High Resolution Mass Spectrometry in Nontarget Screening for Environmental Analysis: A Survey

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Abstract

High Resolution Mass Spectrometry (HRMS) is a transformative tool in nontarget screening (NTS), significantly enhancing the detection and characterization of environmental pollutants. This survey paper examines HRMS's role in environmental analysis, emphasizing its high-resolution capabilities that enable the identification of both known and unknown contaminants. HRMS's integration with advanced chromatographic techniques and innovative methodologies, such as chemical fingerprinting, facilitates comprehensive pollutant profiling and source tracing, expanding the scope of environmental monitoring. The paper highlights HRMS's applications across various matrices, including water, air, soil, and biological samples, underscoring its versatility and importance in assessing ecological and health impacts. Despite its advancements, HRMS faces challenges in data management, standardization, and analytical methodologies, necessitating the development of harmonized protocols and robust quality assurance measures. Future research directions include enhancing sensitivity and specificity, refining data analysis tools, and exploring novel ionization methods to further elevate HRMS's analytical power. These advancements promise to improve environmental monitoring, support regulatory processes, and contribute to effective pollution management strategies, ultimately protecting ecosystems and public health.

1 Introduction

1.1 Overview of High Resolution Mass Spectrometry in Nontarget Screening

High Resolution Mass Spectrometry (HRMS) is integral to nontarget screening, acting as a sophisticated analytical tool for environmental analysis. It excels in detecting and characterizing a diverse range of pollutants that traditional monitoring methods often overlook [1]. By generating detailed chemical fingerprints of environmental samples, HRMS facilitates comprehensive pollutant profiling and source tracing [2].

The versatility of HRMS spans various environmental matrices, from urban stormwater analysis to the investigation of extraterrestrial organic aerosols. Its high-resolution capabilities allow for the detection of subtle chemical features crucial for understanding environmental pollution complexities [3]. The technique's sensitivity and specificity are further refined through optimized ionization processes, such as atmospheric pressure photoionization, which is essential for accurately analyzing complex mixtures like crude oil [4].

Beyond environmental monitoring, HRMS's applications extend to disease diagnostics and drug discovery, underscoring its broad analytical scope [3]. The integration of HRMS with other analytical methods enhances the understanding of complex chemical compositions and transformation processes, as evidenced in studies on chlorinated organic compounds and their environmental impacts.

The significance of high-resolution instruments in enhancing the reliability of molecular annotations is emphasized, which is critical in the context of nontarget screening [5]. HRMS remains a cornerstone

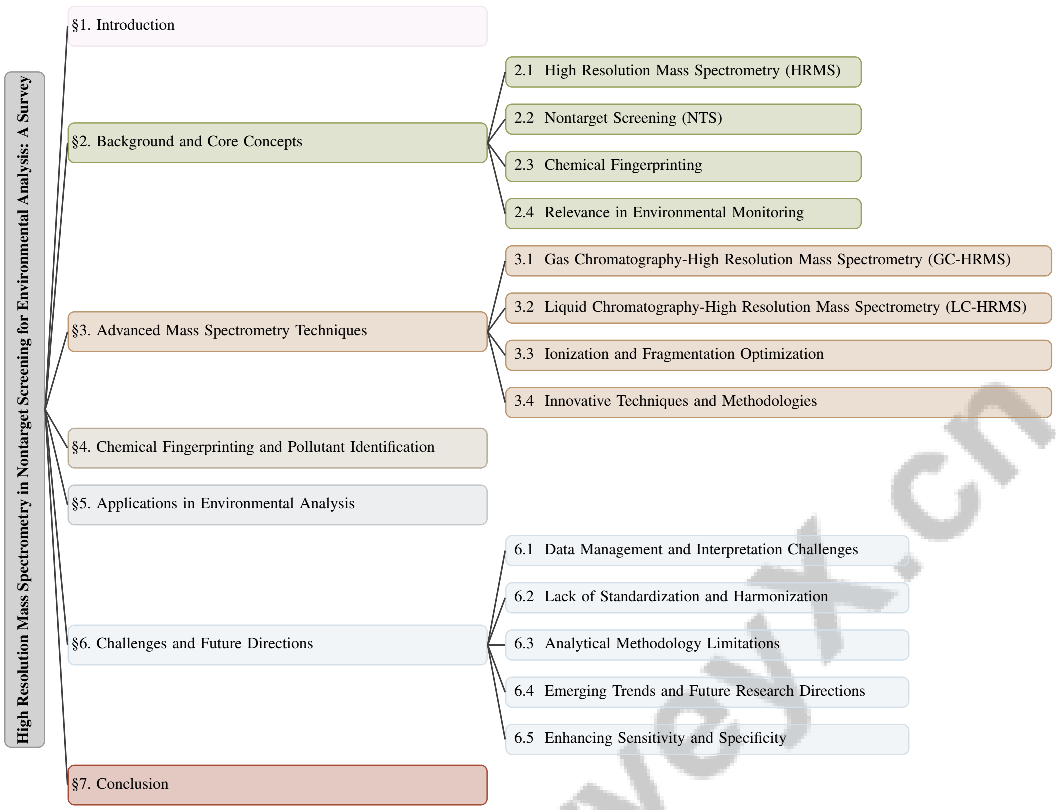

Figure 1: chapter structure

technology in environmental analysis, offering invaluable insights into pollution dynamics and significantly contributing to ecological protection and pollution management.

1.2 Importance of Identifying Characteristic Pollutants

Identifying characteristic pollutants in environmental samples is essential for effective monitoring and management, as traditional analytical methods often lack the sensitivity to detect emerging contaminants prevalent in various matrices. High Resolution Mass Spectrometry (HRMS) greatly enhances this capability through nontarget screening (NTS), which is vital for detecting, identifying, and quantifying both known and unknown substances in complex environmental contexts [6].

HRMS plays a critical role in identifying novel pollutants, such as bromochloro alkanes (BCAs) in indoor environments, which pose health risks as flame retardants and are challenging to detect using conventional methods [7]. It also facilitates the analysis of organic contaminants in highway runoff and fish tissues, providing insights into the environmental impact on sensitive species like adult coho salmon [8]. Furthermore, HRMS aids in characterizing exogenous nanoparticles in human serum, enhancing understanding of the health impacts of ambient particulate matter pollution [9].

Additionally, HRMS elucidates complex chemical signatures associated with specific pollution sources, supporting risk assessments and regulatory actions. For example, detecting carbon isotope compositions in chlorine-isotopologue pairs provides valuable insights into the environmental behavior of organochlorines, significant pollutants [10]. The comprehensive chemical fingerprinting enabled by HRMS addresses the insufficient identification of secondary metabolites from organisms like Penicillium verrucosum, which threaten human health and agricultural productivity [11].

Integrating HRMS into environmental monitoring not only improves pollutant detection but also promotes harmonization of methodologies across laboratories, fostering a coordinated approach to environmental protection and the development of standardized protocols for reproducible molecular networks [6]. This holistic strategy is crucial for addressing inadequacies in current monitoring practices and enhancing the effectiveness of environmental analysis [12].

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1.3 Structure of the Survey

This survey is systematically organized to provide a comprehensive examination of HRMS's role in nontarget screening for environmental analysis. It begins with an introduction highlighting HRMS's significance in detecting and analyzing characteristic pollutants, followed by an overview of its application in nontarget screening. Subsequent sections delve into background and core concepts, elucidating fundamental principles of HRMS, the concept of nontarget screening, and the relevance of chemical fingerprinting in environmental monitoring.

