# The Basics Of Flow Chemistry

## 1 Summary

This application note gives information on the basics of flow chemistry, with particular reference to the Africa system.

## 2 Batch vs Flow Reactions

<table>
<thead>
<tr>
<th>Batch</th>
<th>Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addition of “A” then “B” once</td>
<td>Addition of “A” and “B” continuously</td>
</tr>
<tr>
<td><img src="image1" alt="Batch Diagram" /></td>
<td><img src="image2" alt="Flow Diagram" /></td>
</tr>
</tbody>
</table>

- **Batch**: Traditional batch reactor e.g. round bottom flask, vial, microtitre plate etc.
- **Flow**: Continuous flow micro reactor

## Diagram

1. **Batch** Diagram:
   - Reagent A
   - Reagent B
   - Reaction Mixture

2. **Flow** Diagram:
   - Reagent A
   - Reagent B
   - Reaction Mixture
   - `~200µm`
   - `>5mm`
3 Flow Chemistry

3.1 Flow Rate, Residence Time, Reactor Volume & Production Rate

In a flow reactor, the residence time of the reagents in the reactor chip (i.e. the amount of time that the reaction is heated or cooled) is calculated from the volume of the reactor and the flow rate through it.

\[
\text{Residence time} = \frac{\text{Reactor Volume}}{\text{Flow Rate}}
\]

Therefore, to achieve a longer residence time, you can either pump more slowly and/or use a reactor with a larger volume. In this way, Africa is able to operate with reaction times from a few tens of seconds to a few hours. The Africa software automatically calculates the flow rate required to give the desired residence time.

The software also indicates when the calculated flow rate is either too high or too low for the pumps to supply, and therefore it is necessary to use a larger or smaller chip or to fit larger or smaller syringes to the pumps.

For the same given residence time one can either choose to use a larger reactor (and therefore larger flow rate) or a smaller reactor (and therefore smaller flow rate). The key difference is that with a large reactor, more material will be synthesised in a given time. In practice, this means Africa can be used to synthesise mg to gram quantities.

3.2 Diffusional Mixing in Microreactors

In Africa micro reactors, reagents do not mix by turbulence (as in a round bottom flask); instead, the reagents mix by diffusion. Because the distance across the channel is ≈200µm, the time taken for reagents to completely diffuse is in the order of seconds. At typical Africa flow rates, this corresponds to less than 10mm of flow along reaction channel. Note that the total length of the reactors is ≈1m!

3.3 Pressure

3.3.1 Back Pressure due to flow

When a liquid (the reaction) flows through a “tube” (the reactor) there is an inherent resistance to its flow. This resistance or backpressure is dependent upon a number of physical factors. Thus smaller reactor cross section, longer reactor length, higher flow rates and more viscous liquids all generate higher backpressure. The reactor chips used by the Africa system are specifically designed to generate low backpressure.
3.3.2 Pressurising & Superheating Reactions
Using the Africa Pressurisation Module it is possible to pressurise a reaction by applying a chosen pressure to the output of the reactor. This allows reactions to be heated to temperatures above the boiling point of the solvent, thereby increasing reaction rates.

Examples of the superheating affect that can be achieved include
- DCM @ 100°C (vs 40°C at atmos. press.)
- THF @ 140°C (vs 66°C at atmos. press.)
- Dioxane @ 180°C (vs 100°C at atmos. press.)

3.3.3 Pressurising with Gas Evolution
It is also possible to apply pressure to an Africa flow reactor to suppress the evolution of gas. (This is beneficial because if gas bubbles are formed they can propel the reaction mixture out of the reactor leading to uncertain residence times).

3.4 Heat Transfer
The surface area to volume ratio of the reaction mixture in an Africa flow reactor is very large. This means that heat can be added to or removed from the reaction mixture more rapidly than in a batch reactor. It also means a constant temperature can be maintained for reactions which are exo- or endothermic.

![Graph showing temperature vs time for batch and flow](image)

3.5 Order & Timing of Reagent Addition
In a batch reaction, reagents are typically added sequentially, even when it would be advantageous to add all reagents simultaneously. In an Africa reactor chip up to three reagent streams can be combined simultaneously.

![Diagram of reagent addition](image)
In flow it is possible to achieve exact timing of sequential reagent addition. In this case, more than 1 chip can be used as demonstrated below.