Edge-To-Cloud Digital Twins Aiming At Future Personalized, Preventive and Participatory (P3) Healthcare

Adrian M. Ionescu, EPFL

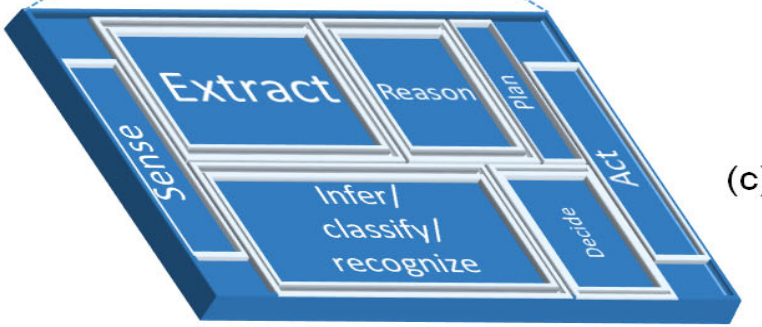
Outline

- **Edge-to Cloud** information processing and **Digital Twins**
- Why this is important for **P3 healthcare?** What is the needed technological platform?
- **Integrated (bio)sensors** for **wearables & implantables**
  - ❑ electrolytes
  - ❑ hormones: cortisol
  - ❑ proteins
- **Digipredict project**
  - ❑ Predicting cytokine storms and cardiovascular implications
  - ❑ Biomarkers, organs on chip and AI
- **Conclusions**

Edge-to-Cloud information processing

(a)

(b)



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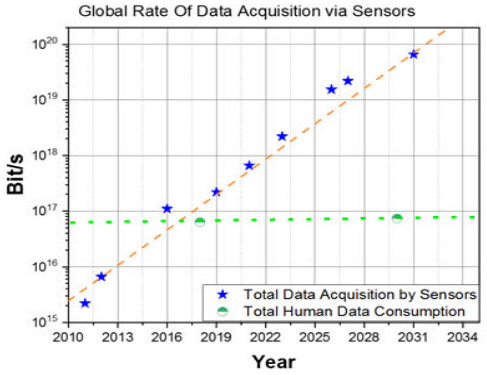
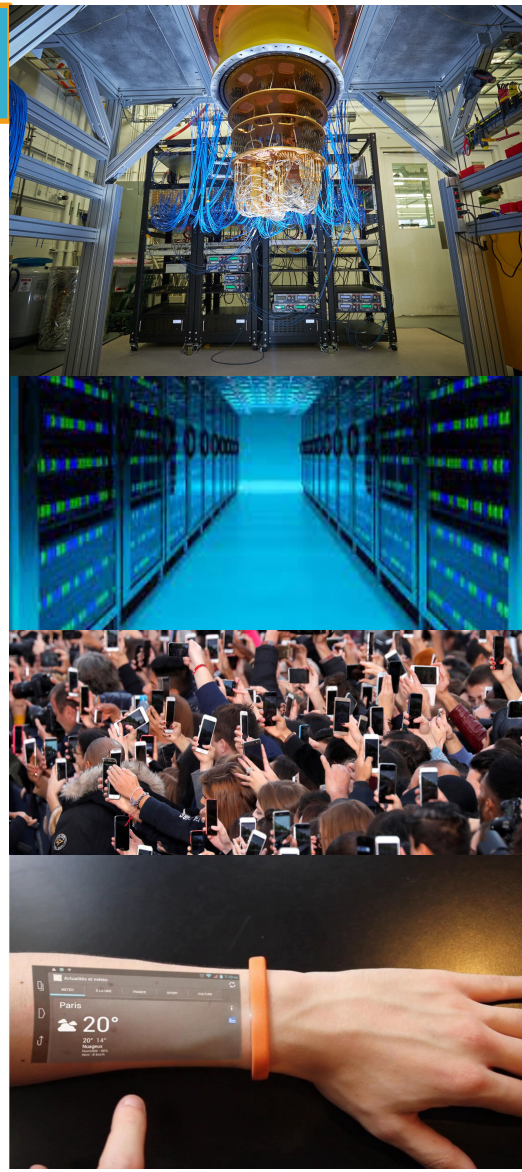
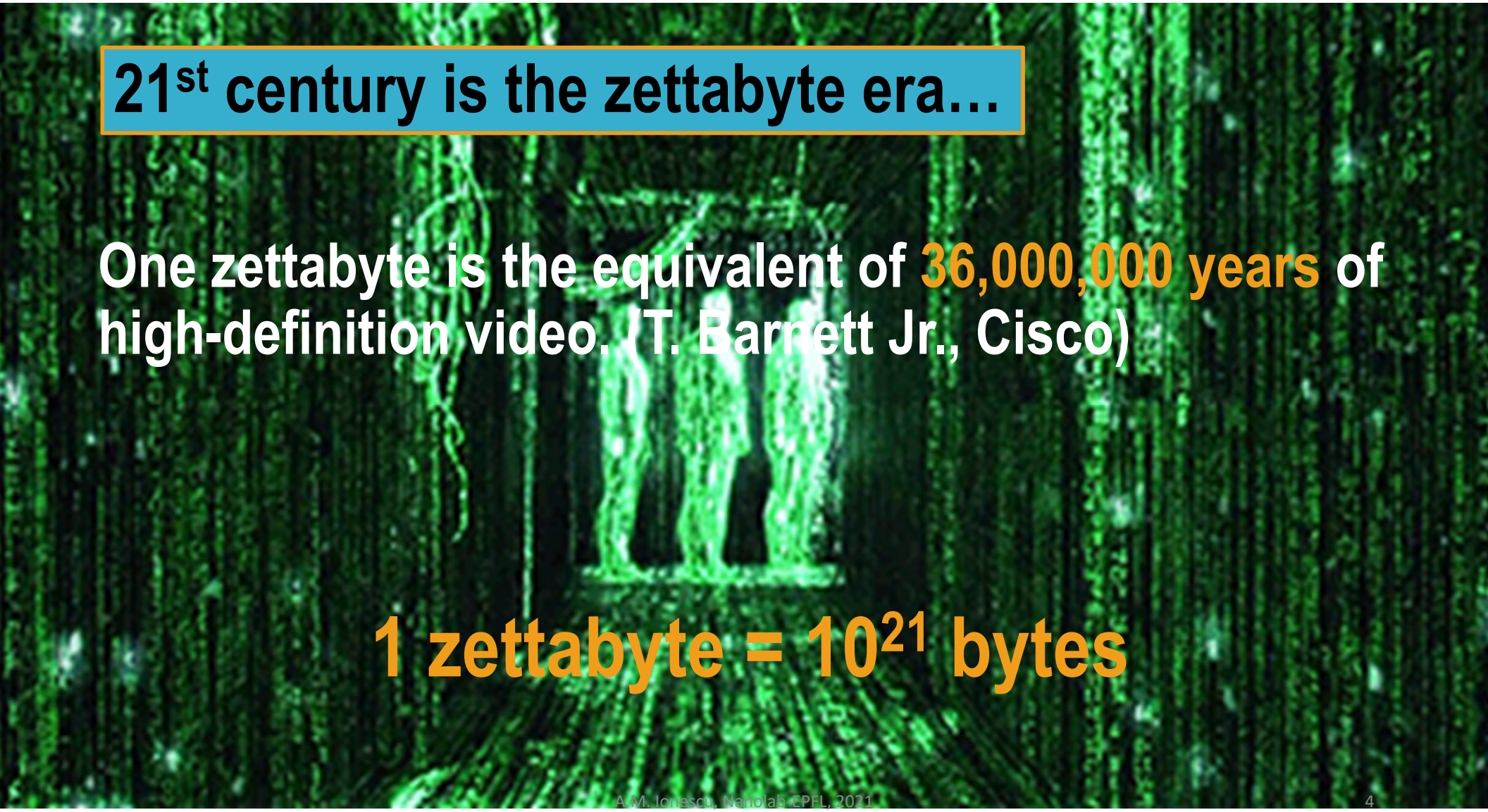






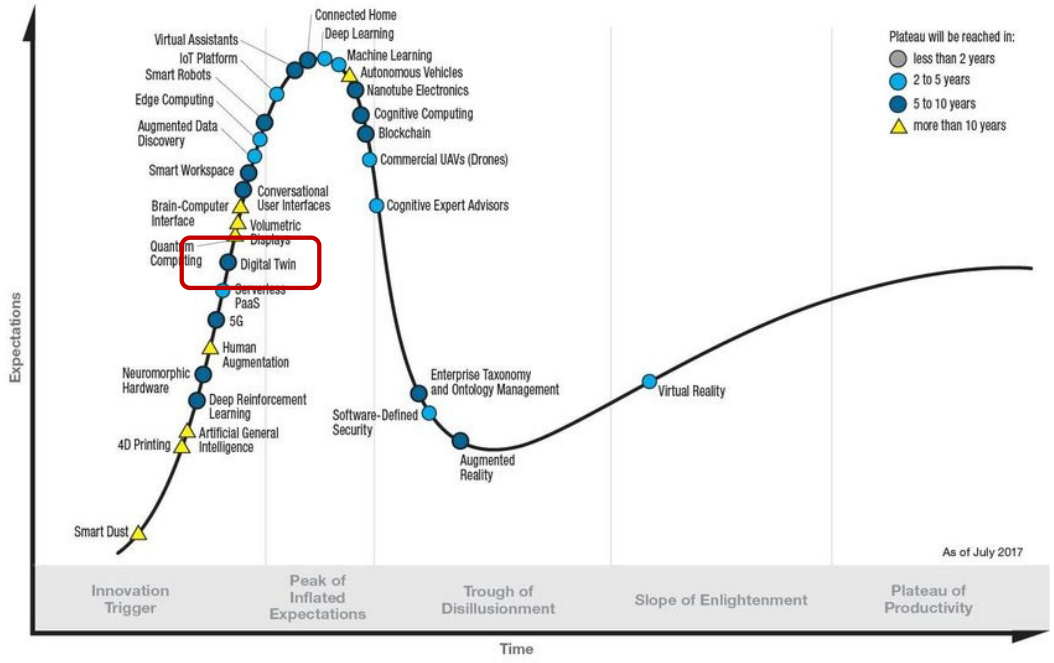
21st century is the zettabyte era…

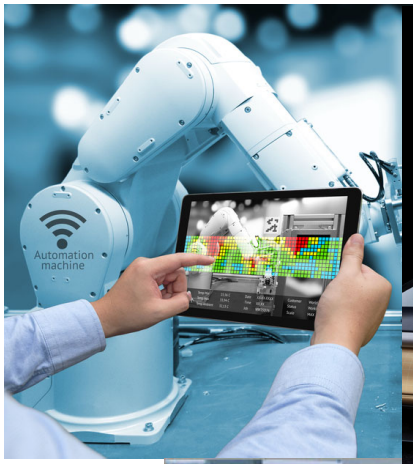
One zettabyte is the equivalent of 36,000,000 years of high-definition video. (T. Barrett Jr., Cisco)

