This workshop will provide an interchange forum on system design, design experiences, EDA, and design methodologies for both of industry and academy. Presentations on theoretical aspects, practical issues, case studies and applications are encouraged. The workshop gives an opportunity for presentation and discussion of advanced work and research. Works in progress and new ideas are also welcome. Special sessions for hot topics will be provided. Proposals for the topics are welcome.

Areas of Interest include, but are not limited to:

- System Design and Design Experiences, Industry Experiences
- Software/Hardware Design for Embedded Systems, Cyber-Physical Systems, IoT, etc.
- New Design Methodologies for MEMS, Bioengineering, Automobile, Environment, etc.
- Reconfigurable System Design
- Design for Manufacturability, Reliability, Security, etc.
- Behavioral/Logic/Layout Synthesis
- Test, Verification and Simulation
- Analog and Mixed-Signal Design

Submission of Papers:
Prospective authors are invited to submit original papers of 3 to 6 pages (for full papers*) or of 2 pages (for short papers), electronically via the web site below. Detailed instructions for paper submission will be available at the web site. Official language is English.

* Best Paper Awards will be selected from full papers.

Key Dates:
- Submission due date: June 13 (Mon), 2016 (Extended)
- Notification of Acceptance: August 5 (Fri), 2016
- Final paper due date: September 9 (Fri), 2016

Questions should be directed to:
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For More and Latest Information:
http://sasimi.jp/
Outline

▲ Introduction
   ▼ Trends in Engineering and Medicine
   ▼ Examples from the medical practice

▲ Cyber-medical systems
   ▼ Sensors
   ▼ Circuits and architectures
   ▼ Systems

▲ Conclusions
The megatrends

▲ Relentless growth of computing, storage and communication technologies
  ▼ Inexpensive terminals providing ubiquitous services
▲ Biomedical sciences becoming more quantitative
  ▼ Societal need of better care at lower costs
▲ Big data issues fueling research and businesses
  ▼ Models, algorithms, architectures to tame data deluge

PRECISION MEDICINE
What is health?

State of complex physical, mental and social well-being and not merely the absence of disease or infirmity.
Where medicine and engineering meet

▲ Data acquisition chains
  ▼ Sequencing DNA, sensing proteins, ...

▲ Data elaboration and transmission means
  ▼ Telemedicine, robotics surgery

▲ Prosthetics, smart implants
  ▼ Sensing, elaborating and actuating

▲ Drug dispensing
  ▼ Off-body, on-body, in-body
Cyber-medical systems objectives

- Bettering **medicine** by electronic means
- Bringing **low-cost** medicine to the people
- Exploiting electronic **well-being** as a **lifestyle**
Cyber-medical systems objectives

▲ Bettering medicine by electronic means
▲ Bringing low-cost medicine to the people
▲ Exploiting electronic well-being as a lifestyle
▲ Opportunities:
   ▼ Synergy of integrated electronic and sensing
   ▼ Platform-based design of electro-sensing systems
   ▼ Connectivity: mobile telephony as backbone
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Conclusions
Point of care

▲ Some molecular tests can be done in real time
   ▼ Efficient and lower cost for routine care
   ▼ Some diagnostics require multiple tests

▲ Emergency situations require real-time measures
   ▼ Patient’s fluids are often connected
   ▼ Local tests and remote diagnosis
Tele-medicine: Monitoring chronic patients

▲ Non-invasive monitors
  ▼ Heart rate, SpO₂, blood pressure

▲ Invasive monitors:
  ▼ Metabolites: glucose, lactate, cholesterol
  ▼ Continuous measurements calibrated in $T$ and $pH$

▲ Wireless challenges
  ▼ Secure transmission
  ▼ Remote powering

[Courtesy: Smartcardia]
Examples

GLUCOSE SENSOR [Senseonics™]

Prototype for human implant [EPFL]

Muti-sensor for lab animals [EPFL]

Current (nA)

Injection Acetaminophen 400mg/kg

Time (min)
Tele-medicine
Remote ultrasound diagnosis

▲ Ultrasound (US) imaging is widely used
   ▼ Standard US needs a radiologist to operate the probe
   ▼ Hard to use in emergencies and in remote areas

▲ 3D Ultrasound can obviate this problem
   ▼ 3D volumes can acquired by non-specialist
   ▼ Then transmitted to medical provider
   ▼ Then sectioned and analyzed remotely

▲ Current 3D systems are bulky, expensive and power-hungry
Tele-medicine
Remote ultrasound diagnosis

▲ Design portable 3D US system
   ▷ Lightweight, low-power, wirelessly connected
▲ Tight integration of probe and beamforming electronics
   ▷ High processing power
   ▷ Heat removal

New 2D probes for 3D image acquisition

Image reconstruction, rotation & sectioning

[Courtesy: Benini, ETHZ]
Patient care support systems

- Drug administration *decision support systems*
  - Drug selection, dosage and timing
- Data acquisition by integrated sensors
  - Continuous and real-time
- Applicable to hospital care
  - In the future will enable also remote care
Smart drug administration

Prof. Thierry Buclin
Head of Clinical Pharmacology and Toxicology Department
Lausanne University Hospital
CHUV
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Technologies

▲ Sensing
  ▷ Electrical, mechanical, optical

▲ Fluidics and transducers
  ▷ Micro tubes, valves, pumps

▲ Data acquisition electronics
  ▷ Discrete, integrated, monolithic with sensor

▲ Packaging
  ▷ Rigid/flexible, bio-compatible
Biosensing targets

- Endogenous metabolites:
  - Glucose, lactate, cholesterol...

- Exogenous metabolites:
  - Drugs, e.g., anti-inflammatory, chemotherapy, ...

- Biomarkers:
  - Tumor growth factors

- DNA, RNA

- Ions (K, Na)

- ...

...
### Integrated sensors sensitivity and range
### Some endogenous metabolites

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Sensitivity ($\mu$A/mM cm$^2$)</th>
<th>Range (mM)</th>
<th>Detection limit ($S/N = 3\sigma$) ($\mu$M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>27.7</td>
<td>0.5 – 4</td>
<td>73</td>
</tr>
<tr>
<td>Lactate</td>
<td>40.1</td>
<td>0.5 – 2.5</td>
<td>28</td>
</tr>
<tr>
<td>Glutamate</td>
<td>25.5</td>
<td>0.5 – 2</td>
<td>195</td>
</tr>
<tr>
<td>ATP</td>
<td>3.42</td>
<td>0.5 – 1.4</td>
<td>208</td>
</tr>
</tbody>
</table>

[Courtesy Carrara, EPFL]
FETs: electronic transducers for chemi/bio-recognition events

▲ Surface potential changes as a function of the ion concentration:
  - pH sensing (H⁺ ions)
  - Other ions (membrane)

MOSFET

ISFET

P. Bergveld et al., IEEE TBME 17(1), 1970

\[
\Delta I_d(pH) \quad \Delta V_{th} = 2.3 \frac{kT}{q} \alpha \Delta pH
\]

\[
S_{out} = \frac{\Delta I_d}{I_d} = \frac{\Delta V_{th}}{SS}
\]
Bio-FETs

Immuno-FET

S
n
D
n
p-silicon

gate oxide

antibody

specific antigen

non-specific antigen

DS

SIGNAL PROCESSING
Relevance of SiNWs

1. Nano size
   - Best interface to proteins

2. Surface-to-volume ratio
   - Larger interaction area
   - Charge confinement

3. Silicon biomodification

4. Compatibility

Reprinted from Curreli et al., IEEE TNANO 7, 2008
SiNW-FETs for Biosensing

Current increase

Current decrease

Reprinted from Patolsky et al., PNAS 101(39), 2004
Voltage-gap SiNW biosensors

Bare NWs

NWs functionalized with Ab

The VoG parameter

Puppo et al. BIOCAS 2014
Applications of Bio SiNW-FETs

Cancer markers detection


DNA detection


Small molecule detection

Design tools for integrated sensors

- Layout generation of the sensor masks
- Sensor and electrical front-end co-simulation
  - Under chemical stimuli
- Signal integrity analysis
  - Crosstalk, drift
- Synthesis of regular array structures
Issues in electrical biosensors

▲ Dimensions and integrated realization
▲ Mediated/non mediated reactions
   △ Stability of organic mediators
▲ Electrode nano structuring
   △ Enhancing performance
▲ 3-Dimensional architectures
SiNWs realized by DRIE and bio-functionalization

Example of fabrication steps

Vertically stack NWs

NiSi contacts

[Courtesy Puppo, EPFL]
Nanostructuring: growing CNTs on Si

Temperature affects yield

Bars: 100nm

Fe Nanoparticles
Fe Non Compact Layer

750 °C
High density
Long and rolls

600 °C
Low density
Short, big and more defective

[Taurino, Nanoscale, 2013]
Nanostructuring (Uric Acid)

2 orders of magnitude sensitivity increase

1 order of magnitude detection limit decrease

[Taurino, Nano Letters, 2014]
Nanostructuring: Au-Pt Nanoferns

Au-Pt nanoferns

Pt tetravalent

Pt divalent
Monolithic and TSV-based integration

[Schienle et al., JSSC 2004]

[Temiz et al., El Letters 2011]

[Temiz et al., Lab on Chip 2012]
Key points

▲ Electrical biosensors are available for various substances
  ▼ Still limited use because of predictability

▲ Strong potential for future growth
  ▼ Integration with front-end electronics
  ▼ Parallel redundant measures

▲ Various nano-materials and technologies can be used because of dimensional compatibility
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Circuits and design

▲ Electrical readout methods:
  ▼ Impedometric
  ▼ Chronoamperometry
  ▼ Cyclic voltammetry

▲ Requirements
  ▼ Low noise (drift)
  ▼ Low power (implants)
Programmable sensing platform

▲ Multiple sensor integration on silicon
  ▼ Electronic resource sharing
  ▼ Various dynamic ranges

▲ Reducing Non-Recurring Engineering (NRE) costs
  ▼ Modular electrode and interface physical design
  ▼ Standard-cell like design

▲ Several families of medical tests where analyses can be done by sensors with similar structures
  ▼ Possibly various current values and ranges of interest
  ▼ Readout circuit sharing/multiplexing
Field-programmable sensing array

▲ Sensor array platform where targets are chosen after silicon fabrication
  ▼ FPGAs are reminiscent of FPGAs
  ▼ Maximal flexibility in application

▲ Programming FPSAs
  ▼ Selecting sensing mediators in last fabrication step
  ▼ Providing sensing mediators via microfluidics
  ▼ Selecting sensing sites on the field by programming
Sensor data analysis

▲ Biosensor integration enables
  ▼ Multiple/simultaneous readout of
    ➢ Same target
    ➢ Different targets

▲ Data elaboration to enhance result quality
  ▼ Reproducibility
  ▼ False positive/negative

▲ Majority and threshold logic play an important role in data processing
  ▼ In situ data processing
SW tools for design and operation

▲ Design tools for sensor subsystems
   ▼ Current DA tools plus sensor design support

▲ On-line support tools
   ▼ Map clinical requirements to specific bio tests
   ▼ Configure system for sensing operation

▲ Conformity check

▲ Redundant checks can increase reliability
Key points

▲ Co-design of electronics and sensing is crucial
  ▶ Achieve low-power consumption
  ▶ Achieve small footprint

▲ Platform-based design
  ▶ Modularity of design can reduce NREs

▲ Electronic technology can be extended upwards
  ▶ Monolithic integration
  ▶ Silicon interposer technologies
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Therapeutic Drug Monitoring (TDM)

- Drug dosage according to the individual pharmacokinetic profile

J. Hiemke / European journal of clinical pharmacology 64.2 (2008): 159-166.
Drug concentration in blood
Smart drug administration

▲ Policy design:
  ◀ Determine the sequence and dose of the drug
▲ Predictive models:
  ◀ Extract system state from external parameters
▲ Close-loop models:
  ◀ Measure system state: drug concentration
▲ Objective:
  ◀ Minimize drug dose/administration
    ➢ subject to drug concentration to be in the permitted band
System-level challenges

▲ Correctness:
   ▷ The system must perform its function in any condition

▲ Security:
   ▷ No medical information leaking to other parties
   ▷ No access from non-authorized sources

▲ Safety:
   ▷ Under no condition the health-device can be a threat
   ▷ Safety must be guaranteed for both patient and operator

▲ Dependability:
   ▷ All devices must work long time in possibly harsh condition
   ▷ Graceful degradation mechanisms
Correctness

▲ Diagnostic systems
  ▼ Accuracy, linearity, limit of detection

▲ Drug administration decision support systems
  ▼ Decisions based on acquired data must be correct

▼ Life-critical systems

The verification problem

▲ Verify that a therapeutic protocol is
  ▼ Consistent
  ▼ Complete
▲ Verify that a drug administration control unit is a correct *implementation* of the protocol
  ▼ Model checking
Formal model of *Imatinib* protocol
Key points

▲ Very few protocols have a formal description
   ▶ Corner cases are hazardous for patients
▲ Personalization of drug dosage is important
   ▶ But still used in few cases
▲ Modeling human body reaction is critical
   ▶ But often hard to achieve in a deterministic way
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Conclusions

▲ New electronic health systems and services will be enabled by advances in biology and medicine, in combination with progress in electronics

▲ The rationalization of health care will provide advanced care to a broader audience at lower cost

▲ Human factors will still be central to decisions in medicine - decision support will be automated