In [6]:

```
%load_ext rpy2.ipython
# Activates R cell magic
```

```
The rpy2.ipython extension is already loaded. To reload it, use:
  %reload_ext rpy2.ipython
```

Part III. HKA

- 1. Divergence Homo-Pongo
- 1. Merge Divergence and Diversity in a pandas dataframe
- 1. Intersection Divergence and Diversity with functional genomic features
- 1. Perform the HKA test

Part IV. Site Frequency Spectrum

Part III. HKA

In [ ]:

```
%%R
install.packages("plotrix", repos="https://cloud.r-project.org")
```

1. Divergence between Homo/Pongo

Update Divergence to identify missing regions in reference alignment

"WG.filtered.maf" from https://doi.org/10.1093/nar/gkaa1269 (https://doi.org/10.1093/nar/gkaa1269)

```
python mafparser.py
```

In [ ]:

```
#mafparser.py

import sys
import re
from string import maketrans

infile = open('WG.filtered.maf', 'rt') # from Divergence pipeline, Kinet
ics paper
outfile = open('Substitutions.bed', 'w+')

parsed = {}

h_motif = None
p_motif = None
r_motif = None


nucl_mapping = maketrans("actgn-","ACTGN-")

def custom_translate(input_string):
   return input_string.translate(nucl_mapping)


for line in infile:
        if line[0] == 's':
                line = line.strip()
                array = re.search('[s]\ +([a-z,A-Z]+[0-9]+)\.[a-z,A-Z]+
([0-9,\.,\_,\-,a-z,A-Z]+)\ +([0-9]+)\ +([0-9]+)\ +([+-])\ +[0-9]+\ +([a-
z,A-z,\-]+)', line)
                if 'hg19' == array.group(1):
                        h_chrom = array.group(2)
                        h_start = array.group(3)
                        h_length = array.group(4)
                        h_strand = array.group(5)
                        h_motif = array.group(6)

                if 'ponAbe2' == array.group(1):
                        p_chrom = array.group(2)
                        p_start = array.group(3)
                        p_length = array.group(4)
                        p_strand = array.group(5)
                        p_motif = array.group(6)

        if line[0] == 'a' and h_motif and p_motif:

                h_motif = custom_translate(h_motif)
                p_motif = custom_translate(p_motif)

                pos = 0
                compare = zip(h_motif, p_motif)
                for nuc in compare:
                        if nuc[0] != '-':
                                if nuc[0] != nuc[1]:
                                        outfile.write('chr'+h_chrom+'\t'
+str(int(h_start)+pos)+'\t'+str(int(h_start)+pos+1)+'\t'+nuc[0]+'\t'+nuc
[1]+'\n')
```

```
                                else:
                                        outfile.write('chr'+h_chrom+'\t'+str(int(h_start)+pos)+'\t'+str(int(h_start)+pos+1)+'\tNo\tNo\n')
                                pos += 1

                h_motif = None
                p_motif = None

        elif line[0] == 'a' and h_motif:
            for i in range(int(h_start), int(h_start) + int(h_length)):
                outfile.write('chr'+h_chrom+'\t'+str(i)+'\t'+str(i+1)+'\tNA\tNA\n')
```

Multithreading

```
array=(1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22)
for a in ${array[*]}; do
       echo chr${a};
       grep -w chr${a} WholeSGDPsnps.bed > chr${a}SGDPsnps.bed ;
       grep -w chr${a} Substitutions.bed > chr${a}Substitutions.bed;
done;
wait
```

2. Merge Divergence and Diversity in a pandas dataframe

"SGDPsnps.bed" from https://doi.org/10.1093/nar/gkaa1269 (https://doi.org/10.1093/nar/gkaa1269)

In [ ]:

```
#merging.py
import pandas as pd
import sys



SNPs = open(sys.argv[1]+'SGDPsnps.bed', 'rt')
Subs = open(sys.argv[1]+'Substitutions.bed', 'rt')

current_chrom = sys.argv[1]

colnames = ['chrom', 'start', 'end', 'homo|pongo|ref|alts|maf']
rows = []
sites = {}

for line in Subs:
    array = line.strip().split('\t')
    try:
        chrom, start, end, homo, pongo = array
    except:
        print(line)
    if chrom == current_chrom:
        key = chrom+'|'+start+'|'+end
        if key in sites:
            print('ERROR: Key should not yet be in directory Sites')
            print(array)
        else:
            sites[key] = [[homo, pongo],['NA','NA','NA']]

for line in SNPs:
    array = line.strip().split('\t')
    chrom, start, end, ref, alts, MAF, discard = array
    if chrom == current_chrom:
        key = chrom+'|'+start+'|'+end
        if key in sites:
            if sites[key][1] == ['NA','NA','NA']:
                sites[key][1] = [ref,alts,MAF]
            else:
                print('ERROR: Sub appearing multiple times')
        else:
            sites[key] = [['NA','NA'],[ref,alts,MAF]]


for site in sites:
    chrom, start, end = site.split('|')
    homo, pongo  = sites[site][0]
    ref, alts, maf = sites[site][1]
    alleles = homo+'|'+pongo+'|'+ref+'|'+alts+'|'+maf
    rows.append([chrom, start, end, alleles])

dataframe = pd.DataFrame(data=rows, columns=colnames)
dataframe.sort_values(by=['start'])
dataframe.to_csv(current_chrom+'Sites.tab', sep='\t')
```

Multithreading

```
for a in ${array[*]}; do
        echo chr${a};
        python merging.py chr${a}
done;
wait

for a in ${array[*]}; do
        cut -f 2-5 chr${a}Sites.tab | tail -n +2 > chr${a}Sites.bed
        grep -w chr${a} hs37d5.quadron.bed > chr${a}.hs37d5.quadron.bed
done;
wait
```

3. Intersection Divergence and Diversity with functional genomic features

In [ ]:

```
#SFScounter3.py
# Makes counts used in HKA
import sys

SFS = open(sys.argv[1], 'rt')
#output = open(sys.argv[1]+'.counted', 'w+')

windows = {}

compared = 0
subs = 0
poly = 0
empty = 0

for line in SFS:
    array = line.strip().split('\t')
    chrom, start, end, call = array[0], array[1], array[2], array[3]

    #if chrom == 'chr2':
    key = chrom+'|'+start+'|'+end

    if key not in windows:
        windows[key] = [0,0,0,0] # [subs, poly,compared,empty]

    try:
        homo, pongo, ref, alts, maf = call.split('|')
        if homo != 'NA':
            compared += 1
            windows[key][2] += 1
        if homo != 'NA' and homo != 'No':
            subs += 1
            windows[key][0] += 1
        if homo == 'No' and ref != 'NA':
            if float(maf) >= 0.05:
                poly += 1
                windows[key][1] += 1
            else:
                compared += 1
                windows[key][2] += 1
        else:
            compared += 1
            windows[key][2] += 1
    except:
        #empty += 1
        #windows[key][3] += 1
        print('ERROR type 2: This should never happen')

for key in windows:
    chrom, start, end = key.split('|')

print(sys.argv[1])
print(poly, subs, compared, empty)
```

```
# List of commands to obtain counts


awk -F "\t" '{if ($7>19) print $0}' hs37d5.quadron.bed > hs37d5.quadron.high.bed
awk -F "\t" '{if ($7<=19) print $0}' hs37d5.quadron.bed > hs37d5.quadron.low.bed

for a in ${array[*]}; do
        echo chr${a}

        grep -w chr${a} Upstream1k.nooverlap > chr${a}.Upstream1k.nooverlap
        bedtools intersect -wa -wb -a chr${a}.Upstream1k.nooverlap -b chr${a}Sites.bed -loj >> Upstream1k.SFS

        grep -w chr${a} FUTR.nooverlap > chr${a}.FUTR.nooverlap
        bedtools intersect -wa -wb -a chr${a}.FUTR.nooverlap -b chr${a}Sites.bed -loj >> FUTR.SFS

        grep -w chr${a} Exons.nooverlap > chr${a}.Exons.nooverlap
        bedtools intersect -wa -wb -a chr${a}.Exons.nooverlap -b chr${a}Sites.bed -loj >> Exons.SFS

        grep -w chr${a} Introns.nooverlap > chr${a}.Introns.nooverlap
        bedtools intersect -wa -wb -a chr${a}.Introns.nooverlap -b chr${a}Sites.bed -loj >> Introns.SFS

        grep -w chr${a} TUTR.nooverlap > chr${a}.TUTR.nooverlap
        bedtools intersect -wa -wb -a chr${a}.TUTR.nooverlap -b chr${a}Sites.bed -loj >> TUTR.SFS

        grep -w chr${a} Downstream1k.nooverlap > chr${a}.Downstream1k.nooverlap
        bedtools intersect -wa -wb -a chr${a}.Downstream1k.nooverlap -b chr${a}Sites.bed -loj >> Downstream1k.SFS

        grep -w chr${a} hg19RM_no_Interspersed.bed > chr${a}.hg19RM_no_Interspersed.bed
        bedtools intersect -wa -wb -a chr${a}.hg19RM_no_Interspersed.bed -b chr${a}Sites.bed -loj >> hg19RM_no_Interspersed.SFS

        grep -w chr${a} hg19Interspersed.bed > chr${a}.hg19Interspersed.bed
        bedtools intersect -wa -wb -a chr${a}.hg19Interspersed.bed -b chr${a}Sites.bed -loj >> hg19Interspersed.SFS

        grep -w chr${a} RepOrigin.nooverlap > chr${a}.RepOrigin.nooverlap
        bedtools intersect -wa -wb -a chr${a}.RepOrigin.nooverlap -b chr${a}Sites.bed -loj >> RepOrigin.SFS


        grep -w chr${a} enhancers.nooverlap > chr${a}.enhancers.nooverlap
        bedtools intersect -wa -wb -a chr${a}.enhancers.nooverlap -b chr${a}Sites.bed -loj >> enhancers.SFS

        grep -w chr${a} EncodeEnhancers.nooverlap > chr${a}.EncodeEnhancers.nooverlap
        bedtools intersect -wa -wb -a chr${a}.EncodeEnhancers.nooverlap -b chr${a}Sites.bed -loj >> EncodeEnhancers.SFS

        grep -w chr${a} promoters.nooverlap >chr${a}.promoters.nooverlap
        bedtools intersect -wa -wb -a chr${a}.promoters.nooverlap -b chr${a}Sites.bed -loj >> promoters.SFS

        grep -w chr${a} hg19CTCF.sorted.bed > chr${a}.hg19CTCF.sorted.bed
        bedtools intersect -wa -wb -a chr${a}.hg19CTCF.sorted.bed -b chr${a}Sites.bed -loj >> hg19CTCF.sorted.bed

        grep -w chr${a} TAD_boundary_regions.nooverlap > chr${a}.TADB.nooverlap
        bedtools intersect -wa -wb -a chr${a}.TADB.nooverlap -b chr${a}Sites.bed -loj >> TADB.SFS

        grep -w chr${a} recomb_hotspots.nooverlap > chr${a}.recomb_hotspots.nooverlap
        bedtools intersect -wa -wb -a chr${a}.recomb_hotspots.nooverlap -b chr${a}Sites.bed -loj >> recomb_hotspots.SFS

        grep -w chr${a} CpGIsland.nooverlap > chr${a}.CpGIsland.nooverlap
        bedtools intersect -wa -wb -a chr${a}.CpGIsland.nooverlap -b chr${a}Sites.bed -loj >> CpGIsland.SFS

        grep -w chr${a} NCNR.nooverlap > chr${a}.NCNR.nooverlap
        bedtools intersect -wa -wb -a chr${a}Sites.bed -b chr${a}.NCNR.nooverlap >> NCNR.SFS

        grep -w chr${a} NCNR.highrecomb.bed > chr${a}.NCNR.highrecomb.bed
        bedtools intersect -wa -wb -a chr${a}Sites.bed -b chr${a}.NCNR.highrecomb.bed >> NCNR.highrecomb.SFS

        grep -w chr${a} NCNR.lowrecomb.bed > chr${a}.NCNR.lowrecomb.bed
        bedtools intersect -wa -wb -a chr${a}Sites.bed -b chr${a}.NCNR.lowrecomb.bed >> NCNR.lowrecomb.SFS


done;
```

```
wait


bedtools intersect -a hs37d5.quadron.high.bed -b NCNR.nooverlap -f 1 >> NCNR.quadron.high.bed
bedtools intersect -a hs37d5.quadron.low.bed -b NCNR.nooverlap -f 1  >> NCNR.quadron.low.bed

bedtools intersect -a hs37d5.quadron.high.bed -b NCNR.highrecomb.bed -f 1 >> NCNR.highrecomb.quadron.high.bed
bedtools intersect -a hs37d5.quadron.low.bed -b NCNR.highrecomb.bed -f 1  >> NCNR.highrecomb.quadron.low.bed

bedtools intersect -a hs37d5.quadron.high.bed -b NCNR.lowrecomb.bed -f 1 >> NCNR.lowrecomb.quadron.high.bed
bedtools intersect -a hs37d5.quadron.low.bed -b NCNR.lowrecomb.bed -f 1  >> NCNR.lowrecomb.quadron.low.bed



awk '{print $7,$8,$9,$10,$5,$6}' OFS='\t' Upstream1k.SFS > Upstream1k.SFS.cut
bedtools intersect -a Upstream1k.SFS.cut -b hs37d5.quadron.high.bed  | cut -f 1-4 > Upstream1k.SFS.high.test
bedtools intersect -a Upstream1k.SFS.cut -b hs37d5.quadron.bed -v  > Upstream1k.SFS.control
python SFScounter3.py Upstream1k.SFS.high.test
python SFScounter3.py Upstream1k.SFS.control
bedtools intersect -a Upstream1k.SFS.cut -b hs37d5.quadron.low.bed  | cut -f 1-4 > Upstream1k.SFS.low.test
python SFScounter3.py Upstream1k.SFS.low.test

awk '{print $7,$8,$9,$10,$5,$6}' OFS='\t' FUTR.SFS > FUTR.SFS.cut
bedtools intersect -a FUTR.SFS.cut -b hs37d5.quadron.high.bed -s  | cut -f 1-4 > FUTR.SFS.high.sens.test
bedtools intersect -a FUTR.SFS.cut -b hs37d5.quadron.high.bed -S  | cut -f 1-4  > FUTR.SFS.high.antisens.test
bedtools intersect -a FUTR.SFS.cut -b hs37d5.quadron.bed -v  > FUTR.SFS.control
python SFScounter3.py FUTR.SFS.high.sens.test
python SFScounter3.py FUTR.SFS.high.antisens.test
python SFScounter3.py FUTR.SFS.control
bedtools intersect -a FUTR.SFS.cut -b hs37d5.quadron.low.bed -s  | cut -f 1-4 > FUTR.SFS.low.sens.test
bedtools intersect -a FUTR.SFS.cut -b hs37d5.quadron.low.bed -S  | cut -f 1-4 > FUTR.SFS.low.antisens.test
python SFScounter3.py FUTR.SFS.low.sens.test
python SFScounter3.py FUTR.SFS.low.antisens.test
```

```
awk '{print $7,$8,$9,$10,$5,$6}' OFS='\t'Exons.SFS > Exons.SFS.cut
bedtools intersect -a Exons.SFS.cut -b hs37d5.quadron.high.bed -s  | cut -f 1-4 > Exons.SFS.high.sens.test
bedtools intersect -a Exons.SFS.cut -b hs37d5.quadron.high.bed -S  | cut -f 1-4 > Exons.SFS.high.antisens.test
bedtools intersect -a Exons.SFS.cut -b hs37d5.quadron.bed -v  > Exons.SFS.control
python SFScounter3.py Exons.SFS.high.sens.test
python SFScounter3.py Exons.SFS.high.antisens.test
python SFScounter3.py Exons.SFS.control
bedtools intersect -a Exons.SFS.cut -b hs37d5.quadron.low.bed -s  | cut -f 1-4 > Exons.SFS.low.sens.test
bedtools intersect -a Exons.SFS.cut -b hs37d5.quadron.low.bed -S  | cut -f 1-4 > Exons.SFS.low.antisens.test
python SFScounter3.py Exons.SFS.low.sens.test
python SFScounter3.py Exons.SFS.low.antisens.test

awk '{print $7,$8,$9,$10,$5,$6}' OFS='\t' Introns.SFS > Introns.SFS.cut
bedtools intersect -a Introns.SFS.cut -b hs37d5.quadron.high.bed -s  | cut -f 1-4 > Introns.SFS.high.sens.test
bedtools intersect -a Introns.SFS.cut -b hs37d5.quadron.high.bed -S  | cut -f 1-4 > Introns.SFS.high.antisens.test
bedtools intersect -a Introns.SFS.cut -b hs37d5.quadron.bed -v  | cut -f 1-4 > Introns.SFS.control
python SFScounter3.py Introns.SFS.high.sens.test
python SFScounter3.py Introns.SFS.high.antisens.test
shuf -n 1000000 Introns.SFS.control > Introns.SFS.control.shuf
python SFScounter3.py Introns.SFS.control.shuf
bedtools intersect -a Introns.SFS.cut -b hs37d5.quadron.low.bed -s  | cut -f 1-4 > Introns.SFS.low.sens.test
bedtools intersect -a Introns.SFS.cut -b hs37d5.quadron.low.bed -S  | cut -f 1-4 > Introns.SFS.low.antisens.test
python SFScounter3.py Introns.SFS.low.sens.test
python SFScounter3.py Introns.SFS.low.antisens.test



awk '{print $7,$8,$9,$10,$5,$6}' OFS='\t' TUTR.SFS > TUTR.SFS.cut
bedtools intersect -a TUTR.SFS.cut -b hs37d5.quadron.high.bed -s  | cut -f 1-4  > TUTR.SFS.high.sens.test
bedtools intersect -a TUTR.SFS.cut -b hs37d5.quadron.high.bed -S  | cut -f 1-4 > TUTR.SFS.high.antisens.test
bedtools intersect -a TUTR.SFS.cut -b hs37d5.quadron.bed -v  > TUTR.SFS.control
python SFScounter3.py TUTR.SFS.high.sens.test
python SFScounter3.py TUTR.SFS.high.antisens.test
python SFScounter3.py TUTR.SFS.control
bedtools intersect -a TUTR.SFS.cut -b hs37d5.quadron.low.bed -s  | cut -f 1-4 > TUTR.SFS.low.sens.test
bedtools intersect -a TUTR.SFS.cut -b hs37d5.quadron.low.bed -S  | cut -f 1-4 > TUTR.SFS.low.antisens.test
python SFScounter3.py TUTR.SFS.low.sens.test
python SFScounter3.py TUTR.SFS.low.antisens.test

awk '{print $7,$8,$9,$10,$5,$6}' OFS='\t' Downstream1k.SFS > Downstream1k.SFS.cut
bedtools intersect -a Downstream1k.SFS.cut -b hs37d5.quadron.high.bed  | cut -f 1-4 > Downstream1k.SFS.high.test
bedtools intersect -a Downstream1k.SFS.cut -b hs37d5.quadron.bed -v  > Downstream1k.SFS.control
python SFScounter3.py Downstream1k.SFS.high.test
python SFScounter3.py Downstream1k.SFS.control
bedtools intersect -a Downstream1k.SFS.cut -b hs37d5.quadron.low.bed  | cut  -f 1-4 > Downstream1k.SFS.low.test
python SFScounter3.py Downstream1k.SFS.low.test


bedtools intersect -a hs37d5.quadron.high.bed -b NCNR.nooverlap -f 1 > NCNR.quadron.high.bed
bedtools intersect -a hs37d5.quadron.low.bed -b NCNR.nooverlap -f 1  > NCNR.quadron.low.bed
cat NCNR.quadron.high.bed NCNR.quadron.low.bed > NCNR.quadron.bed
bedtools intersect -a NCNR.SFS -b NCNR.quadron.high.bed > NCNR.SFS.high.bed.test
bedtools intersect -a NCNR.SFS -b NCNR.quadron.bed -v > NCNR.SFS.control
python SFScounter3.py NCNR.SFS.high.bed.test
shuf -n 10000000 NCNR.SFS.control > NCNR.SFS.control.shuf
python SFScounter3.py NCNR.SFS.control.shuf
bedtools intersect -a NCNR.SFS -b NCNR.quadron.low.bed > NCNR.SFS.low.bed.test
python SFScounter3.py NCNR.SFS.low.bed.test

bedtools intersect -a NCNR.highrecomb.SFS -b NCNR.quadron.high.bed > NCNR.highrecomb.SFS.high.bed.test
bedtools intersect -a NCNR.highrecomb.SFS -b NCNR.quadron.bed -v > NCNR.highrecomb.SFS.control
python SFScounter3.py NCNR.highrecomb.SFS.high.bed.test
shuf -n 10000000 NCNR.highrecomb.SFS.control > NCNR.highrecomb.SFS.control.shuf
python SFScounter3.py NCNR.highrecomb.SFS.control.shuf
bedtools intersect -a NCNR.highrecomb.SFS -b NCNR.quadron.low.bed > NCNR.highrecomb.SFS.low.bed.test
python SFScounter3.py NCNR.highrecomb.SFS.low.bed.test

bedtools intersect -a NCNR.lowrecomb.SFS -b NCNR.quadron.high.bed > NCNR.lowrecomb.SFS.high.bed.test
bedtools intersect -a NCNR.lowrecomb.SFS -b NCNR.quadron.bed -v > NCNR.lowrecomb.SFS.control
```

```
python SFScounter3.py NCNR.lowrecomb.SFS.high.bed.test
shuf -n 10000000 NCNR.lowrecomb.SFS.control > NCNR.lowrecomb.SFS.control.shuf
python SFScounter3.py NCNR.lowrecomb.SFS.control.shuf
bedtools intersect -a NCNR.lowrecomb.SFS -b NCNR.quadron.low.bed > NCNR.lowrecomb.SFS.low.bed.test
python SFScounter3.py NCNR.lowrecomb.SFS.low.bed.test

cut -f 5-8 TADB.SFS > TADB.SFS.cut
bedtools intersect -a TADB.SFS.cut -b hs37d5.quadron.high.bed > TADB.SFS.high.test
bedtools intersect -a TADB.SFS.cut -b hs37d5.quadron.bed -v > TADB.SFS.control
python SFScounter3.py TADB.SFS.high.test
bedtools intersect -a recomb_hotspots.SFS.cut -b hs37d5.quadron.bed -v > recomb_hotspots.SFS.control
python SFScounter3.py recomb_hotspots.SFS.high.test
python SFScounter3.py recomb_hotspots.SFS.control
bedtools intersect -a recomb_hotspots.SFS.cut -b hs37d5.quadron.low.bed > recomb_hotspots.SFS.low.test
python SFScounter3.py recomb_hotspots.SFS.low.test

cut -f 5-8 CpGIsland.SFS > CpGIsland.SFS.cut
bedtools intersect -a CpGIsland.SFS.cut -b hs37d5.quadron.high.bed > CpGIsland.SFS.high.test
bedtools intersect -a CpGIsland.SFS.cut -b hs37d5.quadron.bed -v > CpGIsland.SFS.control
python SFScounter3.py CpGIsland.SFS.high.test
python SFScounter3.py CpGIsland.SFS.control
bedtools intersect -a CpGIsland.SFS.cut -b hs37d5.quadron.low.bed > CpGIsland.SFS.low.test
python SFScounter3.py CpGIsland.SFS.low.test

cut -f 5-8 RepOrigin.SFS > RepOrigin.SFS.cut
bedtools intersect -a RepOrigin.SFS.cut -b hs37d5.quadron.high.bed > RepOrigin.SFS.high.test
bedtools intersect -a RepOrigin.SFS.cut -b hs37d5.quadron.bed -v > RepOrigin.SFS.control
python SFScounter3.py RepOrigin.SFS.high.test
python SFScounter3.py RepOrigin.SFS.control
bedtools intersect -a RepOrigin.SFS.cut -b hs37d5.quadron.low.bed > RepOrigin.SFS.low.test
python SFScounter3.py RepOrigin.SFS.low.test

cut -f 4-7 enhancers.SFS > enhancers.SFS.cut
bedtools intersect -a enhancers.SFS.cut -b hs37d5.quadron.high.bed > enhancers.SFS.high.test
bedtools intersect -a enhancers.SFS.cut -b hs37d5.quadron.bed -v > enhancers.SFS.control
```

```
python SFScounter3.py enhancers.SFS.high.test
python SFScounter3.py enhancers.SFS.control
bedtools intersect -a enhancers.SFS.cut -b hs37d5.quadron.low.bed > enhancers.SFS.low.test
python SFScounter3.py enhancers.SFS.low.test

cut -f 5-8 EncodeEnhancers.SFS > EncodeEnhancers.SFS.cut
bedtools intersect -a EncodeEnhancers.SFS.cut -b hs37d5.quadron.high.bed > EncodeEnhancers.SFS.high.test
bedtools intersect -a EncodeEnhancers.SFS.cut -b hs37d5.quadron.bed -v > EncodeEnhancers.SFS.control
python SFScounter3.py EncodeEnhancers.SFS.high.test
python SFScounter3.py EncodeEnhancers.SFS.control
bedtools intersect -a EncodeEnhancers.SFS.cut -b hs37d5.quadron.low.bed > EncodeEnhancers.SFS.low.test
python SFScounter3.py EncodeEnhancers.SFS.low.test
```

