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Standardized Software Solution for an Automated Data Evaluation in Analytical Measurement

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***Abstract* – To reduce the high degree of manual operation and processing time as well as human errors the automation in chemical analysis has become important in the last years. As a result a fast and automated data evaluation is required to overcome the high amount of measurement data. To enable the integration of various analytical devices with different device software a standardized solution without any programming knowledge should be preferred. Additionally the data evaluation should be accessible via any computer or mobile device within the laboratory network.**

The presented software called *Project ADE* is implemented as a web application to persist in a multi-user environment. To transmit the pre-evaluated results from the device software to the *Project ADE* the exported *XML* report files are uploaded and imported to the *entities database* using the software *Data Upload*. An algorithm identifies the affiliation of a sample within one measurement series with a calculation type (e.g. routine measurement, method validation). The calculated results are presented in tables and diagrams on different information levels (general, detailed for one analyte or sample).

***Keywords* – chemical analysis, data evaluation, data processing, ICP-MS, laboratory automation, mass spectrometry, software development**

I. INTRODUCTION

In modern laboratories the analytical processes are mostly automated. This includes the sample preparation, analysis and data processing and leads to a high amount of data in a short time period [1-5]. Besides routine measurements the method development and validation are important tasks in analytical laboratories. Therefor many experiments are required, what leads to a time consuming evaluation process if this is done manually. The software delivered by the vendors of the analytical devices includes modules for the device control and for a qualitative and quantitative data evaluation. These provided functionalities are often not adequate for the daily laboratory routine, especially for the validation of new methods for the detection of chemical compounds. Thus the data has to be cleaned up to separate the required from the non-relevant data (e.g. flushing samples). Furthermore, statistical analysis and validation calculations [6,7] such as the determination of precision and the limits of detection and quantification [8] are required. Often an additional graphical presentation of the measured data and the calculated results is necessary. These steps are mostly done manually using a spreadsheet software like *Excel* what requires a high manual effort and working time. With the high amount of measurements resulting from the high degree of automation in modern analytical laboratories the data evaluation is a bottleneck. For that reason a fast and automated data evaluation is required [9-11].

II. DATA EVALUATION IN ANALYTICAL LABORATORIES

A. Automated Data Evaluation

The challenge and goal in laboratory automation is the combination of various devices such as laboratory equipment (e.g. centrifuge, thermos shaker, ultrasonic bath), robots for transport or manipulation and analytical instruments. This leads to an increased productivity and flexibility, the minimization of working time as well as possible human errors and a higher sample throughput. Thus huge automated laboratories are able to analyze more than 1,000 samples per day [12]. Methods specialized in high-throughput screening like clinical laboratories or in the field of toxicology [13-15] this is raised up to more than 8,000 samples per day [16,17]. Typically the data evaluation is done by the software provided by the vendor of the analytical devices. Thus many individual software solutions for special data analysis have been reported: e.g. for lipid experiments [18], the identification of proteins and peptides [19], in toxicological studies [13-15], in material sciences [20] and some other analytical applications [20-23].

But also in the daily laboratory routine especially in the method development and validation an automated data evaluation is necessary to overcome the increased sample throughput [9-11]. The integration of such a software is possible since modern laboratories are mostly electronic and paperless [26-30]. This change in

digitalization of data in analytical measurement and the way to handle the high amount of data will change the work in laboratories for a long time [26,30-32].

B. *Digital Laboratory*

The control of an analytical device and the qualitative and quantitative analysis of the measured data is done by the provided software. Thus the integration and automation has to be done on a software level via this device software. Beside the device computer linked to the analytical device, personal computer with various operating systems (e.g. Windows, Macintosh or Linux) are used in the offices of an analytical laboratory. Additionally mobile devices like smartphones and tablets gain growing importance [33-35]. To optimize the workflow of the evaluation process the required software and the analyzed data should be accessible via every device in the laboratory network. A multi-platform solution e.g. a web application with a central data storage running on a webserver can overcome these tasks [36]. Such a solution also reduces the development costs as well as the service effort.

