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ARTICLE

Rapid Bacterial Diagnostics at the Point of Care: Emerging Electrochemical and Raman-Based Approaches

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Abstract

Bacterial infections impose a major clinical and economic burden, which is likely to increase further as antimicrobial resistance rises, reinforcing the need for early detection to accelerate and better target therapy. Conventional culture-based diagnostics are well established, but they are too slow to inform early therapeutic decisions. This review frames the growing need for rapid bacterial diagnostics in the context of acute infection, antimicrobial stewardship, and point-of-care testing. We focus on emerging electrochemical biosensing and Raman-based approaches and compare them with established laboratory methods, including culture, MALDI-TOF MS, nucleic acid amplification tests, sequencing, and antimicrobial susceptibility testing, emphasising where central laboratories remain essential and where near-patient testing could alter clinical management. We highlight clinically relevant targets, recognition strategies, signal generation, materials design, manufacturability, and performance in complex biological matrices. Rather than focusing only on analytical sensitivity, we discuss the practical factors that will determine translation, including reproducibility, workflow integration, validation in real samples, and regulatory readiness. Taken together, the most clinically promising rapid bacterial diagnostics are those that deliver reliable, actionable information within the time window in which treatment decisions can still meaningfully influence outcomes. In this context, the most promising point-of-care systems are not those intended to replace central laboratories, but those designed to complement them by enabling earlier, better-targeted, and more judicious antimicrobial therapy.

1. Clinical Need and Diagnostic Landscape

Bacterial infections still place a heavy burden on healthcare systems, not only because of the illness and deaths they cause, but also because of the cost of managing them.[1] Treating these infections effectively depends on identifying the causative pathogen, and doing so early enough for the result to actually shape clinical decisions. That is why "rapid" is best understood in clinical, not just technical, terms. In sepsis and other acute infections, rapid may mean minutes or a few hours, since even modest delays in appropriate therapy can cause serious consequences.[2–7] In less urgent situations, such as urinary or respiratory tract infections, a same-day response may be sufficient to support targeted treatment and avoid unnecessary empirical prescribing. Conventional culture-based diagnostics, however, generally take 24–72 hours to deliver definitive identification and susceptibility results, making them too slow for many early treatment decisions.[2,5,6] This gap is especially obvious in severe infections such as sepsis, where early recognition and timely antimicrobial therapy are closely tied to patient survival.[2–6] The burden is not only clinical. These infections often lead to longer hospital stays, intensive care admission, and costly management of complications.[3–5] Faster microbiological diagnostics therefore matter at two levels: they can improve outcomes for individual patients and ease pressure on healthcare systems. Just as importantly, earlier pathogen identification makes it easier to move away from broad-spectrum empirical treatment toward more targeted therapy that is, in most cases, more appropriate.[8,9] That point matters even more in the context of antimicrobial resistance (AMR). Empirical antibiotic treatment is often unavoidable, particularly when a patient is critically ill, but the longer broad-spectrum therapy is continued without microbiological clarification, the greater the selective pressure it creates. That, in turn, supports the emergence and spread of AMR.[8,9] Rapid diagnostics can help interrupt this pattern by shortening the time to identification, enabling earlier de-escalation where justified, and, ideally, providing at least some information on likely susceptibility or resistance. Seen this way, rapid bacterial

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diagnostics are not just diagnostic tools; they are also part of the practical machinery of stewardship.[8–11] Even so, central microbiology laboratories remain indispensable. Culture still underpins the field because it yields viable isolates for confirmatory identification, epidemiological work, and phenotypic antimicrobial susceptibility testing. Modern instrumental laboratory methods such as matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS), molecular assays, sequencing, and rapid phenotypic antimicrobial susceptibility testing (AST) have accelerated key steps in the workflow, but they have not eliminated the need for centralised facilities or expert interpretation. The point of point-of-care (POC) and near-patient testing, then, is usually not to replace the central laboratory altogether. It is to bring actionable information closer to the clinical encounter. In the emergency department, intensive care unit, outpatient clinic, or field setting, an earlier result may influence triage, the start or narrowing of therapy, infection-control measures, or the decision to escalate to more comprehensive laboratory testing.[12–14] These pressures shape what next-generation rapid bacterial diagnostics need to deliver.[15] Ideally, they should work directly from clinical samples with little preparation, produce results within a genuinely useful timeframe, and remain reliable in complex biological matrices. They also need to balance analytical performance with practical concerns such as ease of use, robustness, cost, and compatibility with stewardship goals. Where possible, they should go beyond simple organism detection and provide resistance-related information that can guide treatment more precisely.[16] In the end, the most useful rapid diagnostics will not necessarily be the fastest in purely analytical terms, but the ones that deliver dependable, clinically relevant information at the point where it can still change what happens next.

Scope of this Review. This review focuses on electrochemical biosensing and Raman-based optical approaches, especially surface-enhanced Raman scattering (SERS), as two emerging routes for rapid bacterial diagnostics at the point of care.[17,18] They both combine short analysis times with portable instrumentation, potential for miniaturisation, and compatibility with disposable or low-cost formats. Electrochemical methods provide quantitative output through simple electronics and readily manufacturable electrode platforms, whereas Raman offers molecular fingerprinting and, particularly in SERS, strong signal enhancement. In both cases, performance is governed by the chemistry of the sensing interface; in electrochemical platforms by receptor immobilisation, surface charge, electron transfer, antifouling layers, and matrix-tolerant electrode design, and in SERS by reproducible plasmonic substrates with controlled hotspot density, analyte access, surface functionalization, and signal normalisation. Other rapid diagnostic modalities, including nucleic-acid amplification tests (NAATs), sequencing, MALDI-TOF MS, and broader optical screening methods, are discussed only as benchmarks or contextual comparators.

2. Electrochemical and Raman-Based POC Strategies for Rapid Bacterial Detection

2.1 Electrochemical Approaches

Electrochemical biosensing is one of the most compatible strategies for POC bacterial diagnostics.[19,20] Electrochemical measurements can be performed using compact, low-power, and inexpensive instrumentation that can be readily integrated into disposable sensors and microfluidic platforms (**Figure 1A**).[21,22] Another key advantage is the inherently quantitative nature of the signal, since current, potential, charge, or impedance can be directly digitised and correlated with bacteria (or related analyte) concentration.[23] These characteristics make electrochemical biosensors attractive for rapid testing near the patient, where low cost, portability, and operational simplicity are essential. Practical performance is shaped by the choice of bacterial target, the selectivity of the biorecognition layer, the robustness of the signal-generation mechanism, and the manufacturability of the electrode platform.[24] Electrochemical sensing has evolved from proof-of-concept demonstrations toward more translational questions such as matrix tolerance, storage stability, antifouling behaviour, reproducibility, and compatibility with clinical workflows.[25,26]

