



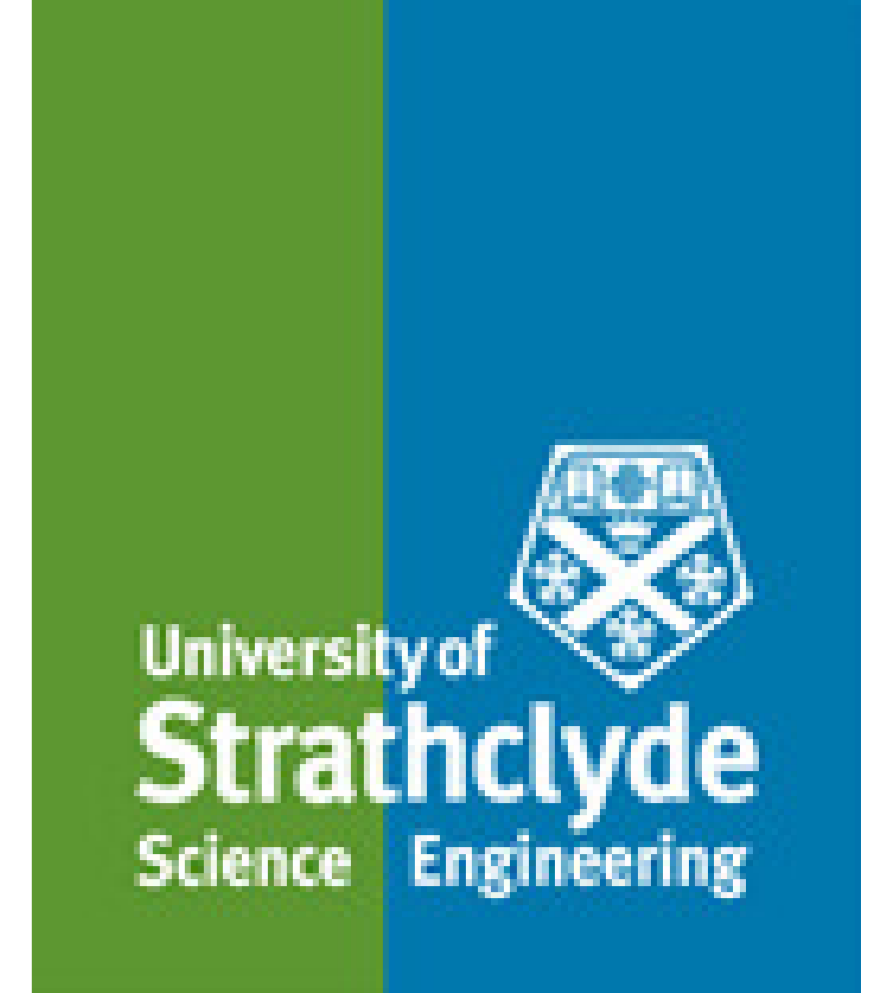
Dziewierz, Jerzy and McGinty, John and Macfhionnghaile, Pol and Svoboda, Vaclav and Sefcik, Jan and Gachagan, Anthony and Nordon, Alison and Marshall, Stephen and Cleary, Alison (2016) Applying hyperspectral imaging to continuous processing of pharmaceuticals. In: Solving problems with spectral imaging, 2016-02-04 - 2016-02-04, London. ,

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Hyperspectral imaging for continuous process development



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Problem statement

In production of high value chemicals as pharmaceuticals, a strict control over the final product attributes like size, purity, morphology, form etc. is required. Traditionally pharmaceuticals are produced in batch mode where it is not possible to fully control process operation and the final product quality varies from batch to batch. Moving from batch processing to continuous operation offers opportunities for improvement in consistency of the product attributes. However, development of advanced techniques for on-line process monitoring and control is needed.

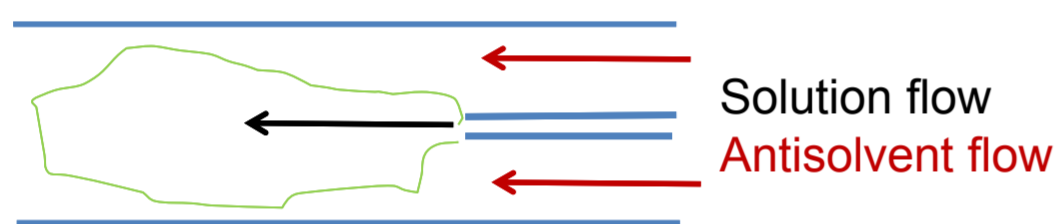
Using hyperspectral camera

The process is continuous crystallisation of a solute of a pharmaceutical compound using antisolvent in tubular crystalliser. Antisolvent crystallisation is a very rapid process, requiring tight control of environment conditions. A feasibility study has confirmed that hyperspectral camera can deliver spatial concentration distribution information not available from other techniques. Hyperspectral images have been acquired to reveal the size and shape of the resulting jet, and relate its properties to the crystals produced.

The process is now being upgraded with computer controlled pumps and hyperspectral compatible photo booth, for long term usability and repeatability of further developments.

Feasibility study results

continuous crystalliser

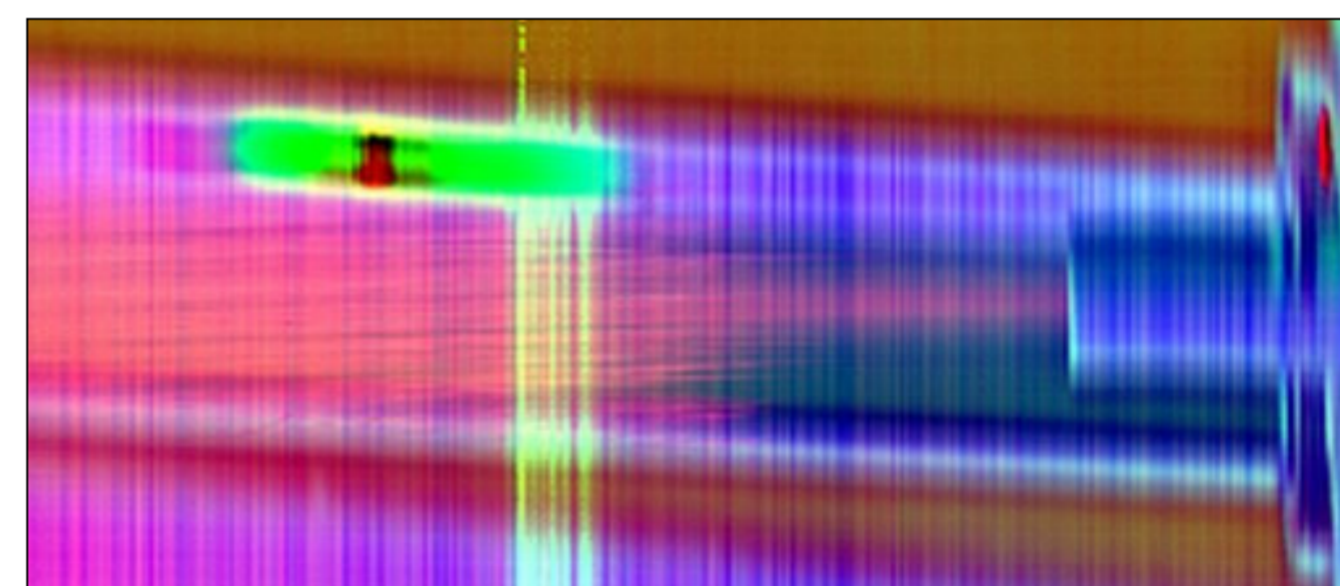


The solution is continuously introduced into the antisolvent flow using a nozzle in the middle of the vessel. The resulting crystallisation process is very rapid and the product properties (crystal size, shape, agglomeration, amount of product recovered from solution) depend heavily on the shape and size of the jet. Hyperspectral images allow distinction of the two chemical compounds that are otherwise white or transparent to human eye. It is possible to obtain quantitative measurements of the mixing properties.

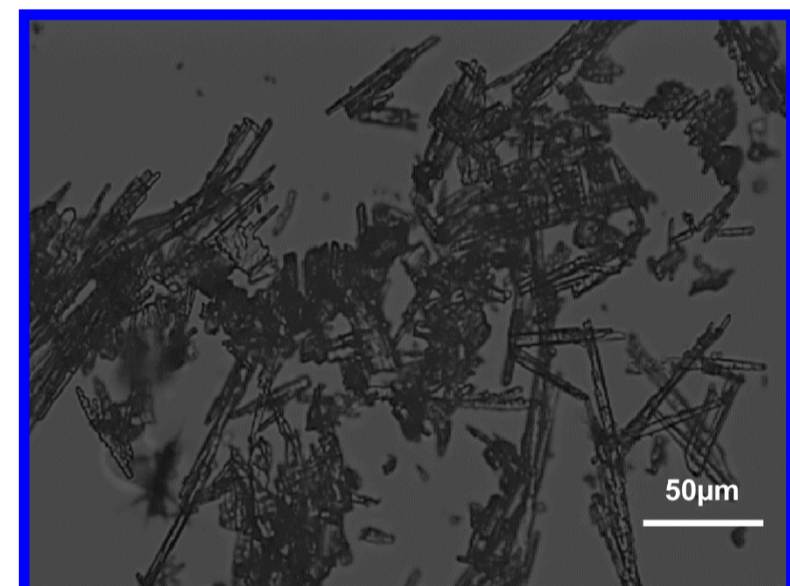
Conditions

Low flow rate
Total flow: 100g/min
20g/min solution
80g/min antisolvent
d=0.5mm,
Re=652,
v=1.70m/s
Residence time=10sec

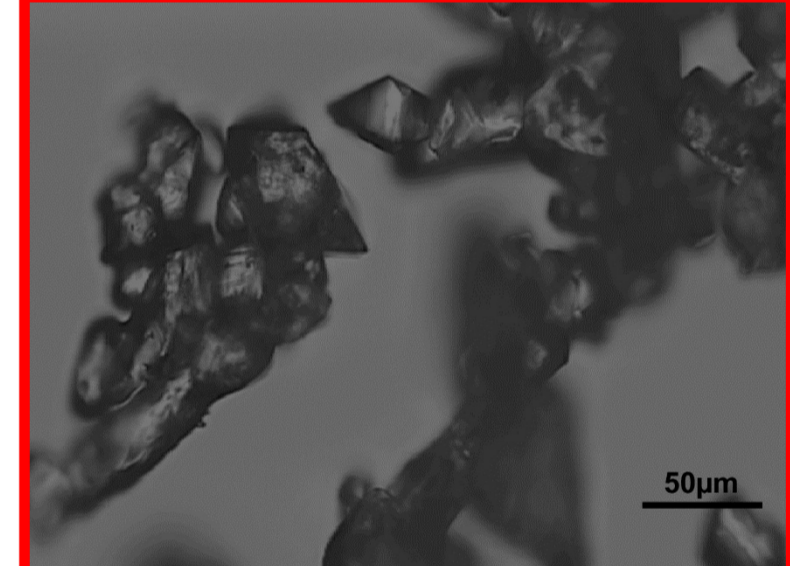
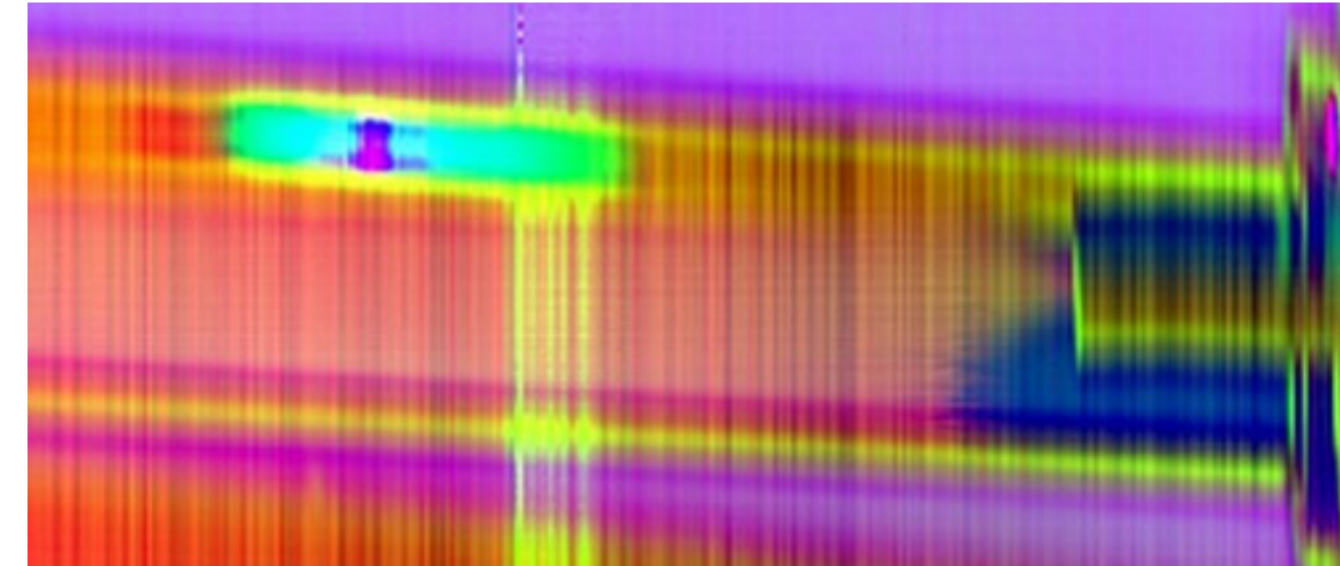
Hyperspectral image



Product image



High flow rate
Total flow: 200g/min
40g/min solution
160g/min antisolvent
d=0.5mm,
Re=1304,
v=3.4m/s
Residence time=5sec

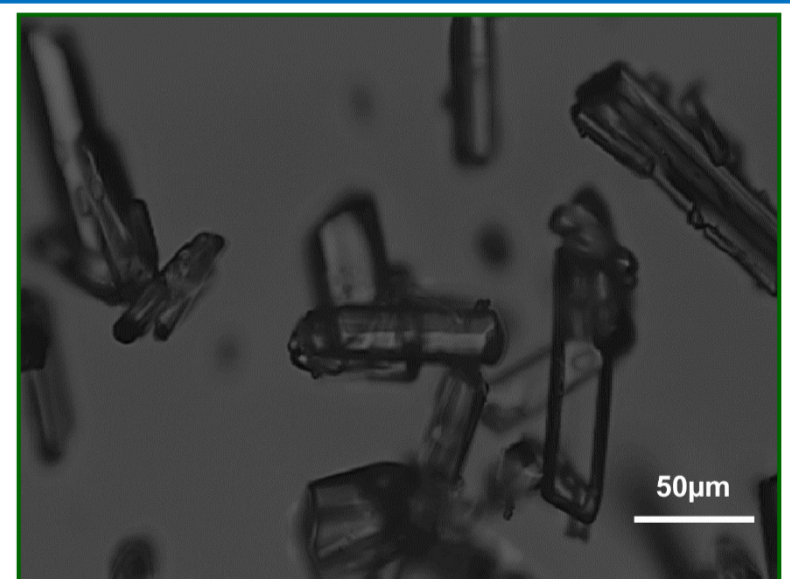


Reference batch crystalliser

For comparison, the same pharmaceutical was crystallised in a batch crystalliser. The resulting product is shown in the microscopic image to the right.

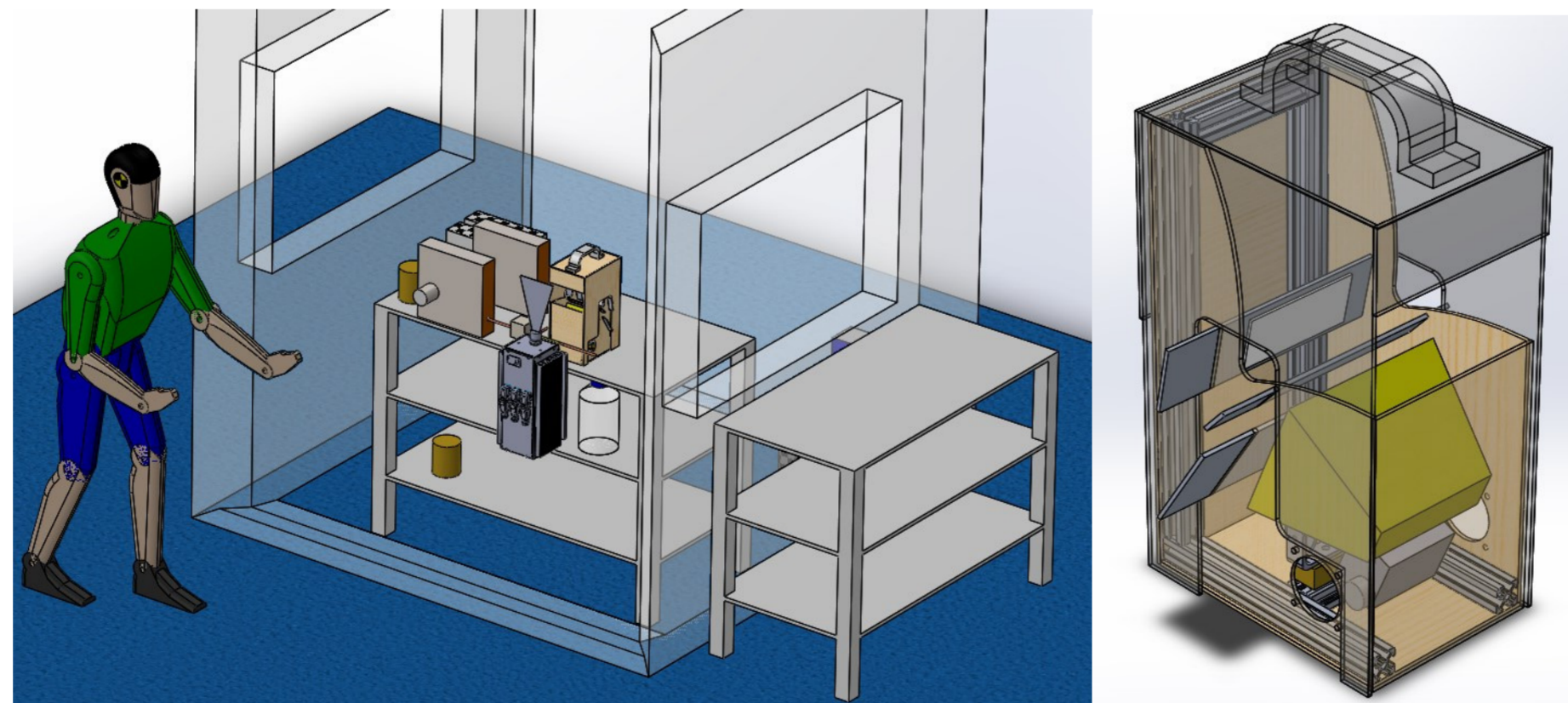
Station type: Mettler Toledo EasyMax

Total volume :100ml
Stir rate: 400rpm,
Cooling: 1°C/min



New experimental setup

The experimental setup is being upgraded to support long term automated experiments with parametric sweeps of flow concentrations, and tighter control of image acquisition parameters.



Experiment automation

A parameter sweep, covering a range of input variables like temperature gradients, flow rate, mixing ratio, e.t.c. can be programmed into the controller to perform a comprehensive study of the system behaviour. Data is carried over local OPC hub and stored in database for easy retrieval into the electronic lab notebook.

A holistic approach is used to design the experimental booth. The path of the light from the source, through the specimen, to the camera, has been optimized for final image quality.

