Bio-mechanical sensing of enzymatic reaction on DNA bundle by silicon nanotweezers

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Host Professor: **H. FUJITA**

Keywords: nanotweezers, molecules, DNA, enzyme, biosensing

Context

Performing biological test by direct molecular manipulation can provide quick and reliable data as noise due to bulk experiment can be reduced. However, these experiments relying on optical or magnetic tweezers have a low throughput since the molecule preparation is done one at a time. To move towards systematic biological or medical analysis, Micro and Nano Systems (MEMS) are the appropriate tools as they can integrate accurate molecular level engineering tools and can be cheaply produced with highly parallel process. This research focuses on this long term goal.

Objectives and Methods

The objective of this project is to demonstrate routine molecules manipulation and systematic bio reaction sensing by MEMS silicon nano tweezers. DNA molecules bundle is trapped by the tweezers from DNA solution and biological reaction is sensed by immersing the trapped bundle in enzyme solution and tracking the mechanical response of the tweezers.

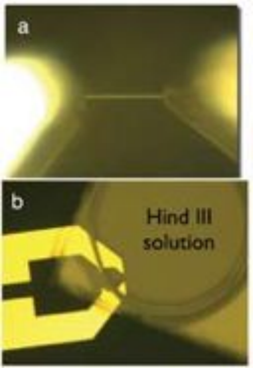

Fig. 1: Trapped DNA bundle and tweezers tips immersion in enzyme solution

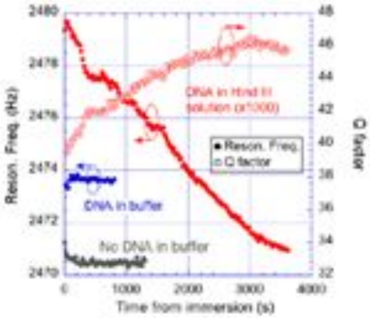

Fig. 2: Tweezers + bundle FR and Q vs. Digestion time. Response without proteins is also shown (witnesses)

Results

DNA bundle is first trapped by the 2 tips of the tweezers, Fig. 1a. The bundle handled by the tweezers is immersed in the enzymatic solution contained in the reaction cell, Fig. 1b. The enzymes, Hind III digest the DNA. The mechanical resonance frequency F_R and Q factor of the tweezers+bundle is extracted in real time as shown in fig. 2. The reduction of F_R and increase of the Q factor give the kinetics of the digestion reaction. This first result proves the feasibility of the molecular based bio-sensing with MEMS nanotweezers.

References and Publications

[1] Collard D., et al., IEEJ Transactions on Electrical and Electronic Engineering (invited), 2009.
[2] Kumemura M., et al., proc. MEMS 2010.

A mechanical switch device made of microfibrillated cellulose sheet

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Host Professor: B. J. KIM

Keywords: biodegradable electronics, cellulose, mechanical switch device

Context

The development of biodegradable nanomaterials for electronic applications such as cellulose is of great interest [1-3]. As cellulose is the most abundant renewable resource of polymer on earth, it may serve as a raw substrate in the fabrication of lightweight, inexpensive, flexible and environmentally-friendly devices.

Objectives

This project is focused on the development of an electrostatically actuated mechanical switch device made of microfibrillated cellulose sheet coated with thin polyimide polymer.

Methods

The studied cellulose sheets reveal a net-like structure composed of tangle of cellulose nanofibres (Fig. 1) leading to a high surface roughness. Moreover, the porous microstructure and the hydrophilic nature of cellulose sheet induce poor dielectric properties.

To overcome these drawbacks, both sides of the sheet are coated with a thin polyimide layer making the surface roughness, moisture sensitivity and insulating behaviour greatly improved.

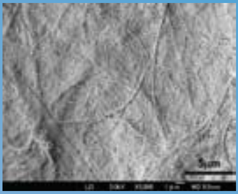

Fig. 1: SEM image of the cellulose nanofibre sheet

Fig. 2: Top view picture of the cellulose-based mechanical switch device

The mechanical switch is fabricated from the polyimide-coated cellulose sheet by implementing very simple processes such as punched-draw pattern defining, metal evaporation through shadow masks and glue assembling. The switch operation uses the principle of an electrostatically deflected cantilever beam (Fig. 2). The electrodes are used for the electrostatic actuation of the cantilever beam and switch detection when the beam is in contact with the substrate (ON state).

Results

The switch ON state is performed for an actuation voltage of 55 V and a distance beam-substrate of ~ 30 µm. Figure 3 shows the switch response when the device is subjected to a 10 Hz square wave signal.

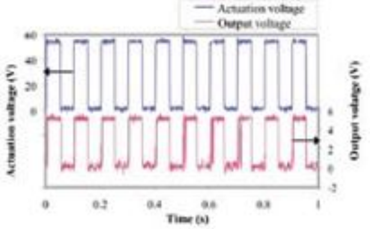

Fig. 3: Switch response through the output voltage measurement for an actuation voltage of 55 V and a distance beam-substrate ~ 30 µm

References and Publications

[1] Couderc S. et al., J. Micromech. Microeng., 19, 2009.
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Integration of bendable/tunable metamaterial structures for RF-applications

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Host Professor: H. TOSHIYOSHI

Keywords: Metamaterial, microtechnologies, tunable, RF, microwave

Context

Since many years, are intensively but separately investigated both (1) microtechnologies implying new and innovative substrate/material as alternative to silicon semiconductor and (2) metamaterial structures for RF and microwave applications exhibiting new behaviors and characteristics.

Objectives

We then propose to mix these two concepts and to investigate the integration of metamaterial structures with plastic-based microtechnologies in order to reach improved performances and functionalities. The objective is to demonstrate that high miniaturization level can be reached as well as tunability of RF-performances.

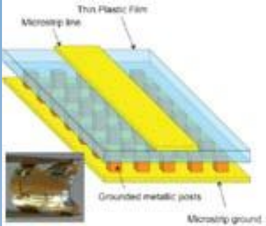

Fig. 1: Investigated metamaterial RF Structure

Methods

An existing technology for the future generation of large and flexible display panels has then been derived for RF applications. The structures consist in periodic metallic posts realized on plastic substrate over which a thin dielectric film, supporting the RF-line, is laminated (Fig. 1). The resulting structures exhibit large bendability suitable for conformal integration on planar and non-planar objects.

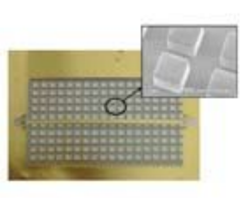

Fig. 2: Micro-fabricated structure

Results

A specific modeling of the proposed structures has been developed and validated [1]. It permits to define suitable design and technology leading to the fabrication and test of proof of concept demonstrators (Fig. 2), which exhibit improved miniaturization level [2] and wide tunability [3] (Fig. 3).This opens a route towards miniature, reconfigurable and mechanically flexible RF and microwave structures.

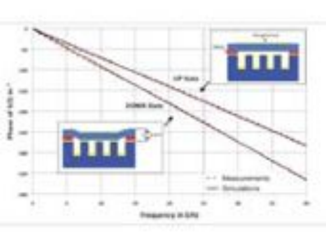

Fig. 3: Phase Shift Tunability

References and Publications

[1] Dubuc D., et al., Metamaterials, 2008.
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Broadband and non invasive Radio-Frequencies/microfluidic sensor dedicated to bioengineering

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Host Professor: **H. FUJITA**

Keywords: sensor, microwave, non-invasive, broadband, microfluidic, bioengineering

Context

In the past decade, the biological and medical fields have been submitted to a tremendous evolution thanks to microtechnologies, which enable the elaboration of lab-on-a-chips for precise manipulation and characterization of biomolecules and cells. Strong researches are thus ongoing on new type of integrated biosensors, which could fulfil the challenges of high sensitivity for small-analysed volume, high compactness, and label free ability.

