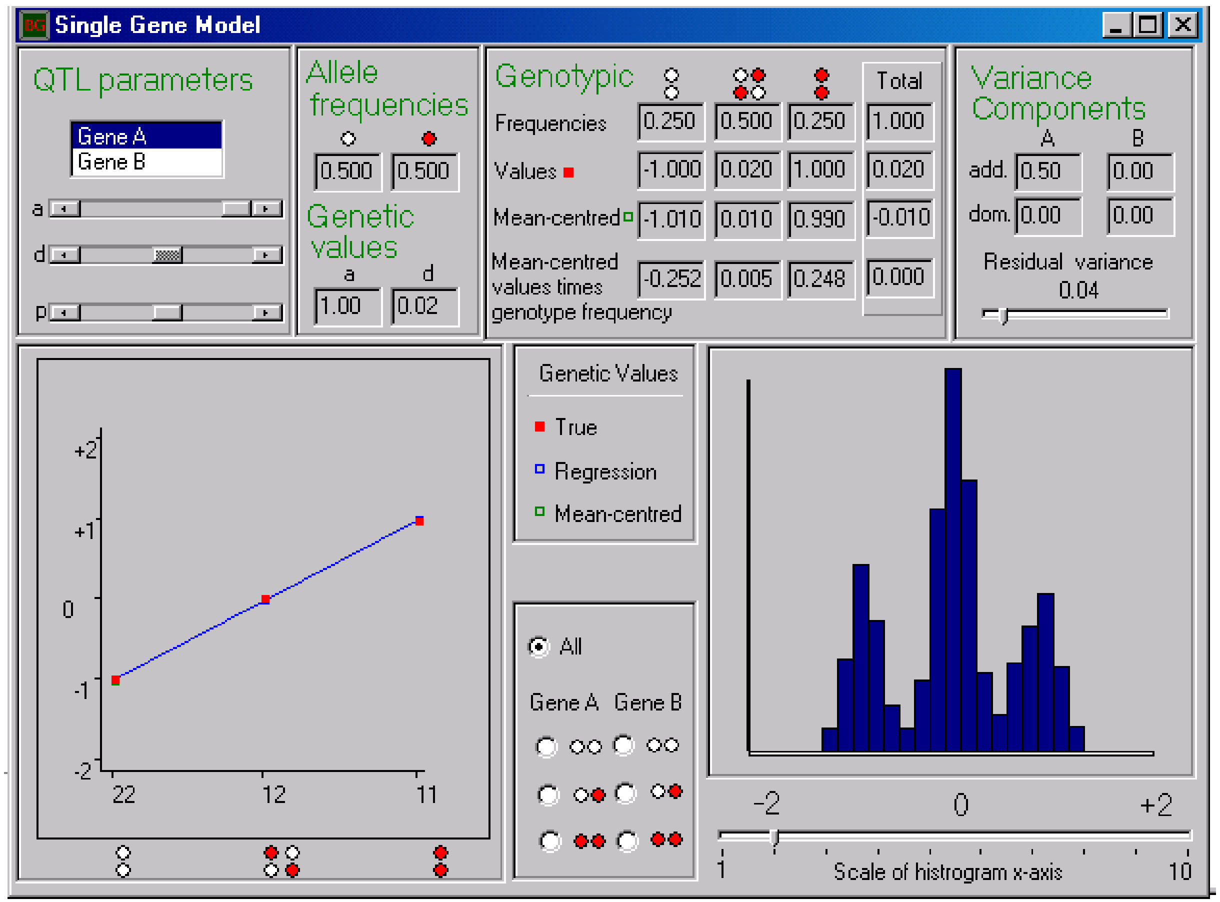
Practical

H:\ferreira\biometric\sgene.exe



Practical

- **Aim** Visualize graphically how allele frequencies, genetic effects, dominance, etc, influence trait mean and variance

Ex1

a=0, d=0, p=0.4, Residual Variance = 0.04, Scale = 2.
Vary a from 0 to 1.

Ex2

a=1, d=0, p=0.4, Residual Variance = 0.04, Scale = 2.
Vary d from -1 to 1.

Ex3

a=1, d=0, p=0.4, Residual Variance = 0.04, Scale = 2.
Vary p from 0 to 1.

Look at scatter-plot, histogram and variance components.

