A 64×64 High-Density Redox Amplified Coulostatic Discharge-Based Biosensor Array in 180nm CMOS

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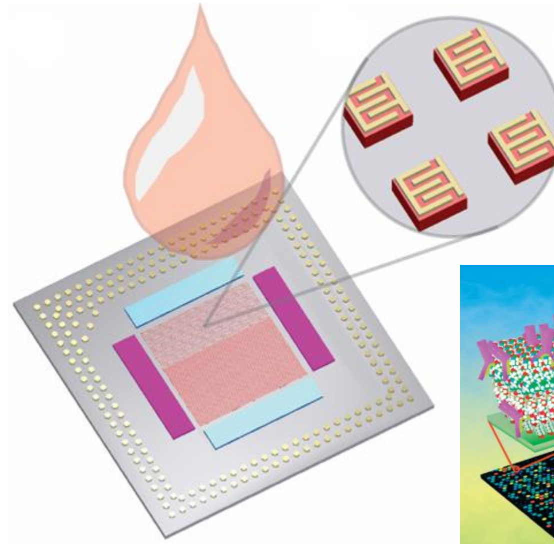
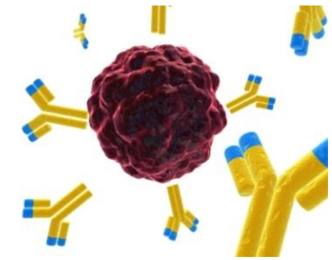
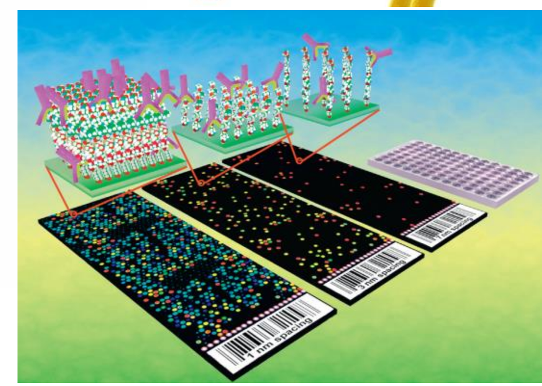
Motivation for Biosensors



High-density Biosensors

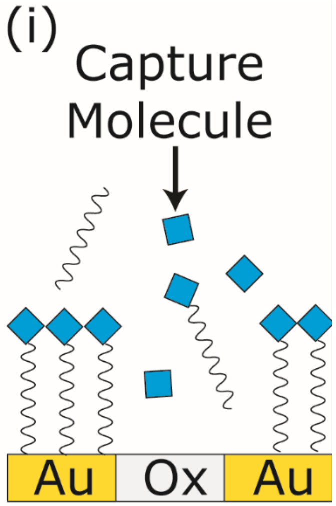







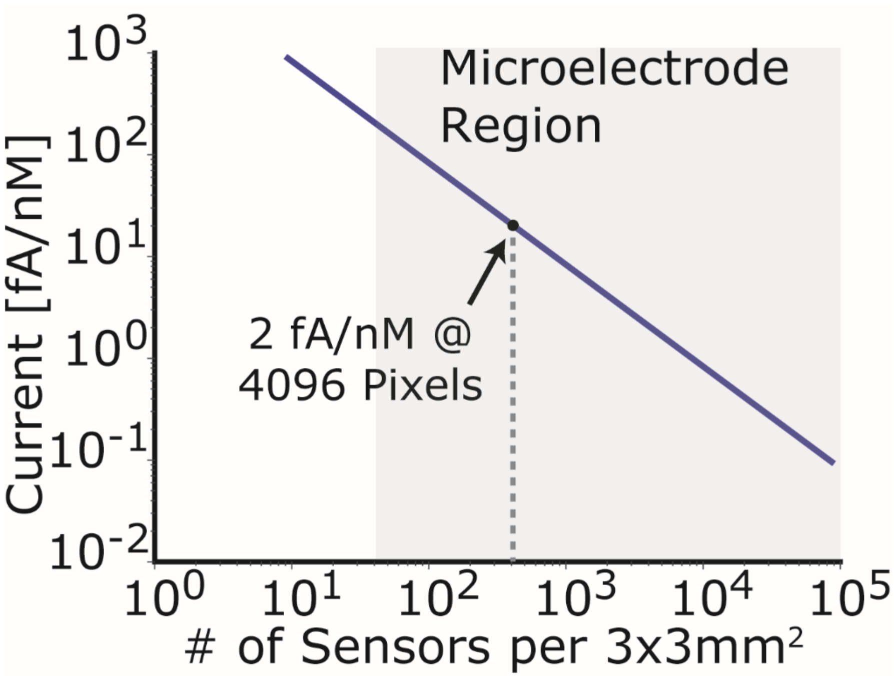
- Biosensors are crucial for modern diagnosis of illness
- Need high-density arrays for parallelized sensing
- Applications in Proteomics, Genomics, Immunosignaturing

