donor bias

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This vignette walks through a series of deconvolution analyses evaluating the impact of between-donor variations on results.

Experiment series 1: ndonors = 2

Let's run a series of experiments keeping ndonor = 2. We start with the simplest example of k = 2 types and G = 2 total markers, one for each type. We will vary the offset from small (2) to medium (5) to large (10). This offset magnitude should be proportional to observed between-donor variances.

```
ndonor = 2
gindexv = c(1, 2)
offsetv \leftarrow c(2, 5, 10)
num.sim <- 50
lexpt <- lapply(offsetv, function(offi){</pre>
  title.append <- paste0("Offset = ", offi, "\n")</pre>
  donor_marker_experiment(gindexv = c(1,2), num.sim = num.sim, ndonor = ndonor,
                           plot.title.append = title.append,
                           sd.offset.pos = offi,
                           sd.offset.neg = offi)
})
## Loading required package: dplyr
## Attaching package: 'dplyr'
## The following object is masked from 'package:Biobase':
##
##
       combine
## The following objects are masked from 'package:GenomicRanges':
##
##
       intersect, setdiff, union
```

The following object is masked from 'package:GenomeInfoDb':

##

intersect

```
## The following objects are masked from 'package: IRanges':
##
       collapse, desc, intersect, setdiff, slice, union
##
## The following objects are masked from 'package:S4Vectors':
##
##
       first, intersect, rename, setdiff, setequal, union
## The following objects are masked from 'package:BiocGenerics':
##
       combine, intersect, setdiff, union
##
## The following object is masked from 'package:matrixStats':
##
##
       count
## The following objects are masked from 'package:stats':
##
##
       filter, lag
## The following objects are masked from 'package:base':
##
##
       intersect, setdiff, setequal, union
names(lexpt) <- paste0("offset:", offsetv)</pre>
```

Randomized marker data

```
knitr::kable(lexpt$`offset:2`$marker.table, align = "c")
```

donor1	donor2	donor.combn.all.mean	donor.combn.all.median	type	marker	marker.type
28	24	26.0	26.0	type1	marker1	type1
4	4	4.0	4.0	type1	marker2	type2
3	3	3.0	3.0	type2	marker1	type1
23	20	21.5	21.5	type2	marker2	type2

knitr::kable(lexpt\$`offset:5`\$marker.table, align = "c")

donor1	donor2	donor.combn.all.mean	donor.combn.all.median	type	marker	marker.type
32	23	27.5	27.5	type1	marker1	type1
8	7	7.5	7.5	type1	marker2	type2
6	6	6.0	6.0	type2	marker1	type1
27	19	23.0	23.0	type2	marker2	type2

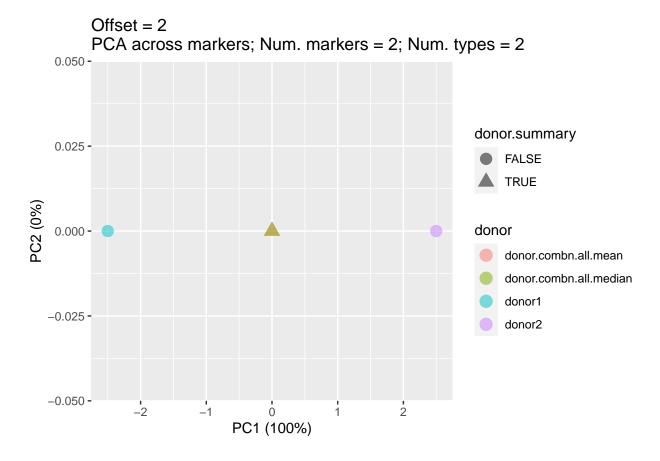
knitr::kable(lexpt\$`offset:10`\$marker.table, align = "c")

donor1	donor2	donor.combn.all.mean	donor.combn.all.median	type	marker	marker.type
39	21	30.0	30.0	type1	marker1	type1
14	13	13.5	13.5	type1	marker2	type2
20	19	19.5	19.5	type2	marker1	type1
40	22	31.0	31.0	type2	marker2	type2

Marker bias plots

PC1 vs. PC2 of donor bias

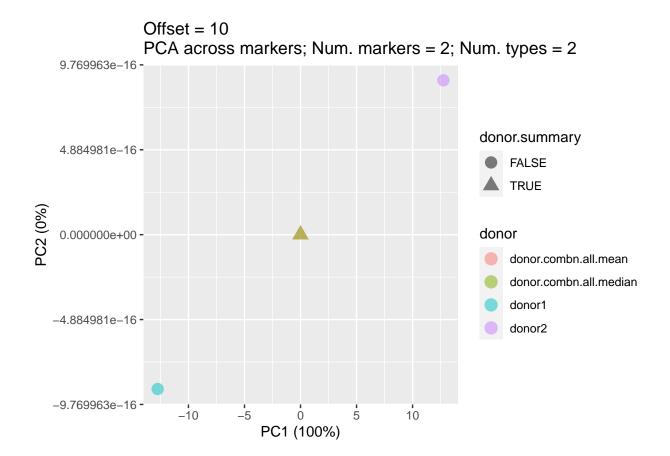
lexpt\$`offset:2`\$lpca.markers\$pca.bydonor\$scatterplot.pc1.pc2



lexpt\$`offset:5`\$lpca.markers\$pca.bydonor\$scatterplot.pc1.pc2

Offset = 5PCA across markers; Num. markers = 2; Num. types = 2 4.884981e-16 donor.summary 2.442491e-16 -**FALSE** TRUE 0.000000e+00 donor donor.combn.all.mean donor.combn.all.median donor1 -2.442491e-16 donor2 -4.884981e-16 **-**3 PC1 (100%)

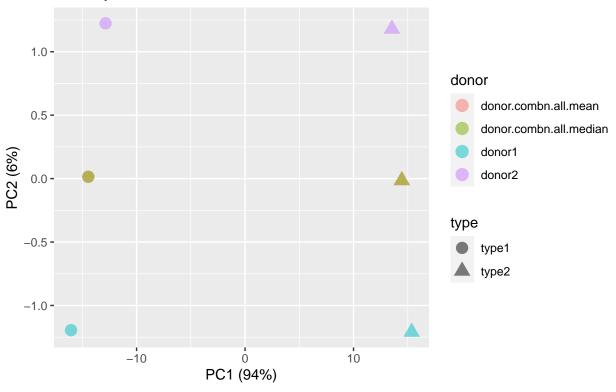
lexpt\$`offset:10`\$lpca.markers\$pca.bydonor\$scatterplot.pc1.pc2



PC1 vs. PC2 of donor, marker variances

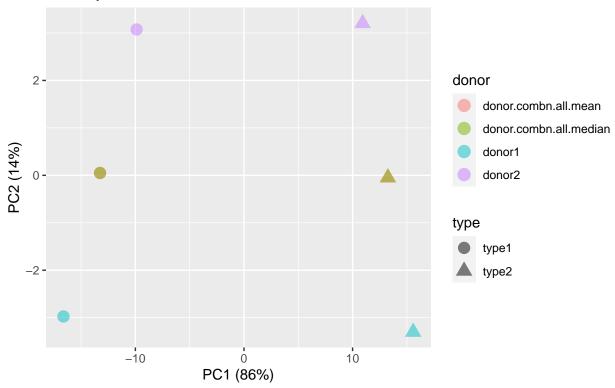
lexpt\$`offset:2`\$lpca.markers\$pca.bydonortype\$scatterplot.pc1.pc2

Offset = 2 PCA by donor, marker; Num. markers = 2



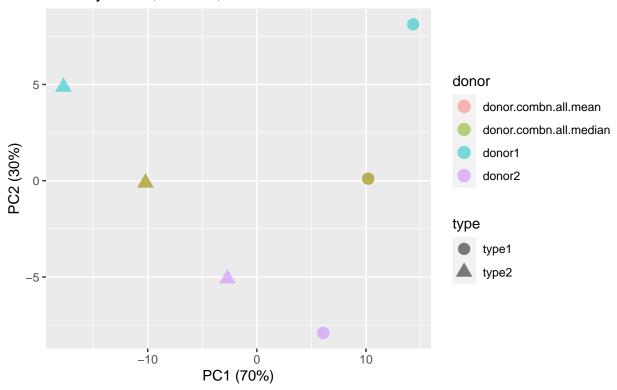
 ${\tt lexpt\$"offset:5"\$lpca.markers\$pca.bydonortype\$scatterplot.pc1.pc2}$

Offset = 5 PCA by donor, marker; Num. markers = 2



lexpt\$`offset:10`\$lpca.markers\$pca.bydonortype\$scatterplot.pc1.pc2

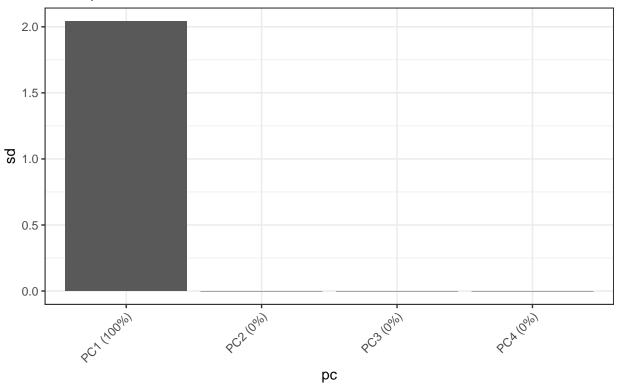
Offset = 10 PCA by donor, marker; Num. markers = 2



Screeplots, PCA by donor

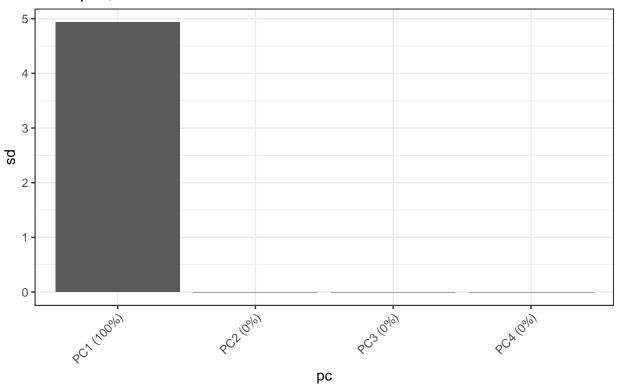
lexpt\$`offset:2`\$lpca.markers\$pca.bydonor\$screeplot

Offset = 2 Screeplot; Num. markers = 4



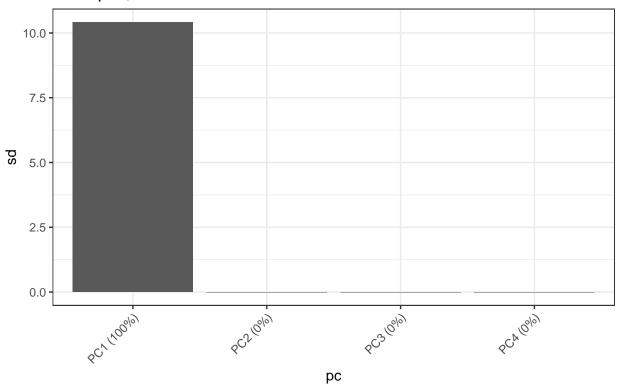
lexpt\$`offset:5`\$lpca.markers\$pca.bydonor\$screeplot

Offset = 5 Screeplot; Num. markers = 4



lexpt\$`offset:10`\$lpca.markers\$pca.bydonor\$screeplot

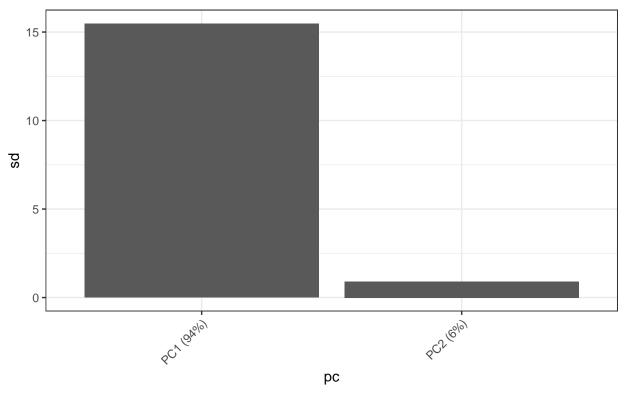
Offset = 10 Screeplot; Num. markers = 4



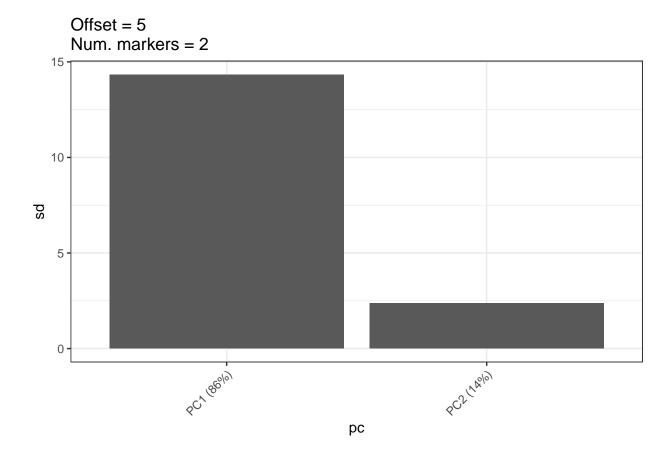
Screeplots, PCA by donor;type

lexpt\$`offset:2`\$lpca.markers\$pca.bydonortype\$screeplot

Offset = 2 Num. markers = 2

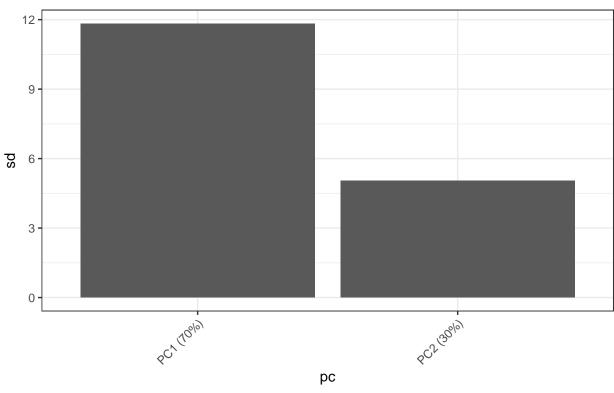


lexpt\$`offset:5`\$lpca.markers\$pca.bydonortype\$screeplot



lexpt\$`offset:10`\$lpca.markers\$pca.bydonortype\$screeplot

Offset = 10 Num. markers = 2



Deconvolution results – all tests

Results table

```
# get all results
dfres <- do.call(rbind, lapply(offsetv, function(offi){
  lres <- lexpt[grepl(paste0("offset:",offi,"$"), names(lexpt))][[1]]$decon.results
  dfresi <- do.call(rbind, lapply(lres, function(resi){resi$dfres}))
  dfresi <- as.data.frame(dfresi)
  dfresi$offset <- offi
  dfresi
}))</pre>
```

