What happened since SWEMSA 2016?

About Research, Education and Applications in Non-Target Screening (NTS)

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NTS reflects a new paradigm analyzing organic molecules in complex mixtures. The analysis procedure, the data evaluation and data interpretation therein are very demanding tasks. SWEMSA workshops were organized within the scope of the FOR-IDENT projects and brought together international and interdisciplinary NTS specialists. A very fruitful core of sustainable discussions and further ideas.

Research and Discussion in NTS

Mass spectrometric screening techniques (in combination with chromatographic separation), such as non-target screening (NTS), have been a major topic regarding measurement principles and data evaluation strategies in scientific research and discussion for years. In addition to the 'classical' metabolomics scene, the environmental analytical community stood out in particular. Both communities discussed the classification and definitions of the screening approaches in detail and categorized them finally almost collectively. For example, an overview article on screening definitions [1] was published by our RISK-IDENT project as early as 2014, and in the following time a categorization concept [2,3] as well as exemplarily scientific applications [4,5] were published by and with colleagues (e.g. from the continuing FOR-IDENT project). This trend in environmental analysis found a first highlight finally last year in the publication of a book with two volumes from in total of twenty-one chapters by international colleagues [6]. The international discussion in the Environmental Analysis consequently led to several conferences and meetings in that years regarding the upcoming Non-Target Screening. The SWEMSA 2016 Workshop for example intended to continue the exciting dialogue that was started earlier in 2016 at the 'Non-Target Conference 2016' in Ascona. SWEMSA 2016 focused thereby on the topics 'Open access platforms in NTS', 'Commercial software solutions in NTS', 'Holistic NTS workflows and solutions' and 'NTS in epidemiology, toxicology, molecule degradation in environmental analysis', bringing together international (leading) scientists from the NORMAN initiative, ESSEM COST Action ES1307, ESSEM COST Action ES1202, NEREUS-COST Action

ES1403 and many other international consortia in environmental analysis. These topics were presented by ten 'environmental' lectures as well as seven 'computational' lectures. However, SWEMSA 2016 tried to combine and to harmonize for the first time various analytical NTS topics and linkages to different disciplines. Participants from disciplines like chemistry, food, forensic, metabolomics and instrumental analysis presented in total further seven talks. The general program featured a solution-focused discussion strategy including flip chart discussions, panel discussions and overview talks. The overall aim of the meeting was to condense and harmonize various common aspects of NTS, to extend the use of software and workflow strategies and to learn about the potential of NTS applied in various disciplines. Later should be strengthened in SWEMSA 2019, thus this time again fourteen talks are in the 'environmental' and/or 'computational' field but this time more than eighteen lectures are given from other disciplines. The successful discussion might be intensified by panel discussions after each slot, i.e. seven in total.

Education in NTS (using open access e-learning and practical concepts)

Simultaneously with the discussion about non-target screening and its data evaluation strategies, there was also a growing recognition that in this type of analysis it is no longer effective and efficient for each laboratory or facility to be on the move as a 'single fighter'. The need for trained and experienced experts in this field of instrumental analysis and data evaluation becomes also more dominating in every laboratory. In recent years, however, this sector has had to contend with the fact that non-academic

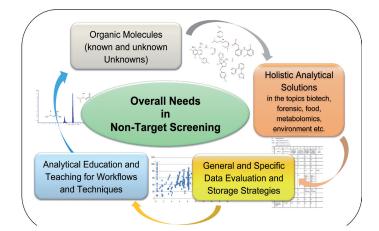**Fig. 1: Open access programs for free application in NTS**

Fig. 2: Concept scheme for NTS needs

training (e.g. to laboratory technicians and chemical-technical assistants) obviously had to lag behind compared to academic education. However, as this has led to an increasing shortage of practical experts in sophisticated instrumental analysis (such as mass spectrometry), it is now time to counteract this and to take new or modern ways of training in order to increase the number of interested youth (mainly in the non-academic environment). One of these ways is the increased use of free apps by young people. So was ten years ago the German Chemnix-Blog [7] started and five years ago the Analytics+-Tool [8]; both open-access (e-learning) tools (see also Figure 1) are targeting young people or trainees and giving them access to interesting analytical topics. Since both learning tools are professionally organized and supervised, it is also ensured that the young people (and not only them) find an exciting introduction to the topic, but at the same time they receive correct information and learning content free of charge. The Chemnix-Blog answers a wide range of questions from the natural sciences in an entertaining way, while Analytics+ deals directly with analytical training. The Analytics+ e-learning platform works on three levels of knowledge, namely learning, practicing and applying. In this context, interested persons can use basic material as well as SPE-[9], HPLC-[10] and GC-[11] simulators and thus expand their experience in instrumental analysis. An examination approach with certification (to prove the successful application of Analytics+) is also available. This is to ensure that this open access concept (including simulator use) can also be used sustainably. The use of the materials and simulators is explained in the tool Analytics+ as well as the currently heavily used screening strategies, e.g. NTS [12]. This

