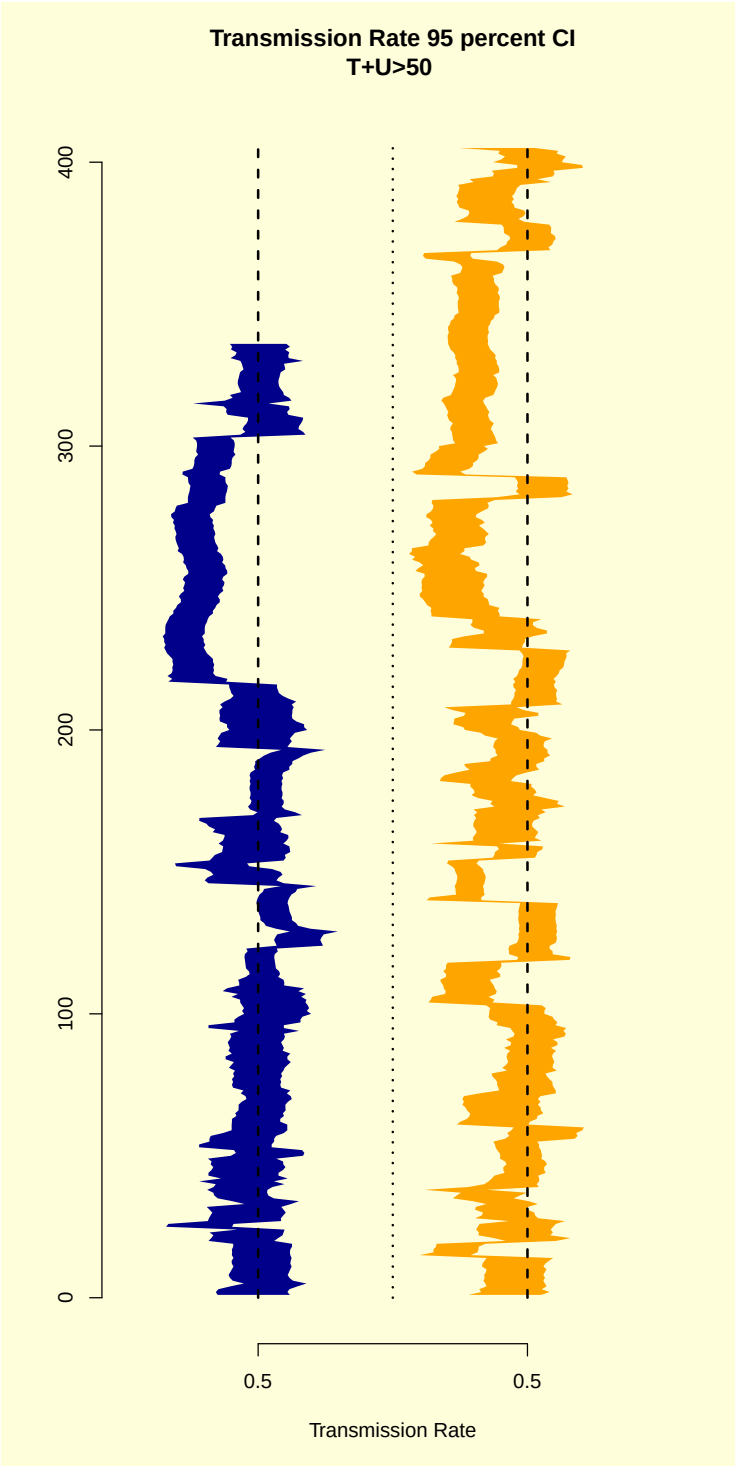
The top CNV component has the followinfg trio-states. Where '1' indicates a deletion and order is F, M, O.

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

GRanges with 3 ranges and 0 metadata columns:
      seqnames                ranges strand
         <Rle>             <IRanges>  <Rle>
  [1]     chr7 [141407267, 141441259]      *
  [2]     chr8 [ 39341981,  39518214]      *
  [3]    chr11 [ 55124465,  55216671]      *
  ---
  seqlengths:
            chr1   chr1_random          chr2 ...          chrY          chrM
       247249719       1663265     242951149 ...      57772954         16571

> freq.beaty <- colSums(cnv(fe.beaty))/2/nrow(cnv(fe.beaty))
> freq.pitt <- colSums(cnv(fe.pitt))/2/nrow(cnv(fe.pitt))
> freq.beaty[index.1.beaty]

 comp1883
0.1023152

> freq.pitt[index.1.pitt]

comp1645
0.116408

> freq.beaty[index.2.beaty]

 comp1994
0.3278566
```


Transmission Rate 95 percent CI
T+U>50
400
300
200
100
0
0.5
0.5
Transmission Rate

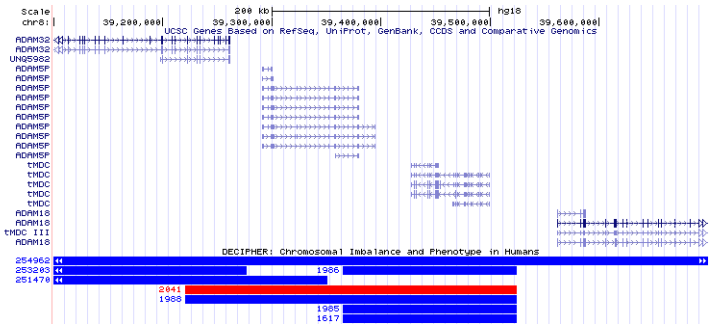


Figure 1: UCSC Genome Browser at chromosome 8 locus.

