The artificial Human – Retina Implants

Talk by Christian Freudiger

Implants are thought to be one of the major methodes to cure all kinds of diseases, from fractures of the skeleton to complex illnesses like the loss of the hearing sense or cardiac defects. To construct those implants in a way that they work in the human body for more than 30 years without causing further damage challenges many research groups worldwide. Doing so the challenges occur at all time and length scales: From the overall macroscopic stability of the implant over micrometer-sized circuits to surface modifications in the nano-world. All of the areas of research always have to be seen in the context of the biological functioning and biocompatibility.

Retinal implant could restore the vision of 2 millions of blinds

The talk by Christian Freudiger was mainly focused on retinal implants that might once restore the vision of over 2 million patients worldwide. One of the main inherited diseases that cause blindness already during early childhood is Retinitis Pigmentosa. Age-related macular degeneration mainly occurs at old age. Both forms of blindness result in a continuous degeneration of the photoreceptor-cells in the retina, which create a nerve-pulse due to stimulation by light and both diseases lead to absolute blindness after years. The only positive finding about these illnesses is that almost all neurons that process the information created by the photoreceptors and transfer it to the visual cortex in the brain stay unaffected. This creates the hope that it will be possible to directly stimulate the neurons by electrodes implanted into the eye and in this way restore the visual sense of patients.

In literature two main concepts are proposed to realize this idea. Both are already in the stage of their development in which they can be implanted into first test candidates and hopefully prove the general functionality of retinal implants:

1. Subretinal approach:
   The subretinal approach is the direct substitution of the photoreceptor cells. If one analyzes the functionality of a photoreceptor, one realizes that it is nothing else than a highly functionalized solar cell: A photon is absorbed in the receptor and a nerve pulse, which simply is an electrical pulse in the order of mV, is created. This is exactly what a solar cell does. It absorbs light and creates a voltage. Therefore, it is believed that it will be possible to build a complete and self-supporting retinal implants by adapting a thin-film solar cell to be implanted into deep layers of the retina.

2. Epiretinal approach:
   The epiretinal approach represents an even more complicated system. The aim is not to construct a single-celled system like a subretinal implant, in which each cell acts on its own, but to contain an information processing unit which modifies the data captured by a normal CCD-camera outside the eye to drive electrodes implanted on top of the retina. The information processing becomes necessary as another type of neurons is stimulated in the epiretinal approach than in the subretinal approach.

The challenge of the neuron-semiconductor-interface

One of the main assaults in the development of retinal implants is the proper design of the electrodes and the proper stimulation parameters. Therefore, it is important to gain the full understanding of the neuronal activity. Relatively basic descriptions of the functionality of neurons date back to the middle of the 20th century:

A neuron is modelled as a membrane that separates the outside world, i.e. a solution of ions of a certain concentration from the inside, another solution of ions of different concentrations. Due to the difference in ionic concentration a potential difference across the membrane builds up in order to maximize the total entropy and minimize the free energy of the system. In thermal equilibrium and for one ion-species this potential is described as Nernst-Potential which can be derived by solving Boltzmann equation for the electrical potential

$$V_{Nernst} = -\frac{k_B \cdot T}{Z \cdot e} \cdot \ln\left(\frac{c_{in}}{c_{out}}\right)$$

with k_B being Botzmann constant, T the absolute temperature, Ze the charge of one ion and c the concentrations in- and outside the cell.

A more detailed study reveals that this simple model of a neuron is not correct by far as living cells are rarely found in thermal equilibrium. A membrane protein, the so called K^+-Na^+-ATPase burns ATP, a molecule rich in energy, to pump sodium ions out of the cell and potassium ions into the cell. As the membrane possesses conductivity a certain leakage current through the membrane always exists, but due to the pumping the system will never end up in an equilibrium state. Still it is possible to describe this model system by the means of statistical mechanics. The solution is the Goldmann equation

$$\Delta V = \frac{2 \cdot g_{Na} \cdot V_{Na}^{Nernst} + 3 \cdot g_K \cdot V_K^{Nernst}}{2 \cdot g_{Na} + 3 \cdot g_K}$$

with V^{Nernst} being the calculated Nernst potentials according to the equation above for the different ion species and g being the different conductivities of the membrane for each species. It can be seen that the resulting potential is a linear combination of the Nernst potentials of the individual ion species weighted by the membrane conductivity for each species. Knowing that the Nernst potential for sodium is positive and for potassium is negative, it can be understood that a neuron might simply change the voltage across its membrane by changing the conductivity of the membrane. This is what actually happens. The membrane contains specific ion-channels that can open and close due to certain stimulation and in this way result in a change of the conductivity of the membrane. A nerve impulse is the timed and spatially synchronized repetition of those events.

This fundamental understanding is the basis for the construction stimulation electrodes. A special type of ion-channels opens and closes in dependence to an external stimulation voltage. They open as soon as a threshold voltage is exceeded and thus lead to a depolarization of the cell membrane, i.e. they create a nerve pulse.

Still it is not that easy to actually apply this theory to living cells and construct a stimulation electrode. The complete mechanism is not jet understood in all details on the basis of molecular level. The research group of Prof. P. Fromherz has been investigating in this area for more than 20 years and made major contributions to the chip-development for laboratory study. Despite the lack of complete understand it has been possible to develop ear-implants containing stimulation electrodes that have been working for many years. This gives rise the hope that it might be possible to find similar systems for the eye.

State-of-the-art-systems and first results from testing

As mentioned above, the current research is at the point, where prototypes have been developed and can now be implanted into first test patients. Although it cannot be expected that these test-implants will restore the vision in a satisfactory manner, first results indicate that biocompatibility does not seem to be an unsolvable problem. In all candidates so far even after 18 month of implantation no infections and rejections have occurred and all systems where still functional.

It is even reported that the patients where able to recognise separate spots of light and even different colors were observed. Still testing proposes that using better models for the processing of the pictures taken by the CCD camera and increasing electrode density will lead to a picture-like assembly of these yet uncontrolled spots of light. In this way there is good hope that it will be possible to implant fully functional devices within the next 10 to 20 years. Still lots of research needs to be done to reach this highly defined goal.