PNNL-38447

Autonomous Synthesis of Metastable Materials Using a Modular Mixed-Flow Reactor

September 2025

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1.0 Introduction

Unraveling atomic-level processes at solid-liquid interfaces is critical for various DOE priority areas, such as energy storage, carbon mineralization, critical element recovery, and novel composite synthesis. In many systems, solid-liquid interactions are dominated by short-lived precipitate intermediates that determine the final composition and structure.[1-5] Study of these intermediates is essential to understanding, modeling, and ultimately tuning the fundamental physico-chemical properties of synthesized precipitates.[3,4,6] However, isolating metastable phases often requires extensive experimentation under highly controlled conditions due to their sensitivity to heterogeneities.[7] Mixed-flow reactors (MFRs) offer a more consistent experimental approach, yet finding optimal conditions still typically relies on trial-and-error, often guided by the researchers' intuition.[8] To address this challenge, an automated MFR-type device, steered by a theory-informed machine learning (ML) algorithm, is needed to synthesize and study metastable materials efficiently.

While MFRs are widely used in catalysis for solid-gas and gas-phase reactions, their use in aqueous precipitation reactions remains limited, often constrained to measuring dissolution rates. The lack of a comprehensive kinetic model tailored to MFR kinetics for suspensions may explain this underutilization. This project developed a variable-volume MFR and an automated kinetic model fit, based on existing kinetic models, [9-12] to make metastable phase synthesis more accessible. The methods was benchmarked using a new Wide-/Small-Angle X-ray Scattering capability (SWAXS), a DOE Office of Science investment. This advancement builds the foundation for studying rapid nucleation and growth kinetics unresolvable by batch reactors and supports ML-based optimization of target properties. Progress on each of the major components of this system are detailed below, with a summarizing schematic shown below (Figure 1).

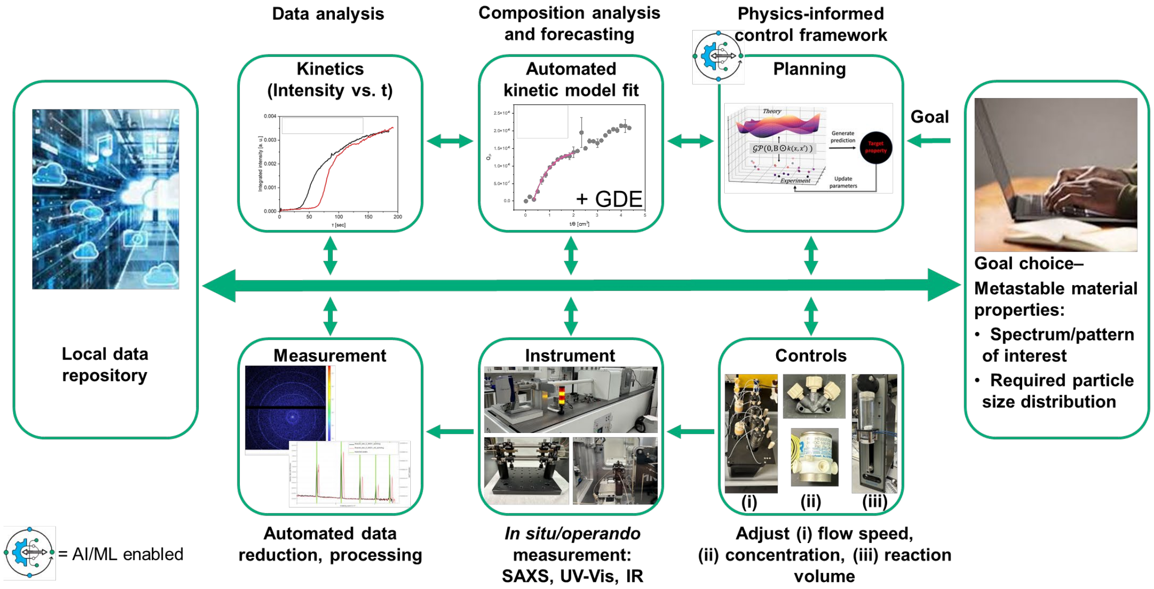

Figure 1. Schematic of the autonomous MFR capability, showing the goal selection on the right, the six components of the system in the middle, and highlighting the integration with the local data repository on the left.

