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Investigation on Applicability and Suitability of Micro Cantilever Based Biosensors for DNA Detection

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Abstract

Highly sensitive and selective DNA detection has attracted extensive attention for its importance in clinical diagnostics, treatment, and various genome projects. Recently there has been a flurry of activities with the use of nano particle labels to detect DNA and proteins. These detection methodologies strongly depend on the availability of a mechanism that traduce and amplify specific DNA binding events to detectable signals. One such DNA detection is technique is micro cantilever bio sensing. The micro cantilever biosensors are becoming popular due to their inherent ability to generate highly sensitive and quantitative measurements with low cost, portability, real time and label-free detection. The capability of the micro cantilever beams of detecting mechanical stress, mass additions and small forces offer encouraging prospects for physical and chemical sensing with high sensitivity and dynamic range. Keeping this in mind, in this paper a brief study on application and feasibility of micro cantilever based DNA detection has been presented.

Keywords: Micro cantilever; DNA detection; Biosensor; Deflection; Cantilever materials

Introduction

A micro cantilever is an extreme sensitive bio sensing transducer responding to detection of the target molecules in nano scale unit [1,2]. Generally, this device consists of a tiny horizontal beam which is fixed on the supporting material at one end of this beam. Another end is normally free for spatial movement according to the molecular interaction at biological recognition area on the beam surface. Micro cantilever-based biosensors have attracted much attention due to their small size, low cost, fast response, high sensitivity, and suitability for parallelization into arrays [3-5]. The biosensors are generally operated in two modes: static bending and dynamic resonance frequency shift [6]. The current methods for measuring micro cantilever bending involve optical, interferometer, piezo resistive, and capacitive detection technologies [7]. In the static case, label-free biosensors have provided common platforms for DNA hybridization [8], biotin-antibody binding [9], and BRAF mutation in RNA from melanoma cells [10]. Biological interaction between target molecules in analyzed samples and specific capture molecules immobilized on a surface of the beam induces structural bending. Deflection length of the micro cantilever beam can be measured by an optical device as found in Atomic Force Microscopy (AFM) application [11-15]. Optical-based detection offers very high sensitivity in determining a deflection length. However, this system requires great precision of the external readout device, laser source assembly, and position sensitive photo detector (PSD) which increases both cost and size of the whole device. A micro cantilever integrated with an embedded piezo resistive material serves as an inexpensive and portable micro cantilever biosensor platform [16,17]. Deflection length of this device is monitored by using the resistance change of piezo resistive material due to structural bending of piezo resistive material inside the beam [18,19]. Several previous studies developed piezo resistive micro cantilever-based DNA sensors to detect the short piece of synthetic DNA targets [8,20-22].

DNA Detection

The detection of DNA is considered to be a milestone in the advancement of microcantilever biosensors. Experiments have shown that deflections of the DNA micro cantilever can be induced by many factors such as length and sequence [23], grafting density and hybridization density of molecules [24], buffer salt solution concentration [25], moisture concentration [26], time, and temperature [27]. The detection of nucleic acid

hybridization is achieved using cantilever arrays where the micro cantilever surface is modified using oligonucleotide chain which reacts with the complementary single chain solution. The cantilever transduces this reaction process into the mechanical deflection. Compared to the commercial silicon nitride, the su8 polymer fabricated cantilever shows enhanced sensitivity for single stranded DNA by a factor of 6 [28-34]. Micro cantilevers have also been investigated for studying the secondary structure of DNA. A comprehensive table of applications of micro cantilever sensor in DNA detection is provided in Table 1.

Table 1: Different applications of Micro cantilevers in DNA detection [28].

