Recent Advances in MEMS Sensor Technology— Biomedical Applications

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icro-electromechanical systems (MEMS) use microminiature sensors and actuators. MEMS technology provides the benefits of small size, low weight, high performance, easy mass-production and low cost. This article is the first part of a three-part series on MEMS sensors. In the present article, we provide a general introduction to MEMS sensing and the primary sensing techniques. Next, MEMS-based bio-medical sensors are explained. We consider MEMS devices that are: designed to detect triglycerides, c-reactive protein, and glucose, respectively; bio-inspired robotic fingers with tissue softness characterization sensors for pressure measurement during surgical procedures; for counting blood cells; acoustic sensors for 2-D sound source localization; pressure measurement sensors on the wings of an insect-like flying robot; and ultra-miniature sensors for intramuscular pressure measurement.

The second part of the series will be dedicated to mechanical sensors. There, some related technologies of MEMS sensors will be discussed including compensation for environmental effects, the Casimir effect, and harvesting of energy for selfpowered sensors. Also, the subject of sensor selection will be addressed. The third part will treat MEMS sensing in the thermo-fluid and electro-magnetic domains.

Sensors and Transducers

Sensors and transducers are necessary to measure excitations (inputs), responses (outputs) and parameter values for a variety of purposes including monitoring, fault prediction, detection and diagnosis, experimental modeling, and control. In practical applications, one should be able to identify and select suitable sensors, model and analyze individual components or the overall systems, and choose parameter values that meet the performance requirements for the intended functions with respect to some specifications. Identification, analysis, selection, matching and interfacing of sensors, and tuning of the integrated system (adjusting parameters to obtain the required response from the system) are essential tasks in the instrumentation and design of a system [1] - [3]. A sensor detects (feels) the quantity that is being measured (the *measurand*). A transducer converts the detected measurand into a convenient form for subsequent use (monitoring, diagnosis, recording, actuation, control, etc.). The transducer signal may be filtered, amplified, and suitably modified prior to this. For example, a piezoelectric accelerometer senses acceleration and converts it into an electric charge; an electromagnetic tachometer senses velocity and converts it into a voltage; and a shaft encoder senses a rotation and converts it into a sequence of voltage pulses. Hence, the terms sensor and transducer are used interchangeably to denote a sensor-transducer unit.

A complex measuring device can have more than one sensing stage. Often, the measurand goes through several transducer stages before it is available for control and actuation purposes. Sensor and transducer stages are functional stages, and sometimes it is not easy or even feasible to separately identify the physical elements associated with them. Furthermore, this separation is not very important in using existing devices. Proper separation of sensor and transducer stages (physically as well as functionally) can be crucial, however, when designing new measuring devices.

Pure transducers depend on nondissipative coupling in the transduction stage. *Passive transducers* (sometimes called *self-generating transducers*) depend on their power transfer characteristics for operation and do not need an external power source. It follows that pure transducers are essentially passive devices. Some examples are *electromagnetic*, *thermoelectric*, *radioactive*, *piezoelectric*, and *photovoltaic* transducers. External power is required to operate active sensors/ transducers, and they do not depend on power conversion characteristics for their operation. A good example is a *resistive* transducer, which depends on its power dissipation through a resistor to generate the output signal.

An active transducer requires a separate power source (power supply) for operation, whereas a passive transducer draws its power from a measured signal (measurand). Since passive transducers derive their energy almost entirely from the measurand, they tend to distort (or load) the measured signal to a greater extent than an active transducer does. Precautions can be taken to reduce such loading effects. On the other hand, passive transducers are generally simple in design, more reliable, and less costly [1] - [3].

MEMS Techniques

MEMS technology provides the benefits of small size, low weight, high performance, easy mass-production, and low cost. Sensing techniques are typically based on piezo-electric, capacitive, electromagnetic and piezoresistance principles [1] – [3]. These sensing technologies are briefly discussed now.

