Design and Analysis of a MEMS Cell Adhesion Device

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Abstract

Cell adhesion studies have applications in many branches of biological science, including pathology, oncology, and cell biology. The biological changes in a cell resulting from mechanical stimuli are not only indicative of cell health, but can also illuminate the underlying mechanical structure of cells in general. We propose a novel MEMS-based device to test cell adhesion. The cell sits atop the device, which consists of several polymer micropillars. As the cell moves, the pillars deflect. A piezoelectric base made of polyvinylidene fluoride (PVDF) converts the mechanical deflection of the pillar to an electrical signal. This signal can be analyzed in order to extract data on the force applied by the cell.
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Introduction

Background
Research in cellular mechanics has established a relationship between mechanical forces on cells and their biological response. The relationship works in both directions: mechanical forces can stimulate biological response and biochemical signals can alter mechanical properties (Bao and Suresh, 2003 and Yang and Saif, 2005). A better understanding of the cellular response to external mechanical stimuli may lead to major advances in many areas of medicine, ranging from treatment of disease to tissue engineering.

There is a deep link between cell structure, function, and mechanical properties; external forces can help regulate cell function, and adhesion of certain types of cells to the extracellular matrix (ECM) can trigger the onset of key cell functions such as growth and motility (Ingber, 2002). Depending on the stiffness of the substrate, cells have been shown to alter their adhesion structure and motile behavior. Remarkably, even their direction of motion may be controllable through the choice of substrate (Pelham and Wang, 1997). Along similar lines, better control of cell orientation would be useful for tissue engineering and implants. The orientation process, called “contact guidance”, has been shown to be a function of external mechanical stimuli from the substrate on which the cells are situated (Bettinger et al. 2006). As another example, vascular cells must sense and respond to shear stress forces (Hsiai, et al. 2004). Similarly, endothelial cells that incorrectly sense and respond to characteristics of shear flow can lead to vascular diseases (Bao and Suresh, 2003). It has even been hypothesized that certain diseases arise when cells are subjected to mechanical forces that deviate from those in their “native” environment (Bao and Suresh, 2003).

Not only do external forces regulate cell function, but the cells themselves often exert forces that are crucial to an organism’s overall health. Many diseases occur because cells stop deforming or correctly modulating forces. For example, heart failure can result from cells that lose their ability to contract (Bao and Suresh, 2003).

Since cellular response to mechanical stimuli is so critical to healthy cell function, it is crucial that we understand the mechanical properties of the cell. MEMS devices that study cell adhesion have great potential to achieve this end.
Overview of Experimental Methods

A number of experimental methods have been developed which enable direct manipulation, stimulation, or observation of a single cell. These methods are very diverse, consisting of magnetic devices, fluid devices, and methods based on substrate stiffness and digital image correlation.

Particle Tracking Methods

Various forms of particle tracking have been utilized to estimate traction forces and image the mechanical response of cells. Particles embedded in a flexible substrate act as fiduciary markers in the embedded particle tracking method (Beningo, et al. 2002 and Munevar, et al. 2001). By tracking the motion of these markers in an optical microscope, the displacement of the substrate in response to cellular traction forces can be imaged at multiple points simultaneously. For substrates of known stiffness, these displacements can be translated into force vectors. The resolution of the optical microscope limits the displacement resolution and subsequent force estimates. The accuracy of the substrate stiffness measurement further limits resolution. In multiple-particle-tracking microrheology, fluorescent microparticles are injected into the cytoplasm of the cell (Tseng, et al. 2002). These particles move with Brownian motion in response to random forces caused by the thermal energy of the system. The magnitude of the particle displacement, which is tracked by an optical system, is a function of the stiffness and viscosity of the surrounding fluid.

Pillar Deflection Methods

Micropatterned substrates are an alternative to particle tracking methods. Here, a rigid substrate is patterned with closely-spaced, flexible pillars of known stiffness (Tan, et al. 2003). These pillars bend in response to traction forces created by a cell placed on top of them. The displacement, which is measured by microscope as in the embedded particle tracking method, is again translated to a force via the known stiffness of the pillars. Like the embedded particle tracking method, the accuracy of this method is limited by the resolution of the optical displacement measurement and the estimation of the pillar stiffness. Our device aims to remove the uncertainty associated with digital image correlation by measuring the displacement of the pillars with a piezoelectric polymer. The electric signal created by the strain on the polymer is used instead to determine the deflection.

Magnetic Methods

In addition to these methods, there have been a number of methods which make use of magnetic forces to test cell adhesion. Most rely on magnetic tweezer technology, which uses magnetic fields to manipulate beads adhered to a test subject, which may be a cell, a protein, or even DNA (Wirtz, et al. 2000).

Magnetic Twisting Cytometry

This method, used by Ingber, et al. in 1993, uses magnetic beads to induce angular strain on the cell membrane. The beads are functionalized to bind to the cell’s extracellular
matrix receptors. The beads are magnetized, and then exposed to an external magnetic field. This applies a particular angular strain to the cell membrane at all points of bead adhesion. Through this type of testing, it was found that the resulting cell response indicates that the extracellular matrix receptor acts also as a mechanoreceptor.

**Magnetic Bead Microrheometry**

In a similar experiment (Bausch, et al. 1998), magnetic beads are bound to the cell in the same way. In this case, a magnetic bead rheometer is set up to expose the cell and attached beads to strong magnetic pulses. The deflection of the beads was monitored by particle tracking. The results provide values for the viscoelastic properties of the cell, and show cell response to actual shear forces (as opposed to the twisting forces in Ingber, et al.). Bausch, et al. claim that this can be used “to evaluate local changes in the cytoskeletal structure caused by local mechanical agitations,” or those caused by binding to the extracellular matrix. That is, this method can be used to probe the cell in a controlled manner and observe the response.

**Microcantilever Methods**

Saif et al. used a MEMS sensor consisting of a single crystal silicon microcantilever beam for in-situ studies of adhesion of living cells. The cantilever is 1200 µm long, 4 µm wide and 11.5 µm deep, with a spring constant of 18.1 nN/µm. It is supported by an anchor attached to the Si substrate. The device was fabricated using standard micromachining processes. The sensor is functionalized by a thin layer of fibronectin, brought into contact with the cell and is then moved by a piezoactuator to apply local deformation to a single living cell attached to a substrate. Because the cantilever presents only a small surface area to the cell, a limited number of adhesion sites are allowed to form. The cantilever is then moved away from the cell; the force interaction between the two is measured from the deformation of the cantilever. In these experiments, bovine endothelial cells were probed. The experiments were repeated with cantilevers 1000 µm long, 1 µm wide, 10 µm deep, with a nominal spring constant of 0.4 nN/µm, and with various geometries at their ends. The resolution of measurement of cantilever deformation for both sets of cantilevers was \( \Delta x \approx 0.5 \, \mu\text{m} \), giving a resolution of force measurement of 9 nN and 0.2 nN for the first and second cantilevers, respectively (Saif, et al. 2003).

Using a similar concept, Mahaffy et al. used AFM-based microrheology to study the viscoelastic behavior at the well-adhered and non-adhered regions of a cell. Thus they were able to correlate elastic strength and Poisson’s ratio to the adhesive state of the cell. The group modified commercial AFM tips by gluing spherical polystyrene beads with radii ranging from 1.5 to 4 µm with standard TEM epoxy. Reverse imaging over a sharp AFM tip ensured that the bead was properly centered (Mahaffy et al. 2004).