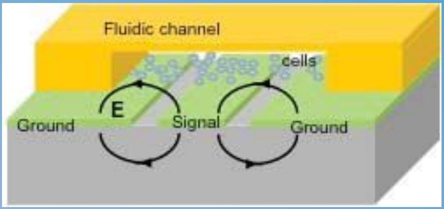

Fig. 1: Schematic view of the RF/fluidic biosensor

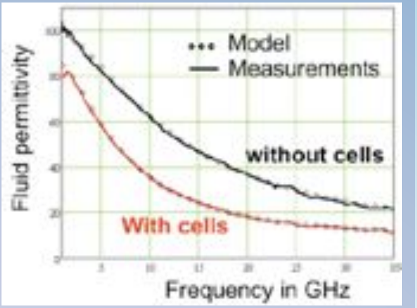

Fig. 2: High frequency dielectric signatures of cells suspensions and medium

Objectives

This project aims consequently to demonstrate that high frequency electromagnetic detection can provide a label free, non-invasive, sensitive, and very compact solution, as well as broadband information for biological and medical engineering.

Methods

The developed biosensor (cf. Fig. 1) takes benefit from MEMS technologies, which easily allies high frequency devices for the non-invasive electromagnetic detection and fluidic channels for biological substances routing and networks.

Results

The validation of the proposed RF analysis technique has been successfully performed on λ-DNA solution [1]. Furthermore, thanks to an appropriate metrology, the high frequency electrical properties of HUVEC human cells over a broadband frequency spectrum have been accurately evaluated (cf. Fig 2) for various cells concentrations [2]. These first results are based on a totally new type of biosensor, which integrates both fluidic network and non-invasive RF detection. It opens a route towards innovative bioengineering tools.

References and Publications

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PDMS-embedded vertical nanosheets of materials for flexible devices

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Host Professor: **H. FUJITA**

Keywords: flexible devices, vertical nanosheets, PDMS, micro-droplet

Context

Flexible devices enable new class of applications that lie outside those addressed with wafer-based microelectronics. Examples include flexible displays, smart textiles, ultrasensitive chemical sensors, active antennas, selective molecule/cell adhesion on biocompatible plastics. Hybrid integration of materials on plastic substrate at low cost, on large area, with nanoscale patterning is still challenging. Material choice and adhesion properties on plastic are limiting factors of actual transfer techniques that mostly concern planar structures (nanowires, planar thin films).

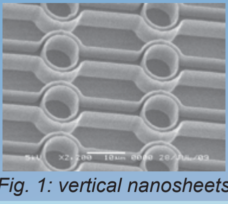

Fig. 1: vertical nanosheets

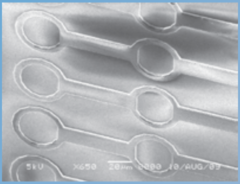

Fig. 2: Au-nanosheets (Au-NS) embedded in PDMS

Objective

The hybrid integration on PDMS of any materials/stacks (semiconductor, metals, dielectrics, ferroelectric, piezoelectric, magnetic …) with a strong adhesion, a nanoscale resolution, on large area, at low cost.

Methods

Fabrication of high density vertical nanosheets (NS) on a silicon substrate using standard MEMS techniques. Those nanosheets can be covered with a wide range of thin films and transferred into the PDMS surface by a mechanical releasing during the peel-off of the cured polymer.

Results

We succeeded in embedding thermally grown SiO2-NS (80nm in width, several mm in length) (Fig. 1) [1], also Au/SiO2/Au-NS (Fig. 2) and self-aligned microdroplet formation on Au patterns [2-3]. Flexible photomask for sub-micron photolithography was also demonstrated by a reusable template engineering [4].

