

# MITRE 1.0 user's manual

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# Chapter 1

## Introduction

MITRE learns interpretable predictive rules that classify hosts or predict host outcomes based on longitudinal observations of their microbiome. For a full explanation of what this means, why it is important, and how MITRE does it, refer to “MITRE: predicting host status from microbiota time-series data”, Elijah Bogart and Georg Gerber (in preparation), and the associated supplementary technical note. For a quick tutorial introduction, see the README.md file, or go to <https://github.com/gerberlab/mitre>. This manual describes how to install and run MITRE, how to format your own data for use with MITRE, what types of output are available, and the options that may be specified in a MITRE configuration file to control its execution.

### 1.1 Installation

The recommended installation procedure is to use `pip` to download MITRE (and any dependencies not already installed) from the Python Package Index:

```
pip install mitre.
```

To install from source, run

```
git clone https://github.com/gerberlab/mitre.git
```

followed by

```
pip install mitre/
```

(note the trailing slash.) To verify that installation was successful, run

```
mitre --test
```

A series of status messages should be displayed, followed by ‘Test problem completed successfully.’

You will need Python 2.7 installed to install and run MITRE. (Note that recent versions of Python 2.7 provide the `pip` command by default.) Only Mac and Linux systems are supported at this time.

## 1.2 Usage

To use MITRE, create a configuration file specifying input data, the operations to be performed, and output types. Then run

```
mitre path_to_configuration_file
```

The MITRE configuration file options, and what happens when MITRE reads a configuration file, are described in detail in chapter 4 below. Rather than writing a configuration file from scratch, it may be easiest to modify a sample configuration file to suit your needs; an example file is provided in chapter 5 below.

# Chapter 2

## Formatting input data for MITRE

This chapter describes, with examples, how to prepare input data files for MITRE.

### 2.1 Required files

#### 2.1.1 Abundance table

The abundance data should be provided as a comma-separated table, with the first row providing OTU IDs and the first column providing sample IDs.

Listing 2.1: Example abundance data table

1	" " , "OTU1 " , "OTU2"
2	"SampleID1 " , 768 , 46
3	"SampleID2 " , 17 , 7545

(Quotes around strings are not necessary.)

#### 2.1.2 Sample metadata table

The sample metadata table specifies an associated subject ID and timepoint for each sample ID. It should be given as a comma-separated table with no header row. No particular ordering is expected.

Listing 2.2: Example sample metadata table

1	SampleID1 , SubjectID1 , 0
2	SampleID2 , SubjectID1 , 27
3	SampleID3 , SubjectID2 , 2

### 2.1.3 Subject data table

The subject data table gives information about each subject, (including the value of whatever variable will be used as the outcome that MITRE will try to predict, though that does not need to be explicitly marked.) It should be given as a comma-separated table with a header row, whose first column is the subject ID. (The first field in the header row is ignored.) Values may be either strings or numbers (but variables that appear to be Boolean may be converted to 0/1; see the note for the ‘outcome\_positive\_value’ option in section 4.4 below.)

Listing 2.3: Example subject data table

1	subjectID , delivery_mode , allergy , week_of_delivery , exposure_count
2	SubjectID1 , cesarean , True , 38.1 , 5
3	SubjectID2 , vaginal , True , 39.9 , 1

### 2.1.4 Pplacer results

This should be the .jplace file created by placing the representative sequences from each OTU on a reference tree of known 16S sequences using the `pplacer` package in maximum likelihood mode.

## 2.2 Optional files

### 2.2.1 Sequence key

If this FASTA file of unique sequences is given, each OTU identifier in the abundance data table that exactly matches one of the sequences will be replaced with the identifier for that sequence in the FASTA file. The same will be done for OTU identifiers in the placement table described below, if it

is given. This is useful when working with tables from DADA2 that use the inferred exact sequences as row and column headers.

## 2.2.2 Pplacer taxonomy table

A comma-separated-value taxonomy table from the `pplacer` reference package used for placement of the OTUs. See <http://fhcrc.github.io/taxtastic/refpkg.html> for a description of the `pplacer` reference package components. The following listing is provided as an aid to identifying the appropriate file, not as a complete example of its necessary properties.

Listing 2.4: Beginning of an example taxonomy table file

```

1 "tax_id", "parent_id", "rank", "tax_name", "root", "below_root",
  "superkingdom", "superphylum", "phylum", "subphylum",
  "class", "subclass", "order", "below_order",
  "suborder", "family", "below_family", "subfamily",
  "tribe", "genus", "below_genus", "subgenus",
  "species_group", "species_subgroup", "species"
2 "1", "1", "root", "root", "1", "", "", "", "", "", "",
  "", "", "", "", "", "", "", "", "", "", "", ""
3 "131567", "1", "below_root", "cellular
  organisms", "1", "131567", "", "", "", "", "", "", "",
  "", "", "", "", "", "", "", "", "", "", ""
4 "2157", "131567", "superkingdom", "Archaea", "1", "131567",
  "2157", "", "", "", "", "", "",
  "", "", "", "", "", "", "", "", "", "", ""
5 "2", "131567", "superkingdom", "Bacteria", "1", "131567",
  "2", "", "", "", "", "", "", "", "", "",
  "", "", "", "", "", "", "", "", "", ""

```

## 2.2.3 Pplacer sequence information

A comma-separated-value table from the `pplacer` reference package used for placement of the OTUs, giving information about the sequences included in the reference package. See <http://fhcrc.github.io/taxtastic/refpkg.html> for a description of the `pplacer` reference package components. The following listing is provided as an aid to identifying the appropriate file, not as a complete example of its necessary properties.

Listing 2.5: Beginning of an example sequence information file

```
1 seqname , tax_id , species_name
2 S000438419 , 53635 , Acidimicrobium ferrooxidans
3 S001416053 , 121039 , Ferrimicrobium acidiphilum
4 S000750001 , 209649 , Ferrithrix thermotolerans
```

## 2.2.4 Placement table

A comma-separated table giving predicted taxonomies for the OTUs in the abundance table, with a header row listing the taxonomic levels at which placements are predicted, from coarsest to finest (last two entries must be “Genus” and “Species”), and with the OTU identifiers in the first column, e.g.:

Listing 2.6: Example placement table

```
1 " " , " Kingdom " , " Phylum " , " Class " , " Order " , " Family " , " Genus " ,
   " Species "
2 "OTU1" , " Bacteria " , " Bacteroidetes " , " Bacteroidia " ,
   " Bacteroidales " , " Bacteroidaceae " , " Bacteroides " , " dorei "
3 "OTU2" , " Bacteria " , " Verrucomicrobia " , " Verrucomicrobiae " ,
   " Verrucomicrobiales " , " Verrucomicrobiaceae " ,
   " Akkermansia " , NA
```

When a placement for an OTU was not predicted at a particular level, the entry should be NA or empty. Note that this is the format that results from passing the output of `dada2`'s `addSpecies` function to `write.csv`.

# Chapter 3

## Quick guide to available MITRE output types

MITRE offers a number of different output options. This section provides a quick guide to how each may be specified in the configuration file.

To generate...

- **An interactive visualization of the MITRE results as an HTML file:** Set ‘gui\_output’ in section ‘postprocessing’ to True.
- **The point estimate of the best rule set, distribution of rule set lengths, and the Bayes factor in favor of the empty rule set, as a text file:** Set ‘quick\_summary’ in section ‘postprocessing’ to True.
- **All of the above, plus the most frequent clusters of similar rule sets seen in the posterior distribution, as a text file:** Set ‘full\_summary’ in section ‘postprocessing’ to True.
- **A table of Bayes factors indicating the strength of the evidence that particular variables or detectors are involved in the true rule list, as a text file:** Set ‘bayes\_factor\_table’ in section ‘postprocessing’ to True.
- **A table describing taxonomically the OTU or group of bacteria corresponding to each variable in the model, as a text file:** Specify an appropriate ‘taxonomy\_source’ and input data files

in section ‘data’, and set ‘aggregate\_on\_phylogeny’ to True in section ‘preprocessing’.

- **Cross-validated accuracy assessments for the MITRE point and ensemble estimators, as text files:** Include either a ‘crossvalidation’ or ‘leave\_one\_out’ section in the configuration file, with all required options given there (see sections 4.9 and 4.10 below.)
- **Convergence diagnostic plots as PDF files:** Set ‘mixing\_diagnostics’ in section ‘postprocessing’ to True.
- **The full suite of outputs necessary to compare MITRE performance against alternative methods:** See section 4.12 below.

Note that in almost all output text files, rules will be expressed in terms of internal variable identifiers (which may be the names of input OTUs, or numbers representing edges in the phylogenetic tree.)

These may be looked up in the variable annotations file (if it has been generated) which provides a taxonomy-based label for each such variable and, for each variable that represents a higher-level group, a list of the OTUs included in that group.

The interactive visualization provides descriptions of the variables visualized detector refers to; where a visualized detector represents a higher-level group, the interface will draw the subtree of the phylogeny corresponding to the group.

# Chapter 4

## Configuration options

### 4.1 How a configuration file is processed

When MITRE reads a configuration file, it attempts to carry out each of the following operations, if the corresponding sections of the configuration file are present:

**preprocessing** Loading, filtering, transforming, and/or annotating the input data, (section 4.5)

**model** Preparing a model object with specified parameters (section 4.6)

**sampling** Drawing samples from the posterior distribution (section 4.7)

**postprocessing** Generating output files, including summaries of the posterior distribution, mixing diagnostics, or the interactive visualization (section 4.8)

**crossvalidation** K-fold crossvalidation: splitting the data across a set number of folds, creating and sampling from a model for each fold, assessing the accuracy of the resulting predictive rules for the held-out data, and writing a summary report (section 4.9)

**leave\_one\_out** As above, but performs leave-one-out crossvalidation instead (section 4.10).

**comparison\_methods** Applying random forest and L1-regularized logistic regression models to predict the outcome, assessing their accuracy by cross-validation, and writing a report (section 4.11).

All sections are optional. When applicable, the results of the ‘preprocessing’ operation will be supplied to the ‘model’ and ‘comparison\_methods’ operations, the results of the ‘model’ step will be supplied to the ‘sampling’ step and the cross-validation methods, and the results of the ‘sampling’ step will be supplied to the ‘postprocessing’ step.

For each operation that depends on an earlier step, however, it is possible to omit the earlier step and instead specify a file of previously generated results to be loaded.

The ‘data’ section (4.4) tells MITRE where to find input data files, and is required if the ‘preprocessing’ section is present.

The ‘description’ section (4.3) provides information about the problem that is used to label output files, and is required. The ‘general’ section (4.2) is optional; it controls options for MITRE operation that apply across all steps in the pipeline.

The ‘benchmarking’ section (4.12) is special. It modifies the normal sequence of operations to apply the comparison methods to the dataset after some steps of filtering, but before the phylogenetic aggregation process; preprocessing is then completed, and cross-validation is performed. This is a convenience method which facilitated the benchmarking calculations presented in the MITRE manuscript.

## 4.2 General

Options allowed in section ‘general’ are:

**verbose** Boolean, optional. If true, MITRE will print progress messages for most steps, including every MCMC iteration. Internally this sets the log level to `logging.INFO`. Default: false.

## 4.3 Description

Options allowed in section ‘description’ are:

**tag** A short string used to generate output filenames. Required.

## 4.4 Data

Options allowed in section ‘data’ are:

**load\_example** Allowed values are ‘bokulich’, ‘david’, ‘digiulio’ or ‘karelia’. If one of these values is given, MITRE will load one of the pre-packaged example datasets, consisting of data from, respectively,

- Bokulich, N. A., et al., “Antibiotics, birth mode, and diet shape microbiome maturation during early life”, *Science Translational Medicine* 8(343): 343ra82 (2016)
- David, L. A., et al., “Diet rapidly and reproducibly alters the human gut microbiome”, *Nature* 505(7484): 559 – 563 (2014)
- DiGiulio, D. B., et al., “Temporal and spatial variation of the human microbiota during pregnancy”, *PNAS* 112(35): 11060 – 11065 (2015)
- Vatanen, T., et al., “Variation in Microbiome LPS Immunogenicity Contributes to Autoimmunity in Humans”, *Cell* 165(4): 842 – 853 (2016),

reprocessed as described in the MITRE supplementary note. If this option is given, no other options in this section are required. Note that the ‘tag’ option, above, is overwritten in this case.

**abundance\_data** Filename or path to a table of OTU abundance data, formatted as described in section 2.1.1. Required, unless ‘load\_example’ is set.

**sample\_metadata** Filename or path to a table giving a subject and time-point for each sample in the abundance table, formatted as described in section 2.1.2. Required, unless ‘load\_example’ is set.

**subject\_data** Filename or path to a table of data about each subject, formatted as described in section 2.1.3. Required, unless ‘load\_example’ is set.

**jplace\_file** Filename or path to pplacer results in .jplace format, as described in section 2.1.1. Required if ‘aggregate\_on\_phylogeny’ is set to True in section ‘preprocessing’, or ‘taxonomoy\_source’ is ‘pplacer’ or ‘hybrid’, unless ‘load\_example’ is set.

- sequence\_key** Filename or path to a FASTA file to be used to rename the OTUs listed in the abundance table, in the case where the name of each OTU is simply a sequence, as in some DADA2 output; see 2.2.1. Optional.
- outcome\_variable** String, specifying which of the columns in the subject data table encodes the outcome that MITRE should try to predict. Subjects for whom this data is not available will be dropped from the calculation. Required, unless ‘load\_example’ is set.
- outcome\_positive\_value** The value of the outcome variable that corresponds to a positive outcome. All other (non-missing) values will be considered a negative outcome. Due to a minor limitation of MITRE’s data parsing system, *if the outcome variable is given as ‘true’/‘false’, ‘True’/‘False’, etc., in the subject data table, the positive value must be given as ‘1’ or ‘0’ in the configuration file.* Other strings or numerical values should work as expected. Required, unless ‘load\_example’ is set.
- taxonomy\_source** String specifying how taxonomic annotations for each variable (i.e., subtree of the overall phylogeny) should be generated. Valid options are ‘table’, ‘pplacer’, and ‘hybrid’ (see the supplement to the MITRE manuscript for a full explanation of these options; in short, ‘table’ labels OTUs from a table and higher clades based on the OTUs they contain, ‘pplacer’ labels all variables based on the pplacer results, and ‘hybrid’ labels variables based on pplacer results except where a species-level placement is given in a table.) If this option is not present, no such annotation will be done. If given, note that the table of annotations will be written to [tag]\_variable\_annotations.txt at the conclusion of the preprocessing step, unless phylogenetic aggregation is not performed.
- pplacer\_taxa\_table** Filename or path to a table from the pplacer reference package, formatted as described in section 2.2.2. Required if ‘taxonomy\_source’ is ‘pplacer’ or ‘hybrid’; otherwise ignored.
- pplacer\_seq\_info** Filename or path to a table from the pplacer reference package, formatted as described in section 2.2.3. Required if ‘taxonomy\_source’ is ‘pplacer’ or ‘hybrid’; otherwise ignored.

**additional\_subject\_covariates** String or comma-separated list of strings specifying additional variables (columns in the subject data table) to be included in the regression calculation. See “Incorporating additional covariates”, section 1.6 of the supplementary note to the MITRE manuscript for full details. These variables should be categorical. For quantitative covariates, see below. Subjects where data for any of these variables are missing will be dropped from the calculation. Optional.

**additional\_covariate\_default\_states** String or comma-separated list of strings specifying, in the appropriate order, the values of the additional covariates to be treated as the default state. For each such covariate, the model will incorporate a change in the odds of the outcome associated with every other value of the covariate, but not this value. Required if ‘additional\_subject\_covariates’ is specified.

**additional\_subject\_continuous\_covariates** String or comma-separated list of strings specifying additional variables (columns in the subject data table) to be included in the regression calculation as quantitative covariates. The name is somewhat misleading, as integer-valued variables are fine here. See “Incorporating additional covariates”, section 1.6 of the supplementary note to the MITRE manuscript for full details. Subjects where data for any of these variables are missing will be dropped from the calculation. Optional.

## 4.5 Preprocessing

See section 2.1 of the MITRE supplementary note for a detailed discussion of the data preprocessing and filtering procedure controlled by the ‘preprocessing’ section of the configuration file. Note that the ordering of the options in the configuration file does not matter. Steps will be carried out in the order the corresponding options are presented below, skipping any for which the corresponding options are not given in the configuration file. Except where specified, any of these options may be omitted.

**min\_overall\_abundance** Numeric value ( $N_{\text{counts,OTU}}$  in the notation of section 2.1). If this is specified, all OTUs with lower total abundance data than this value, summed across all samples, are dropped. (Abundance data is assumed to be measured in 16S read counts at this stage, but this is not enforced.)

- min\_sample\_reads** Numeric value ( $N_{\text{counts, sample}}$  in the notation of section 2.1). If this is specified, all samples where the total abundance data across all (remaining) OTUs sum to less than this value are dropped. (Abundance data is assumed to be measured in 16S read counts at this stage, but this is not enforced.)
- trim\_start** Numeric value ( $t_i$  in the notation of section 2.1). The time to consider as the beginning of the study. (By default, this will be the timepoint of the earliest (remaining) sample.) Samples before this time will be dropped. If this is given, ‘trim\_stop’ must be given also.
- trim\_stop** Numeric value ( $t_f$  in the notation of section 2.1). The time to consider as the end of the study. (By default, this will be the timepoint of the latest (remaining) sample.) Samples after this time will be dropped.
- density\_filter\_n\_samples** Numeric value ( $N_s$  in the notation of section 2.1). If this is given, ‘density\_filter\_n\_intervals’ and ‘density\_filter\_n\_consecutive’ must be given also. The duration of the study will be divided into the specified number of time intervals, and subjects from whom at least the specified number of samples are available in *every* time window formed from the specified number of consecutive intervals are retained; samples from all other subjects are dropped.
- density\_filter\_n\_intervals** Integer ( $N_{w, \text{filter}}$  in the notation of section 2.1). See above.
- density\_filter\_n\_consecutive** Integer ( $N_c$  in the notation of section 2.1). See above.
- take\_relative\_abundance** Boolean. If True, abundance data will be converted to relative abundances by normalizing so that the sum of the data for each sample is 1.0.
- aggregate\_on\_phylogeny** Boolean. If True, introduce new variables corresponding to subtrees of the overall phylogeny of the OTUs, inferred from `pplacer` results given in the ‘jplace\_file’ option above, as discussed in section 2.2 of the supplement. The data for each new variable will be the sum of the data for the OTUs contained in the subtree.

- log\_transform** Boolean. If True, take the natural log of all abundance data. Values less than  $10^{-10}$  will be replaced by  $10^{-6}$  before taking the log.
- temporal\_abundance\_threshold** Numeric value ( $a$  in the notation of section 2.1). If this option is given, ‘temporal\_abundance\_consecutive\_samples’ and ‘temporal\_abundance\_n\_subjects’ must be also. Variables which exceed the abundance threshold in at least the specified number of consecutive samples in the data from each of at least the specified number of subjects will be kept; others will be dropped. If the data has been log-transformed, this should be specified on a log scale.
- temporal\_abundance\_consecutive\_samples** Numeric value ( $N_a$  in the notation of section 2.1). See above.
- temporal\_abundance\_n\_subjects** Numeric value ( $N_i$  in the notation of section 2.1). See above.
- discard\_surplus\_internal\_nodes** Boolean. If true, variables corresponding to subtrees rooted at internal nodes which have only one (remaining) child node after the filtration steps have been applied will be dropped from the analysis.
- pickle\_dataset** Boolean. If true, the MITRE datastructure corresponding to the processed and filtered dataset will be serialized to `[tag]_dataset_object.pickle` at the conclusion of the preprocessing step.

## 4.6 Model

### 4.6.1 Required values

Required or conditionally required options section ‘model’ are:

- load\_data\_from\_pickle** String giving the location of a `dataset_object.pickle` file from a previous preprocessing step. Must be given if no ‘preprocessing’ section in this file. If given, a model for that dataset will be built; otherwise, a model will be built for the result of the ‘preprocessing’ step specified in this file.

**n\_intervals** Integer, required. ( $N_w$  in the notation of chapter 1 of the MITRE supplementary note.) The study duration will be divided into this many intervals and rules will apply to time windows formed one or more consecutive such intervals.

**t\_min** Numeric value, required. ( $W_{\min}$  in the notation of chapter 1 of the MITRE supplementary note.) Rules may apply only to time windows this long or longer.

**t\_max** Numeric value, required. ( $W_{\max}$  in the notation of chapter 1 of the MITRE supplementary note.) Rules may apply only to time windows this long or shorter.

## 4.6.2 Saving the model object

An optional setting allows saving the model for reuse:

**pickle\_model** Boolean. If true, the MITRE datastructure representing the model will be serialized to `[tag]_model_object.pickle` at the conclusion of the model setup step.

## 4.6.3 Advanced settings

The following advanced options, all numeric, are not required. See the indicated sections of the MITRE supplementary note for explanations of their significance.

**prior\_coefficient\_variance**  $\sigma_b^2$  in the notation of section 1.3. (default 100.0)

**hyperparameter\_alpha\_m**  $\alpha_m$  in the notation of section 1.4 (default 0.5)

**hyperparameter\_beta\_m**  $\beta_m$  in the notation of section 1.4 (default 2.0)

**hyperparameter\_alpha\_primitives**  $\alpha_n$  in the notation of section 1.4 (default 2.0)

**hyperparameter\_beta\_primitives**  $\beta_n$  in the notation of section 1.4 (default 4.0)

**hyperparameter\_a\_empty**  $a_\Theta$  in the notation of section 1.4.1 (default 0.5)

**hyperparameter\_b\_empty**  $b_\Theta$  in the notation of section 1.4.1 (default 0.5)

**max\_thresholds**  $N_\theta$  in the notation of section 1.2.4 (default, no maximum)

**max\_rules**  $m_{\max}$  in the notation of section 1.4 (default 10)

**max\_primitives**  $n_{\max}$  in the notation of section 1.4 (default 10)

**window\_concentration\_typical**  $c_{w,\text{typical}} = 1/\lambda_w$  in the notation of section 1.4.3 (default 5.0)

**window\_concentration\_update\_ratio** Controls the standard deviation of the proposal distribution for the update  $\delta_w$  to  $c_W$  relative to  $c_{w,\text{typical}}$  (default 0.2); see section 1.5.4.

**delta\_l\_scale\_mean** Variance of the normal prior distribution of  $\mu_L$  in the notation of section 1.4.3, relative to  $\Delta_L^2$  (default 50.0).

**delta\_l\_scale\_sigma** Upper bound on the range of allowed values for  $\sigma_L$  in the notation of section 1.4.3, relative to  $\Delta_L$  (default 25.0)

**lambda\_l\_offset** Amount by which  $\Lambda_L$  in the notation of section 1.4.3 differs from the median of the logarithms of the subtree weights  $L_i$  (default 0.0).

## 4.7 Sampling

Options allowed in section ‘sampling’ are:

**load\_model\_from\_pickle** String giving the location of a `model_object.pickle` file from a previous model setup step. Must be given if no ‘model’ section in this file. If given, that model will be sampled from; otherwise, the model specified by the ‘model’ section of this file will be used.

**total\_samples** Total number of samples to draw. Either this or ‘sampling\_time’ must be given.

**sampling\_time** Number of seconds to run the sampling process. If present, overrides ‘total\_samples’.

**pickle\_sampler** Boolean. If true, the MITRE datastructure representing the sampler will be serialized to `[tag]_sampler_object.pickle` at the conclusion of sampling.

## 4.8 Postprocessing

The following settings, all optional, may be specified in section ‘postprocessing’:

**load\_sampler\_from\_pickle** String giving the location of a `sampler_object.pickle` file from a previous sampling step. Must be given if no ‘sampling’ section in this file. If given, generate output from the samples drawn by that sampler; otherwise, from the samples drawn as specified in the ‘sampling’ section of this file.

**burnin\_fraction** Number between 0 and 1 giving the fraction of samples to discard as burn-in before analysis. Defaults to 0.05.

**quick\_summary** Boolean. If True, write the point summary, the distribution of rule set lengths, and the Bayes factor in favor of the empty rule set `[tag]_quick_summary.txt`.

**full\_summary** Boolean. If True, write the point summary, the distribution of rule set lengths, the Bayes factor in favor of the empty rule set, and the highest-posterior-probability rule set clusters (see section 3.3 of the MITRE supplement) to `[tag]_full_summary.txt`.

**bayes\_factor\_table** Boolean. If True, write the 10 variables and 10 detectors with the highest Bayes factors supporting their inclusion in the true model, and those factors, to `[tag]_bayes_factor_table.txt`. See section 3.4 of the MITRE supplement.

**gui\_output** Boolean. If true, prepare an interactive visualization of the results as described in section 3.5 of the MITRE supplement and save it to `[tag]_visualization.html`. Note, this output cannot be generated if ‘aggregate\_on\_phylogeny’ is not set.

**bayes\_factor\_samples** Integer. Draw this many samples to estimate the prior distribution over the space of detectors in the process of estimating Bayes factors, if the other options in this section require the estimation of Bayes factors (beyond the Bayes factor for the empty rule set.) Default 10000.

**mixing\_diagnostics** Boolean. If true, plot the sampled values of the likelihood, prior, rule set length (total number of detectors), an arbitrary subset of the auxiliary variables  $\omega$ , and parameters  $f_w$ ,  $c_w$ ,  $\mu_L$ , and  $\sigma_L$  (defined in the MITRE supplementary note) versus MCMC iteration. Results will be saved in `[tag]_likelihood.pdf`, `[tag]_prior.pdf`, etc.

## 4.9 K-fold crossvalidation

Required or conditionally required options in section ‘crossvalidation’ are:

**load\_model\_from\_pickle** String giving the location of a `model_object.pickle` file from a previous model setup step. Must be given if no ‘model’ section in this file. If given, that model will be crossvalidated; otherwise, the model specified by the ‘model’ section of this file will be used.

**n\_folds** Integer; how many folds of cross-validation should be done.

**parallel\_workers** Integer; how many parallel worker processes should be launched.

**burnin\_fraction** Number between 0 and 1 giving the fraction of samples to discard as burn-in before calculating accuracy metrics for each fold.

**total\_samples** Total number of samples to draw for each fold. Either this or ‘sampling\_time’ must be given.

**sampling\_time** Number of seconds to run the sampling process for each fold. If present, overrides ‘total\_samples’.

Non-mandatory options are:

**write\_reports\_every\_fold** Boolean. If True, the quick summary described in section 4.8 will be written after sampling concludes for every fold (`[tag]_0_qr.txt`, `[tag]_1_qr.txt`, etc.) Note that accuracy

metrics in these reports are calculated based on the *training* set for the fold, not the held-out test set.

**write\_full\_summaries\_every\_fold** Boolean. If True, the full summary described in section 4.8 will be written after sampling concludes for every fold (`[tag]_0_full_summary.txt`, `[tag]_1_full_summary.txt`, etc.) Note that accuracy metrics in these reports are calculated based on the *training* set for the fold, not the held-out test set.

**pickle\_results** Boolean. If true, the true outcomes and predicted probabilities of a positive outcome for each subject in each test set under the point and ensemble classifiers will be written (as serialized Python objects) to `[tag]_cv_point_results.pickle` and `[tag]_cv_ensemble_results.pickle` for further analysis.

At the conclusion of crossvalidation, a table of accuracy metrics for the point and ensemble classifiers learned in each fold, applied to the held-out test data for each fold, will be written to `[tag]_mitre_cv_report.txt`.

## 4.10 Leave-one-out crossvalidation

The options for section ‘`leave_one_out`’ are the same as those for section ‘`crossvalidation`’, above, except that ‘`n_folds`’ is not required (and is ignored if given.)

At the conclusion of crossvalidation, a table of accuracy metrics for the predictions made on the left-out subjects for each fold will be written to `[tag]_mitre_leave_one_out_report.txt`.

## 4.11 Comparison

This section supports benchmarking the MITRE models against alternative methods. See the MITRE manuscript for the details of the comparison methods used and an explanation of these parameters. Options in section ‘`comparison_methods`’ are:

**load\_data\_from\_pickle** String giving the location of a `dataset_object.pickle` file from a previous preprocessing step. Must be given if no ‘`preprocessing`’ section in this file. If given, a model for that dataset will be built;

otherwise, a model will be built for the result of the ‘preprocessing’ step specified in this file.

**cv\_type** String, optional. If ‘leave\_one\_out’, assess the performance of the methods by leave-one-out crossvalidation; otherwise, use k-fold crossvalidation.

**n\_folds** Integer, required unless ‘cv\_type’ is ‘leave\_one\_out’, specifying how many folds to use for k-fold crossvalidation.

**n\_intervals** Integer, required.  $N_{w,comparison}$  in the notation of the MITRE manuscript.

**n\_consecutive** Integer, required.  $N_{c,comparison}$  in the notation of the MITRE manuscript.

## 4.12 Benchmarking

If this section is present:

1. Data is loaded following the options in the ‘preprocessing’ section normally, through the step of conversion to relative abundance.
2. The first comparison-methods crossvalidation is run immediately, following the options specified in the ‘comparison’ section of the configuration file as usual. (If log-transformation is specified in the ‘preprocessing’ section, this is applied to the data passed to the comparison methods.) The resulting report will be labeled `[tag]_benchmark_step3_comparison.txt`.
3. Temporal filtering options are applied to a copy of the dataset and a second comparison-methods crossvalidation is run. (Again, if log-transformation is specified in the ‘preprocessing’ section, this is applied to the data passed to the comparison methods.) The resulting report will be labeled `[tag]_benchmark_step4_comparison.txt`.
4. All later actions in the ‘preprocessing’ section are applied to the dataset normally, such as aggregation on the phylogenetic tree and log transformation. A third comparison-methods crossvalidation is run. The resulting report will be labeled `[tag]_benchmark_step5_comparison.txt`.

5. The dataset is used for MITRE crossvalidation, following the options specified in the ‘model’ and ‘crossvalidation’ or ‘leave\_one\_out’ section of the configuration file as usual.

The comparison method F1 scores reported in the manuscript are those from `...step3_comparison.txt` or `...step4_comparison.txt`, whichever are better, to provide the most favorable conditions for the comparison methods.

One option is allowed in this section (but its use is not recommended, as it is likely to lead to confusion.)

**load\_data\_from\_pickle** String giving the location of a `dataset_object.pickle`, *preprocessed up to conversion to relative abundance, but not farther*. If given, this will be loaded and the first part of the preprocessing stage will be skipped; options governing later steps of the preprocessing operation must still be specified in this file.

# Chapter 5

## Example configuration file

This file is also available as `example.cfg` in the MITRE source distribution. It specifies that MITRE should load data from the dietary perturbation study of David et al (2014), reprocessed as described in the MITRE supplementary note, learn rules that will predict whether a subject ate the exclusively plant-based diet or not, and produce text and interactive summaries of the results.

This file cannot be used exactly as is: you will need to edit the paths to the data files, and change the outcome and filtering parameters to whatever is appropriate for your own study. (Alternatively, if you do want to rerun this calculation, you can simply replace the options in the ‘data’ section with `load_example = david` to use the copies of the relevant files included with the MITRE distribution.)

Listing 5.1: Template MITRE configuration file

```
# Note: comments placed on their own lines
# may start with ';' or '#', but
# inline comments should start only with ';'.

[description]
tag = david_diet

[data]
abundance_data = /path/to/your_data/abundance.csv
sequence_key = /path/to/your_data/sequence_key.fa
sample_metadata = /path/to/your_data/sample_metadata.csv
subject_data = /path/to/your_data/subject_data.csv
jplace_file = /path/to/your_data/placements.jplace
```

```
outcome_variable = diet
outcome_positive_value = Plant
taxonomy_source = hybrid
pplacer_taxa_table = /path/to/your_data/taxaTable.csv
pplacer_seq_info = /path/to/your_data/seq_info.csv
placement_table = /path/to/your_data/mothur_placements.csv
```

### [\[preprocessing\]](#)

```
# Note that the order of these options in the configuration file is
# not important. Those filters and transformations selected will be
# applied in the following order:
# overall abundance filter, sample depth filter, window trimming,
# temporal sampling density filter, relative abundance
# transformation, phylogenetic aggregation, log transform,
# temporal abundance filter, surplus internal node filtering.

# Drop RSVs with less than a certain number of reads across
# all samples
min_overall_abundance = 10
# Drop samples with less than a certain total number of reads
min_sample_reads = 5000
# No need to trim the time window here, -5 to 10 is okay
# trim_start = 20
# trim_stop = 30
# Discard subjects with insufficiently dense temporal sampling:
# divide the window up into n_intervals equal pieces,
# then require at least n_samples within every n_consecutive
# consecutive such pieces
# We don't actually need to do this here, the sampling density
# is good for all 20 subjects.
# density_filter_n_samples = 1
# density_filter_n_intervals = 12
# density_filter_n_consecutive = 2
# Select which transformations should be applied to the data.
take_relative_abundance = True
aggregate_on_phylogeny = True
log_transform = False
# Temporal abundance filtration: keep only those taxa which
# exceed a threshold abundance in multiple consecutive observations
# at least once in a minimum number of subjects. Note that the
```

```
# threshold should be on a log scale if the log transform has been
# performed.
temporal_abundance_threshold = 0.001
temporal_abundance_consecutive_samples = 2
temporal_abundance_n_subjects = 4
# Discard taxa representing nodes in the phylogenetic tree not
# required to maintain the topological relationships among
# the other nodes of the tree still included in the model.
discard_surplus_internal_nodes = True
# Save this dataset as a pickle file?
pickle_dataset = True

[model]
# Divide the experiment into this many equal segments and use them
# as the atomic time windows
n_intervals = 10
# Allow rules to apply only to time windows longer than t_min
t_min = 1.0
# Allow rules to apply only to time windows shorter than t_max
t_max = 7.0
pickle_model = True

[sampling]
total_samples = 50000

[postprocessing]
quick_summary = True
full_summary = True
gui_output = True
burnin_fraction = 0.1
```