Self-optimizing platform for green chemistry synthesis

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Nikita A. Ivanov, Sven Kochmann and Sergey N. Krylov
Department of Chemistry, York University, Toronto, Ontario, M3J 1P3

Victoria Corless, Frank Lee and Andrey Yudin
Davenport Research Laboratories, Department of Chemistry, University of Toronto, Toronto, Ontario, M5S 3H6

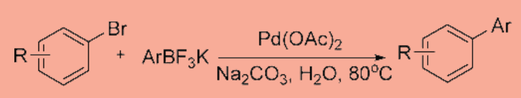
YORK UNIVERSITÉ UNIVERSITY

MOTIVATION

The goal of this project is to develop a continuous and stable system for chemical synthesis and separation with a number of automated feedback mechanisms, capable of adjusting reactant supply & buffer flow rates, as well as electric field intensity. Microscale continuous chemical synthesis is very popular in chemistry, as it offers multiple advantages over classical batch techniques. Microreactors possess laminar flow profiles, short diffusion paths, high surface-to-volume ratio (improved heat exchange) and short mixing times (higher mass transfer coefficient). These advantages allow a high level of control over the reaction by regulating the reactants supply rates, as well as residence times at different intervals. Following synthesis, each substance has to be purified. Current procedures for reactor product analysis break the continuity of the system. Offline methods such as CE or HPLC are often required to calculate the yield and production rate. In contrast, Free Flow Electrophoresis (FFE) allows simultaneous separation of analytes, doesn't break the system continuity and requires no separation matrix. By quickly analysing all products at the FFE outlets, it becomes possible to fine-tune the reactor for specific yields or production rates.

SYNTHESIS

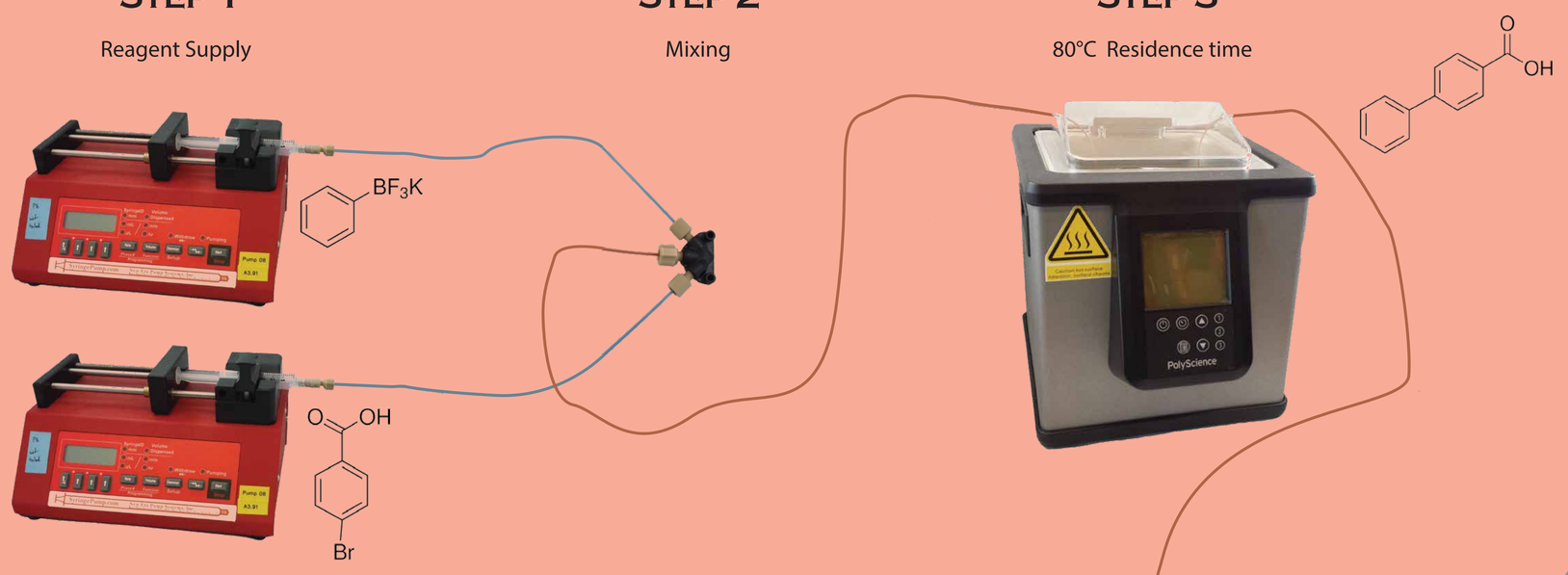
Chemical synthesis is the first step of the platform in development. With the help of our collaborators, we have successfully selected our first "proof of principle" chemical reaction – Suzuki-Miyaura Coupling in water. This particular reaction proved to be exceptionally convenient.
We can resolve every single component by applying an electric field (all elements have a charge at neutral pH). Information from "Detection & Feedback" is analysed and pumping rates are adjusted according to the operator's demands.



Step 1
Reagent Supply

Step 2
Mixing

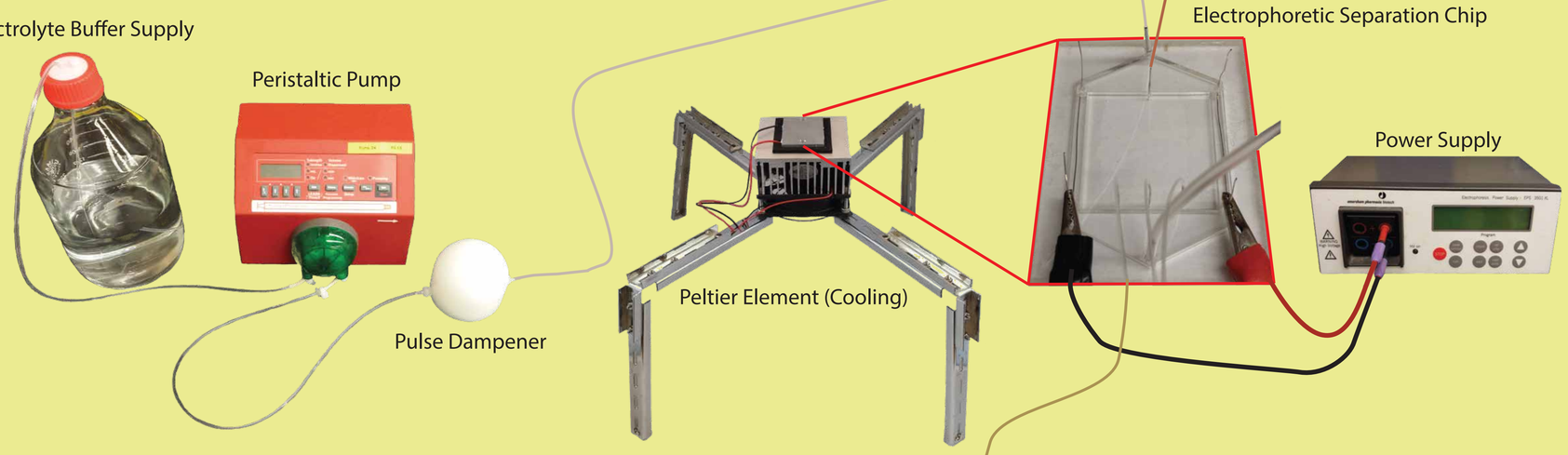
Step 3
80°C Residence time



SEPARATION

Continuous-flow separation is achieved when a continuous-flow microreactor exits into a wide purification channel in which products are separated in the direction orthogonal to the flow and continuously collected at the exit of the channel. An existing continuous flow purification technique, Free Flow Electrophoresis (FFE), is naturally suited for combination with continuous-flow microsynthesis in aqueous solution. For the separation to work at least one or more elements of the reaction need to have a charge when diluted in the FFE electrolyte buffer. Molecules (ex. Toluene pKa=40) that don't acquire a charge within attainable pH buffering ranges remain unresolved in the electric field.
As of now, majority of FFE implementations deal with visible or labelled substances and completely avoid transparent chemical species often used in CFS.

