

Application of the Nanopore in Life-Support Clinical Devices —— ECMO's Promotion

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Abstract:

Nanopore technology has emerged as a transformative tool in modern biomedical science, enabling direct, label-free, and highly sensitive analysis of biomolecules at the single-molecule level. This technology has been widely applied in genomics, proteomics, biosensing, and environmental monitoring, with its rapid advancement indicating broad prospects for medical and clinical applications. In particular, its integration into medical devices could significantly enhance diagnostic accuracy, monitoring capabilities, and treatment personalization. This review explores the potential application of nanopore technology within extracorporeal membrane oxygenation (ECMO), a critical life-support system for patients with severe respiratory or cardiac failure. The study begins by outlining the basic principles and core functions of nanopores, followed by an overview of their potential roles in medical instrumentation, including biosensors, diagnostic platforms, and blood filtration devices. The primary focus is placed on ECMO integration, where nanopores could offer unique advantages in real-time monitoring of blood oxygenation, pathogen detection, and molecular-level biomarker quantification. By analyzing both qualitative and quantitative detection capacities, we demonstrate the feasibility and transformative value of nanopore-based ECMO monitoring systems. Over all, the paper ends with a discussion about future directions, including engineering challenges, clinical validation, and opportunities for personalized medicine. This article emphasizes that nanopore technology, once optimized for stability, scalability, and hemocompatibility, could evolve into a cornerstone of precision monitoring in ECMO and other critical-care technologies.

Keywords: Nanopore technology; ECMO; Application.

1. Introduction

Nanopore technology has drawn significant attention over the past decade for its ability to directly analyze nucleic acids, proteins, and metabolites at the single-molecule level. Unlike conventional biochemical assays, nanopores rely on monitoring ionic current changes as molecules pass through nanoscale pores, allowing high-resolution structural and quantitative information to be obtained in real time [1,2]. These properties position nanopores as an ideal platform for rapid diagnostics and continuous monitoring in clinical contexts.

In parallel, extracorporeal membrane oxygenation (ECMO) has become an indispensable intervention for patients suffering from life-threatening cardiopulmonary dysfunction. However, despite its life-saving potential, ECMO faces major challenges, particularly in continuous, high-fidelity monitoring of blood composition, oxygenation dynamics, and pathogen burden. Current approaches rely on intermittent sampling and external laboratory assays, which are often slow and limited in sensitivity [3]. The convergence of nanopore sensing with ECMO technology presents a novel and potentially revolutionary pathway for improving patient outcomes. Real-time molecular surveillance of circulating blood could enable clinicians to detect early signs of infection, quantify viral loads, assess inflammatory markers, and continuously track oxygen and metabolic balance. This review highlights the fundamental mechanisms of nanopore technology, explores its potential integration into medical devices, and provides a detailed examination of its application within ECMO systems, emphasizing both opportunities and challenges.

2. Fundamentals of Nanopore Technology

Nanopores are nanoscale channels that allow individual biomolecules to pass through under the influence of an electric potential. The principle relies on detecting ionic current fluctuations when a molecule translocates through the pore, generating a unique electrical signature corresponding to its size, shape, or charge distribution [4]. Depending on material composition, nanopores can be broadly classified into biological nanopores, typically formed by protein complexes such as α -hemolysin, and solid-state nanopores fabricated from silicon nitride or other robust materials [5].

Biological nanopores offer superior molecular specificity and reproducibility due to their precise protein architecture, while solid-state nanopores provide durability, tunability, and compatibility with microfabricated systems.

Hybrid nanopores are also emerging as promising alternatives, combining stability with molecular selectivity [6].

The major functional advantage of nanopore technology lies in its ability to perform single-molecule detection without amplification or labeling. Applications span DNA and RNA sequencing, protein identification, pathogen detection, and even environmental toxin monitoring [7,8]. With the advent of advanced analog front-end electronics and molecular “ping-pong” sensing techniques, the resolution and throughput of nanopores have been greatly enhanced [1,4].

In a clinical context, nanopores stand out as powerful biosensing tools. Their small footprint, low power consumption, and scalability make them suitable for portable and continuous monitoring systems.

3. Nanopore Applications in Medical Devices

The clinical potential of nanopore technology extends beyond sequencing and research. Several categories of medical devices can benefit from nanopore integration.

Point-of-care diagnostic platforms – enabling rapid detection of pathogens or biomarkers directly at the bedside. In point-of-care platforms, nanopore sensors can reduce diagnostic delays by directly identifying nucleic acids from pathogens within minutes to hours, a major advantage in emergency or ICU settings.

