

Management of genetic diversity with gene bank material

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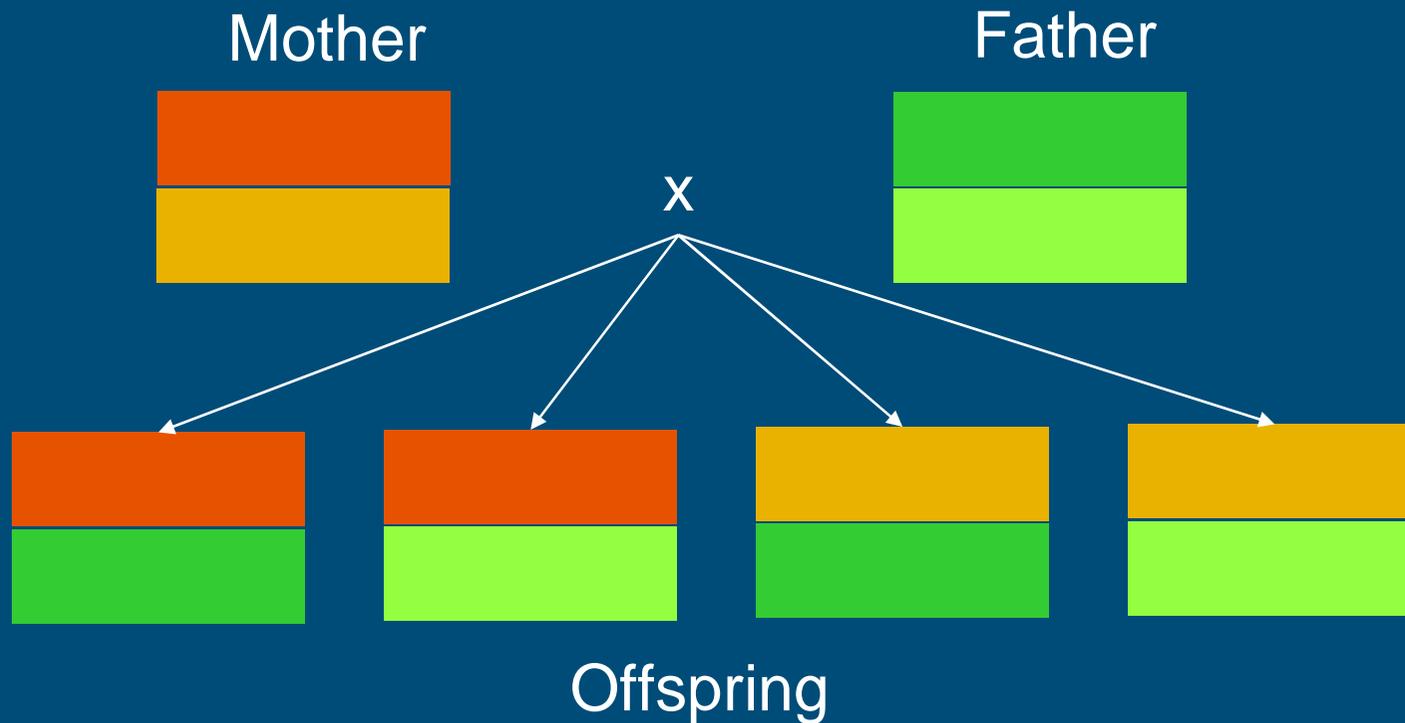
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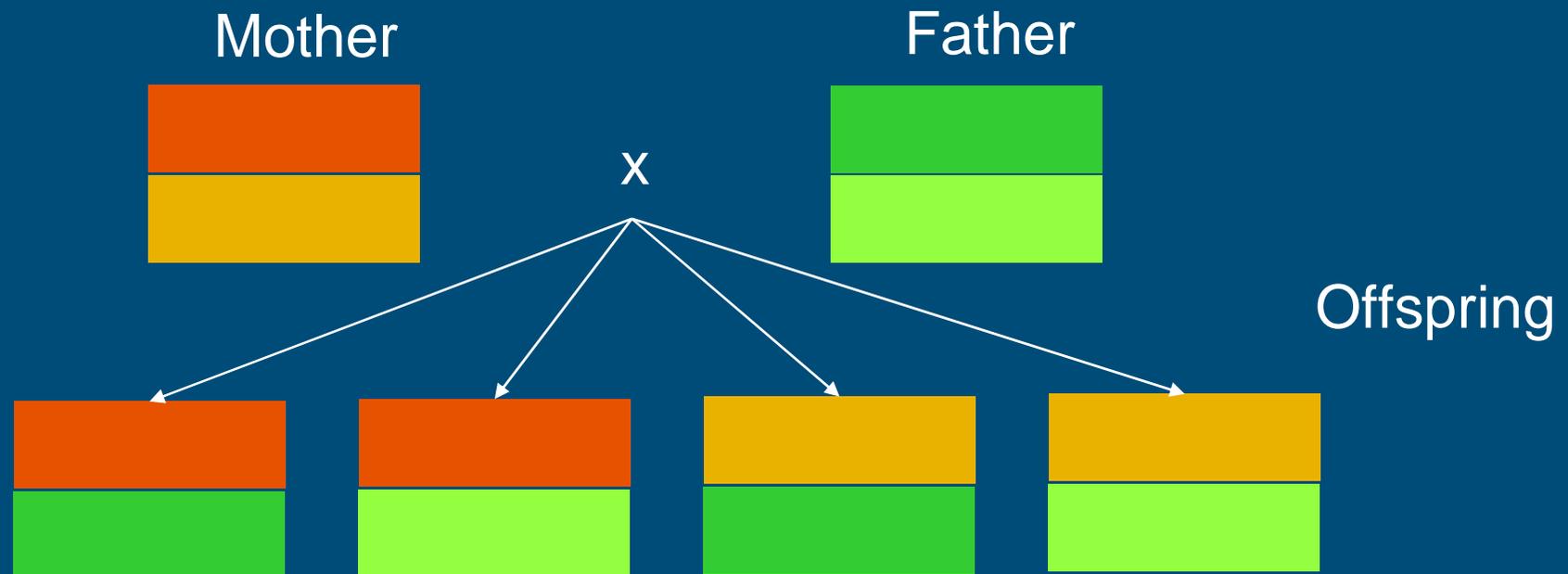
Simple Genetics

