Potassium Sensing in Serum Samples with a GFET

Application Note

Contents

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1 Summary

This application note describes the use of Paragraf's Graphene Field Effect Transistor (GFET) for potassium ion sensing using a PVC-based selective membrane. The study demonstrates clear selectivity for K^+ over common cations, rapid measurement response and practical manual channel functionalization, distinguishing the GFET as a suitable tool for tracking potassium levels at concentrations and sensitivity applicable to biosensing of human and animal kidney function.

2 Relevance of Potassium Measurement

Many industrial applications and processes – including but not limited to agriculture and healthcare – involve measurement of potassium levels. Such measurements can be one-time or continuous, and the sample types to be assessed are as diverse as the application.

Perhaps the largest addressable market for potassium sensing is in healthcare, both human and animal. Potassium ions in blood serum are critical for helping nerves and muscles to send signals, moving nutrients around the body and allowing the heart to function correctly. As such, the concentration of potassium within the blood is a key metric to monitor.

High potassium levels (i.e., hyperkalaemia) can be an indicator of kidney disease, whereas low levels (i.e., hypokalaemia) may indicate a heart problem such as an irregular heartbeat. Additionally, potassium testing can help diagnose high blood pressure, diabetic ketoacidosis or reduced muscle activity[1].

In human healthcare, the clinically relevant range extends from 2 mM to 8 mM where in the upper and lower figures indicate poor outcomes from hypokelemia and hyperkelemia unless acted on promptly.

The experiment described below indicates that real-time, digital measurement for personal monitoring using Paragraf's mass-producible GFET technology is achievable. The GFET provides a platform on which partners may develop a low-cost, at-home blood test to enable patients to manage a range of health concerns through regular potassium measurements.

3 Advantages of Graphene Field-Effect Transistors

The GFET offers a potential solution to the unmet needs in a majority of such applications, with excellent dynamic range, resolution and sensitivity, and small geometry. A change in the surface potential across the transducer and the gate electrode can be monitored in a GFET as a change in the minimum conduction point, also known as the Dirac point (DP), of the GFET transfer curve with respect to the applied gate voltage. This application note provides feasibility evidence of this with sensors capped with a PVC-based membrane with a potassium-selective molecule incorporated.

4 Device Overview: GFET-PV01

The GFET-PV01 is a research-focused transistor with three electrode channels equally spaced around a large central gate, each distanced from one another to permit manual adjustment or adjustment with automated targeted deposition. Pristine graphene devices (genuinely monolayer, free from polymer or metal contamination) were used from stock and represent performance that can be achieved by any scientist without additional equipment.

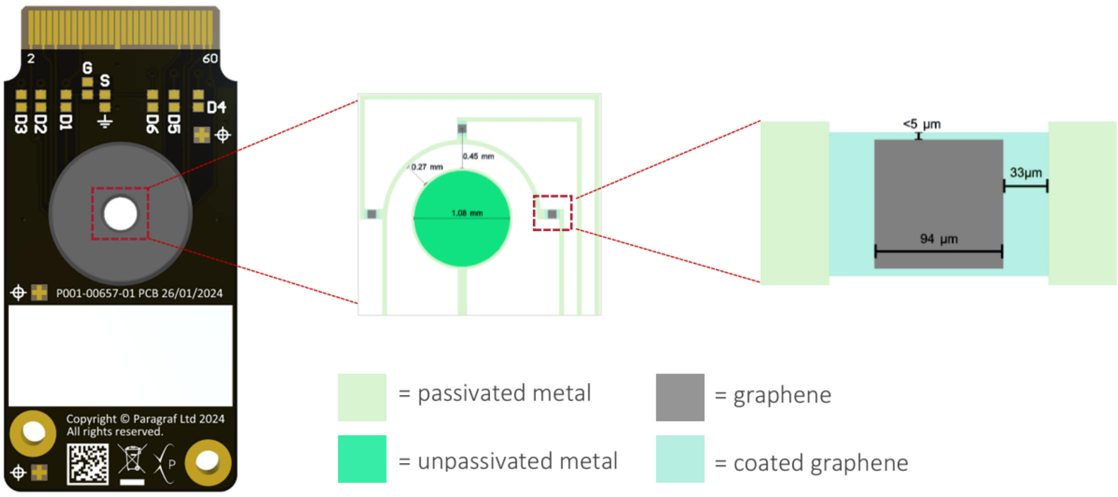

Figure 1. GFET-PV01 sensor layout

Paragraf's GFET is the only commercially scalable graphene device that is manufactured using standard semiconductor processes and equipment, offering unparalleled quality and consistency. These research prototypes were produced by Paragraf's foundry using proprietary technology and industry-leading knowhow in 2D materials.

