Recent Advances in Implantable Medical Systems with Highly-Heterogeneous Integration

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Abstract: ***Future implantable biomedical systems will require power and data telemetry with multiferroic interfaces, signal modulation, low-impedance electrodes with high current injection, remateable connectors - all in a highly miniaturized form-factor with reliability in a reactive aqueous environment. They provide a combination of functions such as neural recording and stimulation, imaging, spectroscopy, electrochemical sensing and others. They, thus, drive the most advanced heterogeneous integration. Advancing system components and their 3D connectivity in small form-factors are both critical to realize such future medical implants. The system components are advanced through innovative nanomaterials, multiphysics-based material designs to achieve the performance metrics, and hybrid additive and semi-additive manufacturing technologies. The integration technologies rely on advanced chiplet fan-out embedding technologies in flexible or rigid-flex substrates that provide seamless but reliable interconnect technologies between the system components. This article will briefly review some of the key functional packaging build blocks towards these heterogeneous 3D implanted medical systems.***

I. INTRODUCTION

Implantable biomedical systems represent the most complex class of heterogeneous systems. They require high functional densities in highly-miniaturized 3D packages, with thin form-factors that are determined by physiological and surgical constraints, and reliability under aqueous and aggressive reactive environments. The systems perform critical functions such as neural recording and stimulation or condition-monitoring through specific biomarkers. These sensors utilize various other modalities such as biophotonics through near-infrared or fluorescence spectroscopy to detect the concentration of critical biomarkers such as glucose, blood oxygenation for hemodynamics or others and wirelessly communicate to an external reader. This requires power and data telemetry, sensing interfaces, and associated data modulation and conversion, all of which lead to the most complex electronic function in a single miniaturized package. The underlying heterogeneous integration technologies are dependent on the power and data rates, size constraints, and process maturity for implantable medical devices. The most important factor for implantable biomedical systems is to be hermetic in aqueous and reactive aging conditions. Hermeticity protects the electronic system from water and reactive chemicals in the target tissue environment. Furthermore, cardiac pacemakers, neural recording systems and neural stimulators also need to provide remateability in a surgical environment. Addressing remateability in electronic packaging would benefit surgeons to troubleshoot failed components and allows minimal intervention to disassemble and reassemble the system.

Because of the reliability constraints and long R&D cycle time to qualify new technologies, implantable medical products tend to utilize pre-approved or established materials and technologies for shorter time to clinical use, while customizing the design and integration advances with power sources, electrode or sensing interfaces to the specific application. In typical implantable technologies, the primary electronics package is sealed in a titanium case with ceramic feedthroughs, with PtIr wire electrodes of high strength and reliability that extend to the target locations. For battery-driven, low-power applications that support few channels, low stimulation current, low duty cycle and long-term applications such as pacemakers, the 3D technologies within the titanium include stacked ICs and packages for signal conditioning and data processing, batteries, capacitors, power regulation and other functions. Key innovations are driven by this existing framework where the titanium case supports a highly-integrated 3D electronics module.

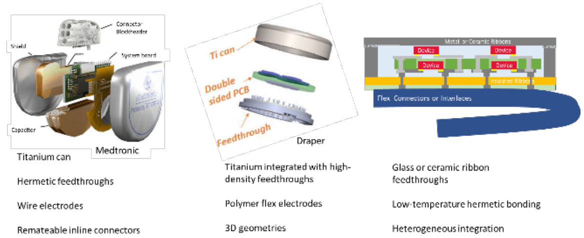

Figure 1: Biomedical devices from titanium can with wired connectors, high-density feedthroughs with titanium connected to flex, and miniaturized 3D packages extended to flex. [1]

For emerging higher-power density, but miniaturized systems such as those used in neuroprosthetics (ex: retinal prosthetics, brain-machine interfaces), the hermetic package supports dozens of feedthroughs, titanium cap and gold braze to achieve higher interconnect density to the external electrode array. The neural interfaces in this case are typically based on microwire bundles, polymer flex electrodes or vertical high-density pin electrode arrays. The trend of Pt feedthroughs in thick-film alumina is now leading to ultraminiaturized glass or ceramic ribbon feedthroughs that can achieve much higher interconnect or channel density with the flex electrode array without compromising reliability. This trend is illustrated in Figure 1, showing implantable systems based on metal can with feedthroughs on the left, migrating to smaller geometries with planar or cylindrical geometries, and eventually to thin electronic nodes or motes that are so miniaturized that they are now being visualized as grains or dust.

