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学 位 論 文 題 目　Study of 3-D Stacked Retinal Prosthesis Chip with Visual Information Processing Functions
(高次視覚情報処理機能を有する三次元積層人工網膜チップの研究)
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論文内容要約

Currently, the world's population is drastically increasing. By the end of this century, the population will be reached more than 10 billion. However, developed countries are noticing increasing aging population and low birthrates. According to United Nations reports, developing countries will also have aging populations in the near future. By 2050, it is expected that 60 years old and older people will reach more than 2 billion in the world. Given these situations, there is concern with regard to the growth in visual impaired and blind people. Currently, there are more than 285 million people with visual impairment in the world, including 39 million blind people. Among those blind people, 32 million people are more than 50 years old. The World Health Organization expects that visual impaired and blind people will increase in the future. The principal causes of blindness are cataracts, glaucoma, uncorrected refractive errors, age-related macular degeneration (AMD), corneal opacities, trachoma, diabetic retinopathy, and so on. Among these causes, cataracts and glaucoma account for approximately 60% of the cases. Most patients suffering from these diseases are living in the developing countries because medical technology is developing in them. In contrast, developed countries have a large number of blind patients suffering from AMD, which is a retinal disease developing in accordance with aging. Addition to AMD, patients of retinitis pigmentosa (RP) also are increasing in accordance with population growth because RP is one of hereditary diseases, which the incidence ranges from 1 in 2000 to 1 in 7000. The retina consists of photoreceptor cells, horizontal cells, bipolar cells, ganglion cells, and so on. The photoreceptor cell converts optical signals into electrical signals. The horizontal cell and the bipolar cell process visual information. The ganglion cell propagates visual information to the brain through the optic nerve system. AMD and RP are retinal diseases that cause photoreceptor cells to degenerate, and patients finally lose visual perception. However, effective medical treatments have not been established yet. In order to recover visual sensation for these patients, several approaches, such as chemical photoswitch, regenerative therapy, optogenetics therapy and retinal prosthesis are proposed.

Retinal prosthesis has shown the best results among the proposed approaches. It consists of photodetectors, processing circuits, and a stimulus electrode array. The photodetector converts optical signals into electrical signals. The processing circuit processes visual information and generates biphasic stimulus current pulses. The stimulus current pattern stimulates remaining retinal cells via a stimulus electrode array. A large scale integration (LSI) chip including processing circuit for generating stimulus current pulses is called a retinal prosthesis chip. There are three types of retinal prostheses: suprachoroidal transretinal stimulation (STS), epiretinal and subretinal prosthesis. In STS type, a stimulus electrode array is implanted into sclera. The photodetector is equipped outside the eyeball. Visual information is acquired by the photodetector and delivered to an internal retinal prosthesis chip wirelessly. The retinal prosthesis chip generates stimulus current patterns. As for epiretinal type, an electrode array is implanted on the retina. Similar to STS type, visual information is acquired by the extaocular photodetector, and delivered to retinal prosthesis chip in the eye. Using an electrode array implanted under the retina, subretinal prosthesis stimulates the retinal cells electrically. The electrode array is formed on LSI chip which has photodiodes, and processing circuit. Therefore, this retinal prosthesis performs both of acquiring visual information and generating stimulus current pulse in the eye.

Conventional retinal prostheses have several problems. The first problem is low resolution. According to several reports, more than 600 to 1000 stimulus electrodes are necessary to recognize writing, objects, and faces. Because the appropriate area for implanting a stimulus electrode array is limited, a high-density arrangement of the electrodes is required. The second problem is in optimizing the photosensitivity. In general, when retinal cells are stimulated with high electrical pulse frequencies, patients can recognize bright light. In the case of stimulation with low-pulse frequencies, patients can recognize dim light. Thus, the retinal prosthesis chip has to generate appropriate current pulse frequencies according to the incident light for recognizing brightness. The third problem is in the implementation of visual information processing. In the retina, photoreceptor cells, horizontal cells, and bipolar cells perform visual information processing. This processing is useful for recognizing objects and faces; however, visual information processing is not implemented in proposed retinal prosthesis chips. The fourth problem is low power consumption. Because retinal cells are damaged by heat, the power consumption of a retinal prosthesis chip should be below 19 mW/mm^2. To ensure high safety, low power operation is strongly required.

We have been developing a fully implantable retinal prosthesis with a three-dimensional (3-D) stacked retinal prosthesis chip. This system consists of an external unit and an internal unit. The external unit is comprised of a transmitter and a primary coil for delivering configuration data and power. The internal unit consists of a secondary coil and a receiver for receiving data and power, a flexible cable, and a 3-D stacked retinal prosthesis chip with a stimulus electrode array. The 3-D stacked retinal prosthesis chip is comprised of a photoreceptor chip, and stimulus current generator chip with visual information processing functions which are vertically stacked and electrically connected by through silicon vias (TSVs). This retinal prosthesis chip can solve the mentioned above issues.

In this study, a photoreceptor chip with high resolution and switchable photosensitivity function, and a stimulus current generator chip with higher visual information processing function for the 3-D stacked retinal prosthesis chip are developed. A retinal prosthesis chip had been developed by our group in a previous study. This chip had 100 pixels and pixel size of 154.7 μm × 143.4 μm. To fabricate a high-resolution retinal prosthesis chip, the pixel circuit of the previous work was thoroughly reviewed and redesigned. Consequently, the pixel circuit area decreases to 90 μm × 90 μm, and a two-dimensional (2-D) retinal prosthesis chip having 24 × 24 pixels was fabricated using 0.35-μm double poly-Si 4-metal complementary metal oxide semiconductor (CMOS) image sensor technology. Characteristics between the incident light intensity and stimulus current pulse frequency of the 2-D retinal prosthesis chip were evaluated. From the evaluation results, the frequency of the stimulus current pulse was 40 Hz at 200 lx. Because humans can recognize a stimulus current pulse frequency more than 40 Hz as a spot of light, patients cannot recognize the light below 200 lx using the 2-D retinal prosthesis chip. Our target photosensitivity is that the stimulus current pulse frequency between 40 Hz and 300 Hz is generated in the incident light from 6 to 600 lx. However, there was a large difference between the target photosensitivity and the measurement results of the 2-D retinal prosthesis chip. From analysis of the measurement results, it was found that the photosensitivity depends on material property of the silicon photodiode. Then, to overcome this issue, a switchable photosensitivity photoreceptor circuit was designed. This circuit has two photosensitivities such as sunlight mode and room light mode. The circuit consists of a large size photodiode, and current mirror circuits, and outputs the current to a visual information processing circuit. Current mirror ratios are set to 0.7 in sunlight mode and 7 in room light mode, respectively. A photocurrent I_{pd} converted at a photodiode is amplified in a current mirror circuit. When patients selects sunlight mode, $0.7 \times I_{pd}$ flows to the visual information processing circuit. In contrast, a current of $7 \times I_{pd}$ flows to the visual information processing circuit in room light mode. In order to evaluate the switchable photosensitivity photoreceptor circuit, a photoreceptor chip was fabricated using 0.35-μm double poly-Si 4-metal CMOS image sensor technology. This chip has 37 × 37 pixels and a pixel size of 75 μm × 75 μm including a photodiode of 30 μm × 50 μm, two metal pads for TSVs, and current mirror circuits. Firstly, a relationship between the incident light intensity and an output current of the switchable photosensitivity photoreceptor circuit was evaluated. The incident light was changed between 1 to 1000 lx. For the evaluation results, the output currents were 1.9 pA to 820 pA in sunlight mode, 12 pA to 8.7 nA, respectively. Next, the photoreceptor circuit connected to the stimulus current generator was evaluated. As results, stimulus current pulse frequencies from 40 to 200 Hz were generated in the incident light between 50 and 600 lx in sunlight mode. In room light mode, pulse frequencies between 40 and 300 Hz were measured in the light of 4 to 100 lx. Therefore, by switching to another photosensitivity, stimulus current pulse frequencies between 40 Hz and 300 Hz were obtained in the light intensity from 4 to 600 lx.

