Free-flow electrophoresis (FFE) in continuous flow organic synthesis

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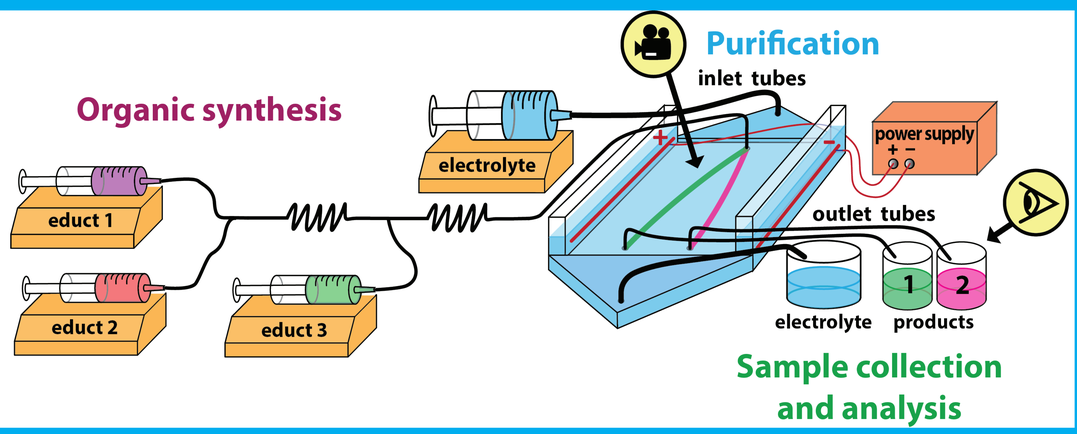
Introduction

Continuous-flow processes have demonstrated their value as a practical tool for organic synthesis by providing several benefits in terms of increased yield, automation capability and safer conditions. Downstream purification of such processes is crucial to ensure high product purity and operation efficiency. Such purification requires continuous-flow separation of hydrophobic compounds, which demands spatial divergence of an input flow of organic mixture into individual streams with minimal technical complexity. Since most organic reactions are incompatible with aqueous solvents, it seemed only logical to search for new non-aqueous electrolyte systems that can be easily implemented and benefit from previously developed FFE ideas and designs.

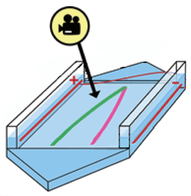
Electrophoresis for organic synthesis?

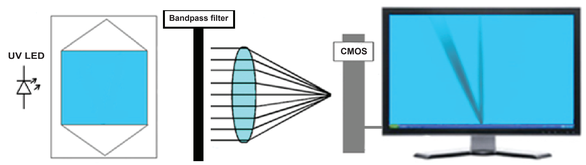
Conventional FFE is limited to aqueous media for separation of hydrophilic compounds. It is advantageous to expand the scope of FFE to hydrophobic compounds. Solubility can be improved by adding organic solvents into aquous background electrolytes (BGEs). However, such modifications suffer from incomplete solvation of purely hydrophobic compounds and are not sufficient to overcome the incompatibility between aqueous phase in FFE and organic chemical processes. Thus, we proposed applying purely non-aqueous solvent (Propylene Carbonate) and BGEs (Tetrabutylammonium-Acetate) to FFE to address these issues.

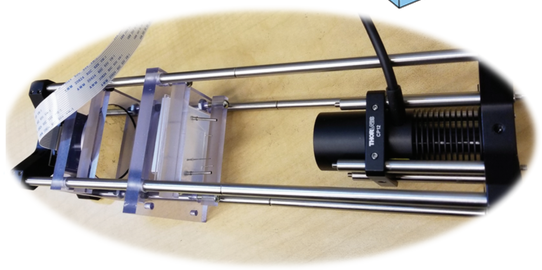


2D UV Imaging

Majority of organic compounds do not absorb in visible spectrum. We are developing tools for imaging directly on the chip.

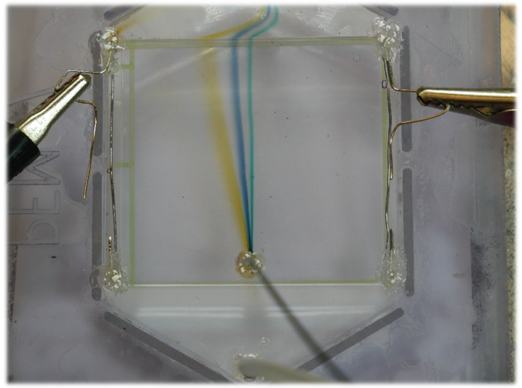






Preliminary results

Ten hours of steady separation of three hydrophobic compounds (Sudan Black B, α-Naphtholbenzein, 2-[4-(Dimethylamino) styryl]-1-methylpyridinium) was achieved with minimal band broading and bubble generation. It is a first step towards establishing NAFFE as a practical tool for downstream purification of organic continuous-flow processes.



Conclusion

We introduce a robust and easy-to-implement continuous-flow separation technique for multiple hydrophobic compounds. It is based on free-flow electrophoresis (FFE), which utilizes an electrical field perpendicular to the input hydrodynamic flow to separate compounds based on their difference in electrophoretic mobility.

Agostino, F. J., Cherney, L. T., Galievsky, V., & Krylov, S. N. (2013). Steady-State Continuous-Flow Purification by Electrophoresis. Angewandte Chemie, 125(28), 7397-7401.

Kochmann, S., & Krylov, S. N. (2018). Quantitative characterization of molecular-stream separation. Analytical chemistry, 90(15), 9504-9509.

Kochmann, S.; Krylov, S.N. Image processing and analysis system for development and use of free flow electrophoresis chips. Lab on Chip 2017, 17, 256-266. (PDF file)

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