Comparison between Field Effect Transistors and Bipolar Junction Transistors as Transducers in Electrochemical Sensors

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Field effect transistors (FET) have been widely used as transducers in electrochemical sensors for over 40 years. In this report, a FET transducer is compared with the recently proposed bipolar junction transistor (BJT) transducer. Measurements are performed on two chloride electrochemical sensors that are identical in all details except for the transducer device type. Comparative measurements show that the transducer choice significantly impacts the electrochemical sensor characteristics. Signal to noise ratio is 20 to 2 times greater for the BJT sensor. Sensitivity is also enhanced: BJT sensing signal changes by 10 times per pCl, whereas the FET signal changes by 8 or less times. Also, sensor calibration curves are impacted by the transducer choice. Unlike a FET sensor, the calibration curve of the BJT sensor is independent of applied voltages. Hence, a BJT sensor can make quantitative sensing measurements with minimal calibration requirements, an important characteristic for mobile sensing applications.

As a demonstration for mobile applications, these BJT sensors are further investigated by measuring chloride levels in artificial human sweat for potential cystic fibrosis diagnostic use. In summary, the BJT device is demonstrated to be a superior transducer in comparison to a FET in an electrochemical sensor.

The application of field effect transistors (FET) as transducers in electrochemical sensors was first described in 1970 by Bergveld. Since then, field effect transistor (FET) based electrochemical sensors have been extensively investigated due to their enhanced sensitivity, resolution, low power, portability and fabrication compatibility with silicon processing technology. Over the years, these electrochemical sensors have been demonstrated to detect both ions and biomolecules, and have several sensing applications, including DNA sequencing and mobile diagnostics. Recently, bipolar junction transistor (BJT) device was proposed as a transducer in an electrochemical sensor. In this study, we compare a FET transducer with the recently proposed BJT transducer. The objective is to evaluate the impact of the transducer type on the performance metrics of an electrochemical sensor.

An electrochemical sensor has two basic components as shown in Fig. 1: the sensing surface (or receptor) and the transducer. The sensing surface interacts with the target analyte and the transducer converts this interaction into a readable electronic signal. The sensor performance characteristics depend on both the components. The sensor selectivity and affinity towards the target analyte depends solely on the sensing surface because the analyte interacts only at the sensing surface as illustrated in Fig. 1. Other performance metrics such as sensitivity, resolution, and calibration depend on both components. Since the present objective is to compare the performance of a FET transducer with that of a BJT transducer in an electrochemical sensor, it is important to ensure that the sensing surface does not impact the evaluation. If the sensing surface and target analyte solution are kept the same, the sensing surface selectivity and target analyte affinity would therefore remain the same; in that case the observed differences in the electrochemical sensor performance metrics could then be attributed to transducers.

In other words, electrochemical sensors that are identical in all details except for the transducer device type (FET versus BJT) must be used to ensure that the transducer comparison is accurate.

In the present study, electrochemical sensors with FET and BJT as transducers are compared. Both the sensors have the same chloride ion sensitive silver chloride sensing surface. Measurements show that the recently proposed BJT transducer is superior in comparison to the widely used FET transducer: both sensitivity and signal...
to noise ratio (SNR) are significantly higher for BJT sensors. More importantly, SNR, sensitivity and calibration curves are independent of measurement voltages for the BJT sensor. This implies that optimal measurements can be made over the entire sensing range with minimal calibration requirements which is a significant advantage, particularly for mobile diagnostic applications. In contrast, sensitivity, resolution and calibration curves are dependent on the applied gate voltage for a FET sensor. Consequently, for the FET sensor, detailed calibration curves are required to obtain accurate quantitative sensing results and also use voltages have to be carefully chosen to ensure maximum sensitivity and resolution. As a demonstration for mobile diagnostic applications, the BJT sensor is further investigated for diagnosing cystic fibrosis which requires accurate measurement of chloride ion in sweat. Sensing measurements are shown to be repeatable and reversible in artificial human sweat. In summary, the BJT is shown to be a superior transducer option for an electrochemical sensor.

Results and Discussion

In this section, electrochemical sensors with FET and BJT devices as transducers are compared. These electrochemical sensors are identical except for the transducer device type to ensure that the transducer comparison is accurate. For the comparison purpose, we have chosen chloride ion sensitive silver chloride sensing surface. Also, these electrochemical sensors are further investigated by for potential cystic fibrosis diagnostic applications.

Electrochemical sensors with FET and BJT as transducers. Figure 2(A) shows the schematic of an electrochemical sensor with bipolar junction transistor (BJT) as the transducer. The sensor consists of a NPN BJT device with its base connected to a silver chloride coated silver (AgCl/Ag) wire that forms the chloride sensitive sensing surface, in contact with the aqueous solution. A miniaturized reference electrode is also immersed in the solution. The BJT device is fabricated using standard silicon processing technology as discussed elsewhere. Post fabrication, the BJT base is connected to an AgCl/Ag wire; the AgCl/Ag preparation is described in the Methods section. The BJT emitter area is $2.5 \times 10^{-7} \text{cm}^2$ (25 $\mu\text{m}^2$) and the sensing surface area is ~0.04 cm$^2$. The voltages applied at the emitter, collector and reference electrode are $V_E$, $V_C$, and $V_B$, respectively. The collector current ($I_C$) is the sensing signal and sensing measurements are made with $V_C = V_B = 0 \text{V}$ and $V_E$ is either varied or set at a fixed value.

The equation for the sensing signal $I_C$ is briefly reviewed:

$$I_C = I_o \cdot \exp\left(\frac{q(V_{BE} + \psi_s)}{kT}\right)$$ (1)

$$=I_o \cdot \exp\left\{2.3\left(V_{BE} + \psi_s\right)/SS\right\}$$ (2)

where, $T$ is the temperature in Kelvin, $k$ is the Boltzmann constant, $I_o$ is a BJT device constant, and $q$ is the electronic charge and $V_{BE} = (V_B - V_E)$. $SS$ is the sub-threshold swing that is defined as the change in $V_{BE}$ corresponding to a decade change in $I_C$ therefore, $SS = 2.3kT/q$ from equation 1. In contrast, the sensing surface potential $\psi_s$ depends solely on the sensing surface charge density associated with bound analyte, and is therefore a characteristic of the sensing surface/analyte interaction.

Figure 2(B) shows the schematic of an electrochemical sensor with a FET device as the transducer. The sensor has an N-type FET device with its gate connected to AgCl/Ag wire with AgCl forming the sensing surface in contact with the solution. A reference electrode is also immersed in the solution. The sensing surface is attached.
to the gate post FET fabrication. The silver chloride sensing surface, reference electrode and FET device area (=25μm²) are the same as those for the BJT sensor. The FET device consists of a dual gate SiO₂/HfO₂ gate dielectric layer with TiN as the gate. SiO₂ thickness is 1.5 nm and is grown by thermal oxidation at 900 °C, and HfO₂ physical thickness is 2.0 nm and is deposited by atomic layer deposition (ALD) at 400 °C. The equivalent oxide thickness (EOT) of the dual layer stack is ~1.8 nm as determined by the accumulation capacitance. TiN thickness is 50 nm and is sputter deposited at 300 °C. More fabrication details of the HfO₂ FET are given elsewhere²³,²⁴. These SiO₂/HfO₂ FETs are advantageous for the transducer application due their significantly lower gate currents in comparison to SiO₂ gate dielectric FETs with heavily doped poly silicon gate. The optimized SiO₂/HfO₂ FET has a low gate current density of about 10⁻³A/cm² at a gate voltage of 1.0 V (Supplementary, Fig. S1). This current density is about 500 times lower than that in a standard SiO₂ FET of similar gate dielectric thickness²³. Since electrochemically induced sensing surface degradation depends on the gate current density, reduced gate current results in improved sensing surface life time. The threshold voltage, sub-threshold swing (SS) and drain current hysteresis (ΔH) are other parameters impacting sensor performance. For example, low threshold voltage implies that the use voltage would be small, a low SS value results in enhanced sensitivity as discussed later, and small ΔH indicates that the sensing signal is reversible with gate voltage sweep. The optimized SiO₂/HfO₂ FET device has threshold voltage of ~0.24 V, SS = 71 mV/decade and ΔH < 1 mV (Supplementary, Fig. S1); these values are comparable to those for a SiO₂ FET device. Hence, these SiO₂/HfO₂ FETs have significantly lower gate currents, an important advantage over SiO₂ FETs.

The FET electrochemical sensor measurements are made as follows. The drain current (I_D) is the sensing signal. The voltages applied at the drain, source, substrate and reference electrode are V_D, V_S, V_SUB and V_G respectively. Sensing measurements are made at room temperature with V_S = V_SUB = 0 V, V_D = 50 mV while V_G applied at the reference electrode is either varied or set at a fixed value. For an electrochemical sensor with FET transducer, the equation for the sensing current I_D on gate voltage (V_G) measured at various [Cl⁻] is I_D = μ_C V_G C_D where I_D is the drain current, μ_C is the transconductance, V_G is the gate voltage and C_D is the dielectric capacitance. Since V_G is either varied or fixed, the drain current is given by equation 1. The dependence of drain current on gate voltage is exponential with gate voltage (V_G) measured at various [Cl⁻] is shown in Figure 3A. The drain current increases exponentially with gate voltage (V_G) measured at various [Cl⁻] and shows a linear dependence at higher V_G. This current density is about 500 times lower than that in a standard SiO₂ FET of similar gate dielectric thickness²³. Since electrochemically induced sensing surface degradation depends on the gate current density, reduced gate current results in improved sensing surface life time. The threshold voltage, sub-threshold swing (SS) and drain current hysteresis (ΔH) are other parameters impacting sensor performance. For example, low threshold voltage implies that the use voltage would be small, a low SS value results in enhanced sensitivity as discussed later, and small ΔH indicates that the sensing signal is reversible with gate voltage sweep. The optimized SiO₂/HfO₂ FET device has threshold voltage of ~0.24 V, SS = 71 mV/decade and ΔH < 1 mV (Supplementary, Fig. S1); these values are comparable to those for a SiO₂ FET device. Hence, these SiO₂/HfO₂ FETs have significantly lower gate currents, an important advantage over SiO₂ FETs.

Comparison between BJT and FET Transducers. Using the electrochemical sensors shown in Fig. 2, sensing measurements are performed for FET and BJT sensors. Measurements are performed in an aqueous KCl solution of varying concentrations (0.01–100 mM). Since KCl is fully ionized in water at room temperature, Cl⁻ and KCl concentrations are assumed to be the same. Figure 3A shows the dependence of the sensing signal I_D on the applied voltage V_BE measured at various chloride concentrations ([Cl⁻]) for the BJT sensor. Symbols denote measurements and solid lines are exponential fits to the data in accordance with equation 1. At each Cl⁻ concentration, I_D increases exponentially as V_BE increases with a sub-threshold swing (SS) of 59 mV/decade, consistent with the room temperature Nernst value. This SS value is same as that for the stand-alone BJT device (Supplementary, Fig. S2), and therefore SS is an intrinsic transducer property. Figure 3B shows the dependence of I_D on gate voltage (V_G) measured at various [Cl⁻] for the FET sensor. At each Cl⁻ concentration, the sensing signal I_D increases exponentially with SS = 71 mV/decade at lower V_G and has a linear dependence at higher V_G, consistent with the FET transfer curve equation. This SS = 71 mV/decade for the FET transducer is same as that for the stand-alone FET device (Supplementary, Fig. S1), thereby indicating once again SS is an intrinsic transducer property.

Figure 2. Electrochemical sensors with BJT and FET as transducers. Identical electrochemical sensors except for the transducer device type. (A) Schematic of an electrochemical sensor with a BJT device as the transducer; BJT base is connected to the silver chloride sensing surface that is immersed in the solution; a reference electrode is also immersed in the solution. Sensing signal (I_S) is measured with the collector voltage (V_C) and the base voltage V_B held at 0 V, whilst the emitter voltage (V_E) is either varied or held constant. (B) Schematic of an electrochemical sensor with a FET device as the transducer; FET gate is connected to the silver chloride sensing surface that is immersed in the solution; a reference electrode is also immersed in the solution. Sensing signal (I_D) is measured with drain voltage V_D = 50 mV, source (V_S) and substrate (V_SUB) voltages held at 0 V, whilst gate voltage V_G is either varied or held constant.

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property. From Fig. 3A,B three main observations can be made. (i) Sensing current versus applied voltage curves are significantly different for BJT and FET sensors; symbols are measurements and solid lines are fits. (ii) Sub-threshold swing are independent of chloride concentration for both sensors and SS for BJT sensor is smaller than that for the FET sensor; symbols are measurements and solid lines are fits. (iii) For both sensors, $I_C$ and $I_D$ curves shift as chloride concentration varies, thus indicating that threshold voltage $V_T$ depends on $[\text{Cl}^-]$; $V_T$ is defined as the applied voltage value corresponding to a constant sensing current of 1 nA. As chloride concentration increases in the solution, more Cl$^-$ bind to the sensing surface, thereby causing $\psi_s$ to shift with a concomitant shift in $V_T$; i.e. $\Delta V_T = \Delta \psi_s$. Figure 3C shows dependence of $V_T$ on $[\text{Cl}^-]$ for BJT and FET sensors: $V_T$ varies reversibly with $\Delta V_T = 57 \pm 1 \text{ mV/pCl}^-$ for both FET and BJT sensors. (D) Transconductance ($g_m$) dependence on sensing current for BJT and FET sensors; $I_C$ is the sensing current for the BJT sensor and $I_D$ is the sensing current for the FET sensor; $g_m$ values are extracted by numerically differentiating transfer curves shown in A and B.

Figure 3. Sensing measurements using BJT and FET electrochemical sensors. (A) Dependence of the sensing signal $I_C$ on applied voltage $V_{BE} (=V_B-V_E)$ in KCl solution of various concentrations for a BJT sensor; symbols are measurements and solid lines are fits. (B) Dependence of the sensing signal $I_D$ on applied gate voltage $V_G$ in KCl solution of various concentrations for a FET sensor; symbols are measurements and solid lines are fits. (C) Threshold voltage $V_T$ dependence on chloride concentration for BJT and FET sensors; $V_T$ values are extracted from transfer curves shown in (A) and (B); different symbols denote different $V_T$ measurement sets; open symbols indicate that measurements are made as $[\text{Cl}^-]$ is increased, and filled symbols indicate that measurements are made as $[\text{Cl}^-]$ is decreased; arrows indicate that $V_T$ dependence on chloride concentration is reversible; solid lines are fits and provide estimations of $V_T$ shifts ($\Delta V_T$) with variation in chloride concentration by a decade: $\Delta V_T = 57 \pm 1 \text{ mV/pCl}^-$ for both FET and BJT sensors. (D) Transconductance ($g_m$) dependence on sensing current for BJT and FET sensors; $I_C$ is the sensing current for the BJT sensor and $I_D$ is the sensing current for the FET sensor; $g_m$ values are extracted by numerically differentiating transfer curves shown in A and B.
that \( g_m \) is an intrinsic transducer property. Using these results from Fig. 3, the performance metrics for BJT and FET sensors are compared as discussed.

An electrochemical sensor sensitivity can be defined as the relative change in the sensing current (I) for a fixed change in the target analyte concentration. From equation 1, sensor sensitivity can be written as:

\[
\Delta I / I = (\Delta \psi_s / I) \cdot (g_m / I)
\]

In the above equation, \( \Delta \psi_s \) is the change in the surface potential corresponding to a fixed analyte concentration change. Figure 3 shows that \( \Delta \psi_s \) is same for both BJT and FET sensors. Hence, for the purpose of transducer comparison, \( \Delta \psi_s \) can be set to 1 V and sensor sensitivities are estimated from equation 3. For the BJT sensor, sensitivity \( \Delta I_c / I_c = g_m / I_c \), where the transconductance is \( g_m = (\delta I_c / \delta V_{BE}) \). Similarly, the FET sensor sensitivity can be written as: \( \Delta I_d / I_d = (\delta I_d / \delta V_G) / I_d \). Using the transfer and transconductance curves shown in Fig. 3, sensor sensitivities at various chloride ion concentrations are estimated and compared. Figure 4A compares the BJT sensor sensitivity with the FET sensor sensitivity. The BJT sensor sensitivity (\( \Delta I_c / I_c \)) is observed to be independent of \( I_c \), implying that sensing measurements can be made with the same high sensitivity over the entire \( I_c \) range of several decades, irrespective of applied \( V_{BE} \). In contrast, the FET sensor sensitivity \( \Delta I_d / I_d \) varies with the sensing signal, and therefore applied \( V_G \) has to be chosen such that \( I_d \) is in the range of 0.05 to 0.5 nA to achieve maximum sensor sensitivity. Also, BJT sensor sensitivity (\( \Delta I_c / I_c \)) is increasingly higher than the FET sensor sensitivity (\( \Delta I_d / I_d \)) for sensing currents > 1 nA. Hence, an electrochemical sensor with a BJT transducer is demonstrated to have superior sensitivity characteristics.

We now discuss calibration curves for BJT and FET electrochemical sensors: the calibration curve is defined as the sensing signal dependence on analyte concentration measured at a fixed applied voltage. To compare these two calibration curves, the sensing signal is normalized by the signal measured at 100 mM KCl concentration. Figure 4B shows the dependence of normalized sensing current on the chloride concentration for BJT and FET sensors at various applied voltages. For the BJT sensor, the normalized \( I_c \) increases by a factor of 10 per pCl, irrespective of the applied voltage \( V_{BE} \). In contrast, normalized calibration curve depends on the applied gate voltage \( V_G \) for the FET sensor. Normalized \( I_d \) increases by a factor of 8 per pCl over a narrow range of \( V_G \) ~ 0.2 to 0.25 V and this dependence becomes weaker at higher \( V_G \). In summary, normalized calibration curves are independent of applied voltage for a BJT sensor, and therefore it is better suited for mobile sensing applications.

Signal to noise ratio (SNR) is another important sensor performance metric. As discussed elsewhere, SNR measures the sensor resolution (i.e. smallest measurable change in ion concentration) and can be written as:

\[
SNR = \Delta \psi_s \cdot g_m / (\sqrt{BW} \cdot \sqrt{S_i(f = 1 Hz)})
\]

where, \( S_i(f = 1 Hz) \) is the sensing current noise power density at 1 Hz, \( g_m \) is the transconductance, and band width \( BW = \ln (f_2/f_1) \) for low frequency cutoff \( f_1 \) and high frequency cutoff \( f_2 \) in the measurement bandwidth. Using equation 4 and assuming \( BW = 1 \) and \( \Delta \psi_s = 1.0 \) V, the SNR per volt can be written as:

\[
SNR \text{ per volt} = g_m / \sqrt{S_i(f = 1 Hz)}
\]
Using equation 5, the SNR is estimated as follows. Sensing current noise power density ($S_I$), signal noise ratio (SNR) and signal resolution comparison: (A) Dependence of $S_I$ at 1 Hz on sensing current for BJT and FET sensors; $I_C$ and $I_D$ are sensing currents for BJT and FET sensors, respectively; blue symbols denote $S_I$ measured in 1 mM KCl, red symbols denote $S_I$ measured in 100 mM KCL, and black symbols denote measurements made on a standard device with no sensing surface or solution; solid lines are power law fits and extracted exponent values are shown in the figure. (B) Comparison of SNR dependence on sensing current for BJT and FET sensors; blue symbols denote measurements made in 1 mM KCl, red symbols denote measurements made in 100 mM KCL, and black symbols denote measurements made on a standard device with no sensing surface or solution. (C) BJT sensor signal $I_C$ dependence as 10 mM KCl solution of 1.6 mL volume is diluted by adding 20 µL of deionized water at each step; $I_C$ is measured at a fixed $V_{BE} = 0.260$ V. (D) FET sensor signal $I_D$ dependence on as 10 mM KCl solution of 1.6 mL volume is diluted by adding 20 µL of deionized water at each step; $I_D$ is measured at a fixed $V_{GS} = 0.284$ V. (E) Mean and standard deviation (error bar) values of sensing signal $I_D$ at various dilution steps; symbols denote mean $I_D (\langle I_D \rangle)$ estimated from BJT sensor data shown in (C); solid line is a power law fit. (F) Mean and standard deviation values of sensing signal $I_D$ at various dilution steps; symbols denote mean $I_D (\langle I_D \rangle)$ estimated from FET sensor data shown in (D); solid line is a power law fit.
In contrast, the maximum SNR is observed at $I_{C} \sim 100 \text{nA}$ for the FET sensor, and therefore the corresponding $V_{G}$ has to be carefully chosen to achieve maximum SNR. From Figs 4A and 5B, we observe that the maximum sensitivity and SNR occur at different sensing current values, and as a result a tradeoff has to be made between sensitivity and SNR for a FET sensor. Since SNR is a measure of the sensor resolution, the above SNR observations are also true for the sensor resolution.

To further highlight the sensor resolution dependence on the transducer choice, a dilution experiment is performed using BJT and FET sensors. Starting with a 10 mM KCl solution of 1.6 mL volume, the solution is diluted in steps by adding 20 µL of deionized water. Each dilution step results in chloride concentration change of $\Delta pC1 \sim 0.0051$. To ensure that the comparison is accurate, the applied voltage ($V_{BE}$ or $V_{G}$) is fixed at a value such that the corresponding sensing current at the initial 10 mM KCl concentration is the same. At each dilution step, the sensing current is measured for about 100 sec after a wait of about 1 minute. Figure 5C shows the BJT sensing signal $I_{C}$ measured at a fixed $V_{BE} = 0.26 \text{ V}$ at various dilution steps. Figure 5D shows dilution experiment results for a FET sensor, where the sensing signal $I_{C}$ is measured at a fixed $V_{G} = 0.284 \text{ V}$. Figures 4C and 5D measurements are analyzed and results are shown in Fig. 5E. Figure 5E shows mean and standard deviation values of BJT sensing current $I_{C}$ at various dilution steps. Mean $I_{C}$ value increases by $\Delta I_{C} \sim 3 \text{ pA}$ per dilution step and the standard deviation $\delta I_{C} \sim \pm 0.15 \text{ pA}$. Since the ratio $\Delta I_{C}/\delta I_{C} \sim 10$ and $\Delta pC1 \sim 0.0051$ at each dilution step, estimated BJT sensor resolution is about 0.0005 which is the highest reported value to the best of our knowledge. Figure 5F shows mean and standard deviation values of sensing current $I_{C}$ at various dilution steps for the FET sensor. Mean $I_{C}$ value increases by $\Delta I_{C} \sim 2.2 \text{ pA}$ per dilution step and the standard deviation $\delta I_{C} \sim \pm 1 \text{ pA}$. Since signal change and signal noise are of comparable magnitude for the FET sensor, FET sensor is unable to resolve $\Delta I_{C}$.

To further highlight the sensor resolution dependence on the transducer choice, a dilution experiment is performed using BJT and FET sensors. Starting with a 10 mM KCl solution of 1.6 mL volume, the solution is diluted in steps by adding 20 µL of deionized water. Each dilution step results in chloride concentration change of $\Delta pC1 \sim 0.0051$. To ensure that the comparison is accurate, the applied voltage ($V_{BE}$ or $V_{G}$) is fixed at a value such that the corresponding sensing current at the initial 10 mM KCl concentration is the same. At each dilution step, the sensing current is measured for about 100 sec after a wait of about 1 minute. Figure 5C shows the BJT sensing signal $I_{C}$ measured at a fixed $V_{BE} = 0.26 \text{ V}$ at various dilution steps. Figure 5D shows dilution experiment results for a FET sensor, where the sensing signal $I_{C}$ is measured at a fixed $V_{G} = 0.284 \text{ V}$. Figures 4C and 5D measurements are analyzed and results are shown in Fig. 5E. Figure 5E shows mean and standard deviation values of BJT sensing current $I_{C}$ at various dilution steps. Mean $I_{C}$ value increases by $\Delta I_{C} \sim 3 \text{ pA}$ per dilution step and the standard deviation $\delta I_{C} \sim \pm 0.15 \text{ pA}$. Since the ratio $\Delta I_{C}/\delta I_{C} \sim 10$ and $\Delta pC1 \sim 0.0051$ at each dilution step, estimated BJT sensor resolution is about 0.0005 which is the highest reported value to the best of our knowledge. Figure 5F shows mean and standard deviation values of sensing current $I_{C}$ at various dilution steps for the FET sensor. Mean $I_{C}$ value increases by $\Delta I_{C} \sim 2.2 \text{ pA}$ per dilution step and the standard deviation $\delta I_{C} \sim \pm 1 \text{ pA}$. Since signal change and signal noise are of comparable magnitude for the FET sensor, FET sensor is unable to resolve $\Delta I_{C}$.

