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EDITORIAL

Special Topic: DNA-Based Biosensors

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While the function of DNA in biology is for storage of genetic information, chemists have developed methods to obtain DNA sequences with catalytic and molecular recognition functions. Thus, DNA is a highly attractive molecule for developing biosensors. DNA probes are known for their detection of complementary DNA and RNA. In addition, DNA aptamers allow for the detection of, essentially, any type of molecule. By coupling DNA with biological elements such as CRISPR-Cas12, highly sensitive detection with signal amplification can also be achieved. Overall, using DNA as a sensor component and as a target are hot areas of research for biomedical diagnosis, environmental monitoring, and food safety.

Journal of Analysis and Testing provides an international academic forum for the publication of original research papers, rapid communications, and critical reviews in all aspects of fundamental and applied analytical chemistry. To highlight the current developments in DNA-based biosensors and to stimulate new thoughts in the field, this Special Issue is focused on biosensors related to DNA. This Special Issue features one review and six research papers.

Zhou, Liu and coworkers from South China Normal University reviewed recent advances in CRISPR-Cas12 based nucleic acid detection, and the authors emphasized the new research methods and means to improve the nucleic acid detection capability of CRISPR-Cas12 including improving sensitivity, integrated detection, design of simplified detection modes and methods for achieving quantitative detection.

For the research papers, they covered a wide range of topics. Liu and Chang and coworkers from Dalian University of Technology reported a G-rich DNA sequence that can form a G-quadruplex (G4) structure even at high temperature and maintain high stability. Since this G4 structure can bind N-methylmesoporphyrin IX (NMM) a fluorescent and thermophilic signal transduction mechanism was demonstrated. This system was used for single nucleotide polymorphism (SNP) detection coupled with a rolling circle amplification platform. Since high temperature could ensure more specific base pairing, this system allowed highly specific detection of DNA or microRNA 21.

Lu and coworkers reported a novel enzyme modulated fluorescence-on sensor for sensitive detection of omethoate, a systemic organophosphorous insecticide. An AT-rich double-stranded DNA was used to template the synthesis of fluorescent copper nanoparticles (CuNPs) as the fluorescent signaling unit. Omethoate was recognized based on its ability to inhibit acetylcholinesterase. This system also included magnetic Fe_3O_4 nanoparticles and graphene oxide (GO) as the single-stranded DNA adsorbent. The sensor detected omethoate with a detection limit of 2.48 nmol/L, and retained functionality in food and environmental samples.

Bi and coworkers reported a dual-signal electrochemical biosensor by self-assembly of pH-activatable i-motif probes on magnetic microparticles (MMPs), which was further coupled with a DNA walker system for signal amplification. A cytosine-rich DNA was hybridized with the DNA walker, and the resulting duplexes are rich in G-C base pairs, providing rich binding sites for doxorubicin (DOX). At acidic pH, the C-rich sequences folded into an i-motif structure, releasing DOX and DNA walker initiators. The magnetic separation can suppress the background, allowing pH monitoring from 4.0 to 7.4, as well as target detection in human serum.

Huang and Liu studied the adsorption of fluorescently labeled DNA and aptamer probes to graphene oxide (GO). Upon adsorption, the fluorescence of the labelled DNA is quenched, which is recovered in the presence of target analytes. Interestingly, the authors found that some of this desorbed DNA would re-adsorb on the GO surface, causing a slow decrease in fluorescence. The explanation for this was related to the surface heterogeneity of GO, where DNA

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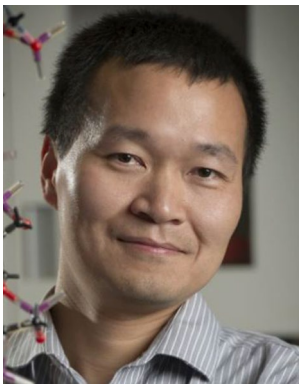
initially desorbs from weaker binding sites in the process of target binding, but re-adsorbs at stronger binding sites. To avoid this re-adsorption in the context of biosensor design, the authors recommend either extensive washing of samples, blocking the GO surface with competing adsorbent or heating to overcome any physical bonds formed during re-adsorption.

Qing and coworkers pinpointed the problem of decreased sensitivity of traditional DNA detachment fluorescent sensors within cells. To address this, the authors integrated a detachment-independent fluorescence-on sensor with cationic dipeptide nanoparticles (CDNs). This modification did not significantly change the fluorescence of the probe, while improving the DNA stability against nuclease degradation. Furthermore, this avoided the potential false negatives from DNA adsorption on traditional nanosurfaces (which are quenching), and accelerated the lighting of the molecular beacon.

Zhang and Wu and coworkers reported a simple enzyme-free DNA sensor for microRNA detection utilizing a multiple signal amplification strategy. The sensing system includes six hairpin DNA strands that were designed for intramolecular hybridization. The DNA hairpin reactants are opened and hybridized with the corresponding complementary DNA strand in the presence of miR-21 via the toehold-mediated hybridization chain reaction and other amplification mechanisms for a very large signal output. Without protein enzymes, this sensing system showed a highly sensitive and selective detection of miR-21, with a limit of detection of 1.8 pmol/L.

This Special Issue only represents a small collection of work in the field of DNA-based biosensors. We hope that they can be useful for readers to get an idea of the current state of research in this field. By reading these papers, some challenges and future research opportunities can also be defined. For example, simplifying the detection systems to make them portable and field deployable is a challenge.

We are very grateful to the authors for contributing high-quality papers to this issue, and the reviewers for their efforts and help in reviewing these manuscripts. We also wish to thank the Editorial Office for their help along the way.



Jue-Wen Liu received his Ph.D. degree from the University of Illinois at Urbana-Champaign in 2005. After postdoctoral research at Sandia National Labs and the University of New Mexico, he joined the Department of Chemistry at the University of Waterloo in 2009. He is currently a full professor there. He received a Fred Beamish Award (2014) and a W.A.E. McBryde Medal (2018) from the Canadian Society for Chemistry for his contribution in bioanalytical chemistry, and an Ontario Early Researcher Award in 2011. He serves an Editor for *Biosensors & Bioelectronics, Trends in Analytical Chemistry* (*TrAC*), an Associate Editor for Chinese Chemical Letters, a Board member for *Journal of Analysis and Testing*, and is on the Editorial Advisory Board of *Langmuir* and *Particles & Particle Systems Characterization*. He is interested in metal-dependent DNAzymes, biointerface science, and nanozymes. Since 2002, he has published over 300 papers, receiving over 32,000 citations with an H-index of 84.

Dik-Lung Ma completed his PhD in 2004 at the University of Hong Kong under the supervision of Prof. C.-M. Che. Between 2005 and 2009, he worked at the University of Hong Kong, the Hong Kong Polytechnic University, and the Scripps Research Institute with Prof. C.-M. Che, Prof. K.-Y. Wong, and Prof. R. Abagyan. He is currently an Associate Professor at the Department of Chemistry, Hong Kong Baptist University. His research mainly focuses on luminescent sensing of biomolecules and metal ions, computer-aided drug discovery and inorganic medicine.