Complementary classification of solid oral dosage forms in ambient conditions by desorption electrospray ionization mass spectrometry and transmission Raman spectroscopy

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Abstract

Discrepancies or defects in active ingredients, excipients and coatings that form solid oral dosage forms can both impact product quality and provide hallmarks of off-brand or counterfeit products. There is therefore a need for rapid and continuous analytical techniques that can assess and classify product differences of intact samples at- or near the production line, or in analytical labs, ideally without resorting to product dissolution.

Here we test the ability of two rapid ambient chemical characterization methods to discriminate between solid dosage forms: desorption electrospray ionization mass spectrometry and transmission Raman spectroscopy. These two techniques are highly complementary, offering greater sensitivity to the analysis of the surface and the tablet bulk, respectively. The data sets generated were then used to test a variety of classification algorithms including linear discriminate analysis, tree-based methods, a simple neural network, and support vector machines (SVM). The highest performing algorithms for DESI-MSI were the SVM, with an additional performance boost when used with a polynomial kernel. For transmission Raman data, a linear discriminant analysis (LDA) model was found to be the most effective.

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The rest of this document is a full list of formatting elements/features supported by Manubot. Compare the input (.md files in the /content directory) to the output you see below.

Basic formatting

Bold text

Semi-bold text

Centered text

Right-aligned text

Italic text

Combined italics and bold

Strikethrough

- 1. Ordered list item
- 2. Ordered list item
 - a. Sub-item
 - b. Sub-item
 - i. Sub-sub-item
- 3. Ordered list item
 - a. Sub-item
- · List item
- List item
- List item

subscript: H₂O is a liquid

superscript: 2¹⁰ is 1024.

unicode superscripts⁰¹²³⁴⁵⁶⁷⁸⁹

unicode subscripts₀₁₂₃₄₅₆₇₈₉

A long paragraph of text. Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip ex ea commodo consequat. Duis aute irure dolor in reprehenderit in voluptate velit esse cillum dolore eu fugiat nulla pariatur. Excepteur sint occaecat cupidatat non proident, sunt in culpa qui officia deserunt mollit anim id est laborum.

Putting each sentence on its own line has numerous benefits with regard to <u>editing</u> and <u>version</u> <u>control</u>.

Line break without starting a new paragraph by putting two spaces at end of line.

Document organization

Document section headings:

Heading 1

Heading 2

Heading 3

Heading 4

Heading 5

Heading 6



Horizontal rule:

Heading 1's are recommended to be reserved for the title of the manuscript.

Heading 2's are recommended for broad sections such as Abstract, Methods, Conclusion, etc.

Heading 3's and Heading 4's are recommended for sub-sections.

Links

Bare URL link: https://manubot.org

<u>Long link with lots of words and stuff and junk and bleep and blah and stuff and other stuff and more stuff yeah</u>

Link with text

Link with hover text

Link by reference

Citations

Citation by DOI [1].

Citation by PubMed Central ID [2].

Citation by PubMed ID [3].

Citation by Wikidata ID [4].

Citation by ISBN [5].

Citation by URL [6].

Citation by alias [7].

Multiple citations can be put inside the same set of brackets [1,5,7]. Manubot plugins provide easier, more convenient visualization of and navigation between citations [2,3,7,8].

Citation tags (i.e. aliases) can be defined in their own paragraphs using Markdown's reference link syntax:

Referencing figures, tables, equations

Figure 1

Figure 2

```
Figure 3

Figure 4

Table 1

Equation 1

Equation 2
```

Quotes and code

Quoted text

Quoted block of text

Two roads diverged in a wood, and I—I took the one less traveled by, And that has made all the difference.

Code in the middle of normal text, aka inline code.

Code block with Python syntax highlighting:

```
from manubot.cite.doi import expand_short_doi

def test_expand_short_doi():
    doi = expand_short_doi("10/c3bp")
    # a string too long to fit within page:
    assert doi == "10.25313/2524-2695-2018-3-vliyanie-enhansera-copia-i-
        insulyatora-gypsy-na-sintez-ernk-modifikatsii-hromatina-i-
        svyazyvanie-insulyatornyh-belkov-vtransfetsirovannyh-geneticheskih-
        konstruktsiyah"
```

Code block with no syntax highlighting:

```
Exporting HTML manuscript
Exporting DOCX manuscript
Exporting PDF manuscript
```

Figures



Figure 1: A square image at actual size and with a bottom caption. Loaded from the latest version of image on GitHub.



Figure 2: An image too wide to fit within page at full size. Loaded from a specific (hashed) version of the image on GitHub.



Figure 3: A tall image with a specified height. Loaded from a specific (hashed) version of the image on GitHub.



Figure 4: A vector .svg image loaded from GitHub. The parameter sanitize=true is necessary to properly load SVGs hosted via GitHub URLs. White background specified to serve as a backdrop for transparent sections of the image.

Tables

Table 1: A table with a top caption and specified relative column widths.

Bowling Scores	Jane	John	Alice	Bob
Game 1	150	187	210	105
Game 2	98	202	197	102
Game 3	123	180	238	134

Table 2: A table too wide to fit within page.

	Digits 1-33	Digits 34-66	Digits 67-99	Ref.
р	3.141592653589 8462643383279			I niday org
е	2.718281828459 5360287471352			nasa gov

 Table 3: A table with merged cells using the attributes plugin.

	Colors		
Size	Text Color	Background Color	
big	blue	orange	
small	black	white	

Equations

A LaTeX equation:

$$\int_0^\infty e^{-x^2} dx = \frac{\sqrt{\pi}}{2} \tag{1}$$

An equation too long to fit within page:

$$x = a + b + c + d + e + f + g + h + i + j + k + l + m + n + o + p + q + r + s + t + u + v + w + x + y + z + 1 + 2 + 3 + 4 + 5 + 6 + 7 + 8 + 9$$
(2)

Special

▲ WARNING The following features are only supported and intended for .html and .pdf exports. Journals are not likely to support them, and they may not display correctly when converted to other formats such as .docx .

LINK STYLED AS A BUTTON

Adding arbitrary HTML attributes to an element using Pandoc's attribute syntax:

Manubot Manubot Manubot Manubot Manubot. Manubot Manubot Manubot Manubot. Manubot. Manubot Manubot. Manubot. Manubot. Manubot. Manubot.

Adding arbitrary HTML attributes to an element with the Manubot attributes plugin (more flexible than Pandoc's method in terms of which elements you can add attributes to):

Manubot Manubot.

Available background colors for text, images, code, banners, etc:

white lightgrey grey darkgrey black lightred lightyellow lightgreen lightblue lightpurple red orange yellow green blue purple

Using the Font Awesome icon set:



Light Grey Banner
useful for general information - manubot.org

1 Blue Banner

useful for important information - manubot.org

♦ Light Red Banner useful for *warnings* - <u>manubot.org</u>

References

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