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Sustainable Point of Care Diagnostics for Human Health and Wellness

18th U.S.-Korea Forum on Nanotechnology: Sensors for Human Cognition, and Sustainability in Semiconductor Manufacturing

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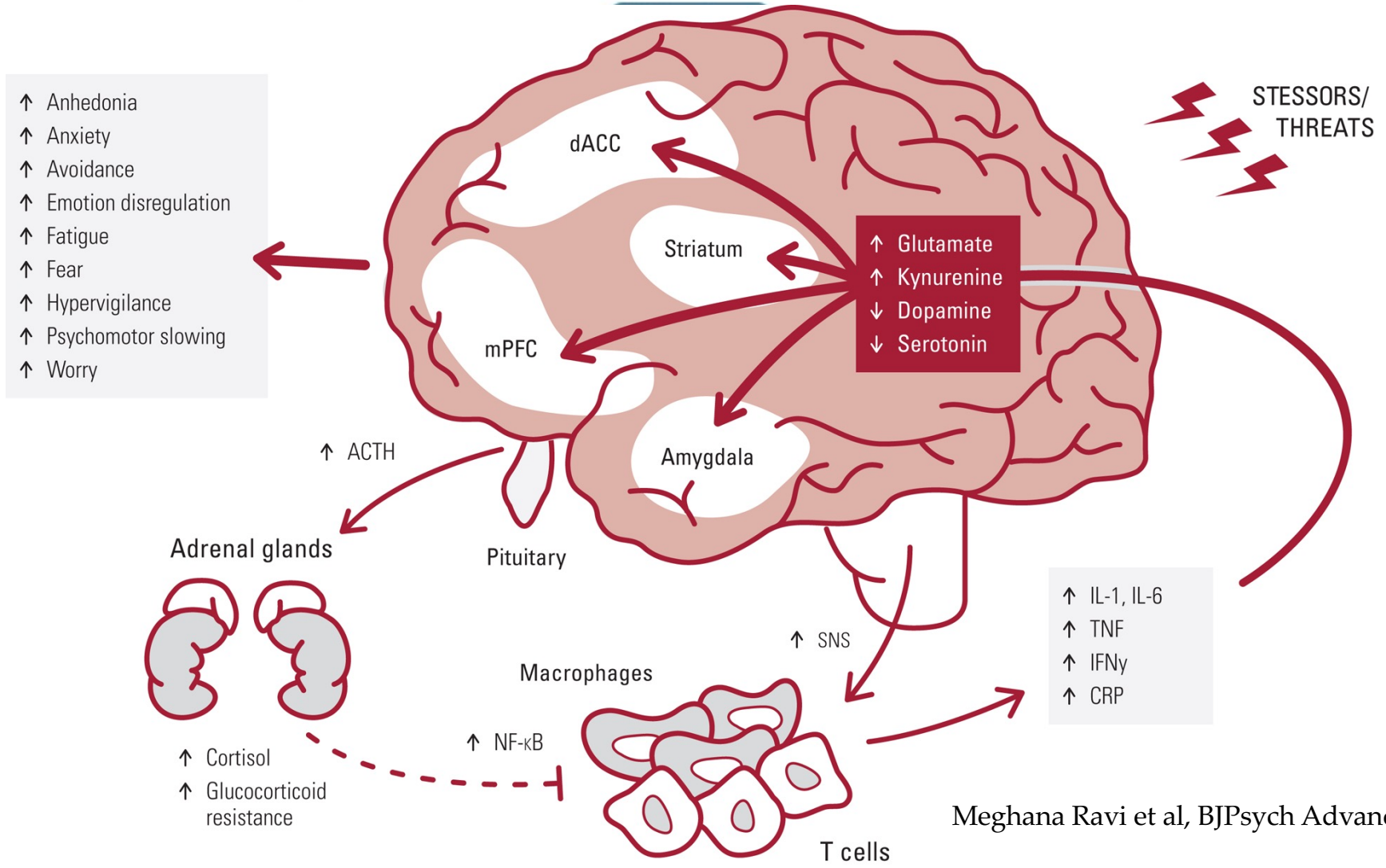
Stress affects Immunity and Cognition

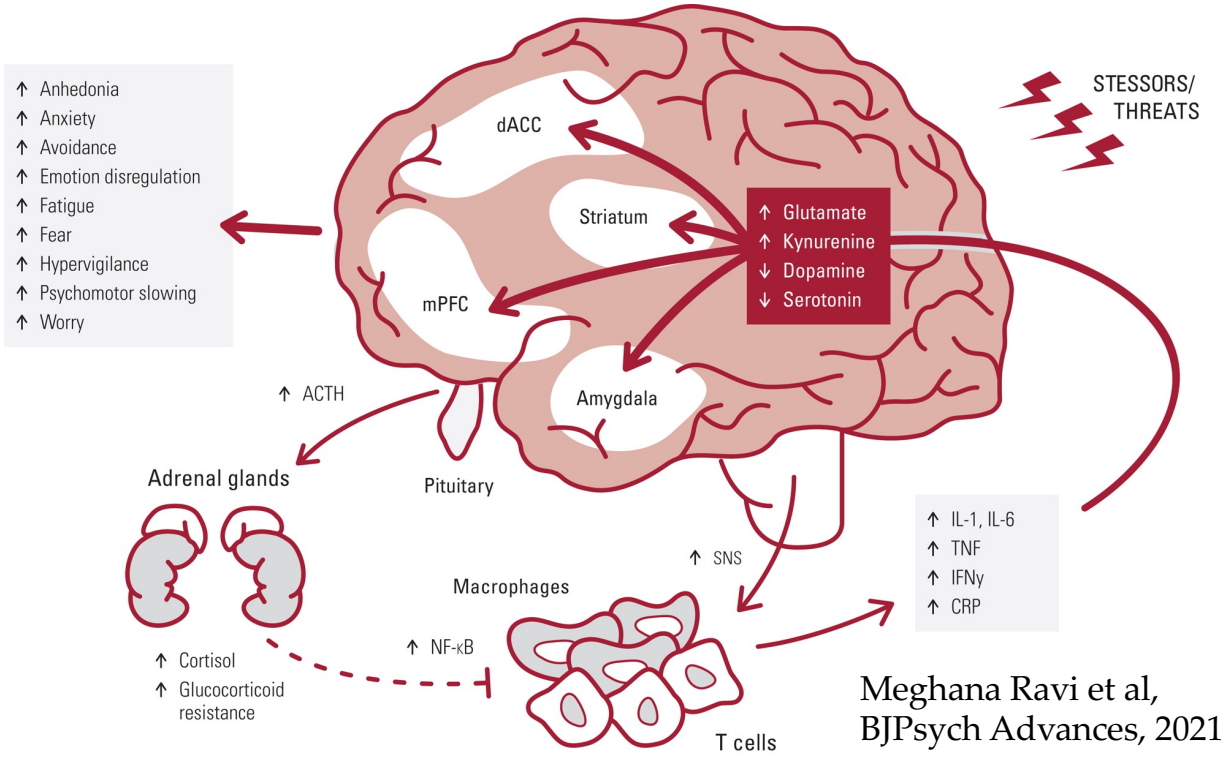
Physical Stressors
Fatigue, Injury, Temperature, Noise etc.

Psychological Stressors
Interpersonal, Life Events, Work etc.



Meghana Ravi et al, BJPsych Advances, 2021

PoC diagnostics for stress, immunity and cognition



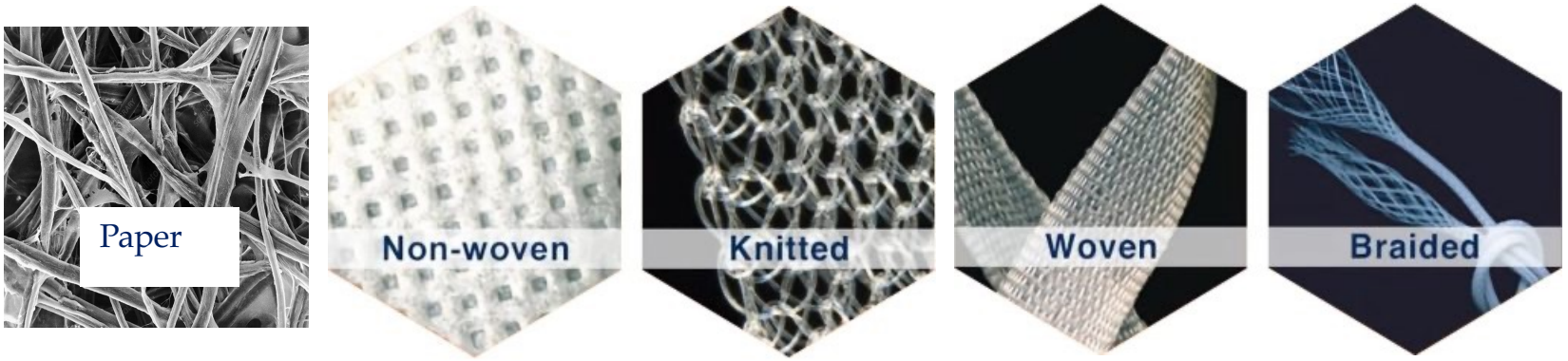
Meghana Ravi et al,
BJPsych Advances, 2021

How do you monitor stress at or near the human?