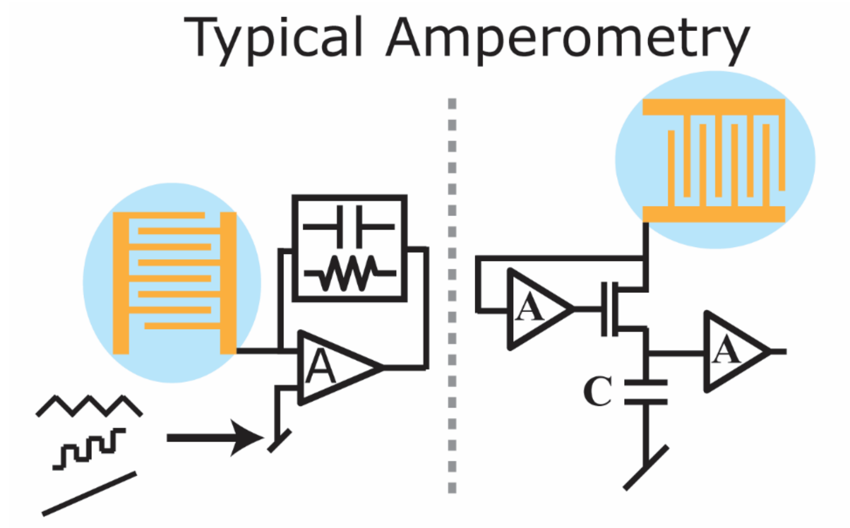
Electrochemical Biosensors



- Binding signal transduced to current $\propto$ concentration
- E-chem biosensors integrate easily with circuits

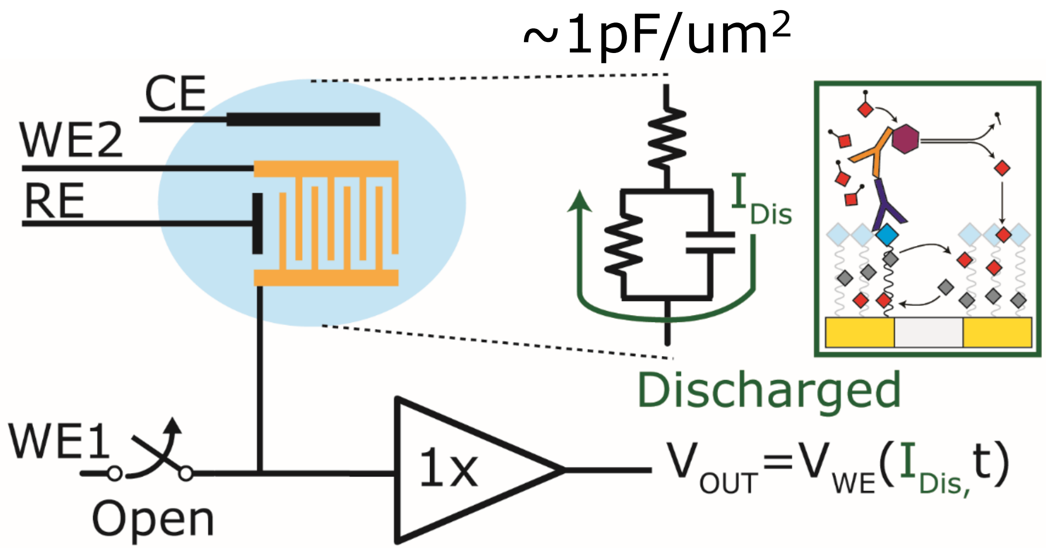
Scaling E-chem sensors





- Sensor size scales with signal
- Higher density requires detection of ultra-low current
- Sensitive potentiostats become area prohibitive