**Substrate Stiffness Methods**

Burton and Taylor used UV irradiation to increase the compliance of transparent elastic substrates fabricated from silicone polymers. Small movements at the cell could then be translated into measurable wrinkles on the substrate. The substrates were calibrated
against force measurements made by flexible microneedles of known stiffness (Burton and Taylor, 1997).

Lo et al. showed that cells can adjust their response depending on the stiffness of their substrate: 3T3 fibroblasts generated significantly stronger traction on stiff substrates than on soft substrates. The stronger mechanical response on stiff substrates may regulate the stability of focal adhesions. In the experiments, the group cultured cells on polycrylimide sheets with a rigidity gradient. Deformations of the sheets due to cell-generated forces were detected by fluorescent beads embedded near the substrate surface (Lo, et al. 2000).

**Fluid Methods**

The influence of laminar shear stress on cell proliferation was investigated by Levesque, et al. (1990) focusing on the effect of both steady and pulsatile shear stress. Bovine aortic endothelial cells exposed to steady flow showed a reduction in the rate of cell proliferation. By increasing the shear stress, the rate of proliferation was totally arrested. Pulsatile shear stress produced an exaggeration of the effect observed in response to steady shear stress with a significant reduction in growth rate.

**Micropipette Aspiration Method**

A micromechanical method was developed in Evans, Berk and Leung (1991), Evans, et al. (1991), and Berk and Evans (1991) to measure the rupture strength of a molecular-point attachment (focal bond) using two micropipettes. The method can be used to study the rupture between two macroscopically smooth membrane capsules. Two membrane capsules are chemically cross-linked in the form of a rigid sphere or are pressurized by large suction to create a stiff sphere outside the pipette. These two nearly perfect spheres are maneuvered by small micropipettes to form a point contact at their poles and then they are separated to test the strength of the contact. The total extension of the deformable cell was measured by electronic video-image analysis of the pipette displacement. The range of forces that can be tested with this technique depends on the properties of the cell (elastic modulus of the membrane, size of the capsule, etc.): for biological membranes, the range is between 1 and 100 pN.
Fabrication

Figure 1: Schematic of a single pillar in the pillar array. Each pillar consists of a polylactide (PLA) column on an element of piezoelectric polyvinylidene fluoride (PVDF). The PVDF is sandwiched between a common top electrode and four bottom electrodes.

The device consists of an array of flexible polylactide (PLA) pillars beneath a soft polydimethylsiloxane (PDMS) membrane. This membrane prevents the cell from sinking between the pillars while providing a more natural, continuous surface on which the cell can adhere. Piezoelectric polyvinylidene fluoride (PVDF) elements at the base of each pillar sense deflection due to traction forces imposed by the cell. Each PVDF element is sandwiched between nickel electrodes to measure voltages resulting from pressure applied to the element.

In each step of the fabrication process, alignment with pre-existing features is critical. For example, the piezoelectric elements and electrodes must be aligned with the pillars such that forces are interpreted correctly. If the piezoelectric element is offset, the voltage output for a given force in the direction of the offset will be reduced. In order to maintain consistent, high-precision alignment through all layers, small alignment pillars are fabricated early in the fabrication process. These pillars, which remain visible in the electron microscope as each subsequent layer is defined by e-beam lithography (EBL), serve as alignment marks throughout the fabrication process. In theory, this allows each layer to be aligned to within ~10 nm (resolution of the EBL system) of the desired position. This offers greater precision than processes using different alignment marks for each layer as each layer is aligned to the same reference mark, minimizing overall deviation. Each lithography step is done using EBL as it offers superior resolution and alignment to that of optical lithography. The entire fabrication process requires 5 masks, one of which is an inversion of another.
Alignment Pillars

Figure 2: Patterning the alignment pillars. (a) Deposit silicon nitride by LPCVD. (b) Spincoat with resist and pattern to create an etch mask for the alignment pillars. (c) Etch nitride by RIE at low pressure to define the alignment pillars.

The alignment pillars are designed to ensure their visibility through each subsequent deposition and patterning step. A layer of silicon nitride is deposited by LPCVD. It is then masked then spincoated with e-beam resist and exposed using the mask shown in Figure 2b. The nitride is then etched through by RIE at low pressure for a highly anisotropic etch. The height of the pillars (defined by the thickness of the silicon nitride film) is chosen such that their top remains exposed as the subsequent layers are added.
**PLA Pillars and Top Electrode**

![Diagram of PLA pillars and top electrode](image)

Figure 3: Process for creating PLA pillars. (a) Spincoat wafer with resist and pattern by EBL to define a mask for etching the Si pillar mold. The alignment pillars are used to align the pattern. (b) Etch wafer by DRIE. (c) Strip resist and silanize wafer to aid release of the PLA. Pour liquid PLA over the mold and cure. (d) Evaporate a nickel film over the PLA to serve as a common top electrode for the PVDF elements.

The silicon wafer serves as a mold for casting the PLA pillars. To create the mold, an e-beam resist etch mask is patterned by EBL using the alignment pillars to align the pattern (Figure 3a). APEX-E e-beam resist is used for its excellent dry etch resistance. While APEX-E has only moderate resolution (0.15 µm) compared to other e-beam resists such as PMMA, it is sufficient for this step as it is used only to define circles 2 µm in diameter. High aspect ratio holes are then etched in the wafer using DRIE (Bosch process, Figure 3b). After etching, the wafer is cleaned and silanized with vapor phase tridecafluoro-trichlorosilane. This prevents the PLA from adhering to the mold upon curing, allowing it to be easily peeled away (Roure et al. 2005). Next, liquid PLA is poured over the mold and cured (Figure 3c). Finally, nickel is deposited by e-beam evaporation over the entire exposed surface. This nickel layer serves as a common ground electrode for all the PVDF elements.


**Patterning PVDF Piezoelectric Elements**

![Diagram of process steps](image-url)

Figure 4: Patterning the piezoelectric elements. (a) Spincoat PVDF over the nickel electrode layer. (b) Spincoat the PVDF with e-beam resist and pattern. The alignment pillars are again used to align the pattern. (c) Etch the PVDF by RIE. (d) Strip resist.

The piezoelectric PVDF elements are patterned at the base of each pillar. Prior to deposition of the PVDF, a short prebake step at 90°C for 15 seconds is performed to drive away any moisture. This improves adhesion of the PVDF to the substrate (Atkinson et al. 2003). A PVDF solution of 15 wt. % is then spincoated on the wafer (Figure 4a). Atkinson, et al. demonstrated this concentration consistently yields a thickness of 1 µm at 4000 rpm with a uniformity of better than 5% in thickness (Atkinson et al. 2003). The wafer is baked at 90°C for 24 hours for curing. The use of a chemically pre-imidized PVDF solution makes these low curing temperatures possible, avoiding damage to the pre-existing PLA polymer features.

After curing, the wafer is spincoated with APEX-E resist and patterned by EBL (Figure 4b). Again the protruding alignment pillars serve as alignment markers to ensure the PVDF elements are properly aligned with the pillars. The mask used in this step is the inverted form of Mask 2 used to define the pillar mold in the silicon wafer. The PVDF is then etched through by oxygen plasma (Figure 4c). The underlying nickel layer serves as an etch stop. Finally, the resist is removed (Figure 4d).
Electrode Forming

Figure 5: Electrode and trace layout. Each piezoelectric PVDF element has four bottom electrodes. The traces are divided into two layers (see also Figure 1) separated by a silicon dioxide dielectric layer to allow for wider traces. The traces in Layer 2 make contact to the electrodes through the dielectric by conductive vias.