Can we do this at low cost using sustainable materials and methods?

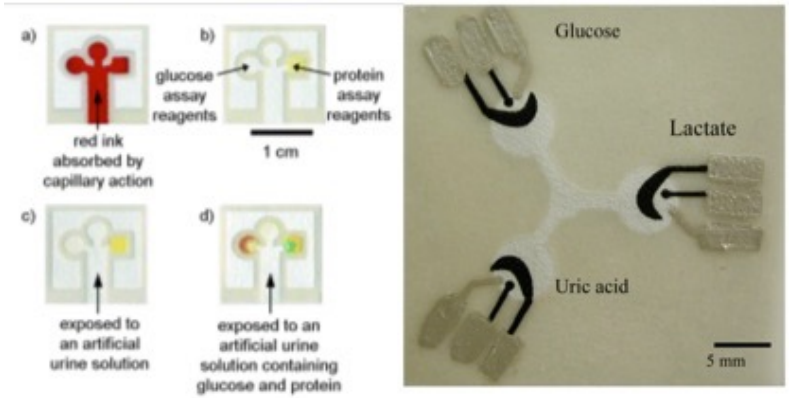
Sustainable Materials for POC Diagnostics

Paper, Thread and Textiles as smart substrate



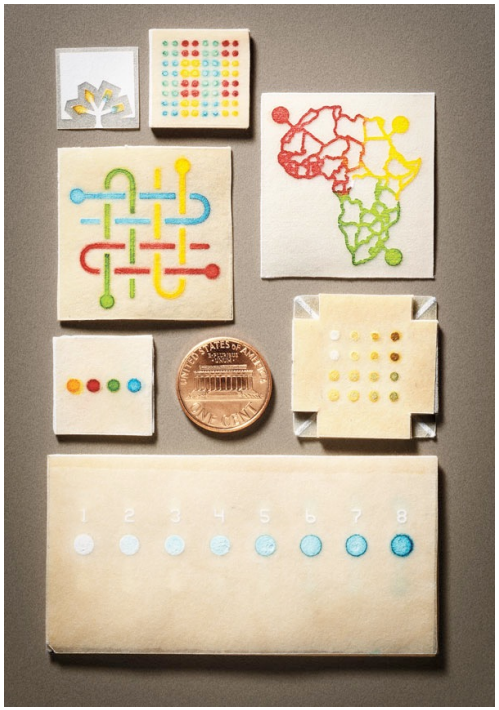
- Naturally biodegradable, environmentally friendly, low cost
- Diversity of materials and processing enables multi-functionality
- Simple processing - Inkjet printing, Dip coating, Roll-to-roll
- Support microfluidic functions to process biological fluids

Paper Analytical Devices and Thread Analytical Devices

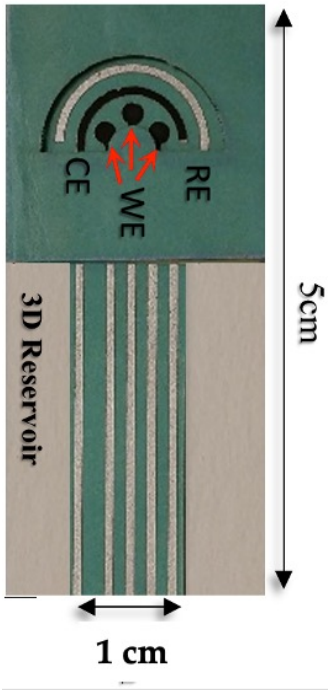


Martinez *et al. 2007 Angew. Chem. Int. Ed*

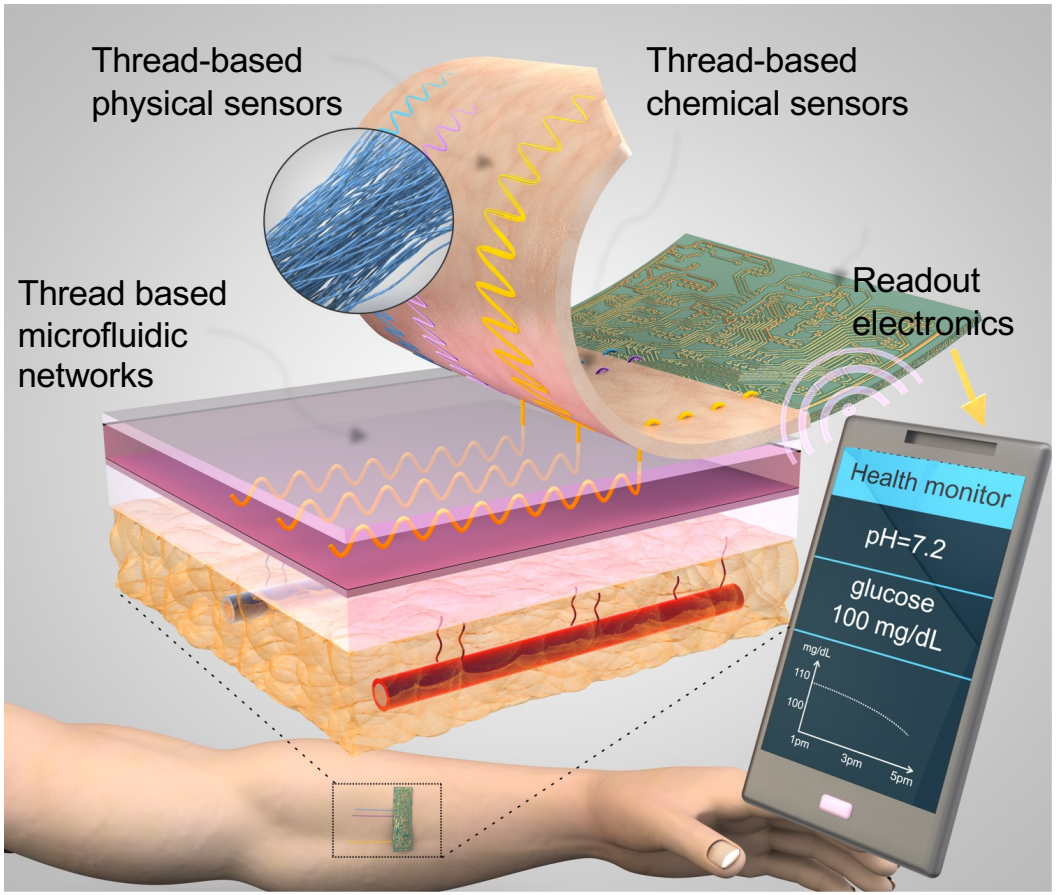
Dungchai *et al. 2009 Anal. Chem*



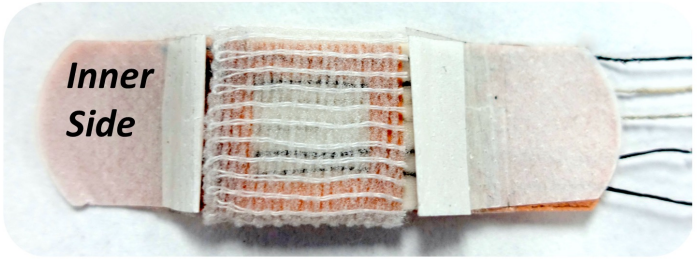
Whitesides Group, Harvard Diagnostics for All, LLC



