Quick Start when calculating MF from Hierarchical Data

Center for Veterinary Biologics - Statistics Section

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INTRODUCTION

This document is intended to supplement function help pages and guide users through the steps of applying functions of the MF package to the evaluation of mitigated fraction when data is arranged in a nested hierarchical structure, first implemented in version 4.3.5. Details of the algorithm are covered in a separate vignette titled Algorithms for calculating MF from hierarchical data. When calculating MF for clustered but not hierarchical data, refer to help pages for functions MFClus and MFClusBoot. For convenience, all help pages can also be accessed via the MF Manual.

Data assumptions. Nested Hierarchical structure.

Examples in this document expect input data to be structured in a *nested hierarchical tree*, as shown in Table 1. If there is only one grouping variable or the experimental design is crossed, it is not appropriate to use this guide as written.

A nested design assumes that the factor level of one variable co-occurs with that of another variable. For example, Pen D exists only within Room Z.

Mitigated Fraction. Bootstrapped and Calculated.

Users have the option of simply calculating the mitigated fraction or simultaneously bootstrapping the mitigated fraction (including confidence interval) and calculating the mitigated fraction. Examples of both options are shown in this document.

Technical requirements.

Examples in this manual were created using MF version 4.4.10, R version 4.4.1 (2024-06-14 ucrt) on Windows. CVB has not tested code usage on other systems.

The package can be found online at: https://github.com/ABS-dev/MF/blob/master/README.md, including installation instructions. It is expected that users have passing familiarity with R code and usage, as CVB does not have resources to address training or IT issues that may occur at external organizations.

Bug reports can be submitted online at: https://github.com/ABS-dev/MF/issues. To expedite resolution, please include a minimal working example and refrain from using confidential data. Incomplete issues may be closed without further investigation. Do not include confidential data as issue tracking is visible to all.

Table 1: Nested hierarchical data structure.

room	pen	litter	tx	lung
	-			5.63
		Litter 11	vac	4.62
		Little 11		9.20
	Pen A		con	7.28
			vac	3.76
		Litter 12		3.86
		Littlei 12		6.31
			con	3.52
Room W		Litter 13	vac	4.36
ROOM W				6.10
		Litter 15		7.87
	Pen B		con	8.34
				5.39
		Litter 14	vac	5.80
		Litter 14		8.28
			con	7.95
				4.86
		T:44 on 15	vac	5.66
		Litter 15		7.66
	Pen C		con	8.52
				4.17
		T::: 10	vac	4.84
	Lit	Litter 16		5.82
			con	7.72
	Pen D	Litter 17	vac	3.60
				4.92
			con	5.22
				5.93
		Litter 18	vac	7.62
				5.04
				8.62
			con	6.27
Room Z				3.79
	Pen E	Litter 19	vac	5.38
		Litter 19		9.45
			con	6.51
			vac	5.30
		Litter 20		4.42
		Litter 20		7.21
			con	6.35
				4.69
		Litter 21	vac	6.04
	Pen F	Litter 21		6.64
			con	7.00
			vac	4.90
		Litter 22		5.37
			con	6.77
		<u> </u>	0011	J

CALCULATED MF

General use.

To calculate mitigated fraction directly from data without bootstrapping, use the function MFClusHier. This function requires four inputs:

- formula: The formula in form y ~ x + a/b/c where y is a continuous response, x is a factor with two levels of treatment, and a/b/c are grouping variables. Nesting is assumed to be in order, left to right, highest to lowest. So a single level of "a" will contain multiple levels of "b" and a single level of "b" will contain multiple levels of "c".
- data: The data table (data.frame or tibble) with variables as identified in formula. If there are extra variables, they will be ignored.
- compare: Treatment groups, a text vector of length two. The first position [1] is treated as the control or reference group to which members of the second position [2] are compared.
- which.factor: One or more variable(s) of interest. This can be any of the grouping variables from the data set. If "All" is specified, a summary MF will be calculated for the whole tree.

Refer to the MFClusHier help page (?MFClusHier) for extended usage details.

Looking at MF for levels of a variable.

The which.factor argument allows users the option of selecting if mitigated fraction should be calculated for levels of a particular variable. In the data from Table 1, it may be of interest to calculate the mitigated fraction for each level of variable "room". It is possible to consider levels from multiple variables simultaneously, and the designator All can be used to evaluate for the entire tree, without breaking out by any variable. Evaluating the value of mitigated fraction for the entire tree is the default behavior, should the user not specify anything to the which.factor argument.

