

## Question 1.b

The probability that the first parent does not contain a given allele can be written as  $P(x_1 \neq A)$ . The second probability is the conditional probability  $P(x_2 \neq A \mid x_1 \neq A)$ , the probabilities of these, respectively are  $(2N-1)/2N$  and  $(2N-2)/(2N-1)$ , and we run this 100 times, so the probability that NONE of the children contain allele  $A$  can be written as follows:

$$(P(x_1 \neq A) * P(x_2 \neq A \mid x_1 \neq A))^N = ((2N-1)/(2N) * (2N-2)/(2N-1))^N = ((2N-2)/2N)^N$$

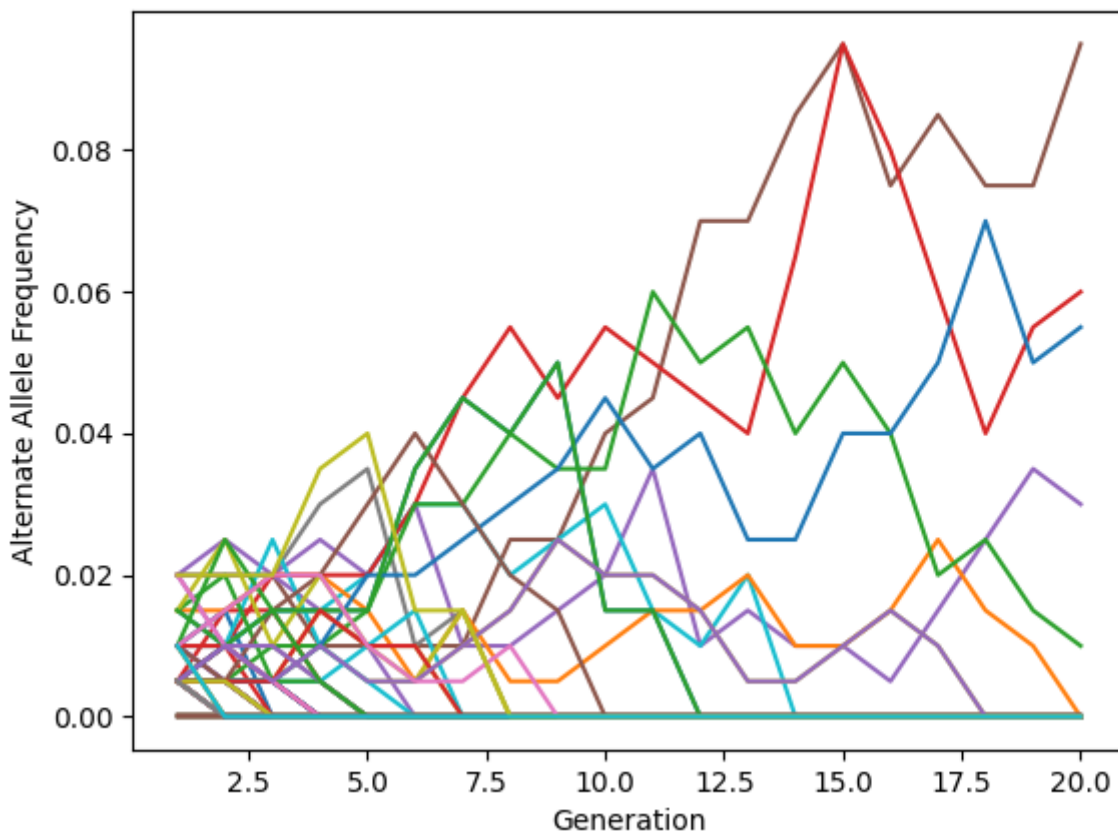
This is the probability of extinction:

$$((2N-2)/2N)^N = 0.366 \text{ when } N=100$$

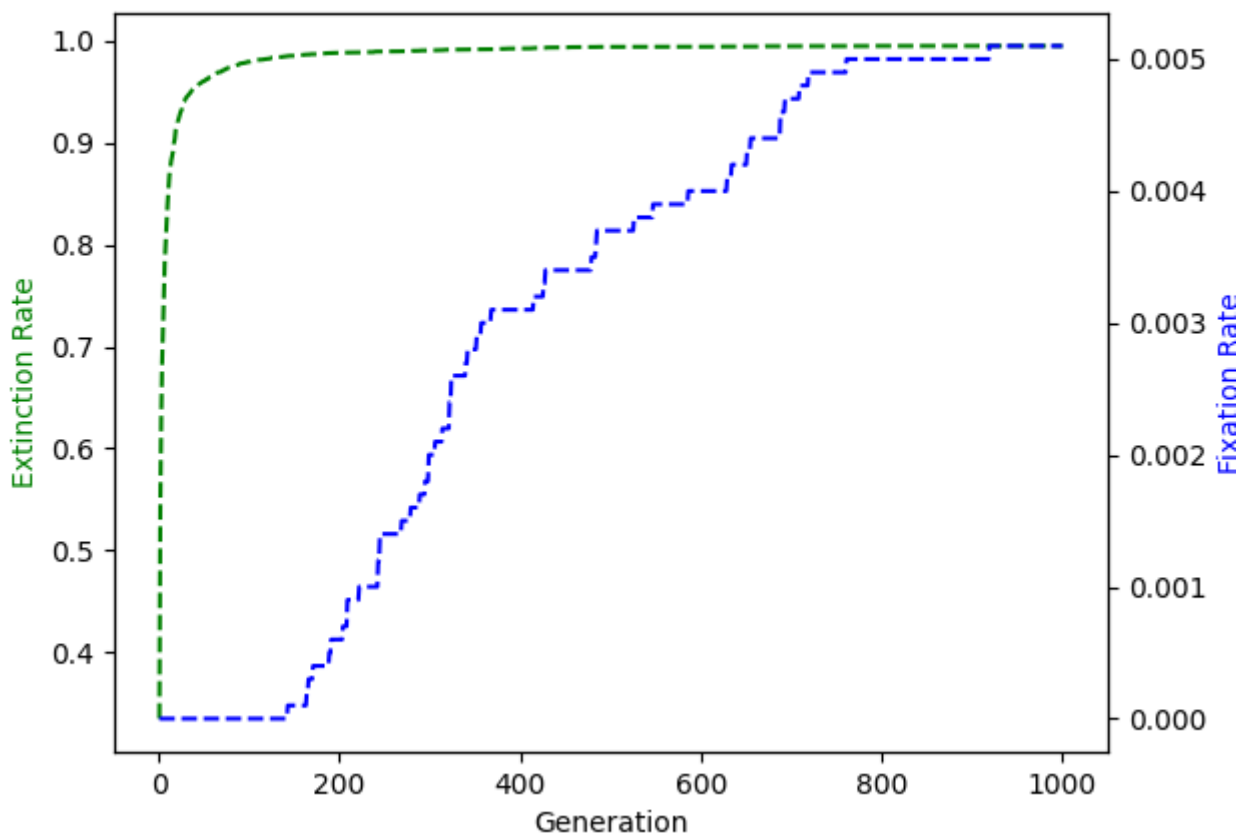
## Question 1.c

The analytical value is very close to the number we get through experimentation, which ranges from 0.39 to 0.34.

## Question 1.d



## Question 1.e



## Question 1.f

The probability that the SNP42 is extinct after one generation can be calculated as follows:

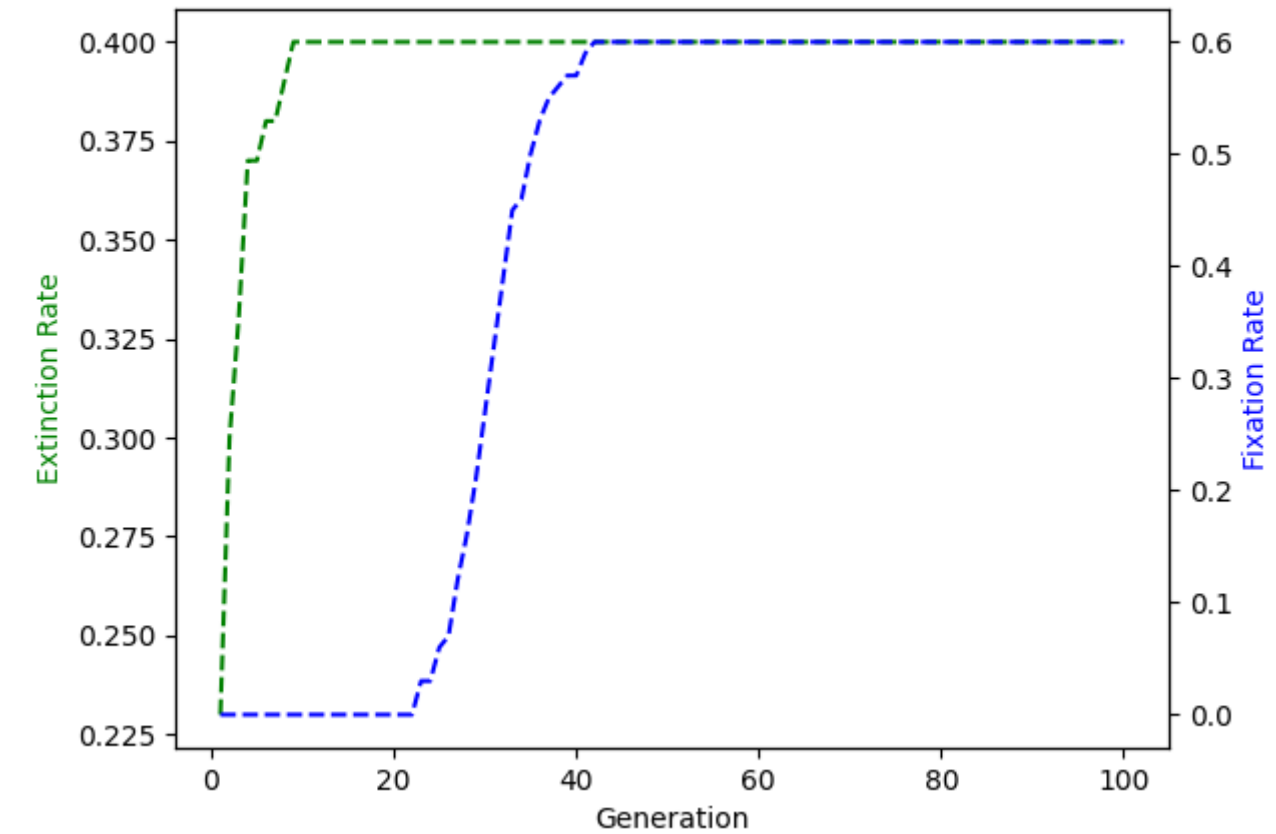
$$P(x_1 \neq \text{SNP42}) * P(x_2 \neq \text{SNP42} | x_1 \neq \text{SNP42})^N = ((2N-1.5)/(2N+0.5) * (2N-2.5)/(2N-0.5))^N$$

