**1 Background**

At the [MSACL](https://www.msacl.org/) conference Dr. Keith Baggerly from MD Anderson Cancer Centre’s Bioformatics and Computational Biology Group spoke about the importance of reproducible research using the Duke University ovarian cancer biomarker scandal as a backdrop. The talk…was…incredible and illustrated how easy it is to introduce catastrophic errors into your research papers through the use of GUI analytical tools. I urge everyone in our field to watch similar talks from Keith discussing biomarker analysis in mass spectrometric proteomic data and microarray data. I were then discussing how to make a submission in the field of clinical chemistry that is reproducible. While this article will will serve as a guide for those who know a little about these and give you a working YAML header and get the citations and cross-references correct.

**2 Overhead**

**2.1 YAML**

RMarkdown articles require a [YAML](https://en.wikipedia.org/wiki/YAML) header to instruct R Markdown how to process your article. This is the YAML code that worked for me. I am sure there are other ways to do this:

---

title: "Reproducible Research: Write your Clinical Chemistry paper using R Markdown"

author:

- Daniel Holmes, MD

date: "February 04, 2018"

documentclass: "article"

header-includes:

- \usepackage{amsmath}

output:

#bookdown::pdf\_document2:

#bookdown::word\_document2

bookdown::html\_document2:

toc: no

pandoc\_args: [

"--csl", "clinical-chemistry.csl" , "--citation-abbreviations", "abbreviations.json"

]

bibliography: bibliography.bib

abstract: |

\*\*Background:\*\* Put

\*\*Methods:\*\* Your

\*\*Results:\*\* Abstract

\*\*Conclusions:\*\* Here

keywords: "bla bla bla"

---

Indenting and spacing really matter a lot in YAML so don’t mess with them. You can generate PDF, MS Word or HTML output as needed by uncommenting and commenting out the output type as appropriate in the YAML above.

**2.2 CSL Files**

CSL files take care of citation formatting for you. Depending on what journal you are making submission to, you will need a different .csl file. They exist for every conceivable journal. In the world of non-reproducible reports, this process is taken care of by reference managers in GUI word processors but since GUI word processors do not produce reproducible research, we must break up with them.

From the YAML, you will see that you need a file called “clinical-chemistry.csl”. Put this file in the same folder as your R Markdown file. The Clinical Chemistry .csl depends on the .csl file of the American Association for Cancer Research but it will be downloaded for you on the fly

Clinical-Chemistry.CSL

|  |
| --- |
| <?xml version="1.0" encoding="utf-8"?> |
|  | <style xmlns="http://purl.org/net/xbiblio/csl" version="1.0" default-locale="en-US"> |
|  | <info> |
|  | <title>Clinical Chemistry</title> |
|  | <id>http://www.zotero.org/styles/clinical-chemistry</id> |
|  | <link href="http://www.zotero.org/styles/clinical-chemistry" rel="self"/> |
|  | <link href="http://www.zotero.org/styles/american-association-for-cancer-research" rel="independent-parent"/> |
|  | <link href="http://www.clinchem.org/site/info\_ar/info\_authors.xhtml#References" rel="documentation"/> |
|  | <category citation-format="numeric"/> |
|  | <category field="medicine"/> |
|  | <issn>0009-9147</issn> |
|  | <eissn>1530-8561</eissn> |
|  | <summary>While not one of the AACR journals, does appear to follow the same style</summary> |
|  | <updated>2012-09-09T21:58:08+00:00</updated> |
|  | <rights license="http://creativecommons.org/licenses/by-sa/3.0/">This work is licensed under a Creative Commons Attribution-ShareAlike 3.0 License</rights> |
|  | </info> |
|  | </style> |

American Association .CSL File

|  |
| --- |
| <?xml version="1.0" encoding="utf-8"?> |
|  | <style xmlns="http://purl.org/net/xbiblio/csl" class="in-text" version="1.0" demote-non-dropping-particle="sort-only" page-range-format="minimal" default-locale="en-US"> |
|  | <info> |
|  | <title>American Association for Cancer Research</title> |
|  | <title-short>AACR</title-short> |
|  | <id>http://www.zotero.org/styles/american-association-for-cancer-research</id> |
|  | <link href="http://www.zotero.org/styles/american-association-for-cancer-research" rel="self"/> |
|  | <link href="http://www.zotero.org/styles/vancouver" rel="template"/> |
|  | <link href="http://www.aacrjournals.org/site/InstrAuthors/ifora.xhtml#references" rel="documentation"/> |
|  | <author> |
|  | <name>Charles Parnot</name> |
|  | <email>charles.parnot@gmail.com</email> |
|  | <uri>http://twitter.com/cparnot</uri> |
|  | </author> |
|  | <category citation-format="numeric"/> |
|  | <category field="medicine"/> |
|  | <summary>Parent style for AACR's journals</summary> |
|  | <updated>2013-02-04T12:00:00+00:00</updated> |
|  | <rights license="http://creativecommons.org/licenses/by-sa/3.0/">This work is licensed under a Creative Commons Attribution-ShareAlike 3.0 License</rights> |
|  | </info> |
|  | <locale xml:lang="en"> |
|  | <date form="text" delimiter=" "> |
|  | <date-part name="year"/> |
|  | <date-part name="month" form="short" strip-periods="true"/> |
|  | <date-part name="day"/> |
|  | </date> |
|  | <terms> |
|  | <term name="retrieved">available</term> |
|  | <term name="section" form="short">sect.</term> |
|  | </terms> |
|  | </locale> |
|  | <macro name="author"> |
|  | <names variable="author"> |
|  | <name sort-separator=" " initialize-with="" name-as-sort-order="all" delimiter=", " delimiter-precedes-last="always"/> |
|  | <label form="long" prefix=", "/> |
|  | <substitute> |
|  | <names variable="editor"/> |
|  | </substitute> |
|  | </names> |
|  | </macro> |
|  | <macro name="editor"> |
|  | <group delimiter=": "> |
|  | <choose> |
|  | <if type="chapter paper-conference" match="any"> |
|  | <text term="in" text-case="capitalize-first"/> |
|  | </if> |
|  | </choose> |
|  | <names variable="editor" suffix="."> |
|  | <name sort-separator=" " initialize-with="" name-as-sort-order="all" delimiter=", " delimiter-precedes-last="always"/> |
|  | <label form="long" prefix=", "/> |
|  | </names> |
|  | </group> |
|  | </macro> |
|  | <macro name="publisher"> |
|  | <group delimiter=": " suffix=";"> |
|  | <choose> |
|  | <if type="thesis"> |
|  | <text variable="publisher-place" prefix="[" suffix="]"/> |
|  | </if> |
|  | <else> |
|  | <text variable="publisher-place"/> |
|  | </else> |
|  | </choose> |
|  | <text variable="publisher"/> |
|  | </group> |
|  | </macro> |
|  | <macro name="access"> |
|  | <choose> |
|  | <if variable="URL"> |
|  | <group delimiter=": "> |
|  | <group delimiter=" "> |
|  | <text term="retrieved" text-case="capitalize-first"/> |
|  | <text term="from"/> |
|  | </group> |
|  | <text variable="URL"/> |
|  | </group> |
|  | </if> |
|  | </choose> |
|  | </macro> |
|  | <macro name="accessed-date"> |
|  | <choose> |
|  | <if variable="URL"> |
|  | <group prefix="[" suffix="]" delimiter=" "> |
|  | <text term="cited"/> |
|  | <date variable="accessed" form="text"/> |
|  | </group> |
|  | </if> |
|  | </choose> |
|  | </macro> |
|  | <macro name="container-title"> |
|  | <choose> |
|  | <if type="article-journal article-magazine chapter paper-conference article-newspaper" match="any"> |
|  | <group suffix="." delimiter=" "> |
|  | <text variable="container-title" form="short" strip-periods="true"/> |
|  | <choose> |
|  | <if variable="URL"> |
|  | <text term="internet" prefix="[" suffix="]" text-case="capitalize-first"/> |
|  | </if> |
|  | </choose> |
|  | </group> |
|  | <text macro="edition" prefix=" "/> |
|  | </if> |
|  | <!--add event-name and event-place once they become available--> |
|  | <else-if type="bill legislation" match="any"> |
|  | <group delimiter=", "> |
|  | <group delimiter=". "> |
|  | <text variable="container-title" form="short"/> |
|  | <group delimiter=" "> |
|  | <text term="section" form="short" text-case="capitalize-first"/> |
|  | <text variable="section"/> |
|  | </group> |
|  | </group> |
|  | <text variable="number"/> |
|  | </group> |
|  | </else-if> |
|  | <else> |
|  | <text variable="container-title" suffix="." form="short"/> |
|  | </else> |
|  | </choose> |
|  | </macro> |
|  | <macro name="title"> |
|  | <text variable="title"/> |
|  | <choose> |
|  | <if type="article-journal article-magazine chapter paper-conference article-newspaper" match="none"> |
|  | <choose> |
|  | <if variable="URL"> |
|  | <text term="internet" prefix=" [" suffix="]" text-case="capitalize-first"/> |
|  | </if> |
|  | </choose> |
|  | <text macro="edition" prefix=". "/> |
|  | </if> |
|  | </choose> |
|  | <choose> |
|  | <if type="thesis"> |
|  | <text variable="genre" prefix=" [" suffix="]"/> |
|  | </if> |
|  | </choose> |
|  | </macro> |
|  | <macro name="edition"> |
|  | <choose> |
|  | <if is-numeric="edition"> |
|  | <group delimiter=" "> |
|  | <number variable="edition" form="ordinal"/> |
|  | <text term="edition" form="short"/> |
|  | </group> |
|  | </if> |
|  | <else> |
|  | <text variable="edition" suffix="."/> |
|  | </else> |
|  | </choose> |
|  | </macro> |
|  | <macro name="date"> |
|  | <choose> |
|  | <if type="article-journal article-magazine article-newspaper" match="any"> |
|  | <group suffix=";" delimiter=" "> |
|  | <date variable="issued"> |
|  | <date-part name="year"/> |
|  | </date> |
|  | <text macro="accessed-date"/> |
|  | </group> |
|  | </if> |
|  | <else-if type="bill legislation" match="any"> |
|  | <group delimiter=", "> |
|  | <date variable="issued" delimiter=" "> |
|  | <date-part name="month" form="short" strip-periods="true"/> |
|  | <date-part name="day"/> |
|  | </date> |
|  | <date variable="issued"> |
|  | <date-part name="year"/> |
|  | </date> |
|  | </group> |
|  | </else-if> |
|  | <else-if type="report"> |
|  | <date variable="issued" delimiter=" "> |
|  | <date-part name="year"/> |
|  | <date-part name="month" form="short" strip-periods="true"/> |
|  | </date> |
|  | </else-if> |
|  | <else> |
|  | <group suffix="."> |
|  | <date variable="issued"> |
|  | <date-part name="year"/> |
|  | </date> |
|  | <text macro="accessed-date" prefix=" "/> |
|  | </group> |
|  | </else> |
|  | </choose> |
|  | </macro> |
|  | <macro name="pages"> |
|  | <choose> |
|  | <if type="article-journal article-magazine article-newspaper" match="any"> |
|  | <text variable="page" prefix=":"/> |
|  | </if> |
|  | <else> |
|  | <group prefix=" " delimiter=" "> |
|  | <label variable="page" plural="never"/> |
|  | <text variable="page"/> |
|  | </group> |
|  | </else> |
|  | </choose> |
|  | </macro> |
|  | <macro name="journal-location"> |
|  | <choose> |
|  | <if type="article-journal article-magazine" match="any"> |
|  | <text variable="volume"/> |
|  | </if> |
|  | </choose> |
|  | </macro> |
|  | <macro name="report-details"> |
|  | <choose> |
|  | <if type="report"> |
|  | <text variable="number" prefix="Report No.: "/> |
|  | </if> |
|  | </choose> |
|  | </macro> |
|  | <citation collapse="citation-number"> |
|  | <sort> |
|  | <key variable="citation-number"/> |
|  | </sort> |
|  | <layout prefix="(" suffix=")" delimiter=","> |
|  | <text variable="citation-number"/> |
|  | </layout> |
|  | </citation> |
|  | <bibliography et-al-min="7" et-al-use-first="6" second-field-align="flush"> |
|  | <layout> |
|  | <text variable="citation-number" suffix=". "/> |
|  | <group delimiter=". " suffix=". "> |
|  | <text macro="author"/> |
|  | <text macro="title"/> |
|  | </group> |
|  | <group delimiter=" " suffix=". "> |
|  | <text macro="editor"/> |
|  | <text macro="container-title"/> |
|  | <text macro="publisher"/> |
|  | <group> |
|  | <text macro="date"/> |
|  | <text macro="journal-location"/> |
|  | <text macro="pages"/> |
|  | </group> |
|  | </group> |
|  | <text macro="report-details" suffix=". "/> |
|  | <text macro="access"/> |
|  | </layout> |
|  | </bibliography> |
|  | </style> |

**2.3 BibTeX**

Reference management in R Markdown is taken care of by BibTeX. You can see from the YAML that we need a bibliography text file called “bibliography.bib”. You can name it whatever you like but you will need to change the YAML accordingly. In any case, any citation you intend to make will have to be in the .bib file.

Below is my bibliography.bib file. I put it in the same folder as my R Markdown file. You make a .bib file using a text file editor (or RStudio) by cutting and pasting the BibTex citations from [Google Scholar](http://labrtorian.com/2018/02/05/reproducible-research-write-your-clinical-chemistry-paper-using-r/scholar.google.com)

@article{shannon2017,

title={Contribution of symmetric dimethylarginine to GFR decline in pediatric chronic kidney disease},

author={Brooks, Ellen R and Haymond, Shannon and Rademaker, Alfred and Pierce, Christopher and Helenowski, Irene and Passman, Rod and Vicente, Faye and Warady, Bradley A and Furth, Susan L and Langman, Craig B},

journal={Pediatric Nephrology},

pages={1--8},

year={2017},

publisher={Springer}

}

@article{li2017wellness,

title={Wellness Initiatives: Benefits and Limitations},

author={Li, Michelle and Diamandis, Eleftherios P and Paneth, Nigel and Yeo, Kiang-Teck J and Vogt, Henrik and Master, Stephen R},

journal={Clinical Chemistry},

volume={63},

number={6},

pages={1063--1068},

year={2017},

publisher={Clinical Chemistry}

}

@article{holmes2005preanalytical,

title={Preanalytical influences on DPC IMMULITE 2000 intact PTH assays of plasma and serum from dialysis patients},

author={Holmes, Daniel T and Levin, Adeera and Forer, Barry and Rosenberg, Frances},

journal={Clinical Chemistry},

volume={51},

number={5},

pages={915--917},

year={2005},

publisher={Clinical Chemistry}

}

**2.4 Journal Abbreviations**

Now, the fussiest thing I had to do was get the references abbreviating properly. We need an abbreviation database. Fortunately, I could download the abbreviation database from the Web of Science as a .csv file and then convert it to a JSON file. This was Stephen’s idea. I had to deal with a couple of badly behaving characters from some journal titles. This script, if embedded in your document, will download the .csv for you and then make the abbreviation database for you. That way your citations will say, “J Clin Pathol” and not “Journal of Clinical Pathology” etc.

```{r, echo = FALSE}

library(RJSONIO)

if(!file.exists("abbreviations.json")){

download.file("<https://ndownloader.figshare.com/files/5212423>","wos\_abbrev\_table.csv")

abbrev <- read.csv("wos\_abbrev\_table.csv", sep = ";", header = TRUE, stringsAsFactors = FALSE)

abbrev$full <- gsub("\\", "\\\\",abbrev$full, fixed = TRUE)

abbrev.list <- list('default' = list('container-title' = abbrev$abbrev.dots))

names(abbrev.list$default$`container-title`) = abbrev$full

write(toJSON(abbrev.list), "abbreviations.json")

rm(abbrev)

rm(abbrev.list)

}

```

**2.5 Citation Management**

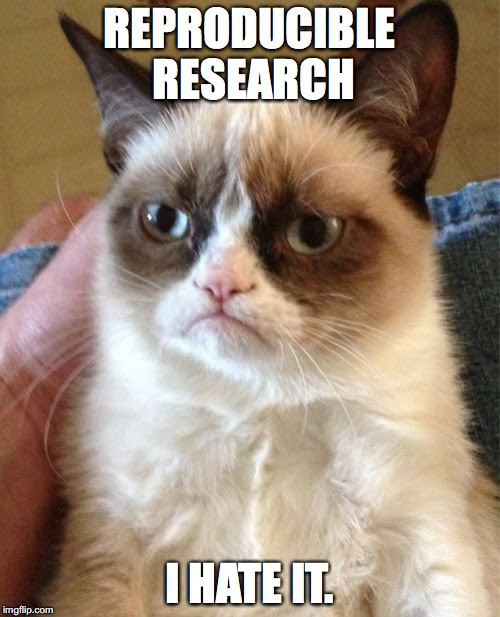
Now we can proceed to cite articles from our .bib file freely inserting syntax like this: [@shannon2017]. Shannon wrote this interesting article on symmetric dimethylarginine (1), Stephen wrote about wellness initiatives with Dr. Diamandis (2) and Dan wrote a paper about PTH when he was a resident (3). That makes for a total of 3 citations in this manuscript. (1–3)

**3 Reporting Your Results**

**3.1 Figures**

You can embed figures in R Markdown as local images or hyperlinks as follows:

![Grumpy Cat does not care about reproducibility](grumpy.jpg)



Grumpy Cat does not care about reproducibility

If you need to do cross-referencing of figures in your document which will change automatically for you if you insert another figure, you can do this by inserting your figure with an R code-chunk and giving the code-chunk a name.

```{r ancient-aliens, fig.height=3, fig.width=2, fig.cap="This is the ancient aliens guy.", echo = FALSE}

knitr::include\_graphics('ancient\_aliens.jpg')

```

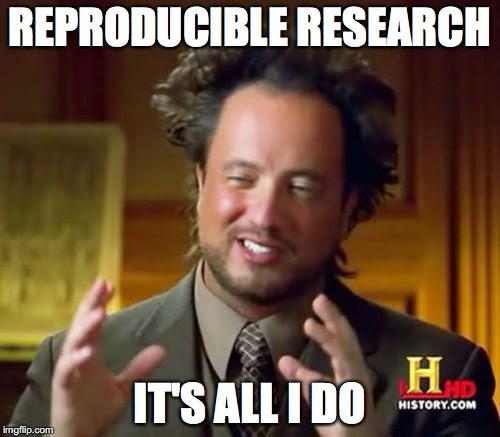


Figure 3.1: This is the ancient aliens guy.

Then you can reference your code chunk using syntax like this: See figure \@ref(fig:ancient-aliens)

and you will automatically create appropriately cross-referenced figures that get automatically numbered like this: See figure [3.1](http://labrtorian.com/2018/02/05/reproducible-research-write-your-clinical-chemistry-paper-using-r/#fig:ancient-aliens). Of course the hallmark of the reproducibility to embed R code right into the document. See for example figure [3.2](http://labrtorian.com/2018/02/05/reproducible-research-write-your-clinical-chemistry-paper-using-r/#fig:example-code)

```{r example-code, fig.cap = "This is a reproducible figure"}

set.seed(10)

x <- runif(100,0,100)

y <- x + rnorm(100,0,0.10)\*x

plot(x,y,

main = "Reproducible Figure",

pch = 16,

col = "blue",

xlab = "Current Method (mmol/L)",

ylab = "New Method (mmol/L)")

abline(lm(y~x), col = "red", pch = 2)

```

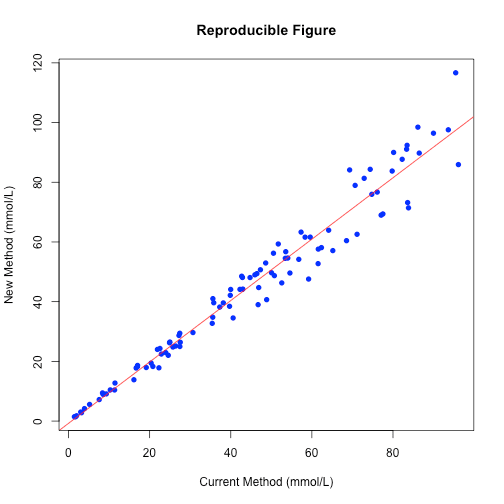


Figure 3.2: This is a reproducible figure

**3.2 Inline Calculations**

When you are reporting your amazing results you can have inline code calculations by syntax that looks like this: &#96r round(median(x),1)&#96 and would result in the median value of \(x\) being reported as 43.9 mmol/L.

**3.3 Tables**

Tables are not a problem either and can be made with the kable() function of the knitr package or with the xtable package. Tables can be crossreferenced analogously to figures.

```{r example-table, echo = FALSE, results = 'asis'}

library(knitr)

library(xtable)

a <- 1:5

b <- 2:6

c <- a\*b

z <- data.frame(a,b,c)

kable(z,

caption = "This is a great table",

col.names = c("First","Second", "Third"))

```

| Table 3.1: This is a great table | | |
| --- | --- | --- |
| **First** | **Second** | **Third** |
| 1 | 2 | 2 |
| 2 | 3 | 6 |
| 3 | 4 | 12 |
| 4 | 5 | 20 |
| 5 | 6 | 30 |

**3.4 Math**

Math works pretty magically using \(\LaTeX\) syntax. For example inline math can be done like so $\sin^2x + \cos^2x = 1$. This will result in: \(\sin^2x + \cos^2x = 1\). And math can also be done as a code block like so:

$$

\oint\_S {E\_n dA = \frac{1}{{\varepsilon \_0 }}} Q\_{inside}

$$

Gauss’ Law says: \[  
\oint\_S {E\_n dA = \frac{1}{{\varepsilon \_0 }}} Q\_{inside}  
\]

Equations can be cross-referenced just like tables and figures.