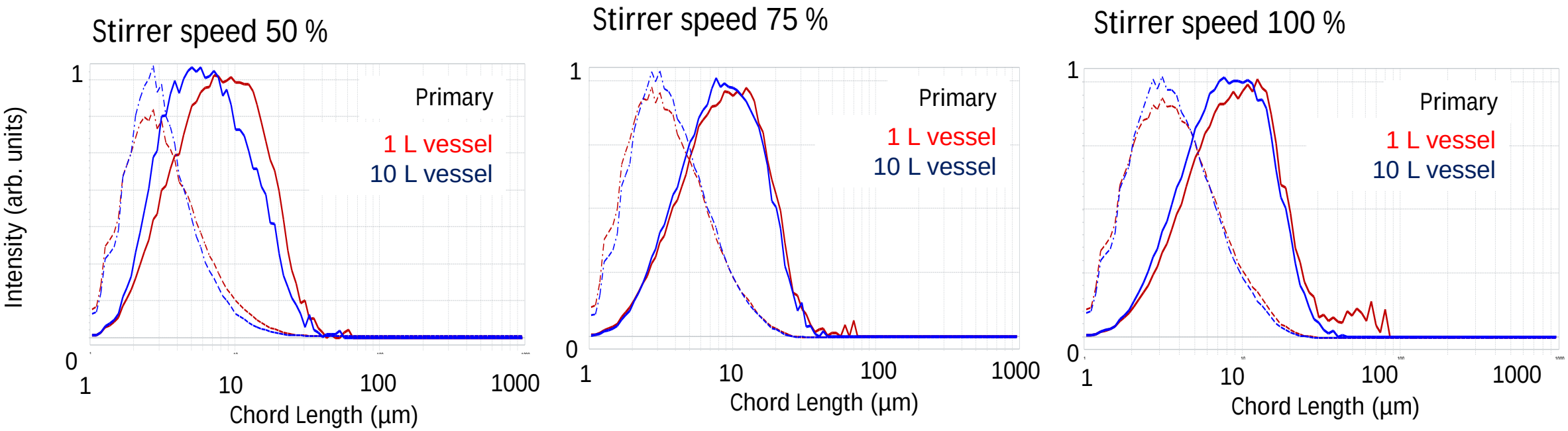


- Main factors stirrer speed, water addition rate, temperature and mixture
- Significant impact of combined factors, e.g. interaction of stirrer speed and oil
  - **This is confirmed by PRBS experiments and model predictive controller (MPC)**
- Other experiments showed that understanding the shape of particle size distribution is crucial for creating a meaningful model – the D90 alone leads to inaccurate predictions
- **Scale-up shows that DOE model seems to be predictive of behaviour on pilot plant scale**