5 Experimental Methods

5.1 Materials and Reagents

To create a consistent potential response from the Ag/AgCl paste used as the gate material, the solutions used to test the devices were controlled to have identical chloride and phosphate concentrations. To do this any changes in KCl concentration are counteracted using an equimolar amount of NaCl. For this trial matrices of electrolyte at physiological ionicity (reference measurement solution) and goat serum are used to compare the impact of the biological molecules in the serum.

Reference measurement solution preparation

- 160 mM phosphate buffered solution
- 5 mM Na_2PO_4H, 5 mM $NaPO_4H_2$
- 150 mM NaCl in DI water

Goat serum

- Available from Abcam (ab138478)
- Added to the reference solution along with 10 mM NaCl

Potassium test solutions

Prepared by substituting NaCl in either reference measurement solution or goat serum with equimolar amounts of KCl, specifically 0.5 mM, 1 mM, 5 mM and 10 mM.

5.2 Potassium-Selective Membrane Preparation

The potassium-selective membrane solution is prepared using a procedure described by Fakih et. al.[2], with the following components:

Potassium ionophore III: 20 mg

- Lipophilic salt potassium tetrakis(4-chlorophenyl) borate: 10 mg
- Poly(vinyl chloride): 330 mg
- Dioctyl sebacate: 660 mg
- THF: 4 mL

A control membrane is also produced with no potassium ionophore. These solutions are placed in an ultrasonic bath for 1 hour to aid dissolution.

5.3 Device Preparation

Each individual graphene track in each GFET device is coated with either potassium-selective membrane, control membrane, or is left uncoated. 1.5 µL of membrane solution is used to deposit over each channel using a positive displacement pipette.

Ag/AgCl (60:40) paste for screen printing is applied to the thin metal gate using a hanging drop under a microscope, ensuring no contact with the graphene channels or contact tracks. The device is then annealed at 100°C for 10 minutes to cure the gate.

5.4 Measurement Equipment

The GFET devices are connected to two source measure units (SMUs) with a custom-built multiplexer device, to switch between graphene channels. The DP is determined using the Paragraf bespoke “Dirac Point Tracking” software, more information about which can be obtained by contacting sales@paragraf.com.

6 Results

6.1 GFET Channel Functionalisation

As indicated in Figure 2, potassium-selective membrane and the control membrane are deposited manually on different channels. The Ag/AgCl gate can be seen in the centre of the image, covering the original gate material.

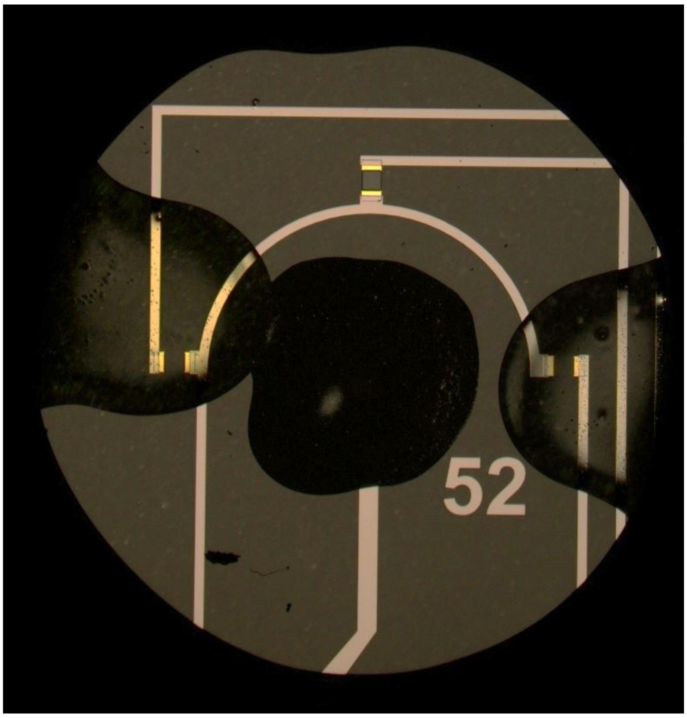

Figure 2. *Optical microscope image (× 2.5 magnification) of the GFET after manual deposition of potassium-selective membrane, control membrane, and Ag/AgCl paste.*

6.2 160 mM Phosphate Buffered Solution

As indicated in Figure 3, a shift in the DP of the potassium-selective membrane can be observed across the range tested of 0.01-10 mM potassium concentration.

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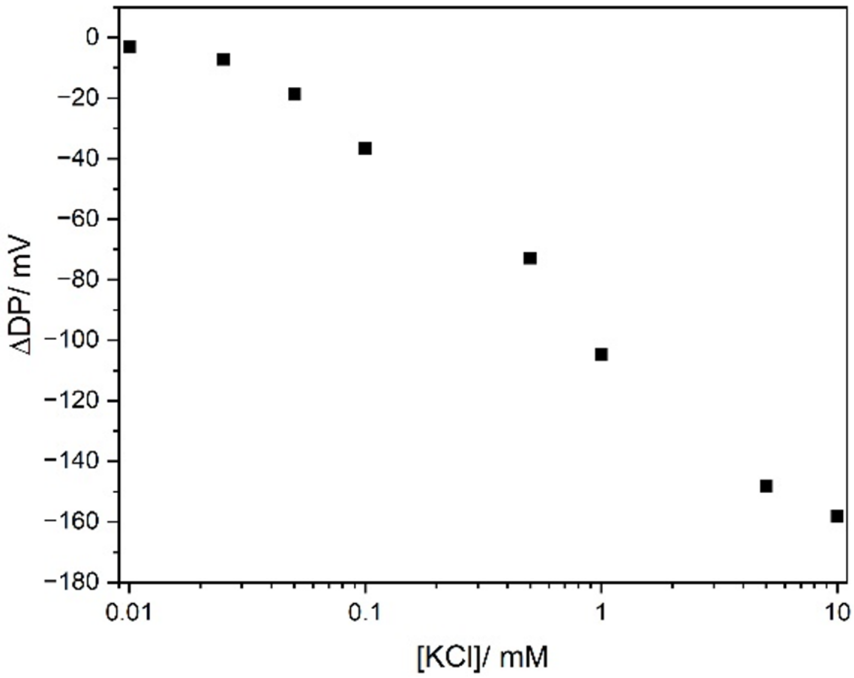

Figure 3. *Change in DP with respect to concentration of KCl in 20 mM phosphate buffered solution for a potassium-selective membrane. Data is taken from continuous DP tracking at 5 minutes per condition.*

As indicated in Figure 4, a shift in the DP of the potassium-selective membrane can be observed against the response of the control membrane across the range tested of 0.5-10 mM potassium concentration.

The response is lower than the previously tested 20 mM phosphate buffered solution (Figure 3) although it is of the same order of magnitude in these higher background ionicity solutions.