This is the probability of survival, so the probability of extinction is:

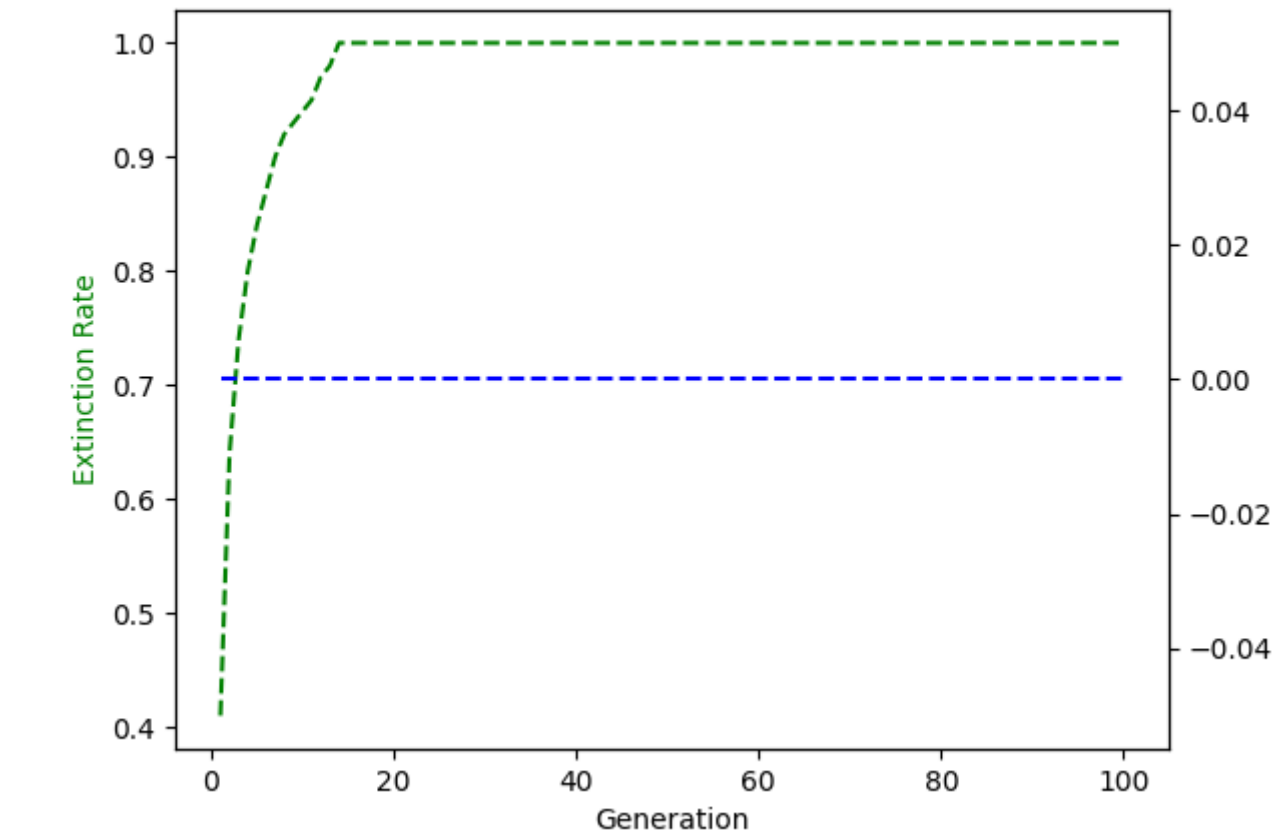
$$((199/200.5)*(198/199.5))^{100} = 0.221$$

This is confirmed by simulation, where it survives in approximately 0.21-0.23 of cases.

## Question 1.g



Question 1.h



## Question 2.b

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A total of 446 SNPs have p\_value lower than 0.05. We would expect 500 SNPs to be significant by chance,  $0.05 \times 10000$ .

## Question 2.c

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See results/snp\_table\_results.csv

```
SNP ID,Uncorrected p-value,Correct p-value,Disease odds ratio for
heterozygous individuals,Disease odds ratio for homozygous alternate
individuals
SNP1000,1.7324820411067143e-16,1.7324820411067143e-
12,1.5828460038986354,2.5099111414900888
SNP2000,9.230118981405191e-
07,0.00923011898140519,1.5034938807737863,2.24862721171446
SNP3000,5.62921270697861e-10,5.62921270697861e-
06,1.5876165280927184,2.027660120652034
SNP4000,4.770371767336931e-
07,0.004770371767336931,1.34410198935276,1.9961757105943152
```

## Question 2.d

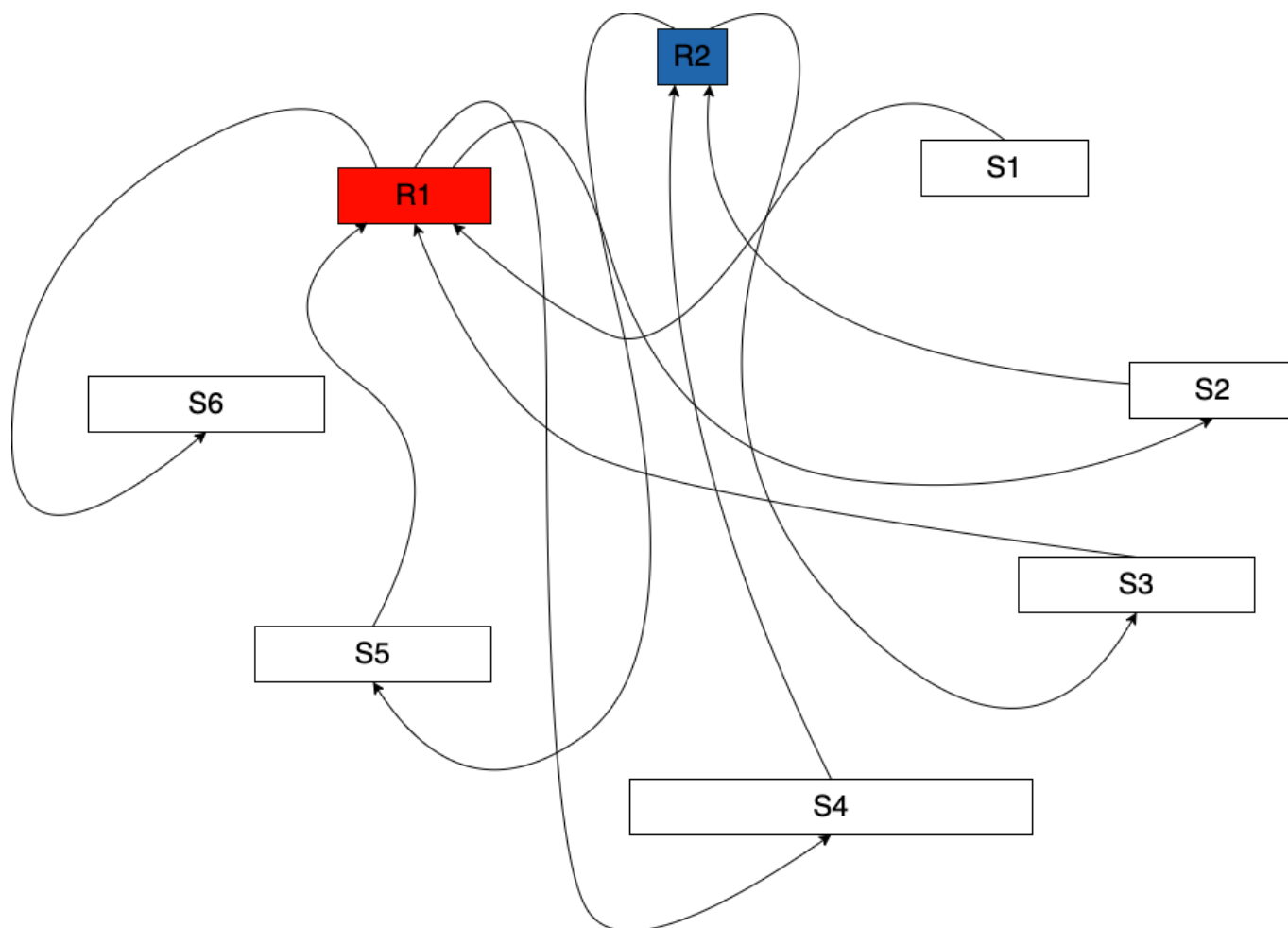
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Mathematically, the chi-squared test checks each variable in our 2-D table of allele counts (0,1,2) and the class observed (disease, no disease). It then uses the calculated expected value (the expected number of counts assuming no correlation) and the observed values (actual allele counts) and the following formula to calculate chi-squared:

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

This is summarized over each of our three alleles. Meanwhile, we calculate the odds ratio as the number of effected individuals given that they have a certain allele. This test, however ignores the expected and observed likelihood of disease vs non-disease, and thus measures the effect size given a disease/non-disease exists, but doesn't help to know if a correlation between allele type and the disease exists.

## Question 3.a



### Question 3.b

Original: S1-R1-S2-R2-S3-R1-S4-R2-S5-R1-S6

1. Switch S3\S5:

S1-R1-S2-R2-S5-R1-S4-R2-S3-R1-S6

2. Switch S2\S4:

S1-R1-S4-R2-S3-R1-S2-R2-S5-R1-S6

3. Switch R2\R4 + R3\R5:

S1-R1-S4-R2-S5-R1-S2-R2-S3-R1-S6

### Question 3.c

Assuming our algorithm is producing reads of 100 base pairs and our sequence contains a 1000 bp short tandem repeat, we will have a lot of fragments that will contain exactly the same bases. Because the goal of our algorithm is to make the shortest path possible, these reads will overlap perfectly and collapse down to a total repeat region of closer to 100, instead of 1000.

### Question 4.a

See data/viterbi\_config.yaml:

```
coding_bases:
AAA: 0.028427703368643392
AAC: 0.0195624104865669
AAG: 0.02352996485784469
AAT: 0.01697670006262792
ACA: 0.013766389458360827
ACC: 0.01555791739494712
ACG: 0.012814377893183295
ACT: 0.014145850858237587
AGA: 0.014807389758907689
AGC: 0.02095432863036262
AGG: 0.009365644639436113
AGT: 0.013888958848586506
ATA: 0.009207815561611267
ATC: 0.018832031243441277
ATG: 0.021212899672756517
ATT: 0.020707510817168446
CAA: 0.024727115203473583
CAC: 0.013796612047731542
CAG: 0.016148936920418886
CAT: 0.014246592822806638
CCA: 0.016661041906978227
CCC: 0.007273569841885486
CCG: 0.013479274859339032
CCT: 0.010638351458491792
CGA: 0.016338667620357263
CGC: 0.019362605590171614
CGG: 0.013470879695624945
CGT: 0.014673067139482287
CTA: 0.009966738361364785
CTC: 0.013032652149749573
CTG: 0.01950028627508265
CTT: 0.015734215832942957
GAA: 0.021316999702811205
GAC: 0.010331088466556186
GAG: 0.01251383103221896
GAT: 0.023177367981853013
GCA: 0.02087373505870738
GCC: 0.01669965966006303
GCG: 0.02251918714666855
GCT: 0.019968736410328737
GGA: 0.010826403125687355
GGC: 0.01812683749145792
GGG: 0.00990293511713772
GGT: 0.01745858245981655
GTA: 0.011071541906138712
GTC: 0.010962404777855574
GTG: 0.020474125265916812
GTT: 0.017643276061526474
TAA: 0.0
TAC: 0.013128357016090171
TAG: 0.0
TAT: 0.014456471915658827
```

```
TCA: 0.019258505560116927
TCC: 0.008888799340475938
TCG: 0.015789623913455935
TCT: 0.012990676331179134
TGA: 0.0
TGC: 0.02162426269474681
TGG: 0.02437787639296754
TGT: 0.01444136062097347
TTA: 0.016424298290240957
TTC: 0.014031676631725996
TTG: 0.02419989892222888
TTT: 0.023712979426811803
coding_len: 990.4515103338633
noncode_len: 1177.8412959912137
noncoding_bases:
  A: 0.26608120198671326
  C: 0.2432772656723154
  G: 0.22580470699802177
  T: 0.26483682534294956
```

## Question 4.d

For results, please see the file `Vibrio_vulnificus_results_compare.yaml`:

```
annotated:
  match_end: 0.314
  match_start: 0.0
  matches_both: 0.361
viterbi:
  match_end: 0.266
  match_start: 0.0
  matches_both: 0.312
```

This shows the fraction of genes from annotated and viterbi that match in the respective field.

## Question 4.a

In order to run the program, first:

```
python3 question_4.py

usage: Viterbi Gene Finding [-h] [--gff GFF] [--fasta FASTA] [--cfg CFG]
                             [--out OUT]

Find Genes using HMMs

optional arguments:
  -h, --help      show this help message and exit
```

```
--gff GFF
--fasta FASTA
--cfg CFG
--out OUT
```

For the output of this, please see results/Vibrio\_cholerae\_viterbi\_genes.csv.

## Question 4.c

For the genes predicted from this, please see results/Vibrio\_vulnificus\_viterbi\_genes.csv.

## Question 4.d

Here are the calculated results, from results/Vibrio\_vulnificus\_results\_compare.yaml.

```
annotated:
  match_end: 0.314
  match_start: 0.0
  matches_both: 0.361
viterbi:
  match_end: 0.266
  match_start: 0.0
  matches_both: 0.312
```

## Question 4.e

### Properties of annotated genes that risk being missed

The predictor is well-tuned to maximize the probability according to the heuristics selected, meaning that it will likely avoid events that lower probability. This includes:

1. Transitions of inter-gene to start
2. Transitions of gene to stop
3. Lower probability codons from the other gene, Vibrio Cholerae

This means that genes and inter-codon regions of shorter length will be avoided. To illustrate this, the average length of genes that were missed by the viterbi algorithm was calculated to be ~330 bases, which is about 1/3 of the length of the average gene length in the gff file, which was ~920 bases. The codon probability is also telling, having an average probability (according to our codon probabilities in the config) of 0.0177, which is about ~3% less frequent.

### Properties of genes predicted by viterbi that don't exist (in annotations)

As mentioned in the previous section, viterbi will theoretically tend to miss smaller genes +/- inter-gene regions if there are short genes interspersed by an inter-gene region, which can be entirely skipped over to create one large gene. In addition, because stop codons are all similarly likely, the first stop codon may be skipped if it gives an opportunity to lengthen the gene. This is evidenced by the fact that the average gene



length of viterbi genes that were partially unmatched by the annotations is ~1066, more than 15% greater than the average codon length ~920.