Implantable Neural Electrodes

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Nerve and muscle cells communicate by transmitting electrical charges comparable to today's technical electronic systems. Hence, trying to treat a medical condition based on an insured or diseased neural or neuro-muscular system by using an electronic treatment device is a rather obvious, promising and very often successful approach. The electrical contact between the electronic device and the biological target is named electrode and - in case of multiple individual contacts - an electrode array. Communication between nervous system and technical system is performed by transfer of electrical charges and works in both directions, permitting to send information to the nervous system by electrically exciting voltage sensitive nerve cells as well as monitoring nervous system electrical activity. This bi-directional communication works very reliable. In fact, reliable enough to make this method the key technology in all modern cardiac pacemakers which are considered life-sustaining devices. Although, transferring electrical charges from one system to the other appears to be trivial at first sight, we have to consider that the biological system utilizes ions as charge carries while electronic systems work by exchanging electronics (or holes). As a consequence, an electrode acts as interface, converting ionic current flow to electronic current flow and vice versa. By doing so, an electrode can only convert a certain amount of electrical charge before building up a critical voltages across its boundary between the aqueous phase (biological system) and the metal (technical system). Its behavior resembles that of a capacitor, which breakdown voltage is in the range of about □ 1 V. Exceeding save voltage limits by injecting a too large charge causes water molecules to dissociate, accompanied by a local pH drift, possibly leading to electrode corrosion and eventually to device failure and biological tissue irritation. But even at electrochemically safe conditions, many metals are likely to corrode when exposed to the harsh body liquids and are therefore unsuitable bio-electrode materials. However, a set of materials demonstrated excellent corrosion resistance and also proved to be non-toxic, making these materials, among other properties, biocompatible. State-of-the-art pacemaker electrode materials are Platinum, Platinum-Iridium, stainless steel, cobalt-based ('super') alloys (e.g. MP35N, Eligloy), and titanium nitride [Love, 2006]. These electrode contacts are joined to wires, usually by laser welding. The wires have to be very corrosion resistant and mechanical tough electrical conductors, for which super alloys, stainless steel or platinum-iridium are favored. The wires are electrically insulated against the body and in multi-wire cables against each other by a polymeric insulator. This insulator must be biocompatible, have good electrical insulation properties, high mechanical strength and must not degrade inside the body. Insulators used in commercial implanted devices are medical grade silicone rubber, polyurethane (elastomer), polyimide, polyesterimide and fluoro-polymers (e.g. FEP). Today's implanted devices that are commercially available for long-term (> 30 days) human implantation use rather limited numbers of such electrodes/wires to interface with the nervous system. E.g. cardiac pacemakers have 2-4 electrode contacts, neuro modulators that are used for reduction of chronic pain sensation use 8-16 electrodes, cochlear implant used for electrical generation of sound impression by profound deaf patients also typically use 16 electrode contacts. An implantable device by Second Sight Medical Products Inc. achieved European Market approval in 2011, utilizes a 60 contact electrode array placed on the retina for restoration of vision in blind patients. For sub-chronic use (implantation time up to 30 days), electrode arrays of larger channel count (typically 64) are implanted onto the cortex of epilepsy patients for localizing pathological tissue. Since the cables of these so-called electrode grids protrude through the skin, these patients are a welcome test population for researches to do fundamental studies eventually leading to the

development of chronically implanted brain-machine-interfaces. Visual implants and brain-machine interfaces are two examples of a new generations of implanted devices that require high density electrode arrays with many contacts for locally highly selective interfacing with the nervous system. However, traditional implant fabrication technologies might not be suitable for producing higher electrode densities. In general, there is a strong discrepancy between the technologies used today in commercial implants and these developed in the academic research environment. A major reason for that is the long time spans associated with the process of approval of the highly regulated process required for commercialization of active implantable medical devices, which is prolonged by proving that a novel fabrication technology or material is actually safe and efficient. The vast majority of today's academic research activities in the area of implantable electrode arrays takes place without taking too much into consideration if the technology under investigation is suitable for later approval but rather focuses on animal experiments, and episodically, on clinical human trials. Not restricting themselves to traditional implant materials opened the world to materials used in micromachining methods, initially developed for electronic integrated circuit production. Micromachining technology based on photolithographic patterning of metals, semiconductors and insulators permits the fabrication of electrode array in the dimensions of single cells (some micrometers). First approaches based on silicon substrates have already been developed in the late 1960, using thin-film metallization (some 100 nanometers film thickness), insulated with a silicon dioxide layer [Wise, 1969]. These devices became and still are very popular in the neuroscience community as a tool for fundamental studies on the nervous system. Twenty years later, polymeric substrates (e.g. polyimide) were introduced [Shamma-Donoghue, 1982] leading to ultra-flexible micromachined neural electrode arrays, allowing the fabrication of e.g. surgical suture-like multi-contact nerve electrode arrays for penetrating peripheral nerves, or cuff-like neural electrode arrays that are wrapped around the peripheral nerve. Both, polymer-based and silicon-based technologies were continuously improved, permitting the realization of three-dimensional electrode arrays that resemble brushes consisting of individual filaments, each carrying multiple electrode contacts, up to 1024 per array [Hetke, 2002]. These devices provide highly localized coupling between the technical system and a volume of the nervous system, which could be a section of a peripheral nerve or a section of the central nervous system. A major difficulty in the development of very high-density electrode is associated with the wiring, which is required for linking each contact to implanted electronics and which usually is more space demanding than the actual electrode array. A solutions to this problem is the integration of electronic circuitry (multiplexer etc.) inside the silicon-based electrode arrays. Another limitation in miniaturization is the capability of the electrode contact to pass electrical charge without damage. The smaller the electrode contacts, the lower the limit of safe charge injection. This aspect is addressed by a variety of electrode coatings that improve the charge injection capacity, either by providing a very rough surface (effectively increasing the surface area) or by using high performance materials such as sputter-deposited iridium oxide or doped conductive polymers (e.g. PEDOT). New approaches of combining electrical coupling to the nervous system with other coupling modes immerged in the past 15 years, starting with shaft-like electrode probes that use microfluidic channels, allowing to locally administer pharmaceutical agents to the neural tissue [Hetke, 2002]. Additionally, electrode arrays received integrated sensors, monitoring pH, temperature, mechanical stress, or the presence of chemical substances (e.g. neurotransmitters), etc.. The past years brought the dawn of optogenetical methods, modifying the membranes of particular cell types in neural tissue by injecting of a fluid containing viruses that alter the cells genes. Exposing these cells to light of a matching wavelengths permits to locally inhibit or facilitate electrical activity in the gene-transfected neuron population. Neural electrode arrays are currently

developed that have electrical stimulation and recording contacts, microfluidic channels for controlled release of gene-transfecting viruses as well as optical waveguides for introducing light of the desire wavelength into the targeted tissue. These electrode arrays promise to be a new powerful tool in fundamental neuroscience. However, time will tell if these methods will also be suitable for treating patients with neural or neuro-muscular conditions in a clinical setting.

References

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