4. Perform the HKA test

In [10]:

```
%%html
<!-- Left aligning the next table -->
<style>
table {float:left}
</style>
```

Simple HKA test

The input data looks as such:

	Poly	Subs
Test	T_{poly}	T_{subs}
Control	C_{poly}	C_{subs}

In [30]:

```
%%R

# VALUES MANUALLY RECOVERED FROM STEP 3


NCNR_fisher <- fisher.test(cbind(c(29040+30118, 179366+232166),c(33137, 276062)))
NCNR_high_fisher <- fisher.test(cbind(c(29040, 179366),c(33137, 276062)))
NCNR_low_fisher <- fisher.test(cbind(c(30118, 232166),c(33137, 276062)))
print(paste('NCNR',NCNR_fisher$estimate,NCNR_fisher$p.value))
print(paste('NCNR High',NCNR_high_fisher$estimate,NCNR_high_fisher$p.value))
print(paste('NCNR Low',NCNR_low_fisher$estimate,NCNR_low_fisher$p.value))


Upstream_fisher <- fisher.test(cbind(c(6948+2448, 36771+18026),c(110740, 909807)))
Upstream_high_fisher <- fisher.test(cbind(c(6948, 36771),c(110740, 909807)))
Upstream_low_fisher <- fisher.test(cbind(c(2448, 18026),c(110740, 909807)))
print(paste('Up',Upstream_fisher$estimate,Upstream_fisher$p.value))
print(paste('Up High',Upstream_high_fisher$estimate,Upstream_high_fisher$p.value))
print(paste('Up Low',Upstream_low_fisher$estimate,Upstream_low_fisher$p.value))

FUTR_fisher_sense <- fisher.test(cbind(c(692+528, 3698+3752),c(51397, 391923)))
FUTR_high_fisher_sense <- fisher.test(cbind(c(692, 3698),c(51397, 391923)))
FUTR_low_fisher_sense <- fisher.test(cbind(c(528, 3752),c(51397, 391923)))
print(paste('5UTR sense',FUTR_fisher_sense$estimate,FUTR_fisher_sense$p.value))
print(paste('5UTR High sense',FUTR_high_fisher_sense$estimate,FUTR_high_fisher_sense$p.value))
print(paste('5UTR Low sense',FUTR_low_fisher_sense$estimate,FUTR_low_fisher_sense$p.value))

FUTR_fisher_antisense <- fisher.test(cbind(c(898+600, 4996+4245),c(51397, 391923)))
FUTR_high_fisher_antisense <- fisher.test(cbind(c(898, 4996),c(51397, 391923)))
FUTR_low_fisher_antisense <- fisher.test(cbind(c(600, 4245),c(51397, 391923)))
print(paste('5UTR antisense',FUTR_fisher_antisense$estimate,FUTR_fisher_antisense$p.value))
print(paste('5UTR High antisense',FUTR_high_fisher_antisense$estimate,FUTR_high_fisher_antisense$p.value))
print(paste('5UTR Low antisense',FUTR_low_fisher_antisense$estimate,FUTR_low_fisher_antisense$p.value))
```

```
Exon_fisher_sense <- fisher.test(cbind(c(195+393, 1151+2343),c(82685, 514590)))
Exon_high_fisher_sense <- fisher.test(cbind(c(195, 1151),c(82685, 514590)))
Exon_low_fisher_sense <- fisher.test(cbind(c(393, 2343),c(82685, 514590)))
print(paste('Exon sense',Exon_fisher_sense$estimate,Exon_fisher_sense$p.value))
print(paste('Exon High sense',Exon_high_fisher_sense$estimate,Exon_high_fisher_sense$p.value))
print(paste('Exon Low sense',Exon_low_fisher_sense$estimate,Exon_low_fisher_sense$p.value))

Exon_fisher_antisense <- fisher.test(cbind(c(968+801, 4274+4718),c(82685, 514590)))
Exon_high_fisher_antisense <- fisher.test(cbind(c(968, 4274),c(82685, 514590)))
Exon_low_fisher_antisense <- fisher.test(cbind(c(801, 4718),c(82685, 514590)))
print(paste('Exon antisense',Exon_fisher_antisense$estimate,Exon_fisher_antisense$p.value))
print(paste('Exon High antisense',Exon_high_fisher_antisense$estimate,Exon_high_fisher_antisense$p.value))
print(paste('Exon Low antisense',Exon_low_fisher_antisense$estimate,Exon_low_fisher_antisense$p.value))

Intron_fisher_sense <- fisher.test(cbind(c(28521+14309,163609+114249),c(4283, 35504)))
Intron_high_fisher_sense <- fisher.test(cbind(c(28521, 163609),c(4283, 35504)))
Intron_low_fisher_sense <- fisher.test(cbind(c(14309, 114249),c(4283, 35504)))
print(paste('Intron sense',Intron_fisher_sense$estimate,Intron_fisher_sense$p.value))
print(paste('Intron High sense',Intron_high_fisher_sense$estimate,Intron_high_fisher_sense$p.value))
print(paste('Intron Low sense',Intron_low_fisher_sense$estimate,Intron_low_fisher_sense$p.value))


Intron_fisher_antisense <- fisher.test(cbind(c(28147+13495,162411+103428),c(4283, 35504)))
Intron_high_fisher_antisense <- fisher.test(cbind(c(28147, 162411),c(4283, 35504)))
Intron_low_fisher_antisense <- fisher.test(cbind(c(13495, 103428),c(4283, 35504)))
print(paste('Intron antisense',Intron_fisher_antisense$estimate,Intron_fisher_antisense$p.value))
print(paste('Intron High antisense',Intron_high_fisher_antisense$estimate,Intron_high_fisher_antisense$p.value))
print(paste('Intron Low antisense',Intron_low_fisher_antisense$estimate,Intron_low_fisher_antisense$p.value))



TUTR_fisher_sense <- fisher.test(cbind(c(973+649, 4999+4698),c(124588, 994407)))
```

```
TUTR_high_fisher_sense <- fisher.test(cbind(c(973, 4999),c(124588, 994407)))
TUTR_low_fisher_sense <- fisher.test(cbind(c(649, 4698),c(124588, 994407)))
print(paste('3UTR sense',TUTR_fisher_sense$estimate,TUTR_fisher_sense$p.value))
print(paste('3UTR High sense',TUTR_high_fisher_sense$estimate,TUTR_high_fisher_sense$p.value))
print(paste('3UTR Low sense',TUTR_low_fisher_sense$estimate,TUTR_low_fisher_sense$p.value))

TUTR_fisher_antisense <- fisher.test(cbind(c(1228+761, 7645+5787),c(124588, 994407)))
TUTR_high_fisher_antisense <- fisher.test(cbind(c(1228, 7645),c(124588, 994407)))
TUTR_low_fisher_antisense <- fisher.test(cbind(c(761, 5787),c(124588, 994407)))
print(paste('3UTR antisense',TUTR_fisher_antisense$estimate,TUTR_fisher_antisense$p.value))
print(paste('3UTR High antisense',TUTR_high_fisher_antisense$estimate,TUTR_high_fisher_antisense$p.value))
print(paste('3UTR Low antisense',TUTR_low_fisher_antisense$estimate,TUTR_low_fisher_antisense$p.value))


Downstream_fisher <- fisher.test(cbind(c(2568+1271, 15724+9880),c(112551, 969230)))
Downstream_high_fisher <- fisher.test(cbind(c(2568, 15724),c(112551, 969230)))
Downstream_low_fisher <- fisher.test(cbind(c(1271, 9880),c(112551, 969230)))
print(paste('Down',Downstream_fisher$estimate,Downstream_fisher$p.value))
print(paste('Down High',Downstream_high_fisher$estimate,Downstream_high_fisher$p.value))
print(paste('Down Low',Downstream_low_fisher$estimate,Downstream_low_fisher$p.value))


Oris_fisher <- fisher.test(cbind(c(48685+19152, 267964+148105),c(632389, 5228028)))
Oris_high_fisher <- fisher.test(cbind(c(48685, 267964),c(632389, 5228028)))
Oris_low_fisher <- fisher.test(cbind(c(19152, 148105),c(632389, 5228028)))
print(paste('Oris',Oris_fisher$estimate,Oris_fisher$p.value))
print(paste('Oris High',Oris_high_fisher$estimate,Oris_high_fisher$p.value))
print(paste('Oris Low',Oris_low_fisher$estimate,Oris_low_fisher$p.value))

Enhancers_fisher <- fisher.test(cbind(c(2549+977, 13572+6937),c(74321, 582596)))
Enhancers_high_fisher <- fisher.test(cbind(c(2549, 13572),c(74321, 582596)))
Enhancers_low_fisher <- fisher.test(cbind(c(977, 6937),c(74321, 582596)))
```

```
print(paste('Enhancers', Enhancers_fisher$estimate,Enhancers_fisher$p.value))
print(paste('Enhancers High', Enhancers_high_fisher$estimate,Enhancers_high_fisher$p.value))
print(paste('Enhancers Low', Enhancers_low_fisher$estimate,Enhancers_low_fisher$p.value))

TADB_fisher <- fisher.test(cbind(c(29642+15607, 170462+119163),c(42631, 357334)))
TADB_high_fisher <- fisher.test(cbind(c(29642, 170462),c(42631, 357334)))
TADB_low_fisher <- fisher.test(cbind(c(15607, 119163),c(42631, 357334)))
print(paste('TADB', TADB_fisher$estimate,TADB_fisher$p.value))
print(paste('TADB High', TADB_high_fisher$estimate,TADB_high_fisher$p.value))
print(paste('TADB Low', TADB_low_fisher$estimate,TADB_low_fisher$p.value))

CpGI_fisher <- fisher.test(cbind(c(10120+5230, 56369+37197),c(85310, 604452)))
CpGI_high_fisher <- fisher.test(cbind(c(10120, 56369),c(85310, 604452)))
CpGI_low_fisher <- fisher.test(cbind(c(5230, 37197),c(85310, 604452)))
print(paste('CpGI', CpGI_fisher$estimate,CpGI_fisher$p.value))
print(paste('CpGI', CpGI_high_fisher$estimate,CpGI_high_fisher$p.value))
print(paste('CpGI', CpGI_low_fisher$estimate,CpGI_low_fisher$p.value))
```

```
[1] "NCNR 1.19757578033276 1.04927592755154e-136"
[1] "NCNR High 1.34877993859284 7.25198589322622e-264"
[1] "NCNR Low 1.0807387388301 3.94971559989767e-20"
[1] "Up 1.40873634375814 1.01583848287047e-178"
[1] "Up High 1.55237345204985 5.48190275270506e-214"
[1] "Up Low 1.11569537925185 6.80979650583152e-07"
[1] "5UTR sense 1.24872277022481 3.98695225141817e-12"
[1] "5UTR High sense 1.42692144166062 2.32853152446011e-16"
[1] "5UTR Low sense 1.07310811510519 0.130850124075054"
[1] "5UTR antisense 1.23610494791617 2.34989859912373e-13"
[1] "5UTR High antisense 1.37061437568979 7.75805317487696e-17"
[1] "5UTR Low antisense 1.07782148904905 0.0907023921474555"
[1] "Exon sense 1.04735266655434 0.30622490919682"
[1] "Exon High sense 1.05438429545317 0.50174635969441"
[1] "Exon Low sense 1.0438986320892 0.437267583734939"
[1] "Exon antisense 1.22433845659533 4.60533472910989e-14"
[1] "Exon High antisense 1.40952921480283 2.25066989426134e-20"
[1] "Exon Low antisense 1.05660929467542 0.153004807032294"
[1] "Intron sense 1.27776964924056 1.54916630041988e-49"
[1] "Intron High sense 1.44501229702771 3.77672638071925e-106"
[1] "Intron Low sense 1.03818082710153 0.0421873147531252"
[1] "Intron antisense 1.29849350615665 5.29049875131616e-56"
[1] "Intron High antisense 1.43658412150075 1.44941026727251e-102"
[1] "Intron Low antisense 1.08159131373222 2.26510293001806e-05"
[1] "3UTR sense 1.33505815218509 4.18003724489921e-25"
[1] "3UTR High sense 1.55351338255059 9.77287595922082e-33"
[1] "3UTR Low sense 1.10257165009094 0.0209128714069089"
[1] "3UTR antisense 1.18189974032086 1.34664259512304e-11"
[1] "3UTR High antisense 1.28206016350631 5.58946109001039e-15"
[1] "3UTR Low antisense 1.04960142951792 0.214547796242716"
[1] "Down 1.29118044402985 3.41203305200329e-45"
[1] "Down High 1.40639568916887 2.07871599208989e-52"
[1] "Down Low 1.10778333898741 0.000720537951066889"
[1] "Oris 1.34788911331848 0"
[1] "Oris High 1.50200280009476 0"
[1] "Oris Low 1.06907097863864 1.92208722674057e-17"
[1] "Enhancers 1.34769815601055 3.7518863981056e-54"
[1] "Enhancers High 1.47224422546273 4.03953372189528e-64"
[1] "Enhancers Low 1.10399097691151 0.00430506334346868"
[1] "TADB 1.30953705648304 3.10368985515179e-307"
[1] "TADB High 1.45761101376159 0"
[1] "TADB Low 1.09780236705632 9.80205696536419e-21"
[1] "CpGI 1.16241165961688 9.48478996686513e-56"
[1] "CpGI 1.27204260611575 1.2213875656606e-94"
[1] "CpGI 0.996220853037997 0.807918064581636"
```

In [31]:

```
%%R
#https://stackoverflow.com/questions/14069629/how-can-i-plot-data-with-c
onfidence-intervals

x <- c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15)


ORs <- c(Upstream_fisher$estimate,
         CpGI_fisher$estimate,
         FUTR_fisher_sense$estimate,
         FUTR_fisher_antisense$estimate,
         Exon_fisher_sense$estimate,
         Exon_fisher_antisense$estimate,
         Intron_fisher_sense$estimate,
         Intron_fisher_antisense$estimate,
         TUTR_fisher_sense$estimate,
         TUTR_fisher_antisense$estimate,
         Downstream_fisher$estimate,
         Enhancers_fisher$estimate,
         Oris_fisher$estimate,
         TADB_fisher$estimate,
         NCNR_fisher$estimate)


Low_ORs <- c(Upstream_low_fisher$estimate,
             CpGI_low_fisher$estimate,
             FUTR_low_fisher_sense$estimate,
             FUTR_low_fisher_antisense$estimate,
             Exon_low_fisher_sense$estimate,
             Exon_low_fisher_antisense$estimate,
             Intron_low_fisher_sense$estimate,
             Intron_low_fisher_antisense$estimate,
             TUTR_low_fisher_sense$estimate,
             TUTR_low_fisher_antisense$estimate,
             Downstream_low_fisher$estimate,
             Enhancers_low_fisher$estimate,
             Oris_low_fisher$estimate,
             TADB_low_fisher$estimate,
             NCNR_low_fisher$estimate)

High_ORs <- c(Upstream_high_fisher$estimate,
              CpGI_high_fisher$estimate,
              FUTR_high_fisher_sense$estimate,
              FUTR_high_fisher_antisense$estimate,
              Exon_high_fisher_sense$estimate,
              Exon_high_fisher_antisense$estimate,
              Intron_high_fisher_sense$estimate,
              Intron_high_fisher_antisense$estimate,
              TUTR_high_fisher_sense$estimate,
              TUTR_high_fisher_antisense$estimate,
              Downstream_high_fisher$estimate,
              Enhancers_high_fisher$estimate,
              Oris_high_fisher$estimate,
              TADB_high_fisher$estimate,
              NCNR_high_fisher$estimate)
```