encouraged the fact that research and discussion has also responsibility to teach the knowledge in a workable way.

Commercial and practical use of NTS

Mass spectrometric non-target screening together with target screening and suspect screening is part of the 'screening family' and includes hidden targets, i.e. 'Known Unknowns' and unknown targets, i.e. 'Unknown Unknowns'. The former often leads to the identification of substances in compound databases as well as analytical databases. The latter are the real unknown substances and can only be described and compared (and remain 'unknown' so far). Current research groups and various NTS instrument and software supplier present(ed) several analytical techniques, practical workflows and data evaluation concepts (see SWEMSA programs 2016 and 2019). A well-known and in the last eight years (by several public institutions) supported substance database is the so-called STOFF-IDENT [13]. This compound database can be used with the non-target screening platform FOR-IDENT [14] and support in the identification of molecules can be consulted there with. The FOR-IDENT platform (see also Figure 1) provides information on retention time, accurate mass, signal intensity as well as fragment spectra and translates this via retention time normalization, molecular formulas and a comparison with in silico fragmentation software into chemical information such as logD, molecular formula and chemical structure. This physico-chemical information can then be compared by the FOR-IDENT platform [14] with the molecules (deposited in the substance databases STOFF-IDENT [13] and PLANT-IDENT (online since mid-2019)). This leads to suggestions for molecular identification which would have to be finally confirmed with reference materials. Further open-access databases for this evaluation strategy in other areas such as food, forensics etc. are in preparation. Thus, in the past, this evaluation strategy has been able to find several molecules that were originally unknown with non-target screening measurements such as in surface waters [3], house dust [15], and red wine [16]. This evaluation strategy is currently spreading worldwide and it can be hoped that many more molecules will be detected through these substance databases. In this way, non-targeted analytics would become a systematic, (first) identifying analysis and, in addition to the experts in the field, it would also be possible for quickly aspiring experts and interested public society to find their way around. The free access would be there. Finally, SWEMSA 2016 and SWEMSA 2019 also will help to translate the NTS knowledge into commercial applications and the use of statistical information.

Conclusions

Main player of the (German) long-term NTS are the RISK-IDENT project (2011-2014) and the continuing FOR-IDENT projects (2015-2017 and 2017-2019). These projects resulted in the workshops SWEMSA 2016 and SWEMSA 2019; in both more than 120 participants were discussing the past, presence and future of Non-Target Screening. The FOR-IDENT platform itself and its compound database family STOFF-IDENT, PLANT-IDENT (and DuftSTOFF-IDENT) become sustainable now and will continue the work in an independent FOR-IDENT club (for membership see https://www.for-ident.org). The e-learning platform Analytics+ (http://www.analyticsplus.org) with various learning strategies and open-access simulators in instrumental analysis became an independent free platform as well supported by professional partners. And last but not least the project strengthened the expertise of experienced NTS partners like the Bavarian Environment Agency, the Zweckverband Landeswasserversorgung Langenau and Berliner Wasserbetriebe. Further more also a new institution for NTS consulting, teaching and research was founded as a consequence and solution for forthcoming NTS tasks, i.e. the Analytische Forschungsinstitut für Non-Target Screening GmbH (AFIN-TS GmbH). All together, we will continue the long-term NTS thinking (like shown in Figure 2) not only in Germany.

Thus we look very positively in the future of NTS and future experts as well as the further dissemination and long-lasting use of platforms in 'open-access e-learning' and for 'open-access data analysis'.

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[8] http://analyticsplus.org

[9] http://analyticsplus.org/?page_id=426

[10] http://analyticsplus.org/?page_id=92

[11] http://analyticsplus.org/?page_id=482

[12] http://analyticsplus.org/?page_id=80

[13] https://www.lfu.bayern.de/stoffident/

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