SCALE-UP/SCALE-DOWN APPROACH

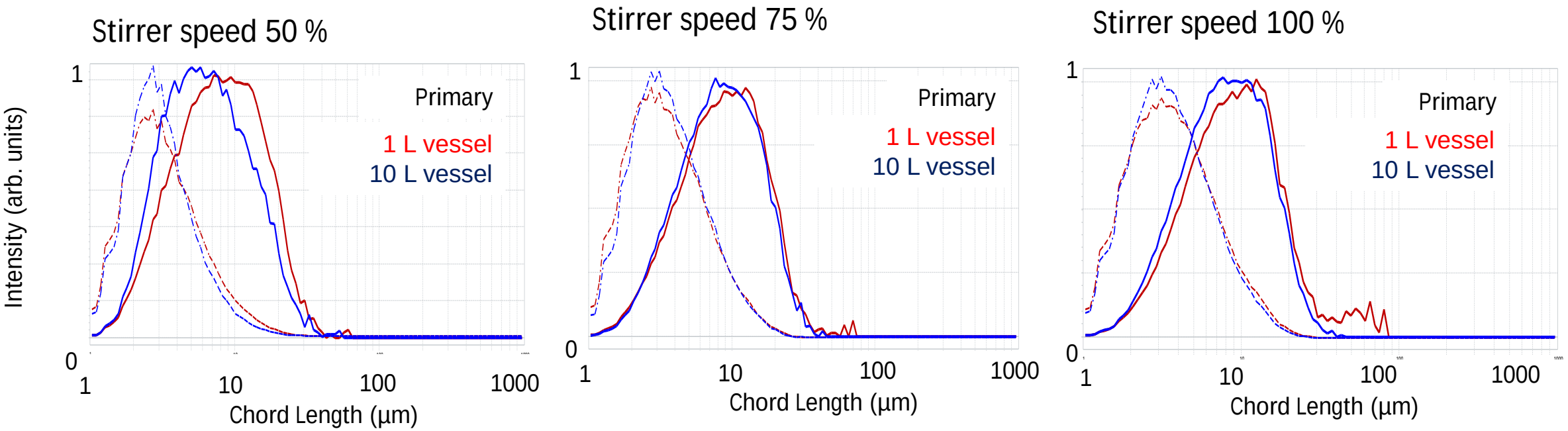


SCALE-UP ON THE PROSPECT CL RIG



Stirrer speeds (rpm)	1 L vessel			10 L vessel		
	1355 (50%)	2033 (75%)	2710 (100%)	675 (50%)	1013 (75%)	1350 (100%)
Percentile c (90) No Wt (µm)	7.34	8.18	8.14	6.41	8.42	8.09
Span (-)	1.92	2.02	1.90	1.62	1.93	1.84