2.0 Flow Cell Development

The project has made significant progress in developing an improved and modular flow cell that prioritizes both accessibility and reproducibility (Figure 2). The experimental flow cell is a silica capillary that is incorporated into a flow loop and held in place by minimal components. The design can be constructed by anyone using off-the-shelf components from major suppliers like ThorLabs and IDEX. This ensures ease of assembly without the need for glue, specialized tools, or equipment. The base, compatible with metric optical breadboard systems, can be used with both laboratory and synchrotron-based setups, enhancing its versatility in diverse research environments. These improvements aim to eliminate user-by-user variability, providing consistent performance across different operators. Additionally, the system's modular design allows for a wide array of experimental conditions and secondary measurements, making it highly adaptable to various applications. This is a significant improvement over flow cells used by PNNL researchers in the past to measure SWAXS at synchrotron light sources.

Figure 2 shows two iterations of the flow cell for the PNNL-based SWAXS instrument. In the first iteration, the system was optimized for stability and to minimize noise (Figure 2 A). This design obstructed the field of view of the instrument, however, limiting its use. Integration of this part uses a vendor-supplied adapter plate. Use of a vendor-supplied adaptor enables the integration of the flow cell with the system, which includes automatic recognition of the sample holder and automatically loaded safety parameters. A second design (Figure 2 B) improved the field of view on the SWAXS detector and allows for additional components to be mounted along with the capillary. This includes mainly calibration standards, which are essential for the automated setup of the instrument. In the future, these additional mounts can be used to develop in situ/operando environments, to measure the sample while applying a magnetic field or while shining a light, for example.

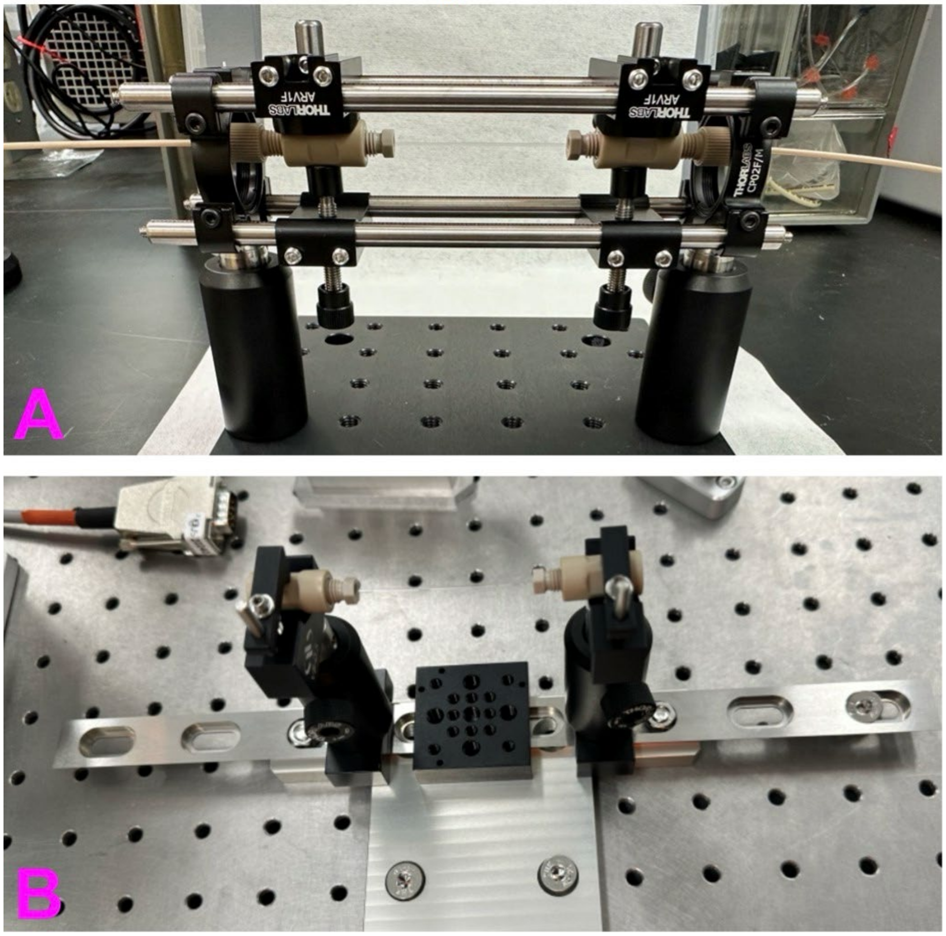

Figure 2. (A) First iteration of the flow cell developed under this project for use in the lab-based SWAXS instrument. (B) Second iteration of the flow cell on the adaptor plate.

3.0 Automated MFR

Design of a stirred, variable volume, automatable reaction vessel was the main challenge for the project (Figure 3). Two key properties that needed to be implemented were i) high chemical compatibility to enable measurements for a large number of different chemical systems and ii) even stirring of the volume to maintain proper mixing needed for the kinetics models to be applicable. These key points were addressed iteratively as the team worked to optimize the reactor specifications. Initial designs established use of a Kloehn syringe pump as the basis for the MFR (Figure 3A). Early iterations produced inadequate stirring and were not leak-proof over the full range of volumes (Figure 3B). Figure 3 C shows the current final design, which features a flexible volume range of 1-2 to 25 mL and stirring capabilities in the 100 to 300 rpm range to ensure precise control over mixing conditions. The system exhibits high chemical compatibility, allowing it to handle a wide variety of chemical environments. The plunger head is 3D printed using a resin-based material, which enables us to tailor reactor materials to specific chemical requirements. This highly adaptable setup makes the reactor suitable for a broad spectrum of applications and experimental setups, while being fully a automatable part of the flow loop.

