

1 **MetaR: simple, high-level languages for** 2 **data analysis with the R ecosystem**

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11 **ABSTRACT**

12 Data analysis tools have become essential to the study of biology. Tools available today were constructed with layers of technology developed over decades. Here, we explain how some of the principles used to develop this technology are sub-optimal for the construction of data analysis tools for biologists. In contrast, we applied language workbench technology (LWT) to create a data analysis language, called MetaR, tailored for biologists with no programming experience, as well as expert bioinformaticians and statisticians. A key novelty of this approach is its ability to blend user interface with scripting in such a way that beginners and experts alike can analyze data productively in the same analysis platform. While presenting MetaR, we explain how a judicious use of LWT eliminates problems that have historically contributed to data analysis bottlenecks. These results show that language design with LWT can be a compelling approach for developing intelligent data analysis tools.

13 **Keywords:** Data analysis, Bioinformatics, Language Workbench Technology, JetBrains MPS, Composable R, R language

14 The modern tools of biology often require biologists to rely on software tools for data analysis. For
15 instance, software tools are required for analysis of high-throughput data, for the study of genome-wide
16 gene expression, genetic or epigenetic. Similarly, most fields of biology require specialized software tools
17 for analysis of microscopy, crystallography or other data. Most analysis software is constructed in a very
18 similar manner: writing a program as a collection of text source code that is compiled into one or more
19 executable analysis tools. Despite the evolution of programming languages, encoding programs as text
20 has been a constant since the invention of the first high-level programming language (FORTRAN Backus
21 [1958, 1978]).

22 In this manuscript, we discuss several drawbacks of encoding programs as text that we believe
23 contribute to common challenges encountered by data analysts. Language Workbenches (LWs) with
24 projectional editors offer an alternative to storing source code as text. These approaches were conceived
25 in the 90s Simonyi [1995] and have since led to the development of robust software development
26 environments Dmitriev [2004], Erdweg et al. [2013]. For this study, we used the Meta-Programming
27 System (MPS, <http://jetbrains.com/mps>), a robust and open-source LW to explore whether
28 LW technology (WLT) can help develop improved data analysis tools.

29 One question we were particularly interested in testing was whether we could create an analysis tool
30 that would blend the boundary between programming/scripting languages and graphical user interfaces.
31 Programming languages such as the R language Ihaka and Gentleman [1996] are frequently preferred for
32 data analysis by experts. They have so far been the most flexible and powerful tools for data analysis, but
33 require a steep learning curve. In contrast, beginners tend to prefer data analysis software with a graphical
34 user interface, which are easier to learn, but eventually are found to lack flexibility and extensibility.
35 We reasoned that blending these two types of interfaces into one tool could provide a simpler way for
36 beginners to learn elements of scripting, improve repeatability and reproducibility of their analyses, and
37 increase their productivity.

38 We found that LWT made it straightforward to develop a data analysis tool that blends the distinction
39 between graphical user interface and scripting. If implementation was straightforward, our design of a
40 novel type of analysis tool was an iterative process that benefited from frequent feedback from users of
41 the tool. In this manuscript, we describe the goals of the language, explain how the tool can be used, and
42 highlight the most innovative aspects of the language compared to other tools used for data analysis, such
43 as the R language Ihaka and Gentleman [1996] or electronic notebooks.

44 The initial focus of MetaR was on analysis of RNA-Seq data and the creation of heatmaps, but the
45 tool is general and can be readily extended to support a broad range of data analyses. For instance, we
46 have used MetaR to analyze data in a study of association between the allogeneic score and kidney
47 graft function Mesnard et al. [2015]. We chose to focus on the construction of heatmaps as a use case and
48 illustration for this study because this activity is of interest to many biologists who obtain high-throughput
49 data.

50 Interestingly, we found that both beginners and experts can benefit from blending user interfaces and
51 scripting. Beginners benefit because the MetaR user interface is much simpler to learn than the full R
52 programming language. Expert users benefit because they can develop high-level language elements
53 to simplify repetitive aspects of data analysis in ways that text-based programming languages cannot
54 achieve.

55 LANGUAGE WORKBENCH TECHNOLOGY PRIMER

56 Since many readers may not be familiar with LWT, this section briefly describes how this technology
57 differs from traditional text-based technology.

58 Text-based programming languages are implemented with compilers that internally convert the text
59 representation of the source code into an *abstract syntax tree* (AST), a data structure used when analyzing
60 and transforming programming languages into machine code.

61 In the MPS LW, the AST is also a central data structure, but the parsing elements of the compilers are
62 replaced with a graphical user interface (called a *projectional editor*) that enables users to directly edit the
63 data structure. Where text-based languages are restricted to programs written as text, a projectional editor
64 can support both textual and graphical user interfaces (such as images, buttons, tables or diagrams) Voelter
65 and Solomatov [2010]. Projectional editors can also offer distinct views of the same AST, implemented as
66 alternative editors. Projectional editors keep an AST in memory until the user saves the program. Saving
67 an AST to disk is done using serialization (loading is conversely done via deserialization to memory AST
68 data structures).

69 The choice of serialization rather than encoding with text has a profound consequence. Serialization
70 uniquely identifies the concept for each node in an AST. This method makes it possible to combine AST
71 fragments expressed with different languages, when the concept hierarchy of the languages supports
72 composition. We have presented examples of language composition in Simi and Campagne [2014],
73 Benson and Campagne [2015]. In this manuscript, we extensively use language composition to extend the
74 R language and provide the ability to embed user interfaces into R programs.

75 Abstract Syntax Tree (AST)

76 An AST is a data structure traditionally used by compilers as a step towards generating machine code.
77 In the MPS Language Workbench, an AST is a tree data structure, where nodes of the tree are instances
78 of concepts (in the object-oriented sense). Figure 1 illustrates the notion of AST nodes, concepts and
79 projectional editor.

80 AST concepts may have properties (values of primitive types), children (lists of other nodes they
81 contain), references (links to other nodes defined elsewhere in the AST). An AST has always a root node,
82 which is used to start traversing the tree. In the MPS LW, AST root nodes are stored in models.

83 Languages

84 In the MPS LW, languages are defined as collection of concepts, concept editors (which together implement
85 the user interface for the language), and other language aspects Campagne [2014]. Each language has a
86 name which is used to import, or activate, the language inside a model. After importing a language into a
87 model, it becomes possible to create ASTs with this language in the model. Creating an AST starts with
88 the creation of a root node. Children of the root node are added using the projectional editor. Children of
89 root nodes, properties and references can be edited interactively in the editor.

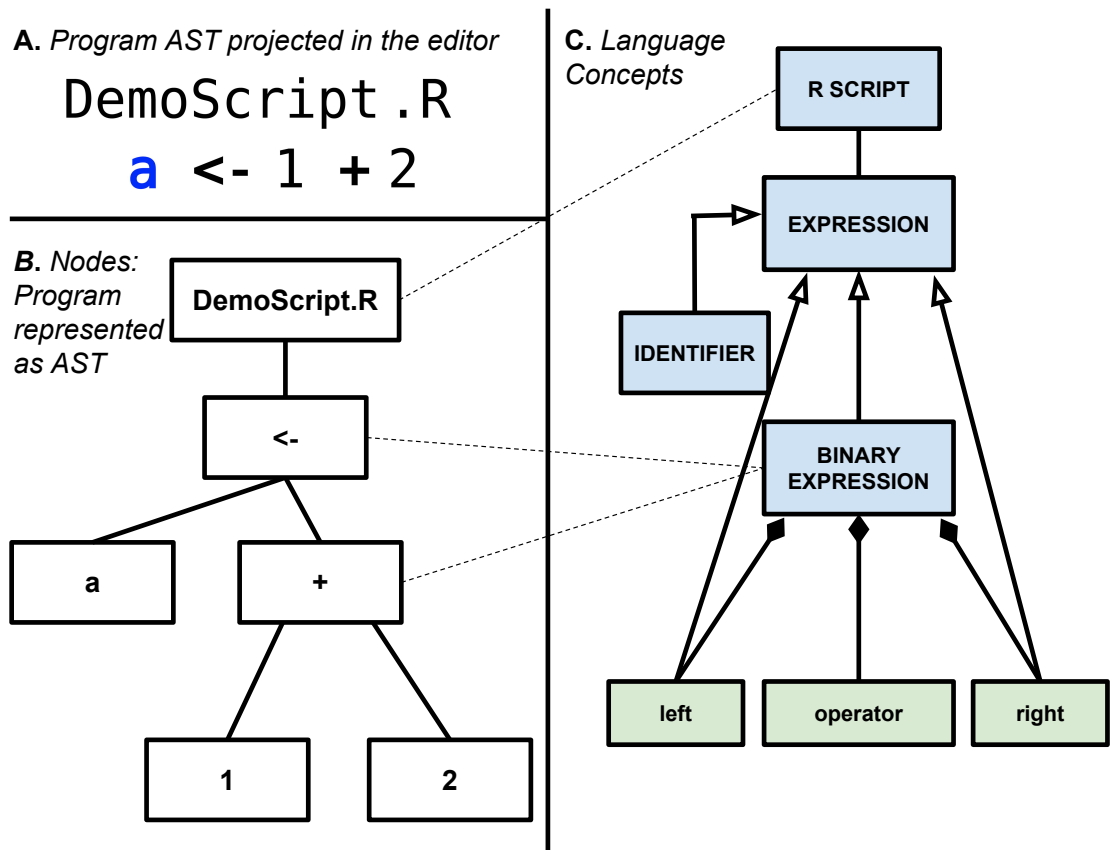


Figure 1. Concepts, Nodes and Projectional Editor. Panel A: Projectional editor showing a simple R script with one assignment expression. Panel B: An abstract syntax tree is shown with nodes that correspond to the program in panel A. Panel C: Language Concepts for the nodes in Panel (B) (shown as blue boxes). Each concept is connected to other concepts with an open-ended arrow to indicate inheritance (e.g., A <- B indicates that B is a sub-concept of A). Green boxes indicate fields of a concept and are connected to the concept that has these fields by a line with a black diamond on the concept that owns the field. This shows that BinaryExpression is a concept that is an Expression and has three fields: left, operator and right. Dotted lines connect nodes to their concept. For instance, the <- and + nodes are instances of BinaryExpression.

90 DESIGN OF A HIGH-LEVEL DATA ANALYSIS LANGUAGE

91 Several decisions must be made when designing a new computational language. Most decisions are driven
92 by design goals. We have designed the MetaR language to address the following goals:

- 93 1. The language should help users who have no knowledge of programming. The goal is to offer a
94 smooth learning curve for beginners used to GUIs. We favor declarative language constructs over
95 flexibility in parts of the language aimed at beginners.
- 96 2. Since a table of data is a frequent input when working with high-throughput data, make Table a first
97 class element of the design. Leverage this element to simplify the annotation of the columns of a
98 table. We rely on the idea that a little formalism (e.g., annotation of table columns) goes a long way
99 to simplify analysis scripts.
- 100 3. Eliminate the need to know the language syntax to help beginners get started quickly. We leverage
101 the MPS LW and its projectional editor to this end (Voelter and Solomatov [2010]). The MPS
102 projectional editor provides interactive features, such as auto-completion, that provide guidance to
103 beginners and experts alike when using the language to develop analyses.
- 104 4. Provide the ability to blend a scripting language with a graphical user interface. We use language
105 composition and the ability of the MPS LW to render nodes with a mix of text and graphical user
106 interface components.
- 107 5. Offer essential data transformations (e.g., joining two tables, taking subsets of rows of a table) via
108 simple, yet composable language elements.
- 109 6. Provide means for experts to use their knowledge of the R language to work-around cases when
110 the MetaR language is not sufficiently expressive to perform a specific analysis. We offer the
111 ability to embed R code inside a MetaR analysis, as well as the ability to write scripts in the R
112 language. In both instances, this variant of the R language supports language composition and
113 enables embedding graphical user interfaces inside script fragments.

114 High-level Design Choices

115 In addition to these goals, the design of MetaR included several strategic choices. We now present these
116 choices and their rationales:

117 **Choice of a Target Language and Runtime System** A language needs a runtime system to execute the
118 code of programs written in the language. A possible choice for a runtime is to target another high-level
119 language (such as Java, or C) but this would require implementing all aspects of data manipulation in the
120 target language. Since the R language (Ihaka and Gentleman [1996]) is widely used for data analysis in
121 biology, we considered using it as a runtime system. Experts biostatisticians and bioinformaticians have
122 developed many R packages that implement advanced analysis for biological high-throughput data. These
123 packages can be used to simplify the implementation of a runtime system for a new data analysis language.
124 We therefore decided that the MetaR language would generate R code in order to take advantage of the
125 packages developed in this language. This decision greatly simplified the implementation of the MetaR
126 language because it removed the need to develop a custom language runtime system.

127 **Data Object Surrogates** MetaR makes extensive use of Data Object Surrogates (DOS, our terminology).
128 A data object surrogate is an object that represents other data (the source data). The surrogate often
129 contains only limited information from the original data source. The DOS contains just enough to facilitate
130 referring to the source data in another context for the purpose of data analysis, but not as much as to
131 represent the entire content of the data source in memory. A good example of DOS is the Table object,
132 which stores information about the columns of a data file. The Table DOS describes the columns of the
133 table, but does not store the data contained in the table. A DOS typically has a name which can be used
134 to refer to the DOS and its source data inside a MetaR model. References to table DOS help users refer
135 to the table as they develop an analysis. Our use of the MPS LW facilitates the creation of DOS. In the
136 MPS LW, we model DOS as concepts of the language. For instance, the Table DOS is represented by a
137 Table concept, whose instances can be created in a model as root nodes. DOS are also used in MetaR to
138 represent plots.

139 **Immutable Data Objects** Many programming languages (of which C, C++, Java, Perl, Python and R
140 are members) make it possible to define variables or objects whose values can be changed (so called
141 mutable variables). While this provides flexibility, it is a frequent source of confusion for beginners until
142 they have developed their own mental model of how program steps modify variable values. During the
143 design of MetaR, we chose to offer immutable objects rather than mutable variables when possible. This
144 makes MetaR analyses easier to reason about because the value of objects cannot be changed after the
145 object is created. Note that design decision does not prevent adding mutable variables to the MetaR
146 language, but simplifies initial learning of the language by complete beginners.

147 **Organization into Languages**

148 We designed MetaR as a collection of MPS languages. The main language, *org.campagnelab.metar* is
149 aimed at beginners with limited computational experience.

150 In the next section, we explain how the MetaR language can be used from the point of view of an
151 end-user. This section also includes highlights of features that differ from the state of the art in data
152 analysis. Please note that exhaustive reference documentation is available elsewhere (see Campagne
153 and Simi [2015]) and the goal of the following paragraphs is to provide a sufficient introduction to data
154 analysis with MetaR that readers can understand the impact of the innovations we tested in developing
155 this tool.

156 **The MetaR Language**

157 **Tables**

158 An example of an immutable DOS is the MetaR Table object. In MetaR, objects of type Table represent
159 tabular data with columns and rows of data. An example of a MetaR Table is shown in Figure 2. A
160 MetaR Table is associated to a data file that contains the actual data of the table in a Tab-Separated Value
161 (TSV). The location of the data file can be specified using Variables (i.e., $\{\text{project}\}$), which offer
162 independence from the local file system structure, and are particularly useful when keeping analyses
163 under source control). A table has columns. Columns have names and types, which determine how data
164 in each column is used. Types of data include string, numeric, boolean and enumeration (a small number
165 of pre-defined categories, such as Male and Female). Figure 2 presents a table of RNA-Seq read counts
166 which was obtained from the Gene Expression Omnibus Seguin-Estevéz et al. [2014] and annotated to
167 enable analysis with MetaR.

168 Annotating a Table consists of two steps: (1) browsing to the file that contains the data. This can be
169 accomplished by clicking on the file dialog button (the little square with . . .) to locate the file. Upon
170 selection of a valid file, the MetaR table node inspects the file and determines column names and types.
171 Names and types are then shown in the Table node (under the Columns heading). (2) Specific columns
172 can be annotated with one or more Column Groups.

173 Users can define arbitrary Column Groups in a different node called “Column Groups and Usages”
174 (shown on the right of Figure 2). If two columns are related, user can define a Group Usage to explicitly
175 document the relation. For instance, in Figure 2, the usage *LPS.Treatment* is defined to indicate that
176 the Column Groups *LPS=no* and *LPS=yes* are two kinds of LPS treatments.

177 Tables and their annotations help users formalize information about data in a table. We find that
178 asking the user to provide such information early on is beneficial because the structure of annotations can
179 be leveraged in other parts of the language to provide intelligent auto-completion, customized for each
180 table of data (for instance, to provide auto-completion for column names when writing expressions, or to
181 select columns to use when joining two tables, examples of intelligent auto-completion is provided in the
182 following sections, see Figure 3).

183 For instance, in the dataset of Seguin-Estevéz et al. [2014], users can indicate which columns contain
184 data for samples that were treated (*LPS=yes*) with lipopolysaccharide (LPS) or not (*LPS=no*). MetaR
185 facilitates the data curation steps of a data analysis project by offering an interactive user interface to
186 help users keep track of annotations. The interface is interactive in several ways: group names can be
187 auto-completed to the groups defined in the “Column Group and Usage” object. Menus are available to
188 add column group annotations to a set of columns that the user has selected. In addition to LPS treatment,
189 Figure 2 shows the *count* annotation, used in an RNA-Seq differential expression analysis to identify
190 which columns contain read counts, the *ID* column group, which uniquely identifies specific rows of the
191 data table and the *heatmap* column group, used to choose which columns groups should be heatmap.

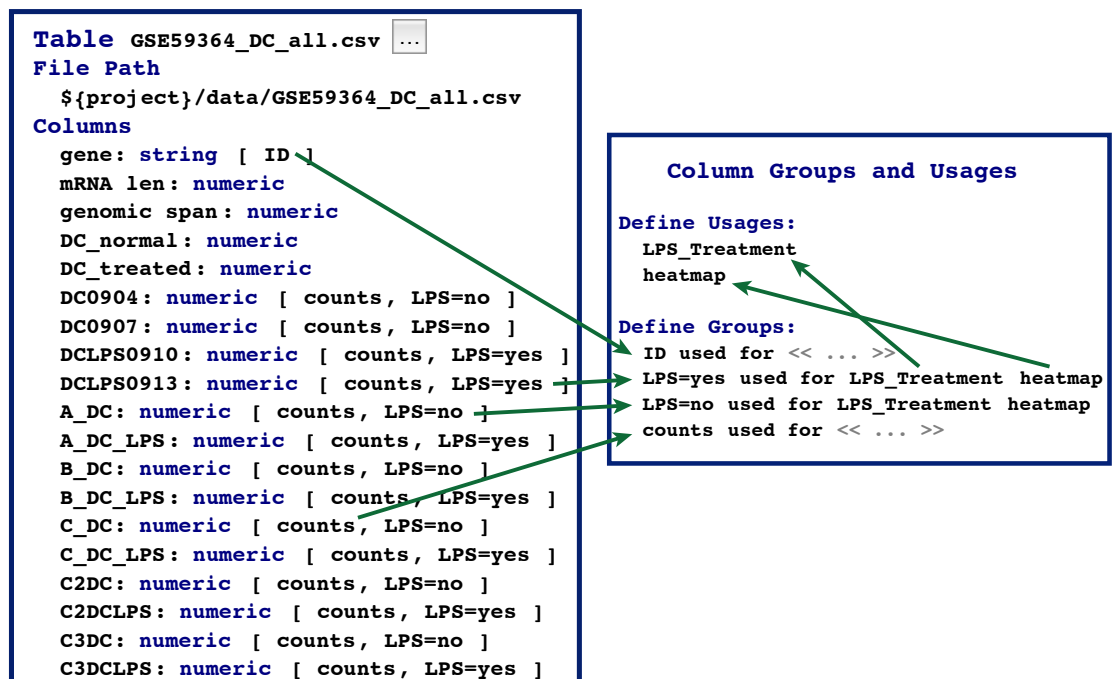


Figure 2. Table and Column Group objects. This figure presents the Table and Column Group objects. Green arrows show some cross-references among nodes of Tables and Column Groups. For instance, the ID group used to annotate the gene column is a reference to the ID group defined under the Column Group and Usage Container.

192 This illustrates that the table annotation mechanism is flexible and can be leveraged by specific statements
 193 of the language, in order to indicate that the statement needs data annotated in a certain way.

194 **Analyses**

195 Analyses make it possible for users to express how data is to be analyzed. Figure 3 presents a MetaR
 196 Analysis node. This analysis is the one we use as a worked example during training sessions we offer at
 197 our institution. The editor of an analysis node offers an interface similar to that of a script in a traditional
 198 editor, but provides a more interactive and intelligent user interface. For instance, auto-completion
 199 is available at every point inside an analysis and suggests possible elements of the language that are
 200 compatible with the context at the cursor position.

201 The user may accept a suggestion and this results in the insertion of the language element at the
 202 position of the cursor. When the context calls for referencing a column of a table, for instance, only
 203 columns of Tables available at this point of the analysis are shown. While it is still possible to make
 204 mistakes when using this interface, mistakes created as a result of typos are less common than in programs
 205 encoded as text, for two reasons:

- 206 • Auto-completion offers a convenient way to set references between objects. Accepting an auto-
 207 completion suggestion helps users avoid typos.
- 208 • Some users choose not to use auto-completion to set references and instead type a referenced node
 209 name. In this case, mis-typed names that cannot be resolved to a valid node are highlighted in red
 210 and in the right margin of the editor (this feature of the MPS LW is available for all languages
 211 developed with the MPS platform). This highlighting draws the attention of the user to the error or
 212 typo. This feature is also important when merging different versions of an analysis placed under
 213 source control or when combining analyses from parts of other analyses (e.g., errors will be clearly
 214 marked after a code fragment is pasted into a new analysis).

215 Auto-completion help is available for the various types of references supported by the MetaR language.
 216 Examples of these can be seen on Figure 3 for tables (whose names are in green), plots (whose names are

Analysis Limma analysis

```

{
  import table GSE59364_DC_all.csv

  subset rows GSE59364_DC_all.csv when true: $(gene) != "Total" -> filtered
  limma voom counts= filtered model: ~ 0 + LPS
  comparing LPS=YES - LPS=NO -> Results

  join ( filtered, Results ) by group ID -> MergedResults
  subset rows MergedResults when true: $(adj.P.Val) < 0.0001 & $(logFC) > 2 | $(logFC) < -2 -> 1% FDR
  heatmap with 1% FDR select data by one or more group LPS=YES, group LPS=NO -> plot HeatmapStyle [
  annotate with 1% FDR ^myOwnTable (manuscript.Limma analysis)
  scale values ^GSE59364_DC_all.csv ^Table (manuscript)
  cluster columns ^MergedResults ^myOwnTable (manuscript.Limma analysis)
  ^Results ^myOwnTable (manuscript.Limma analysis)
  ^filtered ^myOwnTable (manuscript.Limma analysis)
]

multiplot -> PreviewHeatmap [ 1 cols x 1 rows ] 

[ plot ]

  render plot as PDF named "heatmap.pdf"  72dpi
  write Results to "results.tsv" 
}

```

Figure 3. MetaR Analysis. The Analysis node is composed of a list of statements. This analysis works with the table of data presented in Figure 2, removes the row of data where the value *Total* appears in the gene column, performs statistical modeling with Limma Voom to identify genes differentially expressed between LPS treated and control samples, constructs a heatmap and displays the plot as a preview. Finally, the analysis converts the plot to PDF format and writes the joined table (statistics and counts) in the *results.tsv* file.

217 in blue), styles (names shown with a green background and white foreground, such as *HeatmapStyle*), or
 218 Column Group names (shown with a blue grey background and black foreground). Pressing control-B
 219 (or command-B on Mac) with the cursor on these nodes navigates to the destination of the reference (a
 220 menu is also available to help novice users discover this navigation mechanism). References may point to
 221 children nodes defined inside an analysis (e.g., plots), or nodes defined outside the analysis (e.g., tables
 222 and column groups).

223 Importantly, the MetaR user interface can also display buttons and images directly as part of the
 224 language. This feature takes advantage of the ability of the MPS LW to embed arbitrary graphical elements
 225 in the projectional editor. This capability is illustrated in Figure 3 by the “Hide Preview” button and by
 226 the heatmap image shown immediately below the *multiplot* keyword (pressing this button hides the
 227 plot preview).

228 The level of interactivity provided by the MetaR user interface is best conveyed by watching video
 229 recordings of its use. We provide training videos at <http://metaR.campagnelab.org> that help
 230 illustrate how much more interactive the MetaR language is compared to other languages commonly used
 231 for data analysis.

232 Language Composition and Micro-Languages

233 Since MetaR is implemented as a set of MPS languages, it fully supports language composition (Voelter
 234 and Solomatov [2010]). Language composition has no equivalent in text-based programming languages
 235 and many readers may be therefore unfamiliar with this technique. We will use an example to explain the
 236 advantage of this technique for data analysis.

237 Consider the table of results produced by the analysis shown in Figure 3. Users are likely to need
 238 to annotate the subset of genes found differentially expressed with gene names and gene descriptions.
 239 Information such as this is available in the Biomart system Haider et al. [2009].

240 To illustrate language composition, we created a new kind of MetaR statement called `query`
 241 `biomart`, which we defined in a micro-language. A micro-language is a language which provides
 242 only a few concepts meant to extend a host language. In this case, the MetaR language is the host
 243 language and `query biomart` is a concept contributed by the the micro-language. The purpose of this
 244 concept is to connect to Biomart and retrieve data. In the R language, this functionality is provided as a
 245 BioConductor package (called “`biomaRt`”, Durinck et al. [2005])

Analysis Micro Language Example

```

{
  import table results.tsv
  query biomart database ENSEMBL GENES 81 (SANGER UK) and dataset Homo sapiens genes (GRCh38.p3)
    get attributes HGNC symbol from feature of types string with column group annotation select a group
      Description from feature of types string with column group annotation select a group
      Ensembl Gene ID from feature of types string with column group annotation ID
    filters HGNC symbol(s) [e.g. NTN3] from results.tsv when true: ${adj.P.Val} < 0.01
    -> resultFromBioMart
  join ( resultFromBioMart , results.tsv ) by group ID -> Annotated Results
}

```

Figure 4. Example of Micro-language Composition. The `query biomart` statement is defined in a micro-language called `org.campagnelab.metar.biomart`, which extends the host language `org.campagnelab.metar.tables`. The biomart language provides one statement that offers an interactive user interface to help users retrieve data from biomart. This language reuses expressions and tables from the host language. Micro-languages can be enabled or disabled dynamically by the end-user at the level of a model. This example retrieves Human ENSEMBL identifiers and gene descriptions using the HGNC gene symbols used as identifiers in the Results table (see Figure 3 for the analysis that produced Results).

246 Querying Biomart in R consists in calling one of the functions defined in the package with specific
 247 parameters. The statement is very specialized, and for this reason would not typically be part of the core
 248 statements of a text-based programming language. Leveraging language composition, we can offer a
 249 dedicated statement that supports auto-completion in a remote Biomart instance. The statement acts as a
 250 specialized user interface designed to help users retrieve data from Biomart (in very much the same way
 251 that the web-based interface to Biomart helps users query this resource, but here completely integrated
 252 with the MetaR host language).

253 Figure 4 illustrates how the `query biomart` statement can be used to obtain gene annotations. In or-
 254 der to use these statements, end-users of MetaR would declare using both the `org.campagnelab.metar.tables`
 255 (the host language) and `org.campagnelab.metar.biomart` (the micro-language). In this specific case, the
 256 micro-language is provided with the MetaR distribution, but end-users can also implement other micro-
 257 languages to seamlessly combine them with the host language (the process for doing so is described in
 258 the MetaR documentation booklet Campagne and Simi [2015], Chapter 10). This capability makes it
 259 possible to customize the data analysis process for specific problems in much more flexible ways than
 260 would be possible with text-based programming languages: with the `query biomart` statement, we
 261 demonstrated that it is possible to remotely query databases to support auto-completion directly in the
 262 language. In contrast, text-based languages can only be extended in ways compatible with the syntax of
 263 the programming language, and are not able to support such levels of interactivity.

Composable R language

264 In addition to the MetaR language illustrated in Figure 2-4, we have developed a composable R language.
 265 This language models the traditional R language Ihaka and Gentleman [1996], but supports language
 266 composition. Composable R is implemented in the language `org.campagnelab.metar.R` distributed with
 267 MetaR. R programs can be pasted in text form into an RScript root node and the text is parsed and
 268 converted to nodes of the composable R language. In Figure 5, we show the R code equivalent to the
 269 analysis shown in Figure 4. This R script was pasted from the text generated automatically from the
 270 MetaR analysis shown in Figure 4. Executing this script is supported in the MPS LW and yields the same
 271 result that of the simpler MetaR script shown in Figure 4.
 272


```

R Example.R
libDir <- "/Users/fac2003/.metaRlibs "
dir.create(file.path(libDir), showWarnings = FALSE, recursive = TRUE) .libPaths(c(libDir))
dir.create(file.path("/Users/fac2003/R_RESULTS/manuscript "), showWarnings = FALSE, recursive = TRUE)
if ( ! ( require("biomaRt") ) ) {
  if ( ! require("BiocInstaller") ) {
    source("http://bioconductor.org/biocLite.R",
          local = TRUE)
  }
  biocLite(ask = FALSE, c("biomaRt")) library("biomaRt")
}
if ( ! require("plyr") ) { ... } if ( ! require("data.table") ) { ... }
results.tsv <- fread("/Users/fac2003/MPSProjects/git/metar/data/manuscript/results.tsv ",
colClasses = c("character", "numeric", "numeric", "numeric", "numeric", "numeric"))
cat("STATEMENT_EXECUTED/1382062817028347486/\n ")
queryBiomart_1382062817028347636 <- function ( <no parameters> ) {
  output <- c()
  thisDataset <- "hsapiens_gene_ensembl "
  thisMart <- useMart("ensembl", dataset =
thisDataset) attributes <- c("hgnc_symbol", "
description", "ensembl_gene_id")
filtersVector = c() valuesList = c()
filtersVector <- c(filtersVector, "
hgnc_symbol")
data <- results.tsv[
( results.tsv$ "adj.P.Val" <0.01 )
]
valuesList <- c(valuesList, list(tableIds =
as.vector(data$ genes))) output <- getBM(
attributes = attributes, mart = thisMart,
filters = filtersVector, values = valuesList)
colnames(output) <- c("
HGNC_symbol_from_feature ", "
Description_from_feature ", "
Ensembl_Gene_ID_from_feature ") return(
data.table(output, key = colnames(output)))
}
queryBiomart_1382062817028347636 ( ) -> resultFromBioMart
write.table(resultFromBioMart, "/Users/fac2003/R_RESULTS/manuscript/table_resultFromBioMart_0.tsv ",
row.names = FALSE, sep = "\t")
cat("STATEMENT_EXECUTED/1382062817028347636/\n ")
setkey(resultFromBioMart, "Ensembl_Gene_ID_from_feature") setkey(results.tsv, "genes")
results.tsv <- rename(results.tsv, c(genes = "Ensembl_Gene_ID_from_feature "))
tableSuffixes = c(" ", " ")
joiningColumns = c("Ensembl_Gene_ID_from_feature ")
nextTableToMergeInto = resultFromBioMart nextTableToMergeFrom = results.tsv
mergedresults.tsv <- merge(nextTableToMergeInto, nextTableToMergeFrom, by = joiningColumns,
suffixes = tableSuffixes) nextTableToMergeInto = mergedresults.tsv
Annotated_Results <- mergedresults.tsv rm(mergedresults.tsv)
Annotated_Results <- Annotated_Results [ , "genes" ] := Annotated_Results$ "Ensembl_Gene_ID_from_feature " ]
results.tsv <- rename(results.tsv, c(Ensembl_Gene_ID_from_feature = "genes"))
write.table(Annotated_Results, "/Users/fac2003/R_RESULTS/manuscript/table_Annotated_Results_0.tsv ",
row.names = FALSE, sep = "\t") cat("STATEMENT_EXECUTED/1382062817033011970/ ")

```

Figure 5. R language equivalent of the Analysis shown in Figure 4. To produce this figure, the analysis shown in Figure 4 was generated to the R language and the text was pasted in a RScript node of the composable R language. Automatic parsing of the R code into composable R objects yields a composable R version of the biomart example. Notice that boiler plate code needed to import R packages is shown only for the biomaRt package. Subsequent package import statements have been folded { . . . } to save space in the Figure. Folding is directly supported by the MPS LW. Function calls are highlighted in green and are linked to the function declaration in the package stub (end-user can navigate to each function to review its list of arguments, for instance). Comparing the complexity of this code with the equivalent MetaR code shown in Figure 4 makes a strong case for the need for simplified languages for data analysis.

273 **Micro-Languages for the R Language**

274 A composable R language makes it possible to create micro-languages that compose directly with R as
 275 the host language. We demonstrate this capability by adapting the `query biomart` statement shown in
 276 Figure 4 to the R language. Adaptation is simple because both MetaR and R generate to the same target
 277 language (R). In this case, we create a sub-concept of `Expr` (this type represents any R expression), and
 278 define a field of type `Biomart` (the concept that implements `query biomart`). This simple adapter is
 279 sufficient to make it possible to use the `query biomart` user interface inside an R script and is defined
 280 in the language *org.campagnelab.metar.biomartToR*. The result of composing the adapter language with
 281 composable R is shown in Figure 6. We also provide a short video to illustrate the interactive capabilities
 282 of a micro-language combined with composable R (see <https://youtu.be/ZwGj1RPOODQ>).

283 This example illustrates that a composable R language makes it possible to mix regular R code with
 284 new types of language constructs that can include user interfaces elements. This opens up new possibilities
 285 to facilitate repetitive analyses in R, for instance for specific data science domains (e.g., the Biomart
 286 example is useful for bioinformatic data analyses), but also for more general activities where simpler ways
 287 to perform a task would be beneficial. An example of this would be a micro-language to facilitate the use
 288 of packages to replace the boiler-plate package import code found at the beginning of most R scripts.

```

QueryBiomartInR.R
  if ( ! require("data.table") ) {
    install.packages("data.table", repos = "http://cran.us.r-project.org ")
    library("data.table")
  }
  if ( ! require("biomaRt") ) {...}
  if ( ! require("graphics") ) {...}

  query biomart database ENSEMBL FUNGI 29 (EBI UK) and dataset Aspergillus terreus genes (Broad (CADRE))
  get attributes % identity from aflavus homologs of types string with column group annotation select a group
  filters << ... >>
  -> resultFromBioMart
  [BioMart]
  pdf("histogram.pdf")
  hist(resultFromBioMart$percent_identity_from_aflavus_homologs )
  dev.off()

```

Figure 6. Composing Query Biomart with the composable R language. We developed an adapter that makes it possible to use the MetaR `query biomart` statement directly inside a composable R Script. This figure shows how the `query biomart` Expression adapter appears when used inside an R script. Notice how the table and column adapters are used inside a regular `hist()` function call `resultFromBioMart$percent_identity_from_aflavus_homologs`. These adapters make it possible to refer to the table produced by the statement as an R expression and provide auto-completion for column names in the table (determined dynamically based on the query expressed in the `query biomart` statement).

289 **Using R Expressions in the MetaR Language**

290 Figure 7 illustrates that language composition can also be used to embed R expressions inside a MetaR
 291 analysis. This extension is possible because both analyses and R expressions generate code compatible
 292 with the syntax of the R programming language. Providing a way to embed the full language in a simpler
 293 analysis language offers a guarantee that the end-user will not be overly limited by restrictions of the
 294 simpler language.

295 **SOFTWARE**

296 MetaR is distributed as a plugin of the MPS LW. Instructions for installing the software are available
 297 online at <http://metar.campagnelab.org>. Briefly, after installing MPS, users can download
 298 and activate plugins with the Preferences/Plugins (Mac) or Settings/Plugins (Windows/Linux) menu.
 299 Plugins are stored as Zip files on the JetBrains Plugin repository https://plugins.jetbrains.com/category/index?pr=mps&category_id=92 and can also be downloaded and installed
 300 manually from the zip file. Source code (technically, MPS languages serialized to files) are distributed
 301 on GitHub at <https://github.com/campagnelaboratory/MetaR> Campagne et al. [2015].
 302 MetaR (and the MPS LW) are distributed under the open-source Apache 2.0 license.
 303

The screenshot shows a window titled 'MetaR with R'. The top panel displays MetaR code for simulating a dataset and performing a Limma voom analysis. The R code is highlighted in blue. The bottom panel shows the execution progress, including package loading and a table of results.

```

Analysis MetaR with R
{
  simulate dataset with [
    num of samples: 100
    num of genes: 500
    mean when all factors are false: 10
    discrete factors: treatment
    effect size: 3
    continuous covariate: age , range: [ 18 - 100 ] , slope: 3
  ] -> simulatedTable

  limma voom counts= simulatedTable model: ~ 0 + treatment + age
  comparing treatment=No - treatment=Yes -> Results adjusted counts: Adjusted
  // show the top 10 hits using an R expression (limma voom binds the fit3 name to a value)
  — R
  topTable(fit3, coef = 1, number = 10)
  R —

```

```

Run R Script MetaR with R
/Library/Frameworks/R.framework/Versions/3.1/Resources/bin/Rscript /Users/fac2003/MPSPProjects/git/metar,
Loading required package: limma
Loading required package: methods
Loading required package: edgeR
Loading required package: Cairo
Loading required package: data.table
STATEMENT_EXECUTED/1382062817041463098/
STATEMENT_EXECUTED/6795413641515324807/
STATEMENT_EXECUTED/6795413641515324807/

```

	genes	logFC	AveExpr	t	P.Value	adj.P.Val
323	gene_323_treatment	-0.4182245	11.03107	-5.674651	2.001635e-08	1.000817e-05
54	gene_54_treatment	-0.3870329	11.13942	-5.277938	1.722625e-07	4.020041e-05
126	gene_126_treatment	-0.3866908	11.09819	-5.213549	2.412025e-07	4.020041e-05
112	gene_112_treatment	-0.3808808	11.11778	-5.118621	3.936154e-07	4.832646e-05
166	gene_166_treatment	-0.3792082	11.12251	-5.078391	4.832646e-07	4.832646e-05
232	gene_232_treatment	-0.3729548	11.14150	-5.026791	6.274733e-07	5.228944e-05
445	gene_445_treatment	-0.3626018	11.10790	-4.859438	1.440418e-06	1.028870e-04
360	gene_360_treatment	-0.3594876	11.08581	-4.793461	1.985425e-06	1.240891e-04
328	gene_328_treatment	-0.3437431	11.10246	-4.551622	6.230697e-06	3.254523e-04
351	gene_351_treatment	-0.3307637	11.12417	-4.542160	6.509046e-06	3.254523e-04

Figure 7. Composing R Expressions with the MetaR Language. Top panel: this example illustrates that it is possible to use R code inside a MetaR analysis. In this snapshot, R code is delimited by the — R and R — markers and shown with a blue background. Embedding R code in MetaR provides flexibility to perform operations for which MetaR statements have not yet been developed. The analysis shown simulates a dataset using simple parameters and tests the ability of Limma voom, as integrated with MetaR, to call differentially expressed genes. Bottom panel: shows the result of executing the analysis inside the MPS LW. As part of execution, the analysis is converted to R code, this code is run and standard output displayed inside the LW. The STATEMENT_EXECUTED// lines hyperlink the progress of the execution with each specific analysis statement that has been executed.

304 DISCUSSION

305 Data Object Surrogates and Relation to Meta Data

306 DOS are related, but different from metadata. For instance, the Table DOS provides metadata about the
 307 file that contains the tabular data represented by Table nodes. It lists columns, associates columns to
 308 groups and defines group usages. This type of information can be thought of as metadata about the file
 309 that contains the tabular data. However, there is an important difference between DOS and metadata. For
 310 instance, a MetaR Table only provides metadata relevant to the analysis that the user needs to perform. It
 311 makes no effort to provide information that would have a meaning outside of the user's analysis. This
 312 simplification maximizes the benefit of annotation while keeping the effort needed to produce it minimal
 313 and local to the user who actually needs the annotation.

314 Graphical User Interfaces for Data Analysis

315 Programs with graphical user interfaces (GUIs) (also called direct manipulation interfaces Galitz [2007])
 316 are often popular among beginners who are starting with data analysis and have no programming or

317 scripting experience. GUIs are popular in part because they facilitate discovery of software functionality
318 directly when using the software. They do not require prior-knowledge of syntax.

319 Data Analysis software with GUIs constrains how analysis is to be performed and provides clear
320 menus and buttons that make it obvious what the program can do. A user can often discover new ways to
321 perform analysis with these tools simply by browsing the user interface and looking at choices offered
322 in menus and dialogs of the program. While such programs are favored by beginners (because they
323 are relatively easy to learn), more advanced users who need to perform similar analyses across several
324 datasets tend to strongly prefer analysis software that does not require repeating interactions with a GUI
325 for every new dataset that must be studied. The novel approaches we have used to develop MetaR share
326 these advantages with GUIs.

327 A minority of analysis software with GUIs also supports writing and running scripts in their user
328 interface. For instance, JMP from SAS Inc. is an example of a statistical analysis software with GUI that
329 also offers a scripting language. However, when scripting is offered, it is often only loosely integrated
330 with the rest of the interface. Furthermore, users who are familiar with the GUI often need to learn
331 scripting from scratch and do not benefit much from their prior experience using the GUI.

332 **Scripting and Programming Languages for Data Analysis**

333 Scripting and programming languages are popular options for data analysis because analyses encoded
334 in scripts or programs can be reused with different datasets. This makes these options popular among
335 researchers who have programming skills and engage frequently in data analysis. The popularity and
336 power of scripting for data analysis is epitomized by the development of the R language Ihaka and
337 Gentleman [1996], which has become a defacto workhorse of open data science in biology. The versatility
338 of the R language is its strength, but mastering the language requires elements of programming. Learning
339 the R programming language is not as simple as learning how to use a GUI analysis tool and many users
340 who would benefit from data analysis experience difficulties with the steep learning curve involved in
341 learning programming and the R language.

342 In contrast to R, the MetaR language offers a much simpler alternative for users who have no prior
343 programming background. At the same time, the Composable R language offers the means for expert R
344 users to extend the R language with micro-languages in order to provide custom user interfaces. Such
345 interfaces could be used to flatten the learning curve for novice data analysts or to empower expert data
346 analysts with expressive means to encode solution to specific problems. Since both these options are
347 available in the same platform (the MPS LW), users who become skilled with one language acquire
348 transferable skills that help them learn other languages available on the platform.

349 **Impact on Development of User Proficiency**

350 The MetaR high-level language shown in Figure 2-4 is aimed at novice data analysts. An interesting
351 question is whether such a language can help novice data analysts learn skills that are useful when working
352 with a variety of data analysis tasks.

353 If the language is sufficiently general, then novice users may learn skills that they can reuse when
354 learning other general data analysis languages. If the language is too limited, then novice users would
355 only learn a specialized analysis tool similar to existing GUI analysis tools. Rigorously determining to
356 which category the MetaR language belongs would require following users for several months or years
357 while they use the tool and we have not done such a study. However, we think that MetaR can help users
358 transition to more general languages for the following reasons.

359 First, users who learn the high-level MetaR language acquire basic skills that are similar to those
360 needed when working with other languages, including composable R. For instance, users learn to formalize
361 their analysis intent using the constructs offered by the language. This is a very important first step that
362 users with a strong programming background may take for granted, but that is difficult for novice users to
363 acquire when they are distracted with problems of syntax. MetaR avoids syntax distractions and helps
364 novice users focus on the logic of an analysis (e.g., how to combine language elements to achieve the
365 desired analysis).

366 Second, the high-level MetaR language does not offer loops and conditionals. Since these language
367 features are often needed for advanced analysis, many users who reach the point where they will need
368 these language features will need to learn a language like R. MetaR offers composable R for this purpose.
369 Novice users who have first learned the MetaR high-level language will be familiar with the MPS LW
370 platform where composable R is also available. Some skills that users have acquired working with the

371 high-level language will be directly transferable, including: how to run a script, how to navigate references
372 to look at definitions, how to use auto-completion or use intentions to transform the program automatically,
373 how to use source control (seamlessly integrated with the MPS LW). Subsets of the R language will still
374 need to be learned to perform more advanced analysis, but learning can occur in an environment where
375 the user is already comfortable. We believe that such an integrated environment where both high-level and
376 low-level languages of the R ecosystem are offered will facilitate teaching of the many skills needed for
377 data analysis. Formally testing whether this intuition is correct will require comparing cohorts of subjects
378 learning data analysis. Alternatively, the answer may become apparent if a large number of data analysts
379 were to transition to using composable R after initially learning the MetaR high-level language.

380 **Relation to Electronic Notebooks**

381 MetaR shares some similarities to electronic notebooks such as IPython Pérez and Granger [2007], Jupyter
382 (<https://jupyter.org/>) and Beaker (<http://beakernotebook.com/>) notebooks, but also
383 has some important differences.

384 Regarding analogies, both MetaR and notebooks can be used to present analysis results alongside the
385 code necessary to reproduce the results. For instance, the MetaR multi-view plot can be used to show a
386 plot at the location where the statement is introduced in an analysis.

387 MetaR was developed approximately over the course of one year (2015). As such the software cannot
388 be expected to be as feature-rich as software developed for many years. Beside this obvious difference,
389 MetaR has the advantage to support language composition. In contrast, current data analysis notebooks
390 support conventional programming languages constructed using text-based technology. Therefore, the
391 closest that notebooks can approach language composition is to support multiple languages in one
392 notebook, a so-called polyglot feature, available for instance in the Beaker notebook. Polyglot notebooks
393 are useful, but cannot be extended by data analysts to customize languages for the requirements of a
394 specific analysis project or domain. For instance, supporting a simple analysis language like MetaR would
395 not be possible without developing a MetaR compiler and an associated execution kernel for the notebook.
396 Developing and using micro-languages together with the traditional languages supported by the notebooks
397 is also not possible.

398 Hence, the approach taken with MetaR is different from notebooks in two major ways. First, MetaR
399 provides flexibility in designing new languages or micro-languages. It is not constrained by the syntax
400 of a full programming language. Extending MetaR often consists in adding just one statement to an
401 existing language. This promotes collaborative language design and development since many users can
402 acquire sufficient skills to create one or two statements, reusing the building blocks provided by the
403 host language (the steps needed to extend MetaR with a new language statement are described in the
404 user manual Campagne and Simi [2015]). As long as a new statement generates valid R code, a MetaR
405 Analysis that contains this statement will be executable.

406 Second, the syntax of the MetaR languages is not limited to text scripts or programs. Language
407 Workbench technology used to implement MetaR supports graphical notations and diagrams as well
408 as text. These differences combine to make it easier to design and implement custom data analysis
409 abstractions with the LWT approach than it is possible with current electronic notebooks. Interestingly,
410 the R IPython kernel could be used to execute scripts generated from MetaR analyses, which would
411 provide an interactive console similar to that offered in the IPython notebook inside the MPS LW.

412 **Reproducible Research and Education**

413 MetaR analysis and Composable R scripts can be executed seamlessly with an R environment installed
414 inside a docker image (see Methods). Users can enable this feature by providing a few details about the
415 installation of docker on their computer and checking the “Run with Docker” option in the MPS LW. This
416 feature is particularly useful to facilitate reproducible research because docker images can be tagged with
417 version numbers and always result in the same execution environment at the start of an analysis. This
418 makes it possible to pre-install specific versions of R, CRAN and Bioconductor packages in a container
419 and distribute this image with the MetaR analyses or R scripts that implement the analysis inside the
420 container. While this is possible also with R, using docker on the command line, the customization of
421 the MPS LW makes it seamless to run analyses with docker. We are not aware of a similar feature being
422 supported by current R IDEs.

423 We found this feature also particularly useful for training sessions where installation of a working
424 R environment can be challenging on trainees’ laptops. Using docker, we simply request that trainees

425 pre-install Kitematic (available on Mac and Windows), or run docker natively on Linux and download
426 the image we prepared with the packages used in the MetaR training sessions. The ability to run MetaR
427 analysis in docker container results in a predictable installation of dependencies for training session and
428 frees more of the instructor's time to present data analysis techniques.

429 METHODS

430 We have used the MPS Language Workbench (<http://jetbrains.com/mps>), as also described
431 in Campagne [2014] and Campagne [2015]. For an introduction to Language Workbench Technology
432 (LWT) in the context of bioinformatics see Simi and Campagne [2014] and Benson and Campagne [2015]
433 in the context of predictive biomarker model development.

434 Language Design

435 We designed the MetaR MPS languages through an iterative process, releasing the languages at least
436 weekly to end-users at the beginning of the project and adjusting designs and implementations according
437 to user feedback. Full language developments logs are available on the GitHub code repository (<https://github.com/CampagneLaboratory/MetaR>) Campagne et al. [2015]. Briefly, we designed
438 abstractions to facilitate specific analyses and implemented these abstractions with the structure, editor,
439 constraints and typesystem aspects of MPS languages. Generated R code is produced from nodes of the
440 languages using the *org.campagnelab.TextOutput* plugin. An illustration of the steps required to develop
441 one language statement is available in Chapter 10 of the MetaR documentation booklet (see Campagne
442 and Simi [2015]).
443

444 Table Viewer

445 We implemented a Table viewer as an MPS Tabbed Tool, using the MPS LW mechanisms for user
446 interface extension (see Campagne [2015]). The table viewer provides the ability to inspect the data
447 content of any table produced during an analysis, or any input table. When the cursor is positioned over a
448 node that represent a FutureTable (created when running the R script generated from the MetaR Analysis),
449 and the viewer is opened, it tries to load the data file that the analysis would create for this table. If the file
450 is found, the content is displayed using a Java Swing Component in the MPS user interface of the Table
451 Viewer tool.

452 Language Execution

453 MetaR analyses can be executed directly from within the MPS LW. This capability was implemented with
454 Run Configurations (see Campagne [2015], Chapter 5).

455 Execution in a Docker Container

456 In order to facilitate reproducible execution, we implemented optional execution within a Docker container.
457 A docker image was created to contain a Linux operating system and a recent distribution of the R language
458 (provided in the rocker-base image), as well as several R packages needed when executing the MetaR
459 statements. The Run Configuration was modified to enable execution inside a docker container when the
460 user selects a checkbox "execute inside docker container". Information necessary to run with docker (i.e.,
461 location of the docker executable, docker server connection settings and image name and tag) is collected
462 under a tab in the MPS Preferences (Other Settings/Docker).

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