

1 Genotype Likelihoods from Reads

$$\begin{aligned}
L(g = 1) &= p(d | g = 1) \\
&= p(d, g = ra | g = 1) + p(d, g = rb | g = 1) + p(d, g = rc | g = 1) \\
&= \sum_a p(d | g = ra) \times p(g = ra | g = 1)
\end{aligned}$$

Here we do not favour any heterozygous genotype, and all have likelihood 1/3. This may be changed to reflect empirical or dbSNP data

$$\begin{aligned}
L(g = 1) &= 1/3 \sum_a p(d | g = ra) \\
&= 1/3 \sum_a p(d | g = ra, \text{ado}) \times p(\text{ado}) + p(d | g = ra, \text{no ado})(1 - p(\text{ado})) \\
p(d | g = ra, \text{ado}) &= p(d | g = ra, \text{drop r}) * p(\text{drop r}) + p(d | g = ra, \text{drop a}) * p(\text{drop a})
\end{aligned}$$

Here we assume either allele is equally likely to be dropped in an ado event and $p(\text{drop r}) = p(\text{drop a}) = 0.5$. This is unlikely to change.

$$\begin{aligned}
p(d | g = ra, \text{ado}, \text{drop a}) &= \prod_i p(d_i | g = rr) \\
p(d | g = ra, \text{ado}, \text{drop r}) &= \prod_i p(d_i | g = aa)
\end{aligned}$$

2 Cell-locus Posterior probabilities

Using Bayes' rule:

$$\begin{aligned}
p(g = k | d) &= \frac{p(d | g = k) p(g = k)}{p(d)} \\
&= \frac{p(d | g = k) \mu^k (1 - \mu)^{2-k}}{p(d)}
\end{aligned}$$

where k is the mutation rate, a learnable parameter. Note: this parameter may be overestimated if the algorithm finds more mutations, increases the rate prior, and so finds more mutations. There may be no reason for this to converge.

Since $p(d)$ is the same for all values of k at a cell-locus, we do not need to find it and can simply normalise.

3 Probabilistic Hamming distance

The Hamming distance between two sequences s, p both length n is given by

$$\sum_i^n (1 - \delta_{s_i p_i})$$

where δ_{ab} is the Kronecker delta. Since we have a probabilistic tree, we use a similar metric but weighted by the posterior probabilities of the genotypes at each locus:

$$\sum_i^n \sum_{(a,b) \in \{0,1\} \times \{0,1\}} (1 - \delta_{ab}) p(s_i p_i = ab)$$