Nanomaterial-enabled volatilomic systems for portable health diagnostics

Danyao Qu and Hossam Haick*

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Diagnostic technologies are critical for improving health outcomes and extending quality of life. Accurate and timely diagnosis plays a critical role in preventing disease, guiding treatment, and improving clinical outcomes.[1] Over the past century, diagnostic technologies have advanced to enable earlier disease detection and more precise health monitoring, allowing more timely and effective intervention.[2,3] Recently, smart diagnostics driven by artificial intelligence (AI), portable and mobile systems integrated with the Internet of Things (IoT), and noninvasive yet highly accurate detection methods have promised a bright future, although significant technological challenges remain.[4]

Volatilomics-based diagnosis, which analyzes volatile organic compounds (VOCs) released directly by a disease or produced as a consequence of pathological processes in exhaled breath, skin emissions, or other biological sources, offers distinctive advantages: rapid, painless, and repeatable testing without specialized facilities or invasive procedures.[5] However, its diagnostic reliability has historically been constrained by dependence on the clinician's subjective expertise. To address this limitation, mobile and portable electronic noses (E-noses) based on precise disease volatilomics have been developed.[6] These systems can reveal in real time metabolic or pathological changes, require minimal sample, and are well suited for large-scale screening and early detection. They are especially advantageous in resource-limited settings due to their user comfort, compliance, and low cost. Future mobile noninvasive volatilomic diagnostic systems are expected to combine high VOC recognition capability, passive or power-free operation, compact and lightweight design, rapid data processing and transmission, and seamless IoT integration. Achieving these features will heavily rely on advances in nanomaterials.

In this context, nanomaterials—particularly low-dimensional ones—have emerged as key enablers of volatilomic diagnostics. To move beyond a purely descriptive account of zero-dimensional–three-dimensional (0D–3D) systems, we adopt a concise A–T–F framework, comprising accessible interfacial area (A; governing adsorption capacity and kinetics), charge-transport pathways (T; setting transduction gain and noise), and functionalization (F; programming selectivity and robustness). By jointly optimizing A, T, and F, these materials leverage their physicochemical attributes to meet the stringent requirements of next-generation mobile diagnostic platforms, thereby bridging the gap between conceptual smart diagnostics and clinically reliable, real-world applications. Low-dimensional nanomaterials—0D, one-dimensional (1D), and two-dimensional (2D) materials together with 3D nanostructures—are particularly attractive because they provide large accessible area, low-loss and tunable transport pathways, and rich, programmable surface chemistry, which together expand VOC–material interactions and enable multidimensional feature extraction.[7] Representative 0D nanomaterials, such as metal nanoparticles, quantum dots, and semiconductor nanoparticles, rely on tunable conductivity, interparticle tunneling barriers (i.e., energy barriers that electrons must overcome to tunnel between adjacent nanoparticles, strongly influenced by VOC adsorption and surface chemistry), and surface depletion effects to achieve highly sensitive responses to gas adsorption, while their ultrafine size ensures rapid response and recovery. In A–T–F terms, 0D systems provide high A (dense, accessible surface), tunable T (gap/ligand-controlled tunneling), and high F (ligand/thiol chemistry). This profile is exemplified by gold nanoparticle (GNP), which has been used in cancer diagnostics since 2009;[8] subsequent studies showed that VOC–thiol interactions modulate film resistance and that removing trace ligands stabilizes the response, reducing humidity/pressure cross-sensitivities and thereby lowering calibration requirements in E-nose diagnostics (**Figure** 1a, top left).[9] One-dimensional nanomaterials, including electrospun nanofibers, nanowires, nanotubes, nanorods, and nanobelts, offer directional, tunable charge-transport pathways together with a large, readily functionalizable surface area. Within the A–T–F framework, 1D systems deliver high A (open, porous meshes), low-loss, length-matched T (directional percolation), and moderate–high F (surface coatings/defect engineering). As

