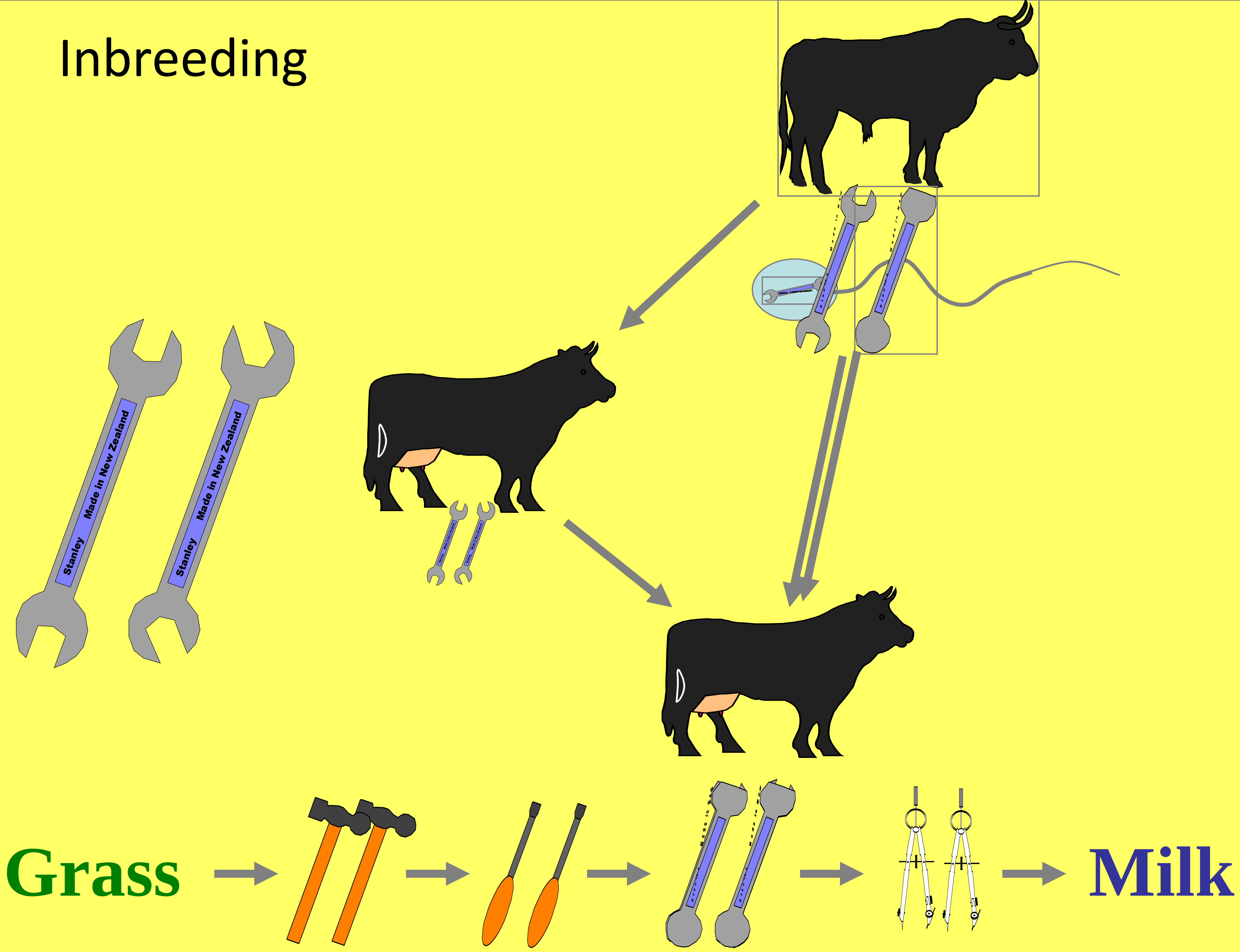
Selection and inbreeding

Inbreeding


Stanley
Made in New Zealand
Stanley
Made in New Zealand
Grass
Milk

So, previous slide illustrates …….

- Inbreeding coefficient

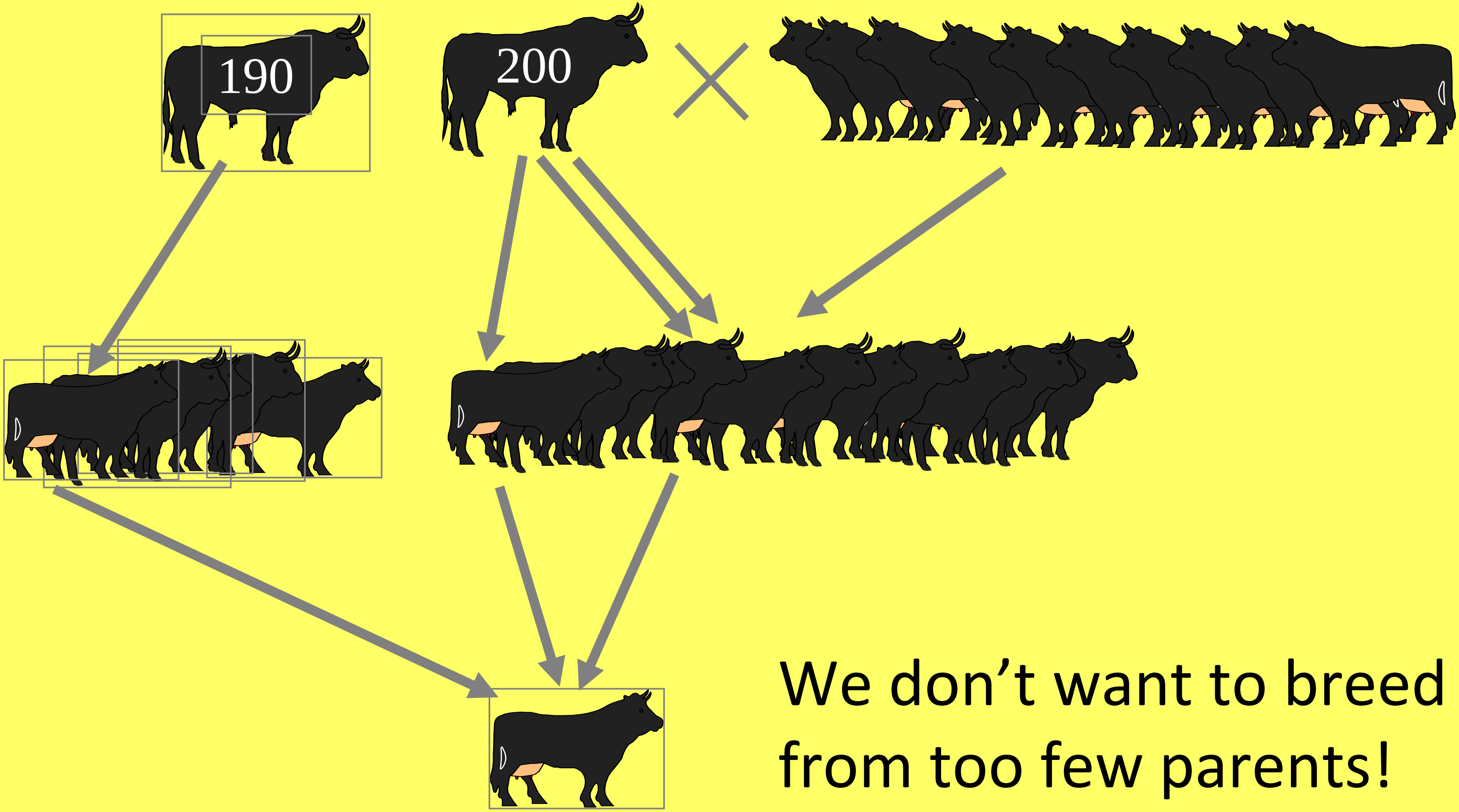
  Animals that have related parents have more chance to carry two alleles that are identical by descend

