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MINI-REVIEW

Specific heavy metal/metalloid sensors: current state and perspectives

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Abstract

Heavy metal(loid)s play pivotal roles in regulating physiological and developmental aspects in living organisms depending on their concentration. For example, a trace amount of heavy metal(loid)s is essential for living organisms, but heavy metal(loid)s in high concentrations negatively affect their physiology and development. Because of rapid industrial developments, heavy metal(loid)s have been accumulating in environmental systems, thereby becoming a threat to human health and the earth's ecosystem. Thus, the development of tools to quantify and monitor heavy metal(loid)s in environmental systems has become essential. Typically, risk has been determined through instrument-based analysis, regardless of the shortcomings regarding expense and duration. Nowadays, the need for alternative tools, besides instrumental analysis, to detect heavy metals has prompted the development of new techniques, and many different methods have been reported from various research areas, including new techniques based on electrochemistry and biological systems. Nonetheless, it seems that the gap between laboratory and fieldwork is still greater than it should be when it comes to applying these systems. In this mini-review, we discuss the current status of heavy metals/metalloid detection techniques, with an emphasis on biosensors. Moreover, we discuss the advantages and disadvantages as well as the mechanisms behind newly developed sensors and make suggestions to improve applicability and to develop new objective targeting sensors. Although many different types of metal(loid) sensors are available, we focused on metal sensors based on biological systems. Additionally, we suggest potent approaches to developing new biosensor systems based on current metal sensor mechanisms.

Keywords Heavy metal sensors · Chemosensors · Electrochemical-based sensors · Bacterial cell-based sensors · Metalloregulators · Split-protein systems

Introduction

Heavy metal/metalloids are naturally present in diverse environmental systems and are essential components for living organisms. However, the influx of large amounts of heavy metal(loid)s into environmental systems has been considered a critical threat to human health because its accumulation is known to cause severe diseases. Since metal(loid)s are not degraded in environmental systems, they tend to accumulate in living organisms. Among the heavy metal(loid)s found in environmental systems, arsenic (As), cadmium (Cd), mercury (Hg), lead (Pb), and chromium (Cr) are highly toxic and known to cause severe diseases even when exposed to small amounts (Järup 2003; Martin and Griswold 2009). In fact, as rapid industrial developments continue, the levels of metal(-loid)s in environmental systems inevitably increases as well. Therefore, monitoring the levels of heavy metal(loid)s in different environmental systems is regarded an essential task; consequently, new techniques such as chemical sensors and biosensors, which are faster and simpler than traditional instrument-based techniques, are being developed.

As concerns regarding heavy metal(loid)s contamination increases, the development of a large number of metal(loid) sensors have been presented from diverse research fields during the last few decades, with a major emphasis on biosensors employing biological materials and analytical tools. For example, Sugunan et al. (2005) reported on the use of heavy metal sensors based on chitosan-capped gold nanoparticles;

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also, Zhang et al. (2011) described using metal sensors based on DNA molecules. The fluorophore-coupled chemicals designed by Winkler et al. (1998) and Ohshima et al. (2004) were developed to detect and measure metals. Furthermore, many other groups also have described metal sensors based on biological systems such as proteins, peptides, and bacterial cells (Chow and Gooding 2006; Harms et al. 2006; Pennella et al. 2003; Robbens et al. 2010). A biosensor has thus been defined as an independently integrated receptor transducer device capable of providing quantitative analytical information using a biological recognition element such as antibodies, antigens, nucleic acid, enzymes, etc. (Thevenot et al. 1999). Therefore, changes in biological elements can be transduced to electrical signals. In fact, this principle applies to all types of sensors, including biosensors. In general, most metal sensors employ metal sensing components responsible for the interacting with specific metal ions; in turn, the interaction between the sensor itself and metal ions provokes various responses including conformational changes in proteins, quenching or emission of fluorophores, spectroscopic shift, and expression of reporter genes. Even if the sensors are generated based on different mechanisms, their common purpose would be the development of rapid and simple detection of metal(loid)s in environmental systems to alarm the threats of pollutants.

In this flooding era of metal sensors, bacterial cell-based sensors (whole-cell bioreporters; WCBs) have been actively investigated in environmental sciences. Because of the numerous advantageous aspects, including the ability to monitor bioavailability, WCBs have been considered an alternative tool for assessing the risks of metal(loid) contamination in diverse environmental systems. However, the term "bioavailability" is controversial and will be discussed later. Briefly, WCBs were generated by fusing the promoter region of metal-responsive operons and reporter genes, which are controlled by transcription regulators and able to represent the presence of target metal ions, respectively. Afterward, efforts in genetic engineering on regulatory circuits in bacterial cells and transcription regulators increased the number of WCBs with improved metal selectivity and specificity (Belkin 2003; Islam et al. 2007; Kang et al. 2018b).

More recently, excellent reviews on WCBs and transcription factor-based biosensors have become available (Fernandez-López et al. 2015; Harms et al. 2006; Mahr and Frunzke 2016). Also, other studies on metal(loid) sensing have been reported from diverse research areas employing the techniques based on electrochemistry, luminescence, nanoparticle, and surface resonance spectroscopy (Gumpu et al. 2015; Keefe et al. 2000; Wing Fen and Mahmood Mat Yunus 2013; Zeng et al. 2011). Although they were based on different techniques, they shared a common goal, to quantify the amount of metal(loid)s in environmental systems to assess the risks. Since various methods to detect heavy metal(loid)s are continuously being developed, it is difficult to follow up on them all. In this regard, we decided to include several metal sensing techniques widely studied and reported: (1) instrument-based analysis, (2) chemical-based sensors, (3) electrochemical technique-based sensors, (4) bacterial cell-based sensors, (5) metal-binding protein-based sensors coupled with DNA probes, and (6) split-protein system-based sensors (Table 1). However, we focused more on discussing metal(loid) sensors based on biological systems such as living bacterial cells, proteins, and DNA. We hope this mini-review would help researchers to gain insights into the current states of metal sensors and to facilitate the development of a new strategy for sensing metal(loid)s.

Instrument-based analysis

The detection and quantification of heavy metal(loid)s in diverse environments have classically been done by employing gas chromatography-mass spectroscopy (GC-MS), high-performance liquid chromatography-mass spectroscopy (HPLC-MS), inductively coupled plasma-mass spectroscopy (ICP-MS), inductively coupled plasma-atomic emission spectroscopy (ICP-AES), etc. Even if other metal(loid) sensors had been developed and claim to replace instrumental analysis, these are still the best methods when it comes to sensitivity and accuracy. However, an instrument-based analysis requires very expensive equipment, a well-trained operator, and time-consuming sample preparation; therefore, it is practically impossible to apply these methods in real time to do on-site analysis. Additionally, it was clear that the lack of bioavailability would be one of the major shortcomings of instrumental analyses.

Although instrumental analyses measure the total amount of metals including effective portions of metal ions and non-effective portions, the total amount of metals would not represent the portion of biologically active metal ions due to the complex nature of environmental systems, especially in soils. Moreover, in some cases, the biologically active portion of metal ions in soils are water-soluble extracts which do not represent the real biologically active portions because the efficiency of extracting biological material varies depending on the composition of soils. Even though a particular sample of bacterial cells presents an IC_{50} (the half-maximal inhibitory concentration), soils with the same amount of metal ions would have no toxic effect, because a large portion of metal ions was non-biologically active due to complexation with other materials in the soil. The biologically active portion of metal ions is known as bioavailability or the bioavailable portion of metal ions. It is thus evident that alternative methods to measure the biologically active portion of heavy metals/metalloids are essential.

Table 1 List of metal/metalloid sensors classified by types of platforms

Type	Target metal(loid)s	Systems/responses	Detection limit	Reference
Chemical-based	Cu^{2+}	Chemicals/fluorescence	100 nM	(Fabbrizzi et al. 1996)
	Zn^{2+}	Dioxotetraaza-anthracene fragment	10 nM	(Dujols et al. 1997)
	Pb^{2+}	Rhodamine B hyrazide	1.3 μM	(Xu et al. 2009)
	Cd^{2+}	NBD-based TRPEN	–	(Kwon et al. 2005)
		Rhodamine B derivative	–	(Choi et al. 2001)
		Anthryl tetra acid		
		Rhodamine-alkyne derivative		
Electrochemical-based	Cd^{2+}	Diverse platform/electric parameters	0.2 μg/L	(Riman et al. 2015)
	Pb^{2+}	Bi_2O_3-SPEs(SWASV)	0.1 μg/L	(Hao et al. 2016)
	Cu^{2+}	MnO_2 nanowire/nickel foam electrode (SWASV)	1.0 μg/L	(Nie et al. 2010)
	Pb^{2+}	Microfluidic devices (uPEDs)	1.0 μg/L	(Reay et al. 1996)
	Cd^{2+}	Microfabricated chips		
	Pb^{2+}			
Bacterial cell-based (*E. coli*)	Hg^{2+}	Genetic system/reporter gene *merR/lux arsR/lux CDABE modified zntR/egfp modified zntR/mcherry cueR/egfp cadC/gfp*	3.1 nM 12 μg/L, 140 μg/L 0.5 μM 0.5 μM 1.0 μM 10 nM/0.1 nM	(Harkins et al. 2004)
	As^{3+}			(Ivask et al. 2007)
	As^{5+}			(Kang et al. 2018a)
	Cd^{2+}			(Kang et al. 2018b)
	Hg^{2+}			(Liao et al. 2006)
	Cu^{2+}			
	Pb^{2+}			
	Sb^{3+}			
Metal binding protein-based	Pb^{2+}	Metal binding protein/DNA probe PbrR691 with pyrrolo-C labeled DNA probes	2 μM 50 nM	(Chen et al. 2005)
	Cu^{2+}	CueR with pyrrolo-C labeled DNA probes		(Chen and He 2004)
	Ag^{+}			
Split-protein system-based	Cd^{2+}	Modified eGFP/fluorescence MBL modified eGFP.		(Lee et al. 2019)
	Cd^{2+}	MBL-modified eGFP		(Kim et al. 2019)
	Hg^{2+}			

Chemical-based sensors

In addition to instrumental-based analyses, diverse sensors that recognize target metal ions have also been developed. For sensors, the key is detecting and quantifying the sensing events between the sensing apparatus and targets as shown in Fig. 1. Of course, the same principles do not just apply to biological system-based sensors but all kind of sensors, including chemical-based sensors and electrochemical technique-based sensors. Concerning biosensors, macromolecules such as proteins and DNA have been employed as sensing apparatus, where these parts detect structural changes. These biologically induced structural changes, such as enzymatic activity, gene expression, and fluorescent emission, function as signals indicating sensing events. Unlike biosensors, chemical-based metal sensors use chelating ligands as sensing apparatus to detect metal-chelate binding by measuring spectroscopic changes, such as fluorescence. All metal(-loid)s and transition metal ions are positively charged, and nitrogen and oxygen-chelating ligands show high affinity toward metal ions; therefore, a chemical-based sensor for metal ions becomes accessible by quantifying signal events.

In general, chemical-based metal sensors using chelating ligands as sensing apparatus are denominated chemosensors. There has been a large number of chemosensors reported in a variety of fields such as synthetic and chemical biology and organic chemistry (Jeong and Yoon 2012; Wu et al. 2011; Xu et al. 2010). In their brief review, Krämer (1998) characterized three fluorescent chemosensors composed of fluorophores and chelating parts for detecting copper ions. The chemicals are fluorescent or nonfluorescent without metal ions, but fluorescence properties were changed to opposite ways with metal ions because the association of metal ions with chemosensors induced the chemical changes; thereby the spectroscopic properties including absorption spectra and fluorescent spectra were changed. Additionally, in their review, Jeong and Yoon (2012) detailed current progress on fluorescent chemosensors for metal ions such as zinc, lead, cadmium, silver, and gold ions. Although the sensing apparatus for each metal ion was different, the recognition event was quantified by simply measuring spectroscopic changes. The use of ligand structures for detecting metal ions is advantageous because of its simplicity, modulating selectivity, and sensitivity. Nonetheless, its application is limited because of the insoluble nature of ligand structures.

