Optical force transducer for visualizing cell mechanotransduction in 3D

DESIGN DOCUMENT

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Table of Contents

List of figures/tables/symbols/definitions

1 Introduction

1.1 ACKNOWLEDGEMENT

1.2 PROBLEM AND PROJECT STATEMENT

Mechanotransduction refers to how cells react physical forces (mechanical stimuli) and translate the forces into biochemical outputs. In mammalian cells, their cytoskeletons allow them to exert forces in nano newton; and physical forces play an important role on biological choices of cells such as stem cell differentiation and tumor formation [1]. Therefore, it is very important to study the forces in cells.

In this project, we aim to collect preliminary results of a fiber-based optical force transducer that can probe forces as low as nN. The optical force transducer is consist of a bare fiber (without coating and majority of cladding) with nanostring, which is used to attach cells, and a laser source. For visualizing the forces, we utilize evanescent field, which occurs at the interface between core and cladding of the fiber during the total internal reflection. The evanescent field can react with the cells to emit light, whose intensity can be used to determine the force.

1.3 OPERATIONAL ENVIRONMENT

In the first testing, we use the exposed fiber functionalized with -CHO group to attach gold nanoparticles. The exposed fiber would be observed under the microscope while the room should be completely dark. In the final testing, we use the exposed fiber with nanostring to attach cells. The observation condition is the same as the previous testing.

1.4 INTENDED USERS AND USES

The product of our project is mainly used for biological research. Therefore, the researchers who interested in the field of mechanotransduction would be the primary users of our product. Since by observing the induced light intensity, researches can visualize cell mechanotransduction.

1.5 ASSUMPTIONS AND LIMITATIONS

The potential users of our product are the researchers in the field of mechanotransduction. Since our product is beneficial for them to visualize cell mechanotransduction.

During the testing period, the laser safety goggles will be needed for protecting the eyes, as the background need to be dark enough to observe the laser through the fiber. The length of the optical fiber should be about 1 meter long. The cost to produce the product shall not exceed one thousand dollars.

In case of the limitations, it's impossible to remove all the cladding from the optical fiber. Because both core and cladding are made of glass, we have to use Hydrogen Fluoride(HF) to etch the cladding part. But the size of optical fiber is in micrometer scale.

1.6 EXPECTED END PRODUCT AND DELIVERABLES

Our expected end product is an optical force transducer used to visualize the mechanotransduction under the microscope. To achieve a high sensitivity, we use simulation tool to optimize the parameters of the optical fiber, which is the major part of our optical force transducer. We expect we can get the optimized parameters by the end of Fall 2017, and finalize our product design by the end of Spring 2018.

2. Specifications and Analysis

To solve the problem, we should create numerical model of the optical force transducer to optimize the parameters, and fabricate the optical fiber to characterize light scattering by the attached nanoparticles. In the theory and numerical modeling, we will use simulation software to build a numerical model for nanofiber with gold nanoparticles; in addition, we will use the model to optimize the sensor parameters. In the fabrication and process development, we will process the optical fiber by stripping the outside layers, adding FC connector and attaching gold nanoparticles. At the end of the phase, we will be able to test the gold nanoparticles immobilization process.

Functional requirement:

- the coating layer and cladding layer should be completely removed
- the gold nanoparticles should be evenly attached onto the optical fiber
- the fiber holder should be made to fit the size of the single mode optical fiber
- the parameter of the numerical model should optimize the efficiency of optical force transducer(nanoparticle size, operation wavelength)
- the laser experiment must be performed in the laser hood room

Non-functional requirement:

- the optical fiber should be cleaned thoroughly after each experiment to minimize the contamination
- the design of the fiber holder/stabler should be simple enough to save more time and resources

2.1 PROPOSED DESIGN

Numerical model and component of optical force transducer:

- Single mode optical fiber holder (for microscope use)
- cubic model of optical fiber stabler for surface chemistry
- complete model of optical force transducer with gold nanoparticles
    - optimize the sensor parameters: fiber diameter, nanoparticle size, and operation wavelength
    - characterize the figure of merits(force sensitivity) and noise sources

Fabrication:

- Optical fiber preparation
    - remove coating, cladding layers
- Surface chemistry
    - capture -NH2 coated AuNPs
    - capture -COOH coated AuNPs
    - immobilize gold nanoparticles
    - exam fiber under optical microscope and SEM
- Laser experiment:
    - making connectors(FC/PC), polish the fiber tip
    - testing the laser beam
- Demonstrate the application of the optical force transducer in cell mechanotransduction
- Characterize the light scattering by the gold nanoparticles attached on the optical fiber
- Functionalize the fiber core and test the gold nanoparticles immobilization process

Fiber surface chemistry protocol I:

I. PVA-GA Surface chemistry for Amine-terminated materials

Prepare containers (centrifuge tubes) for the following processes, including the cleaning process. The fiber should be soaked into the container and gently shaked.

1. Clean the fiber using Acetone, DI and dried in air
2. Prepare PVA (Polyvinylamine) solution (1% - 2% dissolved in DI water). PVA is stored in the fridge (Sweeney 3152)
3. Soak the fiber in PVA for 12 -24 hr (overnight) at room temperature
4. Clean the fiber by soaking in DI water 3x
5. Prepare GA (Glutaraldehyde) 20% solution in DI. GA is stored under the fume hood in Sweeney lab.
6. Soak the fiber in GA solution for 5 hours
7. Clean the fiber by soaking in DI water
8. At this point the fiber tip is functionalized with –CHO group. It is ready to capture amine (-NH2) samples.
9. If the following experiment can't be carried out immediate after the pervious step, fiber should be stored in DI water. DON'T let it dry in air.

II. Capture -NH2 coated AuNPs (gold nanoparticles)
1. Dip the fiber in DI water (2 mins) for quick cleaning.
2. Soak the GA-coated fiber in the solution of AuNPs (with NH2) for 1-4 hrs. Gently shake the fiber during the conjugation process.
3. Pull the fiber out of AuNP solution and dip it in the DI water for a quick cleaning (2 mins)
4. The fiber is ready for imaging. Fiber can be dried at this point.

The above list is the process we have designed to finish the project. In the fabrication process, we need to use a stripper to complete removing the coating layer, and use a fire gun to burn the cladding layer, so the layer can be peeled off completely. Another approach of removing cladding layer is to use the hydrochloric acid. The surface chemistry experiment is shown in the graph above to attach the gold nanoparticles. We also designed a surface chemistry holder to stabilize the optical fiber as shown below. After we finish attaching the gold nanoparticles, we will install the optical fiber into the FC connector, and test the fiber through the laser beam. We need to perform the above