- Genetic defects

  Inbred individuals have more chance to express genetic defects

- Inbreeding depression:

  Heterozygosity has often positive effects on phenotypes (and therefore inbreeding/homozygisty a negative effect >>



We don’t want to breed from too few parents!

Ne = effective population size

Genetic gain and inbreeding

- Select few individuals
- high genetic gain

but

- low Ne and high F

- Select many individuals
- low genetic gain

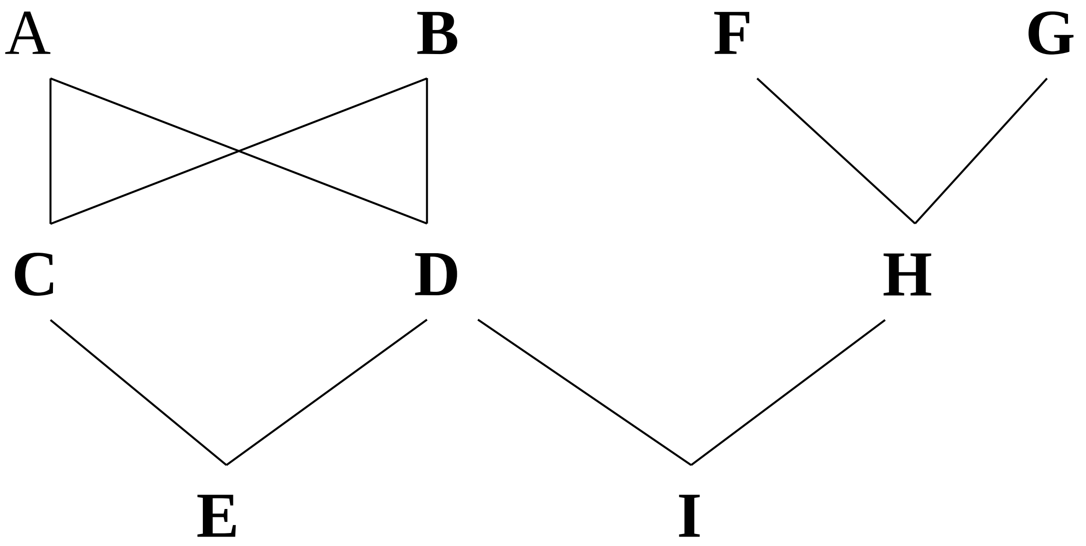
but

- high Ne and low F

Need to balance rates of F and genetic gain

Inbreeding

- Due to the mating of relatives



Which animal(s) in the pedigree are inbred?

Coefficient of inbreeding (F)

- The *coefficient of inbreeding* (F) is the probability that two alleles at a randomly chosen locus are identical by descent (IBD)

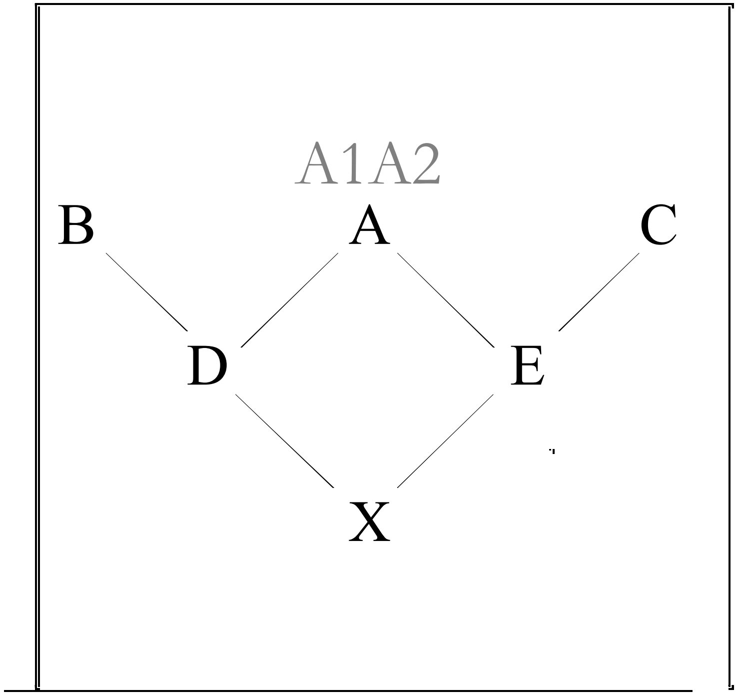
IBD = copies of same alleles from common ancestor

- F ranges from 0 to 1

What is F of individual X?

Recall:

The ***coefficient of inbreeding* (F)** is the probability of 2 alleles at a randomly chosen locus being ***identical by descent***



$$p_{A1A1} = \left(\frac{1}{2} x \frac{1}{2}\right) x \left(\frac{1}{2} x \frac{1}{2}\right) = \frac{1}{16}$$

$$p_{A2A2} = \left(\frac{1}{2} x \frac{1}{2}\right) x \left(\frac{1}{2} x \frac{1}{2}\right) = \frac{1}{16}$$

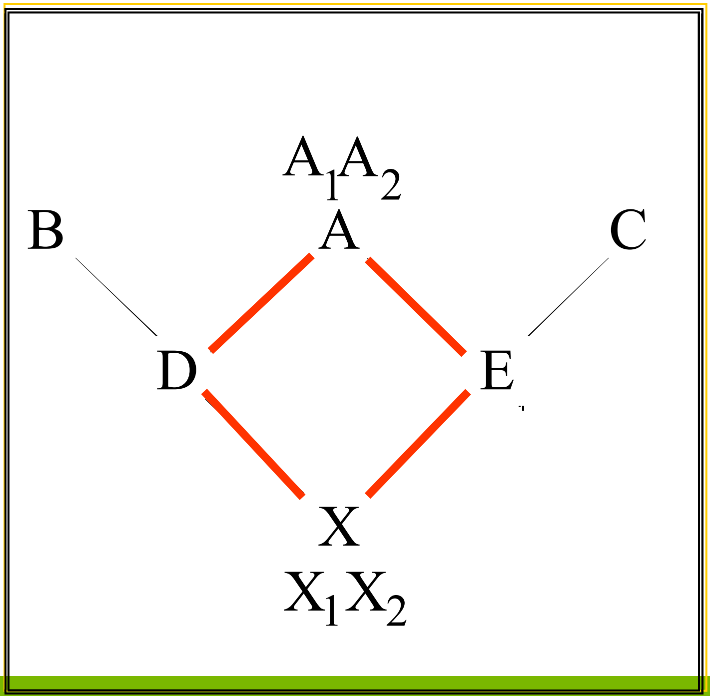
$$F_x = \frac{1}{8}$$

Also: half the relationship among parents

What is F of individual X?

Shortcut ‘loop’ method:

- For one ‘loop’ (path through common ancestor) determine $\frac{1}{2}^n$, where n is the number of individuals in the loop (excluding X)



Loops are:

DAE: $\frac{1}{2}^3$ $\quad F_x = \frac{1}{8}$

Consequences of inbreeding

Inbreeding increases expression of recessive alleles

- Genotype frequencies
  - Non-inbred: q^2 $2pq$ p^2
  - Inbred: q^2+pqF $2pq-2pqF$ p^2+pqF

- Example, q=0.02 (2%)

F	0	0.125	0.25	0.50
Prob. aa (recessive genotype)	0.4 in 1000	2.9 in 1000	5.3 in 1000	10.2 in 1000

Change in genotype frequencies in response to inbreeding

For example, $p=q=0.5$

Genotype	aa	Aa	AA
Frequency	q^2+pqF	$2pq-2pqF$	p^2+pqF
At F=0	0.25	0.50	0.25
At F=0.5	0.375	0.25	0.375
At F=1.0	0.5	0	0.5

Note that allele frequencies do not change

une

Inbreeding depression reduces productivity & viability

- Inbreeding depression
  - Results in lowered performance and viability
  - Reproductive fitness is particularly affected
  - Due to loss of dominance arising from increased homozygosity
- Level of trait depression is variable
  - Often 2-20% decrease in the trait per 10% F

Inbreeding reduces genetic variance

- As individuals become more alike, the *within* population genetic variance decreases

- V_A (with inbreeding) = (1-F) V_A (without inbreeding)

- *Why is this a concern?*

Inbreeding rate

- Inbreeding occurs due to the mating of relatives
- In a closed population inbreeding is inevitable
- Inbreeding rate (ΔF) describes the increase in F over time

The rate of inbreeding

- F at time ‘t’ can be calculated as:

$$F_t = 1 - \left[1 - \frac{1}{2Ne}\right]^t$$

where t is number of generations

- Note that this only holds for no selection and random mating

- More importantly:

Inbreeding Rate ~ $1/2N_e$

  - i.e. need $N_e > 50$ for Inbreeding Rate to be < 1%

    (which maybe about reasonable)

How to restrict inbreeding?

- Mating policies mostly affect
  - progeny inbreeding *(short term)*
  - but not *long term* rate of inbreeding ΔF
  - The long term inbreeding rate depends on ….

effective population size (N_e)

- Long term inbreeding is restricted by restricting the average co-ancestry among selected parents

Effective Population Size: Ne

Accounting for unequal sex ratio

- Effective pop'n size (Ne) reduces towards sex with fewer breeding individuals

$$Ne = \frac{4.N_m.N_f}{N_m + N_f}$$

Males / generation	2	2	2	5	20	1
Females / generation	2	20	200	200	200	99999
N	4	22	202	205	220	100,000
Ne	4	7.3	7.9	19.5	72.7	4

With selection, this formula <u>underpredicts</u> inbreeding (2x)
But it shows that usually, it is controlled by using enough sires

So to prevent inbreeding

- Use enough parents
- Use enough males 10 per generation

- Use males that are not too related to each other

Example of BLUP selection

Terminals - Top 150

Analysis Date Friday, 15 June 2001

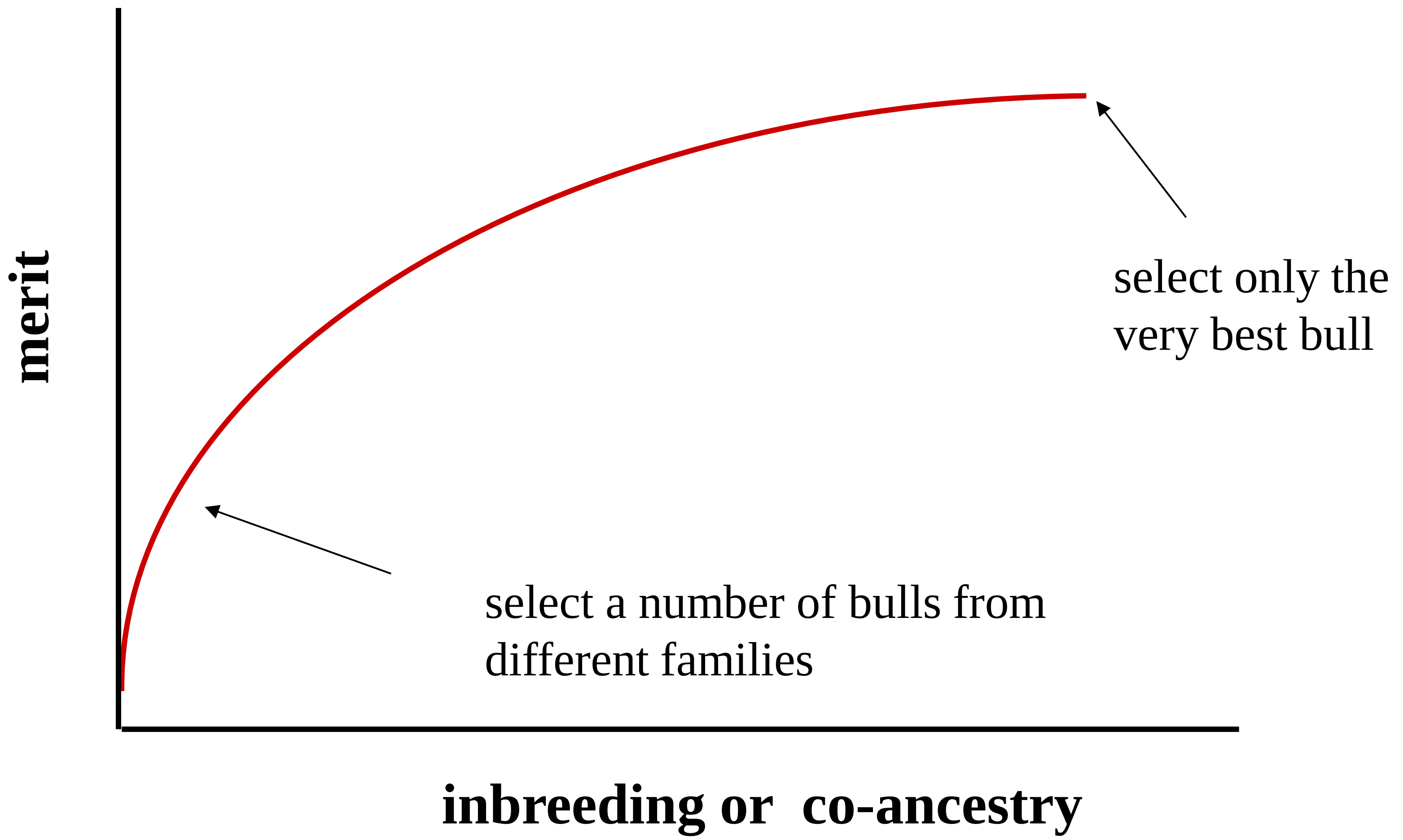
LAMBPLAN

Sires

ID	Stud of breeding	Wwt	Pwwt	Ywt	Pfat	Pemd	Carcase +	Progeny	Inbreeding & Accuracies: Coeff	Weight	Carcase	Sire	Sire of Dam
161972-1999-990196	HILLCROFT FARMS	5.46	14.95	14.94	-1.19	1.62	226.64	38	0.133	83	70	1619721998980093	1630001993930134
162368-1998-980211	KURRALEA	6.60	12.39	12.69	-0.89	2.50	215.20	1148		97	96	1623681994940260	8600401992920175
162204-1999-990453	BETHELREI	8.52	13.38	15.87	-1.18	1.11	211.75	224		93	89	8601221993930205	1619721995950289
161972-1998-980093	HILLCROFT FARMS	5.15	14.40	16.00	-1.08	0.25	207.51	12		80	74	1630001993930134	1603361992920349
161972-1998-980527	HILLCROFT FARMS	8.46	13.45	10.97	-1.66	-0.47	204.10	25		85	76	1619721996960091	1630001993930134
860122-1993-930205	OHIO	6.95	11.94	13.72	-1.60	0.49	203.76	1522		98	97	8601221992920200	8601221987870073
161143-1999-990204	DERRYNOCK	8.39	12.10	12.19	-0.49	2.19	203.60	38		82	76	1623681998980211	1640001993930411
160060-1996-960004	ANNA VILLA	8.56	14.90	16.18	-0.48	0.24	200.47	151		93	87	1632801992920016	1623541990900584
161143-1999-990201	DERRYNOCK	5.43	11.83	11.14	-1.19	0.83	199.83	39		83	77	1623681998980211	1613151995950042
230034-1997-970904	BURWOOD	4.98	11.01	8.82	-2.27	-0.55	198.82	380	0.003	96	92	2300091994940171	2300341994940314
163677-2000-000140	FELIX	6.69	13.56	13.36	-0.59	0.61	197.98	56		70	63	1619721995950289	1600341994940020
160060-1997-970115	ANNA VILLA	6.30	14.47	11.69	-0.42	0.24	196.90	118		90	83	1600601996960004	1600601992920057
162204-1999-990394	BETHELREI	7.42	12.97	14.27	-1.03	0.14	196.85	24		82	74	8601221993930205	1622041996960579
161143-1999-990064	DERRYNOCK	5.10	11.20	10.10	-0.72	1.60	196.01	18		80	74	1623681998980211	1640001994940317
161972-1996-960020	HILLCROFT FARMS	5.32	12.96	10.66	-0.80	0.36	195.20	83		88	75	1630001993930134	
160185-1996-960001	JOLMA	6.19	10.29	10.42	-1.56	0.63	194.57	101		90	83	1630001993930134	1613151991910870
161235-1997-970830	POLLAMBI	7.10	10.69	10.35	-0.88	1.50	194.54	34		87	79	1700991993930002	1612351991910691
163677-1999-990307	FELIX	7.09	12.52	11.59	-1.29	-0.47	192.45	54		83	74	8601221993930205	1636771994940008
162368-1999-990290	KURRALEA	5.53	10.84	10.58	-0.62	1.59	192.11	68		69	62	1623681998980211	1630001993930160
860074-1995-950044	ADELONG	7.17	14.47	13.22	-0.80	-0.94	191.15	448		96	94	8600741993930189	
163000-1998-980575	RENE	7.59	12.01	13.06	-0.50	0.99	190.92	12		71	60	1623681994940260	8600371992920165
162368-1997-970443	KURRALEA	6.58	12.13	7.96	-1.00	0.08	190.69	178		88	83	1640001993930411	8600401992920175
160034-1999-991208	MOSSLEY	5.52	13.45	10.27	-0.53	0.04	190.41	17	0.003	78	70	1621001998980130	1600341994940171
161437-1999-990006	WARRURN	5.41	10.97	10.93	-1.21	0.37	190.26	14		73	65	1604621994940012	1640001993930411

These are sibs so might not select all of them as flock sire

Balancing inbreeding and merit



Balancing Selection and Inbreeding

- Higher selection intensities make bigger gain
- Fewer animals are selected, so also more inbreeding
- This trend is more evident with higher rates of fecundity , e.g. with new reproductive technologies
- Genetic evaluation (BLUP) favors selection of related animals

→rationalization of selection make inbreeding restriction methods a necessity

Jointly optimizing merit and inbreeding

Wray and Goddard, 1994

$x'G + \lambda x'Ax$

λ = penalty on inbreeding

- merit: $x'G$
  - x = vector with each animal's contribution to progeny
  - G = the vector with merit (EBV's) for each animal
- Co-ancestry: $x'Ax$
  - x = vector with each animal's contribution to progeny
  - A = Numerator Relationships Matrix

Remember: $\Delta F = x'Ax/2$ $F_i = 0.5\, a_{ij}$

Vector *x* of animal contributions

Source of animals	Animal#	x = Contribution	
Male candidates	1	0	$\sum = 0.5$
	2	.1	
	3	.05	
	4	0	
	5	.01	
	6	0	
	7	0	
	8	0	
	…	…	
Female candidates	101	0	$\sum = 0.5$
	102	.01	
	103	.01	
	104	.01	
	105	0	
	106	0	
	107	0	
	108	.08	

Note that this does not only determines number of selected sires and dams, but also allows for unequal contributions

Balancing inbreeding and merit

- Restricting co-ancestry but this slows genetic (short term) progress
- How much inbreeding can we afford?
- Often inbreeding is restricted by limiting ΔF to a certain preset value
- This optimal value may depend on your situation (how open is your nucleus?)

