

The logo consists of the letters 'DIT' in a bold, sans-serif font, enclosed within a white square border. The background of the slide features a dark gray grid pattern with a large, light gray curved line on the left side.

DIT

DART-MS Data Interpretation Tool and Other Resources for Seized Drug Analysis

Arun Moorthy (ORCID: 0002-5988-1389)

&

Edward Sisco (ORCID: 0003-0252-1910)

NIST

National Institute of Standards and Technology

Disclaimers

Certain commercial products are identified in order to adequately specify the procedure; this does not imply endorsement or recommendation by NIST, nor does it imply that such products are necessarily the best available for the purpose.

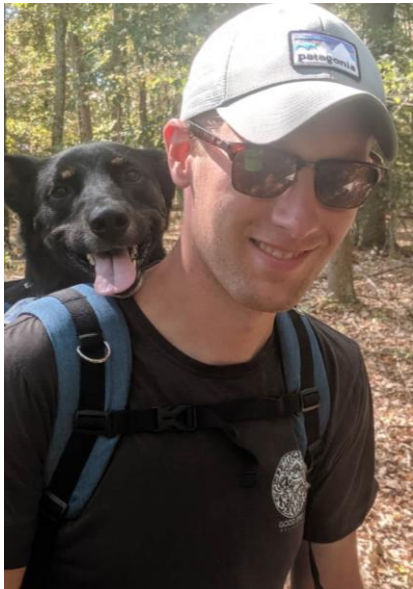
A portion of this work was supported by Award No. 2018-DU-BX-0165, awarded by the National Institute of Justice, Office of Justice Programs, U.S. Department of Justice. The opinions, findings, and conclusions or recommendations expressed in this publication/program/exhibition are those of the author(s) and do not necessarily reflect those of the Department of Justice.



Who We Are / What We Do



Support forensic chemistry disciplines by addressing measurement challenges through collaborative research.

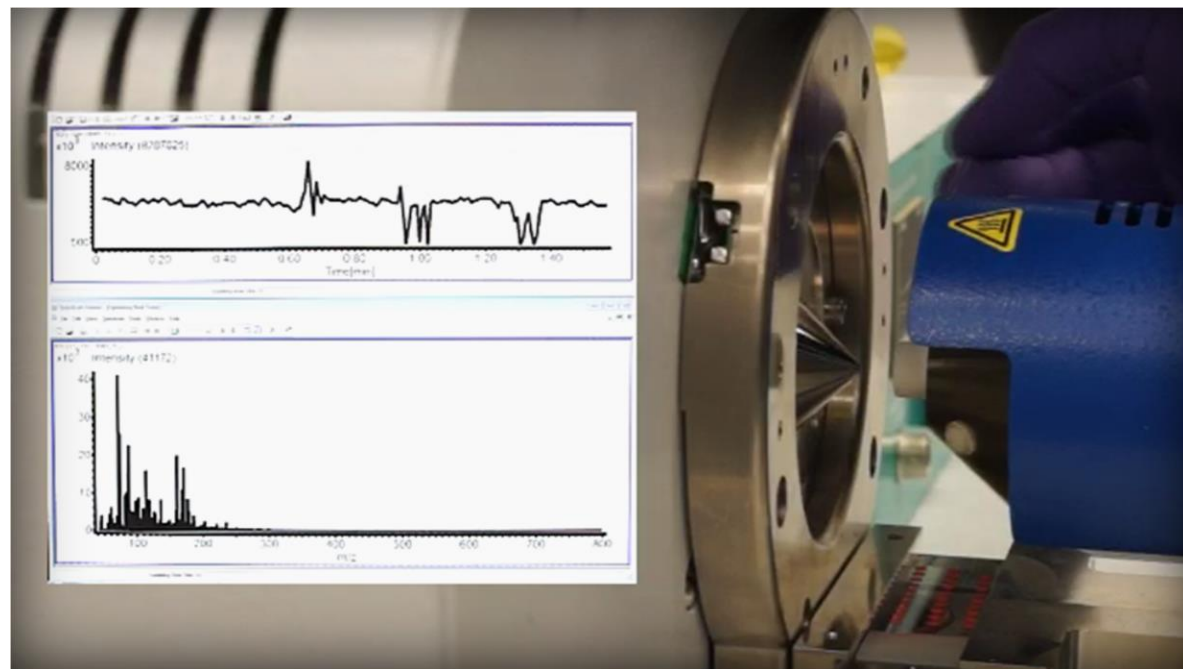


Provide forensic practitioners at all levels (local, state, federal, and international) usable tools and resources.

Fundamentals of DART-MS

- One of many ambient ionization mass spectrometry sources
- Conventional DART-MS uses a heated helium metastable gas stream for sample desorption and ionization
- Allows for analysis of samples with minimal preparation or pre-treatment
- Analysis time 1 s to 5 s
- Typical LODs ng to pg
- Can be coupled to a range of mass spectrometers

