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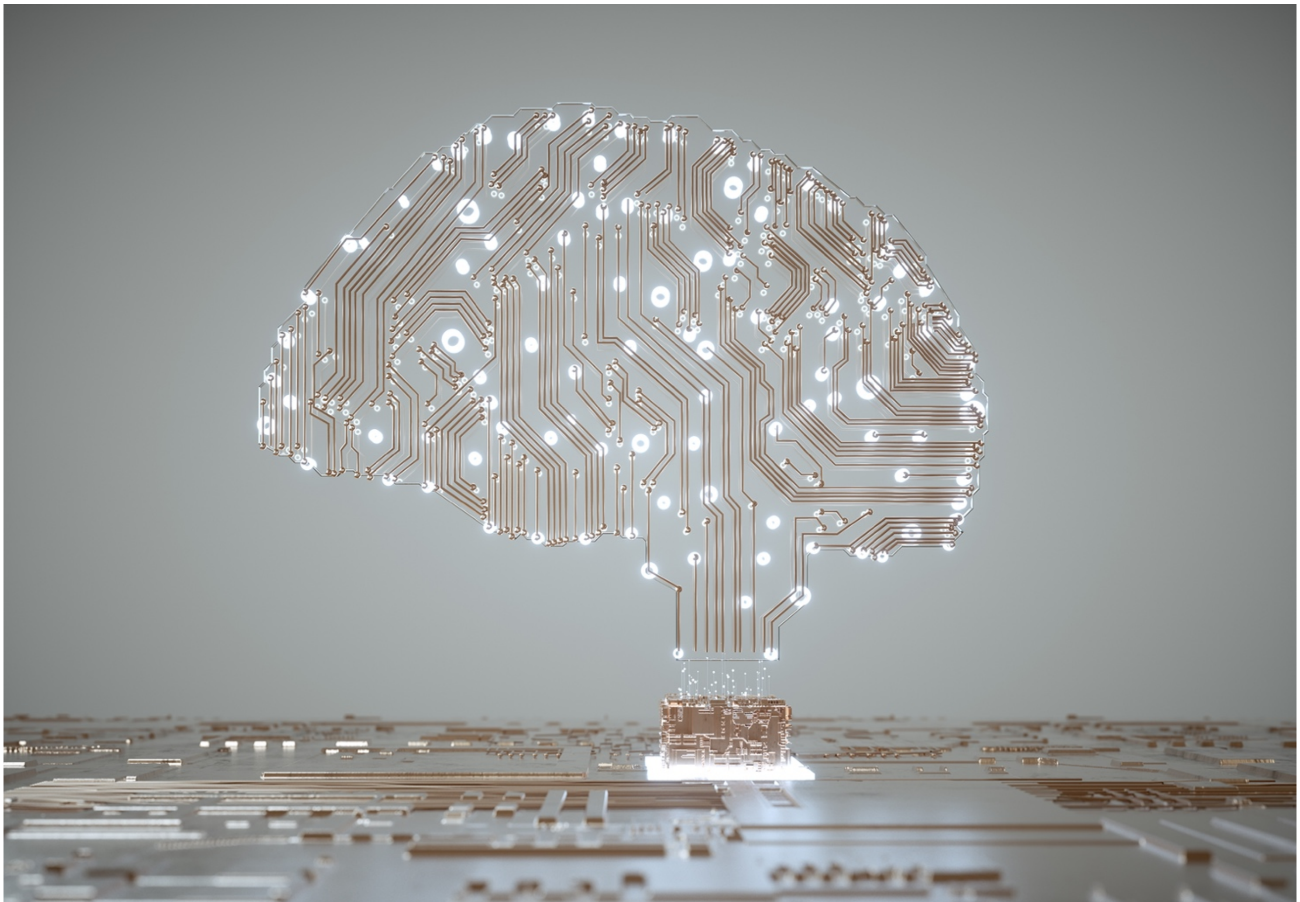

THE FUTURE OF WEARABLE HEALTHTECH

October 2022

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Background

The health and wellness wearable tech market is set for dramatic growth over the next five to ten years. Driven by a potent combination of technical innovation and changing consumer attitudes and demands, the market will encompass a growing diversity of health and wellness applications.

Wearable healtech will be at the heart of the fifth industrial revolution where man not just meets machine but becomes integrated with machine.

We are currently entering a renaissance for wearable tech as the forces of new biology, bio engineering and digital technology collide. The fruits of this renaissance will change our world forever as we see a combination of activities digitizing biology, fuse with activities biologizing digital.

The more biology becomes a component of wearable tech the more this market will encroach on traditional pharma/biotech markets and the greater its growth potential.

This paper aims to highlight how current innovation in this sector could evolve in the future.

Introduction

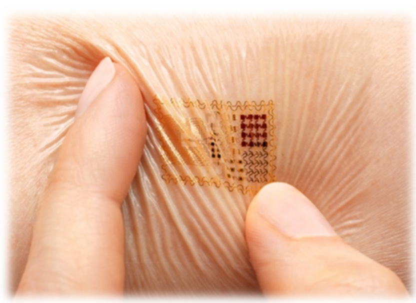
The future of wearable tech is exciting and frankly, inevitable.

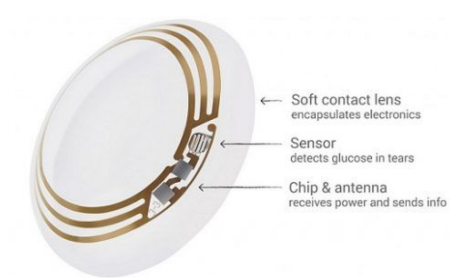
Think about how mobile phones have evolved over a relatively short period of time and how now it is virtually impossible to do without them. Phones are essentially “wearable” tech – right now you have to “wear” them in your hand or pocket but that’s changing.

Wearable tech will become a key component of everyday life involved in both monitoring and managing many aspects of health, wellness and medical treatment.

Firstly, a definition of what we’re talking about always helps to frame everything. From a healthcare perspective, wearable technologies can be defined as a small device that is worn or carried on the body to improve personal health and well-being through diagnosis, treatment, monitoring and prevention.

Today Wearables take many forms and include: clothing, skin patches, watch-like devices, body devices, hearing devices, glasses and contact lenses.





These different devices and formats already cover a very broad spectrum of applications and they will continue to evolve.

Applications

The number of applications for wearable tech is growing, literally by the day, but they can be broadly categorized into three groups:

1. Activity Tracking – Monitors functions such as steps, sleep pattern, heart-rate and calorie intake. These apps/devices intend to provide users with instant feedback to modify their physical behavior for healthy living.

2. Health Monitoring – Supports medical diagnosis of user's health conditions. Recently introduced ECG and glucose monitoring features on wrist-worn wearables fall under this category. Additional features of such devices include providing users with disease updates, news, informative articles, treatment plans, drug information and advice.

This category includes: real-time patient monitoring, sleep monitoring devices, dyspnea and respiratory monitoring, fetal monitoring and obstetric devices, and neuromonitoring devices. Could include monitoring patient compliance and clinical trial participants.

3. Therapeutic Wearable Medical Devices – provides both disease monitoring and therapeutic intervention or treatment, for example insulin pumps that monitor glucose levels and administer insulin. Other areas included devices that measure movement of a limb and support post-operative or trauma physiotherapy.

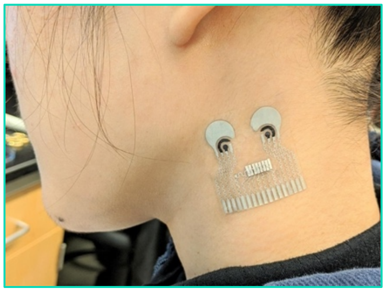
Includes: pain management devices, rehabilitation devices, insulin pumps, and respiratory therapy devices, which provide RPM and therapeutic delivery.

ava

Ava is the first wearable device designed to track, visualize, and understand the menstrual cycle. The parameters tracked include pulse rate, breathing rate, sleep, heart rate variability, and temperature. Once synced with the corresponding app, this data, along with the user's fertility status, is displayed in real time.

In the future wearable tech, either attached to the body or integrated onto/into the body, will be an essential part of day-to-day living. The bigger question is how much of our life will they be involved with? The short answer is, everything.

As technology develops, so too do the applications and utility.



There are two broad forces that are governing the adoption of wearable tech – the development of new technology and the regulations that govern its use.

