Evaluation of the VLSI Adaptation of the Chemfet, a Biosensor for Fluid Analysis

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Abstract:

A biosensor system is presented for identification of properties of a fluid. The class of biosensors studied in this work, are capable of operating as a dielectric constant measurement device. This paper focuses on studying the effectiveness of the VLSI adaptation on the CHEMFET in determining fluidic properties. The objective of this research is to determine metrology infrastructure issues needed for developing multi-sensor System-on-a-Chip (SoC) devices.

1. INTRODUCTION

In a number of areas it would be useful to have available smart sensors that can determine the properties of a fluid and from those make a reasoned decision. Among such areas of interest might be ecology, food processing, and health care. For example, in ecology it is important to preserve the quality of water for which a number of parameters are of importance, including physical properties such as color, odor, and pH, as well as up to 40 inorganic chemical properties and numerous organic ones [1, pp. 363-366]. Therefore, in order to determine the quality of water it would be extremely useful if there were a single system on a chip which could be used in the field to measure the large number of parameters of importance and make a judgment as to the safety of the water. For such, a large number of sensors are needed and a means of coordinating the readouts of the single sensors into a user friendly output from which human decisions could be made. As another example, the food processing industry needs sensors to tell if various standards of safety are met. In this case it is important to measure the various properties of the food, for example the viscosity and thermal conductivity of cream or olive oil [2, pp. 283-287]. In biomedical engineering biosensors are becoming of considerable importance; general theories of different types of biosensors can be found in [3]-[5] while similar devices dependent upon temperature sensing are introduced in [6]. In the biomedical engineering area methods for the selective determination of compounds in fluids, such as blood, urine, and saliva, are indeed very important in clinical analysis. Present methods often require a long reaction time and involve complicated and delicate procedures. One valuable application in the health care area is that of the use of multiple sensors for maintaining the health of astronauts where presently an array of eleven sensors is used to maintain the quality of recycled air [7], although separate control is effected by the use of an external computer. Therefore, the development of inexpensive and miniaturized sensors that are highly selective and sensitive and for which control and analysis is present all on one chip is very desirable. These types of sensors can be implemented with micro-electro-mechanical systems (MEMS). Because the sensors are fabricated on a semiconductor substrate, additional signal processing circuitry can easily be integrated into the chip thereby readily providing functions such as multiplexing and analog-to-digital conversion. In numerous other areas one could find similar uses for a smart multi-sensor array from which easy measurements can be made with a small portable device. These are the types of systems on a chip (SOC) that this research addresses.

The architecture of these systems is given in Figure 1 where there are multiple inputs, sensors, and outputs. In between are smart signal processing elements including built-in self-test (BIST). In this system there may be many classes of input signals (for example, material [as a fluid] and user [as indicator of what to measure]). On each of the inputs there may be many sensors (for example, one material may go to several sensors each of which senses a different property [as dielectric constant in one and resistivity in another]. The sensor signals are treated as an N-vector and combined as necessary to obtain the desired outputs, of which there may be many (such as an alarm for danger and indicators for different properties). For example, a patient with kidney disease may desire a system on a chip that gives an indication of when to report to the hospital. For this an indication of deviation of dielectric constant from normal and spectral properties of peritoneal fluid may be sensed and combined to give the presence of creatinine (a protein produced by the muscles and released in the blood) in the fluid, with the signal output being the percent of creatinine in the fluid and an alarm when at a dangerous level.

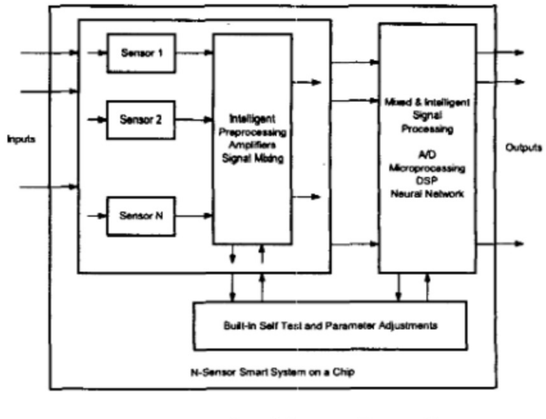

Figure 1. Architecture for N-Sensor Smart System on a Chip

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A multi-function biosensor circuit is analyzed in this paper to provide an example of the expected results that are possible when analyzing the effects of air and fluid after various HF etches.

2. BIOSENSOR CIRCUIT DESCRIPTION

A multi-function smart sensor system can be used to identify the properties of a fluid. This technology is of interest to a number of areas including: ecology, food processing, and health care. In biomedical engineering, biosensors are becoming of considerable importance. In this area biosensors can be used in clinical analyses for the selective determination of properties of fluids including blood, urine, and saliva.

The class of biosensors studied in this work is designed to analyze physical properties of fluids [8]. These sensors are capable of deciphering various characteristics associated with fluids including: color, odor, pH, resistivity, and dielectric constant. The sensors can also discern inorganic and organic chemical properties. Such sensors are implemented using micro-electro-mechanical systems (MEMS) technology. The sensor circuit can be fabricated on a semiconductor substrate that allows for the integration of additional signal processing circuitry onto the chip. An array of such sensors can be used to determine multiple properties of a fluid, using a single chip.

Figure 2 is a schematic of the type of sensor used to detect fluid properties. This example sensor circuit operates as a dielectric constant measurement device. This sensor can be provided as part of an integrated micro-system designed to determine the properties of a fluid. The fluid-sensing transistor in this sensor is a VLSI adaptation of the CHEMFET [10]. The sensor operates as a capacitive-type bridge such that a balance can be set for a normal dielectric constant. In the presence of a fluid, the unbalance that occurs within this sensor bridge is used to evaluate the fluid's dielectric constant. The four CMOS transistors form the bridge: M1, M6, M7, and the fluid-sensing transistor comprised of transistors M2 through M5. The fluid-sensing transistor and transistor M1 are PMOS (p-type MOSFETs) transistors in the diode connected configuration (gate connected to drain) while the lower two, M6 and M7, are NMOS type (one diode connected and the other with a gate voltage control). The output, Vout, of the sensor circuit is taken between the junction of the fluid-sensing transistor and the diode-connected transistor, M7.

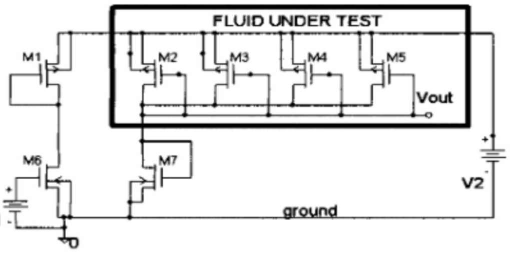

Figure 2. Schematic of biosensor circuit under test. Each transistor has a W/L ratio of 160μ/160μ. The overall W/L ratio of the fluid-sensing transistor is therefore 640μ/160μ.The output of this circuit is taken as the gate of transistor M5.

The transistors, M2 through M5, have openings in their gates to allow fluid to flow between the silicon substrate and the polysilicon gate where the gate oxide has been removed. This allows the fluid to behave as the gate dielectric for that transistor. The fluid-sensing transistor is constructed out of four transistors with all terminals connected in parallel to increase the gain constant parameter KP that is proportional to the dielectric constant.

Fabrication of the sensor is based on a sacrificial etch process, where the silicon dioxide gate dielectric in the fluid-sensing transistor is removed by chemical etch [9]. This activity is accomplished by opening holes in protective layers using the over-glass cut method available in the MOSIS-MEMS fabrication process. Since, in the MOSIS processing that is readily available, these cuts should be over an n-well, the transistor in which the fluid is placed is chosen as a PMOS one. And, since we desire to maintain a gate, only portions are cut open so that a silicon dioxide etch can be used to clear out portions of the gate oxide, leaving the remaining portions for mechanical support. To assist the mechanical support we also add two layers of metal, metal-1 and metal-2, over the polysilicon gate.

The layout of the basic sensor is shown in Figure 3 for M2 constructed from four sub-transistors, this layout having been obtained using the MAGIC layout program. As the latter can be used with different lambda values to allow for different technology sizes, this layout can be used for different technologies and thus should be suitable for fabrications presently supported by MOSIS. Associated with Figure 3 is Figure 4 where a cross section is shown cut through the upper two transistors in the location seen on the upper half of the figure. The section shows that the material over the holes in the gate is completely cut

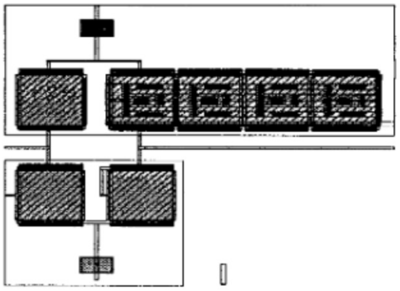

Figure 3: Basic sensor layout

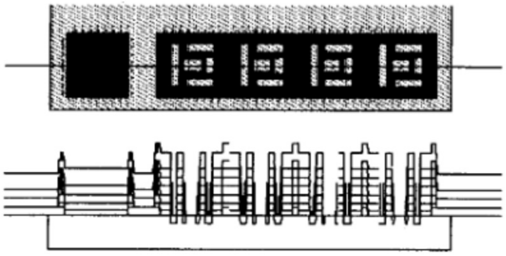

Figure 4: Cross section of upper transistors

away so that an etch of the silicon dioxide can proceed to cut horizontally under the remaining portions of the gate. The two layers of metal can also be seen as adding mechanical support to maintain the cantilevered portions of the gate remaining after the silicon dioxide etch.

3. BIOSENSOR CIRCUIT OPERATION

To study the operation of the sensor we turn to the describing equations. Under the valid assumption that no current is externally drawn from the sensor, the drain currents of M1 and M6 are equal and opposite, ID6=-ID1, and similarly for M2 and M7, ID7=-ID2. Assuming that all transistors are operating above threshold, since M1, M6, and M7 are in saturation they follow a square law relationship while the law for M6 we designate through a function f(Vset,VD1), which is controlled by Vset. Thus,

(Equation 1a)
-ID1 = beta_1·(Vdd-VD1-|Vthp|)^2(1+lambda_p·[Vdd-D2])
(Equation 1b)
ID6=beta_6·[f(Vset,VD1)·(1+lambda_n·VD1)=ID3
(Equation 2a)
-ID2=epsilon·beta(2-5)·(Vdd-VD2-|Vthp|)^2 (1+ lambda_p ·[Vdd-VD2])
(Equation 2b)
ID2= beta_7·(VD2-Vthn)^2(1+lambda_n·VD2) = ID4
where, for the ith transistor,
(Equation 3)
beta_i = KPi·Wi/(2Li), i=1,(2-5),6,7
(Equation 4)
f(x,y) = {(x-Vthn)^2 if x-Vthn<y [M saturation], 2(x-Vthn)y-y^2 if x-Vthn≥ y [M Ohmic]}

Here Vth, KP, and lambda are Spice parameters for silicon transistors, all constants in this case, with the n or p denoting the NMOS or PMOS case, and epsilon is the ratio of the dielectric constant of the fluid to that of silicon dioxide,
(Equation 5)
epsilon = epsilon_fluid/ epsilon_silicon-dioxide.

In order to keep the threshold voltages constant we have tied the source nodes to the bulk material in the layout. In our layout we also choose the widths and lengths of M1, M6, and M7 to be all equal to 100mu and L2/W2 to approximate epsilon. Under the reasonable assumption that the lambda's are negligibly small, an analytic solution for the necessary Vset to obtain a balance can be obtained. When M6 is in saturation the solution is

(Equation 6)
VD1 = Vdd-|Vthp|-(beta_6/beta_1}$^{1/2}$·(Vset-Vthn)
while irrespective of the state of M6
(Equation 7)
VD2={Vthn+(epsilonxbeta_2/beta_7)$^{1/2}$·(Vdd-|Vthp|)/ [1+epsilonxbeta_2/beta_7]$^{1/2}$}

Balance is obtained by setting VD1=VD2. Still assuming that M6 is in saturation the value of Vset needed to obtain balance is obtained from equations (6) and (7) as:

(Equation 8)
Vset=Vthn+{(beta_1/beta_6})$^{1/2}$·(Vdd-|Vthp|-Vthn)/ [1+(epsilonxbeta_2/beta_7})$^{1/2}$}

At this point we can check the condition for M6 to be in saturation, this being that,

VDS ≥VGS-Vthn; since VDS=VD1 and VGS = Vset,
the use of Equation (6) gives

(Equation 9)
Vthn < Vset_{sat} ≤ Vthn+(Vdd-|Vthp|)/ [1+(beta_6/beta_1)$^{1/2}$

Substituting the value of Vset at balance, Equation (8), shows that the condition for M6 to be in saturation at balance is epsilon·beta_2 >= beta_6; this normally would be satisfied but can be guaranteed by making M2 large enough.

Several things will be added to the sensor itself as per Fig. 1. Among these will be a differential pair for direct current mode readout followed by a current mode pulse coded neural network to do smart preprocessing to insure the integrity of the signals. Finally a built in test circuit will be included to detect any breakdown in the sensor operation.

From the layout a Spice extraction was obtained. On incorporating the BiCMOSIS transistor models, the extracted circuit file was run in PSpice with the result for the output difference voltage versus Vset shown in Figure 5. As can be seen there, adjustment can be made over a wide range.

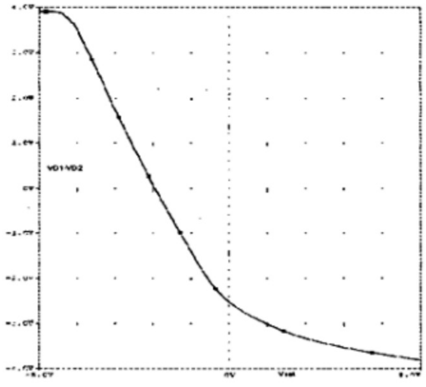

Figure 5: Extracted circuit output voltage versus Vset

Thus it is seen that a sensor sensitive to the dielectric constant of a fluid over an 11 to 1 range of dielectric constant most likely can be incorporated into a multi-sensor chip using standard analog VLSI-MEMS processing one can use the bridge for anomalies in a fluid by obtaining Vset for the normal situation and then comparing with Vset found for the anomalous situation. This could be particularly useful for determining progress of various diseases. For example, one way to determine kidney function and dialysis adequacy is through the clearance test of creatinine. This clearance test is a test for the amount of blood that is cleared of creatinine per time period, which is usually expressed in ml per minute. For a healthy adult the creatinine clearance is 120 ml/min. A renal adult patient will need dialysis because symptoms of kidney failure appear at a clearance of less than 10 ml/min. Creatinine clearance is measured by urine collection, usually 12 or 24 hours. Therefore a possible use for the proposed sensor could be as a creatinine biosensor device for individual patient use so that the patient can monitor the creatinine level at home. An alternate to the proposed biosensor is based on biologically sensitive coatings, often enzymes, which could be used on our M2 transistor in a technology that is used for urea biosensors that are presently marketed for end stage renal disease patients [1.4]. The advantage of the sensor presented here is that it should be able to be used repetitively while enzyme based coatings have a relatively short life.

The same philosophy of a balanced bridge constructed in standard VLSI processing can be carried over to the measurement of resistivity of a fluid. In this case the bridge will be constructed of three VLSI resistors with the fourth arm having a fluid channel in which the conductance of the fluid is measured. Consequently, some of the research effort will go into simultaneously designing the dielectric constant and the resistivity bridges.

4. CONCLUSIONS AND FUTURE WORK

The biosensor circuitry described was fabricated on a multi-technology testbench on a chip. Post-processing in the form of an HF etch was performed on the biosensor. The device was evaluated in the presence of air and water after incremental etch steps. The results of the Input/Output voltage for the biosensor in the presence of air are shown in figure 6.

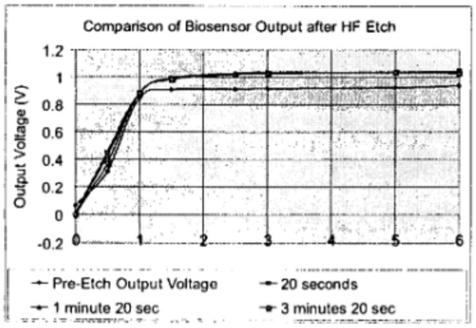

Figure 6: Output Voltage versus Input Voltage for Biosensor versus time in HF solution.

These curves reflect the impact of etching on the function of the biosensor circuit. After 18 minutes of etching and the application of 6V in the presence of water, the biosensor collapses while the remaining circuitry on the testbench continues to perform as expected. Thus, a 15 minute etch was performed on the circuit whose results are reflected in figure 7.

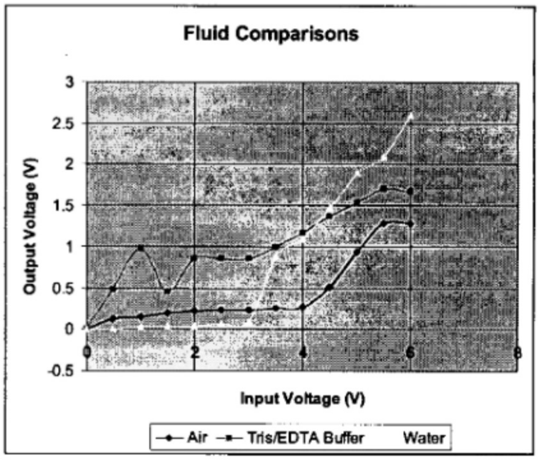

Figure 7: Biosensor Output Voltage versus Voltage Controlled Transistor Input Voltage for various fluids under test.

The biosensor circuit is shown to produce a unique output response for each of the fluids under test. The described biosensor was evaluated in the presence of air, Tris/EDTA Buffer, and Water.

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