DOI: 10.7860/JCDR/2026/89478.24359

Review Article

Dentistry Section

Salivary Biomarkers for Early Detection of Oral Diseases: A Narrative Review of Diagnostic Technologies and Clinical Applications with a Su-Field Systems Analysis

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ABSTRACT

Saliva has emerged as a promising non invasive diagnostic biofluid containing a diverse range of biological molecules, including cytokines, nucleic acids, enzymes, metabolites, extracellular vesicles, and microbial components that reflect physiological and pathological processes within the oral cavity. Owing to its ease of collection, cost-effectiveness, and suitability for repeated sampling, saliva has gained increasing attention as a diagnostic medium for the early detection, monitoring of oral diseases, particularly oral squamous cell carcinoma and periodontal disease. Recent advances in nanotechnology have significantly enhanced the sensitivity and specificity of biosensor platforms, enabling the detection of low-abundance salivary biomarkers with improved analytical performance. Artificial Intelligence (AI) and machine-learning approaches further strengthen diagnostic capabilities by facilitating the interpretation of complex biomarker datasets and supporting clinical decision making. In addition, digital health technologies and teledentistry platforms offer opportunities for real-time data management, remote monitoring, and integration of diagnostic information into routine clinical workflows. This narrative review summarises the biological basis of salivary biomarkers and examines emerging diagnostic technologies relevant to oral disease detection. Furthermore, Substance-Field (Su-Field) analysis, a core Teoriya Resheniya Izobretatelskikh Zadach {TRIZ (in Russian)}, which means Theory of Inventive Problem Solving methodology, is employed as a conceptual systems-engineering framework to identify system-level limitations and guide optimisation of salivary diagnostic systems. The analysis identifies key challenges, including biological variability, signal instability, limited clinical validation, and interoperability barriers, while highlighting potential optimisation strategies. Integration of salivary biomarker science with biosensing technologies, Artificial Intelligence (AI), digital health systems, and Su-Field-guided system optimisation may facilitate the development of reliable chair-side diagnostic platforms for early detection, disease monitoring, and precision oral healthcare.

Keywords: Biosensing, Early diagnosis, Machine learning, Point-of-care systems, Precision medicine, Teledentistry, Translational research

INTRODUCTION

Salivary diagnostics has gained increasing attention as a promising, non invasive alternative to blood-based testing for the detection and monitoring of oral and systemic diseases. Saliva contains a diverse range of biological constituents including proteins, nucleic acids, metabolites, hormones, and microorganisms that reflect physiological and pathological states of the body [1,2]. In the oral cavity, pathological processes such as inflammation, microbial dysbiosis, and tumourigenesis lead to the release of cytokines, enzymes, extracellular vesicles, and nucleic acids from epithelial cells, immune cells, and oral microorganisms into saliva. These biomolecules provide valuable molecular information regarding disease initiation and progression, making saliva a biologically informative diagnostic fluid for oral diseases. Because saliva collection is simple, painless, and cost-effective, it is particularly suitable for chair-side diagnostics and large-scale screening programs in preventive dentistry.

Recent advances in nanotechnology have significantly improved the sensitivity and specificity of biosensors designed for salivary biomarker detection. Nanomaterial-based sensing platforms enable rapid and multiplexed analysis, supporting early disease detection and personalised treatment strategies [3,4]. In parallel, AI and Machine Learning (ML) techniques have emerged as powerful tools for interpreting complex diagnostic datasets and supporting clinical decision making [5]. Digital and mobile health interfaces further enhance accessibility by enabling real-time data transmission, storage, and remote monitoring [6].

Despite these technological advances, the clinical translation of salivary diagnostics into routine dental workflows remains limited. Current systems often function as isolated components rather than integrated ecosystems. Challenges include inconsistent sample handling, signal instability, limited interoperability between devices, and insufficient feedback mechanisms between clinicians and analytical platforms [7]. These issues highlight the need for a structured systems-engineering framework capable of identifying interaction gaps and guiding targeted improvements.

