

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

```
000 001 010 011 100 101 110 111
326  3  14  35  14  32   1  20
```

```
> 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.beaty.obj$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.pitt.obj$cmp.gr[testable.pitt]
> freq.pitt.vec <- freq.pitt.vec[testable.pitt]
```

The CNV components with significant *p*-values (Bonferroni) are given below.

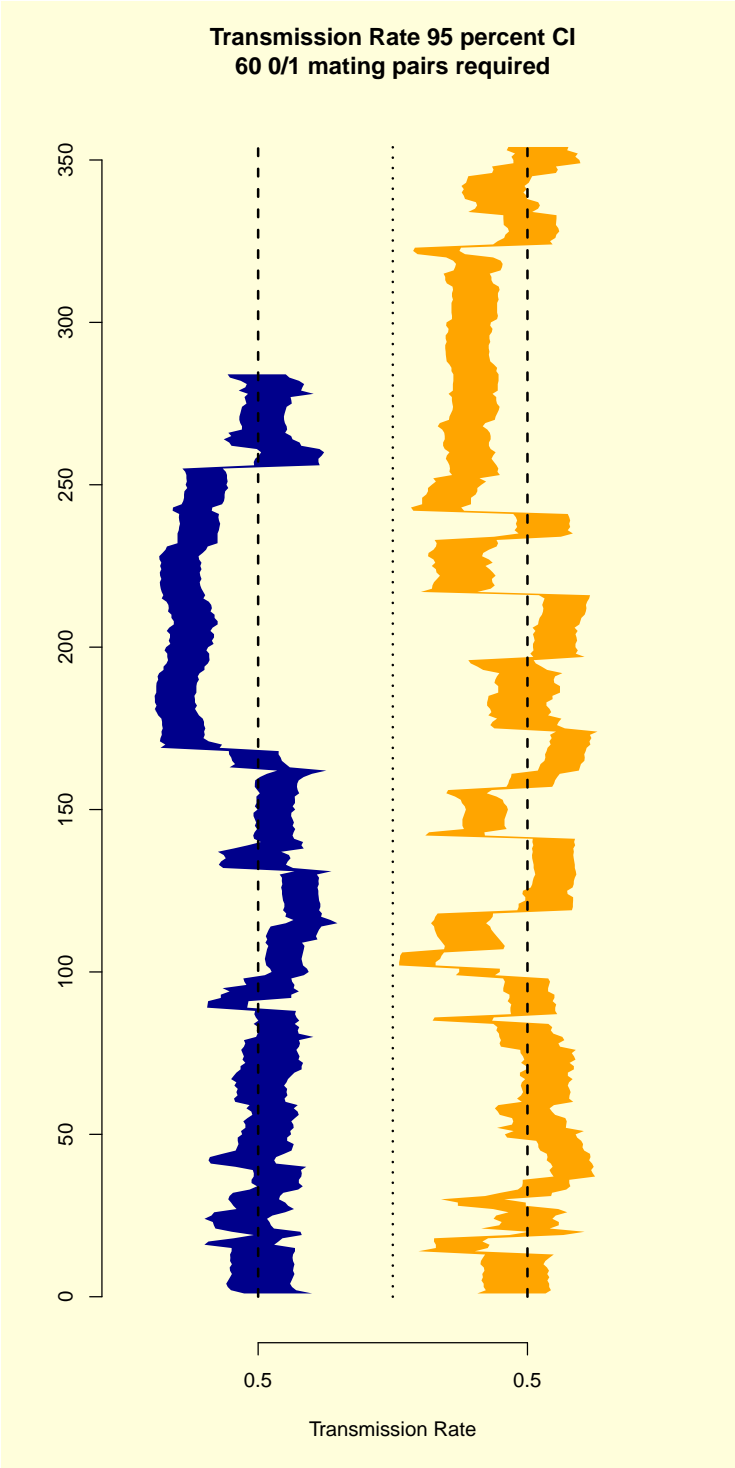
GRanges with 17 ranges and 0 metadata columns:

	seqnames	ranges	strand
	<Rle>	<IRanges>	<Rle>
comp1883	chr7	[141435189, 141439888]	*
comp1994	chr8	[ 39356825, 39370186]	*
comp1995	chr8	[ 39370187, 39379683]	*
comp1996	chr8	[ 39379684, 39393417]	*
comp1997	chr8	[ 39393418, 39401865]	*
...	...	...	...
comp2005	chr8	[39450168, 39457081]	*
comp2006	chr8	[39457082, 39460087]	*
comp2007	chr8	[39460088, 39469612]	*
comp2008	chr8	[39469613, 39476658]	*
comp2009	chr8	[39476659, 39497557]	*

---

seqlengths:

chr1	chr1_random	chr2 ...	chrY	chrM
247249719	1663265	242951149 ...	57772954	16571



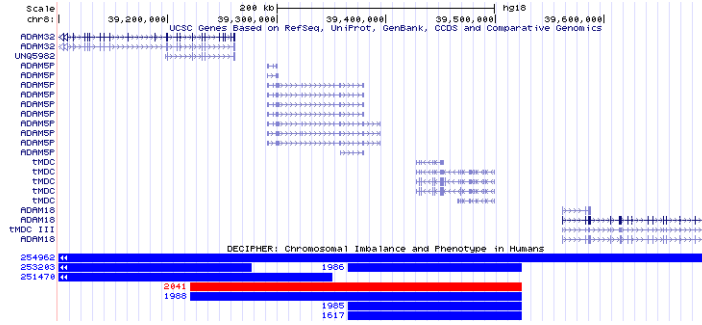


Figure 1: UCSC Genome Browser at chromosome 8 locus.

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

```
function (object)
{
  if (sum(object[c("101", "011", "100", "010")], na.rm = TRUE) >=
    60) {
    T <- sum(object[c("101", "011")], na.rm = TRUE)
    U <- sum(object[c("100", "010")], na.rm = TRUE)
    return(binom.test(x = T, n = T + U, p = 0.5, alternative = "greater")$p.value)
  }
  else {
    return(NA)
  }
}
<environment: namespace:trioClasses>

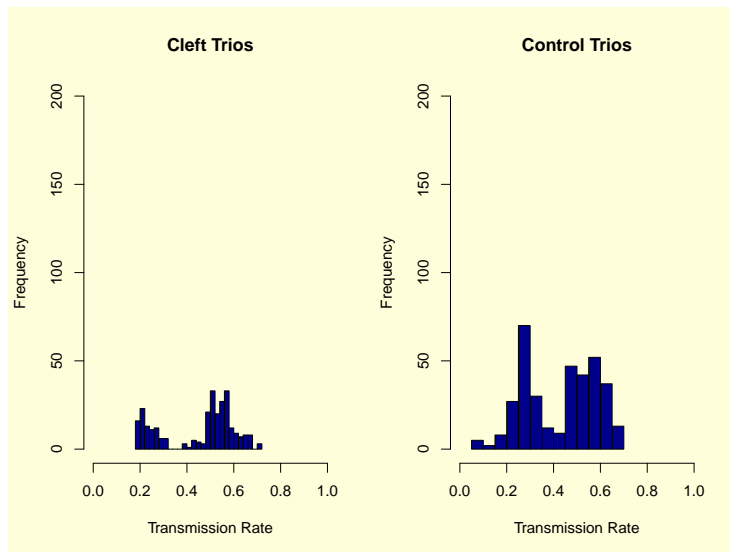
> gr.deletion.pitt <- gr.pitt[values(gr.pitt)$numsnps >= 10 &
  values(gr.pitt)$cn %in% 0:1]
> sum(countOverlaps(gr.deletion.pitt, reduce(locus)))

[1] 649
```

## Methods

### Cleft Data Description

- Performed 284 tests. Bonferroni significant locus has width 4.7 kB.
- *PennCNV* joint HMM
- european, MAD < 0.3, non-WGA, aux  $\neq$  1
- coverage > 10



- 13140 hemi/homozygous deletions identified in 445 trios
- 4288 CNV components
  - Common ( $> 0.01$ ): 284
  - Rare: 0
- Construct trio-states for all CNV components
  - recall that we use indicator variable for hemi/homozygous deletions
- 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.beaty.obj$cmp.gr))])
```

```
[1] NA
```

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

```
[1] NA
```

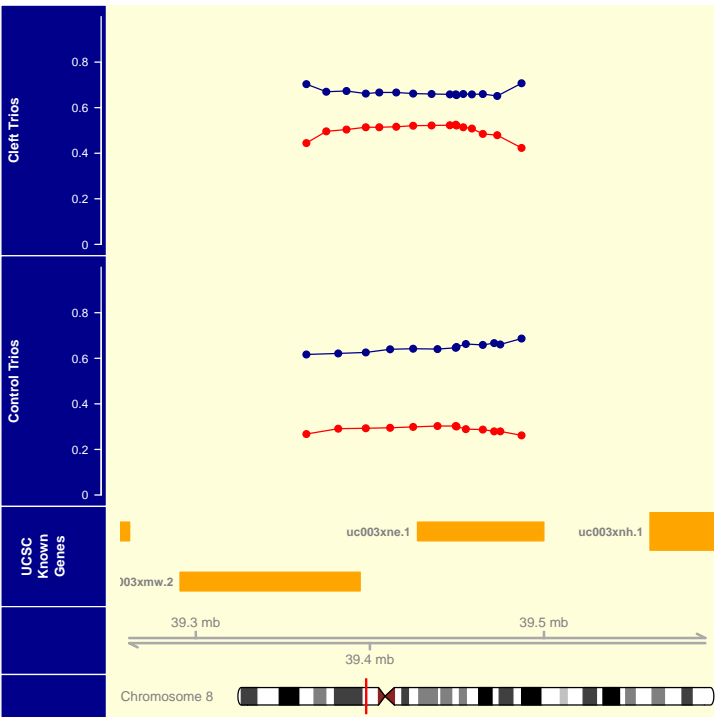


Figure 2:

```

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

[1] 5.784253

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

[1] 3.907709

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

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

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

  comp1883  comp1994  comp1995  comp1996  comp1997  comp1998  comp1999
0.1534155 0.4445689 0.4960806 0.5039194 0.5139978 0.5139978 0.5162374
  comp2000  comp2001  comp2002  comp2003  comp2004  comp2005  comp2006
0.5207167 0.5218365 0.5229563 0.5251960 0.5218365 0.5139978 0.5083987
  comp2007  comp2008  comp2009
0.4848824 0.4792833 0.4232923

```