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Published on: 20 Jan 2021 - [bioRxiv](#) (Cold Spring Harbor Laboratory)

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1 An all-solid-state heterojunction oxide transistor for the rapid detection of 2 biomolecules and SARS-CoV-2 spike S1 protein

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21

22 Abstract

23 Solid-state transistor sensors that can detect biomolecules in real time are highly attractive for
24 emerging bioanalytical applications. However, combining cost-effective manufacturing with
25 high sensitivity, specificity and fast sensing response, remains challenging. Here we develop
26 low-temperature solution-processed In₂O₃/ZnO heterojunction transistors featuring a
27 geometrically engineered tri-channel architecture for rapid real-time detection of different
28 biomolecules. The sensor combines a high electron mobility channel, attributed to the quasi-
29 two-dimensional electron gas (q2DEG) at the buried In₂O₃/ZnO heterointerface, in close
30 proximity to a sensing surface featuring tethered analyte receptors. The unusual tri-channel
31 design enables strong coupling between the buried q2DEG and the minute electronic
32 perturbations occurring during receptor-analyte interactions allowing for robust, real-time
33 detection of biomolecules down to attomolar (aM) concentrations. By functionalizing the tri-
34 channel surface with SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2)
35 antibody receptors, we demonstrate real-time detection of the SARS-CoV-2 spike S1 protein
36 down to attomolar concentrations in under two minutes.
37

1 **Main text**

2 Miniaturised biochemical sensors fabricated via high-throughput manufacturing methods
3 promise cost-effective, large-volume production for use in various technology sectors¹. The
4 present needs for biochemical detection are diverse and include environmental monitoring²,
5 security systems³, and preventative medical care⁴. An ideal biochemical sensing platform
6 should be able to accommodate a wide range of applications in biological and chemical
7 detections with high-sensitivity⁵ and selectivity⁶. Among the various types of sensing platforms,
8 a solid-state transistor sensor is a highly-anticipated tool that could address these requirements
9 as it provides the functionality of a transducer for converting a biochemical interaction into an
10 amplified electrical signal⁷. This characteristic enables direct readout without the need of bulky
11 peripheral driving (opto)electronics, such as amplifiers, excitation light sources and photo-
12 detectors⁸.

13 For the successful use of solid-state transistors as biosensors, the channel should exhibit
14 a large surface area⁹ and tuneable surface chemistry¹⁰. The former allows tethering of a
15 sufficient quantity of molecular receptors whilst the latter helps to preserve charge transport in
16 the channel without unintentionally reacting with the environment. One widely reported
17 biosensor technology platform is based on silicon-nanowire (Si-NW) transistors, but their
18 manufacturing remains technologically demanding^{11,12,13}. Alternative technologies such as
19 solid-state thin-film transistors (TFT) made of metal oxide semiconductors offer scalable
20 manufacturing and intriguing physical properties¹⁴⁻¹⁷. However, due to parasitic gating effects
21 and associated performance deterioration¹⁸⁻²¹, the use of metal oxide transistors as biosensors
22 has remained limited with most effort dedicated on liquid-gated transistors (LGTs)^{6,22-24}. In
23 spite of being one of the most studied device, LGT biosensors face the detrimental Debye
24 screening effect^{6,25,26} – a direct result of the operating principles that rely on electrochemical
25 reactions²⁷, or on the movement of analytes²⁸, upon liquid-gating. Thus managing or
26 overcoming the Debye screening effect is critical for developing ultra-sensitive transistor-
27 based sensor technologies for emerging applications²⁹.

28 Here, we introduce a nanometres-thin In₂O₃/ZnO heterojunction channel and combine
29 it with a geometrically engineered tri-channel architecture several millimetres in size as a
30 universal platform for rapid, selective and ultra-sensitive biosensing. The all-solid-state device
31 features a central sensing channel and two side channels featuring a quasi-two-dimensional
32 electron gas (q2DEG) formed at the buried heterointerface a few nanometres below the
33 channel's surface. The flexible surface chemistry of metal oxides, on the other hand, allows
34 direct functionalisation of different receptors. The unusual channel architecture offers ultrahigh

1 surface-area-to-volume ratio ($10^6 \text{ cm}^2 \text{ cm}^{-3}$) and facilitates nm-proximity between the
2 electrostatic perturbations occurring during surface-tethered receptor and analyte interaction,
3 with the buried q2DEG channel. These unique features enable simultaneous signal transduction
4 and amplification in an all-solid-state TFT platform enabling real-time detection of specific
5 biomolecules down to attomolar (aM) concentrations under physiological relevant conditions.
6 As a proof-of-concept we demonstrate selective sensing of the SARS-CoV-2 (Severe Acute
7 Respiratory Syndrome Coronavirus 2) spike S1 protein in real-time with a limit of detection
8 (LoD) of 865 aM.

9

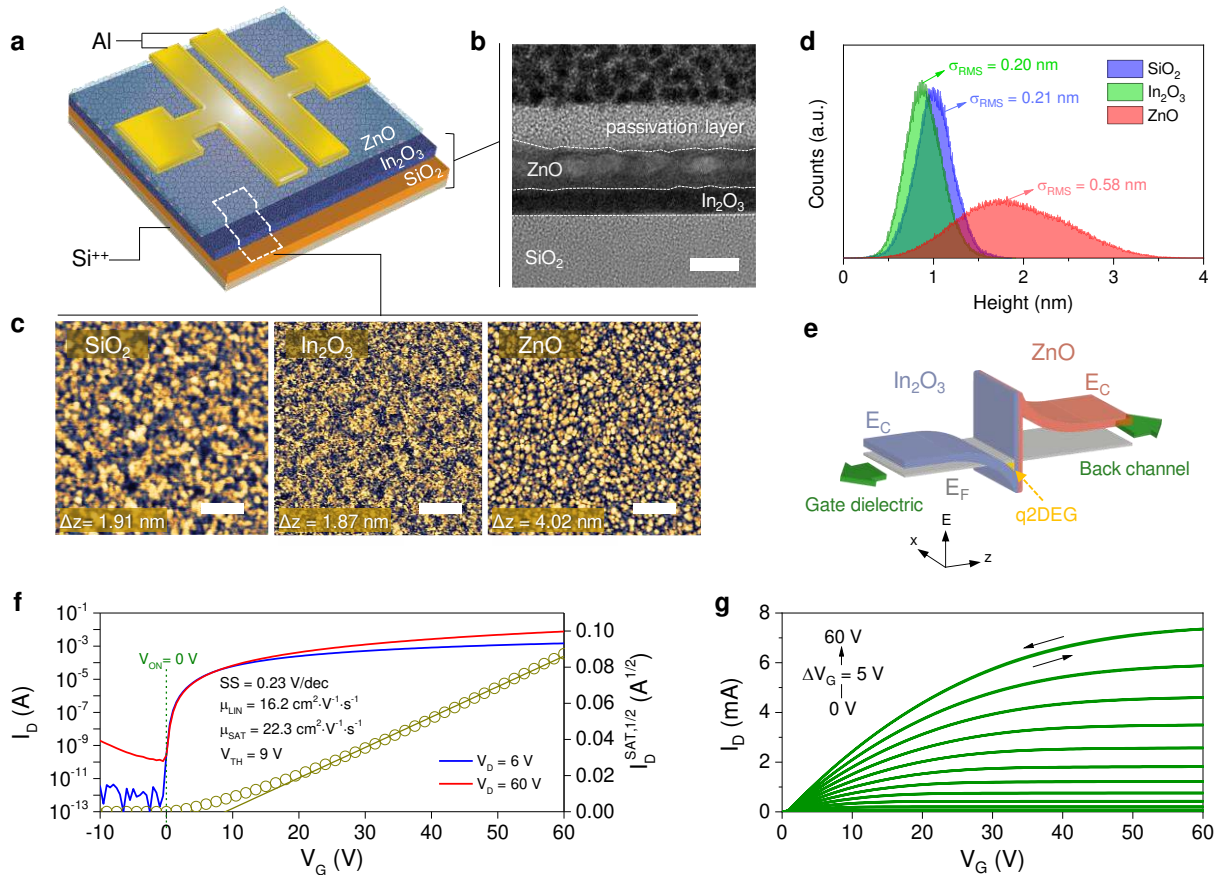
10 **Quasi-two-dimensional oxide heterojunction channel**

11 We hypothesised that our recently developed solution-processed, high electron mobility
12 $\text{In}_2\text{O}_3/\text{ZnO}$ heterojunction (HJ) transistors³⁰ offers unique features that could prove attractive
13 for biosensing. Firstly, the buried electron channel located at the oxide HJ is physically
14 separated from the receptor units tethered on its surface a few nm above^{31,32}. This feature is
15 expected to prevent degradation of electron transport upon sensing (due to Coulomb scattering)
16 and preserve the transistor's performance. This is not the case for most biosensor transistors
17 reported to date where the channel interacts directly with the receptor units and hence the
18 analyte. To overcome this, liquid gating has been exploited for analyte detection in the liquid
19 phase^{6,22,33}. Secondly, the high electron mobility of the HJ TFTs offers the possibility for large
20 electrical signals that are easy to detect and amplify even in large-size devices³¹.