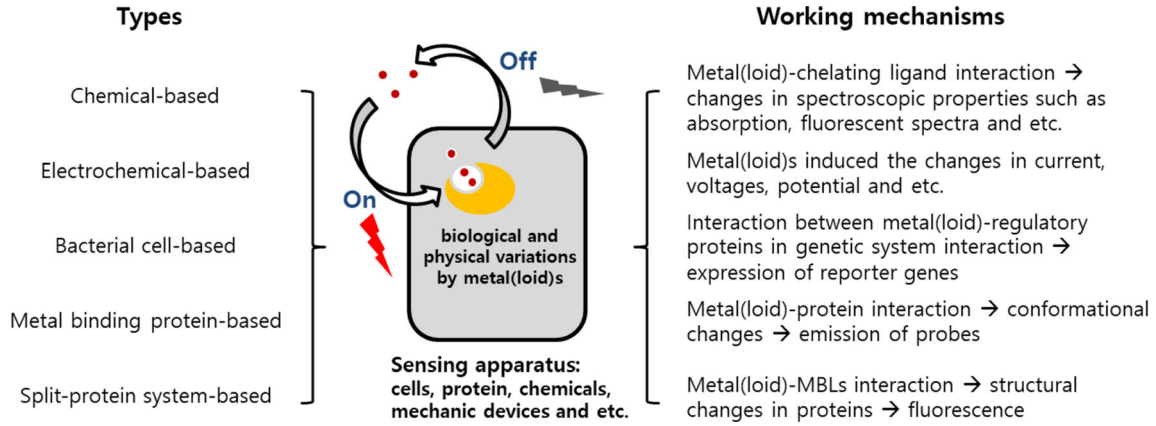

Fig. 1 Illustration for common working mechanisms of current metal(loid) sensors

Electrochemical-based sensors

Besides chemical- and biological-based systems, electrochemical sensors have also been developed (Bansod et al. 2017; Wang et al. 1995). Due to the extensive information regarding electrochemical sensors, we will review these briefly. Even though these techniques are based on electrochemical factors, the general mechanisms share commonalities with the previously mentioned systems. This system detects the variations in the electrochemical parameters such as current, potential, voltage, and electroluminescence depending on the presence or not of metal ions. Thus, when a current is generated through oxidation-reduction reactions, the electrochemical biosensor measures the current. Then, the current can be correlated to either the concentration of the electroactive species present or its rate of production/consumption. The resulting electrical signal is related to the recognition process between the sensors and targets and is proportional to the concentration of the targets. According to previous reports, the sensing platforms for electrochemical-based technique are diverse and include nanomaterials (Waheed et al. 2018; Zhao et al. 2002), microfluidic devices (Nie et al. 2010), microfabricated chips (Reay et al. 1996), and enzyme- or peptide-linked systems (Chow and Gooding 2006; Degani and Heller 1987; Ruger et al. 1998). These electrochemical sensors had been characterized by the electrical signals they are monitoring. Those sensors are categorized by potentiometry, amperometry, chronocoulometry, and voltammetry by characters of electric parameters, even if they employed different platforms. Although this review is focused more on biological system-based sensors, we felt obliged to include electrochemical-based sensors because it is a predominant method for detecting metal ions.

