## THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

## High-mobility graphene field-effect transistors for biosensing applications.

MUNIS KHAN



Department of Microtechnology and Nanoscience (MC2) Quantum Device Physics Laboratory CHALMERS UNIVERSITY OF TECHNOLOGY

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Quantum Device Physics Laboratory Department of Microtechnology and Nanoscience (MC2) Chalmers University of Technology SE-412 96 Göteborg, Sweden Telephone: +46 (0)31-772 1000

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## Abstract

Graphene, a single layer of sp<sup>2</sup>-hybridized carbon atoms arranged in a hexagonal lattice, possesses remarkable electronic, mechanical, and thermal properties, stemming from its linear band structure and Dirac-like charge carriers. These attributes make it a strong candidate for advanced technologies such as high-speed electronics, flexible devices, and biosensors. However, its broader adoption is limited by two key challenges: (i) scalable transfer of high-quality graphene without degrading its intrinsic properties, and (ii) development of stable, sensitive, and reliable biosensing platforms. Existing transfer methods for chemical vapor deposition (CVD) graphene often introduce defects and contamination, while conventional direct current (DC) biosensing techniques suffer from signal drift, hysteresis, and poor signal-to-noise ratios.

This thesis addresses these challenges through two primary research directions. The first focuses on developing a scalable, mechanically non-destructive method for transferring CVD graphene onto target substrates. This method is designed to preserve the material's intrinsic properties by minimizing the introduction of defects, contamination, and strain-induced deformations that typically degrade charge transport. Second, the thesis explores an alternating current (AC) biasing scheme as an alternative to conventional DC measurements in graphene field-effect transistor (GFET) biosensors. The AC-based technique demonstrates improved measurement stability, enhanced sensitivity, and better resilience against environmental fluctuations, offering a more reliable platform for real-time biosensing. Additionally, this approach provides new insights into the dynamic behavior of the graphene-electrolyte interface, a key element in understanding biosensor performance.

Together, these advances aim to overcome longstanding barriers in graphene device fabrication and sensing, contributing to the realization of scalable, highperformance graphene technologies for future healthcare and electronic systems.

**Keywords:** Graphene, Field-effect transistor, Chemical vapor deposition, Hall-effect, Sensors.

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## LIST OF PUBLICATIONS

This thesis is based on the work contained in the following appended papers:

- M. Khan, K. Indykiewicz, P. L. Tam, and A. Yurgens, "High mobility graphene on EVA/PET", Nanomaterials 12, 331 (2022).
- [II] M. Khan, J. Ji, B. Zhou, P. U. Jepsen, P. Bøggild, and A. Yurgens, "High mobility graphene field effect transistors on flexible EVA/PET foils", 2D Materials 11, 035022 (2024).
- [III] M. Khan, I. Mijakovic, S. Pandit, and A. Yurgens, "A complimentary impedance spectroscopy biosensing method with graphene", Preprint arXiv: 2504.02510 (2025).
- [IV] S. Rahimi\*, M. Khan\*, M. L. Santa-Maria, M. Ghaeidamini, A. Yurgens, A. Stahlberg, and I. Mijakovic, "Graphene based CRISPR-Cas9 enhanced cancer biomarker KRAS detection", manuscript in preparation (2025).

OTHER PUBLICATIONS/PATENTS NOT INCLUDED IN THIS THESIS

- 1. Youngwoo Nam, Daewon Gu, Munis Khan, August Yurgens. "Graphene thermocouple fabricated on a flexible and transparent substrate." Aip Advances 14, no. 6 (2024).
- 2. Munis Khan, August Yurgens. "Scalable production of graphene structures." PCT WO2025005856A1 (2023) Patent I.
- August Yurgens, Munis Khan. "Complementary electrochemical impedance spectroscopy method in sensor devices." Patent application, PRV 2530180-5 (2025) Patent II.
- 4. Daewon Gu, Moonnyeong Choi, Kyung Ho Kim, Young Duck Kim, Munis Khan, August Yurgens, Youngwoo Nam. "Low-voltage operating graphene p-n junctions on a plastic substrate." (2025) manuscript in preparation.

## Abbreviations and Symbols

CNP	Charge neutrality point
CPE	Constant phase element
CRISPR	Clustered regularly interspaced short palindromic repeats
CVD	Chemical vapor deposition
DC	Direct current
DOS	Density of states
EDL	Electric double layer
EGFET	Electrolyte-gated field-effect transistors
EIS	Electrochemical impedance spectroscopy
EVA	Ethylene vinyl acetate
FET	Field-effect transistor
GFET	Graphene field-effect transistor
LFN	Low-frequency noise
LPCVD	Low-pressure chemical vapor deposition
PBASE	1-pyrenebutanoic acid succinimidyl ester
PET	Polyethylene terephthalate
PSA	Prostate specific antigen
QHE	Quantum Hall effect
R2R	Roll-to-roll
SNR	Signal-to-noise ratio
TDS	Time-domain spectroscopy
TFT	Thin-film transistors
THz	Terahertz
XPS	X-ray Photoelectron Spectroscopy

## Symbols

$E_F$	Fermi energy
$C_q$	Quantum capacitance
$Q_g$	Total charge

$V_{ch}$	Local electrostatic channel potential
$C_g$	Total gate capacitance
$C_{ox}$	Geometric capacitance
$t_{ox}$	Oxide thickness
$C_{dl}$	Double-layer capacitance
$V_{xx}$	Longitudinal voltage
$V_{xy}$	Transverse (Hall) voltage
$ ho_{xx}$	Longitudinal resistivity
$ ho_{xy}$	Hall resistivity
В	Magnetic field
n	Charge carrier density
$R_H$	Hall coefficient
$n_0$	Residual carrier concentrations
$n_g$	Carrier concentrations induced by gate voltage
$\mu$	Charge carrier mobility
Ι	Current
T	Temperature
V	Voltage
$V_g$	Gate voltage
$V_D$	Dirac voltage
$R_{co}$	Contact resistance
$V_{nl}$	Nonlocal voltage
$E_f$	Fermi energy
$v_f$	Fermi velocity
au	Time constant
ω	Frequency
Z''	Imaginary part of impedance
Z'	Real part of impedance
$R_{SH}$	Sheet resistance
$\sigma$	Conductivity
$\mu_0$	Long-range Coulomb scattering-limited mobility
$\theta$	Mobility degradation at high carrier densities

$n^*$	Disorder-induced residual carrier density
$\mu_H$	Hall mobility
$n_{ m sub}$	Substrate refractive index
$V_{CNP}$	Gate voltage at charge neutrality point
$V_{ds}$	Drain-source voltage

#### Constants

e	Electron charge: $e = 1.602 \times 10^{-19} \text{ C}$
$v_F$	Fermi velocity in graphene: $v_F \cong 1 \times 10^8 \mathrm{cm/s}$
h	Planck's constant
$\hbar$	Reduced Planck's constant
k	Boltzmann constant
$\epsilon$	Permittivity

This thesis is dedicated to my parents, Gigi and Abbu.

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## **1** Introduction

Graphene, a single-atom-thick planar sheet of  $sp^2$ -hybridized carbon atoms arranged in a hexagonal lattice, serves as the two-dimensional (2D) building block of graphite [1]. It is characterized by strong in-plane carbon bonds, which give it remarkable mechanical strength. Weak van der Waals interactions between layers enable easy separation. Although graphene was theoretically studied as early as the 1940s, it was long believed to be unstable in its free-standing form due to its presumed susceptibility to thermal fluctuations and structural deformations [2, 3]. This perception changed in 2004 when Geim and Novoselov successfully isolated graphene using mechanical exfoliation, demonstrating its stability and unique characteristics [4].

Since its isolation, graphene has attracted immense interest across multiple scientific fields due to its exceptional electrical, mechanical, optical, and thermal properties. The interaction between its lattice and charge carriers results in a linear electronic dispersion relation, causing graphene's charge carriers to behave as chiral, massless Dirac fermions. This behavior has led to the observation of remarkable physical phenomena, such as the room-temperature integer quantum Hall effect, the fractional quantum Hall effect under strong magnetic fields, hightemperature ballistic transport, and the Hofstadter's butterfly pattern in graphene subjected to both a magnetic field and a periodic potential [5, 6]. Graphene's extremely high carrier mobility, mechanical flexibility, superior strength, and large surface area make it a highly promising material for next-generation electronic and sensing technologies. Its potential applications range from high-speed transistors and transparent conductive films to advanced sensors and energy storage devices. Despite these promising attributes, challenges remain in scaling up production and integrating graphene into existing technologies, which are critical steps for its widespread adoption.

#### Graphene as a sensing material

Graphene's two-dimensional structure and electronic properties make it highly sensitive to local environmental changes, positioning it as a promising material for sensor applications [7]. Its entire surface area is directly exposed to the environment, allowing efficient interactions with target analytes, an attribute particularly advantageous in biosensing, where graphene enables the detection of biomolecular interactions with high sensitivity [8]. Graphene-based biosensors have demonstrated strong potential for detecting a wide range of biomolecules, including proteins, nucleic acids, and biomarkers. Among these platforms, the graphene field-effect transistor (GFET) has emerged as the most widely studied configuration. In GFETs, graphene serves as the conductive channel, and changes in its conductivity are used to sense the presence of specific biomolecules [9]. Owing to its atomic thickness, graphene exhibits pronounced charge-carrier tuning in response to even minor environmental perturbations, enabling label-free, real-time detection.

Unlike conventional silicon-based field-effect transistors (FETs), which rely on three-dimensional (3D) charge transport, where conduction occurs not only at the surface but also through the bulk, the influence of surface-bound molecules on overall conductivity is limited. This results in reduced sensitivity. In contrast, graphene field-effect transistors leverage the planar geometry and atomic-scale thickness of graphene, ensuring that the entire channel is electrostatically coupled to its surroundings. As a result, surface interactions directly modulate carrier density, leading to significantly enhanced detection sensitivity.

Graphene's high carrier mobility reaching values up to  $10000 \text{ cm}^2/(\text{V s})$  at room temperature further improves device performance over traditional semiconductors. Moreover, the ability to chemically functionalize the graphene surface enables selective binding of specific biomolecules, making GFETs well suited for rapid and targeted clinical diagnostics.

Recent advancements underscore the potential of GFET biosensors in realworld applications. For instance, ultrasensitive detection of SARS-CoV-2 proteins has been demonstrated using GFET platforms [10]. Additionally, integrating GFETs with CRISPR-based gene-editing technologies has led to the development of CRISPR-chip devices capable of detecting specific DNA sequences with high precision and speed [11]. These innovations have further raised interest in GFETbased biosensors for a broad range of diagnostic and environmental monitoring applications.

#### Challenges in large-scale graphene production

Despite its potential, the large-scale implementation of graphene in advanced applications remains challenging, primarily due to difficulties in scalable production while preserving its intrinsic high charge carrier mobility and integrating it seamlessly into functional devices. The production of good-quality, defect-free graphene at an industrial scale remains a formidable challenge. Mechanical exfoliation, the method used in the initial discovery of graphene, produces single-crystal material but is limited to small sizes. Other methods, such as liquid-phase exfoliation [12], can yield graphene-like materials, reduced graphene oxide [13] in bulk, but the material often suffers from structural defects, reduced charge carrier mobility, and inconsistencies in layer thickness. Chemical Vapor Deposition (CVD) has emerged as a promising technique for producing large-area single-layer graphene [14–18]. However, a significant bottleneck in CVD-based production lies in the transfer process, where graphene must be transferred from the metal catalyst to the target substrate for practical applications [19]. This transfer step often introduces defects, contamination, and wrinkles in graphene, all of which can degrade the material properties and limit its reproducibility in device fabrication [20–22].

Numerous transfer techniques have been developed to address these challenges, including roll-to-roll (R2R) methods [23–28], delamination transfer [29], carrier polymer-assisted transfer [20, 21], laser-assisted transfer [30], electrochemical methods [27], frame-assisted techniques [31], and semi-dry transfer [32]. However, none of these methods combine simplicity, high carrier mobility, mechanical flexibility, and long-term protective encapsulation, which explains why no single transfer method has become a standard. The high mobility graphene devices have been achieved in van-der-Waals heterostructures, such as graphene sandwiched between h-BN flakes using dry transfer techniques [33–36], however, these approaches are not scalable and depend on the availability of high-quality 2D materials.

#### Challenges in biosensing

Most graphene-based biosensing devices are designed to operate in liquids, as many biological molecules, including proteins and DNA, require aqueous conditions to maintain their structural integrity and functionality. However, the interaction between graphene and liquid introduces complexities that are not yet fully understood. The electrical double layer formed at the graphene-liquid interface plays a critical role in the sensing mechanism, but detailed studies on its behavior are still lacking [37]. Additionally, the Debye screening effect in highionic-strength solutions poses another challenge, as it reduces the effective sensing range of graphene-based devices. Many biosensors are affected by this issue, limiting their application in physiological conditions where ionic concentrations are high [38]. Understanding and controlling the phenomena at the interface between graphene and liquid is challenging, as nonspecific adsorption often decreases the signal-to-noise ratio, sometimes rendering the signal undetectable [39]. Biosensing is achieved either by detecting shifts in the charge neutrality point (CNP) or changes in conductance or resistance caused by the adsorption of target molecules. However, the accuracy of detection is frequently compromised by issues such as hysteresis, charge trapping, time drifts, and asymmetric transfer curves [40–42]. Furthermore, the adsorption of analytes introduces scattering centers, which alter transconductance and increase disorder within the system [43, 44].

#### Objectives of this thesis

This thesis aims to address two challenges in the field of graphene research:

#### 1. Scalable methods for high-quality graphene

The first objective is to introduce a simple, robust, and scalable methodology to transfer CVD graphene onto target substrates while preserving its pristine quality. The focus will be on developing innovative transfer techniques to minimize defects, contamination, and wrinkles during the transfer process. By achieving a reproducible and scalable transfer method, this work will contribute to the broader goal of integrating graphene into commercial technologies.

#### 2. Enhancing graphene-based biosensing techniques

The second objective is to leverage high-quality graphene devices for biosensing applications. Traditional biosensing methods using direct current (DC) suffer from signal drift, noise, and low sensitivity. The proposed AC-bias approach overcomes these challenges by improving measurement stability and sensitivity. Additionally, this method will provide deeper insights into the graphene-electrolyte interface, leading to a better fundamental understanding of charge transfer mechanisms at this critical junction.

The successful realization of these objectives will have far-reaching implications in multiple domains. A scalable method for producing high-quality graphene will accelerate its adoption in industrial applications, including flexible electronics and medical diagnostics. Furthermore, the introduction of AC-bias-based biosensing can revolutionize graphene-based sensors by offering a more reliable and precise detection method, ultimately advancing healthcare technologies such as disease diagnostics and personalized medicine. By addressing key production and application challenges, this thesis aims to make a substantial contribution to the field of graphene research and pave the way for its widespread utilization in nextgeneration technologies.

Chapter 2 introduces the fundamental physics of graphene, covering its crystal and electronic structure, charge carrier statistics, and quantum capacitance. Key magneto-transport phenomena, including the Hall effect and quantum Hall effect, are explained. The ambipolar field-effect in graphene is described, along with transport model. Finally, relevant electrochemical principles, particularly electrochemical impedance spectroscopy (EIS), are discussed to lay the groundwork for biosensing applications.

Chapter 3 presents a scalable method for transferring CVD-grown graphene onto flexible polymer substrates via hot-press lamination. The process involves graphene growth on copper foils, followed by transfer to Ethylene vinyl acetate (EVA)/Polyethylene terephthalate (PET) lamination foils. Comprehensive electrical and spectroscopic characterization, including Raman spectroscopy and XPS analysis, confirms the quality and mobility of the transferred graphene. (Paper I)

Chapter 4 details a novel fabrication method for flexible GFETs. The process preserves graphene quality, yielding high carrier mobility (8000-10000 cm<sup>2</sup>/(V s)) and enabling observation of the quantum Hall-effect. Device characterization includes Hall effect measurements, field-effect transport measurements, and terahertz time-domain spectroscopy (THz-TDS) analysis. (Paper II, Patent I)

Chapter 5 explores electrolyte-gated GFETs for biosensing, introducing an innovative complementary impedance spectroscopy method that remains stable against electrolyte variations. Sensor fabrication, functionalization, and electrical measurements are discussed, alongside a model for interpreting lock-in measurements and frequency-dependent impedance responses. (Paper III, Patent II)

Chapter 6 demonstrates a CRISPR-Cas9-enhanced GFET biosensor for detecting DNA mutations. The chapter covers GFET functionalization, specificity validation, and time-series measurements. Comparative studies between functionalized and non-functionalized devices highlight enhanced sensitivity. (Paper IV)

Finally, Chapter 7 summarizes advancements in graphene transfer, GFET fabrication, and biosensing, proposing future improvements in functionalization, stability, and commercialization.

## 2 Concepts and theory

This chapter outlines the fundamental theoretical concepts underlying the properties and behavior of graphene, with a focus on its structural, electronic, and electrochemical characteristics. We begin by examining the crystal and electronic structure of graphene, which forms the basis for its unique electronic properties. Next, we discuss charge carrier statistics and quantum capacitance, key factors governing graphene's electrical behavior. The magneto-transport properties of graphene are then explored, including the classical Hall effect and the quantum Hall effect, which highlight its exceptional electronic performance under magnetic fields. Additionally, the ambipolar field-effect in graphene is reviewed, demonstrating its tunable charge carrier nature. Finally, we introduce essential principles in electrochemistry, particularly electrochemical impedance spectroscopy, which plays a crucial role in characterizing graphene-based electrochemical systems. Together, these theoretical foundations provide the necessary background for understanding graphene's applications in electronic and electrochemical devices.

## 2.1 Crystal and electronic structure



Figure 2.1: (a) unit cell consists of two atoms marked with A and B. The primitive vectors are defined as  $a_1$  and  $a_2$  (b) The 2D band structure of graphene, with the Dirac cone zoomed in the band structure to K or K' points. Adopted from [5].

Graphene exhibits a 2D hexagonal crystal structure, as illustrated in Fig. 2.1a.

Its unit cell comprises two carbon atoms, labeled A and B. The entire 2D lattice is formed by repeating this unit cell in a triangular arrangement. The primitive lattice vectors are given by:

$$a_1 = \frac{a}{2} \left(3, \sqrt{3}\right), \quad a_2 = \frac{a}{2} \left(3, -\sqrt{3}\right),$$
 (2.1)

where  $a \cong 1.42$  Å denotes the bond length between directly neighboring carbon atoms A and B. The three  $sp^2$  orbitals are evenly distributed in the *x-y* plane, separated by an angle of 120°. These orbitals form strong covalent bonds between the carbon atoms. This bonding arrangement results in the characteristic hexagonal structure of graphene, as illustrated in Fig. 2.1a, and accounts for its exceptional mechanical strength. The  $2p_z$  orbital, on the other hand, forms outof-plane  $\pi$  bonds with neighboring carbon atoms. These  $\pi$  bonds enable electrons to move freely across the graphene sheet, contributing to its remarkable electronic properties. The electronic band structure of graphene, which describes the allowed energy states as a function of electron momentum, is derived by solving the Schrödinger equation. Using the tight-binding approximation and considering only nearest-neighbor hopping, the energy dispersion relation for graphene can be expressed as [2]:

$$E_{\pm}(k) = \pm t_{\sqrt{3}} + 2\cos\left(\sqrt{3}k_ya\right) + 4\cos\left(\frac{3}{2}k_xa\right)\cos\left(\frac{\sqrt{3}}{2}k_ya\right), \qquad (2.2)$$

where  $k = (k_x, k_y)$  represents the wave vector, and  $t \approx 2.8 \text{ eV}$  is the nearestneighbor hopping energy. The plus and minus signs correspond to the conduction and valence bands, respectively. A 3D plot of this band structure reveals that these two bands intersect at specific points known as the K and K' points (Fig. 2.1b). Their coordinates in momentum space are:

$$K = \left(\frac{2\pi}{3a}, \frac{2\pi}{3\sqrt{3}a}\right), \quad K' = \left(\frac{2\pi}{3a}, -\frac{2\pi}{3\sqrt{3}a}\right)$$

The presence of these K (or K') points implies that graphene has a zero bandgap, classifying it as a semimetal. By expanding the energy dispersion around the K (or K') points, we obtain the approximate relation [5]:

$$E_{\pm}(q) = \pm v_F |q| + O\left[\left(\frac{q}{K}\right)^2\right],\tag{2.3}$$

where q = k - K represents the deviation from the K point, and  $v_F \cong 1 \times 10^8$  cm/s is the Fermi velocity near these points. To first order, the energy dispersion is linear in q, implying that charge carriers behave as massless particles, akin to photons (Fig. 2.1b). Consequently, the charge carrier dynamics near the K (or K') points are governed by the Dirac equation rather than the Schrödinger equation, leading to their designation as Dirac points. These Dirac points contribute to graphene's unique electronic properties, making it a subject of great interest in both fundamental research and engineering applications.

## 2.2 Charge carrier statistics and quantum capacitance

The density of states (DOS), which represents the number of available states per energy interval, can be derived from the dispersion relation. For graphene, the DOS is given by:

$$g(E) = \frac{2}{\pi (\hbar v_F)^2} |E|,$$
 (2.4)

where  $\hbar$  is the reduced Planck constant and  $v_F$  is the Fermi velocity. The DOS, combined with the Fermi-Dirac distribution:

$$f(E_F) = \frac{1}{1 + e^{(E - E_F)/kT}},$$
(2.5)

where  $E_F$  is the Fermi energy, k is the Boltzmann constant, and T is the temperature, is used to calculate the charge carrier concentration in graphene. The Fermi-Dirac distribution describes the probability of an electron occupying a given energy state at a specific temperature and Fermi level position.

Due to the low density of states in graphene, even a small change in the charge carrier concentration can significantly shift the Fermi level. In material systems with low DOS, the quantum capacitance  $(C_q)$  must be considered. The quantum capacitance is defined as the derivative of the total charge  $Q_g$  in graphene with respect to the local electrostatic channel potential  $V_{ch} = E_F/e$ . For pristine graphene, it is expressed as:

$$C_q = \frac{\partial Q_g}{\partial V_{ch}} = \frac{8\pi e^2 kT}{(hv_F)^2} \ln\left[2 + 2\cosh\left(\frac{E_F}{kT}\right)\right]$$
(2.6)

In GFETs, the total gate capacitance  $(C_g)$  is reduced due to the quantum capacitance acting in series with the geometric capacitance  $C_{ox} = \epsilon/t_{ox}$ , where  $\epsilon$  is the permittivity and  $t_{ox}$  is the oxide thickness:

$$C_g = \frac{C_{ox}C_q}{C_{ox} + C_q} \tag{2.7}$$

However, if one capacitance is significantly larger than the other, the total capacitance can be approximated by the smaller capacitance. For example, if the gate oxide thickness is relatively large, then:

$$C_q \gg C_{ox} \implies C_t \approx C_{ox}$$
 (2.8)

In electrolyte-gated GFETs, the quantum capacitance becomes particularly significant due to the comparable magnitudes of the double-layer capacitance  $(C_{dl})$ and the quantum capacitance [45]. In these systems, the double-layer capacitance, which arises from the formation of an ionic charge layer at the graphene-electrolyte interface, is typically in the range of a few  $\mu F/cm^2$ . This value is often on the same order of magnitude as the quantum capacitance of graphene. As a result, the quantum capacitance cannot be neglected, and its inclusion is essential for accurately modeling the device's electrostatic behavior and charge modulation. The interplay between  $C_q$  and  $C_{dl}$  significantly influences the overall gate capacitance and, consequently, the device's performance, making it a critical consideration in the design and analysis of electrolyte-gated GFETs.

## 2.3 Magneto-transport properties of graphene



Figure 2.2: (a) An illustration of a graphene Hall bar structure. A current I is applied, and the longitudinal- and transverse (Hall) voltages Vxx and Vxy are measured in a fourprobe configuration. The magnetic field B is applied out of plane, perpendicularly to the current path. (b) Half-integer quantum Hall effect measured in exfoliated graphene flakes by fixing the magnetic field to B = 12 T and varying the carrier concentration with a bottom electrostatic gate (adopted from [46]).

Graphene's electronic structure, characterized by massless Dirac fermions and linear energy dispersion, gives rise to remarkable magneto-transport properties. When subjected to a perpendicular magnetic field, graphene exhibits behaviors distinct from conventional two-dimensional electron gases, including an unconventional Hall effect and a unique manifestation of the quantum Hall effect [47, 48]. These phenomena hold promise for applications in metrology and future electronic devices.

Graphene's high charge carrier mobility means ballistic transport over micrometer scales, leading to minimal scattering and pronounced quantum effects in the presence of a magnetic field. The application of the magnetic field modifies charge carrier trajectories, resulting in well-defined transport regimes and the formation of discrete Landau levels at high fields. The carrier density in graphene is tunable via electrostatic gating, making it an ideal platform for studying magnetic-fielddependent transport effects.

The Hall effect in graphene allows direct measurement of carrier type and density, while the quantum Hall effect exhibits an unconventional half-integer quantization due to graphene's unique band structure. Additionally, magneto-transport studies in graphene reveal Shubnikov-de Haas oscillations, negative magnetoresistance, and chiral edge states [49], all of which contribute to its potential for advanced electronic applications.

#### 2.3.1 Hall effect

The Hall effect serves as a fundamental method for analyzing the electronic properties of materials. When a current flows through a conductor subjected to a perpendicular magnetic field, the charge carriers experience a Lorentz force that causes their deflection. This deflection generates a transverse voltage, known as the Hall voltage, which depends on the charge carrier density and type (electrons or holes) in the material.

For graphene, the Hall-effect measurements are performed using a configuration shown in Fig. 2.2a, where the current I is applied along the graphene strip, and both longitudinal  $(V_{xx})$  and transverse  $(V_{xy})$  voltages are measured. The longitudinal resistivity,  $\rho_{xx}$ , and the Hall resistivity,  $\rho_{xy}$ , are defined as:

$$\rho_{xx} = \frac{V_{xx}}{I}, \quad \rho_{xy} = \frac{V_{xy}}{I} \tag{2.9}$$

The Hall voltage is given by:

$$V_{xy} = -\frac{IB}{ne},\tag{2.10}$$

where B is the applied magnetic field, n is the charge carrier density, and e is the elementary charge. The Hall resistivity is then expressed as:

$$\rho_{xy} = -\frac{B}{ne} = -R_H B \tag{2.11}$$

where  $R_H$  is the Hall coefficient. Through this method, the type of doping (n-type or p-type) in graphene can be determined, and the mobility of charge carriers can be extracted.

#### 2.3.2 Quantum Hall effect

At high magnetic fields, graphene exhibits the quantum Hall effect, a phenomenon where the Hall resistivity becomes quantized while the longitudinal resistivity vanishes [47]. Unlike in conventional two-dimensional electron gases, where Hall plateaus occur at integer multiples of  $h/e^2$ , graphene's unique band structure results in the half-integer quantum Hall effect [50]. This arises due to the presence of a zero-energy Landau level and the four-fold degeneracy of graphene's electronic states, which include spin and valley degrees of freedom. The Hall resistivity follows the quantization rule [51]:

$$\rho_{xy} = \frac{1}{(g_s \cdot (l + \frac{1}{2}))} \cdot \frac{h}{e^2}, \quad l = 0, 1, 2, \dots$$
(2.12)

where  $g_s = 4$  accounts for both spin and valley degeneracies. As a result, Hall plateaus appear at unconventional resistance values such as 12.9 k $\Omega$ , 4.3 k $\Omega$ , and 2.58 k $\Omega$  (Fig. 2.2b), which are distinct from those observed in traditional semiconductor-based systems.

Another notable feature of the quantum Hall effect in graphene is its robustness at elevated temperatures. While the conventional quantum Hall effect typically requires cryogenic conditions, the high energy separation between graphene's Landau levels allows the effect to be observed even at room temperature in highquality samples. This makes graphene a strong candidate for next-generation resistance standards in metrology [52].

## 2.4 Ambipolar field-effect in graphene

The electronic properties of semiconductors can be effectively modified by applying an electric field, a principle widely employed in field-effect transistors, which form the basis of modern electronics. In conventional metals, this effect is minimal due to the strong screening of the bulk from surface charges. However, graphene's two-dimensional structure enables capacitive gating to induce significant charge densities on the order of  $10^{13}$  cm<sup>-2</sup>, substantially altering graphene's electrical resistivity [4].

Graphene exhibits a bipolar field effect. By adjusting a gate voltage, the carrier concentration can be tuned continuously between electron-dominated (n-type) and hole-dominated (p-type) transport as shown in Fig. 2.3a. This behavior arises from graphene's unique band structure, where conduction and valence bands meet at the Dirac point. At this point, graphene displays maximum resistivity due to



Figure 2.3: The field-effect ambipolar conduction due to the shift of the Fermi level. If a negative gate voltage is applied, the channel is dominated by hole conduction. If a positive gate voltage is applied, the channel is dominated by electron conduction.

residual carrier concentrations  $(n_0)$ , attributed to thermal fluctuations, disorder, impurities, and charge traps in the substrate environment [53]. This residual concentration imposes a lower limit on graphene's conductivity.

Graphene's extremely high charge carrier mobility, reaching  $10^5 \text{ cm}^2/(\text{V s})$  at room temperature [54] and even higher at cryogenic temperatures [55], makes it ideal for high-speed electronics. However, because graphene is a purely twodimensional material, its electrical properties are highly sensitive to surface contaminants, defects, and fabrication conditions. Consequently, both mobility ( $\mu$ ) and residual charge density ( $n_0$ ) depend strongly on these factors.

To characterize graphene's electrical properties, field-effect measurements are commonly employed. In such measurements, a transistor-like configuration controls the carrier concentration using a gate electrode. Assuming carrier mobility is independent of density, the resistance R can be described by a diffusive transport model [56]:

$$R = R_{co} + \frac{N_{sq}}{e\mu} \frac{1}{\sqrt{n_0^2 + n_q^2}}$$
(2.13)

where  $N_{sq} = L/W$  is the geometrical number of squares in the device,  $n_g = (V_g - V_D)C_g/e$  is the carrier concentration induced by gate voltage  $V_g$  relative to the Dirac voltage  $V_D$ , and  $C_g$  is the gate capacitance per unit area. The parameter  $R_{co}$  accounts for constant resistance, absent in four-probe measurements. The field-

effect remains a popular method for investigating graphene's electronic properties and is vital for its application in nanoelectronic devices.

## 2.5 Relevant principles in electrochemistry



Figure 2.4: The three most common models used to describe electric double layers (a) Helmholtz model, (b) Gouy-Chapman model, (c) Gouy-Chapman-Stern model. (adopted from [57])

The use of graphene in chemical and biological sensors necessitates an understanding of certain electrochemical concepts. Specifically, graphene EGFETs (Electrolyte-Gated field-effect transistors) utilize two key notions: electric double layer formation and electrochemical potential windows. When a metal electrode interfaces with an electrolyte, an electric double layer forms. Cations or anions in the electrolyte migrate toward the surface, creating a charge buildup over a short distance of a few nanometers, while the bulk electrolyte remains electro-neutral. Consequently, electric double layer capacitances can be quite large, ranging from a few- to tens of  $\mu F/cm^2$ . Several models describe this phenomenon, including the Helmholtz model, Gouy-Chapman model, and Gouy-Chapman-Stern model. Fig. 2.4 illustrates these three models.

The electric double layer (EDL) describes the distribution of ions near a charged surface in an electrolyte. The earliest model, proposed by Helmholtz, treated the EDL as a simple parallel-plate capacitor with all ions tightly adsorbed onto the surface [58]. While useful in some cases, this model fails to account for the diffusive movement of ions in solution.

The Gouy-Chapman model improved upon this by considering both electrostatic forces and ion diffusion [59, 60]. However, this approach still treated ions as point charges, leading to unrealistic predictions at higher concentrations. The Gouy-Chapman-Stern model combined both approaches, featuring a compact inner layer (Helmholtz) and a diffuse outer layer (Gouy-Chapman) [61].

These classical models had limitations because they ignored the finite size of ions. In reality, ions occupy space and cannot pack infinitely close together. More advanced models, like the modified Poisson-Boltzmann approach, account for these steric effects [62, 63]. These improvements better describe the behavior of ions in concentrated solutions or at high potentials.

Electric double layer capacitance is an interface effect occurring within nanometers of the surface, with the bulk electrolyte remaining electro-neutral. Thus, the electrolyte's thickness or volume does not affect capacitance, contrasting with conventional dielectric capacitors, where capacitance inversely depends on dielectric thickness. Unlike dielectric capacitors, electric double-layer capacitance is voltage-dependent.

Modeling electric double layers is complicated by the fact that high ionic concentrations affect the relative permittivity of the electrolyte. Because of this, electrolyte permittivity is not constant but exhibits some form of spatial dependence. Secondary effects such as these make accurate modeling of electric double layers difficult.

Another crucial concept in graphene EGFET operation is the electrochemical potential window. Although both graphene and electrolytes are conductive, applying a voltage across the graphene-electrolyte interface does not necessarily result in sustained (DC) current. This is because graphene has a wide electrochemical potential window in many electrolytic environments, a feature long recognized in carbon-based electrodes [64].

To sustain a DC current at the graphene-electrolyte interface, a redox reaction must occur at the graphene surface, involving one or more chemical species. For instance, in aqueous NaCl electrolyte, Na<sup>+</sup> must be reduced, Cl<sup>-</sup> must be oxidized, or water must be split to produce oxygen and hydrogen gases. These reactions require overcoming activation barriers, which are relatively high for many graphene-electrolyte interactions, including aqueous NaCl and complex electrolytes like phosphate-buffered saline (PBS).

The graphene-electrolyte interface has a low exchange current density, resulting in a large potential range with negligible current flow. The lack of DC current, coupled with ion migration due to the electric field, means the interface acts as a capacitor. A wide potential window can potentially allow very high charge accumulation, which has spurred research into graphene-based supercapacitors [65– 67]. For graphene EGFET operation, a wide potential window enables gating over a wide range in various electrolytes without inducing redox currents. Absence of redox reactions limits potential damage to the graphene and its electrical properties. It also allows graphene EGFETs to operate without the need for any protective coating or dielectric. This direct interface with the electrolyte enables graphene EGFETs to take full advantage of the high interface capacitances due to electric double layer formation.

#### 2.5.1 Electrochemical impedance spectroscopy

Electrochemical Impedance Spectroscopy (EIS) is a powerful, non-destructive technique widely employed to analyze the dynamic behavior of electrochemical systems. It is especially valued for its ability to deconvolute complex processes based on their characteristic time constants, making it indispensable in fields such as corrosion science, energy storage, biosensing, and solid-state electrochemistry [68, 69].

The core principle of EIS involves applying a small-amplitude sinusoidal voltage perturbation over a broad frequency range and measuring the resulting current response. For the system to qualify as linear and time-invariant, the output current must vary proportionally with the input voltage, and the system's properties must remain constant during the measurement. The measured impedance,  $Z(\omega)$ , is a complex, frequency-dependent quantity composed of a real part (resistance) and an imaginary part (reactance). This impedance spectrum reveals information about the underlying physicochemical processes occurring at the electrodeelectrolyte interface.

Impedance characterizes the total opposition to current flow in systems composed of resistors (R), capacitors (C), and inductors (L). The configuration and values of these passive elements determine the system's overall impedance. When an alternating voltage  $v(t) = V_0 \sin(\omega t)$  is applied, the resulting current takes the form  $i(t) = I_0 \sin(\omega t + \phi)$ , with a phase shift  $\phi$ . The complex impedance is expressed as:

$$Z(\omega) = |Z|e^{j\phi} = |Z|(\cos\phi + j\sin\phi) = Z' + jZ'', \qquad (2.14)$$

where Z' is the real (resistive) component and Z'' is the imaginary (reactive) component. The magnitude and phase angle of the impedance are given by:

$$|Z| = \sqrt{(Z')^2 + (Z'')^2}, \qquad \phi = \tan^{-1}\left(\frac{Z''}{Z'}\right)$$
 (2.15)

In electrochemical impedance spectroscopy, frequency response analyzers employ the orthogonality principle of sine and cosine function measurements.

Key processes probed by EIS include the ohmic resistance of the electrolyte, double-layer capacitance, charge-transfer kinetics of redox reactions, and the diffusive transport of electroactive species. Each of these phenomena operates over distinct time scales and dominates within specific frequency ranges. The characteristic time constant  $\tau$  of such a process is typically defined as  $\tau = RC$ , where Ris resistance ( $\Omega$ ) and C is capacitance (F).

Commercial EIS instruments typically operate across a frequency range of 10  $\mu$ Hz to 1 MHz, though practical limitations exist. At ultra-low frequencies

(e.g., 10  $\mu$ Hz), acquiring a single data point may take over 27 hours, whereas at high frequencies, parasitic effects from cables and instrumentation can distort the measurements. EIS results are commonly displayed using Nyquist and Bode plots. A Nyquist plot graphs the negative imaginary impedance (-Z'') versus the real component (Z'). Bode plots display the impedance magnitude |Z| and phase angle  $\phi$  versus the logarithm of frequency, providing a clearer view of frequencydependent behavior.

Ensuring data reliability is crucial prior to interpreting EIS spectra. The Kramers-Kronig relations serve as a mathematical consistency check, ensuring the real and imaginary components of impedance are physically valid. For EIS data to be considered trustworthy, it must satisfy four essential criteria: *linear-ity, causality, stability,* and *finiteness.* Linearity requires the system to respond proportionally to the excitation signal, such that no harmonic distortion is introduced. Causality ensures that the response arises solely from the applied perturbation. Stability implies that the system returns to its initial state after the excitation is removed, and finiteness guarantees bounded impedance values across the measured frequency range.

In summary, EIS provides detailed insight into the interfacial, kinetic, and mass transport processes within electrochemical systems. Its ability to model these systems using equivalent electrical circuits and to resolve overlapping phenomena in the frequency domain makes EIS a cornerstone of modern electrochemical analysis and diagnostics.

# 3 Scalable transfer of high-quality graphene

Mechanical exfoliation is the earliest method for producing graphene. This technique involves physically peeling thin layers of graphene from bulk graphite using adhesive tape [4]. While this method produces high-quality graphene with minimal defects, its scalability is limited, making it suitable mainly for research purposes rather than large-scale production. Despite its limitations, mechanical exfoliation remains a crucial technique for studying graphene's fundamental properties.

Epitaxial growth is another method widely used for graphene synthesis, particularly for producing high-quality graphene layers on silicon carbide (SiC) substrates. This process involves heating the SiC substrate to high temperatures in a vacuum or inert gas environment, causing the SiC molecules to break down and Si atoms to evaporate, leaving behind a graphene layer. Epitaxial growth is notable for producing graphene with minimal defects and excellent electrical properties, making it highly desirable for electronic applications [70].

In this study, we focus on the use of CVD graphene, which offers a balance between scalability and quality, making it a promising candidate for both research and industrial applications.

## 3.1 Chemical Vapor Deposition (CVD)

Chemical vapor deposition is a widely used method in industry for thin film growth [71–73]. Since the discovery of graphene, extensive research has focused on synthesizing large-area, high-quality graphene through CVD [74–76]. In this method, a carbon-source gas is supplied to a heated metal catalyst, where it decomposes, and the released carbon atoms form graphene. Numerous parameters impact the resulting graphene quality, making optimization crucial. Despite these challenges, CVD remains one of the most effective and scalable methods for graphene production.

Graphene films are typically synthesized on metal substrates such as nickel [75] and copper [74, 76]. Nickel or copper-nickel alloys are commonly used for multilayer graphene growth [77], while copper is preferred for monolayer graphene due to its limited carbon solubility at high temperatures. Platinum has also been reported to facilitate monolayer graphene growth [78]. This study emphasizes



Figure 3.1: (a) A schematic overview of the cold-wall low-pressure CVD chamber. The gases are pre-mixed in the shower head and evenly introduced across the copper foil. The copper foil sits just above a graphite Joule heater (to avoid current flowing through Cu). A thermocouple connected directly to the heater measures the temperature. (b) Temperature profile of a typical graphene deposition cycle on copper.

monolayer graphene synthesis on copper foil. Critical growth parameters include temperature, gas flow rates, chamber pressure, annealing duration, and growth time.

Methane is the most widely used carbon source in graphene synthesis. Hydrogen is also crucial during the process, removing amorphous carbon residues [79]. However, excessive hydrogen can degrade graphene's lattice integrity [80]. Balancing the carbon-to-hydrogen ratio is thus essential for optimal graphene quality.

Several factors affect graphene growth, including substrate material, temperature, pressure, and chamber design. Low-pressure CVD (LPCVD) is often preferred, operating between 1 to 1500 Pa, ensuring uniform deposition and minimizing unwanted reactions [81, 82]. Typical synthesis temperatures range from 800 °C to 1050 °C.

In this study, graphene was synthesized on copper (Cu) foils. A schematic of the chemical vapor deposition chamber and a typical temperature profile for the growth process are illustrated in Fig. 3.1a and b, respectively. Prior to growth, the high-purity Cu foil (25  $\mu$ m thick, 99.995%) is cleaned with acetone and isopropanol to eliminate organic contaminants, followed by treatment with acetic acid to remove the native copper oxide. The CVD system used included a coldwall, low-pressure setup equipped with a graphite Joule heater. Temperature control was achieved using a thermocouple in direct contact with the heater. Gas
mixtures were introduced through a quartz shower head for preheating the gases.

The system was first evacuated to a pressure below 0.1 mbar. Then, gases were introduced to achieve a working pressure of 70 mbar. Heating proceeded under 1000 sccm  $H_2$  and 1000 sccm Ar, raising the temperature to 1000 °C at a rate of 300 °C/min. The Cu catalyst was pre-annealed for 15 minutes to increase Cu domain size and stabilize system conditions. Graphene growth began with a methane  $(CH_4)$  flow rate of 30 sccm for 3 minutes to promote nucleation. The  $CH_4$  flow was then increased to 60 sccm for an additional 6 minutes to facilitate growth. For monolayer graphene synthesis, the partial pressure ratio of  $CH_4$  to  $H_2$ typically ranges from 1:100 to 1:5000 [74], requiring extremely low  $CH_4$  flow rates often well below 1 sccm. Such low flow rates are difficult to control using standard mass flow controllers, making the use of diluted  $CH_4$  mixtures essential. In this work,  $CH_4$  diluted to 5% in high-purity Ar (99.9995%) was used. This dilution not only facilitates precise flow control but also slows down the deposition rate, lowers nucleation density, and suppresses the formation of multilayer graphene [83]. The influence of pressure on graphene synthesis is consistent with Le Chatelier's principle. High methane partial pressure, low hydrogen partial pressure, and reduced total system pressure favor rapid carbon deposition and dense nucleation. In contrast, low methane pressure combined with atmospheric pressure supports the slow growth of large, single-crystal graphene domains [74, 84]. Temperature also significantly affects growth dynamics: while elevated temperatures increase the carbon deposition rate, they simultaneously lower nucleation density, ultimately leading to slower overall growth [85].

#### 3.1.1 The challenge of graphene transfer

Many graphene-based technologies require insulating substrates, such as semiconductors and metal oxides, necessitating a subsequent transfer process to relocate the CVD-grown graphene onto the desired substrate for practical applications [22, 86]. Ensuring precise control throughout this transfer process is crucial to preserving the high quality of the as-deposited graphene. Unfortunately, the transfer process often introduces defects such as cracks, wrinkles, residue, and contamination, which compromise the graphene's quality and performance [87].

#### Slow adoption of graphene technology

Since the first successful demonstration of large-scale graphene synthesis via chemical vapor deposition (CVD) in 2009, the field has experienced phases of high optimism, intense competition, ambitious commercial efforts, and some level of disappointment. Despite the abundance of scientific publications focusing on large-scale graphene production and manufacturing technologies, practical applications remain limited. The commercialization of CVD graphene products faces obstacles beyond cost alone; issues related to consistency, reproducibility, and predictability also hinder its widespread adoption. As previously discussed by Kauling et al. [88] and Bøggild [89, 90], variations in material quality have contributed to mistrust in the market, further delaying commercial uptake.

#### The challenge of graphene transfer

One of the most persistent challenges in large-area graphene production is the transfer process. Graphene is typically grown on a catalytic substrate, such as copper, via CVD and subsequently transferred to a target substrate for device fabrication and integration. For graphene to meet expectations in electronics, optics, and barrier applications, the transfer process must be fast, cost-effective, and capable of preserving the remarkable physical properties of the atomically thin carbon sheet.

However, the extreme thinness of graphene makes it highly vulnerable to contamination, wrinkles, and interface roughness, all of which degrade its quality and consistency, posing significant obstacles to practical implementation. Graphene sheets are highly susceptible to cracking under mechanical strain during cleaning or repeated transfer processes, as well as from sharp tools. Such damage negatively impacts graphene's electrical properties and mechanical stability, potentially leading to inefficient performance or failure in practical applications. Moreover, impurities and structural damage complicate the accurate analysis of graphene's structure-property relationships, posing additional challenges for research and development [91, 92].

The impurities include the growth substrate (e.g., copper foil), the etchant used to dissolve the growth substrate (e.g., ammonium persulfate (APS)), and the polymeric support layer, commonly polymethyl methacrylate (PMMA). While PMMA is frequently used, it tends to promote wrinkle formation and produces significant residue [93–96]. Contaminants can adhere to the surface of graphene, altering its interactions with other materials. This is especially problematic in applications where the surface properties of graphene are crucial, such as in sensors. Additionally, charged impurities can scatter charge carriers within graphene, diminishing their mobility and consequently reducing the material's overall conductivity [21, 97]. Unsurprisingly, the graphene transfer process is crucial yet inherently delicate and challenging. Despite the publication of nearly 3000 scientific articles addressing 2D material transfer [89], many claiming partial or complete solutions, the scientific community remains actively engaged in overcoming these challenges.

Various strategies have been proposed to ensure the effective transfer of defectfree graphene while preserving its unique characteristics [98]. Numerous largescale graphene transfer processes have been documented in the literature to address challenges associated with the large-scale transfer of CVD graphene [98–100]. These processes encompass a wide range of techniques, including roll-to-roll methods [23–28], delamination transfer [29], transfer using various carrier polymers [20, 21], laser-assisted transfer [30], electrochemical methods [27], frame-assisted techniques [31], and semi-dry transfer [32]. To the best of our knowledge, very few, if any, of these methods combine simplicity, consistently high carrier mobility, and mechanical flexibility. This scarcity of a comprehensive solution may explain why, to date, no single transfer method has succeeded in establishing itself as a standard, akin to the CVD-synthesis on copper. The cleanest graphene transfer has been achieved in van-der-Waals heterostructures, particularly in graphene sandwiched between h-BN single-crystal flakes using dry transfer techniques [33–36]. Evidently, this technique is not scalable and relies on the availability and quality of other 2D materials.



## 3.2 Graphene transfer by hot-press lamination

Figure 3.2: (a) Process flow for graphene transfer from Cu foil to PET substrate. (b) SEM image of graphene on EVA/PET. (c) AFM images of graphene transferred to EVA/PET. Adopted from Paper I.

The transfer of graphene from copper to Ethylene vinyl acetate (EVA)/Polyethylene terephthalate (PET) was carried out using a hot-press lamination process followed by chemical etching, as shown in Fig. 3.2a. The Cu foil with graphene was laminated onto EVA/PET foil using a standard office laminator and 125  $\mu$ m-thick lamination pouches. The hot-press lamination process ensured strong adhesion of the graphene to the EVA layer by applying uniform heat and pressure across the sample. This method effectively minimized mechanical damage to the graphene layer during transfer.

Following lamination, the Cu foil was etched using 30% nitric acid (HNO<sub>3</sub>), ensuring complete removal of the metal catalyst. The samples were immersed in the acid solution for a sufficient period (ca. 5 mins) to dissolve the Cu layer without compromising the graphene film. After etching, the films were rinsed in deionized water multiple times to remove any acid residues. Finally, the samples were blow-dried and annealed at 60 °C in nitrogen overnight.

This transfer method effectively mitigated contamination issues common with polymer-assisted transfer techniques, which typically introduce polymer residues that impair graphene's electrical properties. The resulting graphene films exhibited improved characteristics, as confirmed by Hall-effect and Raman measurements, which further demonstrated enhanced electrical performance in comparison to traditional transfer techniques.

## 3.3 Electrical characterization and carrier mobility enhancement

Electrical characterization was conducted on  $1 \times 1$  cm<sup>2</sup> samples using resistivity and Hall-effect measurements via the van der Pauw method. The van der Pauw method is particularly convenient for measuring the sheet resistance of transferred CVD graphene films. In the van der Pauw measurements, four contacts are placed at the edges (periphery) of the graphene. A constant current is applied between an adjacent pair of contacts, and the voltage drop is measured between another adjacent pair of contacts. This configuration allows for the measurement of the sheet resistance without the need for a specific geometric shape. The method employs various configurations of current and voltage measurements to enhance accuracy and address any anisotropy in the sample. To further improve precision, measurements are frequently repeated, and the average resistance values are calculated. This approach helps to reduce errors arising from contact resistance and any inhomogeneities within the sample. For a square or rectangular geometry, two sets of measurements (set A and B) are typically performed to account for both vertical and horizontal conduction within the flake.

An average resistance is then calculated for each set (A and B), and the sheet resistance  $(R_{SH})$  and conductivity  $(\sigma)$  are determined using the following relations:

$$e^{-\pi R_A/R_{SH}} + e^{-\pi R_B/R_{SH}} = 1$$
 and  $\sigma = \frac{1}{R_{SH}}$  (3.1)

The Hall-effect measurements were conducted on the same samples to extract the effective carrier concentration (n). This technique involves applying a perpendicular magnetic field to the sample while measuring the resulting Hall voltage.



Figure 3.3: The time dependence of the (a) mobility, (b) carrier concentration n and (c) sheet resistance  $R_{SH}$ , for a few samples transferred to EVA/PET kept at room temperature (black squares) and at 60 °C in nitrogen flow (red dots). The inset: repeated HNO<sub>3</sub> treatment and annealing show mobility drops with HNO<sub>3</sub> (measurements 3, 5, 7) and increases after annealing at 60 °C overnight (measurements 2, 4, 6). Adopted from Paper I.

By combining these two measurements, the charge-carrier mobility  $(\mu)$  was calculated using the expression:

$$\mu = \frac{1}{eR_{SH}n} \tag{3.2}$$

The carrier mobility quantifies how efficiently charge carriers move through the graphene layer under the influence of an electric field, serving as a parameter for evaluating the material's electronic performance. This method allowed for characterization under ambient air and room temperature conditions.

The Hall-effect measurements (Fig. 3.3) revealed that the graphene transferred to EVA/PET initially exhibited low mobility due to the presence of adsorbed dopants and scattering centers induced by the HNO<sub>3</sub>etching of copper. However, annealing the samples at 60 °C under nitrogen flow significantly improved the

mobility. The initial rapid increase in mobility, followed by stabilization, suggests effective desorption of adsorbed molecules. The maximum achieved mobility values, ranging between 7000–8000 cm<sup>2</sup>/(V s), represent a substantial improvement compared to typical polymer-assisted transferred graphene on SiO<sub>2</sub>, which typically shows mobility in the range of 1000 cm<sup>2</sup>/(V s).

Simultaneously, the carrier concentration was observed to decrease with annealing, indicating reduced doping. This trend aligns with the behavior observed in graphene transferred to  $SiO_2$ , where desorption of molecular species upon annealing similarly enhanced mobility [101]. We also conducted control experiments to quantify the reversibility of the HNO<sub>3</sub> treatment on graphene's electrical properties. Three samples were repeatedly treated with HNO<sub>3</sub> and annealed overnight at 60 °C. As seen in the inset of Fig. 3.3b, the mobility drops every time the samples are treated with HNO<sub>3</sub> (measurements 3, 5, and 7) and increases to higher values after annealing at 60 °C overnight (measurements 2, 4, and 6).

## 3.4 Morphological analysis

SEM imaging (Fig. 3.2b) revealed graphene's surface morphology post-transfer, displaying wrinkles, grain boundaries, and multi-layered regions. Despite the presence of these structural imperfections, the annealed samples maintained high mobility, suggesting that these defects did not significantly hinder electrical performance. AFM image (Fig. 3.2c) reveals a rather rough surface morphology of the sample. The surface morphology is inherited by the copper film during the lamination process.

## 3.4.1 Raman spectroscopy

In Raman spectroscopy, the back-scattered light by the sample is detected, and its wavelength and intensity are analyzed. Part of the light has the same wavelength as the incident light. It is attributed to elastic scattering (Rayleigh scattering). The remaining light has different frequencies (higher or lower) than the incident radiation, because its emission involves inelastic scattering of photons [102]. Possible excitations giving rise to Raman scattering are phonons, plasmons, crystal defects, excitons, etc. The Raman spectrum of graphene exhibits three principal characteristic peaks. The G peak, arising from the zone-center  $E_{2g}$  phonon mode, is common to most graphitic materials and represents in-plane vibrational modes. In contrast, the 2D peak originates from a second-order double-resonant scattering process involving zone-boundary phonons [87]. The D peak shares the same phonon modes as the 2D peak but results from a first-order scattering process. Notably, while the D peak is absent in defect-free graphene due to momentum conservation constraints, it becomes Raman-active when structural defects or edges break the lattice symmetry, permitting single-phonon scattering events [103].



Figure 3.4: (a) The Raman spectra of EVA/PET, graphene transferred to EVA/PET, and CVD graphene on Cu. A symmetric and sharp 2D peak for graphene on Cu indicates the presence of single-layer graphene, confirmed by a low intensity of the D peak. (b) Frequency-correlation Raman map. The G and 2D band frequencies are sensitive to strain and doping. The 2D-vs.-G-frequency plot shows the correlation, with strain and doping lines indicating the effects of mechanical and chemical modifications during transfer. Green and red dots represent measurements before and after annealing, respectively. Adopted from Paper I.

The Raman spectra of EVA/PET, graphene transferred to EVA/PET, and CVD graphene on Cu are presented in Fig. 3.4a. For graphene on Cu, the symmetric and sharp 2D peak confirms the presence of predominantly monolayer graphene, as supported by SEM observations (Paper I). The minimal D peak intensity further attests to the high quality of the CVD-grown graphene. Upon transfer to EVA/PET, the characteristic G and 2D peaks of graphene remain detectable, though the D peak becomes obscured due to overlap with an EVA/PET-derived peak. The observed frequency shifts in the 2D and G peaks reflect mechanical and chemical modifications induced during the transfer process.

**Spatial mapping and strain/doping correlations:** Raman mapping was performed to assess spatial homogeneity by collecting 25 spectra across each sample. Fig. 3.4b illustrates the results for graphene on Cu and graphene on EVA/PET (pre- and post-annealing). The G and 2D band frequencies are sensitive to both strain and doping, as described by Lee *et al.* [104]. A vector model

was employed to differentiate these effects (Fig. 3.4b), with strain represented by a slope of  $\sim 2.2$  (uniaxial stress in charge-neutral graphene) and doping by a slope of  $\sim 0.7$  (variations in charge carrier density).

Strain effects from lamination: The frequency-correlation plot shown in Fig. 3.4b reveals that graphene on Cu (blue dots) clusters near the pristine graphene reference point, indicating negligible strain or doping. In contrast, transferred graphene (green and red dots) exhibits a pronounced vertical shift, primarily in the 2D peak frequency, signaling significant tensile strain. This strain arises from the lamination process, where mismatches in the coefficients of thermal expansion between Cu  $(16.6 \times 10^{-6} \,^{\circ}\text{C}^{-1})$ , EVA  $(180 \times 10^{-6} \,^{\circ}\text{C}^{-1})$ , and graphene  $(-1 \times 10^{-6} \,^{\circ}\text{C}^{-1})$  up to 420  $^{\circ}$ C) [93], combined with non-uniform pressure, induce mechanical deformation.

**Doping dynamics and annealing effects:** Spectral data for graphene immediately after HNO<sub>3</sub> etching (green dots) display a blue-shifted G peak, indicative of *p*-doping due to adsorbed oxygen species [104, 105]. Annealing at 60 °C (red dots) reverses this effect, restoring the G peak position to near-pristine values, consistent with desorption of dopants. The 2D peak position remains stable postannealing, confirming that strain is retained while doping is mitigated. These findings align with Hall-effect measurements and XPS data, underscoring the reversibility of HNO<sub>3</sub>-induced doping [101].

#### 3.4.2 XPS analysis

X-ray Photoelectron Spectroscopy (XPS) is a surface-sensitive analytical technique that probes the elemental composition and chemical states of materials by measuring the kinetic energy of photoelectrons emitted under X-ray irradiation. The method, based on the photoelectric effect, provides quantitative information from the top 1-10 nm of a sample surface with a typical energy resolution of 0.1-1.0 eV and lateral resolution down to 10  $\mu$ m. XPS is particularly valuable for characterizing graphene and 2D materials, enabling identification of dopants, oxygen functional groups, and hybridization states through precise measurement of core-level binding energies.

XPS measurements were conducted to quantify the chemical composition changes induced by HNO<sub>3</sub> etching and subsequent annealing (Fig. 3.5). The atomic percentage of carbon increased from 91.6% to 93.6%, while oxygen content decreased from 8.4% to 6.4% after annealing. High-resolution C1s spectra revealed four components through peak deconvolution using a 70% Gaussian-Lorentzian function with Shirley background correction:  $C(sp^2)$  at 283.5 eV,  $C(sp^3)$  at 284.3 eV, C-O at 285.4 eV, and C=O at 288 eV [23]. The area ratios of these components, analyzed using PHI Multipak<sup>TM</sup> software, demonstrated an increase in  $C(sp^2)$  content



Figure 3.5: High resolution XPS narrow scanned spectra in (a) the C1s region (i) before and (ii) after annealing and (b) O1s region of the graphene on EVA/PET sample. Adopted from Paper I.

and a decrease in oxygen-containing functional groups after thermal treatment.

The introduction of oxygen functional groups by  $HNO_3$  treatment was confirmed by both the C1s and O1s spectra (Fig. 3.5). These groups act as *p*-dopants and are predominantly physisorbed [106], explaining their reversible removal during annealing. The C1s main peak shifted to lower binding energy after annealing, consistent with reduced surface doping. This reversible behavior correlates with Hall mobility measurements (Fig. 3.3b inset), where alternating  $HNO_3$  treatment and annealing cycles produced corresponding decreases and increases in carrier mobility.

The observed 2.0% reduction in oxygen content (from 8.4% to 6.4%) after annealing directly corresponds to the removal of oxygen-containing groups, explaining the enhanced Hall mobility. The O1s spectra (Fig. 3.5b) further confirm this reduction in oxygen-containing groups [107]. Since the EVA/PET substrate remains stable at 60 °C, these changes are attributed specifically to modifications of the graphene surface rather than the underlying polymer. These XPS results provide direct evidence that the mobility enhancement stems from decreased surface contamination in the graphene lattice, consistent with the complementary Raman spectroscopy data.

## 4 Graphene field-effect transistor

Field-effect transistors are essential active components found in nearly all electronic devices. The name "field-effect transistor" is derived from the use of the field effect in their operation [108]. This effect enables the control of current flow between the drain and source terminals by applying an out-of-plane electric field at the gate terminal via a gate potential  $V_q$ .

Field-effect transistors, including metal-oxide-semiconductor and high-electronmobility transistor architectures, operate by modulating charge carrier concentration in their conduction channels. GFETs exhibit a fundamentally distinct behavior: the zero-bandgap nature of graphene enables not only carrier density tuning but also dynamic switching between electron- and hole-dominated conduction regimes within the same channel. This ambipolar behavior, arising from graphene's unique electronic structure, provides additional operational flexibility compared to conventional semiconductor-based transistors.

# 4.1 Fabrication of flexible graphene field-effect transistors

An ideal transistor - the fundamental building block of modern electronics should exhibit a high on/off ratio, high carrier mobility, and long-term stability, among other key characteristics [109]. However, inherent material limitations often necessitate trade-offs in device performance. For instance, graphene-based fieldeffect transistors have low on/off ratios, restricting their use in logic applications. Nevertheless, their exceptionally high carrier mobility makes them promising for high-frequency electronics [110].

A notable milestone in electronics has been the successful integration of graphenebased thin-film transistors (TFTs) on flexible substrates. However, achieving stable and reliable device performance requires optimized gate dielectrics. Critical factors include low operating voltages enabled by high- $\kappa$  dielectrics or reduced residual carrier doping, and mechanical robustness under bending conditions [111].

A major challenge in top-gate GFET fabrication on low-melting flexible substrates is the thermal limitation imposed on gate dielectric processing. Since these substrates cannot withstand high temperatures, post-deposition thermal treatments must remain below 100  $^{\circ}$ C, constraining material choices and device optimization strategies. The graphene used in this study was either commercially sourced (Graphenea or Sigma Aldrich) or synthesized in-house using an AIXTRON Black Magic II cold-wall CVD system.



Figure 4.1: Schematic of fabrication process of (a) bottom-gate GFET (b) top-gate GFET. Adopted from Paper II.

#### 4.1.1 Deposition of gate dielectric: Parylene N

We use a commercial coating system (Specialty Coating Systems (SCS)) to deposit Parylene N (180-200 nm thick) on graphene. Detailed Parylene chemistry and deposition mechanism are described elsewhere [112]. In short, to deposit a layer of Parylene N, a few grams of dimer were placed in an aluminum foil. The dimer was vaporized (sublimated) at 130 - 160 °C. The dimer vapors flowed through the pyrolysis furnace at 650 °C where the Parylene N dimer molecules were converted into monomer ones. The monomer vapor entered the chamber, condensed- and self-polymerized at all surfaces, forming Parylene N film. The deposition usually takes about three hours at room temperature.

#### 4.1.2 Fabrication of bottom-gated GFETs

The fabrication process began with the deposition of Parylene N onto CVD-grown graphene on copper foil, which was temporarily attached to a silicon substrate using a thermal-release tape. A 110-nm-thick gate electrode (Ti/Au/Ti = 5/100/5 nm) was then patterned on the Parylene N layer through standard photolithography, electron-beam evaporation, and lift-off processes. The titanium layers were incorporated to enhance the adhesion between the gate electrode and both Parylene N and EVA [113].

Following gate electrode formation, the copper foil was released from the silicon carrier, and the gate/Parylene/graphene/copper stack was laminated onto an EVA/PET substrate using an ordinary office laminator [paper I]. Graphene was subsequently separated from the copper foil via electrochemical delamination in NaOH solution [114]. To protect the graphene from contamination during further processing, the stack was entirely encapsulated with another Parylene N layer.

Electrical contacts were fabricated using a two-layer resist stack (LOR1A and S1813). The graphene edges were exposed by oxygen plasma etching of the top Parylene layer, followed by angled metal deposition  $(45^{\circ})$  with simultaneous sample rotation (5 rpm).

Finally, the graphene channel was patterned into a Hall-bar geometry using photolithography and oxygen plasma etching. Fig. 4.1a illustrates the complete fabrication process for bottom-gated GFETs.

#### 4.1.3 Edge contacts to graphene

Traditional electrical contacts in graphene devices place metal electrodes on top of the flat surface, but graphene's smooth surface doesn't bond strongly with metals, leading to high contact resistance. Edge contacts solve this problem by connecting metal electrodes to the exposed edge of graphene instead, where stronger bonding occurs due to available atomic orbitals [115]. This approach achieves contact resistance as low as 100  $\Omega \cdot \mu m$ , outperforming conventional top contacts.

This advancement is particularly valuable for high-performance graphene electronics, where minimizing resistance and maintaining material quality are essential. The edge contact geometry offers fabrication flexibility by allowing complete graphene encapsulation before contact patterning, thus preventing processing-induced contamination. The edge contacts fabricated in this study exhibited a specific contact resistance of ~6 k $\Omega \cdot \mu m$ , as measured by the transfer line method. This value is significantly higher than the ~100  $\Omega \cdot \mu m$  typically reported for conventional edge contacts [115, 116], likely due to mechanical deformation of the flexible substrate during bending. Experimental details are provided in the supplementary information of Paper II.

#### 4.1.4 Fabrication of top-gated GFETs

For top-gated devices, graphene on copper was first laminated onto EVA/PET substrates. After patterning the graphene into a Hall-bar structure, Parylene N was deposited as the gate dielectric. The subsequent patterning steps mirrored those of the bottom-gated devices. Finally, a 110-nm-thick gate electrode (Ti/Au = 10/100 nm) was patterned on the Parylene N layer using photolithography, e-beam evaporation, and lift-off processes. The fabrication sequence for top-gated GFETs is depicted in Fig. 4.1b.

To prepare devices without a gate, CVD graphene laminated to EVA/PET was shaped into Hall bars using photolithography and oxygen-plasma etching. This was followed by the deposition of metal contacts, followed by lift-off, using a similar electrode stack as before.

## 4.2 Graphene characterization

The structural properties of CVD graphene transferred onto EVA/PET substrates with Parylene N encapsulation were characterized using Raman spectroscopy and scanning electron microscopy (SEM). Three distinct sample configurations were examined (Fig. 4.2a):

- (i) Graphene directly on EVA/PET.
- (ii) Graphene encapsulated between EVA/PET and Parylene N.
- (iii) Graphene on Parylene N laminated to EVA/PET.

#### 4.2.1 Raman spectroscopy analysis

Raman spectra revealed characteristic G and 2D peaks at  $\omega_G = 1585 \text{ cm}^{-1}$  and  $\omega_{2D} = 2635 \text{ cm}^{-1}$  for configurations (i) and (ii), while configuration (iii) showed slightly shifted peaks at  $\omega_G = 1574 \text{ cm}^{-1}$  and  $\omega_{2D} = 2602 \text{ cm}^{-1}$  (Fig. 4.2b). The shifts in the peak positions are attributed to variations in doping levels and strain within the graphene layers [117]. The D-peak was obscured by overlapping vibrational modes from the EVA/PET substrate.

The observed high I(2D)/I(G) intensity ratio and narrow, symmetric 2D peak shape confirm the excellent structural quality of the transferred graphene [87]. Previous studies have established that the full width at half maximum (FWHM) of the 2D peak serves as a sensitive indicator of strain uniformity, with narrower peaks corresponding to more homogeneous strain distributions [118]. Notably, random nanometer-scale strain variations that broaden the 2D peak have been directly correlated with reduced charge carrier mobility in graphene devices, as demonstrated in hBN-encapsulated systems [36].



Figure 4.2: (a) Schematic of the sample preparation. CVD graphene was transferred to the EVA/PET via hot-press lamination. Parylene N was deposited by CVD. (b) Representative Raman spectra of CVD graphene for the schematic shown in panel (a). SEM pictures of CVD graphene on EVA/PET (c) and on Parylene N (d), respectively (the scale bar is 4  $\mu$ m). Adopted from Paper II.

## 4.2.2 SEM characterization

SEM imaging provided complementary morphological information, revealing characteristic features of CVD-grown graphene (Fig. 4.2c,d). Both graphene on EVA/PET and Parylene N substrates exhibited:

- Darker contrast regions corresponding to multilayer patches.
- Clearly visible grain boundaries.
- Typical polycrystalline morphology consistent with copper-grown CVD graphene.

## 4.3 Electrical characterization

## 4.3.1 Hall-effect characterization of GFET devices

Hall-effect mobility measurements were performed using a perpendicular magnetic field of  $B = \pm 0.16$  T in a four-terminal configuration. The sheet resistance  $(R_{SH})$ of graphene was determined by applying a constant current of 1  $\mu$ A between the I+ and I- electrodes and recording the voltage drop between the S and  $D_x$  terminals (see the inset of Fig. 4.3). The Hall resistance  $(R_{xy})$  was obtained by measuring the voltage drop between S and  $D_y$  under the applied magnetic field. To eliminate the longitudinal resistance contribution caused by contact misalignment,  $R_{xy}$  was anti-symmetrized as



Figure 4.3: Hall-effect mobility and carrier density for the top-gated GFETs (top gate), bottom-gated GFETs (bottom gate), and graphene transferred to EVA/PET with no gate (no gate). Solid vertical lines separate the top, bottom, and no gate devices. The dashed vertical lines separate the devices fabricated in different batches. The inset shows optical images of the devices of respective configurations (scale bars are 75  $\mu$ m). Adopted from Paper II.

$$R_{xy} = \frac{R_{xy}(+B) - R_{xy}(-B)}{2}$$

The carrier concentration was calculated using the relation  $n = B/(eR_{xy})$ , and the Hall mobility was derived from

$$\mu_H = \frac{1}{enR_{SH}},$$

where e is the elementary charge.

The average mobilities for top-, bottom-, and no-gate GFETs were  $6300 \pm 1700$ ,  $2900 \pm 500$ , and  $8100 \pm 1100 \text{ cm}^2/(\text{V s})$ , respectively. These values are consistent with the Raman spectroscopy results, where the reduced mobility in bottom-gated devices corresponds with a lower I(2D)/I(G) ratio and broader full width at half maximum (FWHM) of the 2D peak. The lower carrier mobility of bottom-gated GFETs may be attributed to both the material in contact with the graphene (Parylene N vs. EVA/PET) and differences in the fabrication processes. Notably, Parylene N deposited on top of graphene transferred to EVA/PET does not appear to degrade the device performance.

To assess the consistency of our fabrication method, devices were produced in multiple batches (grouped in between by dashed vertical lines in Fig. 4.3). Both commercial graphene and in-house CVD-grown graphene on copper foils with varying surface roughness and thickness were used. Top- and bottom-gated GFETs were fabricated in groups of 2 - 4 devices per batch, depending on the available size of CVD graphene. In-house graphene was synthesized using the Black Magic II cold-wall CVD system (AIXTRON) on  $25\mu$ m-thick, non-polished Cu foils.

The graphene sources for the different batches shown in Fig. 4.3 are as follows:

- Top-gated (T): T1 Graphenea, T2 In-house, T3 and T4 Sigma Aldrich.
- Bottom-gated (B): B1 Graphenea, B2 and B3 Sigma Aldrich.
- No-gate (N): N1 Sigma Aldrich.

The final surface roughness of the GFETs in all configurations was largely inherited from the morphology of the original copper foils. Despite some variation between samples, the overall charge-carrier mobility remained consistently high. It is worth emphasizing that our fabrication technique appears robust and largely insensitive to the initial copper-foil surface morphology, as high mobilities were observed across devices fabricated from various foil sources, which is typically considered a significant parameter as reported by Lin et al. [119].

#### 4.3.2 Field-effect measurements and device characterization



Figure 4.4: Fitting of  $R(V_g)$  experimental curves to extract the field-effect characteristics. (a) A typical plot of the four-terminal resistance of graphene, R, as a function of the gate voltage,  $V_g$ , of the top-gated GFET measured at room temperature and fitted by the model represented by Eq. 1. (b) Forward and backward voltage sweeps for top-gated GFETs with the channel aspect ratio (L/W) = 2 and 4. (c) The field effect mobility as a function of carrier density. The inset shows the optical image of the top-gated GFETs (the scale bar is 75  $\mu$ m)). Adopted from Paper II.

Several key parameters define the performance of a graphene field-effect transistor. While a considerable amount of research has focused on enhancing the field-effect mobility [56, 120, 121], real-world applications demand not only high mobility but also stable and reproducible device operation.



Figure 4.5: (a) The field-symmetrized Hall resistance of the top-gated GFET as a function of the gate voltage, measured at B = 0.157 T and room temperature. (b) The inverse of the Hall resistance as a function of the gate voltage. The red line is a linear fit. (c) The extracted Hall-mobility as a function of the gate voltage. Adopted from SI of Paper II.

Fig 4.4a displays the four-terminal resistance as a function of gate voltage  $(V_g)$ , along with a fit based on the modified model proposed by Kjell et al. [122], expressed by:

$$R_{\text{total}} = \frac{1}{k\sqrt{n_0^2 + n(V_q)^2}} + \frac{\theta}{k} + R_{co}, \qquad (4.1)$$

where  $k = (W/L)\mu_0 C_{\text{ox}}$  is the transconductance parameter,  $n_0$  is the residual charge-carrier density at the Dirac point,  $\mu_0$  is the long-range Coulomb scatteringlimited mobility, and  $\theta$  accounts for mobility degradation at high carrier densities. The channel width and lengths were  $W = 75 \ \mu\text{m}$ , and  $L = 150 \ \mu\text{m}$  and 300  $\ \mu\text{m}$ , corresponding to aspect ratios of L/W = 2 and 4. The term  $n(V_g)$  represents the gate-induced charge-carrier density, e is the elementary charge, and  $C_{\text{ox}}$  is the gate capacitance per unit area for a 200-nm-thick Parylene N dielectric layer with a relative permittivity  $\varepsilon_r = 2.65$ . The contact resistance  $R_{co}$  represents the sum of the source and drain contact resistances, including access regions not covered by the top gate. All resistance measurements were performed in a four-terminal configuration, rendering  $R_{co} = 0$ . The term  $\theta/k$  plays the role of an effective contact resistance, which was often needed to get a better fitting of experimental transfer curves, even in the four-probe measurements.

The value of  $C_{\text{ox}}$  was extracted from gate-dependent Hall-effect measurements conducted under a perpendicular magnetic field of |B| = 0.16 T. The Hall resistance  $(R_{xy})$  was measured for both positive and negative field orientations and anti-symmetrized according to  $R_{xy} = [R_{xy}(+B) - R_{xy}(-B)]/2$  to eliminate spurious longitudinal contributions arising from contact misalignment (see Fig 4.5a). The carrier density is given by  $n = B/(eR_{xy}) = C_{\text{ox}}(V_g - V_{\text{Dirac}})/e$ , enabling a direct extraction of  $C_{\text{ox}}$  from the linear fit to  $1/R_{xy}$  as a function of  $(V_g - V_{\text{Dirac}})$ (Fig 4.5b). For the top-gate GFET, we estimate  $C_{\text{ox}} = 11.9 \text{ nF/cm}^2$ , which aligns with the calculated value for a 200-nm-thick Parylene N dielectric layer. The gate-dependent Hall mobility exhibits a clear dependence on  $V_g$  (or n), especially away from the charge neutrality point. Fig. 4.4b presents the transfer curves and the extracted parameters  $n_0$  and  $\mu_0$  for devices with two channel lengths (inset of Fig. 4.4c). Forward and backward gate sweeps show negligible hysteresis, indicating the device's stability. Fig. 4.4c shows the extracted hole mobility as a function of carrier density  $n = \frac{C_{\text{ox}}}{e} \sqrt{n_0^2 + n(V_g)^2}$ , fitted using:

$$\mu = \frac{\mu_0}{1 + n/n_{\rm ref}},\tag{4.2}$$

where  $n_{\rm ref} = C_{\rm ox}/(e\theta)$  denotes the characteristic carrier density at which the mobility is reduced to half of its zero-density value  $\mu_0$ .



Figure 4.6: (a) Transfer characteristics of the top- and back-gated GFETs. (b) Drude mobility vs. charge carrier density for the top- and bottom-gated GFETs. (c) and (d) Procedure to extract  $n^*$  from the log-log  $\sigma(n)$  plots. Adopted from Paper II.

Figure 4.6a presents  $R(V_g)$  at room temperature for both top- and bottomgated GFETs. The devices were identical in size ( $W = 75 \ \mu \text{m}$  and  $L = 150 \ \mu \text{m}$ ), with Parylene N gate insulators of thickness 200 nm (top-gated) and 120 nm (bottom-gated). From the model fits in Fig. 4.4a, we extract  $\mu = 2200 \ \text{cm}^2/(\text{V s})$ for bottom-gated devices and  $\mu = 8100 \ \text{cm}^2/(\text{V s})$  for top-gated devices. These values show good agreement with the corresponding Hall mobilities ( $\mu_H = 3000 \ \text{and} 6700 \ \text{cm}^2/(\text{V s})$ , respectively), further validating our extraction approach.

Notably, an asymmetry between the p- and n-branches of the transfer curves for bottom-gated GFETs is observed. This behavior may stem from differing scattering cross-sections of electrons and holes on charged impurities [124, 125], potentially introduced during fabrication or through environmental exposure. Figure 4.6b depicts the carrier density dependence of the mobility, calculated according to the Drude model as  $\mu_D = \sigma/(nq)$ , where  $\sigma$  is the electrical conductivity. At high carrier densities,  $\mu_D$  may degrade due to enhanced momentum relaxation caused by supercollision processes involving lattice defects [126].



Figure 4.7: Mobility versus disorder-induced charge-carrier density  $n^*$  in graphene samples. Field- (solid squares) and Hall-effect (empty squares) mobilities for the top (square) and bottom (circles) gated GFETs. Different colors refer to the field- and Hall-effect mobilities of different devices. The dashed line corresponds to the model in [123], which describes the inverse proportionality between  $\mu$  and  $n^*$ . Adopted from Paper II.

Another metric is the disorder-induced residual carrier density  $n^*$ , which reflects the strength of potential fluctuations experienced by carriers. This parameter is extracted by plotting  $\sigma(n)$  on a double logarithmic scale, as shown in Fig. 4.6c and d. Fig. 4.7 presents the correlation between mobility and  $n^*$ , comparing both  $\mu_0$  (solid symbols) and  $\mu_H$  (open symbols). A consistent inverse relationship  $\mu \propto 1/n^*$  is observed across all devices, in agreement with earlier findings [123]. Overall, these results confirm that our fabrication method yields GFETs with significantly improved mobility and reduced charge inhomogeneity compared to conventional wet-transferred devices on Si/SiO<sub>2</sub> substrates. Additionally, our devices exhibit excellent long-term stability when stored under ambient conditions or a nitrogen atmosphere (see Supplementary Information of Paper II).

#### 4.3.3 Quantum Hall-effect

To further assess device quality, we performed magnetotransport measurements. Fig. 4.8 presents the longitudinal resistance  $(R_{xx})$  and Hall resistance  $(R_{xy})$  as functions of the magnetic field (B), revealing clear signatures of the quantum Hall effect (QHE): a vanishing  $R_{xx}(B)$  and the appearance of a plateau in  $R_{xy}(B)$ 



Figure 4.8: Quantum Hall effect observed (a) in the top-gated GFET and bare graphene transferred to EVA/PET measured at 2 K and (b) at different temperatures for graphene on EVA/PET. The top and bottom horizontal dashed lines represent the resistivity values of 12941  $\Omega$ - and 0  $\Omega$ , respectively. Adopted from Paper II.

in a certain range of  $B > B_{\text{onset}} = 5 - 6$  T.

For the top-gated GFETs at  $V_g = -6$  V and 2 K, we observed QHE onset ( $\nu = 2$ ) below 5 T (Fig. 4.8a). The devices on EVA/PET substrates showed slightly lower onset fields (~4 T). Remarkably, these QHE features persisted up to 100 K in EVA/PET-supported devices (Fig. 4.8b), although with imperfect quantization where  $R_{xy} \neq h/(2e^2)$  and  $R_{xx} \neq 0$ . This behavior aligns with previous reports of disorder effects in CVD graphene, attributed to grain boundaries and multilayer patches [127]. Notably, this represents the first observation of QHE in graphene on flexible polymer substrates. Our devices exhibit two significant advantages:

- Large-scale uniformity (250  $\mu$ m channel length).
- Comparable quality to hBN-encapsulated devices.

The successful observation of QHE in these macroscopic flexible devices suggests exceptional material quality and uniformity, particularly given that our channel dimensions are an order of magnitude larger than typical hBN-encapsulated structures showing similar effects [36, 128, 129].

## 4.4 Terahertz time-domain spectroscopy

The terahertz (THz) frequency range, spanning from 0.3 to 30 THz, corresponds to photon energies between approximately 1 and 100 meV (where 1 THz  $\equiv$  4.1 meV) and electromagnetic field oscillation periods ranging from about 3 ps to



Figure 4.9: Schematic of the THz time-domain spectroscopy setup (a) transmission mode, and (b) reflection mode.

30 fs. These characteristic timescales directly match the fundamental dynamics of charge, lattice, and spin subsystems in condensed matter systems, making THz spectroscopy [130] uniquely suited for investigating phenomena in the regime where  $\omega \tau \sim 1$ , with  $\omega$  representing the electromagnetic wave oscillation frequency and  $\tau$  the characteristic timescale of the elementary processes under study. This capability has enabled significant advances in understanding diverse ultrafast phenomena, including carrier transport dynamics [131], lattice vibrations [132], and strongly correlated electron systems [133].

Ultrafast THz spectroscopy operates through the generation of ultrashort, broadband (typically single-cycle) THz pulses produced by nonlinear down-conversion of femtosecond laser pulses. A key advantage of this technique lies in its direct measurement of the THz electric field, including both amplitude and phase, in the time domain. Fourier transformation of these time-domain signals, measured before and after interaction with the sample, yields the material's complex dielectric function (or equivalent representations such as conductivity or refractive index spectra) across the full THz bandwidth, with sub-picosecond temporal resolution determined by the THz pulse duration. While conventional THz spectroscopy typically employs field strengths below 1 kV/cm to maintain linear response conditions, recent technological advances [134] have enabled nonlinear THz spectroscopy [135] through the generation of intense THz fields exceeding 100 kV/cm. In standard experimental configurations, THz radiation is focused onto the sample with the transmitted or reflected pulse detected (as shown in Fig. 4.9). Given that THz frequencies correspond to sub-millimeter wavelengths, samples must typically exceed several square millimeters in area to overcome diffraction limitations.

#### 4.4.1 Terahertz time-domain spectroscopy system

A Terahertz time-domain spectroscopy (THz-TDS) system manufactured by Toptica (Germany) was employed to construct a THz mapping system. The system generates pulsed terahertz radiation using femtosecond lasers operating at 1.5  $\mu$ m wavelength and InGaAs-based photoconductive switches that function as both THz emitter and detector. Two polyethylene lenses focus the emitted and detected THz radiation onto the samples, achieving a spot size of approximately 600  $\mu$ m. The mapping system incorporates a two-dimensional moving stage with positioning accuracy down to 2.5  $\mu$ m.

The complex transmission coefficient  $t(\omega)$  is obtained through the ratio of Fourier-transformed time-domain signals:

$$t(\omega) = \frac{E_s(\omega)}{E_r(\omega)} \tag{4.3}$$

where  $E_s(\omega)$  and  $E_r(\omega)$  represent the sample and reference signals in the frequency domain, respectively. The complex conductivity  $\sigma$  of graphene is then calculated from the complex transmission using:

$$\sigma = \frac{n_{\rm sub} + 1}{Z_0} \left(\frac{1}{t_f} - 1\right) \tag{4.4}$$

Here,  $n_{\rm sub}$  denotes the substrate refractive index and  $Z_0 = 377 \ \Omega$  is the impedance of free space.

The DC conductivity  $\sigma_{\text{DC}}$ , carrier density n, and mobility  $\mu$  are extracted by fitting the frequency-dependent conductivity to the Drude model:

$$\sigma(\omega) = \frac{\sigma_{\rm DC}}{1 - i\omega\tau} \tag{4.5}$$

where the DC conductivity and mobility are given by:

$$\sigma_{\rm DC} = \frac{e^2 v_F \sqrt{n}}{\hbar \sqrt{\pi}} \tau, \quad \mu = \frac{e v_F \tau}{\hbar \sqrt{n\pi}} \tag{4.6}$$

In these expressions,  $\tau$  represents the scattering time and  $v_F \approx 1 \times 10^6$  m/s is the Fermi velocity of graphene.



#### 4.4.2 THz-TDS measurement

Figure 4.10: Different sample structures of CVD graphene transferred to (a) EVA/PET, (b) CVD graphene transferred on Parylene N, and (c) CVD graphene encapsulated in Parylene N. (d-f) Corresponding THz DC conductivity maps. (g-i) Corresponding histograms of the charge-carrier mobility. The black dashed boxes in the maps represent the areas from which mobility histograms were extracted. Adopted from paper II.

Measurements were performed using a fiber-coupled TOPTICA Teraflash Pro spectrometer system, whose detailed description can be found in previous work [136]. In transmission mode operation, samples were raster-scanned with 200  $\mu$ m steps in the focal plane between emitter and detector, generating spatial conductivity maps with a spot size of approximately 0.3 mm at 1 THz. This approach enabled the extraction of DC conductivity, charge carrier mobility, and density across cm<sup>2</sup>-scale graphene films. Three sample configurations were prepared for THz-TDS analysis, as illustrated in Fig. 4.10a-c: (1) CVD graphene transferred to EVA/PET, (2) graphene on Parylene N, and (3) graphene encapsulated in Parylene N.

The frequency-dependent sheet conductivity  $\sigma_s(\omega) = \sigma_1 + i\sigma_2$  was calculated at each map position using the transmission function:

$$T_{\rm film}(\omega) = \frac{1 + n_{sub}}{1 + n_{sub} + Z_0 \sigma_s(\omega)} \tag{4.7}$$

where  $n_{sub}$  represents the substrate refractive index and  $Z_0$  denotes the vacuum impedance [136, 137]. The measured conductivity spectra were fitted with the Drude model, using  $\sigma_{DC}$  and scattering time  $\tau$  as fitting parameters [136]. Within the framework of semiclassical transport theory [138], we derived carrier density and mobility following the methodology described in [136].

Our THz-TDS results showed good agreement with conventional Hall and fieldeffect measurements, consistent with previous comparative studies on CVD graphene [136, 139, 140]. The slightly higher mobility values obtained via THz-TDS likely stem from sample-to-sample variations and the absence of photolithographic processing for THz-characterized samples, which typically introduces contamination that degrades transport properties.

Notably, Parylene N-encapsulated samples exhibited threefold higher chargecarrier mobility compared to their non-encapsulated counterparts. This enhancement demonstrates the effectiveness of encapsulation in providing long-term stability against environmental factors [141] while offering mechanical protection. The achieved mobility values surpass those reported for other scalable encapsulation approaches, including atomic layer deposition [120].

The conductivity maps and corresponding mobility histograms (Fig. 4.10d-i) reveal uniform electrical properties across the measured areas, with histograms derived from data within the dashed rectangular regions in Fig. 4.10d-f.

# **5** Graphene sensors

Graphene exhibits good potential as a sensing material due to its unique charge carrier transport properties. While its mechanical stability primarily arises from in-plane  $\sigma$ -bonds, carrier transport is facilitated by the  $\pi$ -bonds located above and below the carbon lattice. These  $\pi$ -bonds, which govern graphene's electrical characteristics, are highly responsive to environmental changes, enabling effective transduction—the conversion of chemical signals into electrical ones. The exposed  $\pi$ -bonds provide intrinsic sensitivity to external stimuli, and as an all-surface material, graphene has demonstrated extreme sensitivity, even achieving singlemolecule detection [142, 143].

Beyond its sensing capabilities, graphene's electrical, chemical, mechanical, and optical properties further enhance its suitability for chemical and biological sensing applications. Electrically, graphene exhibits remarkable room-temperature charge carrier mobilities exceeding 50000 cm<sup>2</sup>/(V s), enabling high-speed, high-transconductance sensors [144]. Chemically, graphene's stability allows direct interfacing with electrolytic environments common in biological and chemical sensing, while leveraging the ultrahigh capacitance of electric double layers [145]. It also possesses a wide electrochemical potential window of ~2.5 V in various electrolytes, including physiologically relevant solutions like phosphate-buffered saline [146].

## 5.1 Electrolyte-gated GFET

In electrolyte-gated field-effect transistors (EGFET), the dielectric material separating the gate electrode from the conductive channel consists of an electrolyte (Fig. 5.1a). Electrolytes fundamentally differ from conventional dielectrics in FET operation through their gating mechanism and physical characteristics. Where dielectrics provide electrostatic control via capacitive coupling, electrolytes form electric double layers (EDLs) through mobile ion migration. The structure of a graphene EGFET includes a graphene channel situated between two conductive source and drain electrodes. A portion of the graphene is exposed to the external environment either directly or through surface-functionalization, allowing environmental stimuli to influence the doping level of the graphene. This, in turn, modulates the conductivity of the device. To monitor this conductivity change, graphene EGFETs are integrated with electronic readout systems that



Figure 5.1: (a) Schematic of electrolyte-gated GFET, where gating is achieved via electric double layers formed at the gate-electrolyte and electrolyte-channel interfaces. (b) Carrier density tuning in graphene. Resistance versus gate voltage curves show a shift in the Dirac point after analyte exposure, indicating molecular adsorption.

translate electrical signals into quantifiable information about the surrounding environment. A typical layout of a graphene EGFET is illustrated in Fig. 5.1a.

Upon application of a gate voltage  $(V_g)$ , the electrolyte experiences migration of ionic species according to their polarity: anions (-q) drift toward the positive terminal while cations (+q) move toward the negative terminal. This ionic redistribution creates two spatially separated charge accumulation regions. At the gate-electrolyte interface, the accumulated ions form a screening layer that neutralizes charges on the metal electrode. Simultaneously, at the electrolyte-sample interface, the counterions generate an electric field that induces charge carrier accumulation in the material's surface layer. These two parallel charge separation phenomena, known as electric double layers, operate through similar mechanisms but at distinct interfaces. The formation of EDLs at both interfaces represents the fundamental operating principle of electric double layer transistors (EDLTs), with the nanometer-scale charge separation distance enabling exceptionally high effective gate capacitance.

The formation and properties of EDLs have been extensively investigated both via theoretical [58–61] and experimental [147] approaches. EDLs represent a universal phenomenon occurring at all solid-fluid interfaces. When considering electrolytes as ionic fluids, it becomes apparent that a solid surface's inherent charges can attract ions from the electrolyte even in the absence of an applied potential, resulting in a spontaneous EDL formation. However, such intrinsic double layers typically exhibit weak charge separation, and significant charge accumulation at the electrolyte-solid interface generally requires application of an external voltage.

Fig. 5.1b illustrates the transfer characteristics of a graphene-based electrolyte-

gated field-effect transistor, showing resistance as a function of gate voltage before (blue curve) and after (red curve) exposure to analytes. The red curve exhibits a shift in the Dirac point and a change in resistance ( $\delta R$ ), indicating that molecular adsorption alters the electronic properties of the graphene channel, likely through charge transfer and increased scattering. The smaller  $n_0$  suggests that a GFET with a lower residual carrier concentration would exhibit a sharper and more symmetric transfer curve. This reflects reduced intrinsic doping and improved electrostatic gating, which are desirable for enhancing sensor sensitivity and resolution.

For biomolecule detection, the graphene channel is typically functionalized with specific receptors and left directly exposed to the test solution. This configuration facilitates direct interaction between the graphene surface and target species such as biomarkers, nucleic acids, proteins, or viruses. When these biomolecules bind to the receptors on the graphene, they influence both the electrical double-layer capacitance at the interface and the intrinsic electronic properties of graphene. This interaction modulates the carrier density in the channel, resulting in measurable changes in conductivity. Although pristine graphene lacks inherent selectivity, surface functionalization with appropriate receptors imparts specificity, enabling the selective detection of target biomolecules.

#### 5.1.1 Mechanism of the GFET biosensor

The graphene FET sensing mechanism involves changes in graphene conductivity, governed by the relation  $\sigma = \mu C(V_{\rm g} - V_{\rm Dirac})$ . In electrostatic gating, the binding of a target analyte to an insulating surface layer alters the local gate potential. This causes a shift in the transfer curve [148]. The direct adsorption of target analytes onto the graphene surface results in a direct charge transfer between the analyte and the graphene, which alters its electrical conductivity. However, this method suffers from limited selectivity between different molecules.

Graphene conductance can also be modulated through changes in gate capacitance. When sensing layers are deposited on the graphene, they alter the local permittivity (or dielectric constant), which affects the gate capacitance [149]. Additionally, sensing can be achieved through the variation of carrier mobility. The mobility of charge carriers in graphene can vary due to changes in scattering by charged impurities, and surface-adsorbed analytes can screen these impurities, thereby affecting mobility. In addition, we should note during the actual test that the pH value of the test solution and the ion concentration can also regulate the position of the Dirac point [8, 150].

#### 5.1.2 State-of-the-art

Most GFET biosensors rely on liquid-gate transistor configurations, where an electrochemical gate modulates charge transport in an aqueous environment. Biosensing relies on shifts in the charge neutrality point (CNP), induced by molecular adsorption. However, the precision of detection is often hindered by hysteresis (charge trapping), time drifts, and asymmetric transfer curves [40–42]. Additionally, analyte adsorption introduces scattering centers that modify transconductance and increase disorder in the system [43, 44].

Real-time biosensing using GFETs typically involves monitoring drain-source current or resistance over time at a fixed  $V_g$ . The optimal response occurs in hightransconductance regions [151], but this also amplifies low-frequency noise, which degrades sensitivity [152, 153]. Furthermore, a baseline drift remains a major challenge in GFETs even in the absence of target molecules [154–156]. Traditional methods often assume constant interfacial capacitance and carrier mobility, yet biomolecular interactions with graphene can induce charge-carrier scattering that suppresses mobility [157], while molecular adsorption alters interfacial capacitance [158], complicating accurate sensing. Practical sensor designs must also account for interfacial capacitance variations upon biomolecular adsorption [158].

## 5.2 Complementary impedance spectroscopy method

We demonstrate that using an AC bias enhances biosensor sensitivity and accuracy by simultaneously capturing both resistance and capacitance changes during biomolecular interactions. Unlike traditional methods that focus solely on DC conductivity, our approach utilizes a low-frequency lock-in method to extract the full AC impedance, including reactance. The reactance carries information about the capacitances involved in the measurements. This approach, employing AC bias with low-frequency lock-in detection, provides comprehensive information about dynamic charge transport and electrostatic interactions, directly accessing the series combination of three key capacitances: quantum capacitance  $(C_q)$  [159–161], electrical double-layer capacitance  $(C_{dl})$  [158, 162], and functional layer capacitance  $(C_f)$ . This approach addresses key limitations of conventional DC measurements while providing enhanced sensitivity to biomolecular interactions.

The quantum capacitance, governed by carrier density and Fermi level tuning, can be important in biosensing [163–166]. Analyte adsorption alters graphene's carrier density, leading to measurable shifts in Fermi energy and quantum capacitance [45, 148, 160, 161, 167, 168]. Previous studies relied on buried gate electrodes under high-k dielectrics for quantum capacitance measurements [160, 167]. These architectures, however, complicate fabrication and limit scalability. Our approach eliminates the need for high-k dielectrics, enabling quantum and EDL capacitance measurements using a conventional liquid gate electrode, thus simplifying fabrication while maintaining high sensitivity.

By capturing the full AC impedance, our method enables a more comprehensive characterization of biomolecular interactions at the GFET surface. This approach enhances sensing precision, suppresses noise, and enables real-time biosensing, offering a significant advantage over conventional GFET-based biosensors while maintaining a simplified, scalable device architecture.



## 5.3 GFET sensor fabrication

Figure 5.2: (a) Process flow for graphene transfer from Cu foil to EVA/PET substrate, (b) functionalization, and (c) electrical measurement set-up. Adopted from Paper III.

We report the development of an antibody-functionalized graphene field-effect transistor biosensor that combines the molecular recognition specificity of human prostate-specific antigen (PSA) antibodies with the high sensitivity of graphenebased detection. This biosensing platform enables label-free, rapid, and selective detection of PSA antigens.

Fabrication proceeds through multiple stages of conventional microfabrication processes, followed by surface functionalization via non-covalent attachment of molecular linkers to the graphene surface through  $\pi$ - $\pi$  stacking interactions [169] (Fig. 5.2b). Subsequent immobilization of PSA antibodies is achieved using carbodiimide cross-linking chemistry [170]. To ensure high detection specificity, the graphene surface undergoes additional passivation steps using amino-PEG5 alcohol and ethanolamine hydrochloride to minimize nonspecific adsorption [171, 172]. The GFET fabrication process begins with monolayer graphene grown by chemical vapor deposition on copper foil. This CVD graphene is transferred onto an EVA/PET flexible substrate using hot-press lamination, with pre-patterned electrodes (current-bias, voltage, and gate electrodes) Ti (10 nm)/Au (50 nm) already deposited on the substrate. The copper foil is subsequently removed through wet etching in a diluted nitric acid solution (10% HNO<sub>3</sub> in water).

Following the transfer process, the graphene layer is patterned using standard photolithography techniques and oxygen plasma etching (Fig. 5.2a). To complete the device assembly, a short piece of plastic tube is affixed to the GFET chip using epoxy adhesive, creating a well around the graphene channel for liquid handling during measurements.

#### 5.3.1 Functionalization

The device functionalization was a two-step process combining molecular linker deposition and biological reagent immobilization. Initially, GFET devices were functionalized with 1-pyrenebutanoic acid succinimidyl ester (PBASE) as the molecular linker. Devices were incubated in a 5 mM PBASE solution (in dimethyl-formamide, DMF, Sigma-Aldrich) for 2 hours at room temperature, followed by rinsing with DMF to remove unbound PBASE molecules and blow-drying in nitrogen.

For antibody conjugation,  $30-\mu$ L of Human KLK3/PSA antibody solution (1 mg/mL, Sigma-Aldrich) were applied to the PBASE-functionalized chips and incubated overnight at 4 °C in a humidified environment. Post-incubation, chips were rinsed with deionized water and dried under nitrogen flow. To minimize nonspecific binding, a dual blocking strategy was implemented using:

- 3 mM amino-PEG5-alcohol (Broadpharm, P-22355).
- 3 M ethanolamine hydrochloride (ETA, Sigma-Aldrich).

The blocking procedure involved applying  $30-\mu L$  droplets of each blocking agent sequentially, with 1-hour incubations at room temperature, followed by DI water rinsing and nitrogen drying. Fig. 5.2b illustrates the completed functionalization scheme, showing both the PBASE linker and the PSA antibody successfully anchored to the graphene channel surface.

## 5.4 Electrical measurements

Electrical characterization was performed using a four-probe configuration in  $0.001 \times PBS$  solution to minimize charge screening effects [173]. The measurement system, illustrated in Fig. 5.2c, employed an AC bias voltage ( $V_{\rm b} = 250$  mV at f = 137 Hz) applied through a 1 M $\Omega$  current-limiting resistor to establish a nearly

constant current of  $I_{\rm b} \approx 250$  nA. A Keithley 2604B source meter supplied the DC liquid-gate voltage relative to the current-bias electrode, while a Stanford Research Systems SR830 lock-in amplifier simultaneously recorded both in-phase (X) and quadrature (Y) components of the  $\times 100$  preamplified voltage. For transfer curve measurements, the GFET well was filled with 200  $\mu$ L of 0.001×PBS solution and allowed to stabilize for five minutes before initiating gate voltage sweeps at 10 mV/s, with three consecutive hysteresis-free cycles recorded before and after analyte introduction. Time-series measurements were conducted with the graphene channel biased at its peak transconductance voltage, continuously monitoring Xand Y components during baseline stabilization, analyte introduction (10  $\mu$ L), and subsequent signal stabilization. Between measurements, the system underwent rinsing and refilling with fresh  $0.001 \times PBS$  solution, with the same  $V_{\rm g}$  and  $I_{\rm b}$  as before. All analytes were prepared in 0.001×PBS to maintain consistent pH conditions, with DC measurements performed using the Keithley 2604B source while monitoring V with an HP-34401 multimeter. For frequency-dependent timeseries measurements, the frequency was swept while simultaneously recording the X and Y components, allowing frequency-dependent characterization before and after analyte introduction.

## 5.5 Model



Figure 5.3: Simple model of a liquid-gate biosensor with resistive thin film including the Randles equivalent circuit of the electrochemical cell. C is the effective capacitance of the double layer plus the layer of functional molecules (for graphene, also including its quantum capacitance).  $R_c$  is the charge transfer resistance of the double layer,  $R_s$  is the resistance of electrolyte, and R is the thin-film- or graphene resistance. Adopted from Paper III.

While DC resistance measurements of graphene effectively detect charge redistribution caused by analyte binding in the bio-functional layer, AC measurements offer the additional capability of probing capacitance changes in adjacent layers. This principle extends beyond graphene to any sufficiently thin conductive film with high resistivity (several  $k\Omega$ ), such as NiCr or TaN. It has long been established that variations in the capacitance of the functional layer can detect very small concentrations of analytes using the EIS method [68, 174].

The liquid-gated GFET can be modeled using a distributed Randles equivalent circuit (Fig. 5.3) [68, 69], comprising resistive and capacitive components. A simplified circuit element analysis reveals three key resistances: the solution resistance  $(R_s)$ , charge transfer resistance  $(R_c)$ , and graphene's in-plane resistance (R). Graphene's wide electrochemical window in electrolytes leads to exceptionally high  $R_c$  values  $(R_c \gg R, R_s)$  [146], allowing this component to be neglected. The use of highly diluted buffer (0.001x PBS) ensures  $R_s$  remains significant, with  $R_s \ge R$  under typical measurement conditions.

The graphene-electrolyte interface capacitance arises from three series components: first, the electrical double-layer capacitance  $(C_{dl})$  representing polarized electrode surface ions; second, the bio-functional layer capacitance  $(C_f)$ accounting for antibodies and blocking molecules; and third, the quantum capacitance  $(C_q)$ . Under typical biosensing conditions, the capacitance hierarchy  $C_{dl} \sim C_q \gg C_f$  reduces the total capacitance to  $C \sim C_f$ . For the case where  $R_c = \infty$  and  $R = \epsilon R_s$  with  $\epsilon \ll 1$ , the voltage components across R are given by:

$$X = \frac{\epsilon R_s \left[ 1 + C^2 R_s^2 \omega^2 (1 - \epsilon/2) \right]}{(1 + C^2 R_s^2 \omega^2)}$$
(5.1)

$$Y = -\frac{CR_s^2\epsilon^2\omega}{2(1+C^2R_s^2\omega^2)}$$
(5.2)

These relationships yield an analytical metric through the ratio  $Y/X^2$ , which at low frequencies  $(C^2 R_s^2 \omega^2 < 1)$  simplifies to:

$$\frac{Y}{X^2} = -\frac{C\omega}{2(1+C^2R_s^2\omega^2)} \to -\frac{C\omega}{2}.$$
(5.3)

This metric offers several advantages for biosensing applications, including enabling low-frequency operation with cost-effective electronics, immunity to baseline resistance drifts common in DC measurements, and insensitivity to doping variations caused by environmental factors like pH fluctuations. The pH stability is particularly noteworthy, as even buffer solutions exhibit pH variations with changing ionic strength and temperature [175], making the  $Y/X^2$  ratio a robust measurement parameter that directly probes functional layer capacitance while overcoming many limitations of traditional DC measurements.

#### 5.6 Lock-in measurements

Our lock-in measurements revealed distinct roles for the X and Y components in characterizing GFET response. The X component primarily tracked changes



Figure 5.4: (a) Transfer curves and corresponding (b) time series measurements at  $V_{\rm g}$  -0.05 V and -0.2 V of an PSA antibody functionalized GFET. The red arrows represent the intervals at which 10  $\mu$ L analyte of varying concentration prepared in 0.001X PBS is dropped on GFET sensors containing 200  $\mu$ L 0.001X PBS. Adopted from Paper III.

in graphene channel resistance induced by gate voltage tuning of carrier concentration, while the Y component captured capacitance variations between the liquid gate and graphene channel arising from quantum capacitance and double layer effects. Fig. 5.4a demonstrates these measurements before and after analyte introduction, showing characteristic shifts in both components that indicate modifications to the GFET's electrical properties.

The X component shift reflects alterations in graphene channel resistance due to charge transfer processes initiated by analyte binding [176], which modifies carrier density and shifts the Dirac point. This manifests as resistance changes at fixed  $V_g$ . The Y component shift encompasses changes in the effective capacitance C, driven by multiple mechanisms: quantum capacitance variations [164, 166, 167], electric double layer modifications [68, 158, 162], and local dielectric constant changes as analytes displace water molecules or introduce dipoles [177]. While these effects collectively influence  $C_q$ ,  $C_{dl}$ , and  $C_f$ , the functional layer capacitance  $C_f$  appears dominant in our devices due to its relatively smaller magnitude compared to the other capacitance components.

The more pronounced Y shifts observed in Fig. 5.4a suggest a strong capacitive contribution to the sensing response. To better quantify this effect, we analyzed the metric  $\gamma \equiv Y/X^2$  versus  $V_g$ , which effectively isolates capacitive effects from resistive contributions (see Eq. 5.3). Remarkably,  $Y/X^2$  remains nearly constant across the entire  $V_g$  range, unlike the strongly nonlinear  $X(V_g)$  and  $Y(V_g)$ dependencies. This stability makes  $\gamma$  particularly effective for detecting subtle biomolecular binding effects, offering superior performance for biosensing applications compared to conventional approaches.

Time-series measurements at fixed  $V_g$  (peak transconductance points) further validated this metric's advantages. As shown in Fig. 5.4b, analyte introduction at various concentrations (marked by red arrows) produced distinct responses in X, Y, and  $Y/X^2$ , normalized to the values at t = 0, i.e.,  $\Delta X/X_0 = (X - X_0)/X_0$ , where  $X_0 = X(t = 0)$ , etc. While X exhibited significant baseline drift that obscured analyte responses,  $Y/X^2$  demonstrated stronger response signals, higher signal-to-noise ratio (SNR), and minimal  $V_g$  dependence. These characteristics ensure reliable, consistent detection across different operating conditions, establishing  $Y/X^2$  as a robust sensing parameter that overcomes key limitations of traditional resistance-based measurements.

#### 5.6.1 Selectivity

To evaluate the specificity of our functionalized GFET biosensor, we performed control experiments using both target (PSA) and non-target (bovine serum albumin, BSA) proteins, as shown in Fig. 5.5a. The experimental protocol involved introducing specific concentrations of each protein at timed intervals (marked by red arrows in Fig. 5.5a), following the procedures detailed in the section 5.4. The results demonstrate that the PSA-functionalized GFET responds selectively to its target analyte, showing negligible response to BSA exposure. This confirms the high specificity achieved through our antibody functionalization approach.

Further validation was obtained by comparing responses between functionalized and non-functionalized GFETs exposed to identical PSA concentrations. As evident in Fig. 5.5a, while the non-functionalized device exhibited minimal signal changes attributable to non-specific PSA adsorption on the graphene surface, the antibody-functionalized GFET showed substantially stronger responses. This marked difference highlights the critical role of specific antibody-antigen interactions in generating the observed sensing signals.

The high sensitivity of our biosensor was demonstrated through real-time detection of ultra-low PSA concentrations. As shown in Fig. 5.5b, introduction of 10  $\mu$ L of 50 pg/mL PSA solution (equivalent to 1.6 pM for PSA's molecular weight of 30,000 Da) into the 200  $\mu$ L well produced a clear, high signal-to-noise ratio response (see the inset). This detection capability is particularly significant


Figure 5.5: (a) Selective response of a PSA antibody functionalized GFET towards target analyte PSA (black line) and non-target analyte BSA (blue line), also shown is a response of a non-functionalized (without PSA antibody) GFET to target analyte PSA (red line). (b) Real-time response of a PSA antibody functionalized GFET towards varying concentrations of target analyte PSA, inset shows a SNR to the 50 pg/mL concentration. The red arrows represent the intervals at which 10  $\mu$ L analyte of varying concentration prepared in 0.001X PBS is dropped in the GFET's well filled with 200  $\mu$ L 0.001X PBS. Adopted from Paper III.

for clinical applications, where current diagnostic thresholds for prostate cancer typically consider PSA levels above 4.0 ng/mL as abnormal, with age-adjusted thresholds ranging from 2.5 ng/mL for younger men to 5 ng/mL for older individuals [178]. Our sensor's ability to reliably detect concentrations three orders of magnitude below these clinical thresholds (50 pg/mL versus 2.5-5 ng/mL) demonstrates its remarkable sensitivity and potential for early-stage disease detection.

#### 5.7 Frequency-dependent impedance response

To investigate the frequency-dependent response of our GFET biosensor, we performed systematic lock-in measurements across different frequencies. Fig. 5.6a and Fig. 5.6b show the X, Y, and  $Y/X^2$  as functions of  $V_g$  at 137 Hz and 1000 Hz, respectively, both before and after analyte introduction. The frequency-dependent behavior reveals fundamental insights into the sensing mechanism: at 137 Hz, ions have sufficient time to redistribute, enabling strong electric double-layer formation and efficient carrier tuning in graphene, while at 1000 Hz, the ionic response becomes limited, reducing effective gate control and increasing parasitic capacitance effects [179, 180].

The distinct responses observed at different frequencies offer complementary insights into analyte interactions with the graphene channel. At 137 Hz, the pro-



Figure 5.6: X, Y, and  $Y/X^2$  vs.  $V_g$  at (a) 137 Hz and (b) 1000 Hz, measured before and after target analyte introduction. These lock-in measurements illustrate the frequencydependent behavior of the GFET biosensor: at lower frequency (137 Hz), efficient ionic redistribution enhances gate control, while at higher frequency (1000 Hz), limited ionic mobility and parasitic effects reduce gate control efficiency. Adapted from Paper III.

nounced leftward shift in the  $X(V_g)$  maximum indicates charge transfer doping effects, suggesting efficient carrier density modulation due to well-formed electric double layers. In contrast, at 1000 Hz, the overall reduction in X suggests that changes in interfacial capacitance dominate the response, as the ionic motion becomes limited, impairing effective gate coupling. This frequency-dependent behavior aligns with established electrochemical impedance spectroscopy principles: lower frequencies probe charge transfer resistance, while higher frequencies are more sensitive to variations in double-layer capacitance [68, 181].

Previous electrochemical impedance spectroscopy studies have employed the Constant Phase Element (CPE) model to interpret deviations from ideal capacitive behavior at the electrolyte-graphene interface, which may also explain our current observations. In [182], the interface was shown to exhibit CPE characteristics, with both the admittance parameter  $Q_0$  and the phase factor  $\alpha$  displaying frequency dependence. The study attributed this behavior to charged impurities and structural defects within the graphene lattice, which result in an inhomogeneous charge distribution and, consequently, a frequency-dependent capacitance. Moreover, the inherently low density of states near the Dirac point in graphene renders the phase factor particularly susceptible to local charge fluctuations. Similarly, [180] provided an in-depth analysis of the frequency response of liquid-gated graphene field-effect transistors (GFETs), revealing that signal distortion and reduced transconductance at higher frequencies stem from non-ideal capacitive behavior. At low frequencies, ionic motion in the electrolyte effectively supports double-layer formation, thereby enhancing capacitance and gate modulation efficiency. However, at elevated frequencies, limitations in ionic mobility and the emergence of capacitive leakage currents diminish the effective gate capacitance, weakening the electrostatic control over the graphene channel.

Our frequency analysis demonstrates that the  $Y/X^2$  metric becomes particularly useful at higher frequencies, where capacitive effects become more apparent (Fig. 5.6). Time-series measurements at fixed  $V_{\rm g}$  (Fig. 5.7a) reveal enhanced signal shifts at 1000 Hz. This can be attributed to the fact that the ratio  $Y/X^2$  reflects changes in interfacial capacitance, which become more prominent at higher frequencies. Interestingly, we also observed a reversal in the direction of the shift in X at higher frequencies. This phenomenon can be attributed to the non-ideal behavior of the electrolyte-graphene interface, where variations in interfacial capacitance cause the  $X(V_{\rm g})$  curve to shift downward at elevated frequencies (see Fig. 5.6a). This observation further underscores the influence of CPE-like capacitance effects, wherein charge redistribution and interfacial capacitance dominate, ultimately shaping the high-frequency response of the GFET biosensor.

The biosensor maintains excellent selectivity at 1000 Hz, as evidenced by its negligible response to non-target BSA compared to specific PSA detection (Fig. 5.7b). This frequency-independent specificity confirms that the measured signals originate from specific antibody-antigen interactions rather than non-specific binding. When comparing our AC approach to conventional DC measurements (Fig. 5.7c), the lock-in technique demonstrates superior sensitivity, with  $Y/X^2$  at 1000 Hz providing significantly higher response than DC resistance measurements for the same analyte concentration. This enhancement stems from the method's ability to simultaneously capture resistive and capacitive changes, making it particularly effective for detecting subtle biomolecular interactions that evade conventional detection schemes.



Figure 5.7: (a) Real time response of a PSA antibody functionalized GFET towards varying concentrations of target analyte PSA at different frequencies. Enhanced signal shifts are observed at 1000 Hz, where capacitive effects become more prominent. (b) Normalized  $Y/X^2$  response of target (PSA) and non-target (BSA) at 1000 Hz drive frequency, demonstrating strong specificity and minimal non-specific binding. (c) Normalized DC resistance  $(\Delta R/R_0)$  vs. normalized  $Y/X^2$  response of target (PSA) analyte, highlighting the superior sensitivity of the AC lock-in method. The red arrows represent the intervals at which 10  $\mu$ L analyte of varying concentration prepared in 0.001X PBS is dropped into the GFET-sensor well initially filled with 200  $\mu$ L 0.001X PBS. Adopted from Paper III.

# 6 CRISPR-Cas9 enhanced KRAS mutation detection

Recent advances in whole-genome sequencing have enabled comprehensive identification of disease biomarkers, driving development of targeted nucleic acid detection technologies [183–185]. While established methods like PCR have been optimized over decades for genomic analysis [183], current nucleic acid detection platforms remain constrained by multi-step workflows, expensive reagents, and complex instrumentation requiring trained personnel [186]. These limitations highlight the need for innovative detection strategies that enable rapid, costeffective molecular diagnostics without compromising sensitivity or specificity.

Clustered regularly interspaced short palindromic repeats (CRISPR)-Cas systems have emerged as powerful tools for nucleic acid detection, offering programmable sequence recognition through RNA-guided targeting [187, 188]. We present CRISPR-Chip, a biosensing platform combining CRISPR-Cas9 targeting with GFET technology. This integrated system enables direct detection of target sequences within intact genomic DNA without requiring amplification or optical components. The device features three key innovations:

$$CRISPR-Chip = \underbrace{dCas9-sgRNA}_{Programmable recognition} + \underbrace{Graphene}_{Electronic transduction} + \underbrace{FET}_{Signal amplification}$$
(6.1)

At the core of CRISPR-Chip is a catalytically deactivated Cas9 (dCas9) complex immobilized on a high-mobility graphene channel (>10000 cm<sup>2</sup>/(V s)). The dCas9-sgRNA ribonucleoprotein (dRNP) performs sequence-specific DNA recognition through a two-step process: (1) whole-genome scanning with double-helix unwinding, followed by (2) stable binding at target sites containing the protospacer adjacent motif [189, 190]. Target binding induces charge redistribution that modulates the graphene's (sensing layers') electrical properties, producing a measurable signal change in the transistor output.

The system's programmability arises from the easily customizable 20-nucleotide guide sequence within the sgRNA, while graphene's exceptional charge sensitivity, enhanced by the AC bias method (Section 5.2), enables direct electronic detection of nucleic acid interactions [11, 191]. This integration of molecular recognition and electronic transduction in the CRISPR-Chip platform marks a significant step toward portable, amplification-free nucleic acid diagnostics.

Circulating tumor DNA has emerged as a powerful biomarker in cancer management, enabling non-invasive tumor profiling through liquid biopsies. Circulating tumor DNA facilitates early detection, diagnosis, monitoring of treatment response, and identification of minimal residual disease or relapse. Among the most clinically relevant genetic alterations are mutations in the Kirsten rat sarcoma (KRAS) gene, which are found in over 80% of pancreatic cancers and more than 30% of colorectal, cholangial, and lung adenocarcinomas. Accurate detection of these mutations, including single-nucleotide variants, is crucial for guiding targeted therapies and improving patient outcomes. While PCR-based methods are widely used, they are limited by their complexity, cost, and need for specialized equipment. CRISPR-Cas9-based diagnostics offer a promising alternative, enabling rapid, sensitive, and specific detection of mutations-including single-base changes-under physiological conditions. Here we explore the development of a CRISPR-Cas9 system integrated with a graphene field-effect transistor for precise detection of KRAS mutations, emphasizing the importance of guide RNA design in achieving single-nucleotide specificity. We refer to the KRAS sequence with the mutation we want to detect as the target, and the normal, unmutated sequence as the non-target. Refer to Paper IV for more details.

## 6.1 GFET functionalization



Figure 6.1: Schematics of CRISPR-Chip functionalization. The graphene surface is first functionalized with PBASE. A carboxylate group at the terminal end of the hydrocarbon arm of the linker acts as the dCas9-tethering unit that covalently couples to dCas9, securing the nuclease to the surface of graphene. Any unfunctionalized PBASE molecules are blocked with amino-polyethylene glycol 5-alcohol (PEG). Finally, sgRNA complementary to a gene of interest is introduced and complexes with dCas9 tethered to the graphene surface. Adopted from [11].

The fabrication of the GFET sensor was carried out using the same procedures detailed in Chapter 5, Section 5.3. The fabricated graphene chip was functionalized through a multi-step biochemical protocol. Initially, the surface was incubated with 5 mM PBASE (Sigma-Aldrich) in dimethylformamide for 2 h at room temperature or overnight at 4 °C to enable linker immobilization. Subsequently, 900 ng (10  $\mu$ L) of dCas9 was applied and incubated for 30 min at 37 °C. The chip was then rinsed with nuclease-free water (Fig. 6.1). To block unreacted PBASE sites, the surface was treated with 3 mM amino-PEG5-alcohol (BroadPharm) and 1 M ethanolamine hydrochloride (Sigma-Aldrich), each for 10 min at 37 °C. After blocking, the chip was washed with Milli-Q water. For final dRNP complex formation, an additional 900 ng of sgRNA in nuclease-free water was incubated on the surface for 10 min at 37 °C, followed by a 5 min rinse with nuclease-free water. This final step ensured complete dRNP assembly and yielded a fully functionalized CRISPR-Chip.

#### 6.2 Selectivity

In our lock-in measurements, the X component primarily reflected changes in the graphene channel resistance, modulated by the gate voltage, which alters carrier concentration. Meanwhile, the Y component captured variations in capacitance between the liquid gate and graphene channel, influenced by quantum capacitance and double layer capacitance. These measurements allowed us to distinguish resistive and capacitive contributions.

Lock-in measurements of X and Y versus  $V_g$  were performed before and after target/non-target analyte introduction, as shown in Fig. 6.2, following the procedures detailed in section 5.4. A shift in both components indicates that the analyte alters the sensor's electrical properties. A shift in X suggests changes in channel resistance likely due to charge transfer as indicated by analyte binding. A shift in Y indicates capacitance changes, likely driven by variations in quantum capacitance, functional layer capacitance, and modifications in the electric double layer.

As shown in experimental results, shifts in Y were more pronounced than in X, suggesting a significant capacitive contribution to the sensing mechanism. To further analyze this, we plotted  $Y/X^2$  versus  $V_g$  before and after analyte introduction. This ratio enhances sensitivity to capacitive effects, effectively isolating them from resistive contributions. This parameter provides a more stable and reliable detection metric at the graphene/electrolyte interface, allowing for better analyte differentiation compared to conventional methods.

From Fig. 6.2, it is evident that both target and non-target DNA induce shifts in the GFET response. A non-target DNA can still influence the electrical properties of a GFET due to its negative charge [192], which modifies the local electrostatic environment and affects both the X and Y response. Additionally, weak  $\pi$ - $\pi$ stacking interactions between DNA and graphene can contribute to capacitance variations, even in the absence of specific Cas9 binding [191]. Partial sequence complementarity or off-target interactions may also result in weak binding, leading



Figure 6.2: Transfer curves plotting X, Y and  $Y/X^2$  vs Vg (a) before and after target and (b) before and after non-target, respectively. The X component reflects changes in graphene channel resistance, while Y captures capacitance variations between the liquid gate and graphene, influenced by quantum and double-layer capacitance. Shifts in these signals indicate analyte-induced changes in the sensor's resistive and capacitive properties. Adopted from Paper IV.

to a small but detectable signal. Despite these minor effects, the chip retains high specificity by producing a significantly stronger response for fully complementary target DNA.

Our results indicate that while non-target DNA can cause detectable shifts in X, Y, and  $Y/X^2$ , the shifts caused by the target analyte are more pronounced. This demonstrates the strong target recognition capability of Cas9-sgRNA functionalized GFETs. When the target-adjacent protospacer-adjacent motif sequence is present, complete hybridization occurs, securing the complementary DNA to the graphene surface via the Cas-sgRNA complex. In contrast, DNA sequences with mismatches exhibit lower affinity, leading to their dissociation from the graphene surface [191].

#### 6.2.1 Time-series measurements



Figure 6.3: Real time response of dRNP functionalized GFET to target and non-target in (a) 200  $\mu$ L nuclease-free water (f = 137 Hz) and (b) 200  $\mu$ L nuclease-free water with 400 ng human genomic DNA (f = 1000 Hz), respectively. The red arrows represent the intervals at which analytes of varying concentration are dropped on GFET sensors. Adopted from Paper IV.

To validate this further, we conducted real-time series measurements by fixing  $V_g$  at the peak transconductance point and continuously monitoring  $Y/X^2$  as the analyte was introduced. The GFET was first stabilized in 200  $\mu$ L nuclease-free water at a fixed  $V_g$  before being exposed to different analyte concentrations at specific time intervals, as indicated by the red vertical arrows in Fig. 6.3a. The electrical response was normalized relative to the initial value at t = 0, using the formula  $\Delta S/S_0 = (S - S_0)/S_0$ , where  $S_0$  represents S(t = 0) and S denotes  $Y/X^2$ .

As shown in Fig. 6.3a, the GFET functionalized with dRNP exhibited a distinct response only to the target DNA, confirming its specificity. In the presence of 20 ng (0.09 ng/ $\mu$ L) of target DNA, the normalized GFET response ( $\Delta S/S_0$ ) was 12 times greater than that of the non-target, reflecting an approximately 10-fold increase in the relative target/non-target response compared to previous studies [11, 191]. This enhanced performance of our functionalized GFET is attributed to the high-quality graphene used (>8000 cm<sup>2</sup>/(V s)) and the lock-in measurement technique, which simultaneously captures resistance and capacitance changes during biomolecular interactions. Unlike previous studies where rinsing was required to distinguish target from non-target binding [11, 191], our sensors do not require this additional step, simplifying the detection process.

We further evaluated the specificity of our dRNP-functionalized GFET by performing measurements in the presence of human genomic DNA (Fig.6.3b). For this, 400 ng of human genomic DNA was added to 200  $\mu$ L of nuclease-free water, and the GFET was allowed to stabilize at a fixed  $V_q$ . As illustrated in Fig. 6.3b,

Method	Detection time	Detection limit	Single-point mutation	Ref.
GFET	15 min	$3.3 \text{ ng}/\mu \text{l}$	No	[11]
GFET	40 min	10-60 ng/ $\mu \text{l}$	Yes	[191]
GFET	5 min	0.09 ng/ $\mu \text{l}$	Yes	This work

 Table 6.1: Performance comparison of GFET-Cas9 biosensors

a distinct response was observed only for the target DNA, whereas the response from non-target DNA was negligible. Additionally, when the GFET was exposed to nuclease-free water alone, a slight negative shift was recorded, likely due to the dilution of the overall concentration of 400 ng human genomic DNA in 200  $\mu$ L of nuclease-free water. However, this shift was minimal compared to the pronounced response observed when the GFET was exposed to nuclease-free water containing target DNA.

## 6.3 Functionalized vs non-functionalized GFET



Figure 6.4: (a) Selective response of target analyte to a dRNP functionalized (func. chip) and bare graphene (non-func chip). The functionalized chip shows a significantly stronger signal, confirming specific binding to the Cas9-sgRNA complex, while the bare chip exhibits only minor non-specific interactions. (b) Real-time response of dRNP functionalized chip to target and non-target in 120  $\mu$ L nuclease-free water. The overall signal increases with reduced volume, but the target response remains distinctly higher, demonstrating the sensor's selectivity and the influence of measurement conditions on sensitivity. Adopted from Paper IV.

To further validate our results, we conducted a negative control experiment

using a non-functionalized GFET (bare graphene) to assess whether the observed response was indeed due to target DNA binding to the RNP complex (Fig. 6.4a). The non-functionalized GFET was exposed to both target and non-target analytes, and its response was compared to that of the functionalized GFET. A small shift was observed in the non-functionalized GFET, likely due to non-specific interactions between DNA (target or non-target) and the graphene surface. However, the response of the functionalized GFET to the target DNA was significantly larger, confirming that the majority of the observed signal arises from the specific binding of target DNA to the Cas9-sgRNA complex. This experiment further validated that the capacitive and resistive shifts recorded in functionalized GFETs are primarily due to selective target recognition rather than non-specific adsorption.

To investigate the effect of background volume, we repeated the same measurements using a smaller volume of nuclease-free water (Fig. 6.4b), reducing it from 200  $\mu L$ (as in Fig. 6.3a) to 120  $\mu L$ . Under these conditions, we observed an overall increase in the response for both target and non-target DNA. Despite this proportional increase, the response to the target DNA remained significantly higher than that of the non-target, reinforcing the sensor's ability to differentiate between the two. This finding highlights the impact of background volume on biosensing sensitivity and the importance of optimizing measurement conditions for enhanced detection accuracy.

## 6.4 Frequency-dependent impedance response

Our AC impedance measurements on CRISPR-functionalized GFETs revealed distinct frequency-dependent behaviors that varied significantly with the ionic composition of the surrounding medium (Fig. 6.5). The behavior of the  $Y/X^2$  metric can be quantitatively described using the derived expression in Equation 5.3, which is governed by the parameter  $C^2 R_s^2 \omega^2$ . Depending on its magnitude, the system transitions between two distinct regimes. Although our findings offer valuable insights, the full physical mechanisms behind these behaviors remain only partially understood and require further systematic study.

In ultra-pure water-characterized by extremely low ionic strength, the system exhibits a pronounced  $Y/X^2$  response at lower frequencies (137 Hz), as shown in Fig. 6.5a. This contrasts with the behavior observed in Chapter 5, Section 5.7. In this low-conductivity environment, the lack of free ions leads to a large solution resistance  $(R_s)$ , satisfying the condition  $C^2 R_s^2 \omega^2 \gg 1$ . Under this high-resistance limit, Equation 5.3 simplifies to:

$$\frac{Y}{X^2} \approx -\frac{1}{2CR_s^2\omega} \tag{6.2}$$

This inverse frequency dependence accounts for the observed enhancement of the  $Y/X^2$  response at lower frequencies and the corresponding signal attenuation



Figure 6.5: Real time response of dRNP functionalized GFET to target in (a) 200  $\mu L$  nuclease-free water and (b) 200  $\mu L$  nuclease-free water with 400 ng human genomic DNA, respectively, at different frequencies. The red arrows represent the intervals at which analytes of varying concentration are dropped on GFET sensors. This highlights the influence of sample composition on frequency-dependent sensor behavior.

at higher frequencies.

In contrast, measurements conducted in ultra-pure water spiked with 400 ng of background human DNA (Fig. 6.5b) showed frequency-dependent behavior consistent with previous results (Chapter 5, Section 5.7). Here, the added DNA contributes sufficient ionic species to significantly reduce the solution resistance, placing the system in the  $C^2 R_s^2 \omega^2 \ll 1$  regime across the experimental frequency range. Under this low-resistance condition, Equation 5.3 reduces to:

$$\frac{Y}{X^2} \approx -\frac{C\omega}{2} \tag{6.3}$$

This linear dependence on frequency explains the enhanced  $Y/X^2$  response observed at higher frequencies. The presence of DNA ensures moderate ionic conductivity, thereby favoring a regime where the response scales with  $\omega$ .

These results have meaningful implications for biosensor design and operation.

The shift from low-frequency signal enhancement in ultra-pure water to highfrequency dominance in DNA-containing solutions highlights the critical role of the sample matrix. For applications involving low-ionic-strength media, such as single-molecule detection or microfluidic systems, low-frequency measurements may yield higher sensitivity. Conversely, in complex biological fluids with substantial ionic content, high-frequency operation becomes advantageous, mitigating ionic screening and enabling direct probing of biomolecular interactions at the sensor interface.

However, fully decoupling the various contributing factors, ionic strength, DNA concentration, and frequency response, remains a challenge. Future investigations should systematically vary these parameters to establish a comprehensive theoretical and experimental framework, ultimately leading to robust, optimized sensing protocols for real-world biosensing applications.

## 7 Summary and Outlook

#### Summary

This thesis has explored the development, characterization, and application of graphene-based devices, with a particular focus on scalable fabrication methods and their integration into high-performance electronic and sensing platforms. The study encompasses the development of growth and transfer processes, indepth characterization of the structural, electronic, and transport properties of graphene, and the application of these insights to the realization of sensitive and robust biosensing platforms.

The research commenced with the exploration of scalable transfer methods for high-quality graphene. The study introduced a hot-press lamination process for transferring CVD-grown graphene from copper foils to flexible polymer substrate EVA/PET. This method effectively minimized defects, contamination, and wrinkles, thereby preserving the pristine quality of graphene. Comprehensive electrical and spectroscopic characterizations, including Raman spectroscopy and X-ray photoelectron spectroscopy, confirmed the high quality and mobility of the transferred graphene. The Hall-effect measurements demonstrated significant improvements in carrier mobility, reaching values between 7000-8000 cm<sup>2</sup>/(V s) after annealing. The research highlighted the challenges associated with graphene transfer and proposed solutions to mitigate these issues, thereby contributing to the broader goal of integrating graphene into commercial technologies.

Building upon this foundation, the thesis explored the fabrication and characterization of flexible graphene field-effect transistors. Devices were implemented in both top-gated and bottom-gated configurations, allowing investigation into the impact of gate geometry on device performance. Electrical measurements, including Hall-effect and field-effect characterizations, were employed to extract key parameters such as carrier mobility, sheet resistance, and charge neutrality point. Notably, the devices exhibited high field-effect mobilities and demonstrated near-hysteresis-free transfer characteristics, signifying low defect density and uniform doping. At cryogenic temperatures and under magnetic fields, the devices exhibited quantum Hall features, further validating the intrinsic high quality of the transferred graphene. Additionally, terahertz time-domain spectroscopy was employed as a non-contact tool to probe spatial variations in electrical conductivity and carrier dynamics, offering a powerful technique for process monitoring over large-area graphene devices.

The research further explored the use of electrolyte-gated GFETs for biosensing applications, introducing an innovative complementary impedance spectroscopy method. This approach enhanced measurement stability and sensitivity, providing deeper insights into the graphene-electrolyte interface. This method allowed for the detection of both resistive and capacitive changes at the grapheneelectrolyte interface, thereby improving sensitivity and specificity. The development of antibody-functionalized GFET biosensors for detecting human prostatespecific antigen was demonstrated. These sensors exhibited high sensitivity and specificity, capable of detecting ultra-low concentrations of PSA, which is significant for clinical diagnostics.

In addition, the thesis presented a CRISPR-Chip platform combining CRISPR-Cas9 targeting with GFET technology for the direct detection of target sequences within intact genomic DNA. This integrated system enabled rapid, amplificationfree nucleic acid diagnostics with high precision and speed. The functionalization of GFETs with dCas9-sgRNA complexes allowed for sequence-specific DNA recognition, resulting in measurable signal changes in the transistor output. The platform demonstrated high specificity and sensitivity, making it a promising tool for molecular diagnostics.

#### Outlook

The progress demonstrated in this thesis lays a strong foundation for the continued advancement of graphene-based electronic and biosensing technologies. Nonetheless, several avenues remain open for further exploration and improvement.

While the hot-press lamination process has shown promise, further optimization is needed to enhance the scalability and reproducibility of graphene transfer methods. On the materials side, refinement of the graphene transfer process could include automation, roll-to-roll compatibility, and integration with other two-dimensional materials to create heterostructures with tailored functionalities. The high carrier mobility and flexibility of GFETs make them ideal candidates for a wide array of applications beyond biosensing. For instance, they can be employed in terahertz detectors and modulators for next-generation wireless communication systems, or in sensitive magnetic field sensors for industrial and scientific use. Their mechanical flexibility further opens up integration into wearable electronics, flexible displays, and electronic skins. Realizing these applications will require reliable, scalable manufacturing routes that maintain the performance metrics achieved in this work.

The biosensing capabilities demonstrated in this thesis can be extended to a wider range of disease biomarkers, environmental contaminants, and pathogens. Machine learning algorithms, such as artificial neural networks (ANNs), can improve signal classification and quantification in complex sensing environments. Non-functionalized GFET arrays analyzed with ANNs have shown strong performance in detecting food quality and spoilage indicators [193], offering a pathway to overcome traditional challenges such as sensor-to-sensor variability and bioreceptor instability. At the sensor interface, optimizing the orientation and immobilization of bioreceptors remains crucial. Functionalization using tetrakis(4carboxyphenyl) porphyrin has demonstrated superior antibody orientation efficiency compared to conventional linkers like PBASE, enhancing the sensor's sensitivity and response consistency [194]. The functionalization strategy can be further enhanced by optimizing the surface density of receptors on the graphene, thereby maximizing interaction sites for target analytes. Moreover, substituting conventional antibodies with alternative biorecognition elements such as aptamers, owing to their smaller molecular size, can significantly improve detection efficiency. When integrated with the platform proposed in this work, these improvements are expected to yield substantially higher sensitivity than what has been demonstrated thus far.

Fundamental Understanding of Graphene-Electrolyte Interactions: Gaining a comprehensive understanding of the interactions between graphene and electrolyte environments is essential for optimizing the performance and reliability of GFETbased sensors. Our AC impedance spectroscopy experiments revealed distinct frequency-dependent responses that were strongly influenced by the ionic composition of the surrounding medium. While these observations provide meaningful insight into the combined roles of interfacial capacitance, series resistance, and signal frequency, the full range of physical mechanisms driving this behavior is not yet fully understood. A key challenge remains in disentangling the overlapping effects of ionic strength, analyte concentration, and frequency response factors that are intricately coupled in real sensing environments. To address this, future studies should focus on systematically varying these parameters to build a more detailed theoretical and empirical model of the graphene-electrolyte interface. Such work will be vital for refining sensor design and establishing consistent, high-fidelity measurement protocols for real-world biosensing applications.

In conclusion, this thesis has made significant contributions to the field of graphene research, particularly in the areas of scalable transfer techniques and advanced biosensing applications. The findings and methodologies presented herein provide a solid foundation for future research and development, with the potential to revolutionize various industries, including electronics, healthcare, and environmental monitoring.

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