Sensors with Highly Ordered Nucleotides

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A great deal of research has been carried out for the development of not only sensors targeting nucleotides, but also for sensors employing nucleotides to detect other species. Sensors based on probe molecules with highly ordered nucleotide structures (aptamers or DNAzymes) have recently been reported. Wang et al. reported on a fluorescence turn-on and label-free sensor based on aptamers using the intrinsic quenching power of the G-quadruplex to 4′-aminomethyl-4,5,8-trimethylpsoralen (AMT).1 The developed sensor showed high selectivity and good accuracy for detecting ATP. Liu et al. reported on a colorimetric biosensor for DNAs and proteins by an endonuclease-assisted target-responsive amplification method, and guanine-rich DNAs prolonged by terminal deoxynucleotidyl transferase (TdT).2 The generated guanine-rich DNA formed peroxidase-mimic DNAzyme with hemin. Detection of the target DNA at 1 pM and of thrombin at 100 pM were demonstrated. Zhang et al. reported on a non-label and enzyme-free half adder/subtractor based on the G-quadruplex structure and graphene oxide instead of any expensive free logic operation platform based on the G-quadruplex demonstrated.3

Zhang et al. reported on a non-label and enzyme-free half adder/subtractor based on the G-quadruplex demonstrated. They constructed a series of binary logic gates (AND, OR, INHIBIT, XOR). They also designed a non-label, enzyme-free half adder/subtractor based on the logic gates. Zhou et al. reported on an ultrasensitive and label-free sensing platform for Cd2+ detection containing a G-quadruplex-Cd(II) specific aptamer (GCDSA).3 They found that the GCDSA in a random coil sequence in the absence of Cd2+ is induced to fold into a G-quadruplex structure in the presence of Cd2+ with a detection limit of 0.15 nM. Wang et al. reported on aptamers specific to either Escherichia coli (E. coli) or Staphylococcus aureus, immobilized on a gold substrate to prepare SPR aptasensors for detecting their corresponding bacteria. They demonstrated the detection limits of 1 × 10^4 and 1 × 10^6 CFU/mL, respectively. Mazzafrianto et al. reported on an electrochemical sensor for ochratoxin A (OTA) by using an aptamer having a dithiol-based anchor.4 The sensor was based on a structure-switching signal-on scheme yielding a signal current upon interacting with OTA. They demonstrated high reproducibility and sufficient sensitivity with a detection limit of 113 pM of OTA. Zou et al. reported on a surface-enhanced Raman scattering (SERS) platform for the selective trace analysis of Hg2+ based on poly-thymine (T) aptamer-2-naphthalenethiol (2 NT)-modified Au nanoparticles.7 T aptamer forms a T-Hg2+-T structure with Hg2+, and 2-NT was used as a Raman reporter. The detection limit was 1.0 ppt, far below the limit of 10.0 ppb for drinking water required by the WHO. Weng et al. reported on a DNA electrochemical biosensor based on lambda exonuclease (λ-Exo)-assisted signal amplification.8 The target DNA hybridized with auxiliary DNA having a λ-Exo recognition site; the double strands were cleaved by λ-Exo. The target DNA was released, and continued to hybridize with remaining auxiliary DNA, forming a recycle for target reutilization. Finally, they detected the remaining auxiliary DNA to evaluate the amount of the epidermal growth factor receptor (EGFR) gene, with a detection limit of 10 pM.

Sensors targeting nucleotides have also been updated by those with high sensitivity. Wang et al. reported on an ultrasensitive electrochemical DNA biosensor based on carboxylated multi-walled carbon nanotube/molybdenum disulfide composites (MWCNTs-COOH/MoS2) for detecting the KRAS gene.9 They demonstrated the detection limit of the target DNA achieved down to 3 fM with a linear range from 1 × 10^−3 to 1 × 10^3 M. They demonstrated a determination of the KRAS gene in human serum samples with good accuracy and high precision due to a large conductivity and a large active surface area of the MWCNTs-COOH/MoS2 nanocomposites. Kong et al. reported on an ultrasensitive sensor using reversible addition-fragmentation chain transfer (RAFT) polymerization as a signal amplification strategy for the detection of CYFRA 21-1 DNA fragment.10 They employed magnetic beads modified with peptide nucleic acid probes to specifically capture the CYFRA 21-1 DNA. Hybridization was followed by CPAD tethering to the duplexes, and fluorescent tags were introduced to the duplexes through RAFT polymerization. They demonstrated a detection limit of 0.02 fM with great selectivity against base mismatched DNA.

Nucleotides are feasible to construct probe molecules, which are even complicated and sophisticated, as building blocks. They enable the probes to recognize targets of not only nucleotides, but also other species other than nucleotides, while widely expanding the possibility of sensors. Nowadays, the detection of biomarkers of environmental and biomedical importance becomes more attractive and focused.10-14 Further...
developments of the sensors are expected to play active roles in this field.

**Keywords** Sensors, nucleotides, DNA, RNA, aptamers, DNAzymes

**References**