Bacterial cell-based biosensors

Bacterial cell-based biosensors, also known as whole-cell bioreporters (WCBs), were first reported a few decades ago. Moreover, since their development, they have been thoroughly tested to determine their efficiency for monitoring heavy metal ions in different environmental systems. Microorganisms such as bacteria and fungi have been used as biosensors to detect specific molecules or the overall state of the surrounding environments (Acha et al. 2010). Microorganisms possess genetic components responsible for recognizing external stress factors. In this regard, metal-responsive operon systems have been employed to generate whole-cell bioreporters. In general, the metal sensing apparatus of WCBs are metalloproteins such as ZntR, ArsR, and CueR also play roles as transcriptional factors that regulate the downstream expression of genes in the presence of metal(loid) ions. Thus, WCBs were constructed by recombining genes consisting of the promoter region of the metal-responsive operon and reporter genes. WCBs possess enormous potential as an alternative to instrumental-based analyses as the main advantages of a WCB system reside in its simplicity, cheapness, and ability to measure bioavailability; unsurprisingly, the development and application of WCBs are increasing. Accordingly, there are many excellent reviews on WCBs and on transcription factors being used as sensing apparatus for target metal ions (Fernandez-López et al. 2015; Mahr and Frunzke 2016; Robbens et al. 2010). Therefore, in this review, we would like to discuss how to enhance and enlarge the applicability of WCBs. Transcription factors binding to target metal(loid)s have been identified in bacterial cell bioreporters before, but the number of binding events was limited relative to that of pollutants such as heavy metal(loid) ions. In general, living organisms have broad response mechanisms to external stresses rather than a specific response to a sole target; moreover, they all possess alternative pathways to compensate for certain pathways. Additionally, WCBs maintain homeostasis by controlling the concentration of exogenous materials that cause sensitivity to the cells. Therefore, it would be challenging to increase the number of WCBs to improve selectivity and specificity.

Regarding this issue, we invested our efforts into genetically engineering host cells and biochemically engineer metal-

binding regulatory proteins. As described in previous reports, the selectivity and sensitivity of WCB to metal(loid) ions are modulated by genetically and biochemically engineering host *E. coli* cells and bacterial cells (Kang et al. 2018a; Kang et al. 2018b; Yoon et al. 2018). The WCBs employing the promoter regions of *znt*-operon and *egfp* showed selective responses toward cadmium and mercury because of ZntR a regulatory protein controlling the *znt*-operon, binds to them (Yoon et al. 2016). Thus, it was inferred that metal(loid) selectivity of WCBs could be changed by modulating amino acid sequences for metal binding loops (MBLs). Indeed, the selectivity of WCBs with ZntR was modulated solely to cadmium and mercury by replacing the MBL sequence, CCGTAHSSVYC, to CNHEPGTVCPIC and CPGDDSADC, respectively (Kang et al. 2018a). In contrast, the sensitivity of WCBs can also be enhanced by genetically engineering host cells. However, WCBs with CueR, a regulatory protein in a copper-inducible operon, showed no signal when copper was added in wild type *E. coli* cells, but it responded to copper ions in *E. coli* cells when *copA* was deleted (Kang et al. 2018b). Thus, it was speculated that deleting *copA*, a gene involved in exporting copper in *E. coli*, could cause the accumulation of copper ions in cells, thereby enhancing the sensitivity. This finding supported the idea that the sensitivity of WCB could be modulated by interfering with endogenous homeostasis systems in the host cells.

Of course, there have been many efforts to improve the sensitivity or capability of WCBs by replacing reporter genes and generating genetically engineered bacterial strains (Brutesco et al. 2017; He et al. 2016; Yoon et al. 2016); these efforts have also led to new applications such as targeting various environmental toxins including naphthalene and other organic pollutants (Shemer and Belkin 2019; Sun et al. 2017). Because of the simplicity and cheapness of WCBs, research efforts to target diverse pollutants have also increased. However, there is one major disadvantage, measuring bioavailability, the most advantageous aspect of WCBs, would be measuring the of pollutants in environmental systems, is also this system's weakest point. Although measuring bioavailability was a novel property of WCB, the level of bioavailability measured by WCBs is relative. Because of the nature of WCBs, the portion of metal ions accumulated in the bacterial cells could only be measurable in WCBs, which would vary among different bacterial species. Thus, further studies are required before we can expand the applications of WCBs to include diverse environmental pollutants.

Another critical limitation of the bacterial cell-based biosensors is the size of the target pollutants. Since the WCBs detect the target pollutants accumulated in the cells, other pollutants such as nondegradable phenolic compounds, algal toxins, and perchlorinated chemicals, which cannot enter the cells because of their size, will not be detected. This is an issue that could be solved by changing the sensing system to one that does not use bacterial cells. As an alternative, it would be possible to use a cell-free gene expression system (Carlson et al. 2012; Katzen et al. 2005). If this system were applicable, bacterial host cells would become unnecessary, thereby clearing the issue of entering to the cells. Although the cell-free system has, to our knowledge, not been applied to detect environmental pollutants, it would be worthwhile to verify whether the cell-free systems are applicable or not.

Metal-binding protein-based sensors coupled with DNA probes

Metal(loid) sensors based on biological systems were generally based on proteins able to interact with metal(loid) ions, especially MerR family proteins (Brown et al. 2003; Waldron et al. 2009). Typically, proteins from the MerR family are known as regulatory proteins that play roles as transcription factors to maintain metal homeostasis by inducing the expression of genes related to detoxification or efflux systems of target materials such as metal(loid)s and chemicals. Proteins from the MerR family bind to specific promoter regions of the DNA and undergo conformational changes upon the binding of target metal ions, thereby distorting the DNA duplexes and sending signals downstream (Heldwein and Brennan 2001). In the case of WCB, MerR family proteins were employed as the metal sensing apparatus, and the expression of reporter genes was the quantifiable signal.

Contrary to WCBs, Chen and colleagues analyzed the distortion of DNA duplex using MerR proteins and reported a novel strategy to develop metal ion biosensors with high sensitivity and selectivity (Chen et al. 2005; Chen and He 2004). Most metal biosensors employ transcriptional regulators with metal-interacting domains, and the interaction between metal ions and regulators is indicated by the expression of reporter proteins with enzymatic activity or fluorescence. However, Chen and his colleagues reported in vitro biosensors using metal-binding transcriptional regulators coupled with fluorescent-tagged probes. The nature of metal-binding transcriptional regulators such as BmrR, PbrR, and CueR recognize specific DNA sequences to regulate gene expression, and their structural conformation can change when they bind to metal ions. However, it was vague how the structural conformation was changed until Heldwein and his colleagues described the process (Heldwein and Brennan 2001). The crystal structure of BmrR, a transcriptional activator in *Bacillus substiles*, bound to DNA and a coactivator revealed that BmrR distorted the DNA double helix upon the binding with the coactivators. Based on this finding, they designed a novel metal sensor using DNA probes with a pyrrolo-C label in the middle. Pyrrolo-C emitted a weak fluorescence signal at 435 nm when there was C–G pairing in DNA, but the emission got stronger when G–C pairing was broken. In their

research, they used CueR and PbrR coupled with pyrrolo-C labeled DNA probes for copper and lead ions, respectively. Since the Mer family proteins show the structural similarity, specific metal ion detecting sensors would be obtained by the same system. Nonetheless, these in vitro metal sensors were not widely used and not investigated further. It might be reasoned that fluorescent DNA probes were too expensive to monitor the level of contamination of metal ions.

Split-protein system-based sensors

Since their development, split-protein systems have been used to monitor protein-protein interactions. Proteins such as ubiquitin, dihydrofolate reductase (DHFR), green fluorescent protein (GFP), luciferase, and TEV protease become inactive when split into two fragments but reversed into an active state when the two fragments are in close proximity (Paulmurugan and Gambhir 2003; Shekhawat and Ghosh 2011). Split-protein systems were designed to reassociate when they are close enough to each other; therefore, if a two-part protein such as fluorescent proteins or enzymes was rejoined by target molecules acting as molecular glue, the reactivity of proteins should indicate the presence of target molecules, thereby functioning as biosensors. To elucidate this idea, we put MBLs into the enhanced green fluorescent protein (eGFP) to determine if we could detect metal ions.

Since the breaking point of eGFP for the split-protein system has already been reported, the MBLs were inserted into eGFP between β-strand 9 and 10 to replace loop region (Cabantous et al. 2013). Although the idea was taken from a split-protein system, this was not split protein per se. Nonetheless, inserting the MLBs into the eGFP inactivated it, but activation was restored when it became active when the target metal ions were added (Kim et al. 2019; Lee et al. 2019). The amino acid sequences for the MBLs were obtained from diverse metal-binding proteins and from the findings of our previous studies (Kang et al. 2018a; Kang et al. 2018b). Both CPGDDSADC and CTTCGCG sequences in the MLBs were replaced by DGPV (an amino acid from 191 to 194 in eGFP) and engineered into eGFP to detect cadmium and cadmium/mercury, respectively. Even if the emission signal was relatively weak compared to the eGFP, the reporter gene in WCBs, metal selectivity, was observed. Most importantly, it confirmed that using split-eGFP for metal sensors was possible, and our strategy could be a platform for building new metal sensors.

The reason why we designed this split-protein-based sensor system was to overcome a shortcoming in WCB systems. As mentioned above, the bioavailability of WCBs was defined as the number of metal ions accumulated in bacterial cells, and it could vary depending on the bacterial host species used. If the purified sensing proteins worked as sensor molecules, they would work regardless of the variation in bioavailability caused by the host species. Unfortunately, the genetically engineered eGFP did not behave well as a sensor molecule after purification. Although it showed specificity for the target metal, the signal was too weak for practical applications, suggesting that the insertion of longer MBL sequences hindered the structural stability of eGFP. Consequently, these approaches might be not useful for monitoring metal ions in its current state. Nonetheless, we believe that there is a large potential for biosensors to be created by genetic modification and protein engineering our split-protein systems could be useful as a platform for creating biosensors to target new environmental pollutants

Perspectives

Over the last few decades, considerable attention has been given to monitoring and quantifying heavy metals/metalloids in different environmental systems. Since the accumulation of metal(loid)s in environmental systems is known to be a threat to human health, it was inevitable to monitor and to control the environmental pollutions. To achieve this goal, researchers from diverse academic fields have combined their efforts into developing new strategies. Many different types of metal sensors such as chemosensors, electrochemical-based sensors, bacterial cell-based sensors, metal-binding protein-based sensors coupled with fluorescent probes, as well as split-protein system-based sensors have been developed (Table 1). Nonetheless, they all shared similar functional mechanisms, even though the metal sensors were developed based on different systems. Most of all, the sensing apparatus of the sensors recognize target metal ions, and the reporter represents the interaction between the sensing apparatus and the targets by detecting either conformational changes, spectroscopic changes or electrochemical changes (Fig. 1 and Table 1). Therefore, it would be possible to obtain new metal sensors by making new combinations of sensing apparatus with reporter parts. Since the analytical techniques used to measure metals/metalloids ions are highly advanced, even weak signal changes could be quantified with relative ease. In this review, we discussed the current state of techniques used for monitoring heavy metal/metalloid ions from diverse research fields with an emphasis on biological system-based metal(loid) sensors. Although we were not able to discuss all known metal sensors here, we hope that this review will help to understand the current state of metal(loid) sensors and incite new ideas for developing novel strategies for generating new metal sensors. We believe that the future direction for metal sensors will narrow the gap between the laboratory and the environmental field. Unlike experimental conditions in a laboratory, there are many variables in the environment, such as high acidity or basicity, high salt, and toxicity of contaminants in real fields

where these sensors should be applied. Therefore, it would be more important to figure out how to employ currently available metal(loid) sensors to environmental systems and to continue developing new sensors.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics statement This article does not contain any studies with human participants or animals performed by any of the authors.

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