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Piezoelectric resonators based on self-assembled diphenylalanine microtubes

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Piezoelectric actuation has been widely used in microelectromechanical devices including resonance-based biosensors, mass detectors, resonators, etc. These were mainly produced by micromachining of Si and deposited inorganic piezoelectrics based on metal oxides or perovskite-type materials which have to be further functionalized in order to be used in biological applications. In this work, we demonstrate piezoelectrically driven micromechanical resonators based on individual self-assembled diphenylalanine microtubes with strong intrinsic piezoelectric effect. Tubes of different diameters and lengths were grown from the solution and assembled on a rigid support. The conducting tip of the commercial atomic force microscope was then used to both excite vibrations and study resonance behavior. Efficient piezoelectric actuation at the fundamental resonance frequency ≈ 2.7 MHz was achieved with a quality factor of 114 for a microtube of 277 μm long. A possibility of using piezoelectric dipeptides for biosensor applications is discussed.

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It has been recently found that diphenylalanine (L-Phe L-Phe, FF), the famous core recognition motif of the β -amyloid peptide associated with the Alzheimer's disease, self assembles into the discreet nano- and microtubes (FF tubes) under mild chemical conditions.¹⁻³

Bioinspired FF tubes offer a wide range of attractive properties for microelectronic and microelectromechanical applications including controlled morphology,⁴ thermal and chemical stability,^{5,6} high Young modulus of 27 GPa,⁷ and, last but not the least, high polarization along the longitudinal axis accompanied with a strong piezoelectric effect.⁸ In addition, after annealing above 140–150 °C, FF tubes become electrically switchable in a radial direction thus opening new opportunities for information data storage applications.^{9,10} Strong piezoelectricity¹⁰ (of the order of that in LiNbO_3) is especially beneficial for various biosensor and mass detection applications where micromachined piezoelectric cantilevers based on inorganic materials (such as AlN, GaAs, ZnO, or piezoelectric perovskites) are currently used.^{11,12} Due to the small dimensions of sensing elements and consequent increase of the resonance frequencies, piezoelectric actuation is able to provide extremely small mass sensitivity, single electron efficiency, and fast response, as opposite to magnetomotive, electrostatic, and electrothermal principles.¹³ However, their functionalization is required to reach high enough selectivity for the biomolecules detection.¹⁴ In this work, we realize a prototype of the piezoelectric resonator based on a single FF microtube with high enough resonance frequency and quality factor to be used in above mentioned applications.

For the preparation of FF tubes, commercial diphenylalanine lyophilized powder was purchased from Bachem (Switzerland). FF tubes were prepared in accordance with the standard method¹ by the dissolution of FF powder in 1,1,1,3,3,3-hexafluoro-2-propanol with a concentration of 100 mg/ml. For the tube self assembly, an aliquot of the stock solution was diluted in a deionized water to a final FF concentration of 2 mg/ml and left for self assembly overnight at room temperature. A multitude of tubes of various lengths and diameters ranging from tens of nm to hundreds of μm was obtained (Fig. 1). The resulted FF tubes were studied in two different configurations: (i) suspended ones (cantilever-type) with one edge clamped to a rigid support. For the cantilever-like configuration, the tube edge was picked up with tweezers and placed on the top of a conducting carbon tape (Fig. 2), whereas for the study in (ii) longitudinal extensional mode, the tubes were prepared directly on a patterned

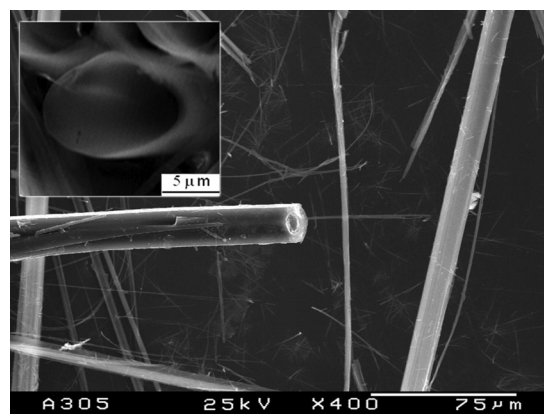


FIG. 1. SEM picture of the solution grown FF microtubes used for the resonance studies. Sufficiently small nanotubes could be grown in the same experiment. The inset shows SEM picture of the vertical tube with slightly asymmetric opening.

