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NEWS

Researchers Combine Wearable Biosensors and Machine Learning to Combat the Opioid Crisis

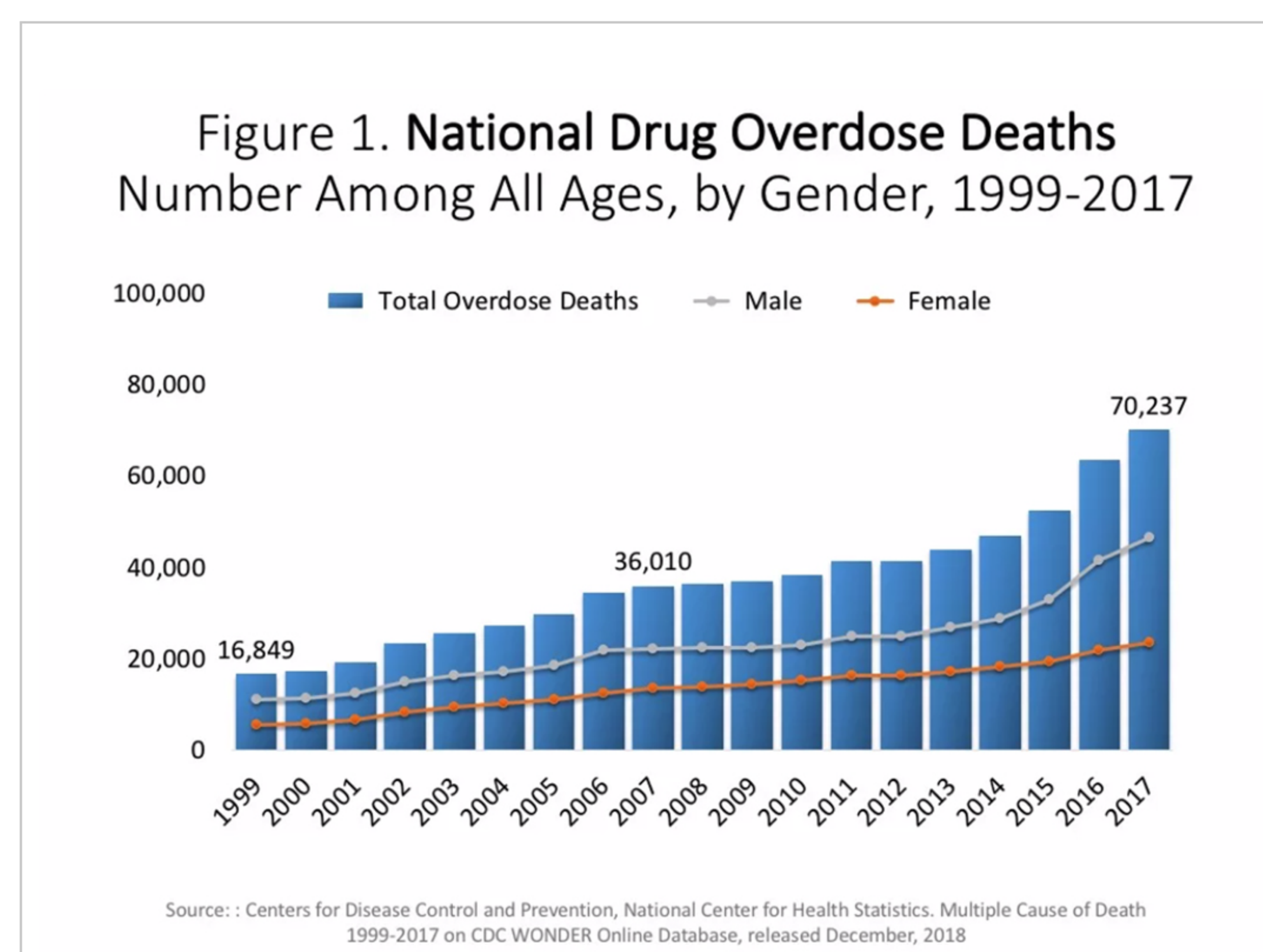
Researchers have combined wearable biosensors with machine learning to aid in treatment for substance abuse.

Wearables have been finding increasing utility in the healthcare industry, from step counters to incentivize fitness to [heart rate monitors for preventative healthcare applications](#). These low-power, small-footprint devices are tricky to design, but their potential to improve health and fitness applications has been inarguable.

Now, in research settings, these little devices are finding a calling in combatting a grave issue that was [declared a public health emergency](#) by the Department of Health and Human Services in 2017: substance abuse.

A Growing Substance Abuse Pandemic

The Centers for Disease Control and Prevention (CDC) has reported an increasing number of opioid-overdose related deaths across the United States with [47,600 reported deaths in 2017 up from 18,515 in 2007](#). Unfortunately, the substance use epidemic has not only affected the United States, but has been reported in many countries around the world, including Canada and France.



Statistics from 1999 to 2017 showing an increasing trend in opioid overdose-related deaths. Image courtesy of CDC WONDER via the [National Institute on Drug Abuse](#).

Members of the scientific community have endeavored to combat this growing epidemic with the help of technology. Of the different technological platforms being explored, wearables present a particular set of advantages, namely the ability to continually track recovering substance abuse disorder patients in their daily lives. Such tracking would assess treatment adherence, facilitating intervention if necessary, as well as alert ambulatory services in times of need.

To pursue this possibility of remote monitoring, a group of researchers and physicians at the University of Texas at Tyler and the University of Massachusetts, Medical School have been investigating using a wearable biosensor to monitor treatment adherence in substance use disorder patients. Their 2019 paper entitled, "[A Machine Learning-based Approach for Collaborative Non-Adherence Detection during Opioid Abuse Surveillance using a Wearable Biosensor](#)" details their study.

Detecting Opioid Use with Wearable Biosensors

The research group utilized the E4 wristband wearable biosensor from Empatica, the same company that makes the [Embrace2 Watch](#), a wearable biosensor for detecting epilepsy in children.



Image of the E4 wristwatch. A single user input button is available to toggle through different operation modes. You can also observe two electrodes on the wrist strap for measuring electrodermal activity. Image courtesy of [Empatica](#).

Unlike the Embrace2 Watch, the E4 has not been FDA cleared, but is instead intended for research purposes. The E4 is packed with a suite of sensing capabilities including heart rate, skin impedance, temperature, and locomotion.

In this study, the research group use the sensor capabilities of the E4 to collect data on active drug users, then applied machine learning techniques to develop predictors for non-adherence of treatment regimens.

Building on Previous Studies

Members of this research group have been working in this technology space for a number of years now as the drug epidemic has, unfortunately, continued to grow. Their earliest study dates back to 2015 in which they employed the Q Sensor, the now-discontinued predecessor of the E4 wearable, to monitor changes in electrodermal activity, skin temperature, and locomotion. The group recorded data from a single patient during his daily activities.



The Q Curve and Q Sensor Pod from Affectiva. Image courtesy of MIT Affective Computing Group.

The Q Sensor was able to detect changes in the recorded physiological signals and such changes were corroborated with self-reported instances of drug use. As one would imagine, retroactively detecting drug use is not particularly amenable to real-time monitoring.

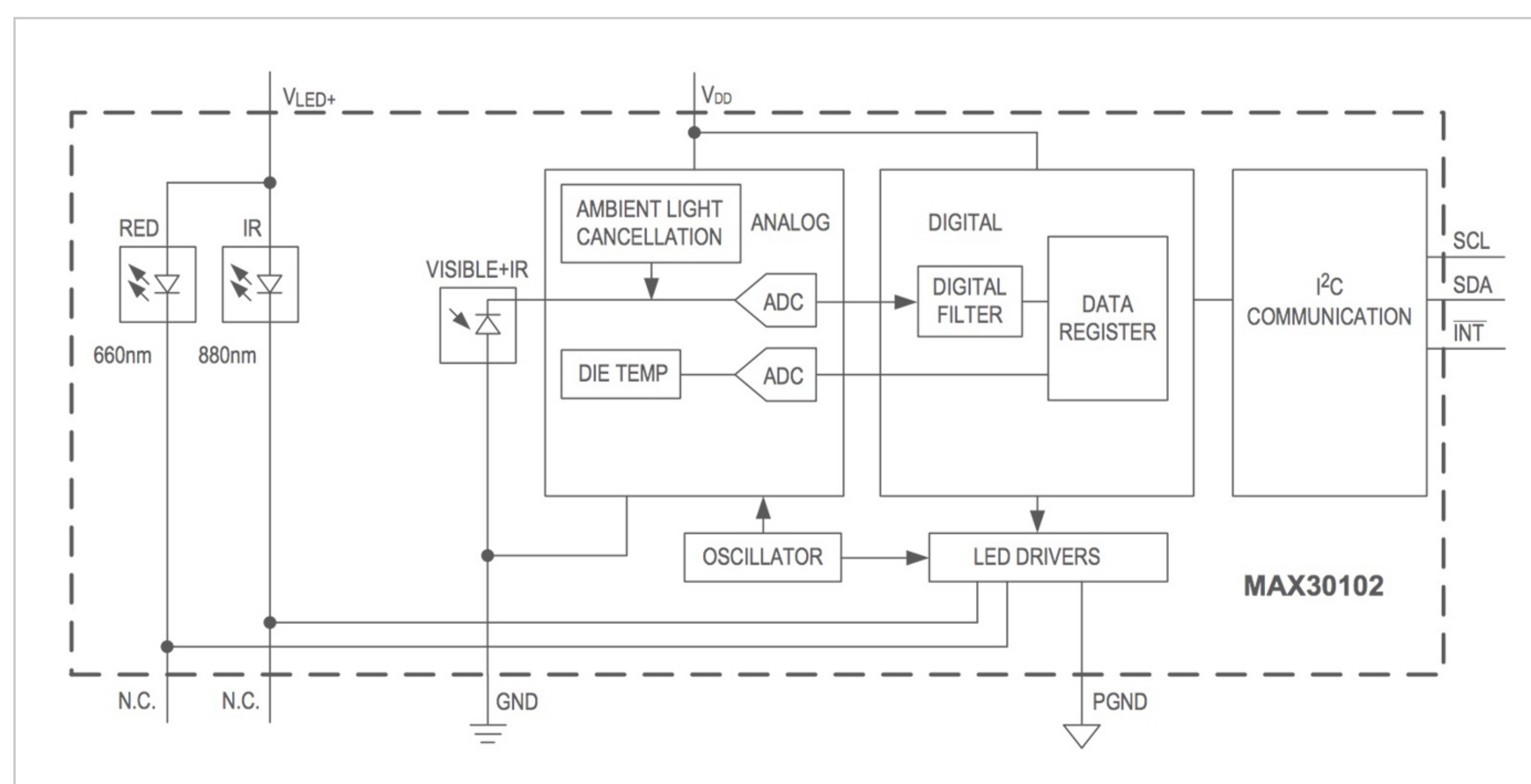
Detecting Opioid Use with Machine Learning

In 2018, the group demoed an algorithm for automatically detecting opioid use again by measuring changes in electrodermal activity, skin temperature, and locomotion. In their 2018 study, titled “[Automatic Detection of Opioid Intake Using Wearable Biosensor](#)”, they improved upon their 2015 paper by utilizing machine learning and pattern recognition to automatically differentiate baseline readings of different physiological signals from abnormal readings elicited by substance use.

Possible Chipsets for Wearable Biosensors

Not many details on the specific chipsets used in the E4 or Q-Sensor wearable are available. However, given the popularity of biometric monitors, we can speculate the use of any number of popular chipsets available for heart rate, such as the AFE4490 from Texas Instruments or the more recent [MAX3010X series of ICs](#) from Maxim Integrated, which have been popularized by the heart rate monitor function in the [Samsung Galaxy series](#) of phones.

Maxim Integrated has been placing emphasis on healthcare applications in many of the hardware components and tools they release, including a [wearable platform for remote biometric monitoring](#) for developers. Maxim, along with Omron and ROHM, also offers [biometric monitoring wearables as end devices](#).



Functional block diagram of the MAX30102. Image from the [MAX30102 datasheet](#). [Click to enlarge](#).

Certainly the MAX30205 human body temperature sensor from Maxim Integrated would be appropriate here or the MLX90632 from Melexis if a designer needed a non-contact IR thermophile route, instead. If you'd like to learn more about this subject, we briefly discussed a few chipsets for EDA in a previous article on wearable static exercise monitors.

From examining the scientific literature, we can clearly see the increasing need for improved processing capabilities on embedded hardware to handle the ever-increasing amount of sensor data required to make intelligent algorithms.

Combating Epilepsy with Wearables and Machine Learning

Biometric-monitoring wearables are common for tracking everyday health—but can they monitor seizures?

Epilepsy is a chronic condition that affects millions of people worldwide. Epilepsy is most commonly characterized by the occurrence of involuntary seizures. Due to the sometimes debilitating nature of these seizures, epilepsy monitoring is of major interest to the medical community.

A team at healthcare wearables startup Empatica has positioned themselves at the forefront of epilepsy monitoring with their recently FDA-cleared, second-generation, wrist-worn wearable called the Embrace2.



The Empatica Embrace2. Image from [Empatica](#)

The Embrace2 is intended for children with epilepsy ages six and up, specifically designed for tonic-clonic seizures, those that cause involuntary convulsions in patients.

According to a [January press release on the FDA's 510\(k\) clearance of the Embrace device](#), it is "the first non-EEG based physiology signal seizure monitoring system to be cleared by the FDA" specifically for use with pediatric populations.

A Wearable that Measures Possible Seizures

The Embrace2 is designed to monitor locomotion as well as electrodermal activity or response (EDA). The goal of the device is to make it more likely for caregivers to be present at the time of a seizure to render assistance.

Let's take a look at what sensors are needed to monitor these factors.



