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Towards a polymeric patch-on-a-chip design

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INTRODUCTION: Since the patch clamp technique was introduced in 1976, it has become one of the most important tools for the investigation of ion transport mechanisms through cell membranes. A major drawback, however, is that despite recent efforts for automation[1] the technique is still not suited for true high throughput investigations as they are needed in the pharmaceutical industry.

To overcome this drawback we study a new approach which we call polymeric patch-on-a-chip. The general design of this approach is sketched out in Fig. 1

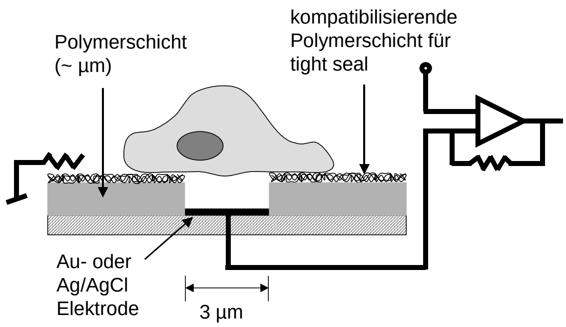

Fig. 1: Patch-on-a-chip design. For details see text.

Here the cell sits on a small hole within a microstructured film and tightly seals the interior of the hole from the medium around the cell. Small electrodes that are placed within the hole and in the medium can then be used to study the ion transport through the cell membrane. Using standard photolithographical techniques this design allows for the generation of many such set-ups on one chip and is therefore in principle well suited for high throughput measurements.[2]

METHODS: The microstructures were generated by using photolithography in a SU8 resist layer. Prior to that the silicon substrate was covered with a structured layer of titanium and gold with a lift off. The modification of the surface of the photoresist was achieved by depositing polymers with photoreactive benzophenone groups which upon UV irradiation for networks that are also chemically linked to the surface. All layers were characterized by XPS and FTIR. The microstructures were characterized by AFM Profiliometer and Light Microscopy.

RESULTS & DISCUSSION: SU-8 technology has been successfully used to generate microstructures with sizes suitable for the approach outlined above. One example is shown in Figure 2. There nine little holes were successfully written into a resist layer. The depth of the holes is of the order of 6 µm and the diameter is 20 µm. Below the resist layer a gold layer which is connected to a big gold spot may later on serve as a connection to the measurement electronics.

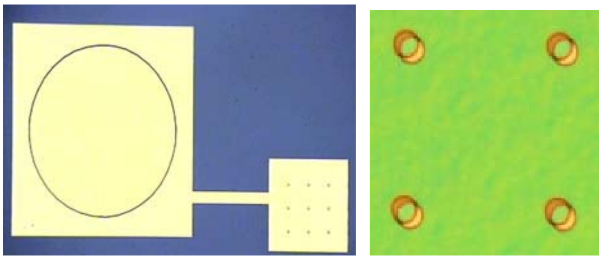

Fig. 2: Test structure for a patch-on-a-chip device.

As SU-8 forms rather hydrophobic surfaces cells cannot be cultured directly on this device. Therefore, we deposited thin coatings of polymers carrying photoreactive groups that upon UV illumination cause the formation of a network. Also bonds to the resist layers are formed and consequently very stable layers are generated that resist delamination even if they were formed from hydrophilic polymers. Using this approach we were able to completely mask the cell hostile properties of the resist. Current investigations concern the deposition of cells such that they come to rest directly above one of the little holes and form a tight seal that separates the inside of the hole from the exterior. Also, other chip designs are studied and optimized in terms of size and spacing.

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