SOP For Mixing Experiments

This document describes the SOP for the mixing experiments conducted at Rutgers University.

Lab Location: C-135, Chemical and Biochemical Engineering

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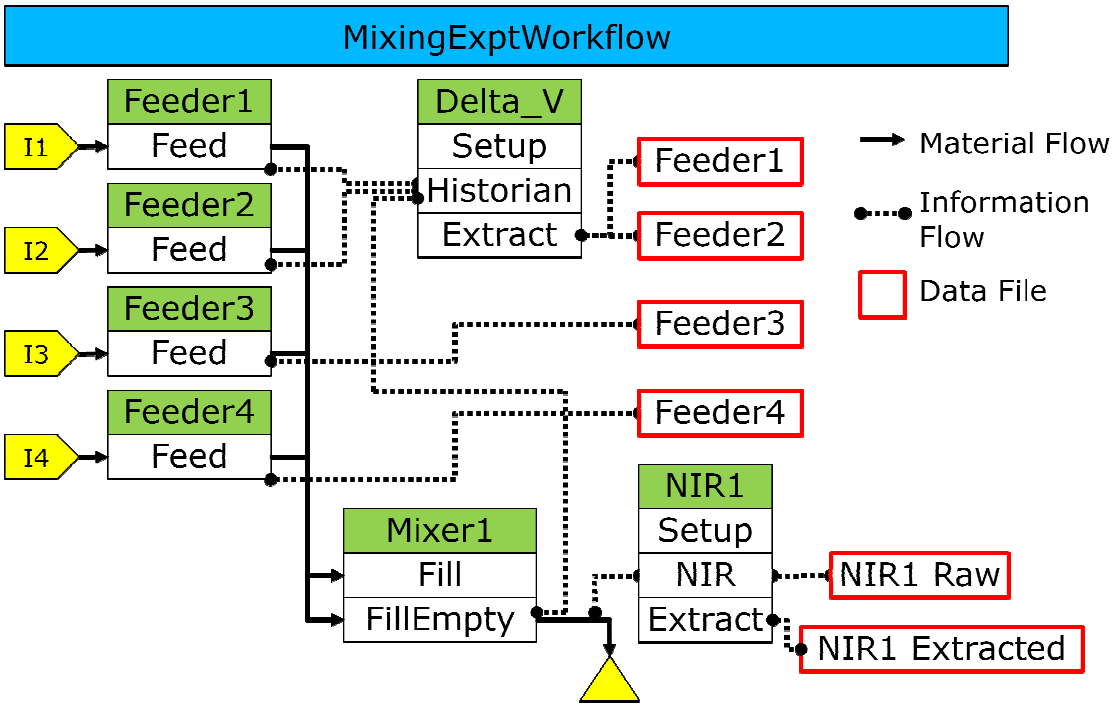
Objective

During each mixing experiment the effect of various operating parameters on the following is studied: mixer hold-up and residence time, residence time distribution in the mixer, and content uniformity of the mixture.

- Hold-up is the amount of powder (kg) in the mixer after flow through the mixer has reached steady state.
- Average residence time is determined from the hold-up (hold-up /feed rate).
- Residence time distribution is calculated from spectral data or off-line analysis by taking samples at different times. From the residence time distribution experiments, the mean residence time and the mean centered variance are calculated to determine the efficiency of the mixer.
- Content uniformity is inferred from the statistical analysis of the spectral data.

Overall Description

The schematic showing the tasks and subtasks of the workflow are shown below. It is based on the input from Eric Jayjock and Juan Osorio.



Up to 4 feeders can be used in a single experiment depending on the mixture being studied. Each feeder handles one component. The material from each feeder falls through a funnel into the inlet of the mixer. At the center of the mixer, a shaft fitted with triangular blades continuously rotates, resulting in a helical motion which pushes the material along the length of the mixer. The material coming of the mixer falls through a pipe, 4" diamenter and 2' long, into a receptacle. An NIR probe is located approximately 1' below the mixer outlet. The tip of the probe is positioned about 1/4" inside the pipe, pointing towards the center of the pipe. The NIR instrument continuously collects the spectral data (every 1 sec?) and saves the spectra in a specified folder along with the values calculated from the data. The spectral data provide the information about the content uniformity of the mixture coming out of the mixer.

(Picture of the experimental setup)

Detailed description

The detailed procedure is organized according to the various operations in the schematic (green rectangles).

Preliminaries:

- Determine the number of components to be mixed for the given experiment, and select the feeders that will be used during the experiment.
- Make sure that the components and experimental equipment are already defined in the database. If they are not, contact the pharmaHUB support.
- Select the duration of the continuous mixing operation, the composition of the resulting mixture (mass fraction of each ingredient) and the throughput of the mixer.
- Compute the amount of each input material that will be consumed during the experiment. Measure and set aside the requisite quantities of each material.
- Perform the initial setup and recommended checks for all the hardware used in the experiment, including connections between the instruments and the Delta-V system where appropriate
- Start the necessary software programs if necessary (Delta-V, NIR etc.)
- Note down the relative humidity, temperature and pressure in the lab
- Note down the lot ids of all the materials used in the experiment
- Create and note down an ID for the experiment. The ID along with other parameters you enter constitute a unique identifier for the experiment for look-up and analysis. Try to generate IDs using some convention which will facilitate subsequent look-up and analysis steps.

Feeders:
Fill each feeder's hopper with the desired material. This could be a one-time or a repetitive step depending on the given experimental conditions. Set the desired flowrate set point for each feeder.

Mixer:
Set the rpm set point, the incline angle and the weir height for the mixer based on the conditions for the given experiment and the mixer being used.

Start-up:
First start the mixer, and then the feeders in sequence. The difference in the starting times for the feeders should be as small as possible. Record data for the feeders and the material coming out of the blender to determine the hold-up, if this has not been done already. After the feed rate out of the mixer reaches steady state, start recording the NIR spectra for residence time distribution. For residence time distribution, an instantaneous input pulse is added in the blender's inlet. Collect samples at the outlet of the blender, for comparison with a different NIR measurement. For mixing homogeneity experiments, start collect time data from the beginning in order to determine when the desired mixing state is reached. Use the data obtained after the mixing state is reached to calculate blend homogeneity (the relative standard deviation).

Hold-up measurement:
After the mixer output reaches a steady state, note down the total mass in the mixer. Mixer hold-up is the difference between total feeder mass minus tear mass. Compute average residence time as mixer mass/total flowrate.

Residence time distribution:
After the measurement of content uniformity, add a measured quantity of a known substance, other than the mixture components, to the mixer input. Note down the substance identity, mass added, and the time at which it was introduced. Measure the NIR spectra for specific amount of time.

Shut-down:
After the predetermined duration, shut down the feeders in sequence and stop recording the NIR data. Let the mixer run until it is empty. As a suitable point stop the mixer. Dispose off the material collected from the mixer.

Post-Processing:
- For the feeders connected to Delta-V, extract the time vs mass data table for the appropriate variable in the historian.
- For the spectral data, execute the chemometrics software that generates the desired properties, such as composition of components. This is automatically generated when it is taking spectral data.

- Note down the file names of the extracted/collected data.
- Use the GUI to record and upload the data on pharmaHUB. You may enter the information throughout the experiment, or as a single session at the end using the required values from the lab notebook.

Data Input through the GUI

In all dialog boxes, the GUI provides choice list for specifying materials and experimental equipment used. Enter appropriate values in the various field in the forms. If a feeder is not used, you do not have to enter any information. All the fields are self-explanatory. Complete all the forms and upload the data clicking the *Submit* button.