FAIR enough?

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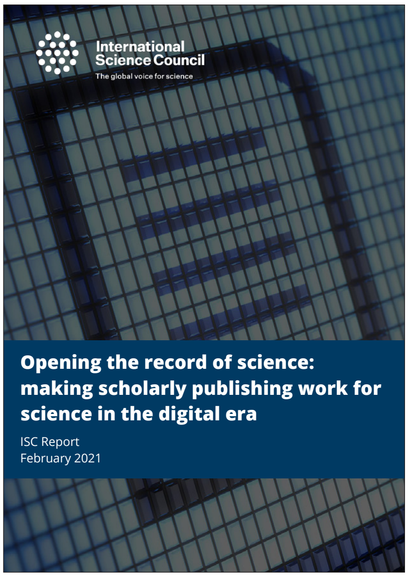
As 2021 arrives with all the promise of beating COVID-19, mixed with the realities of vaccine delays and the threatened breakdown of international consensus on tackling global pandemics, it is a strange feeling to be writing an article about the ability of all to find, access, understand and re-use spectroscopic data. However, effectively and freely sharing information needs to be at the heart of any global effort to beat a pandemic. Although nationalistic tendencies always raise their ugly heads at times of tension, it is only through strong global collaboration and free access to data that we can hope to minimise the damage to our nearest and dearest!

The International Science Council report on Opening the Record of Science

February 2021 has just seen the publication of the ISC Report on Opening the Record of Science: making scholarly publishing work for science in a digital era Figure 1.[1]


International Science Council
The global voice for science

Opening the record of science: making scholarly publishing work for science in the digital era

ISC Report
February 2021

Figure 1. The ISC Report on Opening the Record of Science.

A PDF version of the report is appropriately free to download for those who want to read it in full at https://council.science/wp-content/uploads/2020/06/2020-02-19-Opening-the-record-of-science.pdf. One of the things I like about this report is that it starts with the basics, briefly explaining "Why Science Matters" including the clear statement around the communication of new experiments and new observations publicly communicated through the published record of science. The importance of the publication process is nicely summed up with *"Publication processes that achieve these ends and are adapted to the needs and priorities of the disciplines of science and interdisciplinary collaboration are essential to the function of science as a global public good".*

Who is the ISC?

The International Science Council (ISC) is a non-governmental organisation with a global membership consisting of 40 international scientific Unions and Associations and over 140 national and regional scientific organisations including Academies and Research Councils.

The ISC Report lays down seven Principles for Scientific Publishing around how modern scientific publishing needs to serve us, and which need be durable in the long term:

1) There should be universal open access to the record of science, both for authors and readers.
2) Scientific publications should carry open licenses that allow reuse and text and data mining.

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3) Rigorous and ongoing peer review is essential to the integrity of the record of science.
4) The data/observations underlying a published truth claim should be concurrently published.
5) The record of science should be maintained to ensure open access by future generations.
6) Publication traditions of different disciplines should be respected.
7) Systems should adapt to new opportunities rather than embedding inflexible infrastructures.

For spectroscopists, the Principles around Open Access, Reuse of the Text and the Data and the need to concurrently publish both reinforce the position this column has taken from its inception. We do not have space to go through the whole Report, but it is well worth highlighting their approach to the importance of scientific data, including a very powerful statement that *"Publishing the data is as important, and sometimes more important, than publishing the written text"*. The ISC[2] specifically refer to the FAIR data principles which we have covered in a few articles, including reporting on the IUPAC CODATA Workshop on "Supporting FAIR Exchange of Chemical Data through Standards Development" held in Amsterdam in July 2018,[3] which led to the founding of an IUPAC project in 2019.

IUPAC Project "Development of a standard for FAIR data management of spectroscopic data"

