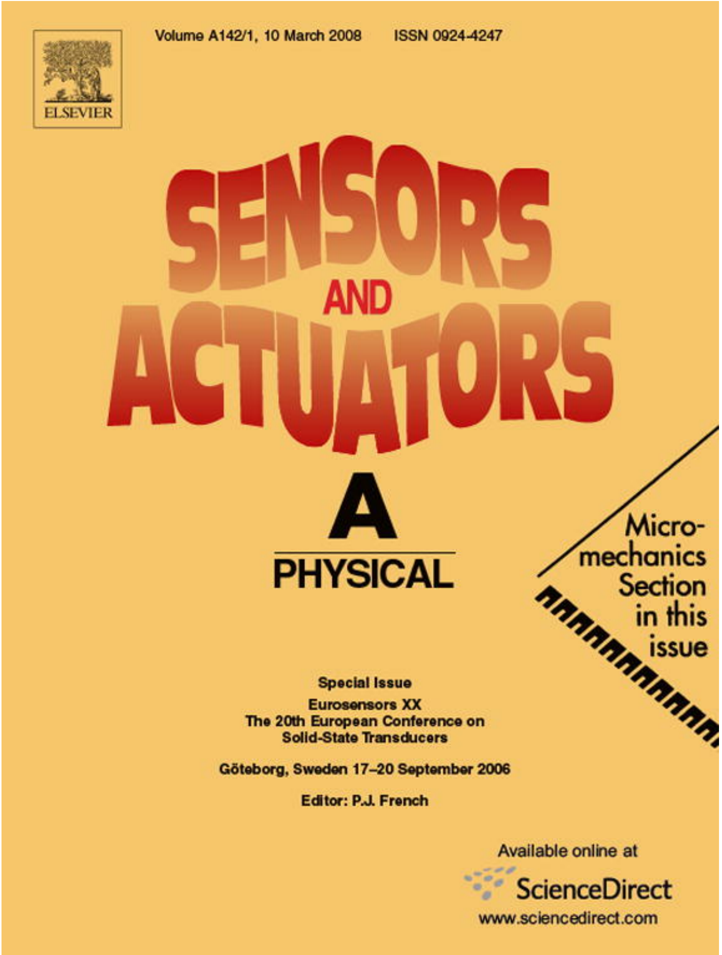
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A novel haptic platform for real time bilateral biomanipulation with a MEMS sensor for triaxial force feedback

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Abstract

A novel triaxial force sensing device developed by the authors with a MEMS sensor as core component is mounted on a subnanometric resolution nanomanipulator having three degrees of freedom (DOF). This sensorized device allows measuring forces on the nanomanipulator tip in the range of 0–3 N for normal and ±50 mN for tangential forces with a resolution of 11 bits. Together with a haptic input device, a setup was created allowing palpation and force feeling. The mathematical model used to drive the master haptic interface force feedback capabilities is based on online force and stiffness measurement. The performance of the novel setup is demonstrated with a cell palpation experiment.

Keywords: Force sensor; MEMS; Phantom; Haptic; Triaxial; Force feedback

1. Introduction

Thanks to the recent developments in micromechatronics, it is nowadays possible to access and manipulate very small objects. Fine movement resolution, force sensing for haptic feedback, high reliability and intuitive master interface are some basic requirements that have to be met by platforms for bilateral micro and nanomanipulation. These systems will spread the field of micro and nanomanipulation beyond the scientific community, and even unskilled operators will be able to interact with the micro and nanoworld. Several systems have been developed addressing this final goal, in particular using AFM as the force sensing principle and having the Phantom (Phantom 1.0, SensAble Technologies Incorporated) [1] or a purposely developed device [2] as haptic interfaces. The AFM tip enables high resolution force sensing, but its use is limited to a narrow force range and to a single degree of freedom.

A scientific field where bilateral micromanipulation platforms have increasingly been applied in the last few years is intracellular injection. Manual manipulation requires long, lengthy training and the success rate is related to the operator experience. Even for a skilled operator, the injection process results in low success rate and poor reproducibility, since he/she has to rely only on visual information coming from optical microscopy and eyestrain significantly affects the final output. Furthermore, since biological cells are irregular in configuration and easily deformable, they can be damaged during manipulation and treatment due to excessive force or hand tremor.

A typical platform for bilateral manipulation in the field of cell injection is composed of a master unit, usually an intuitive and ergonomic controller or joystick that is able to provide a force feedback, and a slave unit, a multi degrees of freedom (DOF) manipulator with micro or nanometric movement resolution. The injecting needle is placed onto the distal end of the slave unit.

Combining force feedback with vision can improve cell injection outcomes since the operator can both feel and see the cell injection process. The role played by force feedback and its advantages during such a procedure are well described in [3]. By reflecting the cellular force signal to the operator through the

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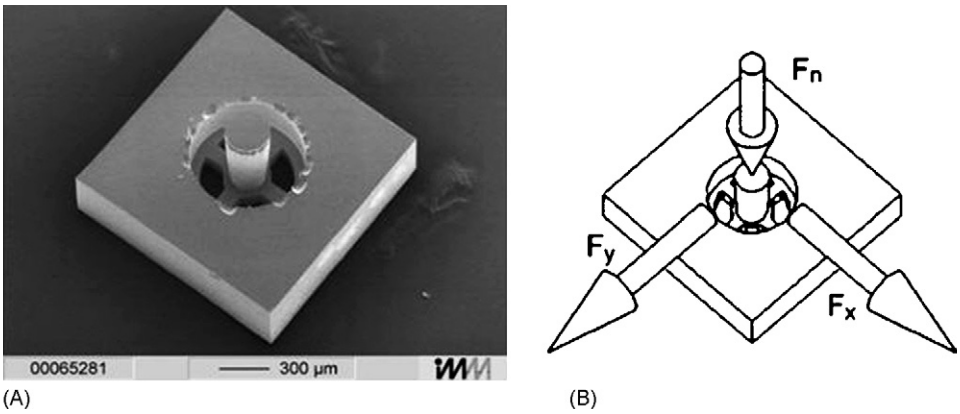

Fig. 1. (A) SEM picture of the bare silicon sensor. (B) Force components on the bare sensor.

haptic interface during bilateral biomanipulation, it is possible to detect clearly the membrane penetration event. Furthermore, the force feedback information to the operator enables minimally invasive injection, reducing any physical damage to the cellular structure, thus increasing the success rate of cell embryonic development. In [4], the force applied by the injecting needle is estimated by contour measurement from the visual system. This may be a critical disadvantage in some injection tasks where real force feedback is required. Placing a real force sensor as close as possible to the injecting tool is of course the most suitable solution. In [5,6], the force sensor is made by piezoelectric polymer, PolyVinyliDene Fluoride (PVDF). This material can be modeled as a capacitor that is able to generate charges on its plates under the effect of pressure, sound or heat. Then, if a charge amplifier is used, a linear relationship exists between the applied force and the corresponding integral of the voltage output from the charge amplifier. Because of this working principle PVDF are more suitable for dynamic loading measurements, than for static ones. The same principle has been also used in [7] to investigate the mechanical properties of single living cells at different stages of cellular development. However, even if PVDF demonstrates to be a suitable sensor for cell biomanipulation, its performance is affected by several unsolved problems such as the pyroelectric effect and the high sensitivity to acoustic waves and ground vibrations that can disturb the sensor readings. Moreover, all these solutions are limited to monoaxial force sensing. Measurement of these forces in three directions is crucial to operators interacting with the haptic display since it provides them with the membrane interaction forces, as they would feel in palpation [8]. However, conventional force sensors have large dimensions and are too heavy to be placed on the tip of a micro or nanomanipulation system. For triaxial high-speed bilateral biomanipulation, it is highly desirable to install a miniaturized multiaxial force sensor directly onto the tool tip. If the size of the sensor is miniaturized, the mass of the sensor reduces dramatically and the resonant frequency of the elastic body, composed of the manipulator and the sensorized tip, increases. This would enable real time bilateral manipulation, where the operator's hand movements are mapped in real time onto the tip of the slave manipulator. A triaxial force sensor fabricated by silicon micromachining for this purpose is reported in [9]. The proposed sensor, having dimensions of 4.5 mm × 5.0 mm × 525 μm without considering cabling and the eventual packaging, is however still bulky for a fine bilateral micro and nanomanipulation platform.

In this paper, a novel haptic platform for real time bilateral micro and nanobiomanipulation with triaxial force feedback is introduced. The core component that enables the multi degrees of freedom force sensing is a MEMS-based silicon triaxial force sensor, properly customized to act as probing end of the slave unit. The sensor, represented in Fig. 1A and described in details in [10,11], allows the measurement of normal and tangential components of an applied force, as in Fig. 1B, with a fully integrated silicon structure. The sensing element consists of a cylindrical mesa and four tethers. A piezoresistor (1 kΩ), dimensioned and positioned to obtain maximum sensitivity, is ion-implanted in each tether and used as an independent strain gauge. The bare sensor force sensitivities are 2 mN for normal and 0.4 mN for tangential loadings.

A nanomanipulator with three degrees of freedom of movement and a nanometric resolution is the slave unit, where the force sensor is mounted on. This system is controlled by a commercial haptic interface, which also applies the triaxial force feedback to the operator. A double vision system focused on the target location completes the setup. In order to evaluate the performances of the proposed platform, it is applied to a cell palpation and injection tasks. However, with just minimal modifications of the probing unit, it can be easily applied to other bilateral manipulation tasks where triaxial force feedback, small dimensions and high movement resolution are key requirements. Examples range from eye surgery [12] to nanomanipulation [13].

2. Design and fabrication of the force sensing device

Two main problems have to be solved in order to apply the bare silicon triaxial force sensor to a real working scenario. First, the four piezoresistors must be electrically connected to the acquisition electronics, then the sensitive part of the MEMS device must be mechanically interfaced with the target in such a way that would not compromise the information about the force orientation and intensity. To achieve this first goal, the MEMS sensor is directly mounted onto a flexible circuit made from

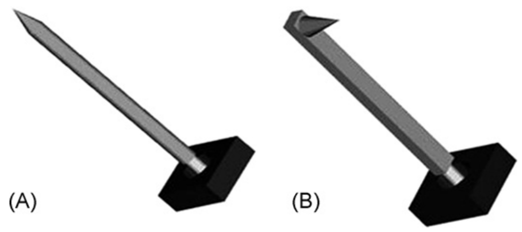

Fig. 2. Axial tip (A) and flat tip with a dedicated probing end bonded onto the sensor (B).

LF9150R Pyralux (DuPont, USA), using a thermally bonded anisotropic conductive tape 5552R from 3M without the need for an extra silicon support, as reported in details in [14]. This bonding technique enables low electrical contact resistances, e.g. below 0.5 Ω, together with excellent mechanical bonding strength.

Two differently shaped tools, represented in Fig. 2, to be mounted on the sensors central pillar, were designed to interface the MEMS device with the target surface. The first design, Fig. 2A, has an integrated tip to allow force sensing in normal direction, while the second one, Fig. 2B, having a rectangular shaped cross section, allows bonding of a range of tips. Four different prototypes of both designs were fabricated, two from stainless steel by μwire Electro Discharge Machining (WEDM AP 200L, Sodick, Japan) and two where the tip was obtained from a 22 gauge needle, that was cut in order to achieve the target length, as explained in the following. The tips were bonded to the sensors central cylindrical mass using cyanoacrylate glue (M-Bond 200 Adhesive, M-Line, USA). For correct alignment, this task was performed with the help of a couple of 3 degrees of freedom cartesian micromanipulators (DC3-R-L, Marzhauser-Wetzlar, Germany) under an optical microscope.

The triaxial force sensing device is carried by an aluminium support, represented in Fig. 3, directly mounted on the tip of a 3 DOF piezoelectric nanomanipulator (MM3A Manipulator, Kleindiek GmbH, Germany). This manipulator allows stepper motor like movements with a resolution in the subnanometer range. Maximum normal forces that can be exerted by the tip are approximately 0.6 N for normal and 50 mN for tangential movements.

Tridimensional static loading simulations of the device were performed, by using FEMLAB 3.0 (Comsol, Sweden), in order to define the proper tip length to fit the sensor force range to the manipulators maximum applicable forces. To calculate the output of the strain gauges during tangential loading, the normal strain component in the direction of force application at the location of the strain gauge was calculated and correlated to the output voltage by a conversion factor obtained by experimental tests. For normal loadings, the normal strain component in the same direction was taken and converted as with the tangential loading.

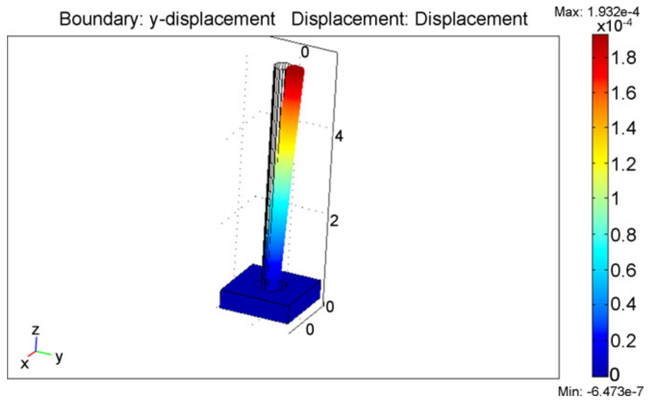

Fig. 4. Boundary plot of the sensor displacement in the y direction in response to a 0.1 N tangential loading at the tip.

Fig. 4 shows a boundary plot of the sensor displacement in the y direction in response to a 0.1 N tangential loading at the tip, while in Fig. 5 a slice plot of the y component of normal strain in response to a 0.2 N tangential loading a the tip is represented. From the simulations results, a tip length of 5 mm was finally chosen in order to have a force sensor that is sensitive enough to the probing movements imposed by the nanomanipulator.

3. Signal processing and data acquisition

The electronic circuit outlined in Fig. 6 is used to acquire three digital signals proportional to the normal force (ADC Normal Loadings) and the tangential forces (ADC Tangential Loadings x, y). Normal loadings result in the same resistance change of all the four piezoresistors, thus the sensor signal is processed in a quarter bridge configuration (the sensing element is R_{x1} in series with R_{x2} parallel to R_{y1} in series with R_{y2}). Tangential forces show opposites fractional changes in resistance, so a half

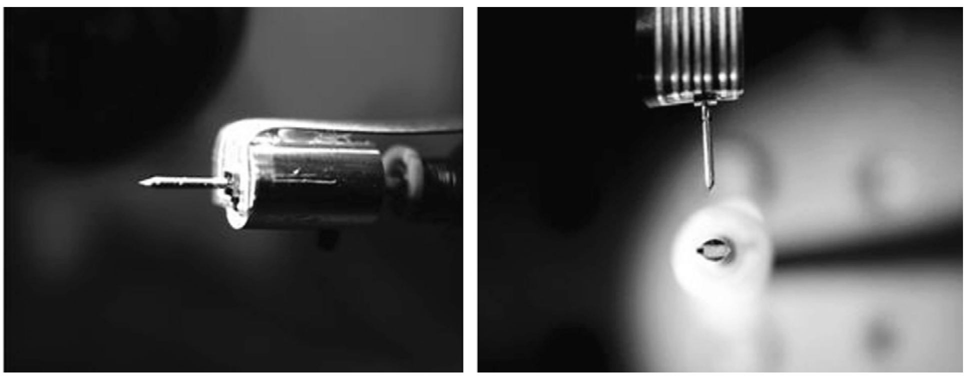

Fig. 3. The triaxial force sensing device mounted onto its aluminium support.

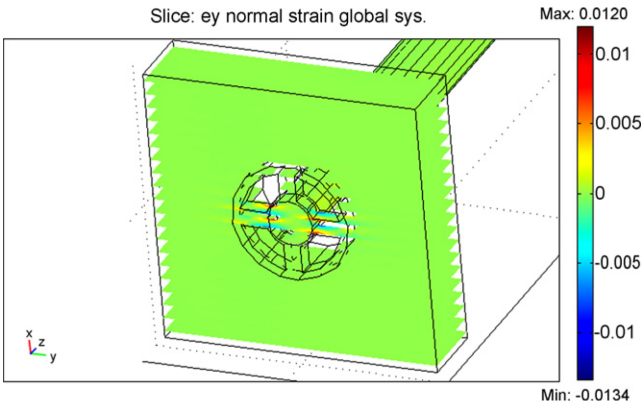

Fig. 5. Slice plot of the y component of normal strain in response to a 0.2 N tangential loading at the tip.

bridge configuration can be used. As no real temperature compensation, e.g. an additional dummy piezoresistor, is included in the MEMS device, temperature changes will appear as an offset in the normal force readings. The Analog Devices AD7730 Analog to Digital Converter (ADC), used for the data conversion, is a programmable 24 bits Sigma Delta ADC with an input range of ± 80 to ± 10 mV, thus no additional amplification is necessary for the bridges outputs. Signal processing is performed with internal components including a programmable amplifier, two fully programmable digital filters, to remove high frequency noise and to set a suitable -3 dB frequency, and a 6 bits Digital to Analog Converter (DAC) to remove the bridges offsets. The ADC Serial Peripheral Interface (SPI) is directly linked to a Personal Computer (PC) printer port. The SPI protocol emulating software is programmed in National Instruments Labview 7.1 under Microsoft Windows XP. The data output rate is programmed to 200 Hz with a -3 dB frequency of 7.8 Hz. This filtering enables an 11 bits real resolution of the sensor readings.

4. Bilateral manipulation system with triaxial force feedback

The whole haptic platform consists of the sensor equipped nanomanipulator and a haptic master interface (Phantom 1.0, SensAble Technologies Inc., USA) and it is represented in Fig. 7. The master interface allows steering of the slave manipulator, while the force signals from the triaxial force sensor allow haptic force feedback.

4.1. Interfacing the haptic controller

To access the Phantom device under Labview 7.1, a Virtual Instrument (VI) based on a Code Interface Node (CIN) was developed. This CIN uses the OpenHaptics TM Toolkit (SensAble Technologies Inc., USA). When initializing the CIN (usually executed when the VI is loaded), the scheduler for the Phantom is started. The VI provides then functions to read the Phantom positions and to set the forces. The code for the CIN

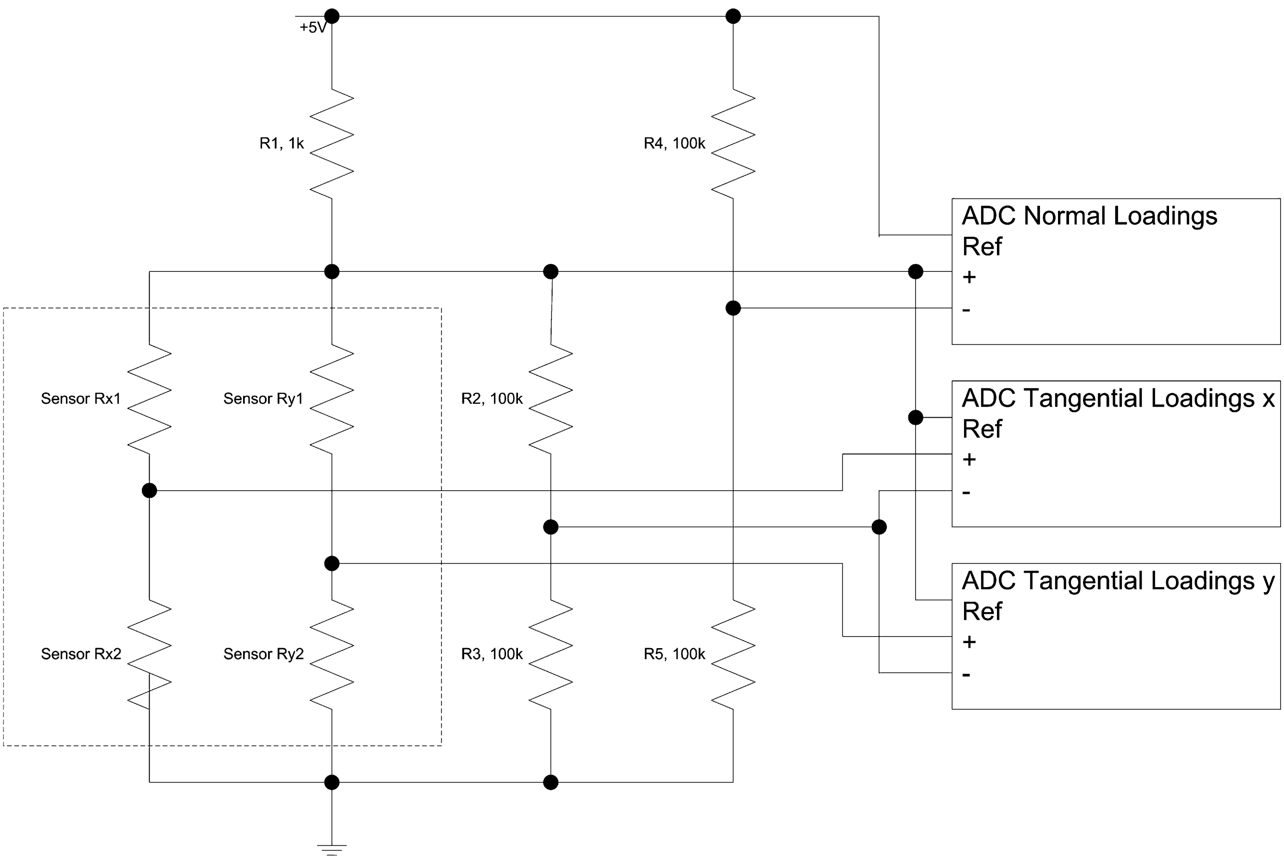

Fig. 6. Electronic circuit layout.

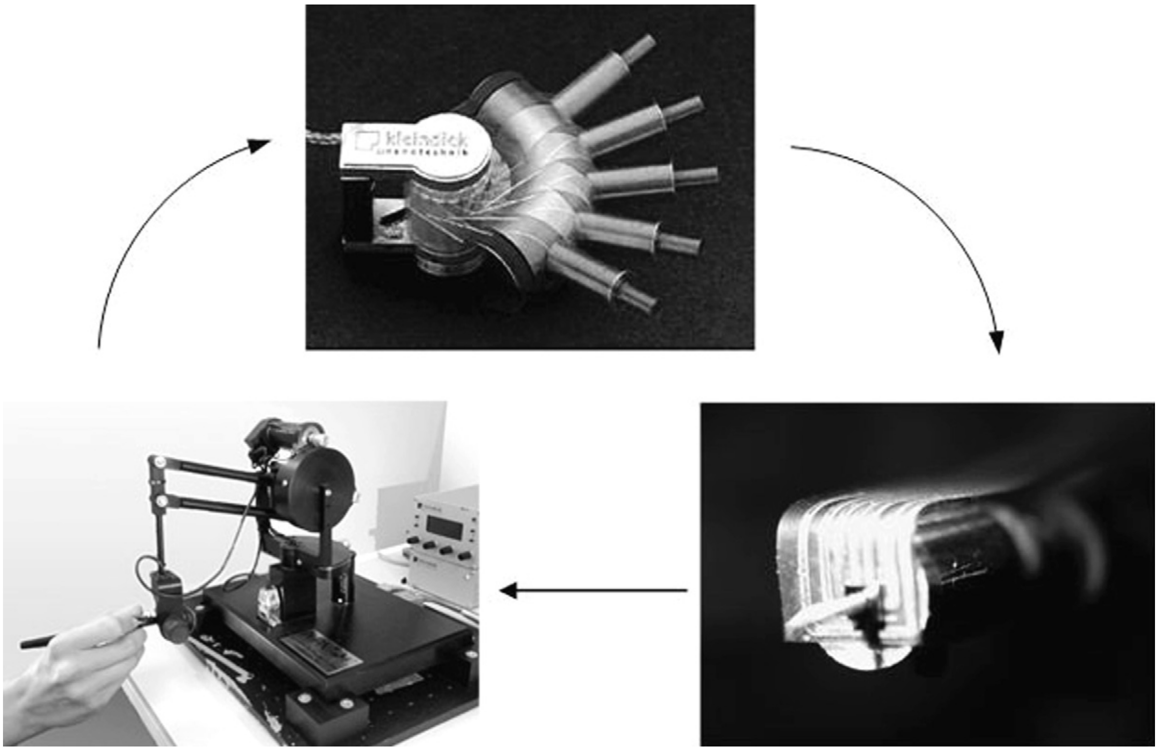

Fig. 7. Bilateral manipulation platform with triaxial force feedback.

Library is written in C and compiled under Microsoft Visual C++. The maximum frequency for position reading and force updating is 1 kHz, given by the Phantom scheduler. This VI has all the necessary capabilities to perform haptic rendering under Labview 7.1.

4.2. Controlling of the nanomanipulator

The master workspace is scaled down by a user definable factor to the working range of the slave manipulator. An implemented kinematical model of the manipulator is used to map the VI Cartesian input variables to the workspace of the manipulator. Changes in the input coordinates are translated into movements in the 3 DOF of the manipulator which are then sent to the manipulator control unit by the PC serial port. One position update cycle takes between 10 ms (small movements) and 500 ms (very large displacements), depending on the size of the calculated steps. Fine movements of the slave nanomanipulator are carried out by applying an analog voltage to the piezoelectric actuators, thus movements in the nanometer range can be achieved. For coarse movements the stick–slip principle [15] is applied. This allows driving the manipulator like a stepper motor, where one coarse step corresponds to one stick–slip driving pulse. However, the displacement of such a step is not constant like a stepper motor, but it depends on friction, forces on the manipulator and environmental variables like temperature and humidity [16]. As no displacement encoders are integrated, a kind of calibration of the manipulator needs to be performed each time these variables are changed. However, it is not necessary to have an exact calibration, as the setup is used by an operator under a microscope, thus allowing visual position feedback.

4.3. Haptic force feedback

The force sensor signals are acquired as described in Section 3, by using a purposely developed board and a Labview VI. From these signals, the three force components in Newtons are calculated via a calibration matrix. These three values are the base for the force feedback through the phantom. The −3 dB frequency of the sensor signals is 7.8 Hz, thus these cannot be directly used for force feedback with the haptic interface, since its scheduler runs at 1 kHz. Therefore, a spring model was introduced. The direction of the force vector is given by the three force components and the spring constant for this model is evaluated from two following and different force sensor readings at two different positions. This allows a kind of palpation and feeling of the objects mechanical surface properties in front of the tip.

To be able to calculate this spring constant k, according to the function $f[N] = k[N/\text{mm}] \times x[\text{mm}]$, x has to be known. As described above, the nanomanipulator steps depend also on the force that is applied to its tip. To evaluate the maximum force where the decrease of the step size is tolerable for force feedback applications, the step size of the manipulator over the applied normal force was recorded with a setup consisting of the manipulator, a six components load cell (ATI NANO 17 F/T, Apex, USA), a linear spring and a laser displacement meter (OptoNCDT 1401, MicroEpsilon, Germany). In the experiment, the manipulator was driven in constant sequences of 10 coarse steps compressing a spring (the force on the manipulator is then given by the Hook's Law for linear springs). The laser displacement meter allows the measurement of the position of the manipulator tip, which can then be used to determine the real step size in

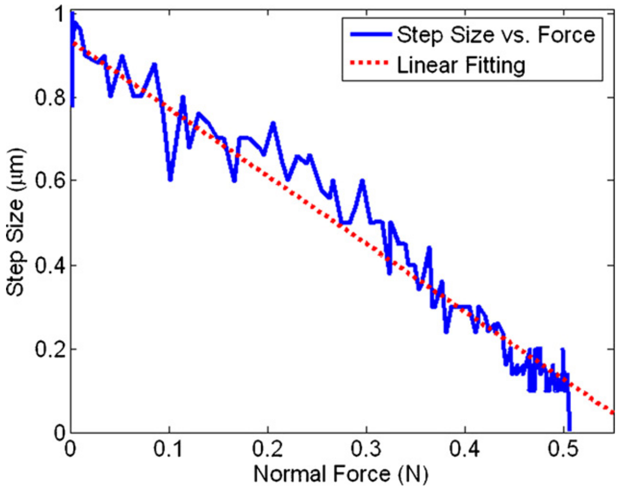

Fig. 8. Nanomanipulator step size versus the force on the tip.

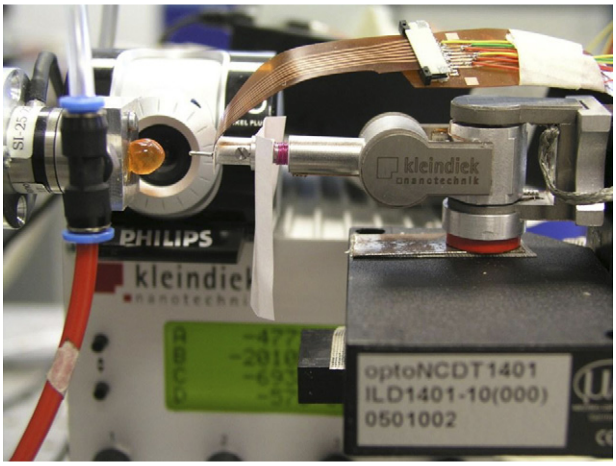

Fig. 9. Cell palpation and injection setup.

micrometer(s). The output of this calibration is plotted in Fig. 8. A maximum normal force of 100 mN, that corresponds to an 80% decrease of the step size, was chosen as acceptable force limit for the bilateral telemanipulation.

5. Cell palpation and injection experiments

In order to test the setup capabilities for real time bilateral biomanipulation with triaxial force feedback, a cell palpation and insertion task was chosen. Salmon fish eggs were selected as target cells as in [5], where the force sensor had just one DOF.

The setup described in Section 4 was extended with a suction plate mounted for holding the salmon fish egg. The suction plate is screwed on a six components load cell (ATI NANO 17 F/T, Apex, USA), which allows validation of the force signals from the device. The typical diameter of a salmon fish egg ranges from 4 to 6 mm. A picture of the slave side of the platform is showed in Fig. 9.

Fig. 10 shows the whole microrobotic palpation and injection procedure. First, the sensing probe approaches and contacts the cell outer membrane, controlled by the master interface under visual feedback (1). Then (2) the probe touches the cellular wall and starts pushing against it (3), transferring the force feedback to the operator. As soon as the membrane rupture force is reached (4), the operator feels a sudden drop in the force and understands that the injection event occurred. This procedure was carried out with the operator trying to maintain a uniform pushing speed.

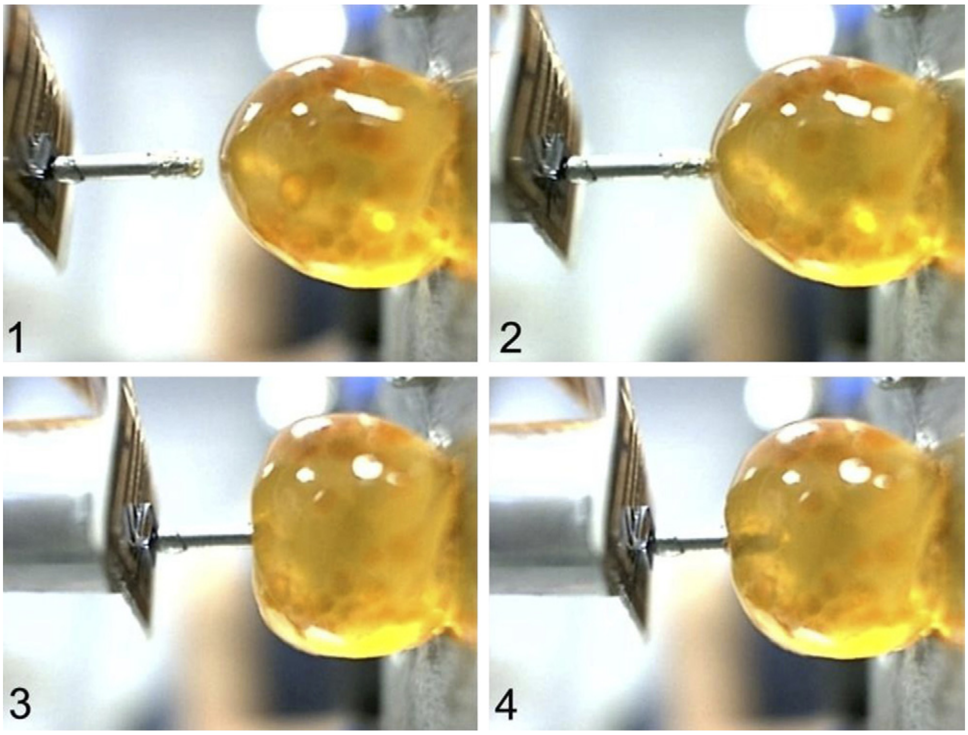

Fig. 10. Different phases of cell palpation.