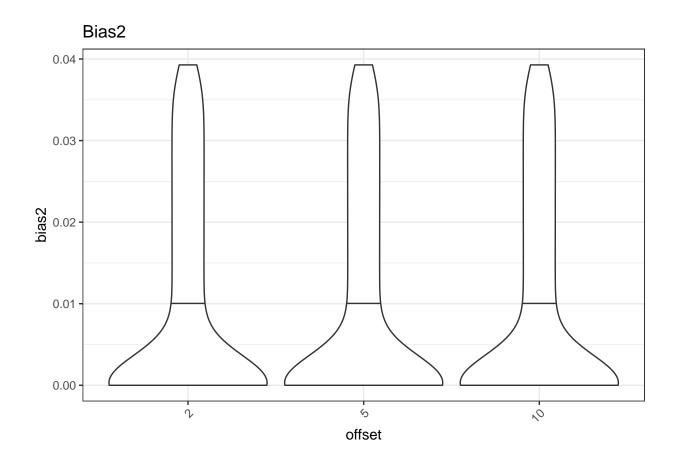
Bias violin plots

```
dfres$offset <- as.factor(dfres$offset)

ggplot(dfres, aes(x = offset, y = bias1)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias1") + theme(axis.text.x = element_text(angle = 45, hjust = 1))</pre>
```

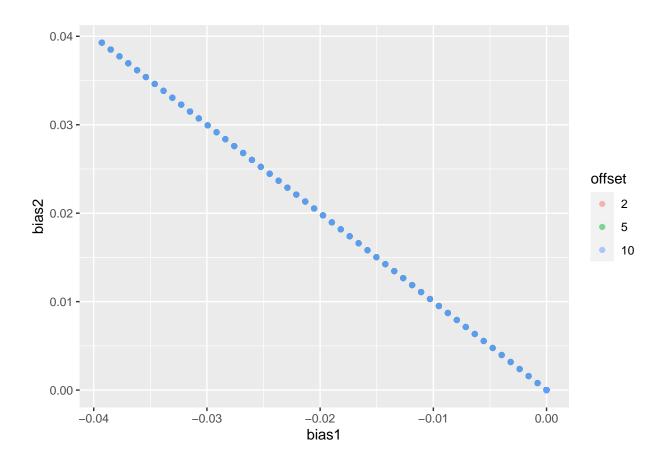


```
ggplot(dfres, aes(x = offset, y = bias2)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias2") + theme(axis.text.x = element_text(angle = 45, hjust = 1))
```

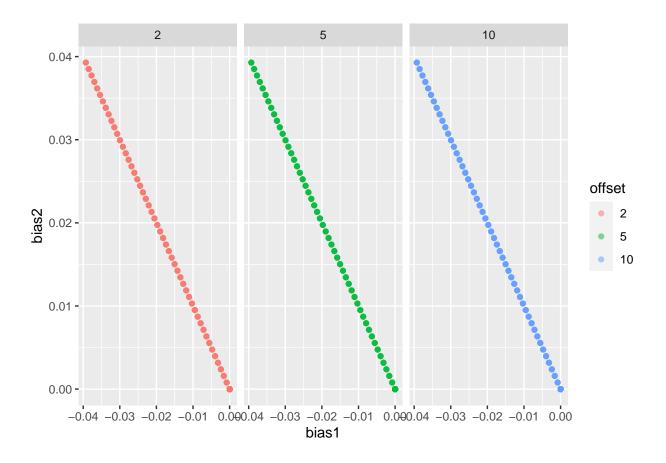


Bias scatterplots

```
ggpt <- ggplot(dfres, aes(x = bias1, y = bias2, color = offset)) + geom_point(alpha = 0.5) ggpt
```

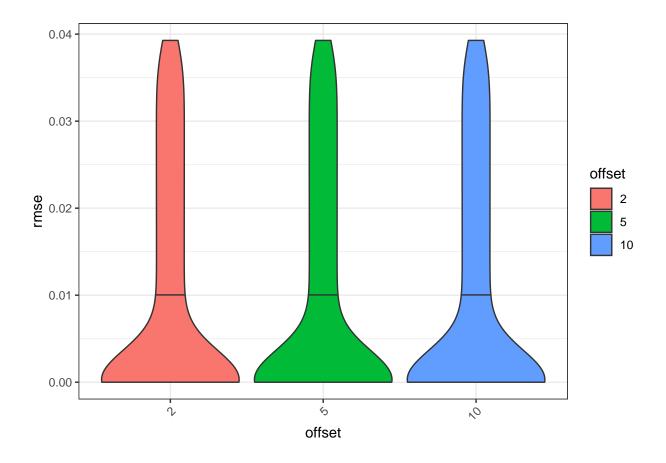


ggpt + facet_wrap(~offset)



RMSE violin plot

```
ggplot(dfres, aes(x = offset, y = rmse, fill = offset)) +
geom_violin(draw_quantiles = 0.5) + theme_bw() +
theme(axis.text.x = element_text(angle = 45, hjust = 1))
```



Deconvolution results – without S transformations

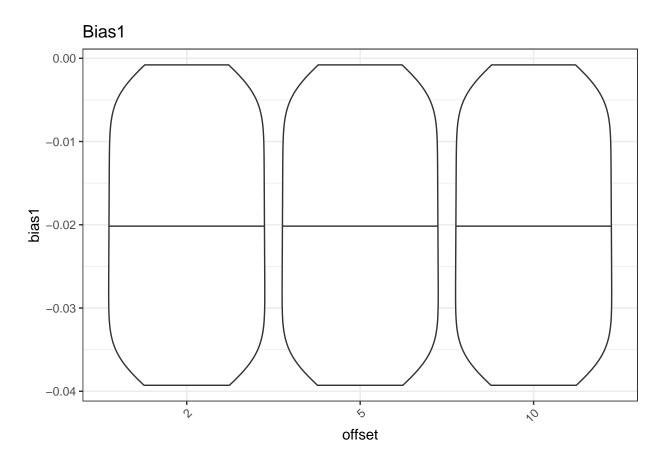
Results table

```
dfres.all <- dfres
dfres <- dfres.all[dfres.all$zs_transform==FALSE,]</pre>
```

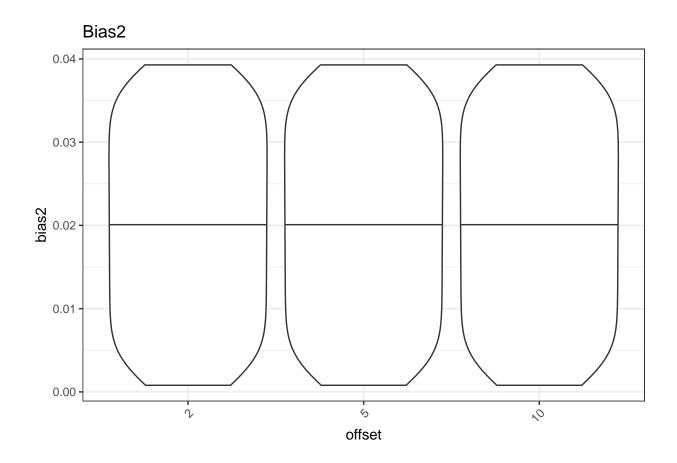
Bias violin plots

```
dfres$offset <- as.factor(dfres$offset)

ggplot(dfres, aes(x = offset, y = bias1)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias1") + theme(axis.text.x = element_text(angle = 45, hjust = 1))</pre>
```

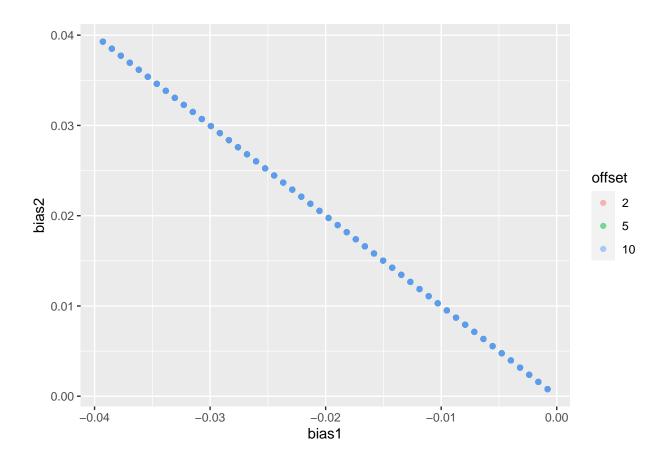


```
ggplot(dfres, aes(x = offset, y = bias2)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias2") + theme(axis.text.x = element_text(angle = 45, hjust = 1))
```

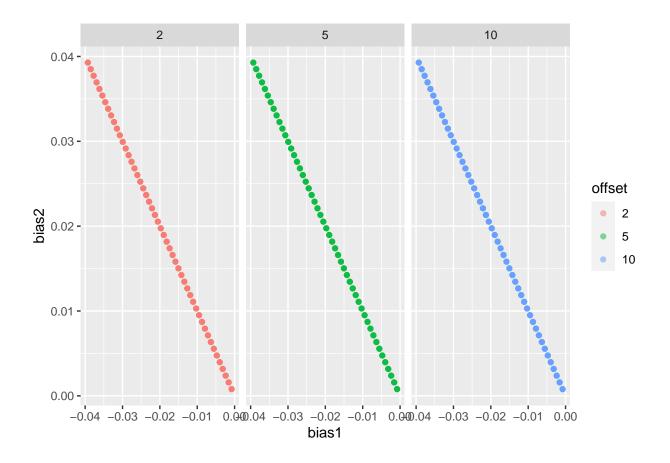


Bias scatterplots

```
ggpt <- ggplot(dfres, aes(x = bias1, y = bias2, color = offset)) + geom_point(alpha = 0.5) ggpt
```

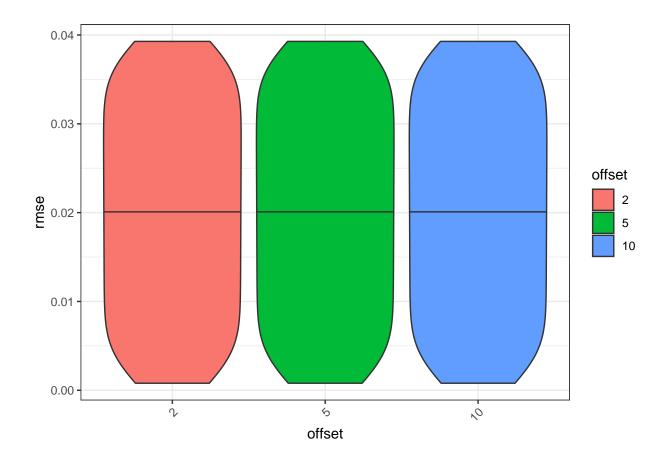


ggpt + facet_wrap(~offset)



RMSE violin plot

```
ggplot(dfres, aes(x = offset, y = rmse, fill = offset)) +
geom_violin(draw_quantiles = 0.5) + theme_bw() +
theme(axis.text.x = element_text(angle = 45, hjust = 1))
```



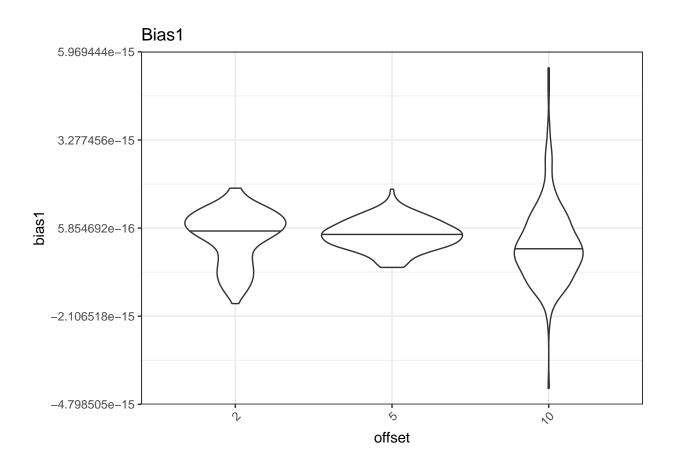
Deconvolution results – with S transformations

```
dfres <- dfres.all[dfres.all$zs_transform==TRUE,]</pre>
```

Bias violin plots

```
dfres$offset <- as.factor(dfres$offset)

ggplot(dfres, aes(x = offset, y = bias1)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias1") + theme(axis.text.x = element_text(angle = 45, hjust = 1))</pre>
```

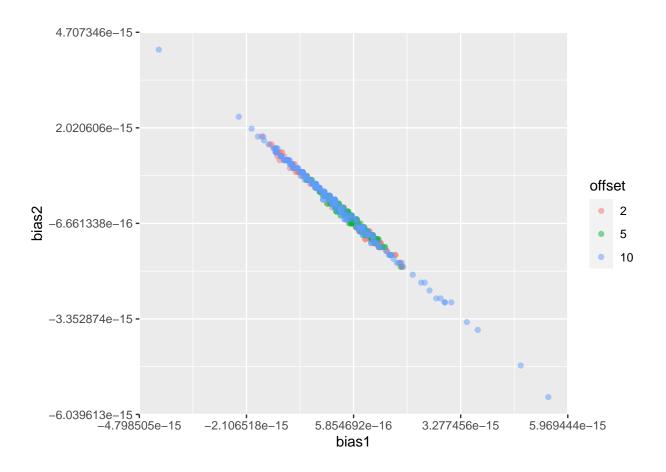


```
ggplot(dfres, aes(x = offset, y = bias2)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias2") + theme(axis.text.x = element_text(angle = 45, hjust = 1))
```

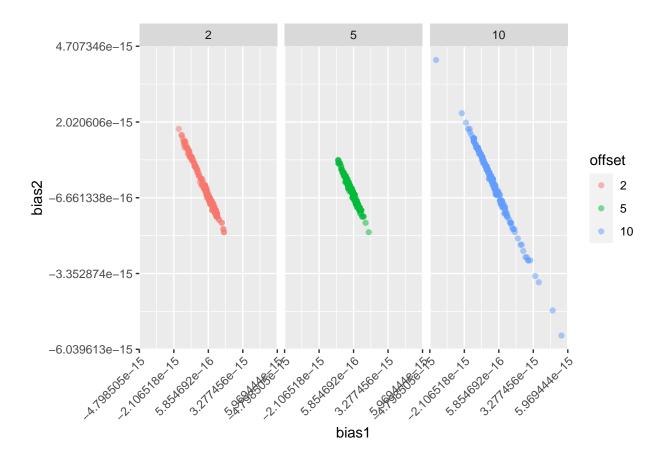


Bias scatterplots

```
ggpt <- ggplot(dfres, aes(x = bias1, y = bias2, color = offset)) + geom_point(alpha = 0.5) ggpt
```

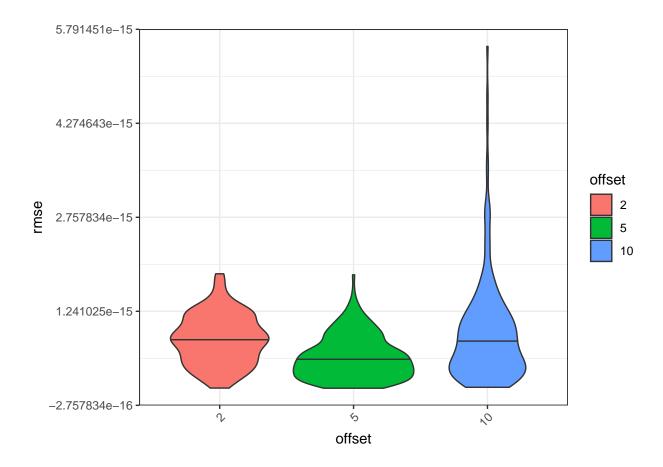


ggpt + facet_wrap(~offset) + theme(axis.text.x = element_text(angle = 45, hjust = 1))



RMSE violin plot

```
ggplot(dfres, aes(x = offset, y = rmse, fill = offset)) +
geom_violin(draw_quantiles = 0.5) + theme_bw() +
theme(axis.text.x = element_text(angle = 45, hjust = 1))
```



Experiment series 1: ndonors = 10

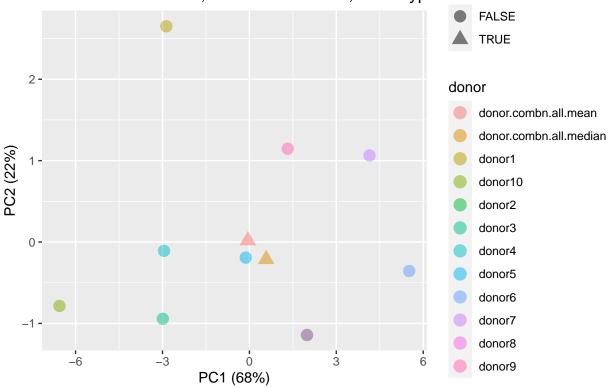
Building on the simple 2-donors case above, we now simulate 10 donors with the same progression in random offset increase.

Marker bias plots

PC1 vs. PC2 of donor bias

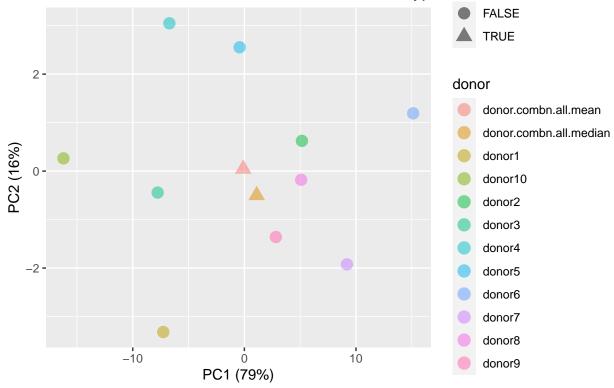
lexpt\$`offset:2`\$lpca.markers\$pca.bydonor\$scatterplot.pc1.pc2

Offset = 2 PCA across markers; Num. markers = 2; Num. types & 20r.summary



lexpt\$`offset:5`\$lpca.markers\$pca.bydonor\$scatterplot.pc1.pc2

Offset = 5 PCA across markers; Num. markers = 2; Num. types dogor.summary



lexpt\$`offset:10`\$lpca.markers\$pca.bydonor\$scatterplot.pc1.pc2

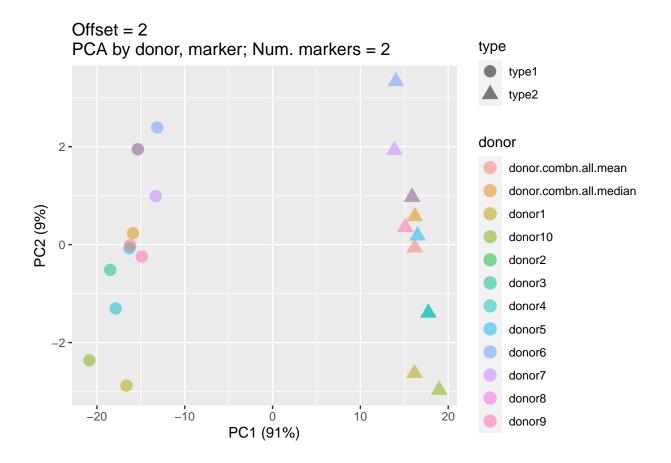
Offset = 10PCA across markers; Num. markers = 2; Num. types dozor.summary 5 -FALSE TRUE donor donor.combn.all.mean 0 donor.combn.all.median PC2 (16%) donor1 donor10 donor2 donor3 -5 donor4 donor5 donor6 donor7 donor8 -20 20 -40

donor9

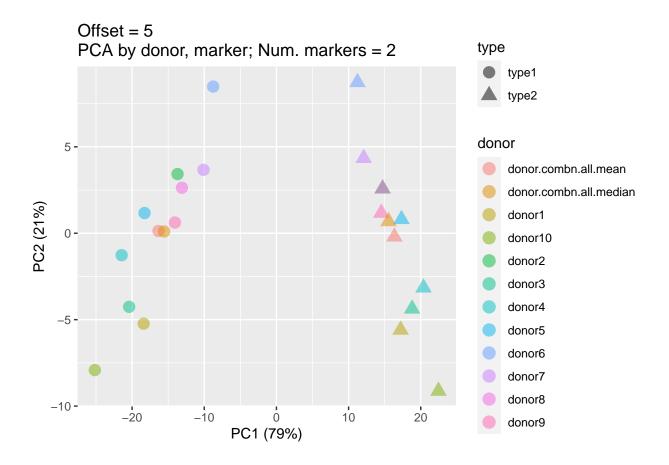
PC1 vs. PC2 of donor, marker variances

lexpt\$`offset:2`\$lpca.markers\$pca.bydonortype\$scatterplot.pc1.pc2

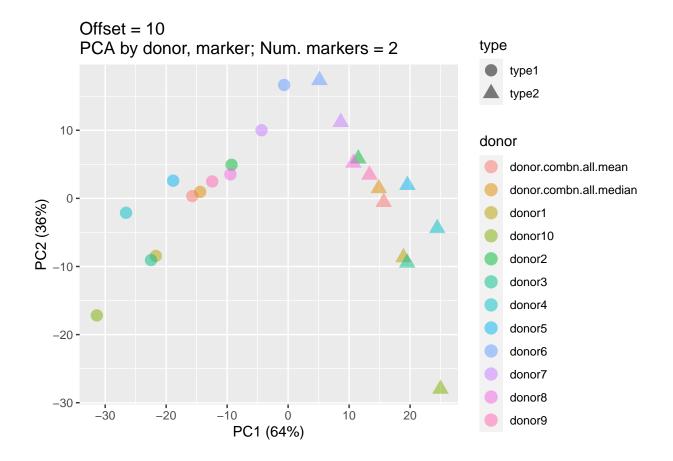
PC1 (77%)



lexpt\$`offset:5`\$lpca.markers\$pca.bydonortype\$scatterplot.pc1.pc2



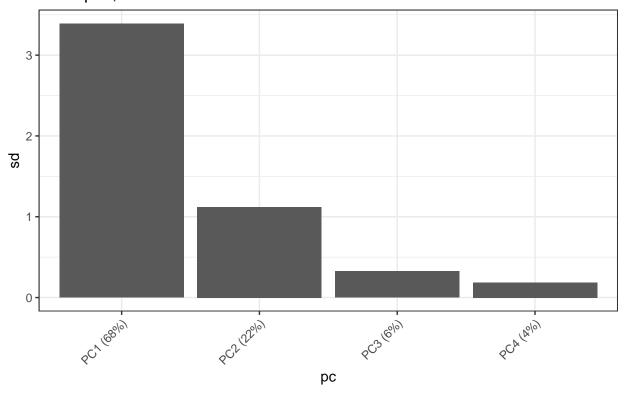
lexpt\$`offset:10`\$lpca.markers\$pca.bydonortype\$scatterplot.pc1.pc2



Screeplots, PCA by donor

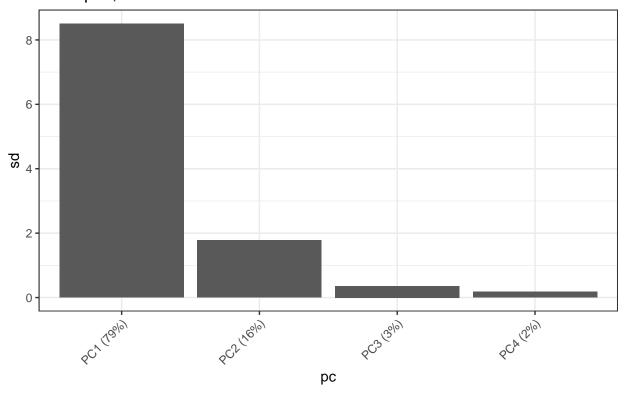
lexpt\$`offset:2`\$lpca.markers\$pca.bydonor\$screeplot

Offset = 2 Screeplot; Num. markers = 4



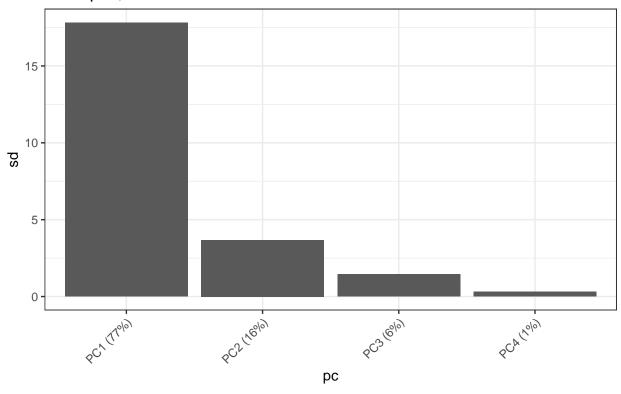
lexpt\$`offset:5`\$lpca.markers\$pca.bydonor\$screeplot

Offset = 5 Screeplot; Num. markers = 4



lexpt\$`offset:10`\$lpca.markers\$pca.bydonor\$screeplot

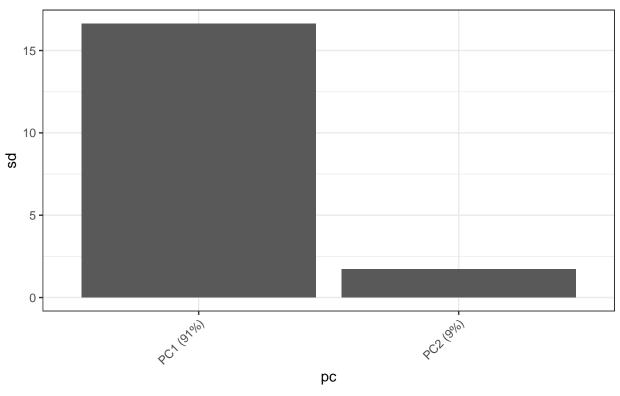
Offset = 10 Screeplot; Num. markers = 4



Screeplots, PCA by donor;type

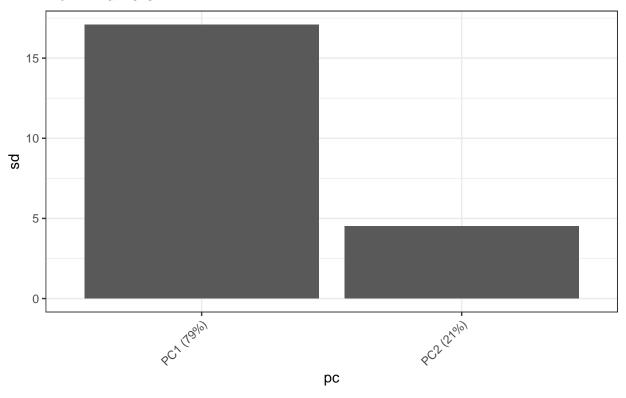
lexpt\$`offset:2`\$lpca.markers\$pca.bydonortype\$screeplot

Offset = 2 Num. markers = 2



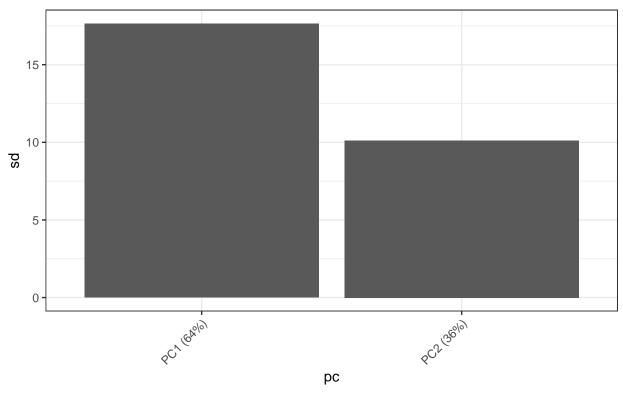
lexpt\$`offset:5`\$lpca.markers\$pca.bydonortype\$screeplot

Offset = 5 Num. markers = 2



lexpt\$`offset:10`\$lpca.markers\$pca.bydonortype\$screeplot

Offset = 10 Num. markers = 2



Deconvolution results – all tests

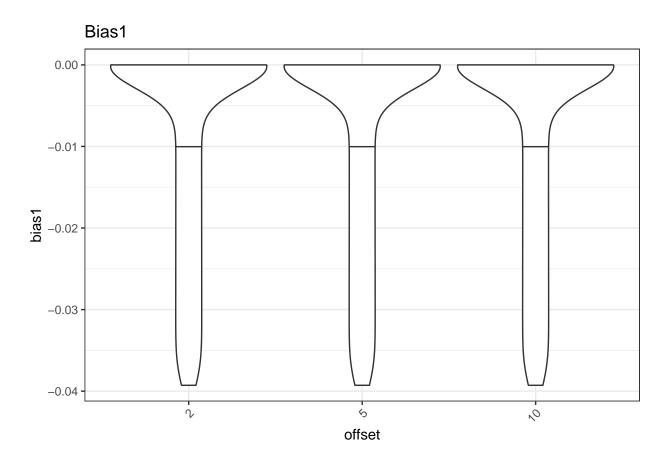
Results table

```
# get all results
dfres <- do.call(rbind, lapply(offsetv, function(offi){
  lres <- lexpt[grepl(paste0("offset:",offi,"$"), names(lexpt))][[1]]$decon.results
  dfresi <- do.call(rbind, lapply(lres, function(resi){resi$dfres}))
  dfresi <- as.data.frame(dfresi)
  dfresi$offset <- offi
  dfresi
}))</pre>
```

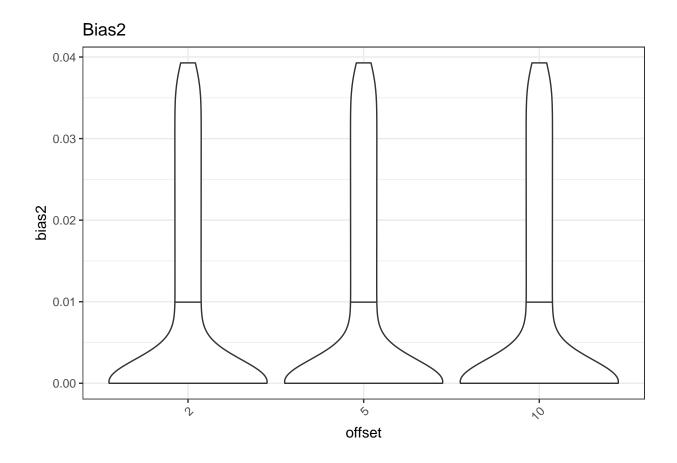
Bias violin plots

```
dfres$offset <- as.factor(dfres$offset)

ggplot(dfres, aes(x = offset, y = bias1)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias1") + theme(axis.text.x = element_text(angle = 45, hjust = 1))</pre>
```

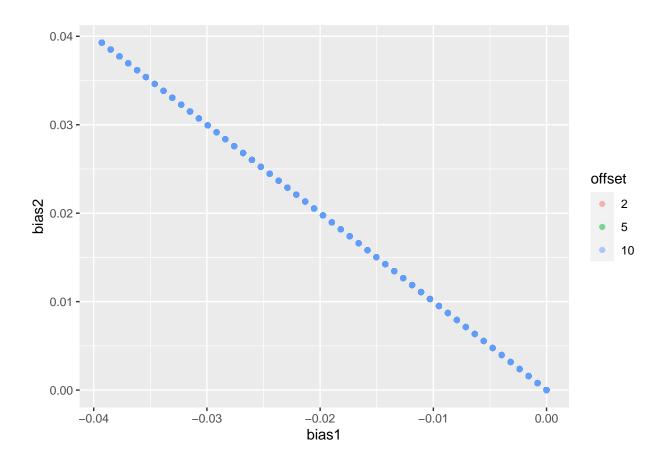


```
ggplot(dfres, aes(x = offset, y = bias2)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias2") + theme(axis.text.x = element_text(angle = 45, hjust = 1))
```

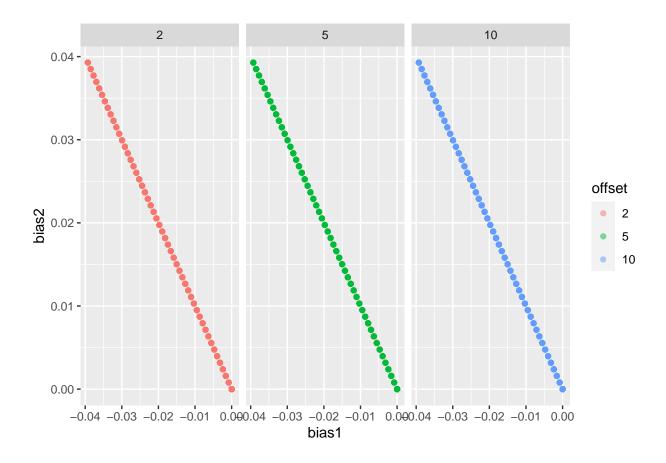


Bias scatterplots

```
ggpt \leftarrow ggplot(dfres, aes(x = bias1, y = bias2, color = offset)) + geom_point(alpha = 0.5) ggpt
```

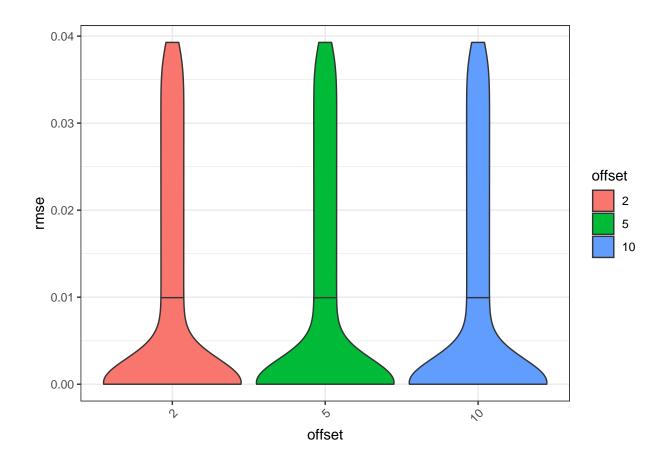


ggpt + facet_wrap(~offset)



RMSE violin plot

```
ggplot(dfres, aes(x = offset, y = rmse, fill = offset)) +
geom_violin(draw_quantiles = 0.5) + theme_bw() +
theme(axis.text.x = element_text(angle = 45, hjust = 1))
```



Deconvolution results – without S transformations

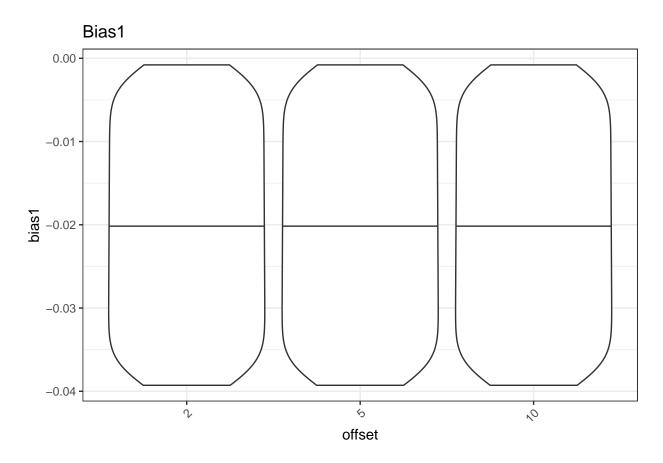
Results table

```
dfres.all <- dfres
dfres <- dfres.all[dfres.all$zs_transform==FALSE,]</pre>
```

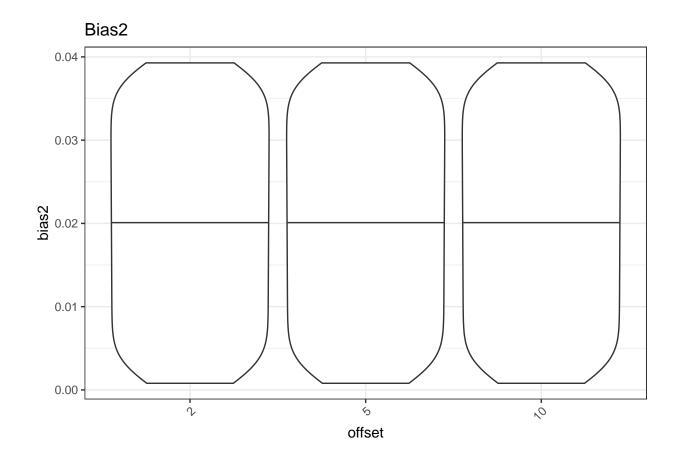
Bias violin plots

```
dfres$offset <- as.factor(dfres$offset)

ggplot(dfres, aes(x = offset, y = bias1)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias1") + theme(axis.text.x = element_text(angle = 45, hjust = 1))</pre>
```

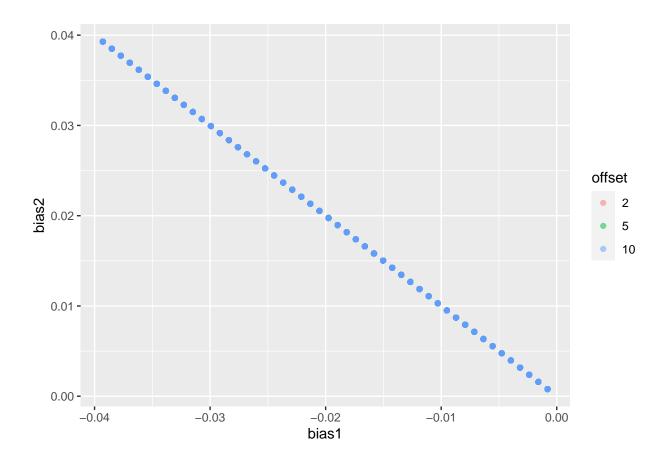


```
ggplot(dfres, aes(x = offset, y = bias2)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias2") + theme(axis.text.x = element_text(angle = 45, hjust = 1))
```

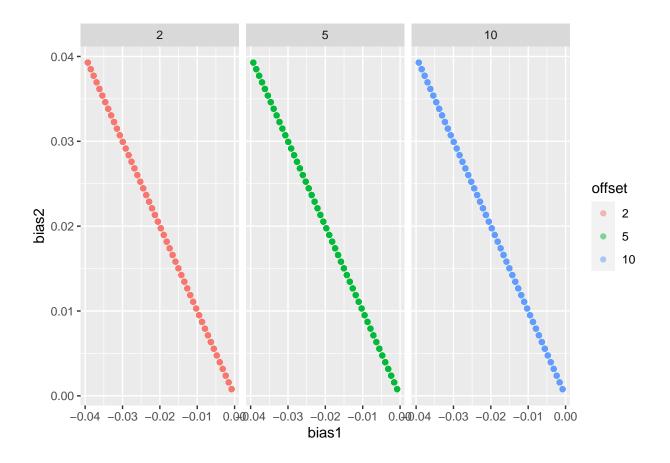


Bias scatterplots

```
ggpt \leftarrow ggplot(dfres, aes(x = bias1, y = bias2, color = offset)) + geom_point(alpha = 0.5) ggpt
```

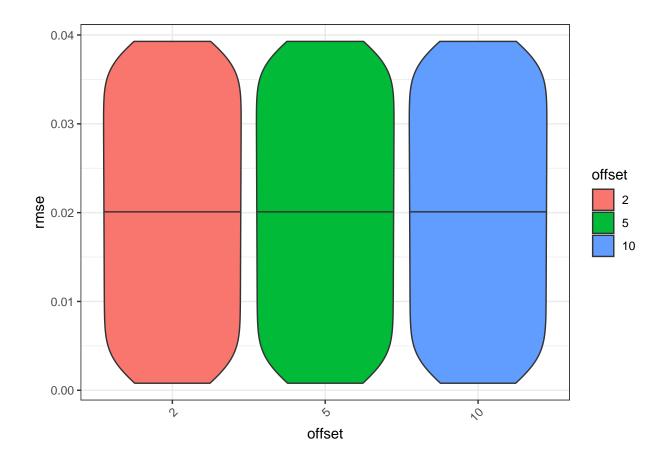


ggpt + facet_wrap(~offset)



$\mathbf{RMSE} \ \mathbf{violin} \ \mathbf{plot}$

```
ggplot(dfres, aes(x = offset, y = rmse, fill = offset)) +
geom_violin(draw_quantiles = 0.5) + theme_bw() +
theme(axis.text.x = element_text(angle = 45, hjust = 1))
```



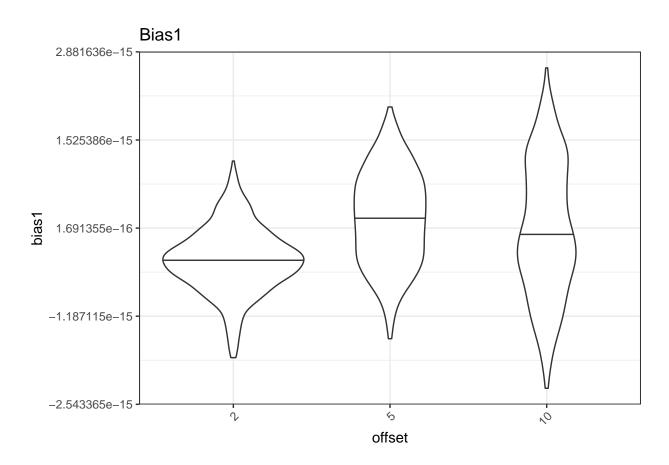
Deconvolution results – with S transformations

```
dfres <- dfres.all[dfres.all$zs_transform==TRUE,]</pre>
```

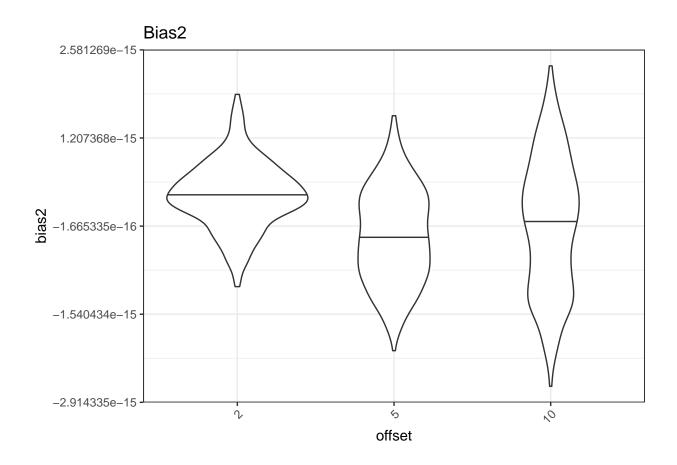
Bias violin plots

```
dfres$offset <- as.factor(dfres$offset)

ggplot(dfres, aes(x = offset, y = bias1)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias1") + theme(axis.text.x = element_text(angle = 45, hjust = 1))</pre>
```

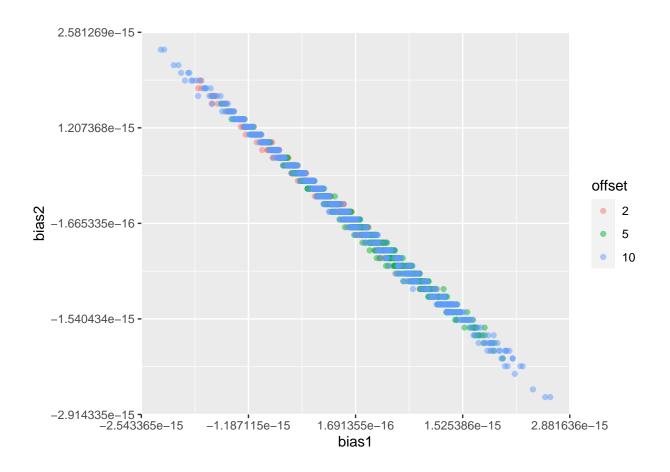


```
ggplot(dfres, aes(x = offset, y = bias2)) + geom_violin(draw_quantiles = 0.5) +
    theme_bw() + ggtitle("Bias2") + theme(axis.text.x = element_text(angle = 45, hjust = 1))
```

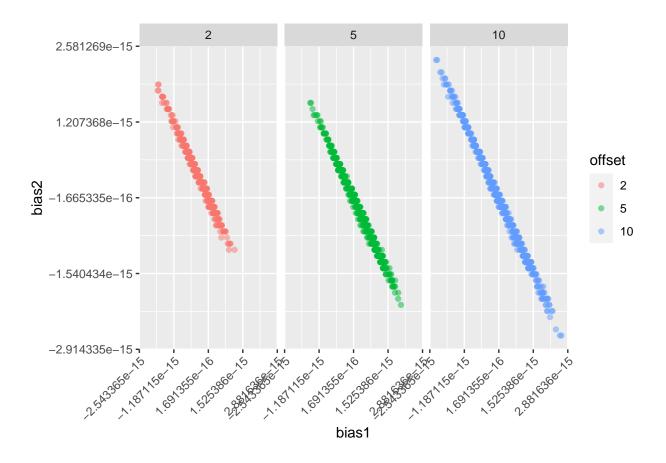


Bias scatterplots

```
ggpt <- ggplot(dfres, aes(x = bias1, y = bias2, color = offset)) + geom_point(alpha = 0.5) ggpt
```



ggpt + facet_wrap(~offset) + theme(axis.text.x = element_text(angle = 45, hjust = 1))



RMSE violin plot

```
ggplot(dfres, aes(x = offset, y = rmse, fill = offset)) +
geom_violin(draw_quantiles = 0.5) + theme_bw() +
theme(axis.text.x = element_text(angle = 45, hjust = 1))
```