Image from Empatica

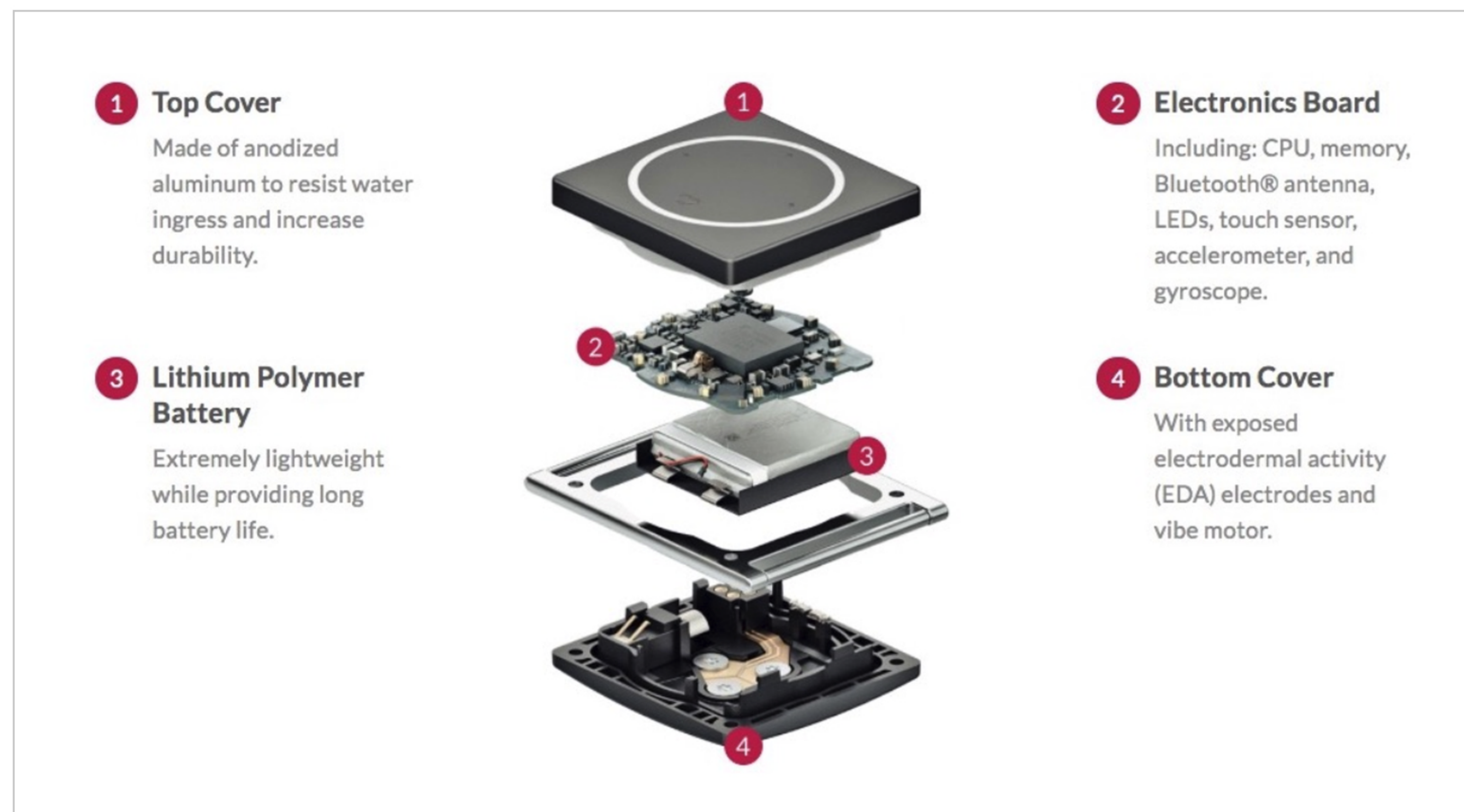
Using Accelerometers to Measure Locomotion

Of these two physiological quantities, locomotion is probably the more recognizable of the two to most readers.

The Embrace2 tracks locomotion using accelerometers which have become a mainstay in the semiconductor industry. These accelerometers are tiny MEMS (microelectromechanical machines) devices that measure the linear acceleration of an object with respect to gravity. Accelerometers are widely employed in consumer electronics for detecting orientation for switching between landscape and portrait mode in cell phones, free fall for elderly fall alert monitors, and for detecting steps in pedometers and smartwatches to name a few examples.

Since epilepsy results in seizures, Empatica is able to use the accelerometer data to quantify the length and intensity of the convulsion, sending an alert to a caretaker or loved one when a seizure is detected.

Gyroscopes are also reportedly in the device to allow similar measurements regarding orientation.



The Q Curve and Q Sensor Pod from Affectiva. Image courtesy of [MIT Affective Computing Group](#).

Measuring Electrodermal Activity with Electrodes

Between locomotion and EDA, most people are probably less familiar with EDA. EDA (also known as GSR or galvanic skin response) is an indirect measure of the human body's sympathetic nervous response or "flight-or-fight" response.

The sympathetic nervous system (SNS) is the body's center for responding to arousal due to external stimuli. The activities of the SNS can be detected by measuring local changes in skin conductance often between two fingers or on the wrist, in the case of a wrist-worn device like the Embrace2. Such changes in skin conductance are elicited due to the activation of sweat glands right below the surface of skin that secrete minute amounts of sweat, a conductive solution, consequently increasing the measured skin conductance.

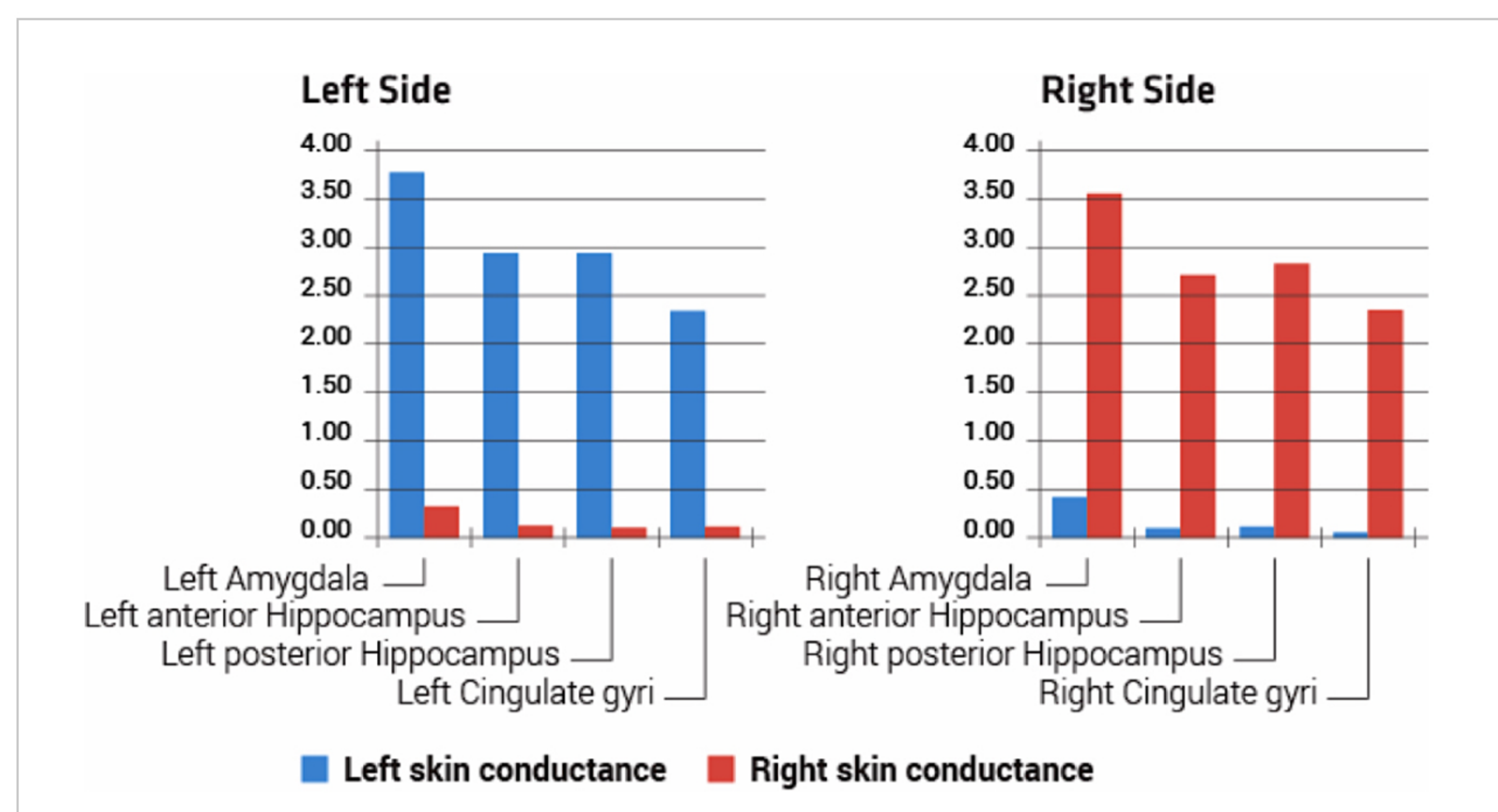


Image from [Empatica](#)

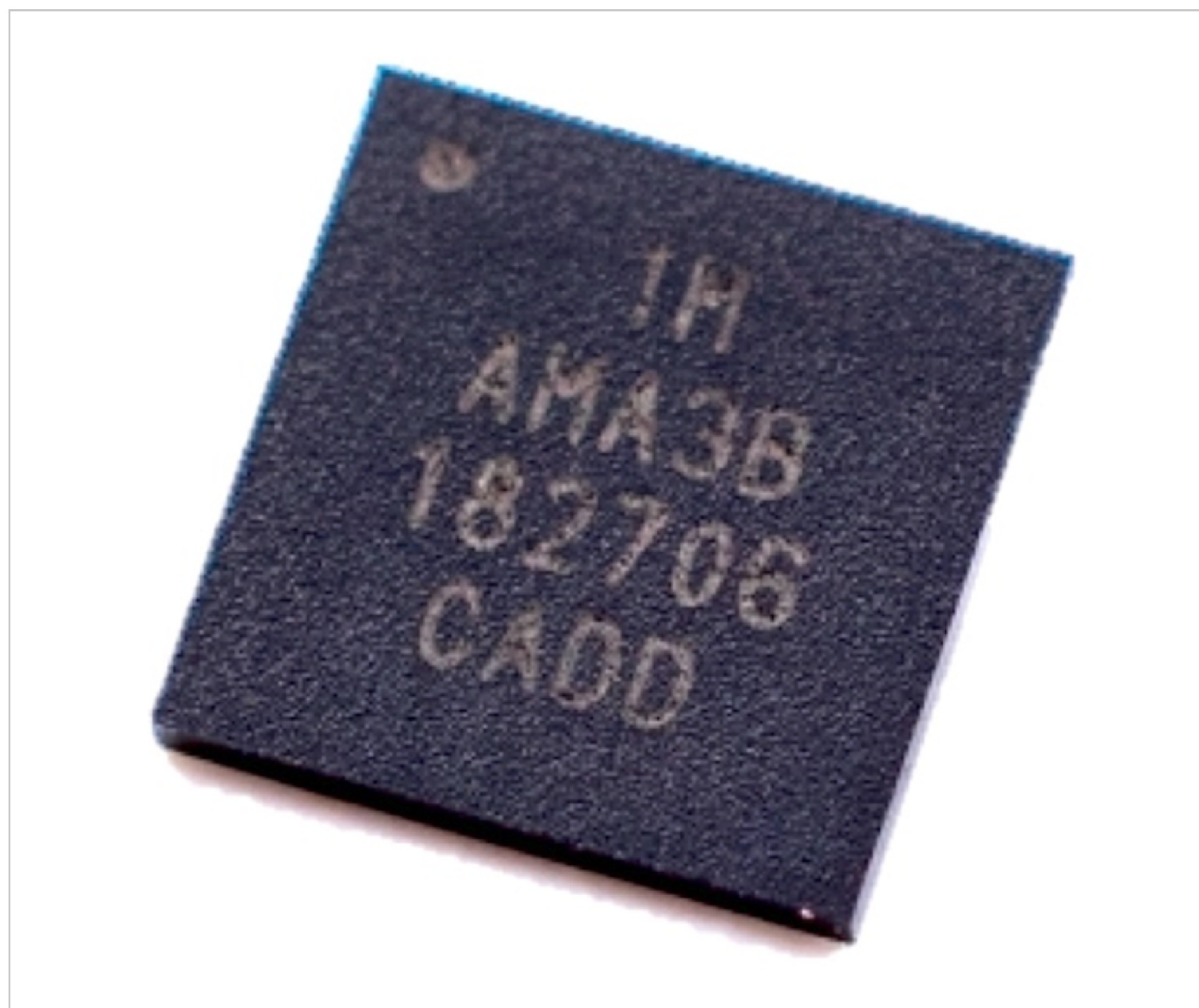
EDA has been used in [biometric monitoring wearables](#) over the past few years—and famously used in lie detectors for decades. EDA, however, is not necessarily specific to any particular stimuli (skin conductance can be impacted by a number of emotional responses). For this reason, Embrace2 had a challenging task in using such a technology for detecting seizures. Nevertheless, Empatica has been able to develop a working product that was able to pass the scrutiny of the FDA.

According to [Empatica's website](#), the company is choosing to utilize EDA in this context based on [2015 research](#) that suggests that a seizure that "strongly stimulates the amygdala" could cause large EDA, among other citations of [neuroscience](#) journal articles.

Machine Learning and Embedded Systems

Empatica openly admits that the technology isn't perfect and that false positives and false negatives are a certainty, unfortunately. Nevertheless, the development of technologies to help people with epilepsy continues and Empatica is proud to be a part of this active area of research continually refining their device and algorithms with each new patient.

Empatica's work demonstrates the need for more sophisticated sensing modalities and artificial intelligence to combat chronic illnesses such as epilepsy. Recent developments in reducing the computation intensity of machine learning algorithms have given rise to technologies such as Intel's Loihi, Movidius's Myriad 2, and most recently Ambiq Micro's Apollo3 Blue microcontroller, an ARM Cortex-M4F processor running TensorFlow Lite.



The Apollo3 Blue microcontroller from Ambiq Micro is also available on the SparkFun Edge Board, which can run TensorFlow. Image from [Ambiq Micro](#)

Hopefully Empatica and other medical device companies continue to improve and refine their technologies turning to the semiconductor industry for each new and more capable chipset.

Future Uses of Biometric Monitoring

Biometric-monitoring wearables have been gaining popularity over time. As the relevant algorithms for interpreting sensor data advance, even **component manufacturers are making health wearables**.

But Empatica is tackling something beyond monitoring steps, heart rate, and blood oxygen levels.

The promise of a wearable for monitoring such seizures could, dare I say, extend into predicting the occurrence of these seizures. While Empatica makes no claims on seizure prediction, such a feature would make a world of difference to those managing their epilepsy.



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INDUSTRY ARTICLE

Creating an Integrated and Unobtrusive Diabetes Management System

By: Steven Dean, Business Marketing, Signal Processing, Wireless and Medical Division, ON Semiconductor

The World Health Organization (WHO) suggests that globally more than 400 million people live with Diabetes and that since 1980, the number of people has nearly quadrupled. These are just numbers, but the real tragedy in them is that this disease can lead to serious health complications such as blindness, stroke, lower limb numbness and amputation, heart attacks, and of course even death.

Measurement and monitoring are key to the effective management of both Type 1 and 2 Diabetes. Typical and traditional measuring techniques involve using a Blood Glucose Meter (BGM). Another technology option in the marketplace that is used by both Type 1 and 2 diabetics, are Continuous Blood Glucose meters (CGMs). The advantages of continuous measurements are many, one of which is learning more of what a human body does, or how blood glucose changes continuously over time given various daily routines, such as physical activity, diet, and even sleep. Therapies can and do improve as a result as more is known about a body's behaviors over time, continuously, rather than discretely.

Since these meters typically measure interstitial fluid subcutaneously, up until very recently, calibration with blood on a periodic schedule was required - this requires the 'old school' finger prick. However, as technologies have advanced, some CGMs can now avert the need for calibration to whole blood.

The microelectronic nature of the continuous blood glucose monitoring system is generally the same with a few key exceptions. And since these devices are typically body worn, size matters meaning much higher levels of integration and effective power management to foster optimum levels of efficiency of the semiconductor devices used in them are now required.