The TRIZ offers a systematic methodology for analysing and optimising complex technical systems. Su-Field analysis, a core TRIZ tool, represents systems as interactions between substances and fields and enables identification of incomplete, insufficient, or harmful interactions [8-13]. Applying Su-Field analysis to salivary diagnostic platforms provides a novel interdisciplinary perspective for identifying system-level limitations, improving interactions among diagnostic components, and guiding optimisation strategies that integrate engineering principles with clinical dentistry.

Therefore, the present narrative review aims to summarise current evidence on salivary biomarkers and emerging diagnostic technologies for oral diseases, including nanobiosensors, AI-based analytics, and digital health platforms. Furthermore, it applies Su-Field analysis as a conceptual systems-engineering framework to identify system level limitations and propose optimisation strategies for the development of reliable and clinically adaptable chair-side diagnostic systems.

Fundamentals of Salivary Diagnostics

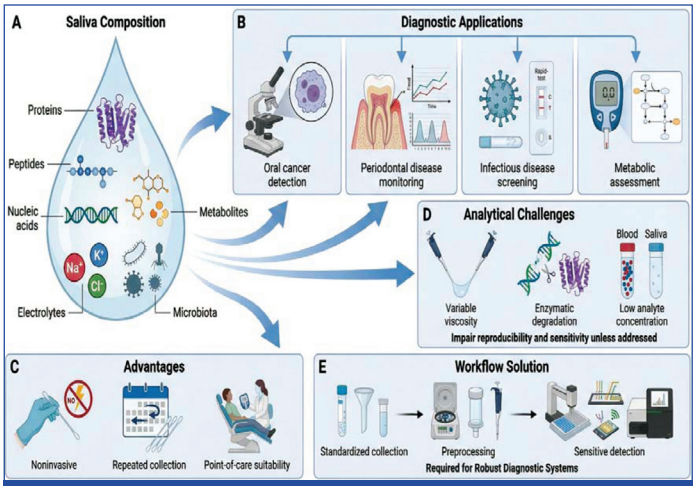
Saliva is a composite biofluid containing proteins, peptides, nucleic acids, metabolites, electrolytes, and microbiota that can serve as diagnostic fingerprints for oral and systemic disease [1,3,7]. Salivary diagnostics have demonstrated applications in oral cancer detection, periodontal disease monitoring, infectious disease screening, and systemic metabolic assessment [9,14,15]. During disease progression, damaged epithelial cells, activated immune cells, and microbial communities release inflammatory mediators, nucleic acids, and metabolic by-products into saliva, providing measurable molecular signatures that can be exploited for diagnostic purposes. Representative salivary biomarkers, their detection platforms, and clinical applications are summarised in [Table/Fig-1] [7,9,14-17].

Disease/Condition	Salivary biomarker(s)	Biological role	Detection method	Clinical application	Sensitivity/Specificity (where reported)
Oral squamous cell carcinoma	IL-8, miRNA panels	Tumour-associated inflammation and carcinogenesis	Nanobiosensor / PCR	Early cancer detection	Moderate to high diagnostic accuracy reported in systematic reviews; values vary across biomarkers and studies.
Periodontal disease	MMP-8, IL-1β	Connective tissue degradation and inflammation	Immunoassay / Biosensor	Disease monitoring	Moderate to high sensitivity and specificity reported for active periodontal disease detection.
Viral infections	Viral RNA (e.g., SARS-CoV-2)	Pathogen detection	RT-PCR / Microfluidics	Rapid screening	High sensitivity and specificity reported for saliva-based RT-PCR assays.
Systemic metabolic disorders	Cortisol, glucose metabolites	Stress and metabolic status indicators	Electrochemical Biosensor	Systemic health monitoring	Diagnostic performance varies according to analyte and platform.

[Table/Fig-1]: Representative salivary biomarkers, detection platforms, and clinical applications [7,9,14-17].
PCR: Polymerase chain reaction, IL-8: Interleukin 8, RT-PCR: Reverse transcription PCR, MMP: Matrix metalloproteinases, SARs-CoV-2: Severe acute respiratory syndrome coronavirus 2

Advantages of saliva sampling include non invasiveness, ease of repeated collection, and suitability for point-of-care testing in dental settings [3,7].

However, saliva presents analytical challenges such as variable viscosity, enzymatic degradation, and low analyte concentrations relative to blood, which can reduce reproducibility and analytical sensitivity [7,16]. Robust diagnostic systems therefore require standardised collection methods, preprocessing, and sensitive detection platforms [Table/Fig-2].



[Table/Fig-2]: Overview of saliva-based diagnostics showing: (a) Saliva composition; (b) Diagnostic applications; (c) Advantages; (d) Analytical challenges; and (e) Workflow solutions.
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Biological Basis and Sources of Salivary Biomarkers in Oral Disease

Salivary biomarkers originate from multiple biological sources within the oral cavity. These biomarkers may be categorised into proteins, cytokines, enzymes, nucleic acids, metabolites, extracellular vesicles, and microbial products, each reflecting different pathological mechanisms associated with oral disease progression. During inflammatory, infectious, or neoplastic processes, epithelial cells, immune cells, periodontal tissues, and oral microorganisms release cytokines, enzymes, nucleic acids, metabolites, and extracellular vesicles into saliva [7,15,16]. For example, inflammatory mediators such as Interleukin-8 (IL-8) and matrix metalloproteinases are elevated during periodontal tissue destruction, whereas tumour-associated micro Ribonucleic Acids (RNAs) and cytokines may be released by malignant cells in oral squamous cell carcinoma [7,14]. These molecular alterations provide the biological foundation for saliva-based diagnostic technologies and support the development of non invasive biomarker detection platforms for early disease identification and monitoring [7,14,15].

Su-Field Analysis Framework

Su-Field analysis is a core analytical tool of the Theory of Inventive Problem Solving (TRIZ) that models systems as interactions between substances (S) and operative fields (F). It is widely used in engineering to identify incomplete, insufficient, or harmful interactions within complex systems and to develop targeted optimisation strategies [8]. In the present review, Su-Field analysis is applied conceptually to evaluate salivary diagnostic systems and identify opportunities for improving clinical performance.

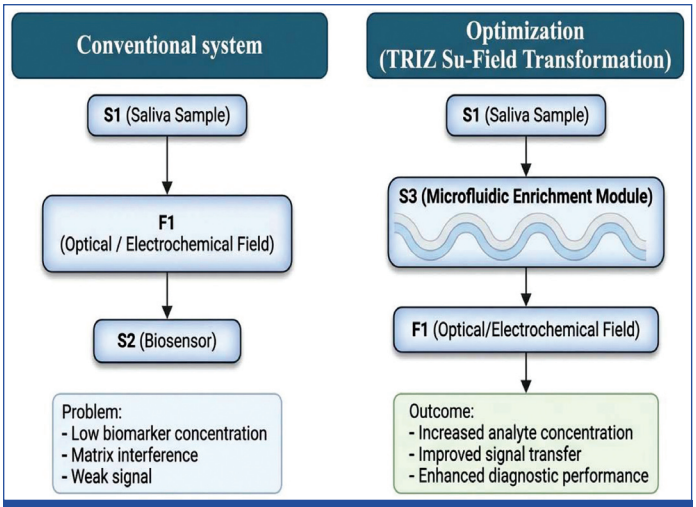
In a salivary diagnostic platform, the system can be represented using Su-Field models, where substances (S) interact through an operative field (F). Representative Su-Field models within salivary diagnostic systems include:

- S1 (saliva sample) - F (optical/electrochemical field) - S2 (biosensor transducer)
- S1 (saliva) - F (microfluidic hydrodynamic field) - S2 (sample-preparation module)
- S1 (biosensor output) - F (informational/algorithmic field) - S2 (AI analytics)

An illustrative Su-Field model for saliva-based biosensing is shown in [Table/Fig-2]. In a conventional diagnostic system, the saliva sample (S1) interacts with the biosensor (S2) through an optical or electrochemical field (F1). However, low biomarker concentration and matrix interference may weaken signal transfer, resulting in reduced analytical performance. To address this limitation, an auxiliary substance (S3), such as a microfluidic enrichment module, may be introduced between the sample and the biosensor. This modification improves analyte concentration, enhances signal transmission, and increases diagnostic reliability. According to TRIZ principles, the addition of auxiliary substances or transforms an insufficient system into a more complete and effective system as illustrated in [Table/Fig-3] [8].