Wearable biosensors—for continuous monitoring of metabolic markers in chronic disease management. For wearable biosensors, their portability allows continuous tracking of glucose, lactate, or urea, potentially improving chronic disease management and patient compliance.

Blood purification systems – such as hemodialysis or hemoperfusion, where nanopores may act as molecular sieves. In blood purification systems, nanopores not only enhance selectivity in removing toxins but also provide real-time assessment of treatment efficacy by continuously monitoring residual molecules in circulation.

Extracorporeal circulation systems, including ECMO – where nanopores can provide real-time insight into oxygenation levels, pathogen load, and biomarker fluctuations [9,10]. Most notably, ECMO systems represent a particularly promising field for nanopore integration. Current ECMO management relies on intermittent laboratory testing, which can delay clinical decisions and requires frequent blood draws. Embedding nanopore sensors into ECMO circuits could allow Continuous infection monitoring, Biochemical balance assessment, and Anticoagulation and drug monitoring.

Each of these applications leverages the unique ability of

nanopores to deliver sensitive, continuous, and miniaturized monitoring, representing a significant advancement over traditional biochemical assays.

4. Nanopore Integration into ECMO

4.1 Feasibility and Advantages

The integration of nanopore sensing into ECMO is technically feasible due to the compatibility of nanopores with fluidic systems and their ability to function in complex biological samples. Unlike traditional assays, nanopores provide label-free analysis and can directly assess whole blood samples without extensive preprocessing [6]. In ECMO, patient survival often depends on rapid detection of complications such as sepsis, hemolysis, or inadequate oxygenation. Nanopores can continuously monitor blood composition, enabling early intervention. Their single-molecule sensitivity allows detection of pathogens or biomarker shifts before they manifest clinically [9]. Furthermore, solid-state nanopores demonstrate high chemical stability and can be engineered for hemocompatibility, an essential factor for long-term ECMO use [3].

From an engineering perspective, ECMO circuits already contain multiple monitoring ports for pressure, oxygen saturation, and flow rate. Integrating a nanopore module into these circuits would not require fundamental redesign but rather the addition of a microfluidic branch channel in which blood could flow past the nanopore sensor in real time. Advances in microfluidics and lab-on-a-chip platforms suggest that such integration could be achieved with minimal additional blood loss or dead space.

Another critical advantage is the potential to reduce reliance on intermittent laboratory testing. In conventional ECMO practice, clinicians frequently extract blood samples for gas analysis and biochemical testing, which can both delay decision-making and contribute to iatrogenic anemia. A nanopore-based sensor could provide continuous readouts, minimizing blood draws and improving patient safety. Additionally, because nanopores are capable of multiplexed detection, they could theoretically replace several existing monitors with a single integrated platform, simplifying ECMO system architecture. This capacity for consolidation is especially attractive in critical care environments where device overload is a common challenge.

Overall, nanopores can offer a unique combination of miniaturization, high throughput, and specificity, positioning them as an attractive solution for next-generation ECMO monitoring systems.

4.2 Qualitative Detection Capabilities

Nanopore technology in ECMO can be leveraged for qualitative detection of pathogens, metabolites, and other biomarkers. Continuous surveillance of blood during ECMO is particularly important for infection management, as bloodstream infections are a major risk. Nanopores can identify bacterial DNA, viral RNA, or even small-molecule toxins directly from circulating blood samples [8,9]. Pathogen identification is a key advantage. For example, nanopores can differentiate between bacterial species or viral genotypes within minutes, significantly reducing diagnostic turnaround compared to culture methods [2]. Moreover, nanopores are capable of detecting single-molecule events such as mutations, enabling rapid identification of drug-resistant strains.

In addition to pathogens, nanopores may detect small biomolecules linked to organ dysfunction or systemic inflammation. For instance, monitoring inflammatory cytokine fragments, metabolites, or hemolysis markers could provide early warning signals of ECMO-associated complication.[8] Such qualitative detection provides clinicians with a broad molecular picture, complementing traditional clinical parameters. This approach transforms ECMO from a primarily supportive intervention into an intelligent, diagnostic-enabled platform capable of guiding real-time therapeutic adjustments. Nanopores can also provide qualitative insights into immune system activation. By detecting fragments of circulating DNA, microRNAs, or oxidative stress markers, clinicians could anticipate complications such as hemolysis-induced kidney injury or systemic inflammation. This molecular-level surveillance represents a paradigm shift in ECMO monitoring, shifting from reactive intervention toward proactive complication prevention.