2.1.1 Detection Targets

Electrochemical assays can be designed for several targets, including whole cells, cell lysates, secreted biomarkers, and nucleic acids or their amplification products (**Figure 1B**).[27,28] Whole-cell detection is appealing because it addresses the actual presence of the pathogen and may require only limited sample preparation.[28] At the same time, it is often complicated by non-specific adsorption, low bacterial abundance, and the difficulty of distinguishing closely related organisms in complex samples. Lysate-based detection[29] improves access to intracellular components and can generate stronger or more reproducible signals, but it adds a lysis step and may sacrifice information about cell viability.[30] Secreted biomarkers, such as toxins, enzymes, metabolites, or quorum-sensing molecules, offer another attractive route because they are soluble and can often be accessed more quickly than intact cells. Their presence may also reflect ongoing bacterial activity. Still, these analytes are not always uniquely linked to viable pathogen burden, which limits straightforward interpretation.[31] Nucleic acid detection generally offers the highest specificity, since it can be directed toward species-, strain, or resistance-associated sequences.[32] In many cases, though, this comes with the need for upstream amplification, with electrochemistry functioning as the final readout stage. This is particularly relevant in CRISPR-assisted formats, where sequence recognition is coupled to an electrochemical reporter system.[33,34] In practice, the selection of the target should be guided by the intended clinical use of the assay,[35] rather than solely by the lowest reported limit of detection.[36] Whole-cell, lysate-based, and secreted-biomarker assays are useful for rapid detection, triage, or monitoring of

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bacterial activity.[37,38] Nucleic-acid assays provide more specific information by detecting species-, strain-, or resistance-associated sequences, which is highly therapeutically relevant information; however, the presence of a resistance gene does not necessarily prove phenotypic resistance.[39] Assays intended to support susceptibility-related decisions must therefore measure the bacterial response to antibiotic exposure more directly, for example, by assessing changes in viability, metabolism, impedance, or redox activity after a brief antibiotic exposure. Once the target and intended clinical role are clear, the next design question is how to build a recognition interface capturing the target reliably at the electrode surface.[40]

2.1.2 Biorecognition Strategies

Selectivity at the electrode surface is usually achieved through antibodies, aptamers, peptides, lectins, bacteriophages, or nucleic acid probes, as shown in **Figure 1C**.[41,42] Antibody-based electrochemical biosensors remain widely used because they offer established affinity toward bacterial surface structures or secreted toxins. Their use in POC settings, however, is not without drawbacks. Orientation at the surface can be difficult to control, proteins may denature during storage or immobilisation, and cross-reactivity can reduce analytical specificity.[43] Aptamers are often presented as an attractive alternative because they are produced synthetically, are straightforward to chemically modify, and can be integrated well into electrochemical signal designs.[44] They are especially useful in redox-labelled formats. Even so, their performance in complex clinical matrices is often less impressive than in buffered model systems, which remains an important practical limitation.[45] Peptides and lectins provide additional recognition options, particularly in settings where broader-spectrum capture, lower cost, or greater robustness is preferred over absolute specificity.[46,47] Bacteriophages and phage-derived proteins are also highly interesting for whole-cell sensing, since they bring biologically evolved recognition and may preferentially bind viable bacteria.[48] For molecular assays, nucleic acid probes still dominate, as they allow selective targeting of pathogen-specific genes and resistance determinants.[49] Across all of these strategies, the central translational question is not simply how strongly the receptor binds its target, but whether the recognition layer remains stable, selective, and manufacturable under realistic POC storage and operating conditions.[50] Thus, receptor performance is inseparable from the electrode material, because surface chemistry governs loading, orientation, electron transfer, antifouling behaviour, and stability.

2.1.3 Electrode and Interfacial Materials

Recent advances in nanomaterials have expanded the range of available materials that can support immobilisation of the biorecognition element while maintaining sufficient conductivity of the electrode transducing layer.[51] In this context, graphene-based materials, MXenes,[52,53] carbon nanotubes,[54] metallic nanoparticles,[55,56] metal oxides,[57,58] conducting polymers,[59,60] and hybrid composites[61] (**Figure 1D**) have been explored to improve receptor binding, electron transfer, catalytic amplification, antifouling behaviour, or mechanical robustness. Graphene and its derivatives are particularly attractive because they combine a high accessible surface area, favourable electronic properties, and chemically tunable surfaces.[62–64] Controlled functionalization further expands this material portfolio by enabling dual-functionalized, Janus-type, or doped derivatives such as nitrogen-containing analogues.[65–68] Carboxyl- and ethynyl-functionalized derivatives provide a suitable platform for bioconjugation strategies, including carbodiimide coupling and click chemistry, which can be used to immobilise biorelevant systems such as antibodies, aptamers, or nucleic acid probes.[69,70] However, graphene-based materials should be viewed as one option rather than a default solution. Printed carbon inks, carbon black, AuNP-modified electrodes, PEDOT:PSS or polypyrrole layers, magnetic-particle-assisted formats, and MXene-containing composites[71–73] may be equally or more appropriate depending on the target organism, sample matrix, readout mode, and intended point-of-care workflow. From a translational perspective, the decisive question is therefore not whether a platform uses a particular nanomaterial, but whether the electrode material supports a stable, reproducible, matrix-tolerant, and manufacturable sensing interface. Actual performance remains largely dependent on surface chemistry, antifouling design, storage stability, and batch-to-batch reproducibility, variables that deserve more attention than they often receive in proof-of-concept studies.[74,75]

2.1.4 Signal Generation and Readout Modes

Electrochemical bacterial sensors rely on several main readout modes, most notably voltammetric or amperometric, potentiometric, and impedimetric approaches. Voltammetric and amperometric methods are widely used because they provide sensitive and quantitative current-based signals while relying on relatively simple electronics.[37] These formats are well-suited to redox mediators, enzyme labels, and catalytic amplification strategies, and they can be implemented readily in disposable sensor platforms.[76] Potentiometric sensing is encountered less often, but it can be useful when bacterial recognition leads to measurable changes in potential through ion flux, pH shifts, or membrane-associated phenomena. Its low power demand is attractive, although in practice, issues such as signal drift and reference-electrode instability can limit robustness.[37,77] Impedimetric sensing is particularly appealing for POC use because it often allows label-free detection.[78] When bacteria or biomolecules bind to the electrode surface, they alter the interfacial electrical properties, making it possible to monitor the event directly without additional reporters.[79,80] The drawback is that impedance signals are also highly sensitive to matrix effects and non-specific fouling.[81] More generally, the choice between label-free and labelled sensing reflects a familiar trade-off; label-free systems simplify the workflow, whereas labelled or catalytic approaches provide stronger and more robust signals, albeit at the cost of greater assay complexity.

