



Playing with Droplets

Modular Droplet-based Microfluidics with Sensory Particles

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Microfluidic devices are powerful analytical tools with appealing features such as miniaturized size, low reagent and sample consumption, rapid response and short measurement times. As society wants to be ever better, earlier and more comprehensively informed about critical factors in life, work, and the environment, the demand for powerful measurement devices for use outside of the laboratory constantly increases.

Whether for environmental monitoring, the detection of hazards, process control or point-of-care diagnostics, one of the most promising formats for in-the-field liquid sample analysis are microfluidic devices. Although tremendous progress has been achieved in analytical tool integration and miniaturization in the past two decades, a wealth of synergisms can still be expected from a combination of sensitive optical detection, in particular fluorescence, with the chemical sensing power of tailored indicator particles and the processing opportunities that miniaturized analytical systems offer. However, a significant part of the non-academic community is still hesitant to exploit microfluidics widely, presumably because of the complexity of the required infrastructure for the manufacturing of customized chips and their instrumental environment. Alternative approaches use modular sys-

tems that offer high flexibility as well as facile handling and assembly. Such low-cost devices cannot only be used for single-liquid applications, but liquid-liquid droplet handling is also possible while relying on “off-the-shelf” components.

Modular Off-the-shelf Microfluidics

Typically, microfluidic systems are constructed in monolithic form by means of microfabrication and, increasingly, by additive manufacturing techniques. The desire to make microfluidic technology more accessible has led to the notion of “modular microfluidics”, where users can build a fluidic system using a toolkit of building blocks [1,2]. This approach is analogous to the electronics industry where discrete electronics design (breadboards) can often provide a faster time-to-market than ASICs (application specific integrated cir-

uits). In modular microfluidics, discrete standard components or commercially available cross-junctions can be used, allowing designers to build large-scale microfluidic systems in three dimensions that are modular, diverse and predictable by simple network analysis techniques. For example, a modular approach for building a droplet-based system for optical sensing would require four integral steps of droplet generation, mixing, storage/reaction and optical interrogation.

Tubing System for Droplet Handling

For optical fluorescence sensors, droplet-based liquid handling is essential because small confined volumes allow better to reach signal intensities required for trace detection. Considering this, a modular microfluidic setup was conceived entirely from micrometer-sized PTFE (polytetrafluoroethylene) and PFA (perfluoroalkoxyalkane) tubes connected by commercially available micro-connectors. This flexible design is also advantageous as it offers to integrate multiple inlets or biphasic stop-flow setups, which in turn enable many ways of sensory particle handling.

As in conventional microfluidic chips, stable and homogeneous water droplets were generated in a commercial micro T-cross because of the shear forces and interfacial tension at the fluid-fluid interface. The continuous organic phase that has a lower interfacial tension with the channel walls was injected in-line with the outlet while the aqueous phase was injected perpendicularly. Depending on the flow rates, droplets were generated with frequencies from 0.5 to 1.5 Hz and volumes from 25 to 300 nL.

Mixing, reaction and/or extraction were then achieved by chaotic advection in the outlet tube (PFA) that was simply rolled in a serpentine around a metallic bar. Optimization of the fluidic system was then greatly facilitated by its modularity: a 2-fold decrease of the flow rates for instance could be simply achieved by shortening the tube with scissors instead of going through the whole manufacturing cycle for a new chip. Such simple adaption of the tubing length is usually sufficient to obtain quantitative reaction or extraction. Moreover, the use of tubes with inert PTFE-PFA walls resulted in highly reproducible experiments with no memory effects, even when dispensing with regular rinsing cycles of the fluidic system. Besides flexibility, PFA tubes are

