Genomic Selection in Dairy Cattle

Jack Dekkers

Current status

Challenges

Opportunities

Larry Schaeffer. 2006, J. Anim. Breed. Genet.

Table 1 Schedule of progeny testing activities

Time (months)	Activity
0	Elite dams chosen and bred.
9	Bull calves born from elite dams
21	Test matings of young bulls made
30	Daughters of young bulls born
45	Daughters of young bulls bred
54	Daughters calve and begin first lactation
57	First estimated breeding values for young bulls from test day model
64	Daughters complete first lactations, keep or cull young bulls

Table 2 Four pathways of selection, progeny testing

$\Delta G = 4.68 / 21.75 = 0.22\ \sigma_g/yr$

Pathway	Selection %	Accuracy i	r_{TI}	Generation Interval, L	$i \times r_{TI}$
Sire of bulls	5	2.06	0.99	6.5	2.04
Sire of cows	20	1.40	0.75	6	1.05
Dams of bulls	2	2.42	0.60	5	1.45
Dams of cows	85	0.27	0.50	4.25	0.14
Total				21.75	4.68

Table 3 Four pathways of selection, genome-wide strategy

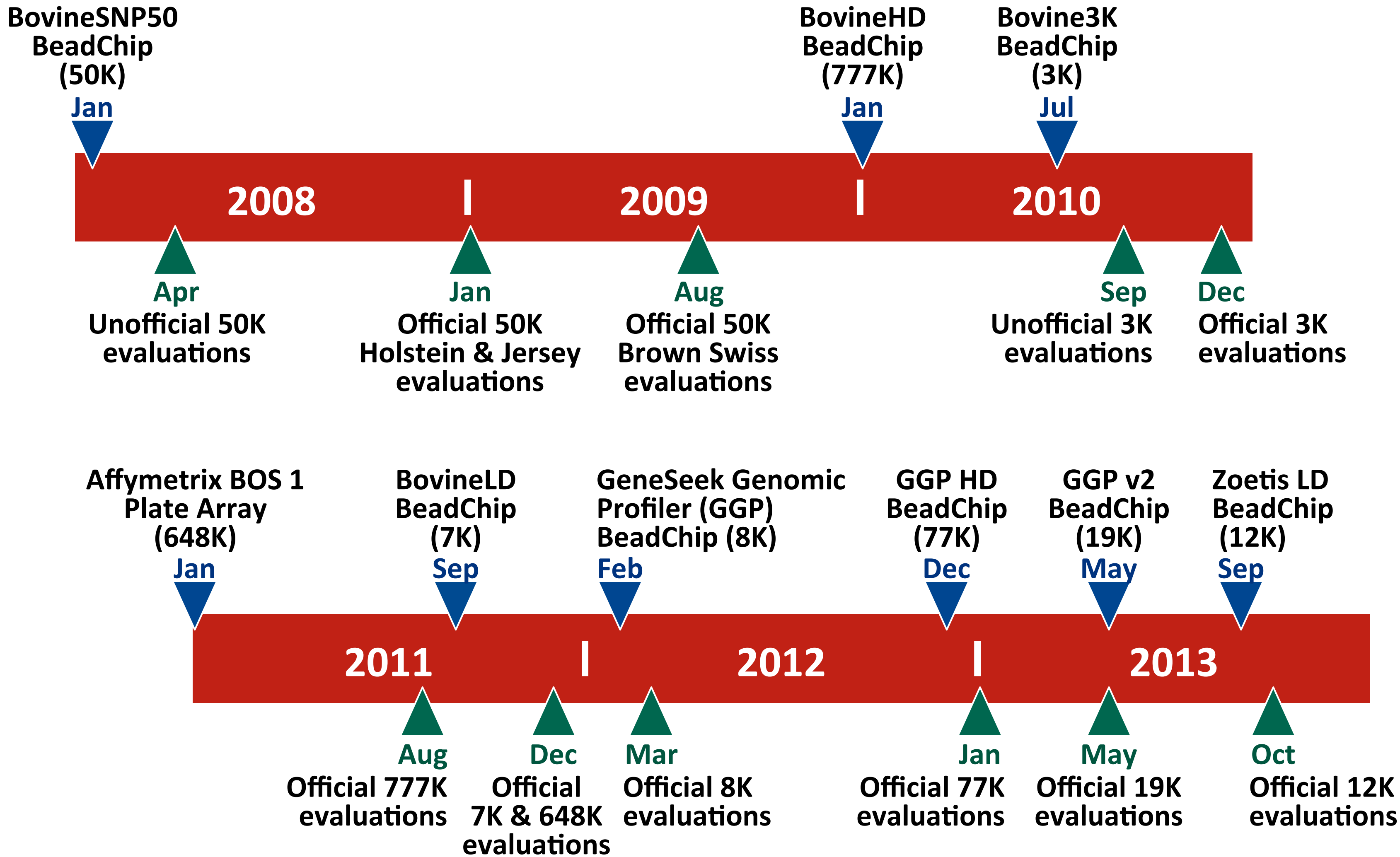
$\Delta G = 4.55 / 9.75 = 0.47\ \sigma_g/yr$

