A 201mV/pH, 375 fps and 512×576 CMOS ISFET Sensor in 65nm CMOS Technology

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Outline

- Introduction
- Ion sensitive field effect transistor (ISFET)
- High-sensitivity CMOS ISFET array sensor
- Results
- Conclusion

Personalized Diagnosis Needs Mobility

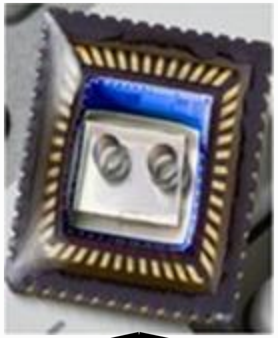
Speed of analysis

Bio Lab Equips

Equipment and labor cost

Validation rate

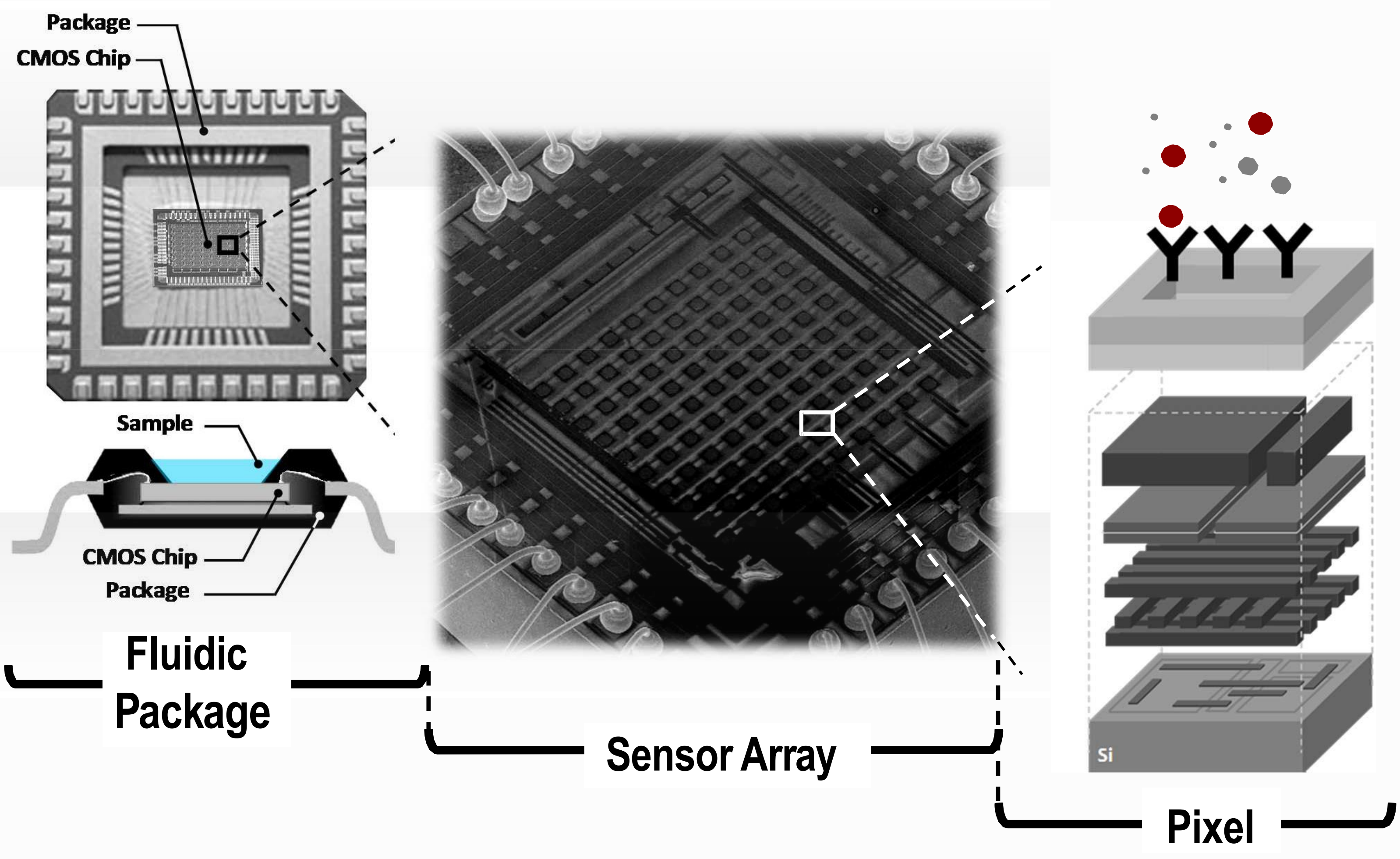
Microscope on-chip



Point-of-Care Clinic Diagnosis	Biological Sample Analysis	Disease Analysis Drug Development

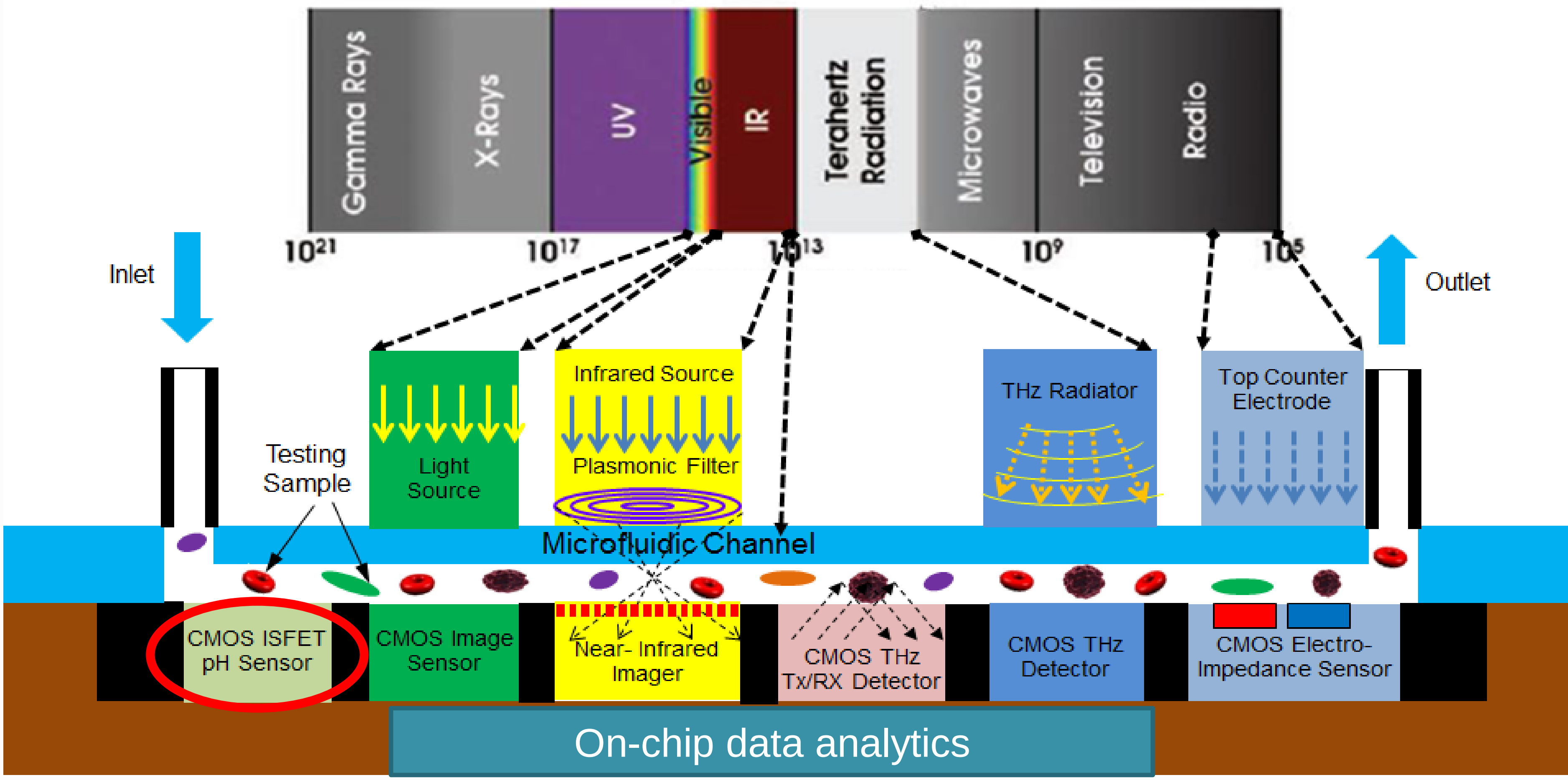
Biomedical instrument miniaturization towards portable/wearable solution

