



HETEROGENEOUS INTEGRATION ROADMAP

2020 Edition

Chapter 4: Medical, Health and Wearables

<http://eps.ieee.org/hir>

The HIR is devised and intended for technology assessment only and is without regard to any commercial considerations pertaining to individual products or equipment.

We acknowledge with gratitude the use of material and figures in this Roadmap that are excerpted from original sources.
Figures & tables should be re-used only with the permission of the original source.



Table of Contents

To download additional chapters, please visit
<http://eps.ieee.org/hir>

CHAPTER 1: HETEROGENEOUS INTEGRATION ROADMAP: DRIVING FORCE AND ENABLING TECHNOLOGY FOR SYSTEMS OF THE FUTURE	
CHAPTER 2: HIGH PERFORMANCE COMPUTING AND DATA CENTERS	
CHAPTER 3: THE INTERNET OF THINGS (IOT)	
CHAPTER 4: APPLICATIONS FOR MEDICAL, HEALTH AND WEARABLES	
EXECUTIVE SUMMARY	1
INTRODUCTION	1
SCOPE	3
DRIVERS AND EXAMPLES	3
INTERCONNECT REQUIREMENTS	6
SUBSTRATE MATERIALS, TRACE FABRICATION, AND ASSEMBLY	7
EXAMPLES OF RECENT ADVANCES AND EMERGING TECHNOLOGIES	9
MATERIALS AND POWER	12
CHALLENGES.....	12
CHAPTER 5: AUTOMOTIVE	
CHAPTER 6: AEROSPACE AND DEFENSE	
CHAPTER 7: MOBILE	
CHAPTER 8: SINGLE CHIP AND MULTI CHIP INTEGRATION	
CHAPTER 9: INTEGRATED PHOTONICS	
CHAPTER 10: INTEGRATED POWER ELECTRONICS	
CHAPTER 11: MEMS AND SENSOR INTEGRATION	
CHAPTER 12: 5G COMMUNICATIONS	
CHAPTER 13: CO DESIGN FOR HETEROGENEOUS INTEGRATION	
CHAPTER 14: MODELING AND SIMULATION	
CHAPTER 15: MATERIALS AND EMERGING RESEARCH MATERIALS	
CHAPTER 16: EMERGING RESEARCH DEVICES	
CHAPTER 17: TEST TECHNOLOGY	
CHAPTER 18: SUPPLY CHAIN	
CHAPTER 19: SECURITY	
CHAPTER 20: THERMAL	
CHAPTER 21: SIP AND MODULE SYSTEM INTEGRATION	
CHAPTER 22: INTERCONNECTS FOR 2D AND 3D ARCHITECTURES	
CHAPTER 23: WAFER-LEVEL PACKAGING (WLP)	

Chapter 4: Applications for Medical, Health and Wearables

Executive Summary

With increasing interest in miniaturization, there is a need for packages that provide greater functionality in a smaller space. This technology roadmap recognizes miniaturization as a major driver in consumer-electronics-based health monitors, diagnostics devices, and aids, as well as implantable medical devices. While traditional

medical electronics remain conservative in the adoption of advanced packaging and assembly technology, the emerging area of connected and distributed healthcare (including wearables attached directly to the skin) is in the early stages, and many new materials and assembly methods are in development. The roadmap outlines today's technology examples, including the materials and deposition methods, and discusses trends and challenges as the technology moves forward. The roadmap recognizes the need for the integration of heterogeneous electronics in a high-density design. Both 2D and 3D structures will continue in production. An increasing number of products will also need to communicate and send data, balance power and thermal budgets, and are expected to drive the use of radio systems. The roadmap for these devices is covered in the 5G/RF Communications chapter.

There is increasing interest in wireless medical and health monitoring. The adoption and continued innovation in flexible hybrid electronics is expected to drive this industry in the years to come. Miniaturization will drive the need for packages that provide greater functionality in thinner and smaller spaces for both medical-grade- and consumer-grade-based health monitors, as well as implantable and other medical devices. While traditional medical electronics may remain conservative in design, the adoption of flexible hybrid electronics for wearables is attractive due to the advantages in comfort and form factor. The integration of a variety of components and die (including thinned and unpackaged processors, memory, sensors, MEMS, RF, optical, etc.) together with printed circuits on thin flexible substrates will create the next generation of wearable medical systems. Many new materials, assembly methods and applications are demonstrated in the literature. Prototypes are available for evaluation from a variety of companies. The ability to integrate power sources (thin batteries, RF induction and energy harvesting), sensors (chemical, electrical, optical and MEMS), RF (components and communications) and displays in thin flexible and comfortably wearable formats will be critical. This chapter will describe these technologies, including target applications, materials, deposition methods, components, device integration, and reliability; it will discuss trends and challenges expected in the coming years. The following is an initial summary of flexible hybrid electronics applications for medical, health and wearable technologies that are relevant to the progress needed over the next 10 to 15 years.

1. Introduction

Medical and healthcare products including hearing aids – implantable devices such as pacemakers, defibrillators, and neurostimulators, as well as portable monitoring systems such as a smart inhaler – are increasingly challenged by the need for miniaturization. Miniaturization is a major driver in consumer electronics-based health monitors and aids, as well as implantable devices and portable systems. Manufacturers of cardio implants, such as pacemakers and defibrillators, and neurostimulators, cochlear implants, and insulin pumps are investigating the use of heterogeneous integration to achieve the goals of smaller form factors with increased performance. Novel heterogeneous SiP (System-in-Package) integration configurations enable these devices to meet user needs. MCPs (Multi-Chip Packages) have been in production for a few decades, primarily for improved time-to-market and for critical heterogeneous integration needs. A variety of package types are used, including lead-frame, wafer level packages (WLP), fan-out WLP (FO-WLP), and laminate packages such as land grid arrays (LGAs) and ball grid arrays (BGAs). Flex circuit is common across product types. Laminate substrates are also popular. Traditional interconnect methods continue to include flip chip and wire bond while embedded die solutions, where interconnect is realized by plating, are moving into production. New methods such as printed electronics and 3D printing are emerging. Roll-to-roll and panel processing are being adopted. Low power is key for many applications, and new developments in battery, battery management, and energy harvesting are needed. All these technologies have to be optimized for cost and at the same time be sustainably compliant to an increasingly aware customer base as well as global environmental legislations.

Market studies and industry literature [1] describe sensors for medical wearable applications and a detailed description of the currently available sensors, the application, the company that produces it, and its market

Send corrections, comments and suggested updates to the TWG chair, using our HIR SmartSheet:

<https://rebrand.ly/HIR-feedback>

(regulatory) status. Examples include: Cefaly, a forehead wearable for migraine headache prevention; Backtrack Skyn, a wrist wearable for blood alcohol monitoring; and CarePredict: Tempo, a wrist wearable ADL activity monitor. Applications for maternal and neonatal care that include Ovulation Tracking and TempTraq baby temperature monitoring are available. These devices are not limited to human use, and devices for veterinary applications that include multiparameter sensors for respiration, heart rate, and distance are also available.

Representative Sensors for Medical Wearables typically include the following types:

- ECG, PPG, Microphone, Inertial, Ultrasound, Electrochemical, Temperature, Pressure, EEG, and their wearable formats for which they are available are presented in a tabulated list (i.e., wristband, patch, headset, etc.)
- Optical and Electrical Sensors are described for the detection of heart rate, cardiac function, blood pressure, oximetry, and UV sensing.
- Ultrasound Sensors for urinary incontinence.
- Chemical Sensors for glucose monitoring, sweat, blood, and tears analysis
- Microfluidics for analytes collection using MEMS-produced microneedles and micropumps
- pH sensors in microfluidic patch and needle array formats
- Pressure Sensors for blood pressure monitoring, respiratory monitoring and treatment (eg, sleep apnea), gait analysis, and strain gauges for interocular pressure measurement (glaucoma).
- MEMS microphones for use in hearing aids and cochlear implants.
- Inertial Sensors for rehabilitation monitoring, activity tracking, and fall detection.
- Dosage and fluid level counting.
- Thermopiles for body temperature monitoring, especially for women's health (i.e., hormone changes).

Medical Wearables Supply Chain

This section describes the suppliers and manufacturers of sensors and systems that make up the wearables ecosystem. These are strongly linked to IoT and mobility products and also require IT networks, cloud computing, software, and AI developers. The ecosystem is evolving such that single sensor producers are working to develop multisensory capability, and eventually devices with fully integrated multiplexed sensing, analysis, and communications capability.

Challenges:

- Current wearables such as activity trackers do not have sufficient accuracy to be used for medical applications.
- In the consumer market for medical wearables, the user is a consumer, not a patient, leading to variability in device use and thus data.
- Standards have not yet been set to ensure consumers, patients, and doctors can rely on data integrity across many devices.
- Mobile Phone applications are needed for use with smartphones capable of interfacing to new devices.
- Data use acceptance within the medical community.

