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Commentary

Next Wave Diagnostic Tools Using CRISPR and Advanced Sensor Technologies

Tariq Hassan*

Department of Molecular Diagnostics, Nile Valley University, Cairo, Egypt

DESCRIPTION

In contemporary biomedicine, the ability to detect a single strand of nucleic acid or a tiny shift in molecular concentration can make all the difference. Recent advances in CRISPR based detection systems and advanced biosensor platforms are reshaping diagnostic possibilities, blending molecular biology, photonics, and materials science. This article explores how CRISPR/Cas systems are adapted for ultrasensitive detection of nucleic acids, and how biosensor innovations plasmonic systems, quantum sensing, graphene based transistors, and label free formats push diagnostic resolution to new levels.

CRISPR/Cas systems offer a natural specificity: A guide RNA leads the Cas enzyme to its complementary target, then cleavage occurs. In diagnostic adaptation, this specificity is coupled with "collateral cleavage" activity: Once the target is bound, the activated Cas enzyme cleaves nearby reporter probes (often short nucleic acids tagged with a fluorophore and quencher). The cleavage event releases the fluorophore, producing a detectable signal. Because that cleavage may affect many reporter molecules per target binding, the system shows intrinsic signal amplification, helping detect very low target loads.

To further boost sensitivity, researchers embed CRISPR systems within plasmonic nanomaterials. Plasmonics exploits collective oscillations of electrons in metallic nanostructures, sensitive to changes in local refractive index or to electromagnetic field enhancements. When a plasmonic nanoparticle or thin metal film is functionalized with CRISPR components, target binding and collateral cleavage lead to local optical changes (shifts in resonance or enhanced fluorescence), thereby enhancing readout sensitivity. One review describes how combining CRISPR/Cas modules with plasmonic nanostructures improves signal strength and reduces background noise, enabling detection of viral RNA, small molecules, or proteins with greater performance.

Another strand involves integrating CRISPR with novel reporters or signal transducers. For example, systems using Aggregation Induced Emission (AIE) luminogens have been developed: The Cas cleavage of a reporter leads to a controlled aggregation change that amplifies fluorescence. When combined with spherical nucleic acid architectures, such platforms offer substantial improvements in sensitivity relative to traditional CRISPR detection. On the biosensor side, plasmonic sensors themselves remain widely explored. Surface Plasmon Resonance (SPR) and Localized Surface Plasmon Resonance (LSPR) sensors monitor shifts in peak resonance wavelengths or intensity as biomolecules bind at metallic surfaces. In diagnostics, label free, real time monitoring is possible, and coupling with nanostructured metals or dielectric layers refines detection limits. A study on plasmonic biosensors outlines their continuous evolution and how researchers balance sensitivity, specificity, and ease of fabrication.

Graphene is now central in many biosensor designs. Its high electron mobility, large surface area, and ability to interface with biomolecules make it ideal for Field Effect Transistor (FET) sensors. In a graphene FET architecture, binding of a nucleic acid or protein on the graphene channel modulates local charge distribution, thereby altering device conductance. Because graphene is extremely sensitive to surface adsorption events, even small binding events can produce detectable signals. A comprehensive study highlights applications of graphene FET sensors for DNA/RNA detection, including rapid virus detection.

Graphene works well also in optical sensing. In plasmonic or Surface-Enhanced Raman Scattering (SERS) systems, graphene or graphene derivatives can interact with metallic nanostructures to quench fluorescence background, stabilize binding regions, or help amplify Raman signals. The combination improves signal clarity when detecting low concentration biomarkers. Quantum sensing is emerging as a complementary direction. Some devices use Nitrogen Vacancy (NV) centers in diamond defects in the diamond lattice with spin properties sensitive to magnetic or electric perturbations. In a recent proposal, NV centers were coupled with molecular transducers to convert presence of viral RNA to magnetic noise changes, which are read out optically. In one SARS CoV 2 sensor, theoretical models suggested detection sensitivity down to a few hundred RNA copies, with minimal false negatives.

Correspondence to: Tariq Hassan, Department of Molecular Diagnostics, Nile Valley University, Cairo, Egypt, E-mail: tariq.hassan@nvu.edu.eg

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