X10e: Patch a Gap in Healthcare

R42 Demo Day, Aug 16, 2024

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What if you were able to continuously learn about your health without a blood test?

Our Mission

Develop evidence based non-invasive e-skin sensors for measuring your body's signals; anytime, anywhere

70%

medical decisions relying on **invasive laboratory tests**[1]

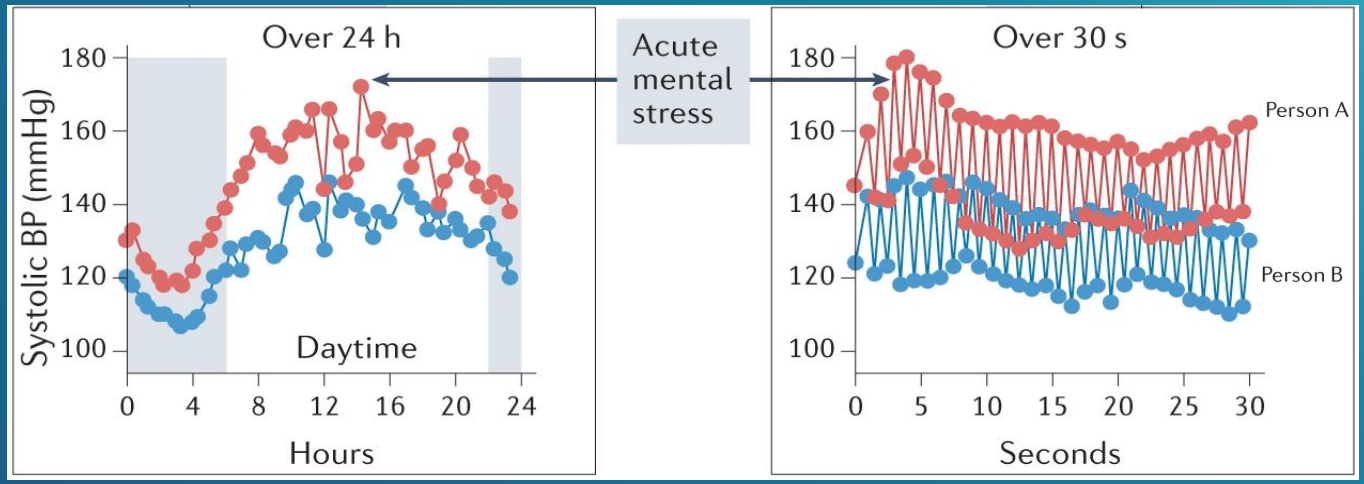
40%

US patients **skip** annual physical exams[1]

Less invasive => more frequent tests = **Earlier Diagnosis**

1) Schutte, A.E., Kollias, A. & Stergiou, G.S. Blood pressure and its variability: classic and novel measurement techniques. Nat Rev Cardiol 19, 643–654 (2022)

Biomarkers vary between 10-40% in a day



Non-invasive, continuous monitoring = **Early & Insightful Data**

1) Schutte, A.E., Kollias, A. & Stergiou, G.S. Blood pressure and its variability: classic and novel measurement techniques. Nat Rev Cardiol 19, 643–654 (2022)

Redefining wearables
From wellness to clinical utility

Wellness

- Limited sensor technology (**Vital signs:** T^0, HR, BP)
- Designed for healthy consumers
- User misinterpretation

Clinical

- Emerging technology (**single metric**: glucose)
- Designed for those with medical needs
- Clear actionable signal

Wearables market ↑ from **$150M** in **2016** to **~$31B** in **2026**

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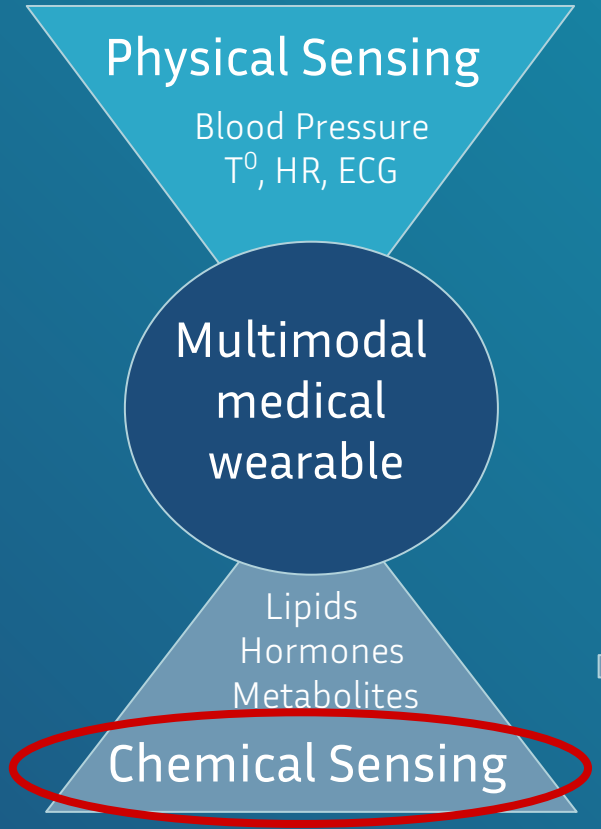
Solution: Multimodal sensor technology

Comprehensive and insightful health overview



→ Traditional, vital signs

→ Expand to other molecules

Metabolic Syndrome

A progressive cluster of conditions requiring continuous monitoring

Impact on health

- Increased risk of:
  - diabetes
  - heart disease
  - stroke
- 1/3rd of the US population[1]
- Double healthcare cost[2]

In the clinic

- Increased Body Mass Index
- Increased blood pressure
- Elevated Triglycerides
- Reduced Cholesterol
- Elevated Fasting Glucose

1. The Global Pandemic of Metabolic Syndrome, NCBI
2. Health care utilization and costs by metabolic syndrome risk factors, NCBI

Identifying Biomarkers for Metabolic Syndrome

Biomarker	Macromolecule Group	Function
Glucose	Carbohydrate	Main energy source
Triglycerides	Lipid	Energy storage and transport
Cholesterol	Lipid	Cell membrane structure
Insulin	Hormone	Regulates blood glucose levels
Leptin	Hormone	Regulates hunger and metabolism
Adiponectin	Hormone	Enhances insulin sensitivity, reduces inflammation
Uric Acid	Purine metabolite	Waste product of purine metabolism
C-reactive protein (CRP)	Protein	Marker of inflammation

Specific & Predictive

Identifying Biomarkers for Metabolic Syndrome

Biomarker	Macromolecule Group	Function	In Sweat
Glucose	Carbohydrate	Main energy source	Yes
Triglycerides	Lipid	Energy storage and transport	No
Cholesterol	Lipid	Cell membrane structure	No
Insulin	Hormone	Regulates blood glucose levels	No
Leptin	Hormone	Regulates hunger and metabolism	No
Adiponectin	Hormone	Enhances insulin sensitivity, reduces inflammation	No
Uric Acid	Purine metabolite	Waste product of purine metabolism	Yes
C-reactive protein (CRP)	Protein	Marker of inflammation	No

