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Flexure-FET biosensor to break the fundamental sensitivity limits of nanobiosensors using nonlinear electromechanical coupling

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In this article, we propose a Flexure-FET (flexure sensitive field effect transistor) ultrasensitive biosensor that utilizes the nonlinear electromechanical coupling to overcome the fundamental sensitivity limits of classical electrical or mechanical nanoscale biosensors. The stiffness of the suspended gate of Flexure-FET changes with the capture of the target biomolecules, and the corresponding change in the gate shape or deflection is reflected in the drain current of FET. The Flexure-FET is configured to operate such that the gate is biased near pull-in instability, and the FET-channel is biased in the subthreshold regime. In this coupled nonlinear operating mode, the sensitivity (S) of Flexure-FET with respect to the captured molecule density (Nc) is shown to be exponentially higher than that of any other electrical or mechanical biosensor.

In other words, while Sflexure ∼ eγNc(Nc−Nc0), classical electrical or mechanical biosensors are limited to Sclassical ∼ γNc or γNc ln(Nc), where γ are sensor-specific constants. In addition, the proposed sensor can detect both charged and charge-neutral biomolecules, without requiring a reference electrode or any sophisticated instrumentation, making it a potential candidate for various low-cost, point-of-care applications.

Nanoscale biosensors are widely regarded as a potential candidate for ultrasensitive, label-free detection of biochemical molecules. Among the various technologies, significant research has focused on developing ultrasensitive nanoscale electrical (1) and mechanical (2) biosensors. Despite remarkable progress over the last decade, these technologies have fundamental challenges that limit opportunities for further improvement in their sensitivity (Fig. 1A) (3–6). For example, the sensitivity of electrical nanobiosensors such as Si-Nanowire (NW) FET (field effect transistor) (Fig. 1B) is severely suppressed by the electrostatic screening due to the presence of other ions/charged biomolecules in the solution (7), which limits its sensitivity to vary linearly (in subthreshold regime) (3, 7) or logarithmically (in accumulation regime) (4, 7, 8, 9) with respect to the captured molecule density Nc. Moreover, the miniaturization and stability of the reference electrode have been a persistent problem, especially for lab-on-chip applications (1). Finally, it is difficult to detect charge-neutral biological entities such as viruses or proteins using charge-based electrical nanobiosensor schemes.

In contrast, nanomechanical biosensors like nanocantilevers (10, 11) (Fig. 1C) do not require biomolecules to be charged for detection. Here, the capture of target molecules on the cantilever surface modulates its mass, stiffness, and/or surface stress (5, 11, 12). This change in the mechanical properties of the cantilever can then be observed as a change in its resonance frequency (dynamic mode), mechanical deflection, or change in the resistance of a piezoresistive material (static mode) attached to the cantilever (6, 13). Unfortunately, typical optical detection schemes (10) require complex instrumentation which may preclude them from many low-cost point-of-care applications. Further, the response of nanomechanical biosensors varies only linearly (5) or logarithmically (6, 14, 15) with the change in the mass or surface stress of the cantilever, and therefore these sensors may not be sufficiently sensitive to detect target molecules at very low analyte concentrations, unless sophisticated, low-noise setup is used.

To overcome the respective limitations of classical electrical and mechanical nanoscale biosensors, we propose the concept of a Flexure-FET biosensor that integrates the key advantages of both technologies but does not suffer from the limitations of either approach. The Flexure-FET consists of a nanogate channel biased through a thin-film suspended gate (Fig. 1D). Although the structure is similar to that of a suspended-gate FET (16), nano-electromechanical (NEM) FET (17), or resonant gate transistor (18), we call the device Flexure-FET to emphasize its distinctive nonlinear operation specifically optimized for ultra-sensitive detection of biomolecules. As shown in Fig. 1E, the ultra high sensitivity arises from the coupling of two electromechanical nonlinear responses, namely (i) spring-softening (19) in which stiffness decreases nonlinearly with the applied gate bias Vc and vanishes at the pull-in point (for detailed discussions on pull-in instability, see refs. 20, 21), and (ii) subthreshold electrical conduction (22) in which current depends exponentially on the surface potential (Fig. S1). Such nonlinear electromechanical coupling enables exponentially high sensitivity for Flexure-FET sensors (Fig. 1A), which is fundamentally unachievable by exclusive use of existing nanoscale electrical or mechanical biosensors. Moreover, the reliance of change in stiffness (23, 24) ensures screening-free detection of charged/neutral molecules, with no need for a reference electrode, and the measurement of drain current for detection requires no complex instrumentation. It should be noted that from a mechanical perspective, the Flexure-FET operates close to pull-in instability, a critical point. Similar critical point sensing has also been reported for vapor sensors (25) that operate close to bucking-instability (25) and for mass sensors that operate close to saddle-node bifurcation (26), and their higher sensitivity has been confirmed experimentally. However, beyond the critical point sensing, the integrated transistor-action in the subthreshold regime provides the Flexure-FET an additional exponential sensitivity (and simpler direct current readout) that could not be achieved by the classical nonlinear sensor schemes.

Theory of Flexure-FET
Sensor Configuration Before Target Capture. The operating principle of Flexure-FET can be understood using the well established...
spring-mass model (Fig. 2) (17, 18). With the application of gate bias \( V_G \), the gate moves downward toward the dielectric (y vs. \( V_G \) curve in Fig. 1E); and the corresponding increase in gate capacitance is reflected in the increased drain current \( I_{DS} \), as shown in Fig. 1E. The static behavior of the device is dictated by the balance of spring and electrostatic forces; i.e.,

\[
k(y_0 - y) = \frac{1}{2} \varepsilon_0 E_{air}^2 A,
\]

where \( k \) is the spring constant, \( y_0 \) is the air-gap, \( y \) is the position of the gate electrode, \( \varepsilon_0 \) is the permittivity of free space, \( E_{air} \) is the electric field in the air, and \( A = WL \) is the area of the gate electrode.

The electric field below the membrane \( E_{sub} \) is equal to \( \varepsilon_s E_s(\psi_s) \), where \( \varepsilon_s \) is the dielectric constant of the substrate, and

\[
E_s(\psi_s) = \frac{2qN_A}{\varepsilon_0 \varepsilon_s} \left[ \psi_s + \left( e^{\frac{\varphi_s}{k_B T}} - 1 \right) \frac{k_B T}{q} \right] - \left( \frac{n_i}{N_A} \right)^2 \left( \psi_s - \left( e^{\frac{\varphi_s}{k_B T}} - 1 \right) \frac{k_B T}{q} \right).
\]

where \( E_s(\psi_s) \) is the electric field at the substrate-dielectric interface (22, page 64, for a detailed derivation of Eq. 2a), \( \psi_s \) is the surface potential, \( q \) is the charge of an electron, \( N_A \) is the substrate doping, \( k_B \) is the Boltzmann constant, \( T \) is the absolute temperature, and \( n_i \) is the intrinsic carrier concentration in the substrate. The voltage drop in air \( (\psi_s, E_s(\psi_s)) \), dielectric \( (\varphi_s, E_s(\psi_s)) \), and substrate \( (\psi_s) \) can be related to the applied gate bias \( V_G \) as follows

\[
V_G = \left( y + \frac{V_d}{\varepsilon_d} \right) \varepsilon_s E_s(\psi_s) + \psi_s,
\]

where \( y_d \) is the dielectric thickness and \( \varepsilon_d \) is the dielectric constant. Eqs. 1 and 2 are solved self-consistently for \( y \) and \( \psi_s \) at each \( V_G \). The corresponding inversion charge density \( (Q_i) \) in the channel and drain current \( (I_{DS}) \) are given by

\[
Q_i = \frac{q m_n^2}{N_A} \int_{0}^{\psi} \frac{e^{\frac{\varphi_s}{k_B T}} - 1}{E_s(\psi_s)} d\psi,
\]

\[
I_{DS} = \mu_n L Q_i \frac{V_{DS}}{W},
\]

where \( \mu_n \) is the channel mobility for electrons, \( V_{DS} \) is the applied drain to source voltage. Fig. 1E shows the steady-state response of Flexure-FET as a function of biasing voltage \( V_G \), obtained from the numerical simulations of Eqs. 1-4.

**Flexure-FET Response to Target Capture.** For transduction, the proposed Flexure-FET biosensor utilizes the change in suspended gate stiffness from \( k \) to \( k + \Delta k \) due to the capture of biomolecules. The change in stiffness due to the capture of biomolecules has been demonstrated by several recent experiments of mass sensing using nanocantilever-based resonators (12, 27, 28) (Fig. S2). This well known observation of stiffness change has been attributed to the change in the membrane thickness, Young’s modulus, and/or surface stress of the beam (12, 23,
Indeed, Craighead (27) suggests its use as a basis of a new class of mechanical biosensor.

In the following analysis, we model change in $k$ by change in the effective thickness $H$ of the gate ($\Delta H$), although it should be stressed that the conclusions do not depend on the particular hypothesis regarding $\Delta k$. For now, we ignore the details of the spatial distribution of molecules associated with random sequential adsorption (31) and assume a uniform distribution of adsorbed molecules on the sensor surface. Therefore, the conservation of volume suggests $\Delta H = NA_sH_t$, where $N_s$ is the area density, $A_s$ is the effective cross-sectional area, and $H_t$ is the effective thickness of the target molecule. Using the fact that $k = \frac{\alpha \epsilon_{rel} \Gamma t^3}{2H^2}$, the change in stiffness $\Delta k$ due to $\Delta H (\ll H)$ can be related to adsorbed molecule density $N_s$ as follows:

$$\frac{\Delta k}{k} \approx \frac{3N_sA_sH_t}{H}.$$  \[5\]

For simplicity, we have taken the Young’s modulus of captured molecules to be the same as that of the membrane, but this is obviously not necessary, and the theory can be generalized by the methods developed in Tamayo, Ramos, Mertens, and Calleja (23).

Combining Eqs. 1 and 2b, we get $k(y_0 - y) = \epsilon_0 A_s(V_G - y_s)^3/2$. Now, the change in gate position $\Delta y$ for small change in stiffness $\Delta k$ due to capture of biomolecules is given as

$$(3y_0 - y_0)\Delta y + (y - 3y_0)\Delta y \approx \frac{\epsilon_0 A_s(V_G - y_s)^3}{2}\frac{\Delta k}{k^2}.$$  \[6\]

If Flexure-FET is biased close to pull-in ($V_G \approx V_{Pi}$, $y \approx \frac{1}{3} y_0$), the nonlinear $\Delta y^2$ term dominates the linear $\Delta y$ term in Eq. 6. It is essential to bias the Flexure-FET in this nonlinear, close-to-pull-in regime for maximum sensitivity. Using Eqs. 5 and 6, we find

$$\Delta y \approx \sqrt{\frac{\epsilon_0 A_s(V_G - y_s)^3}{2} \frac{\Delta k}{k^2}} \approx \beta \sqrt{N_s},$$  \[7\]

where $\beta = \sqrt{\frac{3\epsilon_0 A_s(V_G - y_s)^3 A_s H_t}{2(y_0 - y)}}$ is a bias and device dependent constant.

Since the electrostatic force in subthreshold regime is given by $\frac{1}{2} \epsilon_0 E_{air}^2 A = qe_s N_A A$ (Eq. 2a), the corresponding change in the surface potential $\Delta \psi_s$, is obtained by perturbation of Eq. 1; i.e.,

$$\Delta \psi_s = \frac{-k \Delta y + \Delta k(y_0 - y)}{q e_s N_A A}.$$  \[8\]

Using Eqs. 2a, 3, and 4, we can calculate the drain current $I_{DS}$ in the subthreshold regime as follows,

$$I_{DS} \approx \frac{\mu_n C}{W} \left( \frac{V_{GS}}{N_s} \right) \left( \frac{q \beta T}{\eta} \right) \left( \frac{q e_s N_A}{\sqrt{N_s}} \right) e^{V_{DS}/V_{th}}.$$  \[9\]

Now, the ratio of the drain current before ($I_{DS1}$) and after ($I_{DS2}$) capture of biomolecules (in terms of the change in surface potential $\Delta \psi_s$) is given by

$$\frac{I_{DS1}}{I_{DS2}} \approx \exp\left( -\frac{q \Delta \psi_s}{k_B T} \right).$$  \[10\]

Using Eqs. 8 and 10, the ratio $I_{DS1}/I_{DS2}$ is given by

$$I_{DS1} \approx \exp\left( \frac{k_B T e_s N_A A}{k_B T e_s N_A A} \right).$$  \[11\]

Therefore, if Flexure-FET is operated close to pull-in and in subthreshold regime, sensitivity $S$ (using Eqs. 5, 7, and 11) is given by

$$S_{Flexure} = \frac{I_{DS1}}{I_{DS2}} \approx \exp(\gamma_1 \sqrt{N_s} - \gamma_2 N_s).$$  \[12\]

where $\gamma_1 = \frac{k_B}{k_B T e_s N_A A}$ and $\gamma_2 = \frac{3(y_0 - y)e_s N_A A}{k_B T e_s N_A A}$. The sensitivity $S$ is defined as $I_{DS1}/I_{DS2}$, because $I_{DS}$ decreases after capture (see next text section).

Eq. 12 is the key result of the paper and shows how nonlinear interaction between mechanical (spring-softening) and electrical (subthreshold) aspects of sensing leads to an exponential sensitivity to capture of biomolecules. Such gain in sensitivity is impossible to achieve exclusively by electrical or mechanical sensing mechanisms.

Numerical Confirmation of Flexure-FET Response. The compact analytical expression of sensitivity of the Flexure-FET sensor can be validated by the self-consistent numerical solution of Eqs. 1-4. The results for the change in sensor characteristics due to the capture of biomolecules are summarized in Fig. 3. For example, Fig. 3A shows $\Delta y$ vs. $V_G$ before and after capture of target molecules. After the capture, the gate moves up (for a fixed $V_G$) due to increased restoring spring force (because of increase in the $k$; Fig. 3A). Interestingly, change in gate position $\Delta y$ is maximum close to pull-in due to spring-softening effect, as shown in Fig. 3B (see Figs. S3, S4 and S5 in SI Text for experimental validation). The change in gate position $\Delta y$ is directly reflected in change in $I_{DS}$. Fig. 3C shows $I_{DS}$ vs. $V_G$ before and after capture of biomolecules. Interestingly, $I_{DS}$ decreases after capture due to increased separation between the gate and the dielectric (hence decreased capacitance). The corresponding ratio of the currents

\[Fig. 3. \] Change in the sensor characteristics due to capture of target molecules on the surface of the gate, (A) $\Delta y$ vs. $V_G$ before and after capture, and (B) corresponding change in the position of gate electrode $\Delta y$ vs. $V_G$. The $\Delta y$ increases rapidly near pull-in due to spring-softening effect. The capture of target molecules is directly mirrored in the change in $I_{DS}$. (C) $I_{DS}$ vs. $V_G$ before and after capture, and (D) corresponding ratio of the two currents $I_{DS1}$ (before capture) and $I_{DS2}$ (after capture) as a function of $\Delta y$. Symbols denote the numerical simulation and solid line analytical formula (Eq. 11). The device considered has the following typical parameters: $L = 4 \mu m$, $W = 1 \mu m$, $H = 40 \ nm$, $E = 200 \ GPa$, $y_0 = 100 \ nm$, $y_d = 5 \ nm$, $e_l = 11.7$, $e_d = 3.9$, $N_A = 6 \times 10^{16} \ cm^{-3}$.\]
threshold regime, orders of magnitude change in Flexure-FET close to mechanical pull-in and in electrical subthreshold regime, orders of magnitude change in stiffness or captured molecule density can be extraordinarily sensitive; indeed, zeptogram mass detection (8, 9) as well.

Comparison with Classical Sensors

Next we compare the sensitivity of the proposed Flexure-FET sensor with the current nanoscale electrical/mechanical biosensors. Fig. 4A indicates that the Flexure-FET sensors are exponentially sensitive to change in stiffness or captured molecule density $N_t$ (symbols: numerical simulation, solid line: analytical result; Eq. 12). In the following, we explain the origin of linear (or logarithmic) sensitivity for electrical and mechanical nanoscale biosensors.

Electrical Nanobiosensors. For Si-NW FET biosensors, which also have the optimal sensitivity in subthreshold regime (3), sensitivity $S$ is defined to be the ratio of conductance $G$ (after) and $G_0$ (before) capture of target molecules (assuming conductance increases after the capture). Therefore, using Eq. 9, $S$ can be approximated as

$$S_{\text{SiNW}} \equiv \frac{G}{G_0} \approx \exp \left( \frac{q \Delta \psi \rho}{k_B T} \right). \quad [13]$$

Unfortunately, the detection of biomolecules in a fluidic environment involves electrostatic screening by other ions in the solution.

Consequently, the surface potential scales logarithmically with biomolecule density; i.e., $(q/k_B T) \Delta \psi \propto \ln(\delta N_t)$ (7), where $\delta$ is a constant that depends on ionic strength and properties of dielectric/fluid interface. Therefore, optimal sensitivity of Si-NW biosensors is given by

$$S_{\text{SiNW}} \propto \delta N_t. \quad [14]$$

In Fig. 4B, $S$ is plotted against volume concentration $\rho$, as the captured molecule density $N_t \propto \rho$ [linear regime of Langmuir isotherm (7)]. Therefore, all the conclusions regarding the dependence of sensitivity on $N_t$ also hold for $\rho$. It should be noted that the reported sensitivity in the subthreshold regime (3) is actually sublinear (Fig. 4B), below the maximum sensitivity limit defined by Eq. 14 that can be achieved in this sensing regime. In the accumulation or the inversion regimes, $S_{\text{SiNW}} \propto \rho$, and therefore, $S_{\text{SiNW}} \propto \ln(N_t)$, as shown in Fig. 4B (4, 7). Similar logarithmic dependence of sensitivity was reported in other references (8, 9) as well.

Mechanical Nanobiosensors. For nanomechanical biosensors such as resonance mode nanocantilever, the sensitivity $S$ is defined as $o_0/\omega$, where $\omega$ is the resonance frequency after the capture of target biomolecules, and $o_0$ is the resonance frequency before capture. Using the well known fact that $\omega = \sqrt{k/\rho}$, where $k$ is the stiffness and $m$ is the initial mass of the cantilever, $S$ is given by

$$S_{\text{Res}} \equiv \frac{o_0}{\omega} \approx 1 + \frac{1}{2} \frac{\Delta m}{m} = 1 + \frac{1}{2} \frac{N_t W L m^*}{m}. \quad [15]$$

where $m^*$ is the mass of individual biomolecule and $\Delta m = N_t W L m^*$ is the added mass of the biomolecules. Therefore, the sensitivity of mechanical biosensor can only vary linearly with $N_t$. This theoretical prediction is confirmed by experimental data (5) in Fig. 4C. We emphasize that the nanomechanical biosensors—with careful design and appropriate instrumentation—can be extraordinarily sensitive; indeed, zeptogram mass detection (32) has been reported. Eq. 15 simply suggests that the sensitivity of such sensor still varies linearly with respect to $N_t$.

It is also important to realize that the linear sensitivity with $N_t$ is achieved only if the change in stiffness due to capture of molecules is negligible. In general, however, capture of target molecules increases stiffness of the membrane. If this increase in stiffness compensates the corresponding increase in the mass, there might be no change in resonance frequency at all (12, 28), and the sensitivity could be vanishingly small. One must independently measure the change in the stiffness (29, 30) to decouple the mass effect from stiffness effect so that the mass of the adsorbed molecule can be correctly estimated. In contrast, the Flexure-FET relies only on the change in the stiffness and works in the static mode, and therefore requires no more than a simple measurement of the drain current.

Another class of nanocantilever sensor involves operation in the static mode, where the capture of the target molecules introduces a surface stress, which in turn bends the cantilever. The displacement $\Delta \nu$ of the tip can in principle be measured using sophisticated optical readout methods, but a simpler approach can be used instead: One can measure the change in surface stress by measuring the change in the resistance of a piezoresistor attached to the cantilever. For these piezoresistive-based cantilever biosensors, the sensitivity is defined as the ratio of resistance before ($R_0$) and after ($R$) the capture of biomolecules. Fig. 4D shows a logarithmic dependence of $S$ on $\rho$. Similar logarithmic dependence for surface stress change has also been reported (14, 15). We therefore conclude that these static mode sensors do not exceed linear sensitivity limit of classical sensors.
We summarize the results discussed in this section in Fig. 1A, where the sensitivity of various types of nanobiosensors has been plotted against normalized Ns, defined as the ratio of the measured quantity (either ρ or Ni) to the minimum measured ρ or Ni of the available data. Fig. 1A allows us to conclude that the Flexure-FET biosensor will be exponentially more sensitive compared to existing nanoscale electrical or mechanical biosensors.

Finally, we emphasize that each of the three sequential physical phenomena associated with the operation of Flexure-FET (stiffness change due to capture of biomolecules, pull-in instability, subthreshold conduction) (Fig. S1) has been individually confirmed by numerous experiments based on electromechanical resonators (18, 33) and suspended-gate FET (34). We provide a summary of these experiments in the SI Text (Figs. S2, S5, and S6). In the SI Text, we also suggest that a simple reconfiguration of existing electromechanical resonators or suspended-gate FET in Flexure-FET mode can give rise to exponential sensitivity (Fig. S7).

**Conclusion**

In this paper, we have demonstrated how the Flexure-FET nanobiosensor achieves exponentially high sensitivity by combining two nonlinear characteristics of spring-softening and subthreshold conduction. This extreme high sensitivity of Flexure-FET, therefore, breaks the fundamental limits of linear or logarithmic sensitivity of classical nanoscale electrical or mechanical biosensors. There are broad ranges of applications that can benefit from this sensitivity gain. For example, the current genome sequencing schemes require PCR (polymerase chain reaction) amplification of DNA strands because of the lower sensitivity of existing biosensors. The high sensitivity of Flexure-FET can eliminate the requirement of multiplication step and hence reduce the cost of sequencing. In addition, we recall that the proposed sensing scheme (i) can detect both charged and charge-neutral molecules, (ii) does not rely on reference electrode (the fundamental roadblock of Si-NW type biosensors), and (iii) obviates the need for any sophisticated and difficult-to-integrate instrumentation. The sensitivity of Flexure-FET can be further enhanced by choosing a softer membrane (having low stiffness) such as some polymer with low Young’s modulus or an ultrathin membrane like graphene. Finally, let us emphasize that the sensing scheme is very general, which converts any change in the mechanical property of the gate electrode or change in the air-gap in the drain current of the FET channel. Therefore, the proposed idea is not necessarily restricted to biomolecules detection but should find broader applications in gas/chemical/pressure sensing as well.

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Supporting Information

Jain et al. 10.1073/pnas.1203749109

SI Text
In this document we discuss the proof-of-concept of Flexure-FET biosensor and justify the various claims made in the paper using the experimental data available in the literature. Before we show the proof-of-concept, we want to mention that the operation of Flexure-FET consists of three main pieces: (i) stiffness change due to capture of biomolecules, (ii) operating the gate near pull-in instability for maximum change in the displacement, and (iii) subthreshold conduction of the FET for exponential sensitivity (Fig. S1). In the following sections we validate each of the three pieces and their combined actions.

Experimental Validation of Stiffness Increase Due to Capture of Biomolecules. The operating principle of the proposed Flexure-FET is based on the increase in the stiffness of a cantilever or fixed-fixed beam due to the capture of biomolecules. This increase in the stiffness due to capture of biomolecules has been reported by several groups (1–4). Fig. S2 shows one such dataset for percentage increase in the stiffness due to capture of proteins on different cantilevers (2). It should be noted that percentage increase could be as high as 50%. We have shown in the article that even a 5–10% increase in the stiffness results in two to three orders of magnitude change in the drain current.

Experimental Validation That Operation Close to Pull-In Instability Results in Maximum Change in the Displacement (Δy) Due to Change in the Stiffness (Δk). The second part of the operation of Flexure-FET; i.e., biasing the gate near pull-in maximizes Δy, has also been demonstrated in large numbers of experiments on electromechanical resonators (Figs. S3–S5) (5, 6). In the following, we interpret the experiments from the perspective of its application in Flexure-FET.

We recall that capture of biomolecules changes the stiffness k \( \propto \frac{EWH}{t} \) due to change in the thickness t of the gate. Since \( \frac{\Delta E}{E} = 3 \frac{\Delta H}{H} + \frac{\Delta W}{W} + \frac{\Delta t}{t} = 3 \frac{\Delta t}{t} \), where the subscript 0 indicates initial values, we note that the nonlinear sensitivity of Δy on Δk can be equivalently demonstrated by changing the beam length L (5) or Young’s modulus E (6).

Fig. S4A shows the response of two electromechanical resonators (5) having different lengths. Their differential nonlinear response \( \Delta y(V_g) \equiv y(k(L_1), V_g) - y(k(L_2), V_g) \) for two different lengths, \( L_1 = 310 \mu m \) and \( L_2 = 510 \mu m \), is shown in Fig. S4B. Similarly, Fig. S5A shows the response of an electromechanical resonator (6) at two different temperatures. Nathanson, Newell, Wickstrom, and Davis (6) assume that an increase in temperature decreases the Young’s modulus. The corresponding differential nonlinear response \( \Delta y(V_g) \equiv y(k(T_1), V_g) - y(k(T_2), V_g) \) for two different temperatures (or different Young’s modulus), \( T_1 = 30^\circ C \) and \( T_2 = 80^\circ C \), is shown in Fig. S5B. These experiments confirm that that any change in \( \Delta k \) is reflected in nonlinear new response in Δy, and Δy is maximum close to pull-in instability—a key assertion of the Flexure-FET concept.

Experimental Validation That Drain Current in Flexure-FET Depends Exponentially on the Gate Position (y) in Subthreshold Regime. Fig. S6 shows the response of a suspended-gate FET (7). The structure of suspended-gate FET is similar to the proposed Flexure-FET, and therefore the experimental data is directly relevant. The symbols in Fig. S6B show the measured drain current as a function of gate voltage (7). Our numerical simulations (solid line in Fig. S6B) based on Eqs. 1 and 2 in the main text reproduce the experimental data very well. The drain current has been obtained using the following expression

\[
I_{DS} = \frac{q n^2}{N_A} \mu m \frac{W}{L} V_{DS} \int_0^{\psi_s} e^{\frac{qV_g}{kT_0}} - 1 \, dv,
\]

where the underlap factor \( m \sim 5.5 \) accounts for the fact that the membrane does not overlap the source/drain completely (8). Fig. S6C shows the drain current as a function of the position of the gate (y) confirming that drain current depends exponentially on y in subthreshold region. Therefore, any change in gate position will result in exponential change in the drain current. Hence, all the three pieces of the Flexure-FET operation namely change in stiffness due to capture of biomolecules (Fig. S2), maximum change in gate position occurs close to pull-in due to change in stiffness (Figs. S4 and S5) and the exponential dependence of transistor drain current on the gate position in subthreshold (Fig. S6) are supported by experiments. In the following we conclude this discussion by showing the sensitivity of the devices discussed above when reconfigured in the Flexure-FET mode.

Response of Existing Devices When Reconfigured to Flexure-FET Mode. If the devices discussed above were reconfigured in the Flexure-FET mode, we anticipate the following response. If a transistor was integrated with the electromechanical resonators discussed in Figs. S4 and S5 and operated in the subthreshold regime, according to the theory discussed in the article, the overall response will be given by

\[
\frac{I_{DS1}}{I_{DS2}} = \exp \left( \frac{k_1 (A_1)(y_0 - y_1) - k_2 (A_2)(y_0 - y_2)}{k_B T \epsilon_2 N_A} \right),
\]

where \( I_{DS1}, k_1, y_1, A_1 \) are initial drain current, stiffness, position, and area of the beam, whereas \( I_{DS2}, k_2, y_2, A_2 \) are drain current, stiffness, position, and area due to stiffness change. In Eq. S2 all the parameters are known experimentally except the doping of the substrate \( N_A \). For a typical doping concentration (\( N_A = 5e14 - 5e16 \) cm\(^{-3}\)), the ratio of drain currents \( \frac{I_{DS1}}{I_{DS2}} \) changes by two to three orders of magnitude, confirming the exponential sensitivity of this class of devices (Fig. S7 A and B). Similarly, if the membrane stiffness of suspended-gate FET was changed by approximately 30–35% (keeping all other parameters to be the same and underlap factor \( m = 1 \) in Eq. S1), a similar two to three order magnitude change in drain current is expected (Fig. S7C).


Jain et al. www.pnas.org/cgi/doi/10.1073/pnas.1203749109

**Fig. S1.** Flow chart showing three main pieces of Flexure-FET operation for achieving exponential sensitivity. The flow chart also shows the references which are used to validate the various pieces.

**Fig. S2.** Experimental validation of the first part (Part 1 in Fig. S1); i.e., change in stiffness due to capture of biomolecules on different nanocantilever devices (2).
Fig. S3. Schematic of an electromechanical resonator.

Fig. S4. Demonstration of nonlinear sensitivity of $\Delta y$ on $\Delta k$ using the response of two electromechanical resonators with different lengths (5). (A) Equilibrium position of beam as a function of applied bias. Symbols are the experimental data (5), and the dotted line is the numerical simulations based on Eqs. 1 and 2 in the article. Different symbols correspond to $L = 510 \mu m$ (empty square) and $L = 310 \mu m$ (empty circle). (B) Difference in the equilibrium position $\Delta y$ as a function of gate voltage suggests that maximum change in $\Delta y$ occurs close to pull-in instability.

Fig. S5. Demonstration of nonlinear sensitivity of $\Delta y$ on $\Delta k$ using the response of an electromechanical resonator at two different temperatures (6). (A) Equilibrium position of the beam as a function of applied bias for two different temperatures $80 \degree C$ (empty square) and $30 \degree C$ (empty circle). Symbols are the experimental data, and the dotted line is the numerical simulations based on Eqs. 1 and 2 in the article. (B) Change in beam position $\Delta y$ is due to change in temperature (and hence stiffness).

Fig. S6. Response of a suspended-gate FET (7). (A) Micrograph of the suspended-gate FET. (B) Measured drain current as a function of gate voltage. Symbols are the experimental data, and the solid line is the numerical simulation. (C) Corresponding drain current as a function of the position of gate ($y$) showing that drain current depends exponentially on $y$.

Fig. S7. Response of existing devices reconfigured to operate in Flexure-FET mode. (A, B) If a transistor is integrated with the existing electromechanical resonators (5, 6), drain current $I_{DS1}/I_{DS2}$ changes by two to three orders of magnitude, as suggested in the article. (C) The response of suspended-gate FET (7) (with underlap factor $m = 1$) due to stiffness change ($\Delta k = 30-35\%$) also suggests similar improvement.