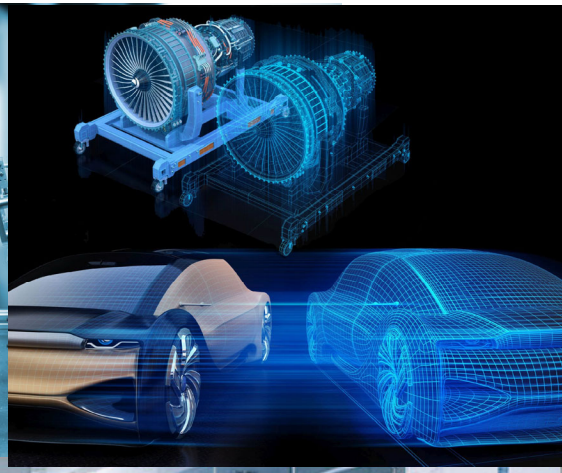
1 zettabyte = 10^{21} bytes

Digital Twins as mainstream use for future digitalization

- **Digital Twins** **of all objects, products and services**
- By 2022, over 2/3 of companies that have implemented IoT will have deployed at least one digital twin in production



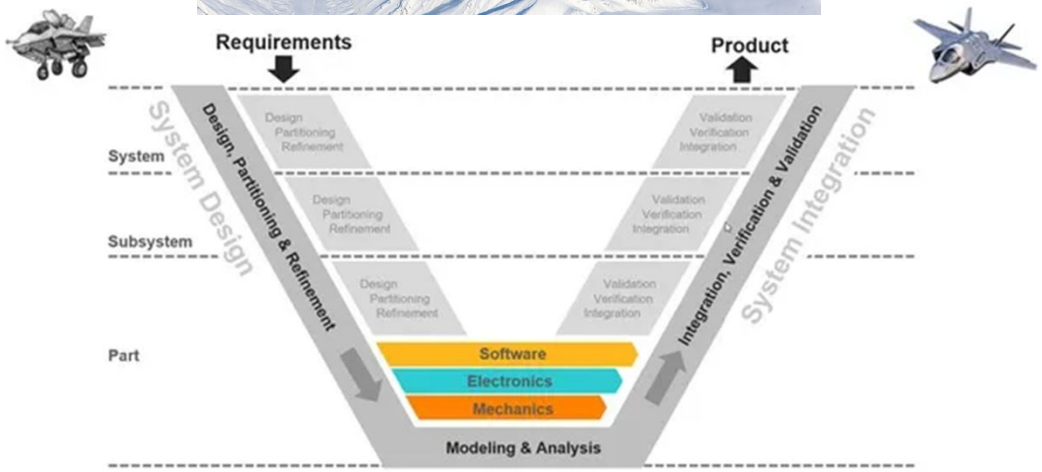




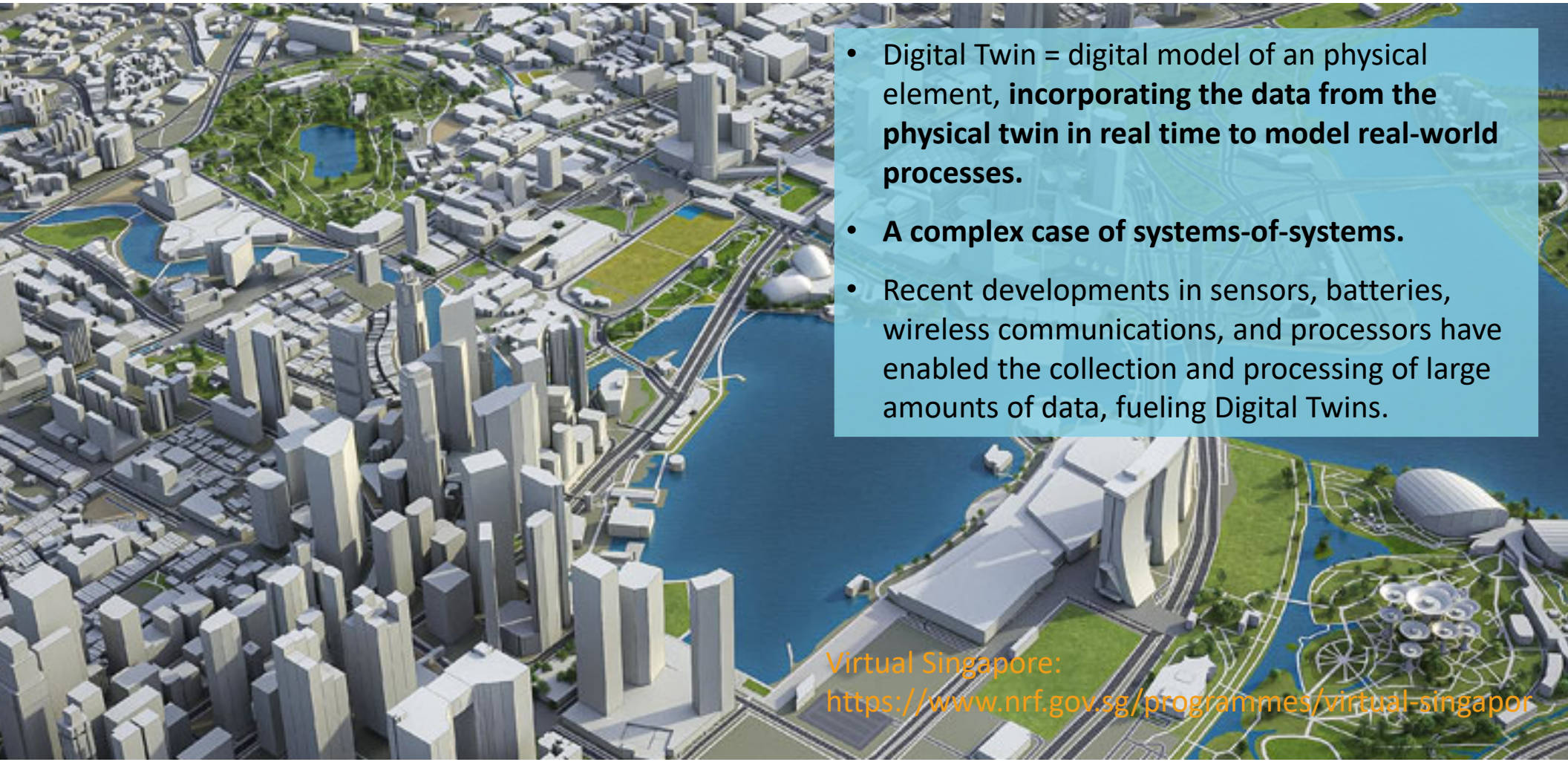
A.M. Ionescu, Nanolab-EPFL, 2021

System-of-Systems need Digital Twins: the F-35

- **200,000 parts** made by **1,600 suppliers**
- houses **3,500 integrated circuits**
- **>20,000,000 lines of software** code.
- designers face **hugely intricate hardware/software interaction** and interactions at the system level across **multiple domains**—mechanical, electronic, thermal, etc.



Can Digital Twins Transform Cities Environment?



- Digital Twin = digital model of an physical element, **incorporating the data from the physical twin in real time to model real-world processes.**
- **A complex case of systems-of-systems.**
- Recent developments in sensors, batteries, wireless communications, and processors have enabled the collection and processing of large amounts of data, fueling Digital Twins.