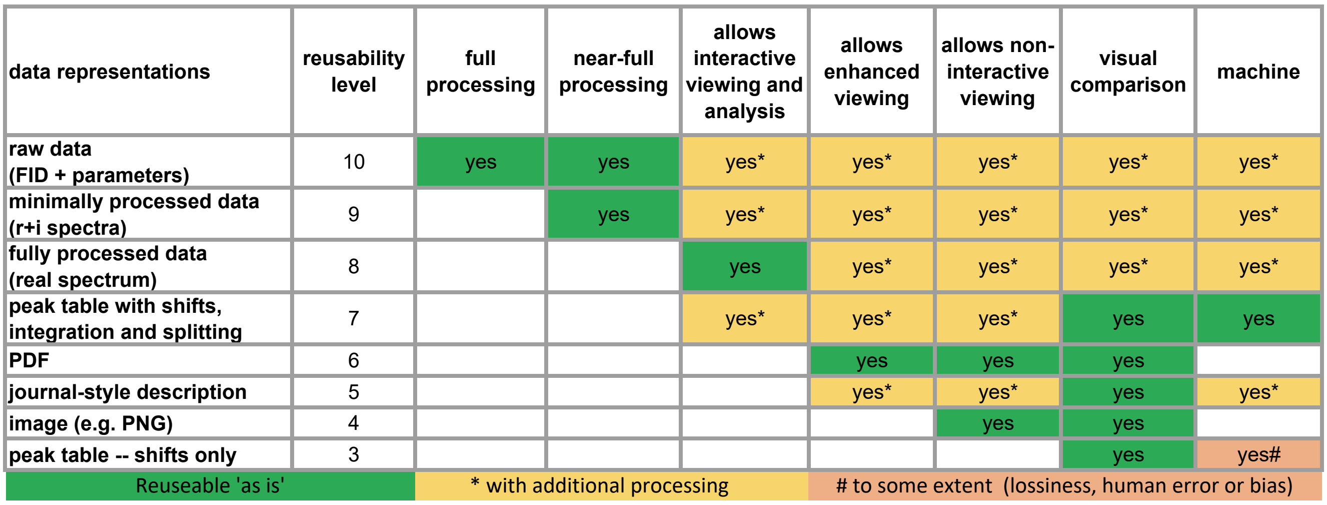
The objective of this project is to apply FAIR data principles to spectroscopic data in the field of chemistry building on IUPAC's extensive expertise in this area. The project will develop standards for the production and dissemination of digital data objects that contain enough spectral data and metadata that they can be:
(a) findable through semantic searches on the web,
(b) available through standard interfaces,
(c) interoperable and transferable between systems and
(d) readable and reusable over time, for both humans and machines.

The IUPAC FAIRSpec Project

Following the Amsterdam workshop, a proposal was submitted to IUPAC for a project to follow up on many of the actions agreed at the workshop. The project, under the title of *Development of a Standard for FAIR Data Management of Spectroscopic Data*, was launched under the auspices of the IUPAC Committee on Publications and Cheminformatics Data Standards right at the start of the COVID epidemic on 18 March 2020 (https://iupac.org/project/2019-031-1-024). The project objectives are shown in the textbox. There has been a lot of work done this year around exactly what role IUPAC, as the standardisation body for chemistry, can play in the FAIR initiative. Clearly IUPAC's ownership and responsibility for many cheminformatics data standards, especially the JCAMP-DX series of spectroscopic data standards, places IUPAC in a special position to respond when the environment for which these standards were originally crafted changes radically. FAIR is just such a ground-breaking change, where the correct storage and accessibility with data processing opportunities means that the "minimum essential metadata" approach of the original standards needs to be brought up to date by standardising the majority of the relevant metadata with a spectroscopic data set. Indeed, this column challenged the spectroscopic community in a relatively recent article called "Are you taking your Metadata seriously?".[4]

The project team have produced a useful figure as they continue to assess the current state of available data collections. It is reproduced in Figure 2 for the example of NMR data.

One advantage of IUPAC projects being able to draw on some of the top innovators in the field is that we have people who are actively *FAIRifying* their own working environments. The

