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An Enhanced ISFET Readout Circuit for Biosensing

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Abstract **-Ion Sensitive Field Effect Transistor (ISFET) Sensors are widely used in bio sensing which plays an important role in healthcare. The ISFET consist of an ion sensitive layer which is able to detect the concentration of a specific type of ion even in the presence of other ionic components. The reaction between the solution and the sensitive membrane modulates the drain current of the ISFET that is proportional to the ion concentration of the sensing element. The ISFET output signal is acquired by a readout circuit. The ISFET Sensor circuits are very compatible with CMOS technology. ISFETs in CMOS are manufactured in the same way as regular MOSFET but with a floating gate extended to the top of the metal. An advantage of using ISFETs for bio sensing is their extremely low power operation when kept in weak inversion. The most commonly used readout circuit consists of Operational Amplifiers. In this work the Operational Amplifiers of the readout circuit are replaced by Folded Cascode Amplifiers. The power consumption of the readout circuit using Folded Cascode Amplifier with Regulated Cascode Current Mirror is very less when compared with other readout circuits.**

Keywords— ISFET, Readout Circuit, CMOS, Bio sensing, Folded Cascode Amplifiers.

I. INTRODUCTION

Biosensing plays an important role in healthcare. Rapid diagnosis of diseases at their initial stage is critical for effective clinical outcomes and promotes general public health. Complementary Metal Oxide Semiconductor (CMOS) biosensors are commonly used due to its smaller size and lower power [1]. Biosensor is a combination of bio-element and sensor element. There are wide range of applications for biosensors such as biomedical, industry, and military applications. The bio-element may be an enzyme, antibody, living cells or tissue and the sensing element may be electric current or electric potential[9]. semiconductor technologies can be used to fabricate compact and cost effective biosensors with high performance[6].Since various types of sensing methods are used, the ISFET sensors has shown high sensitivity towards ion concentration[11].ISFET is known as a PH sensor[4].The passivation layer at the top is sensitive to hydrogen Ions[13].The structure of ISFET is similar to that of a MOSFET and the gate metal is replaced by an ion sensitive layer. The ISFETs have many inherent features such as small dimensions and low sample volumes which makes it suitable for many applications[10].The ISFET devices are very useful in PH detection due to their high sensitivity to ions. Nowadays CMOS circuits are commonly used in the industry due to their low cost and solid performance, especially in low frequency applications, such as biosensing .wheatstone bridge based ISFET readout circuit is very useful for noise compensation[17].ISFET sensor circuits with various pixel structures can be used for biosensing[18].ISFET is a chemical sensor device .The readout circuit will convey the PH change that takes place in ISFET into an electrical signal [5].Potentiostats can be used to set the required potential value[15].CMOS technology can be used for the fabrication of ISFET which includes an intermediate gate formed by some conducting layers. In recent years numerous electrochemical biosensors have been developed and proposed for detection of various diseases based on specific biomarkers taking advantage of their features including sensitivity, selectivity, low cost and rapid response. A change in threshold voltage of ISFET can be used to find the PH change of a solution[16].Implementation of the ISFET in standard CMOS technology can be enabled using extended gate approach[19].A biosensor is a sensing device comprised of a combination of a specific biological element and a transducer. A specific biological element recognizes a specific analyte and the changes in the biomolecule are usually converted into an electrical signal. Electrochemical biosensors are mainly used for the detection of hybridized DNA,DNA-binding drugs, glucose concentration, etc. The underlying principle for this class of biosensors is that many chemical reactions produce or consume ions or electrons which in turn cause some change in the electrical properties of the solution which can be sensed out and used as measuring parameter[14].Biosensors are detection platforms which comprise not only biological samples and biochemical systems but also electronic components ion-sensitive field effect transistors (ISFETs) have been used to detect a variety of biomolecules whose charges alter the current or threshold voltage of the transistor . ISFETs can be built into large-scale arrays by CMOS compatible technology, offering the promise of highly parallel, all-electrical biomolecule sensing in a true chip-scale construct. The ISFET can be used as PH sensor since it can detect chemical and biological phenomena[20].Ion sensitive field-effect transistor in DNA sequencing application is gaining popularity because of its capability to work massive parallel sensor arrays, especially when integrated in CMOS technology fabrication with inherent scalability from silicon at low cost.

II. DIFFERENT TYPES OF BIOSENSORS

1.AMPEROMETRIC

Amperometric Biosensors are stimulated by a DC voltage.The output response of this type of biosensor is a DC respose current.The input DC source can be step,multistep,ramp

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potential or constant source.This stimulus can be applied across the electrode-electrolyte interface.This input stimulus can be used as the driving force which is essential for the biorecognition process.The biosensor that use a constant voltage stimulus is known as amperometric biosensors.Amperometric biosensors can be used in pesticide monitors,enzyme biosensors and immunosensors.

2.IMPEDIMETRIC

In Impedimetric biosensors,the input stimulus will be a sinusoidal voltage or current signal with variable frequency. The resulting current or voltage will be measured. The phase or amplitude change of the resulting signal contains the information of the biorecognition event. This type of measurement is known as Electrochemical Impedance Spectroscopy(EIS) and it can be used in a wide range of applications. Impedimetric biosensors measure the AC electrical impedance of the electrode electrolyte interface at equilibrium. Impedimetric biosensors can be used in monitoring bilayer lipid membranes and detecting small molecules of biological relevance.The most important advantage of impedimetric biosensors is that the stimulus voltage signal is very small and it does not cause any damage or disturb the bio-recognition layers.

3.POTENTIOMETRIC

In potentiometric biosensors when there is no current flow between electrode,a DC electrical potential is measured.A new approach involves applying a controlled DC current and measuring the resulting potential.This potential will be Proportional to the analyte concentration. Potentiometric biosensors are commonly used in the past because of its high selectivity,simplicity and low cost.There are potentiometric biosensors that involves redox reactions.They are known as redox potential biosensors.Redox potential biosensors are used for the detection of glucose and DNA.In potentiometric biosensors the current response is a combination of the sensor response current and the electrode doublelayer charging current that is modeled by a double layer capacitance.This charging current is very large and difficult to filter out.This limits the resolution of potentiometric biosensor.

4.ISFET

ISFET Sensing circuits are very useful in detecting the PH of a solution. ISFET sensors are one of the commonly used sensing circuits.One of the commonly used method to measure ion concentration in a solution utilizes ion sensitive field effect transistor(ISFET).The ISFET operates in a manner similar to that of a metal oxide semiconductor field effect transistor(MOSFET).ISFET biosensors can be used for measuring antigen-antibody bonding reactions,DNA detection and enzyme sensing.In biosensors like amperometric,impedimetric and potentiometric ,the transducer is an electrode but in ISFET biosensor,the transducer is the gate oxide layer.ISFET output current can be measured by a readout circuit similar to that of an amperometric or impedimetric biosensor.

III. AMPLIFIERS USED FOR READOUT CIRCUIT

Amplifiers are the most important part of the readout circuit.In this work three different amplifiers are compared and analysed.The power consumption and gain of the amplifiers are also compared.Folded Cascode Amplifiers can be used to obtain high amplification[7].

1.FOLDED CASCODE AMPLIFIER

The figure below shows the schematic diagram of folded cascode amplifier. The transistors PM1 and PM2 form the input differential pair. Transistor PM3 is used to provide the required bias current for the input differential pair. The transistors NM8, NM9, PM1 and PM2 form the input cascode tube. The transistors NM8, NM9, NM10 and NM11 forms the cascode current mirror [6].Folded cascode amplifiers can be used in readout circuits because it provides high range of amplification and the power consumption is also less when compared with other types of amplifiers.

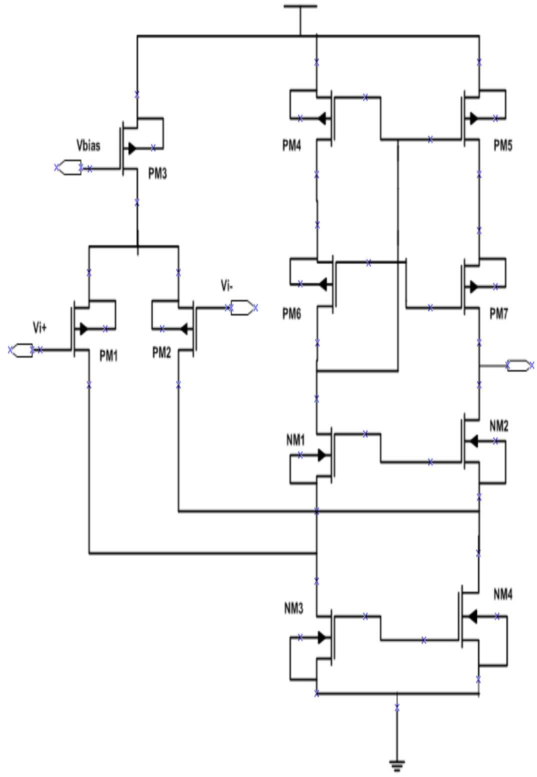

Figure.1.Schematic diagram of Folded Cascode Amplifier

2. FOLDED CASCODE AMPLIFIER WITH HIGH IMPEDANCE CURRENT MIRROR

The schematic diagram of folded cascode amplifier with high impedance current mirror is shown in figure.2.The transistors PM1 and PM2 are used as the input differential pair transistors. The transistor NM2 and NM5 are maintained at same saturation level [8].The transistor PM6 is forced to produce a current which is equal to the biasing current, thus the steady state of transistor PM6 is achieved. This amplifier provides higher range of amplification when compared with folded cascode amplifier and low power folded cascode amplifier.

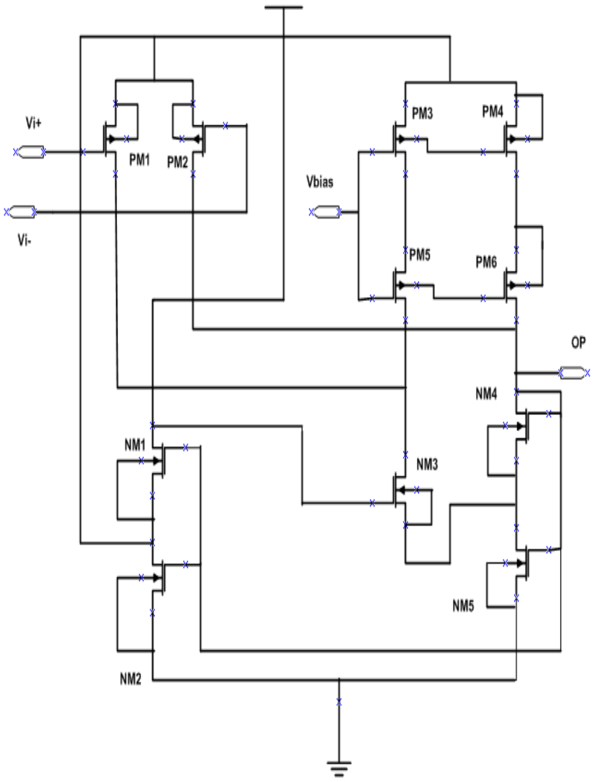

Figure.2.Schematic diagram of Folded Cascode Amplifier With High Impedance Current Mirror

3. FOLDED CASCODE AMPLIFIER WITH REGULATED CASCODE CURRENT MIRROR

Figur.3. shows a folded cascode amplifier with regulated cascode current mirror. The transistor PM9 and PM11 are connected in cascade form and it increases the output impedance. The transistor PM1 and PM2 forms the input differential pair. The transistors PM12 and PM14 are used to compensate any deviation in the output current [4].The most important advantage of folded cascode amplifier with regulated cascode is that it reduces the power consumption. This amplifier circuit also provides high amplification.

