Protein Binding on Functionalized Charged Graphene Quantum Dots

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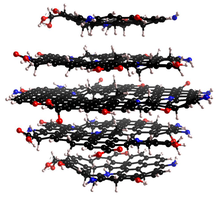
Abstract

Graphene quantum dots (GQDs) have emerged in nanobiotechnology as useful tools for numerous biomedical applications, including non-invasive cellular imaging, drug delivery, and gene targeting. Several studies have shown the successful uptake of GQDs in healthy and cancerous cells. While some in vitro and in vivo studies highlight mechanisms underlying GQD internalization in cells, there is a gap in our understanding of GQD interactions with complex biological media, such as blood serum. Proteins in biofluid environments adsorb to the surface of nanoparticles such as carbon nanotubes, forming the "protein corona." Graphene quantum dots have an abundance of charged surface functional groups, which are likely to interact with complementary charged regions in proteins. Herein, we investigate the interactions of individual proteins with negatively charged sodium citrate and reduced graphene oxide-derived GQDs, as well as positively charged nitrogen-doped GQDs. This study will advance our understanding of protein-GQD interactions in physiological environments, ultimately guiding the optimization of GQDs for biomedical applications.

Introduction

Graphene Quantum Dots (GQDs)

- **Water soluble**
- **Nano-sized**
- **Exhibit successful cell-internalization**
- **Numerous biological applications:**
  - **Drug delivery**
  - **Cell imaging**
  - **Gene targeting**



Interactions with Protein

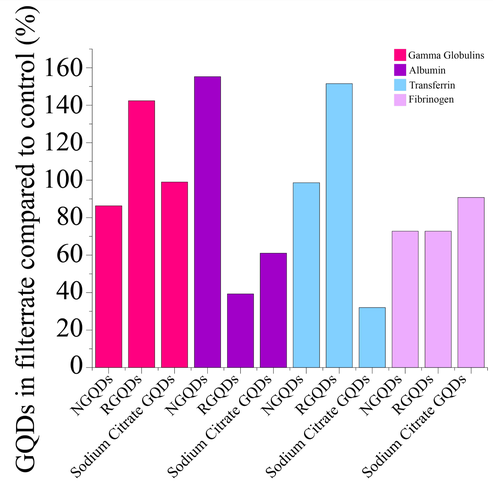
- **Lack of understanding of GQD interactions with biological media**
- **Utilize GQDs of different sizes and charges**
- **Through a simple centrifugation experiment, we aim to understand how size and charge affect GQD–protein interactions.**

Charge & Size of GQDs & Protein

GQD Type	Size (kDa)	Zeta Potential (mV)	Experimental Concentration
NGQDs	~10.5	+1.8 mV	1 mg/mL
RGQDs	~48	–49.4 mV	1 mg/mL
Sodium Citrate	~5.4	–51.8 mV	1 mg/mL

Protein	Size (kDa)	Net Charge (Physiological pH)	Experimental Concentration
Gamma Globulins (IgG)	~150	Slightly negative	11.5 mg/mL
Albumin	~66	Negative	45 mg/mL
Transferrin	~80	Negative	3 mg/mL
Fibrinogen	~340	Negative	3 mg/mL

Results



Interpretation

Gamma Globulins

- **NGQDs:** Moderate binding → electrostatic attraction reduces passage
- **RGQDs:** Increased passage → electrostatic repulsion + dispersion dominates
- **Sodium Citrate:** Minimal interaction → small size + negative charge → free passage

Albumin

- **NGQDs:** Increased passage → weak binding + dispersion/stabilization
- **RGQDs:** Strong retention → hydrophobic adsorption
- **Sodium Citrate**: Moderate retention → weak surface interactions

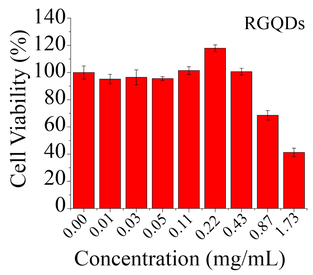
Transferrin

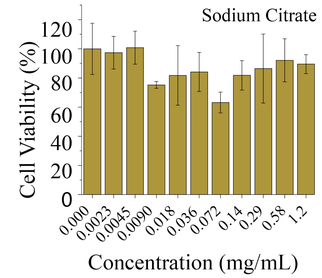
- **NGQDs:** Near-neutral → weak interaction
- **RGQDs:** Increased passage → electrostatic repulsion dominates
- **Sodium Citrate**: Strong retention → likely structural/ionic interactions

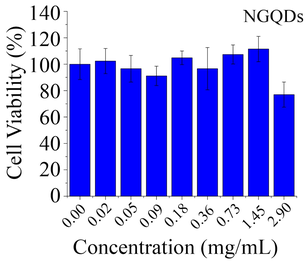
Fibrinogen*

- Difficult to interpret results due to aggregation

Biocompatibility Assay







Conclusion

- GQD–protein interactions depend on **charge, size, and protein structure**, not charge alone.
- **NGQDs** show mixed behavior (binding or increased passage) depending on the protein.
- **RGQDs** exhibit dual behavior: retention (Albumin, Fibrinogen) vs enhanced passage (Gamma, Transferrin).
- **Sodium citrate** shows minimal interaction overall, with some protein-specific retention.
- **Protein structure strongly influences outcomes**, with fibrinogen showing aggregation effects.
- Relative changes in filtrate recovery show that **protein-induced effects (binding, dispersion, or aggregation) dominate over intrinsic GQD properties**, highlighting the importance of the biological environment in determining nanoparticle behavior.

References

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