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1 *Viewpoint*

2 **Community Sewage Sensors for Monitoring Public Health**

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12 Wastewater-based epidemiology (WBE) has been shown to be an innovative approach  
13 for monitoring drug use in communities by quantifying drug residues (so-called “drug  
14 biomarkers”) in sewage<sup>1, 2</sup>. WBE has thus far been validated by assessing illicit drug use  
15 trends across Europe, with the evaluation of spatial differences and temporal changes in the  
16 levels of specific biomarkers in sewage from 42 cities in 21 European countries (total  
17 population 24.74 million)<sup>1</sup>. It is hypothesized that sewage contains additional information on  
18 the lifestyle, health and pollutant exposure of a community which could also be obtained by  
19 the analysis of sewage biomarkers<sup>2</sup>. In fact, feces and urine from either humans or animals  
20 carry many biomarkers and pathogens, which could and enter the sewer system from a carrier  
21 of the disease in the community, e.g. patients at hospitals. Those pathogens such as bacteria,  
22 viruses and parasites in wastewater are hazardous to humans because they might cause  
23 epidemics in population. However, human hazards can be minimized if those pathogens  
24 could be monitored at an early stage in the community. Unlike illicit drug use trends,  
25 infectious diseases require rapid or even real-time detection to assess whether there is a need  
26 for the containment of the disease carriers to certain areas and prevent the development of an  
27 epidemic. To this end, there is a need to develop novel analytical tools that are able to  
28 accurately and rapidly monitor low levels of biomarkers/pathogens with minimal sample  
29 processing by unskilled personnel at the site of sample collection. **Emerging biosensing  
30 technology will play a key role in the in situ quantitative analysis of biomarkers and  
31 pathogens in sewage due to rapid response times, low cost, minimal sample processing, high  
32 data resolution and ability to operate remotely. Community sewage sensors employed to  
33 detect biomarkers of health and diseases at a population-level have therefore the clear  
34 potential to provide real-time data for the assessment of community-wide health.**

35 Biosensors have emerged as powerful tools for the detection of disease biomarkers for  
36 both healthcare and environmental monitoring. A biosensor is a small device with a  
37 biological receptor (DNA, antibody, protein etc.) that generates a signal (electrochemical,  
38 optical, piezoelectric, nanomechanical, mass sensitive etc.) in the presence of an analytical  
39 target (analyte). Compared to conventional analytical tools, biosensors can provide rapid  
40 response times, ultra-sensitive detection of biomolecules, and the potential to be miniaturized

41 for portable assays requiring minimal sample processing. Moreover, this approach could be  
42 employed, not only for the detection of pathogens, but also for the monitoring of more  
43 general public health indicators such as obesity, diabetes, high blood pressure and sexually  
44 transmitted infections. For example, a recent report demonstrates that the level of an  
45 American city's obesity could be predicted by analyzing the bacterial community structure  
46 found in sewage<sup>3</sup>. Such an approach providing near real-time and continuous data would  
47 serve as an early warning sensing system to help agencies, such as the "Centre for Disease  
48 Control and Prevention" (CDC) in the United States, to make effective interventions to  
49 prevent the spread of epidemics, evaluate the effects of interventions and in turn increase the  
50 effectiveness of their policies and use of valuable resources. For example, in 2003 the  
51 effective interventions of CDC in the United States helped reduced spread of severe acute  
52 respiratory syndrome (SARS) to a minimum level.

53 A large number of biosensors have been developed for the detection of disease  
54 biomarkers and pathogens in samples such as urine, sera and saliva (Table 1). Although  
55 sewage is a complex matrix, spurious effects, such as nonspecific interactions can be  
56 minimized provided that an ultra-high affinity probe such as an aptamer is used to target  
57 specific analytes, as well as by calculating the differential response of a probe and a reference  
58 chip. As an example, a macrocantilever-based label-free biosensor can quantitatively detect a  
59 prostate cancer biomarker ( $\alpha$ -methylacyl-CoA racemase; AMACR) directly in patients' urine  
60 without any sample preparation<sup>4</sup>. Hence, there is the clear potential to develop a wider range  
61 of innovative community sensors to quantitatively assess sewage profiles and patterns of  
62 factors related to health and illness within populations using WBE. Additionally, biosensors  
63 have the potential to be miniaturized to a handheld device for point-of-care analysis that may  
64 facilitate the monitoring of infectious diseases in developing countries where the occurring  
65 rate (such as malaria, acquired immune deficiency syndrome (AIDS) and tuberculosis) is  
66 extremely high. For instance, a plasmonic enzyme-linked immunosorbent assay (ELISA) has  
67 been developed to ultra-sensitively detect an HIV-1 capsid antigen p24 at concentrations as  
68 low as 1 attogram per millilitre in serum of HIV-infected patients with the naked eye<sup>5</sup>. In this  
69 sensor, the ELISA enzyme controls the aggregation of nanoparticles, rising a blue colour if a  
70 target protein is present otherwise a red colour if no target. All of these biosensors can  
71 potentially be used in sewage matrices as community sensors to assess urinary and fecal  
72 biomarkers/pathogens for the monitoring of public health using WBE, while also providing a  
73 means of collecting data for epidemiological and socio-economic studies. Community  
74 sewage sensors arrays can be customized designed for the monitoring of different  
75 biomarkers/pathogens in a single assay. Their use could be of considerable economic and  
76 societal impact especially in resource-constrained areas. More importantly, biosensing  
77 technology platforms can be utilized to collect information on community-wide health in  
78 order to report to health agencies as an early prevention measurement and effective  
79 interventions. Although the selectivity and long-term stability of community sensors as well  
80 as environmental susceptibility to deterioration of bio-recognition are yet to be addressed, we  
81 envisage that the rapid and real-time monitoring of health in communities will soon be  
82 possible.

83 Table 1 Examples of biosensors used for the detection of infectious diseases and pathogens

Infectious diseases	Biosensors and its transducers	Biomarkers/pathogens
HIV	Plasmonic ELISA	protein biomarkers
	Impedimetric, voltammetric and amperometric proteins biosensors	HIV virus lysate, HIV-1 protease
	Mechanical sensors	HIV CD4 T cell number
Tuberculosis	Electrochemical PCR-free mycobacterium tuberculosis (MTB) genomic sensors	PCR-free MTB nucleic acid or cells
Others diseases	Fluorescent peptides sensors	Drug resistant chronic myelogenous leukemia
Pathogens	Fluorescent array, evanescent wave fibre-optic, laser cytometry, electrochemical and mass sensitive DNA/antibodies sensors	Pathogenic Bacillus species like Bacillus anthracis and bacillus cereus
	Optical, electrochemical and mass sensitive DNA/ aptamers/antibodies biosensors	campylobacter species for campylobacteriosis
	Fluorescent, electrochemical and piezoelectric antibody/lectin/ganglioside biosensors	cholera toxin from bacterium Vibrio cholera
	Optical, electrochemical, mass sensitive antibodies/antimicrobial peptides/aptamers/bacteriophages biosensors	Escherichia coli, like E coli O157:H7; Listeria monocytogenes,; Salmonella; Shigella spp, Staphylococcus aureus; viral threats (smallpox viral hemorrhagic fevers, viral encephalitis etc.)

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