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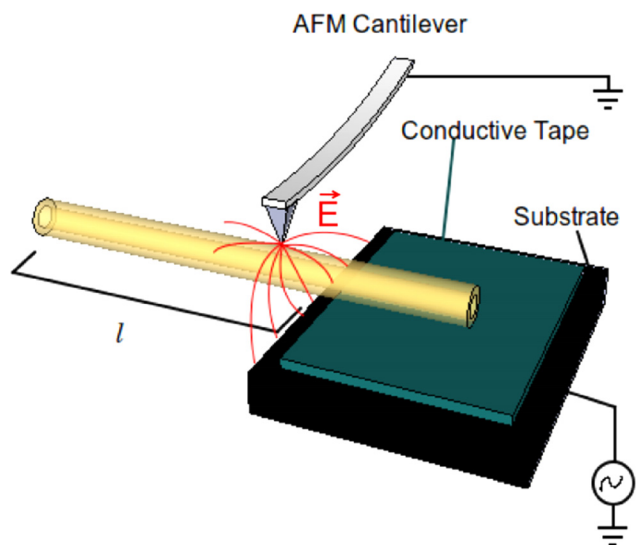


FIG. 2. Schematic of the FF tube arrangement on the rigid substrate. AFM cantilever is used to excite piezoelectric resonances and to measure induced vibrations as a function of frequency. Red arrows are used to highlight inhomogeneous distribution of electric field that helps to induce bending resonances in the system.

glass substrate coated with Au in order to have a conducting electrode. The vibrational response was investigated using an atomic force microscopy (AFM) setup where the conducting tip is used both to excite the piezoelectric vibrations and to study the vibrational response via an additional lock-in amplifier connected to the photodiode and synchronized with the driving voltage. The measurement scheme is analogous to that used in the piezoresponse force microscopy (PFM)¹⁵ but the external ac driving was replaced with the internal one commonly used in AFMs for the cantilever resonance calibration. For the experiments, we used a modified commercial AFM (Ntegra Prima, NT-MDT) and soft metallized cantilevers ($\sim 7.4 \text{ N m}^{-1}$ PPP-NCSTPt, Nanosensors). It should be noted that the asymmetric driving method used in our work (Fig. 2) is able to excite both purely extensional and bending modes due to the non-uniform distribution of the applied electric field which somehow imitates the situation in monomorph cantilever-based piezoelectric structures.¹⁶ The driving voltage was typically 2–3 V and frequency range up to 10 MHz. In order to separate spurious peaks from the true vibrational signal, the same procedure was performed with the cantilever tip in contact with the nonpiezoelectric substrate and $30 \mu\text{m}$ above the tube. The peaks appeared in contact with the tube (and not related to the cantilever resonance) were only selected for the analysis. Carbon tape electrodes were cut and put on a plastic holder manually. Metal electrodes were sputtered with a SEM coating unit (E5000 Polaron Equipment Ltd.) and the exposure time 5 min.

Figure 3 represents the measured amplitude of the deflection (DFL) signal in respect to the excitation frequency for the cantilever configuration shown in Fig. 2 for two different tip positions. The studied tube was $885 \mu\text{m}$ long and $13 \mu\text{m}$ in diameter. The measured resonance frequencies and respective quality factors are shown in the inset to Fig. 3. As it is clear from the figure, the peaks shift to higher frequencies with increasing distance between the voltage application point (AFM tip) and the clamping point. However, the ratio