Danyao Qu, Department of Chemical Engineering and Russell Berrie Nanotechnology Institute, Technion–Israel Institute of Technology, 3200003 Haifa, Israel; danyaoqu@gmail.com
Hossam Haick, Department of Chemical Engineering and Russell Berrie Nanotechnology Institute, Technion–Israel Institute of Technology, 3200003 Haifa, Israel; hhossam@technion.ac.il
*Corresponding author
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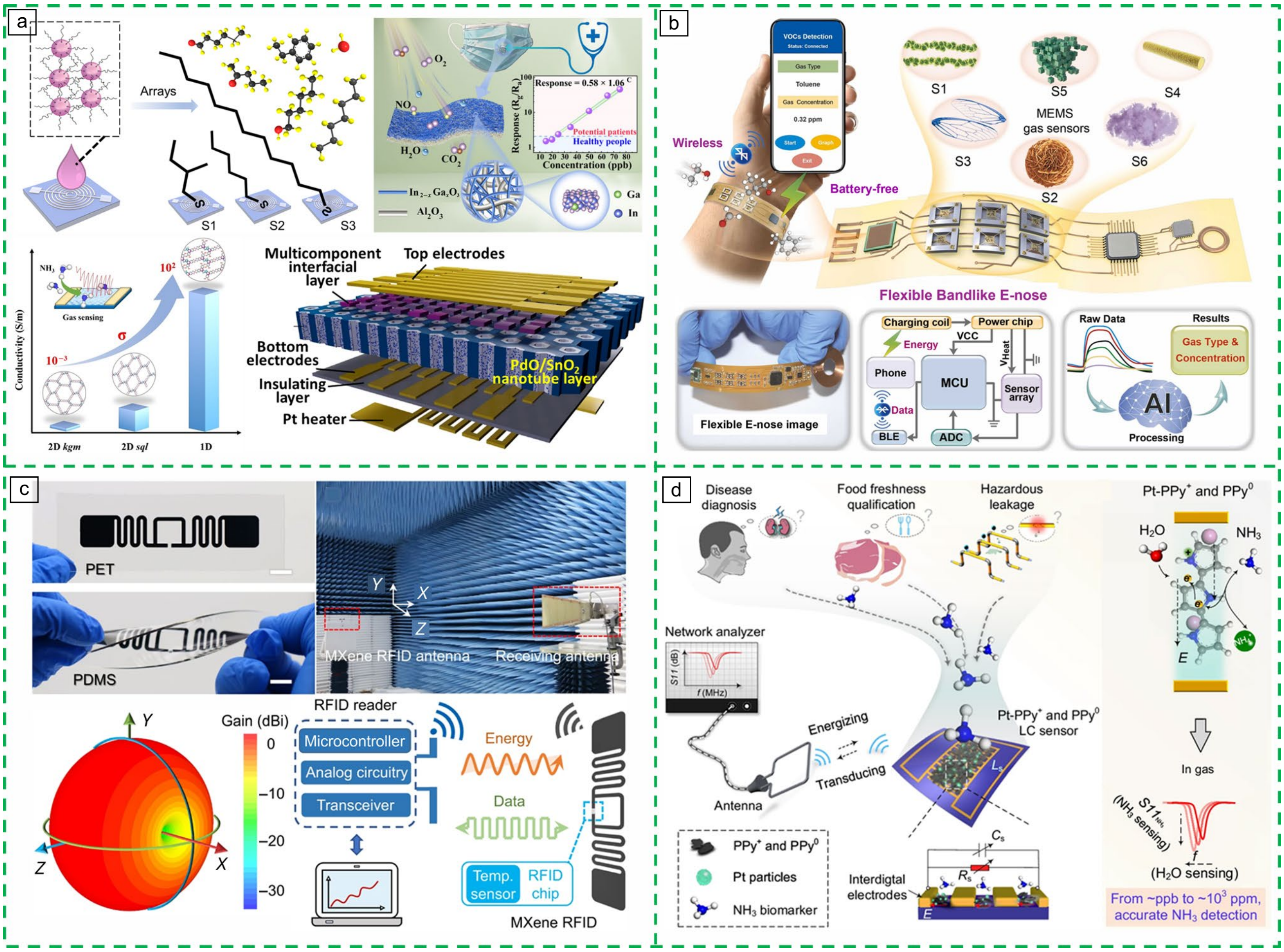

Figure 1. Nanomaterials and integration strategies for mobile health diagnostics. (a) (Top left-0D) gold nanoparticle chemiresistive element with an organic ligand shell;[9] (top right-1D) electrospun mesh for NO sensing;[10] (bottom left-2D) conductive Cu–metal–organic framework thin film illustrating selective adsorption and charge-transfer pathways;[11] (bottom right-3D) 3D nanotube-array platform with ultrathin PdO/SnO_2 layers enabling up to 10,000 addressable sensors.[12] (b) Wireless, flexible, band-like E-nose architecture integrating a sensing array, power supply, measurement and processing units, and wireless communication.[13] MEMS, microelectromechanical systems; VCC, voltage vommon vollector; MCU, microcontroller unit; BLE, bluetooth low energy; ADC, analog-to-digital converter. (c) MXene radio-frequency identification (RFID) system with antennas on PET/PDMS, showing measured and simulated radiation patterns and the RFID tag mechanism.[14] (d) Passive wireless inductor-capacitor (LC) chemical sensor testing platform based on Pt–PPy^+ and PPy^0.[15]

a representative example, electrospun $In_{1.98}Ga_{0.02}O_3$–Al_2O_3 nanofiber meshes exhibit high porosity and mechanical flexibility (Figure 1a, top right), enabling stable and reliable NO sensing under deformation, which is critical for the diagnosis of NO-related diseases such as asthma and pneumonia.[10] Two-dimensional nanomaterials encompass both advanced 2D materials—such as MXenes, black phosphorus, transition-metal dichalcogenides, and graphene with its derivatives—as well as conventional thin films, including metal oxides and conductive metal–organic frameworks (MOFs). Advanced 2D materials offer exceptionally large accessible area, abundant surface terminations, and atomic-scale thickness, enabling very low detection limits, whereas conventional thin films trade part of the ultimate sensitivity for greater compatibility with microelectronic manufacturing. In A–T–F terms, 2D materials as a class typically provide very high A (two-sided exposure and short diffusion paths), low-loss T (planar, in-plane transport), and high F (rich surface terminations or pore chemistry), enabling low detection limits and straightforward microelectronic integration. For example, conductive Cu-MOF thin films combine ordered porosity with electrical conductivity for efficient gas recognition, and the *kgm*-Cu-MOF-3 has achieved NH_3 detection down to 10.8 ppb—a clinically relevant biomarker for chronic kidney disease and liver disorders—highlighting its potential in noninvasive diagnostics (Figure 1a, bottom left).[11] Representative 3D nanomaterials are typically nanoporous frameworks with hierarchical architectures. By combining high surface areas with spatial complexity, these materials significantly enhance analyte capture efficiency and enable multipoint recognition and high-throughput detection beyond the reach of 0D, 1D, and 2D systems. Their interconnected porous networks further facilitate the simultaneous capture and identification of multiple VOCs. In A–T–F terms, 3D architectures exhibit extremely high A (hierarchical porosity with convective access), engineered T (scaffolded thin shells and heterojunctions), and high F (shell composition and surface-site design). For instance, ultrathin PdO/SnO_2 layers deposited on 3D nanotube arrays (Figure 1a, bottom right) have enabled the fabrication of up to 10,000 individually addressable chemiresistive sensors[12] (i.e., sensors that detect gases through resistance changes caused by surface charge transfer upon analyte adsorption), achieving ppb-level sensitivity to disease-related biomarkers, such as acetone, a well-recognized volatile biomarker of diabetes. Such architectures underscore the unique potential of 3D nanostructures for multiplexed, high-throughput, noninvasive diagnostics. Overall, the rational design of gas-sensitive nanomaterials centers on three levers: A—maximize accessible area; T—engineer low-loss, length-matched transport paths; F—implement stable, selective functionalization. In parallel, controllable synthesis and uniform device fabrication are essential for scalable production and clinically reliable deployment.

