

FORENSICS @ NIST

#NISTForensics

# NPS Data Hub

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

Aaron Urbas

Forensics @ NIST, Nov 8, 2018

# Outline

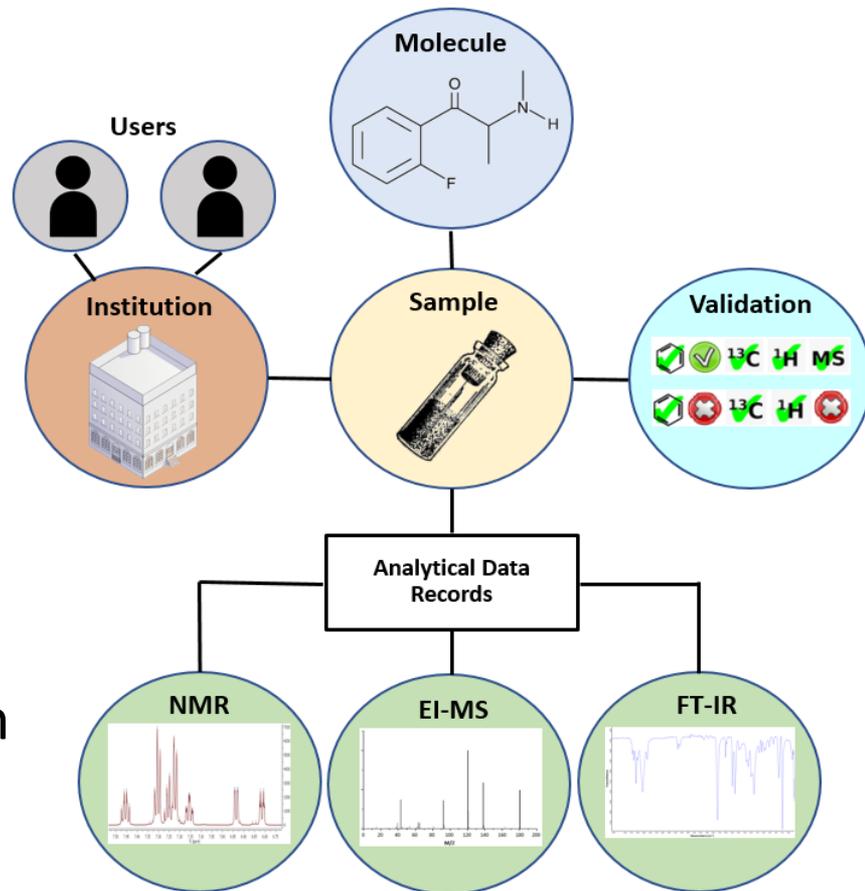
- ❑ NPS Data Hub Concept
- ❑ NPS DH Inner Workings
- ❑ Where We Are So Far with the NPS DH
- ❑ NPS Related Activities
  - ❑ NMR Spin System Analysis for Data Verification
  - ❑ Mixture Analysis with Raman Spectroscopy



# 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

Navigate through pages (list mode) or molecules (detail mode)

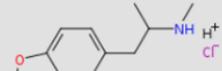
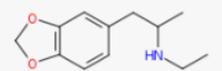
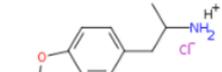
# Molecules Per Page

Add/Remove columns in list view and save view here

Click on column headers to sort by or remove columns

Search parameters Search result Toggle View Mode Create New Molecule Search dialog: Molecule

163 molecules 1 / 17 Detail mode 10 lines Columns New Print Export Refresh Quick search Copy query URL

Structure	Molecule names	Formula	CAS No.	Safety data sheet	MW	Tags
	<b>MDMA</b> ; 1-(1,3-benzodioxol-5-yl)-N-methylpropan-2-amine hydrochloride; S(+)-3 4-MDMA HCL; N,α-dimethyl-1,3-benzodioxole-5-ethanamine, monohydrochloride; ...	C <sub>11</sub> H <sub>16</sub> ClNO <sub>2</sub>	64057-70-1	<a href="#">Cayman Chemical</a>	229.71	Phenethylamines
	<b>MDE</b> ; N-ethyl-α-methyl-1,3-benzodioxole-5-ethanamine, monohydrochloride; Eve; 3,4-Methylenedioxyethylamphetamine; 1-(1,3-Benzodioxol-5-yl)-N-ethylpropan-2-amine.hydrochloride; ...	C <sub>12</sub> H <sub>17</sub> NO <sub>2</sub>	74341-78-9	<a href="#">Lipomed</a>	207.27	Phenethylamines
	<b>DFMDA</b> ; DIFMDA; Difluoromethylenedioxyamphetamine ; -(2,2-Difluoro-1,3-benzodioxol-5-yl)propan-2-amine	C <sub>10</sub> H <sub>12</sub> ClF <sub>2</sub> NO <sub>2</sub>			251.66	Phenethylamines

Open Molecule Detail View

Select Molecule

# Samples From Users Institution

Add (+) New Sample

Total # Samples

Add (+) New Analytical Data

View Available Analytical Data Sets

Clicking on Structure Opens Detail View



# FORENSICS @ NIST

## #NISTForensics

# Molecule Search Result Page (Detail View)

Info Search molecule x

Search parameters Search result **Toggle View Mode**

Add New Sample

Search dialog: Molecule

1 / 152 List mode New Print Export Refresh selected Quick search Copy query URL Search molecule at suppliers CSearch

## MDMA

Molecule names	IUPAC	Sample identifier	Lot no.	Institution	Comment	Validation status
<input checked="" type="radio"/> MDMA	<input type="checkbox"/>	control sample	45NR040	BKA - Bundeski		
<input type="radio"/> 1-(1,3-benzodioxol-5-yl)-N-methylpropan-2-amine hydrochloride	<input type="checkbox"/>					
<input type="radio"/> S(+)-3,4-MDMA HCL	<input type="checkbox"/>					
<input type="radio"/> N,α-dimethyl-1,3-benzodioxole-5-ethanamine, monohydrochloride	<input type="checkbox"/>					
<input type="radio"/> (±)-3,4-Methylenedioxymethamphetamine hydrochloride	<input type="checkbox"/>					

