

# Package ‘titeR’

November 22, 2016

**Title** Tools for analyzing and visualizing antibody titer data

**Version** 0.0.1.0027

**Description** This package contains methods to calculate endpoints from antibody titer data and visualize titers.

**Depends** R (>= 3.0.2)

**Imports** tidy,  
dplyr,  
grid,  
ggplot2

**BugReports** <https://github.com/stefanavey/titeR/issues>

**License** CCO

**LazyData** true

**RoxygenNote** 5.0.1

**Suggests** knitr,  
rmarkdown

**VignetteBuilder** knitr

## R topics documented:

+.uneval . . . . .	2
Barplot . . . . .	2
BubbleChart . . . . .	3
CalculateD0NormPaired . . . . .	5
CalculatePadjMFC . . . . .	6
CalculateSAdjMFC . . . . .	7
CalculateStdNorm . . . . .	8
FormatTiters . . . . .	9
GetEqn . . . . .	10
Multiplot . . . . .	11
titeR . . . . .	12
Year1_Titers . . . . .	12
Year2_Titers . . . . .	13
<b>Index</b>	<b>14</b>

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<code>+.uneval</code>	<i>Addition for <code>aes()</code> and <code>aes_string()</code></i>
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### Description

`+.uneval` is a helper function to allow adding `aes` and `aes_string` in `ggplot2`

### Usage

```
## S3 method for class 'uneval'
a + b
```

### References

<http://stackoverflow.com/questions/28777626/how-do-i-combine-aes-and-aes-string-options>

### Examples

```
library(ggplot2)
v1 <- "mpg"
v2 <- "qsec"
ggplot(mtcars, aes(x=wt)) + ylab("") +
  geom_line(aes_string(y=v1) + aes(color="one")) +
  geom_line(aes_string(y=v2) + aes(color="two")) +
  scale_color_manual(name="Val", values=c(one="#105B63", two="#BD4932"))
```

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Barplot	<i>Titer bar plots.</i>
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### Description

Barplot plots the baseline and day 28 titers

### Usage

```
Barplot(dat_list, subjectCol = "SubjectID", cols = 1, groupVar = NULL,
  colors = c("#A6CEE3", "#1F78B4", "#B2DF8A", "#33A02C", "#FB9A99", "#E31A1C",
    "#FDBF6F", "#FF7F00"))
```

### Arguments

<code>dat_list</code>	a named list like the one returned by <a href="#">FormatTitters</a> .
<code>subjectCol</code>	the name of the column specifying a subject ID. Default is "SubjectID".
<code>cols</code>	numeric specifying how many columns to layout plot
<code>groupVar</code>	an optional character string specifying a grouping variable. May be either a variable in <code>dat_list</code> or an endpoint. Default is NULL
<code>colors</code>	a vector of colors specifying bar colors. If <code>dat_list</code> contains more than 4 elements, you must specify your own colors.

**Value**

(invisibly) a list of ggplot2 object(s).

**Author(s)**

Stefan Avey

**Examples**

```
## Prepare the data
strains <- c("A_California_7_2009", "A_Perth_16_2009", "B_Brisbane_60_2008")
titer_list <- FormatTitters(Year1_Titters, strains, subjectCol = "YaleID", otherCols = "AgeGroup")

## Bar plot of a single strain
Barplot(titer_list[strains[1]], subjectCol = "YaleID")

## Bar plot of all 3 strains
Barplot(titer_list, subjectCol = "YaleID")

## Can improve readability of previous plot by separating into groups
## For example, group by AgeGroup
Barplot(titer_list, subjectCol = "YaleID", groupVar = "AgeGroup")
```

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BubbleChart

---

*Bubble Chart*


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**Description**

BubbleChart visualizes baseline vs fold change in titers

**Usage**

```
BubbleChart(dat_list, fit = NULL, yMinZero = FALSE,
  eqSize = 6/log2(length(dat_list) + 1), subjectCol = "SubjectID",
  colorBy = NULL, xlimits = c(1.5, 10.5), xbreaks = 2:10,
  ylimits = c(-0.5, 10), ybreaks = seq(0, 10, 2), plot = TRUE, cols = 2,
  ...)
```