The integration of such a software in an existing laboratory network is easily possible since modern laboratories are mostly electronic and paperless. As opposed to this the integration of multiple analytical devices from different vendors with various software is more complex, since the provided export formats (e.g. Excel, csv, XML) and the style (e.g. table layout) of the measured data depend on the manufacturer.

The presented software solution *Analytical Data Evaluation (ADE)* should overcome the challenges mentioned above. It was developed as a web application using the ASP.NET framework and the Model View Controller (MVC) principle. The measurement data provided by the analytical devices and additional required data for the data evaluation is saved in a database on the same web server. Thus every user in the laboratory environment has access via a common web browser to all data from the integrated devices and the functionalities of the *Project ADE*. The overall objective is to obtain a standardized and automated data evaluation for all analytical devices in elemental and structural analysis available in the laboratories of this institute.

III. SYSTEM CONCEPT

The general workflow of the data evaluation using the *Project ADE* is shown in figure 1. To automate the export for the pre-evaluated report files provided by the device quantification software it is essential to adjust the *Data Analysis (DA) Method* in the *Acquisition Method* of the device software. Furthermore information tags following a naming convention should be added to the sample names. These tags are used by the *Project ADE* to get additional information about the samples (e.g. sample type, known concentration and unit) and how to handle them inside the calculation algorithm (e.g. calculation type, affiliation of the samples). After these necessary manual steps the samples are analyzed by the analytical device and the measured results are quantitative calculated and exported in a *XML* report file. This file is detected and the contained information is added to the entities database by the software *Data Upload* which observes the report folder. Afterwards the user has to adjust additional information for the samples (e.g. sample preparation) and analytes (e.g. shown in results) and add the measurement series to an evaluation project. An algorithm sorts the included samples by their related calculation type and calculates the results. Finally these results are presented in tables and diagrams.

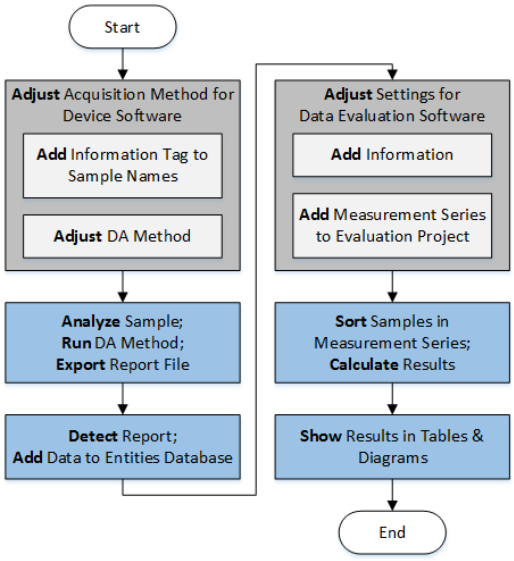

Fig. 1. General workflow of the automated data evaluation using the Project ADE (gray: necessary manual settings; blue: automated steps; DA – Data Analysis)

The *Project ADE* consists of different software modules to achieve a standardized and automated data evaluation in analytical measurement. The *web application* and the *web service* grant an access to the *functionalities* of the *Project ADE* and the measurement data obtained from the analytical devices. While the *web application* provides a graphical user interface (GUI) for a user to machine interaction, the *web service* is optimized for a machine-to-machine interaction, as it is required by the module *Data Upload*. This software module enables an automated upload and import of the measured data to the *entities database*. The relational database manages the whole data required by the *Project ADE*. This includes the user account information and their roles, the information about the projects, measurement series and its settings as well as the information about the analytical devices and the linked device software. Additionally a translator for the *PubChem* database [37] using the power user gateway (*PUG*) [38] was included to complete the information for the analytes with the molecular formula, the molecular weight and exact mass, the simplified molecular input line-entry system (*SMILES*), the international chemical identifier (*InChi*) and with synonyms as well as a picture of the structure.

Former development steps of the analytical data evaluation software use the *Excel* format for the report files to transfer the measured data from the device software [24,25]. Indeed the tables in this format are suited to the presentation of the results to the user but *Excel* is not optimized to transport data from one software to another. In this case the *XML* format is better qualified since the structure of such files is known using the related schema. So the tags inside a *XML* file are used to find the

required information about the batch, sample, analyte or its qualifier. Due to the fact that all *XML* reports exported from one device software have the same schema it is possible to link these information on the software level inside the *entities database*. The user has to adjust these linkage only once for each device software. In case of the *Excel* format such connection between the kind of the information and the information itself is not possible because the included information is not labeled. Additionally the *XML* report contains the unfiltered pre-evaluated data from the device software in contrast to the *Excel* file with preselected information. So it was possible to add result pages with detailed information in addition to the final concentration for each sample and analyte: e.g. retention time and the area, width, height and symmetry of the related detector signal.

IV. SOFTWARE IMPLEMENTATION

To overcome the gap for the information transport between the device software and the additional data evaluation using the *Analytical Data Evaluation* the software *Data Upload* was developed. This module of the *Project ADE* observes the report folder of the device software, using the *FileSystemWatcher* class from the *.NET* framework (figure 2).

```
FileSystemWatcher watcher = new FileSystemWatcher(_settings.ReportFolderPath);
watcher.NotifyFilter = NotifyFilters.LastAccess | NotifyFilters.LastWrite |
NotifyFilters.FileName | NotifyFilters.DirectoryName;
watcher.IncludeSubdirectories = true;
watcher.EnableRaisingEvents = true;
watcher.Created += new FileSystemEventHandler(watcher_OnChanged);
GC.KeepAlive(watcher);
```

Fig. 2: FileSystemWatcher class used to observe a folder to detect new report files

For a full automated data upload and import to the *entities database* the software *Data Upload* needs only three information: the report folder path, the device and related software saved in the *entities database*. The user has to adjust these settings only at the first start. Afterwards this software runs as a background-task. Figure 3 shows the workflow of the software *Data Upload*.

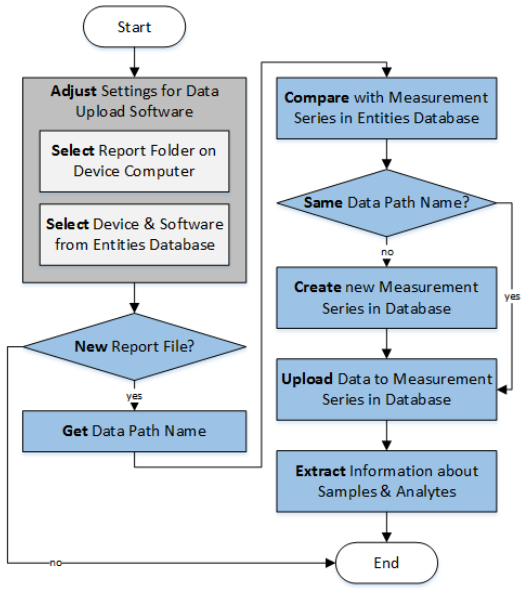

Fig. 3: Workflow of the automated upload and import process using the software Data Upload

When the *FileSystemWatcher* detects a new file the algorithm checks if it is a report file related to the selected device software. As a next step the data path name is extracted from the *XML* report file and compared with the measurement series inside the *entities database*. If the data path name matches with an existing measurement series the data is updated, else a new measurement series is created first. As a last step the information about the samples and analytes are extracted from the *XML* report file using the mentioned linkage for each software with the related *XML-Schema*.

Once the user adds the necessary information for the samples (e.g. sample preparation) and the analytes (e.g. shown in results) included in the uploaded measurement series the results are calculated. Therefor the samples have to be sorted by its related calculation types in the information tags included in the sample name.