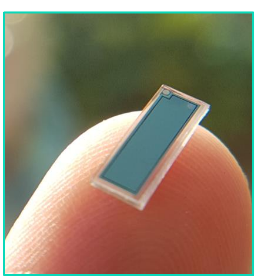
New technology is being driven by advancements in biology as well as digital "inorganic" technology and includes things like sensors, active materials, wireless connectivity, and batteries.

Technological Developments

Digital Technology

Batteries

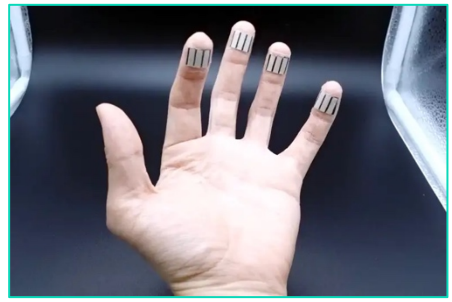
Battery technology is particularly important for wearable tech as device size is a critical component of utility. The ideal battery will be small, lightweight and store enough energy to power ever increasing functions for long periods of time without the need to recharge frequently and the ability to re-charge many times.



Energy density and biocompatibility are key challenges now being met by developments in solid-state technology. Solid-state batteries have longer life spans of up to 10 years (up to 5x longer) and lower leakage currents (10x smaller), making them suitable for low power wireless charging. The Stereax M50 is an example of new solid-state technology which is less than 1mm thick and can be stacked to add energy density.

Clearly the more battery technology advances to match these criteria the more subtle the device can become. However higher levels of energy stored in unstable environments near the body and the need to be biocompatible so that they do not pose a risk of leakage will bring further regulatory hurdles.

For smaller energy requirements other sources are being tapped directly from the body. For example small biofuel cells being developed at UCSD can harvest enough energy from the sweat on a person's fingertips to power wearable medical sensors that track health and nutrition – and because our fingertips are one of the sweatiest parts of the body, the sensors could be powered all day.



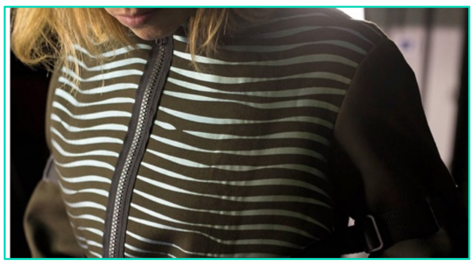
The Internet of Things

Wearable tech is one the pioneers of the internet of things, or IoT - a system of interrelated computing devices, mechanical and digital machines, objects, animals or people that are provided with unique identifiers (UIDs) and the ability to transfer data over a network without requiring human-to-human or human-to-computer interaction.

As the IOT expands so too will the utility for wearable tech, connecting the wearer to other devices, datasets and observers. As a result, many medical device companies are already evolving their business models away from being providers of products to patient care management organizations. For example, AliveCor's electrocardiogram (ECG) home monitoring along with its platform, application and other accessories, or clinical-grade biometric sensors from MC10. The MC10 BioStamp system collects and processes raw data into recognizable clinical metrics including vital signs, activity/actigraphy and posture classification, sEMG, and sleep metrics. The ability to collect consistent, relevant and standardized medical and "real world" data represents a very significant opportunity for enhancing the efficiency of clinical trials and the resulting claims for the tested treatment. MC10 was recently bought by Dassault Systemme's MediData, indicating the growing interest in the value of this kind of data.

Senseonics Eversense for monitoring blood glucose levels in people with diabetes. The Eversense CGM System provides continuous glucose monitoring for up to 90 days via an under-the-skin sensor, a removable and rechargeable smart transmitter, and a convenient app for real-time diabetes monitoring and management.

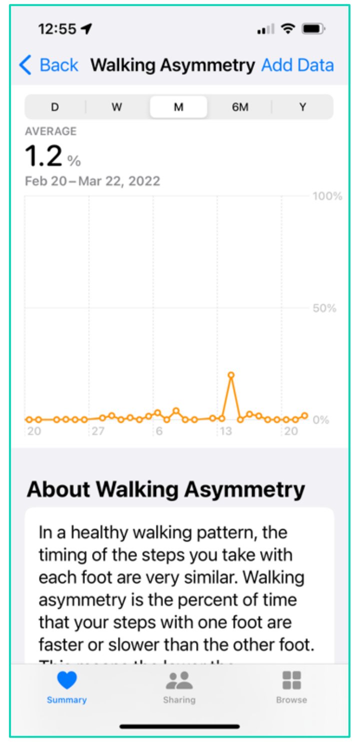
By connecting monitoring wearable devices to other devices and to places, the IoT enhances the reach and efficiency of caregivers, (an extremely important factor for economies with aging populations), in monitoring their patients remotely, improve healthcare access, reduce costs, save time, and enable early detection of deterioration. Consequently, digitization of medical diagnostic and monitoring processes are focusing on outcome, reduction in risk, and metered usage. In the future, IoT devices are anticipated to be aimed at prevention and wellness management, technology convergence, and value-based healthcare.