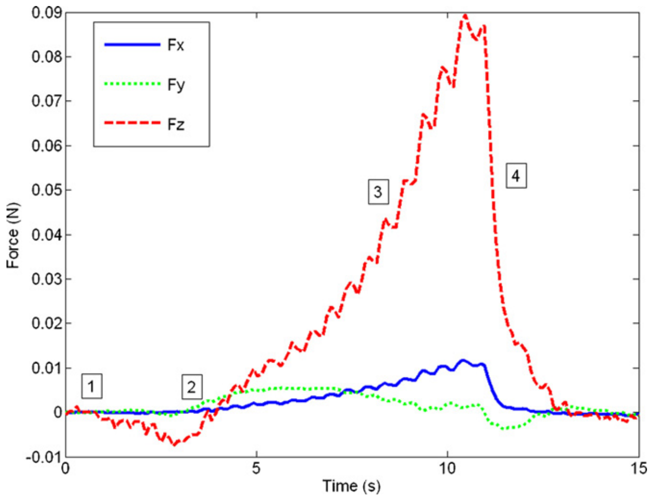

Fig. 11. Force signals from the force sensor during the different phases of cell palpation.

The force recordings acquired by the developed sensor during this experimental procedure are plotted in Fig. 11. These signals can be compared with the ones acquired by the reference load cell, located underneath the cell suction plate, that are plotted in Fig. 12.

The stiffness is important for modeling deformable tissues for accurate haptic force feedback. Together with the force on the tip of the slave manipulator and the coordinates of the master controller, a spring model is used to drive the force feedback capabilities of the master interface. To allow an accurate "feeling" of material properties it is therefore important to calculate the "local" stiffness, which is given by the first derivation of the force over displacement plot (Fig. 13). In the test setup, a laser displacement meter was used to validate the step size of the nanomanipulator. From the force plots it is possible to observe that the nanomanipulator moves like a stepper motor, with steps in the order of 150 μm (the manipulator is driven in sequences of each 1500 coarse steps). The maximum force that occurred in the experiment was 90 mN. The step size decreased

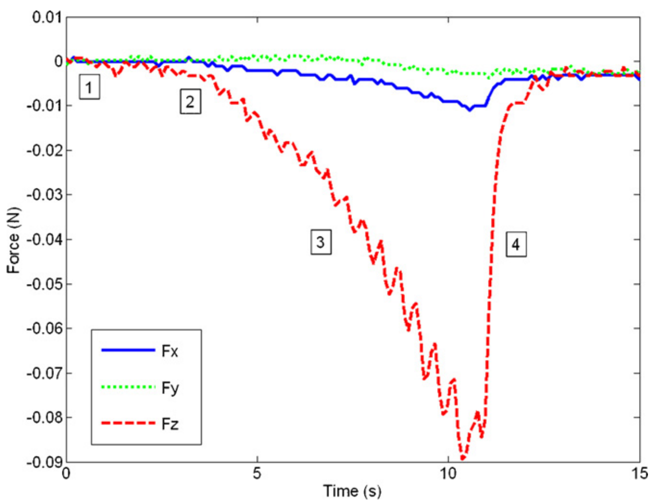

Fig. 12. Force signals from the reference load cell during the different phases of cell palpation.

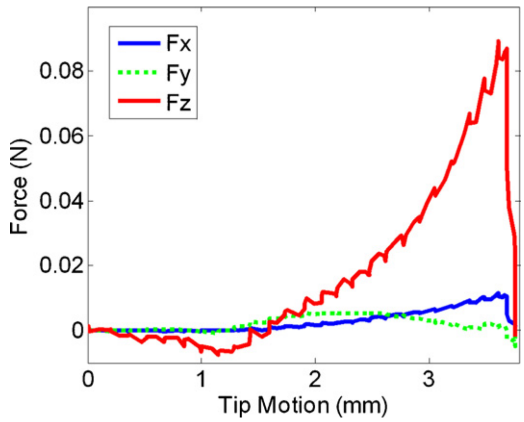

Fig. 13. Force signals from the reference load cell during the different phases of cell palpation.

by approximately 20% according to Fig. 8. For haptic force feedback applications like the one presented in this paper, manually guided by an operator with vision feedback under a microscope, there is no need for a high accuracy laser displacement measurement, as the "local" stiffness can also be calculated by the change of force over each steps of movement.

6. Conclusions and future work

Several working prototypes of triaxial MEMS force sensor with a steel tip in the axial direction were manufactured. The achieved force ranges and resolutions are:

- Normal forces: 0.3 N range and 11 bits resolution.
- Tangential forces: ±50 mN range and 11 bits resolution.

Figs. 11 and 12 are the force over time plots recorded with the triaxial MEMS sensor device and respectively with a commercial six components load cell. These plots show comparable signals, especially for normal loading. For tangential forces it is clearly visible that the novel sensor has better performances in terms of sensitivity.

The main advantages of the developed device are being lightweight and highly miniaturized and therefore it is suitable to be mounted on a high resolution nanomanipulator, without compromising its movement capabilities. In a haptic setup like the one described above, the device is one of the core components that allow the operator to feel all the three components of an applied force when, for example, performing a palpation or an injection task. A misalignment of the tip during palpation or injection will result in relatively high tangential force components. By feeling these components, the operator can correct the slave movement, thus increasing the positive outcome of the procedure. Difficult tasks, like cell injection, usually require long, extensive experience. Performing such a task with a haptic station with triaxial force feedback then become also feasible for low skilled operators.

Work in the near future will be focused on the validation of different haptic feedback strategies and to the use of the developed system for mechanical characterization of biological micro samples. Furthermore, since the used nanomanipulator is compatible with the high vacuum environment of Focused Ion Beam (FIB) working chamber, the setup will be also used for haptic bilateral manipulation under FIB vision. Finally, a redevelopment of the MEMS sensor is planned including miniaturisation, smaller signal to noise ratio, higher resolution, increased mechanical robustness and a dummy resistor for temperature compensation.

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Biographies

Arne Sieber finished his studies of electrotechniques biomedical engineering in 1999 at the Technical University of Graz, Austria. From 1997 to 2001, he gained his first industrial research experiences at AVL Medical Instruments in Graz, Austria. The next 4 years, he worked for Roche Diagnostics in R&D of electrochemical and optical sensors. He finished his PhD about electrochemical sensors in 2002. Actually, he is working as a researcher in R&D of microsensors and actuators for ARC Seibersdorf Research GmbH. Within a knowledge transfer program, he was integrated in a research team at CRIM Lab of Scuola Superiore Sant'Anna in Pisa, Italy, for the last year.

Pietro Valdastri received his Laurea degree in electronic engineering (with honors) from the University of Pisa in February 2002, and the PhD degree in biomedical engineering from Scuola Superiore Sant'Anna, Pisa, in 2006. From 2002, he joined the CRIM Lab of the Scuola Superiore Sant'Anna in Pisa as a research assistant. Main research interests are in the field of implantable biotelemetry, MEMS-based biosensors, and capsular endoscopy. He is working on several European projects for the development of minimally invasive biomedical devices.

Keith Houston completed his bachelor and research masters degree in mechanical engineering at the University of Limerick in Ireland in 2002. After graduation, he joined the precision engineering industry in Northern Ireland until 2004 when he joined the CRIM Lab of Scuola Superiore di Sant'Anna to begin a PhD in teleoperation of micromanipulation processes. He is also involved in microrobotics and design of micromanipulation tools.

Clemens Eder completed both his masters degree in 2001 and his PhD in biomedical engineering and science in 2005, both at the University of Aalborg, Denmark. His PhD thesis covered biomechanical and electrophysiological methods to assess motor recovery of stroke survivors. He is currently holding a postdoctoral position at the ARTS lab of the Polo Sant'Anna Valdera in Pontedera, Italy. He is working on the development of a teleoperation system for micromanipulation using sensorized end-effectors. His main interests are teleoperation and robotic devices for medical applications.

Oliver Tonet received the MSc degree in physics from the University of Pisa, Italy, in 1997, and the PhD degree in biomedical robotics from Scuola Superiore Sant'Anna, Pisa, in 2002. He has been Laboratory Assistant at the Fermi National Accelerator Laboratory, Batavia, IL, and Visiting Researcher at INRIA, Sophia-Antipolis, France. Since 2003, he is Assistant Professor in Bioengineering at Scuola Superiore Sant'Anna. His main research interests are in the field of action and perception enhancement in biomechatronic systems for teleoperation and minimally invasive computer-assisted surgery. His research is carried out in the context of national and European projects.

Arianna Menciassi (MS, 1995; PhD, 1999) joined the CRIM Lab of the Scuola Superiore Sant'Anna (Pisa, Italy) as a PhD student in bioengineering with a research program on the micromanipulation of mechanical and biological micro-objects. The main results of the activity on micromanipulation were presented at the IEEE International Conference on Robotics & Automation (May 2001, Seoul) in a paper titled Force Feedback-based Microinstrument for Measuring Tissue Properties and Pulse in Microsurgery, which won the ICRA2001 Best manipulation paper award. In the year 2000, she was offered a position of Assistant Professor in Biomedical Robotics at the Scuola Superiore Sant'Anna and in

June 2006 she obtained a promotion to Associate Professor. Her main research interests are in the field of biomedical microrobotics, bio-mimetics, microfabrication technologies, micromechatronics and microsystem technologies. She is working on several European projects and international projects for the development of minimally invasive instrumentation for medical applications and for the exploitation of micro and nanotechnologies in the medical field.

Paolo Dario received his doctorate degree in mechanical engineering from the University of Pisa, Italy, in 1977. He is currently a Professor of Biomedical Robotics at the Scuola Superiore Sant'Anna in Pisa. He has been Visiting Professor at Brown University, at the Ecole Polytechnique Federale de Lausanne, and at Waseda University. He was the founder of the ARTS (Advanced Robotics Technologies and Systems) Laboratory and is currently the Coordinator of the CRIM (Center for the Research in Microengineering) Laboratory of the Scuola Superiore Sant'Anna, where he supervises a team of about 70 researchers and PhD students. He is also the Director of the Polo Sant'Anna Valdera of the Scuola Superiore Sant'Anna. His main research interests are in the fields of medical robotics, biorobotics, neuro-robotics and micro/nanoengineering. Specifically, he is active mainly in the design of miniature and microrobotics systems for endoluminal surgery, and in advanced prosthetics. He is the coordinator of many national and European projects, the Editor of two books on the subject of robotics, and the author of more than 200 scientific papers (90 on ISI journals). He is Editor-in-Chief, Associate Editor and member of the Editorial Board of many international journals. He has been a plenary invited speaker in many international conferences. Prof. Dario has served as President of the IEEE Robotics and Automation Society in the years 2002–2003, and he is currently Co-Chair of the Technical Committees on Bio-robotics of the same Society. Prof. Dario is an IEEE Fellow, a Fellow of the European Society on Medical and Biological Engineering, and a recipient of many honors and awards, such as the Joseph Engelberger Award. He is also a member of the Board of the International Foundation of Robotics Research (IFRR). He is the General Chair and Program Chair of the 1st IEEE RAS/EMBS Conference on Biomedical Robotics and Biomechatronics (BioRob 2006), and the General Chair of the IEEE International Conference on Robotics and Automation (ICRA 2007).