CMOS-Integrated Biosensors



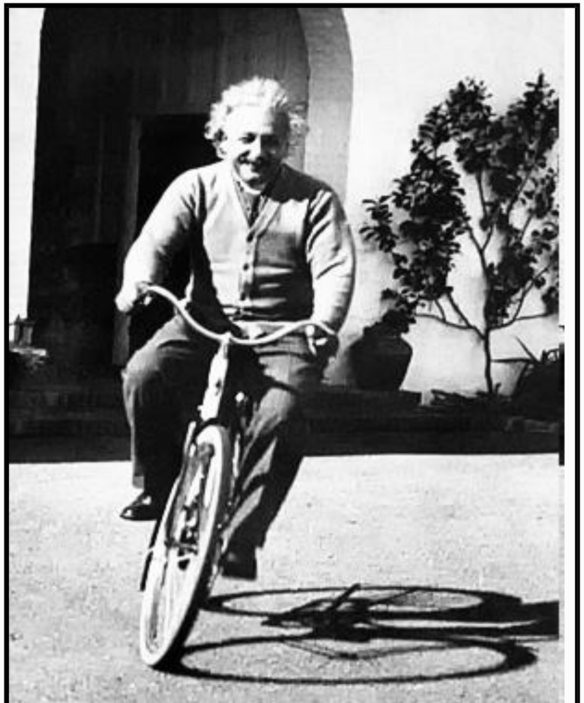
Miniaturization by integrated circuits in CMOS technology

Lab on CMOS



- **Large-arrayed, multi-spectrum, multi-modal sensor:** electrical, optical and chemical
- **Smart on-chip data analytics:** compressive, super-resolution, machine learning
- **Microfluidic channel:** molecules, tissues, cells, and biofilms

Why DNA Sequencing?



Albert Einstein (1879-1955)
Greatest Achievement: Theory of Relativity

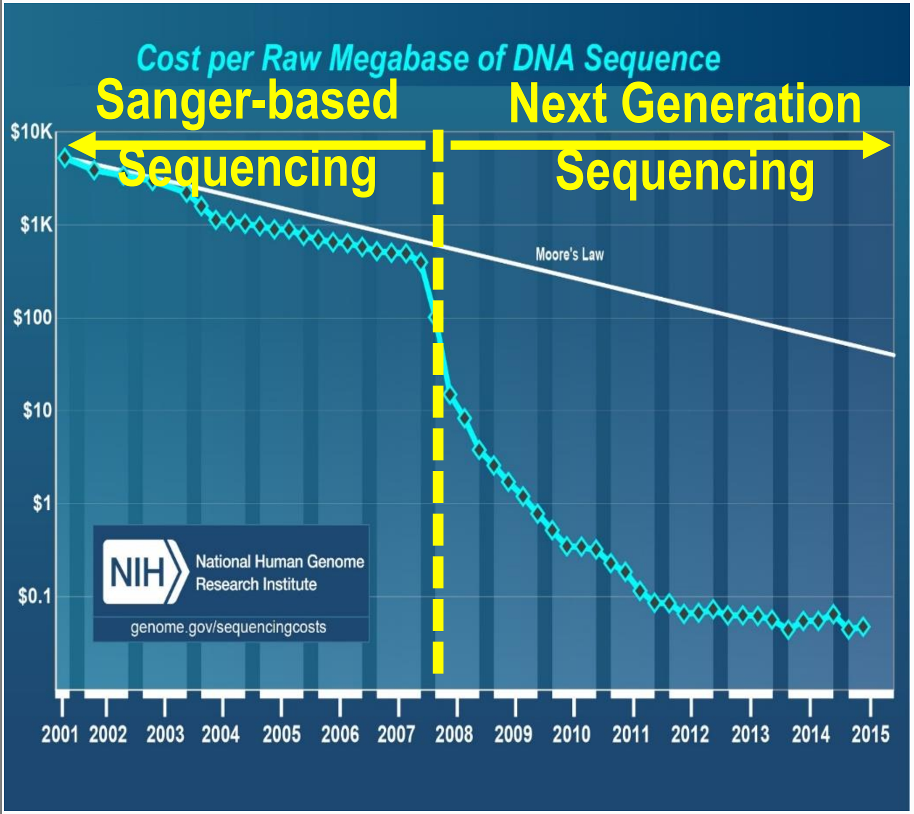
–

Bobo the Chimp (1995-Now)
Greatest Achievement: Shown Above

= **1.5% DNA Difference**

Small details in the DNA can make a huge difference if one can sense, detect and analyze the sequence!

DNA Sequencing and Moore's Law



Method	Read length	Reads per run	Time per run	Cost per 1 million bases (US$)
Ion torrent sequencing	400 bp	80 million	2 hours	$1
Pyrosequencing (454)	700 bp	1 million	24 hours	$10
Illumina sequencing	50~300 bp	6 million	1~11 days	$0.05~$0.15
Sanger sequencing	400~900 bp	N/A	20 minutes ~3 hours	$2400

High demand for low-cost sequencing

CMOS compatible sequencing system

High-throughput sequencing

Data from the NHGRI Genome Sequencing Program (GSP) : Available at: www.genome.gov/sequencingcosts.

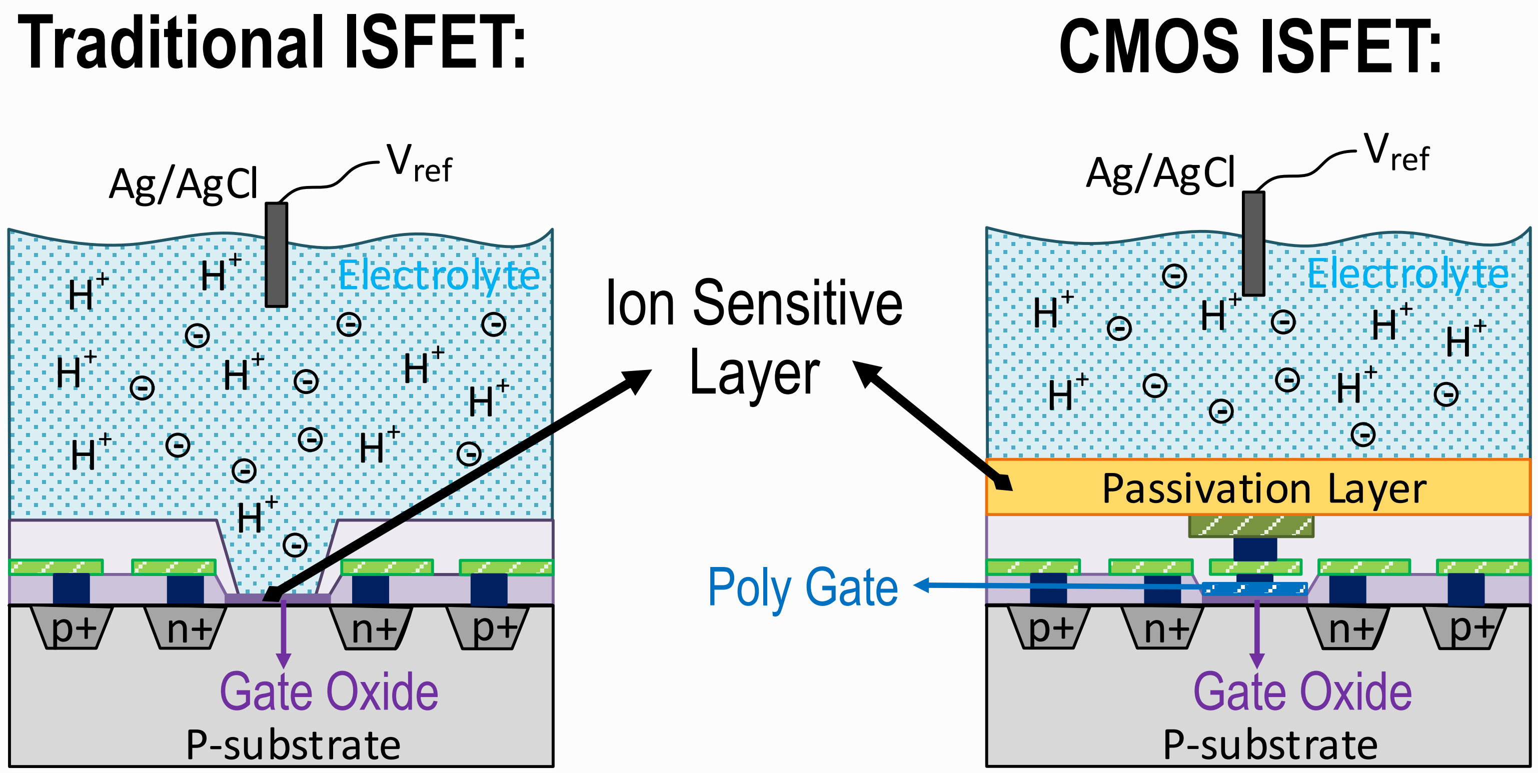
Ion Sensitive Layer in Semiconductor Devices

- **Ion sensitive layer contains chemical groups that can donate or accept a proton from electrolyte**
  - Gate oxide SiO_2 layer: SiOH site
  - Passivation Si_3N_4 layer: SiOH and $SiNH_2$ site

$$SiOH \rightleftharpoons SiO^- + H_s^+ \qquad (1)$$
$$SiOH_2^+ \rightleftharpoons SiOH + H_s^+ \qquad (2)$$
$$SiNH_3^+ \rightleftharpoons SiNH_2 + H_s^+ \qquad (3)$$

- **SiO_2 vs. Si_3N_4 layer$\rightarrow$ Traditional ISFET vs. CMOS ISFET**

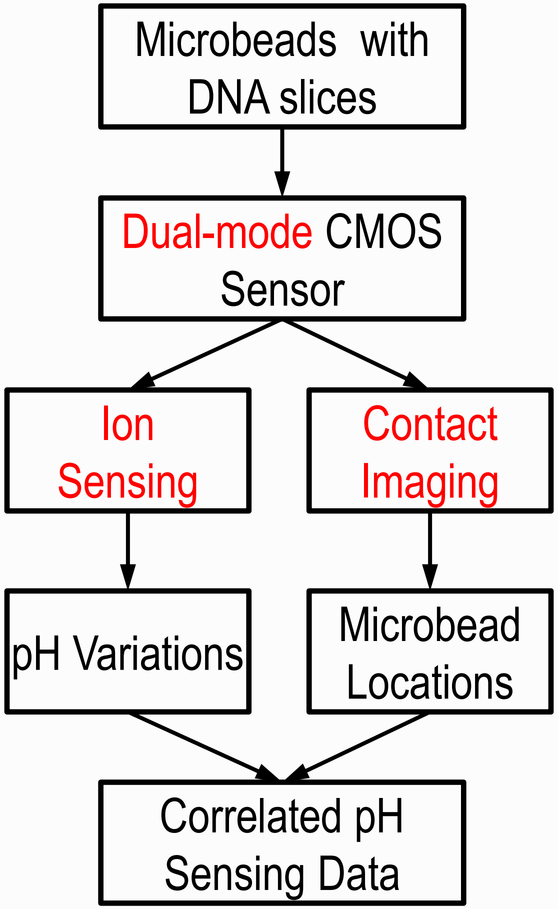
ISFET by Standard CMOS Technology

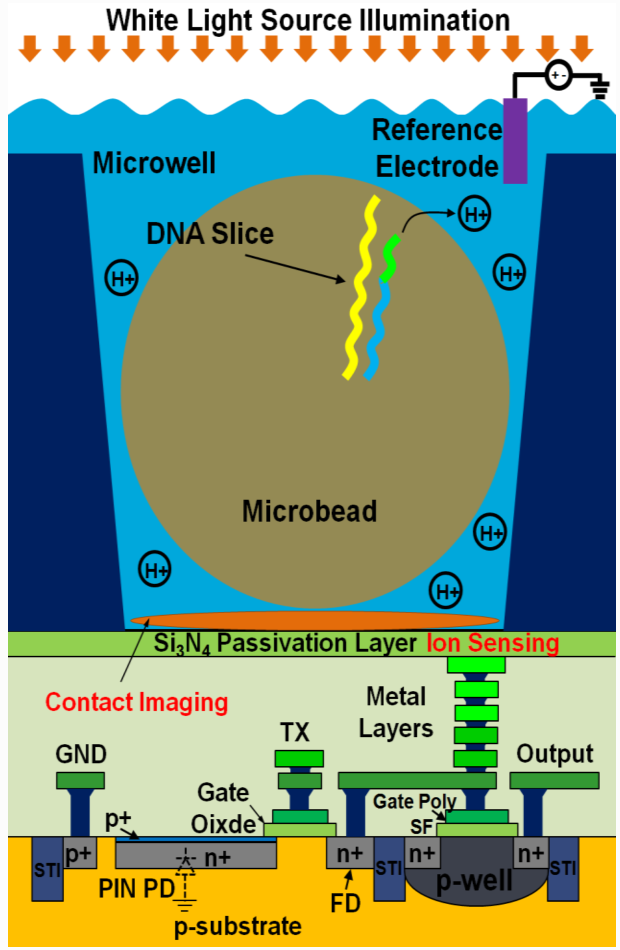


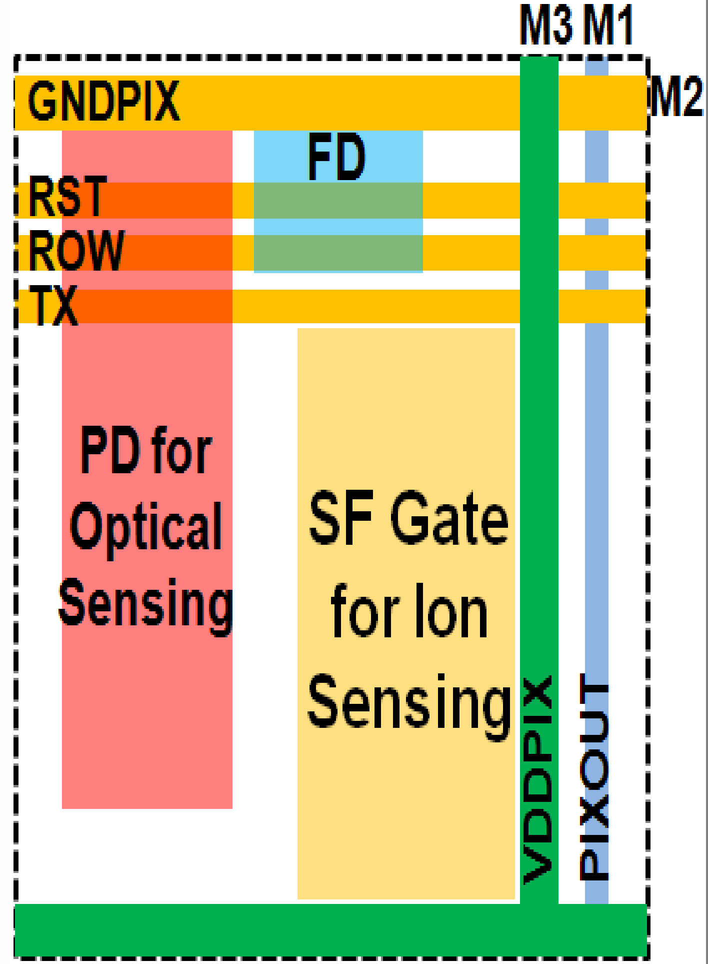
- ❑Special process
- ❑High cost

- ❑Compatible with commercial CMOS process
- ❑Low cost

Our Previous Work: CMOS Ion-Image Sensor



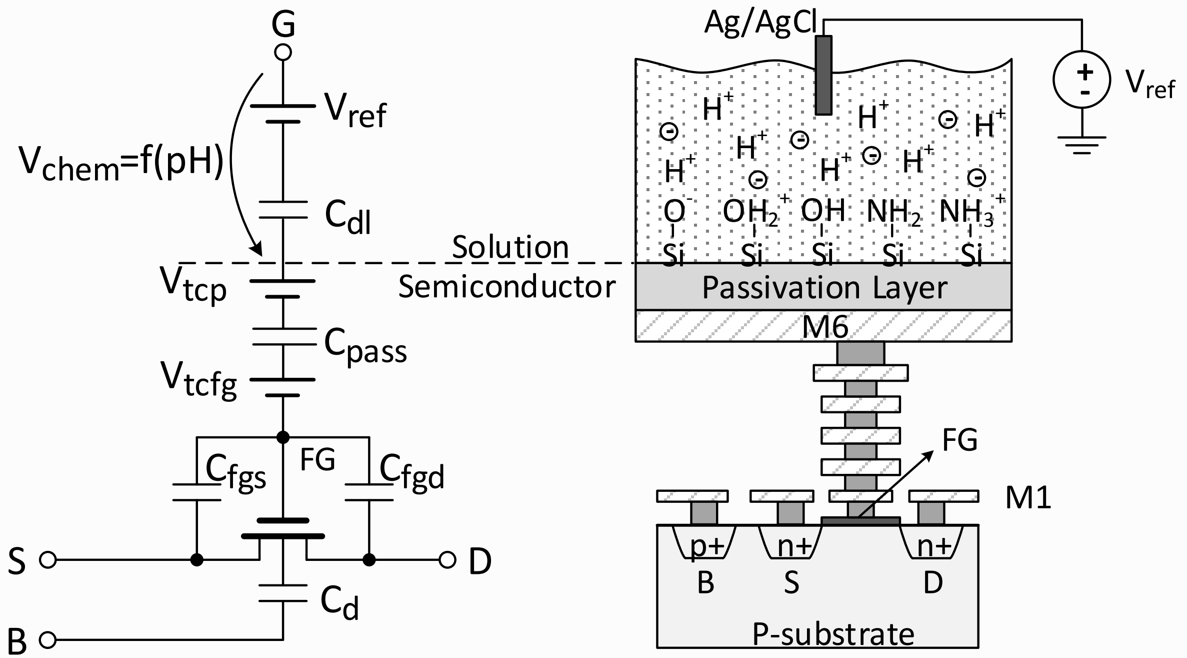




CIS based Contact Imaging + ISFET based Ion Sensing

CMOS ISFET Device Model

- Stacked capacitance and trapped charge effects are depicted



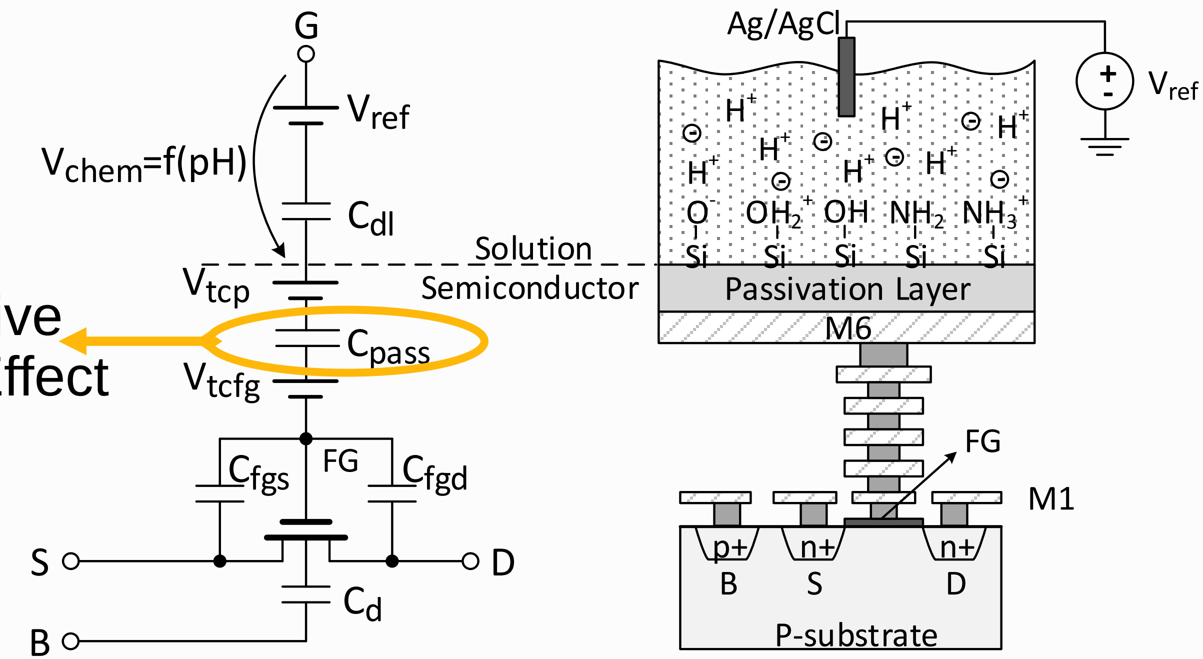
$$V_{th(ISFET)} = V_{chem} + V_{tc} + V_{th(MOSFET)}/A$$

$$A = \frac{C_{pass}}{C_{pass} + C_{ox}//C_d + C_{fgd} + C_{fgs}}$$

CMOS ISFET Challenge 1: Sensitivity Attenuation

- **ISFET floating gate voltage to pH sensitivity is reduced by the factor A**

Capacitive Division Effect

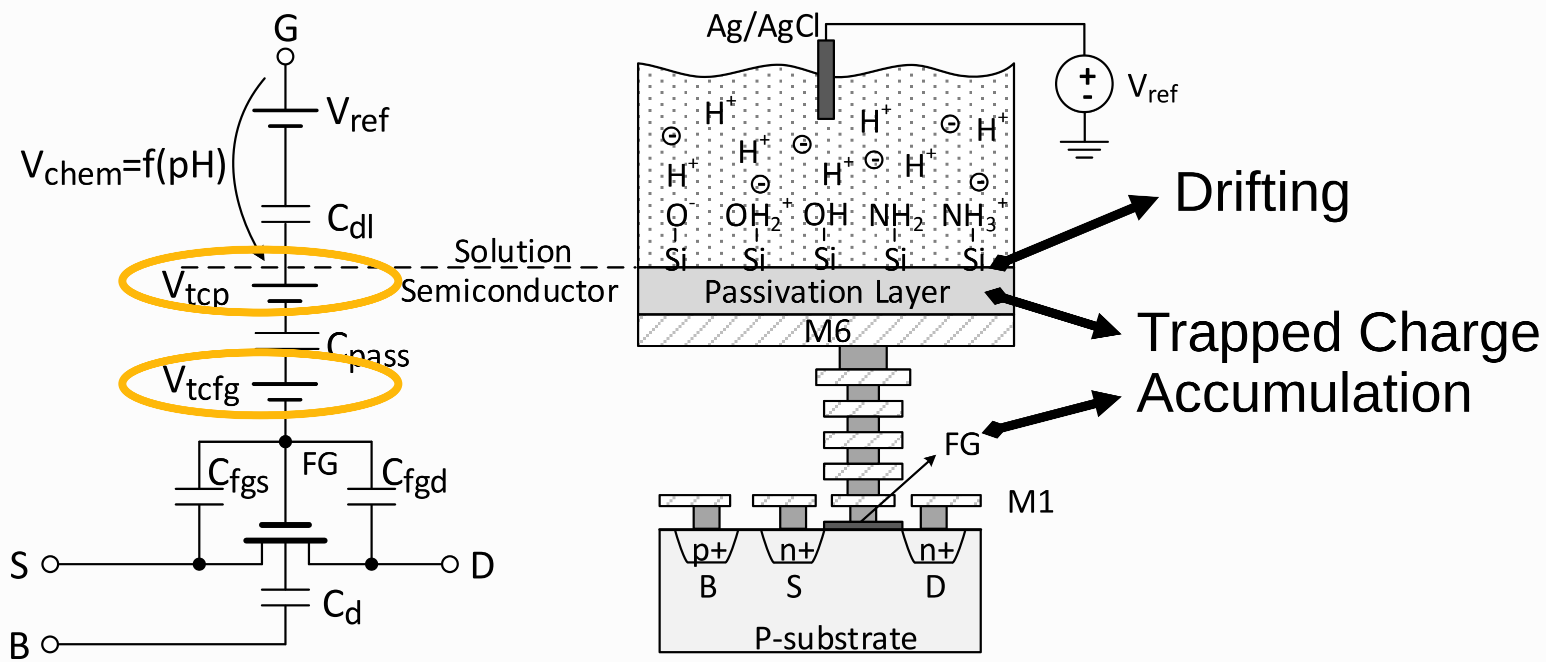


$$\Delta V_{FG} = A \cdot \Delta V_{chem} = A \cdot 2.303 \alpha U_T \cdot \Delta pH$$

$$A = \frac{C_{pass}}{C_{pass} + C_{ox}//C_d + C_{fgd} + C_{fgs}}$$

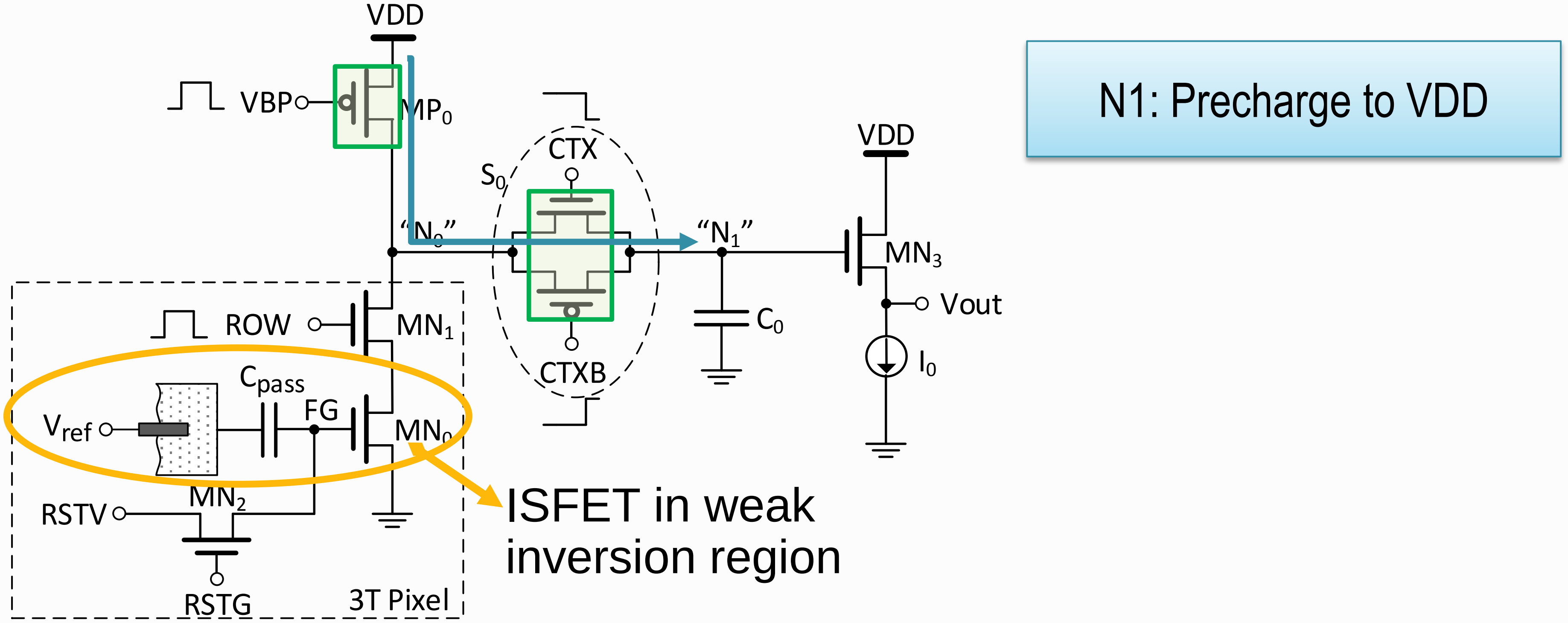
CMOS ISFET Challenge 2: Trapped Charge and Drift

- ❑ **Accumulated trapped charge → large and unpredictable threshold voltage deviation**
- ❑ **Drift → time-varying threshold voltage drift**



This Work: pH-to-Time-to-Voltage conversion (pH-TVC) Scheme

- **Operation principle: change of pH → change of ISFET Vth and drain current → change of N0 discharge time → change of N1 voltage**



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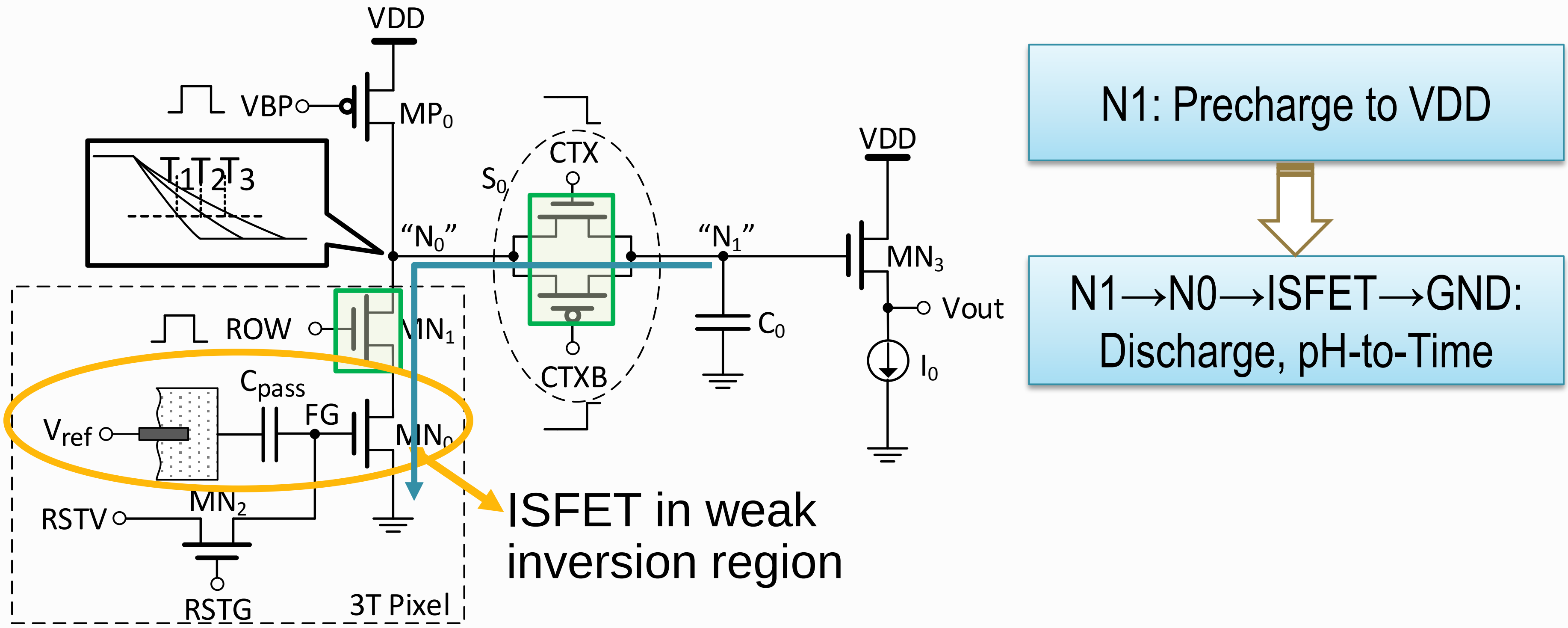

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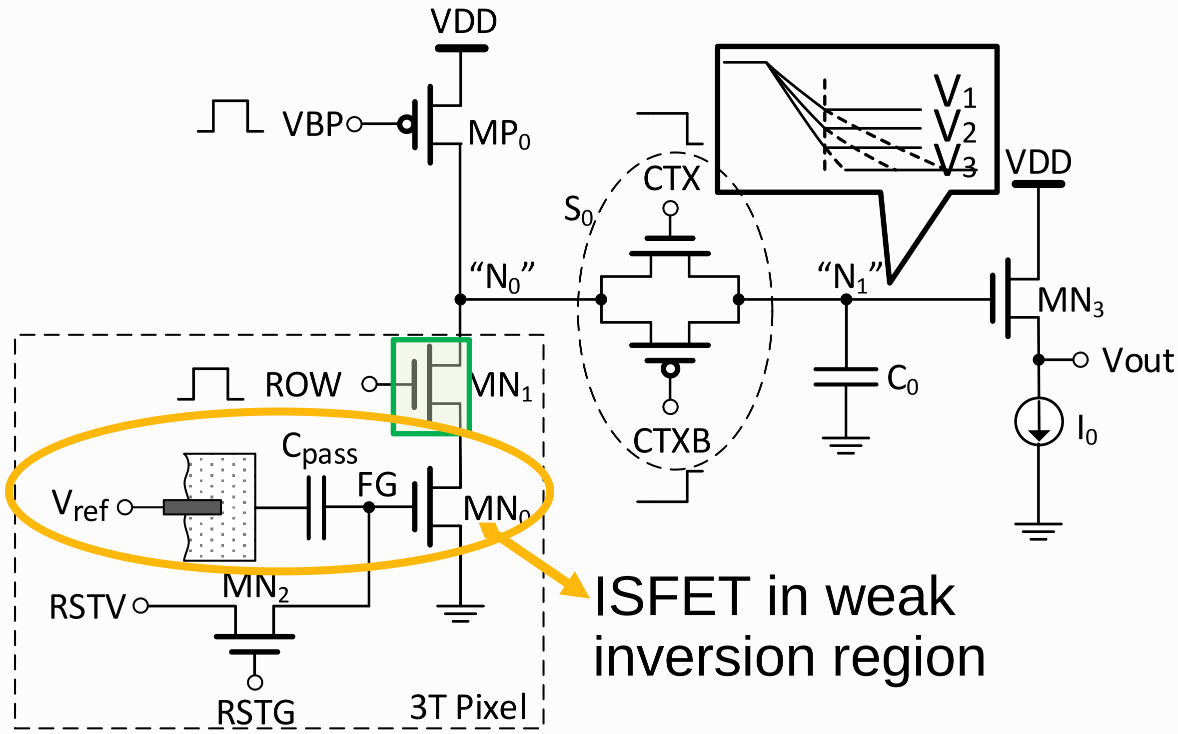


N1: Precharge to VDD

N1→N0→ISFET→GND: Discharge, pH-to-Time

N1: Voltage output (close S_0) pH-to-time-to-Voltage

Sensitivity Optimization

- **ISFET output voltage at node 'N1' ΔV_{pH} is exponential to pH change, hence the capacitive division effect is compensated**

Weak inversion ISFET: $$I_D = I_0 \cdot K \cdot \exp \frac{-A \cdot 2.303\alpha U_T pH}{nU_T} \quad (1)$$

Solution with an initial pH_1: $$\Delta V_{pH1} = V_{DD} - V_{pH1} = I_{pH1} \cdot \frac{\Delta t}{C_0} \quad (2)$$

Solution pH value change to pH_2: $$\Delta V_{pH2} = V_{DD} - V_{pH2} = I_{pH2} \cdot \frac{\Delta t}{C_0} \quad (3)$$

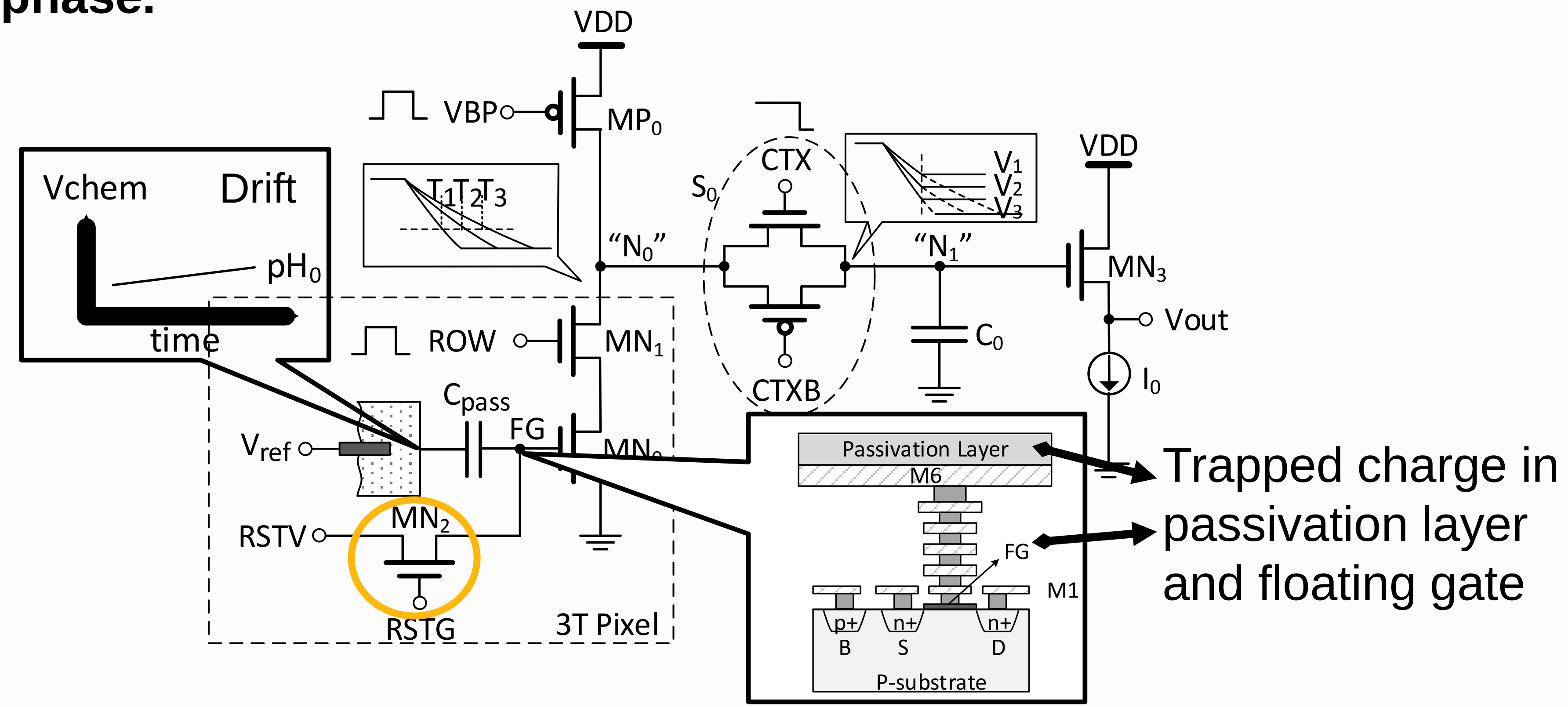
pH-related ΔV at "N1": $$\Delta V_{pH} = V_{pH1} - V_{pH2} = \Delta V_{pH1} \cdot \left(\frac{I_{pH2}}{I_{pH1}} - 1\right) \quad (4)$$

pH sensitivity to ΔV_{pH} : $$\Delta V_{pH} = \Delta V_{pH1} \cdot \left[\exp \frac{A \cdot 2.303\alpha U_T \cdot \Delta pH}{nU_T} - 1\right] \quad (5)$$

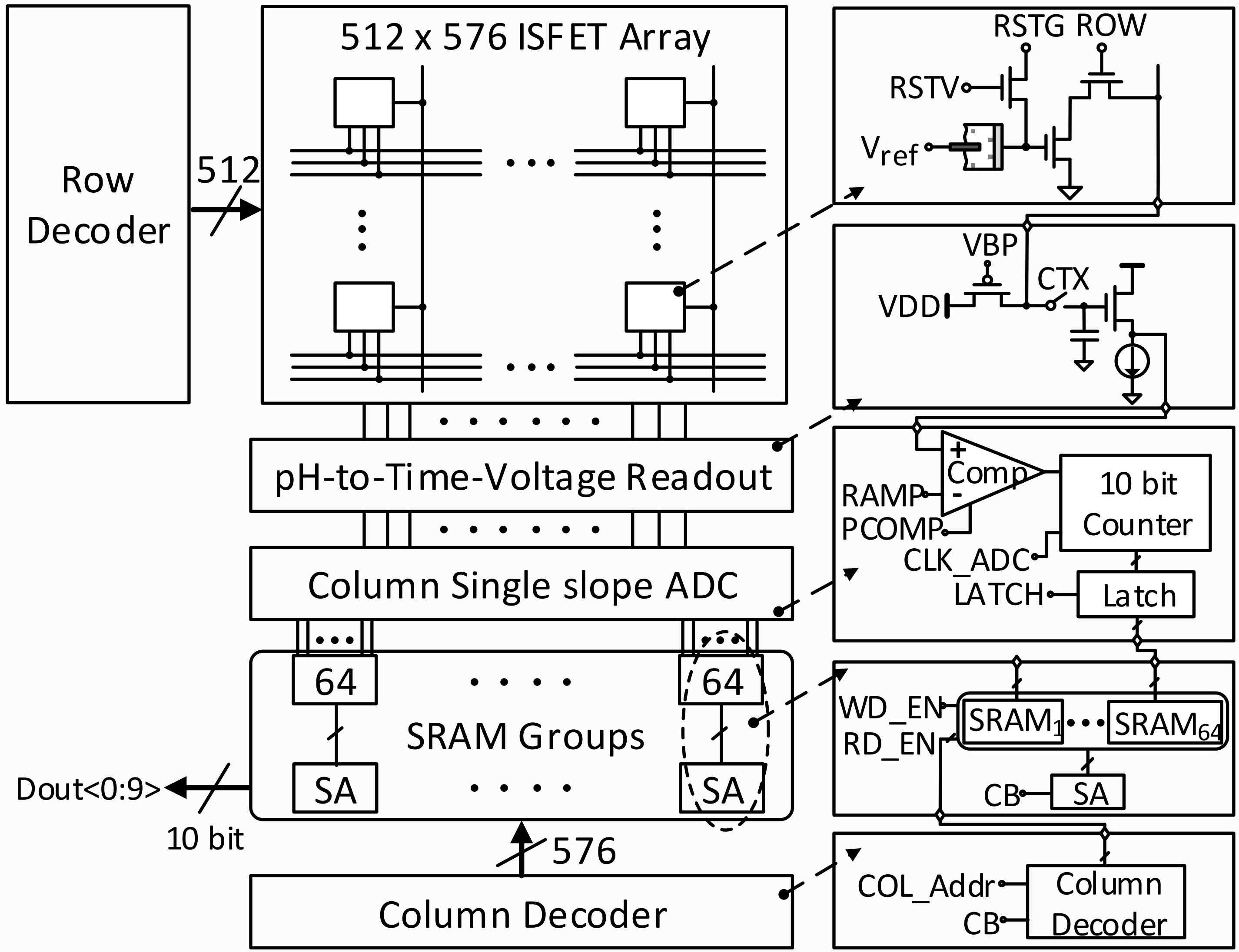
Where $$A = \frac{C_{pass}}{C_{pass} + C_{ox}//C_d + C_{fgd} + C_{fgs}}$$

Elimination of Trapped Charge and Drift

- ❑ Trapped charge in FG can be eliminated through reset device MN_2
- ❑ Trapped charge in passivation layer can be removed using ultraviolet (UV) radiation
- ❑ Drift effect can be ignored by fixing FG voltage to RSTV in reset phase.

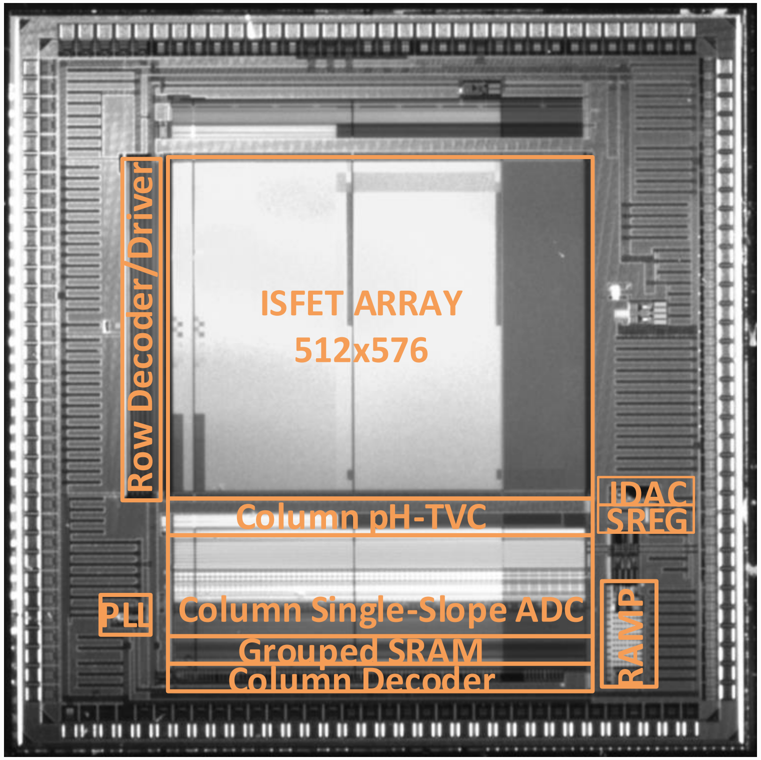


CMOS 512×576 ISFET Sensor Top Architecture



ISFET Sensor Summary

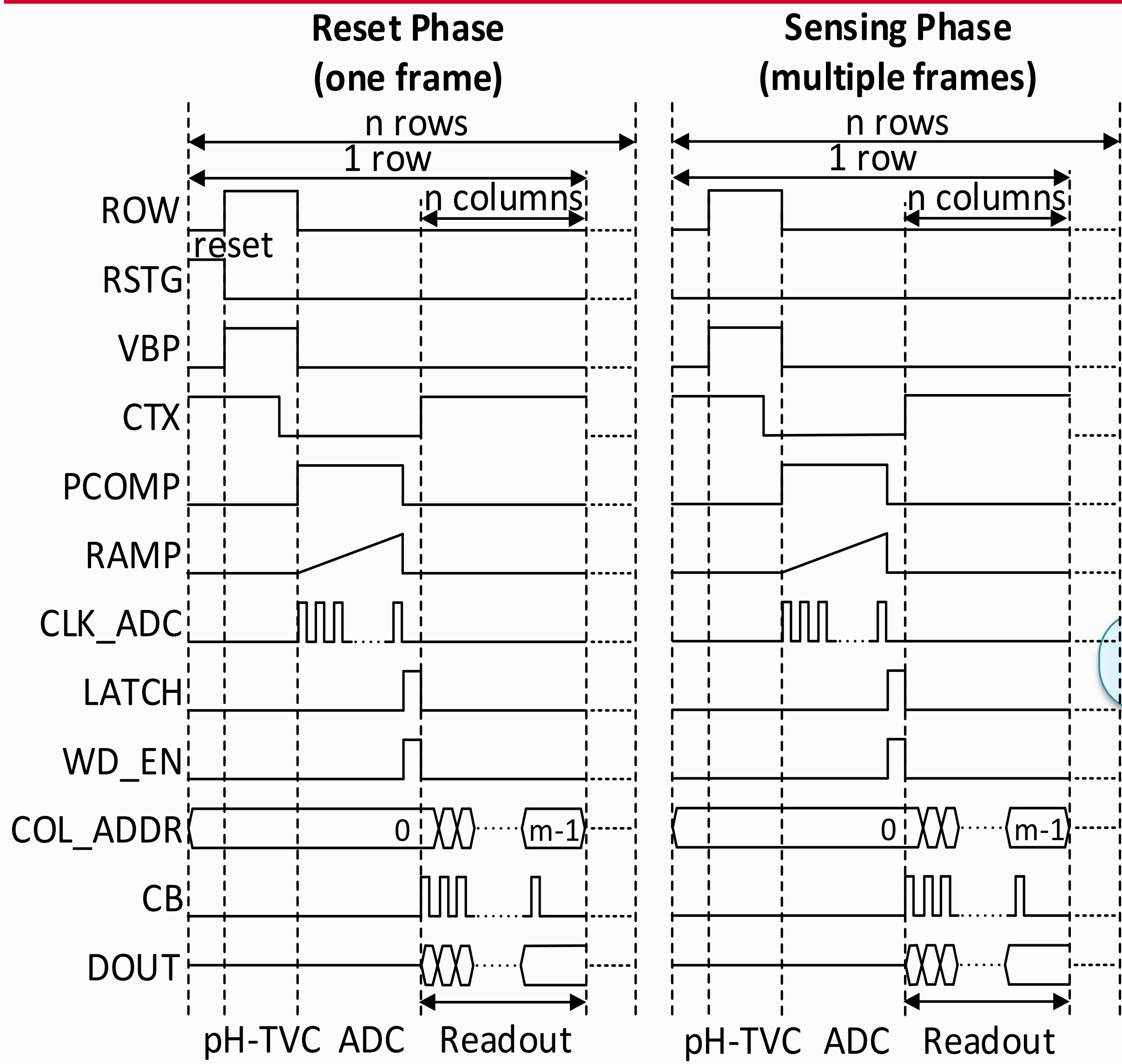
- ❑512×576 pixel array with 3.9um×3.9um chemical sensing area
- ❑201mV/pH sensitivity and 375 fps readout speed



5mm x 5mm TSMC 65nm CMOS

	[9]	[10]	[3]	**This paper**
Process	0.35μm CMOS	0.35μm CMOS	0.18μm CMOS	**65nm CMOS**
ISFET size (μm/μm)	-	5/0.35	4.8/0.3	**0.4/0.28**
Pixel pitch (μm×μm)	14×14	11.2×11.2	10×10	**4.4×4.4**
Array size	16×16	64×64	64×64	**512×576**
Sensitivity (mV/pH)	17	20	26.2	**201**
Frame rate (fps)	333	100	1200	**375**

