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FNSNF

Microfluidic Sample Preparation for IR-Detection of Cocaine in Human Saliva

Philip Wägli, Alexandra Homsy, Nico F. de Rooij

Ecole Polytechnique Fédérale de Lausanne (EPFL), Sensors, Actuators and Microsystems Laboratory (SAMLAB), Neuchâtel, Switzerland

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
samlab The Sensors, Actuators and Microsystems Laboratory

Motivation:

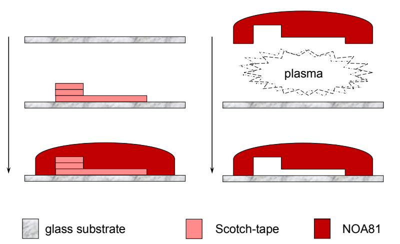
The aim of the project is the detection of cocaine in human saliva by attenuated total reflection infrared (ATR-IR) spectroscopy. Since water is adsorbing the IR light of interest, we decided to bring the analyte to an IR-transparent solvent (tetrachloroethlyene, PCE) by droplet-based liquid-liquid extraction.

Benefits of droplet-based liquid-liquid extraction:
- faster diffusion (increased interface)
- cocaine preconcentration (ratio of flow rates of different phases)

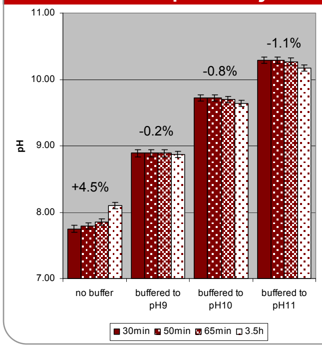
filtration → pH adjustment → Droplet Generation → Liquid-Liquid Extraction → Droplet Merging → ATR-IR Spectroscopy →

Microfluidic Chip Fabrication:

Rapid prototyping with UV-curable adhesive NOA81 [1] using Scotch-tape masters:



pH Adjustment:

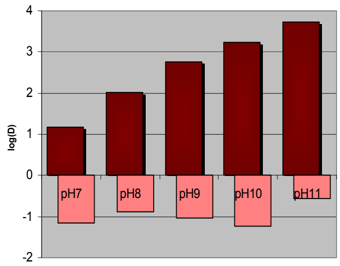


ISFET measurement

saliva buffering systems:

- bicarbonate buffer (changing by exposure to air)
- phosphate buffer
- protein buffer system (buffering acids)

Distribution Coefficient:



UPLC-MS measurement

cocaine in PCE:
@ pH 7, 94%
@ pH >8, >99%

$$\log D = \log\left(\frac{c_{cocaine(PCE)}}{c_{cocaine(saliva)}}\right)$$

$$pKa_{cocaine} = 8.6$$

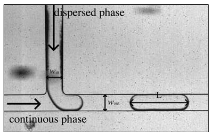
$$pKa_{benzylegognine} = 2.3/11.2$$

Improved Droplet-Based Liquid-Liquid Extraction:

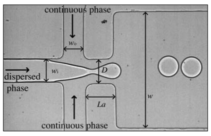
Droplet Generation

State of the Art:

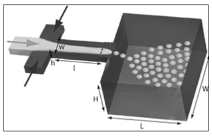
Microfluidic methods for droplet generation:



T-shaped junction [2]
(shear-stress, flow obstruction)

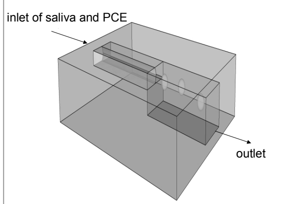


Flow-focusing device [3,4]
(hydrodynamic focusing)

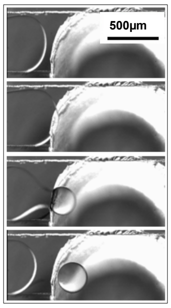


Nano terrace – reservoir [5]
(capillary focusing)

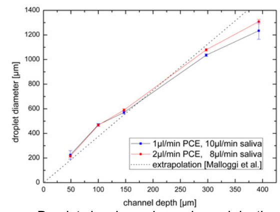
IrSens:



3D schematic of droplet generation step in microfluidic channel (100µm to 1000µm)

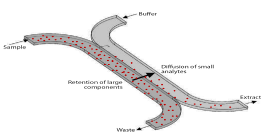


Droplet generation process during 30ms
(8µl/min saliva, 2µl/min PCE)

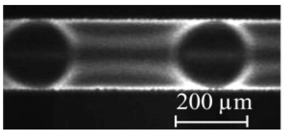


Droplet size depends on channel depth.

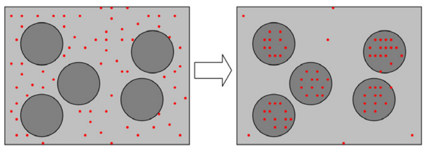
Liquid-Liquid Extraction



Microfluidic H-filter [6]

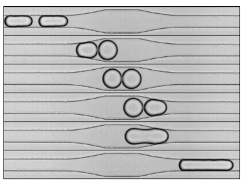


Droplet-based liquid-liquid extraction [7]

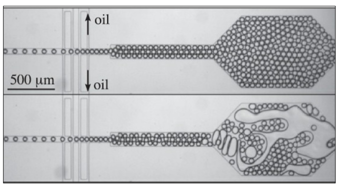


Schematic of improved droplet-based liquid-liquid extraction

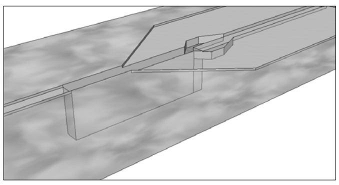
Droplet Merging



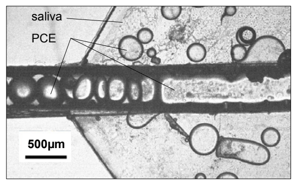
Separation-driven coalescence [8]



Phase inversion device [8]



3D schematic of droplet merging device



Microscope image of merging zone
(15µl/min saliva, 6µl/min PCE)

[1] Wägli, Ph., et al., *Norland optical adhesive (NOA81) microchannels with adjustable wetting behavior and high chemical resistance against a range of mid-infrared-transparent organic solvents*, Sens. Act. B, 2011.**156**(2): 994-1001.
[2] Thorsen, T., et al., *Dynamic pattern formation in a vesicle-generating microfluidic device*, Phys. Rev. Lett., 2001. **86**(18): 4163-4166.
[3] Anna, S.L., et al., *Formation of dispersions using flow-focusing in microchannels*, Appl. Phys. Lett., 2003. **82**(3): 364–366.
[4] Dreyfus, R., et al., *Ordered and disordered patterns in two phase flows in microchannels*, Phys. Rev. Lett., 2003. **90**: 144505.
[5] Malloggi, F., et al., *Monodisperse colloids synthesized with nanofluidic technology*, Langmuir, 2009. **26**(4): 2369-2373
[6] Yager, P., et al., *Microfluidic diagnostic technologies for global public health*, Nature, 2006. **442**(7101): 412-418.
[7] Mary, P., et al., *Microfluidic droplet-based liquid-liquid extraction*, Anal.Chem, 2008. **80**: 2680-2687.
[8] Bremond, N., et al., *Propagation of Drop Coalescence in a Two-Dimensional Emulsion: A Route towards Phase Inversion*, Phys. Rev. Lett., 2011. **106**(21): 214502.