HETEROGENEOUS INTEGRATION ROADMAP

2019 Edition

Chapter 4: Medical, Health and Wearables

http://eps.ieee.org/hir

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Chapter 4: Medical, Health and Wearables

This chapter is in preparation, and will be integrated into the Roadmap at version 1.1, planned for the end of 2019. In its place is the following summary and a series of slides giving the current status of applications of flexible hybrid electronics to medical, health and wearable technologies that is relevant to the progress needed over the next 10 to 15 years.

Executive Summary

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 that significantly advance packaging and assembly technologies is in the early stages. 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) and RF (components and communications) in thin, flexible and comfortably wearable formats will be key. This chapter will describe these technologies including the target applications, the materials, deposition methods, components, device integration and reliability. It will discusses trends and challenges expected in the coming years.

Heterogeneous Integration Roadmap

Medical, Health and Wearables

Mark D. Poliks (Binghamton University), Jan Vardaman (TechSearch International, Inc.) & Nancy Stoffel (GE)
Wilfred Bair (NextFlex), Jason Marsh (formerly at NextFlex)
and the NextFlex Community

Disclaimer: The material contained herein is biased towards Flexible Hybrid Integration approaches as a consequence of the NextFlex contribution. It is recognized that many rigid and semi-rigid approached are also widely used and should be part of the HIR.

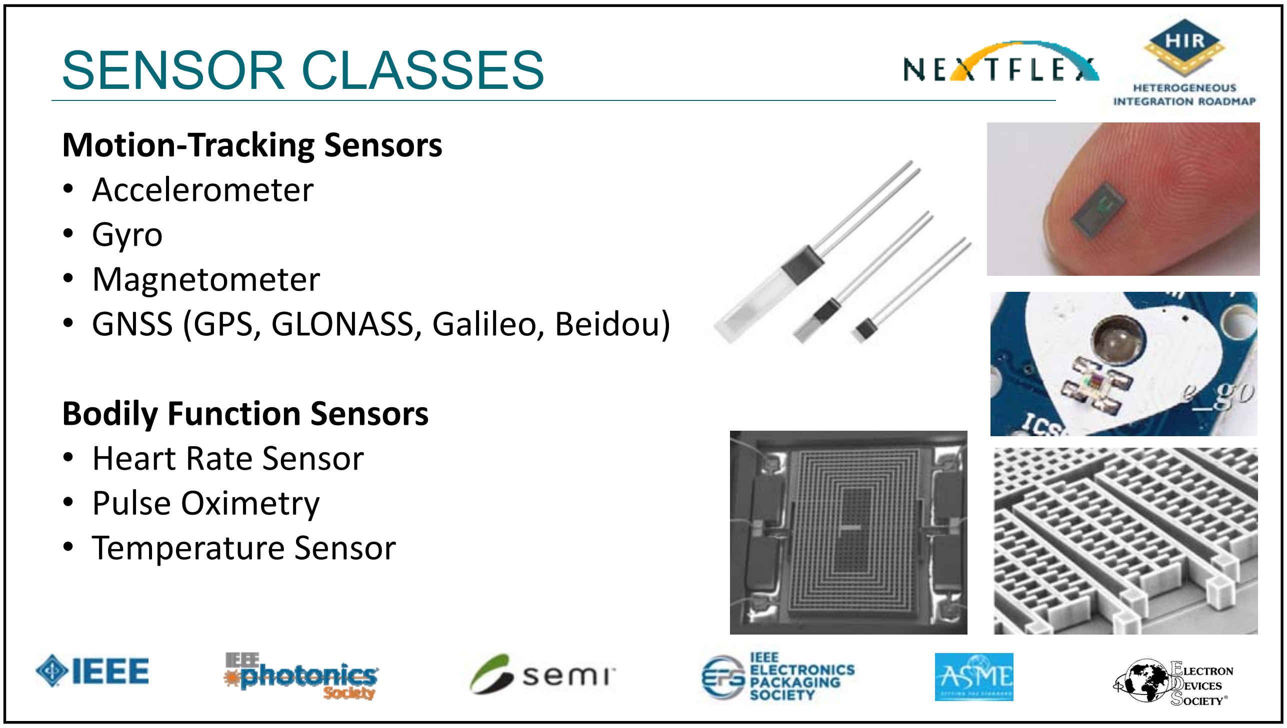
Application Space: focus on wearable devices