General Technology Trends:

- Increasing miniaturization
- Lower Power consumption and Energy production/harvesting
- Increasing Accuracy
- Increasing Connectivity
- Shape, flexibility, and conformance improvements for wearability
- Toward noninvasive skin wearable
- From electrochemical toward optical sensing

Market studies [2] describe the global forecast for growth in the medical wearable device markets from 2018 through 2024. The report shows revenue growth, during this period, increasing from \$7B to \$32B. The sale of sensors for medical device applications will dominate the growth with an increase over the period (of approximately 21.6%) to \$2.8B. In 2018 the dominant sensors were pressure and microphone units integrated into respiratory and hearing aid devices. The largest growth areas will be devices for sensing respiratory and movement disorders, metabolic and

cardiovascular monitoring, blood glucose level monitoring, and drug delivery. These will be primarily incorporated in banded wearable devices such as smartwatches. Such applications are enabled by shrinking size and increased functionality of microelectronic sensors capable of near-field wireless communication to increasingly ubiquitous smartphones, which in turn are able to easily connect to the internet. This provides a grand scheme of interconnection for data transmission in support of medical monitoring and diagnostics.

Currently, no wearable products with high conformability and flexibility have successfully reached the market, although this is indeed the goal. The majority of currently marketed wearables are for fitness monitoring including heart rate, activity, sleep quality, and temperature, and are incorporated into wrist-worn (89%) smartwatches. Developers are focusing on multiplexed sensing devices that integrate multiple sensing capabilities (with lowest power consumption and added energy harvesting) into flexible and conformal (e.g., skin wearable) packaging formats. These will require the development of thin and flexible sensor, logic, memory, and battery components. Currently, many new and novel sensors are under development such as those for sleep apnea, oxygen diffusion to track wound healing, and for chemical analysis of biofluids such as sweat, saliva, blood, and tears.

Limitations in the use of wearable medical devices include high cost, incompatibility across all smartphone operating systems, and a lack of data format standards. Devices must not only be comfortable, but also their proper use is dependent upon the wearer and as such are prone to variable responses. There is also a lack of understanding by medical professionals relating to how to acquire, utilize, and interpret data. In terms of device vetting, there is also a lack of available data supporting their safety, accuracy, reliability, and effectiveness, all necessary for the establishment of regulatory standards for their manufacture, performance and use. As evidence, very few Class II and Class III flexible wearable medical devices have been approved for sale in the US due to the need to meet ISO standards and gain FDA approval. These approvals can delay marketing of a medical device significantly. In the US the typical time (delay) required for launching a new medical device due to these approval requirements is 1-3 years, compared to a much shorter (typical) 45-day delay for marketing non-medical consumer electronics. For globally marketed products, even more regulations may apply.

2. Scope

This roadmap chapter has a two-fold purpose:

- Define products and their packaging requirements.
- Examine materials and package trends, including substrate materials and features.
- Analyze new manufacturing trends such as flexible manufacturing with printed electronics.
- Devices continue to be populated with a wide variety of sensors such as air quality particle counters, humidity, temperature, pH. Currently several of these sensors are discrete and need individual assembly to the substrate i.e., PCB. This drives the size of the smart device larger than the predecessor. Miniaturization and integration structure that do multi-modal sensing will help enable smarter but thinner devices.

The chapter is organized into three primary areas:

- Product examples including the substrates, devices, interconnect methods, and packages
- Substrate trends
- Manufacturing trends
- Challenges

3. Drivers and Examples

"Nanopackaging for Component Assembly and Embedded Power in Flexible Electronics: Heterogeneous Component Integration for Flexible Systems" [3] describes which applications and products drive the growth of flexible and printed electronics. Drivers typically include flexible displays, aviation and automotive, wearable health and medical devices, bioelectronics, and devices for IoT. The functions of a flexible package may include sensing, computing, communication, and power management. Flexible electronics have requirements different from traditional print-and-etch rigid PWB electronics. They require:

- Flex Substrate: supports wiring and components
- Interconnection and component assembly: Flexible conductive adhesives, flexible (eg, nano copper) interconnects, new assembly technology i.e. thinned die pick and place, lower temperature solders
- Flexible power supplies/batteries/energy harvesting: solar, piezoelectric, thermoelectric, inductors, pyro- and triboelectric

- Printed discrete elements including flexible capacitors and inductors

General trends and expectations include:

- Flexible electronics typically require all components of the system be flexible.
- Majority of flex substrates are organic, and hence processing and applications are limited to lower temperatures.
- Commercial economic viability requires existing manufacturing infrastructure be adapted to fabricate these electronics.
- Materials for printing electronics on substrates are deficient in electrical properties compared to traditional materials i.e. lower-conductivity conductors, higher dielectric constant dielectrics.
- Inferior adhesion and materials (if used) mean lower resistance to stressing, and hence lower thermal and mechanical reliabilities.
- Energy storage capacity and power delivery is deficient compared to traditional devices. Conventional batteries and semiconductors do not perform as expected when stretched or bent, thus developments in materials and their combined usage are required here.
- Flexible electronics cannot currently match the transistor density of traditional rigid electronics. Hence, the requirement for flexible hybrid electronic devices.

Medical and healthcare products including implantable devices such as pacemakers, defibrillators, and neurostimulators, insulin pumps, hearing aids and cochlear implants, as well as portable image and monitoring systems such as smart inhalers, air quality monitors, continuous glucose monitors, and point-of-care diagnostic devices are increasingly challenged by the need for miniaturization. Miniaturized packaging for many sensor and human-machine interface (displays, radios) applications is required for healthcare products, including biometric sensors. Sensor and communication gateway and power use is expected to increase. Heterogeneous integration of electronics in a high-density design is required to not only reduce size but to integrate performance and reduce power consumption. An increasing number of products will need to communicate and send data, driving the use of radio systems that will also be in the form of heterogeneous integration.

Medical devices that are permanently implanted or used within the body for limited periods are constrained by considerations of the biocompatibility of the surfaces, hermeticity, and toxicity of construction materials. In many cases, the strength and rigidity or flexibility of the structure may be important for long term use. Surfaces in contact with tissue are often coated to minimize inflammatory responses and to prevent tissue damage. These considerations are application dependent and must be taken into account during the earliest stages of the design process, and will guide solution pathways, often requiring different materials than used in standard consumer electronics.

Medical implantable devices such as pacemakers have decreased in size, from when the first pacemakers were introduced as external units in 1957 to implantable devices that required surgery, and now to small leadless products that are a fraction of the size and do not require surgery. Both Abbott's (formerly St. Jude) Nanostim and Medtronic's Mica are delivered to the heart via a catheter snaked up through the femoral artery. Medtronic indicates its pacemaker required extremely dense electronics packaging. The integrated circuits are very thin and are stacked on top of each other and packaged in a very dense module. The laminate substrate is ultra-thin. The pacemaker has wireless functionality, so Medtronic redesigned its own wireless antenna integrated into the device. ECGs are also expected to use SiP. A prototype flexible hybrid electronics module 2-inches by 2-inches has been developed by i3Electronics to wirelessly monitor EEG output through a surface-mounted Bluetooth module attached to a patient. Modules include 8-channel (12 bit) analog-to-digital converters, SRAM, and flash memory. Examples of other technologies include:

- Neurostimulation modulation requires small form factor electronics, and many new packaging configurations are under investigation. [4] A typical product may contain two die and 100 passive components. These devices are mounted on a PCB substrate. Die sizes are typically 7 mm x 7 mm and include a transceiver. The requirements for neural stimulation probes include biocompatibility and hermetic connections. Implants under the cranium (skull) must be low power and highly efficient to prevent brain fluid temperature changes. [5] For long-term implant stability and to avoid scar tissue formation, the probes should have mechanical properties and surface chemistry similar to the surrounding tissue. [6]

- Smaller Cochlear implants that require miniaturization of electronics are under development. Pill cameras also need high-density packaging, including stacked die, to meet form factor requirements. In one example, three flip chip die and 96 SMT are mounted on the substrate and encapsulated. A full RF module contains five components (Transceiver, SAE filter, crystal, ferrite, and diode) plus an integrated passive device.
- Balloon catheters with electrodes for neurostimulation or ablation use extremely flexible ultra-thin two-layer liquid crystal polymer film (LCP) build-up with 50 μ m thickness. There is one thermistor per electrode, coupled with the thin film layers. The LCP has 25 μ m lines and spaces and one-sided Cu plating with 100% via-fill. The surface finish is electroplated gold on Cu for a short-term implant.
- Ultrasound imaging products typically use off-the-shelf components instead of custom devices. Devices include analog, digital signal processors (DSPs), and field programmable gate arrays (FPGAs). Ultrasound modules have been fabricated using 14 μ m line and space single-sided flex with 11 μ m line and space double-sided flex with 25 μ m through vias.
- Hearing devices (hearables) include ear buds, hearing aids, and Cochlear implants. Devices include MCU, audio CODEC, switches, battery chargers, Flash memory, amplifiers, controllers, and digital signal processors. Hearing aids originally used ceramic substrates, but many have transitioned to include FR-4 or BT-resin for the rigid circuit and flex circuit. In some cases, the flex circuit is folded, and multiple die are attached. Bending zones have interconnects between different assembly portions. Low loss dissipation is required for the substrate. Often an integrated electromagnetic shielding is used.