Optimizing genetic contributions

- Maximize objective function

$$x'G + \underline{\lambda} x'Ax$$

λ = *inbreeding penalty*

Question: what is best value for λ ?

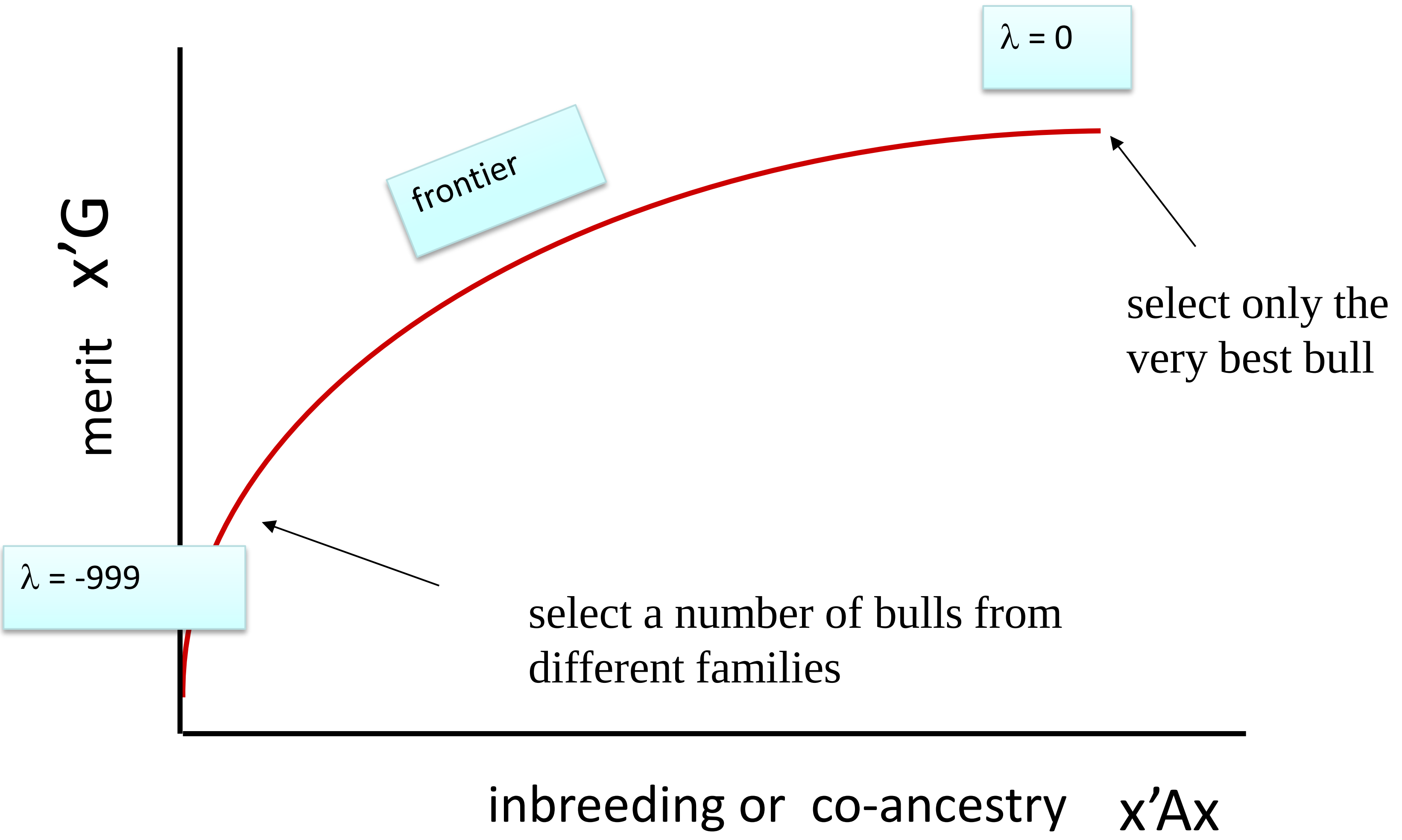
How much inbreeding can we afford?

Could preset rate of inbreeding (e.g. 1%) and determine λ accordingly (Meuwissen, 1997)

Alternative: look at graph (next slide)

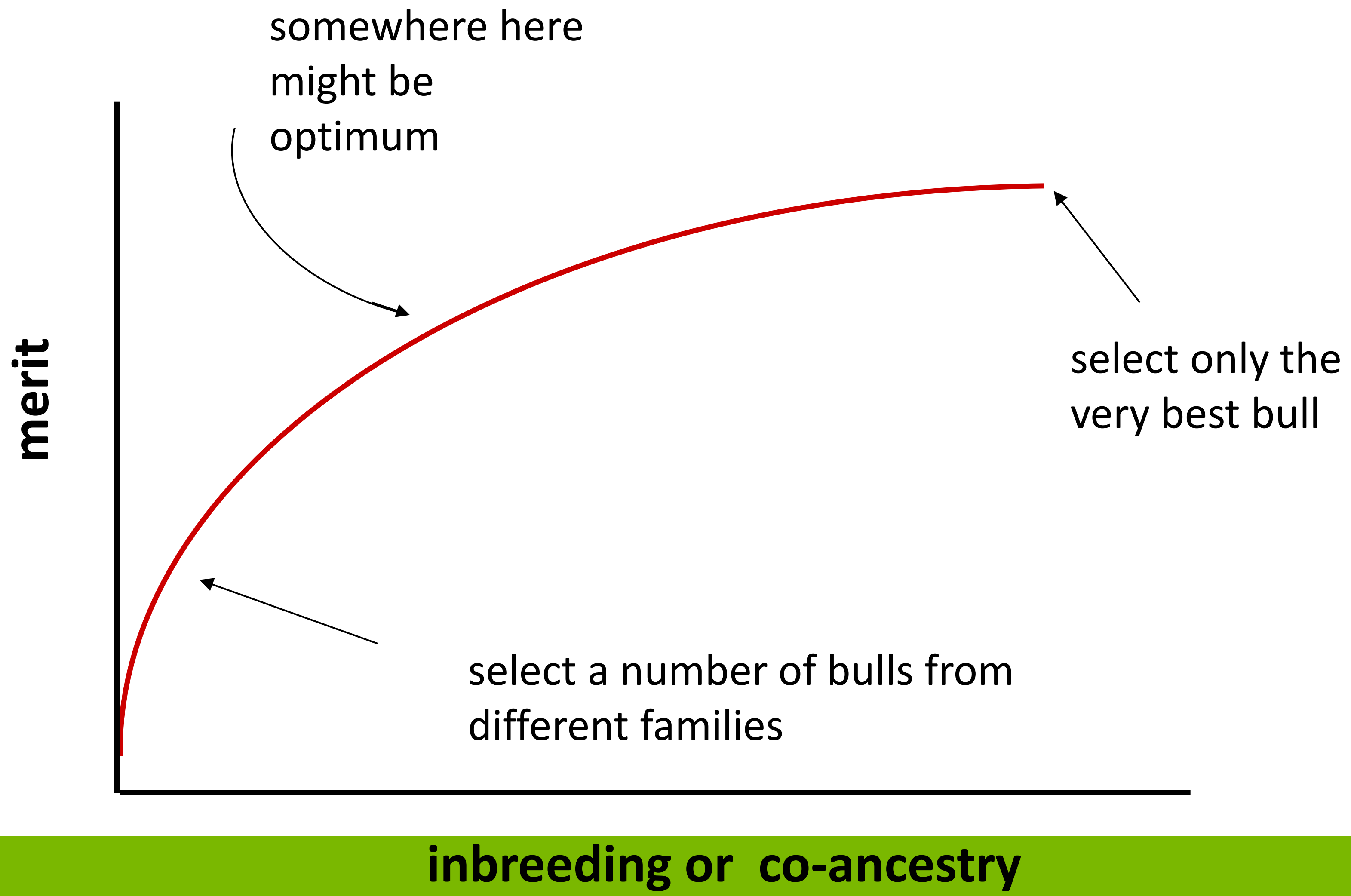
Balancing inbreeding and merit

$x'G + \underline{\lambda} x'Ax$



Balancing inbreeding and merit

This graph will look different for each population



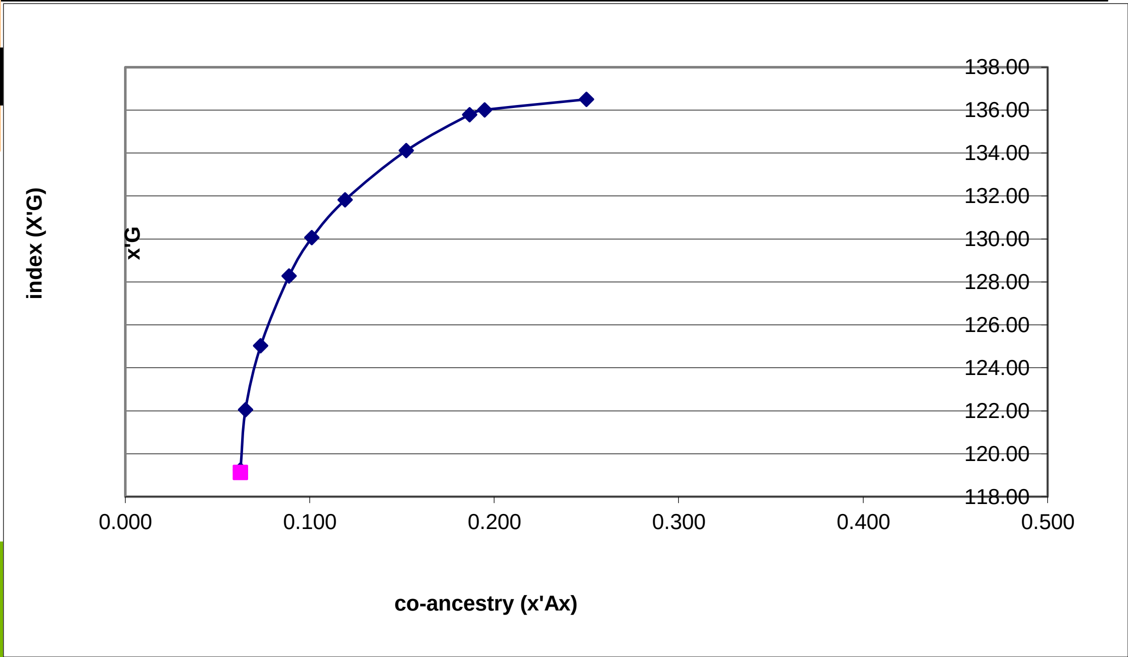
Example Optimal Contributions

xGxAx.xls

	X	nmales	nfemales	G	Relationships Matrix							
Male 1	**0.125**	4	4	**127**	**1.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Male 2	0.125			**122**	0.00	**1.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Male 3	0.125			**150**	0.00	0.00	**1.00**	**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Male 4	0.125			**109**	0.00	0.00	0.00	**1.00**	**0.00**	**0.00**	**0.00**	**0.00**
Female 1	0.125			**120**	0.00	0.00	0.00	0.00	**1.00**	**0.00**	**0.00**	**0.00**
Female 2	0.125			**123**	0.00	0.00	0.00	0.00	0.00	**1.00**	**0.00**	**0.00**
Female 3	0.125			**89**	0.00	0.00	0.00	0.00	0.00	0.00	**1.00**	**0.00**
Female 4	0.125			**113**	0.00	0.00	0.00	0.00	0.00	0.00	0.00	**1.00**

Find optimal contributions

average merit of progeny	x'G	119.12
Inbreeding weight	λ	**-9999999.0**
·rage co-acestry of progeny	x'Ax	0.063