1 / 2 [ 1 - 5 / 8 ]

CAS No. 64057-70-1 Sum formula C11H16ClNO2

MW 229.71 Monoisotopic mass 229.08696

InChi InChi=1S/C11H15NO2.ClH/c1- InChiKey LUWHVONVCYWRMZ-UHFFFAO

Stereo SMILES [Cl-].CNC(C)Cc1ccc2OCoc2c1.[f SMILES [Cl-].CNC(C)Cc1ccc2OCoc2c1.[f

[Google](#) [PubChem](#)

Comment

**Tags** Drug Class(es)

Phenethylamines

Structure uncertain

Created by riedel (Nov 7, 2016 4:56:03 AM)  
Last change by schoenberger (May 5, 2017 12:07:40 PM)

**Analytical data**

- control sample (BKA - Bundeskriminalamt) - (45NR040) (12)
  - NMR (11)
  - MS: 3,4-MDMA.MSP (MS)

**Available Analytical Data**  
Clicking on a data set will open the data browsing tree in this panel.



FORENSICS @ NIST

#NISTForensics

# Adding New Molecules

**Add molecule** Info Search molecule x Search molecule at su... x Search analytical data x Search literature x

Save & exit Save | [There is one more molecule with this molecular structure in the database.](#)

## AM-2201

Molecule names + IUF

- AM-2201
- [1-(5-Fluoropentyl)-1H-indol-3-yl]-1-naphthalenylmethanone
- [1-(5-fluoropentyl)-1H-indol-3-yl]-1-naphthalenyl-methanone
- 1-[[5-Fluoropentyl)-1H-indol-3-yl]-(naphthalen-1-yl)methanone

**This information was automatically populated from chemical structure or CAS #**

CAS No. 335161-24-5 Sum formula C<sub>24</sub>H<sub>22</sub>FNO

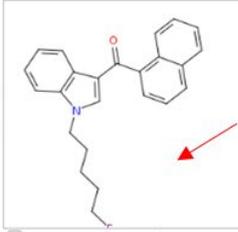
MW 359.44 Monoisotopic mass 359.16854

InChi InChiKey

Stereo SMILES FCCCCn1cc(C(=O)c4cccc4cccc44) SMILES FCCCCn1cc(C(=O)c4cccc4cccc44)

Comment SWGDrug Monograph

Tags + Cannabinoids

 Drag & Drop Chemical Structures

Structure uncertain

**Physical data**

Melting point (°C, low-high) Boiling point (°C, low-high) at bar

Refractive index (20°C) Degree of unsaturation 14 Density (20°C)

**Safety data**

**Properties**

MSDS and CoA (2) +



FORENSICS @ NIST

#NISTForensics

# Analytical Data Browsing

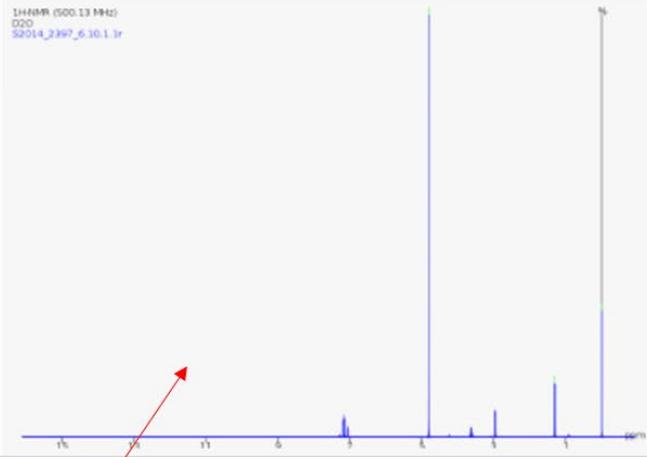
**Analytical data**

#1 (BKA - Bundeskriminalamt) (9)

- NMR (8)
  - D2O (8)
    - 1H: 1H (JCamp 1D)
      - Attached files: NMRshiftDB - vali...
    - 13C: 13C (SDF)
      - Attached files: CSearch - Validat...
      - Attached files: CSearch - Validat...
    - more (6)
      - DFMDA.mnova (NMR)
      - PDF report page 1
      - PDF report page 2
      - PDF report page 3
      - PDF report page 4
      - PDF report page 5
    - MS: DFMDA.MSP (MS)

Report Export Refresh selected | NMRshiftDB

Molecule	DFMDA	Sample
Method	1H	1H-NMR (500.13 MHz) D2O S2014_2397_6.10.1.3r
Comment	<div style="border: 1px solid gray; height: 40px;"></div>	



More data of this set of measurements

Downloads Data File →

Mouseover Menu For Spectrum Window

- Download
- Zoom
- Interactive viewer
- Search for similar data

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



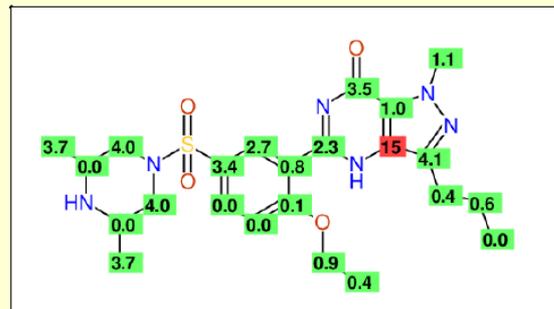
# Integration with CSEARCH

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

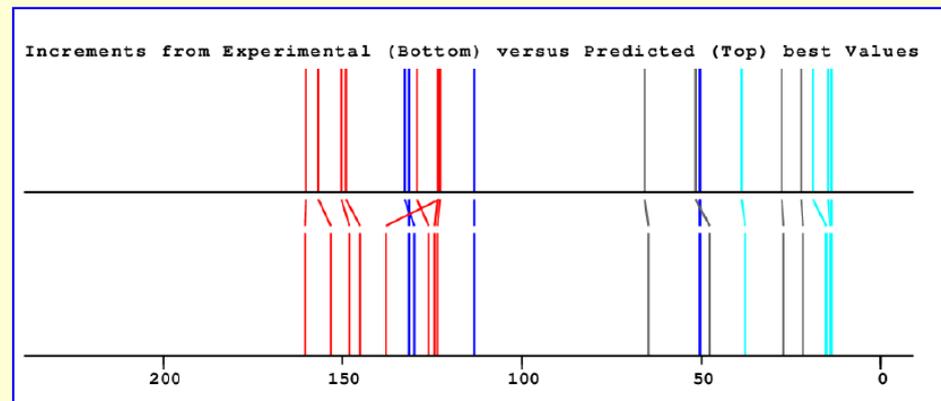
- ❑ Evaluation of proposed structure with associated  $^{13}\text{C}$  assignments
- ❑ Based on SDF file format (chemical structure + peak assignments)
- ❑ “Robot-referee” provides a fully automated, detailed report (HTML) evaluating proposed structure and associated  $^{13}\text{C}$  assignments.
-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

## Predicted/Experimental Comparison Excerpt

Differences between predicted and experimental data in ppm



Comparison of Experimental versus Predicted Chemical Shift Values



Overall deviation between predicted and experimental data is 2.2ppm



FORENSICS@NIST

#NISTForensics

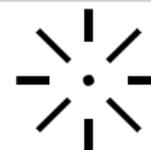
# Where Are We So Far

- ❑ 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

What do you want to do?



Search for a dataset



Create a dataset



Personal settings



Help

Do you want to start with a different function?  ▼

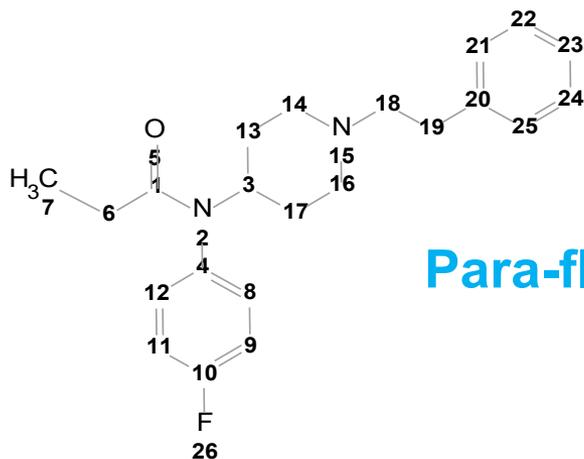


FORENSICS @ NIST

#NISTForensics

# Can We Get More From $^1\text{H}$ 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.  $^{19}\text{F}$



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 CH <sub>2</sub>	2.082	J(6)	14.56
		J(6-7)	7.89
7 CH <sub>3</sub>	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
		J(11-9)	1.5
11 CH	7.156	J(11-12)	8.43
		J(11-26)	8
		J(12-8)	1.5
12 CH	7.019	J(12-11)	8.43
		J(12-26)	5
		J(13'-3)	5.78
13' CH <sub>2</sub>	1.645	J(13'-13'')	12.29
		J(13'-14')	8.01
		J(13'-14'')	5.65
		J(13''-3)	5.78
13'' CH <sub>2</sub>	2.031	J(13''-13')	12.29
		J(13''-14')	5.65
		J(13''-14'')	8.01

⋮



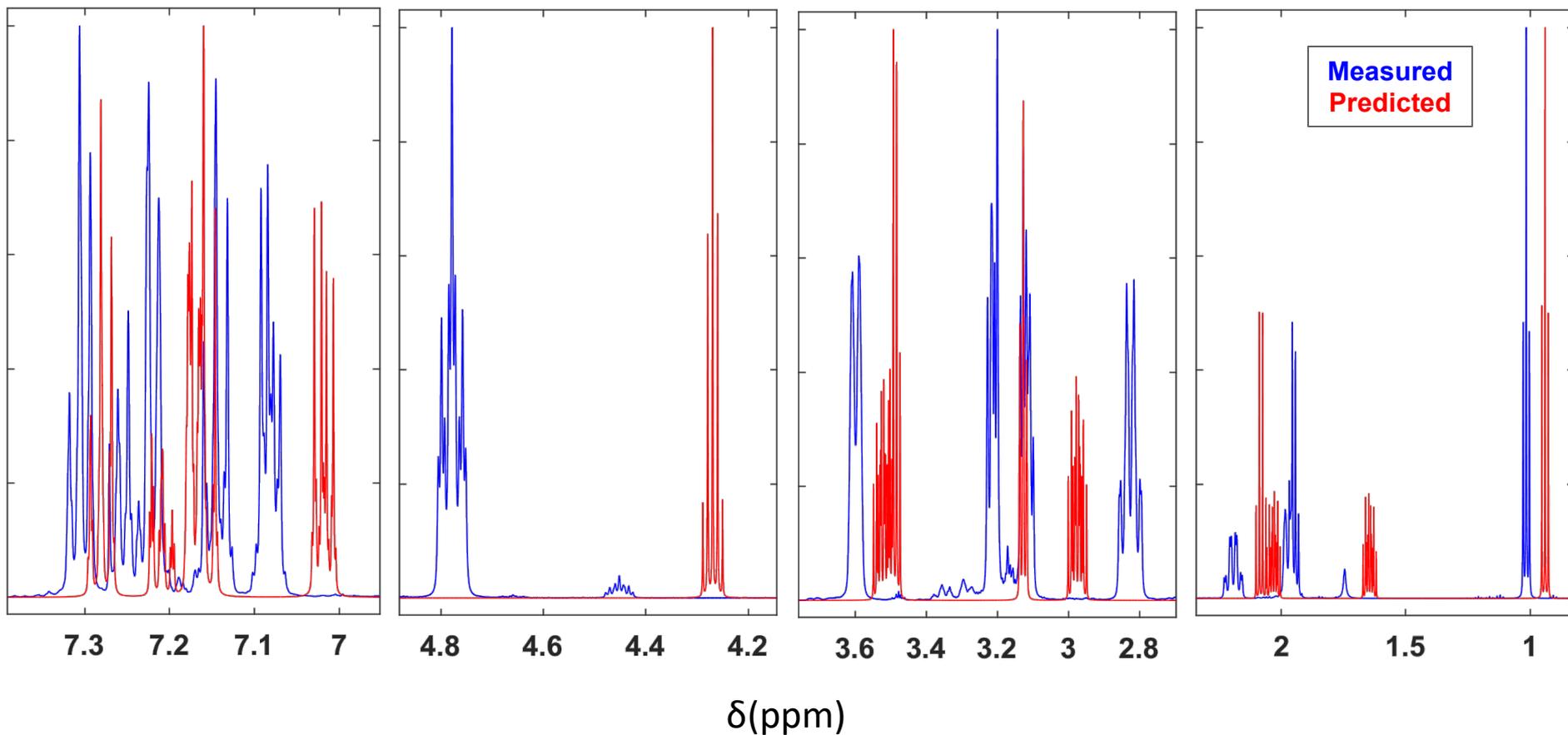
# Outline

- ❑ 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**



# Predicted $^1\text{H}$ NMR Spectra

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



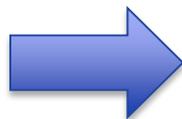
FORENSICS @ NIST

#NISTForensics

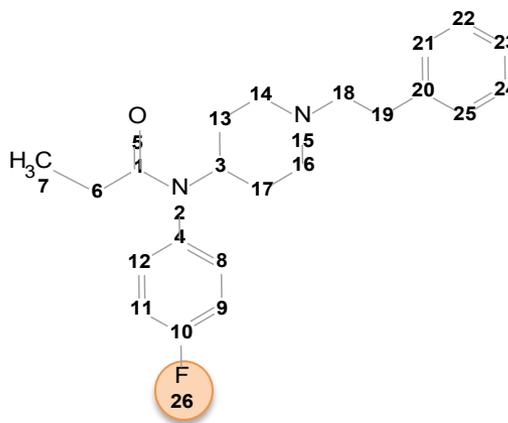
# Quantum Mechanical Spectral Analysis (QMSA)

## 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



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

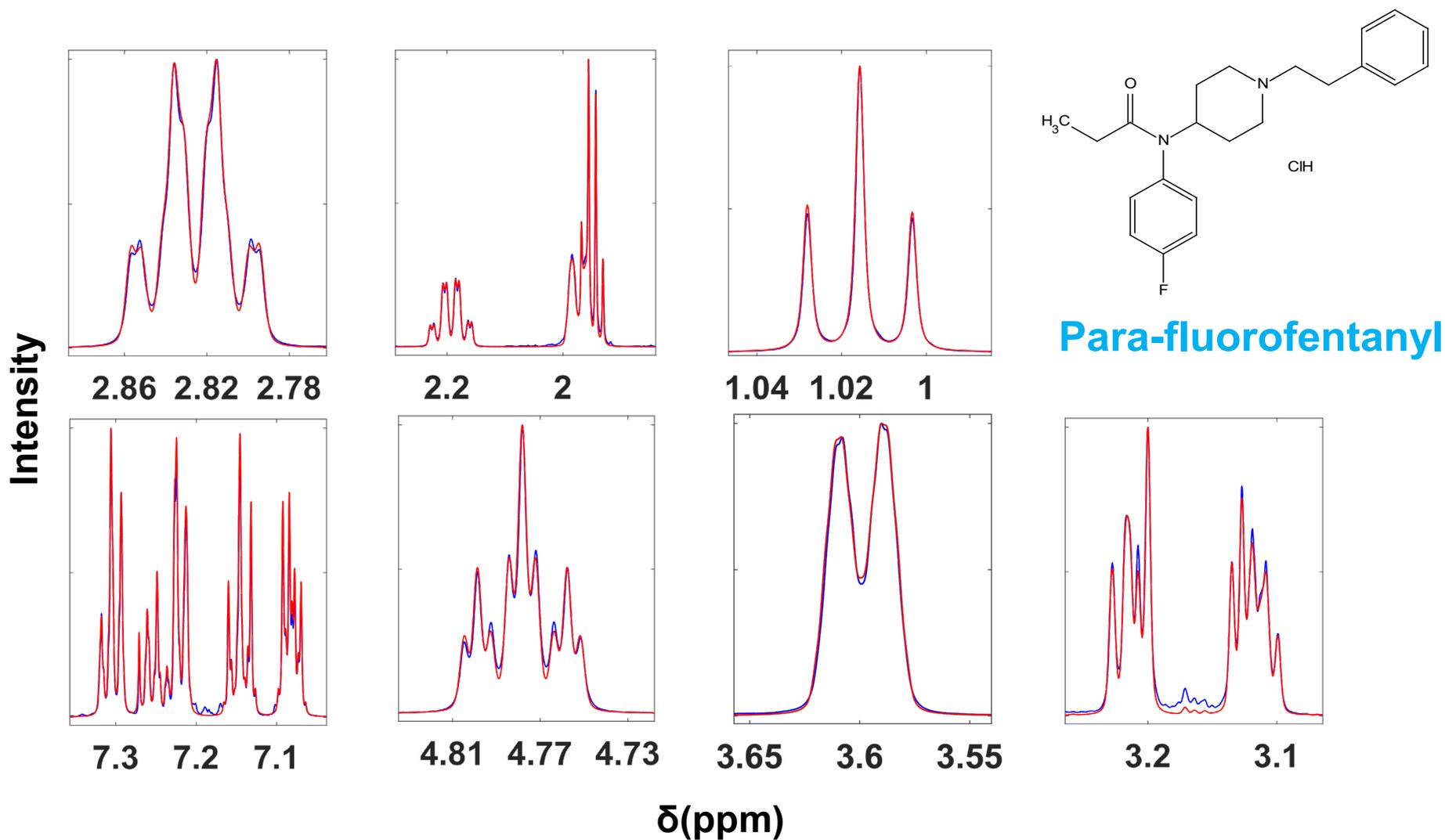
Atom	Shift (ppm)	J (Hz)	
3 CH	4.778	J(3-13')	12.3336
		J(3-13'')	3.6189
		J(3-17')	12.3336
		J(3-17'')	3.6189
6 CH2	1.9495	J(6)	14.56
		J(6-7)	7.4367
7 CH3	1.0157	J(7-6)	7.4367
		J(7)	6.99
8 CH	7.0817	J(8-9)	8.663
		J(8-12)	3.1175
		J(8-26)	4.7923
9 CH	7.1451	J(9-8)	8.663
		J(9-11)	2.6866
		J(9-26)	8.0205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



FORENSICS@NIST

#NISTForensics

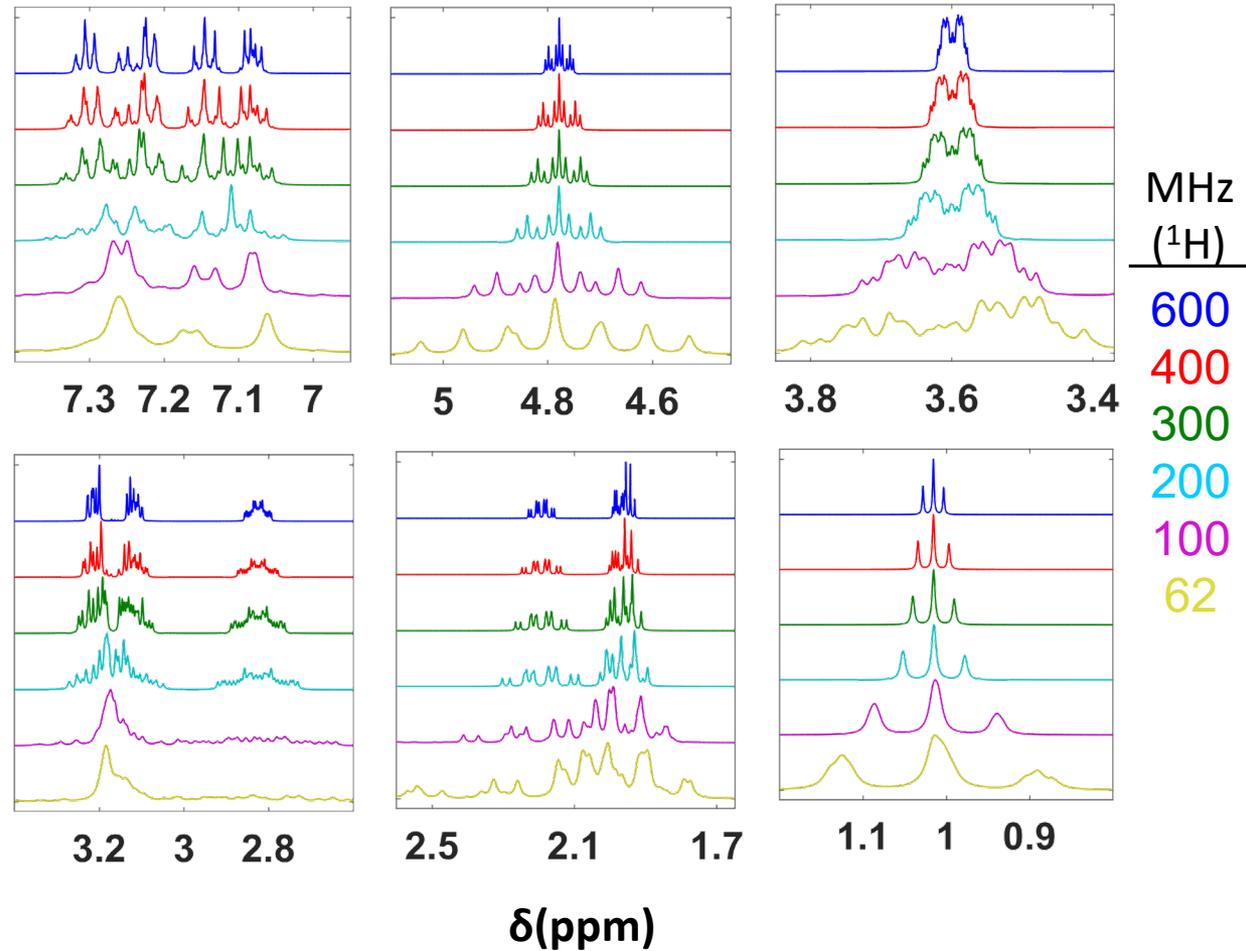
# $^1\text{H}$ QM Spectral Analysis @ 600 MHz



# Field Translation of $^1\text{H}$ Spectra

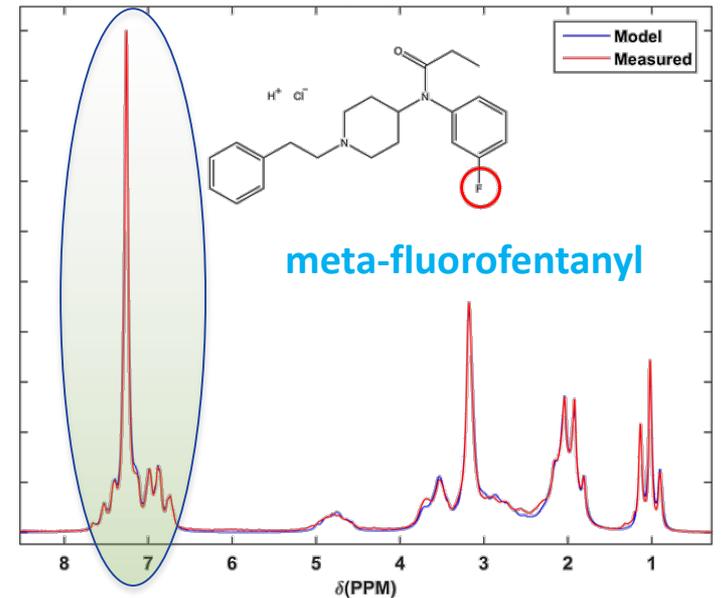
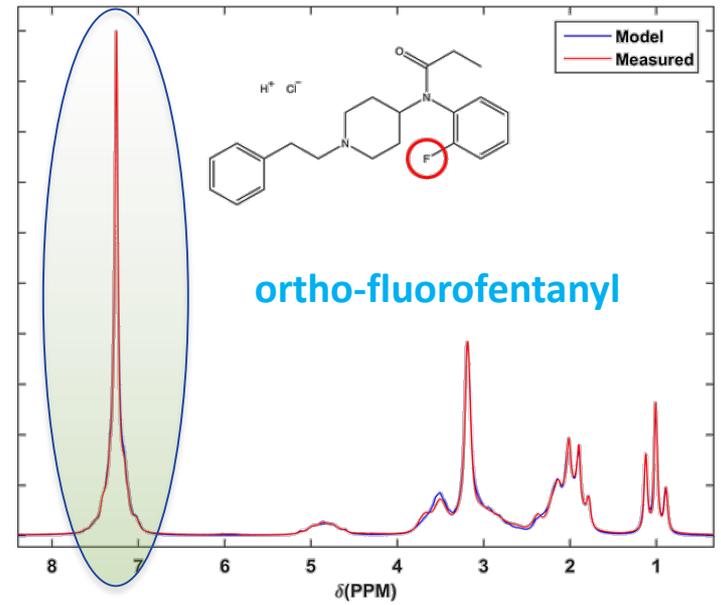
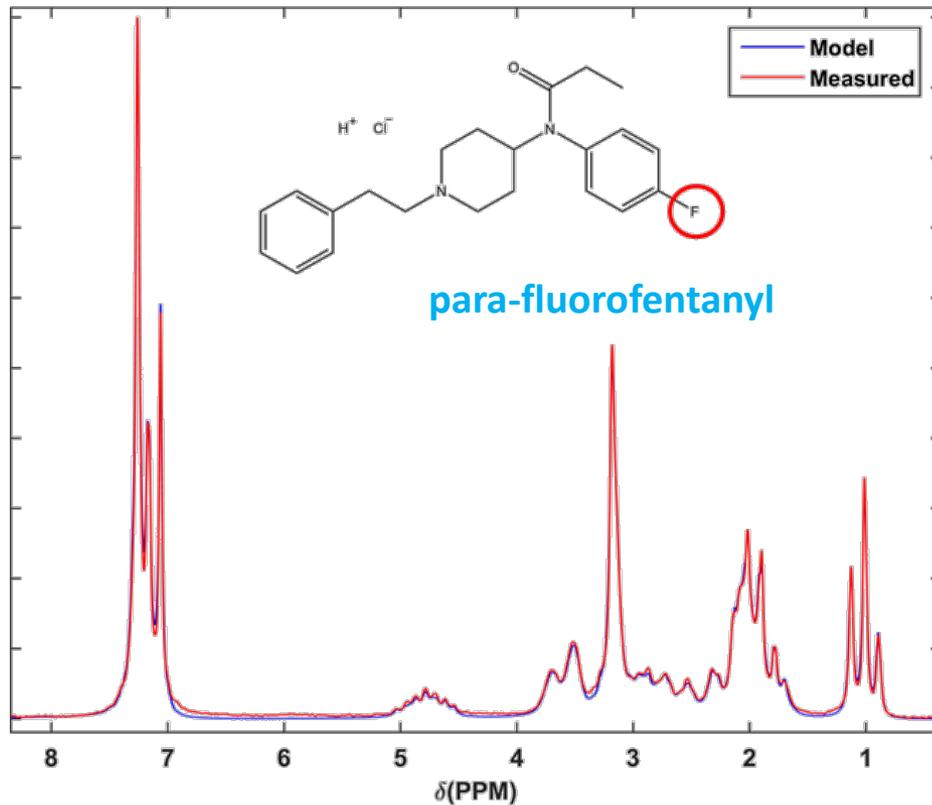
## QM Model Evaluated at Various Field Strengths

- ❑ Chemical shift ( $\delta$ ) 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

