Biosensors and Bioelectronics 89 (2017) 201–211

Contents lists available at ScienceDirect

Biosensors and Bioelectronics

journal homepage: www.elsevier.com/locate/bios

Nucleic acid-functionalized transition metal nanosheets for biosensing applications

Liuting Mo [a], Juan Li [a,b], Qiaoling Liu [a,**], Liping Qiu [a], Weihong Tan [a,c,*]

[a] Molecular Sciences and Biomedicine Laboratory, State Key Laboratory for Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering and College of Biology, Collaborative Innovation Center for Molecular Engineering and Theranostics, Hunan University, Changsha 410082, China
[b] The Key Lab of Analysis and Detection Technology for Food Safety of the MOE and Fujian Province, State Key Laboratory of Photocatalysis on Energy and Environment, College of Chemistry, Fuzhou University, Fuzhou 350002, China
[c] Department of Chemistry and Department of Physiology and Functional Genomics, Center for Research at the Bio/Nano Interface, UF Health Cancer Center, University of Florida, Gainesville, FL 32611-7200, USA

A R T I C L E I N F O

Article history:
Received 3 December 2015
Received in revised form
20 February 2016
Accepted 17 March 2016
Available online 18 March 2016

Keywords:
Transition metal nanomaterials
Nucleic acids
Aptamers
Biosensors
Nanosheets

A B S T R A C T

In clinical diagnostics, as well as food and environmental safety practices, biosensors are powerful tools for monitoring biological or biochemical processes. Two-dimensional (2D) transition metal nanomaterials, including transition metal chalcogenides (TMCs) and transition metal oxides (TMOs), are receiving growing interest for their use in biosensing applications based on such unique properties as high surface area and fluorescence quenching abilities. Meanwhile, nucleic acid probes based on Watson-Crick base-pairing rules are also being widely applied in biosensing based on their excellent recognition capability. In particular, the emergence of functional nucleic acids in the 1980s, especially aptamers, has substantially extended the recognition capability of nucleic acids to various targets, ranging from small organic molecules and metal ions to proteins and cells. Based on π-π stacking interaction between transition metal nanosheets and nucleic acids, biosensing systems can be easily assembled. Therefore, the combination of 2D transition metal nanomaterials and nucleic acids brings intriguing opportunities in bioanalysis and biomedicine. In this review, we summarize recent advances of nucleic acid-functionalized transition metal nanosheets in biosensing applications. The structure and properties of 2D transition metal nanomaterials are first discussed, emphasizing the interaction between transition metal nanosheets and nucleic acids. Then, the applications of nucleic acid-functionalized transition metal nanosheet-based biosensors are discussed in the context of different signal transducing mechanisms, including optical and electrochemical approaches. Finally, we provide our perspectives on the current challenges and opportunities in this promising field.

Contents

* Corresponding author: Molecular Sciences and Biomedicine Laboratory, State Key Laboratory for Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering and College of Biology, Collaborative Innovation Center for Molecular Engineering and Theranostics, Hunan University, Changsha 410082, China.
** Corresponding author.
E-mail addresses: qlliu@iccas.ac.cn (Q. Liu), tan@chem.ufl.edu (W. Tan).

http://dx.doi.org/10.1016/j.bios.2016.03.044
0956-5663/

1. Introduction

Two-dimensional (2D) transition metal nanomaterials, including transition metal chalcogenides (TMCs) and transition metal oxides (TMOs), which possess planar morphology and ultrathin thickness, have received growing interest in the fields of electronics (Lembke et al., 2015; Radisavljevic et al., 2011b), sensors (Li et al., 2012; Sarkar et al., 2015; Yang et al., 2013), catalysis (Voiry et al., 2013; Xie et al.., 2013), and energy harvesting (Chhowalla et al.., 2013; Sun et al., 2014b). Moreover, these 2D nanosheets provide outstanding biosensing performance owing to their unique physical, chemical and electronic properties (Pumera and Loo, 2014; Xu et al., 2013). In particular, their unique structure and specific surface area favor high loading efficiency for biomolecules. Many transition metal nanosheets also possess intrinsic fluorescence quenching abilities (Goswami et al., 2013; Liu and Lu, 2007; Sakai et al., 2005), which could be applied in fluorescence resonance energy transfer (FRET)- and chemiluminescence resonance energy transfer (CRET)-based sensing platforms (Zhu et al., 2013). More importantly, they are biocompatible and readily dispersed in aqueous solutions without surface modification or surfactants, making them suitable in biosensing applications.