A clinically robust salivary diagnostic system requires stable transfer of information or energy across these fields and compensatory mechanisms to mitigate harmful interactions, such as enzymatic degradation, non specific binding, and sample variability. Su-Field transformation rules therefore provide a structured framework for identifying system limitations and guiding targeted optimisation of biosensing, analytical, and digital-health components [8].

Application of Su-Field analysis to salivary diagnostic systems reveals several recurring system-level limitations. In nanobiosensor platforms, insufficient interaction between the analyte and the sensor transducer may occur due to low biomarker concentrations and adsorption competition from abundant salivary proteins. In addition, harmful interactions such as non specific binding, signal interference,



[Table/Fig-3]: Conceptual Su-Field model illustrating optimisation of saliva-based biosensing systems. Introduction of an auxiliary substance (S3), represented by a microfluidic enrichment module, strengthens the interaction between the saliva sample (S1) and the biosensor (S2), thereby improving signal transmission and diagnostic performance. Adapted from TRIZ Su-Field principles [8].
Figure generated by author

and photobleaching in optical assays may reduce analytical performance. According to TRIZ principles, these limitations can be addressed through the introduction of auxiliary substances or fields that strengthen system interactions. Examples include surface-passivation layers, high affinity functionalised capture probes, on-chip sample-cleaning strategies such as magnetic bead capture or size-exclusion membranes, and signal-amplification approaches using enzymatic labels, catalytic nanoparticles, or nucleic acid amplification techniques [18,19].

The Su-Field evaluation presented in this review is conceptual and based on established TRIZ principles and published engineering literature rather than dedicated computational modelling software [8].

Nanobiosensing in Salivary Diagnostics

Nanomaterials such as gold nanoparticles, graphene, carbon nanotubes, quantum dots, and nanostructured electrodes have significantly enhanced the performance of biosensors by increasing surface area, improving electron transfer, and enabling signal amplification [20,21]. Recent microfluidic-integrated nanobiosensor platforms have demonstrated point-of-care capabilities for the detection of salivary biomarkers, with rapid assay times and detection limits approaching clinically relevant concentrations [6,18]. Several studies have reported successful detection of salivary biomarkers, including IL-8, microRNAs, and tumour-associated proteins associated with oral squamous cell carcinoma, highlighting the potential of nanobiosensing technologies for early disease detection and monitoring [9,14,20].

Emerging Technologies in Salivary Diagnostics

a. **Artificial Intelligence (AI) and data analytics:** The ML and Deep Learning (DL) approaches have been applied to salivary proteomics, metabolomics, and imaging outputs to classify disease states and predict clinical outcomes [5,22]. However, several challenges continue to limit clinical implementation of AI in healthcare. Limited and non representative datasets may introduce dataset bias, reducing model generalisability across diverse patient populations. In addition, domain shift between training and real world clinical environments can adversely affect model performance [22-24]. Explainable Artificial Intelligence (XAI) has emerged as an important approach for improving transparency, interpretability, and clinician trust in AI-assisted decision making [22-24]. Transfer learning has also been increasingly utilised to improve model performance when large annotated datasets are unavailable, particularly in healthcare applications involving limited clinical data [23,24]. From a Su-Field perspective, these challenges represent incomplete informational fields that may hinder reliable integration of AI into salivary diagnostic systems.

   Strategies to complete informational fields include creation of standardised multicentre annotated datasets, application of transfer-learning techniques to adapt models to new cohorts, incorporation of explainable AI methods to provide human-interpretable outputs, and implementation of closed-loop learning systems in which algorithm predictions are continuously validated against clinical outcomes to improve performance over time [22-24].

b. **Digital interfaces and clinical integration:** Mobile apps, cloud platforms, and Electronic Health Record (EHR) connectors enable secure storage, visualisation, and clinician-patient communication for salivary diagnostic data. Teledentistry workflows have expanded dramatically since Coronavirus 2019 (COVID-19), demonstrating remote triage and monitoring use-cases that can incorporate point-of-care saliva testing [25]. Linking saliva-based diagnostic platforms with electronic dental records may enable longitudinal monitoring of biomarker profiles and support personalised disease risk assessment.

Su-Field analysis reveals unstable informational fields due to inconsistent data formats and limited interoperability across dental software and hospital EHRs. Adoption of interoperability standards-particularly Health Level Seven – Fast Healthcare Interoperability Resources (HL7 FHIR) and open EHR templates- facilitates structured data exchange, enabling downstream AI analytics and longitudinal patient monitoring [26,27]. Additionally, cybersecurity, data privacy {Health Insurance Portability and Accountability Act (HIPAA/ General Data Protection Regulation (GDPR) considerations}, and user-centred interface design are essential to maintain trustworthy and usable digital ecosystems [28]. Regulatory considerations are becoming increasingly important for AI-assisted diagnostic systems. Regulatory agencies such as the United States Food and Drug Administration (FDA) and European regulatory authorities require evidence of safety, effectiveness, transparency, and continuous performance monitoring before clinical implementation [28].

Application of su-field analysis in salivary diagnostic systems: Building upon the Su-Field framework described above, the principles of Su-Field transformation can be applied to identify practical interventions that strengthen interactions among sensing, analytical, and digital-health components. These system-level optimisation strategies provide a roadmap for improving the performance, reliability, and clinical translation of salivary diagnostic systems.

System-Level Optimisation Strategies

Applying Su-Field transformation rules across the sensing-analytics-interface pipeline highlights that effective chair-side salivary diagnostics requires coordinated optimisation of multiple interconnected subsystems rather than isolated technological upgrades. Each design principle represents a targeted intervention that strengthens system interactions and reduces instability in real clinical environments.

1. **Modular microfluidic front-end:** A modular microfluidic front-end serves as the first stabilisation layer between the biological sample and the sensing platform. Saliva is a complex and variable fluid containing mucins, enzymes, microorganisms, and debris that can interfere with sensor performance. Microfluidic pre-processing modules can incorporate filtration, dilution, mixing, and analyte concentration steps within disposable cartridges. These modules standardise sample volume, reduce viscosity, and remove interfering substances before detection. From a Su-Field perspective, this module functions as an auxiliary substance that converts harmful saliva-sensor interactions into stable and reproducible signal transfer. Modular design also enables plug-and-play replacement, simplifies sterilisation, and supports scalability in routine dental clinics [6,11].

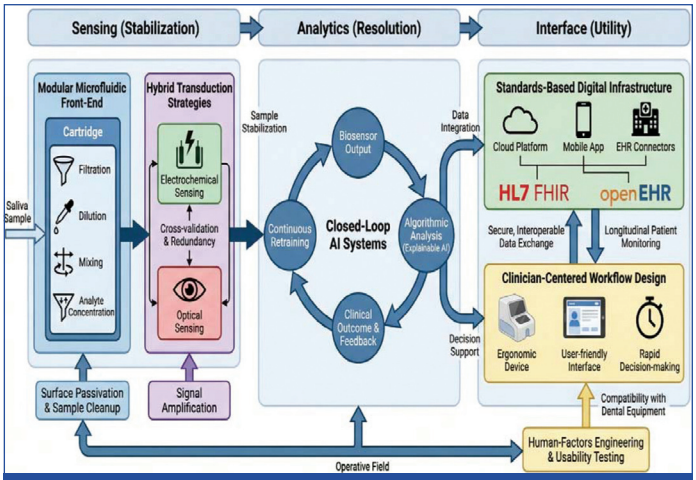
2. **Hybrid transduction strategies:** Hybrid transduction combines multiple sensing modalities most commonly electrochemical and optical detection to enhance analytical robustness. Electrochemical sensors provide high sensitivity and quantitative output, while optical methods such as fluorescence or plasmonic sensing offer strong specificity and multiplexing capability. Integrating these modalities within a single platform enables cross-validation of results, reduces false positives, and improves diagnostic confidence in complex salivary matrices. In Su-Field terms, hybrid transduction strengthens operative fields and introduces redundancy, thereby increasing system resilience. Such multimodal architectures are particularly valuable for detecting low-abundance biomarkers associated with early disease stages [10,20].
3. **Closed-loop AI systems:** Closed-loop AI systems create continuous feedback between data acquisition, algorithmic analysis, and clinical outcomes. Instead of static machine-learning models, adaptive systems are periodically retrained using new patient data and validated against confirmed diagnoses. This feedback loop improves predictive accuracy over time and reduces model drift. Incorporating explainable AI techniques allows clinicians to interpret algorithmic decisions, increasing trust and facilitating adoption. Within the Su-Field framework, closed-loop AI completes informational fields by reinforcing bidirectional communication between the analytical engine and real world clinical performance [12,23,28].
4. **Standards-based digital infrastructure:** A standards-based digital infrastructure ensures interoperability among diagnostic devices, dental software, and EHRs. Frameworks such as HL7 FHIR enable structured data exchange, secure cloud storage, and integration with existing healthcare information systems. This infrastructure supports longitudinal patient monitoring, remote consultation, and large-scale data aggregation for research and quality improvement. From a systems perspective, standardised digital architecture stabilises informational interactions and prevents fragmentation. It also facilitates regulatory compliance, cybersecurity protection, and future scalability [26,27].
5. **Clinician-centred workflow design:** Even technologically advanced diagnostic tools will fail if they disrupt clinical workflow. Clinician-centred design emphasises ergonomic usability, minimal training requirements, and seamless integration into routine dental procedures. Interfaces should present results clearly, support rapid decision making, and avoid excessive cognitive load. Chair-side devices must be compact, easy to disinfect, and compatible with existing equipment. Human-factors engineering and user-experience testing are essential to ensure adoption. In Su-Field terms, optimising human-system interaction strengthens the final link in the diagnostic chain, transforming technological capability into practical clinical value [13].

Together, these strategies form an integrated optimisation framework that aligns engineering innovation with clinical usability. Their coordinated implementation is essential for translating salivary diagnostic technologies from laboratory prototypes into reliable, scalable tools for preventive dentistry [Table/Fig-4] [13,29].

The principal system components, associated limitations, Su-Field classifications, and corresponding optimisation strategies are summarised in [Table/Fig-5] [7,16,18,20,22-24,26-28].

Future Directions for Clinical Translation of Salivary Diagnostics

Advancing chair-side salivary diagnostics from promising prototypes to routine clinical tools requires coordinated progress across clinical validation, device engineering, regulatory science, and healthcare integration. The following priority areas represent critical directions for future research and development.



[Table/Fig-4]: Su-Field optimisation framework.
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System component	Identified limitation	Su-Field classification	Optimisation strategy
Saliva sample interface	Matrix interference and variability	Harmful interaction	Microfluidic pre-processing and stabilisation
Nanobiosensor surface	Low analyte abundance	Insufficient field	Signal amplification and surface functionalisation
AI analytics	Dataset bias and poor interpretability	Incomplete informational field	Multicentre datasets and explainable AI
Digital interface	Interoperability and security gaps	Unstable informational field	Standards-based secure architectures

[Table/Fig-5]: System-level limitations in salivary diagnostics and Su-Field-guided optimisation strategies [7,16,18,20,22-24,26-28].

1. **Multicentre validation and standardised clinical protocols:** One of the most important future directions for clinical translation of salivary diagnostics is the establishment of large multicentre validation studies using standardised saliva collection and analysis protocols. Variability in saliva collection techniques, sample storage conditions, biomarker extraction methods, and analytical platforms limits comparability of diagnostic accuracy, biomarker performance, and clinical outcomes across studies and may hinder regulatory approval. Collaborative multicentre trials can generate robust datasets that reflect diverse patient populations and real world clinical settings. Shared, curated datasets also enable benchmarking of diagnostic performance and facilitate the training and validation of reliable AI models. Such standardisation is essential for developing evidence-based clinical guidelines and accelerating regulatory acceptance of salivary diagnostic devices [12,14].
2. **Plug-and-play microfluidic cartridge development:** Future device engineering should focus on user-friendly, disposable microfluidic cartridges that integrate sample preprocessing, reagent storage, and detection within a compact system. These cartridges must maintain reagent stability at room temperature, minimise manual handling, and operate with minimal training to suit busy dental environments. Advances in microfabrication, material science, and reagent stabilisation can enable robust cartridges that are scalable and cost-effective. Plug-and-play designs also support modular system upgrades and simplify maintenance, which are crucial for widespread adoption in clinical practice [6,11].
3. **Regulatory frameworks for AI-assisted diagnostics:** As AI becomes increasingly integrated into diagnostic platforms, regulatory frameworks must evolve to address issues of safety, transparency, and accountability. Future research should support the development of regulatory standards that require continuous performance monitoring, post-market surveillance, and clear reporting of algorithm updates. Adaptive AI systems must demonstrate consistent accuracy across diverse

populations and maintain audit trails that allow traceability of clinical decisions. Collaboration between researchers, clinicians, and regulatory agencies will be necessary to create governance models that balance innovation with patient safety [23,28].

4. **Integration into preventive dental care pathways:** Another critical direction is embedding salivary diagnostics within structured preventive care pathways. Research should evaluate how chair-side salivary testing can inform screening programs, longitudinal disease monitoring, and personalised treatment planning. Cost-effectiveness analyses are needed to demonstrate economic value for healthcare systems and private practices. Integration with digital health platforms can enable population-level surveillance and remote monitoring, supporting preventive dentistry and early intervention strategies. Evidence from digital dentistry and clinical decision support research suggests that such integration can improve patient outcomes when aligned with clinician workflows [9,13].

Collectively, these future directions emphasise that the maturation of salivary diagnostics depends on interdisciplinary collaboration and systems-level thinking. Progress in validation science, device engineering, regulatory policy, and clinical integration will determine whether salivary diagnostics becomes a routine component of precision oral healthcare.

DISCUSSION

The expanded analysis presented in the present review highlights that the future success of salivary diagnostics depends less on isolated technological breakthroughs and more on the deliberate engineering of integrated, clinically usable systems. Although substantial progress has been achieved in nanobiosensing, AI, and digital health platforms, their translation into routine dental workflows requires coordinated optimisation across biological, technical, and human factors domains [6,7,10]. Su-Field analysis provides a structured systems framework to identify weak, missing, or harmful interactions and to guide rational improvements that enhance reliability and clinical relevance [8].

A fundamental issue in salivary diagnostics is the intrinsic biological variability of saliva. Salivary composition is influenced by circadian rhythms, hydration status, medication use, oral hygiene, and systemic health conditions [16,30]. Such variability can introduce noise that masks low-abundance biomarkers and compromises analytical reproducibility. Previous studies emphasise the importance of standardised sampling protocols and preanalytical controls to improve diagnostic reliability [3,7]. From a Su-Field perspective, these challenges represent unstable interactions between the biological substance (saliva) and the sensing interface. Integration of microfluidic pre-processing and stabilisation modules can normalise sample conditions and strengthen signal transfer [5,11].

Nanobiosensor technologies have demonstrated remarkable sensitivity improvements through nanostructured materials and advanced surface functionalisation [20,31]. Recent point-of-care platforms show promise for rapid detection of salivary biomarkers associated with oral cancer and infectious diseases [6,10,14]. However, real world clinical adoption requires devices that are robust, cost-effective, and simple to operate in dental environments. Hybrid sensing strategies combining electrochemical and optical modalities can improve analytical confidence and system resilience against matrix interference [10,20].

AI-driven analytics further expand diagnostic capabilities by enabling pattern recognition across complex salivary datasets [5,12,22]. However, concerns regarding dataset bias, generalisability, and interpretability may hinder clinician acceptance [23,28]. Establishing multicentre datasets, external validation protocols, and explainable AI frameworks is essential for trustworthy deployment. Within the Su-Field framework, these measures complete informational fields by reinforcing feedback loops between algorithmic predictions and clinical outcomes. Unlike traditional narrative reviews that primarily summarise individual biomarker studies, the present review provides a systems-level perspective by integrating biosensing technologies, AI analytics, and digital health infrastructures to highlight pathways for clinical translation of salivary diagnostics.

Digital integration determines whether salivary diagnostics can be embedded into everyday dental workflows. Interoperable information systems enable secure data exchange and integration with EHRs [26,27]. Adoption of standardised frameworks such as HL7 FHIR supports scalable digital infrastructures [28]. Evidence from digital dentistry research shows that clinician-centred usability and workflow compatibility are critical for technology adoption [13,31].