- Hierarchy of Accuracy
  - Clinical (clinical grade, high accuracy critical)
    - Patient monitoring, diagnosis and therapy
  - Occupational
    - Factory or harsh conditions
  - Extreme Performance
    - Military, Public Safety/Homeland Security, Professional Athletics)
    - Mentally & physical demanding settings
  - Wellness/Fitness (non-critical relative accuracy)
    - General personal use -- information only
- Wearables based on COTS components (2016 and before)
  - Pulse, heart-rate, temperature (basic non-medical grade vitals)
- Wearables based on non-COTS (2017 and after)
  - Form Factor
    - Conformability
    - Stretch-ability
    - Transparency
    - Semi-Breathability
  - Basic medical grade vitals
  - Physiological: ECG, EEG, SpO2, BP, RR, temperature and more
  - Motion, strain and pressure sensors
  - Integrated multi-sensor systems
  - Fluid and biomarker analysis (using micro fluidic systems)
    - Sweat sampling (absorption and wicking)
    - Interstitial fluid and blood (micro needles)

WEARABLES 2016

Sensors & Devices

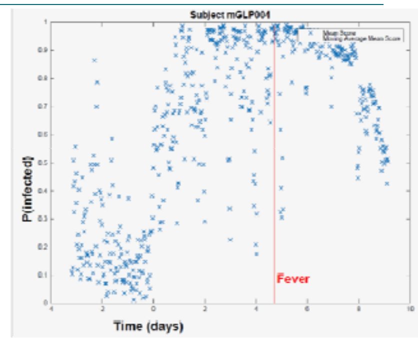
- Motion-Tracking Sensors
  - Accelerometer
  - Gyro
  - Magnetometer
  - GNSS (GPS, GLONASS, Galileo, Beidou)
- Bodily Function Sensors
  - Heart Rate Sensor
  - Pulse Oximetry
  - Temperature Sensor
  - Chemical
  - Electrical
  - RF


SENSOR CLASSES
Motion-Tracking Sensors
• Accelerometer
• Gyro
• Magnetometer
• GNSS (GPS, GLONASS, Galileo, Beidou)
Bodily Function Sensors
• Heart Rate Sensor
• Pulse Oximetry
• Temperature Sensor


WEARABLES 2018-2021
Form Factor
• Conformability
• Stretchability
• Transparency
• Semi-Breathability
Sensors
• Chemical
• Electrical
• RF

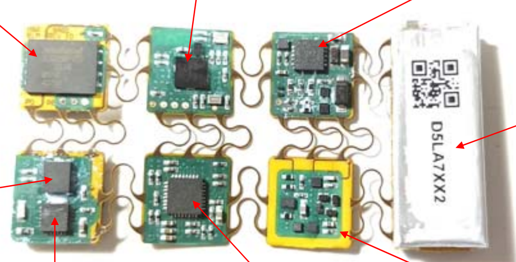
MEASURING PEOPLE

- Biomarker Examples
  - Neuropeptides (NpY, Orexin A..)
  - Cytokines
  - Catecholamines
  - Corticosteroids
  - PSMA/Antigens
  - Glucono Lactone(glucose oxidase)
  - Saccharide (boronic acid)