Example Optimal Contributions

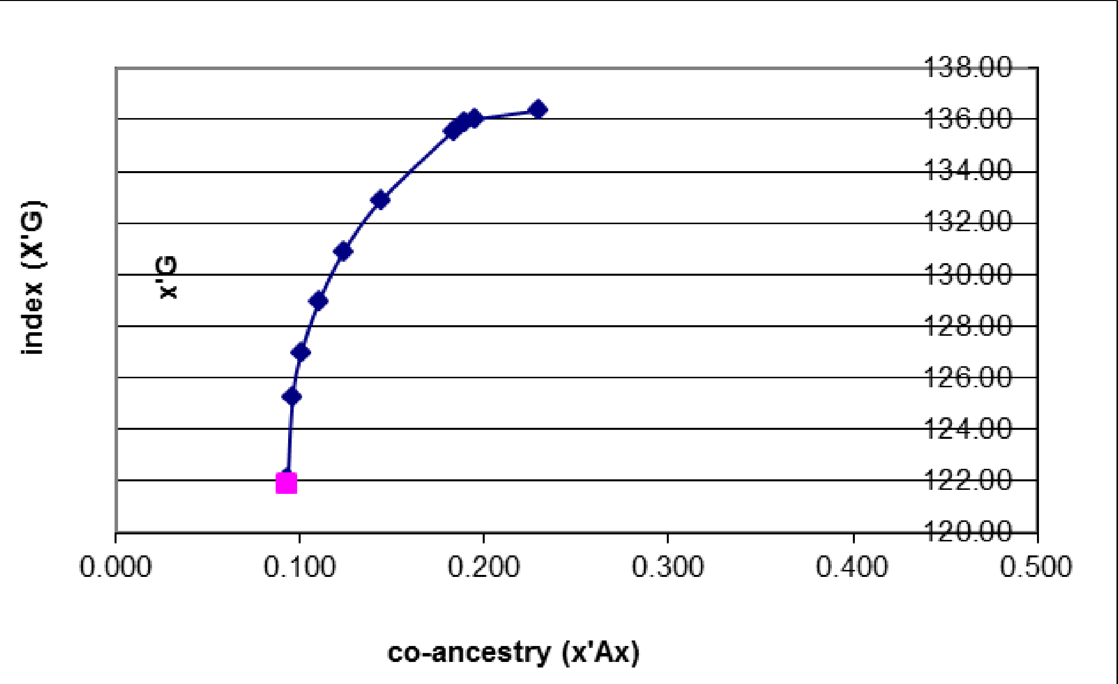
xGxAx.xls

	X	nmales	nfemales
Male 1	**0.127**	4	4
Male 2	0.108		
Male 3	0.129		
Male 4	0.136		
Female 1	0.189		
Female 2	0.177		
Female 3	0.049		
Female 4	0.085		

Find optimal contributions

G	Relationships Matrix							
127	**1.00**	**0.00**	**0.25**	**0.00**	**0.00**	**0.00**	**0.50**	**0.00**
122	0.00	**1.00**	**0.00**	**0.25**	**0.00**	**0.00**	**0.00**	**0.50**
150	0.25	0.00	**1.00**	**0.00**	**0.00**	**0.00**	**0.25**	**0.00**
109	0.00	0.25	0.00	**1.00**	**0.00**	**0.00**	**0.00**	**0.25**
120	0.00	0.00	0.00	0.00	**1.00**	**0.00**	**0.00**	**0.00**
123	0.00	0.00	0.00	0.00	0.00	**1.00**	**0.25**	**0.00**
89	0.50	0.00	0.25	0.00	0.00	0.25	**1.00**	**0.00**
113	0.00	0.50	0.25	0.25	0.00	0.00	0.00	**1.00**

average merit of progeny	x'G	121.91
Inbreeding weight	λ	-99999999.0
rage co-acestry of progeny	x'Ax	0.093



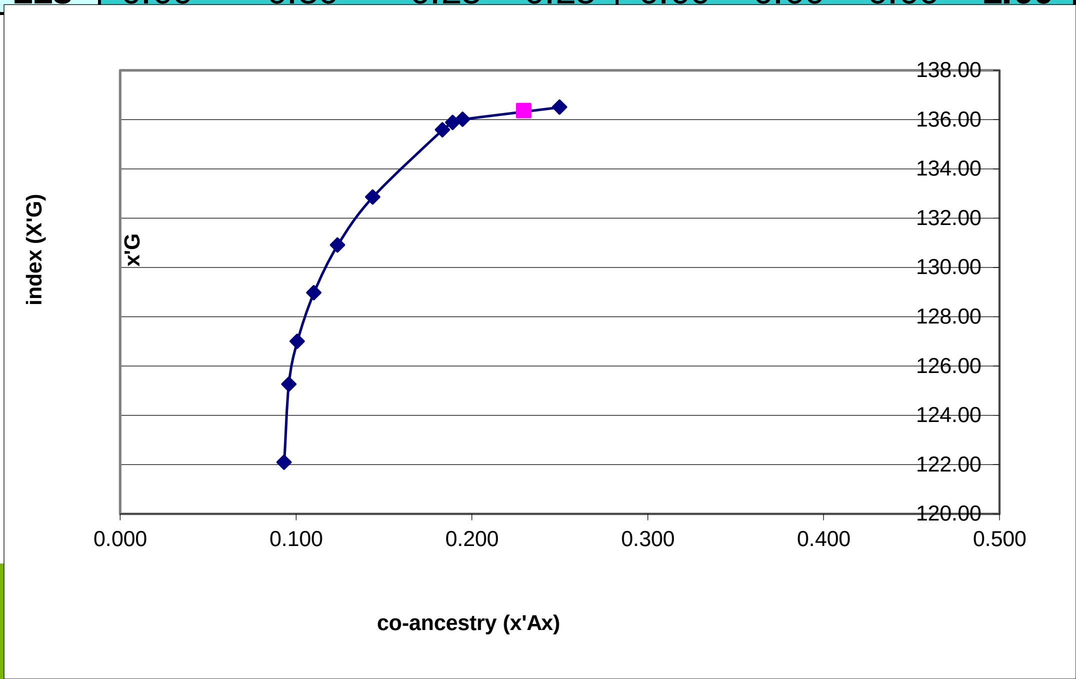
Example Optimal Contributions

xGxAx.xls

	X	nmales	nfemales	G	Relationships Matrix							
Male 1	**0.000**	4	4	**127**	**1.00**	**0.00**	**0.25**	**0.00**	**0.00**	**0.00**	**0.50**	**0.00**
Male 2	0.000			**122**	0.00	**1.00**	**0.00**	**0.25**	**0.00**	**0.00**	**0.00**	**0.50**
Male 3	0.500			**150**	0.25	0.00	**1.00**	**0.00**	**0.00**	**0.00**	**0.25**	**0.00**
Male 4	0.000			**109**	0.00	0.25	0.00	**1.00**	**0.00**	**0.00**	**0.00**	**0.25**
Female 1	0.000			**120**	0.00	0.00	0.00	0.00	**1.00**	**0.00**	**0.00**	**0.00**
Female 2	0.500			**123**	0.00	0.00	0.00	0.00	0.00	**1.00**	**0.25**	**0.00**
Female 3	0.000			**89**	0.50	0.00	0.25	0.00	0.00	0.25	**1.00**	**0.00**
Female 4	0.000			**113**	0.00	0.50	0.25	0.25	0.00	0.00	0.00	**1.00**

Find optimal contributions

average merit of progeny	x'G	136.50
Inbreeding weight	λ	**0.0**
rage co-acestry of progeny	x'Ax	0.250



