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J. GHAYMOUNI, B. CAGNEAU (канд.техн.наук, доц.)**, S. TOPSU** (д-р техн.наук, доц.)**,**
L. CHASSAGNE (д-р техн.наук, проф.)**, Y. ALAYLI** (д-р техн.наук, проф.)
University of Versailles, Laboratory LISV, 78035 Versailles, France
jaouad.ghaymouni@uvsq.fr, barthelemy.cagneau@uvsq.fr, suat.topcu@uvsq.fr

INTERACTIONS BETWEEN NANOTUBES AND CANCER CELLS WITH AN OPTICAL TWEEZER AND A HAPTIC COUPLING

We develop a new optical tweezer with force feedback features. This will be done thanks to the development of an accurate system based on laser interferometric techniques. An optical tweezer also ensures an accurate positioning as far as objects with nanometric size are concerned. Force feedback will be performed using a haptic device, a mechanical device with several active degrees of freedom. We plan to provide the user with forces involved during the manipulation. These forces are at the piconewton level and must be amplified with a bilateral coupling before rendering.

Nanotechnology, laser interferometry, optical tweezer, haptic.

1. Introduction

3D manipulation at nanoscales still remains a challenge due to contact forces that occur. These forces are quite difficult to model depending on the geometry of the objects and it is thus a problem to control/anticipate them. Using an *optical tweezer* seems to be a promising solution since no physical contact is established with the object while manipulating it. Basically, the laser beam is focused with an objective so that, in the focal plane, it creates an attractive force to the center of the trap allowing the manipulation of the object. However, the magnitude of the forces is very low (a few piconewton) and force measurement is a major issue. Two main issues will be addressed through this project, named NanoCan:

- The first one consists in providing efficient tools to the user so that he or she can easily manipulate the objects in 3D. An interesting solution could be the use of haptic interfaces since they allow real-time interactions with the manipulated objects. However, one must also ensure that the manipulation can be performed in an accurate and easy way, without being an expert. To overcome these difficulties, force feedback may be added to provide local information about the interactions between the objects.
- The second issue of this project consists in modeling cell-cell interactions and cell-laser interactions. One can expect to better understand the phenomena that occur at this scale and to evaluate the accuracy thanks to the experimental setup.

The first application will exhibit the mechanisms of interactions between cancer cells and carbon nanotubes. Basically, the nanotubes are functionalized with a ligand and can thus interact with a receptor which is specific to cancer cells. Since the complex ligand-receptor is created, the temperature of the nanotubes is locally increased using a light with adequate wavelengths. As a result, cancer cells are destroyed without killing other cells. This very promising application may lead to a new therapy for cancers.

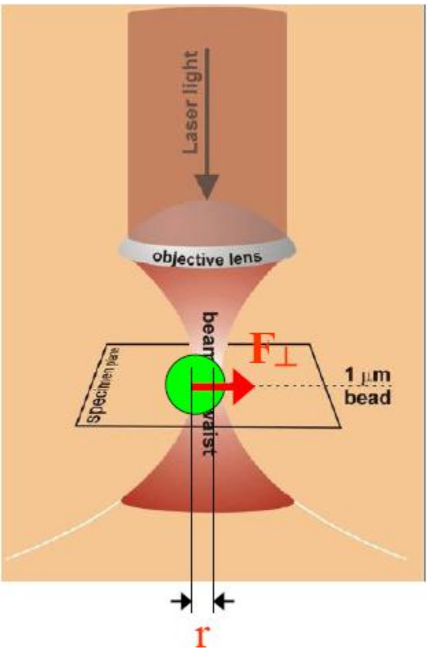

Figure 1 – Principle of an optical tweezer – Haptic device

2. Principle. 2.1 Description of the project

Optical tweezer has been first developed in the middle of the '70's by Ashkin et al. [1]. However, it has been deeply studied and developed only a few years ago while nanotechnologies emerged. Biology, physics and medicine constitute most of the known applications [2]. Optical tweezers allow the measurement of mechanical forces [3] exerted on molecules but also DNA manipulation.

A bilateral coupling (a control scheme dedicated to haptic devices) is thus necessary to provide forces to the user. However, deriving a control law with high performances is still a challenge especially for applications at nanoscales. Two huge scale factors are used to link the macro-world (user frame) to the nano-world (object frame). The stability of the system depends on the ratio of the factors [4], [5]. A few solutions have been considered to overcome this problem [6]. However, the same solutions may lead to a lack of transparency and, consequently, the forces transmitted to the user are deteriorated.

2.2 Optical tweezer dedicated to the oncology

Thanks to their mechanical, electronic, physical and chemical properties, the nanotubes have a high potential not only for material structures but also in medicine. Monolayer nanotubes could be used for anticancer therapies. The main advantage is that they are able to strongly absorb a selective range of wavelengths (between 700 and 1100 nm). This inherent property seems to be useful in order to destroy cancer cells. The temperature of the nanotubes is increased while inserting them into the cells.

Recalling that the biological systems are not sensitive to the same wavelengths, only the potential cancer cells will be affected by this operation. The last step is to select only the cancer cells in this subarea. In order to do that, the nanotubes must be inserted into the organism in a selective way. This is done by functionalizing the nanotubes with a ligand which is the complement of a native receptor on the cancer cell.

Since I arrived in LISV, our team acquired skills in near field microscopy and nanodisplacements. We decided to use these competences to build a new setup dedicated to optical tweezers using dipole trapping and emission field microscopy. One of the milestones of this project is to study the interactions between the nano-objects and biological cells. It will be thus possible to better understand the process about the selective insertion of nanotubes into the organism (described above). Moreover, NanoCan allows a better knowledge concerning the toxicity of the nanotubes.

A partnership will be formed with a hospital and a laboratory working on biology. First contacts are already made and a PhD student (Hoda Sbeity) is working on this aspect in collaboration with the University of Beirut.

3. Experimental setup and discussion

The prototype will be designed with respect to a conventional architecture:

- 1 microscope with an objective x100 and a numerical aperture 1,3
- 1 laser Nd:YAG able to deliver a high power and a collimated beam
- 1 laser He-Ne (633nm, 6mW) to perform position measurement based on interferometry
- 1 camera with high definition and real-time capabilities
- 1 haptic device (Omega 3D by Force Dimension)

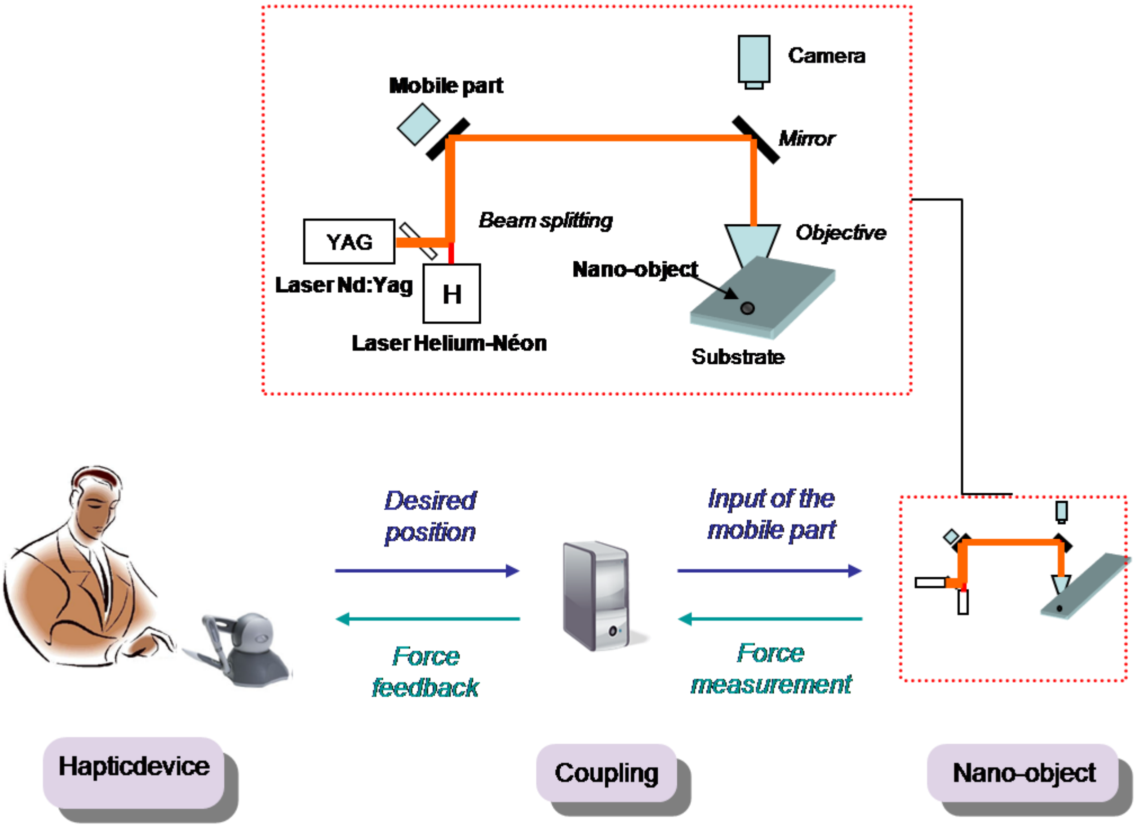

Figure 2 – Haptic coupling and optical tweezer for nanomanipulation

The first challenge concerns the optical tweezer. Usually, position measurement is realized using techniques based on interferometry or laser deflection. These techniques allow for precise measurement with high resolution (typically 1ms for the time resolution and 1nm for the spatial resolution) [8-9]. However, the measure of the position is often disturbed by the thermal noise. The particle, which is trapped, is frequently in collision with solvent molecules. The thermal noise is thus a limit for the spatial resolution. It can be reduced if a more rigid optical tweezer. This can be achieved using a laser with high power. However, as far as biological applications are concerned, increasing the power may lead to the destruction of the cells due to the variation of the temperature.

The second challenge concerns the haptic coupling that must ensure the transparency and the stability of the system (these two criteria are widely used [7] to evaluate the performances of any haptic coupling). The transparency consists in providing the user with phenomena encountered at nanoscales. However, assuming that we develop a system with perfect transparency, the thermal noise will also be reflected to the user and this can be very disturbing. As a consequence, it seems necessary to filter the force signal so that thermal noise can be canceled. Moreover, using high scaling factors may lead to a lack of stability as stated above. These factors must be taken into account while synthesizing the controller used in the bilateral coupling.

4. Conclusions

3D manipulation at nanoscales still remains a challenge due to contact forces that occur. These forces are quite difficult to model depending on the geometry of the objects and it is thus a problem to control/anticipate them. With our system, we expect to control the position of the nano-objects with sub-nanometric repeatability and accuracy without increasing the power of the laser. Consequently, the manipulation of cells may be improved since they will not be destroyed using a high power.

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ГАЙМУНИЖ., КАНЁ Б., ТОПСЮ С.,
ШАСАНЬ Л., АЛАЙЛИ Я.
Версальский университет, лаборатория LISV, Франция

Интеракция нано-трубок с раковыми клетками с помощью оптического пинцета и тактильной связи. Мы разрабатываем новый оптический пинцет, особенностью которого является обратная связь по силе. Она будет реализована благодаря новой точной системе, основанной на лазерных интерферометрических технологиях. Оптический пинцет обеспечивает точное позиционирование объектов нанометрического размера. Обратная связь по силе будет осуществляться с использованием тактильного механического устройства с несколькими степенями свободы. Мы планируем дать почувствовать пользователю силы, участвующие в манипулировании. Эти силы находятся на пиконьютоновом уровне и должны быть усилены двунаправленной связью перед их обработкой.

Нанотехнологии, лазерная интерферометрия, оптический пинцет, тактильная связь.

ГАЙМУНІ Ж., КАНЬО Б.,ТОПСЮ С.,
ШАСАНЬ Л., АЛАЙЛІ Я.
Версальський університет, лабораторія LISV, Франція

Інтеракція нано-трубок з раковими клітинами за допомогою оптичного пінцету та тактильного зв'язку. Ми розробляємо новий оптичний пінцет, особливістю якого є зворотний зв'язок за силою. Він буде реалізований завдяки новій точній системі, що базується на лазерних інтерферометричних технологіях. Оптичний пінцет забезпечує точне позиціонування об'єктів нанометричнихрозмірів. Зворотний зв'язок за силою буде здійснюватись з використанням тактильного механічного пристрою з декількома ступенями свободи. Ми плануємо дати відчути користувачеві сили, які приймають участь в маніпулюванні. Ці сили мають піконьютонний рівень і повинні бути посилені двонаправленим зв'язком перед їх обробкою.

Нанотехнології, лазерна інтерферометрія, оптичний пінцет, тактильний зв'язок.