

CHARACTERIZATION OF TRANSLATION OF FUSED SILICA MICROPIPETTES IN NON-RECTILINEAR TRAJECTORIES

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INTRODUCTION

In vivo imaging technologies such as confocal endomicroscopy used for clinical histology applications, as well as *in vivo* patch clamping electrodes used in neuroscience research require very precise and stable positioning of probes within a living test subject [1-2]. For these procedures to be as minimally invasive as possible the probes need to navigate through the body's canals and cavities to reach the region of interest and are often guided using flexible and reconfigurable guide tubes in complicated non-rectilinear trajectories. Current technology used for controlling the translation of such probes within the guide tubes do not have the requisite axial resolution (1-2 μm) that will allow imaging or recording of electrophysiological activity from single cells [2]. Understanding the mechanical parameters that affect the performance of such systems will allow the development of micrometer resolution actuation systems.

We have developed an experimental methodology in combination with flexible multibody simulations to study the translation of flexible polyimide coated fused silica micropipettes (typically used for *in vivo* electrophysiology studies) telescoping within Teflon tubing that are configured in rigid predetermined curved configurations. We are investigating the performance of this translation system over a wide spectrum of geometrical (bend radii, arc length, tubing to capillary diameter clearance) and physical (preload,

frictional force) parameters and the results of this study will help in developing a basis for design of more complex non-rectilinear probes.

EXPERIMENTAL SETUP

Shown in Figure 1 is the experimental setup being used to study the geometrical parameters that affect the translation of fused silica capillaries. It consists of: a) linear actuation system comprising a piezomotor and linear stage capacitive sensing system. The fused silica micropipettes (658 μm outer diameter) are attached to the linear stage for actuation using a micropipette holder and are routed through Teflon guide tubes (21 gauge, or 724 μm inner diameter) that are fixed in predefined circular grooves in an acrylic plate wedged between two aluminum plates. The aluminum plates have holes corresponding to the grooves where the Teflon guide tubes terminate and allow the normal entry and exit of the micropipettes. An aluminum disc is attached via a precision-machined shaft translating in a linear roller bearing to the end of the micropipette acts as the ground plate for the capacitive position sensor. Thus actuation of the micropipette by the piezomotor results in corresponding axial displacement of the ground plate that can be measured.

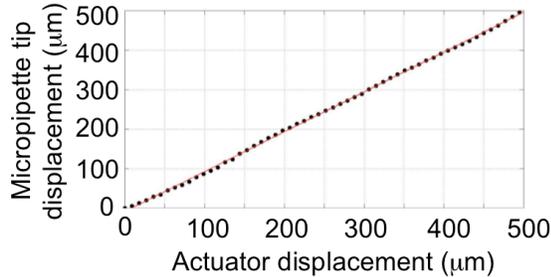
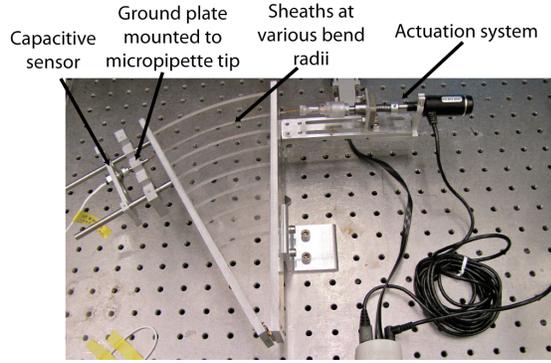


FIGURE 1: (top) Photograph of experimental setup used for characterizing micropipette translation. (bottom) Representative plot of micropipette translation through a Teflon guide tube configured at 160 mm bend radius and 45° arc angle ($r^2=0.987$).

This setup allows characterization of the linearity of micropipette translation through guide tubes of radii ranging from 80, 100, 120, 140, 160, 180, 200 and 220 mm respectively and spanning arc angles of 45°. Shown in Figure 1b is a representative plot of translation of a micropipette through a Teflon guide tube having a 160 mm bend radius and spanning an arc angle of 45° at step input of 10 μm . We were able to measure good linearity in the micropipette tip displacement ($r^2=0.987$) in all bend radii configurations.

In a second set of experiments, we measured the hysteresis in translation of the micropipette and in various geometrical configurations during bi-direction motion. The results are shown in Table 2 and accompanying Figure 2. The input displacement of the micropipette is 10 steps of 50 μm forward and 10 steps back. As it can be seen, there is an inverse linear correlation between the measured hysteresis and the bend radius, that is, the hysteresis is largest for the smallest bend radius for the same spanned arc length. The quantification of this relationship between hysteresis and geometric configuration will guide the design of future devices that required bi-directional non-rectilinear translation.

TABLE 1: Measured hysteresis for 658 μm diameter micropipette translating inside of 21 gauge (724 μm) Teflon tubes through an arc of 45°.

Bend Radius	Hysteresis
80 mm	45 μm
120 mm	-
160 mm	33 μm
200 mm	26 μm

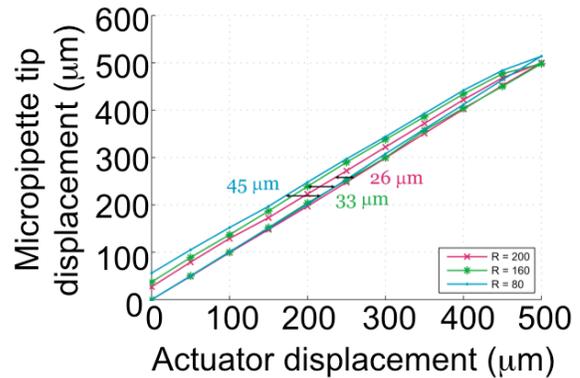


FIGURE 2: Measured hysteresis in displacement at various bend radii. The results show an inverse correlation between bend radius and hysteresis.

MULTIBODY SIMULATIONS

A multibody system analysis approach based on non-linear finite elements using SPACAR [3] is used to model the micropipette [4]. The multibody approach allows for modeling with a limited number of elements whilst obtaining accurate results. A micropipette is modeled as a series of interconnected flexible beam elements. Each beam has six deformation modes: axial, torsion and four bending deformation modes. The beams are connected at nodal points. At the nodal points external forces such as the normal reaction and friction forces can be applied. The guide tube is modeled as a tube of uniform circular cross-section with flexible walls with centerline tracing a circular arc. The contact force between the micropipette and the guide tube depends on the distance and rate of approach between them. Three regions are used; a no contact region, a full contact region, and a transition region in between to make the model continuous. In the full contact region the interaction between the micropipette and the wall results in a normal force that depends linearly on the displacement of the micropipette

wall interface, that is, a constant stiffness regime. In addition, a velocity dependent damping force is added. With the normal nodal force and tangential velocity known, a Stribeck based continuous friction model is implemented. The friction is increased at low velocity to represent static friction. The friction force always acts opposite to the direction of motion on the tangent plane at the point of contact. Simulations can be carried out both for the insertion of the micropipette as well as for the fine positioning of the tip. During a simulation the nodal displacement and force acting at the various nodes have been obtained depending on position and time.

Figure 3 shows the forces acting at the first two nodes at the distal end of the micropipette when it is inserted into the guide tube, neglecting friction. Only the first two nodes are considered for the sake of clarity, though similar plots can be obtained for all nodes. It can be observed that the end node is making contact with the outer wall of the tube all the time, whereas the penultimate node is making contact with the inner wall as expected. Clearly the nodes experience different forces. Figure 4 shows the magnitude of forces acting at the first two distal nodes in time. The penultimate node experiences a larger force in the beginning when the end node started making contact with the tube.

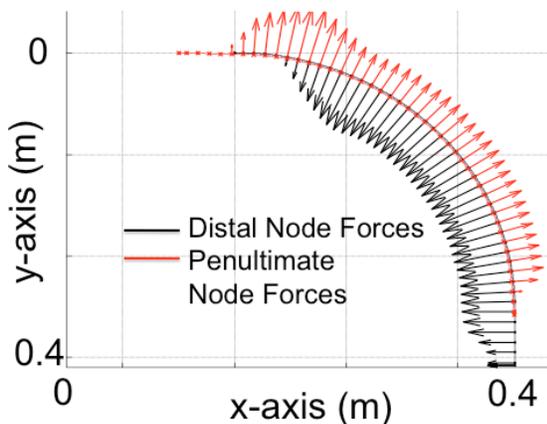


FIGURE 3: Forces as a function of space at the two distal nodes while inserting micropipette translating into tubes through an arc of 45°.

