

Supporting Information

Quantum-Electrostatic Modelling of Graphene FET Biosensors for β 2-Microglobulin Detection

Ghassem Baridi^a, Leonardo Martini^b, Maria Celeste Maschio^{b,c}, Stefano Corni^c,
Giorgia Brancolini^c, Francesco Rossella^b and Luigi Rovati^a

^a Department of Engineering "Enzo Ferrari", University of Modena and Reggio Emilia, Via P. Vivarelli, 10, 41125 Modena, Italy

^b Department of Physics, Computer Science and Mathematics, University of Modena e Reggio Emilia, Via Campi 213/a, I-41125 Modena, Italy

^c Istituto Nanoscienze - CNR, S3, Via G. Campi 213/A, Modena, Italy

Figure S1. Protein-Surface Docking:

Statistical analysis of protein-surface encounter complexes for wild-type β 2-m obtained from rigid-body Brownian dynamics docking. Relative cluster populations and corresponding energy contributions during adsorption on graphite are reported. Simulations were performed in aqueous buffer at an ionic strength of 2.5 mM.

The most populated clusters are obtained from 5000 BD trajectories for the wild type. They represent the initial approach of the protein to the surface and they reveal more than five recurring binding poses, corresponding to different early-stage orientations. Configuration a1 is the most energetically stable due to an extended interaction patch. Contact residues are defined within a distance of ≤ 4.5 Å from the graphene surface.

Label	RelPop % (a)	U_{Rep}^pr (b)	U_{ds}^e (c)	U_{ds}^h (d)	LJ (e)	contact residues (f)		
Wild Type								
a1	4	-87.40	18.72	-9.03	-97.09	Asp34 Glu44 Asn83 Gln89	Glu36 Arg45 Val85 Pro90	Glu47 Arg81 Ser88
a2	44	-55.85	7.21	-6.75	-56.31	Ile1 Pro32 Thr86	Gln2 Ser33 Ile35	Arg3 Thr4 Ser61
a3	16	-55.44	20.10	-7.03	-68.51	Ala15 Glu74	Glu16 Arg97	Asn17 Asp98
a4	9	-52.24	8.01	-5.82	-54.42	Pro32 Asp53	Ser33 Phe56	Asp34 Trp60
a5	27	-50.76	5.70	-4.98	-51.48	Gln2 Val85	Val85 Ser88	

(a) Relative population of the cluster

(b) U_{repr} : total interaction energy of the representative of the given cluster, in kT with T=300 K

(c) U_{ds}^e : electrostatic desolvation energy of the representative complex, in kT

(d) U_{ds}^h : non-polar (hydrophobic) desolvation energy of the representative complex, in kT

(e) LJ: Lennard Jones contribution of the representative complex, in kT

(f) residues in contact with the surface at a distance $d \leq 4.5$ Å

Figure S2. Protein Radius of Gyration from Atomistic Molecular Dynamics Simulations:

Radius of gyration of the wild-type protein, showing the total Rg and its components along the x, y, and z axes, averaged over trajectories from conventional MD in water, conventional MD on graphene, and T-REMD simulations on graphene.

Wild type	<i>water</i> (Å)	<i>MD on graphite</i> (Å)	<i>TREMD on graphite</i> (Å)
R_{gtot}	14.23 ± 0.01	14.16 ± 0.01	14.13 ± 0.01
R_x	11.39 ± 0.13	12.07 ± 0.05	12.00 ± 0.06
R_y	11.55 ± 0.12	9.54 ± 0.06	9.70 ± 0.07
R_z	11.71 ± 0.12	12.80 ± 0.02	12.72 ± 0.01

Change 12, change 21 The COMSOL Multiphysics model considers a pH-7 aqueous electrolyte droplet placed on the graphene surface, where the formation of an electric double layer (EDL) at the graphene–electrolyte interface governs the electrostatic potential distribution and the resulting Dirac point shift. Graphene is modeled as a charged boundary interacting with mobile proteins in the electrolyte, while bulk boundary conditions are applied far from the interface to ensure the decay of the electrostatic potential toward its bulk value.

Due to the large disparity in characteristic length scales between the atomically thin graphene layer and the surrounding micrometer-scale domains, a non-uniform meshing strategy is adopted. The mesh is strongly refined in the vicinity of the graphene–electrolyte interface, where steep potential and protein concentration gradients occur, while coarser elements are used in regions with weak field variations. Mesh-convergence tests were performed to verify numerical accuracy, confirming that the calculated potential profiles and Dirac point shifts are insensitive to further mesh refinement. Figure SI.3 illustrates the mesh distribution employed in the simulations.

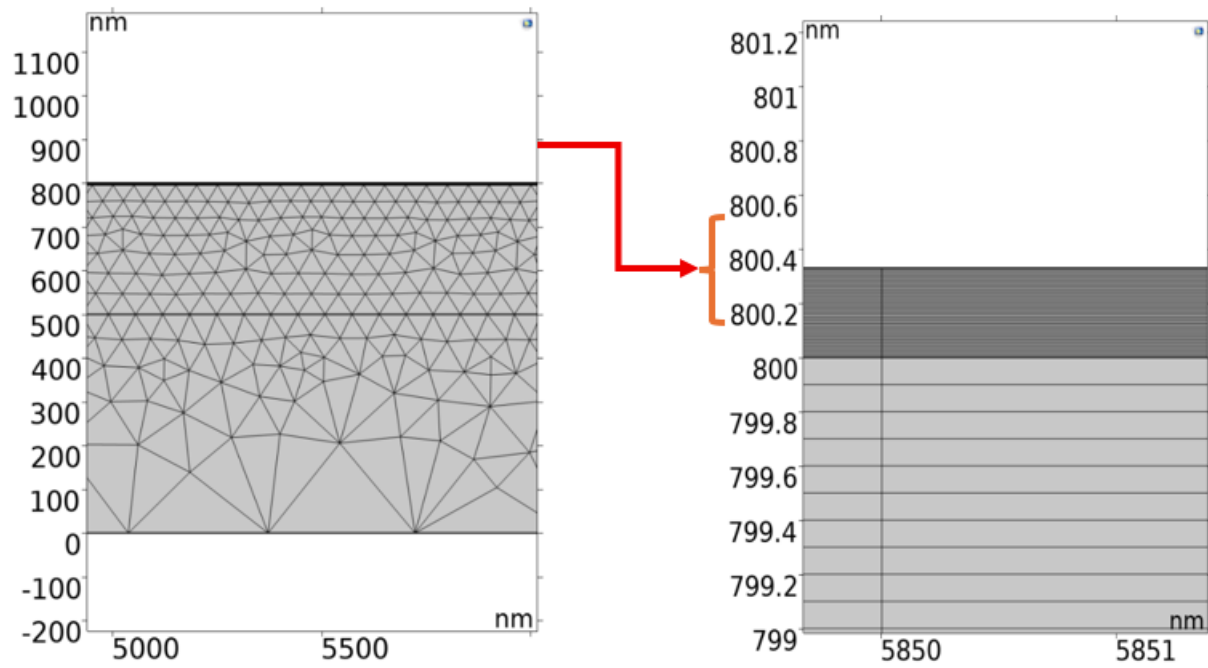


Figure S3. Meshing features employed in the simulations, with different level of refinement. (left) overall view of the computational mesh for the graphene field-effect transistor; (right) zoomed-in view highlighting the finer mesh applied in the graphene layer and the adjacent region to improve numerical accuracy.