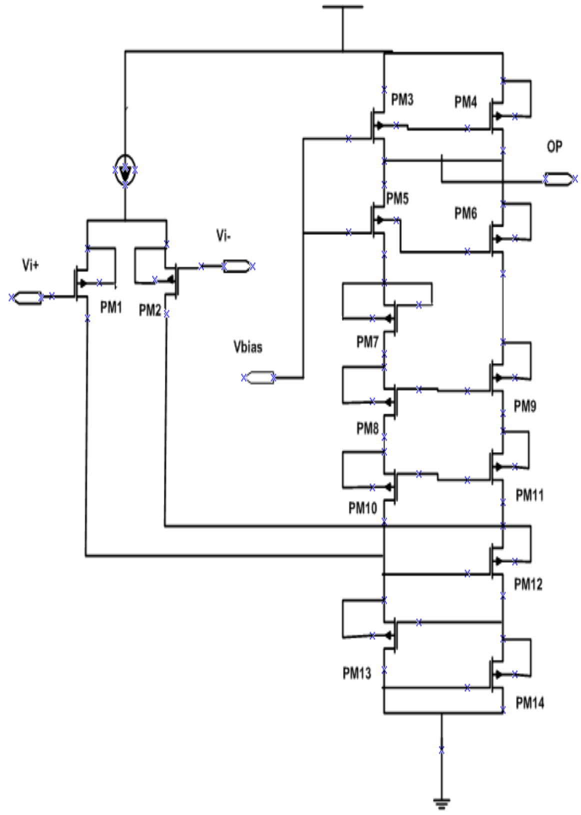

Figure.3.Schematic diagram of Folded Cascode Amplifier With Regulated Cascode Current Mirror

IV. READOUT CIRCUITS

The output signal obtained from the ISFET is very feeble so it is necessary to amplify the signal. The readout circuit is used for this purpose. There are various types of readout circuits that can be used for the purpose of amplification.The ISFET sensor can be formed by integrating the ISFET with the readout circuit. Readout Circuits are very important in ISFET sensing circuits.In this work readout circuits using three different types of amplifiers are compared and analysed.Readout circuits have two main functions (i)provide working point is ISFET and (ii)read voltage or current signal out.The two types of readout circuits are current mode readout circuits and voltage mode readout circuits.Comparing with the voltage mode circuit,current mode circuit has the following advantages such as lower voltage supply,high signal response speed and the current output is more suitable for A/D conversion.In the case of sensing circuits voltage mode is also very useful.

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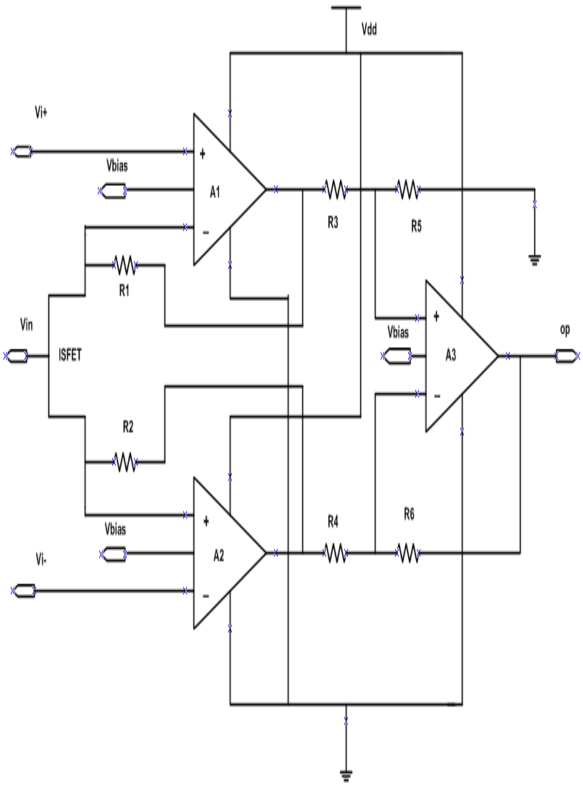

