

## **Synthetic biosensors for detection of cryptic elemental cycles**

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Of life's limiting micronutrients, iron is essential for nearly all life functions and is linked to major biological element cycles. However, understanding Fe oxidation states, such as the ratio of ferric to ferrous iron in the environment is challenging due to the low concentration and rapid turnover of these ions, which makes the application of conventional measurement approaches particularly expensive, cumbersome, and destructive. Synthetic biology offers new approaches to detect the cycling of Fe and other cryptic processes. Microbes can be engineered to detect low levels of these elements and then report on their perception of concentrations. The recent development of indicator gases as reporters allows nondestructive biosensing, reading out microbially detected concentrations of compounds in the headspace of incubation experiments.

Here we report on our efforts to develop biosensors to nondestructively detect Fe in soils and sediments. To do this, we domesticated a microbial two component signal transduction system (TCS). TCSs are composed of a sensor and a response regulator protein. In most cases, the sensor is phosphorylated in the presence of its cognate ligand, which is then transduced to a response regulator protein that binds DNA to modulate the expression of a reporter gene that synthesizes a rare indicator gas.

We engineered biosensors based on ferric specific BasS-BasR TCS and on ferrous specific BqsS-BqsR TCS. These TCSs enable the measurement of bio-available iron ions at environmentally-relevant concentrations. We tested the ferric sensor by assaying gene expression in the presence of both a ferric chelator, deferoxamine mesylate, and a gradient of ferric nitrate. We find the ferric biosensor is responsive to changes in concentration of ferric nitrate. Ongoing efforts are using quantitative models to tune the dynamic range and the detection threshold. This synthetic biologic design framework represents a simple method to design tools for monitoring the availability of a cryptically cycling compound.