21 We fabricated metal oxide HJ transistors using the staggered bottom-gate, top-contact
22 (BG-TC) architecture shown in **Fig. 1a**. High-resolution transmission electron microscopy
23 (HRTEM) analysis (**Fig. 1b**) of the channel reveals the formation of a well-defined HJ channel
24 with thickness in the range of 8-10 nm. Atomic force microscopy (AFM) measurements show
25 the existence of smooth layers as being deposited sequentially (**Fig. 1c-d**). In_2O_3 exhibits the
26 lowest peak-to-peak height (ΔZ) of 1.87 nm with a root-mean-square roughness (σ_{RMS}) value
27 of 0.20 nm, which are comparable to that of SiO_2 ($\Delta Z = 1.91 \text{ nm}$, $\sigma_{\text{RMS}} = 0.21 \text{ nm}$). Subsequent
28 deposition of ZnO atop In_2O_3 leads to a slightly rougher topography ($\Delta Z = 4.00 \text{ nm}$, $\sigma_{\text{RMS}} =$
29 0.58 nm) indicative of a more textured surface^{31,34}.

30 The $\text{In}_2\text{O}_3/\text{ZnO}$ forms a type-II heterojunction where electrons migrate from the
31 conduction band (CB) of ZnO to that of In_2O_3 , leading to the formation of a q2DEG (**Fig. 1e**)³².
32 The latter resembles 2DEG systems found in high electron mobility transistors (HEMTs) based
33 on epitaxial inorganic heterointerfaces³⁵. Although uncommon, the existence of q2DEG in

1 disordered/non-epitaxial heterointerfaces has been predicted, further corroborating our
 2 findings and conclusions³⁶. **Fig. 1f** and **1g** show representative sets of transfer and output
 3 current-voltage (I-V) characteristics for a In₂O₃/ZnO HJ transistor with electron mobility and
 4 current on-off ratio of >22 cm² V⁻¹ s⁻¹ and >10⁸, respectively. The presence of the q2DEG
 5 system at the In₂O₃/ZnO interface is responsible for the electron current across the channel and
 6 the high electron mobility measured³².



7

8

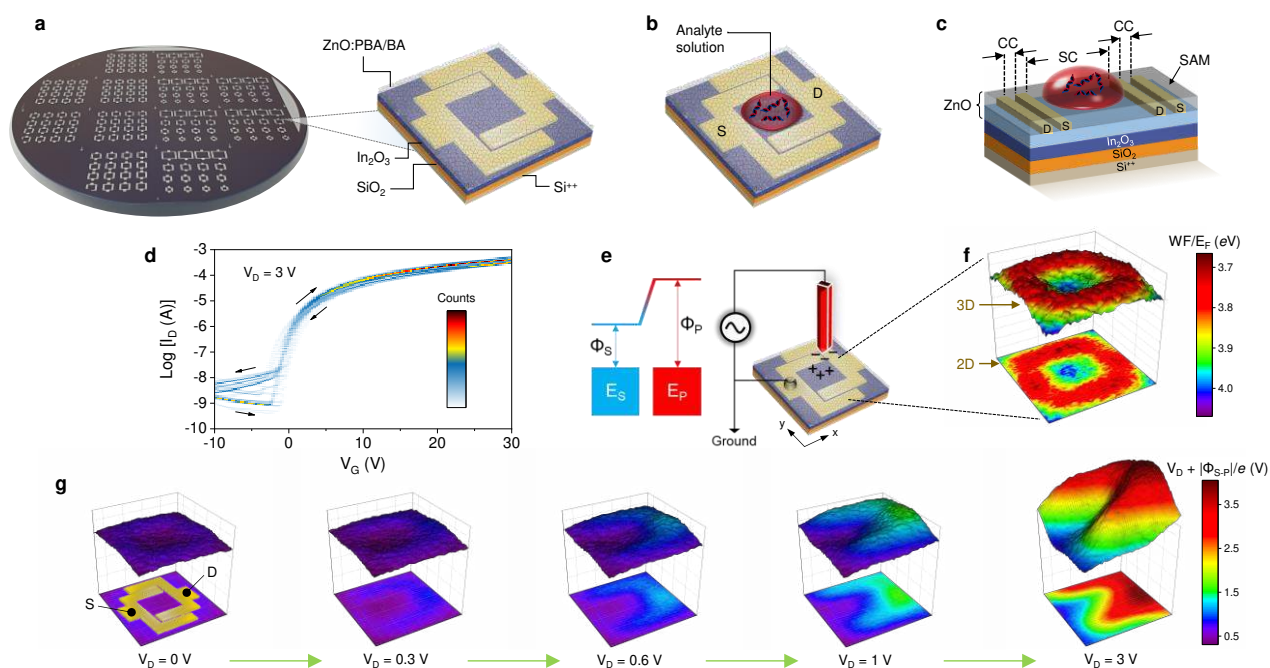
9 **Figure 1 | Fabrication and testing of metal oxide heterojunction transistors.** **a**, Schematic
 10 of an In₂O₃/ZnO heterojunction transistor. **b**, HRTEM cross-sectional image of the channel
 11 region (scale bar = 5 nm). **c**, Intermittent AFM topography images of SiO₂, In₂O₃ and ZnO
 12 surfaces (scale bar = 200 nm). **(d)** Height histogram extracted from the AFM data for each
 13 sequentially deposited layer. Corresponding peak-to-peak height difference (ΔZ) and root
 14 mean square surface roughness (σ_{RMS}) were derived from AFM image analysis. **e**, Schematic
 15 of energetic diagram for the In₂O₃/ZnO heterointerface. The discontinuity in the conduction
 16 band between ZnO and In₂O₃ results to the electron migration from ZnO to In₂O₃, resulting in
 17 the formation of a q2DEG. **f,g**, Representative current-voltage (I-V) characteristics for a
 18 In₂O₃/ZnO transistor: **(f)** transfer and **(g)** output characteristics. Important device parameters
 19 are shown in **(f)**. These include turn on voltage (V_{ON}), threshold voltage (V_{TH}), subthreshold
 20 swing (SS), linear mobility (μ_{LIN}), and saturation mobility (μ_{SAT}).

21

22

1 All solid-state tri-channel transistor sensor

2 To investigate the suitability of the $\text{In}_2\text{O}_3/\text{ZnO}$ transistors for biosensing, we fabricated devices
 3 based on a tri-channel configuration on 4-inch Si wafers (**Fig. 2a**). The source-drain (S-D)
 4 electrodes are deposited atop the $\text{In}_2\text{O}_3/\text{ZnO}$ channel followed by the deposition of another
 5 ultrathin (2-4 nm) protective ZnO layer. Next the known deoxyribonucleic acid (DNA)
 6 intercalator^{37,38} 1-pyrenebutyric acid (PBA) was functionalised directly to ZnO ³⁹ acting as the
 7 DNA receptor. A second functionalisation step using butyric acid (BA) was also applied to
 8 ensure complete passivation of the ZnO surface (see **Supplementary Note 1** and
 9 **Supplementary Figure 1**). The presence of the PBA molecules was verified using ultraviolet–
 10 visible (UV-Vis) absorption measurements before and after functionalisation as evidenced by
 11 the appearance of distinct absorption peaks associated with the pyrene unit (**Supplementary**
 12 **Figure 2**). The completed device consists of two identical ‘conventional’ channels (hereafter
 13 termed CC) 100 μm in length (L), formed on the sides, and a third long (L = 2000 μm) ‘sensing’
 14 channel (hereafter termed SC) formed in the central region of the device between the S-D
 15 electrodes (see **Supplementary Figure 3**). This unique channel layout offers a large sensing
 16 area channel where the analyte-containing solution can be easily applied while avoiding direct
 17 contact with the S-D electrodes (**Fig. 2b-c**) which is known to induce parasitic gating effects⁴⁰.
 18



