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Review

Engineering biology-enabled sensors for environmental monitoring

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Environmental monitoring is essential to protect the ecosystem and human health. Currently, there is a limited number of deployable sensors for emerging contaminants. Biology-enabled sensing methods are addressing this gap by using biological components as sensors. This review provides a perspective on recent advances in biology-enabled sensors, with a focus on cell-free sensors, whole-cell sensors, and multicellular sensors. These tools can be leveraged to produce sensitive, deployable, and at times rapid sensing technologies. Many sensor-related studies have focused on deployment in aqueous matrices that are optically transparent. This perspective paper extends beyond aqueous environments to examine emerging approaches for biology-enabled monitoring of analytes in soil and air. By comparing sensing mechanisms, sensitivity, limit-of-detection, and response time across different matrices, this review highlights tradeoffs in sensor performance. Finally, this review outlines future directions for improving biology-enabled sensors to make them more robust, scalable, and capable of real-time sensing for comprehensive environmental monitoring.

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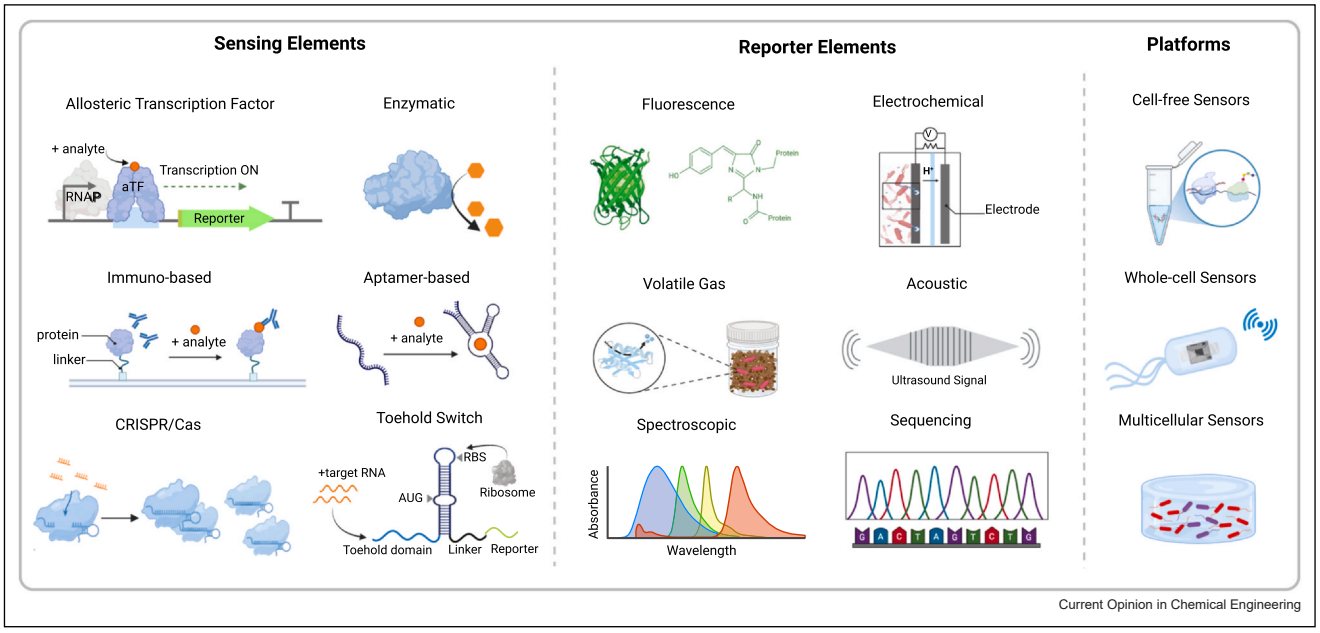
Introduction

Environmental monitoring and detection of pollutants is crucial for mitigating the harmful impacts of contaminants (*e.g.*, pharmaceuticals, pesticides, microplastics, heavy metals, and pathogens). As emerging contaminants increasingly occur at trace concentrations and across various matrices, this makes *in situ* detection challenging. Addressing these issues requires scalable and sensitive technologies, for which biosensors hold promise. Biology-enabled sensors are analytical tools that incorporate biological components, including whole cells, enzymes, nucleic acids, or bioinspired structures, to detect physical, chemical, and biological stimuli and transduce them into measurable outputs. Traditional environmental monitoring approaches leverage techniques such as spectroscopy, high-performance liquid chromatography (HPLC), gas chromatography (GC), inductively coupled plasma mass spectrometry (ICP-MS), and nucleic acid sequencing. While these tools provide high accuracy and sensitivity, they require discrete sampling, sample processing, specialized expertise, and costly instrumentation, making them impractical for continuous on-site deployment. Biology-enabled sensors can offer distinct features to overcome these challenges, including producing human-detectable outputs and having fast response times in complex matrices that enable real-time *in situ* environmental monitoring that can support rapid on-site management or remote intervention. In this review, we summarize recent advances in the application of biosensors in diverse environments, including water, soil, and air. We focus on classifying biosensors based on biological unit (*e.g.*, cell-free, whole-cell, multicellular), sensing mechanism, output signal modality, and highlight their figures-of-merit including limit-of-detection (LOD) and response time (RT) (Table S1). Nearly all examples highlighted in this review were contributed to the field within the past 5 years. We offer perspectives on the challenges associated with the diverse environments (*e.g.*, water, soil, air) in which these biosensors have been deployed and the unique challenges for achieving low LOD and fast RT using varying biological units as sensors within these environments.

Fundamental biosensor components

Biosensors are composed of three modules: (i) a *sensor module* that converts the environmental information into biochemical signals, (ii) a *processing module* that computes the input signals, and (iii) an *output module* that produces a detectable response [1]. Sensor modules leverage diverse classes of biomolecules to detect input signals. These

Figure 1



Components of biology-enabled sensing devices. Bio-hybrid sensors can be divided into three functional modules: *Sensing elements*, illustrating biochemical recognition mechanisms such as allosteric transcrption factors, enzymatic conversion, immuno-recognition, aptamer binding, CRISPR/Cas detection, and toehold switches. *Reporter elements*, depicting output signal modules including fluorescence, electrochemical, volatile compound synthesis, acoustic/ultrasound signals, spectroscopic, and high-throughput sequencing. *Platforms*, showing the biological units of operation for deployment - cell-free systems, whole-cell, and multicellular sensors. Created in BioRender.

include protein-based allosteric transcription factors, antibodies, and enzymes; nucleic acid-based aptamers and toehold switches; or protein-nucleic acid complexes such as CRISPR/Cas systems (Figure 1) [2]. Processing modules can be simple input/output processes such as transcription/translation or additional layers can be added to enable computation through Boolean logic gates (*e.g.*, AND, OR, NOR, XOR) to integrate multiple inputs and encode decision-making processes [3–9] or for storing memory of past events by utilizing toggle switches, recombinase-based memory, or CRISPR-based recording circuits [10–14]. Output modules generate detectable signals such as fluorescent, spectroscopic, electrochemical, gaseous, acoustic, or nucleic acid signals (Figure 1). The choice of components used for each of these modules impact the biosensor performance (*e.g.*, LOD, RT, matrix compatibility) and require careful consideration of the environment-specific challenges for field deployment (Figure 2). For example, fluorescent and spectroscopic output modules can enable low-cost, human-readable analysis in the field but perform poorly in opaque samples. By contrast, electrochemical, gaseous, and acoustic outputs are particularly advantageous for environments with high extinction coefficients [2]. The use of these components in cell-free, whole-cell, and multicellular biosensors, as well as challenges for environmental deployment, are discussed in the following sections.

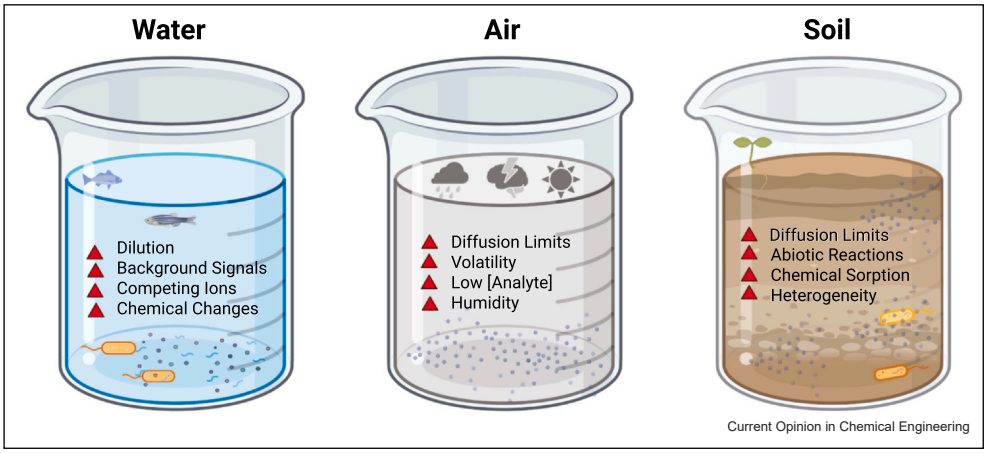
Cell-free biosensors

Principles of cell-free systems

Cell-free systems (CF) utilize cellular lysates or isolated biomolecules as the biological unit for sensing. Cytosolic materials, including RNA polymerases and ribosomes needed for transcription and translation, are removed from the cell, and reactions are performed *in vitro* in test tubes or in paper-based formats that contain freeze-dried components that can be rapidly activated by the addition of water or aqueous sample matrices. Additionally, CF sensors have been integrated into paper-based microfluidic devices that enable integration of upstream sample processing and extraction prior to analyte detection, allowing for field deployment of complex sample isolation processes [15].

CF sensing platforms have distinct advantages relative to cellular sensor platforms as they are not restricted by membrane permeability limitations, biocontainment, or genetic instability, and one can readily control reaction variables such as pH or ionic strength. Largely, CF biosensors can be categorized into sensors that use DNA, RNA, or protein circuits for sensing and typically utilize optical outputs such as fluorescence or spectroscopic outputs, but have also been implemented with electrochemical and nucleic acid outputs [16].

Figure 2



Challenges of sensing in environmental matrices of water, air, and soil. The efficacy of biology-enabled devices is modulated by the physicochemical properties of the target matrix. *Water* samples are mainly restricted by analyte dilution, high background signals, and ionic interference. *Air* monitoring encounters challenges such as gas-phase diffusion kinetics, volatility, low analyte concentration, and fluctuations in humidity. *Soil* matrices face restricted mass transfer (diffusion limits), abiotic reactions, chemical sorption, and heterogeneity of the substrates. Created in BioRender.

Applications of cell-free biosensors in aqueous environments

CF biosensors often use DNA circuits that leverage allosteric transcription factors (aTFs) to regulate transcription of reporter genes. aTFs have been used for sensors that respond to small molecules, including heavy metals (*e.g.*, Hg, Pb) [17] or organic compounds such as the pesticide pentachlorophenol [18], the drug cocaine [19], or human biomarkers such as bile acids [20] in both water and complex matrices, including wastewater and urine. CF sensors constructed using aTFs typically have LODs on the order of 10^{-9}–10^{-6} M, which are primarily defined by the affinity of the aTF for their corresponding ligands (Table S1). To enable detection of protein analytes, recently a split-T7 RNA polymerase was developed into an immunosensor by fusing pairs of affinity domains to control reassembly of the polymerase with a 10^{-8} M LOD [4]. Because this utilizes biomolecular recognition and dimerization for sensing, this system can easily be generalized to new target protein analytes by swapping the affinity domains. As an alternative to protein-based transcription factors and RNA polymerases, RNA riboswitches can also be utilized to control transcription in DNA circuits. For example, the fluoride-responsive riboswitch *crcB* can be used to control transcription of fluorescent or spectroscopic reporters with a 10^{-5} M LOD below the U.S. EPA (< 2 ppm, 1×10^{-4} M) and WHO limits (< 1.5 ppm, 7.9×10^{-5} M) in rural Kenyan water samples [21].

DNA circuits enable signal amplification by coupling the binding of an analyte to a sensing element to gene expression, but they are typically characterized by slower RT (typically several hours) than other circuits, as transcription and translation processes are required, which limits their utility for continuous, real-time sensing. However, DNA circuits can be sped up by selecting RNA-based reporter elements that do not require protein translation [3,5] or by coupling aTF binding to outputs that do not rely on transcription/translation, such as CRISPR/Cas-mediated DNA cleavage [6]. For example, the recently developed ligand-responsive artificial protein-protein communication (LIRAC) system converts aTF binding events to Cas12a-mediated transcleavage of quenched fluorescent nucleotide probes that reduces RT from 2 h to 10 min. LIRAC was able to detect Cu(II) and parabens in both lacustrine and riverine water samples by generating both fluorescent and spectroscopic lateral flow outputs [6].

RNA circuits are also frequently used in CF biosensor systems to regulate the translation of mRNA transcripts into proteins. RNA circuits typically utilize toehold switches to regulate protein synthesis. Toehold switches utilize a stem-loop RNA structure to occlude ribosome binding to the mRNA, thereby limiting translation. Upon binding of a trigger nucleic acid, the stem-loop unfolds, enabling ribosome access to the ribosomal binding site to initiate protein translation. Because these sensors rely on nucleic acid base pairing to control loop formation, they are easily designed to respond to diverse target sequences [22]. For example, toehold switches have been designed to detect Zika virus with a 2–14 h RT and a 10^{-9} M LOD and when coupled with nucleic acid sequence-based amplification (NASBA) can achieve enhanced sensitivity down to a 10^{-18} M LOD [23]. The ability to amplify nucleic acid analytes with initially low abundance enables this exceptionally high sensitivity.

CF systems are the ideal deployment setting for RNA circuits that respond to nucleic acids, as CF systems do not suffer from transport limitations associated with cellular uptake of environmental nucleic acids.

As an alternative to DNA and RNA circuits, protein circuits that depend on the direct actuation of protein or enzymatic activity to trigger output signal generation can be used for CF sensing. As transcription and translation are not required for signal production in protein circuits, these systems typically have rapid RT (s-min) and are often operated as purified proteins rather than in the context of CF expression systems. For a detection element, protein circuits often rely on allosteric protein switches that respond to target ligands to actuate signal production. These are typically developed using protein engineering techniques such as protein splitting, circular permutation, or domain insertion. For example, by using domain insertion, glucose dehydrogenase was engineered as a platform to detect ligands that are not the native substrate glucose and to convert these into electrochemical signals that can be measured using simple glucometer devices [24]. This was utilized to detect the endocrine disrupting molecule 4-hydroxytamoxifen with a 4 min RT and a 10^{-7} M LOD [24]. Additionally, a per- and polyfluoroalkyl substances (PFAS) sensor was developed by fusing a split-human liver fatty acid binding protein to circularly permuted GFP that could generate a fluorescent signal upon binding of perfluorooctanoic acid in creek water with a 5 min RT and a 10^{-7} M LOD [25]. While promising, the ppb sensitivity of this sensor remains well above the < 10 pM sensitivity needed to assess if samples meet the recent U.S. EPA drinking water standards (4 ppt, 9.66×10^{-12} M). To achieve LOD at this stringent level, paper-based microfluidic devices have been reported to achieve pM LOD of PFOA in wastewater samples by performing capillary flow assays that measure device wetting rates, which are impacted by competitive molecular interactions between PFOA and either purified protein (*e.g.*, albumin, casein) and cellulose fibers [26]. With the emergence of generative deep learning models for protein design, the ability to design new protein sensors for emerging environmental contaminants is rapidly expanding [27,28].

Extending cell-free biosensing beyond aqueous environment

Many CF biosensors have been developed and examined in aqueous matrices because of sample homogeneity, chemistry compatibility, and as a feature of rehydrating lyophilized lysates. Complex environments such as soils and sediments can inhibit CF expression systems through sorption to particulates or enzyme degradation, which has limited their direct application within these matrices (Figure 2). Nonetheless, recent efforts using protein circuits that do not rely on transcription/translation have expanded CF sensing for gaseous analyte detection in aerosols in the field. Several electronic nose (eNose) devices have been developed for sensing volatile organic compounds (VOCs) in the gas phase by embedding olfactory receptors onto ion-sensitive field-effect transistors to detect esters, aldehydes, alcohols, and terpenes with 10^{-14}–10^{-7} M LODs depending on the receptor and 1 s to 5 min RTs [29–32]. For example, a plant pathogen eNose was developed that generates electrical signals in response to the bacterial volatiles 2,3-butanediol (BDO) and 2-phenylethyl alcohol (PEA) with RT of 10 seconds and was used in a portable bioelectronic device to detect pathogens in fruit orchards [29]. While these atmospheric sensors illustrate how biomolecules can be directly used as sensors in non-aqueous environments, additional efforts are needed to extend cell-free systems into complex matrices such as soils [33]. Recently, encapsulation of CF expression systems into cell-like lipid vesicles is emerging as an approach for potentially extending CF biosensors into these complex non-aqueous environments [34]. Additionally, microfluidic devices could be utilized to perform in-field analyte extraction from soil samples, facilitating the use of CF biosensors without the risk for matrix incompatibilities [35,36].

Whole-cell biosensors

Principles of whole-cell biosensors

Whole-cell (WC) biosensors also leverage DNA, RNA, and protein circuits to detect analytes, but instead of depending on isolated biomolecules, these platforms utilize living cells as the biological unit for sensing. A distinct advantage of WC biosensors relative to CF biosensors is that WC biosensors can self-replicate, repair, and maintain themselves without continuous supplementation, which can lead to lower cost, longer shelf-lives, and increasing scalability for monitoring. Additionally, WC biosensors provide measurements of the bioavailable fraction of analytes in the environment, which have been shown to vary relative to the total abundance in the environment [35].

Whole-cell biosensors in aqueous matrices

WC biosensors also utilize DNA circuits that rely on allosteric transcription factors to convert chemical signals to gene expression outputs. For instance, WC mercury sensors have been developed by using the MerR aTF to activate expression of either fluorescent or spectroscopic reporters and have achieved 10^{-9} M LODs, below the WHO drinking water thresholds (6 ppb, 2.9×10^{-8} M) [37]. These WC biosensors were applied for environmental monitoring of water samples from gold mining sites in Peru. Analogously, arsenite sensors that leverage the ArsR aTF detected arsenite with a 10^{-8} M LOD in both marine and freshwater, again below the WHO drinking water threshold (10 ppb, 1.3×10^{-7} M) [38]. WC sensor DNA circuits have been deployed in a

microfluidic device called Dynomics to enable genome-scale sensors that rely on transcriptome-wide responses to analytes using promoter libraries linked to fluorescent reporter production [39]. When coupled to machine learning, Dynomics could be used for continuous monitoring and prediction of the presence of heavy metals in urban water and mine spill samples.

One distinct class of transcription factors that are available within WC systems, but unavailable in CF systems, are two-component systems (TCSs) [40]. TCSs rely on sensor kinase domains that are often embedded in the cell membrane to activate intracellular response regulators that control gene expression. The reliance on a membrane-embedded component limits their use in membrane-less CF systems [41]. TCSs are versatile components for WC biosensors. For example, the PhoR-PhoB TCS has been utilized in an *Escherichia coli* WC biosensor to detect inorganic phosphate in lacustrine and riverine water samples with a 10^{-5} M LOD, below the allowable international discharge standard (10^{-5}–10^{-4} M) [42]. Because the phosphorylation dynamics between the histidine kinase and response regulators can be tuned, TCSs have customizable response functions that can achieve higher fold change relative to one-component aTFs, but typically have higher LODs due to lower-affinity sensor kinases [43]. Recently, synthetic TCSs using aTFs in place of sensor kinases were developed to regulate the expression of response regulators taking advantage of both the lower LOD of aTFs and the enhance dynamic range of TCSs [43]. As with CF sensors, DNA circuits in WC sensors generally have slow RTs (h-d) that are exacerbated by the requirement for cell growth to enable transcription and translation.

In addition to DNA circuits, RNA circuits can also operate in WC biosensors. However, as these circuits typically respond to nucleic acid signals their utility as sensors is distinct from their use in CF systems as the cell envelope presents a barrier limiting transport of exogenous nucleic acids. Instead, these sensors are useful for responding to the transcription of genes encoded within the cells that make up the WC biosensor. For example, recently, the Ribozyme-ENabled Detection of RNA (RENDR) system was developed that utilizes a split ribozyme to detect specific RNA signals and was applied as a sensor for monitoring the expression of antibiotic resistance genes, and was shown to be able to control diverse outputs, including fluorescent, gaseous, and spectroscopic signals [44]. Similarly, a truncated ribozyme called a catalytic RNA was used to generate nucleic acid barcode signals in response to plasmid conjugation to sense horizontal gene transfer events in wastewater that could be quantified using DNA sequencing [45].

In addition to DNA and RNA circuits, protein circuits can be used to control output signals in living cells with fast RTs. The same PFAS sensor described as a CF sensor in the earlier section was also deployed in *E. coli* cells, but exhibited a diminished fluorescent signal and had 10^{-6} M LOD, 10-fold higher than the CF version of this sensor, likely caused by membrane transport limitations and placing this sensor even further from the EPA standard (4 ppt, 9.66×10^{-12} M) [45]. As an alternative to engineered proteins, sensors can be constructed that leverage native metabolic pathways that operate at the protein level. For example, electroactive microbes that oxidize organic matter and transfer electrons to an anode have been used as continuous sensors for biochemical oxygen demand (BOD) in wastewater with a 1 h RT and a 10^{-4} LOD, below the EPA 30 day average BOD standard (30 ppm, 9.3×10^{-4} M) [46]. In this system, cellular metabolism plays a dual role of sensing and transducing, highlighting how the flow of biological energy can be used to capture and transmit information about environmental signals. However, this system is non-specific, responding broadly to organic metabolic substrates. To enable molecular specificity, engineered proteins can be used to control the flow of electrons through metabolism. For example, engineered ferredoxin switches have been developed that respond to endocrine disrupting molecules and used to control the production of electrical signals generated *via* extracellular electron transfer, achieving < 3 min RT in urban riverine waters [7].

One limitation of the previously described biosensors is that they provide a snapshot of analytes in the environment. One unique feature of WC systems for biosensing is that sensing cells can persist in environments for extended times and be programmed with memory circuits as processing modules. For example, recombinase-based memory circuits can be used to flip discrete DNA segments and store memory of exposure events in wastewater samples [10]. Extending on this, CRISPR-Cas acquisition circuits can be utilized to continuously record nucleic acid barcode signals in response to transient stimuli, providing a history of environmental exposures as has been illustrated with Record-seq [43], TRACE [44], and Retro-Cascorder [46]. However, these recording systems have been primarily deployed in the gut microbiome or in pure cultures but are poised for deployment in environmental settings.

Extending whole-cell biosensing beyond aqueous environment

Similar to CF sensors, most WC biosensors target analytes in aqueous conditions due to efficient cell-analyte contact [47]. Unlike CF sensors, WC sensors have been deployed in heterogeneous matrices such as soils as cellular units can protect sensor function from matrix inference with the biomolecular components (Figure 2).

For example, RNA and memory circuits have been utilized to control the production of fluorescent outputs to detect 2,4,6-trinitrotoluene (TNT) in the surface of soils with 10^{-5} M LOD, well above the EPA drinking water standard (2.5 ppb, 1.1×10^{-8} M) but in a useful range for detecting buried explosives [48]. Hyperspectral reporters that leverage metabolites with unique absorbance spectra can enable detection using remote hyperspectral cameras up to 90 m above the survey site, furthering detection on soil surfaces over large spatial areas [9,47–49]. However, due to the use of visual outputs in both cases, these WC sensors were limited to use on the soil surface. To sense deeper within soils where visual reporters cannot be detected, reporter genes that generate gaseous signals have emerged as useful outputs for WC biosensors deployed in soils [9,48–50].

A potentially useful output for high opacity sediment or wastewater matrices are acoustic reporters that produce gas vesicles, which can be used as contrast agents for ultrasound imaging [51]. While these have been used in the human body, they have not been explored for environmental sensing. Other strategies for deploying WC sensors into soil environments include encapsulation into hydrogel materials that enable cells to be maintained in aqueous microenvironments, enhancing sensor longevity in the environment [52,53]. For example, WC sensors encapsulated in alginate/polyacrylic acid hydrogel beads placed on the surface of sand were able to detect TNT from buried landmines by producing luminescent reporters [54]. Additionally, recording circuits have been deployed as processing modules in soils to store histories of analyte detection as DNA sequences. For example, sentinel cells were modified for enhanced DNA uptake to record environmental DNA (eDNA) sequences. In this system, target DNA uptake causes the excision of a terminator to turn on expression of a fluorescent protein, achieving a 10^{-12}–10^{-15} M LOD for target DNA sequences and maintaining a nucleic acid record that avoids environmental degradation for weeks and can be later detected using DNA sequencing [48].

Applications of multicellular biosensors in the environment

Extending on WC sensors, multicellular (MC) biosensors, where environmental inputs are detected *via* interactions between populations of cells, have emerged as a strategy for robust biosensing at large scales [55]. MC biosensors can leverage specialized sensor cells that respond to input signals and communicate sensing events to information processing cells, which can enable multi-input sensing or transmission of sensing signals over long distances. For example, the gaseous output signals used for deep soil sensing described in section above have been utilized for cell signaling to enable cells deep in soils to communicate with cells at the surface of soils to generate visual signals that enable mapping of the heterogenous distribution of target analyte hotspots within field settings [55]. Additionally, MC biosensors have been developed that employ soil microbes as sensor cells and produce chemical signals that activate fluorescent reporter production in plants, extending the output signal above the soil. This modular system enabled the plants to respond to diverse input signals by simply exchanging the microbial sender cells [56]. Similarly, MC biosensors have been developed where sensor microbes convert analytes into molecules that trigger reporter cells to produce electrical signals, again allowing for modularity to adapt to different environmental contaminants by simply modifying the microbial community composition [57]. In addition to cell communication, MC sensors can be developed to have specialist cells that enhance sensor longevity. For example, engineered living materials have been developed that function as sensors while producing a material scaffold that enhances sensor cell viability. For example, SynSCOBY biosensors have been constructed by co-culturing bacterial cellulose-producing *Komagataeibacter rhaeticus* with *Saccharomyces cerevisiae* that are engineered to respond to β-estradiol, which can pose threats to vertebrates living in aqueous environments [58]. By growing the sensor cells in the ELM matrix, these sensors could be desiccated and revived after 4 months to grow new sensor materials. Utilizing a division-of-labor approach in MC sensors can improve capabilities beyond what can be achieved with a single cell type.

Challenges and future outlooks

Despite having distinct advantages as outlined above, cell-free, whole-cell, and multicellular sensors exhibit several unique limitations that can be exacerbated by matrix properties when deployed for environmental sensing (Figure 2). In CF systems, the lack of cellular membrane barrier provides distinct advantages for overcoming transport limitations that impede RT and increase LODs, this also renders CF systems more susceptible to interference from salts, pH fluctuations in aquatic sensing application or desiccation in soil or atmospheric sensing applications. Recent encapsulation efforts offer potential solutions by mimicking the cellular membrane, but come with the tradeoff of introducing transport challenges [57]. Additionally, freshly isolated CF expression reactions have short shelf lives, but this can be extended up to >6 months in a refrigerator following lyophilization. To extend the shelf life of CF biosensors at ambient temperatures, additional work is needed to identify why reactions stop or components degrade [58]. In addition to shelf-life, one challenge with CF systems is the cost associated with producing cell lysates. Advances in reagent optimization have increased CF accessibility; for example, the RFopt formulation developed by Olsen et al. [59] reduced reagent cost by two orders of magnitude ($4513/$L_{CFE}$ →

$143/L$_{CFE}$) while simplifying chemical complexity and enhancing reproducibility.

One challenge with WC and MC biosensors is that membrane transport can limit sensitivity toward analytes, resulting in higher LODs than their CF counterparts. This can be overcome by deploying sensor modules onto the cell surface rather than intracellularly, but this can limit the ability to use DNA and RNA circuit elements [60]. Another challenge for deploying WC and MC sensors into the environment is the risk of release of engineered organisms into the environment. There are multiple available biocontainment strategies for limiting environmental persistence of engineered microbes to limit risks of release that have recently been reviewed elsewhere [61]. While it is important to consider, the evidence supporting the risk of environmental damage or runaway propagation of engineered organisms that informs regulatory policy remains limited, and the regulatory framework governing environmental deployment varies widely across jurisdictions [61,62]. A remaining challenge for environmental biosensing is the ability of engineered microorganisms to retain viability and functionality in resource or nutrient-limiting environments, such as those needed for atmospheric and soil sensing applications (Figure 2). Efforts to overcome this through material encapsulation using cell coating such as hydrogels [7,52–54,63] or metal-phenolic networks [64] offer potential solutions to this challenge and also can at times improve sensor performance [7,54]. An alternative approach to cellular encapsulation is to generate cyborg cells by polymerizing hydrogels within cells [65]. This approach has the benefit of both biocontainment and extending sensor viability, but comes with a tradeoff that the cells no longer self-replicate.

Beyond the challenges associated with the choice of biological platform, the choice of sensing, processing, and output modules directly impacts biosensor performance. Biosensors relying on DNA circuits generally have slower RT than those that rely on RNA or protein circuits. To achieve real-time sensing capabilities, biosensors should be designed to utilize protein and RNA switches that can directly control output signal generation. Sensors relying on aTFs and TCS as sensing modules have LODs between 10^{-4} and 10^{-9} M, while sensors utilizing olfactory receptors have lower sensitivities between 10^{-11} and 10^{-14} M. Sensors that respond to nucleic acids can achieve highly sensitive 10^{-9}–10^{-18} LODs when coupled to nucleic acid amplification techniques. In many cases, these LODs are sufficient to be useful for environmental monitoring, surpassing the sensitivities needed to meet regulatory requirements, but in some cases, such as for the detection of PFAS, the strict regulatory thresholds are beyond what is readily achievable using biomolecules alone. The emergence of protein design tools is poised to enable the development of generalizable protein circuits that can achieve high-sensitivity detection with rapid response times.

Conclusion

Over the past few years, biology-enabled sensors have evolved into versatile technologies that can translate chemical information into measurable outputs with enhanced temporal resolution and field deployability. By leveraging diverse biological units — including cell-free, whole-cell, and multicellular systems — biosensors can extend sensing in multiple environmental matrices and provide information about the chemical environment that can enable actionable interventions. With these platforms involving multiple layers of control at the DNA, RNA, and protein levels, they are able to harness the diverse biomolecular mechanisms by which cells interpret their environments and translate these into measurable signals. Moving forward, there is a need to improve sensitivity and reliability in environments beyond aqueous systems, where there are transport limitations, heterogeneity, and interference challenges that can affect the sensor performance. Integrating memory systems, bioelectronics, and machine learning-guided design will be broadly essential for the development of next-generation sensors that enable long-term environmental monitoring in the field and support real-time interventions. Beyond supporting scalable deployment, standardized safety frameworks and regulatory approaches for evaluating the risks of engineered organism release through field trials are needed to ensure responsible implementation.

Data Availability

No data were used for the research described in the article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.coche.2026.101269.

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- •• of outstanding interest

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