Real-Time, Non-Invasive Biomarker Sensing on the Wrist

How integrated photonics will revolutionize mobile biomarker monitoring

Rockley® Photonics

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rockleyphotonics.com

Abstract

In recent years, there have been several significant technological advances for monitoring and assessing human health and wellbeing. Portable and wearable electronic devices are now widely available to consumers, and tens of millions of devices are sold each year. Many of these products rely on a core set of non-invasive optical sensing technologies. Light-emitting diodes (LEDs) shine into the skin to monitor specific parameters related to underlying health conditions. Gathering critical photoplethysmography (PPG) data by using green LEDs, for example, has become the foundation upon which consumer wearables collect meaningful health metrics, including heart rate, respiration rate, sleep patterns, and more.

While LED-based sensors have become ubiquitous in nearly all wearable devices, they have considerable limitations. Most notably, LED-based sensors in mobile devices are limited by the detection capabilities of visible and near-infrared (NIR) light. While larger benchtop equipment may have the capability to monitor biomarkers using more powerful light sources to achieve a wider spectral range, mobile LED-based solutions simply do not provide sufficient optical power over the spectral ranges needed to monitor key biomarkers.

What if there were a mobile sensor that could extend light's measurement capabilities into a completely new range of wavelengths to reveal more about the wearer's health?

At Rockley® Photonics, we believe that our silicon photonics platform will tremendously impact biomarker measuring and monitoring — in several important ways:

- By using sensors based on a much larger slice of the infrared spectrum, the Rockley platform provides the range needed for wearable devices to detect a wider selection of biomarkers, including ethanol, lactate, and glucose.

- By producing many discrete and individually generated light sources from a single photonics integrated circuit (PIC), the Rockley platform provides the accuracy needed to discern this wider selection of biomarkers.

- By integrating multiple sensing capabilities into a small module, the Rockley platform provides a complete solution that easily fits into a compact form factor.

These proprietary hardware technologies are paired with Rockley's on-device analytics to create a stand-alone mobile platform for measuring and analyzing key biomarkers. With this mobile platform, we have created a new class of sensor with the potential to deliver the level of measurement and analysis needed for consumer wearables and medical monitoring devices. This sensor technology is built upon a scalable platform that significantly reduces cost barriers for mass market deployment and widespread adoption.

Overview of Biomarker Monitoring

Limitations of Current Monitoring

The conventional approach to testing patients and monitoring biomarkers has remained unchanged for decades. Technicians draw blood from patients in a medical facility, and lab equipment analyzes those blood samples to determine the presence, absence, or concentrations of specific elements or biomarkers within the blood. While this traditional process certainly provides important diagnostic information, this lab-based approach has significant drawbacks:

- High cost of instrumentation
- Dependency on manual processes
- Limited patient access
- Inconvenience for patients
- Limited ability to measure trends over time

Newer mobile approaches, such as wearables using PPG sensors, overcome the disadvantages of in-lab monitoring, but they have their own limitations. These sensors leverage a very narrow band on the light spectrum — i.e., visible and near-infrared (NIR) light — and therefore have limited detection capabilities. Moreover, the low signal-to-noise ratio (SNR) of these sensors limits their accuracy and precision. Applying complex and often customized algorithms can sometimes improve performance for a specific use case but typically will not overcome the inherent limitations of the hardware.

Even with their limitations, current in-lab and mobile solutions will continue to fill an important role for monitoring biomarkers based on use case and patient needs. In addition to these traditional methods, however, there is an expanding need and desire for both mobile and in-home solutions that provide accurate and cost-effective monitoring of key biomarkers.

Growing Demand for Mobile Monitoring

The global consumer wearable market has seen double-digit growth year over year, driven by the increased attention among consumers on health issues, along with the declining cost of wearable devices. Annual smartwatch shipments are projected to exceed 130 million units by 2025, and annual shipments of wristband devices and wireless earbuds have been forecasted to grow to 90 million and 300 million units, respectively, by 2025. (See Figure 1.)

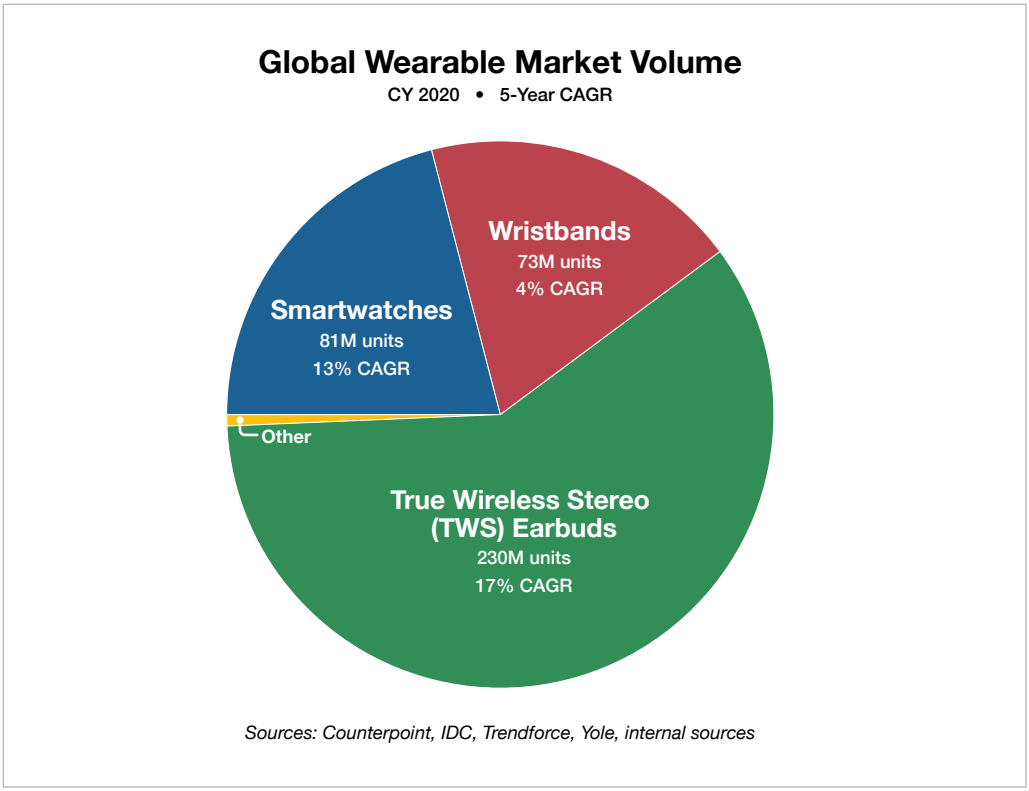

Figure 1: Growth projections for wearable device market

Recent advances in LED technology have been a key driver in this market and have lowered the barrier to entry for manufacturers. Because LED-based sensors can detect biomarkers in a non-invasive manner, they are extremely convenient for use in different form factors, such as smartwatches and wristbands. The table below outlines the biomarker monitoring capabilities of several popular manufacturers:

Table 1: Biomarker monitoring abilities of popular wearables

	Heart Rate	Oxygen (SpO2)	ECG Monitoring	Sleep Patterns	Respiration Rate	Blood Pressure
Apple	✓	✓	✓	✓	✓	
FitBit	✓	✓	✓	✓	✓	
Garmin	✓	✓		✓	✓	
Huami	✓	✓	✓	✓	✓	
Huawei	✓	✓	✓	✓	✓	
Samsung	✓	✓	✓	✓	✓	✓

Based on publicly available information as of July 2021. Subject to change without notice.

Changing the Game

Rockley Photonics has developed a full-stack silicon-photonics-based sensing platform that integrates many proprietary advances in photonics and analytics. This new platform has the potential to transform and elevate the biomarker monitoring capabilities of consumer wearables and medical devices.

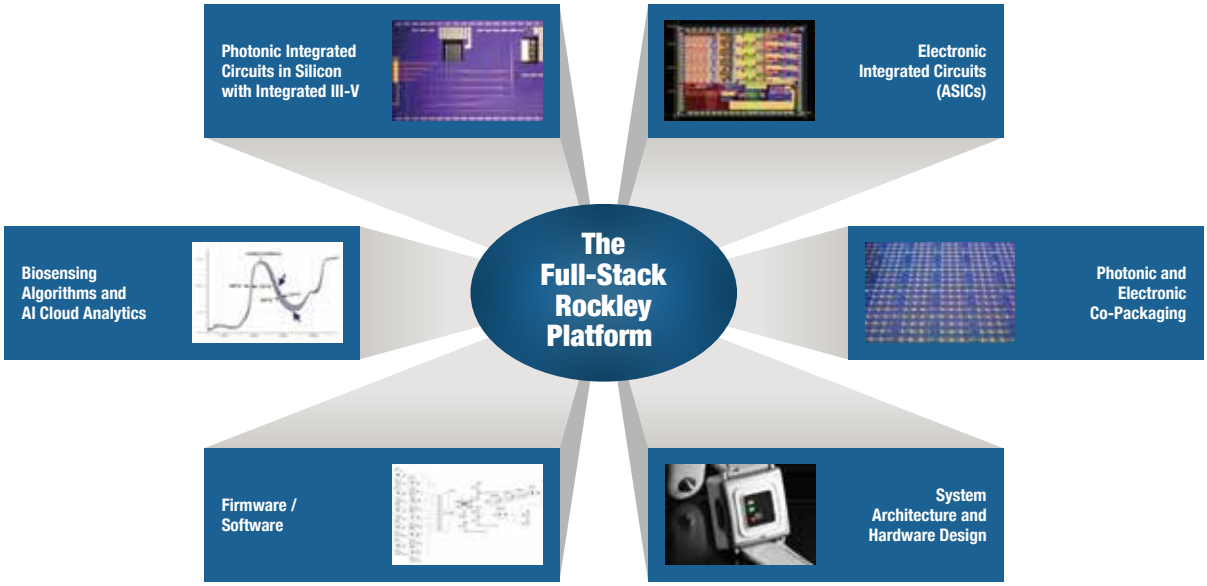

Figure 2: Key components of Rockley's full-stack sensing platform

Rockley's sensing platform augments the LED solutions used in today's wearable devices with a proprietary solution using a photonic integrated circuit (PIC). Representing a fundamental breakthrough in mobile spectroscopy, this unique chip-sized hardware solution could have a tremendous impact on providing real-time, non-invasive insights into a person's health and wellbeing.

Rockley has achieved this breakthrough by developing a complete and secure end-to-end (module-to-cloud) solution that leverages several innovative technologies:

- Rockley's spectrophotometer chip provides a significantly broader spectral range (approximately one hundred times broader) by emitting numerous distinct laser lines over a wide range of wavelengths.
- Rockley's multi-micron-waveguide photonics-optimized platform enables the manufacturing of compact circuitry with high integration densities, thereby substantially increasing the number of lasers and sampling wavelengths.
- Rockley's data science platform includes application-level algorithms and applies deep learning across raw spectral and biomarker data to generate holistic and actionable health insights.

In summary, Rockley has effectively created a “clinic on the wrist” platform that is ideally suited to enabling advanced biomarker tracking in both the mobile wearable and medical technology markets. The following sections of this paper provide further details about the technologies behind the Rockley sensing platform.

Figure 3: Rockley wristband with standalone sensor module containing photonic ICs and application firmware

Spectroscopy for Health Monitoring

The use of spectroscopy in wearable devices has enhanced the ability to provide non-invasive health monitoring. This advance would not have been possible without two important improvements in optical technologies:

- Miniaturizing the size of both the light emitter and detector
- Eliminating the need for a monochromator grating or filter by using light sources that have narrower emission spectra.

LEDs have become the most prevalent light source used in consumer wearables mostly due to their wide availability. In addition, they are now powerful enough to penetrate through the skin and into tissue, while also being small enough to fit into a mobile wearable device.

For example, smartwatches and wristbands today use high-intensity green LEDs to detect changes in blood volume, the measurement of which enables the monitoring of vital signs like heart rate and respiration rate. With each heartbeat, capillaries expand and contract as blood volume changes. When blood volume increases, green light absorption by hemoglobin reaches its peak, then diminishes between beats. This change in light absorption is detected by a photodetector. Interpreting this data to provide useful insights about biomarkers is a mature, well-established procedure and has become a standard for wearable monitoring devices.

Mobile LED technology has proven to be an effective light source for detecting certain biomarkers, but it falls short in three critical areas.

While mobile LED technology has proven to be an effective light source for resolving blood components that have strong absorbance signatures in the visible and near-infrared range, it falls short in three critical areas: (1) power efficiency, (2) signal strength, and (3) the spectral range and resolution for targeted biomolecule quantification, particularly in blood, tissue, and skin.

Solutions using a much broader region of the infrared (IR) spectrum can detect these components, but such an IR-based process typically requires a lab-based benchtop system. In addition to the large, bulky equipment, conventional benchtop spectroscopy systems often have other significant drawbacks, including low power efficiency and inadequate signal strength.

Rockley's Sensing Platform

Overcoming the Challenges of LEDs

The Rockley sensing platform adds to the capabilities of the LED-based spectroscopy solutions commonly used in wearable devices today with a module that uses a photonic integrated circuit (PIC) chip to generate numerous discrete, narrow-linewidth laser lines across the spectral range of interest. Leveraging a bevy of patented and proprietary technologies, Rockley successfully addresses all three drawbacks related to the conventional LED approach:

- ***Spectral resolution***
  Rockley's silicon photonic lasers have an extremely narrow linewidth that dramatically increases the spectral resolution to a level similar to that produced by a monochromator.

- ***Integration density***
  Rockley's high-density laser integration technology allows for the inclusion of numerous lasers onto a compact chip, while covering a very broad spectral range.

- ***Spectral power efficiency***
  Rockley's proprietary lasers emit an optimal level of optical power (several milliwatts) concentrated into narrow lines at each individual IR wavelength.

The resulting performance optimization, miniaturization, and range expansion of our sensors enable the transmission of a greater amount of optical power through tissue at only the desired wavelengths, thereby gathering the high signal-to-noise ratio and high-fidelity absorption information needed to resolve a wide range of targeted blood constituent species. Moreover, a design that separates the transmission optics into specific, precise wavelengths reduces the complexity of the downstream detection system.

Silicon-Photonics-Based Spectrophotometer

The LED-based sensing solutions built into current wearables typically use visible and NIR light to measure a range of biomarkers: blood oxygen, heart rate, heart rate variability, respiration rate, and blood pressure. However, there are many biomarkers present in the body (such as in skin, blood, or interstitial fluid) that are not easily detectable with visible or NIR light. Rockley's silicon photonics technology can integrate lasers covering a significantly broader spectral range. This ability to reach deep into the infrared spectrum with high resolution enables the detection of biomarkers undetectable by visible and NIR light.

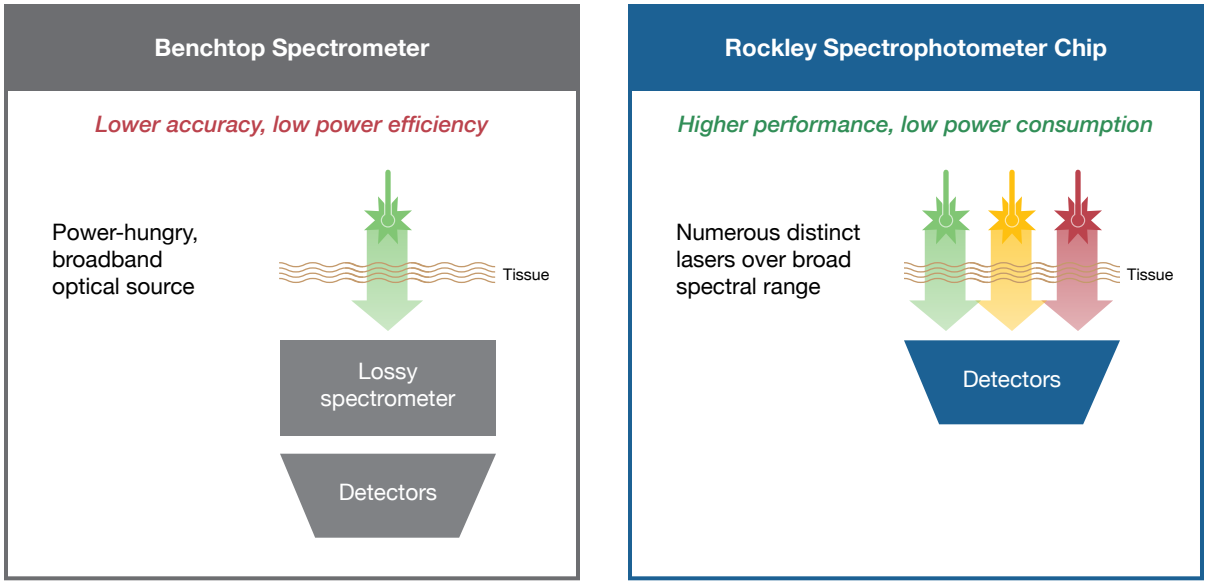

Figure 4: Comparison of benchtop spectrometer to Rockley's spectrophotometer chip

Furthermore, Rockley's integrated narrow-linewidth laser array technology acts like a monochromator on a chip, emitting light in precisely defined laser lines that are many times narrower than an LED's emission spectrum. Leveraging Rockley's proprietary multi-micron waveguide platform, the laser emission wavelength is also far less sensitive to manufacturing variations, giving lasers the potential to be more accurate than LEDs. By adding an array of these proprietary lasers, Rockley's spectrophotometer chip provides approximately one hundred times broader spectral range than a single LED.

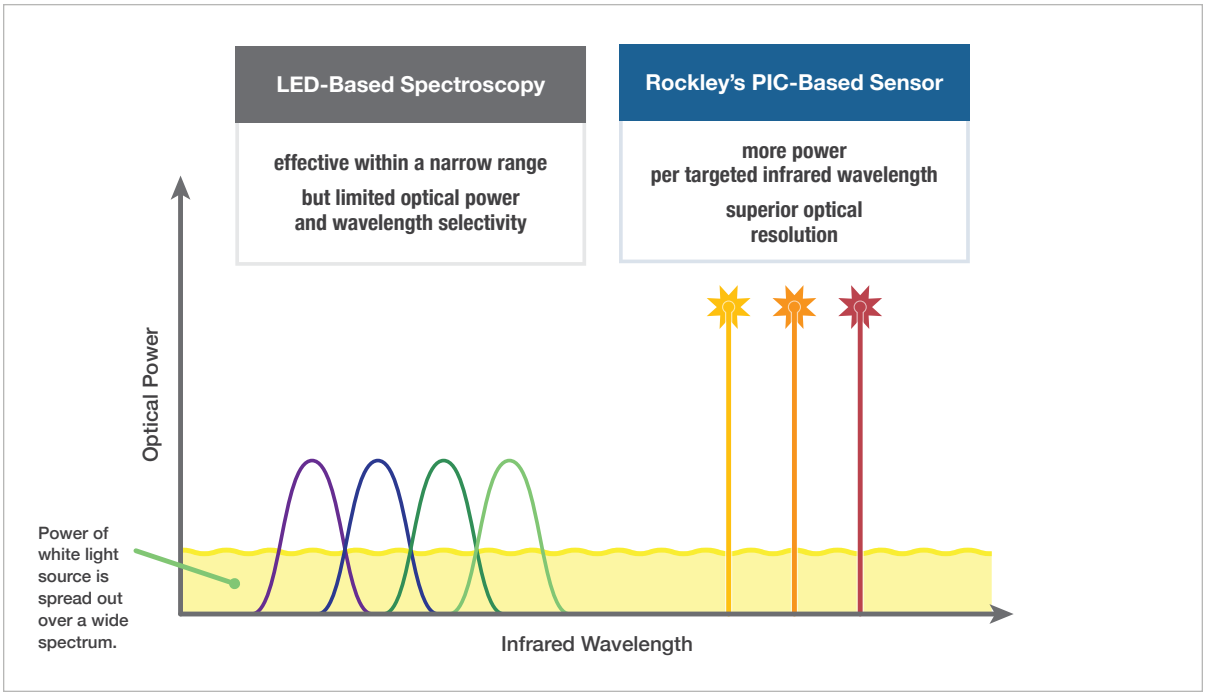

Figure 5: Rockley spectrophotometer chip solution, as compared to conventional LED- and spectrometer-based solutions

Multi-Micron Silicon Photonics Platform

Rockley's integrated laser-based spectrophotometer chip is based on a third-generation silicon photonics process that enables optical systems that are smaller, more robust, more power efficient, and easier to use. Using both larger-than-standard waveguide size and proprietary laser integration technology, the Rockley platform optimizes photonic performance, adds new functionality, and enables high-yield manufacturability.

Rockley's custom multi-micron-waveguide photonics-optimized platform[1] has multiple competitive advantages for spectroscopy applications in terms of both performance and manufacturability. Here are some of the advantages provided by the Rockley platform:

Rockley's spectrophotometer chip enables optical systems that are smaller, more robust, more power efficient, and easier to use.

1 A. J. Zilkie et al., "Multi-Micron Silicon Photonics Platform for Highly Manufacturable and Versatile Photonic Integrated Circuits," in IEEE Journal of Selected Topics in Quantum Electronics, 25 (5), pp. 1-13 (2019)

- Reduced III-V-to-PIC coupling losses
- Significantly lower waveguide losses
- Higher waveguide power handling
- Polarization independence
- Ubiquitous integration of III-V actives in their native known-good-die form
- Ultra-broad-band performance
- Lower sensitivity to manufacturing variations of gratings and filters needed for lasers

By providing these key improvements, the Rockley platform allows the manufacturing of compact circuitry with high integration densities and the broad-spectrum optical I/O needed for biomarker detection.