Identifying Biomarkers for Metabolic Syndrome

Biomarker	Macromolecule Group	Function	In Sweat	In Interstitial fluid
Glucose	Carbohydrate	Main energy source	Yes	Yes
Triglycerides	Lipid	Energy storage and transport	No	Yes
Cholesterol	Lipid	Cell membrane structure	No	Yes
Insulin	Hormone	Regulates blood glucose levels	No	Yes
Leptin	Hormone	Regulates hunger and metabolism	No	Yes
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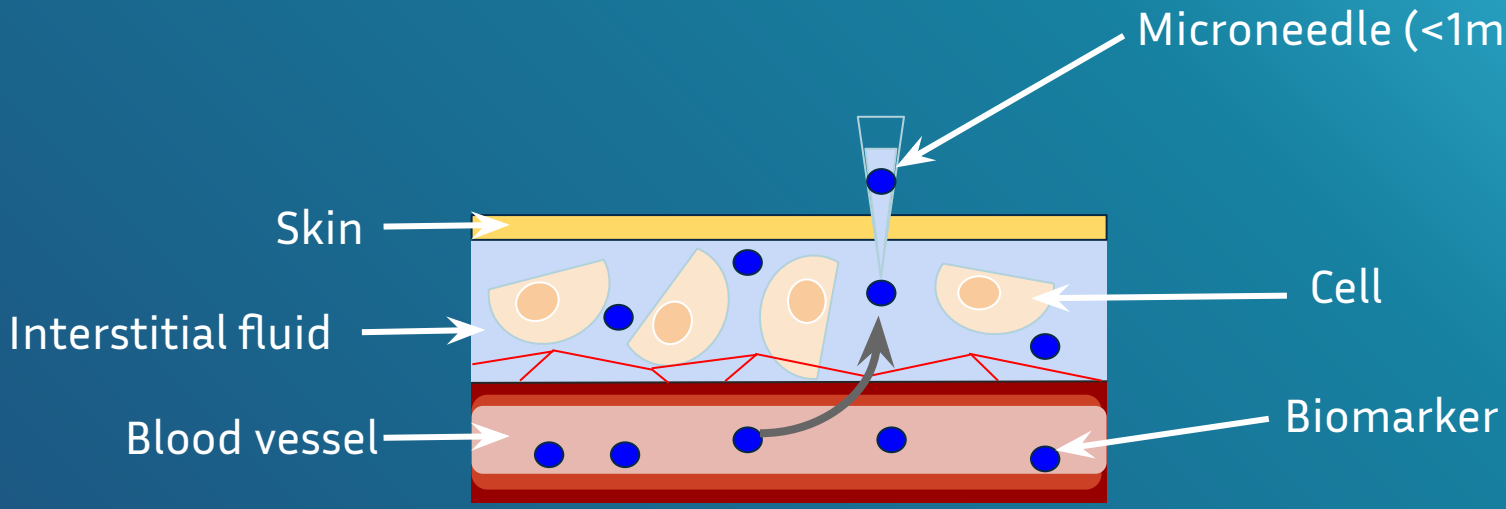
Uric Acid	Purine metabolite	Waste product of purine metabolism	Yes	Yes
C-reactive protein (CRP)	Protein	Marker of inflammation	No	Yes

Interstitial Fluid: Golden Reservoir for Biomarkers



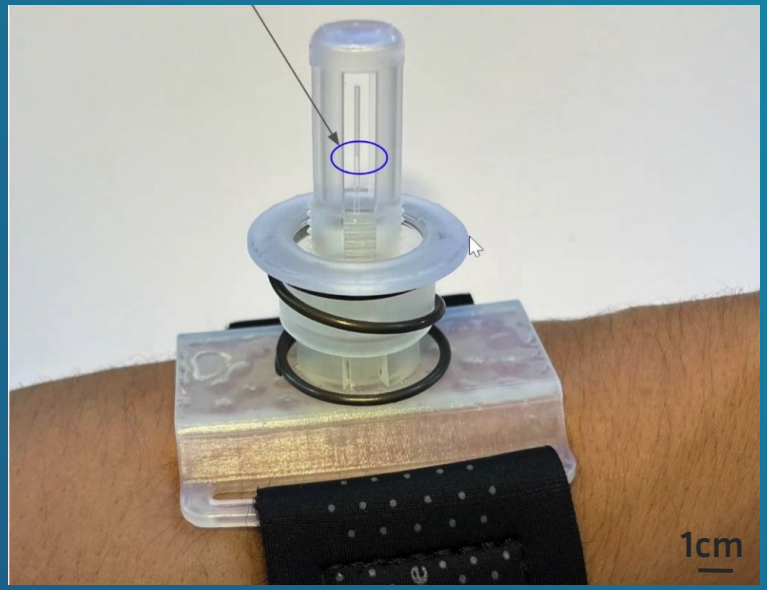
➡ Non-invasive nor painful extraction

- What are our biomarker concentration in the interstitial fluid?

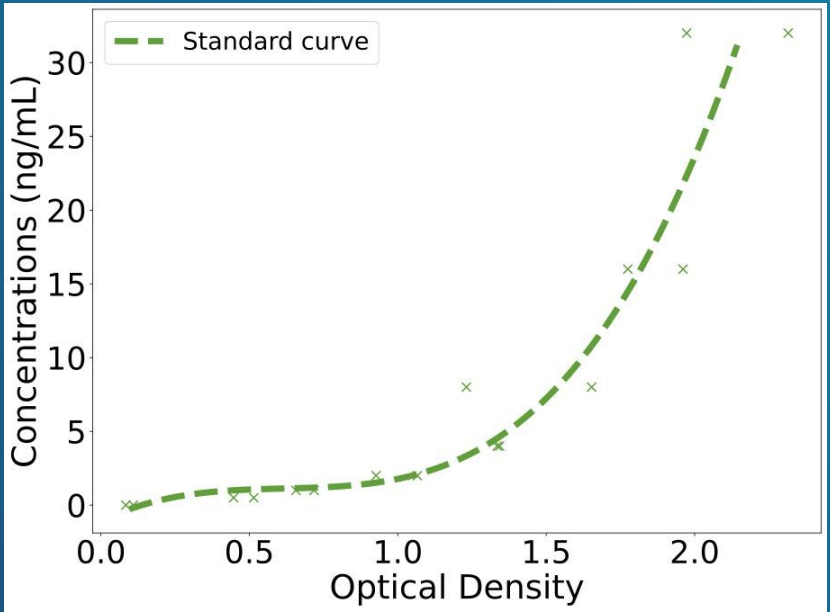
Extraction of Interstitial Fluid versus Blood

