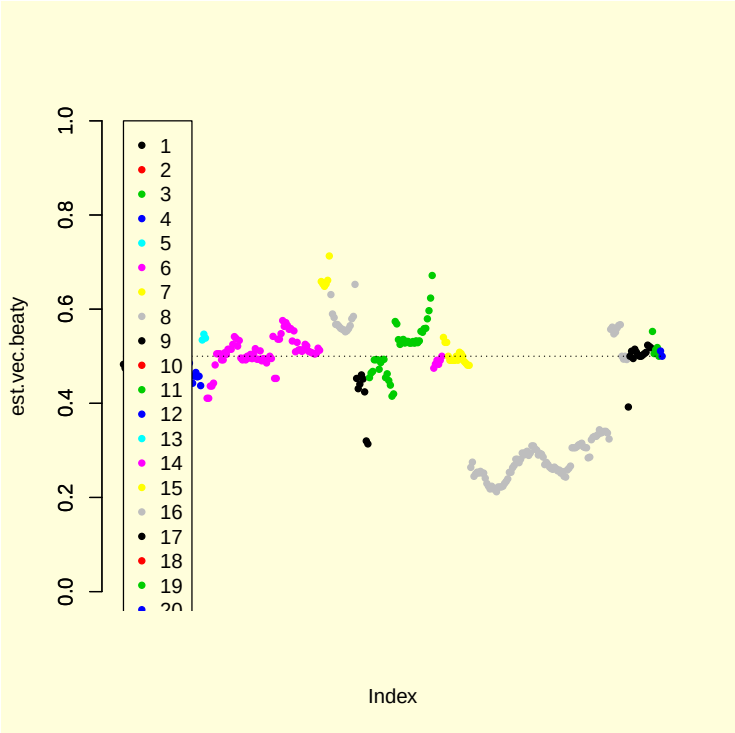
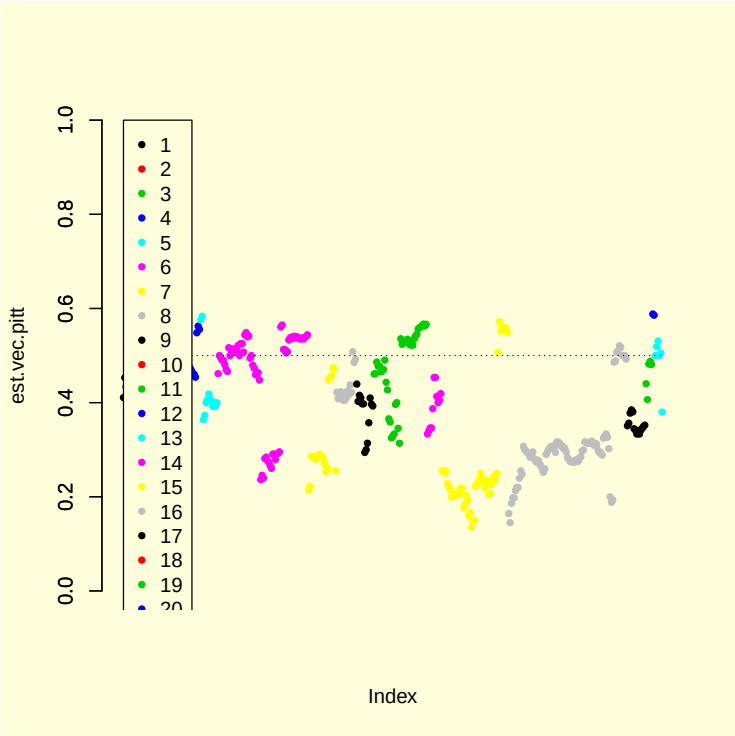


The top CNV component has the followinfg trio-states. Where '1' indicates a deletion and order is F, M, O.

