Review

Mass Spectrometry-Based Techniques Towards OMICS 2.0

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Review

Education Made Easy with Lab-on-a-Chip, or One Tool—Mass-Spectrometry-Based Techniques, OMICS 2.0 and Society 5.0

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Abstract: The literature was scoped to help place mass spectrometric (MS) platforms in the spotlight of the life sciences, as a tool of OMICS and OMICS 2.0 technologies. Moreover, today's appliances are so handy, that they literally place a whole lab on a single chip. Methods of OMICS (and the most recently developed term OMICS 2.0) are tackled, having in mind their aptness for educational purposes, as well as their feasibility. This same topic was highlighted in many reviews that have been periodically published. The author's initial interest was the forensic application of MS, but since these interests changed, terms such as "biosensors" were also examined, so the review included means of discovery of efficient biomarkers and clinical therapeutic targets. Aside of simply reviewing the research status and the future perspectives, this article tackles terms such as Society 5.0 and OMICS 2.0. However, within the framework of this review, physical chemistry, bioinformatics, or specific software solutions were not specifically studied. Since the topic of generating permanent collections of digital content for retrospective analysis was also reviewed, the need for loads of data – cloud storage was discussed in the context of MS. These large quantities of data are easier to operate with if generated by MS, rather than by any other commercially available assay. In this manner, the review has strengthened an in-depth understanding of the applications of MS.

Keywords: cost; mass spectrometry; OMICS; OMICS 2.0: Society 5.0

1. Introduction

One of the universally used - powerful and flexible tools of any laboratory is actually a hybrid of gas chromatography (GC) and mass spectrometry (MS). MS is one of the main analytical technologies on which the ''-omics'' approaches are based [1,2]. the emerging concept of OMICS 2.0 pushes it even further into the foreground [3,4].

Essentially, we use this exquisite combination to separate mixtures of complex composition, count analytes and identify unknown compounds represented by peaks on the spectrogram [5–7]. Both techniques are highly precise and swift, and they both have proven to be exceptionally operative and informative when combined. This appliance is used for analyzing chemical mixtures in drug screening and addiction recovery monitoring, forensic, environmental, and trace analysis, and is a technique with supreme sensitivity and selectivity [6,8]. The rationale for this "hybridization" is that it is not possible to make an accurate identification of a particular molecule by a GC or MS alone. However, when these two analytical methods are combined, they allow efficient substance identification [9,10]

2. Blood-Alcohol Determination

Toxicology assessment is performed by the field's golden standard - headspace gas chromatography with flame ionization detection (HS-GC-FID) [11–13]. This method is merely a variation of the apparatus drafted in Figure 1.

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It provides key information as to the type of substance present in an individual and the amount of those substances [14]. Basically, a person's blood alcohol concentration is a function of the total amount of alcohol in the person's system divided by the total body water [15,16]. Though, total body water is the preferred method to use in forensic blood-alcohol calculations rather than the volume of distribution of pure ethanol [17]. Though, alcohol has a hydrophilic affinity , what renders it more "water-demanding" for alcohol to be distributed in.

2.1. GC-MS

Separation science and analytical technique are combined, and blood is the preferred specimen. Since the GC is a separation technique here, certain outputs of the separation are inputs in the analytical part, and that input has its features. For instance, the interval between the injection of a sample into the glass coil and the detection of substances in that sample is called retention time (RT). It's the unique and substance-specific time required for the solute to pass through a chromatographic column [18]. Most often, separation and analysis devices are merged (hyphenated) into a unique instrument via a heated transfer line. For that reason, we call these techniques – "hyphenated" analytical techniques. The GC utilizes a capillary column (Figure 1). The separation abilities of that capillary column depend on the column's dimensions as well as the properties of the analyte. An individual feature of components constituting the analyte will stimulate the separation of the molecules as the sample/analyte travels the length of the column.

Each molecule is further broken by MS into ionized fragments and fragments are identified using their mass-to-charge ratio [10]. This can be used to determine the molecular weight and elemental composition, thus chemical structures of molecules. Each ion has its particular mass-to-charge ratio.

