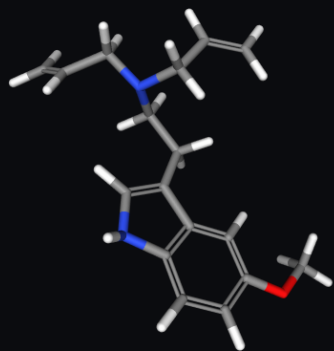




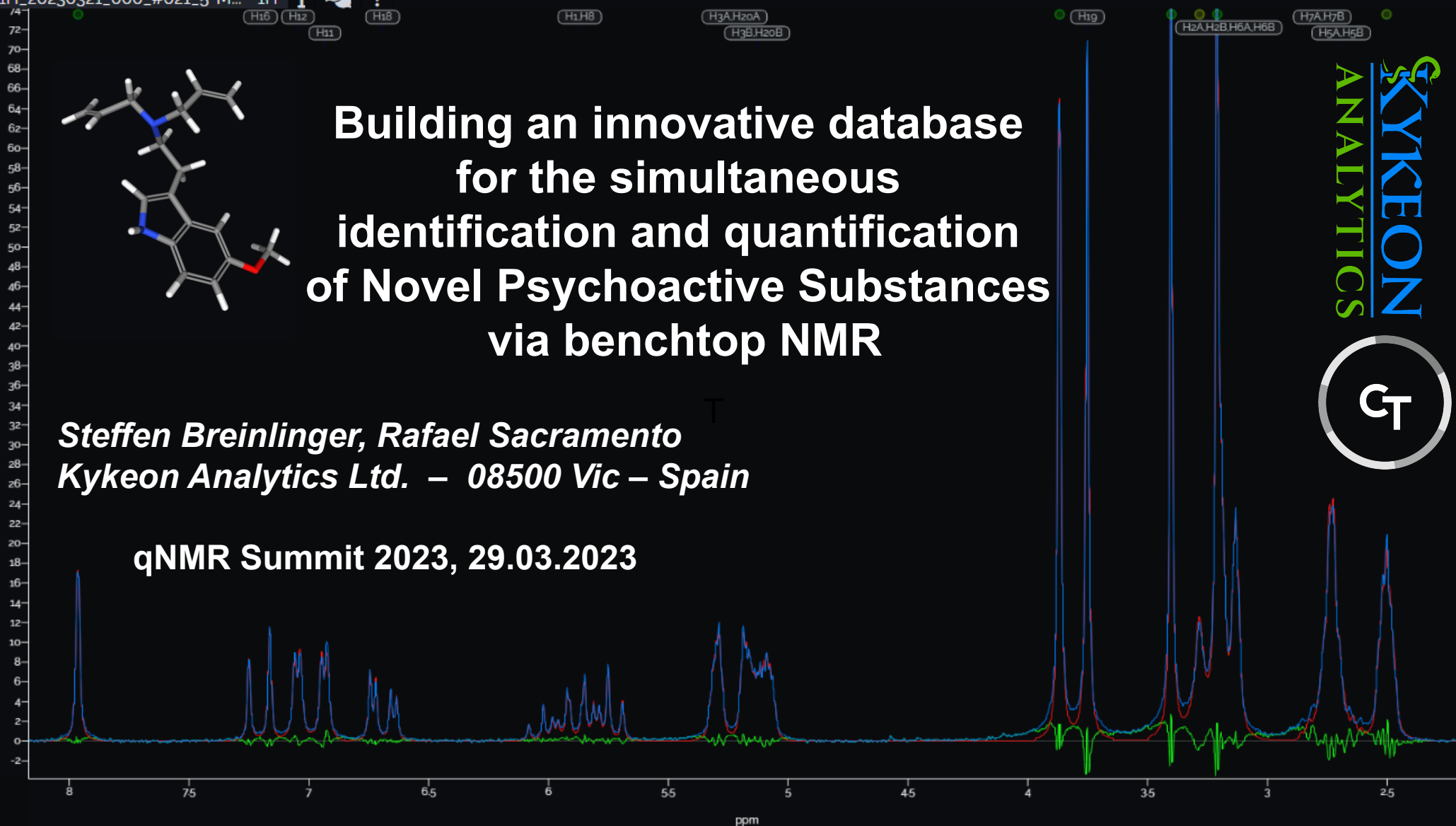
Building an innovative database for the simultaneous identification and quantification of Novel Psychoactive Substances via benchtop NMR

Steffen Breinlinger, Rafael Sacramento
Kykeon Analytics Ltd. – 08500 Vic – Spain

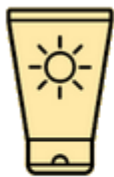
qNMR Summit 2023, 29.03.2023

KYKEON
ANALYTICS

CT



Harm reduction



SUNSCREEN



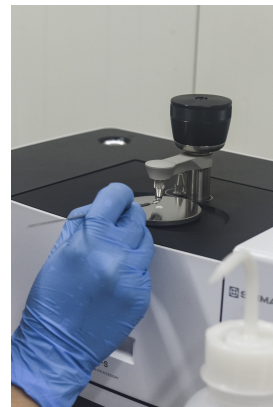
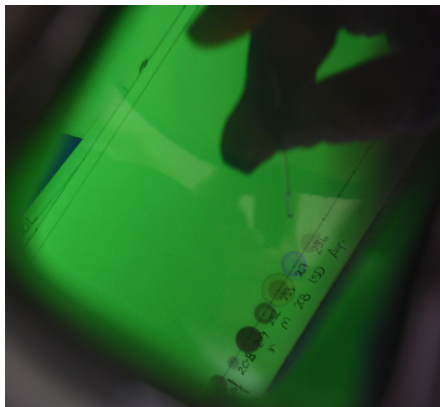
BICYCLE HELMET



SEATBELT

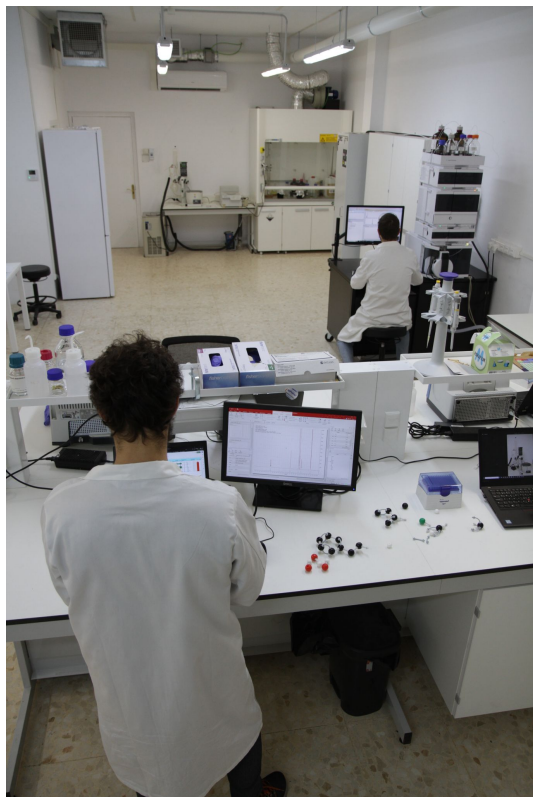
- Reduce risks and harms associated with a behavior
- Multidisciplinary approach
- No value judgment: Pragmatic perspective

Substance testing



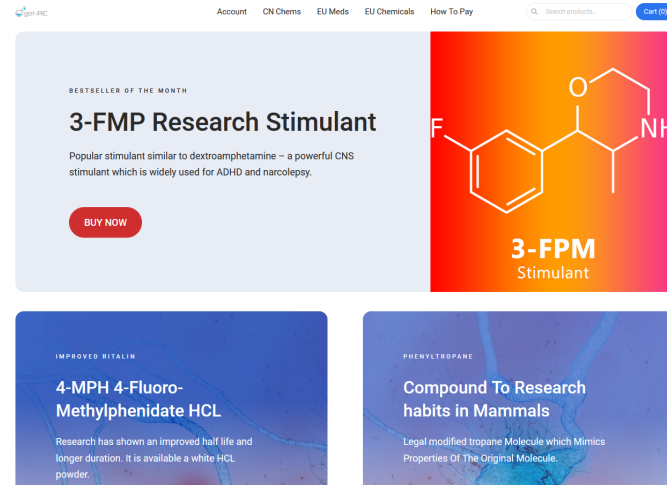
- Allows for informed decision making
- Dosage and purity / adulterants
- Drug market adapts to prohibition
- Multiple techniques available – Lab based or *in situ*

Kykeon Analytics



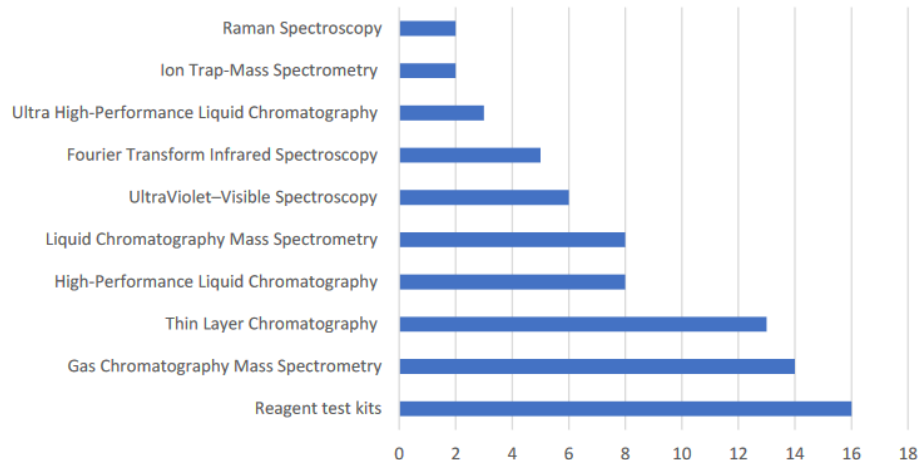
- Public service initiative to provide analytical services to people and organizations at no or low cost
- Use of FTIR, LC-MS and NMR

Market analysis – “legal” shops



- Variety of Novel Psychoactive Substances
- Sold as “not for human consumption” for legal reasons
- Useful for building our database
- Variable content, sometimes high purity, sometimes potentially lethal adulteration/mislabeling

Other harm reduction organizations



- 30+ organizations worldwide, most use simple reagent kits and/or TLC
- Difficult to identify new trends with less advanced techniques
- Kykeon offers help with analysis of unknowns, establishing libraries and training

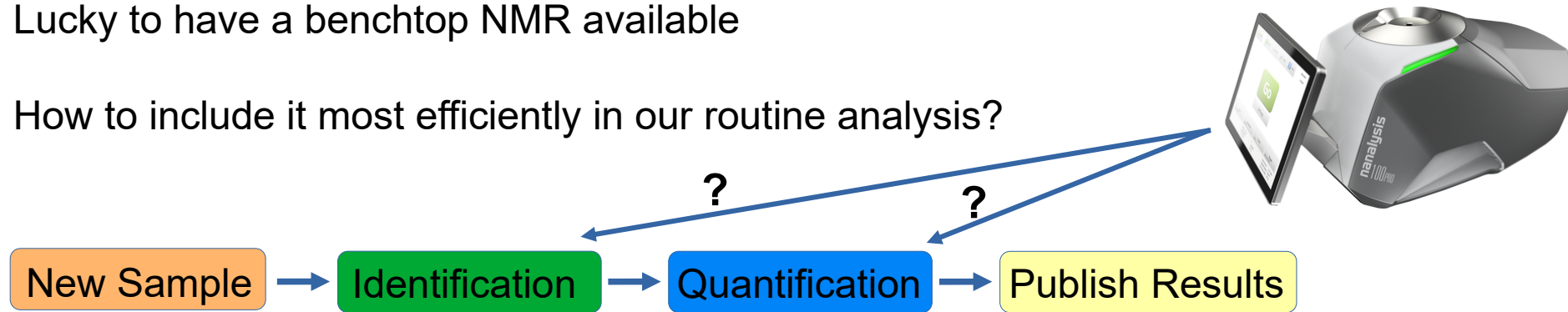
***In situ* analysis – Summer festivals**



- Very high demand
- High effectiveness – Research shows most people with adulterated substances throw them away
- Use of TLC, FTIR, HPLC and potentially benchtop NMR

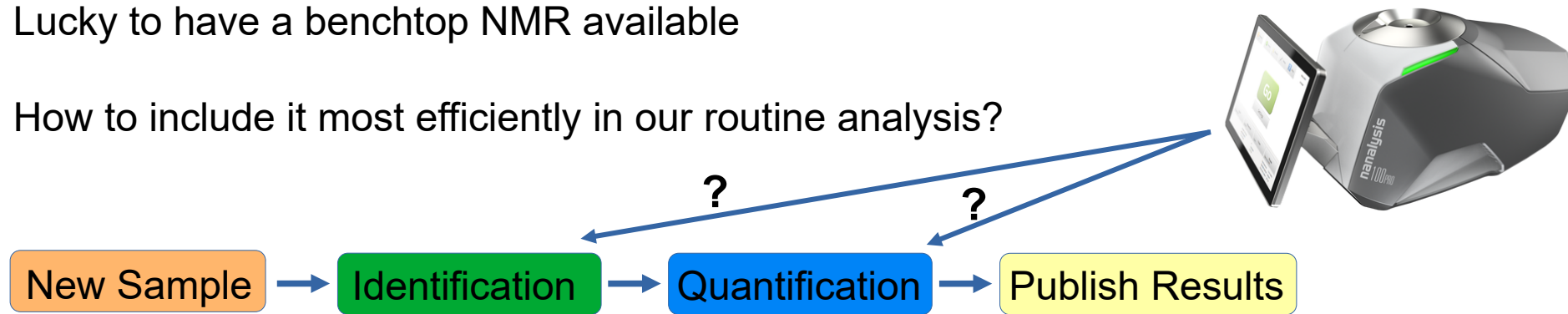
Why create this database?

- Lucky to have a benchtop NMR available
- How to include it most efficiently in our routine analysis?



Why create this database?

- Lucky to have a benchtop NMR available
- How to include it most efficiently in our routine analysis?



- Stumbled upon **Cosmic Truth** and the concept of **quantum mechanical spin analysis**
- Game changer for benchtop NMR as a dereplication tool in routine (forensic) analysis (**one-step identification and quantification**)



- based on permanent magnets
- smaller footprint
- no consumeables
- almost no maintenance
- easy operation

- lower field strength (< 200 MHz):

↓ signal dispersion ↓ sensitivity

→ **signal overlap, 2nd order effects**

→ **complex spectra**

Quality Control / Forensics / Routine Analysis = mainly Dereplication

Requirements:

- easy sample preparation ✓
- quantitative ✓ (**X** → only if no signal overlap)
- quick (analysis time, no external calibration) ✓
- 100 % reproducible ✓
- unambiguous identification **X**

Quality Control / Forensics / Routine Analysis = mainly Dereplication

Requirements:

- easy sample preparation ✓
- quantitative ✓ (**X** → only if no signal overlap)
- quick (analysis time, no external calibration) ✓
- 100 % reproducible ✓
- unambiguous identification **X**

**Impossible with
conventional spectral
analysis!!!**

→
**signal overlap, 2nd order effects
complex spectra**

**(especially for
multi-component mixtures)**

- (ppm), (Hz) are extremely reproducible
- (ppm), (Hz) are instrument/field independent
- (ppm), (Hz) can be extracted from NMR spectra
- NMR spectra can be calculated from δ (ppm), J (Hz)
- (ppm), (Hz) are natural constants (under defined experimental conditions)
 - δ (ppm), J (Hz) + $\omega_{1/2}$ (Hz) bound to analyte and NMR experimental conditions by Quantum Mechanical principles
 - **provide computational access to fully replicate experimental spectra**

Calculated spectra are **unique molecular fingerprints** (“Profiles”)

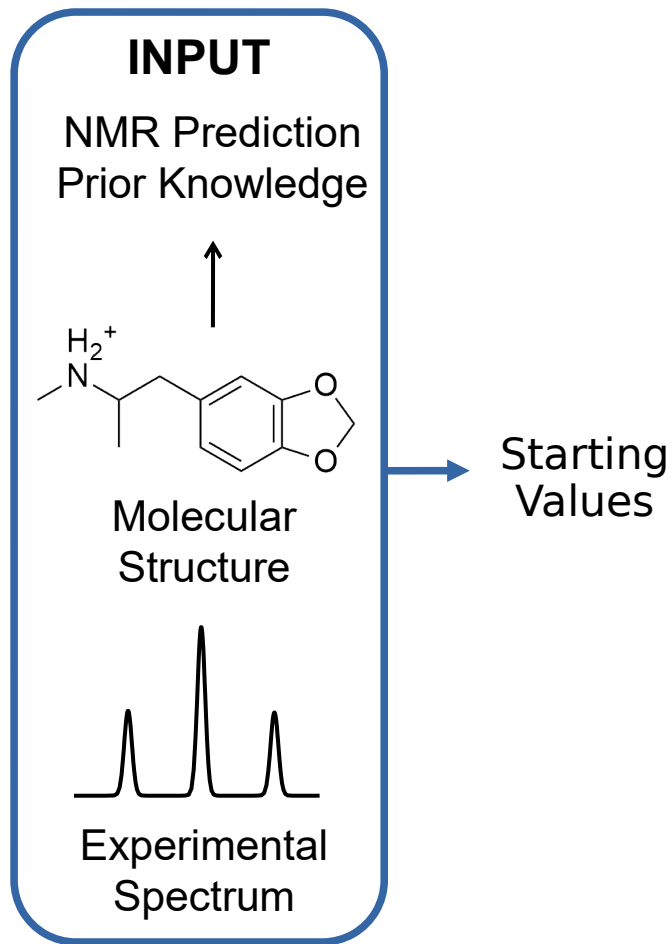
Essential NMR parameters (δ , J , $\omega_{1/2}$) have to be correct and **complete!**

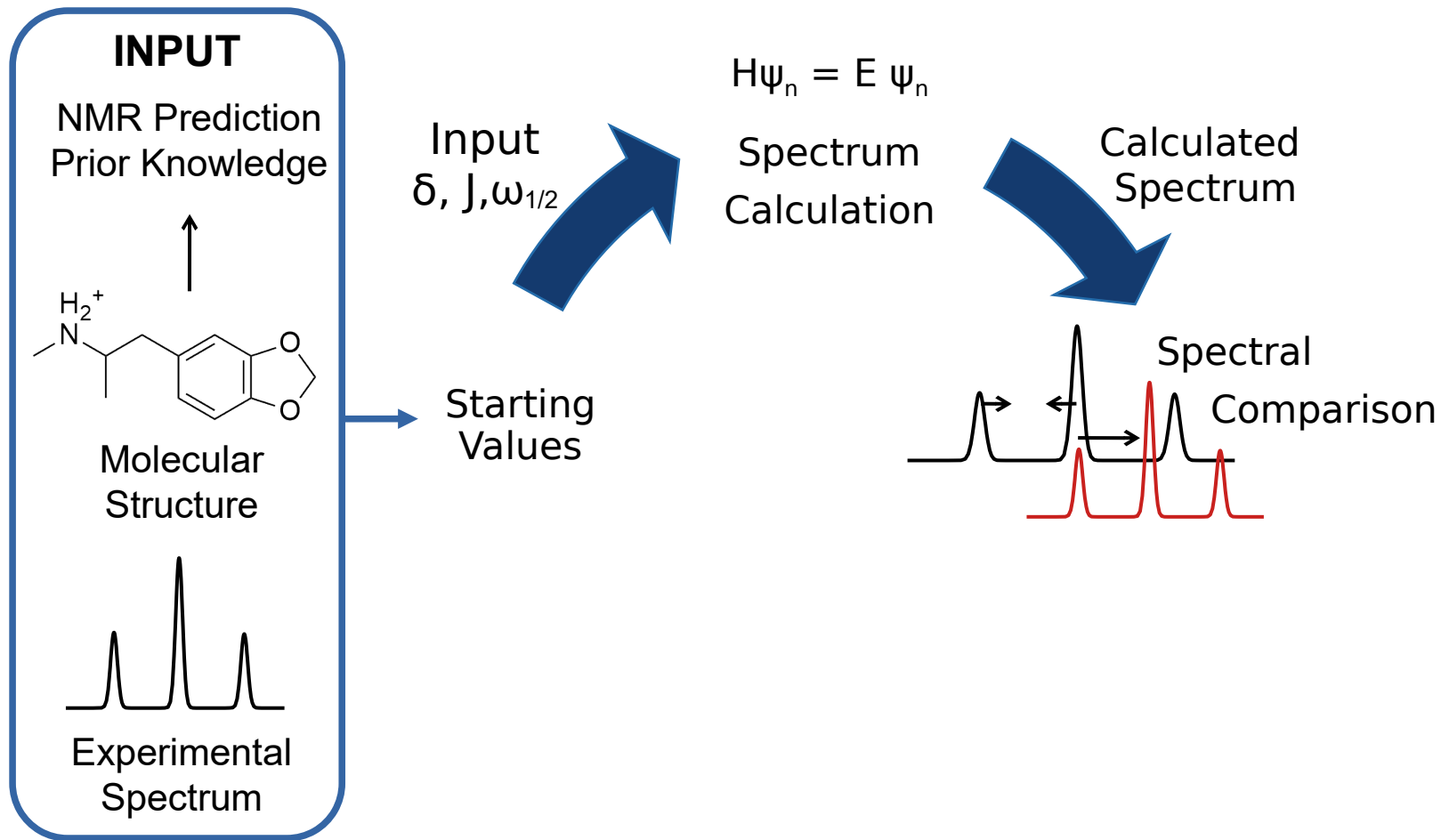
→ Determination of these parameters (and thus of profiles) via **Quantum mechanical spectral analysis**

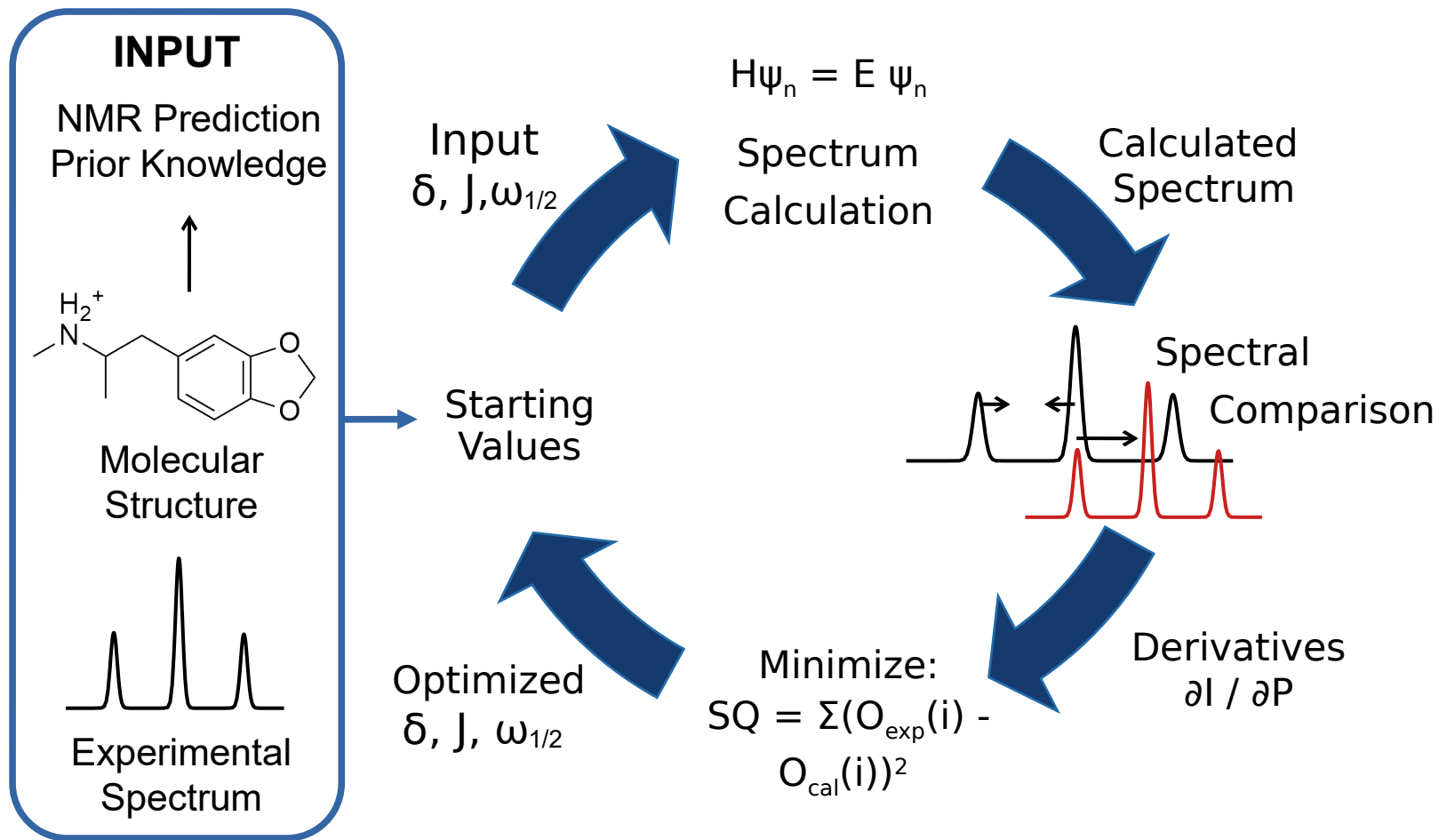
→ **Iterative process:**

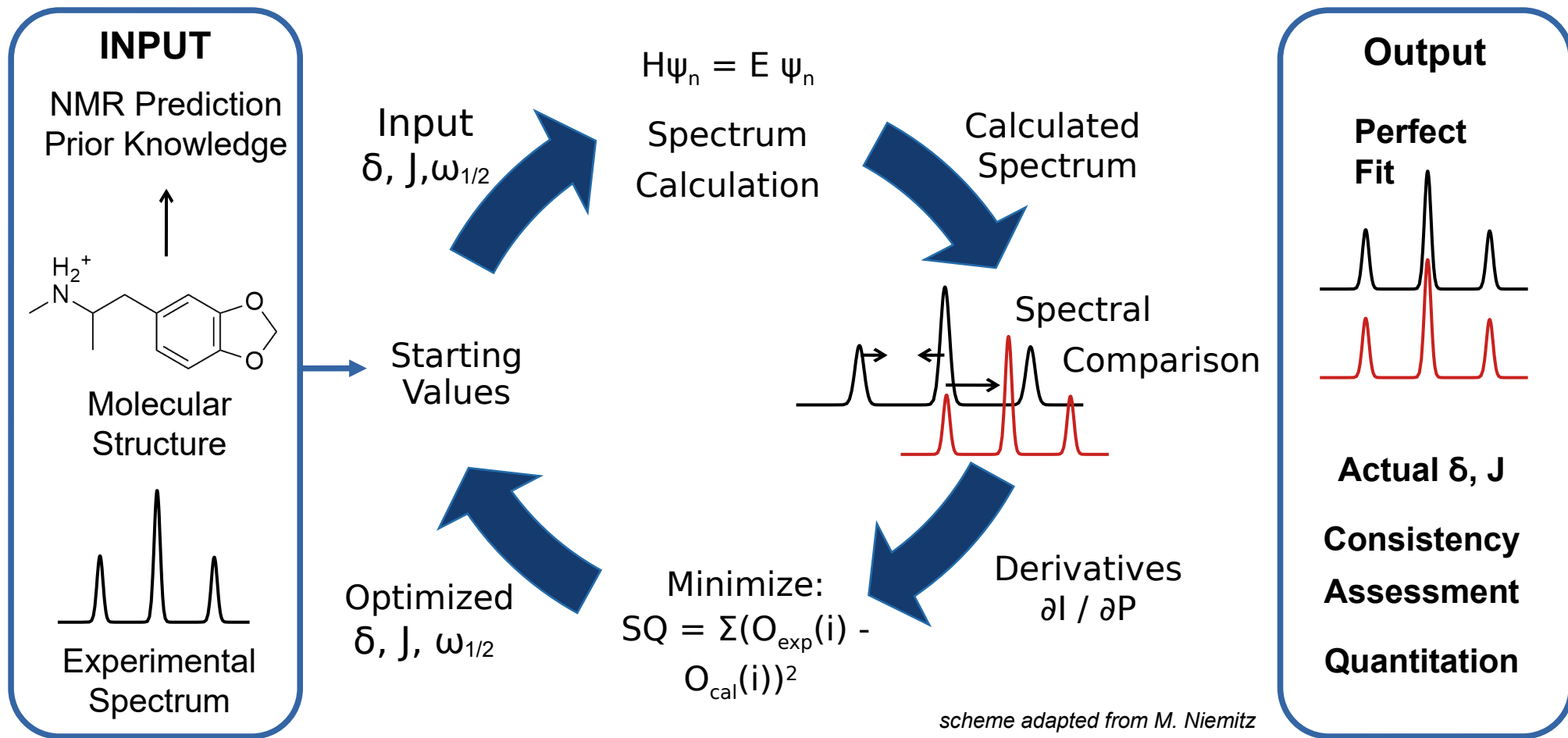
¹H iterative functional Spin Analysis (HifSA)











Cosmic Truth - <https://ct.nmrsolutions.io/> (Sign up)

Web browser based software to perform HifSA, build profiles and evaluate NMR data!

Cosmic Truth - <https://ct.nmrsolutions.io/> (Sign up)

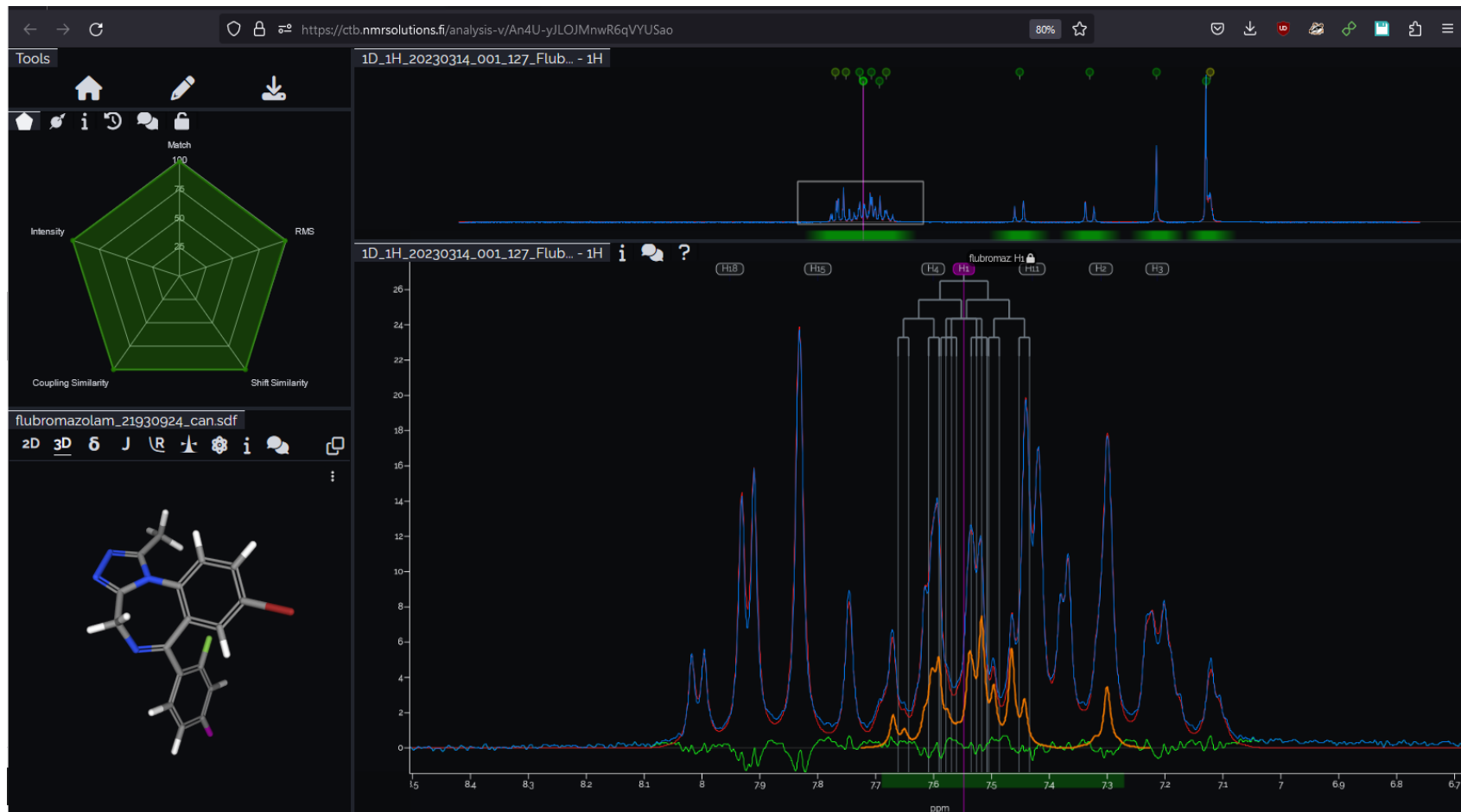
Web browser based software to perform HifSA, build profiles and evaluate NMR data!

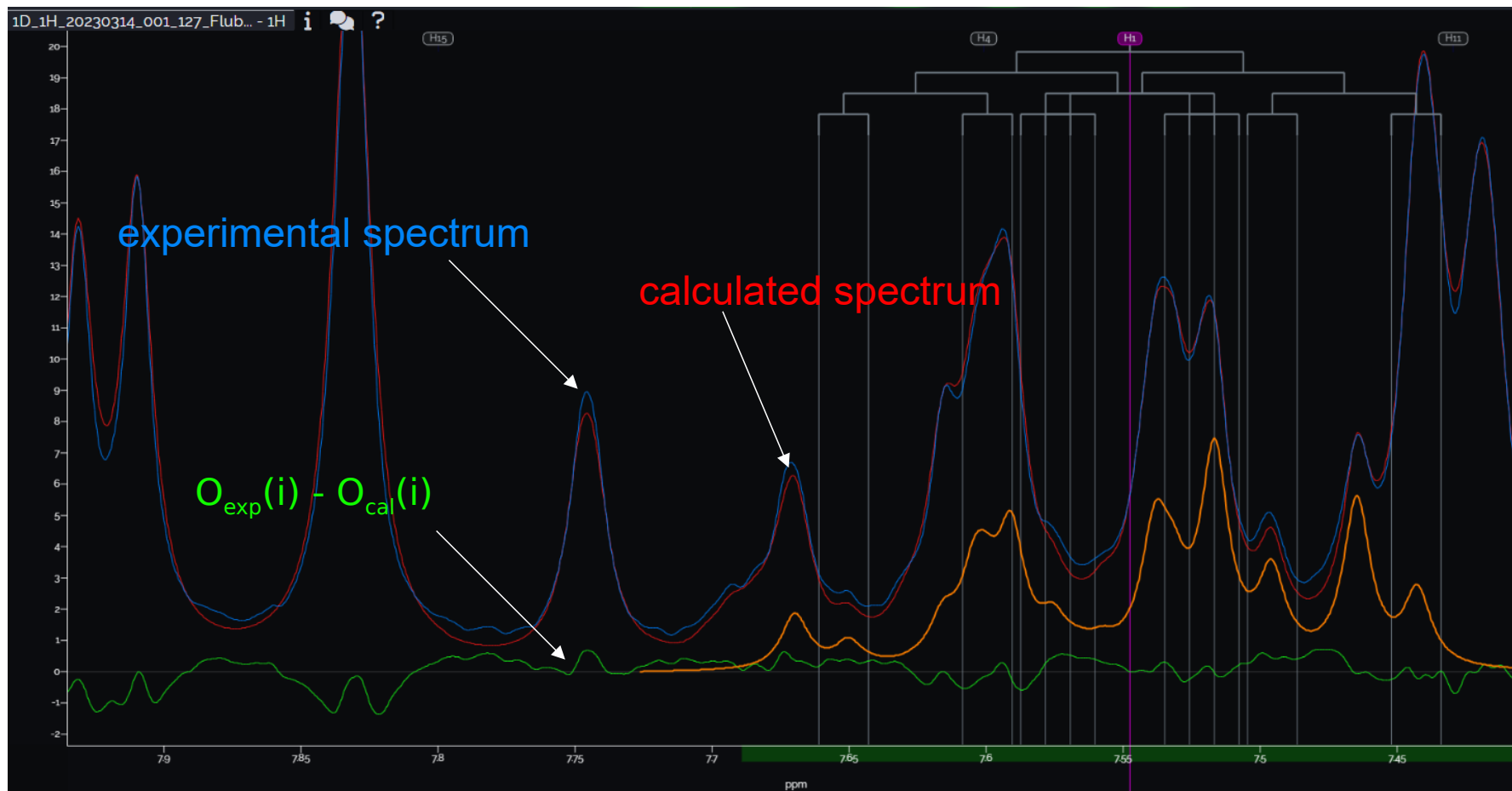
Profile database building:

- Profiles for simple molecules built from 100 MHz data in automation with CT
- More complex molecules require high field ^1H NMR spectra (>400 MHz)
- → high field profiles converted into low field profiles via CT
- Profiles saved in CT and imported into Mnova Database

Introduction – Benchtop NMR – QMSA/HifSA – Cosmic Truth – Workflow and Conclusions

Tryptamines		Phenethylamines / Cathinones		Arylcyclohexylamines		Diverse	
400 MHz data		400 MHz data		400 MHz data		400 MHz data	
5-MeO-DALT	-	2-MMC	✓	MXPr	✓	Ibogaine	✓
5-MeO-DMT	-	3-CMC	-	DCK	✓	NEP HCl	✓
4-HO-MiPT	✓	2C-B-FLY	-	MXiPr	✓	5-MAPB	✓
4-AcO-DET	-	bk-2C-B	-	2-FDCK	✓	6-APB	✓
4-HO-MPT	✓	3-FEA	✓	DMXE	✓	5-MMPA	✓
5-MeO-DiPT	-	2-FMA	✓	A-PHiP	✓	3-FPM	✓
5-MeO-MiPT	-	3-FMA	✓	3F-PCP	✓	Eutylone	✓
5-Br-DMT	-	2-FEA	✓	FXE	✓	1,4-DMAA	-
5-Cl-DMT	-	Methallylescaline	-	5-FDCK	✓	Isopropylphenidate	✓
AMT	✓	BOH-2C-B	-	3-MeO-PCP	✓	Phenibut	✓
4-AcO-DMT	-	PEA	✓			Flubromazolam	✓
4-HO-DPT	✓	3-FMC	✓	Synthetic Cannabinoids		Troparil	✓
MET	✓	2C-C	-			4F-MPH	✓
DPT	✓	2C-D	-	THJ-2201	✓	4C-MAR	✓
EPT	✓	2C-E	-	JWH-210	✓	Levamisol	✓
4-AcO-MET	✓	3-MMC	-	5-Br-ADB-INACA	✓	4-CEC	✓
4-HO-MET	✓	3-FEA	✓				
4-HO-EPT	✓	3-MMA	✓	7-ADD	✓	d1 40s, aq 4.4s, Pulse 90°, sw 20 ppm Points 8896 --> zf to 64k = dr 0.02 ns 32 scans Gain 25 (1/3 of max) T 306K	
4-HO-DET	✓			ADB-BUTINACA	✓		
4-HO-DET	✓						
4-AcO-EPT	✓						





ctb.nmr solutions.fi/data

🏠🔍🌟🔧📄👤⋮

🏠🔍🌟🔧📄👤⋮

📊

Data Manager & Import

OwnSharedAll

tgLF

TypeNameSolventModified

👁️✎️➡️⋮

1D_1H_20230314_001_127_Flubromazolam_26.4DMSO-d64 days ago

Remarks:
Tags: BenzodiazepinesX LF ProfileX Add...
Source:
Created: 03/14/2023 Modified: Last Tuesday at 11:48 PM

👁️✎️➡️⋮

1D_1H_20221130_006_#046_4-HO-MIPT-FumarDMSO-d65 days ago

Remarks:
Tags: LF ProfileX TryptamineX Add...
Source:
Created: 03/13/2023 Modified: Last Monday at 3:09 PM

👁️✎️➡️⋮

1D_1H_20230314_002_021_5-MeO-DALT_22.7mgDMSO-d68 days ago

Remarks: - IS: Maleic Acid --> influence on shifts. Extra Profile.
Tags: LF ProfileX QUANTX Add...
Source:
Created: 03/16/2023 Modified: 03/17/2023

👁️✎️➡️⋮

1D_1H_20221130_014_#115_5-Cl-DMT_0.1565MDMSO-d69 days ago

Remarks: manually Phased
Tags: LF ProfileX TryptamineX Add...
Source:
Created: 03/16/2023 Modified: 03/16/2023

👁️✎️➡️⋮

1D_1H_20230306_000_050_3-FEA-HCL_28.19mgDMSO-d69 days ago

Remarks:
Tags: LF ProfileX PhenethylamineX Add...
Source:
Created: 03/16/2023 Modified: 03/16/2023

👁️✎️➡️⋮

1D_1H_20230310_003_114_5-Br-DMT_39.03mgDMSO-d612 days ago

Remarks:
Tags: LF ProfileX TryptamineX Add...
Source:

Import Data

Drag and drop your files here.

📁

📊

🧪

📁

📊

🧪

New Analysis Data

TypeNameSolventModified

👁️✎️✕⋮

1D_1H_20230321_000_#021_5-MeO-DALT_15.1mgDMSO-d65 minutes ago

👁️✎️✕⋮

5-meo-dalt_50878551_babel.sdfDMSO-d65 minutes ago

👁️✎️✕⋮

CaffeineDMSO-d65 minutes ago

👁️✎️✕⋮

DMSO-d5DMSO-d65 minutes ago

👁️✎️✕⋮

H2ODMSO-d65 minutes ago

New Analysis

Name:1D_1H_20230321_000_#021_5-MeO-DALT_15.1mg_#120_Caffeine_12mg_21032023

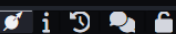
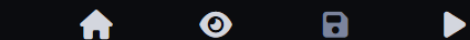
Remarks:

- Spinsystem from Annw6aYgQysveVLSz_kTPl

- Caffeine as Internal STD

⚙️📄▶️✕

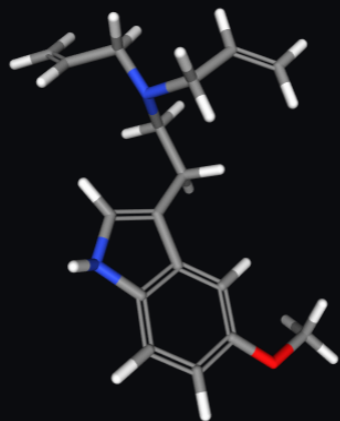
Tools



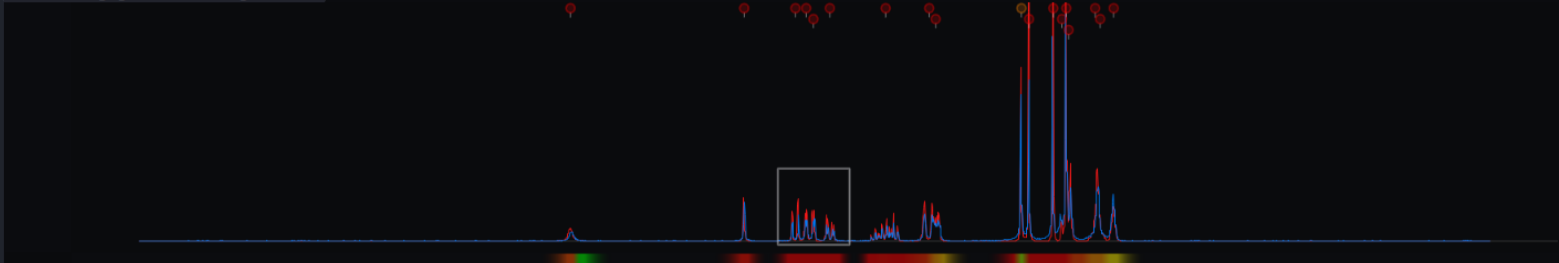
Filter...

Mode	Name	Population	WLRMS
	Caffeine	23.381	0.658
	DMSO-d ₆	43.558	0.401
	H ₂ O	4.477	0.461
	5-meo-dalt_508785_28.584		0.674

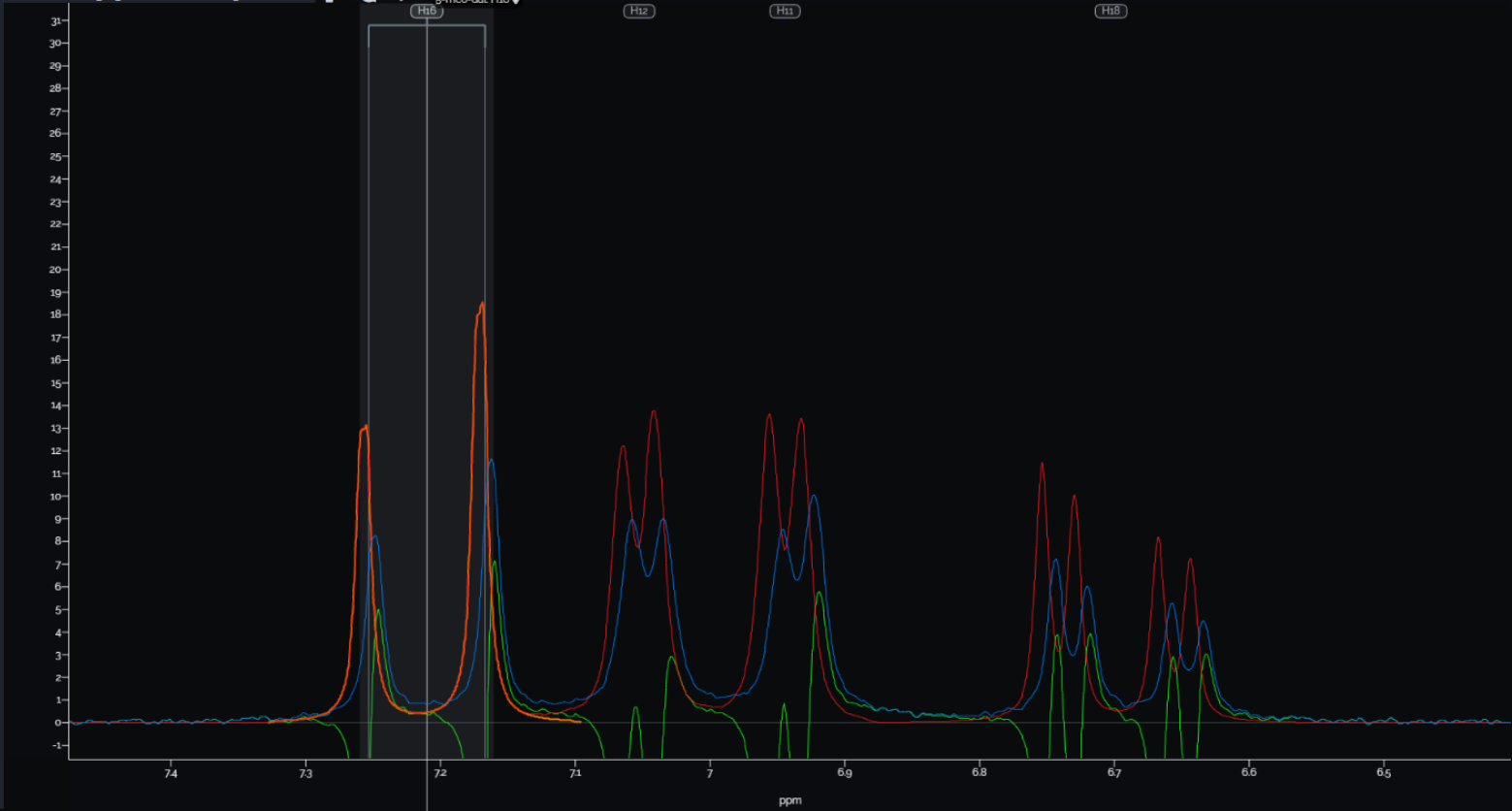
5-meo-dalt_50878551_babel.sdf



1D_1H_20230321_000_#021_5-M... - 1H



1D_1H_20230321_000_#021_5-M... - 1H



Tools

Filter...