Since the discovery of the double helix structure, nucleic acids have been employed in biosensors as recognition elements based on Watson-Crick base-pairing rules. In particular, the emergence of functional nucleic acids in the early 1980s further extends recognition capability (Guerrier-Takada et al., 1983; Kruger et al., 1982). Functional nucleic acids are specific oligonucleotides capable of folding into distinct three-dimensional structures and performing functions beyond carrying genetic information. Among them, aptamers are single-stranded oligonucleotides with specific recognition abilities through receptor-ligand interactions. Aptamers are selected by a technique known as “systematic evolution of ligands by exponential enrichment” (SELEX), and they exhibit high affinity towards a wide range of targets, such as small organic molecules, metal ions, proteins and cells (Ellington and Szostak, 1990; Fang and Tan, 2010; Tuerk and Gold, 1990). Therefore, the introduction of aptamers can significantly expand the application scope of nucleic acid-based biosensors (Chen et al., 2011, 2015a; Shukoor et al., 2012; Tan et al., 2013; Yasun et al., 2012; Zheng et al., 2015). Metallo-base pairs also provide a feasible recognition strategy for biosensing. Through specific metal ion coordination between thymine (T) and Hg^{2+}or cytosine (C) and Ag^{+}, T-Hg^{2+}-T and C-Ag^{+}-C base pairs are formed with high stability (Miyake et al., 2006; Tanaka et al., 2002; Wagenknecht, 2003). This strategy was employed in biosensors for selective detection of metal ions (Dave et al., 2010; Tortolini et al., 2015). In sum, owing to their powerful recognition properties, nucleic acid-based biosensors, especially aptasensors, have found a broad range of applications in the fields of bioanalysis and biomedicine e (Kong et al., 2011; Li et al., 2010; Liu et al., 2012; Lubin and Plaxco, 2010; Tan et al., 2012; Tang et al., 2015; Wang et al., 2009; Zhao et al., 2015c).

The new wave to incorporate nanomaterials into biosensors has spawned many studies reporting on the integration of nucleic acids into transition metal nanosheet-based biosensors to improve sensing performance (Chen et al., 2015b; Wang et al., 2010; Yang et al., 2010; Zhu et al., 2015). Specifically, π-π stacking interaction between transition metal nanosheets and nucleic acids promotes facile assembly into biosensing systems. In addition, the high loading efficiency of nucleic acids can enhance biosensor sensitivity and recognition performance. Meanwhile, transition metal nanosheets can serve as carriers of nucleic acids, and by preventing nuclease degradation in complex environment, their many practical applications can be realized, in particular those involving clinical diagnostics. The first nucleic acid-functionalized transition metal nanosheet-based biosensor was reported by Zhu et al. (2013) for the detection of nucleic acids and small molecules. From then on, various biosensing systems have been continuously developed, with the scope of target analytes ranging from small molecules to large biomolecules (e.g., proteins). Besides detection in buffer solutions, driven by the needs of biomedicine and clinical diagnostics, increasing attention has been paid to the detection in more complex systems (e.g., living cells). Several research groups have successfully employed this system in intracellular imaging and detection (Jia et al., 2015; Zhao et al., 2014). Therefore, the combination of 2D transition metal nanomaterials and nucleic acids has resulted in many novel strategies for biosensing applications.

In this review, we provide an overview of nucleic acid-functionalized transition metal nanosheets in biosensing applications. The structure and properties of 2D transition metal nanomaterials are first discussed, emphasizing the interaction between transition metal nanosheets and nucleic acids. Next, we present recent progress in coupling nucleic acids and transition metal nanosheets to detect various targets in the context of different signal transducing mechanisms, including optical and electrochemical approaches. Finally, future perspectives and challenges are discussed.

2. Structure and properties of transition metal nanosheets

2D transition metal nanosheets are graphene analogs with atomic thickness and planar structure. Compared with graphene composed of only carbon, 2D transition metal nanomaterials constitute a large family and provide greater flexibility and diversity of composition, structure and functionality. TMCs are MX2-type compounds where M is a transition element of groups IV, V, and VI, and X is a chalcogen, such as S, Se, and Te (Doran, 1980; Yoffe, 1990). For example, layered MoS_2 consists of a sandwich structure of Mo atoms between two layers of S atoms, exhibiting strong in-plane covalent bonding and weak out-of-plane interaction, therefore enabling exfoliation from bulk 3D materials into 2D nanosheets (Ataca and Ciraci, 2011; Brent et al., 2015; Huang et al., 2013b; Leonard and Talin, 2011; Schwierz, 2011). Single- or few-layer nanosheets present many attractive properties over their bulk counterparts and, as such, cater to wide applications in nanoelectronics (Lee et al., 2015; Radisavljevic et al., 2011a; Wu et al., 2014; Yin et al., 2012), catalysis (Chianelli et al., 2006; Gao et al., 2015; Huang et al., 2013a), energy harvesting (Jaramillo et al., 2007; Sun et al., 2014a) and biomedicine (Chen et al., 2015b; Cheng et al., 2014). On the other hand, TMOs are composed of oxygen atoms bound to transition metals. Generally, these oxide nanosheets exhibit high stability and tunable properties owing to diversity of chemical composition and crystal structure (Geng et al., 2010; Ma et al., 2006; Osada and Sasaki, 2009, 2012). For example, manganese, molybdenum and tungsten oxides possess facile redox activity (Ma and Sasaki, 2010; Sasaki, 2007), while titanium and zinc oxides show photocatalytic activity (McLaren et al., 2009; Wang and Sasaki, 2014). Therefore, TMO nanosheets are widely applied in the fields of photocatalysis (Cai et al., 2015; Deng