Beyond measurement and monitoring, the techniques and technologies used for the delivery of insulin are also advancing with closed loop systems integrating continuous monitoring with insulin delivery via what has been termed the artificial pancreas. This is resulting in better, more convenient healthcare and more positive long-term outlooks for the many millions living with diabetes.

Measuring Blood Sugar Levels

Traditional BGMs can be purchased commercially at a pharmacy or any drug store chain. With a supplied lancet device (a very small, thin needle), a finger prick exposes a small drop of blood which is exposed to a test strip inserted in the meter.

There is typically some AC or DC excitation voltage or current applied to the blood sample as it chemically interacts with the test strip. The derived result is read back by the data converter. After a brief wait for the microcontroller to complete computations, the resultant blood glucose level is displayed on a screen.

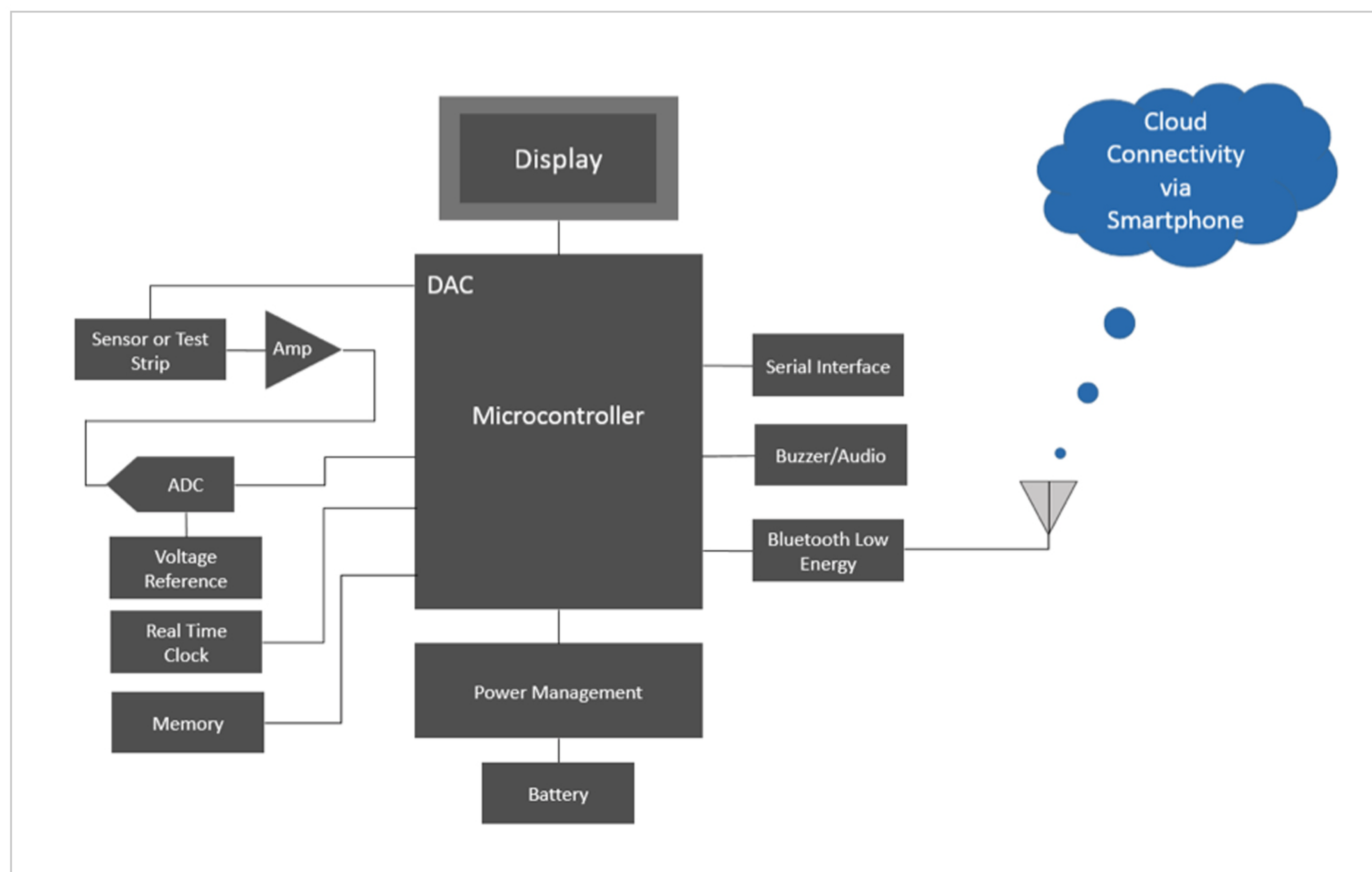


Figure 1. Simplified Blood Glucose Meter (BGM) Diagram

Unlike the Embrace2 Watch, the E4 has not been FDA cleared, but is instead intended for research purposes. The E4 is packed with a suite of sensing capabilities including heart rate, skin impedance, temperature, and locomotion.

Continuous Blood Glucose Measurement

The system architecture of Continuous Glucose Meters (CGM) now commonly integrates the A/D and D/A, and input/output functions into one monolithic piece of silicon, typically a custom ASIC AFE or ASSP. When coupled with a BLE and MCU in a small WLCSP package such as the RSL10, this helps to meet the challenge of making the permanently worn devices as unobtrusive and practical as possible for users.

Aside from the circuitry, another major factor contributing to size is the power cells that are required. In a hand-held BGM for example, one or two AA, AAA, or AAAA batteries are common. These would be too weighty and large for a CGM, so power cell size and chemistry often dictates a coin-cell form factor. To make this feasible, system power must be carefully managed. Peak and total currents must be minimized, as the maximum current that can be sourced from a coin cell battery is dramatically reduced in comparison to its AA cousins. A further consideration is the discharge profile. If using a silver oxide battery chemistry for example, these typically produce a maximum of 1.55 V, with useful life down to 1.2 V. If using a manganese dioxide chemistry, then nominal voltage is 1.5 V with useful life down to 1.0 V.

Insulin delivery: Injectors

Insulin has been traditionally self-administered when needed with a clinical grade syringe and needle just as one would receive an injection at the doctor's office. There are many types of insulin marketed and available today. Rapid, short, intermediate and long-acting types of insulin may be injected separately or mixed and combined as appropriate to meet specific needs.

Most recently, alternatives to subcutaneous injections have come onto the market. One such alternative is a jet injector which delivers insulin in a fine stream through and into the skin. Another is injector pens, which deploy the insulin more automatically, through an ultra-fine needle. Convenience and comfort greatly improve usually along with the benefit of reduction of fear to inject.

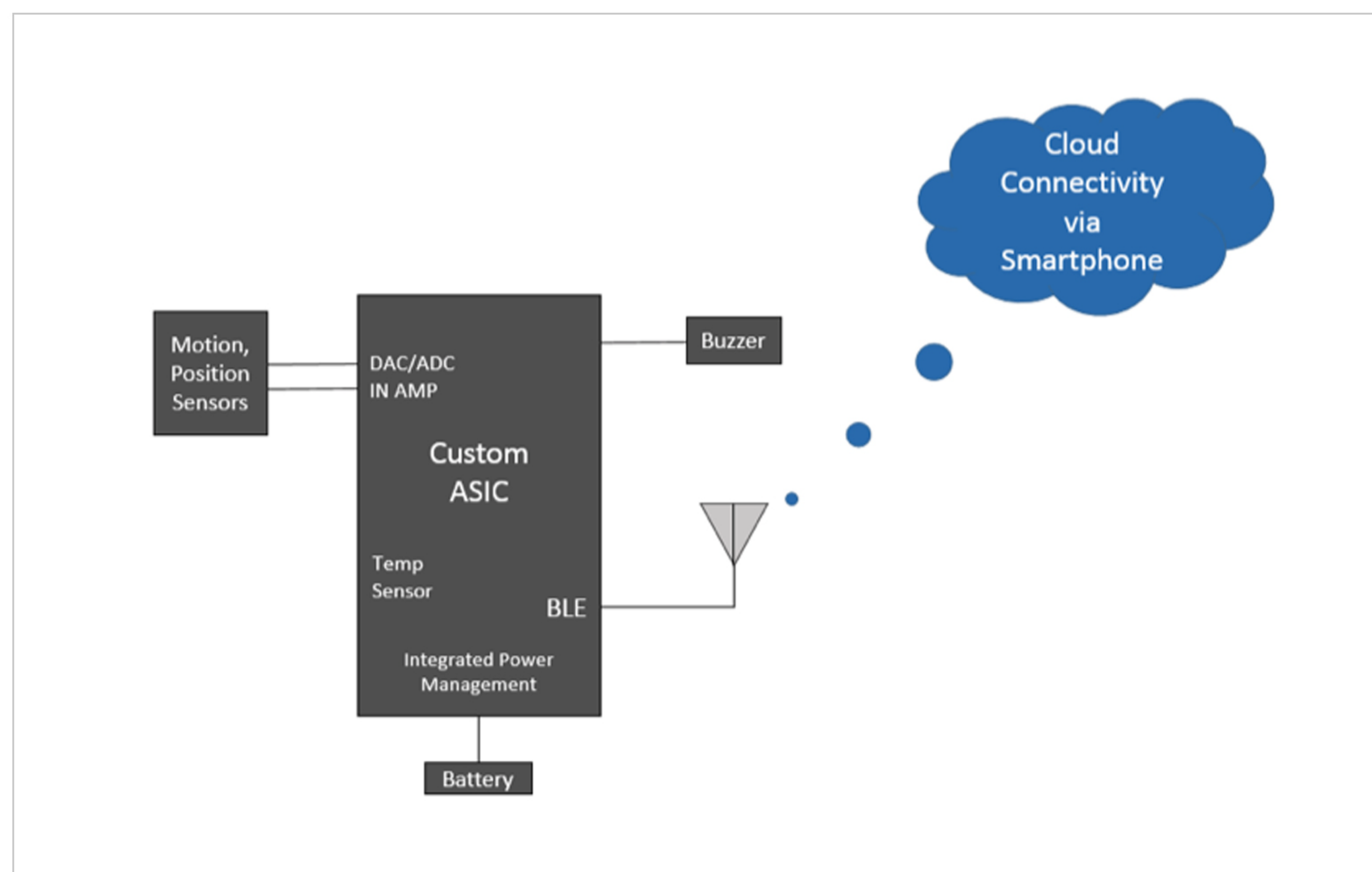


Figure 2. Smart Injector Pen Diagram

These alternative devices are more commonly becoming electro-mechanical and 'smart' in nature just like traditional blood glucose meters. Pens are being designed with microcontrollers and Bluetooth Low Energy radios with the purpose of capturing and reporting discrete injection times, volumes, and more.

Insulin delivery: Pumps

An insulin pump accurately controls the delivery of insulin for both Type 1 and some Type 2 diabetic patients, but are more commonly prescribed to type 1 patients. These pumps are a critical piece of the puzzle playing their part eventually in a 'closed loop' system - the artificial pancreas. Continuous measurement of blood glucose in a system with an insulin pump receiving this data, along with proper delivery control and algorithms creates the artificial pancreas, the holy grail of diabetes management.

When a CGM is in place to substitute the need for multiple daily finger sticks, it's simply a better method for measurement leveraging continuous data rather than a few discrete data points. Likewise, the ability to remove low blood sugar and high blood sugar situations throughout the day is an improved method of delivery. A so-called artificial pancreas means patients no longer need to worry about nocturnal hypoglycemia, or low blood glucose levels during sleep or about the frequency of measurement or injections. This can greatly improving their health, quality of life and likely also longevity.

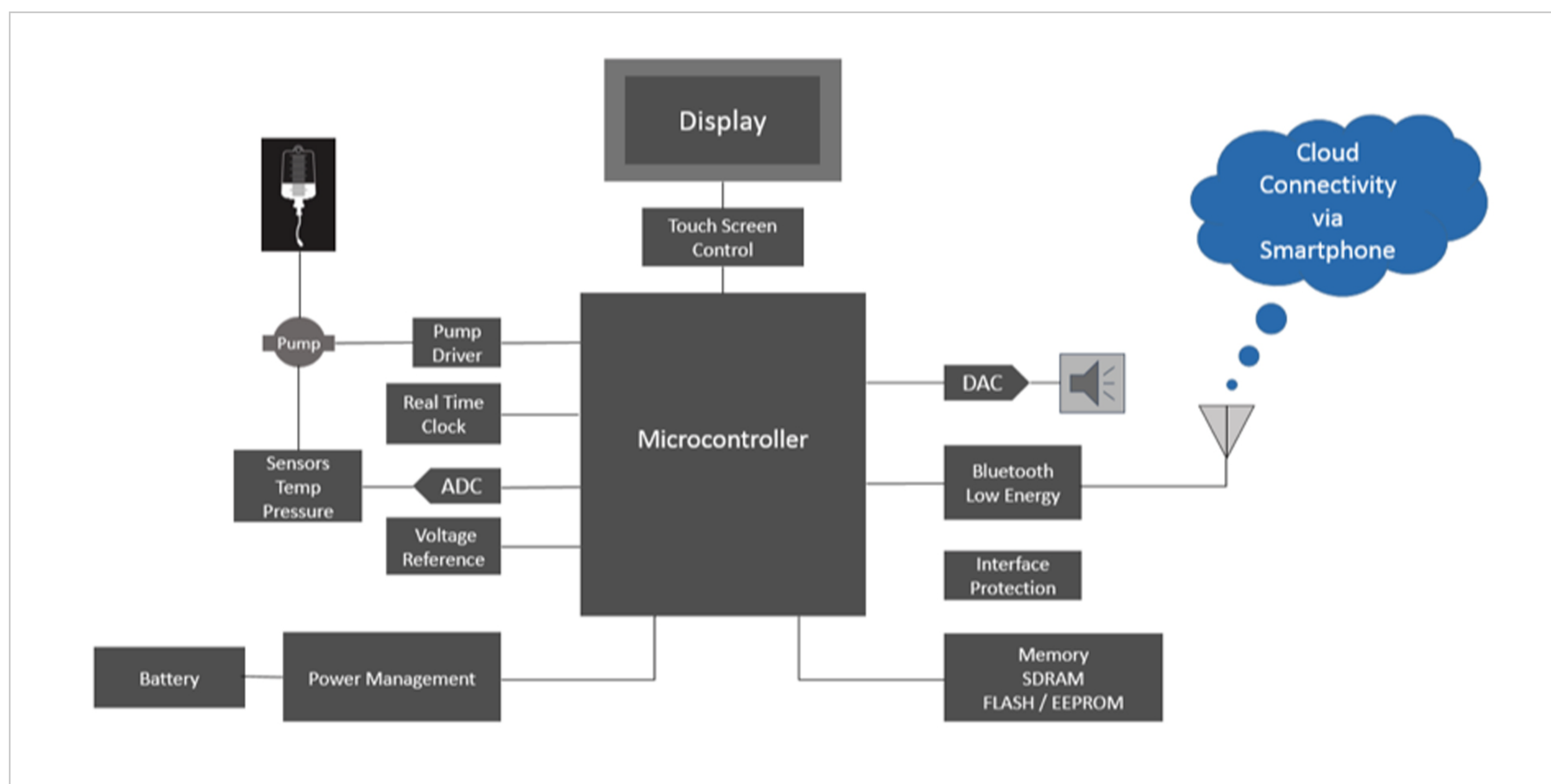


Figure 3. Simplified Insulin Pump System Diagram

As can be imagined with automated insulin delivery, the need for system safety, reliability, and accuracy are paramount which makes the selection of technology, system and component providers by equipment makers is vitally important.