Coulostatic Discharge Technique

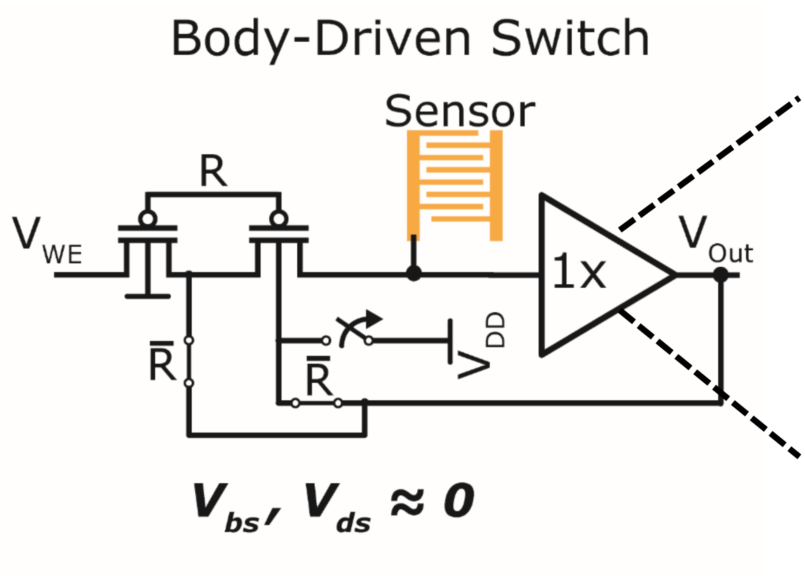


Discharging Stage

Charging Stage

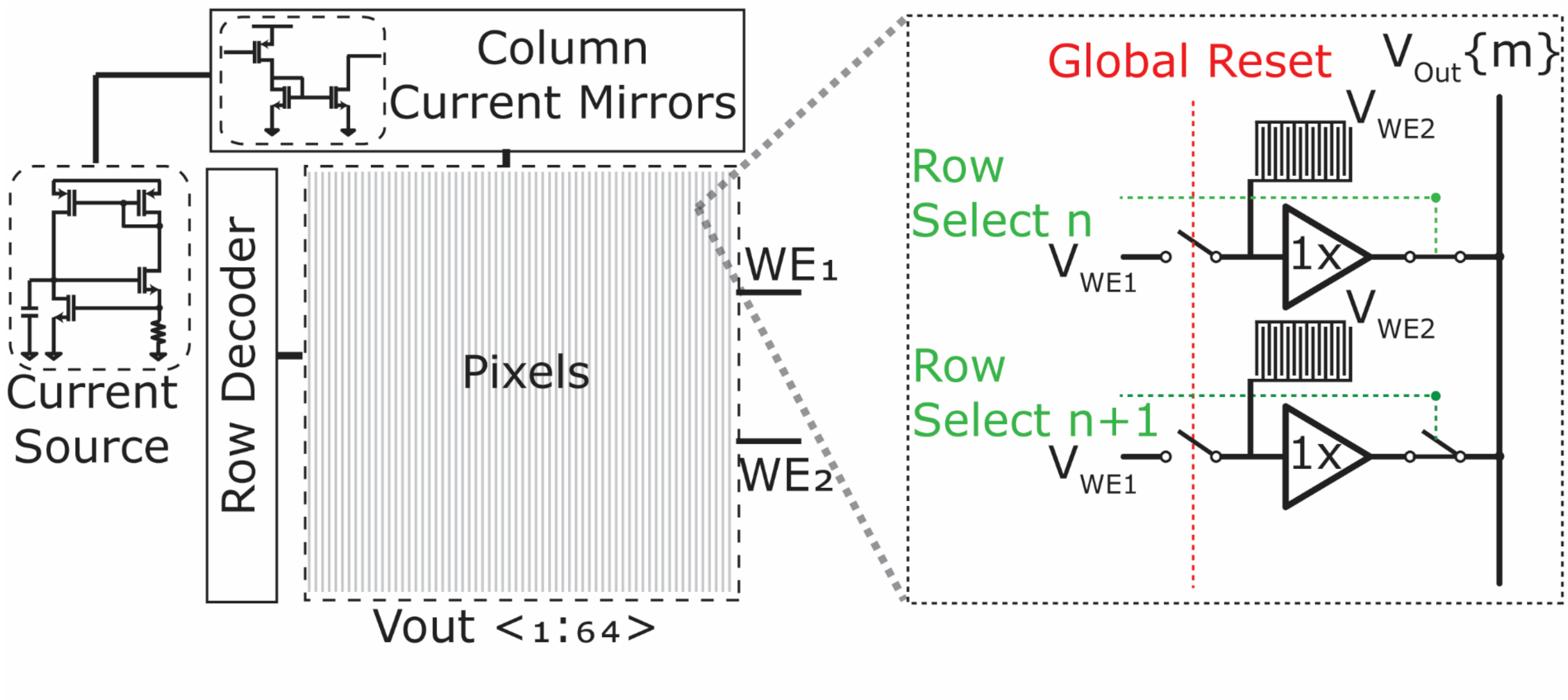
- Convert *current* measurement to *voltage over time*
- Reduces circuitry, only buffer and switch needed
- Capacitance scales with size, discharge rate constant
- Sensor node ultra-sensitive to leakage through switch

Low Leakage Switch



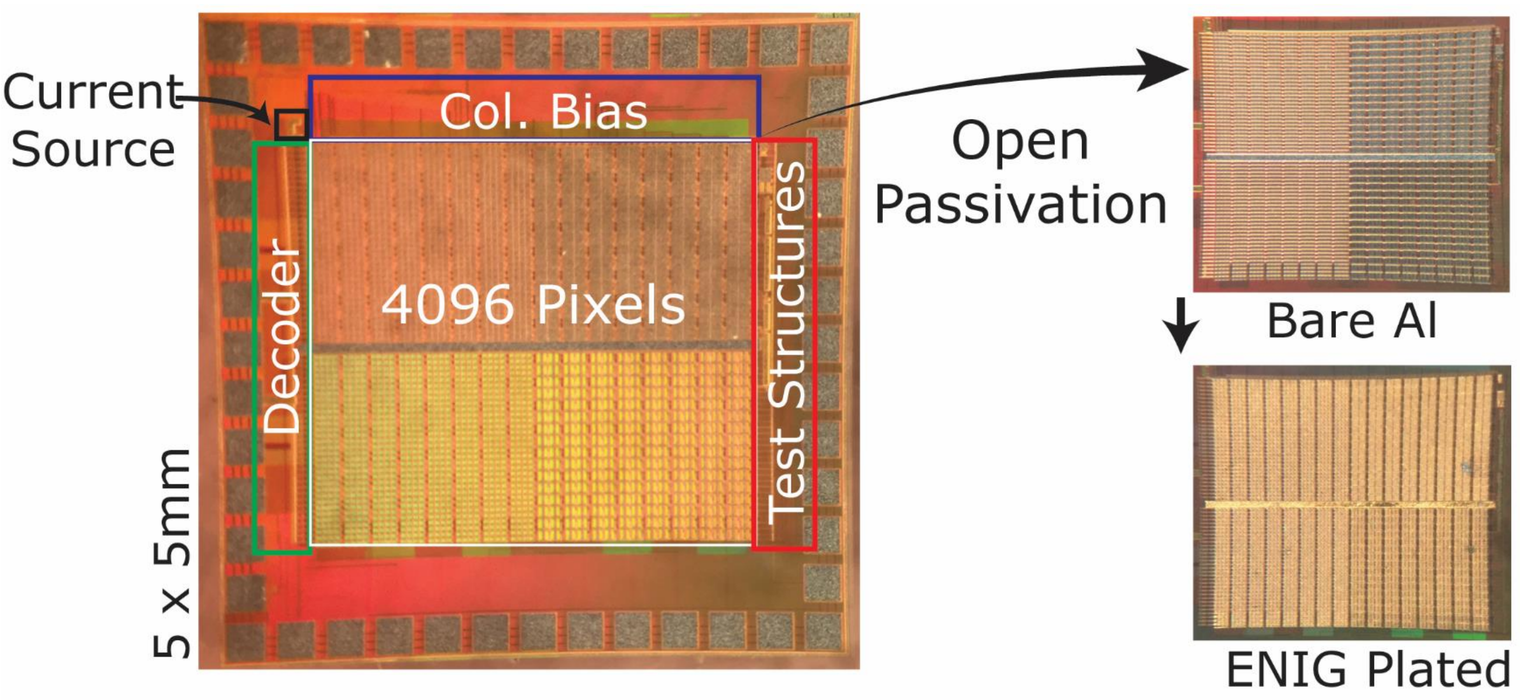
- Body-driven switch designed to minimize leakage
- Pixel circuitry designed for compactness and minimal devices
- Leakage was measured to be sub-femptoampere

Coulostatic Discharge Array



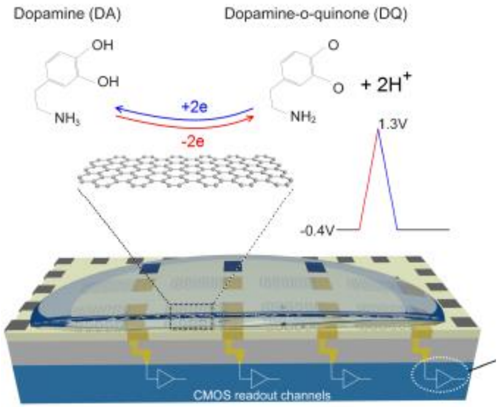
- Packed and arranged like an imager with row decoder
- Bias current is shared between every 4x4 grouping

Integrated Discharge Array

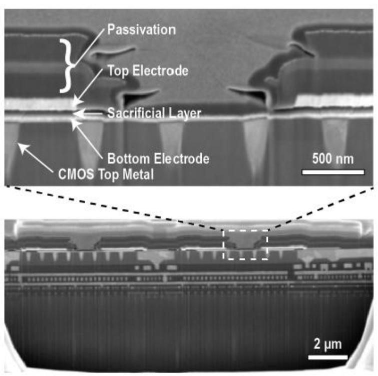


- 64x64 biosensor array in 0.18 CMOS, 50x50μm^2 pixels
- In-pixel circuitry implements Coulostatic Discharge
- Sensors on top metal with passivation opened
- **Only gold plating, no complex post-processing**

Sensor Structure

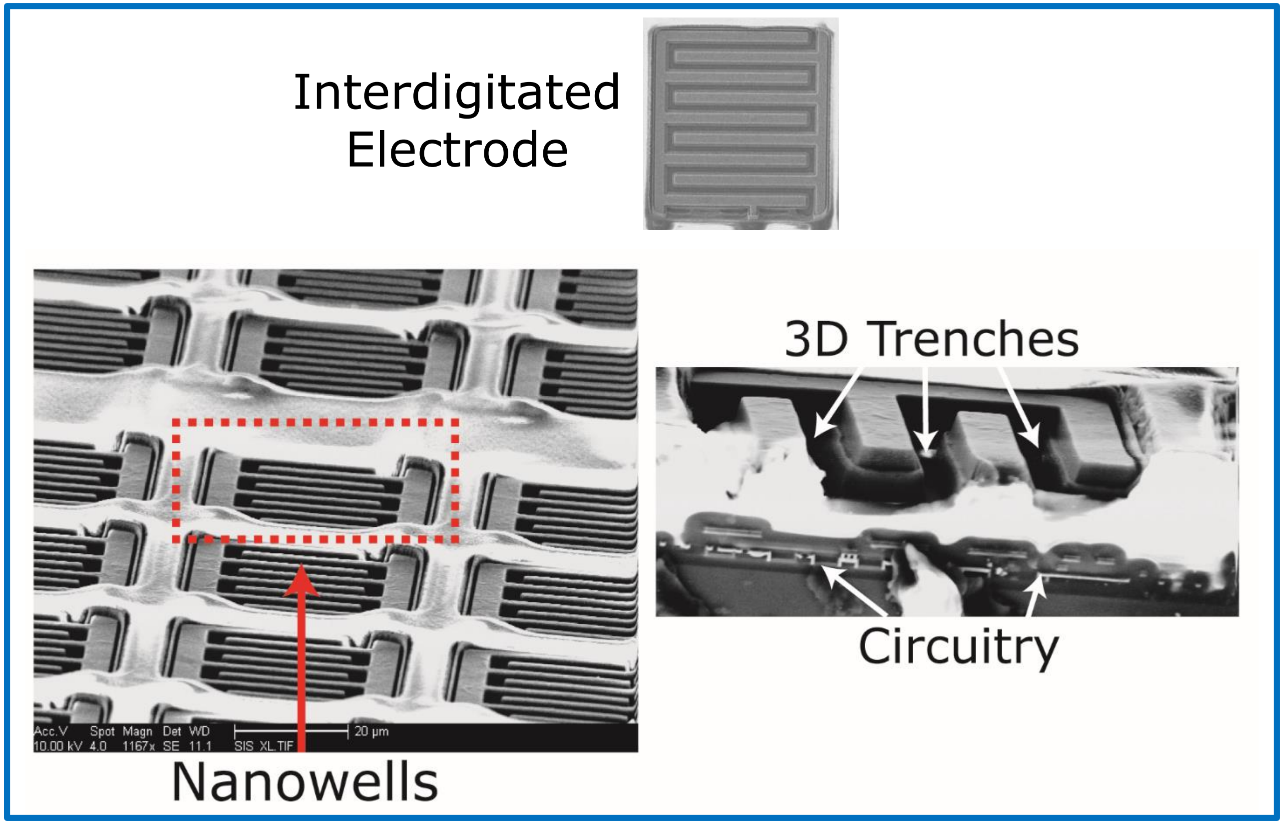


[Nasri, ISSCC, 2017]



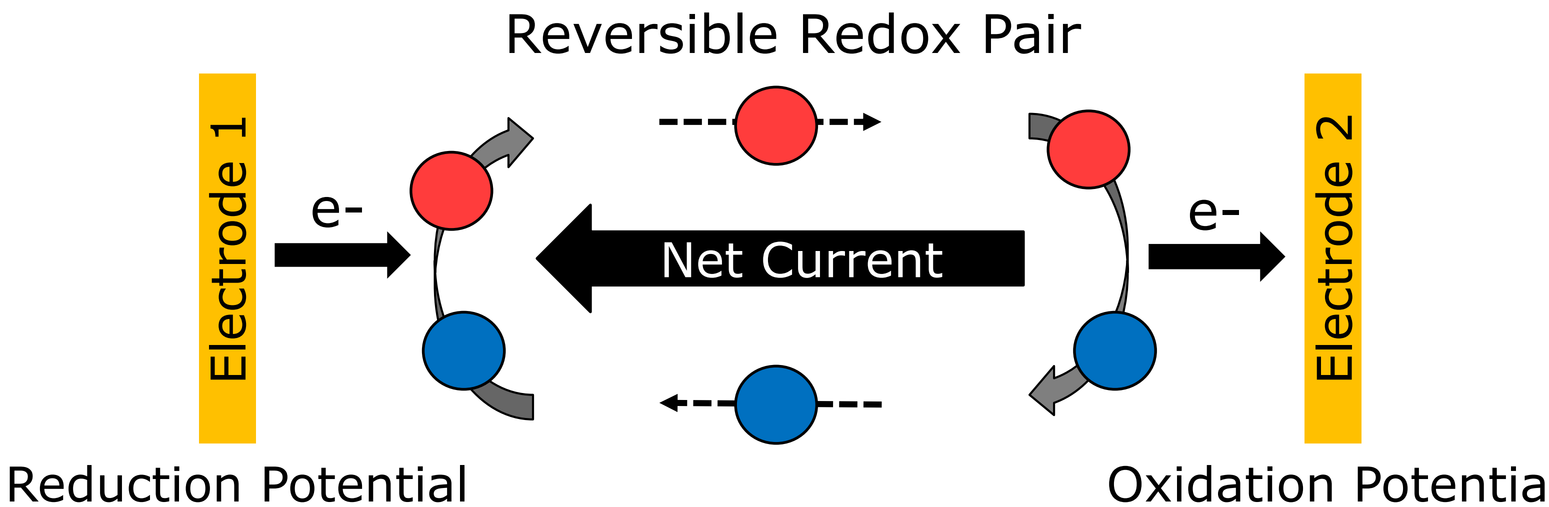
[Hall, ISSCC, 2016]

This Work



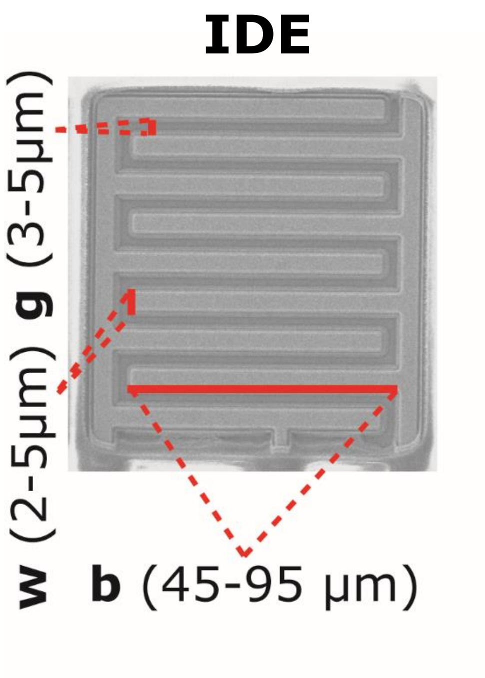
- No advanced post-processing for higher sensitivity
- Etching of passivation to create 3D structures
- 3D trenches allow for amplification via ***redox cycling***

Redox Cycling for Signal Amplification



- Shuttling (redox cycling) produces amplification
- Offset the effects of scaling
- Requires proper sizing to increase amplification factor

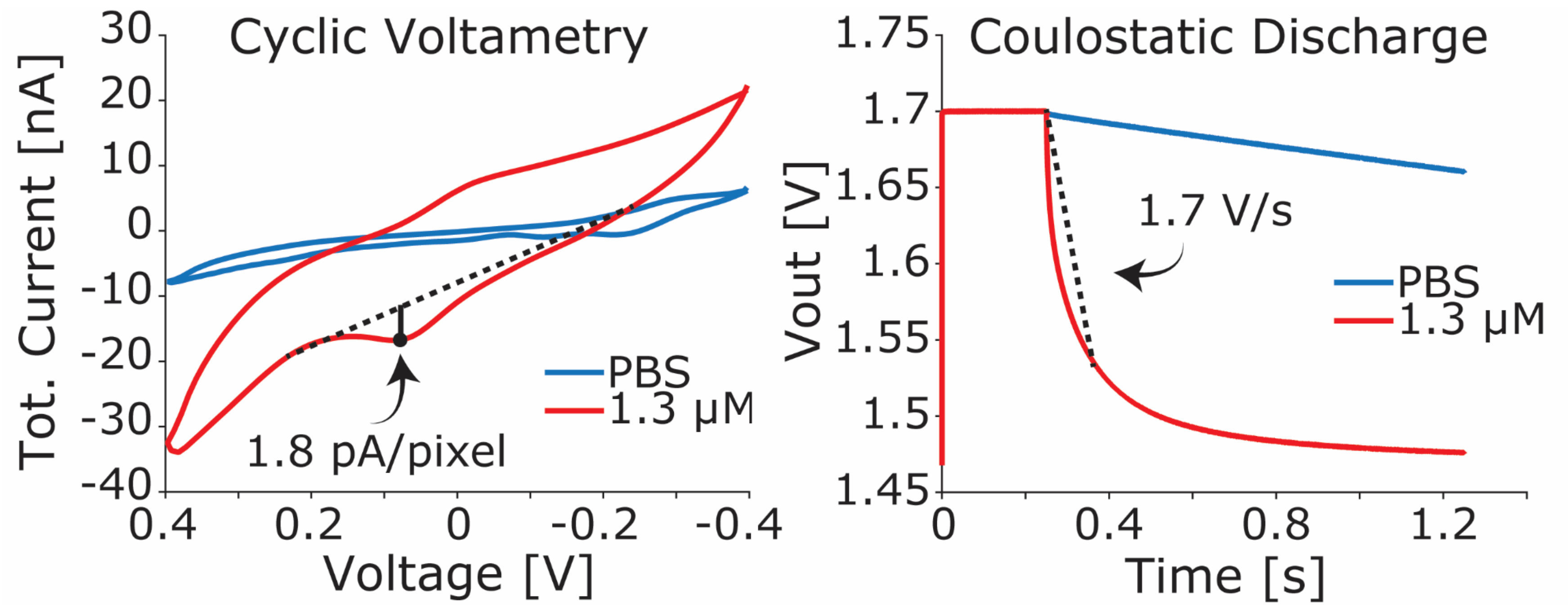
On-Chip Sensor Designs



- Studied 4 different designs sweeping w, b, and g
- Max amplification at minimum gap and width sizing
- 3D trench structure traps redox molecules

Biological Measurements

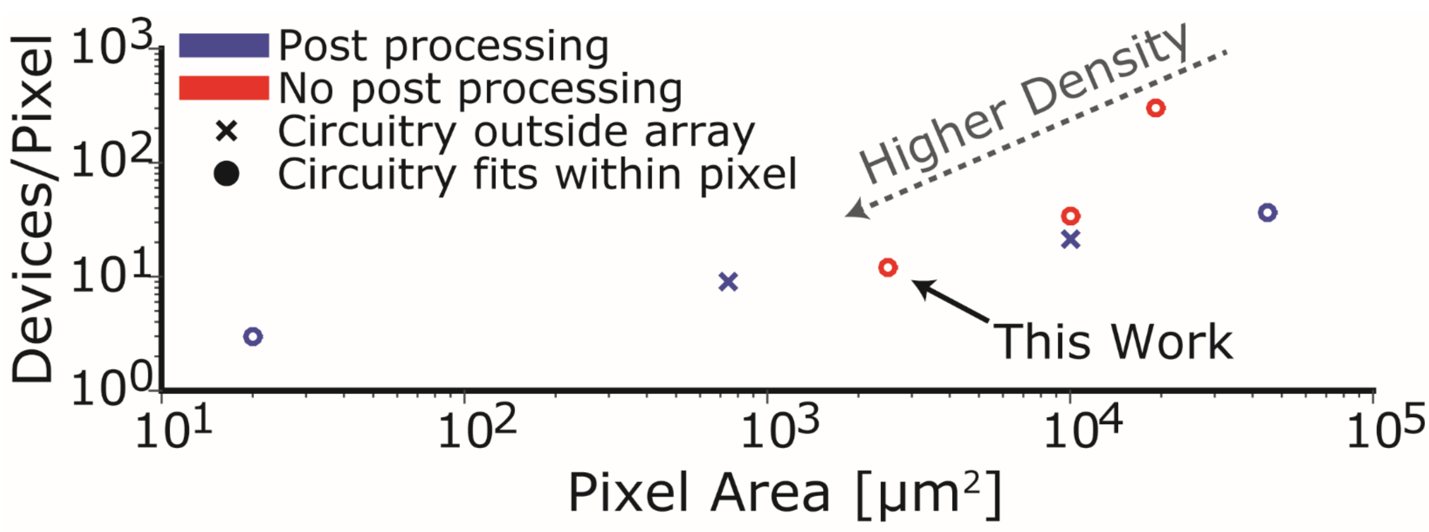
Rubella Vaccination Screening Assay



- Able to detect 1.3µM anti-Rubella antibody
- 1.8 pA with amperometry vs 1.7 V/s with discharge

Comparison

	ISSCC '05	ISSCC '10	BIO '13	AC '14	ISSCC '16	ISSCC '17	*THIS WORK*
Tech.	0.18	0.35	0.5	0.35	0.032	0.065	*0.18*
# Pixels	50	100	100	1,024	8,192	4	***4,096***
Density [#/mm²]	52.1	69.4	1,046	100	50,000	22.2	***400***
Pixel Area [µm²]	19,200	10,000	745	10,000	20	45,000	*2,500*
Devices / Pixel	301	34	>9*	21**	3	37	*12*
Technique	MULT.	EIS	CA	AMP.	CD	FSCV	*CD*
Post Processing	NO	NO	YES	YES	YES	YES	***NO***



Conclusion

Difficult to balance sensitivity and scalability with typical E-Chem techniques in biosensor arrays

Our solution:

- Use Coulostatic Discharge to shrink measurement circuitry to 400 pixels/mm^2
- Design in-pixel ultra-low-leakage (sub-fA) readout circuitry
- Design sensor geometry and leverage open passivation trenches for 10.5 times signal amplification

Result:

- Achieve the highest density amperometric array with no additional post-processing steps
- Successful detection of anti-Rubella demonstrated as progress towards a complete vaccination panel

Acknowledgements

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Thanks!

Questions?