A Molecular Dynamic Study to the Chiral Graphene Quantum Dots

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Introduction

Graphene-based materials enrich physical and chemical phenomena associated with optical properties of chiral nanostructures and facilitate their applications in biology. To study their applications to biology and further guide the design of nanomaterials, we need to understand the interactions of nanomaterials with biological systems. Here, we used molecular dynamic (MD) simulation to study the biocompatibility of chiral graphene quantum dots (GQDs) to the cellular membrane.

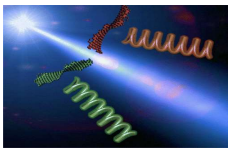

Figure 1, Graphene quantum dots (GQDs) represent single-layer of graphene of a size less than 30 nm. This innovative nanomaterial has stable photoluminescence and the wavelength is adjusted by the size of the graphene.

- We revealed the dynamics of a GQD entering cellular membrane.
- We found that the membrane was selective to the chirality of GQDs.
- And we proposed that the disturbance of the membrane was the origin of such chiral selectivity.

Methods

MD simulation was performed by NAMD with CHARMM36 force field at room temperature (310 K). Most calculation was completed on FLUX, the Linux-based high-performance computing cluster at the University of Michigan.

Structures of GQDs

Covalent attachment of L/D-cysteine to the edges of GQDs leads to the chiral helical buckling of GQDs. Using MMFF algorithm, we calculated the molecular geometries of pristine GQD and L/D GQDs (Figure 2).

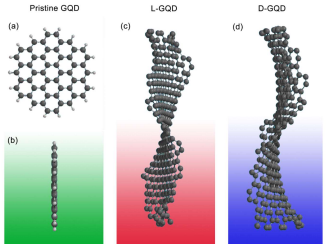

Figure 2, On the left (a,b) are the equilibrium geometries of small unmodified GQDs display nearly perfect molecular flatness. On the center (c) and right (d), when, L– or D-cysteine ligands were added around the circumference of GQD, an increase of buckling deformation was observed. The chirality of the ligands is noted on the top of the image; they were removed for clarity.

GQDs Enter Membrane

Applying a invented force in the MD simulation to drag the GQD through the membrane, we observed the dynamics of the insertion (Figure 3).

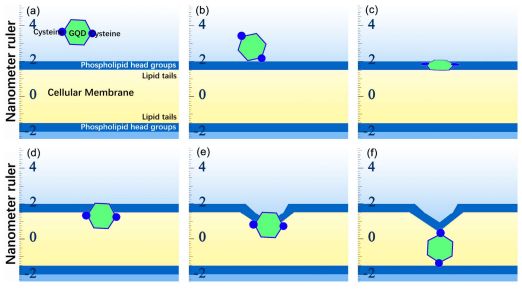

Figure 3, a serial of pictures depicted the important steps during a D-GQD entering the cellular membrane. Cysteine groups and phospholipid head groups are hydrophilic. The graphene matrix and the lipid tails are hydrophobic. (a) The GQD stayed in water with random orientation. (b) Once the GQD was close to the membrane, electrostatic force attracted one of the cysteine groups to the surface. (c) Then GQD lied flatly to maximize hydrophilic contacts. (d) Continuing dragging GQD down firstly sank the GQD perpendicularly into the membrane, (e) and then bent the membrane. (f) When enough force was accumulated, one of the cysteine detached from the upper leaflet and the GQD suddenly turned 90 degree.

Chiral Biocompatibility

Chiral nanostructures may exhibit different biological activity depending on their handedness. We tested how L/D-GQDs affect the viability of human liver HepG2 cells, and observed toxicity differentiation depending on chirality (Figure 4).

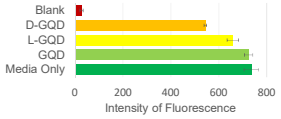

Figure 4, viability of HepG2 cells were measured by the intensity of fluorescence after treating with 0.015mg/ml GQDs for 1 hour.

There can be multiple biological pathways for how the chirality of GQDs affects cellular functions. In this study, interactions of the GQD stereoisomer with cellular membranes were evaluated using unbiased MD simulations. From the simulations, D-GQDs entered the head group region after tens of nanoseconds (Figure 5a) with the graphene parts of the GQDs lay perpendicularly to the bilayer plane (Figure 5e). But, in all cases, the L-GQDs never entered the bilayer (Figure 5b).

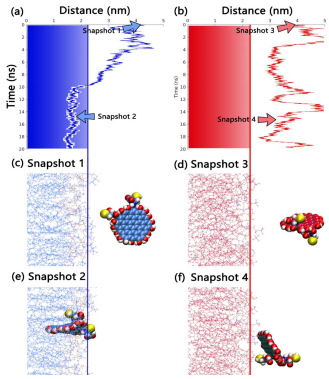

Figure 5, the 20 ns trajectories of the simulations of (a) L– and (b) D- GQDs entering membrane. There are two snapshots at (c) t = 0 ns and (e) t = 15 ns for L-GQD, and two snapshots at (d) t = 0 ns and (f) t = 15 ns for D-GQD.

Scan the QR code to watch videos.

To study the origin of the chiral selectivity, we used biased MD to drag both L/D-GQDs into the membrane. From the simulations, we found that when the GQD was inside the membrane, the L-GQD creates larger deformation to the cellular membrane than the D-GQD.

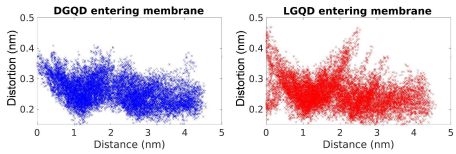

Figure 5, the correlations between the distortions of the membrane and the distances between centers of mass of GQDs and the membrane. Distortion was evaluated by the standard deviation of the z axis of positions of the phospholipid head groups. Each plot included data from four simulations. We ran each simulation for 200 ns.

Conclusions

1. We determined the molecular structure of L/D-GQDs.
2. We studied the biocompatibility of GQD by simulating the process of a GQD molecule entering the cellular membrane.
3. *In vitro* evaluation of GQDs with liver cells demonstrated their low cytotoxicity and differentiation of cytotoxicity between GQD stereosomers. Result from simulations implied that cellular membranes were likely to play the central role in the differentiation.

Acknowledgements

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