



innovative process development solutions  
Full Laboratory & Plant


## Chemical Understanding: The Key to Continuous Processing

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## Continuous vs Batch



	BATCH	CONTINUOUS
<b>STRENGTHS</b>	Cheap reactors Covers a variety of reaction types Versatility from reactions to crystallisations Established scale up steps	Wide range of reactors Wider operating ranges Excellent heat exchange Easier scale up Smaller footprint Cheaper service infrastructure More easily controlled Enables specific technologies e.g. photochem; hazardous Fits into existing plant set-ups Clearer ROI Safer to operate and control
<b>WEAKNESSES</b>	Expensive infrastructure Limited operating ranges e.g. b.p. Heterogeneous reactions and niche techniques scale poorly e.g. photochem Poor heat exchange (runaway) Extended processing times OOS takes out a whole batch; Reworks	Specific reactors may not suit custom synth paradigm Perceived as expensive Less experience across industry



## Introduction

We will present:


- Our approach
- Continuous vs Batch
- What IntensiChem do; Operation Envelopes; Enabling Chemistry
- Gases in flow; High Pressure Gas-Liquid Assessment
- Photochemical development; Process Optimisation
- Work up; The route to scale up of flow processing
- Summary

## Continuous vs Batch

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<b>WEAKNESSES</b>	Expensive infrastructure Limited operating ranges e.g. b.p. Mass transfer frequently an issue Poor heat exchange (runaway) Extended processing times Niche techniques scale poorly e.g. photochem	Specific reactors may not suit custom synth paradigm Perceived as expensive Less experience across industry

YOUR CHEMISTRY  
 CAN BE  
 LIBERATED FROM  
 BATCH



## Our Approach

IntensiChem provide process development services to the fine chemical industry and associated sub-sectors.


Chemical manufacturing is competitive. We want to give our clients the commercial differentiator.

We recognise that batch processing has limitations.

We know flow processing meets this need and offers value.

The key is to understand what the chemistry needs, not to fit the process into whatever equipment is available.

Chemical + Process Understanding
→
Dedicated Continuous Manufacturing Equipment



## What IntensiChem do

We offer flow development services with the view on scalability.



Current flow chemistry laboratory systems exist at a cost, however, thermal performance and pressure capability is limited.  
**We can operate from 1µl/min ? 3.2L/min up to 500 °C.**

We can offer the wide applicabilities of flow processing without constraining the client to laboratory equipment or batch conditions.

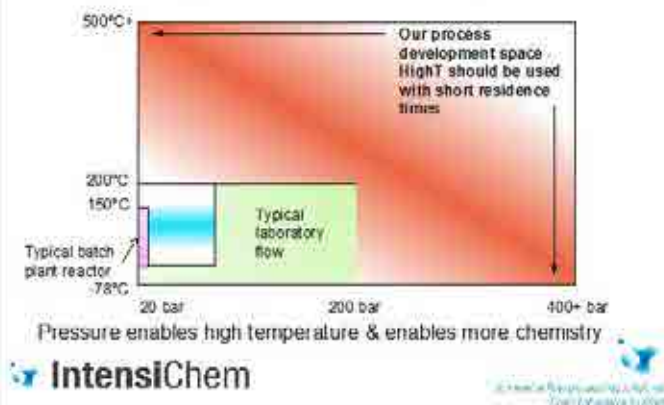
Possible applications:

Hydrogenation	Photochemistry
High pressure	Control of reactive reagents and products
High temperature	<b>Oxidation</b>
Nitration	<b>Ozonolysis</b>
Energetic process intermediates	

Solids can be used, but equipment selection is more challenging.

## Operational Envelopes



## Gases in Flow

We offer bespoke assessments and solutions for g-l reactions

Off-the-shelf solutions exist for gases in flow

- few, if any, are inherently scalable at commercial concentrations

Our approach to using gases in flow is based on scale up

We have internal know-how on delivering scalable g-l reactions

e.g. hydrogenation: 8h & messy 50% yield improved to 3s & 95%



Pressures >100 bar

Excellent selectivity

Residence times of seconds

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## Enabling chemistry (cont.)

A high temperature reaction at ~230 °C, gave 10% yield over 5-8h with 90% undesired material (1:9 selectivity).

Reaction assessment in batch - incomplete by the client due to low boiling inputs and off-gassing at 350 °C.

In-house reactor design enabled investigation from 350-450 °C.

Pressures from 70 – 180 bar investigated

Yields of 60% demonstrated with no optimisation

Selectivity of 1:1 easily achieved, with up to 4:1 demonstrated

No solvent was used

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## High Pressure Gas Liquid Reaction Assessment



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## Gases in Flow

Poor dissolution or mixing can lead to compromised flow regimes



Courtesy of Prof. R. Krishna, University of Amsterdam - [http://ci-c4.chem.uva.nl/Single/Capillary/sample\\_videos\\_flow\\_regime.html](http://ci-c4.chem.uva.nl/Single/Capillary/sample_videos_flow_regime.html)

Compromised flow leads to problems on scale up

Pressure is useful – avoids potential mass transfer issues

Batch can suffer here!

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## Photochemical Development

Designs are kept simple and bespoke to the process required



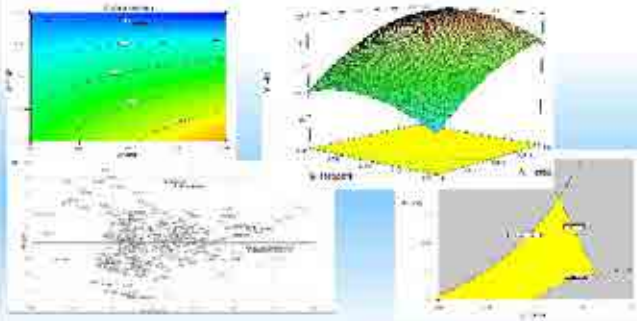
Simple, scalable designs keep costs lower

A benzylic-type bromination was reduced from 30h to 30s

Yield increased from 89% to 99%

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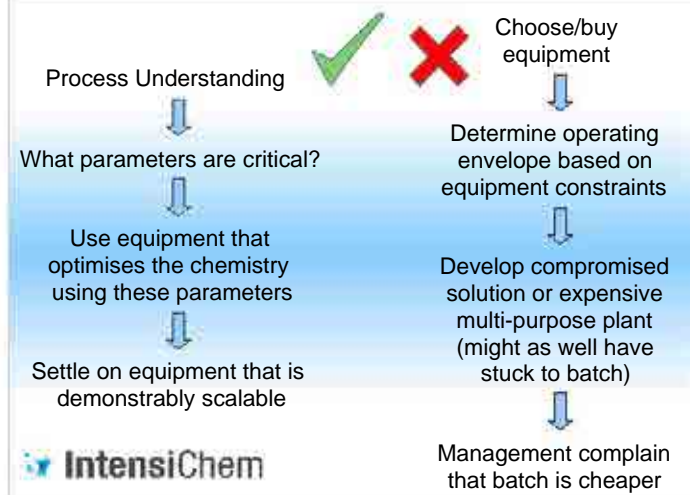
## Process Optimisation



Process modelling speeds up and quantifies optimisation.

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## Work-up assessments



- Counter current columns
- Centrifugal extractors
- Continuous distillation
- Recycle strategies
- Crystallisations: OBR or CSTR

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## Manufacturing the Solution

Developing chemical & process understanding  $\longleftrightarrow$  Equipment selection

IntensiChem can assess flow technologies offered by companies such as Chemtrix, Alfa Laval, Ehrfeld, Coming, NiTech...

We aim to deliver a complete process solution, using existing process technologies, if appropriate.

The true value of continuous can be realised with a dedicated manufacturing set-up

No reactor – batch or continuous – is universal  
Universal chemically compatible pumps don't exist  
Dedicated process equipment keeps costs down

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## Process Scale Up

Our laboratory activity will generate process understanding

We can achieve throughput through reducing reaction times to minutes or seconds.

Even smaller lab equipment based rigs can deliver small commercial quantities: 200ml/min ? 30-90kg/day

Our current largest laboratory pump at 3.2L/min @ 10% concentration = ~14MT/month

It is important to demonstrate the process at intermediate scale with small, demonstrably scalable process flow technology

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## Summary

IntensiChem can offer flow process development services not possible with current laboratory based offerings.

IntensiChem's scalable approach is to minimise constraints that are built into the current batch paradigm.

Access is possible to a large range of:  
Temperatures: -78 - 500 °C  
Pressures: 400 bar +  
Flow rates: 1µl/min – 3.2L/min

We're not a vendor, so not constrained to technology or conditions.  
And don't push a technology until the process is understood.

Dedicated process equipment means not having too many pumps, control systems or redundant equipment in general.

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