DART-MS: Direct Analysis in Real Time Mass Spectrometry



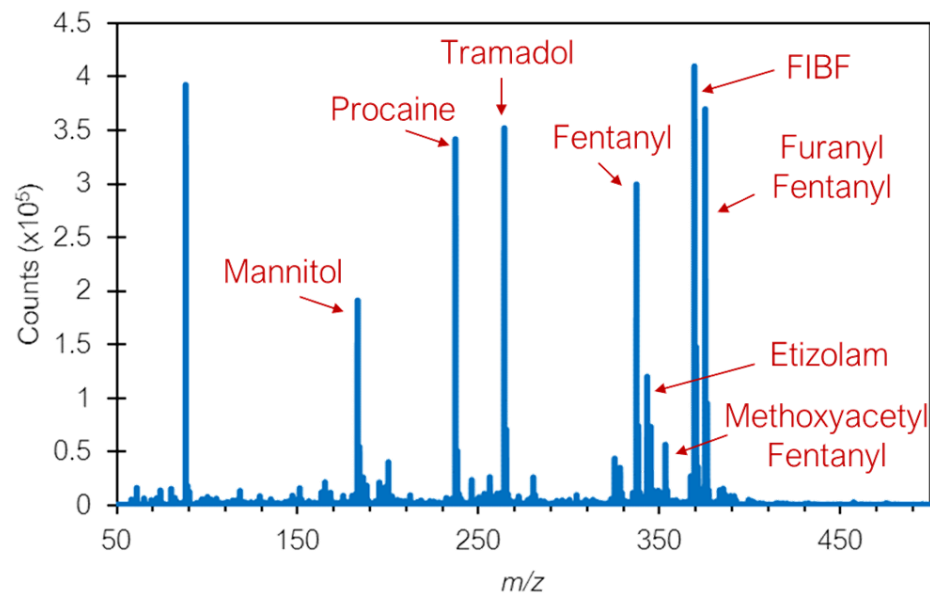
DOI: 10.1016/j.forc.2020.100294

**DART-MS Review
Article**

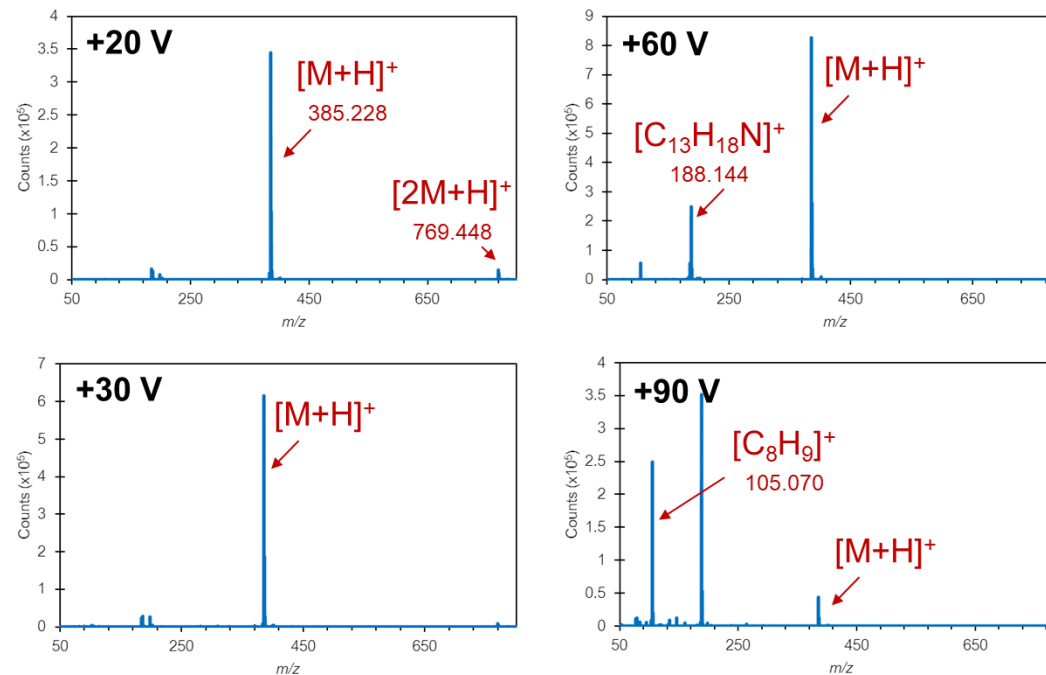


Fundamentals of DART-MS

One of the limitations of DART-MS is difficulty searching spectra due to lack of chromatography



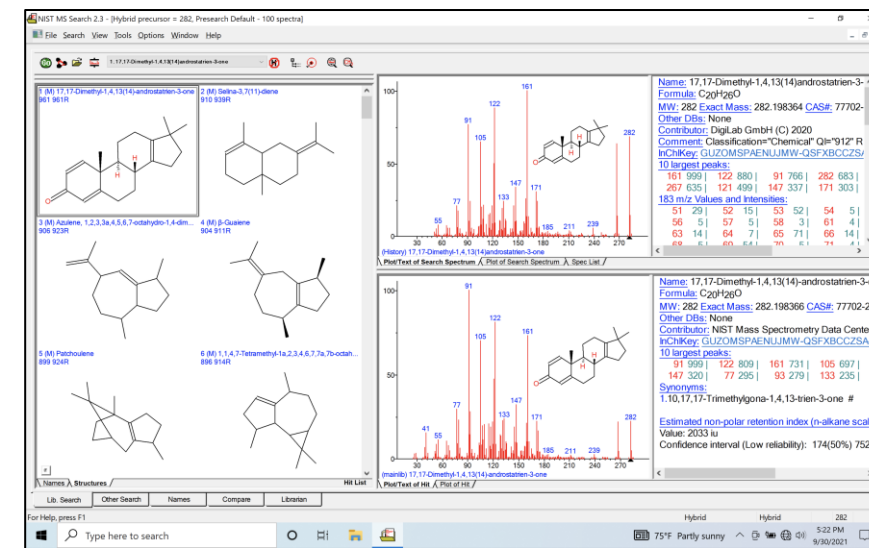
Even with high resolution, assigning compounds can be difficult



Can leverage is-CID to fragment compounds for more specific identification

Data Interpretation in Traditional MS

- NIST has several existing tools to help interpret traditional electron impact mass spectra (EI-MS):
 - **Automated Mass Spectral Deconvolution and Identification (AMDIS):** Automates extraction of GC/MS data files to generate consistent/reproducible mass spectra.
 - **Mass Spectral (MS) Search/Interpreter:** A comprehensive tool for interacting with mass spectral libraries, including a variety of useful search algorithms and data interpretation tools.
 - **Fentanyl Classifier:** A tool specifically for interacting with mass spectra of potential fentanyl analogs, attempting to localize the site of modification.
- To most effectively use these tools, a reference library is required



<https://chemdata.nist.gov/>

Search Results
[Instructions](#)

FentanyL Classifier

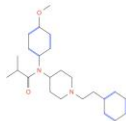
The FentanyL Classifier is a prototype implementation of "augmented mass spectral library searching". The software was designed for demonstration purposes. The authors cannot guarantee the accuracy of results generated using the FentanyL Classifier, and cannot validate claims of others using this software.

Choose Query Spectrum (MSP File)

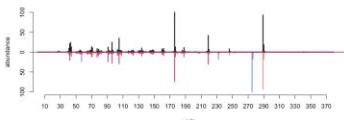
Browse... 463403.MSP

[View Structure](#)

Potential structure based on library search results. **Disclaimer:** The authors do not guarantee the accuracy of this result or claims of other based on results generated using this tool.


CN(Cc1ccccc1)CCOC(=O)c2ccc(O)cc2

Molecular weight information was contained in the Query MSP. The nominal MW of 380 Da was employed in the Hybrid Search.



m/z	Relative Intensity (%)
380	100
395	~80
154	~10
169	~10
184	~10
199	~10
214	~10
229	~10
244	~10
259	~10
274	~10
289	~10
304	~10
319	~10
334	~10
349	~10
364	~10

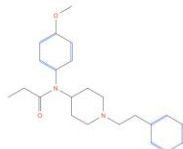
HR List Hit Map [FentanyL Structure Definition](#)

Show [33] entries

Name	HMZ	DM	SM
1 para-Methoxyfentanyl	892	14	0.81
2 Isobutyl fentanyl	806	30	0.71
3 Butanal fentanyl	793	30	0.7
4 Ethoxycarbonyl fentanyl	578	14	0.511
5 Tetrahydrofuranyl fentanyl	577	2	0.52
6 Isobutyryl fentanyl	566	16	0.511
7 p-Fluorofentanyl	563	26	0.511
8 Methoxycarbonyl fentanyl	550	28	0.47
9 ortho-Methylfentanyl	548	30	0.5
10 Tetrahydrofuran fentanyl D5	547	2	0.49

Library Compound:

Name: para-Methoxyfentanyl
 Formula: C20H26NO3
 Exact Mass: 346.2011
 MolWt: 344
 ICHMN: [COPD/Hydrocodone](#)
[XANTHANOL](#)


CCOC(=O)N(c1ccc(O)cc1)CCCN(CC2=CC=CC=C2)C2

Two Key Challenges

1. Developing is-CID mass spectral libraries
 - Procuring and measuring relevant compounds
 - Determine whether spectra are appropriate measurements of compounds
 - Confirm all non-spectral data is correct (e.g. molecular formula, name, etc.)