Delivering Actionable Insights

As smart wearables (watches, wristbands, apparel, etc.) grow in popularity, they are increasingly becoming an important access point for providing health-related information to the end-user. However, to provide insights that are timely, accurate, and relevant, these devices must go beyond simple data collection and pass-through reporting. They must communicate news that *means something* to the wearer — i.e., that conveys actionable intelligence that helps consumers make decisions about their health and welfare.

Smart wearables should provide insights that help consumers make decisions about their health and well-being.

While existing sensors provide insights into several key health-related issues, Rockley's new sensing platform provides a deeper level of helpful information about a wider range of biomarkers. The following table outlines the detection capabilities of existing LED-based sensors and Rockley's photonics-based solution and their connection to various health conditions:

		Cardiovascular Disease	Diabetes	Physical Activitiy	Respiratory Illness
Infrared	Glucose	✓	✓	✓	✓
	Lactate	✓		✓	✓
	Core Body Temp.	✓	✓	✓	✓
	Hydration	✓	✓	✓	✓
	Alcohol	✓	✓		
Visible / NIR	Oxygen (SpO2)	✓			✓
	Respiration Rate	✓			✓
	Heart Rate / HRV	✓	✓	✓	✓
	Blood Pressure	✓	✓	✓	✓
Affected U.S. Population		**18M**	**34M**	**37M**	**28M**

Table 2: Multi-parameter monitoring has the potential to address various disorders

On the Wrist and In the Cloud

By combining its laser-based spectrophotometer capabilities with on-device analytics, the Rockley sensing platform is a self-contained solution for smart wearables to measure and analyze key biomarkers. In addition, Rockley's cloud platform augments these stand-alone capabilities with predictive analytics based on biomarker trends.

Leveraging recent advances in machine learning and AI, the Rockley cloud platform analyzes large data sets gathered across several key dimensions (number of subjects, population samples, time frames, time duration, clinical annotations, etc.). With a deeper understanding of the relationship between spectral data and individual biomarkers,

Rockley's platform improves the ability of wearables to monitor health conditions and support varying use cases and applications.

Figure 6: Rockley's stand-alone wristband, augmented by app and cloud analytics

When combined with the application of existing science related to optical biomolecule detection, these newly gained insights will allow Rockley to explore more effective ways to harness measurements of critical biomarkers in fields such as cardiology, nephrology, oncology, and more. Through an integrated analysis of both traditional biomarkers and targeted biomarkers, Rockley's advanced analytical toolkit has the potential to enhance or create new physiological and behavioral measures to identify, influence, or even predict health-related outcomes.

Conclusion

As a pioneer in silicon photonics, Rockley Photonics has developed numerous game-changing technologies that enable a wide variety of applications across multiple industries. Among these applications, biomarker monitoring is particularly well suited to Rockley's unique platform. By combining our PIC technology with our in-house spectrophotometer, data analysis, and machine learning expertise, Rockley is developing a highly accurate, highly manufacturable, and highly cost-effective full-stack platform for monitoring health and wellness biomarkers in the consumer wearable and medical technology markets.

All the capabilities of the full-stack platform are integrated into a single, compact module that delivers non-invasive, real-time monitoring of a broad range of physiological measurements and health and wellness parameters, including core body temperature, body hydration, lactate, ethanol, urea, glucose, and more. (See Figure 7.)

The Rockley sensing platform takes mobile biomarker monitoring to a whole new level, and we are not resting on our laurels. By expanding our data science capabilities internally and externally with partners, we will extend the functionality of the sensing platform beyond the detection of primary physiological signals to a deeper understanding of the complex interplay between biomarker signals. This enhanced analysis of accessible biomarkers has the potential to help predict and provide better insights to disease progression and management.

About Rockley Photonics

A global leader in silicon photonics, Rockley is developing a comprehensive range of photonic integrated circuits and associated modules, sensors, and full-stack solutions. From next-generation sensing platforms specifically designed for mobile health monitoring and machine vision to high-speed, high-volume solutions for data communications, Rockley is laying the foundation for a new generation of applications across multiple industries. Rockley believes that photonics will eventually become as pervasive as microelectronics, and it has developed a platform with the power and flexibility needed to address both mass markets and a wide variety of vertical applications.

Formed in 2013 by Dr. Andrew Rickman (who previously founded the first commercial silicon photonics company, Bookham Technology), Rockley is uniquely positioned to support hyper-scale manufacturing and address a multitude of high-volume markets. Rockley has partnered with numerous Tier-1 customers across a diverse range of industries to deliver the complex optical systems required to bring transformational products to market.