Regulatory agencies increasingly require rigorous validation of AI-assisted diagnostic systems and continuous performance monitoring to ensure patient safety [30]. In addition, economic considerations and cost-effectiveness analyses will influence implementation in clinical practice. Interdisciplinary collaboration among dentists, engineers, and data scientists is essential to address these translational challenges.

Despite promising technological developments, variability in salivary biomarker expression among individuals and across disease stages remains a major challenge for standardisation of saliva-based diagnostics. As a narrative synthesis, it does not provide quantitative meta-analysis of diagnostic accuracy. Rapid technological evolution may outpace available published evidence [9,31]. Furthermore, empirical validation of Su-Field-guided optimisation requires future clinical trials. Despite these limitations, the framework presented here offers a structured roadmap for integrating diverse technological advances into cohesive diagnostic ecosystems. Cost-effectiveness remains an important consideration for large-scale implementation of saliva-based diagnostics. Future studies should evaluate economic feasibility, especially in low-resource and community-based settings where non invasive screening tools may provide substantial public health benefits.

Overall, the discussion underscores that the next generation of salivary diagnostics will emerge from the convergence of biosensing innovation, intelligent analytics, and interoperable digital infrastructure [9,13]. A systems-engineering perspective guided by Su-Field principles provides a coherent strategy for transforming laboratory technologies into reliable chair-side tools.

For salivary diagnostics to become clinically meaningful, integration into routine dental workflows is essential. Chair-side salivary testing has the potential to support early detection of oral squamous cell carcinoma, risk assessment for periodontal disease progression, and screening for systemic conditions such as diabetes or viral infections. In practical terms, an optimised system would involve standardised saliva collection, automated microfluidic pre-processing, rapid biosensor-based detection, and AI-assisted interpretation delivering a clear risk stratification output to the clinician within minutes.

Such real-time diagnostic support could enhance preventive care strategies, enable timely referrals, and facilitate personalised treatment planning. In community and resource-limited settings, portable saliva-based diagnostic platforms may expand access to early disease screening and reduce barriers associated with blood-based testing. By aligning technological innovation with clinician-centred workflow design, salivary diagnostics can evolve from experimental prototypes into scalable tools that strengthen preventive and precision dentistry. In high-risk populations such as tobacco users and individuals with potentially malignant oral disorders, saliva-based diagnostic tools may provide a non invasive strategy for early screening of oral squamous cell carcinoma.

From a clinical perspective, the integration of salivary biomarker detection with rapid biosensor platforms and AI-assisted analysis could enable chair-side screening tools that support early identification of oral cancer and other oral diseases in routine dental practice.

Limitation(s) and Research Gaps

Although salivary diagnostics shows significant potential for non invasive disease detection, several limitations remain. Variability in saliva composition, differences in collection methods, and preanalytical factors may affect biomarker stability and diagnostic reproducibility. Many biosensor technologies and AI models also require large multicentre datasets for reliable clinical validation. Future research should focus on standardised saliva collection protocols, large-scale clinical trials, and integration of diagnostic platforms into routine dental workflows.

CONCLUSION(S)

Salivary biomarkers offer significant potential for the non invasive early detection and monitoring of oral diseases. Advances in nanobiosensing technologies, AI, and digital health platforms have enhanced the diagnostic capabilities of saliva-based testing. Su-Field analysis highlights key system-level challenges and provides a conceptual framework for identifying opportunities for optimisation and clinical integration. Continued interdisciplinary collaboration and clinical validation are essential for translating salivary diagnostics into reliable chair-side tools for precision oral healthcare.

Acknowledgement

The authors would like to acknowledge interdisciplinary contributions from the fields of dentistry, bioengineering, and health informatics that have advanced research in salivary diagnostics. No external editorial assistance was used in the preparation of this manuscript.

Authors' contribution: All authors contributed to the conceptualisation, literature review, analysis, and manuscript preparation. All authors read and approved the final manuscript.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 30, 2026
- Manual Googling: Jul 09, 2026
- iThenticate Software: Jul 11, 2026 (1%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Apr 01, 2026**
Date of Peer Review: **May 27, 2026**
Date of Acceptance: **Jul 14, 2026**
Date of Publishing: **Sep 01, 2026**