experiment process step by step to finish the project.
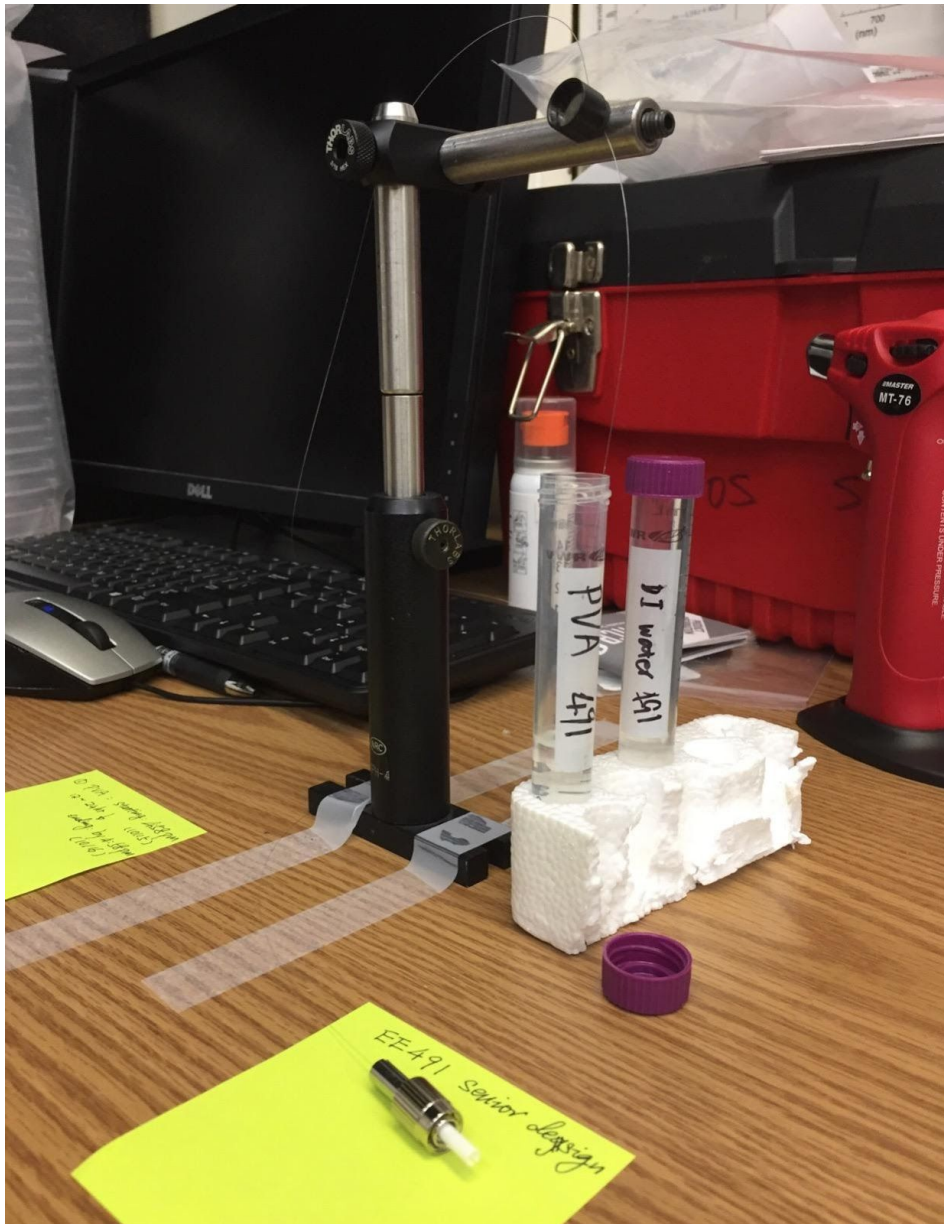
2.2 DESIGN ANALYSIS

We have finished creating the numerical model of the experiment, which is the optical fiber transducer attached with the gold nanoparticles in three dimensional model. The fabrication of optical fiber has already started. To process the optical fiber, the coating layer and cladding layer should be removed to start the attachment of the gold

nanoparticles. At Week six, the coating layer has already been removed by the stripper tool, and we have completed the first trial of surface chemistry based on the first optical fiber model created. The gold nanoparticles have successfully attached onto the optical fiber; nevertheless, we are preparing our second trail of surface chemistry, and in the process of finding new method to effectively remove the cladding layer.

The weakness of our design of fabrication process is the removal of the cladding layer, it is an essential step for next stage of experiment, using the fire gun cannot remove the cladding layer evenly, and the optical fiber can be broken easily because it is made by glass. Although we have completed the trail one experiment, we are still working on the improvement of cladding layer removal by trying new method like using Hydrochloric acid. When the optical fiber was attaching the gold nanoparticles, it is more likely to turn fragile, and it could break into pieces even dipped into deionized water.

The strength of our design is the numerical model, we have successfully created the optical force transducer model. For sensor parameters, we will be able to optimize the sensor parameters like adjusting the fiber diameter and nanoparticle size.

3   Testing and Implementation

3.1 INTERFACE SPECIFICATIONS

- Comsol (simulation)
- SolidWork (Design the research components)
- Scanning Electron Microscope(observing gold nanoparticles)
- Chemicals used in surface chemistry(PVA, GA, Acetone, DI water, and AuNPs solutions)

For the software and simulation part, we use the solid work to design fiber holders for observing purposes under the microscope. We will use solid work to design the shape of the fiber in precise measurement, and then ask ETG to print out the real holder. The fiber holder will be used as a tool to stabilize the optical fiber under the microscope. Also, we

will use the Comsol to do the simulation. The basic model for the optical fiber will be built in Comsol, and gold nanoparticles will be added.

For observing the gold nanoparticles, we will send the samples to SEM to observe whether the gold nanoparticles have successfully attached.

3.2 HARDWARE AND SOFTWARE

- Comsol (simulation)

Comsol is a software that could simulate the 2-D and 3-D model by designing the exterior structure and applying the physics equations. In our project, we will use Comsol to design a 2-D model of optical force transducer made by the optical fiber and gold nanoparticles, and then optimize the efficiency by adjusting the parameters of the nanoparticle size and operation wavelength.

- SolidWork (Design the research components)

SolidWork is a computer program that can build models in 2D sketch. We use SolidWork to design the components of our project like the optical fiber holder.

- Scanning Electron Microscope(observing gold nanoparticles)

The Scanning Electron Microscope is used for observing the attachment of the gold nanoparticles on the optical fiber, it uses electrons to form an image with high resolution, so it can closely observe the particles at high magnification which cannot be replaced by the fluorescence microscope[2].

- Chemicals used in surface chemistry(PVA, GA, Acetone, DI water, and AuNPs solutions)

The chemicals are used for attaching the gold nanoparticles on the optical fiber.

3.3 PROCESS

Before assembling the optical force transducer, we need to finish creating the numerical model in ComSol. We need to find out the size of appropriate single mode optical fiber and the diameter of the gold nanoparticles in the solution to determine the basics of the model.

After the raw model of the transducer has been created, we can start taking care of the optical fiber that will be used in the sensor. We need to conduct series of experiment to attach the gold nanoparticles on the fiber using the surface chemistry plan, then choose the successful attached fiber to insert into the FC connectors. Finally, the fiber core can be functionalized and the immobilization can be continued.

At the same time, we need to make the fiber holder, and check whether the fiber can fit into the V-groove or not. As long as it can fit inside, we use two magnets on both side of the holder. Thus, we are able to put the holder under the microscope and detect what is going on inside of the fiber.

3.4 RESULTS

We have successfully finished the simulation in ComSol, and trying to convert the 2-D model into 3-D model to utilize the settings. Our group have learned to use the software and creating models.

For the fabrication process, we have finished stripping off the cladding layers and coating layer, but most of our experiment failed by breaking the optical fiber. The optical fiber is very fragile after it is coated with gold nanoparticles, the reason is due to the thickness and the result of surface chemistry. But we have already assembled the one meter optical fiber into the FC connector, we need to find the best solution to stabilize the fiber after the gold nanoparticles has been attached.

For making the first holder, everything was successful, but the problem appeared when ETG do not have the tool to cut a V-groove as small as the optical fiber, it is the area to place the optical fiber on the fiber holder as shown in the picture below. Due to the fact

that V-groove need an extremely precise tool, we decide to use the U-groove instead of the V-groove, it will be much easier and cheaper.

