One of the greatest challenges in modern medicine is the ability to provide accurate diagnostic laboratory tests in developing countries and in remote areas where conventional analytical laboratories are lacking. Imagine running a clinic in a remote area of rural Africa, the Canadian arctic, on a military field base or even in a small rural community in Ontario and having the ability to provide accurate, rapid, point-of-care diagnostic lab tests without the infrastructure of a full analytical laboratory! There’s no need for a cumbersome or expensive mass spectrometer, a spectrophotometer, a flow cytometer or even a centrifuge because the application of microfluidics engineering to medical diagnostics has enabled laboratory tests to be performed on a small microchip the size of a credit card that you can carry around in your pocket and may only require the use of a battery as a power source for analysis! As futuristic as this idea seems, the application of microfluidics engineering to the development of medical diagnostic tests is very much a reality.

Microfluidics engineering is a multidisciplinary field of engineering where the intersection of the fields of physics, chemistry, engineering and biotechnology have come together to develop chips on which the analysis of fluids can occur on a microscale level. A particularly interesting application of microfluidics engineering technology is the development of a lab-on-a-chip; a platform on which one or more laboratory tests are integrated onto a small chip a few square centimetres in size that uses a very small volume of fluid for analysis. Several microliters of a variety of biological fluids including blood, cerebrospinal fluid, urine, feces or saliva can be added to the lab-on-a-chip for analysis. These chips utilize a wide variety of techniques for analysis. The most successful lab-on-a-chip applications integrate all aspects of sample preparation, sample separation, signal amplification and signal detection on a single chip. These chips can be easily adapted for use in remote regions since specialized laboratory personnel are not needed for analysis - you simply need to apply the sample to the chip and the technology takes care of the rest. In addition to their small size and portability, the applications of lab-on-a-chip platforms have a wide variety of advantages to the field of medicine and are listed in Box 1 (adapted from references (1-3)). A variety of molecular biology, immunology and biochemical techniques have been adapted for use on lab-on-a-chip platforms including protein assays, nucleic acid assays, cell sorting, and biological analyte detection. Since lab-on-a-chip technology has a wide variety of applications in medicine we will now focus on two areas of interest where we feel the technology will be rapidly applied; the detection of infectious microorganisms from biological samples and the microscale detection of biological analytes.

Arguably, one of the most important and exciting applications of these devices is in the early and accurate diagnosis of infectious diseases in the developing world. The ability to rapidly detect an infection, assess an infected patient’s health status and the application of this technology to epidemiological studies in the field are invaluable. In order to be a useful tool in the developing world several design challenges need to be overcome; the reagents and the chip itself need to be stable at a wide variety of temperatures since refrigeration of the components may not always be feasible in the developing world, the cost of the chips needs to be low and the chips need to have a small power source for operation since reliable electrical infrastructure is not found in all parts of the world. Research and development work is being undertaken to adapt lab-on-a-chip technology for the detection of many microorganisms from biological samples including; HIV (reviewed in (8)), malaria (reviewed in (9-10)), tuberculosis, diathelial diseases, pertussis, and dengue fever. One exciting lab-on-a-chip application for the detection of enteric infections is the Disposable Enterics Card (DEC) which is able to detect the presence of Campylobacter jejuni, Escherichia coli O157:H7, Shigella dysenteriae, Shiga Toxin-producing Escherichia coli (STEC) and Salmonella from a sample of feces all on one microchip. The DEC lab-on-a-chip technology combines several laboratory assays to detect the bacteria (see Figure 1 and Figure 2 for a schematic of the chip). Briefly, a sample of feces is applied to the chip and bacteria from the sample are captured on the chip by using specific antibodies to each bacterium of interest. These antibodies are located in several different areas of the chip. The bacteria are subsequently lysed using buffers and the bacterial DNA is captured on a silica resin contained within the chip. The purified bacterial DNA is subsequently amplified using a standard molecular biology technique called the polymerase chain reaction (PCR) with DNA primers specific for a gene in each bacterial species of interest. The end of each primer has been designed to contain a fluorescent molecule. After the amplification of the bacterial DNA using PCR, fluorescent molecules are now found at the ends of each.