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
```



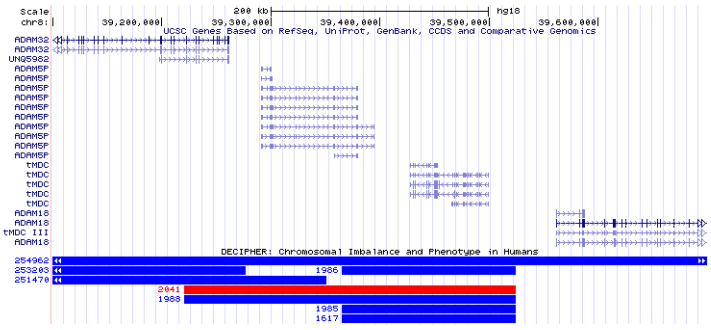
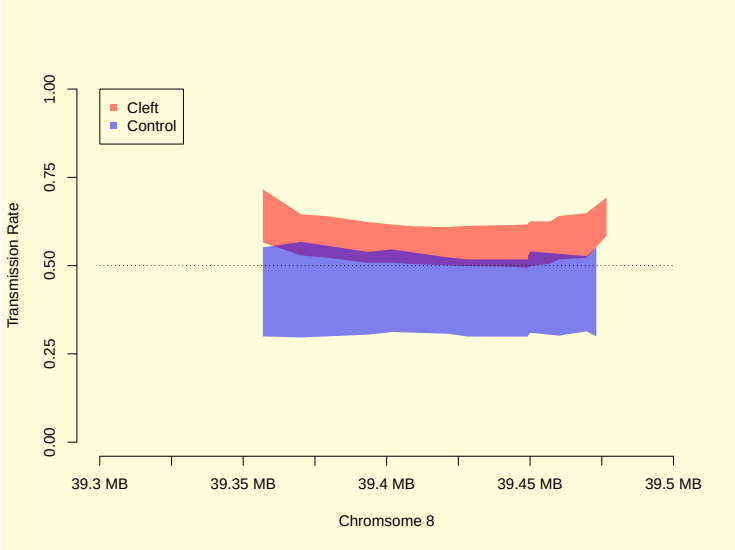


Figure 1: UCSC Genome Browser at chromosome 8 locus.




```
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
```

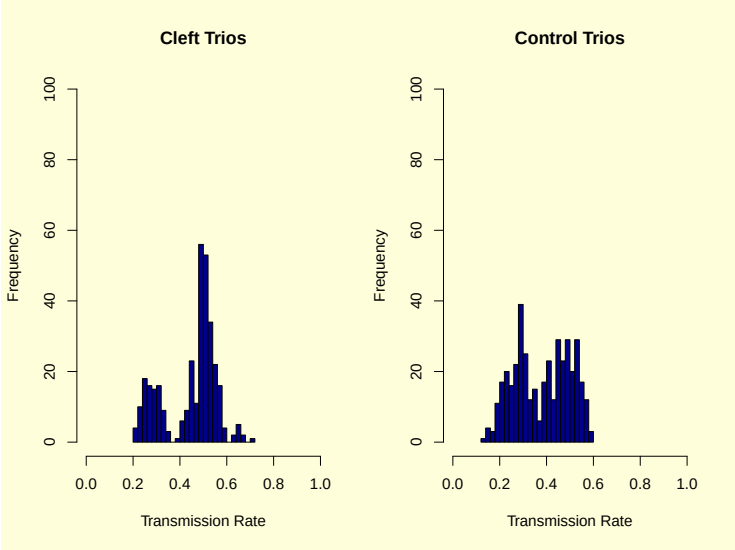
```
> freq.pitt[index.2.pitt]

 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")

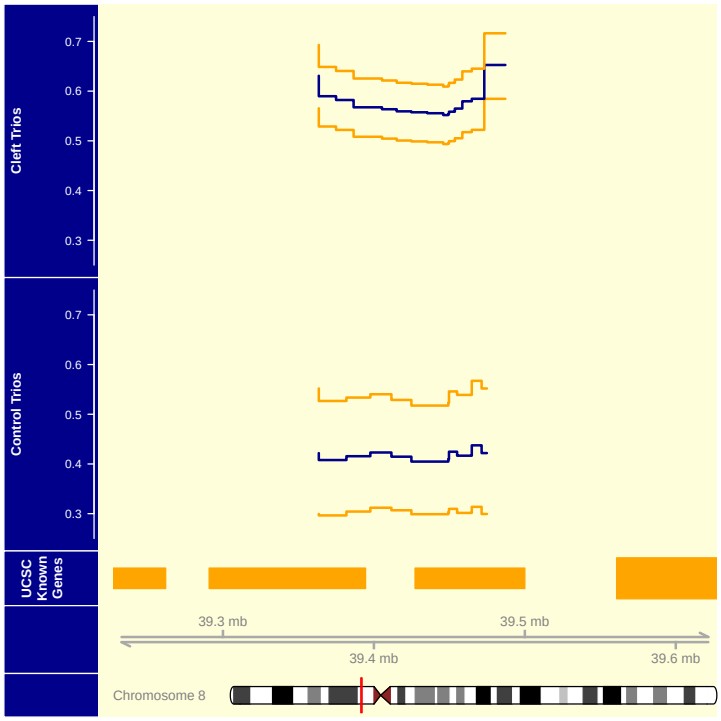

Cleft Trios
0.7
0.6
0.5
0.4
0.3
Control Trios
0.7
0.6
0.5
0.4
0.3
UCSC Known Genes
39.3 mb
39.5 mb
39.4 mb
39.6 mb
Chromosome 8

Figure 2:

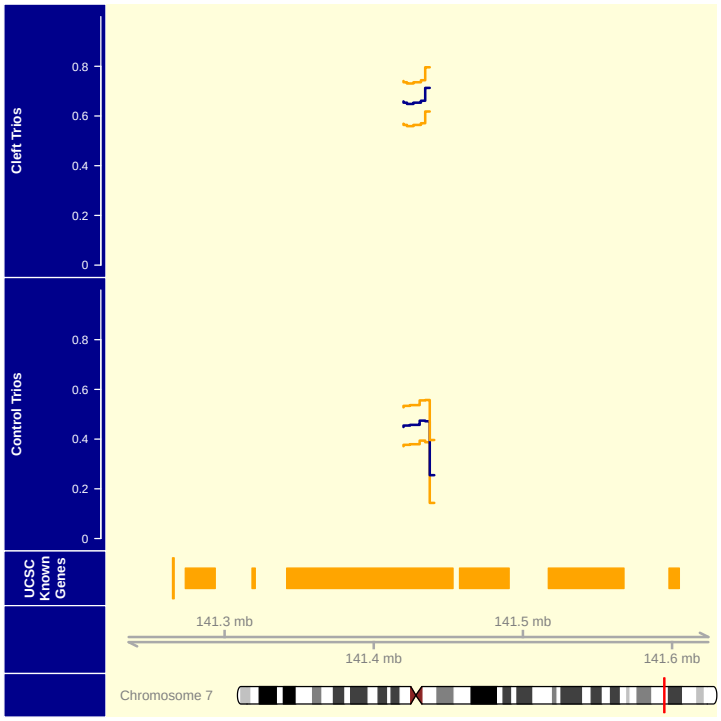

Cleft Trios
0.8
0.6
0.4
0.2
0
Control Trios
0.8
0.6
0.4
0.2
0
UCSC Known Genes
141.3 mb
141.5 mb
141.4 mb
141.6 mb
Chromosome 7

Figure 3:

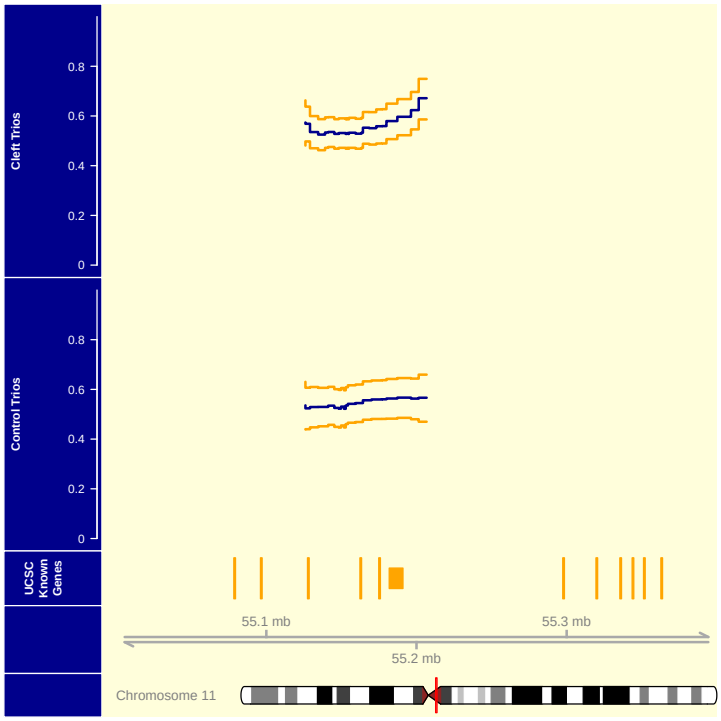

Cleft Trios
0.8
0.6
0.4
0.2
0
Control Trios
0.8
0.6
0.4
0.2
0
UCSC Known Genes
55.1 mb
55.3 mb
55.2 mb
Chromosome 11

Figure 4: