

MICROMETER-SCALE CHEMICAL ANALYSIS USING HEATED AFM CANTILEVER AND
MASS SPECTROMETER

BY

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THESIS

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ABSTRACT

This thesis presents the development of a micrometer-scale chemical analysis method using a heated atomic force microscope (AFM) cantilever and mass spectrometer. Simulations investigate the underlying transport mechanisms within the system and the impact of various design parameters. The way to optimize the system is suggested based on the simulation results. A heated microcantilever is used to thermally desorb a micrometer-sized sample by applying thermal energy. Thermally desorbed species are transported through the micro capillary to the vacuum chamber and are deposited onto the plate inside the chamber. The collected species on the plate can be analyzed by a mass spectrometer or fluorescence microscope. The microcantilever is resistively heated and can be operated up to 1000 °C, which enables applications to various samples with a high decomposition or boiling temperature. In the present work, a caffeine sample and rhodamine B sample were successfully analyzed. The caffeine sample was detected by MALDI mass spectrometry, and rhodamine B sample was detected by fluorescence microscopy.

This thesis is dedicated to my beloved family for their limitless love and continued encouragement.

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I would like to thank my advisor, Professor William Paul King, for guiding and encouraging me to concentrate my energy on research. I am also grateful for Professor Jonathan Sweedler in the Chemistry department for his effort in working as a team on this project. I would like to thank Troy Comi and Sage Dunham in Professor Sweedler's group for their help with experiments. Finally, I would like to thank to my colleagues in Professor King's group for their help and friendship.

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CHAPTER 1: INTRODUCTION

Mass spectrometry is an analytical chemistry technique that identifies the chemical compositions of samples by measuring the mass to charge ratio of gas-phase ions of compounds [1]. Mass spectrometry has significantly contributed to studies of physical chemistry since its invention more than a hundred years ago [2]. For the past few decades, there have been various attempts to improve the spatial resolution of mass spectrometry [3-7]. The typical Matrix-Assisted Laser Desorption/Ionization (MALDI) technique has a spatial resolution around 100 μm because it uses laser beams with a 100 μm diameter [4]. Many researchers have improved the spatial resolution of MALDI by focusing the laser beam with a lens [7] or by slightly overlapping the laser beam at each shot [4], allowing for spatial resolutions of 25 μm and 40 μm , respectively. Studies on near-field laser ablation have also been applied to mass spectrometry, and have achieved a 5 μm spatial resolution by using a SNOM tip [5]. Because the contacting area of the AFM cantilever tip is typically 20~30 nm, the heated AFM cantilever combined with mass spectrometry is expected to have a spatial resolution of 30 nm. This thesis describes the development of a chemical analysis system with highly improved spatial resolution using a heated AFM cantilever combined with a mass spectrometer

Atomic Force Microscopy (AFM) has become one of the most important and versatile tools for nanoscale research [8]. AFM utilizes a nanometer-sized tip located at the end of a micrometer scale cantilever. When the tip contacts the sample surface, the deflection of the microcantilever is measured by laser, so one can calculate the topography and mechanical properties of the sample [9]. Although AFM has great capabilities of measuring topography and many other mechanical properties of the sample, not many researchers have tried to identify the chemical compositions of a sample with AFM. Considering that AFM has successfully shown the coupling between topographic data and elastic modulus data [10],

pioneering the way to identify chemical compositions with AFM will lead to understanding complex material properties at the nanoscale.

A heated AFM cantilever is a silicon microcantilever integrated with heating elements. It was originally designed for high-density data storage because of its ability to apply heat energy onto a nanometer-scale area [11-12]. The free end of the cantilever is low doped with phosphorus while the legs are highly doped with phosphorus, which makes the free end have high electrical resistance. Due to its high resistance, the free end region has more intense Joule heating which allows the tip to be heated up to 1000 °C when current passes through the cantilever [13]. By using this heated tip, nanometer-scale thermal desorption is achievable, and the technique can improve the spatial resolution of mass spectrometry [14-16]. AFM operates under ambient conditions, which leaves the possibility to analyze the living cell.

The hybrid systems of a heated AFM cantilever and mass spectrometer (MS-AFM) at atmospheric pressure conditions have been suggested recently [14-16]. By serially connecting AFM and mass spectrometer, thermal desorption and chemical analysis can be operated in real-time. Thermally desorbed species are transported through a capillary, and then, they are ionized by electrospray ionization or APCI Corona Needle at the outlet of the capillary before they are transported into the mass analyzer [14-15]. However, the sampling efficiency and ionization efficiency could not be improved at the same time since the instruments are coupled in real-time [15].

This thesis describes a hybrid system of a mass spectrometer and AFM that can obtain chemical information at the micrometer-scale. As opposed to the previous works for MS-AFM, we suggest a way to maximize the sampling efficiency and ionization efficiency at the same time by collecting and analyzing samples independently. The general system operation, simulation results with different design parameters, and experimental setup and results are discussed. The simulation results provide the insights into general system operation. From the experiments, we achieved micrometer-scale spatial resolution. Caffeine and fluorescence samples are successfully detected through MALDI, SIMS, fluorescence microscopy and a fluorescence microplate reader.

CHAPTER 2: MODELING AND RESULTS

2.1 Simulation modeling

The 100 mm long stainless steel capillary and ambient air are modeled and analyzed by the 3-dimensional finite element analysis method. The air part forms the cuboid shape as shown in the Figure 2.1, and each side of the air is set to atmospheric pressure, 1 atm. Average outlet air velocity is applied to the capillary outlet as a boundary condition. Since the simulation model is symmetric with respect to the vertical plane, only half of the system is modeled and the symmetric boundary condition is applied for efficient computation. Capillary inner diameter, wall thickness, height, and the horizontal distance between the capillary inlet and species are investigated as the design parameters in the simulations. The capillary is placed in parallel with the sample surface. Throughout the simulation, the range of each design parameter is set by considering the experimental setup parameter values at the reference material [15].

Three major assumptions are made throughout the simulations. First, all the transported species are present from the beginning of the simulations. It is an appropriate assumption since the thermal desorption process has a significantly smaller time constant compared to the entire transport process. The heating process of a heated AFM cantilever shows a time constant on the order of 100 μ s [13] while the entire transport process shows a time constant on the order of 1 s. Second, the concentration of the species is dilute enough to be predicted by the transport of diluted species model. This is a reasonable assumption because the spatial scale of the thermal desorption process is relatively small compared to the entire system. The entire height of the AFM cantilever tip is around 1 μ m and the largest diameter is also around 1 μ m. Third, the temperature of the thermally desorbed species is room temperature. This assumption is

reasonable because the cooling process of the thermally desorbed species has a relatively small time constant compared to the transport phenomena.

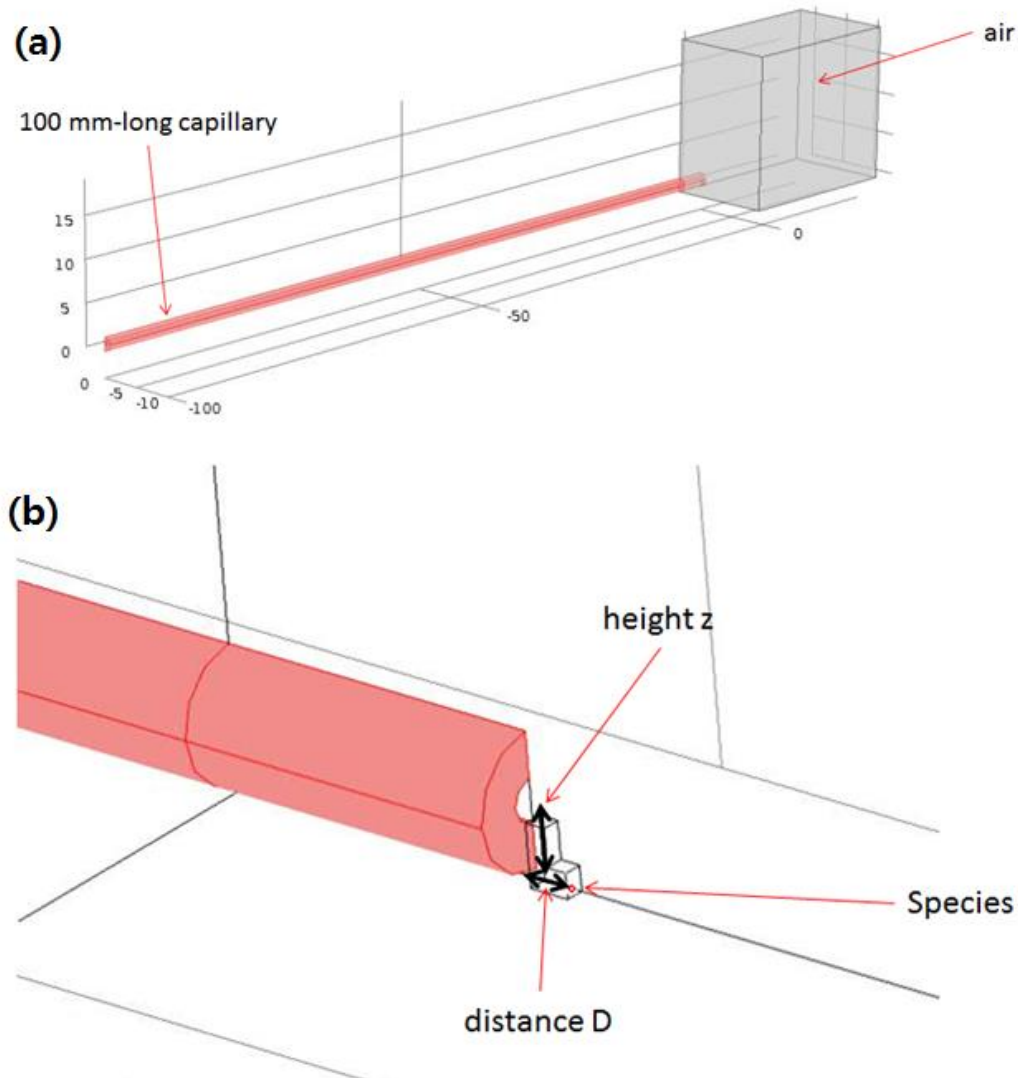


Figure 2.1 (a) Simulation model of MS-AFM system. The air pressure is set to an atmospheric pressure. (b) Simulation model around the capillary inlet. Capillary inner diameter, wall thickness, height, and the horizontal distance between the capillary inlet and species are investigated as the design parameters.