MEMS in TEM (updated): In previous work, we observed in real-time the melting of a Si-NW [5]. Recently, we achieved a precise control of the retractation process to form a "neck" on the Si-NW (Fig. 3) and obtained a variation of the thermal conductance as a function of the Si-NW diameter [6]. Near-field radiations characterization are under investigation.

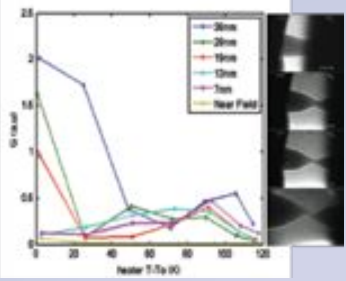

Fig. 3: MEMS in TEM. Si-NW "neck"

References and Publications

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[4] Jalabert L. et al., MEMS'10.
[5] Jalabert L. et al., Proc. IEEE Transducer'09.
[6] Jalabert L. et al., submitted to Int. Conf on Phonon'10.

Modeling and control of MEMS tweezers for direct bio-mechanical sensing of bio-reactions on DNA

Contact Researcher: Nicolas LAFITTE

Host Professor: H. FUJITA

Keywords: MEMS tweezers, modeling, control, DNA, biosensing

Context

Nowadays, a huge interest exists on systematic and real-time biological analysis. Whereas experiments relying on optical or magnetic tweezers have a low throughput since the molecule preparation is done one at a time, our research means to demonstrate DNA molecule manipulation and characterization by micro machined silicon based tweezers (Fig. 1).

Fig. 1: MEMS tweezers

Objectives

Currently, the resolution achieved is in order of hundred of molecules of λ-DNA. Thanks to the development of a new method of resonance frequency characterization and a precise control design, it is expected to reach the sensing of a single molecule of DNA, competing with optical or magnetic tweezers resolutions.

Methods

The increase of MEMS complexity and the immutable dimension downscaling implies the need to have a system robust to parameter uncertainty and external disturbances, in order to improve performances of the system. The application of control methods to the tweezers would lead to higher degrees of certainty and reliability of operations in physically demanding environments.

Results

Although many factors play a crucial role in the successful design and implementation of control system, control design begins by examining the plant's dynamic behavior, with the objective of developing a mathematical model whose behavior accurately replicates that of the real plant (Fig. 2).

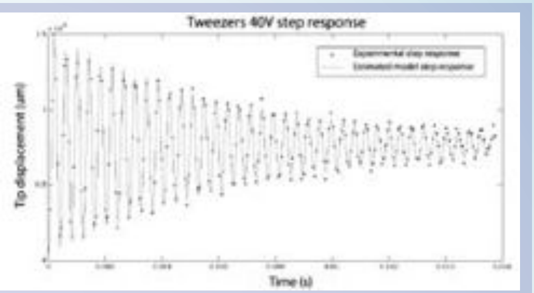


Fig. 2: Experimental and estimated model step response

The purpose of the developed mathematical model is to serve as a basis for subsequent control system design and simulation. Different sophisticated control methods have been developed fulfilling several and different types of disturbance rejection specifications. The synthesis and the implementation of a robust control algorithm upstream of the MEMS device to control its behavior constitute the next major step of the project.

Silicon neural network circuits for smart-MEMS systems

Contact Researcher: Timothée LEVI, Dr
Host Professor: T. KOHNO
Keywords: silicon neuron, neural network, MEMS

Context

Neuromorphic engineering is a research field where microelectronic encounters biology. Our main aim is to design networks of silicon neurons, a silicon analog of neuronal cell, that are applicable to integrated controller of MEMS devices to realize neuromorphic smart MEMS devices. Silicon neuron is electrical circuit that is analogous to biological neurons. Conventionally, it was designed mainly in the following two attitudes. One is to realize circuitry that is as close to biological neuron as possible, which enlarges circuit size and complexity terribly. Another is to realize simple and compact circuitry that can be utilized to construct large-scale silicon neural networks.

