Comment on Wearable lateral flow assays for cortisol monitoring with time-dynamic sweat sampling and sensing by electrochromic timers

ZhiLing Di*
School of Mathematics and Physics, Hebei University of Engineering, Handan 056038, China
Nature Sensors 2026, 1, 85-98. DOI: 10.1038/s44460-025-00005-z

Wearable biosensors for real-time biomarker monitoring represent a frontier in analytical chemistry. In a study published in Nature Sensors, Cho et al. reported a wearable lateral flow platform using paper-based microfluidics and plasmonic gold nanoflowers for noninvasive monitoring of cortisol in human sweat. The device integrates carbachol iontophoresis, electronic timing circuits or BSA-gated microfluidic delay valves for time-dynamic sampling, and electrochromic timers to record collection events, offering a new approach for stress management and circadian rhythm research.

Regarding analytical methods for wearable sensors, a key contribution of this study is identifying the limitations of existing electrochemical sensors in time-dynamic detection,[1,2] and addressing this issue through innovative design. The authors analyzed in the introduction the current state of electrochemical methods, noting they "require electronics for sensing and offer limited capacity for the time-dynamic detection," and proposed two temporal sampling strategies — electronic timing circuits and BSA-gated microfluidic delay valves. This trajectory from problem identification to solution design reflects the systematic and targeted nature of the research.

Regarding timer design, the study used a polyaniline electrochromic timer to record sampling time and incorporated a pretreatment channel to remove reductive interferents in sweat. The authors tested the effect of ascorbic acid on electrode color, demonstrating the timer's responsiveness to potential interferents. Future studies could further strengthen this approach by providing quantitative data on pretreatment efficiency and systematically evaluating interference from other reducing substances in sweat.

In terms of iontophoresis process simulation, the study employed finite element analysis to calculate electric field distribution and sweat generation rate. The skin conductivity parameters were sourced from the study by Peters et al,[3] and the carbachol diffusion coefficient was derived from the report by Muller et al.[4] The simulation results indicated that sufficient sweat could be collected at a distance of 1.5 mm from the stimulation site. Further validation through statistical analysis of the agreement between simulation and experimental data would strengthen the reliability of these findings.

In terms of fluid dynamics simulation, the study used COMSOL Multiphysics to model fluid flow in the paper-based microfluidic channels,[5,6] with an inlet flow rate of 1 μl min^{-1}, which falls within the physiologically relevant sweat rate range of 0.5-1.0 μl min^{-1}. This provides a reasonable flow condition for subsequent experimental validation.

The study employed the Brooks and Corey model to simulate capillary pressure in the BSA-gated microfluidic delay valves,[7] and combined it with the Nernst-Brunner equation to describe the BSA dissolution mechanism.[8] The simulation results showed that after BSA dissolution, the contact angle decreased, allowing fluid to pass through the valve structure. The use of these established models provides a solid theoretical foundation for understanding the valve timing mechanism in paper-based microfluidic systems.

In terms of human trials, the study validated the device's ability to monitor circadian rhythms. The cortisol fluctuation patterns of three participants were consistent with trends observed in salivary cortisol, demonstrating the device's potential for real-world stress monitoring. The authors suggested that cortisol monitoring could aid in managing sleep patterns and stress-related disorders.[9-13] The correlation coefficients between sweat and salivary cortisol (r=0.73) and between sweat and serum cortisol (r=0.73) indicate good agreement with established measurement methods.

In summary, the wearable sweat cortisol sensor developed by Cho et al. represents a significant advancement in the field of noninvasive hormone monitoring, with its time-dynamic sampling and colorimetric detection design demonstrating innovation. The successful correlation with saliva and serum assays validates sweat as a reliable biofluid for cortisol detection, opening new possibilities for stress research and personalized health management. The platform's ability to track circadian variations and stress responses in real time lays a foundation for future applications in sleep monitoring, mental health assessment, and endocrine studies.

AUTHOR INFORMATION

Corresponding Author
*E-mail:2208936483@qq.com.
Notes
The authors declare no competing financial interest.

REFERENCES

1. Parlak, O., Keene, S. T., Marais, A., Curto, V. F. & Salleo, A. Molecularly selective nanoporous membrane-based wearable organic electrochemical device for noninvasive cortisol sensing. Sci. Adv. 4, eaar2904 (2018).
2. Wang, B. et al. Wearable aptamer-field-effect transistor sensing system for noninvasive cortisol monitoring. Sci. Adv. 8, eabk0967 (2022).
3. Peters, M. J., Stinstra, J. G. & Hendriks, M. Estimation of the electrical conductivity of human tissue. Electromagnetics 21, 545–557 (2001).
4. Muller, W., Misgeld, U. & Heinemann, U. Carbachol effects on hippocampal neurons in vitro: dependence on the rate of rise of carbachol tissue concentration. Exp. Brain Res. 72, 287–298 (1988).
5. Chowdhury, I. U., Mahapatra, P. S. & Sen, A. K. Shape evolution of drops on surfaces of different wettability gradients. Chem. Eng. Sci. 229, 116136 (2021).
6. Chowdhury, I. U., Mahapatra, P. S., Sen, A. K., Pattamatta, A. & Tiwari, M. K. Autonomous transport and splitting of a droplet on an open surface. Phys. Rev. Fluids 6, 094003 (2021).
7. Brooks, R. H. & Corey, A. T. Properties of porous media affecting fluid flow. J. Irrig. Drain. Div. 92, 61–88 (1966).
8. Siepmann, J. & Siepmann, F. Mathematical modeling of drug dissolution. Int. J. Pharm. 453, 12–24 (2013).
9. Weber, C. J., Clay, O. M., Lycan, R. E., Anderson, G. K. & Simoska, O. Advances in electrochemical biosensor design for the detection of the stress biomarker cortisol. Anal. Bioanal. Chem. 416, 87–106 (2024).
10. Ok, J., Park, S., Jung, Y. H. & Kim, T. I. Wearable and implantable cortisol-sensing electronics for stress monitoring. Adv. Mater. 36, e2211595 (2024).
11. Kim, S. et al. Soft, skin-interfaced microfluidic systems with integrated immunoassays, fluorometric sensors, and impedance measurement capabilities. Proc. Natl Acad. Sci. USA 117, 27906–27915 (2020).
12. O'Byrne, N. A., Yuen, F., Butt, W. Z. & Liu, P. Y. Sleep and circadian regulation of cortisol: a short review. Curr. Opin. Endocr. Metab. Res. 18, 178–186 (2021).
13. Zee, P. C. & Goldstein, C. A. Treatment of shift work disorder and jet lag. Curr. Treat. Options Neurol. 12, 396–411 (2010). REFERENCES