Figure 6: Patterning the bottom electrodes and traces. (a) Spincoat with PDMS. (b) The bottom electrodes are formed by EBL, evaporation, and liftoff. (c) Deposit silicon dioxide by PECVD. (d) Etch small holes for vias through the oxide by RIE. (e) Sputter nickel over the entire surface, filling
the vias. Define traces in the nickel by spincoating with resist, patterning by EBL, then etching with a wet chemical etch. (f) Conformally coat the entire top surface with parylene by CVD.

Each pillar has four individually addressable bottom electrodes. Due to the large number of traces required to address these electrodes, the traces are separated into two layers with a silicon dioxide dielectric and vias between them. In this way, two of the traces for each piezoelectric element exist in the first layer and the other two in the second layer (as shown in Figure 5).

To create the electrodes, the wafer is first spincoated with PDMS (Figure 6a). This PDMS layer serves as a support for the first layer of traces. After spincoating, a brief low-pressure oxygen plasma etch is conducted to remove any residual PDMS covering the PVDF elements. This ensures the electrodes will make direct contact with the PVDF. PDMS is used here due to its relatively low Young’s modulus compared to PVDF. This concentrates the majority of the load in the stiffer PVDF elements, maximizing their voltage output.

The bottom electrodes and first layer of traces are then patterned on the PVDF/PDMS layer (Figure 6b) by EBL, evaporation, and liftoff. Again the protruding alignment pillars are used for alignment. Before defining the second layer of traces, a silicon dioxide dielectric layer with conductive vias must be formed. These vias allow this second layer of traces to access the electrodes. First, silicon dioxide is deposited by PECVD (Figure 6c). The use of plasma in the PECVD process allows deposition at low temperatures, avoiding damage to the PDMS and PLA features. Next, via holes are etched through the oxide (Figure 6d) using a mask defined by EBL and RIE. Nickel is then sputtered over the entire surface. This nickel fills the via holes, making electrical contact with the electrodes beneath. The wafer is then spincoated with resist and patterned to define the second layer of traces. Then the unmasked nickel is removed in a wet chemical etch (Figure 6e). Finally, a rigid layer of parylene is deposited by CVD (Figure 6f). This parylene layer serves as a bonding agent to bond the existing features to a support wafer.

**Wafer Bonding**

![Wafer Bonding Diagram](image)

Figure 7: Process for wafer bonding using parylene. (a) Turn the wafer over and bring it into contact with another silicon support wafer. Heat the wafers to form a bond between the parylene and support wafer. (b) Pull away the original mold wafer.
Before removing the mold, the structures must be bonded to a support wafer. The wafer is turned over and brought into contact with another silicon support wafer (Figure 7a). They are then heated to 130°C which causes additional cross-linking in the parylene, resulting in bonding between the parylene and new silicon support wafer (Kim and Najafi, 2003). This bonding process was chosen over others as it is effective at low temperatures and does not require direct contact between two silicon surfaces. At 130°C, the bond strength is similar to that of a soft solder joint (Kim and Najafi, 2003). Finally, the original mold wafer is pulled away. The PLA releases cleanly from the silicon mold due to the silanization treatment performed before it was cast.

**Thin PDMS Membrane**

![Diagram of PDMS membrane process](image)

Figure 8: Transferring thin PDMS membrane. (a) Begin with a bare silicon wafer. (b) Spincoat with photoresist. (c) Spincoat with diluted PDMS (allows for thinner films). (d) Turn over and bring onto contact with pillar array. (e) Lift away support wafer.

A thin PDMS membrane is bonded across the tops of the pillars to prevent the cell from sinking between the pillars and to create a continuous surface to which the cell can adhere. Lee, et al. demonstrated a process for fabricating thin free-standing PDMS membranes (Lee, J., 2005). Here the membrane is fabricated on a separate wafer then transferred to the pillars in a later step. First, a polished silicon wafer is spincoated with photoresist (Figure 8b). This prevents the PDMS membrane from adhering strongly to the wafer, allowing for easy transfer. It is then spincoated with diluted PDMS pre-polymer to form a thin film (Figure 8c). In order to make extremely thin PDMS membranes, the PDMS pre-polymer is diluted with hexane to a ratio of 1:5 PDMS to hexane by weight. This reduces the viscosity, allowing thinner, more uniform films to be spincoated. After spincoating, both the membrane wafer and pillars are treated in oxygen plasma for one minute and brought into contact (Figure 8d). This forms an irreversible bond between the tops of the pillars and the PDMS membrane (Jo, B.-H., et al., 2000). This bonding process will not damage the soft pillars as it does not require additional external force. The support wafer is then peeled away (Figure 8e).
**Biological and CMOS Compatibility**

The cell must adhere properly to the PDMS membrane in order to spread and behave naturally. This requires functionalization of the membrane. After completion of the fabrication, the device is treated in oxygen plasma for two minutes. This makes the PDMS membrane hydrophilic and facilitates adsorption of fibronectin and other organic materials (Roure et al. 2005). Without this treatment and functionalization, it is unlikely that the cell will adhere and spread naturally on the surface.

All processes used in the fabrication of this device are CMOS compatible. This allows for the possibility of adaptation to sophisticated methods of multiplexing which require solid-state electronic devices to be cofabricated within the layers of the device. For example, Vettiger et al. embedded diodes and switches in an array of individually addressable piezoelectric actuators (Vettiger et al. 2002). With the addition of these solid state devices, they were able to reduce the number of traces required to access individual actuators. In our case, the fabrication is simplified by using an individual trace for each electrode, thus increasing the yield. This also enables both sensing and actuating of individual pillars. In the multiplexed scheme, a single bad diode or switch could potentially eliminate the functionality of an entire row and column of pillars. However, if the number of pillars in the array were to be increased significantly, a multiplexing scheme similar to that of Vettiger et al. may become necessary.
Structural Analysis

Linear Piezoelectricity Theory

Under small field conditions the linear theory of piezoelectricity can be applied and its constitutive relation for a sensor (piezoelectric direct effect) is [1, 2]

$$D_i = e_iE_j + d_{ij}\sigma_j \quad i = 1, 2, 3 \quad j = 1, 2, ..., 6$$

(1)

where $D_i$ is the electric displacement (C/m$^2$), $e_i$ is the electric permittivity (C/V/m), $E_j$ is the applied electric field (V/m), $d_{ij}$ the piezoelectric coefficients (C/N), and $\sigma_j$ the stress components. If there is no external electric field, eq. (1) can be simplified to

$$D_i = d_{ij}\sigma_j \quad i = 1, 2, 3 \quad j = 1, 2, ..., 6$$

(2)

The piezoelectric matrix is

$$d = \begin{bmatrix} 0 & 0 & 0 & 0 & d_{15} & 0 \\ 0 & 0 & 0 & d_{24} & 0 & 0 \\ d_{31} & d_{32} & d_{33} & 0 & 0 & 0 \end{bmatrix}$$

(3)

The generated charge $q$ (C) is

$$q = \int_{\text{electrode area}} D_i dA_i \quad i = 1, 2, 3$$

(4)

where $dA_i$ is the infinitesimal electrode area normal to the $i$ direction.