CMOS ISFET Sensor Timing

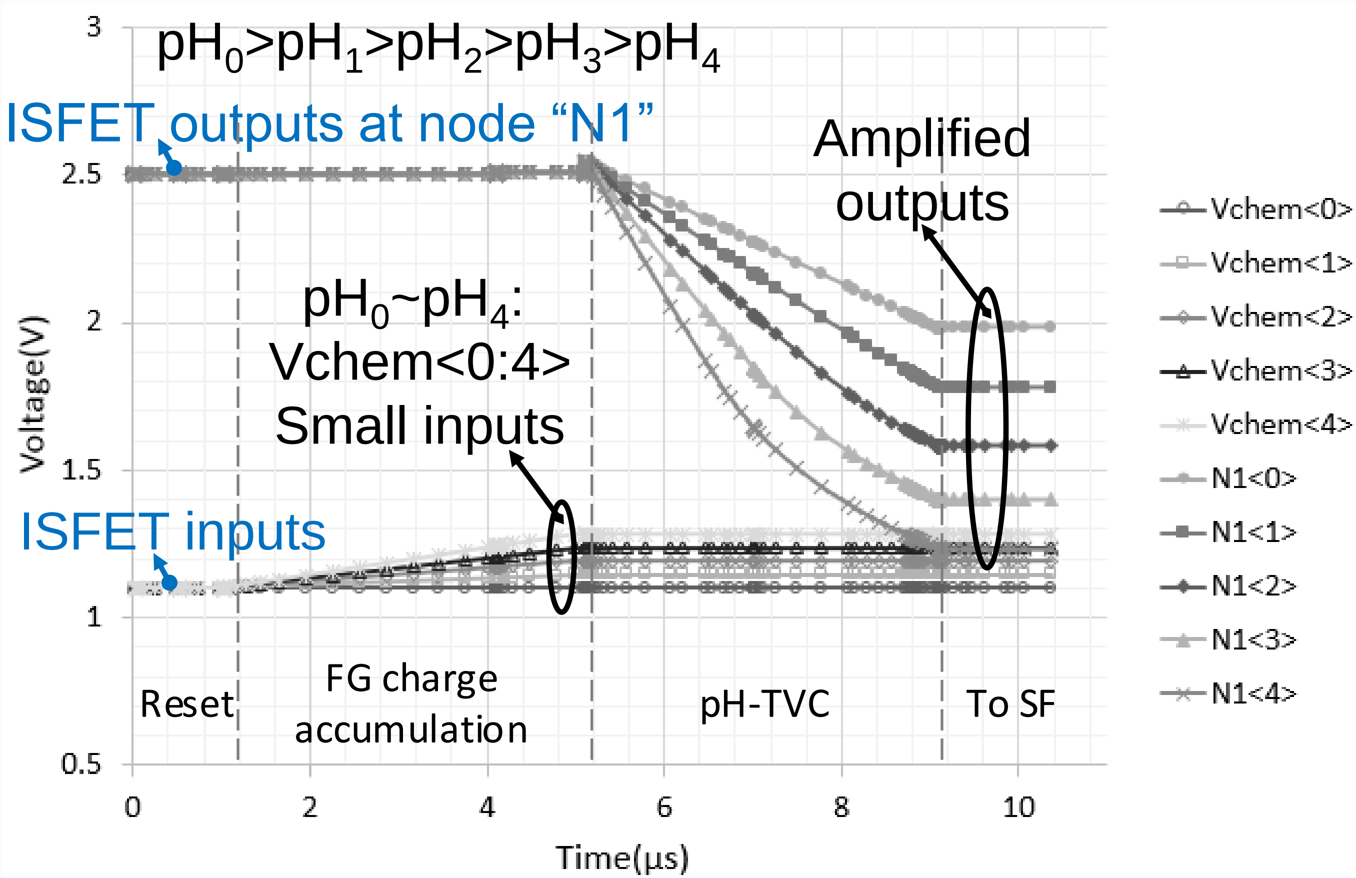


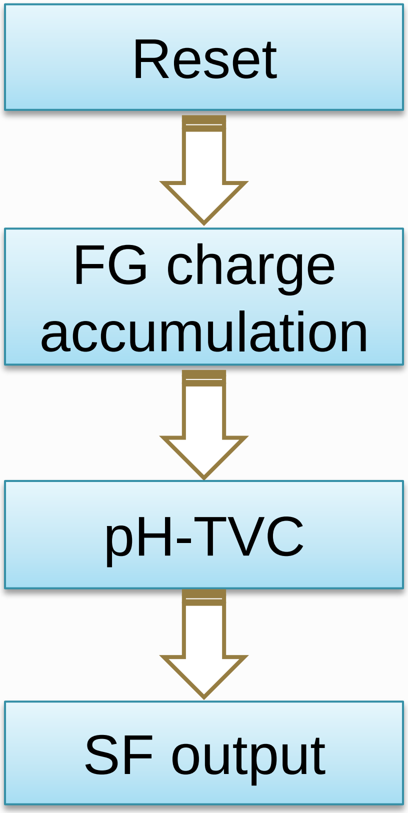
1 Reset phase (remove drift and trapped charge)

Sensing phase (keep cycling to track pH change trends)

Initial Results and Discussions I

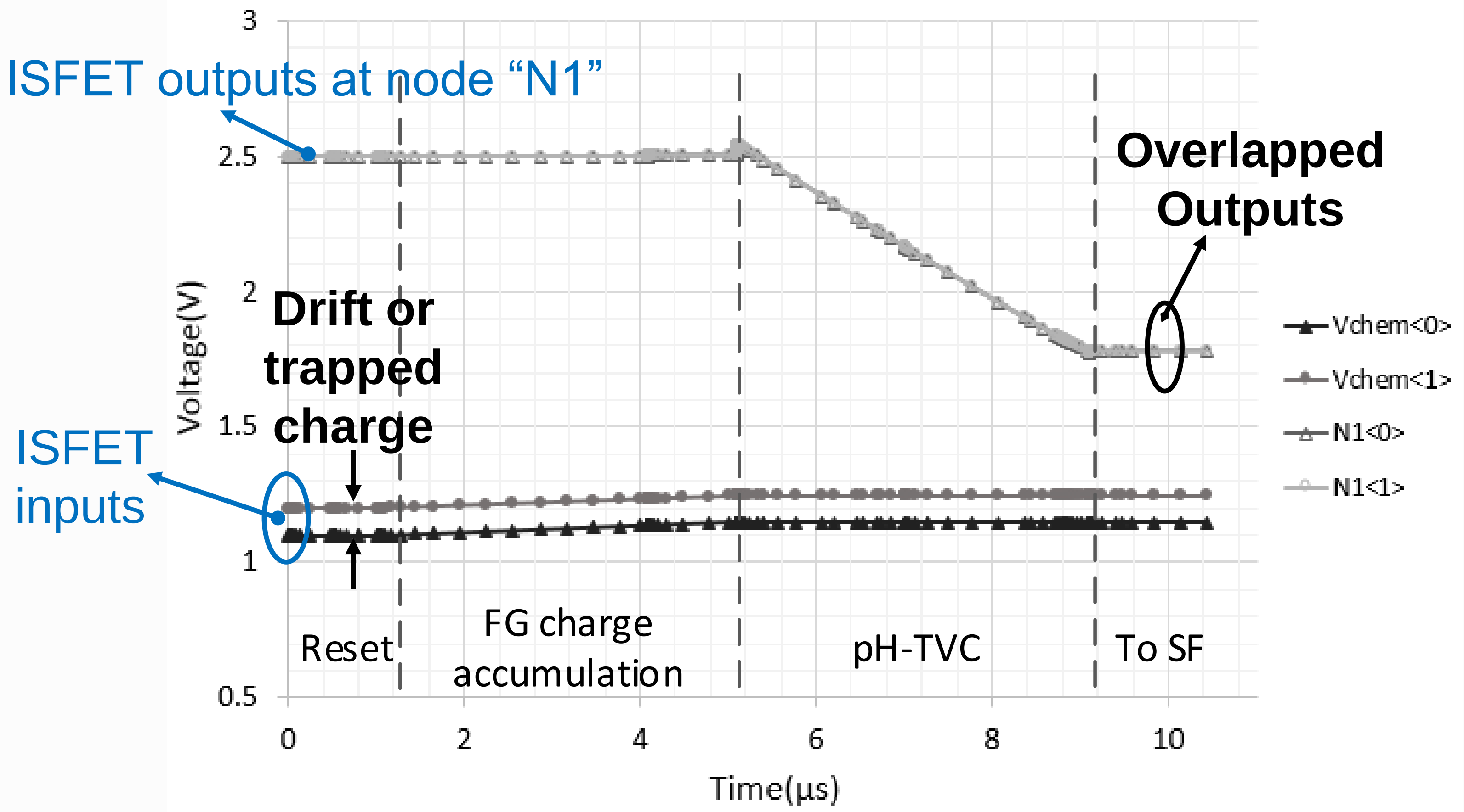
- pH sensitivity is largely improved
- A maximum of 201mV/pH sensitivity at node "N1".





Initial Results and Discussions II

- FG voltage is fixed to RSTV in reset phase
- The system is immune to drift and trapped charge effect



Conclusion

- This paper addresses two major issues faced by CMOS ISFET sensor:
  1. Low ISFET pH sensitivity
  2. Trapped charge and drift effects

- The proposed pH-TVC readout scheme compensates pH sensitivity reduction; and Reset removes non-ideal effects such as trapped charge and drift

- A 201mV/pH, 375 fps and 512×576 CMOS ISFET sensor is designed and fabricated with support by TSMC sensor team

Thank You!

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