Pathway	Selection %	Accuracy i	r_{TI}	Generation Interval, L	$i \times r_{TI}$
Sire of bulls	5	2.06	0.75	1.75	1.54
Sire of cows	20	1.40	0.75	1.75	1.05
Dams of bulls	2	2.42	0.75	2	1.82
Dams of cows	85	0.27	0.50	4.25	0.14
Total				9.75	4.55

History of genomic evaluations

BovineSNP50 BeadChip available	Dec. 2007
First unofficial evaluation released	Apr. 2008
Official evaluations for Holsteins and Jerseys	Jan. 2009
Official evaluations for Brown Swiss	Aug. 2009
Monthly evaluation	Jan. 2010
Official 3K evaluations	Dec. 2010
BovineLD BeadChip available	Sept. 2011
Official evaluations for Ayrshires	Apr. 2013
Weekly evaluation	Nov. 2014

Progression of chips and genomic evaluations



Why genomics works for dairy cattle

- Extensive historical data available
- Well-developed genetic evaluation program
- Widespread use of AI sires
- Progeny-test programs
- High-value animals worth the cost of genotyping
- Long generation interval that can be reduced substantially by genomics

Wiggans

How is Genomic Selection changing dairy breeding?

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Embryo Transfer

Superior progeny-tested bull

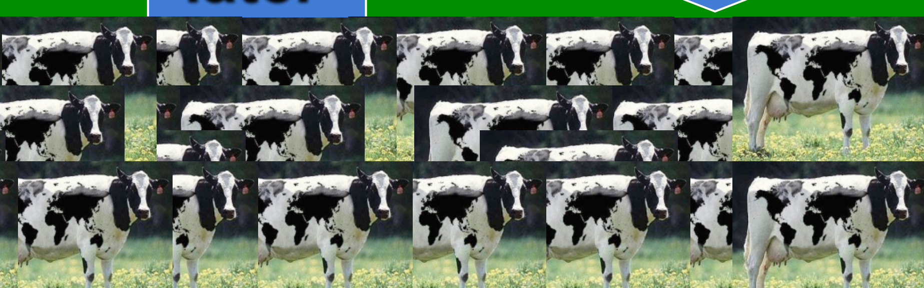
Superior genome-tested young bull

5 yrs & $$$$$$ later

Pro-geny Testing

DNA sam-ples

< 6 mo & $$ later



Illumina Bovine 50k Beadchip

Reliability gains

Reliability (%)	Ayrshire	Brown Swiss	Jersey	Holstein
Genomic	37	54	61	70
Parent average	28	30	30	30
Gain	9	24	31	40
Reference bulls	680	5,767	4,207	24,547
Animals genotyped	1,788	9,016	59,923	469,960
Exchange partners	Canada	Canada, Interbull	Canada, Denmark	Canada, Italy, UK

Source: VanRaden, Advancing Dairy Cattle Genetics: Genomics and Beyond presentation, Feb. 2014