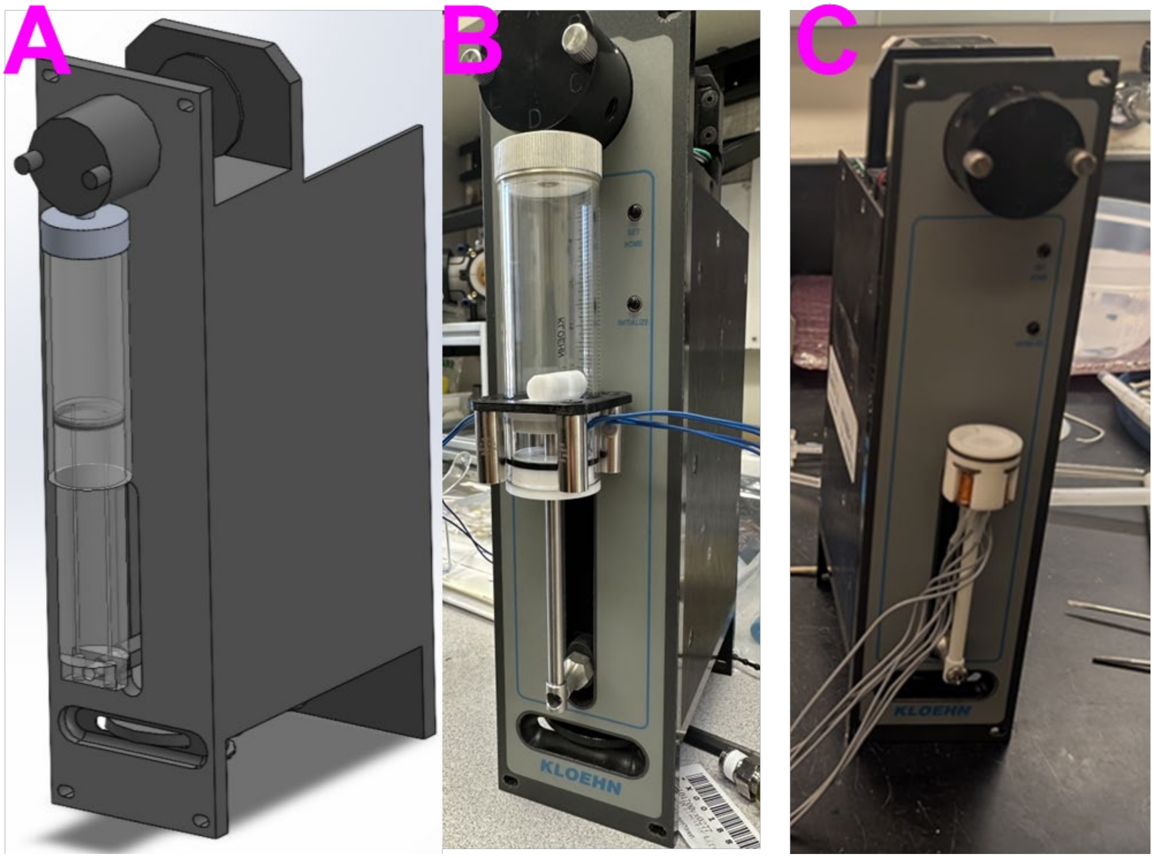

Figure 3. (A) Initial design of the automatable MFR. (B) The stirring was originally added on the outside of the syringe, using 1 N magnets. (C) Later designs moved the stirring into the plunger, to make better contact with the magnetic stir bar.

4.0 Integration with automated SWAXS system

After we completed assembly and testing of the automated components, primarily syringe pumps to control the flow rate, the variable volume MFR, and a set of programmable solenoids to control fluid flow, we needed to integrate this set-up with the SWAXS system. The first step was the automatic alignment of the flow cell. In its current iteration, the vendor-supplied chipped adaptor plate will let the system know that the flow cell has been loaded and where to expect pre-loaded calibrant samples. The system will then automatically move the sample stage to find and measure the calibrant. Successful calibration will update all the motor positions, so that both the sample and instrument detector locations are now indexed. This enables the system to automatically find the sample and set up measurements at specific sample-to-detector locations. This is a key advancement towards the goals of this project and relies on the open-source pyFAI library (Figure 4). Use of this library also opens the door for future iterations of this setup to quickly process data and automatically screen for specific experiment outcomes.

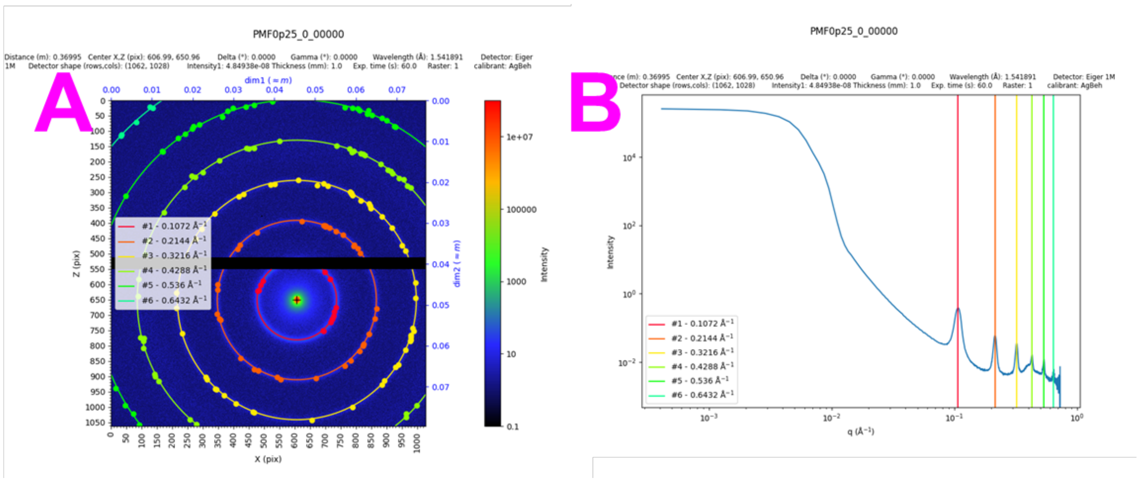

Figure 4. Sample output of the automated alignment script showing (A) the 2D raw data with an overlay of the refined peak positions and (B) the equivalent 1D data in log-log space after reducing the data using a radial integral. The colors match between the two panels, with solid lines indicating the refined peak positions and colored dots representing pixels that were used to come up with initial guesses for each peak.