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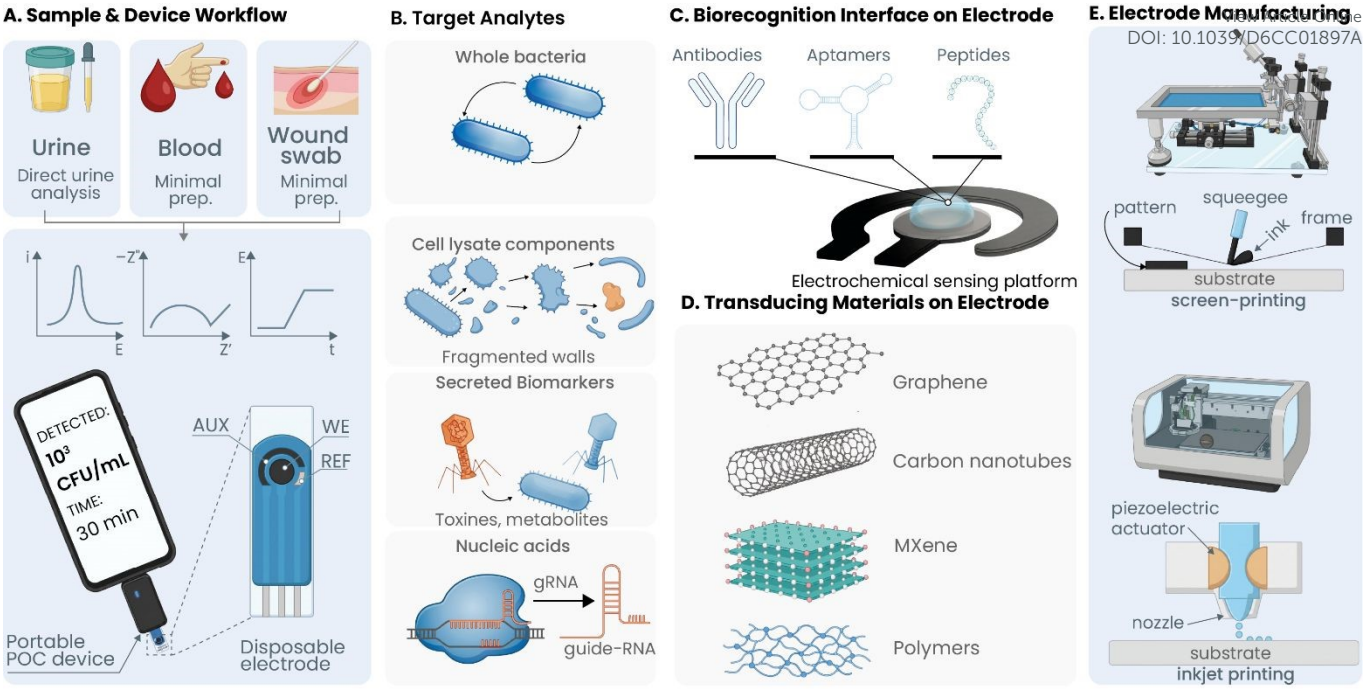

Figure 1. Schematic overview of electrochemical POC strategies for bacterial pathogen detection. **(A)** A representative workflow is shown from the collection of clinically relevant samples, including urine, blood, and wound swabs, to rapid readout using a portable POC device and disposable electrode. **(B)** The main analytical targets include whole bacteria, lysate-derived cell components, secreted biomarkers, and nucleic acids. **(C)** Selectivity at the electrode surface is achieved through different biorecognition layers, including antibodies, aptamers, and peptides. **(D)** The figure highlights representative transducing materials used at the electrode interface, including graphene, carbon nanotubes, MXene, and polymers. **(E)** Scalable electrode fabrication approaches, including screen printing and inkjet printing, illustrate the manufacturing routes that support translation toward disposable electrochemical diagnostic platforms. The figure was created using BioRender.com and Adobe Illustrator.

2.1.5 Electrode Platforms and Manufacturing

Electrode fabrication becomes a critical consideration in translating electrochemical biosensors from laboratory demonstrations to manufacturable devices (**Figure 1E**). Screen-printed electrodes (SPEs) constitute the most practical platform for POC electrochemical sensing because they are inexpensive, scalable, and readily adapted into disposable integrated devices.[82] SPEs can be produced on ceramic, plastic, or flexible substrates and easily configured as complete three-electrode systems.[83] Inkjet-printed electrodes offer finer digital patterning and more efficient use of functional materials, which is particularly attractive when working with advanced inks, including expensive nanomaterials and biocomponents.[84–86] They are well-suited to form-factor optimisation, rapid prototyping and customised device architectures.[87] Flexible and wearable formats are gaining more attention, especially for wound-related sensing, but they bring a different set of requirements, including mechanical robustness, resistance to moisture, and stable performance under repeated deformation.[88,89]

2.1.6 Representative Case Studies and Benchmarking

The electrochemical sensing literature contains many encouraging examples of bacterial detection, but direct comparison between studies is often difficult. Differences in target choice, sample matrix, preparation workflow, and reporting standards make it hard to judge which approaches are genuinely closer to clinical use.[37] For that reason, benchmarking should focus less on record-low limits of detection alone and more on metrics that are meaningful in practice.[41] Urine is one of the more promising matrices for electrochemical sensing, partly because it is relatively accessible and urinary tract infections remain a major use case for rapid triage.[90,91] Blood is far more demanding: bacterial concentrations are often low, while matrix interference is high, so direct detection usually requires enrichment, lysis, or molecular amplification.[92] Swab and wound samples are also attractive for planar or flexible electrochemical devices, but their heterogeneity and often polymicrobial nature make interpretation more complicated.[93,94] Across all of these sample types, the most informative studies are those that report time-to-result from sample to answer, validate performance in real matrices, and compare results directly against culture or PCR. Reproducibility, false-positive behaviour, storage stability, and workflow simplicity are equally important. In the end, electrochemical POC diagnostics are most convincing when they combine reliable recognition chemistry, manufacturable electrode platforms, matrix-tolerant interfaces, and benchmarking that is clinically realistic rather than merely analytically impressive.[95,96]

2.2 Raman-Based Optical Approaches

2.2.1 Realistic Role in POC Bacterial Workflows

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Optical methods offer a complementary approach to bacterial detection, providing spatially resolved, chemically informative signals without direct electrical contact with the sample. Raman spectroscopy, especially SERS, combines molecular specificity with the potential for miniaturised, portable instrumentation (**Figure 2A**). Their main value is not simply rapid readout, but the ability to extract biochemical fingerprints, discriminate bacterial phenotypes, and support multiplexed analysis when combined with suitable substrates and data-processing workflows. Moreover, optical signals are spatially resolvable. This spatial resolution enables integrated "lab-on-a-chip" architectures that simultaneously map morphology and chemical concentration, providing diagnostic depth previously reserved for centralised pathology labs.[97] Among optical methods, Raman spectroscopy is a rapid technique that often eliminates the need for complex, time-consuming laboratory analyses.[98] It also provides precise measurements, enabling ultrasensitive multiplexed detections required for many clinical applications.[99,100] Additionally, Raman spectroscopy can be simply combined with other optical and non-optical methods to enable accessible sample handling and processing of clinical patient samples without the need for complex wiring, often using disposable optics or measuring kits.[101] Furthermore, its integration with microscopy enables high spatial resolution (< 1 µm) and hyperspectral imaging, providing one more level of information.

2.2.2 Fingerprints, Strengths, and Limitations

The specificity of a bacterial Raman spectrum is a function of stoichiometric proportions of biomolecules, including proteins, lipids, carbohydrates, and nucleic acids.[102] The spectral region of interest can be divided into two discrete regions: the high-wavenumber region and the fingerprint region, separated by a silent region (**Figure 2B**). The high-wavenumber region (2,800–3,800 cm^{-1}) is dominated by –CHx, –N–Hx, and –O–H stretching vibrations. Spectral data from this region offer remarkable precision in discriminating between cell wall types (Gram-positive vs Gram-negative), with an accuracy approaching 100 %.[103] On the other hand, the fingerprint region (400–1,800 cm^{-1}) is where key diagnostic markers reside. The phenylalanine ring-breathing mode at 1,003 cm^{-1} serves as a stable internal reference for protein content. This band, together with bands characteristic of dipicolinate and amino acids, was used to study bacterial endospores.[104] The DNA spectral band at 785 cm^{-1} (phosphorus diester O–P–O bonds) tracks, for example, nucleic acid fragmentation during antibiotic exposure.[105] The amide I band (1,650–1,670 cm^{-1}) provides essential insight into secondary protein structures and overall cellular viability.[106] The entire Raman spectrum can be used to discriminate between *Escherichia coli* strains using a combination of Raman microscopy and chemometric methods.[107] Similar results were also obtained for nine clinical species of bacteria isolated from clinical samples,[108] or 11 bacterial mutants of *E. coli* MDS42.[109] Despite its non-destructive nature and single-cell resolution, spontaneous Raman scattering is inefficient: only approximately 1 in 107 photons undergo the Raman effect. This necessitates long acquisition times and sophisticated baseline correction to mitigate the high autofluorescence background inherent in biological complex matrices. These limitations explain why SERS has become the more practically attractive Raman-based strategy for bacterial diagnostics in complex or low-biomass samples.

2.2.3 SERS as the Practical Raman Route for Real Samples

SERS addresses the intrinsic weakness of the Raman effect by utilising the localised surface plasmon resonance (LSPR) of noble metal nanostructures (**Figure 2B**). When an analyte is adsorbed onto or placed near the formed plasmonic "hotspots", the Raman signal is amplified by factors of up to 10^{10}. This allows the detection of single bacterial cells or viral particles directly from complex matrices, including whole blood,[110] tissue samples,[111] and even wastewater.[112] The evolution of SERS substrates has shifted from simple stochastic colloidal systems to complex 3D architectures, including structured surfaces fabricated via electron-beam lithography or glancing-angle deposition.[113–115] These architected models provide uniform hotspot distribution and precisely regulated nanogaps. Moreover, 3D scaffolds, such as metallic foams and vertically aligned nanorod arrays, present other interesting approaches.[116–118] These hierarchical structures extend hotspot density into the third dimension, thereby prolonging photon lifetimes through multiple scattering events. When integrated into flexible polymer or cellulose substrates, these "swab-and-sense" platforms enable conformal, in situ detection of bacteria on complex, non-planar surfaces such as wound beds or food products.[119] Furthermore, by employing surface cell-imprinting, these matrices can be engineered with bio-specific cavities tailored for target bacterial strains, effectively mitigating matrix interference and enhancing selectivity.[120] To move beyond qualitative detection, advanced calibration models are required. Such models are usually based on a set of Internal Standards (IS).[121] Incorporating SERS probability models allows for signal normalisation and enables qualitative analysis of a single molecular target over a 9-order-of-magnitude concentration range.[122] The next applicable calibration strategy to achieve quantitative information is Digital SERS, which is primarily used at ultra-low concentrations where intensity-based metrics usually fail.[123,124] Digital SERS treats detection as a binary "on/off" event across a pixelated substrate, deriving concentration from the fraction of active hotspots via a Poisson distribution. The last example of a quantitative approach is an application of a SERS Performance Factor (SPF).[125] This metric reflects intrinsic sensitivity by comparing the slopes of concentration-dependent SERS and standard Raman curves.

2.2.4 Label-Free vs Tag-Based SERS

The choice between label-free and tag-based SERS usually involves a fundamental trade-off between speed, simplicity, and specificity. Label-free profiling measures the intrinsic Raman signature of the pathogen. It is rapid and low-cost, providing a direct readout of the cellular physiological state (e.g., metabolic activity or antibiotic stress).[126] However,

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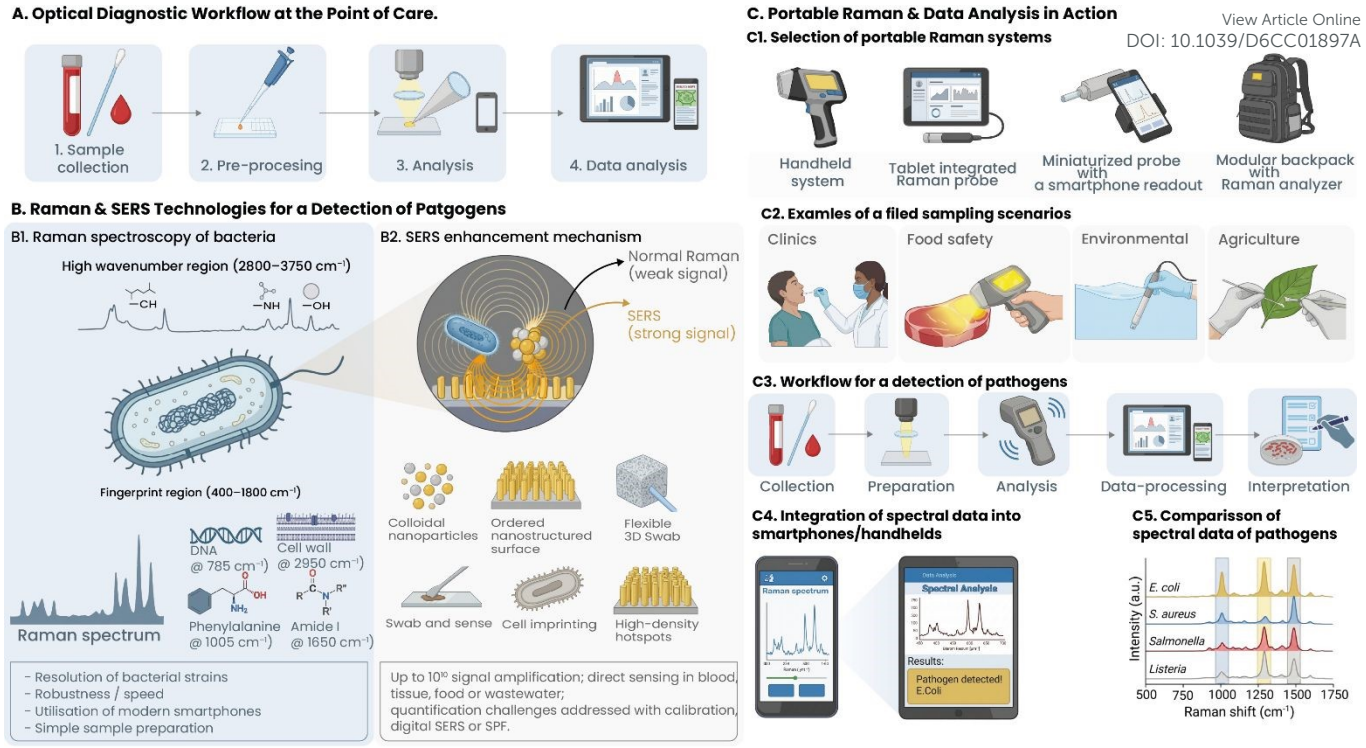

Figure 2. Schematic overview of Raman/SERS-based point-of-care strategies for bacterial pathogen detection. **(A)** A simplified workflow is shown from sample collection and preprocessing to spectral acquisition and data analysis. **(B)** The figure highlights the basis of bacterial Raman detection and the signal enhancement achieved by SERS, together with representative substrate and sampling formats. **(C)** Portable Raman instrumentation, field and near-patient sampling scenarios, smartphone-assisted analysis, and spectral discrimination of representative pathogens illustrate the potential of these approaches for rapid decentralised testing. The figure was created using BioRender.com and Adobe Illustrator.

because the SERS enhancement effect decays rapidly with distance from the surface (r^{-6}), the signal is dominated by the outermost cell wall components. This similarity across strains usually requires a powerful machine learning or more advanced AI models to extract these small discriminative features.[127,128] Tag-Based SERS, including immuno and aptamer based techniques utilizes plasmonic cores functionalized with a Raman reporter and a recognition element, such as Immuno-SERS, which employs monoclonal antibodies in sandwich architectures to isolate targets from complex backgrounds,[129,130] offering unparalleled specificity, or aptamer-SERS, which uses synthetic DNA/RNA "chemical antibodies".[131] Aptamers are considerably more stable and cheaper in production than antibodies, might be stored at room temperature, can be fully engineered to undergo conformational changes upon target binding. This change initiates a displacement of the Raman reporter, which results in a highly quantifiable "signal-on" or "signal-off" transition. While tag-based methods excel in multiplexing (by using reporters with distinct, non-overlapping peaks), they increase assay complexity and also preparation time. From a clinical perspective, label-free methods are primarily suitable for fingerprint identification and phenotype distinction,[132] whereas labelled SERS is better suited for targeted pathogen identification or multiplex detection of selected markers.[133,134] Resistance information can be approached indirectly through resistance-associated spectral phenotypes, reporter panels, or antibiotic-induced changes in bacterial metabolism and viability, but these outputs should not be treated as equivalent to phenotypic AST unless they are benchmarked against susceptibility testing in clinically representative samples.[135]

2.2.5 Portable Raman and Data Analysis

The synergy between handheld hardware and chemometric processing drives the transition of Raman diagnostics to the field (**Figure 2C**). Handheld spectrometers, while rugged, often suffer from lower laser powers and limited integration times. Sophisticated data-driven tools are usually required to compensate for these hardware limitations, including machine learning methods such as support vector machines (SVMs) and Random Forests, as well as convolutional neural networks (CNNs). Recent reviews highlight the integration of SERS with artificial intelligence and microfluidic lab-on-chip formats as a practical route toward point-of-care diagnostics. AI can help interpret complex spectra, while microfluidics can standardise enrichment, mixing, washing, and sample handling in compact devices.[136] Portable Raman systems are, at the same time, getting smaller and smarter, approaching pocket-sized form factors at decreasing cost.[137,138] To address the limitations of the spectral intensity and interferences, Botto et al. utilised unsupervised Partial Least Squares Discriminant Analysis (PLS-DA) regression coefficients, combined with accuracy score maximisation in stratified k-fold cross-validation, to analyse 17 isolates belonging to the genera *Pseudomonas* spp., *Stenotrophomonas* spp., and *Erwinia* spp.[139] Similarly, to utilize

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a portable Raman system, Thomsen et al. developed a procedure allowing for the analysis of antibiotic-resistant and susceptible phenotypes by utilizing a spectral transformer (ST) machine learning (ML) model.[140] Interestingly, Zhao developed a working portable Raman system and in a combination with a frequently available paper- based SERS substrate (originally aimed for a tobacco packaging) and used them to detect *Staphylococcus aureus* and *Shigella flexneri* in a pork meat.[141] These examples demonstrate a trend in Raman detection of pathogens towards simple, field-manageable sample preparation, enabled by advanced signal processing and miniaturisation of hardware. Machine-learning-assisted Raman and SERS can help to reveal weak multivariate spectral differences that are difficult to assign peak by peak, especially in label-free bacterial profiling and phenotype discrimination.[127,132,142] Its diagnostic value, however, depends on diverse training data and validation beyond a single instrument, strain set, or controlled matrix.[143] Future studies should therefore include external test sets, cross-site testing, calibration transfer between instruments and substrate batches, standardised preprocessing, and transparent uncertainty reporting.[143] Machine learning is best viewed as an interpretive layer, not a substitute for robust substrates, chemistry, and clinically realistic benchmarking.[136,144] At present, Raman/SERS is most credible in controlled workflows using cultured or enriched material, defined matrices, or standardised preprocessing. Direct POC analysis of low-burden, heterogeneous clinical specimens remains largely preclinical because matrix interference, bacterial recovery, substrate reproducibility, and cross-site transfer still limit routine use.[145]

2.2.6 Complementary Optical Modalities in the Context of Raman-based Workflows

Although this review focuses on Raman, several complementary optical methods help define the broader landscape of POC testing. Colourimetric assays, including smartphone-assisted platforms, are attractive for simple screening because they provide a visually accessible readout, but they generally offer lower molecular specificity.[146,147] Fluorescence methods can be sensitive and spatially informative, although they usually require labelled reagents and careful background control.[148] SPR/LSPR platforms provide label-free monitoring of binding events, but their performance in clinical matrices can be limited by nonspecific adsorption and refractive index changes.[149] DHM and related phase-imaging approaches are better suited for monitoring bacterial growth, segmentation, or microfluidic culture behaviour than for direct molecular identification.[150] These methods are therefore mentioned here as complementary technologies, rather than as a second major focus of the review.

2.3 Comparative Perspective: Electrochemical vs Raman POC Strategies

Electrochemical and Raman platforms both offer routes toward rapid POC bacterial diagnostics, but they address this goal through different analytical strengths, practical constraints, and clinical use cases. Electrochemical systems align well with low-cost, near-patient testing because the hardware is simple, low-power, and readily adaptable to disposable sensors. The main weakness is connected with real samples, where fouling, non-specific adsorption, interference, and low bacterial counts can make performance less reliable, particularly in blood samples.[151,152] Raman approaches provide richer molecular information useful for label-free profiling, multiplexed analysis, and in some cases phenotypic discrimination,[153] but this added information depends on reproducible substrates, signal normalisation, spectral preprocessing, and robust data analysis.[154,155] For this reason, electrochemical platforms are currently most plausible for accessible matrices such as urine, wound exudate, or swabs, whereas Raman is strongest when molecular specificity or multiplexed readout is worth the added complexity. In bloodstream infections, both approaches still face major preanalytical barriers and should be viewed as triage or complementary tools to culture and phenotypic AST, not as replacements for them.[156] The intended use, therefore, has to be defined by the matrix and the decision context. Urine and wound or swab samples are the nearest-term settings for low-cost electrochemical screening or swab-compatible SERS; respiratory samples require stronger preprocessing because mucus, viscosity, and host background complicate both readouts.[157–159] In sepsis or bloodstream infection, especially in ICU or emergency-department workflows, greater device complexity may be acceptable if the result is rapid and actionable,[160] whereas field settings favour simple, robust, reagent-stable formats. Clinical actionability also requires more than binary pathogen detection.[156,160] For stewardship, the most useful platforms should identify resistance determinants, monitor antibiotic-induced changes in viability or metabolism,[39] or provide early susceptibility-related information. Electrochemical assays may do this through resistance-gene detection or viability/metabolite readouts, while Raman can capture antibiotic-response fingerprints or resistance-associated spectral phenotypes.[161] Both methods should therefore be benchmarked by their ability to support escalation, de-escalation, or earlier susceptibility-informed treatment, not by detection sensitivity alone. To make the practical comparison between the discussed technologies more explicit, **Table 1** summarises their main analytical targets, typical performance ranges, operational strengths, and translational limitations. A related cross-cutting issue is amplification, which influences both analytical sensitivity and practical point-of-care feasibility. In nucleic-acid assays, PCR and qPCR remain highly sensitive, whereas isothermal methods such as LAMP or RPA are better suited to decentralised testing because they reduce instrumentation requirements.[162] Electrochemical platforms may further improve sensitivity through enzyme labels, redox cycling, catalytic nanoparticles, nanostructured electrodes,[76] or CRISPR-coupled reporter cleavage,[33] while Raman approaches rely on plasmonic signal enhancement, reporter tags, internal standards, and digital SERS formats.[131,153,154] These strategies can substantially lower detection limits, but they may also

increase assay time, reagent complexity, washing steps, contamination risk, and susceptibility to matrix inhibition.[163]

3. Benchmarking, Validation, and Clinical Translation of Rapid Bacterial Diagnostics

The value of a rapid bacterial diagnostic is not determined solely by how quickly it produces a signal, but by how quickly it provides information that is actually useful in a clinical decision-making context relative to the existing microbiology workflow.[164] In practice, the most meaningful benchmark is therefore not an idealised proof-of-concept measured in buffer, but the established sequence of culture, species identification, and antimicrobial susceptibility testing (AST) that still underpins most treatment decisions. A strong, rapid test should be judged by whether it shortens the path to meaningful action, whether that means targeted therapy, de-escalation, triage, or escalation to central laboratory testing, rather than by analytical sensitivity alone.[165]

3.1 Laboratory Gold Standards for Bacterial Pathogen Identification

Conventional culture remains the clinical reference standard because it recovers viable organisms, supports phenotypic identification, and enables downstream AST. Its weakness, of course, is time, as shown in **Figure 3.** Enrichment, subculture, and susceptibility testing usually take at least overnight, and often longer, while contamination, low pathogen burden, and prior antibiotic exposure can further reduce recovery or complicate interpretation.[165] MALDI-TOF MS has substantially changed routine laboratory identification by allowing rapid and accurate species-level assignment once isolated colonies, positive blood-culture material, or otherwise enriched biomass are available.[166,167] Even so, direct-from-sample analysis remains much more difficult, especially in blood and similarly complex matrices, where low bacterial abundance, host background, and mixed infections can all interfere with performance.[168] NAATs, particularly PCR and qPCR, are now the most mature rapid alternatives for targeted pathogen detection, while isothermal amplification methods provide an important bridge toward simpler, lower-instrumentation testing closer to the patient.[169,170] Sequencing and metagenomic approaches offer the broadest diagnostic scope and can reveal polymicrobial or uncultivable organisms,[171] but in most cases, they still depend on specialised sample preparation, strict contamination control, and substantial bioinformatic support. For that reason, they currently fit more naturally into advanced laboratory workflows than into routine POC use.[172] AST cuts across all of these approaches. Genotypic assays can rapidly identify known resistance determinants, but phenotypic AST remains the clinically decisive endpoint because it reflects expressed susceptibility rather than genetic potential alone, even if that usually comes at the cost of time.[156]

3.2 Clinical Benchmarking

Clinical benchmarking merits at least the same level of attention as analytical sensitivity.[173,174] To make such benchmarking transparent, rapid bacterial diagnostic platforms should be compared using a common set of quantitative and operational descriptors, including the analytical target, the clinically relevant sample matrix, the reported limit of detection, the total sample-to-answer time, the sample preparation requirements, the comparator method, and the level of validation (**Table 1)**.[175] For bacterial diagnostics, reported limits of detection are difficult to compare because they may be expressed as CFU mL^{-1}, genome copies, colony equivalents, or molecular biomarker concentrations, and because values obtained in buffer often differ from those obtained in urine, blood, wound exudate, sputum, or food-related matrices.[176,177] Therefore, representative performance ranges are more informative than isolated best-case values. Electrochemical bacterial sensors commonly report 10^1–10^4 CFU mL^{-1} in simplified or moderately complex matrices, with assay times ranging from minutes to 1–2 h, depending on enrichment,

