From sample to sensor

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Abstract

Point-of-Care (PoC) diagnostics is a term concerning diagnostic methods and devices that can be conducted at the patient side in a fast and easy manner. This means they can be used in a wide set of contexts from global pandemics to environments in which healthcare infrastructure is not properly established. This doctoral thesis concerns itself with several aspects of Point-of-Care diagnostics.

In the first part, the actual use of PoC in low-income countries is analyzed and several bottlenecks are identified. For this, the whole value chain is examined, including the fundamental research, the market distribution and the end-user application of PoC diagnostics, in order to find the most important aspects contributing to its success or failure. Identified elements include problems with misguided research philosophies, problems with distribution and stock management as well as limited end-user trust. This part of the thesis unveils important aspects and design considerations that were essential for the consecutive chapters as it became evident that, for example, 3D printing can be a valuable tool for on-demand research and production of PoC devices in low-income countries.

The third chapter concerns itself with the heat-transfer method, a proof-of-application for its use in diagnosis of urinary tract infections is established, using samples of several volunteers of different genders. The method is shown to work in clinically relevant ranges down to 10^4 CFU. Furthermore, it is shown that a fast sample analysis is necessary to guarantee correct diagnostics results. This shows that rapid PoC diagnosis on the spot is the best mode of action, especially in low-income countries where, as we showed in the first part, a proper cold chain is not necessarily guaranteed.

New methods of microfluidic manufacturing, suitable for low-income countries, are demonstrated in the consecutive chapters. First a Form2 3D printer is benchmarked for its capability to produce microfluidic channels, both inside and on the surface of the print. It was found that embedded channels are easier to produce the more orthogonally they are in respect to the buildplate, and the larger they are. Channels on the surface were tremendously easier to produce than channels embedded in the print. The size limit of embedded channels was 500 µm compared to 250 µm for surface channels. This finding was used to improve on 3D printed microfluidics further by the development of ‘topographical vacuum sealing’. Here the channels are 3D printed as groves on the surface and then consecutively closed using a low-resolution vacuum forming process. In this process, a heated thermoplastic is stretched over the 3D printed substrate and a vacuum applied. With this, the thermoplastic is aligned to the macro-topography of the substrate but does not intrude into the micro-sized channel due to their small size. A wide range of surface geometries can be covered and several angles from 90° to 270° were tested. This technique enables the construction of open channels via 3D printing, which in turn allows smaller channel sizes while at the same time keeping the benefit of 3D printing, the ability to cover wide form factors, intact.