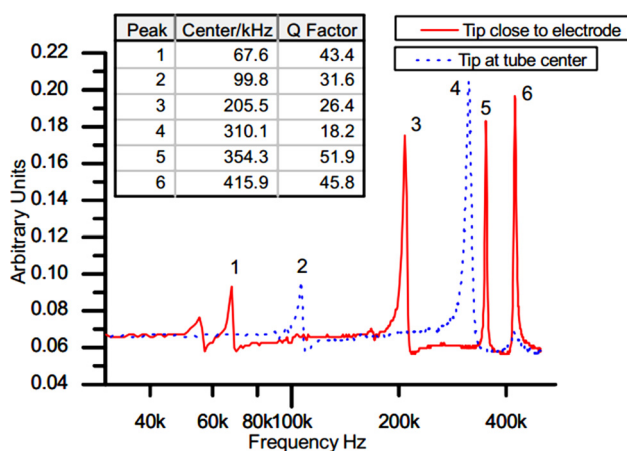


FIG. 3. Piezoelectric resonances excited in the FF microtube of $885 \mu\text{m}$ long and $13 \mu\text{m}$ in diameter in a cantilever configuration. Solid line represents the resonance structure for the AFM tip located in the middle. Dotted line is the example of the resonance peaks for the AFM tip close to the support. Table in the set summarizes resonance frequencies and quality factors for both configurations.

between the 2nd and 1st resonance modes is approximately the same, being about 3.05–3.1. The quality factors are in the range 20–50 and are close to that reported for piezoelectrically driven polyvinylidene fluoride (PVDF) fibers prepared by electrospinning.¹⁷

Decreasing the tube length to $277 \mu\text{m}$ (in this case, the tube diameter was $8 \mu\text{m}$) leads to the drastic increase of the resonance frequency to about 2.53 MHz with a concomitant increase of the quality factor (114.4 for the DFL peak) (Fig. 4). The observation of the lateral (LF) signal further supports the piezoelectric nature of the resonance and possible coupling between longitudinal and transverse signals as was earlier observed in PFM measurements.¹⁸ The measurements were done in an unclamped situation with both ends of the tube free.

So as to identify the nature of the vibrational response measured experimentally, we used the simple mechanical equations for the free and clamped thin uniform rod (or cylinder) in both extensional and transverse modes.¹⁹ Although the density of diphenylamine tubes is unknown so far, we used data for the

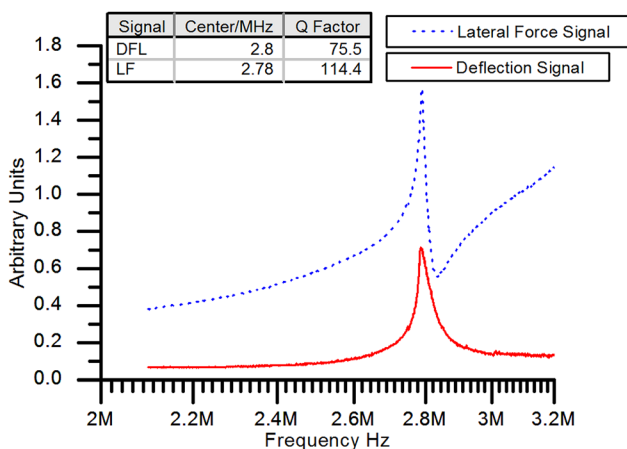


FIG. 4. Piezoelectric resonance of a FF microtube ($277 \mu\text{m}$ long and $13 \mu\text{m}$ in diameter) in both DFL and LF modes. The inset shows extracted resonance frequencies and quality factors.

material in the crystal form: $\rho = 1.233 \text{ g/cm}^3$.³ The Young modulus was estimated earlier via the indentation studies.⁷

For the clamped cylinder (cantilever configuration), the resonance frequency can be estimated via a following equation:

$$\omega_r = \lambda_r^2 \left(\frac{EI}{\rho A} \right)^{\frac{1}{2}}, \quad (1)$$

where E is the Young modulus, I is the second moment of inertia, A is the transverse area, and λ_i is the wavelength of the i th-mode. For the first two fundamental modes: $\lambda_1 l \approx 1.9$ and $\lambda_2 l \approx 4.7$. The ratio between the frequencies of the second and first resonance modes is thus about 6.1, i.e., approximately 2 times greater than found experimentally (Fig. 3). In case of the clamped-pinned configuration (which is closer to experimental situation), the ratio is 3.24 and thus approaches to that observed in the experiment. The absolute values of the resonance frequency estimated by Eq. (1) are very close to the experimental results but the accuracy of the calculations is limited due to incorrect boundary conditions and rough estimation of input parameters.