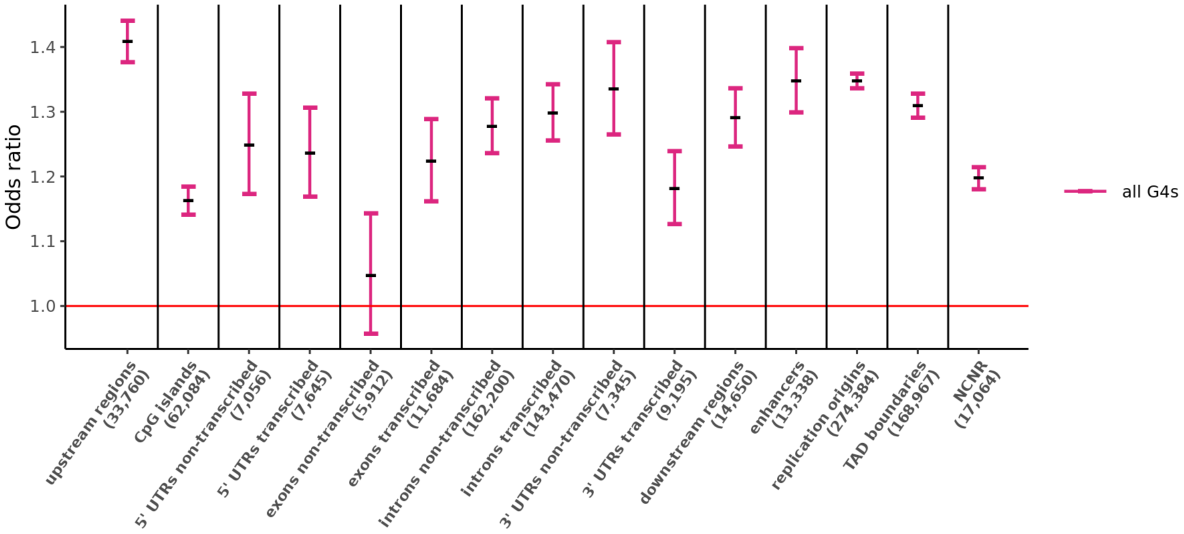
```
Ls <- c(Upstream_fisher$conf.int[1],
        CpGI_fisher$conf.int[1],
        FUTR_fisher_sense$conf.int[1],
        FUTR_fisher_antisense$conf.int[1],
        Exon_fisher_sense$conf.int[1],
        Exon_fisher_antisense$conf.int[1],
        Intron_fisher_sense$conf.int[1],
        Intron_fisher_antisense$conf.int[1],
        TUTR_fisher_sense$conf.int[1],
        TUTR_fisher_antisense$conf.int[1],
        Downstream_fisher$conf.int[1],
        Enhancers_fisher$conf.int[1],
        Oris_fisher$conf.int[1],
        TADB_fisher$conf.int[1],
        NCNR_fisher$conf.int[1])


Low_Ls <- c(Upstream_low_fisher$conf.int[1],
            CpGI_low_fisher$conf.int[1],
            FUTR_low_fisher_sense$conf.int[1],
            FUTR_low_fisher_antisense$conf.int[1],
            Exon_low_fisher_sense$conf.int[1],
            Exon_low_fisher_antisense$conf.int[1],
            Intron_low_fisher_sense$conf.int[1],
            Intron_low_fisher_antisense$conf.int[1],
            TUTR_low_fisher_sense$conf.int[1],
            TUTR_low_fisher_antisense$conf.int[1],
            Downstream_low_fisher$conf.int[1],
            Enhancers_low_fisher$conf.int[1],
            Oris_low_fisher$conf.int[1],
            TADB_low_fisher$conf.int[1],
            NCNR_low_fisher$conf.int[1])


High_Ls <- c(Upstream_high_fisher$conf.int[1],
             CpGI_high_fisher$conf.int[1],
             FUTR_high_fisher_sense$conf.int[1],
             FUTR_high_fisher_antisense$conf.int[1],
             Exon_high_fisher_sense$conf.int[1],
             Exon_high_fisher_antisense$conf.int[1],
             Intron_high_fisher_sense$conf.int[1],
             Intron_high_fisher_antisense$conf.int[1],
             TUTR_high_fisher_sense$conf.int[1],
             TUTR_high_fisher_antisense$conf.int[1],
             Downstream_high_fisher$conf.int[1],
             Enhancers_high_fisher$conf.int[1],
             Oris_high_fisher$conf.int[1],
             TADB_high_fisher$conf.int[1],
             NCNR_high_fisher$conf.int[1])

Us <- c(Upstream_fisher$conf.int[2],
        CpGI_fisher$conf.int[2],
        FUTR_fisher_sense$conf.int[2],
        FUTR_fisher_antisense$conf.int[2],
        Exon_fisher_sense$conf.int[2],
        Exon_fisher_antisense$conf.int[2],
        Intron_fisher_sense$conf.int[2],
        Intron_fisher_antisense$conf.int[2],
        TUTR_fisher_sense$conf.int[2],
        TUTR_fisher_antisense$conf.int[2],
        Downstream_fisher$conf.int[2],
        Enhancers_fisher$conf.int[2],
        Oris_fisher$conf.int[2],
        TADB_fisher$conf.int[2],
        NCNR_fisher$conf.int[2])


Low_Us <- c(Upstream_low_fisher$conf.int[2],
            CpGI_low_fisher$conf.int[2],
            FUTR_low_fisher_sense$conf.int[2],
            FUTR_low_fisher_antisense$conf.int[2],
            Exon_low_fisher_sense$conf.int[2],
            Exon_low_fisher_antisense$conf.int[2],
            Intron_low_fisher_sense$conf.int[2],
            Intron_low_fisher_antisense$conf.int[2],
            TUTR_low_fisher_sense$conf.int[2],
            TUTR_low_fisher_antisense$conf.int[2],
            Downstream_low_fisher$conf.int[2],
            Enhancers_low_fisher$conf.int[2],
            Oris_low_fisher$conf.int[2],
            TADB_low_fisher$conf.int[2],
            NCNR_low_fisher$conf.int[2])


High_Us <- c(Upstream_high_fisher$conf.int[2],
             CpGI_high_fisher$conf.int[2],
             FUTR_high_fisher_sense$conf.int[2],
             FUTR_high_fisher_antisense$conf.int[2],
             Exon_high_fisher_sense$conf.int[2],
             Exon_high_fisher_antisense$conf.int[2],
             Intron_high_fisher_sense$conf.int[2],
             Intron_high_fisher_antisense$conf.int[2],
             TUTR_high_fisher_sense$conf.int[2],
             TUTR_high_fisher_antisense$conf.int[2],
             Downstream_high_fisher$conf.int[2],
             Enhancers_high_fisher$conf.int[2],
             Oris_high_fisher$conf.int[2],
             TADB_high_fisher$conf.int[2],
             NCNR_high_fisher$conf.int[2])
```

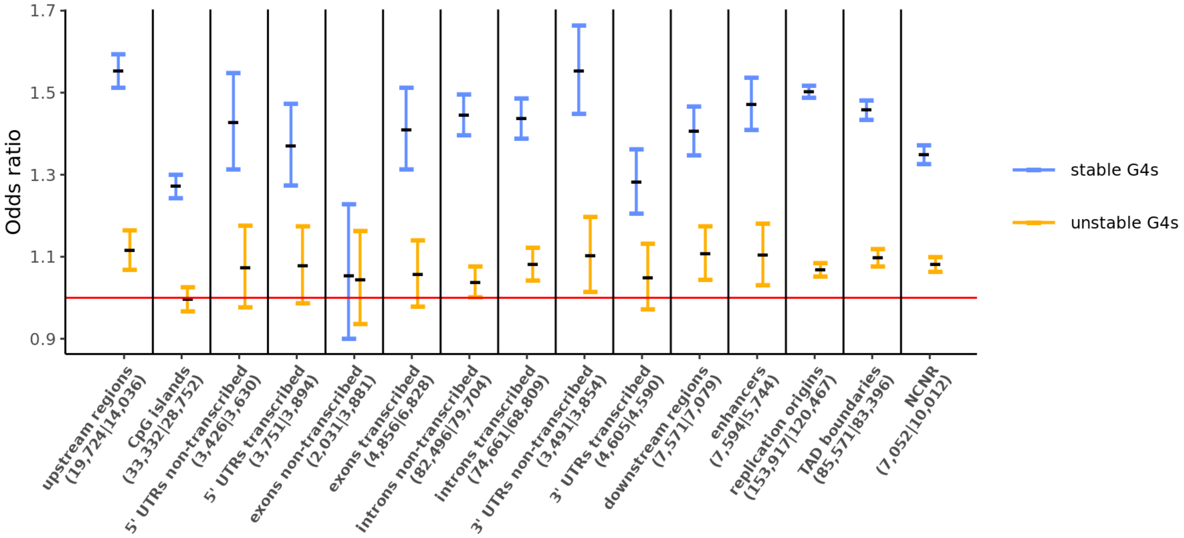
In [32]:

```
%%R
library(ggplot2)
library(grid)
library(gridExtra)
```

In [33]:

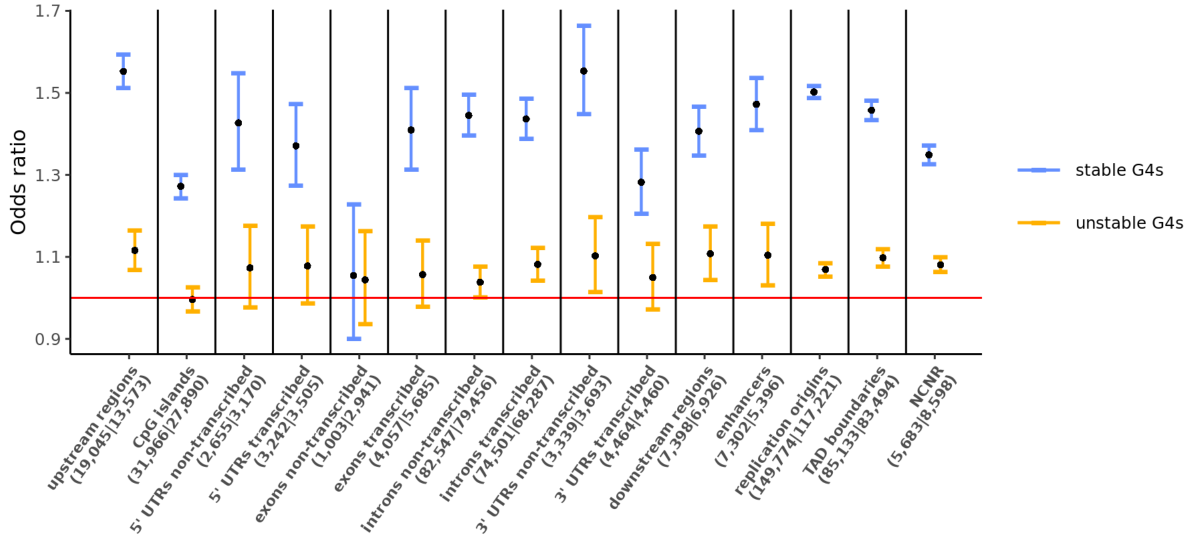
```
%%R -w 9 -h 10 --units in -r 200


xlegend = c("upstream regions\n(33,760)", "CpG islands\n(62,084)","5' UT
Rs non-transcribed\n(7,056)",
            "5' UTRs transcribed\n(7,645)","exons non-transcribed\n(5,91
2)",
            "exons transcribed\n(11,684)","introns non-transcribed\n(16
2,200)",
            "introns transcribed\n(143,470)","3' UTRs non-transcribed\n
(7,345)",
            "3' UTRs transcribed\n(9,195)","downstream regions\n(14,65
0)","enhancers\n(13,338)",
            "replication origins\n(274,384)","TAD boundaries\n(168,967)"
,"NCNR\n(17,064)")



dataf <- cbind.data.frame(xlegend,x,ORs,Low_ORs,High_ORs,Ls,Low_Ls,High_
Ls,Us,Low_Us,High_Us)
names(dataf) <- c("xlegend","x","ORs","Low_ORs","High_ORs","Ls","Low_Ls"
,"High_Ls",
                  "Us","Low_Us","High_Us")

cols <- c("all"="#DC267F",
          "high"="#648FFF",
          "low"="#FFB000")


g1 <- ggplot(dataf,) +
   geom_segment(aes(x=(x), xend=(x), y=Ls, yend=Us, colour="all"), size=
0.75) +

   geom_point(aes(x=(x), y=ORs),shape='-', size=7) +
   geom_point(aes(x=(x), y=Us, colour="all"),shape='-', size=10) +
   geom_point(aes(x=(x), y=Ls, colour="all"),shape='-', size=10) +


   geom_hline(yintercept=1, color="red") +
   geom_vline(xintercept=1.5, color="black") +
   geom_vline(xintercept=2.5, color="black") +
   geom_vline(xintercept=3.5, color="black") +
   geom_vline(xintercept=4.5, color="black") +
   geom_vline(xintercept=5.5, color="black") +
   geom_vline(xintercept=6.5, color="black") +
   geom_vline(xintercept=7.5, color="black") +
   geom_vline(xintercept=8.5, color="black") +
   geom_vline(xintercept=9.5, color="black") +
   geom_vline(xintercept=10.5, color="black") +
   geom_vline(xintercept=11.5, color="black") +
   geom_vline(xintercept=12.5, color="black") +
   geom_vline(xintercept=13.5, color="black") +
   geom_vline(xintercept=14.5, color="black") +


   theme_classic() + labs(subtitle="Classic Theme")+
   scale_x_continuous(limits = c(0.7,15.1),  breaks=c(1,2,3,4,5,6,7,8,9,
10,11,12,13,14,15),labels=xlegend) +
   theme(axis.text.x=element_text(angle = 55, hjust = 1,family="sans",fa
ce="bold",size=8)) +
   scale_colour_manual(name="",values=cols,labels="all G4s") +
   labs(title="", subtitle="", y="Odds ratio", x="", caption="",family=
"sans")


xlegend = c("upstream regions\n(19,724|14,036)", "CpG islands\n(33,332|2
8,752)","5' UTRs non-transcribed\n(3,426|3,630)",
            "5' UTRs transcribed\n(3,751|3,894)","exons non-transcribed
\n(2,031|3,881)",
            "exons transcribed\n(4,856|6,828)","introns non-transcribed
\n(82,496|79,704)",
            "introns transcribed\n(74,661|68,809)","3' UTRs non-transcri
bed\n(3,491|3,854)",
            "3' UTRs transcribed\n(4,605|4,590)","downstream regions\n
(7,571|7,079)","enhancers\n(7,594|5,744)",
            "replication origins\n(153,917|120,467)","TAD boundaries\n(8
5,571|83,396)","NCNR\n(7,052|10,012)")

dataf <- cbind.data.frame(xlegend,x,ORs,Low_ORs,High_ORs,Ls,Low_Ls,High_
Ls,Us,Low_Us,High_Us)
names(dataf) <- c("xlegend","x","ORs","Low_ORs","High_ORs","Ls","Low_Ls"
,"High_Ls",
                  "Us","Low_Us","High_Us")

cols <- c("all"="#DC267F",
          "high"="#648FFF",
          "low"="#FFB000")


g2 <- ggplot(dataf,) +
   geom_segment(aes(x=(x+0.1), xend=(x+0.1), y=Low_Ls, yend=Low_Us, colo
ur="low"), size=0.75) +
   geom_segment(aes(x=(x-0.1), xend=(x-0.1), y=High_Ls, yend=High_Us, co
lour="high"), size=0.75) +

   geom_point(aes(x=(x+0.1), y=Low_ORs),shape='-',size=7) +
   geom_point(aes(x=(x-0.1), y=High_ORs),shape='-',size=7) +
   geom_point(aes(x=(x+0.1), y=Low_Us, colour="low"),shape='-', size=10)
+
   geom_point(aes(x=(x+0.1), y=Low_Ls, colour="low"),shape='-', size=10)
+
   geom_point(aes(x=(x-0.1), y=High_Us, colour="high"),shape='-', size=1
0) +
   geom_point(aes(x=(x-0.1), y=High_Ls, colour="high"),shape='-', size=1
0) +

   geom_hline(yintercept=1, color="red") +
   geom_vline(xintercept=1.5, color="black") +
   geom_vline(xintercept=2.5, color="black") +
   geom_vline(xintercept=3.5, color="black") +
   geom_vline(xintercept=4.5, color="black") +
   geom_vline(xintercept=5.5, color="black") +
   geom_vline(xintercept=6.5, color="black") +
   geom_vline(xintercept=7.5, color="black") +
   geom_vline(xintercept=8.5, color="black") +
   geom_vline(xintercept=9.5, color="black") +
   geom_vline(xintercept=10.5, color="black") +
   geom_vline(xintercept=11.5, color="black") +
   geom_vline(xintercept=12.5, color="black") +
   geom_vline(xintercept=13.5, color="black") +
   geom_vline(xintercept=14.5, color="black") +

   theme_classic() + labs(subtitle="Classic Theme")+
   scale_x_continuous(limits = c(0.7,15.1),  breaks=c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15),labels=xlegend) +
   theme(axis.text.x=element_text(angle = 55, hjust = 1, face="bold",family="sans",size=8)) +
   scale_colour_manual(name="",values=cols,labels=c('stable G4s','unstable G4s')) +
   labs(title="", subtitle="", y="Odds ratio", x="", caption="",family="sans")

grid.arrange(g1,g2,nrow=2)
G <- arrangeGrob(g1,g2,nrow=2)
ggsave(file='HKA.pdf',G, width=9, height=10, dpi=300)
```


Odds ratio
1.4
1.3
1.2
1.1
1.0
upstream regions (33,760)
CpG islands (62,084)
5' UTRs non-transcribed (7,056)
5' UTRs transcribed (7,645)
exons non-transcribed (5,912)
exons transcribed (11,684)
introns non-transcribed (162,200)
introns transcribed (143,470)
3' UTRs non-transcribed (7,345)
3' UTRs transcribed (9,195)
downstream regions (14,650)
enhancers (13,338)
replication origins (274,384)
TAD boundaries (168,967)
NCNR (17,064)
all G4s


Odds ratio
1.7
1.5
1.3
1.1
0.9
upstream regions (19,724|14,036)
CpG islands (33,332|28,752)
5' UTRs non-transcribed (3,426|3,630)
5' UTRs transcribed (3,751|3,894)
exons non-transcribed (2,031|3,881)
exons transcribed (4,856|6,828)
introns non-transcribed (82,496|79,704)
introns transcribed (74,661|68,809)
3' UTRs non-transcribed (3,491|3,854)
3' UTRs transcribed (4,605|4,590)
downstream regions (7,571|7,079)
enhancers (7,594|5,744)
replication origins (153,917|120,467)
TAD boundaries (85,571|83,396)
NCNR (7,052|10,012)
stable G4s
unstable G4s

In [799]:

```
%%R -w 9 -h 5 --units in -r 200


xlegend = c("upstream regions\n(19,045|13,573)", "CpG islands\n(31,966|27,890)","5' UTRs non-transcribed\n(2,655|3,170)",
            "5' UTRs transcribed\n(3,242|3,505)","exons non-transcribed\n(1,003|2,941)",
            "exons transcribed\n(4,057|5,685)","introns non-transcribed\n(82,547|79,456)",
            "introns transcribed\n(74,501|68,287)","3' UTRs non-transcribed\n(3,339|3,693)",
            "3' UTRs transcribed\n(4,464|4,460)","downstream regions\n(7,398|6,926)","enhancers\n(7,302|5,396)",
            "replication origins\n(149,774|117,221)","TAD boundaries\n(85,133|83,494)","NCNR\n(5,683|8,598)")

dataf <- cbind.data.frame(xlegend,x,ORs,Low_ORs,High_ORs,Ls,Low_Ls,High_Ls,Us,Low_Us,High_Us)
names(dataf) <- c("xlegend","x","ORs","Low_ORs","High_ORs","Ls","Low_Ls","High_Ls",
                  "Us","Low_Us","High_Us")

cols <- c("all"="#DC267F",
          "high"="#648FFF",
          "low"="#FFB000")



g <- ggplot(dataf,) +
   geom_segment(aes(x=(x+0.1), xend=(x+0.1), y=Low_Ls, yend=Low_Us, colour="low"), size=0.75) +
   geom_segment(aes(x=(x-0.1), xend=(x-0.1), y=High_Ls, yend=High_Us, colour="high"), size=0.75) +

   geom_point(aes(x=(x+0.1), y=Low_ORs),shape=16) +
   geom_point(aes(x=(x-0.1), y=High_ORs),shape=16) +
   geom_point(aes(x=(x+0.1), y=Low_Us, colour="low"),shape='-', size=10) +
   geom_point(aes(x=(x+0.1), y=Low_Ls, colour="low"),shape='-', size=10) +
   geom_point(aes(x=(x-0.1), y=High_Us, colour="high"),shape='-', size=10) +
   geom_point(aes(x=(x-0.1), y=High_Ls, colour="high"),shape='-', size=10) +

   geom_hline(yintercept=1, color="red") +
   geom_vline(xintercept=1.5, color="black") +
   geom_vline(xintercept=2.5, color="black") +
   geom_vline(xintercept=3.5, color="black") +
   geom_vline(xintercept=4.5, color="black") +
   geom_vline(xintercept=5.5, color="black") +
   geom_vline(xintercept=6.5, color="black") +
   geom_vline(xintercept=7.5, color="black") +
   geom_vline(xintercept=8.5, color="black") +
   geom_vline(xintercept=9.5, color="black") +
   geom_vline(xintercept=10.5, color="black") +
   geom_vline(xintercept=11.5, color="black") +
   geom_vline(xintercept=12.5, color="black") +
   geom_vline(xintercept=13.5, color="black") +
   geom_vline(xintercept=14.5, color="black") +

   theme_classic() + labs(subtitle="Classic Theme")+
   scale_x_continuous(limits = c(0.7,15.1),  breaks=c(1,2,3,4,5,6,7,8,9,
10,11,12,13,14,15),labels=xlegend) +
   theme(axis.text.x=element_text(angle = 55, hjust = 1, face="bold",fam
ily="sans",size=8)) +
   scale_colour_manual(name="",values=cols,labels=c('stable G4s','unstab
le G4s')) +
   labs(title="", subtitle="", y="Odds ratio", x="", caption="",family=
"sans")

grid.arrange(g)
G <- arrangeGrob(g)
ggsave(file='HKA_highlow.pdf',G, width=9, height=5, dpi=300)
```