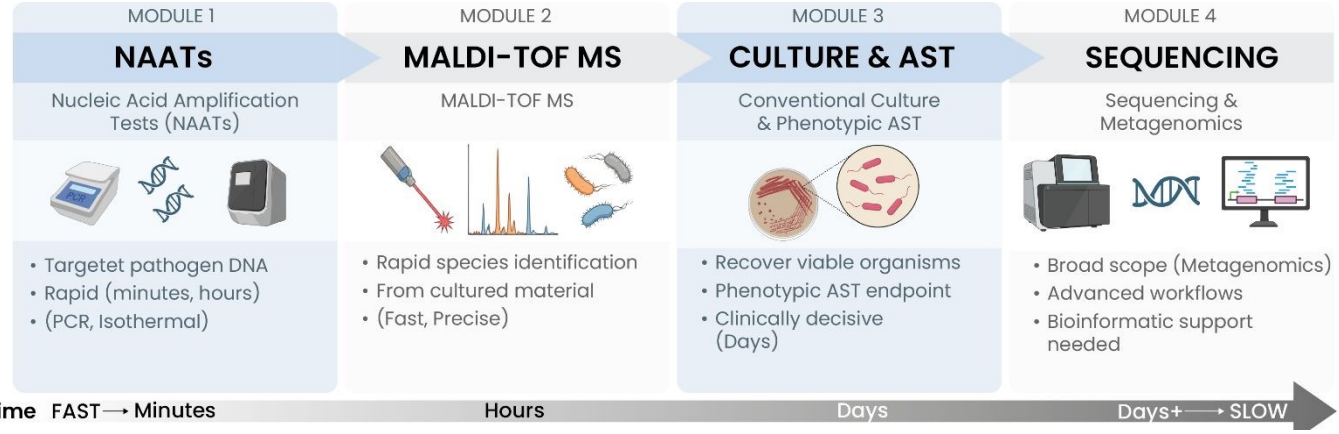

Figure 3. Overview of major diagnostic modules for bacterial pathogen identification across different time scales. NAATs provide rapid targeted detection within minutes to hours, MALDI-TOF MS enables fast species identification from cultured material, culture with phenotypic AST remains the clinically decisive but slower reference method, and sequencing/metagenomics offers the broadest scope at the cost of greater workflow complexity and longer turnaround. The timeline highlights the trade-off between speed, diagnostic breadth, and laboratory requirements. The figure was created using BioRender.com and Adobe Illustrator.

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labelling, or amplification.[18,177] SERS can reach single-cell to 10^2–10^5 CFU mL^{-1} under favourable conditions, but performance depends on substrate reproducibility, capture efficiency, acquisition time, and chemometric robustness.[178,179] These values should be read as indicative and matrix-dependent. Reported sensitivity, accuracy, or classification performance is meaningful only when the experimental context is clear.[180–182] Many electrochemical and Raman studies demonstrate excellent analytical performance in buffer, spiked samples, enriched cultures, or carefully controlled matrices, but these results do not necessarily translate directly to routine clinical specimens.[152,183–185] Real-world applicability depends on additional factors, including bacterial recovery from the sample, matrix-induced fouling or optical background, operator-dependent preprocessing, assay failure rate, and validation against clinically accepted comparator methods. Therefore, high-performance claims are most meaningful when supported by testing in relevant biological matrices, transparent sample-to-answer workflows, and independent validation using clinically representative samples.[174,175] The influential studies rely on prospective cohorts, or at least carefully curated retrospective ones, together with blinded analysis, transparent comparator definitions, and prevalence-aware reporting of sensitivity, specificity, positive predictive value, and negative predictive value.[180] Just as importantly, they report operational characteristics such as time-to-result from sample to answer, failure rate, number of operator steps, and any measurable effect on treatment escalation, de-escalation, or triage.[181] In many cases, these parameters say more about real clinical usefulness than an exceptionally low detection limit ever could. Future studies should report, at a minimum, the intended clinical use, the sample matrix and volume, the matrix-specific LOD, the total sample-to-answer time, the preprocessing and user steps, the comparator method, the assay failure rate, and the validation level.[24,176] They should also state whether the assay is intended for pathogen detection, resistance marker identification, or susceptibility-related decision support.[135] This makes it easier to separate proof-of-concept sensitivity from clinical actionability, and to judge detection limits alongside workflow complexity, matrix tolerance, and decision relevance. For spectral and optical platforms that rely on chemometrics or machine learning, internal cross-validation alone is insufficient.[182] More convincing validation should include independent external test sets, cross-site generalisation, calibration transfer between instruments or substrate batches, uncertainty reporting, and transparent reporting frameworks such as TRIPOD+AI when predictive models are involved.[174] These details may seem technical, but they are exactly what determine whether a platform is robust enough to move beyond a single well-controlled study.

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Table 1. Representative benchmarking parameters for electrochemical and Raman/SERS point-of-care bacterial diagnostics.*

Technology	Analytical target	Representative LOD range	Typical time-to-result	Common sample types	Clinical role/Key strengths	Main limitations
Electrochemical whole-cell sensors	Intact bacteria captured by an antibody, aptamer, peptide, lectin, or phage	~10^1–10^4 CFU mL^{-1}	~10–60 min, longer if enrichment is needed	Urine, wound swabs, food samples, diluted blood	Quantitative readout, low-cost electronics, disposable electrodes	Matrix fouling, non-specific adsorption, and limited validation in true clinical cohorts
Electrochemical nucleic-acid sensors	Species or resistance genes, often after amplification	~10–10^3 genome copies or equivalent	~30–120 min	Blood after extraction, urine, and respiratory samples	High specificity, resistance-marker detection possible	Extraction/amplification increases complexity and contamination risk
Electrochemical secreted-biomarker sensors	Toxins, enzymes, metabolites, quorum-sensing molecules	Highly analyte-dependent; often nM–pM or equivalent bacterial burden	~10–60 min	Urine, wound fluid, culture supernatants	Can indicate bacterial activity	Biomarker may not map directly to viable pathogen burden
Spontaneous Raman	Intrinsic bacterial biochemical fingerprint	Usually requires isolated/enriched cells or a high bacterial load	Seconds to minutes per spectrum; longer, including preprocessing	Colonies, enriched samples, urine or sputum after processing	Label-free, single-cell information, phenotypic insight	Weak scattering, fluorescence background, demanding data analysis
Label-free SERS	Enhanced intrinsic bacterial surface signals	Single-cell to ~10^2–10^5 CFU mL^{-1} depending on substrate and matrix	~10–60 min	Urine, swabs, food, environmental samples, selected blood workflows	Rapid spectral fingerprinting, potential strain discrimination	Substrate variability, matrix interference, and limited cross-site validation
Tag-based SERS	Antibody/aptamer-mediated pathogen capture with Raman reporters	Often ~10–10^3 CFU mL^{-1} under optimized conditions	~30–120 min	Urine, serum/plasma after preparation, swabs, food matrices	High specificity, multiplexing	More assay steps, higher reagent complexity, batch-to-batch reproducibility

*Ranges are representative rather than absolute; matrix, preprocessing, target organism, assay format, enrichment, and comparator method strongly affect reported performance.

3.3 Matrix effects and mitigation strategies

Biological matrices shape rapid bacterial diagnostics at every step, from pathogen recovery and target accessibility to signal generation and interpretation.[186] This is particularly important for point-of-care workflows, where extensive purification or specialist troubleshooting is usually unrealistic. Matrix interference is one reason why assays that perform well in buffer often lose reliability in clinical samples.[187,188] The challenge is matrix-specific. Urine is accessible and often contains clinically relevant bacterial loads, but variation in pH, ionic strength, salts, proteins, urea, and debris can affect receptor binding, electrode response, nanoparticle stability, and optical background.[189] Blood is much more complicated.[151,190] Bacterial counts may be very low, while blood cells, plasma proteins, haemoglobin, coagulation factors, and host DNA create strong interference. Respiratory samples, sputum, wound exudates, and swabs add viscosity, mucus, tissue debris, polymicrobial content, and uneven bacterial distribution.[191] Limit of detection should therefore be reported

