Session 11 – CMOS Biochips and Bioelectronics

A Sub-1 μW Multiparameter Injectable BioMote for Continuous Alcohol Monitoring

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Motivation: Alcohol Sensing for Treatment

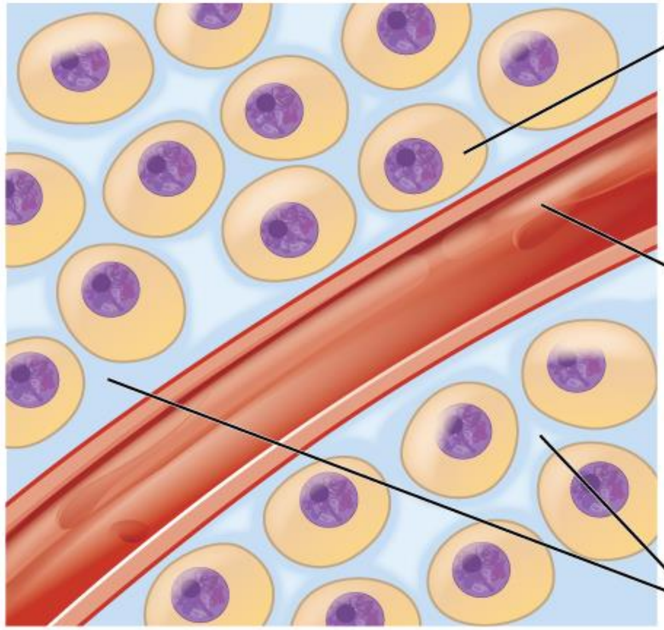
Alcohol abuse prevention
- Short term
- Limited supervision
- Relapse

Alcohol breath analyzers
- Short term
- User initiation
- Inaccurate (>0.1% BAC)

Laboratory blood test
- Short term
- Inaccessible
- Takes hours of time

Needs: accurate, long term, continuous alcohol monitoring

Motivation: ISF-Based Sensor

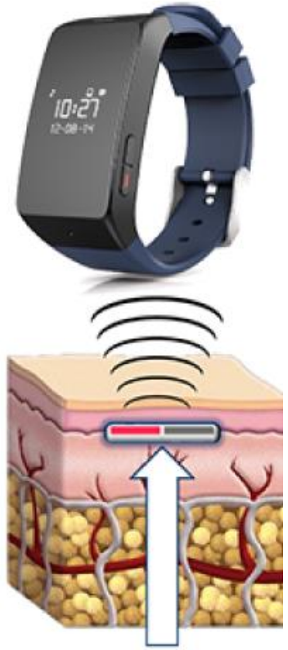


Benefits:

- High correlation with actual blood alcohol content (BAC)
- Located right below skin surface → allows near-field communication
- Quasi-stationary → sensor doesn't flow around

Need to build ISF-based (injectable) sensor & readout circuit

System Overview



Low E_{total} is essential to extend the wearable device work time w/o recharging

Typically < 0.1% for near-field coupling, determined by size and distance

$$E_{total} = (P_{reader} + P_{chip}/Eff_{link}) \times T_{test}$$

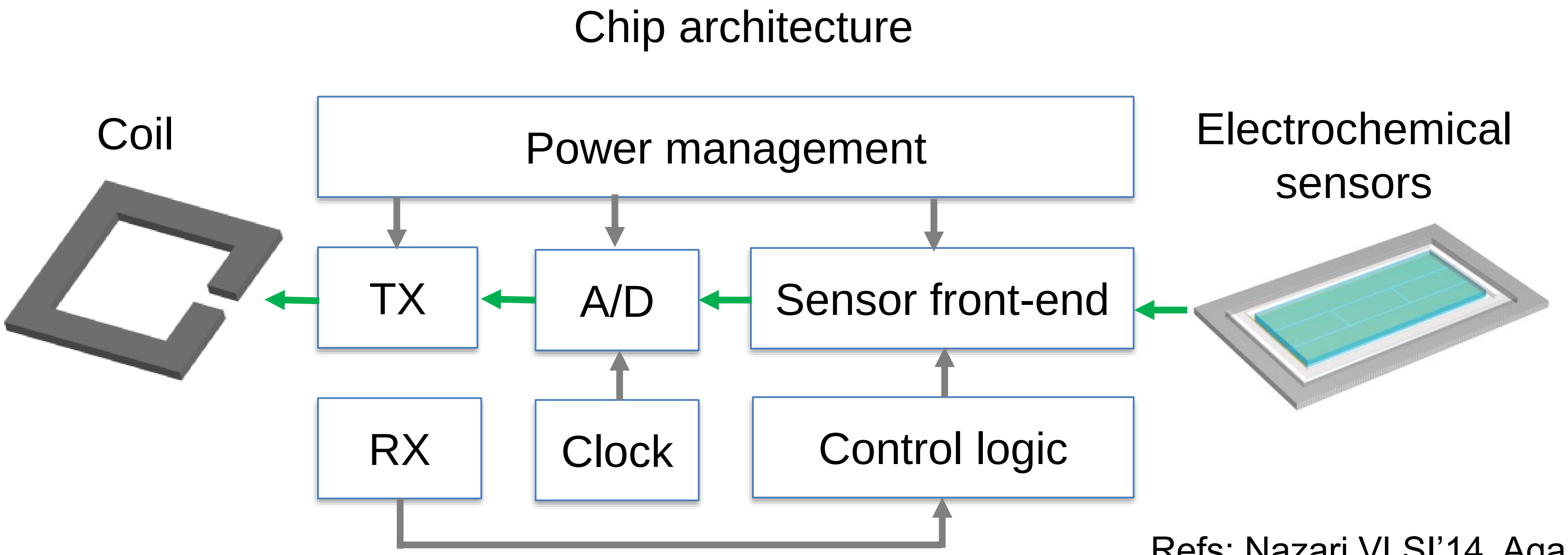
Determined by circuits

Determined by both circuits & sensing methodology

Design Requirements:

- Low power
- Fast measurement
- Tiny size: fully integrated sensors, antenna; battery-less
- High selectivity: cancel biological interference

Prior-Art



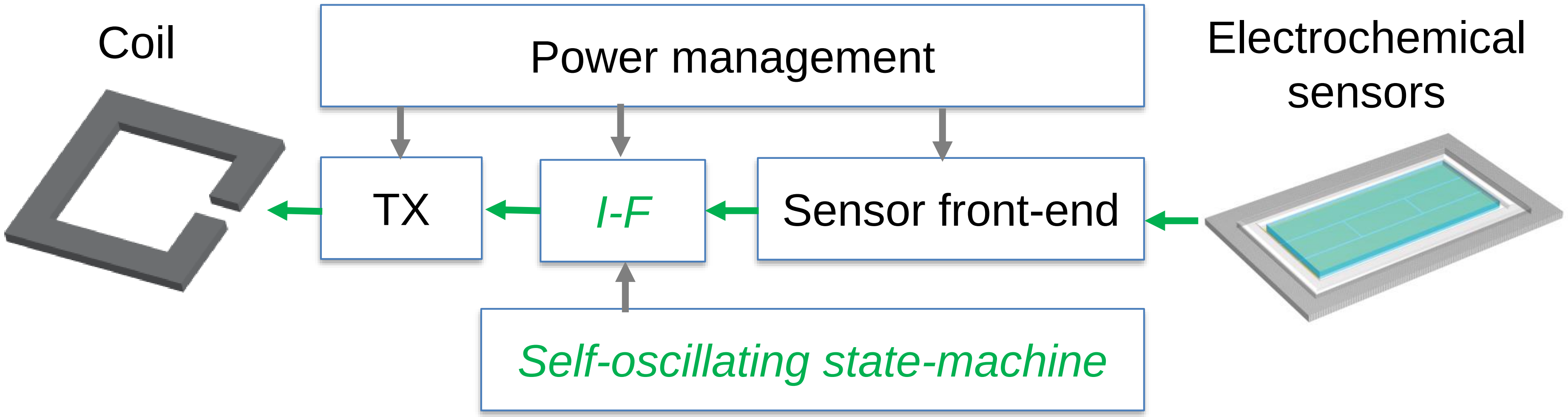
Refs: Nazari VLSI'14, Agarwal VLSI'17

Problems:

- Power hungry low-jitter clock and A/D converter
- RX is required for controlling sensing, digitizing and transmitting data

Proposed Work

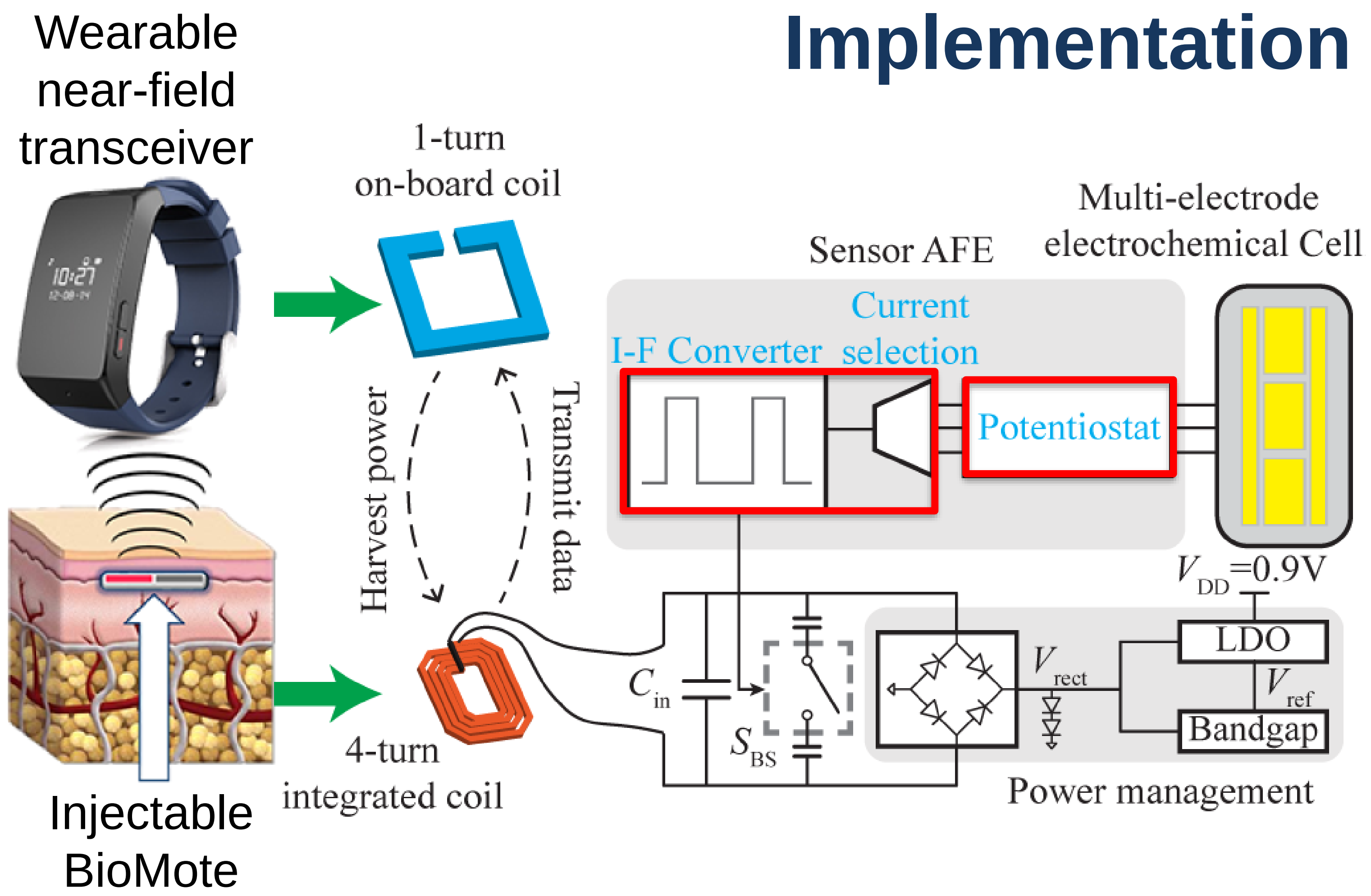
Chip architecture



Benefits:

- Transfer clock-shaped analog data through TX → no need for on-chip clocking and digitizing
- Measurement is cycled by state-machine → no RF downlink

Implementation

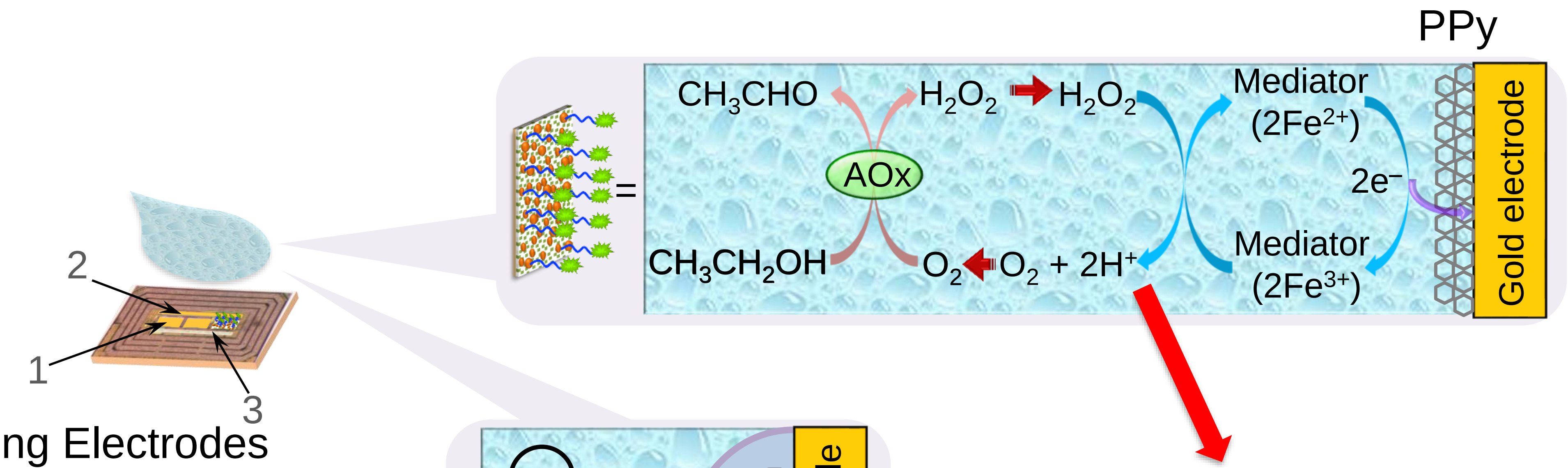


Highlights:

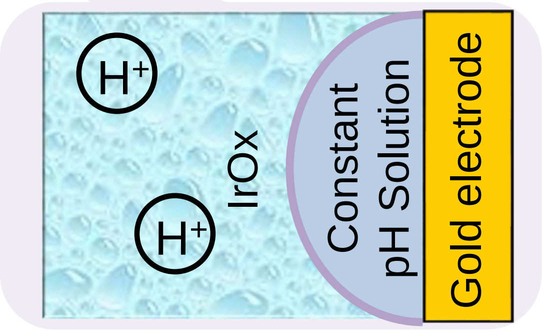
- A low-power potentiostat w/ current-control loop & current starved amplifier consumes < 0.5 μW
- Self-oscillating I-F removes the need for clocking & digitizing

First reported sub-1 μW fully integrated, injectable biosensor

Alcohol Assay Sensing Method



1: 3-Gold Working Electrodes (WEs)
2: Gold Counter Electrode (CE)
3: pseudo Silver Reference Electrode (RE)

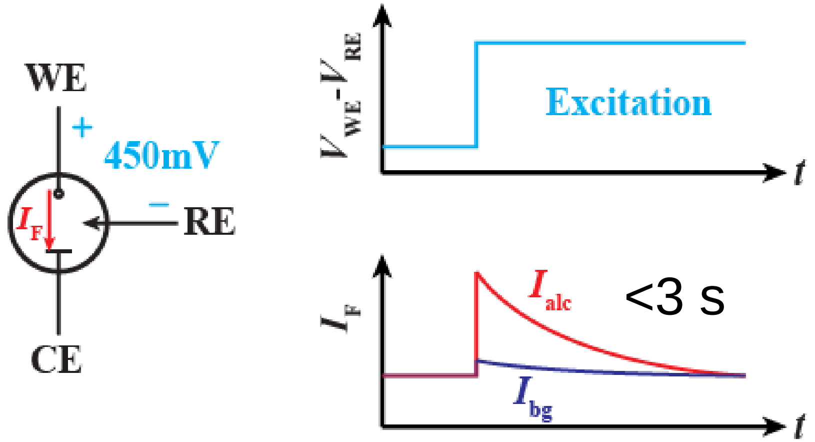


Problem:
Solution pH affects reaction rate

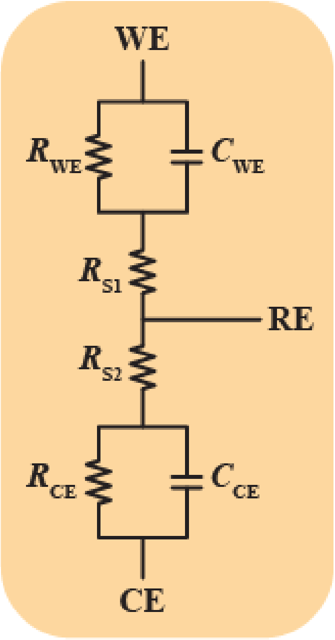
Solution: Multi-electrode test cancels background signal and pH

Alcohol Assay Sensing Method

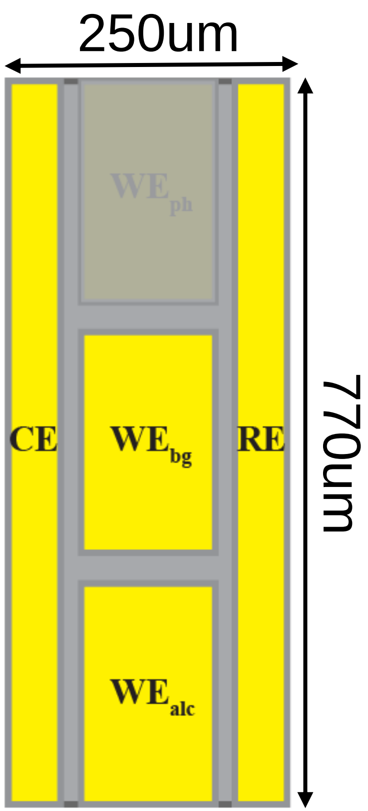
Chronoamperometry



Electrode Model



Electrode Layout

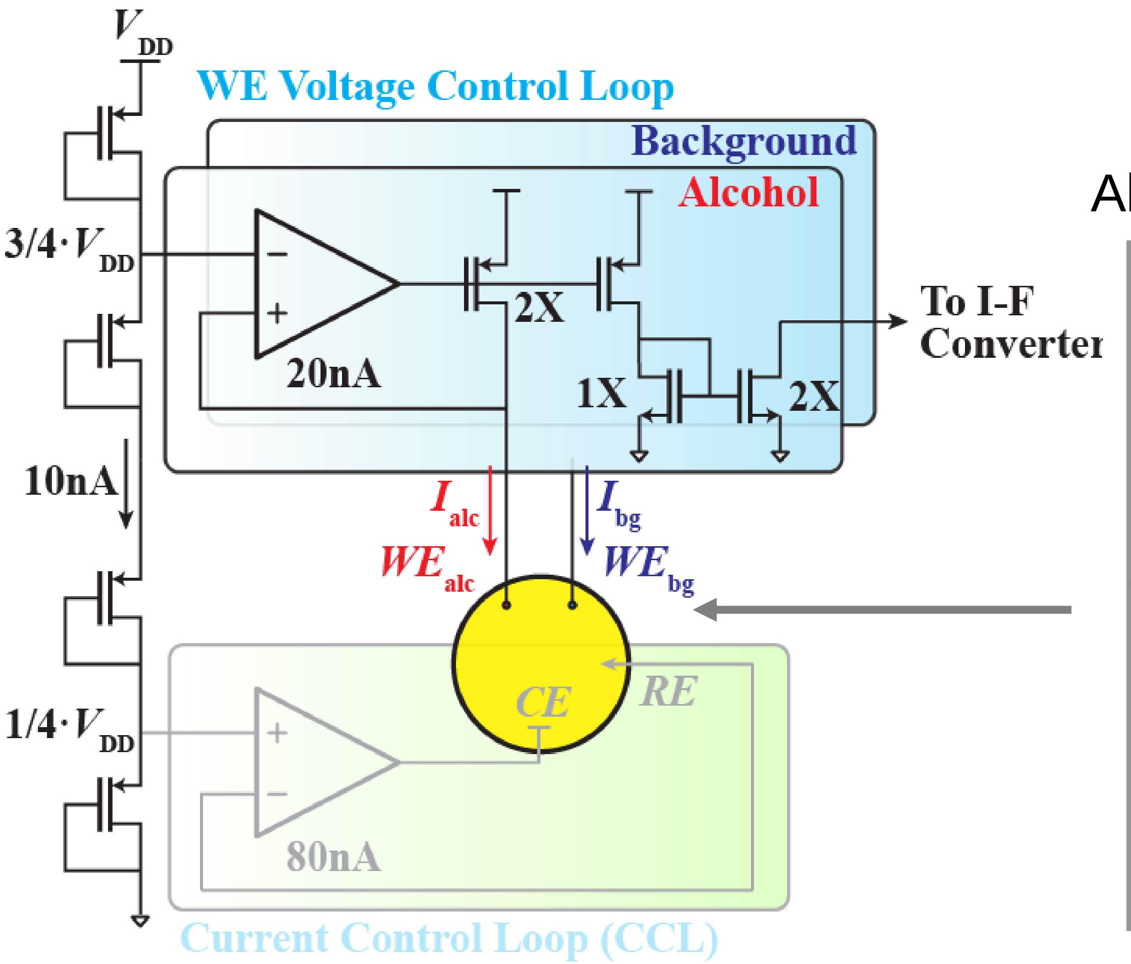


Cottrell equation:

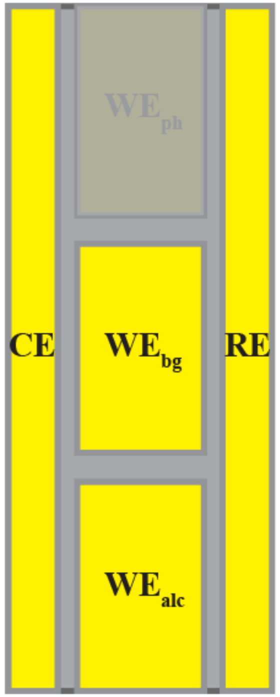
$$I_F(t) = \frac{nFAC_0\sqrt{D_0}}{\sqrt{\pi t}}$$

Low noise circuit (<3 nA) is required due to micro-electrodes

Potentiostat



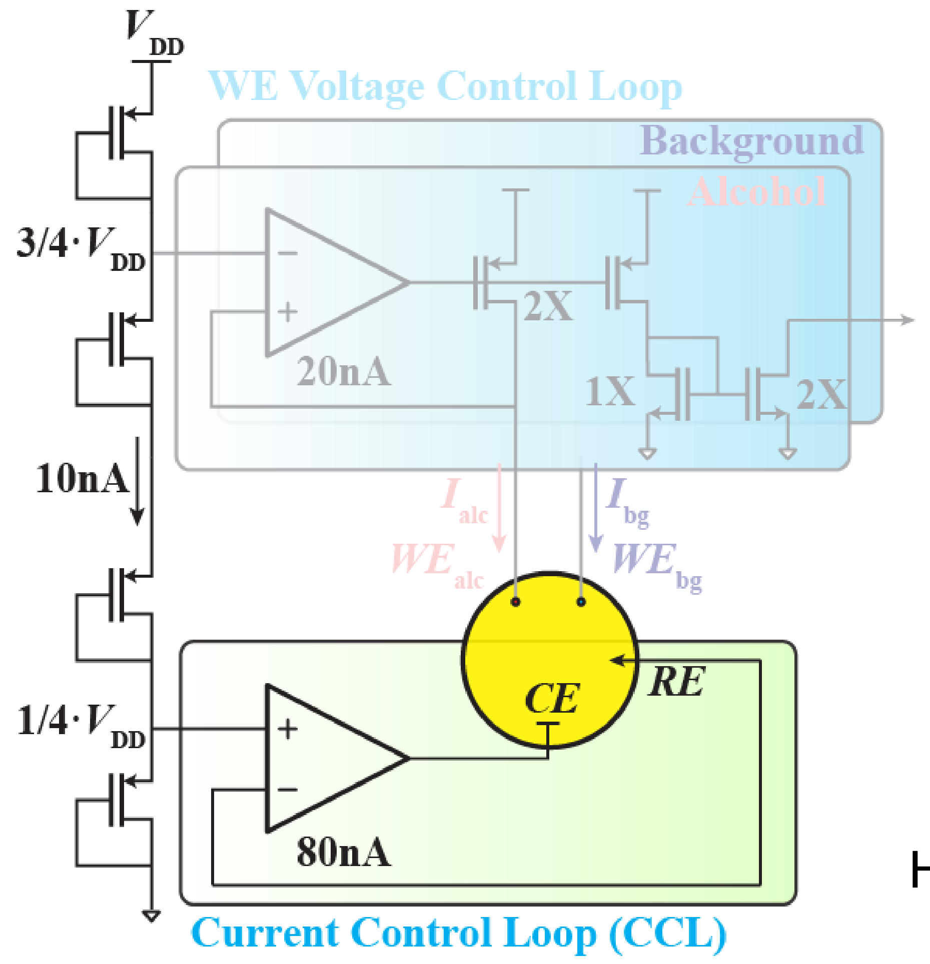
Alcohol assay



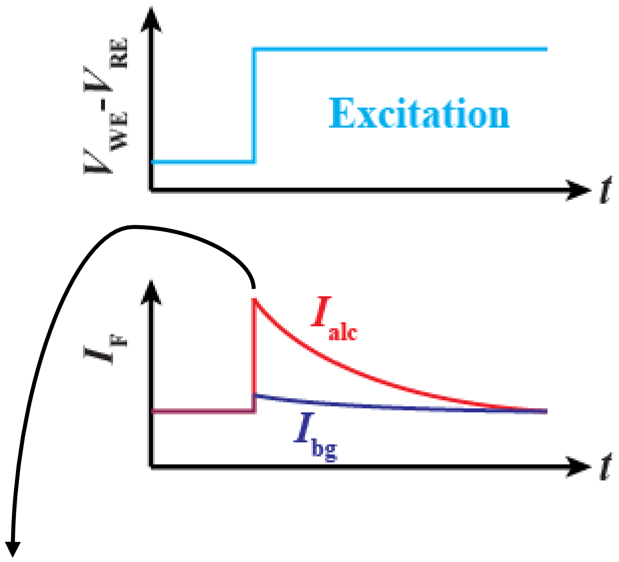
Benefits of Voltage Control Loops:

- Set WE potential to 3/4·V_{DD} and measure I_{DUT} separately.
- Reduce kickback from I-F converter using current mirror.

Potentiostat



Chronoamperometry



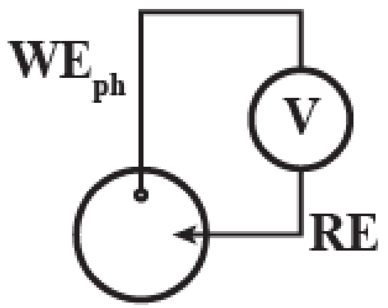
High current at start-up

Benefits of CCL:

- Set RE potential to $V_{DD}/4$.
- Limit current < 80 nA → reduce power consumption during start-up.
- Set dynamic range (~26 dB) based on ethanol physiological level (0.01–0.2% BAC).

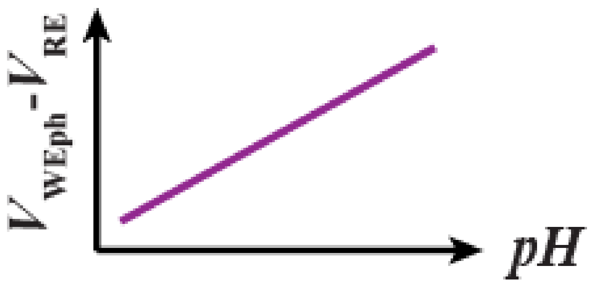
pH Sensing Method

Potentiometry:

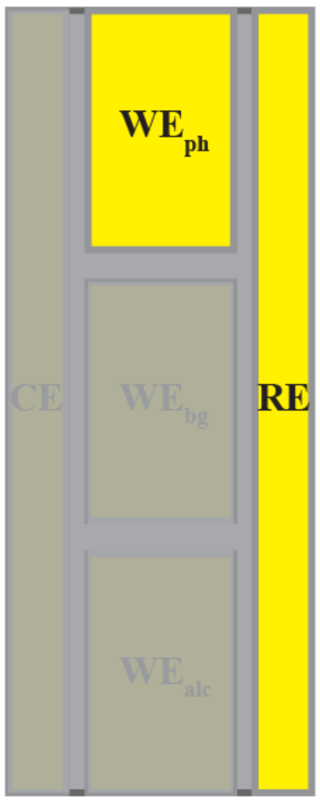


Simplified Nernst equation:

$$E = E_0' - 0.0591 \cdot pH$$



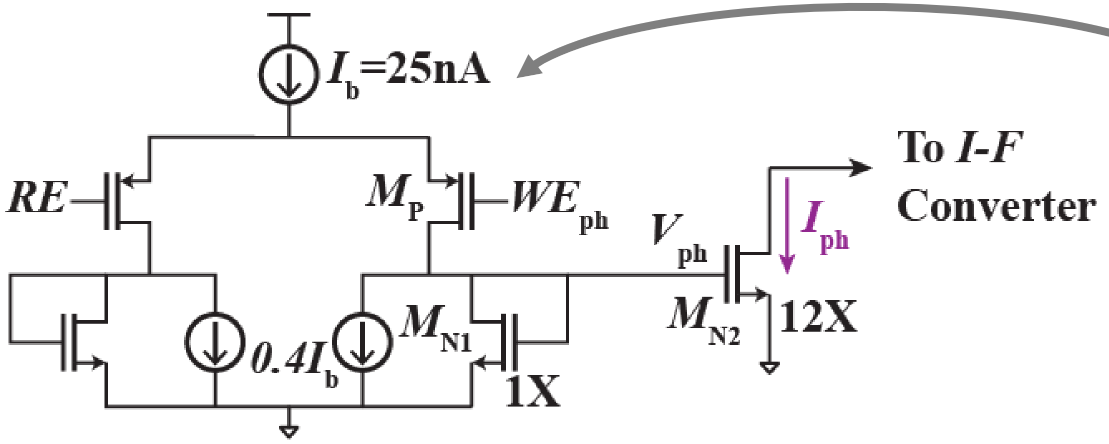
Electrode Layout



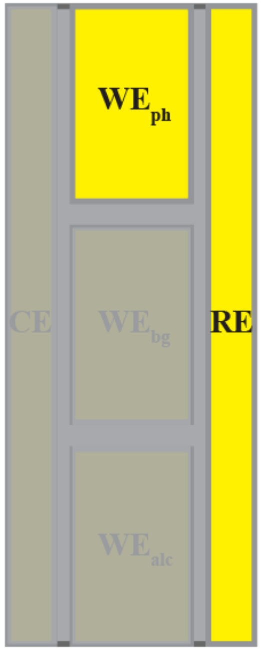
pH channel digitally corrects the measured ethanol concentration.

pH Amplifier

Open-loop transconductance amplifier



Alcohol assay



$$G_{ph} = g_{mp} \frac{W_{N2}}{W_{N1}} = 12 g_{mp} = 1.2 \mu S$$

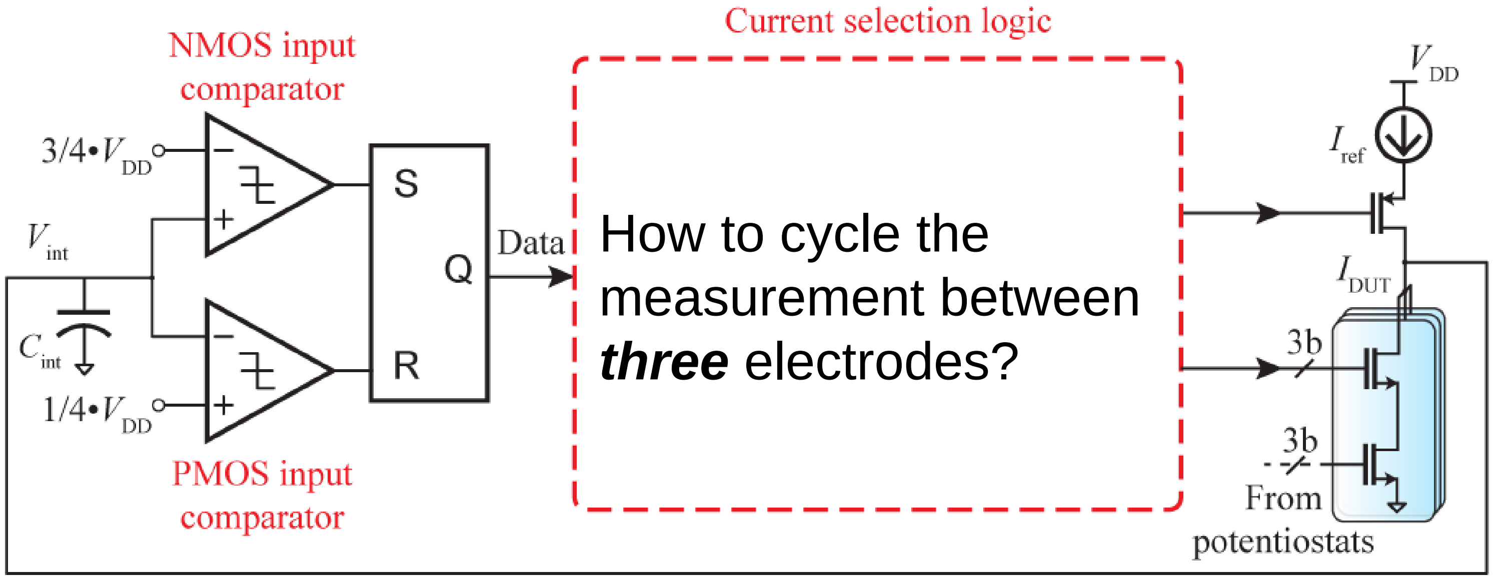
Benefit:

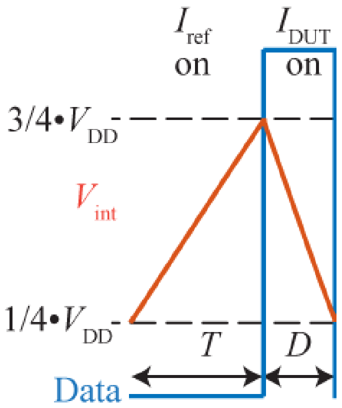
- Current starving reduces baseline current and improves power efficiency by 5X

Potential issues:

- Moderate dynamic range & linearity due to open-loop operation. However, the physiological pH range is very limited (6.8 – 7.4)
- Gain error & offset can be removed w/ 2-point calibration

I-F Converter





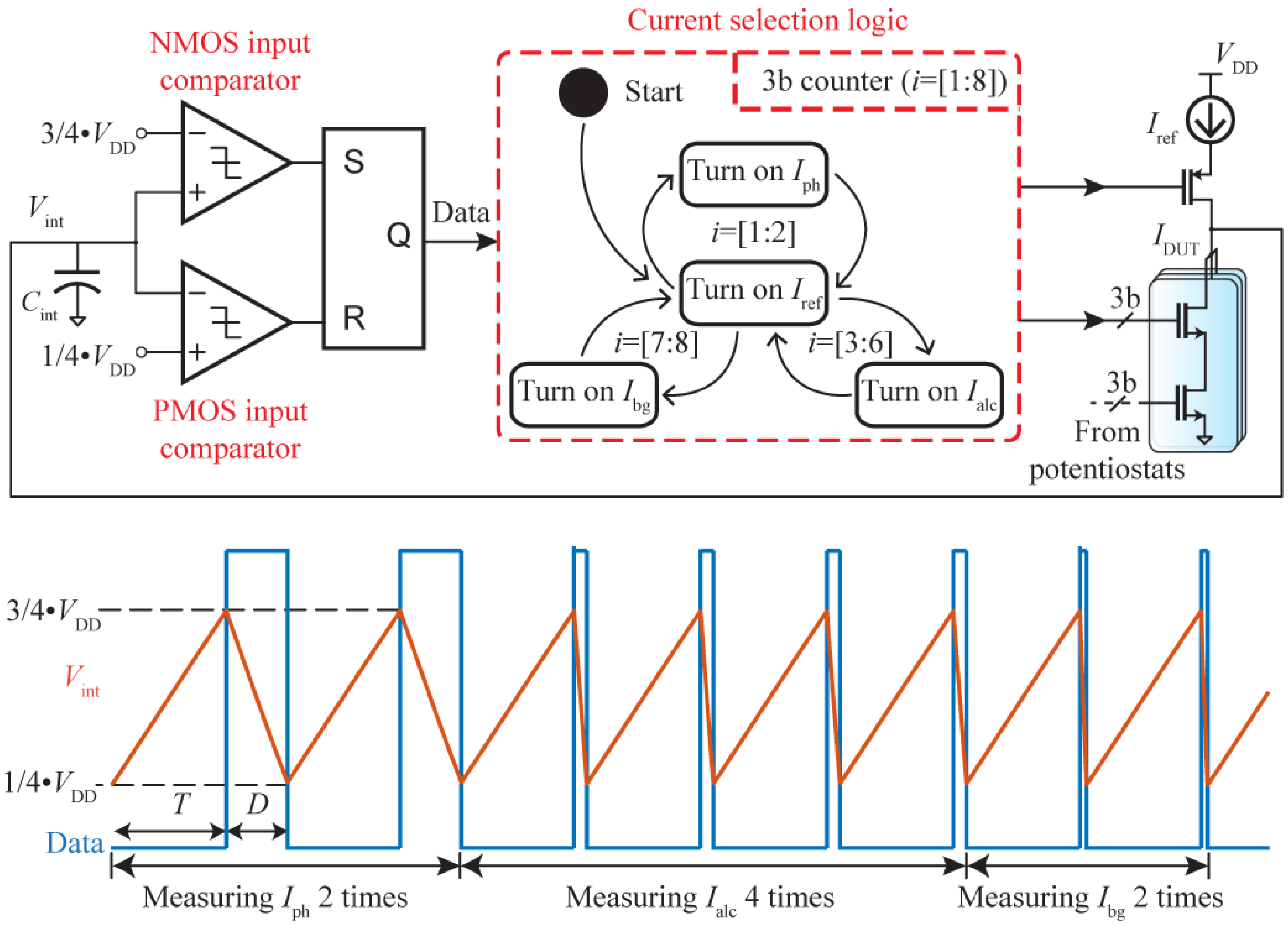
$$T = \frac{V_{DD} C_{int}}{2 I_{ref}}$$

$$D = \frac{V_{DD} C_{int}}{2 I_{DUT}}$$

$\Rightarrow$ $I_{DUT} \propto T/D$

I_{DUT} can be measured without knowing V_{DD} & C_{int}

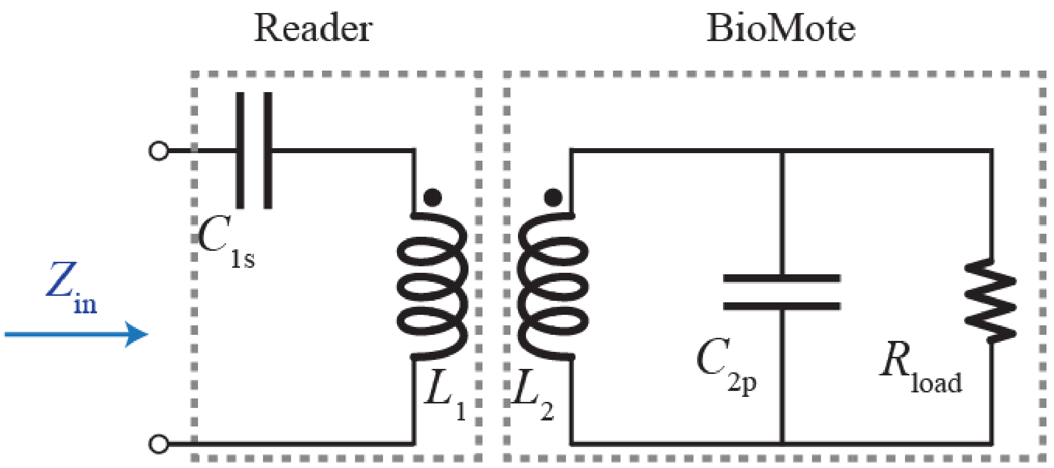
I-F Converter



Benefits:

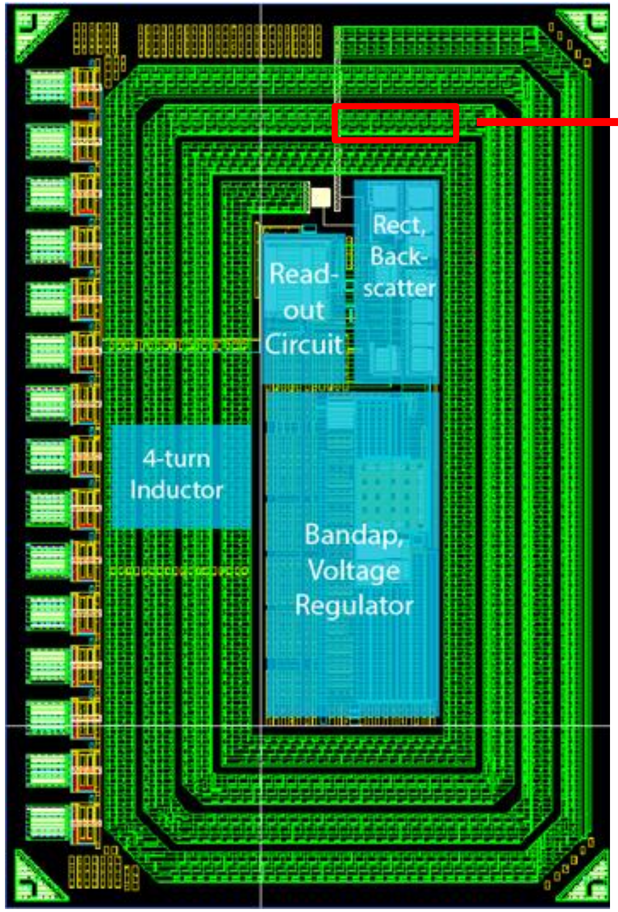
- Requires no additional timer
- 2-4-2 pattern distinguishes each I_{DUT}, and reduces noise by averaging
- Only 300 pW power w/ custom stacked digital logic

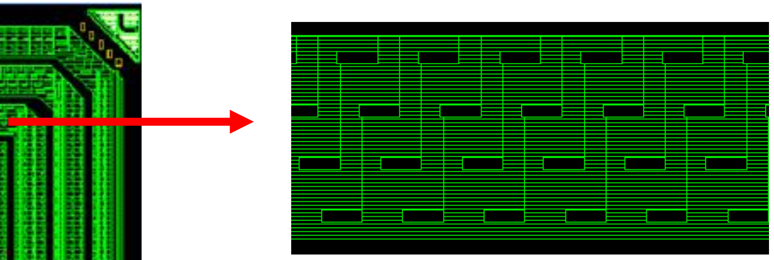
Wireless Power Transfer (WPT)



- Resonant frequency: 985 MHz due to link efficiency & tissue compatibility [1]
- $L_1 C_{1s} = L_2 C_{1p} = \frac{1}{\omega^2} \rightarrow Z_{in}$ is purely real at resonant frequency
- Chose $L_2 = 40\ \mathrm{nH}$, $C_{2P} = 0.7\ \mathrm{pF}$ balance link efficiency & backscatter signal

[1] O'Driscoll ISSCC'09

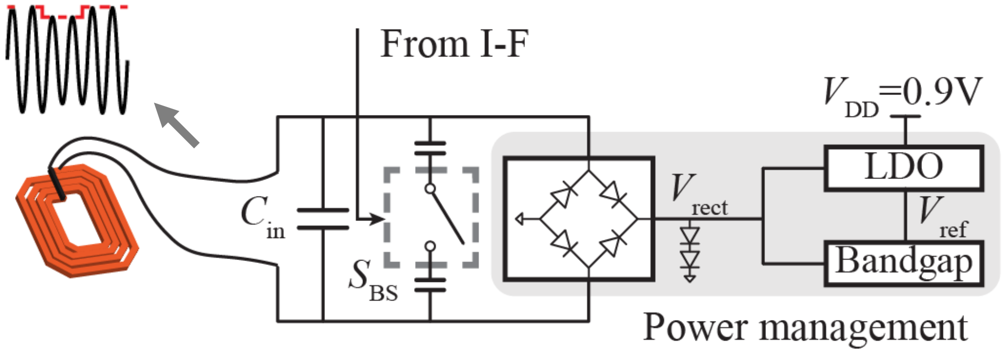


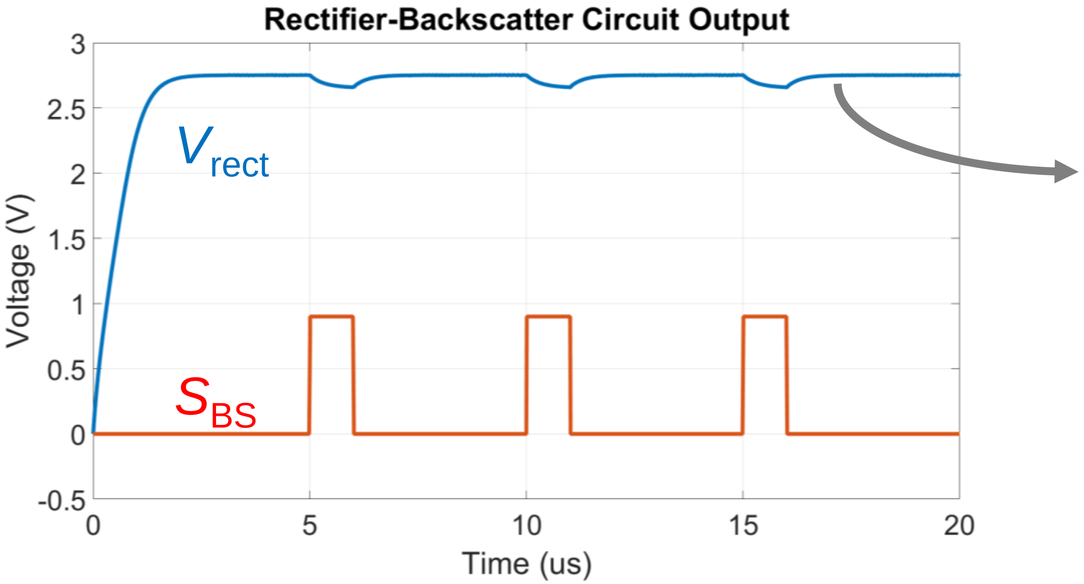


- Putting circuits and electrodes inside the coil to minimize chip area
- Making slots on the coil to pass DRC

Q drops from 15.2 to 10

Backscatter (BS) Uplink





Benefit: no additional power cost

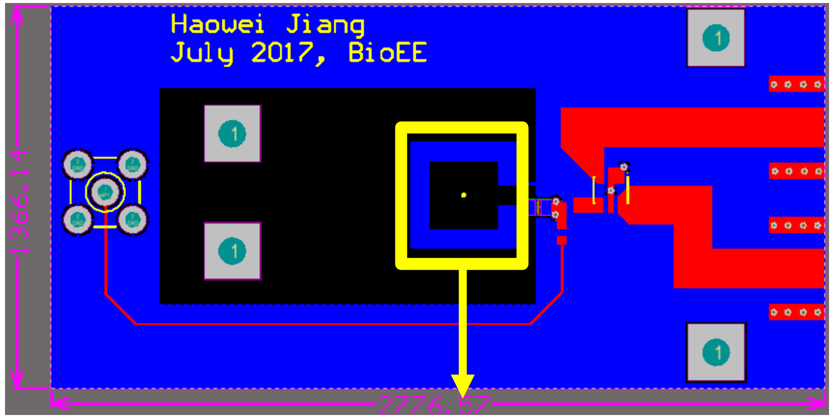
Small bypass capacitor → fast start-up, but large droops on supply

Design choice:
The 2nd tank resonant frequency moves by ~100 MHz → 0.4% modulation & 3 mV droops

Optimized for low droops due to fast start-up requirement

WPT & BS Measurement Setup

RF board

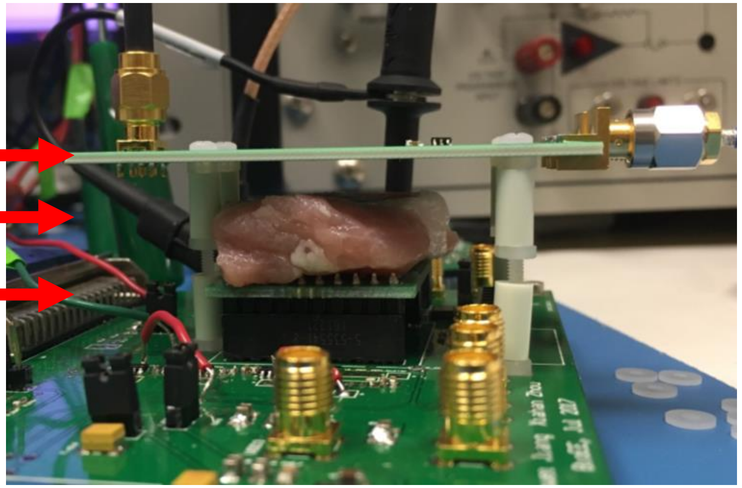


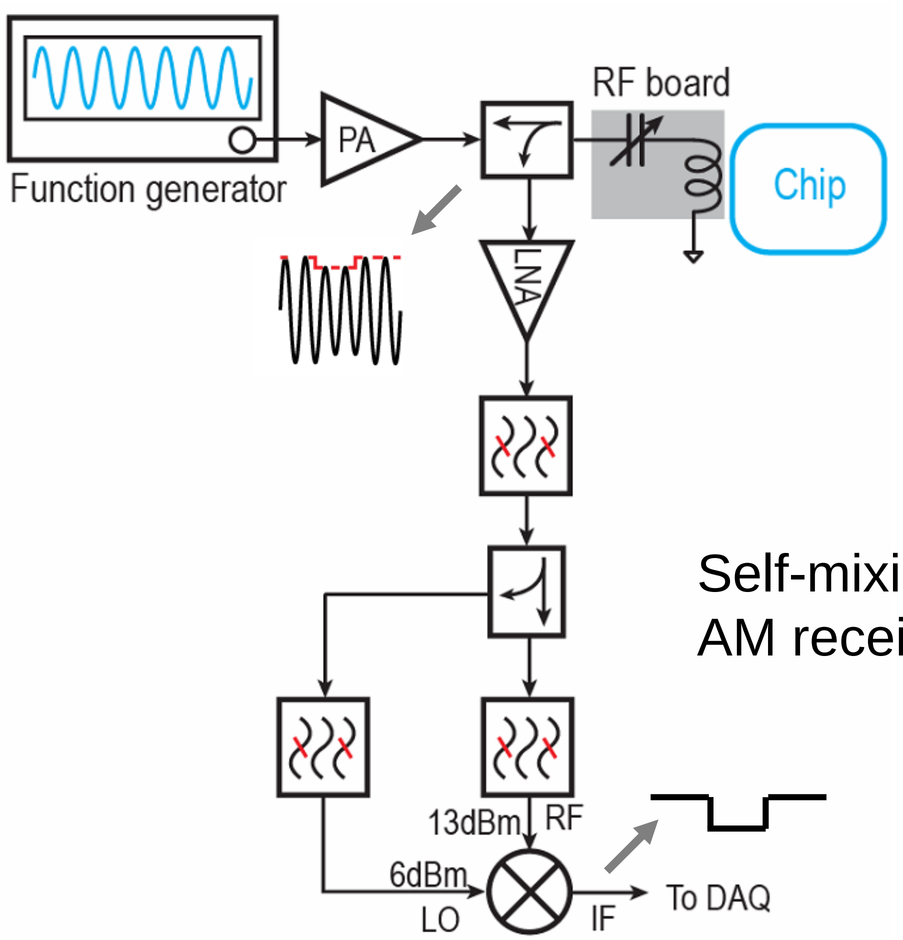
Primary coil: 8×8mm^2, 19nH

RF Board

Pork tissue

Chip

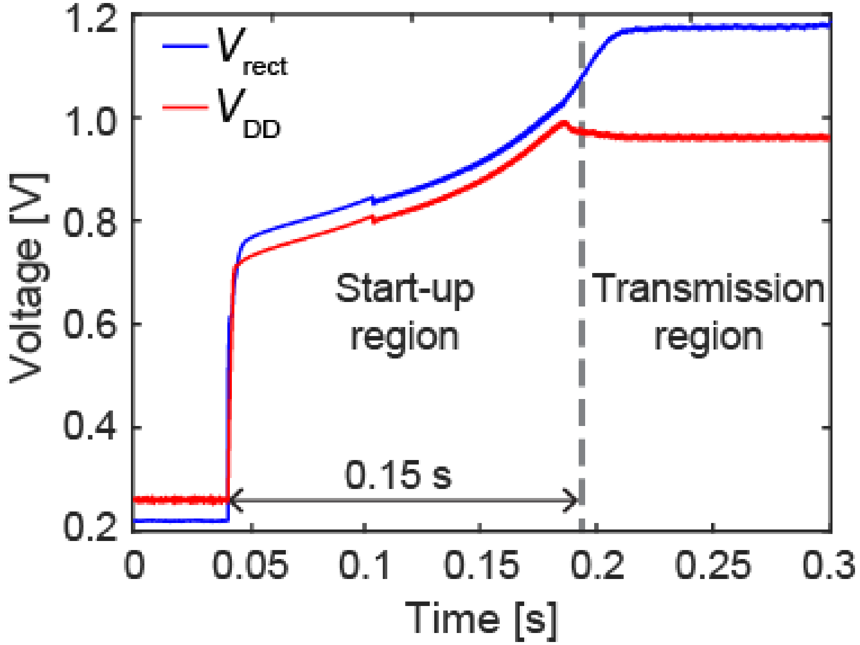




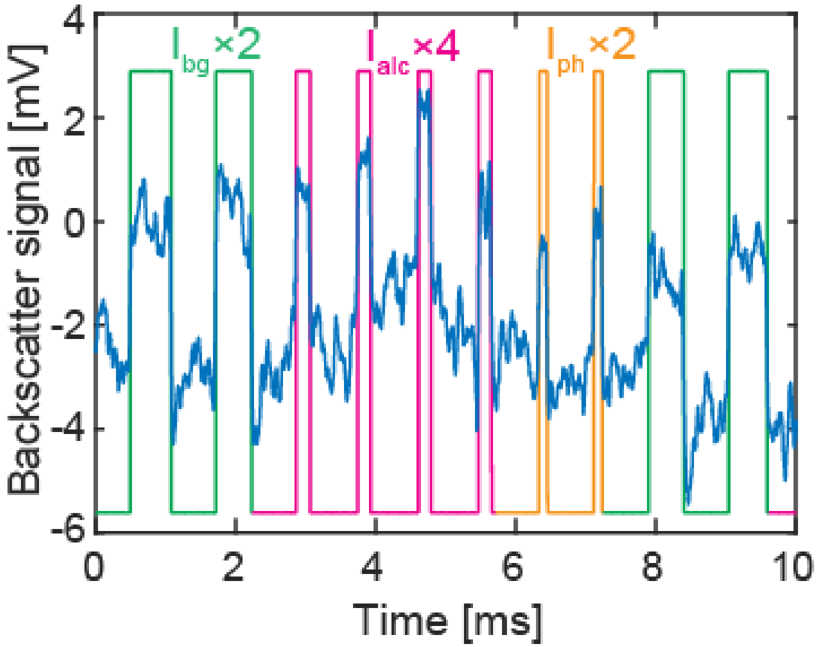
Self-mixing AM receiver

Measurement Results (Wireless)

Wireless power transfer



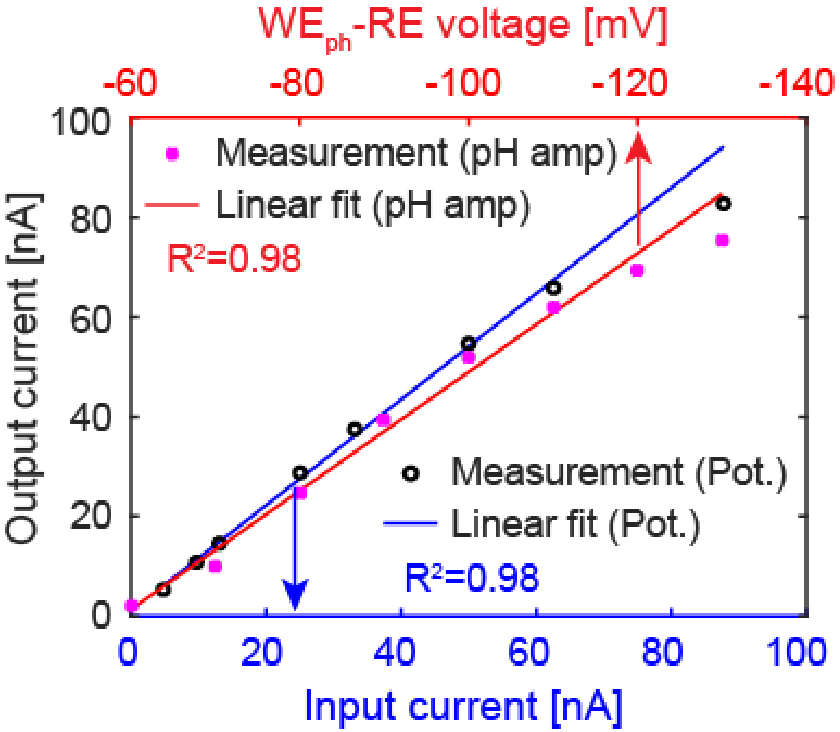
Backscatter signal



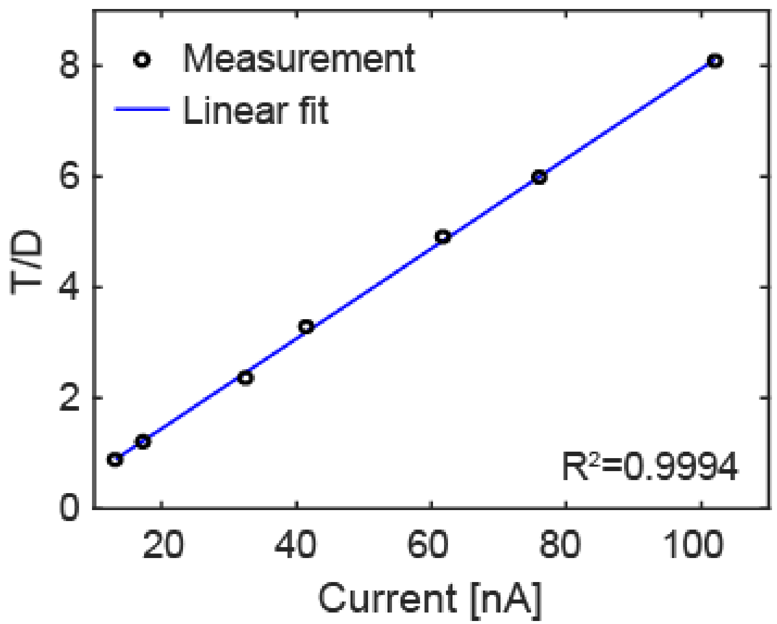
- Carrier frequency: 985 MHz; link efficiency: 0.033% via 2 mm tissue gap
- Fast start-up: 0.15 s; small supply droops: 3 mV
- BS signal modulation depth: 0.2%. Large drift caused by 1/*f* noise AM RX

Measurement Results (AFE)

Multi-parameter potentiostat

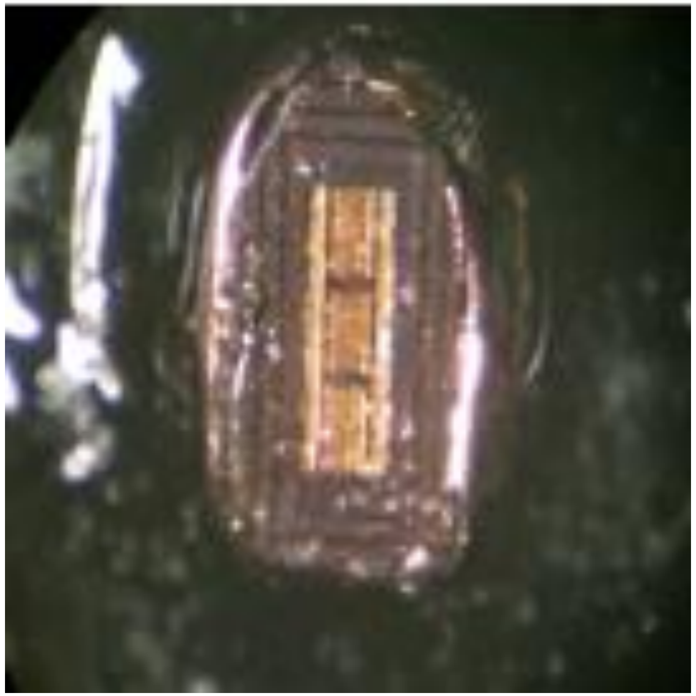


I-F converter

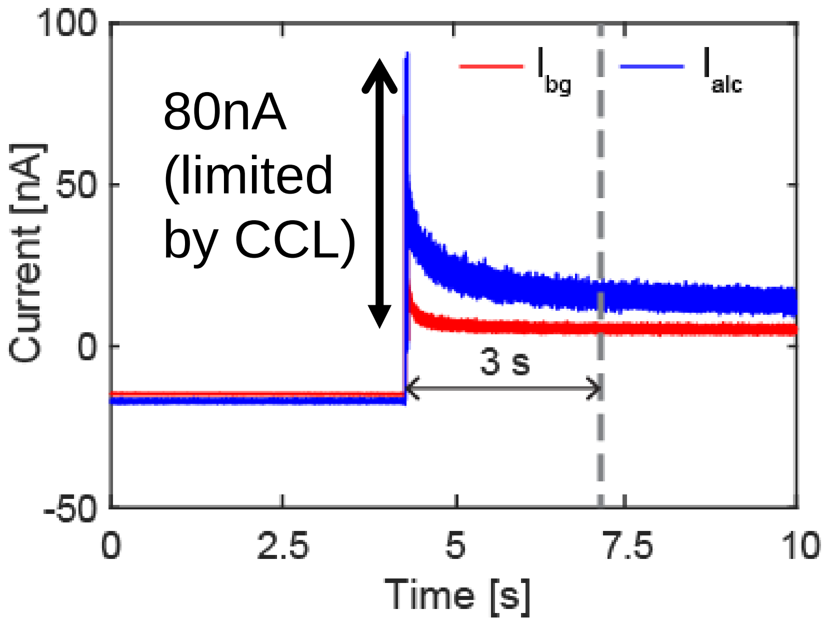


- Potentiostat dynamic range: 2.5 – 80 nA (30.2 dB)
- pH amplifier dynamic range: 0.5 – 70 mV (43 dB)
- I-F converter covers larger dynamic range than potentiostat & pH amplifier

Measurement Results (Biological)



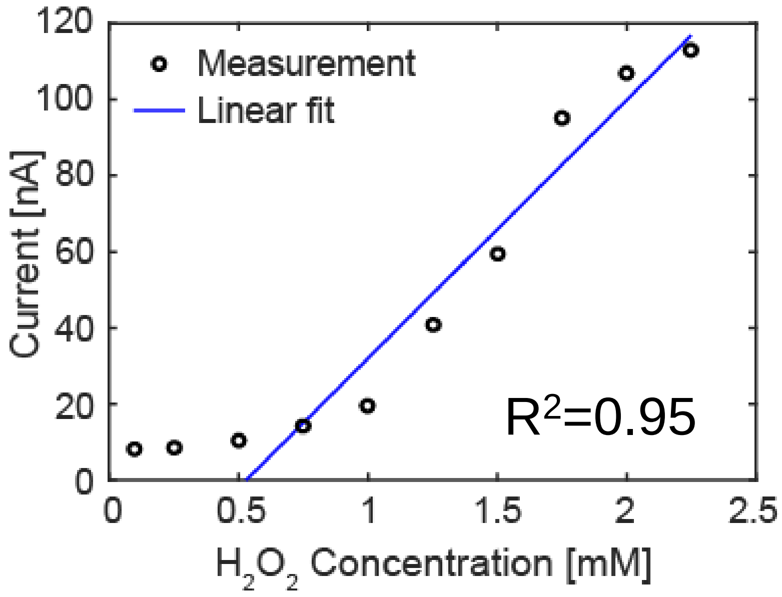
Transient response



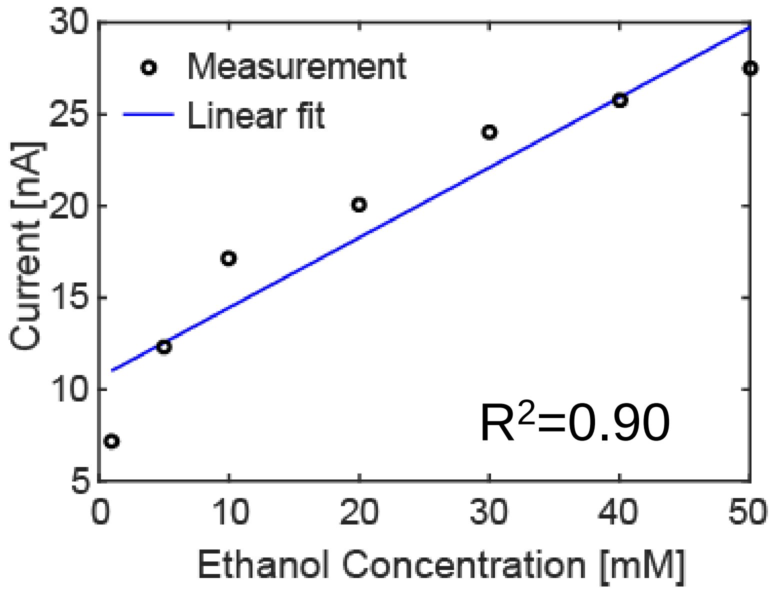
- Sensor electrodes have been plated and functionalized before testing.
- High start-up current is limited by CCL.

Measurement Results (Biological)

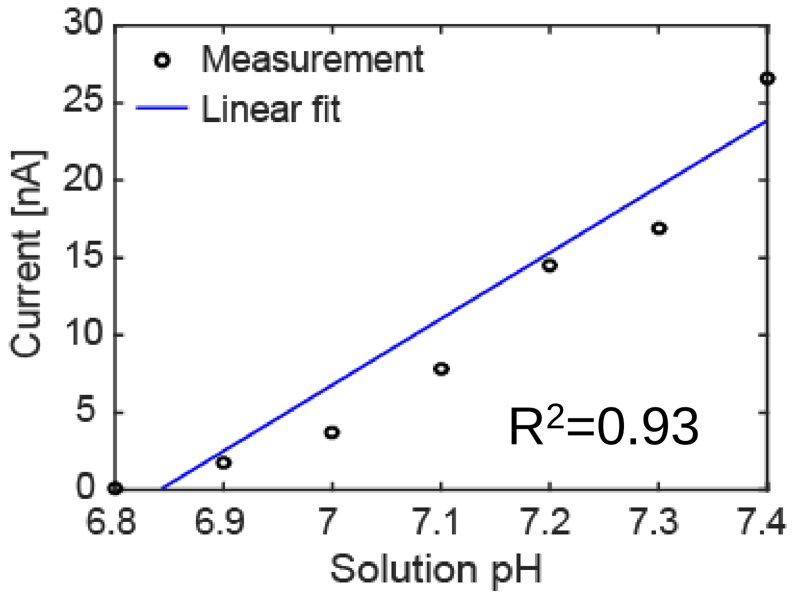
H_2O_2 transfer curve



Ethanol transfer curve

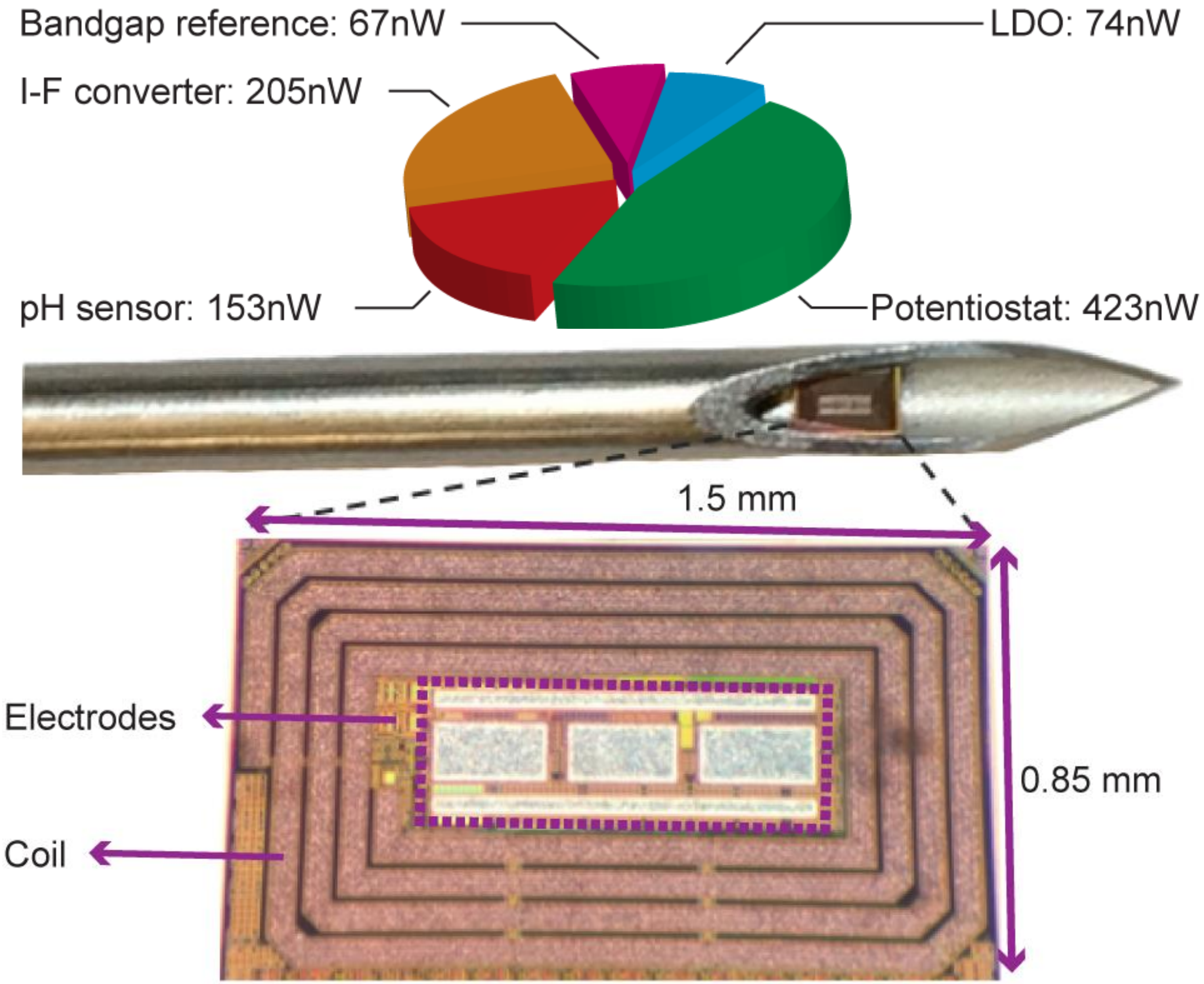


pH transfer curve



- Proper ethanol range (0.0046 – 0.23 %) is covered.
- Proper pH range (6.8 – 7.4) is covered.

Power Breakdown & Die Photo



16-gauge syringe (1.19mm diameter)

Prior Fully-Implantable Biosensors

Parameter	Ahmadi TBioCAS'09	Liao JSSC'12	Nazari VLSI'14	Kilinc JSEN'15	Agarwal VLSI'17	This Work
Tech. (nm)	180	130	180	180	65	65
Carrier Freq. (MHz)	13.56	1,800	915	13.56	900	985
Supply (V)	1.8	1.2	1.2	1.8	1	0.9
Power (µW)	198	3	6	1,500	4	0.97
Sensitivity (nA)	1	2	12[1]	13	0.1	2.5 (alc.); 0.5 mV (pH)
Dynamic Range (dB)	60	37	32	48	71	30.1 (alc.); 43 (pH)
Size (mm)	4×8	10 (diameter)	1.4×1.4	12×12	1.2×1.2	0.85×1.5
Detection Technique	Amp.[2]	Amp.[2]	Amp.[2] + Volt.[3]	Amp.[2] + Volt.[3]	Amp.[2]	Amp.[2] + Volt.[3]
Analyte	Glucose	Glucose	Glucose	APAP	H_20_2	Ethanol/H_20_2
Multi-parameter?	No	No	No	BG[4]	No	BG[4] + pH
External Components	Sensor, coil, capacitor	Sensor, coil	None	Sensor, coil, capacitor	None	None

[1] Read from figure
[2] Amperometry
[3] Potentiometry
[4] Background

Conclusion

- A wireless, fully-integrated injectable BioMote was designed for continuous, long-term alcohol monitoring

- Key challenges: **background cancellation**, **low-power** & **fast measurement**

- To address this, we:
  - Developed a low-power multiparameter potentiostat enabling differential measurements to cancel background interference.
  - Developed a self-oscillating I-F converter and potentiostat w/ current control loop to minimize power.
  - Minimized measurement time w/ fast start-up and chronoamperometry.

- Result: **a first-reported sub-1 μW fully-integrated, injectable biosensor**

Acknowledgments

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- CARI Therapeutics for market discussions
- NSF, NIH and Samsung for funding