	Measurement	Input Needed	Connection	Continuous
Temperature	Electrical	Voltage	Skin Contact Electrodes	Yes
Electrocradiogram	Electrical	Passive	Adhesive Electrodes	Yes
Photoplethysmograph	Optical	Light	Adhesive Sensor	Yes
Electrolytes	Potentiometry	Wicked Sweat/Blood	Wick	Yes
Blood Gasses	Amperometry	Capillary Blood	Microneedle	Yes
DNA Markers	DNA	Nucleic Acid Amplification/Fluid Sample	Swab/Tissue Sample	No
Protien Markers	Eletrochemical/Optical	Swabbed Blood/Sweat/Urine/Sweat	Swab	Maybe

SUNY BINGHAMTON EVAL (MC-10 BIOSTAMP)

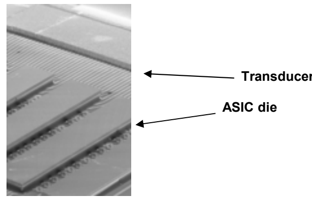


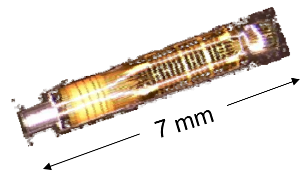
I3, UIC AND BINGHAMTON UNIVERSITY

Early (2010) FHE Product:

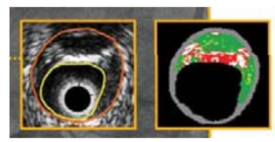
Five ASIC die in 1 mm diameter

Intravascular Ultrasound (IVUS) is a catheter-based system that allows physicians to acquire images of diseased vessels from inside the artery.





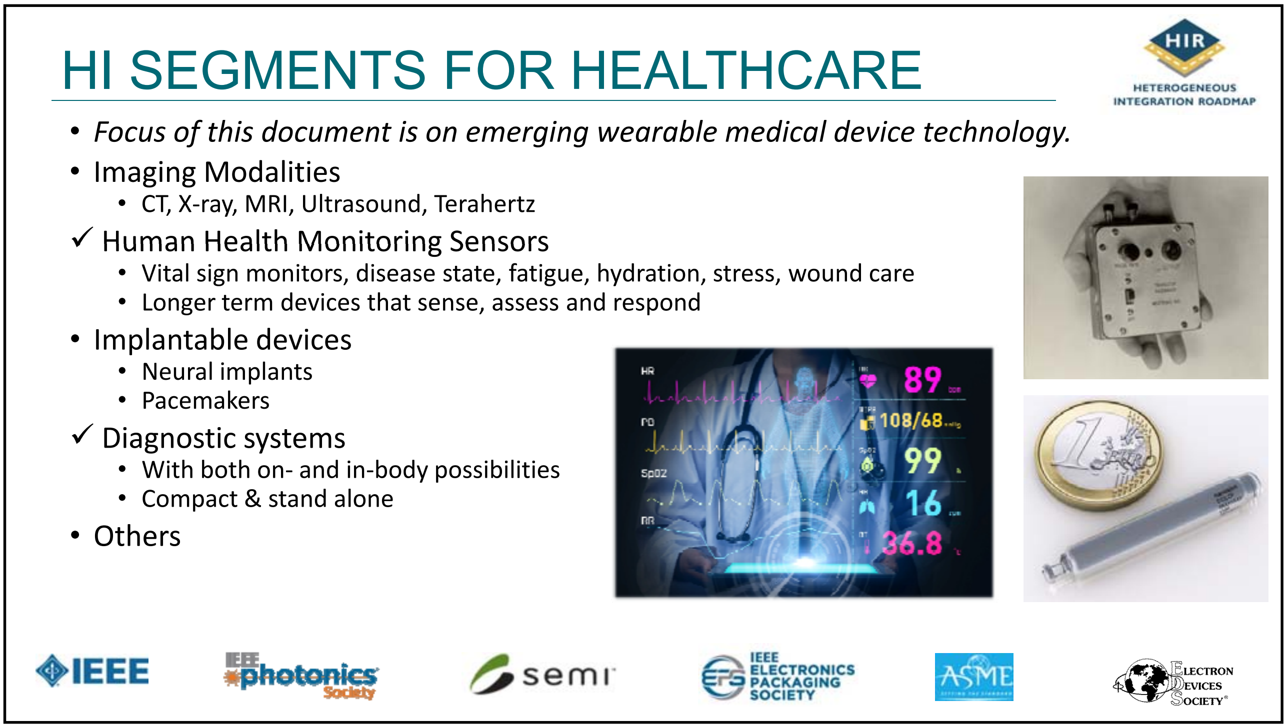
Part Description
Description: Flexible polyimide substrate with transducer (receiver / transmitter)
Dielectric: Polyimide, 12.5 µm
LW/LS: 14 µm / 14 µm
Flip Chip: 22 µm bumps, 70 µm pitch

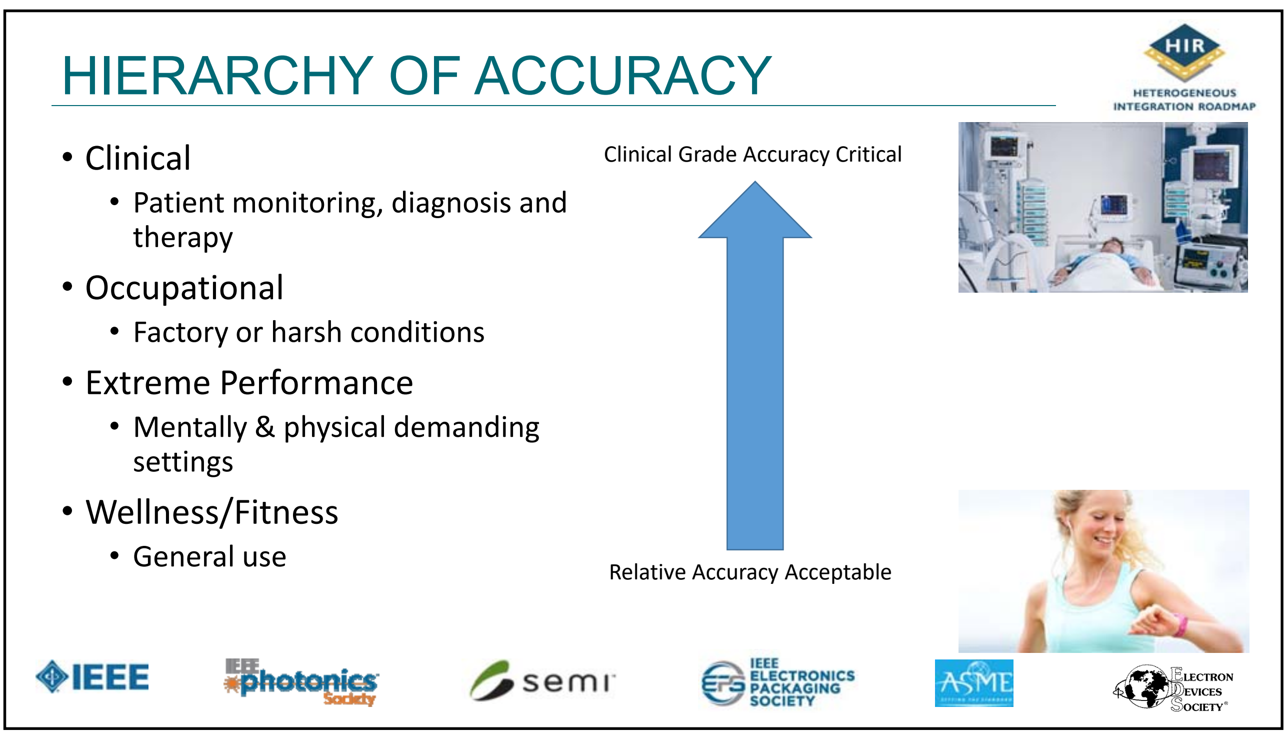


Endicott Interconnect (i3), Universal Instruments & Binghamton University

Heterogenous Integration for Healthcare

- Imaging Modalities (much follows other sections of HIR)
  - CT, X-ray, MRI, Ultrasound and Terahertz
- Human Health Monitoring Sensors
  - Vital sign monitors, disease state, fatigue, hydration, wound care
  - Longer term devices that sense, assess and respond
- Implantable devices
  - Neural implants
  - Pacemakers
- Diagnostic systems
  - With both on- and in-body possibilities
  - Compact & stand alone
- Other related applications
  - Neonatal
  - Smart wound care
  - Smart PPE
  - other


HI SEGMENTS FOR HEALTHCARE
HIR
HETEROGENEOUS INTEGRATION ROADMAP
• Focus of this document is on emerging wearable medical device technology.
• Imaging Modalities
• CT, X-ray, MRI, Ultrasound, Terahertz
✓ Human Health Monitoring Sensors
• Vital sign monitors, disease state, fatigue, hydration, stress, wound care
• Longer term devices that sense, assess and respond
• Implantable devices
• Neural implants
• Pacemakers
✓ Diagnostic systems
• With both on- and in-body possibilities
• Compact & stand alone
• Others
89
108/68
99
16
36.8
IEEE
photonics Society
semi
IEEE ELECTRONICS PACKAGING SOCIETY
ASME
ELECTRON DEVICES SOCIETY


HIERARCHY OF ACCURACY
HIR
HETEROGENEOUS INTEGRATION ROADMAP
• Clinical
• Patient monitoring, diagnosis and therapy
• Occupational
• Factory or harsh conditions
• Extreme Performance
• Mentally & physical demanding settings
• Wellness/Fitness
• General use
Clinical Grade Accuracy Critical
Relative Accuracy Acceptable
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ASME
ELECTRON DEVICES SOCIETY

Substrates, Materials and Device Integration

- Rigid, flexible and ultra-thin
- Silicon, glass, ceramic, polymer (PI, PET, LCP, TPU), fabric, paper
- Plated metals (Au, Pt, Cu, etc.)
- Printed metal inks/pastes: (Ag, Cu, etc.)
- Printed & dispensed materials including dielectrics, encapsulants, sealants etc.

- Device integration
  - Electronic (active & passive)
  - RF (communications)
  - Optical (emitters and sensors)
  - Micro-fluidic
  - Other: MEMS, temperature, GPS etc…

Literature review and summary

- The following slides are *examples* of current literature in the field that demonstrate clear trends and capabilities being implemented in prototype hardware for initial testing that often involves human subjects.

- Pictures and diagram will be added.
- Additional literature will be added in the narrative version of this document.

Materials and Structures toward Soft Electronics

- Summary from Advance Materials, **2018**, 30, 1801368 by C. Wang, C. Wang Z. Huang and S. Xu. (with 656 references)
- Materials for Soft Electronics
  - Hydrogels, liquid metals, conductive polymers, and nanomaterials.
- Structural Designs for Soft Electronics
  - Wave/wrinkle, island bridge, origami, kirigami, textiles, cracks, and interlocks.

Flexible Hybrid Electronics: Direct Interfacing of Soft and Hard Electronics for Wearable Health Monitoring

- Summary from Advanced Functional Materials, **2016**, 26, 8764-8775 by Y. Kahn, M. Garg, M. Poliks, K. Ghose, J. Turner and A. Arias and others (with 28 references)
- Wearable Sensor Patch
- Single-substrate integration by direct printing of sensors
- Inkjet printed Au ECG electrodes
- Stencil-printed nickel oxide thermistors
- Fabrication of the WSP
- Real-time ECG signal monitoring

A Wearable Electrochemical Platform for non-invasive simultaneous monitoring of Ca^{2+} and pH

- Summary from ACS Nano, 2016
- Authors include: H. Hyein, W. Gao, Z. Shahpar, R. Davis and A. Javey and others (with 43 references)
- Demonstrated a wearable electrochemical device for continuous monitoring of ionized calcium and pH of body fluids using a disposable and flexible array of sensors interfaced with a flexible PCB.

Highly flexible, wearable and disposable cardiac biosensor for remote and ambulatory monitoring

- Summary from Nature Partner Journals Digital Medicine, 2018.
- Authors include: S. Lee, G. Ha, D. Wright, J. Rogers, R. Ghaffari and others (with 49 references)
- A highly flexible epidermal design and clinical implementation of a novel ECG and hear rate logging wearable sensors that is low-cost, light-weight and capable of energy harvesting. Device communicates using standard near field communication approaches.

Battery-free, stretchable optoelectronic system for wireless optical characterization of the skin

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- Summary from Science Advances Research Article, e1600418, 2016.
- Authors include: J. Kim, G. Salavatore, H. Araki, S. Xu, J. Rogers and others (with 31 references)
- Introduces an 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.
- Application to arterial blood flow, tissue oxygenation etc.

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Flexible Electronics toward wearable sensing

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- Summary from ACS Accounts of Chemical Research, 2018.
- Authors include: W. Gao, H. Ota, D. Kiriya, K. Takei and A. Javey (with 48 references)
- Summary of recent studies on the design of flexible electronics devices and systems for physical and chemical monitoring.
- Material innovation, sensor design, device fabrication, system integration and human studies toward continuous and noninvasive wearable sensing are discussed.

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Nano-packaging for component assembly and embedded power in flexible electronics

- Summary from IEEE Nanotechnology Magazine, 2018.
- Authors include: N. Shahane, P. Raj, C. Nair, V. Smet, C. Buch and R. Tummala (with 56 references)
- Heterogeneous component integration for flexible systems
- Next-generation electronics systems
- Anatomy of flex packages
- Flex substrates
- Interconnects and component assembly
- Flexible power supply: storage, harvesting and conversation

Flexible and stretchable power sources for wearable electronics

- Summary from Science Advances, 3, e1602051, 2017.
- Authors include: A. Zamarayeva, A. Ostfeld, M. Wang, J. Duey, I. Deckman, B. Lechene, G. Davis, D. Steingart and A. Arias (with 50 references)
- Unique approach that demonstrates mechanically robust, intrinsically safe, silver-zinc batteries.
- Approach uses current collectors with enhanced mechanical design, such as helical springs and serpentines as structural support and backbone for all battery components.

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A wearable patch for continuous monitoring of sweat electrolytes during exertion

- Summary from Lab Chip, 2018, 18, 2632–2641
- Authors include: A Alizadeh, A Burns, R Lenigk, R Gettings, J Ashe, A Porter, M McCaul, R Barrett, D Diamond, P White, P Skeath and M Tomczak. (with 35 references)
- 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.

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HIR HETEROGENEOUS INTEGRATION ROADMAP

BROAD RANGE OF MATERIALS AND DEVICES

- Substrates
  - Rigid, flexible and ultra-thin
  - Silicon, glass, ceramic, polymer (PI, PET, LCP, TPU), fabric, paper
  - Plated metals (Au, Pt, Cu, etc.)
  - Printed & dispensed materials
- Device integration
  - Electronic (active & passive)
  - RF (communications)
  - Optical (emitters and sensors)
  - Micro-fluidic
  - Other: MEMS, temperature, GPS etc...
  - Power
- Packaged for a wide range of size, shape and other physical attributes

Dressing	Manufacturer	Base Material
Telfa	Medtronic	PET
Tegaderm	3M	PET
ProFore	Smith & Nephew	Si
Dermanet	DeRoyal	Si
Colactive	Covalon Tech	Biodegradeable
Petrolatum	Cardinal Health	Cellulose Acetate
ComfiTel	Dermarite	Si
CutiCell	BSN	Si
Meptiel One	Mölnlycke	Soft Si

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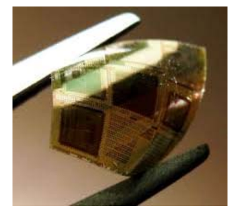
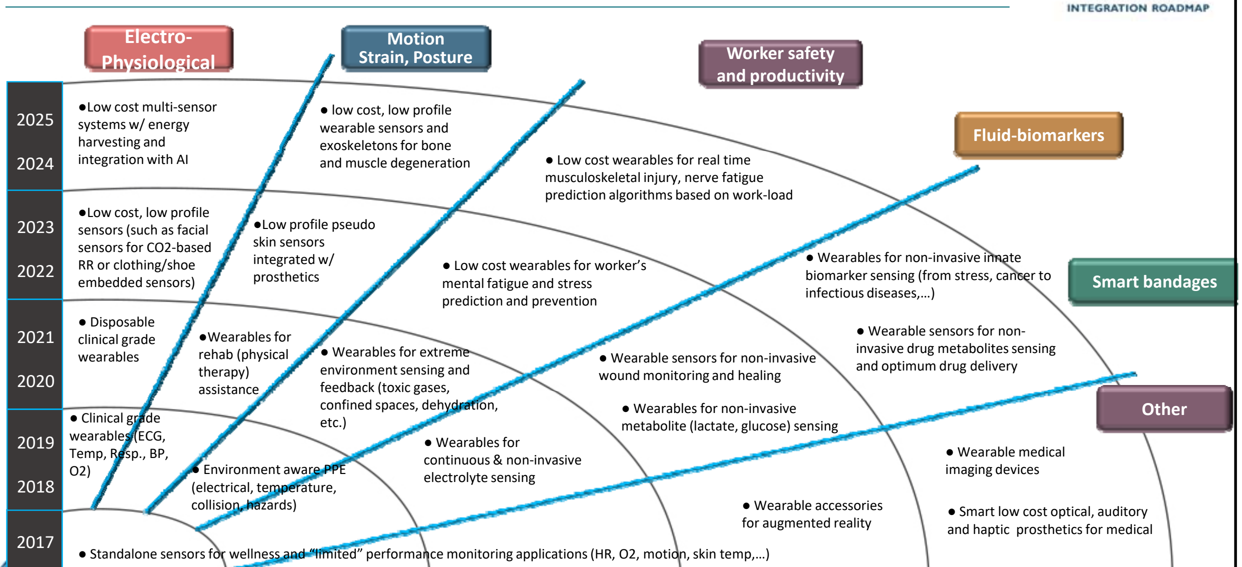
MEDICAL HIR OBJECTIVES

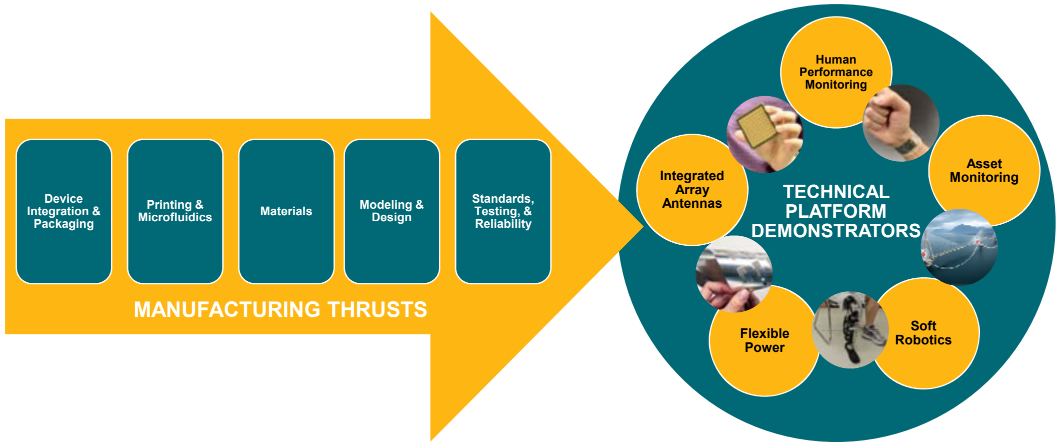
- Physiological: ECG, EEG, SpO2, BP, RR, temperature and more
- Motion, strain and pressure sensors
- Fluid level and fluid bio-marker sensors
- Smart bandages
- Smart PPE
- Integrated multi-sensor systems
- Communications
  - Device integrated antennas (Bluetooth)
  - Advanced printed antennas solutions for multi sensor on-body applications
- Energy Management
  - Batteries, inductive charging to harvested energy
  - Compact, safe, high energy density batteries