in the matrix that matches the intended clinical use, not only in buffer or simplified media. In electrochemical biosensors, matrix effects commonly appear as electrode fouling, non-specific adsorption, altered charge-transfer resistance, pH or ionic-strength shifts, inhibition of redox or enzymatic reactions, and reduced access to the recognition layer.[152] This is particularly problematic for label-free impedimetric systems, where non-specific interfacial changes can mimic binding.[183] Mitigation usually relies on antifouling and blocking layers, PEG-based[192] or zwitterionic interfaces,[193,194] dilution or washing, selective capture, magnetic preconcentration, filtration, or microfluidic separation.[195–197] In Raman, matrix effects appear as autofluorescence, broad backgrounds, optical scattering, competitive adsorption, nanoparticle aggregation, and inconsistent contact between bacteria and hotspots.[163,184] Proteins, salts, mucus, or host debris can mask label-free SERS signals, while tag-based assays may suffer from reduced capture efficiency or non-specific reporter binding.[185] Practical mitigation includes clarification, enrichment, immunomagnetic or aptamer-mediated capture, controlled washing, filtration, microfluidic concentration, more robust substrate functionalization, internal Raman standards, standardised preprocessing, and external validation of chemometric models.[198–200] Matrix assessment should therefore include bacterial recovery, matrix-specific LOD, background signal, false-positive behaviour, sample volume, preprocessing, failure rate, and workflow compatibility.[176]

3.4 Manufacturing, Regulation, and Real-World Deployment

Ultimately, translation depends on whether a sensing concept can be turned into a reproducible sample-to-answer product.[201] For bacterial diagnostics, that usually means integrating lysis, enrichment, fluid handling, biosafety, and contamination control into a disposable cartridge or another tightly controlled workflow.[202] A platform that performs well only after extensive manual preprocessing may still have value in a central laboratory, but it is unlikely to function as a true POC device. Manufacturing, therefore, needs to be considered early rather than treated as a late-stage engineering detail.[203] Electrochemical systems must demonstrate scalable electrode fabrication, stable interfacial chemistry, and batch-level quality control,[204] whereas Raman/SERS and related optical methods must address substrate reproducibility, signal standardisation, and shelf-life without relying on cold-chain storage.[205] Usability matters just as much. Low operator burden, effective error-proofing, minimal maintenance, and secure integration into laboratory information systems or electronic health records often determine whether a device is actually suitable for use in the emergency department, ICU, outpatient clinic, or field setting.[206,207] Regulatory evidence should likewise be built in from the start rather than assembled afterwards. In Europe, the IVDR requires evidence for scientific validity, analytical performance, and clinical performance in relation to the intended use.[208] In parallel, manufacturing should be developed within an appropriate medical-device quality system, typically ISO 13485,[209] with traceability, risk management, and post-market surveillance embedded throughout the product lifecycle. Overall, the rapid bacterial diagnostics most likely to achieve clinical adoption will not be those that simply report the lowest limits of detection, but those that combine honest benchmarking in real samples with reproducible manufacturing, usable workflows, and a credible route to implementation.

4. Future Perspectives

Rapid bacterial diagnostics will have the greatest clinical impact not when they are merely fast in analytical terms, but when they provide information early enough to change treatment decisions, support triage, and improve antimicrobial stewardship. In that sense, the most useful point-of-care and near-patient tests are unlikely to replace central microbiology laboratories, but rather to complement them by delivering earlier actionable results while culture, MALDI-TOF MS, molecular assays, sequencing, and phenotypic AST continue to provide confirmation, broader characterisation, and definitive susceptibility data.

Among emerging decentralised approaches, electrochemical biosensors remain especially attractive because they align naturally with the practical requirements of point-of-care use, including portability, low cost, straightforward electronics, and compatibility with disposable formats. Their future success, however, will depend less on achieving ever lower detection limits than on solving more translational problems, such as matrix tolerance, antifouling behaviour, storage stability, reproducible surface functionalization, and scalable manufacturing. Raman-based strategies, particularly SERS, offer complementary strengths through their rich molecular specificity and potential for multiplexed detection in complex samples. Also in this domain, the key challenge is not proof-of-concept sensitivity alone, but the development of robust substrates, transferable calibration strategies, and data-analysis workflows that remain reliable across instruments, batches, and clinical settings. Across both fields, future progress is also likely to be accelerated by artificial intelligence (AI), particularly through improved data analysis, predictive modelling, and agentic systems that support interpretation and decision-making.[210,211] At the same time, AI may help lower practical barriers to adoption by enabling more intuitive handling of complex outputs, for example, through natural language processing-based interfaces that make advanced diagnostic systems easier to use in routine clinical practice.[145]

Across both fields, the next phase of progress will depend on more rigorous and clinically honest benchmarking. Studies that use real patient samples, report time-to-result from sample to answer, compare performance directly with standard-of-care methods, and address usability, failure rates, and workflow

integration will be far more valuable than demonstrations in simplified laboratory media. More broadly, the technologies most likely to succeed will be those designed around specific clinical decisions rather than around abstract analytical performance. The future of rapid bacterial diagnostics, therefore, lies not in a single universal platform but in well-validated, application-focused systems that combine robust sensing with manufacturability, regulatory readiness, and clear clinical utility.

5. Conclusions

This review highlights the clinical rationale for rapid bacterial diagnostics and examines two technically mature routes toward decentralised implementation: electrochemical biosensing and Raman-based detection, particularly SERS. Both approaches offer genuine advantages for POC use. Electrochemical platforms excel in their portability, low cost, and quantitative signal output. Raman/SERS offer their rich molecular specificity and multiplexing capability. However, neither field has yet produced devices that consistently meet the standards required for clinical adoption, namely robust performance in complex biological matrices, validated clinical utility, and regulatory approval. Progress will require a shift in focus from proof-of-concept demonstrations toward honest, clinically grounded benchmarking. The most impactful future diagnostics will not be those with the lowest detection limits in buffered model systems, but those that deliver reliable, actionable results in real patient samples, integrate seamlessly into existing clinical workflows, and provide information specific enough to guide treatment. In that context, electrochemical biosensors and Raman-based platforms are best understood not as replacements for central laboratory diagnostics, but as complementary tools that can provide earlier, more targeted information at the point of clinical decision-making. Their success will ultimately be measured not by analytical performance alone, but by their ability to improve patient outcomes and also support the responsible use of antibiotics.

Author contributions

P.J. contributed to conceptualisation, writing of the original draft, review and editing, visualisation, and funding acquisition. V.R., M.K., O.Z., D.P., and M.O. contributed to the writing of the original draft and to the review of the manuscript. M.O. contributed to conceptualisation, manuscript review and editing, and funding acquisition.

Conflicts of interest

M.O. discloses his share in InSiliBio (France), focused on biosimulations, and ATOMIVER (Czechia), focused on supercapacitor electrode materials, companies.

Data availability

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No new primary research data were generated or included as part of this review article.

Declaration of Generative AI in Scientific Writing

During the preparation of this manuscript, the authors used ChatGPT 5.5 to assist with language editing and improving readability. All content was subsequently reviewed and revised by the authors, who take full responsibility for the accuracy and integrity of the work.

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Data availability

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