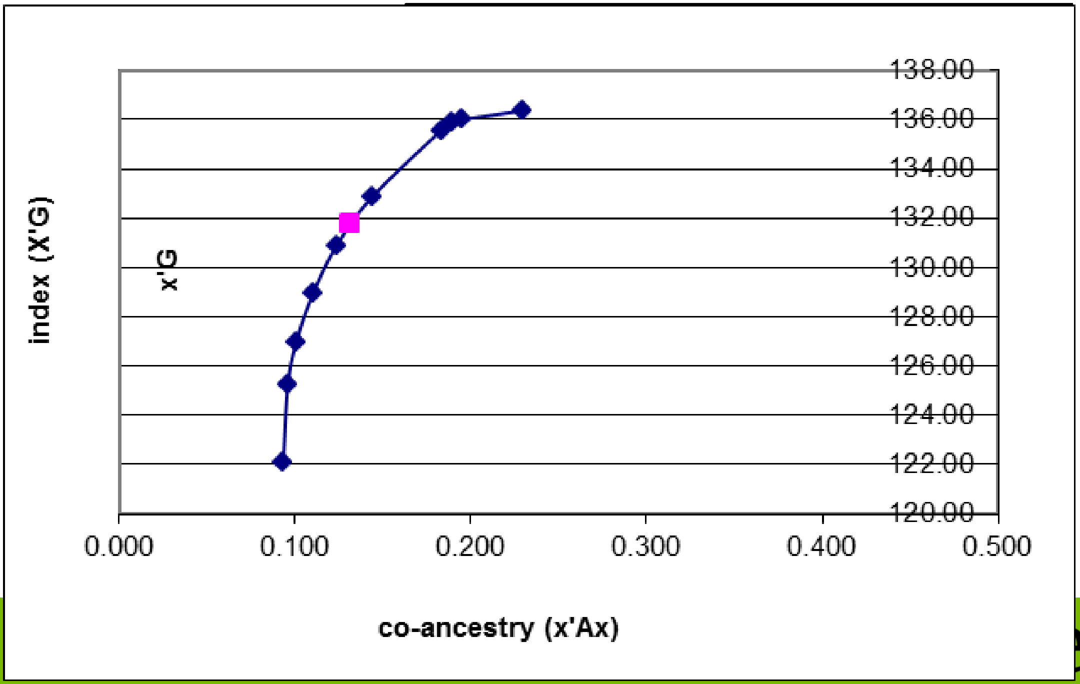
Example Optimal Contributions

xGxAx.xls

	X	nmales	nfemales
Male 1	**0.063**	4	4
Male 2	0.076		
Male 3	0.361		
Male 4	0.000		
Female 1	0.208		
Female 2	0.238		
Female 3	0.000		
Female 4	0.055		
average merit of progeny	x'G		131.75
Inbreeding weight	λ		-50.0
rage co-acestry of progeny	x'Ax		0.132

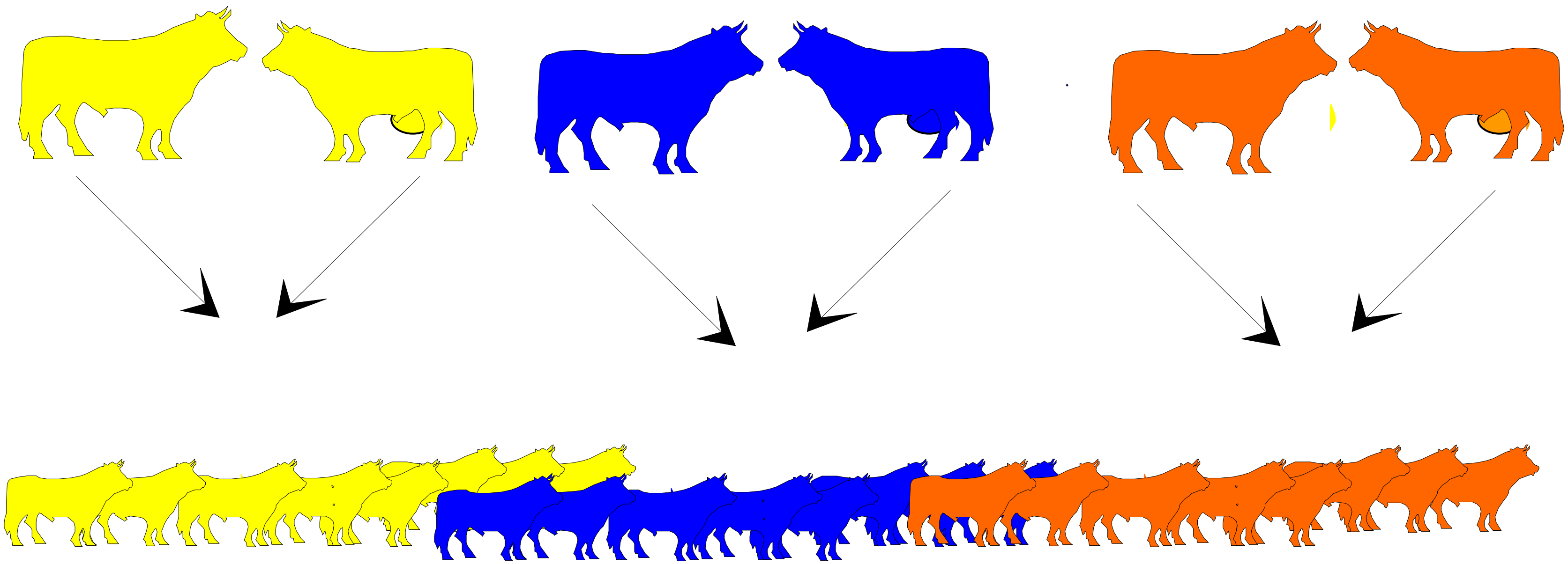
Find optimal contributions

G	Relationships Matrix							
127	**1.00**	0.00	0.25	0.00	0.00	0.00	0.50	0.00
122	0.00	**1.00**	0.00	0.25	0.00	0.00	0.00	0.50
150	0.25	0.00	**1.00**	0.00	0.00	0.00	0.25	0.00
109	0.00	0.25	0.00	**1.00**	0.00	0.00	0.00	0.25
120	0.00	0.00	0.00	0.00	**1.00**	0.00	0.00	0.00
123	0.00	0.00	0.00	0.00	0.00	**1.00**	0.25	0.00
89	0.50	0.00	0.25	0.00	0.00	0.25	**1.00**	0.00
113	0.00	0.50	0.25	0.25	0.00	0.00	0.00	**1.00**



This is more than simply moving back from BLUP to mass selection (penalizing family info)

Between versus within family selection



Own information (performance or *genotype*):

More variation within families

More within-family selection – ***less inbreeding***

Advantage of genomic selection

Ultimately, genetic gain is about utilizing Mendelian sampling Variance

Conclusion Optimal Contribution Selection

- OCS is the only sensible selection method
  - Optimality subject to some degree of subjectivity
  - Separates best prediction of merit from selection rule
  - Play with number of parents as well as progeny per selected parent → optimizes contributions
  - Different from simply giving more weight to family info
- Hard to deterministically predict response to OCS