The voltage across the sensor electrodes $V$ is

$$V = \frac{q}{C_p}$$

(5)

where $C_p$ is the capacitance of the sensor and, for the case of a parallel plate capacitor is

$$C_p = \frac{e_\perp \cdot A_c}{h}$$

(6)

where $e_\perp$ (C/V/m) is the electric permittivity in the direction orthogonal to the electrode plate and $A_c$ is the area of the capacitor plate and $h$ the distance between the plates.
Beam Analysis

From linear elastic beam bending theory the state of stress in the piezoelectric material is uniaxial and

$$\sigma_z = \frac{M_y \cdot x}{I} = \frac{64 \cdot M_y}{\pi \cdot D^4} \cdot x$$

$$= \frac{64 \cdot M_y}{\pi \cdot D^4} \cdot r \cdot \cos \vartheta$$  \hspace{1cm} (7)

Combining eqs. (2), (3), (4), and (7) we obtain

$$q = \iint_{A_y} d_{33} \sigma_{33} dA_3 = \iint_{A_y} \frac{64M_y}{\pi D^4} \cdot r \cos \vartheta d\vartheta dr$$

$$= d_{33} \frac{64M_y}{\pi D^4} \int_{D/2-s-\varphi/2}^{D/2} \int_{\varphi/2}^{\varphi/2} r^2 \cos \vartheta d\vartheta dr$$

$$= d_{33} \frac{64M_y}{\pi D^4} \int_{D/2-s-\varphi/2}^{D/2} \int_{\varphi/2}^{\varphi/2} r^2 \cos \vartheta d\vartheta dr$$

$$= d_{33} \frac{64M_y}{\pi D^4} \cdot \left(3 \cdot D^2 - 6 \cdot D \cdot s + 4 \cdot s^2\right) \cdot \sin(\varphi/2)$$

$$= \frac{32 \cdot M_y \cdot d_{33}}{3 \cdot \pi} \cdot \left(3 \cdot D^2 - 6 \cdot D \cdot s + 4 \cdot s^2\right) \cdot \sin(\varphi/2)$$

$$= \frac{32 \cdot M_y \cdot d_{33}}{3 \cdot \pi} \cdot \frac{D^4}{\text{geometry of the electrode}}$$

With this geometry, the area of one electrode is

$$A_e = \int_{D/2-s-\varphi/2}^{D/2} \int_{\varphi/2}^{\varphi/2} r d\vartheta dr = \frac{s \cdot (D-s) \cdot \varphi}{2}$$  \hspace{1cm} (9)

Combining eqs. (5), (6), (8), and (9) we obtain
\[ V = \frac{q}{C_p} = \frac{q \cdot h}{e_\perp \cdot A} \]
\[ = \frac{h}{e_\perp} \cdot \left( \frac{2 \cdot M_y \cdot d_{33}}{s \cdot (D - s) \cdot \varphi} \cdot \frac{3 \cdot \pi}{D^4} \right) \left( 3 \cdot D^2 - 6 \cdot D \cdot s + 4 \cdot s^2 \right) \cdot \sin(\varphi/2) \]
\[ = \frac{64 \cdot d_{33}}{3 \cdot e_\perp \cdot \pi} \left( \frac{3 \cdot D^2 - 6 \cdot D \cdot s + 4 \cdot s^2}{(D - s) \cdot D^4 \cdot \varphi} \right) \cdot \sin(\varphi/2) \cdot h \cdot M_y \]  

The moment \( M_y \) is a function of \( z \)
\[ M_y = F_x \cdot (L - z) \]
where \( F \) is the force that the cell exerts in the \( x \) direction at the top of the pillar.
If \( h << L \) we can assume that \( M_y \) is constant over \( h \) and equal to the average value on this region
\[ \overline{M_y} = F_x \cdot \left( L - \frac{h}{2} \right) \]

Combining eqs. (10) and (11) we obtain an expression for the voltage among a couple of electrodes
\[ V = \frac{64 \cdot d_{33}}{3 \cdot e_\perp \cdot \pi} \left( \frac{3 \cdot D^2 - 6 \cdot D \cdot s + 4 \cdot s^2}{(D - s) \cdot D^4 \cdot \varphi} \right) \cdot \sin(\varphi/2) \cdot h \cdot \left( L - \frac{h}{2} \right) \cdot F_x \]  

**Parametric Study**

Equation (12) can be used to study how the voltage \( V \) varies with the geometric parameters \( D, s, L, h, \) and \( \varphi \). On each plot only one of the five parameters is varied and the other four are fixed to the reference values of \( D_0 = 2 \mu m, s_0 = 1 \mu m, h_0 = 1 \mu m, L_0 = 20 \mu m, \) and \( \varphi_0 = 80^\circ \). The force exerted by the cell is varied between 10 nN and 100 nN. The pillar is made of PLA while the piezoelectric material is PVDF. The material properties are reported in the following table [1, 3].

<table>
<thead>
<tr>
<th>Material</th>
<th>Quantity</th>
<th>Value</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVDF</td>
<td>Young's modulus, ( E )</td>
<td>5</td>
<td>GPa</td>
</tr>
<tr>
<td></td>
<td>Piezoelectric constant, ( d_{33} )</td>
<td>-33</td>
<td>pC/N</td>
</tr>
<tr>
<td></td>
<td>Electric permittivity, ( e_{33} )</td>
<td>0.106</td>
<td>nC/(V·m)</td>
</tr>
<tr>
<td>PLA</td>
<td>Young's modulus, ( E )</td>
<td>3.760</td>
<td>GPa</td>
</tr>
</tbody>
</table>
Figure 10: Voltage vs. pillar diameter for several forces

Figure 11: Voltage vs. pillar height for several forces
Figure 12: Voltage vs. electrode separation for several forces

Figure 13: Voltage vs. electrode width for several forces
The “nominal value” represents the final geometry selected for the micropillars. The force exerted by a cell is expected to range from 10 – 100 nN on a single pillar; from the graphs above, this corresponds to an output voltage range of 55 - 550 mV, which is acceptable.

**Final Design**

The final design parameters are $D = 2 \, \mu m$, $s = 1 \, \mu m$, $h = 1 \, \mu m$, $L = 20 \, \mu m$, and $\varphi = 80^\circ$. The response curve $V = V(F)$, voltage output as a function of the magnitude of the force in the $x$ direction, for one electrode is represented in Figure 15.
Inverse Analysis

In-plane Force
Let’s first consider the in-plane force. In general, we will have a force of modulus $F$ at an angle $\alpha$ from the $x$ axis.
Eq. (7) becomes

\[ \sigma_z = \frac{M_y \cdot x + M_x \cdot y}{I} = \frac{64}{\pi \cdot D^4} \left( M_y \cdot x + M_x \cdot y \right) \]

\[ = \frac{64}{\pi \cdot D^4} \left( M_y \cdot r \cdot \cos \theta + M_x \cdot r \cdot \sin \theta \right) \]  

(13)

where the moment components are

\[ \begin{align*}
M_y &= F_x \cdot (L - z) \\
M_x &= F_y \cdot (L - z)
\end{align*} \]

and the force components are

\[ \begin{align*}
F_x &= F \cdot \cos \alpha \\
F_y &= F \cdot \sin \alpha
\end{align*} \]