V. EXPERIMENTAL

A. Causal Investigation of Biliary Stent Occlusion

Biliary endoprosthesis stents made of plastic (Teflon, polyethylene or polyurethane) or metal (stainless steel or nickel titanium alloy) [39,40] are used to prevent blockages caused by cancer [41]. While plastic stents have a reduced stent migration, tumor overgrowth and sludge formation, metal stents have a significant less stent occlusion and a reduced risk of recurrent obstruction [42]. To prevent occlusion by using new coating material for bile duct stents the components of the blockage material have to be analyzed. Analog to gallstones the congested stents contain calcium and magnesium [43], which can be verified via an *inductively coupled plasma linked to a mass spectrometer* (*ICP-MS*).

The measurement series for the validation of the acquisition method were additionally used to determine the effectiveness of the automated data evaluation using the developed software *ADE* compared to the manual data evaluation using *Excel* spreadsheet software.

B. Automated Data Evaluation Using ICP-MS

The *ICP-MS* is used for a fast and sensitive determination of the concentration of chemical elements (e.g. heavy metals in environmental samples) [44]. The *Data Analysis (DA) Method* adjusted in the device software *MassHunter Workstation for ICP-MS* is used to automate the export of the measured and quantified results. These generated reports are detected and uploaded by the software *Data Upload*.

Using the automated result export the device software creates the required *XML* file only temporarily to transfer the information into the *Excel* report file. To keep these files the report has to be generated manually via the quantification module of the *MassHunter* software. Thereby more files than the required *XML* report are created (e.g. image files) which requires a lots of storage capacity and should be deleted. After the upload via the *web application* or by the software *Data Upload* the user has to adjust some information about the sample preparation (e.g. weight, volume, dilution), select the analytes to be shown in the results and add the measurement series to an evaluation project. Afterwards the results are calculated and shown in tables and diagrams for each included calculation type.

Figure 4 illustrates the calculation process. First the results are corrected with an optional second internal standard to eliminate possible mistakes which happened during the sample preparation. Thereafter the units are converted to the desired unit considering the sample preparation values (weighted portion, dilution and volume). The information tags added to the sample name are used to sort the samples by their calculation type and calculate the related results. For the sample group with the calculation type *Recovery Rate* and *Calibration* special calculations are required. For the *Recovery* Rate for example the percentage deviation in relation to the expected value is calculated. Finally for each sample group except the *Calibration* the statistic values (e.g. average and standard deviation) are calculated and the required data for the charts are collected.

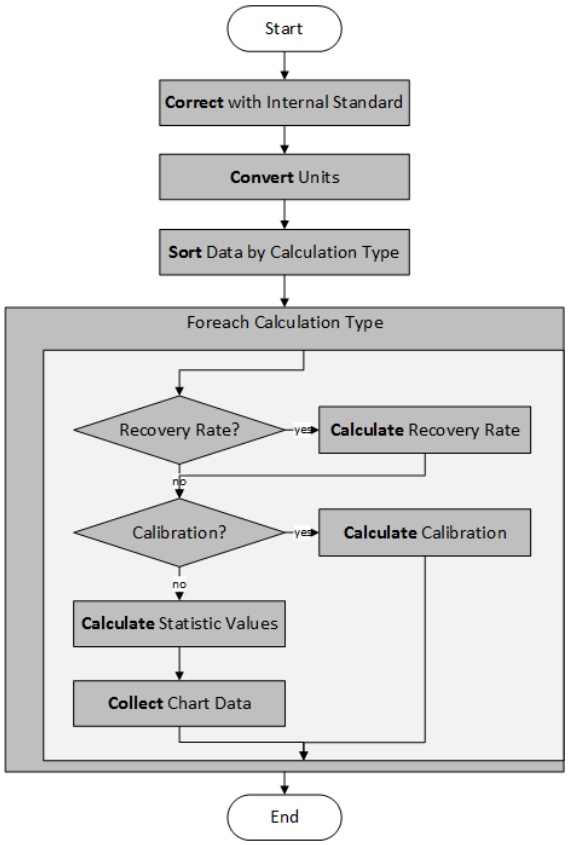

Fig. 4: Workflow of the calculation process

After the calculation process is finished the results are send from the web server to the browser on the client computer to display them in form of tables and charts in different information level (general information, information by analyte, information by sample).