Architecting an Artificial Pancreas

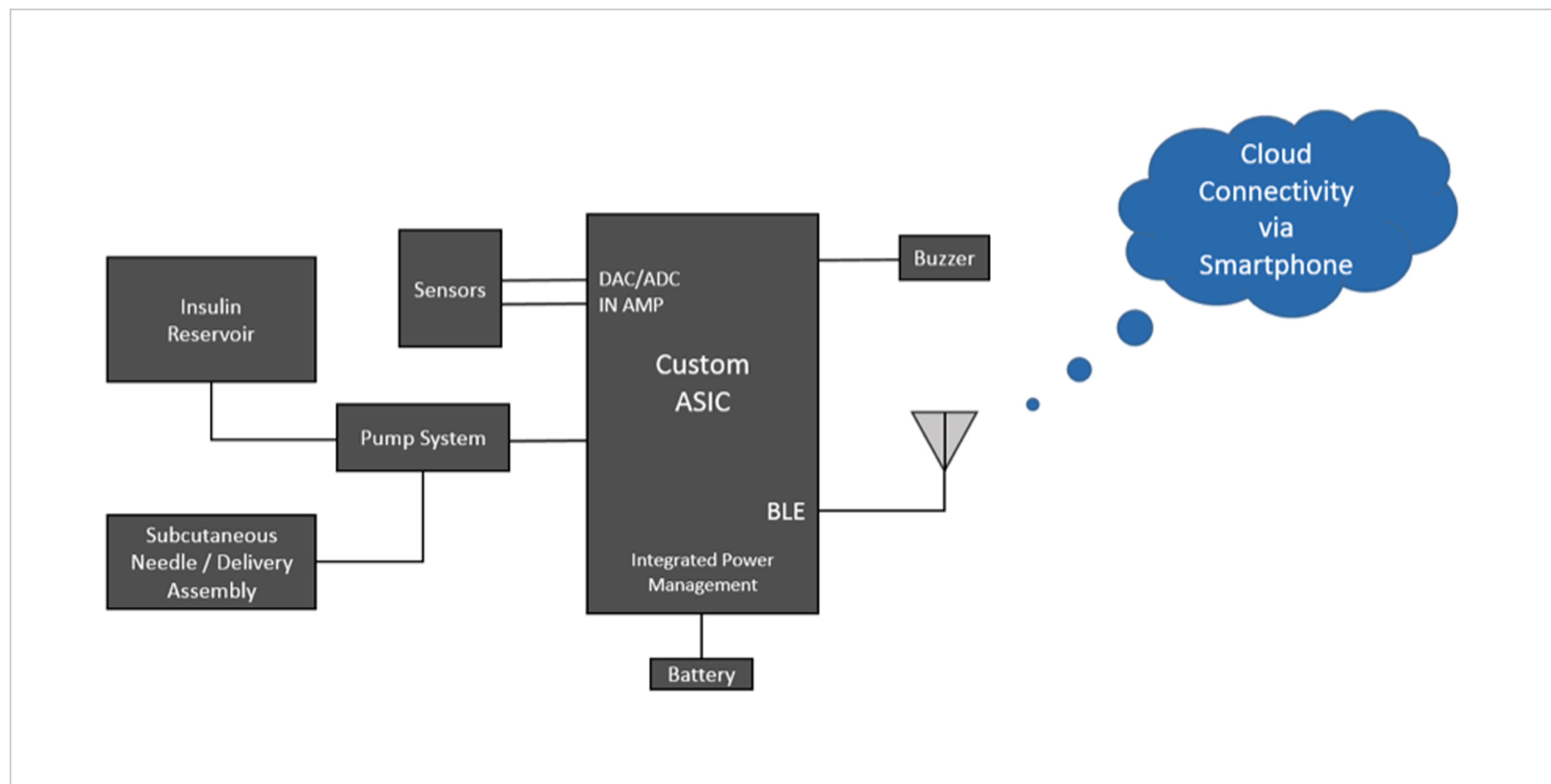


Figure 4. Artificial Pancreas Diagram

Physical designs for an artificial pancreas vary greatly, albeit they are body-worn or affixed by the user's belt. The architecture shown depicts the most common scheme utilizing a highly integrated custom ASIC which will include all Analog Front End (AFE) blocks, power management, MCU or control block, and an integrated Bluetooth Low Energy radio to facilitate communications. All systems will include an insulin reservoir of some type, a pump or actuator system with appropriate driver mechanism, a catheter or cannula system delivering insulin via a subcutaneous needle, and sensors of various types (motion, pressure, temperature, blood glucose) as well. The key difference to discrete or disconnected measurement systems is continuous and closed-loop feedback.

Several sensors beyond the blood glucose sensor, such as low-g accelerometers and temperature sensors in the body worn device can be employed to monitor activity levels that can be used to improve dosage algorithms. These sensors continuously provide information regarding physical exertion and environment from an external perspective, while also providing continuous information regarding blood glucose levels. Artificial Intelligence (AI) can be employed such as to estimate near and intermediate term insulin therapy required.

Most systems communicate using Bluetooth Low Energy to a cloud-connected smartphone. Some however, use a headless body-worn pod which communicates with a separate control system or what is sometimes referred to as a Personal Device Manager (PDM). In these cases, the PDM is used for user interaction and can be used as the open-loop (not closed-loop) control system. The PDM is also what then provides the cloud connectivity, usually via Wi-Fi or LTE.

With cloud connectivity caregivers can be notified and involved. Further, with cloud computing, even further functionality can be garnered from big data analytics and population management.

Going beyond IC integration, in some cases, even passive components are being integrated in advanced 3D hybrid modules along with a highly integrated semiconductor ASIC. This is where the benefits in size, weight, and performance really pay off.

The Bluetooth Low Energy Radio of Choice:

Referencing back to the need for coin cell operation and low power operation, devices such as ON Semiconductor's RSL10 Bluetooth® 5 certified radio SoC can provide an appropriate choice for enabling communication to and from the artificial pancreas solution. The RSL10 offers the industry's lowest power consumption as verified by the EEMBC and has been qualified recently for use in implantable/life critical medical applications. It is especially suited for ultra-low power battery-operated devices. It uses the Arm® Cortex®-M3 Processor and ON Semiconductor's LPDSP32 Digital Signal Processor to give the robustness needed to support complex designs. On-board 384 KB Flash and 160 KB RAM provides users with flexible programming options. RSL10 also provides ample room for the Bluetooth Low Energy stack and the ability to develop Firmware Over-the-Air (FOTA) applications.

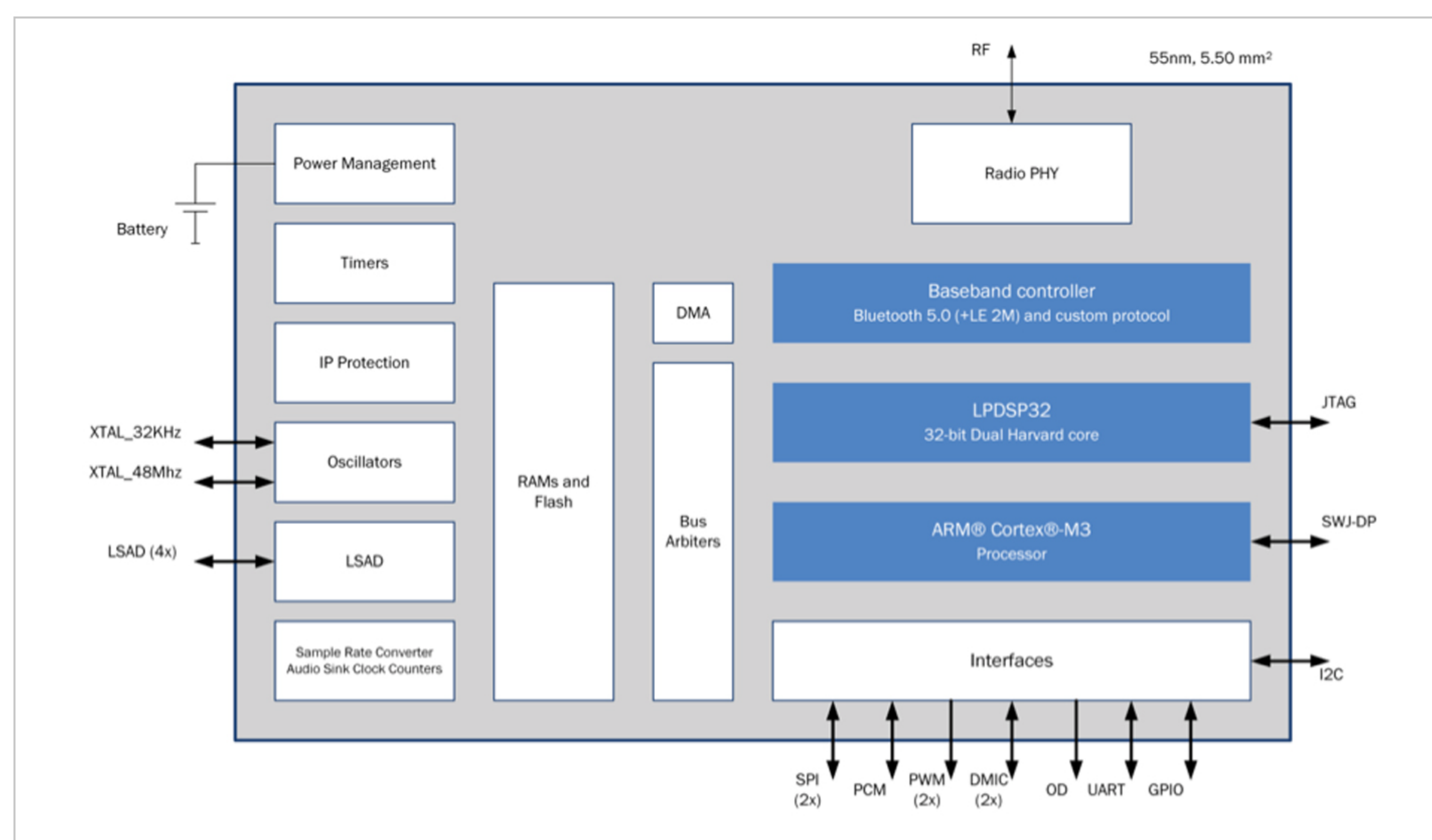


Figure 5. RSL10 System Diagram

One less-known benefit of the RSL10 is that ON Semiconductor's Bluetooth Low Energy IP can be re-spun into an ultra-low-power custom ASIC, meeting the needs to cover the wide variety of sensors and sensor interfaces. As unique D/A and A/D conversion in both the measurement systems and insulin delivery systems are common, customization is nearly always required. In insulin delivery systems for example, perhaps only Bluetooth Low Energy transmit is required, reducing overhead in the baseband RF and controller. Many applications are high volume and/or potentially disposable, so it's key to be as efficient as possible on silicon to save both cost and size.



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TECHNICAL ARTICLES

How to Design a Bluetooth Low Energy Circuit with Sensor Technology

Tutorial on designing a Bluetooth Low Energy (aka Bluetooth Smart) circuit with the ability to measure 9-axis motion, humidity, and temperature.

In this article, I'm going to cover the circuit design for a Bluetooth Low Energy (BLE) product that features an accelerometer, magnetometer, and gyroscope, as well as sensors for measuring humidity and temperature.

One of many possible applications for this design would be a small device to monitor the shipping conditions of critical items during transit. After shipment, the data from the journey can be downloaded over the BLE link to be analyzed. Did employees mishandle the item? Maybe play football with it? This device can tell you.

Also, keep in mind that this design is highly extensible—it would not be difficult to incorporate other types of sensors.

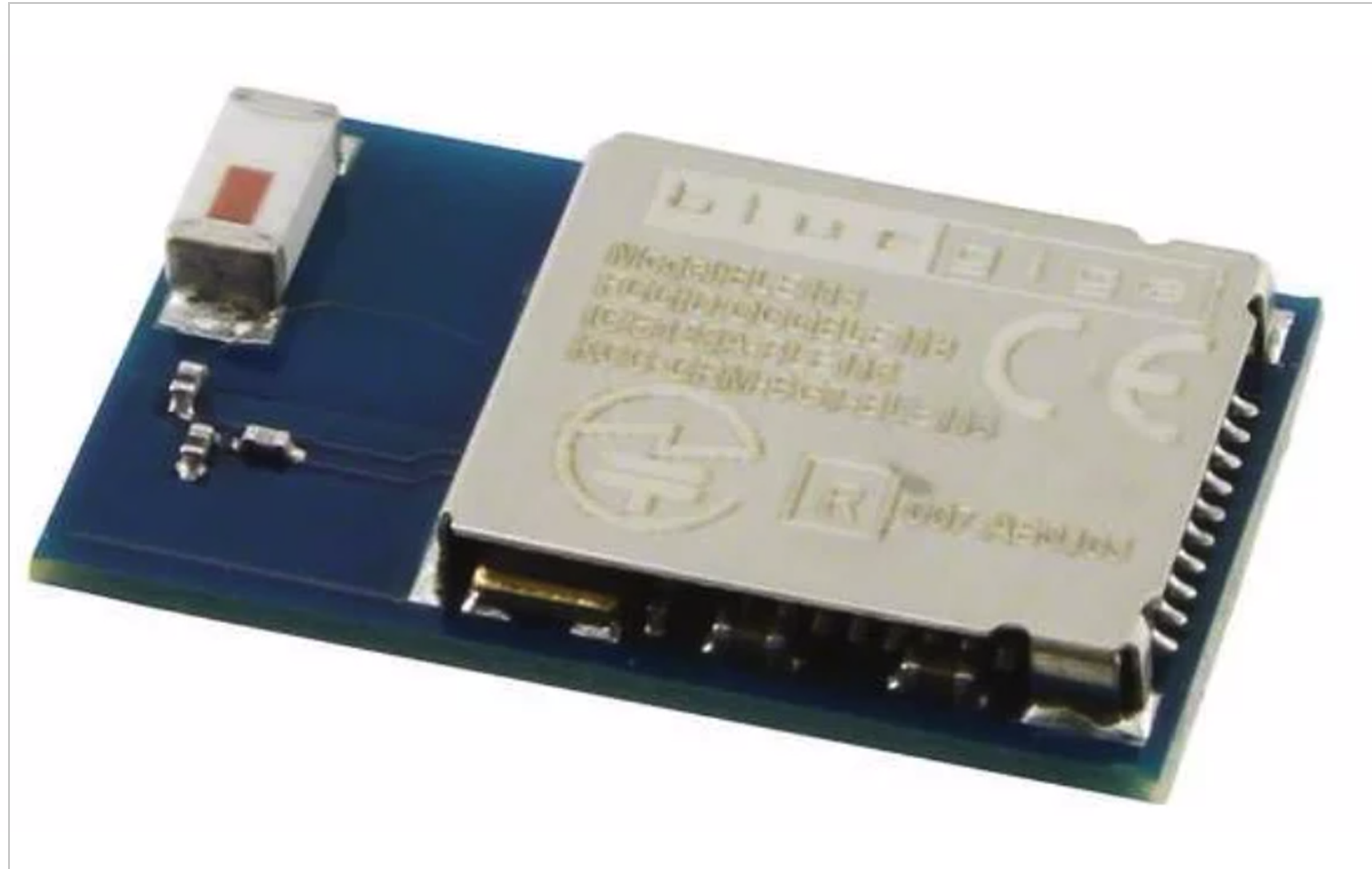
NOTE: Throughout this article I will be using the following terms interchangeably: Bluetooth Low Energy, Bluetooth LE, BLE, and Bluetooth Smart. They all mean the same thing.

Bluetooth Low Energy / Bluetooth Smart

Designing a new Bluetooth product, or any wireless product, can be somewhat challenging for the inexperienced. This is primarily due to the complexity of the PCB layout for the RF (radio frequency) section. Fortunately, in BLE microchips, most of the RF circuitry is internal, so you don't need to worry about much more than the layout for the antenna.

Bluetooth Low Energy is a very popular open wireless standard for short-range communication. The range is typically about 50 feet, although this can be significantly increased with the use of a range extender circuit that either increases the receiver sensitivity, increases the transmission power, or both.

As the name implies, Bluetooth LE is a low-energy version of "classic" Bluetooth and thus is more appropriate for ultra-small devices powered by a single watch battery. BLE is the primary **wireless technology for Internet of Things (IoT)** products.



Example of a Bluetooth LE module. Image courtesy of [Digi-Key](#).

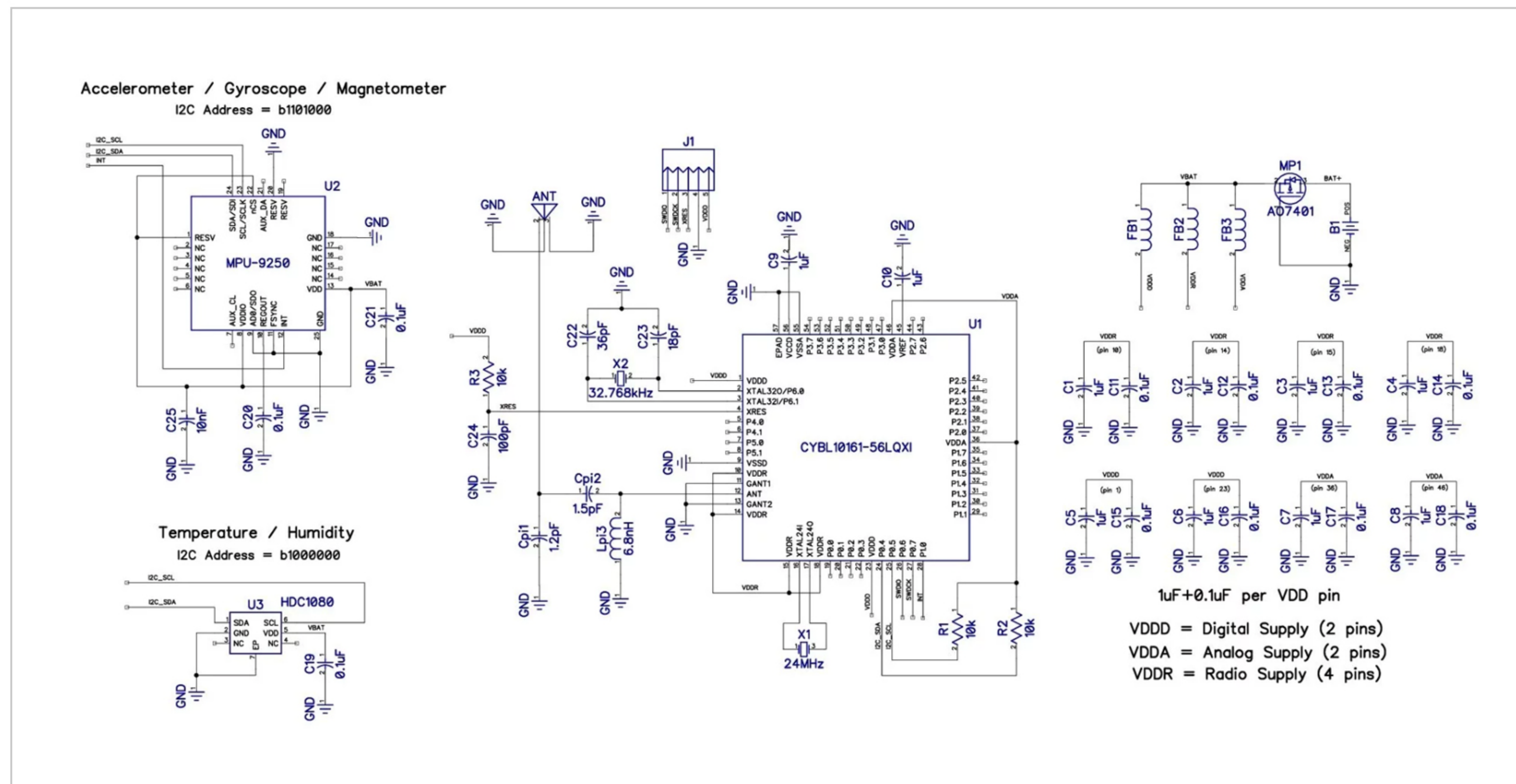
BLE is designed for devices that require only intermittent transmission of relatively small packets of data, rather than, for example, streaming audio. Most modern smartphones and tablets support Bluetooth Low Energy. It is supported by Android versions 4.3+ and by Apple iOS versions 4s+.

Bluetooth Smart devices communicate using radio frequencies in the 2.4 GHz industrial, scientific, and medical (ISM) band. BLE-enabled devices can support a wide array of applications and products, from remote controls and smart toys to short-range monitoring with wireless sensors. BLE devices are covered by version 4.0+ of the Bluetooth specification.

Integrating BLE into a system can be accomplished by [selecting a microcontroller](#) that offers BLE functionality or by using a BLE module. The use of a module will simplify the design and drastically reduce certification costs—but it will also increase the production cost. However, in most cases, a non-module BLE solution only makes economic sense once manufacturing volumes exceed about 500k units.

One such BLE microcontroller is a member of the Cypress CYBL10X6X family based on an ARM Cortex-M0 processor. One nice thing about the Cypress line of BLE microcontrollers is that they also offer BLE modules based on these microcontrollers. This can make the transition from a module solution to a more-customized solution a smoother process..

Schematic



The project's schematic. [Click to enlarge.](#)

BOOM

Quantity	Value	Name and Datasheet	RefDes	Description
1		CYBL10161-56LQXI	U1	Cypress BLE microcontroller
1		MPU-9250	U2	InvenSense 9-axis motion sensor
1		HDC1080	U3	Texas Instruments humidity/temperature sensor
1	24MHz	NX2520SA- 24.000000MHZ	X1	Microcontroller crystal
1	32.768kHz	ABS06-32.768KHZ-9-T	X2	Microcontroller crystal
1		W3008	ANT	Bluetooth chip antenna
10	1 μ F	GRM188R61C105KA93D	C1-C10	Ceramic capacitor
11	0.1 μ F	CC0603KRX7R7BB104	C11-C21	Ceramic capacitor
1	36pF	GRM1555C1H360JA01D	C22	Ceramic capacitor
1	18pF	CBR04C180F5GAC	C23	Ceramic capacitor
1	100pF	GRM1555C1H101JA01D	C24	Ceramic capacitor
1	10nF	CC0603KRX7R9BB103	C25	Ceramic capacitor
1	1.2pF	GRM1555C1H1R2CA01D	Cpi1	Ceramic capacitor
1	1.5pF	GJM1555C1H1R5BB01D	Cpi2	Ceramic capacitor
1		AO7401	MP1	P-channel MOSFET
3		BLM18AG102SN1D	FB1, FB2, FB3	Ferrite bead
1	6.8nH	L-07C6N8JV6T	Lpi3	Inductor
3	10k	RC0603JR-0710KL	R1, R2, R3	Resistor
1		22232051	J1	Programming connector

Components Discussion

The main components are the Bluetooth Low Energy microcontroller (U1, CYBL10161), the motion sensor (U2, MPU9250), and the humidity sensor (U3, HDC1080). The system is powered by a 3.7 V lithium polymer battery.

There are two crystal oscillators used by the [Cypress CYBL10X6X](#): the 24MHz external crystal oscillator (ECO) and the 32.768kHz watch crystal oscillator (WCO). The Cypress microcontroller includes internal, tunable load capacitors for the 24MHz crystal. Thus, in contrast to crystal-oscillator circuits for most microcontrollers, the 24MHz crystal in this design requires no external load capacitors.

The Cypress microcontroller is programmed via a Serial Wire Debug (SWD) interface on connector J1.

All power pins on each IC have bypass capacitors and use the recommended values given in the datasheets. Ferrite beads FB1, FB2, and FB3 provide some noise isolation between the digital, analog, and RF sections of U1.

Most components in a design need a clean, stable voltage. Power supply capacitors should be placed near the power supply pins on each IC to stabilize and filter the power. These [decoupling capacitors](#) provide a local storage reservoir and lower the effective impedance on the power supply traces as seen by the IC power pins.

Usually, designers will place a 1.0 μ F (or larger) capacitor in parallel with a 0.1 μ F or 0.01 μ F capacitor in order to achieve [low impedance across a wide band of frequencies](#). Capacitors of X7R [dielectric are sufficient](#) for use as power supply bypass capacitors.

For highly sensitive components, such as this RF microcontroller, a ferrite bead should also be included. This creates a low-pass filter that suppresses high-frequency power supply noise generated by other parts of the system. This design uses three ferrite beads (FB1, FB2, and FB3), one for each VDD supply (digital, analog, and radio) required by the microcontroller.

Humidity / Temperature Sensor

U3 is a digital humidity sensor (the [HDC1080 from Texas Instruments](#)) and is connected to the controller through an I2C serial interface. The device can measure relative humidity with up to 14 bits of resolution with accuracy better than $\pm 4\%$ over a temperature range of -20°C to 70°C .



Image courtesy of [ClosedCube](#).

The HDC1080 can also measure temperature over the range of -40°C to $+125^{\circ}\text{C}$ with accuracy better than 0.6°C . In addition to measuring temperature and humidity, the HDC1080 includes a battery monitoring circuit which will set a status bit if the battery is below 2.8 V. The supply voltage range is 2.7 to 5.5 V.

I2C is an addressable serial bus, so each I2C slave device in the system must have a unique address. For the HDC1080, the 7-bit address is pre-set to b1000000. The MPU-9250 motion sensor allows you to choose between two addresses: b1101000 or b1101001. The least significant bit is set to one or zero by tying the AD0 pin high or low. Note that pull-up resistors (R1 and R2) are required for each of the two I2C lines.

The device manufacturer provides recommendations concerning the placement of the sensor on the PCB. For example, the HDC1080 should not be placed close to any heat-generating components.

Power and ground planes in the PCB should not run under the device, because they could provide an unwanted thermal path to the sensor. In fact, slots should generally be placed around the device to separate it as much as possible from the rest of the board.

9-Axis Motion Sensor

U2 is a motion sensor ([MPU-9250 from InvenSense](#)) that includes a 3-axis accelerometer, a 3-axis gyroscope, and a 3-axis magnetometer (compass).



Image courtesy of [InvenSense](#).

This type of sensor detects movement of the device itself and is not to be confused with ultrasonic or infrared sensors that detect motion of a nearby object (such as those used in motion-activated lights).

The MPU-9250 includes nine analog-to-digital converters, each having 16 bits of resolution. The MPU-9250 interfaces to the microcontroller via the I2C bus.

The Antenna

When not using a pre-certified BLE module with a built-in antenna, one of the most critical aspects of the design will be the antenna and the transmission line between the antenna and the transceiver.

There are two choices for the BLE antenna: a chip antenna or a PCB-trace antenna. A chip antenna has the advantages of smaller size and simplified tuning. A trace antenna is designed into the PCB itself. The main advantage of a trace antenna is the reduced unit cost. In fact, because the antenna is just a trace on the PCB, the antenna is essentially free.

However, chip antennas are rather cheap, so in most cases a chip antenna is a better choice—at least initially.

This design uses a chip antenna from Pulse Electronics. Once your product achieves large production volumes, you may want to replace the chip antenna with a PCB-trace antenna in order to reduce your unit cost and improve the profit margin.

PCB trace antennas tend to be more problematic to tune, however, and many times they require several PCB revisions in order to optimize tuning. Modifications to the PCB will also have a more pronounced impact on a trace antenna's tuning versus that of a chip antenna.

Antennas always need to be tuned for peak performance. Tuning is a complex process that requires a special type of testing chamber that shields and absorbs all types of radio waves. So antenna tuning is usually best outsourced to vendors specializing in tuning. In many cases, though, the antenna manufacturer ([Johanson Technology](#), [Pulse Electronics](#), and [Taoglas](#), for example) will offer tuning services for new designs incorporating one of their antennas.

An antenna will normally require the use of a pi-network for tuning the antenna (i.e., altering the impedance of the antenna so that it more closely matches the impedance of the transceiver). The capacitor and inductor values used in the pi-network are adjusted so as to maximize the power transfer between the antenna and the RF transceiver.

If optimizing the operating range isn't extremely critical for your product, then a chip antenna doesn't necessarily need to be tuned for BLE, at least for early testing.

Critical aspects of the antenna layout must be adhered to in order for the antenna to operate correctly. The designer must pay careful attention to recommendations in datasheets and application notes.

You can determine the PCB transmission line dimensions for achieving proper impedance matching by using a special calculator such as the free tool [AppCad from Avago](#).

Certifications

Each country has its own regulations concerning the emission of radio frequencies, and every BLE system must be in compliance. In the United States, the [FCC regulates emissions](#) in the 2.4 GHz ISM band, and if the product is sold commercially, FCC certification is required.

FCC certification usually costs a minimum of about \$10,000 for a custom-chip (i.e., non-module) solution (which is classified as an "intentional radiator"), versus only about \$1,000 for a solution using a BLE module (classified as a "non-intentional radiator").

Both "classic" Bluetooth and Bluetooth Low Energy require you to pay an \$8,000 licensing fee. This is true whether you use a pre-certified module or a chip solution.

The designer of a BLE system should be aware that significant testing expense, certification cost, and design effort can be avoided by using a pre-certified BLE module.

If you would like to learn more about developing a new electronic product, check out my [Ultimate Guide - How to Develop a New Electronic Product](#).



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Exploring UC Berkeley's Wearable Sweat Sensor for Monitoring Dehydration

Researchers develop a wearable sensor for detecting important analytes in sweat for monitoring dehydration.

In this article, we will explore the specifics behind the University of California, Berkeley's wearable sweat sensor they recently published about in [Nature Letters](#).



View of the wearable sweat sensor worn on the wrist. Image courtesy of [UC Berkeley](#).

Biosensors

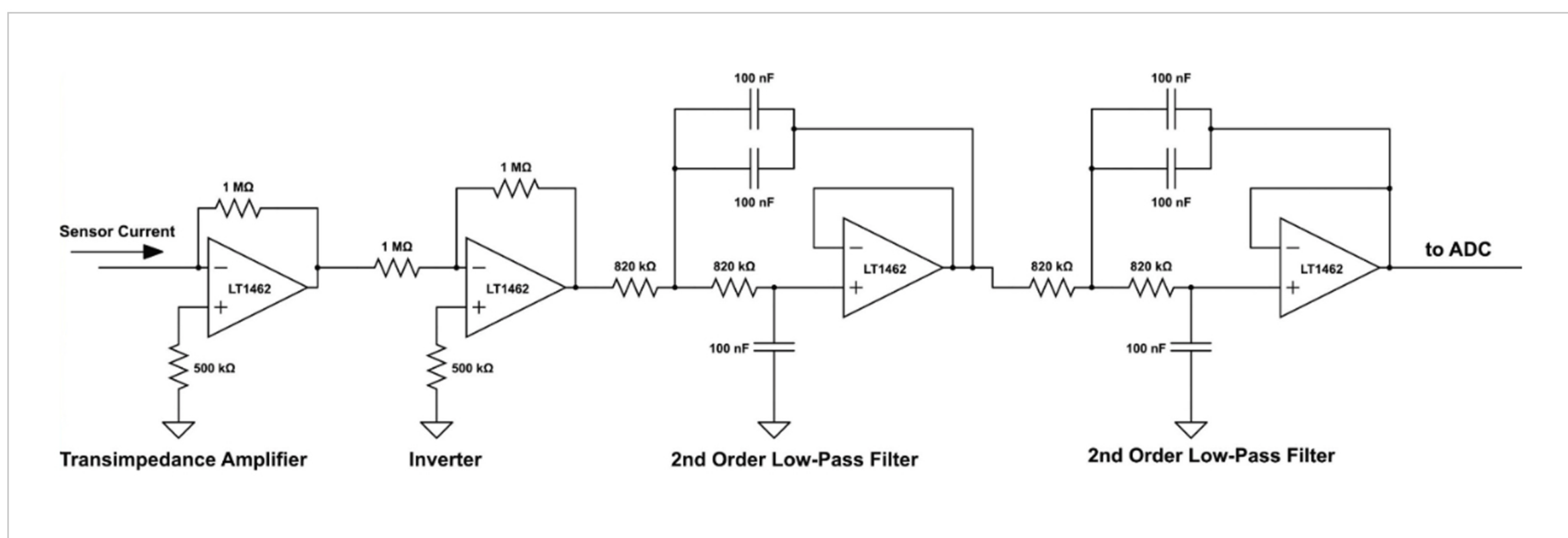
One of the more interesting classes I have taken thus far in grad school has to be Biosensors.

In this class, we detail the development of biosensors over the last few decades in research and consumer technologies. A biosensor can be described as a device that measures a specific biological quantity and transduces the biological quantity into a form that can be read and interpreted by a person.

One common type of biosensor is the glucometer, which allows diabetics to monitor their blood sugar levels and their insulin regimen. Of course, being the EE at heart that I am, I tend to pay pretty close attention to the electronics design that accompanies some of these sensors.

Gao et al. detail their design for “fully integrated wearable sensors arrays for multiplexed in situ perspiration analysis.” In their paper, they analyze human sweat for a few important biomarkers, namely glucose, lactate, sodium (Na⁺), and potassium (K⁺). These biomarkers provide important information regarding hydration status and overall fitness. Surprisingly, very simple circuits can perform these measurements.

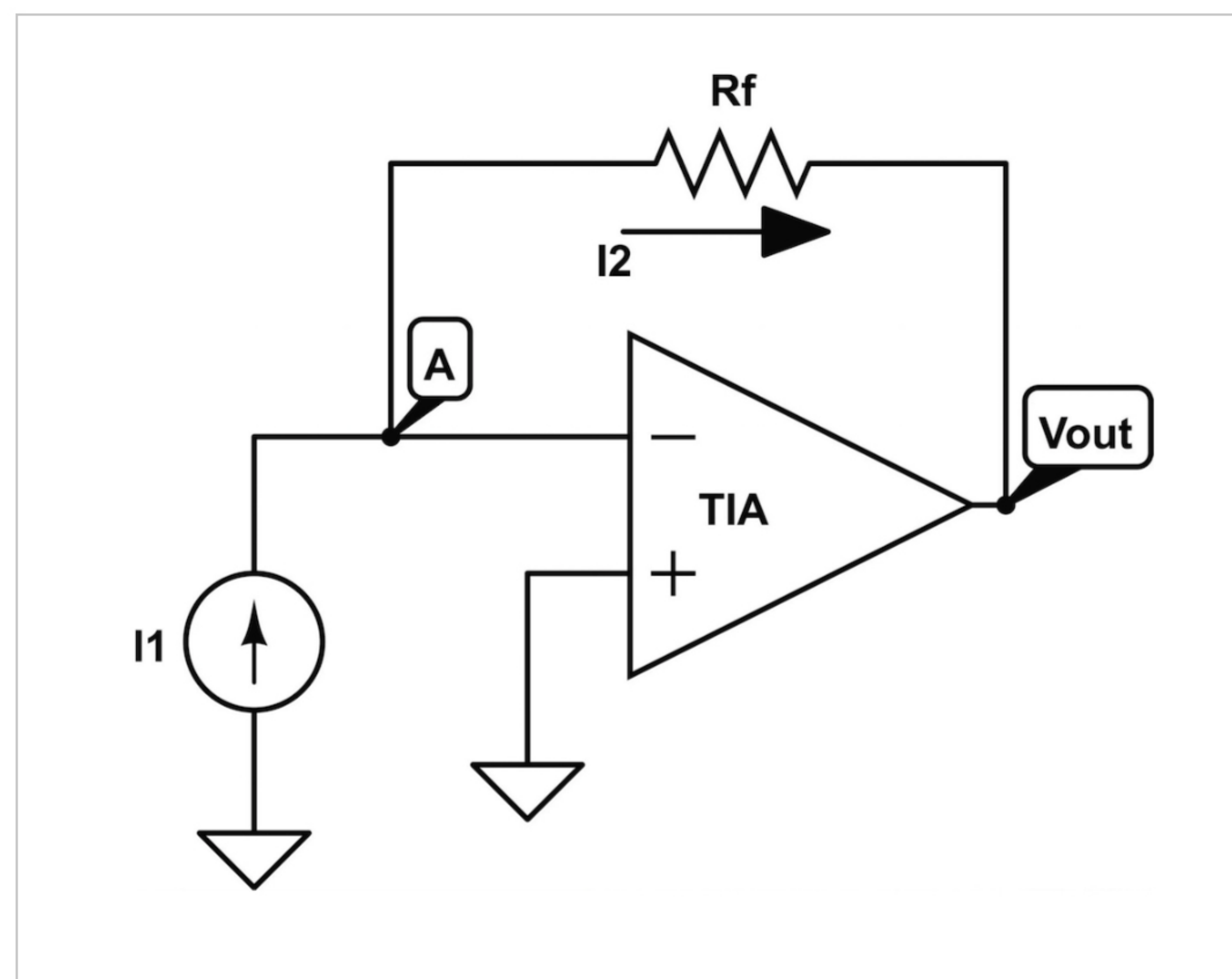
Let's take a look at the circuit configurations.



Schematic diagram of the glucose and lactate sensor. Image content recreated from [Nature Letters](#).

Glucose and Lactate Sensing with a Transimpedance Amplifier (TIA)

At the heart of their glucose and lactate sensor is a transimpedance amplifier (TIA), or “current-to-voltage converter.” A transimpedance amplifier, as the name suggests, converts an input current to a voltage. Let's analyze this further.



General schematic of a transimpedance amplifier (TIA) or "current-to-voltage converter".

Satisfying Kirchhoff's Current Law (KCL)

Remember your basic [Kirchhoff's Current Law](#) (KCL) relationship. If a current, let's say I_1 , flows into a node, another current, equal to I_1 , flows out of the node. Looking at our schematic of a basic transimpedance amplifier, if a current, I_1 , flows into Node A, we must also have an equal current, I_2 , flowing out of Node A to satisfy KCL.

Now we get into Ohm's Law which states that $V = I \times R$. Our op amp produces a voltage at its output to drive a current across R_f in order to satisfy KCL (or sink a current depending on the direction of current flow and your preferred convention of positive current flow). In this way, we obtain current-to-voltage conversion with a pretty simple relationship.

The Inverter

Next, they add an inverter to correct the phase inversion from the transimpedance amplifier. Notice the resistor from the non-inverting pin to ground. This is a slight modification to the typical inverting amplifier configurations that many are used to. The purpose of this resistor is to help correct for input bias currents that can add noise at the output of the circuit distorting the glucose or lactate measurement.

From our basic op amp rules, we know that no current flows into the inputs of the op amp and that the voltages at the op amp inputs are the same. Unfortunately, it's not quite that simple.

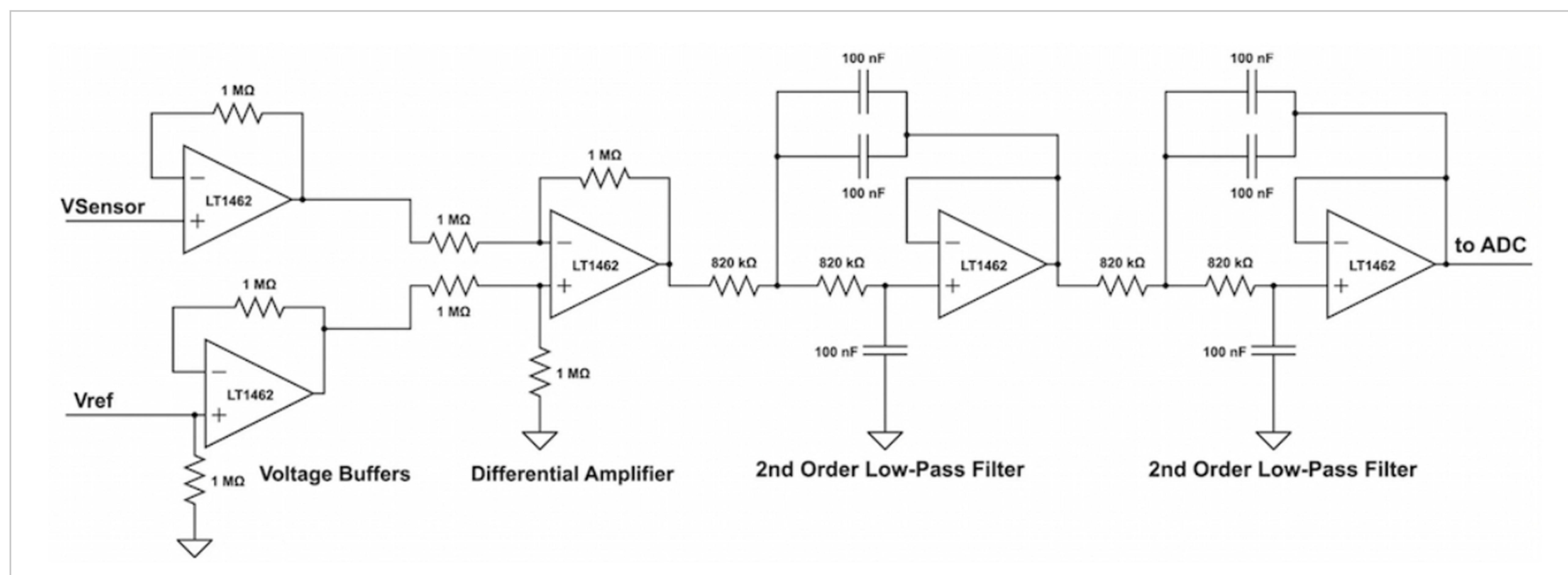
Bias currents can cause the non-inverting input and inverting input to have different voltages. For a low-gain amplifier, this is probably not that big a deal. It's also not problematic if the ratio of the input voltage (V_{in}) to the input resistance (R_{in}) is relatively large. Decent amplifiers have input bias currents in the nanoamperes (nA), so we figure if V_{in}/R_{in} is on the order of milliamps, we are a few orders of magnitude higher than our noise.

Gao et al. use an input resistance of $1\text{ M}\Omega$. And we can figure that the input voltage (from the output of the transimpedance amplifier) is probably in the millivolt range. This means that V_{in}/R_{in} will probably be around a few nanoamps, which is right in our noise margin. Gao et al. place a resistor at the non-inverting pin to help correct for the bias currents. As you examine the full schematic a bit further, you will see that the researchers use this trick in pretty much all their op amp stages. They are being quite careful in managing their input bias currents.

Second-Order Low-Pass Filters

Next, we have two 2nd-order low-pass filters to get rid of unwanted noise using the popular [Sallen-Key topology](#). Connecting these two filters in series leads to a four-pole response that provides steep roll-off for frequencies above the cutoff. These biosensors are operating at about 1Hz, so bandwidth is certainly not a limiting factor in the amplifier or filter design.

Sodium and Potassium Sensing with a Differential Amplifier



Schematic diagram of the Na^+ and K^+ sensor. Image content recreated from [Nature Letters](#).

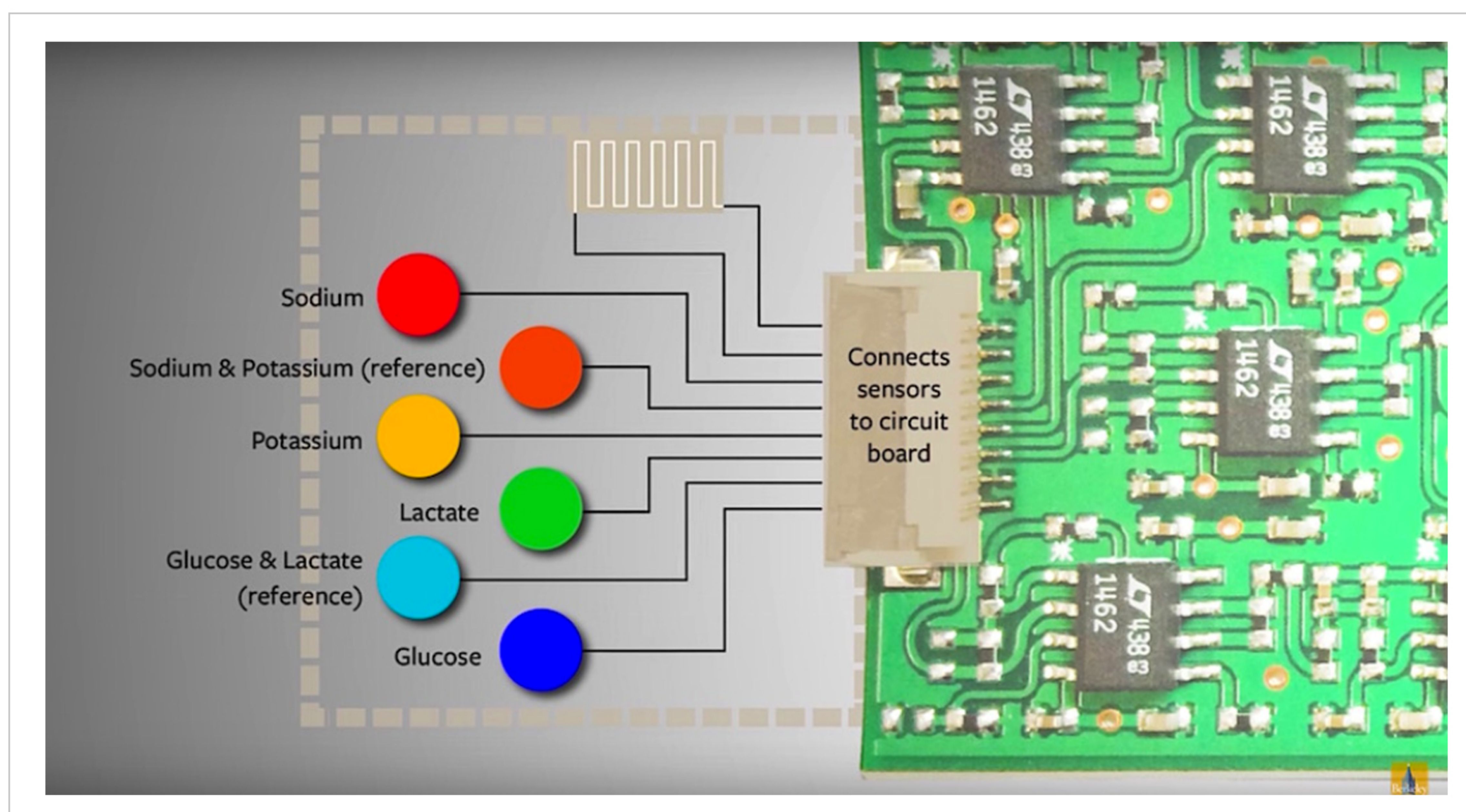
For the Na⁺, K⁺ measurement systems, Gao et al. utilize a simple differential amplifier stage with two buffered inputs. An interesting aspect of the design is the use of the buffer amplifiers to interface the circuit to the bioelectrical system.

Metals are often used as electrodes for performing bioelectric measurements. Metals are great conductors of electricity. In bioelectrical systems, however, there are a number of complications that affect the impedance of a metal. I won't go into too much detail but, when a metal is placed into a biological system, an electrode-fluid interface develops. This electrode-fluid interface has a highly variable impedance. In order to nullify the effect of the variable electrode-fluid impedance, a buffer amplifier is used as the first stage.

A buffer amplifier has a very large input impedance, much larger than the variable impedance of the electrode-fluid interface. As a result, we obtain a faithful measurement of the voltage of our bioelectrical system without loading the system, itself. The resulting voltage generated from the system is subtracted from a reference voltage—a standard technique in bioelectrical measurements—using a differential amplifier. The circuit is further conditioned with two 2nd-order low-pass filters before being processed by a microcontroller.

The entire circuit design is on a flexible printed circuit board, allowing the device to conform to the skin.

Finally, and this is a personal favorite of mine, the analog signal is digitized by the ADC on an



The board's flexible sensor array. Screenshot courtesy of the UC Berkeley.

In Summary: A Research Paper with Implications for Health and Wellness

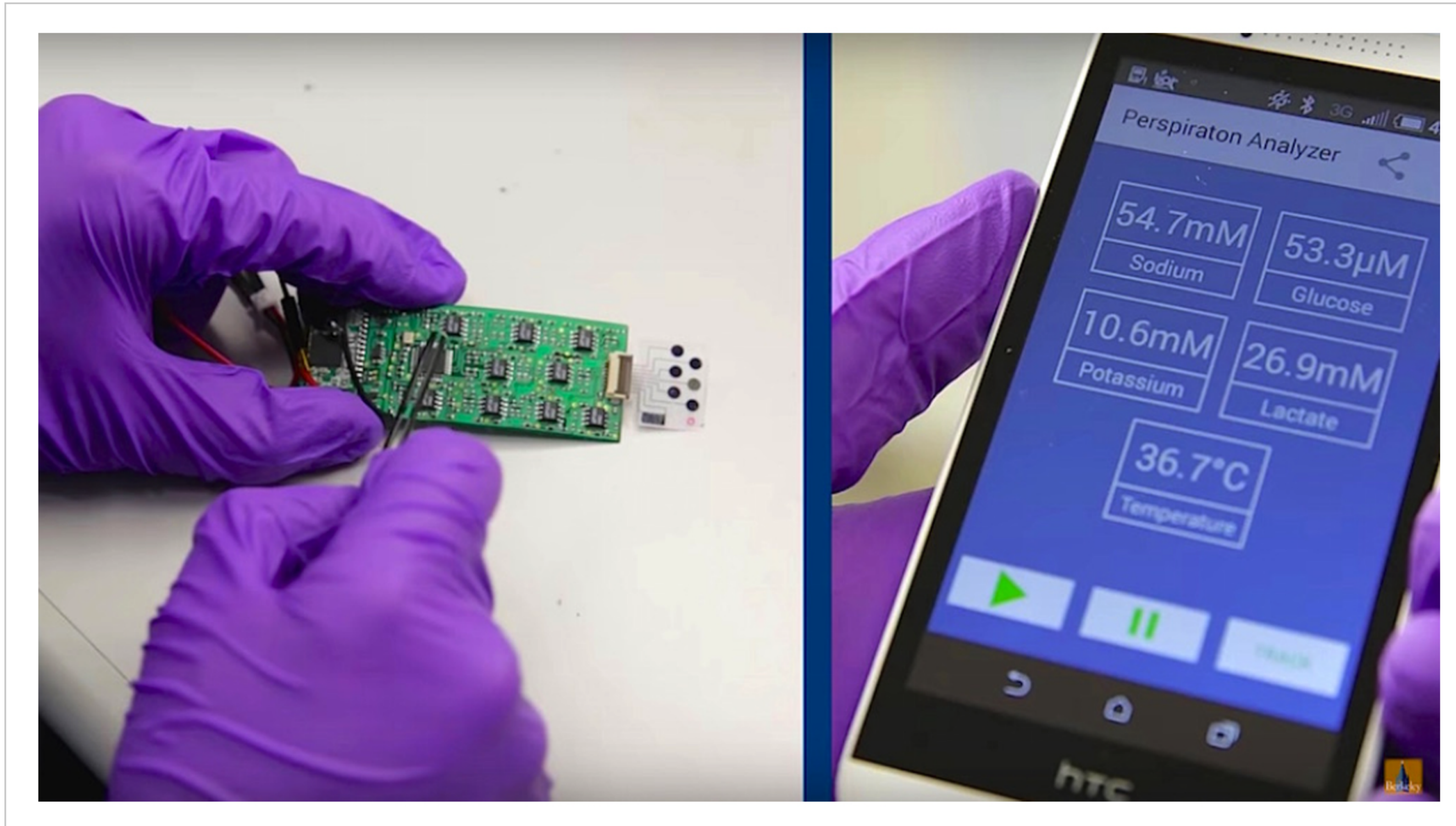
Overall, I was really impressed by the detail the researchers went into in developing their sensing circuit. I would also like to propose a few suggestions for thought.

For starters, they built four separate amplifier stages for each of their four biosensors (glucose, lactate, Na⁺, K⁺). Admittedly, glucose and lactate required a different sensing configuration compared to Na⁺ and K⁺. Nevertheless, the use of a simple two-channel multiplexer like the [TS5A9411](#) from Texas Instruments could very quickly simplify the circuit by essentially cutting their design in half. I have personally found the TS5A9411 to be a pretty good option for interfacing between electrochemical cells due to its low on-resistance (10Ω max at VCC = 5V) and on-capacitance (8.5pF). Furthermore, with a low operating voltage (down to 2.5V) and small footprint (SC70-6, 2.2mm × 2mm), the TS5A9411 is a decent option for sensitive switch applications for bioelectrical systems.

Several ICs have been developed for bioelectrical sensing. The [LMP91000](#), also from Texas Instruments, is an integrated analog front-end for electrochemical sensing (I've been using "bioelectrical" instead of "electrochemical"—but, in this context, they can be considered interchangeable). It is capable of performing both the current-to-voltage conversion for glucose and lactate and the differential measurements for Na⁺ and K⁺, which makes the IC pretty versatile. Use of the LMP91000 essentially cuts their design down to a single chip, which is outstanding. Maybe they found that it was necessary to explicitly design each amp stage in order to maintain sensitivity and configurability for each biomarker.

Furthermore, research papers are often presenting proof-of-concepts. From the title, we understand that the focus was more on detecting these biomarkers in sweat, in real-time, with a wearable device, than on the circuit design, itself. We can surmise that further optimization of the circuit design will soon follow.

All that being said, Gao et al. built an impressive device for simultaneous measurement of four important biomarkers of hydration and fitness. Their project also demonstrates that there is a need for experienced electrical and electronics engineering in a variety of fields including chemistry, biological science, and biomedical engineering.



The sensor and its accompanying app. Image courtesy of [UC Berkeley](#).

Biosensors have extraordinary impact in the consumer and research space ranging from applications in glucose monitoring to cancer detection. In recent years, the quantified-self movement has increased the demand for wearable biosensors, prompting researchers to investigate new ways to bring laboratory technologies to the hands and homes of consumers.

Featured image used courtesy of the [University of California, Berkeley](#).

NFC-Powered Sweat Biosensor for Glucose and Lactate

Researchers at Northwestern University Center for Bio-Integrated Electronics are championing the development of sweat biosensors with their latest glucose and lactate sensors.

What Are Sweat Biosensors?

Sweat biosensors are devices that monitor a given physiological quantity in sweat, often being worn on the arm or the back shoulder as these locations experience high sweat production compared to the rest of the body. Oftentimes, sweat biosensors are designed for analyzing biomarkers such as glucose, lactate, or sodium, providing information on glycemic content, muscle activity, or hydration.

Sweat biosensors have seen increased interest in the medical device industry and in academia as they present a unique opportunity for non-invasively monitoring important biomarkers for health and fitness applications as well as for medical diagnosis and treatment.

Researchers at Northwestern University Center for Bio-Integrated Electronics, led by Professor John Rogers, are among those championing the investigation of wearable sweat biosensors. One of their recent publications titled “Battery-free, skin-interfaced microfluidic/electronic systems for simultaneous electrochemical, colorimetric, and volumetric analysis of sweat” highlights their efforts.

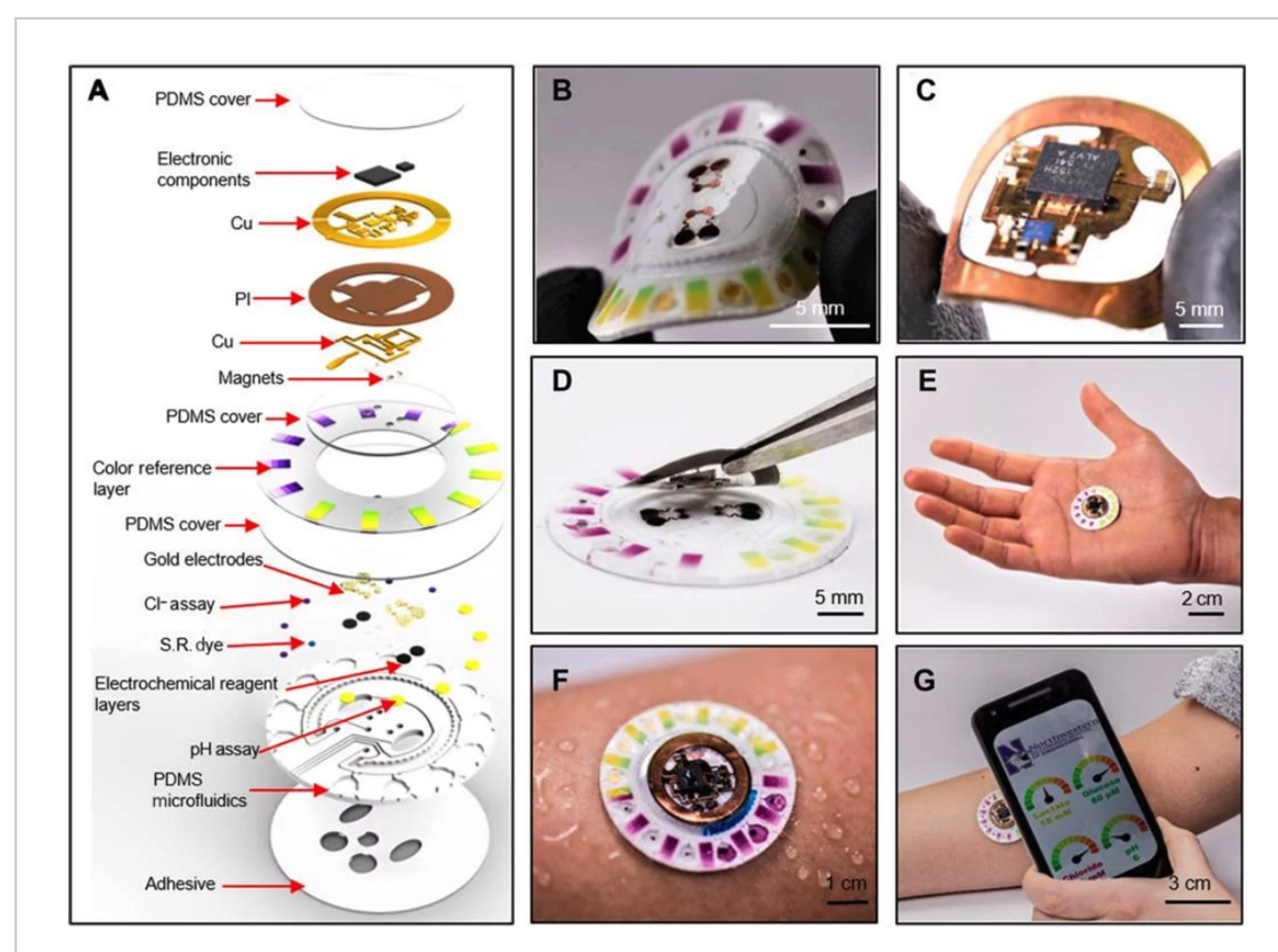
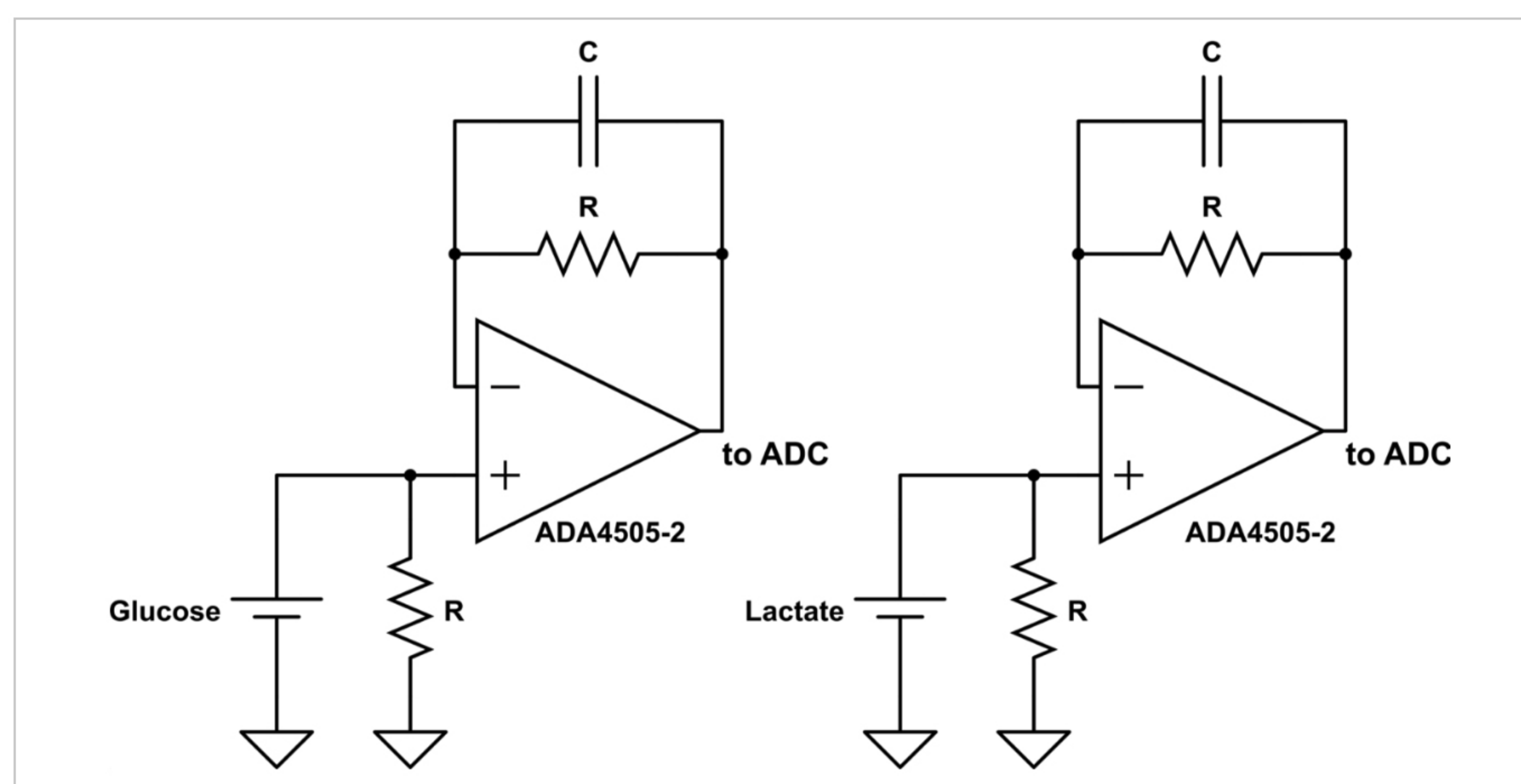


