

## No Need to PANIC



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### Overview of the Newsletter

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Practical  
Applications of NMR  
in Industry Conference



Wako

# qNMR symposium in Tokyo and qNMR Japan Committee (by Takako Suematsu, JEOL RESONANCE Inc.)



qNMR symposium in Tokyo was held on 31th of Oct.. This symposium is commemorative symposium for founding qNMR Japan Committee. Several companies and institutions have been working on qNMR activities since



around 2005, but qNMR community in Japan was established officially. qNMR Japan Committee object is shown [here](#). We are going to improve the web-page and we hope it will be communication tool with qNMR community in the world.

The theme of qNMR symposium in Tokyo was "Recent Progress and Future Prospects for qNMR". The symposium was intended to establish a platform for information exchange and educational activities related to qNMR as the next-generation of quantitative analysis, representing the ultimate goal of the committee. Specifically, participants learned about the latest ISO application and standardization activities, while engaging in an interactive program that provided an opportunity to utilize and share the research and activities of participants, including brainstorming of ideas for broader dissemination. The program was as shown here.



## Greetings Ministry of Economy, Trade and Industry (JAPAN)

13:05 – 13:15 **"Introduction of qNMR Japan Committee"**, *Secretary-General*

13:15 – 13:45 **"Status report on standardization activities"** - Including the prompt report for Inter laboratory comparison study, *Toru Miura (FUJIFILM Wako Pure Chemical Corporation)*

13:45 – 14:45 **"Calculation, Documentation, and Dissemination of qNMR Data"**, *Dr. Guido Pauli (University of Illinois at Chicago)*

15:00 – 16:00 **"Quo Vadis?" The Future of qNMR**, *Dr. Bernd Diehl (Spectral Service)*

16:00 – 17:30 **"Open discussion"**

Discussion topic: Next Steps in Moving qNMR Technology forward

- 1) Food Analysis
- 2) Education

As the result, about 50 people attended the symposium. There were a lot of fruitful discussions. We are ready for the starting variety of activities as qNMR Japan Committee. The activities details will be posted soon on our webpage.



## ValidNMR Fellow 2018/2019 is Elina Zailer



**Once is not habitual!** I am very grateful to become a second time the BrukerValidNMR fellow for Excellence in NMR Validation presented by PANIC. As a business development manager at Spectral Service (Cologne, Germany) and a PhD student at the University of Würzburg (Germany) I combine industry and education. My mission is to provide education and awareness in NMR Validation through fostering communication and progress in the community. Any great ideas, suggestions or publications? - contact me at [elina\(at\)validnmr.com](mailto:elina(at)validnmr.com)! I am looking forward to supporting you!



# SUMMIT 2018

The **q** in NMR

(by Michael Maiwald, BAM)

**The 2018 qNMR summit in Würzburg attracted over 55 participants from various countries and was filled with talks spanning a variety of topics.**



After the successful spring meeting in Japan the series of qNMR satellite meetings was continued with the 2018 qNMR Summit in Würzburg/Germany held October 11-12, 2018 at the Julius Maximilians University of Würzburgs Institute for Pharmacy and Food Technology, organized by Ulrike Holzgrabe's Group. Contributors and guests came broadly mixed from local European Industry, research, instrument and software manufacturers and authorities. Participants from Japan, U.S.A., New Zealand, or Australia made the meeting once more very international.



The Summit started with a qNMR Workshop organized by Mestrelab Research. It was opened by James Hook (University of New South Wales) with his keynote talk taking the audience into the world of chlorine, oxygen, and nitrogen qNMR.

