A Cheap and Reliable Lateral Flow Test for Small Molecules

Technology Description

Figure 1: Overall appearance of our new lateral flow test system. The paper strip contains several laser structured channels and structured conjugate pads for quantitative measurement of pharmaceutical ingredients.

Rapid tests, based on antigen-detection of relevant marker structures, play an ever-increasing role in modern medical diagnostics. One of the drawbacks of such assays is that they often only provide a qualitative result or detect only large analytes. Here we present a new architecture for the overall design of such diagnostic tests, which expands the applicability of lateral flow tests. Our newly invented multi-channel structure allows multiple measurements on a single strip\(^1\), thus permitting the analysis of multiple analytes simultaneously\(^2\). Another considerable advantage of our invention is the possibility of an internal calibration by the realisation of the standard addition method on a lateral flow test for a quantitative readout. In addition, a switchable barrier between conjugate pad and test line ensures sufficient incubation time for reaching equilibrium between recognition element and analyte, and therefore enables a non-competitive assay for small analytes.

Innovation

Up to now:
- Sandwich-Assay for large analytes
- Competitive assay for small analytes
- Single qualitative measurements

Now:
- Laser-based multi-channel structuring for analysis of several different analytes
- Non-competitive assay for small molecules
- Switchable barrier
- Quantification of low molecular weight compounds

Market Potential / IP Status

A predicted substantial increase of the market for point-of-care testing (POCT) within the next years (worldwide market volume predicted to be 50 billion US dollar in 2026, up from 23 billion in 2018)\(^3\) will bring huge demands especially for new and better lateral flow tests. The internal calibration for such testing made possible by our new invention can be a door opener for new applications in medical and general diagnostics.

German patent granted: DE 10 2021 214 853 B3
PCT-application filed

Applications

- POCT, especially therapeutic drug monitoring
- Residues of small organic compounds in food and feed samples
- Quantification of small organic compounds (e.g. pesticides or EDCs) in water samples
- Faster doping controls due to parallel measurements of up to 6 analytes.

Contact:
Dr. Rolf Hecker
Eberhard Karls Universität Tübingen
Technology Transfer Office
Keplerstraße 2
72074 Tübingen · Germany
+49 7071 29 7263
r.hecker@uni-tuebingen.de
www.technologietransfer.uni-tuebingen.de

Prof. Dr. Günter Gauglitz
Eberhard Karls Universität Tübingen
Physical and Theoretical Chemistry
Auf der Morgenstelle 18
72076 Tübingen · Germany
+49 7071 29 76927
guenter.gauglitz@ipc.uni-tuebingen.de
**Proof of Concept**

### Fabrication Method

Our invention permits structuring several channels on a single test stripe at µm-precision using a laser technique. This method guarantees waterproof channel walls with fully fluidic separation of all channels for multiparametric measurements. We use a laser technology for ablating partly a nitrocellulose layer that lies on top of a polyester base. Figure 2 depicts the cross sectional area of the laterally structured channel’s sidewall. The laser energy has been applied on the right side, ablating completely the nitrocellulose membrane and thus forming the channel. Absolutely tight lateral walls are achieved by applying additional energy directly at the channel wall.

Furthermore, the created structures can be used to integrate on-off structures such as valves on the system. Practical implementations achieved in our investigation include mechanical actuated barriers based on a small gap oriented perpendicular to the channel, or optical actuated barriers based on special molecules capable of polarity change in presence of light. Incorporating barriers introduces the potential to establish a pre-incubation period for the entire system, imparting distinctive attributes to the assay.

### Rapid and Precise Internal Calibration via Standard Addition Method

Our invention permits internal calibration with a standard addition method on the test strip. This allows correction of matrix effects and a reliable quantitative readout.

Figure 3 shows an example with amitriptyline, a common antidepressant. On the conjugate pad increasing amounts of amitriptyline were added to the sample leading to a decrease of the signal on the test line (from top to bottom). This shows that the standard addition method can be integrated into the test strip by adding known analyte concentrations onto the structured conjugate pad.

Furthermore we developed a software for an automated numerical procedure for the determination of the sample concentration.

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**References**