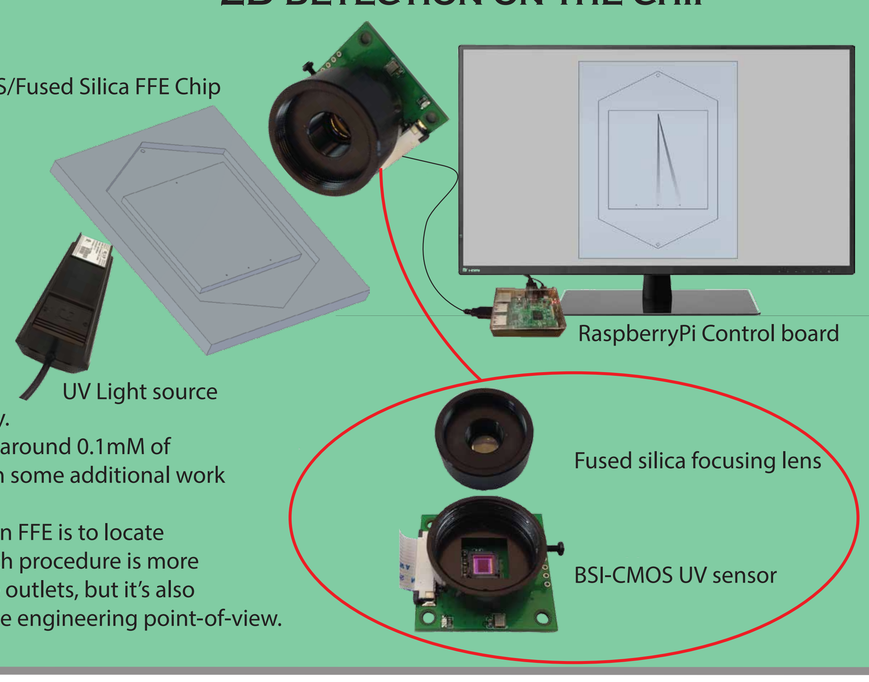
Free Flow Electrophoresis



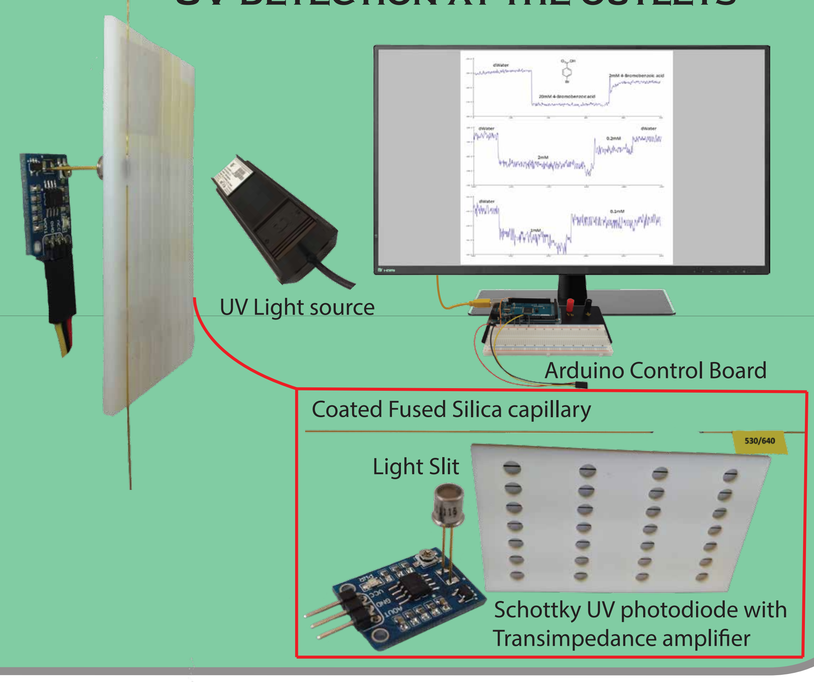
DETECTION & FEEDBACK

Most organic compounds are invisible to a naked eye. Much of our effort has been put into developing potential ways of detecting chemical species on the chip and after FFE separation. Machine vision ideas have been adapted from other fields such as dissolution and atmospheric chemistry.
Based on a simple design, we have assembled our first prototype from the UV lamp, 3D printed light slit, UV sensor, microcontroller board and polyimide coated fused silica capillary.
Without any optimisation the practical LOD was around 0.1mM of 4-Bromobenzoic acid. We are confident that with some additional work lower LODs could be achieved.
Another approach to organic species detection in FFE is to locate them directly on the chip during separation. Such procedure is more advanced and more useful than detection at the outlets, but it's also substantially more diffcult to implement from the engineering point-of-view.

2D detection on the chip



UV detection at the outlets



References

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2. Liu, L.; Dong, Y.; Pang, B.; Ma, J. The Journal of organic chemistry 2014, 79, 7193-7198.

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