In the case of extensional vibrations, the analytical solution for the resonance frequency of a tube with both edges free is simply given by

$$\omega_r = \frac{n\pi}{l} \sqrt{\left(\frac{E}{\rho} \right)}, \quad (2)$$

where the resonance frequency is inversely proportional to the length of the tube and does not depend on the transverse area in this case. This equation predicts much higher frequencies for the studied tubes (8 MHz for the cantilever configuration and 51 MHz for the free tube for the given dimensions). Also, the ratio between the two first fundamental resonances does not fit to the experimental data. Most probably, we were able to excite bending resonances in both configurations and the values of the resonance frequencies can be roughly approximated with Eq. (1). The fundamental resonance scales as $1/l^2$, so we foresee much higher resonance frequencies and quality factors in shorter tubes. Already in a $277 \mu\text{m}$ long tube, the resonance lies in the MHz range and we can apparently approach several hundreds of MHz for the tubes of a few tens of microns in length. In this case, a better control of the tube growth and using patterning and microfabrication methods²⁰ will be required. The quality factors could be also increased as the quality of the tubes should increase with decreasing their size, especially for single-walled nanotubes that can be obtained by the crystallization in diluted solutions. As of today, the quality factors are in between those observed in soft PVDF cantilevers fabricated by electrospinning¹⁷ and micromachined ones based on SiN resonators.²¹

The major advantage of using self-assembled dipeptides as piezoelectric biosensors is their much easier biofunctionalization. In inorganic materials based on piezoelectric oxides, the common practice is to cover the active surface with a covalent bonded metal such as gold (and due to poor adhesion a buffer layer such as Cr might be required).²² This

is due to the fact that the thiol groups frequently used for self-assembly and functionalization have a high affinity with gold, forming strong bonds that help to ensure that the gold-ligand interaction is stronger than the ligand-receptor interaction, not to mention that the high quality of a gold layer and necessity of its annealing are typically required. The deposition of the buffer and metal layers will further change the rigidity of the cantilever with unpredictable change of the cantilever performance. Therefore, often a non-piezoelectric extension is required to decouple driving and sensor parts.²³ On the contrary, the surface of peptides can be readily functionalized. For example, it can be done by absorbing free amide and carboxylic groups on the surface of peptides serving as binding sites to anchor biological molecules. It should be mentioned that the tubes geometry can be beneficial for biosensing because of their hollow structure. High binding capabilities of peptide tubes have been already used for the label-free detection of antibodies and heavy metals.^{24,25} In these experiments, antibody-conjugated peptide nanotubes were positioned at the gap between metallic electrodes and the binding event between virus and nanotubes generated the impedimetric signal for pathogen detection. While this biochip can detect viruses at a concentration of 100 CFU ml^{-1} or higher, reuse of the sensor for multiple measurements is not straightforward due to the strong interaction between pathogens and antibodies on the peptide nanotube. The observed resonance behavior has a great potential for the easy removal of the biomolecules non-specifically adsorbed on the peptide nanotube surface leading to improved selectivity of biosensor. Even more possibilities are foreseen in thermally annealed tubular structures⁶ where a stable polarization switching is observed due to the rotation of the radial polarization component.⁹ This will allow controlling hydrogen bond orientation, which can give additional opportunities for biofunctionalization by switching functional groups “on” and “off,” i.e., by making them more or less sterically accessible.

In conclusion, in this work, we demonstrated that the self-assembled diphenylalanine microtubes prepared from the solution can be used as piezoelectric resonators with the potential to perform sensing and actuating functions in micro- and nanoelectromechanical systems. The sharp piezoelectric resonance in the MHz range with the quality factor >100 are demonstrated. These parameters can be further improved by scaling down the sizes of the devices down to a few μm and sub- μm ranges. Purely organic nature, light weight, intrinsic multifunctionality, and possibility of controlling surface properties make self-assembled dipeptide tubes a material of choice for various applications.

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