![Figure 1. A Schematic Diagram of the Disposable Enterics Card (DEC) lab-on-a-chip Technology.](image-url)
amplified molecule of bacterial DNA. The next step in the process is to detect the amplified bacterial DNA. To do this, a laser light is directed at the sample. The fluorophore emits fluorescent light which can be detected if the sample is positive for the bacteria. Unfortunately, the DEC testing still requires the use of a small machine for the PCR reaction and PCR product detection which limits its ability to adapt to field conditions. This technology would be useful in a small analytical laboratory or clinic but its usefulness would be limited under field conditions.

A second application of technology to lab-on-a-chip capability is the detection of analytes such as electrolytes from a small sample of blood. The iSTAT, a device manufactured by Abbott Diagnostics, has the capability of rapidly analyzing analytes in a few drops of blood. The developers of the iSTAT have miniaturized electrodes by depositing electrode arrays onto silicon cartridges to create a biosensor. A few drops of blood deposited into a sample chamber are able to enter the cartridge by capillary action. Once the sample is in the cartridge it can be treated with chemical reagents prior to analysis. At the analytical stage the cartridge is inserted into a handheld electromechanical read-out device that provides a power source and controls the temperature of the chip. The electrode arrays deposited on the silicon membrane can then be used to measure the concentration of various blood electrolytes, gases, and other analytes using potentiometry (measuring the electric potential).

**Figure 2.** Biochemical steps of the analysis in the chip. (A) Feces sample is applied to the chip and enters the sample well. Various types of bacteria in the sample are represented by different ovals. Different surface proteins on each type of bacteria are denoted by rectangles and triangles. (B) Antibodies specific to surface proteins on the bacteria of interest capture the bacteria in the chip. This example shows black coloured bacteria captured in the upper chamber and grey coloured bacteria in the lower chamber. Bacteria whose surface proteins are not bound by the antibodies are washed away. (C) Captured bacterial cells are lysed in buffer and bacterial DNA is purified on silica resin. (D) Purified bacterial DNA is eluted from the resin and enters the PCR amplification chamber. (E) A bacterial gene of interest is amplified using a standard molecular biology technique called PCR. Small DNA molecules (primers) specific for the gene of interest are found in this chamber. Primers are denoted as arrows in the diagram and are linked to a fluorophore (a fluorescent molecule) denoted by a star. (F) The gene of interest is amplified exponentially (there are many copies) and now contains fluorophores on each end. (G) Amplified bacterial DNA fluoresces when laser light is shone on the sample giving a readout, thus, leading to the diagnosis of the infection.

**Box 1: Advantages of lab-on-a-chip technology**
- Small size (credit card or smaller), portability
- Small sample volumes, less invasive
- Rapid analysis, short processing times
- Low cost
- No need for highly trained laboratory technicians to perform the test
- May run using a battery for power (no need for electrical infrastructure)
- Reduced reagent consumption due to small volumes
- High reproducibility
- Reduced exposure to hazardous materials or infectious agents due to small volumes
- Minimal risk of sample contamination
- Convenient disposal
- Elimination of human error (you add the sample to the chip and the chip takes care of the rest)

Adapted from references (1-3).
amperometry (measuring the flow of an electrical current) or conductimetry (measuring the conductance) of the sample. These values are then displayed on a screen. Different chips are used for different analytical applications and each chip is disposed of after one use. All the chips use the same handheld electromechanical read-out device.

We have only focused on two applications of lab-on-a-chip technology; however, there are numerous uses for this technology and many approaches to the miniaturization of biochemical, molecular biology and chemical assays for use on microchips. The miniaturization of medical technologies may very well revolutionize the delivery of medical care in the near future. Is your pocket ready for the lab-on-a-chip?

REFERENCES