B144 Development of Microchip-Based Sample Processing Systems for Forensic DNA Analysis

James P. Landers, PhD and Jerome P. Ferrance, PhD, University of Virginia, Departments of Chemistry and Pathology, PO.Box 400319, McCormick Road, Charlottesville, VA 22904*

This talk will discuss the development of modular and integrated microchip-based technologies that can be utilized in expediting sample processing and analysis steps for forensic DNA analysis

The impact of this talk will be to explore the developments in microfluidic processing and analyses which are applicable to forensic DNA analysis.

Forensic DNA analysis is a multistep process that involves a diverse array of molecular and analytical techniques executed in a sequential manner with STR analysis as the final step. Individually, these steps are time-consuming and labor-intensive, which has resulted in a slow throughput rate for forensic analysis and contributed to the backlog of samples awaiting forensic DNA testing. One approach for reducing analysis time for the individual processes involved in forensic DNA analysis is to exploit miniaturized technologies. In particular, microfluidic devices have been utilized in biochemical processes and analyses that are applicable to forensic work, with the added benefit that they can be designed with monotasking functionality, or in an integrated format for multiple process execution on a single device.

The last decade has seen an explosion of efforts to miniaturize sample preparation steps, such as DNA extraction and PCR amplification, with the expressed goal being to expedite the molecular diagnostic evaluation of human samples. These efforts have demonstrated, unequivocally, that the microminiaturization of analytical processes on microchip platforms can lead to enhanced efficiency and a reduction in time (versus conventional methods). In addition, optimized microchip sample processing can accommodate small sample sizes and does so with minimum reagent consumption. This has been demonstrated with the microchip-based extraction of nucleic acids from complex samples including whole blood, PCR amplification of specific genomic targets in volumes (as low as a few hundred nanoliters) on microchips, microchip electrophoretic separations for DNA analysis, and, to a lesser extent, with chip-based sorting of blood cells in labyrinth-like silicon structures.

The power of analytical microchip technology for carrying out analytical processes rapidly and efficiently can be exploited in numerous ways by the forensic community. Traditional forensic DNA analysis methods, such as differential extraction, DNA purification and quantitation, STR amplifications, and capillary electrophoretic separations, can be replaced with equivalent microchip methods that provide a equivalent, if not higher, level of confidence. One embodiment of a forensic microdevice design involves a 'modular' approach, which aims to develop stand-alone, dedicated instrumentation that accepts single-task, single use microchips designed for automated analysis. These are being developed for cell sorting, DNA extraction, and PCR amplification processes. These microdevices are designed in a 'task-conscious' manner so that easy introduction into the conventional sample processing work-flow is possible. An alternative embodiment, the 'integrated' approach, is being pursued to create multi-task microchips capable of carrying multiple processes in a sequential manner. This requires the seamless interfacing of at least two different chip microstructures, both fluidically and electrically, so that a single sample can be processed through multiple steps automatically. Challenges here are multidisciplinary in nature, requiring efforts in electrical and mechanical engineering, surface science, polymer chemistry, molecular biology and analytical chemistry to be brought to bear on the problem.

Ultimately, one can envision a forensic micro-total analysis system ($_0$-TAS) that could accept a sample, extract and sort cells if required, purify and quantify the DNA, amplify the target sequences of interest and then electrophoretically separate the fragments with the single base pair resolution required to generate an STR profile of forensic utility. For rape kit evidence in particular, this type of microdevice processing will provide male and female DNA analysis from a single swab in a reasonable amount of time, allowing faster evidence processing for current cases, and contributing to reducing the significant backlog of cases which currently exist.

Microchip Technology, Integrated Microdevices, Sample Processing