As the micropipette advances further into the tube, the first two distal nodes experience larger forces than the other nodes.

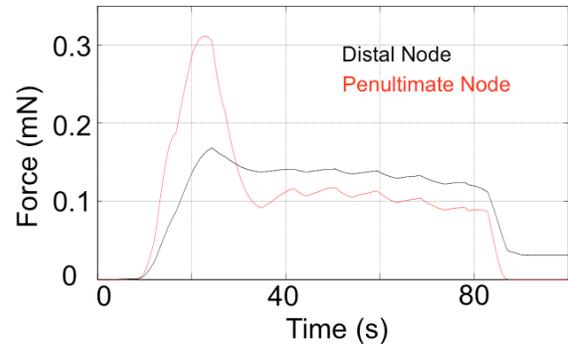


FIGURE 4: Forces as a function of time at the two distal nodes while inserting micropipette translating into tubes through an arc of 45°.

A similar input displacement to the experiments presented earlier at a slightly larger velocity is used in the simulations. The results for three simulations are shown Table 2 and Figure 5. Two simulations are performed with a friction coefficient $\mu = 0.02$ and one with a friction coefficient of $\mu = 0.2$. This range of the friction coefficient can be found for Teflon on Teflon contact. The bend radius is $R = 80$ mm and $R = 120$ mm.

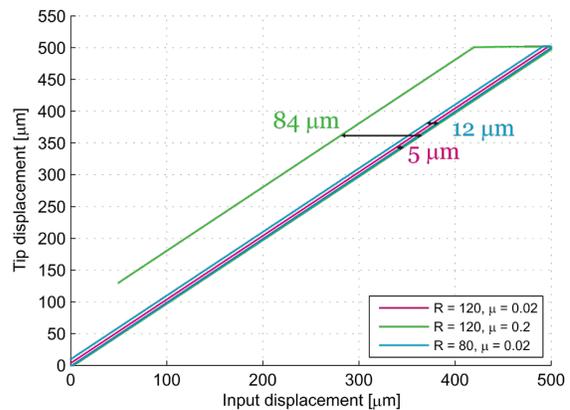


FIGURE 5: Simulated hysteresis in displacement at various bend radii.

The simulations show a larger hysteresis for a smaller bend radius, which is in agreement with the experiments. The nodal forces increase due to a decreased bend radius of the micropipette, which causes friction and therefore hysteresis to increase. The hysteresis also increases for

larger friction coefficients. The simulated hysteresis ranges from 5-84 mm for $R = 120$ mm which is due to the large spread in friction coefficient and large radius. The experimental data for $R = 120$ mm is not available. The experimental hysteresis of $R = 80$ mm and $R = 160$ mm is similar to the simulation results for $R = 120$ mm. The experimental values, with a measured friction coefficient of about 0.10 to 0.14, fit within the results of the simulation.

TABLE 2: Simulated hysteresis for 658 μm diameter micropipette translating inside of 21 gauge (724 μm) Teflon tubes through an arc of 45°.

Bend Radius (mm)	Friction Coefficient	Hysteresis (μm)
80	0.02	12
120	0.02	5
120	0.2	84

CONCLUSIONS

The experiments conducted show that it is possible to achieve highly precise translation of flexible micropipettes in defined non-rectilinear trajectories. We have shown that by varying the bend radius systematically, we can quantify the relationship between hysteresis and geometrical configuration. Both experimentally and through simulations, we have shown an inverse linear correlation between the measured hysteresis and the bend radius, that is, the hysteresis is largest for the smallest bend radius for the same spanned arc length. In the future more simulations will be set up to verify the experimental data with more accurate radii and friction coefficients. Currently the simulations are slow and very sensitive to input parameters such as the friction coefficient. More superficial models are being worked on using a state friction models or other integrators. This combined approach of experimental measurement and multibody simulations can be extended to screen a wide range of geometrical configurations and in future be used to accurately predict the translation of such tubes in arbitrary curved configurations.

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