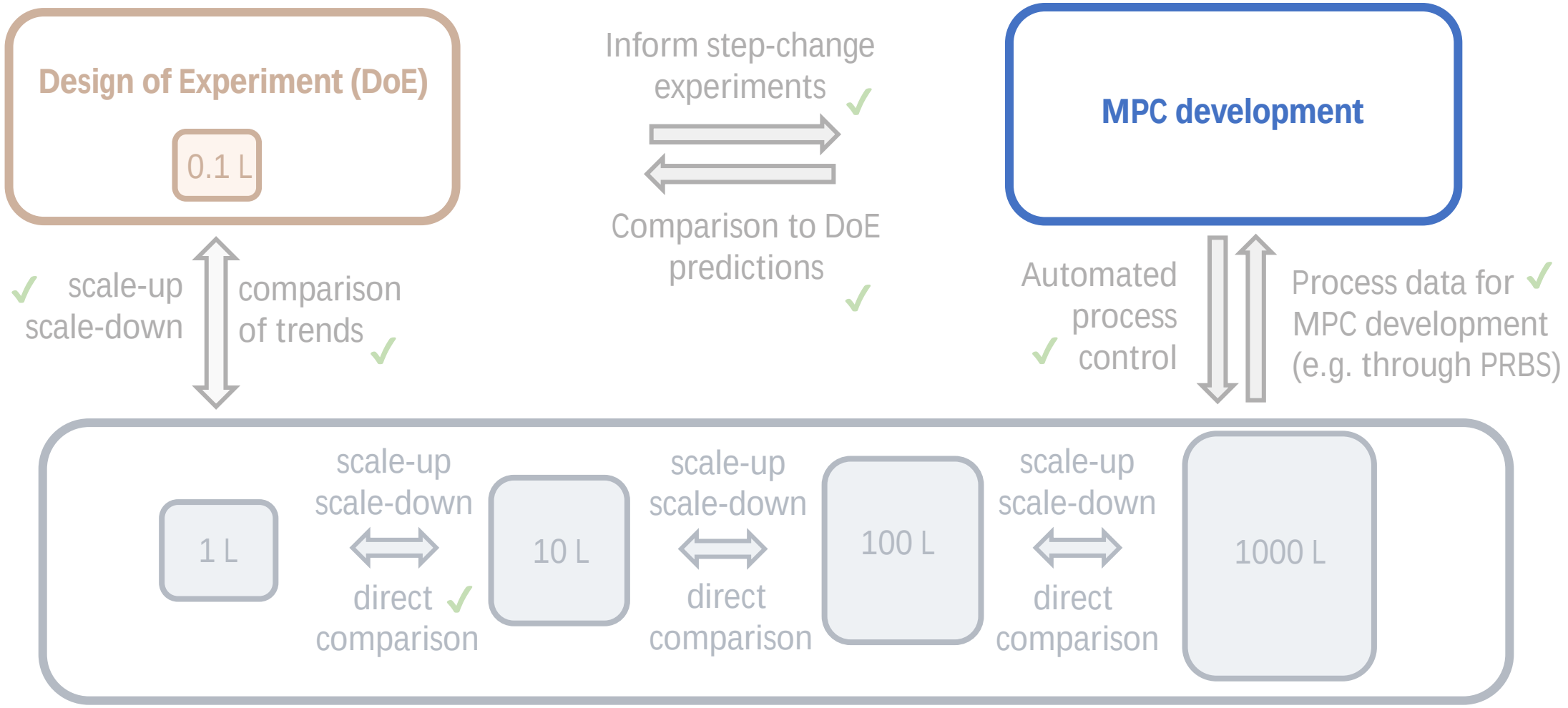
SCALE-UP ON THE PROSPECT CL RIG



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

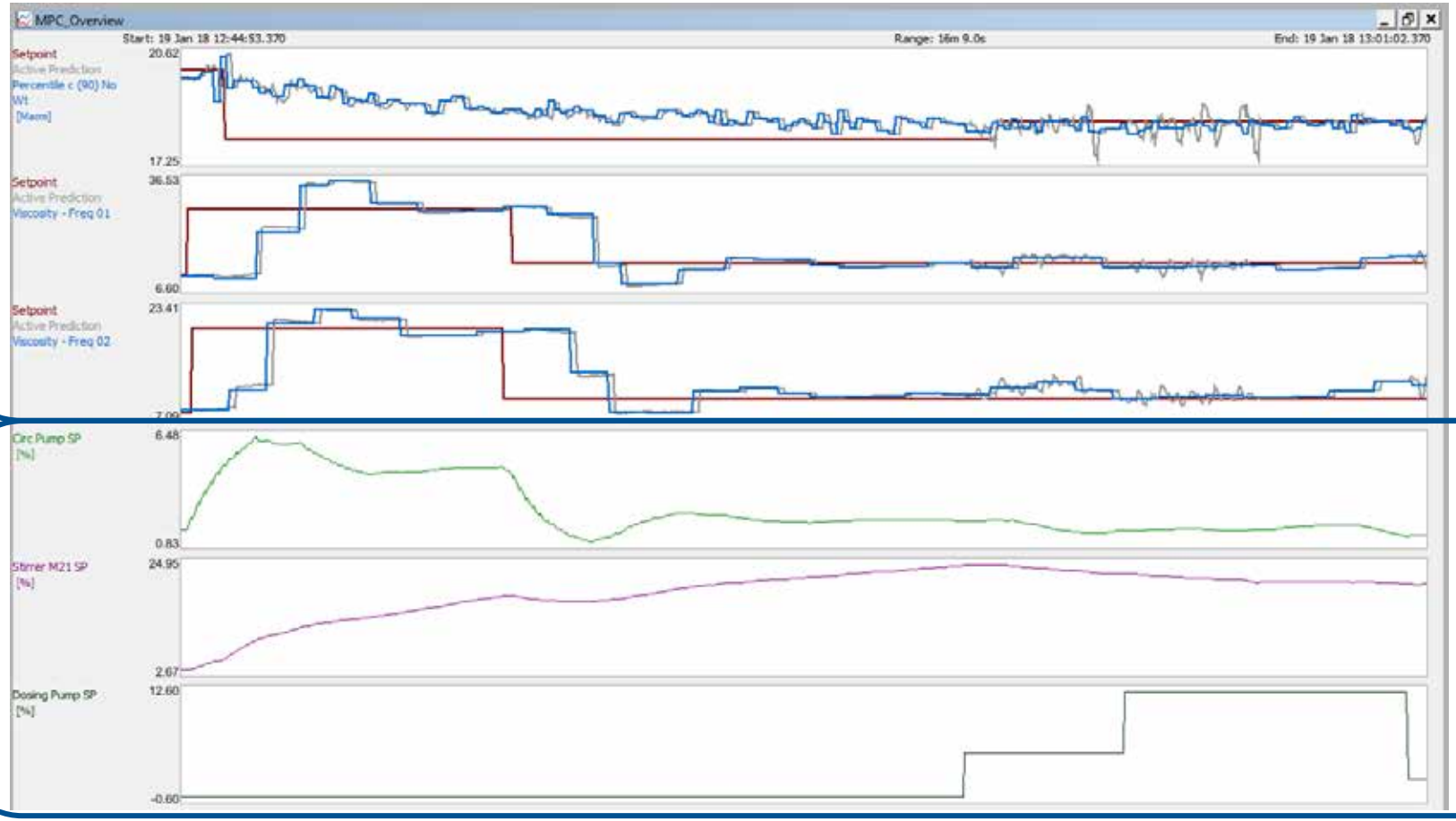
- Control of particle size, viscosity and stability when scaling up/down
- DOE trends can be confirmed on larger scales – more validation experiments to follow