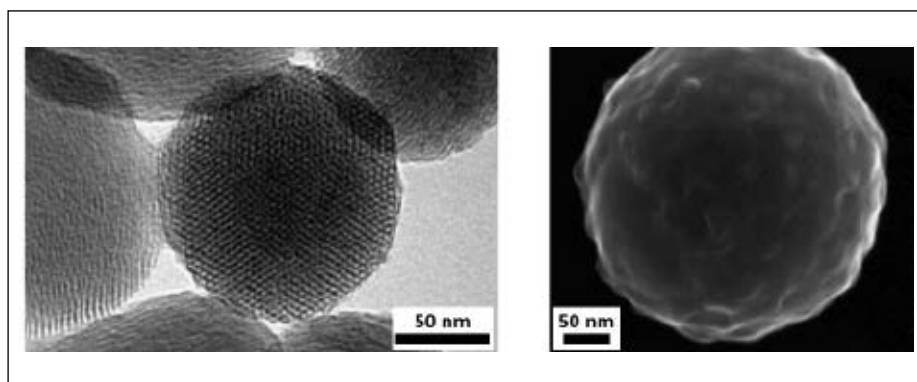


Fig. 1: Sensory particles used in microfluidic chips: a) MCM-41-type MSNs and b) SiO₂ core/MIP shell microparticles

also transparent, facilitating direct fluorescence signal collection.

Integration of Fluorescent Sensory Particles

This concept was adapted recently for two different sensory particles, silica core microparticles that carry a few-nanometer thin molecularly imprinted polymer (MIP) shell which indicates the pesticide 2,4-dichlorophenoxyacetic acid (2,4-D) by fluorescence enhancement [3] and a mesoporous silica nanoparticle- (MSN) based gated indicator release system for Hg²⁺

trace detection in drinking water [4]. The SiO₂ core-MIP shell particles contain a fluorescent probe monomer co-polymerized directly into the MIP layer which “lights up” upon binding of the small-molecule analyte 2,4-D. These particles are employed in the organic phase. The analyte is thus extracted from the water phase and indication happens in the organic phase. Homogeneous water droplets were generated in the chloroform carrier fluid in a T-shaped microdroplet generator without pre-treatment and both, extraction and indication were achieved in 100 s.

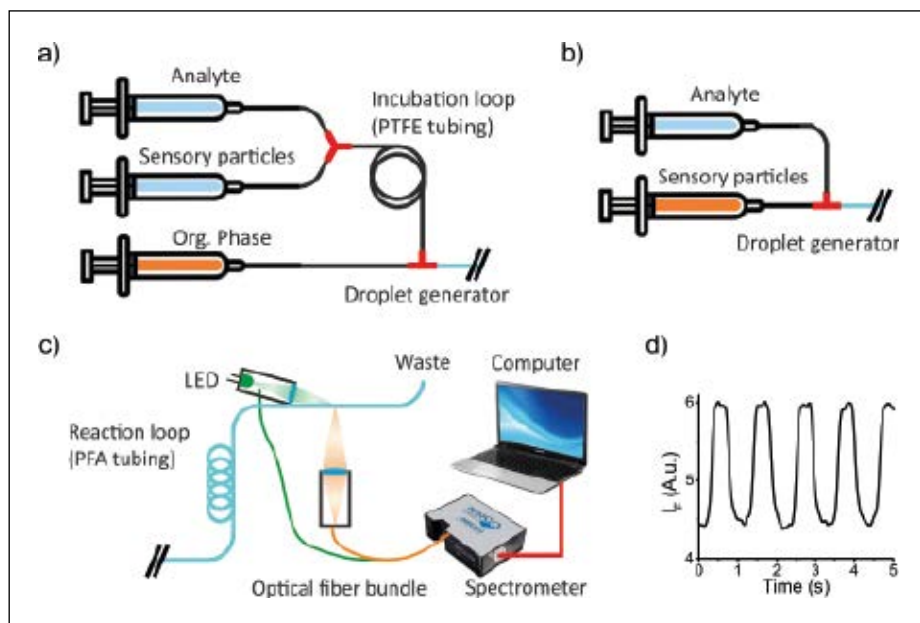


Fig. 2: Scheme of the modular microfluidic system based on PTFE and PFA tubing. Assembly until droplet generation for a) the gated indicator release system for Hg^{2+} detection and b) SiO_2 core/MIP shell particles for 2,4-D detection. c) Reaction and optical detection setup for fluorescence analysis of droplets. d) Typical signal measured by the spectrometer with single-droplet fluorescence.

The gated indicator release system consists of MSNs that were loaded with an indicator dye before the pore openings were capped with stoppers that react selectively with Hg^{2+} . These particles are employed in the water phase. If Hg^{2+} is present, uncapping occurs, the dye is released into the water phase and subsequently extracted into the organic phase. Therefore, an incubation step had to be implemented prior to droplet generation in the organic phase, which was accomplished simply by use of a tube with an appropriate length. Aqueous sample and MSN suspension were injected into an incubation loop using a Y-connector, equivalent to 100 s of dwell time, before homogeneous water droplets were generated in a dichloromethane carrier fluid within a T-shaped microdroplet generator. Quantitative phase transfer of the dye occurred in ca. 8 min.

Complete Analytical Device

Fluorescence detection required a modular optical setup for which a standard opto-mechanical filter cube was used. Because tubes were used, any angle between exciting beam and emission collection optics is possible, allowing us to use 90° for optimum suppression of scattered light. Not only is this angle often difficult to realize in conventional microfluidic chips, but also is the tubing approach much more flexible regarding mounting LED excita-

tion source and detection optics. To improve the signal-to-noise ratio, a band pass filter was inserted between LED and the lens used to focus the beam into the tube. Fluorescence light was focused through a band pass filter and collected through a bundle of six optical fibers into a USB spectrometer. After signal acquisition, numerical data treatment with logic equations allowed to extract the fluorescence intensity of the organic phase containing either the core-shell MIP particles or the released dye, depending on which assay was carried out. Use of the logic equations along with separation of the signals from both phases facilitated identification and removal of outliers that may have arisen from gas bubbles or particle aggregates.

The setup performed well for both sensors with acceptable standard deviation for the fluorescence measurement of 0.5–1% after signal acquisition for 100 s. Concentrations of 2,4-D and Hg^{2+} down to 20 nM and 0.1 nM, respectively, were detectable with a linear range up to μM concentrations, principally matching the EU, WHO and/or EPA requirements for ground and drinking water [5–7].

Outlook

For an actual real-time monitoring device, most of the electronic and fluidic parts can be further integrated and miniaturized, e.g., by replacing the spectrom-

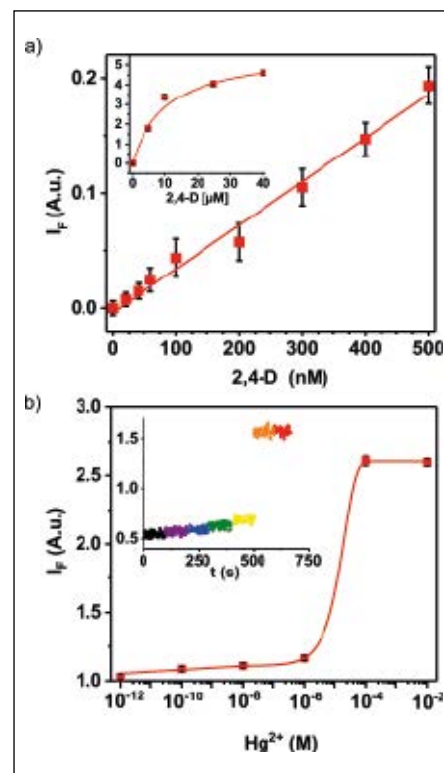


Fig. 3: Calibration curves obtained from the combination of the modular microfluidic system with the sensor particles for increasing concentration of 2,4-D a) and Hg^{2+} b) in water.

eter with photodiodes, the computer-based numerical post-treatment with electronic onboard handling or the syringe pump for sample handling by a bypass from a drainage system or any other outlet of a potentially contaminated water body/system.

Given the modularity of the presented platform, that are of both, the microfluidics and the sensory particles, this toolbox harbours an enormous potential for the development of single or multiplexed integrated chemical sensors for the monitoring of a larger number of relevant, less hydrophilic chemical parameters in liquid samples of not only environmental but also pharmaceutical, food chemical, biochemical or medical interest.

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