Models

Models

- Intentional simplification of complex relationships
  - Eliminate extraneous detail, focus on key parameters
  - Appropriate and useful first approximations
- Evaluate fit of data to model
  - Poor fit may implicate violation of model assumptions
  - Refining of models tells us which parameters most important
- Population genetics relies heavily on mathematical models
  - Specify the mathematical relationships among parameters that characterize a population

Random Mating

- One of the most important models in population genetics
- Frequency of mating pairs determined by genotype frequencies

Male Genotype Frequency	Female Genotype Frequency		
	A_1A_1 (P_F)	A_1A_2 (H_F)	A_2A_2 (Q_F)
A_1A_1 (P_M)			
A_1A_2 (H_M)			
A_2A_2 (Q_M)			

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A_1A_1 (P_M)	P_MP_F	P_MH_F	P_MQ_F
A_1A_2 (H_M)	H_MP_F	H_MH_F	H_MQ_F
A_2A_2 (Q_M)	Q_MP_F	Q_MH_F	Q_MQ_F

Random Mating

- One of the most important models in population genetics
- Frequency of mating pairs determined by genotype frequencies
- Also called ‘panmictic’ model

Non-overlapping Generations

Birth
Reproduction
Death

Birth
Reproduction
Death

Birth
Reproduction
Death

Generation t -2

Generation t -1

Generation t

Hardy-Weinberg Model

- Both models convenient first approximations for complex populations
- What happens when we combine them?
- What are consequences of random mating in a non-overlapping generation model?

Godfrey Harold Hardy

Wilhelm Weinberg

HW Model Assumptions

- Discrete generations
- Random mating
- Sexual reproduction
- Diploid
- Bi-allelic locus
- Allele frequencies equal in males, females
- Large population size
- No migration
- No mutation
- No selection

Hardy-Weinberg Principle

- One of first major principles in population genetics
- Describes relationship between genotype frequency and allele frequency
  - Equilibrium state
- Autosomal locus will alleles A, a
  - Frequencies of A, a: p, q
- Genotypes AA, Aa, aa

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  - Frequencies of A, a: p, q
- Genotypes AA, Aa, aa
  - HW frequencies: p^2, $2pq$, q^2

Hardy-Weinberg Principle

Frequency(A) = p
Frequency(a) = q

Frequency(AA) = P
Frequency(Aa) = H
Frequency(aa) = Q

Mating
AA x AA
AA x Aa
AA x aa
Aa x Aa
Aa x aa
aa x aa

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Mating	Frequency of Mating
AA x AA	
AA x Aa	
AA x aa	
Aa x Aa	
Aa x aa	
aa x aa	

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Mating	Frequency of Mating
AA x AA	P^2
AA x Aa	
AA x aa	
Aa x Aa	
Aa x aa	
aa x aa	

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Mating	Frequency of Mating
AA x AA	P^2
AA x Aa	$2PH$
AA x aa	
Aa x Aa	
Aa x aa	
aa x aa	

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$P' =$

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$$P' = P^2 + \frac{1}{2}2PH + \frac{1}{4}H^2$$

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$$P' = P^2 + \frac{1}{2}2PH + \frac{1}{4}H^2 = \left(P + \frac{H}{2}\right)^2$$

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$$H' = \frac{1}{2}2PH + 2PQ + \frac{1}{2}H^2 + \frac{1}{2}2HQ$$

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$$H' = \frac{1}{2}2PH + 2PQ + \frac{1}{2}H^2 + \frac{1}{2}2HQ = 2(P + \frac{H}{2})(Q + \frac{H}{2})$$

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$$Q' = \frac{1}{4}H^2 + \frac{1}{2}2HQ + Q^2$$

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$$Q' = \frac{1}{4}H^2 + \frac{1}{2}2HQ + Q^2 = \left(Q + \frac{H}{2}\right)^2 = q^2$$

$$p' =$$

Hardy-Weinberg Principle

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$$p' = P' + \frac{1}{2}H'$$

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$$p' = P' + \frac{1}{2}H' = p^2 + \frac{1}{2}2pq = p(p + q)$$

Hardy-Weinberg Principle

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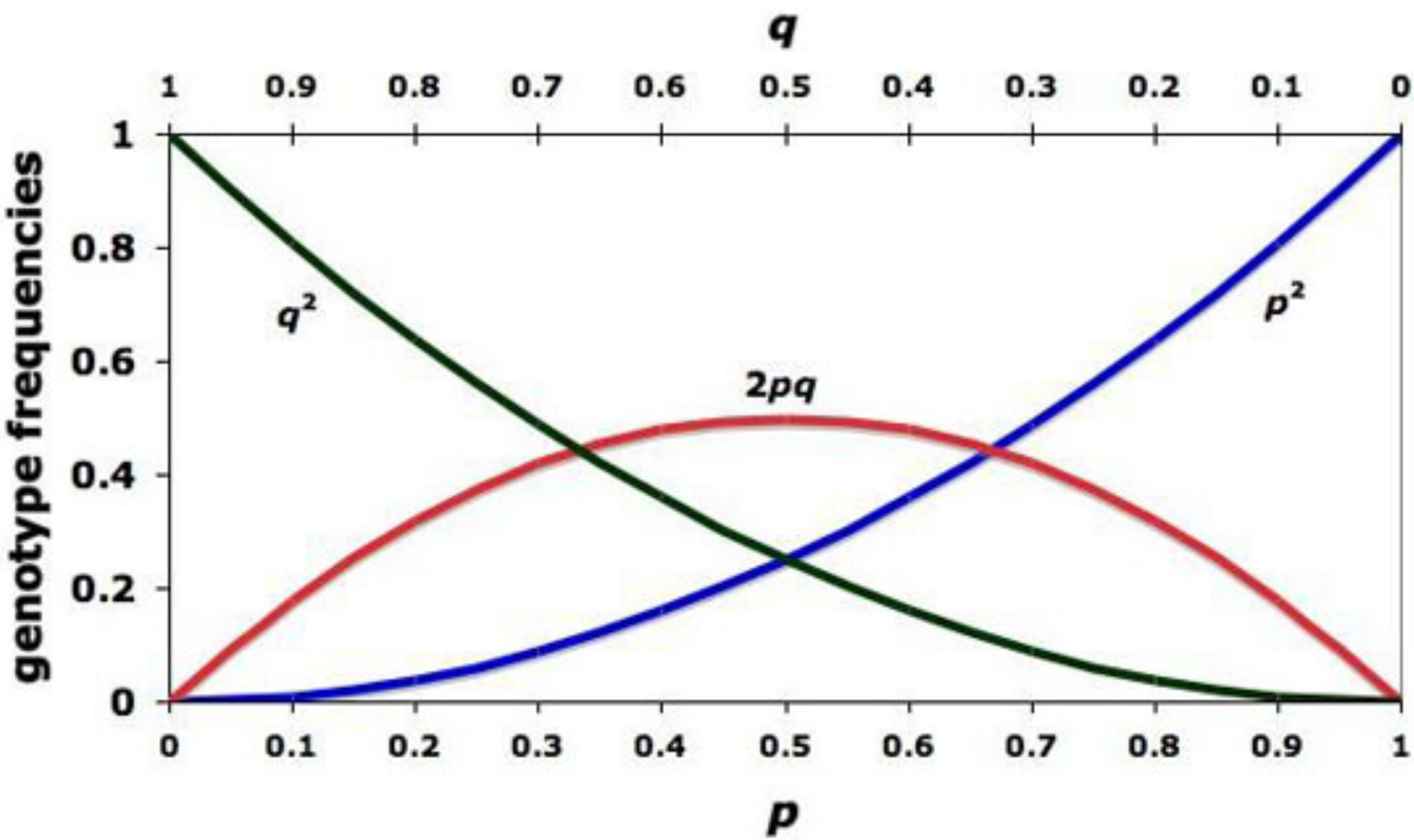
$$p' = P' + \frac{1}{2}H' = p^2 + \frac{1}{2}2pq = p(p+q) = p$$

$$q' = Q' + \frac{1}{2}H' = q^2 + \frac{1}{2}2pq = q(q+p) = q$$

- Allele frequency unchanged across generations
  - Mendelian inheritance itself preserves variation
- HWE achieved in ONE generation
  - Equal allele frequencies in males & females, discrete generations

HWE Genotype Frequencies



Hardy-Weinberg Principle

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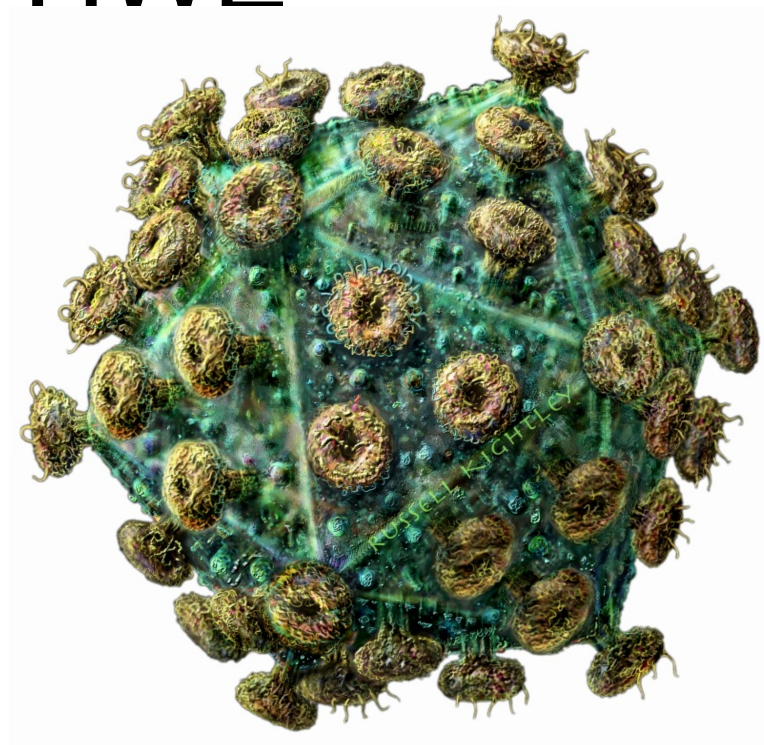
- Describes relationship between genotype frequency and allele frequency
  - Equilibrium state
- Autosomal locus will alleles A, a
  - Frequencies of A, a: p, q
- Genotypes AA, Aa, aa
  - HW frequencies: p^2, $2pq$, q^2
- Once at HWE, allele & genotype freq constant

Example test of HWE

- *CCR5Δ*
- 338 individuals sampled
  - Denmark, Germany



	Observed	Expected
CCR5/CCR5	265	
CCR5/CCR5Δ	66	
CCR5Δ/CCR5Δ	7	

Lucotte and Mercier 1998

Example test of HWE

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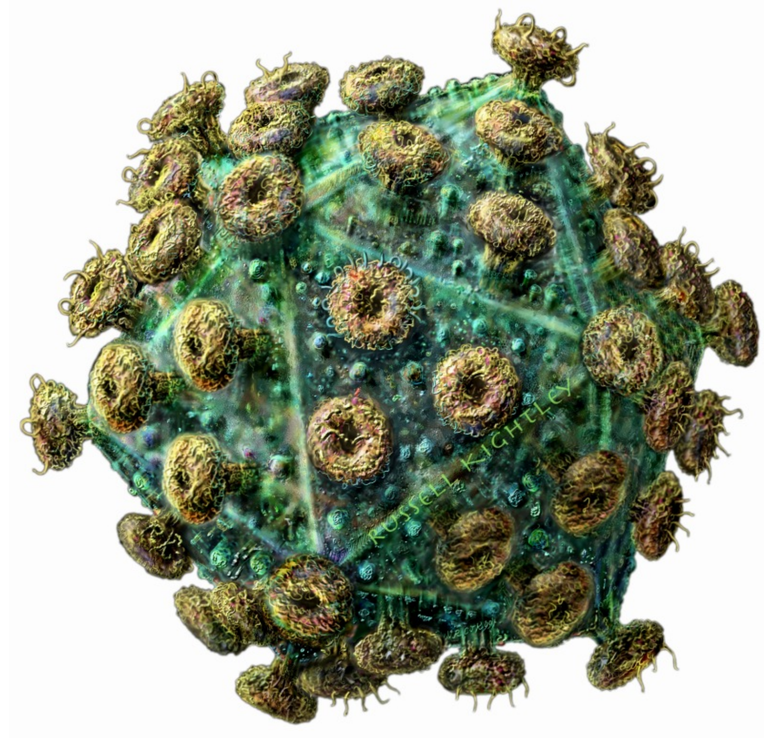


	Observed	Expected
CCR5/CCR5	265	
CCR5/CCR5Δ	66	
CCR5Δ/CCR5Δ	7	

$$\hat{p} = \frac{265 + \frac{1}{2}(66)}{338} = 0.882$$

$$\hat{q} = \frac{7 + \frac{1}{2}(66)}{338} = 0.118$$

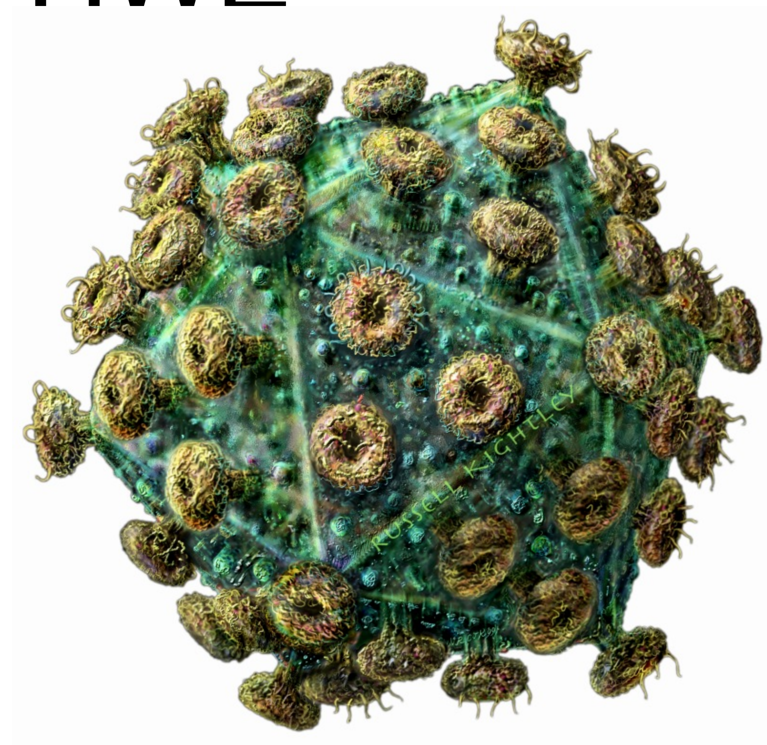
$$P = \hat{p}^2 = (0.882)^2 = 0.78$$

$$H = 2\hat{p}\hat{q} = 2(0.882)(0.118) = 0.21$$

$$Q = \hat{q}^2 = (0.118)^2 = 0.01$$

Lucotte and Mercier 1998

Example test of HWE



- *CCR5Δ*
- 338 individuals sampled
  - Denmark, Germany

	Observed	Expected
CCR5/CCR5	265	262.9
CCR5/CCR5Δ	66	70.4
CCR5Δ/CCR5Δ	7	4.7

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

$$\chi^2 = \frac{(265 - 262.9)^2}{269.2} + \frac{(66 - 70.4)^2}{70.4} + \frac{(7 - 4.7)^2}{4.7}$$

$$\chi^2 = 1.42$$

df = Number of data classes - number parameters estimated from data – 1

df = 3 - 1 – 1 = 1 $P = 0.25$