Holstein prediction accuracy

Trait	Bias*	Reliability (%)	Reliability gain (% points)
Milk (kg)	−80.3	69.2	30.3
Fat (kg)	−1.4	68.4	29.5
Protein (kg)	−0.9	60.9	22.6
Fat (%)	0.0	93.7	54.8
Protein (%)	0.0	86.3	48.0
Productive life (mo)	−0.7	73.7	41.6
Somatic cell score	0.0	64.9	29.3
Daughter pregnancy rate (%)	0.2	53.5	20.9
Sire calving ease	0.6	45.8	19.6
Daughter calving ease	−1.8	44.2	22.4
Sire stillbirth rate	0.2	28.2	5.9
Daughter stillbirth rate	0.1	37.6	17.9

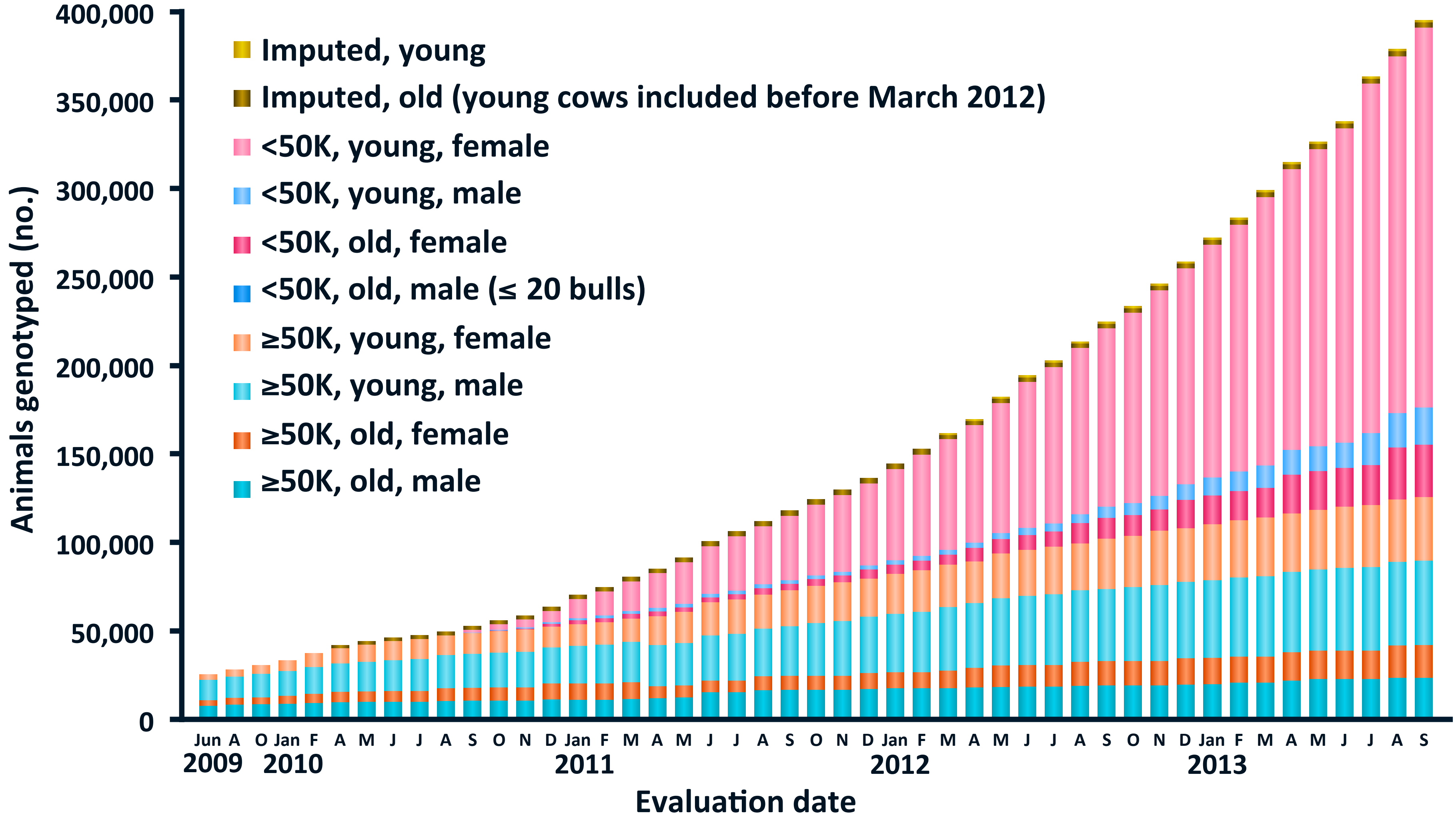
*2013 deregressed value – 2009 genomic evaluation

Holstein prediction accuracy

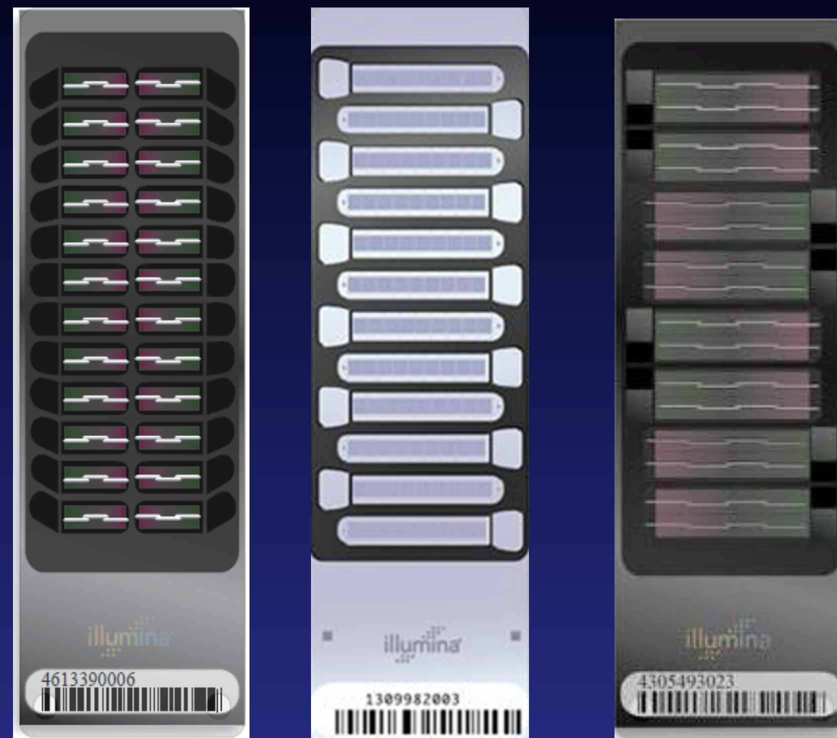
Trait	Bias*	Reliability (%)	Reliability gain (% points)
Final score	0.1	58.8	22.7
Stature	–0.2	68.5	30.6
Dairy form	–0.2	71.8	34.5
Rump angle	0.0	70.2	34.7
Rump width	–0.2	65.0	28.1
Feed and legs	0.2	44.0	12.8
Fore udder attachment	–0.2	70.4	33.1
Rear udder height	–0.1	59.4	22.2
Udder depth	–0.3	75.3	37.7
Udder cleft	–0.2	62.1	25.1
Front teat placement	–0.2	69.9	32.6
Teat length	–0.1	66.7	29.4

*2013 deregressed value – 2009 genomic evaluation

Genotypes evaluated



Can you afford genomic testing?



Number of SNP	9K	50K	800K
U.S. Price	€32	€92	€184
International price	€41	€100	€192

