Comment

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Low-cost and rapid sensors for wastewater surveillance at low-resource settings

Zhugen Yang

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Wastewater surveillance enables tracking infectious disease dynamics and community prevalence quantification for public health. However, the testing requirement of centralized laboratories and well-trained staff challenges underserved areas and low-resource settings. The development of new rapid and low-cost sensors enables in-field testing of wastewater from the community to the individual building levels for early warning of pandemics.

Wastewater surveillance, or wastewater-based epidemiology, enables rapid pathogen detection and community prevalence quantification[1], and is currently being performed in over 70 countries worldwide for regional and national surveillance programs. Wastewater surveillance not only provides prevalence data for governments and health agencies but can also provide an early warning alert, as was the case in London and New York when the polio virus was recently detected. However, most wastewater samples are sent to laboratories, with analysis involving either polymerase chain reaction (PCR) – a gold standard analytical method – or genome sequencing, for identifying new variants. These methods incur a long delay in reporting results[2]. The lack of diagnostic centres and trained staff impede the more widespread use of wastewater surveillance, especially in low-resource settings and underserved communities, for example, low- and middle-income countries (LMICs). Unfortunately, the regions in the Global South typically have a high prevalence of infectious diseases, including tuberculosis, malaria, acquired immunodeficiency syndrome (AIDS), dengue, Ebola, hepatitis, influenza, zika, norovirus, SARS-CoV-2 and monkeypox virus[3]. It is therefore essential to develop rapid and low-cost methods for on-site wastewater surveillance in resource-limited areas.

In addition to challenges related to the length of the analysis time (wherein nucleic acid degradation may occur during wastewater storage and transport), the presence of PCR inhibitors in wastewater may lead to inconsistent results. Therefore, rapid and in situ testing is needed to overcome these limitations, enabling the sensitive detection of low concentrations of pathogens in wastewater whilst providing real-time monitoring to generate sufficiently large data sets for early warning systems[4]. The methods must apply to underserved areas without sewage networks by testing point sources (for example, nature pooling sites)[3].

Low-cost and rapid sensor development

Low-cost and rapid sensor technologies (for example, colorimetrical sensors, lateral flow devices (LFD), paper microfluidic devices) have been developed for the diagnosis of pathogens in the field[5,6]. However, wastewater analysis remains significantly challenging for such sensors due to the low concentrations of pathogenic biomarkers and the complexity and variability of the matrix (for example, inhibitors prevent signal amplification). Implemented techniques must: (1) be sensitive and specific; (2) provide comprehensive and objective data; (3) realize results in real-time; (4) be able to monitor multiple diseases and pollutants, even those which are typical; (5) be scalable and cost-effective; and (6) be easy-to-use and demand no specialist resources.

Nanomaterials including noble metal nanoparticles, carbon-based nanomaterials and nanotechnologies have significantly contributed to improving the analytical performance (for example, sensitivity and specificity) of biosensors. In addition to antibodies, new highly specific biological receptors such as DNases, phages, and peptides can also be generalized for use in biosensors. Emerging biotechnology (for example, CRISPR/Cas-enabled sensor technology[7–9]), engineering approaches such as microfluidics (for example, low-cost paper-based microfluidics), and electronics can be further explored to develop integrated biosensing platforms for wastewater analysis. In addition to the improved analytical performance, the developed sensor devices must be stable enough to withstand long-term storage (for example, reagents) and fluctuations in environmental conditions.

The LFD device is a typical example of the application of sensors for COVID-19 diagnosis. More novel devices have been developed to aid the mass screening of SARS-CoV-2 in the COVID-19 pandemic; these are low-cost, easy-to-operate, rapid and sensitive, and could potentially be deployed in the field. For example, Wu et al. developed an isothermal NASBA (nucleic acid sequence–based amplification) sequencing–based high-throughput test, which provides results within 1 to 2 hours, using either fluorescence detection or an LFD readout and thus potentially making it scalable to the population level[10]. Another example is a face-mask-integrated sensor, developed as a complementary method for diagnosing COVID-19 based on nasopharyngeal sampling. It includes a reservoir for hydration, a surface area sample collection pad, a wax-patterned microfluidic paper-based analytical device and an LFD assay strip[11].

Testing wastewater in the field

Low-cost and rapid sensors have recently shown a clear potential for the detection of pathogens in wastewater (Fig. 1). For example, a paper-based microfluidic device has been developed for the multiplexed detection of pathogens and successfully tested in Indian farms[12] and in Uganda for malaria[6]. The device has been further demonstrated as a point-of-care diagnosis tool for active hepatitis C virus (HCV) infection, comprising a loop-mediated isothermal amplification (LAMP) chamber and LFD nucleic acid detection strips, giving a visually-read and user-friendly result in less than 40 min[13]. An LFD integrated with LAMP for testing genetic biomarkers in wastewater[14] was subsequently proposed for detecting SARS-CoV-2 in wastewater[7]. A low-cost, rapid,

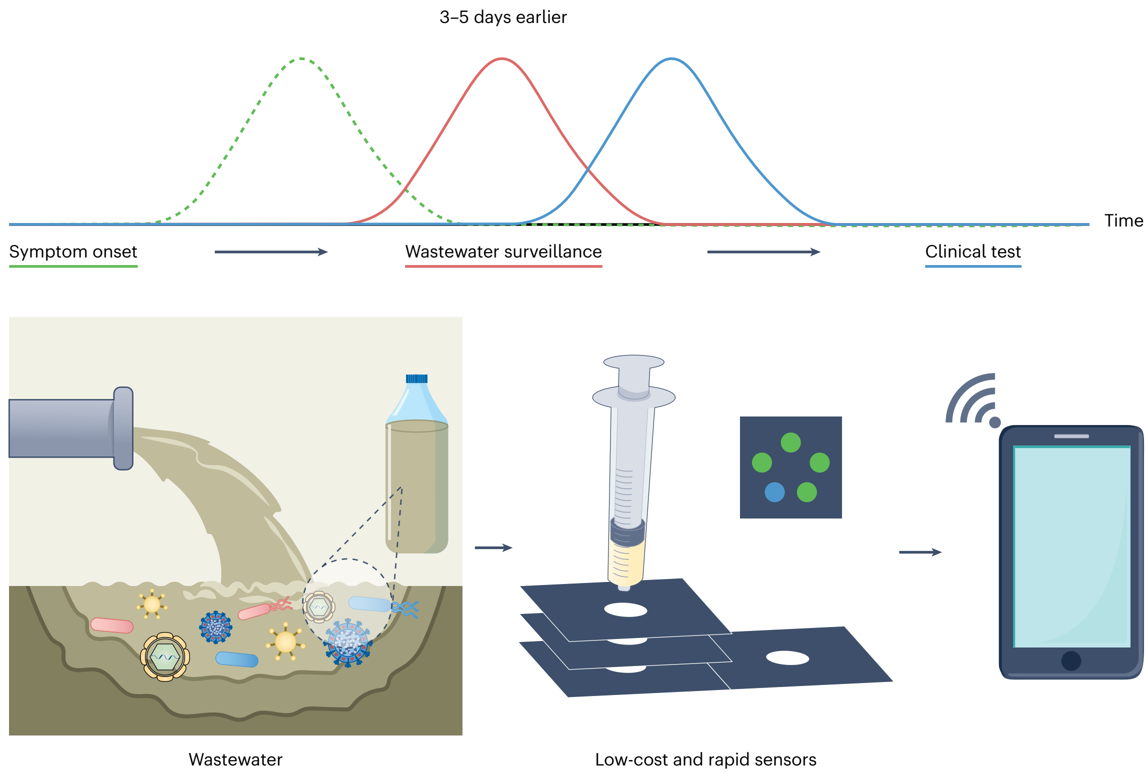

Fig. 1 | Low-cost sensors for rapid and on-site wastewater surveillance. Wastewater surveillance provides earlier diagnosis than clinical testing for infectious diseases, even for people with mild or no symptoms; low-cost and rapid sensors (such as paper microfluidics devices) enable rapid and on-site testing of pathogens in wastewater at low-resource settings, even in the field. For example, origami paper sensors provide multiplexed detection of pathogens in a single device, and the image shows the signal from the detection of three pathogens together with two controls (positive and negative, where the blue circle is negative and the green circles are positive)[12]. The near real-time data can be collected and interpreted for public health management.

and user-friendly multiplexed paper microfluidic platform has been developed for the detection of SARS-CoV-2 and influenza in wastewater[15], which could achieve on-site virus detection within 90 minutes at a London quarantine hotel, demonstrating its potential application in LMICs and resource-limited areas.

To further implement those sensors in low-resource settings, they will need further to be designed to: (1) achieve device operation under highly variable environmental conditions, (2) simplify field sensor replacement, (3) facilitate data communication and (4) minimize the possibility of sensor scaling. In addition to solving these and other technical problems, data security and confidentiality will also need to be taken into consideration. For example, an end-to-end smartphone-based platform was established for malaria diagnosis based on multiplex LAMP assay and LFD testing in rural Uganda, which combined deep learning algorithms for local decision support and blockchain technology for secure data management[5]. The newly-developed sensors can be further extended for the evaluation of antimicrobial resistance.

A look ahead

Wastewater surveillance can provide early warning of community-level outbreaks and predict infection trends within the population as well as reflect the dynamics of interaction between people and their environment, based on markers for long-term chronic diseases. Wastewater can be used to track infectious disease dynamics from the community level to the building level and from sources ranging from sewers and wastewater treatment plants (WWTPs) to surface waters and point sources (for example, natural pooling sites)[3]. In the future, artificial intelligence, big data analytics and the Internet of Things (IoT) can be combined with sensors and sensor networks for wastewater surveillance. Artificial Intelligence devices can perform multi-step analysis to predict disease profiles using various algorithms even in lower-resource settings, which provides the potential for a more robust response to future pandemics.

Developing fully deployable rapid wastewater sensors will need collective efforts of academic researchers, medical professionals, industrial engineers, and government agencies. These stakeholders must collectively explore and improve sensor performance, statistical analysis and models as well as hardware design for rapid sensors to enable real-time monitoring in low-resource settings in order to help protect global public health.

Zhugen Yang
School of Water, Energy and Environment, Cranfield University, Cranfield, UK.
e-mail: zhugen.yang@cranfield.ac.uk

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Competing interests

The authors declare no competing interests.