```
> freq.pitt[index.2.pitt]

 comp1793
0.2577605

> freq.beaty[index.3.beaty]

 comp2009
0.3188947

> freq.pitt[index.3.pitt]

 comp1805
0.2588692

> freq.beaty[index.4.beaty]

 comp2610
0.1467513

> freq.pitt[index.4.pitt]

comp2356
0.154102

> summary(freq.beaty[index.1.full.beaty])

     Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
0.0003734 0.0067210 0.1070000 0.0690100 0.1131000 0.1135000

> summary(freq.pitt[index.1.full.pitt])

    Min.  1st Qu.   Median     Mean  3rd Qu.     Max.
0.001109 0.016210 0.121400 0.081830 0.129200 0.129700
```

```
> summary(freq.beaty[index.2.full.beaty])

     Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
0.0003734 0.3359000 0.3574000 0.2984000 0.3620000 0.3645000

> summary(freq.pitt[index.2.full.pitt])

     Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
0.0005543 0.2633000 0.2716000 0.2352000 0.2752000 0.2788000

> summary(freq.beaty[index.3.full.beaty])

     Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
0.0007468 0.1822000 0.2110000 0.1940000 0.2255000 0.2274000

> summary(freq.pitt[index.3.full.pitt])

     Min.   1st Qu.    Median      Mean   3rd Qu.      Max.
0.0005543 0.1818000 0.1924000 0.1795000 0.1973000 0.2040000

> trioClasses:::trans.tab

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

> trioClasses:::trans.rate

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) {
        return(binom.test(x = T, n = T + U, p = 0.5))
    }
```