Virtual Singapore:
https://www.nrf.gov.sg/programmes/virtual-singapor

Digital Twins of All Humans

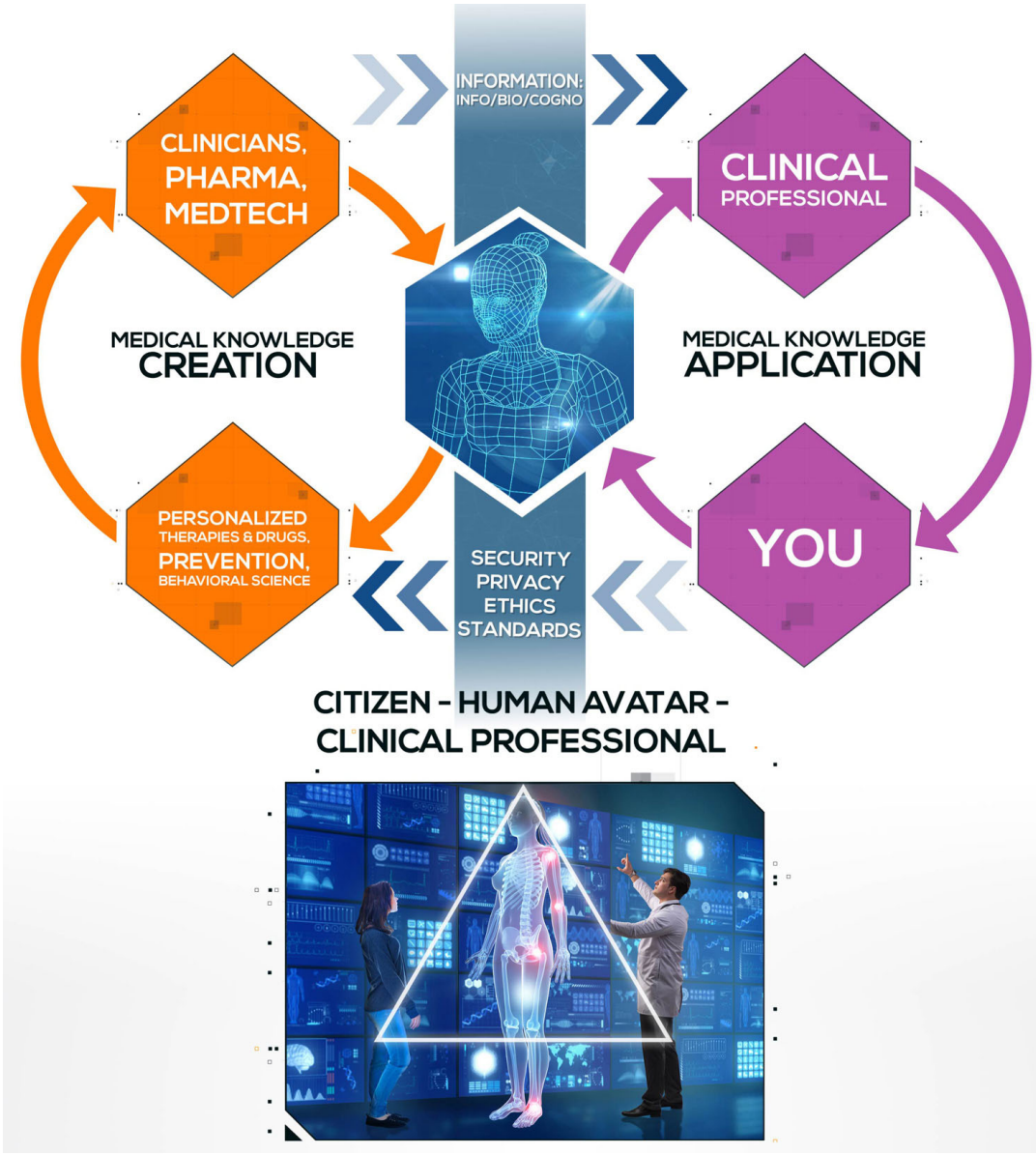
- Reactive healthcare is unsustainable
- Digital twins will apply to people too…
- Towards a more sustainable Personalized, Preventive and Participatory (P3) Healthcare

The missing link…

… for **breaking barriers** between Medical Knowledge Creation and Medical Knowledge Application

… for creating the **triangle Citizen – Human Avatar – Clinical Professional**

… for a **sustainable** healthcare in 21st Century

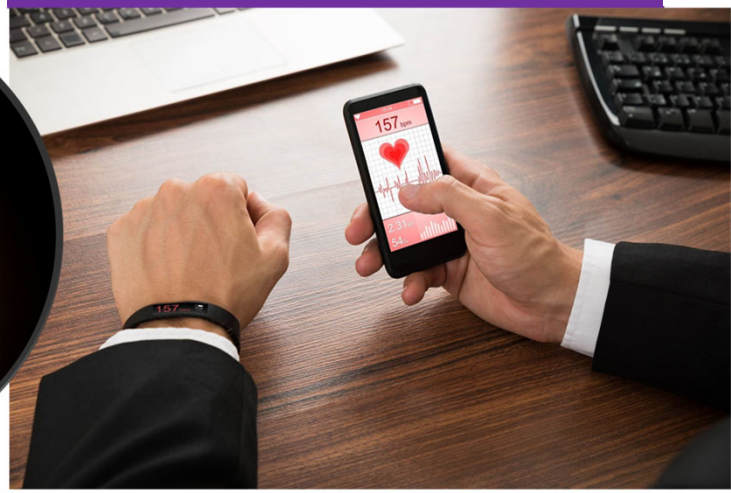


Thinking out-of-the-box the future of P3 healthcare

- What's the **real opportunity** for future Digital Twins in P3 healthcare?

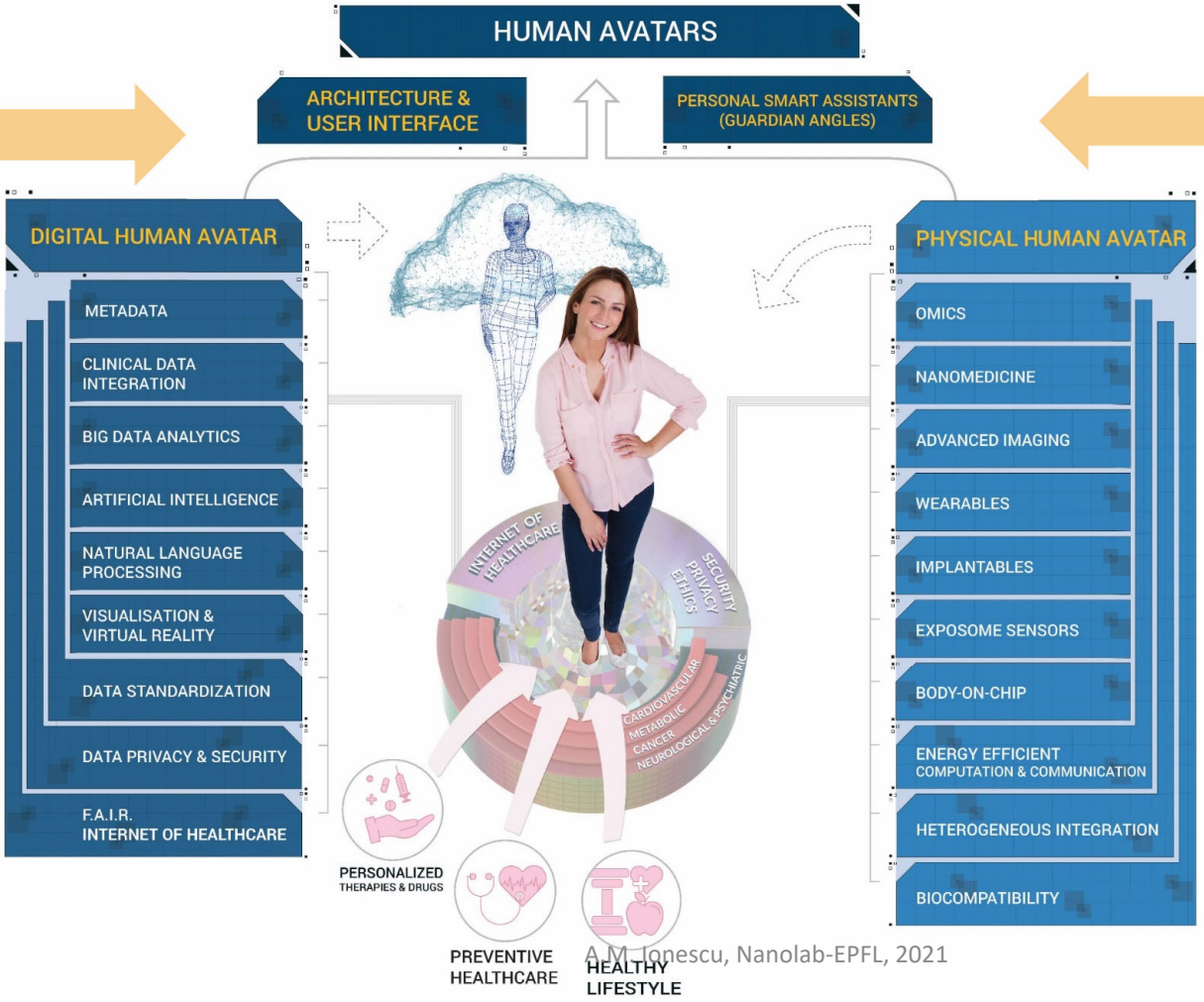
The value of being sick

The value of NOT being sick = healthy?



Edge-to-Cloud Digital Twin Integrative Technology Platform

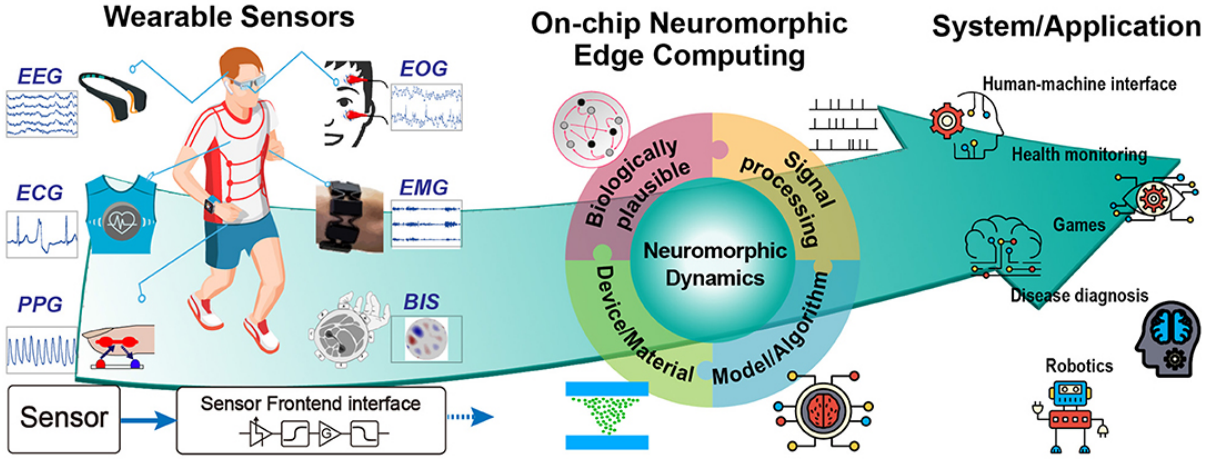
Big Data
AI
IoH



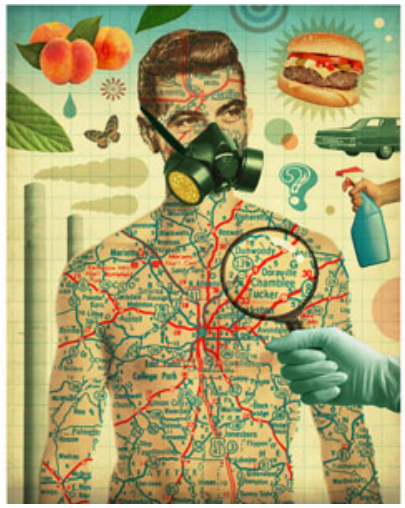
Data
Generator
Technology
Body-On-Chip

Technologies for Edge Artificial Intelligence…

- **Requirements**
  - Real-time
  - Energy efficient
  - Physical footprint
  - Robustness
  - Security and privacy
- **Functions**
  - Sense
  - Extract
  - Classify
  - Reason and decide
  - Act
- **How? Think future platforms:**
  - CPU &digital accelerators
  - In-memory
  - In-sensor



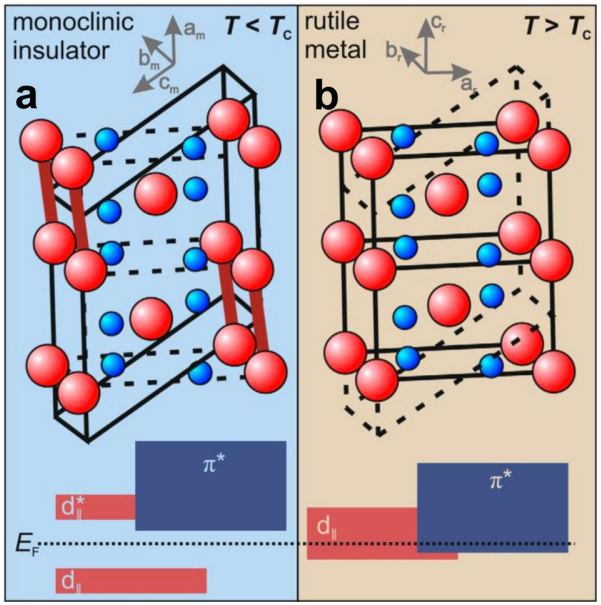
E. Covi et al., Front. Neurosci., May 2021.

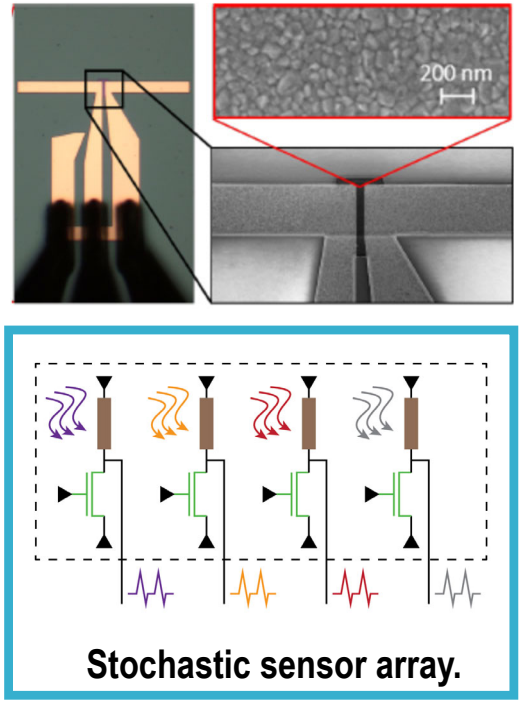


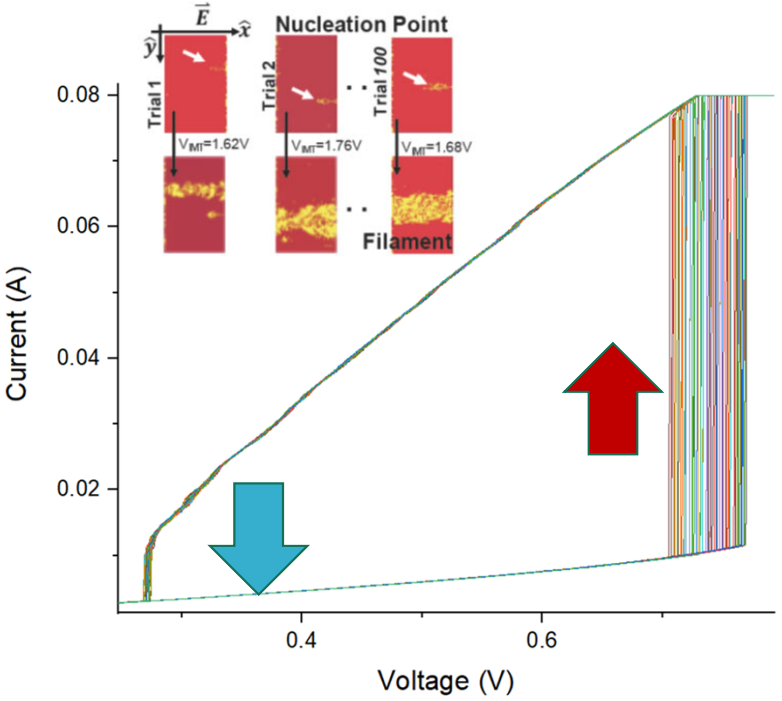
Exposome: a measure of the environment's impact on health.

Ex#1: Stochastic spiking sensors: GHz to THz sensing

- Combined Mott-Peierls stochastic IMT/MITphase transitions in vanadium dioxide (VO_2) exploited to build memristive sensors.

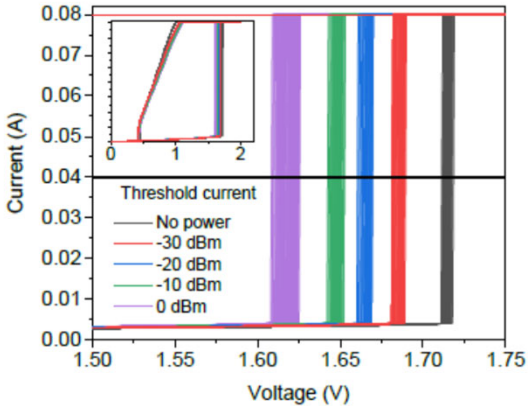


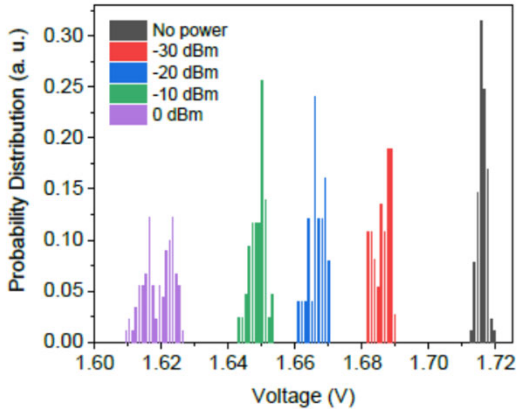


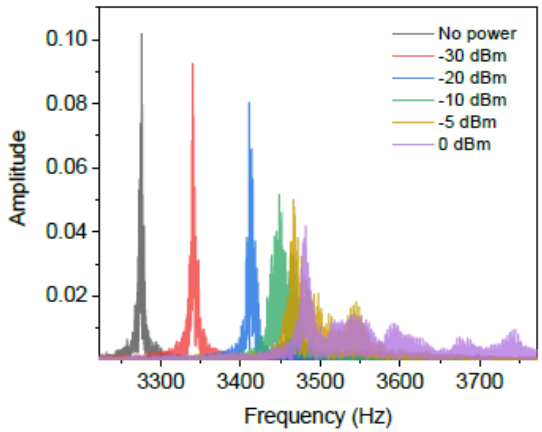


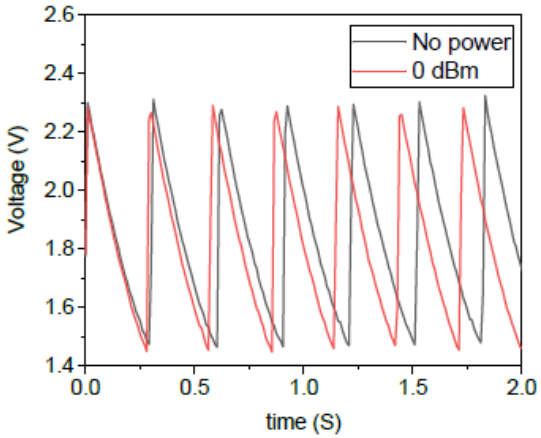
F. Qaderi et al, in revision, Nature Com, 2021.

Millimeter-wave to near-terahertz spiking sensors based on vanadium dioxide IMT/MIT transitions

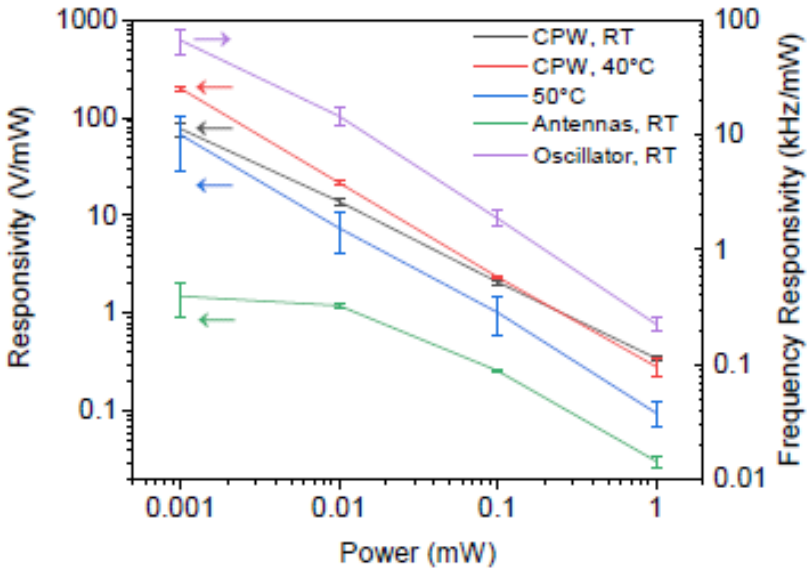




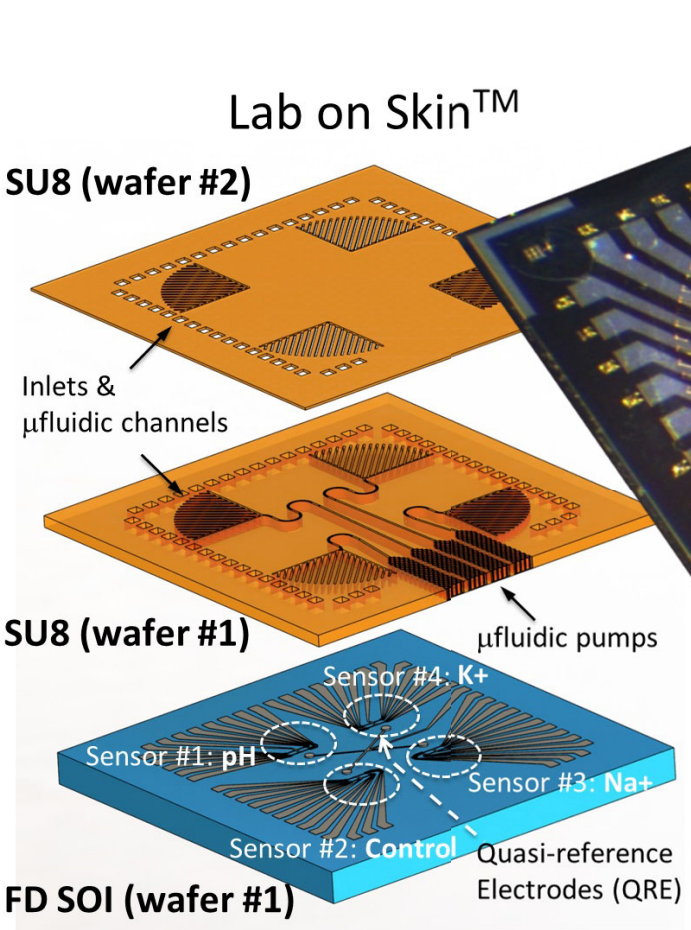




- Capable to detect with record energy efficiency any **wave power from GHz to THz**.
- Extendable to IR and UV sensing, for **event detection.**
- Inspired by insect spike signaling.

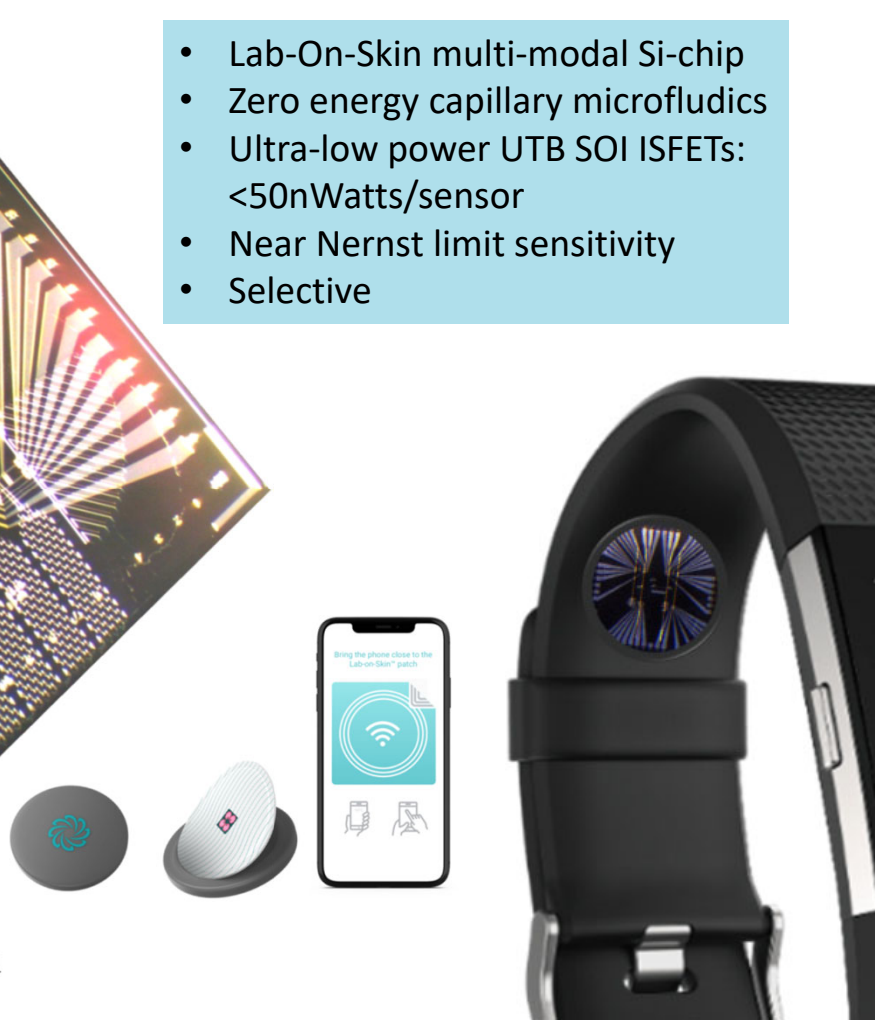


Ex#2: Real-time multi-modal sweat analysis

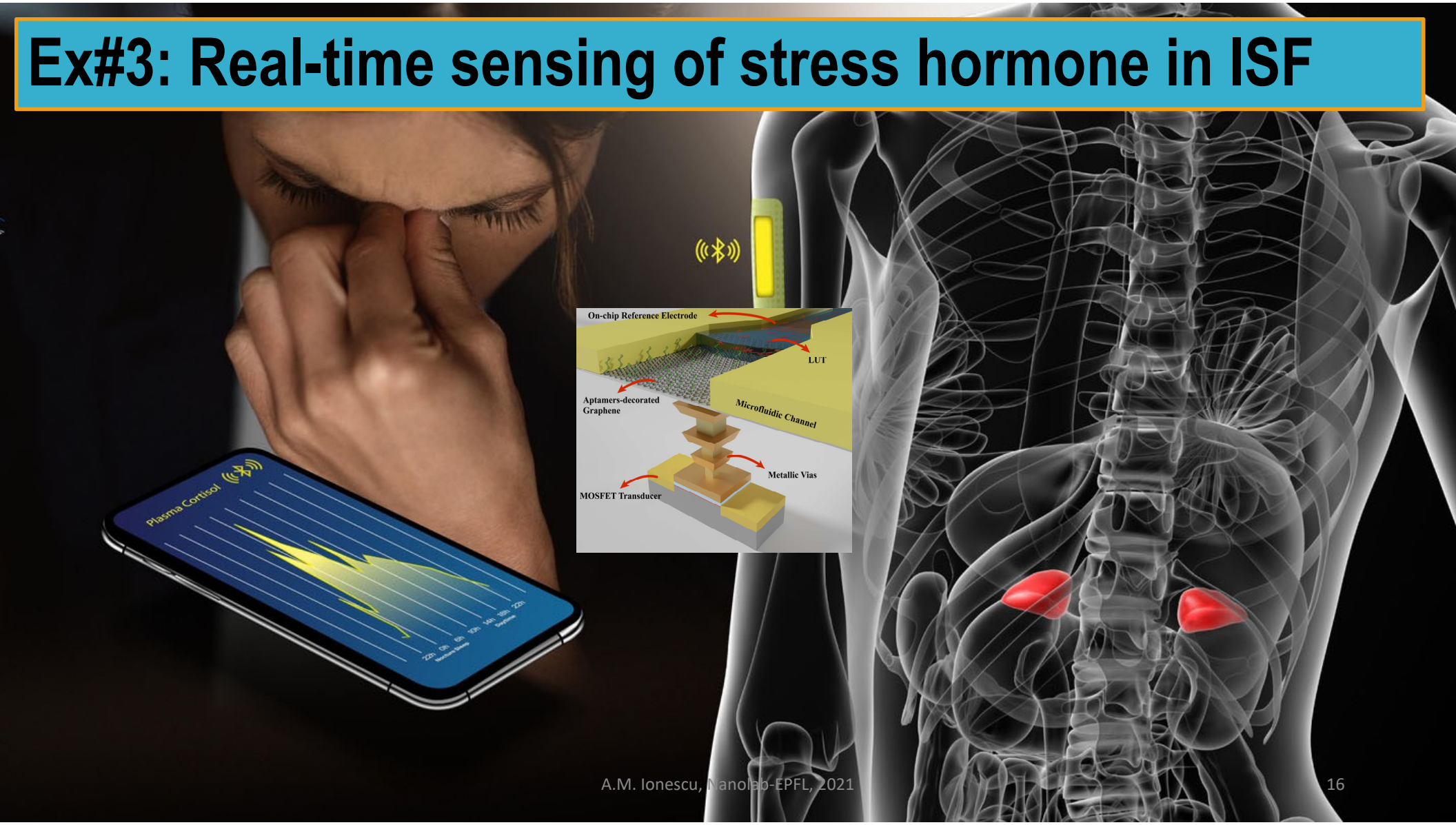


F. Bellando et al., IEDM 2017.

- Lab-On-Skin multi-modal Si-chip
- Zero energy capillary microfludics
- Ultra-low power UTB SOI ISFETs: <50nWatts/sensor
- Near Nernst limit sensitivity
- Selective



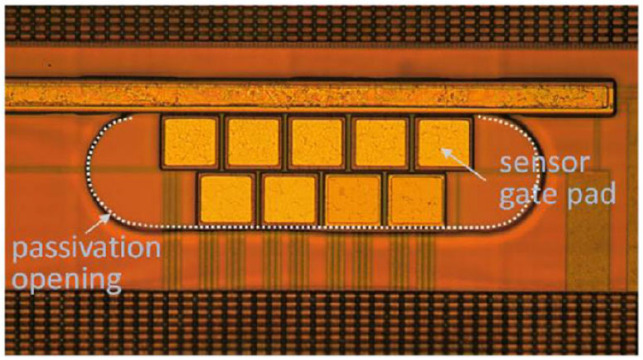
Ex#3: Real-time sensing of stress hormone in ISF

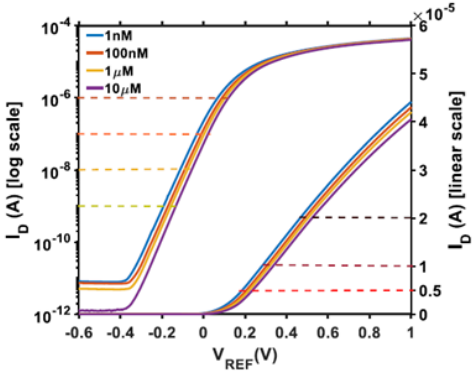


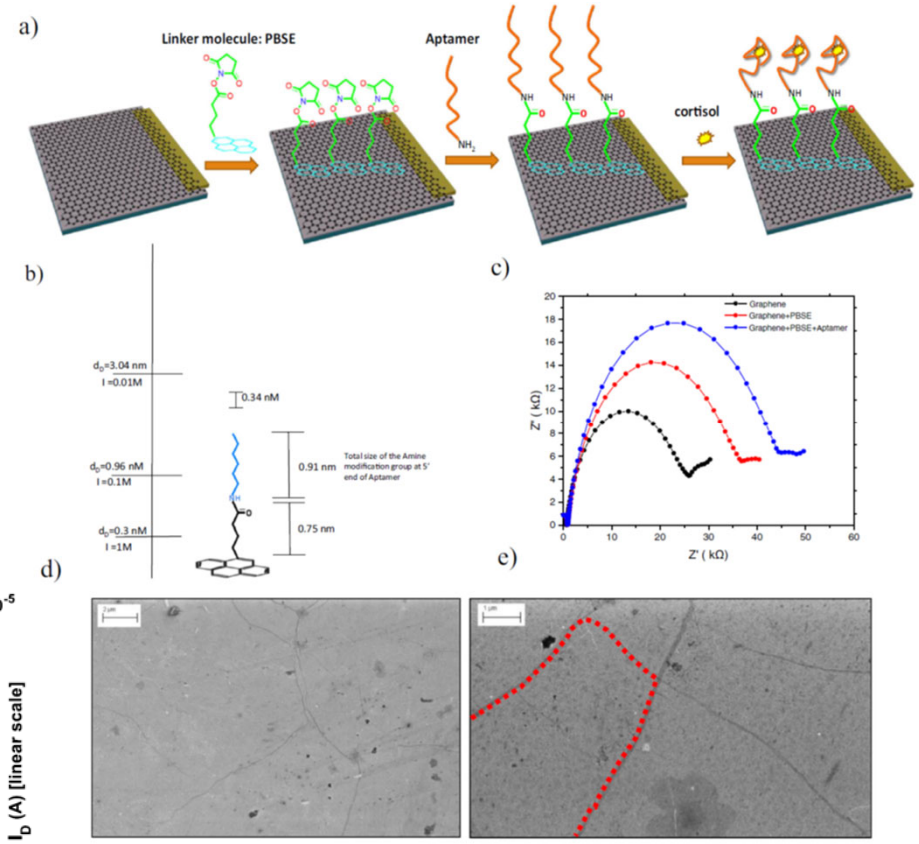
Aptamer/graphene cortisol 2D sensor

Aptamer-based functionalized gate metal electrodes in BEOL

- ✓ Synthesized *in vitro*
- ✓ Low batch variability
- ✓ Highly stable
- ✓ Less sensitive to T
- ✓ Tailored for varying degrees of affinity
- ✓ Covalently immobilized



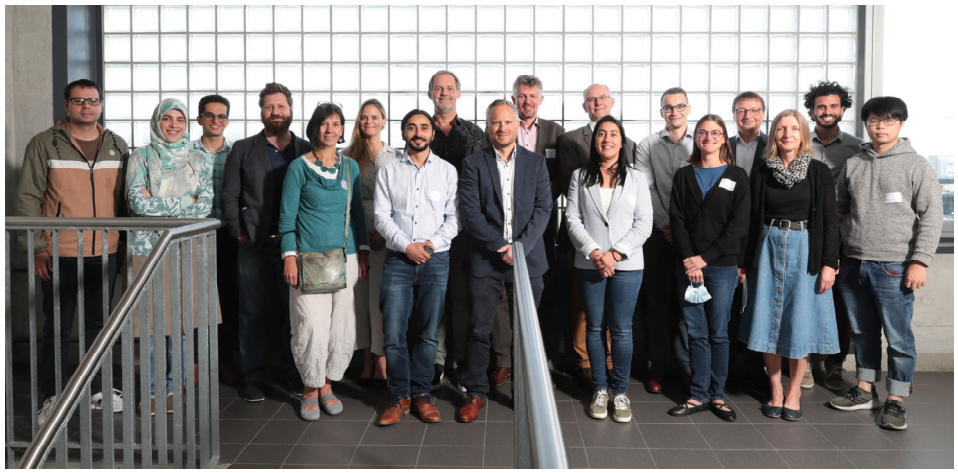




N. Shokoofeh and A.M. Ionescu, Coms Mat 2020.

The DIGIPREDICT FET Proactive Project

DIGIPREDICT proposes the first of its kind Edge AI Digital Twin, designed, developed and calibrated on experiments, based on the interaction between Digital Biomarkers, Organ-On-Chip (OoC) and Artificial Intelligence (AI) at Edge technologies, with the goal of identifying a specific dynamic digital fingerprint of the complex disease progression and building and assistive tools for medical doctors and patients. We will combine scientific and technical excellence in multiple disciplines and we aim at building a new interdisciplinary community in Europe centred on Digital Twins.

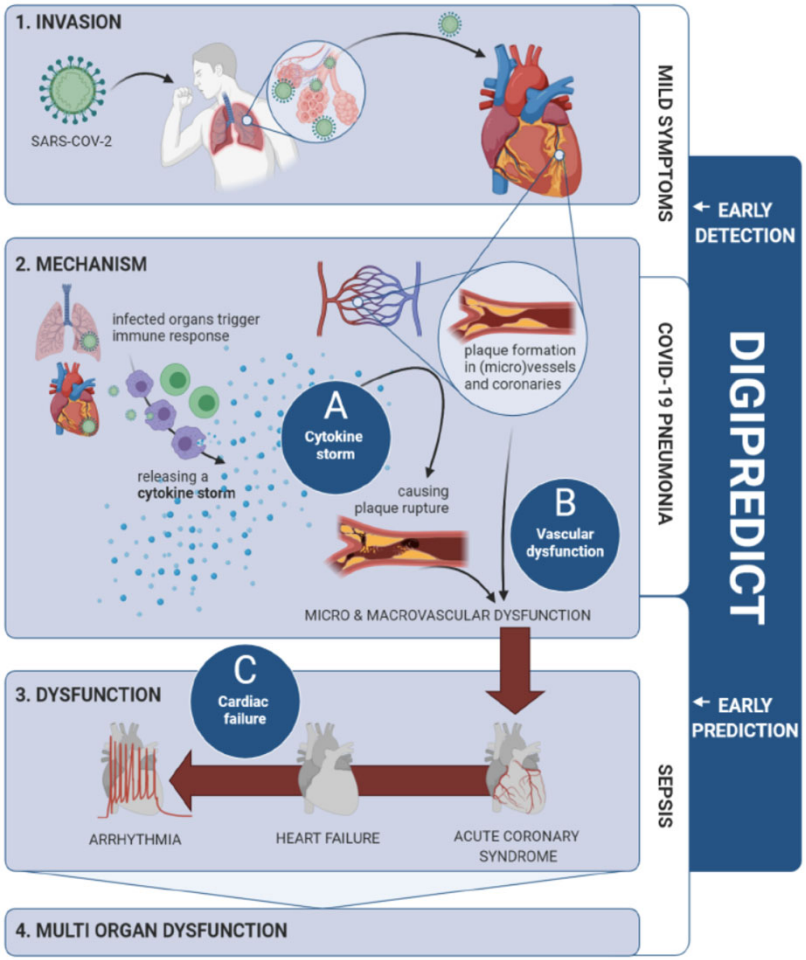


A.M. Ionescu, Nanolab

DIGIPREDICT develops digital-twin technology improving diagnostics methods for COVID-19

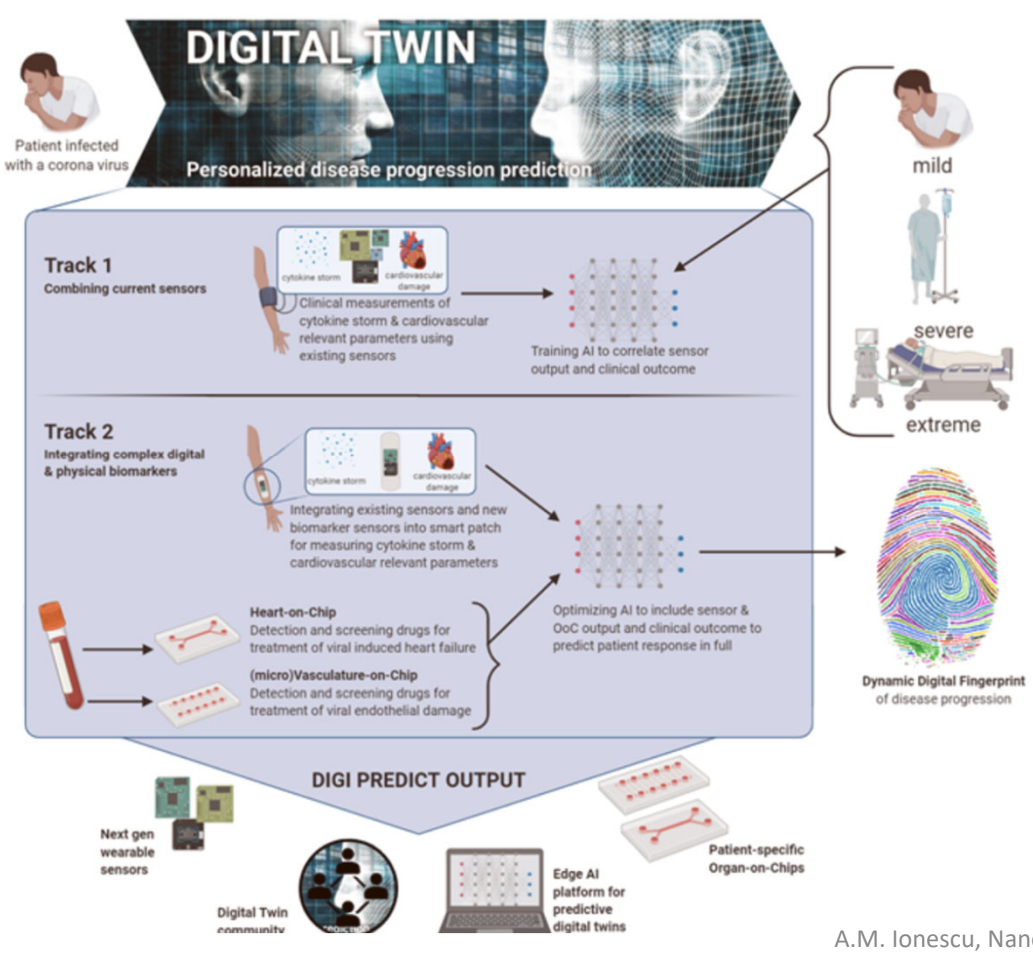
https://ec.europa.eu/newsroom/horizon2020/items/699059

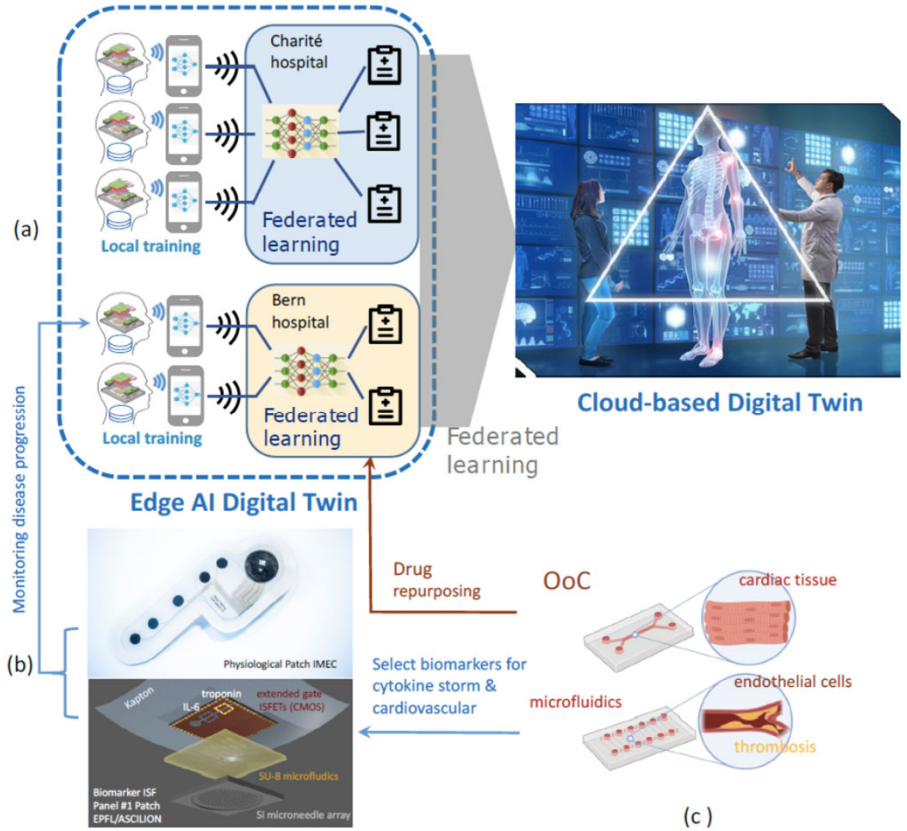
DIGIPREDICT: Digital Twins @ the Edge



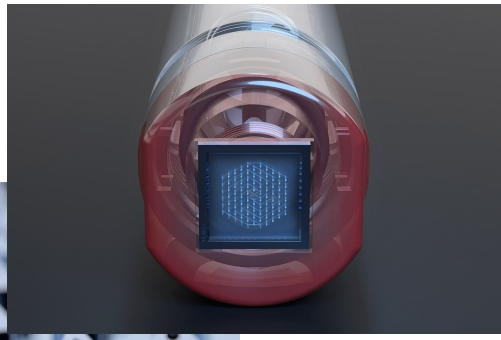
- **Early detection**: High risk COVID-19 patients can be early identified from **Digital Fingerprints**
- **Personalized therapy**: Supportive therapy as well as referral decisions can be personalized and administered to patients with the highest need.
- **A new Digital Twin tool for P3 Healthcare**: empowers citizens and provide medical doctors with a new assistive and predictive healtcare tool, the Digital Twin from Edge to Cloud.
- Building a broad **Digital Twin interdisciplinary community** in Europe.

The DIGIPREDICT concept, implementation & validation

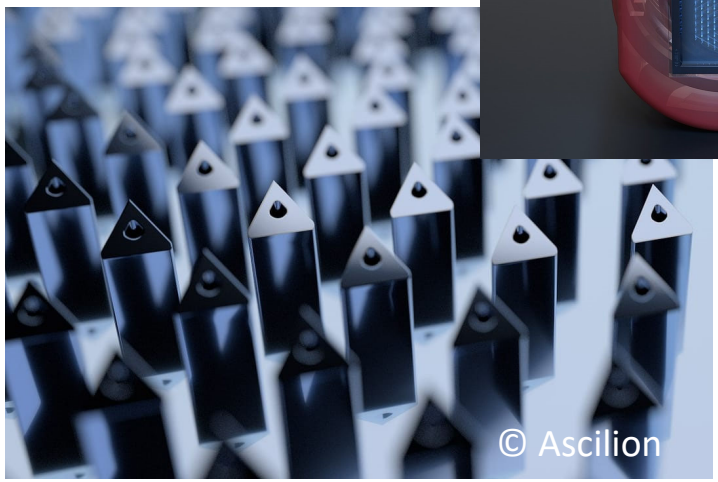




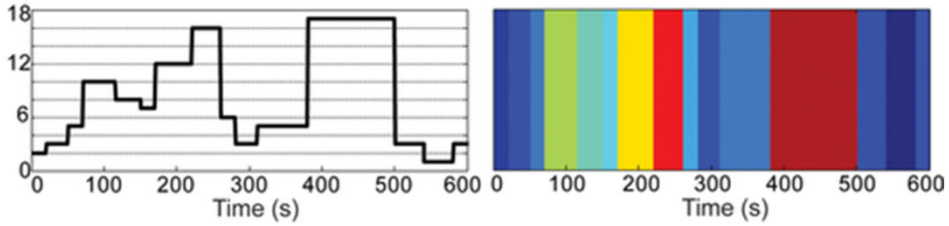
Ex#4: Digipredict biomarker smart patch



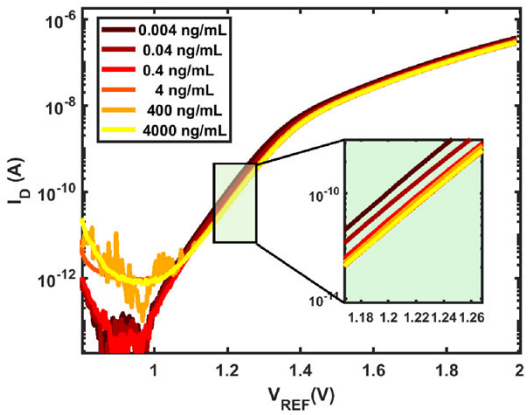
Develop **sensors co-integrated with MEMS needle arrays for collecting ISF and detecting biomarkers** relevant for cytokine storm and cardiovascular system:

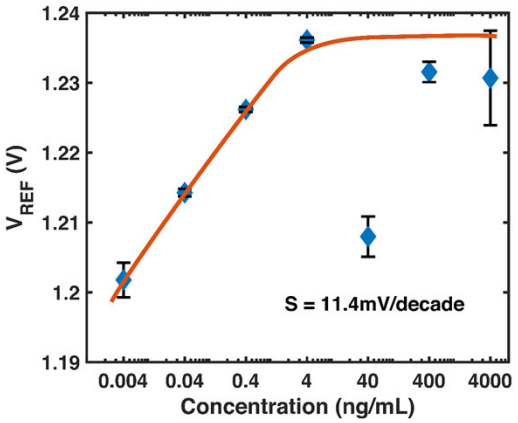


- Multimodal sensing: IL-6 and troponin + Na+, K+
- Dynamics of change/monitoring
- Enable quasi-cont. monitoring
- Wirelessly connected
- ML algorithm & visualisation interface

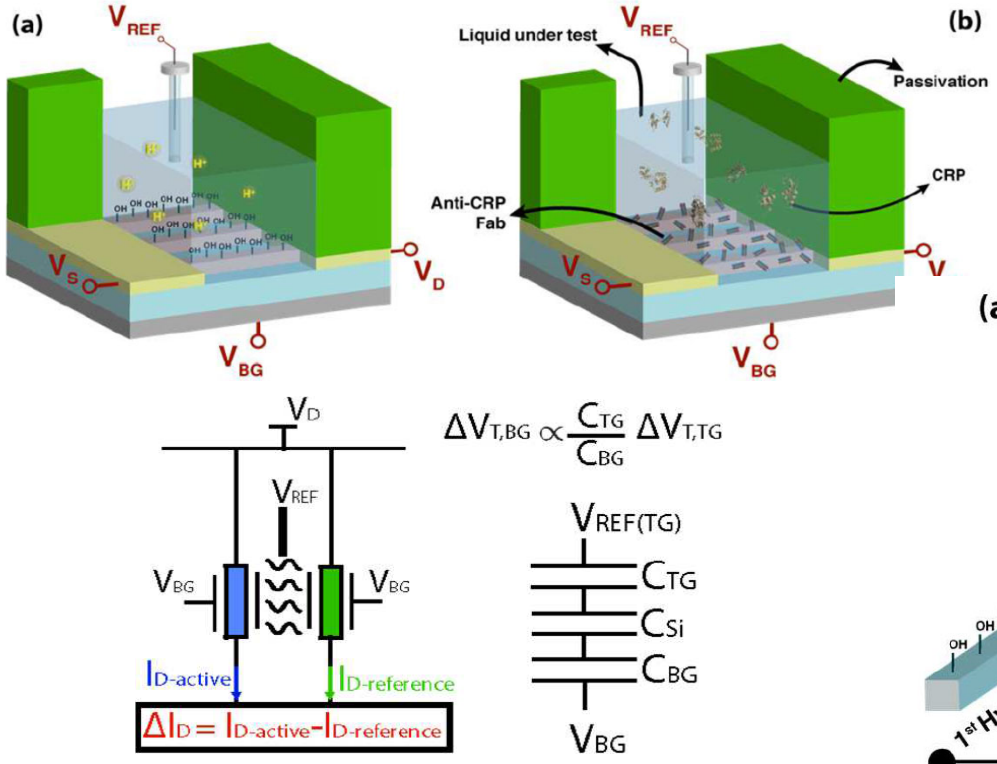


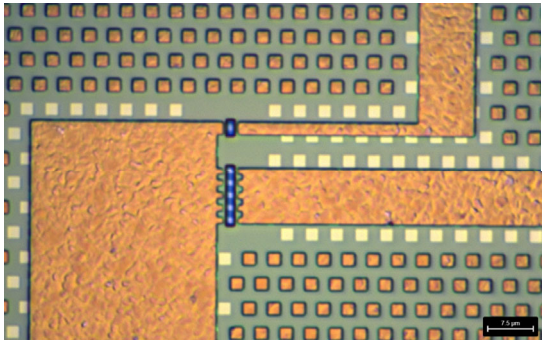
Troponin detection in-vitro

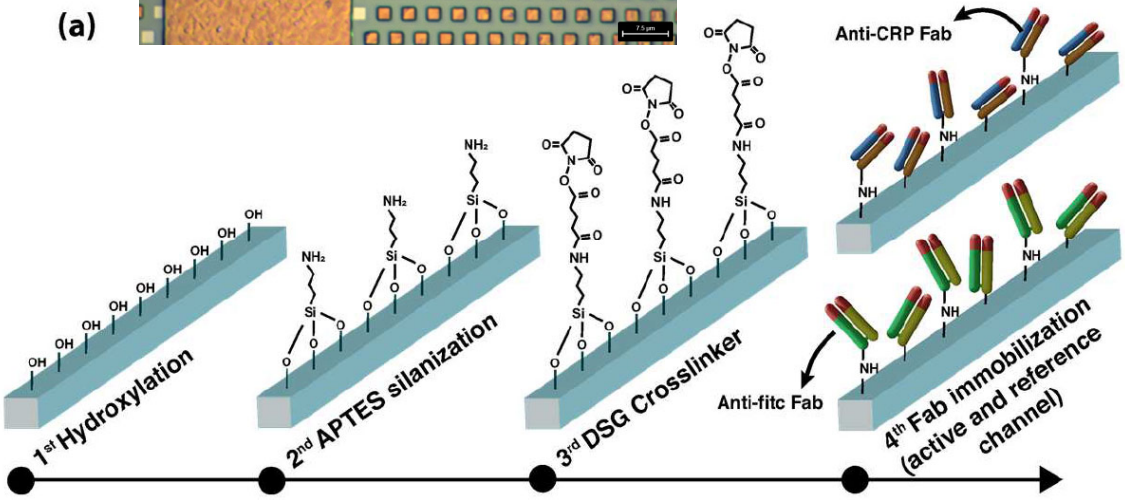




Detection of inflammation markers: C-Reactive protein with nanobody functionalized Si NW FETs



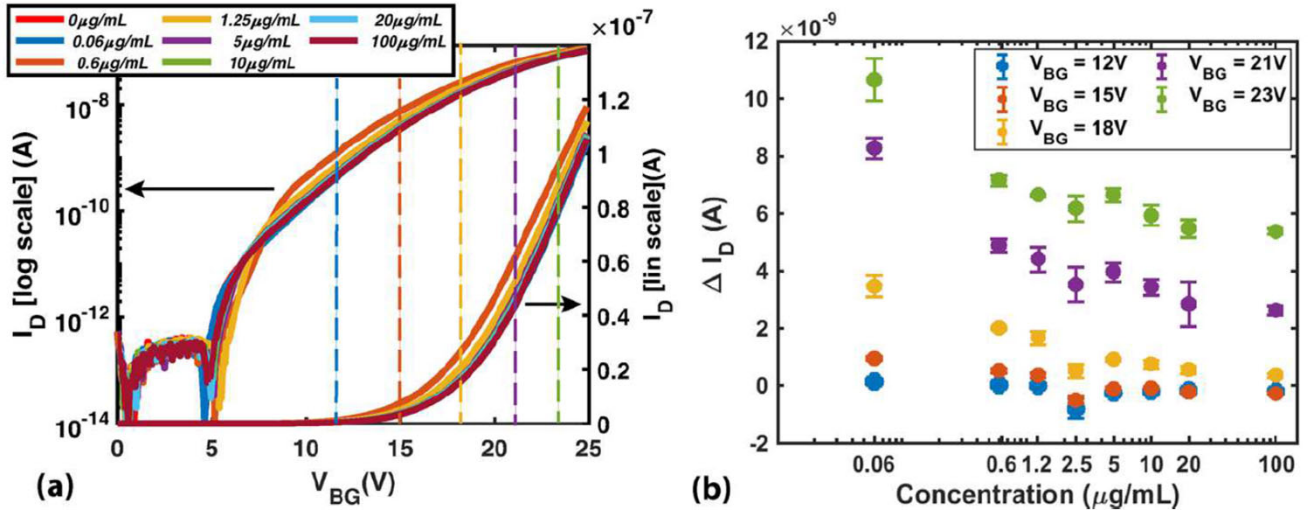




L. Capua et al, to appear @ IEDM 2021.

C-RP sensor proof of concept

	Transducer Technology	Capturing Probes	Detection Range	Sample Dilution	Protein Sensitivity	pH Sensitivity	Reference Subtaction Mode	Drift Assesment in Buffer
Lee et al. 2016 [4]	HEMT	Antibodies	0.01~1000ng/ml	Needed	Not reported	Not investigated	No	No
Kutovyi et al. 2020 [5]	SiNWs (No BG amplification)	Antibodies	0.0001~100ng/ml	Needed	~20mV/decade	32.5mV/pH	No	No
Park et al. 2019 [6]	Capacitive	RNA Aptamers	100~500pg/ml	Needed	Not reported	Not investigated	No	No
Capua et al. (this work)	SiNWs (**BG amplification**)	Fab Antibodies fragments	0.5~100ug/ml Physiological Range	Not Needed	1.2nA/decade	Super-Nernstian ~3V/pH	YES	YES



Conclusions

- **Digital Twins** expected to enable the 21st century paradigm change for a sustainable P3 healthcare: needs innovations in hardware-software co-design and multidisciplinary platforms.
- **Biosensors and Exposome sensory systems** as Edge AI data generators for multi-modal, real-time sensing.
- **Digipredict Project: interception of the trajectory of cytokine storm and cardiovascular implications**. Technology to be developed in 2 years and first validations within next 4 years.

Thank You!