Piezoelectric Sensors

Some substances, such as barium titanate, single-crystal quartz, and lead zirconate-titanate (PZT) can generate an electrical charge and an associated potential difference when they are subjected to mechanical stress or strain. This piezoelectric effect is used in piezoelectric transducers. The governing equation (constitutive equation) of a piezoelectric element is

$$D_i = e_{ii} S_i + \varepsilon_0 \varepsilon_{ik}^S E_k \tag{1}$$

Here D_i is the combined dielectric displacement (also called electric displacement) in the *i*th orthogonal direction (*Note: i* = 1, 2, 3 are three orthogonal directions in three-dimensions) due to six mechanical strain components S_i (3 normal strains and 3 shear strains) and three orthogonal electric field components E_k (in three dimension). Also *e* denotes the piezoelectric strain coefficient, ε_0 is the permittivity (dielectric constant) of a vacuum, and ε_k^s is the relative permittivity of the material between different pairs of directions i and k, at constant strain (denoted by the superscript *S*). The constant ε_0 is equal to 8.854 × 10⁻¹² farads per meter (F/m). An equivalent circuit of a piezoelectric microsensor is given in Fig. 1.

The dielectric displacement in the direction (denoted by 3) normal to a pair of parallel plates of a piezoelectric capacitor of facing area *A* and carrying a charge *Q* is given by



Fig. 1. Equivalent circuit for a piezoelectric microsensor.

$$D_3 = \frac{Q}{A} \tag{2}$$

This is indeed the charge per unit area. When there is no external electric field *E*, equation (1) may be written for axis 3 as

$$D_{3} = e_{31}S_{1} + e_{32}S_{2} + e_{33}S_{3} = e_{31}(S_{1} + S_{2}) + e_{33}S_{3}.$$
 (3)
Note: $e_{31} = e_{32}$

Capacitive Sensors

A capacitor is formed by two plates which can store an electric charge. The charge generates a potential difference which may be maintained using an external voltage. The capacitance *C* of a two-plate capacitor is proportional to *A*, the common (overlapping) area of the two plates, and ε , the dielectric constant (or permittivity) which depends on the dielectric properties of the medium between the two plates. *C* is inversely proportional to *d*, the gap width between the two plates. A change in any one of these three parameters may be used in the sensing process. Capacitive sensors are compatible with most mechanical structures, and they have high sensitivity and low temperature drift. An equivalent circuit for a capacitive sensor is shown in Fig. 2.

The capacitance of a parallel plate capacitive transducer is given by:

$$C = \frac{\varepsilon_r \varepsilon_0 A}{d} \tag{4}$$

where ε_r and ε_0 denote the relative and vacuum permittivity, respectively.

Electromagnetic Sensors

Sensors that employ the principle of electromagnetic induction are termed variable-inductance or electromagnetic sensors. Those variable-inductance transducers that use a non-magnetized ferromagnetic medium to alter the reluctance (magnetic resistance) of the flux path are known as *variable-reluctance transducers*. Magnetic force on a magnet placed in an external magnetic field is given by:

$$F = \frac{1}{2\mu_0} B^2 S \tag{5}$$

where *F* denotes the magnetic force, μ_0 is the permeability of free space, and *B* and *S* are the magnetic field intensity and area of the ferromagnetic material perpendicular to the magnetic field.



Fig. 2. Equivalent circuit for a capacitive sensor.

Piezoresistive Sensors

Piezoresistive sensors use the change of the electrical resistance in material when it has been mechanically deformed. The resistance of a piezoresistor is given by:

$$R = \frac{\rho \times l}{t \times w} \tag{6}$$

where ρ , *l* and *t* denote the resistivity, the length, and the thickness and of the piezoresistor, and *w* is the width of the contact. ρ depends on the doping concentration of the piezoresistor. In particular, strain gauges sometimes make use of piezoresistive sensors.

Next, we present recent advances in MEMS sensor technologies related to biomedical applications, bio sensing and bio-inspired sensing.