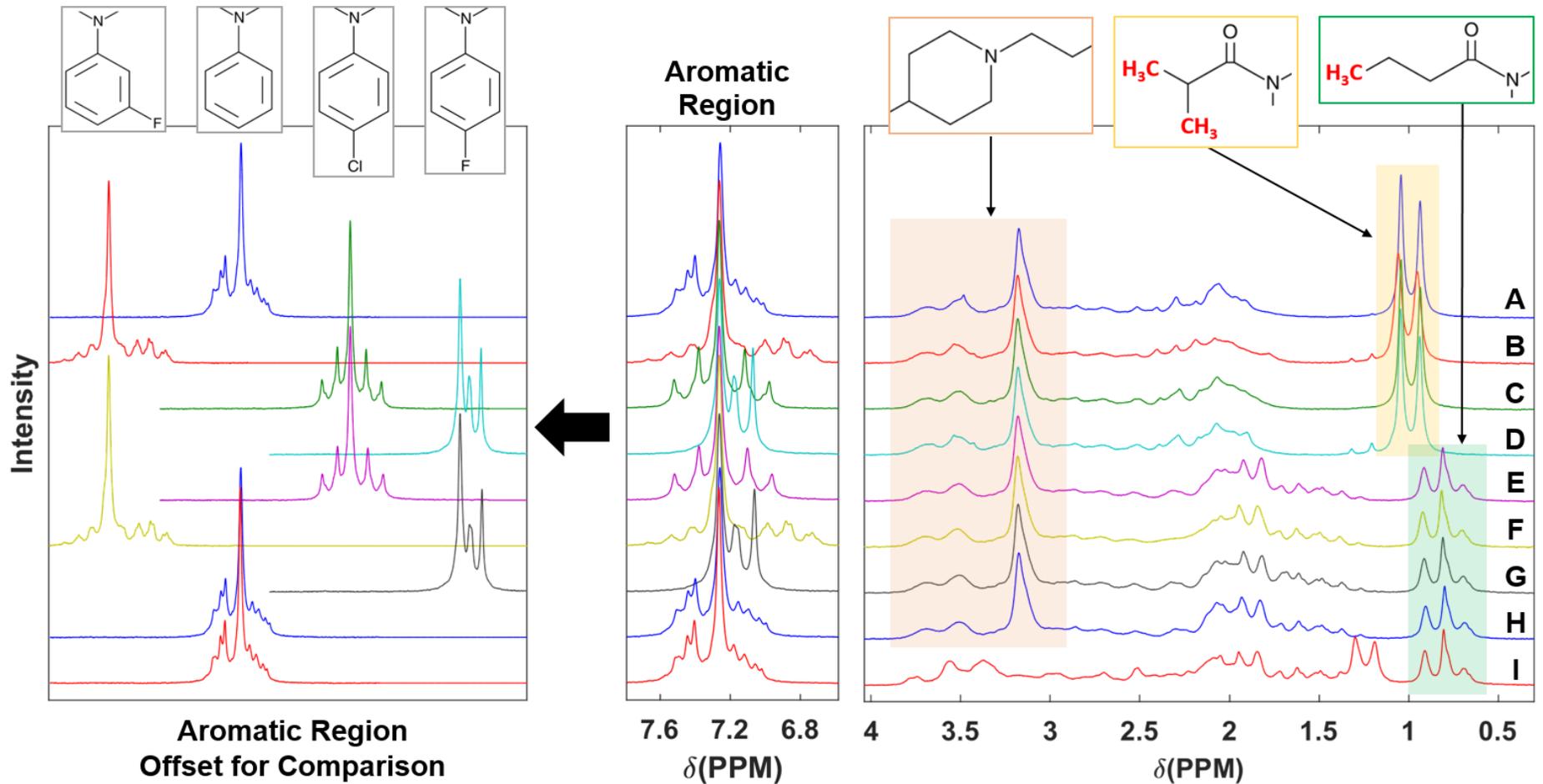


# Isomer Differentiation On a Benchtop NMR

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

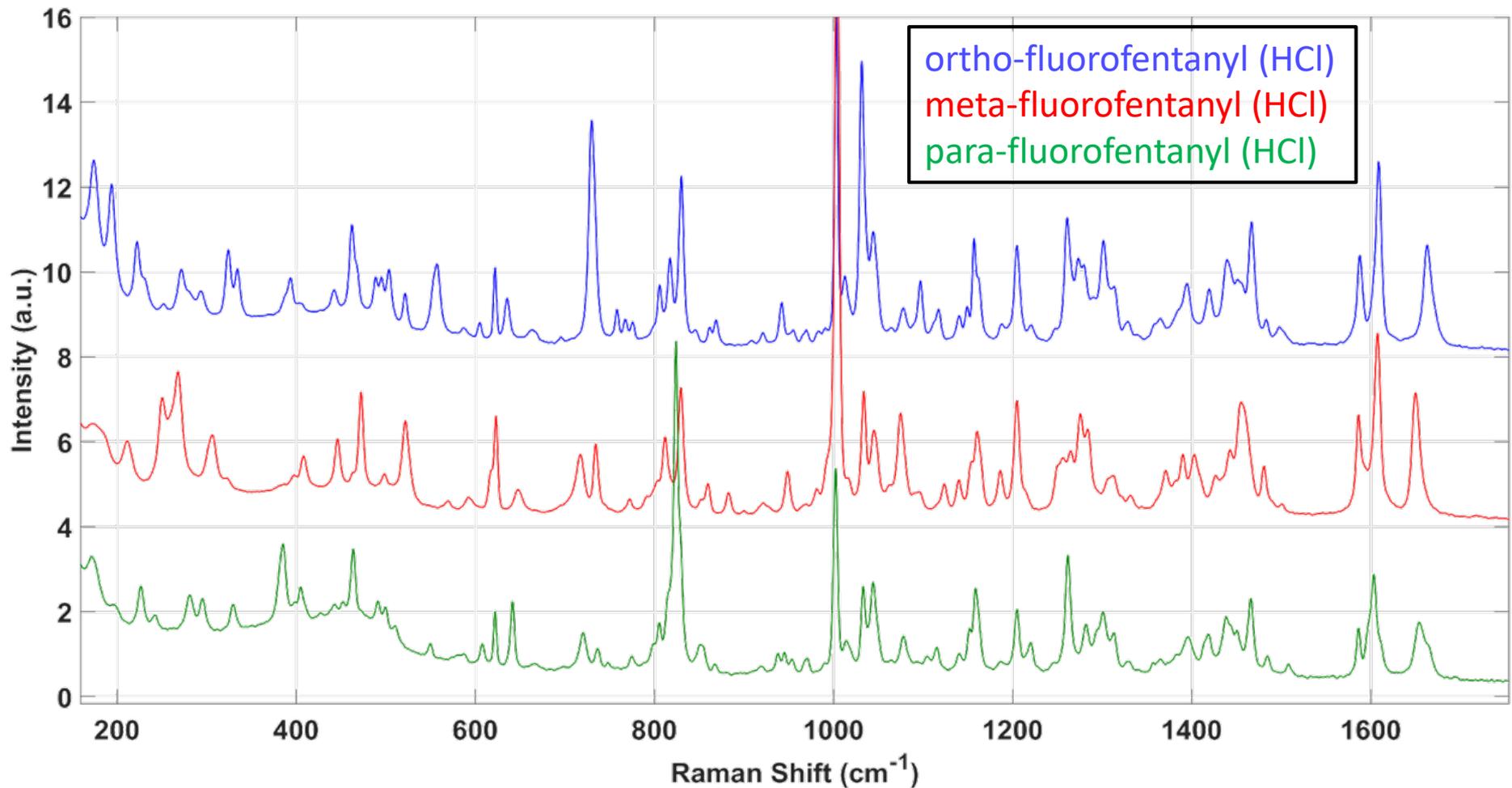


# Butyrl Fentanyl Isomers (<sup>1</sup>H NMR, 62 MHz)



# Raman Spectroscopy, Fluorofentanyl Isomers

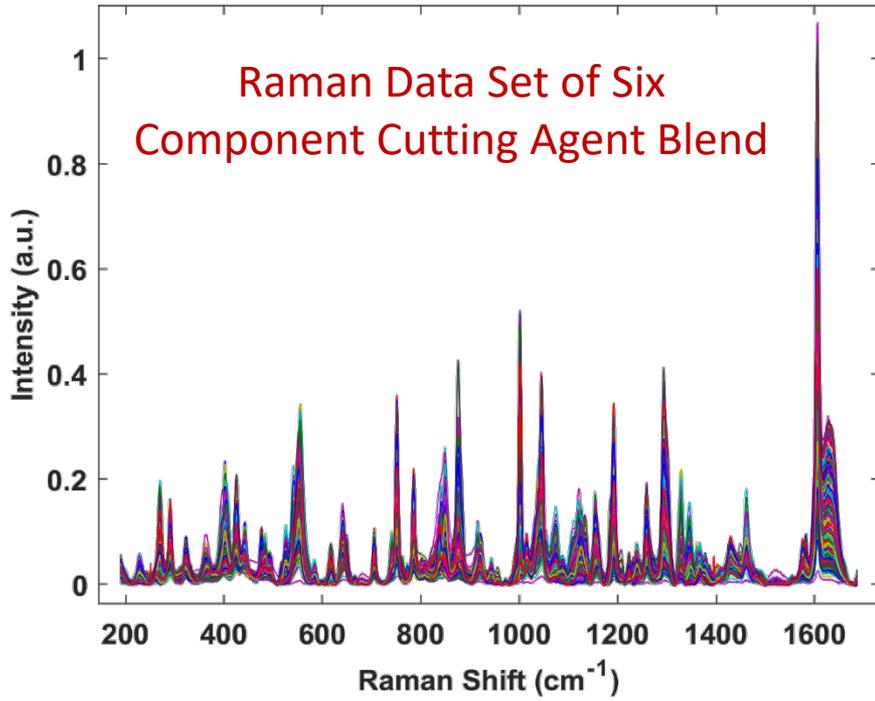
1064 nm Raman Spectra



FORENSICS @ NIST

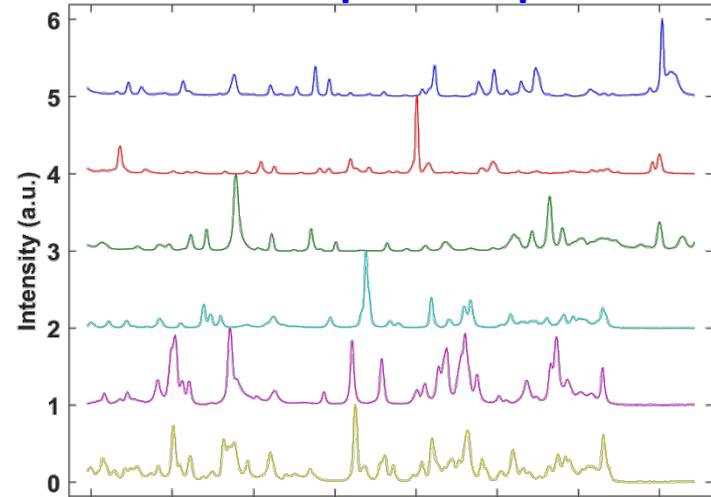
#NISTForensics

# Raman Mixture Analysis

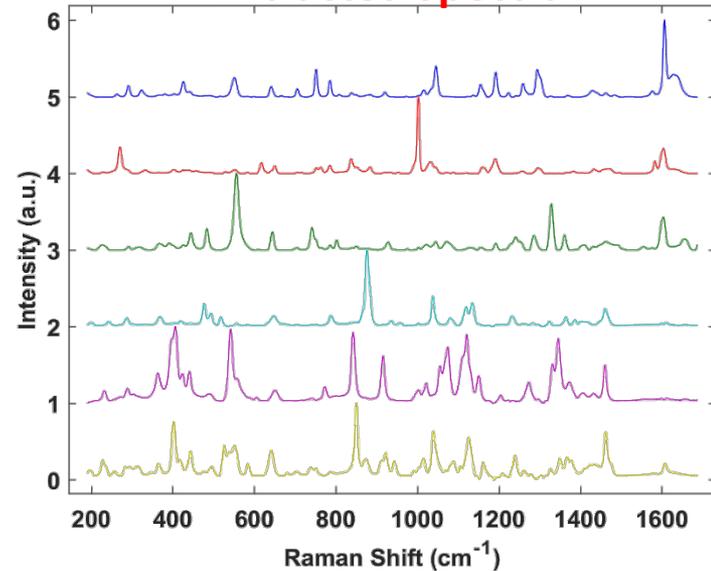


Multivariate Curve Resolution (MCR)

Pure Component Spectra



Extracted Spectra



# Acknowledgements

## **NPS Data Hub**

Torsten Schoenberger (Federal Criminal Police Office of Germany, BKA)

Charlotte Corbett (Drug Enforcement Administration, STRL)

Katrice Lippa (Chemical Sciences Division, NIST)

Felix Rudolphi (Sciformation Consulting Gmb, Bad Vilbel, Germany)

Wolfgang Robien (Department for Organic Chemistry, University of Vienna)

## **NMR QMSA & Benchtop NMR Work**

Jonathan Duffy (Department of Forensic Sciences, George Washington University)

Ioan Marginean (Department of Forensic Sciences, George Washington University)

Matthias Niemitz (NMR Solutions Oy, Kuopio Finland)

## **Raman Spectroscopy**

Peter Trask (Chemical Sciences Division, NIST)

## **Funding**

**NIST Special Programs Office**

# Thank You!



**FORENSICS @ NIST**

**#NISTForensics**