5.0 Development and application of automated kinetic model

The final automated step to enable autonomous operation of the MFR setup was development and implementation of a kinetics model that can be automatically fit to incoming SWAXS measurements. The purpose of this model is to quickly measure a nucleation rate for a given set of experimental conditions. After some iteration on the ideal model to use, we settled on a physics-based derivative model, adapted from Jensen (2001). This model was initialized on previously acquired data from SAXS measurements at a synchrotron user facility (Figure 5). Figure 5A shows the primary measurement, which is the SAXS curve at low q, where the X-ray scattering is primarily caused by the smallest dimension of nucleating particles. As the number of precipitated particles increases, the signal gets more intense. This intensity can be reduced to the integrated area under the curve, as shown in Figure 5B, and plotted as a function of reaction time. Here, we show the example of amorphous calcium phosphate (ACP) nucleation with (red) and without (black) an organic additive in solution. The additive primarily causes the reaction to be delayed, as evidence by the low integrated intensity early into the reaction. To turn this purely qualitative observation into a quantitative signal, two transformations of the data are necessary.

First, the integrated intensity is turned into the Porod Invariant, Q_P, which is a direct measure of the number of particles in solution. Second, the x-axis is transformed into the number of MFR volumes that have cleared the reaction vessel. This transformation requires knowledge of the flow rate of the reaction and the reactor volume. Because both of these are actively controlled by the automated system, both are known and can be used for this transformation. The resulting plot, shown in Figure 5 C, is now the input for the automated fitting routine developed under this project. Briefly, a least-squares fit is performed on the incoming data to determine i) a lag-time before the reaction begins, ii) a slope of the initial rise in the signal, and iii) the location of an inflection point after which the precipitation rate slows down again. If the mass density of the precipitating phase is known, the result is a delay time and a measured nucleation rate. With these in hand, the system can now iterate the hardware setup to optimize for specific rates. In line with the original purpose of this project, this can be used for any measurement (scattering, spectroscopy, etc.) of a reacting system and builds the basis for the composition analysis and forecasting, as outlined in Figure 1.

Completion of this part of the project enabled the very first fully automated measurements, as shown in Figure 5 D. After automatic calibration and measurement setups, the system automatically completed two measurements of ACP nucleation on the lab-based SWAXS instrument. The data in grey were a repeat of the conditions shown in Figure 5C at higher concentrations. After this experiment, the system then automatically adjusted the reactor volume from 10 mL to 1.5 mL and repeated the experiment at an the same flow rate, shown in magenta. Using this smaller reaction volume, the system can “zoom in” on the kinetics that precede nucleation phenomena. In this case, we observed rapid formation and dissolution of a previously unknown pre-cursor in a part of the reaction curve where we only expected a flat signal. *This initial experiment demonstrates that the automated experimental platform we built under this project A) is ideally suited for measurements of the kinetics of short-lived intermediates and B) can access kinetic regimes previously inaccessible to lab-based systems, revealing previously unknown phenomena for well-characterized systems.*