SCALE-UP/SCALE-DOWN APPROACH



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

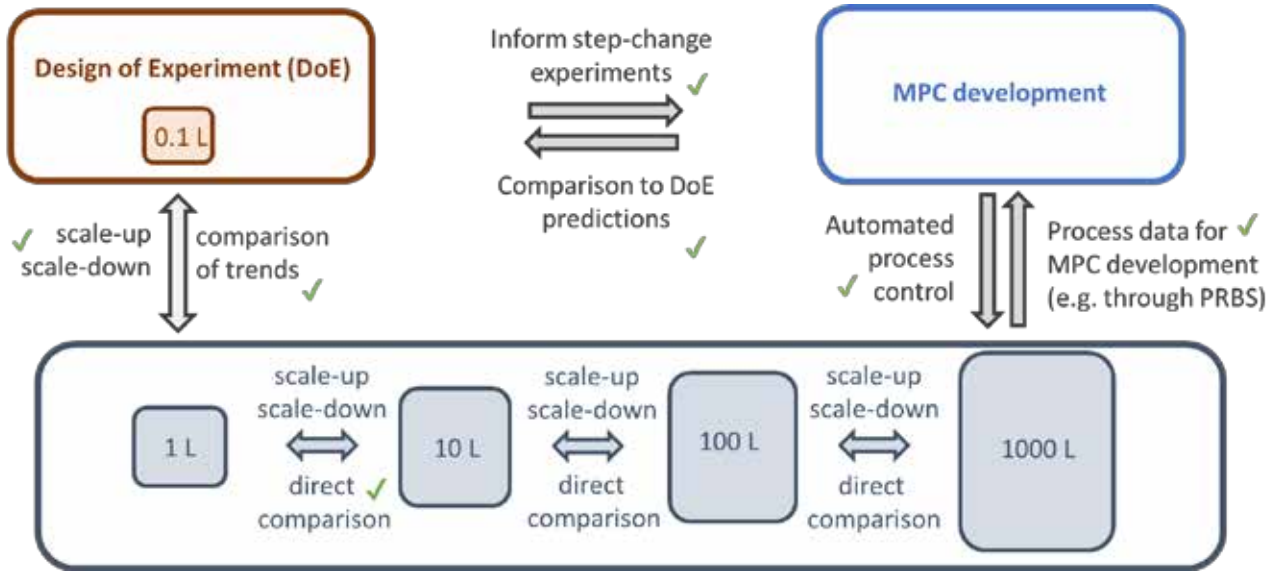
Manipulated variables

(stirrer speed, dosing rate,...)

SUMMARY AND NEXT STEPS

Summary:

- Successful scale-up from 100 mL to 10 L
- Development of MPC for advanced process control
- Qualitative agreement between DoE and MPC



Next steps:

- Quantitative validation of DoE scale-up up to 100 L scale
- Scale-up of MPC through adaptive modelling
- Test predictive scale-up approach on new model system

THANK YOU

for more information

please get in touch...

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