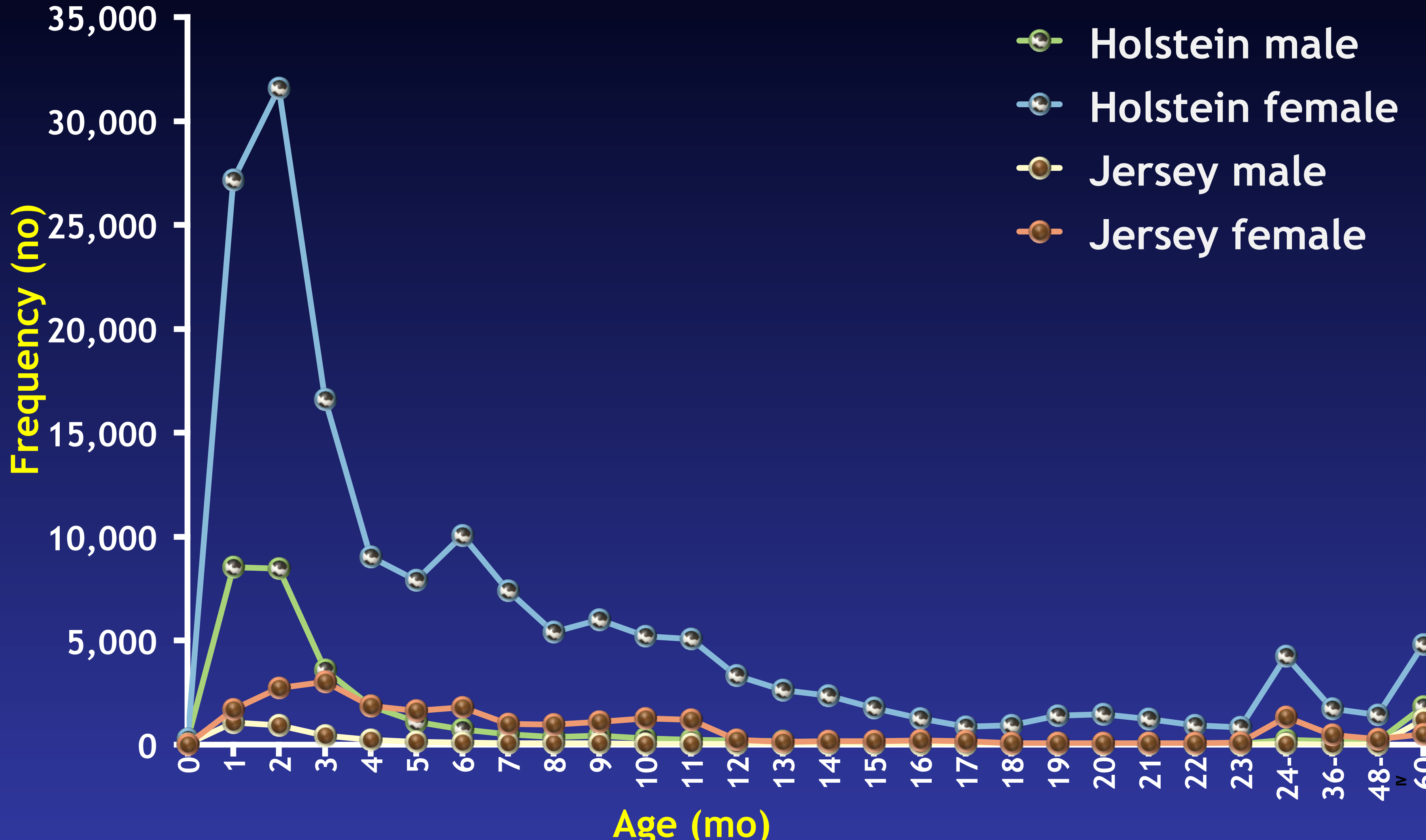
SNP count for different chips

Chip	SNP (no.)	Chip	SNP (no.)
50K	54,001	GP2	19,809
50K v2	54,609	ZLD	11,410
3K	2,900	ZMD	56,955
HD	777,962	ELD	9,072
Affy	648,875	LD2	6,912
LD	6,909	GP3	26,151
GGP	8,762	ZL2	17,557
GHD	77,068	ZM2	60,914

2014 genotypes by chip SNP density

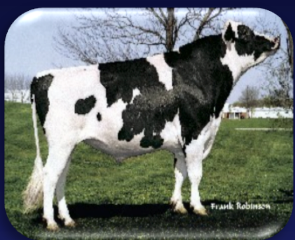
Chip SNP density	Female	Male	All animals
Low	239,071	29,631	268,702
Medium	9,098	14,202	23,300
High	140	28	168
All	248,309	43,861	292,170

Genotypes by age (last 12 months)