Sonkusale et al, Analyst 2018



Microsystems and Nanoengineering 2016, npj Flexible Electronics 2020, Analyst 2021, ACS Appl. Mater. Interfaces 2019, Sens. & Act: A Physical 2020, Adv Func Mat 2017



pH
Na+
Lactate
Reference
NH_4^+

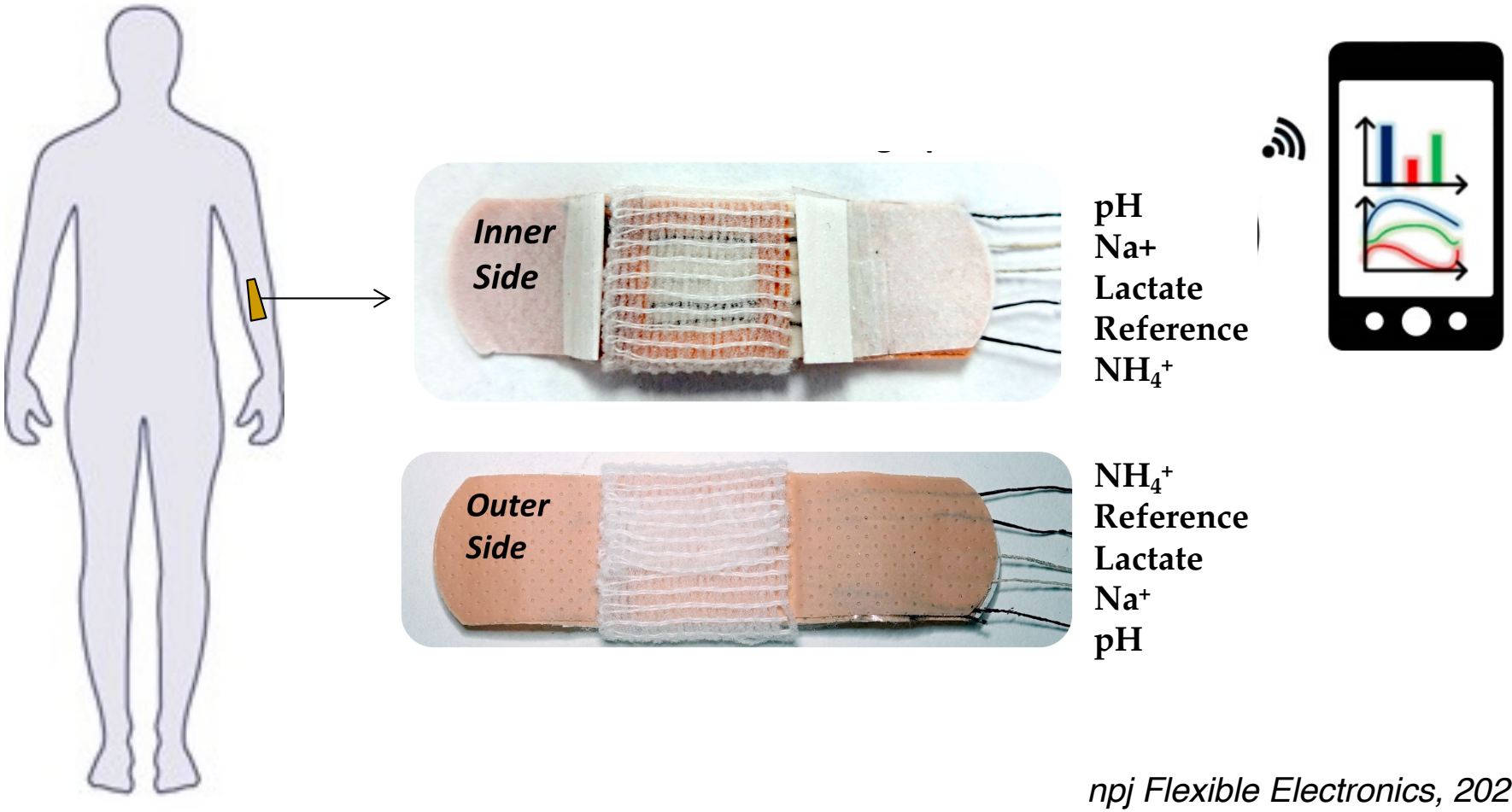
Outline

- Fatigue sensing Thread Analytical Devices (TAD)
- Stress sensing floss for detection of salivary cortisol
- Inflammation monitoring distance based paper analytical device (dPAD)

Wearable Sweat Sensing Patch to Monitor Fatigue

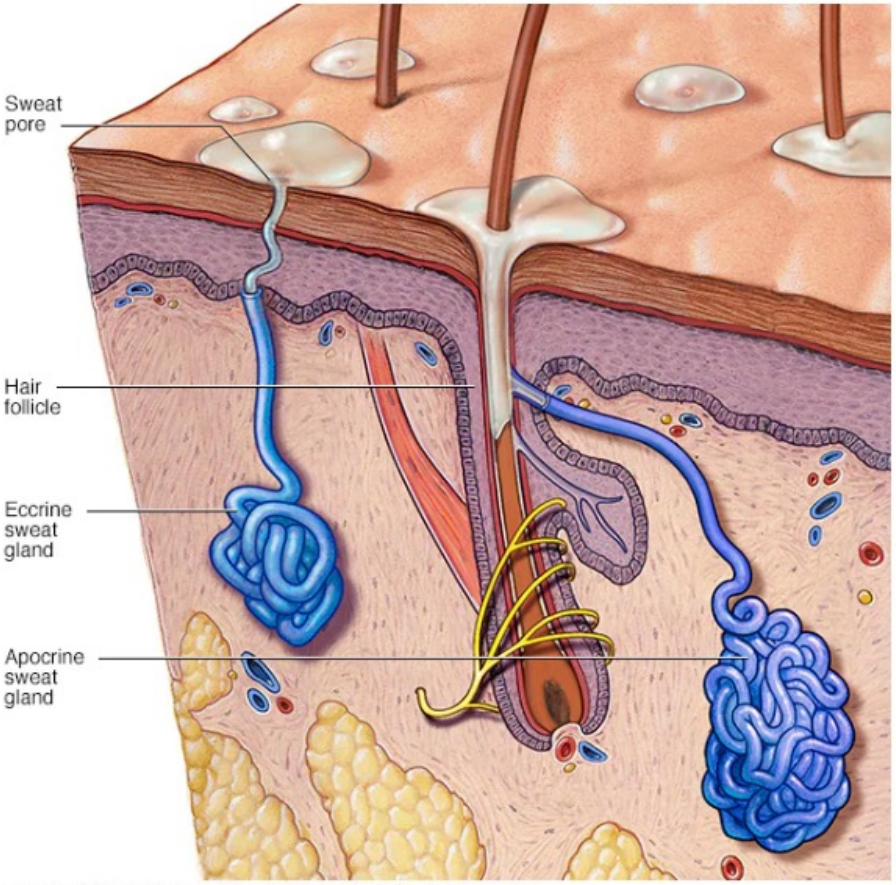
Can we detect fatigue from sweat?

