Complex ORAL health products (CORAL)
Characterisation, modelling and manufacturing challenges

P. Angeli, W. Weheliye, S. Migliozzi

EPSRC funded project on
Future Formulation for Complex Products
£2M over 4 years

Team

Chemical Engineering

Panagiota Angeli: Two-phase flows, mixing, intensified processing, laser based flow diagnostics (PIV, LIF)

Luca Mazzei: Two-phase flows, particulate systems, CFD, numerical modelling

Mechanical Engineering

Stavroula Balabani: experimental fluid mechanics, particle suspensions, RheoPiv, optical shearing, microstructure interactions

Manish Tiwari: nanotechnology, rheology, AFM

Mathematics

Helen Wilson: rheology, non-Newtonian fluids, mathematical analysis

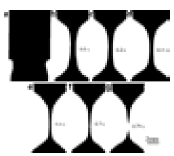
5 PDRAs and 4 PhD students

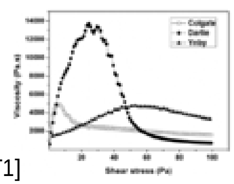
Methodology

UCL

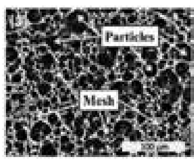
Characterisation

WP1. Characterize the local and bulk rheological properties of oral product formulation mixtures





Self-thinning[MKT1]



Toothpaste viscosity & microstructure (Liu et al, K-A Rheo J., 27, 2015)

Prediction

WP2. Mathematical modelling to derive constitutive equations

$$\mu = \frac{\tau_y}{\dot{\gamma}} + k|\dot{\gamma}|^{n-1}$$

WP 3. Formulate a continuum description of the flows of such mixtures

[www.pharmaceuticalonline.com]

Scale up & Manufacturing

WP 4. Understand scale up issues & Develop continuous manufacturing processes

[www.comsol.com]

mm to mm | cm | m

CORAL: A multidisciplinary, multiscale approach to oral care formulation challenges

Current Progress

Small scale studies

- Rheological characterisation of particle suspensions in Newtonian media
- Studies of interparticle forces using AFM

CFD modelling

- Implementing the mixture approach for suspensions of spherical particles in Newtonian fluids
- Validation of model against control experiments
- Expand model to non-Newtonian systems using experimental rheology data

Manufacturing approaches

-Mixing of viscous fluids with non-Newtonian properties.
-Addition of solids

To aid detailed flow field and mixing experiments in some cases matching refractive index solids are used.

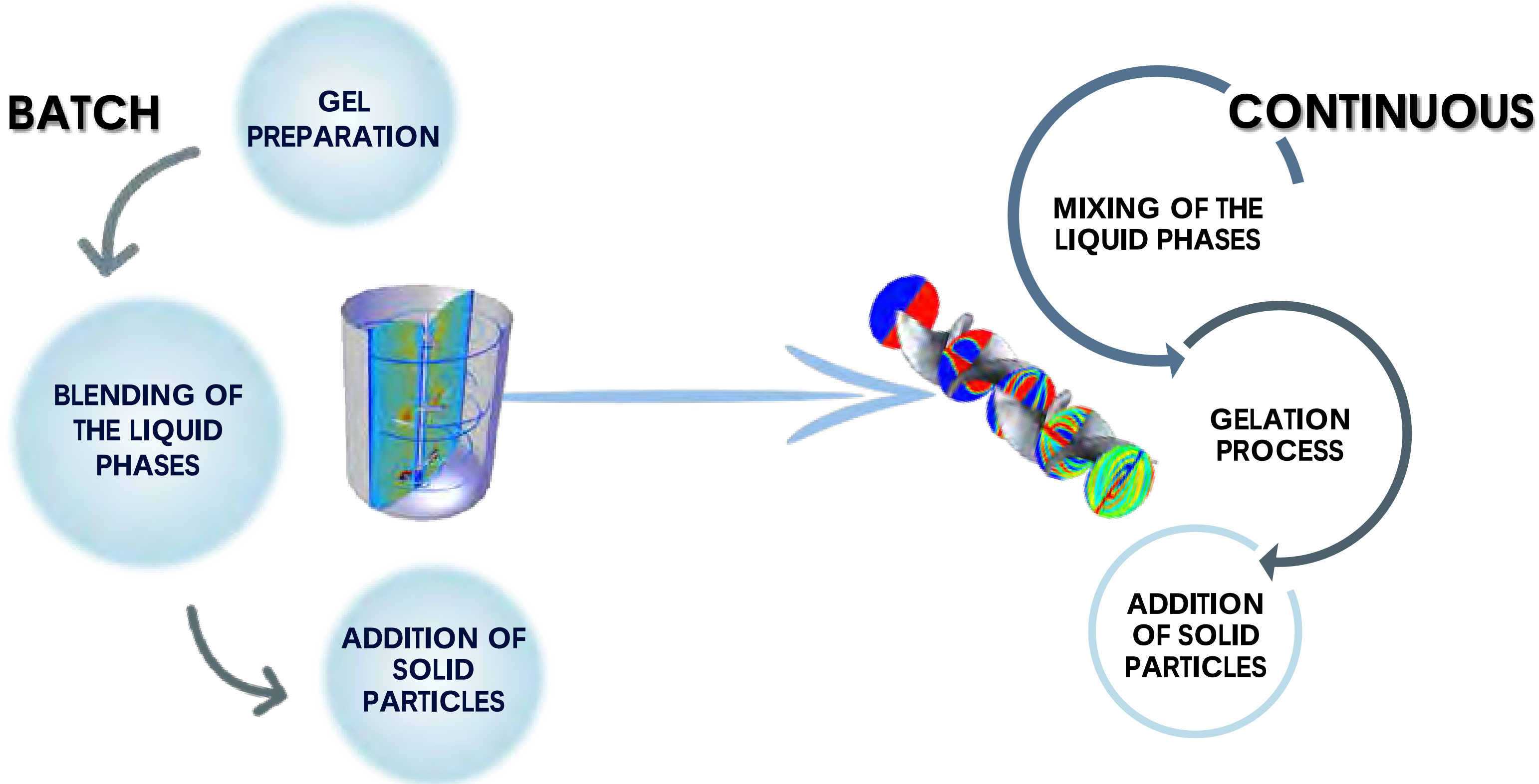
- Batch mixing in a stirred tank – Dr W Weheliye

Glycerol + high viscosity gel
Solids addition

- Continuous mixing in a static mixer – S Migliozzi

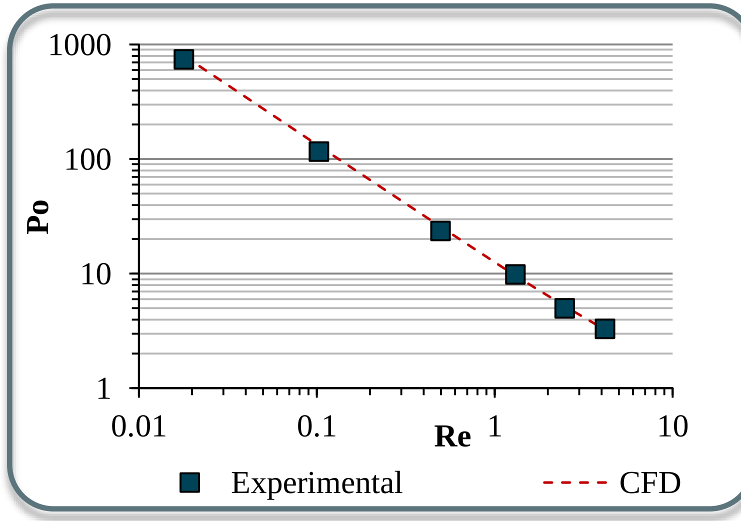
Glycerol + polymer suspension (before gelation) – low viscosity mixing
Gelation
Solids addition

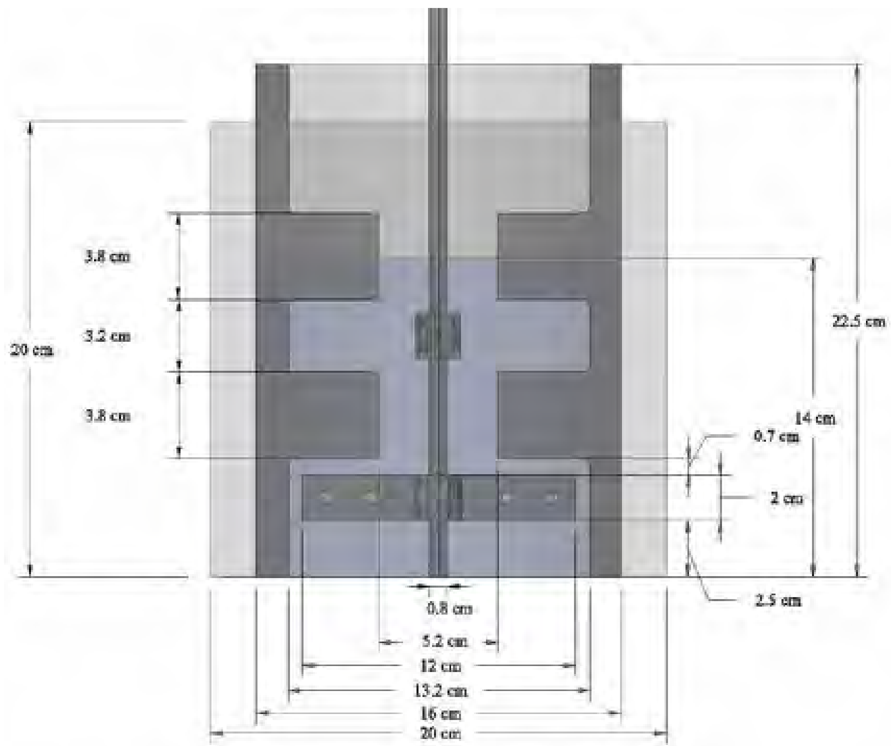
Manufacturing approaches

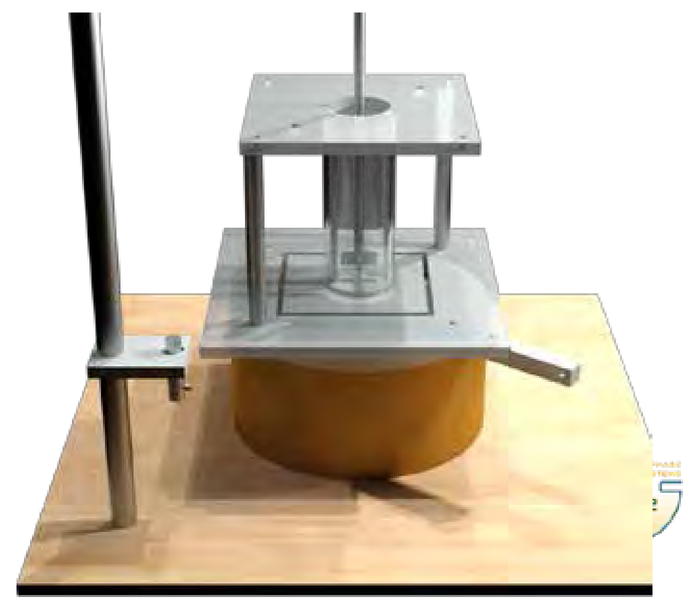


Batch mixing of non-Newtonian fluids

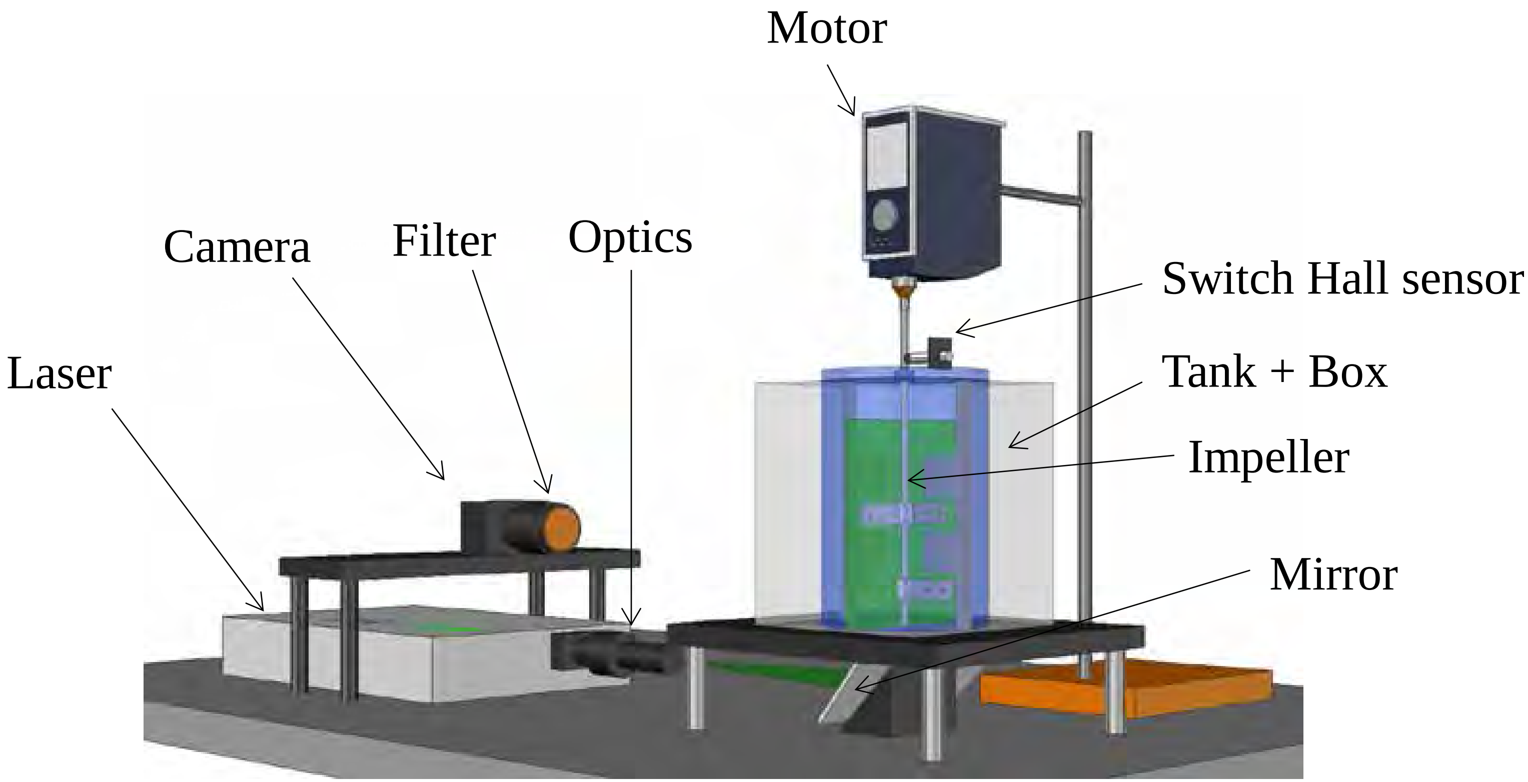
- Study the mixing of gel/glycerol in a mixing tank “similar” to the pilot plant scale
  - Velocity profiles (Hydrodynamics)
  - Mixing time
  - Validation







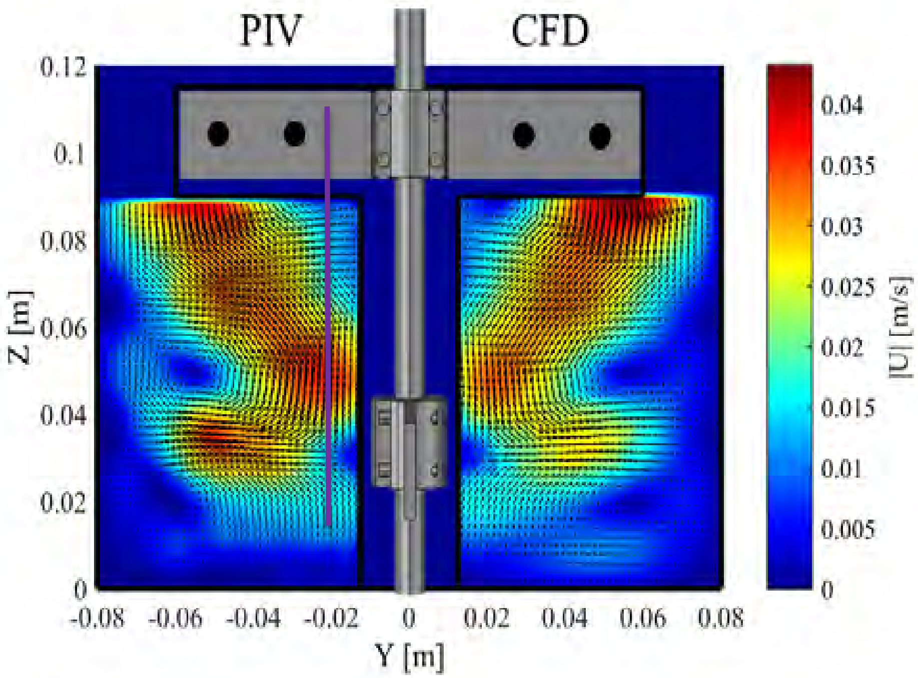
Velocity profile measurements - Particle Image Velocimetry (PIV)

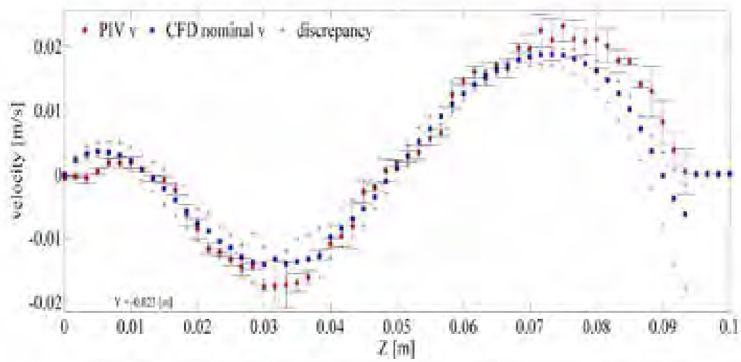


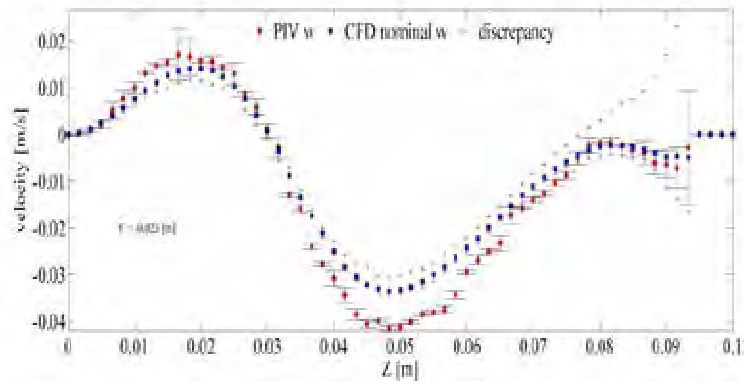
- Fluids: gel and glycerol
- Polymer particles coated with Rhodamine 6G

Batch mixing of non-Newtonian fluids

r = -0.023 m



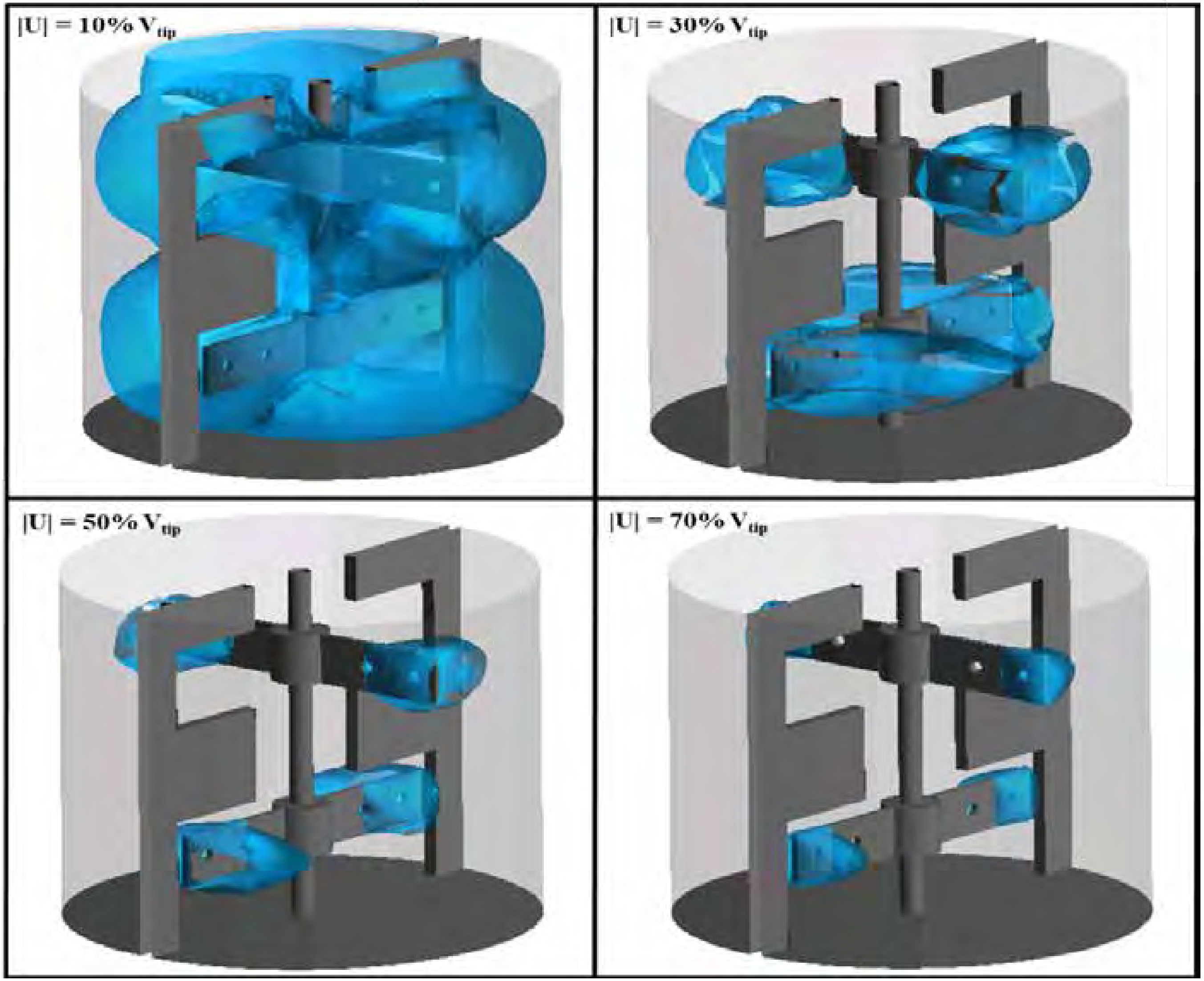




r = -0.023 m

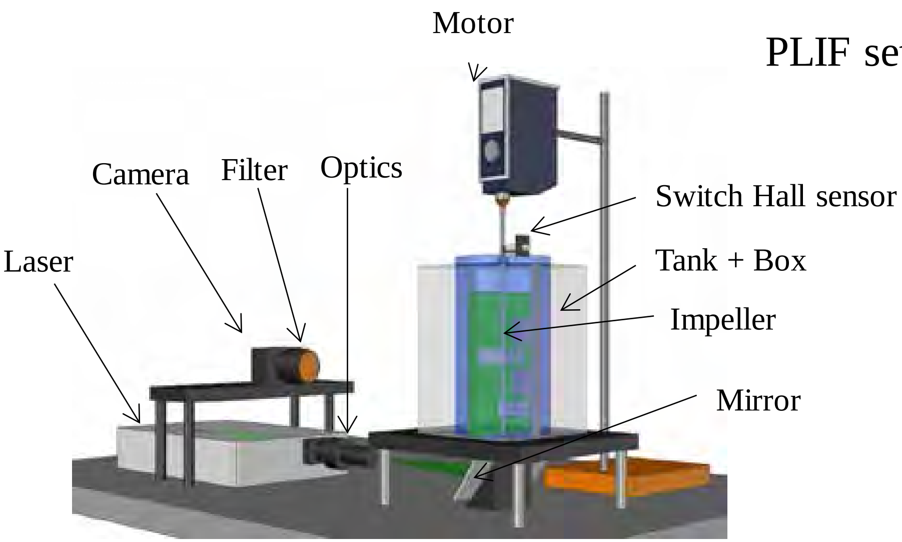
Gel 5%, 40 rpm, 49ºC ± 1ºC

Batch mixing of non-Newtonian fluids

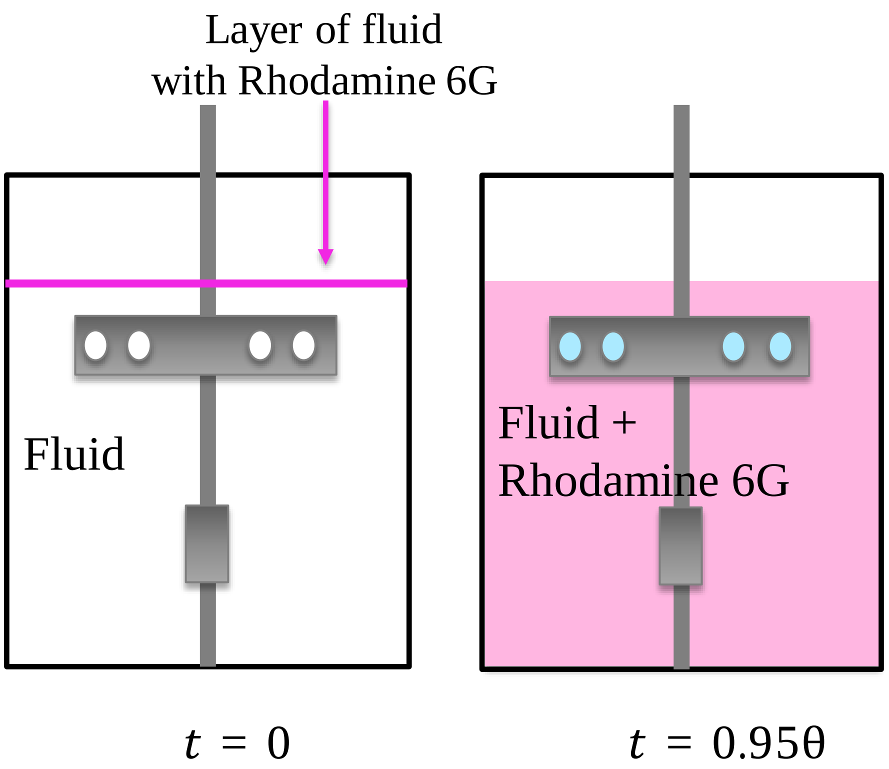


Batch mixing of non-Newtonian fluids

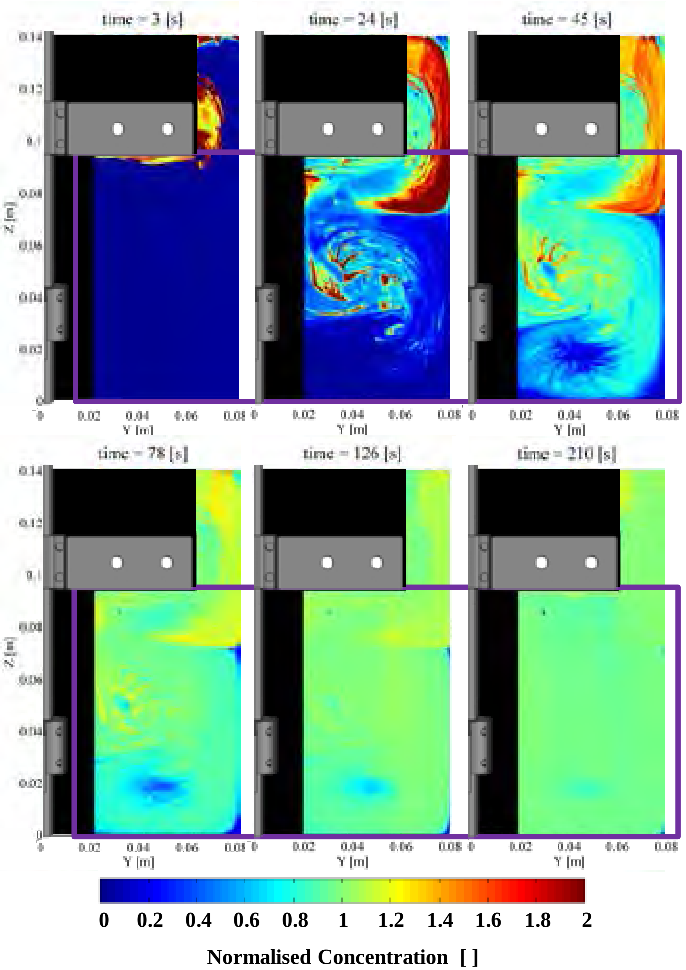
- Fluids: gel and glycerol
- Tracer: Rhodamine 6G



PLIF setup

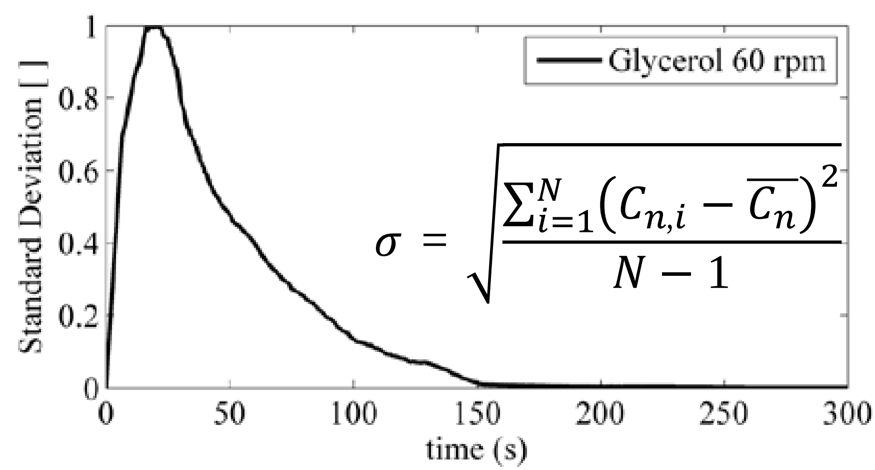


Mixing time – experiment



% gel	% glyc	T (ºC)	Imp Speed (rpm)
0	100	22.0	60

$$C_n = \frac{C - C_0}{C_\infty - C_0}$$

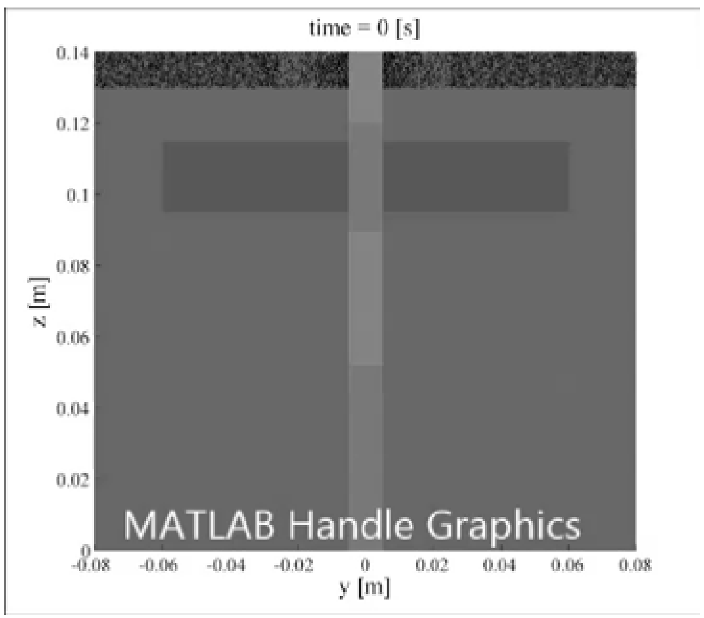


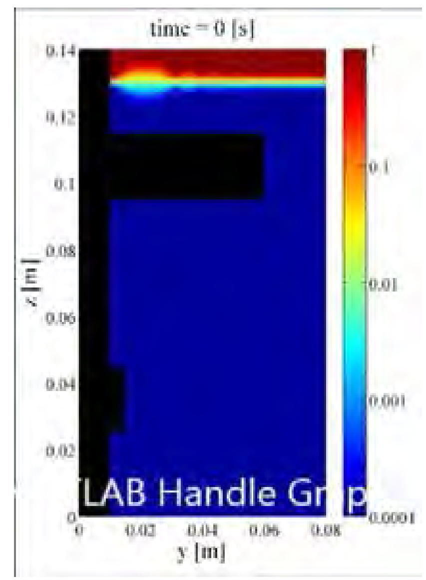
$$\sigma = \sqrt{\frac{\sum_{i=1}^{N}\left(C_{n,i} - \overline{C_n}\right)^2}{N-1}}$$

Mixing time - CFD

- CFD à Solve flow field with Fluent
- Export velocity profiles into Matlab
- Track particles with Matlab
- #particles à concentration

$$\mathbf{u}_P = \left(\sum_{i=A}^{D} \frac{1}{\mathbf{d}_i} \right)^{-1} \sum_{i=A}^{D} \frac{\mathbf{u}_i}{\mathbf{d}_i}$$

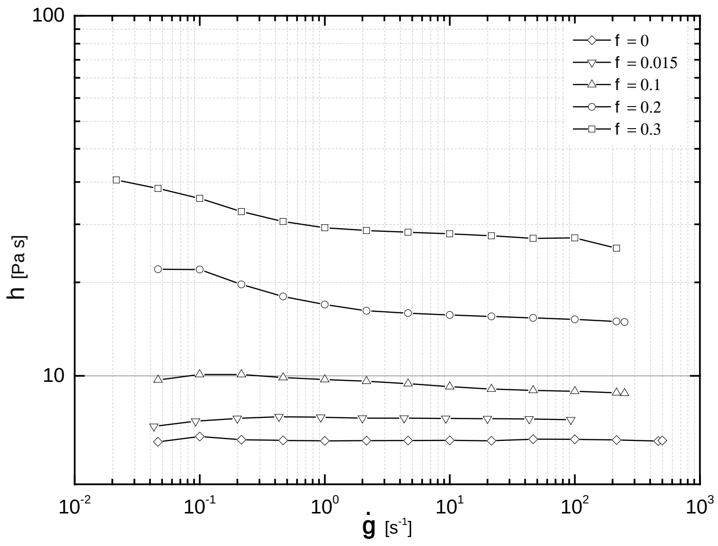




Simulations of liquid-particle suspensions

Current Results:

- Behaviour perfectly Newtonian up to 10% vol PMMA
- Slightly Non-Newtonian at 20% and 30% vol
- Torque Measurements



Future work:

- Simulate the stirring of homogeneous suspensions (at different solid volume fraction) in order to predict the impeller torque.
- Carry out PIV and PLIF measurements to examine the flow and mixing dynamics.
- Compare the CFD and the experimental results for liquid-particle suspensions

Continuous mixing – Design

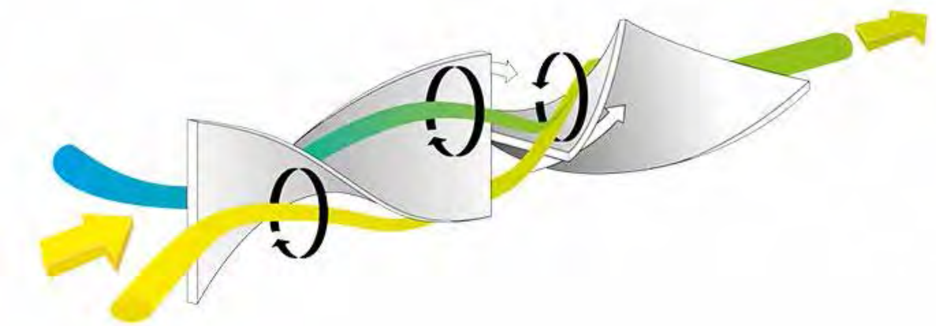
ü Approach plug flow

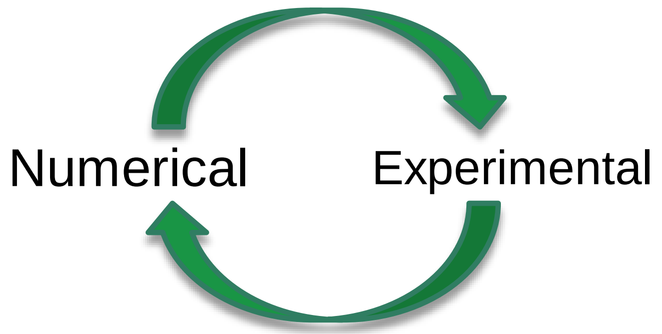
ü Good mixing at low shear rates

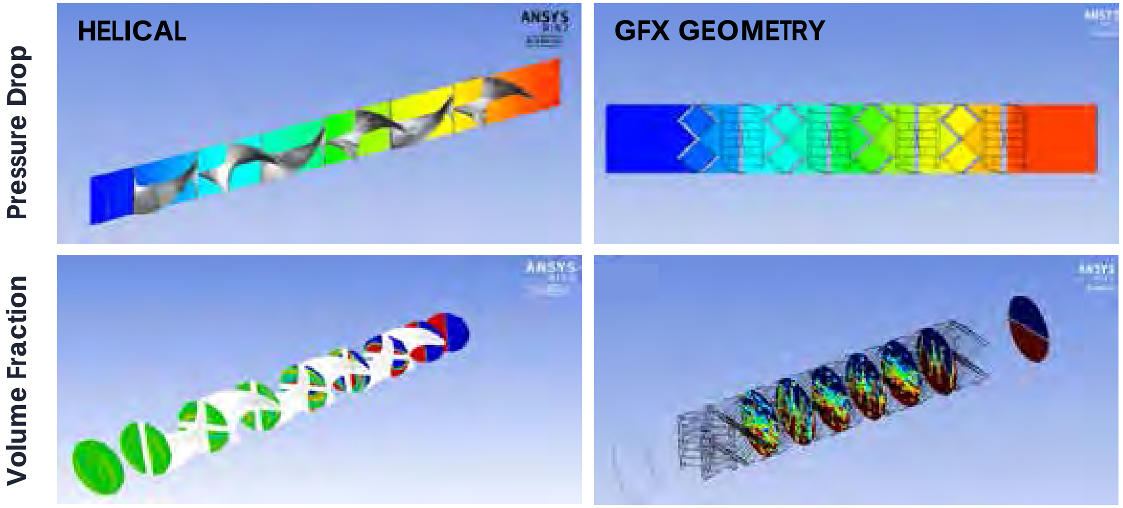
ü Short residence time

ü Small space required

ü Low maintenance, operative and equipment costs

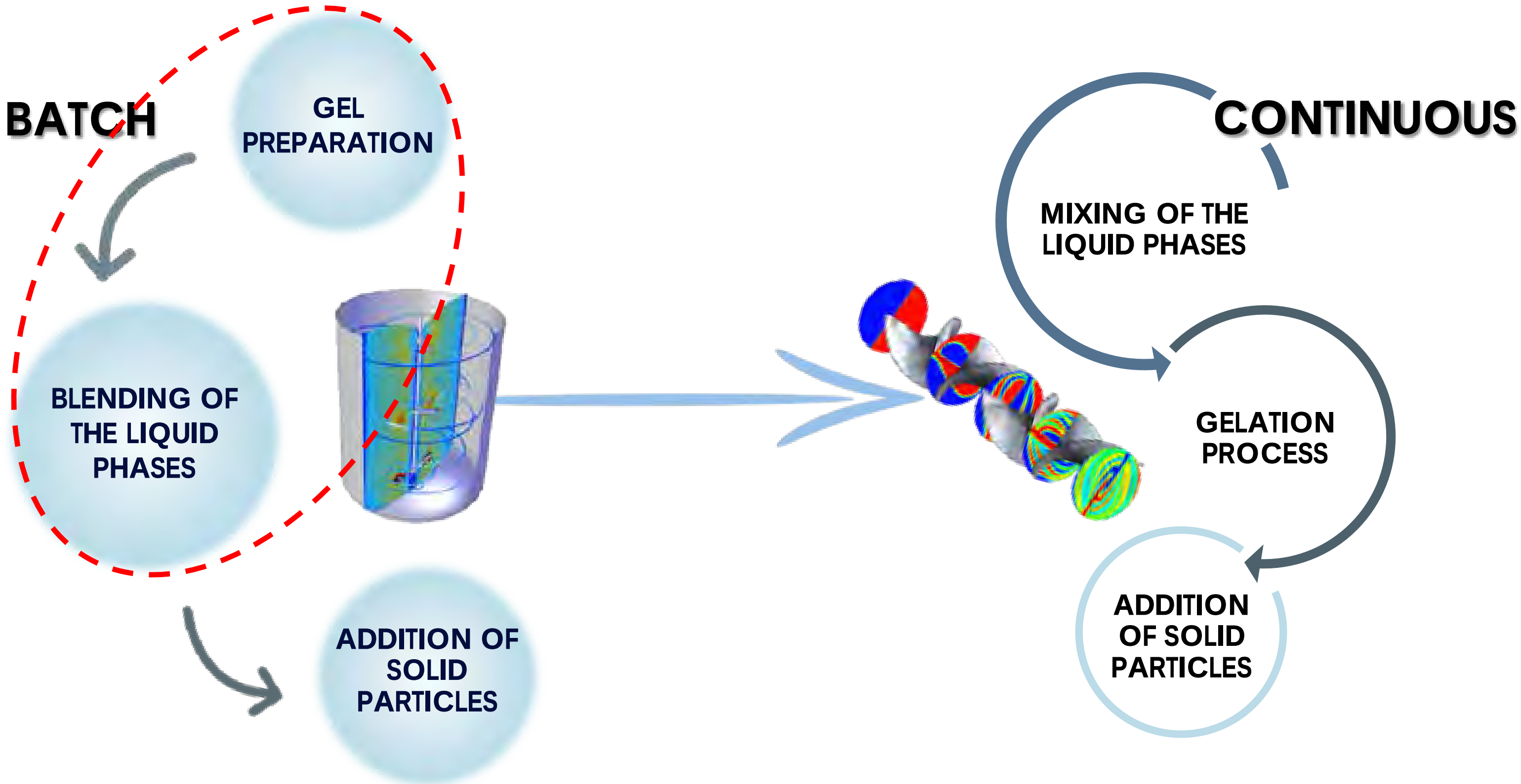






Rheology of the fluids flowing trough the mixer

Continuous mixing – Process of interest



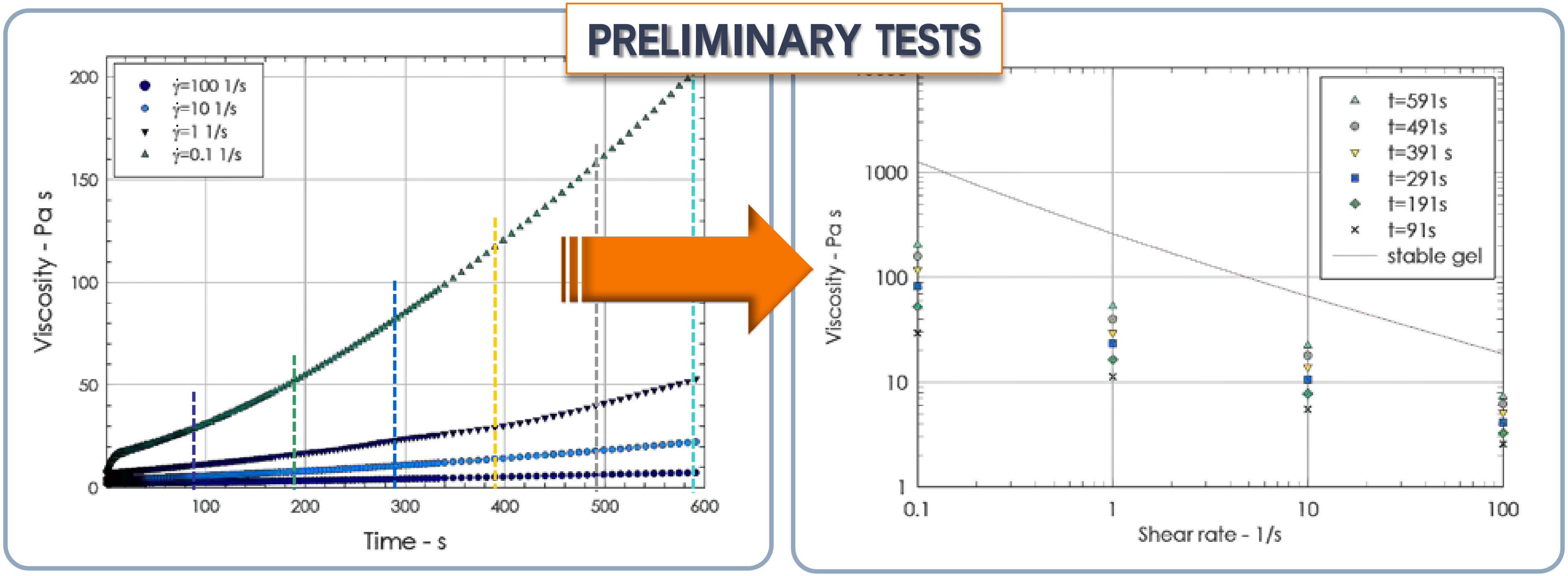
V Higher compactness

V Shorter operating times

V Lower viscosity ratio

V Lower operating temperature

Continuous mixing – Rheology of the mixture



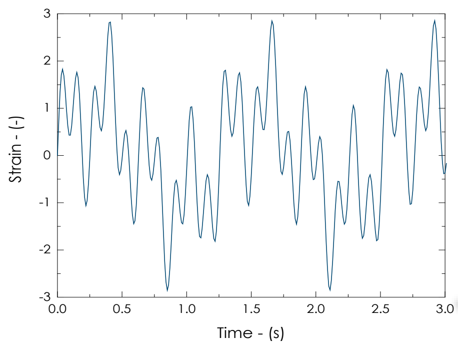
Pre-mixed mixture (Glycerol+suspension at 70%wt) 60mm 0.995° cone plate geometry (T=25°C), TA Instrument rotational rheometer

The kinetics of the gelation process depends on

V TEMPERATURE V GLYCEROL CONCENTRATION V SHEAR RATE

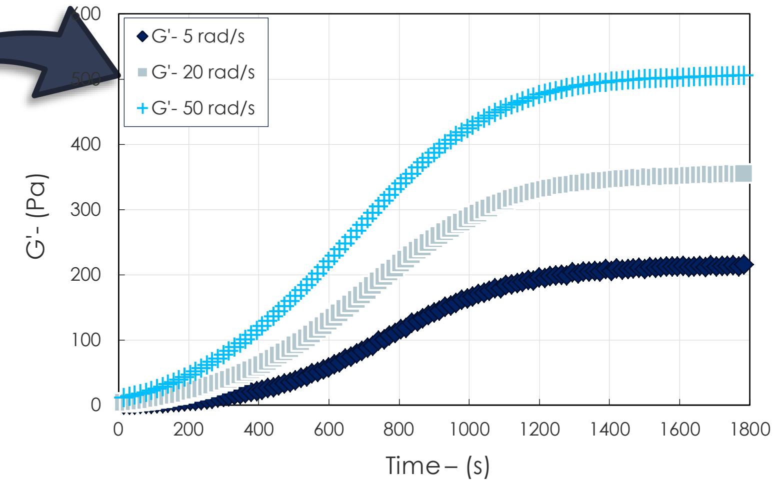
Continuous mixing – Kinetics of gelation

