PROVIDING TECHNICAL SOLUTIONS FOR MOLECULAR DIAGNOSTICS
Enrichment of bacterial cells from blood is a necessity and a significant challenge in the molecular diagnostics industry. To address this, the Fraunhofer LSE team has developed a device that can selectively destroy blood cells, enrich the bacterial cells, wash and rinse the concentrated cells and dispense the bacterial cells onto a microscopic slide ready for further analysis. The “Bacterial Concentrator” is a specialized multi-compartment device that works within a standard swinging bucket centrifuge. The chambers are separated by metering valves that transfer concentrated bacteria from one chamber to another. The device can isolate bacteria from 10 milliliters of blood with starting concentrations as low as 10 bacteria per milliliter. The resulting bacteria are purified successfully enough to conduct real-time PCR directly on the output.

Molecular diagnostics is a new enabling area of healthcare with enormous potential over conventional diagnostic assays. However, the molecular assays are complex, requiring skilled operators, expensive reagents and multiple instruments. This makes these assays more expensive than conventional ones. One solution to this problem is a microfluidic “lab-on-a-chip” to combine automation, smaller reagent volumes and a single instrument to complete the diagnostic assay. The team at Fraunhofer CMI, with help from Boston University and Fraunhofer IPT, has developed a fully integrated lab-on-a-chip instrument for the detection of bacteria from liquid samples.

The system conducts bacterial lysis, nucleic acid isolation and concentration, polymerase chain reaction (PCR), and end-point fluorescent detection. To enable truly low-cost manufacture of the single-use disposable chip, the plastic chip was designed in a planar format without any active components to be amenable to injection molding. A novel porous polymer monolith (PPM) embedded with silica is used to lyse bacteria and isolate the nucleic acids from clinical samples. The chip is made of a thermoplastic with a high melting temperature to allow PCR, good UV transmissibility for UV-curing of the PPM, and low auto-fluorescence for fluorescence detection of the amplicon.
Sensor Integration for Lab-on-a-Chip

To use lab-on-a-chip for mobile diagnostics, the system integration of fluidic components and sensors have to be a part of the development process for these devices. Furthermore, the quality of the diagnostic results and the mobility of the entire system depend on the development of the instrumentation. The Fraunhofer LSE group in cooperation with RWTH Aachen University, designed a micro positioning stage with the integration of fiber based sensors and all needed fluid handling components. During the development process, Fraunhofer was able to maintain the high usability requirements in combination with the needed repeatability of the diagnostic results.

Shear Cell

To effectively combat the emerging threat and dissemination of bacterial resistance to antibiotics, new fast phenotypically-based clinical tests to identify antibiotic susceptibility are required. Standard susceptibility testing relies on the passive observation of bacterial growth inhibition in the presence of antibiotics, often requiring more than 24 hours. The Fraunhofer LSE group, in collaboration with Harvard Medical School, has developed a new rapid method for antibiotic susceptibility testing of bacterial species. Mechanical and chemical stressors are applied to initiate biosynthetic pathways involved in bacterial responses to antibiotics. Strains susceptible to the antibiotic are killed under these conditions while resistant bacteria survive. Comparing the rate of bacterial death in the presence and absence of antibiotic allows this method to circumvent the need for bacterial growth. The method was implemented on a microfluidic platform integrated with an optical microscopy detection system. Using this method, the methicillin resistance of more than 20 staphylococcal strains (MRSA) was identified in less than 60 minutes per test.
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