Monitor sweat biomarkers using electrochemical sensing threads



npj Flexible Electronics, 2020

Human sweat contains useful biomarkers



Electrolytes

- Na^+, K^+, Ca^{2+}, NH_4^+, Cl^-, H^+

Metabolites

- Lactate, Glucose, Urea, Uric Acid, Creatinine

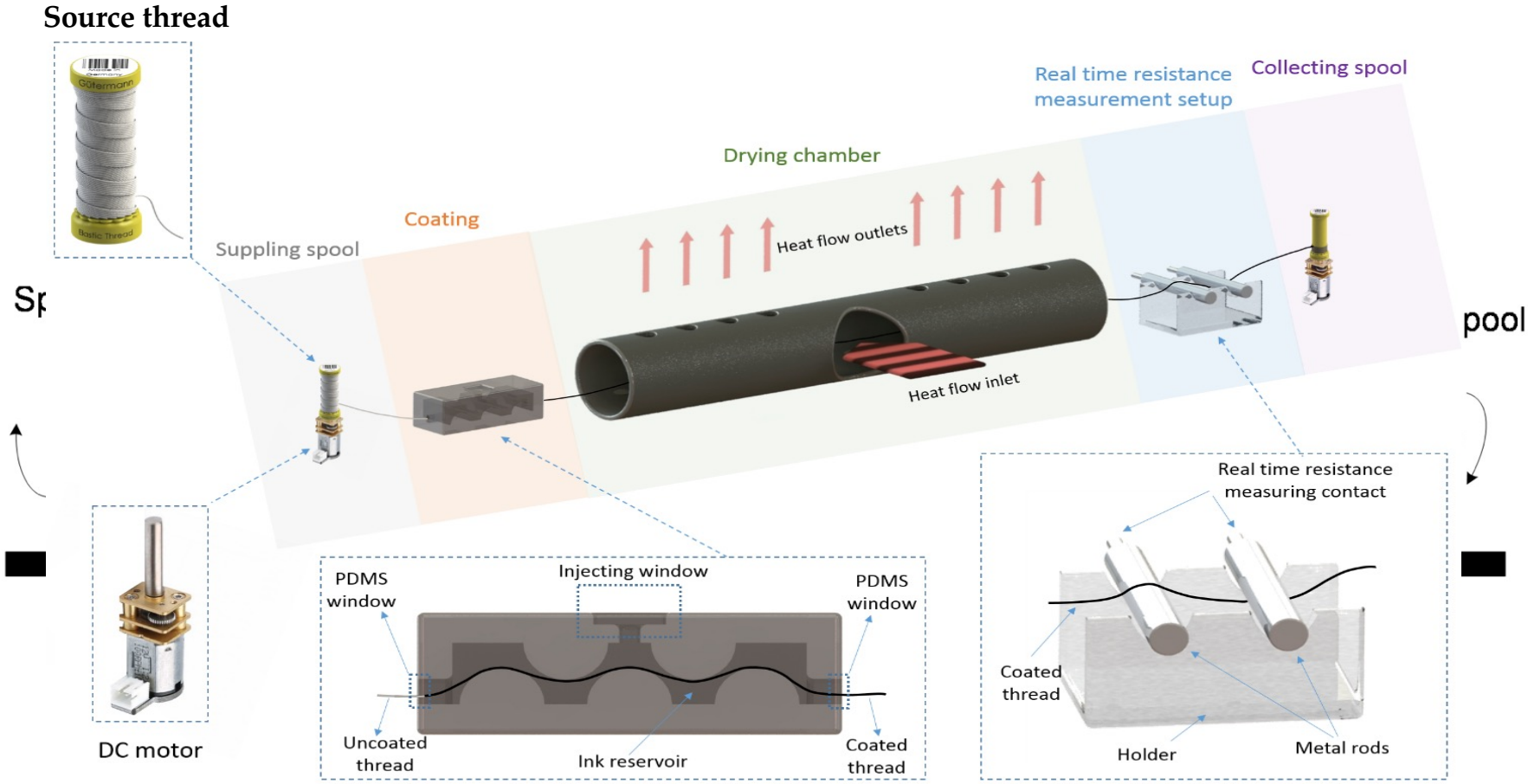
Proteins and Peptides

- Amino Acids, Cortisol, DHEA

Xenobiotics

- Heavy metals such as Cu, Hg, Cd, Zn, Pb, As, Ni
- Ethanol
- Drugs
- Cosmetics

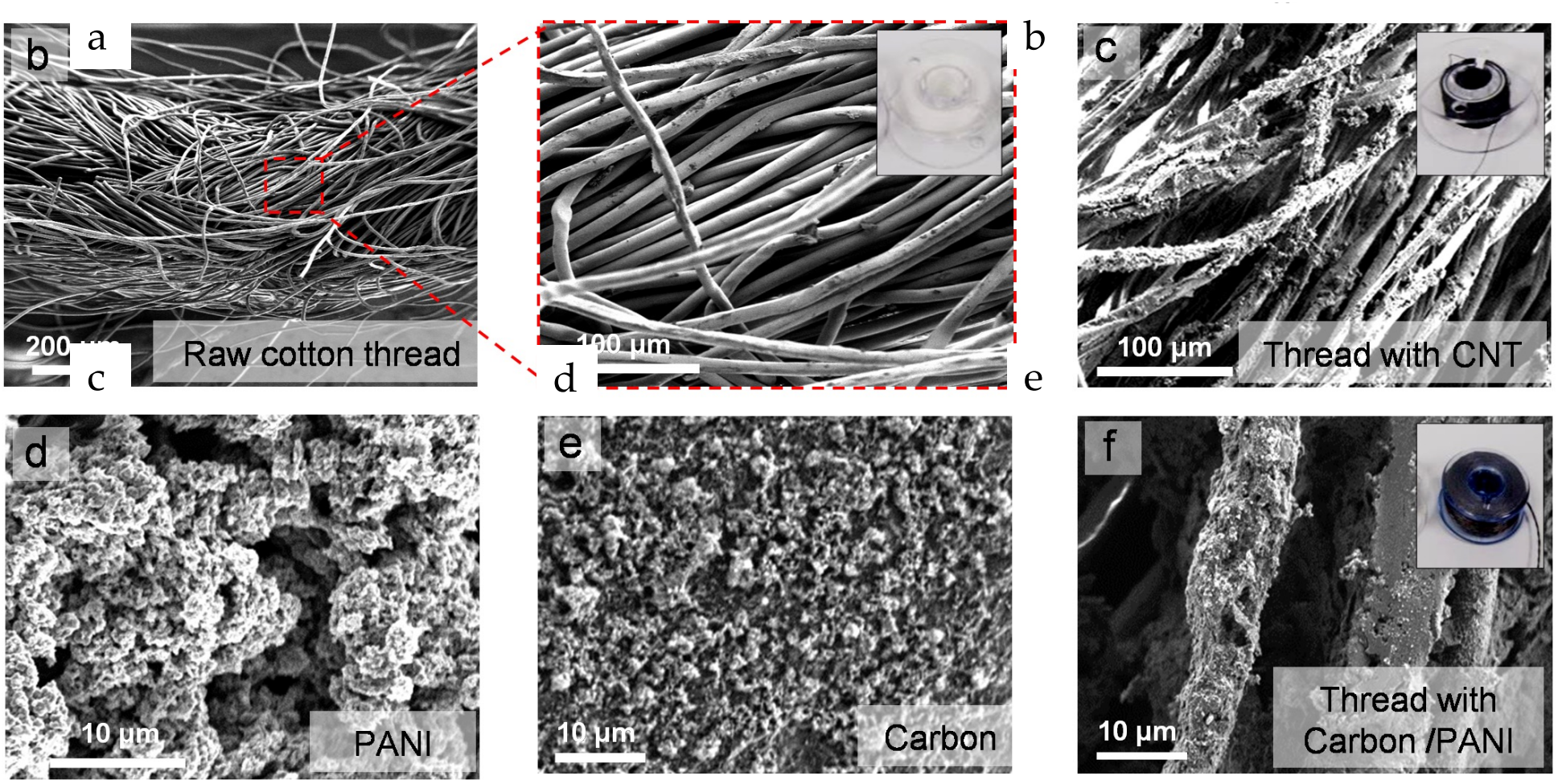
Threads can be functionalized to make sensors



- Threads are functionalized using a continuous ***reel-to-reel dip-coating & drying*** approach.
- Enables realization of multifunctional sensing threads that are thin, flexible, stitch-able, braid-able, weave-able and knit-able.

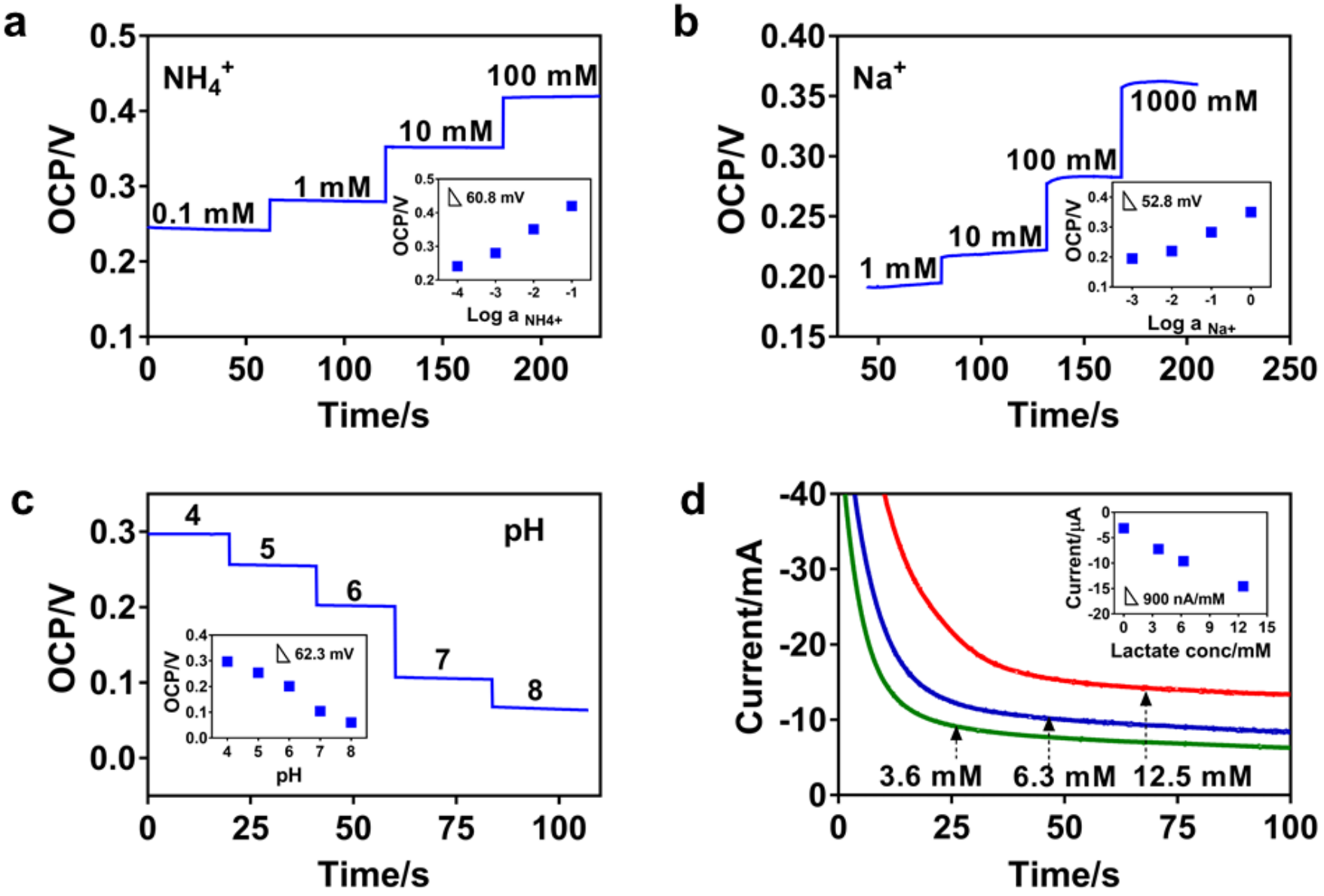
Microsystems and Nanoengineering, 2016
Sensors and Actuators: A, 2020

Conductive and Sensing Threads



Microsystems and Nanoengineering, 2016

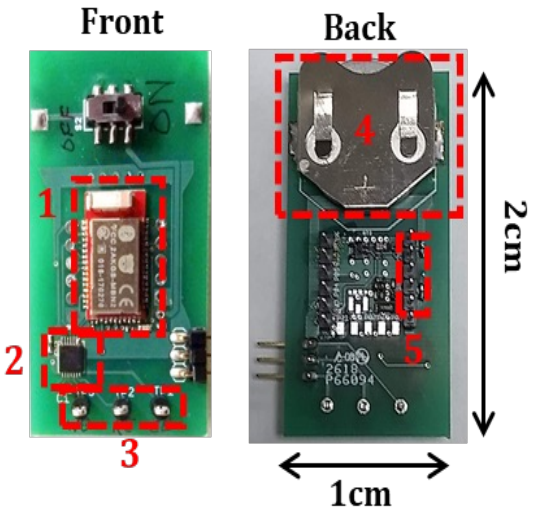
Performance: Ion and Metabolite sensing threads

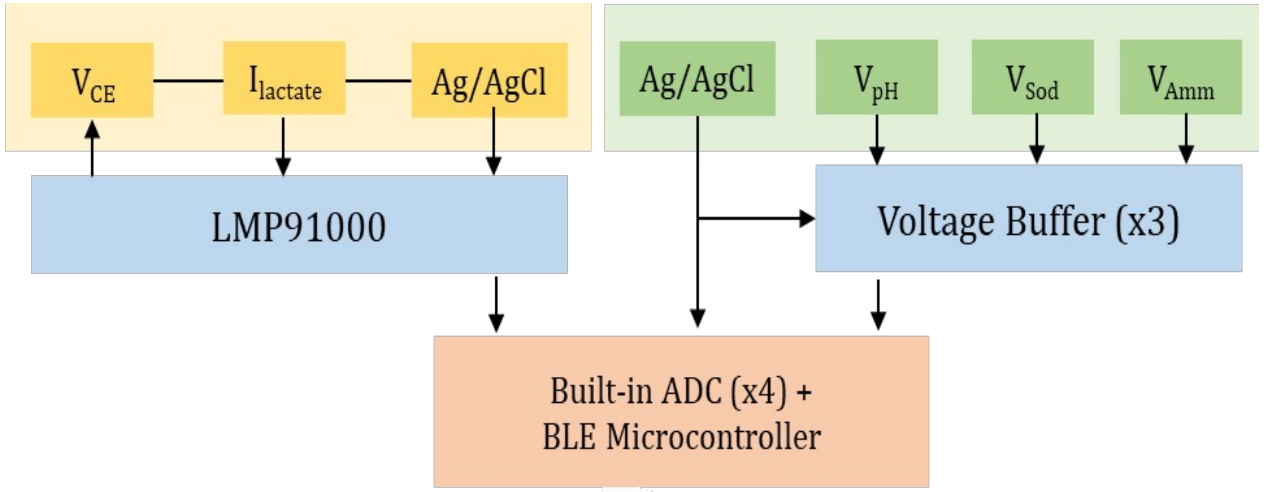


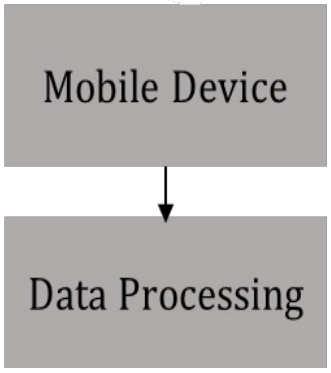
npj Flexible Electronics, 2020

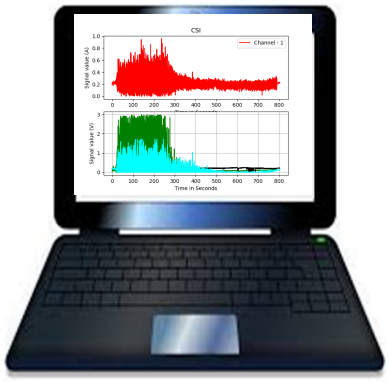
Stamp sized electronics board

Use off-the shelf chipsets to realize miniaturized electronics button for readout and wireless communication





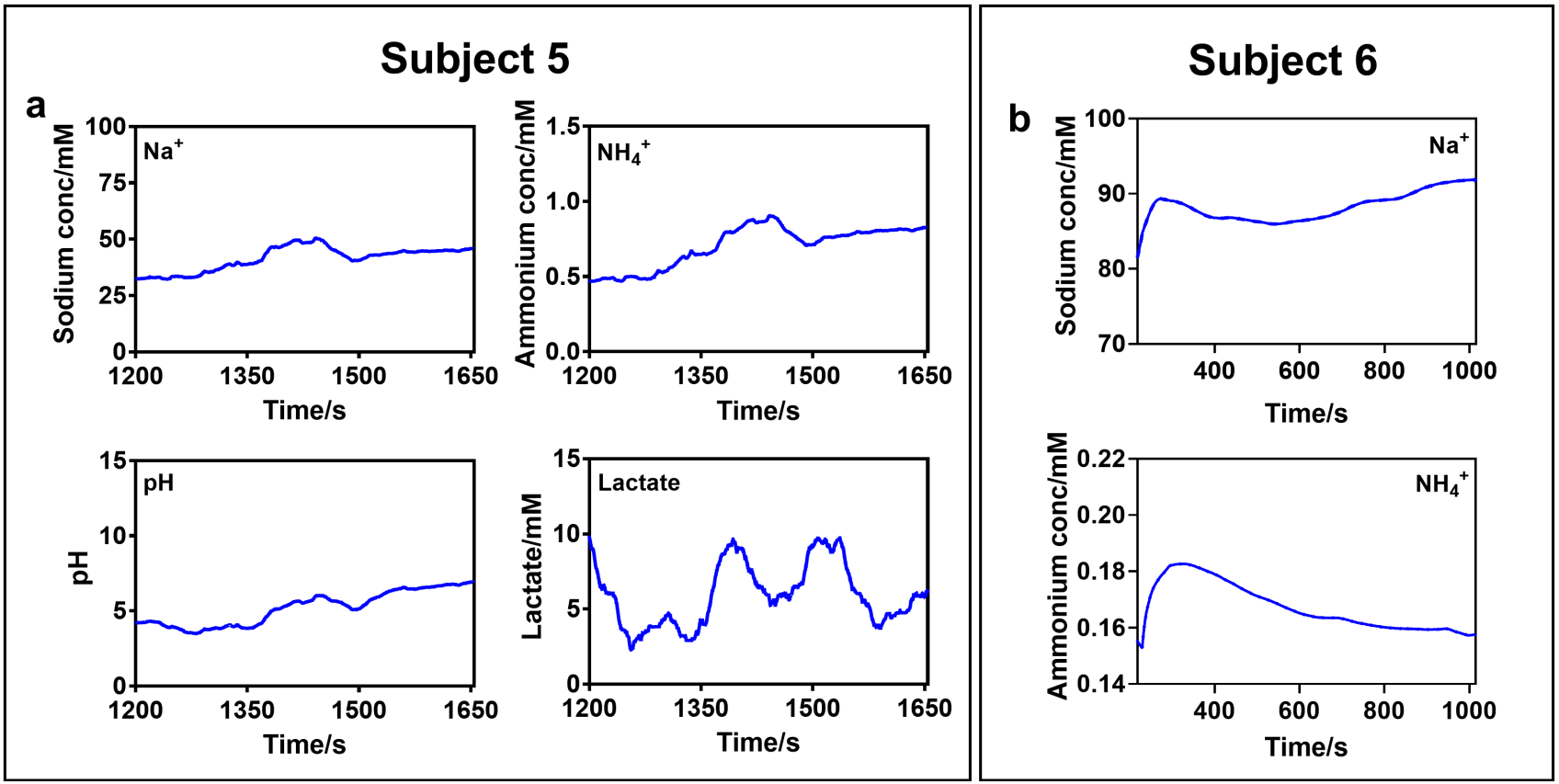




1) Red Bear BLE Module MB-N2 containing the Nordic Semiconductor nRF52832 SoC and chip antenna, 2) LMP91000 Configurable Potentiostat, 3) Amperometric Connectors, 4) Battery Holder CR2032 (3.6 V lithium-ion) battery holder, 5) Potentiometric connectors

npj Flexible Electronics, 2020

Maximum Exertion VO_{2max} studies in Humans



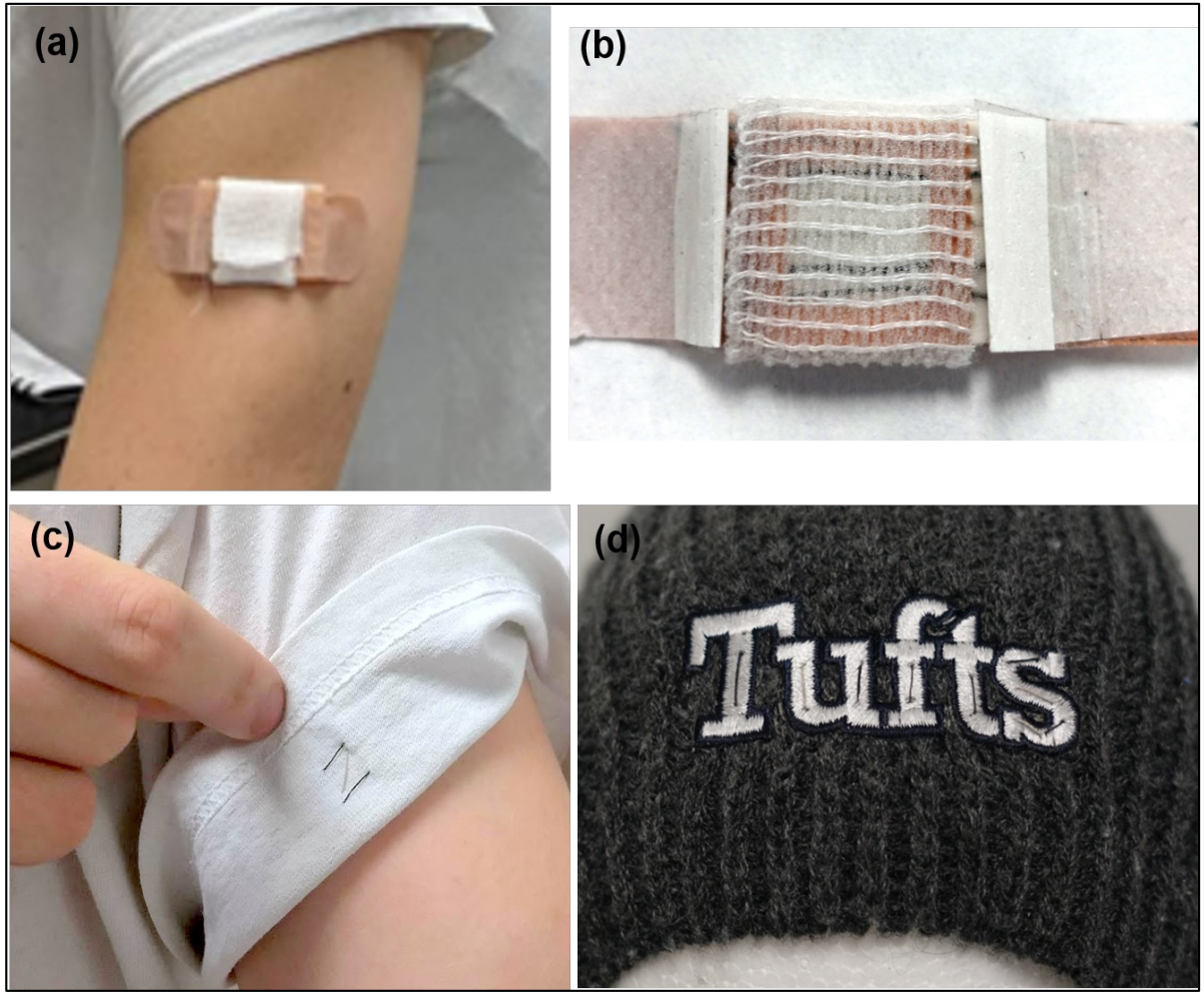
a) Sensor patch on the forehead during the stationary cycling

b) Waist belt integrated with sensor patch and the electronic during treadmill run.

Observed correlations :
Higher VO_2 is associated with higher sodium (r = .847, p < .001) and **lower ammonium** (r = -.785, p = .001).
Higher VO_2 is associated with higher pH (r = .773, p = .003) and **lower ammonium** (r = -.812, p = .001), but not sodium (p = .064).

npj Flexible Electronics, 2020

Threads can go where nothing else can!