FHE APPLICATION VIEW



NEXTFLEX FOCUS



Data Processing

- microprocessors
- memory
- A/D converters and filters
- Integration of communications (optional)

Communications

- Wired (conventional protocols with cables)
- Wireless (Bluetooth, WiFi and beyond)
  - Device integrated antennas
  - Advanced printed antennas solutions for multi sensor on-body applications
  - Applications with integrated near-field power and communications

Power & Energy Management

- Wired
- Batteries, inductive charging to harvested energy
  - Compact, safe, high energy density batteries
  - Coin cells and conventional batteries
  - “Flexible” unpackaged batteries
  - Wireless charging (conventional)
  - Wireless near-field activated low power systems
  - Harvested energy based power (thermal or mechanical)

Integration

- Packaged for a wide range of size, shape and other physical attributes
  - Conventional packaged components & interconnects
  - Unpackaged bare die
  - Unpackaged thin bare die
  - Printed interconnects

Manufacturing

- Pick/Place, Assembly and Reflow
  - Conventional pick/place with solder assembly
  - Low temperature solder assembly
  - Highly localized laser based reflow
  - Photonic based reflow
  - Other printed interconnect (aerosol jet print
- Thin-die handling, pick/place
- Direct printed interconnect
- Thin substrate handling (frames, fixtures or R2R)
- Stretchable substrate handling (frames, fixtures or R2R)

ELEMENTS FOR MEDICAL FHE

- Circuitization
  - Die < 100 I/O & pitch > 200 µm
  - Flexible and stretchable substrates
    - Single-layer to multi-layer
  - Printed vs plated conductors
- Non-printed components
  - Flexible interposers
  - Thin die (flip-chip) bonding
    - 50 µm to 10 µm wafers
    - Need unpackaged die
- Device Assembly
  - Methods (PnP) for 50 to 10 µm thick die
  - Embedded passive & active components
  - Panel to Roll
- Encapsulation
  - For single to multiple die
  - Flexible/Conformable

CURRENT ROADMAP NEEDS

- Unpackaged thin die
- Compliant interconnect and attach methods
- Stretchable and conformable substrates (films and textiles)
- Flexible low Dk/Df
- Printed passives and RF
- Metal-like printed conductors
  - Thermal, laser, photonic based metal oxide reduction/particle-flake sintering
  - Use of (localized) reducing gas (hydrogen/nitrogen) processes
- Embedded components
- Encapsulation for range of environments
  - On-body, in-body, high/low temperatures/humidity
- Scalable manufacturing
  - Panels to rolls

HI AND THE PATH TOWARDS FHE

- Devices are evolving into full systems with different building blocks, which may include but are not limited to sensors, actuators, MEMS, RF communication, power electronics, GPUs, CPUs, and memory
- The current approach is to offer a high density integration of different building blocks in a SiP, 2.5D Interposer or 3D integration.
- FHE offers a less dense but overall system integration in a flexible format ideal for wearable devices, replacing Silicon interposers with plastic film substrates
- Both lithography based subtractive processing as well as additive and semi additive manufacturing options are available for FHE systems