Another difference between these two electrochemical sensors is the voltage applied to the aqueous solution by the reference electrode. In the case of a BJT sensor, the reference electrode applies $0 \text{ V}$ to the solution during sensing measurements. In contrast for the FET sensor, the reference electrode applies a voltage $|V_{G}| > 0 \text{ V}$ to the solution during sensing measurements. This $|V_{G}| > 0 \text{ V}$ can cause interference, particularly if the sensing is being performed on voltage gated ion channel proteins such as those embedded in neuron membranes. Hence, BJT sensors are better suited for a wider range of biological systems. Lastly, like a FET transducer, a BJT is also compatible with silicon processing technology and can be integrated with automation circuitry on a single chip. Both FET and BJT can easily be miniaturized to 0.1 $\text{mm}^2$ but the FET is easier to further scale down. In summary, this comparative study demonstrates that the electrochemical sensor with a BJT as the transducer has significantly enhanced sensing characteristics in comparison to that with a FET transducer.

**Cl$^-$$^*$ Sensing in Artificial Human Sweat for Diagnostic Applications.** Since electrochemical sensors with BJT as transducers have significantly enhanced sensing characteristics, they are further investigated for as a potential candidate for hand-held diagnostic application for Cystic Fibrosis disease that requires the measurement of [Cl$^-$] in human eccrine sweat. Chloride sensing measurements are performed using artificial human sweat that are similar in chemical composition to the human eccrine sweat. Measurements are performed on a set of seven artificial sweat samples that have been diluted by varying amounts with ultrapure water: the sweat percentage ranged from 100 (no dilution) to 0.8 (125 times dilution). Figure 6A shows measured BJT sensor transfer curves for undiluted and diluted sweat samples. For each sample, IC increases with increasing $V_{BE}$ in accordance with equation 2 with an exponent that corresponds to $25 \text{ °C}$. This dependence is similar to that observed in aqueous KCl solutions (Fig. 3A). Also, $I_{C}$ curves are observed to shift towards the left with decreasing sweat percentages, thereby indicating that $[\text{Cl}^+]$ is decreasing. In Fig. 6B, the sensing signal ($I_{C}$) reversibility and reproducibility in sweat is investigated. $I_{C}$ is measured for about 100 sec at a fixed $V_{BE} = 0.2 \text{ V}$ for each artificial sweat sample. Measurements are made on samples in the order of first decreasing and then increasing sweat concentration. $I_{C}$ is observed to be repeatable and reversible within 4% of error. Though, the focus is on BJT sensor, similar sensing measurements are also performed with the FET sensor to verify that chloride sensitivity comparisons are same in sweat as those of Fig. 4B. In Fig. 6C, the solid line denotes the chloride calibration curves for BJT and FET sensors, obtained by fitting sensing signals measured in for KCl solutions (solid symbols) at constant applied voltage $V_{BE} = V_{G} = 0.2 \text{ V}$. From the fits, the calibration curve equation for the BJT sensor is $I_{C} = 4.3 \times 10^{-13}[\text{Cl}^+]^{1.03}$, and the calibration curve equation for the FET sensor is $I_{C} = 5.5 \times 10^{-13}[\text{Cl}^+]^{0.8}$. Using calibration curves and sensing signals at $V_{BE} = V_{G} = 0.2 \text{ V}$ (open symbols), chloride concentration values are estimated for undiluted and diluted sweat samples for both BJT and FET sensors. Similar analysis is also performed for BJT and FET sensing currents measured at another applied voltage $V_{BE} = V_{G} = 0.4 \text{ V}$ as shown in Fig. 6D. From Fig. 6C,D, two main observations can be made. (i) Sensing signal increases with a power law dependence on the [Cl$^-$] with an exponent value of $\sim 1.0$ that is independent of the applied voltage $V_{BE}$ for the BJT sensor, whereas the exponent decreases from $-0.8 \text{ V}$ to $-0.6$ as the applied voltage $V_{G}$ increases from 0.2 V to 0.4 V. (ii) Since the exponent magnitude is higher for the BJT sensor data, the BJT sensor has higher chloride sensitivity than the FET sensor. These two observations obtained using sweat samples are consistent with those obtained using KCl solutions as shown in Fig. 4B. To verify the accuracy of sensor measurements, chloride concentrations are also calculated by using the supplier provided chloride concentration value of 65 mM for the undiluted sweat and the known sweat dilution percentage. The calculated and measured chloride concentration results are compared in Fig. 6E; solid line denote calculated results and open symbols are $[\text{Cl}^+]$ measurements from Fig. 6C,D using BJT and FET sensors. Measurements are in agreement with calculated values of chloride levels in artificial sweat samples for both sensors.
Since artificial sweat has amino acids, minerals and metabolites, it is possible that these amino acids and metabolites would nonspecifically bind to the sensing surface, and thus cause signal drifts or degrade the sensitivity to chloride ions. To evaluate these effects, the silver chloride sensing surface is incubated in 100% artificial sweat for total time of 168 hours (1 week); intermittently the incubation is interrupted and chloride sensing measurements are made in the incubating sweat. Figure 7A shows the measured dependence of IC on VBE after various incubation times. From the figure, the transfer curves show a small shift of ~3 mV after a week of incubation. Since the curve shifted back when re-measured in fresh sweat, the observed drift is attributed to a slight increase in the chloride ion concentration due to the sweat evaporation during the long incubation period. Hence, the sensing signal shows negligible (< 1 mV) drift after one week of incubation in artificial human sweat. This result is understandable because sweat is mostly (99%) water with low concentrations of biomolecules and as a result non-specific binding is minimal.

To measure the impact of week long incubation in sweat on the sensing surface sensitivity to chloride ions, the calibration curve at a fixed VBE = 0.2 V is measured as a function of incubation time as shown in Fig. 7B. The calibration curve (IC versus [Cl\(^-\)]) remains unchanged with incubation time, thus indicating that the silver chloride sensing surface is not degraded with prolonged incubation in sweat. At the end of the week long incubation, the sensing signal IC at a fixed VBE = 0.3 V is repeatedly measured 6000 times in sweat as shown in Fig. 7C. The signal shows no drifts with repeated measurements and has 0.13% noise which is similar to the noise measured before incubation. In summary, incubation in artificial sweat does not induce signal drifts, calibration curve degradation or noise increase for the BJT sensor.
Conclusion
BJT and FET transducers are compared by performing sensing measurements on two electrochemical sensors that are identical in all details, except for the transducer device type. This comparative study demonstrates that an electrochemical sensor with the BJT transducer has significantly enhanced sensing characteristics in comparison to that with the widely used FET transducer. The BJT sensor has sensitivity and resolution and calibration curves that are independent of the use voltages. Hence, BJT sensors are particularly well suited for making high sensitivity and resolution sensing measurements with minimal calibration requirements and are well suited for mobile sensing applications. As a demonstration for mobile diagnostic applications, the BJT electrochemical sensor is investigated by measuring chloride levels in artificial human sweat and is shown to be a viable option for portable cystic fibrosis diagnosis.

Methods
Chloride ion sensing surface preparation. The silver chloride is used as the chloride ion (Cl\(^{-}\)) sensing surface for both BJT and FET sensors. It is prepared by the electrochemical anodization of a silver (Ag) wire (Sigma Aldrich, part# 265586, ≥ 99.99%; 1 mm diameter) in a chloride solution. To prepare a silver chloride coated silver wire, a silver wire is first cleaned by sonication in ethanol (~5 mins) followed by rinse in ultrapure Millipore water. The cleaned silver wire is used as the anode and a platinum wire (Sigma Aldrich, part# 267201, 99.99%) is used as the cathode in an electrolytic cell. Since KCl\(^{28}\), HCl\(^{29}\) and their mixtures\(^{30}\) have been widely used as an electrolyte for anodization of the Ag wire, we have evaluated different electrolytic solution with the aim of identifying the best recipe. The results are summarized in Table S1 in Supporting Information Section. As shown in Table S1, the recipe that uses 1 M HCl as the electrolytic solution with a constant current of 2 mA/cm\(^{2}\) for 15 minutes produced a silver chloride surface with highest chloride sensitivity and least drifts during electrical measurements. The silver chloride surface prepared by this recipe is used for all sensing measurements.

Materials used in sensing measurements. All sensing measurements are performed in air at room temperature using either potassium chloride (99.5%, Sigma Aldrich) aqueous solution using or synthetic human Eccrine sweat (Pickering Laboratories, http://www.pickeringtestsolutions.com) of 100 μL volume. Ultrapure water with resistivity of 18.2 MΩ at 298 K is used for making potassium chloride (KCl) solutions and for sweat dilution. The reference electrode is a leak free commercially available reference electrode (Innovative Instruments, Inc., Florida) with outer diameter of 1 mm.

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Author Contributions
S.Z. conceived the experiments, analyzed the results and wrote the main manuscript text. All authors conducted experiments and reviewed the manuscript.

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