Extraction of Interstitial Fluid versus Blood

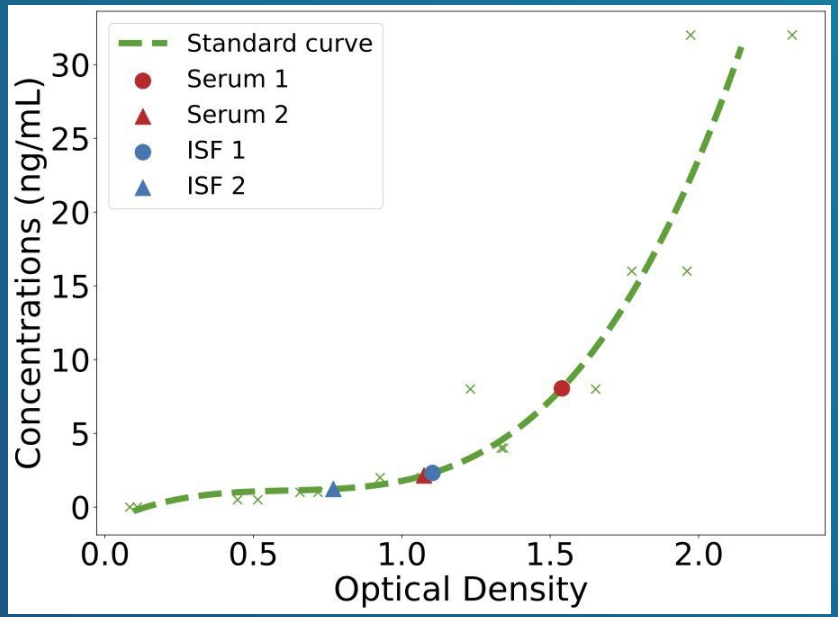
Meniscus shows interstitial fluid in the vial

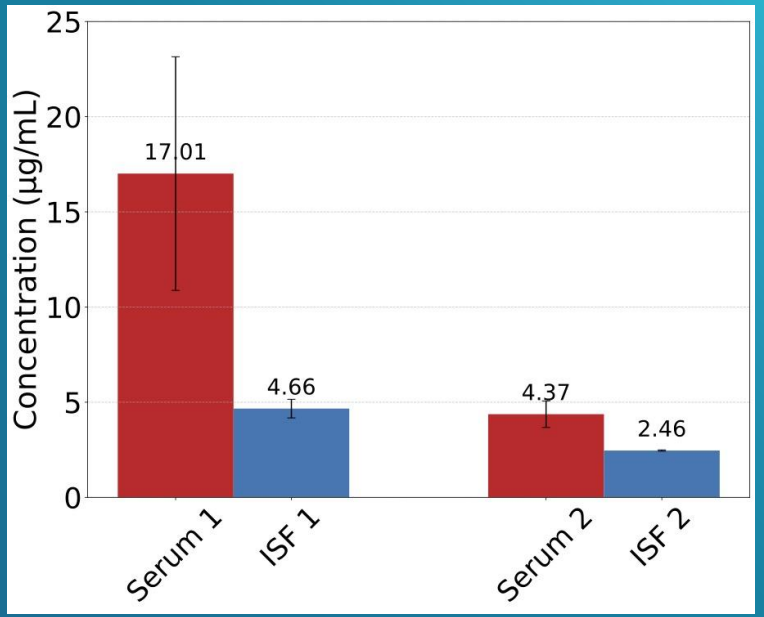


Biomarker Concentration Findings



Biomarker Concentration Findings

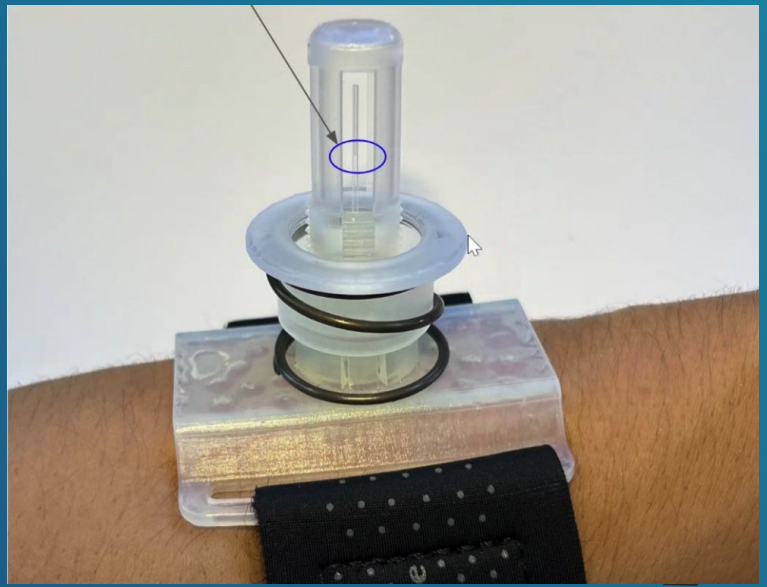




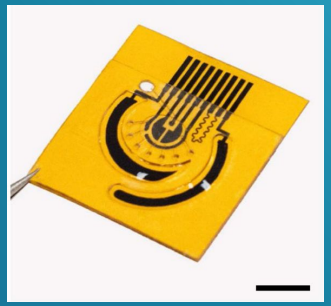
➡ 2- to 3-fold less hormone (adiponectin) in ISF than in Blood