Evaluating is-CID Mass Spectra

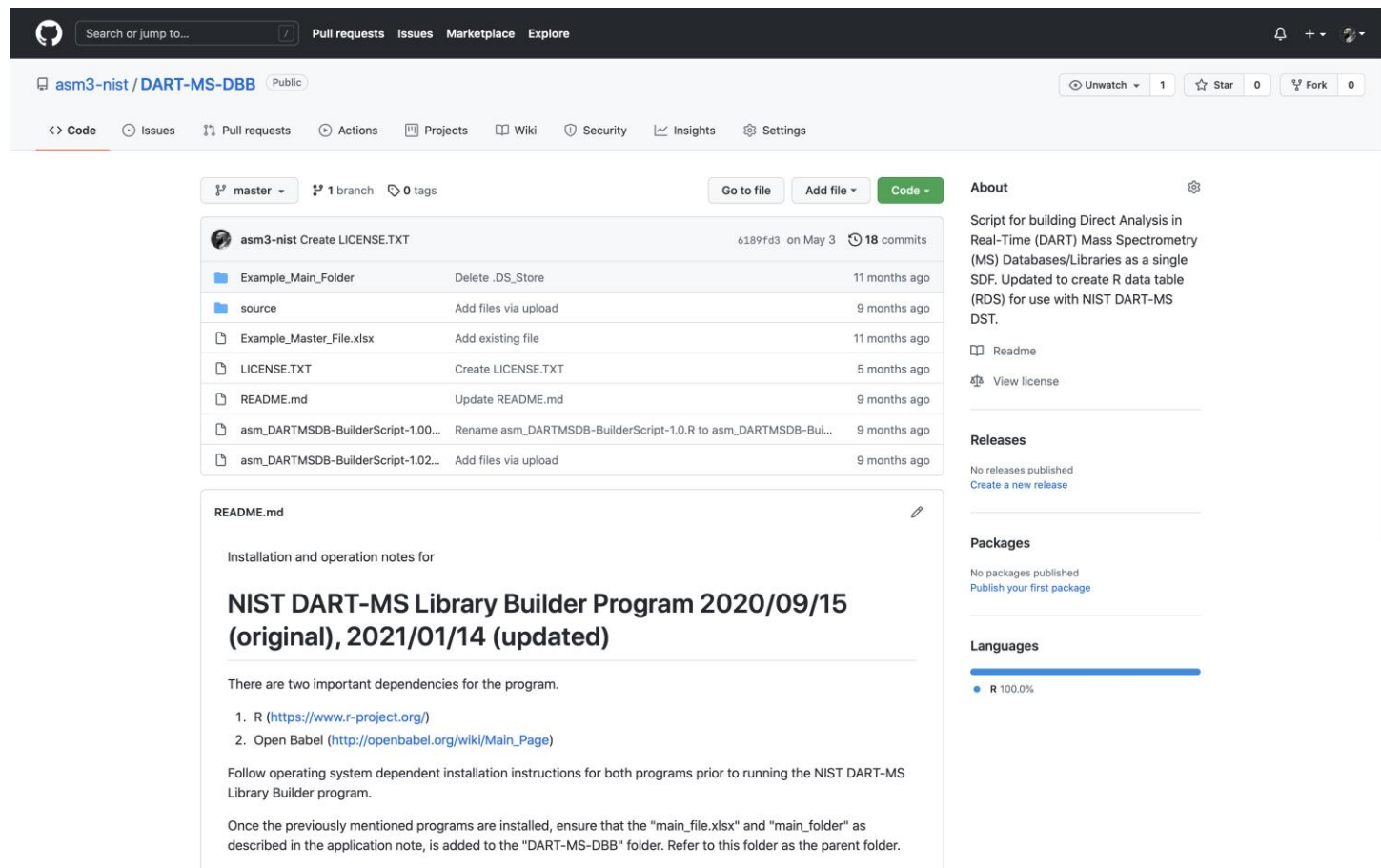
1. Developed a simple script with several filters and algorithms to assist in evaluating library mass spectra

```
You are welcome to redistribute it under certain conditions.  
Type 'license()' or 'licence()' for distribution details.  
  
Natural language support but running in an English locale  
  
R is a collaborative project with many contributors.  
Type 'contributors()' for more information and  
'citation()' on how to cite R or R packages in publications.  
  
Type 'demo()' for some demos, 'help()' for on-line help, or  
'help.start()' for an HTML browser interface to help.  
Type 'q()' to quit R.  
  
> source("asm_DARTMSDB-BuilderScript-1.07.R")  
NIST DART-MS Database Builder v.1.07  
Revised September 7th, 2021.  
  
data.table 1.14.0 using 1 threads (see ?getDTthreads). Latest news: r-datatable.com  
*****  
This installation of data.table has not detected OpenMP support. It should still work but in single-threaded mode.  
This is a Mac. Please read https://mac.r-project.org/openmp/. Please engage with Apple and ask them for support. Check r-datatable.com for  
updates, and our Mac instructions here: https://github.com/Rdatatable/data.table/wiki/Installation. After several years of many reports of  
installation problems on Mac, it's time to gingerly point out that there have been no similar problems on Windows or Linux.  
*****  
Loading required package: grid  
  
Welcome to enviPat version 2.4  
Check www.envipat.eawag.ch for an interactive online version  
  
Loaded all external packages.  
Loaded all custom functions ('source/asm_Functions/')  
  
There are 1 potential master files currently in the directory.  
  
1: 210825_HeLibrary_Cicada_SmilesUpdate.xlsx  
  
Click to stop screen recording (integer value) for creating database: █
```



Evaluating is-CID Mass Spectra

1. Developed a simple script with several filters and algorithms to assist in evaluating library mass spectra
2. Made the script and test files open-source and publicly available through github:
<https://github.com/asm3-nist/DART-MS-DBB>

A screenshot of the GitHub repository page for 'asm3-nist / DART-MS-DBB'. The page shows the repository name, a search bar, and navigation links like 'Pull requests', 'Issues', 'Marketplace', and 'Explore'. Below these are tabs for '<> Code', 'Issues', 'Pull requests', 'Actions', 'Projects', 'Wiki', 'Security', 'Insights', and 'Settings'. The main content area displays a file tree with items like 'Example_Main_Folder', 'source', 'Example_Master_File.xlsx', 'LICENSE.TXT', 'README.md', and two 'asm_DARTMSDB-BuilderScript' files. The 'README.md' file is selected, showing its content which includes installation and operation notes, dependencies (R and Open Babel), and instructions for running the program. The right sidebar contains sections for 'About' (describing the script's purpose), 'Releases' (no releases published), 'Packages' (no packages published), and 'Languages' (R 100.0%).

