# Ion-sensitive field-effect transistors

### **Basics and Applications**

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# Introduction

- Introduction of potentiometric sensors
  - Measuring the electrical potential difference at a solid/liquid interface
  - Nernst Equation
    - $\Delta \phi = RT/F \ln a_{i1}/a_{i2}$
    - $a_{i1,2} = f_i c_i = activity of ions i$
  - Constant potential drop at the inner surface of the bulb
  - Contact between inner KCI solution and the outer solution
  - Electrochemical couple



Fig.1 Cross sectional view of combined pH electrode.

# Introduction

- Problem of miniaturizing
  - Less stable

→ problematic for in vivo measurments

- Bergveld 1970: "Development af an Ion-Sensitive Solid-State Device for Neurophysiological Measurements"
- Advantage of chip technology
  - cheaper
  - Improved characteristics
  - Reproducability
- Ion-Sensitive Field-Effect Transistor (ISFET)
  - small and rigid
  - fast response





# Introduction



- Industry: Development of patents
- Markets:
  - Food industry
  - Biomedical industry
- Biocompatibility is still a big problem for in vivo measurements
- Future: inline-monitoring of industrial processes

- Metal Oxide Semiconductor
  - Field effect: Voltage  $V_{\rm G}$  induces charges at the surfaces  $\rightarrow$  electric field
  - Ideal MOS-structure
    - W<sub>M</sub> = W<sub>Si</sub>
    - perfect insulator
    - no charges inside the oxide





- Apply a voltage V<sub>G</sub>
  - Inducing surface charges /space charges
  - Bending: due to surface charges/applied potential



Ψ<sub>S</sub> = potential at the semiconductor surface, determines the bending
Calculation by solving Poisson Equation
Boundary conditions:
i) electric field E = 0 inside sc

ii) electric field  $E \sim Q_S$ 

Leads to a relation between surface charges  $Q_s$  and the surface Potential

 $\Psi_s$ = 0 = Flatband condition (ideal MOS)

P-type semiconductor

 $V_{\rm G}$  < 0

 $E_{F,M}$  increasement

 $\rightarrow$  upward bending

Accumulation fo holes at the sc/ oxide inetrface



#### $V_{G} > 0$

 $E_{F,M}$  decreasement

 $\rightarrow$  downward bending

Depletion of charge carriers (holes) negative space charge

(insulating layer)



P-type semiconductor

 $V_G >> 0$ : Inversion Strong downward bending  $\rightarrow$  $E_i < E_F$ :  $E_F$  closer to  $E_C$  than to  $E_V$  $N_e > N_h$ 

Strong depletion:

SC far away from Equilibrium n \* p =  $n_i^2$   $\rightarrow$  generation of electron-hole couples accumulation of electrons at the Si/Ox interface



#### n – type semiconductor

# Distribution of surface charge $\rm Q_s$



Equivalent situation, with changed polarity



Strong inversion definition:

$$\Psi_s(inv) = 2\Psi_b$$

Threshold voltage  $U_T$ :

voltage required to induce and inversion layer

$$U_T = U_G(inv) = 2\Psi_b + \Psi_i$$

$$\Psi_{i} \equiv \frac{-Q_{D}}{C_{i}} = \frac{-Q_{D}}{\varepsilon_{i}} d_{i} \equiv \text{potential across}$$
the insulator

 $-Q_D \equiv -qN_A^-W_d$  = depletion region charge





Flat-band voltage: 
$$U_{FB} = \frac{\Delta W_{m/Si}}{q} - \frac{Q_i}{C_i}$$
  $\Longrightarrow$   $U_T = U_{FB} - \frac{Q_D}{\varepsilon_i} d_i + 2\Psi_b$ 

Voltage required to induce and inversion layer: first must achieve flat-band condition, then accommodate the charge in the depletion region and finally induce the inversion region



- a) accumulation:
  - $C = C_{max} = Ci$
- b) depletion:
  - $1/C = 1/Ci + 1/C_{s}$

C < C<sub>max</sub>

c) inversion:

low frequencies (< 100 Hz)

 $C = C_{max}$ 

high frequencies (> 100 Hz)

recombination/regeneration of electron – hole couples cannot keep up with voltage variation

 $\rightarrow$  depletion zone acts as a dielectric

 $C = C_{min}$ 

# MOSFET operation



# MOSFET operation

Integration:

$$I_D = K \left( \left( U_G - U_T \right) U_D - \frac{U_D^2}{2} \right)$$

for  $U_D < U_G - U_T$  linear region  $U_D = U_G - U_T = \text{pinch off}$ inversion channel vanishes  $\rightarrow$  depletion remaining

U<sub>D</sub> > U<sub>G</sub> − U<sub>T</sub> = saturation Lenght of channel reduces →Resistance increases → I<sub>D</sub> stays constant  $I_D = K \frac{(U_G - U_T)^2}{2}$ 



# MOSFET operation



 $U_T$  depends of oxide thickness: small  $d_i \rightarrow big C_i \rightarrow small U_T$ limit: electric field strength for break through

# ISFETs

Basic Idea: removal of the metal plate of an MOSFET and expose the oxide to an electrolyte

Important: encapsulation of the chip

U<sub>G</sub>: Potential applied between reference electrode and earth

Possible Respond mechanisms:

1. Interfacial potential at electrolyte-oxide interface (s.MOSFET)

2. Diffusion of species through the oxide

Diffusion: slow process (d  $_{oxide}$  ~1000 A, t ~ 10<sup>4</sup> s)

no dependence of oxide thickness has been watched

ightarrow not the major respond mechanism

(current drift)



### ISFETS EOS-system



Electrolyte/Oxide/Semiconductor Interface

#### Inner Helmholtz Plane (IHP)

- $\cdot$  Specifically adsorbed ions
- · amphoteric hydroxyl groups

#### Outer Helmholtz Plane (IHP)

 $\cdot$  closest approach of solvated ions

#### Diffuse (Gouy-Chapman) Layer

 $\cdot$  diffuse charge region into the bulk electrolyte

# ISFETS EOS-system



flat band potential ( $\psi_{\rm S}$ =0)

$$U_{FB} = U_{Ref} - \psi_0 + \chi^{sol} - \frac{W_{Si}}{q} - \frac{Q_i}{C_i}$$

 $U_{\text{Ref}} \equiv$  reference electrode potential  $\psi_0 \equiv$  potential drop in the electrolyte

#### Potential drop across:

- Solution (Bulk  $\rightarrow$ 

diffuse layer  $\rightarrow$  OHP  $\rightarrow$  IHP

- Oxide /Electrolyte surface dipoles
- Capacitance of the oxide
- Oxide/Semiconductor interface dipoles
- Semiconductor

 $W \equiv Si$  work function

 $Q_i / C_i \equiv$  oxide potential drop

 $\chi^{sol} \equiv$  electrolyte surface dipole potential

### ISFETS EOS-system

#### First Approach: Nernst Equation

Interface between solid (oxide) and liquid (electrolyte)

Equilibrium:  $\mu_i^{ox} = \mu_i^{sol}$ 

**Electrochemical Potential in one phase** 

 $\mu_i = \mu_i^0 + RT \ln a_i + z_i F \Phi$ 

a<sub>i</sub> = activity of component i a<sub>ox</sub>= 1

Potentialdifference:Galvani Potential

$$\Delta \Phi = \Phi_{sol} - \Phi_{ox} = \Delta \mu_i^0 + RT/F \ln (a_i^{sol})$$

For 
$$i = H^+$$
:  $U_{interface} = E_0 + RT/F \ln(a_{H^+})$ 

In real measurements: strong derivations from Nernstian behaviour For good insulators ( $Si_3N_4$ ,  $Al_2O_3$ ) thermodynamic equilibrium between electrolyte and oxide cannot be achieved

### pH-sensitivity and Site-Binding Model

Amphoteric behaviour of Oxides



### pH-sensitivity and Site-Binding Model

Equilibrium of H<sup>+</sup> between the oxide surface and the bulk solution  $\Psi o$  = potential difference between surface and bulk solution =  $\Psi s - \Psi b$ 

 $[H^+]_s$  related to  $[H^+]_b$  by equating the electrochemical potential

$$\implies \mu_{H^+}^S + kT \ln[H^+]_S + q \psi_0 = \mu_{H^+}^b + kT \ln[H^+]_b$$

$$[H^+]_S = [H^+]_b \exp\left(\frac{-q \psi_0}{kT}\right) \exp\left(\frac{\mu_{H^+}^b - \mu_{H^+}^S}{kT}\right)$$

$$\implies [H^+]_S = [H^+]_b \exp\left(\frac{-q \psi_0}{kT}\right)$$
Boltzmann...

### pH-sensitivity and Site-Binding Model

Number of Surface sites:  $N_s = \sum [OH_2^+] + \sum [O^-] + \sum [OH]$ Results in a surface charge  $\sigma_0(pH) = \sum [OH_2^+] - \sum [O^-]$ 

$$\sigma_0 = 0 \rightarrow pH_{pzc} = pH$$
, at which the total surface charge is zero

 $\longrightarrow [M - O^{-}] = [M - OH_2^+]$ 

With previous equations , this is leading to:

$$2.303 \cdot (\mathrm{pH}_{\mathrm{pzc}} \ - \ \mathrm{pH}) \ = \ \frac{\mathrm{e}\psi_0}{\mathrm{kT}} \ + \ \ln\left(\frac{\left[\mathrm{M} - \mathrm{OH}_2^+\right]}{\left[\mathrm{M} - \mathrm{O}^-\right]}\right)^{\frac{1}{2}}$$

pH-sensitivity and Site-Binding Model



$$-\psi_0 = \frac{\sigma_d}{C_H} + \frac{2kT}{q} \sinh^{-1} \left( \frac{\sigma_d}{\left( 8kT\varepsilon\varepsilon_0 n^0 \right)^{1/2}} \right)$$

the in Helmholtz double layer

potential drop in the diffuse layer

when the ion concentration in the solution  $(n^0)$  is

 $\psi_{0} = \frac{-\sigma_{d}}{C_{I}} = -\sigma_{d} \left( \frac{1}{C_{II}} + \frac{2kT}{q} \left( 8kT\varepsilon\varepsilon_{0}n^{0} \right)^{1/2} \right)$ 

# ISFETS pH-sensitivity and Site-Binding Model

using the charge neutrality equation

$$\sigma_0 + \sigma_d = -(Q_{Si} + Q_i)$$

$$\implies \sigma_0 = -\sigma_d \qquad \sigma_0 = \psi_0 C_d$$

linear relation between surface charge and potential

### pH-sensitivity and Site-Binding Model

Leading to an expression for the pH sensitivity of an ISFET



### pH-sensitivity and Site-Binding Model

Sensitivity depends on the used oxide material



pH-sensitivity and Site-Binding Model



#### pH-sensitivity and Site-Binding Model



# ENFETs Concept

Functionalisation of oxide surfaces

Deposition of polymeric membranes on the gate insulator

 $\rightarrow$  Matrices for immobilisation of enzymes

Common material: polyvinylchloride (PVC)

Immobilisation mechanisms

- i) entrapment in polymeric network
- ii) entrapment in gel matrix
- iii) crosslinking with multi-functional agent
- iv) covalent bonding to sensor surface



Fig. 4. Methods of enzyme immobilisation: a) entrapment in gel matrix, b) crosslinking with multi-functional agent, c), d) covalent bond with and without bi-functional agent respectively

### **ENFETs** Example

#### Glucose ENFET



ISFET

Glucose Glucose Gluconic acid Gluconic acid Gox Gox Gox Gox 0, H<sub>2</sub>0<sub>2</sub> H<sub>2</sub>0<sub>2</sub> 0, local pH change local pH change local pH change SiO<sub>2</sub>