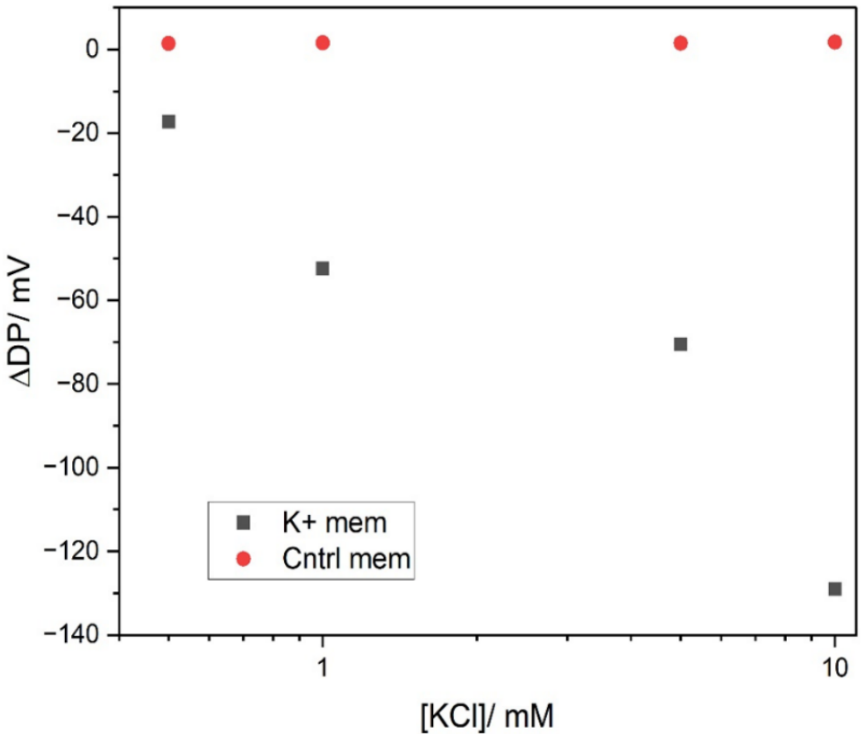

Figure 4. *Change in DP with respect to concentration of KCl in a 160 mM phosphate buffered solution of a GFET with a potassium-selective membrane and a control membrane deposited. Data is taken from continuous DP tracking at 5 minutes per condition.*

6.3 Goat Serum

The results from the tests in goat serum can be seen in Figure 5. In goat serum, a reduction in response is observed; however, by comparing to the control membrane, a response at 1 mM can be resolved even with a signal of −1.6 mV. The reason for this loss in response has not been investigated but is not due to the higher ionicity of solution, as evidenced by the data in Figure 5.

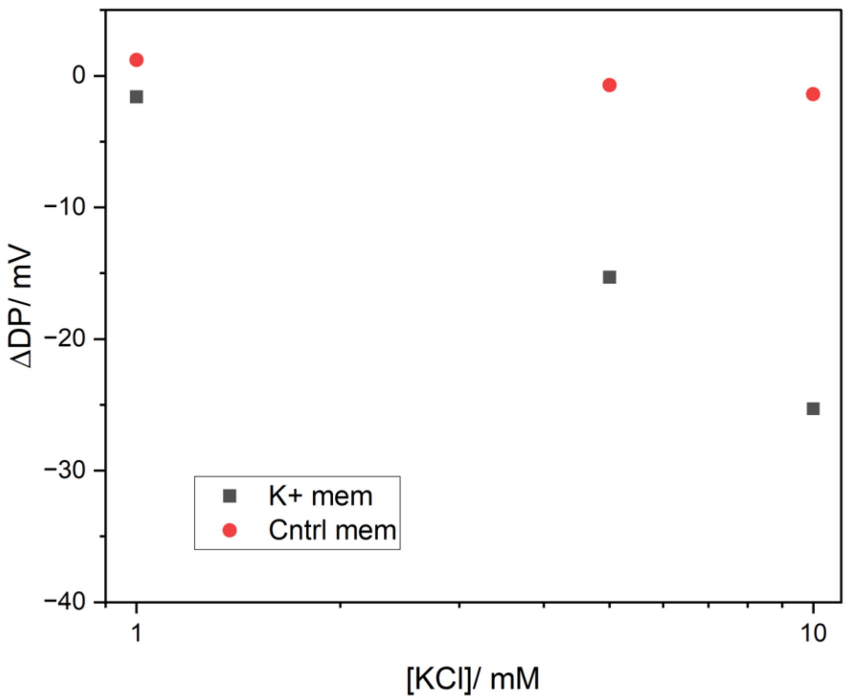

Figure 5. Change in DP with respect to concentration of KCl in goat serum of a GFET with a potassium-selective membrane and a control membrane deposited. Data is taken from continuous DP tracking at 5 minutes per condition.

7 Data Disclaimer

The data shared herein is intended to serve as evidence of use case and exemplification that can be replicated independently. Further experimentation may build on these tests to establish specific product or application alternatives that meet specific needs or research interests.

8 Next Steps

If you would like to try GFET for your own molecular sensing experiments, and learn more about other promising applications of graphene sensing, please visit our web site. GFET devices, as well as the plug-and-play GFET Discovery Kit data acquisition system, are in stock and on sale now at our Online Store.

For custom pricing on larger orders, or to access our foundry services for bespoke solutions, please email sales@paragraf.com.

We would welcome the opportunity to discuss your specific requirements and are actively looking for partners and collaborations to support you in your graphene applications. Please get in touch via enquiries@paragraf.com.

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9 References

1. Anthony J. Viera, MD, MPh, And Noah Wouk, MD. Potassium Disorders: Hypokalemia and Hyperkalemia. American Family Physician, 92, 6 (2015)
2. Fakih, I., Durnan, O., Mahvash, F. et al. Selective ion sensing with high resolution large area graphene field effect transistor arrays. Nat Commun 11, 3226 (2020). https://doi.org/10.1038/s41467-020-16979-y

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