Integration into Wearable Sensor

Meniscus shows interstitial fluid in the vial

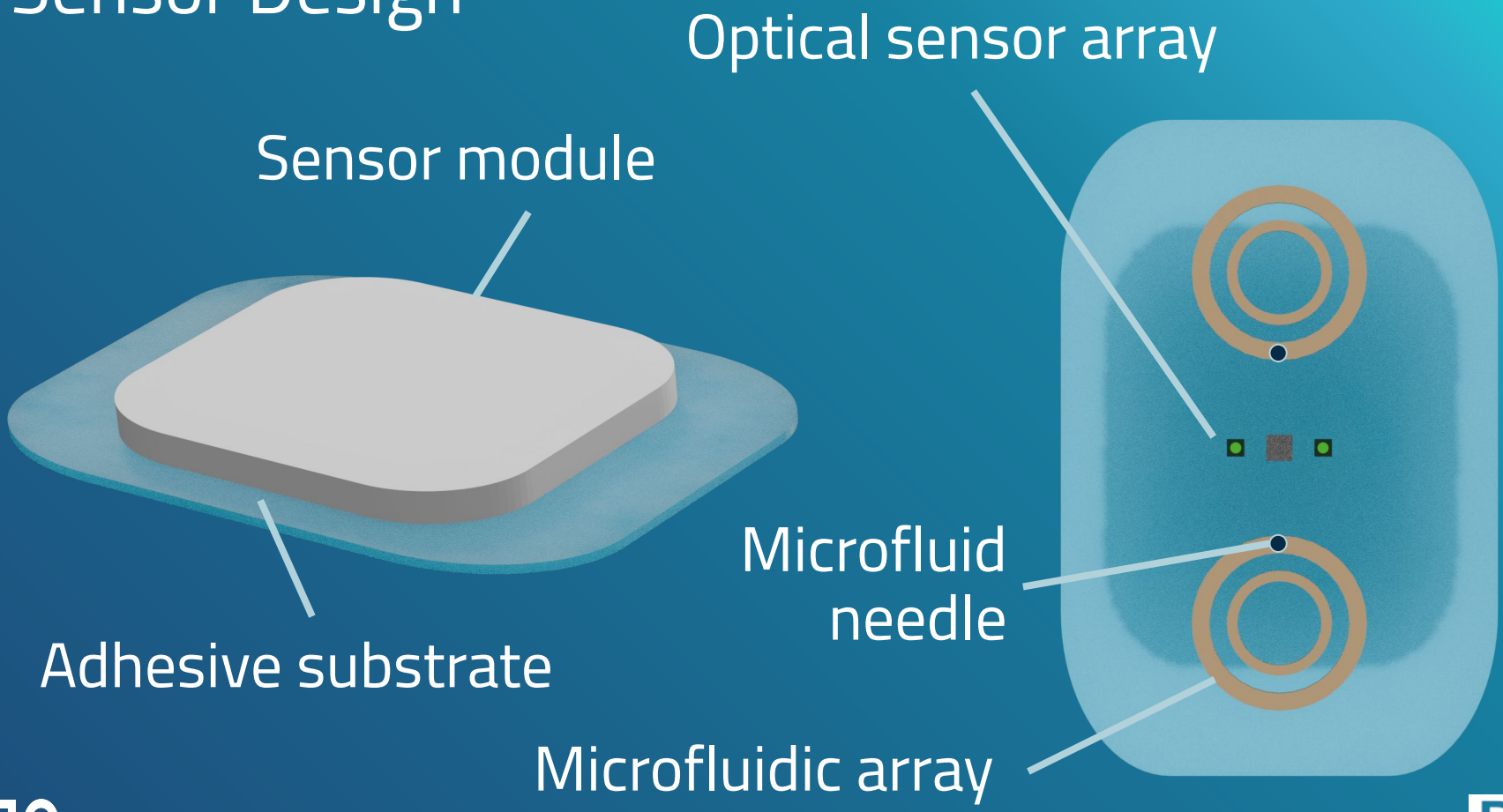


***In situ* analysis**
with microfluidic



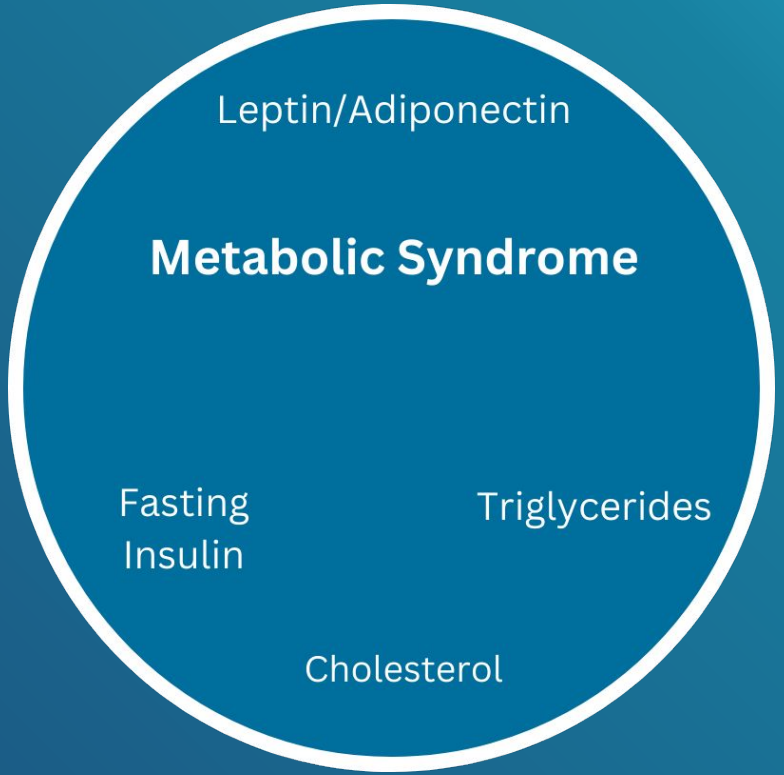
Wang *et al.*, A wearable electrochemical biosensor for the monitoring of metabolites and nutrients, Nature BioEng (2022)

Sensor Design

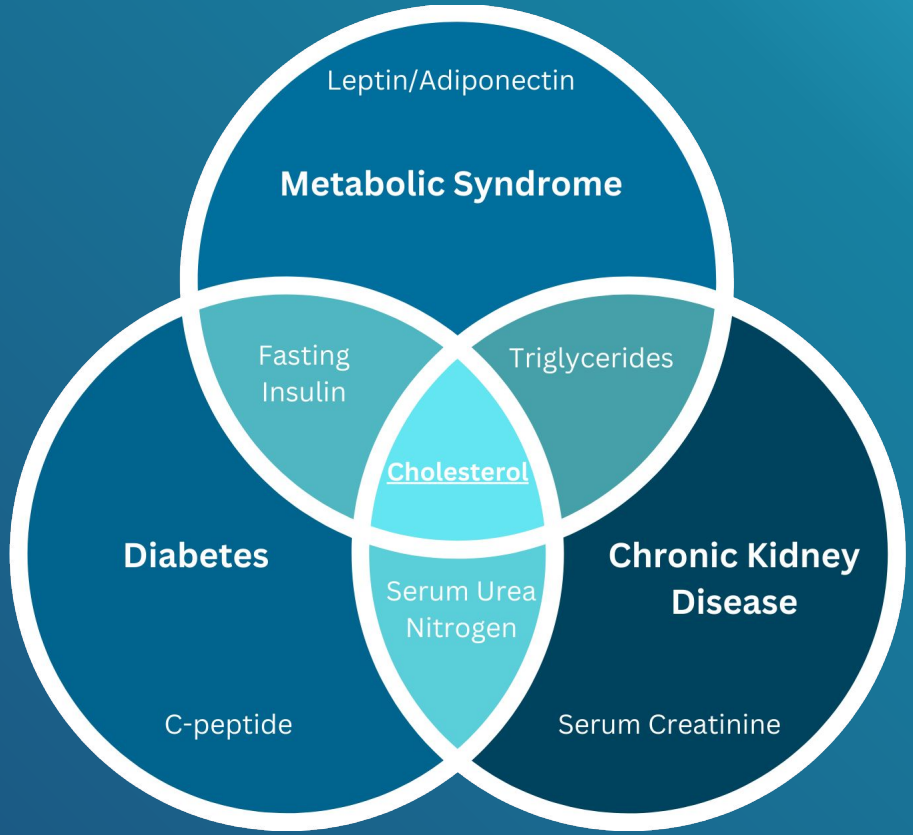


Sensor Prototype

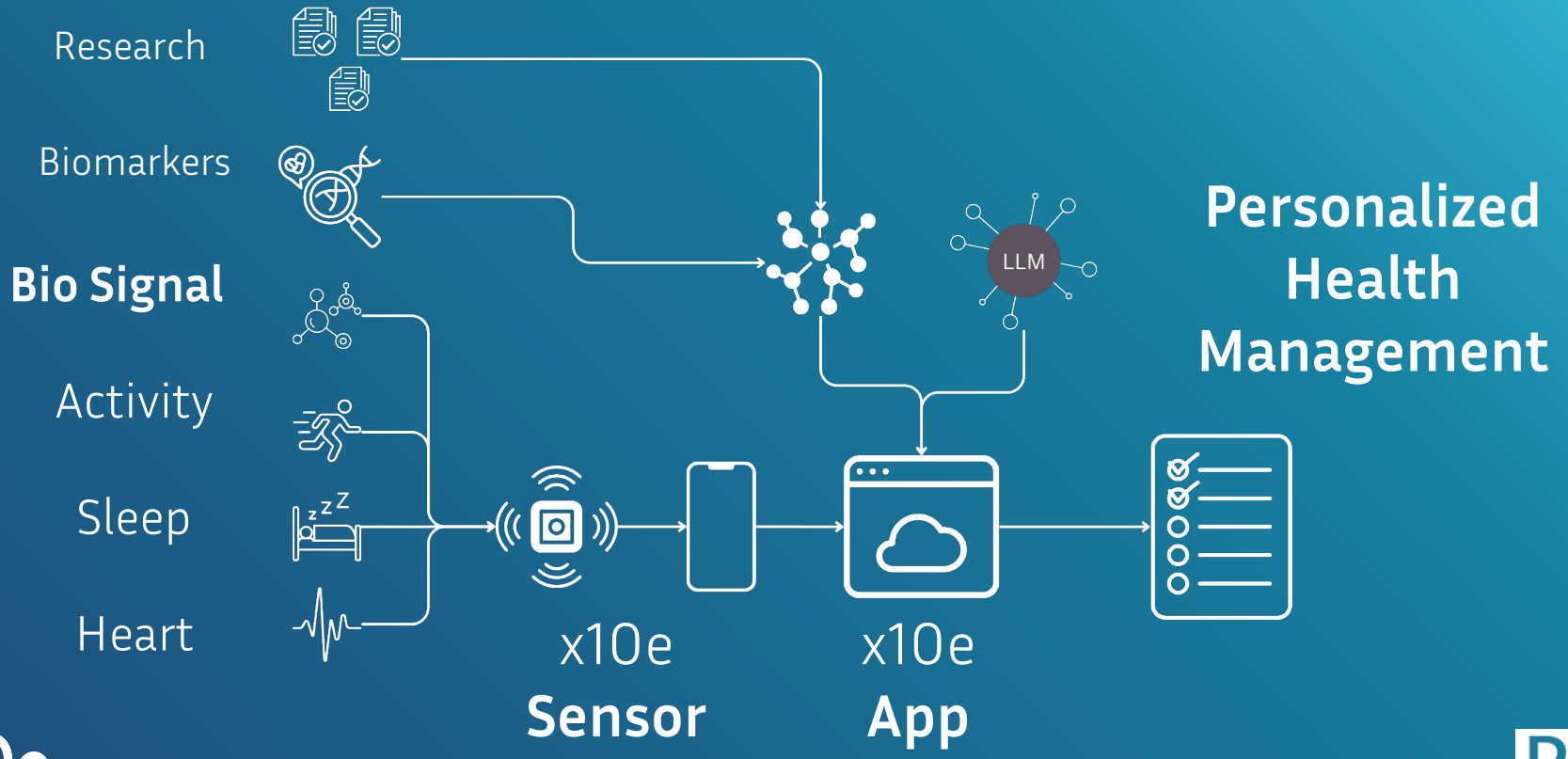
Continuous monitoring of biomolecules for metabolic and chronic diseases



Continuous monitoring of biomolecules for metabolic and chronic diseases



Generative Health Model



Business Model

- Revenue: recurring revenue based on subscription of device
- Leverage insurance companies reimbursement (CPD codes)
- Sales motion: B2B2C via medical distributors

Expertise in Biophysics, Sensors, and Bioengineering

Silvia Veronese, PhD
Founder and CEO X10e
Mentor

Yann Sakref, PhD
BioPhysicist
PhD in Physics
École Normale Supérieure

Mark MelnyKowycz, PhD
Sensor Engineer
PhD in Physics
Ecole Polytechnique de Zurich

Anupama Mahabhashyam
Technical Product lead
Broadcom
Stanford Business School

Julian Pena
BioEngineer
BS Bioengineering
University of California at Merced

Cristina Dalle Ore, PhD
Sensor Technology Expert
NASA, Bayer Crop Science
Fellow Mentor

Amit Goldman, EMBA
DigitalDx Ventures
Longevity Education Hub

Shaun Ranadé
BioEngineering
USPTO, Colgate

Carnegie Mellon,
BS Engineering, Medical

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THANK YOU

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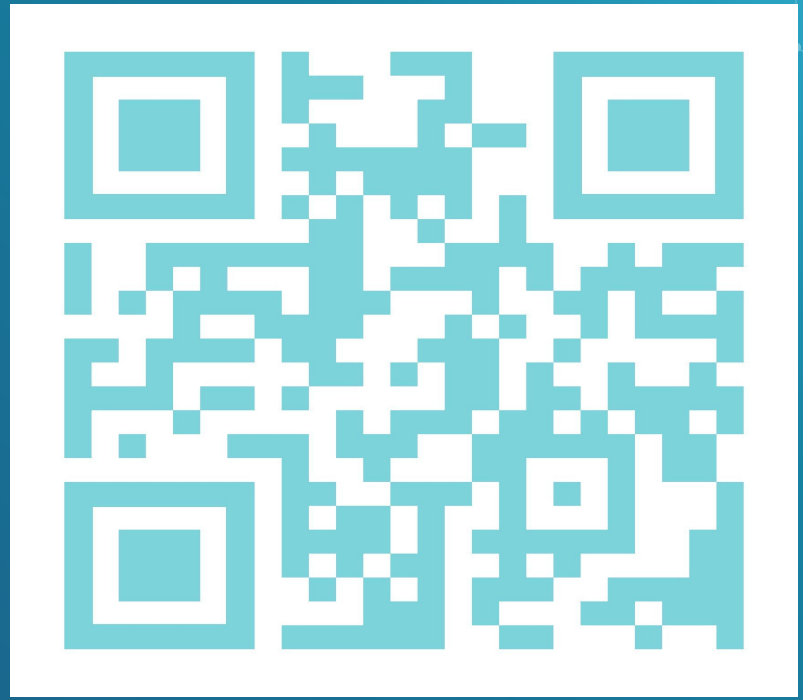
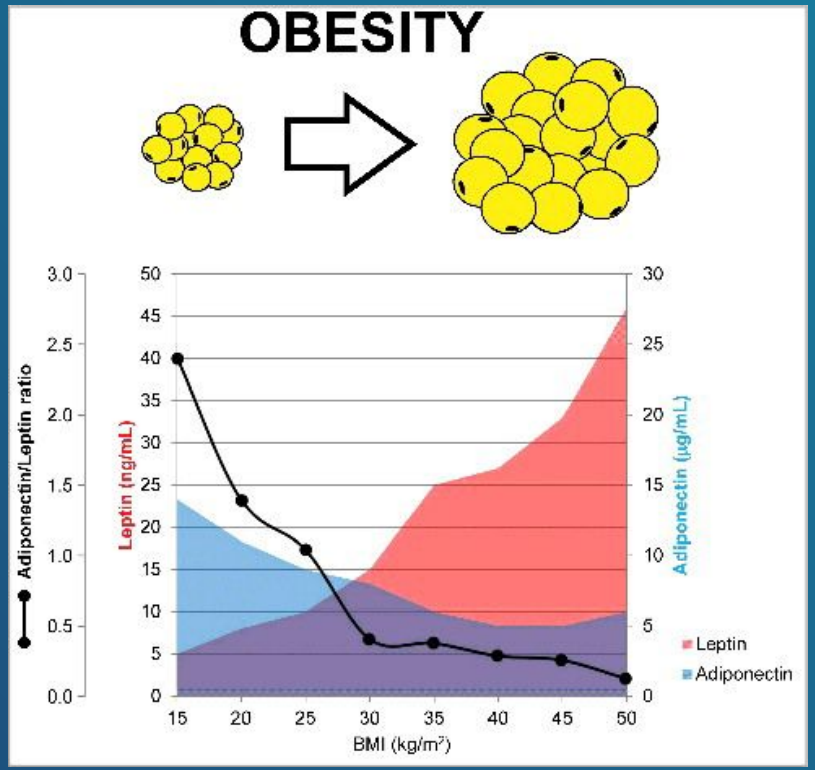


