Steady-State Continuous-Flow Purification: Key to Small-Scale Chemical Manufacturing

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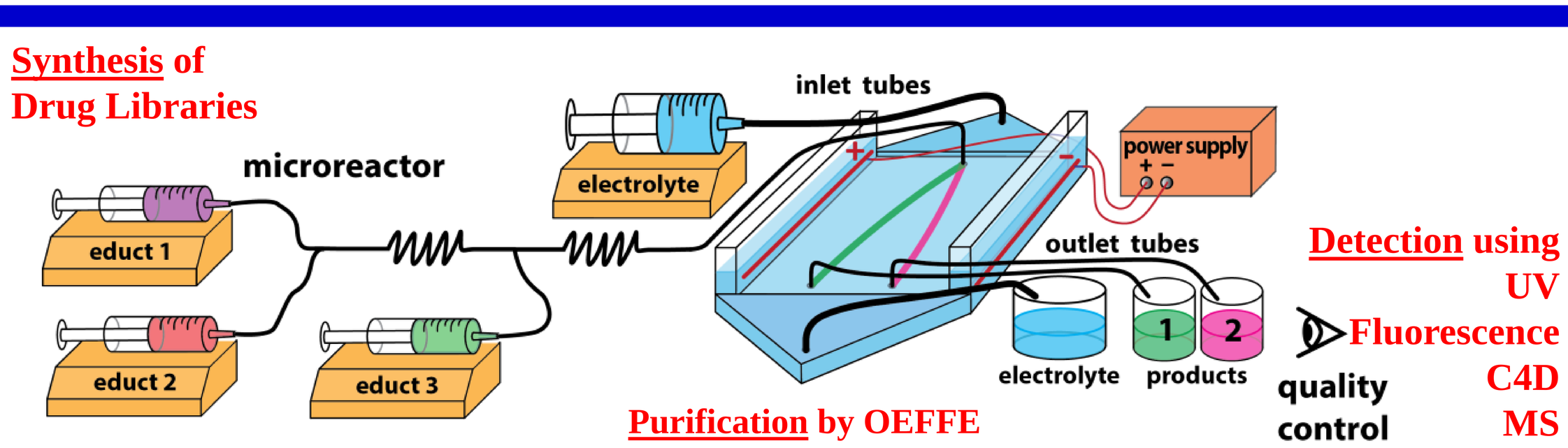
Motivation

Continuous microsynthesis has a number of important advantages over batch synthesis (control, greater yields, 'greener'). To fully exploit these advantages, continuous-flow microsynthesis should be followed by continuous-flow purification in a compatible scale. A practical and universal combination has not yet been realized due to a lack of a suitable purification technique. Free flow electrophoresis (FFE) is naturally suited for combination with continuous-flow microsynthesis in aqueous solution. Ideally, continuous monitoring throughout the entire scheme should be available. See the figure below for our suggested scheme.



Purification by Open-Electrolyte FFE (OEFFE)

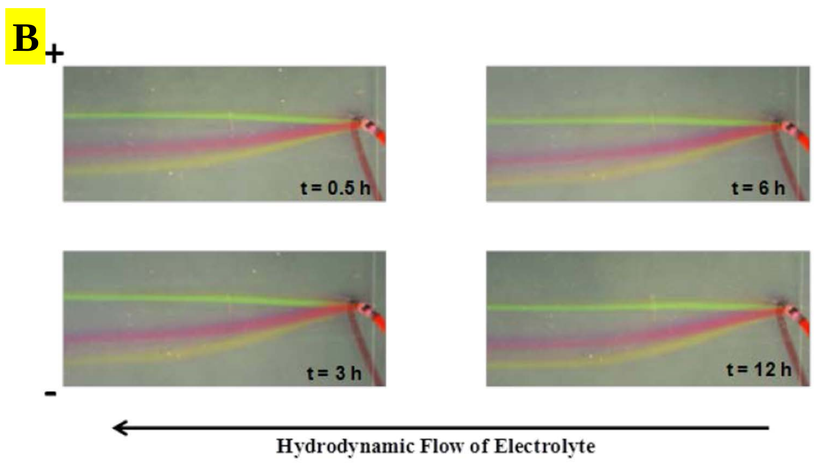
Advantages:

A) Steady-State Bubble Removal

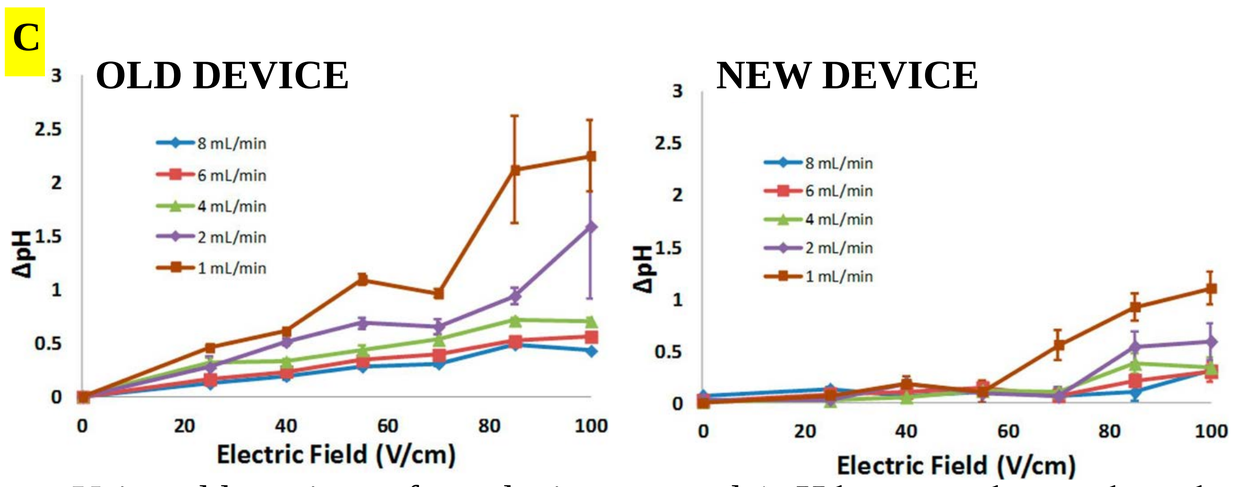
B) Long-Term Steady-State Separation

C) Steady-State pH Uniformity

Chimneys evacuate bubbles, and prevent their interference with separation quality



Fluorescein, rhodamine B, and rhodamine 6G (all at 250 mM) are separated using OEFFE over 12 hours using an electric field strength of 67 V/cm, a sample flow rate of 10 µL/min, and a buffer (10 mM HEPES at pH = 7.5) flow rate of 8 mL/min.[1]



Using old versions of our devices created ΔpH between the anode and cathode. By changing the channel geometry in new devices we have minimized the ΔpH over a broad range of flow rates and electric field strengths, without compromising the quality of separation.[2]

Conclusions and References

Our developing work using OEFFE as a continuous-flow purification technique can facilitate the integration of continuous-flow synthesis-purification-detection. Currently, we are pursuing FFE-MS assemblies. FFE-MS would enable the label-free detection of a wide variety of analytes. Our desire is to develop a continuous-flow platform of small-molecule drug libraries, which could be used as a rapid approach for combinatorial chemistry. Such a platform would be profoundly useful for both academic and industrial labs.

[1] F.J. Agostino *et al.* Angew. Chem. Int. Ed. DOI: 10.1002/anie.201300104

[2] F. J. Agostino *et al.* Anal. Chem. DOI: 10.1021/ac501081b