The top CNV component has the followinfg trio-states. Where '1' indicates a deletion and order is F, M, O.

```
> est.list.beaty <- lapply(binom.list.beaty, FUN = trioClasses:::get.est)
> ci.list.beaty <- lapply(binom.list.beaty, FUN = trioClasses:::get.ci)
> testable.beaty <- !is.na(ci.list.beaty)
> ci.mat.beaty <- matrix(unlist(ci.list.beaty[testable.beaty]),
      nrow = sum(testable.beaty), ncol = 2, byrow = TRUE)
> est.vec.beaty <- as(est.list.beaty, "numeric")[testable.beaty]
> gr.cnp.beaty <- cnv.obj.beaty$cmp.gr[testable.beaty]
> freq.beaty.vec <- freq.beaty.vec[testable.beaty]

> est.list.pitt <- lapply(binom.list.pitt, FUN = trioClasses:::get.est)
> ci.list.pitt <- lapply(binom.list.pitt, FUN = trioClasses:::get.ci)
> testable.pitt <- !is.na(ci.list.pitt)
> ci.mat.pitt <- matrix(unlist(ci.list.pitt[testable.pitt]),
      nrow = sum(testable.pitt), ncol = 2, byrow = TRUE)
> est.vec.pitt <- as(est.list.pitt, "numeric")[testable.pitt]
> gr.cnp.pitt <- cnv.obj.pitt$cmp.gr[testable.pitt]
> freq.pitt.vec <- freq.pitt.vec[testable.pitt]
```
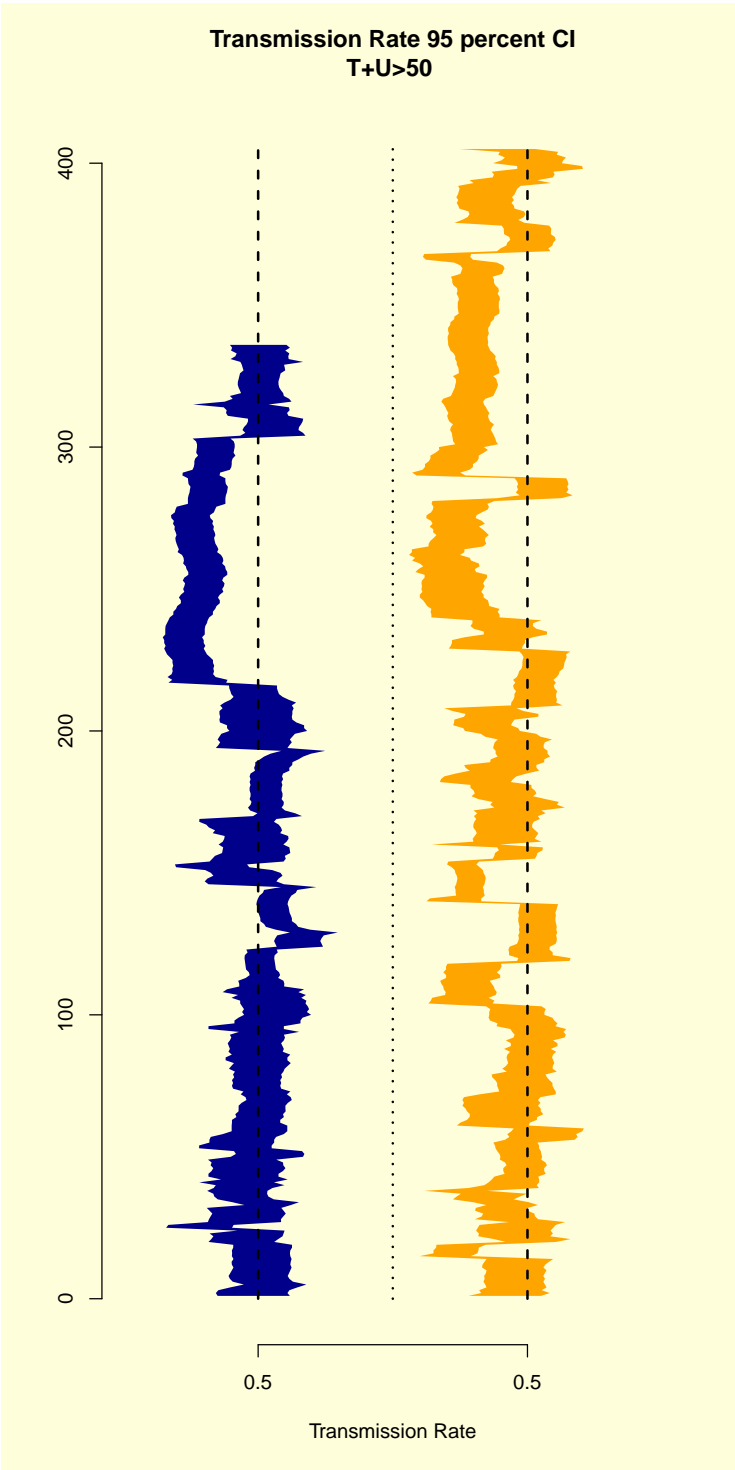
The CNV components with signiifcant p-values (Bonferroni) are given below.

```
GRanges with 4 ranges and 0 metadata columns:
          seqnames                    ranges strand
             <Rle>                 <IRanges>  <Rle>
  comp1883     chr7 [141435189, 141439888]       *
  comp1994     chr8 [ 39356825,  39370186]       *
  comp2009     chr8 [ 39476659,  39497557]       *
  comp2610    chr11 [ 55204004,  55209499]       *
  ---
  seqlengths:
           chr1  chr1_random         chr2 ...         chrY         chrM
      247249719      1663265    242951149 ...     57772954        16571
```

All CNV components are contiguous and the total width is 4.7 kB.

```
function (object)
{
    T <- sum(object[c("101", "011", "122", "212", "111", "112",
        "112")], na.rm = TRUE)
    U <- sum(object[c("100", "010", "121", "211", "111", "110",
        "110")], na.rm = TRUE)
    if (T + U >= 50) {
```

Transmission Rate 95 percent CI
T+U>50

Transmission Rate

2

Figure 1: UCSC Genome Browser at chromosome 8 locus.

```
        return(binom.test(x = T, n = T + U, p = 0.5, alternative = "greater")$p.value)
    }
    else {
        return(NA)
    }
}
<environment: namespace:trioClasses>

> gr.deletion.pitt <- gr.pitt[values(gr.pitt)$numsnp >= 10 &
      values(gr.pitt)$cn %in% 0:1]
> sum(countOverlaps(gr.deletion.pitt, reduce(locus)))

[1] 1237
```

Methods

Cleft Data Description

- Performed 336 tests. Bonferroni significant locus has width 4.7 kB.

- *PennCNV* joint HMM

- european, MAD < 0.3, non-WGA, aux $\neq 1$

- coverage > 10

- 14857 hemi/homozygous deletions identified in 445 trios

- 4288 CNV components

    Common (> 0.01): 336

    Rare: 0

- Construct trio-states for all CNV components

    recall that we use indicator variable for hemi/homozygous deletions

3
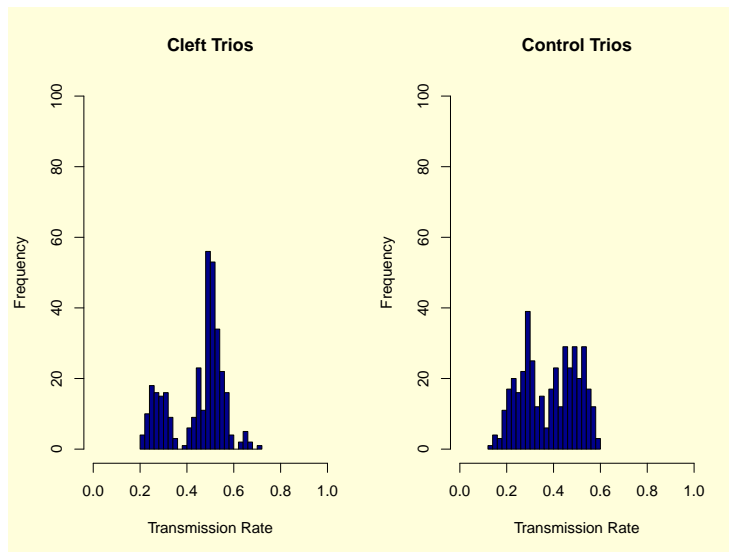
- must be at least 5 informative mating pairs

    01x and 10x

- count transmissions and perform binom.test (See "trans.tab")

```
> mean(est.vec.beaty[subjectHits(findOverlaps(reduce(locus),
    cnv.obj.beaty$cmp.gr))])

[1] NA

> mean(est.vec.pitt[subjectHits(findOverlaps(reduce(locus),
    cnv.obj.pitt$cmp.gr))])

[1] NA

> mean(-log10(trans.vec[subjectHits(findOverlaps(reduce(locus),
    cnv.obj.beaty$cmp.gr))]))

[1] 4.850908

> mean(-log10(trans.vec.pitt[subjectHits(findOverlaps(reduce(locus),
    cnv.obj.pitt$cmp.gr))]))
```
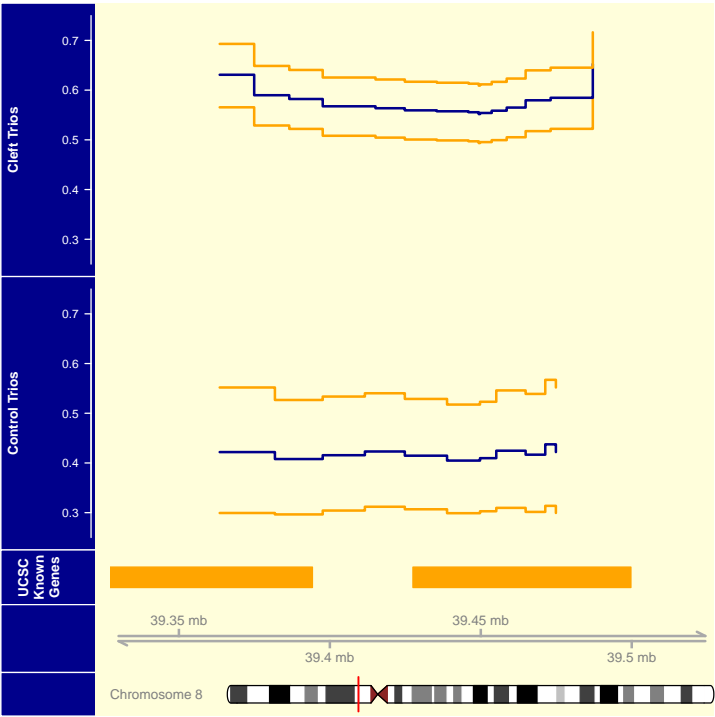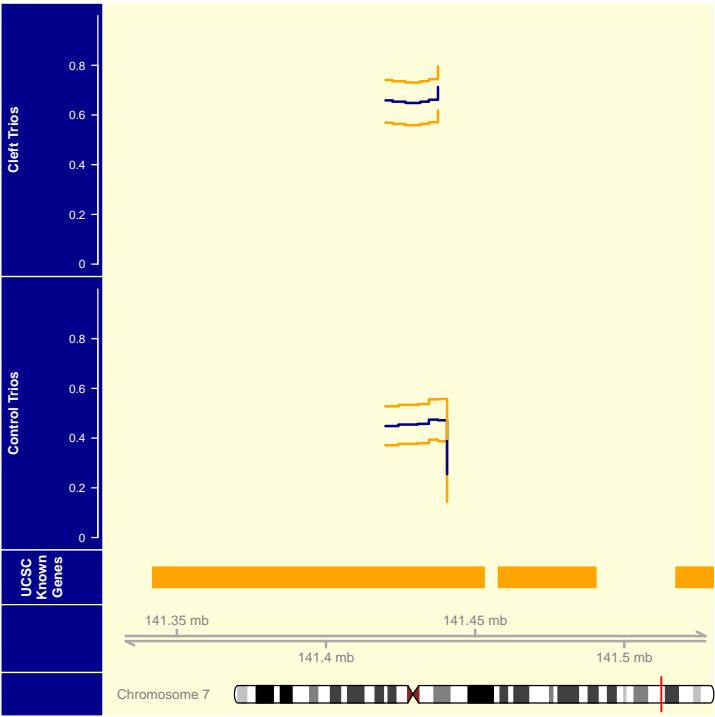
Figure 2:

Figure 3:
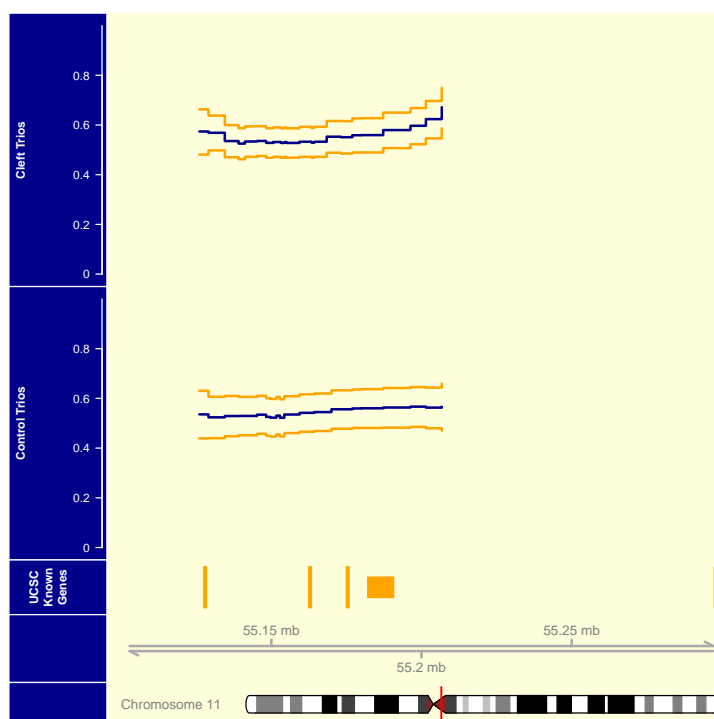
Figure 4:

```
[1] NA

> freq.pitt.vec[subjectHits(findOverlaps(reduce(locus), cnv.obj.pitt$cmp.gr))]

<NA> <NA> <NA> <NA>
  NA   NA   NA   NA

> freq.beaty.vec[subjectHits(findOverlaps(reduce(locus), cnv.obj.beaty$cmp.gr))]

<NA> <NA> <NA> <NA>
  NA   NA   NA   NA
```