Design Approach for Moving from Batch to Continuous: Oscillatory Baffled Reactor (OBR) Technology

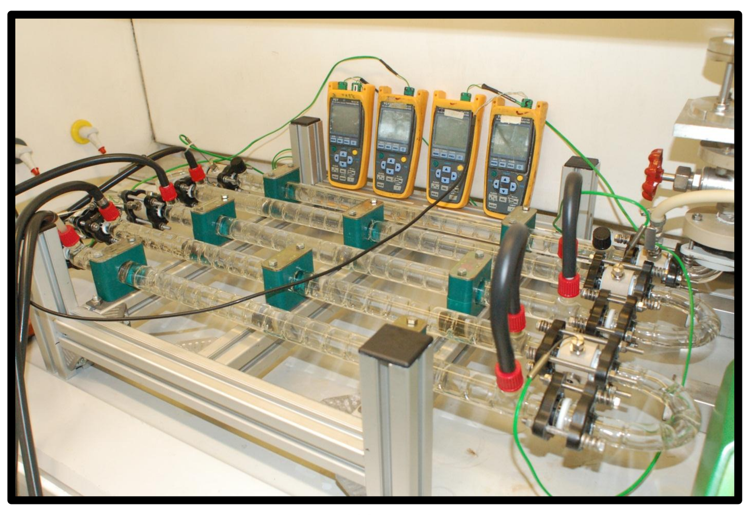
Thomas McGlone, Craig Johnston, Alastair Florence, Lihua Zhao and Vishal Raval

The Potential Benefits of Continuous Manufacturing (CM)

- More efficient use of raw materials and solvents and minimisation of waste/disposal
- Improved yield/conversion rates/product reliability in addition to enhancing chemical reactions which may have been otherwise limited in a batch - type setup
- Consistent and reproducible output as opposed to batch to batch variability
- Improved heat/mass transfer with particular suitability towards varying physical forms which exist for specific processes
- Reductions in energy consumption for running processes in addition to reactor downtime for maintenance and cleaning
- More efficient use of physical plant space
- Significant reduction in process development required for scale up operations

Oscillatory Baffled Reactors (OBRs)

Batch OBR



Small COBR

Plant COBR

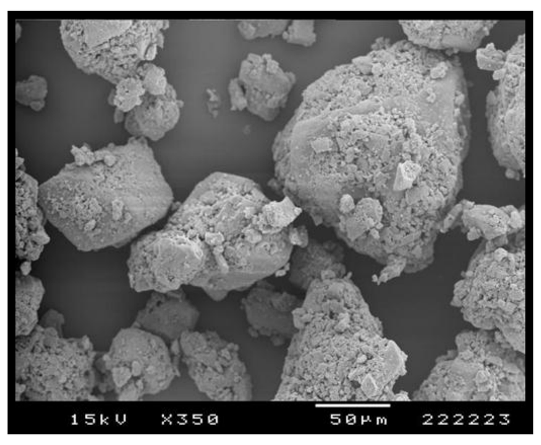
- Tubular network containing periodically spaced orifice baffles superimposed with oscillatory motion of a fluid
- Mixing is provided by the generation and cessation of eddies when flow interacts with the baffles and with repeating cycles of vortices, strong radial motions are created, giving uniform mixing in each inter - baffle zone and cumulatively along the length of the tube
- COBR systems can achieve *plug - flow conditions* at laminar (non - turbulent) flows
- Unlike microreactors, COBRs can handle solid suspensions and slurries well in addition to more viscous systems

Investigation of Cooling Crystallisation

- Plant scale cooling crystallisation, batch to batch variability, isolation issues