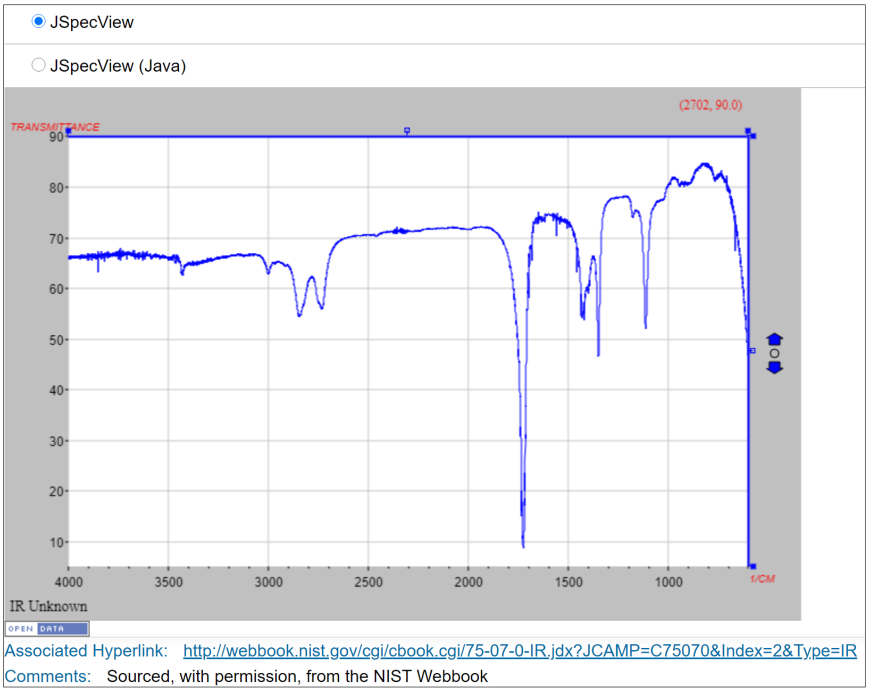


data representations	reusability level	full processing	near-full processing	allows interactive viewing and analysis	allows enhanced viewing	allows non-interactive viewing	visual comparison	machine
raw data (FID + parameters)	10	yes	yes	yes*	yes*	yes*	yes*	yes*
minimally processed data (r+i spectra)	9		yes	yes*	yes*	yes*	yes*	yes*
fully processed data (real spectrum)	8			yes	yes*	yes*	yes*	yes*
peak table with shifts, integration and splitting	7			yes*	yes*	yes*	yes	yes
PDF	6				yes	yes	yes	
journal-style description	5				yes*	yes*	yes	yes*
image (e.g. PNG)	4					yes	yes	
peak table -- shifts only	3						yes	yes#

Reuseable 'as is' | * with additional processing | # to some extent (lossiness, human error or bias)

Figure 2. How reusable are our NMR data in scientific publications.

following sections will show a few examples of how this work is progressing.


● JSpecView

○ JSpecView (Java)

Associated Hyperlink: http://webbook.nist.gov/cgi/cbook.cgi/75-07-0-IR.jdx?JCAMP=C75070&Index=2&Type=IR

Comments: Sourced, with permission, from the NIST Webbook

Figure 3. ChemSpider data example.

Example of accompanying spectroscopic data from ACS Publications: submission of real data (Jeff Lang)

In February of 2020, ACS Publications began a programme to encourage authors to submit their original data for NMR, including free induction decay (FID) files, acquisition data and processing parameters in a zip file as Supporting Information with their manuscript at submission time. Two journals, *The Journal of Organic Chemistry* and *Organic Letters* joined this programme by publishing a joint editorial.[5] The goal was to utilise existing scholarly infrastructure to encourage data publication and gauge support for data publication from the chemistry community.

In the first year of the programme, these two journals published nearly 200 manuscripts with NMR primary data, demonstrating early support. These data are available during manuscript review and receive a DOI upon publication. ACS provided a tool for authors to package the primary data with metadata like structure identifiers, ORCID and funding identifiers. These would better align the resulting package with the FAIR data principles,[6] but authors have preferred to package the data themselves, often forgoing such metadata. Future efforts will focus on the incentives and workflow needed to solicit this metadata in a scalable way.

Example of accompanying spectroscopic data from the Royal Society of Chemistry: ChemSpider (Mark Archibald)

ChemSpider contains approximately 400,000 community-submitted NMR, IR, UV-vis and mass spectra (most come from existing collections or projects). Although this is a significant set of spectra, it represents a tiny percentage of >100 million total ChemSpider records. ChemSpider records can be found by searching on structure, text, experimental or calculated properties, or combinations thereof. However, it is not currently possible to limit a search to only records containing spectra—the user must click through to the record to discover if a spectrum is present. Spectra within ChemSpider records are freely available to all users (Figure 3 is an example ChemSpider entry for acetaldehyde). At present, the ChemSpider APIs do not enable retrieval of spectra, limiting opportunities for machine processing. The majority (~300,000) are in JCAMP format, so they rate highly for reusability. An interactive viewer (JSpecView) allows visualisation of JCAMP spectra on the record page.

