# Characterization of Ion Sensitive Field Effect Transistors for Cellular Scale pH Measurement

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## Abstract:

**Commercially-available ion-sensitive field effect transistors (ISFETs) are ideal for use as potential of hydrogen (pH) sensors in space- and material-limited applications. However, drift continues to be a major obstacle to precision and accuracy in ISFET measurements. Though it may not be possible to entirely eliminate drift in currently manufactured ISFETs, techniques have been developed that may aid in the prediction and minimization of its effects. In this work, a unique approach was used where relays were integrated into the ISFET control circuit in order to determine the effect of electric field change on drift. Drift characterization was performed by varying the pH of the solution to which the five identical ISFETs were exposed and the frequency at which the relays were switched on and off. A correlation was found between the pH of the solution and the rate of drift. Switching off was found to decrease drift in the subsequent on period.**

## Introduction:

Good cell culture practice is essential to the fabrication of many of the products of biotechnology. A variety of factors influence the growth and health of cells in culture including temperature, nutrient concentration, oxygen levels, and pH. Consequently, pH is a parameter which should be optimized in culture for favorable proliferation [1]. Additionally, the measurement of pH can communicate valuable information about growth and cell death in culture [2].

ISFETs are a type of field effect transistor whose conductivity is regulated, not by a gate electrode, but by the ion concentration of the solution in direct contact with the ion-sensitive substrate. As a result, ISFETs are sensitive to hydrogen ion concentration, and the resulting current through the transistor can be used to measure pH levels in micro-scale devices.

A major drawback to ISFET use in practice is the incidence of drift, or change in current despite a constant pH, which lowers the accuracy and precision of the measurements taken by the device. However, drift is not random noise but is in fact a result of the movement of mobile ions in solution which neutralize dangling charges along the oxide layer or diffuse into the oxide layer itself. Consequently, drift may be minimized and predicted. The purpose of this body of work is to answer two questions: "Can we characterize drift?" and "What effect does modulating electric field have on drift?"

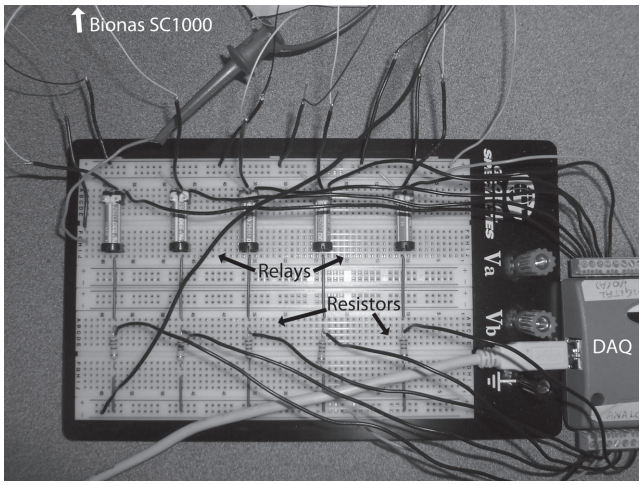


*Figure 1: The experimental circuit featuring SPST Reed Relays with inset showing the switching cycles for the five ISFETs.*

## Methods:

Data was taken from multiple ISFETs on the commercially-available Bionas metabolic chip SC1000. The chip was integrated into a circuit incorporating SPST Reed Relays, shown in Figure 1. To determine the current through each of the five ISFETs, a data acquisition module was employed, taking voltage measurements over every ISFET's corresponding resistor. The reference electrode in the solution was set to -2V while the switches were set to "on."

Custom MATLAB® code controlled data collection, switching each ISFET at a different frequency over three hours (see Figure 1). In order to answer the question of whether or not a change in electric field could affect drift, the ISFET switching experiment was repeated, employing pH buffers with values 4, 7, 10 and 12.

Analysis of the collected data was performed via curve-fitting to the linear region of each "on" region, neglecting any non-linear behavior at the start of the run, as is accepted practice when dealing with ISFETs. The slope of the line of best fit gives an approximation of drift over time in amps per second.

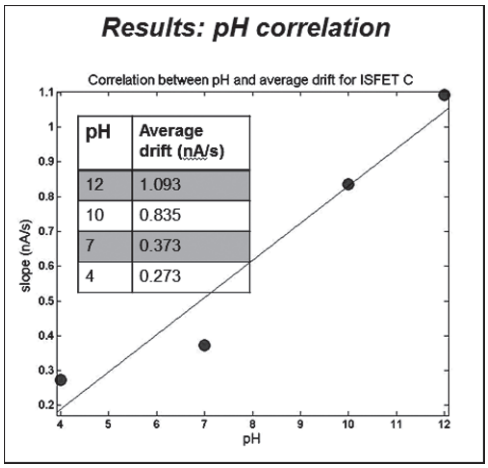


*Figure 2: Correlation between pH and drift with average values in the table inset.*

## Results:

A correlation was found between average drift as measured by the slope of the line of best fit and the pH of solution, as shown in Figure 2. Additionally, drift was found to decrease, on average, following the first switch in ISFET C, as shown in Figure 3. For ISFET D, the same trend was found to be true of the first "on" period following a switch; however, the results following the second switch were inconclusive. For trials with pH 4 and 12, the average drift of the third "on" period was less than the second while, for trials with pH 7 and 10, the average drift of the third "on" period was greater than the second, as illustrated in Figure 4.

## Conclusions:

Further work is needed in this area; in order to conclusively answer the question of whether a drift-decreasing trend continues past the first switch in ISFET D, a larger data set is needed to decrease the possibility of experimental error being responsible for inconsistencies in results. However, a correlation between pH and drift was found, indicating that prediction and subtraction of drift is possible with further work. In addition, switching was found to decrease drift, indicating that multiple ISFETs and a switching pattern could be employed to create a system with measurably lower drift.


## Acknowledgements:

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## References:


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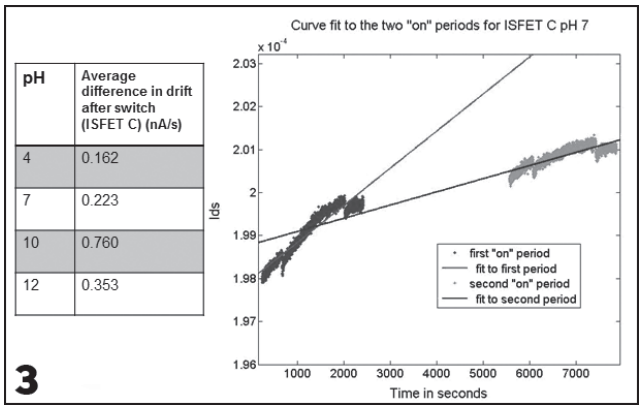


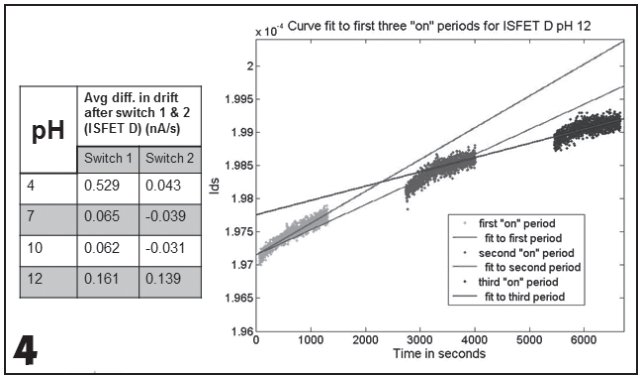


*Figure 3, top: Average difference in drift after the first switch. The diagram illustrates the process by which drift was determined for ISFET C.*

*Figure 4, bottom: Average difference in drift after each switch. Note the decreasing slopes in each successive set of data.*