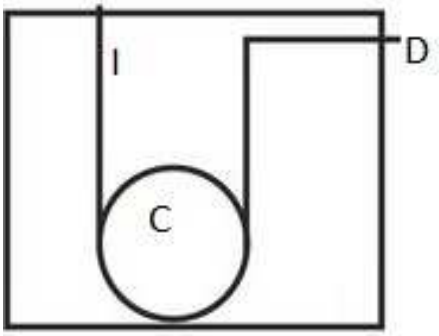

Figure 1. Schematic of standard GC-MS; (I) – input/ injection; (C) – capillary column: (D) – detection device.

The usefulness of hyphenated instruments is evident in many separation processes as they are common tools in industry and research.

2.2. Semiquantitative Widmark Equation

Still, the first and the most popular calculation method is the Widmark equation [19] which is. based on oxide-reduction reaction and the amount of ethanol is calculated indirectly. This is the most widespread form of the equation to assess blood alcohol concentration. It utilizes a known amount of bichromate solution (potassium bichromate and *Acidum sulfuricum*), followed by titration of superfluous bichromate with hyposulphate solution.

It accounts:

a) the hypothetical initial blood alcohol concentration (before any metabolism has occurred).
b) amount of pure ethanol consumed.
c) fraction of blood volume that is water.
d) total body water of an individual [15,20,21].

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The simplified version of the Widmark equation is: blood-alcohol concentration = [Alcohol consumed in grams / (Body weight in grams x r)] x 100.

In this formula, "r" is the gender constant, and equals 0.55 for females and 0.68 for males [22].

3. „OMICS"

The word „OMICS" refers to a field of study in biological sciences that ends with -OMICS, such as genomics, transcriptomics, proteomics, or metabolomics [23]. It is a vernacular expression - suffix -OMICS is used frequently to describe something big and refers to a field of study in life sciences that focuses on large-scale data/information - such as proteomics, genomics, metabolomics, etc. [24]. Proteomics and genomics were the first „OMICS" formed to date, and now there are lots of closely related scientific disciplines. Some of these disciplines gave birth to new scientific fields and covered narrower arrays of a specific scientific field [25].

Approaches based on MS and steered to answering the problems of petroleomics, foodomics, humeomics, and exosomics; or those problems related to inorganic sciences - are merely mentioned. The most compelling consideration is paid to „OMICS" related to the life sciences as those represent the majority of today's „OMICS [2]. Notwithstanding this explanation, there are „OMICS" outside of the life sciences circle. On the other hand, working with copious data, whatsoever, is not complete without statistical, and mathematical processing of databases. Generally speaking, MS laid a foundation for the set of „OMICS" disciplines, and many of them took shape as sciences after some new advances in the field of MS [26].

Additional advances in scientific culture and responsible innovation are called OMICS 2.0. It is driven by systems-oriented thinking, meta-analysis, and independent social science analyses that help bridge the current gaps between omics technologies and society [3].

3.1. Possibilities

GC-MS can be used for an assortment of applications comprising the detection of potentially toxic chemicals in foods to the quantitation of organic contaminants in water, the determination of pesticide residues to the characterization of ingredients [27]. As previously said on many occasions, distinguishing compounds of a mixture to separate them is performed by injecting a gaseous sample (analyte) into a carrier gas (usually an inert or an unreactive gas). With this procedure, a mobile phase is produced. this is a gaseous mixture driven through a capillary column - stationary phase [10].

It was not until 1977 that GC-MS was admitted to the court as evidence [28], and nowadays GC-MS can be used to study liquid, gaseous or solid samples. The analysis begins with the GC, where the sample is effectively vaporized into the mobile phase and separated into its various components using a capillary column coated with a stationary (liquid or solid) phase. As elements of our analyte are separated, each element drops down the column at a different time based on its properties. Once the components leave the GC column, they are ionized and fragmented by the MS using electron or chemical ionization sources. Ionized molecules and fragments are then accelerated through the instrument's mass analyzer. It is here that ions are separated based on their different m/z ratios. In the context of metabolome/ metabolomics, MS-based laboratory techniques should be regarded only as a tool for researchers to dive deeper into the metabolome and explore all metabolites.

Dealing with substances that will be detected at very low levels, or with will be very little information about their toxicity, would result in controversies over whether the concentrations found pose a significant risk to the public health or the environment, he added Drug testing, as an example, can be carried out for multiple reasons: pathology, healthcare, and the anti-doping of both humans and animals [29]. Their concentration in biological fluids is usually very low, so their detection requires the GC-MS, additionally, the molecules in merit are often very small (<650 Daltons) [8,30,31].

however, compound identification and reliable quantification are greatly complicated owing to the chemical complexity and dynamic range of the metabolome [32]. GC-MS data acquisition can be performed to enable the detection and quantification of many thousands of metabolite features as part of MS-based metabolomics.