Combining eqs. (2), (3), (4), and (13) we obtain the following four expressions for the four electrode couples (1, 2, 3, and 4)

\[ q_1 = \iint_{A_1} d\sigma dz da = \iint_{A_1} d\sigma dz \frac{64}{\pi \cdot D^4} \left( M_y \cdot r \cdot \cos \theta + M_x \cdot r \cdot \sin \theta \right) rd\theta dr \]

\[ = \frac{64}{\pi \cdot D^4} \iint_{\phi/2}^{\phi} \left( M_y \cdot r \cdot \cos \theta + M_x \cdot r \cdot \sin \theta \right) rd\theta dr \]

\[ = 128 \cdot d_{33} \cdot \frac{D^3}{8} \left( \frac{D}{2} - s \right)^3 \cdot \sin (\phi/2) \cdot M_y \]

\[ = \frac{128 \cdot d_{33}}{3 \cdot \pi} \cdot \frac{D^3}{8} \left( \frac{D}{2} - s \right)^3 \cdot \sin (\phi/2) \cdot M_y \]

\[ q_2 = \iint_{A_2} d\sigma dz da = \iint_{A_2} d\sigma dz \frac{64}{\pi \cdot D^4} \left( M_y \cdot r \cdot \cos \theta + M_x \cdot r \cdot \sin \theta \right) rd\theta dr \]

\[ = \frac{64}{\pi \cdot D^4} \iint_{\phi/2}^{\phi} \left( M_y \cdot r \cdot \cos \theta + M_x \cdot r \cdot \sin \theta \right) rd\theta dr \]

\[ = 128 \cdot d_{33} \cdot \frac{D^3}{8} \left( \frac{D}{2} - s \right)^3 \cdot \sin (\phi/2) \cdot M_x \]

\[ = \frac{128 \cdot d_{33}}{3 \cdot \pi} \cdot \frac{D^3}{8} \left( \frac{D}{2} - s \right)^3 \cdot \sin (\phi/2) \cdot M_x \]
\[ q_3 = \int_{A_3} d_3 \sigma_{33} dA_3 = \int_{A_3} d_3 \frac{64}{\pi \cdot D^3} (M_y \cdot r \cdot \cos \vartheta + M_x \cdot r \cdot \sin \vartheta) \, rd \vartheta dr \]
\[ = \frac{d_3}{3} \frac{64}{\pi \cdot D^3} \int_{D/2}^{\varphi/2} \int_{\varphi/2}^{\varphi} \left( M_y \cdot r \cdot \cos \vartheta + M_x \cdot r \cdot \sin \vartheta \right) \, rd \vartheta dr \]
\[ = -\frac{128 \cdot d_3}{3 \cdot \pi} \frac{D^3}{8} \left( \frac{D}{D - s} \right)^3 \sin \left( \frac{\varphi}{2} \right) \cdot M_y \]
\[ = -q_1 \]
\[ q_4 = \int_{A_4} d_3 \sigma_{33} dA_4 = \int_{A_4} d_3 \frac{64}{\pi \cdot D^3} (M_y \cdot r \cdot \cos \vartheta + M_x \cdot r \cdot \sin \vartheta) \, rd \vartheta dr \]
\[ = \frac{d_3}{3} \frac{64}{\pi \cdot D^3} \int_{D/2}^{\varphi/2} \int_{\varphi/2}^{\varphi} \left( M_y \cdot r \cdot \cos \vartheta + M_x \cdot r \cdot \sin \vartheta \right) \, rd \vartheta dr \]
\[ = -\frac{128 \cdot d_3}{3 \cdot \pi} \frac{D^3}{8} \left( \frac{D}{D - s} \right)^3 \sin \left( \frac{\varphi}{2} \right) \cdot M_x \]
\[ = -q_2 \]

Using eq. (14)-(17), eq. (10) becomes
\[
\begin{cases}
V_1 = V_3 = -\frac{64 \cdot d_3}{3 \cdot \pi} \frac{\left( 3 \cdot D^2 - 6 \cdot D \cdot s + 4 \cdot s^2 \right) \cdot \sin \left( \frac{\varphi}{2} \right) \cdot h}{\left( D - s \right) \cdot D^4} \cdot M_y \\
V_2 = V_4 = -\frac{64 \cdot d_3}{3 \cdot \pi} \frac{\left( 3 \cdot D^2 - 6 \cdot D \cdot s + 4 \cdot s^2 \right) \cdot \sin \left( \frac{\varphi}{2} \right) \cdot h}{\left( D - s \right) \cdot D^4} \cdot M_x 
\end{cases} \quad (18)
\]

The moments \( M_x \) and \( M_y \) are functions of \( z \)
\[
\begin{cases}
M_y = F_x \cdot (L - z) \\
M_x = F_y \cdot (L - z)
\end{cases}
\]

If \( h \ll L \) we can assume that \( M_x \) and \( M_y \) are constant over \( h \) and equal to the average value on this region
\[
\begin{cases}
\bar{M}_y = F \cdot \cos \alpha \cdot \left( L - \frac{h}{2} \right) \\
\bar{M}_x = F \cdot \sin \alpha \cdot \left( L - \frac{h}{2} \right)
\end{cases} \quad (19)
\]

Combining eqs. (18) and (19) we obtain an expression for the voltage among each couple of electrodes
\[
\begin{aligned}
V_1 = -V_3 &= \frac{32 \cdot d_{33}}{3 \cdot e_\perp \cdot \pi} \cdot \frac{(3 \cdot D^2 - 6 \cdot D \cdot s + 4 \cdot s^2) \cdot h \cdot (2 \cdot L - h) \cdot \sin(\varphi/2)}{(D - s) \cdot D^4 \cdot \varphi} \cdot F \cdot \cos \alpha \\
V_2 = -V_4 &= \frac{32 \cdot d_{33}}{3 \cdot e_\perp \cdot \pi} \cdot \frac{(3 \cdot D^2 - 6 \cdot D \cdot s + 4 \cdot s^2) \cdot h \cdot (2 \cdot L - h) \cdot \sin(\varphi/2)}{(D - s) \cdot D^4 \cdot \varphi} \cdot F \cdot \sin \alpha
\end{aligned}
\]  
(20)

If we define

\[
\Psi \equiv \frac{32 \cdot d_{33}}{3 \cdot e_\perp \cdot \pi} \cdot \frac{(3 \cdot D^2 - 6 \cdot D \cdot s + 4 \cdot s^2) \cdot h \cdot (2 \cdot L - h) \cdot \sin(\varphi/2)}{(D - s) \cdot D^4 \cdot \varphi}
\]

eqs. (20) become

\[
\begin{aligned}
V_1 &= \Psi \cdot F \cdot \cos \alpha \\
V_2 &= \Psi \cdot F \cdot \sin \alpha \\
V_3 &= -\Psi \cdot F \cdot \cos \alpha \\
V_4 &= -\Psi \cdot F \cdot \sin \alpha
\end{aligned}
\]  
(21)

**Out-of-plane Force**

The out-of-plane component of the force \( F_z \) has the same influence on all the four electrodes because the charge for all of them is

\[
q_z = \int_A d_{33} \sigma_{33} dA = \int_A d_{33} \frac{F_z}{A} \cdot \rho \, d\vartheta \, dr
\]

\[
= d_{33} \frac{F_z}{A} \int_A \rho \, d\vartheta \, dr
\]

\[
= d_{33} \frac{F_z}{A} \cdot A
\]

\[
= d_{33} \cdot F_z
\]  
(22)

thus for eqs. (5), (6), (9), and (22) the voltage on each of the electrode couples is

\[
V_z = \frac{q \cdot h}{e_\perp \cdot A_e}
\]

\[
= \frac{d_{33} \cdot h}{e_\perp \cdot A_e} \cdot F_z
\]

\[
= \frac{2 \cdot d_{33} \cdot h}{e_\perp \cdot s \cdot (D - s) \cdot \varphi} \cdot F_z
\]

\[
= \Psi_z \cdot F_z
\]  
(23)

where \( \Psi_z \) is a constant depending on the geometry and the material properties.
Total voltage output

Combining eqs. (21) and (23) we obtain the total voltage output for each electrode

\[
\begin{align*}
V_1 &= \Psi \cdot F \cdot \cos \alpha + \Psi_z \cdot F_z \\
V_2 &= \Psi \cdot F \cdot \sin \alpha + \Psi_z \cdot F_z \\
V_3 &= -\Psi \cdot F \cdot \cos \alpha + \Psi_z \cdot F_z \\
V_4 &= -\Psi \cdot F \cdot \sin \alpha + \Psi_z \cdot F_z
\end{align*}
\]

where the quantities \( F, \alpha, \) and \( F_z \) are to be determined solving the system of equations.

Using the first three eqs. (24) we obtain

\[
\begin{align*}
F_z &= \frac{V_1 + V_3}{2 \cdot \Psi_z} \\
F &= \frac{|V_1 - V_3| \cdot \sqrt{V_1^2 - 2 \cdot V_1 \cdot V_3 + 2 \cdot V_2^2 - 2 \cdot V_2 \cdot V_3 + V_3^2}}{\sqrt{2 \cdot \Psi_z \cdot (V_1 - V_3)}} \\
\alpha &= \arccos \left[ \frac{|V_1 - V_3|}{\sqrt{2 \cdot V_1^2 - 2 \cdot V_1 \cdot V_3 + 2 \cdot V_2^2 - 2 \cdot V_2 \cdot V_3 + V_3^2}} \right]
\end{align*}
\]

where

\[
\begin{align*}
\Psi_z &= \frac{2 \cdot d_{33} \cdot h}{e_{\perp} \cdot s \cdot (D - s) \cdot \phi} \\
\Psi &= \frac{32 \cdot d_{33} \cdot \left(3 \cdot D^3 - 6 \cdot D \cdot s + 4 \cdot s^2\right) \cdot h \cdot (2 \cdot L - h) \cdot \sin(\phi/2)}{3 \cdot e_{\perp} \cdot \pi \cdot (D - s) \cdot D^4 \cdot \phi}
\end{align*}
\]

Finite Elements analysis

In order to analyze the stress field between the electrodes, a Finite Element (FE) analysis has been conducted on ANSYS.

Geometry

To represent the behavior of a single pillar subject to a distributed force applied to its tip, the FE model has to represent only a quarter of the structure if symmetry and antisymmetry boundary conditions are applied to two of its faces. If the force is in the \( x \) direction, then the surface with normal in the \( y \) direction (yellow surface in Figure 17) needs to have a symmetry constraint while the surface with normal in the \( x \) direction (orange surface in Figure 17) needs to have an antisymmetry constraint.
**Constraints**

All the rotations and displacements of the bottom area of the SiO2 layer are imposed equal to zero (assumption of perfectly rigid substrate). While the on the other two faces are applied a symmetry and an antisymmetry constraint in order to simulate periodic pillars for the worse case in which the focus applied to two neighbor pillars has opposite direction.

**Loads**

The force of 100 nN is applied to the upper surface of the pillar as a uniformly distributed pressure.

**Mesh**

The mesh of the FE model is mapped and the element size decreases gradually from the boundaries to the area of interest (where the piezoelectric material is). The size of the elements has been chosen with a convergence analysis. The element type used is the 3D 20 node structural solid (ANSYS element 95). The pictures below report several views of the meshed model.
Figure 18: Meshed pillar model in top, side, and perspective views
Figure 19: Element sizing throughout the mesh
Material properties

The model has four materials which properties are reported in the following table.

<table>
<thead>
<tr>
<th>Material</th>
<th>Young’s modulus (GPa)</th>
<th>Poisson’s ratio</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVDF (Polyvinylidene Fluoride)</td>
<td>0.350–1.100</td>
<td>0.1</td>
<td>[1, 4]</td>
</tr>
<tr>
<td>PLA (Polylactic acid)</td>
<td>3.690-3.830</td>
<td>0.3-0.5</td>
<td>[3]</td>
</tr>
<tr>
<td>PDMS (polydimethylsiloxane)</td>
<td>360-870 10^{-6}</td>
<td>0.5</td>
<td>[5]</td>
</tr>
<tr>
<td>SiO₂ (Silicon Dioxide)</td>
<td>73</td>
<td>0.165</td>
<td>[6]</td>
</tr>
</tbody>
</table>

Figure 20 shows the position of each kind of material in the FE model.
Results

Stress field

Figure 21: The stress field in the deflected pillar
Figure 22: Close-up of stresses in the deflected pillar

Figure 23 reports the principal stress in the z direction $\sigma_z$ along a vertical path (in the z direction) at 0.5 um from the outside of the pillar. The graph clearly shows that the stress is almost constant in the 1 um thick piezoelectric material (PVDF) and thus we can use the average $\sigma_z$ stress over this area to compute the voltage output. This assumption was done in eq. (19).
Displacement

The displacement of the tip of the pillar in the $x$ direction due to a force of 100 nN in the $x$ direction applied to the tip of the pillar is 0.0684 um, as shown in the following picture. The value that can be obtained from the beam theory assuming that all the deformation takes place in the PLA is

$$\delta_x = \frac{F_x \cdot L^3}{3 \cdot E \cdot I} = \frac{F_x \cdot L^3 \cdot 2^6}{3 \cdot E \cdot \pi \cdot D^4} = 0.077 \ \mu m$$

which is close to the FE solution.
Resonant Frequency
The deformation of a cantilever beam due to a force at the tip is
\[ v(y) = \frac{F}{EJ} \left( \frac{L}{2} y^2 - \frac{y^3}{6} \right) \]  
(27)
The force that gives \( v(L) = 1 \) is
\[ F = \frac{3EJ}{L} \]  
(28)which substituted in eq. (27) gives
\[ d(y) = \frac{3}{L^3} \left( \frac{L}{2} y^2 - \frac{y^3}{6} \right) \]  
(29)The equivalent mass \( m^* \) and stiffness \( k^* \) for a 1D lumped model are
The resonance frequency is

\[ f = \frac{1}{2\pi} \sqrt{\frac{k^*}{m^*}} = \frac{\sqrt{770}}{88\pi} \sqrt{\frac{ED^2}{L^2\rho}} \quad (31) \]

For PLA we have \( \rho = 1250 \text{ kg/m}^3, \ D = 2\times10^{-6} \text{ m}, \ E = 3.76\times10^9 \text{ Pa} \) and \( L = 20\times10^{-6} \text{ m} \) thus

\[ f = 17.41 \text{ Hz} \quad (32) \]
Electrical Considerations

Frequency Response
The simplest model of our device is a slab of PVDF polymer between two gold plates. The plates are electrically connected to the circuitry of the chip by long, narrow Ni wires. A simple model of the circuit can then be constructed as follows:

![Figure 25: A lumped-element model of the system](image)

In this model, a resistor corresponding to the resistance of the polymer ($R_{PVDF}$) is in parallel with the capacitance ($C_{PVDF}$) between the two electrodes. That is, since they share the two voltages, they are modeled in parallel. The resistances of the long narrow Ni wires are included in the two $R_{wire}$ resistors. The capacitance and resistance of the polymer ($C_{PVDF}$ and $R_{PVDF}$, respectively) can easily be calculated as

$$C_{PVDF} = \frac{\varepsilon A}{d} \quad \text{and} \quad R_{PVDF} = \frac{\rho_{PVDF} d}{A}$$

where $\varepsilon$ is the permittivity of the PVDF, $A$ is the area of the plates (which can be calculated from the geometry), and $d$ is the gap between the plates. The values needed to calculate $R_{PVDF}$ and $C_{PVDF}$ can be taken from the specification sheet for Symalit PVDF 1000 from Quadrant Engineering Plastic Products.

$$C_{PVDF} = \frac{7.4 \times \varepsilon_0 \times 0.5236 \mu m^2}{1 \mu m} = 34.3 \times 10^{-18} F$$

$$R_{PVDF} = \frac{(10^{18} \Omega \mu m)(1 \mu m)}{0.5236 \mu m^2} = 1.91 \times 10^{18} \Omega$$

For the Ni wires, a resistivity of 63.1 n$\Omega$*m is assumed (Farrell and Greig, 1968). The wires will have a cross-sectional area of roughly 100 nm x 100 nm ($10^{15}$ m$^2$) and will
likely by less than 20 \, \mu m long (the longest will have to span from the center of the pillar array to the edge).

\[ R_{\text{wire}} = \frac{P_{\text{Ni}} \ell}{A} = \frac{(63.1 \times 10^{-9} \Omega m)(20 \times 10^{-6} m)}{523.6 \times 10^{-15} m^2} = 2.41 \Omega \]

So, the resistances and capacitance are known, and a transfer function for the model can be developed by simply combining impedances and taking the output across \( Z_P \):

\[
Z_P = \frac{1}{\frac{1}{Z_{PR}} + \frac{1}{Z_{PC}}} \text{, so } Z_{EQ} = 2Z_W + \frac{1}{\frac{1}{Z_{PR}} + \frac{1}{Z_{PC}}} = \frac{2R_W + R_P + 2R_W R_P C_p s}{1 + R_P C_p s}
\]

\[
H(s) = \frac{Z_P}{Z_{EQ}} = \frac{R_P}{R_P + 2R_W + 2R_W R_P C_p R_p s}
\]

A Bode plot of this transfer function can be made in Matlab so that the frequency response of the electrical portion of the device can be examined. The Bode plot (Figure 27) shows that low frequencies, where our system will be excited, are several orders of magnitude away from the cutoff frequency, which is at roughly \( 5 \times 10^{15} \text{ rad/sec} \).
Additionally, we can check that the time response of the PVDF is long enough that a
signal can be obtained with data acquisition equipment. Time constant \( \tau = R_{PVDF}C_{PVDF} \),
so we can calculate \( \tau = 65.5 \text{ s} \). This is large enough to ensure that the signals obtained by
the pillar array will not decay too quickly.

**Noise**

The noise inherent in the electrical circuit described above can largely be attributed to
thermal noise in the PVDF RC system. This noise can be quantified as long as the
resistance and temperature are known. Resistance was calculated above, and the
temperature will be assumed to be above room temperature in order to account for some
electrical heating. In order to ensure good performance, we therefore assume a worst-case
temperature condition of 150° F. The RMS thermal noise voltage across the capacitor can
then be found by the same process as in Senturia:

\[
V_{RMS} = \sqrt{4k_BTR\Delta f}
\]

where \( k_B \) is the Boltzmann constant, \( k_B=1.38065\times10^{-23} \text{ J/K} \), \( T \) is the temperature, \( R \) is the
value of the resistor, and \( \Delta f \) is the noise bandwidth. The noise bandwidth can be found by
integrating the transfer function over all frequencies. That is, the noisy PVDF system can
be modeled as the same resistor and capacitor from above. The noisy resistor can be
replaced by a noiseless resistor of the same value and a thermal noise voltage source:
The circuit is a simple voltage divider with the output across the capacitor. So,

\[
\frac{V_{\text{OUT}}}{V_{\text{IN}}} = \frac{Z_C}{Z_R + Z_C} = \frac{1}{sC} \frac{1}{R + \frac{1}{sC}} = \frac{1}{1 + RC}\]

Now \(\Delta f\) can be calculated by integrating the square of the magnitude of this transfer function over all frequencies.

\[
\Delta f = \int_{0}^{\infty} \frac{1}{1 + (2\pi f RC)^2} df = \frac{1}{4RC} = 0.0038 \text{ Hz}
\]

Now \(\Delta f\) is known, so we can calculate \(V_{\text{RMS}}\), the RMS noise voltage, using the formula above. \(V_{\text{RMS}}\) is then found to be 0.1364 mV. This value is less than 1% of the expected voltage output, so the thermal noise is acceptable. The resolution of the device is therefore primarily determined by the geometry of the device. That is, uncertainty in the fabrication process will propagate uncertainty in the calculation of the force from the electrical signal.

**Other Components**

**CMOS Circuitry**

In addition to the pillar device, there are several other CMOS components involved (amplifiers, filters, etc.) These circuits can be included on the same chip as the pillars, or the outputs can be routed out to a printed circuit board. The advantage of directly outputting the signals is that other commercially available components can be used, rather than designing these components from scratch so that they can be built on the chip. A circuit board will be necessary in any event, as the chip will be packaged so that it can be connected to a data acquisition unit or a computer for data processing.

**Actuation**

One key advantage of piezoelectric technology is that it can easily run in reverse. That is, the primary goal of this device is to sense cellular motion and forces, but the same mechanism can be used to actuate a pillar for the purpose of stimulating the cell. Rather
than sensing the voltage between the electrodes of the pillar, a voltage can instead be applied to it. The piezoelectric polymer will strain in response to the electrical input, which in turn will tilt the pillar.

The voltages necessary to achieve the desired mechanical output will be higher than those sensed for the same mechanical input due to losses in the material. These losses are characterized by the electromechanical coupling factor $k$, which for PVDF is ~0.1 to 0.3. The coupling factor $k$ is defined in Schwartz, 2002, as either

\[ k^2 = \frac{\text{stored mechanical energy}}{\text{input electrical energy}} \quad \text{or} \quad k^2 = \frac{\text{stored electrical energy}}{\text{input mechanical energy}} \]

Assuming a value of $k = 0.1$, we can then estimate that the input voltage to achieve a particular deflection will have to be 10 times as large as the voltage output from that same deflection (mechanical energy is proportional to deflection squared, electrical energy is proportional to voltage squared, so $k$ is proportional to deflection over voltage). In other words, if the pillar is deflected $x$ nm and produces a $y$ volt output, then $10y$ volts must be applied in order to deflect the pillar by $x$ nm. This is only an estimate, however, as actual values will be dependent on the geometry, fabrication tolerances, and material properties of the PVDF. The actuation would likely have to be calibrated experimentally.

