# Electrical Detection of DNA Molecules

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**This high quality abstract was presented at the BMES 2007 Annual Fall meeting**

**The Problem.** Early detection of pathogens has long been a critical issue for food safety and public health. In the past decades, much research has been done for rapid detection of microorganisms that cause outbreaks of food-borne illness. However, most of these methods are time consuming and labor intensive requiring a high level of expertise. Our research group has been working on developing simple, automated and portable microfluidic devices for rapid detection of microorganisms based on label-free electrical measurements and impedance spectroscopy. Typically, nucleic acid-based methods are still considered the gold-standard for detection and identification of microorganisms due to their high specificity and selectivity as compared to antibody-based assays. The test of choice for detection of target DNA molecules is Polymerase Chain Reaction (PCR). Conventional PCR requires the introduction of fluorescent labels in the solution mix, which produce light when incorporated into the amplified DNA product.

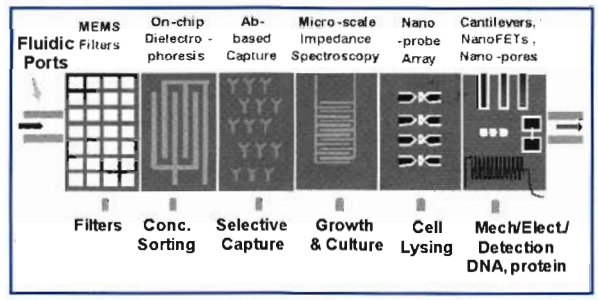


**Figure 1: Schematic of a modular lab on a chip for detection of microorganisms.**

New methods for the label free detection of the amplified nucleic acid product would reduce the cost and make it easier to miniaturize the measurement apparatus. Hence, label-free detection of DNA molecules is a quest of utmost importance.

**Detector on a Chip.** A schematic of an integrated lab on a chip device is shown in Figure 1, where the appropriate module could be integrated depending on specific applications and the analysis to be performed. The final step of any such analysis is the identification of the target microorganism. The direct electrical detection of DNA in solution is potentially a very attractive option, especially if differences in length and concentrations can be detected directly without any labels or attaching the molecules to a surface. It has been known that the presence of dsDNA molecules suspended in solution can be detected directly without any labels by measuring the impedance of the solution that the molecules are suspended in, provided that the concentration of the molecules is above a critical threshold. We used microscale devices with integrated metal electrodes to perform electrical impedance measurements

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## DNA Molecules

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of solutions with DNA molecules and found that the threshold of detection is about 1×108 molecules/μL in de-ionized water. This corresponds to approximately nM concentration for a 400 bp (base pair) dsDNA (double stranded DNA) molecule. The impedance magnitude was found to decrease as the concentration of the 400 bp dsDNA was increased. Similarly, at fixed concentrations, the impedance magnitude was also found to decrease as the length of the dsDNA molecule was increased. We fitted the measured impedance data to an equivalent circuit model and our results show that the extracted dielectric capacitance and conductance of the solution increase with molecule length and concentration owing to a corresponding increase in number of DNA dipoles and counter-ions in solution. We also found that the threshold of electrical detection was about 1×1016 molecules/μL in PCR solution (i.e. in the presence of all components necessary to perform PCR).

**The Goal.** It should be possible to directly detect the amplified product of PCR reactions using electrical means as long as the amplified molecules can remain concentrated in a very small volume. So a solution could be used with about 1000 bacterial cells flown through a channel with the bacteria confined in a 0.1 nL volume. If the bacteria were lysed and the target DNA segments were amplified in 30 cycles (amplified by 1×109 times), and if the amplified product was confined to the same volume, then the amplified product would change the electrical properties of the solution. We envision a cartridge with an electrical and fluidic interface to a hand held reader, where the entire assay can be performed in a miniaturized format to provide information of identification of target pathogenic microorganism based on detection of target nucleic acids. ◆

## Canver's Corner

*Matt Canver*

*Do you have a question that is burning inside you, but you can't get a straight answer? Do you want to know about biomedical engineering, school, career, or life? Matt Canver at the University of Pennsylvania will answer all your questions. Just email them to him at canver@seas.upenn.edu*

**Question: What** can I do with a degree in Biomedical Engineering?

The race to develop the latest life-saving technology has often involved the intersection of engineering with the biomedical sciences. Influential medical advances such as the defibrillator and the heart-lung machine exemplify the possible success of such an interaction. As the population continues to age and health issues flood the media, biomedical engineering's place in society continues to grow. Engineers number 1.5 million in the work force, with 20% of those being biomedical engineers. Strikingly, the U.S. Bureau of Labor Statistics has predicted a steep growth in biomedical engineer employment through 2016. In addition to this wide marketability, a biomedical engineering degree has the advantage of versatility. Here are some common paths taken by students after receiving a Bachelor's degree in biomedical engineering:

### *Graduate School*

Many graduates elect to pursue further study to obtain either a Master's or Doctoral degree in biomedical engineering. These advanced graduate degrees open many additional job possibilities, especially in the biotechnology industry and academia. Medical school is also a popular choice for biomedical engineering graduates. The strong technical background provides a sound basis for tackling clinical problems. The option for a combined MD/PhD path, totally about 8 to 9 years, is becoming increasingly common. Business school is another frequent path for biomedical engineers. A Master's in Business Administration (MBA) can open many doors, particularly in industry jobs or in developing your own biotechnology company.

### *Workforce*

It is common for graduates to enter the workforce after graduation. This is no

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