In [629]:

```
%%R

NCNR_fisher_highvlow <- fisher.test(cbind(c(29040, 179366),c(30118, 232166)))
print(paste('NCNR high v low',NCNR_fisher_highvlow$estimate,NCNR_fisher_highvlow$p.value))
print(NCNR_fisher_highvlow)

Upstream_fisher_highvlow <- fisher.test(cbind(c(6948, 36771),c(2448, 18026)))
print(paste('Up high v low',Upstream_fisher_highvlow$estimate,Upstream_fisher_highvlow$p.value))

FUTR_fisher_sense_highvlow <- fisher.test(cbind(c(692, 3698),c(528, 3752)))
print(paste('5UTR sense high v low',FUTR_fisher_sense_highvlow$estimate,FUTR_fisher_sense_highvlow$p.value))

FUTR_fisher_antisense_highvlow <- fisher.test(cbind(c(898, 4996),c(600, 4245)))
print(paste('5UTR antisense high v low',FUTR_fisher_antisense_highvlow$estimate,FUTR_fisher_antisense_highvlow$p.value))

Exon_fisher_sense_highvlow <- fisher.test(cbind(c(195, 1151),c(393, 2343)))
print(paste('Exon sense high v low',Exon_fisher_sense_highvlow$estimate,Exon_fisher_sense_highvlow$p.value))

Exon_fisher_antisense_highvlow <- fisher.test(cbind(c(968, 4274),c(801, 4718)))
print(paste('Exon antisense high v low',Exon_fisher_antisense_highvlow$estimate,Exon_fisher_antisense_highvlow$p.value))

Intron_fisher_sense_highvlow <- fisher.test(cbind(c(28521, 163609),c(14309, 114249)))
print(paste('Intron sense high v low',Intron_fisher_sense_highvlow$estimate,Intron_fisher_sense_highvlow$p.value))

Intron_fisher_antisense_highvlow <- fisher.test(cbind(c(28147, 162411),c(13495, 103428)))
print(paste('Intron antisense high v low',Intron_fisher_antisense_highvlow$estimate,Intron_fisher_antisense_highvlow$p.value))

TUTR_fisher_sense_highvlow <- fisher.test(cbind(c(973, 4999),c(649, 4698)))
print(paste('3UTR sense high v low',TUTR_fisher_sense_highvlow$estimate,TUTR_fisher_sense_highvlow$p.value))

TUTR_fisher_antisense_highvlow <- fisher.test(cbind(c(1228, 7645),c(761, 5787)))
print(paste('3UTR antisense high v low',TUTR_fisher_antisense_highvlow$estimate,TUTR_fisher_antisense_highvlow$p.value))

Downstream_fisher_highvlow <- fisher.test(cbind(c(2568, 15724),c(1271, 9880)))
print(paste('Down high v low',Downstream_fisher_highvlow$estimate,Downst
ream_fisher_highvlow$p.value))

Oris_fisher_highvlow <- fisher.test(cbind(c(48685, 267964),c(19152, 1481
05)))
print(paste('Oris high v low',Oris_fisher_highvlow$estimate,Oris_fisher_
highvlow$p.value))

Enhancers_fisher_highvlow <- fisher.test(cbind(c(2549, 13572),c(977, 693
7)))
print(paste('Enhancers high v low', Enhancers_fisher_highvlow$estimate,E
nhancers_fisher_highvlow$p.value))

TADB_fisher_highvlow <- fisher.test(cbind(c(29642, 170462),c(15607, 1191
63)))
print(paste('TADB high v low', TADB_fisher_highvlow$estimate,TADB_fisher
_highvlow$p.value))

CpGI_fisher_highvlow <- fisher.test(cbind(c(10120, 56369),c(5230, 37197
)))
print(paste('CpGI high v low', CpGI_fisher_highvlow$estimate,CpGI_fisher
_highvlow$p.value))
```

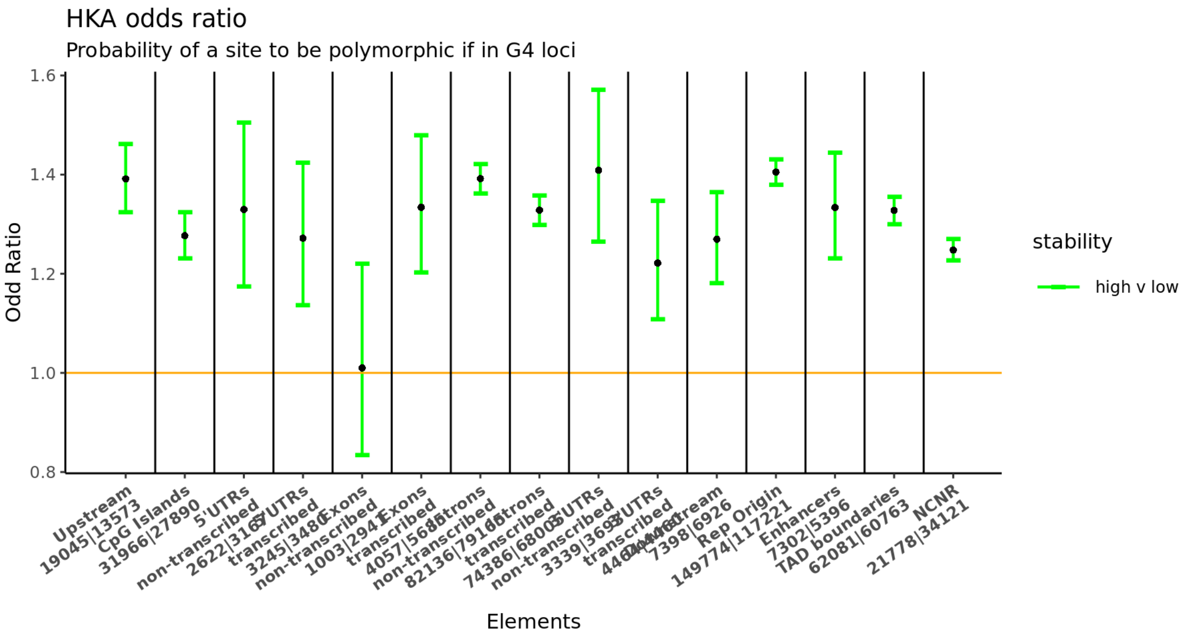
```
[1] "NCNR high v low 1.24803212199888 2.03096795917292e-139"

        Fisher's Exact Test for Count Data

data:  cbind(c(29040, 179366), c(30118, 232166))
p-value < 2.2e-16
alternative hypothesis: true odds ratio is not equal to 1
95 percent confidence interval:
 1.226629 1.269821
sample estimates:
odds ratio
  1.248032

[1] "Up high v low 1.391361316676 1.37581691424796e-40"
[1] "5UTR sense high v low 1.3296931671024 4.74793622558623e-06"
[1] "5UTR antisense high v low 1.27165625421897 2.08642841926392e-05"
[1] "Exon sense high v low 1.01004161018301 0.924490759669745"
[1] "Exon antisense high v low 1.33398583946064 3.37929520593627e-08"
[1] "Intron sense high v low 1.39187230668259 2.13359010469109e-205"
[1] "Intron antisense high v low 1.32825370372033 6.67036600042132e-14
5"
[1] "3UTR sense high v low 1.40890723277994 3.05020142754629e-10"
[1] "3UTR antisense high v low 1.22147251744749 4.89626113825615e-05"
[1] "Down high v low 1.26952019645597 5.04731362195521e-11"
[1] "Oris high v low 1.40499124626619 1.59729058702294e-314"
[1] "Enhancers high v low 1.33351484824448 5.85885135919754e-13"
[1] "TADB high v low 1.32770284888875 4.89594437883419e-161"
[1] "CpGI high v low 1.27686510239527 2.19482568093664e-41"
```

In [630]:

```
%%R
#https://stackoverflow.com/questions/14069629/how-can-i-plot-data-with-c
onfidence-intervals

x <- c(1,2,3,4,5,6,7,8,9,10,11,12,13,14,15)

#print(length(x))

ORs <- c(Upstream_fisher_highvlow$estimate,
         CpGI_fisher_highvlow$estimate,
         FUTR_fisher_sense_highvlow$estimate,
         FUTR_fisher_antisense_highvlow$estimate,
         Exon_fisher_sense_highvlow$estimate,
         Exon_fisher_antisense_highvlow$estimate,
         Intron_fisher_sense_highvlow$estimate,
         Intron_fisher_antisense_highvlow$estimate,
         TUTR_fisher_sense_highvlow$estimate,
         TUTR_fisher_antisense_highvlow$estimate,
         Downstream_fisher_highvlow$estimate,
         Oris_fisher_highvlow$estimate,
         Enhancers_fisher_highvlow$estimate,
         TADB_fisher_highvlow$estimate,
         NCNR_fisher_highvlow$estimate)



Ls <- c(Upstream_fisher_highvlow$conf.int[1],
        CpGI_fisher_highvlow$conf.int[1],
        FUTR_fisher_sense_highvlow$conf.int[1],
        FUTR_fisher_antisense_highvlow$conf.int[1],
        Exon_fisher_sense_highvlow$conf.int[1],
        Exon_fisher_antisense_highvlow$conf.int[1],
        Intron_fisher_sense_highvlow$conf.int[1],
        Intron_fisher_antisense_highvlow$conf.int[1],
        TUTR_fisher_sense_highvlow$conf.int[1],
        TUTR_fisher_antisense_highvlow$conf.int[1],
        Downstream_fisher_highvlow$conf.int[1],
        Oris_fisher_highvlow$conf.int[1],
        Enhancers_fisher_highvlow$conf.int[1],
        TADB_fisher_highvlow$conf.int[1],
        NCNR_fisher_highvlow$conf.int[1])




Us <- c(Upstream_fisher_highvlow$conf.int[2],
        CpGI_fisher_highvlow$conf.int[2],
        FUTR_fisher_sense_highvlow$conf.int[2],
        FUTR_fisher_antisense_highvlow$conf.int[2],
        Exon_fisher_sense_highvlow$conf.int[2],
        Exon_fisher_antisense_highvlow$conf.int[2],
        Intron_fisher_sense_highvlow$conf.int[2],
        Intron_fisher_antisense_highvlow$conf.int[2],
        TUTR_fisher_sense_highvlow$conf.int[2],
        TUTR_fisher_antisense_highvlow$conf.int[2],
        Downstream_fisher_highvlow$conf.int[2],
        Oris_fisher_highvlow$conf.int[2],
        Enhancers_fisher_highvlow$conf.int[2],
        TADB_fisher_highvlow$conf.int[2],
        NCNR_fisher_highvlow$conf.int[2])
```

In [631]:

```
%%R -w 9 -h 5 --units in -r 200

xlegend = c("Upstream\n19045|13573", "CpG Islands\n31966|27890","5'UTRs
\nnon-transcribed\n2622|3167",
            "5'UTRs\ntranscribed\n3245|3480","Exons\nnon-transcribed\n10
03|2941",
            "Exons\ntranscribed\n4057|5685","Introns\nnon-transcribed\n8
2136|79165",
            "Introns\ntranscribed\n74386|68005","3'UTRs\nnon-transcribed
\n3339|3693",
            "3'UTRs\ntranscribed\n4464|4460","Downstream\n7398|6926","Re
p Origin\n149774|117221",
            "Enhancers\n7302|5396","TAD boundaries\n62081|60763","NCNR\n
21778|34121")


dataf <- cbind.data.frame(xlegend,x,ORs,Ls,Us)
names(dataf) <- c("xlegend","x","ORs","Ls","Us")

cols <- c("all"="gold",
          "high"="red",
          "low"="blue",
          "high v low"="green")


ggplot(dataf,) +
   geom_segment(aes(x=(x), xend=(x), y=Ls, yend=Us, colour="high v low"
), size=0.75) +

   geom_point(aes(x=(x), y=ORs),shape=16) +
   geom_point(aes(x=(x), y=Us, colour="high v low"),shape='-', size=10)
+
   geom_point(aes(x=(x), y=Ls, colour="high v low"),shape='-', size=10)
+

   geom_hline(yintercept=1, color="orange") +
   geom_vline(xintercept=1.5, color="black") +
   geom_vline(xintercept=2.5, color="black") +
   geom_vline(xintercept=3.5, color="black") +
   geom_vline(xintercept=4.5, color="black") +
   geom_vline(xintercept=5.5, color="black") +
   geom_vline(xintercept=6.5, color="black") +
   geom_vline(xintercept=7.5, color="black") +
   geom_vline(xintercept=8.5, color="black") +
   geom_vline(xintercept=9.5, color="black") +
   geom_vline(xintercept=10.5, color="black") +
   geom_vline(xintercept=11.5, color="black") +
   geom_vline(xintercept=12.5, color="black") +
   geom_vline(xintercept=13.5, color="black") +
   geom_vline(xintercept=14.5, color="black") +


   theme_classic() + labs(subtitle="Classic Theme")+
   scale_x_continuous(limits = c(0.7,15.1),  breaks=c(1,2,3,4,5,6,7,8,9,
10,11,12,13,14,15),labels=xlegend) +
   theme(axis.text.x=element_text(face="bold",angle = 35, hjust = 1)) +
   scale_colour_manual(name="stability",values=cols) +
   labs(title="HKA odds ratio", subtitle="Probability of a site to be polymorphic if in G4 loci", y="Odd Ratio", x="Elements", caption="")
```



Part IV. Site Frequency Spectrum

NCNR

In [632]:

```
NCNR_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/NCNR.SFS.high.bed.test')
NCNR_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/NCNR.SFS.low.bed.test')
NCNR_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/NCNR.SFS.control.shuf')

NCNR_high_infile.seek(0)
NCNR_low_infile.seek(0)
NCNR_ctrl_infile.seek(0)

def list_MAFs(infile):

    already_parsed = {}
    MAFs = []
    for line in infile:
        array = line.strip().split('\t')
        key = array[0]+'|'+array[1]+'|'+array[2]
        #print(key)
        #break
        SFS = array[3]
        MAF = SFS.split('|')[4]


        if MAF != 'NA':
            if key not in already_parsed:

                if float(MAF) < 1: #remove fixed
                    MAF = float(MAF)

                    if MAF > 0.5:
                        if MAF >1:
                            print('ISSUE')
                            break
                            MAF = 1
                        MAF = 1-MAF

                    if float(MAF) > 0.001792115*2: #remove single- and doubletons
                        MAFs.append(MAF)

        already_parsed[key] = 0

    return(MAFs)

MAFs_high = list_MAFs(NCNR_high_infile)
MAFs_low = list_MAFs(NCNR_low_infile)
MAFs_ctrl = list_MAFs(NCNR_ctrl_infile)

min(MAFs_high)
```

Out[632]:

```
0.00537634408602
```

In [633]:

```
%%R -i MAFs_ctrl,MAFs_high,MAFs_low

MAFs_high <- as.numeric(as.character(MAFs_high))
MAFs_low <- as.numeric(as.character(MAFs_low))
MAFs_ctrl <- as.numeric(as.character(MAFs_ctrl))
MAFs <- c(MAFs_high,MAFs_low)

print(min(MAFs_high))
print(min(MAFs_low))
print(min(MAFs_ctrl))
```

```
[1] 0.005376344
[1] 0.005376344
[1] 0.005376344
```

In [634]:

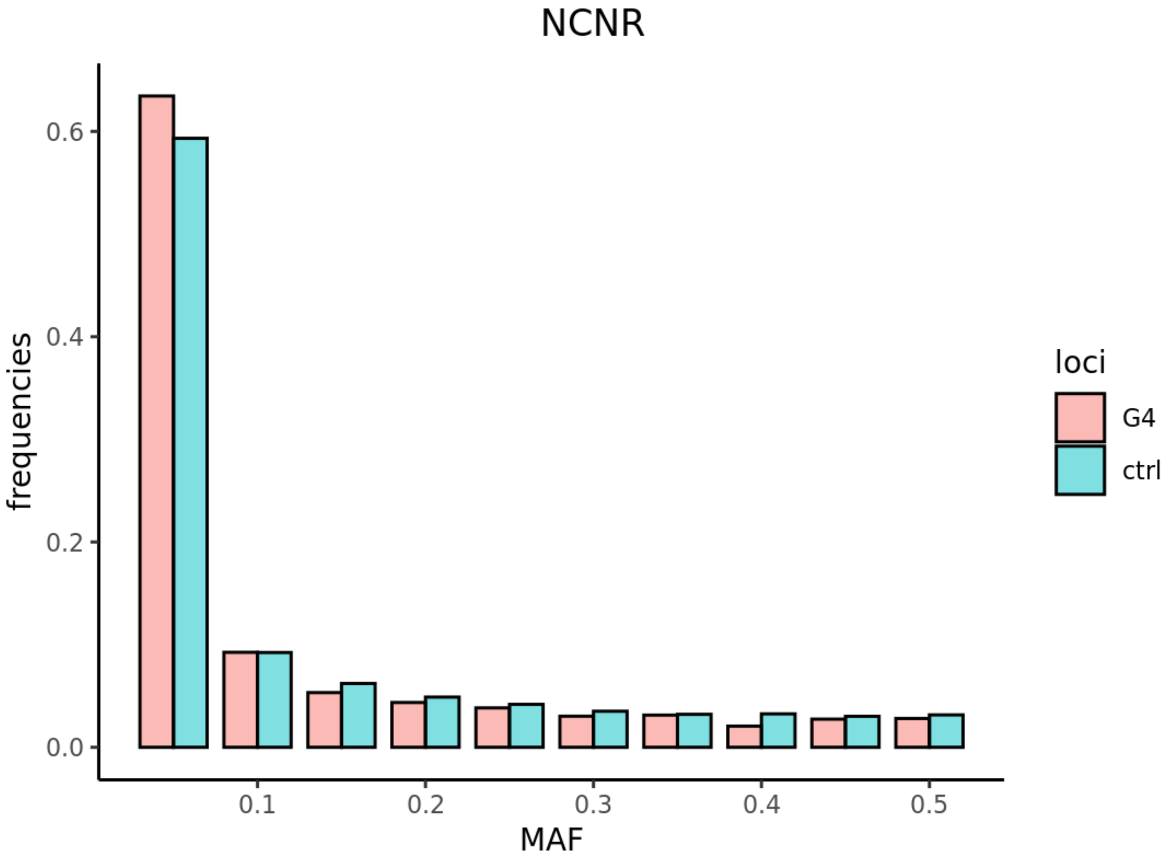
```
%%R

KS <- ks.test(MAFs_high,MAFs_ctrl)
print(KS)

KS <- ks.test(MAFs_low,MAFs_ctrl)
print(KS)

KS <- ks.test(MAFs,MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  MAFs_high and MAFs_ctrl
D = 0.069026, p-value = 4.12e-10
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  MAFs_low and MAFs_ctrl
D = 0.030042, p-value = 0.05207
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  MAFs and MAFs_ctrl
D = 0.0464, p-value = 3.035e-08
alternative hypothesis: two-sided
```

In [765]:

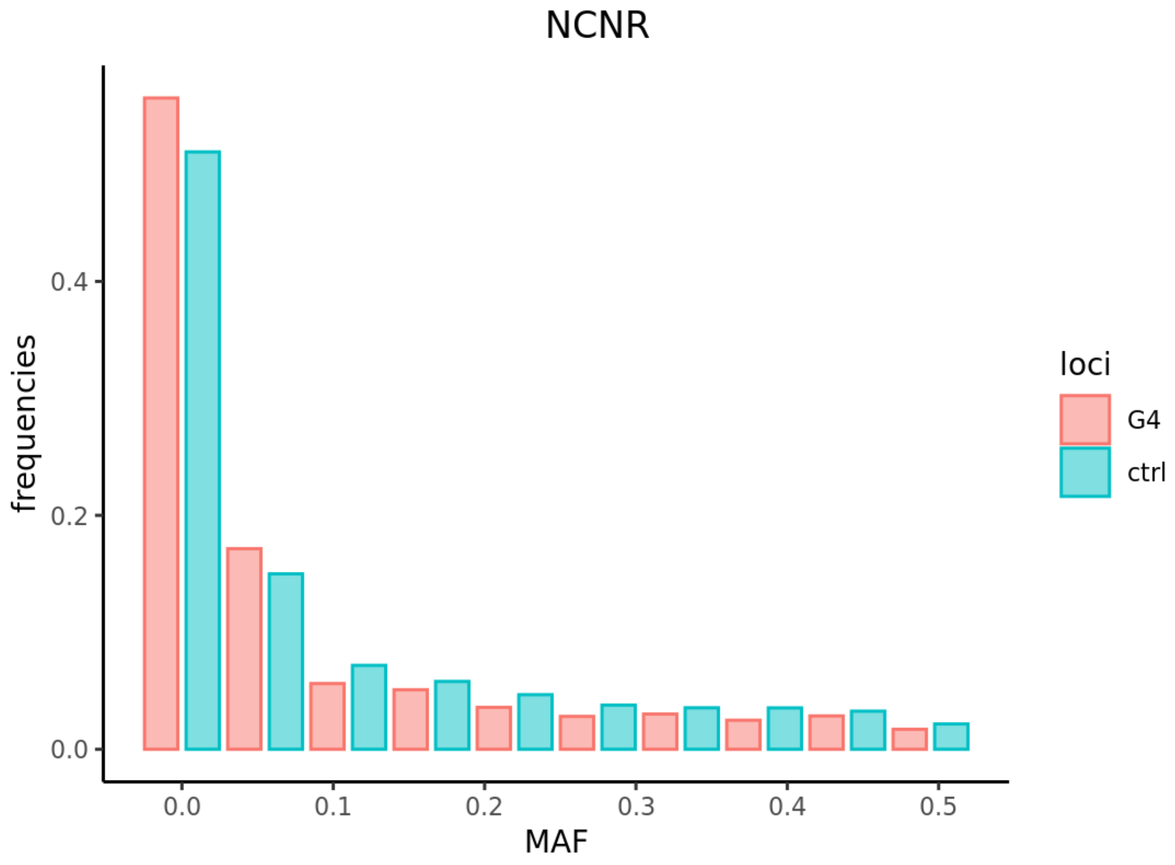
```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)


hist_high <- hist(MAFs, plot=FALSE, breaks = 10)$density / sum(hist(MAFs
, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist
(MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',leng
th(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="ide
ntity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("NCNR",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.63450998   G4
2 0.10 0.09252357   G4
3 0.15 0.05327779   G4
4 0.20 0.04363078   G4
5 0.25 0.03836878   G4
6 0.30 0.03025652   G4
```



In [749]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)

toplot <- cbind.data.frame(c(MAFs_high,MAFs_ctrl),c(rep('G4',length(MAFs
_high)),rep('ctrl',length(MAFs_ctrl))))
colnames(toplot) <- c('MAF', 'loci')



p1 <- ggplot(data=toplot, aes(x=MAF, fill=loci, colour=loci)) +
    geom_histogram(aes(y=2*(..density..)/sum(..density..)),position=posi
tion_dodge2(preserve = "single", padding = 0.2, width = 0.5), bins = 10,
alpha = .5)+
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("NCNR",gp=gpar(fontsize=12,font=1)))
```



In [636]:

```
UP_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Upstream1k.SFS.high.test')
UP_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Upstream1k.SFS.low.test')
UP_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Upstream1k.SFS.control')

UP_MAFs_high = list_MAFs(UP_high_infile)
UP_MAFs_low = list_MAFs(UP_low_infile)
UP_MAFs_ctrl = list_MAFs(UP_ctrl_infile)
```

In [637]:

```
%%R -i UP_MAFs_ctrl,UP_MAFs_high,UP_MAFs_low

UP_MAFs_high <- as.numeric(as.character(UP_MAFs_high))
UP_MAFs_low <- as.numeric(as.character(UP_MAFs_low))
UP_MAFs_ctrl <- as.numeric(as.character(UP_MAFs_ctrl))
UP_MAFs <- c(UP_MAFs_high,UP_MAFs_low)
```

In [639]:

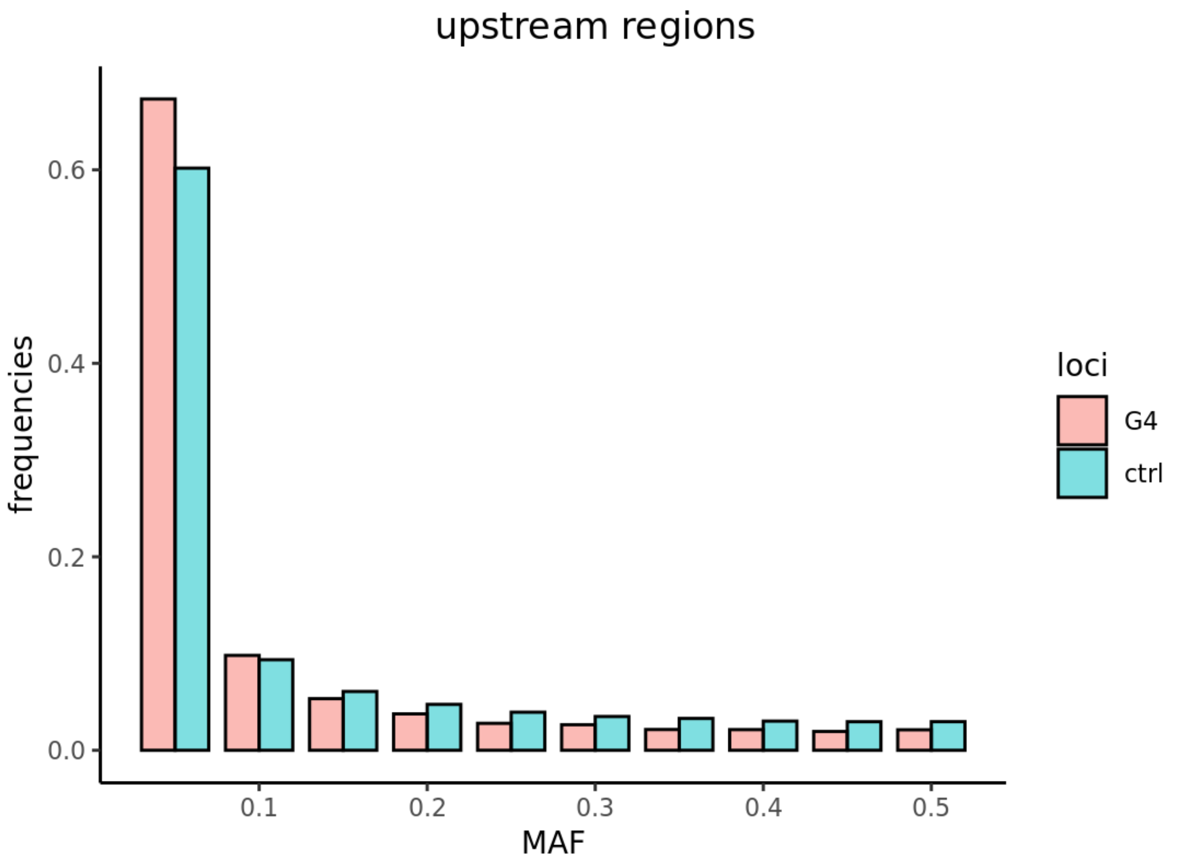
```
%%R

KS <- ks.test(UP_MAFs_high,UP_MAFs_ctrl)
print(KS)

KS <- ks.test(UP_MAFs_low,UP_MAFs_ctrl)
print(KS)

KS <- ks.test(UP_MAFs,UP_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  UP_MAFs_high and UP_MAFs_ctrl
D = 0.087849, p-value < 2.2e-16
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  UP_MAFs_low and UP_MAFs_ctrl
D = 0.044375, p-value = 4.421e-07
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  UP_MAFs and UP_MAFs_ctrl
D = 0.077158, p-value < 2.2e-16
alternative hypothesis: two-sided
```

In [767]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)



hist_high <- hist(UP_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(U
P_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(UP_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(h
ist(UP_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',leng
th(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="ide
ntity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("upstream regions",gp=gpar(fontsize=12,font
=1)))
```

```
     x        MAF loci
1 0.05 0.67322600   G4
2 0.10 0.09809183   G4
3 0.15 0.05336911   G4
4 0.20 0.03762671   G4
5 0.25 0.02784735   G4
6 0.30 0.02641622   G4
```



In [641]:
```
FUTR_sense_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/FUTR.SFS.high.sens.test')
FUTR_sense_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/FUTR.SFS.low.sens.test')
FUTR_sense_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/FUTR.SFS.control')

FUTR_sense_MAFs_high = list_MAFs(FUTR_sense_high_infile)
FUTR_sense_MAFs_low = list_MAFs(FUTR_sense_low_infile)
FUTR_sense_MAFs_ctrl = list_MAFs(FUTR_sense_ctrl_infile)
```

In [642]:

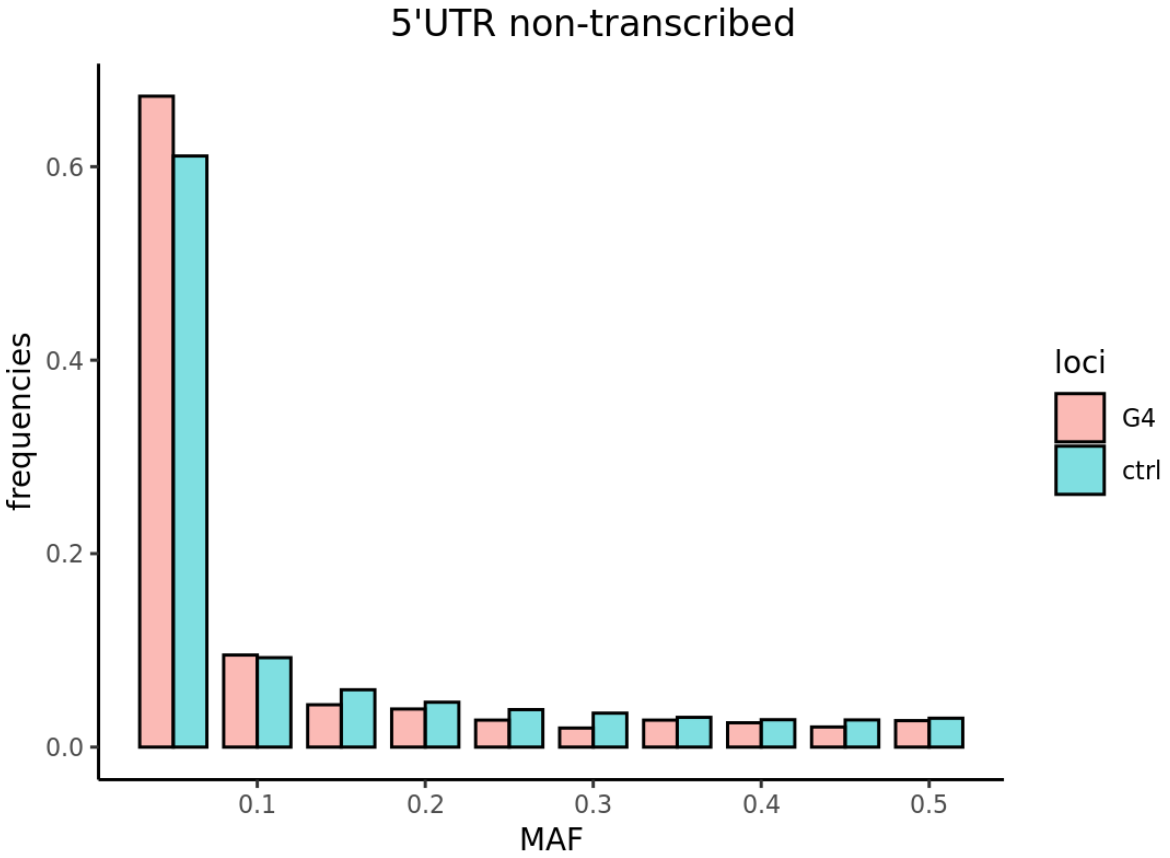
```
%%R -i FUTR_sense_MAFs_ctrl,FUTR_sense_MAFs_high,FUTR_sense_MAFs_low

FUTR_sense_MAFs_high <- as.numeric(as.character(FUTR_sense_MAFs_high))
FUTR_sense_MAFs_low <- as.numeric(as.character(FUTR_sense_MAFs_low))
FUTR_sense_MAFs_ctrl <- as.numeric(as.character(FUTR_sense_MAFs_ctrl))
FUTR_sense_MAFs <- c(FUTR_sense_MAFs_high,FUTR_sense_MAFs_low)

KS <- ks.test(FUTR_sense_MAFs_high,FUTR_sense_MAFs_ctrl)
print(KS)

KS <- ks.test(FUTR_sense_MAFs_low,FUTR_sense_MAFs_ctrl)
print(KS)

KS <- ks.test(FUTR_sense_MAFs,FUTR_sense_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  FUTR_sense_MAFs_high and FUTR_sense_MAFs_ctrl
D = 0.080046, p-value = 3.664e-06
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  FUTR_sense_MAFs_low and FUTR_sense_MAFs_ctrl
D = 0.063373, p-value = 0.003958
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  FUTR_sense_MAFs and FUTR_sense_MAFs_ctrl
D = 0.068319, p-value = 1.159e-07
alternative hypothesis: two-sided
```

In [769]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)


hist_high <- hist(FUTR_sense_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(FUTR_sense_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(FUTR_sense_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(FUTR_sense_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("5'UTR non-transcribed",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.67286652   G4
2 0.10 0.09518600   G4
3 0.15 0.04376368   G4
4 0.20 0.03938731   G4
5 0.25 0.02789934   G4
6 0.30 0.01969365   G4
```



In [644]:

```
FUTR_antisense_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/FUTR.SFS.high.antisens.test')
FUTR_antisense_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/FUTR.SFS.low.antisens.test')
FUTR_antisense_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/FUTR.SFS.control')

FUTR_antisense_MAFs_high = list_MAFs(FUTR_antisense_high_infile)
FUTR_antisense_MAFs_low = list_MAFs(FUTR_antisense_low_infile)
FUTR_antisense_MAFs_ctrl = list_MAFs(FUTR_antisense_ctrl_infile)
```

In [645]:

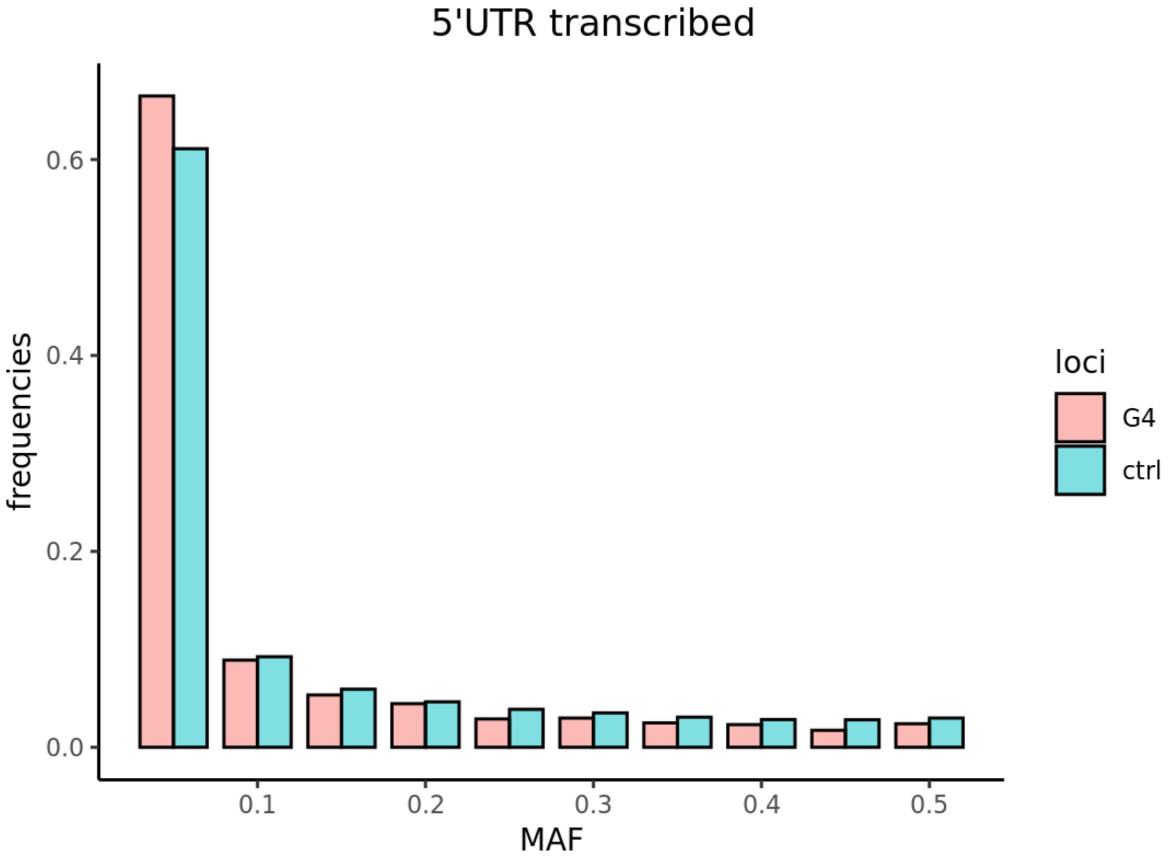
```
%%R -i FUTR_antisense_MAFs_ctrl,FUTR_antisense_MAFs_high,FUTR_antisense_MAFs_low

FUTR_antisense_MAFs_high <- as.numeric(as.character(FUTR_antisense_MAFs_high))
FUTR_antisense_MAFs_low <- as.numeric(as.character(FUTR_antisense_MAFs_low))
FUTR_antisense_MAFs_ctrl <- as.numeric(as.character(FUTR_antisense_MAFs_ctrl))
FUTR_antisense_MAFs <- c(FUTR_antisense_MAFs_high,FUTR_antisense_MAFs_low)

KS <- ks.test(FUTR_antisense_MAFs_high,FUTR_antisense_MAFs_ctrl)
print(KS)

KS <- ks.test(FUTR_antisense_MAFs_low,FUTR_antisense_MAFs_ctrl)
print(KS)

KS <- ks.test(FUTR_antisense_MAFs,FUTR_antisense_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  FUTR_antisense_MAFs_high and FUTR_antisense_MAFs_ctrl
D = 0.094906, p-value = 1.295e-10
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  FUTR_antisense_MAFs_low and FUTR_antisense_MAFs_ctrl
D = 0.014183, p-value = 0.993
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  FUTR_antisense_MAFs and FUTR_antisense_MAFs_ctrl
D = 0.060648, p-value = 2.129e-07
alternative hypothesis: two-sided
```

In [770]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)



hist_high <- hist(FUTR_antisense_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(FUTR_antisense_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(FUTR_antisense_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(FUTR_antisense_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("5'UTR transcribed",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.66488652   G4
2 0.10 0.08900757   G4
3 0.15 0.05340454   G4
4 0.20 0.04450378   G4
5 0.25 0.02892746   G4
6 0.30 0.02981753   G4
```



In [647]:

```
exon_sense_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Exons.SFS.high.sens.test')
exon_sense_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Exons.SFS.low.sens.test')
exon_sense_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Exons.SFS.control')

exon_sense_MAFs_high = list_MAFs(exon_sense_high_infile)
exon_sense_MAFs_low = list_MAFs(exon_sense_low_infile)
exon_sense_MAFs_ctrl = list_MAFs(exon_sense_ctrl_infile)
```

In [648]:

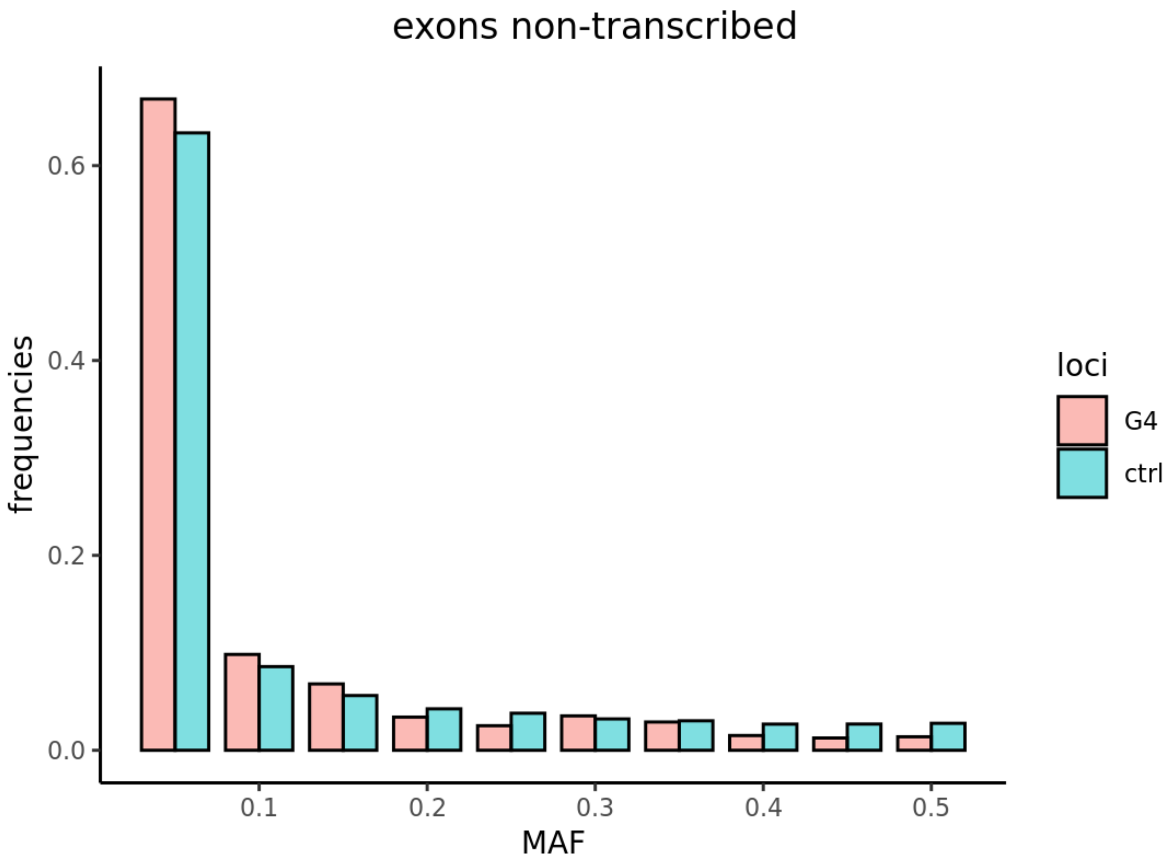
```
%%R -i exon_sense_MAFs_ctrl,exon_sense_MAFs_high,exon_sense_MAFs_low

exon_sense_MAFs_high <- as.numeric(as.character(exon_sense_MAFs_high))
exon_sense_MAFs_low <- as.numeric(as.character(exon_sense_MAFs_low))
exon_sense_MAFs_ctrl <- as.numeric(as.character(exon_sense_MAFs_ctrl))
exon_sense_MAFs <- c(exon_sense_MAFs_high,exon_sense_MAFs_low)

KS <- ks.test(exon_sense_MAFs_high,exon_sense_MAFs_ctrl)
print(KS)

KS <- ks.test(exon_sense_MAFs_low,exon_sense_MAFs_ctrl)
print(KS)

KS <- ks.test(exon_sense_MAFs,exon_sense_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  exon_sense_MAFs_high and exon_sense_MAFs_ctrl
D = 0.053537, p-value = 0.4323
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  exon_sense_MAFs_low and exon_sense_MAFs_ctrl
D = 0.072533, p-value = 0.008014
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  exon_sense_MAFs and exon_sense_MAFs_ctrl
D = 0.059776, p-value = 0.00719
alternative hypothesis: two-sided
```

In [772]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)



hist_high <- hist(exon_sense_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(exon_sense_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(exon_sense_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(exon_sense_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("exons non-transcribed",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.66834805   G4
2 0.10 0.09836066   G4
3 0.15 0.06809584   G4
4 0.20 0.03404792   G4
5 0.25 0.02522068   G4
6 0.30 0.03530895   G4
```



In [650]:
```
exon_antisense_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Exons.SFS.high.antisens.test')
exon_antisense_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Exons.SFS.low.antisens.test')
exon_antisense_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Exons.SFS.control')

exon_antisense_MAFs_high = list_MAFs(exon_antisense_high_infile)
exon_antisense_MAFs_low = list_MAFs(exon_antisense_low_infile)
exon_antisense_MAFs_ctrl = list_MAFs(exon_antisense_ctrl_infile)
```

In [651]:

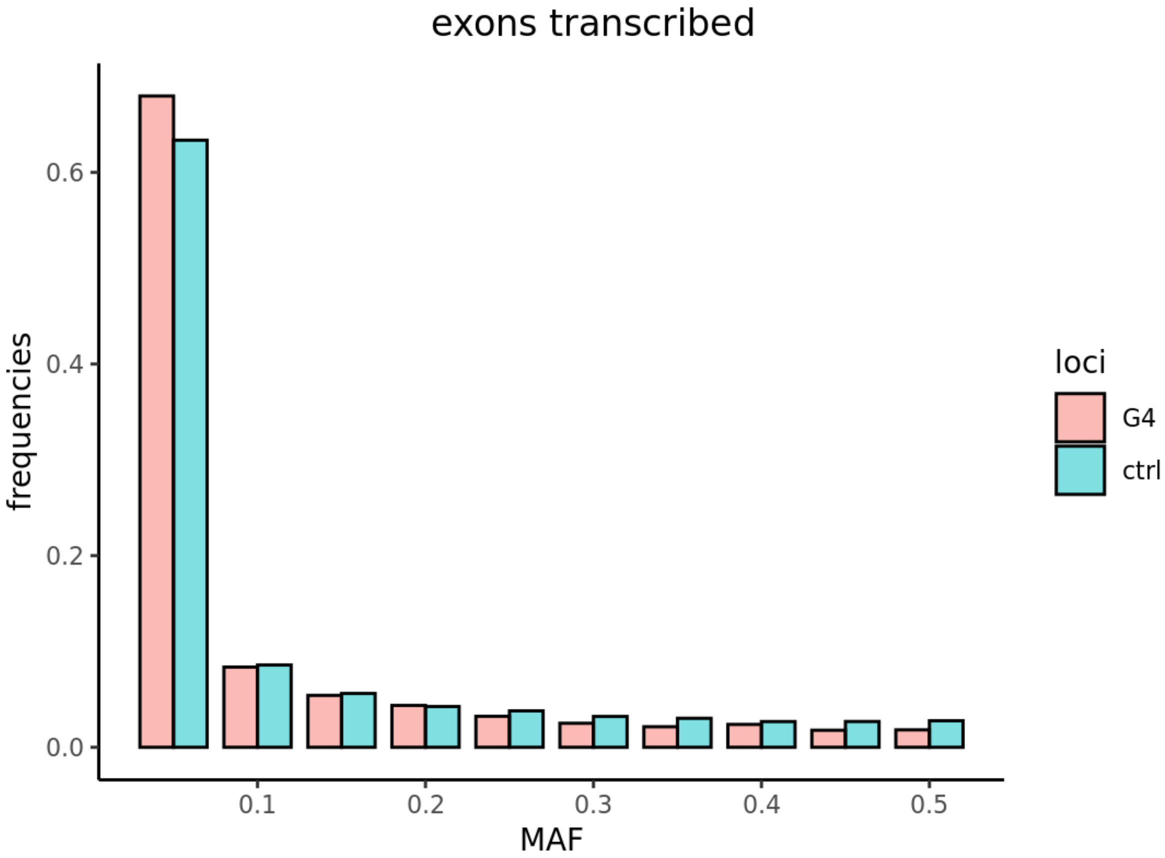
```
%%R -i exon_antisense_MAFs_ctrl,exon_antisense_MAFs_high,exon_antisense_MAFs_low

exon_antisense_MAFs_high <- as.numeric(as.character(exon_antisense_MAFs_high))
exon_antisense_MAFs_low <- as.numeric(as.character(exon_antisense_MAFs_low))
exon_antisense_MAFs_ctrl <- as.numeric(as.character(exon_antisense_MAFs_ctrl))
exon_antisense_MAFs <- c(exon_antisense_MAFs_high,exon_antisense_MAFs_low)

KS <- ks.test(exon_antisense_MAFs_high,exon_antisense_MAFs_ctrl)
print(KS)

KS <- ks.test(exon_antisense_MAFs_low,exon_antisense_MAFs_ctrl)
print(KS)

KS <- ks.test(exon_antisense_MAFs,exon_antisense_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  exon_antisense_MAFs_high and exon_antisense_MAFs_ctrl
D = 0.061063, p-value = 7.954e-05
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  exon_antisense_MAFs_low and exon_antisense_MAFs_ctrl
D = 0.043147, p-value = 0.03487
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  exon_antisense_MAFs and exon_antisense_MAFs_ctrl
D = 0.048741, p-value = 2.022e-05
alternative hypothesis: two-sided
```

In [773]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)


hist_high <- hist(exon_antisense_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(exon_antisense_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(exon_antisense_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(exon_antisense_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("exons transcribed",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.67974121   G4
2 0.10 0.08370400   G4
3 0.15 0.05418520   G4
4 0.20 0.04367165   G4
5 0.25 0.03234937   G4
6 0.30 0.02507076   G4
```



In [653]:

```
intron_sense_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Introns.SFS.high.sens.test')
intron_sense_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Introns.SFS.low.sens.test')
intron_sense_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Introns.SFS.control.shuf')

intron_sense_MAFs_high = list_MAFs(intron_sense_high_infile)
intron_sense_MAFs_low = list_MAFs(intron_sense_low_infile)
intron_sense_MAFs_ctrl = list_MAFs(intron_sense_ctrl_infile)
```

In [654]:

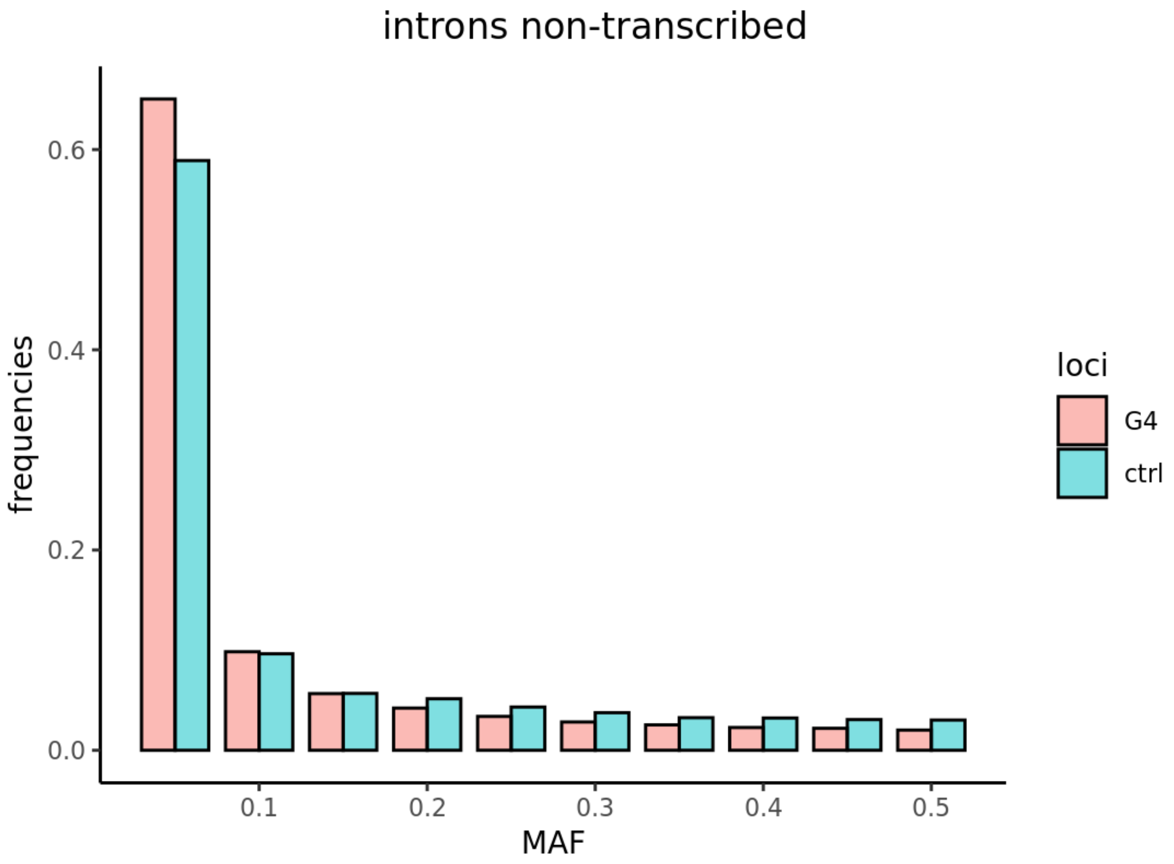
```
%%R -i intron_sense_MAFs_ctrl,intron_sense_MAFs_high,intron_sense_MAFs_l
ow

intron_sense_MAFs_high <- as.numeric(as.character(intron_sense_MAFs_high
))
intron_sense_MAFs_low <- as.numeric(as.character(intron_sense_MAFs_low))
intron_sense_MAFs_ctrl <- as.numeric(as.character(intron_sense_MAFs_ctrl
))
intron_sense_MAFs <- c(intron_sense_MAFs_high,intron_sense_MAFs_low)

KS <- ks.test(intron_sense_MAFs_high,intron_sense_MAFs_ctrl)
print(KS)

KS <- ks.test(intron_sense_MAFs_low,intron_sense_MAFs_ctrl)
print(KS)

KS <- ks.test(intron_sense_MAFs,intron_sense_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  intron_sense_MAFs_high and intron_sense_MAFs_ctrl
D = 0.079739, p-value < 2.2e-16
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  intron_sense_MAFs_low and intron_sense_MAFs_ctrl
D = 0.033549, p-value = 2.793e-05
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  intron_sense_MAFs and intron_sense_MAFs_ctrl
D = 0.066349, p-value < 2.2e-16
alternative hypothesis: two-sided
```

In [775]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)



hist_high <- hist(intron_sense_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(intron_sense_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(intron_sense_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(intron_sense_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("introns non-transcribed",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.65051669   G4
2 0.10 0.09841992   G4
3 0.15 0.05659944   G4
4 0.20 0.04215259   G4
5 0.25 0.03382426   G4
6 0.30 0.02825501   G4
```


introns non-transcribed

In [656]:

```
intron_antisense_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Introns.SFS.high.antisens.test')
intron_antisense_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Introns.SFS.low.antisens.test')
intron_antisense_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Introns.SFS.control.shuf')

intron_antisense_MAFs_high = list_MAFs(intron_antisense_high_infile)
intron_antisense_MAFs_low = list_MAFs(intron_antisense_low_infile)
intron_antisense_MAFs_ctrl = list_MAFs(intron_antisense_ctrl_infile)
```

In [657]:

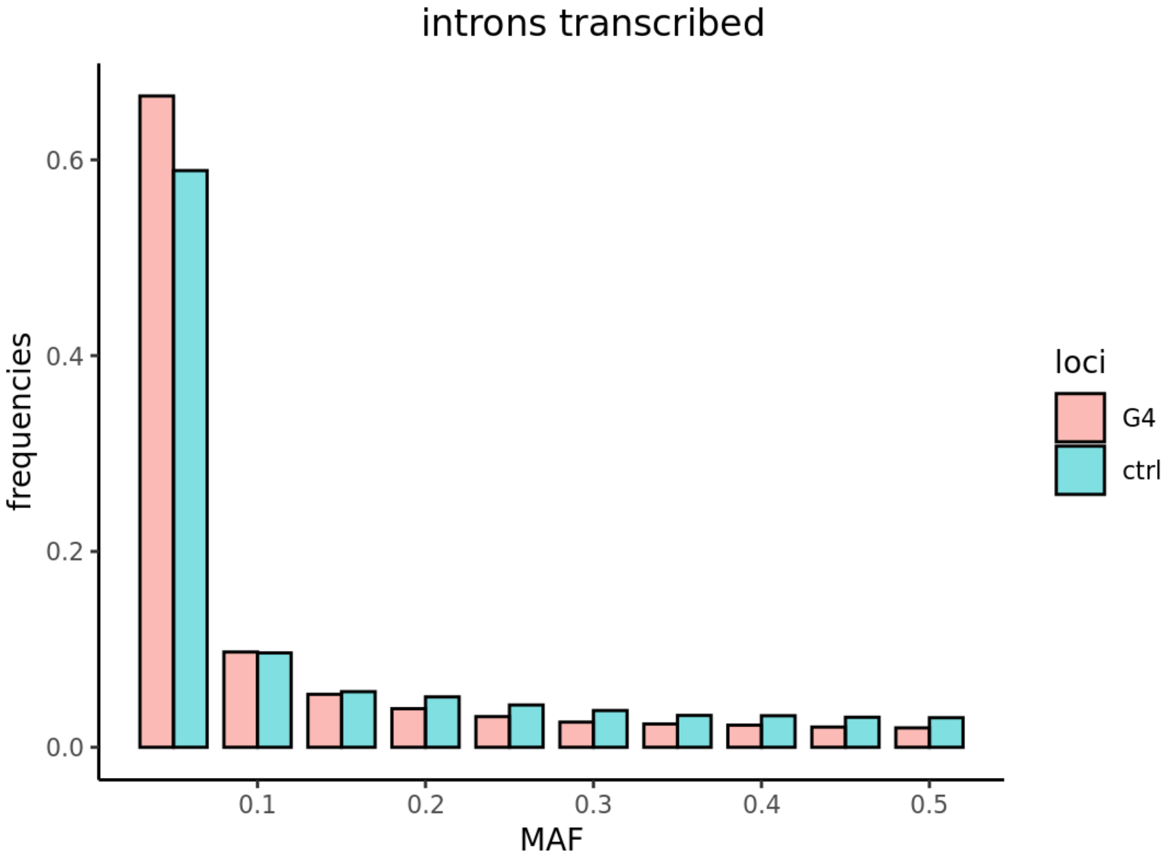
```
%%R -i intron_antisense_MAFs_ctrl,intron_antisense_MAFs_high,intron_antisense_MAFs_low

intron_antisense_MAFs_high <- as.numeric(as.character(intron_antisense_MAFs_high))
intron_antisense_MAFs_low <- as.numeric(as.character(intron_antisense_MAFs_low))
intron_antisense_MAFs_ctrl <- as.numeric(as.character(intron_antisense_MAFs_ctrl))
intron_antisense_MAFs <- c(intron_antisense_MAFs_high,intron_antisense_MAFs_low)

KS <- ks.test(intron_antisense_MAFs_high,intron_antisense_MAFs_ctrl)
print(KS)

KS <- ks.test(intron_antisense_MAFs_low,intron_antisense_MAFs_ctrl)
print(KS)

KS <- ks.test(intron_antisense_MAFs,intron_antisense_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  intron_antisense_MAFs_high and intron_antisense_MAFs_ctrl
D = 0.089356, p-value < 2.2e-16
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  intron_antisense_MAFs_low and intron_antisense_MAFs_ctrl
D = 0.059009, p-value = 1.332e-15
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  intron_antisense_MAFs and intron_antisense_MAFs_ctrl
D = 0.080358, p-value < 2.2e-16
alternative hypothesis: two-sided
```

In [776]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)


hist_high <- hist(intron_antisense_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(intron_antisense_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(intron_antisense_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(intron_antisense_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("introns transcribed",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.66520778   G4
2 0.10 0.09731726   G4
3 0.15 0.05410631   G4
4 0.20 0.03942478   G4
5 0.25 0.03133141   G4
6 0.30 0.02571584   G4
```



In [659]:
```
TUTR_sense_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/TUTR.SFS.high.sens.test')
TUTR_sense_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/TUTR.SFS.low.sens.test')
TUTR_sense_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/TUTR.SFS.control')

TUTR_sense_MAFs_high = list_MAFs(TUTR_sense_high_infile)
TUTR_sense_MAFs_low = list_MAFs(TUTR_sense_low_infile)
TUTR_sense_MAFs_ctrl = list_MAFs(TUTR_sense_ctrl_infile)
```

In [660]:

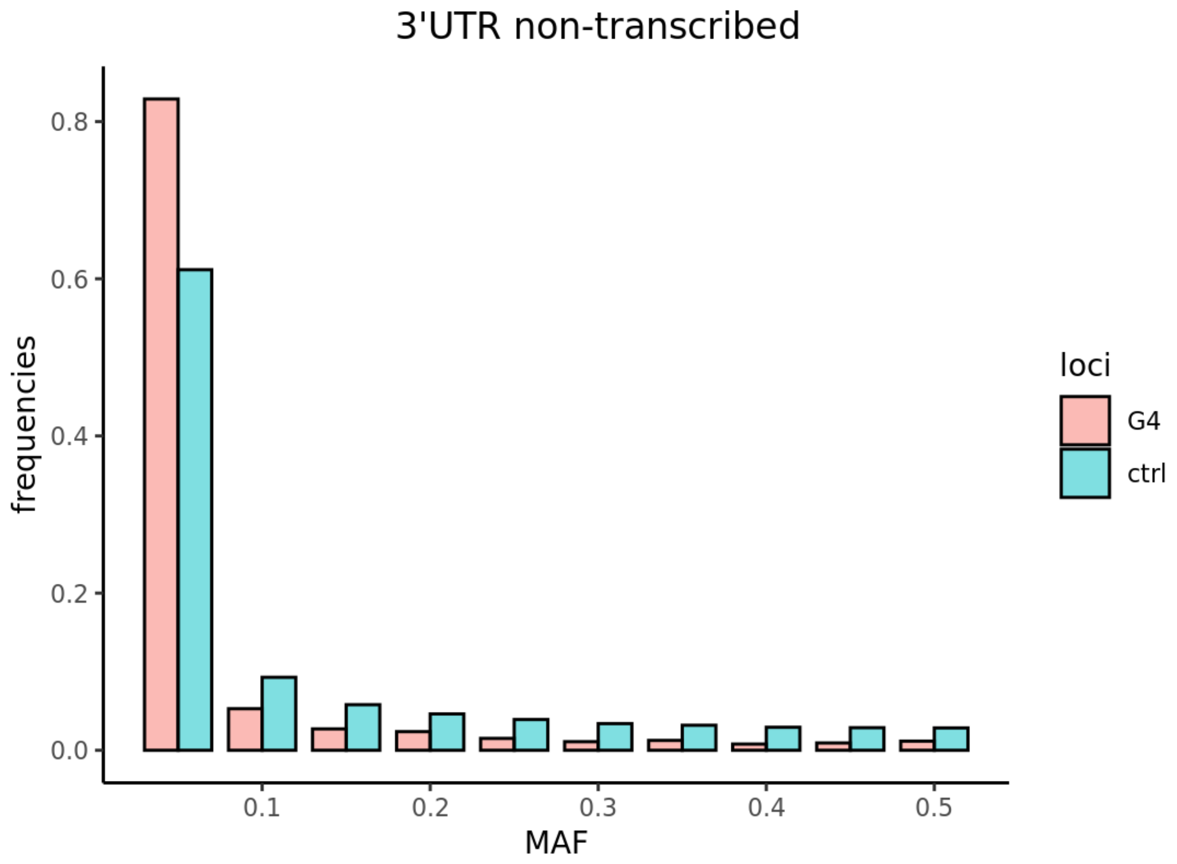
```
%%R -i TUTR_sense_MAFs_ctrl,TUTR_sense_MAFs_high,TUTR_sense_MAFs_low

TUTR_sense_MAFs_high <- as.numeric(as.character(TUTR_sense_MAFs_high))
TUTR_sense_MAFs_low <- as.numeric(as.character(TUTR_sense_MAFs_low))
TUTR_sense_MAFs_ctrl <- as.numeric(as.character(TUTR_sense_MAFs_ctrl))
TUTR_sense_MAFs <- c(TUTR_transcribed_MAFs_high,TUTR_sense_MAFs_low)

KS <- ks.test(TUTR_sense_MAFs_high,TUTR_sense_MAFs_ctrl)
print(KS)

KS <- ks.test(TUTR_sense_MAFs_low,TUTR_sense_MAFs_ctrl)
print(KS)

KS <- ks.test(TUTR_sense_MAFs,TUTR_sense_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  TUTR_sense_MAFs_high and TUTR_sense_MAFs_ctrl
D = 0.071724, p-value = 4.522e-07
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  TUTR_sense_MAFs_low and TUTR_sense_MAFs_ctrl
D = 0.050348, p-value = 0.02361
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  TUTR_sense_MAFs and TUTR_sense_MAFs_ctrl
D = 0.49855, p-value < 2.2e-16
alternative hypothesis: two-sided
```

In [777]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)



hist_high <- hist(TUTR_sense_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(TUTR_sense_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(TUTR_sense_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(TUTR_sense_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("3'UTR non-transcribed",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.82874084   G4
2 0.10 0.05290083   G4
3 0.15 0.02720614   G4
4 0.20 0.02371817   G4
5 0.25 0.01511452   G4
6 0.30 0.01092896   G4
```



In [662]:

```
TUTR_antisense_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/TUTR.SFS.high.antisens.test')
TUTR_antisense_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/TUTR.SFS.low.antisens.test')
TUTR_antisense_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/TUTR.SFS.control')

TUTR_antisense_MAFs_high = list_MAFs(TUTR_antisense_high_infile)
TUTR_antisense_MAFs_low = list_MAFs(TUTR_antisense_low_infile)
TUTR_antisense_MAFs_ctrl = list_MAFs(TUTR_antisense_ctrl_infile)
```

In [663]:

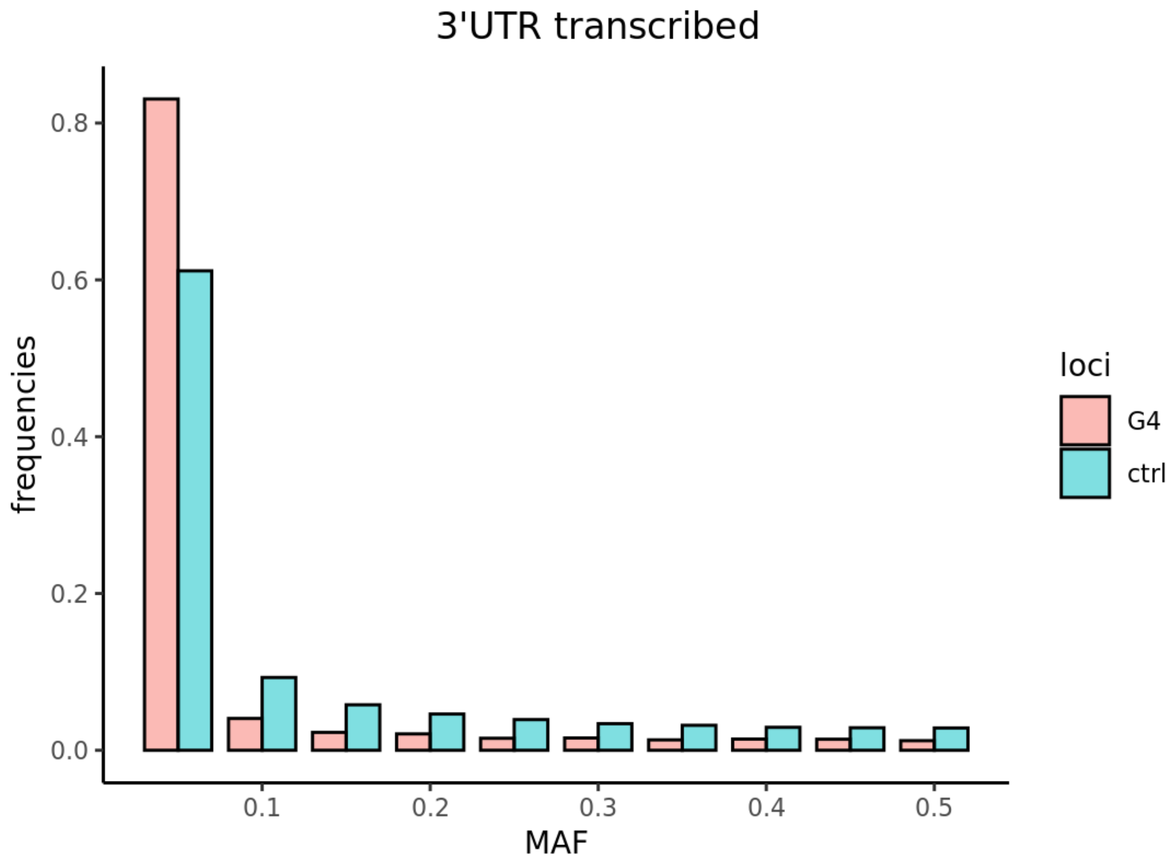
```
%%R -i TUTR_antisense_MAFs_ctrl,TUTR_antisense_MAFs_high,TUTR_antisense_MAFs_low

TUTR_antisense_MAFs_high <- as.numeric(as.character(TUTR_antisense_MAFs_high))
TUTR_antisense_MAFs_low <- as.numeric(as.character(TUTR_antisense_MAFs_low))
TUTR_antisense_MAFs_ctrl <- as.numeric(as.character(TUTR_antisense_MAFs_ctrl))
TUTR_antisense_MAFs <- c(TUTR_template_MAFs_high,TUTR_antisense_MAFs_low)

KS <- ks.test(TUTR_antisense_MAFs_high,TUTR_antisense_MAFs_ctrl)
print(KS)

KS <- ks.test(TUTR_antisense_MAFs_low,TUTR_antisense_MAFs_ctrl)
print(KS)

KS <- ks.test(TUTR_antisense_MAFs,TUTR_antisense_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  TUTR_antisense_MAFs_high and TUTR_antisense_MAFs_ctrl
D = 0.028793, p-value = 0.07669
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  TUTR_antisense_MAFs_low and TUTR_antisense_MAFs_ctrl
D = 0.02272, p-value = 0.6326
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  TUTR_antisense_MAFs and TUTR_antisense_MAFs_ctrl
D = 0.53102, p-value < 2.2e-16
alternative hypothesis: two-sided
```

In [778]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)


hist_high <- hist(TUTR_antisense_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(TUTR_antisense_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(TUTR_antisense_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(TUTR_antisense_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("3'UTR transcribed",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.83070208   G4
2 0.10 0.04058321   G4
3 0.15 0.02284547   G4
4 0.20 0.02089525   G4
5 0.25 0.01532318   G4
6 0.30 0.01569465   G4
```



In [665]:

```
Down_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Downstream1k.SFS.high.test')
Down_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Downstream1k.SFS.low.test')
Down_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Downstream1k.SFS.control')

Down_MAFs_high = list_MAFs(Down_high_infile)
Down_MAFs_low = list_MAFs(Down_low_infile)
Down_MAFs_ctrl = list_MAFs(Down_ctrl_infile)
```

In [666]:

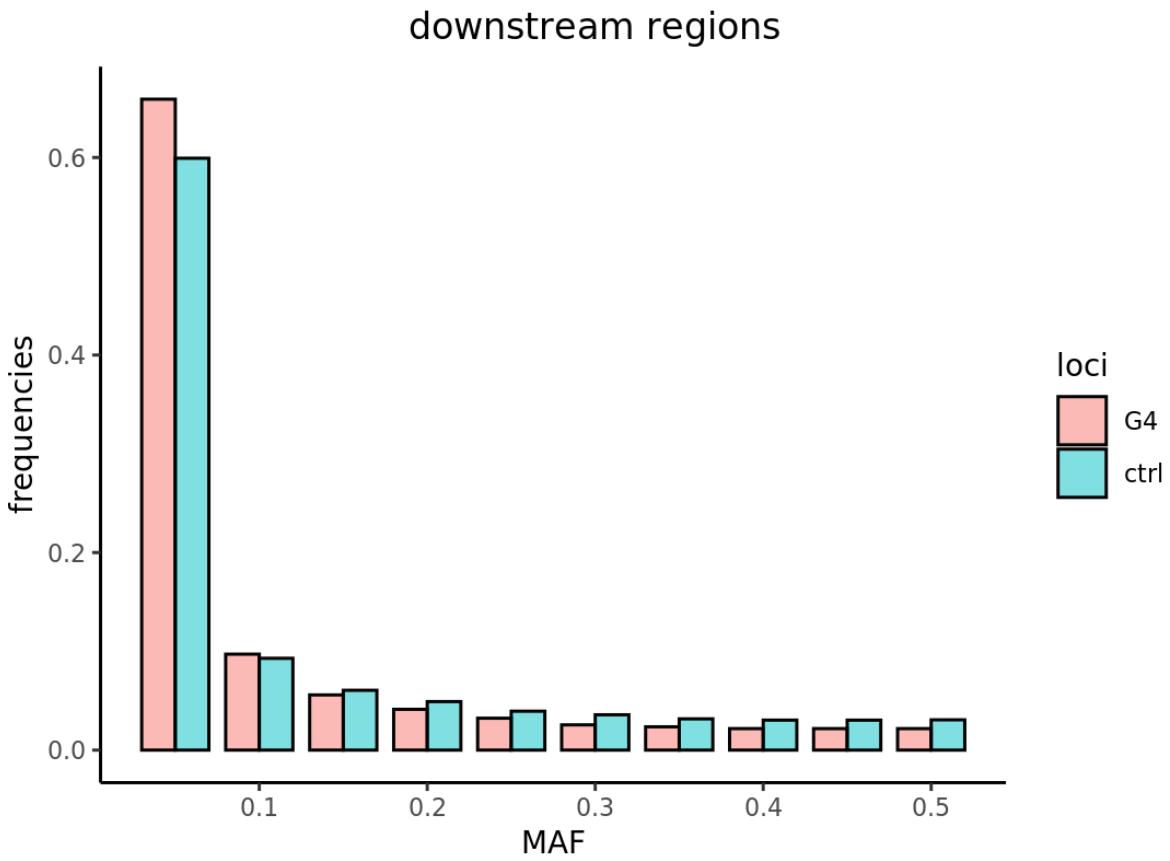
```
%%R -i Down_MAFs_ctrl,Down_MAFs_high,Down_MAFs_low

Down_MAFs_high <- as.numeric(as.character(Down_MAFs_high))
Down_MAFs_low <- as.numeric(as.character(Down_MAFs_low))
Down_MAFs_ctrl <- as.numeric(as.character(Down_MAFs_ctrl))
Down_MAFs <- c(Down_MAFs_high,Down_MAFs_low)

KS <- ks.test(Down_MAFs_high,Down_MAFs_ctrl)
print(KS)

KS <- ks.test(Down_MAFs_low,Down_MAFs_ctrl)
print(KS)

KS <- ks.test(Down_MAFs,Down_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  Down_MAFs_high and Down_MAFs_ctrl
D = 0.075798, p-value < 2.2e-16
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  Down_MAFs_low and Down_MAFs_ctrl
D = 0.043864, p-value = 0.00118
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  Down_MAFs and Down_MAFs_ctrl
D = 0.065295, p-value < 2.2e-16
alternative hypothesis: two-sided
```

In [779]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)


hist_high <- hist(Down_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(Down_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(Down_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(Down_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("downstream regions",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.65903987   G4
2 0.10 0.09713644   G4
3 0.15 0.05586749   G4
4 0.20 0.04126895   G4
5 0.25 0.03228523   G4
6 0.30 0.02554745   G4
```



In [668]:

```
RepOrigin_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/RepOrigin.SFS.high.test')
RepOrigin_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/RepOrigin.SFS.low.test')
RepOrigin_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/RepOrigin.SFS.control')

RepOrigin_MAFs_high = list_MAFs(RepOrigin_high_infile)
RepOrigin_MAFs_low = list_MAFs(RepOrigin_low_infile)
RepOrigin_MAFs_ctrl = list_MAFs(RepOrigin_ctrl_infile)
```

In [669]:

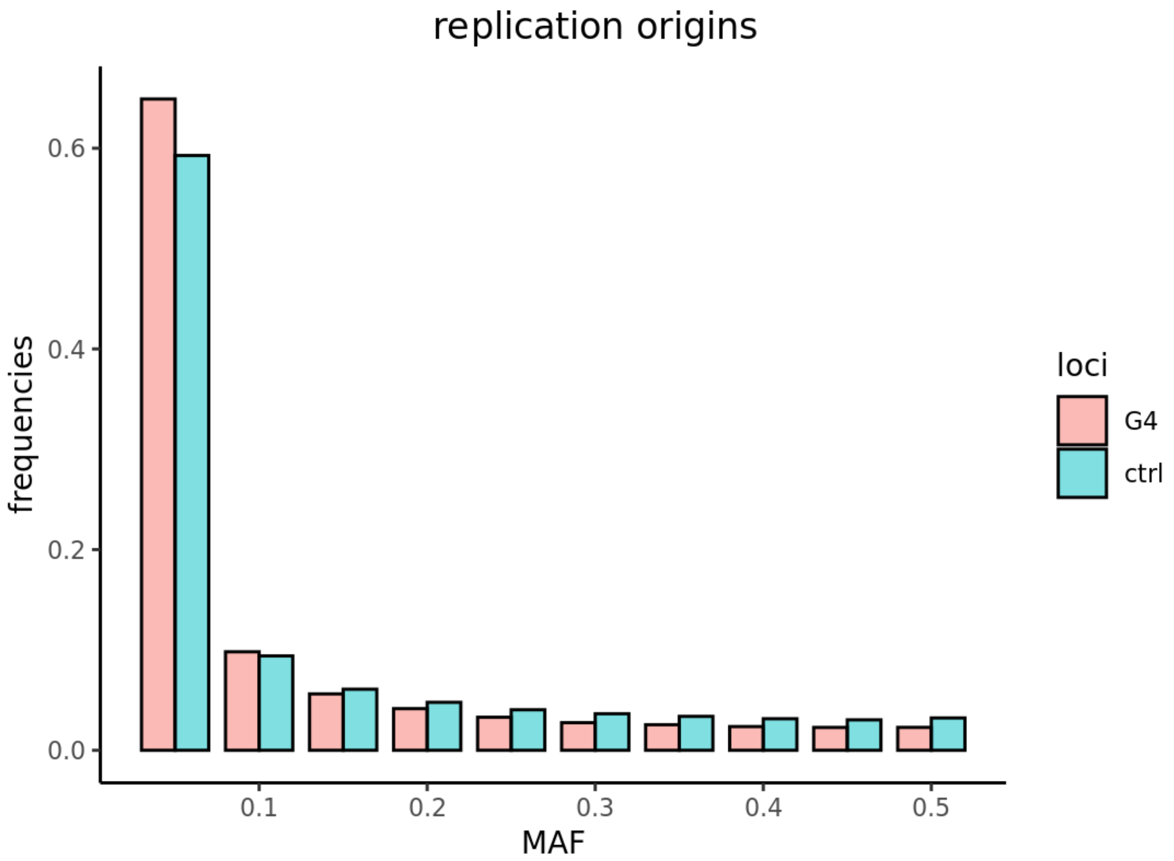
```
%%R -i RepOrigin_MAFs_ctrl,RepOrigin_MAFs_high,RepOrigin_MAFs_low

RepOrigin_MAFs_high <- as.numeric(as.character(RepOrigin_MAFs_high))
RepOrigin_MAFs_low <- as.numeric(as.character(RepOrigin_MAFs_low))
RepOrigin_MAFs_ctrl <- as.numeric(as.character(RepOrigin_MAFs_ctrl))
RepOrigin_MAFs <- c(RepOrigin_MAFs_high,RepOrigin_MAFs_low)

KS <- ks.test(RepOrigin_MAFs_high,RepOrigin_MAFs_ctrl)
print(KS)

KS <- ks.test(RepOrigin_MAFs_low,RepOrigin_MAFs_ctrl)
print(KS)

KS <- ks.test(RepOrigin_MAFs,RepOrigin_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  RepOrigin_MAFs_high and RepOrigin_MAFs_ctrl
D = 0.072784, p-value < 2.2e-16
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  RepOrigin_MAFs_low and RepOrigin_MAFs_ctrl
D = 0.022511, p-value = 1.161e-12
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  RepOrigin_MAFs and RepOrigin_MAFs_ctrl
D = 0.060897, p-value < 2.2e-16
alternative hypothesis: two-sided
```

In [780]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)


hist_high <- hist(RepOrigin_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(RepOrigin_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(RepOrigin_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(RepOrigin_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("replication origins",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.64907669   G4
2 0.10 0.09814519   G4
3 0.15 0.05617655   G4
4 0.20 0.04150186   G4
5 0.25 0.03291979   G4
6 0.30 0.02751505   G4
```



In [672]:
```
enhancers_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/enhancers.SFS.high.test')
enhancers_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/enhancers.SFS.low.test')
enhancers_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/enhancers.SFS.control')

enhancers_MAFs_high = list_MAFs(enhancers_high_infile)
enhancers_MAFs_low = list_MAFs(enhancers_low_infile)
enhancers_MAFs_ctrl = list_MAFs(enhancers_ctrl_infile)
```

In [673]:

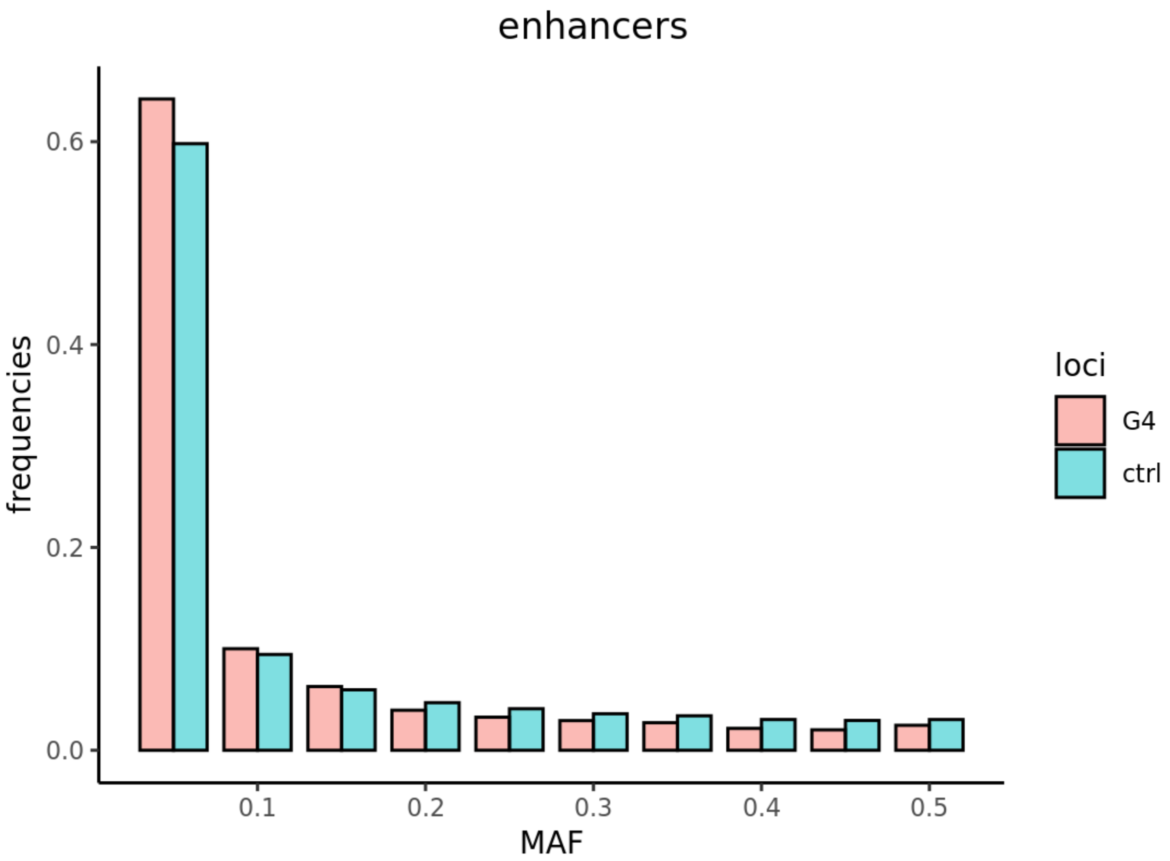
```
%%R -i enhancers_MAFs_ctrl,enhancers_MAFs_high,enhancers_MAFs_low

enhancers_MAFs_high <- as.numeric(as.character(enhancers_MAFs_high))
enhancers_MAFs_low <- as.numeric(as.character(enhancers_MAFs_low))
enhancers_MAFs_ctrl <- as.numeric(as.character(enhancers_MAFs_ctrl))
enhancers_MAFs <- c(enhancers_MAFs_high,enhancers_MAFs_low)

KS <- ks.test(enhancers_MAFs_high,enhancers_MAFs_ctrl)
print(KS)

KS <- ks.test(enhancers_MAFs_low,enhancers_MAFs_ctrl)
print(KS)

KS <- ks.test(enhancers_MAFs,enhancers_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  enhancers_MAFs_high and enhancers_MAFs_ctrl
D = 0.055282, p-value = 2.376e-12
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  enhancers_MAFs_low and enhancers_MAFs_ctrl
D = 0.054629, p-value = 0.0001994
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  enhancers_MAFs and enhancers_MAFs_ctrl
D = 0.054013, p-value = 2.109e-15
alternative hypothesis: two-sided
```

In [781]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)


hist_high <- hist(enhancers_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(enhancers_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(enhancers_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(enhancers_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("enhancers",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.64209180   G4
2 0.10 0.10011195   G4
3 0.15 0.06284983   G4
4 0.20 0.03950104   G4
5 0.25 0.03262434   G4
6 0.30 0.02926595   G4
```



In [675]:

```
TADB_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/TADB.SFS.high.test')
TADB_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/TADB.SFS.low.test')
TADB_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/TADB.SFS.control.shuf')

TADB_MAFs_high = list_MAFs(TADB_high_infile)
TADB_MAFs_low = list_MAFs(TADB_low_infile)
TADB_MAFs_ctrl = list_MAFs(TADB_ctrl_infile)
```

In [676]:

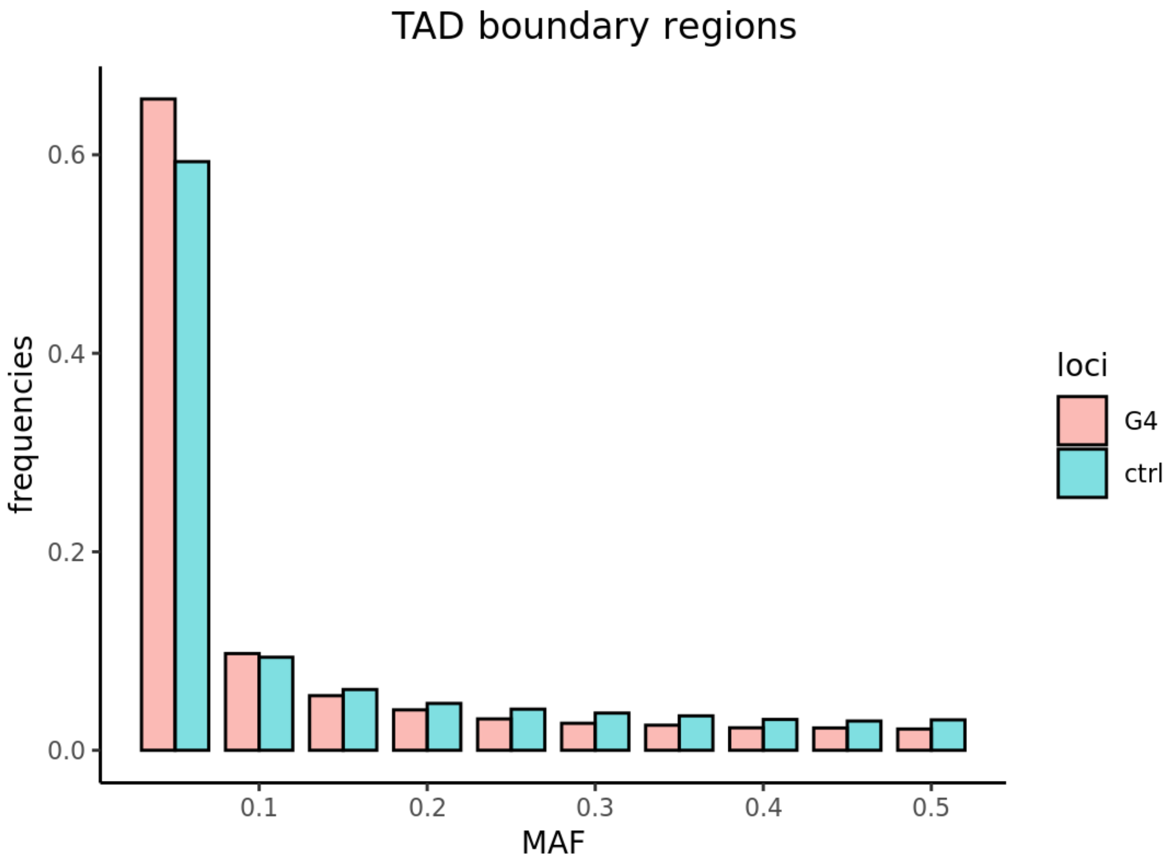
```
%%R -i TADB_MAFs_ctrl,TADB_MAFs_high,TADB_MAFs_low

TADB_MAFs_high <- as.numeric(as.character(TADB_MAFs_high))
TADB_MAFs_low <- as.numeric(as.character(TADB_MAFs_low))
TADB_MAFs_ctrl <- as.numeric(as.character(TADB_MAFs_ctrl))
TADB_MAFs <- c(TADB_MAFs_high,TADB_MAFs_low)

KS <- ks.test(TADB_MAFs_high,TADB_MAFs_ctrl)
print(KS)

KS <- ks.test(TADB_MAFs_low,TADB_MAFs_ctrl)
print(KS)

KS <- ks.test(TADB_MAFs,TADB_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  TADB_MAFs_high and TADB_MAFs_ctrl
D = 0.080175, p-value < 2.2e-16
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  TADB_MAFs_low and TADB_MAFs_ctrl
D = 0.039796, p-value < 2.2e-16
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  TADB_MAFs and TADB_MAFs_ctrl
D = 0.067812, p-value < 2.2e-16
alternative hypothesis: two-sided
```

In [782]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)


hist_high <- hist(TADB_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(TADB_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(TADB_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(TADB_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("TAD boundary regions",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.65619298   G4
2 0.10 0.09745349   G4
3 0.15 0.05501555   G4
4 0.20 0.04071656   G4
5 0.25 0.03159320   G4
6 0.30 0.02718645   G4
```



In [678]:

```
CpGI_high_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/CpGIsland.SFS.high.test')
CpGI_low_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/CpGIsland.SFS.low.test')
CpGI_ctrl_infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/CpGIsland.SFS.control')

CpGI_MAFs_high = list_MAFs(CpGI_high_infile)
CpGI_MAFs_low = list_MAFs(CpGI_low_infile)
CpGI_MAFs_ctrl = list_MAFs(CpGI_ctrl_infile)
```

In [679]:

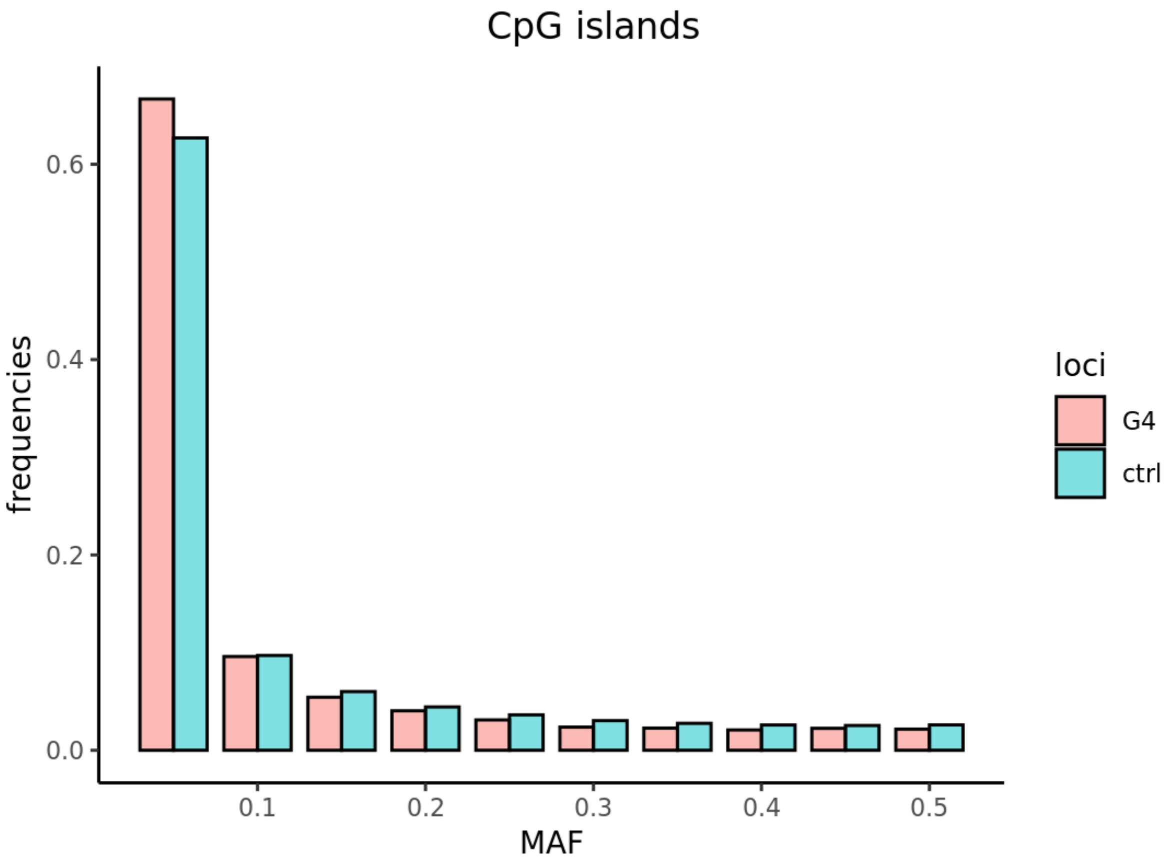
```
%%R -i CpGI_MAFs_ctrl,CpGI_MAFs_high,CpGI_MAFs_low

CpGI_MAFs_high <- as.numeric(as.character(CpGI_MAFs_high))
CpGI_MAFs_low <- as.numeric(as.character(CpGI_MAFs_low))
CpGI_MAFs_ctrl <- as.numeric(as.character(CpGI_MAFs_ctrl))
CpGI_MAFs <- c(CpGI_MAFs_high,CpGI_MAFs_low)

KS <- ks.test(CpGI_MAFs_high,CpGI_MAFs_ctrl)
print(KS)

KS <- ks.test(CpGI_MAFs_low,CpGI_MAFs_ctrl)
print(KS)

KS <- ks.test(CpGI_MAFs,CpGI_MAFs_ctrl)
print(KS)
```

```
        Two-sample Kolmogorov-Smirnov test

data:  CpGI_MAFs_high and CpGI_MAFs_ctrl
D = 0.054079, p-value < 2.2e-16
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  CpGI_MAFs_low and CpGI_MAFs_ctrl
D = 0.020424, p-value = 0.002847
alternative hypothesis: two-sided


        Two-sample Kolmogorov-Smirnov test

data:  CpGI_MAFs and CpGI_MAFs_ctrl
D = 0.040372, p-value < 2.2e-16
alternative hypothesis: two-sided
```

In [783]:

```
%%R -w 5.5 -h 4 --units in -r 200

library(scales)
library(plotrix)


hist_high <- hist(CpGI_MAFs, plot=FALSE, breaks = 10)$density / sum(hist(CpGI_MAFs, plot=FALSE, breaks = 10)$density)
hist_ctrl <- hist(CpGI_MAFs_ctrl, plot=FALSE, breaks = 10)$density / sum(hist(CpGI_MAFs_ctrl, plot=FALSE, breaks = 10)$density)
x <- seq(0.05,0.5,0.05)

toplot <- cbind.data.frame(c(x,x),c(hist_high,hist_ctrl),c(rep('G4',length(hist_high)),rep('ctrl',length(hist_ctrl))))
colnames(toplot) <- c('x','MAF', 'loci')
print(head(toplot))

p1 <- ggplot(toplot) +
    geom_bar(aes(fill = loci, x=x, y=MAF), position = "dodge", stat="identity", colour="black", width = 0.04, alpha = .5) +
    theme_classic() +
    scale_x_continuous(breaks=seq(0,0.5,0.1)) +
    labs(y="frequencies", x="MAF") +
    theme(text=element_text(size=10,family="sans"))

grid.arrange(p1,top=textGrob("CpG islands",gp=gpar(fontsize=12,font=1)))
```

```
     x        MAF loci
1 0.05 0.66681343   G4
2 0.10 0.09598239   G4
3 0.15 0.05430196   G4
4 0.20 0.04043295   G4
5 0.25 0.03107687   G4
6 0.30 0.02373876   G4
```



In [11]:

```
infile = open('/nfs/brubeck.bx.psu.edu/scratch6/wilfried/nonB/Selection_Errors/Exons.nooverlap', 'rt')

length = 0

for line in infile:
    array = line.strip().split('\t')
    currentlength = int(array[2]) - int(array[1]) + 1
    length += currentlength


print(str(length)+' bp in Exons')
```

```
33683716 bp in Exons
```

In [12]:

```
infile = open('/nfs/brubeck.bx.psu.edu/scratch6/wilfried/nonB/Selection_Errors/Exons.Quadron.intersect', 'rt')


length = 0

for line in infile:
    array = line.strip().split('\t')
    if array[4] != '-1':
        start, end, G4start, G4end = int(array[1]), int(array[2]), int(array[4]), int(array[5])

        if G4start < start:
            G4start = start

        if G4end > end:
            G4end = end

        currentlength = G4end - G4start + 1
        length += currentlength

print(str(length)+' bp of G4s in Exons')
```

```
590145 bp of G4s in Exons
```

In [13]:

```
print(str(33683716-590145)+' bp of Exons without G4')
```

```
33093571 bp of Exons without G4
```

In [21]:

```
infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Exons.SFS.high.sens.test', 'rt')

span = 0
count = 0

for line in infile:
    chrom, start, end, SFS = line.strip().split('\t')
    span += int(end) - int(start) + 1

    homo, pongo, ref, alt, MAF = SFS.split('|')

    if ref != 'NA' and homo == 'NA':
        count += 1

print(str(count)+' SNPs in '+str(span)+' bp')
```

```
82 SNPs in 81366 bp
```

In [22]:

```
infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Exons.SFS.high.antisens.test', 'rt')

span = 0
count = 0

for line in infile:
    chrom, start, end, SFS = line.strip().split('\t')
    span += int(end) - int(start) + 1

    homo, pongo, ref, alt, MAF = SFS.split('|')

    if ref != 'NA' and homo == 'NA':
        count += 1

print(str(count)+' SNPs in '+str(span)+' bp')
```

```
490 SNPs in 339140 bp
```

In [19]:

```
infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Exons.SFS.control', 'rt')

span = 0
count = 0

for line in infile:
    chrom, start, end, SFS, score, strand = line.strip().split('\t')
    span += int(end) - int(start) + 1

    homo, pongo, ref, alt, MAF = SFS.split('|')

    if ref != 'NA' and homo == 'NA':
        count += 1

print(str(count)+' SNPs in '+str(span)+' bp')
```

```
25811 SNPs in 63142846 bp
```

In [25]:

```
%%R
fisher.test(cbind(c(82 + 490, 81366 + 339140),c(25811, 63142846)))
```

```
        Fisher's Exact Test for Count Data

data:  cbind(c(82 + 490, 81366 + 339140), c(25811, 63142846))
p-value < 2.2e-16
alternative hypothesis: true odds ratio is not equal to 1
95 percent confidence interval:
 3.057339 3.615870
sample estimates:
odds ratio
  3.327667
```

In [26]:

```
infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/E
xons.SFS.high.sens.test', 'rt')

span = 0
count = 0

for line in infile:
    chrom, start, end, SFS = line.strip().split('\t')
    span += int(end) - int(start) + 1

    homo, pongo, ref, alt, MAF = SFS.split('|')

    if homo != 'NA':
        count += 1

print(str(count)+' FNSs in '+str(span)+' bp')
```

```
36885 FNSs in 81366 bp
```

In [27]:

```
infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/E
xons.SFS.high.antisens.test', 'rt')

span = 0
count = 0

for line in infile:
    chrom, start, end, SFS = line.strip().split('\t')
    span += int(end) - int(start) + 1

    homo, pongo, ref, alt, MAF = SFS.split('|')

    if homo != 'NA':
        count += 1

print(str(count)+' FNSs in '+str(span)+' bp')
```

```
155558 FNSs in 339140 bp
```

In [8]:

```
infile = open('/nfs/brubeck.bx.psu.edu/scratch5/wilfried/nonB/Mutation/Exons.SFS.control', 'rt')

span = 0
count = 0

for line in infile:
    chrom, start, end, SFS, score, strand = line.strip().split('\t')
    span += int(end) - int(start) + 1

    homo, pongo, ref, alt, MAF = SFS.split('|')

    if homo != 'NA':
        count += 1

print(str(count)+' FNSs in '+str(span)+' bp')
```

```
30134931 FNSs in 63142846 bp
```

In [28]:

```
%%R
fisher.test(cbind(c(36885+155558, 81366+339140),c(30134931, 63142846)))
```

```
        Fisher's Exact Test for Count Data

data:  cbind(c(36885 + 155558, 81366 + 339140), c(30134931, 63142846))
p-value < 2.2e-16
alternative hypothesis: true odds ratio is not equal to 1
95 percent confidence interval:
 0.9537570 0.9641387
sample estimates:
odds ratio
 0.9589287
```

In [ ]: