Liquid-liquid mixing facilities for development of model predictive control for industrial scale-up:

PROSPECT CL project

cpi

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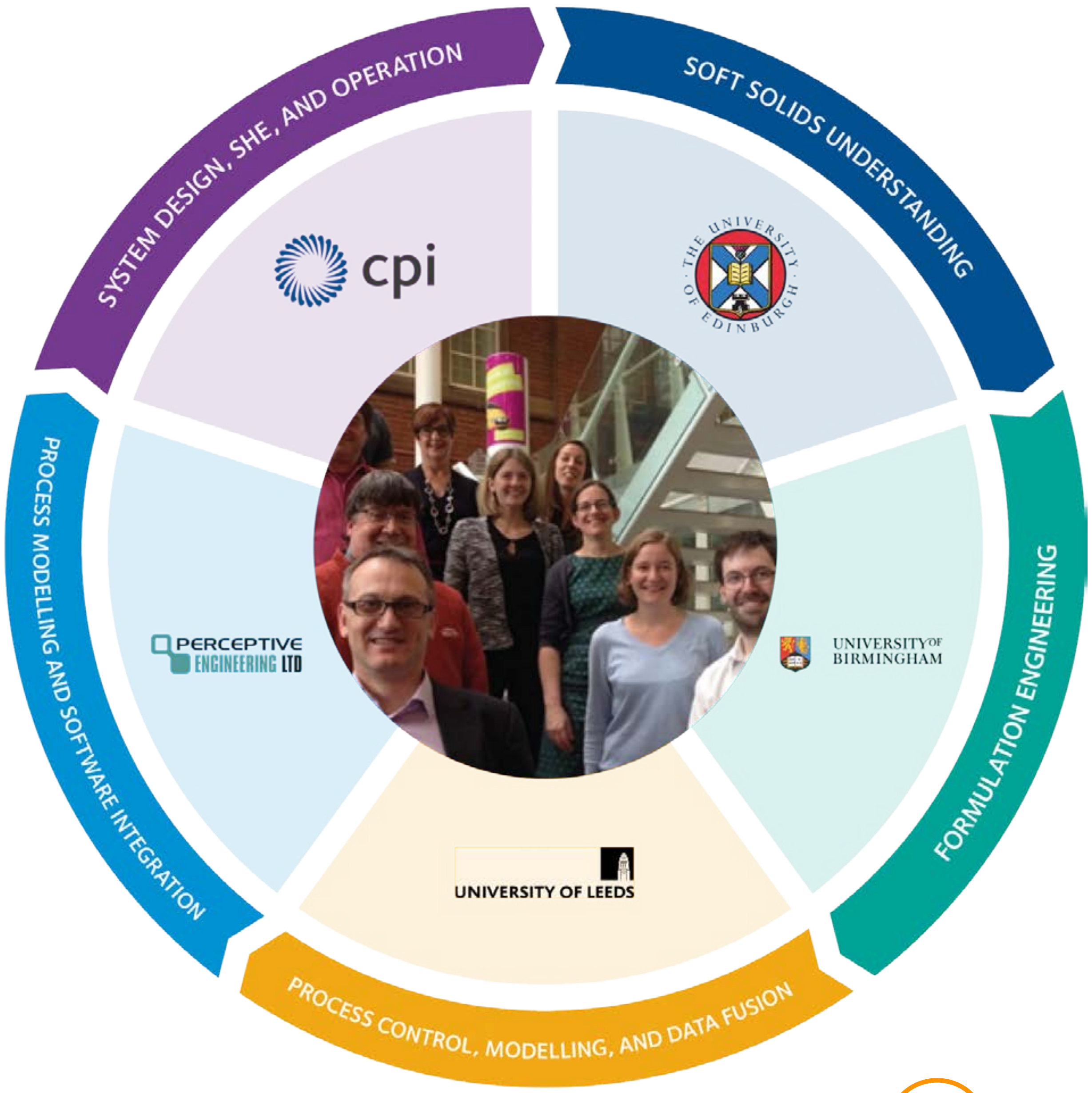
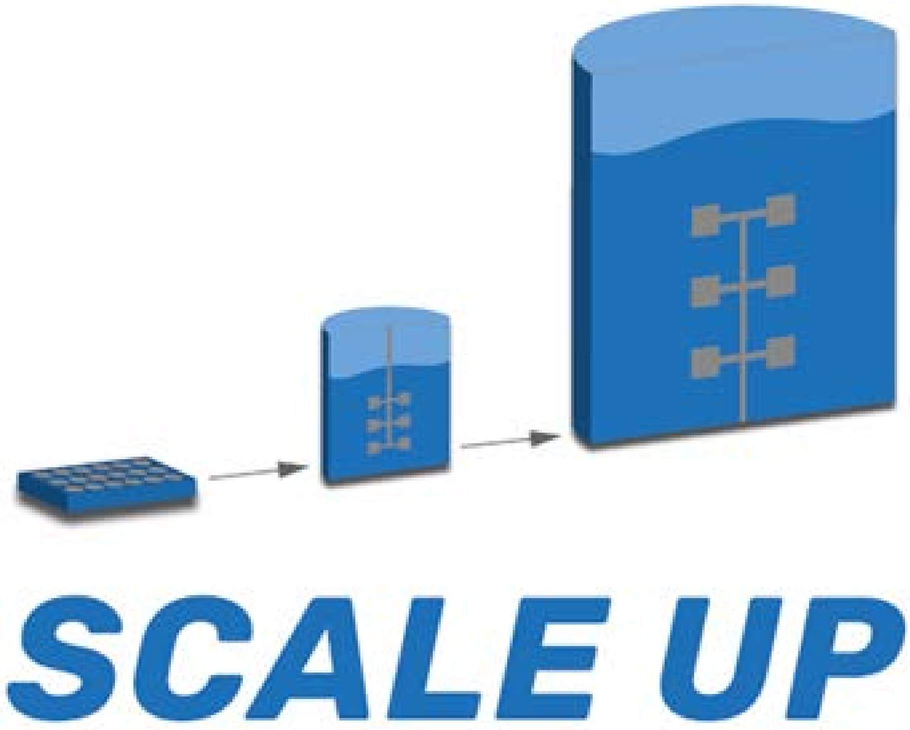


Outline

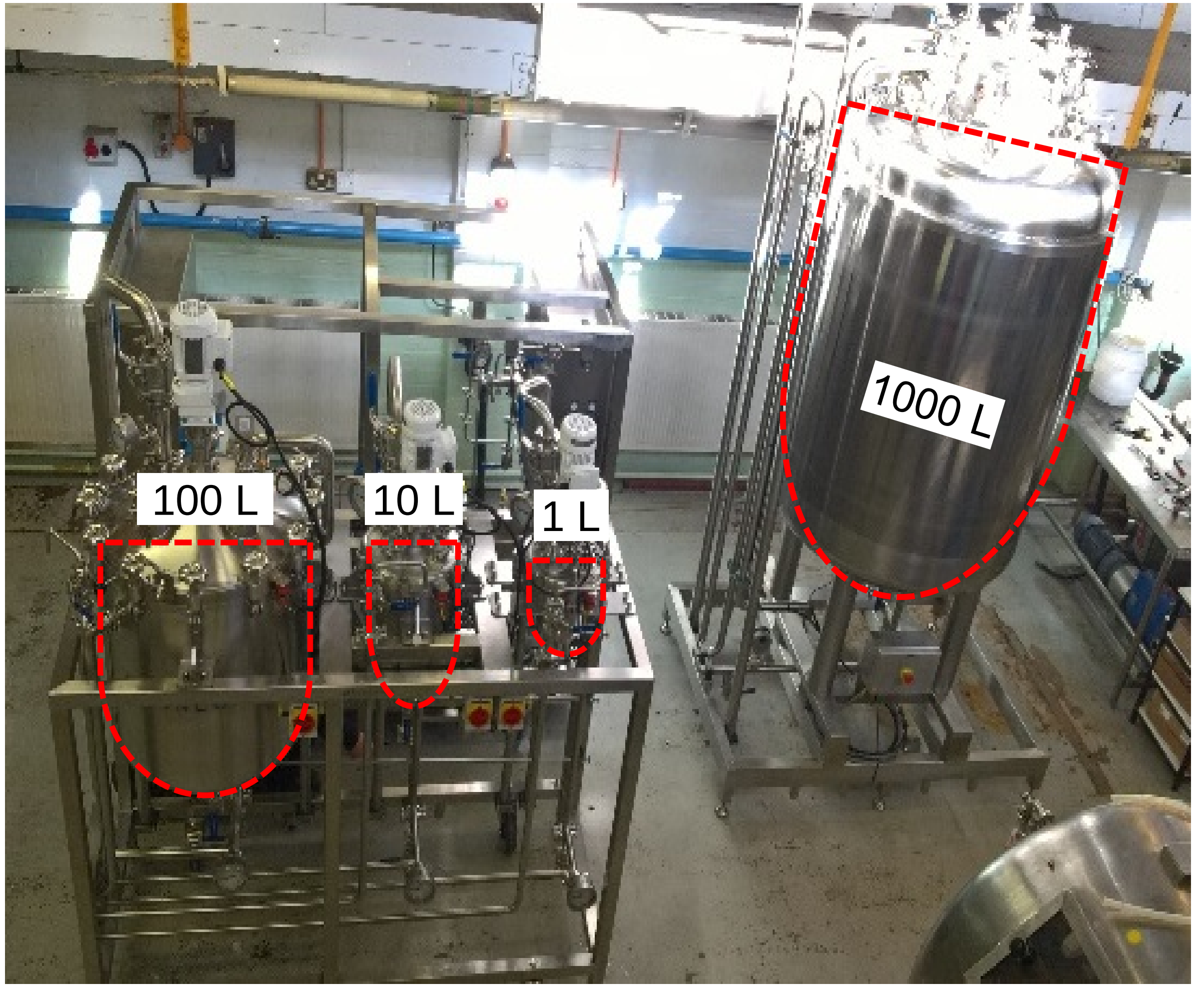
1. Introduction of scale-up rig;
2. Validation and characterisation methodology:
   – In-line measurement validation
   – Characterisation of model formulations/rig behaviours;
3. A successful scale-up case study

- Scale up and manufacturability
- Develop a formulation and get it to market quickly
- Want equipment that will produce the same product on different length scales



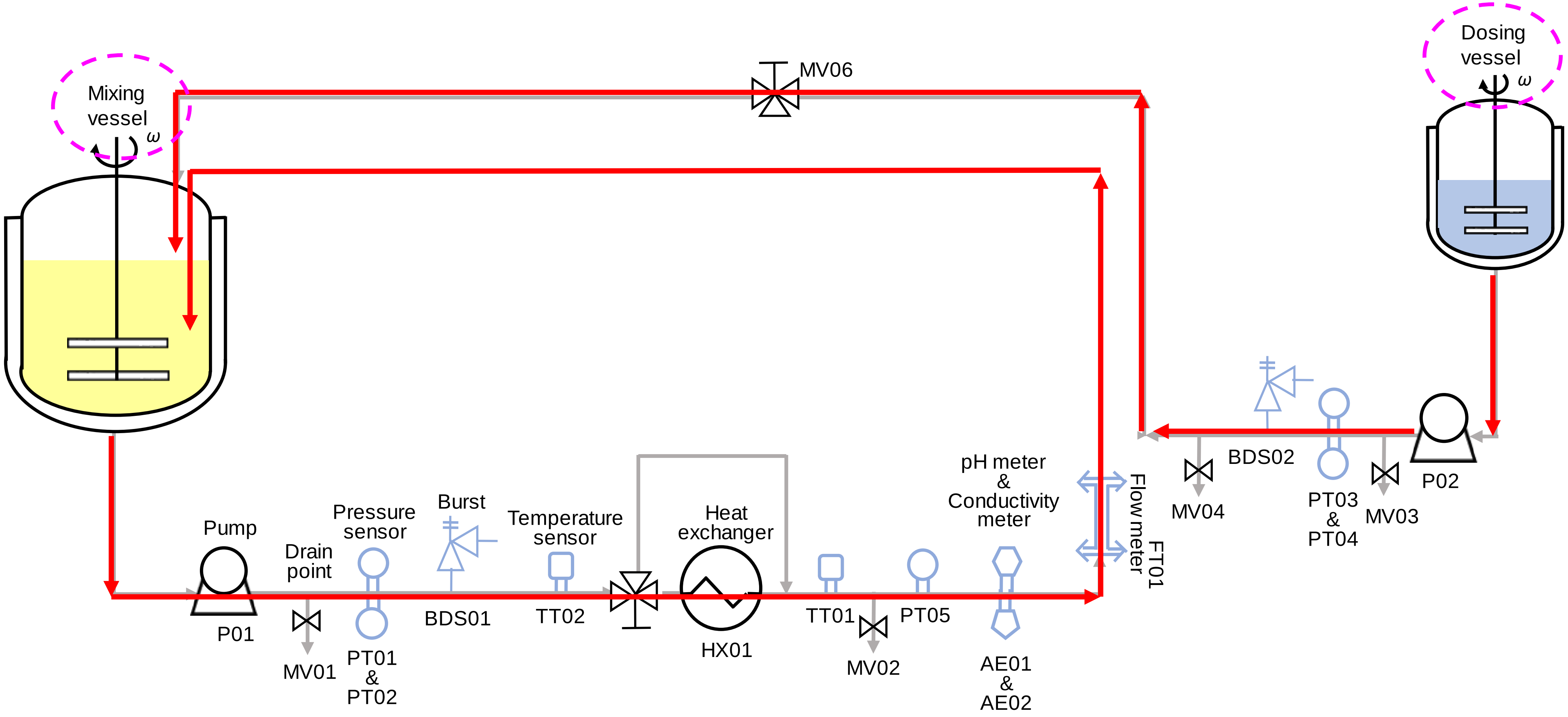
- picture from web

PROSPECT CL – **P**roving of **R**eal-w**O**rld **S**calable **P**r**E**di**C**tive **T**ools /**T**echnologies for **C**omplex **L**iquids

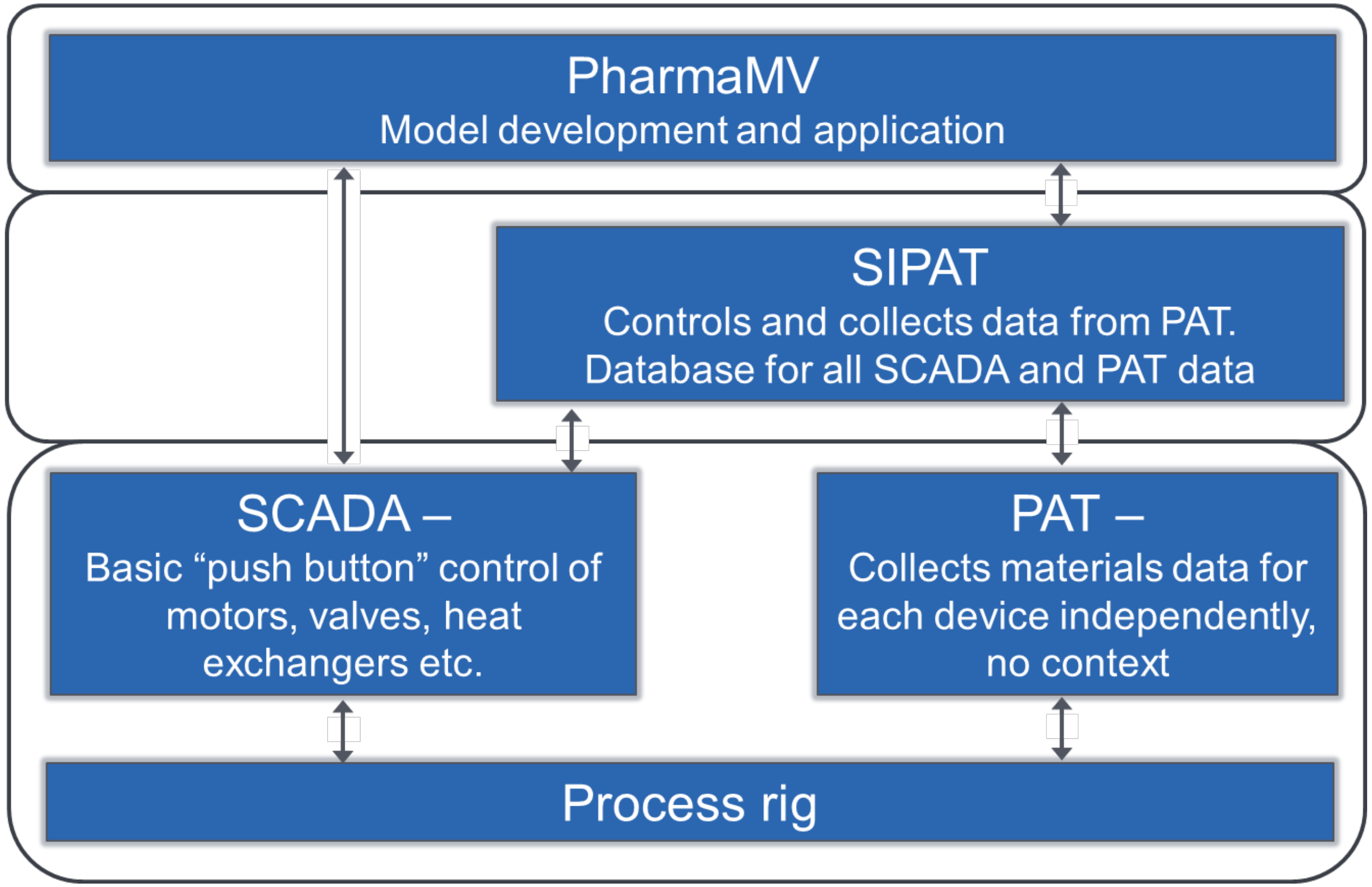


The scale-up rig

Flexible configurations for lab-scale investigation (e.g., 1 L) & industry production (e.g., 1000 L)



The Digital Infrastructure



PROSPECT CL

Phase 1 (@CPI):
before 2017

Procure and build basic kit

→

Phase 2 (@UoB):
2018-2019

Commission, characterisation, understanding of the rig behaviour

→

Phase 3 (@CPI):
2020 –

Deliver and operate rig at CPI

PROSPECT CL – Proving of Real-wOrld Scalable PrEdiCtive Tools /Technologies for Complex Liquids

National Formulation Centre facility: 1, 10, 100, 1000 L vessels and instrumentation

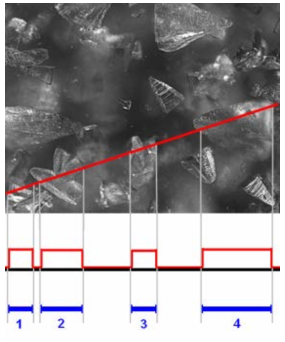
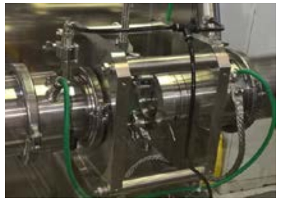
- Complex liquid mixing/processing scale-up loop;
- Representative model formulations;
- Platform to test/validate Process Analytical Technology (PAT) for process monitoring and product quality control use.

The flow rig – processing parameters

- High shear mixers
- Jacket heating
- Temperature range 4-90 °C
- Powerful pump for high viscosity loop

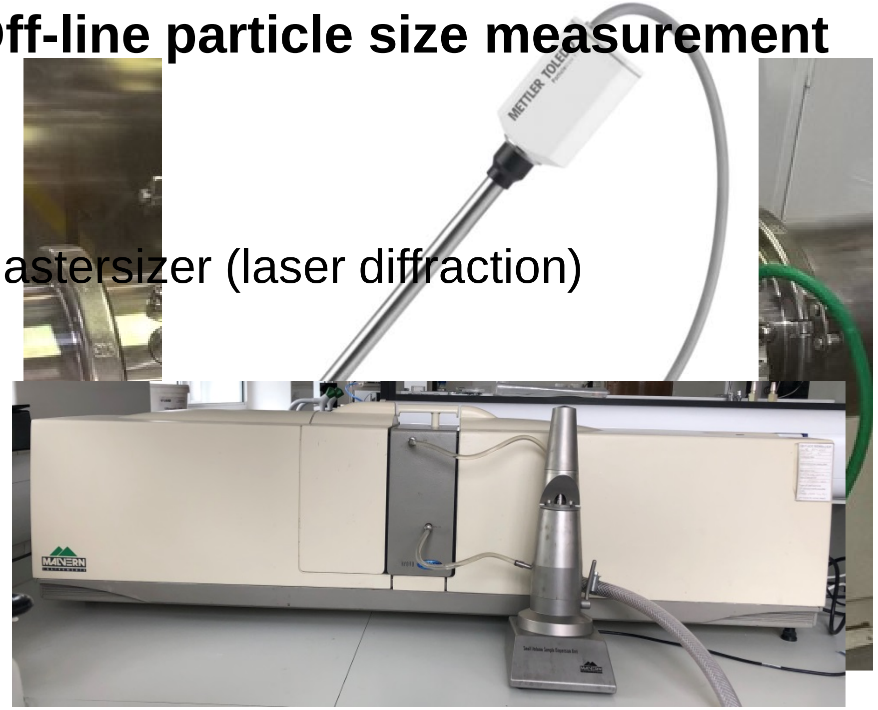
	Limits
T_{min} (°C)	4
T_{max} (°C)	90
1 L mixer speed (rpm)	5700
Max. 10 L mixer speed (rpm)	5700
Max. 100 L mixer speed (rpm)	5700
Max. 1000 L mixer speed (rpm)	250 (3000 after 03/2020)
Recirculation max flow (L/min)	9.4
Dosing max flow (L/min)	8.9

Process Analytical Technology (and off-line measurements)

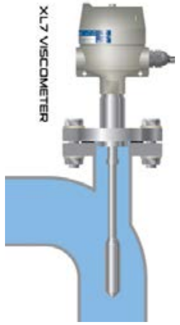
Particle characterisation		
ParticleView	Real-time microscopy for emulsification, crystallization, suspensions, *etc.*	
Focused Beam Reflectance Measurement (FBRM®)	In-process particle size measurement for emulsification, dissolution, disintegration, *etc*.	
Insitec	Real-time monitoring and control; of particle sizes in emulsions, suspensions and slurries.	

Off-line particle size measurement

Mastersizer (laser diffraction)



Process Analytical Technology (and off-line measurements)

In-line viscosity measurement		
RheoJet	High accuracy and robustnesss; instant feedback for real-time process optimisation and continuous product control	

Off-line rheology behaviour characterisation

TA instrument rheometer

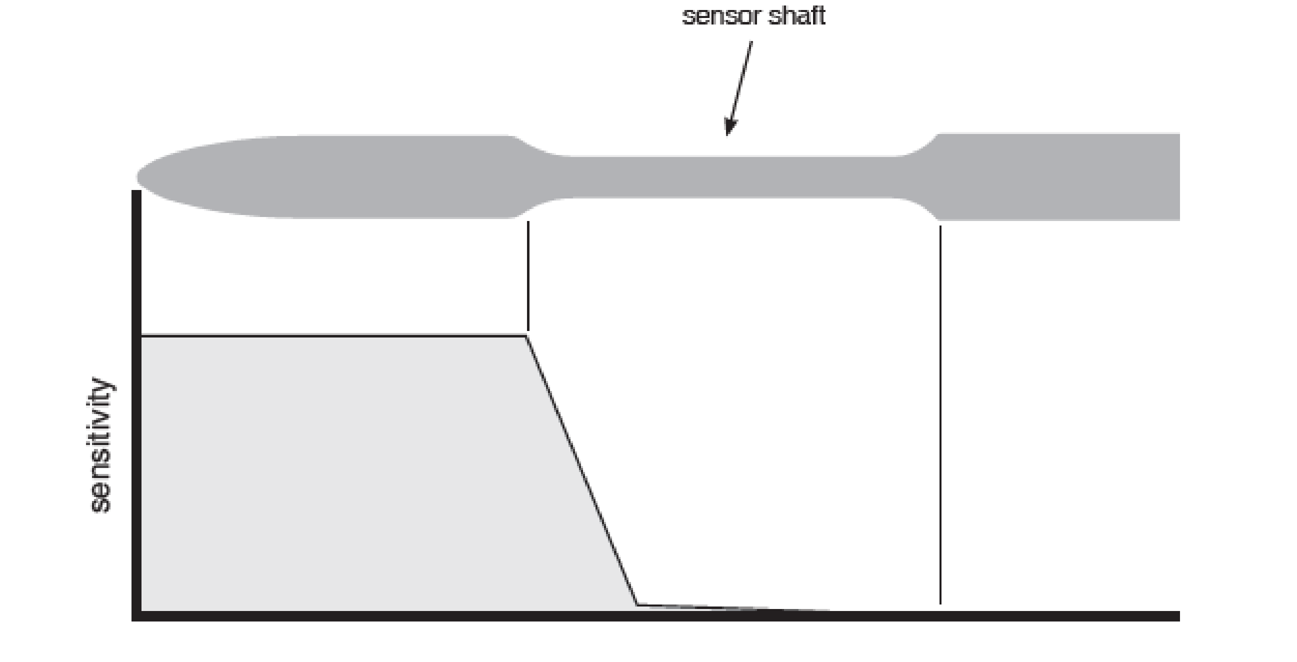
In-line measurement validation

Validation of Hydramotion Rheojet – In-line viscometer

From User Manual

- Orientation independent
- Fluid depth sufficient to cover bob

Figure 2. *Sensitivity profile of the sensor element*



Previous Adapter

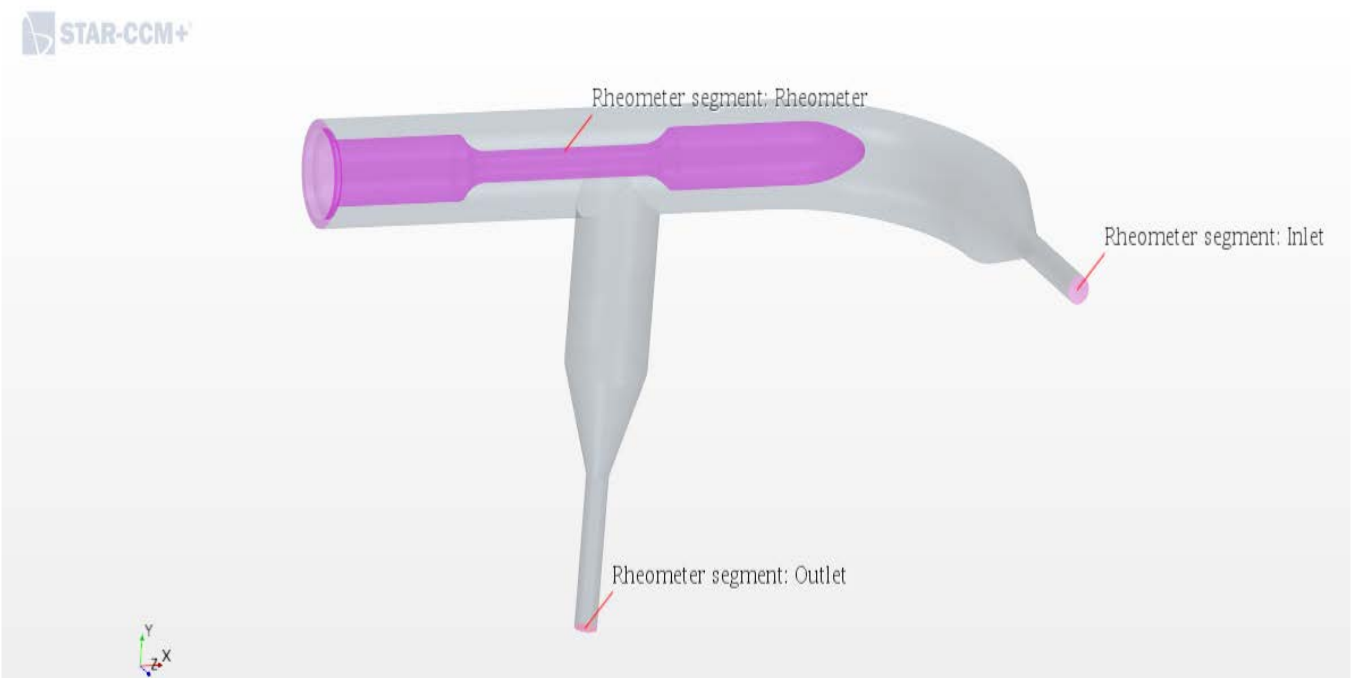
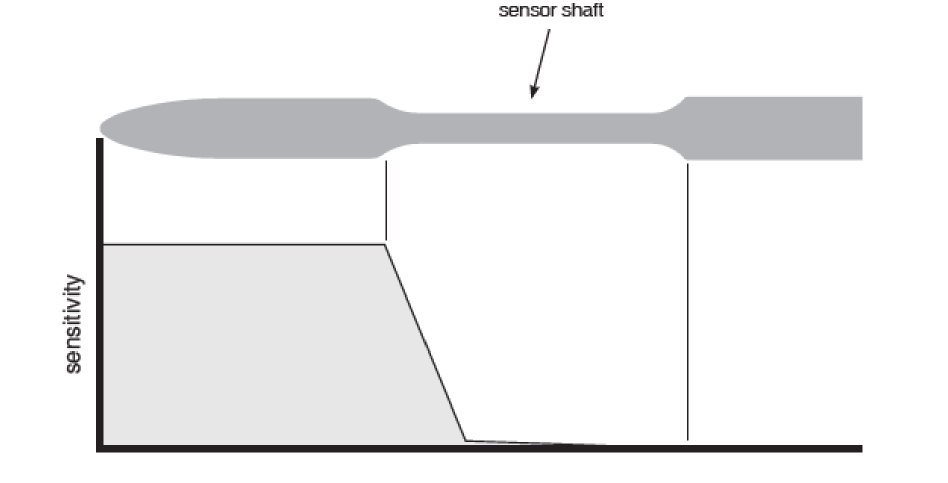
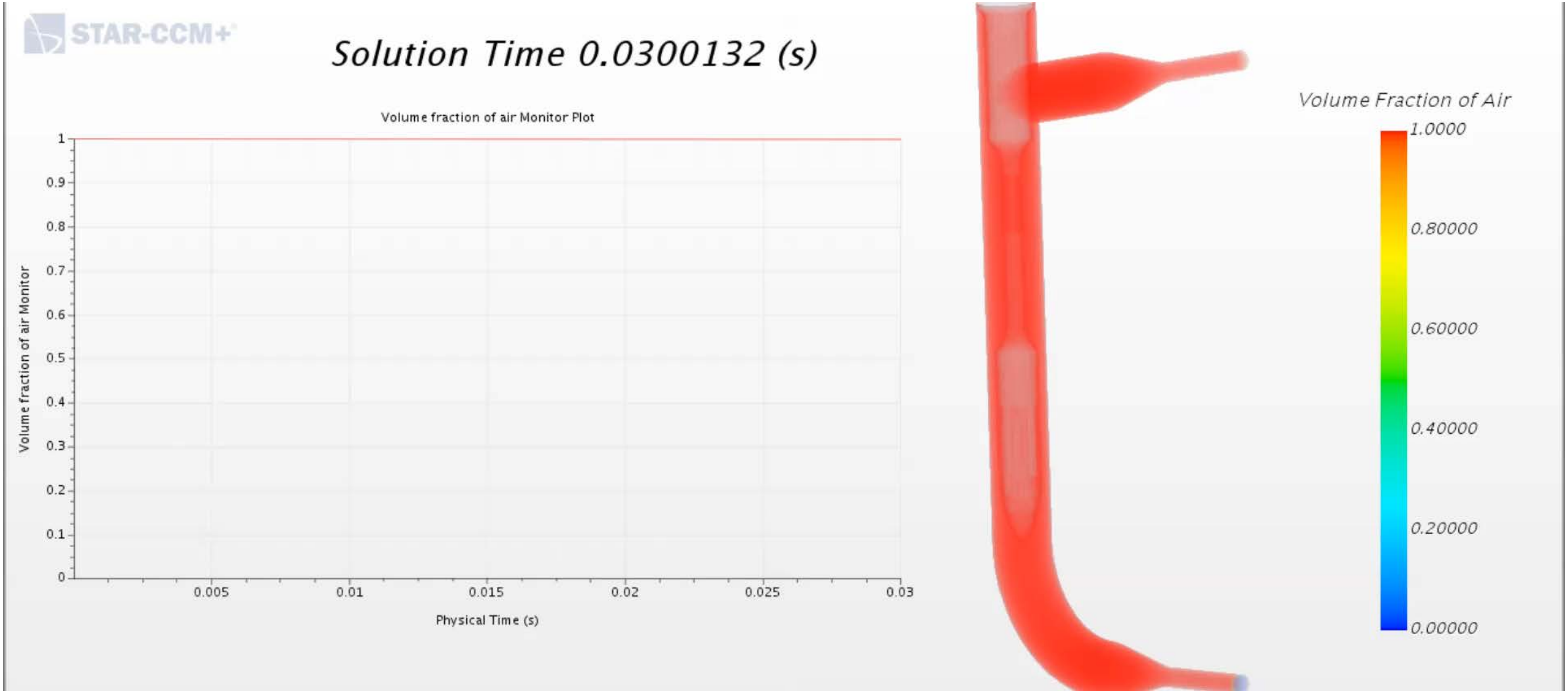


Figure 2. *Sensitivity profile of the sensor element*

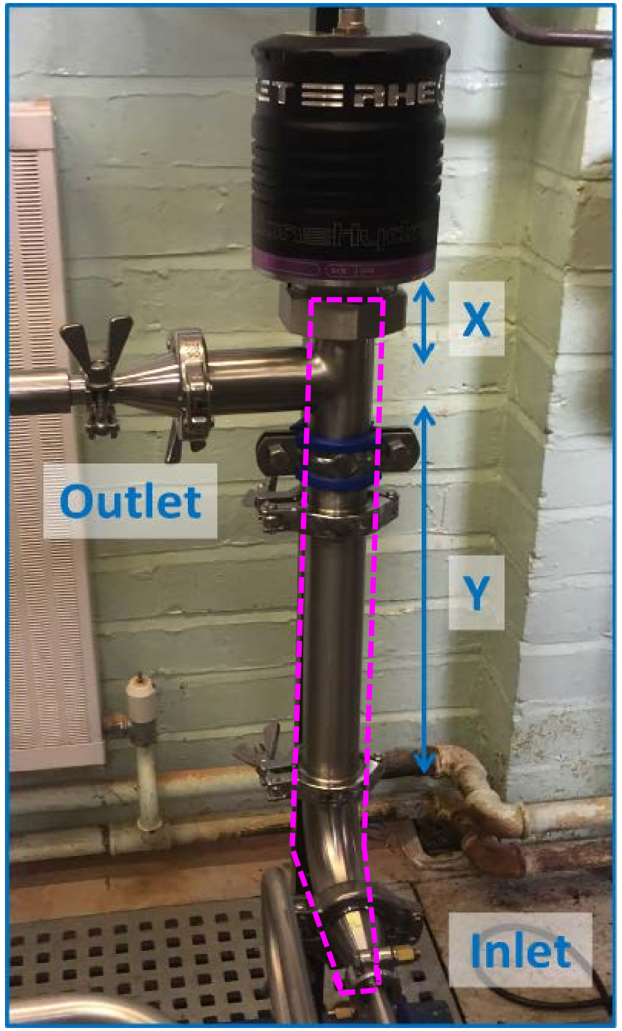


- CFD calculations- ascertain how fluid flow pattern changes with adapter geometry
- Modelling transient fluid velocity and change in volume fraction of fluid

RheoJet validation – CFD New Adapter

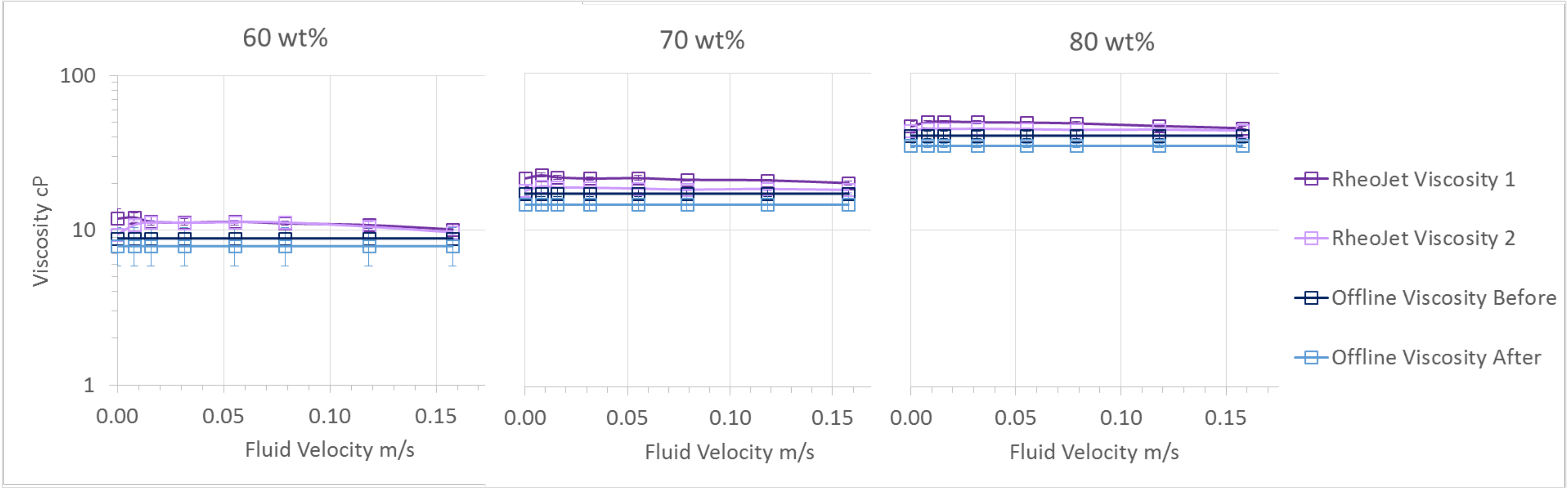


RheoJet validation – New Adapter



- Installation & commissioning of new adapter on current flow loop
- Prepare glycerol & water solutions of known concentrations
- Record measurements with RheoJet in loop at set pump speeds (increasing from 5%)
- Take sample for offline rheology tests
- Compare results to literature values & offline readings.

RheoJet validation – Glycerol solutions



- Similar readings between in-line RheoJet and offline rheometer – reasonable error
- Viscosity independent of fluid velocity / pump speed– Newtonian fluid
- Viscometer does a relative viscosity measurements whereas offline rheometer gives apparent viscosity values across a range of shear rates

RheoJet validation

Summary:

- Adapter issues - presence of air bubbles and preferential flow along one side of the sensor
- Effect of adapter geometries using CFD
- New adapter - reliable and repeatable results given for Newtonian fluids

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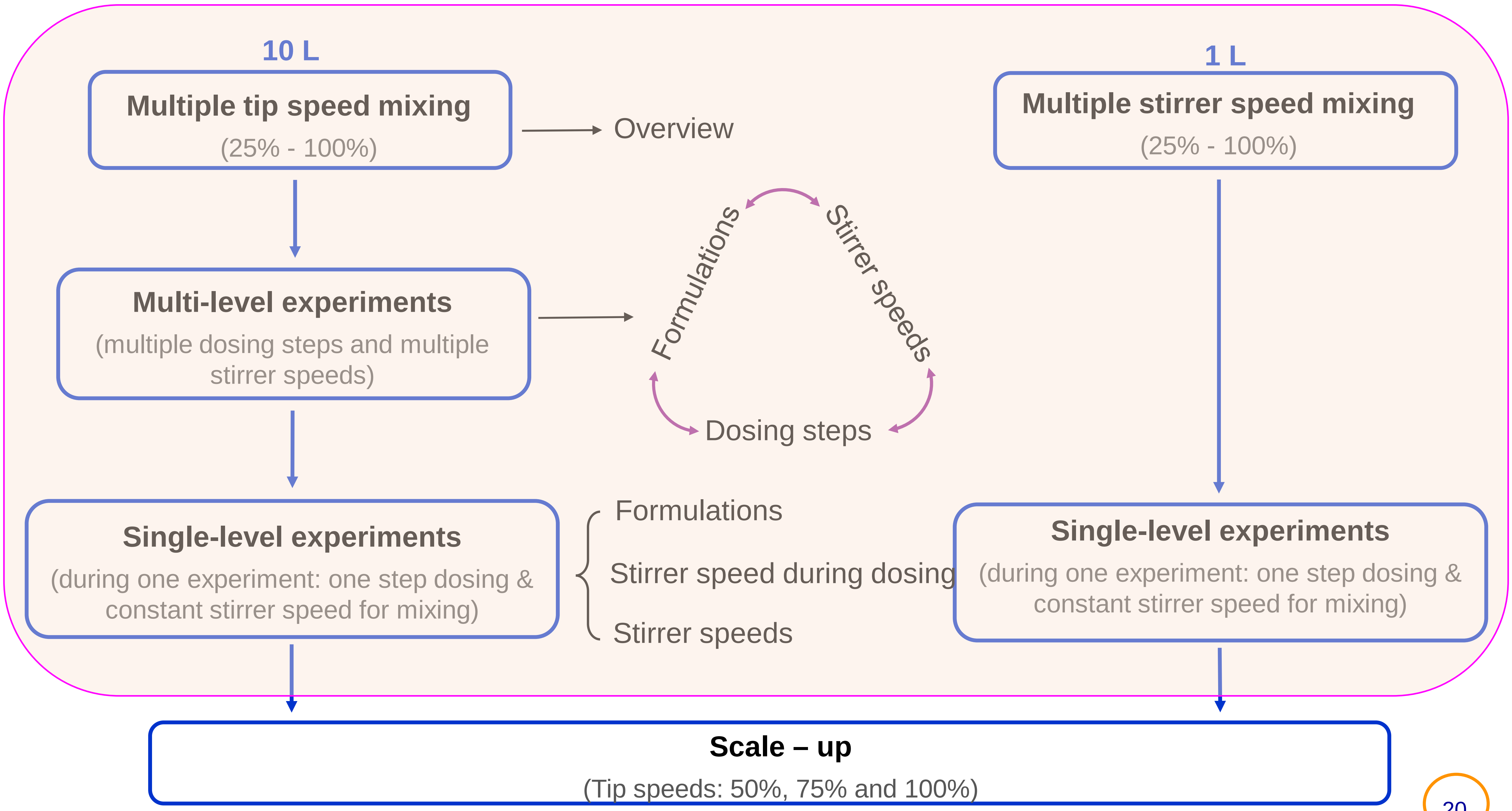
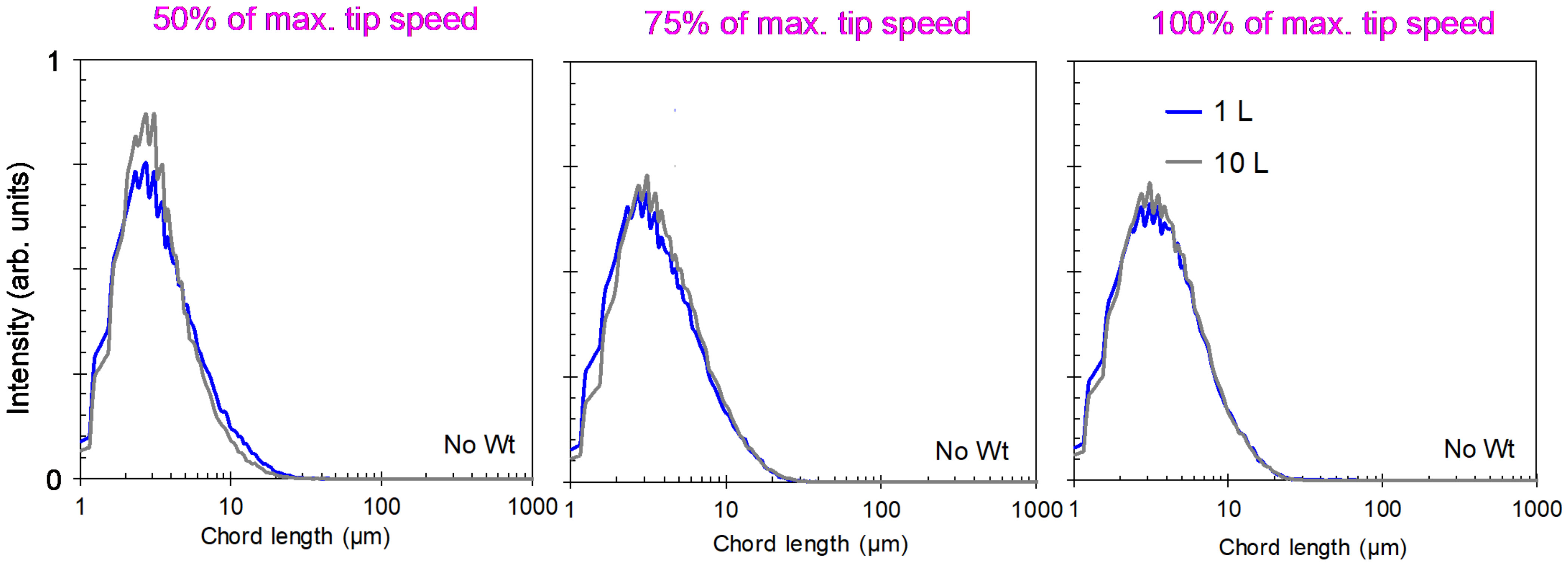
Development of an experiment methodology for scale-up


10 L
Multiple tip speed mixing
(25% - 100%)
Overview
1 L
Multiple stirrer speed mixing
(25% - 100%)
Multi-level experiments
(multiple dosing steps and multiple stirrer speeds)
Formulations
Stirrer speeds
Dosing steps
Single-level experiments
(during one experiment: one step dosing & constant stirrer speed for mixing)
Formulations
Stirrer speed during dosing
Stirrer speeds
Single-level experiments
(during one experiment: one step dosing & constant stirrer speed for mixing)
Scale – up
(Tip speeds: 50%, 75% and 100%)

1 L *vs* 10 L

Scale – up

(Tip speeds: 50%, 75% and 100%)



Model formulation:

- 54.5% of Vegetable oil
- 44.6% of water
- 0.9% of PGPR (emulsifier)
  - polyglycerol polyricinoleate (PGPR)

Tip speed (%)	1 L vessel			10 L vessel		
	50	75	100	50	75	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

Summary and future work

1. Rig has been commissioned and tested with different model formulations;

2. A methodology for characterisation of an emulsion model and identification of operation window has been developed;

3. 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
   - MPC for advanced process control will be developed based on experimental data

4. Transfer to CPI Jan – March 2020.

Acknowledgments

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