Biological Sensors

MEMS-based biological sensors are applied in physiological, medical, and health applications. Several examples of such sensors are presented now.

Triglyceride Biosensor

Triglyceride measurement is in demand in the food and oil industries. Composite porous silicon/polysilicon micro-cantilevers are used in biosensing applications, such as triglyceride sensing. Micro-cantilevers are able to transduce a variety of

chemical and physical phenomena into mechanical motion. Micro-cantilevers have been employed in detecting cells, proteins, heavy metals, and other chemical and biological species. Arrays of these cantilevers are MEMS technology provides the benefits of small size, low weight, high performance, easy massproduction, and low cost.

capable of detecting multiple parameters simultaneously.

In chemical and biochemical sensing, the micro-cantilever surface is coated with a suitable chemical substance through self-assembled alkanethiols, organosilane films, direct



Fig. 3. A triglyceride biosensor with a cantilever beam in liquid. The cantilever beam's dimensions: length = $100-200 \mu m$, width = $10-20 \mu m$, thickness = $2 \mu m$. A 2 μm thickness of polysilicon is deposited by LPCVD on 1.6 μm thermal oxide.

covalent attachment of molecular receptors, or dip coating. Micro-cantilever mass increases when the biomolecules adhere to the coated cantilever surface. Variation in the cantilever mass changes the natural frequencies of the cantilever which is detected by a Doppler vibrometer. Porous layers on the surface of the micro-cantilever provide a larger sensing area for the sensor. Porous silicon provides a large surface area with a small volume.

A triglyceride biosensor [4] is illustrated in Fig. 3. Such a biosensor can have a cantilever beam with length = $100-200 \mu m$, width = $10-20 \mu m$, and thickness = $2 \mu m$. A $2 \mu m$ thickness of polysilicon is deposited by LPCVD on 1.6 μm thermal oxide for this sensor.

Bio-MEMS Sensor for C-Reactive Protein Detection

Proteins have many biological functions in the human body. Proteins catalyze the biochemical reactions to transport and store nutrients, provide protection from viruses/bacteria, and transmit biological signals. C-reactive protein (CRP) concentration in human serum is below 1 μ g/mL in a healthy body. CRP can increase to 100 and in some cases up to 500 times due to infection. Increasing the CRP in the bloodstream may cause cardiovascular disease and heart attacks, a major cause of death. Development of low cost CRP detection is crucial for human health monitoring.

The CRP sensing techniques allow detection of biologi-

cal molecules. Fluorescence based bio-sensing is the most common technique in biological molecule sensing. However, this technique requires a complicated labeling process of target molecules with dye and is expensive. A

quires a complicated labeling process of target molecules with dye and is expensive. A
200 µm long micro-cantilever in a wireless MEMS sensor is realized to detect disease related CRP [5]. Cross-biolinker binding on the sensor is performed by injecting self-assembled molecules into the sensor to adhere to a gold-coated silicon nitride micro-cantilever. AntiCRP is then injected to the sensor and adheres to the cantilever surface. Biomolecular interactions between CRP and antiCRP change the intermolecular nanomechanical inter-



actions within the biolinker layer and bend the cantilever. The

Fig. 4. Schematic diagram of a bio-MEMS sensor for C-reactive protein detection. Dimensions: length = $200 \ \mu m$, width = $40 \ \mu m$ [5].

deflection of the micro-cantilever is measured optically or using piezoresistive techniques. Fig. 4 is a schematic of a bio-MEMS sensor for C-reactive protein detection. It is 200 μ m by 40 μ m [5].

Detection of Glucose

Glucose is measured in diabetic patients to monitor blood sugar levels. Commercially available enzymatic Continuous monitoring of glucose for diabetes management can also be attained by a magnetically driven vibrating micro-cantilever that is similar to an affinity glucose sensor except the oscillating membrane is replaced with a micro-cantilever. changes due to affinity binding between glucose and poly (acrylamide-ran-3acrylamidophenylboronic acid) (PAA-ran-PAAPBA). The cantilever is placed in a micro-chamber filled with PAA-ran-PAAPBA solution. When glucose permeates through a membrane and binds to the phenylboronic acid moiety of the polymer, it changes the viscosity of the solution. Changes in the

electrochemical detection implants for continuous glucose monitoring provide irreversible measurements. These sensors consume glucose throughout the measurement and therefore change the equilibrium of glucose concentration in the tissue. This results in inaccuracy in the sensed glucose level. MEMS sensors based on the binding of glucose do not affect sensed glucose measurement.

Membrane-based sensors: Glucose may be monitored by MEMS sensors [6] – [7] which operate based on the binding of glucose. These methods do not consume glucose and so they give the actual glucose level. In MEMS affinity glucose sensors, glucose permeates through a semipermeable membrane into a micro-chamber filled with a solution of a biocompatible glucose-specific synthetic polymer called poly (acrylamide-ran-3-acrylamidophenylboronic acid). Raising the glucose level in the chamber changes the viscosity of the solution. A flexible Parylene diaphragm placed inside the micro-chamber vibrates due to an external magnetic field, and the vibration of the diaphragm changes with the variation in the solution. The damped vibration of the diaphragm is detected using the capacitance principle and is converted into the glucose level as the final sensor reading.

Microcantilever-based sensors: Continuous monitoring of glucose for diabetes management can also be attained by a magnetically driven vibrating micro-cantilever that is similar to an affinity glucose sensor except that the oscillating membrane is replaced with a micro-cantilever. The principle of operation is affinity binding. The cantilever detects viscosity



Fig. 5. A MEMS affinity sensor for detection of glucose. Its length and width are each approximately 750 $\mu m.$

viscosity of the solution vary the damping of the vibration behavior of the cantilever in the solution. The vibration behavior of the cantilever is monitored by an optical lever setup (Fig. 5).

Fig. 5 is a MEMS affinity sensor for detection of glucose [6], [7]. Using this device, readings of glucose concentrations in the range of 27 mg/dL to 324 mg/dL are possible. Such sensors have a response time of approximately 3 min.

Continuous monitoring: An important issue for diabetic patients is the fluctuation of blood sugar level throughout the day. "Finger pricking" is the common method used for blood sampling and glucose level measurement. However, this method can only provide the blood sugar level at the time of the measurement. Continuous blood sugar monitoring is a more desirable approach in glucose level examination.

Continuous monitoring of biological fluids such as tears, mucus, sweat and saliva has been reported. It has been found that:

- ▶ Tear glucose level changes with a delay of approximately 5 min when the blood sugar level changes.
- "Soft-MEMS" techniques enable fabrication of flexible electrochemical sensors for bioinstrumentation in the eye. Biocompatible polymers (phospholipid polymer or MPC polymer) are used as the material for the flexible sensors. MPC polymer has a molecular configuration similar to a cell membrane which allows it to fit



Fig. 6. Schematic diagram of a MEMS force sensor in protein delivery. The cantilever thickness = $5 \ \mu$ m; the device size is approximately $5 \ mm$ x $5 \ mm$.

into the shape of the eye. Monitoring the blood sugar level is performed by measuring the current variation induced by the enzyme reaction of glucose oxidase immobilized PMD membrane which is calibrated to the glucose concentration in the tear.

- Other MEMS-based glucose level measurement techniques include the use of electrochemical, impedance, eletrophoretic, thermal, optical, and colorimetric principles.
- Continuous monitoring of glucose for diabetes management can also be attained by magnetically driven vibrating micro-cantilevers.