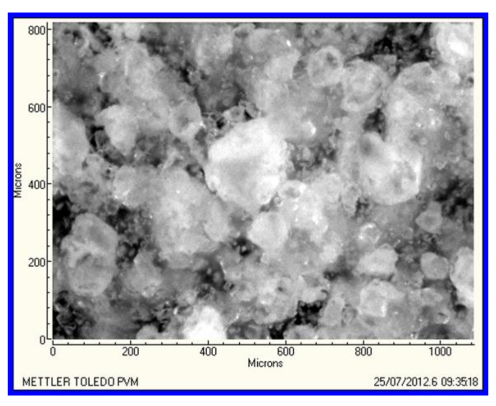
Saturation

Full de-supersaturation

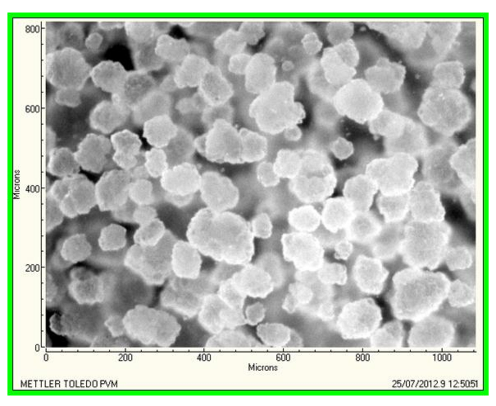


SEM image of plant isolated material

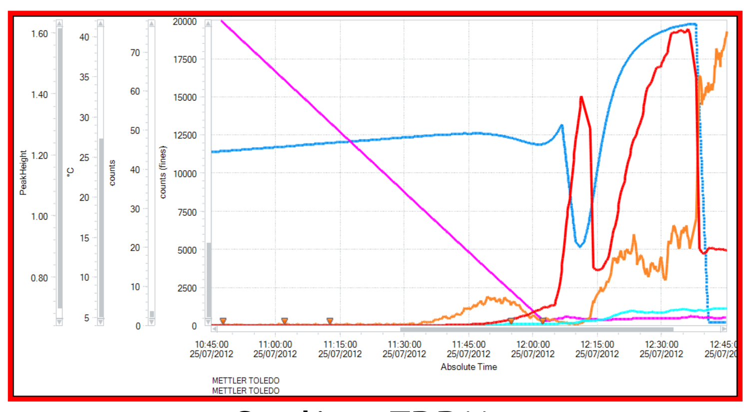
- On-line FBRM, PVM, and ReactIR™ monitoring:†



Before dissolution



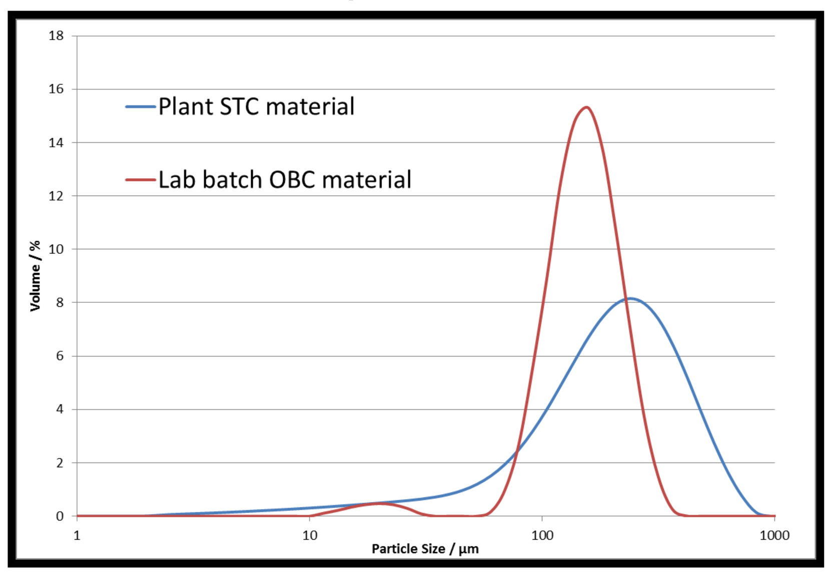
Full de-supersaturation

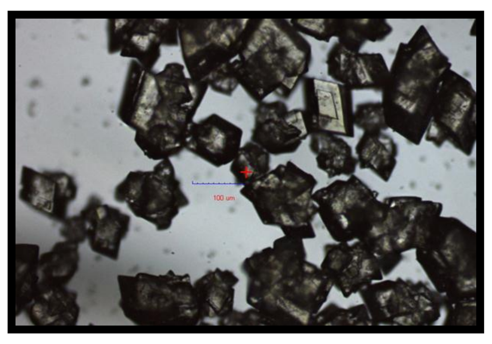


On-line FBRM

- Initial batch OBC Results:

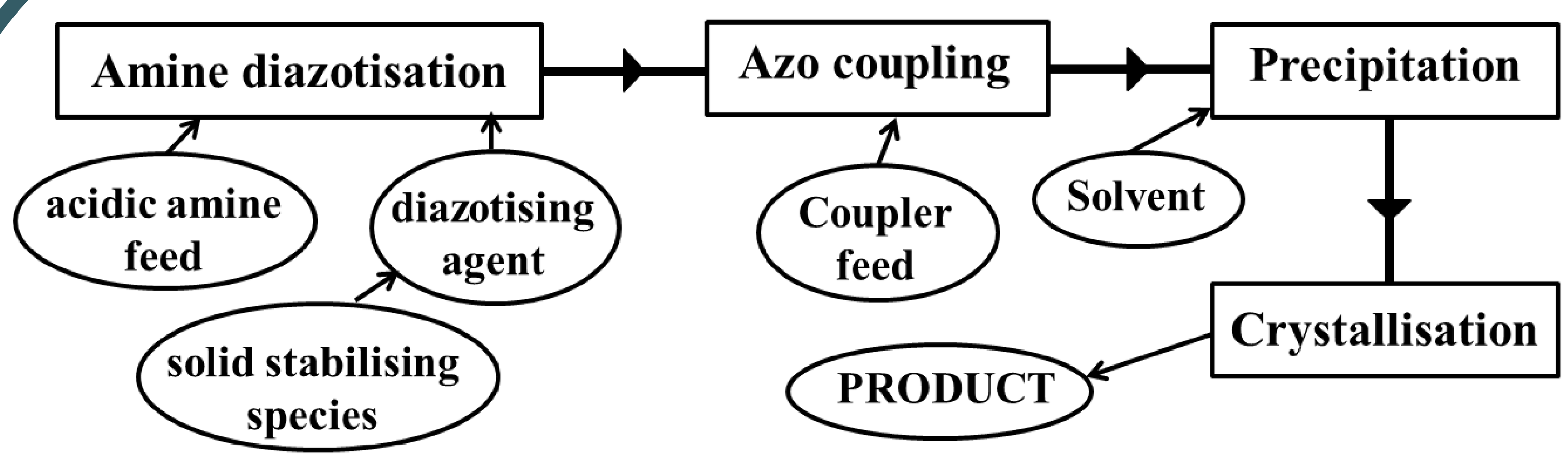
Malvern data for isolated material:



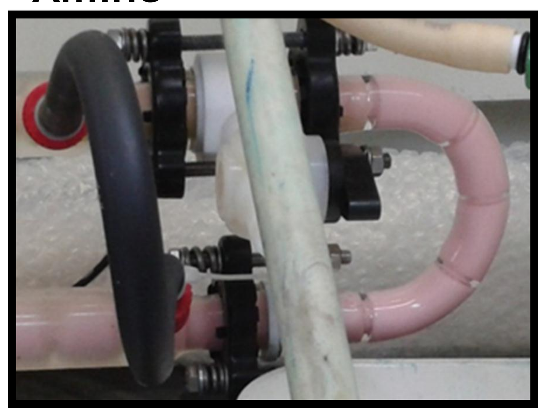


Microscope image of isolated material

Telescoping Continuous Reaction and Crystallisation



Amine

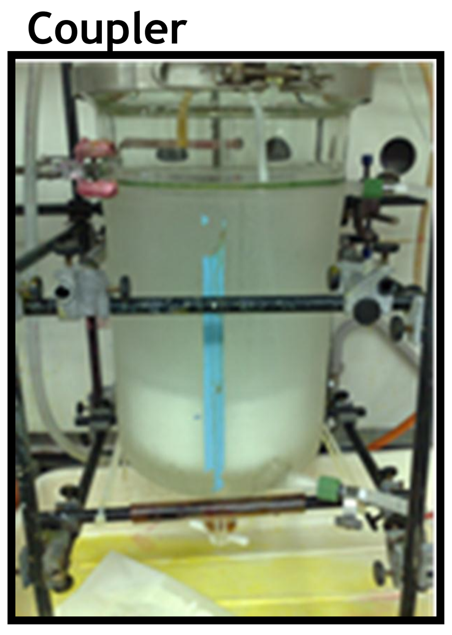


- Highly acidic media
- Physical form change
- Viscous slurry (>100 cP)
- Chemically unstable vs. temp. and time
- Freezing point 3-5 °C

Diazo

- Highly acidic media
- Chemically unstable vs. temp. and time
- Gaseous decomp. products (N_2), stabiliser can be added but increase in gas formation
- Slurry

Coupler

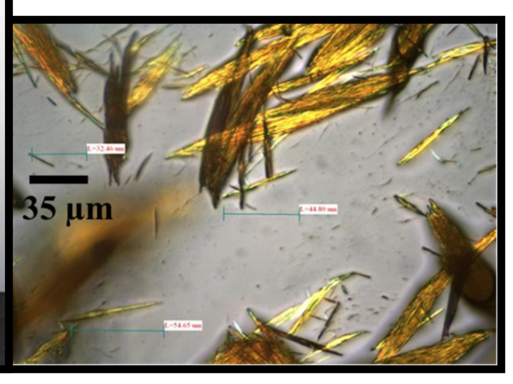


- Solvent slurry
- Fine dispersion

Azo Coupling

- Extremely viscous slurry
- Chemically unstable vs. temp. and time
- Toxic by-product (<0.1 wt./wt. %)

Product



- Chemically unstable vs. temp. and time
- Variable, mm sized agglomerates

- Obtained significant learning and improved understanding of process
- Feasibility for continuous OBR alternative not fully verified due to process verging on the limits of COBR kit and design space

Design Approach for Developing a COBR Process

- **Phase 1: Gathering existing data.**
  - Mixing, slurries or solutions, concentrations
  - Addition rates, solids or liquids
  - Temperature control, exotherms
  - Crystallisation, 1° and 2° nucleation kinetics, seeding, cooling/antisolvent/evaopration, attrition, polymorphs
  - Reagent/product stability
  - PAT – what is currently used and what would be beneficial
  - *Residence time* including hold periods
- **Phase 2: Batch OBR Experimentation**
  - Initial comparison between oscillatory and stirred mixing
  - Define minimal oscillatory conditions for particle suspension and/or reagent conversion
- **Phase 3: Designing COBR System**
  - Physical data – densities, viscosities available?
  - Determine suitable flow rates based on oscillatory Reynolds number/net flow Reynolds number ratio
- **Phase 4: COBR Experimentation**
  - Demonstration of equivalent improved product yield over batch?
  - Realisation of enhanced product quality/physical form via continuous crystallisation/precipitation?

†Ian Haley, Jon Goode and Caroline Edwards (Mettler-Toledo) are acknowledged for contributions