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On the analytical theory of a graphene-based resistive biosensor

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A single-sheet graphene (through which an electric current is passed) encapsulated by a massive semiconductor substrate and an organic macromolecule (biomolecule–antibody) is considered as a resistive biosensor. The organic macromolecule (biomolecule–antigen) being tested is placed on top of the antibody. Expressions for the concentrations of current carriers in graphene before and after the antigen placement are obtained within the framework of simple models. The conditions under which the presence of an antigen changes the type of conductivity of graphene are determined.

Keywords: encapsulated graphene, antibody (bioreceptor), antigen (biomarker).

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1. Introduction

In recent years, in the field of graphene sensors the interest of researchers noticeably shifted from resistive gas sensors [1–4], intended for environmental monitoring, to the development of resistive biosensors suitable for medical express analyses [5–12]. The gas sensor is an epitaxial single-sheet graphene (epigraphene), the adsorption of gas molecules on which causes a change $\Delta\sigma$ in the conductivity of the graphene layer σ, which is detected by the sensor. A more complex structure of the biosensor is schematically presented in the Figure: in the initial state the sensor contains single-sheet graphene, encapsulated between a semiconductor substrate and an antibody Ab, or a bioreceptor, which is an organic macromolecule [11]; during the measurement the tested biomolecule–antigen Ag, or biomarker is brought into contact with Ab [11,12]. The interaction of Ag with Ab changes the conductivity of encapsulated graphene, which serves as an indicator of its presence. Thus, for both gas and biosensors, the change in current in graphene is determined. From a theoretical point of view, it is necessary to determine the resulting change in relative conductivity $\Delta\sigma/\sigma = \Delta\nu/\nu + \Delta\mu/\mu$, where ν is concentration of current carriers[1] and μ is their mobility. In this paper, we will present estimates of the ratio $\Delta\sigma/\sigma$ based on two previously proposed models: the encapsulated structure [13] and the dangling bonds of antibody [14].

2. Encapsulated Graphene

To describe encapsulated single-layer graphene, we will use the approach developed in the paper [13]. Assuming that single-layer graphene is enclosed between plates representing substrate and antibody, we represent its Green's function $G(\omega, \mathbf{k})$ in the form

$$G^{-1}(\omega, \mathbf{k}) = \omega - \varepsilon_D - tf(\mathbf{k}) - \sum_{sub}(\omega) - \sum_{Ab}(\omega). \quad (1)$$

Here ω is energy variable, ε_D is energy of the Dirac point, t is energy of electron hopping between nearest neighbors in graphene, $f(\mathbf{k})$ is dispersion function, equal in the low-energy approximation to $\pm 3|\mathbf{k}|a/2$, where a is the distance between nearest neighbors in graphene and $\mathbf{k}$ is wave vector measured from the Dirac point [15]. The functions $\sum_{sub}(\omega)$ and $\sum_{Ab}(\omega)$ are self-energy parts that describe the influence of the substrate and antibody, respectively, on the electronic spectrum of free graphene. Self-energy parts can be presented in the form

$$\sum_{sub(Ab)}(\omega) = \Lambda_{sub(Ab)}(\omega) - i\Gamma_{sub(Ab)}(\omega). \quad (2)$$

The functions of the half-width of graphene levels induced by the labs are equal to

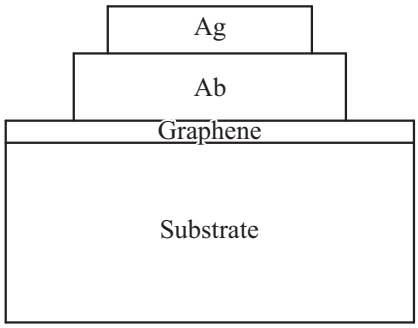
$$\Gamma_{sub(Ab)}(\omega) = \pi V^2_{sub(Ab)}\rho_{sub(Ab)}(\omega), \quad (3)$$

where $V_{sum(Ab)}$ is matrix element of the graphene interaction with the substrate (antibody), $\rho_{sub(Ab)}(\omega)$ is density of states of the substrate (antibody). The functions of the shift of graphene levels induced by the labs are

$$\Lambda_{sub(Ab)}(\omega) = V^2_{sub(Ab)}P\int_{-\infty}^{\infty}\rho_{sub(Ab)}(\omega')(\omega-\omega')^{-1}d\omega', \quad (4)$$

where P is symbol of the main value of the integral. Thus, the form of the functions $\Gamma_{sub(Ab)}(\omega)$ and $\Lambda_{sub(Ab)}(\omega)$ is uniquely determined by the densities of states $\rho_{sub(Ab)}(\omega)$.

[1] To denote the concentration, we use here the symbol ν, since the symbol n is used further to denote the occupation number of graphene atoms.



Schema of graphene-based resistive biosensor. Ab is antibody (bioreceptor macromolecule), Ag is antigen (biomarker macromolecule). The current propagates along the graphene sheet.

Further we will consider a semiconductor substrate, to describe the density of states of which we will use the Haldane–Anderson model [16]:

$$\rho_{sub}(\Omega) = \begin{cases} \rho_s, & |\Omega| \geq E_b/2, \\ 0, & |\Omega| < E_g/2 \end{cases} \tag{5}$$

where $\Omega = \omega - \omega_0$, E_g is the substrate band gap, the center of which corresponds to the energy ω_0, $\rho_s = \text{const}$. Then $\Gamma_{sum}(\Omega) = \pi V_{sub}^2 \rho_s$ at $|\Omega| \geq E_g/2$ and 0 in other cases, so

$$\Lambda_{sub}(\Omega) = \rho_s V_{sub}^2 \ln \left| \frac{\Omega - E_g/2}{\Omega + E_g/2} \right|. \tag{6}$$

3. Model of antibody dangling bonds

The interaction of Ab antibody with the semiconductor substrate will be described by the model of dangling bonds of the border fragments of the Ab biomolecule with energies ε_i and concentrations $N_i = m_i/S$, where m_i is number of dangling bonds of type i per unit cell of graphene with area $S = 3\sqrt{3}a^2/2$ [14]. Let us represent the density of states of Ab biomolecule in the form

$$\rho_{Ab}(\omega) = \sum_i N_i \rho_i(\Omega_i), \quad \rho_i(\Omega_i) = \frac{1}{\pi} \frac{\gamma_i}{\Omega_i^2 + \gamma_i^2}, \tag{7}$$

where $\Omega_i = \omega - \varepsilon_i$ and $\gamma_i = \text{const}$ is the intrinsic half-width of the dangling i-th bond occurring due to its interaction with the rest of Ab biomolecule. Then, in accordance with (4), we obtain

$$\Gamma_{Ab}(\omega) = \pi \sum_i N_i V_i^2 \rho_i(\Omega_i)$$

and

$$\Lambda_{Ab}(\omega) = \sum_i N_i \lambda_i(\Omega_i), \quad \lambda_i(\Omega_i) = \frac{\Omega_i V_i^2}{\Omega_i^2 + \gamma_i^2}. \tag{8}$$

In the future, we will consider the weak coupling of encapsulated graphene with the labs, i. e. assume $\Gamma_{sub(Ab)}(\omega) \ll t$.

Parameters of silicon carbide polytypes (in eV)

Polytype	3C	8H	21R	6H	15R	27R	4H
E_g	2.40	2.86	2.96	3.00	3.06	3.13	3.23
$-(\omega_9 - \varepsilon_D)$	0.70	0.51	0.50	0.45	0.36	0.34	0.29

Neglecting the functions $\Gamma_{sub(Ab)}(\omega)$ compared to $\Lambda_{sub(Ab)}(\omega)$ (see corresponding justification in [17]), we can represent the density of states of encapsulated graphene as

$$\rho(\omega) = \begin{cases} 2|w|/\xi^2, & |w| \leq \xi, \\ 0, & |w| > \xi, \end{cases} \tag{9}$$

where $w = \omega - \varepsilon_D - \Lambda_{sub}(\omega)$, $\xi = t\sqrt{2\pi\sqrt{3}}$ [18]. Let us set $\varepsilon_D = 0$ and, based on the regime of weak coupling of the lab is graphene, we will assume that

$$w \approx \omega - \Lambda_{sub}(0) - \Lambda_{Ab}(0).$$

At zero temperature, the occupation number of atom of encapsulated graphene is

$$n = \int_{-\xi}^{\varepsilon_F} \rho(\omega) d\omega,$$

where ε_F is Fermi level, from where we get

$$n = \begin{cases} (\xi + \varepsilon_F)(\xi - \varepsilon_F + 2\Lambda_0)/\varepsilon^2, & \varepsilon_F < \Lambda_0 \\ 1 + \varepsilon_F(\varepsilon_F - 2\Lambda_0)/\xi^2, & \varepsilon_F > \Lambda_0, \end{cases} \tag{10}$$

where $\Lambda_0 = \Lambda_{sub}(0) + \Lambda_{Ab}(0)$. Note that the carrier concentration is $\nu = 2(n-1)/S$: at $n < 1$, encapsulated graphene has hole conductivity, at $n > 1$ is electronic conductivity.

Let us now connect Ag antigen to the Ab antibody. Note that each antibody interacts with a strictly specific unique element of the antigen, which allows this antigen detection [10,11,19]. speaking generally about this interaction, we will assume that the antigen influence on the antibody is reduced to a shift in the energies of dangling bonds and change in their broadening: ε_i and γ_i become respectively into $\bar{\varepsilon}_i = \varepsilon_i + \Delta\varepsilon_i$ and $\bar{\gamma}_i = \gamma_i + \Delta\gamma_i$. Then the occupation number of atoms of encapsulated graphene in the presence of antigen is still determined by the formulas (10), but with Λ_0 replacement by $\bar{\Lambda}_0 = \Lambda_{sub}(0) + \bar{\Lambda}_{Ab}(0)$, where

$$\bar{\Lambda}_{Ab}(0) = \sum_i N_i \bar{\lambda}_i(0) \quad \text{and} \quad \bar{\lambda}_i(0) = -\bar{\varepsilon}_i V_i^2/(\bar{\varepsilon}_i^2 + \bar{\gamma}_i^2).$$

At the same time, we assumed that the position of the Fermi level is determined exclusively by the massive substrate, and therefore we set $\bar{\varepsilon}_F = \varepsilon_F$.

4. Results and discussion

Let's assume for simplicity that $|\Delta\varepsilon_1|$, $|\Delta\gamma_i| \ll \gamma_i$. Then

$$\Delta\Lambda_0 = \bar{\Lambda}_0 - \Lambda_0 = \sum_i N_i \Delta\lambda_i,$$

where

$$\Delta\lambda_i = \bar{\lambda}_i - \lambda_i \approx -\Delta\varepsilon_i V_i^2/(\varepsilon_i^2 + \gamma_i^2).$$

The difference in the occupation numbers of encapsulated graphene in the presence and absence of antigen is equal to $\Delta N = \bar{n} - n - 2(\xi + \varepsilon_F)\Delta\Lambda_0/\xi^2$ at $\varepsilon_F \leq \Lambda_0, \bar{\Lambda}_0$ and $\Delta_n = \bar{n} - n = -2\varepsilon_F\Delta\Lambda_0/\xi^2$ at $\varepsilon_F > \Lambda_0, \bar{\Lambda}_0$. As $t \sim 3\,\text{eV}$ [15], we have $\xi \sim 10\,\text{eV}$, which means that for lightly doped graphene ($|\varepsilon_F|/\xi \ll 1$) difference Δn is a quantity of the smallness of second order. Difference of concentrations of carriers $\Delta\nu = \bar{\nu} - \nu = 2\Delta n/S$ has the same order of smallness.

If in the absence of antigen $\varepsilon_F < \Lambda_0$, and in its presence $\varepsilon_F > \bar{\Lambda}_0$, then $\Delta n \approx -2\Lambda/\xi$. In the opposite situation, when without the antigen $\varepsilon_F > \Lambda_0$, and in its presence $\varepsilon_F < \bar{\Lambda}_0$, we have $\Delta n \approx 2\Lambda_0/\xi$, i.e. values of the first order of smallness. This is the situation that is most suitable for testing. Thus, one should achieve a situation where the Fermi level lies within the energy interval $(\varepsilon_D + \Lambda_0, \varepsilon_D + \bar{\Lambda}_0)$. Extrapolating the result obtained in the approximation of weak coupling graphene–lab to the general case, we can say that the best version of the sensor operation is realized when the introduction of antigen biomolecule changes the type of graphene conductivity in the original structure of the substrate–graphene–antibody. It seems that to implement such mode the condition $\varepsilon_D \sim \varepsilon_F$ shall be met. According to [20,21], the work function of undoped graphene is $\phi \approx 4.5\,\text{eV}$. The Table shows the values E_g and $\omega_0 - \varepsilon_D = \phi - (\chi + E_g/2)$ for polytypes of SiC (material often used in sensors), taken from the paper [22]. It is easy to see that the ratio $|\omega_0 - \varepsilon_D|/E_g$ can be considered small.

Thus, to achieve the condition $\varepsilon_D \sim \varepsilon_F$ a relatively weak level of doping of polytypes of SiC and/or graphene is required. The same condition can be achieved by applying an electrostatic field [23], using, for example, FET circuit [12].

We considered here the mode of weak coupling between graphene and the plates not only for the purpose of the problem simplification. The fact is that in the strong strong coupling regime, when $\Gamma_{sub(Ab)}(\omega) > t$, the graphene loses its unique specificity. Moreover, in the limit $\Gamma_{sub(Ab)} \gg t$ we get a set of individual carbon atoms attached to the substrate and the antibody.

5. Conclusion

In this paper we obtained the analytical estimate of the ratio $\Delta\nu/\nu = \Delta n/n$ and identified the conditions under which encapsulated graphene before and after the antigen addition has different types of conductivity. If $|\Delta\nu/\nu| \gg |\Delta\mu|/\mu$, then the results obtained are also valid for the ratio $\Delta\sigma/\sigma$. Note that estimation of the ratio $\Delta\mu/\mu$ for encapsulated graphene is much more difficult than determination of the ratio $\Delta n/n$ [24]. If, however, short-range scattering on neutral impurities prevails in encapsulated graphene, then we can assume that $|\Delta\mu|/\mu \ll 1$, since the addition of antigen shall not create additional scattering centers at the antibody — graphene interface. If Coulomb scattering on charged centers prevails, then the presence of the antigen shall manifest itself, since the charges of dangling bonds change. According to existing concepts [24,25], mobility μ is inversely proportional to the density of charged i-centers N, but does not depend on the concentration of current carriers ν [2]. Thus, the problem of theoretical determination of the ratio $\Delta\sigma/\sigma$ remains open and requires additional experimental studies for solution. For the same reason, it is quite difficult to estimate the approximations made in the paper.

In this paper, where zero-gap graphene was considered, we did not discuss the issue of the role of temperature, since the effect of temperature on the electronic state of adsorbates was considered by us earlier in the paper [26]. In the future, we plan to consider slotted (semiconductor) graphene, where temperature determines its carrier concentration.

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Conflict of interest

The author declares that he has no conflict of interest.

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