```
    else {
        return(NA)
    }
}
<environment: namespace:trioClasses>
```

Methods

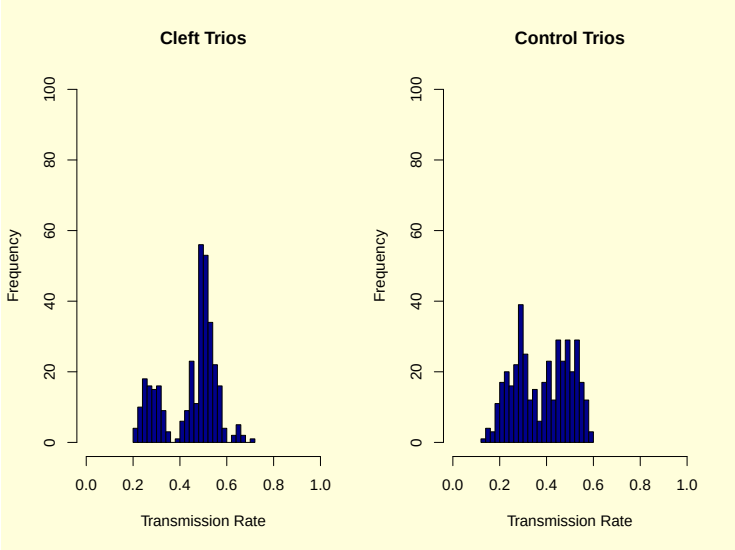
Cleft Data Description

- Performed 336 tests.
- *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): 660

  Rare: 3628
- Construct trio-states for all CNV components

  0,1,2 variable for normal, hemizygous and homozygous, respectively
- $T + U > 50$
- count transmissions and perform binom.test (See "trans.tab")


Cleft Trios
Control Trios
Frequency
0
20
40
60
80
100
0.0
0.2
0.4
0.6
0.8
1.0
Transmission Rate

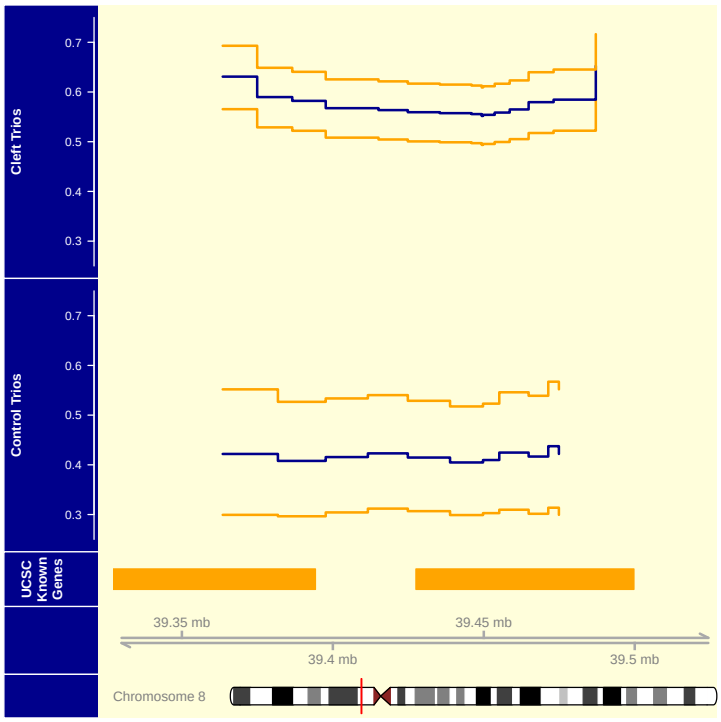

Cleft Trios
Control Trios
0.7
0.6
0.5
0.4
0.3
UCSC Known Genes
39.35 mb
39.45 mb
39.4 mb
39.5 mb
Chromosome 8

Figure 2:

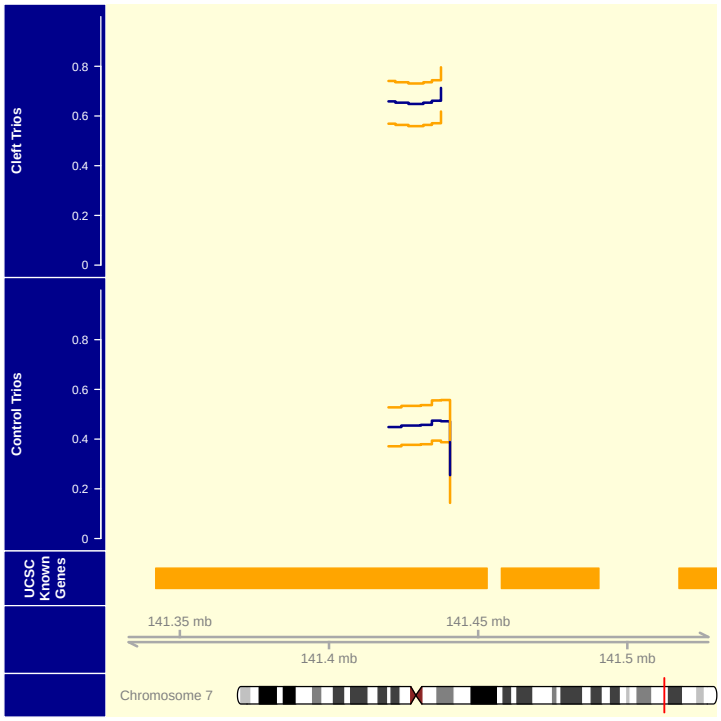

Cleft Trios
0.8
0.6
0.4
0.2
0
Control Trios
0.8
0.6
0.4
0.2
0
UCSC Known Genes
141.35 mb
141.45 mb
141.4 mb
141.5 mb
Chromosome 7

Figure 3:

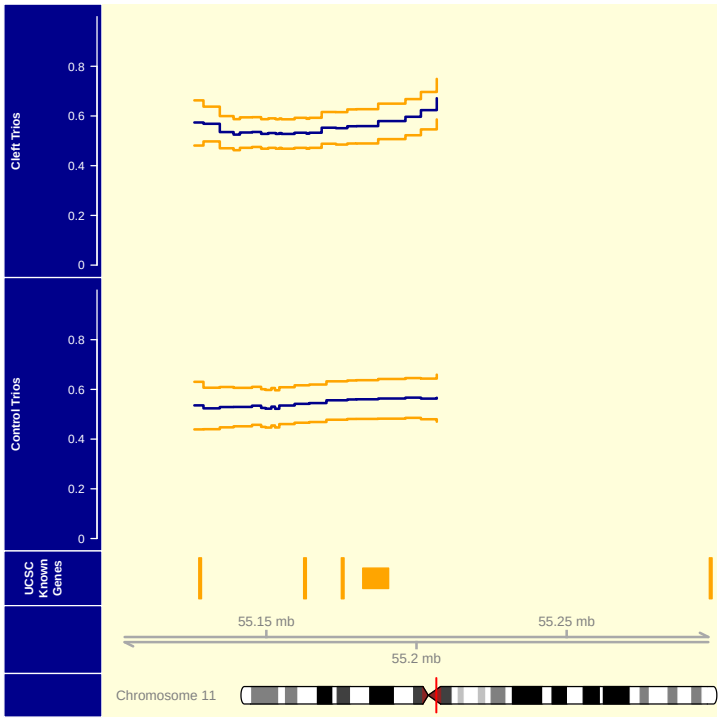

Cleft Trios
0.8
0.6
0.4
0.2
0
Control Trios
0.8
0.6
0.4
0.2
0
UCSC Known Genes
55.15 mb
55.25 mb
55.2 mb
Chromosome 11

Figure 4: