Artificial Intelligence for Mass Spectrometry and Nuclear Magnetic Resonance Spectroscopy

Florian Fricke†, Safdar Mahmood∗, Javier Hoffmann∗, Marcelo Brandalero∗, Sascha Liehr‡,
Simon Kern‡, Klas Meyer‡, Stefan Kowarik⋆, Stephan Westerdick†, Michael Maiwald‡, Michael Hübner∗
† *Ruhr-Universität Bochum (RUB), Germany*
∗ *Brandenburgische Technische Universität (B-TU), Germany*
‡ *Bundesanstalt für Materialforschung und -prüfung (BAM), Germany*
⋆ *University of Graz, Austria*

***Abstract*—Mass Spectrometry (MS) and Nuclear Magnetic Resonance Spectroscopy (NMR) are critical components of every industrial chemical process as they provide information on the concentrations of individual compounds and by-products. These processes are carried out manually and by a specialist, which takes a substantial amount of time and prevents their utilization for real-time closed-loop process control. This paper presents recent advances from two projects that use Artificial Neural Networks (ANNs) to address the challenges of automation and performance-efficient realizations of MS and NMR. In the first part, a complete toolchain has been developed to develop simulated spectra and train ANNs to identify compounds in MS. In the second part, a limited number of experimental NMR spectra have been augmented by simulated spectra to train an ANN with better prediction performance and speed than state-of-the-art analysis. These results suggest that, in the context of the digital transformation of the process industry, we are now on the threshold of a possible strongly simplified use of MS and MRS and the accompanying data evaluation by machine-supported procedures, and can utilize both methods much wider for reaction and process monitoring or quality control.**

***Index Terms*—industry 4.0, cyber-physical systems, artificial neural networks, mass spectrometry, nuclear magnetic resonance spectroscopy**

I. INTRODUCTION

The miniaturization of computing devices can be seen as a vital enabler of the fourth industrial revolution, namely the Industry 4.0. By combining intelligent sensor networks with physical processes in the form of Cyber-Physical Systems (CPSs), it is possible to realize exciting new applications such as flexible production, convertible factories, customer-centered solutions, optimized logistics, and resource-saving recycling management. *Modular Chemical Production*, in particular, where configurable physical modules can be flexibly connected to develop new processes, could substantially accelerate the development of new special chemicals and lead to faster market launches.

Among the requirements for modular chemical production is a *chemical process* and a *quality control sytem* based on special chemical sensors. These sensors collect data that can be used later to assess the concentration of selected chemical components and the presence of undesired by-products. Today, standard chemical sensors are based on optical spectroscopic methods such as near-infrared, infrared, or Raman spectroscopy, all of which have to be calibrated to the specific chemical components under analysis. This process requires a considerable degree of expertise and often causes expenditures in the amount of an analytical instrument's purchase price. Two commonly used methods are currently coming to the fore, as we show in this article, which were previously considered as being too complicated for process analytics: Mass Spectrometry (MS) and Nuclear Magnetic Resonance Spectroscopy (NMR). With the help of machine-supported training and data analysis methods, we use these examples to provide potential approaches for the change towards much-simplified applicability.

For example, artificial intelligence (AI) techniques offer an attractive solution for complex training procedures, such as image recognition, which can also be used for chemical spectra to extract valuable information from a dynamic chemical process. Especially the use of artificial neural networks (ANN) has already shown first promising results for similar processes in the field of chemistry [1]–[6]. In all these studies, ANNs have proven their capability to improve accuracy and speed up the process of spectral analysis. Furthermore, when combined with interpretation techniques, they can identify important features in spectra [7]. ANNs are particularly useful when other linear models fail due to the complexity within the spectra.

In this paper, we present a brief background on topics addressed in this work (Section II), and then we present **our contributions, which can be summarized as follows:**

- We present the design of a miniaturized mass spectrometer for in-process use, along with a toolchain for the automatic training of ANNs that can identify compounds out of the measured spectra (Section III);
- We present a methodology for the augmentation of simulated spectra and training of ANNs that can predict compounds from an NMR spectrum faster and more accurate than the state-of-the-art (Section IV);

Our results suggest that ANNs can be a key technology in enabling in-process MS and NMR to support Industry 4.0.

II. BACKGROUND

MS and NMR spectroscopy are indispensable tools for analysis in different science fields, which have undergone enormous

---

This work was partially funded by the *Bundesministerium für Wirtschaft und Energie* (*BMWi*). The authors would like to thank their colleagues Lukas Wander and Martin Bornemann-Pfeiffer for their support in conducting the experiments.

978-3-9819263-5-4/DATE21/©2021 EDAA

technical development in recent years. Just a few years ago, both methods were too sophisticated and were sensitive to their environment. Thus, they required costly, large-scale research equipment and staff with a high level of expertise. Nowadays, these methods have improved in stability and are easier to apply so that a sample can be taken and analyzed offline by instructed staff. This approach is useful for basic research or quality assurance but cannot be used for direct process control. Besides, the analysis usually has to be performed manually, which not only requires an available specialist but can also be time-consuming. MS and NMR can now be advanced considerably by using Artificial Intelligence (AI) and Machine Learning).

In this work, we show approaches that lead to a novel calibration concept for spectroscopic and spectrometric sensors using ML. These approaches lead to a considerably shorter procedure for modeling, require less calibration data than traditional ones, and can be efficiently implemented in Field Programmable Gate Arrays (FPGAs) [8]. The methods described here could significantly enhance the real-time release and continuous production as well as traditional batch chemistry for fine chemicals.

One of the critical challenges in this field, however, is the acquisition of the massive amounts of data needed for the training of ANNs. Such data is usually not available for chemical processes due to the limited number of measurement devices and their typical intervals. Thus, the term *Big Data* as a prerequisite for data-driven evaluation procedures is not appropriate for the process industry because even with quantitatively large data sets, information is typically only available for campaigns about a few batches with a series of measurement data that do not exhibit sufficient variance for a data-driven evaluation – not comparable with the data sets from large Internet groups. In the process technology environment, the term *Smart Data* is more appropriate. Smart Data includes, among other things, the clever selection of data for analysis and the combination of data-driven procedures and expert knowledge for their analysis. *In this work, we address this problem by using simulated variants of the measured data (i.e., synthetic MS and NMR spectra), a form of data augmentation.* Past works [4], [9] have used similar procedures, although not in the context of MS nor NMR.

In the first application, a miniaturized mass spectrometer for controlling closed-loop processes was developed, enabling more efficient process quality control than offline methods. Our second application demonstrates a moderately complex process analytical problem, where an industrial organic synthesis step with four reactants was observed by medium-resolution NMR spectroscopy. The spectroscopic calibration model was addressed using ANNs in combination with the presented process-analytical method (low-field NMR) and with the proposed approach to generate meaningful training data [10].

A. Chemical Information and Process Models

Sensors that react directly or indirectly to changes in the target components are needed in order to achieve chemically specific measurements. The measurements must be as precise as possible (i.e., undisturbed by other components such as the solvent) as well as with sufficient sensitivity – such as MS. *Direct analytical methods*, such as NMR spectroscopy, would be the optimum where the signal obtained is independent of matrix effects and is causally linked to a concentration of a component in a multicomponent mixture.

The improvement of production parameters, space-time yield, or energy efficiency can only be achieved by data- or knowledge-based models from the raw data via a more detailed description of the material on several scale levels. Nowadays, typically multivariate tools and algorithms are used for automated feature extraction, such as the extraction of chemical information from the data sources using Principle Component Analysis (PCA), Partial Least Squares (PLS), or Latent Discriminant Analysis (LDA), is currently done manually and is time-consuming. However, access to consistently compiled data alone is not sufficient for this purpose, because the understanding of the process is often hidden as so-called *expert knowledge* in the design of the process and its control and is usually undocumented.

To find an acceptable way to control *chemical* processes and so that sensors and actuators can better meet the requirements of digital transformation and the associated tasks in the future, they must be equipped with *intelligent* functions that also accumulate the expert knowledge, e.g., in the form of process models. For a holistic process analytical approach and such decision support systems, the semantic level (context information brought together with sensor data) must be considered beyond the pure interface definition (syntax, such as data acquisition, data connectivity, and data integrity). Efficient communication with all the components in the system is thus key are will require novel architectures [11].

B. Mass Spectrometry

Spectroscopy defines the observation of the interaction that electromagnetic radiation causes over atoms and molecules. The advantages of mass spectrometry include the identification of structures, the qualitative and quantitative analysis of the composition of a sample. There are two necessary steps for mass spectrometry: Ionization and Ion-Separation. The ionization consists on adding ions to the sample, so that the sample starts to fragment or decay in its own ions. The behaviour of this fragmentation depends on the molecules contained in the given sample which allows the identification of the elements contained. To avoid interaction between ions, this process is normally done in vacuum. The next step is the separation of the ions released by the sample. To accomplish this, a dynamic electrical field is generated, which separates the ions due to their different acceleration properties based on the influence of the field and its own mass and charge. Other mass spetrometers use static magnetic fields along with individual flight paths (Figure 1 bottom left) or times of flight for individual ions. The spectrometer, thus, records the mass-to-charge relation of the ions.

The analysis of the results obtained can be done qualitatively or quantitatively. In this work, we will concentrate in the quantitative approach. In such analyses, the *resolution* indicates the capacity to differentiate and catalogue the ions according to their mass. A high resolution indicates that two elements

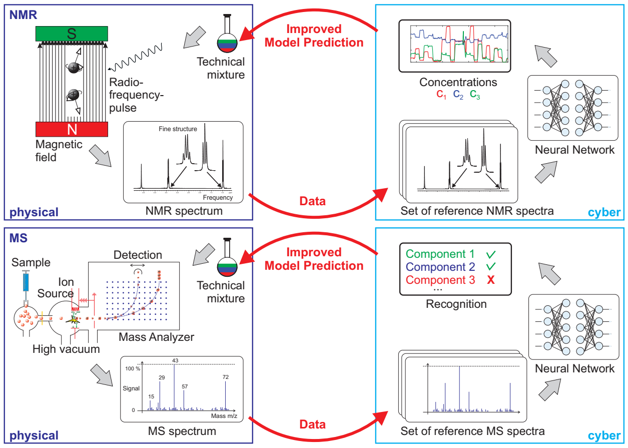

Fig. 1. Cyber-physical systems for MS (bottom) and NMR (top) applications. MS: The ion separation by a static magnetic field results in individual flight paths for fragments and molecules of the sample, which were generated in an ionization chamber. A detector collects intensities for various mass-to-charge ratios. NMR: The effect is based on interactions of electromagnetic radiation in the radio frequency range (typically 300–1200 MHz) with atomic nuclei (nuclear spins) that occur in strong external magnetic fields. Resonances are recorded with a radio frequency antenna yielding spectra for individual atom groups in a chemical molecule. Both, MS and NMR spectra can be analyzed by neural networks to predict quantitative information such as the concentrations of individual components in a complex mixture within seconds.

with similar mass can still be differentiated, while in the case of low resolution this is not the case, both elements would be catalogued as the same one.

C. NMR Spectroscopy

NMR (Nuclear Magnetic Resonance) spectroscopy is today one of the most important instrumental analytical methods in the natural sciences and medicine. Because of its ability to obtain unambiguous structural information non-destructively, it has become indispensable in chemistry, biochemistry, and pharmacy (high-resolution NMR spectroscopy of liquids), physics and materials research (solid-state NMR spectroscopy), and medicine (magnetic resonance imaging).

High-resolution NMR spectroscopy is particularly suitable for the non-invasive study of the properties and behavior of complex multicomponent mixtures under technical conditions. [12] It is one of the few non-invasive analytical methods that are able to provide quantitative and, at the same time, detailed chemical-structural information on complex reacting mixtures, e.g., on the type of reactions taking place or on by-products. In contrast to routine NMR spectroscopy, which usually aims at qualitative information, sample preparation in which the analytes are dissolved or diluted in deuterated solvents is not suitable for technical mixtures – especially in online operation. Nevertheless, if the NMR parameters and experimental conditions are carefully selected, it is also possible to analyze undiluted technical mixtures quantitatively under increased pressure and at high temperature, even those with high electrolyte concentrations or extreme pH values.