**Arguments**

dat_list	a named list like the one returned by <a href="#">FormatTitters</a> . Values are assumed to be log2-transformed.
fit	what type of fit to add. Current options are "lm" for linear model, "exp" for exponential, or NULL for no smoothing.
yMinZero	a logical specifying whether fitted y values below 0 should be set to 0.
eqSize	Text size of the equation. Only relevant if fit is not NULL
subjectCol	the name of the column specifying a subject ID. Default is "SubjectID".
colorBy	a character string specifying an endpoint to colorBy or NULL (default) for no coloring.
xlimits	the x-axis limits (passed to scale_x_continuous)

<code>xbreaks</code>	the x-axis breaks (passed to <code>scale_x_continuous</code> )
<code>ylimits</code>	the y-axis limits (passed to <code>scale_y_continuous</code> )
<code>ybreaks</code>	the y-axis breaks (passed to <code>scale_y_continuous</code> )
<code>plot</code>	logical indicating whether to plot or not. Default is TRUE
<code>cols</code>	numeric specifying how many columns to layout plot
<code>...</code>	other arguments besides <code>method</code> and <code>subjectCol</code> passed to <a href="#">CalculateSAdjMFC</a> .

### Details

This plot was designed for HAI titer data with baseline columns and fold change columns for multiple strains.

### Value

(invisibly) a list of ggplot2 objects.

### Author(s)

Stefan Avey

### See Also

`FormatTiters`

### Examples

```
## Prepare the data
strains <- c("A_California_7_2009", "A_Perth_16_2009", "B_Brisbane_60_2008")
titer_list <- FormatTiters(Year2_Titers, strains, subjectCol = "YaleID",
                          otherCols = "AgeGroup")

## Basic plot without any fitted model
BubbleChart(titer_list)

## Change layout to plot 3 strains in a single column
BubbleChart(titer_list, cols = 1)

## Add a linear fit
BubbleChart(titer_list, fit = "lm", subjectCol = "YaleID")

## Add an exponential fit
BubbleChart(titer_list, fit = "exp", subjectCol = "YaleID")

## Add coloring by age
BubbleChart(titer_list, fit = "exp", subjectCol = "YaleID", colorBy = "AgeGroup")
```

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`CalculateD0NormPaired` *CalculateD0NormPaired*

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## Description

`CalculateD0NormPaired` calculates the normalized day 0 titer paired with the titer with maximum normalized fold change

## Usage

```
CalculateD0NormPaired(dat, fcStdCols = grep("fc_std_norm", colnames(dat),  
  value = TRUE))
```

## Arguments

<code>dat</code>	data frame containing <code>fcStdCols</code>
<code>fcStdCols</code>	column names containing the titer fold changes for each strain standardized across subjects

## Details

If there are multiple strains that have the maximal fold change, choose the day 0 titer that is higher since this will allow for a greater adjustment and better chance of being a high responder.

Column names containing the day 0 titers for each strain standardized across subjects are assumed to follow the same pattern as `fcStdCols` with "d0" replacing "fc" in the name.

## Value

a numeric vector containing the values from `d0StdCols` that correspond to the maximum over the strains of `fcStdCols`

## Author(s)

Stefan Avey

## Examples

```
## First Example
```

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CalculatePadjMFC	<i>CalculatePadjMFC</i>
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---

## Description

CalculatePadjMFC calculates the paired, adjusted maximum fold change (padjMFC)

## Usage

```
CalculatePadjMFC(dat, fcCol = "fc_norm_max_ivt", d0Col = "d0_norm_paired",
  discretize = c(0.2, 0.3), scaleResiduals = FALSE,
  responseLabels = paste0(c("low", "moderate", "high"), "Responder"), ...)
```

## Arguments

<code>dat</code>	the data containing the columns <code>fcCol</code> and <code>d0Col</code>
<code>fcCol</code>	character string specifying the name of the fold change column from <code>dat</code>
<code>d0Col</code>	character string specifying the name of the day 0 column from <code>dat</code>
<code>discretize</code>	a vector of quantiles in (0, 0.5] specifying where to make the cutoff for low, moderate and high responses. Default is 20% and 30%.
<code>scaleResiduals</code>	Logical. Should residuals be scaled inversely by the square of the confidence intervals from the linear model.
<code>responseLabels</code>	names for low, moderate and high responses
<code>...</code>	Additional arguments passed to <code>lm</code>

## Details

Calculate the paired, adjusted maximum fold change (padjMFC) from `fc_norm_max_ivt` and `d0_norm_paired` using linear regression to remove the effect of baseline titers. Missing (NA) values are handled and any missing values in `fcCol` and `d0Col` will also be missing in the output.

## Value

A list with the first element named "linearModel" for the linear model and then "padjMFC" containing the continuous padjMFC metric and one additional element for each value of `discretize` giving the discrete labels.

## Author(s)

Stefan Avey

## See Also

`lm`

## Examples

```
## First Example
```

---

CalculateSAdjMFC

*Calculate SAdjMFC*


---

## Description

CalculateSAdjMFC calculates the baseline-adjusted maximum fold change (MFC) for each viral strain

## Usage

```
CalculateSAdjMFC(datList, subjectCol = "SubjectID", method = c("lm", "exp"),
  yMinZero = FALSE, scoreFun = max, fcCol = "fc", d0Col = "d0",
  normalize = TRUE, discretize = c(0.2, 0.3), scaleResiduals = FALSE,
  responseLabels = paste0(c("low", "moderate", "high"), "Responder"),
  na_action = "na.fail", ...)
```

## Arguments

datList	a list with one data frame for each strain and each data frame containing the columns fcCol and d0Col. The order of each data frame must be the same and they must be the same dimensions. In addition, each data frame must be sorted by d0Col from low to high.
subjectCol	the name of the column specifying a subject ID. Default is "SubjectID".
method	a character string specifying the method used to model the relationship between day 0 and fold change values. One of either "lm" for a linear model or "exp" for an exponential model.
yMinZero	a logical specifying whether fitted y values below 0 should be set to 0.
scoreFun	a function applied to all (potentially scaled) residuals for each subject to determine the endpoint. Default is max but sum may also be useful to quantify the total response.
fcCol	character string specifying the name of the fold change column in each element of datList
d0Col	character string specifying the name of the day 0 column in each element of datList
normalize	Logical specifying whether residuals should be normalized with the inverse normal transform. Default is TRUE.
discretize	a vector of quantiles in (0, 0.5] specifying where to make the cutoff for low, moderate and high responses. Default is 20% and 30%.
scaleResiduals	Logical. Should residuals be scaled inversely by the square of the confidence intervals from the linear model.
responseLabels	names for low, moderate and high responses
na_action	how should missing NA values be treated. Default is "na.fail"
...	Additional arguments passed to lm if method == "lm" or nls if method == "exp"

**Details**

Calculates the baseline-adjusted fold change for each strain of virus using (unnormalized) fold change and baseline titers. Linear regression or an exponential curve is used to remove the effect of baseline titers on fold changes. The score function (scoreFun) is used to combine the adjusted fold change across multiple strains. Missing (NA) values are handled by being returned as missing in the endpoints in the output

**Value**

A list with the following elements: "models": the models calculated on each strain separately (with names the same as on datList) "residualMatrix": the matrix of residuals "SAdjMFC": a list containing the continuous and discrete SAdjMFC metrics

**Author(s)**

Stefan Avey

**See Also**

lm, nls

**Examples**

```
## First Example
```

---

CalculateStdNorm

*Calculate Normalized Titers*

---

**Description**

CalculateStdNorm calculates the standardized d0 or fc titers

**Usage**

```
CalculateStdNorm(dat, type, fcToOne = FALSE, idCol = "SubjectID",
  cols = grep(paste0(type, "_[AB]"), colnames(dat), value = TRUE))
```

**Arguments**

dat	Data frame containing fcStdCols
type	What should be standarized. Either "d0", or "fc".
fcToOne	Logical. Are titer fold changes allowed to be less than 1 or should these be changed to 1 before standardization? Default is FALSE and no changes will be made. Only relevant when type == "fc"
idCol	Name of column containing subject IDs
cols	column names containing the titer measurements for each strain



**Details**

This must be run on only 1 cohort at a time because titers will be normalized across all subjects. The median is used but unlike the original reference, the standard deviation is calculated rather than the maximum absolute deviation.

**Value**

A data frame like `dat` but with standardized columns added

**Author(s)**

Stefan Avey

**References**

Tsang JS, et al. (2014) Global analyses of human immune variation reveal baseline predictors of postvaccination responses. *Cell* 157(2):499–513.

**Examples**

```
## First Example
```

---

FormatTiters	<i>Format antibody titers.</i>
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---

**Description**

FormatTiters formats titers into a list with one tidy data frame per viral strain

**Usage**

```
FormatTiters(titers, strains, subjectCol = "SubjectID",
  otherCols = vector(mode = "character"), d0Cols = paste0("d0_", strains),
  fcCols = paste0("fc_", strains), fcMinZero = TRUE, log2Transform = TRUE)
```

**Arguments**

<code>titers</code>	a data frame containing the titer information
<code>strains</code>	the names of the virus strains
<code>subjectCol</code>	the name of the column specifying a subject ID. Default is "SubjectID".
<code>otherCols</code>	a character vector specifying which additional columns of titers to retain. (Defaults to an empty character vector).
<code>d0Cols</code>	the column names of day 0 (baseline) columns
<code>fcCols</code>	the column names of fold change columns
<code>fcMinZero</code>	should negative fold changes be set to 0? Default is TRUE
<code>log2Transform</code>	logical specifying whether titer values should be log2 transformed

**Value**

a list of data frames with one data frame per viral strain containing the baseline ("d0"), fold change ("fc") and any other columns specified by the otherColumns argument.

**Author(s)**

Stefan Avey

**Examples**

```
strains <- c("A_California_7_2009", "A_Perth_16_2009", "B_Brisbane_60_2008")
titer_list <- FormatTiters(Year1_Titers, strains, subjectCol = "YaleID")
```

---

GetEqn

*Get Formatted Model Equation*


---

**Description**

GetEqn gets the equation for various models in a human readable format

**Usage**

```
GetEqn(m)
```

**Arguments**

m                      a model object

**Author(s)**

Stefan Avey

**References**

original lm\_eqn and inspiration from this SO post <http://stackoverflow.com/questions/7549694/ggplot2-adding-regression-line-equation-and-r2-on-graph>.

**Examples**

```
## First Example
```

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Multiplot

---

Multiple ggplot2 plots on the same page

---

## Description

Multiple Plot Function for ggplot

## Usage

```
Multiplot(..., plotlist = NULL, cols = 1, layout = NULL)
```

## Arguments

...	ggplot objects
plotlist	a list of ggplot objects
cols	Number of columns in layout
layout	A matrix specifying the layout. If present, 'cols' is ignored

## Details

If the layout is something like `matrix(c(1,2,3,3), nrow=2, byrow=TRUE)`, then plot 1 will go in the upper left, 2 will go in the upper right, and 3 will go all the way across the bottom.

## Author(s)

R Cookbook

## References

[http://www.cookbook-r.com/Graphs/Multiple\\_graphs\\_on\\_one\\_page\\_%28ggplot2%29/](http://www.cookbook-r.com/Graphs/Multiple_graphs_on_one_page_%28ggplot2%29/)

## Examples

```
library(ggplot2)

## This example uses the ChickWeight dataset, which comes with ggplot2
## First plot
p1 <- ggplot(ChickWeight, aes(x=Time, y=weight, colour=Diet, group=Chick)) +
  geom_line() +
  ggtitle("Growth curve for individual chicks")

# Second plot
p2 <- ggplot(ChickWeight, aes(x=Time, y=weight, colour=Diet)) +
  geom_point(alpha=.3) +
  geom_smooth(alpha=.2, size=1) +
  ggtitle("Fitted growth curve per diet")

# Third plot
p3 <- ggplot(subset(ChickWeight, Time==21), aes(x=weight, colour=Diet)) +
  geom_density() +
  ggtitle("Final weight, by diet")
```

```

# Fourth plot
p4 <- ggplot(subset(ChickWeight, Time==21), aes(x=weight, fill=Diet)) +
  geom_histogram(colour="black", binwidth=50) +
  facet_grid(Diet ~ .) +
  ggtitle("Final weight, by diet") +
  theme(legend.position="none")      # No legend (redundant in this graph)

Multiplot(p1, p2, p3, p4, cols=2)

```

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titerR	<i>titerR - An R package for antibody titer data</i>
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### Description

titerR - An R package for antibody titer data

---

Year1_Titers	<i>Year 1 titers.</i>
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---

### Description

Antibody titers to 3 strains of influenza in a cohort of young and older adults from Yale during the 2010-2011 flu season.

### Usage

Year1\_Titers

### Format

A data frame with 42 rows and 11 variables:

**YaleID** subject identifier, unique

**AgeGroup** age of subject. 20-35 (Young), >= 65 (Older)

... Other columns follow the format <type>\_<strain> where <type> is either Day 0 ("d0"), Day 28 ("d28"), or fold change ("fc").

### References

Thakar J, et al. (2015) Aging-dependent alterations in gene expression and a mitochondrial signature of responsiveness to human influenza vaccination. *Aging (Albany NY)* 7(1):38-52.  
<https://www.ncbi.nlm.nih.gov/pubmed/25596819>

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Year2_Titers	<i>Year 2 titers.</i>
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---

**Description**

Antibody titers to 3 strains of influenza in a cohort of young and older adults from Yale during the 2011-2012 flu season.

**Usage**

Year2\_Titers

**Format**

A data frame with 69 rows and 11 variables:

**YaleID** subject identifier, unique

**AgeGroup** age of subject. 20-35 (Young), >= 65 (Older)

... Other columns follow the format <type>\_<strain> where <type> is either Day 0 ("d0"), Day 28 ("d28"), or fold change ("fc").

**References**

Thakar J, et al. (2015) Aging-dependent alterations in gene expression and a mitochondrial signature of responsiveness to human influenza vaccination. *Aging (Albany NY)* 7(1):38-52.  
<https://www.ncbi.nlm.nih.gov/pubmed/25596819>

# Index

- \*Topic **HIPC**
  - BubbleChart, [3](#)
  - CalculateSAdjMFC, [7](#)
  - FormatTiters, [9](#)
- \*Topic **aveytoolkit**
  - GetEqn, [10](#)
- \*Topic **datasets**
  - Year1\_Titers, [12](#)
  - Year2\_Titers, [13](#)
- +.uneval, [2](#)
- Barplot, [2](#)
- BubbleChart, [3](#)
- CalculateD0NormPaired, [5](#)
- CalculatePadjMFC, [6](#)
- CalculateSAdjMFC, [4](#), [7](#)
- CalculateStdNorm, [8](#)
- FormatTiters, [2](#), [3](#), [9](#)
- GetEqn, [10](#)
- Multiplot, [11](#)
- titeR, [12](#)
- titeR-package (titeR), [12](#)
- Year1\_Titers, [12](#)
- Year2\_Titers, [13](#)