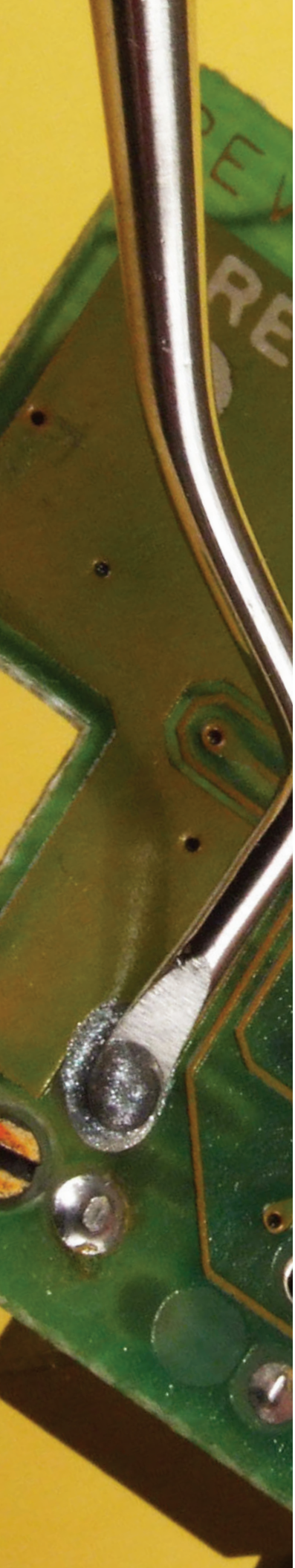

MASTERBOND®
CASE STUDY

EP3HTSMed Novel Microchannel Array for Assessing Nerve Regeneration in Potential Prosthetics

Master Bond Inc. 154 Hobart Street, Hackensack, NJ 07601 USA
Phone +1.201.343.8983 | Fax +1.201.343.2132 | main@masterbond.com

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Application

Recent advances in robotics have been used to improve the functionality and utility of prosthetic devices for persons with amputations (PWA). Despite the advancements, the integration of upper and lower limb prostheses still faces many challenges in enabling truly biomimetic functionality between the user and the prosthetic device.[1] An ideal prosthesis would possess bidirectional neural communication—existing neural signals from the user could be interpretated and sent to the device resulting in actuation while sensors present on the device itself would send signals back to the user's nervous system providing sensory feedback. Long-term efficacy also requires that the device have a high biocompatibility, enable nerve regeneration, and impart limited pathology to the remaining nerve fibers and surrounding tissues.

More simplistic devices are low resolution and utilize skin surface electromyography (EMG) to capture and process signals from residual muscle fibers in the effected limb enabling communication to the prosthetic device; these techniques provide limited biospatial resolution and limit the intuitiveness of the user interface. Other devices utilizing implantable microarrays provide a high degree of resolution as they can measure signals from individual nerve units; however, these devices have limited clinical efficacy as the mechanical stiffness of the interface results in damage to the nerve fibers. Recent advances in the field explore regenerative microchannel peripheral nerve interfaces that provide sensory and control communication with a high degree of resolution and selectivity while employing mechanically compliant interfacing materials to support the health of the existing nerve.

Previous studies have demonstrated that the size and geometry of the channels may negatively affect the health and proliferation of the existing nerve via chronic inflammation and mechanical compression. The authors, Maimon et al, sought to devise and test a novel microchannel array with 16-20 channels and assess the extent of nerve regeneration that is critical to the long-term efficacy of these devices. Both active and passive types were tested with one of the active types including an axially oriented collagen scaffold that was hypothesized to allow for greater nerve proliferation while minimizing incompatibility and inflammatory response. The extent to which an input signal applied to a nerve resulted in muscle firing was evaluated along with electromyography data. Immunofluorescence was employed to determine the extent of motor nerve regeneration within the microarray channels. The devices constructed utilized Master Bond EP3HTSMed, a USP Class VI certified, highly conductive epoxy for use in medical device assembly.

Key Parameters and Requirements

Adhesives and sealants used in the construction of implantable medical devices must meet strict biocompatibility and toxicity requirements. The United States Pharmacopeia, USP, maintains rigorous protocols that must be undergone prior to the use of any plastic, rubber, adhesive or sealant in a medical device—depending on the nature of the product, different requirements must be met. Of the USP's requirements, Class VI certification is the most rigorous and requires tests to assure that the material or its leachates will impart no systemic toxicity to the subject. This testing protocol requires the test material to be extracted with a suitable solvent, such as polyethylene glycol or a sodium chloride solution, with this

extract then being injected intravenously and intracutaneously into a test animal. During the prescribed period, the test animal is monitored for various symptoms that may indicate the potential for systemic toxicity. Additionally, the product material itself will be implanted with subsequent observation for signs of toxicity. Any adhesive or sealant used in the construction of an implantable microarray device must then meet the USP Class VI requirements. The authors chose Master Bond EP3HTSMed which is certified to be compliant with USP Class VI.

The authors used standard fabrication methods in the construction of the microarray devices.[1] Photolithography was used to define an SU-8 mold onto a silicon wafer—a 200 μm layer of Elastomeric polydimethylsiloxane (PDMS) was then spin-coated onto the mold and was then thermally cured. The spin-coated PDMS layers were removed and this process was repeated to create multiple PDMS layers that were then stacked, aligned and bonded. Metallic tracing integrated into a ribbon cable was used to electrically connect each electrode in the array via a percutaneous port to external recording and stimulating devices. Master Bond EP3HTSMed, a silver-filled conductive epoxy meeting USP Class VI requirements, was used to secure and seal the electrical connections with the through-holes of the ribbon cable. Pin-grid array (PGA) techniques were used to connect the microchannel array, bond pads and the ribbon cable with all connections being done with Master Bond EP3HTSMed with the final interface being embedded in silicone. **Figure 1** includes images of the various component assemblies as well as the final construction.

In addition to the USP Class VI requirements for biocompatibility, an epoxy system used in this type of application must have a high degree of conductivity to provide a sound electrical connection. Master Bond EP3HTSMed is a conductive, silver-filled epoxy system possessing exceptionally low volume resistivity of <0.001 ohm-cm. This epoxy system exhibits high shear strength and a convenient and rapid cure schedule. Master Bond EP3HTSMed is a single-component system with an unlimited working time at room temperature providing for forgiving assembly and rapid cure in 20-40 minutes at 300°F.

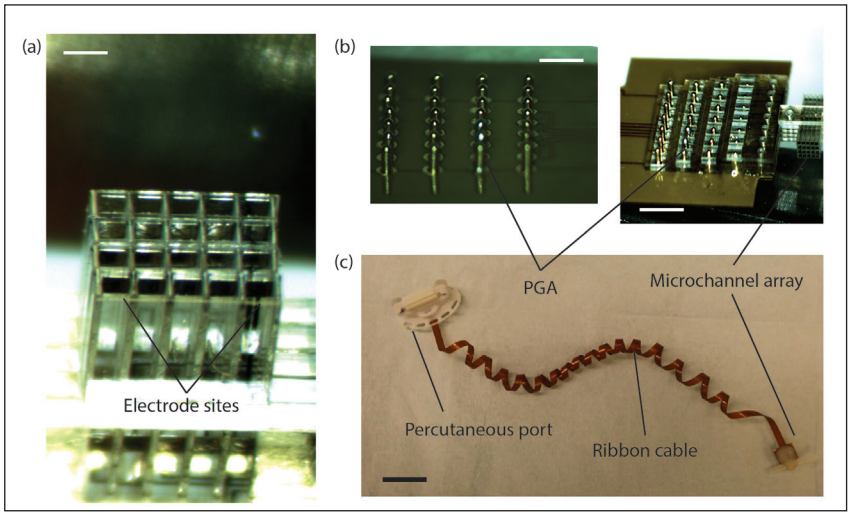

***Figure 1.** The assembled SU-8 microchannel array with Pt electrodes (a), Electrical connections between array electrodes and ribbon cable performed with PGA techniques (b), Overview of system including the microchannel array, ribbon cable and the percutaneous port.*[1]

Results

Five months after implantation of the devices into the test animals, rats and ferrets, the authors conducted tests to ascertain the extent of nerve regeneration within the channels using EMG recordings and immunofluorescence. The discussed work employed larger channels, 200 μm, in an attempt to avoid constriction of the thick layer of connective tissue that encapsulates growing axons during regeneration; this adverse effect was reported in a previously published work using 110 μm channels.[1] They found that this increase in channel size did not show a significant increase in axon counts nor did it address the issue of tibial nerve fibers regenerating around the device itself. This suggests that the chronic inflammation due to the presence of a foreign object or its resulting mechanical pressure during the nerve regeneration process is geometry-independent. The axially oriented collagen scaffold used in one construction did not show any benefit in inhibiting neuroma formation suggesting that this material is still being interpreted as a foreign body during the five-month nerve regeneration period. This work contributes significant information to understanding nerve regeneration in the context of biomimetic prosthetics and provides additional insights into the design of future studies within this field.

References

[1] Maimon, B., Zorzos, A. N., Song, K., et al. (2016). Assessment of Nerve Regeneration through a Novel Microchannel Array. International Journal of Physical Medicine and Rehabilitation. 4:2. DOI: 10.4172/2329-9096.1000332