Mode	Name	Population	WLRMS
	Caffeine	23.381	0.658
	DMSO-d5	43.558	0.401
	H2O	4.477	0.747
	5-meo-dalt_508785	28.584	0.546

Caffeine

2D 3D

INFO

Name: Caffeine

Remarks:

Source:

Created: Today at 8:20 PM

Modified: Today at 8:20 PM

Tags:

CTKey: SsfqbYHdcLUHDX2ack7L6M

Solvent: DMSO-d6

Temperature: 306.0 K

pH: 7.0

Purity: 100.000 %

Concentration: Not Defined

Weight: 12.000 mg

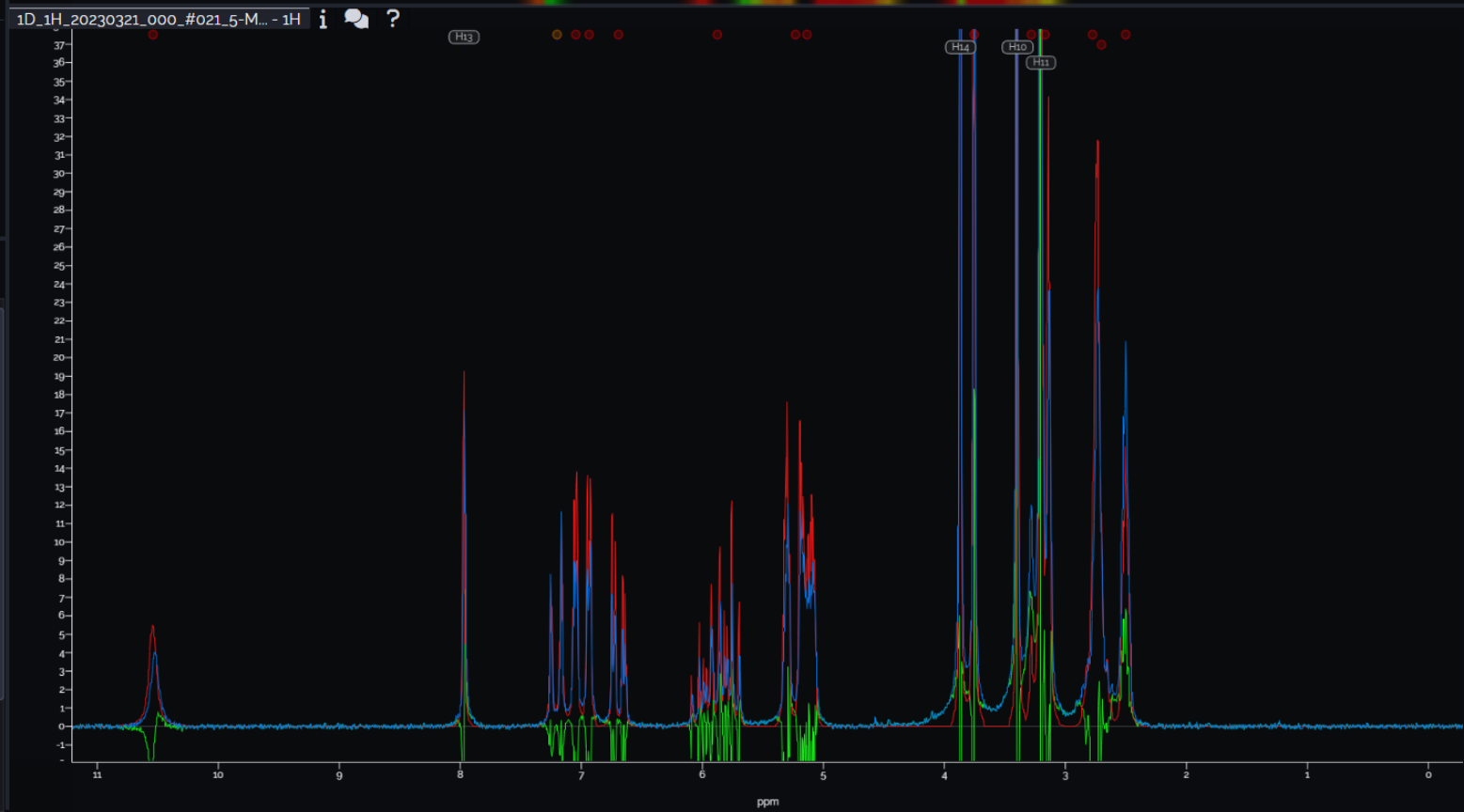
Volume: 0.600 ml

SSType: Calibrant

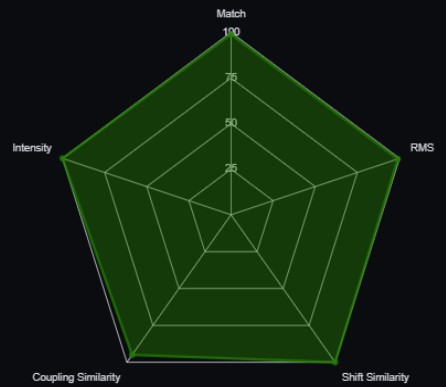
Any:

InChI key: RYYVLZVUUVJGH-UHFFFAOYSA-N

Formula: C₈H₁₀O₂N₄



Tools



5-meo-dalt_50878551_babel.sdf



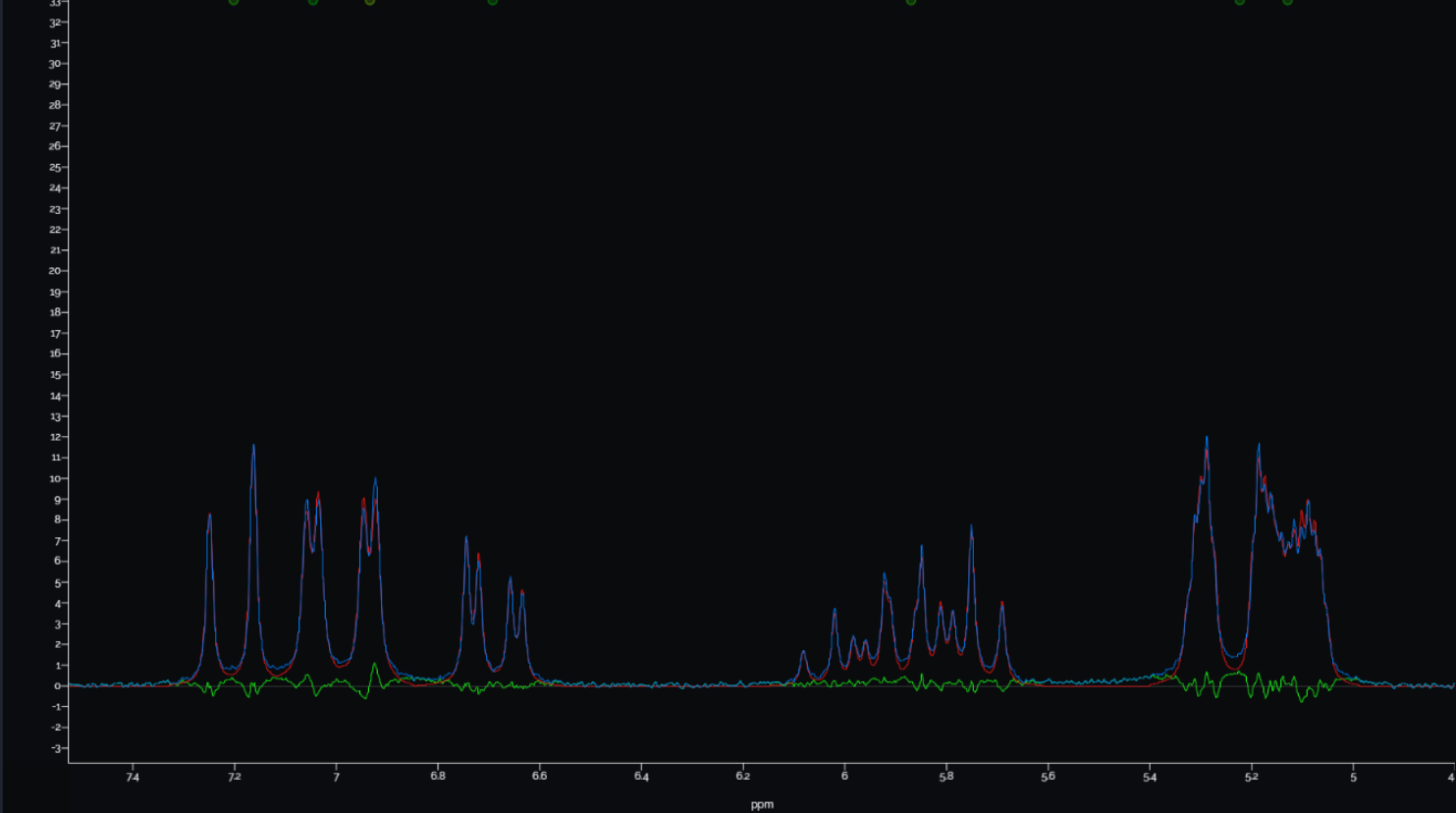
INFO

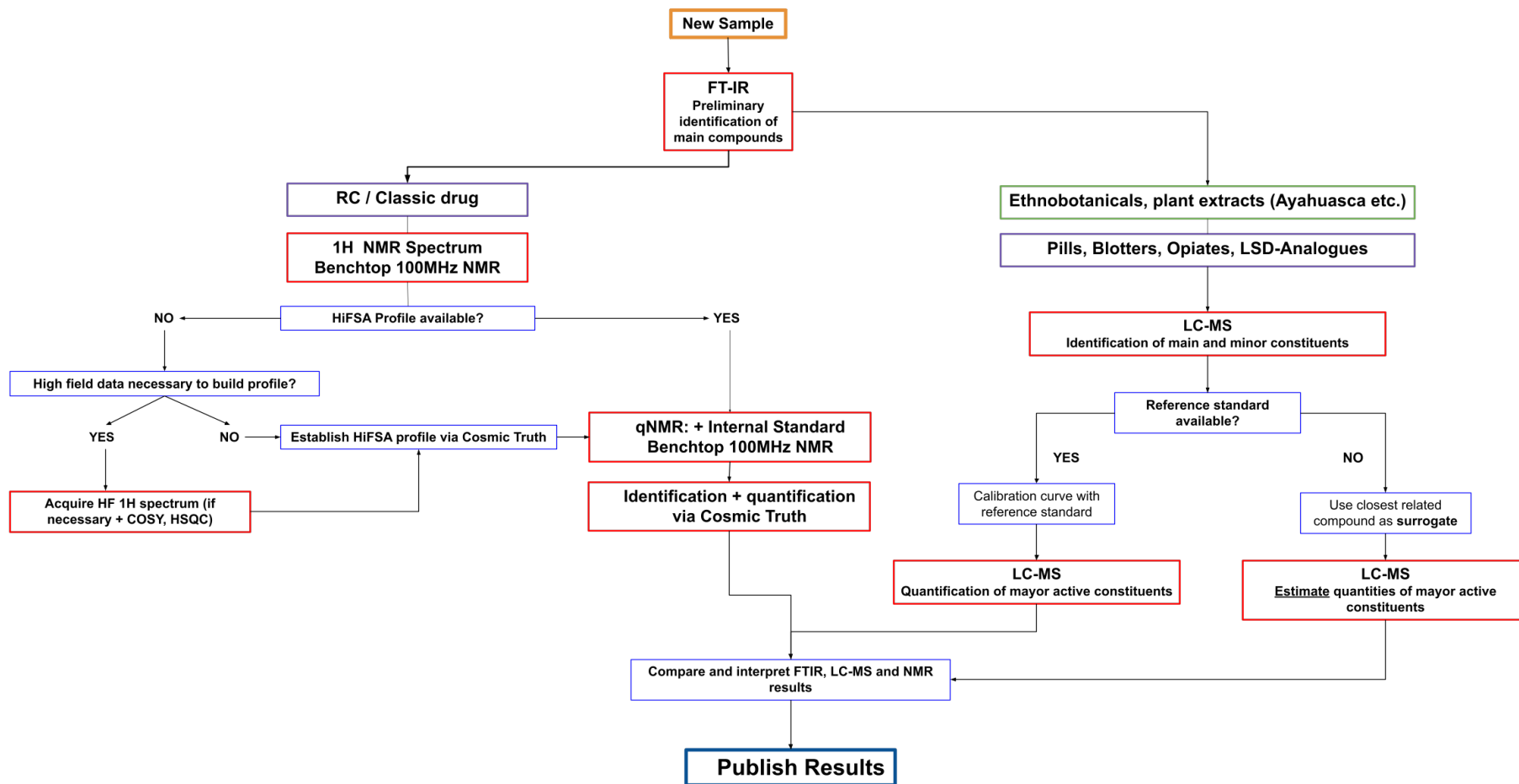
Name: 5-meo-dalt_50878551_babel.sdf
 Remarks:
 Source:
 Created: Today at 1:39 PM
 Modified: Today at 1:43 PM
 Tags:
 CtKey: SsX6lxoKgsIXHnNczTzIA
 Solvent: DMSO-d6
 Temperature: 306.0 K
 pH: 7.0
 Purity: 97.913 %
 Concentration: 24.641 mg/ml
 Weight: 14.785 mg
 Volume: 0.600 ml
 SS17: Solute
 AType: Output
 InChI key: HGRHWEAUHXYNPN-UHFFFAOYSA-N
 Formula: C₁₇H₂₂ON₂
 MW: 270.370
 Ref. MW: MW
 Field strength: 2.36849

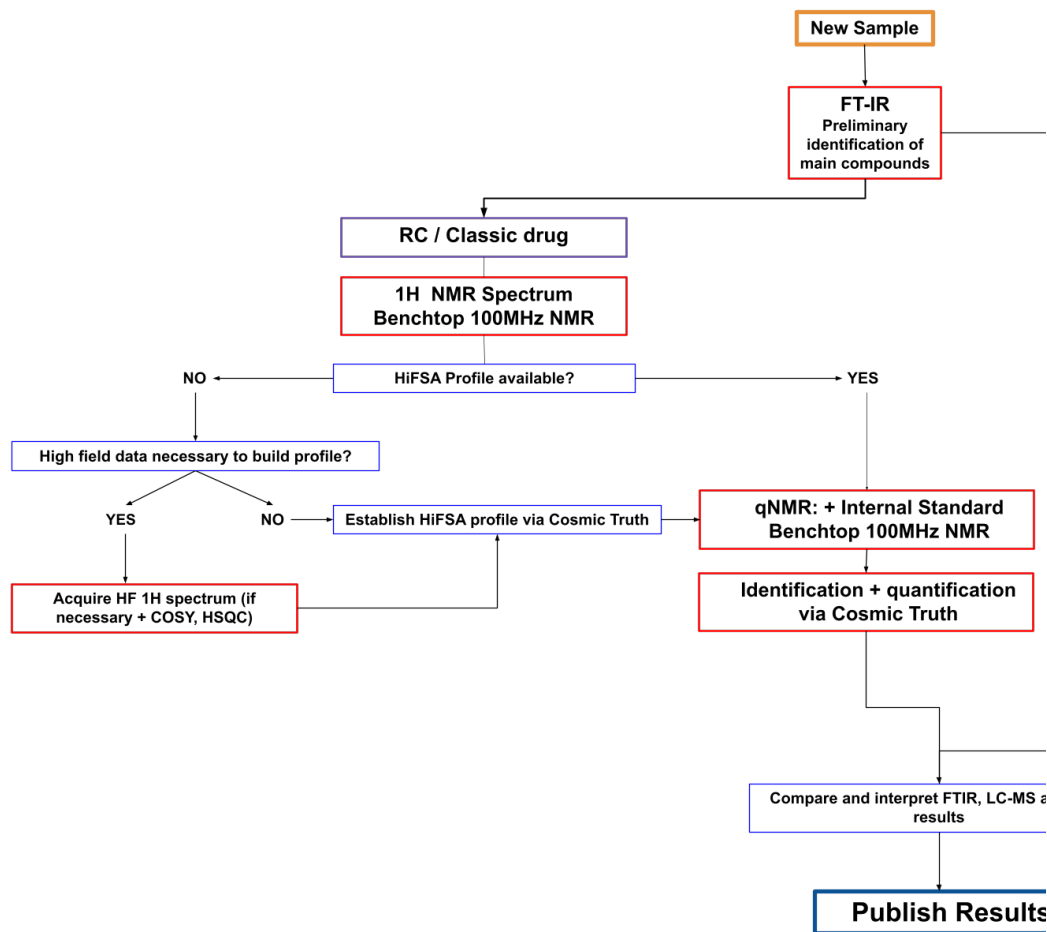
1D_1H_20230321_000_#021_5-M... - 1H



1D_1H_20230321_000_#021_5-M... - 1H







Acknowledgements

- Kykeon Analytics Team for funding, support and opportunities
- Matthias Niemietz and whole team of CT for the privileged access to their software as well as their continuous support with all our questions
- Nanalysis for their customer support
- Friends and families