Design and simulation of MEMS based Intra ocular Drug delivery Device

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ABSTRACT: There is an increasing need to develop devices for drug delivery to address ocular diseases such as glaucoma, age-related macular degeneration (AMD). Conventional ocular drug delivery devices are not capable of being refilled and doesn’t enable targeted drug delivery. But, MEMS devices help us to achieve the accurate drug delivery. The existing device have drawbacks like inconsistent performance of actuators, low cracking pressure of valves, getting damaged after repeated deliveries. By doing required modifications, the drug can be delivered to specific area at desired time and also it can deliver minor volumes of drug. In this paper, we design and simulate the micro pump with parylene bellows and check valves to overcome the existing drawbacks. By applying the required pressure, the drug will be released from reservoir to the targeted site with very accurate measures. With its high accurate delivery, the usage of drug volume can be reduced.

Keywords: Ocular Drug Delivery, MEMS, Parylene Bellows, Actuators, Cracking Pressure, Check Valves.

1 Introduction

Micro Electro Mechanical systems (MEMS) are small integrated devices or systems that combine electrical and mechanical components. Their size ranges from the sub micrometer level to the millimeter level (100nm – 1mm). In each system there can be any number of components, from a few to millions. MEMS is highly used in the integrated circuit industry to add mechanical elements like beams, gears, springs etc., to devices.

Now-a-days, MEMS technology is being applied for the miniaturization and integration of conventional devices and it is basically done on a common silicon substrate. Silicon is the most commonly used material due to its excellent electrical properties and outstanding mechanical properties. This helps us to sense, control and activate mechanical processes on the micro scale and generates effects on the macro scale. MEMS are not only about miniaturization of mechanical systems; they are also a new paradigm for designing mechanical devices and systems [1].

MEMS are classified into sensors and actuators. These MEMS sensors are used to measure the mechanical, thermal, biological, chemical, optical and magnetic phenomena. The actuators are used to respond by moving, positioning, regulating, pumping and filtering, thereby controlling the environment for some desired outcome or purpose [2]. By using these sensors and actuators, many applications have been derived. Few applications include inkjet-printer cartridges, accelerometer, miniature robots, micro engines, locks inertial sensors, micro mirrors, optical scanners, micro actuator, fluid pumps and transducer, pressure and flow sensors.

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MEMS proved to be a revolutionary technology in various fields like mechanical, space exploration, automation, medical etc. It has wide range of applications in the medical field and this technology is referred to as BIO MEMS.

Bio MEMS is an abbreviation of biological/biomedical micro electro mechanical systems (MEMS) and refers to a special class of MEMS where biological matter is analysed, manipulated or integrated as part of a transducer mechanism of a physical device. Biomedical microsystems (BioMEMS) integrate microscale sensors and actuators, microfluidics, micro-optics, and structural elements with computation, communications, and controls for application to medicine for the improvement of human health. Derived from the microfabrication technology used to make integrated circuits, Bio MEMS is revolutionizing the world by enhancing the way medicine is practiced and delivered [3].

The three new areas of Bio MEMS in medicine are: 1) surgical micro systems (intelligent micro-invasive surgical tools); 2) diagnostic micro systems (biochips and related micro instrumentation); and 3) therapeutic micro systems (health care management systems)[3]. BIO-MEMS functioning is sometimes comparable with micro total analysis systems (μTAS). Bio-MEMS is more focused on biological applications using mechanical parts and micro fabrication technologies. This signifies a lab-on-a-chip concept, which is concerned with miniaturization and integration of laboratory processes and experiments into single (often micro fluidic) chips [4].

Bio-MEMS is a branch which constitutes of material sciences, clinical sciences, medicine, surgery, electrical engineering, mechanical engineering, optical engineering, chemical engineering, and biomedical engineering [2]. Few of its major applications include genomics, proteomics, molecular diagnostics, point-of-care diagnostics, tissue engineering, single cell analysis and implantable micro devices [4].

Advancement in micro electromechanical system has facilitated the micro fabrication of polymeric substrates and the development of the novel class of controlled drug delivery devices [5]. (Bio MEMS) provide many opportunities for improved drug delivery like Low-dose vaccinations and painless transdermal drug delivery. This is achieved using micro needles which reach the targeted region accurately by piercing through skin. On the other hand, Low-power, low-volume Bio MEMS pumps and reservoirs can be implanted to complete the job which can't be performed by conventional pumping systems. These systems develop phenomenally and capitalize on their simpler integration with other MEMS-based systems such as computer controls and telemetry [7].

Recent advances in the field of micro fabrication have offered the possibility to develop controlled release systems for drug delivery and this efficient drug delivery plays a major role in disease treatment and remains an important challenge in medicine. There are two kinds of delivery devices: micro reservoir and micro/nano fluidic devices [10]. Drug delivery is the method or process of administering a pharmaceutical compound to achieve a therapeutic effect in humans or animals. Delivering drug at controlled rate, slow delivery, targeted delivery are other very attractive methods and have been pursued vigorously. The method of drug delivery is different for different parts of our body.

In our paper, we explained about delivering drug to the posterior part of eye. Ocular drug delivery has been a major challenge to pharmacologists and drug delivery scientists due to its unique anatomy and physiology. Static barriers (different layers of cornea, sclera, and retina including blood aqueous and blood–retinal barriers), dynamic barriers (choroidal and conjunctival blood flow, lymphatic clearance, and tear dilution), and efflux pumps in conjunction pose a significant challenge for delivery of a drug alone or in a dosage form, especially to the posterior segment[9].

In general, the eye consists of anterior and posterior segment. The front part of eye is called anterior segment and it’s easy to treat this part of eye. The conventional methods used for treating the anterior part are oral drugs, eye drops, intra ocular injections. But for posterior segment of eye (i.e, inner part of eye), it’s very difficult to deliver drugs to the targeted site with the existing conventional methods.

It has been proven that, less than 5% of the drug applied is capable of penetrating through the physiological barriers which include the ocular surface epithelium, the tear film and internal barriers of the blood-aqueous and blood-retina barriers. So we have to increase the efficiency...
of drug delivered to the targeted site, with reduced medication. In order to achieve this, MEMS based intraocular drug delivery concept can be used. This concept greatly reduces the systemic side effects. The need for repetitive surgeries to treat the infected site can also be reduced with this model. The existing delivery device has fixed drug to be delivered at fixed instants of time. Once it is been implanted into the body, its release rate and concentration cannot be changed. The other drawback of this model is that, it can’t be refilled. In order to refill it, the device has to be surgically removed, filled with required medication and should be implanted again using surgery. Adding to it, the drug delivery is achieved only by manually depressing the reservoir. Due to this, the device is getting damaged after repeated deliveries.

To overcome the above discussed issues, we designed and simulated a new device which consists of drug reservoir, parylene bellows micro pump, MEMS check valves. In this model, the micro pump contains two pyrolyzed - nafion-coated platinum electrodes immersed in an electrolyte to provide more catalyst surface area. The bellows mechanism used in this model is feasible and allows for greater achievable deflections at lower applied pressures. By applying the required pressure, the drug will be released from reservoir to the targeted site with very accurate measures. With its high accurate delivery, the usage of drug volume can be reduced.

2. DESIGN CONCEPT

As mentioned above, our drug delivery device consists of drug reservoir, parylene bellows micro pump, MEMS check valves. Using polyethylene glycol (PEG) – moulding process, the parylene bellows are fabricated with two convolutions and is used in this model [12]. It is followed by coating with parylene C.

In all the conventional models used till now, the drug delivery is achieved only by applying pressure manually. This doesn’t assure the accurate volumes of drug delivery at the targeted site. Adding to this, the space occupied by the device is approximately equal to 200cm³ in which only the 1/4th is being filled with drug. This is one of the greatest disadvantages to be overcome [15].

2.1 Working Mechanism

The ease of operation is achieved by electrically controlled circuitry having actuators. In our proposal the bellows electrolysis actuator is utilized. This actuator consists of platinum electrodes, as it is highly biocompatible. The basic mechanism of bellows actuator is based on electrolysis concept. In this an electrical circuit operating by varying minimal currents is used. This triggers the electrolysis reaction and generates gases responsible for the expansion and contraction of the bellows [14].

These bellows consisting of Pt electrodes are filled with electrolyte (water). When the electrical pulse is applied, the electrolyte splits up into hydrogen and oxygen gases as a result of electrolysis. Due to the release of gases it generates pneumatic pressure which is imposed on the inner portion of bellows. This creates a driving force and causes the bellows to expand. As the bellows is

![Fig 1.1 The existing model using cantilever mechanism](image)
surrounded by drug, its expansion causes the drug to flow from reservoir through the cannula to reach the targeted site appropriately. The outflow can be altered by switching between on and off states of electric circuit attached to it. Also the flow rates of drug are controlled by changing the applied pressures. This is done by varying the current applied to the circuit.

When the current supply is terminated, the platinum electrode acting as a catalyst makes the gases to recombine and form water again and this electrolysis is a reversible reaction and this process is continuous.

The optimum current applied for efficient drug release is 0.2 to 1 mA. When this level of current is applied, the pressure of about 3.5kPa (approx) is generated. This constitutes to the flow rates ranging between micro liters to nano liters. One more advantage of bellows is that, the space available for drug in a device is greatly increased [14]. Considering all these advantages, parlyene C bellows are proved to be more compatible for usage in any drug delivery device. So this mechanism is implemented in our proposed reservoir to control the course of drug to the targeted site.

![Figure 2.1 Basic working demonstration[14] a) Depicts the initial status of the drug delivery system, b) Depicts the drug delivery during pressure applied, c) Depicts the refilling process of the reservoir](image)

### 3. SIMULATION & RESULT

By using COMSOL version 4.2a multi physics software we are designing and simulating our proposed model. COMSOL Multiphysics is a cross-platform finite element analysis, solver and multiphysics simulation software. This software allows conventional physics based user interfaces and coupled systems of partial differential equations(PDE’s). It provides unified work flow for electrical, mechanical, fluid and chemical applications. User may drag and drop tools or do programming to design their model.

In this paper we designed a silicon reservoir with curved edges, parylene bellows mechanism. This reservoir is refillable whenever it is needed. The drawing tools like rectangles, squares, bezier polygons have been utilized to frame the reservoir.

![Fig 3.1 Two Dimensional model of the proposed reservoir](image)

The above drawn 2D model is extruded to form the 3 dimensional view of the reservoir. The whole
structure is made up of silicon as it is highly biocompatible. For this the pressure is applied at the range of micro Pascals and their corresponding displacements are tabulated.

Figure 3.2 3Dimensional model of proposed reservoir

4. CONCLUSION

In our proposal, we have framed an efficient method to provide medication to the posterior part of the eye by parylene bellows, and thereby monitoring the level and refilling it when the reservoir is devoid of drug. It can greatly reduce the amount of drug getting dissolved in the blood thereby reducing the side effects. In the previous Model, for the delivery of drug cantilever is been used. In cantilever concept, the amount to be delivered cannot be controlled accurately. This will be overcomed by using the concept of increase in pressure corresponding to the amount of drug flow to the targeted site. Using parylene bellows, the pressure is applied and the displacement of the bellows in the upward direction is observed. Depending on this displacement, the amount of drug being delivered can be determined. In this paper, we applied different pressures to the bellows and tabulated its corresponding resulted displacements. With this analysis, the drug volumes can be delivered at the required minimal quantities when compared to other existing models. It is highly useful in making the drug to be used properly.

The material used in this is highly bio-friendly that is silicon. The compatibility of the silicon is appreciable, because it doesn’t break for the applied pressure. The models’ design is curved on the edges to reduce the stocking of drug at the edges. The proposal will be a success due to the immense quality of the material being used and the efficient mechanism being proposed.

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