Some conclusions

1. Additive genetic variance depends on

    allele frequency p

    & additive genetic value a

    as well as

    dominance deviation d

2. Additive genetic variance typically greater than dominance variance

Biometrical model for single biallelic QTL

1. Contribution of the QTL to the Mean (X)

2. Contribution of the QTL to the Variance (X)

3. Contribution of the QTL to the Covariance (X,Y)

Biometrical model for single biallelic QTL

3. Contribution of the QTL to the Cov *(X,Y)*

$$Cov(X,Y) = \sum_i (x_i - \mu_X)(y_i - \mu_Y) f(x_i, y_i)$$

	AA (*a*-*m*)	*Aa* (*d*-*m*)	*aa* (-*a*-*m*)
AA (*a*-*m*)	$(a-m)^2$		
Aa (*d*-*m*)	$(a-m)(d-m)$	$(d-m)^2$	
aa (-*a*-*m*)	$(a-m)(-a-m)$	$(d-m)(-a-m)$	$(-a-m)^2$

Biometrical model for single biallelic QTL

3A. Contribution of the QTL to the Cov *(X,Y)* – MZ twins

$$Cov(X,Y) = \sum_i (x_i - \mu_X)(y_i - \mu_Y) f(x_i, y_i)$$

	AA *(a-m)*	***Aa*** *(d-m)*	***aa*** *(-a-m)*
AA *(a-m)*	$p^2(a-m)^2$		
Aa *(d-m)*	$0\ (a-m)(d-m)$	$2pq(d-m)^2$	
aa *(-a-m)*	$0\ (a-m)(-a-m)$	$0\ (d-m)(-a-m)$	$q^2(-a-m)^2$

$$Cov(X,Y) = (a-m)^2p^2 + (d-m)^2 2pq + (-a-m)^2q^2$$

$$= 2pq[a+(q-p)d]^2 + (2pqd)^2 = V_{A_{QTL}} + V_{D_{QTL}}$$

Biometrical model for single biallelic QTL

3B. Contribution of the QTL to the Cov (X,Y) – Parent-Offspring

	AA $(a-m)$	***Aa*** $(d-m)$	***aa*** $(-a-m)$
AA $(a-m)$	$p^3(a-m)^2$		
Aa $(d-m)$	$p^2q\,(a-m)\,(d-m)$	$pq\,(d-m)^2$	
aa $(-a-m)$	$0\,(a-m)(-a-m)$	$pq^2\,(d-m)(-a-m)$	$q^3(-a-m)^2$

- *e.g.* given an *AA* father, an *AA* offspring can come from either *AA* x *AA* or *AA* x *Aa* parental mating types

AA x *AA* will occur $p^2 \times p^2 = p^4$
and have *AA* offspring Prob()=1

AA x *Aa* will occur $p^2 \times 2pq = 2p^3q$
and have *AA* offspring Prob()=0.5
and have *Aa* offspring Prob()=0.5

Therefore, P(*AA* father & *AA* offspring) $= p^4 + p^3q$

$= p^3(p+q)$

$= p^3$

Biometrical model for single biallelic QTL

3B. Contribution of the QTL to the Cov (X,Y) – Parent-Offspring

	AA $(a-m)$	***Aa*** $(d-m)$	***aa*** $(-a-m)$
AA $(a-m)$	$p^3(a-m)^2$		
Aa $(d-m)$	$p^2q\,(a-m)(d-m)$	$pq\,(d-m)^2$	
aa $(-a-m)$	$0\,(a-m)(-a-m)$	$pq^2\,(d-m)(-a-m)$	$q^3(-a-m)^2$

$$Cov\,(X,Y) = (a-m)^2p^3 + \ldots + (-a-m)^2q^3$$

$$= pq[a+(q-p)d]^2 = \tfrac{1}{2}V_{A_{QTL}}$$

Biometrical model for single biallelic QTL

3C. Contribution of the QTL to the Cov (*X*, *Y*) – Unrelated individuals

	AA *(a-m)*	***Aa*** *(d-m)*	***aa*** *(-a-m)*
AA *(a-m)*	$p^4 (a-m)^2$		
Aa *(d-m)*	$2p^3q\,(a-m)(d-m)$	$4p^2q^2\,(d-m)^2$	
aa *(-a-m)*	$p^2q^2 (a-m)(-a-m)$	$2pq^3\,(d-m)(-a-m)$	$q^4 (-a-m)^2$

$$Cov\,(X,Y) \;=\; (a-m)^2 p^4 + \ldots + (-a-m)^2 q^4$$

$$= 0$$

Biometrical model for single biallelic QTL

3D. Contribution of the QTL to the Cov *(X,Y)* – DZ twins and full sibs

	¼ genome	¼ genome	¼ genome	¼ genome
# identical alleles inherited from parents	**2**	**1** (father)	**1** (mother)	**0**

¼ (2 alleles) + ½ (1 allele) + *¼ (0 alleles)*

MZ twins — *P-O* — *Unrelateds*

$$Cov(X,Y) = \tfrac{1}{4}\,Cov(MZ) + \tfrac{1}{2}\,Cov(P\text{-}O) + \tfrac{1}{4}\,Cov(Unrel)$$

$$= \tfrac{1}{4}(V_{A_{QTL}} + V_{D_{QTL}}) + \tfrac{1}{2}\left(\tfrac{1}{2}V_{A_{QTL}}\right) + \tfrac{1}{4}(0)$$

$$= \tfrac{1}{2}V_{A_{QTL}} + \tfrac{1}{4}V_{D_{QTL}}$$

Summary…

- Biometrical model predicts contribution of a QTL to the mean, variance and covariances of a trait

$$Mean(X) = a(p-q) + 2pqd$$ ← *Association analysis*

$$Var(X) = V_{A_{QTL}} + V_{D_{QTL}}$$ ← *Linkage analysis*

$$Cov(MZ) = V_{A_{QTL}} + V_{D_{QTL}}$$

$$Cov(DZ) = \tfrac{1}{2}V_{A_{QTL}} + \tfrac{1}{4}V_{D_{QTL}}$$

On average!

↓ 0, 1/2 or 1

↓ 0 or 1

↓ For a sib-pair, do the two sibs have 0, 1 or 2 alleles in common?

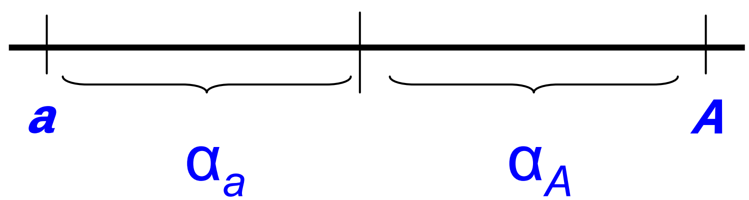
IBD estimation / Linkage

Biometrical model for single biallelic QTL

2A. Average allelic effect (α)

The deviation of the allelic mean from the population mean

	Allele *a*	Population	Allele *A*
Mean (*X*) →	?	$a(p-q) + 2pqd$	?



	AA	*Aa*	*aa*	Allelic mean	Average allelic effect (α)
	a	*d*	*-a*		
A	*p*	*q*		$ap+dq$	$q(a+d(q-p))$
a		*p*	*q*	$dp-aq$	$-p(a+d(q-p))$

Biometrical model for single biallelic QTL

- Denote the average allelic effects
  - $\alpha_A = q(a+d(q-p))$
  - $\alpha_a = -p(a+d(q-p))$

- If only two alleles exist, we can define the *average effect of allele substitution*
  - $\alpha = \alpha_A - \alpha_a$
  - $\alpha = (q-(-p))(a+d(q-p)) = (a+d(q-p))$

- Therefore:
  - $\alpha_A = q\alpha$
  - $\alpha_a = -p\alpha$

Biometrical model for single biallelic QTL

2A. Average allelic effect (α)

2B. Additive genetic variance

The variance of the average allelic effects

$\alpha_A = q\alpha$
$\alpha_a = -p\alpha$

	Freq.	Additive effect	
AA	p^2	$2\alpha_A$	$= 2q\alpha$
Aa	$2pq$	$\alpha_A + \alpha_a$	$= (q-p)\alpha$
aa	q^2	$2\alpha_a$	$= -2p\alpha$

$$V_{A_{QTL}} = (2q\alpha)^2 p^2 + ((q-p)\alpha)^2 2pq + (-2p\alpha)^2 q^2$$
$$= 2pq\alpha^2$$
$$= 2pq[a+d(q-p)]^2$$

$d = 0,\ V_{A_{QTL}} = 2pqa^2$

$p = q,\ V_{A_{QTL}} = \frac{1}{2}a^2$