The program on the first day covered a Workshop on automatic qNMR where the incredible progress of NMR experiment automation and data analysis under quantitative aspects was shown. Meanwhile, the user is supported with several options and functions, which allow full workflows from experiment design to experiment certificates. The Workshop was followed by a session on regulatory affairs, which started with the topics NMR in GxP environments, ISO standardization of qNMR, and the role of qNMR in the European Pharmacopeia. Two impressive success stories from industrial users gave the audience a feeling for the importance of qNMR spectroscopy in industry spanning from automated product releases of specialty chemicals to reference methods and the market registration of diagnostics in pharma. Finally, a focus was laid on the good weighing practice for accurate qNMR sample preparation. The first day was rounded by several panel discussions and a remarkable poster program. It ended properly with a wine tasting in the spaciouly wine cellars of Juliusspital, one of the largest and most recognized wine cellars in Germany. Some participants recognized that Würzburg's pubs close at 2:00 am during the week.

The second day started (in the presence of all wine tasters) with a keynote "Updates and Future Vision of qNMR at U.S. Pharmacopeia" of Yang Liu (USP). It was followed by a couple of short talks spanning a bridge from basic methods to applications as well as a special session on low-field NMR spectroscopy in qNMR. Benchtop NMR instruments are rapidly developing and become interesting for quality control applications or purity analyses. The second day was also accompanied by panel discussions and poster program. It was framed by the keynote given by Bernd Diehl (Spectral Service AG, Cologne).

The 2018 qNMR summit in Würzburg was all in all a very successful and fruitful event. It was proposed to hold the next meeting in spring 2020 somewhere in Europe. Finally I'd like to acknowledge the perfect organization by the organizing committee and the local organization by all contributors of Ulrike Holzgrabe's Group, first and foremost Curd Schollmayer. **See you in 2020!**

## **qNMR: a superior method of quantitative analysis?** (by Ron Crouch)

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Nuclear magnetic resonance (NMR) spectroscopy has long been a preferred method for organic compound analysis, but now quantitative NMR (qNMR) is making waves in a field that has so far been reliant upon chromatography. NMR spectroscopists have known of the flexibility and utility of qNMR for quite a long time but now the word is spreading further afield.

Analysis by NMR has a quantitative performance in principle, but it has previously been considered big, expensive, low-sensitivity and altogether complicated when compared to chromatographic methods. However, that's all changing, with qNMR attracting attention from a variety of fields for the reliability of the results it can achieve. The fact that an NMR measurement is inherently quantitative without requiring a reference standard for routine analysis affords both power and convenience. In fact, a qNMR result of an unknown mixture based on an external calibration of the instrument on a known sample can easily reach 1% accuracy or better. It is not surprising to NMR folks to find that an NMR spectrometer can actually be more precise than a scale. The technique can be more accurate than typical weighing errors.

## What is qNMR?

NMR methodology enables primary and secondary metabolites to be identified and quantified, delivering high-throughput spectroscopic and structural information on a wide range of metabolites simultaneously. The principle difference from other quantitative analytical techniques is that it is an absolute method, which does not require the same standard substance as an analyte. Hydrogen within the molecules can be observed and measured with NMR, so even if the molecules are different, the presence of hydrogen means that quantitative analysis is possible. This is extremely useful for quantification of new compounds, and means that calibration curves are not required for this analysis.

With qNMR it is possible to confirm the proportion of a target component in a sample, and to determine the absolute amount (content) of the components of interest. This is useful for samples that include multiple components, such as polymers and chemical products. Of course, liquid chromatography can also be used to perform separation and analysis to determine the ratio of components in a sample. However, even though analysis with NMR is not a separation analysis, the properties of NMR can be exploited to perform very effective results.