The circuitry necessary to enable this actuation is fairly simple, and commercial systems are available. Input can be taken from a computer regarding the deflection desired and the coordinates of the pillar (or pillars) to deflect. Multiplexors and amplifiers on the chip can then simply apply the necessary voltage to the appropriate electrodes.

**Multiplexing**

Lastly, a time-multiplexing-type scheme for the processing of output voltages was considered. The most promising design followed the scheme employed in the IBM “Millipede” which used row-enabling, column-addressing in order to individually access an individual cantilever in the entire square array. This was achieved by placing a Schottky diode in series with each cantilever. If a cantilever was located in a row being enabled, but not in a column being addressed, the diode would be operated in reverse. The Schottky diode also had the function of reducing crosstalk between each cantilever. Our group originally considered using a similar scheme for our array of pillars, however our array is much smaller and it would not be feasible to insert one diode for each pillar.
Figure 29: (a) Schematic for multiplexing in the Millipede (Lutwyche, M.I., Despont, M. et al., 2000); (b) Application of row-enabling, column-addressing to an array of pillars
Resolution and Sensitivity

The sensitivity of a device is affected by many factors, such as its material and geometry. The performance of the device can be assessed from several perspectives, which are described in this section. Our array of micropillars takes as an input the forces exerted by a live cell, and convert them to a voltage output. The size of this voltage range then, is one indication of the possible achievable resolution. The dependence of this range on each design parameter of the pillars is examined. Finally, some aspects of the resulting pillar displacement and pillar time response are discussed.

Material Choice

The choice of polyvinylidene fluoride (PVDF, molecular formula -(CH2CF2)n-) as the sensor material at the base of the pillar is due to its high piezoelectricity. Its $d_{33}$ piezoelectric constant (piezoelectric strain coefficient along the 3-3 direction) is -33 pC/N, which is relatively high. In fact, its voltage output is ten times higher than that of piezo-ceramics such as lead zirconate titanates (PZTs). The strong piezoelectric activity is due to the large electronegativity of the fluorine atoms, thus the material is able to accommodate a large dipole moment. If a piezoelectric strip formed in the 3-3 plane is compressed, it is free to expand along the 1-1 and 2-2 directions, and the output charge can be expressed as $Q = d_{33}F$. Normally, the output charge would depend on the combination of $d_{11}$, $d_{22}$ and $d_{33}$, however because the PVDF film is so thin, the output charge is mainly due to the 3-3 direction.

Device Resolution

Figure 10 through Figure 14 indicate that changing the pillar diameter or the angle $\phi$ of the electrode do not affect the output voltage range greatly. The pillar height and the distance between electrodes on the other hand, affect the voltage range linearly, as indicated in the figures below. The slope of the line indicates the sensitivity of the output range to the change in the pillar geometry.
On the other hand, the output voltage range does not vary linearly with the radial width of the electrode:
The voltage range increases with decreasing radial width of the electrode, however a minimum width is dictated by microfabrication processes. Our chosen electrode width of 0.5µm still results in a sufficiently wide output voltage range.

The smallest force detectable by the pillar array must produce an output voltage that exceeds the voltage due to the noise in the system, which was calculated to be 0.1364 mV. It is evident that this value is very small compared to the expected output voltage range of the device, which is 55-550mV. The pillar output voltage varies linearly with the applied force as indicated in Figure 32.

The device resolution is given by

$$\Delta F [nN] = \frac{V [mV]}{5.5061}$$
The resolution, as limited by the system noise is therefore

$$\Delta F = \frac{0.1364 \text{ mV}}{5.5061} = 0.0248 \text{ nN}$$

This would indicate that if system noise were the limited factor, the micropillar array would be extremely sensitive, being able to detect changes in force of much less than 1 nN. However, it is more likely that the system performance will be limited by imperfections in the geometry due to microfabrication.

The geometry of the electrodes is limited by the resolution of the lithographic processes during microfabrication. E-beam lithography however, can obtain resolution of a few tens of nanometers. From Figure 13 and Figure 14 it is evident that slight changes in the nominal values of the electrode radial width and angle $\phi$ will not affect the output voltage. Rather, the total height of the pillar, $L$, will have a greater effect. The final height of the pillars is determined by the resolution of the DRIE process. Very careful control of the etching process should allow for 1$\mu$m precision, thus we shall assume that the pillar height will be $20 \pm 1 \mu$m. Variations in the pillar height will affect the voltage output more for larger applied forces, as indicated by Figure 11. At $F = 100 \text{ nN}$, the voltage output could range from 560-580 mV, a difference of 20mV.

Similarly, the thickness of the PVDF layer affects the output voltage linearly, with a greater slope for larger applied forces (Figure 11). Microfabrication processes can achieve a layer uniformity of 4%, so that the PVDF layer could vary over a 0.08$\mu$m range. At $F = 100\text{nN}$, $\Delta V[\text{mV}] = 450\Delta x[\mu\text{m}]$. This results in an output voltage range of 36 mV.

Lastly, the variation in pillar diameter during fabrication can affect the output voltage. The gradient of the voltage is plotted against different diameters in Figure 33 for an applied forces of 100nN.
At a diameter of 2µm, the gradient is -30mV/µm. High-resolution e-beam lithography can achieve accuracy of 30nm or better so we can assume that the pillar diameter will be 2 ± 0.03 µm. This results in a voltage range $\Delta V = (30\mu V/\mu m)(0.06 \mu m) = 1.8$ mV.

Therefore the greatest variation in output voltage occurs due to changes in the PVDF layer thickness. A 36 mV range affects the device resolution as follows:

$$\Delta F = \frac{36 \text{ mV}}{5.5061} = 6.54 \text{ nN}$$

If the pillar height, pillar diameter and thickness of the PVDF layer all deviated from the nominal values, their combined effect on the output voltage would not necessarily be equal to the sum of their individual effects. However, an assumption that this is in fact the case can provide an estimate of a worst-case scenario. The maximum total variation in output voltage then, is $V = 20 + 1.8 + 36 \text{ mV} = 57.8$ mV. The worst-case device resolution then becomes $\Delta F = 10.50 \text{ nN}$.

**Pillar Displacement**

Hooke’s law can be used to determine the displacement $\delta$ of the pillar due to an applied force $F$:

$$F(\delta) = k \delta, \text{ where } k \text{ is the spring constant of the pillar, given by }$$

$$k = \frac{3EI}{H^3}$$

$E$ is the Young’s modulus, $I$ is the moment of inertia and $H$ is the pillar height.

For a pillar with a circular cross-section,
\[ I = \pi D^{4}/64 \]

\[
k = \frac{3\pi E D^{4}}{64 H^{3}}
\]

Therefore, \[ k = \frac{3\pi E D^{4}}{64 H^{3}} \]

For our geometry, the height of the pillar not including the thickness of the PVDF layer is 19\(\mu\)m, and \(D=2\mu m\). In order for the pillar deflection to be a sufficiently small value, \(E\) is required to be fairly large. This is the reason for the choice of poly(lactic acid) (PLA) to form the bulk of the pillar. PLA has a Young’s modulus ranging from 3690-3830 MPa. Using a value of \(E = 3.7\) GPa results in a pillar stiffness \(k\) of 1.271 N/m. An applied force of 100 nN then, will give a deflection of only 78.7 nm, ensuring that two adjacent pillars being bent towards each other are in no danger of touching.
References