Figure.4.Readout circuit using Folded Cascode Amplifier with High Impedance Current Mirror readout

V. SIMULATION RESULTS

1. SIMULATION RESULTS OF AMPLIFIER CIRCUIT

The simulation of different amplifier circuits is done using Cadence Virtuoso in 180nm technology.Figure.5 shows the transient response of folded cascode amplifier. The power dissipation of this amplifier is 183.7 mW. Figure.6 shows the transient response of folded cascade amplifier with high impedance current mirror. The power dissipation of this amplifier is 363.6 mW. Figure.7 shows the transient response of folded cascode amplifier with regulated cascode current mirror. The power dissipation of this amplifier is 39.47 mW. The Analysis Table shows the performance summaries of the different amplifier circuits.

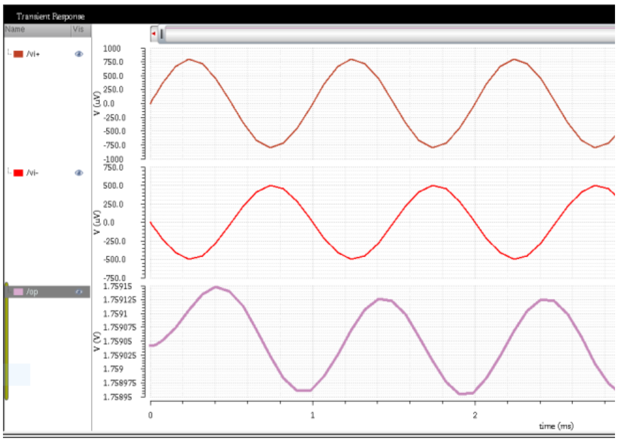

Figure.5.Output waveform of Folded Cascode Amplifier

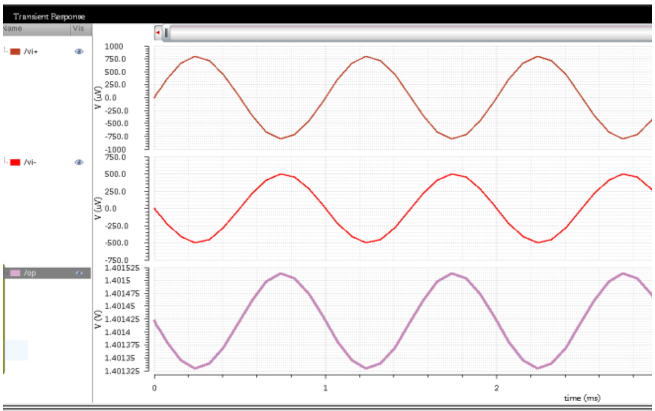

Figure.6.Output waveform of Folded Cascode Amplifier with High Impedance Current Mirror

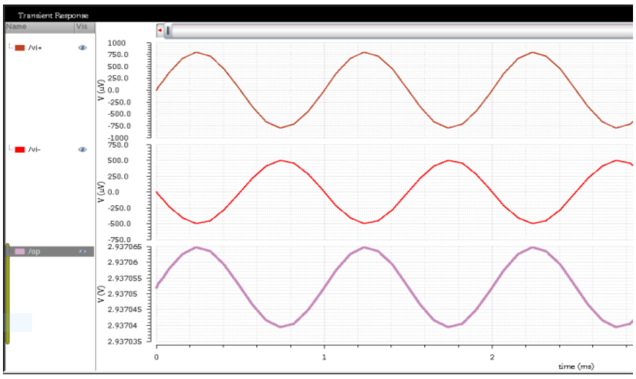

Figure.7.Output waveform of Folded Cascode Amplifier with Regulated Cascade Current Mirror

