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EDITORIAL

ABC Spotlight on Analytics 4.0

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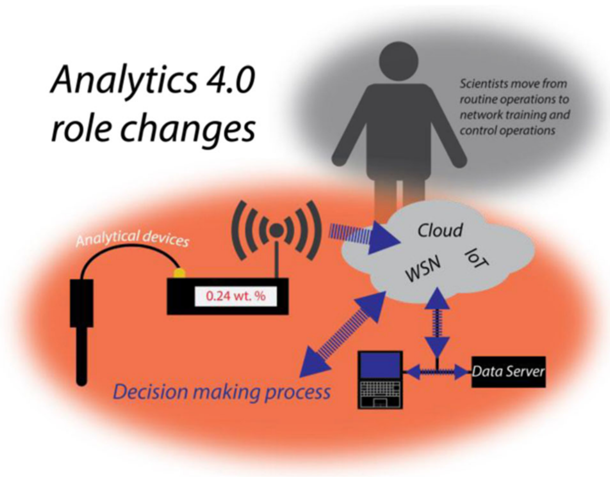

Analytical chemistry plays a key role in our daily life, albeit often not realized by the layman, and is a crucial contributor to areas such as food safety, health care, production processes, environmental monitoring, forensics, and life sciences research.

With an ever-evolving Internet of Things (IoT), i.e., the increasing automation and networking within and of industrial processes, businesses, and our homes, it is obvious that analytical chemistry will become an integral part of the IoT and will contribute by providing analytical data for decision-making processes just as it does off-line in today's analytical facilities. Analytics 4.0 describes technologies ready for automation, and for connection to IT and computing technologies to realize data transmission, interpretation, learning, and self-evolution. It is associated with a dramatic decentralization of data generation, expanding from centralized labs to individuals, to remote sensing locations, and to the cloud. Analytics 4.0 is thus the evolution that analytical chemistry is undergoing as it becomes an inevitable part of the IoT.

Today, the chemical industry plays a leading role in the advancement of Analytics 4.0 by integrating analytical chemistry directly into process lines (termed process analytical technology, PAT) and hence stepping away from the traditional use of separate, external sensors in the decision-making process. Gouveia et al. have shown the suitability of different spectroscopic methods and their importance as PAT elements either applied in quality monitoring of a chemical synthesis process routine or in the design of process layouts for a scale-up from batch to continuous production lines [1]. Hence, automated analytical chemical technology is embedded in the overall process control. It is coupled to up- or downstream decision-making steps and hence directly influences the outcome of the whole process in real time, as opposed to being a disconnected, passive sensing element that requires human interaction to cause a reaction. Furthermore, Gouveia and colleagues illustrate how such an integrated small-scale solution provides the understanding needed for translation to large-scale production.

Analytics 4.0 will often rely on multi-sensing solutions to obtain the required reliability in an automated system. This may be achieved by connecting and networking analytical devices of the same type at different locations or by incorporating different analytical (detection) methods for orthogonal verification of results. Obtaining the same answer through independent methods has a long tradition in analytical chemistry. In automated situations as envisioned in the IoT this need is even greater and research for orthogonal detection strategies for the same analyte are in high demand. Uteschil et al. have, for example, presented the combination of time-of-flight ion mobility spectrometry (TOF-IMS) together with laser-induced fluorescence detection [2]; hence, spectroscopic and mass-based data are obtained during the same analysis. The authors demonstrate that this combination delivers not

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only more precise molecular information from IMS (i.e., the specific drift times) but also optical parameters such as fluorescence lifetimes or emission maxima, thus gathering simultaneous in-depth information on the analytes. Many of the exquisite hyphenated, complex technologies developed over the last decades, or traditional combinations of microbiological and biochemical methods, or verifications of molecular biological results through immunological staining fall into the same orthogonal detection approach strategy. Developing these technologies toward Analytics 4.0 performance is an important grand future task and highly desirable for multidimensional analysis.

In this day and age high-throughput screening (HTS) is a highly automated process with semiautomated data processing and minimal user interaction in the pharmaceutical industry. Further progress can link combinatorial syntheses with HTS, which is more an IT and engineering task than an analytical challenge. At the same time though, the development of new screening procedures, alternatives to the ubiquitous microtiter plate format, is desirable as many analytical answers cannot be obtained in such a format, and as applications outside of centralized facilities would also benefit from screening strategies. Jagannadh et al. [3] demonstrated a microscopy method with the potential to screen large entities of cells in a short timeframe and with reasonably priced equipment, e.g., for blood cell counting in a point-of-care (POC) diagnostics setting. Combined with chemometric techniques, e.g., principal components analysis (PCA) and other algorithms, with neuronal networks and with deep learning strategies this can become a more interaction-independent tool.

Portable sensors may be the one analytical technology that the layperson can directly associate with as it relates to interconnected, automated Analytics 4.0. Many people voluntarily wear accessories that incorporate sensors, whether these are simple step counters, pulse monitors, or temperature sensors. Wearable glucose sensors, ECG monitors, smartphones with interactive health monitoring apps have entered our daily life and find acceptance with the users. Smartphones, smart homes, and smart cars are at the forefront of making our lives “more convenient”. Thus, it is foreseeable that the (bio)chemical sensors that are part of the Trillion Sensor Vision will drive the development of Analytics 4.0. In fact, where possible, today’s published portable (bio)analytical sensors describe their potential for wireless data transmission, which is a mandatory necessity for Analytics 4.0. Also, in most scenarios, data acquisition via cell phone is suggested. Chen et al. recently presented a smartphone add-on for the optical readout of colorimetric assays as demonstrated with an ELISA for zearalenone, which is a fungal toxin relevant in food safety testing [4]. Also, Gao et al. have built a smart wristband multiple sensor array for multiple physiological parameter monitoring based on sweat analysis [5]. Their device is able to monitor levels of lactate, glucose, Na^+, K^+, and temperature via enzyme- or ion-selective electrodes or microwires with at least 5 weeks of long-term stability. Data are sent via a Bluetooth module to a smartphone for readout and logging. Furthermore, Sharma et al. have presented an amperometric, microneedle-based in vivo glucose-monitoring device, with state-of-the-art performance also during a short clinical testing phase in humans [6]. Such multi-analyte ex vivo and in vivo sensing applications will define the progress of portable sensing and are an important cornerstone of the future Analytics 4.0.

One of the greatest challenges for wearable in vivo or in situ sensors may be the integration of sample preparation and analyte preconcentration steps with the detection module, all to be located in a simple device that does not require user interaction and can be used in the long term. Hence, this is an area of intensive research and great needs. Much success has been seen through the development of lab-on-a-chip systems. While not wearable, these tend to be portable devices in which analytical operations are miniaturized. For example, Furutani et al. recently demonstrated a portable system for highly complex bioanalytical challenges. The size of a suitcase, it incorporates a real-time PCR system for on-site pathogen detection [7]. Microfluidics-based liquid handling and integrated system design allows processing from sampling to result output. Their system compares well to a conventional PCR setup and was demonstrated for *E. coli* detection.

In the present day, rapid, portable, and low-cost detection of analytes based on DNA or RNA information remains challenging because of complex sample preparation and expensive amplification and detection assay requirements. Yet, nucleic acid-based sensing is of great interest also for Analytics 4.0 as observable phenotypes and many diseases are associated with specific genomic information. Next generation sequencing (NGS) has the potential to become the routine technology for nucleic acid testing in the lab, in screening applications, but also in the POC setting. Using sufficient computing power, wireless data transmission, and cloud technology, large databases will be created as sources for automated data analysis.

Connectivity, data readout, storage, sharing, and logging are as important to Analytics 4.0 as these are integral elements of the IoT. Connection between devices is highlighted in the review by Lopez-Barbosa et al. on the future of POC disease detection, emphasizing the role of the IoT [8]. The unfolding independence of user operation and the evolution of standalone analytical devices (not only automatically reporting results but also being integrated in decision-making routines with closed loop sensing and feedback control systems) will prepare Analytics 4.0 for the IoT. Stenzel has written an exciting article on sensor systems onboard the International Space Station (ISS) [9]. Here, the onboard sensor system is a complete wireless sensor network (WSN), connecting and coupling all single sensing elements together into one large, intercommunicating entity. Expansion of this approach to different application areas (such as smart homes, environmental monitoring, health care, industrial processes) is highly projectable. Although no (bio)chemical techniques and sensors are included yet onboard the ISS's own WSN (rather microscale sensors for temperature, humidity, pressure, or light), the architecture can be a blueprint for the integration with any aforementioned Analytics 4.0 sensor or system and those off-line sensors used already onboard for ISS-based experiments.

Such multi-orthogonal, autonomously reacting, large sensor networks can be realized, as long as interfaces, communication protocols, and data formats are standardized. Also, low and sustainable energy consumption is a mandatory requirement for WSNs and any portable sensor approaches. Here, low-power communication, microelectromechanical system (MEMS) devices, and a photovoltaic energy harvesting system avoid batteries and improve the independence of the networked system on the ISS. Obviously, benchtop measurement devices will profit equally from all of these described developments, and added connectivity will boost interoperability, automation, user independence, processing, and many more features.

Analytics 4.0 is a step toward an Internet of Analytical Things, in which networked analytical labs communicate with distributed sensors, providing information which drives automated decision-making. Application areas include health care, smart homes, food and agricultural systems, environmental monitoring, and industrial processes. It will be a highly relevant, important, and in fact necessary resource for the goal of solving ubiquitous challenges in our societies. It should be noted though that with a "trillion sensor vision", with the integration of Analytics 4.0 into the IoT, and with the desired unlimited analytical possibilities come great responsibilities related to cybersecurity, data privacy, and a fair evolution. Making these aspects part of our scientific communications is our responsibility.

References

1. Gouveia FF, Rahbek JP, Mortensen AR, Pedersen MT, Felizardo PM, Bro R, et al. Using PAT to accelerate the transition to continuous API manufacturing. Anal Bioanal Chem. 2017;409:821–32.
2. Uteschil F, Kuklya A, Kerpen K, Marks R, Telgheder U. Time-of-flight ion mobility spectrometry in combination with laser-induced fluorescence detection system. Anal Bioanal Chem. 2017;409:6279–86.
3. Jagannadh VK, Bhat BP, Nirupa Julius LA, Gorthi SS. High-throughput miniaturized microfluidic microscopy with radially parallelized channel geometry. Anal Bioanal Chem. 2016;408:1909–16.
4. Chen Y, Fu Q, Li D, Xie J, Ke D, Song Q, et al. A smartphone colorimetric reader integrated with an ambient light sensor and a 3D printed attachment for on-site detection of zearalenone. Anal Bioanal Chem. 2017;409:6567–74.
5. Gao W, Emaminejad S, Nyein HYY, Challa S, Chen K, Peck A, et al. Fully integrated wearable sensor arrays for multiplexed in situ perspiration analysis. Nature. 2016;529:509–14.
6. Sharma S, Huang Z, Rogers M, Boutelle M, Cass AE. Evaluation of a minimally invasive glucose biosensor for continuous tissue monitoring. Anal Bioanal Chem. 2016;408:8427–35.
7. Furutani S, Naruishi N, Hagihara Y, Nagai H. Development of an on-site rapid real-time polymerase chain reaction system and the characterization of suitable DNA polymerases for TaqMan probe technology. Anal Bioanal Chem. 2016;408:5641–9.
8. Lopez-Barbosa N, Gamarra JD, Osma JF. The future point-of-care detection of disease and its data capture and handling. Anal Bioanal Chem. 2016;408:2827–37.
9. Stenzel C. Deployment of precise and robust sensors on board ISS—for scientific experiments and for operation of the station. Anal Bioanal Chem. 2016;408:6517–36.

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