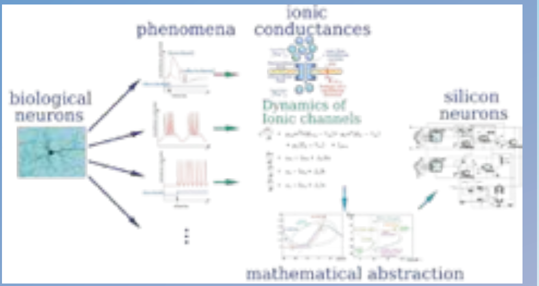


Fig. 1: Methodology of design of Silicon neurons

Objectives

In the nerve system, biological actuators such as muscles and secretion glands have their own local neural network system in peripheral nerve system. We have started to realize a MEMS actuator device that has local controller circuit built in the device itself. A kind of array of our silicon HCO will be used for the local controller circuit in the same manner as the nerve system.

Methods

Professor Kohno proposed a new design methodology that allows us to design the system equations utilizing mathematically abstracted description of neuronal phenomena. We designed small-scale silicon neural networks combining our silicon neurons via silicon synapses. Our first silicon neural network is a silicon half center oscillator (HCO).

References and Publications

[1] Kohno T. et al., Neurocomputing Journal, 2008.

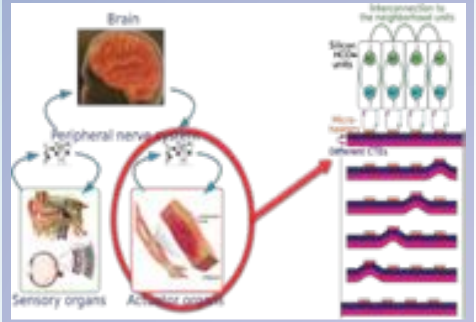


Fig. 2: Smart-MEMS System

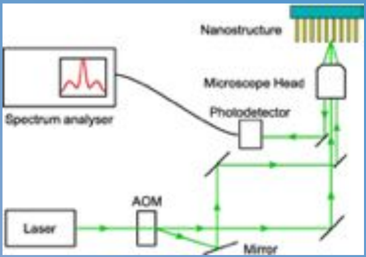
Mechanical nano-sensor for nano-particle recognition

Contact Researcher: Christian PIGOT, Dr.
Host Professor: A. HIBARA

Keywords: dynamic light scattering, nano-pillars, sensor, nano-particle, thermal actuation

Context

Nowadays, the most sensitive mass sensors are microsized sensor based on mechanical frequency. They have a very high sensibility and a very high resolution, up to tens of atoms in vacuum [1]. The downscaling to the nanosize is expected to increase the sensitivity and the resolution of such sensor. However, technological barrier remains on the actuation means and measurement of the resonance frequencies.



Principle of dynamic light scattering measurement

Objectives

In the present project, we aim at demonstrating that thermal actuation is sufficient to excite mechanical resonance of nanostructure. Effectively, the chocks of the molecules constituting the surrounding medium on the nanostructure can be considered as a white noise. This noise excites every mechanical frequency including the resonances frequencies. The input energy is sufficient to induce measurable displacements both in gaseous and liquid environment.

Methods

A network of vertical gold nanowires is used. Due to their high aspect ratio, a few resonant modes keep a good quality factor, even in liquid. The high number of nanowires allows having a significant signal that can be simply measured. The measurement will be achieved on each resonator at the same time by dynamic light scattering [2][3].

Results

In this work we expect to improve the understanding of the interaction of nanowires with their surrounding medium. It will also offer new opportunities for applications of NEMS (Nano-ElectroMechanical Systems). This resonators network leads to the qualitative and quantitative characterisation of the composition of a medium. With this technology, we especially expect to develop a powerful tool for nanoparticles characterisation.

References and Publications

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