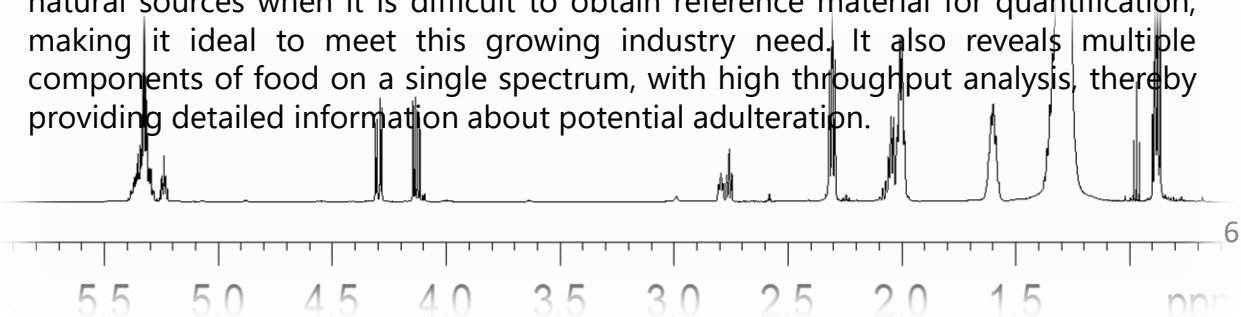
From an NMR spectrum you can identify, as well as measure, the compounds that you analyze, so it delivers both qualitative and quantitative analysis simultaneously without changing the measurement conditions – a key benefit to scientists in many fields of analysis, from food and drug analysis, to natural products and forensics.

## Practical applications

The USP (United States Pharmacopeia) Food Fraud Database lists hundreds of incidents of economically motivated adulteration (EMA), substitution, counterfeiting/mislabelling of food products, e.g. olive oil and milk powder, and some adulterants such as melamine. Techniques like chromatography can provide a detailed profile of food but require a lot of sample prep and manual processes, which means they're expensive and time-consuming.

Reference materials are indispensable for accurate analysis of hazardous substances in food, however, regulators have not been able to keep pace to provide RMs for the growing number of organic compounds that might require analysis.

qNMR allows for accurate (and rapid) quantification of analytes derived from natural sources when it is difficult to obtain reference material for quantification, making it ideal to meet this growing industry need. It also reveals multiple components of food on a single spectrum, with high throughput analysis, thereby providing detailed information about potential adulteration.



In the field of metabolomics, in vitro cell based studies are used in many areas of research, including cancer cell metabolism, immune metabolism, regenerative medicine and drug effectiveness. The common goal of all of them is to understand and decipher the influence and involvement of metabolism on/in biological effects and mechanisms, and integrate this information onto metabolic maps. Detailed quantitative metabolic data is required and qNMR is a non-destructive technique that can be used to analyze several core features of cellular metabolism.

### qNMR gains momentum

qNMR isn't a new tool for analysis; rather an under-used technique that is becoming increasingly popular among analytical chemists due to its growing reputation for making analysis easier. Fairly complex mixtures can easily be analysed without the time consuming and tedious step of separation. The technique is increasingly used across multiple industries and its merits are becoming widely known across applications. As industries employing NMR techniques invest in technology capable of ever more complex research and analysis, we believe that NMR will become a standard method for quantitative analysis in the future.

<https://www.sciencedirect.com/science/article/pii/S0003267017306037>

C.H. Johnson, J. Ivanisevic, G. Siuzdak Metabolomics: beyond biomarkers and towards mechanisms Nat. Rev. Mol. Cell Biol., 17 (2016), pp. 451-459

## Interested in 'Quantitative NMR Methods for Reaction and Process Monitoring'?

(by Michael Maiwald, BAM)



We invite you to join NMRPM 2019!

**31st January and 1st February 2019**

**University of Kaiserslautern**

**Curious? Visit: <http://nmrpm.mv.uni-kl.de/home.html>**

**Poster submission deadline:**

**30th November**

**Registration deadline:**

**28th December**

The symposium brings scientists who apply NMR methods for reaction and process monitoring in academia and industries together, with the goal to narrow the gap between what is achieved with NMR techniques under ideal conditions and what is possible under conditions relevant to industrial applications.