NMR spectroscopy is a direct analytical comparison method. This means that it exhibits a direct correlation between the signal area in the spectrum and the number of observed nuclei in the active sample region and allows for a calibration-free relative quantification compared to the *counting* of nuclear spins. In combination with a reference compound of known quantity or a single-point calibration, e.g., on a pure reactant, absolute quantification becomes feasible. This makes NMR spectroscopy a very promising method for online reaction monitoring applications. [12]

With the availability of compact benchtop NMR instruments, a very wide range of applications for NMR spectroscopy has opened up, and the instruments can be used in a fume hood or in a production environment. The application of NMR spectroscopy is currently in technical readiness level 7 (TRL 7 – i.e., system prototype demonstration in an operational environment). Work is presently underway to fully integrate an NMR analyzer and the associated data evaluation via MTP in the sense of quality control and process control unit. [13]. Previous works have already shown that this is achievable [14]

III. A MINIATURIZED MASS SPECTROMETER FOR IN-PROCESS USE

A. Toolflow

The MiMEP project addressed the development of a a miniaturized mass spectrometer for use within chemical processes. To assist in the development of new chemical processes and have a toolflow that can also be applied to other systems, we developed a complete toolflow that includes the following tools:

- an ideal *line spectra simulator* (Step 1 in Fig. 2) that can generate ideal mass spectrometers for arbitrary compounds based on already-known spectra;
- a *simulator of the portable mass spectromenter* (Step 3 in Fig. 2) that takes into account all the nonidealities of the real measuring device and can produce a non-ideal a mass spectrum matching those characteristics (given an ideal spectrum);
- a tool for the *automatic generation of the mass spectrometer simulator* (Step 2 in Fig. 2) based on measured data from the real measuring device;
- a tool for the *automatic training of ANNs* (Step 4 in Fig. 2) that can identify the chemical compounds from the non-ideal mass spectra.

The tool for spectrum simulation addresses the issue that many spectra with labels are required to train the networks, but the mass spectrometer prototype was not able to provide them. The simulation tool thus creates a big amount of ideal line spectra with definable concentration ranges for all compounds (Tool 1) and to use a tool, that applies the characteristics of the real mass spectrometer to those (Tool 3). As the mass spectrometer prototype has been used in various configurations within the project, the automation of the extraction of the measurement systems characteristics from a small number of measured spectra was desired. This task is handled by a tool, which requires some labeled mass spectrums from the mass spectrometer prototype as input and extracts the characteristics like the shape of the peaks, the kind and strength of the noise, the shift on the horizontal axis and some more (Tool 2).

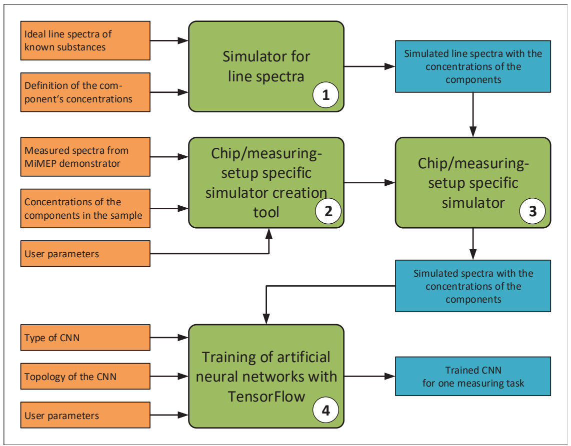

Fig. 2. Toolchain Overview

Using those characteristics, the ideal line spectra are transformed to the simulated mass spectra, that mimic the behavior of the mass spectrometer. Using this tool, the creation of ten-thousands of spectra can be achieved in minutes. This has been done, to comprehend which measurements have been used to train the simulators and which data has been used to train a specific network. The process of designing and training the ANN is primarily defined by the TensorFlow Framework, which is used in this project. To enable the integration of the database and to allow the automated evaluation of different network topologies using the same training data, various tools have been developed. The tools, that assist in the definition phase, allow the definition of one or more network topologies and the training- and validation datasets to use without modifying the source code. The whole training process can then run without user interaction. Backend tools help with the evaluation of the trained networks with different training datasets, the selection of the best-performing networks, based on selectable quality criteria and the export of analysis data to spreadsheet applications or data analysis tools, e.g., MATLAB or Pandas. Additionally, a tool to export the desired ANN for used on embedded platforms is available.

Apart from the software, an embedded system, that is able to run the ANN and to graphically present the analysis result has been developed. The system is based on the Nvidia Tegra platform. These systems combine a Multicore ARM processor and an embedded GPU in a SoM (System-on-Module). For the prototype of our embedded system, the Nvidia Jetson Nano development Kit has been used. It comprises a Quadcore ARM A57, a Nvidia Maxwell GPU, 4 GiB RAM and various interfaces. This system has been combined with a 7 inch monitor and integrated into a 3D-printed case. The system uses a full-featured Linux distribution and is able to run the TensorFlow ANN on the CPU and the embedded GPU. It allows fast iterations as the adoption of all software components and the ANN can be done like on a desktop system. Performance measurements show that the system could be replaced by a smaller and cheaper system in the future.

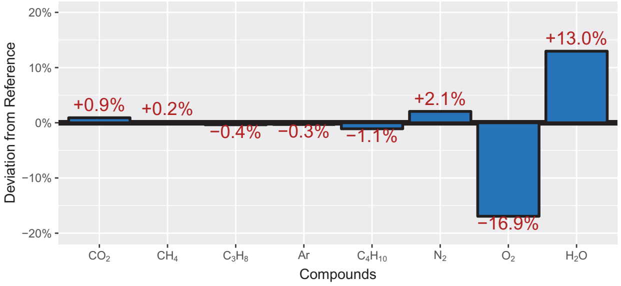

Fig. 3. Results of the MMS when identifying the compounds in a sample spectra.

B. *Results*

We evaluated several different ANNs topologies with both the simulated and measured spectra, checking the accuracy they would achieve in identifying compound concentrations from the spectra. In most cases, we used ANN with 951 inputs and 8 outputs. The number of inputs directly corresponds to the range and the resolution of the m/z-axis, the number of outputs equals the number of dectectable components. The results achieved with simulated spectra were promising, with the best ANN achieving an average MAE of around 0.01 %. To evaluate the networks with measured data, we mixed gases with known spectra by using mass flow controllers, allowing us to create mixtures with controlled concentrations of compounds. The mass spectra of the mixtures have been measured with the MMS prototype and the ANN has been used to infer the compound concentrations. Figure 3 shows, that for most of the compound the mean error is smaller than 2 %. Evaluations showed that this could partly be explained with impurities and changes in the configuration of the prototype. In future versions, we plan to introduce additional inputs to the ANN, which provide parameters of the system and the environment to evaluate their impact on the quality of the results. Another reason could be that the simulator only considers a static system state, fluctuations of certain parameters, such as the displacement of the peaks do not affect the simulated values. Two substances in Figure 3 show big deviations of up to 15 %. Oxygen (O_2) is underestimated and Water (H_2O) is overestimated, which can be explained by the aforementioned impurities. H_2O was no purposed compound, but air humidity caused a signal in the reference measurement, which was not considered while creating the simulator. Therefore, the ANN is able to detect water, but the reference gas should not contain water. So, it is possible that O_2 is partially recognized as H_2O.

IV. MACHINE-ASSISTED MODEL BUILDING OF ONLINE NMR SPECTRA

As already mentioned, data-driven methods for predicting quantitative information from complex process analytical data require very large training data sets together with contextual information. These are typically not available if a process development is still in its early stages or the chemicals involved are still being modified. Usually only a few hundred or a few thousand specific data sets are available. Data for the validation of online methods obtained by sampling and comparative analysis are even smaller. We have therefore based our study on a data set which corresponds to this typical framework: different reaction conditions for an organic lithiation reaction were generated with the help of laboratory equipment and measured simultaneously online using two methods: medium-resolution and high-resolution NMR spectroscopy resulting in a set of 300 spectra as raw data basis with four compound concentrations as the four labels of interest.

The experimental setup is based upon a laboratory scale flow reactor, the chemical example reaction used, NMR spectra acquisition, data enhancement, and ANN model building and ANN concentration prediction is depicted in Figure 4.

A. *Simulation of synthetic training spectra*

Similar to the MS example, we again used an NMR line spectra simulator to generate a large number of synthetic training data covering the full concentration range of interest. The simulator uses NMR spectra of the pure components, which have been fitted with an indirect hard modelling (IHM) approach that can also be used for an analysis of the spectra [15]. Linear combinations of the parametric models of pure component spectra can then be calculated to generate NMR spectra for arbitrary values of the four compound concentrations. Note, that the IHM approach has advantages compared to just a linear combination of the experimental pure component spectra. Firstly, noise in the experimental spectra would be inaccurately scaled and added in the linear combination of experimental spectra. Secondly, the mixing of compounds in solution may shift single NMR peaks within a pure component spectrum. A linear combination of experimental pure component spectra would neglect this effect, but it is included in our spectra simulator through shifting and broadening peaks in our parametric model. Overall, the approach allows the initial training data set to be arbitrarily sized and distributed along different prediction variables.

B. *Training of Artificial neural networks*

We first conducted an optimization of the neural network architecture to arrive at a small but accurate neural network, capable of running on limited hardware in cyber-physical systems. We optimized the architecture through trying out fully connected, convolutional and locally connected neural networks with different depths. After finding that fully connected layers need to have significantly more trainable parameters than convolutional layers we further optimized the number of layers, average or max-pooling layers, size of the pooling or strides, number of filters, the number of fully connected layers after the convolutional layer and their type of activation function. We finally arrived at a comparatively simple model of just a single, locally connected 1d convolutional layer and a single flatten layer connected to the four output variables of the four concentrations. Training this neural network, we found that after 50 epochs the performance on the experimental dataset is best. However we continued training for 400 epochs, despite the risk of overfitting to synthetic data, because we want the neural network to perform well over the full range of concentrations, not just the ones available in our experimental low field NMR test dataset. Note, that one limitation of the ANN methodology is that the resulting model can only reproduce those changes that lie within the training label range, so application is limited to parameter ranges within the training data.

C. *Results*

For predicting compound concentrations, both the optimized ANN and state-of-the-art model predictions from IHM were benchmarked against accurate high field NMR reference data. The best performing ANN consists of only three layers with 10532 trainable parameters in total, organized as follows: 1) locally connected 1-D convolutional layer (4 filters, strides and kernel size 9); Flattening Layer; Fully connected layer with 4 output neurons for the prediction of four concentration values. This ANN performs better than an IHM analysis as its results have a 24 % lower mean square error. Beyond being more accurate, the ANN analysis takes only 0.9 ms for predicting a single spectrum batch on an Intel i7-8565U CPU (1.8 GHz) with Keras and TensorFlow and is therefore more than 1000 times faster than an IHM analysis. This is relevant for online monitoring applications and may in the future enable not only an analysis of the compound concentrations but also real-time estimates of error margins. This shows that it is generally possible to apply ANN approaches to low-field NMR data with limited experimental data.

V. CONCLUSIONS

In this paper we present new methods, to deploy artificial intelligence, in our case neural networks, in measurement systems from the chemical industry. We hope that our approach will facilitate and accelerate the integration of smart sensors into the digital infrastructure. With that we could move to the threshold of a possible use of MS and NMR for reaction and process monitoring extending the toolbox of chemically specific process analytical methods for process industry. We are already discussing to use the proposed AI methods in other analyzers like, e.g., Near Infrared Spectroscopy or for combinations of analytical methods.

Concepts based fundamentally on cyber-physical systems will change production processes and, e.g., enable new topologies of plant modules which are not economic today or are not even possible for control or safety reasons. Such fully integrated and intelligently networked systems and processes require reliable and powerful automation nodes that are operated within the modular plant. This so-called edge computing requires high computing power for increasingly complex control algorithms, machine-supported learning algorithms and cryptology for secure data transfer and it leads to the implementation of suitable platforms with processor architectures, which meet the requirements such as hard real-time capability, high data throughput and computing efficiency.