The survey explores advanced mass spectrometry techniques, emphasizing the capabilities of both gas chromatography-high resolution mass spectrometry (GC-HRMS) and liquid chromatography-high resolution mass spectrometry (LC-HRMS) in pollutant detection. It discusses optimizing ionization and fragmentation processes in HRMS to enhance detection accuracy, highlighting innovative methodologies such as automated fragment identification for electron ionization mass spectrometry (EI-HRMS) and applying design of experiments (DOE) to refine atmospheric pressure photoionization techniques for crude oil analysis. Furthermore, it reviews advancements in retention time prediction models, which improve suspect and non-target screening of emerging contaminants, underscoring significant analytical capability improvements afforded by these innovations [13, 4, 14, 15].

In the section on chemical fingerprinting and pollutant identification, the survey examines methodologies for creating chemical fingerprints and their applications in identifying environmental pollutants, followed by a discussion on integrating data and analysis techniques that enhance the identification process.

The applications of HRMS in environmental analysis are explored, emphasizing its effectiveness in detecting a wide range of pollutants across diverse matrices, including water, air, soil, and sediment. This approach leverages suspect and non-target screening (NTS) methodologies to identify organic contaminants and assess their impacts on ecosystems and human health. Guidance from the NORMAN Association underscores the importance of harmonizing analytical techniques and data interpretation across laboratories, while recent studies illustrate HRMS's successful application, particularly in analyzing urban stormwater runoff and biological samples, to prioritize and characterize toxicants in complex environmental mixtures [8, 16]. Additionally, HRMS's role in biological and ecological risk assessments is discussed, highlighting its importance in regulatory monitoring.

Challenges and future directions are identified in the penultimate section, addressing issues related to data management, standardization, and analytical methodology limitations. Emerging trends and future research directions are proposed to enhance HRMS's applications, with a focus on improving sensitivity and specificity.

The survey concludes by summarizing critical findings, emphasizing HRMS's essential role in nontarget screening for environmental monitoring. It underscores the necessity for harmonized protocols and enhanced methodologies in NTS, which could significantly improve the detection and identification of emerging contaminants. Furthermore, it highlights the potential for future advancements in mass spectrometry techniques to enhance regulatory frameworks, facilitate data sharing, and ultimately strengthen environmental protection efforts [17, 16].The following sections are organized as shown in Figure 1.

2 Background and Core Concepts

2.1 High Resolution Mass Spectrometry (HRMS)

High Resolution Mass Spectrometry (HRMS) is indispensable in environmental analysis due to its high mass accuracy and resolution, essential for identifying both known and unknown pollutants [18]. It measures mass-to-charge ratios with precision, enabling the differentiation of complex chemical mixtures and comprehensive profiling of environmental samples [6]. Integration with advanced chromatographic techniques, such as Trapped Ion Mobility Spectrometry coupled with Fourier Transform Ion Cyclotron Resonance Mass Spectrometry (TIMS-FTICR MS), enhances HRMS's analytical capacity, as demonstrated in studies of Titan's haze [18]. Gas chromatography-high resolution mass spectrometry (GC-HRMS) provides detailed isotopic information, revealing carbon isotope ratios and isotopologue distributions of organochlorines [10].

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HRMS's versatility is further highlighted by its ability to observe two-dimensional isotope fractionations through GC-double focus magnetic-sector high resolution mass spectrometry (GC-DFS-HRMS) [19]. This capability is crucial for elucidating complex chemical interactions and transformations in environmental chemistry. In untargeted mass spectrometry data analysis, HRMS constructs molecular networks that accurately depict chemical space, addressing data interpretation challenges and enhancing result reproducibility [6]. The Diamond Molecular Balance (DMB) exemplifies innovative HRMS applications, utilizing diamond nanostructures for precise mass measurement [20].

Recent advancements in HRMS and non-target screening solidify its role in environmental monitoring, providing critical insights into pollution dynamics by identifying emerging contaminants across ecosystems. Through advanced chemical screening techniques and effect-based monitoring, HRMS significantly contributes to ecological protection and pollution management, aiding in developing targeted strategies for mitigating chemical risks [12, 21, 15, 1, 16].

2.2 Nontarget Screening (NTS)

Nontarget Screening (NTS) is a crucial methodology in environmental analysis, enabling the identification of unknown compounds across various matrices without prior knowledge of their presence. This technique addresses the limitations of traditional target analysis methods, which may overlook numerous environmental chemicals [16]. NTS is particularly relevant in studies of bromochloro alkanes (BCAs), which are often unmonitored despite their environmental and health risks as flame retardants [7].

NTS encompasses target, suspect, and non-target screening stages, each employing distinct strategies to broaden contaminant detection [17]. This systematic approach allows for identifying a wider range of contaminants, as evidenced in studies of highway runoff and aquatic species exposure [8]. High-performance liquid chromatography coupled with high-resolution mass spectrometry (LC-HRMS) enhances the separation and identification of complex mixtures, improving detection capabilities. However, challenges like inaccurate retention time predictions necessitate improvements in predictive models [15]. Reliable metabolite annotation remains critical, with strategies like false discovery rate control essential for minimizing errors [5].

Innovative software solutions, such as LipidMatch, enhance lipid identification accuracy using rule-based approaches and comprehensive in silico fragmentation libraries [22]. Compound-specific isotope analysis (CSIA) techniques, particularly those exploring concurrent two-dimensional isotope fractionations, enrich NTS's analytical depth by enabling detailed isotopic studies of halogenated organic compounds [19].

NTS is a vital tool in environmental monitoring, providing a robust framework for identifying and assessing unknown pollutants. Mass spectrometry-based non-target analysis, especially through platforms like patRoon, extends beyond environmental science, enhancing the understanding of complex ecological dynamics and facilitating the identification and mitigation of potential environmental and health risks associated with chemical contaminants [8, 17, 21].

2.3 Chemical Fingerprinting

Chemical fingerprinting is a key approach in environmental analysis, utilizing High Resolution Mass Spectrometry (HRMS) to create detailed profiles of chemical constituents within a sample. This method is essential for pollutant identification, allowing for the characterization of complex mixtures and detection of both known and unknown compounds [2]. By analyzing unique mass spectral patterns, chemical fingerprinting aids in tracing the sources and pathways of pollutants, enhancing the understanding of their ecological and health impacts.

The process generates unique spectral signatures for each compound, valuable for tracing origin and transformation in the environment. This is particularly useful for identifying pollutants undetectable by conventional methods, such as emerging contaminants and complex mixtures like crude oil [4]. HRMS's high resolution and sensitivity enable the detection of subtle isotopic variations, providing insights into the environmental behavior of organochlorines [10].

Chemical fingerprinting is also instrumental in identifying secondary metabolites from microorganisms, which can impact human health and agriculture. For instance, profiling metabolites from Penicillium verrucosum reveals potential risks associated with their presence in food and feed [11].

Integrating chemical fingerprinting with advanced data analysis techniques, such as molecular networking and in silico fragmentation libraries, enhances compound identification accuracy, addressing challenges in data interpretation and reproducibility.

2.4 Relevance in Environmental Monitoring

The integration of High Resolution Mass Spectrometry (HRMS) and Nontarget Screening (NTS) into environmental monitoring frameworks significantly enhances pollutant detection and characterization, overcoming traditional analytical methods' limitations. These advanced techniques are crucial for analyzing complex chemical mixtures, including unknown or unexpected contaminants, thereby providing comprehensive insights into environmental pollution [16]. HRMS's ability to generate high-resolution mass spectra facilitates the identification of subtle chemical features, enabling pollutant detection that may otherwise remain undetected [19].

Advanced mass spectrometry techniques, such as TIMS-FTICR MS, underscore HRMS's relevance in environmental monitoring by elucidating the structural complexity of compounds like tholins in extraterrestrial atmospheres [18]. This capability is mirrored in terrestrial applications, where HRMS is crucial in characterizing exogenous nanoparticles in human samples, highlighting its importance in assessing health impacts from environmental pollution [9].

The complexity of fungal secondary metabolomes presents challenges in environmental analysis, with existing methods often struggling to detect and characterize unknown metabolites [11]. HRMS addresses these challenges by providing the sensitivity and specificity necessary for comprehensive profiling of complex biological and environmental samples. The Diamond Molecular Balance (DMB), with exceptional mass resolution and broad dynamic range, exemplifies HRMS's potential in analyzing diverse samples, enhancing its utility in environmental monitoring [20].

In metabolomics, accurately estimating the false discovery rate (FDR) remains challenging due to the high dimensionality of data and biological sample complexity [5]. Developing standardized procedures for NTS is essential to improve result comparability across laboratories and enhance environmental assessment reliability [16]. This is particularly crucial in effect-based monitoring for toxicity fingerprints and effect-directed analysis, vital for understanding chemical impacts in environmental monitoring [12].

The integration of HRMS and NTS methodologies in environmental monitoring establishes a comprehensive framework for pollutant identification and assessment. This approach enhances the detection and characterization of emerging contaminants, enabling researchers and regulators to better understand environmental contaminants' complexities and their potential impacts on ecosystems and human health. Implementing harmonized protocols, robust data management systems, and developing open-access databases are essential for maximizing NTS utility in regulatory contexts and improving chemical management strategies [15, 21, 17, 8, 16]. This holistic approach is crucial for advancing regulatory measures and ecological risk assessments, ultimately contributing to more effective environmental protection and management strategies.

3 Advanced Mass Spectrometry Techniques

In advanced mass spectrometry, various methodologies significantly enhance pollutant detection and characterization. Notably, Gas Chromatography-High Resolution Mass Spectrometry (GC-HRMS) is particularly effective for analyzing complex contaminant mixtures, offering crucial insights into environmental analysis and monitoring. Table 1 presents a comparative analysis of advanced mass spectrometry techniques, underscoring their distinct features and applications in environmental pollutant detection and characterization. Figure 2 presents a hierarchical overview of advanced mass spectrometry techniques, categorizing major methodologies such as GC-HRMS and Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS). This figure highlights their capabilities and recent innovations that further enhance pollutant detection and analysis, thereby illustrating the landscape of contemporary advancements in this field.

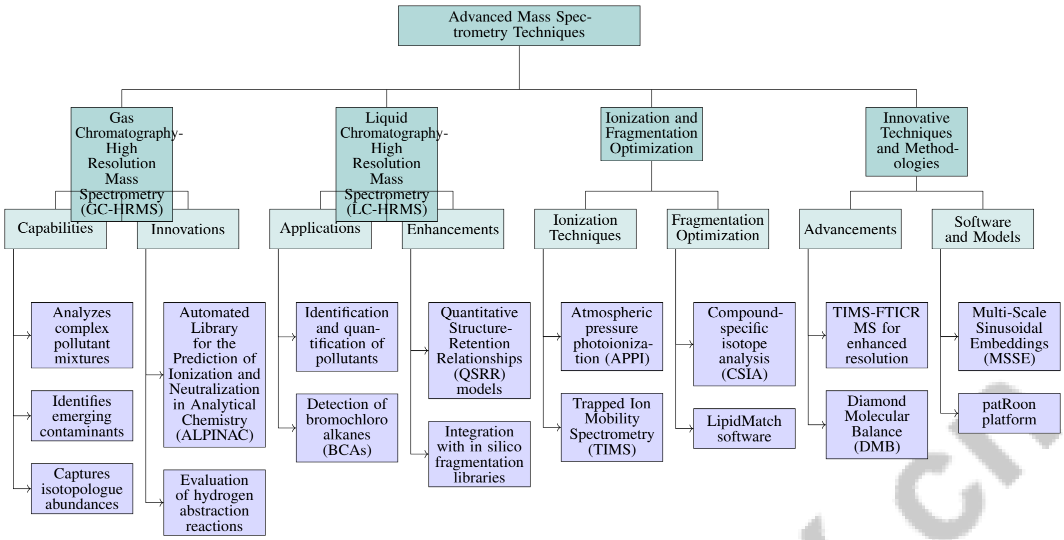


Figure 2: This figure presents a hierarchical overview of advanced mass spectrometry techniques, categorizing major methodologies like GC-HRMS and LC-HRMS, their capabilities, and recent innovations enhancing pollutant detection and analysis.

3.1 Gas Chromatography-High Resolution Mass Spectrometry (GC-HRMS)

GC-HRMS is a powerful technique in environmental analysis, adept at identifying complex pollutant mixtures, including emerging contaminants [1]. It combines gas chromatography's separation capabilities with mass spectrometry's high-resolution detection, enabling precise chemical identification. GC-HRMS excels in capturing isotopologue abundances, such as chlorine isotopologues, aiding source identification and enhancing pollutant origin understanding [2]. It also measures isotope fractionations in halogenated compounds, offering insights into their environmental behavior [19].

Innovative methodologies like the Automated Library for the Prediction of Ionization and Neutralization in Analytical Chemistry (ALPINAC) enhance GC-HRMS capabilities by automating fragment formula annotation of unknown compounds [14]. GC-HRMS also evaluates reaction efficiencies, such as hydrogen abstraction, crucial for understanding chemical transformations and environmental impacts [23]. Applications extend to analyzing specific compounds like perchloroethylene and trichloroethylene with GC-DFS-HRMS, showcasing its versatility in environmental monitoring [24, 10].

3.2 Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS)

LC-HRMS is essential in identifying and quantifying environmental pollutants, offering superior separation and mass accuracy for complex mixtures. It detects a wide range of contaminants, including bromochloro alkanes (BCAs) in indoor environments, crucial due to their flame retardant use and health risks [7]. Its sensitivity and resolution make it ideal for analyzing such compounds in intricate matrices like indoor dust.

The development of Quantitative Structure-Retention Relationships (QSRR) models enhances LC-HRMS by improving retention time predictions, refining unknown pollutant identification [15]. LC-HRMS is pivotal in metabolomics, profiling metabolites in biological samples to elucidate environmental pollutants' biochemical effects and health impacts [8, 12, 17, 21]. Integration with advanced data analysis techniques, like in silico fragmentation libraries, improves metabolite identification reliability, contributing to robust environmental assessments.

LC-HRMS's exceptional sensitivity and separation capabilities facilitate known and unknown contaminant detection, supporting effective non-target analysis across laboratories [21, 13, 15]. Its application in both environmental and biological contexts underscores its importance in advancing pollution dynamics understanding and their ecological and health implications.

3.3 Ionization and Fragmentation Optimization

Optimizing ionization and fragmentation processes in HRMS enhances detection accuracy and sensitivity, critical in environmental analysis of complex pollutant mixtures [4]. Atmospheric pressure photoionization (APPI) improves ionization efficiency in complex mixtures like crude oil [4]. Trapped Ion Mobility Spectrometry (TIMS) coupled with Fourier Transform Ion Cyclotron Resonance Mass Spectrometry (FTICR MS) exemplifies ionization advancements, separating ions based on mobility to enhance resolution and accuracy [18].

Fragmentation optimization, through compound-specific isotope analysis (CSIA) techniques, enables detailed isotopic fractionation studies, providing insights into halogenated organic compounds' environmental behavior [19, 10]. Software solutions like LipidMatch enhance fragmentation analysis by utilizing comprehensive in silico fragmentation libraries, improving complex lipid mixtures' identification accuracy [22].

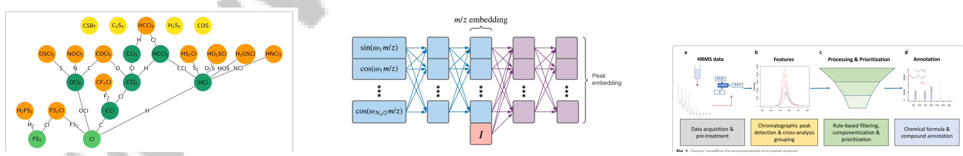
3.4 Innovative Techniques and Methodologies

Recent HRMS advancements have improved analytical capabilities, enabling detailed environmental analyses. TIMS-FTICR MS enhances resolution and accuracy, identifying complex structural motifs [18]. The Diamond Molecular Balance (DMB) achieves mass detection over a wide range with exceptional resolution, enhancing HRMS precision [20].