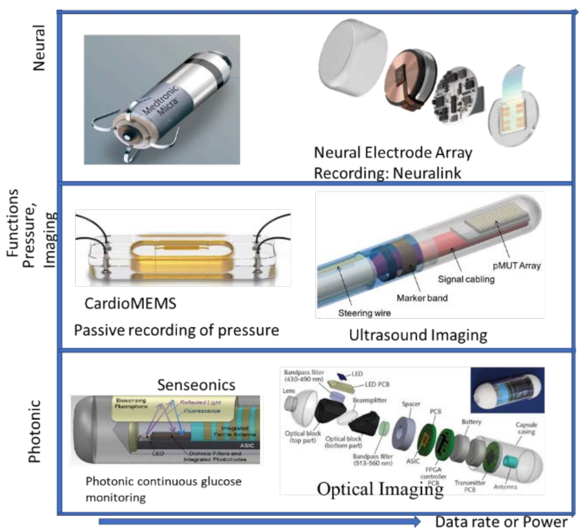

Figure 2: Spectrum of biomedical devices for health-monitoring, imaging, spectroscopy and neural recording. [Neuralink [2]; Camera pill [3]; Glucose fluoroscence monitor [4], CardioMEMS pressure sensing [5]; ultrasonic imaging Array [6].

More functional medical systems incorporate imaging with higher telemetry bandwidth. These are injected into the body as wireless camera pills or endoscopes or smart imaging catheters that can collect images, process them and communicate them to outside. For such wireless imaging systems, the heterogeneously-integrated 3D system is packaged into a cylindrical pill with electromagnetically and optically-transparent windows. The system components involve antenna and RF transmitter on one end, lens + CMOS camera + ASIC on the other hand, with a battery in the middle. This 3D package pill can communicate images to an external reader around the waist. Alternative ultrasonic imaging systems are based on piezoelectric arrays (256-512) that are 3D integrated with a flex using silicon interposers with through-vias to underneath flex that support the signal processing chips. Emerging 3D heterogeneously-integrated package architecture details of these systems are illustrated in Figure 2.

Thin and flexible hermetic ribbon packages will have pervasive role in all future neuro, spectroscopic, imaging and multimodal sensing technologies. However, present flex-packaging only focuses on discrete and prepackaged components, limiting their ability for integration in hermetic ribbons. Embedded and fan-out interconnects with thin bare dies or their sub-units such as chiplets will enable such hermetic packages where the chiplets are embedded in the flex core, and sandwiched between metal-ceramic ribbon windows. Strength and handling are a major concern at smaller thickness. Ultra-thin and ultra-tough hermetic ribbons are the need of the future. These are extended with low-electrical impedance and mechanically-compliant nanoelectrodes for higher sensitivity to low voltage neural signals and also to inject higher current at lower voltages for stimulation. The team at FIU are advancing such flex ribbon packaging to not only include the signal processing and photonic chips, but also with miniaturized high-power-density modules, drivers and switches to control the timing of the LEDs and integrate the wireless sensing. This report highlights some of the recent advances in implantable device packaging.

II. RECENT ADVANCES IN IMPLANTABLE SYSTEM BUILDING BLOCKS

Zero-power Passive Neural Recording: For neural recording, biosensing or other monitoring functions, biomedical systems are going through major innovations that are driven not only by advances in the sensing interfaces but also through new simplified signal conditioning and data telemetry topologies. In the simplest architecture, a zero-power telemetry scheme is widely adapted to monitor neural activity at critical areas. The incoming RF signal is backscattered to carry the neural signal with it, which can be demodulated through an external reader. The measured action potentials are wirelessly communicated through the backscattered RF signal that carries the sensing information, as shown in Figure 3. Such topologies do not need power telemetry and rectification as the internal components do not need any DC bias, and are completely passive. FIU has recently advanced such passive neural recording with thin flex substrates, as shown in Figure 3. With topology advances, continuous recording neural potentials of 15-20 microvolts are now showing to be feasible with this approach [7, 8].