MEMS Force Sensor in Protein Delivery

Mechanical properties of soft hydrogel microcapsules as a protein delivery mechanism have been studied using a MEMS capacitive force sensor illustrated in Fig. 6 [8]. The sensor can measure both the normal and tangential forces on the soft hydrogel microparticles [8] and is capable of resolving forces up to 110 μ N with a resolution of 33.2 nN along two independent axes with linear response and minimized cross-axis coupling. These results are used to characterize the mechanical properties of hydrogel microcapsules so that the controlled delivery of therapeutic agents (e.g., protein drugs) and the encapsulation of living cells is possible. Due to their hydrophilic nature that resembles living tissues, they exhibit high biocompatibility.

Hydrogel microcapsules offer a suitable environment for stabilizing proteins as a result of their capability of

holding a large quantity of water. Hydrogel microcapsule characteristics include high deformability and diameters in the range of 1 to $100 \,\mu$ m, which is comparable with most biological cells. The mechanical strength of hydrogel microcapsules determines if they can survive

Current blood cell counters are bulky and are not suitable for use at point-of-care. MEMS technology can overcome this limitation.

in the needle tract during injection, in the blood capillaries, and in the applied tissues. It is necessary to preserve their integrity during processing to avoid dose dumping, cell death, or immunoresponse. Characterization of the mechanical properties of hydrogel microcapsules using MEMS capacitive sensors allows developers to design efficient drug and cell delivery systems.

Tissue Softness Characterization

In open surgery, most trauma to the patient is caused by the incisions when accessing the surgical site rather than by the surgical procedure itself. Minimally invasive surgery (MIS) allows smaller incisions, less pain during the recovery period, reduced blood loss and scarring, faster recovery time, shorter hospitalization, fewer complications due to infection, better prognosis, better cosmetic results, and reduced overall costs. The surgeon needs to distinguish between different types of tissue in the body when making an incision into the tissue and identify the type of tissue (e.g., fatty, muscular, vascular, or nerve) that is being incised. Inaccurate classification of a tissue may lead to cutting of nerve tissues with consequences such as loss of motor control in patients.

MIS tools require the ability to measure the force magnitudes applied to the grasped tissues and quantify the tissue softness. In an MIS procedure, it is necessary to measure the local distribution of the force in the grasped tissue. Presence of any anatomical feature (e.g., lumps or tubular features, pulsating or nonpulsating features) in the grasped tissue causes an unusual change in the force distribution and generates a concentrated load at the contact surface. Therefore, the sensor should be able to detect and locate concentrated loads. Surgical tools should measure tissue properties such

> as elasticity and identify the type of tissues, locate tumors, and detect the abnormal stiffness of organs. Thus, the need for identification and classification of different types of tissue during surgery is an important issue in the design of surgical tools.

MEMS tactile sensors, in conjunction with existing MIS graspers, offer tactile sensing capabilities for endoscopic surgery. This tactile sensor measures the magnitude and location of force and tissue softness. The sensor is fabricated



Fig. 7 A MIS smart grasper and MEMS tactile sensors for quantifying tissue softness. Approximate size of a sensing unit: 7mm x 2 mm.



Fig. 8. Schematic diagram of the blood counter sensor. Sensor size: 10 mm x 5 mm x 0.8 mm. Gap through which the injected blood flows = $80 \mu m$.



Fig. 9. Schematic diagram of the fly-ear inspired 2-D sound source localization sensor. Size of silicon membrane: thickness = 0.5μ m, radius = 590μ m. The beam is made of alternating layers of silicon nitride and silicon oxide of size 1200 μ m x 300 μ m x 3 μ m.

from a uniaxial polyvinylidene fluoride (PVDF) film [9]. It is composed of a suspended beam with PVDF films which detect beam deflections. When a compressive grasping force is applied to the beam, the PVDF films compress or extend (Fig. 7). This configuration is used to measure the softness of tissues. When a constant grasping force is applied, a soft tissue produces less force on the beam than a harder tissue. A smaller force generates a smaller deformation of the beam. In this manner, the tissue softness is determined by detecting the beam deformation.

A Blood Cell Counter

Blood consists of plasma and blood cells. Blood cells are divided into red blood cells, white blood cells and platelets. Commercial blood cell counters are based on an aperture-impedance method and a light scattering method. Current blood cell counters are bulky and are not suitable for use at pointof-care. MEMS technology can overcome this limitation. A MEMS sensor for counting blood cells in humans has been realized. The sensor's output is a voltage that is proportional to the blood count [10]. When a diluted blood sample is injected into the aperture, the change in the electrical resistance due to the passing blood cell is measured and is proportional to the volume of the cells. The number of blood cells is determined by counting from the total number of electrical pulses (Fig. 8). Red and white blood cells are distinguished by the difference in the pulse heights they cause. There is a linear relationship between the red blood cells and the measured counts.

Acoustic Sensors

MEMS acoustic sensors assist human hearing using piezoresistive, condenser and piezoelectric methods. Although new hearing devices such as digital hearing aids and cochlear implants are used today, the MEMS acoustic method is still applied in cell phones, micro-personal digital assistants, portable multimedia players, and voice recognition [11].

A MEMS micro-sensor for 2-D sound source localization has been developed that detects a sound's source in two dimensions described by the azimuth and elevation angles by using three mechanically coupled circular fiber-optic membrane systems (Fig. 9). This acoustic sensor is 1200 μ m x 300 μ m x 3 μ m [12]. It is inspired by the hearing organ of the fly *Ormia ochracea*. MEMS capacitive based microphones allow detection of small pressure gradients. A low-coherence capacitive fiber-optic interferometer measures the acoustic pressure from the small pressure gradients produced by the membrane oscillations and localizes the sound source. The fly-ear inspired sensor offers better amplification in both the directional cues and directional sensitivity detection when compared to other MEMS sound sensors [12].

Wing Pressure Measurement

Design and analysis of insect-like flying robots (ornithopters) require a knowledge of the pressure applied to their wings during flight. For this, a pressure sensor with a weight at least ten times lighter than the wings should be used [12]. For instance, the wing length and weight of a hawk moth is about 50 mm and 100 mg, respectively. This requires a sensor that weighs about 10 mg and performs well in flight. A MEMS-based pressure sensor that measures differential pressure may be employed to evaluate the aerodynamic forces of the flapping wings of the insect-type ornithopter. The sensing is carried out using a micro-cantilever with a piezoresistive layer on its surface whose resistance varies when subjected to mechanical stresses. Deflections of the cantilever due to aerodynamic forces change the resistance of the piezoresistor which is calibrated to measure pressure fluctuations. With this sensor, pressure measurements in the frequency range of 0-1 kHz have been realized.

Ultraminiature MEMS

Treatment of neuromuscular diseases requires assessment of the patients' muscles. Common muscle strength assessment techniques include manual muscle testing, instrumented strength testing, and electromyography. Pressure is developed inside a muscle as the contracting muscle fibers apply pressure on the interstitial fluid volume. There is a linear relationship between intramuscular pressure (IMP) and joint torque [14]. By attaching an ultraminiature capacitive MEMS sensor to the muscle tissue, the IMP can be measured using the change in capacitance. The sensor grips the surrounding muscle tissue with anchors to minimize movement of the pressure sensor during muscle contraction.

Conclusions

Sensors at the micro/nano scale are useful in a wide range of applications in medical science, biosensing,, and the design of biologically-inspired sensors. This article is the first of a threepart series. It introduced the subject of MEMS sensing and recent advances in MEMS sensor technology in the domain of biomedical sensing. Bio-sensing and bio-inspired sensors are making an impact on technological development, innovation and progress in biomedical applications.

Part 2 of the series is dedicated to mechanical sensors. Related technologies of MEMS sensors will be discussed including compensation for environmental effects, the Casimir effect, and harvesting of energy for self-powered sensors. The subject of sensor selection will also be addressed. Part 3 will explore MEMS sensing in the thermo-fluid and electro-magnetic domains.

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