Genomic prediction of progeny test

0 1 2 3 4 5



Select parents, transfer embryos to recipients

Calves born and DNA tested

Calves born from DNA-selected parents

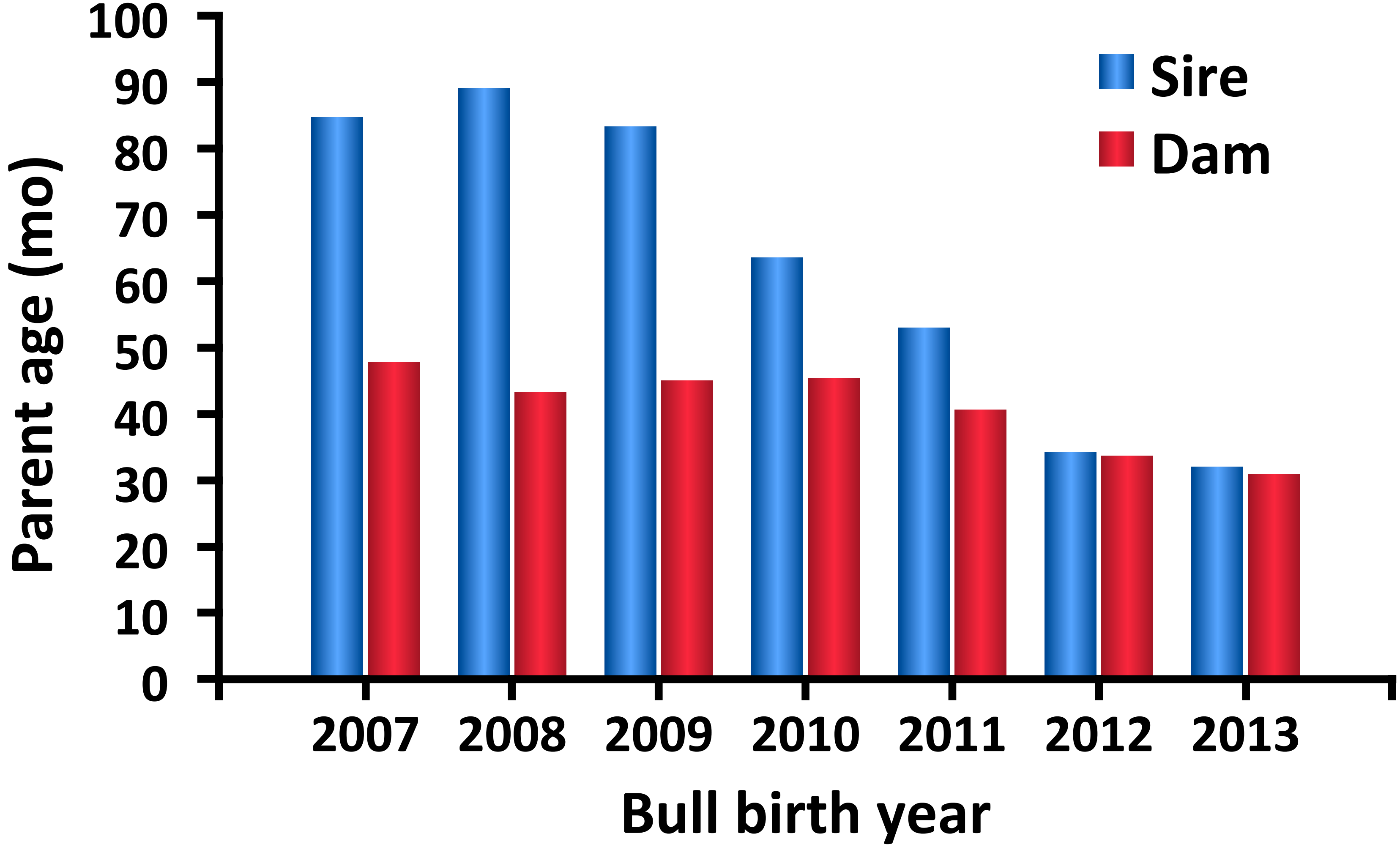
Bull receives progeny test

Reduce generation interval from 5 to 2 years

Marketed Holstein bulls

