# Recent Advances in the Applications of MXene Quantum-Dots for Biosensing

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**Abstract.** MXene quantum dots (MQDs) are a burgeoning novel material that stands out for its excellent physicochemical properties. It is especially effective in serving as biosensing materials. It can be utilized as a biomarker for health conditions or as a marker for remnant chemical composites. Recently, there have been a great deal of advancements in the development of MGDs. It is requisite to recapitulate the progress achieved, providing a systematic summary of recent developments. This paper systematically reviews the latest applications of MQDs in biosensing. MQDs are used to detect metabolites and disease biomarkers through electrochemical, conventional fluorescent, and ratiometric fluorescent strategies, enabling sensitive detection of all sorts of biomarkers. In addition, MQD-based fluorescent and ratiometric fluorescent sensors are applied to monitor environmental pollutants and food contaminants. Modification strategies, including elemental doping, noble metal loading, and nanocomposite superposition, significantly improve the sensitivity and selectivity of sensors. Despite remarkable progress, challenges including large-scale synthesis, biocompatibility, and device portability still exist. Refinement can be made, such as optimizing preparation methods, enhancing biocompatibility, and promoting clinical transformation. This review offers a thorough reference for the design and future development of MQD-based biosensors.

**Keywords:** MXene quantum dots, Application, Biosensing, Recent advances.

## 1. Introduction

MXene quantum dots (MQDs) garnered from two-dimensional materials, MXene (transition metal carbides, nitrides, and carbonitrides), have exhibited enormous potential for application in biosensing for their excellent physicochemical properties. The MQDs are produced when the MXene is reduced to the nanoscale. The newly attained materials have demonstrated many novel properties while preserving some of the parent materials' merits. The MQDs have large surface areas, ample surface terminations, high biocompatibility, low toxicity, high hydrophilicity, surface tunability, high electric conductivity, gorgeous stability, abundant active sites, etc. The applications of MQDs in biosensing have manifested their increasing significance. Biosensing technology has been ubiquitously employed as an efficient method for clinical diagnosis, environmental surveillance, and food security control, providing highly selective, efficient, sensitive, and safe detection.

In recent years, many research teams have achieved great success in refining MQDs-based detection methods. However, there are still limitations to be tackled, such as the scalable and facile synthesis of MQDs, the integration of MQDs with other methods, etc. Hence, it is requisite to present a systematic recapitulation of the latest developments of applications of MQDs in biosensing. Herein, the recent progress in the application of MQDs in biosensing has been followed, providing comprehensive insights into current innovations. The paper aims to provide a systematic summary of recent studies and provide valuable references for researchers. It is anticipated that this work will inspire more innovative studies in terms of MQD's biosensing technology.

## 2. MQDs for Metabolites and Biomarker Detection

### 2.1. Electrochemical Methods

Cancer poses a great threat to human health. An early and accurate identification of tumor cells does substantial favor to clinical therapy. Electrochemical methods have been widely adopted, utilizing the ultrasensitivity, high selectivity, efficiency, and high biocompatibility of MQDs.

Safarpoor et al. have developed an ultrasensitive electrochemical method for prostate cancer biomarker detection, presenting a cost-efficient diagnostic method for early identification of prostate cancer. The prostate antigen is widely considered to be a biomarker for the detection of prostate cancer. The team first synthesized Ti3C2 MQDs and V2C MQDs. PANI@Ti3C2 MXene quantum dots-Au NPs and V2C quantum dots@Au-NPs were then produced, respectively, which was followed by the construction of an immunosensor based on a glassy Carbon electrode (GCE) adopting the sandwich type. The electrode was modified by PANI@Ti3C2 with antibody Ab1 conjugated and was further processed utilizing bovine serum albumin to shroud the non-specific binding sites, after which the electrode was completed through conjugation of Ab2 attached to V2C quantum dots@Au-NPs composites [1].

The construction of electrodes can be further refined to enhance the sensitivity of detection. A recent innovation has exploited the synergistic effects of three nanocomposites to fabricate electrodes. Gharehaghaji et al. have proposed a practical approach for ovarian-specific antigen (CA-125) inspection, which is beneficial to early identification of ovarian cancer. They fabricated a glassy carbon electrode embellished by a hierarchical nanocomposite of electrodeposited gold nanoparticles, MQDs polished with self-assembled Prussian blue nanoparticles, and further functionalized with optimized concentrations of streptavidin and anti-CA-125 antibodies (AuNP/PB/MXene QD/GCE). The outstanding performance of the sensor is ascribed to the synergistic effects of miscellaneous constituent nanocomposites [2].

Ranjbari et al. have designed a label-free biosensor using PBA-Au-MXene quantum dot nanocomposites, which allows electrochemical early screening of miR-122. They have successfully transformed non-conductive poly (n-butyl acrylate) into a conducting compound via the integration of Au-MXene QDs, which is followed by loading it onto a GCE and covalent immobilization of thiolated antisense single-stranded DNA (ssDNA) probes through thiol-Au bonds. They managed to convert non-conductive poly (n-butyl acrylate) into a conductive composite, enhancing the electrical conductivity of PBA while retaining its structural flexibility [3].

### 2.2. Doping Strategy

Doping MQDs has emerged as a successful strategy to tailor the properties for advanced applications. Common dopants include sulphur, phosphorus, nitrogen, and various sorts of metals.

Govindaraju et al. developed the first biosensing platform based on iron-nitrogen co-doped MXene quantum dots (FeNMQDs) for monitoring normetanephrine, a metabolite of norepinephrine and a potential biomarker for neuroendocrine tumors. MXene nanosheets were first prepared, and Fe- and N-co-doped MQDs were obtained via sonication and hydrothermal treatment with ethylenediamine and $FeCl_3$. Electrochemical tests confirmed that the FeNMQDs-modified GCE achieved a low detection limit of 13.85 nM with a linear range from 50 μM to 200 μM [4].

Rajeev et al. have developed boron-nitrogen-doped $Ti_3C_2T_x$ MQDs (BNMQDs) for the detection of creatinine (CRT), which can be employed as a biomarker for acute kidney injury. The $Ti_3C_2T_x$ MQDs were first synthesized via a hydrothermal route, and B-N co-doping was achieved by combining the quantum dots with p-phenylenediamine and boric acid. The sensing electrode was fabricated using carbon fiber paper (CFP). The newly prepared sensor exhibited detection from 0.104 to 135 μM, with a detection limit of 34.53 nM and a quantitation limit of 104.65 nM [5].

Paul and Kim constructed a sensing platform for L-ascorbic acid using screen-printed electrodes modified with C-Pd co-doped MQDs supported by a metal-organic framework (MOF). Pd nanoparticles were integrated into C-doped MQDs and combined with a Fe-based MOF to form MIL-

PdMNQDs. Screen-printed electrodes and GCEs modified with this composite were fabricated for selective electrochemical detection of L-ascorbic acid in buffers, human serum, and artificial sweat, showing great potential for precision medicine applications [6].

These doping methods have shown positive effects in improving the properties of MQDs, making them more suitable for clinical applications.

### 2.3. Fluorescent Method

The fluorescence detection method founded on Förster resonance energy transfer (FRET) has been widely used. FRET is a distance-dependent non-radiative energy transfer process in which an excited fluorescent donor imparts energy to a ground-state fluorescent acceptor, resulting in the quenching of donor fluorescence and the enhancement of acceptor fluorescence.

Yang et al. have integrated $Ti_3C_2T_x$ MQDs and $MnO_2$ nanosheets to construct a label-free system for ultrasensitive and selective detection of glutathione. The FRET phenomenon between $Ti_3C_2T_x$ MQDs and manganese dioxide nanosheet (MnNS) contributes to the on-off detection system. The MnNS is capable of quenching the fluorescence of $Ti_3C_2T_x$ QDs in the absence of GSH, while the quenching effect is subdued in the presence of excessive GSH owing to its calibre of transforming the $MnO_2$ NS to $Mn^{2+}$ [7].

Li et al. proposed a FRET-driven fluorescent aptasensor for detecting low-density lipoprotein (LDL), an important biomarker for cardiovascular diseases. S-doped graphitic carbon nitride quantum dots were synthesized via a hydrothermal reaction using citric acid and thiourea as precursors. These quantum dots conjugated with LDL aptamers served as fluorescent donors, while MXene-supported Au nanoparticles acted as acceptors. The sensing mechanism relies on FRET. The fluorescence is quenched in the absence of LDL, while in the presence of LDL, fluorescence will experience a recovery, the extent of which strongly correlates to the concentration of LDL [8].

### 2.4. Ratiometric Fluorescent Method

Ratiometric fluorescent detection is an advanced sensing technique that determines target concentrations by calculating the intensity ratio of two distinct fluorescence emission peaks at different wavelengths, with one peak serving as a stable internal reference and the other as a responsive signal toward the analyte. It has a stronger ability to remain stable against external interference in contrast to traditional single fluorescence methods. Lin et al. have devised a ratiometric fluorescence monitoring method for 2,6-dipicolinic acid (DPA). The blue fluorescent MQDs were first synthesized. A composite probe, MQDs-EDTA-$Eu^{3+,}$ was constructed via coordination between MQDs, EDTA, and $Eu^{3+}$. $Eu^{3+}$ was surrounded by water molecules, which are able to quench the fluorescence emitted by $Eu^{3+}$ in the absence of DPA, leaving the 445 nm blue fluorescence of MQDs observed. DPA, as an outstanding ligand of $Eu^{3+}$, can surrogate water molecules to produce the MQD-EDTA-$Eu^{3+}$-DPA conpound, triggering red fluorescence of $Eu^{3+}$ at 616 nm through energy transfer from DPA to $Eu^3$, while the blue MQD emission remains unaltered. The fluorescence intensity ratio $F_{616}/F_{445}$ displays a marvelous linear relationship with the concentration of DPA, providing a facile method for precise analysis of DPA [9].

## 3. MQDs for the Detection of Chemical Composites in Environments and Food

### 3.1. Fluorescent Method

The most adopted method in the surveillance of chemical compounds is the fluorescence method, thanks to its feasibility and high sensitivity.

Nguyen et al. have N-doped $Ti_3C_2$ MXene QDs (N-MQDs) prepared by cutting $Ti_3C_2$ MXene nanosheets with the assistance of ammonia via a hydrothermal method. N-MQDs bear a remarkable character of fluorescence, which can be quenched by tetracycline. The fluorescence quenching performance of N-MQDs in the presence of different tetracycline concentrations was examined in the

range of 0.50-300 mM, with results in conformity with the Stern-Volmer equations to a great extent. FRET and inner filter effect were responsible for the procedure [10].

Hu et al. have developed a novel tactic to synthesize $Ta_2C$ MXene using low-temperature molten salt etching, which was subsequently transformed into $Ta_2C$ MQDs through hydrothermal delamination and a simultaneous amination process, producing fluorescent probes for oxytetracycline, an antibiotic. The probe shows a linear detection range of 0.5 to 400 μm and a low detection limit of 0.186 μm. The innovative method of synthesizing the precursors of MQDs and the excellent physicochemical properties of $Ta_2C$ MQDs highlight the promising application of $Ta_2C$ MQDs in monitoring oxytetracycline in food and the environment [11].

Han et al. established a fluorescent sensing platform for 2,4,6-trinitrophenol (TNP) using amino-functionalized MQDs ($NH_2$-MQDs). N-(2-aminoethyl)-3-aminopropyl trimethoxysilane was used as the amine reservoir. The fluorescence of MQDs-$NH_2$ is effectively quenched by TNP through FRET and the inner filter effect, forming the basis of TNP detection. The probe achieves a linear range of 0.05-20 μM and a detection limit of 17 nM [12]. Rajamanikandan et al. have devised $Nb_2C$ MQDs fluorescence probes for the precise detection of the antibiotic chloramphenicol (CPL). Bluish-green-emitting N-S co-doped Nb2C MXene quantum dots were prepared with glutathione as a nitrogen and sulfur source. The MQDs have a peak of 427 nm when being stimulated with 330 nm light. The fluorescence of MQDs is effectively quenched by CPL by forming complexes between the MQDs and the CPL antibiotic, which fail to emit fluorescence. The sensor has a detection range from 20 μm to 240 μm with a limit of detection of roughly 76.3 nM [13].

### 3.2. Ratiometric Fluorescent Method

Liu et al. have proposed a ratiometric fluorescence detector for the examination of ofloxacin, an antibiotic. The probe was constructed employing L-tryptophan and cerium (Ce)-functionalized $Ti_3C_2$ MQDs, which show perfect photoluminescence. The intensity of fluorescence at 433 nm plummeted with the addition of ofloxacin via a core mechanism of static quenching, while the intensity of fluorescence at 495 nm increased with the addition of ofloxacin due to L-tryptophan and cerium (Ce)-functionalized $Ti_3C_2$ MQDs-ofloxacin complex formation. The research presents an effective tactic to tackle the menace of residual ofloxacin to human health [14].

Chen et al. have developed a novel ratiometric fluorescent probe based on the MIL-53(Fe)-$NO_2$ metal-organic frameworks (MOF) and nitrogen-doped $Ti_3C_2$ MQDs (NTiMQDs) for the sensitive and green monitoring of formaldehyde in food matrices. The MIL-53(Fe)-$NO_2$ MOF exhibits intrinsic oxidase-mimicking activity, catalyzing the oxidation of o-phenylenediamine (OPD) into the 2, 3-diaminophenazine (DAP) with yellow fluorescence emitting at 560 nm. The N-$Ti_3C_2$ MQDs emit stable blue fluorescence at 450 nm. DAP quenches the blue fluorescence of N-$Ti_3C_2$ MQDs via a strong inner filter effect. Ofloxacin is capable of depleting free OPD in the system and inhibiting DAP formation, which weakens the inner filter effect, restoring the MQDs'450 nm fluorescence and reducing DAP's 560 nm fluorescence. The fluorescence intensity ratio $F_{450}/F_{560}$ was used as the ratiometric parameter. While the system offers advantages, key limitations were noted. A long time of detection retards real-time detection. The system has not yet been adapted into a portable device for real-time analysis [15].

## 4. Conclusion

In summary, MXene quantum dots (MQDs) have evolved into prospective and appealing material for advanced biosensing thanks to their excellent and unique properties. Recent studies have successfully developed MQD-integrated electrochemical, fluorescent, and ratiometric fluorescent sensors for the detection of critical disease biomarkers, metabolites, environmental pollutants, and food additives. Modification strategies such as elemental doping, noble metal loading, and nanocomposite construction have greatly enhanced sensing sensitivity and selectivity, showing their rapid development. Despite remarkable progress, key limitations, including scalable and green

synthesis of high-quality MQDs, long-term biosafety, anti-interference ability in complex matrices, and device portability, still need to be addressed. Future research should focus on simplifying preparation routes, improving biocompatibility for in vivo applications, developing smartphone-integrated systems, and promoting the clinical and commercial transformation of MQD-based biosensing technologies. The sensitivity and selectivity of sensors can be further optimized for detection with higher precision requirements.

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