electroluminescent textiles. The transmissivity of the gold textile electrodes and the luminance of the final electroluminescent devices can be tuned by varying the repeating loop structure of the knit pattern and also by stretching the knit textile substrate. Such dynamic, post-fabrication control over optical characteristics is difficult to achieve using traditional micro- and nano-fabrication approaches.

Commonly available, mass-produced textiles and premade garments can, in theory, be transformed into a plethora of dynamically responsive human-machine interfaces upon being coated with films of electronic materials, such as metals and conducting polymers. The definitive hurdle is that premade garments and fabrics have densely textured, three-dimensional surfaces that display roughness over a large range of length scales, from microns to millimeters. Tremendous variation in the surface morphology of metal- or polymer-coated fibers and fabrics can be observed with different coating or processing conditions.[5] In turn, the morphology of the metal or polymer layer determines device performance and, most importantly, ruggedness and lifetime. To date, reactive coating methods have been the most successful at creating electronic coatings directly on the surface of any premade garment or textile;[6] however, further processing innovations that increase coating speed and reduce toxic or solvent waste are always welcome. Ideally, new coating methods need to work without the need for specialized surface pretreatments, detergents, or fixing agents while also yielding uniform and conformal coatings that are notably wash-stable and withstand mechanically demanding textile manufacturing routines.

1. Meng, K., Zhao, S., Zhou, Y., Wu, Y., Zhang, S., He, Q., Wang, X., Zhou, Z., Fan, W., Tan, X., and Yang, J. (2020). A Wireless Textile-Based Sensor System for Self-Powered Personalized Health Care (Matter).

2. Kiaghadi, A., Homayounfar, S.Z., Gummeson, J., Andrew, T.L., and Ganesan, D. (2019). Phyjama: Physiological Sensing via Fiber-Enhanced Pyjamas. Proc. ACM Interact. Mob. Wearable Ubiquitous Technol. *3*, 89.

3. Homayounfar, S.Z., and Andrew, T.L. (2020). Wearable Sensors for Monitoring Human Motion: A Review on Mechanisms, Materials, and Challenges. SLAS Technol. *25*, 9–24.

4. Wu, Y., Mechael, S.S., Lerma, C., Carmichael, R.S., and Carmichael, T.B. (2020). Stretchable Ultrasheer Fabrics as Semitransparent Electrodes for Wearable Light-Emitting e-Textiles with Changeable Display Patterns (Matter).

5. Allison, L., Hoxie, S., and Andrew, T.L. (2017). Towards seamlessly-integrated textile electronics: methods to coat fabrics and fibers with conducting polymers for electronic applications. Chem. Commun. (Camb.) *53*, 7182–7193.

6. Andrew, T.L., Zhang, L., Cheng, N., Baima, M., Kim, J.J., Allison, L., and Hoxie, S. (2018). Melding Vapor-Phase Organic Chemistry and Textile Manufacturing To Produce Wearable Electronics. Acc. Chem. Res. *51*, 850–859.

Preview

Don't Sweat It: The Quest for Wearable Stress Sensors

Amay J. Bandodkar,[1,2] Roozbeh Ghaffari,[1,3] and John A. Rogers[1,2,3,*]

A nervous sweat may seem like an inconvenience, but your body could be releasing important signals. Herein, Gao and colleagues develop a wearable sensor with integrated microfluidics, immunoassays, and electronics for tracking cortisol in sweat—as a biomarker of stress.

Stress is an intense, natural, and universal reaction that guides both cognitive and physical processes with beneficial short-term consequences attributed to "fight-or-flight" responses and harmful long-term consequences to health. Recent studies show that chronic stress accumulated over time can lead to debilitating outcomes such as cancer, coronary heart disease, accidental injuries, lung disease, liver disease and suicide.[1] The World Health Organization estimates that stress-related disorders are one of the leading causes of disability globally and classifies stress as the "health epidemic of the 21st century".[2] According to the American Psychological Association, over 80% of workers in the United States suffer from work-related stress, costing businesses a staggering $300 billion annually.[3]

Although the underlying causes can vary widely, the frequency and intensity of stressful events are rising sharply, due in part to the increasing influence of social media on daily life.[4] Extensive research suggests that such stress can exacerbate or even cause serious medical conditions beyond those described

[1]Querrey Simpson Institute for Bioelectronics, Northwestern University, Evanston, IL 60208, USA

[2]Department of Materials Science and Engineering, McCormick School of Engineering, Northwestern University, Evanston, IL 60208, USA

[3]Department of Biomedical Engineering, McCormick School of Engineering, Northwestern University, Evanston, IL 60208, USA

*Correspondence: jrogers@northwestern.edu

https://doi.org/10.1016/j.matt.2020.03.004

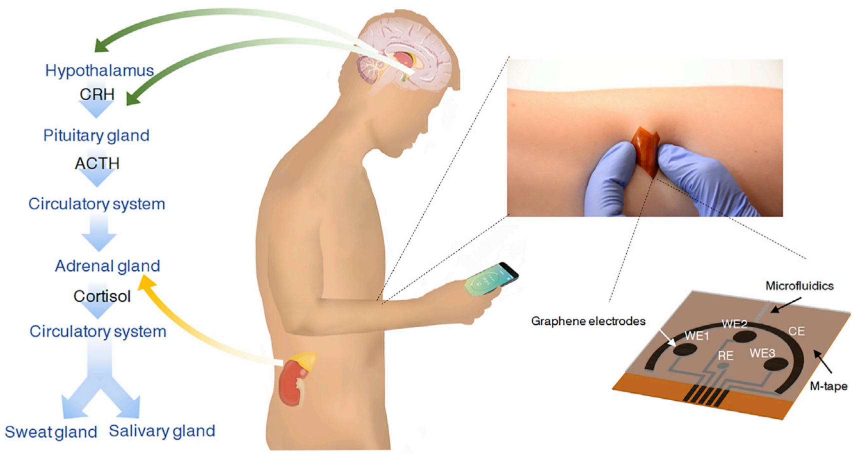

Figure 1. Wearable Sensor with Integrated Microfluidics, Immunoassays, and Electronics for Tracking Cortisol Levels in Sweat as a Biomarker of Stress

above, including depressive and post-traumatic disorders, Alzheimer's and Parkinson's diseases, inflammatory conditions, and diabetes.[5] The clinical standard for assessing stress relies on questionnaires and surveys. The subjective nature of these techniques lack both quantitative rigor and temporal resolution necessary to aid in the development of precise medical interventions. Methodologies are, however, beginning to shift to techniques that exploit biochemical markers that are known to quantitatively relate to stress levels. A team of researchers at Caltech, led by Prof. Wei Gao, report an important contribution to this area of research in the form of a monitoring system that accurately captures instances of stress based on evaluation of key biomarker concentrations in sweat.[6] The sensor platform leverages a collection of advances in nanotechnology, sweat sampling, immunosensing, and flexible, wireless electronics.

At physiological levels, stress activates the sympathetic nervous system, the hypothalamic pituitary adrenal axis, and the immune system, collectively resulting in elevated levels of cortisol—a hormone that controls the body's "fight-or-flight" reaction.[7] As a result, the concentration of cortisol yields a diagnostic correlate for stress.[8] The conventional method for quantifying cortisol levels requires collection samples of blood using standard clinical techniques, and then analysis for cortisol using benchtop instrumentation. The result yields accurate measurements of cortisol levels but only at discrete time points, performed by trained personnel in specialized facilities. Practical limitations associated with these procedures prevent rapid medical interventions, thereby increasing the potential for stress related health complications. Emerging methods that rely on chemical analysis of hair and saliva provide non-invasive alternatives, but they retain requirements for manual collection and measurement. The wearable device reported by the Caltech team promises to enable continuous, real-time assessments of cortisol levels in a non-invasive, automated fashion through analysis of small volumes of sweat. The result could fundamentally change the way that we monitor stress levels on a daily basis.

Sweat possesses several important attributes that are attractive for this type of non-invasive, autonomous physiological monitoring. For example, the human body produces a considerable amount of this relatively underexplored class of biofluid.[9] More importantly, sweat contains a rich mixture of important biochemical markers,[10] including cortisol,[11] that can yield insights into health status. Nevertheless, most prior studies of sweat focus mainly on handful of electrolytes, metabolites, and minerals.

The work of Torrente-Rodríguez et al.[6] represents a significant contribution to this growing field in the form of graphene-based, wireless, wearable devices capable of measuring cortisol levels in sweat, as it emerges from the surface of the skin (Figure 1). Systematic benchtop and human subject studies demonstrate the key features and capabilities of this system as well as strong correlations between cortisol levels in sweat, blood serum, and saliva samples. The results have direct implications for the continuous, accurate monitoring of stress levels, without the need for surveys or specialized equipment.

The design and fabrication of these devices build on the authors' expertise in graphene-based sweat sensors.[12] The process begins with synthesis of graphene on a flexible film of polyimide via directed laser ablation. A layer of a conducting polymer–poly(pyrrole propionic acid) – grown on top of the graphene exposes surface chemical groups that promote attachment of an anti-cortisol monoclonal antibody designed to selectively bind cortisol via the (1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) and N-hydroxysulfosuccinimide (Sulfo-NHS) cross-linker. Proof of concept testing uses manually collected sweat diluted with buffer containing a fixed amount of enzyme-labeled cortisol (horseradish-peroxidase-labeled cortisol). Introducing such a sample onto the sensor leads to competitive binding between cortisol in the sweat and the enzyme-labeled cortisol. Adding hydroquinone—a molecule that reacts with enzymes on the sensor surface—produces hydrogen peroxide. An integrated wireless electronic system that applies a negative potential (−0.2 V) to the sensor leads to electrochemical reduction of the hydrogen peroxide and production of an associated current that serves as a signal with magnitude proportional to the concentration of cortisol.

An integrated version of this sensor exploits microfluidic handling capabilities to allow the binding step to be performed directly while the device is on the skin. With this platform, sweat cortisol levels measured in human subjects during and post-exercise show strong correlations to corresponding concentrations in blood and saliva. These levels also exhibit expected variations associated with daily circadian rhythms, intense physical activity, and stress induced by placing a hand in cold water, where each study demonstrates different aspects of applicability in practical scenarios.

Beyond the monitoring of cortisol, these systems may have broader utility in the application of sweat in biochemical monitoring of the physiological status. Specifically, the combination of graphene electrodes, immunosensing techniques, flexible electronics, and skin-compatible microfluidics have great potential in non-invasive health tracking, ranging from mental health management, military training, and human performance to cancer treatment and cardiac therapy. Combining these biochemical sensing capabilities with co-integrated systems for measuring biophysical signatures such as body temperature, heart rate, respiration rate, blood pressure, and others suggest a promising future for personalized, data-enabled health care and preventative medicine.

1. Yao, B.C., Meng, L.B., Hao, M.L., Zhang, Y.M., Gong, T., and Guo, Z.G. (2019). Chronic stress: a critical risk factor for atherosclerosis. J. Int. Med. Res. *47*, 1429–1440.

2. Kalia, M. (2002). Assessing the economic impact of stress--the modern day hidden epidemic. Metabolism. *51*, 49–53.

3. American Psychological Association (2019). 42 Worrying Workplace Stress Statistics. https://www.stress.org/42-worrying-workplace-stress-statistics.

4. Aalbers, G., McNally, R.J., Heeren, A., de Wit, S., and Fried, E.I. (2019). Social media and depression symptoms: A network perspective. J. Exp. Psychol. Gen. *148*, 1454–1462.

5. Deak, T., Quinn, M., Cidlowski, J.A., Victoria, N.C., Murphy, A.Z., and Sheridan, J.F. (2015). Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress *18*, 367–380.

6. Torrente-Rodríguez, R.M., Tu, J., Yang, Y., Min, J., Wang, M., Song, Y., Yu, Y., Xu, C., Ye, C., IsHak, W.W., et al. (2020). Investigation of Cortisol Dynamics in Human Sweat Using a Graphene-Based Wireless mHealth System. Matter *2*, this issue, 921–937.

7. Kraemer, W.J., French, D.N., Spiering, B.A., Volek, J.S., Sharman, M.J., Ratamess, N.A., Judelson, D.A., Silvestre, R., Watson, G., Gómez, A., and Maresh, C.M. (2005). Cortitrol supplementation reduces serum cortisol responses to physical stress. Metabolism *54*, 657–668.

8. Herane Vives, A., De Angel, V., Papadopoulos, A., Strawbridge, R., Wise, T., Young, A.H., Arnone, D., and Cleare, A.J. (2015). The relationship between cortisol, stress and psychiatric illness: New insights using hair analysis. J. Psychiatr. Res. *70*, 38–49.

9. Taylor, N.A.S., and Machado-Moreira, C.A. (2013). Regional variations in transepidermal water loss, eccrine sweat gland density, sweat secretion rates and electrolyte composition in resting and exercising humans. Extrem. Physiol. Med. *2*, 4.

10. Harvey, C.J., LeBouf, R.F., and Stefaniak, A.B. (2010). Formulation and stability of a novel artificial human sweat under conditions of storage and use. Toxicol. In Vitro *24*, 1790–1796.

11. Russell, E., Koren, G., Rieder, M., and Van Uum, S.H. (2014). The detection of cortisol in human sweat: implications for measurement of cortisol in hair. Ther. Drug Monit. *36*, 30–34.

12. Yang, Y., Song, Y., Bo, X., Min, J., Pak, O.S., Zhu, L., Wang, M., Tu, J., Kogan, A., Zhang, H., et al. (2020). A laser-engraved wearable sensor for sensitive detection of uric acid and tyrosine in sweat. Nat. Biotechnol. *38*, 217–224.