The transport of diluted species assumes that diluted species are transported through diffusion and convection phenomena. The “Transport of Diluted Species” model from the Comsol Multiphysics

software (COMSOL Inc., Burlington, MA) is used for the entire simulation. The governing mass balance equation becomes [20]:

$$\frac{\partial c}{\partial t} + \mathbf{u} \cdot \nabla c = \nabla \cdot (D \nabla c) + R$$

where c is the concentration of the species (mol/m^3), $\mathbf{u}$ is the velocity vector (m/s), R is a reaction rate expression for the species ($\text{mol}/(\text{m}^3 \cdot \text{s})$), and D is the diffusion coefficient (m^2/s). In the present work, no chemical reaction is assumed, and thus R becomes zero. Simulations throughout the entire project are performed based on this governing equation [20].

The initial concentration is given to the hole of the simulation model. Figure 2.2 presents the initial concentration profile of the species. The species spread slightly over the hole at the beginning of the simulation to avoid discontinuity of the concentration. As discussed previously, the assumption that the transported species are present at the beginning of the simulation is appropriate since the thermal desorption process happens very quickly compared to the transport phenomena. All the cases have the same initial concentration profile to accurately compare the transport efficiencies. The radius of the hole and its height are both set to $1 \mu\text{m}$. The size of the hole matches well with the cantilever tip size.

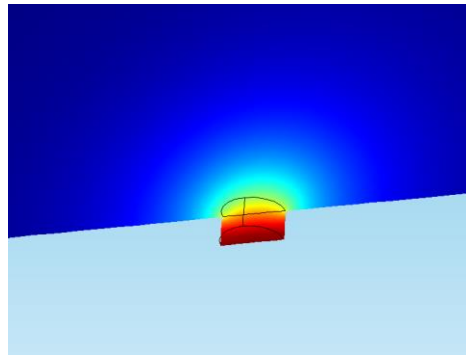


Figure 2.2 Initial concentration of the species at the hole(0 s). The species spread slightly at the beginning to avoid the discontinuity of the concentration. All the cases have the same initial concentration profile to accurately compare the transport efficiencies. The radius of the species hole is $1\mu\text{m}$ and the height of the hole is also set to $1 \mu\text{m}$.

The standard simulation is performed with the design parameters of outer diameter(OD)=3.175 mm, inner diameter(ID)=2.0828 mm, $t=0.55$ mm, $z=0.1$ mm, $D=0.5$ mm, $V=0.073$ m/s, diffusivity= $1\text{E-}09$ m^2/s . Other than the standard simulation, each design parameter is investigated with the standard values as the center value. Figure 2.3 presents the simulation results of the standard model. Figure 2.3 (a) shows the 2-dimensional total flux plot at $t=0$ s. Due to the zero air flow, no total flux is found in Figure 2.3 (a). However, the total flux values show up as the species moves with the air flow as shown in Figure 2.3 (b). The total flux becomes the greatest at $t=1.54$ s, and then, it gets smaller until all the species are transported. As shown in Figure 2.3, most of the species are located at the bottom of the capillary when the species are sampled to the capillary inlet. Quantitative analysis of the standard model is discussed in the simulation results section.

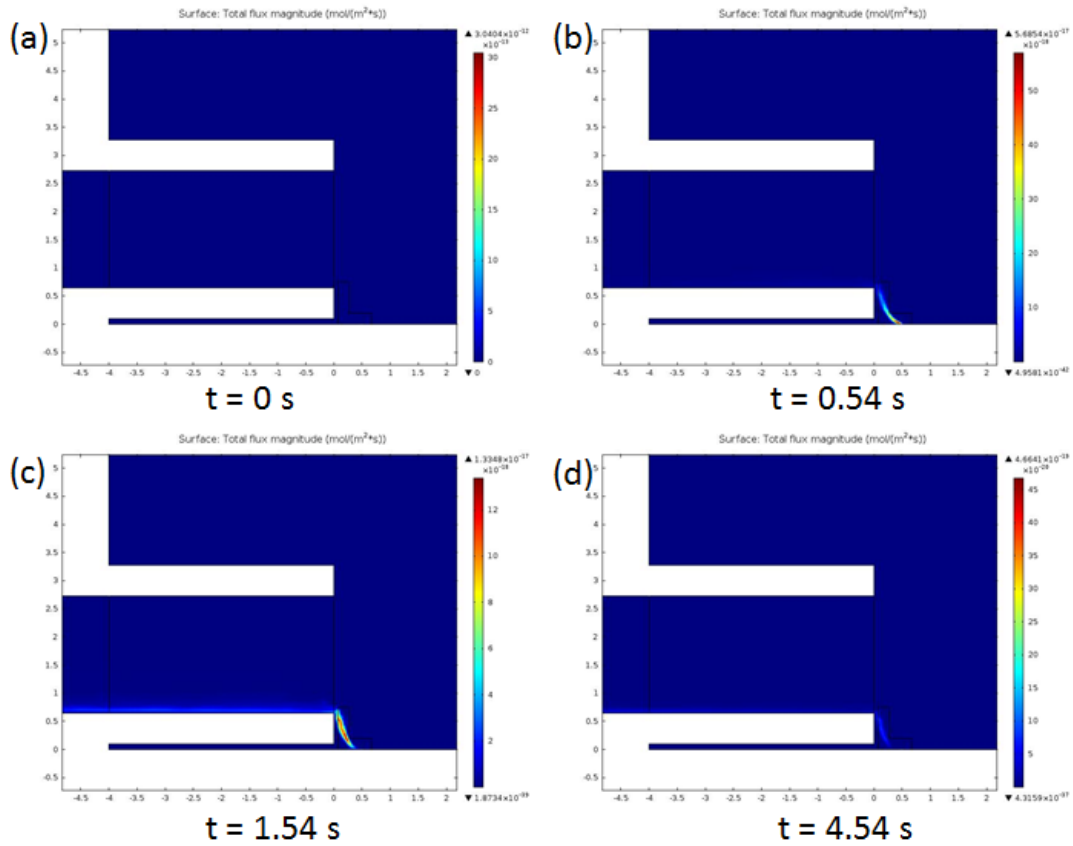


Figure 2.3 2-dimensional total flux profile. The simulation is performed with the parameters of OD=3.175 mm, ID=2.0828 mm, $t=0.55$ mm, $z=0.1$ mm, $D=0.5$ mm, $V=0.073$ m/s, diffusivity= $1\text{E-}09$ m^2/s . (a) Total flux at $t = 0$ s. (b) Total flux at $t = 0.54$ s. (c) Total flux at $t = 1.54$ s. (d) Total flux at $t = 4.54$ s

2.2 Simulation results

The experimental setup has too many design parameters to optimize only with experiments. By simulating the design with different values of the design parameters, the system is optimized and the underlying mechanism of transport is discussed. Here, four parameters are investigated: capillary inner diameter, wall thickness, distance from capillary inlet to the sample, and average air velocity through the capillary. The total flux of species at the capillary inlet is calculated in each case to compare the sampling efficiency. The schematic simulation model and design parameters are shown in Figure 2.4.

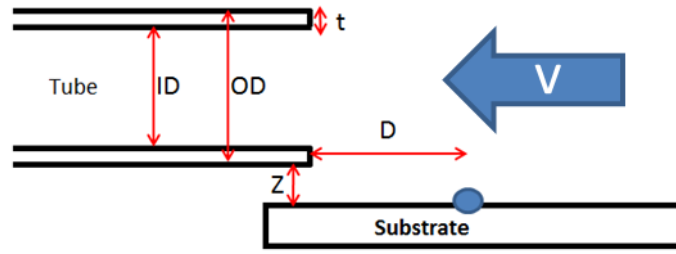


Figure 2.4 Schematic of simulation model. ID (capillary inner diameter), t (capillary wall thickness), D (distance from capillary inlet to sample), and V (average air velocity) are the investigated parameters.

First, the distance from the inlet to sample is investigated. Figure 2.5 shows the total flux at the capillary inlet when the distance from the inlet to the sample varies from 0.2 mm to 10.0 mm. As expected [15], the species are sampled more quickly when the distance D is shorter, and thus, the system has better sampling efficiency when the distance D is shorter. The air velocity decreases rapidly as the distance from capillary inlet increases. When the distance D is large, the air around the initial location of species is relatively slow. Thus, transporting the species from the initial location to the capillary inlet takes more time.

However, as shown in Figure 2.5, we also found that the sampling efficiency decreases when the distance D value is too small ($D=0.2$ mm). This happens because the disturbance of air flow caused by the boundary layer effect around the capillary inlet prevails over the advantage of the shorter distance D . The air flow around the wall forms the boundary layer due to the effects of friction and viscosity. When the

distance D is very small, the boundary layer is formed around the species, which eventually interferes with the sampling efficiency of the system.

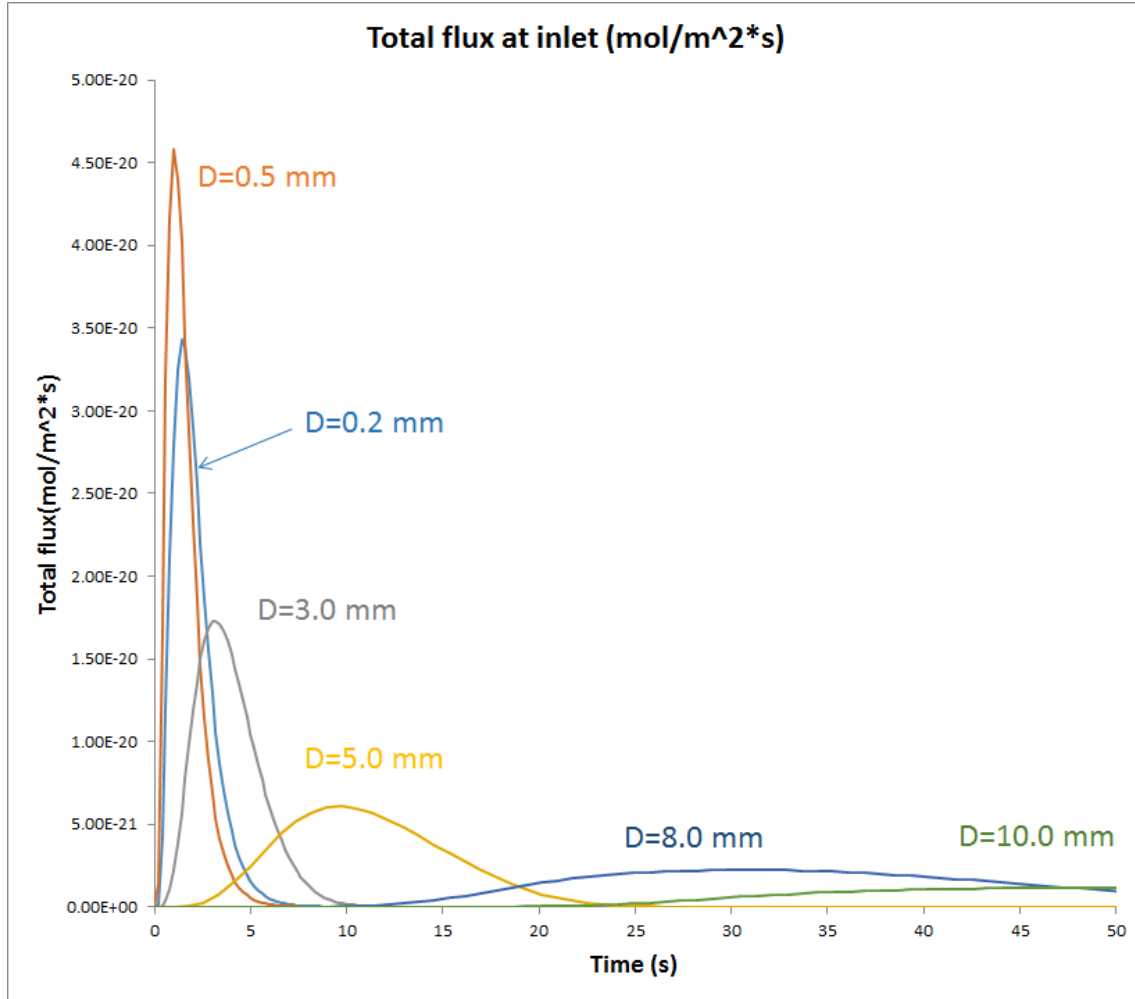


Figure 2.5 Total flux at the capillary inlet when the distance from the inlet to sample varies from 0.2 mm to 10.0 mm. The system has better sampling efficiency when the distance D is shorter. However, if the distance D value is too small ($D=0.2$ mm), the system starts to have worse sampling efficiency due to the boundary layer effect around the capillary inlet. Other parameters are set to $OD=3.175$ mm, $ID=2.0828$ mm, $t=0.55$ mm, $z=0.1$ mm, $V=0.073$ m/s, diffusivity= $1\text{E-}09$ m^2/s [15].

The sampling efficiency monotonically increases as the capillary wall thickness decreases. The change in the position of the capillary center is the most critical factor that affects the sampling efficiency. The position of the capillary center moves toward the bottom wall as the wall thickness of the capillary becomes smaller. Since the air velocity along the capillary center is the largest velocity, air around the

species flows faster when the capillary center is close to the bottom wall. Figure 2.6 clearly shows this advantage of the thinner capillary wall thickness.

The boundary layer effect is another factor that affect the sampling efficiency in this case. When the capillary wall thickness is small, the boundary layer effect along the vertical surface of the capillary inlet is reduced, which makes the air flow in the vertical direction quicker. Due to the efficiency of the air flow along the vertical direction, the species are transported more quickly, and thus, the sampling process becomes more efficient.

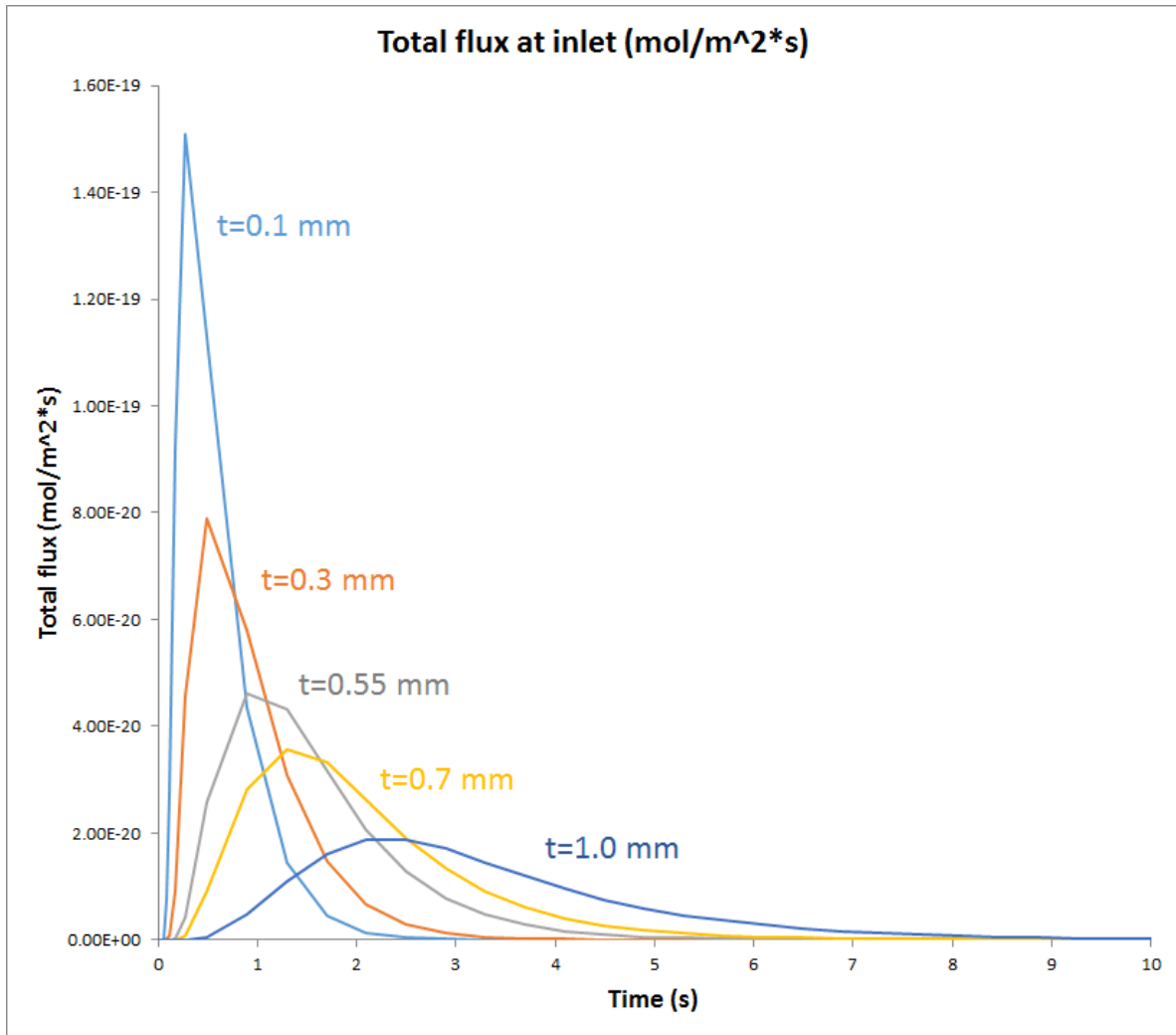


Figure 2.6 Total flux at capillary inlet when the capillary wall thickness varies from 0.1mm to 1.0mm. The system has better sampling efficiency when the capillary wall thickness is thinner. Other parameters are set to OD=3.175 mm, D=0.5 mm, z=0.1 mm, V=0.073 m/s, diffusivity= $1\text{E}-09 \text{ m}^2/\text{s}$.

Figure 2.7 shows the total flux multiplied by the capillary inlet area when the inner diameter varies from 1.5 mm to 5.0 mm. Total flux basically means the amount of species which passes through a certain cross-section per unit area each second. Since this dimension describes a quantity per unit area, the value cannot be compared when the area of each case is different. For example, although the total flux value is fixed, the amount of species which passes through the capillary will increase as the area becomes larger. Therefore, for this parameter, total flux values are multiplied by the capillary inlet area before they are plotted in order to compare the sampling efficiency.

Based on the area multiplied by total flux plot, we found that the sampling efficiency is almost independent of the capillary inner diameter size. This is due to the balance of two major factors. The first factor is the position of the capillary center. The capillary moves upward as the inner diameter increases, which makes the sampling process less efficient. The second factor is the volumetric air flow rate. Since the average air velocity is fixed, the larger capillary has a larger volumetric air flow, which makes the sampling more efficient. When the capillary inner diameter increases, the movement of the capillary center decreases the sampling efficiency, but the increased volumetric air flow compensates for this decrease. Thus, the change in capillary inner diameter has little effect on the sampling efficiency.

