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Tunable graphene quantum point contact transistor for DNA detection and characterization

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Abstract

A graphene membrane conductor containing a nanopore in a quantum point contact (QPC) geometry is a promising candidate to sense, and potentially sequence, DNA molecules translocating through the nanopore. Within this geometry, the shape, size, and position of the nanopore as well as the edge configuration influences the membrane conductance caused by the electrostatic interaction between the DNA nucleotides and the nanopore edge. It is shown that the graphene conductance variations resulting from DNA translocation can be enhanced by choosing a particular geometry as well as by modulating the graphene Fermi energy, which demonstrates the ability to detect conformational transformations of a double-stranded DNA, as well as the passage of individual base pairs of a single-stranded DNA molecule through the nanopore.

1 Introduction

In recent years, there has been immense interest in finding a low-cost, rapid genome sequencing method [1, 2, 3]. Amongst such methods, the use of solid-state nanopore (SSN) membranes is a promising new technology that can lead to tremendous advancement in the field of personalized medicine [4]. In a SSN device, a nanometer-sized membrane with a nanopore separates an ionic solution into two chambers. When a DNA molecule is electrophoretically driven across the membrane through the nanopore, it can be probed electronically, allowing the passing nucleotides to be detected. The detection methods include measuring ionic blockade currents [5], recording the electrostatic potential induced by the DNA using a semiconductor capacitor [6], and using transverse currents to probe translocating DNA in a plane perpendicular to the translocation direction [7].

For these approaches, biomolecular sensors with graphene membranes appear well suited for DNA sequencing. Graphene is a two-dimensional allotrope of carbon, whose thickness of ~ 3.35 Å is comparable to the base separation and can resolve translocating DNA at a very high resolution, revealing detailed information about its nucleotides [8, 9, 10]. Recent

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experiments have demonstrated the successful detection of both double-stranded DNA (dsDNA) [11, 12, 13] and single-stranded DNA (ssDNA) [14] using graphene-based nanopores. Unlike many solid-state membranes, graphene is electrically active and can readily conduct electronic currents. Moreover, it can be cut into narrow strips called graphene nanoribbons (GNRs), for which edge shape determines their electronic properties [15, 16, 17, 18]. The size of the graphene band-gap and the density of electronic states at a particular energy can be altered by changing the width, edge shape, lattice chirality, and presence of any nanopores. In addition, the position and shape of a nanopore can similarly affect the electronic states, influencing the magnitude of the graphene electrical conductance as well as its behavior under electrostatic disturbances [19].

Theoretical and first-principles-based calculations suggest micro-Ampere edge currents pass through GNR membranes as well as the possibility of distinguishing base pairs of DNA with graphene nanopores [9, 10]. Experiments have demonstrated that micro-ampere sheet currents can arise in GNRs with nanopores [20]. Such structures have the ability to detect DNA molecules by observing variation in the sheet current when the biomolecules pass through the pore [21]. In this context, a multi-layer graphene nanopore transistor with a gate-controlled, electrically active GNR membrane shaped as a quantum point contact (QPC) was recently proposed to detect the rotational and positional orientation of dsDNA [19, 22]. The QPC edge shape offers advantages over pristine edges as it introduces stringent boundary conditions on the electronic wavefunctions with selective sensitivity on the electrostatic environment. This property results in a large enhancement of the conductance sensitivity whenever the carrier density is modulated by a transistor gate, thereby improving the capability of discerning a nucleotide signal from the background noise. The multi-scale model relies on a Poisson-Boltzmann formalism to account for DNA electrostatics in an ionic solution combined with a transport model based on Non-Equilibrium Greens Function (NEGF) theory. The proposed device architecture also allows for the presence of additional electronic layers within the membrane to alter the electrostatic profile of the nanopore, such as for the control of DNA motion, as has been shown in a previous study with doped silicon capacitor layers [23, 24].

This paper outlines a comprehensive review on the ability of GNRs with a QPC geometry (g-QPC) to detect and characterize the passage of both double and single-stranded DNA molecules in a variety of configurations. In particular, we demonstrate the ability of a g-QPC to detect the helical nature of dsDNA, to sense the conformational transitions of dsDNA subjected to forced extension, and to distinctively count base pairs of a passing ssDNA molecule through the nanopore. Our study also shows that both the position of the nanopore as well as the electrical bias on a gate electrode can drastically influence the conductance variation in response to the charge carried by a biomolecule. In addition, we show that the diameter and shape of the pore both play a significant role in the sensitivity of the conductance signal to the nucleotides of a ssDNA molecule.

2 Methods

In order to investigate the conductance response to the translocation of a DNA molecule through a g-QPC nanopore, we have developed a comprehensive multi-scale, multi-phase

model. First, a molecular dynamics simulation is performed to obtain the trajectories of the translocating DNA molecule. Next, we extract the ionic and molecular charge configuration to find the electrostatic potential in the g-QPC membrane for each trajectory time step (snapshot) by solving the Poisson equation over the whole electrolyte-membrane domain. Finally, the electrostatic potential is used to calculate the electronic and transport properties of the g-QPC during the DNA translocation. Each of these three steps is outlined below.

DNA Atomic Charge Model

The atomic coordinates and charges of a DNA molecule are described using all-atom molecular dynamics (MD) simulations. There are three DNA charge models employed in the study, namely, an ideal 24 base pair dsDNA model, conformations of a 15 base pair dsDNA strand obtained from a forced extension from a helical (B-form) to a zipper (zip-form) conformation, and one linear conformation of a 16 base pair ssDNA obtained from MD simulations.

The atomic coordinates of the initial structure of the DNA molecules were built using the program X3DNA [25], and the topology of the DNA, along with missing hydrogen atoms, was generated using psfgen [26]. The 15 base pair dsDNA (16 base pair ssDNA) molecule was placed in a water box and neutralized at 1 M KCl (0.3 M KCl). The dimensions of the solvated system was $70 \text{ \AA} \times 70 \text{ \AA} \times 110 \text{ \AA}$ ($60 \text{ \AA} \times 60 \text{ \AA} \times 180 \text{ \AA}$) and contained about 52,000 atoms (64,000 atoms). All molecular dynamics simulations were performed using NAMD 2.9 [26], using periodic boundary conditions. CHARMM27 force field parameters were employed for DNA [27], ions and TIP3P water molecules [28]. The integration time step used was 2 fs with particle-mesh Ewald (PME) full electrostatics with grid density of $1/\text{\AA}^3$. Van der Waals energies were calculated using a 12 $\text{\AA}$ cutoff, and a Langevin thermostat was assumed to maintain constant temperature at 295 K [29].

The system was first minimized for 4000 steps, then heated to 295 K in 4 ps. After heating, the DNA was constrained, and a 500 ps-equilibration was conducted under NPT ensemble conditions, using the Nosé-Hoover Langevin piston pressure control at 1 bar [29]. After the system acquired a constant volume in the NPT ensemble, 1.5 ns-equilibration was conducted in an NVT ensemble. Steered Molecular Dynamics (SMD) simulations [30, 31] were employed to induce forced extension of DNA molecule. The dsDNA was stretched by pulling both strands on one end of the dsDNA at a constant velocity of 1 $\text{\AA}/\text{ns}$ along the z -direction, while harmonically restraining the other end. In the case of the ssDNA molecule the 5' end of the strand was pulled at a constant velocity of 10 $\text{\AA}/\text{ns}$, restraining the 3' end of the strand. The pulled atoms were attached to one end of a virtual spring; the other end of the spring, a dummy atom, was moved at a constant pulling speed along the pulling direction. The pulled atoms experience a force $f = -k[z(t) - z(t_0) - v(t - t_0)]$, where $z(t_0)$ is the initial position of the dummy atom attached to the spring. The spring constant k was chosen to be equal to $3k_B T_0 / \text{\AA}^2$ (k_B is the Boltzmann constant; $T_0 = 295 \text{ K}$), corresponding to a thermal RMSD deviation of $\sqrt{k_B T_0 / k} \approx 0.6 \text{ \AA}$, typical for SMD simulations [30, 31, 32, 33]. After a 60 ns (6 ns) SMD simulation, the dsDNA molecule (ssDNA molecule) underwent a molecular extension of 53 $\text{\AA}$ (73 $\text{\AA}$).

Self-Consistent Determination of Electric Potential

The electronic transport properties of the g-QPC depend on the induced electrostatic potential $\phi(\mathbf{r})$ on the membrane due to the DNA charges in the nanopore. The local potential can be obtained self-consistently by solving the Poisson equation,

$$\nabla \cdot [\varepsilon(\mathbf{r}) \nabla \phi(\mathbf{r})] = -e[K^+(\mathbf{r}) - Cl^-(\mathbf{r})] - \rho_{DNA}(\mathbf{r}). \quad (1)$$

and using a Newton-multigrid method inside a 3D box containing the g-QPC in solution [19]. In eq. 1, ε is the local permittivity, and the RHS includes the charge of ions in solution (K^+, Cl^-) as well as ρ_{DNA} , the DNA charges present in the system. The electrolyte distributions obey Boltzmann statistics [6]

$$K^+(\mathbf{r}) = c_0 \exp\left[-\frac{e\phi(\mathbf{r})}{k_B T}\right], \quad Cl^-(\mathbf{r}) = c_0 \exp\left[\frac{e\phi(\mathbf{r})}{k_B T}\right] \quad (2)$$

Here, K^+ and Cl^- are the local electrolyte concentrations, where c_0 is the nominal concentration of the solution. A typical translocation bias across the membrane is less than 0.5 V, a regime in which eq. 2 is valid [14]. A nonuniform 3D grid with 256 points in each dimension is used to discretize the system. The grid near the nanopore has a larger resolution to improve accuracy in the electrostatic potential induced by the DNA. Neumann boundary conditions are enforced on the sides of the box, while Dirichlet boundary conditions are used for the top and bottom of the box ($V_{TOP} = V_{BOTTOM} = 0$ V).

Electronic Transport Properties of Graphene Nanoribbons

The fluctuations of the potential $\phi(\mathbf{r})$, induced by DNA translocation as obtained from eq. 1, are used to calculate the transport properties of the g-QPC within the tight-binding approximation, for which the Hamiltonian reads [8, 34]

$$H = \sum_{i,\mu} [\varepsilon_\mu - e\phi(\mathbf{r}_i)] a_i^{\mu\dagger} a_i^\mu + \sum_{\substack{\langle ij \rangle \\ \mu\nu}} V_{\mu\nu}(\vec{n}) a_i^{\mu\dagger} b_j^\nu + V_{\nu\mu}(\vec{n}) b_j^{\nu\dagger} a_i^\mu \quad (3)$$

Here, e_μ is the on-site energy of an electron in state μ located at position i , $\phi(\mathbf{r}_i)$ is the electrostatic potential at position i , and $a_i^{\mu\dagger}/b_i^{\mu\dagger}$ and a_i^μ/b_i^μ are creation and annihilation operators for an electron in state μ at position i for the graphene A/B sublattice, respectively. The states μ, ν are the p_z, d_{yz} , and d_{zx} orbitals of atomic carbon [35]. The inclusion of the d states in the basis improves the description of the electronic structure by allowing for the inclusion of edge-passivation by hydrogen. The transfer integrals $V(\vec{n})$, where $\vec{n}$ is the unit displacement between positions i and j , are determined by fitting to *ab initio* calculations [35]. All tight-binding parameters are taken from Boykin et al [34].

After determining the Hamiltonian, the electronic properties of the g-QPC are obtained using the non-equilibrium Green's functions (NEGF) formalism. The Green's function $\mathbf{G}$ is written

$$\mathbf{G}(E)=[E - \mathbf{H}]^{-1} \quad (4)$$

In real space, it is written

$$[E \pm i\eta - H(\mathbf{r}, \mathbf{r}')]G(\mathbf{r}, \mathbf{r}')=\delta(\mathbf{r} - \mathbf{r}') \quad (5)$$

$\mathbf{H}$ is the Hamiltonian, and η is an infinitesimally small number to ensure solutions are found. One can divide the g-QPC lattice into three sections, two leads (L) on either side of a conductor (C). Then, eq. 4 can be written

$$\begin{bmatrix} G_L & G_{LC} & 0 \\ G_{CL} & G_C & G_{LC} \\ 0 & G_{CL} & G_L \end{bmatrix} = \begin{bmatrix} E - H_L & V_{LC} & 0 \\ V_{CL} & E - H_C & V_{LC} \\ 0 & V_{CL} & E - H_L \end{bmatrix}^{-1} \quad (6)$$

Taking $V_{LC}=V_{CL}^\dagger$ yields

$$G_C=[(E+i\eta)I - H_C - \sum_\alpha \sum_\alpha]^{-1} \quad (7)$$

where $\sum_\alpha \equiv V_{\alpha C}^\dagger [E - H_\alpha]^{-1} V_{\alpha C}$ is the “self energy” of lead α .

The transmission $T(E)$ between the leads 1 and 2 is given by [36]

$$\bar{T}_{12} = -Tr[(\sum_1 - \sum_1^\dagger)G_C(\sum_2 - \sum_2^\dagger)G_C^\dagger]. \quad (8)$$

and is used to find the conductance at a source-drain bias V_{DS}

$$G = \frac{2e}{V_{DS}h} \int_{-\infty}^{\infty} \bar{T}(E)[f_1(E) - f_2(E)]dE \quad (9)$$

Here, $f_\alpha(E) = f(E - \mu_\alpha)$ is the probability of an electron occupying a state at energy E in the lead α , and $(\mu_1 - \mu_2)/e = V_{DS}$ is the bias across the conductor. We take $f(E)$ as the Fermi-Dirac distribution function and the temperature as 295 K. The Fermi energy E_F is set equal to μ_1 . In practice, E_F can be adjusted by an external gate bias as proposed in a previous work [22]. In this analysis, it is taken to be an external parameter without any loss of generality.

3 Results and Discussion

Electronic Detection of dsDNA Helicity

In this study, we consider g-QPCs with leads measuring ~ 8 nm wide and a constriction measuring ~ 5 nm wide (figure 1). Each g-QPC has a 2.4 nm diameter nanopore located in one of two positions: the geometric center of the g-QPC (figure 1a) or vertically offset (y

direction) from the geometric center (figure 1b). A schematic diagram of a DNA molecule electrophoretically translocating across the g-QPC membrane through a nanopore is shown in figure 2.

The charge distributions from an ideal 24 base pair B type dsDNA, containing only adenine and thymine base pairs, in a 1 M KCl solution were translocated through the nanopores of the described g-QPCs. The corresponding potential distributions in the plane of the graphene membrane were obtained as outlined in eq. 1.

At the start of the translocation (snapshot 0), the bottom of the strand is at a distance 3.5 Å above the g-QPC membrane, and the translocation axis of the dsDNA is coaxial with the center of the nanopore. The dsDNA is then rigidly translocated 0.25 Å per time step (snapshot) through the nanopore until the DNA has passed through the pore completely. After the last snapshot, the top of the DNA strand is 13.5 Å below the g-QPC membrane. The charge distribution arising from the dsDNA at each snapshot is fed into the Poisson solver, yielding the electrostatic potential on the g-QPC membrane at each time step.

Because of the heavy screening due to the electrolytic ions in solution, the potential on the g-QPC membrane is mainly induced by the charges in the immediate vicinity of the nanopore. As a result, the charge distribution inside the pore is effectively due to a thin slice of the DNA strand located within the membrane plane. In effect, the electrostatic potential “rotates” in-place (see e.g. [19]). Since each slice of the DNA strand has a reflection symmetry, the resulting potential should also have the same symmetry.

Figure 3 shows the conductance in the g-QPC during the translocation of the dsDNA while the g-QPC is gate biased so as to achieve three different carrier concentrations: $p_1 \approx 7 \times 10^{12} \text{ cm}^{-2}$ ($E_F = -0.25 \text{ eV}$), $p_2 \approx 1 \times 10^{12} \text{ cm}^{-2}$ ($E_F = 0 \text{ eV}$), and $n_1 \approx 4 \times 10^{12} \text{ cm}^{-2}$ ($E_F = 0.25 \text{ eV}$). The g-QPC geometries considered had the nanopore in one of two positions, the first of which is located in the center of the g-QPC (g-QPCa) (figure 1a). As seen in figure 3a, for $p = p_1$, the average conductance $\bar{G}$ was found to be $\sim 15 \mu\text{S}$, and the conductance variations dG have a magnitude of less than $0.1 \mu\text{S}$, which is $< 1\%$ of $\bar{G}$. As the hole concentration is reduced to p_2 , $\bar{G}$ jumps to $\sim 26 \mu\text{S}$, while dG similarly increases to $\sim 1.4 \mu\text{S}$, or more than 5% of $\bar{G}$. Finally, for the n-type concentration n_1 , $\bar{G} \approx 9 \mu\text{S}$, while the $dG \approx 0.5 \mu\text{S}$, or 6% of $\bar{G}$. Though the conductance is indeed smaller, the variations dG increase relative to the overall signal.

The significant change in both conductance magnitude and magnitude variation dG are due to the complex boundary conditions introduced by the QPC and nanopore edge. These boundary conditions give rise to a nonuniform electron density around the nanopore, which changes as the carrier concentration is adjusted by the gate bias. The DNA, then, interacts differently with the electron (and hole) density at different carrier concentrations, as well as at different points during the translocation through the pore, eliciting a marked difference in the behavior of the conductance. As a result, small gate voltage adjustments can cause significant improvements in the ability to identify the DNA signal from the background. Additionally, it is worth noticing that though changes in carrier concentrations can largely reduce the magnitude of the conductance signal, as seen when switching from p-type (p_2) to

n-type (n_1), the variations dG can actually increase with respect to the overall signal, enhancing the detection of the DNA helix.

In the case of g-QPCb (figure 1b), when the pore is positioned 2 nm above the location of the center of the GNR constriction, the behavior of the mean conductance $\bar{G}$ is significantly different from the conductance behavior of g-QPCa. For p_1 , $\bar{G}$ is $\sim 91 \mu S$, about six times the conductance of g-QPCa at the same concentration, while $dG \approx 1.1 \mu S$, less than 2% of the signal. When p is changed to p_2 , $\bar{G}$ drops to $\sim 27 \mu S$, in contrast to the conductance increase in g-QPCa for the same carrier concentration change. The variations dG are only $\sim 0.3 \mu S$, which is negligible when compared to the signal magnitude. For the n-type GNR ($E_F = 0.25$ eV), $\bar{G}$ drops even further to $\sim 16 \mu S$, but dG increases to $1.4 \mu S$, or 9% of the signal. This different behavior of G at the same values of n is another consequence of the complex boundary conditions of the QPC edge and nanopore. In particular, moving the pore around the QPC center changes the sign of the differential transconductance for the p-type g-QPCs. However, the conductance behavior of g-QPCb is similar to that of g-QPCa in the sense that small changes in carrier concentration can cause significant modulation of $\bar{G}$ and dG . A more in-depth discussion on the interaction of the boundary and electronic properties of the g-QPC can be found elsewhere [19, 22].

For all carrier concentrations and nanopore positions, the conductance traces display a periodic behavior, repeating after a period of ~ 130 snapshots, as a consequence of helical nature of the dsDNA itself. The electrostatic potential rotation converges to its original position after one full helical pitch has translocated, which for 130 snapshots at $0.25 \text{ \AA}$ per snapshot yields a distance of ~ 3.3 nm for the DNA pitch. In addition, the initial and final halves of each period are related by a mirror symmetry, as shown in figure 3. The g-QPC lattice's y-axis reflection symmetry, coupled with the DNA molecule's own reflection symmetry, yields an identical conductance after the DNA potential is reflected about the y-axis, or when θ is transformed to $2\pi - \theta$ (figure 3g). In other words, potentials at an angle θ yield the same conductance for potentials at angles $2\pi - \theta$. The mirror effect within each period is present in all conductance curves.

Detection of Helical to Zipper Conformational Transformation

Another potential application of the g-QPC as a biomolecular sensor is the detection of the conformational changes DNA undergoes inside the nanopore. A poly(AT)₁₅ dsDNA molecule was stretched using SMD simulations to achieve forced extension of the DNA molecule. SMD simulations were performed by harmonically restraining both 3' and 5' terminal phosphate atoms on one end, while the corresponding atoms at the other end were pulled at a constant velocity of $1 \text{ \AA/ns}$. The length of the dsDNA molecule changed from $52 \text{ \AA}$ to $103 \text{ \AA}$ over the course of a 60 ns SMD simulation. The dsDNA undergoes a series of conformational changes, starting in the helical form (B-DNA) and gradually unwinding into a planar zipper-like form (zip-DNA). In the zip-DNA conformation, the hydrogen bonds on the complementary base pairs are broken, and the base pairs interlock in a zipper-like fashion. The conformations of both dsDNA type can be seen in figure 4a.

The transformation between the helical and zipper conformations of the dsDNA molecule can be detected by the g-QPC device by calculating the transverse electronic conductance of

the graphene membrane [37]. Each conformation was rigidly translocated (translocated at a rate of 0.5 Å per snapshot) through the nanopores in both g-QPCa and g-QPCb at $p = p_2$ over a series of snapshots, and the electrostatic potential from the DNA charges was calculated for each snapshot.

Figure 4b shows the conductance in g-QPCa as a function of the electrostatic potential of each snapshot. When the dsDNA is helical in shape, the proximity of the DNA charges to the nanopore edge generates significant potential variations on the g-QPC membrane, and as described earlier, the electrostatic potential induced by the DNA charge effectively rotates in the plane of the membrane. As a result, the conductance variation dG is $\sim 0.8 \mu\text{S}$, or 9% of the mean conductance $\bar{G} \approx 9 \mu\text{S}$. On the other hand, when the dsDNA is in the zip-type, its cross-sectional area becomes smaller than that of B-DNA, resulting in a greater distance between the DNA charge and the nanopore edge. Thus, the electrolyte (Debye length $\sim 3 \text{ Å}$) screens the electrostatic potential on the nanopore edge significantly. In addition, because the zip-type DNA is no longer helical, the membrane potential does not vary significantly as the DNA translocates. As a result dG vanishes, and the signal is virtually constant at $\bar{G} = 9.2 \mu\text{S}$. When the dsDNA is pulled through g-QPCb, a similar behavior occurs. Hence, in B conformation, dG is $1.2 \mu\text{S}$, i.e. $\sim 8\%$ of $\bar{G} = 16 \mu\text{S}$. In the zip conformation, on the other hand, the conductance G is flat at a constant value of $16.2 \mu\text{S}$.

Our simulations indicate that the g-QPC can clearly differentiate between the two types of DNA. At both pore positions, the change from a significant conductance variation of $\sim 8\text{-}9\%$ of the signal to a constant value can be readily observed. In addition, moving the nanopore position in a g-QPC can enhance the value of the conductance, as well as the variation amplitude, especially when combined with a tunable gate electrode. An interesting point to note is the gating effect of the DNA strand itself on the g-QPC. Because of the DNA's proximity to the nanopore edge in the B-DNA conformation, its electrical charges actually bias the constriction, inducing a different mean conductance, which is an additional confirmation the transformation has occurred.

Electronic Detection of ssDNA Nucleotide Translocation

We also use SMD to stretch a 16 base pair ssDNA, comprising of 4 repetitions of the DNA segment A-T-G-C, from a canonical helical conformation to a linear, ladder-like form. The ssDNA molecule was solvated in a 0.3 M KCl electrolyte solution, and the terminal phosphate atom on the 5' end of the ssDNA was pulled with a constant velocity of 10 Å/ns . The terminal phosphate atom on the 3' end of the DNA was harmonically constrained to its initial position, until the nucleotides in the central region of the ssDNA acquired a linear conformation. The molecular length of the ssDNA changed from 55 Å to 128 Å over the course of the simulation, and the base pairs collectively tilted towards the 5' end of the DNA [38].

The stretched ssDNA, which adopts a linear configuration due to forced extension, was placed inside a nanopore within a g-QPC and translocated at a rate of 1 Å per snapshot along a direction perpendicular to the graphene plane to mimic electrophoretic translocation of the DNA through the graphene nanopore (see figure 2). As mentioned earlier, we showed that the rotation of the electrical potential of the DNA charge distribution, arising from DNA

helicity, within the graphene plane causes a modulation in the electronic conductance through the graphene membrane. In the present study, we choose a ladder-like conformation for ssDNA to ensure that the conductance modulations are solely due to the linear translocation of the DNA as opposed to any effective rotation of the electrostatic potential in the graphene plane.

First, we investigate the ssDNA translocation through a circular nanopore with a 1.2 nm diameter at three different locations in the g-QPC at a carrier concentration $p = p_2$. Figure 5 shows the transverse electronic conductance of the g-QPC as a function of ssDNA snapshot. We consider two orientations of the DNA molecule, one where the base pairs are aligned in the direction of transverse electronic current, herein referred to as ssDNA-x (see figure 5d), and the second where the base pairs are aligned in the direction perpendicular to the transverse electronic currents, herein referred to as ssDNA-y (see figure 5d).

Figure 5a displays the conductance traces for the center of the nanopore aligned to the geometric center of the g-QPC. For both DNA orientations, the conductance displays a series of peaks and valleys corresponding to the passage across the graphene membrane of individual nucleotides attached to the negatively charged phosphate backbone. The variation in electrical potential on the nanopore edge due to the motion of charges on the DNA molecule during the translocation process induces a variation of the local carrier concentration along the edge of the graphene nanopore, altering its conductance [19].

The particular snapshot when a nucleotide's center of mass passes the graphene membrane is denoted with a vertical black dashed line in figure 5. As can be readily seen, these snapshot locations correlate with the valleys in the conductance curve, identifying a conductance valley with the passage of a single nucleotide. The magnitude of the conductance at a particular snapshot is determined by the spatial orientation of the nucleotide within the nanopore, which can fluctuate significantly. However, the percentage change in conductance between nucleotides can be in excess of 15%, indicating the possibility to distinguish the charges of a passing nucleotide from the rest of the system.

In particular, the magnitude of the conductance variations for ssDNA-y is $\sim 0.03 \mu\text{S}$ to $\sim 0.05 \mu\text{S}$, or 10 to 17% of the overall signal. These variations are approximately three times larger than those for ssDNA-x for two reasons. First, there is a larger electronic density of states in g-QPCa above and below the nanopore (along the y-direction) compared to the density of states on either side (x-direction). Secondly, the nucleotides of ssDNA-y are closer to the larger electron density compared to ssDNA-x. As a result, changes in electrical potential have a more significant effect on the conductance.

When the pore geometry is altered, such as when changing its position, shape, or size, the boundary conditions restricting the allowed electronic states in the QPC are likewise changed, so various conduction channels around the Fermi energy may open or close. Depending on the transmission probability of each of these channels, an overall larger or smaller current can arise. An in-depth discussion on the effects of geometry on the electronic states and electronic transmission is reported in [19].

In order to determine the effect of the pore position on the conductance sensitivity, we chose to study g-QPCs with a 1.2 nm diameter pore in two alternate positions, shown in figure 5b and c, where the nanopore center is offset from the QPC geometric center by 1 nm and 2 nm, respectively, along the y-direction defined in figure 5. Because the trajectory of ssDNA remains unchanged for each pore position, the conductance of the QPC with a pore at position 'b' (figure 2b) has conductance minima at the same nucleotide positions as that with the pore at 'a' (figure 5a). However, for ssDNA-y, the width of these variations is noticeably smaller. Similarly, for ssDNA-y, the width of the minima is further reduced for a QPC with a pore at position 'c' (figure 5c). This is because there is a smaller interaction between the charges on the DNA backbone and the GNR electronic conduction states as the pore is placed closer to the edge. The negative backbone charges tend to attract positive holes in the g-QPC, enhancing the hole conduction and masking the nucleotide signal. As the nanopore is placed closer to the edge, however, the influence of the backbone becomes negligible, especially when the backbone is outside of the g-QPC, as in the case of pore 'c' (figure 5c). As a result, the nucleotide charges are solely responsible for the conductance variation, enhancing the detection of the nucleotide passage event.

In the case of the ssDNA-x, as the pore is placed closer to the edge, the nucleotide signal becomes indiscernible. The nucleotide and the conducting holes of the GNR are too far to interact strongly, when the nanopore is far from the QPC center, and cannot to be detected. On the other hand, in the ssDNA-y orientation, the nucleotides are adjacent to the conduction charges, and the conductance dips can be clearly seen.

The most striking effect of the changing boundary conditions when varying the pore position is their influence on the conductance magnitude. When the pore is moved from the nanopore center 'a' to position 'b', the conductance is amplified by almost two orders of magnitude, while at position 'c', the conductance is reduced by a factor of ~ 10 . Such drastic changes in the conductance magnitude with alternate pore positions suggest that the conductance magnitude is a strong function of lattice geometry. However, finer control of the conductance magnitude can be achieved by adjusting electronic carrier concentration in the g-QPC via a gate electrode [22]. It is clear that positioning the pore closer to the boundary negates the influence of the phosphate backbone on the conductance, and hence increases the ability for the current to detect only the nucleotide.

In figure 6 we display the conductance variation due to ssDNA-y, for a 2 nm circular pore (figure 6b), and a 0.8 nm by 1.2 nm elliptical pore at the g-QPC center (figure 6c), in addition to the 1.2 nm circular pore (figure 6a) discussed earlier. The primary result of increasing the circular pore diameter to 2 nm is the suppression of the interaction between the ssDNA molecule and the electronic conduction states (figure 6b). Since the ssDNA is in the center of the pore, the electrolytic screening, with a Debye length of 0.5 nm, causes the electric potential to become significantly smaller at the pore edge. Variations can still be seen at the same locations as the 1.2 nm pore, but they are significantly smaller, varying in magnitude by 1%.

