Balancing Selection and Inbreeding

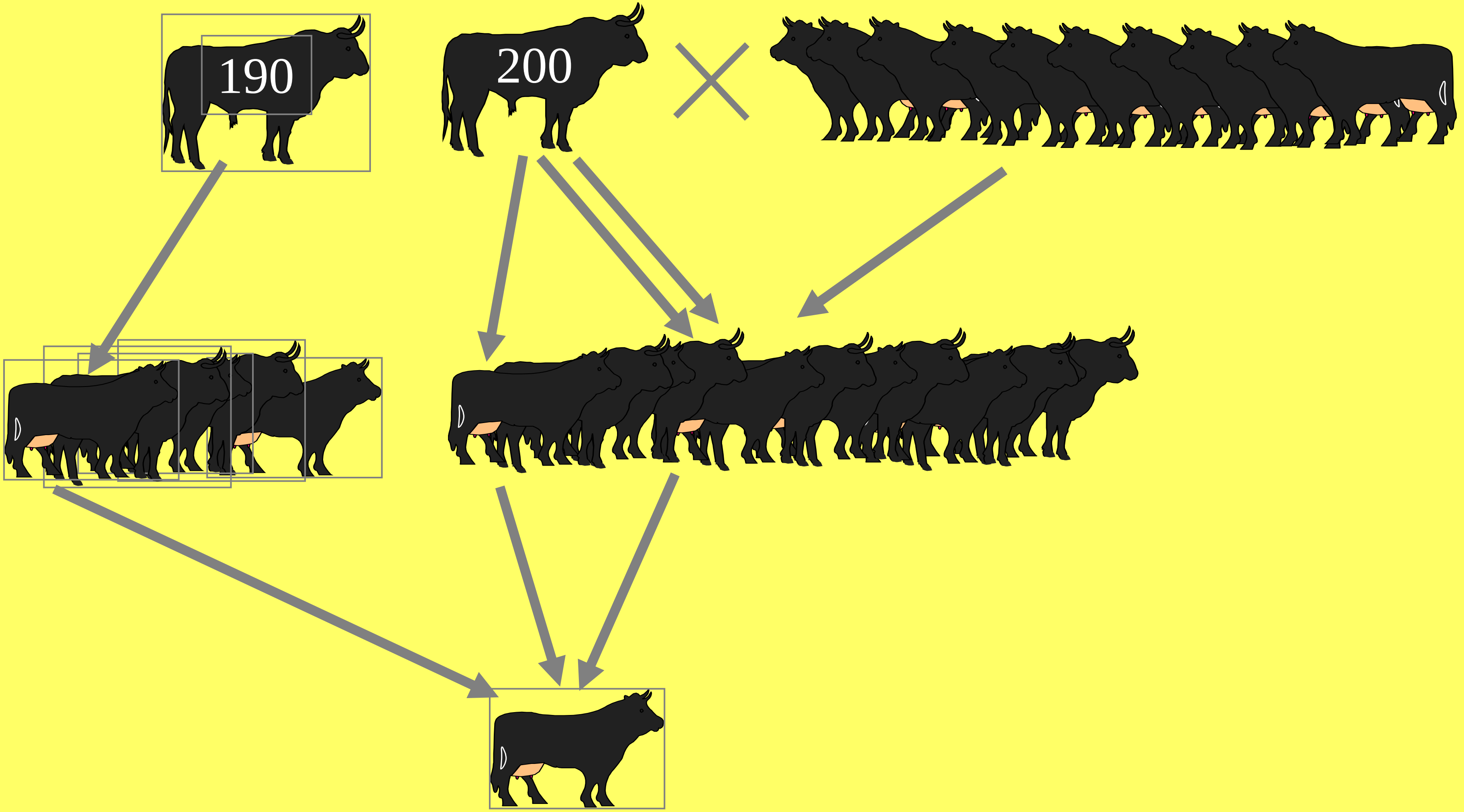
- Higher selection intensities make bigger gain
- Fewer animals are selected, so also more inbreeding
- This trend is more evident with higher rates of fecundity
- Effect of new reproductive technologies
- Genetic evaluation (BLUP) favors selection of related animals

- →rationalization of selection make inbreeding restriction methods a necessity

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*

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


190
200

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 underpredicts inbreeding (2x)
But it shows that usually, it is controlled by using enough sires

A feature of BLUP

- BLUP uses family information (and more so at lower heritabilities)

- Selection on BLUP EBVs can thus results in higher inbreeding than selection on phenotypes alone

- Best strategy: Balance merit and genetic diversity
  - Start selecting from top, but leave an animal out if sibs have been selected already

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	Inbreeding & Accuracies: Weight	Inbreeding & Accuracies: 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	86012219929202[illegible]	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	WARBURN	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

More theoretical

- BLUP selection leans on family info
- Causing co-selection of relatives

- Reducing weight on family info is like moving from BLUP to mass selection

- Inbreeding rate depends on emphasis on
  - Between vs Within Family selection
  - Family info versus Mendelian Sampling info

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 determine number of selected sires and dams, but also allows for unequal contributions

How to find an optimal x?

Meuwissen, 1997

- Optimize gain at a fixed rate of inbreeding (C)
- Max(xG |constrain x'Ax=C, sum of x = 0.5 per sex)
- Use a Langrange multipliers to solve for x.

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?)

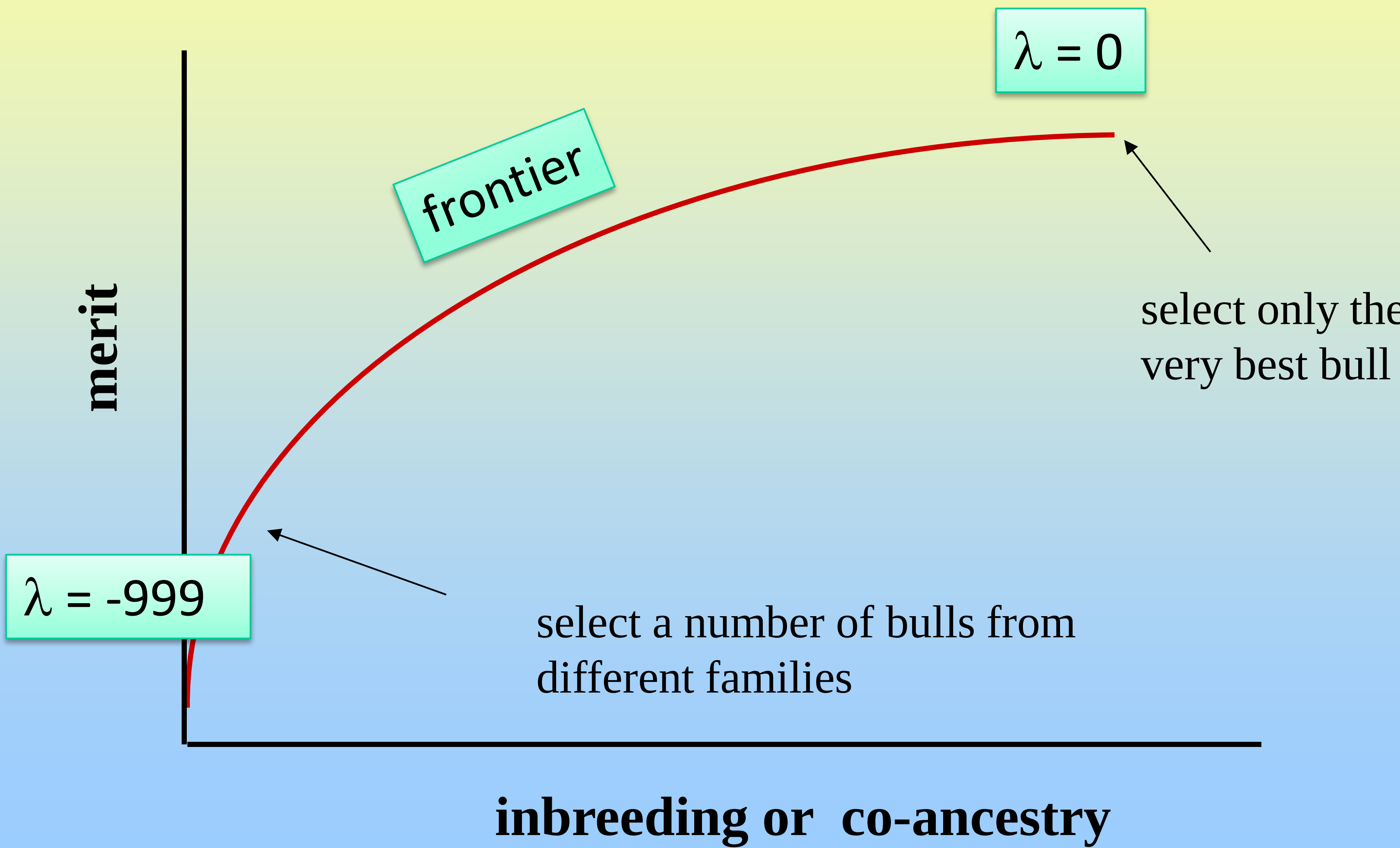
How to find an optimal x?

$x'G + \lambda x'Ax$

Kinghorn, 2000-ish

- Draw a frontier by varying λ
- For given λ Max($x'G + \lambda x'Ax$ | constrain sum of x=0.5 per sex)
- Use Differential Evolution multipliers to solve for x
  - Versatile, can easily set other constraints, minuse, maxuse

Balancing inbreeding and merit



Optimizing genetic contributions

- Maximize objective function

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

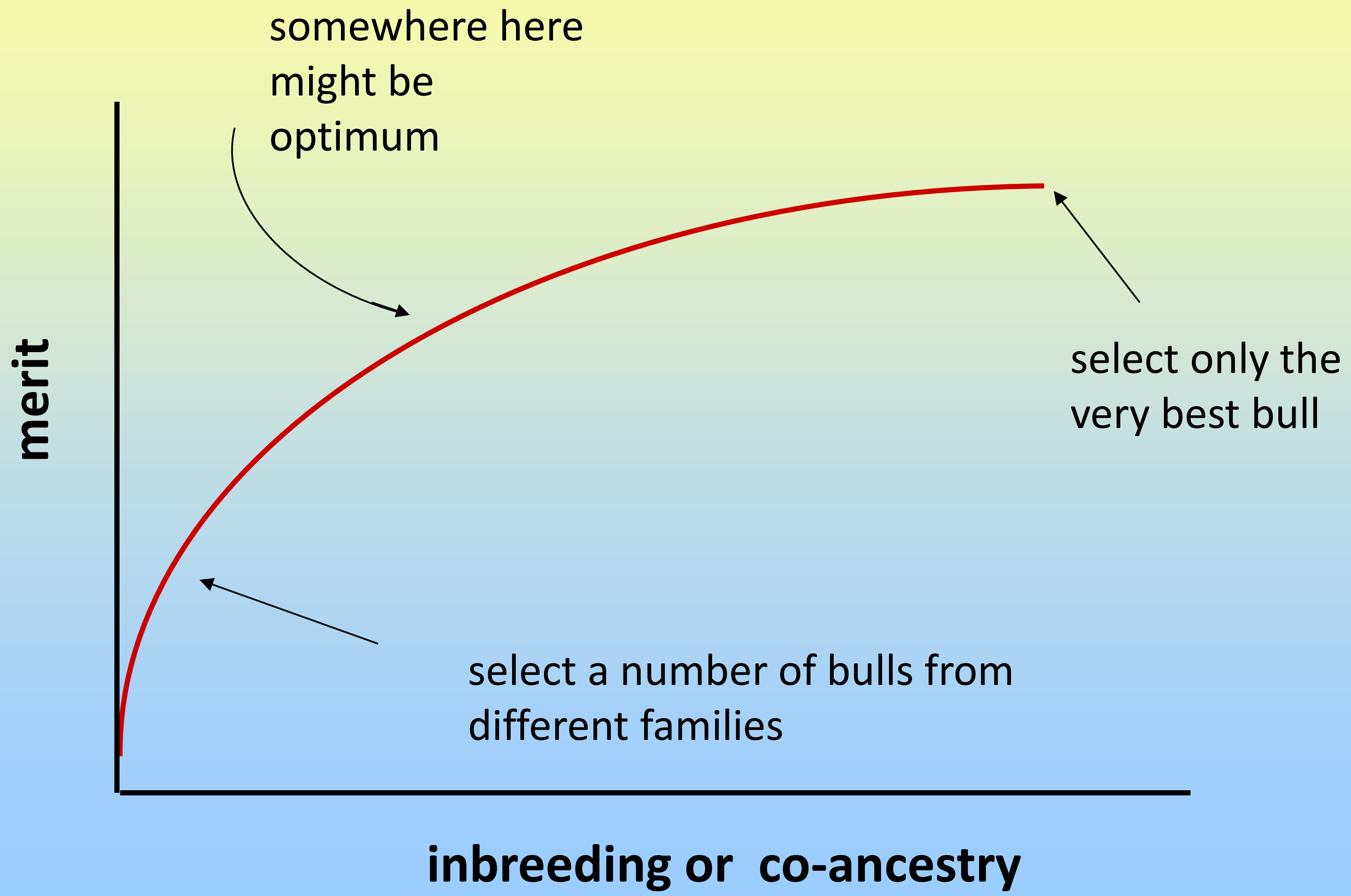
Question: what is best value for λ ?

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

Alternative: look at graph (next slide)

Balancing inbreeding and merit

This graph will look different for each population



Some expansion

- Account for juvenile matings (last year’s)
  - Augment A-matrix
- Various other constrains
  - end up below frontier ‘cost of constraint’
- Overlapping generations

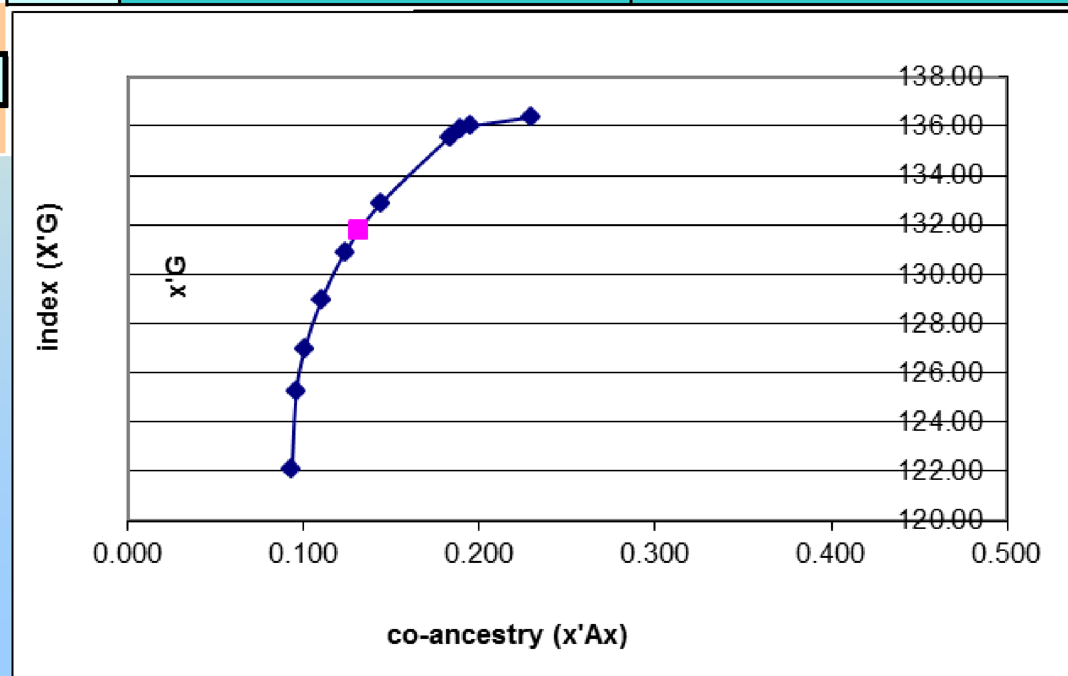
Example Optimal Contributions

xGxAx.xls

	X	nmales	nfemales	G	Relationships Matrix							
Male 1	**0.063**	4	4	**127**	**1.00**	**0.00**	**0.25**	**0.00**	**0.00**	**0.00**	**0.50**	**0.00**
Male 2	0.076			**122**	0.00	**1.00**	**0.00**	**0.25**	**0.00**	**0.00**	**0.00**	**0.50**
Male 3	0.361			**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	0.208			**120**	0.00	0.00	0.00	0.00	**1.00**	**0.00**	**0.00**	**0.00**
Female 2	0.238			**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	0.055			**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	131.75
Inbreeding weight	λ	**-50.0**
rage co-acestry of progeny	x'Ax	0.132



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

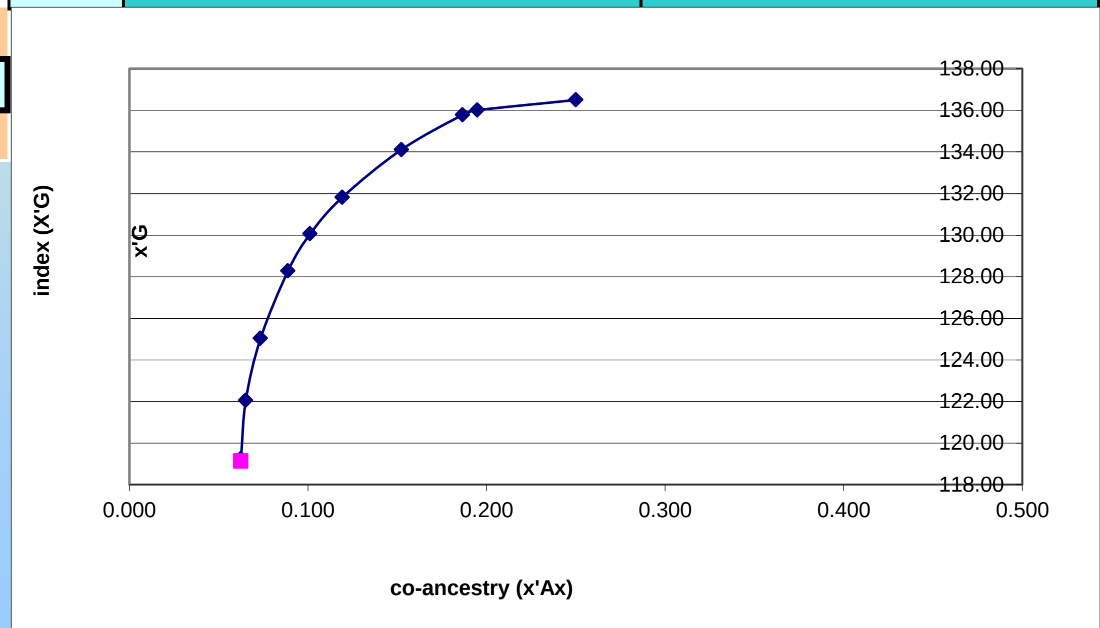
Example Optimal Contributions

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

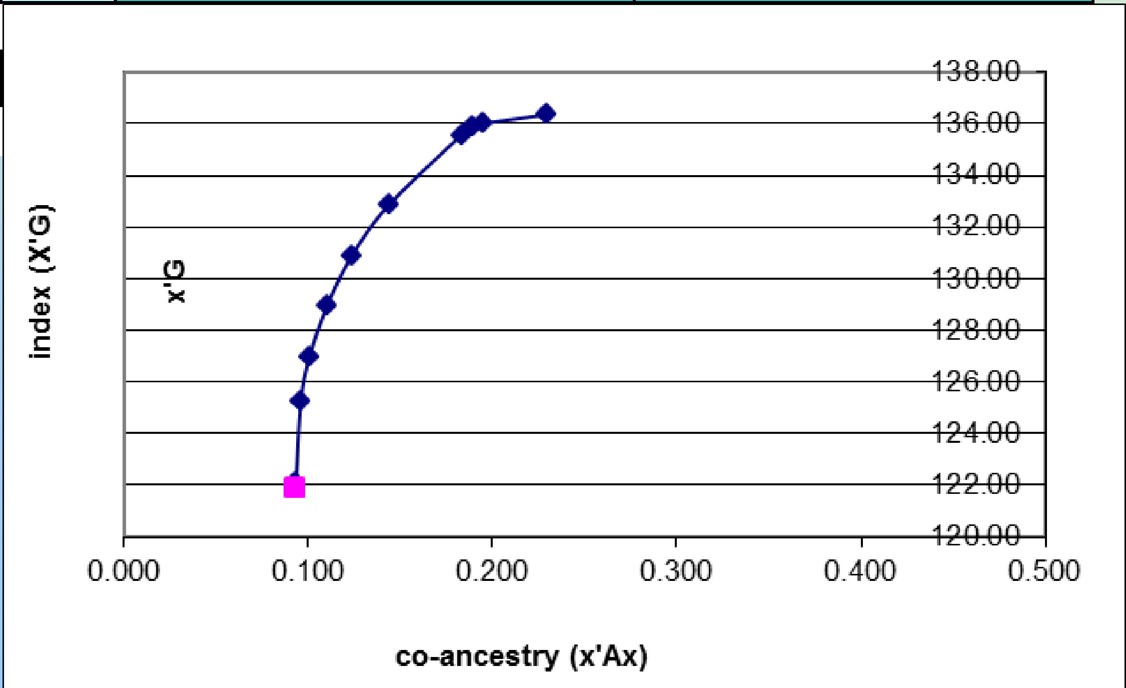
xGxAx.xls

	X	nmales	nfemales
Male 1	**0.127**	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



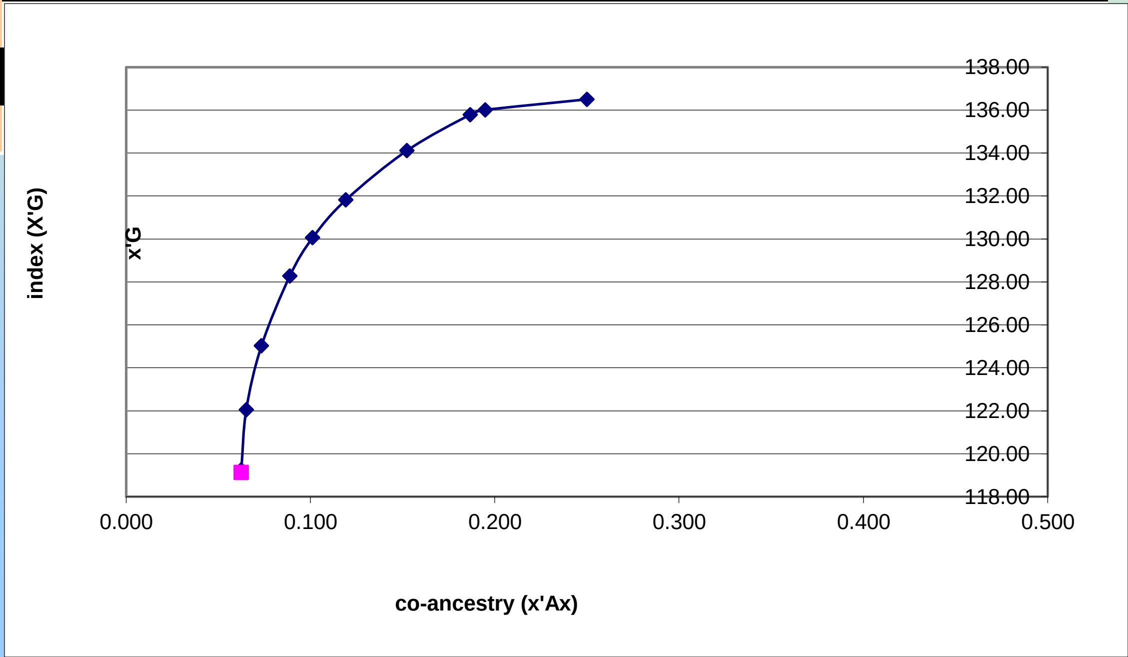
Example Optimal Contributions

xGxAx.xls

	X	nmales	nfemales	G	Relationships Matrix							
Male 1	**0.125**	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

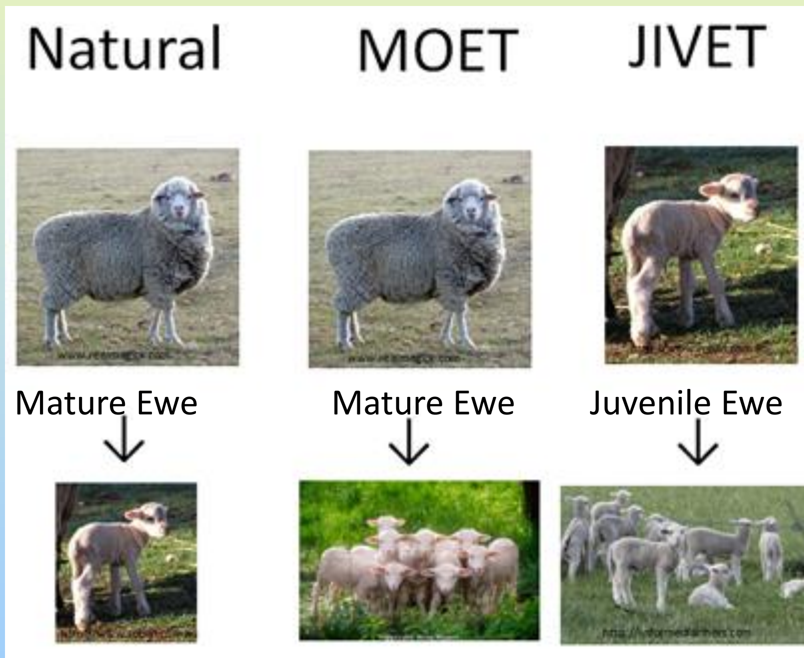
average merit of progeny	x'G	119.12
Inbreeding weight	λ	**-9999999.0**
rage co-acestry of progeny	x'Ax	0.063



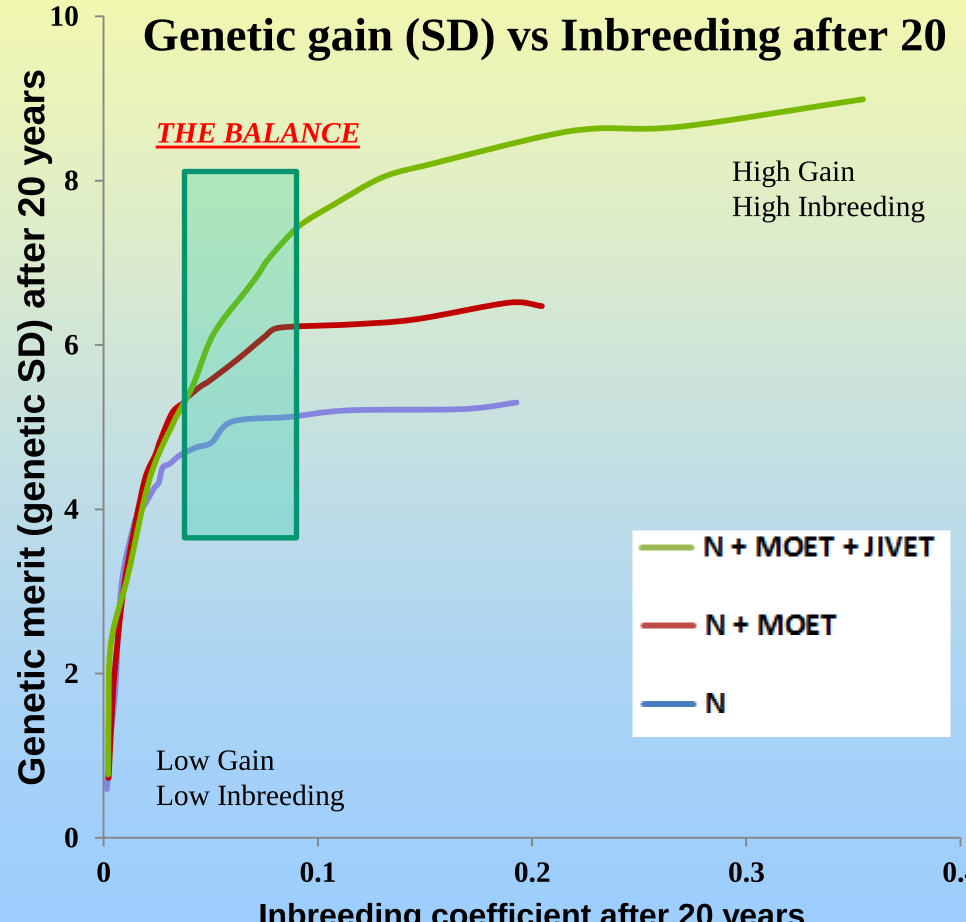
Genetic Gain vs Inbreeding
while using female reproductive technologies

Tom Granleese, 2014

Reproductive technologies



1 Lamb　　Many Lambs　　Loads of Lambs



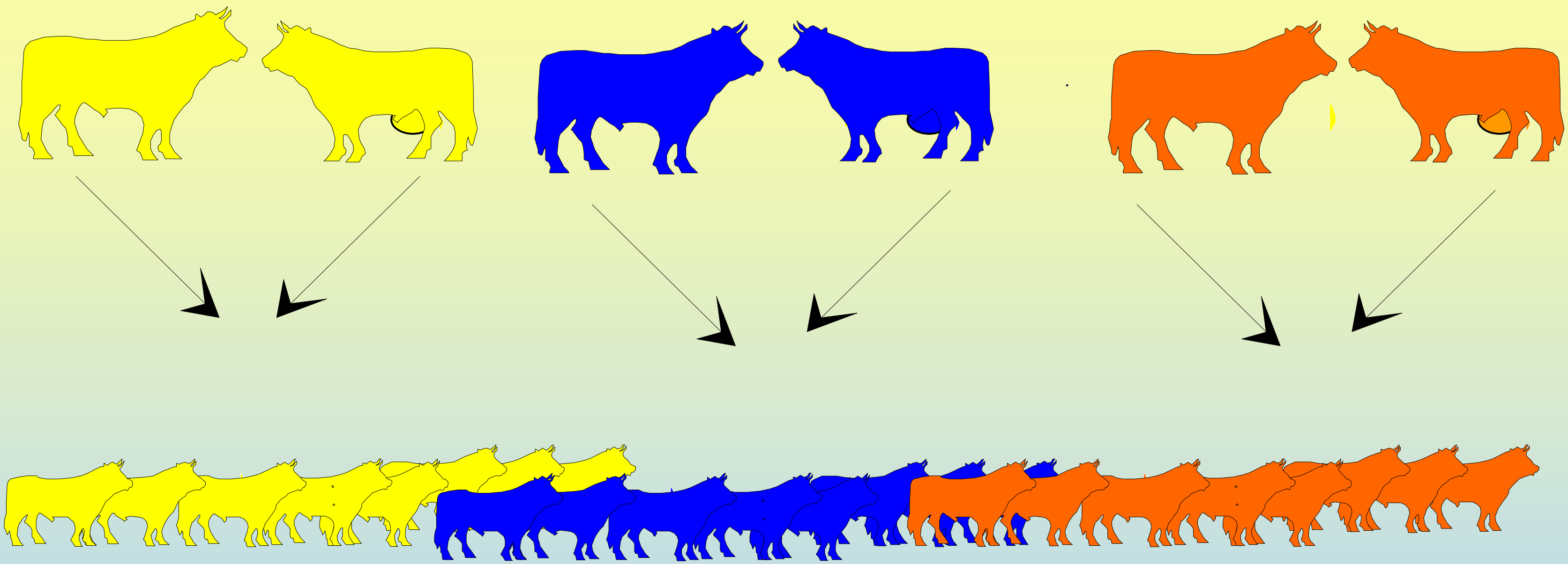
Optimal Contribution Selection with reproductive technologies

Granleese 2014

Prop females allocated to

	AI/N	MOET	JIVET	TOTAL FEMALES*	Males Used*	Females per male
AI/N + MOET + JIVET (GS)	0.24	0.32	0.44	47	19	2.5
AI/N + MOET + JIVET	0.26	0.35	0.39	57	20	2.9
AI/N + MOET (GS)	0.34	0.66		98	18	5.4
AI/N + MOET	0.34	0.66		100	19	5.3
AI/N (GS)	1.00			276	14	19.7
AI/N	1.00			277	14	19.8

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

- Hard to deterministically predict response to OCS