The Multi-Scale Sinusoidal Embeddings (MSSE) method significantly enhances chemical analyses' accuracy and depth, using sinusoidal functions to embed mass-to-charge values, advancing spectral library searches and chemical property predictions [3]. Software platforms like patRoon integrate tools and algorithms, facilitating non-target analysis workflows and improving environmental monitoring efficiency [6, 25, 21].

Chemical multifingerprinting techniques enhance nanoparticle characterization, contributing to pollution source identification. The Global Natural Product Social (GNPS) system integrates community-driven data analysis tools, enhancing mass spectrometry research collaboration and reproducibility [21, 6, 3, 22].

Innovations in HRMS methodologies, including retention time prediction models and the patRoon platform, transform environmental science by facilitating efficient suspect and non-target screening of emerging contaminants [21, 8, 12, 15].



(a) The image depicts a chemical compound tree, showing the relationships between various compounds through their chemical structures.[14]

(b) A neural network architecture for peak embedding[3]

(c) Generic Workflow for Environmental Non-Target Analysis[21]

Figure 3: Examples of Innovative Techniques and Methodologies

As shown in Figure 3, innovative techniques and methodologies in advanced mass spectrometry enhance chemical analysis accuracy and efficiency. The first image illustrates a chemical compound tree, elucidating structural relationships between compounds. The second image depicts a neural network architecture for peak embedding in mass spectrometry data, facilitating result interpretation. The third image outlines a workflow for environmental non-target analysis, systematically dividing data processing and analysis stages. These examples highlight modern mass spectrometry's strategies for tackling complex analytical challenges [14, 3, 21].

Feature	Gas Chromatography-High Resolution Mass Spectrometry (GC-HRMS)	Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS)	Ionization and Fragmentation Optimization
Detection Capability	Complex Pollutant Mixtures	Wide Range Contaminants	Enhanced Accuracy
Innovative Feature	Automated Fragment Annotation	Qsrr Models	Appi And Tims
Application Context	Environmental Monitoring	Metabolomics	Complex Mixtures

Table 1: Comparison of advanced mass spectrometry methods highlighting their detection capabilities, innovative features, and application contexts. This table delineates the specific advantages of Gas Chromatography-High Resolution Mass Spectrometry (GC-HRMS), Liquid Chromatography-High Resolution Mass Spectrometry (LC-HRMS), and ionization and fragmentation optimization techniques in the context of environmental monitoring and pollutant analysis.

4 Chemical Fingerprinting and Pollutant Identification

4.1 Applications in Pollutant Identification

High Resolution Mass Spectrometry (HRMS) is indispensable for pollutant identification via chemical fingerprinting. The CP-Seeker method effectively identifies bromochloro alkanes (BCAs), pollutants linked to health risks due to their flame retardant use, showcasing HRMS's capability in detecting substances often missed by traditional methods [7]. HRMS has also revealed novel organic contaminants in urban stormwater runoff and fish tissues, emphasizing its role in identifying environmentally hazardous pollutants [8]. Further, HRMS has traced exogenous nanoparticles in human serum and pleural effusion, linking them to combustion emissions and illustrating its utility in understanding pollution pathways [9]. The detection of 98 secondary metabolites from Penicillium verrucosum, including novel compounds, highlights HRMS's ability to delineate complex chemical profiles in environmental samples, essential for assessing secondary metabolite risks in food and feed [11]. Advanced retention time prediction models have enhanced the identification of transformation products and biocides, improving pollutant detection precision [15]. Additionally, analyzing carbon isotope ratios from chlorine-isotopologue pairs offers insights into organochlorine pollutant sources, showcasing HRMS's capability in tracing pollutant origins and understanding environmental behavior [10].

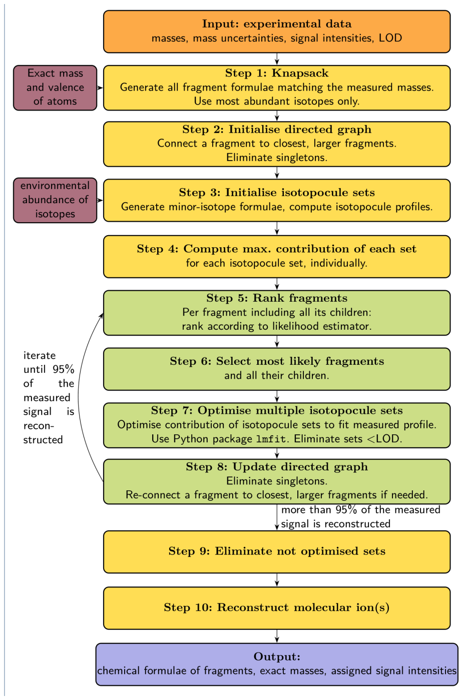
4.2 Integration of Data and Analysis Techniques

Integrating diverse data and analytical techniques enhances pollutant identification and characterization using HRMS. Molecular networking facilitates visualizing complex chemical relationships, improving mass spectrometry data interpretability by identifying related compound clusters, thus refining chemical fingerprints and aiding novel pollutant discovery [6]. Computational tools like LipidMatch, utilizing in silico fragmentation libraries, improve complex lipid mixture annotation accuracy, addressing interpretation challenges [22]. The development of Quantitative Structure-Retention Relationships (QSRR) models provides a framework for predicting unknown compound retention times in LC-HRMS analyses, enhancing pollutant identification precision [15]. In nontarget screening, integrating high-resolution data with advanced statistical methods, such as false discovery rate control, is crucial for minimizing annotation errors and improving metabolite identification reliability [5]. This precision is vital in environmental metabolomics, where accurate compound identification evaluates pollutant impacts on biological systems.

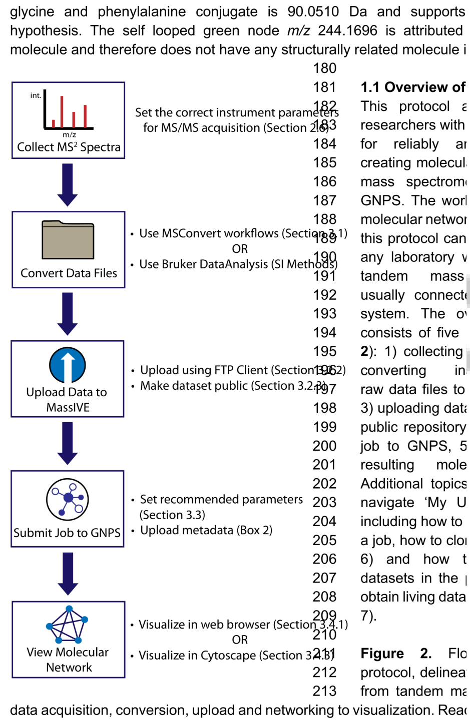
Harmonizing data analysis methodologies across laboratories ensures result comparability and enhances reproducibility in environmental assessments. Platforms like patRoon and LipidMatch facilitate analytical protocol sharing and tool development, promoting collaborative research. For instance, patRoon optimizes non-target analysis workflows, while LipidMatch enhances lipid identification through unique fragmentation libraries. Initiatives like the Global Natural Product Social (GNPS) molecular networking framework support community knowledge integration, enabling reproducible molecular networks connecting chemical insights to biological questions. These tools foster collaboration, enhance accessibility, and improve complex data analysis reproducibility, driving scientific innovation [6, 21, 22].

The integration of diverse data and advanced analytical techniques in HRMS significantly enhances environmental pollutant identification. This comprehensive framework for environmental monitoring and risk assessment employs methodologies such as high-resolution mass spectrometry and predictive modeling to analyze complex chemical compositions and trace pollution pathways effectively. Utilizing non-target screening and retention time prediction models allows researchers to identify known and emerging contaminants, improving understanding of environmental risks and monitoring efficacy

[1, 21, 15]. These advancements are crucial for elucidating pollution dynamics and developing effective management strategies.



(a) The image depicts a flowchart illustrating a process for reconstructing chemical formulae from experimental data, including exact masses, mass uncertainties, signal intensities, and LOD values. The flowchart is divided into ten steps, each representing a distinct phase of the process.[14]



(b) Steps for Generating a Molecular Network from Tandem Mass Spectrometry Data[6]

Figure 4: Examples of Integration of Data and Analysis Techniques

As illustrated in Figure 4, the integration of data and analysis techniques in chemical fingerprinting and pollutant identification is exemplified through flowcharts that facilitate the reconstruction of chemical formulae and the generation of molecular networks from complex datasets. The first flowchart outlines a ten-step process for reconstructing chemical formulae from experimental data, incorporating critical parameters such as exact masses, mass uncertainties, signal intensities, and limit of detection (LOD) values. Each step signifies a distinct phase in data processing, emphasizing the meticulous approach necessary for accurate experimental interpretation. The second flowchart presents a five-step procedure for creating a molecular network from tandem mass spectrometry (MS/MS) data, beginning with MS² spectra collection and progressing through systematic data conversion and analysis, ultimately resulting in a molecular network construction. Together, these visual representations highlight the importance of integrating diverse data and analytical methodologies to enhance understanding of chemical compositions and pollutant sources, thereby advancing environmental chemistry and forensic analysis [14, 6].

5 Applications in Environmental Analysis

The increasing environmental challenges necessitate advanced analytical methods for effective pollutant monitoring across diverse matrices. High Resolution Mass Spectrometry (HRMS) stands out for its exceptional sensitivity and specificity in detecting and characterizing environmental contaminants, playing a pivotal role in various applications, particularly in water analysis.

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5.1 Detection and Analysis of Pollutants in Water Matrices

HRMS significantly enhances pollutant detection and analysis in water matrices, crucial for environmental monitoring and water quality management. Its application in river water analysis offers insights into pollutant concentrations, supporting early warning systems essential for aquatic ecosystem protection and human health [1]. By integrating HRMS with advanced workflows like proFIA, initially used in human serum, detection accuracy and sensitivity in complex water matrices are improved, facilitating pollutant quantification at trace levels [25].

The high-resolution capabilities of HRMS allow for detailed chemical species characterization, enabling the identification of both known and novel contaminants, which aids in tracing pollution sources and understanding contaminant dynamics in aquatic environments. This comprehensive approach, including paired water and biological tissue sample analysis, prioritizes toxicants, assesses bioavailability, and models pollutant pathways, enhancing ecosystem and human health protection strategies [1, 8, 21].

Advanced screening techniques in HRMS facilitate the identification of emerging contaminants and transformation products, prioritizing high-risk contaminants and supporting comprehensive chemical mixture assessments, thereby bolstering ecosystem and human health protection [8, 12, 15]. By providing detailed chemical insights and supporting early detection systems, HRMS is integral to improving environmental monitoring and protection strategies.

5.2 Applications in Atmospheric and Air Quality Analysis

HRMS is vital for air pollutant analysis, enhancing air quality assessment and understanding atmospheric chemical compositions. It excels in detecting and characterizing complex organic aerosols, significant air pollution contributors with implications for health and climate change [18]. Techniques like TIMS-FTICR MS enable detailed analysis of atmospheric samples, identifying structural motifs crucial for understanding chemical processes [18].

HRMS provides comprehensive chemical fingerprints of atmospheric samples, identifying unknown pollutants and tracing pollution sources, essential for effective air quality management. This approach, combined with advanced screening and modeling, enhances our understanding of atmospheric chemical dynamics, supporting ecosystem and human health protection [1, 8, 16].

Beyond detection, HRMS assesses the biological impacts of air pollution, such as characterizing exogenous nanoparticles in human samples, highlighting its utility in evaluating health risks from particulate matter [9]. By offering detailed chemical insights, HRMS aids in developing targeted interventions to mitigate health effects.

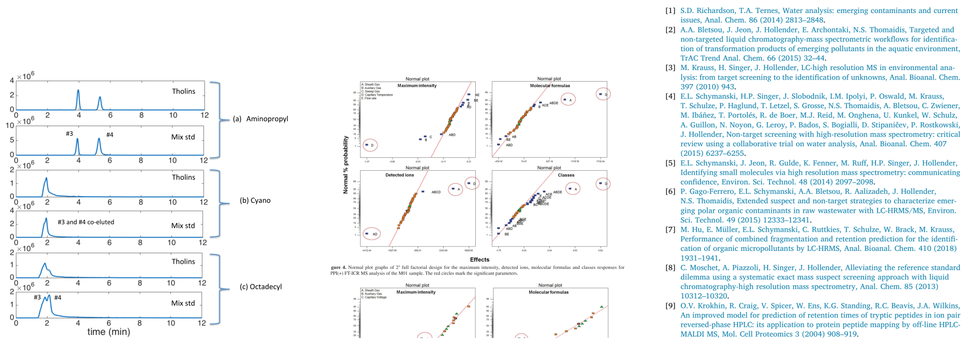
The application of HRMS in atmospheric analysis represents significant advancements in pollutant detection and characterization. Its high-resolution capabilities deepen our understanding of atmospheric chemistry, enabling precise identification of complex compounds and interactions, facilitating targeted strategies to improve air quality and safeguard health [21, 17, 4, 16, 26].

Figure 5 showcases various analytical techniques in environmental analysis, focusing on atmospheric and air quality. The HPLC chromatograms illustrate solvent retention time variations, the factorial design graphs demonstrate mass spectrometry's analytical power, and the water analysis segment highlights evolving challenges and methodologies in water quality analysis [26, 4, 15].

5.3 Soil and Sediment Analysis

HRMS is indispensable for non-target screening of pollutants in soil and sediment matrices, enhancing the detection and characterization of complex chemical mixtures. Its application is crucial for evaluating environmental quality and regulatory compliance, necessitating ongoing development in data management and quality assurance [17, 21, 16]. Understanding pollutant distribution and fate in terrestrial environments is vital for effective monitoring and remediation strategies.

HRMS generates detailed chemical fingerprints, identifying both known and emerging contaminants, enhancing environmental monitoring comprehensiveness. Advanced techniques like high-resolution mass spectrometry detect a broad range of contaminants in complex mixtures, critical for ecosystem and human health protection [21, 15, 17, 1, 8]. High-resolution capabilities also provide insights into pollutant sources and transformation processes in soil and sediment samples.



[1] S.D. Richardson, T.A. Ternes, Water analysis: emerging contaminants and current issues, Anal. Chem. 86 (2014) 2813–2848.
[2] A.A. Bletsou, J. Jeon, J. Hollender, E. Archontaki, N.S. Thomaidis, Targeted and non-targeted liquid chromatography-mass spectrometric workflows for identification of transformation products of emerging pollutants in the aquatic environment, TrAC Trend Anal. Chem. 66 (2015) 32–44.
[3] M. Krauss, H. Singer, J. Hollender, LC-high resolution MS in environmental analysis: from target screening to the identification of unknowns, Anal. Bioanal. Chem. 397 (2010) 943.
[4] E.L. Schymanski, H.P. Singer, J. Slobodnik, I.M. Ipolyi, P. Oswald, M. Krauss, T. Schulze, P. Haglund, T. Letzel, S. Grosse, N.S. Thomaidis, A. Bletsou, C. Zwiener, M. Ibáñez, T. Portolés, R. de Boer, M.J. Reid, M. Onghena, U. Kunkel, W. Schulz, A. Guillon, N. Noyon, G. Leroy, P. Bados, S. Bogialli, D. Stipaničev, P. Rostkowski, J. Hollender, Non-target screening with high-resolution mass spectrometry: critical review using a collaborative trial on water analysis, Anal. Bioanal. Chem. 407 (2015) 6237–6255.
[5] E.L. Schymanski, J. Jeon, R. Gulde, K. Fenner, M. Ruff, H.P. Singer, J. Hollender, Identifying small molecules via high resolution mass spectrometry: communicating confidence, Environ. Sci. Technol. 48 (2014) 2097–2098.
[6] P. Gago-Ferrero, E.L. Schymanski, A.A. Bletsou, R. Aalizadeh, J. Hollender, N.S. Thomaidis, Extended suspect and non-target strategies to characterize emerging polar organic contaminants in raw wastewater with LC-HRMS/MS, Environ. Sci. Technol. 49 (2015) 12333–12341.
[7] M. Hu, E. Müller, E.L. Schymanski, C. Ruttkies, T. Schulze, W. Brack, M. Krauss, Performance of combined fragmentation and retention prediction for the identification of organic micropollutants by LC-HRMS, Anal. Bioanal. Chem. 410 (2018) 1931–1941.
[8] C. Moschet, A. Piazzoli, H. Singer, J. Hollender, Alleviating the reference standard dilemma using a systematic exact mass suspect screening approach with liquid chromatography-high resolution mass spectrometry, Anal. Chem. 85 (2013) 10312–10320.
[9] O.V. Krokhin, R. Craig, V. Spicer, W. Ens, K.G. Standing, R.C. Beavis, J.A. Wilkins, An improved model for prediction of retention times of tryptic peptides in ion pair reversed-phase HPLC: its application to protein peptide mapping by off-line HPLC-MALDI MS, Mol. Cell Proteomics 3 (2004) 908–919.

(a) Comparison of HPLC Chromatograms for Different Solvents[26]

(b) Normal Plot Graphs of 25 Full Factorial Design for the Maximum Intensity, Detected Ions, Molecular Formulas, and Classes Responses for PPI (+) FT-ICR MS Analysis of the M01 Sample[4]

(c) Water Analysis: Emerging Contaminants and Current Issues[15]

Figure 5: Examples of Applications in Atmospheric and Air Quality Analysis

Integrating HRMS with advanced chromatographic techniques enhances analytical power, allowing for separation and identification of complex mixtures. This approach identifies a wide range of contaminants, including POPs and heavy metals, supporting environmental protection and management efforts [8, 12, 21].

HRMS enhances understanding of pollutant interactions with soil constituents, facilitating the identification and characterization of emerging contaminants and transformation products. This knowledge is crucial for assessing bioavailability and mobility, influencing environmental behavior and potential risks [2, 21, 15, 16].

5.4 Biological and Ecological Risk Assessment

HRMS is essential for assessing biological and ecological risks of environmental pollutants, crucial for understanding pollutant interactions with biological systems and evaluating health and ecological impacts. Its high-resolution capabilities enable detailed characterization of chemical mixtures in biological matrices, facilitating the identification of both known and emerging contaminants [9].

HRMS elucidates pollutant pathways in biological systems, supporting internal exposure and toxicological effect assessments, vital for evaluating pollution health risks. Characterizing exogenous nanoparticles in human samples highlights HRMS's utility in tracing pollution sources and understanding biological impacts [9].

In ecological assessments, HRMS evaluates pollutant effects on species and ecosystems, identifying novel contaminants affecting aquatic environments and supporting conservation efforts [8]. This approach identifies pollutants threatening biodiversity and ecosystem health.

HRMS's integration with advanced data analysis techniques enhances risk assessment reliability. In silico fragmentation libraries and molecular networking improve mass spectrometry data interpretation, identifying transformation products and metabolites crucial for ecological impact understanding [22].

HRMS is vital in biological and ecological risk assessments, offering comprehensive chemical insights for evaluating pollutant effects. Advanced platforms like patRoon enhance non-target analysis workflow efficiency, improving risk evaluation reliability and supporting targeted risk management strategies for health and ecological integrity protection [2, 21].

6 Challenges and Future Directions

6.1 Data Management and Interpretation Challenges

High Resolution Mass Spectrometry (HRMS) encounters significant challenges in data management and interpretation, which are crucial for ensuring reliable analytical outcomes. Methodological inconsistencies in liquid chromatography (LC) across laboratories lead to divergent compound elution profiles, complicating result interpretation and comparability. A standardized retention time index (RTI) system has been proposed to harmonize retention times and enhance compound identification in suspect and non-target screening, utilizing a calibrated set of reference compounds and predictive models to improve reproducibility and facilitate accurate inter-laboratory comparisons [2, 13, 24, 15]. The challenge is exacerbated by insufficient experimental data on compound elution.

The complexity of electron ionization mass spectra also presents a hurdle, with approximately 40

Reliance on external isotopic standards in compound-specific isotope analysis introduces variability, as these standards may not always represent environmental samples [19], affecting isotopic measurement precision. Moreover, optimizing ionization processes, such as atmospheric pressure photoionization, requires validation across diverse crude oil types to ensure applicability [4]. Variability in ionization efficiency due to sample preparation and intrinsic sample properties further complicates HRMS analyses.

Analyzing complex mixtures, such as bromochloro alkanes (BCAs) and pentachloro alkanes (PCAs), presents additional challenges due to the intricate nature of these compounds. Limited sample sizes in studies of inhaled ultrafine particles may also hinder comprehensive analyses [9]. Innovative software solutions, like patRoon, provide user-friendly interfaces and integrate multiple algorithms for non-target analyses without extensive computational expertise [21]. However, accurately identifying bioavailable and toxicologically relevant non-target features remains challenging, particularly in complex environmental matrices where in vivo biotransformations may obscure detection [8]. Addressing these challenges is vital for enhancing HRMS reliability and accuracy in environmental analysis, ultimately aiding effective monitoring and management strategies. Integrating spatial information into molecular annotation and categorizing methods based on false discovery rate (FDR) control and spatial analysis approaches offer promising avenues for improving data interpretation [5].

6.2 Lack of Standardization and Harmonization

The effectiveness of High Resolution Mass Spectrometry (HRMS) in environmental analysis is significantly hampered by a lack of standardization and harmonization in methodologies, complicating data interpretation and validation. The absence of standardized protocols in non-target screening (NTS) methodologies leads to variability in analytical approaches, complicating the assessment of environmental impacts [17]. Inconsistencies in sampling protocols across sites further exacerbate this issue, undermining HRMS reliability for environmental monitoring [1].

A critical challenge in HRMS applications is the lack of standards for quantifying many novel compounds, hindering accurate environmental impact assessments. This underscores the urgent need for standardized reference materials and protocols to ensure reliable quantification across studies [27]. The reliance on user-defined parameters in analytical tools, such as LipidMatch, introduces additional variability, highlighting the necessity for standardized lipid identification methodologies to enhance reproducibility and comparability of findings [22].

Addressing these issues necessitates a concerted effort to establish harmonized protocols and methodologies in HRMS applications. Implementing standardized monitoring protocols for chemical contaminants in environmental assessments would enhance data interpretation precision and validation. Such efforts would improve the reliability of evaluations and support effective pollution management strategies through advanced screening techniques, effect-based monitoring, and data integration. By tackling the complexities of chemical mixtures and their ecological impacts, standardization can lead to more informed decision-making and prioritization of management measures, ultimately contributing to healthier ecosystems and improved public health outcomes [8, 12, 21, 16].

AI-generated, for reference only.

6.3 Analytical Methodology Limitations

Despite advancements, current analytical methodologies in mass spectrometry encounter several limitations affecting their effectiveness in environmental analysis. A significant challenge is the inability to distinguish sources when isotopologue distributions are too similar, even with differing bulk isotope ratios, hindering pollution source tracing in complex matrices [2].

The discretization of mass-to-charge (m/z) values can result in the loss of critical chemical information, a challenge that the Multi-Scale Sinusoidal Embeddings (MSSE) method addresses by enabling more precise data interpretation [3]. However, the complexity of certain mixtures, such as tholins, complicates the analysis of all possible isomers due to the extensive number of detected peaks, challenging the identification and characterization of individual components [26].

The proposed gas-flow dynamics suppression method, while innovative, may not be universally applicable across all ion types or mass spectrometry setups, as its effectiveness can depend on specific experimental conditions [28]. Similarly, despite advancements in Trapped Ion Mobility Spectrometry coupled with Fourier Transform Ion Cyclotron Resonance Mass Spectrometry (TIMS-FTICR MS), challenges persist in resolving extremely complex mixtures, indicating inherent limitations in current methodologies [18].

The Diamond Molecular Balance (DMB) method, though revolutionary in measuring mass with high precision, may encounter challenges related to pressure fluctuations and positional accuracy during measurements, affecting result reliability [20].

To address these limitations, improvements can be made by enhancing mass spectrometric resolution and accuracy through innovative data processing algorithms and advanced computational models. Expanding the applicability of novel ionization and fragmentation techniques across various experimental conditions could significantly enhance the robustness of methodologies, particularly in non-target analysis for atmospheric trace gases, where gas chromatography coupled with electron ionization high-resolution mass spectrometry (GC-EI-HRMS) has shown effectiveness in identifying unknown compounds. This is crucial given the ongoing challenges in detecting and characterizing halogenated organic compounds and emerging pollutants in complex environmental samples [23, 14]. Standardizing protocols and developing comprehensive reference materials would facilitate consistent quantification across studies, ultimately enhancing environmental monitoring and pollution management strategies.

6.4 Emerging Trends and Future Research Directions

Emerging trends in High Resolution Mass Spectrometry (HRMS) emphasize the need for advancing data-sharing infrastructures, developing harmonized guidelines for non-target screening (NTS), and improving training for personnel involved in environmental monitoring [16]. These initiatives aim to enhance HRMS consistency and reliability across various environmental contexts. Future research should prioritize refining chemical signatures and conducting comprehensive toxicity assessments on identified compounds to address evolving trends in HRMS applications [27].

Expanding retention time index (RTI) databases and refining prediction models are essential to enhance HRMS applicability across a broader range of compounds [13]. This expansion will facilitate more accurate predictions and improve the identification of unknown pollutants in complex environmental matrices. Additionally, integrating structural elucidation methods and enhancing algorithm efficiency for larger datasets and more complex molecules are critical for advancing HRMS capabilities [14].

Exploring enhancements to embedding techniques, such as Multi-Scale Sinusoidal Embeddings (MSSE), could broaden their applications in metabolomics and other mass spectrometry domains [3]. This exploration could improve data interpretation and deepen understanding of complex chemical interactions. Furthermore, refining methods for broader applicability across various organochlorine compounds and exploring their potential in other environmental contexts are important research areas [24].

Optimizing sampling synchronization and integrating additional data sources are promising directions for enhancing pollutant detection predictive capabilities [1]. These improvements will contribute to more accurate environmental assessments and effective pollution management strategies. Additionally, refining algorithms in tools like proFIA for improved performance in challenging datasets and exploring integration with other analytical techniques are vital for advancing metabolomic profiling [25].

Future research should also focus on refining methods for analyzing complex organic materials and exploring additional chromatographic techniques to improve separation efficiency [26]. Expanding the application of Design of Experiments (DOE) to other analytical techniques in petroleomics and exploring additional parameters to enhance mass spectrometry performance are crucial for advancing HRMS methodologies [4]. These efforts will support the continued evolution of HRMS as a powerful tool in environmental analysis and beyond.

6.5 Enhancing Sensitivity and Specificity

Enhancing the sensitivity and specificity of High Resolution Mass Spectrometry (HRMS) techniques is pivotal for advancing environmental analysis, particularly in detecting and characterizing complex chemical mixtures. Future research should focus on refining methodologies to improve these analytical parameters, ensuring accurate and reliable pollutant detection. A promising area of exploration is the refinement of hydrogen abstraction (H-abstraction) reaction methods, crucial for understanding organic pollutant transformation processes. Enhancing the sensitivity and specificity of these methods will provide deeper insights into H-abstraction reactions, thereby improving HRMS analytical capabilities [23].

In addition to methodological advancements, computational approaches are critical for enhancing HRMS techniques. Developing sophisticated algorithms and data analysis tools can significantly improve the interpretability and reproducibility of molecular networks, essential for accurate pollutant identification. Recent experiments have demonstrated statistically significant improvements in molecular network reproducibility and interpretability, highlighting the potential of computational advancements to enhance HRMS applications [6].

Furthermore, integrating advanced ionization and fragmentation techniques can enhance HRMS sensitivity and specificity. Optimizing these processes will improve detection limits and accuracy, enabling trace-level contaminant identification in complex environmental matrices. This comprehensive approach, integrating methodological refinements and cutting-edge computational innovations, is set to significantly enhance HRMS analytical capabilities. By facilitating more efficient non-target screening and data processing, this strategy will support effective environmental monitoring and pollution management initiatives, addressing the complex challenges posed by chemical contamination in ecosystems [12, 21, 15].

7 Conclusion

High Resolution Mass Spectrometry (HRMS) serves as a pivotal technology in the realm of nontarget screening, significantly advancing the field of environmental analysis. Its high-resolution capabilities enable the precise detection and characterization of a wide array of pollutants, including those previously unidentified, thereby expanding the horizons of environmental monitoring. The integration of HRMS with nontarget screening methodologies provides a comprehensive framework for the identification of emerging contaminants, alongside an evaluation of their ecological and health implications. The establishment of harmonized protocols and rigorous quality assurance measures is crucial to ensure the reliability and comparability of results across diverse studies.

Moreover, the survey underscores the importance of adopting holistic approaches that take into account the complex interactions within chemical mixtures and their subsequent ecological impacts. Such approaches are instrumental in improving water quality management and bolstering environmental protection efforts. Anticipated advancements in mass spectrometry techniques, particularly in data analysis innovations and novel ionization methods, are poised to enhance the sensitivity and specificity of HRMS applications further. These technological developments promise to enrich our understanding of environmental chemical dynamics and human exposure, thereby supporting more effective regulatory frameworks and pollution management strategies.

References

[1] Maria Cairoli, André van den Doel, Berber Postma, Tim Offermans, Henk Zemmelink, Gerard Stroomberg, Lutgarde Buydens, Geert van Kollenburg, and Jeroen Jansen. Monitoring pollution pathways in river water by predictive path modelling using untargeted gc-ms measurements, 2022.

[2] Caiming Tang and Jianhua Tan. Fingerprinting of compound-specific chlorine isotopologue distribution of organochlorines by gc-hrms, 2017.

[3] Gennady Voronov, Rose Lightheart, Joe Davison, Christoph A. Krettler, David Healey, and Thomas Butler. Multi-scale sinusoidal embeddings enable learning on high resolution mass spectrometry data, 2023.

[4] Jandyson M Santos, Marcos A Pudenzi, Alberto Wisniewski Jr, Márcia C Breitkreitz, and Marcos N Eberlin. Optimization of atmospheric pressure photoionization for the crude oil analysis using ultra-high resolution mass spectrometry. *Journal of the Brazilian Chemical Society*, 30(4):819–829, 2019.

[5] Andrew Palmer, Prasad Phapale, Ilya Chernyavsky, Regis Lavigne, Dominik Fay, Artem Tarasov, Vitaly Kovalev, Jens Fuchser, Sergey Nikolenko, Charles Pineau, et al. Fdr-controlled metabolite annotation for high-resolution imaging mass spectrometry. *Nature methods*, 14(1):57–60, 2017.

[6] Reproducible molecular networkin.

[7] Thomas J Mcgrath, Julien Saint-Vanne, Sébastien Hutinet, Walter Vetter, Giulia Poma, Yukiko Fujii, Robin E Dodson, Boris Johnson-Restrepo, Dudsadee Muenhor, Bruno Le Bizec, Gaud Dervilly, Adrian Covaci, and Ronan Cariou. Detection of bromochloro alkanes in indoor dust using a novel cp-seeker data integration tool, 2024.

[8] Bowen Du, Jonathan M Lofton, Katherine T Peter, Alexander D Gipe, C Andrew James, Jenifer K McIntyre, Nathaniel L Scholz, Joel E Baker, and Edward P Kolodziej. Development of suspect and non-target screening methods for detection of organic contaminants in highway runoff and fish tissue with high-resolution time-of-flight mass spectrometry. *Environmental Science: Processes & Impacts*, 19(9):1185–1196, 2017.

[9] Dawei Lu, Qian Luo, Rui Chen, Yongxun Zhuansun, Jie Jiang, Weichao Wang, Xuezhi Yang, Luyao Zhang, Xiaolei Liu, Fang Li, et al. Chemical multi-fingerprinting of exogenous ultrafine particles in human serum and pleural effusion. *Nature communications*, 11(1):2567, 2020.

[10] Caiming Tang, Jianhua Tan, Yujuan Fan, Ke Zheng, Qiuxin Huang, and Xianzhi Peng. Observation of inconsistent carbon isotope compositions of chlorine-isotopologue pairs of individual organochlorines by gas chromatography-high resolution mass spectrometry, 2019.

[11] Thaïs Hautbergue, Olivier Puel, Souria Tadrist, Lauriane Meneghetti, Michel Péan, Marcel Delaforge, Laurent Debrauwer, Isabelle P Oswald, and Emilien L Jamin. Evidencing 98 secondary metabolites of penicillium verrucosum using substrate isotopic labeling and high-resolution mass spectrometry. *Journal of Chromatography B*, 1071:29–43, 2017.

[12] Werner Brack, Beate I Escher, Erik Müller, Mechthild Schmitt-Jansen, Tobias Schulze, Jaroslav Slobodnik, and Henner Hollert. Towards a holistic and solution-oriented monitoring of chemical status of european water bodies: how to support the eu strategy for a non-toxic environment? *Environmental Sciences Europe*, 30:1–11, 2018.

[13] Reza Aalizadeh, Nikiforos A Alygizakis, Emma L Schymanski, Martin Krauss, Tobias Schulze, Maria Ibanez, Andrew D McEachran, Alex Chao, Antony J Williams, Pablo Gago-Ferrero, et al. Development and application of liquid chromatographic retention time indices in hrms-based suspect and nontarget screening. *Analytical chemistry*, 93(33):11601–11611, 2021.

[14] Myriam Guillevic, Aurore Guillevic, Martin Vollmer, Paul Schlauri, Matthias Hill, Lukas Emmenegger, and Stefan Reimann. Automated fragment identification for electron ionisation mass spectrometry: application to atmospheric measurements of halocarbons, 2021.

[15] Reza Aalizadeh, Maria-Christina Nika, and Nikolaos S Thomaidis. Development and application of retention time prediction models in the suspect and non-target screening of emerging contaminants. *Journal of Hazardous materials*, 363:277–285, 2019.

[16] Juliane Hollender, Emma L Schymanski, Lutz Ahrens, Nikiforos Alygizakis, Frederic Béen, Lubertus Bijlsma, Andrea M Brunner, Alberto Celma, Aurelie Fildier, Qiuguo Fu, et al. Norman guidance on suspect and non-target screening in environmental monitoring. *Environmental Sciences Europe*, 35(1):75, 2023.

[17] Juliane Hollender, Bert Van Bavel, Valeria Dulio, Eivind Farmen, Klaus Furtmann, Jan Koschorreck, Uwe Kunkel, Martin Krauss, John Munthe, Martin Schlabach, et al. High resolution mass spectrometry-based non-target screening can support regulatory environmental monitoring and chemicals management. *Environmental Sciences Europe*, 31(1):1–11, 2019.

[18] Christopher P. Rueger, Julien Maillard, Johann Le Maitre, Mark Ridgeway, Christopher J. Thompson, Isabelle Schmitz-Afonso, Thomas Gautier, Nathalie Carrasco, Melvin A. Park, Pierre Giusti, and Carlos Afonso. Structural study of analogues of titan s haze by trapped ion mobility coupled with a fourier transform ion cyclotron mass spectrometer, 2019.

[19] Caiming Tang and Jianhua Tan. Simultaneous observation of concurrent two-dimensional carbon and chlorine/bromine isotope fractionations of halogenated organic compounds on gas chromatography, 2019.

[20] Donggeun Lee, Seung-Woo Jeon, Chang-Hwan Yi, Yang-Hee Kim, Yeeun Choi, Sang-Hun Lee, Jinwoong Cha, Seung-Bo Shim, Junho Suh, Il-Young Kim, Dongyeon Daniel Kang, Hojoong Jung, Cherlhyun Jeong, Jae pyoung Ahn, Hee Chul Park, Sang-Wook Han, and Chulki Kim. Diamond molecular balance: Revolutionizing high-resolution mass spectrometry from mda to tda at room temperature, 2024.

[21] Rick Helmus, Thomas L Ter Laak, Annemarie P van Wezel, Pim de Voogt, and Emma L Schymanski. patroon: open source software platform for environmental mass spectrometry based non-target screening. *Journal of Cheminformatics*, 13(1):1, 2021.

[22] Jeremy P Koelmel, Nicholas M Kroeger, Candice Z Ulmer, John A Bowden, Rainey E Patterson, Jason A Cochran, Christopher WW Beecher, Timothy J Garrett, and Richard A Yost. Lipidmatch: an automated workflow for rule-based lipid identification using untargeted high-resolution tandem mass spectrometry data. *BMC bioinformatics*, 18:1–11, 2017.

[23] Caiming Tang, Jianhua Tan, Yujuan Fan, and Xianzhi Peng. Ascertaining hydrogen-abstraction reaction efficiencies of halogenated organic compounds on electron ionization mass spectrometry, 2019.

[24] Caiming Tang and Jianhua Tan. Compound-specific chlorine isotope analysis of organochlorines using gas chromatography-double focus magnetic-sector high resolution mass spectrometry, 2017.

[25] Alexis Delabrière, Ulli Hohenester, Benoit Colsch, Christophe Junot, François Fenaille, and Etienne Thévenot. profia: A data preprocessing workflow for flow injection analysis coupled to high-resolution mass spectrometry, 2017.

[26] Thomas Gautier, Isabelle Schmitz-Afonso, David Touboul, Cyril Szopa, Arnaud Buch, and Nathalie Carrasco. Development of hplc-orbitrap method for identification of n-bearing molecules in complex organic material relevant to planetary environments, 2016.

[27] Seth Newton, Rebecca McMahen, James A Stoeckel, Michael Chislock, Andrew Lindstrom, and Mark Strynar. Novel polyfluorinated compounds identified using high resolution mass spectrometry downstream of manufacturing facilities near decatur, alabama. *Environmental science & technology*, 51(3):1544–1552, 2017.

[28] Uma Namangalam, Salvi Mohandas, Hemanth Dinesan, and Sunil Kumar S. Suppression of collision-induced dissociation in a supersonically expanding gas, 2024.

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