For the second holder, our team have already designed a CAD graph using a solid cube to stabilize the optical fiber during the surface chemistry, but we found out magnets are strong enough to stabilize the fiber during the experiment.
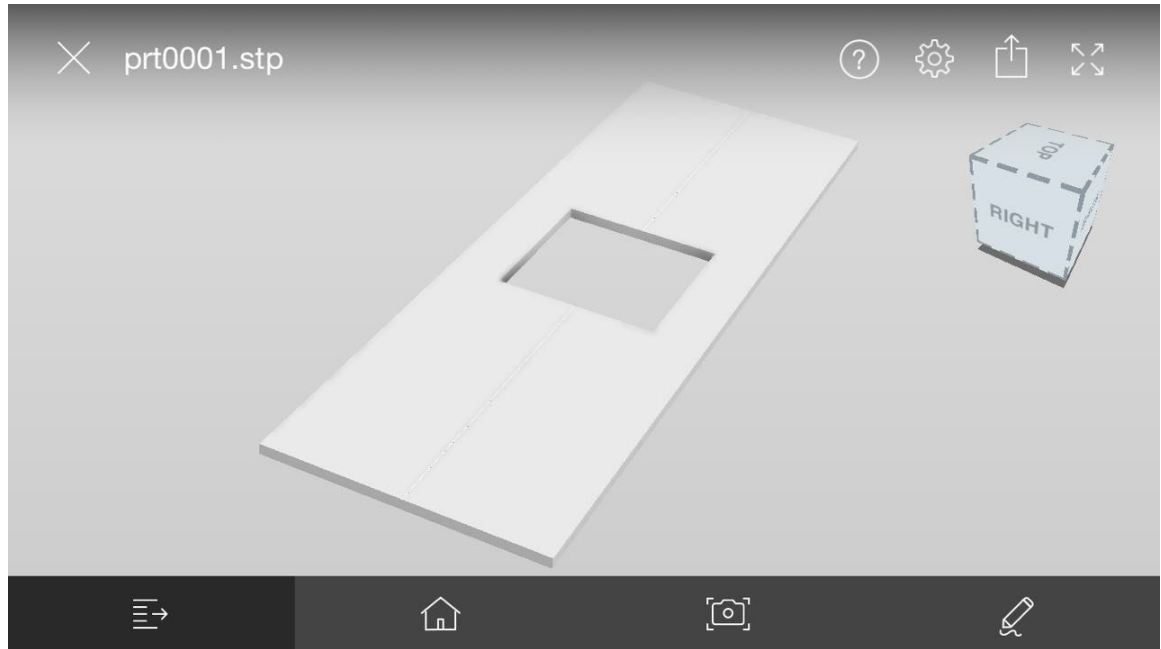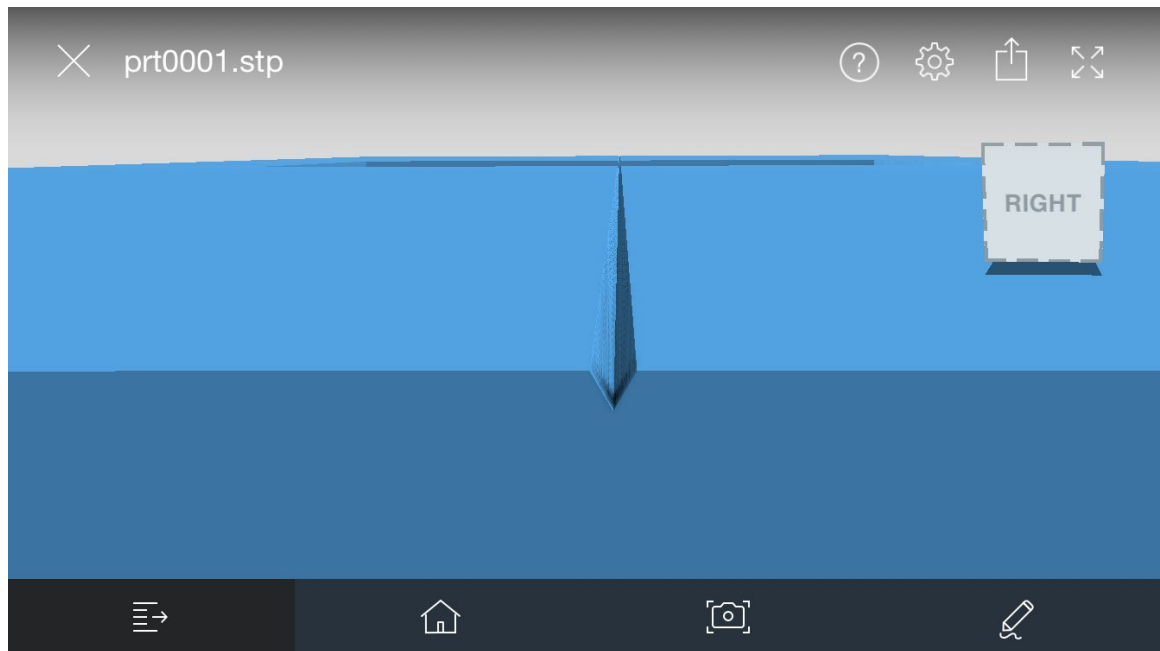
4 Closing Material

4.1 CONCLUSION

In this project, We are trying to fabricate a bare fiber based optical biosensor to visualize nanoparticles. So far, we have successfully completed the following steps: simulation modeling, surface chemistry, removal of coating for optical fiber, laser coupling, and installation of FC connector in optical fiber. After that, we are planning to complete the following steps in the remaining time of fall 2017: Yalun and Quan: Using Wet etching to remove the cladding of optical fiber; Jiameng and Qinming: Running simulations to find the optimised parameters for fiber and nanostring.

4.2 REFERENCES

[1] Paluch, E. K., Nelson, C. M., Biais, N., Fabry, B., Moeller, J., Pruitt, B. L., … Federle, W. (2015). Mechanotransduction: use the force(s). BMC Biology, 13, 47. http://doi.org/10.1186/s12915-015-0150-4

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4.3 APPENDICES