Fast Fourier Transforms analysis

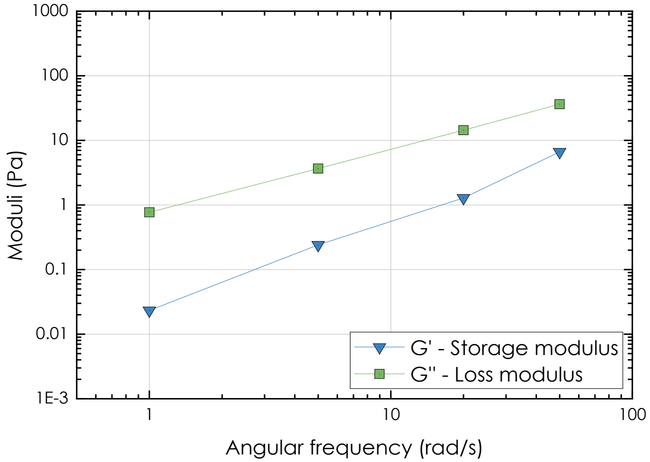


$$\gamma(t) = \sum_{i=1}^{n} \gamma_{i0} \sin(\omega_0 k_i t)$$

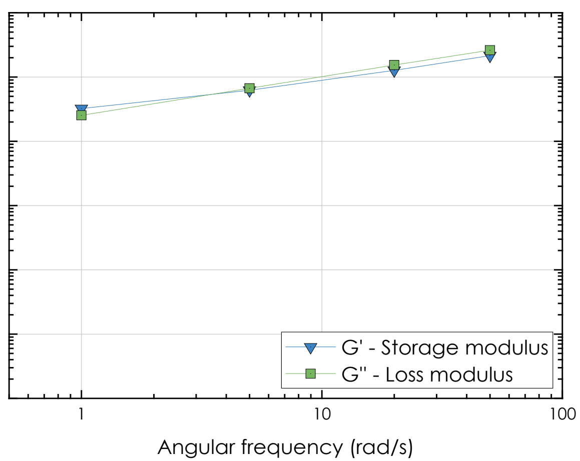
- Acquisition time: 7.3 s



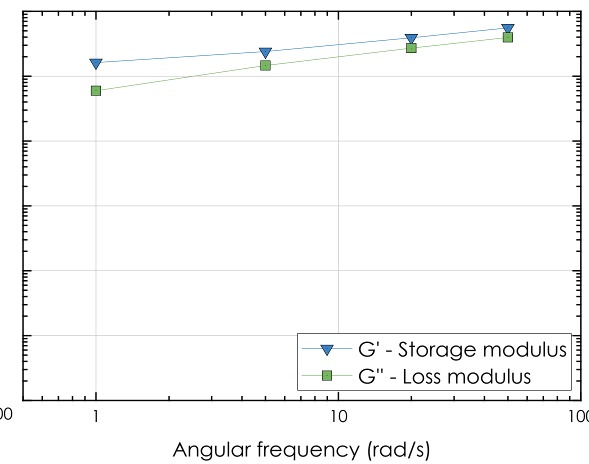
t=0



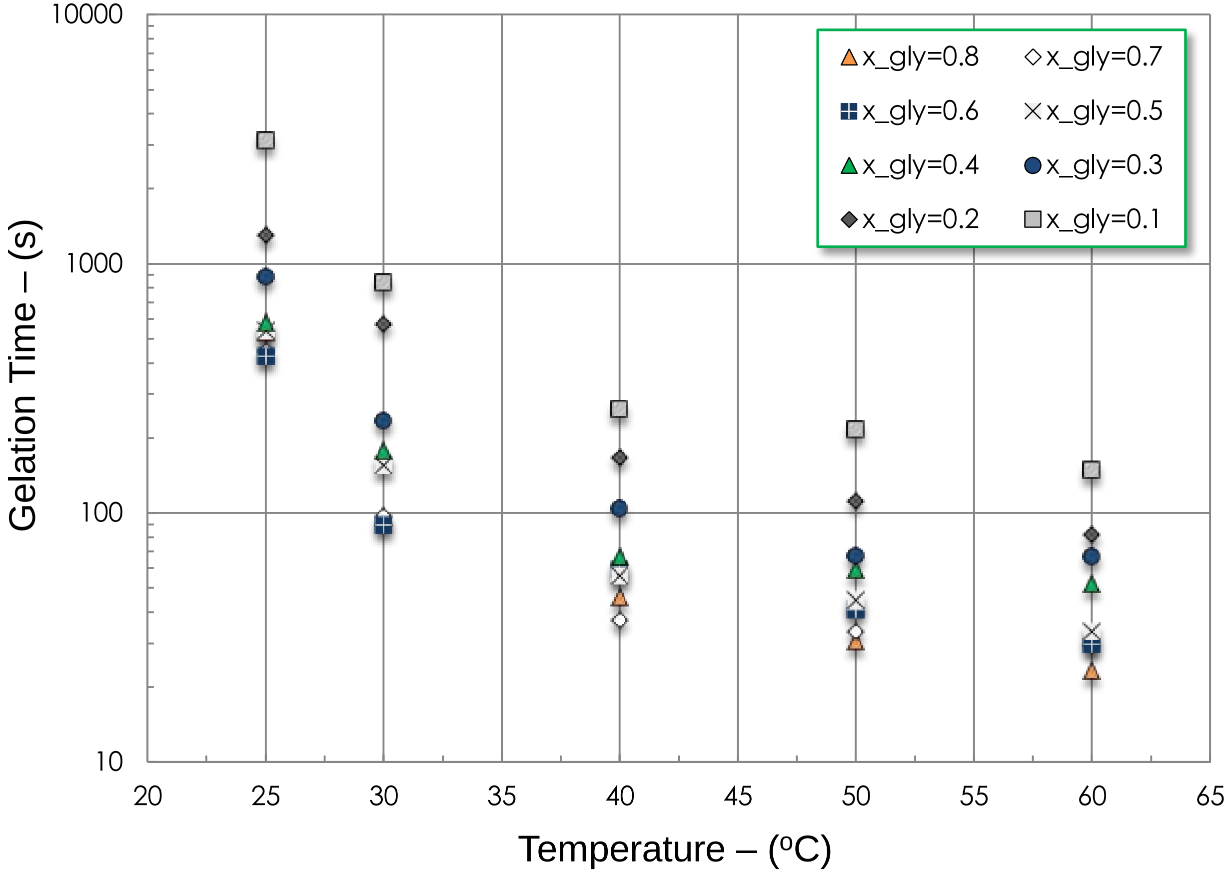
t=680s



t=1800s

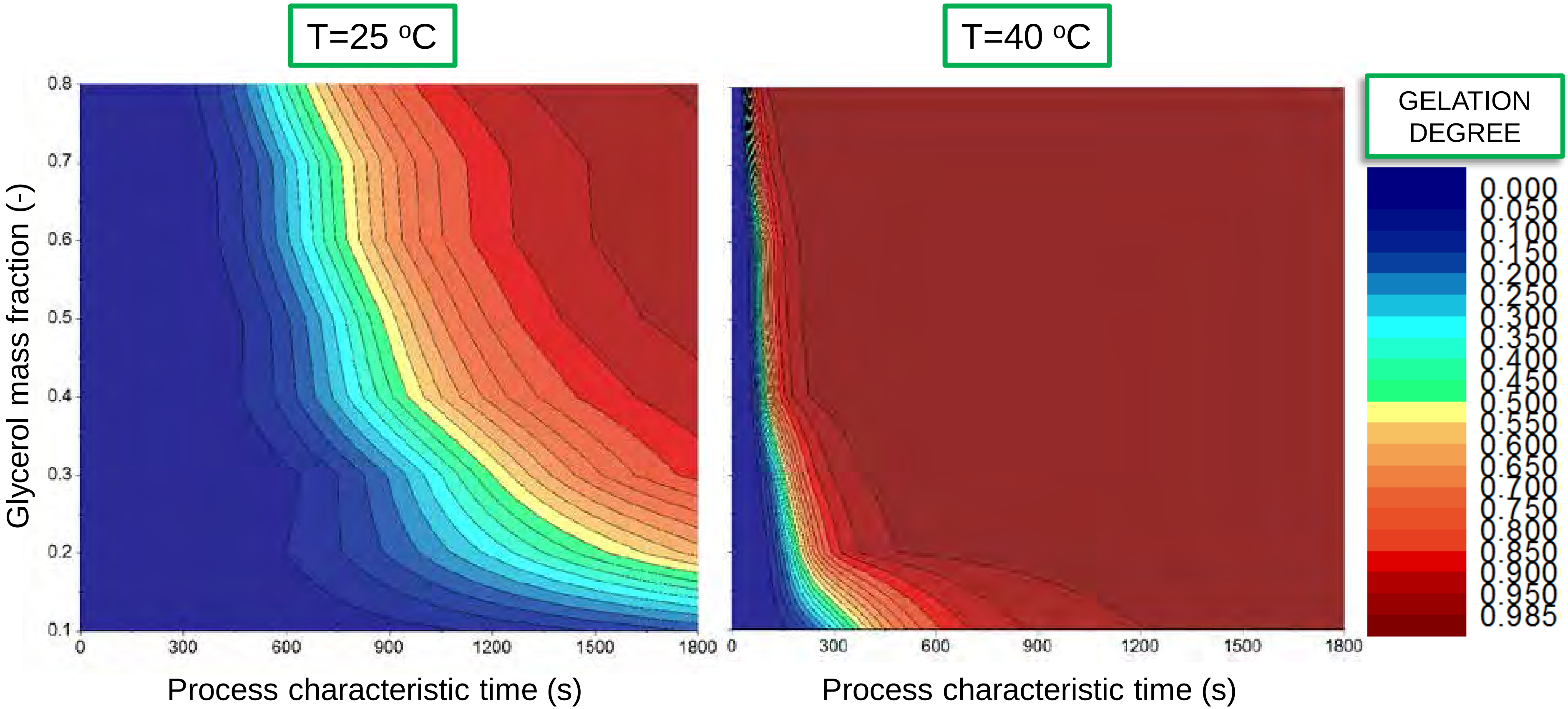


Continuous mixing – Kinetics of gelation



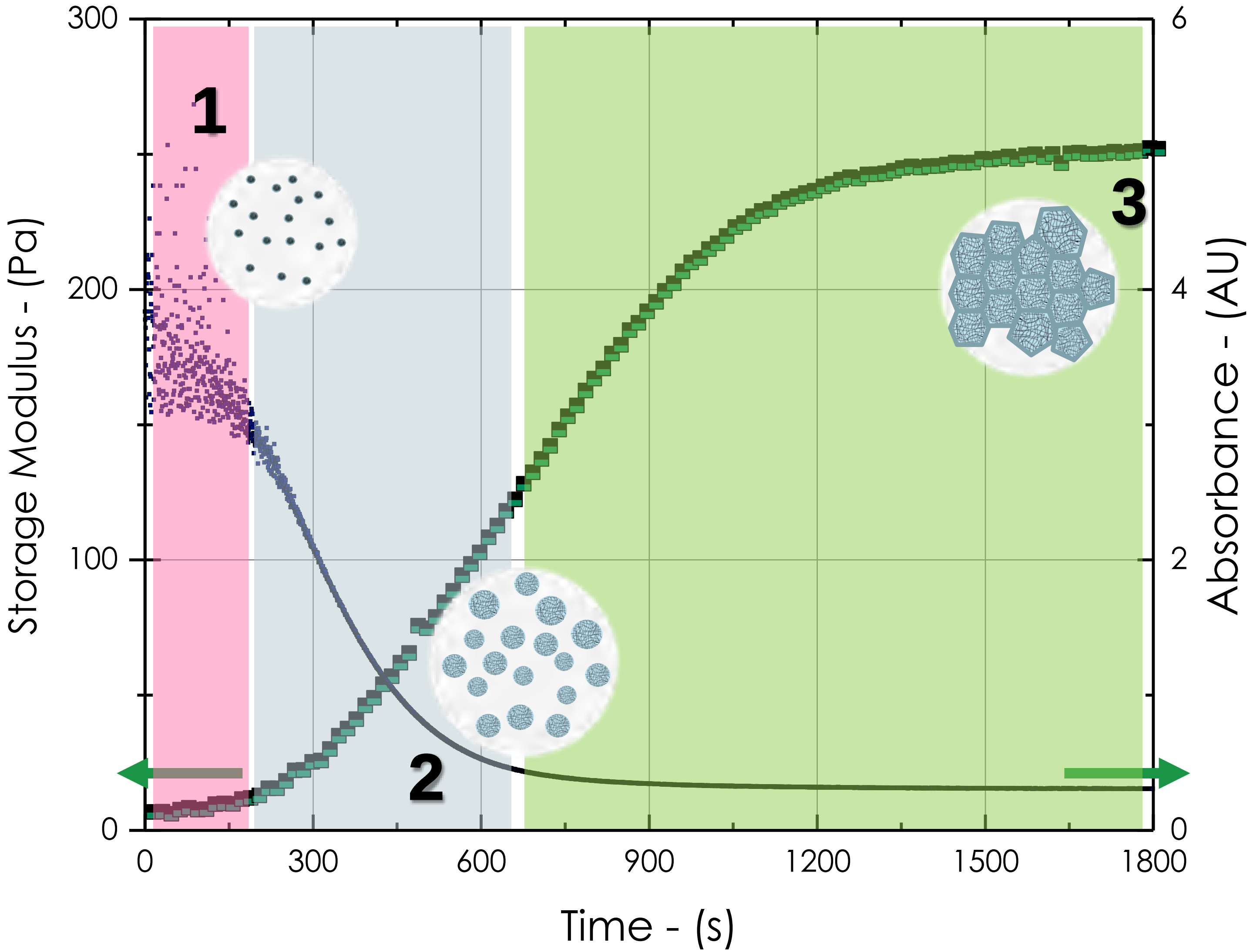
- The accelerating effect of glycerol on the gelling time can be clearly observed.
- The gelling process is strongly dependent on temperature.