Common coding examples.

Default case, looking only at whole tree:

```
MFClusHier(formula = lung ~ tx + room / pen / litter, data = a)
```

Selecting a single variable to evaluate for each factor:

Selecting multiple variables, including the entire tree:

Basic Output.

The default display of MFClusHier output is a table with one row for each unique mitigated fraction calculated. A unique mitigated fraction value will be calculated for each level of the variables identified by the user in the argument which.factor (see previous discussion). The total number of rows is the sum of the number of unique levels for each grouping variable the user specified. The value "All" will add one row to this table.

```
mf_multiple <- MFClusHier(formula = lung ~ tx + room / pen / litter, data = a,</pre>
                            which.factor = c("room", "litter", "All"))
mf multiple
##
                                       U con_N vac_N con_medResp vac_medResp
      variable
                    level
                             MF N1N2
## 1
                   Room W 0.83
                                   24 22
                                             12
                                                   12
                                                             7.795
                                                                          4.850
           room
## 2
                   Room Z 0.91
                                   22 21
                                             11
                                                   12
                                                             6.640
                                                                          4.980
           room
## 3
        litter Litter 11 1.00
                                       4
                                              2
                                                    2
                                                             8.240
                                                                          5.125
## 4
        litter Litter 12 0.00
                                       2
                                              2
                                                    2
                                                             4.915
                                                                          3.810
                                              2
                                                    2
## 5
        litter Litter 13 1.00
                                    4
                                       4
                                                             8.105
                                                                          5.230
                                                    2
                                       4
                                              2
## 6
        litter Litter 14 1.00
                                                             8.115
                                                                          5.595
## 7
                                       4
                                              2
                                                    2
                                                                          5.260
        litter Litter 15 1.00
                                    4
                                                             8.090
                                              2
                                                    2
        litter Litter 16 1.00
                                       4
## 8
                                                             6.770
                                                                          4.505
## 9
        litter Litter 17 1.00
                                       4
                                              2
                                                    2
                                                             5.575
                                                                          4.260
## 10
        litter Litter 18 0.50
                                       3
                                              2
                                                    2
                                                                          6.330
                                                             7.445
                                              2
                                                    2
## 11
        litter Litter 19 1.00
                                       4
                                                             7.980
                                                                          4.585
                                              2
                                                    2
## 12
        litter Litter 20 1.00
                                       4
                                                             6.780
                                                                          4.860
                                              2
                                                    2
## 13
        litter Litter 21 1.00
                                    4
                                       4
                                                             6.820
                                                                          5.365
        litter Litter 22 1.00
                                    2
                                       2
                                                    2
                                                             6.770
## 14
                                              1
                                                                          5.135
                      All 0.87
## 15
                                   46 43
                                             23
            All
                                                   24
                                                             7.210
                                                                          4.910
```

The table columns are:

- variable: Which variable was considered when evaluating MF for the row.
- level: A unique factor level of the variable which was considered when evaluating MF for the row.
- MF: Mitigated fraction calculated value.
- N1N2: Sum of the n1n2 values from the rank table for the factor level of that row.
- U: Sum of the u values from the rank table for the factor level of that row.
- con_N & vac_N: Sum of the counts from the rank table matching the particular factor level of the row. Note that the left hand side of the underscore will match values passed by user to compare.
- con_medResp & vac_medResp: Median of responses for each comparison group matching the particular factor level of the row. Note that the left hand side of the underscore

will match values passed by user to argument compare.

Advanced usage.

This section covers the technical description of how to access the rank table from MFh() and summarize using MFnest(). For a full discussion of the algorithms used in these functions and how they are related, see Algorithms for calculating MF from hierarchical data.

Rank table.

To access the rank table, use the **MFh** field of the output object from MFClusHier(). For example:

```
thisMFh <- mf multiple$MFh
thisMFh
##
                       litter con medResp con n w vac medResp vac n n1n2 u
        room
               pen
## 1
      Room W Pen A Litter 11
                                     8.240
                                                2 7
                                                           5.125
                                                                           4 4
                                                2 5
                                                                     2
                                                                           4 2
      Room W Pen A Litter 12
                                     4.915
                                                           3.810
## 3 Room W Pen B Litter 13
                                                2 7
                                                           5.230
                                                                     2
                                                                           4 4
                                     8.105
## 4 Room W Pen B Litter 14
                                     8.115
                                                2 7
                                                                     2
                                                                           4 4
                                                           5.595
                                                2 7
     Room W Pen C Litter 15
                                     8.090
                                                           5.260
                                                                     2
                                                                           4 4
## 6 Room W Pen C Litter 16
                                     6.770
                                                2 7
                                                                     2
                                                                           4 4
                                                           4.505
      Room Z Pen D Litter 17
                                     5.575
                                                2 7
                                                                     2
                                                                           4 4
                                                           4.260
    Room Z Pen D Litter 18
                                                2 6
                                                                     2
                                                                           4 3
                                     7.445
                                                           6.330
      Room Z Pen E Litter 19
                                     7.980
                                                2 7
                                                           4.585
                                                                     2
                                                                           4 4
## 10 Room Z Pen E Litter 20
                                                2 7
                                                                     2
                                                                           4 4
                                     6.780
                                                           4.860
                                                                           4 4
## 11 Room Z Pen F Litter 21
                                     6.820
                                                2 7
                                                           5.365
                                                                     2
## 12 Room Z Pen F Litter 22
                                                1 3
                                     6.770
                                                           5.135
                                                                     2
                                                                           2 2
```

Alternatively, calculate rank table directly by using the MFh() function:

```
MFh(formula = lung ~ tx + room / pen / litter, data = a)
```

```
##
                       litter con medResp con n w vac medResp vac n n1n2 u
        room
                pen
      Room W Pen A Litter 11
                                     8.240
                                                2 7
                                                           5.125
                                                                      2
                                                                           4 4
## 2
      Room W Pen A Litter 12
                                     4.915
                                                2 5
                                                           3.810
                                                                      2
                                                                           4 2
                                                2 7
                                                           5.230
                                                                      2
                                                                           4 4
      Room W Pen B Litter 13
                                     8.105
## 4 Room W Pen B Litter 14
                                     8.115
                                                2 7
                                                           5.595
                                                                      2
                                                                           4 4
                                                2 7
                                                                      2
                                                                           4 4
## 5
     Room W Pen C Litter 15
                                     8.090
                                                           5.260
                                                                      2
                                                                           4 4
## 6 Room W Pen C Litter 16
                                     6.770
                                                2 7
                                                           4.505
                                                2 7
                                                                      2
                                                                           4 4
## 7
      Room Z Pen D Litter 17
                                     5.575
                                                           4.260
## 8 Room Z Pen D Litter 18
                                     7.445
                                                2 6
                                                                      2
                                                                           4 3
                                                           6.330
      Room Z Pen E Litter 19
                                     7.980
                                                2 7
                                                           4.585
                                                                      2
                                                                           4 4
## 10 Room Z Pen E Litter 20
                                     6.780
                                                2.7
                                                           4.860
                                                                      2
                                                                           4 4
## 11 Room Z Pen F Litter 21
                                     6.820
                                                2 7
                                                           5.365
                                                                      2
                                                                           4 4
## 12 Room Z Pen F Litter 22
                                     6.770
                                                1 3
                                                           5.135
                                                                      2
                                                                           2 2
```

The output table includes the following information, used to calculate the Basic Output table as described previously:

- con_n & vac_n: Counts of observations for each treatment for a particular instance of unique factor level of a variable. Note that the left hand side of the underscore will match values passed by user to compare.
- n1n2: Product of counts, con_n * vac_n.
- w: Wilcoxon statistic.
- u: Mann-Whitney statistic.
- con_medResp & vac_medResp: Median observed response for each treatment group in a particular instance of unique factor level. Note that the left hand side of the underscore will match values passed by user to compare.

There is one row for each unique combination of factor levels across all variables. This table shows the initial statistics as determined by the experimental design. Refer to the vignette for algorithm design Algorithms for calculating MF from hierarchical data for in-depth discussion of how the rank is used to evaluate mitigated fraction values.

The rank table is not affected by changes to the which.factor argument.

Reproducibility.

The rank table can be used to re-calculate the mitigated fraction values, for example if the user intends to explore a different selection to the which.factor argument. To do this, use the function MFnest which takes the following input arguments:

- Y: MFh field output as from MFClusHier()
- which.factor: As above.

For example:

```
MFnest(thisMFh, which.factor = "pen")
```

```
##
     variable level
                        MF N1N2 U con N vac N con medResp vac medResp
## 1
          pen Pen A 0.50
                              8 6
                                       4
                                              4
                                                       6.795
## 2
          pen Pen B 1.00
                              88
                                       4
                                              4
                                                      8.115
                                                                   5.595
## 3
          pen Pen C 1.00
                              88
                                       4
                                              4
                                                      7.690
                                                                    4.850
## 4
          pen Pen D 0.75
                              8 7
                                       4
                                              4
                                                      6.100
                                                                    4.980
          pen Pen E 1.00
                              88
                                       4
                                              4
                                                                    4.860
## 5
                                                       6.860
## 6
          pen Pen F 1.00
                              6 6
                                       3
                                              4
                                                      6.770
                                                                   5.135
```

This is the same output as if the user had initially selected for variable "pen":

```
##
     variable level
                       MF N1N2 U con_N vac_N con_medResp vac_medResp
## 1
          pen Pen A 0.50
                              8 6
                                      4
                                             4
                                                     6.795
                                                                  4.240
                              88
                                      4
                                             4
## 2
          pen Pen B 1.00
                                                     8.115
                                                                  5.595
```

##	3	pen	Pen	С	1.00	8	8	4	4	7.690	4.850
##	4	pen	Pen	D	0.75	8	7	4	4	6.100	4.980
##	5	pen	Pen	E	1.00	8	8	4	4	6.860	4.860
##	6	pen	Pen	F	1.00	6	6	3	4	6.770	5.135

BOOTSTRAPPED MF

General use.

The function MFClusBootHier allows for a bootstrapping approach to calculating mitigated fraction values. Input arguments are:

Same as in non-bootstrapped usage (i.e. MFClusHier)

- formula: The formula in form y ~ x + a/b/c where y is a continuous response, x is a factor with two levels of treatment, and a/b/c are grouping variables. Nesting is assumed to be in order, left to right, highest to lowest. So a single level of "a" will contain multiple levels of "b" and a single level of "b" will contain multiple levels of "c".
- data: The data table (data.frame or tibble) with variables as identified in argument formula. If there are extra variables, they will be ignored.
- compare: Treatment groups, a text vector of length two. The first position [1] is treated as the control or reference group to which members of the second position [2] are compared.
- which.factor: Variable(s) of interest. This can be any of the grouping variables from the data set. If "All" is specified, a summary MF will be calculated for the whole tree.

Additional arguments

- nboot: Number of bootstrapping events.
- boot.unit: Boolean whether to sample observations from within those of the same core.
- boot.cluster: Boolean whether to sample which clusters are present. If TRUE, some trees have all the clusters represented in the original data while others only have a subset.
- alpha: Complement of the confidence level. As used in MFClusBoot.
- seed: Used to initialize random number generator for reproducibility.

A "core" is the unique combination of variable levels from the data, including the compare designation. In Table 1, one core would be Room W/Pen A/Litter 11/vac and another would be Room Z/Pen F/Litter 22/con.

A "cluster" is the the unique combination of variable levels from the data, without the compare designation. In Table 1, the first four observations are from the same core, Room W/Pen A/Litter 11.

Refer to the MFClusHier help page (?MFClusBootHier) for extended usage details.

Further discussion regarding the bootstrapping algorithm can be found in Algorithms for

calculating MF from hierarchical data.

Common coding examples.

Default case, looking only at whole tree and bootstrapping both at the cluster and unit levels:

Specifying what bootstrapping sampling to occur:

Adjusting the number of bootstrapping events and alpha:

Basic output.

The default display of MFClusBootHier is a table with one row for each unique mitigated fraction calculated, just like in the non-bootstrapped approach. However, instead of summary statistics about the calculated mitigated fraction, there are values summarizing the mitigated fraction from a bootstrapped population.

##		variable	level	${\tt median}$	${\tt etlower}$	etupper	${\tt hdlower}$	${\tt hdupper}$	mf.obs
##	1	room	Room W	0.83	0.50	1.0	0.60	1.0	0.83
##	2	room	Room Z	0.92	0.75	1.0	0.80	1.0	0.91
##	3	litter	Litter 11	1.00	1.00	1.0	1.00	1.0	1.00
##	4	litter	Litter 12	0.00	0.00	0.0	0.00	0.0	0.00
##	5	litter	Litter 13	1.00	1.00	1.0	1.00	1.0	1.00
##	6	litter	Litter 14	1.00	1.00	1.0	1.00	1.0	1.00
##	7	litter	Litter 15	1.00	1.00	1.0	1.00	1.0	1.00
##	8	litter	Litter 16	1.00	1.00	1.0	1.00	1.0	1.00
##	9	litter	Litter 17	1.00	1.00	1.0	1.00	1.0	1.00
##	10	litter	Litter 18	0.50	0.50	0.5	0.50	0.5	0.50
##	11	litter	Litter 19	1.00	1.00	1.0	1.00	1.0	1.00
##	12	litter	Litter 20	1.00	1.00	1.0	1.00	1.0	1.00
##	13	litter	Litter 21	1.00	1.00	1.0	1.00	1.0	1.00
##	14	litter	Litter 22	1.00	1.00	1.0	1.00	1.0	1.00
##	15	All	All	0.88	0.71	1.0	0.75	1.0	0.87

The variable columns are:

- variable: Which variable was considered when evaluating MF for the row.
- level: A unique factor level of the variable which was considered when evaluating MF for the row.
- median: Median of mitigated fractions calculated from the bootstrapped population.
- etlower: Lower value of equal tailed range of mitigated fractions calculated from the bootstrapped population.
- etupper: Upper value of equal tailed range of mitigated fractions calculated from the bootstrapped population.
- hdlower: Lower value of the highest posterior density range of mitigated fractions calculated from the bootstrapped population.
- hdupper: Upper value of the highest posterior density range of mitigated fractions calculated from the bootstrapped population.
- mf.obs: Mitigated fraction value calculated from data input, without bootstrapping.

Advanced usage.

This section covers the technical description of how to access the bootstrapped results and use the MFnestBoot() function. For a full discussion of the algorithms of how MFhBoot(), MFnestBoot() and MFClusBootHier are related, or details of the bootstrapping algorithm, see Algorithms for calculating MF from hierarchical data.

Bootstrapping step output.

The bootstrapping stage is the most computationally intensive, so a user may wish to bypass this step subsequently if the only change are values being passed to the which.factor or alpha arguments. Access bootstrapping step outputs using the MFhBoot field of the output object. For example:

```
this_boot_mfh <- mfboot_multiple$MFhBoot
this_boot_mfh</pre>
```

```
## $bootmfh
## # A tibble: 120,000 x 11
##
      bootID con medResp con n
                                       w vac_medResp vac_n
                                                                   n1n2 room
                                                                                         litter
                                                                  u
                                                                                  pen
##
        <int>
                     <dbl> <dbl> <dbl>
                                                <dbl> <dbl> <dbl> <dbl> <chr>
                                                                                  <chr> <chr>
                                                           2
    1
                      8.24
                                2
                                       7
                                                 5.12
                                                                  4
##
            1
                                                                        4 Room W Pen A Litter 1
    2
                                2
                                       7
                                                 5.23
                                                           2
##
            1
                      8.10
                                                                  4
                                                                        4 Room W Pen B Litter 1
                                2
                                       7
                                                           2
                                                                  4
##
    3
            1
                      8.10
                                                 5.23
                                                                        4 Room W Pen B Litter 1
                                2
                                       7
                                                           2
##
    4
            1
                      8.10
                                                 5.23
                                                                  4
                                                                        4 Room W Pen B Litter 1
    5
            1
                      8.12
                                2
                                       7
                                                 5.60
                                                           2
                                                                  4
                                                                        4 Room W Pen B Litter 1
##
##
    6
            1
                      8.12
                                2
                                       7
                                                 5.60
                                                           2
                                                                  4
                                                                        4 Room W Pen B Litter 1
    7
                                2
                                       7
                                                           2
            1
                      8.09
                                                 5.26
                                                                  4
                                                                        4 Room W Pen C Litter 1
##
                      8.09
                                2
                                       7
                                                 5.26
                                                           2
                                                                  4
                                                                        4 Room W Pen C Litter 1
##
    8
            1
                                2
                                       7
                                                           2
##
    9
            1
                      8.09
                                                 5.26
                                                                  4
                                                                        4 Room W Pen C Litter 1
```

```
## 10
            1
                      5.57
                               2
                                      7
                                                4.26
                                                          2
                                                                4
                                                                       4 Room Z Pen D Litter 1
  # i 119,990 more rows
##
## $clusters
##
        room
                pen
                        litter clusterID
## 1
      Room W Pen A Litter 11
      Room W Pen A Litter 12
                                        2
##
      Room W Pen B Litter 13
                                        3
## 3
     Room W Pen B Litter 14
                                        4
     Room W Pen C Litter 15
                                        5
## 5
      Room W Pen C Litter 16
                                        6
## 7
      Room Z Pen D Litter 17
                                        7
      Room Z Pen D Litter 18
                                        8
      Room Z Pen E Litter 19
## 9
                                        9
## 10 Room Z Pen E Litter 20
                                       10
## 11 Room Z Pen F Litter 21
                                       11
## 12 Room Z Pen F Litter 22
                                       12
##
## $compare
## [1] "con" "vac"
##
## $mfh
## # A tibble: 12 x 10
##
                                                       w vac medResp vac n n1n2
      room
              pen
                    litter
                               con medResp con n
                                                                                        u
##
      <chr>
              <chr> <chr>
                                      <dbl> <dbl> <dbl>
                                                                <dbl> <dbl> <dbl> <dbl> <
                                       8.24
                                                                           2
                                                                                  4
##
    1 Room W Pen A Litter 11
                                                 2
                                                       7
                                                                 5.12
                                                                                        4
    2 Room W Pen A Litter 12
                                       4.92
                                                 2
                                                       5
                                                                 3.81
                                                                           2
                                                                                  4
                                                                                        2
##
##
    3 Room W Pen B Litter 13
                                       8.10
                                                 2
                                                       7
                                                                 5.23
                                                                           2
                                                                                  4
                                                                                        4
                                                 2
                                                                           2
    4 Room W Pen B Litter 14
                                                       7
                                                                                  4
                                                                                        4
##
                                       8.12
                                                                 5.60
##
    5 Room W Pen C Litter 15
                                       8.09
                                                 2
                                                       7
                                                                 5.26
                                                                           2
                                                                                  4
                                                                                        4
##
    6 Room W Pen C Litter 16
                                       6.77
                                                 2
                                                       7
                                                                 4.50
                                                                           2
                                                                                  4
                                                                                        4
                                                 2
                                                       7
                                                                           2
    7 Room Z Pen D Litter 17
                                       5.57
                                                                 4.26
                                                                                  4
                                                                                        4
    8 Room Z Pen D Litter 18
                                                 2
                                                                           2
                                                                                  4
                                                                                        3
##
                                       7.44
                                                       6
                                                                 6.33
    9 Room Z Pen E Litter 19
                                                 2
                                                       7
                                                                           2
                                       7.98
                                                                 4.58
                                                                                  4
                                                                                        4
## 10 Room Z Pen E Litter 20
                                                 2
                                                       7
                                                                 4.86
                                                                           2
                                                                                  4
                                                                                        4
                                       6.78
                                                 2
## 11 Room Z Pen F Litter 21
                                                       7
                                                                 5.36
                                                                           2
                                       6.82
                                                                                  4
                                                                                        4
## 12 Room Z Pen F Litter 22
                                                 1
                                                       3
                                                                           2
                                                                                  2
                                                                                        2
                                       6.77
                                                                 5.14
##
## $seed
## [1] 150
```

It is possible to calculate mfboot_multiple\$MFhBoot directly by using the MFhBoot() function, however this executes the bootstrapping stage again. To get the same output with both approaches, the seed argument must be the same value.

This output is a list of four objects:

- bootmfh: The rank table of all the bootstrapped data sets. This is formatted as the rank table for non-bootstrapped data with designation of a single bootstrapping instance using the additional variable bootID. Values for bootID are simply 1:nboot.
- clusters: Unique clusters in the data.
- compare: User-supplied value passed to compare argument.
- mfh: The rank table from user-supplied data; formatted as for non-bootstrapped data.

Note that in the particular case of boot.cluster = FALSE, although all nboot instances will be the same clusters as input data, observed responses will vary due to sampling of the cores. The case of both boot.cluster and boot.unit as FALSE is simply calculating MF from data without any bootstrapping.

Reproducibility.

To bootstrap from the same data in a reproducible manner, numerical value for the **seed** argument in MFClusBootHier. If no value for **seed** is specified, the function defaults to a value of **sample(1:1e+05, 1)** and subsequent iterations may yield different summaries.

Since the bootstrapping step is the most computationally intensive, a user may wish to use the bootstrapped rank table to recalculate mitigated fraction for levels of different variables or a different alpha for calculating confidence intervals. This is possible using the MFnestBoot function, which takes the following input arguments:

- x: MFhBoot field output as from MFClusBootHier.
- which.factor: As above.
- alpha: As above.

For example:

```
MFnestBoot(this_boot_mfh, which.factor = c("pen", "All"), alpha = 0.1)
## Complete separation observed for variable(s): pen
## $mfnest details
## # A tibble: 63,224 x 8
               variable, level [7]
## # Groups:
##
      variable level bootID
                                 U
                                   N1N2 con N vac N
##
      <chr>
               <chr> <int> <dbl> <dbl> <dbl> <dbl> <dbl> <dbl>
   1 All
               All
                           1
                                47
##
                                      48
                                             24
                                                   24 0.958
```

```
## 2 All
                                                    24 0.833
               All
                           2
                                 44
                                       48
                                             24
  3 All
               All
                           3
                                 39
                                       46
                                             23
                                                    24 0.696
##
## 4 All
               All
                           4
                                 43
                                       46
                                             23
                                                    24 0.870
## 5 All
               All
                           5
                                 37
                                       40
                                             20
                                                    24 0.85
## 6 All
               All
                                 45
                                       46
                                             23
                                                    24 0.957
                           6
## 7 All
               All
                           7
                                 46
                                       48
                                             24
                                                    24 0.917
## 8 All
               All
                           8
                                 39
                                       44
                                             22
                                                    24 0.773
## 9 All
               All
                           9
                                 48
                                       48
                                             24
                                                    24 1
## 10 All
               A11
                          10
                                 41
                                       44
                                             22
                                                    24 0.864
## # i 63,214 more rows
##
## $mfnest summary
## # A tibble: 7 x 8
##
     variable level median etlower etupper hdlower hdupper mf.obs
##
              <chr>
                      dbl>
                               <dbl>
                                       <dbl>
                                                <dbl>
                                                        <dbl>
                                                                <dbl>
## 1 pen
              Pen A
                     0.5
                              0
                                           1
                                                 0
                                                               0.5
                                                            1
## 2 pen
              Pen B
                     1
                              1
                                           1
                                                 1
                                                            1
                                                                1
## 3 pen
              Pen C
                     1
                              1
                                           1
                                                 1
                                                            1
                                                               1
              Pen D 0.75
## 4 pen
                              0.5
                                           1
                                                 0.5
                                                            1
                                                               0.75
## 5 pen
              Pen E 1
                              1
                                           1
                                                 1
                                                            1
                                                               1
## 6 pen
              Pen F
                                           1
                                                            1
                                                 1
                                                               1
## 7 All
                      0.875
                              0.708
                                                 0.75
                                                            1 0.870
              All
                                           1
##
## $seed
## [1] 150
```

APPENDIX

Code for example data.

```
a <- data.frame(
  room = paste("Room", rep(c("W", "Z"), each = 24)),
  pen = paste("Pen", rep(LETTERS[1:6], each = 8)),
  litter = paste("Litter", rep(11:22, each = 4)),
  tx = rep(rep(c("vac", "con"), each = 2), 12)
)
set.seed(76153)
a$lung[a$tx == "vac"] <- round(rnorm(24, 5, 1.3), 2)
a$lung[a$tx == "con"] <- round(rnorm(24, 7, 1.3), 2)
a <- a[-48, ]</pre>
```

Session details for this manual.

```
sessionInfo()
## R version 4.4.1 (2024-06-14 ucrt)
## Platform: x86 64-w64-mingw32/x64
## Running under: Windows 11 x64 (build 22631)
##
## Matrix products: default
##
##
## locale:
## [1] LC COLLATE=English United States.utf8 LC CTYPE=English United States.utf8
## [3] LC_MONETARY=English_United States.utf8 LC_NUMERIC=C
## [5] LC TIME=English United States.utf8
##
## time zone: America/Chicago
## tzcode source: internal
## attached base packages:
## [1] stats
                 graphics grDevices utils
                                                datasets methods
                                                                    base
##
## other attached packages:
## [1] lubridate 1.9.3 forcats 1.0.0
                                                                             purrr 1.0.2
                                           stringr 1.5.1
                                                            dplyr 1.1.4
  [6] readr 2.1.5
                         tidyr 1.3.1
                                          tibble_3.2.1
                                                            ggplot2_3.5.1
                                                                             tidyverse 2.
## [11] kableExtra 1.4.0 knitr 1.47
                                          MF 4.4.10
##
## loaded via a namespace (and not attached):
     [1] CVBdevtools 0.0.0.9003
                                           remotes 2.5.0
##
     [3] rlang_1.1.4
##
                                           magrittr 2.0.3
     [5] clue 0.3-65
                                           GetoptLong 1.0.5
##
##
     [7] git2r 0.33.0
                                          matrixStats 1.3.0
##
     [9] compiler 4.4.1
                                           systemfonts 1.1.0
    [11] png 0.1-8
##
                                           callr_3.7.6
##
    [13] vctrs_0.6.5
                                          profvis 0.3.8
    [15] pkgconfig 2.0.3
##
                                           shape 1.4.6.1
##
    [17] crayon 1.5.3
                                           fastmap 1.2.0
    [19] backports_1.5.0
                                           ellipsis_0.3.2
    [21] utf8 1.2.4
##
                                          promises 1.3.0
##
    [23] rmarkdown 2.27
                                          tzdb 0.4.0
##
    [25] sessioninfo 1.2.2
                                          ps 1.7.7
    [27] tinytex 0.51
                                           xfun_0.45
##
    [29] cachem 1.1.0
                                           later 1.3.2
##
    [31] parallel 4.4.1
                                           cluster 2.1.6
##
    [33] R6 2.5.1
                                           stringi 1.8.4
```

```
##
    [35] pkgndep 1.99.3
                                           RColorBrewer 1.1-3
    [37] pkgload 1.4.0
##
                                           Rcpp 1.0.12
##
    [39] iterators 1.0.14
                                           usethis 2.2.3
    [41] IRanges_2.38.1
                                           timechange_0.3.0
    [43] httpuv 1.6.15
##
                                           tidyselect 1.2.1
    [45] rstudioapi 0.16.0
                                           yaml_2.3.9
    [47] doParallel 1.0.17
                                           codetools_0.2-20
    [49] miniUI 0.1.1.1
                                           processx 3.8.4
##
    [51] pkgbuild 1.4.4
                                           plyr 1.8.9
##
    [53] shiny 1.8.1.1
                                           withr_3.0.0
##
    [55] evaluate_0.24.0
                                           desc_1.4.3
##
    [57] sifr 0.0.3.9000.0.0.1696492414 urlchecker 1.0.1
##
    [59] xml2 1.3.6
                                           circlize 0.4.16
    [61] pillar 1.9.0
                                           rsconnect 1.3.1
##
    [63] foreach_1.5.2
                                           stats4_4.4.1
    [65] rex 1.2.1
##
                                           generics 0.1.3
    [67] codeDiagnostics 0.1.4
                                           hms 1.1.3
##
##
    [69] BiocVersion 3.19.1
                                           S4Vectors 0.42.1
    [71] munsell_0.5.1
                                           scales_1.3.0
##
    [73] xtable 1.8-4
                                           glue 1.7.0
    [75] lazyeval 0.2.2
                                           tools 4.4.1
    [77] data.table 1.15.4
##
                                           fs 1.6.4
    [79] grid_4.4.1
                                           cyclocomp_1.1.1
##
    [81] lintr 3.1.2
                                           devtools 2.4.5
##
    [83] colorspace 2.1-0
                                           colt 0.1.1
##
    [85] cli 3.6.3
                                           fansi 1.0.6
##
    [87] viridisLite 0.4.2
                                           svglite_2.1.3
##
    [89] ComplexHeatmap 2.20.0
                                           gtable 0.3.5
##
    [91] hash 2.2.6.3
                                           digest 0.6.36
##
    [93] BiocGenerics_0.50.0
                                           rjson_0.2.21
##
    [95] htmlwidgets 1.6.4
                                           memoise 2.0.1
##
    [97] htmltools 0.5.8.1
                                           pkgdown 2.1.0
    [99] lifecycle 1.0.4
                                           GlobalOptions 0.1.2
## [101] mime_0.12
```