Once the feasibility of machine-supported learning and evaluation systems has been demonstrated, the next step is to investigate how these systems can be automatically and reliably adapted to perturbations or changes in parameters within the life cycle of a production. Especially the advantage of a fast

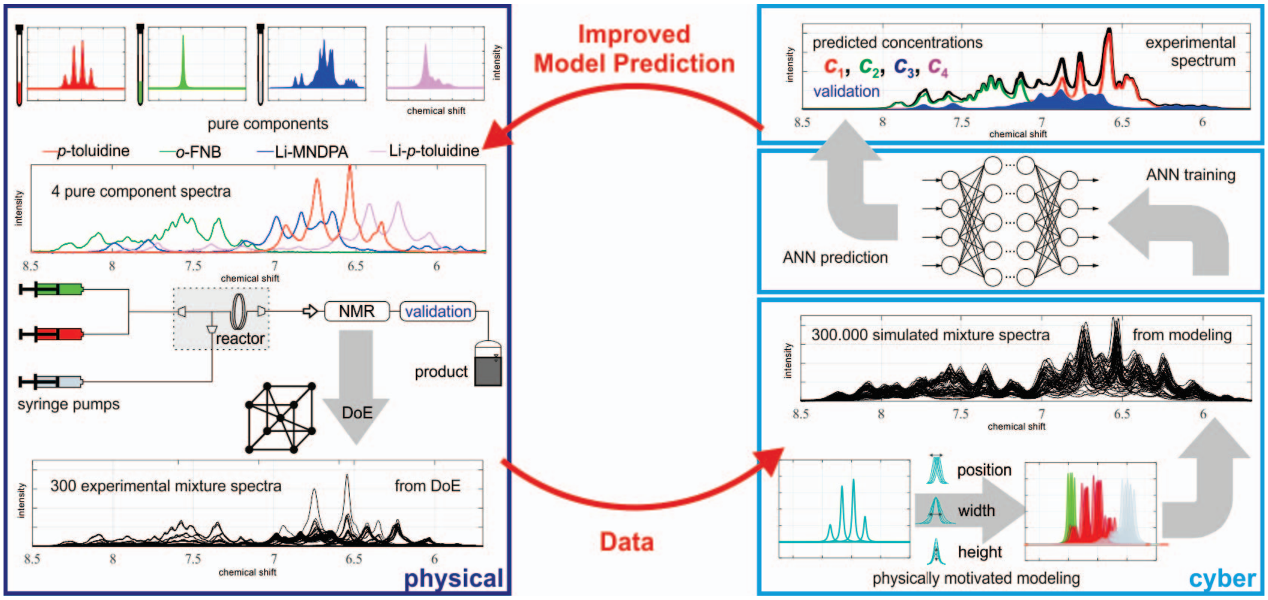

Fig. 4. The synthesis of nitro-4′-methyldiphenylamine (MNDPA) by aromatic substitution of p-toluidine and 1-fluoro-2-nitrobenzene (o-FNB) is a relevant example for the pharmaceutical industry [14]. p-Toluidine was activated by a proton exchange with the organolithium compound lithium bis(trimethylsilyl)amide (Li-HMDS), giving four relevant components in all mixtures, as shown in the upper left figure. The flow reactor (middle left) was operated along a DoE yielding representative mixture spectra (bottom left). These were enhanced to 300.000 spectra on basis of a physically motivated simulation method (bottom right). ANN model building and ANN concentration prediction of the abovementioned is depicted in the upper right. On the left side is the physical part of the cyber-physical system, on the right side the virtual part. The data predicted by ANN were validated against a reference method used in parallel with low field NMR spectroscopy.

computing time will make it possible to use machine-supported analysis methods to increase functional safety, e.g., by not only evaluating process data but also checking them against potential hazard indicators from the data.

The precision of the results show, that there is still research required to optimize the methods by investigating the used neural networks and training methods. However, the results are very promising and the advantages to use AI in this domain are very visible. The next steps in the research will be the optimization of the used AI algorithm to improve the precision and simultaneously the optimization for the integration into embedded systems for edge computing.

REFERENCES

[1] E. C. Ferreira, D. M. Milori, E. J. Ferreira, R. M. Da Silva, and L. Martin-Neto, "Artificial neural network for cu quantitative determination in soil using a portable laser induced breakdown spectroscopy system," *Spectrochimica Acta Part B: Atomic Spectroscopy*, vol. 63, no. 10, pp. 1216–1220, 2008.

[2] T. Väänänen, H. Koskela, Y. Hiltunen, and M. Ala-Korpela, "Application of quantitative artificial neural network analysis to 2d nmr spectra of hydrocarbon mixtures," *Journal of chemical information and computer sciences*, vol. 42, no. 6, pp. 1343–1346, 2002.

[3] J. R. Long, V. G. Gregoriou, and P. J. Gemperline, "Spectroscopic calibration and quantitation using artificial neural networks," *Analytical Chemistry*, vol. 62, no. 17, pp. 1791–1797, 1990.

[4] J. Liu, M. Osadchy, L. Ashton, M. Foster, C. J. Solomon, and S. J. Gibson, "Deep convolutional neural networks for raman spectrum recognition: a unified solution," *Analyst*, vol. 142, no. 21, pp. 4067–4074, 2017.

[5] P. Zhang, Z. Gui, L. Hao, X. Zhang, C. Liu, and Y. Shang, "Signal processing for diffuse correlation spectroscopy with recurrent neural network of deep learning," in *2019 IEEE Fifth International Conference on Big Data Computing Service and Applications (BigDataService)*, pp. 328–332, 2019.

[6] A. B. Risum and R. Bro, "Using deep learning to evaluate peaks in chromatographic data," *Talanta*, vol. 204, pp. 255–260, 2019.

[7] M. Fukuhara, K. Fujiwara, Y. Maruyama, and H. Itoh, "Feature visualization of raman spectrum analysis with deep convolutional neural network," *Analytica chimica acta*, vol. 1087, pp. 11–19, 2019.

[8] F. Kästner, O. N. Guzmán, B. Janßen, J. Hoffmann, and M. Hübner, "Analysis of hardware implementations to accelerate convolutional and recurrent neuronal networks," *International Journal on Advances in Software*, vol. 10, no. 3 & 4, pp. 308–323, 2017.

[9] C. M. Bishop, "Neural networks and their applications," *Review of scientific instruments*, vol. 65, no. 6, pp. 1803–1832, 1994.

[10] S. Kern, S. Liehr, L. Wander, M. Bornemann-Pfeiffer, S. Müller, M. Maiwald, and S. Kowarik, "Artificial neural networks for quantitative online nmr spectroscopy," *Analytical and Bioanalytical Chemistry*, vol. 412, pp. 4447—-4459, 2020.

[11] F. Kaestner, D. Kuschnerus, C. Spiegel, B. Janssen, and M. Huebner, "Design of an efficient communication architecture for cyber-physical production systems," in *2018 IEEE 14th International Conference on Automation Science and Engineering (CASE)*, pp. 829–835, 2018.

[12] M. Maiwald, H. H. Fischer, Y.-K. Kim, K. Albert, and H. Hasse, "Quantitative high-resolution on-line nmr spectroscopy in reaction and process monitoring," *Journal of Magnetic Resonance*, vol. 166, no. 2, pp. 135–146, 2004.

[13] K. Meyer, S. Kern, N. Zientek, G. Guthausen, and M. Maiwald, "Process control with compact nmr," *TrAC Trends in Analytical Chemistry*, vol. 83, pp. 39–52, 2016.

[14] S. Kern, L. Wander, K. Meyer, S. Guhl, A. R. G. Mukkula, M. Holtkamp, M. Salge, C. Fleischer, N. Weber, R. King, *et al.*, "Flexible automation with compact nmr spectroscopy for continuous production of pharmaceuticals," *Analytical and bioanalytical chemistry*, vol. 411, no. 14, pp. 3037–3046, 2019.

[15] D. Chen, Z. Wang, D. Guo, V. Orekhov, and X. Qu, "Review and prospect: Deep learning in nuclear magnetic resonance spectroscopy," *Chemistry – A European Journal*, vol. 26, no. 46, pp. 10391–10401, 2020.