Using standardised spectroscopic metadata to facilitate cross-continent data enhancement workflows (Robert Hanson)

In discussions within the project, it has become clear that the chemical structure representation may well be one of the most important "metadata" objects associated with spectra. In an earlier column,[7] a scheme was introduced whereby an NMR spectrum could be predicted (initially ^{1}H, but now ^{13}C as well) and the input could be a name of the compound or a 2D structure drawn with JSME. This relied on the generation of sufficient information that could be forwarded to nmrdb.org at the École Polytechnique Fédérale de Lausanne (EPFL) for processing (Figure 4).[8–10]

Chemical structure metadata, such as connection tables between the atoms or simply the chemical name input, allows the processing to begin, as Table 1 shows.

NMRDB references

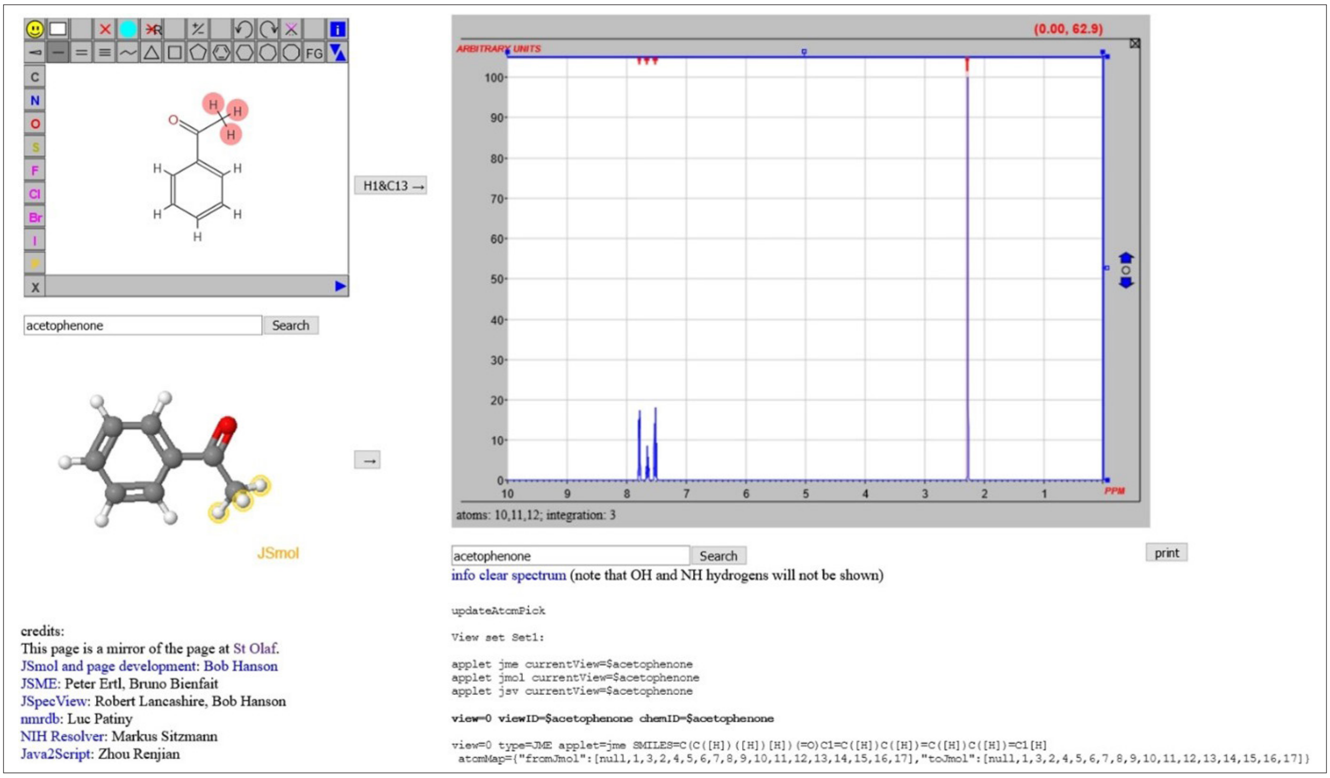
The following services are available, compatible with HTML5, where a SMILES string is embedded in the call.

^{1}H NMR prediction: https://www.nmrdb.org/service.php?name=nmr-1h-prediction&smiles=c1ccccc1CC

^{13}C NMR prediction: https://www.nmrdb.org/service.php?name=nmr-13c-prediction&smiles=c1ccccc1CC

COSY prediction: https://www.nmrdb.org/service.php?name=cosy-prediction&smiles=c1ccccc1CC

HSQC/HMBC prediction: https://www.nmrdb.org/



acetophenone Search

atoms: 10,11,12; integration: 3

acetophenone Search

info clear spectrum (note that OH and NH hydrogens will not be shown)

```
updateAtomPick

View set Set1:

applet jme currentView=$acetophenone
applet jmol currentView=$acetophenone
applet jsv currentView=$acetophenone

view=0 viewID=$acetophenone chemID=$acetophenone

view=0 type=JME applet=jme SMILES=C(C([H])([H])[H])(=O)C1=C([H])C([H])=C([H])C([H])=C1[H]
 atomMap={"fromJmol":[null,1,3,2,4,5,6,7,8,9,10,11,12,13,14,15,16,17],"toJmol":[null,1,3,2,4,5,6,7,8,9,10,11,12,13,14,15,16,17]}
```

credits:
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JSME: Peter Ertl, Bruno Bienfait
JSpecView: Robert Lancashire, Bob Hanson
nmrdb: Luc Patiny
NIH Resolver: Markus Sitzmann
Java2Script: Zhou Renjian

Figure 4. From structures to spectra using trans-continental data processing.

Table 1. Path of information exchange starting from a structure and from a name.

From drawing a structure:	
JSME > SMILES (no H atoms)	local
SMILES > NCI > 2D SDF file (with H atoms)	USA
2D SDF file > JSME for display	
SMILES > NCI > 3D SDF file	USA
From typing a name:	
name > NCI > 2D SDF file (with H atoms)	USA
2D SDF file > JSME for display	local
name > NCI > 3D SDF file	USA
Then from either method:	
3D SDF file to JSmol and sent to EPFL	local
Generates modified 3D mol file, sends to Lisbon	Switzerland
Generates chemical shift+coupling+atom correlation matrix, sent to EPFL	Portugal
EPFL applies a second-order coupling algorithm and line broadening then sends spectral data, assignment and (modified) 3D mol file	Switzerland
2D and two 3D model atom numbering is reconciled using fully elaborated SMILES matching.* Annotated JCAMP-DX file and 3D mol displayed. Interactive atom/peak selection is enabled.	local

*see https://chemapps.stolaf.edu/jmol/jsmol/correlate.htm

service.php?name=hmbc-prediction&smiles=c1ccccc1CC

All predictions:
https://www.nmrdb.org/service.php?name=all-predictions&smiles=c1ccccc1CC

^{1}H NMR prediction was possible thanks to the tool of the FCT-Universidade NOVA de Lisboa developed by Yuri Binev and Joao Aires-de-Sousa.[11]

Incorporating FAIR principles into undergraduate teaching (Henry Rzepa)

As a final example, Henry Rzepa has been developing a novel approach to capturing and disseminating NMR spectroscopic data, which incorporates the basic FAIR principles into an undergraduate student experiment illustrating the synthesis of an organic ester from carboxylic acid and phenolic components.[12]

Each student in a year class is assigned a different combination of reactants, chosen so that the resulting synthesis produces a new-to-science molecule. Following workup, the student submits the sample for NMR analysis and the resulting instrument dataset is acquired/processed to produce a spectrum from the raw FID. The students then participate in group analysis of their individual spectra.

Finally, the student moves to publishing the primary instrumental data in a FAIRsharing data repository[13–14] in the form of both a ZIP archive and processed versions also containing an annotated spectrum (MestreNova archive + JCAMP-DX). The student adds further core metadata to the record and initiates workflows which include generating a chemical identifier (InChI string and key) and a free-to-use MestreNova dataset Access license.[15]

Publication produces a metadata record registered against a persistent identifier (DOI),[16] the latter eventually appearing in the student's ORCID researcher profile. The metadata has sufficient information to allow a variety of complex Finding searches to be undertaken[12] and includes Access information allowing potentially unsupervised machine Interoperation and Reuse of the data for e.g. further AI-based spectral analysis.[12]

Conclusions

So, we already do have some good examples of interoperability between diverse systems, but, as you can see from the examples above, they are pretty much all reliant on the developers' knowledge of the specifics of the raw spectroscopic data sets they receive, as opposed to being able to call on standardised definitions for the metadata in spectroscopy outside of the limited use in JCAMP-DX standards.

Everyone please, stay safe!

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