SiP formats include embedded die in Cu-polyimide flex circuits. In one structure the thinned die is embedded in an adhesive-based polyimide film flex circuit with Cu features. Conductive paste is used for via connections. The die are prepared for embedding with a fan-in RDL WLP process. Examples in production include embedding of a single die with 5 to 9 wiring layers with a total thickness of 280 to 500 μ m and a two-die stack with 10 to 13 wiring layers and a thickness of 580 to 700 μ m. In the future, three-die single stacks and two stacks will be in production. There will be 14 to 16 wiring layers and the thickness will be 800 to 980 μ m. The module size will be 9.9 mm x 6.6 mm x 0.85 mm with for the two stacks of three die each. The embedded die size is 3.2 mm squared, and the I/O pitch of the embedded chip is 0.4 mm [7].

Embedded subsystems in substrates for medical applications also include insulin pumps, cochlear implants, and cardiac implants. A two-layer SiP was fabricated with 35 μ m copper line spacing using a semi-additive process, and many fine blind and through vias were fabricated. Die stacking processes have been demonstrated. In one example the module was only of 3.48 mm x 3.48 mm x 1.5 mm [8]. Applications include:

- A Cochlear implant fabricated with LCP as a biocompatible material without copper for a long-term implant. Features are 125 μ m traces on 250 μ m pads and structures have 15 μ m lines and spaces. Au and Pt are used for electrodes. Au is used for good adhesion and flexible properties. The implant uses 90% wires of platinum and 10% iridium. Up to 24 wires are connected to an audio processor. The electrode array and coil are injected with silicone and cured. The final device is housed in a titanium block.
- A short-term embedded blood glucose sensor is embedded for 30 days in the human body and measures capacitive electric current charge; it is typically a three-electrode system with a counter electrode, a reference electrode, and a work electrode.
- Smartwatches and fitness bands are a wearable that may or may not be classified as medical devices. Devices in these products include Flash and DRAM, controllers, an RF front end module (FEM), heart rate sensor, application processor with modem, power management IC (PMIC), WiFi, Bluetooth, NGSS receiver, antenna switch, USB switch, and Hall Effect sensor.

Point-of-care diagnostic and drug delivery devices include MCU, audio CODEC, switches, battery chargers, Flash, amplifiers, controllers, displays and digital signal processors. They also include sensors for air quality, sweat, humidity, temperature, motion, Hall, proximity, contact, mechanical operation, and counter sensors. Several of these platforms may end up on flexible substrates made of PET or thermoplastic polyurethane (TPU). Increasing integration but minimizing heat dissipation will be critical in such applications. The terminations of such devices will also have to consider the potential for assembly on silver ink traces with conductive adhesives or extremely low temperature solders.

Stretchable and printable medical electronics, including textiles, are in the early stages of development and in some cases the devices are printed and in others the devices are attached using adhesives or surface mount technology

(SMT). In some cases, the electrodes are screen printed on (TPU film substrates and bonded to a textile by a hot melt adhesive. Silver micro-flakes are mixed with a TPU film and heat-cured to make a stretchable fabric. In some cases, the width of the line is 520 μm and the space is 480 μm [9].

Sensors attached directly to the skin are increasingly used to monitor health, athletic performance, and muscle and nerve conditions. Sensors placed on a fingernail are in development. A wearable fingernail deformation sensor system uses a 40 μm thick silicon strain sensor, a three-axis accelerometer, and an RF module to transmit the signal. Handle tape is used to attach the silicon layers [10].

Many new developments are taking place in smart textiles in many organizations, including universities and start-ups. For example, Carnegie Mellon University researchers have developed a self-healing circuit material that can repair itself. The material is composed of liquid metal droplets suspended in a soft elastomer. This is the foundation of the self-repair process. The material can be used in self-healing electrical circuits, which when produced with conductive traces of this material, remain fully and continuously operational if severed or punctured [11]. In another example, researchers at the University of California San Diego have fabricated a stretchable electronic patch with wireless monitoring that can be worn on the skin, similar to a bandage.

A sensor patch system has been fabricated using a Tegaderm polymer film with a Cu sensor electrode fabricated on it. The sensor patch is placed over a cannula needle inserted into the patient's vein for drug or fluid delivery to detect skin swelling. The sensor electrode pattern is laser machined onto a 400 μm thick silicon wafer, and the polymer film is attached to the back of the stencil wafer and a sputtering process is used to pattern the sensor electrode and pad. The first layer of metal is Ti, acting as an adhesive layer between the second metal layer, Cu, and the polymer film. The 2 μm Cu layer is sputtered, followed by a thin (200 angstroms) layer of Au (to act as a passivation layer). The conductors are attached with double-sided conductive film [12].

Embedded die are used for other sensor applications. Assembly of ultra-thin die on flexible substrates is challenging. In one example, a small, thin die is embedded in a flexible substrate using a FO-WLP process with fine-pitch wiring. Small 2.5mm x 2.5mm die with 100 μm thickness are embedded. Devices include photodiodes and a micro-LED driver. The structure can be mounted on a curved human fingernail and used for trans-nail pulse wave monitoring [13]. In another approach, a thinned die is embedded using a highly flexible elastomeric molding compound, polydimethylsiloxane (PDMS), using a FO-WLP process. This embedded substrate approach allows a 2 mm bending range. Foldable displays have been demonstrated, and the technology can be used for multi-channel surface electromyography systems or optogenetics for neural implants [14]. Other examples include the following:

- Wireless, implantable, stretchable biosensor systems have been developed, comprised of a miniaturized capacitive sensor and inductive coil without a battery. In some cases, the capacitive sensor is fabricated using aerosol jet printing of silver nanoparticles and polyimide. Silicone elastomer is used to encapsulate the sensor prior to conformal integration onto a medical stent [15].
- Examples of heterogeneous integration include the fabrication of an ECG monitor with a microcontroller/Bluetooth, antenna, ECG electrodes, analog front-end on a 2-inch x 2-inch polyimide substrate with 64 plated Cu through holes. Capacitive electrodes are formed by alternate deposition of 166 layers of Al_2O_3 and TiO_2 . The total thickness is 103 nm, the dielectric constant is 120, and 0.53 microF/cm^2 [16].
- A wearable passive pH sensor for health monitoring consisting of Ag/AgCl and Sb/Sb₂O₃ electrodes and a transponder consisting of an RF front end and an antenna has been fabricated. The electrodes are fabricated and connected to Cu pads on a 380 μm thick PTFE substrate. The sensor tag and transponder are integrated into a mouthguard. An energy-harvesting method is used instead of a battery to power the system [17].
- Ultra-small passive devices are used in a variety of products. In some cases, integrated passives are used. Examples include Murata's IPDIA used for pacemakers, medical sensors, and brain stimulation.

4. Interconnect Requirements

Wire-bond interconnects continue to be used in some applications for connections between die and package or board. Au wire is most common. An increasing number of products require 3D integration to achieve desired form factors. The 3D integration can take the form of stacked die with wire bonds. Within-Package Interconnects enable lateral connections between two nodes or electrodes. Package-to-Board Interconnects are between the package and the next level, typically the motherboard, and are referred to as the second level interconnect (SLI).

Wafer level packages (WLP) and flip chip interconnect are also increasingly used in consumer wearables. The number of WLPs in smartwatches and fitness products continues to increase from none to a few in early products to four to nine in fitness bands and as many as 27 in today's smartwatches with health or medical functions. The number of WLPs in a smartwatch has increased from 18 to 27, for the highest-end modes. Many of these are found inside the SiP. Fan-out WLPs with multiple die are also being adopted. These are considered examples of heterogeneous integration. Increased use of SiPs is expected in formats that include wire bond, flip chip, and WLP. Driven by miniaturization, functionality, and durability, SiPs may take the form of embedded die.

Flip chip continues to be used for a variety of products ranging from hearing aids and pacemakers to smartwatches. Typically, the flip chip devices are <5 mm x 5 mm and have fewer than 200 bumps. The bumps can be gold stud bump (formed with a modified ball bond process), Pb-free solder, or conductive adhesive. In some cases, a Cu pad may be formed on the die, and an embedded die process is used. A key metric is the flip-chip bump pitch. Flip-chip bump pitch ranges from 150 to 300 μm . In the future, bump pitch may decrease to 120 μm . Table 1 shows a 5-year roadmap for the traditional flip-chip pitch.

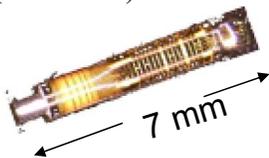
Table 1. Die-Substrate Interconnect Pitch Roadmap

Year of Production	2018	2019	2020	2021	2022	2023	2024
Au Wire bond (μm)	40	35	35	30	30	30	30
Flip chip bump pitch	150-300	150-300	130-300	130-300	130-300	130-300	120-300

Interconnect approaches for the emerging flexible system in package wearables require interconnections between die, passive components, RF components, and power sources. Additionally, there is often the need to connect to elements external to the flexible system, including electrodes, sensors, switches, power sources, and data transfer. Connections made within the flexible system generally are needed to connect components, die, and batteries. Methods used include printed interconnects, printed bumps, anisotropic conductive adhesives, conductive adhesives, solder, as well as some novel materials and methods. In many cases, the interconnections must be made at relatively low temperatures due to the substrate's thermal stability or functionalized coatings on sensors. Connections made to external sensors or wires often utilize snaps, clinch connectors, magnets, and flex connectors. These connections may involve conductive adhesive as well as mechanical interlocking. The transition from the soft substrate to hard components or connectors is challenging, and methods are often developed to reinforce areas, provide graded mechanical transitions and provide strain relief. Methods of connection are not yet fully developed or standardized.

5. Substrate Materials, Trace Fabrication, and Assembly

One of the most advanced medical devices was fabricated by Endicott Interconnect (successor to IBM Microelectronics, Endicott, NY) and assembled with the participation of Universal Instruments. This was an early (circa 2010) FHE-based Intravascular Ultrasound (IVUS), a catheter-based system consisting of five ASIC die in 1 mm diameter package. The IVUS allows physicians to acquire images of diseased vessels from inside the artery. The systems consist of a flexible polyimide substrate dielectric 12.5 μm in thickness with a segmented transducer (receiver/transmitter). The semi-additively plated copper had 14 μm lines and spaces, the five thinned (25 μm) ASIC die were flip-chip assembled and had 22 μm bumps at a 70 μm pitch. This device is one of the first examples of flexible hybrid electronics and remains one of the most advanced.



Once assembled and singulated from a larger panel, the individual devices were rolled into a diameter of 1 mm. The IVUS is a single-use device and is disposed of after use.

The substrate is the backbone of an electrical device, and it interconnects components electrically and acts as a mechanical carrier for the components. The substrate technology helps to achieve the form factor and can determine the reliability and performance of the device. A variety of substrate materials are used in medical electronics, including ceramic substrates such as LTCC, flex circuit, and laminate substrates including BT resin and FR-4. Rigid substrates based on glass-reinforced materials are also used, and often there is a combination of rigid and flex. Liquid crystal polymer films are also used for some devices. The focus for the future will be biocompatible substrates. Cover materials include solder mask (for short term) and LCP for flexible applications, and Parylene coatings.

The typical flex circuit for many applications is a two-layer (no adhesive layer) or a three-layer (adhesive layer) processed in a roll-to-roll format. In some cases, via connections are formed with paste. Applications include pacemaker/defibrillator, hearing aids, and implantable sensors and electrodes. Line and space dimensions are typically 25 to 35 μm ; however, capabilities do exist to manufacture 10 μm dimensions. Cu metal is most common;

additively deposited noble metals (such as Au or Pt) are used as surface finishes and for implantable (electrode) applications.

- Plated metal circuits on lower-cost substrates such as PET (see the picture on the right) will emerge as a compromise between conductivity and cost in certain applications.
- Wearable electronics in the form of implanted or skin-attached products are in development, but the work is still in the early stages. TPU, polyimide (Kapton and Upilex), and PET are being used for skin patches.
- The terminations of devices on such substrates will also have to consider the potential for assembly on silver ink traces with conductive adhesives or extremely low temperature solders.
- Knitting or weaving conductive threads into textiles is under development with Ag, Cu, Sn, or Ni alloy metalized threads. Coating or deposition of conductive polymers is under investigation.



Conductors (typically inks) are deposited by aerosol jet, inkjet, or screen printing. Features of 10 μm line and space have been fabricated. Inkjet droplets (pico-liter in volume) can be jetted by thousands of individually addressable nozzles at the same time and are deposited in a non-contact manner. Inkjet printing is proposed as a low-cost direct patterning method to provide higher resolution than weaving. Inkjet printing for semiconductor packaging applications requires higher accuracy and reliability than today's inkjet printer technology. It requires the use of piezo driven heads used in large-scale graphics printers. A high-precision motion platform, precise pattern rendering, modular design, head inspection, and easy maintenance are required. These requirements add cost to a semiconductor inkjet system, but the total cost is significantly less than the BEOL lithography in use today. Other advantages to inkjet printing for BEOL include quick change of patterning (digital printing), efficient use of materials (fewer subtractive processes, if any), ability to handle larger-area substrates (panel size), and significant cost reductions (compared to lithography). Inkjet printing can be used to fill vias, trenches, and cavities from a micron to a millimeter in thicknesses.

Inkjet materials will be critical to the success of applying printed electronics to BEOL technologies. Materials come in several groupings: dielectrics (such as polyimide), fast-curing UV polymers, resists for etch or plating masking, and conductive inks. The most popular of the conductive inks are Cu and Ag nanoparticle suspensions in solvents that cure below 150°C. Ink materials must have viscosities in the 2-20 centipoise (cP) range, controlled surface tension, and uniform particle sizes and particle loading. Future ink materials could include special adhesives, graphene, quantum dot ink, sensor materials, optical sensors, biomaterials, and passive component materials (resistors and capacitors). Carbon nanotube (CNT) is also under investigation.

Inks can be printed at room temperature and take about 15 minutes to dry. There is no need to pause the deposition process for the ink to dry. Layers can be printed one over another while curing, with no effect on the final material's properties. New inks continue to be developed that can improve the performance and manufacturability of printed electronics. Cu paste for screen printing has been developed that provides high adhesive strength to glass, PET, polyimide, FR4, and ITO, and high conductivity of 20 to 30 microOhm/cm using a low-temperature (120°C) sintering process; some Cu inks require a reducing atmosphere for sintering. It is capable of printing 50 μm lines/spaces. It is targeted to replace Ag paste in applications. Black phosphorus, a two-dimensional material similar to graphene, has been incorporated into an ink that is compatible with conventional inkjet printers. The material can be printed on silicon, so it can be used to make transistors or photodetectors. It could be printed on plastic and used to make flexible displays, or on glass for transparent devices. While not as conductive as graphene, black phosphorus is believed to be sensitive to a greater region of the electromagnetic spectrum, including infrared, making it suitable for the development of optoelectronic devices including solder cells, light emitters, optical fibers, and sensors [18].

- Inkjet printing of electrodes on paper and then transfer as a temporary tattoo has also been reported. Silver-flake ink has been used [19].
- One of the challenges is printing on a rough and porous surface; therefore, coating an interface layer on fibrous substrates before printing is being proposed. A polyurethane-based ultraviolet curable paste has been proposed as an interface layer to fill pores in textiles and improve surface roughness before an antenna is printed. Ag nanoparticle inks have been demonstrated [20].

- More conventional methods of component attachment to flexible circuits have also been proposed. Circuits have been mounted with SnBiAg or SAC305 solder on Cu clad stretchable material [21].
- Anisotropic conductive adhesive film (ACF) has been demonstrated to provide good electrical connections with a low-temperature process. In one example, 50µm thick silicon chips with Cu/Ni/Au bumps using ACF and thermo-compression bonding were attached to a substrate. The Cu-patterned polymer flexible substrate uses a polyester/rayon woven fabric with a 12µm thick Cu foil and 40µm thick B-stage adhesive (styrene-isoprene-styrene block copolymer elastomer) added during fabrication. Stable joint resistance has been reported after 12mm radius convex and concave bending [22]. Companies are also investigating and moving into production with flip chip attached to PET flex circuits using ACA and advanced z-axis materials.