Figure showing different facets of the sweat biosensor particularly highlighting its multilayered construction as well as its battery-less operation. Image from the [Rogers Research Group](#)

Voltage Buffer for Potentiometric Glucose and Lactate Sensors

The analog front-end is fairly simple requiring only a simple voltage follower with integrated RF filters. The glucose and lactate sensors are potentiometric sensors, meaning they output a small voltage proportional to the concentration of glucose or lactate present in the sweat sample being analyzed. This same operation is the basis of common laboratory pH probes and requires fairly simple hardware, consisting of a low-noise voltage buffer, to implement.



Schematic of glucose and lactate potentiometric sensors. Each signal is buffered and filtered before digitizing to remove extraneous noise. Image content recreated from Science Advances.

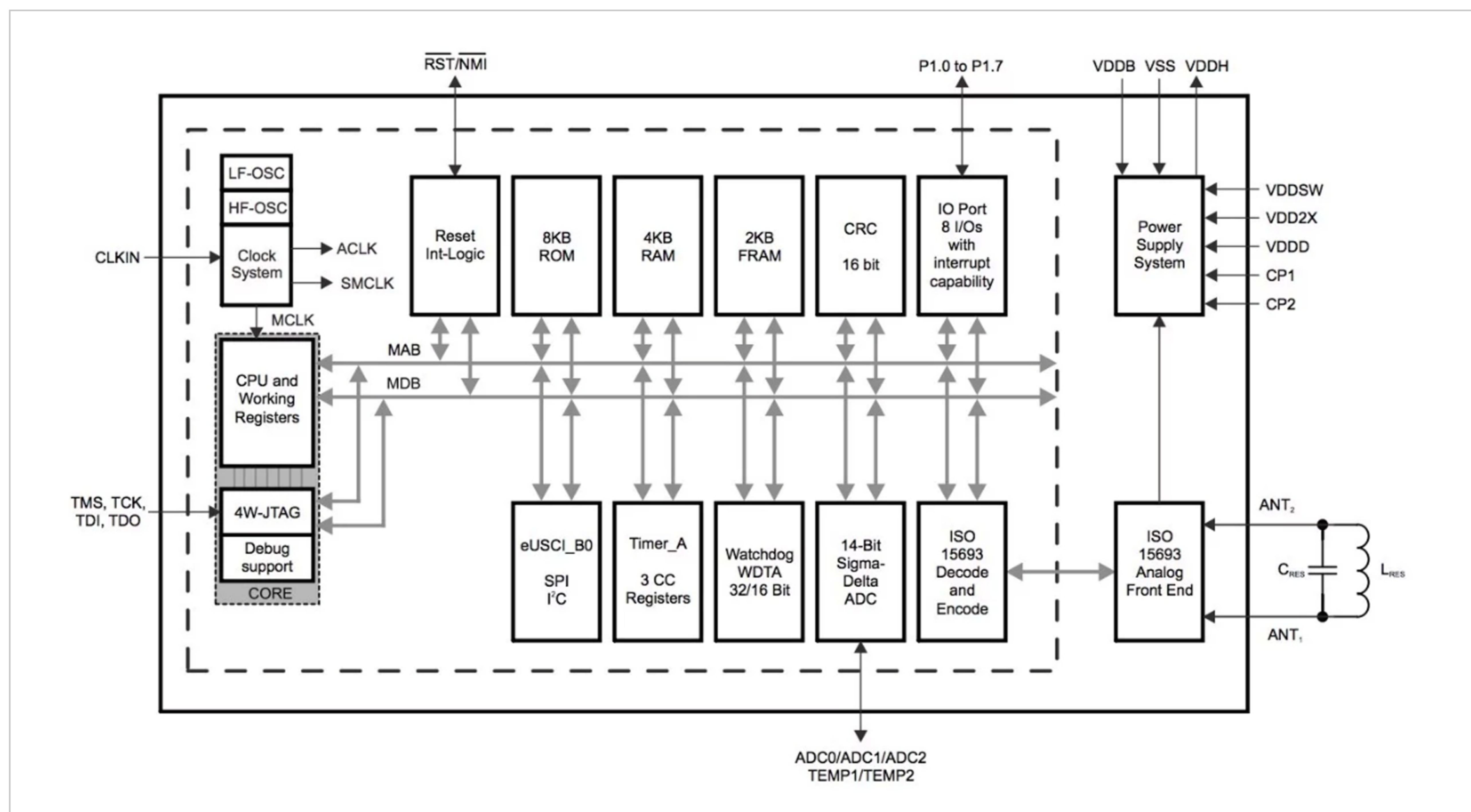
The research group included a capacitor in the feedback network of the follower circuit to decrease bandwidth and reduce noise. The signal is then read by a 14-bit analog-to-digital converter.

Wireless Power through NFC

One of the key features highlighted by the research team is the battery-less operation of their device. Instead of powering the device with a standard primary or secondary cell battery, the Rogers Research Group instead chose to employ a wireless powering scheme craftily leveraging NFC (near-field communication) for both power and communication.

This technique is famously utilized in consumer NFC tags for short-range wireless communication between the tag and an NFC-enabled smart device. Even though NFC has not completely taken over the consumer electronics industry like many previously predicted, NFC is finding growing use in enabling contactless payment using mobile phones and smartwatches.

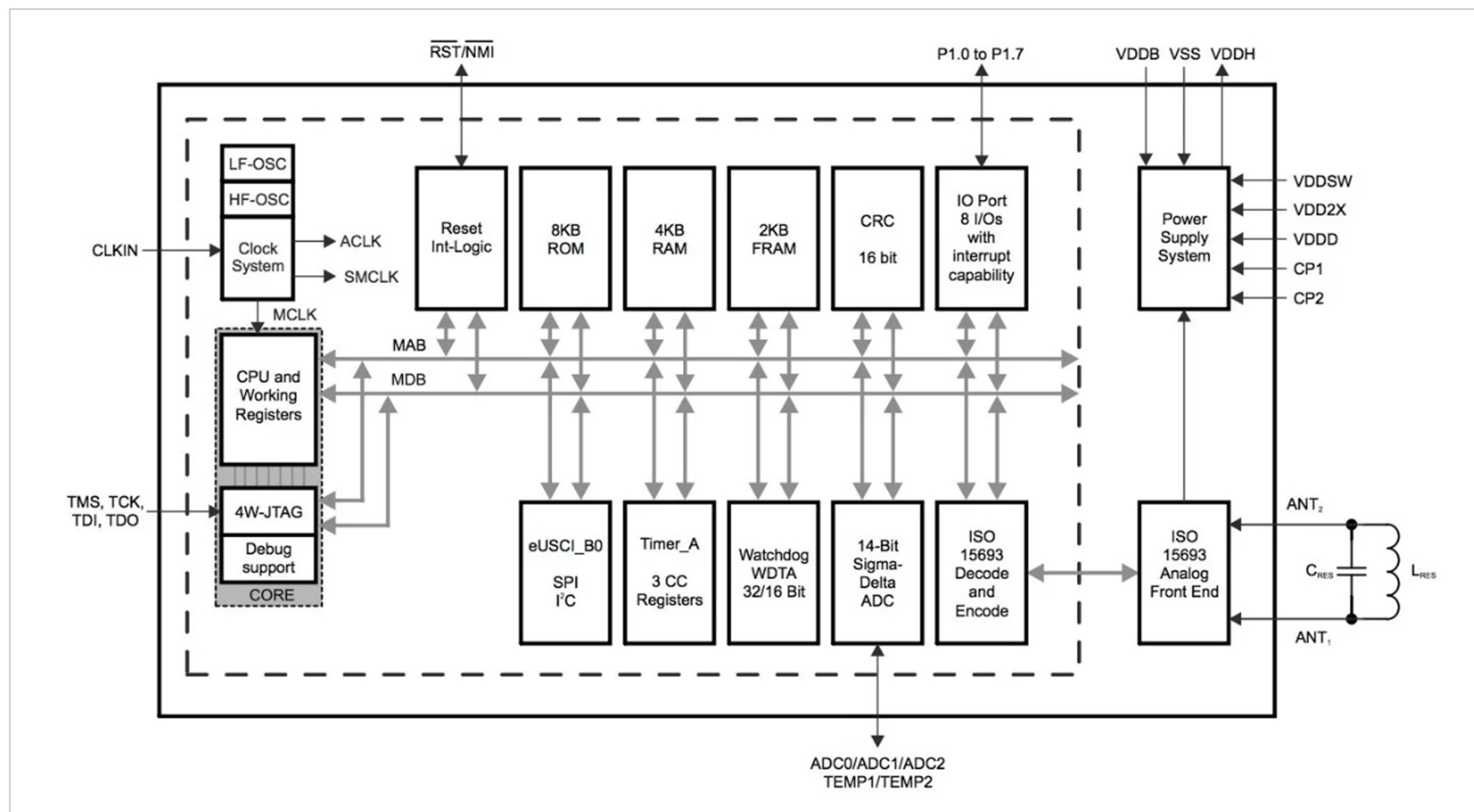
NFC provides a very modest amount of power, so it is necessary that the circuit operates at extremely low power. They utilized the RF430FRL152H sensor transponder from Texas Instruments which is designed for operating on a small battery or, more interestingly, on a magnetic field.



The functional block diagram of the Texas Instruments RF430FRL152H. Image from the [RF430FRL152H datasheet](#).

The RF430FRL152H has an incredibly low operating voltage of 1.45 V and is designed to handle the unregulated, variable power provided by an intermittent magnetic field.

The RF430FRL152H includes Texas Instruments' popular low power MSP430 microcontroller architecture, which boasts one of the lowest operating voltages in the industry. The Rogers group mention buffering the sensor signals with the ADA4505-2, a small footprint, zero-crossover, low noise, low operating voltage amplifier. Minimal footprint is critical for ensuring the sensor remains inconspicuous when worn on the body. Zero-crossover and low noise are necessary to minimize distortion since the signals from the glucose and lactate sensors have a very small dynamic range and are not amplified (because an amplifier, rather than a unity-gain buffer, would require additional passive components).



Data showing sensor glucose and lactate measurements from the sensor compared to traditional laboratory techniques. Image from the Rogers Research Group

Some In-House Fabrication

The NFC antenna fabrication was performed in-house using photolithography to pattern conductive traces onto a flexible printed circuit board material (DuPont Pyralux AP8535R) separated by a layer of polyimide and encapsulated by a silicone material for waterproofing. Developing the NFC antenna in-house presents the research group with the greatest flexibility in quality control resulting in excellent antenna performance with high Q, even at modestly high bend radii.

Early Feasibility Studies

The researchers demonstrated their device's ability to measure different biomarkers while powering the device using an NFC-enabled smartphone as well as from a custom designed large-scale antenna for continuous monitoring while riding a stationary bike. The results are, of course, preliminary, but are promising nonetheless.

Sweat biosensors are notorious for baseline drift, variability due to temperature, and variability due to corroding of the sensing elements leading to lower signal-to-noise ratio over time with increasing wear. Though this paper does not address these issues specifically, other concerns such as the hypoallergenic adhesive and the miniaturization of the analog front-end presented interesting solutions to very challenging issues facing sweat biosensors.

The Case for Lower Power and Miniaturization

This paper demonstrates the need for miniaturization and for more flexible powering options in order to develop advanced biomedical technology as well as the need for wafer scale integrated circuits for reducing device footprint. Miniaturization and decreased power consumption are particularly critical for wearable sensors as such sensors rely on being discreet and long-lasting. This paper also presents key opportunities for industry-academia relations that would streamline the development of new medical technology by leveraging each partner's particular specialties.

Semiconductor companies can provide chipsets with advanced feature sets and low power, fabrication houses can provide academics tape out space for turning their prototypes into custom integrated circuits, and academia can provide the testing centers for the high-risk work that companies would like to explore.



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