## Thursday, 31<sup>st</sup> January

### Session 1 (09:15 – 10:45)

- **Thermodynamic and kinetic studies in NMR flow setups** E. von Harbou, University of Kaiserslautern, DE
- **High-resolution compact NMR spectroscopy for reaction monitoring and process control** K. Singh, Weizmann Institute, Rehovot, ISR
- **A continuous flow-batch hybrid reactor for commodity chemical synthesis enabled by inline NMR and temperature monitoring** C. Schotten, University of Leeds, UK

### Session 2 (11:15 – 12:45)

- **Accelerating chemical process development and manufacturing by online NMR spectroscopy** M. Maiwald, BAM, DE
- **Applications of new 400MHz HTS power-driven magnet NMR technology for online reaction monitoring** M. Silva Elipse, Amgen, USA

### Session 3 (13:45 – 15:15)

- **Reaction monitoring analytics: Bringing it all together** M. Bernstein, MestreLab, UK
- **Quantitative NMR using a quantum mechanical spectral model** D. Holland, University of Canterbury, NZ
- **SINC: A new software for the automated and simultaneous phase and baseline correction of NMR data** K. Neymeyr, University of Rostock, DE

### Session 4 (15:45 – 16:45)

- **Microscale NMR hardware for applications** J. Korvink, Karlsruhe Institute of Technology, DE
- **Poster speed lecture**

### Poster session (16:45 – 19:00)

### Conference dinner @ 21 Café – Bar - Lounge

## Friday, 1<sup>st</sup> February

### Session 5 (09:30 – 10:30)

- **Applications of low and high field magnetic resonance in heterogeneous catalysis** M. Mantle, University of Cambridge, UK
- **Interleaved time-resolved non-uniform sampling NMR for reaction monitoring** M. Urbanczyk, University of Oulu, FIN
- **Online measurements with benchtop NMR: Reactions and beyond** J. Kolz, Magritek, DE

### Session 6 (11:00 – 12:15)

- **Advanced solid-state NMR techniques for revealing the structure of heterogeneous catalysts** T. Gutmann, University of Darmstadt, DE
- **Hyperpolarization enables fast reaction monitoring in diluted systems** K. Münnemann, University of Kaiserslautern, DE

### Workshop – Mestrelab





# ValidNMR Workshop 2018 – Agenda

## March 7, 2019

Welcome		
08:15	Coffee is served	
08:30	Welcome – Opening Statements	Torsten Schönberger (BKA) & Michael Maiwald (BAM)
08:50	Presentation: "QbD principles applied to NMR methods "	Ian Clegg (Bruker Biospin Inc.)
09:10	Presentation: "Good Weighing Practices"	TBD
09:30	Presentation: "Good Weighing Practice for accurate qNMR sample preparation"	Tucker Rubino (Mettler-Toledo GmbH)
09:50	Break	
10:10 Workshop Session #1: Design of Analytical Procedures		
	(A) Establish an Analytical Target Profile (ATP)	Session Leader: José G. Napolitano (AbbVie)
	(B) Identify the Critical Quality Attributes of qNMR	Session Leader: Dan Sorensen (Eurofins Alphora)
	(C) Plan Qualification of the Analytical Instrument	Session Leader: Christoph Freudenberger (Bruker Biospin Inc.)
11:40	Presentation: "ValidNMR Website and Wiki"	Kristie Adams (Steelyard Analytics)
12:00	Lunch	
13:00	Presentation: "Tackling 'dark' uncertainty in SI traceable qNMR analysis of peptides and glycans"	Cailean Clarkson (LGC)



<b>13:20</b>	<b>Workshop Session #2: Verification of Analytical Procedures</b>	
	(D) Plan the Analytical Control Strategy and VerificationBD”	Session Leader: Torsten Schönberger (BKA)
	(E) Design of Experiments	Session Leader: TBD
	(F) Use Statistical Tools for Evaluation of Measurement Uncertainty	Session Leader: Michael Maiwald (BAM)
<b>14:50</b>	<b>Open Forum – Q&amp;A, Discussions</b>	
15:15	The Workshop Adjourns – Closing Statements	Torsten Schönberger (BKA) & Michael Maiwald (BAM)
15:30	ValidNMR Business Meeting ValidNMR committee members (open to observers and interested parties)	
17:30	The ValidNMR Business Meeting Adjourns	



**Want to be featured in the next ValidNMR newsletter?**

The deadline for submissions and contributions to the next newsletter is January 15, 2019.  
Please contact us at [committee\(at\)validnmr.com](mailto:committee(at)validnmr.com)!



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