Summary of Trends in Materials for Flexible Hybrid Electronics

	Now	Emerging	Future
Enables	Basic applications, performance and process specific requirements to enable early technology demonstrations.	Establish supplier base for functional material sets, in-situ characterization tools, establish databases that enable technology adoption.	Product and application specific materials, sources, process and integration requirements that enable technology adoption/manufacturing.
Substrates	20% elongation, <10% deformation over 1000 cycles,	Flex/stretch for extreme environments, >5yr lifetime, low loss (such as <0.0003 at >10GHz with high permeability, low magnetic loss.) Substrates that are in-vivo, soft tissue compatible	30-50% elongation, <10% deformation over 1000 cycles, biodegradable substrates for sustainability
Active	Temperature, humidity, pressure transductive inks, force and haptic sensing media	Long use life transductive ink for T, humidity, pressure, shock, strain, chemical sensing, tunable magnetic/varactors, in-vivo micro-stress/strain	Printed actives for battery/energy storage, conformal energy harvesting, high resolution transducer array for artificial skin
Passive/Conductor	Improve conductivity <4X bulk metal, low T cure <130C, high T solderable >230C, stretch 20%	...plus: printed alternative to Cu, bidirectional elongation w/ 10% resistivity change at 1000 cycles, printable at <10µm,	...plus: flexible battery electrodes, improved conductivity <2X bulk metal, stress absorbing conductor for via/interconnect
Passive/Insulator	Substrate & process compatible dielectrics, encapsulants and selective permeable membranes for low cure (<130C). High T>230C stable, stretchable >20% elongation w/ <10% deformation @ 1000 cycles.	Biocompatibility, >L band compatibility, >5yr use lifetime in natural environment, high dielectric constant.	<0.0003 loss at 10GHz, use at 260C; 30-50% elongation w/ <10% deformation @1000 cycles, super-hydrophobic, biodegradable, in-vivo and microfluidic compatible, flexible NIR plastic & waveguide materials

Trends in Device, Integration, Packaging and Assembly of Flexible Hybrid Electronics

	Now	Emerging	Future
Enables	Thinned die and compliant assembly methods. Stretchable and conformal substrates. Flexible low dielectric and low loss RF materials.	Clothing/textile substrates for wearable applications. Printed features for RF and hi-speed function. Flexible interposed for fine-pitch die attach	Embedded components and integrated passives. Encapsulation for harsh environments. From sheets to roll based device assembly.
Circuitization	Low I/O (<100) and pitch (>200µm) for controllers, memory, communication w/ compliant chip attach	Flexible substrates w/ stretchable circuitry, RF materials, textile substrates	Multi-layer flex circuits w/ internal power/ground, vias and embedded function. Printed conductors, transmission lines, dielectrics, vias RCL, sensors and 3D features
Non-printed components	Thin die flip-chip bonding Stress/defect free die thinning & dicing for <50µm wafers	Flexible interposer for fine-pitch, <50 µm thick die. Reliable interconnect/assembly of <50µm die. Thinning/dicing of <10 µm wafer. Non-contact methods	Interposers for <10µm die, stretchable interposers w/ embedded components. Assembly of <10µm die, integration of power sources and passives. Embedded passive components
Device assembly	Pick/place of <50µm die w/o interposers	Assembly of FHE interposers with fine-pitch for <50µm die. From sheets to roll based assembly	Assembly of <10µm die with, w/o interposer, non-contact methods, embedding passive/active in high density flex, roll based assembly
Encapsulation	Single-die, sheet/batch process Flexible & conformable	Multi-mode & higher I/O count Sustainability/recyclability	High-volume/low cost R2R Harsh environment applications

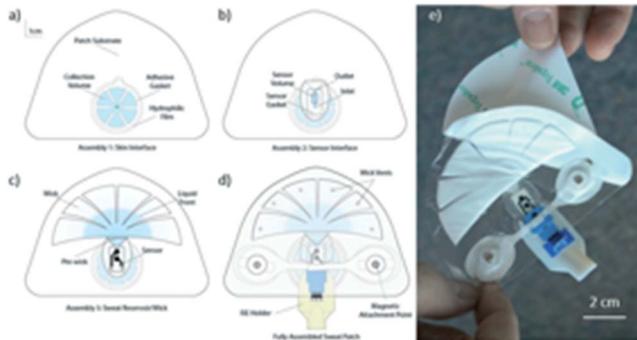
6. Examples of Recent Advances and Emerging Technologies

Recently a review article, "A New Frontier of Printed Electronics Flexible Hybrid Electronics," was published by Y. Kahn and colleagues [23]. This is an excellent summary of the state-of-the-art literature on flexible hybrid electronics (FHE) technology as applied to applications that include wearable medical devices.

Recently work at the University of Connecticut reported "Smart Bandages to Heal Chronic Wounds" that consists of a mobile platform-based, wirelessly controlled bandage to deliver medication to a wound using miniature needles.

The device facilitates healing without removing the bandage and has the potential to change the way diabetic wounds are treated [24]. A similar effort was conducted at Purdue and supported by NextFlex.

"A Wearable Electrochemical Platform for Noninvasive Simultaneous Monitoring of Ca^{2+} and pH" [25] describes wearable and disposable PET flex for concurrent pH, temperature, Ca^{2+} sensing. Sensor Flex is interfaced to a concurrently worn rigid circuit board that enables selective real-time quantitative analysis and wireless transmission of Ca^{2+} in body fluids such as sweat, tears, and urine with pH and temperature correction.



"A wearable patch for continuous monitoring of sweat electrolytes during exertion" [26] is the demonstration of a fully integrated, wireless, wearable, and flexible sweat sensing device for non-obtrusive and continuous monitoring of electrolytes during moderate to intense exertion as a metric for hydration status. The focus of this work is two-fold: 1) design of a conformable fluidics system to suit conditions of operation for sweat collection (to minimize sensor lag) with rapid removal of sweat from the sensing site (to minimize effects on sweat physiology). 2) integration of Na^+ and K^+ ion-selective electrodes

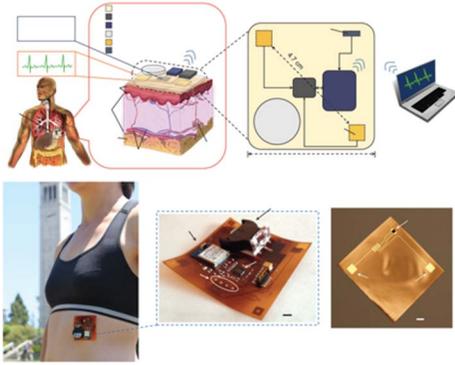
(ISEs) with flexible microfluidics and low noise small footprint electronic components to enable wireless, wearable sweat monitoring. While this device is specific to electrolyte analysis during intense perspiration, the lessons in microfluidics and overall system design are likely applicable across a broad range of analytes. The device is composed of a flexible disposable sensor/microfluidics module and a reusable electronics module. Key challenge: clinical acceptance. Potential shortcoming: not accurate at low perspiration rates.

"Flexible Electronics toward Wearable Sensing" [27] is a summary of recent studies on the design of flexible electronic devices and systems for chemical and physical monitoring. It discusses material innovations, sensor design, device fabrication, system integration, and human studies employed toward continuous noninvasive wearable sensing.

"Battery-free, stretchable optoelectronic systems for wireless optical characterization of the skin," [28] introduces active optoelectronic systems that function without batteries and in an entirely wireless mode, with examples in thin, stretchable platforms designed for multiwavelength optical characterization of the skin. Magnetic inductive coupling and near-field communication (NFC) schemes deliver power to multicolored light-emitting diodes and extract digital data from integrated photodetectors in ways compatible with standard NFC-enabled platforms, such as smartphones and tablet computers. Examples in the monitoring of heart rate and temporal dynamics of arterial blood flow, in quantifying tissue oxygenation and ultraviolet dosimetry, and performing four-color spectroscopic evaluation of the skin demonstrate the versatility of these concepts. The results have potential relevance in both hospital care and at-home diagnostics.

"Highly flexible, wearable, and disposable cardiac biosensors for remote and ambulatory monitoring" [29] reports on advancing contemporary cardiac and heart rate monitoring devices that capture physiological signals using optical and electrode-based sensors. However, these devices generally lack the form factor and mechanical flexibility necessary for use in ambulatory and home environments. It reports an ultrathin (~ 1 mm average thickness) and highly flexible wearable cardiac sensor (WiSP) designed to be minimal in cost (disposable), lightweight (1.2 g), water-resistant, and capable of wireless energy harvesting. Theoretical analyses of system-level bending mechanics show the advantages of WiSP's flexible electronics, soft encapsulation layers, and bio-adhesives, enabling intimate skin coupling. A clinical feasibility study conducted in atrial fibrillation patients demonstrates that the WiSP device effectively measures cardiac signals matching the Holter monitor and is more comfortable. WiSP's physical attributes and performance results demonstrate its utility for monitoring cardiac signals during daily activity, exertion, and sleep, with implications for home-based care. The WiSP device is comparable in size to a standard adhesive bandage ($58 \text{ mm} \times 25 \text{ mm} \times 1 \text{ mm}$) and streams physiological data to commercial smartphones via standard near-field-communication (NFC) for use in both ambulatory and home-based settings.

