

# Volatile Organic Compound Detection Using Insect Odorant-Receptor Functionalised Field-Effect Transistors

by

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# Acknowledgements

Thanks for all the fish.



# Abstract

This is a thesis skeleton written with quarto. Make a copy of this thesis repo and start to write!

Make a new paragraph by leaving a blank line.



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# 1. Introduction

This is a book created from markdown and executable code.

See for additional discussion of literate programming.

[1] 2



## **2. Carbon Nanotube and Graphene Field-Effect Transistors**

### **2.1. Device Functionalisation**

### **2.2. Insect Odorant Receptors**



### **3. Carbon Nanotube and Graphene Field-Effect Transistors as Biosensor Platforms**



## **4. Fabrication of Carbon Nanotube Network and Graphene Field-Effect Transistors**

This chapter discusses the fabrication processes for both the carbon nanotube network and graphene transistors. Experimental optimisation of the transducer element is critical for biosensor work, and large numbers of transducers were required for testing various biosensor functionalisation processes. Therefore, these processes were developed to rapidly fabricate devices with reproducible device characteristics appropriate for biosensing work. Also outlined in this chapter are the characterisation techniques taken to test the quality and reproducibility of these fabrication processes.

### **4.1. Deposition of Carbon Nanotubes**

#### **4.1.1. Solvent-Based**

#### **4.1.2. Surfactant-Based**

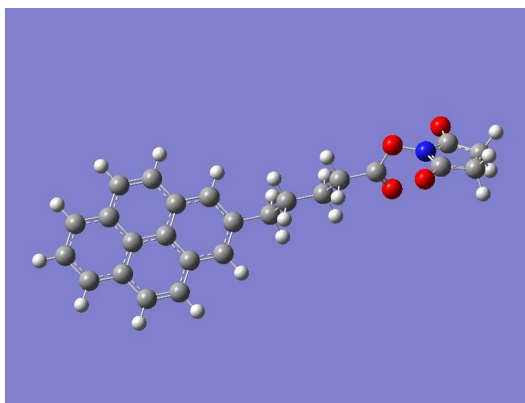




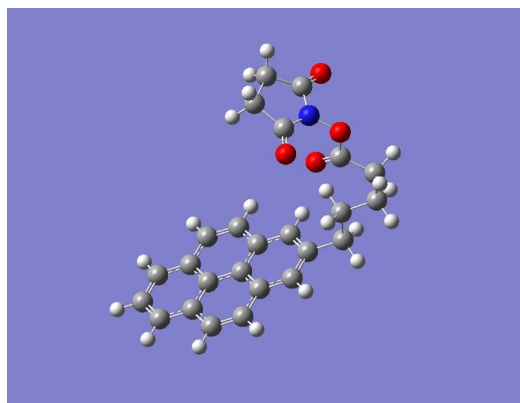
## 5. Functionalisation of Carbon Nanotubes and Graphene with Odorant Receptors

### 5.1. Linker molecules

#### 5.1.1. 1-Pyrenebutanoic acid N-hydroxysuccinimide ester (PBASE)



(a) Hartree-Fock energy: -3427728.67 kJ/mol  
(9 s.f.)



(b) Hartree-Fock energy: -3427729.66 kJ/mol  
(9 s.f.)

Figure 5.1.: Two conformations of PBASE molecule with geometry optimised via *ab initio* calculation (computed using Gaussian 16 [1]). The difference between computed Hartree-Fock energies is 1.0 kJ/mol, small enough that the existence of both molecular conformations is physically possible.

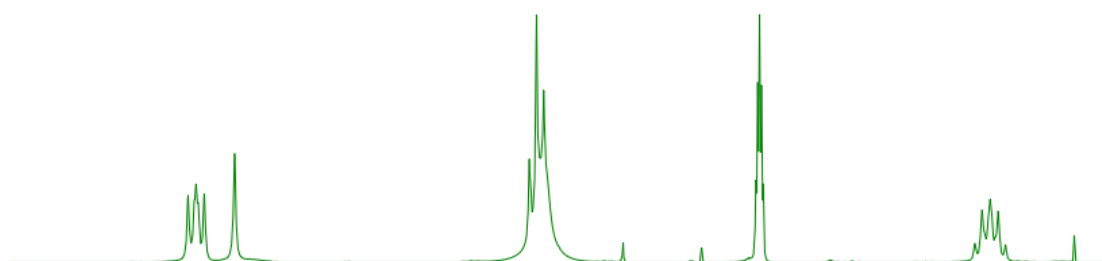
1-Pyrenebutanoic acid N-hydroxysuccinimide ester (variously known commercially and in the literature as 1-Pyrenebutyric acid N-hydroxysuccinimide ester, PBASE, PBSE, PASE, Pyr-NHS, PyBASE, PANHS) is a aromatic, bifunctional molecule commonly used for tethering biomolecules to the carbon rings of graphene and carbon nanotubes. The optimised molecular structure of PBASE is shown in Figure 5.1.

The non-covalent functionalisation of proteins onto a single-walled carbon nanotube using PBASE was first reported by Chen *et al.* in 2001 [2]. Two methods for protein functionalisation and immobilisation were successfully used, with the only differences being the solvent used to dissolve the PBASE powder (DMF, methanol) and the final

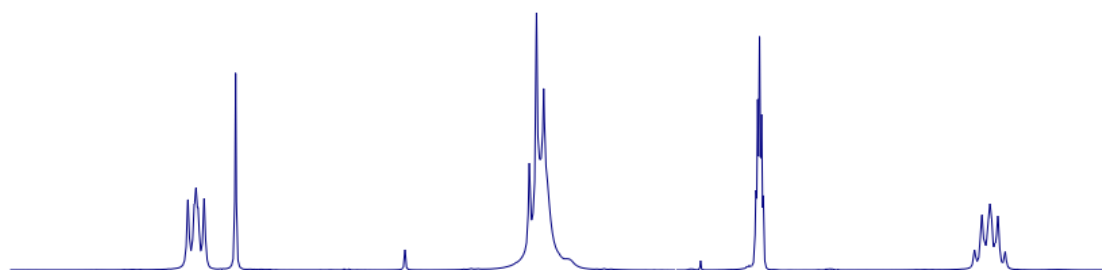
concentration of the resulting solutions (6 mM, 1 mM respectively). The lower concentration may have been used for PBASE in methanol as PBASE powder appears to dissolve poorly in methanol at higher concentrations. Cella *et al.*, Campos *et al.*, Zheng *et al.* and Ohno *et al.* all directly cite Chen *et al.* when discussing functionalisation with PBASE [3]–[6]. Other groups using PBASE for graphene or carbon nanotube functionalisation do not explicitly reference Chen *et al.* in their methodology, but it is apparent they often draw on one of these two original methods. This common ancestry becomes apparent from the high frequency of methods detailing the use of 6 mM PBASE in DMF and 1 mM PBASE in methanol, as seen in Table 5.1.

However, despite this shared heritage, it is also apparent from Table 5.1 that there is a large degree of variation in the methods used for PBASE functionalisation. Various electrical characterisation, microscopy and spectroscopy techniques have been used to demonstrate successful functionalisation. However, there has historically been little justification provided for the exact parameters used in the procedure. As noted by Zhen *et al.* and Hinnemo *et al.*, there is more generally a lack of systematic research into formation of pyrene-derivative monolayers on graphene and other carbon nanomaterials, despite the wide use of this chemistry in the literature [7], [8].

We purchased PBASE from two suppliers, Sigma-Aldrich and Setareh Biotech. Sigma recommends DMF and methanol as suitable solvents for dissolving PBASE alongside chloroform and DMSO. Setareh Biotech indicates methanol can be used for dissolving PBASE. The two suppliers have conflicting information for suitable storage of PBASE, with Sigma recommending room temperature storage while Setareh Biotech recommends storage of  $-5$  to  $-30^{\circ}\text{C}$  and protection from light and moisture. Figure 5.2 compares the shapes of NMR spectra of PBASE from each supplier dissolved in DMSO, alongside a blank DMSO spectrum.



(a) Sigma PBASE in DMSO



(b) Setareh PBASE in DMSO



(c) Blank (DMSO only)

Figure 5.2.: Comparison of NMR spectrum profiles (arbitrary units)

## 5. Functionalisation of Carbon Nanotubes and Graphene with Odorant Receptors

Table 5.1.: Comparison of PBASE functionalisation processes used for immobilisation of proteins and aptamers onto liquid-gated CNTFET and graphene FET sensors

Solvent	Channel	Conc. (mM)	Incubation type	Time (hr)	Rinse steps	References
DMF	CNTs	5	Immersed	1	PBS	Maehashi <i>et al.</i> [9]
		6	Immersed	1	DMF, PBS	García-Aljaro <i>et al.</i> [10]
		6	Immersed	1	DMF	Chen <i>et al.</i> [2]
		6	Immersed	1	DMF	Cella <i>et al.</i> [3]
		6	Immersed	1	DMF	Das <i>et al.</i> [11]
	Graphene	-	-	2	DMF	Kwong Hong Tsang <i>et al.</i> [12]
		-	-	20	-	Wiedman <i>et al.</i> [13]
		0.2	Immersed	20	DMF, IPA, DI water	Gao <i>et al.</i> [14]
		1	100 $\mu$ L droplet	6	DMF, IPA, DI water	Nekrasov <i>et al.</i> [15]
		5	Immersed	1	DMF, DI water	Hwang <i>et al.</i> [16]
		6	6 $\mu$ L droplet	2	DMF, DI water	Nur Nasufiya <i>et al.</i> [17]
		10	10 $\mu$ L droplet	2	DMF, DI water	Campos <i>et al.</i> [4]
		10	Immersed	2	DMF, PBS	Kuscu <i>et al.</i> [18]
		10	Immersed	1	DMF	Xu <i>et al.</i> [19]
		10	Immersed	12	DMF, ethanol, DI water	Khan <i>et al.</i> [20]
2-Methoxyethanol	Graphene	1	Immersed	1	DI water	Ono <i>et al.</i> [21]
Methanol	CNTs	1	Immersed	1	Methanol, DI water	Zheng <i>et al.</i> [5]
		1	Immersed	2	Methanol	Kim <i>et al.</i> [22]
	Graphene	5	Immersed	2	-	Sethi <i>et al.</i> [23]
		5	Immersed	1	Methanol, PBS	Ohno <i>et al.</i> [6]
DMSO	CNTs	10	-	1	DI water	Lopez <i>et al.</i> [24]
		10	Immersed	1	PBS	Strack <i>et al.</i> [25]

## 6. Results

What I found out.

See for more detailed results



## 7. Vapour Phase Sensing with Transistor Biosensors

### 7.1. Testing Vapour Delivery System

#### 7.1.1. System Description

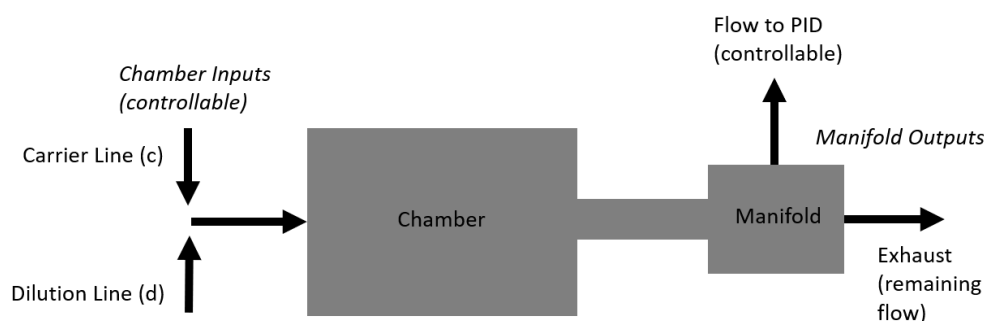


Figure 7.1.: Vapour Delivery System - Schematic of device chamber and manifold

#### 7.1.2. Temperature and Humidity Indicator

#### 7.1.3. Photoionisation Detector

##### Bubbling Vapour

First year report: ““First, a 200 sccm flow of N<sub>2</sub> gas was sent through the dilution line to the device chamber until 1000 s. Then, the flow controller three-way valves were manually adjusted so that the same 200 sccm flow was directed through 50 mL of EtOH analyte in the carrier line. This continued until 2200 s, where the valves were again manually adjusted so that 200 sccm clean N<sub>2</sub> again flowed through the device chamber. The resulting current across the device channel was monitored over this time, and is shown in Figure 19. A response to EtOH exposure and removal is visible.”“ ”





## 8. Summary

In summary, this book has no content whatsoever.

[1] 2



## A. Photolithography

This section details some of the standard photolithography procedures used in the device fabrication processes detailed in Chapter 4. Photolithography was performed with both positive and negative photoresists (also known as “resists”). Photolithography with the positive resist used here required a single softbake step, while with negative resists a second

The nitrogen ( $\geq 99.99\%$ ) and oxygen (99.7%) used in photolithographic work was supplied by BOC Limited New Zealand. Deionised (DI) water was taken from a Synergy® UV Water Purification System. The DI water had a measured conductivity of  $(1.4 \pm 0.1) \mu\text{S cm}^{-1}$ , compared to tap water with a measured conductivity of  $(7.8 \pm 0.2) \mu\text{S cm}^{-1}$ .

### A.1.



## B. Python Code for Data Analysis



## C. Vapour Delivery System

### C.1. Technical Notes

Two LabView Virtual Instruments (VIs) were adapted from pre-existing VIs for operating the mass flow controllers and monitoring vapour flow into the device chamber, as well as monitoring temperature and humidity in the vapour delivery system's manifold. These VIs were named " " A third VI was developed in parallel which combined the first two Virtual Instruments, alongside allowing the sequence of values to control the mass flow controllers.

From Honours report: " " Figure 12 gives the right side of the front panel of the LabView VI sample with vapour.VI, which lets us preset an autonomously-performed vapour sensing sequence. Each row in each array module corresponds to a different step in this sequence. The 'howManySteps' module lets us set how many of these steps are performed. The 'Durations Array' module determines the length of time in seconds each step is performed over. The 'Carrier Flows Array' and 'Dilution Flows Array' modules let us set the carrier flow and dilution flow, respectively, in standard cubic centimetres per minute (sccm) through the gas rig at each step. The carrier flow pushes analyte vapour into the vapour-sensing device chamber, while dilution flow is used to modify the flow behaviour of the analyte vapour entering the chamber. The vapour sensing sequence as depicted in Figure 12 was used for all vapour sensing runs in this investigation. At the end of the sequence, the data collected about the vapour sensing process was saved as an .lvm file. " " "

### C.2. Future Improvements





# Bibliography

- [1] J. A. M. J. Frisch and G. W. Trucks and H. B. Schlegel and G. E. Scuseria and M. A. Robb and J. R. Cheeseman and G. Scalmani and V. Barone and G. A. Petersson and H. Nakatsuji and X. Li and M. Caricato and A. V. Marenich and J. Bloino and B. G. Janesko and R. G. J. E. Peralta, F. Ogliaro, et al. *Gaussian~16 Revision C.01*. 2016.
- [2] R. J. Chen, Y. Zhang, D. Wang, et al. “Noncovalent sidewall functionalization of single-walled carbon nanotubes for protein immobilization”. In: *Journal of the American Chemical Society* 123.16 (2001), pp. 3838–3839. ISSN: 00027863. DOI: 10.1021/ja010172b. URL: <http://pubs.acs.org>.
- [3] Lakshmi N. Cella, Pablo Sanchez, Wenwan Zhong, et al. “Nano aptasensor for Protective Antigen Toxin of Anthrax”. In: *Analytical Chemistry* 82.5 (Mar. 2010), pp. 2042–2047. ISSN: 00032700. DOI: 10.1021/ac902791q. URL: <https://pubs.acs.org/doi/full/10.1021/ac902791q>.
- [4] Rui Campos, Jérôme Borme, Joana Rafaela Guerreiro, et al. “Attomolar label-free detection of dna hybridization with electrolyte-gated graphene field-effect transistors”. In: *ACS Sensors* 4.2 (Feb. 2019), pp. 286–293. ISSN: 23793694. DOI: 10.1021/acssensors.8b00344. URL: <https://pubs.acs.org/doi/full/10.1021/acssensors.8b00344>.
- [5] Han Yue Zheng, Omar A. Alsager, Bicheng Zhu, et al. “Electrostatic gating in carbon nanotube aptasensors”. In: *Nanoscale* 8.28 (July 2016), pp. 13659–13668. ISSN: 20403372. DOI: 10.1039/c5nr08117c. URL: <https://pubs.rsc.org/en/content/articlehtml/2016/nr/c5nr08117c> <https://pubs.rsc.org/en/content/articlelanding/2016/nr/c5nr08117c>.
- [6] Yasuhide Ohno, Kenzo Maehashi, and Kazuhiko Matsumoto. “Label-free biosensors based on aptamer-modified graphene field-effect transistors”. In: *Journal of the American Chemical Society* 132.51 (Dec. 2010), pp. 18012–18013. ISSN: 00027863. DOI: 10.1021/ja108127r. URL: <https://pubs.acs.org/doi/full/10.1021/ja108127r>.
- [7] Xue V. Zhen, Emily G. Swanson, Justin T. Nelson, et al. “Noncovalent monolayer modification of graphene using pyrene and cyclodextrin receptors for chemical sensing”. In: *ACS Applied Nano Materials* 1.6 (June 2018), pp. 2718–2726. ISSN: 25740970. DOI: 10.1021/ACSANM.8B00420/ASSET/IMAGES/LARGE/AN-2018-00420J\_0004.JPEG. URL: <https://pubs.acs.org/doi/full/10.1021/acsanm.8b00420>.

- [8] Malkolm Hinnemo, Jie Zhao, Patrik Ahlberg, et al. “On Monolayer Formation of Pyrenebutyric Acid on Graphene”. In: *Langmuir* 33.15 (Apr. 2017), pp. 3588–3593. ISSN: 15205827. DOI: 10.1021/ACS.LANGMUIR.6B04237/ASSET/IMAGES/LARGE/LA-2016-04237V\_0003.JPEG. URL: <https://pubs.acs.org/doi/full/10.1021/acs.langmuir.6b04237>.
- [9] Kenzo Maehashi, Taiji Katsura, Kagan Kerman, et al. “Label-free protein biosensor based on aptamer-modified carbon nanotube field-effect transistors”. In: *Analytical Chemistry* 79.2 (Jan. 2007), pp. 782–787. ISSN: 00032700. DOI: 10.1021/ac060830g. URL: <https://pubs.acs.org/doi/full/10.1021/ac060830g>.
- [10] Cristina García-Aljaro, Lakshmi N. Cella, Dhamanand J. Shirale, et al. “Carbon nanotubes-based chemiresistive biosensors for detection of microorganisms”. In: *Biosensors and Bioelectronics* 26.4 (Dec. 2010), pp. 1437–1441. ISSN: 09565663. DOI: 10.1016/j.bios.2010.07.077.
- [11] Basanta K. Das, Chaker Tili, Sushmee Badhulika, et al. “Single-walled carbon nanotubes chemiresistor aptasensors for small molecules: Picomolar level detection of adenosine triphosphate”. In: *Chemical Communications* 47.13 (Mar. 2011), pp. 3793–3795. ISSN: 1364548X. DOI: 10.1039/c0cc04733c. URL: <https://pubs.rsc.org/en/content/articlehtml/2011/cc/c0cc04733c> <https://pubs.rsc.org/en/content/articlelanding/2011/cc/c0cc04733c>.
- [12] Deana Kwong Hong Tsang, Tyler J. Lieberthal, Clare Watts, et al. “Chemically Functionalised Graphene FET Biosensor for the Label-free Sensing of Exosomes”. In: *Scientific Reports* 9.1 (Sept. 2019), pp. 1–10. ISSN: 20452322. DOI: 10.1038/s41598-019-50412-9. URL: <https://www.nature.com/articles/s41598-019-50412-9>.
- [13] Gregory R. Wiedman, Yanan Zhao, Arkady Mustaev, et al. “An Aptamer-Based Biosensor for the Azole Class of Antifungal Drugs”. In: *mSphere* 2.4 (Aug. 2017). ISSN: 23795042. DOI: 10.1128/msphere.00274-17. URL: [/pmc/articles/PMC5566834/](https://pmc/articles/PMC5566834/) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5566834/?report=abstract> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5566834/>.
- [14] Zhaoli Gao, Han Xia, Jonathan Zauberman, et al. “Detection of Sub-fM DNA with Target Recycling and Self-Assembly Amplification on Graphene Field-Effect Biosensors”. In: *Nano Letters* 18.6 (June 2018), pp. 3509–3515. ISSN: 15306992. DOI: 10.1021/acs.nanolett.8b00572. URL: <https://pubs.acs.org/doi/full/10.1021/acs.nanolett.8b00572>.
- [15] Nikita Nekrasov, Natalya Yakunina, Averyan V. Pushkarev, et al. “Spectral-phase interferometry detection of ochratoxin a via aptamer-functionalized graphene coated glass”. In: *Nanomaterials* 11.1 (Jan. 2021), pp. 1–10. ISSN: 20794991. DOI: 10.3390/nano11010226. URL: <https://www.mdpi.com/2079-4991/11/1/226/html> <https://www.mdpi.com/2079-4991/11/1/226>.

- [16] Michael T. Hwang, B. Landon Preston, Lee Joon, et al. “Highly specific SNP detection using 2D graphene electronics and DNA strand displacement”. In: *Proceedings of the National Academy of Sciences of the United States of America* 113.26 (June 2016), pp. 7088–7093. ISSN: 10916490. DOI: 10.1073/pnas.1603753113. URL: <https://www.pnas.org/doi/abs/10.1073/pnas.1603753113>.
- [17] Mohd Maidin Nur Nasyifa, A. Rahim Ruslinda, Nur Hamidah Abdul Halim, et al. “Immuno-probed graphene nanoplatelets on electrolyte-gated field-effect transistor for stable cortisol quantification in serum”. In: *Journal of the Taiwan Institute of Chemical Engineers* 117 (Dec. 2020), pp. 10–18. ISSN: 18761070. DOI: 10.1016/j.jtice.2020.12.008.
- [18] Murat Kuscü, Hamideh Ramezani, Ergin Dinc, et al. “Graphene-based Nanoscale Molecular Communication Receiver: Fabrication and Microfluidic Analysis”. In: (June 2020). arXiv: 2006.15470. URL: <https://arxiv.org/abs/2006.15470v2>.
- [19] Shicai Xu, Jian Zhan, Baoyuan Man, et al. “Real-time reliable determination of binding kinetics of DNA hybridization using a multi-channel graphene biosensor”. In: *Nature Communications* 8.1 (Mar. 2017), pp. 1–10. ISSN: 20411723. DOI: 10.1038/ncomms14902. URL: <https://www.nature.com/articles/ncomms14902>.
- [20] Niazul I. Khan, Mohammad Mousazadehkasin, Sujoy Ghosh, et al. “An integrated microfluidic platform for selective and real-time detection of thrombin biomarkers using a graphene FET”. In: *Analyst* 145.13 (June 2020), pp. 4494–4503. ISSN: 13645528. DOI: 10.1039/d0an00251h. URL: <https://pubs.rsc.org/en/content/articlehtml/2020/an/d0an00251h> <https://pubs.rsc.org/en/content/articlelanding/2020/an/d0an00251h>.
- [21] T Ono, K Kamada, R Hayashi, et al. “Lab-on-a-graphene-FET detection of key molecular events underpinning influenza 2 virus infection and effect of antiviral drugs 3 Running title: Graphene-FET detects reactions in an influenza infection MAIN TEXT”. In: *bioRxiv* (Mar. 2020), p. 2020.03.18.996884. DOI: 10.1101/2020.03.18.996884. URL: <https://doi.org/10.1101/2020.03.18.996884>.
- [22] Jun Pyo Kim, Byung Yang Lee, Joohyung Lee, et al. “Enhancement of sensitivity and specificity by surface modification of carbon nanotubes in diagnosis of prostate cancer based on carbon nanotube field effect transistors”. In: *Biosensors and Bioelectronics* 24.11 (July 2009), pp. 3372–3378. ISSN: 09565663. DOI: 10.1016/j.bios.2009.04.048. URL: <https://pubmed.ncbi.nlm.nih.gov/19481922/>.
- [23] Jagriti Sethi, Michiel Van Bulck, Ahmed Suhail, et al. “A label-free biosensor based on graphene and reduced graphene oxide dual-layer for electrochemical determination of beta-amyloid biomarkers”. In: *Microchimica Acta* 187.5 (May 2020), pp. 1–10. ISSN: 14365073. DOI: 10.1007/s00604-020-04267-x. URL: <https://link.springer.com/article/10.1007/s00604-020-04267-x>.

## *Bibliography*

- [24] Ryan J. Lopez, Sofia Babanova, Kateryna Artyushkova, et al. “Surface modifications for enhanced enzyme immobilization and improved electron transfer of PQQ-dependent glucose dehydrogenase anodes”. In: *Bioelectrochemistry* 105 (Oct. 2015), pp. 78–87. ISSN: 1878562X. DOI: 10.1016/j.bioelechem.2015.05.010. URL: <https://pubmed.ncbi.nlm.nih.gov/26011132/>.
- [25] Guinevere Strack, Robert Nichols, Plamen Atanasov, et al. “Modification of carbon nanotube electrodes with 1-pyrenebutanoic acid, succinimidyl ester for enhanced bioelectrocatalysis”. In: *Methods in Molecular Biology* 1051 (2013), pp. 217–228. ISSN: 10643745. DOI: 10.1007/978-1-62703-550-7\_14. URL: <https://pubmed.ncbi.nlm.nih.gov/23934807/>.