The Holst Centre's connected cuddle vest with integrated haptic technology gives people the opportunity to experience a friends' touch, (even in times of social distancing). Fourteen haptic motors positioned around the upper body and arms create vibrotactile patterns that feel like a caress or even a firm hug. The vest is controlled at a safe distance by a phone or tablet, creating a new form of intimacy. However, it's not hard imagine the medical applications of this connected technology; a pumping compression of a calf muscle to support poor flow at the behest of a struggling heart. Or a reassuring virtual pat on the back when you've reached your exercise goals.

Now you can even pay for all of this with just a swipe of your hand. Walletmor has created an implantable chip that allows you to use your hand to pay. Purewrist is an independent digital wallet, where you store your funds. Walletmor uses is near-field communication or NFC, the contactless payment system in smartphones.

Big Data and AI



One of the key aspects of wearable tech is the ability to collect large amounts of accurate, standardized and consistent data (big data) about a variety of bodily functions and process and interactions. When properly analyzed, big data can be very powerful in providing insights for business strategy and, importantly, healthcare. Combine Big Data with advances in Artificial intelligence (AI) (software that mimics aspects of human intelligence), and we begin to see some very exciting possibilities, especially when it comes to predicting the future. Predictive analytics promises to bring a whole new level of utility to wearables, something that the big tech players are already fully engaged in. Apple's iPhone Health App currently collects movement and auditory data and allows input on sleep, blood glucose, heart rate and your full medical records. One example of how big data and AI can function together is buried within Apple's data collection directly from iPhone – asymmetry. iPhone currently collects data about how symmetrical (or asymmetrical) your steps are. A number of large clinical studies[1] have shown that changes in gait (or asymmetry) could be used to predict changes in cognitive and kinetic function. eg the onset of dementia. 1. *JAMA Network Open.* 2020;3(2):e1921636.

Hinlab is developing a wearable replacement for the traditional hospital bedside monitor to measure blood pressure, heart rate, oxygen saturation etc. At first glance doesn't seem to be a big deal but if you give every patient in the ward one of these, start collecting data, and apply AI based predictive analytics, then it becomes more interesting. Deterioration of patients health can be predicted more rapidly, via pattern recognition of bio-signal trend variation. You could literally see the spread of an infection from ward to ward or detect cardiovascular or respiratory disease earlier, so that the correct resources could be mustered at the appropriate time.

Augmented Reality

Augmented reality (AR) superimposes computer-generated content over a live view of the world and integrates digital information with the user's environment in real time. Wearable sensors can contribute to the data and information in real time to deliver live "views" of the wearer's health.

AR in healthcare is the development of applications that empower patients to play a more proactive role in their own care in areas like chronic pain and mental health.

By helping to visualize things that are currently somewhat opaque there are applications for both patients and healthcare professions. Patients can use it to help better describe symptoms, while physicians can more accurately identify treatment approaches.

For example AR software built into smart glasses superimposes real-time data directly from a dental scanner, enabling a dentist to build precise crowns or caps or surgeons to properly align incision points for less patient trauma. Accuvein (shown opposite) allows the visualization of veins to aid accurate intravenous injection.

Metaverse

The metaverse, a domain of the internet where individuals engage with or immerse themselves within virtual worlds with the help of digital tools. Big Tech and Big Commerce are all carving out a stake in the Metaverse. Why? Because the metaverse will become an extension of the real world, where you can spend real money.

A number of Metaverse applications are currently being researched for the treatment/management of mental health conditions including phobias, PTSD, anxiety disorders, hallucinations, and delusions. The metaverse has the potential to change the way we seek support from friends, family, or healthcare professionals. Digital health metaverse experiences might include patients attending virtual reality (VR) group therapy sessions, surgeons planning out procedures on anatomical holograms, or expectant mothers practicing breastfeeding techniques in augmented reality.

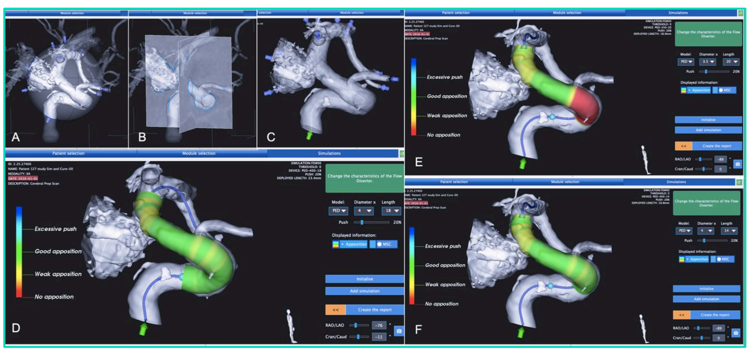
AppliedVR is harnessing the unique properties of immersive therapeutics, we are delivering a bio-psycho-social solution to address the bio-psycho-social condition of chronic pain.

BehaVR translate proven science into immersive and engaging XR therapeutics for mental and behavioral health.

XRHealth has developed VR based therapist supported treatments for Autism Spectrum Disorder, Anxiety, Pain, Fibromyalgia that are reimbursed by insurance companies.

However, the concept of Digital Twins will likely see significant development in the coming years. Digital Twins: representations of real-world entities that exist in virtual worlds and can be manipulated to glean insights for healthcare decision making. The use of digital twins in the healthcare industry is already revolutionizing clinical processes and hospital management by enhancing medical care with digital tracking and advancing modeling of the human body.

Digital twin technology acts as a bridge between the physical and the digital world. By using sensors to measure a physical asset, scientists and engineers are able to collect a wealth of data that can be mapped into a virtual model. This data-charged model can be analyzed to offer crucial information about how the physical thing will respond to the real world. A digital twin helps understand not only how a product or system is currently performing, but also how it may perform in the future.



For example Sim & Size enables visualization of cerebral blood vessels for preoperational planning and precise sizing for neurovascular interventions and surgery. It uses an actual image of the patient produced by 3D rotational angiography. It allows surgeons to computationally model more accurate placement and apposition of NeuroInterventional devices.

Digital Twins are currently being developed by Unlearn to “replicate” patients for clinical trials, which will lower costs and time to completion.

Babylon uses responses to a questionnaire about lifestyle and family history to create a Digital Twin which gives users insights about their current health and risk factors for future conditions along with practical recommendations for staying healthy.

A digital twin should represent a living data system that can take in longitudinal biodata over time and track and learn from that evolving data set to give a reflection of a person’s health and more importantly health trajectory. This starts with measuring and tracking biodata such as cholesterol levels, vitamin panels, and medical imaging results. It will also need to include more complex datapoints, such as genomic, epigenetic, metabolomic, and immune function data. It is easy to imagine how this can evolve as wearable sensors evolve to collect data on an individual’s genetic makeup, physiological characteristics, and lifestyle.

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Sensors

Sensors quantify dynamic biological signals in real time and are consequently a key driver of wearable tech – the more we can measure the greater the applications. Currently built-in sensors in wearables, such as accelerometers, gyroscopes, magnetometers, pulse and moist sensors which can be used for continuous monitoring of physiological and movement related variables have been the mainstay in the wearable platform. However, we are at the beginning of a paradigm shift in healthcare delivery attributed to the development of nanomaterials and improvements made to non-invasive bio-signal detection systems alongside new approaches for data acquisition and interpretation.

For example, a collaboration of researchers at the Massachusetts Institute of Technology and the Rhode Island School of Design have developed a new kind of fiber material that is able to detect a heartbeat, handclaps or even faint sounds, unlocking a new avenue for wearable technology that can be worked into clothing.

The researchers used a material that was piezoelectric. This means it can generate an electric charge in response to being moved (or in this case, an individual moving about while wearing a fabric). This provides a way for the fabric to convert sounds into signals that can be tracked, or to activate something. Wearing an acoustic garment, you might talk through it to answer phone calls and communicate with others," says Wei Yan, the lead author who is now an assistant professor at the Nanyang Technological University in Singapore. "In addition, this fabric can imperceptibly interface with the human skin, enabling wearers to monitor their heart and respiratory condition in a comfortable, continuous, real-time, and long-term manner."

Roswell is integrating molecules with electronics to achieve the ultimate in biosensor scalability. This scalability, combined with the ability to monitor molecular activity at single-molecule resolution, will unlock the future of science.

In addition, the discovery of new biomarkers and the use of bioaffinity recognition elements like aptamers and peptide arrays brings a number of science disciplines together – engineering, physics, material science and biology working from both ends to drive innovation – digitizing biology at one end and "biologizing" digital at the other end.

Biological Technology

Advances in inorganic digital technology will no doubt have a profound positive impact on wearables but it is the developments in Biological Technology that will be the real drivers. Specifically, the convergence of biological and digital information systems promises to facilitate unprecedented insight into, and control of, biological systems ranging from single cells, multi-cellular organisms, and entire ecosystems.

Biological systems use biochemicals for information storage (nucleic acids), energy processing (metabolism), growth (biomass) and reduction/oxidation (redox) reactions that involve electron transfer. Interfacing human digital and electrical systems to measure and control biology can be achieved by converting cellular signals, such as metabolite and protein concentrations into electrical or electromagnetic radiation signals using synthetic biology tools, such as biosensors, optogenetics, electrogenetics, and established concepts in bioelectrochemistry.

There are two key drivers of biosensor development, the biorecognition element and the transducer that translates the recognition signal into usable data.

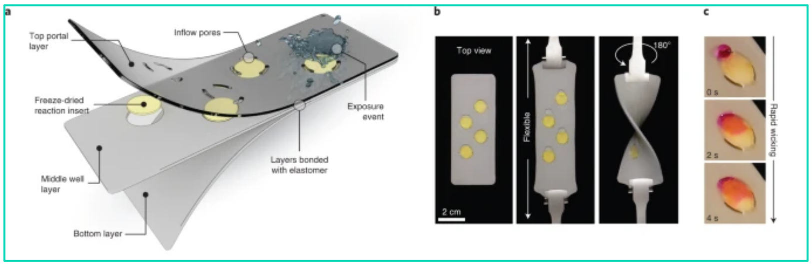
In biology, organic biosensors are a class of genetically encoded biological molecules, proteins, cells, or cell consortia that can be used to detect and respond to target ligands with high specificity and sensitivity. Biosensors can be comprised of protein, RNA, or DNA structures, depending on the application and its requirements, and can be either naked molecules, or functional within cells and their native regulatory components. Life also frequently transfers information using forms of electromagnetic radiation, such as luminescence (chemical to light conversion), fluorescence (light to light conversion), and iridescence (structural light diffraction). Life has evolved highly complex systems, such as photosynthesis, these systems can convert energy, and therefore information, between optical and chemical forms.

This new and growing insight into biological systems is now being leveraged through Synthetic Biology. Synthetic Biology or SynBio is a multidisciplinary area of research that seeks to create new biological parts, devices, and systems, or to redesign systems that are already found in nature.

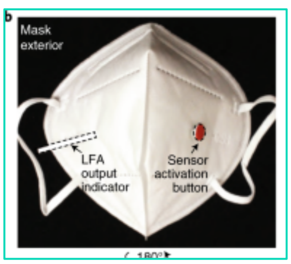
Outputs from SynBio research are providing new varieties of modular biosensors for the design of custom biological circuits. In parallel, recent developments in wireless technology, wearable electronics, smart materials and functional fibers with new mechanical, electrical and optical properties have led to sophisticated biosensing systems.

New protein research, for example, highlights specific capabilities relevant to biosensor development. Under the right conditions, they can act as tiny, current-carrying wires, useful for a range human-designed nanoelectronics.

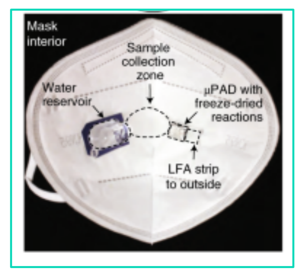
Integrating synthetic biology into wearables could expand opportunities for noninvasive monitoring of physiological status, disease states and exposure to pathogens or toxins.



Professor Jim Collins from Wyss institute reports on the design and validation of various wearable FDCF (wFDCF) sensors for small molecule, nucleic acid and toxin detection.



Wearable technology has detected viral or bacterial nucleic acid signatures in fluid samples with sensitivities rivaling those of traditional laboratory tests at ambient temperatures.



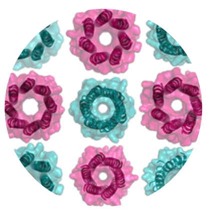
The sensors can be highly modular and adapted to various form factors, such as clothing or face masks.

The INSPECTR platform from Sherlock Biosciences can be programmed to distinguish targets based on single nucleotide differences without an instrument at ambient temperature. When INSPECTR's unique molecular sensors detect the presence of a nucleic acid target, a reporter protein is produced. This protein output can be designed to generate a signal tailored to any medium, providing a simple diagnostic readout. This novel approach enables the rapid development of molecular diagnostic tests that are low cost, easy-to-use and broadly applicable.

Monod Bio is developing biosensors that can quickly detect viral proteins, toxins, antibodies, or other molecules. The sensors are built from engineered proteins developed at the Institute for Protein Design.

Monod's sensors rely on two components. One component is a protein that recognizes a target. Upon target recognition the protein shifts from a closed to an open state. In its open state, the protein is able to bind the second component of the sensor. When the two bind, the sensor lights up. The light is emitted from luciferase, a light-emitting enzyme.

Rosa Biotech has developed the Pandra biosensing platform. Pandra uses protein design combined with machine learning to detect the faint chemical signature given off by chronic diseases. This approach is a departure from traditional biosensors that can only detect one kind of molecule. It is achieved through arrays of designed barrel-forming peptides with a back-end cloud database and machine learning algorithms. To develop a new sensor, requires only annotated samples to screen a designed peptide library and train new models.



Biological devices are being reimagined as advanced cyber-physical systems through their integration with digital and mechanical length scales.

These outputs of synthetic biology and novel inorganic tech developments are being used to create two-way communication between organic and inorganic data platforms. Two-way bio-informational functionality could enable organism-to-organism signaling through an Internet of Biological Things (IoBT), which in turn could connect to an Internet of Things.

Networks of biosensors and biological devices could be distributed across disparate geographies connected through an always-on information exchange. This could revolutionize human health, how we interact with ourselves, each other, and physical objects.

Over time, this could allow for the controlled release of chemicals from engineered gut microbiota to be integrated with wearable and smart phone technologies. In the longer term, this could supplement the oral ingestion of medicines (particularly for paralyzed patients) as well as ensure a patient's medicine levels are more carefully calibrated to their needs through the real-time monitoring of bodily fluids via biosensors.

This paper reports successful smartphone-controlled optogenetically engineered cells that enable semiautomatic glucose homeostasis.

Another study has explored the mind-controlled expression of genes. It describes the design of a synthetic mind-controlled gene switch that enables human brain activities and mental states to wirelessly program the transgene expression in human cells. This type of remote control of gene expression may provide new treatment opportunities in future gene- and cell-based therapies.

We could literally see when a particular gene expression has taken place.

Longer-term applications include viewing health information on a personal device reported via a subcutaneous optogenetic device with bioelectrical monitoring properties. Engineered microbiomes could both report real-time patient data and deliver on-demand pharmaceuticals in situ.

The Market Opportunity

The wearable healthtech market is predicted be one of the largest and fastest growing markets of the next decade.

Wearable healthtech has the potential to disrupt a number of parallel markets and at the same time lower healthcare costs significantly. Cost savings are driven by better treatments and better resource management.

Consumer-Led Healthcare

Healthcare is in the midst of a transformation into a patient-centric, consumer-led model. The traditional inefficient and costly model: a person seeks medical help from the doctor - the only source of information and the doctor makes decisions based on a fragmented medical history or medical records. The rich sets of available data generated by wearable technologies now make patients the point of care. Consumer-led healthcare will change patient care pathways, driving the industry to grow and collaborate in new ways, both with patients around their own health and with partners and innovators. Wearables will primarily support people living healthy lives, and then diagnostic and therapeutic abilities will follow, led by the user themselves at the point of care.

Accountability

Digital technologies and combined data enable a more holistic EHR, medical studies, clinical experience, and experience constructing a more holistic medical picture at both the micro and macro level. This is changing the distribution of data and responsibility with the patient as the point of care and more deeply engaged in medical decisions. At some point, clinicians will no longer be the “keepers” of patient medical data but rather, will consult the latest data provided to them by their patients from their wearables and sensors.

Regulators

As the capabilities of wearables increased, the FDA has grappled with how to regulate the new technology. Originally, wearables were not considered medical devices unless they made claims about treating specific diseases or conditions. However, as the technology of wearables advanced, the FDA regulated some new features. For instance, Apple released an EKG feature on its watch to detect Atrial Fibrillation. Since it was meant to detect Atrial Fibrillation (an irregular heartbeat), Apple could not classify the feature as a general wellness device and the feature needed to be FDA cleared.

WellDoc's diabetes platform for example, has been FDA approved as a digital therapeutic. What makes this a therapeutic versus an informational tool versus a diagnostic? Welldcoc Diabetes tracks blood glucose levels just like any other blood glucose meter. In the traditional monitoring model, a patient will review their blood glucose data and then decide how to adjust their insulin dosage accordingly. In the Welldoc model, the Welldoc platform tells the patient precisely how much insulin to inject. This changes the paradigm from patient/doctor making the dosing decision to the technology platform making the dosing decision (to drive clinically tested outcomes). This "dosing decision" makes the platform a therapeutic and not a monitoring device and this in turn requires a full FDA therapeutic approval.

As the impact of biosensors and syn-bio develops in the wearable platform, regulators will need to consider the devices and their software in many categories; diagnostic, medical device, digital therapeutic, and just straight therapeutic. Although the FDA could exercise its regulatory power over the wearable industry, a more permanent solution is likely to require updates to the Food, Drug and Cosmetic Act and this may slow down the growth of the market.

Reimbursement

Reimbursement has taken a while to align with digital tech innovation generally but as the cost-benefit cases begin to build around resource and manpower utilization, payers will be driving the change through reimbursement. Good data analytics and AI will be able to demonstrate this the harder part is changing older health provision and delivery models.

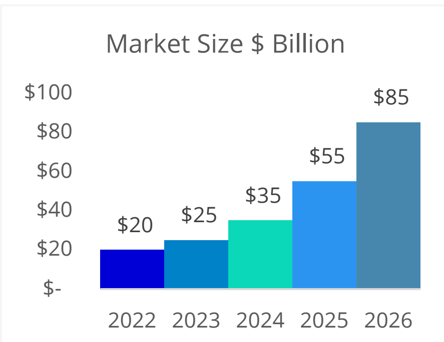
Additionally, as strong therapeutic benefits grow so too will reimbursement, but this will require significant investment in good quality clinical trials and pharmaco-economic studies. This in turn will require strong pharma/biotech type leadership and management at the helm of new innovating companies.

Privacy

Beyond regulatory and reimbursement challenges are new and additional legal dynamics for manufacturers marketing their smart wearables. Most prominently, these concern the privacy and security of the processed data. New levels of detail and insight into an induvial will be available through the data collected by new devices and this will bring new levels of concern about privacy. There will be additional legal requirements regarding the application of the device, such as the liability for malfunction, the professional regulations of medical users, and the data processed.

MARKET OPPORTUNITY

With such a broad application across a number of markets, we've seen some quite dramatic differences in predictions for the wearable healthtech. Clearly these differences are dependent on what aspects are included. We believe a reasonable estimate is around USD 17 billion in 2020 with expected growth at a compound annual growth rate (CAGR) of around 28% from 2021 to 2028 to well over $100 billion.



Eckuity Market Estimates

A greater focus on health and wellness and a growing elderly population will see fitness, remote monitoring and personalized medicine as key sectors of growth but the arrival of more therapeutic applications will accelerate growth dramatically.

While some of this developmental work is still in early-stage development, the potential value is clear to the market. Ziylo has developed an innovative technology platform, which could be a key component to enable the next generation of insulin, able to react and adapt to glucose levels in the blood, therefore eliminating the risk of hypoglycaemia - dangerously low blood sugar levels - and leading to better metabolic control for people living with the disease.

Ziylo was acquired by Novo Nordisk in deal worth $800 million.

What is clear is that Wearable Healthtech will be highly disruptive as its impact will spread across many market sectors – from healthcare deliver, to diagnostics, to therapeutics. Key to successful investment is understanding precisely which technologies, market sectors and regulatory factors will ultimately drive market growth.