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1 Identifying the Source of Blockage

1.1 Visual Inspection

The Asia flow chemistry system is designed to allow the inspection of the majority of the reaction pathway visually. The first point of identifying where any potential blockage has occurred is to visually inspect the flow pathway in sequence.

1) Are the bottled reagents still in solution?
2) Are there any obvious particles observed in the syringes?
3) Are there any blockages in the tubing from the pump to the reactor?
4) Are there any blockages in the reactor itself?
5) Are there any blockages in the tubing from the reactor to the back pressure regulator?
6) Are there any blockages in the tubing from the bpr to the collector (product collector/automated collector)?

1.2 Pressure release

If you cannot see where the blockage occurs through a visual inspection then a systematic inspection of the reaction pathway is required. This is done by releasing the connections in sequence allowing you to see where the build-up of system pressure is released.

1) Start the pumps at a low flow rate to build up pressure in the system, if a blockage is present the system pressure will rise, switch off the pumps before the system reaches the maximum pressure rating of the system to minimise damage.
2) Use the pressure reading shown either through Asia manager or the pump screen, if the pressure drops when releasing the connection drops then the blockage is located in that position. Start from the last connection in your reaction pathway in the following sequence;
    a. Release the connection to the Collector.
    b. Release the connection to the Asia Pressure Controller
    c. Release the connection to the input of the reactor (chip or tube). If more than one reactor is connected in series release the connection to the last reactor first to see which reactor contains the blockage.
    d. Release the connection to the Asia Reagent Injector (if used).

Once the position of the blockage is identified then you can begin to resolve this. If the blockage is obvious then rectifying the issue should be straightforward.

1.3 Common Sources of Blockages

If your reagent solutions are completely homogeneous at room temperature then it is probably unlikely that they will be the problem and precipitate in the reagent bottles.

It is generally observed that most blockages occur when the reagents/reactants are mixed i.e. when a reaction occurs. This can manifest itself in the formation of an insoluble product, by-product or salt formation.

This may occur either at the point of mixing, as the reaction occurs, as the reaction exits a reactor (when it sees a change on temperature) or at a point of restriction.

With this in mind common points of blockages occur at:

1) The mixing section of a chip or tube reactor
2) The point of exit of chip or tube reactor
3) The BPR chip and diaphragm

Care should also be taken when using the Asia Reagent Injector. To avoid the reagent coming out of solution in the injection loop a suitable compatible system solvent needs used to be used. As aliquots are introduced from the injection loop the trailing end of the reagent plug are exposed to the system solvent, if this is likely to cause the reagent to come out of solution a blockage is likely to form in the loop itself.

2 Unblocking the System

2.1 Choosing a Recovery Solvent

It is assumed that the chemistry being performed on the system is known and some understanding of possible products, by-products and salts is known. With this in mind a solvent can be selected that will have a high chance of dissolving any blockage that may be formed. This is known as the 'recovery solvent'. It may be necessary to use more than one recovery solvent to fully remove the blockage.

As a general guide the following tips can be followed to help in selecting the correct recovery solvent.

1) Water - If the blockage is suspected to be an inorganic acid or base or salt
2) Polar Organic Solvents – If the blockage is suspected to be organic
    a. DCM/Methanol
    b. Acetone
    c. Acetonitrile
    d. DMSO
3) Acids – Useful for metal deposits from catalytic systems
    a. 2M HCl/MeOH

Note however if using stainless steel reactors then strong acids are incompatible.

2.2 Unblocking Tubing

If the blockage has been identified to be in a length of tubing connecting any two modules or reactors it should be straightforward in removing any blockage.

The simplest was to do this is to connect one end of the tubing to a luer lock syringe fitting and push through the recovery solvent to remove the blockage. Care should be taken if not using a luer lock syringe as the pressure generated in trying to push the solvent through may cause the syringe and connector to fly off.

If the blockage is not easily removed replacing the length of tubing is the quickest solution.

2.3 Standard Chip Cleaning

The simplest way to clean chips after use is to leave the chip connected to the system and use the pumps to pass a recovery solvent through them.

However, it will be necessary to purge the tubing prior to the chip with the recovery solvent selected.

1) Replace the solvent or reagent solution with the recovery solvent you wish to use in the Asia Pressurized Input Store, remove the reactor input tubing to the reactor and pump a suitable volume of solvent to waste to ensure the reactor input tubing is completely full with the recovery solvent.
2) Re-connect the reactor input and make sure the output is not connected to the BPR begin pumping the recovery solvent at a low flow rate.

It is advisable to pump at low flow rates to avoid over pressurising the system. To avoid over-pressurising the system when unblocking a reactor;

1) pump just one channel at a low flow rate
2) ensure the BPR is not connected
3) set the over-pressurisation limit to that below the maximum operating pressure of the syringe used

It may be necessary to reverse the flow through the reactor. To do this simply connect the tubing containing the recovery solvent to the output and connect a ‘spare’ length of tube to the input.

The direction of the flow of solvent will depend on where the blockage has occurred. If the blockage is near the input then reversing the flow through the reactor may help pump this out rather than pumping it ‘through’ the reactor.

If the blockage in a reactor is proving to be stubborn there are other techniques that may assist in removing the issue;

1) Raising the reactor temperature to assist in solubility. Note however if you are raising the temperature above the recovery solvent boiling point make sure the BPR is connected and the Pressure Controller set to an appropriate setting.
2) Place the reactor in an ultrasound bath whilst pumping. This will aid in breaking up a solid blockage, helping its removal.
3) As a last resort it may be possible for chips only to pyrolize the contents of the chip using the heater and then pumping NaOH (aq) to dissolve the contents.