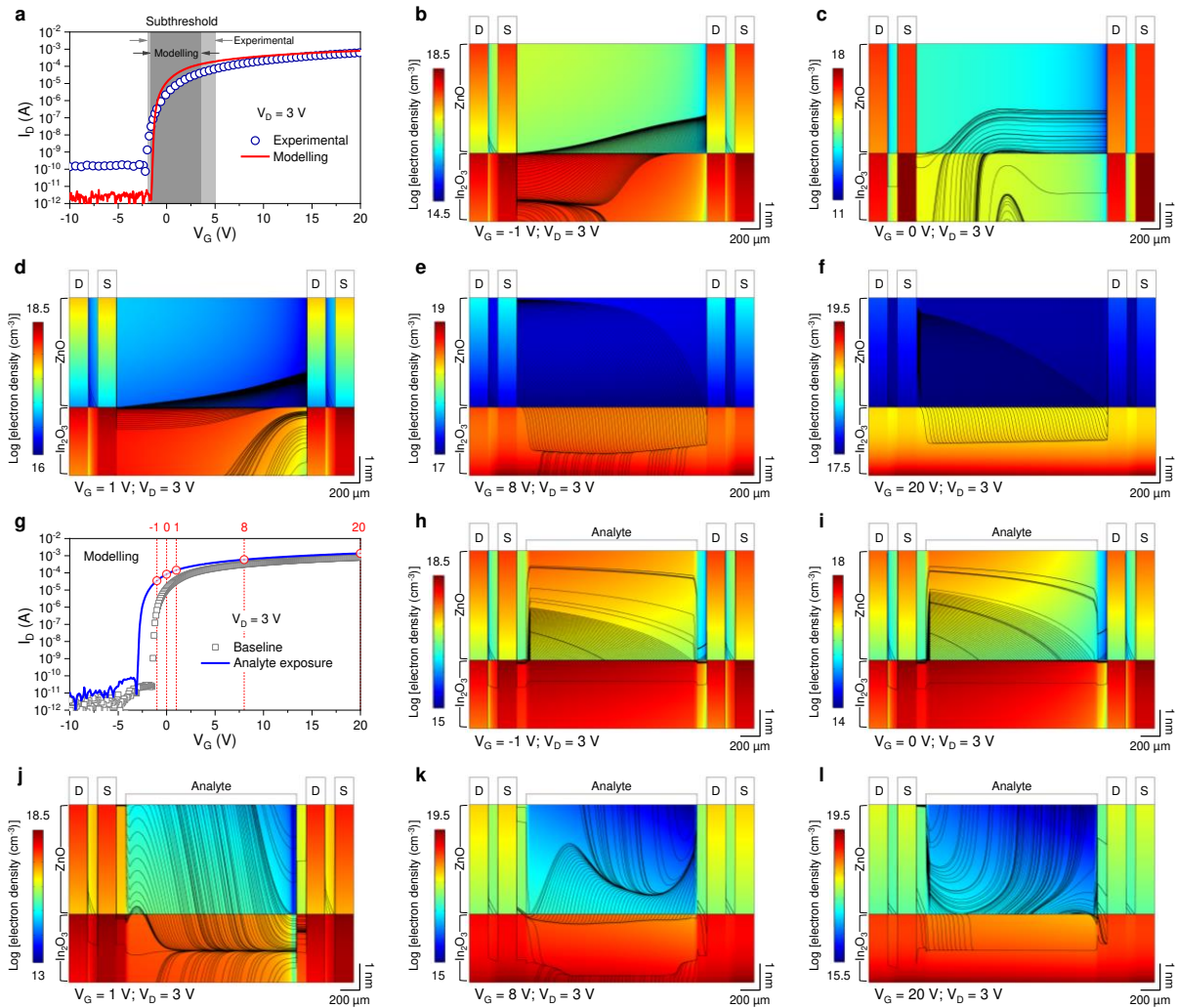
19

20 **Figure 2 | Design and structures of tri-channel transistor sensors.** **a**, Tri-channel $\text{In}_2\text{O}_3/\text{ZnO}$
 21 heterojunction transistors fabricated on a 4-inch $\text{Si}^{++}/\text{SiO}_2$ wafer and schematic of the channel
 22 architecture. The source-drain (S-D) electrodes are covered by the top ZnO layer. The receptor
 23 molecule pyrenebutyric acid (PBA) and passivation molecule butyric acid (BA) are chemically

1 tethered onto the ZnO surface. **b**, Illustration of the direct application of analyte solution on
2 the millimetre-scale sensing channel (SC) area of the sensor. **c**, Schematic of the tri-channel
3 transistor depicting the location of the analyte solution within the SC and two conventional
4 channels (CCs) on the sides. **d**, Density plots of forward-backward dual sweeps of current-
5 voltage characteristics measured from 30 individual tri-channel transistor sensors. **e**, Schematic
6 of the scanning Kelvin probe (SKP) setup used. The SKP method relies on the application of a
7 voltage to offset the surface potential between the sample (Φ_S) and the tip (Φ_P). The magnitude
8 of this voltage is then used to calculate the energy difference between the sample (E_S) and the
9 tip (E_P). **f**, 2D (top)/3D (bottom) maps of the electrostatic potential across a tri-channel
10 transistor measured by SKP. The WF for the embedded Al-electrode areas is measured to be \approx
11 3.8 eV while the E_F for the SC is \approx 4.0 eV. **g**, Electrostatic potential maps measured at different
12 source-drain potentials: $V_D = 0, 0.3, 0.6, 1, 3$ V. The relative positions of the S-D electrodes
13 are shown in the 2D map for $V_D = 0$ V.
14
15

16 In **Supplementary Figures 4** and **5**, we plot the transistor transfer and output
17 characteristics, respectively, measured before and after PBA and BA functionalisation. Unlike
18 conventional transistor biosensors^{22,41}, our tri-channel device shows negligible changes in its
19 operating characteristics after receptor functionalisation. The narrow parameter distribution is
20 better illustrated in **Fig. 2d** which shows the density plots⁴² of the dual-sweep transfer
21 characteristics for 30 individual tri-channel transistors fabricated on a single wafer. Critically,
22 the tri-channel transistors exhibit robust operation even when subjected to 90 repeated dual I-
23 V sweeps with negligible leakage current (I_G) which is critical for optimal device operation and
24 signal amplification (**Supplementary Figure 6**)⁴³. These data demonstrate the high operational
25 stability and reproducibility of the proposed tri-channel HJ transistor architecture.

26 To better understand the electrostatic potential landscape across our unconventional tri-
27 channel device, we performed scanning Kelvin probe (SKP) measurements (**Fig. 2e**). **Fig. 2f**
28 shows the two-dimensional (2D, bottom) and three-dimensional (3D, top) work function (WF)
29 or Fermi energy (E_F) maps for a tri-channel device measured. The influence of the buried Al
30 electrodes beneath the ZnO results in local WF changes (3.8-4 eV), with the higher potential
31 observed in the middle of the SC region. SKP measurements were also performed while
32 applying a drain bias (V_D) in the range of 0-3 V (**Fig. 2g**; the respective location of the device
33 illustrated for $V_D = 0$ V image). The application of low voltages (e.g. $V_D = 0.6-1$ V) causes a
34 substantial change within the SC, while increasing the applied bias to 3 V affects the potential
35 landscape across the entire SC region, suggesting strong coupling between the SC and the two
36 side CCs. Thus, the tri-channel architecture appears to enable spatially decoupling of the signal
37 transduction occurring within the SC region from the current-driving CCs.



1

2 **Figure 3 | Physical principles of tri-channel transistor sensors.** a, Transfer current-voltage
3 characteristics of tri-channel transistor sensors obtained from experiment and modelling using
4 COMSOL Multiphysics®. The applied drain voltage (V_D) was +3 V, and the subthreshold
5 regions are indicated in grey. b,c,d,e,f, Corresponding COMSOL simulations showing the
6 electron density distributions along the cross-section of the $\text{In}_2\text{O}_3/\text{ZnO}$ heterostructure under
7 the source (S) and drain (D) electrodes and the electron flow streamlines within the channel
8 regions, with different gate voltages (V_G) applied: (b) -1 V; (c) 0 V; (d) 1 V; (e) 8 V; (f) 20 V,
9 and a constant $V_D = 3$ V. g, Modelled transfer current-voltage characteristics ($V_D = 3$ V)
10 for baseline and under the exposure of simulated surface-charged analytes. h,i,j,k,l, Corresponding
11 COMSOL electron density distributions under the influence of simulated analytes when
12 applying $V_D = 3$ V and $V_G =$ (h) -1 V; (i) 0 V; (j) 1 V; (k) 8 V; (l) 20 V to the sensors. The
13 electrodes and analytes are shown to indicate their positions with respect to the devices.

14

15 To understand how the tri-channel geometric impacts the electrical characteristics of
16 the sensor, we modelled the device operation using the COMSOL Multiphysics® simulation
17 software. **Fig. 3a** shows the simulated and measured transfer characteristics for a representative
18 transistor. The various material and device parameters used in the modelling were adopted from

1 our previous studies on the same materials^{31,44,45}. The small difference seen in the subthreshold
2 region between the modelled and experimental data is attributed to the presence of trap states
3 in the channel^{46,47}, while the higher off current measured experimentally is due to the use of a
4 common Si⁺⁺ gate substrate and the un-patterned layout of the In₂O₃/ZnO channel. Apart from
5 these minor discrepancies, the model provides a good description of the tri-channel transistor
6 operation and validates its applicability.

7 The main function of a transistor biosensor is to induce a perturbation in the channel
8 current upon exposure to an external stimulus (analyte). To best illustrate this process in our
9 sensor, we used the post-processing streamline tool for visualising the electron concentration
10 and the streamlines of the channel current flow. **Fig. 3b-f** show the static distributions of the
11 electron density and the streamlines of the current flow within the In₂O₃/ZnO heterostructure
12 biased at V_D = 3 V and V_G = -1, 0, 1, 8 and 20 V. The results are in good agreement with our
13 experimental observations and reveal the staggering enhancement in the current density within
14 the In₂O₃ of the heterointerface^{31,46}. Next, we modelled the electrical characteristics of the
15 device in the presence of an analyte. We hypothesize that the analyte species interacts with the
16 surface-tethered receptor units and induce free charges at the surface of the SC region. To
17 establish the sensing condition close to the limit of detection for our sensor, we assumed the
18 number of additional charges induced by the analyte to be equivalent or lower than the number
19 of mobile charges in the channel. Based on the literature⁴⁸ and our own measurements on
20 similar metal oxide heterointerface channels³¹, device operation should remain largely
21 unaltered when the additional electron concentration remains below 10¹⁷ cm⁻³.³⁴ To ensure that
22 this condition is satisfied, we used a more conservative estimation for the analyte-induced
23 electron concentration of 10¹⁶ cm⁻³ and a channel thickness of 10 nm (**Fig. 1b**). The equivalent
24 surface charge density due to analyte was then derived from the modelling yielding a value of
25 $\approx 10^{10}$ cm⁻², which will be considered for the different device operating scenarios next.

26 **Fig. 3g** shows the modelled transfer characteristics for a tri-channel (inset, **Fig. 3g**)
27 In₂O₃/ZnO sensor while **Supplementary Figure 7** displays similar calculations for a single
28 layer In₂O₃ and a heterojunction In₂O₃/ZnO transistors based on the conventional channel
29 geometry (insets in **Supplementary Figure 7a,c**) before (baseline) and after exposure to
30 analyte (analyte exposure). The tri-channel In₂O₃/ZnO transistor shows a large response to the
31 analyte (surface charge $\approx 10^{10}$ cm⁻²) with the transfer curve shifted towards more negative V_G
32 bias. This is not the case for In₂O₃ and In₂O₃/ZnO transistors with conventional channel
33 geometry (**Supplementary Figure 7b,d**), where the analyte induces only a small perturbation
34 in the current around the subthreshold region consistent with filling of sub-gap states⁴⁹. The

1 modelled electron density and current flow for the tri-channel transistor biased at $V_D = 3$ V and
2 $V_G = -1, 0, 1, 8$ and 20 V, are presented in **Fig. 3h-l**, whilst the corresponding modelling results
3 for the conventional channel In_2O_3 (at $V_D = 3$ V, $V_G = 1$ V) and $\text{In}_2\text{O}_3/\text{ZnO}$ (at $V_D = 3$ V, $V_G =$
4 -1 and 1 V) transistors are shown in **Supplementary Figure 8a-b** and **8c-f**, respectively.
5 Strikingly, we find that unlike the geometrically engineered heterojunction $\text{In}_2\text{O}_3/\text{ZnO}$
6 transistors (**Fig. 3h-l**), electron flow in the In_2O_3 device is pinned at the interface with the gate
7 dielectric while being fully decoupled from the surface/analyte (**Supplementary Figure 8b**).
8 From these data we conclude that the tri-channel design is highly sensitive to the presence of
9 surface charges as compared to conventional channel design, while single layer In_2O_3 channel
10 transistors are not ideal for all-solid-state biosensing applications.

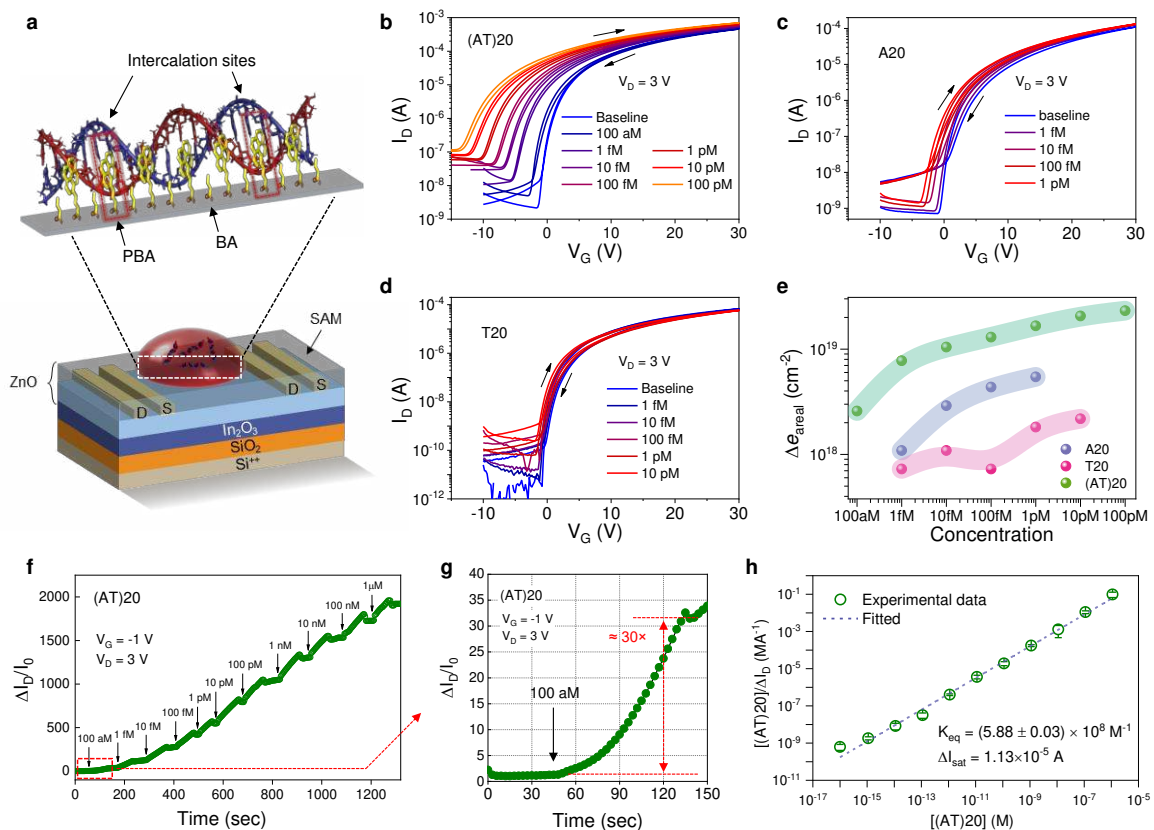
11 Next, we considered the scenario where the heterojunction transistor is operated in
12 depletion ($V_G = -1$ V) and in the presence of analyte (i.e. additional $\approx 10^{10}$ cm^{-2} on the SC
13 surface). Clear perturbations in the current flow are observed for both the tri-channel
14 $\text{In}_2\text{O}_3/\text{ZnO}$ (**Fig. 3h-l**) and the conventional channel designs of $\text{In}_2\text{O}_3/\text{ZnO}$ (**Supplementary**
15 **Figures 8d** and **8f**) transistors. The broader distribution of streamlines seen in the tri-channel
16 is consistent with the large negative shift in the turn-on voltage (V_{ON}) of the device seen in **Fig.**
17 **3g**. Regardless of the biasing scenarios (depletion or accumulation), the tri-channel architecture
18 shows much stronger coupling to the analyte. Specifically, we find the electron flow
19 streamlines to extend ≈ 1 nm beneath the SC surface (**Fig. 3h-l**) due to the asymmetric design
20 of the source-drain electrodes⁵⁰, which prevent the local electric field to fully pinch-off the
21 channel for V_G between -1 to 1 V. As the V_G increases ($+20$ V), the benefits associated with
22 the presence of a q2DEG in the $\text{In}_2\text{O}_3/\text{ZnO}$ become even more apparent as the area beneath the
23 sensing surface remains free from electrostatic screening induced by the gate (**Fig. 3l**).
24 Nevertheless, it is known to be more advantageous for solid-state transistor sensors to be
25 operated within the subthreshold region as it yields optimal sensitivity due to high signal gain⁵¹.

26

27 **Receptor engineering for ultra-sensitive and real-time biosensing**

28 To demonstrate that the working principle of our all-solid-state tri-channel transistor is
29 fundamentally different from that of conventional liquid-gated sensors, we studied the ability
30 of our transistors to detect different types of DNAs (analytes) dispersed in deionised (DI) water
31 rather than in a high ionic strength solution. We note that the latter is essential for the function
32 of liquid-gated transistor sensors in order to drive the analyte towards the semiconducting
33 channel, which in turn modulates its transconductance via electrochemical processes⁶. To prove
34 that our sensors do not rely on such processes, the DI-water based solutions containing double-

1 stranded DNA (dsDNA) and single-stranded DNA (ssDNA) of different sequences, were
 2 applied directly onto the SC area while recording the device's response. **Fig. 4a** depicts the
 3 envisioned interaction between dsDNA and PBA where the pyrene units on PBA intercalate
 4 into the dsDNA⁵². **Fig. 4b-d** show the measured transfer characteristics ($V_D = 3$ V) for different
 5 concentrations of 20 base-pair segments of synthetic DNAs based on single-stranded adenine
 6 (A) [abbreviated as A20], and thymine (T) [abbreviated as T20], as well as their
 7 complementary dsDNA (AT)20. For (AT)20, a much larger change in the transistor's transfer
 8 characteristics is observed with the lowest dsDNA concentrations studied down to 100 aM (**Fig.**
 9 **4b**). The strong response is attributed exclusively to the intercalation of the pyrene units into
 10 the minor grooves of the double-stranded (AT)20 since the presence of DI water has no
 11 measurable effect (**Supplementary Figure 9**). The progressive shift of V_{ON} towards more
 12 negative V_G seen in **Fig. 4b** is consistent with the modelling results of **Fig. 3g** where we
 13 considered the presence of additional free charges on the surface of the SC. This observation
 14 indicates that pyrene-NDA association generates free electrons that are eventually injected into
 15 the channel. Further evidence supporting our hypothesis comes from sensing experiments
 16 involving the single-stranded A20 (**Fig. 4c**) and T20 (**Fig. 4d**) where only minute changes are
 17 observed in the transistors' characteristics due to the absence of pyrene-NDA intercalation.