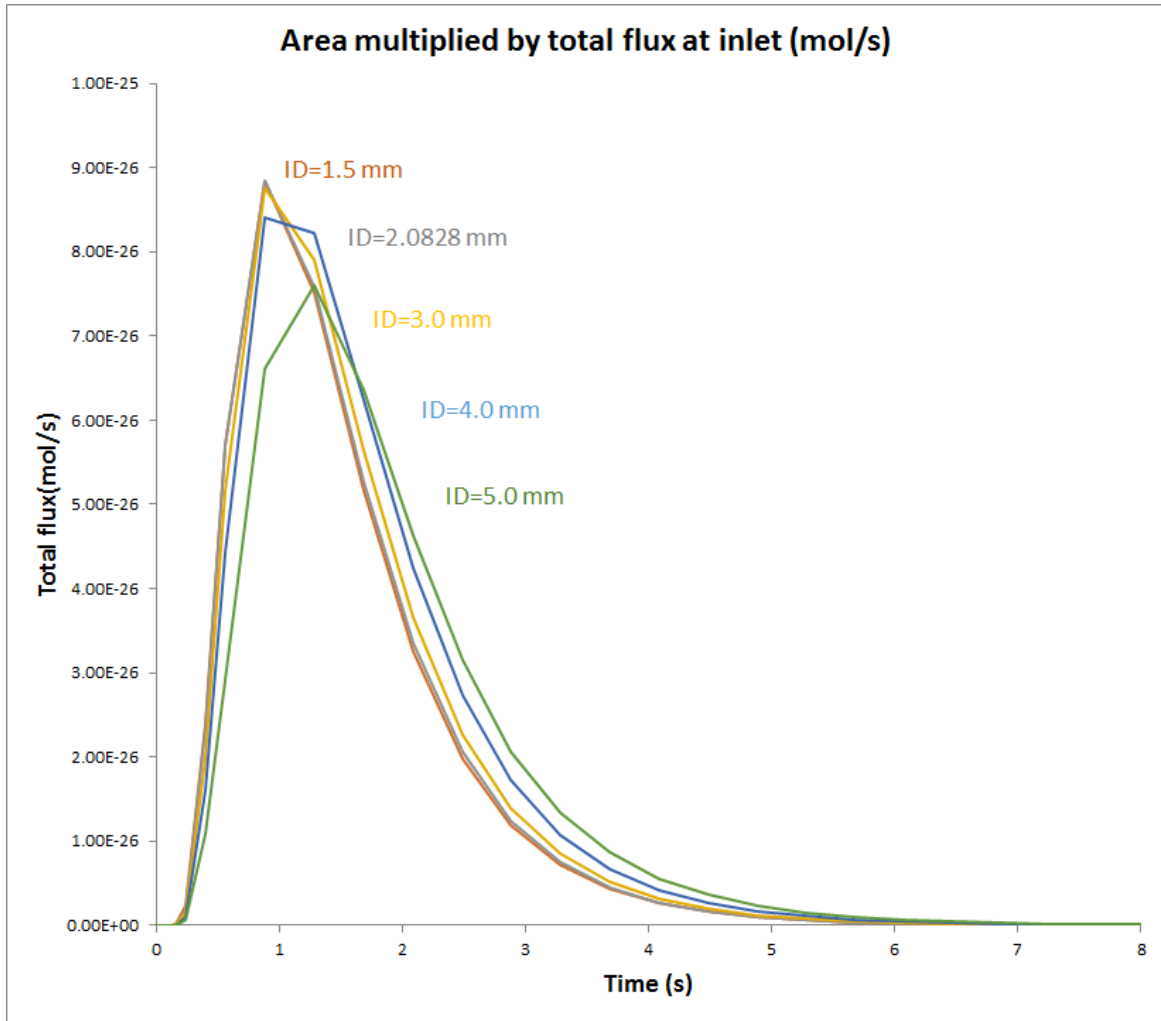


Figure 2.7 Total flux multiplied by the capillary inlet area when the inner diameter varies from 1.5 mm to 5.0 mm. One cannot compare the sampling efficiency with total flux if each case has a different inlet area. Thus, area multiplied by total flux (mol/s) is plotted on this figure. Other parameters are $D=0.5$ mm, $z=0.1$ mm, $t=0.55$ mm, $V=0.073$ m/s, diffusivity= $1E-09$ m^2/s .

The total flux plots at the capillary inlet when the average air velocity through the capillary varies from 0.01 m/s to 0.15 m/s are shown in Figure 2.8. The sampling process becomes more efficient as the air velocity increases. This is simply because the faster air flow transports the species more quickly. However, at the same time, in a real-time coupled system, the higher air velocity will decrease the ionization efficiency as the species stays less time in the ionization region [15].

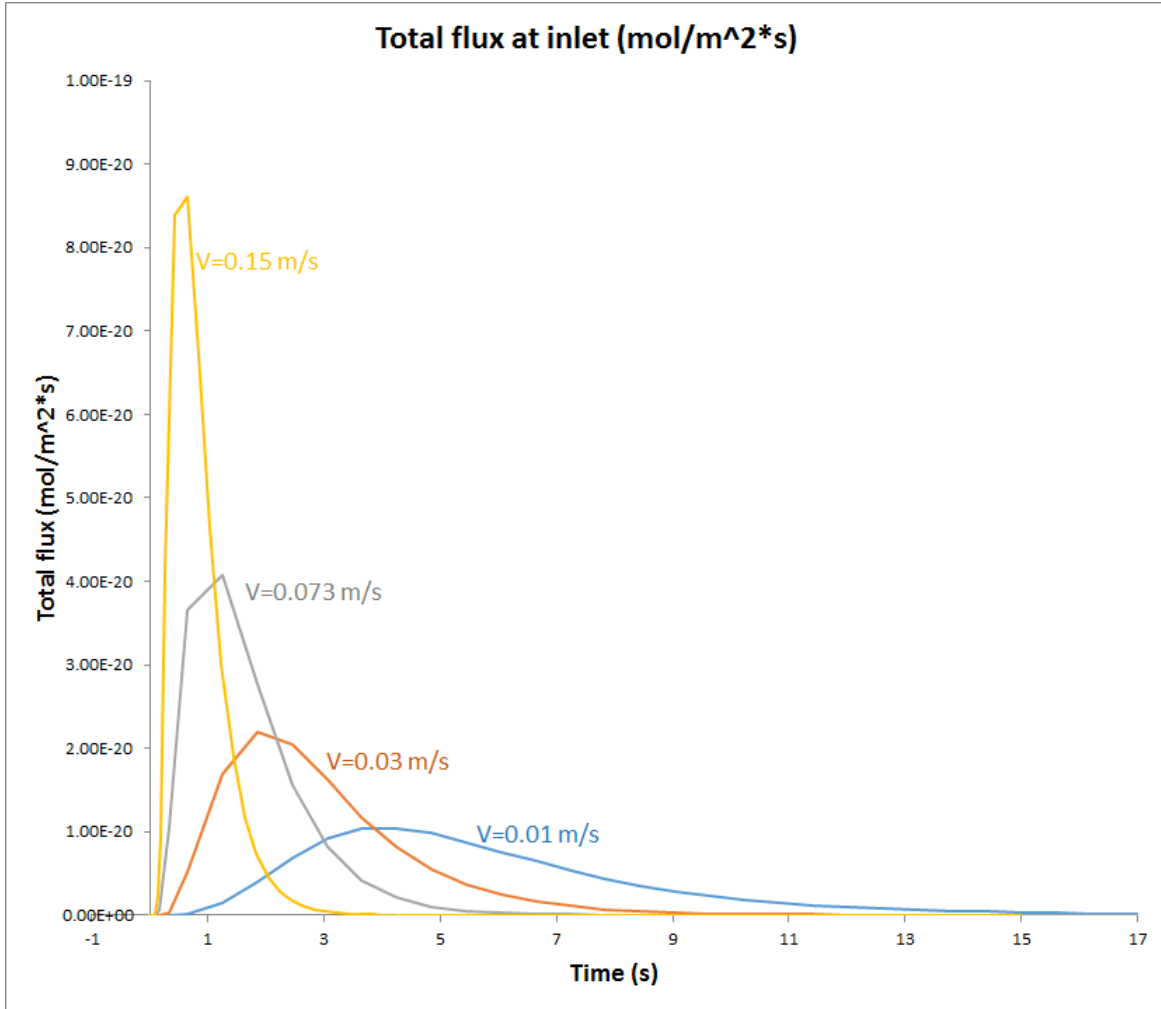


Figure 2.8 Total flux at capillary inlet when the average air velocity through the capillary varies from 0.01 m/s to 0.15 m/s. The system has better sampling efficiency when the air velocity is greater. Other parameters are set to OD=3.175 mm, D=0.5 mm, z=0.1 mm, t=0.55 mm, diffusivity=1E-09 m^2/s .

Figure 2.9 shows the total flux multiplied by the capillary inner area at the capillary outlet when the inner diameter varies from 1.5 mm to 5.0 mm. As opposed to the previous four simulation results which describe the transport mechanism from the sample to the capillary inlet, i.e. sampling efficiency, this simulation result describes the transport mechanism of species inside the capillary. The plot shows the total flux multiplied by the inner area at the end of the 100 mm-long stainless steel capillary. Since the sampling efficiencies at each inner diameter are the same as those shown in Figure 2.7, the total flux plots at the outlet of the capillary can be used to compare the transport efficiency inside the capillary. The plots

indicate that the transport mechanism of the species inside the capillary depends on the size of the inner diameter, with smaller diameters having better transport efficiency.

The most critical factor for this result is the diffusion. When the species are sampled into the capillary inlet, most of the species are located around the bottom of the capillary inlet where the air flow is the slowest. The species have higher horizontal speed as they diffuse to the center of the capillary. Since the air velocity at the capillary center is the same for each case, the species at the smaller capillary undergo a higher velocity increase as they diffuse to the capillary center. Thus, the transport efficiency inside the capillary is better when the capillary inner diameter is smaller.

Based on the above results, an eccentric cone shaped capillary inlet design is suggested. The simulation result with different inner diameters shows that the sampling efficiency mainly depends on the average air velocity rather than on the volumetric air flow rate. By narrowing the entrance of the capillary, air velocity can be increased multiple times with the same volumetric flow rate. Since the volumetric flow rate is unchanged, the species will stay the same amount of time in the ionization region. Thus, the capillary with an eccentric cone shaped entrance is expected to have higher sampling efficiency without the loss of ionization efficiency. Our eccentric cone shaped entrance capillary model and the straight capillary model are simulated at the same conditions in order to compare their efficiency.

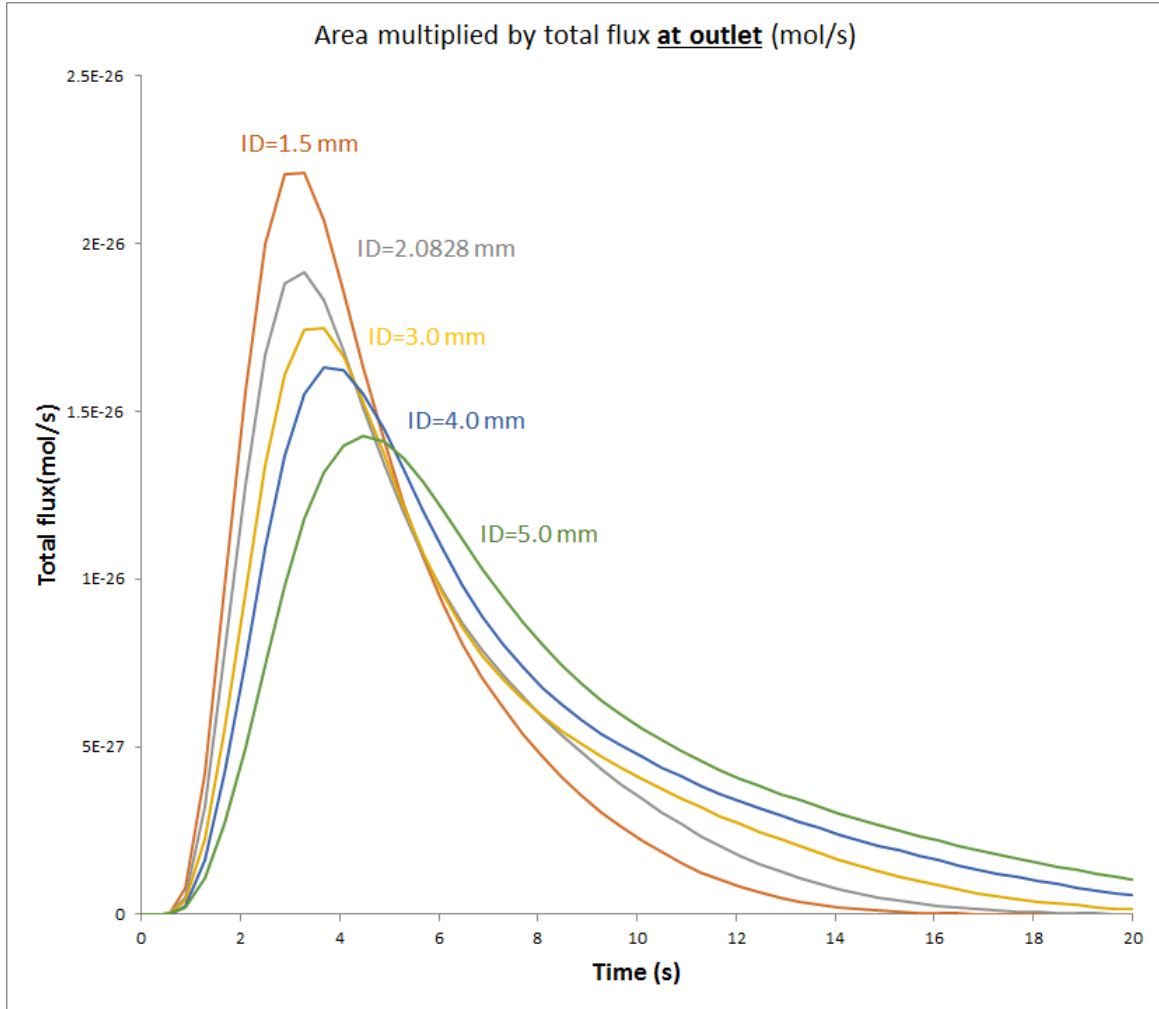


Figure 2.9 Total flux multiplied by capillary inner area at the capillary outlet (100 mm) when the inner diameter varies from 1.5 mm to 5.0 mm. The smaller inner diameter capillary transports the species more quickly. Other parameters are $D=0.5$ mm, $z=0.1$ mm, $t=0.55$ mm, $V=0.073$ m/s, diffusivity= $1E-09$ m^2/s .

As shown in Figure 2.10, the capillary outlet inner diameter is set as the same as the simulation model in Figure 2.3 to compare the efficiency. The inlet inner diameter is set to 0.5 mm, but the wall thickness is held constant. The total capillary length is set to 10 cm in both cases, and the eccentric cone shaped region is set to 5 mm. To make the volumetric flow rate the same, the average inlet velocity increases from 0.073 m/s to 1.286 m/s due to the change in the inlet area.

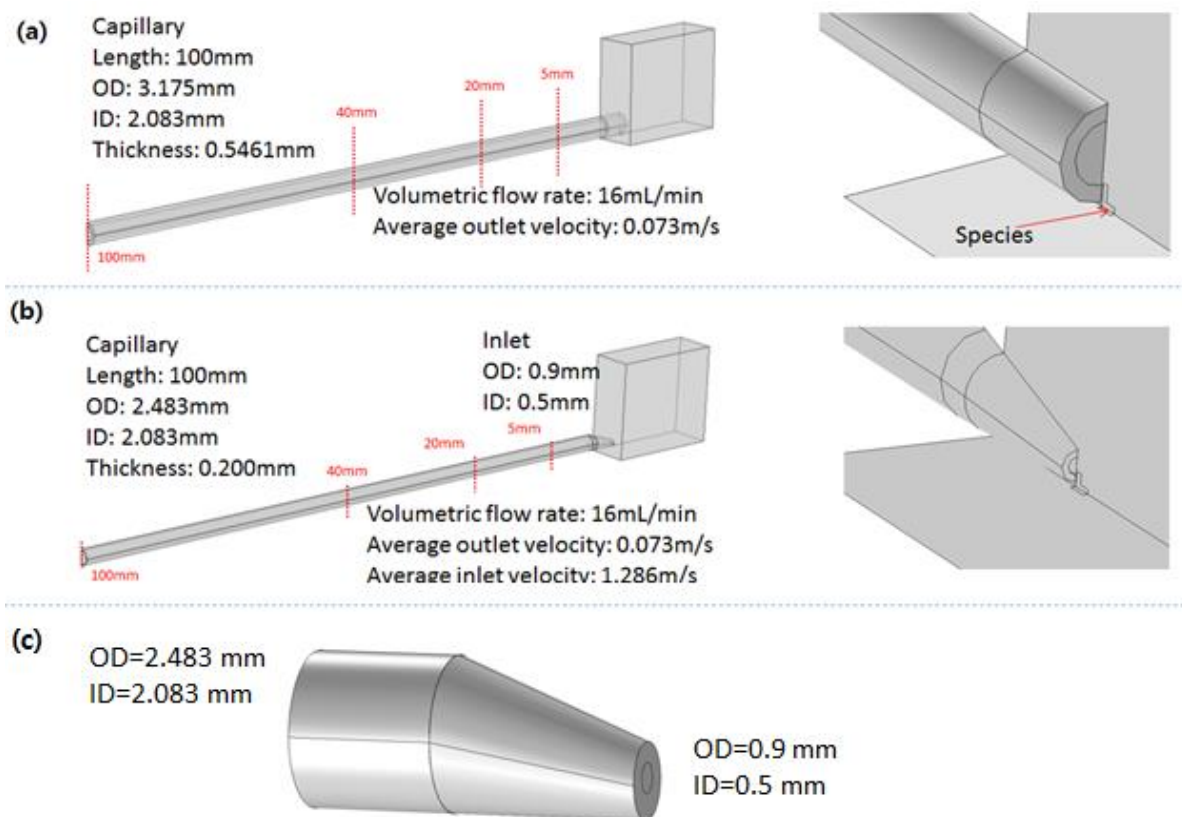


Figure 2.10 (a) Straight capillary simulation model used in Figure 2.3. (b) Simulation model of our design. The total capillary length is set to 10cm. Other parameters are shown in the figure. (c) Eccentric cone shaped capillary entrance. Inlet inner diameter is narrowed down to 0.5 mm with a constant wall thickness.

The eccentric cone shaped entrance capillary shows better sampling efficiency. As shown in Figure 2.11 (c), the eccentric cone shaped entrance capillary has the peak flux at 0.1 s while the straight capillary has the peak at 1.1 s. The peak time in our design is 11 times smaller than the peak time with a straight capillary, representing a significantly improved sampling efficiency. Figure 2.11 (f) shows that our design still has an earlier peak time and higher peak flux even at a distance of 100 mm after the entry, which means that the overall transport efficiency is also better with an eccentric cone shaped entrance capillary. Furthermore, it will not lose ionization efficiency even in the serially coupled system, since the outlet velocities are the same for the two capillary designs.

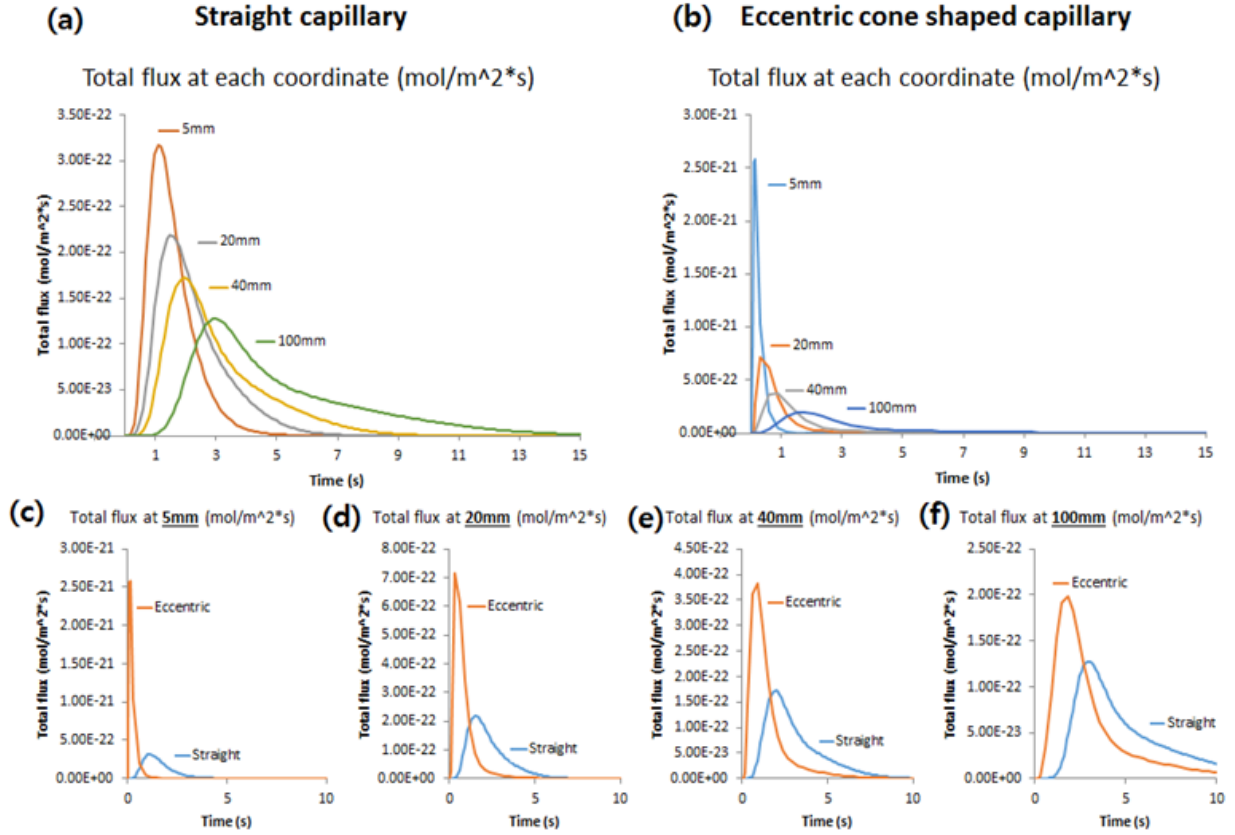


Figure 2.11 (a) Total flux plots at each coordinate of the straight capillary. (b) Total flux plots at each coordinate of the eccentric cone shaped entrance capillary. (c) Total flux plots at 5 mm of the straight and eccentric cone shaped capillaries. (d) Total flux plots at 20 mm of the straight and eccentric cone shaped capillaries. (e) Total flux plots at 40 mm of the straight and eccentric cone shaped capillaries. (f) Total flux plots at 100 mm of the straight and eccentric cone shaped capillaries.

CHAPTER 3: EXPERIMENTS AND RESULTS

3.1 Apparatus Schematic

MS-AFM is a technique combining heated AFM and mass spectrometry that can identify the chemical compositions of a sample at a micrometer-scale. Figure 3.1 shows the schematic for the experimental setup of the MS-AFM system. A heated AFM cantilever operates in ambient conditions, and it can be heated up to 1000 °C. When the heated AFM cantilever contacts the sample, the area around the cantilever tip is thermally desorbed. Thermally desorbed species are liberated from the sample and transported into the chamber due to the lower pressure inside the chamber. The transported species stick on the collecting plate in the chamber [17] before the mass spectrometer analyzes the species on the plate.

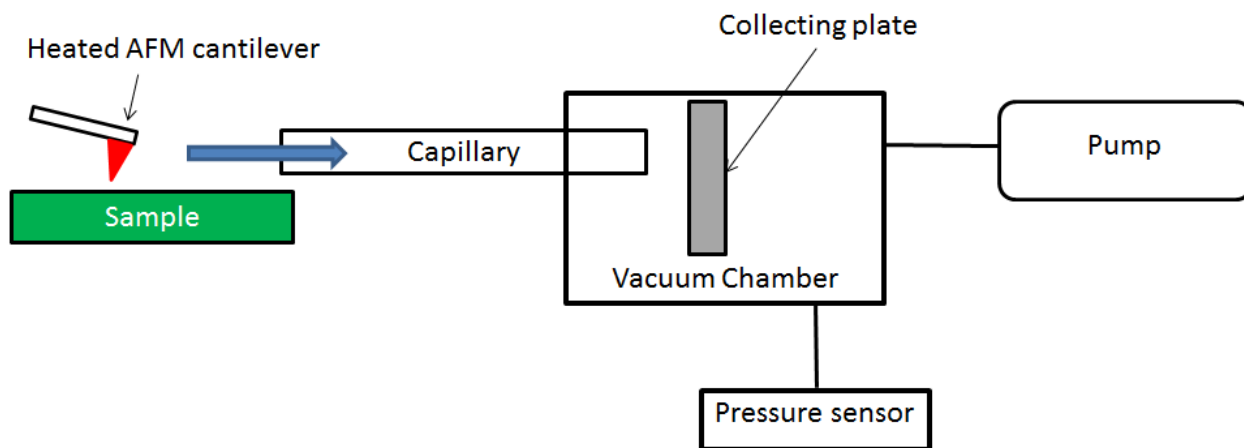


Figure 3.1 2D schematic of the experimental setup. A heated AFM cantilever operates in ambient conditions, and the vacuum chamber pressure is maintained lower than the atmospheric pressure. Thermally desorbed species are transported through the capillary and collected on the plate due to the pressure difference.

3.2 Experimental setup

The vacuum chamber is located next to the AFM, and the pump is connected to the chamber providing lower pressure. The pressure inside the chamber is manually controlled by adjusting the knob on the pump. Two source meters are used to heat up the AFM cantilever and the stainless steel capillary. Figure 3.2 (b) shows how the heated AFM cantilever is connected to the source meter with the electrical wire. The source meter, sense resistor, and the heated AFM cantilever are connected in series, and the cantilever tip temperature is calibrated with respect to the total voltage beforehand. Figure 3.2 (a) shows the experimental setup for the MS-AFM system.

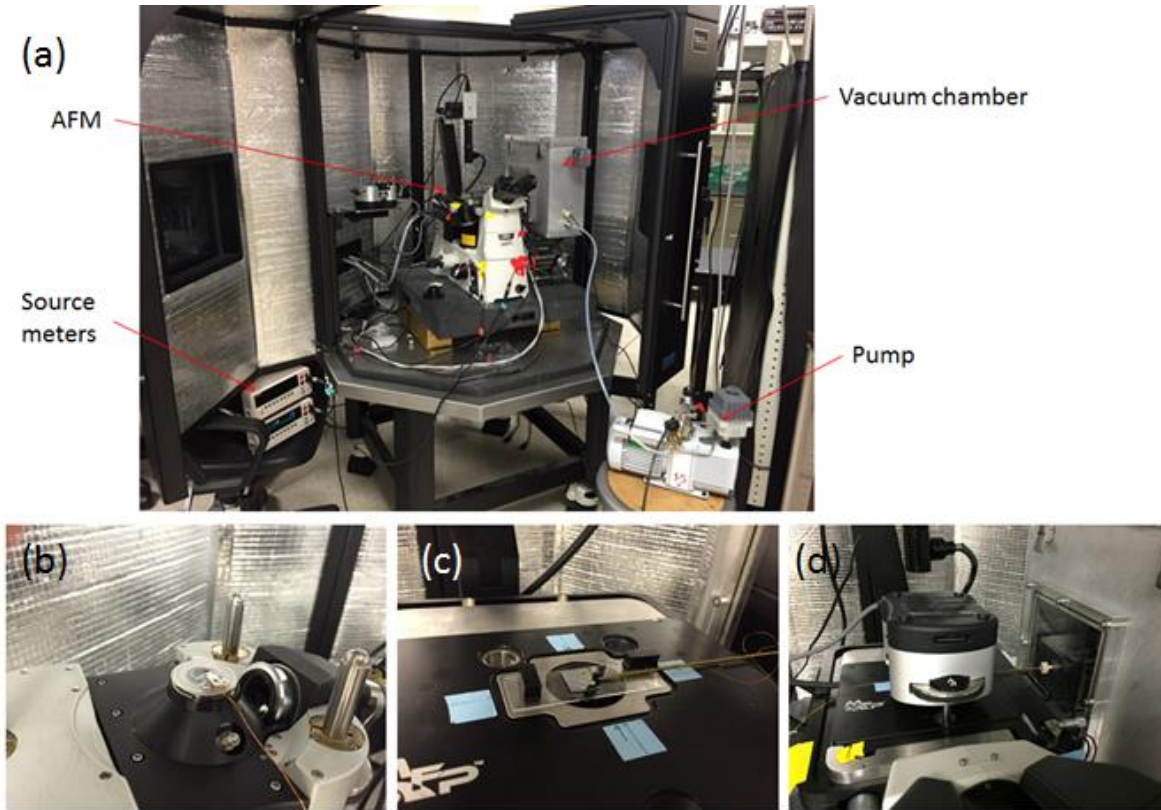


Figure 3.2 (a) Experimental setup for MS-AFM operation. The vacuum chamber is located next to the AFM, and the pump is connected to the chamber to lower the pressure. Two source meters are used to heat up the AFM cantilever and the stainless steel capillary. (b) The heated AFM cantilever is connected with the source meter by electrical wires. (c) Positioning of stainless capillary and the sample under the AFM head. (d) The experimental setup when the AFM is being operated.

The chamber body is made of aluminum, and the chamber door and window are acrylic plates. A rubber ring is inserted between the acrylic plate and aluminum body and covered with Apiezon L Grease to prevent leakage. The pressure gauge is directly connected to the chamber to check the pressure inside the chamber. The motion stage is fixed on one side of the chamber body and connected to the computer by electrical wires. The collecting plate is mounted on the motion stage, so the position of the plate can be controlled by the computer outside the chamber without opening the door. The acrylic window has a hole for the stainless steel capillary to pass. The capillary is inserted in the hole and its outlet is spaced 5 mm away from the collecting plate. Figure 3.3 shows the chamber design.

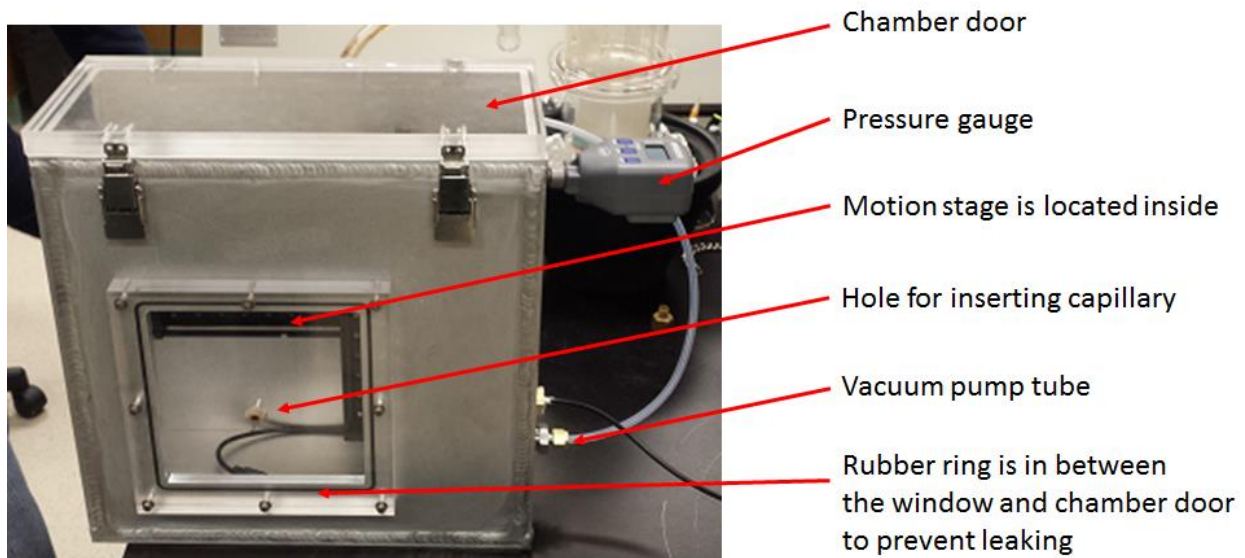


Figure 3.3 The chamber design. The chamber body is made of aluminum, and the chamber door and window are acrylic plates. The pressure gauge is directly connected to the chamber to check the pressure inside the chamber. The motion stage is located in the chamber, and it moves the collecting plate attached to the stage.

3.3 Cantilever characterization

The electrical and thermal characterization of the heated AFM cantilever is performed before it is used in the MS-AFM system. Figure 3.4 shows the schematic for the electrical circuit for the heated AFM cantilever characterization. The heated AFM cantilever, sense resistor, and sourcemeter are serially connected. The multimeter is connected in parallel with the sense resistor to measure the resistance of the heated AFM cantilever since the cantilever resistance varies with respect to the temperature. By measuring the voltage drop across the sense resistor at each voltage, one can deduce the resistance of the heated AFM cantilever without directly measuring it. For the entire characterization process and further experiments, a 10 k Ω sense resistor is used.

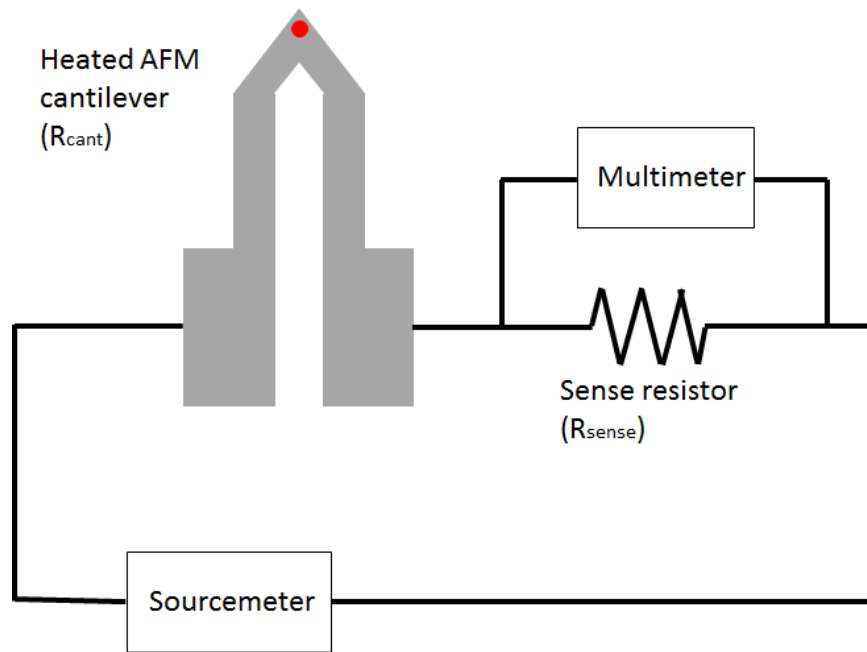


Figure 3.4 2D Schematic for the electrical circuit for the heated AFM cantilever characterization. The heated AFM cantilever, sense resistor, and sourcemeter are serially connected. The multimeter is connected in parallel with the sense resistor to measure the resistance of the heated AFM cantilever with respect to the temperature. The red spot on the heated AFM cantilever represents the cantilever tip.

The heated AFM cantilever is electrically and thermally characterized through IV characterization and Raman spectrometry. The electrical circuit shown in Figure 3.4 is used to perform IV characterization. Different values of source voltage are applied through the source meter and the current and voltage across the sense resistor is measured at each source voltage. Voltage across the cantilever, cantilever resistance, and power generated at the cantilever can be calculated from the measured values. The Raman laser is focused on the cantilever around the tip, and the signal is measured at different total voltages. Based on the Raman signal, the temperature of the cantilever at each total voltage is calculated [18]. By combining the IV characterization results and Raman spectrometry results, the cantilever temperature and resistance curves with respect to the total voltage and generated power at the cantilever are respectively derived [13]. The characterization results are used to predict the tip temperature during the thermal desorption process. Figure 3.5 shows electrical and thermal characterization results of the heated AFM cantilever generated by IV characterization and Raman spectrometry.

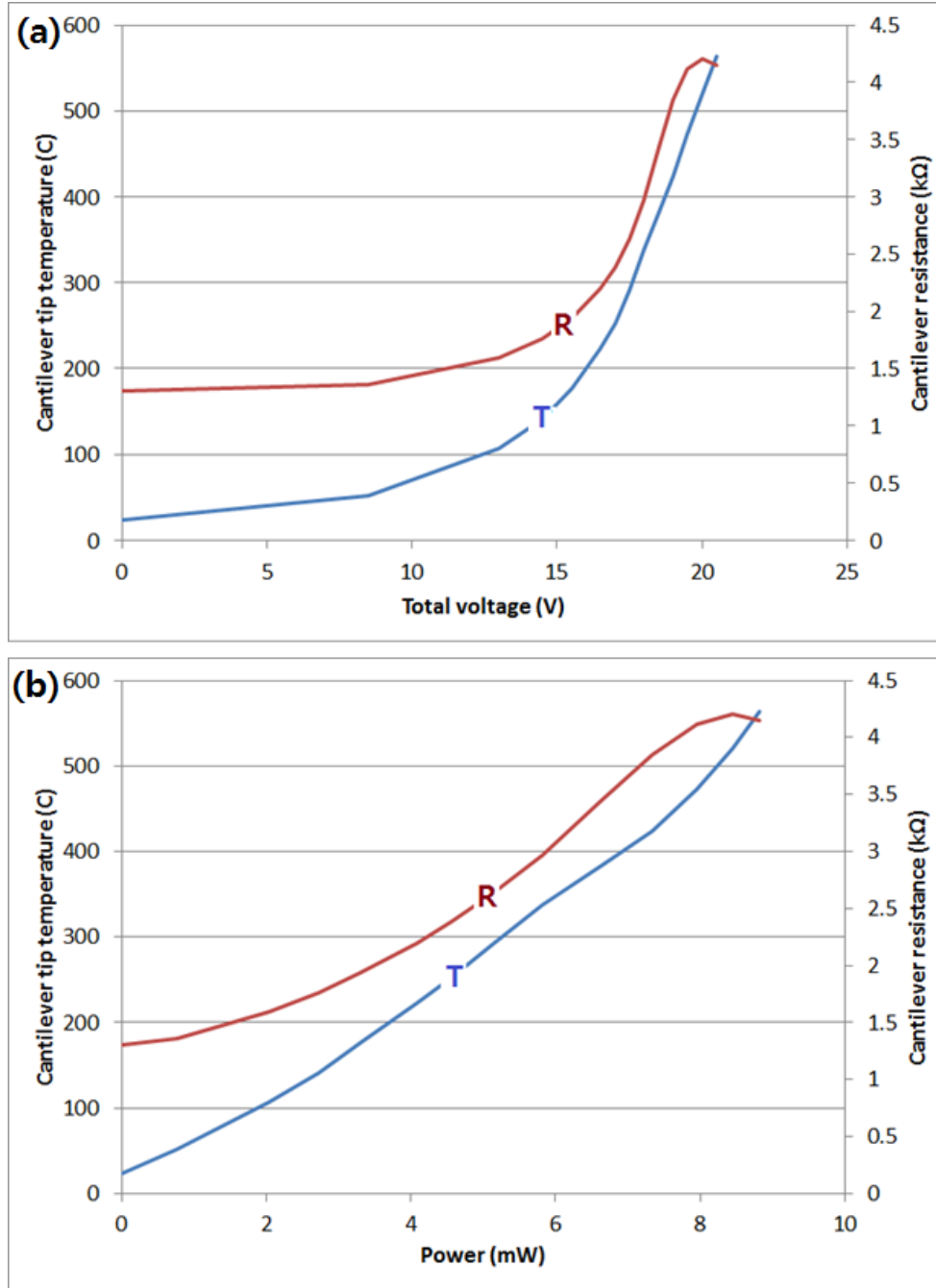


Figure 3.5 Electrical and thermal characterization results of a heated AFM cantilever. (a) The cantilever tip temperature and resistance are plotted with respect to total voltage applied by the sourcemeter. (b) The cantilever tip temperature and resistance are plotted with respect to the generated power at the cantilever.

3.4 Experimental results

50 mg/mL of DHB(2,5-Dihydroxybenzoic acid), 0.1 mg/mL of caffeine, and 0.1 mg/mL of Rhodamine B are dissolved in 80:20 H₂O: ACN solution. Rhodamine B is mixed to analyze the MS-AFM system with fluorescence microscopy, and caffeine is mixed to be analyzed with mass spectrometry due to its high sensitivity in a mass spectrometer. DHB forms a matrix around Rhodamine B and caffeine so that it minimizes decomposition of Rhodamine B during thermal desorption processes. The sample is made by spraying the solution on the conductive ITO glass. The sprayer is custom designed to spray the solution through the capillary tube by applying a pressure. For this sample, the pressure was set to 20 psi. Figure 3.6 shows the microscope picture and fluorescence microscope picture of the mixed DHB, caffeine and Rhodamine B sample.

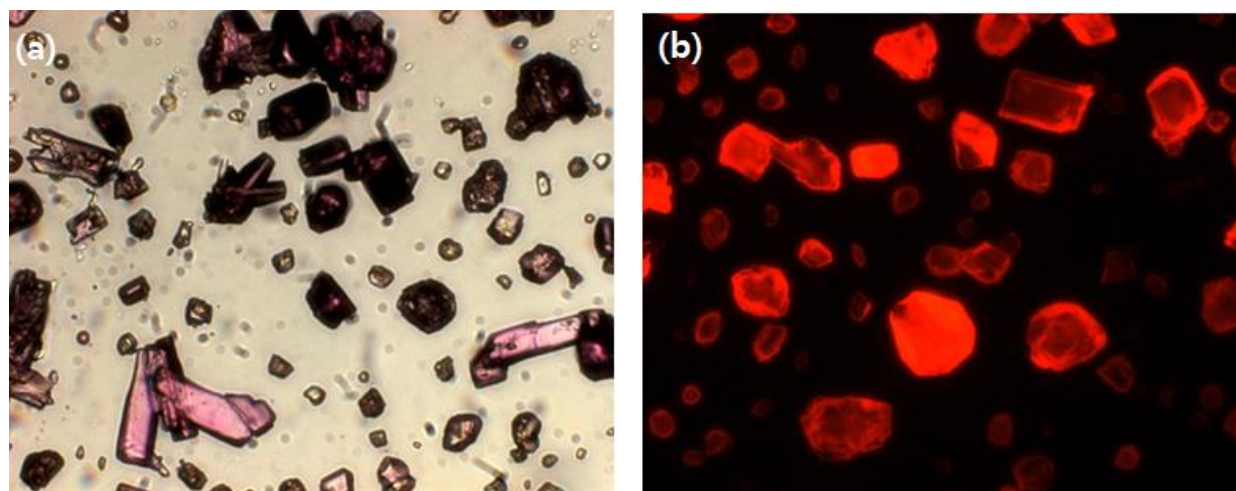


Figure 3.6 (a) Microscope picture of DHB, caffeine, and Rhodamine B sample on ITO glass. (b) Fluorescence microscope picture of DHB, caffeine, and Rhodamine B sample on ITO glass.

The heated AFM cantilever is operated on the DHB+caffeine+Rhodamine B for a 40 μm X 40 μm area. The total voltage was 20 V, and the sense resistor was 10 k Ω . The cantilever tip was operated at 517 $^{\circ}\text{C}$, and the vacuum chamber was maintained to 0.789 atm to sample the species from outside of the chamber. Due to the pressure difference, the air outside the chamber is inhaled into the chamber, and the

thermally desorbed species are also transported through the capillary. When the species moved out of the capillary outlet, they stuck on the ITO glass.

Figure 3.7 (a) shows the microscope picture of the collected species on the glass. The spot formed on the glass is mostly dust, thus, a fluorescence microscope is used to see if the thermally desorbed species are on the spot. The fluorescence microscope casted a light on the spot for 60 seconds, and the spot showed the clear fluorescence signal shown in Figure 3.7 (b). In order to check if the fluorescence signal is noise, the light was also illuminated at the clean spot for the control experiment. As shown in Figure 3.7 (c), the clean spot was also exposed to light for 60 seconds, and did not show any fluorescence signal.

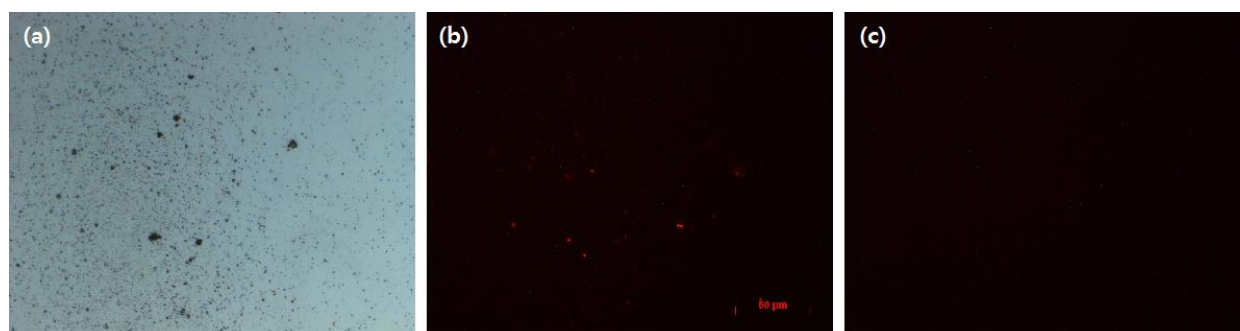


Figure 3.7 (a) Microscope picture of the sample collected in the vacuum chamber. (b) Fluorescence microscope picture of the sample collected in the vacuum chamber. The sample is exposed for 60 seconds in the fluorescence microscope, and the fluorescence signal is detected. The tip is operated with a temperature of 517 °C, and the capillary is heated to 55 °C during the thermal desorption process. The pressure inside the vacuum chamber was maintained at 0.789 atm. (c) Fluorescence microscope picture of the clean spot without species. The spot is exposed for 60 seconds in the fluorescence microscope.

Figure 3.8 shows the fluorescence microscopy results at different tip temperatures. As shown in Figure 3.8, the amount of dust on the spot is not reproducible [19]. There was no clear relationship between the cantilever tip temperature and fluorescence signal intensity, but a signal was detected for all tip temperature cases. Two major factors should be considered. First, the tip with the higher temperature thermally desorbs a greater amount of the species around the tip. Due to the heat conduction through the

sample, not only the exact spot of contacting area but also the around area has the increased temperature. Thus, the cantilever tip with the higher temperature thermally desorbs more amount of the sample.

However, if the tip temperature is too high, there is a possibility that the high temperature decomposes or fragments the sample. For the fluorescent sample especially, it is not possible to detect the species once it is decomposed during the thermal desorption process. Due to the contributions of these two factors, we were not able to find a clear relationship between the tip temperature and fluorescence signal intensity.

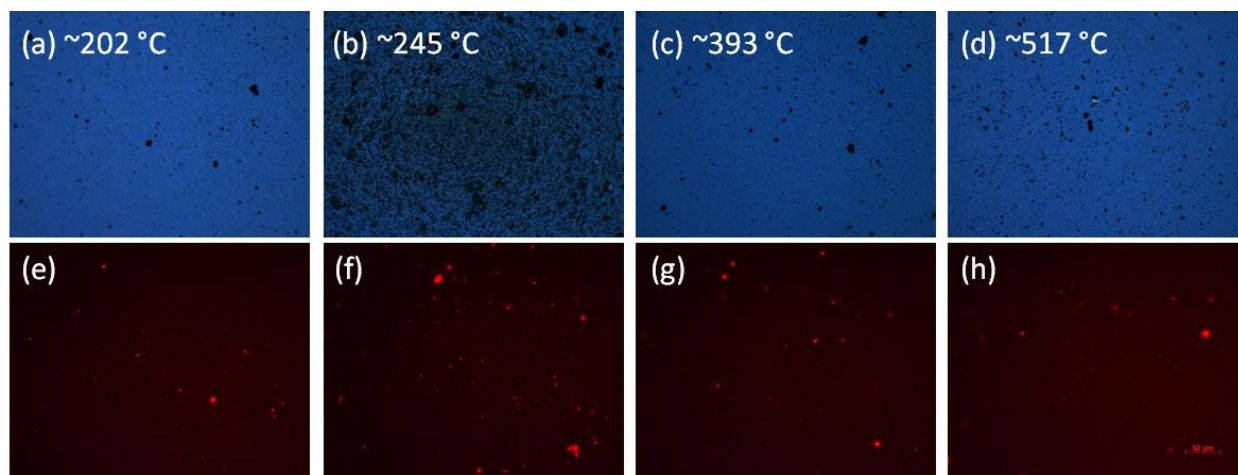


Figure 3.8 (a) Microscope picture of collected species with 202 °C tip temperature. (b) Microscope picture of collected species with 245 °C tip temperature. (c) Microscope picture of collected species with 393 °C tip temperature. (d) Microscope picture of collected species with 517 °C tip temperature. (e) Fluorescence microscope picture of collected species with 202 °C tip temperature. (f) Fluorescence microscope picture of collected species with 245 °C tip temperature. (g) Fluorescence microscope picture of collected species with 393 °C tip temperature. (h) Fluorescence microscope picture of collected species with 517 °C tip temperature. Stainless capillary was heated to 55 °C and the vacuum chamber is operated by 0.789 atm during thermal desorption process.

Figure 3.9 plots the MALDI-MS results of the Blank DHB matrix, collected species, and the caffeine control sample. MALDI-MS was performed on the spot of collected species. The blank DHB matrix sample and DHB with caffeine sample were also analyzed by MALDI-MS for the control experiments. The blank DHB matrix sample did not show any clear signal from MALDI. Considering that the caffeine's molecular mass is 194.19 g/mol, the signals from the collected species were very close to

the exact caffeine signal. The difference between the exact caffeine signal and our sample signal is considered to be a result of fragmentation of the caffeine sample during thermal desorption.

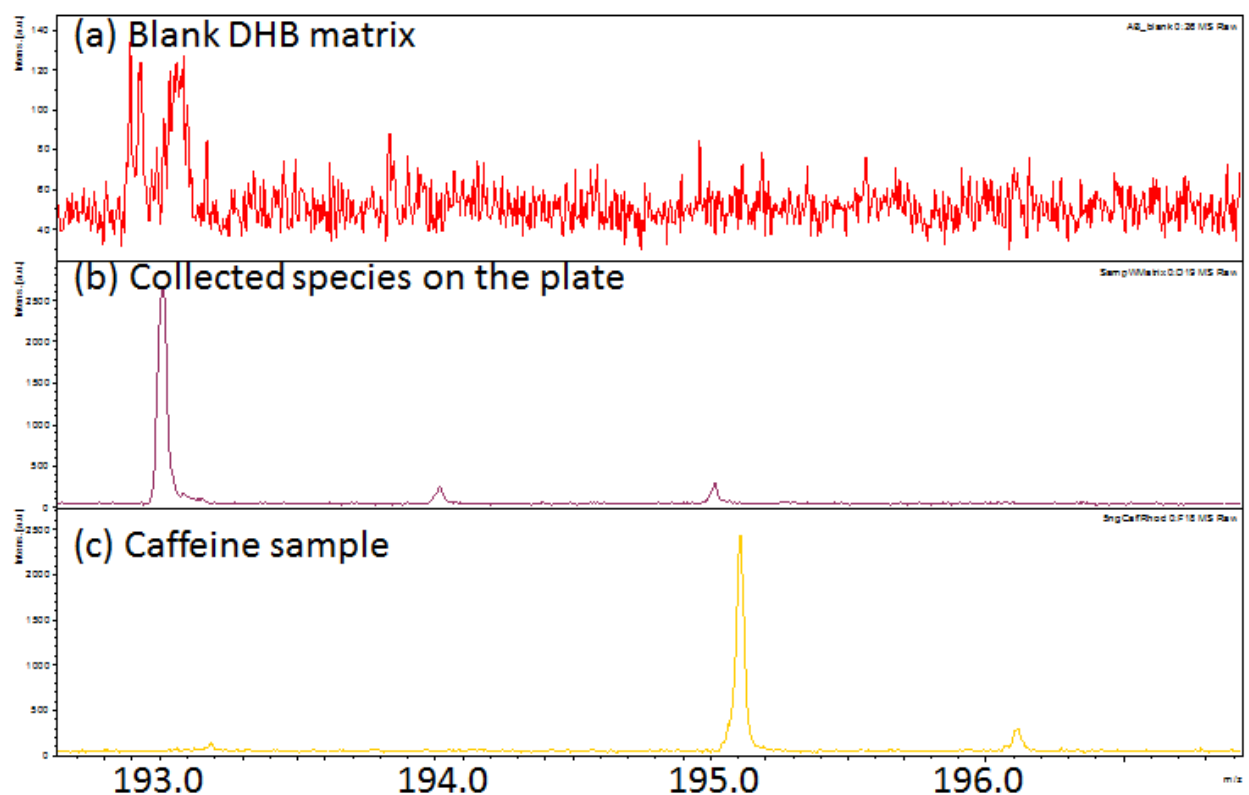


Figure 3.9 (a) MALDI-MS signal from blank DHB matrix. (b) MALDI-MS signal from the collected species on the ITO glass. (c) MALDI-MS signal from caffeine sample for the control experiment.

CHAPTER 4: CONCLUSIONS

Simulations for the hybrid heated AFM cantilever and mass spectrometer system successfully optimized the system's transport efficiency. The optimal distance between the capillary inlet and the sample exists. Decreasing the capillary wall thickness and capillary inner diameter improves the overall transport efficiency. Based on the results of the simulations, an eccentric cone shaped entrance is suggested as the best capillary inlet design to maximize the sampling efficiency. By comparing the transport efficiency results of the straight capillary with the eccentric cone shaped entrance capillary, improvement in sampling efficiency with the latter design is shown.

Experimental work demonstrates the basic instrumental setup and system operation. Rhodamine 6G and caffeine were successfully transported and analyzed through a mass spectrometer and fluorescence microscope. Thermally desorbed and collected species of the Rhodamine B and caffeine sample showed the fluorescence signal in a fluorescence microscope. The mass spectrometer also detected the caffeine signal from the collected species. From the experimental work, we verified the validity of MS-AFM design at a micrometer-scale.

Future work will focus on improving the spatial resolution of the MS-AFM system to nanometer-scale. This will require the optimization of the MS-AFM system. Fluorescence species will be used to quantitatively optimize the system. The deposited species on the collecting plate will emit more light as the amount of species is greater. By comparing the light emission quantitatively, the best experimental conditions can be chosen, and thus, the system can be optimized. Achieving nanometer-scale spatial resolution will help overcoming the current spatial resolution limit of mass spectrometry.

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