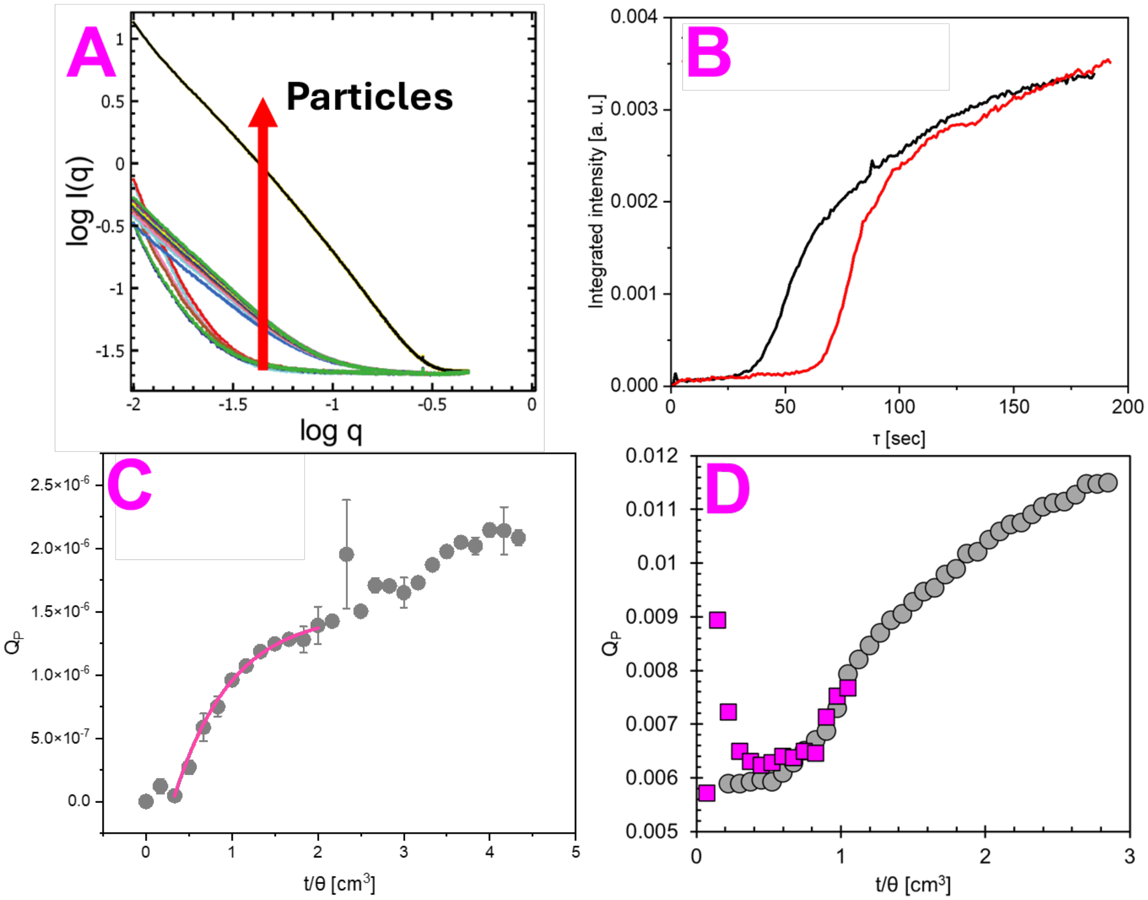

Figure 5. SAXS-based measurements of precipitation kinetics. (A) Time-resolved measurements show nucleation of particles. (B) Automatic integration of the SAXS curves demonstrates progression of the reaction with (red) and without (black) an additive present. (C) Example of automated data reduction and fitting with a first-order reaction kinetics model. (D) Comparison of two nucleation measurements on the lab-based system reveals our experimental platform works and is able to access kinetic regimes that have not been previously possible, especially on lab-based systems

6.0 Future Work

Developments from this project are already used by other LDRD initiatives (NETS) and DOE-BES base programs to automate existing workflows and develop set-ups for synchrotron user facilities. Future work will focus on the last component of the initially formulated goal of this project: To create a fully autonomous experimental platform for metastable material synthesis. This was not achieved under the current proposal due to the difficulties in building the fully automated system. We will, however, continue to pursue implementation of autonomy, specifically to support future investments to study critical element chemistry and isotopic separations. To this end, we are preparing an LDRD proposal aimed to build an upgraded, combined infrared (IR) spectroscopy-SWAXS flow cell that can optimize and run both measurement independently.

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