



Overcoming Wearable Market Limitations Through Bioactive Nitric Oxide Monitoring

Published: October 2, 2024





Sports scientists are continuously searching for new, data-driven ways to gain performance advantages in sport and fitness. At the top, a mere 1% difference in speed, agility or strength marks the difference between a win and a loss. Illustratively profound, this could be clenching an Olympic gold medal, or settling with silver, separated only by a significant tenth of a second (or less). Rightfully so, the pursuit to improve the efficiency and effectiveness of training and recovery continues, often led by new ways to gain physiological insight. Sometimes, millions of dollars are riding on it.

The athletic market is attractive, thirsty for obtaining a novel edge over competitors, with high opportunity for adoption of new measurements and technologies. On the opposite end of the fitness spectrum, the average, health-conscious adult makes up a large proportion of the US population - much larger than paid athletes. Informational goals are differentiated: athletes require data that defines the potential of a career, where exercise and wellness enthusiasts would like to understand where their body's baseline lies across the fitness continuum.

For the health-conscious majority, understanding how to lay a pathway toward improved wellness and general functional performance is most important. This could be taking vitals and constructing an exercise plan to improve blood pressure, resting heart rate, and weight. To get there, it is common to use steps, miles walked or run, minutes cycled, or time in a given heart rate zone. These are obtainable and task-oriented goals to guide people to an often arbitrary objective of "better." But for the general physio-info consumer, what actually and understandably indicates *better*?

It may sound counterintuitive, but its more sensible to deliver simplified data, or less overall. This does not necessarily mean less *collected* data, but less information being delivered to avoid bombarding the user and turning them off altogether. Simplifying information into neatly packaged and actionable notifications may mean the difference between getting off the couch and taking off the device.

Apple's gamified rings and Whoop's AI coach are a solid and market-proven attempt at providing a solution to both the sedentary and enthusiast masses. But the data going into and being provided by these platforms isn't exactly novel, at least not anymore. There is a lot of replication between device manufacturers using the same LED-based technologies to re-package already well-understood information into niche or new biometrics. Examples include stress or strain scores, and sleep. In reality, the insights are typically an amalgam of heart rate, variability in heart rate, motion, skin temperature, respiratory rate, and sometimes blood oxygen saturation.



Sports bioinformatics expert and Chief Physiologist [Evan Peikon](#) collecting data using a [NNOXX One](#) device while running.

This repackaging has left a void. From a performance perspective, the elite and amateurs have spoken, and spoken somewhat loudly. They want information that can be collected by one device, and ideally delivered to one platform. They want it to not interfere with what they are doing, and they would prefer it to be non-invasive, like a smartwatch or band. The consumers do not want it to look like they are wearing anything prescribed by a doctor. But technology dreams do not always come true quickly. The pursuit to deliver glucose and lactate monitors that can satisfy the needs of professional triathletes and cyclists in a way that replaces 1500 ear lobe sticks a season is further in the distance than most people realize. Why? Measuring stuff through the skin (and deeper) is just hard, and doing it accurately is even more difficult.



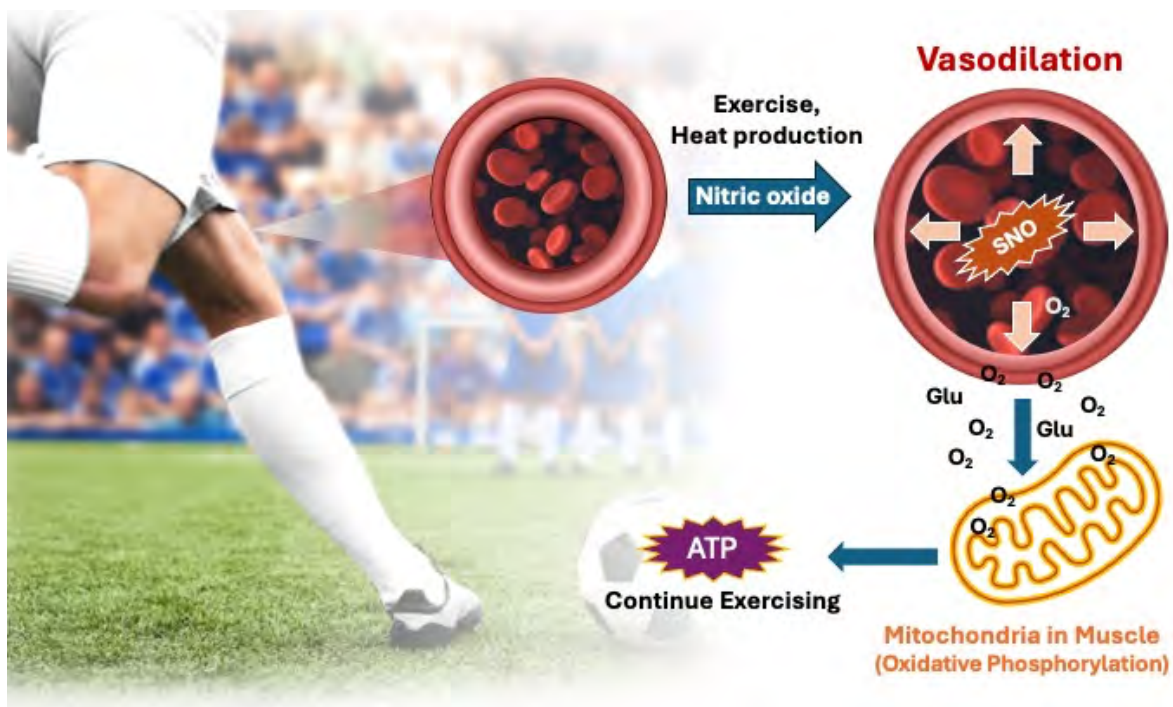
The Physiological Advantage That Breaks Market Barriers

There are two major hurdles in the wearable technology race:

1. Provide truly new insights, and,
2. Do it in a way that satisfies the needs of the people using the information.

Interestingly, hematological and genetic research in the area of nitric oxide physiology has come to a complimentary head with the creation of a monitoring device by [NNOXX Inc.](#) There are several reasons NNOXX could provide a solution to both unmet needs.

It's well understood by most that regular exercise is beneficial for [cardiovascular fitness](#) and health, protecting the heart and reducing the risk of cardiovascular disease, improving contractility, ejection fraction and vascular compliance. Hematological adaptations also occur, such as greater blood plasma volume and red blood cell / hemoglobin upregulation to carry more oxygen.



Exercise stimulates bioactive nitric oxide (SNO) to be produced and released from red blood vessels in small blood vessels in working muscle. SNO causes the small vessels to dilate, allowing more nutrients and oxygen to be delivered when demand is high. This allows metabolic pathways such as the TCA cycle and oxidative phosphorylation to synthesize a greater amount of ATP so the amount of work (exercise) demanded can be accomplished.

Acutely, one impact of exercise on the vascular system is the stimulation of [nitric oxide](#) (NO) production, a primary regulator of blood pressure and blood flow. Nitric oxide, alongside other important vasodilators, shunts blood to areas where oxygen demand has



increased. It is also locally produced, helping to direct blood to the periphery and [skin](#) for cooling when core temperature starts to rise and the body starts producing and dissipating heat in response to [exercise](#). Over time with training, a faster and greater nitric oxide response results.

So how is the NNOXX device able to address some of the current problems facing wearable device developers?

1. The NNOXX platform provides information based on two important and relatively new biometrics: muscle oxygen saturation (SmO_2) and [bioactive nitric oxide](#) (S-nitrosohemoglobin, or SNO-Hb). SNO-Hb is a specific nitric oxide derivative that directs blood flow at a microvascular level based on changes in oxygen tension within red blood cells.
 - A change in muscle oxygen saturation tells us the fraction of oxygen that is being used by the working muscle to perform, and how quickly the body can reach a steady state by upping flow and delivery of oxygen where its needed (e.g. getting supply to meet demand).
 - The production of bioactive nitric oxide (SNO-Hb) will tell you how quickly and intensely your body is responding to the new oxygen and nutrient demand. Nitric oxide stimulates an increase in blood flow to the specific area that is needed.
2. The biomarkers provide valuable, regional insights into actual muscle performance. This can be transformed into understanding recovery, readiness before the next workout, inferring real-time uptake of oxygen and nutrients, and how well these systems are adapting to training.
3. Over time, if training and conditioning are effective, trends in overall nitric oxide response and production should increase. Changes and stabilization of muscle oxygenation during steady state should be faster.

What does all of this mean? NNOXX can provide a tissue-level perspective of how well the body is functioning during an exercise session, if the body is [ready](#) for the next session, and if the exercises being chosen are appropriate and effective based on an immediate individual assessment.

One major benefit of the device measurements and software platform is that it can be used during a large number of exercise conditions. Running, cycling, resistance exercise, rowing, climbing - all of these modalities stimulate a need for increased oxygen and nutritive fuel and therefore an increased need for regional, muscular blood flow.



Opportunities in the Clinical Landscape

Outside of sport, much can be reaped from monitoring nitric oxide for health. Metabolic diseases, Alzheimer's dementia and injury rehabilitation all benefit immensely from physical activity, which is why it is a first-line choice in disease prevention and sometimes even prescribed therapy.

It has been shown that [prescribing exercise](#) improves patient compliance beyond simply recommending exercise and changes to lifestyle habits. This has propelled the development of global strategies like the [Exercise is Medicine Initiative](#) to promote education on the importance in integrating exercise into clinical practice guidance.



From the perspective of how and where the NNOXX device monitors and delivers exercise-related data, several conditions can benefit two-fold. Patients with muscular degeneration or atrophy, oxygenation or similar musculoskeletal condition not only benefit from regular exercise, which strengthens muscles and improves neural control, but can now gain insight into how muscles are improving locally, instead of inferring with whole body or indirect measurements, or through expensive imaging like an MRI.

Those with vascular conditions, such as peripheral artery disease (PAD), also benefit from physical activity, and it is often prescribed both prior to and after intervention through cardiac rehabilitation. Exercise stimulates new blood vessel formation (angiogenesis), improving blood flow to tissues and regions of the body impacted by diminished flow. The implementation of the NNOXX platform could provide insights to clinicians related to vascular adaptations to the exercise being conducted through muscle oxygenation and nitric oxide monitoring.

These applications are pivotal, translating to more populations in need on a global scale, and like athletics, also have millions of dollars at stake. From a developmental



perspective, wearable devices are attempting to penetrate these markets but come up against challenging regulatory barriers for therapeutic use as an approved medical device. Performance standards, the need for alarms or continuous data reporting and integration with hospital-based servers are difficult to overcome depending on the device application and indications.

But barriers are crumbling quickly. The Monarch external Trigeminal Nerve Stimulation (eTNS) System received a medical device clearance from FDA in 2020 for use in treating ADHD. iRhythm Technologies developed the ZEUS system, software connecting their EKG patches to the Zio smartwatch, receiving clearance in 2022. OxiWear, a small ear-based wearable that measures blood oxygen saturation, received FDA [clearance](#) as a Class II oximeter in August 2024. Others monitor fall risk, some offer a whole remote patient monitoring solution (Current Health) for practitioners.

So far, there has been little to no guidance for practitioners on how to implement exercise programs designed as therapeutic tools based on regional, tissue-level monitoring. There are also no FDA cleared wearable, smart devices servicing this need. [Cardiac rehabilitation](#), physical therapy, and preventative at-home prescriptions can benefit tremendously. As the efficacy of the nitric oxide metric is proven through condition-focused clinical trials, NNOXX could be the first to potentially change exercise-focused care paradigms and improve the quality of life for millions.

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