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ボッシュプロセスによる神経細胞ネットワークハイスループットスクリーニングプレナーパッチクランプチップの製作

Fabrication of planar patch clamp chip for the neuron-network high throughput screening by Bosch process

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Neurodegenerative diseases such as Alzheimer's disease (AD) and amyotrophic lateral sclerosis (ALS) are intractable diseases for which neither cause nor reliable treatment method is established. The reason why these diseases are so difficult is; it is not easy to sample neurons, the affected parts, during the lifetime of the patients, and there has never been suitable methods of analyzing the function of the neuron-network. The measurement of ion-channel current, which contains the information with the release of the neuro-transmitter molecules at the synapse is considered to be the most useful method for analyzing the neuron-network function. It is expected that the incubation-type planar patch clamp finds its useful application in the high throughput screening device of neuron-network. Concerning this application, we have developed the cell cage substrate. The one segment of the cell cage substrate is shown in Fig. 1, by which spatially homogeneous neuron-network can be formed and long term incubation is possible (more than one month). Until now, we have used polycarbonate chip formed by hot embossing and focused ion beam micro-fabrications. However, this fabrication method has limitations for manufacturing multi-points measurement device, since it is too expensive and low efficiency. In this work, we have examined to develop a new method of chip fabrications. We have examined to form the micro-structures shown in Fig.1 by using Si(SOI) substrate and micro fabrication process combining photo-lithography and Bosch processes.

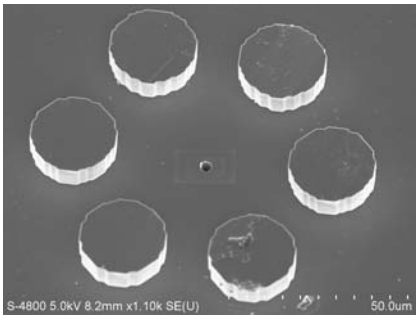

Fig.1 The SEM image of one segment of the planar patch clamp chip (Si).

Bosch process, named after the inventor Robert Bosch, is widely used for fabrication of high aspect ratio microelectromechanical system (MEMS) which need a highly anisotropic etch process to create almost vertical structure in silicon wafers. It consists of a series of time multiplexed etching and passivation processes using SF_6 and C_4F_8 gases. With the optimized condition which control the flow rate of SF_6 , C_4F_8 , O_2 etc. and other parameters like applied bias voltage and bias power, it can etch the silicon wafer almost vertically with smoothed sidewall.

Substance	Si	AZ1500	SU-8	SiO_2
Etching rate (μm/min)	2.85	0.075	0.075	0.023

As a first step, we have investigated the etching rate of the Si, positive photo resist, negative photo resist and SiO_2 as shown in the table.

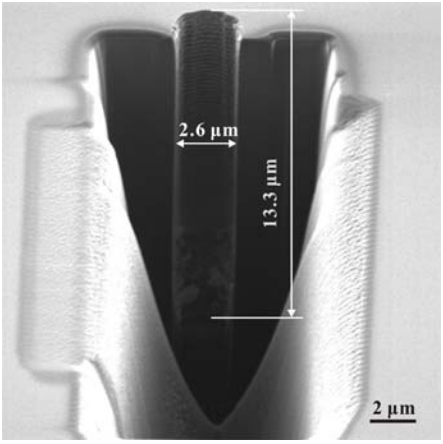

Fig. 2 Cross section image of the micro-pore formed by Bosch process 100 cycles.

We can see the etching rate is almost the same between positive photo resist and the negative photo resist. The etching rate of SiO_2 is about one third of positive photo resist. The etching rate of silicon is about 40 times faster than that of the positive photo resist. The etching rate of silicon strongly depends on the etching area of silicon surface. Close to the micro-pore size (~2 μm diameter) the etching rate of silicon decreases to about half of the value of the large area. Figure 2 shows the SEM image of the deep etching with micro-pore of diameter 2.6 μm. Cross sectional structure was formed by FIB and observation angle was 45 degrees. The etching sidewall is almost vertical and smooth which is considered to be suitable for the micro-pore of the planar patch clamp chip. The fabrication of the micro-pore has long been an important challenge of the planar patch clamp chip, especially for the high throughput applications which require the high density of measuring points. Present results show that new high quality and mass productive fabrication way can be opened by the Bosch process for the first time. It is expected that high throughput screen device with multi-channel current measurement will play a important role in elucidation of mechanisms of neurodegenerative diseases.