**Table S1.** Comparison of the advantages and disadvantages of various simplification strategies.

|  |  |  |  |
| --- | --- | --- | --- |
| Simplification strategy | | Advantage | Disadvantage |
| Extraction-free detection strategy | Heat/chemical cracking | Simple and fast operation; Extremely low cost; No solid-phase carrier dependence | Low nucleic acid purity; Limited sample applicability; Poor repeatability |
| Magnetic bead purification | Simple operation and easy to automate; High purity and low risk of contamination; Wide range of application | Residual risk of magnetic beads; High equipment dependence; Higher cost |
| Membrane-based purification | Easy and fast operation; High purity nucleic acid extraction; Wide range of applications | Potential risks of cross-contamination; Membrane binding capacity limitations; and risk of sample loss |
| Microfluidic-based purification | High efficiency and speed; high integration and automation; ultralow sample/reagent consumables | High technical complexity; Cost and commercialization bottlenecks |
| CRISPR/Cas-based enrichment | High specificity; Suitable for low abundance nucleic acids; High compatibility for point-of-care testing | CrRNA-dependent design; Potential off-target effects |
| Amplification-free detection strategy | Signal conversion strategy | Rapid, high sensitivity detection; Portable and low-cost | High technical complexity; Requires sample preprocessing; Low commercial maturity |
| Signal enhancement strategy | Ultrahigh sensitivity; High signal amplification; Portability and low-cost | Nanomaterial synthesis and modification complexity; Cost and large-scale production issues; Background signal interference |
| Target/signal enrichment strategy | Ultrahigh sensitivity and single-molecule detection; High-throughput multiplexing capability; Low risk of contamination | High technical complexity; Expensive equipment; Complex data analysis |
| Cascade signal amplification strategy | Enhanced signal amplification; Ultrahigh specificity; Multiplexing potential; Compatible with complex samples | Complex reaction system; Risk of nonspecific signaling; High requirements for sample purity |
| Integrated response strategy | Traditional one-pot detection | Simplified operating procedures and reduced cross-contamination | Risk of target and primer degradation; Low sensitivity |
| Optimized one-pot detection | Simplified operating procedures and reduced cross-contamination; Amplification is compatible with CRISPR assays | Complex and costly reagent design; Limited sensitivity |
| Microfluidic integrated detection | Automation and integration; Rapid detection and low sample consumption; Portability and POC potential; Multidetection capability | Technical complexity; Cost and scale-up challenges; Amplification dependence |
| Simple output strategy | Ultrasensitive lateral chromatography system | Simple operation and no complex instruments are required; Low cost, suitable for large-scale applications; It is highly portable and suitable for on-site detection | Restricted sensitivity, dependent on nucleic acid amplification; Weak quantification; Limited multiplexing capability |
| Smartphone readout system | Portability and ubiquity; Real-time data processing and sharing; Low cost and scalability | Dependence on smartphone performance; Ambient light interference; Standardization challenges |
| Integrated small readout system | High sensitivity; Low-cost equipment and user-friendliness; | Relies on preamplification; Requires signal conversion design; Patent barriers |