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NPS Data Hub

A Web–based Community Driven Analytical Data Repository for New Psychoactive Substances

Aaron Urbas

Forensics @ NIST, Nov 8, 2018

NIST
National Institute of Standards and Technology
U.S. Department of Commerce

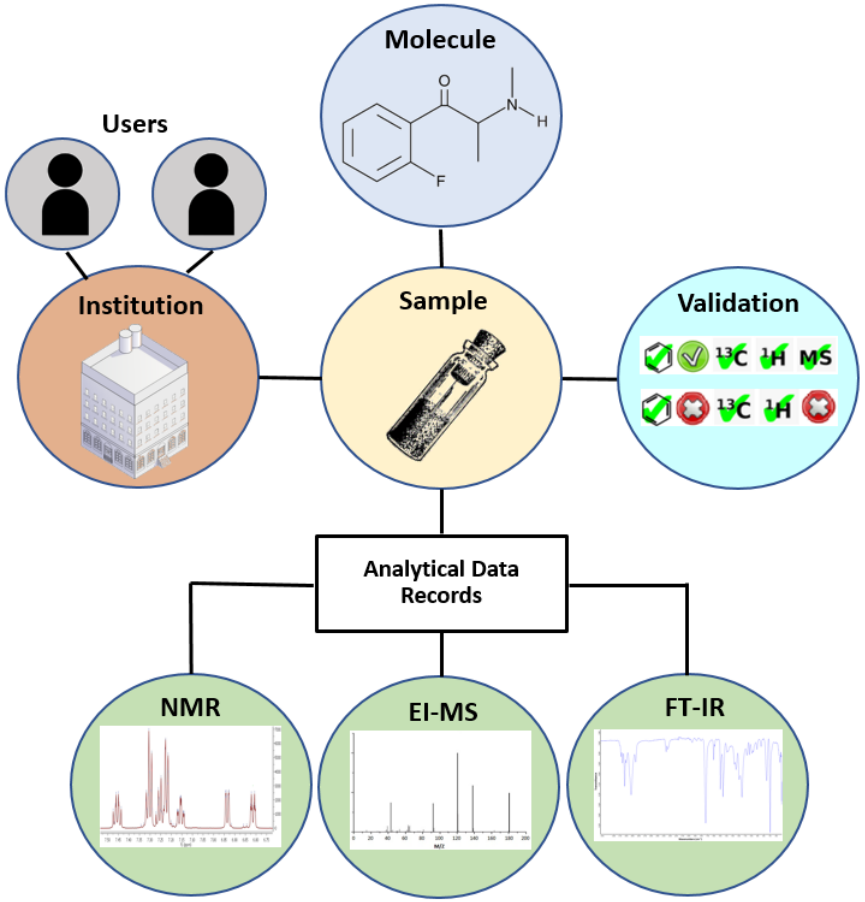
Outline

- NPS Data Hub Concept
- NPS DH Inner Workings
- Where We Are So Far with the NPS DH
- NPS Related Activities
  - NMR Spin System Analysis for Data Verification
  - Mixture Analysis with Raman Spectroscopy

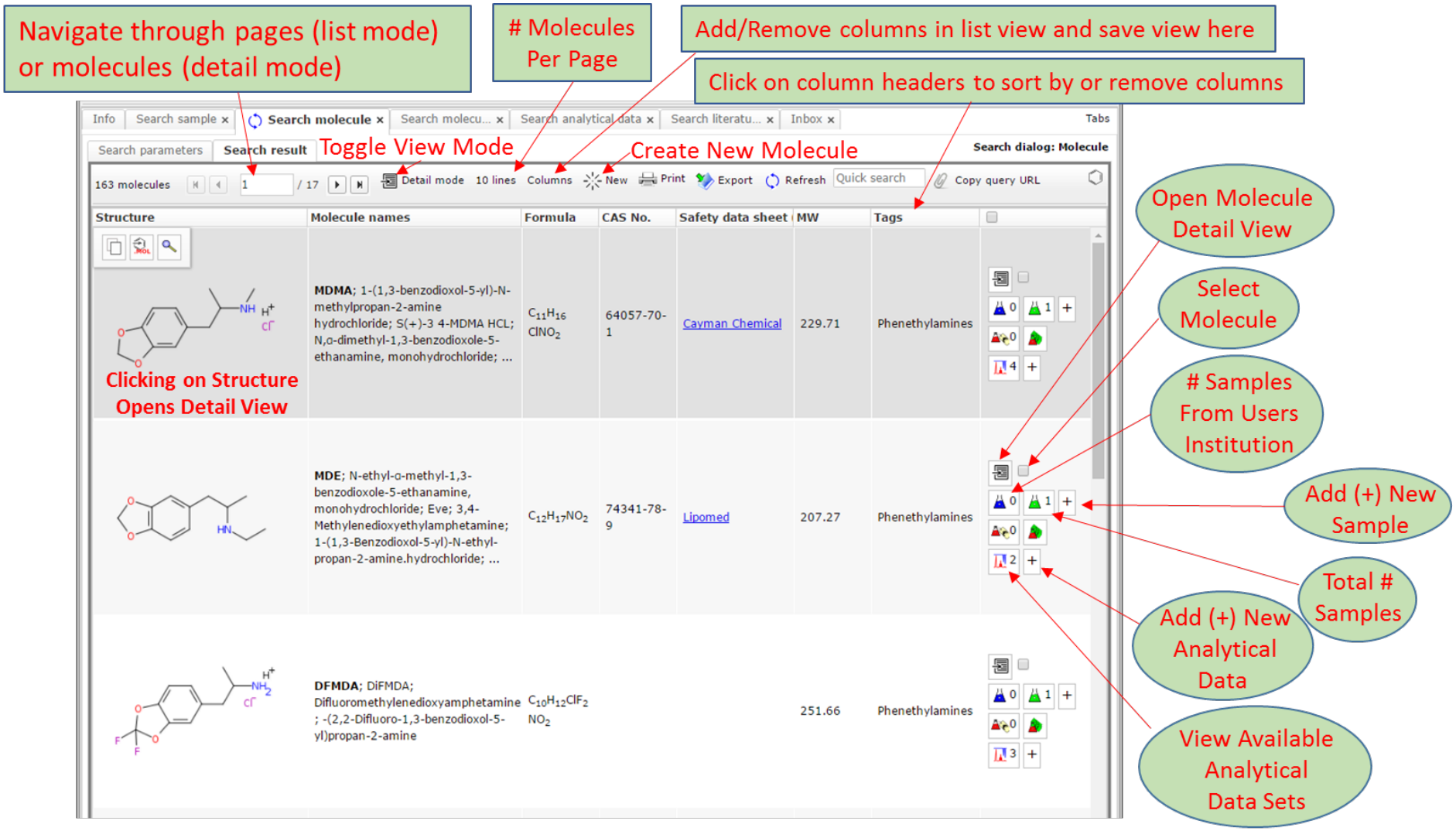
NPS Data Hub Concept

- Web-based data repository for analytical data associated with novel psychoactive substances
- Goal is to be supported and maintained by experts in the international forensic community
- Data integrity based on both peer-review and, when feasible, objective data evaluations (e.g. Structure verification/confirmation tools)
- Built on web-based ELN platform

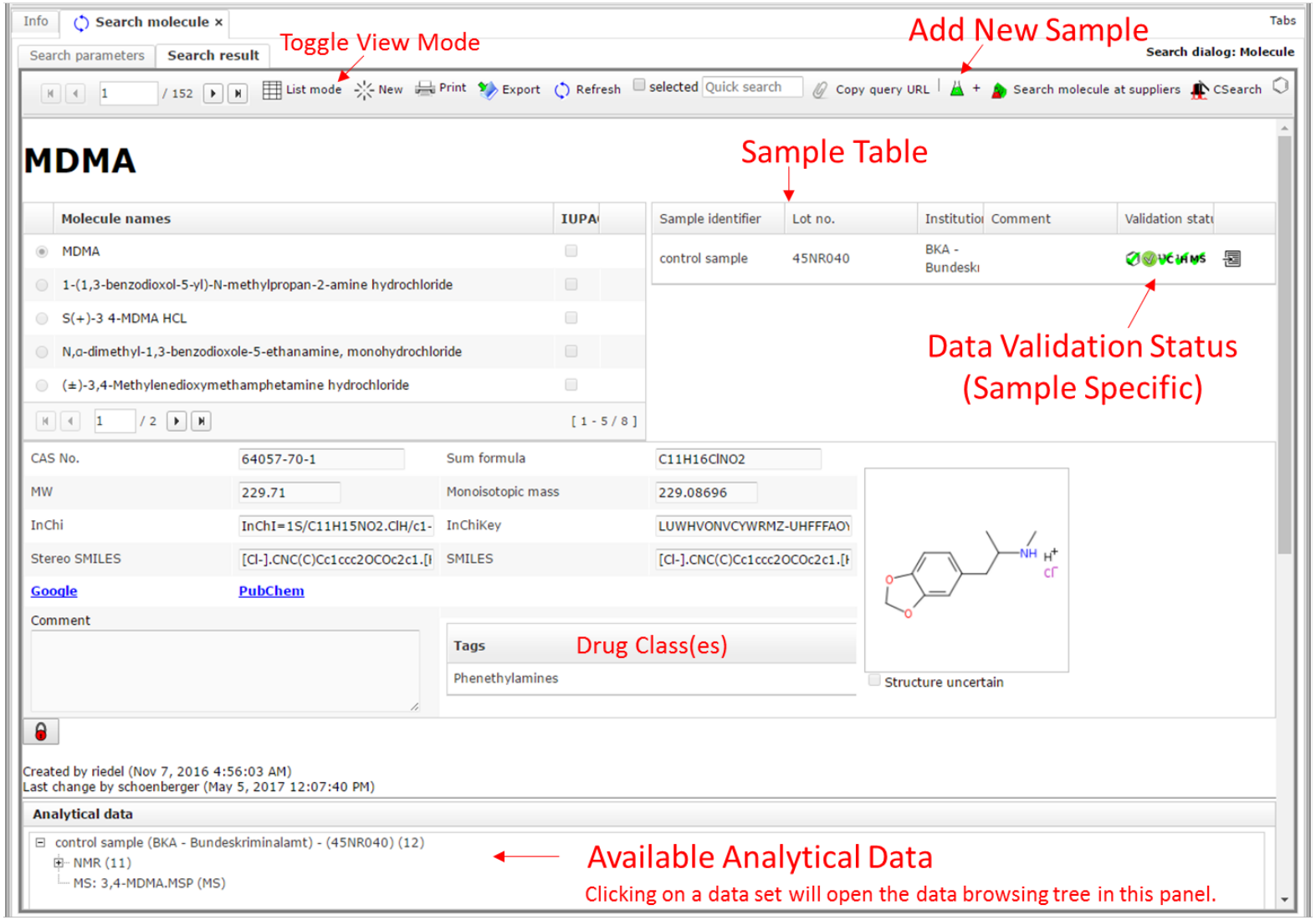
Basic Database Architecture



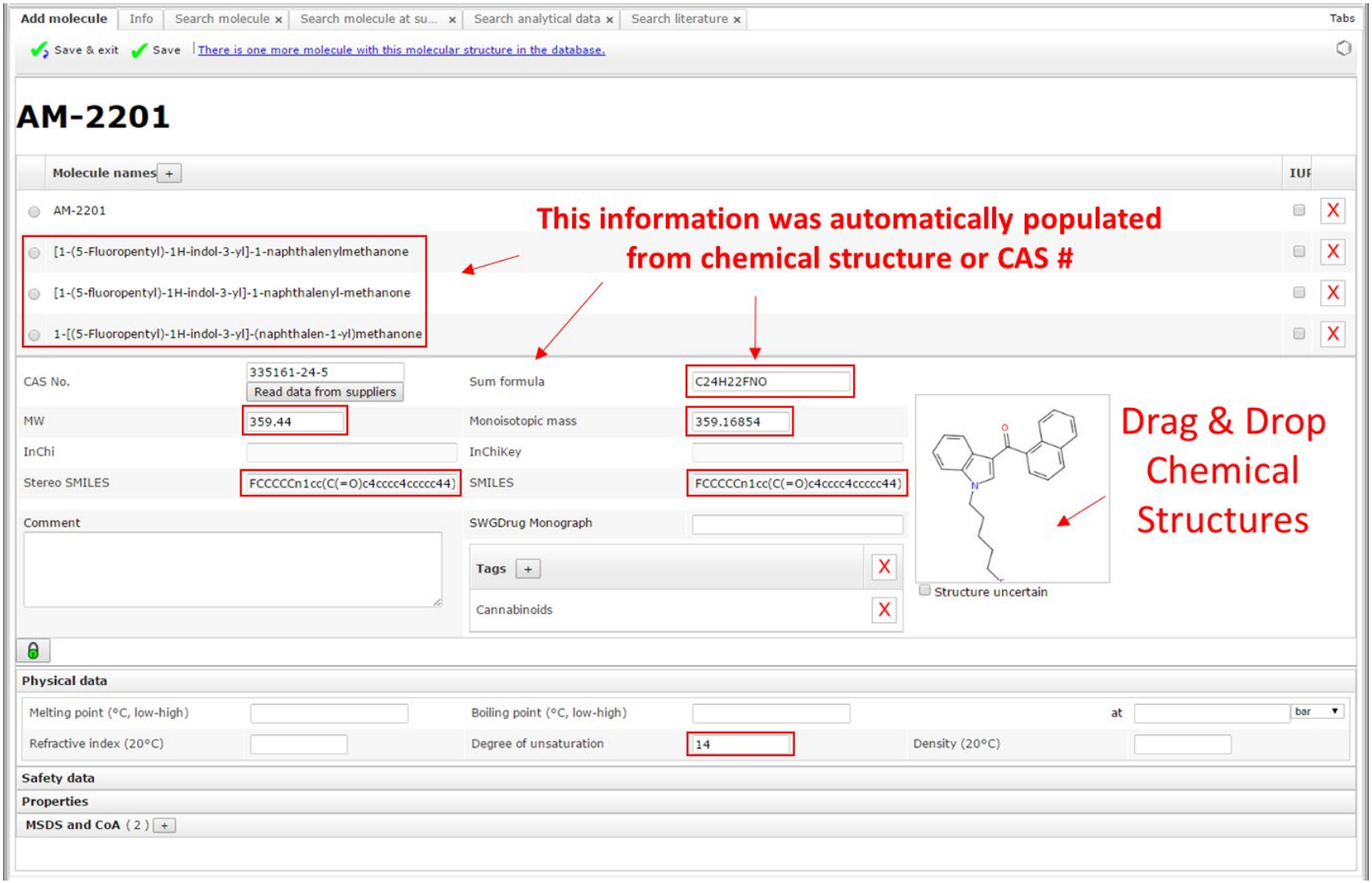
Browsing Molecules and Search Results



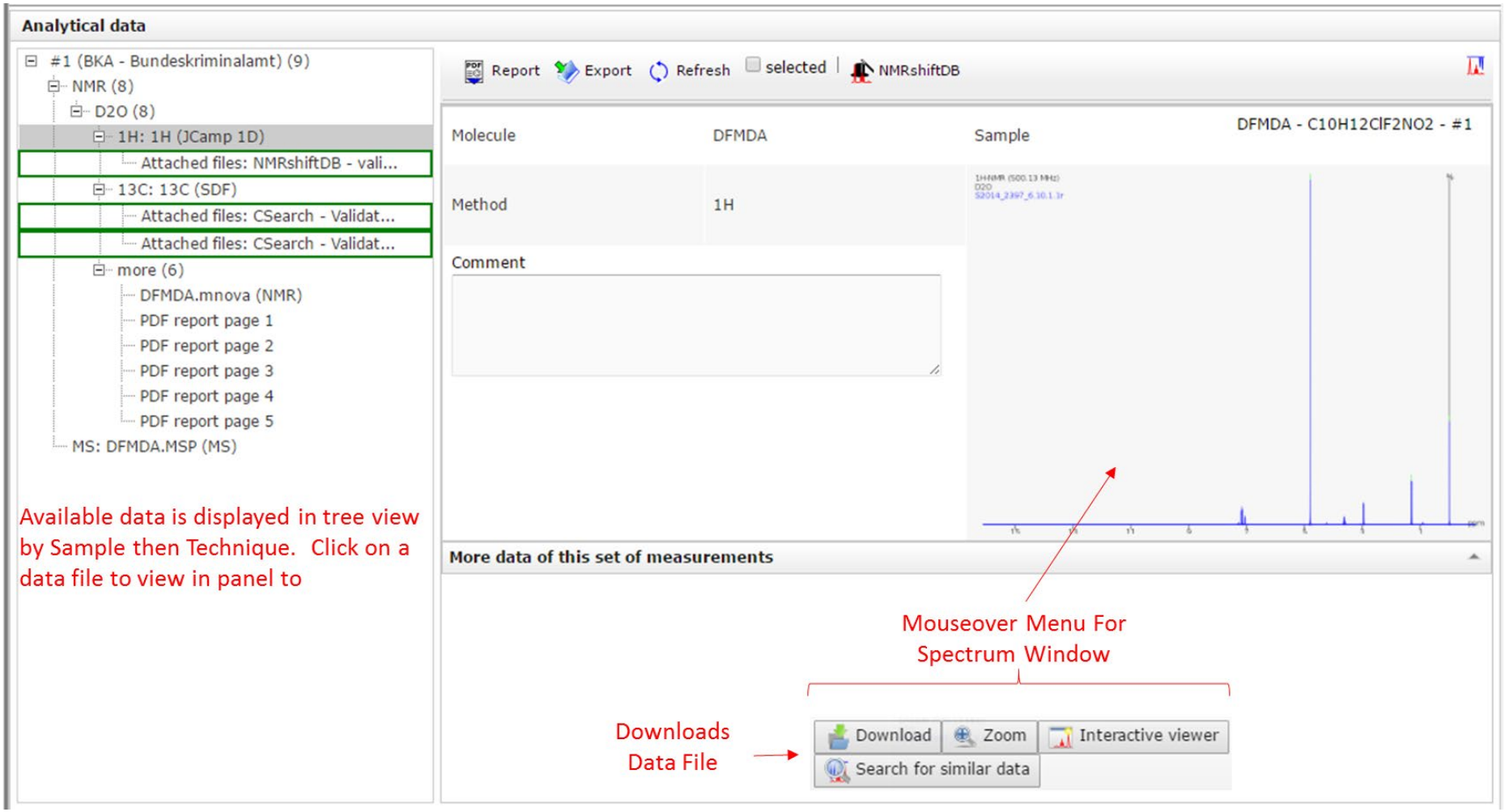
Molecule Search Result Page (Detail View)



Adding New Molecules



Analytical Data Browsing



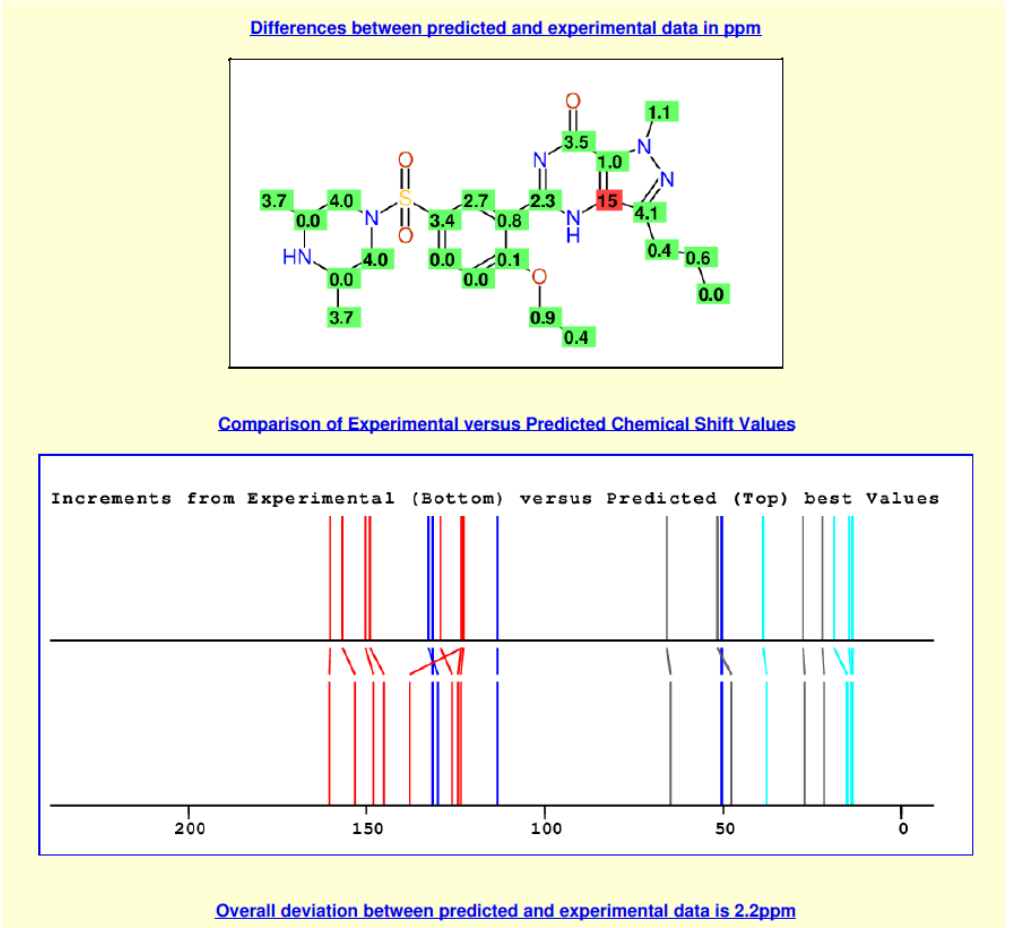
Available data is displayed in tree view by Sample then Technique. Click on a data file to view in panel to

Integration with CSEARCH

http://nmrpredict.orc.univie.ac.at/

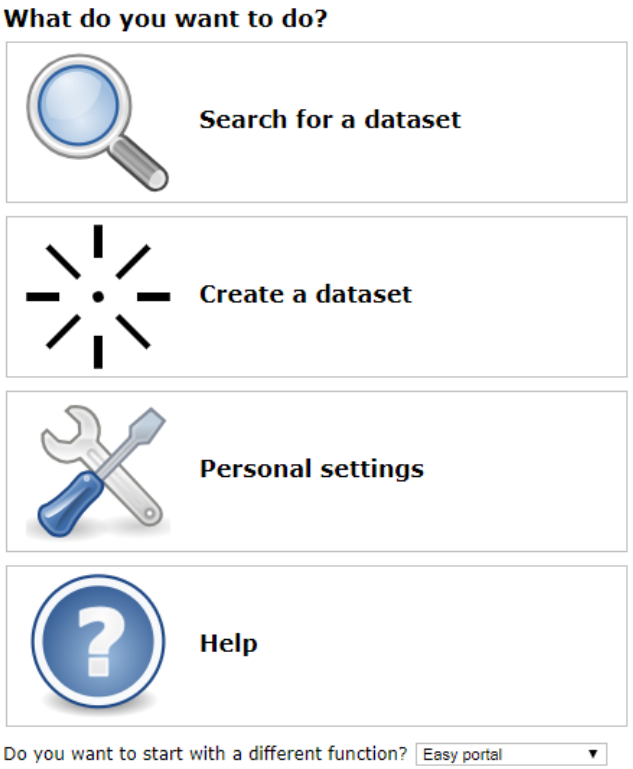
- Evaluation of proposed structure with associated ^{13}C assignments
- Based on SDF file format (chemical structure + peak assignments)
- "Robot-referee" provides a fully automated, detailed report (HTML) evaluating proposed structure and associated ^{13}C assignments.
- Report includes a qualitative valuation to accept, revise or completely reject proposed structure assignments.
- Report stored along with analytical data

Predicted/Experimental Comparison Excerpt



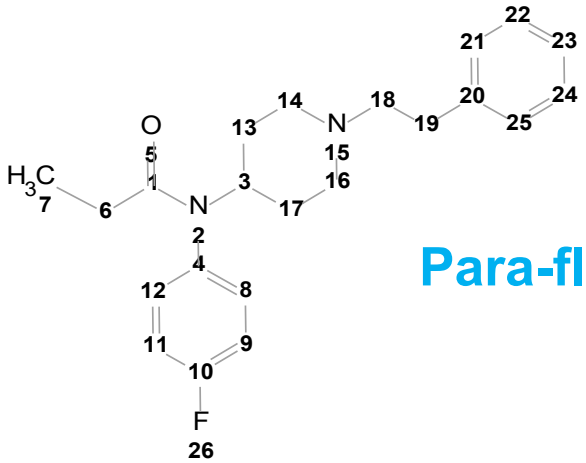
Where Are We So Far

- Approximately 400 registered users
- Database contains data related to 800+ substances
  - Varying amounts of data, some compounds with NMR, EI-MS data, some with NMR, MS, IR/Raman, some with MS peak tables only (RESPONSE)
- Compiling/collecting analytical data (NMR, Raman so far) on a number (65) of fentanyl analogs
- Currently sifting through data from >200 molecules provided by DEA STL
- Refining the interface to improve usability
- ENFSI Drug Working Group on Databases considering using Data Hub



Can We Get More From ^{1}H NMR Spectra?

- Wealth of structural information available
- Proton counts
- Chemical shift structure correlations
- Connectivity via couplings and coupling constants
- Indirect heteronuclear information through coupling, e.g. ^{19}F



Para-fluorofentanyl

Predicted Chemical Shifts & Coupling Constants

Atom	Shift (ppm)	J (Hz)	
3 CH	4.27	J(3-13')	5.78
		J(3-13'')	5.78
		J(3-17')	5.78
		J(3-17'')	5.78
6 CH2	2.082	J(6)	14.56
		J(6-7)	7.89
7 CH3	0.94	J(7-6)	7.89
		J(7)	6.99
8 CH	7.019	J(8-9)	8.43
		J(8-12)	1.5
		J(8-26)	5
9 CH	7.156	J(9-8)	8.43
		J(9-11)	1.5
		J(9-26)	8
11 CH	7.156	J(11-9)	1.5
		J(11-12)	8.43
		J(11-26)	8
12 CH	7.019	J(12-8)	1.5
		J(12-11)	8.43
		J(12-26)	5
13' CH2	1.645	J(13'-3)	5.78
		J(13'-13'')	12.29
		J(13'-14')	8.01
		J(13'-14'')	5.65
13'' CH2	2.031	J(13''-3)	5.78
		J(13''-13')	12.29
		J(13''-14')	5.65
		J(13''-14'')	8.01

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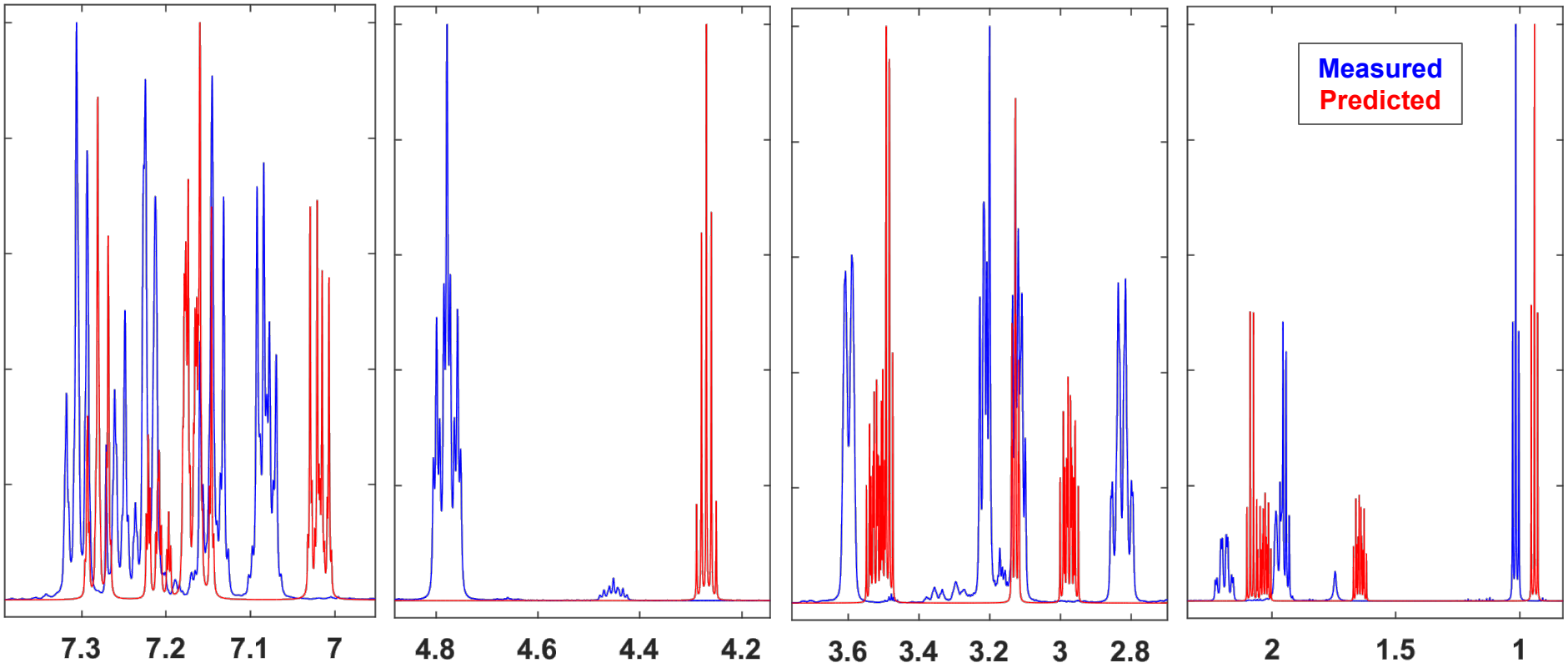
Predicted ^{1}H NMR Spectra

Measured vs Predicted Para-Fluorofentanyl H Spectra (600 MHz)



Quantum Mechanic Spectral Analysis (QMSA)

Predicted Chemical Shifts & Coupling Constants

Atom	Shift (ppm)	J (Hz)	
3 CH	4.27	J(3-13')	5.78
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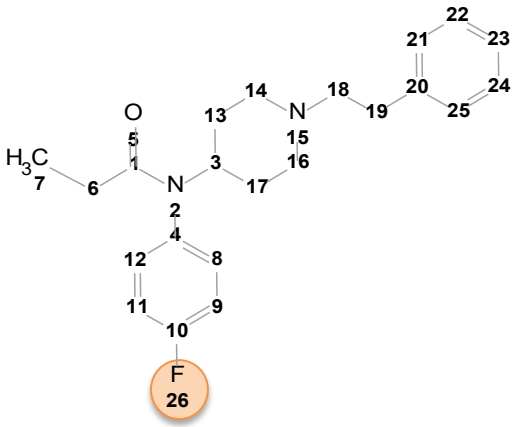
		J(9-26)	8
11 CH	7.156	J(11-9)	1.5
		J(11-12)	8.43
		J(11-26)	8
12 CH	7.019	J(12-8)	1.5
		J(12-11)	8.43
		J(12-26)	5
13' CH2	1.645	J(13'-3)	5.78
		J(13'-13'')	12.29
		J(13'-14')	8.01
		J(13'-14'')	5.65
13'' CH2	2.031	J(13''-3)	5.78
		J(13''-13')	12.29
		J(13''-14')	5.65
		J(13''-14'')	8.01

⋮

Long story short….



Para-fluorofentanyl

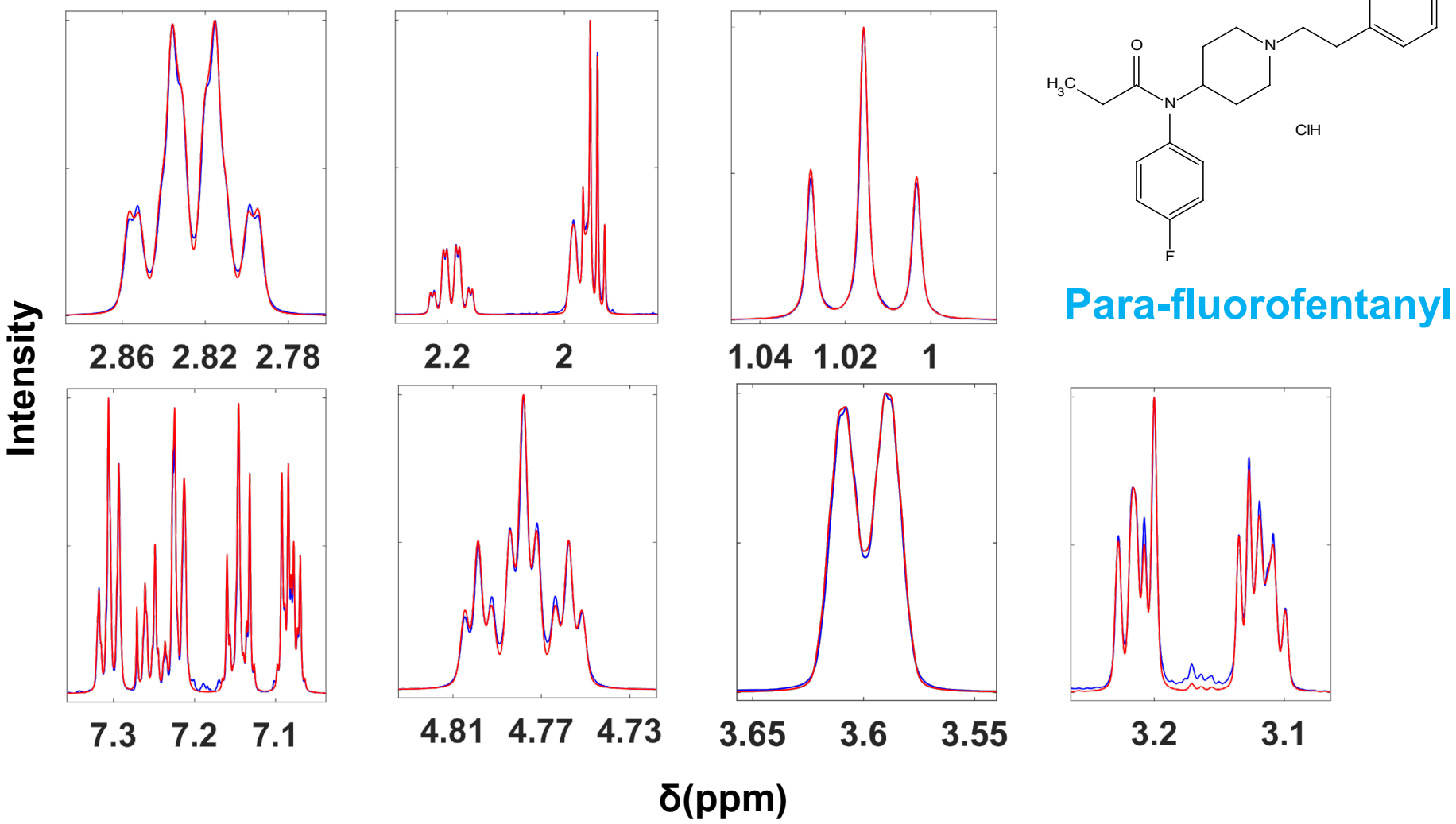
There are a total of 117 chemical shifts and couplings being fit for this molecule, the tables only represent a subset.

Fit Chemical Shifts & Coupling Constants

Atom	Shift (ppm)	J (Hz)	
3 CH	4.778	J(3-13')	12.3336
		J(3-13'')	3.6189
		J(3-17')	12.3336
		J(3-17'')	3.6189
6 CH2	1.9495	J(6)	14.56
		J(6-7)	7.4367
7 CH3	1.0157	J(7-6)	7.4367
		J(7)	6.99
8 CH	7.0817	J(8-9)	8.663
		J(8-12)	3.1175
		J(8-26)	4.7923
9 CH	7.1451	J(9-8)	8.663
		J(9-11)	2.6866
		J(9-26)	8.0205
11 CH	7.1451	J(11-9)	2.6866
		J(11-12)	8.663
		J(11-26)	8.0205
12 CH	7.0817	J(12-8)	3.1175
		J(12-11)	8.663
		J(12-26)	4.7923
13' CH2	2.1927	J(13'-3)	12.3336
		J(13'-13'')	-13.6442
		J(13'-14')	13.0136
		J(13'-14'')	4.2744
13'' CH2	1.9738	J(13''-3)	3.6189
		J(13''-13')	-13.6442
		J(13''-14')	3.1651
		J(13''-14'')	3.1276

⋮

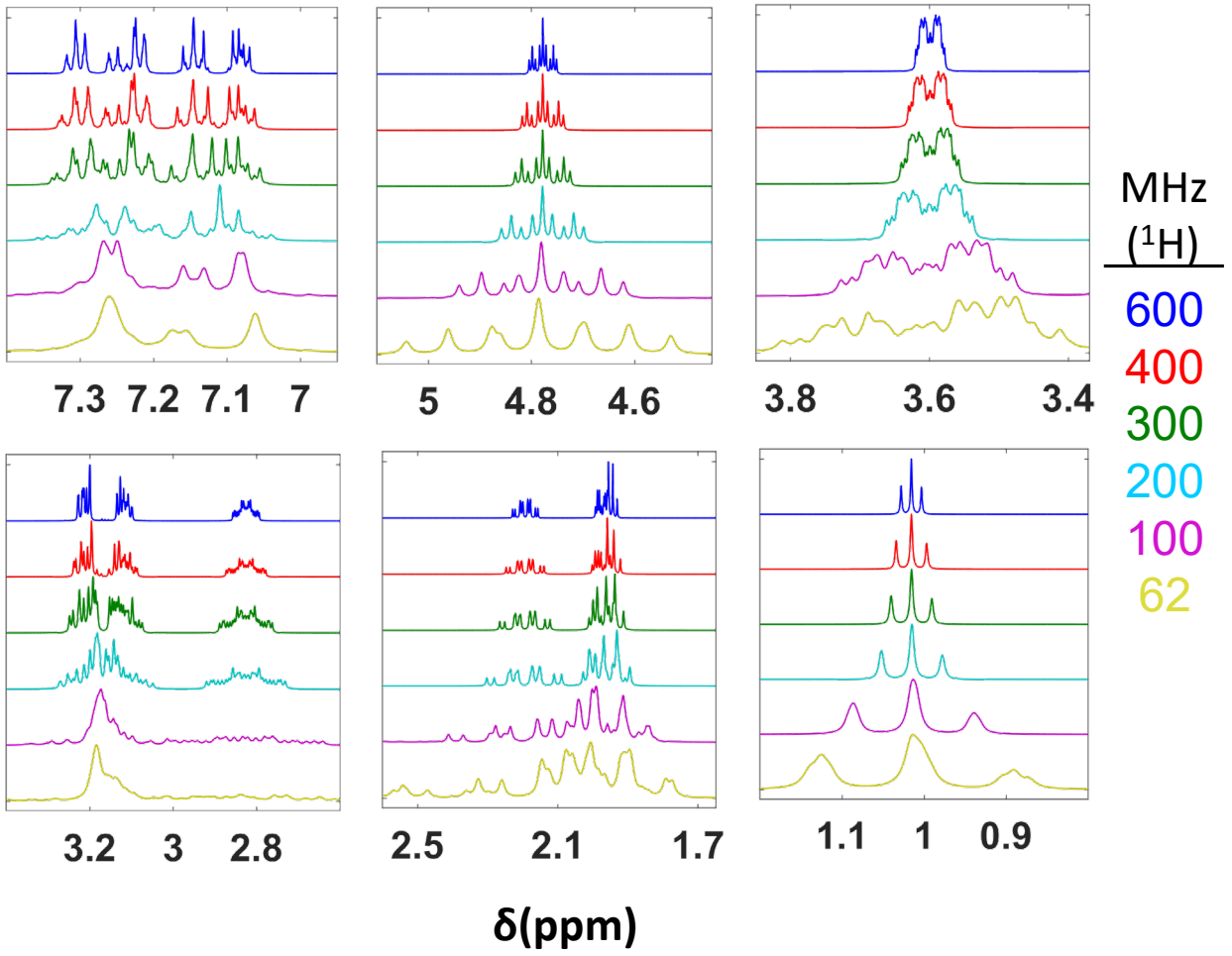
^{1}H QM Spectral Analysis @ 600 MHz



Field Translation of ^{1}H Spectra

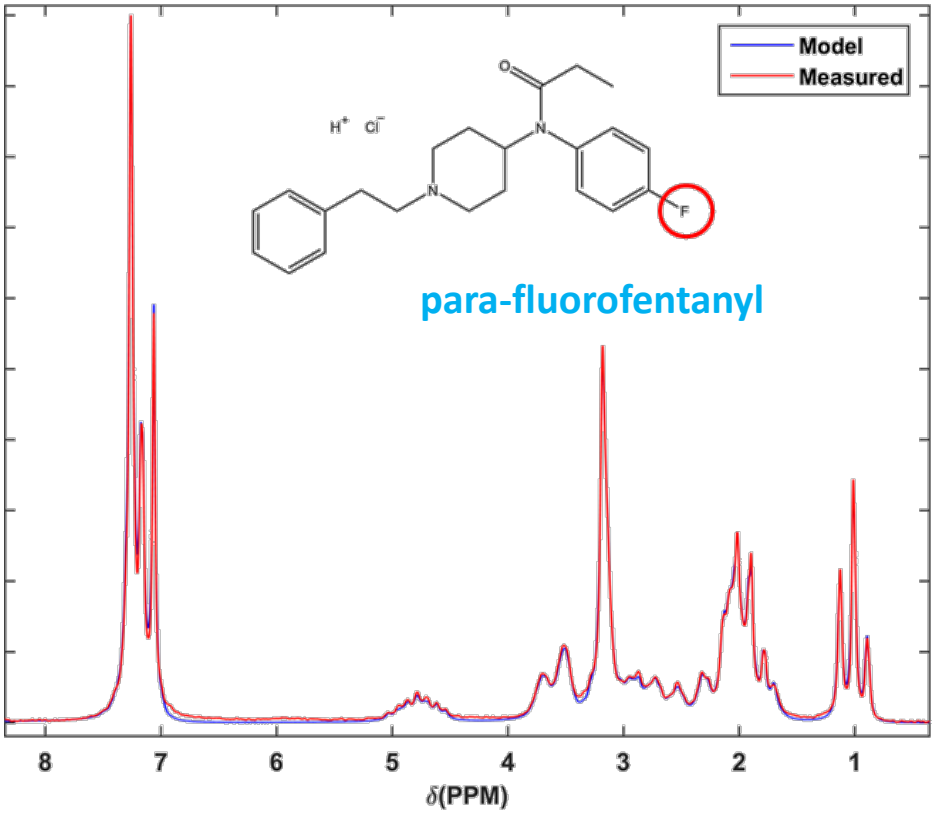
QM Model Evaluated at Various Field Strengths

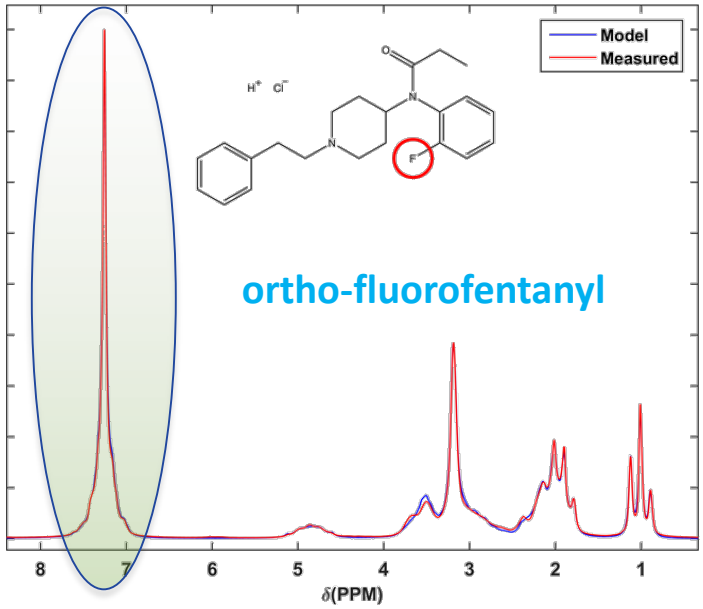
- Chemical shift (δ) is a unitless frequency ratio expressed in ppm that is independent of magnetic field strength
- Coupling constants (Hz) are field strength independent
- The End Result:
  While the chemical shift of a proton resonance remains constant in ppm, the couplings and associated splitting patterns do not
- The QM spin system analysis is field independent and thus portable to any field for reproducing the spectral information

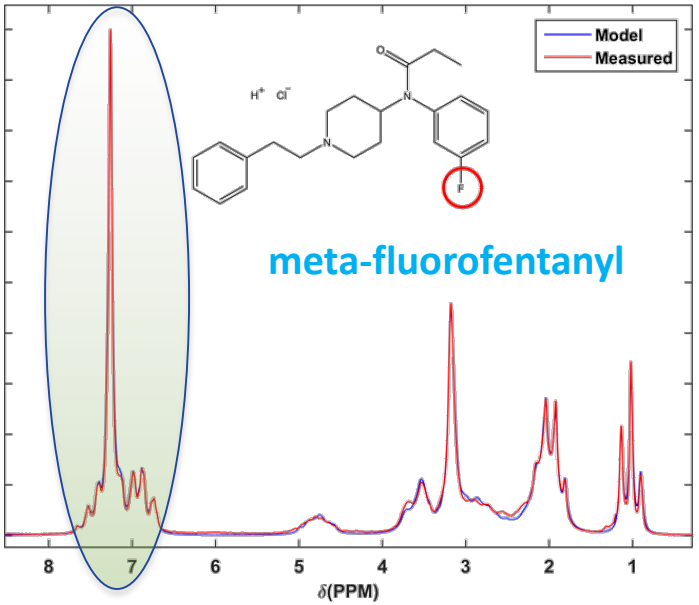


Isomer Differentiation On a Benchtop NMR

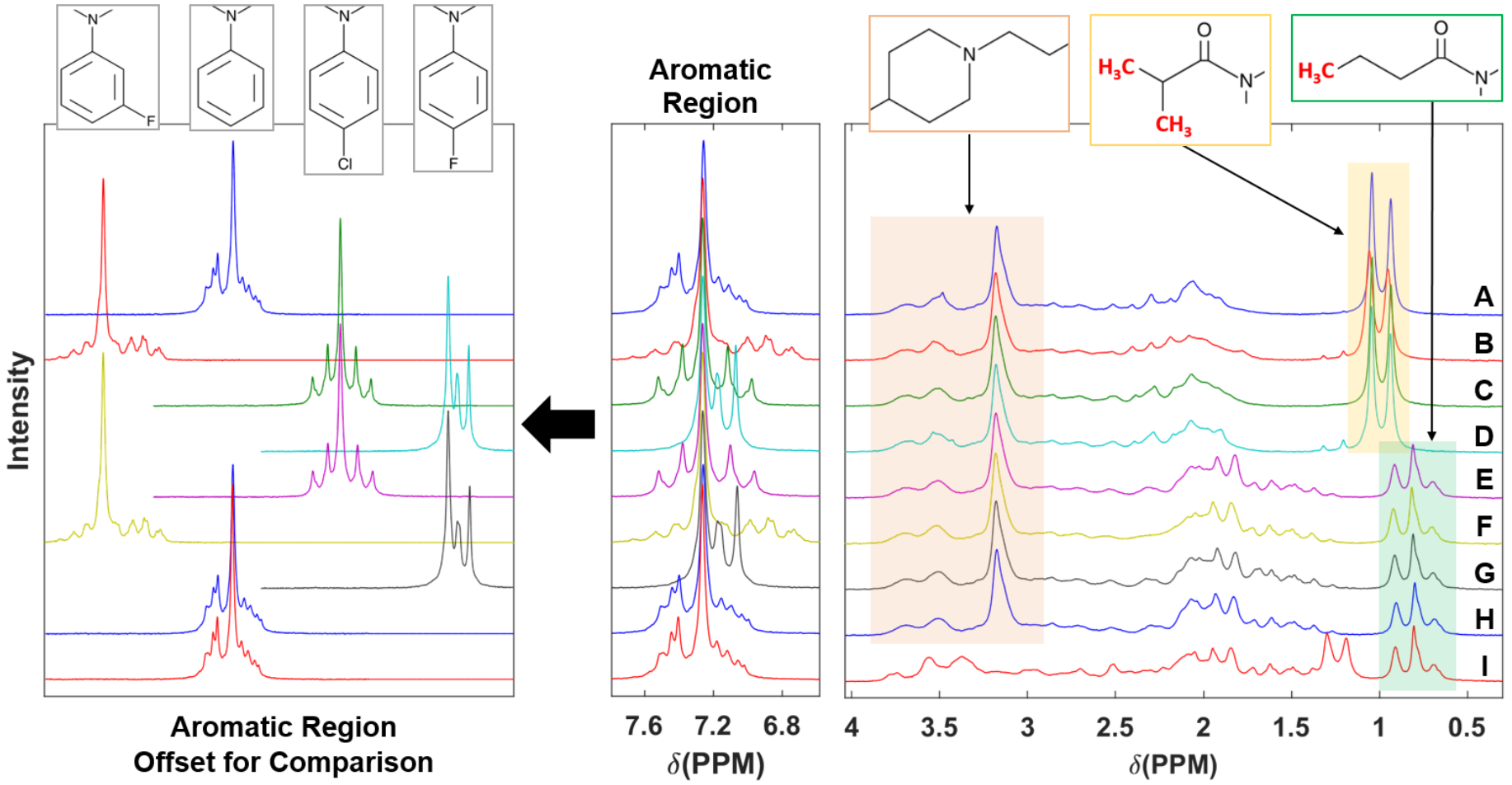
- 600 MHz QMSA ^{1}H Spectra Translated to 62 MHz
- Experimental 62 MHz ^{1}H Spectra





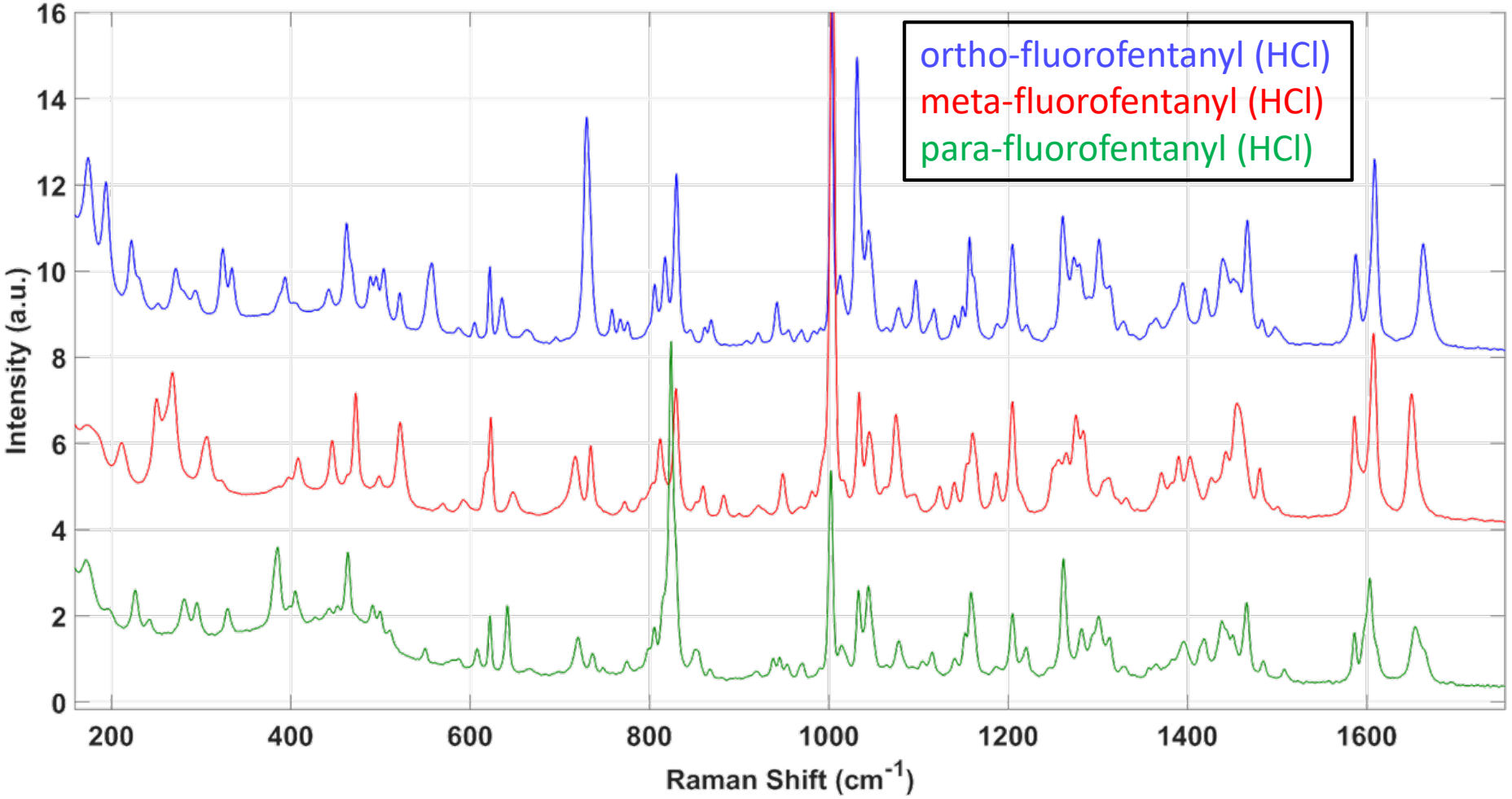


Butyrl Fentanyl Isomers (^{1}H NMR, 62 MHz)

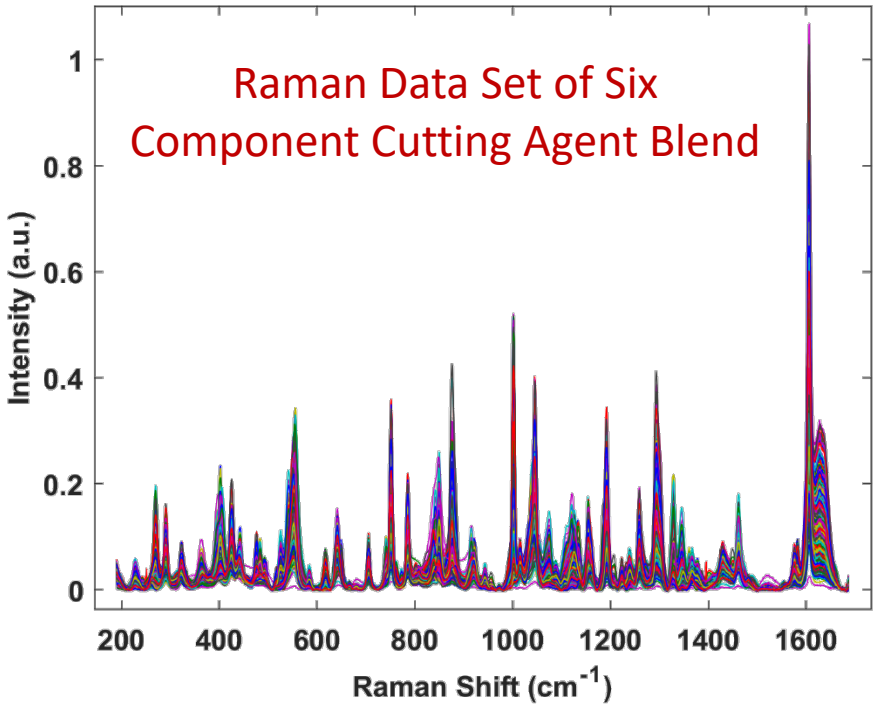


Raman Spectroscopy, Fluorofentanyl Isomers

1064 nm Raman Spectra

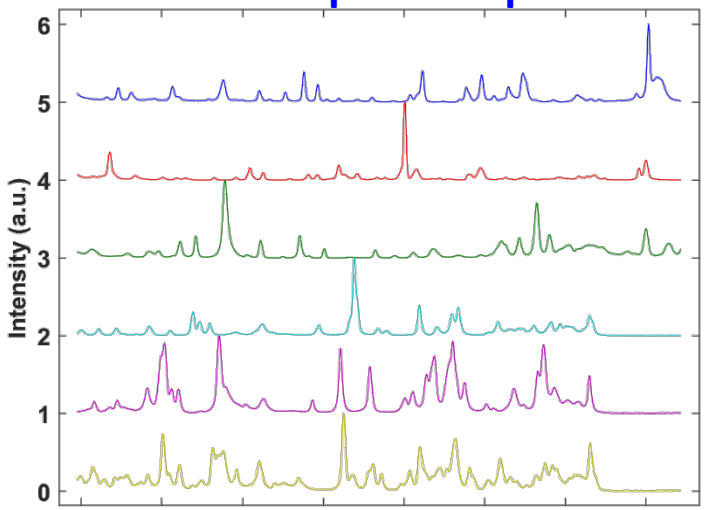


Raman Mixture Analysis

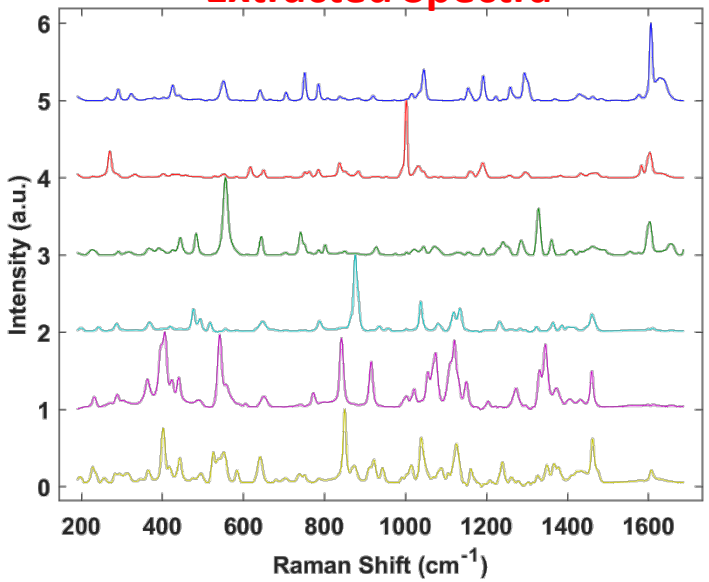


Multivariate Curve Resolution (MCR)

Pure Component Spectra



Extracted Spectra



r^2
0.948
0.928
0.931
0.959
0.963
0.937

Acknowledgements

NPS Data Hub

Torsten Schoenberger (Federal Criminal Police Office of Germany, BKA)
Charlotte Corbett (Drug Enforcement Administration, STRL)
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Raman Spectroscopy

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Thank You!