Continuous mixing – Operating maps



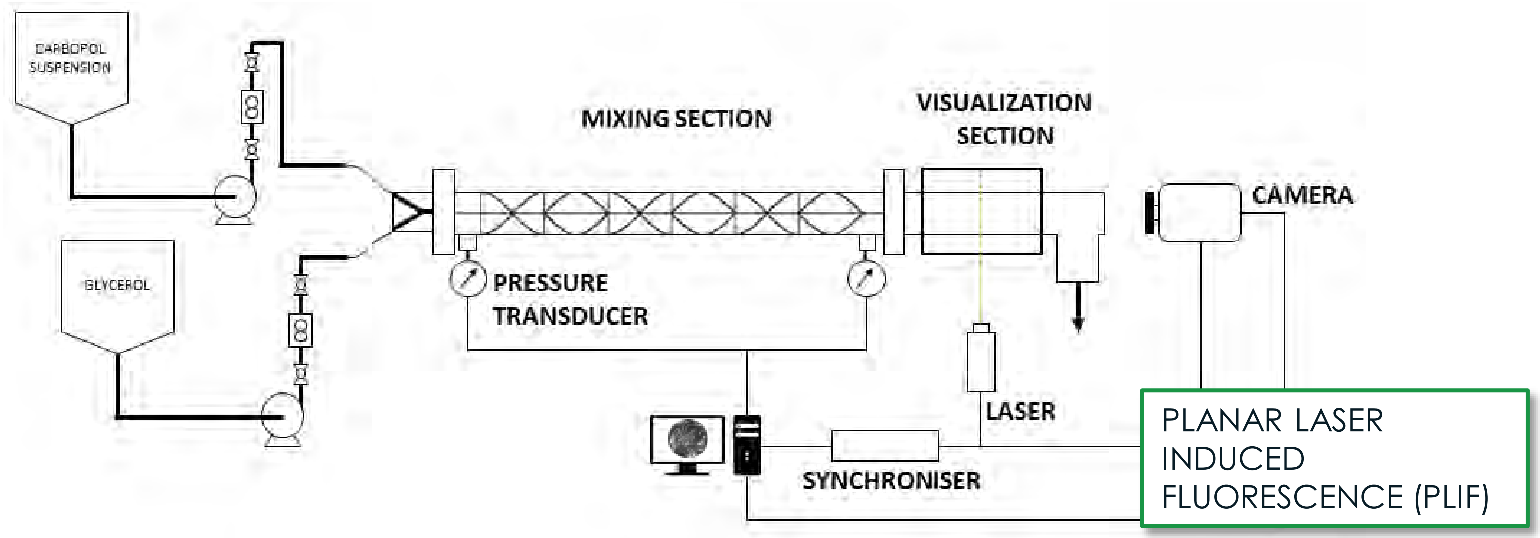
$$\text{GELATION DEGREE} = \frac{G' - G'_0}{G'_\infty}$$

Continuous mixing – Mechanism of gelation

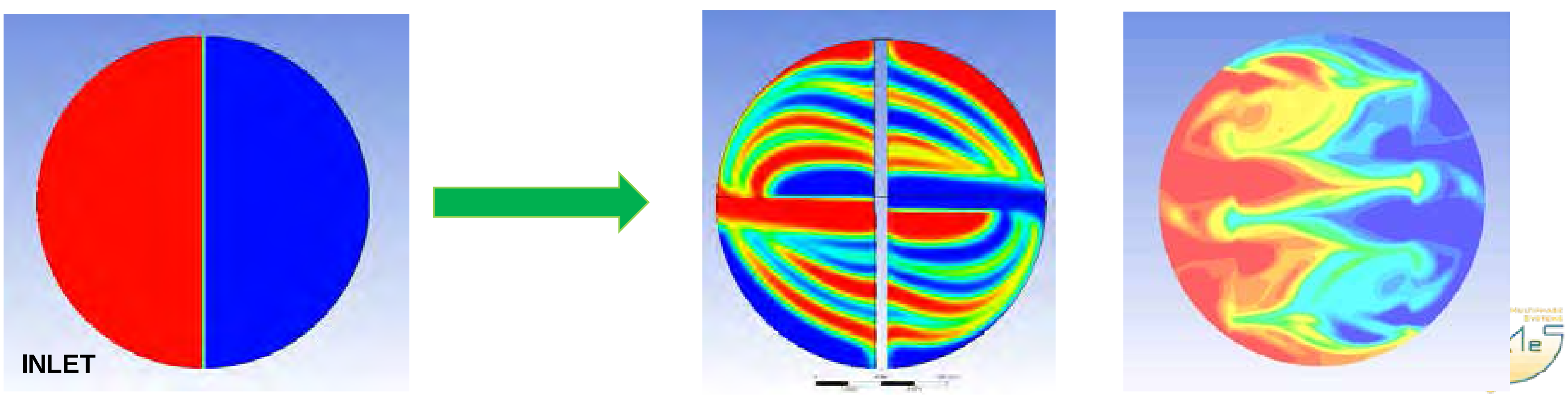


Continuous mixing – Current and Future work

- **Experimental** investigation of the mixing process



- **Numerical** investigation of the mixing process



ThAMeS: The Advanced Multiphase Systems
https://www.ucl.ac.uk/multiphase-advances-research/index

Thank you for your attention!

EPSRC
Engineering and Physical Sciences Research Council

gsk GlaxoSmithKline Consumer Healthcare