

Carbon, Graphene and Graphene Oxide Quantum Dots for Analytical Biochemistry Research

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Editorial

Graphene quantum dots (GQDs) have emerged rapidly as a new class of attractive fluorescence nano-probes ever since they were made from coal in 2013 by the Rice University lab of chemist James Tour [1,2]. They offer 2-10 nm size, good quantum yield, high photostability, tunable photoluminescence, flexible molecular structure, easy functionalization, excellent bio-compatibility, stable dispersion in water, and facile hydrothermal synthesis. A method for forming GQDs included adding an organic starting material to a vessel and heating the material to within 20°C of its boiling temperature for a time no longer than ten minutes [3]. Their chemical inertness and low toxicity have triggered numerous studies on their unique properties in interdisciplinary science and engineering research over the last several years [4]. Different sized GQDs with a narrow size distribution could be obtained via gel electrophoresis of the crude GQDs prepared through a photo-Fenton reaction of graphene oxide [5]. It was illustrated that the photoluminescence emissions of the well-defined GQDs originated mainly from the peripheral carboxylic groups and conjugated carbon backbone planes. GQDs enhanced sulfur/sulfide utilization, proving that C-S bonding could occur [6]. Graphene oxide quantum dots (GOQDs) exhibited photoluminescence color variation from orange-red to blue as their size was reduced, with electron transitions from the graphene π^* orbital to the oxygen n orbital [7]. The electronic properties and mechanisms involved in quantum-confined photoluminescence can be applied to research in analytical biochemistry. Chiral nanostructures can greatly enrich the chemical property of graphene-based materials to facilitate their applications in biology. Covalent attachment of l/d-cysteine moieties to GQDs led to their helical buckling due to chiral interactions at the edges [8]. Exposure of liver HepG2 cells to the l/d-GQD stereoisomers revealed a noticeable difference in their toxicity. Molecular dynamics simulations demonstrated that d-GQDs have a stronger tendency to accumulate within the cellular membrane than l-GQDs.

A fluorometric sensing platform based on tyramine-functionalized GQDs was able to detect a spectrum of metabolites with high sensitivity and specificity, as demonstrated in multi-parametric blood analysis for cholesterol, glucose, l-lactate and xanthine [9]. This metabolite profiling technique could be developed for the diagnosis of metabolic disorders and associated diseases, such as diabetes, gout, hypertension, lactic acidosis and obesity. A highly sensitive fluorometric method was developed for inorganic pyrophosphatase activity detection based on the disaggregation and aggregation of GQDs [10]. Copper ions triggered the severe aggregation of GQDs with rich carboxyl groups, which resulted in effective fluorescence quenching. With the addition of pyrophosphate, the quenched fluorescence was effectively recovered owing to its strong interaction with Cu^{2+} . Under catalytic hydrolysis by pyrophosphatase, the

pyrophosphate- Cu^{2+} complex was rapidly disassembled and the GQDs fluorescence was re-quenched. This method is highly sensitive and selective for the detection of pyrophosphatase, with a detection limit down to 1 mU mL^{-1} . One potential application is the diagnosis of pyrophosphatase-related diseases and screening of pyrophosphatase inhibitors in biological systems.

Carboxylic carbon quantum dots (cCQDs) functioned as a nano-quencher in the detection of nucleic acid based on a homogeneous fluorescent assay [11]. The principle lied in the different propensity of single-stranded DNA and double-stranded DNA to adsorb onto the surface of cCQDs. A superior range of detection, at least 3 orders of magnitude, was achieved; the potential to distinguish single-base mismatch was also exhibited. This may meet the high demand for simple, sensitive and selective DNA biosensors, particularly in disease diagnostics, environment monitoring, and food safety. A sensor for the detection of specific microRNA sequences was developed by exploiting mainly the π - π stacking interaction between the sp² carbon atoms of GQDs and the nucleobases of single-stranded DNA anchored on upconversion nanoparticles to enhance the upconversion emission [12]. Hybridization of the single-stranded DNA chains with their complementary microRNA sequences blocks the capacity of the upconversion nanoparticles to interact with the GQDs. That resulted in a reduction of the fluorescent enhancement, depending on the concentration of microRNA sequences down to a detection limit of 10 μM . A dual-emission and two-photon GQDs probe for bioimaging of hydrogen peroxide in biological systems [13]. A boronate merocyanine fluorophore was used as both a target-activated trigger and the dual-emission fluorescence modulator. Their fluorescence response is rapid and specific for mapping the production of hydrogen peroxide in living cells and deep tissues, with a quantitative detection limit of 0.05 μM .

GQDs were modified by grafting hexylamine or oleylamine to generate surfactant behavior [14]. Precise control of interfacial activity was demonstrated by varying the alkylamine density on the GQDs. The excellent tunability of GQDs' surface property highlights their potential use as a surfactant with novel functionality for stabilizing colloidal nanoparticles in analytical biochemistry research experiments. GQDs were used as an immobilized template on screen printed electrodes for the construction of a sensor platform based on electrochemical impedance spectroscopy [15,16]. The GQDs-modified electrode was conjugated with highly specific anti-myoglobin antibodies for the sensitive detection of myoglobin, a cardiac biomarker, in the presence of other competing proteins. The limit of detection was 0.01 ng/mL which is comparable to standard ELISA techniques. GQDs were added in a capillary electrophoresis method for the separation of cinnamic acid and its derivatives with direct UV detection. Excellent separation was achieved in eighteen minutes,

mainly attributing to the interaction of GQDs with isoferulic acid, sinapic acid and cinnamic acid.

Quantum dots have been used in food science mostly as a marker to either detect pathogenic bacteria or track proteins in the food matrix to give a better understanding of their role [17]. The most widely used quantum dots consist of a CdSe core functionalized in different ways and coated with polymers for better attachment to bacteria and proteins. The strong luminescent property of GQDs can be utilized to stain bacterial cells via a facile translocation into the cytoplasm [18]. *In vitro* experiments showed that GQDs exhibited very low cytotoxicity owing to their ultra-small size and high oxygen content; *in vivo* bio-distribution experiment of GQDs revealed no accumulation in the main organs of mice even after multiple doses and fast clearance through the kidneys [19]. The lack of obvious toxicity results obtained so far shows a promising future for more GQD applications in the food industry. Carbon dots are carbon nanoparticles that have very interesting optical properties and photocatalytic functions. They were highly effective in killing bacteria with visible light illumination, even under room lighting conditions [20]. These photoinduced bactericidal functions can provide many opportunities in a variety of bacteria control applications.

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