18

1 **Figure 4 | Tri-channel transistor sensor for synthetic DNA sensing.** **a**, Illustration of the
2 envisioned intercalation between the pyrene units and dsDNA. **b,c,d**, Transfer I-V
3 characteristics ($V_D = 3$ V) measured from PBA/BA functionalised tri-channel transistor sensors
4 with the presence of three different DNA analytes of **(b)** (AT)20; **(c)** A20; **(d)** T20 at different
5 analyte concentrations. **e**, Plot of the increase in areal charge carriers Δe_{areal} that results from
6 the sensing activity of the tri-channel transistor sensor to the analytes as a function of analyte
7 concentration. Δe_{areal} is calculated from the shift in the turn-on voltage of the device upon the
8 application of analyte solution. AT(20) shows the highest response due to its interaction via
9 intercalation with pyrene units of the PBA-functionalised tri-channel transistor sensor. **f**, Real-
10 time response signal measured from a PBA/BA functionalised solid-state tri-channel transistor
11 sensor operated at $V_G = -1$ V and $V_D = 3$ V upon exposure to synthetic (AT)20 with
12 concentrations from 100 aM to 1 μ M. **g**, recorded response to 100 aM showing ≈ 30 times
13 enhancement in I_D . The arrows indicate the time when the different analyte concentrations were
14 applied to the SC area of the tri-channel transistor. **h**, Fitting of experimental results of synthetic
15 AT(20) sensing at different analyte concentrations according to the Langmuir adsorption
16 isotherm. The error bars denote standard deviations from three real-time measurement sets.
17

18 In an effort to quantify the sensor's response, we analysed the change in V_{ON} as a
19 function of increasing analyte concentration. This shift reflects the increase in the electron
20 concentration (Δe_{areal}) within the channel and is given as⁵³

$$21 \quad \Delta e_{\text{areal}} = \frac{C_{\text{areal}}[V_{\text{ON}}(\text{conc.}) - V_{\text{ON}}(\text{init.})]}{q} \quad (1)$$

22 Here, C_{areal} is the areal capacitance of the gate dielectric (34.4 nF cm^{-2}), q is the elementary
23 charge, $V_{\text{ON}}(\text{init.})$ is the initial V_{ON} measured in the presence of blank solution (no analyte),
24 and $V_{\text{ON}}(\text{conc.})$ is the transistor's V_{ON} measured upon application of the analyte at each
25 concentration. For simplicity, we assume all electrons are confined in a two-dimensional plane
26 at the vicinity of the oxide HJ³². **Fig. 4e** shows the evolution of Δe_{areal} as a function of analyte
27 concentration measured using a tri-channel sensor. (AT)20 induces the highest Δe_{areal} , a direct
28 consequence of the large V_{ON} shift observed in **Fig. 4b**. These results demonstrate
29 unambiguously that pyrene-(AT)20 intercalation produces signals several orders of magnitude
30 larger than the non-intercalating ssDNAs A20 and T20 and showcase the ability of the tri-
31 channel sensor to differentiate between double and single stranded DNAs without the need for
32 complex fluorescence labelling⁵⁴. To this end, the DNA conformation with respect to the
33 substrate (i.e. lying-down or standing up), should not be critical as sensing relies exclusively
34 on the charge transfer upon pyrene-DNA association. This hypothesis is corroborated by the
35 sensor's ability to selectively detect different analytes, such as avidin and SARS-CoV-2 spike
36 S1 protein, which will be discussed latter. The ability of our sensor to facilitate such a strong

1 coupling between the minute receptor-analyte interactions and charge transport, without
2 compromising the channel transconductance (g_m) (**Supplementary Note 2** and
3 **Supplementary Figure 10**), is attributed to three unique device attributes:

- 4 (i) The geometrical engineered tri-channel design that enables strong coupling
5 between current transport and receptor-analyte interactions within the sensing area
6 of the channel.
- 7 (ii) The use of a high electron mobility $\text{In}_2\text{O}_3/\text{ZnO}$ channel featuring a spatially-
8 separated (buried) q2DEG system.
- 9 (iii) The versatile surface chemistry and the electronic properties of the metal oxide
10 employed.

11 Due to the diverse range of biosensor transistor technologies^{5,6} there is currently no
12 clear consensus on the important figures of merit that can be used to define the performance of
13 such devices. Here we attempt to draw an analogy from the field of phototransistors, since both
14 types of sensors act as transducers with a highly V_G -dependent response and define two
15 practical figures of merit namely the responsivity (R_{analyte}) and sensitivity (S_{analyte})
16 (**Supplementary Note 3** and **Supplementary Figure 11**). We first investigated the suitability
17 of our tri-channel biosensor TFTs for real-time sensing of (AT)20 at an extremely broad range
18 of analyte concentrations (10^{-18} to 10^{-6} M), while simultaneously assessing the sensors' ability
19 to operate in aqueous conditions^{9,55}. Specifically, we monitored the evolution of ΔI_D at $V_G = -$
20 1 V and $V_D = 3$ V, as a function of time for different (AT)20 concentrations. The biasing
21 condition were chosen to maximise the sensor's response by operating it in the subthreshold
22 region⁵¹ (**Supplementary Figure 12**). **Fig. 4f** shows a representative real-time recording of
23 $\Delta I_D/I_0$ (where $I_0 = 3.16 \times 10^{-8}$ A) for analyte concentrations in the range 10^{-18} to 10^{-6} M, where
24 a clear response across the entire range is observed. Even at 100 aM of (AT)20, the tri-channel
25 TFT shows a significant increase in the ΔI_D by ≈ 30 times (**Fig. 4g**) in under 2 min. This
26 represents the highest response signal reported to date for biosensing transistors, including
27 liquid-gated devices^{5,6,24}. Importantly, the sensor's sensitivity can be tuned by the V_G as shown
28 in **Supplementary Figure 13** where the S_{analyte} is plotted vs. (AT)20 concentration for different
29 V_G (-1, 0, +1 V). Even at sub-optimal biasing conditions (i.e. $V_G = 1$ V), the measured I_D for
30 100 aM (AT)20 increases to 4.2 μA ($\Delta I_D \approx 2.8$ μA) which is $\approx 300\%$ higher than the baseline
31 signal ($I_0 \approx 1.4$ μA) (**Fig. 4b**). The large ΔI_D indicates that the actual sensitivity of the tri-
32 channel sensors is well below 100 aM. To this end, we note that in the literature the most
33 frequently reported parameter is the LoD, which is determined by the minimum detectable
34 signals that are often far from suitable for real-time monitoring^{5,6,41,56}.

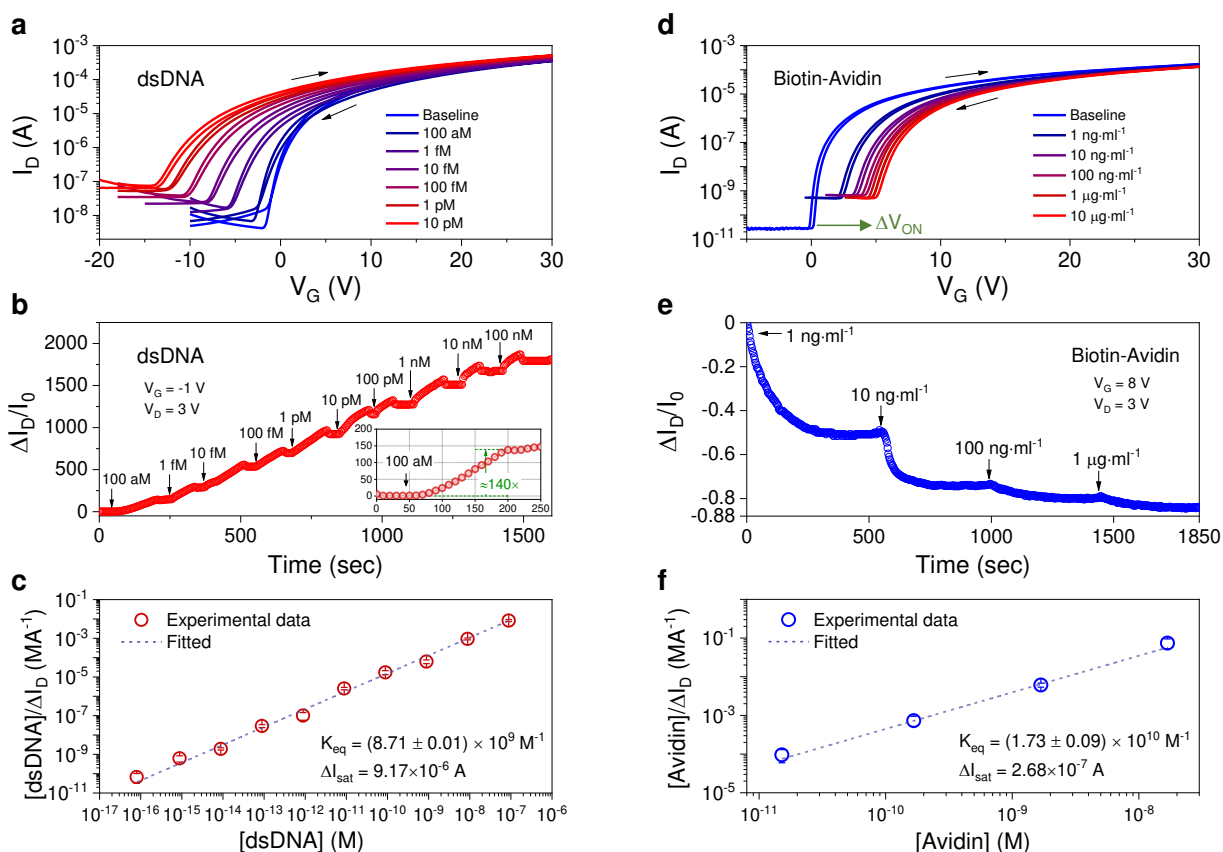
1 To further demonstrate the capabilities of our high S_{analyte} sensor, we analysed the
2 sensing kinetics using the linear form of the Langmuir adsorption isotherm^{57,58}.
3 **Supplementary Figure 14a** displays a series of such measurements taken from **Fig. 4f** but
4 replotted by setting the time (t) at which the different concentrations of analyte were applied,
5 to 0 sec. **Supplementary Figure 14b** shows a representative trace for 1 pM of (AT)20 where
6 three different sensing stages can be clearly distinguished:

- 7 (i) Concentration-limited diffusion stage where the receptor-analyte reaction rate
8 is determined by the diffusive transport of the analyte on the sensor's surface as
9 its concentration increases.
- 10 (ii) Association of analyte with the tethered receptor moieties i.e. 'primary' sensing
11 process.
- 12 (iii) Dissociation of analyte-receptor complexes before reaching a thermodynamic
13 equilibrium.

14 The rate of the 'primary' sensing process depicted in **Supplementary Figure 14b** is
15 representative of a zero-order reaction and is independent of the analyte concentration or the
16 method with which the analyte solution is being applied. For each concentration, a distinct peak
17 between association and dissociation stages is observed and attributed to the immobilisation of
18 analyte species by the tethered receptors⁵⁹⁻⁶¹. Therefore, and regardless of the sensing method,
19 the existence of two-phase kinetics relates solely to the association and dissociation stages.
20 Using the high fidelity sensing data from **Supplementary Figure 14**, the equilibrium constant
21 (K_{eq}) was calculated yielding values of $(5.88 \pm 0.03) \times 10^8 \text{ M}^{-1}$ (**Fig. 4h**).

22 In addition to short synthetic DNA, we have also tested natural dsDNA extracted from
23 calf thymus tissue, which has much longer DNA sequences. **Fig. 5a-b**, respectively, show the
24 transfer characteristics ($V_D = 3 \text{ V}$) and real-time response recorded at fixed $V_D = 3 \text{ V}$ and V_G
25 $= -1 \text{ V}$ (**Supplementary Figure 15**, $I_0 = 2.63 \times 10^{-8} \text{ A}$). The response is similar to that recorded
26 for (AT)20 indicating that the sensing mechanism remains identical for the natural dsDNA.
27 Even when aM concentration of the dsDNA is applied, the recorded signal ($\Delta I_D/I_0$) increases
28 by more than 100× (inset of **Fig. 5b**), further corroborating the unprecedented sensitivity of
29 the tri-channel sensor. When compared to (AT)20, the sensor exhibits stronger response to
30 natural dsDNA with a higher binding constant K_{eq} of $(8.71 \pm 0.01) \times 10^9 \text{ M}^{-1}$ (**Fig. 5c**). This
31 difference is attributed to the stronger interaction between the longer sequence of calf thymus
32 DNA and the surface-tethered pyrene receptor.

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Figure 5 | Attomolar detection of natural biomolecules. **a**, Transfer characteristics ($V_D = 3 V$) of a PBA/BA functionalised tri-channel transistor sensor measured in the presence of natural dsDNA extracted from calf thymus. **b**, Real-time response of the tri-channel transistor sensor to different concentrations (100 aM to 100 nM) of natural dsDNA. Inset: The sensor's response to a 100 aM of the analyte is ≈ 140 times higher than the baseline signal. For this experiment the device was operated at $V_G = -1 V$ and $V_D = 3 V$. **c**, Fitting of the experimental results for natural dsDNA at different analyte concentrations according to the Langmuir adsorption isotherm. The error bars denote standard deviations from three real-time measurement sets. **d**, Transfer characteristics ($V_D = 3 V$) measured from a biotin-functionalised tri-channel transistor sensor subject to different concentrations of avidin. **e**, Real-time response obtained from the biotin-based tri-channel transistor sensor biased at $V_G = 8 V$ and $V_D = 3 V$. The avidin concentration was varied from 10 ng ml⁻¹ to 1 μ g ml⁻¹. The arrows indicate the time when the avidin was applied to the SC area of the sensor. **f**, Fitting of experimental results of avidin sensing at different analyte concentrations according to the Langmuir adsorption isotherm. The error bars denote standard deviations from three real-time measurement sets.

We also investigated the possibility of sensing the formation of the positively charged biotin-avidin pair – an important complex for biochemical analysis⁶². For this purpose, we first functionalised the ZnO surface with biotin, acting as the receptor, and then applied avidin (the analyte) dispersed in DI solution at different concentrations. **Fig. 5d** reveals a systematic shift in V_{ON} of the transistors towards more positive V_G with increasing avidin concentration. This indicates a continuously reducing electron concentration in the channel due to the positively

1 charged nature of avidin and its electron accepting character. **Fig. 5e** shows real-time sensing
2 of different concentrations of avidin. Here a higher voltage bias of $V_D = 3$ V, $V_G = 8$ V
3 (**Supplementary Figure 16**, $I_0 = 1.89 \times 10^{-5}$ A) was used in order to compensate for the large
4 positive shift in V_{ON} upon biotin-avidin association. Analysis of the binding constant between
5 avidin and surface-immobilised biotin (**Fig. 5f**) yields a K_{eq} of $1.73 (\pm 0.09) \times 10^{10} \text{ M}^{-1}$. This
6 value is lower than that reported for free avidin-biotin pairs (10^{13} – 10^{15} M^{-1})^{63,64} – a result most
7 likely attributed to the smaller number of tethered biotin receptors.

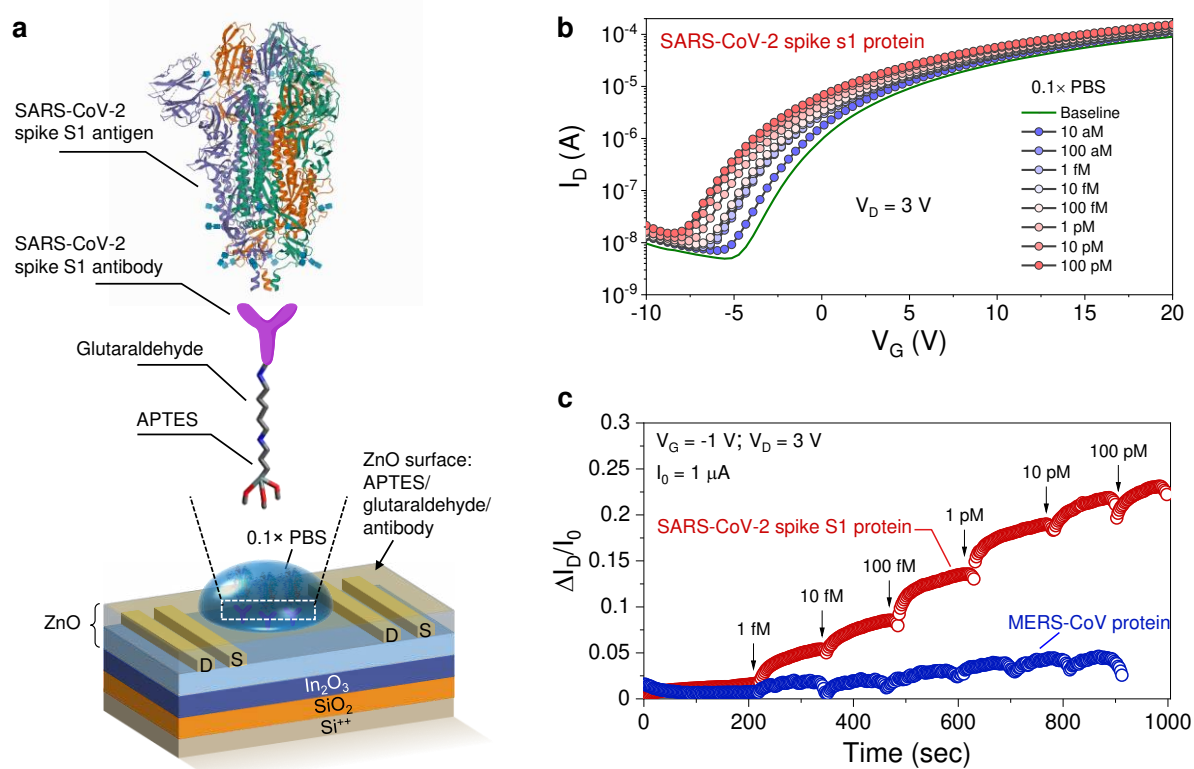
8 To summarize, the sensing mechanism in our all-solid-state tri-channel transistor
9 sensors is starkly different to that of liquid-gated sensor platforms^{5,6,22-28}. The sensing process
10 is modelled by considering the generation of free charges on the SC's surface upon receptor-
11 analyte association (**Fig. 3g-l**) and its strong coupling to the channel current. The higher
12 gradients in the electron flow streamlines observed towards the HJ/analyte interface and the
13 higher electron density highlight how excess charges are introduced and transported across the
14 device upon receptor-analyte interaction. Importantly, the sensor can be easily repurposed via
15 receptor engineering to detect both negatively (i.e. DNAs) as well as positively charged (i.e.
16 biotin-avidin) analytes. In the case of biotin-avidin interaction the channel current was found
17 to reduce due to the electron accepting nature of the formed complex. Another important
18 feature of the tri-channel sensor is the large size SC and its ability to accommodate a high
19 density of receptors which in turn enable dynamic sensing over an extraordinary wide range of
20 analyte concentrations (**Supplementary Figure 14**).

21

22 **Detection of SARS-CoV-2 spike S1 protein**

23 To demonstrate the potential of the tri-channel transistors in a real-world sensing scenario, we
24 engineered the surface of the SC by immobilizing SARS-CoV-2 antibody acceptors designed
25 for specific binding to the SARS-CoV-2 spike S1 protein (**Fig. 6a**)⁵⁶. The receptor-binding
26 domain (RBD) of the spike protein is known to bind the human cell receptor angiotensin-
27 converting enzyme 2 (ACE2), followed by subsequent viral entry. During binding the
28 positively charged polybasic cleavage site on the spike protein binds strongly with the
29 negatively charged human cell receptor ACE2⁶⁵. We hypothesized that such interaction would
30 induce electrostatic perturbations that are detectable by the tri-channel sensor. The sensing
31 scheme is rather straightforward and could prove highly versatile for the detection of the new
32 corona virus and other pathogens of interest.

1 To test our hypothesis, we first examined the ability of the sensor to operate under
 2 physiological-relevant conditions. The antibody-tethered tri-channel sensor show negligible
 3 response upon application of different concentrations of the high ionic strength phosphate
 4 buffered saline (PBS) solution onto the SC (**Supplementary Figures 17 and 18**). Next, a series
 5 of PBS solutions containing different concentrations of the SARS-CoV-2 spike S1 protein were
 6 prepared and applied to the SC of the sensor while the transfer characteristics were recorded
 7 for each analyte concentration (**Fig. 6b** and **Supplementary Figure 19a**). A clear and
 8 systematic shift in V_{ON} towards more negative gate voltages with increasing analyte
 9 concentration, is observed. Strikingly, even at 10 aM the sensor's response remains large and
 10 clearly visible in the quasi-static transfer characteristics of **Fig. 6b** indicating a high sensitivity.



11
 12 **Figure 6 | Detection of SARS-CoV-2 spike protein.** **a**, Schematic of the SARS-CoV-2 spike
 13 S1 protein detection. The SARS-CoV-2 spike S1 antibody is anchored onto the sensor platform
 14 after the sequential modification of oxide surface with 3-aminopropyltriethoxysilane (APTES)
 15 and glutaraldehyde. **b**, Transfer characteristics ($V_D = 3$ V) of a fully functionalised tri-channel
 16 transistor sensor measured in the presence of the SARS-CoV-2 spike protein in 0.1× phosphate-
 17 buffered saline (PBS, baseline). **c**, Real-time response of the tri-channel transistor sensors to
 18 different concentrations (1 fM to 100 pM) of the SARS-CoV-2 spike protein and the MERS-
 19 CoV protein in 0.1× PBS.

20

21 To further demonstrate the versatility of the tri-channel sensor, we performed real-time
 22 sensing measurements of the SARS-CoV-2 spike S1 protein. Prior to this the sensor was biased
 23 at $V_G = -1$ V and $V_D = 3$ V to acquire a stable baseline channel current of ≈ 1 μ A ($\Delta I_D / I_0 = 0$).

1 Following, PBS solutions containing varying concentrations of the SARS-CoV-2 spike S1
2 protein were applied sequentially to the SC while the sensor current being recorded in real-
3 time (**Supplementary Figure 19b**). Evidently, the sensor can detect the analyte across an ultra-
4 wide range of concentrations (aM to pM) demonstrating the tremendous potential of the
5 technology. Similar to dsDNA real-time sensing data, the recorded signal ($\Delta I_D/I_0$) for each
6 concentration increases and reaches an equilibrium followed by a small dip due to the
7 diffusion limited, association and dissociation stages discussed previously (**Supplementary**
8 **Figure 14b**).

9 Lastly, we evaluated the specificity of our sensor towards the SARS-CoV-2 spike S1
10 protein by comparing its real-time response against that of Middle East respiratory syndrome
11 coronavirus (MERS-CoV) spike protein due to their genome similarities⁶⁶. As can be seen in
12 **Fig. 6c**, the tri-channel sensor can differentiate between the two proteins under physiological
13 relevant conditions. For the MERS-CoV protein, the sensor shows no response with the signal
14 remaining largely unaltered with increasing analyte concentration from 1 fM to 100 pM. On
15 the contrary, exposure of the device to SARS CoV-2 spike S1 protein leads to a strong and
16 systematic signal increase with increasing SARS-CoV-2 spike S1 protein concentration. The
17 lowest concentration at which these differences are detectable can be deduced from **Fig. 6c**
18 yielding a value of approximately 1 fM⁵⁶. The LoD⁶⁷ was estimated by applying the
19 International Union of Pure and Applied Chemistry (IUPAC) protocol⁶⁸ to the calibration plot
20 for SARS-CoV-2 spike S1 protein in **Supplementary Figure 19c** yielding a value of 865 aM.

21

22 **Conclusions**

23 We have developed a simple-to-manufacture, millimetre-scale, all-solid-state metal oxide
24 transistor sensor that can detect the presence of biomolecules down to attomolar concentrations
25 in real time while being operated under physiologically relevant environments. The unique
26 device architecture combines high sensitivity and a large dynamic range in an all-solid-state
27 sensing platform capable for analyte sensing in the liquid-phase. The versatile surface
28 chemistry of the metal oxides employed allows for the incorporation of different receptor units
29 (e.g. antibodies, enzymatic recognition elements, aptamers), which is anticipated to enable the
30 detection of a broader range of biomolecules with extraordinary sensitivity and specificity.
31 Furthermore, the ability to distinguish between negatively and positively charged biomolecules
32 as well as between the SARS-CoV-2 and MERS-CoV spike proteins, showcases the
33 universality of the sensor platform, which could be exploited for addressing the most urgent
34 sensing applications.

1 **METHOD**

2 **Preparation of metal-oxide precursors.** ZnO and In₂O₃ precursor solutions were prepared by
3 dissolving zinc oxide (99.99%; Sigma-Aldrich) in ammonium hydroxide (50% v/v; Alfa Aesar)
4 at a concentration of 10 mg ml⁻¹ and anhydrous indium nitrate (99.99%; Indium Corporation)
5 in 2-methoxyethanol (99.8%; Sigma-Aldrich) at a concentration of 20 mg ml⁻¹, respectively.
6 As-prepared solutions were then stirred rigorously at room temperature for 24 h before use.
7 This process yielded clear transparent oxide precursor solutions.

8
9 **Fabrication of low-dimensional oxide transistors.** Heavily doped silicon (Si⁺⁺) wafers with
10 a thermally grown SiO₂ top-layer (100 nm) were used as the common gate electrode and the
11 gate dielectric, respectively. Prior to the semiconductor deposition, the substrates were
12 sonicated in a solvent bath each lasting for ≈10 min in the following sequence: 1) deionised
13 (DI) water with a Decon 90 detergent (5 vol%); 2) DI water; 3) acetone; 4) isopropanol. The
14 solvent residue was dried with dry nitrogen over the substrate surface. As the last cleaning step,
15 the substrates were exposed to ultraviolet (UV) ozone treatment for 10 min. The In₂O₃ ultra-
16 thin film was deposited by carrying out spin-casting of the as-prepared precursor solution onto
17 the Si substrates at 6000 rpm for 30 s in ambient air, followed by a post-deposition thermal-
18 annealing process for 60 min at 200 °C in ambient air. The top ZnO layer was deposited with
19 the same procedure as that for the In₂O₃ layer. Fabrication of the transistors (channel
20 width/length = 1000/100 μm/μm) was completed with thermal evaporation of 40-nm thick Al
21 top source and drain (S–D) electrodes through a shadow mask in high vacuum (≈10⁻⁶ mbar).

22
23 **Transistor characterisation.** Electrical characterisation of transistors was carried out using
24 three micro-positioners (EB-700, EVERBEING), a homemade probe station and an Agilent
25 B2902A source/measure unit in a nitrogen-filled glove box.

26
27 **Self-assembled layer preparation and surface modification.** To prepare the modified device
28 for DNA sensing, firstly 1-pyrenebutyric acid (PBA, 97%; Sigma-Aldrich) solution (1 mg ml⁻¹
29 ¹ in anhydrous tetrahydrofuran (THF)) was applied on the surface of the transistor for 30 min
30 and thoroughly rinsed with THF and dried under nitrogen atmosphere. Butyric acid (BA, ≥
31 99%; Sigma-Aldrich) solution (1 mg ml⁻¹ in anhydrous THF) was then applied to the PBA
32 modified surface for 30 min and thoroughly rinsed with THF and dried under nitrogen
33 atmosphere. To prepare the modified device for avidin sensing, biotin (99%; Sigma-Aldrich)

1 solution (0.8 mg ml⁻¹ in anhydrous ethanol) was first applied on the surface of the transistor for
2 30 min and thoroughly rinsed with ethanol and dried under nitrogen atmosphere. BA was then
3 applied to fully passivate the uncovered surface following the same procedures above as for
4 DNA sensor device.

5
6 **Analyte preparation and sensing.** Deoxyribonucleic acid from calf thymus (Type XV,
7 Activated, lyophilised powder), avidin (lyophilised powder, ≥10 units/mg protein), A20, T20,
8 (AT)20, were purchased from Sigma and used as received. All analytes were well dissolved in
9 MilliQ water (18.2 MΩ·cm/25 °C) to reach the desired concentration according to the solution
10 preparation instruction provided by the supplier. For the sensing process, the analyte solution
11 was constantly applied onto the sensing area, and the electrical properties of the sensor devices
12 were then recorded. For the real time sensing, the channel current was monitored during the
13 continuous and consecutive application of analyte solution of different concentrations onto the
14 same sensor device.

15
16 **Ultraviolet–visible spectroscopy measurements.** The ultraviolet–visible (UV-Vis)
17 transmission measurements were performed using a Shimadzu UV-2600 UV–Vis
18 spectrophotometer. The samples were prepared on quartz substrates using the same deposition
19 parameters described in the Methods section for oxide thin-film deposition and self-assembled
20 monolayer formation.

21
22 **High-resolution transmission electron microscopy measurement.** The samples for high-
23 resolution transmission electron microscopy (HRTEM) analysis were prepared using the
24 focused ion beam processing technique. A gold-plated layer with thickness of 5 nm was coated
25 on sample via sputtering before the sample preparation to make its surface more conductive.
26 The HRTEM images were acquired at 300 kV by a FEI Titan G2 80–300 microscope equipped
27 with a high-brightness Schottky-field emission electron source and a high-resolution Gatan
28 imaging filter Tridiem energy-filter.

29
30 **Atomic Force Microscopy measurement.** Atomic force microscopy study was carried out in
31 tapping mode using an Agilent 5500 atomic force microscope in ambient atmosphere. The
32 approximate resonance frequency of the cantilever was 280 kHz and force constant was ≈60
33 N·m⁻¹.

1

2 **Scanning Kelvin probe measurement.** Scanning Kelvin probe investigations were carried out
3 using a KP Technology system (model SKP5050/APS02) with a 1 mm tip. Scanning was
4 achieved by taking an individual Kelvin probe (KP) measurement in one location and then
5 moving the motorised stage to bring the sample in position for the next KP measurement. This
6 was repeated until data was gathered in a grid pattern of 60×60 points, spanning an area of ca.
7 4 mm × 4 mm. For each point location the tracking feature built into the software made sure to
8 keep the average tip-to-sample-distance constant. Additional drain bias in the range of 0 to 3
9 V was applied using a Keithley B2400 Source-Meter unit. The W_F and E_F values were
10 calculated using Silver as the reference material. All measurements were carried out in ambient
11 air at room temperature and relative humidity of ca. 25 %.

12

13 **Real-time sensing data analysis of (AT)20, natural dsDNA from calf thymus and avidin.**

14 The sensors' real-time recordings to synthetic dsDNA (AT)20 (**Fig. 4h**), natural dsDNA (**Fig.**
15 **5c**) and avidin (**Fig. 5f**) at different analyte concentrations were fitted according to the linear
16 Langmuir adsorption isotherm equation⁵²: $C_{\text{analyte}}/\Delta I_D = C_{\text{analyte}}/\Delta I_{\text{sat}} + 1/\Delta I_{\text{sat}}K_{\text{eq}}$, where ΔI_{sat} is
17 the change of the saturated channel current upon increasing the concentration of analyte, and
18 K_{eq} is the binding constant of the analyte with its corresponding receptor.

19

20 **Solution preparation and device fabrication for spike S1 protein sensing experiments.** The

21 3-aminopropyltriethoxysilane (APTES) solution (99%), glutaraldehyde solution (70% in H₂O),
22 and phosphate buffered saline (PBS, pH 7.4, 10×) solution were purchased from Merck. SARS-
23 CoV-2 spike S1 antibody (40150-R007), SARS-CoV-2 (2019-nCoV) Spike S1-His
24 Recombinant Protein (40591-V08B1), MERS-CoV Spike/S1 Protein (S1 Subunit, aa 1-725,
25 His Tag) (40069-V08H) were purchased from Sino Biological (China). All chemicals were
26 used as received without further purification. Stock solutions of spike proteins were prepared
27 using nuclease-free water and further diluted to different concentrations in 0.1× PBS where
28 necessary. For the SARS-CoV-2 spike protein sensing, the tri-channel transistors were first
29 treated with UV-irradiation for 10 min, APTES solution (2 wt%) in toluene was pipetted onto
30 the oxide surface and left for 15 min, followed by rinsing with toluene and annealing at 120 °C
31 for 1 h. A glutaraldehyde (GA) linker was added to the terminal amino (-NH₂) groups of
32 APTES using a solution of 0.8% GA in DI water for 10 min at room temperature, followed by
33 rinsing with DI water and dried with a stream of N₂ gas. Next, a spike antibody solution (200

1 $\mu\text{g mL}^{-1}$) was applied onto the surface of the functionalised device and kept at room
2 temperature for 5 h in order to immobilise the spike S1 antibodies via covalent bonding. To
3 complete the immobilisation process, the devices were rinsed with $0.1\times$ PBS to remove
4 unbound antibodies. The presence of the antibodies on the surface of the sensing channel was
5 verified via atomic force microscopy. The SARS-CoV-2 spike structure in **Fig. 6a** was adopted
6 from the PDB ID: 6VYB⁶⁹.

7
8 **Device modelling and simulations.** The oxide transistor sensors were modelled and simulated
9 using the semiconductor module in COMSOL Multiphysics. The cross-sectional model was
10 constructed based on the actual device dimensions shown in **Supplementary Figure 3**. The
11 oxide semiconductors were modelled based on material parameters taken from our previous
12 reports^{31,32,70}. The semiconducting $\text{In}_2\text{O}_3/\text{ZnO}$ interface was modelled as a continuous quasi-
13 Fermi-level heterojunction. The S-D electrodes were modelled as Ohmic contacts whilst the
14 gate was modelled using the Thin Insulator Gate node, employing the same SiO_2 dielectric
15 condition as the actual device stack. The analyte was modelled as equivalent surface charges
16 with a density of 10^{10} cm^{-2} . All the other boundaries were modelled as insulations, indicating
17 no normal flux such as current and electric displacement fields. Due to the large aspect ratio of
18 the ultrathin oxide structures, the mapped mesh was generated for the entire transistor channel
19 area with fine rectangular meshes.

20
21 **Data Availability:** The data that support the plots within this paper and other findings of this
22 study are available from the corresponding authors upon reasonable request.

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16 **Acknowledgement**

17 The authors would like to thank Prof. Arnab Pain, as well as Olga Douvropoulou and Raushan
18 Nugmanova from the Biological and Environmental Science and Engineering (BESE) Division
19 at KAUST (Saudi Arabia) for fruitful discussion and assistance with the materials related to
20 the coronavirus spike protein sensing, and Dr Cheng Sheng Lin from Pitotech Co. Ltd (Taiwan)
21 for useful suggestion and assistance in device modelling and simulation. P.P. and A.D.M.
22 would like to acknowledge the postdoctoral funding for A.D.M. from Vidyasirimedhi Institute
23 of Science and Technology (VISTEC). T.D.A. A.S., A.S., W.A., and H.F. acknowledge
24 financial support from King Abdullah University of Science and Technology (KAUST) and
25 KAUST Solar Centre.

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27 **Author contributions**

28 Y.-H.L., Y.H., M.H. and T.D.A. conceived the project. Y.-H.L. and Y.H. designed the
29 experiments. Y.-H.L. designed and fabricated the tri-channel transistor sensors and thin-film
30 samples, conducted the electrical characterisation, and analysed the device data. Y.H. prepared
31 analytes, processed self-assembled monolayers and contributed to the molecular intercalation
32 and kinetics analyses. W.S.A. and Abhinav S. performed additional sensing experiments and
33 contributed to the analysis of the sensing data. Y.-H.L. and Y.H. performed the UV-Vis

1 measurement. C.-H.L. performed device modelling with Y.-H.L., T.-H.C. and X.-W.X. and
2 analysed the simulation results with Y.-H.L. P.P. and A.D.M. performed analyses on device
3 parameters. H.F. carried out the scanning Kelvin probe measurement, collected the electrostatic
4 potential data, assisted the analysis of the device data, and provided suggestion on the sensing
5 measurement. Akmaral S. conducted the TEM characterisation. Y.-H.L., Y.H., M.H. and
6 T.D.A. deduced the sensing mechanism and electronic process. T.D.A. supervised the whole
7 project. All the authors discussed the results and contributed to the writing of the paper.

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15 **COMPETING INTERESTS**

16 The authors declare no competing financial interests.