"Flexible Hybrid Electronics: Direct Interfacing of Soft and Hard Electronics for Wearable Health Monitoring" [30] describes interfacing of soft and hard electronics as a key challenge for flexible hybrid electronics. Here, a single substrate interfacing approach is reported, where soft devices, i.e., sensors, are directly printed on Kapton polyimide substrates that are widely used for fabricating flexible printed circuit boards (FPCBs). Utilizing a process flow compatible with the FPCB assembly process, a wearable sensor patch is fabricated using inkjet-printed gold



electrocardiography (ECG) electrodes and a stencil-printed nickel oxide thermistor. The ECG electrodes provide 1 mV_{p-p} ECG signal at 4.7 cm electrode spacing, and the thermistor is highly sensitive at normal body temperatures and demonstrates temperature coefficient, $\alpha \approx -5.84\% K^{-1}$ and material constant, $\beta \approx 4330 K$. This sensor platform can be extended to a more sophisticated multi-sensor platform where sensors fabricated using solution-processable functional inks can be interfaced to hard electronics for health and performance monitoring, as well as internet of things applications.

New stretchable electronic patches could transform rehabilitation and long-term care [31]. Prof. John A. Rogers at Northwestern University is developing a wearable patch that could record acoustics within the body, such as sounds within a joint or vibrations from speech. The goal was to build a soft, wireless, skin-interfaced device with the form factor of a bandage and the functions of a stethoscope to continuously and precisely measure the body's subtle mechanical and acoustic signatures. The result yielded a real diagnostic and treatment tool to measure a rehabilitating stroke patient's patterns of speech and swallowing. The result, the first wearable device designed for the throat, is a "much more personalized, quantitative approach to rehabilitation." The throat sensor is just one in a portfolio of innovations developed in Northwestern's Center for Bio-Integrated Electronics. Rogers and his collaborators have developed materials and design approaches that transform electronics from traditional rigid silicon circuits into soft, conforming, thin devices that integrate with the body while transmitting real-time information wirelessly to both physicians and machine-learning algorithms that can find new patterns within data.

The team has also developed devices that can be worn on the body to measure sweat rate and chemistry, or to quantify exposure to solar UV radiation, as well as devices that can be implanted within the body to harvest energy from organs and automatically treat abnormal heart conditions. "The patch had to be constructed so that people forget it's there once they put it on," Rogers was quoted: "We strive on the engineering and materials side to make it fully skin-like and physically imperceptible."

In "Smart Skin - Electronics that stick and stretch like a temporary tattoo" [32], engineers developed a device platform that combines electronic components for sensing, medical diagnostics, communications and human-machine interfaces, all on an ultrathin skin-like patch that mounts directly onto the skin with the ease, flexibility and comfort of a temporary tattoo.

Application Roadmap for Wearable Flexible Hybrid Electronics

	Now	Emerging	Future
Electro Physiological	Clinical grade wearables (ECG,EMG, Temperature, Respiration, BP, O ₂)	Disposable clinical grade wearable. Low cost, low profile sensors (such as facial sensors for CO ₂ -based RR or clothing/shoe embedded sensors)	Low-cost multi-sensor systems w/ energy harvesting and integration with AI
Motion, Strain & Posture	Wearables for rehab (physical therapy) assistance	Low profile pseudo skin sensors integrated w/ prosthetics	Low cost, low profile wearable sensors and exoskeletons for bone and muscle degeneration
Worker Safety & Productivity	Environment aware PPE (electrical, temperature, collision, hazards)	Extreme environment sensing and feedback (toxic gases, confined spaces, dehydration, etc.); for worker's mental fatigue and stress prediction and prevention	Low-cost wearables for real time musculoskeletal injury, nerve fatigue prediction algorithms based on work-load
Fluid Biomarkers Smart Bandages	Continuous & non-invasive electrolyte sensing	Non-invasive wound monitoring and healing; sensors for non-invasive metabolite (lactate, glucose) sensing	Non-invasive drug metabolites sensing and optimum drug delivery; non-invasive innate biomarker sensing (from stress, cancer to infectious diseases,...)
Other		Wearable accessories, such as flexible displays, for augmented reality	Wearable medical imaging devices; Smart low cost optical, auditory and haptic prosthetics for medical

7. Materials and Power

"Materials and Structures toward Soft Electronics" [33] presents a comprehensive discussion of the strategies in materials innovation and structural design to build soft electronic devices and systems on non-planar surfaces. For each strategy, the presentation focuses on the fundamental materials science and mechanics, and example device applications are highlighted where possible. Finally, perspectives on the key challenges and future directions of this field are presented.

The implications of soft electronics integrating with nonplanar objects are multifold. First, the intimate contact between the device and the nonplanar object will allow high-quality data to be collected. With rigid electronics, air gaps at the interface between the device and the object reduce the contact area, and can potentially introduce noise and artifacts, which compromise signal quality. Second, foldable, low-profile devices can enable mobile and distributed sensing, which hold great promise for Internet-of-Things technology. Finally, in the area of medical devices, which is probably the major driving force of this field at present, soft electronics have similar mechanical properties and thus cause minimal irritation to the human skin, which can be a key enabling technology for continuous healthcare.



and artifacts, which compromise signal quality. Second, foldable, low-profile devices can enable mobile and distributed sensing, which hold great promise for Internet-of-Things technology. Finally, in the area of medical devices, which is probably the major driving force of this field at present, soft electronics have similar mechanical properties and thus cause minimal irritation to the human skin, which can be a key enabling technology for continuous healthcare.

Two strategies can be applied to achieve stretchability in electronics: 1) materials innovation, by developing novel materials that are stretchable in single or aggregated forms; 2) structural design, by making non-stretchable materials into specific structures that can absorb the applied strain without fracturing, e.g., by inducing mixed modes of mechanical deformations. In this review, we summarize state-of-the-art advances in both strategies, covering a broad range of topics (see

figure), including hydrogels, liquid metals, conductive polymers, and nanomaterials for the material approach, and waves/wrinkles, "island-bridges," textiles, origami, kirigami, cracks, and interlocks for the structural approach. Outlooks on the challenges in the field and possible future research directions are included in this review.

Power sources are critical for nearly all wearable devices. A number of companies are offering flexible or printed batteries (e.g. Imprint Energy, ITN Energy Systems, NGK, Blue Spark, etc.). "A Review of Advanced Flexible Lithium-Ion Batteries" [34] describes flexible Li-ion battery technology for flexible electronics with special focus on the selectivity of flexible electrode/electrolyte materials, cell structure design, and full cell assembly process. Traditional Li-ion battery materials and structures are brittle. There is a need to use flexible materials for the electrodes, current collectors, solid-state-electrode, and structural design of the cells. Examples are materials for anode, cathode, and electrolyte such as graphene, carbon nanofibers or cloth, carbon nanotubes, and carbon paper.

Alternate approaches for power are reported in "Flexible and stretchable power sources for wearable electronics." [35] There are no previous reports of wire/ribbon batteries with fatigue resistance sufficient for wearable applications; a helical band spring for omni-directional flex, or a serpentine shaped battery, accommodates stretch along the length. This is a unique approach that demonstrates mechanically robust, intrinsically safe silver-zinc batteries. This approach uses current collectors with enhanced mechanical design, such as helical springs and serpentes, as a structural support and backbone for all battery components. Wire-shaped batteries that are based on helical band springs are resilient to fatigue and retain electrochemical performance over 17,000 flexure cycles at a 0.5-cm bending radius. Serpentine-shaped batteries can be stretched with tunable degree and directionality while maintaining their specific capacity. Finally, the batteries are integrated, as a wearable device, with a photovoltaic module that enables recharging of the batteries.

8. Challenges

Medical devices, especially implantable devices, are driven by the requirement of miniaturization. At the same time, there is a push to lower cost and maintain reliability. Medical implantable devices must last more than nine years, have <10 ppm process defects, and have no customer complaints. Known good die is required for assembly.

Emerging technologies for medical electronics include smart fabrics and skin patches. There are a number of issues that need to be addressed for commercialization of these developments. Highly conductive, conformal electrode materials are needed to reduce contact impedance with human skin. Facile patterning and integration procedures for large-area multi-channel electrodes with high throughput and low cost are required. Good adhesion between the electrodes and the substrate materials to avoid delamination after multiple uses is required.

