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

Adrian M. Ionescu, EPFL
• 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) Diagram illustrating the edge-to-cloud information processing concept. The triangle represents the transition from edge to cloud with increasing data processing capacity: CMOS (trillions), Neuromorphic (billions), Quantum (millions), and Cloud (billions). The cloud represents very high processing capacity (>10^17 FLOPS) and AI, with high latency (x10^9). The edge shows extreme edge processing (>10^8 IPS).

(b) Diagram showing the process of data acquisition (extract, sense, infer, classify, recognize).

(c) Graph depicting the global rate of data acquisition via sensors over time, showing exponential growth.

(d) Image showing a real-world application of edge-to-cloud processing, such as in the cloud data center and a live event with many people using mobile devices.
21st century is the zettabyte era...

One zettabyte is the equivalent of $36,000,000$ years of high-definition video. (T. Barnett 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.

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 NOT being sick = healthy?

The value of being sick

- Creation: $75bn
  New ways to discover drugs

- Diagnosis: $7.2tr
  Diagnose at earlier stages, saving lives and money

- Prevention
  Whole-life tracking, management and health
Edge-to-Cloud Digital Twin Integrative Technology Platform

Big Data
AI
IoH

Data Generator Technology
Body-On-Chip

© Health EU
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

---

**Exposome**: a measure of the environment’s impact on health.
Ex#1: Stochastic spiking sensors: GHz to THz sensing

- Combined Mott-Peierls stochastic IMT/MIT phase transitions in vanadium dioxide (VO$_2$) exploited to build memristive sensors.

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

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

F. Bellando et al., IEDM 2017.

A.M. Ionescu, Nanolab-EPFL, 2021
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.

A.M. Ionescu, Nanolab-EPFL, 2021
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.

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 healthcare 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

© Ascilion
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

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

A.M. Ionescu, Nanolab-EPFL, 2021
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 the next 4 years.

Thank You!

A.M. Ionescu, Nanolab-EPFL, 2021