

Dynamic Wetting behaviour at Flexible and Tuneable Two-Dimensional Material Interfaces [CarboWet]

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Project Summary

Layered materials such as graphene present a unique opportunity to study discrete material properties in two-dimensions (2D), which are fundamental to the development of future key technologies. Wetting of 2D surfaces is one of such key topics, which is central to the implementation of 2D materials as sensors, energy storage, catalysis, smart membranes etc. Understanding of the wetting behaviour of 2D materials demands special attention to their versatile mechanical (flexible) and physicochemical characteristics, which are influenced by factors inherent to the material surface and its dependence on external parameters such as pH, humidity, temperature and electromagnetic fields. Due to the complex dynamic interplay of these parameters, a unified understanding of the wetting behaviour at 2D interfaces is fundamental.

This project aims to establish an excellent experimental framework to study the wetting behaviour of 2D material based solid-liquid interfaces and to communicate experimental findings for further progress in this modern field. The influence of substrates, layer-thickness, chemical composition and surface properties originating from nanoscale features of the 2D-materials will be characterized with state-of-the-art nanofabrication and surface characterization tools available in the project consortium. In addition, wetting behaviour of 2D-on-polymer surfaces and their bio-specific transducer interfaces will be studied from nano-to-micro dimensions.

Control of wetting properties on 2D material surfaces have significant consequences in their usage as highly-sensitive electrical transducers, where realization of biomolecular interactions at surfaces remains a universal challenge due to various factors at nanoscale affecting the wetting properties of the 2D surfaces. This proposal aims to construct and to understand smart 2D interfaces with selective tuning of their wetting behaviour. Sophisticated surface modification approaches will be developed rendering nanostructured 2D-material surfaces with multipurpose functional groups (MFGs). The MFGs will support selective linking of dendritic polymers with tuneable physicochemical characteristics and will act as 'anchors' for bio-specific receptors. Increased wettability of such graphene-based '2D islands' will allow highly specific, localized interactions between receptor-analyte pairs and help to minimize non-specific adsorption. Positioning biomolecules away from the 2D-material surface using MFG-dendritic polymers will also suppress ionic-shielding in liquids with high ionic-strength towards electronic biomolecule detection beyond Debye-screening of charges. The wetting-engineered 2D-material interfaces will be validated in a relevant bioassay for efficient detection of novel cancer disease biomarkers.

1 State of the art and preliminary work

Wetting of flexible substrates is probably the most well-known phenomena one sees in everyday life. Study of wetting behaviour of new and advanced material surfaces also underscores major developments in key technology areas. Even as the science of wetting at flexible surfaces has progressed tremendously in last decades encompassing bulk to micro to nanostructured surfaces, proper understanding of wetting behaviour at flexible substrates that experience profound changes in their physicochemical properties upon wetting remain elusive. Explaining the wetting behaviour of such 'adaptive' flexible substrates and development of new tools and techniques is critical for a fundamental understanding of many basic functions of nature as we know it. Beyond nature, elastomeric materials such as hydrogels, porous surfaces, polymer brushes etc. are prime examples of substrates exhibiting a 'dynamic' wetting behaviour due to altering composition of surface, change in chemical nature and induction of stress upon contact with liquids. In order to gain detailed understanding of these multiple factors that play role in regulating wetting behaviour of such substrates, efforts are being made to develop tools and technique to study related solid-liquid interfaces, in multiscale approaches. Interestingly, such detailed studies into discovering influence of different inherent and external parameters of dynamic wetting phenomena and governing interrelations have been mainly focused on 'bulk' systems.

Remarkably, with the earlier discovery of graphene and more recent developments in nanoscience towards realization of two-dimensional (2D) material systems, *a unique class of interfaces emerge which consist of characteristic 'bulk-less' flexible and adaptive substrates*. As the unique set of material properties of 2D materials catapults them into next generation applications spearheaded by fast electronics and optoelectronics, emergence of new applications prove their excellence in key technology areas (Figure 1). Thereby, deep understanding of wetting behaviour of 2D material systems invite significant interests for future solutions in areas such as energy storage, catalytic surfaces, filtration membranes, smart wearable devices, biological and environmental sensors etc.[1-5]

In this regard, graphene serves as an ideal substrate. It is well-known that graphene as atomic lattice of sp² hybridized Carbon atoms exhibits maximum surface-to-volume ratio, making it highly responsive to the outer environment (pH, humidity, temperature, light).[1] Atomic layers of graphene are thermodynamically stable and can be produced in large sizes up to centimetre scales with homogeneous surface characteristics.[6, 7] Despite atomically thin, graphene is strong and flexible, as it was demonstrated by the realization of various platforms by suspending graphene between support structures.[8-10] The physicochemical nature of graphene surfaces is regulated by various factors such as Carbon-to-Oxygen ratio as a result of lattice defects and by the presence of oxidative functional groups which may vary for different syntheses approaches.[11] It is to recollect that graphene also benefit from its various Carbon-chemistry approaches which have been adapted for surface functionalization of graphene so as to control their physicochemical properties and surface functionalities.[12] Overall, graphene can be regarded as a model-system, where it is extremely plausible to study 2D material as flexible and adaptive substrates and to build-up workable experimental platforms for a detailed study of wetting behaviour with a new outlook towards future applications.

In this joint proposal by FUB and RWTH, we aim to build-up on our current strengths in synthesis, surface chemistry, system integration and application development to realize an experimental framework which focuses on studying the wetting mechanisms at 2D material surfaces. The project framework constitutes of two strategic domains where we deploy our know-how in handling of 2D materials to realize protocols for fabrication of graphene platforms with systematic variation in configuration and physicochemical properties in order to facilitate studying wetting behaviour and analysis in a detailed, routine manner with high throughput and standardization capabilities. In

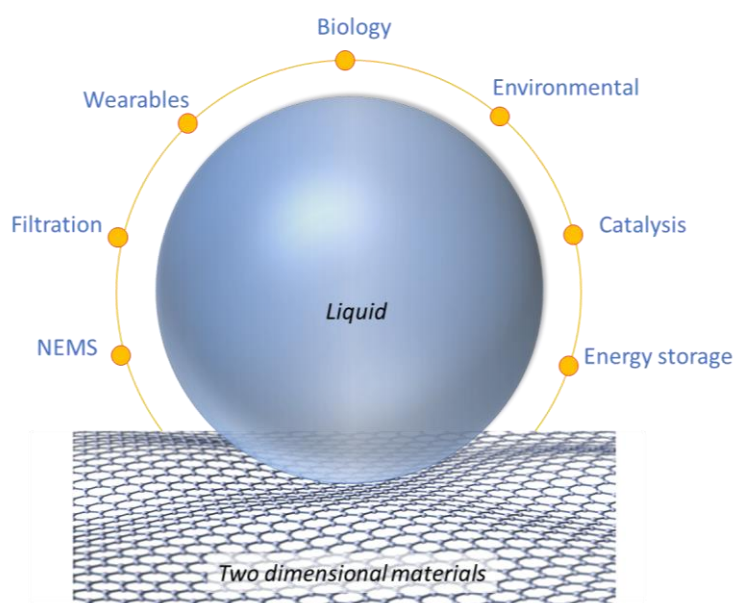


Figure 1: A liquid droplet sits on a graphene lattice. Formation of this novel solid-liquid interface on a bulk-less flexible and adaptive two-dimensional substrate is central to many key application areas in the 21st century.

this regard, the project also benefits here from establishing a working link to the leading experimentalists and theoreticians in the field and are also part of this special focus programme SPP2171 on the study of dynamic wetting behaviour of flexible, adaptive and switchable substrates. In parallel, we plan to exploit the findings of initial results on the wetting behaviour of graphene and graphene based materials (GBM) such as reduced graphene oxide (rGO). Towards this goal, we aim to realize graphene based platforms with tuneable wetting behaviour towards realizing a biosensor which demonstrates enhanced molecular interaction and solve pressing issues of selectivity and sensitivity of label-free electrical biosensors.[13] Translating the potential of our innovative surface chemistry approaches which provide a common route for controlling the wetting and bio-specificity, an exemplary platform showing 'on-demand' enhanced detection of cancer-related biomarkers will be demonstrated as a biosensor by the conclusion of this project. Considering the nature of ambitious goals this proposal represents, we like to further elaborate on the current state of the art towards studying the wetting of 2D material surfaces, challenges and our preliminary work towards addressing contemporary challenges and pertaining to the experimental framework of this proposal.

Soon after the discovery of graphene and demonstration of field-effect, ion-sensitive field-effect transistor (ISFET) based on graphene were fabricated and deployed as biosensors. Integration of such a biosensor platform in general involves surface functionalization of graphene and immobilization of receptor biomolecules towards the assembly of a biofunctional layer specific for an analyte of interest.[14] As evident from numerous reports, while graphene based label-free electrical biosensors show extremely low limits of detection, exceeding far compared to their nanomaterial counterparts such as nanowires, achieving a highly reproducible sensor response for high throughput screening isn't always easy.[15] Behind this problem, lies the control over solid-liquid interface where it is extremely important to have homogeneous coverage of biofunctional layer of tuneable physicochemical characteristics such as surface charge.[16] In general, achieving more homogeneity of the physicochemical characteristics on surfaces is to some extent supported by alternate biofunctional layers where receptor molecules may be embedded in a polymer matrix such as hydrogels, polymer brushes, conductive polymers and so on. Such solutions however are limited to bio-applications or have adverse effect on the inherent advantages of using a 2D material like graphene. Inherent properties of 2D surfaces based on materials like graphene, transition metal chalcogenides, transition metal nitrides and carbides are also gaining importance for other applications such as energy storage.[2] In other examples, selective permeation through 2D materials is an attractive approach for making next generation smart-membranes.[17] In all these examples, it becomes critical to make use of the pristine 2D surfaces and wetting of these surfaces is central to their performance and reliability in key future technology areas.

Fundamental insights into surface-water interactions at 2D materials have been sparse and so far there is no unified theoretical understanding of the mechanisms governing the wetting phenomena. As shown in figure 2 against an ideal graphene lattice (figure 2i), completely different interfaces can be realized with (and without a substrate underneath) where depending on the synthesis and transfer process, density of lattice-defects (fig 2ii) density of functional groups (fig 2iii), and number of graphene layers (figure 2iv). The effect of these interfaces on the wetting of graphene as well as effect of external factors underpin an important research question. In the wake of contrasting reports by static angle measurements carried out on graphene on a substrate, Raj et al carried out a detailed study on graphene layers deposited on copper, thermally grown silica and glass substrates using dynamic contact angle

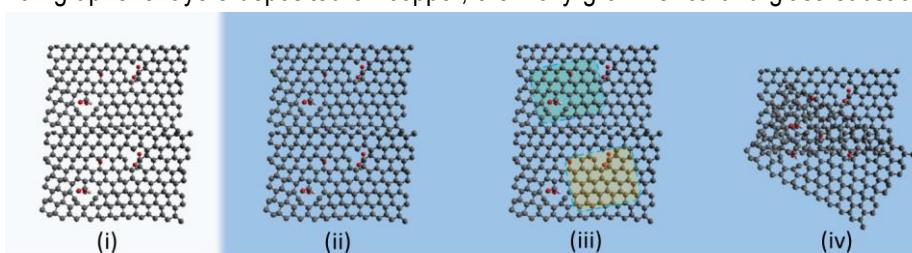


Figure 2: All within one surface: A 2D material such as Graphene forms different interfaces expected to influencing the wetting behaviour. (i) A perfect graphene lattice that can be experimentally constructed representing a near-ideal two-dimensional interface where bulk influence on the wetting properties of a surface are expected to be negligible, (ii) effect of substrate influencing the ideal 2D surfaces comes into play, (iii) the 2D surface may have different heterogeneities coming from the localized defects, or functional groups, and (iv) overlapping of ideal surfaces which is expected to influence the wetting. Thereby, a graphene surface or a graphene-like surface presenting a unique opportunity to understand dynamic and adaptive wetting at flexible surface at microscopic levels.

measurements backed with detailed surface characterizations.[18] The results showed that presence of defects resulted in extremely high contact angle hysteresis in CVD graphene on substrate. Changing the number of layers (mono. bi and tri-) didn't show any changes in the advancing contact angles whereas receding contact angles showed significant variations. The corresponding molecular

dynamics simulations and theoretical calculations also supported these results. These observations however, were restricted to platforms where graphene sheets form very loose interlamellar couplings.

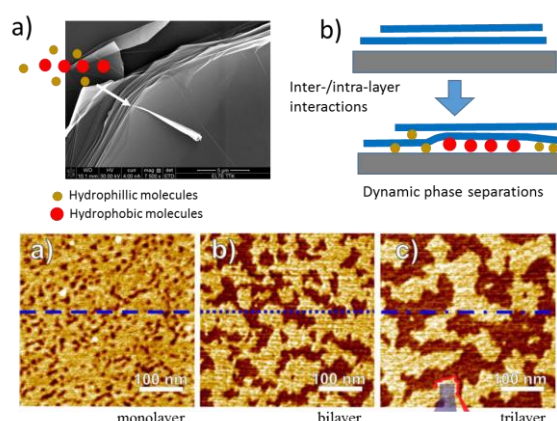


Figure 3: Dynamic phase separation in confined spaces between mica and different layers of graphene

simulation models to provide molecular insight into 2D material-wafer interactions taking account of the interplay of electrostatic and van der Waals (vdW) forces that switch dominant roles in different interface configurations. For example, the vdW screening per layer from few-layer graphene is shown to decrease in strength with each added layer and become stronger with doping in the single-layer graphene.[20] While such forces can be indirectly measured by AFM in dry conditions, direct measurements of such forces while in contact with liquid remains to be realized and require new experimental insights. In all of these studies, graphene layers were put on different substrates where phenomena such as wetting transparency on silicon gold and copper were reported while other reports negligible effect of substrate on graphene-water interactions. At microscopic scales, the influence of the size/volume of the droplet and the presence of foreign substances may also affect the wetting behaviour at 2D surfaces as shown by micro-wettability of picolitre volume droplets at single layer graphene.[21] Studying wettability of suspended 2D layers may provide critical insight at microscopic levels where substrate-2D material interactions can be minimized and experimental observations can be systematically correlated to sort and long range interactions between droplets and their effect on wettability.[22] Placing graphene on soft substrates is also known to have a profound effect on the wetting behaviour. In preliminary findings, it was reported that surface stress of polymer substrate increases with increasing graphene layers and it is significantly larger than that of the bare substrates.[23] In other studies about the formation of thin films and reasons for wetting stability are predicted for graphene in configurations as shown in figure 4. A change in polarization factors for graphene on substrates may result in different alignments of vdW forces and electrostatic interactions and a propensity towards wetting, while suspended graphene experiences an arrested growth of the liquid film triggering surface instabilities and dewetting pattern formations.[18]

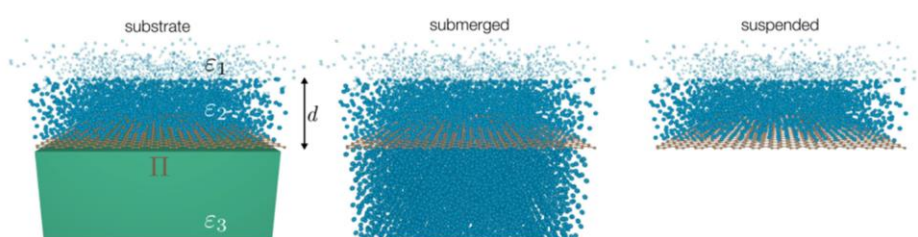


Figure 4: Wetting at Graphene: All possible three conditions where graphene sits on a substrates of a dielectric constant (ϵ_{sub}), is submerged and suspended in a medium with a dielectric constant (ϵ_{med}). Sengupta et al. (PRL, 120, 2018) study wetting and growth of liquid films on a 2D surface using a computation model and propose insights into critical microscopic phenomena at the interface.

As it is clear that low dimensional nanomaterials exhibit unique physicochemical properties to realize surfaces with tailored specificities, they have recently emerged as promising systems for nanomedicine [24-26]. Among such nanomaterials, one- or few-atom thick, two-dimensional (2D) nanostructures including silicate clays, metal dichalcogenides, transition metal oxides, black phosphorous, and graphene derivatives have attracted much attention due to their prominent optoelectronic, photothermal, and photodynamic properties along with outstanding drug loading capacity and fast cellular uptake[27-30]. Efficiency of 2D nanomaterials for theranostic applications depends strongly on their surface chemistry, which is defined by a combination of parameters including functionality, charge, heteroatom doping, defects, edges, number of layers, and the biomolecular corona [31]. All these factors must be standardized or clearly defined to shed more light on the mechanisms of nanobio interactions (at the interface of biosystems and 2D nanomaterials) and to pioneer further development for biomedical applications [32-

34]. In addition, surface modification of 2D nanomaterials results in more effective cancer theragnosis by tuning/dictating their biological properties including cell recognition, intracellular localization, programmed cell death, renal clearance [35]. Graphene derivatives, which are consisting fused benzene rings with oxygen containing functional groups, are especially interested for drug delivery, biosensing and tissue engineering, with strong contributions to the other nanomedicine area [36]. However, preparation of graphene derivatives with defined structure, in particular defined functionality, is a big challenge on the way to the realization of future biomedical devices. In any case, there remain considerable gaps between experimental and theoretical limitations which should be considered in revising the theoretical understanding of these new interfaces. [37-52] Know-how of dynamic wetting processes at flexible surfaces remains elusive and requires deeper understanding of the effects of surface architectures. There are many efforts undertaken into the study of dynamic process of wetting and dewetting on flexible substrates which can deform under lateral traction forces.[53, 54] Here, a unified experimental and theoretical framework for real 2D surfaces is missing at this point. This proposal aims to provide this framework by considering thin film graphene and other layered systems with systematic architectures deployed for the study of wetting behaviour.

Preliminary work

Large area high quality surface modification of substrates: The primary aim of surface modification is to enable reproducible and homogenous substrates that facilitate immobilization of other molecules and nanomaterials without agglomeration effects. For this, Siloxane chemistry is one of the most used approaches for research and industry

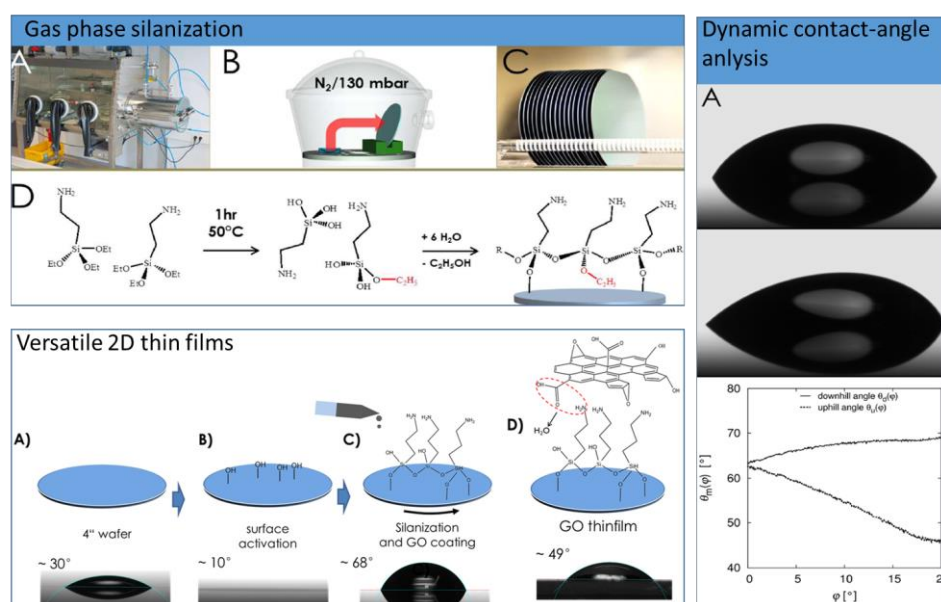


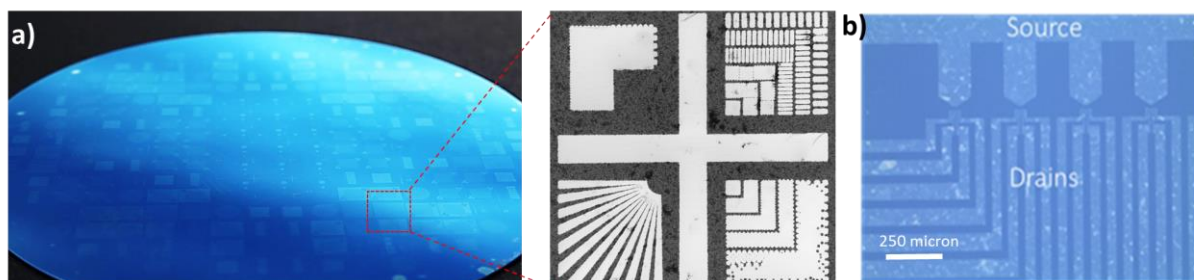
Figure 5: Large area surface modification using gas-phase evaporation techniques, wetting analysis of surface modified substrates, and preparation of graphene based thin films from graphene oxide flakes. Demanding surface chemistry protocols realized towards routine realization of atomic thin films at wafer scale.

Glycidoxypropyltrimethoxysilane (GPTES), and 1H,1H,2H,2H-perfluorooctyl-trichlorosilane (FOTS) to realize very high quality ultrathin siloxane coatings at wafer scale.[55] The ultra-thin siloxane layers, were investigated thoroughly to verify our protocols for high reproducibility and coating quality using high-resolution surface-characterization methods such as FT-IR, AFM, XPS, Ellipsometry and drop shape analysis and high precision dynamic contact angle measurements. Figure 5 show the gas phase silanization process used for surface modification of 4 inch silicon and glass wafers and a snapshot of dynamic contact angle analysis of such siloxane layers for quality control of wettability characteristics. With our protocol we are able to coat several wafers simultaneously during one synthesis.

Graphene based thin films: The siloxane layers prepared in a process such as described above were later on used for immobilization of graphene oxide flakes and realization of high quality graphene oxide (GO) thin films on glass and silicon wafers.[56] For the realization of GO thin-films, we worked out a brand-new exfoliation low temperature exfoliation followed with desalination (LTEDS) protocol yielding high GO flakes with high density of oxidative surface functional groups and very low residual salt content as by-product of the chemistry used in the exfoliation process. GO stock solution is spin-coated onto surface modified wafers and incubated for covalent immobilization. The standardized process-line offers a unified approach for routine fabrication of thickness controlled GO thin films on

applications. Possibility of rendering surfaces with specific functional groups using different types of silane molecules make them attractive for wide spread use. It is fundamental to understand the reaction conditions of the silanes, the process of the siloxane layer formation, and the possible influence of the substrate morphology in order to realize high quality and large area coatings. In past years we have cultivated know-how to use silanes such as Aminopropyltriethoxysilane (APTES),

glass/silicon wafers. The GO thin films served as building block for the top-down fabrication of 2D devices for sensor applications.



GO can be converted to semiconducting reduced GO (rGO) films by thermal annealing procedures and can be

Figure 6: Patterned graphene based thin-films. (a) A 4 inch silicon wafer micro-patterned by photolithography, SEM image of test structures, and (b) GO films patterned using nanoimprint lithography.

patterned in standard top-down lithography processes for desirable architectures as shown in figure 6.

2D device architectures: Several biosensor platforms and technologies based on GBMs have been developed by Pachauri et. al. in the last years. As shown in the bottom figure here, combination of top-down fabricated nanoelectrode arrays covered with CVD grown graphene was used for highly-sensitive detection of cardiac disease biomarkers such as Myeloperoxidase (MPO) and Fatty acid binding proteins (FABP) from concentrated physiological buffers. Development of sensor platforms based on the use of micro/nano-electrode arrays (MEAs and NEAs respectively) at wafer-scale and using CVD graphene as a transducer material while facilitating a high throughput fabrication process, also provides advantages over other platform for the capability of sensing globular biomolecules in concentrated buffers [57]. The group is currently developing such MEA/NEA-Graphene interfaces further and investigate the underlying signal transduction mechanism responsible for superior sensor performance of such for biosensor applications. Other than the sensor platforms based on CVD graphene, there has been an intensive focus on using chemically produced GO as an alternative for biosensor realization at the wafer-scale. The group has in last years established a new nanofabrication protocol which provides a front-end-of-line (FEoL) integration of chemically produced GO.[56] The image on the right in figure 7 shows a typical device produced out of such a FEoL integration of chemically produced GO. The platforms were used in several label-free biomolecular assays. GO thin-films produced via FEoL process were also used as classical Au/glass SPR chips with rGO thin films as functional layers showed promising results. It was found that the bipolar electronic property of rGO allows an enhancement of the SPR signals by applying bias voltages to the rGO thin films in an electrochemical SPR setting. Thereby, a remarkably limit-of-detection for prostate cancer protein biomarkers was achieved (Lu, 2018). Furthermore, several straightforward protocols for the fabrication of microelectrode arrays based on rGO were demonstrated. For example micro-patterned rGO arrays were used to electrically monitor the cell–substrate adhesion.[58] Also several bottom-up fabricated sensor platforms using single flakes of GO as transducer material were realized with remarkably high yields.[59] The use of rGO as a transducer material in these reports are among the foremost studies carried out of this kind for the realization of cell-substrate impedance spectroscopy with single-cell resolution as well as impedance based molecular sensing of glucose.[60] The GO based sensor were mounted on a measurement platform equipped with a fluidic cell and can be deployed point-of-care using homebuilt portable measurement units [61]. The GrO based sensors react to changes of pH value and can be used for biosensing. When the pH of the solutions varies from pH 6 to pH 8, the device shows a bipolar transport behaviour with an ON/OFF ratio of around one order of magnitude, and the devices demonstrate a slightly dominant p-type transport characteristics (at anodic side). Such GO devices were recently shown as biosensor platform using GrO layers

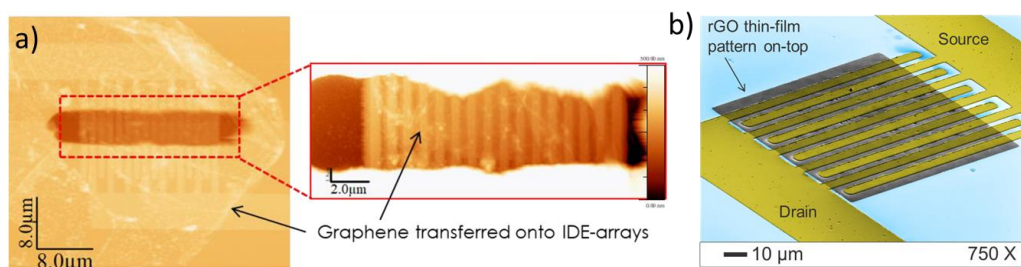


Figure 7: Graphene based electrical devices for biosensor applications. (a) CVD graphene transferred onto electrode arrays shown by AFM characterization, and (b) SEM image of a typical rGO based device.

as an electrical transducer that is able to distinguish single nucleotide polymorphisms (SNPs), in the high ionic strength of a physiological buffer.[62] It is known that SNPs in DNA and resulting configurational changes are associated with grave disorders e.g. neurodegenerative conditions and therefore serve as unique biomarkers [63, 64]. It was shown that chemically exfoliated GrO can be used as a suitable transducer material for the realization of label-free sensor platforms in a simpler, scalable, bottom-up fabrication approach with very low device-to-device variations in sensor characteristics. GO sensors are able to distinguish SNPs at analyte DNA concentrations as low as 5 nM. Interestingly, while the GrO based devices showed a field-effect behaviour in an electrochemical gate similar to that of graphene, it was found that the thicknesses of biofunctionalized layers also played a pivotal role in determining the biosensor response – which needs to be elaborated further by carrying out systematic studies. Based on our findings, we believe that the effect of such delicate changes in biomolecular conformations during analyte-receptor binding can be studied in much detail using advanced high-resolution spectrometry techniques such as circular dichroism (CD) spectroscopy and atomic force microscopy techniques. In order to develop understanding of such phenomena on liquid-solid interface and their effect on the electrical properties of the 2D materials based biosensor platforms, a collaboration has been started with the research group of Prof. XianPing Chen from Chongqing University China, where using multiscale modelling methods, we aim at designing an experimental framework to further elaborate on such biomolecular interactions.

Stepwise, controlled modification of Graphene platforms: The functionality of graphene platforms dominate their interactions at biointerfaces and dramatically influence the reproducibility of the obtained results. There are two main methods for functionalization of graphene derivatives: i) covalent and ii) noncovalent functionalization. Formations of covalent bonds is a robust method with a high stability at complex media but it disturb the π -conjugated system of graphene derivatives and show a high adverse effect on their optical and electrical properties [65, 66]. Noncovalent functionalization, on the other hand, do not affect the chemical structure of graphene platforms but at the cost of their stability [67]. Recently, we have solved this problem by demonstration a new functionalization method so called “non-destructive covalent functionalization” [68]. In this method carbon nanomaterials are functionalized covalently by triazine functional groups through nitrene [2+1] cycloaddition reaction at ambient conditions. The covalently attached

triazine functional groups do not disturb the π -conjugated system of carbon nanomaterials and do not show any adverse effect on their

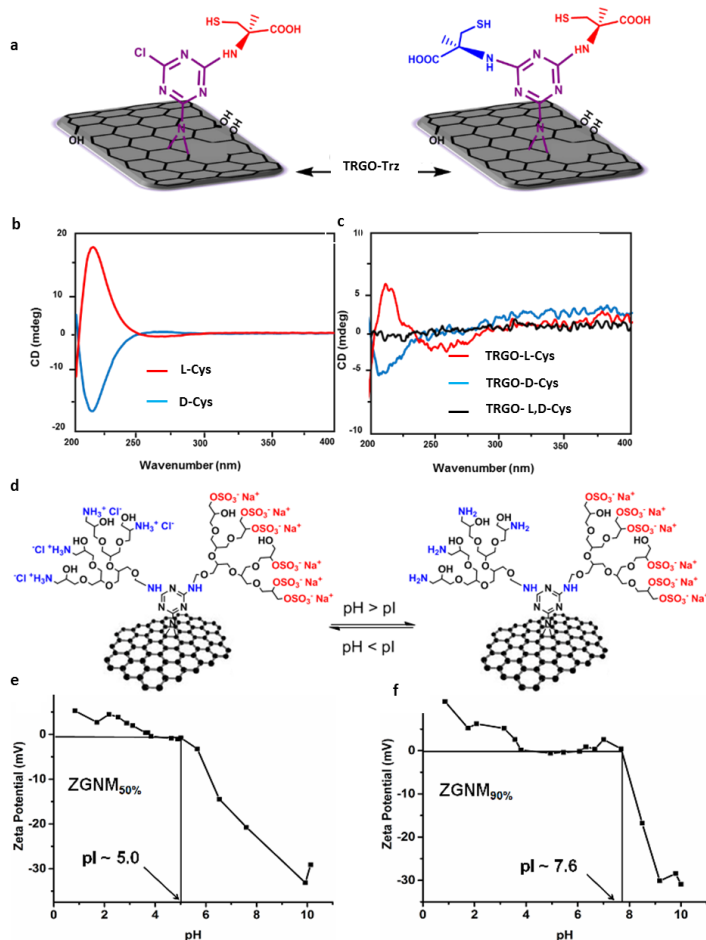


Figure 8. a) Stepwise attachment of the L-cysteine and D-cysteine (L-Cys and D-Cys, respectively) to a triazine-functionalized graphene sheet (TRGO-Trz), showing the ability of this method for the construction of graphene platforms with defined functionality. b) Circular dichroism (CD) spectra of free L-Cys and D-Cys. c) CD spectra of TRGO-Trz₁-L-Cys (red), TRGO-Trz₁-L,D-Cys (black) and TRGO-Trz₁-D-Cys (blue). d) Zwitterionic graphene sheets synthesized by stepwise conjugation of polyglycosulfate and polyglycerolamine branches to their triazine functional groups. While the polyglycosulfate branches are negatively charged at pH > 2, the polyglycerolamine branches switch to positive or neutral states by manipulating the pH. Isoelectric point (pI) of zwitterionic graphene sheets could be changed by manipulation of the number of their amino functional groups. e, f) The zeta-potential titration curves of zwitterionic sheets synthesized using polyglycerolamine with 50% and 90% amino functional

intrinsic optical and electrical properties. Beside non-destructive feature, this covalent functionalization method provide a new strategy for the controlled post-modification of graphene derivatives (Figure 1a)[69, 70]. The controlled post-modification of graphene platforms is investigated by stepwise attachment of a variety of (macro)molecules to the triazine-functionalized thermally reduced graphene sheets (TRGO-Trz). In addition to other spectroscopy methods, stepwise conjugation of L- and D-cysteine to TRGO-Trz to produce graphene sheets with different stereochemistry was proved using Circular dichroism (CD)

spectra (Figure 1b,c). Graphene platforms with defined functionality, in terms of density and type of functional groups, for different biomedical applications are produced by this method. For example, zwitter-ionic graphene sheets with the ability of controlled trapping and release bacteria are synthesized, by this method, and they have been used to study the mechanism of bio-interactions of bacteria at graphene/bacteria interface (Figure 1d). Stepwise and controlled post-modification of triazine-functionalized graphene sheets are accomplished in aqueous solutions and at ambient conditions (25 °C–45 °C)[69]. This is crucial, when bioligands are covalently conjugated to graphene platforms. Most of bioligands and proteins are not compatible with the harsh conditions such as high temperatures and organic solvents, leading to denaturation and loss of their biological function. The first and second chlorine atoms of triazine functional groups can be substituted by moderate nucleophiles such as amino groups at 25 °C and 40 °C, respectively, in aqueous solutions [32, 70]. Controlled and stepwise nucleophilic substitution, through changing the temperature, enable us to attach two different objects to the same triazine functionality and production well-defined graphene platforms in term of functionality [32]. Accordingly, polyglycerol and molecular receptors will be conjugated to triazine-functionalized graphene sheets, step by step and in ambient conditions, to synthesize graphene platforms for specific interactions with the target biosystems.

Spectroscopic and Microscopic characterization of functionalized graphene platforms: Number of layers, lateral size, crystallinity, elemental composition and physicochemical properties of graphene based 2D networks were characterized by methods such as Scanning force microscopy (SFM), SEM characterization techniques [36]. As shown in figure 9, SFM in tapping and quantitative nanomechanical mapping mode (QNM) characterize functionalization of graphene platforms.

Increasing the thickness of graphene upon functionalization is an indicator for the successful attachment of functional groups on its surface. The triazine homogeneity and dispersion could be analyzed by measuring the surface roughness of graphene before and after functionalization (Figure 9b,c). The morphology of graphene sheets in aqueous solutions and even their functionality could be investigated by cryo-TEM. Attachment of hydrophilic polymers onto the surface of graphene sheets, through triazine functional groups, causes a flat conformation in aqueous solutions (Figure 9d). In such conformation the high surface area of graphene platform is accessible for biosystems and strong interactions by

multivalency effect could be observed. Also type of functionality of graphene sheets could be investigated by cryo-TEM images. For example, a graphene platform with polyglycerolamine functionality is able to load gold nanoparticles by electrostatic interactions and this could be directly observed by cryo-TEM imaging (Figure 9e). Composition, functionality and structure of graphene platforms could be further investigated and proved by X-ray photoelectron spectroscopy (XPS) and near edge X-ray absorption fine structure (NEXAFS). The composition and all elements in the structure of the functionalized graphene platforms could be detected in the XPS survey spectra. Different carbon atoms concerning graphene platform and functionalities in the

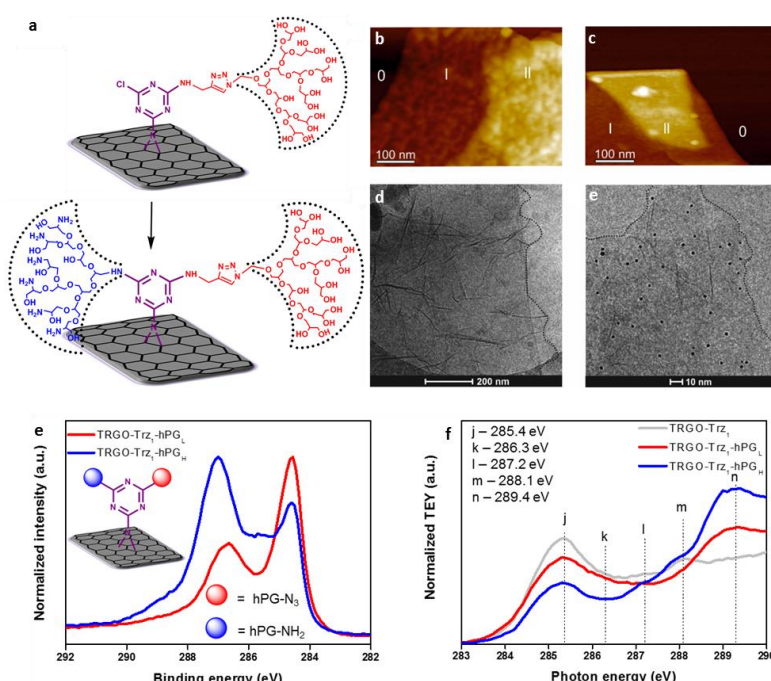


Figure 9. a) Stepwise conjugation of polyglycerol to TRGO-Trz. In the first step polyglycerol was conjugated to TRGO-Trz by click reaction to produce a graphene platform with the low density of polyglycerol branches. In the second step nucleophilic reaction between amino functional groups of polyglycerol and second chlorine atoms of triazine functionality results in graphene platform fully covered by polyglycerol. b) TM-SFM height image of mica (0), covered with single (I) and double (II) layers of post-modified TRGO-Trz by replacement of one Cl atom with a polyglycerol molecule (TRGO-Trz-hPGL). Spherical objects on the surface of graphene are belong to polyglycerol branches. c) TM-SFM height image of mica (0) covered with single (I) and double (II) layers of post-modified TRGO-Trz by replacement of both Cl atoms with hPG molecules (TRGO-Trz-hPGH). TRGO-Trz-hPGH have a height of 11 ± 2 nm, suggesting an integrated polyglycerol layer with the height of 4–5 nm on both sides of functionalized TRGO-Trz. d) Cryo-TEM image of TRGO-Trz-hPGL and e) TRGO-Trz-hPGH after incubation with gold nanoparticles (Sheets boundaries are highlighted by dotted lines). f) highly resolved C1s spectra of TRGO-Trz-hPGL and TRGO-Trz-hPGH. g) expanded low energy section of C K-edge NEXAFS of TRGO-Trz before and after reaction with hPG derivatives.

C1S peak are detected and their intensity are used to calculate the density of each functional group. The Density of polyglycerol branches conjugated to the surface of graphene platform could be detected by ratio of C=C and C-O peaks at 273.7-285.8 eV and 286.3-287.3 eV, respectively (Figure 9e). In the NEXAFS spectra, the C K-edge spectrum (Figure 10f) the TRGO-related π^* resonance intensity (j) decreases with increasing polymer coverage, because polyglycerol coverage attenuates the electron signal originating from the TRGO substrate. Also a resonance peak (n) at 289.4 eV, which is assigned to C–H* resonances, proves covalent functionalization of graphene platform (Figure 9f). The thermal stability and composition of functionalized graphene sheets can be investigated by thermal gravimetric analysis (TGA). Organic functional groups and polyglycerol shell, usually, decompose at temperatures lower than 400 °C. However, graphene platforms decompose at temperatures higher than 500 °C. Therefore, the weight ratios of functionalities and graphene platforms and consequently the density of functional groups can be found by TGA thermograms.

Tuning the wettability and specific interactions of graphene platforms with biosystems: In order to gain control over the biointeractions of graphene, their mechanisms at the nano-biointerfaces should be fully understood.[71-81] The structural parameters and exposure of graphene derivatives must be defined, however, before any systematic study on the mechanism of their biointeractions.[73, 75, 82] One of the most important structural parameters that strongly affect the behaviour of graphene derivatives at biointerfaces is the functionality of these nanomaterials.[69, 83, 84] Graphene sheets could be functionalized, covalently, by many chemical reactions including cycloaddition reactions, esterification, radical addition reactions.[85-87] However, most of usual covalent functionalization are not controlled processes and do not result in surfaces with defined functionalities in terms of number, position, and type of

functional groups.[66] Recently, we have demonstrated a new covalent functionalization method based on nitrene [2+1] cycloaddition reaction at ambient conditions for controlled functionalization of graphene and carbon nanotubes .[68] In addition to nondestructive features, controlled post-modification of the functionalized graphene sheets and construction of two-dimensional platforms with a defined dual functionality is possible by this method.[70] For example, stepwise conjugation of negatively and positively charged (macro)molecules to the surface of graphene sheets result in the two-

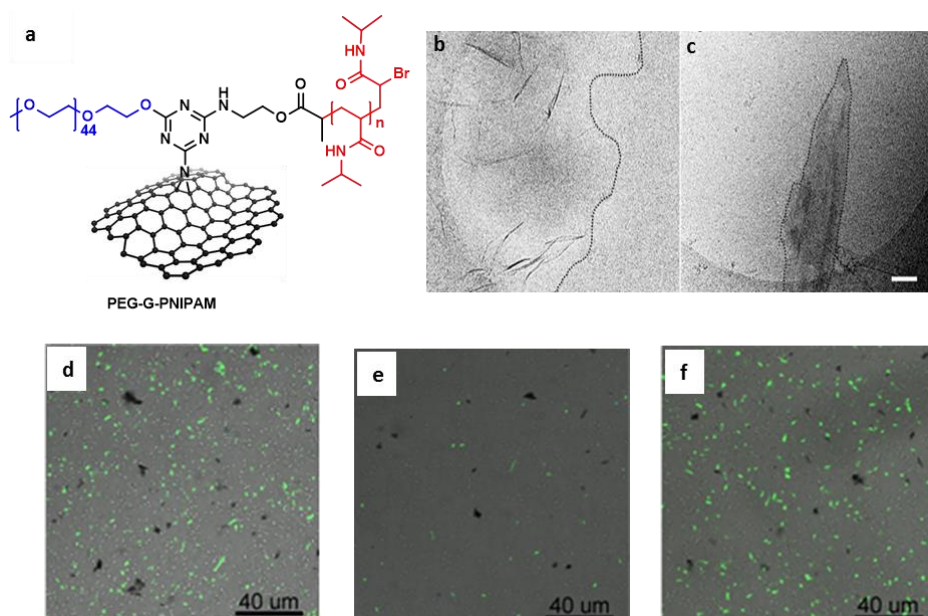


Figure 10. a) Graphene sheet with polyethylene glycol (left) and poly(N-isopropylacrylamide) (right) functionalities. Cryo-TEM images of functionalized graphene sheets at 25 °C (b) and 40 °C (c). Contour of the graphene assemblies is enhanced by dotted lines. Scale bar is 100 nm. CLSM images of FITC labelled *E. coli* incubated with the functionalized graphene sheets at d) 25 °C, e) 40 °C and f) subsequently cooled down to 25 °C.

dimensional nanomaterials. Interaction between these zwitterionic 2D nanomaterials and bacteria could be controlled by changing the pH. The potency of this method to study the mechanism of graphene biointeractions and control such interactions at graphene/bacteria interfaces was further examined by synthesizing a thermosensitive graphene platform with the defined functionality (Figure 10a). The conformation (morphology) of the functionalized graphene sheets in aqueous solutions changed from flat to rolled states by rising the temperature, from 25 °C to 40 °C, and crossing the lower critical solution temperature (LCST) of system. This is an example of the changing of exposure of graphene platforms by a smart functionality. Accordingly, hydrophobic interaction between bacteria and surface of graphene platform was investigated using this system. Because surface of graphene platforms change from hydrophilic state to hydrophobic by changing the temperature of aqueous solution from 25 °C to 40 °C. Confocal laser scanning microscopy (CLSM) images of the FITC labelled *E. coli* that are incubated with the functionalized graphene sheets at different temperatures are shown in figure 10d-f. While in the hydrophilic state (25 °C) a significant quenching of the fluorescence of bacteria cannot be seen, it decreased at 40 °C significantly. This experiment shows that *E. coli* is interacting with the surface of bacteria when it is in the hydrophobic state. Recovering

the fluorescence upon cooling down the temperature shows that the hydrophobic interactions between graphene surface and bacteria are reversible. This is an example, showing how the physicochemical properties of graphene platforms and therefore their interactions at biointerfaces can be controlled by a defined functionality. We have shown that density of triazine functional groups conjugated to the surface of carbon based nanomaterials could be manipulated by performing functionalization reactions at different temperatures or by repeating the functionalization reactions on one batch[68, 70].

1.1 Project-related Publications and Principal Investigators

1. W-M. Munief, R. Lanche, X. Lu, S. Ingebrandt, V. Pachauri*, Wafer-scale fabrication of microelectrode arrays on optically transparent polymer foils for integration of flexible nanoscale devices, *IoP Flexible and Printed Electronics* 2018, 3, 004001
2. W-M. Munief, F. Heib, F. Hempel, X. Lu, M. Schwartz, V. Pachauri, R. Hempelmann, M. Schmitt, S. Ingebrandt*, Silane deposition via gas-phase evaporation and high-resolution surface characterization of the ultra-thin siloxane coatings. *Langmuir* 2018, 34 (35), 10217–10229
3. X. Lu, W-M. Munief, F. Heib, M. Schmitt, A. Britz, S. Grandthyll, F. Müller, J-U. Neurohr, K. Jacobs, H. M. Benia, R. Lanche, V. Pachauri*, R. Hempelmann, S. Ingebrandt, Front-end-of-line integration of Graphene oxide for Graphene based electrical platforms, *Advanced Materials Technologies* 2018, 3 (4), 1700318
4. R. Lanche, V. Pachauri*, W-M Munief, A. Mueller, M. Schwartz, P. Wagner, R. Thoelen, S. Ingebrandt, Graphite oxide sensors are able to distinguish single nucleotide polymorphisms in physiological buffers, *Elsevier FlatChem - Chemistry of Flat Materials* 2018, 7, 1-9
5. L. E. Delle, V. Pachauri*, S. Sharma, O. Shaforost, H. Ma, M. Adabi, R. Lilischkis, P. Wagner, R. Thoelen, N. Klein, R. O'Kennedy, S. Ingebrandt, ScFv-modified Graphene-coated IDE-arrays for 'label-free' screening of cardiovascular disease biomarkers in physiological saline, *Biosensors and Bioelectronics* 2018, 102, 574–581
6. A. Setaro, M. Adeli*, M. Gläske, D. Przyrembel, T. Bisswanger, G. Gordeev, F. Maschietto, A. Faghani, B. Paulus, M. Weinelt, R. Arenal, R. Haag*, and S. Reich*, Preserving π -conjugation in covalently Functionalized carbon nanotubes for optoelectronic applications. *Nat. Comm.* 2017, 8, 14281.
7. A. Faghani, I. S. Donskyi, M. F. Gholami, B. Ziem, A. Lippitz, W. E. S. Unger, C. Böttcher, J. P. Rabe, R. Haag*, and M. Adeli*, Controlled covalent Functionalization of thermally reduced graphene oxide to generate defined bifunctional 2D nanomaterials, *Angew. Chem. Int. Ed.* 2017, 56, 2675.
8. Z. Tu, K. Achazi, A. Schulz, R. Mülhaupt, S. Thierbach, E. Rühl, M. Adeli*, R. Haag*. Combination of Surface Charge and Size Controls the Cellular Uptake of Functionalized Graphene Sheets. *Adv. Funct. Mater.* 2017, 1701837.
9. M. F. Gholami, D. Lauster, K. Ludwig, J. Storm, B. Ziem, N. Severin, C. Böttcher, J. P. Rabe, A. Herrmann, M. Adeli, R. Haag. "Functionalized Graphene as Extracellular Matrix Mimics: Toward Well-Defined 2D Nanomaterials for Multivalent Virus Interactions", *Adv. Funct. Mater.* 2017, 1606477.
10. I. Donskyi, M. Drüke, K. Silberreis, D. Lauster, K. Ludwig, C. Kühne, W. Unger, C. Böttcher, A. Herrmann, J. Darnedde, M. Adeli, R. Haag. Interactions of Fullerene-Polyglycerol Sulfates at Viral and Cellular Interfaces. *Small* 2018, 14, 1800189.

1.1.1 Articles published by outlets with scientific quality assurance, book publications, and works accepted for publication but not yet published. -

1.1.2 Patents

1.1.2.1 Pending

IWE1: None

FUB: FU: M. Adeli, B. Ziem, R. Haag Controlled Functionalization Of Carbon Based Nanomaterials, EU Patent application 2014.

1.1.2.2 Issued

1. V. Pachauri, A. Ahmad, K. Balasubramanian, K. Kern, Autosynthesizer for the controlled synthesis of nano- and sub-nanostructures, European Patent 2010, US Patent 20110311438, EP2370205A1, MPI for Solid State Research Stuttgart/Max Planck Innovation GmbH

2 Objectives and work programme

2.1 Anticipated total duration of the project

The proposed work-packages in this proposal are planned to be completed in a maximum of **three (3) years**.

2.2 Objectives

As discussed in the beginning, this proposal aims to set an experimental framework for the study of dynamic wetting behavior at flexible and adaptive two-dimensional materials and focuses on graphene based material for realization of original objectives. The objectives of this ambitious projects are therefore clearly outlined for effective outcomes along the three years running period and are discussed below in three separate sections:

A. Fabrication of platforms for studying wetting behaviour of 2D substrates: Multiscale approach to the study of

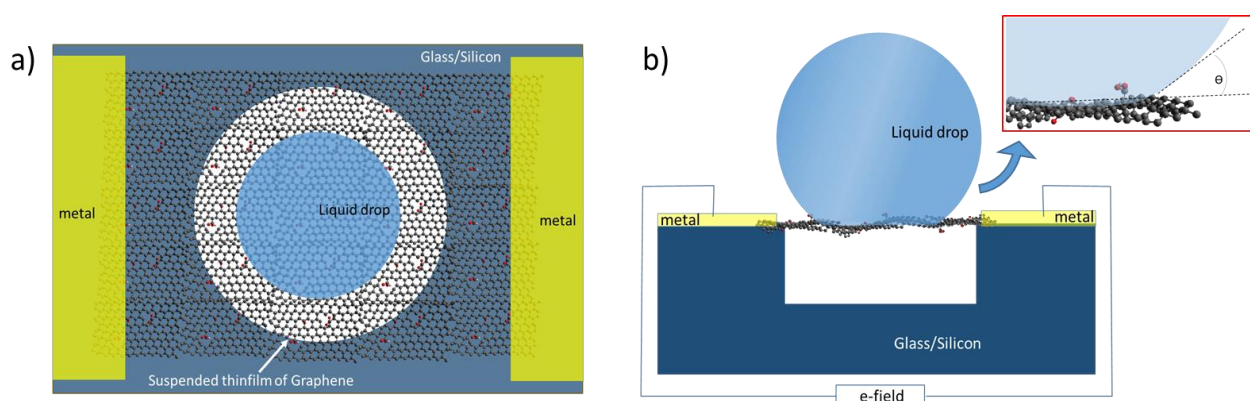
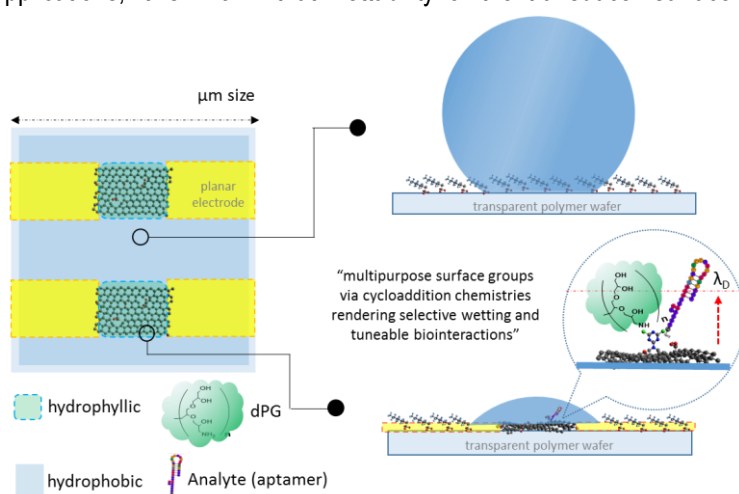


Figure 11: Proposed graphene based chips (a) top-view, (b) side-view for studying the wetting behaviour influenced by intrinsic parameters and substrate interactions.

wetting behaviour at graphene substrates is systematically structures into grouping of parameters that are expected to influence the wetting process. Here it is required to compare the wetting phenomena of graphene surfaces in different possible configurations i.e. single, double, multiple atomic layers with varying density of defects, C/O ratio in suspended and on-top-of-substrate conformations. In order to realize experimentally, we will work out glass or silicon chips with micro and nanosized holes for the suspension of graphene films as shown in figure 11. The wetting behaviour will be studies at micron and sub-micron scales using state of the art characterization tools. Localized wetting at the interfaces will be studied in detailed using high precision and high throughput analysis of wetting behaviour using conventional as well as microscopic (confocal) drop-shape analysis methods. Effect of electrical field on the wetting properties of bare graphene thin-films will be investigate in a specially build set-up.

B. Surface modification of 2D substrates for enhanced localized wetting: Graphene and other 2D materials form ideal surfaces and electrical and optical transducers and assembly of sensor platforms. For biosensing applications, it is known that wettability of the transducer surface is central to the overall performance of the



selective biointeractions.

C. Tuneable interfaces for enhanced molecular binding: Density and distribution of bioreceptors anchored onto graphitic surface through -triazene functional groups will eventually determine the efficiency of biomolecular interactions. Exemplary platform to demonstrate enhanced biointeractions will be realized for detection of cancer specific biomarkers such as Prostate specific antigens (PSA). PSA specific aptamers will be immobilized on the patterned 2D transducer via cycloaddition chemistry approach to render biofunctional layer with tuneable wetting. These islands of enhanced biointeractions will be realized as field-effect transistor based devices on optically transparent flexible substrates.

2.3 Work programme including proposed research methods

The scientific goals and objectives of this proposal as outlined above clearly go beyond the state-of-the-art in studying wetting phenomena at the two-dimensional material's surfaces. The objectives have been set clearly on the basis of our previous findings and the common strengths of the work groups involved in this proposal. The realization

of the graphene based thin-films in different forms and architectures, and surface modifications for rendering special wetting functionalities and the underlying mechanism have been set in a highly interactive work programme between the main partners and links for sharing of the experimental data with theoreticians have been made. For efficient management of this three years project, the work programme is divided into three distinct work-packages (WPs). The WPs have been further divided into distinct tasks and deliverables

WP1: Assembly of 2D interfaces

Thin-films for the study of wetting behaviour at 2D interfaces will be prepared in this WP jointly by FUB and RWTH and the team at the RWTH will take the lead. The realization of high quality thin-films with controlled surface and material properties is crucial for the following studies of the wetting behaviour in WP2 and the development of tuneable and adaptive interfaces for enhanced biomolecular interactions(WP3). Building up on the know-how at RWTH on the surface modification techniques, thin-films preparation and substrate transfer protocols from our previous works, the team will work towards realization of thin-films of GBMs (graphene and rGO) in suspended form and on optically transparent flexible polymer wafers. The deliverables set for this WP are especially demanding and require knowledge and experimental skills in surface modification strategies, nanofabrication and elaborate surface characterization methods including Elliposmetry, Wetting behaviour analyses, AFM, optical microscopy and SEM tools.

T1.1: Substrate modification and characterization: As laid out in the objectives we aim to make use of two different platforms for the study of wetting behaviour. First, high quality glass wafers with very low surface roughness and other heterogeneities will be used for the fabrication of specialized chips with scaffolds that can support the suspension of thin-films as shown in the figure 11 in the objectives section. Secondly, optically transparent polymer films based on polyimides will be used as a flexible substrate.[Ref] For robust attachment of graphitic surfaces onto the substrate, it is required to render the substrates with highly uniform surface characteristics.[] This surface modification of glass and polymer wafers will be achieved using our high-quality gas-phase salinization methods, optimized and standardized using surface characterization tools. In addition, we will work out new surface modification approaches for preparing glass and polymer substrates with suitable chemical functionalities for Triazene chemistry.[Ref] This requires rendering the glass and polymer substrates with amino functional groups, where a suitable surface modification process will be worked out and standardized.

T1.2: Graphene based thin-films: Large-area graphene from CVD and/or epitaxy growth methods will be used for single and multi- atomic layer films in suspended and on-substrate configurations. This requires realization of high quality surface transfer of graphene from their growth substrate to glass/polymer substrates. The processes used for this kind of transfer usually involves coating a solvable polymer on graphene as a support-layer. The graphene sample is then placed in a etch-bath to remove the substrate used for the CVD/epitaxy growth, thereby leaving graphene layer attached to polymer support layer. Due to complexities of using polymer coating, liquid mediated transfer, it is usually difficult to carry out large area transfer of high quality graphene layers. In this task, we aim to further investigate the substrate transfer process for graphene and overcome current challenges.[88, 89] Other than this, rGO thin-films in suspended configuration will be prepared by realization of thin films on an etch-able (dissolvable) substrates and carry out a substrate transfer. Realization of thin films of rGO on flexible wafers will be carried out in an approach similar to the preparation of thin films over glass and silicon wafers. Graphene-based flakes will be modified with known density of triazine groups (G-Trz) including 1/25, 1/100 and 1/300 (triazine/graphene carbon atoms) in a non-destructive nitrene [2+1] cycloaddition reactions at different temperatures. The triazine groups on graphene flakes are expected to provide superior covalent attachment to the surface modified glass/polymer substrates. Thin films will be surface characterized using state of the art characterization tools such as AFM, Elliposmetry, Fluorescence, Raman, X-ray photoelectron spectroscopy, and techniques to ascertain the thickness, size, and material composition.

T1.3: Patterning and surface characterizations: During this task, graphene and rGO thin-films will be undergo top-down nano-/microfabrication process. For this, photolithography and nanoimprint lithography masks and moulds, respectively will be designed by us. In case of suspended thin-film configuration of graphene, we will try two different approaches for comparison of yield and quality of nanofabrication. In one approach, substrate will have scaffolds cast out into a sacrificial layer before the transfer of graphene and further processing. In the second approach, an under etching of sacrificial layer will be carried out after structuring of graphene and rGO thin-films. The second approach may be advantageous for its applicability to both graphene and rGO will common lithography process-steps. The platforms prepared here, in some cases, are expected to undergo thermal step (especially for system integration in WP3) which will be carried out using Rapid thermal annealing process followed with spectroscopic and electrical characterizations for material and electrical properties respectively.

WP2: High precision analysis of wetting-(de)wetting behaviour

This WP is aimed at establishing a workable experimental setup for studying the wetting behaviour of 2D interfaces made of graphene and rGO produced in the WP1. Following the objectives sketched out in this proposal, WP1 provides thin film platforms which are flexible,

T2.1: Basic characterization: Post processing, platforms will be characterized for their wetting properties. High precision dynamic drop shape analysis methods will be used as a work-horse platform for the routine characterization. The vdW screening of standard substrates was earlier reported by few-layer graphene and MoS₂, we will here use a similar approach for direct determination of the vdW forces from thin film platforms.[20]. The surface stress in suspended graphene and graphene on optically transparent polymers will be measured using a specialized set-up available with our collaboration partners within SPP2171 (Vollmer and Butt, MPI Mainz; Thiele, Uni. Münster) where a confocal microscope is used to characterized cropping behaviour in microscopic dimensions. It is known that when a liquid droplet contacts a soft elastic substrate, a deformed microscopic region emerges at the vicinity of the contact line, and the shape of this region can be used to calculate the surface stress directly.

T2.2: Selective and site-specific surface chemistry: Nanopatterned thin films post processing (after annealing) will be surface modified with known density of triazine groups so as to provide multipurpose functional groups as “physicochemical anchors” for stepwise and covalent attachment of dendritic polyglycerols as well as bio-receptors (figure). In order to achieve consistent physicochemical characteristics at these interfaces, high throughput surface analyses using spectroscopy, microscopy and electrochemistry approaches will be carried out. The wetting behaviour analysis of these interfaces will be carried out similar to as laid out in T2.1.

T2.3: Influence of ionic composition and temperature: ionic composition such as pH and ionic strength of the solution are expected to affect the wetting properties of the graphene platforms modified with nanogels functional layers. Additionally, we will also study if the influence of temperature significantly alters the wetting properties of the platforms. The results of influence of these parameters on wettability fluctuations will be communicated with the group of Prof. Christian Holm, University Stuttgart for further investigations where they plan to extend their existing Lorentz Boltzmann electro kinetics model with implicitly dissolved solvent and ions towards developing a model for explicit coupling of polymers. As a theory group, Prof. Holms has developed excellent know-how to study the effect of pH and template on the wettability of polymer brush layers on surfaces and experimental findings of this WP are expected to allow understanding of influences from pH, applied electrical field and physical characteristics of flexible substrates.

WP3: Tuneable 2D interfaces for enhanced Biointeractions

Selected graphene platforms with appropriate wetting characteristics will be used for decoration of biofunctional layers and demonstration of enhanced and on-demand wetting capabilities of the new graphene based platforms.

T3.1: Microsystem integration of 2D interfaces: Layout for fabrication of electrical sensors in ISFET configuration will be worked out during this task followed with lithography process for actual chip fabrication. Nanoimprint lithography and Photolithography tools will be used respectively, to pattern graphene or rGO thin-films and patterning of electrically conductive electrodes of a metal layer forming ohmic contact with graphene patterns. Following this, the devices will be contact passivated and surface characterized. The devices will be thoroughly tested for their sensor characteristics and optimized for sensor operation. All these steps will follow chip encapsulation steps for fluidic handling and realization of external electrical contacts in AC/DC readout configuration.

T3.2: Biomodification of selected 2D interfaces: Density of bio-receptors and wettability of platforms will be manipulated using graphene sheets with different density of triazine functional groups. This will enable us to investigate the effect of bioligand density and wettability on the interactions between platforms and biosystems and optimize the biosensor for the stronger but specific interaction with the target macromolecules. Here, aptamer sequences specific to cancer-biomarker proteins (e.g. prostate specific antigens) or fragmented antibodies (such as fatty acid binding protein specific and myeloperoxidase specific) will be covalently bonded to the triazine functional

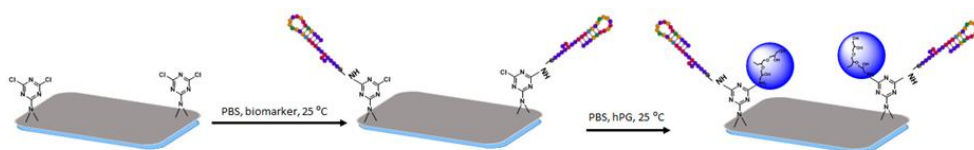


Figure 6. Stepwise attachment of biomarkers and hPG to 2D platforms by nucleophilic reactions between amino functional groups of these objects and triazine groups of graphene flakes. The wettability and density of biomarkers will be tuned using 2D platforms with different density of triazine groups.

The nanopatterned platforms with different density of triazine functional groups, they will be exposed to a PBS solution of biomarkers. 2D

platforms will be then washed with water and PBS, vigorously, to remove any physically absorbed biomarker (Figure

6). Attachment of biomarkers to the platforms as well as their density will be measured by complementary surface characterization techniques by spectroscopy and microscopy methods. 2D platforms with different density of biomarkers will be constructed using precursors with different triazine density.

the composition of 2D platforms could be realized by XPS and NEXAFS. The survey XPS spectra will show the elements and their abundance by which the conjugation of biomarkers to the surface of 2D platforms could be investigated. Improved nitrogen content upon conjugation of biomarkers will be counted for the attached biomarkers and will be used to calculate the density of biomarkers onto the surface of 2D platforms. The next step is to attachment hyper-branched polyglycerols (hPG) to the 2D platforms having different density of biomarkers (Figure 6). Attachment of hPG will improve the wettability of 2D platforms which is crucial for the efficient interactions between biosystems. Covalent attachment of hPG to the 2D platforms will be investigated by AFM and XPS. Topology and increasing the thickness of 2D surfaces upon reaction with hPG indicate attachment of this polymer to the graphene flakes. Also a special peak for carbons of polyglycerol in the C1S peak of XPS spectra, around 277 eV, is an indicator for the attachment of hPG to graphene flakes and preparation of the final 2D platforms with desired wettability.

T3.3: Enhanced binding of biomolecules and assay validation: The new FET platforms realized on optically transparent polymers will be deployed for label-free electrical sensing of biomolecules and the enhanced binding/interaction of receptor analyte will be validated using parallel optical sensing approach.

The following **Gantt chart** summarizes the work-packages distributed between the project partners and associated milestones and deliverables.

	M3	M6	M9	M12	M15	M18	M21	M24	M27	M30	M33	M36
WP1	T1.1											
		T1.2										
			T1.3									
WP2		T2.1										
				T2.2								
				T2.3								
WP3							T3.1					
										T3.2		
											T3.3	

Positioning and impact

The detection of biomolecules is crucial for many areas of healthcare, clinical medicine, food safety, environmental monitoring and homeland security, ranging from uncovering and diagnosing disease to the discovery and screening of new drug molecules and to giving off early warning against health agents. With the advent of nanotechnology, research into nanomaterial-based transducers has triggered a hot research topic in recent years. 2D materials have been widely explored for biosensor systems due to the high surface-to-volume ratio, excellent conductance, low surface resistance, and high field-effect carrier mobility and so on. The experimental methods in developing new biosensors for various applications is common but expensive, time consuming and labour intensive. In order to push the current know-how on 2D material electronics for sensor applications. Specifically for biosensors, there are efforts being made to develop a unified theoretical framework and understanding of solid-liquid interface of 2D materials. Multiscale modelling approaches are common which rely on modelling of electronic transport using DFT and/or similar methods, modelling of solid liquid interface and molecular dynamics simulations. The modelling of solid-liquid interfaces of 2D materials is, however, not reliable for the lack of experimental correlations to similar theoretical observations in other material systems. Therefore, the project proposed here underlines the critical need to investigate the wetting heterogeneities at the solid-liquid interface of 2D materials that come from their inherent characteristics and means to exploit them for new technologies. The establishment of the experimental framework at 2D material interface which also builds on the expertise of this consortium caters the objectives of SPP2171 very well in exploring the dynamic wetting at flexible and adaptive wetting phenomena at new flexible surfaces. In this regard, this proposal makes bold observations of the opportunities that are expected to come across by working on surfaces that do not have bulk-properties and can be modified in robust controlled manner for manipulating their wetting properties and study the influence of microscopic/macroscale, chemical and physical factors.

The outcomes of projects are expected to eventually help other computational approaches based on multi-scale modelling that will help not only in providing a Fundamental understanding of the material behaviour and phenomenon at nano- and micro-scale, respectively, but also in setting protocols for optimizing the device efficiency

with less extensive experimental testing, resulting in cleaner and energy-efficient development. This project is also well-embedded into the concentrated activities towards understanding and multi-purpose applications of novel 2D material systems at RWTH Aachen University. Several institutes are joining their efforts under the umbrella of the *Aachen Graphene & 2D-Materials Center* (<http://www.graphene.ac/>), of which IWE1 is soon to be part of with expertise in 2D materials based biosensor technologies. This centre provides a remarkable infrastructure as well as attracts researchers with international track records in the rising field of 2D materials towards Aachen to work on key future technologies based on 2D materials. The know-how in 2D material research from various research groups including IWE1 is being consolidated at the Centre for Micro and Nanosystems Technology (CMNT) under a new initiative called ForLab2DForME supported by BMBF. This joint initiative is dedicated towards technological and industry-near integration of 2D materials and realization of technology demonstrators in key areas. A new fabrication clusters with high-end equipment for synthesis, processing and characterization of future 2D materials will be set-up at CMNT. Access to these high-class facilities will give a further boost to foundation of this proposal for carrying out basic study of the 2D material-liquid interfaces and greatly benefit in achieving the deliverables and objectives. The researchers working on this proposal will be joining into these activities and interact with a mix of internal reports as well as renowned, international guest speakers during our regular seminar meeting. The platform serves as a catalysts for the researchers working in different fields of 2D materials to come together and explore new science with 2D materials.

2.4 Data handling

Data will be acquired and stored to ensure accessibility to all the researchers related to this project. The data management plan will be discussed in the beginning of the project and implemented in accordance with institutional guidelines. The coordinators on both sides will be responsible for overall quality assurance. Detailed protocols for extracting data from primary and secondary sources will be developed, piloted, refined and agreed. RWTH has a Data Management Team which will provide support during these tasks. Online resources of RWTH will be also utilized as well and project data will be backed up and secured on a regular basis at RWTH and FUB via intranet that will be hosted by RWTH or FUB. The PIs will oversee the overall data management process, ensuring metadata production, cross-checks, back-ups and other quality control activities. Each Beneficiary will be responsible for routine supervision of the dataset development, extraction, processing of the datasets. Finally, both partners will be responsible for dealing with quality and sharing and archiving of data.

Dissemination of results. Data of not sensitive nature and/or subject to confidentiality agreements will be made open-access via institution based on-line repositories and dedicated website resources. Where possible, we will use beneficiary-based online and/or electronic archives or those provided by RWTH. The results of the consortium will be disseminated as efficiently as possible through the scientific, engineering and medical community to achieve maximum impact. We will exploit all possible dissemination channels: publication in high-impact international journals (as previously achieved by the consortium: Nature Nanotechnology, Scientific Report, ACS, Wiley publications etc.) as well as communications at conferences in the different fields.

Communication to the public. Where possible, publications in popular science journals will be used. There will be various local communication endeavors in particular Science Festivals with talks/workshops to convey our work and create interest amongst the wider public. Outreach in high schools will be a particular focus. RWTH conducts various study courses and research programs at the interface of physics, material science, engineering, biological sciences and nanotechnology including workshops and seminars in relevant areas or direct training of students.

Knowledge protection. There is a high chance that some of the schemes and techniques developed by the consortium will result in international patents. PIs and partners of this proposal hold several patents and are therefore well acquainted with the IPR protection aspects. Furthermore, members have experience in spinning out their research into start-ups and to other industry players.

2.5 Other information

The experiments planned in the project do not involve humans or animals. The biomaterials will be procured from commercial sources. The results obtained in the proposed work-programme will comply with the DFG and EU established standards.

2.5.1 Risk management and methodology

Risks for nanofabrication: The substrate transfer processes for CVD grown graphene involves of different chemicals, which may result in doping or impurities in graphene. Property fluctuations arising from such impurities are not desirable and shall be accounted for, while carrying out the data-acquisition and modelling work. Also the substrate transfer may result in irregular interfaces due to folds and material edges exposed to the environment. Eventually, errors and discrepancies coming out of such issues may be sorted using statistical approaches. While the

nanoimprint is relatively an easier, cost-effective and cleaner process to carry out reliable nanofabrication processes, issues with mould design, imprinting process and gaps in transfer of mould structures may result in device variations. Even as such risks are low, a high throughput e-beam lithography tool will be made available to carry out the nanofabrication process.

Risks for surface modifications: We aim to practice site-specific and identical surface modification strategies on the nanopatterned graphene thin films for chemical surface functionalization of polymer layers as well as immobilization of biomolecules. Spotting pico-litre to nanolitre volumes on nanostructured surfaces has been previously achieved by us using microspotting technique. The microspotting may sometime result in inhomogeneous density distributions. In careful optimizations, we aim to minimize such variations and minimize the risk. Eventually, all wet bio-immobilization methods may be useful to minimize such variations.

Risks from collaborations: Interdisciplinary and international collaborations are not easy and therefore require frictionless co-working aptitude. We will schedule a bi-monthly tele-conference, student exchanges and annual face-to-face meetings for the critical review and monitoring of the work-progress.

Risks in theoretical modelling and simulation framework: The accuracy of the models cannot be guaranteed. Therefore, modelling tasks should be strongly interacted with the experimental characterization and verification. We will ensure the measures for intensive communication with collaborators for theoretical work.

2.5.2 Project organization and means implemented

Consortium

FUB is one of Germany's most distinguished universities in the basic science as well as humanities and social sciences. The research institutes of FUB have been reorganized into four interdisciplinary areas so called clusters since 2003. Also Charité –Universitätsmedizin Berlin is a relatively new institute which is created by combining the medical institutions of Freie Universität Berlin and the Humboldt University Berlin. FUB is consisting 12 departments and is one of 11 elite German universities that receive strong funding for the future planes and researches. The Department of Biology, Chemistry, Pharmacy is one of the most active of FUB and is divided to three different institutes: including the *Institute of Biology*, the *Institute of Chemistry and Biochemistry* and the *Institute of Pharmacy*. The institute of chemistry and biochemistry together with the many local research centers have strong collaborations with other universities and many scientific associations around the world. Prof. Rainer Haag's group is one of the biggest research groups in this institute and it is contributing in many researches and scientific programs. The focus of his group is synthesis of biocompatible macromolecules and their hybrids for the future biomedical applications. The synthesis and functionalization of macromolecules, in particular polyglycerol derivatives, and their applications in biomedical applications, ranging from drug delivery to pathogen interactions and functional surfaces. In the past decade, Prof. Rainer Haag has published more than 350 paper in the international scientific journals and issued more than 25 patents. He has a strong scientific network around the world. In 2014 Prof. Mohsen Adeli was invited to join the department as guest professor and to develop new hybrid nanomaterials for the pathogen interactions leading to many high ranked scientific publications and two issued patents.

In this project, the synthesis of polyglycerol derivatives and controlled functionalization of graphene will be performed by both groups at FUB. The surface characterization techniques of this group will be used for the characterization of the synthesized materials.

Prof. Dr. Rainer Haag is a leading expert in the field of macromolecular chemistry and materials science. He investigates the synthesis of the new dendritic polymers, in particular polyglycerol, and their hybrids as well as biomedical applications of the synthesized materials. In the past decade, variety of dendritic polymers and their bioconjugates are synthesized by his group and they have been used for many biomedical applications ranging from drug delivery to tissue engineering. More recently, he has focused on interactions between pathogens and nanomaterials including nanogels and carbon surfaces. His studies on interactions between pathogens and nanomaterials has revealed many significant parameters and their crucial roles at this biointerfaces. He published more than 350 research articles in international journals. He is owner of more than 25 patents and a member of editorial board of high impact scientific journals. He is the organizer of many associations including SFB765.

Prof. Mohsen Adeli is a professor of macromolecular chemistry at Freie Universität Berlin. His main research interests include design and synthesis of hybrid nanomaterials composed of macromolecules and carbon-based nanomaterials, with a keen interest in their biomedical applications. Nondestructive functionalization of carbon nanotubes by nitrene mediated [2+1] cycloaddition reactions at ambient conditions is another objective of his research group. Recently, he also focused on the behaviour of polymer-functionalized carbon nanomaterials at the nano-biointerface: Biointeractions, cellular uptake pathways, intracellular trafficking and localization as well as intracellular stimuli-responsive behaviour of two-dimensional nanostructures are ongoing projects in his research group. By understanding and combining basic synthetic and physical organic chemistry of (macro)molecules and

one- and two-dimensional carbon nanomaterials, Prof. Adeli investigates challenges in materials and life sciences as an interdisciplinary research field. He authored almost 100 scientific papers and holds over seven patents.

RWTH is the largest technical university in Germany with 45,377 students enrolled in 157 degree programs. The number of foreign students (9,651 students from 131 countries) and RWTH's international network (of formalized collaborations) with over 100 universities worldwide highlight its international reputation. RWTH offers 18 graduate programs among which are eight so-called Research Training Groups funded by the German Research Foundation (DFG). The RWTH is one of 11 German Universities of Excellence and receives additional funding for one graduate school and two clusters of excellence from the Excellence Initiative of the BMBF and the DFG. The university has strong ties with industry, and one of Germany's hubs for university spin-off companies. The Institute of Materials in Electrical Engineering 1 (IWE1) at RWTH Aachen University focuses on research in the field of microsystems with clean room facilities to circuit packaging, thin film and micro-electroplating technologies, respectively.

Dr. Vivek Pachauri (PhD in Physics, Chemistry and Biology undergraduate) is group leader for new materials and interfaces integration to micro and nanoscale systems and currently establishing this new direction at IWE1. He has a multidisciplinary track-record with strong interests in assembly of new nanomaterials for sensor applications with keen interests in improving the nanomaterial interfaces and device-concepts for biomedical applications. In recent years, he has developed know-how in self-assembly, substrate-transfer, thin-film preparation and nanostructuring of GBMs and other nanomaterials. System-integration of nanostructured GBMs, surface modification, and novel approaches for electrical and optical readout concerning basic-issues with reproducible sensor-performance, standardization are key focus in the activities of his research group. He has authored about 20 peer-reviewed articles in various journals in the related scientific fields and currently holds one international patent for automated synthesis of nano and sub-nanomaterials. He has co-supervised >5 PhDs and several masters theses independently. In his research group at IWE1, currently active members include one post-doctoral fellow, 2 doctoral students, 1 master's thesis students and several other students working on topic with 2D materials integration. Among them, Humboldt-fellow **Dr. Satish Kumar** is a PhD in in Engineering Sciences with a focus on Nano-Materials Engineering and Electrochemical Biosensors Development. **Ms. Xiaoling Lu** (MSc. Physics) has experience with the assembly of devices based on GBMs and implementation of impedance and Surface Plasmon Resonance (SPR) based biosensor concepts. A new doctoral student **Ms. Yue Chang** (M.S. Material Science) with knowledge in thin-film physics, computational materials physics and nanomaterials analysis joins Dr. Pachauri's research group in November 2018.

At IWE1, with Prof. Ingebrandt (Director, IWE1) establishing a novel direction with a laboratory for cell cultures on technical substrates for the recording from individual cells, we have overall expertise on biosensor development and nanofabrication methods, label-free, multichannel biosensors, biosensor integration of PoC devices, electrophysiology, cell culture techniques. Besides this, additional know-how in terms of clean room and technical laboratory and general scientific skills is coming from Dr. Xuan-Thang Vu (PhD in Physics) who has long experience with nanofabrication techniques and assembly of the nanoscale electrical sensors using silicon based platforms. Dr. Vu will be closely co-supervising the new doctoral student from this project on tasks related to the clean-room processes. In addition, the field of microfluidics with focus on the development of sensors and actuators in microfluidic systems is chaired by Prof. Dr.-Ing. U. Schnakenberg with focus on electrical impedance spectroscopy, surface acoustic wave sensors, localized SPR spectroscopy, pneumatically driven actuators, digital microfluidics, and magnetic tweezers.

3 Requested modules/Funds

Partners	Salaries	Consumables	Facilities	Equipment	Travel / Exchanges/publ.	Overheads	total
FUB	145 k€	36 k€	6 k€	10 k€	13 k€	42 k€	252 k€
RWTH	199 k€	30 k€	20 k€	10 k€	13 k€	54 k€	326 k€
Total Sum: 578 k€							

3.1. Basic Module

3.1.1 Funding for Staff

On FUB side, We apply for two PhD students and a part-time position for a technician. The distribution of the staff of WP is shown in the grant chart below. PhD1 will be jointly supervised by Rainer Haag and Mohsen Adeli. He or she will have a background in chemistry and will carry out the synthetic work of WP1-3. In addition to standard chemical characterization (NMR, UV-vis and infrared spectroscopy, elemental analysis, TGA and so forth), the student will also be trained in the advanced characterization techniques that are characteristic for working with carbon nanomaterials like graphene derivatives.

On RWTH side, a doctoral candidate will be hired for the research work on the development of different architectures of GBM based thin-films, wetting characterizations and related technology development leading to a Dr. Eng. Degree from the Department of Electrical Engineering and Information Technology. This doctoral position is required and calculated as 100 percent full time according to the current regulations at the RWTH Aachen.

3.1.2. Direct Project Costs

3.1.2.1. Equipment up to Euro 10,000, Software and Consumables

On the FUB side, we apply for a small spin coating device to prepare the respective chip surfaces. RWTH asks for a high resolution drop shape analysis set-up.

On FUB side, the consumables will be spent for chemicals, high purity solvents, small glassware and chips for surface characterizations. On RWTH side, consumables money which will be spent towards buying the high quality wafers (Silicon, Glass and Polymers) to be used as substrates for elaborate characterization of the thin-films and standardization for the further characterizations. High quality Graphene (CVD or Epitaxy) samples with different lattice compositions will be procured from commercial sources. Graphene oxide flakes for preparation of GO and rGO thin-films will be produced in the lab using our exfoliation protocol, however, we need to buy high quality graphite crystals as source material. Photolithography masks and nanoimprint lithography mould for the nanopatterning of Graphene based thin-films will be procured from quality-tested manufacturers. In addition, we require some chemicals and other electronic and fluidic parts for surface modifications, wet-chemistry approaches and device packaging demonstrating tuneable interface. For all this we ask for a sum of 30k over three years. In addition we request for 20k for usage of dedicated measurement facilities.

3.1.2.2. Travel Expenses

3.1.2.2. Participation in the workshops organized by SPP2171 and other relevant conferences and workshops has been planned for the doctoral students working on this projects. Several SPP2171 are planned for the next 3 years which will give the students and PIs an opportunity to communicate their findings to the peers with in this special focused programme as well as to the wider audience active in the field in Germany. In addition, students are will be encouraged to participate in international or European conference of high relevance to and to make academic links with research groups world-wide. In addition, we ask for a sum of 5k euro over three years for each PhD candidates for secondments between FUB-RWTH and other work partners in SPP2171. The students will spend average 3 weeks per semester working with the partners. For these activities, we ask for travel budget of the total sum of € 25k over 3 years.

Student	PI	Expenses over 3 years
PhD1	Rainer Haag	4k€
	Mohsen Adeli	4k€
PhD2	Vivek Pachauri	7k€
Secondments (stay/accommodation)		10
Total		25k€

3.1.2.3 Other Costs

3.1.2.4 Project-related publication expenses: RWTH asks for a total of 1000 euro as project-related publication expenses.

4 Project requirements

4.1 Employment status information

Last name	First name	Employment status	Funding body
Haag	Rainer	Permanent	FUB
Adeli	Mohsen	Guest professor (50%)	FUB
Pachauri	Vivek	Tenured	DFG*

*A letter of support from the IWE1, RWTH Aachen for Dr. Pachauri is submitted along with this proposal.

4.2 First-time proposal data

Pachauri, Vivek

4.3 Composition of the project group

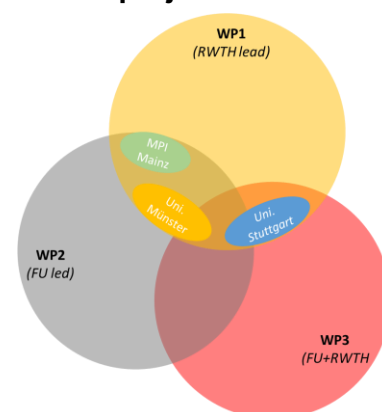
List only those individuals who will work on the project but will not be paid out of the project FUBnds. State each person's name, academic title, employment status, and type of FUBnding.

Name	Academic Title	Institution	Employment status	Type of FUBnding	Role in the project
Rainer Haag	Professor	FUB	Permanent	FUB	PI
Vivek Pachauri	Dr.	RWTH	Tenured	DFG	PI
Mohsen Adeli	Professor	FUB	Permanent	FUB	Co-PI
Cathleen Schlesener	Technician	FUB	Permanent	FUB	Analytics
Xuan Thang Vu	Dr.	RWTH	Permanent	RWTH	Cleanroom processes
Satish Kumar	Dr.	RWTH	Fixed	Humboldt	2D materials Electrochemistry
Xiaoling Lu	M.Sc.	RWTH	Fixed	RWTH	Surface modification
Yue Chang	M.S.	RWTH	Fixed	CSC	Thin-film physics
Uwe Schnakenberg	Prof. Dr.-Ing.	RWTH	Permanent	RWTH	Fluidics

4.4 Cooperation with other researchers

4.4.1 Researchers with whom you have agreed to cooperate on this project

The proposed project makes strong links with leading scientific groups in Germany who are active in the field and are interested in questions sought for exploration in this project. Within the network of SPP2171, the project makes collaborative links with the experimentalists and theoreticians who are also interested in scientific questions related to wetting behavior at two-dimensional interfaces and the effect of other parameters on such 2D surfaces exhibiting dynamic and adaptive wetting properties. The figure on the right side shows the project links with other applicants of the SPP2171. For analysis of wetting behavior at micro and sub-micron scales, we establish a link with the group of Prof. Butt and Prof. Vollmer at MPI Mainz (WP1 and WP2). For the theoretical understanding of observations on graphene films and graphene films modified with polymers, and influence of external factors we have established links with the research groups of Prof. Thiele at University Munster. Their expertise sit between WP1, 2 and 3 of this proposal and closely linked with WP2. Collaborative link with Prof. Holm at University Stuttgart has strong overlap with the tasks outlined in WP3 of this proposal.



4.4.2 Researchers with whom you have collaborated scientifically within the past three years

IWE1, RWTH Aachen:

Rolf Hempelmann (Uni Saarbruecken), **Yannick Coffinier** (IEMN Lille), **Prof. Fred Lisdat** (TH Wildau), **Prof. Karin Jacobs** (Uni Saarbruecken), **Denis Flandre** (UC Louvain), **Prof. Xian-Ping Chen** (Chongqing Uni. China), **Prof. Patrick Herrmann Wagner**, (KU Leuven University, Belgium); **Prof. Ronald Thoelen**, (Hasselt University, Belgium);

Prof. Kannan Balasubramanian (Humboldt University Berlin, Germany); **Prof. Klaus Kern** (MPI for Solid State Research Stuttgart, Germany); **Dr. Hadj Mohamed Benia** (MPI for Solid State Research Stuttgart, Germany); **Dr. Alexis Vlandas** (IEMN Lille, France); **Prof. Chandramouli Subramaniam** (IIT Bombay, India); **Prof. Hatice Altug** (EPFL, Switzerland); **Dr. Pedro Estrela** (University Bath, United Kingdom); **Prof. Richard O’Kennedy** (Dublin City University, Ireland); **Prof. Norbert Klein** (Imperial College London, United Kingdom); **Dr. Jaroslav Katrlík** (Slovak Academy of Sciences, Slovakia); **Prof. Joao Pedro Conde** (INESC MN, Portugal); **Prof. Martin Eickhoff** (University Giessen, Germany); **Prof. Florian Lang** (Tübingen University Germany); **Dr. Yogesh Singh** (Tübingen University Germany).

ICB, FUB Berlin:

Peter Fratzl (MPI-KG, Golm), **Anna Gorbushina** (BAM, Berlin), **Andreas Lendlein** (HZG, Geesthacht/Teltow), **Wolfgang Maison** (U. Hamburg), **R. Mülhaupt** (U. Freiburg), **Jürgen Rabe** (HU Berlin), **Bart Ravoo** (U. Münster), **Peter Seeberger** (MPI-KG, Golm), **Holger Stephan** (Helmholtz-Zentrum Dresden-Rossendorf), **Arne Thomas** (TU Berlin), **Zhibin Guan** (Uni California), **J. Kitzhakkedathu** (UBC Vancouver), **Dusica Maysinger** (McGill, Canada), **G. Multhaupt** (McGill Montreal, Canada), **Ronit Satchi** (Tel Aviv Uni.), **Sunil Sharma** (Delhi University, India), **David Weitz** (Harvard University USA), **Zhiyuan Zhong** (Soochow University, China)

4.5 Scientific equipment

Imaging SPR and CD spectrometer (RWTH): SPR and Circular dichroism spectroscopy techniques remain as gold-standards in analysis of molecular binding and conformations in media or on surfaces. In order to investigate the localized changes in the orientation and conformations of polymeric layers and receptor biomolecules and influence of external parameters, is a critical know-how that we hope to develop in the research group. This know-how will then be immensely useful for the characterization of liquid-solid interfaces based on 2D materials and work as a standard platform for the analysis of intra-molecular and intermolecular interactions that are limited to conformational changes (for example single nucleotide polymorphisms in DNA) yet have significant effect on the device properties. To underline the importance of this collaboration and these subjects for the future research direction of the institute, the IWE1 will invest about a sum of >100.000 € from the start-up funds of IWE1 to procure and establish these important tool and set further ground work towards the activities with graphene and 2D materials systems with tuneable interfaces.

Atomic Force Microscopy for analysis of surfaces in liquids (RWTH): With the new focus on developing know-how in tuneable 2D interfaces at IWE1, procurement of a new AFM platform for surface characterization of nanopatterned surfaces is planned for the coming year. The new AFM platforms will be equipped with electrical measurement modes for microscopic characterization of the electrical properties of the nanostructured materials. More importantly, the new AFM will include capabilities to carryout surface characterizations in liquids for analysis of biofunctional layers, polymer layers and living cells which complements to overall activities of the various research groups active at IWE1. For this IWE1 will invest 50% of the cost of new AFM (~200k€) while Dr. Pachauri is working towards acquiring third party funding for the remaining 50% budget for this equipment. Other than this, IWE1 has two separate clean room facilities for nanofabrication processes and surface modification, polymeric layers integration (fluidics) packaging and electrical and optical measurement platforms. The nanofabrication processes are carried out in a state-of-the-art Central laboratory for Micro and Nanotechnology (CMNT) at RWTH Aachen which is a shared user facility of Department of Physics and Faculty of Electrical Engineering and Information technology. The facility provides a cleanroom of 509 m² of class 5 (DIN EN ISO 14644-1) which will be further expanded to about 1000 m² in next years to cater the demand of new fabrication requirements with novel materials. These facilities are run by highly trained technical staff but also allow for academic and scientific exploration and training of the new students. The tools in the class 5 clean rooms include processes such as Annealing chambers, Atomic Layer Deposition, Chemical Vapour Deposition, Dicing, Dry and Wet Etching, e-beam Lithography, Metallization, Nanoimprint Lithography, Oxidation chambers, Photolithography, Physical Vapour deposition, Wafer bonding. Characterization tools for thin films such as Contact Angle Measurements, Ellipometry, scanning electron microscopy etc. are also available as direct access to IWE1. The cleanroom facility directly managed by IWE1 house a state-of-the-art silicone lab for the processing of polymeric layers, a lab for studying wetting phenomena for micromanipulation such as electrowetting and separate labs for wet-chemistry. Two other labs are well equipped with device packaging, electrical (AC and DC transistor readout techniques) and optical characterization (fluorescence spectroscopy and microscopy techniques) tools. The institute has special know-how on dealing with fabrication issue pertaining flexible polymers as substrates and produced several platforms with quality standards for clinical validations in recent years.

Bibliography:

1. Zhang, J., et al., *Environmentally responsive graphene systems*. Small, 2014. **10**(11): p. 2151-64.
2. Anasori, B., M.R. Lukatskaya, and Y. Gogotsi, *2D metal carbides and nitrides (MXenes) for energy storage*. Nature Reviews Materials, 2017. **2**(2).
3. Balasubramanian, K. and K. Kern, *25th anniversary article: label-free electrical biodetection using carbon nanostructures*. Adv. Mater., 2014. **26**(8): p. 1154-1175.
4. Novoselov, K.S., et al., *2D materials and van der Waals heterostructures*. Science, 2016. **353**(6298): p. aac9439.
5. Mas-Balleste, R., et al., *2D materials: to graphene and beyond*. Nanoscale, 2011. **3**(1): p. 20-30.
6. Asadi, K., et al., *Up-scaling graphene electronics by reproducible metal-graphene contacts*. ACS Appl Mater Interfaces, 2015. **7**(18): p. 9429-35.
7. Lyon, T.J., et al., *Upscaling high-quality CVD graphene devices to 100 micron-scale and beyond*. Applied Physics Letters, 2017. **110**(11).
8. Bolotin, K.I., et al., *Ultrahigh electron mobility in suspended graphene*. Solid State Communications, 2008. **146**(9-10): p. 351-355.
9. Zhang, P., et al., *Fracture toughness of graphene*. Nat Commun, 2014. **5**: p. 3782.
10. Shivaraman, S., et al., *Free-standing epitaxial graphene*. Nano Lett, 2009. **9**(9): p. 3100-5.
11. Kian Ping Loh, et al., *The chemistry of graphene*. J. Mater. Chem., 2010. **20**: p. 2277–2289.
12. Wick, P., et al., *Classification framework for graphene-based materials*. Angew. Chem. Int. Ed. Engl., 2014. **53**(30): p. 7714-7718.
13. Pachauri, V. and S. Ingebrandt, *Biologically sensitive field-effect transistors: from ISFETs to NanoFETs*. Essays in Biochemistry, 2016. **60**(1): p. 81-90.
14. Zhang, A. and C.M. Lieber, *Nano-Bioelectronics*. Chem. Rev., 2016. **116**(1): p. 215-257.
15. Janegitz, B.C., et al., *The application of graphene for in vitro and in vivo electrochemical biosensing*. Biosensors and Bioelectronics, 2017. **89**: p. 224-233.
16. Macedo, L.J.A., et al., *Bioelectronics and Interfaces Using Monolayer Graphene*. ChemElectroChem, 2018.
17. Borini, S., et al., *Ultrafast graphene oxide humidity sensors*. ACS nano, 2013. **7**(12): p. 11166–11173.
18. Sengupta, S., et al., *Theory of Liquid Film Growth and Wetting Instabilities on Graphene*. Phys Rev Lett, 2018. **120**(23): p. 236802.
19. Severin, N., et al., *Reversible dewetting of a molecularly thin fluid water film in a soft graphene-mica slit pore*. Nano Lett, 2012. **12**(2): p. 774-9.
20. Stanislav Tsoi, et al., *van der Waals Screening by SingleLayer Graphene and Molybdenum Disulfide*. ACS Nano, 2014. **8**(12): p. 12410–12417.
21. Peng, S., D. Lohse, and X. Zhang, *Microwetting of supported graphene on hydrophobic surfaces revealed by polymerized interfacial femtodroplets*. Langmuir, 2014. **30**(33): p. 10043-9.
22. Ondarcuhu, T., et al., *Wettability of partially suspended graphene*. Sci Rep, 2016. **6**: p. 24237.
23. Du, F., et al., *Surface stress of graphene layers supported on soft substrate*. Sci Rep, 2016. **6**: p. 25653.
24. Matea, C.T., et al., *Quantum dots in imaging, drug delivery and sensor applications*. International Journal of Nanomedicine, 2017. **12**: p. 5421-5431.
25. Xu, G., et al., *New Generation Cadmium-Free Quantum Dots for Biophotonics and Nanomedicine*. Chemical Reviews, 2016. **116**(19): p. 12234-12327.
26. Hong, G., et al., *Carbon Nanomaterials for Biological Imaging and Nanomedicinal Therapy*. Chemical Reviews, 2015. **115**(19): p. 10816-10906.
27. Mao, H.Y., et al., *Graphene: Promises, Facts, Opportunities, and Challenges in Nanomedicine*. Chemical Reviews, 2013. **113**(5): p. 3407-3424.
28. Barua, S., et al., *Nanostructured MoS₂-Based Advanced Biosensors: A Review*. ACS Applied Nano Materials, 2018. **1**(1): p. 2-25.
29. Choi, G., et al., *Anionic clay as the drug delivery vehicle: tumor targeting function of layered double hydroxide-methotrexate nanohybrid in C33A orthotopic cervical cancer model*. International Journal of Nanomedicine, 2016. **11**: p. 337-348.
30. Qian, X., Z. Gu, and Y. Chen, *Two-dimensional black phosphorus nanosheets for theranostic nanomedicine*. Materials Horizons, 2017. **4**(5): p. 800-816.
31. Tu, Z., et al., *Multivalent Interactions between 2D Nanomaterials and Biointerfaces*. Advanced Materials, 2018. **30**(33): p. 1706709.
32. Tan, K.H., et al., *Functionalized 2D nanomaterials with switchable binding to investigate graphene–bacteria interactions*. Nanoscale, 2018. **10**(20): p. 9525-9537.
33. Tu, Z., et al., *Functionalized graphene sheets for intracellular controlled release of therapeutic agents*. Nanoscale, 2017. **9**(47): p. 18931-18939.
34. Tu, Z., et al., *Combination of Surface Charge and Size Controls the Cellular Uptake of Functionalized Graphene Sheets*. Advanced Functional Materials, 2017. **27**(33): p. 1701837.

35. Tu, Z., et al., *Directed Graphene-Based Nanoplatfoms for Hyperthermia: Overcoming Multiple Drug Resistance*. *Angewandte Chemie International Edition*, 2018. **57**(35): p. 11198-11202.
36. Burnett, T., R. Yakimova, and O. Kazakova, *Mapping of Local Electrical Properties in Epitaxial Graphene Using Electrostatic Force Microscopy*. *Nano Letters*, 2011. **11**(6): p. 2324-2328.
37. Wei, N., C. Lv, and Z. Xu, *Wetting of graphene oxide: a molecular dynamics study*. *Langmuir*, 2014. **30**(12): p. 3572-8.
38. Taherian, F., et al., *What is the contact angle of water on graphene?* *Langmuir*, 2013. **29**(5): p. 1457-65.
39. Shin, Y.J., et al., *Surface-energy engineering of graphene*. *Langmuir*, 2010. **26**(6): p. 3798-802.
40. Metya, A.K., S. Khan, and J.K. Singh, *Wetting Transition of the Ethanol–Water Droplet on Smooth and Textured Surfaces*. *The Journal of Physical Chemistry C*, 2014. **118**(8): p. 4113-4121.
41. Liu, J., et al., *Water wettability of graphene: interplay between the interfacial water structure and the electronic structure*. *RSC Advances*, 2018. **8**(30): p. 16918-16926.
42. Kozbial, A., et al., *Study on the surface energy of graphene by contact angle measurements*. *Langmuir*, 2014. **30**(28): p. 8598-606.
43. Chialvo, A.A., L. Vlcek, and P.T. Cummings, *Surface Strain Effects on the Water–Graphene Interfacial and Confinement Behavior*. *The Journal of Physical Chemistry C*, 2014. **118**(34): p. 19701-19711.
44. Belyaeva, L.A., et al., *Hydrophilicity of Graphene in Water through Transparency to Polar and Dispersive Interactions*. *Adv Mater*, 2018. **30**(6).
45. Ashraf, A., et al., *Doping-Induced Tunable Wettability and Adhesion of Graphene*. *Nano Lett*, 2016. **16**(7): p. 4708-12.
46. Andrews, J.E., et al., *Wetting dynamics of a water nanodrop on graphene*. *Phys Chem Chem Phys*, 2016. **18**(34): p. 23482-93.
47. Tian, T., et al., *Doping-Driven Wettability of Two-Dimensional Materials: A Multiscale Theory*. *Langmuir*, 2017. **33**(44): p. 12827-12837.
48. Ramos-Alvarado, B., S. Kumar, and G.P. Peterson, *On the wettability transparency of graphene-coated silicon surfaces*. *J Chem Phys*, 2016. **144**(1): p. 014701.
49. Kozbial, A., et al., *Are Graphitic Surfaces Hydrophobic?* *Acc Chem Res*, 2016. **49**(12): p. 2765-2773.
50. Khalkhali, M., et al., *Wetting at the nanoscale: A molecular dynamics study*. *J Chem Phys*, 2017. **146**(11): p. 114704.
51. Hung, S.-W. and J. Shiomi, *Dynamic Wetting of Nanodroplets on Smooth and Patterned Graphene-Coated Surface*. *The Journal of Physical Chemistry C*, 2018. **122**(15): p. 8423-8429.
52. Herrera, C., et al., *Nanowetting of Graphene by Ionic Liquid Droplets*. *The Journal of Physical Chemistry C*, 2015. **119**(43): p. 24529-24537.
53. Papadopoulos, P., et al., *Wetting on the microscale: shape of a liquid drop on a microstructured surface at different length scales*. *Langmuir*, 2012. **28**(22): p. 8392-8.
54. Mammen, L., et al., *Effect of nanoroughness on highly hydrophobic and superhydrophobic coatings*. *Langmuir*, 2012. **28**(42): p. 15005-14.
55. Munief, W.M., et al., *Silane Deposition via Gas-Phase Evaporation and High-Resolution Surface Characterization of the Ultrathin Siloxane Coatings*. *Langmuir*, 2018. **34**(35): p. 10217-10229.
56. Lu, X., et al., *Front-End-of-Line Integration of Graphene Oxide for Graphene-Based Electrical Platforms*. *Advanced Materials Technologies*, 2018: p. 1700318.
57. Delle, L.E., *ScFv-modified graphene-coated IDE-arrays for 'label-free' screening of cardiovascular disease biomarkers in physiological saline*. *Biosensors and Bioelectronics*, 2018. **102**: p. 574-581.
58. Lanche, R., et al., *Routine fabrication of reduced graphene oxide microarray devices via all solution processing*. *Phys. Status Solidi A*, 2013. **210**(5): p. 968-974.
59. Lanche, R., et al., *Reduced graphene oxide-based sensing platform for electric cell-substrate impedance sensing*. *Phys. Status Solidi A*, 2014. **211**(6): p. 1404-1409.
60. Lanche, R., et al., *Graphite oxide multilayers for device fabrication: Enzyme-based electrical sensing of glucose*. *physica status solidi (a)*, 2015. **212**(6): p. 1335-1341.
61. Nguyen, T.C., et al., *Handheld readout system for field-effect transistor biosensor arrays for label-free detection of biomolecules*. *physica status solidi (a)*, 2015. **212**(6): p. 1313-1319.
62. Lanche, R., et al., *Graphite oxide electrical sensors are able to distinguish single nucleotide polymorphisms in physiological buffers*. *FlatChem*, 2018. **7**: p. 1-9.
63. LaFramboise, T., *Single nucleotide polymorphism arrays: a decade of biological, computational and technological advances*. *Nucleic Acids Res*, 2009. **37**(13): p. 4181-93.
64. von Bubnoff, A., *Next-generation sequencing: the race is on*. *Cell*, 2008. **132**(5): p. 721-3.
65. Cameron, J.S., et al., *Accurate thickness measurement of graphene*. *Nanotechnology*, 2016. **27**(12): p. 125704.
66. Park, J. and M. Yan, *Covalent Functionalization of Graphene with Reactive Intermediates*. *Accounts of Chemical Research*, 2013. **46**(1): p. 181-189.
67. Georgakilas, V., et al., *Noncovalent Functionalization of Graphene and Graphene Oxide for Energy Materials, Biosensing, Catalytic, and Biomedical Applications*. *Chemical Reviews*, 2016. **116**(9): p. 5464-5519.
68. Setaro, A., et al., *Preserving π -conjugation in covalently functionalized carbon nanotubes for optoelectronic applications*. *Nature Communications*, 2017. **8**: p. 14281.

69. Gholami, M.F., et al., *Functionalized Graphene as Extracellular Matrix Mimics: Toward Well-Defined 2D Nanomaterials for Multivalent Virus Interactions*. *Advanced Functional Materials*, 2017: p. 1606477-n/a.
70. Faghani, A., et al., *Controlled Covalent Functionalization of Thermally Reduced Graphene Oxide To Generate Defined Bifunctional 2D Nanomaterials*. *Angewandte Chemie International Edition*, 2017. **56**(10): p. 2675-2679.
71. Bhatia, S., L.C. Camacho, and R. Haag, *Pathogen Inhibition by Multivalent Ligand Architectures*. *Journal of the American Chemical Society*, 2016. **138**(28): p. 8654-8666.
72. Cho, H., U. Jammalamadaka, and K. Tappa, *Nanogels for Pharmaceutical and Biomedical Applications and Their Fabrication Using 3D Printing Technologies*. *Materials*, 2018. **11**(2): p. 302.
73. Yin, P.T., et al., *Design, Synthesis, and Characterization of Graphene–Nanoparticle Hybrid Materials for Bioapplications*. *Chemical Reviews*, 2015. **115**(7): p. 2483-2531.
74. Parlak, O., A.P.F. Turner, and A. Tiwari, *On/Off-Switchable Zipper-Like Bioelectronics on a Graphene Interface*. *Advanced Materials*, 2014. **26**(3): p. 482-486.
75. Kostarelos, K. and K.S. Novoselov, *Exploring the Interface of Graphene and Biology*. *Science*, 2014. **344**(6181): p. 261-263.
76. Romero-Vargas Castrillón, S., et al., *Interaction of Graphene Oxide with Bacterial Cell Membranes: Insights from Force Spectroscopy*. *Environmental Science & Technology Letters*, 2015. **2**(4): p. 112-117.
77. Movahedi, S., et al., *Edge-functionalization of graphene by polyglycerol; A way to change its flat topology*. *Polymer*, 2013. **54**(12): p. 2917-2925.
78. Namazi, H. and M. Adeli, *Solution proprieties of dendritic triazine/poly(ethylene glycol)/dendritic triazine block copolymers*. *Journal of Polymer Science Part A: Polymer Chemistry*, 2005. **43**(1): p. 28-41.
79. Zhang, N., et al., *Rapidly Probing Antibacterial Activity of Graphene Oxide by Mass Spectrometry-based Metabolite Fingerprinting*. *Scientific Reports*, 2016. **6**: p. 28045.
80. Gao, Y., et al., *Impact of graphene oxide on the antibacterial activity of antibiotics against bacteria*. *Environmental Science: Nano*, 2017. **4**(5): p. 1016-1024.
81. Zou, X., et al., *Mechanisms of the Antimicrobial Activities of Graphene Materials*. *Journal of the American Chemical Society*, 2016. **138**(7): p. 2064-2077.
82. Qi, J., et al., *Poly(N-isopropylacrylamide) on two-dimensional graphene oxide surfaces*. *Polymer Chemistry*, 2012. **3**(3): p. 621-624.
83. Qi, Z., et al., *Multivalency at Interfaces: Supramolecular Carbohydrate-Functionalized Graphene Derivatives for Bacterial Capture, Release, and Disinfection*. *Nano Letters*, 2015. **15**(9): p. 6051-6057.
84. Rojas-Andrade, M.D., et al., *Antibacterial mechanisms of graphene-based composite nanomaterials*. *Nanoscale*, 2017. **9**(3): p. 994-1006.
85. Li, Y., et al., *Graphene microsheets enter cells through spontaneous membrane penetration at edge asperities and corner sites*. *Proceedings of the National Academy of Sciences*, 2013. **110**(30): p. 12295-12300.
86. Liu, S., et al., *Antibacterial Activity of Graphite, Graphite Oxide, Graphene Oxide, and Reduced Graphene Oxide: Membrane and Oxidative Stress*. *ACS Nano*, 2011. **5**(9): p. 6971-6980.
87. Georgakilas, V., et al., *Functionalization of Graphene: Covalent and Non-Covalent Approaches, Derivatives and Applications*. *Chemical Reviews*, 2012. **112**(11): p. 6156-6214.
88. Zhang, G., et al., *Versatile Polymer-Free Graphene Transfer Method and Applications*. *ACS Appl Mater Interfaces*, 2016. **8**(12): p. 8008-16.
89. Delle, L.E., et al., *ScFv-modified graphene-coated IDE-arrays for 'label-free' screening of cardiovascular disease biomarkers in physiological saline*. *Biosens Bioelectron*, 2018. **102**: p. 574-581.