One of the main issues encountered when electrically sensing a DNA molecule, translocating through a nanopore, is the stochastic fluctuations of the DNA molecule itself,

disrupting the conductance variations due to the passage of a nucleotide. Employing an elliptical pore can restrict the lateral fluctuations of translocating base pair. For this purpose we analyze the conductance due to ssDNA-y translocating in an elliptical pore with a major and minor axis diameter equal to 1.2 nm and 0.8 nm respectively (figure 6c). As can be seen, the conductance variations become much more uniform and well defined when the ssDNA-y is translocating through the elliptical pore. The pore edge is screened less by the electrolyte, because the phosphate backbone of the DNA is closer to the pore atoms. As a result, the conductance signal reflects the passage of the phosphate atoms more than the nucleotides themselves. The conductance variations are still significant, having a magnitude 3% of the overall conductance.

4 Conclusion

We have outlined a comprehensive methodology for simulating a g-QPC device for the purpose of biomolecular detection and characterization for a variety of potential medical and health applications, particularly DNA identification and genome sequencing. The proposed device is capable of sensing the motion and rotational position of dsDNA and ssDNA translocating through a nanopore, the conformational changes of a dsDNA molecule under forced extension, and the passage of single nucleotides across the graphene membrane. The pore geometry, position, and size, when combined with a variable carrier concentration, play crucial roles in the sensitivity of the device to the potential induced on the membrane by the translocating molecules.

The applications of this device are not limited to those outlined in this study. For example, detection of methylated cytosine can be an early indication of particular cancers. Additionally, our method is general enough to analyze the structure of other biomolecules. In this context, many biomolecules, particularly proteins, undergo structural transformations depending on the environment, so the ability to quickly and easily characterize their structures is of fundamental interest. Furthermore, experimental nanopores can be used to investigate single molecule conformation by force spectroscopy. For instance, when a DNA molecule is stretched inside a nanopore, the DNA molecule undergoes structural conformation. Being able to detect such conformational changes electronically, as well as the ability to correlate them with measured ionic currents and force experienced by the DNA, could make nanopores more attractive in force spectroscopy measurements.

Presently, differentiating individual nucleotides from one another is a large obstacle facing this class of device. Future avenues for investigation involve the addition of control gates in a multilayer stack containing the g-QPC to adjust the position and speed of any translocating molecules, reducing stochastic fluctuations and thereby enhancing the conductance signal [19]. Statistical analysis on large data sets can also be employed to further improve the identification of nucleotides from one another.

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Figure 1. The lattice of a) a 5 nm g-QPC with a 2.4 nm diameter centered nanopore (g-QPCa) and b) a 2.4 nm diameter edge nanopore (g-QPCb).

Figure 2. Schematic of the g-QPC system used to calculate transverse electronic conductance. Shown in the figure is an ssDNA, which arose from a MD simulation of forced extension, being translocated through the nanopore under a translocation bias. Transverse electronic conductance was computed for the five base pairs shown in the inset of the figure.

Figure 3.

Conductance of g-QPCa for a) $p = p_1$, b) $p = p_2$, and c) $n = n_1$, and conductance of g-QPCb at d) $p = p_1$, e) $p = p_2$, and f) $n = n_1$ as a dsDNA helix is translocated through the nanopore. One full period of the helix rotation is shown between the dotted lines, g) Cross section of dsDNA potential in nanopore plane at rotational position θ .

Figure 4.

Conductance of a) g-QPCa and b) g-QPCb at $n=n_2^+$ as a B-DNA (red) and a zip-DNA (green) is translocated through the nanopore. c) The initial (B-DNA) and final (zip-DNA) conformations of the morphological transformation.

Figure 5.

Conductance as a function of DNA position (snapshot) arising in a g-QPC due to translocation of 5 base pairs of a ssDNA molecule in a linear ladder-like conformation (see inset Figure 2). The dips in the conductance correspond to the translocation of a single base pair through the nanopore. Three different 1.2 nm diameter nanopore geometries are investigated: the nanopore center is (a) aligned to the geometric center of the graphene membrane, (b) offset by 1 nm from the geometric center, and (c) offset by 2 nm from the geometric center. (d) A schematic of the g-QPC nanopore with ssDNA inside. For each of the geometries the base pairs were translocated in two different configurations: ssDNA-x, where the base pairs are aligned in the direction of transverse electronic current (x direction) and ssDNA-y where the base pairs are aligned in direction perpendicular to the transverse electronic currents (y direction).

Figure 6.

Influence of pore size and shape on the electronic conductance variation due to translocation of a 5 base pair long ssDNA segment in a linear ladder-like conformation, (a) circular pore with diameter = 1.2 nm, (b) circular pore with diameter = 2 nm, and (c) elliptical pore with major and minor axis diameters equal to 1.2 nm and 0.8 nm respectively.