While advances in nanomaterials have significantly enhanced the sensitivity and selectivity of VOC detection, translating these material-level improvements into practical health-care solutions requires their integration into compact diagnostic platforms. Current mobile diagnostic systems, such as wireless and flexible band-like E-nose designs (Figure 1b) and microelectromechanical systems (MEMS)-based gas sensors, typically consist of a sensing unit, energy supply, signal processing module, and wireless transmission component.[13] However, dedicated power modules are often bulky, and onboard chips for real-time measurement and processing add size and complexity. This limits miniaturization and hinders integration into wearable or discreet portable formats. One approach to overcoming this limitation is to relocate power supplies and processing units to external hubs, leaving only the sensing unit on the body, while maintaining robust low-latency wireless links and energy-efficient communication to ensure accurate real-time data transmission. There, advanced antenna technology becomes promising for both miniaturization and reliable data transmission.

An MXene-based antenna and measurement system (Figure 1c), fabricated using printing techniques, has demonstrated performance comparable to commercial antennas.[14] Further miniaturization requires balancing tradeoffs among electrical length, operating wavelength, substrate dielectric properties, and the use of wave-absorbing materials in the antenna's interspaces. Advanced nanomaterials such as MXenes, graphene, conductive polymers, and carbon nanotubes are promising candidates due to their high conductivity, flexibility, and compatibility with scalable manufacturing methods such as roll-to-roll printing, screen printing, and solution-based deposition. Many of these antenna materials are also inherently gas-sensitive, offering opportunities to integrate sensing and communication functions into a single device. An example of such integration is a wireless inductor–capacitor (LC) chemical sensor (Figure 1d), in which the antenna itself acts as the sensing element.[15] Changes in the sensitive material modify the resonant properties of the circuit, enabling passive communication–sensing operation without a dedicated power source. Another promising approach is to functionalize Radio-Frequency Identification (RFID) antennas as gas sensors, creating RFID tags that detect VOCs passively and wirelessly. Recent developments in miniaturized RFID chips, reaching sizes as small as $0.15\ mm \times 0.15\ mm$, open possibilities for ultracompact sensing tags. Multiple tags can be deployed as wireless passive sensor arrays to enable pattern recognition for complex odor profiles.

Moving forward, the advancement of nanomaterial and volatilomics-based noninvasive diagnostics will rely on multiple converging directions. Scalable and reproducible synthesis of high-performance nanomaterials is essential to ensure long-term stability, while the integration of VOC sensing with wireless communication will enable truly integrated sensing–communication systems. Miniaturized and potentially passive devices, supported by telecommunication frameworks such as RFID, LC, and Long Range (LoRa), can eliminate bulky power sources and achieve seamless connectivity. At the same time, several challenges must be addressed to achieve clinical translation, including standardized sampling protocols, reproducibility across diverse clinical and environmental conditions, and the ability to distinguish disease-related VOCs from dietary or lifestyle confounders. The long-term durability of devices under real-world conditions also remains a major hurdle. Beyond material and device innovation, regulatory readiness through validated clinical protocols, ethical oversight, and data privacy compliance will be critical. In addition, AI-driven analytics capable of handling complex and multidimensional VOC data sets will be indispensable for improving accuracy and reducing false outcomes. By combining advances in materials, wireless-enabled devices, regulatory frameworks, and AI-powered interpretation, future volatilomics platforms can evolve into compact, reliable, and widely accessible diagnostic systems.

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Conflict of interest

The authors declare no conflicts of interests or other disclosures.

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