

bdots

Abstract

The Bootstrapped Differences of Timeseries (bdots) was first introduced by Oleson (and others) as a method for controlling type I error in a composite of serially correlated tests of differences between two time series curves in the context of eye tracking data. This methodology was originally implemented in R by Seedorff 2018. Here, we revist the original package, both expanding the underlying theoretical components and creating a more robust implementation.

1 Introduction

In 2017, Oleson et al. introduced a method for detecting time-specific differences between (group? idk rewrite this sentence) functions in time. This largely centered around bootstrapping and computing a series of highly correlated t -statistics and using estimates of the autocorrelation as an adjustment for the family-wise error rate, presented in the context of the Visual World Paradigm (VWP), an experimental paradigm combining eyetracking with an interactive environment to measure dynamics in language processing. In 2018, **bdots** was introduced on CRAN to perform a limited version of the analysis proposed in Oleson. Here, we introduce **bdots v2**, an update to the CRAN package that broadly expands the capabilities of the original.

This paper is not intended to serve as a complete use guide for the **bdots** package. Rather, the purpose is to showcase major changes and improvements to the package, with those seeking a more comprehensive treatment directed to the package vignettes. Updates to the **bdots** package have been such that there is little resemblance to the original. Rather than taking a “compare and contrast” approach, we will first enumerate the major changes, followed by a general demonstration of the package use:

1. Simplified user interface
2. User defined curves
3. Permit fitting for arbitrary number of groups
4. Updates to bootstrapping algorithm and introduction of permutation test

5. Automatic detection of paired tests based on subject identifier
6. Allows for non-homogenous sampling of data across subjects and groups
7. Introduce formula syntax for bootstrapping difference function
8. The fitted `bdots` object inherits from `data.table` class

Bootstrapped differences in time series The high level motivation of `bdots`, abstracted from the particulars, is more or less as follows: we are often interested in generally comparing time series between two or more groups and in particular, identifying a window of time in which they differ significantly without a priori specification of any regions. A full(er) review of previous methods can be found in Seedorff, though here we limit the scope of interest to specifying that we are interested in “developing a statistical tool to (1) detect differences in two time series (such as the VWP) and (2) to offer a precise characterization of the time window in which a difference occurs [?].” This is subsequently done in two steps. First, we use a bootstrapping procedure to estimate the group distributions of two time series; and second, we use either a FWER correction or permutation testing to identify time windows in which differences occur.

A typical instantiation of this problem occurs when we have two groups (or experimental conditions, etc.) in which individual subjects have an associated time series. For example, we may be interested in comparing the growth of a particular tumor in mice over time between a control group and several candidate treatment groups. It’s assumed that each group has some distribution of associated functions in time, and we are interested in identifying windows in time in which these distributions of functions are significantly different. This is done by analyzing the difference of timeseries.

The original `bdots` package was predicated on comparing differences between dense, highly correlated time series by first specifying functional forms and then performing statistical tests on each of the observed time points. With version 2.0, capabilities have drastically improved, and `bdots` is able to fit parametric functions to any type of data observed in time. Along with methodological improvements, we have included more options in determining statistical significance in the differences of curves, utilizing a **robust** permutation testing framework when the assumptions of autocorrelation do not hold. In addition to methodology, a number of quality-of-life improvements have also been made, greatly simplifying syntax, creating more **robust** functions, and including a collection of useful methods for handling returned objects.

In summary, `bdots` has transitioned from a package focused exclusively on densely sampled timeseries assuming a limited number of functional forms to a **robust** framework for identifying time windows of significant difference across a wide breadth of timeseries-adjacent data.

2 Methodology and Overview

A standard analysis using **bdots** consists of two steps: estimating distributions of functions for groups of interest and then determining where in time the difference of these functions is statistically significant.

[can maybe delete this par since i kinda say it in next section] In addition to changes in the underlying methodology of the original **bdots** package, version 2.0 introduces permutation testing for situations in which assumptions of autocorrelation do not hold. These changes have impacts on both the estimation of the group distributions, as well as for identifying significant time windows. A fuller treatment of these methodologies is given in chapter 3.

2.1 Creating Group Distributions

Broadly, there are two steps to performing an analysis with the **bdots** package: fitting the curves to observed data and bootstrapping differences between groups. The first step involves specifying an underlying curve f , which is assumed to be parametric¹. Along with the observed data y for each i th subject, **bdots**, via fitting with **gnls**, returns a set of parameters along with an estimate of their covariance.

$$F : f \times y_i \rightarrow N(\hat{\theta}_i, V_i), \quad (1)$$

where θ is a length- p vector representing the parameters of the function.

Once the fits have been made, we are ready to estimate the generating distributions for the groups being compared. The bootstrapping algorithm for each group is as follows (this does not address the new issue with paired **bdots** from **bob**):

1. For a group of size n , select n subjects from the group, *with replacement*. This controls for the between subject variability
2. For each selected subject, draw a set of parameters from the distribution $\theta_i^* \sim N(\hat{\theta}_i, V_i)$. This permits us to account for within subject variability
3. For each of the resampled θ_i^* , find the b th bootstrap estimate for the group $\theta_b = \frac{1}{n} \sum_{i=1}^n \theta_i^*$
4. Perform this sequence B times

The end results is a $B \times p$ matrix containing a bootstrapped sample of the group distribution for θ . Each row of this matrix is used to create a $1 \times T$ vector representing f_θ evaluated at T time points. This results

¹the option to include non-parametric functions is anticipated in the future work of this package. The process will be similar, however, with θ then representing the number and location of the knots for splines

in a $B \times T$ matrix representing a collection of bootstrapped curves evaluated at each time point, in total representing a bootstrapped distribution of the curves.

Group distributions in hand, we next attend to identifying regions in which a statistically significant difference between curves is present, choosing from one of the two methods currently available.

2.2 Evaluating significance differences

There are a number of methods included in the `bdots` package for identifying windows where time series differ significantly. First, there are a collection of FWER alpha adjustments, including Oleson’s method (2017). New to version 2.0 are methods related to permutation testing. A review of the theoretical considerations, as well as underlying assumptions for each are briefly presented here.

2.2.1 Permutation Testing

maybe switch order of this and fwer

The simplest method implemented for identifying time-specific differences is permutation testing, ideal when minimal assumptions can be made on the observed data.

We begin by computing a t -statistic of the difference at each time point,

$$T(t) = \frac{|\bar{f}_1(t) - \bar{f}_2(t)|}{\sqrt{\frac{1}{n_2} \text{Var}(f_1(t)) + \frac{1}{n_2} \text{Var}(f_2(t))}}, \quad (2)$$

or, in the case of paired groups,

$$T(t) = \frac{\bar{f}_D(t)}{\sqrt{\frac{1}{n} \text{Var}(f_D(t))}}. \quad (3)$$

Next, we go about creating a null distribution against which to test our hypothesis that there is no difference between each group at each time point. We do this with permutations, the algorithm being as follows: for two groups, with n_1 and n_2 subjects in each:

1. Assign to each subject a label indicating group membership
2. Randomly shuffle the labels indicating membership, creating two new groups with n_1 and n_2 subjects in each
3. Recalculate the t -statistic, $T(t)$ and record the maximum of each permutation

The collection of maximum values for $T(t)$ will serve as the null distribution against which to compare our observed $T(t)$. Regions in which the observed t statistic are beyond the specified α in the null distribution are then considered significant.

2.2.2 FWER Adjustment

In addition to permutation testing, there are also adjustments that can be made to control for the family-wise error rate. As was done with permutation testing, we begin by computing a t -statistic at each time point for the observed data,

$$T(t) = \frac{|\bar{f}_1(t) - \bar{f}_2(t)|}{\sqrt{\frac{1}{n_2} \text{Var}(f_1(t)) + \frac{1}{n_2} \text{Var}(f_2(t))}}, \quad (4)$$

or, again in the case of paired groups,

$$T(t) = \frac{\bar{f}_D(t)}{\sqrt{\frac{1}{n} \text{Var}(f_D(t))}}. \quad (5)$$

Unlike the case with the permuted data, we have no need for a null distribution, instead determining significance by considering the observed statistics against a modified α . Adjustments that can be made include all of the adjustments found in `stats::p.adjust`, as well as the adjustment “oleson” used in the original `bdots` package. In short, the “oleson” adjustment makes use of an autocorrelation parameter to adjust for the highly correlated series of t -statistics. A full treatment of this methodology, along with a comparison to other FWER adjustments and adjustments based on FDR, is included in Oleson 2017.

3 Standard Analysis

3.1 Example Data

The `bdots` package now has support for data with non-homogenous time sampling across subjects and trials. We illustrate this with a worked example where we will consider a study (source?) comparing tumor growth for the 451LuBr cell line in mice with repeated measures in five treatment groups.

A standard analysis using `bdots` consists of two steps: fitting subject specific curves and determining the group distributions through bootstrapping.

```
> head(mouse)
```

	Volume	Day	Treatment	ID
1:	47.432	0	A	1
2:	98.315	5	A	1
3:	593.028	15	A	1
4:	565.000	19	A	1
5:	1041.880	26	A	1
6:	1555.200	30	A	1

Figure 1: Illustration of Mouse data

3.2 Fitting Curves

The curve fitting process is performed with the `bfit` function (previously `bdotsFit`), taking the following arguments:

```
bfit(data, subject, time, y, group, curveType, cores, ...)
```

(need to add/talk about an `AR1` argument that fits data with this assumption or not)

The dataset being analyzed is passed into the `data` argument and should be in long format. The experimental conditions or groups being analyzed are passed into the `group` argument: unlike previous iterations of `bdots`, an arbitrary number of groups can be fit at once, assuming that they all adopt the same parametric form (for example, the four parameter logistic). The `subject` argument is the subject identifier column. Here, it is important to note that if a paired design is being conducted that the subject identifiers are the same between groups. That is, when determining the regions of significant differences in the bootstrapping step, the paired status between two groups is determined by comparing the intersection of two groups with themselves. `time`, of course, is the name of the column containing time, and `cores` tells the fitter how many computer cores to use in a parallel environment (the default is half). Each of `subject`, `time`, and `y`, are length one character vectors representing columns of the dataset used in `data`, while `group` is a character vector (of varying length), also column(s) found in `data`. Finally, there is the `curveType` argument which is discussed in the next section.

Curve functions New here is `curveType`, where we specify the (parametric) curve that we wish to fit to the dataset provided in `bfit`. Unlike the previous arguments taking either a `data.frame` or character vector, this argument takes a function call, for example, `logistic()`. The motivation for this is detailed in the appendix, but in short, it allows one to provide additional arguments to the fitting curve. For example, provided with `bdots` are a number of common parameteric functions (with their default arguments) including `logistic()`, `doubleGauss(concave = TRUE)`, `expCurve()`, and `polynomial(degree = 5)`. `bfit` will also accept user-

created curves, and a detailed vignettes for writing your own can be found with `vignette("bdots")`.

Return object and generics The function `bfit` returns an object of class `bdotsObj`, inheriting from class `data.table`. As such, each row uniquely identifies one permutation of subject and group values. Included in this row are the subject identifier, group classification, summary statistics regarding the curves, and a nested `gnls` object. Several methods exist for this object, including `plot`, `summary`, and `coef`, returning a matrix of fitted coefficients returned from `gnls`.

Fit Codes (assumption of autocorrelation may change)

One column included in `bdotsObj` is `fitCode`, a numeric summary statistic ranked from 0 to 6 detailing information about the quality of the fitted curve. By default, `bfit` assumes autocorrelation in the fitting of individual subject curves. The `gnls` function is not always able to accommodate this, and in situations in which the fitting algorithm fails, it will try again, dropping the AR(1) assumption. An indication of whether an AR(1) model was fit or not, in conjunction with a range of R^2 values, gives rise to the value for `fitCode`, presented in Table 1. The method for determining the `fitCode` can be seen in the following lines:

```
AR1 <- # determines if AR1 status
fitCode <- 3L*(!AR1) + 1L*(R2 < 0.95)*(R2 > 0.8) + 2L*(R2 < 0.8)
```

A fit code of 6 indicates that `gnls` was unable to successfully fit the subject's data.

fitCode	AR(1)	R^2
0	TRUE	$R^2 > 0.95$
1	TRUE	$0.8 < R^2 < 0.95$
2	TRUE	$R^2 < 0.8$
3	FALSE	$R^2 > 0.95$
4	FALSE	$0.8 < R^2 < 0.95$
5	FALSE	$R^2 < 0.8$
6	NA	NA

Table 1: fit codes, though less relevant for other types of data so idk really what to do about it. nothing for the dissertation, at least

Future work on the package will seek to modularize the evaluation of fit quality, allowing users more freedom in creating a hierarchy of fitted values.

3.2.1 Worked example (fitting)

We begin by fitting our mouse data using the `bdots` fitting function, `bfit`

```
mouse_fit <- bfit(data = mouse, subject = "ID", time = "Day",
  y = "Volume", group = "Treatment", curveType = expCurve())
```

As the object `fit` is of class `data.table`, the default print option simply prints it as it would any other `data.table` or `data.frame`. A summary method is included, providing information on the type of fit, diagnostics for each group, and diagnostics for fits overall. An example of this summary for a single treatment group is included here:

```
> summary(mouse_fit[Treatment == "A", ])
```

```
bdotsFit Summary
```

```
Curve Type: expCurve
Formula: Volume ~ x0 * exp(Day * k)
Time Range: (0, 106) [31 points]
```

```
Treatment: A
Num Obs: 10
Parameter Values:
      x0      k
172.232953 0.056843
#####
##### FITS #####
#####
AR1,      0.95 <= R2      -- 2
AR1,      0.80 < R2 <= 0.95 -- 1
AR1,      R2 < 0.8      -- 0
Non-AR1,  0.95 <= R2      -- 0
Non-AR1,  0.8 < R2 <= 0.95 -- 3
Non-AR1,  R2 < 0.8      -- 4
No Fit                                -- 0
```

```
All Fits
Num Obs: 42
Parameter Values:
      x0      k
102.487118 0.053662
#####
##### FITS #####
#####
AR1,      0.95 <= R2      -- 4
AR1,      0.80 < R2 <= 0.95 -- 2
AR1,      R2 < 0.8      -- 0
Non-AR1,  0.95 <= R2      -- 9
Non-AR1,  0.8 < R2 <= 0.95 -- 16
Non-AR1,  R2 < 0.8      -- 11
No Fit                                -- 0
```

Figure 2: Abridged summary of mouse fit data

The default plotting method plots each of the fitted subjects, including observed and fit data. See Figure 3 for a plot of the first four fitted subjects.

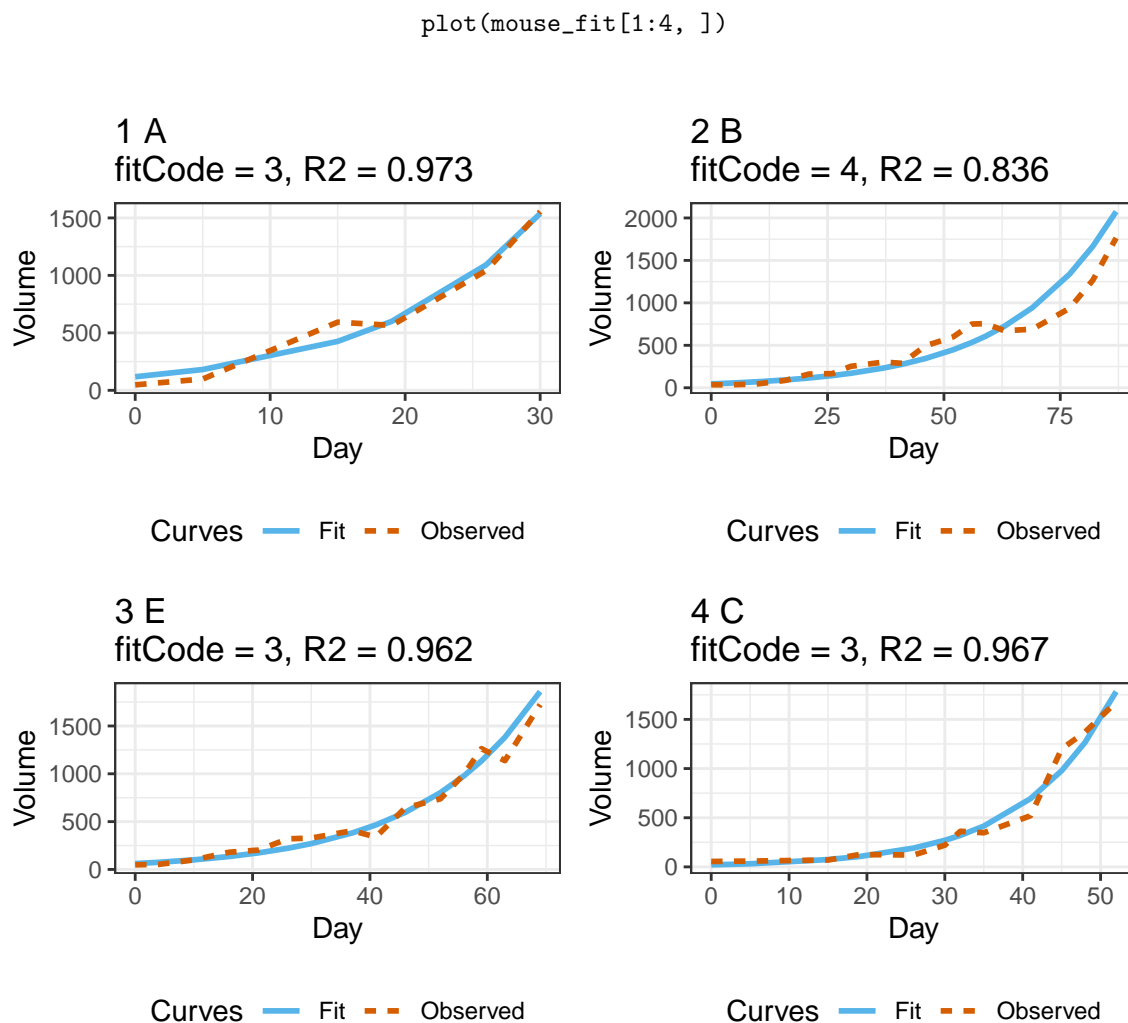


Figure 3: No longer using scale image saweet. But i would like to include a generic/no ggplot2 in the final version

3.3 Bootstrapping

Once fits have been made, we are ready to begin estimating the group distributions. This is done with the bootstrapping function, `bboot`. The number of options included in the `bboot` function have expanded to include a new formula syntax for specifying the analysis of interest as well as to include options for permutation testing. A call to `bboot` takes the following form

```
(singleMeans we should discuss)
bboot(formula, bdObj, Niter, alpha, padj, permutation, singleMeans, cores, ...)
```

By default, the method for determining significance when comparing the difference of two time series is the permutation method, as this makes the fewest assumptions while maintaining an appropriate type I error rate and adequate power (see chapter 3). While `permutation = TRUE`, the argument to `padj` is ignored; otherwise, adjustments can be made to the specified `alpha` to control FWER as was presented in the original `bdots` package. Regardless of what method is used for determining significance, bootstrapping as detailed in Chapter 3 is still used for determining group distributions. Finally, in contrast to the previous `bdots`, there is no longer a need to specify if the groups are paired; `bboot` determines this automatically based on the subject identifiers in each of the groups.

A key component of the bootstrapping function is specifying which groups in our dataset we are wishing to analyze and how. This is done with a formula syntax unique to `bdots` explained in the next section.

3.3.1 Bootstrapping Formula

As the `bfit` function is now able to create fits for an arbitrary number of groups, we rely on a formula syntax in `bboot` to specify precisely which groups differences we wish to compare. Let `y` designate the outcome variable indicated in the `bfit` function and let `group` be one of the group column names to which our functions were fit. Further, let `val1` and `val2` be values of two of the groups in that same column. The general syntax for the `bboot` function takes the following form:

$$y \sim \text{group}(\text{val1}, \text{val2})$$

Note that this is an expression in R and is written without quotation marks used in a character vector. To give a more concrete example, suppose we wished to compare the difference in tumor growth curves for treatments A and B in our mouse data (see Figure 1 for column names and values). We would do so with the following syntax:

$$\text{Volume} \sim \text{Treatment}(\text{A}, \text{B})$$

There are two special cases to consider when writing this syntax. The first is the situation that arises in the case of nested groups, the second when a difference of difference analysis is conducted. Details on both of these cases are handled in the appendix.

3.4 Summary and Analysis

Let's begin first by running `bboot` using bootstrapping to compare the difference in tumor growth between treatment groups A and E in our mouse data using permutations to test for regions of significant difference.

```
mouse_boot <- bboot(Volume ~ Treatment(A, E), bdObj = mouse_fit, permutation = TRUE)
```

This returns an object of class `bdotsBootObj`. A summary method is included to display relevant information:

```
> summary(mouse_boot)

bdotsBoot Summary

Curve Type: expCurve
Formula: Volume ~ x0 * exp(Day * k)
Time Range: (0, 106) [31 points]

Difference of difference: FALSE
Paired t-test: FALSE
Difference: Treatment

FWER adjust method: Permutation
Alpha: 0.05
Significant Intervals:
      [,1] [,2]
[1,]   15  46
```

There are a few components of this worth identifying when reporting the results. First, included at the top is the name of the function used, its expression in R, and the range of time points considered. Below this is information related to the provided formula, namely: is this a difference of difference, are the elements of the groups paired, and what grouping was used in determining the differences. The final section includes information on the FWER, including the method used and the level at which significance was determined. When using one of the autocorrelated alpha-adjusted parameters, estimated of the autocorrelation and the adjusted alpha are also presented. Finally included is a matrix of significant intervals. This is NULL if no significant differences were found at the specified alpha; otherwise one row is included for each disjointed region of significance.

In addition to the provided summary output, plotting methods are available

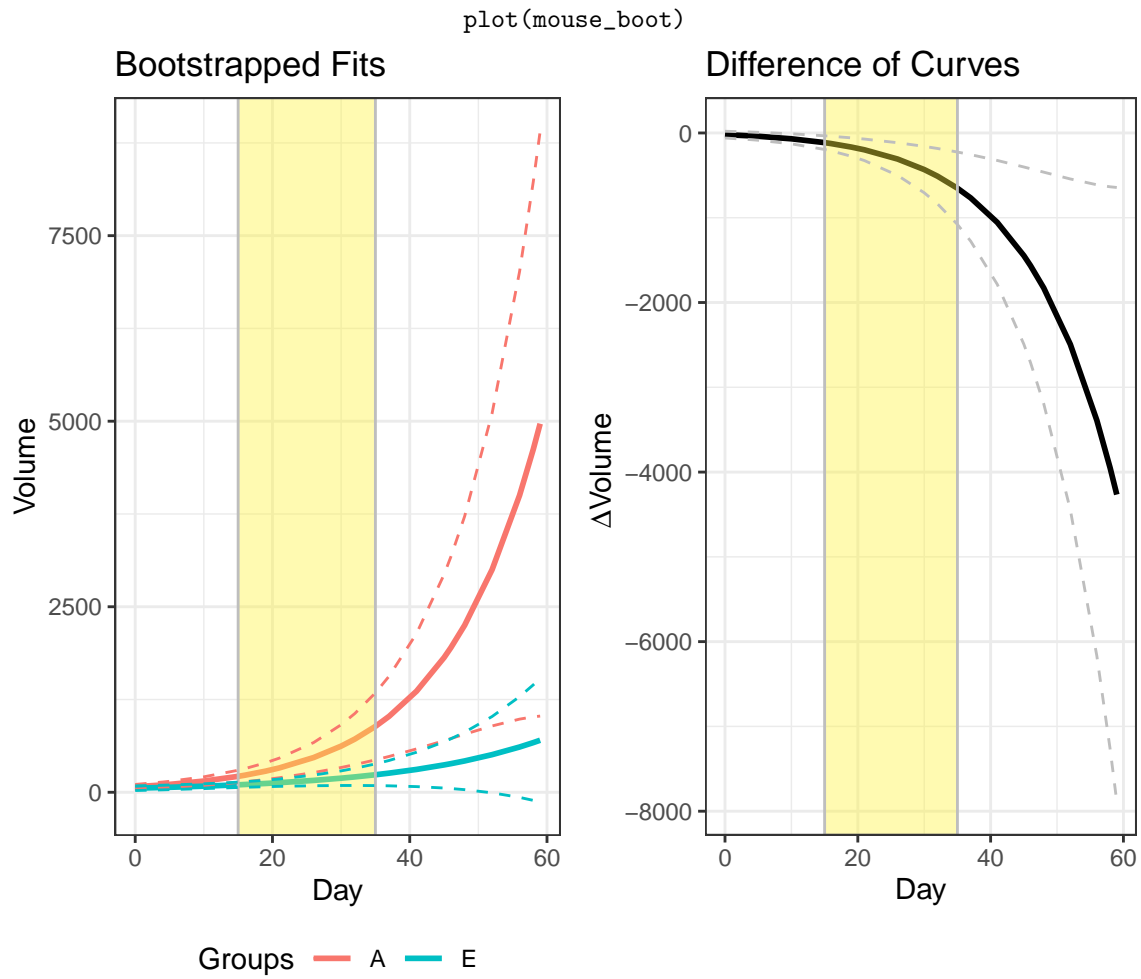


Figure 4: These confidence intervals are based on the bootstrap (permutation only does significance testing). I will go through and investigate this more closely later, my guess is this is related to the fact that we are using the intersection of time points to fit curves while most data (maybe) only goes out to half way. will investigate later. Because obviously values of 100,000 are way the eff out of what is even remotely reasonable. UPDATE: I cheated and cut time to max out at 60 instead of 105. Can consider how else to resolve this. Also, NOTE: significant region did change somewhat considerably when cutting max time with less time being evaluating resulting in larger regions being significant

Depending on user needs, these plots can be recreated both without confidence bands or without the additional difference curve

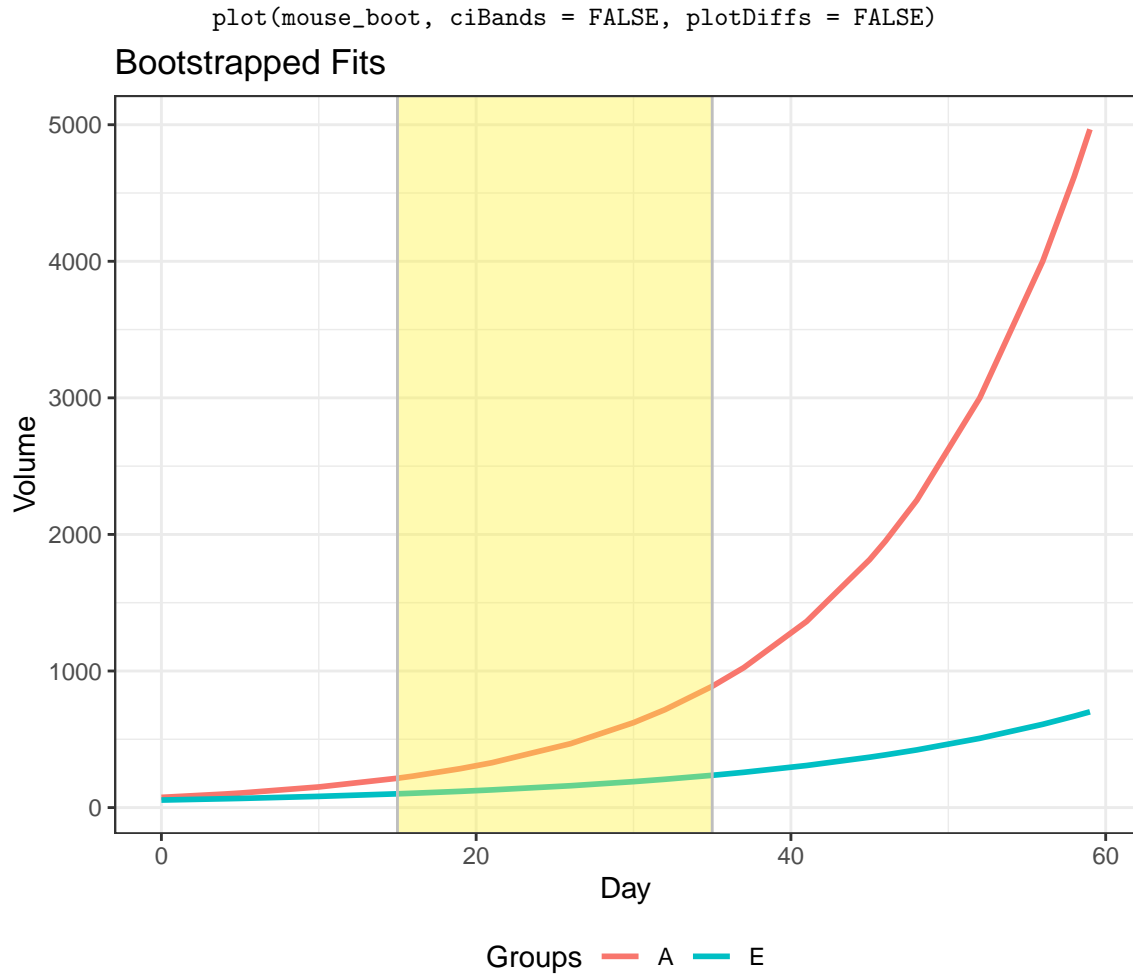


Figure 5: obviously this has same issue with previous.

4 Extras

Let's do a brief tour of some of the other additions to `bdots` that probably doesn't warrant its own section for use

Do I mention non-homogenous sampling elsewhere? could also illustarte with saccades, idk

4.1 Non-homogenous sampling

[not sure if i need this section or if i should elaborate]

The `bdots` package now has support for data with non-homogenous time sampling across subjects or trials. For example, here is data collected comparing tumor growth for 451LuBr cell line in mice with repeated measures and five treatment groups

It is not a problem to fit these groups and perform our bootstrapping analysis either on the union of

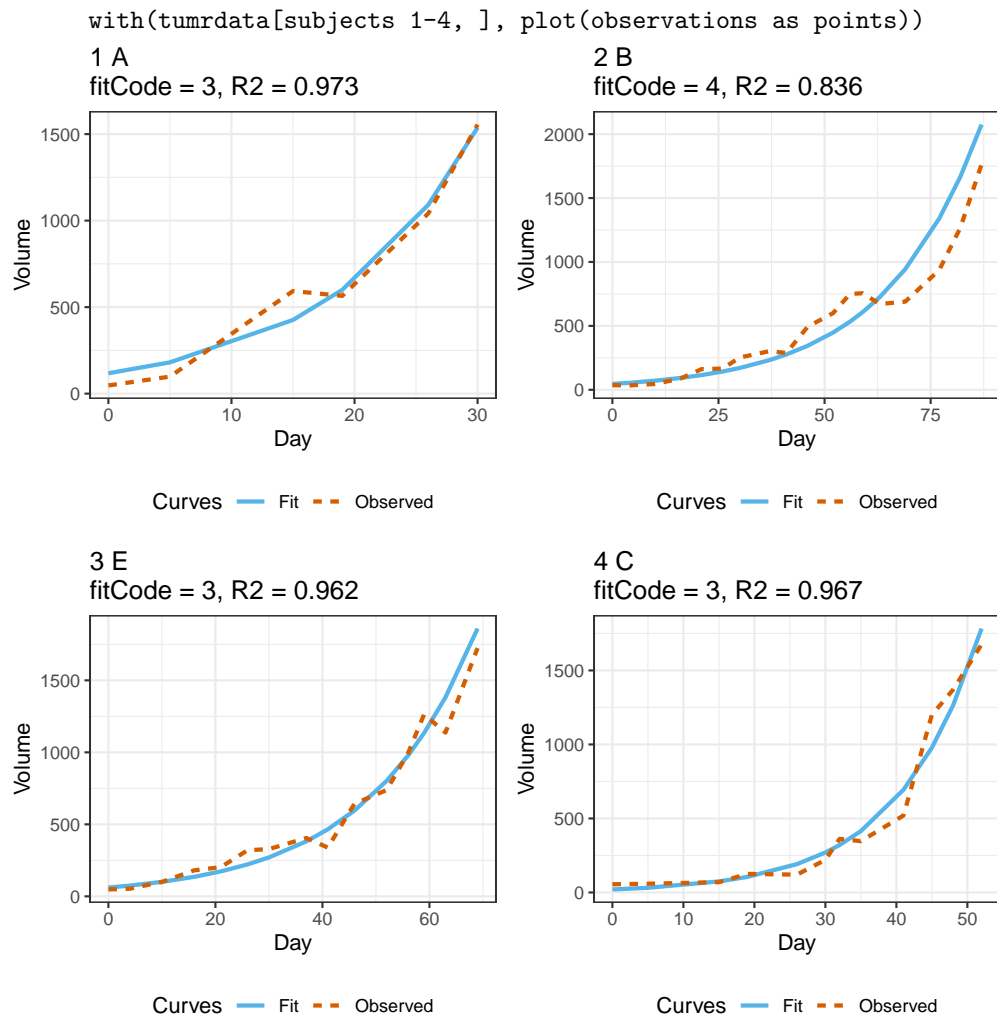


Figure 6: mousey data

observed time, or some custom range in between

example?

`bdots` also allows for repeated observations, as is the case with saccade data from the VWP. Here, an individual subject has 30 trials with saccades taken at the trial level. That is, rather than taking a sequence of observations for each subject, `bfit` allows for an unordered set with observations and associated time, $\mathcal{S}_i = \{(y_j, t_j)\}$ across j observations. As this relates to the VWP, you can read more about his development in my dope ass other paper called chapter 2.

4.2 Refitting

There are sometimes situations in which the fitted function returned by `bfit` is a poor fit. This is largely a consequence of the sensitivity of the `nlme::gnls` function used in `bfit` for fitting the non-linear curves. Sensible starting parameters are computed as a part of the curve fitting functions (i.e., `logistic()`, but see the vignettes for more details), though these can often be improved upon. The quality of the fit can be evidenced by the `fitCode` or via a visual inspection of the fitted functions against the observations for each subject. When this occurs, there are several options available to the user, all of which are provided through the function `brefit` (previously `bdotsRefit`). `brefit` takes the following arguments:

```
brefit(bdObj, fitCode = 1L, quickRefit = FALSE, numRefits = 2L, paramDT = NULL)
```

The first of these arguments, outside of the object itself, is `fitCode`, indicating the minimum fit code to be included in the refitting process. This is a convenient way to limit the refitting process to those of a particular quality. Given the sensitivity of `nlme::gnls` to the starting parameters, one can often try automatically refitting all of the specified subject by simply jittering the previous set of parameters and comparing the updated fit to the original; this is done by setting `quickRefit = TRUE`, with `numRefits` indicating how many attempts the fitter should make in doing so.

Finally, `paramDT` allows for a `data.table` with columns for subject, group identifiers, and parameters to be passed in as a new set of starting parameters. This `data.table` requires the same format as that returned by `bdots::coefWriteout`. The use of this functionality is covered in more detail in the `bdots` vignettes and is a useful way for reproducing a `bdotsObj` from a plain text file. When `quickRefit = FALSE`, the user is put through a series of prompts whereby for each subject to be refit, in addition to being given a series of diagnostics:

```

Subject: 11
R2: 0.837
AR1: FALSE
rho: 0.9
fitCode: 4

Model Parameters:
      x0      k
53.186497 0.051749

Actions:
1) Keep original fit
2) Jitter parameters
3) Adjust starting parameters manually
4) Remove AR1 assumption
5) See original fit metrics
6) Delete subject
99) Save and exit refitter
Choose (1-6):

```

Along with this is given a plot of the original fit, side-by-side with the suggested alternative.

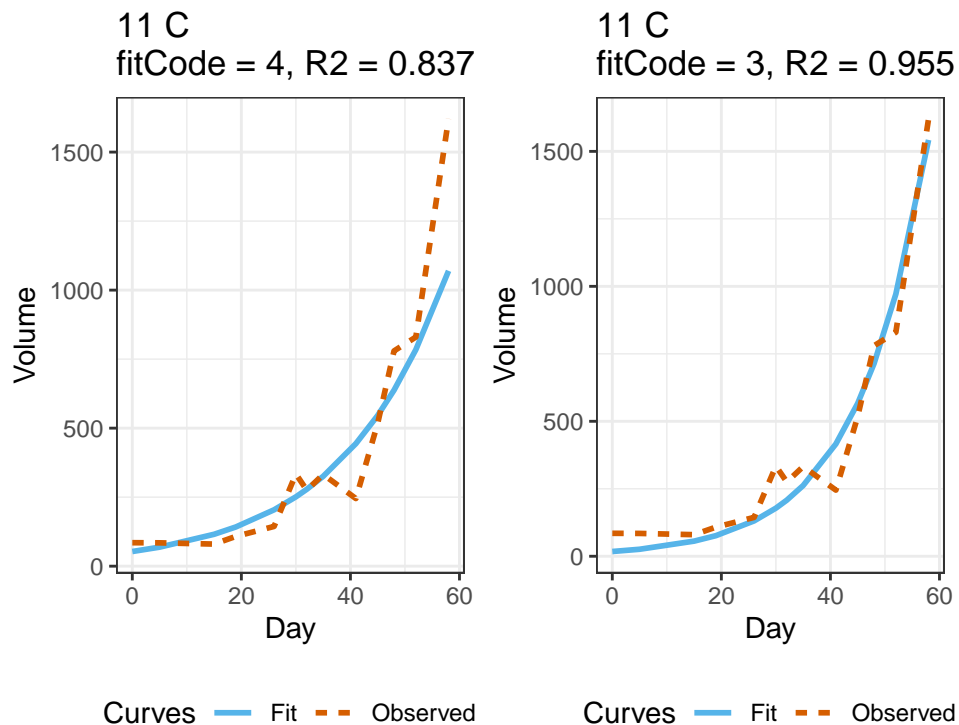


Figure 7: before and after refit: man i am good at picking new parameters

As the menu item suggests, users have the ability to end the manually refitting process early and save where they had left off. To retain previously refit items and start again at a later time, pass the first refitted

object back into the refitter as such:

```
refit <- brefit(fit, ...)
refit <- brefit(refit, ...) # pass in the refitted object
```

A final note should be said regarding the option to delete a subject. As **bdots** now automatically determines if subjects are paired based on subject identifiers (necessary for calculations in the significance testing step), it is critical that if a subject has a poor fit in one group and must be removed that he or she is also removed from all additional groups in order to retain paired status. This can be overwritten with a final prompt in the **brefit** function before they are removed. The removal of subjects can also be done with the ancillary function, **bdRemove**, useful for removing subjects without undergoing the entire refitting process.

4.3 User created curves

Continue to ponder if this worth elaborating on

4.4 Correlations

There are sometimes cases in which we are interested in determining the correlation of a fixed attribute with group outcome responses across time (what such a case may be, I have no idea). This can be done with the **bcorr** function (previously **bdotsCorr**), which takes as an argument an object of class **bdotsObj** as well as a character vector representing a column from the original dataset used in **bfit**

```
bcorr(fit, "value", ciBands, method = "pearson")
```

This returns a thing that can be plotted. Idk, it really doesn't seem that important

4.5 α Adjustment

Finally, we consider an extension to the **p.adjust** function, **p_adjust**, identical to **p.adjust** except that it accepts method **"oleson"** and takes additional arguments **rho**, **df**, and **cores**. **rho** determines the autocorrelation estimate for the oleson adjustment while **df** returns the degrees of freedom used to compute the original vector of t-statistics. If an estimate of **rho** isn't available, one can be computed on a vector of t-statistics using the **ar1Solver** function:

```
t <- diffinv(rnorm(100))
rho <- ar1Solver(t)
unadj_p <- pt(t, df = 10)
adj_p <- p_adjust(unadj_p, method = "oleson", df = 10, rho = rho)
```

5 Discussion

First paragraph of conclusion. Maybe say things like here are the problems `bdots` has tried to solve, etc., idk it just needs to be reconciled with the last paragraph, which i kinda like.

While significant improvements have been made, there is of course room for further expansion, and it is this area that we are most excited about future directions. The most obvious of these is the need to include support for non-parametric functions, the utility of which cannot be overstated. Not only would this alleviate the need for the researcher to specify in advance a functional form for the data, it would implicitly accomodate more heterogeneity of functional forms within a group. Along with this, the current implementation is also limited in the quality-of-fit statistics used in the fitting steps to assess performance. R^2 and the presence of autocorrelation are relevant to only a subset of the types of data that can be fit, and allowing users more flexibility in specifying this metric is an active goal for future work. In all, future directions of this package will be primarily focused on user interface, non-parametric functions, and flexibility in fit metrics (this last sentence kind of sucks).

The original implementation of `bdots` set out to address a very narrow set of problems which it succeeded in doing. Previous solutions beget new opportunities, however, and it is in this space that the second iteration of `bdots` has sought to expand. Since then, the interface between programmer and application has been significantly revamped, creating a simple, reproducible workflow that is able to quickly and simply address a far broader range of problems. This includes not only introducing support for a far wider variety of types of data but also expanding the methods by which data can be analyzed through the introduction of user-specified parametric curves. Further, the implementation of the underlying methodology has been improved and expanded upon, offering far better coverage of the estimated distributions, as well as increasing the methods by which significance testing is conducted, accomodating a broader range of underlying assumptions. Finally, a full suite of ancillary functions have been added, ranging from simple quality of life additions (methods, refitting) to those that add (can't say expand again) (?) analytical questions (?) (correlation function, etc.). Concluding sentence. The end.

Appendix A - custom curves

From an R programming perspective, this is perhaps the most novel and interesting portion of the new package update. Worked use-case examples are included in the pacakge vignettes, so here we will limit discussion to the theoretical considerations when implementing it since it's actually pretty neat (I think). plus it adds length to my dissertation and everybody knows longer == more intelligent

Appendix B - Fitting non-nested groups

(currently just copy pasted from the body of document, not edited so no need to really review)

First, there would be some function of sorts, something like `makeUniqueGroups` which would create a new group column with each permutation of previous groups being given a unique identifier. Doing this on the vehicle example would look something like `fit <- makeuniquewhatever` resulting in the following grouping structure (for example) (and maybe you could specify group name and values who knows, kinda like factor this is just a working thought example)

Origin	Class	Color	bgroup
foreign	car	red	A
		blue	B
	truck	red	C
		blue	D
domestic	car	red	E
		blue	F
	truck	red	G
		blue	H

To then investigate differences in outcome between a foreign red car and a domestic blue truck would simply then be

$$y \sim \text{bgroup}(A, H)$$

yeah not like sexy or anything but whatever it would work.

Appendix X

Copy and paste hard data example here

We will illustrate use of the updated `bdots` package with a worked example, using an artificial dataset to help detail some of the newer aspects of the package. The dataset will consist of outcomes for a collection of vehicles, consisting of eight distinct groups. These groups will be nested in order of vehicle origin (foreign or domestic), vehicle class (car or truck), and vehicle color (red or blue). Further, vehicles of different color but within the same origin and class groups will be considered paired observations. A table detailing the relationship of the groups is shown here:

Origin	Class	Color
foreign	car	red
		blue
	truck	red
		blue
domestic	car	red
		blue
	truck	red
		blue

Table 2: table of stuff

Origin	Class	Color
foreign	car	red
		blue
	truck	red
		blue
domestic	car	red
		blue
	truck	red
		blue

Table 3: table of stuff

The outcome here is simply y due to a lack of creativity, but the functional form assumed (and used in data generation) follows the four parameter logistic,

$$f_{\theta}(t) = b + \frac{p - b}{1 + \exp\left(\frac{4s}{p-b}(x - t)\right)}, \quad (6)$$

where b , p , s , and x represent the baseline, peak, slope, and crossover points, respectively

The formula argument serves two functions in `bboot`: first, it specifies the collection of curves we wish to investigate the difference between, and second, it determines if we are interested in directly comparing the differences or the difference of differences between curves.

To begin, let's reintroduce the structure of the groups we have in our dataset. Recall that we have foreign and domestic cars and trucks, and each of these vehicles comes in red and blue. Recall also that the different colors of each vehicle are considered paired observations.

Beginning with a simple case, suppose we want to investigate the difference in outcome between foreign

and domestic vehicles. Notionally, we would write

$$y \sim \text{Origin}(\text{foreign}, \text{domestic}).$$

Note that this involves the grouping variable, `Origin`, with the two values we are interested in comparing, `domestic` and `foreign`. With this specification, the distribution of functions considered in `domestic` include all red and blue domestic cars and trucks.

If we wanted to limit our investigation to only foreign and domestic *trucks*, we would do this by including an extra term specifying the group and the desired value. In this case,

$$y \sim \text{Origin}(\text{foreign}, \text{domestic}) + \text{Class}(\text{truck}).$$

To compare only foreign and domestic *red* trucks, we would add an additional term for color:

$$y \sim \text{Origin}(\text{foreign}, \text{domestic}) + \text{Class}(\text{truck}) + \text{Color}(\text{red}).$$

There are also instances in which we might be considered in the interaction of two groups. Although there is no native way to handle interactions in `bdots`, this can be done indirectly through the difference of differences (McMurray et al 2019, though truthfully I still don't understand why). To illustrate, suppose we are interested in understanding how the color of the vehicle differentially impacts outcome based on the vehicle class. In such a case, we might look at the difference in outcome between red cars and red trucks, and then again the difference between blue cars and blue trucks. Any difference between these two differences would give information regarding the differential impact of color between each of the two classes. This is done in `bdots` using the `diffs` syntax in the formula:

$$\text{diffs}(y, \text{Class}(\text{car}, \text{truck})) \sim \text{Color}(\text{red}, \text{blue})$$

Here, the *outcome* that we are considering is the difference between vehicle classes, with the outcome of interest being color. This is helpful in remembering which term goes on the LHS of the formula.

Similar as to the case before, if we wanted to limit this difference of differences investigation to only include domestic vehicles, we can do so by including an additional term:

$$\text{diffs}(y, \text{Class}(\text{car}, \text{truck})) \sim \text{Color}(\text{red}, \text{blue}) + \text{Origin}(\text{domestic}).$$

The formula syntax was originally contrived to make comparisons within groups or within nested groups. Conceivably, however, one could be interested in making the comparison between domestic red trucks and foreign blue cars. Doing so requires a bit of a work around. Examples detailing how one might go about doing this are included in appendix B.