APPENDIX

Project Details

Leptin and Adiponectin



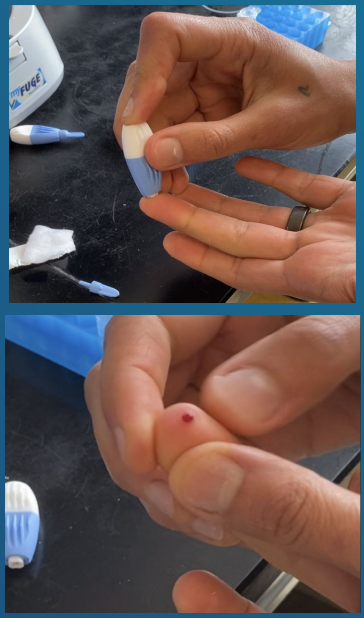
- Obesity, coronary artery disease and the metabolic syndrome (MS) are characterized by an increase in circulating leptin concentrations, in parallel to a decrease in blood levels of adiponectin.

- Leptin -which has an appetite regulating effects- increases due to Leptin resistance
- Adiponectin -which has insulin sensitizing effect- decreases due to chronic inflammation and insulin resistance.

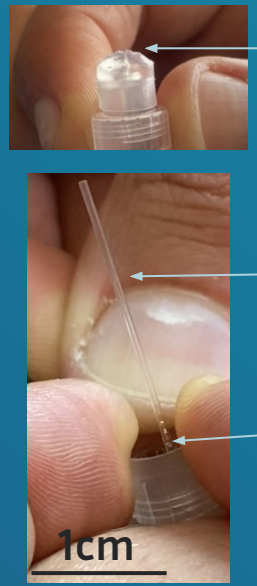
(López-Jaramillo, P. et al. 2014; Frühbeck et al. 2017)

Experiment with ISF Labs

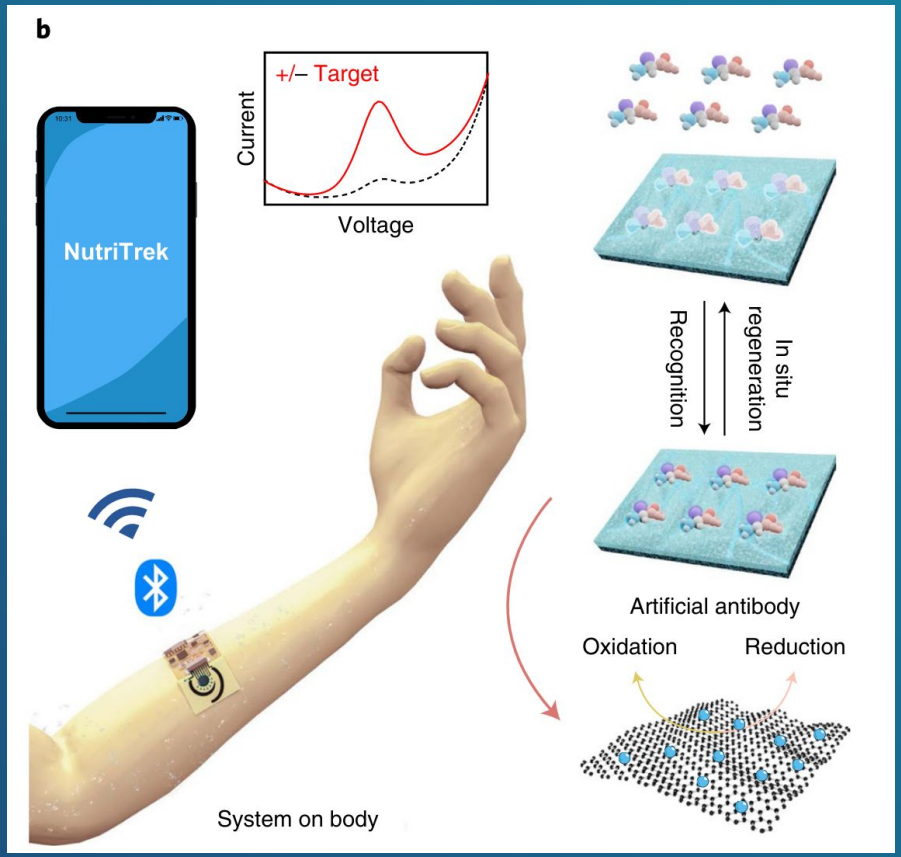
Blood extraction:



Interstitial fluid extraction:



Artificial Antibodies: Molecular Imprinted Polymer



Majority of metabolites non-electroactive

➡ Indirect detection

A RAR (redox-active nanoreporter) layer sandwiched between the graphen and MIP layer: selective adsorption reduces exposure to RAR.

Wang *et al.*, A wearable electrochemical biosensor for the monitoring of metabolites and nutrients, Nature BioEng (2022)

