EUROPEAN SYNCHROTRON RADIATION FACILITY

INSTALLATION EUROPEENNE DE RAYONNEMENT SYNCHROTRON

ESRF

Experiment Report Form

The double page inside this form is to be filled in by all users or groups of users who have had access to beam time for measurements at the ESRF.

Once completed, the report should be submitted electronically to the User Office via the User Portal:

https://wwws.esrf.fr/misapps/SMISWebClient/protected/welcome.do

Reports supporting requests for additional beam time

Reports can be submitted independently of new proposals – it is necessary simply to indicate the number of the report(s) supporting a new proposal on the proposal form.

The Review Committees reserve the right to reject new proposals from groups who have not reported on the use of beam time allocated previously.

Reports on experiments relating to long term projects

Proposers awarded beam time for a long term project are required to submit an interim report at the end of each year, irrespective of the number of shifts of beam time they have used.

Published papers

All users must give proper credit to ESRF staff members and proper mention to ESRF facilities which were essential for the results described in any ensuing publication. Further, they are obliged to send to the Joint ESRF/ ILL library the complete reference and the abstract of all papers appearing in print, and resulting from the use of the ESRF.

Should you wish to make more general comments on the experiment, please note them on the User Evaluation Form, and send both the Report and the Evaluation Form to the User Office.

Deadlines for submission of Experimental Reports

- 1st March for experiments carried out up until June of the previous year;
- 1st September for experiments carried out up until January of the same year.

Instructions for preparing your Report

- fill in a separate form for each project or series of measurements.
- type your report, in English.
- include the reference number of the proposal to which the report refers.
- make sure that the text, tables and figures fit into the space available.
- if your work is published or is in press, you may prefer to paste in the abstract, and add full reference details. If the abstract is in a language other than English, please include an English translation.

ESRF	**Experiment title:** In Situ Studies of Resonant Acoustic Mixing	**Experiment number**: CH-4805
Beamline: ID31	**Date of experiment**: from: 11/11/16 to: 15/11/16	**Date of report**:
Shifts: 12	**Local contact(s)**: Maria Blanco (maria.blanco@esrf.fr)	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

Adam Michalchuk, University of Edinburgh and Novosibirsk State University, Russia*

Stuart Kennedy, University of Edinburgh*

Karl Hope, University of Edinburgh*

Colin Pulham, University of Edinburgh

Report:

Resonant Acoustic Mixing (RAM) technology, by the Resodyn Corporation, has become a highly popular processing technology for the pharmaceutical and energetic materials communities. This experiment sought to build on previous experience of *in situ* mechanochemistry to investigate the real-time processes occurring under Resonant Acoustic Mixing in a LabRAM 1. To the best of our knowledge, this experiment was the **first** example of real-time *in situ* synchrotron investigation of this device. A number of key processes were investigated over the course of this experiment: 1) Optimising experimental procedures to obtain high quality diffraction data from RAM processes; 2) follow the effects of RAM treatment conditions on single phase systems; 3) follow the effects of RAM treatment conditions on multi-phase systems, with particular focus on co-crystallisation; and 4) follow in real time the ability of RAM to mix powdered materials on the small scale.

In this experiment, we have successfully studied these phenomena, and data are being processed for publication in peer-reviewed journals.

1. Data Collection Scheme

Data collection proves particularly difficult for real-time *in situ* studies of mechanochemical processes. With a new mechanochemical reactor being investigated, focus was on optimising data collection strategies for this new device. Due to the flexibility of sample containers allowed by the RAM, high quality data was attainable for robust analysis of solid-state processes. A thorough examination of collection time, position and geometry was performed to ensure highest quality data were attained.

2. Single-Phase Transformations under RAM

A number of single phase transformations were followed *in situ* throughout this experiment. Particular interest in following solid → solid transformations, and obtaining detail into the real-time effects of RAM

treatment on particle integrity. A number of interesting transformations were observed under RAM conditions, and the intensity and rates under which they were observed demonstrate key attributes as to the intensity and applicability of the RAM to treating solid materials. Collection of high-Q range data was achieved for investigation of microstructural development during RAM treatment. This experiment offered unique insights into the relative capacity of RAM for powder treatment over conventional mixing and mechanochemical technologies.

3. RAM-Induced Co-Crystallisation

The beam time provided by the ESRF has allowed us the time to systematically explore a number of key technological parameters associated with the RAM technology. In particular, following the effects of these parameters on the co-crystallisation of model compounds.

3.1 Co-Crystallisation

The particular strength of real-time *in situ* investigation is its ability to directly follow a solid + solid transformation through time, without the need to perturb the system. In the present experiment, the rate of co-crystallisation was followed for a number of model organic molecular systems. Of particular interest was the model system of glycine + oxalic acid dihydrate, which we have previously followed *in situ* by ball milling. This experiment therefore offered a direct comparison of the efficiency and processes occurring for the same system in two very different mechanochemical reactors. The processes were found to differ between the two reactors. These findings are of great importance for industrial application of mechanochemical technologies, where intelligent selection of mechanical processing techniques is clearly of critical importance.

Further co-crystallisation processes were monitored, including those of pharmaceutical interest. We again discovered unique differences between the processes which occur under ball milling conditions and under RAM treatment conditions, and believe these results will be of great interest to both industrial and academic communities. It was particularly notable that some co-crystallisations were not completed due to the inherent energies associated with the RAM technologies, but instead intermediates were trapped. This work is currently being supported by computational and *ex situ* mechanochemical investigation, and will provide unique insight into the nature of mechanochemical co-crystallisations.

3.2 Kinetics of Co-Crystallisation

As a new technology, the community remains largely unaware of the effects of various working parameters on reactive processes. We therefore explored the effects of various G-force settings on the rates of multi-component crystallisations, with and without the addition of liquids. Contrary to widespread belief, these studies showed that a simple correlation between treatment intensity and reaction rate was not always straightforward. For some of the investigated co-crystallisations, increasing RAM intensity was met with an increase in the reaction rate, however, in others there was no obvious effect on the reaction rate.

A particularly surprising feature of these investigations was the discovery that G-force can be used to tune the results of a multi-component crystallisation processes. This was seen for a number of the systems investigated.

It is typically found that RAM co-crystallisations required the addition of small quantities of solvent (that is, liquid assisted grinding, LAG). Thus the rates of co-crystallisation were also followed across a series of solvents, in which materials are known to be soluble, and those in which they are not. Notable effect on the rate of RAM-induced crystallisation was observed, and trends currently being analysed.

4. Mixing

Built primarily as a mixing device, considerable interest has surrounded the ability of RAM technology to homogeneously mix powder systems. This experiment offered the first opportunity to monitor the local mixing of powder + powder systems by RAM technologies. Particular interest rested in the ability to monitor the rates of this mixing as a function of the RAM parameters. A number of experiments were also performed

to assess the relative rates of mixing and reactive chemistry. This allowed for the first time to establish new insights into phenomena obtained by us, and others, through RAM treatment of powders.

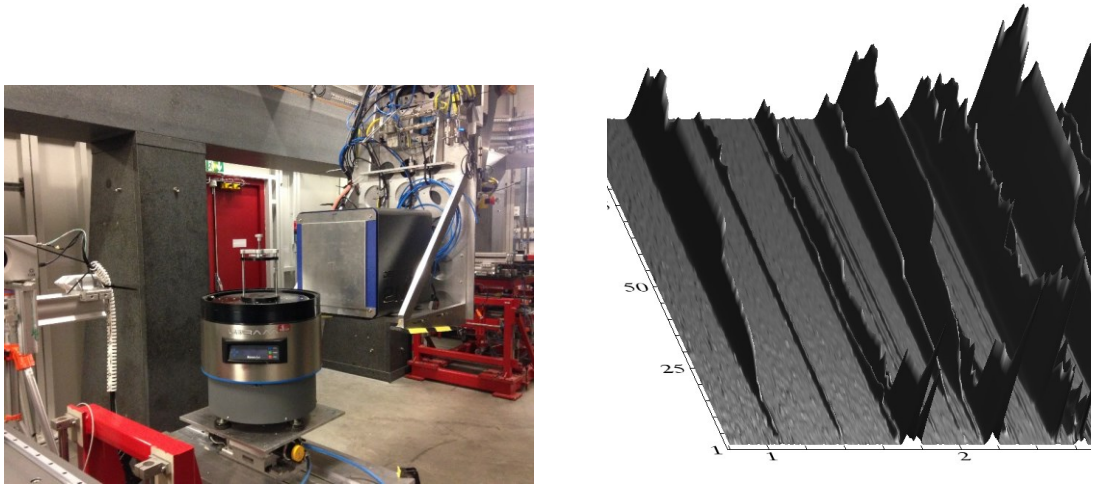

Fig. (Left) RAM installed on ID31 beamline. (Right) Successful monitoring of Co-crystallisation under RAM treatment.