State of the Art and Perspectives on the Fabrication of Functional Contact Lenses

Sajina Tinku1, 2
1BioMEMS Group, CMM
Fondazione Bruno Kessler
Povo, Trento 38050, Italy
2ICT Doctoral School,
University of Trento
Trento, Italy
tinku@fbk.eu

Andrea Adami
BioMEMS Group, CMM
Fondazione Bruno Kessler
Povo, Trento 38050, Italy
andadami@fbk.eu

Leandro Lorenzelli
BioMEMS Group, CMM
Fondazione Bruno Kessler
Povo, Trento 38050, Italy
lorenzel@fbk.eu

Abstract
Functional multi-purpose contact lenses have recently attracted attention as suitable means to exploit the characteristics of eyes to diagnose diseases and for drug delivery. In this paper, we provide insights into the design and fabrication of specific prototype contact lenses suitable for wearers with dry eye conditions. The main objective is to integrate a combined system, which constitutes a biosensor for hydration monitoring and a saline solution delivery system, embedded on flexible polymer based substrates. We discuss the state of art and current research progress in smart contact lenses and provide initial hints of the proposed solution and identify specific challenges.

Author Keywords
Smart contact lenses; micro-fabrication; polymer; PDMS; impedance sensors; drug delivery systems

ACM Classification Keywords
Micromechanical systems; Flexible and printed circuits; Bio embedded electronics
Introduction
The endless possibilities and wide domains of application trends have increased the research potential on smart contact lenses, thanks to the recent breakthroughs in Nanotechnology [1]. Human eye is an exceptional organ with remarkable processing power, which can be exposed in a more natural way by using contact lenses. It is predicted that, by 2020, contact lenses will be the ultimately preferred display console for wearable devices, which will provide enhanced possibilities for the augmented reality vision [2]. Besides visual enhancements, other domains of application of smart contact lenses include medical health monitoring and telemedicine, low vision, defense and security.

In particular, healthcare monitoring applications are recently receiving attention mainly focusing on non-invasive and continuous health monitoring of the wearers biomarkers and health indicators, and drug delivery through smart contact lenses. Sensors built on to the smart lenses will monitor the health parameters, for example, the blood glucose level, and cholesterol level to name a few. These non-invasive monitoring provides similar indication possible from a biochemical analysis, and will aid in continuous health monitoring. When combined with appropriate electronics and other control circuits and antennas, the lens could transmit this information directly to the concerned health professional, without the need of invasive measures and laboratory chemistry, which will eventually be safe and reliable.

Smart contact lenses will also provide the possibility in the medical field for diagnosing diseases by examining eye tear, the retina and other parts of the eye [3].

Apart from the health monitoring and diagnosis, research on drug-delivering smart contact lenses is also currently ongoing, which will benefit mainly optical ailment sufferers.

This is made possible with a combination of biosensors, which detect the ailment and dispense drug doses evenly for as long as the lens is worn. This is a more effective method of drug delivery to the eye than using sporadic eye drops, which has many disadvantages, in particular for chronic ailments. The idea of “smart” contact lenses that can superimpose information on the wearers’ field of view has been around for a while, but the contact lenses that use embedded sensors and electronics to monitor disease and dispense drugs in a controllable manner are quite new topics. Such devices may eventually be able to measure the level of cholesterol or alcohol in your blood and flash up appropriate warning signals.

We focus our attention beyond the state of the art towards the mass market application of smart contact lenses by addressing the common problem faced by contact lens wearers, which is the dry eye condition caused by decreased tear production as a disease condition and also due to the contact lens use [4].

The rest of the paper is structured as follows; we present the state of art and current research progress on smart contact lenses, and provide insights into the design and fabrication of specific prototype contact lenses suitable for wearers with dry eye conditions. Our main objective is to integrate a combined system, which constitutes a biosensor for hydration monitoring and a saline solution delivery system, embedded on flexible polymer based substrates.
State of the Art
The current progresses on smart lenses are in two main areas, in the medical field and in information and communication technologies (ICT). The possibility of incorporating micro/nanostructures, optics and electronics into the contact lens are the main areas of investigation. The utilization of functionalized contact lens, meaning, the material with which the lens are made are treated with special chemical groups, will allow for characteristic chemical reactions, which can be used as indications of certain physiological conditions of the eye as well as the human body.

The same principle is used in the development of blood glucose monitoring using contact lens. The authors in [5] have patented this technology for sensing blood sugar levels using contact lens. The contact lens will change the color if the sensor in the contact lens detects glucose in eye tears. The technology for this type of smart contact lens is cheaper of the lot, as it requires only the addition of a sensor, which is fluorescent on the usual soft contact lens.

For the same application another group from university of Pittsburgh is studying the possibility of incorporating photonic crystals for measuring the glucose level of eye tears. Another research in this area is in the use of nano-particles in lenses to measure the sugar level in eye tears [6]. Shown in Table 1 is the comparison of concentration of components in tears and blood. The concentration of various components in tears are comparable to that of blood, which means that analysis of tears can also provide diagnostic results like in normal blood tests.

Smart contact lens research is also ongoing in the diagnosis of IOP (intra ocular pressure) for Glaucoma patients. Glaucoma is a disease if untreated can lead to blindness.

<table>
<thead>
<tr>
<th>Component</th>
<th>Tear concentration</th>
<th>Blood concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na+</td>
<td>120-165mM</td>
<td>130-145mM</td>
</tr>
<tr>
<td>K+</td>
<td>20-42mM</td>
<td>3.5-5mM</td>
</tr>
<tr>
<td>Ca2+</td>
<td>0.4-1.1mM</td>
<td>2.0-2.6mM</td>
</tr>
<tr>
<td>Mg2+</td>
<td>0.5-0.9mM</td>
<td>0.7-1.1mM</td>
</tr>
<tr>
<td>Cl-</td>
<td>118-135mM</td>
<td>95-125mM</td>
</tr>
<tr>
<td>HCO3-</td>
<td>20-26mM</td>
<td>24-30mM</td>
</tr>
<tr>
<td>Glucose</td>
<td>0.1-0.6mM</td>
<td>4.0-6.0mM</td>
</tr>
<tr>
<td>Urea</td>
<td>3.0-6.0mM</td>
<td>3.3-6.5mM</td>
</tr>
<tr>
<td>Lactate</td>
<td>2- 5 mM</td>
<td>0.5-0.8mM</td>
</tr>
<tr>
<td>Pyruvate</td>
<td>0.05-0.35mM</td>
<td>0.1-0.2mM</td>
</tr>
<tr>
<td>Ascorbate</td>
<td>0.008-0.04mM</td>
<td>0.04-0.06mM</td>
</tr>
<tr>
<td>Total Protein</td>
<td>~ 7 g/L</td>
<td>~ 70 g/L</td>
</tr>
</tbody>
</table>

Table 1 Comparison of the concentration of biological and chemical components in tear and blood [8]

The use of point of care diagnostic tool like contact lens with pressure sensors can monitor and help in identifying the problem much quicker and more comfortable. The experimentation of MEMS (Micro electromechanical systems) and NEMS (Nanoelectromechanical systems) in this area is used to measure the changes of the shape of the eye during
the change of the ocular pressure. The sensor is in direct touch with the eye surface facilitating the accurate measurement of the changes of eye pressure. Tiggerfish a smart contact lens made by Sensimed, and has a sensor with strain gauges to monitor the pressure difference [7].

The possibility of embedding drug delivery systems together with the sensor in the smart contact lens is also another direction of research. The authors in the article [9] use two polymer layers for the lens fabrication and the drug to be delivered is sandwiched between the layers. One of the polymer layers is biodegradable and the drug delivery is based on the ratio of the relative volume of the biodegradable polymer to the amount of drug stored. Similar efforts are also progressing to identify the permeable polymer layers for the use of drug delivery systems on the contact lens.

The use of micro fabrication techniques, with the addition of electronics, optoelectronics and displays open up the application range for using smart contact lens. One such work is towards the realization of heads up display. These displays will help the user to access all the data necessary for them in real time without the need of looking away from their field of focus. In [11], the authors succeeded in realizing a wireless-powered contact lens with single pixel displays. The contact lens developed by Innovega group has built-in optical devices. Such lenses when used with special spectacles yield a high-resolution view [12].

In Figure 1, a conceptual sketch of smart contact lens inspired from literature is shown, where the periphery is an antenna, which collects RF energy from an outside transmitter. There is a circuit, which provides DC power to the whole system. LEDs, which are the display, are in the center of the lens. Photovoltaic components are also placed in for energy harvesting and storage. To complete this conceptual model there is also a biosensor that is designed to perform analysis on the biomarkers and provide results which will be transmitted to an external system through the telecommunication module [10].

**Beyond State of the Art**

Dry eye condition is a common eye problem. Statistics show that Dry eye problem is one of the major causes for people visiting eye specialists. Some of the various reasons are the certain diseases, use of certain
medications, increased use of computer, hormonal changes especially in women during pregnancy, environmental conditions, aging and eye surgeries and most importantly the use of contact lens, which will create irritation by evaporating eye tears [10]. The main treatment for dry eye condition is the use of over the counter artificial tears, the use of which will moisturize the eye surface. Upon usage, major portion around 90 % is lost and only a very small portion is retained for the actual therapy [13][14].

The smart contact lens proposed in our work will be a state of the art micro-machined polymer contact lens with a drug delivery system, which can deliver saline solutions or commercially available artificial tear solutions. Incorporating a hydration sensor into the contact lens together with a drug delivery system is the core of the work.

In [15], the authors developed an impedance sensor for skin hydration monitoring. Impedance sensor is a patch of flexible polymer substrate with various geometries of electrode patterns for the skin resistance measurement. The skin electrical impedance determines skin moisture levels. The skin electrical impedance is in a correlation with the water content in the biological tissues and conductivity of skin changes with the skin hydration levels [16][17].

The challenging problem for our work is to adopt this principle of the hydration sensor into the contact lens. The drug/saline solution delivery is another challenging quest in this work. The possibility of micromachining polymers especially PDMS will be investigated. In [18], the authors managed to create submicron PDMS structures using conventional technological processes such as lithography, reactive ion etching and think film releasing techniques.

In [15], the authors developed an impedance sensor for skin hydration monitoring. Impedance sensor is a patch of flexible polymer substrate with various geometries of electrode patterns for the skin resistance measurement. The skin electrical impedance determines skin moisture levels. The skin electrical impedance is in a correlation with the water content in the biological tissues and conductivity of skin changes with the skin hydration levels [16][17].

The challenging problem for our work is to adopt this principle of the hydration sensor into the contact lens. The drug/saline solution delivery is another challenging quest in this work. The possibility of micromachining polymers especially PDMS will be investigated. In [18], the authors managed to create submicron PDMS structures using conventional technological processes such as lithography, reactive ion etching and think film releasing techniques.

Figure 2. Molding method used for fabrication of smart contact lens

The possible solution for our work will be to create reservoirs to store drug in submicron patterns on the contact lens substrates. The integration of sensor and drug/saline delivery system is a major challenge in realizing the smart lens. We need to minimize the scales of devices and make possible the integration of devices into a small area of the contact lens, without obstructing the normal view. The assurance of safety and reliability are the most important outcomes expected of the fabricated smart contact lens.

We will evaluate the fabrication techniques, materials used, technology for patterning the sensor and the controlled saline solution/drug delivery mechanisms. In spite of the technology used, the devices should be easy to use, wearable and unobtrusive. The ease of use and reliability are the major concerns regarding the
performance of a working device. The aim is to research on means to make the devices thinner, durable, low-cost and with increased lifetime.

The current interest is towards polymer MEMS, which will be taken into consideration for the fabrication of the sensors. The possibility of using standard Si-technology will also be investigated. With various research activities in the same field, our objective will be to integrate the devices at a system level, which promises to give an efficient output compared to the state of the art devices. The conductive polymer is one of the major research lines in the front, which needs to be thoroughly investigated before proceeding to the subsequent steps. The use of flexible substrates will enable the sensors to be adapted for use with any part of the body.

For the curved shape of our eyes, a curved sensor is required for the correct monitoring of the biological parameters. The molding is done as shown in Figure 2 differently from the conventional way of fabricating soft contact lenses. The final aim is to make the devices and the system simpler and cheaper to be fabricated with very high efficiency.

Conclusions and future work

Smart contact lenses are receiving considerable interest in healthcare monitoring and for drug delivery. Further, these functional contact lenses will also provide the possibility in the medical field for diagnosing diseases by examining eye tear, the retina and other parts of the eye. There are several fundamental to be addressed while building multipurpose contact lenses.

An important challenge is related to the compatibility of the different lens modules between each other and with the material from which lens are fabricated. Further, all the devices of the lens need to be miniaturized and integrated into a very small area in the contact lens without obstructing the field of view of the lens wearer. Last but not least, the safety of the eye needs to be ensured by using biocompatible substances.

In this paper, we provided insights into the design and fabrication of smart contact lenses suitable for wearers with dry eye conditions. We discussed the state of art and current research progress in smart contact lenses and provided initial hints of possible solutions. We presented the outline of a combined system, which constitutes a biosensor for hydration monitoring and a saline solution delivery system, embedded on flexible polymer based substrates.

As future work, we plan to study in detail the design of the system specifically focusing on the requirements for each step of the framework. Further, an analysis of the polymer substrates is currently ongoing to identify the most suitable and flexible substrate for the smart contact lens.

References

[1] Legerton J. The future is now: unveiling smart lenses. Rev Cornea Contact Lens. 2011 May;147(4):17-