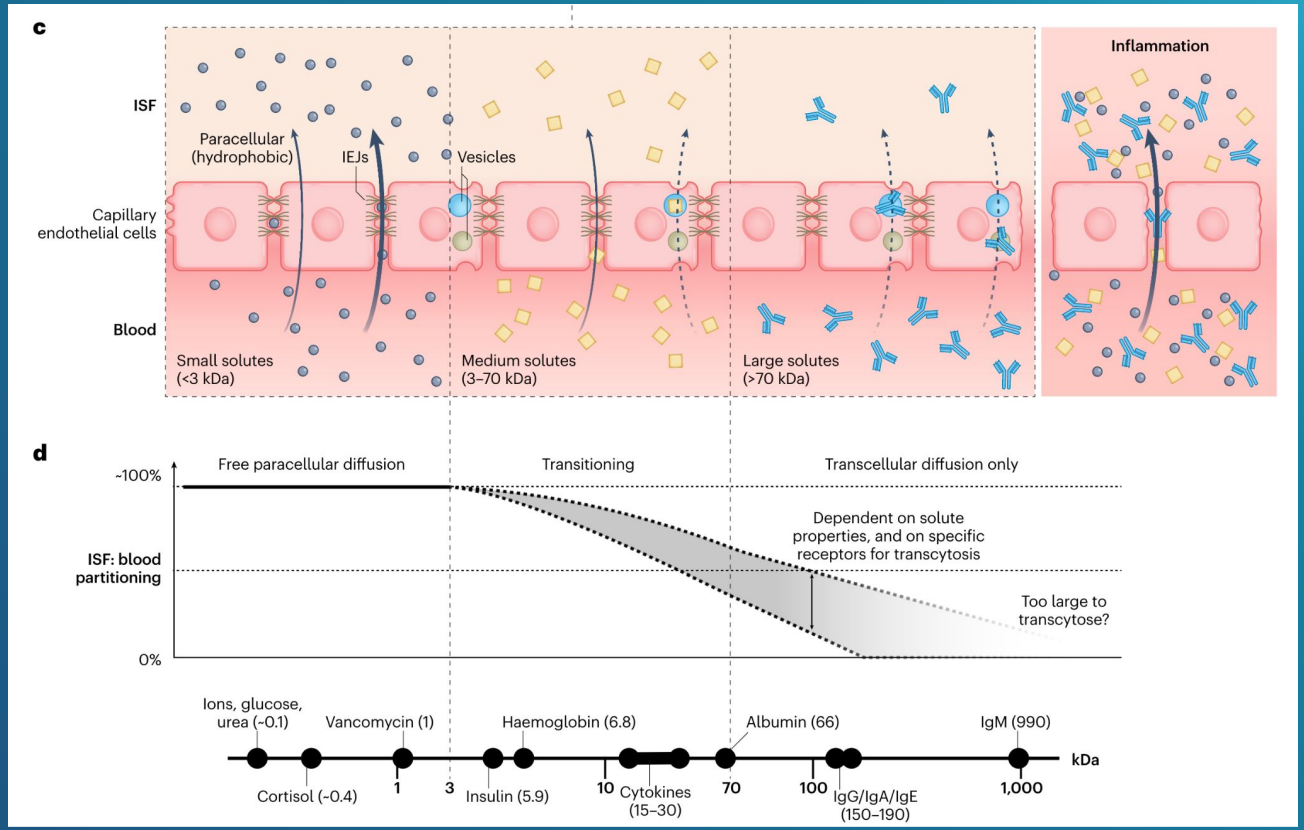
Biomarkers in the sweat

Table 1 Key analytes in sweat and associated health conditions

Analyte category	Analyte	Health condition	Ref.
Electrolytes	Na^+	Dehydration, hyponatremia, electrolyte imbalance	40–43,45,47
	Cl^-	Dehydration, cystic fibrosis	17,50,51
	K^+	Hypokalemia, muscle cramps	52,53
	Ca^{2+}	Myeloma, cirrhosis, renal failure, acid–base balance disorder	54
	NH^{4+}	Shift from aerobic to anaerobic metabolic conditions	9,41,55
	PH	Pathogenesis of skin diseases, wound healing	30,38,43,143
Metabolites	Glucose	Diabetes	17,33,52,103
	Lactate	Shift from aerobic to anaerobic metabolic conditions	7,11,58,37
	Alcohol	Inebriation	16,76,77
	Uric acid	Renal dysfunction, gout	61,144
Drugs	Caffeine	Coronary syndrome, hypertension, Depression	63,145
	Levodopa	Parkinson's disease	64,89
Trace metals	Zn^{2+}	Stress and immune system-induced muscle damage	44,66,67
	Cu^{2+}	Rheumatoid arthritis, Wilson's disease, cirrhosis of the liver	44,66,68
Other analytes (hormones, cytokines, proteins, etc.)	Interleukin 6	Insulin activity, immune responses in cancer therapy	69,70,145
	Cortisol	Stress	59,69,72,73
	Tyrosine	Metabolic disorders, tyrosinemia	74
	Neuropeptide Y	Stress	30,75

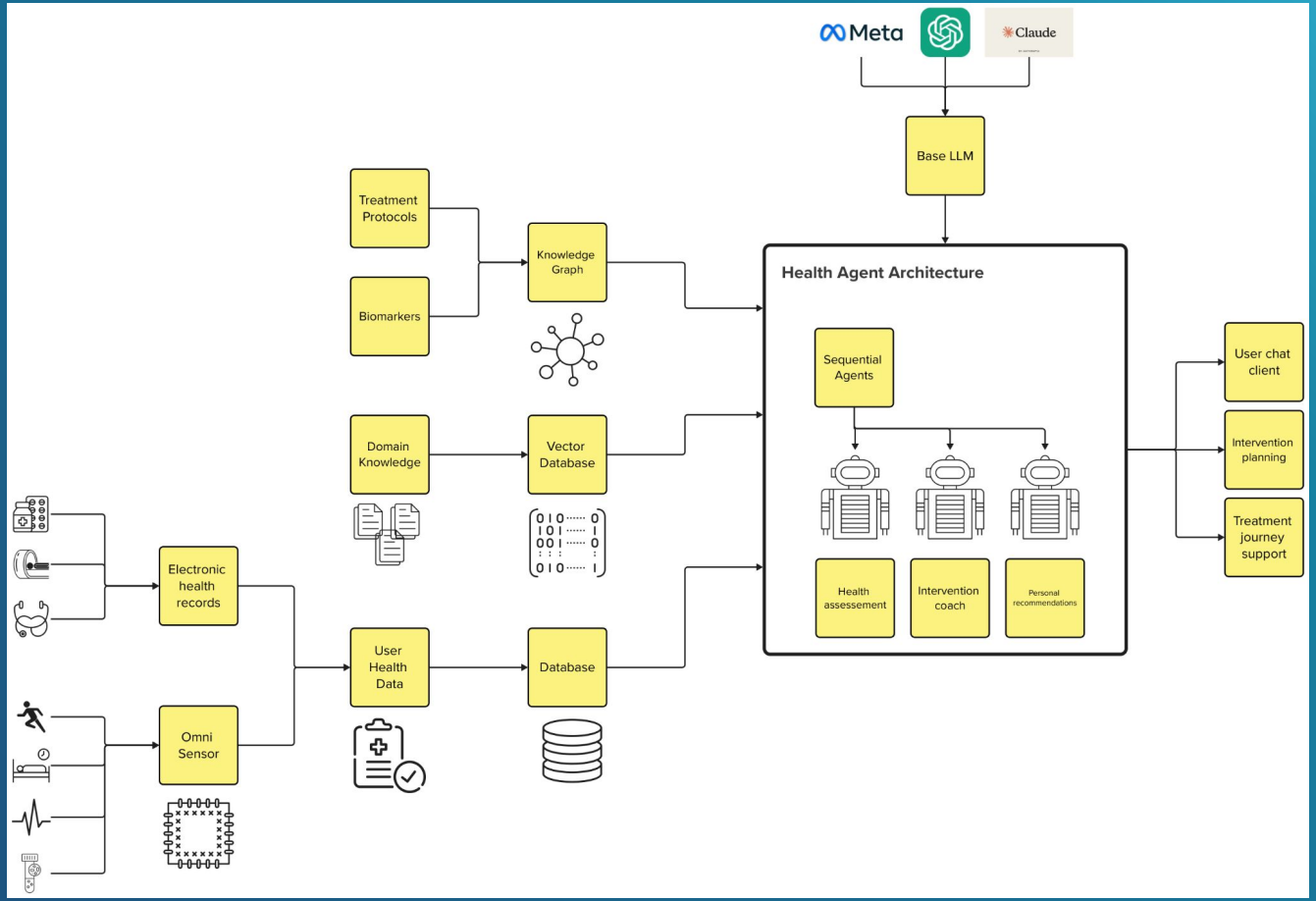
Gao *et al.*, Wearable and flexible electrical sensors for sweat analysis: a review, Microsystem and Nanoengineering (2023)

Biomarkers diffusion to ISF



Friedel *et al.*, Opportunities and challenges in the diagnostic utility of dermal interstitial fluid, Nature Biomedical Eng. (2022)

Health Agent Architecture:



Competitors in Wearables:

Feature/Characteristic	Apple Watch	Fitbit Sense	Garmin Venu 2	Withings ScanWatch	Samsung Galaxy Watch 4	Dexcom G6	Abbott FreeStyle Libre	GlucoTrack	Lumen
Device Type	Smartwatch	Smartwatch	Smartwatch	Smartwatch	Smartwatch	Glucose Monitor	Glucose Monitor	Glucose Monitor	Metabolic Tracker
Fitness Tracking	✔	✔	✔	✔	✔	✘	✘	✘	✘
Heart Rate Monitoring	✔	✔	✔	✔	✔	✘	✘	✘	✘
ECG Monitoring	✔	✔	✘	✔	✔	✘	✘	✘	✘
SpO2 Monitoring	✔	✔	✔	✔	✔	✘	✘	✘	✘
Glucose Monitoring	✘	✘	✘	✘	✘	✔	✔	✔	✘
Stress Monitoring	✘	✔	✘	✘	✔	✘	✘	✘	✘
Body Composition Analysis	✘	✘	✘	✘	✔	✘	✘	✘	✘
Blood Pressure Monitoring	✘	✘	✘	✘	✔	✘	✘	✘	✘
Metabolic Tracking	✘	✘	✘	✘	✘	✘	✘	✘	✔
Unique Features	Integration with Apple	EDA sensor for stress	Advanced fitness metrics,	Medical-grade ECG, sleep	Body composition analysis,	Continuous glucose monitoring	Flash glucose monitoring,	Non-invasive glucose	Measures CO2 levels to indicate
	ecosystem, fall detection	monitoring, skin temperature	Pulse Ox sensor	apnea detection	Wear OS, blood pressure	with alerts and data sharing	real-time data, easy to use	monitoring with ultrasonic,	metabolic state
		sensor						electromagnetic, and thermal	
Market Presence	Strong global presence	Strong presence, acquired by	Strong in fitness-focused	Niche market, focus on	Strong global presence,	Leading in diabetes	Strong presence in diabetes	Emerging player,	Niche market, focus on
	and large user base	Google	market	medical-grade features	especially in Asia	management	care	specialized focus	metabolic health

Cristina

Unique technology means improved health

Cardiovascular
- Vascular flow
- Cardiac output

Blood Vessel mgmt
- Volumetric Blood Flow
- Blood Pressure
- Analysis of pulsatile part of the blood stream

Biomarkers
- Electrolytes (sodium, potassium, chloride, ammonium, and calcium)
- Metabolites (glucose, lactate, and alcohol)

Vitals
- Heart rate
- Temperature
- Motions
- ECGs

Small molecules
- Cortisol
- Urea
- Tyrosine

Hormonal

Testosterone Total/Free
Prolactin
DHEA-Sulfate
Estradiol (E2)
Luteinizing Hormone (LH)
Follicle Stimulating Hormone (FSH)
Anti-Mullerian Hormone (AMH)
Sex Hormone Binding Globulin (SHBG)

Cristina

Unique technology means improved health:

- Cardiovascular -

Pathophysiology

- Vascular flow
- Cardiac output

Biomarkers

- Electrolytes (sodium, potassium, chloride, ammonium, and calcium)
- Metabolites (glucose, lactate, and alcohol)

Small molecules

- Cortisol
- Urea
- Tyrosine

Daily Management

- Volumetric Blood Flow
- Blood Pressure
- Analysis of pulsatile part of the blood stream

Vitals

- Heart rate
- Temperature
- Motions
- ECGs

Hormonal

Testosterone Total/Free
Prolactin
DHEA-Sulfate
Estradiol (E2)
Luteinizing Hormone (LH)
Follicle Stimulating Hormone (FSH)
Anti-Mullerian Hormone (AMH)
Sex Hormone Binding Globulin (SHBG)

Cristina

Unique technology means improved health:

- Diabetes -

Physiology

- Weight gain
- Glucose excess
- Insulin deficiency/resistance

Biomarkers

- Metabolites (glucose, lactate, and alcohol)

Small molecules

- high levels of free fatty acids

Periodic Management

- A1C

Vitals

- Weight monitoring
- Glucose monitoring

Hormonal

- Insulin
- Glucagon
- Amylin
- GLP1

-

Cristina

Unique technology means improved health:

- Breast Cancer -

Pathophysiology

- DNA
- Genetic mutations

Periodic Management

- Mammogram
- Family history

Biomarkers

- Histological:
  - Hormone receptors, HER2,Ki-67
- Serological:
  - Ki-67, CA 15-3, BAX, and Bcl-2

Vitals

–

-

-

-

Small molecules

- HER2
- CDK4/6 inhibitors
- EGFR inhibitors
- Afatinib
- Cabozantinib

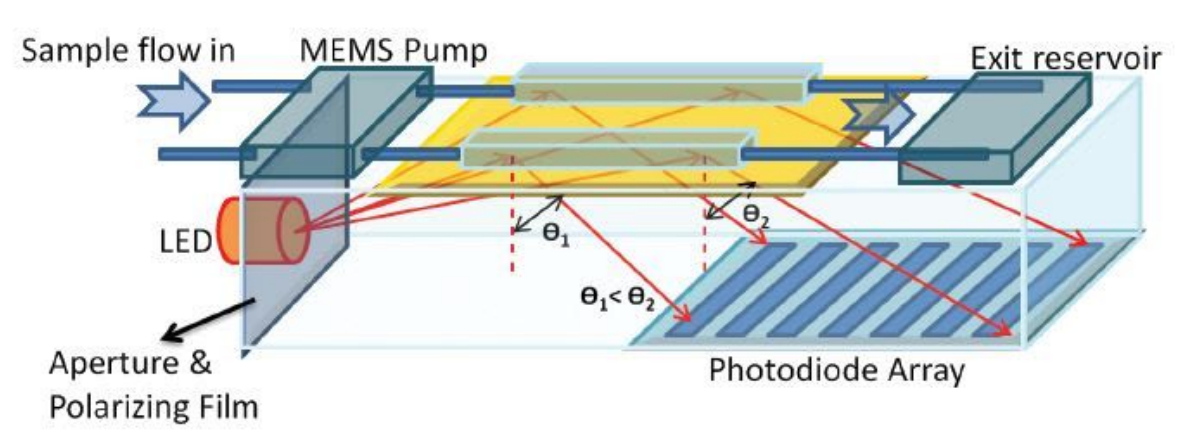
Hormonal

- Estrogen
- Progesterone

Cristina

Unique technology means improved health:

- Hardware schematics -



Low-Cost, Portable Biosensor for Blood Protein Detection

Cristina

- Unique technology means improved health:
  - Logos -

Chemical sensing for Metabolic Syndrome
Summary

1. **Biomarkers of metabolic syndrome**.
2. I**nterstitial fluid**: minimally invasive and very informative.
3. **Preliminary testing** for measuring the concentration of these biomarkers in interstitial fluid.

⇨ Stepping stones towards wearables

Targeted Markets and Use cases

Markets

Medical Devices

Consumer Technology

Use Cases

- In-hospital/Remote Patient Monitoring
- Clinical Trials
- Continuous Monitoring
- Medication Tracking

- Fitness Tracking
- Stress Management
- Sleep Analysis

*Source: IDTechEx, IDC. **Short-wave infrared.

Julian

LLM modeling