C. *Results of the Repeatability Validation Measurement Series for the Causal Investigation of Biliary Stent Occlusion*

The results of one measurement series are separated by their calculation type and displayed in different information level. The general information level of the repeatability measurement series contains a table with the final concentration for each analyte in each sample, the calculated average and standard deviation as well as a graph with this calculated values (figure 5).

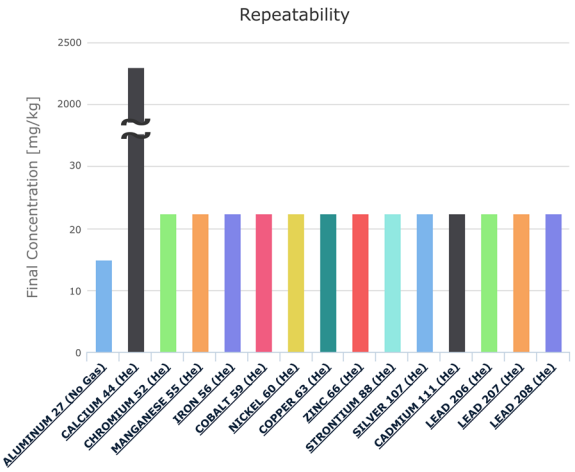

Fig. 5: Repeatability measurement result: average final concentration for each analyte

In case of the elemental analysis (e.g. *ICP-MS*) the detailed result pages for the samples and analytes do not contain additional result information like in case of the structural analysis (e.g. *gas chromatography mass selective detector – GC-MSD*). In this case beside the final concentration, information about the retention time and their difference to the expected one as well as detailed information about the peak of the chromatography (area, symmetry, height, width and signal to noise ratio) are shown.

The main goal of the developed software is the automation of the data evaluation to minimize possible human errors and to reduce the required time. For the presented validation measurement the data evaluation process was performed in a manual way using *Excel* spreadsheet software and automatically using the software *ADE*. The process was divided into the following steps:

1. Filter the data from the device software
2. Select analytes for result pages
3. Add internal standard
4. Add sample preparation values
5. Correct values with internal standard
6. Convert values with sample preparation
7. Calculate statistics (e.g. average)
8. Generate diagrams

Except the necessary manual steps 2-3 the required time could be reduced for all the other steps, in total by more than 90% from over one hour to less than 5 minutes.

VI. CONCLUSIONS

The presented software solution enables a fast and effective data evaluation of measured data from various analytical devices for elemental and structural analysis. With the exception of a few necessary manual inputs (e.g. information tags) the complete process is automated. Additionally new analytical devices and their related software can be integrated into the *Project ADE* in a standardized way using the *XML* format. Therefor a typical *XML* export file from a device software is linked with the corresponding entity *software* inside the database of the *Project ADE* and analyzed to find the required data in the files from the measurement series. Since the data

evaluation software is a web application running on a webserver the data has to be uploaded from the device computer. Using a web application allows the user to access the functionalities of the *Project ADE* via a web browser from any computer or mobile device independently from the operating system. To upload and import the measured data to the entities database the software *Data Upload* is used. To automate the export of the result files from the device software this possibility has to be provided by the device software.

In future work an intelligent decision maker will be included to help the user to interpret the chromatograms and mass spectra in the right way to quantify the right chemical compound. Therefore the results of structural and elemental analysis will be combined with additional information (e.g. source) for sample and the possible compounds.

VII. ACKNOWLEDGMENT

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