■ Base rule

- DNA in two copies
- DNA: 50% from mother, 50% from father



Simple Genetics



- Offspring mixture of infinite number of genes

- 50% shared with either parent
- 0%, 50%, 50% or 100% shared with full sib
- = on average 50%

Relatedness coefficient (= r)

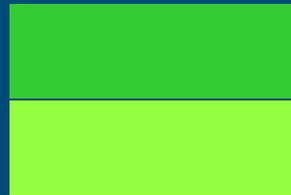


Inbreeding

Mother



Father



X



X

Daughter



Offspring

- Increase relatedness
- Decrease variation
- 25% same copy

Inbreeding coefficient (= F)



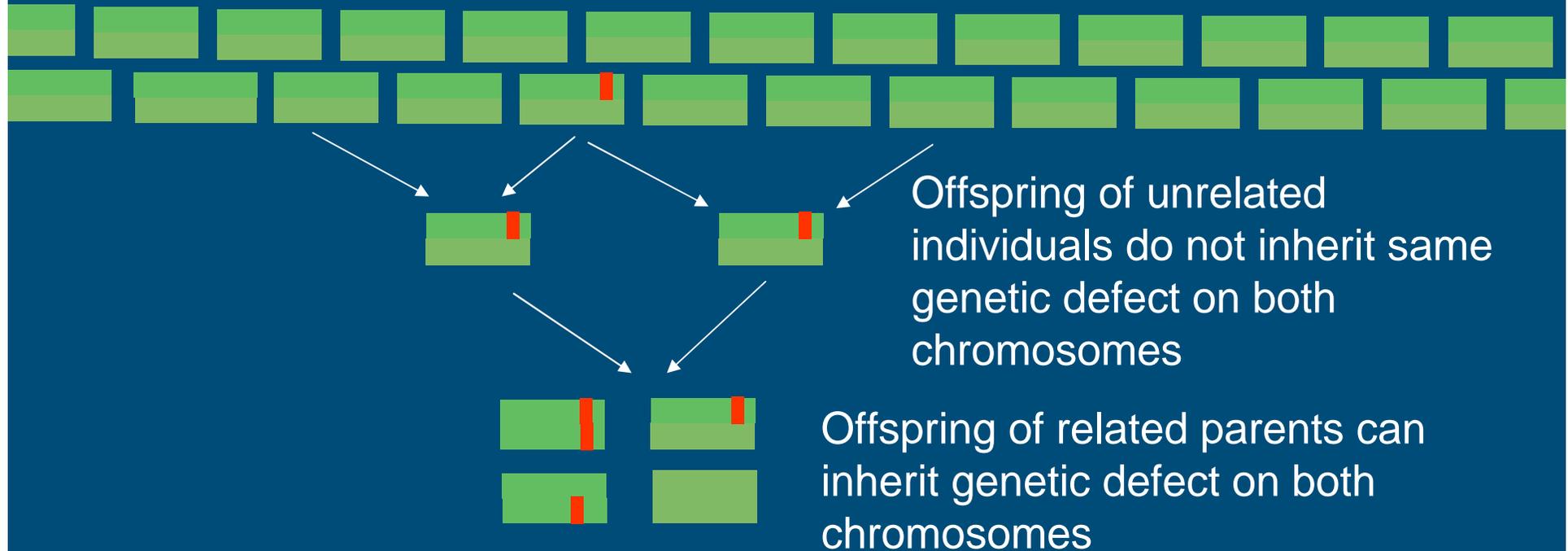
Inbreeding

- The offspring of two related individuals is inbred
 - The closer the relatedness of the parents the higher the inbreeding of the offspring
 - Inbreeding unavoidably increases in a closed population
 - The smaller the population the higher the inbreeding rate in the population
 - Strong selection -> more inbreeding
 - The higher the inbreeding the lower the genetic diversity
 - The higher the inbreeding the more congenital defects
 - The higher the inbreeding the lower the performance (inbreeding depression)
 - Inbreeding is not heritable



Why more genetic defects with inbreeding?

Each defect rare, but many recessive defects around



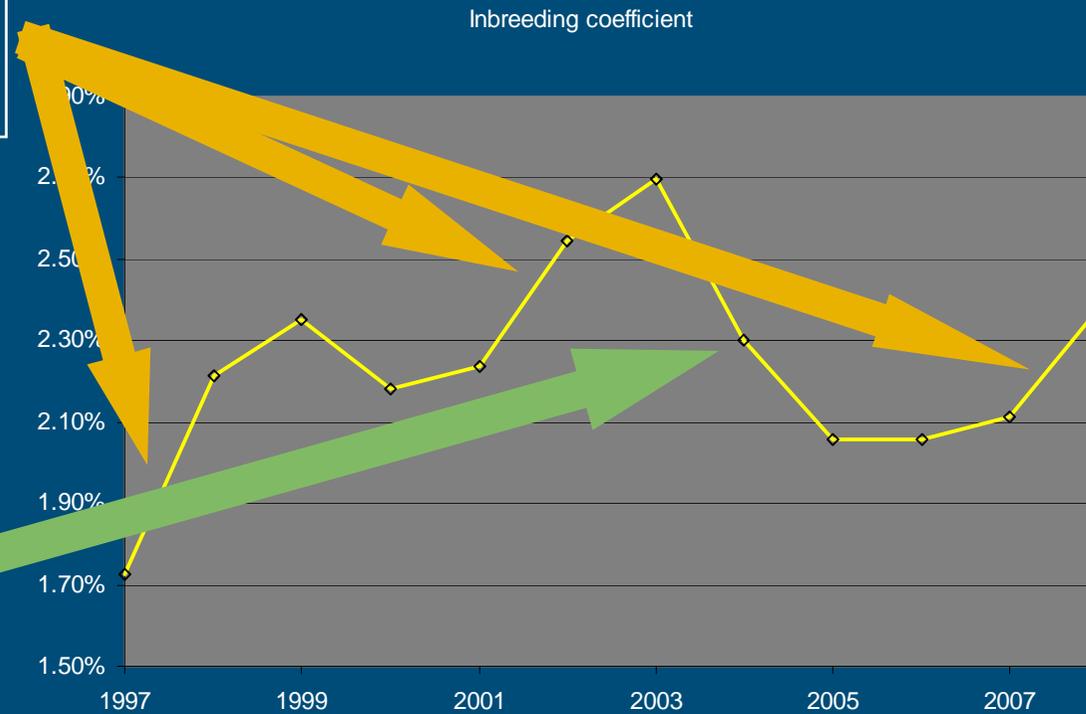
F : = Probability that genetic defect is expressed



Inbreeding in a sheep population

Periods with high inbreeding rate

Period with decrease in inbreeding



Slope of line: Inbreeding rate $\rightarrow \Delta F$



A-matrix

- Relatedness between all individuals in the population
 - On diagonal $1 + F$
- Pedigree needed
 - > 5 or more generations
 - No markers needed
 - But can be estimated with markers
- Higher relatedness
 - More DNA in common
 - Less diversity
- Blocks of more and less related individuals
 - Overview of distribution within a breed



A-matrices

Individual ID	123	157	149	202	197	173	168	159	220	221	219	224	223	226	225	222	205
123	1.000	0.031	0.250	0.109	0.344	0.219	0.094	0.031	0.047	0.109	0.227	0.555	0.180	0.102	0.164	0.070	0.094
157	0.031	1.063	0.063	0.090	0.096	0.066	0.082	0.406	0.504	0.148	0.151	0.119	0.135	0.145	0.137	0.635	0.111
149	0.250	0.063	1.125	0.285	0.262	0.750	0.219	0.078	0.107	0.281	0.270	0.264	0.701	0.248	0.514	0.170	0.215
202	0.109	0.090	0.285	1.137	0.298	0.363	0.314	0.090	0.147	0.802	0.382	0.288	0.376	0.391	0.415	0.278	0.317
197	0.344	0.096	0.262	0.298	1.162	0.426	0.334	0.096	0.240	0.299	0.731	0.322	0.281	0.317	0.363	0.198	0.504
173	0.219	0.066	0.750	0.363	0.426	1.188	0.391	0.074	0.149	0.359	0.391	0.287	0.553	0.373	0.771	0.211	0.387
168	0.094	0.082	0.219	0.314	0.334	0.391	1.031	0.082	0.146	0.305	0.314	0.194	0.257	0.663	0.343	0.188	0.686
159	0.031	0.406	0.078	0.090	0.096	0.074	0.082	1.125	0.699	0.102	0.104	0.072	0.096	0.098	0.094	0.260	0.111
220	0.047	0.504	0.107	0.147	0.240	0.149	0.146	0.699	1.137	0.169	0.215	0.119	0.149	0.168	0.170	0.347	0.254
221	0.109	0.148	0.281	0.802	0.299	0.359	0.305	0.102	0.169	1.233	0.544	0.450	0.536	0.547	0.575	0.469	0.314
219	0.227	0.151	0.270	0.382	0.731	0.391	0.314	0.104	0.215	0.544	1.150	0.467	0.488	0.510	0.549	0.429	0.408
224	0.555	0.119	0.264	0.288	0.322	0.287	0.194	0.072	0.119	0.450	0.467	1.055	0.438	0.403	0.449	0.365	0.203
223	0.180	0.135	0.701	0.376	0.281	0.553	0.257	0.096	0.149	0.536	0.488	0.438	1.139	0.476	0.624	0.415	0.263
226	0.102	0.145	0.248	0.391	0.317	0.373	0.663	0.098	0.168	0.547	0.510	0.403	0.476	1.147	0.539	0.424	0.499
225	0.164	0.137	0.514	0.415	0.363	0.771	0.343	0.094	0.170	0.575	0.549	0.449	0.624	0.539	1.178	0.436	0.349
222	0.070	0.635	0.170	0.278	0.198	0.211	0.188	0.260	0.347	0.469	0.429	0.365	0.415	0.424	0.436	1.104	0.211
205	0.094	0.111	0.215	0.317	0.504	0.387	0.686	0.111	0.254	0.314	0.408	0.203	0.263	0.499	0.349	0.211	1.170

	123	157	149	202	197	173	168	159	220	221	219	224	223	226	225	222	205
123	1.179	0.611	0.346	0.307	0.419	0.354	0.216	0.388	0.562	0.348	0.381	0.760	0.320	0.209	0.520	0.666	0.391
157	0.611	1.290	0.318	0.173	0.508	0.139	0.237	0.343	0.475	0.460	0.472	0.362	0.346	0.068	0.218	0.860	0.565
149	0.346	0.318	1.054	0.450	0.347	0.699	0.184	0.243	0.413	0.529	0.429	0.289	0.705	0.362	0.530	0.449	0.335
202	0.307	0.173	0.450	1.135	0.362	0.393	0.013	0.157	0.450	0.724	0.493	0.617	0.669	0.316	0.562	0.480	0.383
197	0.419	0.508	0.347	0.362	1.249	0.587	0.307	0.432	0.376	0.277	1.041	0.500	0.408	0.146	0.425	0.514	0.499
173	0.354	0.139	0.699	0.393	0.587	1.077	0.138	0.262	0.332	0.341	0.612	0.341	0.552	0.320	0.775	0.382	0.328
168	0.216	0.237	0.184	0.013	0.307	0.138	0.977	0.563	0.267	-0.073	0.337	0.057	0.156	0.408	0.061	0.056	0.386
159	0.388	0.343	0.243	0.157	0.432	0.262	0.563	1.138	0.635	-0.001	0.365	0.334	0.187	0.391	0.160	0.237	0.273
220	0.562	0.475	0.413	0.450	0.376	0.332	0.267	0.635	1.046	0.265	0.269	0.638	0.306	0.587	0.442	0.470	0.309
221	0.348	0.460	0.529	0.724	0.277	0.341	-0.073	-0.001	0.265	1.128	0.421	0.394	0.733	0.153	0.493	0.638	0.439
219	0.381	0.472	0.429	0.493	1.041	0.612	0.337	0.365	0.269	0.421	1.343	0.270	0.589	0.166	0.351	0.501	0.454
224	0.760	0.362	0.289	0.617	0.500	0.341	0.057	0.334	0.638	0.394	0.270	1.183	0.504	0.344	0.657	0.668	0.412
223	0.320	0.346	0.705	0.669	0.408	0.552	0.156	0.187	0.306	0.733	0.589	0.504	1.122	0.373	0.624	0.676	0.688
226	0.209	0.068	0.362	0.316	0.146	0.320	0.408	0.391	0.587	0.153	0.166	0.344	0.373	1.038	0.247	0.163	0.322
225	0.520	0.218	0.530	0.562	0.425	0.775	0.061	0.160	0.442	0.493	0.351	0.657	0.624	0.247	1.264	0.535	0.377
222	0.666	0.860	0.449	0.480	0.514	0.382	0.056	0.237	0.470	0.638	0.501	0.668	0.676	0.163	0.535	1.130	0.479
205	0.391	0.565	0.335	0.383	0.499	0.328	0.386	0.273	0.309	0.439	0.454	0.412	0.688	0.322	0.377	0.479	1.024



Some basic rules for genetic management

- Try to enlarge the population
- Avoid excessive use of a small number of sires
- Avoid matings between close relatives
 - Father/daughter, full brother/sister etc.
- Exchange individuals between farms, villages, etc.



Genetic management and relatedness

- Genetic diversity
 - 1 – average relatedness
- Average inbreeding next generation
 - $0.5 * \text{average relatedness of parents}$
- Management of genetic diversity and inbreeding
 - Minimise average relatedness
 - = Minimise inbreeding in next generation(s)



Use of more animals as parents

- Strongest inbreeding with use of a few sires
 - E.g. 1 bull inseminates 50% of the cows -> 50% of next generation = half sibs ($r > 25\%$)
- Restrictions on excessive use of sires needed
 - Limit maximum number of matings per sire
 - Maximum on offspring per sire (e.g. no more than 50 inseminations)
 - Maximum on sire sons that can be entered in herd book
 - Etc.
- Gene Bank material can help
 - More sires (and possibly dams) available as parent



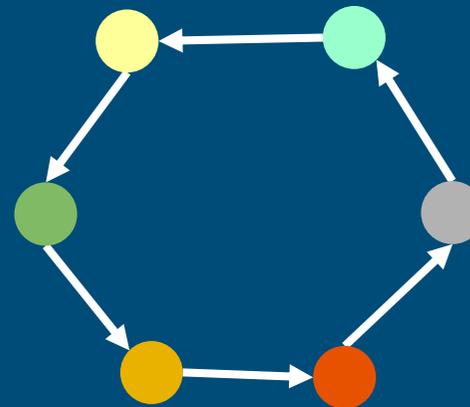
Mate less related parents

- Inbreeding is $0.5 * r$ of parent
- After selection of parents choose least related sire for each dam
- Does not prevent inbreeding in the long run
- Avoids offspring with very high inbreeding coefficients
- Gene Bank material can help
 - Older animals generally less related



Rotational mating

- Most breeds in herds
 - Less related between herds, more within herds
- Rotational mating: use sires from other herds
- Simplest form: breeding circle
 - Each herd uses sires from neighbor herd



Practical advantages breeding circle

- Very effective in reducing inbreeding
- Each year same structure
 - Once started nothing needs to be changed
- Circle can be adapted to population structure
 - Minimal geographic distances
 - Avoidance of “incompatible” herds
- New herds can be incorporated easily
- Requires trust between different owners



Veluws Heideschaap

- 3000 animals
- Ten herds of roughly equal size
- After problems with congenital defects breeding circle started 15 years ago
- Interrupted by FMD



Result

- Breeding circle maintained > 15 years
- Good agreement
 - Right to pick rams from neighboring herd
 - Fixed price per ram
- Limited number of professional herds
- Congenital defects disappeared



Optimal contributions

- Most sophisticated method to minimise relatedness
- Average relatedness
 - $r = c'Ac$
 - c = contribution vector of parents to next generation
 - E.g. 0.50 0.25 0.20 0.04 0.01 0.00 0.00 0.00 0.00 0.00
- Optimal contribution
 - First derivative (with restriction $\Sigma c = 1$)
 - $c_{\min} = (A^{-1}1_n) / (1_n' A^{-1}1_n)$
- Best method to select candidates for a gene bank

Sonesson & Meuwissen 2001 Genet. Research **77**: 285-292



Example $c'Ac$

$$A = \begin{matrix} & 1.00 & 0.50 & 0.10 & 0.05 \\ & 0.50 & 1.00 & 0.15 & 0.05 \\ & 0.10 & 0.15 & 1.20 & 0.60 \\ & 0.05 & 0.05 & 0.60 & 1.00 \end{matrix}$$

$$r = c'Ac = \sum a_{ij} \cdot c_i \cdot c_j$$

$$c = 0.25 \quad 0.25 \quad 0.25 \quad 0.25 \quad r = 0.44$$

$$c = 0.40 \quad 0.10 \quad 0.40 \quad 0.10 \quad r = 0.51$$

$$c = 0.00 \quad 0.00 \quad 0.50 \quad 0.50 \quad r = 0.85$$

$$c = 0.27 \quad 0.26 \quad 0.15 \quad 0.32 \quad r = 0.43 = \text{Minimised}$$



Gencont

- Software program that determines optimal contributions
- Extra restrictions
 - Contributions sum to 1
 - No negative contributions
 - Contributions of mothers sum to 0.5
 - Contributions of fathers sum to 0.5
- Extra options
 - Fix number of fathers/mothers
 - Restrict contributions to maximum
 - Equal contribution for all selected mothers/fathers
 - Selection on trait value
 - Marker Estimated A-matrix
 - Overlapping generations

$$c = \frac{A^{-1}Q \left(2r_1 (Q'A^{-1}Q)^{-1} (r_1 s + Q'Jr_2) \right)}{2r_1^2} + \frac{Jr_2}{r_1}$$



Example use of Gencont



Holland Genetics (CRV) uses Optimal Contribution to select bulls for their breeding program of Holstein Friesians

sons determined with OC

naam	vader	m.vader	DPS	aantal zonen vaders TopSelect
Woud. Russel	Jabot	Amos	517	20
Bobstar 50	Jabot	Sammy	511	15
Jesther	Mountain	Elton	474	12
Carousel Sierra	Jabot	Aerostar	465	8
Manat	Mandel	Bell Rex	455	13
Looking Major	Celsius	Sunny Boy	449	5
Melchior	Celsius	Sunny Boy	437	5
R. Marshall	Mandel	Southwind	426	8
Etazon Addison	Mountain	Elton	406	4
Ol. P. Tugolo	Prelude	Blackstar	402	7
Moet H. Hertz	Jabot	Bell Troy	394	0
Bertrand	Celsius	Nordkap	390	0
Delta Swinger	Celsius	Captain	385	0
Etazon Slogan	Mountain	Elton	381	3
Reg. J. Denver	Jabot	Leadman	376	0
Mid. Jimbo	Celsius	Sunny Boy	368	0

Tabel 1 – Voorbeeld selectie via TopSelect

Method to use depends on existing situation

- Commercial nucleus
 - Reliable pedigree, full control over mating and # offspring, single herd
 - Optimal Contribution no restrictions
- Single herd no control on litter size
 - Optimal Contribution equal contribution of females
- Heath sheep
 - Few large flocks, no pedigree, different owners (who like each other)
 - Breeding circle
- Other situations
 - Limited control over breeding
 - Other measures
 - Maximise # matings per sire
 - Limit # offspring of single dam (sire) to be entered in herd book
 - ...