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3.1.1. MS-Based Quantitative Strategies and Analysis of Proteome, Genome, and Transcriptome

Cells are continuously operational biochemical laboratories, and in their versatility, biological systems are incredibly complex. The result is an almost inexhaustible object of research [2]. The term "genome" was something that changed throughout history, so instead of the totality of genes in all chromosomes (what was its original meaning), it now designates the complete set of DNA in organisms, including all of its genes [2]. The elementary monomeric units of DNA and RNA macromolecules are nucleotides, consisting of nitrogenous bases, monosaccharides, and phosphoric acid residues. Molecules of purine (adenine, guanine) and pyrimidine (thymine, cytosine) structures act as nitrogenous bases for DNA. The same bases are included in the nucleotides of RNA molecules, except that thymine in them is replaced by uracil. In DNA and RNA, these nitrogenous bases bind to monosaccharides deoxyribose and ribose, respectively, forming nucleosides. In nucleotides, the latter is phosphorylated at the primary OH group of a monosaccharide, and this phosphate [33].

Even though qRT-PCR is considered the gold standard in transcriptome techniques due to its accuracy and sensitivity, RNA-seq turns out to be equivalent[16,17]. Transcriptomics can either refer to exploratory analysis of the entire transcriptome, primarily using RNA sequencing (RNA-seq) [34], or to targeted analysis of known RNAs using techniques such as gene expression panels (GEPs).

Of all MS-based quantitative strategies, in the analysis of nucleic acids most often used is matrix-assisted laser desorption/ionization–mass spectrometry (MALDI-MS), recently improved with the time-of-flight (ToF) feature [35]. This appliance should nevertheless recoil due to high initial costs, especially since it does not require trained laboratory personnel [36]. Interestingly, RNAs are more stable than DNA, so the latter are preliminarily converted into RNA by in vitro transcription.

The scope of delivery of RNAs formed in one or a series of cells of an organism is called a "transcriptome" [37,38]. It consists of ribosomal (rRNA), transport (tRNA), and messenger (mRNA) RNA [39,40]. Out of those three forms of RNA, mRNA serves as a transmitter of genetic information [41,42], After translation, these RNAs are rapidly degraded. Though, the complete transcriptome is a subject of interest in transcriptomics [43]. During translation, tRNAs take part as an intermediate between nucleic acids and proteins: they attach activated amino acid residues and transfer them to the site of synthesis of protein polypeptide chains rRNAs do not participate in the process of information transfer and constitute the bulk of the ribosomes. The sequence of nucleotides in mRNA molecules contains all the information about the amino acid sequence in a protein chain.

All types of RNA are synthesized on a DNA template, and the sequence of ribonucleotides in them is complementary to the sequence of deoxyribonucleotides in DNA. Molecules of purine (adenine, guanine) and pyrimidine (thymine, cytosine) structures act as nitrogenous bases for DNA. The elementary monomeric units of DNA and RNA macromolecules are nucleotides, consisting of nitrogenous bases, monosaccharides, and phosphoric acid residues. Though, the same bases are included in the nucleotides of RNA. Except that thymine is replaced by uracil. In DNA and RNA, these nitrogenous bases bind to monosaccharides deoxyribose and ribose, respectively, forming nucleosides Monosaccharides deoxyribose or ribose are phosphorylated in nucleotides, and this phosphate group phosphorylates the OH group of a monosaccharide of another nucleotide, because of which macromolecules of nucleic acids are formed.

Quantitative strategies relying on MS and MS within genomics/transcriptomics are only logical MS led to the concept of "OMICS". And nowadays sequencing and MS are basic experimental tools in investigating the omics of a given biological system. Since a substantial amount of information is obtainable from sequencing-based methods, MS-based techniques can be used to investigate proteome, metabolome, and interactomes that do not involve DNA/RNA [44].

An enormous number of processes simultaneously occur in all of our cells. Accordingly, the proteome is more of a challenge than the human genome [45]. Not only its scale is estimated at over 1 million proteins but the increase in proteomic diversity is further increased by protein post-translational modifications (PTMs) [46]. Precisely the analysis of PTMs could provide a comprehensive vision of molecular mechanisms for various diseases [47]. Though, these modifications of proteins following protein biosynthesis are generally enzymatic. It refers to changes in the polypeptide chain as a result of adding distinct chemical parts to amino acid residues

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To be blunt, PTMs are the foundation of complicated cellular processes, such as cell division, growth, differentiation, signaling, and regulation, the same as various processes included in the maintenance of protein structure and integrity [48].

PTMs also regulate the metabolism and defense processes, cellular recognition, and morphology alternation [49]. Consequently, analysis of PTMs is important for the study of cell biology and disease diagnostics and prevention. The worldwide studies of different PTMs and the proportion change of different proteins could provide new insights into the clinical approach [25].To highlight the relevance of MS in the analysis of PTM, statistics of each PTM experimentally and putatively detected have been compiled using proteome-wide information from the Swiss-Prot database [50].

Many physiological functions can be overviewed using MS-based quantitative strategies developed to quantify glycoprotein expression levels on a large scale [51]. Proteomics based on MS is made feasible by the availability of gene and genome sequence databases and technical and conceptual advancements in many areas [52–55]. Typically, mass spectrometry can cover a range of functions [56]. Time-of-flight (TOF), quadrupole (Q), Fourier transforms ion cyclotron resonance (FT-ICR), and ion trap (IT) that are used generally in labs, are usually combined in proteomics in one MS (triple quadrupole (QqQ), Q-IT, Q-TOF, TOF-TOF, IT-FTMS, etc.) [57].

3.1.2. MS-Based Quantitative Strategies, Food, and Environment

Food science and nutrition interact with disciplines such as pharmacology, medicine, and biotechnology. Conversely, the discipline that we call environmental health, specifically environmental toxicology provides critical information and knowledge for regulatory agencies, decision-makers, and others. To help them, scientists may take advantage of MS, and students of all health-related sciences should be familiar with it.

Today's appliances aim to identify and quantify complex protein (peptides) mixtures in a single experiment [58,59] in which modern analytical chemistry must provide accurate, precise, and robust methods. These methods have to be able to determine any toxic compounds or organisms that might be present in food at very low concentrations. Foodomics is a portmanteau coined in 2009 as "a discipline that studies the Food and Nutrition domains through the application and integration of advanced -OMICS technologies to improve consumer's well-being. Detection of exogenous contaminants in food, food safety, quality, and traceability with MS-based "OMICS" is always a complex area, health, and knowledge". Foodomics requires a combination of food chemistry, biological sciences, and data analysis [60]. A framework of knowledgeability required for the average medical student in the field falls greatly beyond the topic of food cOMICS, so this review shall focus specifically on MS and its application.

In the framework of environmental health, MS is mainly the environmental toxicology tool used to put programs and policies in place to limit our exposure to these substances, thereby preventing or reducing the likelihood that a disease or other negative health outcome would occur [61]. MS has its inevitable position in wastewater-based epidemiology for the determination of small and large molecules as biomarkers of exposure [62,63].

4. A Systematic Review of Mass Spectrometry and OMICS

To conduct this review, Web of Science Core Collection, PubMed, and Jisc Library databases were searched for: mass spectrometry and OMICS, sustainability, and cost.

From the published articles, only those that appeared after 2015 were selected. The initial search (with "AND" as an operator) yielded 51 results from the Web of Science Core Collection. 36 results were found in PubMed, and 5 document results were found in the Jisc Library databases.

From the total number of 92 articles, we excluded 20 duplicates and 6 unrelated articles. The remaining 66 articles were all written in English, no article included a single case report. A total of 66 articles were used for this systematic review and the PRISMA flow diagram can be seen in Figure 2.

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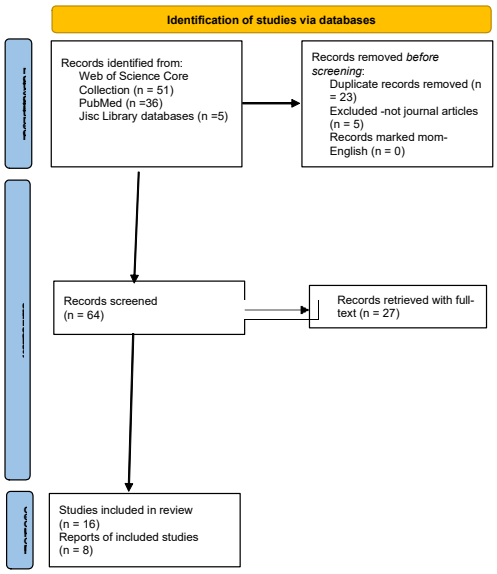

Figure 2. PRISMA diagram of the systematic review of the published articles, only those that appeared after 2015 were selected with "and" as an operator.

5. Immunoassay or Mass Spectrometry—Affordability

Immunoassays use specific antibodies, while MS exploits measuring the mass-to-charge ratio of ionized molecules to quantify an analyte. Many clinical analytes can be measured using either immunoassay or mass spectrometric methods and choosing the method to use can be a demanding decision dependent on a variety of factors. Most shortened, immunoassays are traditionally used for larger molecules (eg, proteins) while mass spectrometry is more commonly used to detect small molecules (eg, drugs) [64–66].

Some laboratories employ both techniques, but generally choice depends on the clinical need [67]. Immunoassays are generally reliable and accurate; they are more automated and decrease the sample preparation required [68]. Considering the findings of Liu et al. in particular the effects of deep learning on the computational time of the algorithm, the use of deep learning in the MS should be encouraged [69]. For the most part, MS-based methods have lower limits of quantification than immunoassays and are therefore useful for measuring very low analyte concentrations [70]. Conversely, due to its potential to provide greater analytical sensitivity and specificity MS is increasingly used, especially at low levels [55].

Interfering substances and sample impurities alter the measurable concentration of an analyte, can be relatively common, and vary widely between patients and assay platforms. Although the matrix may affect both immunological and mass spectrometric methods, the effects tend to be more prevalent in immunoassays because sample extraction or separation methods are less common.

Immunoassays are generally commercially developed, while mass spectrometric methods are often laboratory-developed and can therefore be substantially different from one another [71–73]. Both methods suffer from this lack of standardization. Considering the variety of assay platforms, the lack of standardization and discrepant results between laboratories without actual reference intervals are understandable. Competing manufacturers independently develop and offer a variety of assay platforms, reagents, antibodies, and standards; which all contribute to different results and reference intervals. Conversely, mass spectrometric methods are often laboratory-developed and can therefore be substantially different from one another.

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5.1. Feasibility

Regardless of its importance in substance identification [9], when deciding between immunoassay and mass spectrometry for other analyses, the best option will depend on the needs, goals, and patient population.

The chief disadvantage of MS methods is that they are not easily integrated into core laboratory automation. Additionally, they require personnel (although, the "new" MALDI-ToF does not) with specialized training, and, due to batch processing, tend to have longer turnaround times (which has been successfully reduced). In contrast, immunoassays tend to be more easily automated and require less training but are more susceptible to interference and can require higher-priced reagents, hence costing more to run [36,69,74,75].

On the other hand, the cost of running LC-MS practically does not exist, however financial considerations for purchasing an MS are substantial. After explaining the financial components that must be considered when purchasing an MS system, it is unavoidable to calculate the return on investment [76,77]. Insignificant operating expenses in comparison to intimidating initial costs could ultimately be used as an excuse, together with an argument that currently there is no alternative in the market [78,79].

To evaluate the cost-effectiveness and return on investment, when deciding on investing in a new MS instrument, the price of an MS instrument, as well as all other (recurring) costs, should be considered (i.e., service contract, reagents, consumables, etc.). that are necessary to keep a workflow current with access to technology advancements, as well as service, training, and support. Before making such a decision, it is necessary to insure against equipment obsolescence [80,81].A systematic review of mass spectrometry and sustainability/ mass spectrometry and cost

To finalize this review with data on sustainability, Web of Science Core Collection, PubMed, and Jisc Library databases were searched for: mass spectrometry and, sustainability; with "and" as a logical operator. The search returned 3 items. Unfortunately, they were outdated, so excluded from the literature review.

Simply put, the fact that the literature search yielded no results, or no studies make its publication harder. However, its value is to invite researchers to contribute to the field.

6. Sustainable MS-Based Quantitative Strategies

Mass spectrometry is a key analytical technique in receiving the required molecular information from minute amounts of samples present in the gas, solid, or liquid phase. This is crucial for many applications in life science and environmental science-oriented „OMICS" [82]. Conclusively, progress in all these fields would contribute to the long-term vision originating from the project's objectives, specifically molecular isomer differentiation or weighing the chemical bonds in a molecule directly by mass spectrometry. All these approaches could leave a deep impact on physical, (bio)chemical, and life sciences. The envisioned scientific achievements in health and sustainability applications may translate into improved drug discovery, early diagnosis, and prognosis for preventive and personalized medicine. The planet and humanity should further benefit from an increase in the sustainability of energy production and processing.

Sounded alarms of various governmental or nongovernmental organizations and independent researchers alerted us of rapid and global progress that could seal this generation's and generations to come fate. Namely, we could all face a future steeped in inequity and climate crises. As MS is practically zero-waste technology we could all pull our weight without compromising the ability of future generations to meet their own needs. Without actually knowing what sustainability looks like in practice.

Therefore, perhaps it is sound to expect that machine learning algorithms and deep learning could further improve the sustainability of mass spectrometry since it improves library retrieval accuracy, the accuracy of spectral library retrieval, and reduces the computational time of the algorithm by more than 2 hours in the study of Liu et al. [69].

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Everyone wants it, but all may have different ideas in their heads of what that means. However, it will need a whole collection of ambitious strategies to achieve meaningful change. So, it is not a matter of asking how exactly to get there, but to start walking.

Even if favoriting MS-based quantitative strategies is a small step for overall sustainability, it is the start of a long journey toward a sustainable future, and it may turn out to be an unparalleled notch-up for some future pandemics [83,84].

At the moment, considerable efforts are invested in the development of sustainable nanosystems as front-end technology for MS [85].

Likewise, in the framework of the Community Research and Development Information Service (CORDIS) of the European Commission, there is a project funded by the EU's framework programs for research and innovation of the rapid screening and identification of illegal drugs by IR absorption spectroscopy and gas chromatography as well as an initiative to redefine MS into a breakthrough platform for real-time noninvasive breath analysis with single ion detection of intact viruses and bacteria and post-analysis molecular characterization, so Ms has a future as a sustainable method of the tomorrow [86–88].

6.1. A Systematic Review of Mass Spectrometry and Sustainability/ Mass Spectrometry and Sustainability

To finalize this review with data on sustainability, Web of Science Core Collection, PubMed, and Jisc Library databases were searched for: mass spectrometry and, sustainability; with “AND” as a logical operator In the next query, “sustainability” was replaced with “sustainability”.

No results at all were obtained in reference to this query, so like in the previous case, the literature search yielded no results, or no studies were included in our scope. Mass Spectrometry and OMICS 2.0 in the Society 5.0

The extremely new concept of Society 5.0 is like a guide to social development and can have a profound impact on all points of society, as it emphasizes the potential of the individual-technology relationship [89]. We gave such a catchy name to the “super-smart” society that does not bother with lame questions like “ELISA or MS?”. Indeed, just like Industry 4.0, which is the digital transformation of manufacturing, Society 5.0 aims to tackle several other challenges by going far beyond just the digitalization of the economy [90–92]. Digitalization in the present context extends to all levels of society and ITS (digital) transformation. The omnipresent diffusion of new technologies has recently led to a dramatic adjustment of the techniques and technologies in almost all countries [93]. Internet, robots, self-driving cars, and artificial intelligence are all“new” risks [94–96]. Therefore, it has many pretty comprehensive consequences even for this “ELISA or MS” dilemma. For instance, the emerging “digital ELISA” (single-molecule detection platform) can.be combined with the concept of multiplexing. In this way, extremely low serum concentrations of proteins detectable by “digital ELISA” are rendered even more convenient by adding the option of employing multiple analytes, using several types of nanomaterial-based biosensors [97,98]. On the other hand, MS has become a standard for the analysis of different substances in the clinical laboratory [99].

Aside from its unique strength in performing analysis, MS has a remarkable ability to generate permanent collections of digital content for retrospective analysis [100]. Substances such as antibiotics, immune-suppressive drugs, drug metabolites in former addicts, or therapeutic antibodies used for the treatment of different diseases can all be scooped by the MS. High-resolution, mass-accurate data can demand infrastructure capable of managing 1 GB/h of data. Such enormous quantities of data are generated not only by life science investigators but, increasingly, by those working in industries that depend on high-volume processes like characterizing the presence of metabolites and their biotransformations. In Society 5.0 application of OMICS technologies is tackled in diverse and complementary global settings. We call this concept - OMICS 2.0 [3,26,65]. This leap forward furthers the improvement of the quality of life of all people in a sustainable world [101].

Talking specifically of MS, resulting RTs and *m/z* can be summed, plotted, and stored as a series of data acquired by modern digital instruments. Collections of data yielded from such material can be made available in a cloud computing model that enables storing data and files on the internet through a cloud computing provider [102,103]. With data obtained by MS-based quantitative

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strategies, it is feasible to identify those compounds. However, recent works, such as that of Meissner et al. herald its use in proteomics [55]. Samples are generally dissolved or diluted in a solvent and then injected into the heated inlet port. However, some other methods of sample preparation may also be involved [104]. The liquid sample is vaporized in the hot inlet and converted to gas [105]. The separated compounds then leave the column and enter a detector. The time taken to travel through the column and reach the detector is called retention time [106].

7. Machine Learning and Artificial Intelligence (AI) Approaches

Involving the "metaverse" in this topic might seem a bit inappropriate, and that owes to articles on the metaverse are often illustrated with images of people in VR headsets [107]. However, nearly all people who use metaverse platforms access them otherwise. Chatbots, modern digitalized user interfaces, and e-learning platforms are nothing, but a tool used by humans to observe and interact in a fully or partially synthetic digital environment [82,108].

Machine learning and artificial intelligence (AI) approaches are indispensable components of this concept and have revolutionized multiple disciplines, including toxicology [109,110]. AI-influenced artificial neural networks (ANN) can be employed in forensic science analysis for various purposes. Basically, it is the use of multiple weighted inputs that are summed to produce an output that is then analyzed [111]. AI-augmented toxicology lab offers the most elegant method of dodging space limitations since the need to store several thousands of skeets in large physical archives practically waved [112,113]. Evidently, AI has the potential to outperform most forensic medicine specialists skilled in toxicology in the setting of a toxicological laboratory [114]. Thus, it may soon automate and standardize. Though plots used in AI datasets are visually different from the original, however, proper demands for data storage makes CNNs optimal in this regard [12,115–117]. Deep learning AI models are currently being used in analytical procedures as an assessment to help with efficiency, consistency, and decision making. Unfortunately, they still keep the forensic specialist skilled in toxicology at the center of the assessment. By all accounts it will remain so, at least in the near future [118,119].

Present state-of-the-art toxicology is far away from some anecdotal attainments [120–122]. Learning from the input data mimics the functioning of neurons and their communications to convey complex behavior. This progress follows the progress in the preparation and processing of input material, accessibility of large datasets goes hand-by-hand with the expansion in algorithms' structure. On the other hand, progress in computing programming ignited diligence for learning on the AI-constructed machines built for high-dimensional output of data [123]. A model for the near future comprises the forensic medicine specialist skilled in toxicology enhanced by a real-time artificial intelligence systems' second-review [124,125].

We propose a novel strategy for deep learning in toxicological laboratories. Machines trained and validated by toxicology, from subjects that covered diverse and representative clinical cases, as seem usually in everyday practice [126]. This would yield an AI system that can handle large amounts of toxicological reports without potential disturbances commonly experienced by professionals in the field (space or time limitations, for instance) [127,128]. It will drastically alleviate the heavy clinical burden of daily work. This would also be a generalizable tool for other professions with similar background knowledge.

8. Conclusions

Currently, the concept of systems biology prevails on the big scientific scene and is the talk of the town in biology. Leading methods of such scientific approach include interrelated „OMICS" sciences: transcriptomics, genomics, proteomics, and metabolomics. Perhaps we should all have great hopes for the smooth transition of MS to deep learning, environment because that environment has proven to eliminate timewasters, rendering MS an out-of-favor method [82]. Results of MS yielded in the scope of these „OMICS" sciences generally generate a large number of permanent collections, which are supposed to be best-taken care of in cloud storage. This digital content is available

afterward for subsequent analysis, as to why this method is increasingly attractive in the digitalized society – Society 5.0 [65].

For time being no single method is generally preferred. When deciding between immunoassay and MS-based techniques, the best option will depend on the needs, goals, and patient population. Both methods are subject to impurities and contaminations, but the effects tend to be the most prevalent in immunoassays. Maybe, it is time to introduce MS-based strategies to an approach to gathering information from several "omes ("multi-OMICS").

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