Evaluating is-CID Mass Spectra

1. Developed a simple script with several filters and algorithms to assist in evaluating library mass spectra
2. Made the script and test files open-source and publicly available through github:
<https://github.com/asm3-nist/DART-MS-DBB>
3. Wrote a paper summarizing the methods:
DOI: 10.1021/jasms.0c00416



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Creation and Release of an Updated NIST DART-MS Forensics Database

Edward Sisco*, Arun S. Moorthy, and Laura M. Watt

Cite this: *J. Am. Soc. Mass Spectrom.* 2021, 32, 3, 685–689
Publication Date: February 11, 2021
<https://doi.org/10.1021/jasms.0c00416>
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SUBJECTS: Fragmentation, Reaction mechanisms, Molecules, >

Abstract

Facing increasing caseloads and an everchanging drug landscape, forensic laboratories have been implementing new analytical tools. Direct analysis in real time mass spectrometry (DART-MS) is often one of these tools because it provides a wealth of information from a rapid, simple analysis. The data produced by these systems, while extremely useful, can be difficult to interpret, especially in the case of complex mixtures, and therefore, mass spectral databases are often used to assist in interpretation of data. Development of these databases can be expensive and time-consuming and often relies on manual evaluation of the underlying data. The National Institute of Standards and Technology (NIST) released an initial DART-MS in-source collisional-induced dissociation mass spectral database for seized drugs in the early 2010s but it has not been updated to reflect the increasing prevalence of novel psychoactive substances. Recently, efforts to update the database have been undertaken. To assist in development of the database, an automated data evaluation process was also created. This manuscript describes the new NIST DART-MS Forensics Database and the steps taken to automate the data evaluation process.

KEYWORDS: DART-MS, database, library, seized drugs, data evaluation

Supporting Information

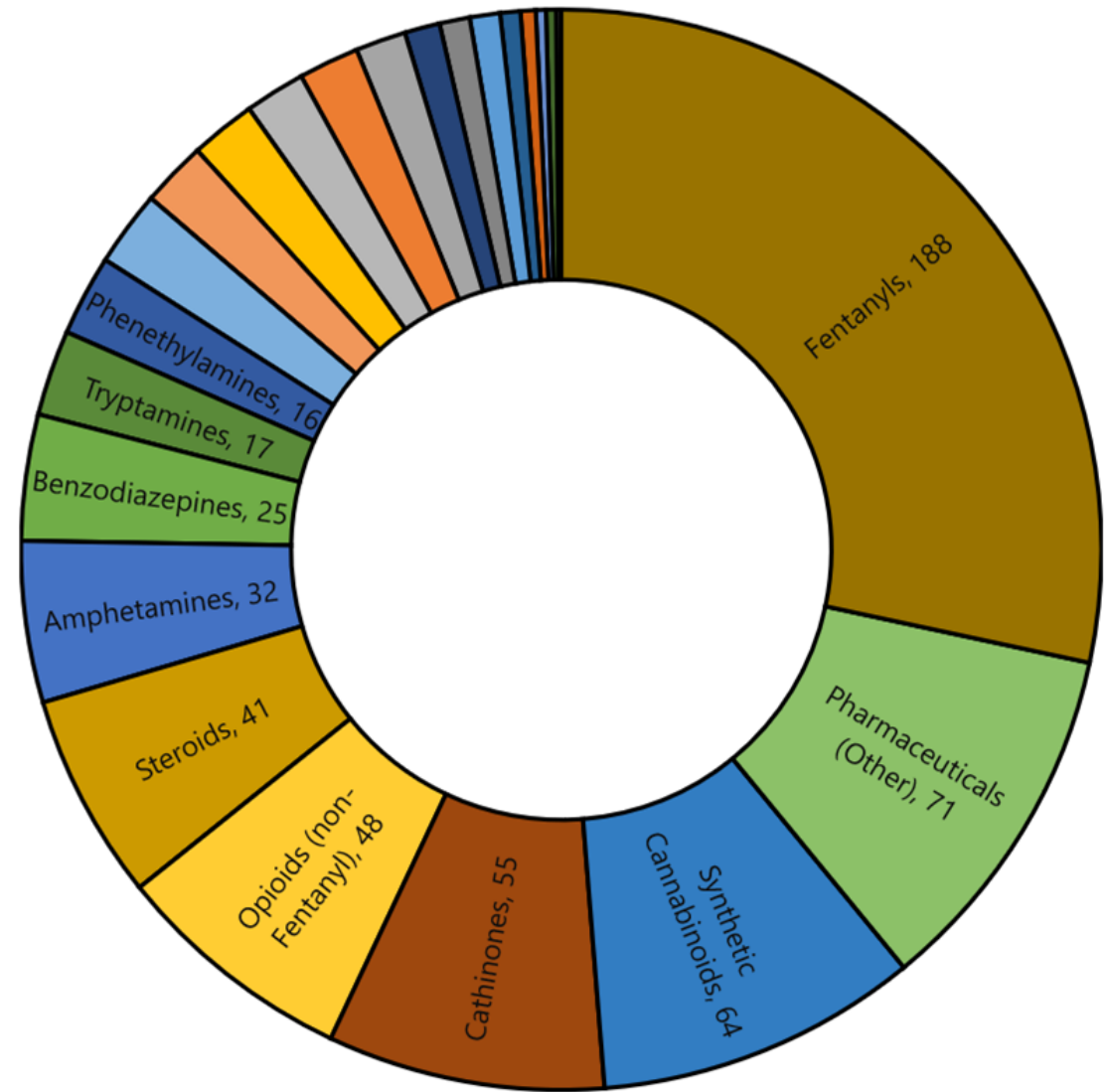
The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jasms.0c00416>.

DART-MS Library

Over the last 24 months, significant efforts have been made to update the DART-MS database

- 895 compounds and growing
- 3 is-CID spectra per compound
- 131 entries were carried over from the original library

Update 4 (Dragonfly) recently released



<https://doi.org/10.18434/mds2-2313>



Two Key Challenges

1. Developing is-CID mass spectral libraries
 - Procuring and measuring relevant compounds
 - Determine whether spectra are appropriate measurements of compounds
 - Confirm all non-spectral data is correct (e.g. molecular formula, name, etc.)
2. Searching is-CID mass spectra
 - Multiple (coupled) is-CID mass spectra collected per query
 - Query is rarely a pure compound in real-world analysis

Searching is-CID Mass Spectra

1. Developed the Inverted Library Search Algorithm (ILSA) for mixture analysis with multiple is-CID mass spectra

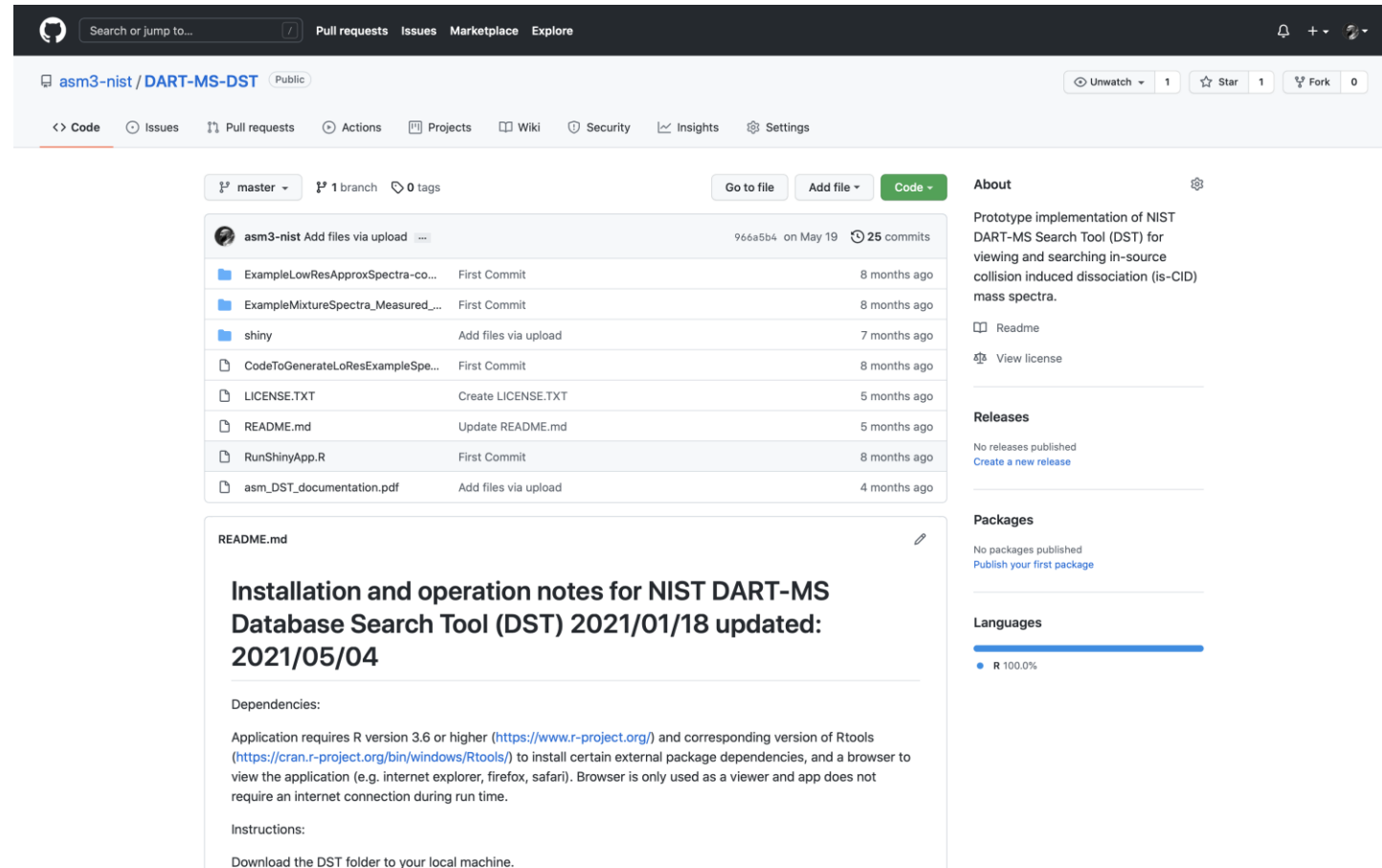
```
08444-1A.txt
Target m/z: 194.118821 (pm)
3,4-Methylenedioxymethamphetamine: FPIE-based Index: 0.835 RevMF-based Index: 0.883
Butamben: FPIE-based Index: 0.421 RevMF-based Index: 0.404
Methedrone: FPIE-based Index: 0.548 RevMF-based Index: 0.335
Target m/z: 163.075983 (pm)
Target m/z: 195.121086 (pm)
Target m/z: 423.205903 (pm)
Target m/z: 192.102651 (pm)
Target m/z: 164.07897 (pm)
Target m/z: 194.203044 (pm)
Target m/z: 206.11782 (pm)
Target m/z: 425.204212 (pm)
Target m/z: 208.132971 (pm)
3,4-Methylenedioxyethylamphetamine: FPIE-based Index: 0.916 RevMF-based Index: 0.778
Methamphetamine Methyl Carbamate: FPIE-based Index: 0.444 RevMF-based Index: 0.529
WARNING: An illegal reflective access operation has occurred
WARNING: Illegal reflective access by org.apache.poi.util.SAXHelper (file:/Library/Frameworks/R.framework/Versions/4.0/Resources/library/xlsxjars/java/poi-ooxml-3.10.1-20140818.jar) to constructor com.sun.org.apache.xerces.internal.util.SecurityManager()
WARNING: Please consider reporting this to the maintainers of org.apache.poi.util.SAXHelper
WARNING: Use --illegal-access=warn to enable warnings of further illegal reflective access operations
WARNING: All illegal access operations will be denied in a future release
Target m/z: 194.281316 (pm)
Target m/z: 424.209288 (pm)
Target m/z: 385.213268 (pm)
Target m/z: 356.186154 (pm)
Target m/z: 312.124129 (pm)
Target m/z: 337.119564 (pm)
Target m/z: 196.12353 (pm)
Target m/z: 194.364582 (pm)
Target m/z: 468.145979 (pm)
Target m/z: 193.105379 (pm)
2-Fluorophenyl Cyclopentyl Ketone: FPIE-based Index: 0.278 RevMF-based Index: 0.353
Target m/z: 190.086991 (pm)
Target m/z: 387.226501 (pm)
4'-Fluoro, para-fluoro-trans-3-methyl Fentanyl: FPIE-based Index: 0.606 RevMF-based Index: 0.606
```



Searching is-CID Mass Spectra

1. Developed the Inverted Library Search Algorithm (ILSA) for mixture analysis with multiple is-CID mass spectra
2. Implemented the algorithm as a simple application and made it publicly available through github:

<https://github.com/asm3-nist/DART-MS-DST>



The screenshot shows the GitHub repository page for `asm3-nist / DART-MS-DST`. The repository is public and has 1 star, 1 fork, and 0 issues. The main content area displays a list of files and their commit history:

File	Commit	Time
ExampleLowResApproxSpectra-co...	First Commit	8 months ago
ExampleMixtureSpectra_Measured_...	First Commit	8 months ago
shiny	Add files via upload	7 months ago
CodeToGenerateLoResExampleSpe...	First Commit	8 months ago
LICENSE.TXT	Create LICENSE.TXT	5 months ago
README.md	Update README.md	5 months ago
RunShinyApp.R	First Commit	8 months ago
asm_DST_documentation.pdf	Add files via upload	4 months ago

The README.md file is displayed below the file list, containing the following text:

Installation and operation notes for NIST DART-MS Database Search Tool (DST) 2021/01/18 updated: 2021/05/04

Dependencies:

Application requires R version 3.6 or higher (<https://www.r-project.org/>) and corresponding version of Rtools (<https://cran.r-project.org/bin/windows/Rtools/>) to install certain external package dependencies, and a browser to view the application (e.g. internet explorer, firefox, safari). Browser is only used as a viewer and app does not require an internet connection during run time.

Instructions:

Download the DST folder to your local machine.

The right sidebar shows the repository's metadata, including the description: "Prototype implementation of NIST DART-MS Search Tool (DST) for viewing and searching in-source collision induced dissociation (is-CID) mass spectra." It also includes links for Readme, View license, Releases, Packages, and Languages.

Searching is-CID Mass Spectra

1. Developed the Inverted Library Search Algorithm (ILSA) for mixture analysis with multiple is-CID mass spectra

2. Implemented the algorithm as a simple application and made it publicly available through github:

<https://github.com/asm3-nist/DART-MS-DST>

3. Wrote a paper summarizing the algorithms:

DOI: 10.1021/jasms.0c00416



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A New Library-Search Algorithm for Mixture Analysis Using DART-MS

Arun S. Moorthy* and Edward Sisco

Cite this: *J. Am. Soc. Mass Spectrom.* 2021, 32, 7, 1725–1734
Publication Date: June 17, 2021
<https://doi.org/10.1021/jasms.1c00097>
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SUBJECTS: Fragmentation, Algorithms, Reaction mechanisms, ...

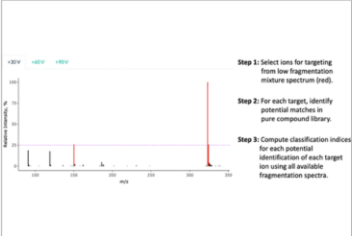
Abstract

Forensic analysis of seized drug evidence often involves determining whether the components of an unknown mixture are illicit compounds. One approach to this task is to screen the evidence using direct analysis in real time mass spectrometry (DART-MS) to make presumptive identifications. This manuscript introduces a new library-search algorithm that enhances presumptive identifications of mixture components using a series of in-source collision-induced dissociation mass spectra collected through DART-MS. The multistage search, titled the Inverted Library-Search Algorithm (ILSA), identifies potential components in a mixture by first searching the lowest fragmentation mass spectrum for target peaks, assuming these peaks are protonated molecules, and then scoring each target peak with possible library matches. As a proof of concept, the ILSA is demonstrated through several example searches of model seized drug mixtures of acetyl fentanyl, benzyl fentanyl, amphetamine, and methamphetamine searched against a small library of select compounds and the freely available NIST DART-MS Forensics Database. Discussion of the search results and several open areas of research to further extend the method are provided. This new approach for presumptive identification provides analysts with refined information about mixture components and will be of immediate importance in forensic analysis using DART-MS. A prototype implementation of the ILSA is available at <https://github.com/asm3-nist/DART-MS-DST>.

KEYWORDS: algorithms, DART-MS, library searching, mass spectrometry, seized drug analysis

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jasms.1c00097>.



Step 1: Select ions for targeting from low fragmentation mixture spectrum (red).

Step 2: For each target, identify potential matches in pure compound library.

Step 3: Compute classification indices for each potential identification of each target ion using all available fragmentation spectra.

Functional research

Functional research



Usable product

Functional research  Usable product

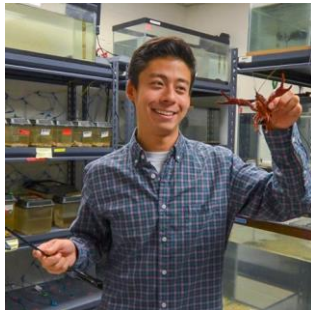
Funding



Expertise



Ruthie
Corzo



Stephen
Tennyson

End-Users

Harris County
Institute of Forensic
Sciences (Texas)



Virginia Department
of Forensic
Sciences



U.S. Customs and
Border Protection
INTERDICT Lab

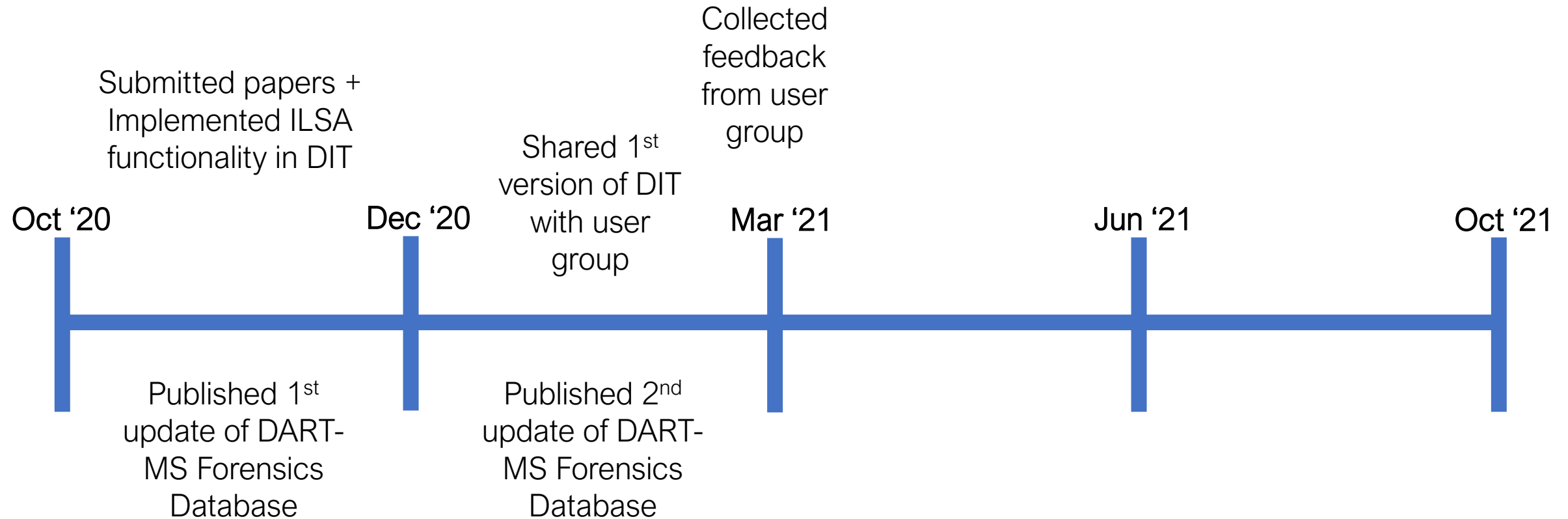


Maryland State Police
Forensic Sciences
Division



Food and Drug
Administration
Forensic Chemistry
Center

Development of the Data Interpretation Tool (DIT)



Survey 1 – Important Features & Bug Report

DART Search Tool Survey

Questions

Responses 7

DART Search Tool Survey

Form description

Your name:

Short answer text

Rate how impactful the inclusion of the following features would be for the way that you analyze data.

No opinion

Not impactful / not...

Somewhat impactf...

Highly impactful / ...

Ability to search sy...

Ability to save a se...

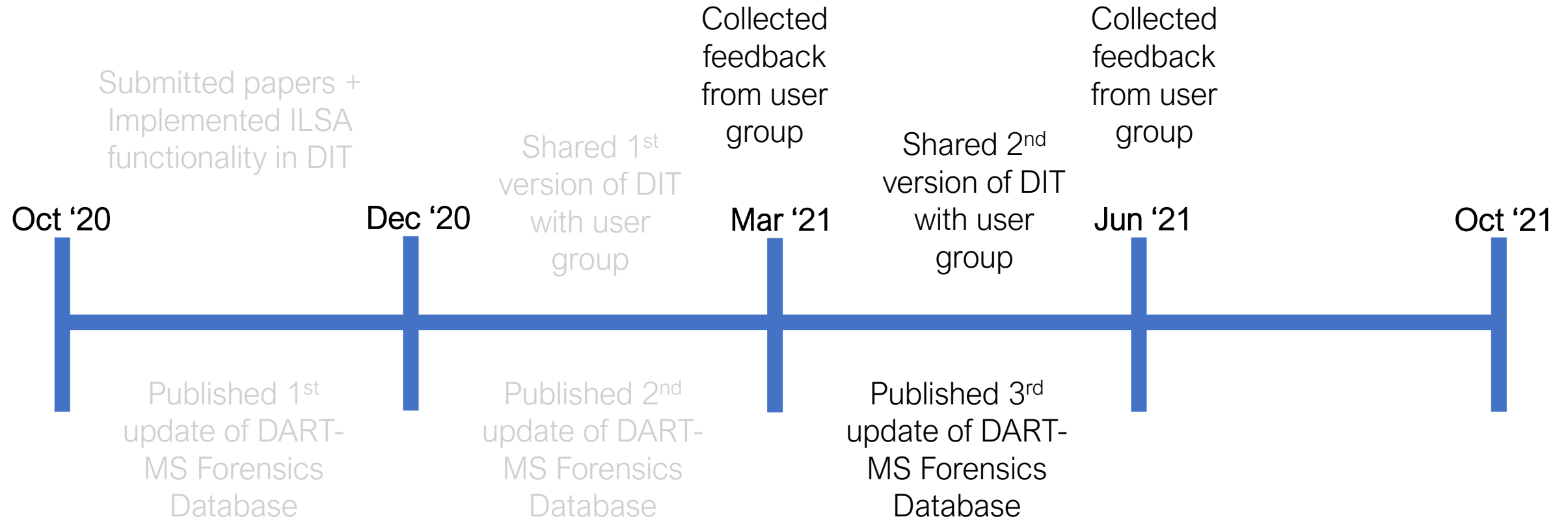
Ranking of search r...

Ability to print spec...

Ability to batch sa...

Ability to overlay / ...

Development of the Data Interpretation Tool (DIT)



Survey 2 – General Comments & Bug Report

Questions Responses 2



DART Search Tool Survey

Form description

Your name:

Short answer text

Please provide any feedback on the new version of the software you have. *

Long answer text

Are there other features that you would like to see added to the DART Search Tool prior to public release in October? *

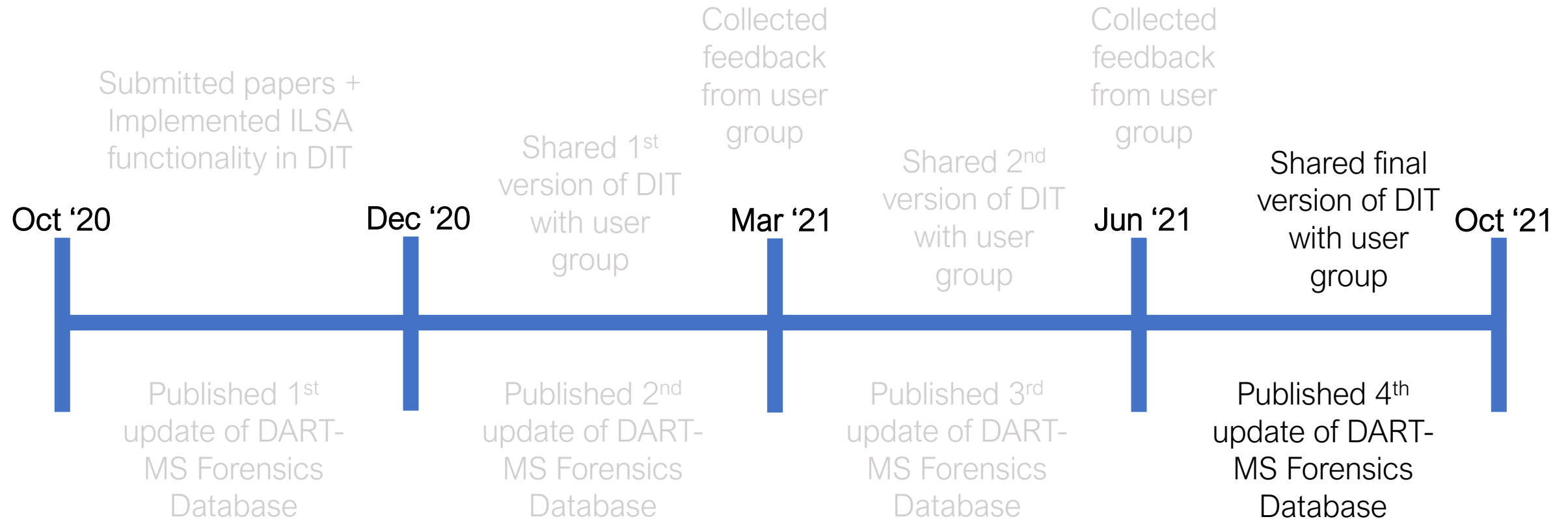
Long answer text

Is there anything missing in the report (Expanded View) that you would like to see added? *

Long answer text



Development of the Data Interpretation Tool (DIT)



DIT

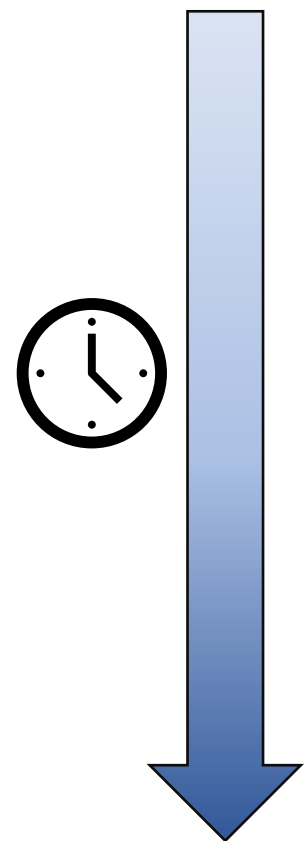
So how does this
thing work?



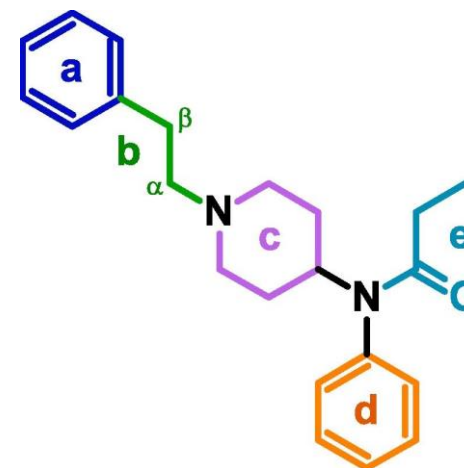
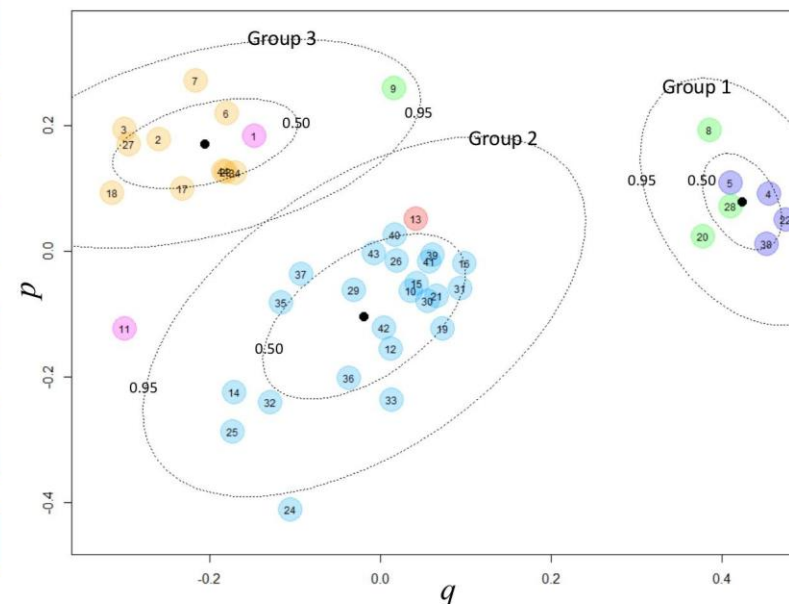
<https://doi.org/10.18434/mds2-2448>



Future Features



- Negative mode library
- Database builder
- Batch processing
- Tools for identification of unknowns
- Datamining



DOI: 10.1016/j.forc.2020.100237



Other Resources – Landing Page

An official website of the United States government [Here's how you know](#)

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PROJECTS/PROGRAMS

Methods, Software Tools, and Resources for Forensics Laboratories with DART-MS or other AI-MS Techniques

Summary

With increasing backlogs and more complex samples, forensic chemistry laboratories need new technologies that rapidly provide accurate analytical results. Many laboratories are adopting Direct Analysis in Real Time Mass Spectrometry (DART-MS) to meet this need. DART-MS enables laboratories to obtain mass spectra, or molecular “fingerprints,” from samples in seconds instead of tens of minutes. Because this technique is highly sensitive, very little of the sample is handled or consumed during analysis. This reduces the risk of accidental exposure when analyzing highly toxic compounds such as fentanyl.

We are developing a suite of methods, software tools, and resources to help forensic laboratories adopt and implement DART-MS and other ambient ionization mass spectrometry (AI-MS) techniques. These include databases, mass spectral search tools, analytical methods, and example validation documents.

The NIST DART-MS Forensics Database 2020, an evaluated collection of mass spectra of seized drugs, cutting agents, and related compounds, is available for [download from the NIST website](#).

UPDATE March 5, 2021: This database has been updated with spectra for an additional 100 compounds, mainly benzodiazepines, cathinones, synthetic cannabinoids, and tryptamines.

This project is part of [NIST's ongoing effort](#) to help labs detect and identify synthetic opioids and other drugs efficiently, reliably, and safely. If you have any questions, please contact %20DARTdata@nist.gov.

DESCRIPTION

The development of methods, software tools, and resources for forensic laboratories using DART-MS or other AI-MS techniques is a collaborative effort between the Surface and Trace Chemical Analysis



ORGANIZATIONS

Material Measurement Laboratory
Materials Measurement Science Division
Surface and Trace Chemical Analysis Group

NIST STAFF

Edward Sisco
Thomas P. Forbes
Elizabeth Robinson
Arun Moorthy

CONTACT

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edward.sisco@nist.gov
(301) 975-2093

PROJECT STATUS

Ongoing

<https://bit.ly/3ry0Kyx>



Other Resources – Validation Package

NIST PUBLIC DATA REPOSITORY 1.5.0 About | Help | Search | Cart 0

Data Publication

Templates for the Implementation of DART-MS for Seized Drug Analysis

Edward Sisco, Amber Burns

Contact: Edward Sisco..

Identifier: doi:10.18434/mds2-2424

Version: 1.0.0 Last modified: 2021-06-14 00:00:00

Description

This dataset includes templates to assist with laboratory implementation of direct analysis in real time mass spectrometry (DART-MS) for seized drug analysis. These templates should be modified as necessary to meet the needs of the particular laboratory.

Certain commercial equipment, instruments, or materials are identified in this paper in order to specify the experimental procedure adequately. Such identification is not intended to imply recommendation or endorsement by NIST, nor is it intended to imply that the materials or equipment identified are necessarily the best available for the purpose.

These opinions, recommendations, findings, and conclusions do not necessarily reflect the views or policies of NIST or the United States Government.

Research Topics:

Forensics: Drugs and toxicology

Subject Keywords:

DART-MS, Forensics, Seized Drug, Implementation, Validation

Data Access

Go To...

Top

Description

Data Access

Record Details

View Metadata

Export JSON

Use

Citation

Fair Use Statement

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Dataset Metrics

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2 unique users

44.72 MB downloaded

Contains:

- Template SOP
- Template Validation Plan
- Validation Data Workup Sheets
- Validation Run Sheets
- Template Maintenance Plan
- Search Lists

Coming Soon: Training

Can help reduce validation time by up to 1-year

<https://doi.org/10.18434/mds2-2424>





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<https://bit.ly/3ry0Kyx>

