Assignment A1: HWE

Choose 3 out of the 5 exercises.

[A1-1] The Agouti Gene

[A1-2] Scarlet Tiger-Moth

[A1-3] 1 Locus, 3 Alleles

[A1-4] Brown Hare

[A1-5] Bitter Taste

[A1-1] The Agouti Gene

Genotype of agouti rabbits : AA or Aa (n=60)

Genotype of non-agouti rabbits : aa (n=51)

$f(aa) = q^2 = \frac{51}{111} = 0.46 \Rightarrow$ 46% are non-agouti rabbits

$q = \sqrt{0.46} = 0.68 \Rightarrow f(a) = 0.68$

$p + q = 1 \Rightarrow p = 1 - 0.68 = 0.32 \Rightarrow f(A) = 0.32$

$f(AA) = f(A)^2 = p^2 = 0.10$

10% of the animals in this population are homozygous agouti rabbits.

A1-2 - Scarlet Tiger-Moth

Scarlet Tiger Moth (*Callimorpha dominula)*

A1-2 - Scarlet Tiger-Moth

Scarlet Tiger Moth (*Callimorpha dominula)*

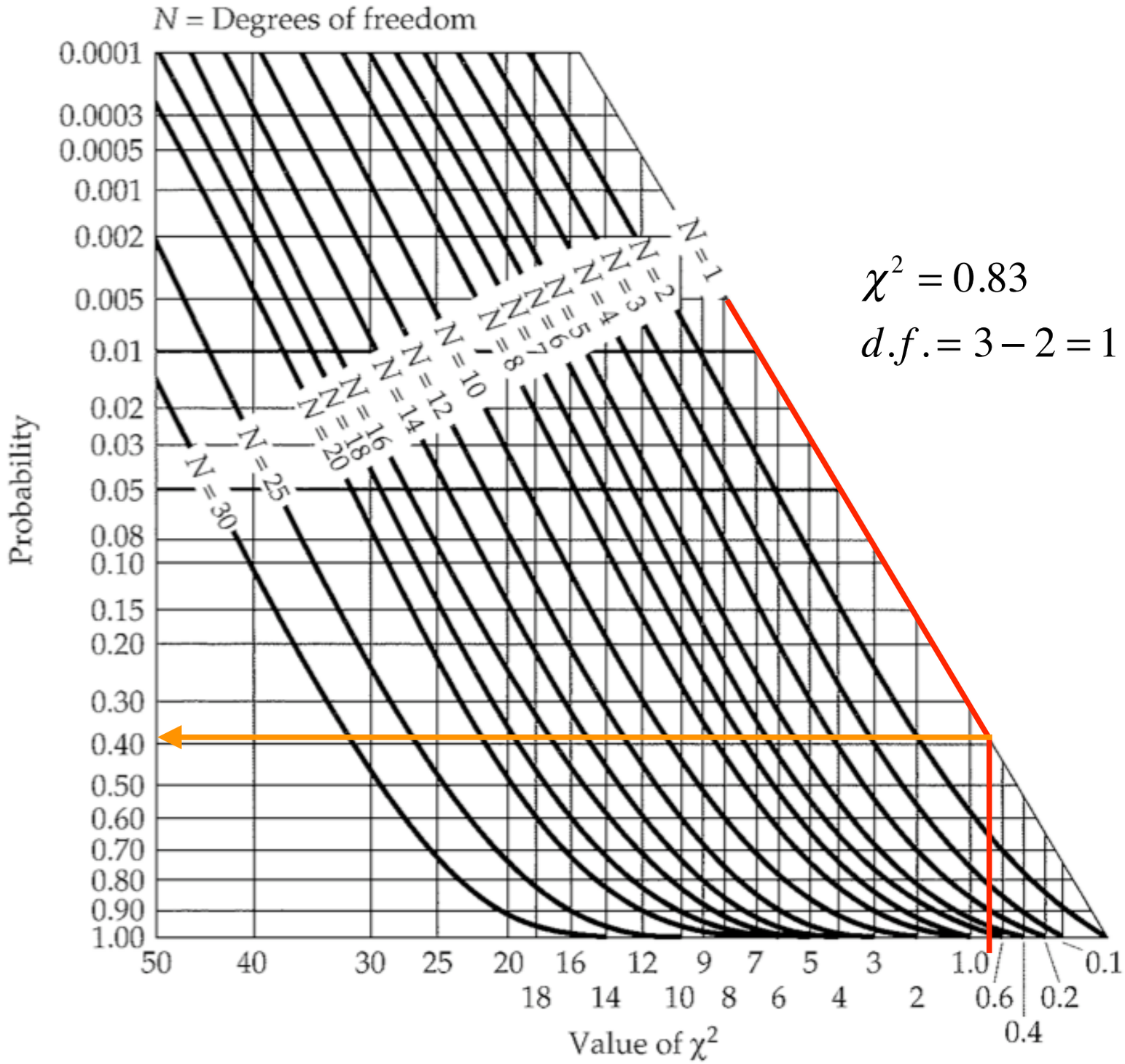
	AA (white-spotted)	Aa (intermediate)	aa (little spotting)	sum
$N_{observed}$	1469	138	5	1612
$N_{expected}$	1467.4	141.2	3.4	1612
$\frac{(obs-exp)^2}{exp}$	0.0017	0.0725	0.7529	0.8272

(a) Allele Frequency: $p = \frac{1469}{1612} + \frac{1}{2}\frac{138}{1612} = \frac{1538}{1612} = 0.954 \quad q = 1 - 0.954 = 0.046$

(b) HW expectation:

$$f(A_1A_1)_{exp} = p^2N = 1467.4$$
$$f(A_1A_2)_{exp} = 2pqN = 141.2$$
$$f(A_2A_2)_{exp} = q^2N = 3.4$$

(c) Pearson's chi-square test: $\chi^2 = 0.83$



$$\chi^2 = 0.83$$

$$d.f. = 3 - 2 = 1$$

1-pchisq(χ^2, d.f.)

p=0.362

```
library(HardyWeinberg)
x <- c(AA = 1469,Aa = 138,aa = 5)
HWtest=HWChisq(x, c = 0, verbose = TRUE)
```

```
Chi2     =   0.8309
p-value  =   0.3620
D        =  -1.6029
```

⇒The population of Scarlet Tiger-Moth seems to be at HW at this locus.

```
Chi2 : value of the chi-square statistic
p-value : p-value of the chi-square test for Hardy-Weinberg equilibrium
D : half the deviation from Hardy-Weinberg equilibrium for the AB genotype
```

[A1-3] 1 Locus, 3 Alleles

Example: 1 locus 3 alleles							
Genotypes	AA	AB	AC	BB	BC	CC	Sum
Counts	17	86	5	61	9	0	178
Frequencies	0.096	0.483	0.028	0.343	0.051	0	1.000

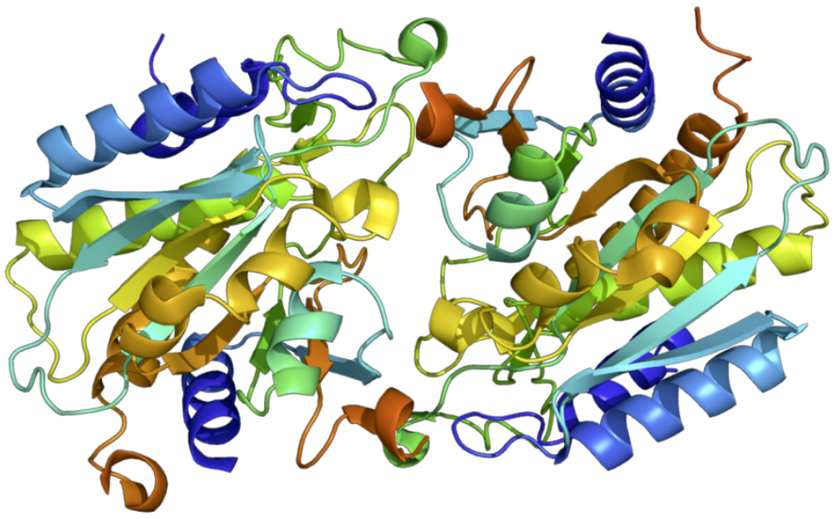
Allele frequencies

$f(A) = 0.096 + 0.5(0.483+0.028) = \mathbf{0.351} \Rightarrow 35.1\%$

$f(B) = 0.343 + 0.5(0.051+0.483) = \mathbf{0.609} \Rightarrow 60.9\%$

$f(C) = 0.000 + 0.5(0.051+0.028) = \mathbf{0.039} \Rightarrow 3.9\%$

[A1-4] Brown Hare



Aminoacylase-1 is an enzyme that in humans is encoded by the **ACY1** gene*

	Genotype	Observed
1	100/100	4
2	100/81	6
3	81/81	14
4	100/66	4
5	81/66	7
6	66/66	3
	Total	38

Is the sampled population in Hardy-Weinberg proportions at locus ACYI?

	Genotype	Observed	Expected
1	100/100	4	2.1
2	100/81	6	9.7
3	81/81	14	11
4	100/66	4	4
5	81/66	7	9.2
6	66/66	3	1.9
Total		38	37.9

C

$$N_{100/100} = \hat{p}^2 N_{total}$$
$$N_{100/81} = 2\hat{p}\hat{q} N_{total}$$
$$N_{81/81} = \hat{q}^2 N_{total}$$
$$N_{100/66} = 2\hat{p}\hat{r} N_{total}$$
$$N_{81/66} = 2\hat{q}\hat{r} N_{total}$$
$$N_{66/66} = \hat{r}^2 N_{total}$$

A

$$\hat{p} = \frac{2N_{100/100} + N_{100/81} + N_{100/66}}{2N_{total}} = \frac{8+6+4}{76} = 0.237$$

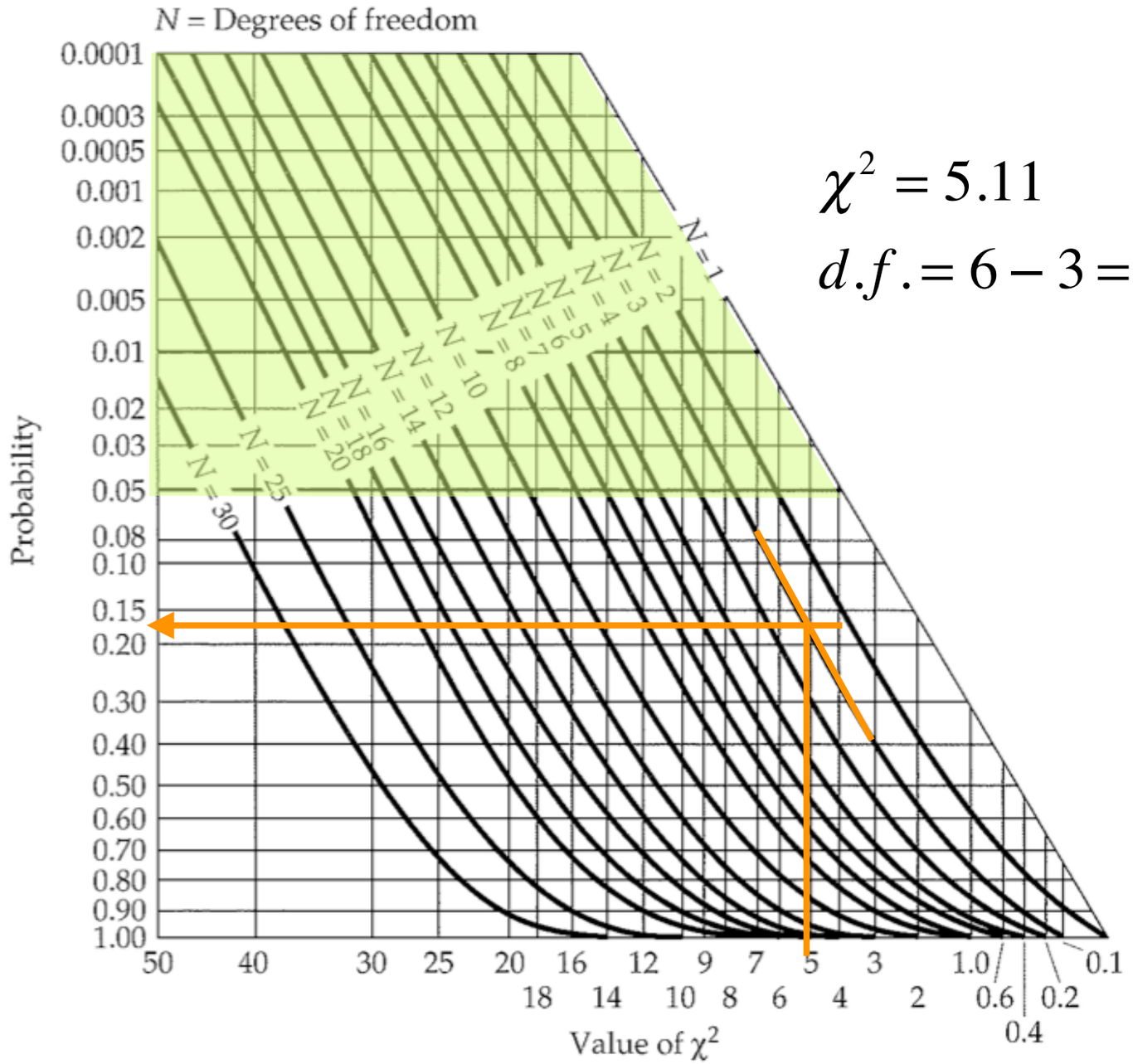
$$\hat{q} = \frac{2N_{81/81} + N_{100/81} + N_{81/66}}{2N_{total}} = \frac{28+6+7}{76} = 0.539$$

$$\hat{r} = \frac{2N_{66/66} + N_{100/66} + N_{81/66}}{2N_{total}} = \frac{6+4+7}{76} = 0.224$$

B

	Genotype	Observed	Expected	$(o-e)^2/e$
1	100/100	4	2.1	1.72
2	100/81	6	9.7	1.41
3	81/81	14	11	0.82
4	100/66	4	4	0.00
5	81/66	7	9.2	0.53
6	66/66	3	1.9	0.64
	Total	38	37.9	**5.11**

$$\chi^2 = \sum \frac{(\text{oberved} - \text{expected})^2}{\text{expected}} = 5.11$$



$\chi^2 = 5.11$

$d.f. = 6 - 3 = 3$

1-pchisq(χ^2, d.f.)

p=0.164

⇒ We accept the H_0. The sampled population of brown hare is at HW equlibrium at locus ACY1.

[A1-5] Bitter Taste

Genetic, Functional, and Phenotypic Diversity in TAS2R38-Mediated Bitter Taste Perception

Abstract

Mutational polymorphism in the TAS2R38 bitter taste receptor is a key determinant of threshold taste detection of isolated compounds, such as phenylthiocarbamide (PTC) and propylthiouracil (PROP), as well as complex orosensation-mediated traits such as diet choice and smoking habits. These relationships are accounted for, in part, by 2 common alleles differing in functionality, TAS2R38-PAV and TAS2R38-AVI. However, TAS2R38 harbors extensive additional polymorphism whose functional significance remains unknown. To examine this variation, we ascertained genetic diversity in 56 Caucasian subjects via whole-gene sequencing, analyzed allele-specific responses to 5 TAS2R38 agonists (PTC, PROP, goitrin, methimazole, and sinigrin) using *in vitro* assays, and assessed genotypic associations with threshold detection phenotypes. Sequencing identified 3 single-nucleotide substitutions encoding 3 amino acid changes (C145G/P49A, C785T/A262V, and A886G/I296V), which combined to form 6 haplotypes in our sample. *In vitro* assays revealed a continuous range of response across alleles, and associations with threshold were significant for all single nucleotide polymorphisms ($P < 0.002$) and PAV/AVI haplotypes ($P < 0.001$). Haplotypes other than PAV and AVI did not exhibit phenotypic associations in our sample, possibly as a result of their low frequencies. However, prior studies have indicated that these alleles are common in some global regions, suggesting that alleles rare in our sample may be phenotypically relevant in other populations.

Behrens et al. (2013) Genetic, Functional, and Phenotypic Diversity in TAS2R38-Mediated Bitter Taste Perception.

```
### [E] Bitter Taste

# Diplotype    145   785   886 Counts
# AAI / PAV     GC    CC    AG       1
# AAV / AVI     GG    CT    GA       2
# AVI / AVI     GG    TT    AA       9
# PAI / PVI     CC    CC    AA       1
# PAV / AAV     CG    CC    GG       3
# PAV / AVI     CG    CT    GA      27
# PAV / PAV     CC    CC    GG      12
# PAV / PVI     CC    CC    AA       1
```

```
## ------------------
## Locus 145
## ------------------

# N(GG)= 2 +  9 =11
# N(CC)= 1 + 12 +  1 = 14
# N(GC)= 1 +  3 + 27 = 31

l145   <- c(GG = 11, CC = 14, GC = 31)
HWtest <- HWChisq(l145 ,c = 0 , verbose = TRUE)

# Chi-square test for Hardy-Weinberg equilibrium (autosomal)
# Chi2 = 0.682 DF = 1 p-value = 0.409 D = 1.540 f = -0.110

# => P-value > 0.05 - We assume locus is in HW proportions.
```

```
## ------------------
## Locus 785
## ------------------

# N(CC)= 1 + 1 + 3 + 12 + 1 = 18
# N(TT)= 9
# N(CT)= 2 + 27 = 29
```

```
l785   <- c(CC = 18, TT = 9, CT = 29)
HWtest <- HWChisq(l785, c = 0, verbose = TRUE)

# Chi-square test for Hardy-Weinberg equilibrium (autosomal)
# Chi2 = 0.224 DF = 1 p-value = 0.636 D = 0.862 f = -0.063

# => P-value > 0.05 - We assume locus is in HW proportions.
```

```
## ------------------
## Locus 886
## ------------------

# N(AA)= 9 +  1 +  1 = 11
# N(GG)= 3 + 12 = 15
# N(AG)= 1 +  2 + 27 = 30
```

```
l886   <- c(AA = 11, GG = 15, CT = 30)
HWtest <- HWChisq(l886, c = 0, verbose = TRUE)

# Chi-square test for Hardy-Weinberg equilibrium (autosomal)
# Chi2 = 0.331 DF = 1 p-value = 0.564 D = 1.071 f = -0.076

# => P-value > 0.05 - We assume locus is in HW proportions.
```