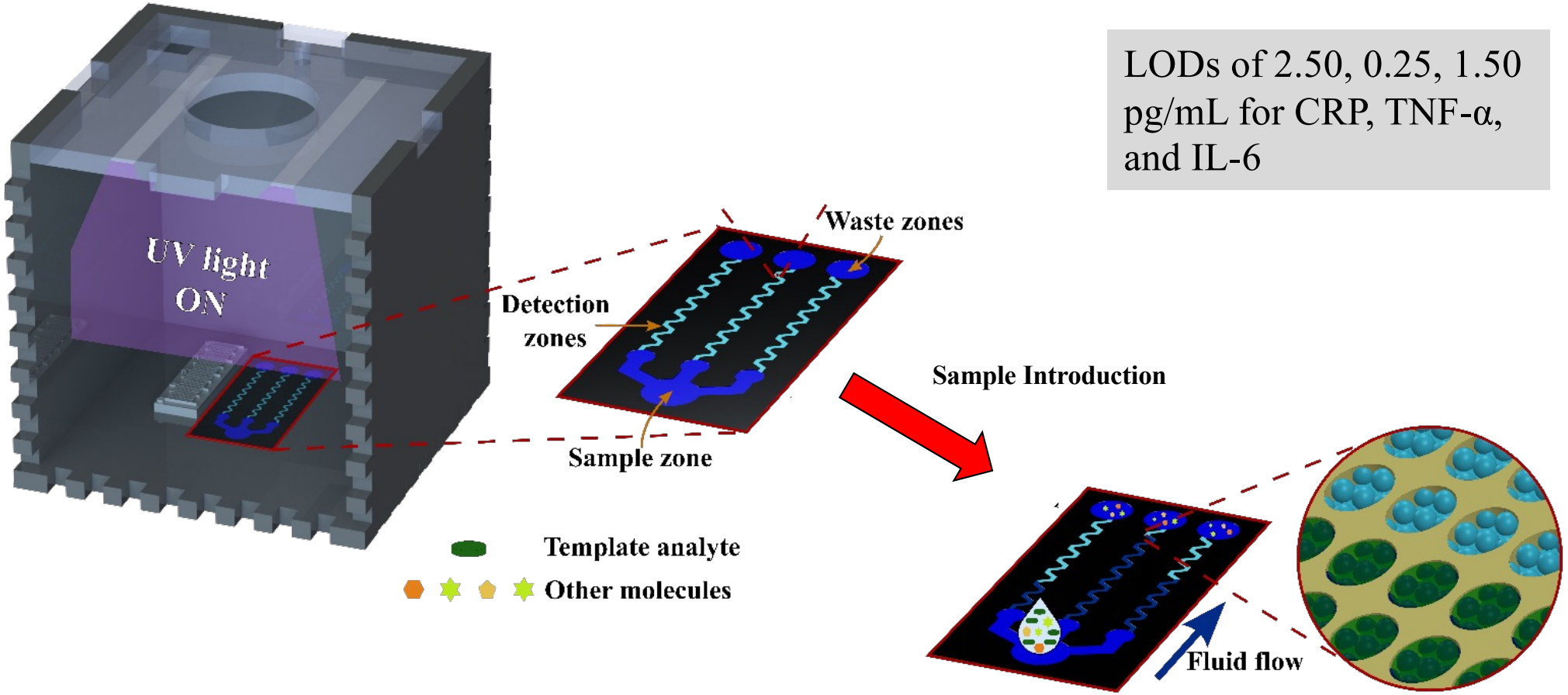


Distance based PAD for multiplexed cytokine detection

Can we detect cytokine levels due to inflammatory conditions?

Use Carbon Dots and Molecularly Imprinted Polymer (CD@MIPs) for distance based quantification : Measure the length of chemical reaction in detection zone

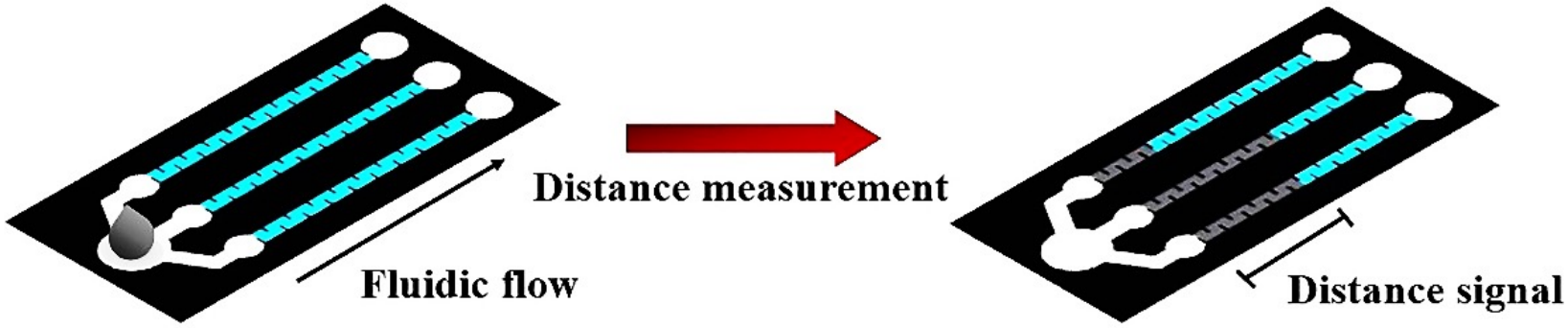
LODs of 2.50, 0.25, 1.50 pg/mL for CRP, TNF-α, and IL-6

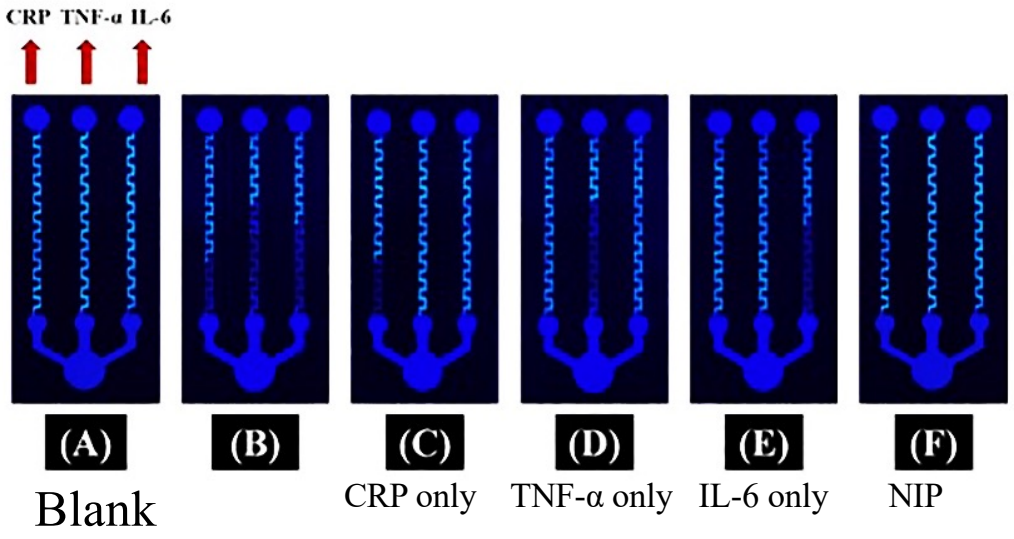


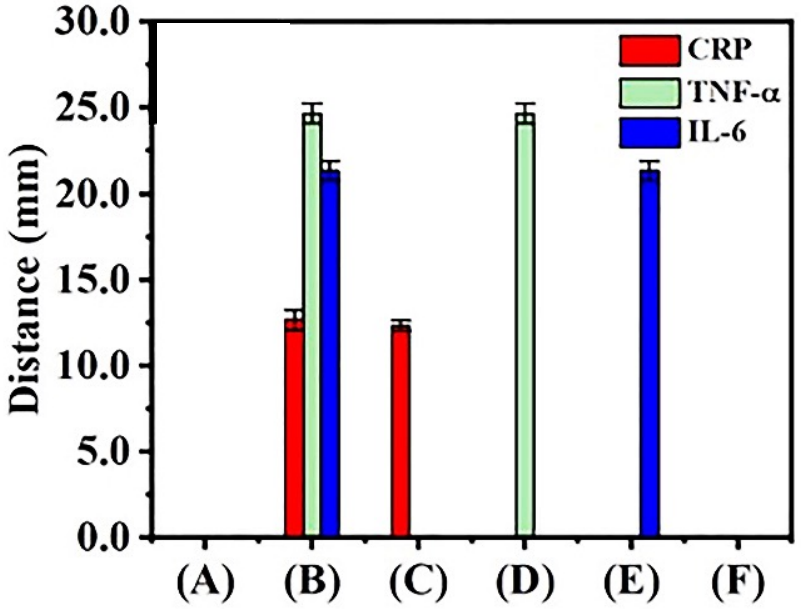
Lab on Chip, 2024

CDs@MIP dPAD: Workflow and Readout

(1) Add sample **(2) Shine UV light**



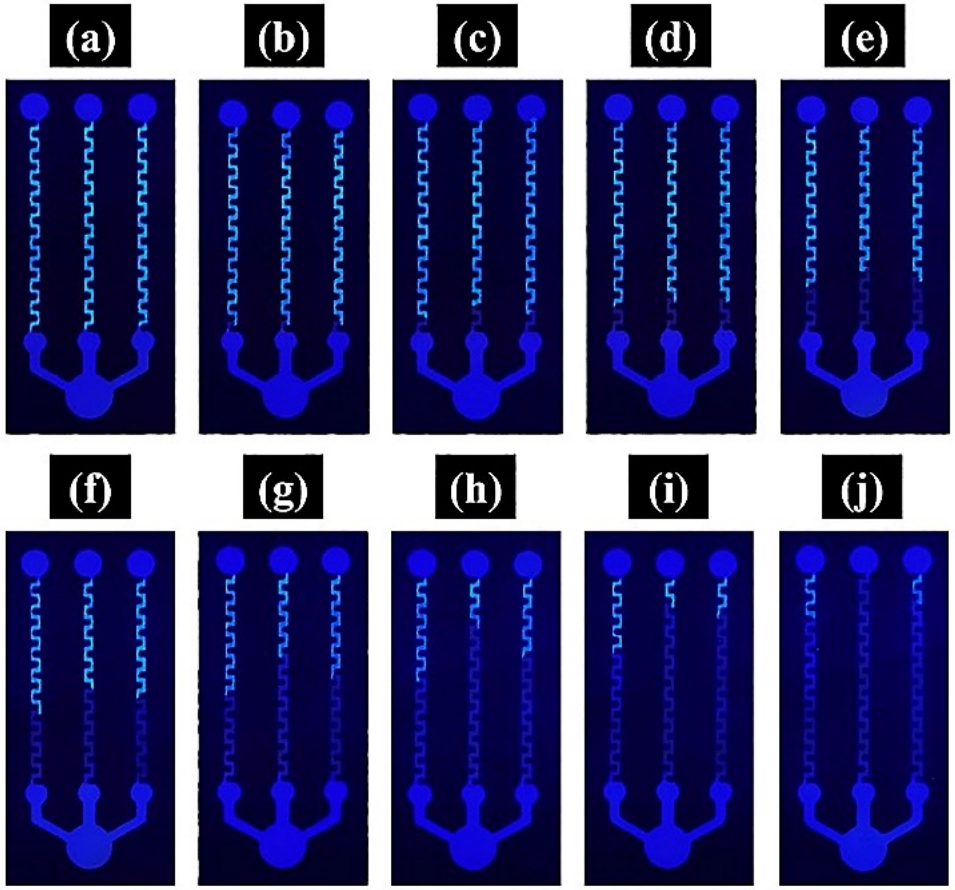


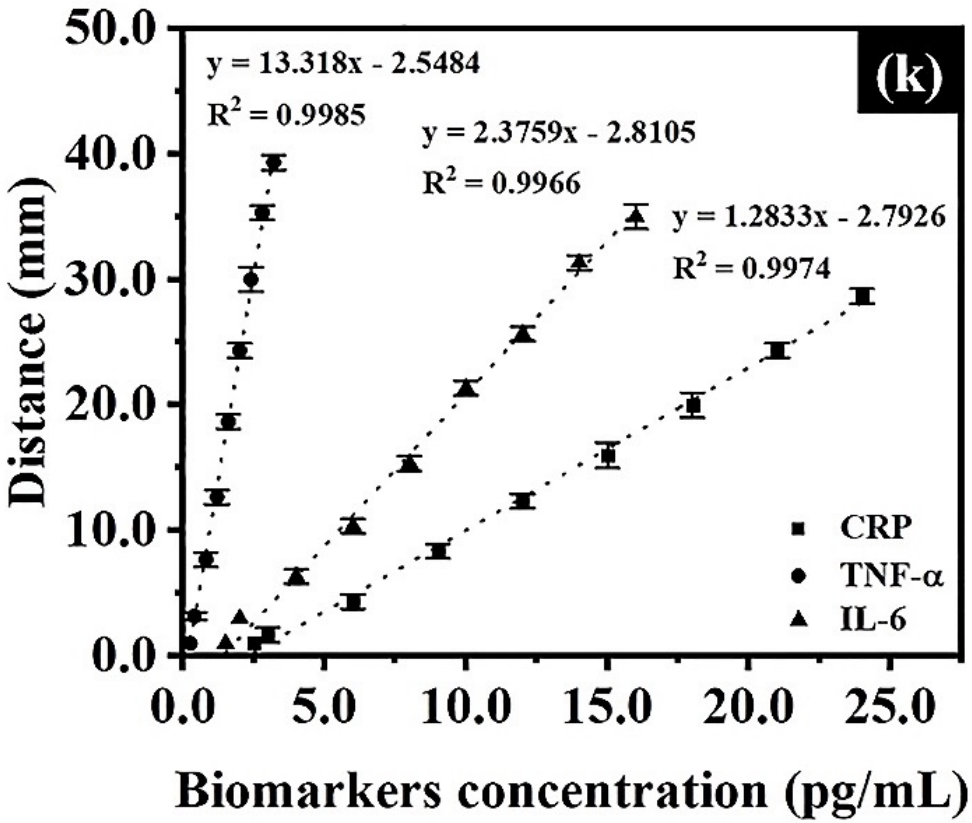


CRP (12.0 pg/mL), TNF-α (2.0 pg/mL), and IL-6 (10.0 pg/mL)

Lab on Chip, 2024

CDs@MIP dPAD: Results





(a) blank, (b) 2.50, 0.25, 1.50, (c) 3.0, 0.40, 2.0, (d) 6.0, 0.80, 4.0, (e) 9.0, 1.2, 6.0, (f) 12.0, 1.6, 8.0, (g) 15.0, 2.0, 10.0, (h) 18.0, 2.4, 12.0, (i) 21.0, 2.8, 14.0, and (j) 24.0, 3.2, 16.0 pg/mL for CRP, TNF-α, and IL-6, respectively.

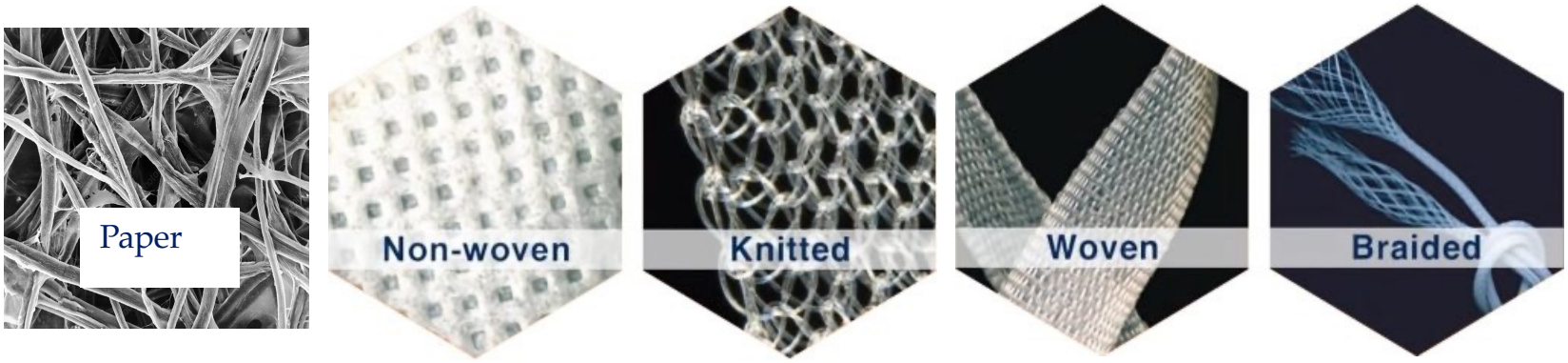
Lab on Chip, 2024

CDs@MIP dPAD: State-of-the-art Comparison

Analytes	Method	Linear range (pg/mL)	LOD (pg/mL)	Reference
CRP	Colorimetric	$117.0 \times 10^3 – 10.0 \times 10^6$	117.0×10^3	10
	Electrochemiluminescence	$10.0 – 1000 \times 10^3$	4.60	18
	Fluorescent	$500.0 – 1.0 \times 10^6$	300.0	42
	SRP-aptamer	$10.0 – 100.0 \times 10^3$	10.0	43
	Electrochemical	$10.0 \times 10^3 – 150.0 \times 10^6$	1.50×10^3	44
	dPADs@CDs@MIPs	2.50 – 24.0	2.50	This work
TNF-α	Colorimetric	$1.0 \times 10^3 – 100.0 \times 10^3$	600.0	6
	Electrochemical	$10.0\text{-}500 \times 10^3$	10.0	17
	Resonance Raman	0.049 – 0.195	0.09	45
	Fluorescent	$250.0 – 250.0 \times 10^3$	123.0	46
	SERS	$173.0 – 520.0 \times 10^3$	173.0	47
	dPADs@CDs@MIPs	0.25 – 3.20	0.25	This work
IL-6	dPADs immunosensor	0.05 – 25.0	0.05	7
	LFIA	$2.0 – 5.0 \times 10^2$	370.0	11
	Magnetic colorimetric	$0.10 – 1.0 \times 10^4$	40.0	12
	Electrochemical	0.50 – 5.0	500.0	13
	Photothermal	0.03 – 0.36	0.02	16
	dPADs@CDs@MIPs	1.50 – 16.0	1.50	This work

Conclusion

Paper and Thread Analytical Devices for stress, fatigue and cognition



- Naturally biodegradable, environmentally friendly, low cost
- Diversity of materials, methods and processing enables multi-functionality
- Facilitates microfluidic functions for sample acquisition, treatment, processing, sensing and transduction
- Facilitates electrochemical, Colorimetric, Fluorescent Based Detection

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- Dr. Ira Herman, Tufts U

Sponsors of the lab!

THANK YOU!

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