ANALYSIS TABLE FOR AMPLIFIERS

Sl No	Amplifier Circuit	Power (mW)	Gain (dB)
1	Folded Cascode Amplifier	183.7	21
2	Folded Cascode with High Impedance Current Mirror	363.6	25
3	Folded Cascode with Regulated Cascode Current Mirror	39.47	27

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2. SIMULATION RESULT OF READOUT CIRCUIT

The simulation of various readout circuits are done using Cadence Virtuoso in 180 nm technology.The power consumption of readout circuit using folded cascode amplifiers 365.6 mW.The power consumption of readout circuit using folded cascode amplifiers with high impedance current mirror circuit is 628.2 mW.Figure.8. shows the transient response of Folded Cascode Amplifier with Regulated Cascode Current Mirror. The power consumption of this circuit is 71.2 mW.The power consumption of this readout circuit is very less when compared with other readout circuits.

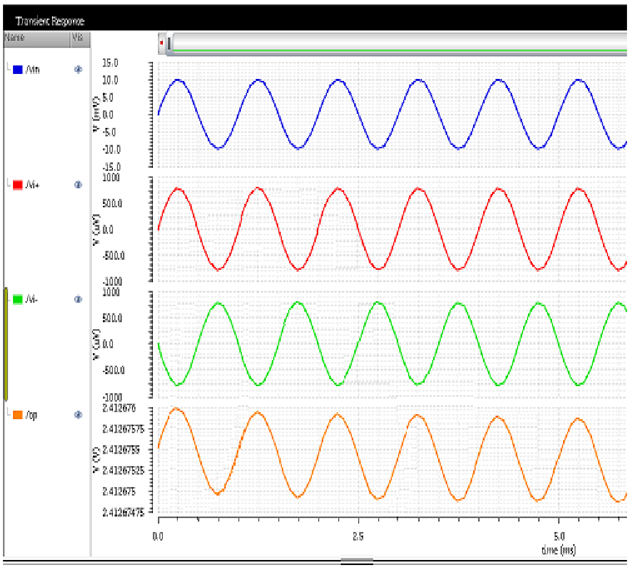

Figure.8. Output waveform of Readout Circuit using Folded Cascode Amplifier with Regulated Cascode Current Mirror

ANALYSIS TABLE FOR READOUT CIRCUITS

Sl No	Readout Circuit Using	Power (mW
1	Folded Cascode Amplifier	365.6
2	Folded Cascode with High Impedance Current Mirror	628.2
3	Folded Cascode with Regulated Cascode Current Mirror	71.2

VI. CONCLUSION

ISFET Sensing circuits are very useful in the Biorecognition processes which helps us for the early detection of various diseases. It is a simple integration with measurement electronics.The ISFET consist of an ion sensitive layer which is able to detect the concentration of a specific type of ion even in the presence of other ionic components.The ISFET Sensor circuits are very compatible with CMOS technology.The main advantage of the ISFET is that it can integrate with the MOSFET and the standard transistors of integrated circuits.Another advantage of using ISFETs for bio sensing is their extremely low power operation when kept in weak inversion.The response of ISFET is very fast which makes it suitable for biosensing processes.In this work different types of amplifiers are analysed and compared. These amplifiers can be used in readout circuits which plays an important role in amplification.The power consumption of Folded Cascode Amplifier with Regulated Cascode Current Mirror is less when compared with other amplifiers.The power consumption of this amplifier is 39.4mW and the gain is 27dB.The power consumption of readout circuit using this amplifier is 71.2mW.From the analysis Folded Cascode Amplifier with Regulated Cascode Current Mirror is suitable for readout circuits since it provides higher amplification and less power consumption.

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