Qualitative analysis is particularly important in ECMO because complications often arise suddenly and progress rapidly. For instance, septicemia in ECMO patients can lead to systemic inflammatory response syndrome (SIRS), coagulopathy, and multi-organ dysfunction. Traditional blood cultures may take up to 48 hours, whereas nanopore sequencing can identify pathogens in under two hours, and in some experimental settings, in less than 30 minutes. Furthermore, nanopores allow direct identification of co-infections or mixed microbial populations, which are often missed by standard culture. In an ECMO context, such rapid and comprehensive pathogen profiling could enable clinicians to tailor antimicrobial therapy almost immediately, reducing unnecessary broad-spectrum antibiotic use and slowing resistance development.

4.3 Quantitative Monitoring Capabilities

Beyond detection, nanopores can deliver quantitative monitoring of key physiological indicators. In ECMO, precise regulation of oxygen delivery and waste removal is critical. Nanopore systems could be embedded into ECMO circuits to continuously measure oxygen saturation and metabolic byproducts, reducing reliance on intermittent arterial blood gas tests [3].

Viral load quantification is another crucial application. For patients with viral pneumonia or systemic infection, nanopores can measure viral RNA concentrations in real time, enabling personalized antiviral therapy. Similarly, nanopores may quantify bacterial DNA loads, allowing early assessment of antibiotic efficacy [10]. Nanopores also show promise in monitoring protein biomarkers. For example, Chen et al. demonstrated improved detection of RBP4 protein in urine samples using solid-state nanopores, suggesting that similar strategies could be applied to ECMO blood monitoring [11]. Quantitative tracking of protein fragments, metabolic intermediates, and coagulation markers could greatly improve patient safety. Furthermore, nanopores can be tuned to monitor electrolytes, small metabolites, and even drug levels. Such capability would allow continuous optimization of pharmacological management, anticoagulation, and fluid balance during ECMO support.

Quantitative nanopore monitoring could directly complement existing ECMO performance indices. For example, real-time measurement of lactate concentration could serve as a continuous marker of tissue perfusion, while monitoring inflammatory cytokines such as IL-6 could provide early warning of cytokine storm or systemic inflammation. These data could be algorithmically integrated with traditional hemodynamic and oxygenation parameters to create a more holistic, precision-based assessment of patient status.

Drug monitoring represents another major area of opportunity. ECMO alters the pharmacokinetics of many medications due to drug sequestration within the circuit. This makes dosing unpredictable and increases the risk of under- or over-treatment. By enabling continuous monitoring of drug levels such as antibiotics, anticoagulants, or sedatives, nanopores could allow for precise, individualized dosing strategies in ECMO patients.

In a word, nanopores could play a role in long-term optimization of ECMO therapy. Quantitative data on blood components could help predict clot formation or membrane fouling in the oxygenator, enabling preemptive system maintenance. Similarly, continuous monitoring of hemolysis markers could reduce the risk of renal injury or multi-organ dysfunction. These applications highlight the

transformative potential of nanopore technology in moving ECMO toward predictive and adaptive therapy rather than static support. Nanopore-based quantitative monitoring could transform ECMO into a closed-loop system, where therapeutic parameters are continuously optimized according to real-time molecular data.

5. Conclusion

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Nanopore technology represents a powerful frontier in molecular sensing, with wide-ranging implications for clinical practice. By integrating nanopores into ECMO systems, clinicians could access a continuous stream of molecular-level information, enhancing the ability to detect infections, quantify biomarkers, and optimize oxygenation management.

The feasibility of this integration is supported by recent advances in nanopore engineering, including improved selectivity, stability, and hemocompatibility. However, challenges remain, particularly in ensuring long-term stability of nanopores in whole blood environments, preventing clogging, and scaling up production for clinical-grade devices.

Looking forward, the convergence of nanopores with artificial intelligence and microfluidics could produce intelligent ECMO systems capable of predictive analytics and personalized treatment. Such systems may automatically adjust oxygen delivery, fluid balance, or antimicrobial therapy based on real-time molecular feedback. Beyond ECMO, similar applications may extend to dialysis, cardiopulmonary bypass, and implantable biosensors, further underscoring the transformative potential of nanopores.

In conclusion, nanopore technology has the potential to redefine ECMO from a life-support system into a diagnostic and therapeutic platform. While technical and clinical validation steps remain, the trajectory of nanopore research strongly suggests that such integration could become a reality within the next decade, opening a new era of precision critical care.

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