Application	Mode of Operation	Research Outcome
DNA melting [29]	Static	Changes in temperature and ionic strength are required for observation of melting process of DNA
DNA molecular motor [30]	Static	Different pH values of buffer result in DNA conformation change which drives repeatedly cantilever deflection, similar to working of motor.
Hybridization [31]	Static	A micro cantilever array is used for the detection of mismatch in the DNA hybridization
Secondary structure of Oligonucleotides [32]	Static	The effect on the surface properties of cantilever beam due to the secondary structure of nucleic acids is studied
Detection [33]	Static	Single stranded DNA attached to cantilever surface is used to detect DNA hybridization
Detection	Dynamic	get an amplified detection signal with a Limit of detection10−15 M
Hybridization [34]	Dynamic	A sensitivity of 2 x 10−18 mol is achieved in human serum

One such micro cantilever based mechanical resonance DNA detection using gold nano particle-modified probes has been demonstrated in [35]. The measurement of the mass change of a micro fabricated cantilever which is induced by DNA hybridization through the shift of the resonance frequency of the cantilever is the main focus. The attachment of gold nanoparticles on the cantilever reflects the hybridization which is then chemically amplified by gold nano particle-catalyzed nucleation of silver in a developing solution. The gold–thiol covalent bonding link the capture DNA strands on the cantilever as shown in Figure 1 & 2, following that the cantilever is dipped into the target DNA solution for hybridization. After that the DNA strands labelled with gold particles, are hybridized on the other end of target DNA through complementary interactions. When exposed to photographic developing solution the gold nano particles act as nucleating agent for the growth of silver. Detectable frequency shift is seen from the growth of silver particles by increasing the effective mass of the micro cantilever, which can be readily detected.

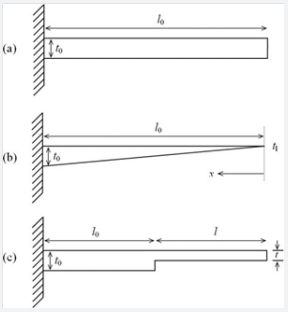

Figure 1: Illustration of (a) rectangular (b) triangular and (c) step cantilever designs.

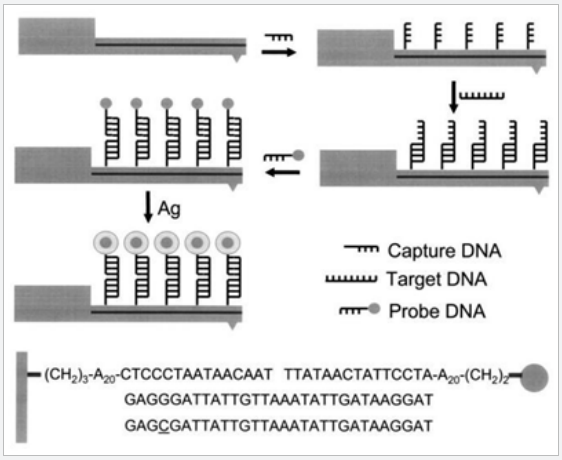

Figure 2: Scheme of micro cantilever based DNA detection using nano particle probe and the sequences of capture DNA, target DNA, probe DNA, and single base pair mismatched DNA [35].

Materials

A wide range of materials have been investigated for micro cantilever sensors. Most popular materials include silicon and silicon based materials like silicon nitride and silicon dioxide because these materials resonate with high Q-values and have low energy dissipation. In addition to traditional silicon based materials the magneto elastic and piezoelectric materials exhibit unique properties of both actuation and sensing [36]. The piezoelectric materials occur in many forms such as single crystals (e.g. Quartz), piezo ceramic (PZT), thin film (e.g.,

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sputtered ZnO) and polymer materials such as poly vinyle dene chloride (PVDF and SU8). A comprehensive table of commonly used materials for the sensing applications of materials is provided below Table 2 [37,38].

Table 2: Materials used for sensing applications.

Material	Material Property		
	Young's Modulus (Gpa)	Poisson's Ratio (V)	Density (Gm/Cc)
Silicon	170	0.26	2.32
SiO2	64	0.25	2.22
Al2O3	415	0	4
Porous Silicon	106.8	0	2.32
Poly Silicon	160	0.22	2.32
Silica	73	0.17	2.20
Si3N4	315	0.27	3.18
Si3N4	315	0.27	3.18

Conclusion

This paper investigated the application of micro cantilever biosensors for DNA detection and it was observed that the unique structural features of micro cantilever provides several advantages such as high sensitivity, high throughput, high mass detection accuracy, small volume, and low cost. Given the current advancements in the field of Micro-Electro-Mechanical Systems (MEMS), in future micro cantilevers with ability of parallel detection of multiple species at the same time by patterning different capture DNA strands can be designed.

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