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A silicon-based MEMS vibrating mesh nebulizer for inhaled drug delivery

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Abstract

This paper presents a silicon-based MEMS vibrating mesh nebulizer capable of producing micro droplets for inhaled drug delivery. The device concept, design, fabrication, and measurements are presented. The core element of the nebulizer (vibrating mesh) was fabricated using silicon process and consists of 1000 tapered micro-sized apertures. During operation the mesh vibrates at high frequency with the bending profile corresponding to the 02 resonance mode. The droplet diameter measured at the device output is 3.75 µm and a typical output rate is 0.45 ml / min.

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Peer-review under responsibility of the organizing committee of the 30th Eurosensors Conference

Keywords: Nebulizer, MEMS, silicon, piezoelectric, aerosol, liquid atomization.

1. Introduction

A nebulizer is a device that converts liquid medicine into medical aerosol that is inhaled into the lungs to treat pulmonary and systemic diseases. Control of droplet size plays a crucial role in delivering of medication to the lungs and the optimum droplet size of 1 to 6 µm for efficient delivery and treatment is required. Droplets larger than 6 µm deposit preliminarily in the mouth and throat whereas droplets smaller than 1 µm may be exhaled.

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Current commercial nebulizer technologies can be divided into three main categories: (i) jet nebulizers, (ii) ultrasonic nebulizers and (iii) mesh nebulizers [1-3]. Jet nebulizers exploit the venturi effect, and use pressurized gas to draw liquid up through the capillary tube from the reservoir. This process generates a wide range of droplet sizes that are filtered out by a baffle, which take larger droplets from aerosol and return them to the reservoir. Jet nebulizers can deliver a limited range of formulations and are commercially available for many years. However, they have limited portability due to their need for compressed gas and additional gas tubing and are not suitable for the aerosolization of suspensions. Ultrasonic nebulizers use a bulk piezoelectric crystal that vibrates at high frequency and generates acoustic signal traveling through the liquid towards the liquid surface. This induces capillary waves at the liquid surface and produce aerosol. In general, ultrasonic nebulizers have many limitations compared to jet nebulizers. For instance, bulk piezoelectric crystals tend to generate a heat that may destroy heat-sensitive medications and once again are not suitable for the aerosolization of suspensions. One of the most recent nebulizer technologies currently on the market is the actively vibrating mesh nebulizer. A generic concept of vibrating mesh technology is explained in Fig 1. It consists of a mechanically vibrating plate perforated with micro-size apertures, (Fig. 1(a)). The mesh is assembled with the metallic holder and piezoelectric (PZT) ring actuator (Fig 2(b)). During operation the liquid is in contact with the top surface of the mesh, which is excited into out-of-plane vibration by the laterally vibrating PZT actuator. Alternating vibration of the mesh builds up alternating pressure in the liquid in the vicinity of the mesh pushing the liquid through the apertures and ejecting aerosol droplets on the other side of the mesh [5]. Commercially available vibrating mesh nebulizer is demonstrated in Fig. 1(c). Vibrating mesh technology is advantageous over other technologies as it does not destroy the medication due to heat and high pressure, the nebulization process is fast and quiet, and the nebulizers are small and portable. Despite these developments, there is still a need to enhance the device performance and also to reduce the manufacturing cost as it incurs a relatively high price compared to other commercial technologies. The objective of this work was to advance the state of the art mesh nebulizer technology by employing MEMS (Micro-Electro-Mechanical Systems) fabrication techniques to develop a silicon-based vibrating mesh. Current commercial mesh devices are made of metal alloys and are fabricated using electroforming and laser drilling techniques. These techniques could potentially be replaced with a high volume MEMS silicon–based process as described in this work as it has the potential to reduce the total technology cost (e.g. high volume, high yield and uniform mesh process) and improve performance in terms of reliability, minimum aperture size and functionality by further integration of other system components such as piezoelectric actuator and electronic sensors.

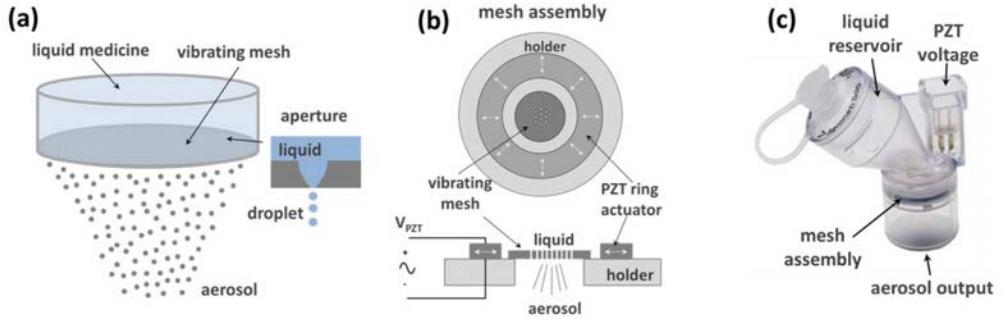

Fig. 1. (a) A concept of vibrating mesh nebulizer technology, (b) schematic drawing of mesh assembly composed of mesh, holder and PZT actuator, and (c) commercially available vibrating mesh nebulizer from Aerogen Ltd.

2. Results

2.1. Mesh design and fabrication

It has been demonstrated that mechanically vibrating membranes with apertures against a bulk liquid generates an aerosol [5]. It has also been demonstrated that the most efficient atomization occurred when the membrane was operated at the second harmonic mode (02) with the frequency range of tens of kHz. Therefore, for the silicon-based

vibrating mesh in this work the initial design target was assumed to be 02 mode and 100 kHz operation frequency. In order to identify the required thickness of the membrane to obtain the assumed operation conditions a modal analysis in COMSOL was performed. A simple 3D model of a membrane mechanically fixed around its periphery was used. The material properties of silicon were assumed to be E = 170 GPa - Young's modulus, ν = 0.28 - poison ratio, ρ = 2329 kg / m^3 - material density, and the membrane was assumed to be free of material stress. Simulation predicts that for the assumed membrane diameter R of 4 mm the 02-mode at 100 kHz can be obtained if the silicon is 25 µm thick, (Fig. 2(a)). The analytical results using formula as in Fig. 2(a) [6] show good agreement with the simulation results. Modal simulation was also performed on the model with up to 2000 apertures patterned in the membrane with 80 µm pitch size and the change in the resonance frequency was obtained to be less than 5 %.

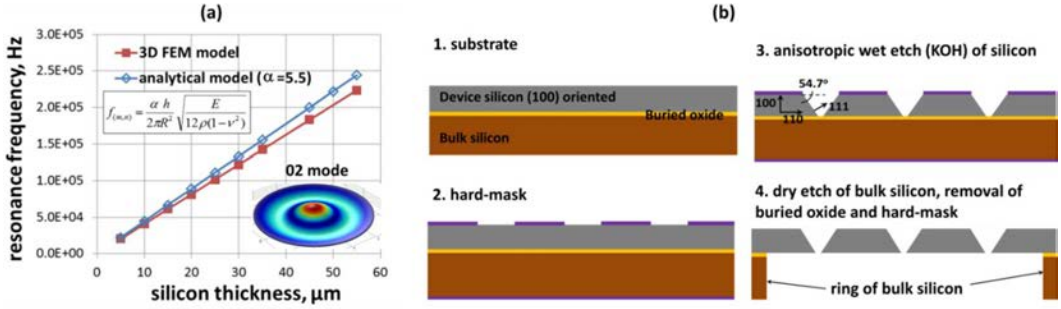

Fig. 2. (a) Simulated and calculated results of the 02 resonance against the silicon thickness for membrane diameter of 4 mm, (b) fabrication process of the silicon mesh where the KOH etch is used to pattern the apertures and the DRIE etch is used to release the bulk silicon.

For proof-of-concept of silicon nebulizer the prototypes were fabricated from the silicon-on-insulator (SOI) wafer with 25 µm device silicon, 1 µm buried oxide and 500 µm bulk silicon. The process flow is shown in Fig. 2(b). The process starts with the deposition and pattern of the hard-mask on the front and back side of the SOI substrate. The hard-mask was composed of two layers, i.e. 100 nm of silicon nitride and 35 nm layer of silicon dioxide. In the following step, the device silicon was etched to the buried oxide using an anisotropic wet etch in KOH (potassium hydroxide) with the etch rate of ≈1 µm per minute. The KOH etching of (100) oriented silicon results in a pyramid shaped apertures along <100> plane with the walls formed from four <111> planes that are angled to the surface at 54.7°. Afterwards, etching of the bulk silicon was performed using a dry etch technique (DRIE, Deep Reactive Ion Etching) that is isotropic, i.e. unlike to KOH the DRIE is not controlled by the silicon crystal planes. This was followed by the removal of the buried oxide and hard-mask.

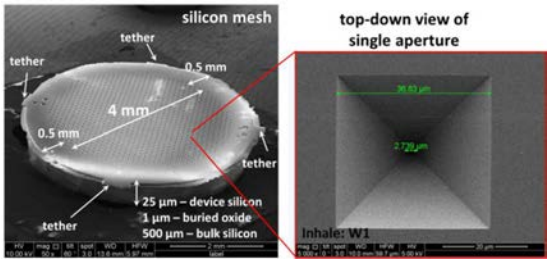

Fig. 3. SEM images of silicon mesh and the top-down view of a single aperture demonstrating pyramidal shape of the aperture.

Figure 3 shows the SEM of the fabricated mesh with 1000 pyramidal apertures separated by 120 µm pitch. Note that the diameter of the active area is 4 mm whereas the total diameter of the device is 5 mm and this is due to 0.5 mm wide ring of bulk silicon left around the device for post-fabrication handling and assembly. After the DRIE etch, the devices were removed from the wafer manually by breaking off four suspending tethers as indicated in Fig. 3. The target dimensions of the apertures in this paper were 38 µm for the top opening and 2.5 µm for the bottom opening.

2.2. Device electromechanical response and aerosol performance

The silicon mesh devices were assembled into the nebulizer as briefly described in Fig. 1 and their response was measured with the Laser Doppler Vibrometer (LDV). Figure 4(a) shows a typical response of the device when a fast frequency sweep at low driving voltage was performed. It demonstrates multiple resonance peaks with the 02 mode at ≈90 kHz, which is only 10% lower than the value predicted by the model. Figure 4(b) shows typical results of the displacement at the centre of the device against the voltage amplitude on the PZT when the device is driven at the 02 frequency. These results show that the device displacement increases linearly from 4 to 10 µm with voltage applied to the actuator.

The ability of the silicon mesh to aerosolise 0.9 % saline was assessed using a spray analyser and a typical result is illustrated in Fig. 4(c). The measurements show that the volumetric-mean-diameter of the droplets is 3.75 µm and around 75 % of all generated droplets are smaller than 6 µm, which is beneficial for efficient medicine delivery to the lungs. The output rate from this device was 0.45 ml / min. This performance is comparable to the devices presented in research papers and available commercially [4].

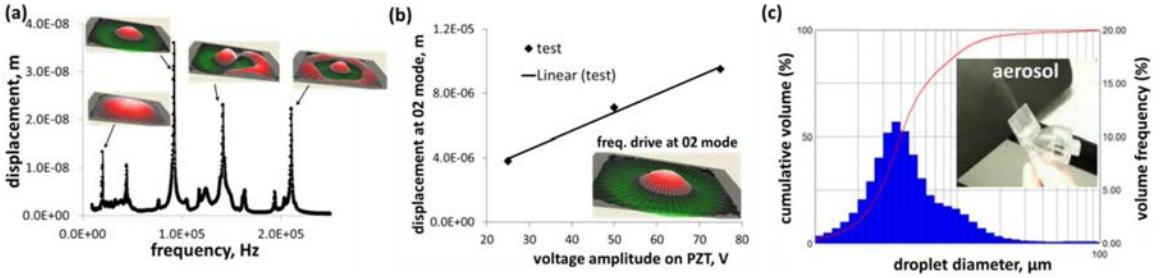

Fig. 4. Measured performance of silicon nebulizer (a) displacement against driving frequency demonstrating multiple frequency modes, (b) displacement against voltage amplitude, and (c) distribution of droplets from the nebulizer.

3. Conclusions

The results presented in this paper demonstrate that with MEMS technology we have been able to design and manufacture a silicon-based vibrating mesh nebulizer. The performance of silicon nebulizer is comparable to existing metal-based mesh nebulizers in that it is capable of generating highly respirable aerosol droplets with a relatively fast output rate. The device was fabricated in silicon MEMS process that use wet anisotropic etch to pattern the apertures in the silicon and dry isotropic process to release the device from the substrate.

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