- Fabrics used in sensing garments or systems must be non-irritating to the wearer's skin. The Oeko-TEX® Standard 100 certifies that textiles do not contain substances harmful to humans.
- Products must pass bend and stretch tests, and often wash testing. IPC's D-70 E-Textiles Committee has released IPC WP-024, White Paper on Reliability and Washability of Smart Textile Structures.
- Acceleration factors will have to be developed for new stacks to be able to assess lifetime.
- Improvements in inks with higher conductivity are needed.
- TPU substrates offer limited protection against strain localization in traces when deformed. Repeated stretching and the effects of temperature and humidity can cause issues [36].
- Battery life is a concern and research is under way in energy harvesting and development of new battery methods.
- The terminations of such devices will also have to consider the potential for assembly on silver ink traces with conductive adhesives or extremely low temperature solders.
- Compatibility of encapsulation materials with inks, substrates and conductive adhesives.

9. Summary

This chapter has accomplished two primary objectives: to present drivers and methods for selected medical wearables, and to discuss emerging trends in developing future medical wearables devices.

- "Wearable" devices will increasingly use thinned silicon devices mounted to flexible, conformal, or stretchable substrates.
- Substrates will include thin plastic films, non-woven papers, and fabrics. Devices will be laminated onto garments.
- A diverse range of sensors making use of electrochemical, microfluidic, optical, and electrical-mechanical devices/transducers will be integrated to provide advanced functions. The "wearable" device will be "heterogeneously integrated" in the diversity of components, materials, non-traditional interfaces, and assembly.
- Microfluidic technologies will allow body fluids to be wicked from the surface of the skin or below the skin (using micro-needles). Fluids will be analyzed onboard and results will be wirelessly communicated to mobile devices for further processing. "High-performance" will be on the mobile device.
- Plated Cu metal circuits will migrate to printed metals and/or stretchable liquid metal conductors, depending on the application. However, plated metal circuits on lower cost substrates such as PET will emerge as a compromise between conductivity and cost in certain applications. Interconnects will be compliant to mechanical deformation and diverse environments.
- Wireless communications will dominate. RF antennas and components will be printed for low-cost applications.
- Low power devices will operate based on RF induction.
- Power density in (flexible) Li-ion batteries will continue to limit function and duration of use.
- The need for standards, test and design for reliability (for the application) will be on-going.

10. Acknowledgments

TWG members: Mark D. Poliks, Mark Schadt (Binghamton University), E. Jan Vardaman (TechSearch International, Inc.), Girish Wable (Jabil), Nancy Stoffel (GE Global Research), S.V. Sreenivasan (UT, Austin), Chan (Binghamton University), Scott M. Miller (NextFlex), and Suresh K. Sitaraman (Georgia Institute of Technology). The TWG members would like to acknowledge the many contributions of industry experts: Grace O'Malley and iNEMI for providing input and to Jason Marsh and Wilfred Bair (formerly of NextFlex). We would also like to acknowledge the contributions of the other TWGs. Mark Poliks and S. V. Sreenivasan acknowledge the support from NSF Award Number 1840406 that funded the "NSF-NextFlex Joint Workshop on Accelerating Innovative Manufacturing Technology for Flexible Hybrid Electronics."

Appendix

The present version of this chapter reflects a preliminary draft of a much larger document. The following outline can serve as a basis for the next editions.

1. Heterogenous Integration for Healthcare
 - a. Imaging Modalities (much follows other sections of HIR)
 - i. CT, X-ray, MRI, Ultrasound and Terahertz
 - b. Human Health Monitoring Sensors
 - i. Vital sign monitors, disease state, fatigue, hydration, wound care
 - ii. Longer term devices that sense, assess and respond
 - c. Implantable devices
 - i. Neural implants
 - ii. Pacemakers
 - d. Diagnostic systems
 - i. With both on- and in-body possibilities
 - ii. Compact and stand alone
 - iii. Durable and Disposable
 - e. Other related applications
 - i. Neonatal
 - ii. Smart wound care
 - iii. Smart PPE
 - iv. Geriatric Assistance or Aging in place: a combination of devices that help to improve the quality of life for the aging population
 - v. other
2. Application Space
 - a. Hierarchy of Accuracy
 - i. Clinical (clinical grade, high accuracy critical)
 1. Patient monitoring, diagnosis and therapy
 - ii. Occupational
 1. Factory or harsh conditions
 - iii. Extreme Performance
 1. Military, Public Safety/Homeland Security, Professional Athletics
 2. Mentally and physical demanding settings
 - iv. Wellness/Fitness (non-critical relative accuracy)
 1. General personal use -- information only
 - b. Wearables based on COTS components (2016 and before)
 - i. Pulse, heart rate, temperature (basic non-medical grade vitals)
 - c. Wearables based on non-COTS (2017 and after)
 - i. Form Factor
 1. Conformability
 2. Stretch-ability
 3. Transparency
 4. Semi-Breathability
 - ii. Basic medical grade vitals
 - iii. Physiological: ECG, EEG, SpO₂, BP, RR, temperature and more
 - iv. Motion, strain and pressure sensors
 - v. Integrated multi-sensor systems
 - vi. Fluid and biomarker analysis (using micro fluidic systems)
 1. Sweat sampling (absorption and wicking)
 2. Interstitial fluid and blood (micro needles)
3. Substrates and Materials
 - a. Rigid, flexible and ultra-thin
 - b. Silicon, glass, ceramic, polymer (PI, PET, LCP, TPU), fabric, paper
 - c. Plated metals (Au, Pt, Cu, etc.)

- d. Printed metal inks/pastes (Ag, Cu, etc.)
- e. Printed and dispensed materials including dielectrics, encapsulants, sealants etc.
- 4. Sensors & Devices
 - a. Motion-Tracking Sensors
 - i. Accelerometer
 - ii. Gyro
 - iii. Magnetometer
 - iv. GNSS (GPS, GLONASS, Galileo, Beidou)
 - v. Gesture and Proximity
 - b. Bodily Function Sensors
 - i. Heart Rate Sensor
 - ii. Pulse Oximetry
 - iii. Temperature Sensor
 - iv. Chemical
 - v. Electrical
 - vi. RF
 - vii. Electroencephalography (EEG) and surface electromyography (sEMG)
 - c. Device integration
 - i. Electronic (active & passive)
 - ii. RF (communications)
 - iii. Optical (emitters and sensors)
 - iv. Micro-fluidic
 - v. Other: MEMS, temperature, GPS, etc...
- 5. Data Processing
 - a. microprocessors
 - b. memory
 - c. A/D converters and filters
 - d. Integration communications (optional)
- 6. Communications
 - a. Wired (conventional protocols with cables)
 - b. Wireless (Bluetooth, WiFi and beyond)
 - i. Device integrated antennas
 - ii. Advanced printed antenna solutions for multi sensor on-body applications
- 7. Flexible Displays (OLED, Electrochromic)
- 8. Power and Energy Management
 - a. Wired
 - b. Batteries, inductive charging to harvested energy
 - i. Compact, safe, high energy density batteries
 - ii. Coin cells and conventional batteries
 - iii. "Flexible" unpackaged batteries
 - iv. Wireless charging (conventional)
 - v. Wireless near field activated low power systems
 - vi. Harvested energy-based power (thermal or mechanical)
- 9. Integration
 - a. Packaged for a wide range of size, shape and other physical attributes
 - i. Conventional packaged components and interconnects
 - ii. Unpackaged bare die
 - iii. Unpackaged thin bare die
 - iv. Printed interconnects
- 10. Manufacturing
 - a. Pick/Place, Assembly and Reflow
 - i. Conventional pick/place with solder assembly
 - ii. Low temperature solder assembly

- iii. Highly localized laser based reflow
 - iv. Photonic based reflow
 - v. Other printed interconnect (aerosol jet print)
 - b. Thin-die handling, pick/place
 - c. Direct printed interconnect
 - d. Thin substrate handling (frames, fixtures or R2R)
 - e. Stretchable substrate handling (frames, fixtures or R2R)
- 11. Roadmap and Technology Needs
 - a. Unpackaged thin die
 - b. Compliant interconnect and attach methods
 - c. Stretchable and conformable substrates (films & textiles)
 - d. Flexible low Dk/Df
 - e. Printed passives and RF
 - f. Metal-like printed conductors
 - i. Thermal, laser, photonic based metal oxide reduction/particle-flake sintering
 - ii. Use of (localized) reducing gas (hydrogen/nitrogen) processes
 - g. Copper plated traces on PET
 - h. Embedded components
 - i. Encapsulation for range of environments
 - i. On-body, in-body, high/low temperatures/humidity
 - j. Scalable manufacturing
 - i. Panels to rolls

References

1. "Medical Prevention" Yole Development, 2019
2. Siari, A.; Mouly, J. "Medical Wearables: Market and Technology Trend 2019 Report," Yole Development, 2019
3. Shahane, N.; Raj, P.M.; Nair, C.; Smet, V.; Buch, C.; Tummala, R.R. Nanopackaging for Component Assembly and Embedded Power in Flexible Electronics. *IEEE Nanotechnology Magazine*, December 2018, pp 6-18.
4. Joseph J. Pancrazio, Felix Deku, Atefeh Ghazavi, Allison M. Stiller, Rashed Rihani, Christopher L. Frewin, Victor D. Varner, Timothy J. Gardner, Stuart F. Cogan, "Thinking Small: Progress on Microscale Neurostimulation Technology," *Neuromodulation* 2017; 20: 745–752. DOI: 10.1111/ner.12716
5. Joong Hoon Lee, Hanseop Kim, Jeong Hun Kimac and Sang-Hoon Lee, "Soft Implantable Microelectrodes for Future Medicine: Prosthetics, Neural Signal Recording and Neuromodulation," *Lab Chip*, 2016, 16, 959. DOI: 10.1039/c5lc00842e
6. Nikita Obidin, Farita Tasnim, and Canan Dagdeviren, "The Future of Neuroimplantable Devices: A Materials Science and Regulatory Perspective," *Adv. Mater.* 2020, 32, 1901482. DOI: 10.1002/adma.201901482
7. N. Ueta, "Flexible Circuit Board Package Embedded with Multi-stack Dies," NORPAC, June 2019.
8. D. Manassis et al., "Large-Scale Manufacturing of Embedded Subsystems-in-Substrates and a 3D-Stacking Approach for a Miniaturized Medical System Integration," EMPC, Grenoble, France, September 9-12, 2013.
9. Y. Hu et al., "Stretchable and Printable Medical Dry Electrode Arrays on Textiles for Electrophysiological Monitoring," *IEEE 69th Electronic Components and Technology Conference*, May 2019, pp. 243-248.
10. K. Sakuma et al., "A Wearable Fingernail Deformation Sensing System and Three-Dimensional Finite Element Model of Fingertip," *IEEE 69th Electronic Components and Technology Conference*, May 2019, pp. 270-276.
11. E. Montalbano, "Carnegie Mellon University Researchers Have Developed a Self-Healing Circuit Material That Can Repair Itself for Use in Wearable Electronics and Soft Robots, Among Other Applications," *Materials and Assembly*, June 13, 2018.
12. R. Lim et al., "Simulation Analysis of a Conformal Patch Sensor for Skin Tension and Swelling Detection," *IEEE 67th Electronic Components and Technology Conference*, May 2017, pp. 2,104-2,109.
13. Y. Susumago et al., "Mechanical and Electrical characterization of FOWLP-Based Flexible Hybrid Electronics (FHE) for Biomedical Sensor Applications," *IEEE 69th Electronic Components and Technology Conference*, May 2019, pp. 264-268.
14. A. Alam et al., "Heterogeneous Integration of a Fan-Out Wafer-Level Packaging Based Foldable Display on Elastomeric Substrate," *IEEE 69th Electronic Components and Technology Conference*, May 2019, pp. 277-282.
15. R. Herbert et al., "Stretchable, Implantable Nanomembrane Biosensor for Wireless, Real-Time Monitoring of Hemodynamics," *IEEE 69th Electronic Components and Technology Conference*, May 2019, pp. 1,233-1,239.
16. M. Poliks, "Development of a Wearable Flexible Hybrid Electronics ECG Monitor," *Flex*, February 2019.

17. S. Mondahl, "A Wearable Passive pH Sensor for Health Monitoring," IEEE 69th Electronic Components and Technology Conference, May 2019, pp. 1,240-1,245.
18. "Hybrid Nanomaterials Engineering Group Researchers Successfully Incorporated Black Phosphorus into Ink that is Compatible with Conventional Inkjet Printers," China Daily, August 25, 2017.
19. S. Tuominen et al., "Screen Printed Temporary Tattoos for Skin-Mounted Electronics," IEEE 69th Electronic Components and Technology Conference, May 2019, pp. 1,252-1,257.
20. H. Lao et al., "Inkjet-Printed Filtering Antenna on a Textile for Wearable Applications," IEEE 69th Electronic Components and Technology Conference, May 2019, pp. 258-263.
21. W. Liu, "Development of Flexible Hybrid Electronics Using Reflow Assembly with Stretchable Film," IEEE 69th Electronic Components and Technology Conference, May 2019, pp. 1,272-1,278.
22. S. Jung et al., "A Study on the Flexible Chip-on-Fabric (COF) Assembly using Anisotropic Conductive Films (ACFs) Materials," IEEE 69th Electronic Components and Technology Conference, May 2019, pp. 283-288.
23. Y. Kahn, A. Thielens, S. Muin, J. Ting, C. Baumbauer, and A. C. Arias, *Advanced Materials*, 2019.
24. Published in "Advanced Functional Materials" UConn Today, February 13, 2020.
25. Nyein, H.Y.Y.; Gao, W.; Shahpar, Z.; Emaminejad, S.; Challa, S.; Chen, K.; Fahad, H.M.; Tai, L-C.; Ota, H.; Davis, R.W.; Javey, A. *ACS Nano* 2016 10 (7), 7216-7224 DOI: 0.1021/acsnano.6b04005
26. Alizadeh, A.; Burns, A., Lenigk, R.; Gettings, R.; Ashe, J.; Porter, A.; McCaul, M.; Barrett, R.; Diamond, D.; White, P.; Skeath, P.; Tomczak, M. A., *Wearable Patch for Continuous Monitoring of Sweat Electrolytes During Exertion. Lab Chip*, 2018,18, 2632-2641 <https://doi.org/10.1039/C8LC00510A>
27. Gao, W.; Ota, H.; Kiriya, D.; Takei, K.; Javey, A. *Acc. Chem. Res.* 2019, 52(3), 523-533. <https://doi.org/10.1021/acs.accounts.8b00500>
28. Kim, J.; Salvatore, G.A.; Araki, H.; Chiarelli, A.M.; Xie, Z.; Banks, A.; Sheng, X.; Liu, Y.; Lee, J.W.; Jang, K.I.; Heo, S.Y.; Cho, K.; Luo, H.; Zimmerman, B.; Kim, J.; Yan, L.; Feng, X.; Xu, S.; Fabiani, M.; Gratton, G.; Huang, Y.; Paik, U.; Rogers, J.A. *Science Advances [Online]* 2016, 2(8), 1-10. e1600418 DOI: 10.1126/sciadv.1600418
29. Stephen P. Lee, Grace Ha, Don E. Wright, Yinji Ma, Ellora Sen-Gupta, Natalie R. Haubrich, Paul C. Branche, Weihua Li, Gilbert L. Huppert, Matthew Johnson, Hakan B. Mutlu, Kan Li, Nirav Sheth, John A. Wright Jr., Yonggang Huang, Moussa Mansour, John A. Rogers, Roozbeh Ghaffari, Highly flexible, Wearable, and Disposable Cardiac Biosensors for Remote and Ambulatory Monitoring. *npj Digital Med* 1, 2 (2018) doi:10.1038/s41746-017-0009-x
30. Khan, Y., Garg, M., Gui, Q., Schadt, M., Gaikwad, A., Han, D., Yamamoto, N. A., Hart, P., Welte, R., Wilson, W., Czarnecki, S., Poliks, M., Jin, Z., Ghose, K., Egitto, F., Turner, J. and Arias, A. C. (2016), Flexible Hybrid Electronics: Direct Interfacing of Soft and Hard Electronics for Wearable Health Monitoring. *Adv. Funct. Mater.*, 2016, 26, 8764-8775. doi:10.1002/adfm.201603763
31. Ashford, E., *Redefining Wearable Technology. TechXplore Newsletter*, Aug. 24, 2018. <https://techxplore.com/news/2018-08-redefining-wearable-technology.html>
32. University of Illinois at Urbana-Champaign, *Smart skin: Electronics that stick and stretch like a temporary tattoo. Science News*, Aug. 11, 2011. <http://esciencenews.com/articles/2011/08/11/smart.skin.electronics.stick.and.stretch.a.temporary.tattoo>
33. Wang, C. F., Wang, C. H., Huang, Z. L., Xu, S., *Adv. Mater.* 2018, 30,1801368. <https://doi.org/10.1002/adma.201801368>
34. Tao, T., Lu, S. G., Chen, Y., *Adv. Mater. Technol.* 2018, 3, 1700375, <https://doi.org/10.1002/admt.201700375>
35. Zamarayeva, A.M.; Ostfeld, A.E.; Wand, M.; Duey, J.K.; Deckman, I.; Lechene, B.P.; Davis, G.; Steingart, D.A.; Arias, A.C. *Science Advances [Online]* 2017: 3(6), 1-10. e1602051 DOI: 10.1126/sciadv.1602051
36. R. Sivasubramony et al., "Assessing the Reliability of Highly Stretchable Interconnects for Flexible Hybrid Electronics," IEEE 69th Electronic Components and Technology Conference, May 2019, pp. 768-776.