Glucose oxidase immobilised at the insulator surface

#### Reaction in membran layer

Glucose +  $O_2$  +  $H_2O_2$  Glucose oxidase Gluconate +  $H^+$  +  $H_2O_2$ 

local pH change induced by enzyme biocatalyzed transformations

Detection of pH change with ISFET structure

 $\rightarrow$  Detection of glucose

#### Control of the pH of a solution = coulometry

Coulometric generation of H<sup>+</sup> / OH <sup>-</sup> by electrochemical reactions at generating electrodes

$$2H_20 + 2e^- \rightarrow H_2 + 2 \text{ OH}^- \quad \text{Reduction} \\ 2H_20 \rightarrow 0_2 + 4e^- + 4 \text{ H}^+ \quad \text{Oxidation}$$

Coulometry is an absolute method of ion generation

Boundary conditions

- i) well known stoichiometry
- ii) no side reactions occur
- iii) Current efficiency ~ 100%

Sensor signal can be adjusted, to induce a defined change of pH

#### Modified ENFET

Generating platinum electrodes arround gate

Excellent stability of urease  $\rightarrow$  ideal sensitive enzyme

Immobilised in polyacrylamide membrane





Limitation for simple ENFET

 $C_{\mbox{\scriptsize buffer}}$  , enzyme kinetics and reaction equilibrium depend on pH

ENFET: Strongly nonlinear response

Dynamic range depends on composition of the sample

Sensor/Actuator System:

ENFET measures pH inside membrane

 $\rightarrow$  pH control through coulometric generation of H<sup>+</sup>/OH<sup>-</sup>

Response of ENFET $\partial V$	$V_{out} / \partial[S] = EB / \beta$
--------------------------------	--------------------------------------

B = sensitivity of ISFET	E = enzymatic sensitivity
$\beta$ = buffer capacity	[S] = substrate concentration

E > 0 = acidic reaction E < 0 = alkaline reaction

Similar: electrochemical actuator

 $\partial V_{out} / \partial I = AB / \beta$ Small changes in pH: I = current through generating electrode A = sensitivity of sensor-actuator system  $\partial V_{\text{out,current}} = -\partial V_{\text{out,enzyme}}$  $\partial I/\partial [S] = -E/A$ independent from buffer Linear response on [S] capacity membrane enzyme urea reaction pН controller actuator V<sub>set</sub> ISFET Vout



Measurement set-up for the pH-static enzyme sensor

Response of a classical ISFET-based enzyme sensor (open symbols) compared with that of the pH-static sensor (filled symbols) in sample solutions with different buffer

capacity.  $\blacktriangleright$  : low buffer;  $\blacktriangleright$  : medium buffer;  $\Delta$ : high buffer

### Basic Principle

- Interaction of biological system with a FET structure
- Electrochemical processes in cells
  - Cell membrane: embedded ion channels allow ion transfer
  - Potential drop:
  - action potential: induced change of permeability

#### **Depolarisation**

Opening of quick channels  $\rightarrow$  Potentialstep in U<sub>Membrane</sub>





### Insect antenna

- Information of [S] is transformed in an electrical signal
- Polarisation in sensing hairs
- Total dipole along the anten
- Receptorpotential →
   action potential





- Coupling of antenna and FET
  - electrolyte
  - constant-Voltage mode: change of antenna potential causes change in FET surface potential
  - local peak in  $I_D([S])$



C) Sensorkopf mit Antennenhalter und FET



A) Whole-Beetle-Anordnung



#### B) isolated-Antenna-Anordnung

 Correlation between peak amplitude and [S] → sensing of [S]

- Possible application
  - Agriculture (Leptinotarsa decemlineata)
  - Fire detection(Phaenops cyanea)



# Surface Charge sensitivity DNA sensor



- Gate potential controlled by the electrical charge associated with the gate interface.
- · surface charge sensitivity ?

 $\sigma_0 = \sqrt{8kT\varepsilon\varepsilon_0 n^0} \sinh($ 

Surface charge density and surface potential

#### DNA: intrinsic negative charge at sugarphosohate backbone

#### Probe DNA: bound to PLL surface



- Target DNA: binding to complementary DNA
- →surface charge
- →depletion
- $\rightarrow$ region,potential change

Probe DNA: bound to PLL surface

noncomplementary DNA:

 $\rightarrow$  No binding



# Surface Charge sensitivity DNA sensor

Measurment of the differential surface potential enables DNA detection





Direct electrical sign al 1

Advantages of wide-bandgap materials:

i) no generation of unwanted charge carriers (optical, thermal)

ii) Strong chemical bondings  $\rightarrow$  mechanical and thermal stability

Sensor concept: modulation of charge carrier density in 2DEG near the AlGaN/GaN interface

Formation of a 2DEG:

Dicontinuity of microscopic dipole density in the wurzite crystal at the AlGaN / GaN interface

Strong electronegativity of N

 $\rightarrow$  dipolemoments along the bondings between Ga – N / Al - N



#### AlGaN / GaN heterostructure

Different strength of ionic bonds of III-nitrides

Change of macroscopic polarisation P at the
 AIGaN / GaN interface

$$P_{AIGaN} > P_{GaN}$$

Electrostatics Surface charge with 
$$\sigma = P$$
 = opposite sign at the two surfaces perpendicular to P

$$\implies E = \sigma / \varepsilon_0(\varepsilon - 1)$$

Internal electric field permanent polarisation

Internal interface: consider  $\Delta P = P_{AlGaN} - P_{GaN}$ 

=

Surface charge  $+\sigma$  at AlGaN / GaN Surface charge  $-\sigma$  at terminated at AlGaN surface

Interacts with surrounding compensating ions



Surface charge between GaN / substrate interface can be neglected

Potential landscape:

 $+\sigma \implies$  downward bending accumulation of electrons High density n<sub>e</sub> ~ 10<sup>13</sup> cm<sup>-2</sup>

2DEG: seperated from surface through insulating AlGaN layer

 $\rightarrow$  strong confinement

Ion sensitive:

X<sup>+</sup>/X<sup>-</sup> adsorbed → e<sup>-</sup> gained / lost in 2DEG affects conductivity / current





Further advantages:

- high signal to noise ratio
- chemically stable
- no toxic to living cells

great potential for physiological measurements (e.g. cell potentials)

Improved heterostructure

n – doped channel: GaN:Si

p – doped bulk: GaN:Mg

 $\rightarrow$  Strong confinement of 2DEG

→ Enhanced sensitivity



#### PROPERTIES

- large bandgap (5.45 eV)
- H-termination
- O-termination
- good biocompatibility



#### formation of dipoles

diamond

adsorbate layer



diamond adsorbate layer

- Surface conductivity of H-terminated diamond (Transfer-Doping-Model)
  - air exposure is essential
  - spontaneously formation of acidic water layer
  - redox reaction

```
2 \text{ H}_3\text{O}^+ + 2 \text{ e}^- \Rightarrow \text{H}_2 + 2 \text{ H}_2\text{O}
```

electron transfer into the liquid ( $\mu_e < E_F$ )





- pH-sensitivity of Oterminated diamond
  - Ozon treatment of Hterminated surfaces
  - amphoteric behaviour
    - $\mathrm{C-OH}\ \rightleftharpoons\ \mathrm{C-O^-}\ +\ \mathrm{H^+}$
    - $C OH + H^+ \rightleftharpoons C OH_2^+$
  - pH-sensitivity:
     site binding model

modulation of 2-D hole gas at Hterminated sites



(a) low pH - reducing accumulation of holes in the channel



(b) high pH - enhancement of hole density in the channel

- Ion Sensitivity (Kawarada,2002)
  - H terminated diamond shows sensitivity to anions and cations

(e.g.Cl<sup>-</sup> ,l<sup>-</sup> ,Br <sup>-</sup>)

- No sensitivity at
- O-terminated surfaces

#### Not reproducable so far





#### lateral modulation of the conductive channel

-Н -Н

-0

-H

-H -O

-0

-H -H

(b) crossection

-OH

- pH-sensitive Device
  - Combination of "conducting" H -terminated and "pH -sensitive"
    - O -terminated areas





# Conclusions

- ISFET: basis for many bio-/chemical sensors
- Miniaturizing and high integration
- No commercial breakthrough, caused by: – High drift
  - Miniaturization of reference electrodes (insufficient stability)
  - Exposure to corrosive electrolytes (lifetime): improved passivating necessary

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# THANK YOU FOR YOUR ATTENTION!

**Questions?**