Multiferroic power telemetry: For most wireless sensing applications, the sensing signal needs to be conditioned through analog and digital signal processing chains, load modulation, timers and switches. All these need DC bias and hence a power telemetry link with rectification is needed in all these cases. Therefore, one of the key features of implantable bioelectronics is wireless power telemetry. Most batteryless implantable devices are based on magnetically-coupled coils referred to as inductive links. These near-field links not only power the devices but also to modulate the load of an incoming RF signal and backscatter to provide the data. However, the receiving coils are usually limited in size because they are implanted in the human body, which may affect the power transfer efficiency as the mutual coupling and Quality factor dramatically reduces with size. In order to achieve higher power transfer efficiency, new transduction mechanisms based on multiphysics phenomena such as piezo-magnetostrictive coupling is developed for telemetry in unprecedented geometries of sub-mm dimensions. Piezo-magnetostrictive power telemetry is advantageous compared to pure piezoelectric power delivery because it can be focused with magnetic lenses better than ultrasonic power but also because the maximum magnetic field power input inside the body at low frequencies is 100 mW/mm^2 as opposed to ultrasonic power with 10X lower limits. Unlike inductive link, the delivered power can retain high power transfer efficiency even with smaller receiving units. By utilizing piezo-magnetostrictive stacks as flexible films, power sources can be thus integrated in the flex package core. This approach is illustrated in Figure 3 through a biophotonic package on Metglas®/PVDF/Metglas® stack.

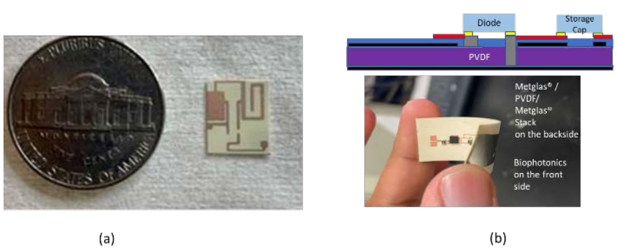

Figure 3: FIU's advances in passive (zero-power) neural recording (a). Leadframe molded diodes (not shown) are assembled to complete the circuit. Wireless biophotonic system with piezo-magnetostrictive power telemetry inside the flex carrier (b).

Hermetic feedthroughs: Ceramic-to-metal feedthroughs are the universal "gold" standard in implantable medical devices such as pacemakers and cochlear implants. Ceramic feedthroughs are stronger and more reliable, enabling a key paradigm shift in high-reliability packages. Through-glass via interposers (TGV) are being widely studied for high-bandwidth 2.5D interposers in high-performance computing. For biomedical implants, the via density is not as high but need to be hermetic, with biocompatible metals such as platinum, tungsten or others. The TGV interposer is manufactured from high-quality borosilicate glass, fused silica, and sapphire to adhere to hermeticity and biocompatibility requirements. Schott Promoceler® designed a process for glass-metal feedthroughs with high thermal expansion coefficient glass that enables it to firmly shrink onto the tungsten vias to create a hermetic seal, as illustrated in Figure 4. Hermiticity of 10^{-12} millibar - liter/second was achieved. Glasses have ~10x higher compressive strength than its tensile strength. Bonding flex electrode arrays to the feedthrough pads is the next challenge.

Figure 4: Evolution of feedthroughs from cofired ceramic-platinum to glass feedthroughs, further aided by glass-to-glass seamless bonding [9, 10].

Remateable Connectors: The need for remateable interconnects increases as the complexity of implantable systems escalates with higher electrodes counts and connection nodes that extend to various parts of the body under the associated physiological constraints. The remateability feature provides the ability to connect and disconnect different components for troubleshooting, such as during component failures, without the need for removing the whole system. Universal requirements of remateable interconnections can be defined in terms of mechanical, electrical, thermal, material, and reliability performance. In terms of mechanical performance, insertion, extraction, and retention forces must be low while retaining low contact resistance. The prevalent remateable connectors are based on linear array of axially-arranged pins with ring contacts on the male side that are pressed against a terminal spring contact on the female side. This concept has been adopted in generations of neuroimplants as a "gold" standard [11]. The technology is advanced to utilize PtIr springs and gold ring contacts to allow a linear array channel system with low retention and extraction forces on the compressible springs. The configuration allows self-interlocking and provides a near-hermetic seal by adding microscrews as redundancy. This trend is illustrated in Figure 5. Remateable connectors are further advanced by Jung et al. [12] to achieve a multi-channel inline connector system that addresses the current limitations of inline connectors such as expandability, contamination, and replaceable parts caused by wear and tear. An innovative approach to address this problem was demonstrated by FIU using compressible and deformable z-elastomer interposers [13]. The designed test vehicles consisted of a z-interposer in a flexible liquid crystal polymer (LCP) substrate that can be interconnected with feedthroughs, all clamped together using microscrews for a strong connection. Such flexible area-array remeatable interconnects are now being qualified for hermiticity to achieve performance stability without compromising the reliability of the interconnects.

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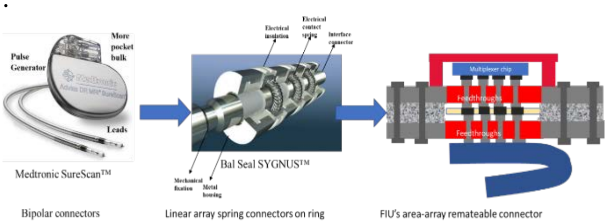

Figure 5: Evolution of remeatable connectors for implantable devices from linear spring-locked pins to area-array connectors [14].

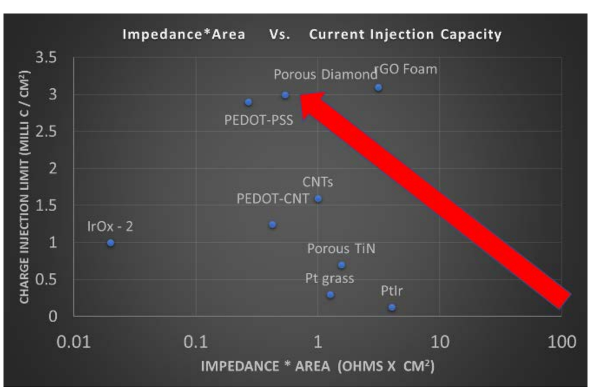

Figure 6: Low-impedance electrodes with high surface area and high-current injection electrodes for neurostimulation and recording. Redrawn from [15].

Low-impedance Neural interfaces: The most prominent materials used in electrodes for neural recording and stimulation are linear wire arrays of Pt-Ir. These are proven for long-term use in peripheral nervous systems under complex physiological environment where the wires are subjected to bending and twisting loads. The impedance of the electrodes is largely determined by the area of exposure of the metal. The high impedance of current electrode structures limits the selectivity of neural signal. Lowering the impedance increases electrode sensitivity and increases the electric change transfer during stimulation. Since the increased surface area is directly related to lowering of impedance, nanostructured surfaces that can increase the surface area without increasing the lateral electrode dimensions are utilized to improve signal quality and miniaturize the electrodes for safer surgical procedures. Such electrodes should also be reliable against mechanical loads and long-term chemical stability of surface without degradation. Porous platinum black coatings, activated iridium oxide, or gold pillars coated with PEDOT-PSS (poly(3,4-ethylenedioxythiophene – polystyrene sulphonate) are emerging as candidates because of their electrochemical, chemical and mechanical stability. This trend is illustrated in Figure 6 through a material map where the current injection limit and the normalized impedance are shown on each axis.. We recently advanced this approach with biocompatible porous metal wire electrodes of more than 100X increase in area, leading to low-impedance interfaces. These electrodes architectures with sintered nanometal are readily compatible with existing PtIr microwire arrays, resulting in faster time to clinical use with minimal disruption to the product architecture.

III. SUMMARY

Implantable biomedical implants drive the most advanced heterogeneous integration technologies at nanoscale with next-generation materials and processes in order to improve functional density, and reliability in the required form-factor. Key building blocks in all these technologies involve high-density feedthroughs, remateable connectors, hermetic sealing and functional integration to advance sensing, power, and data telemetry. This article highlights such key building blocks. In the future, power sources, photonics, analog signal chain, wireless communication interfaces will be co-packaged by embedding and fan-out interconnects, leading to high performance with physiology-driven form-factors through true heterogeneous system integration.

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