As mentioned above, visual information processing is performed in the retina. By implementing visual information processing such as edge enhancement in a retinal prosthesis chip, patients can easily recognize human faces and objects. For this study, implementing edge enhancement function in retinal prosthesis chip was performed. Firstly, to select an appropriate edge enhancement algorithm, Lena image of 37 × 37 pixels was processed by digital image processing using a 3 × 3 operator. The compared algorithms were gradient filter, Prewitt filter, Sobel filter, unsharpe mask, and Laplacian filter. Because gradient filter, Prewitt filter, and Soble filter have directivity, edge enhancement accuracy of these algorithms depends on directions. In contrast, unsharp mask and Laplacian filter do not have directionality. Among two algorithms, eight-neighbor Laplacian filter has the best edge enhancement accuracy. However, a circuit area of eight-neighbor Laplacian filter became large. Then, four-neighbor Laplacian filter was selected. This algorithm has better edge enhancement accuracy next eight-neighbor Laplacian filter. Furthermore, small circuit area would be realized. In four-neighbor Laplacian filter, the edge of the image is calculated by $P_O = (P_T + P_R + P_B + P_L) - 4P_C$, where P_O is a pixel value of the output image, and P_T, P_R, P_B, P_L, P_C are pixel values of top, right, bottom, left, and the center, respectively. A stimulus current generator chip with an edge enhancement function using four-neighbor Laplacian filter was fabricated using 0.18-μm 1 poly-Si 6 metal CMOS mixed-signal technology. This chip has 37 × 37 pixels with pixel size of 75 μm × 75 μm. The pixel includes an edge enhancement circuit using four-neighbor Laplacian filter, a stimulus current generator, and two metal pads for connecting to a switchable photosensitivity photoreceptor circuit. The pixel is connected to four-neighbor pixels such as top, right, bottom, and left. The edge enhancement circuit consists of current mirror circuits and performs the four-neighbor Laplacian calculation of $I_{EE} = I_{tot} - I_C = 0.5\ \{0.25(I_T + I_R + I_B + I_L) - I_C\}$, where I_{EE} is an output current of the edge enhancement circuit, and I_T, I_R, I_B, I_L, and I_C are the output current of top, right, bottom, left, and the center of a switchable photosensitivity photoreceptor circuit, respectively. Firstly, an edge enhancement circuit was evaluated. An input current equivalent to the output current of the photoreceptor circuit, I_C, was changed from 1 pA to 1000 pA using a source meter and I_{tot} was changed 1.25, 12.5, and 125 pA, respectively. When I_{tot} is 12.5 pA, stimulus current pulse was generated more than I_C of 12.5 pA. From the evaluation results, it was found that the edge enhancement function was successfully performed. Additionally, the power consumption of the 3-D stacked retinal prosthesis chip with an edge enhancement function was evaluated in SPICE simulation. From the simulation results, effective power reduction was confirmed. By using the edge enhancement function, a 36% power reduction can be realized. Therefore, implementing an edge enhancement function in a retinal prosthesis chip is effective for power reduction.

In order to fabricate the 3-D stacked retinal prosthesis chip, 3-D integration technology is used. This technology has several reliability issues such as thermal, mechanical stress and strain, and metal contamination. These problems affect the device characteristics and lead to fatal system errors. In this study, we focused on mechanical stress and strain by chip bending, and metal contamination from copper-TSVs. In the 3-D integration process, the LSI chip is thinned and bonded to other LSI chips. Among these chips, adhesive and metal microbumps exist. Because of mismatches in the thermal expansion coefficients between the adhesive and metal microbumps, large mechanical stress and strain arise, induced by expansion or shrinkage of the band gap of silicon and electron mobility change. Additionally, to electrically connect these chips, via holes are formed from the backside surface of the silicon substrate. After that, silicon dioxide and barrier metal are deposited. Finally, via holes are filled with copper. Because copper atoms diffuse into the silicon substrate, poor coverage of the barrier metal induces the copper contamination from the copper-TSVs. The diffused copper creates an energy level in the forbidden band for silicon. In order to evaluate these reliability issues, the retention characteristics of dynamic random access memory (DRAM) were measured. First, the effects of stress and strain were evaluated. The initial chip thickness was 200 μm. The DRAM chip was bonded to an interposer and thinned to 50, 40, 30, and 20 μm. The retention time of 20 μm thickness condition decreased to 50% compared with 200 μm thickness condition. Next, the retention characteristics were evaluated for a DRAM contaminated with copper from TSVs. After the via holes were filled with copper, the DRAM chip was annealed at 200, 250, and 300 °C. From the evaluation results, at an annealing temperature of 300 °C, the retention characteristics deteriorated. The tail distribution of the retention characteristic was enhanced at an annealing temperature 300 °C.

As a result of this study, a photoreceptor chip with a switchable photosensitivity function and a stimulus current generator chip with an edge enhancement function were fabricated for a 3-D stacked retinal prosthesis chip with higher visual information processing function. Additionally, a reliability evaluation of 3-D integration technology for fabricating a 3-D stacked LSI chip was performed. By using these chips and technology, the 3-D stacked retinal prosthesis chip with edge enhancement function will realize.