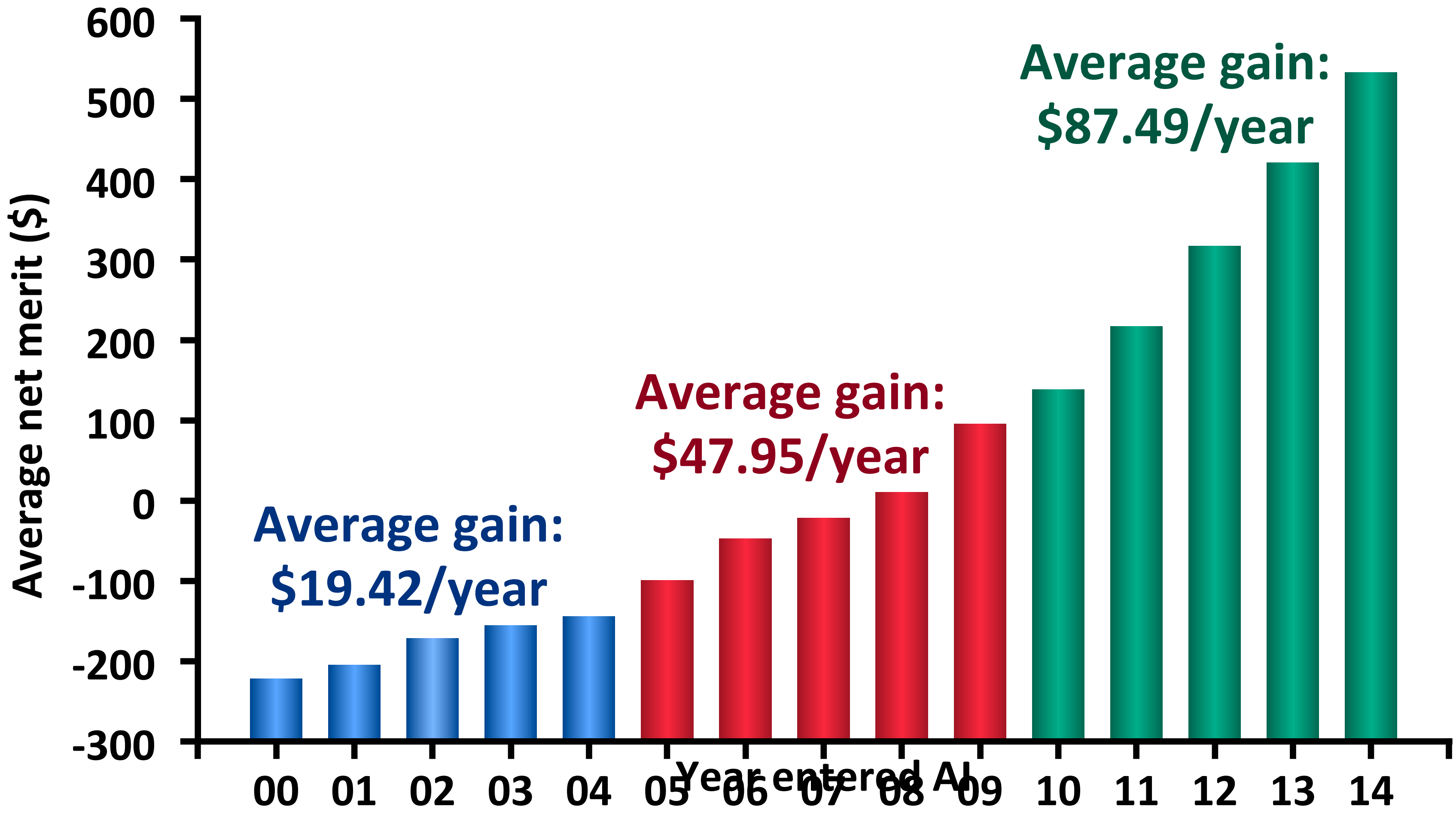
Year entered AI	Traditional progeny-tested	Genomic marketed	All bulls
2008	1,768	170	1,938
2009	1,474	346	1,820
2010	1,388	393	1,781
2011	1,254	648	1,902
2012	1,239	706	1,945
2013	907	747	1,654
2014	661	792	1,453

Parent ages for marketed Holstein bulls

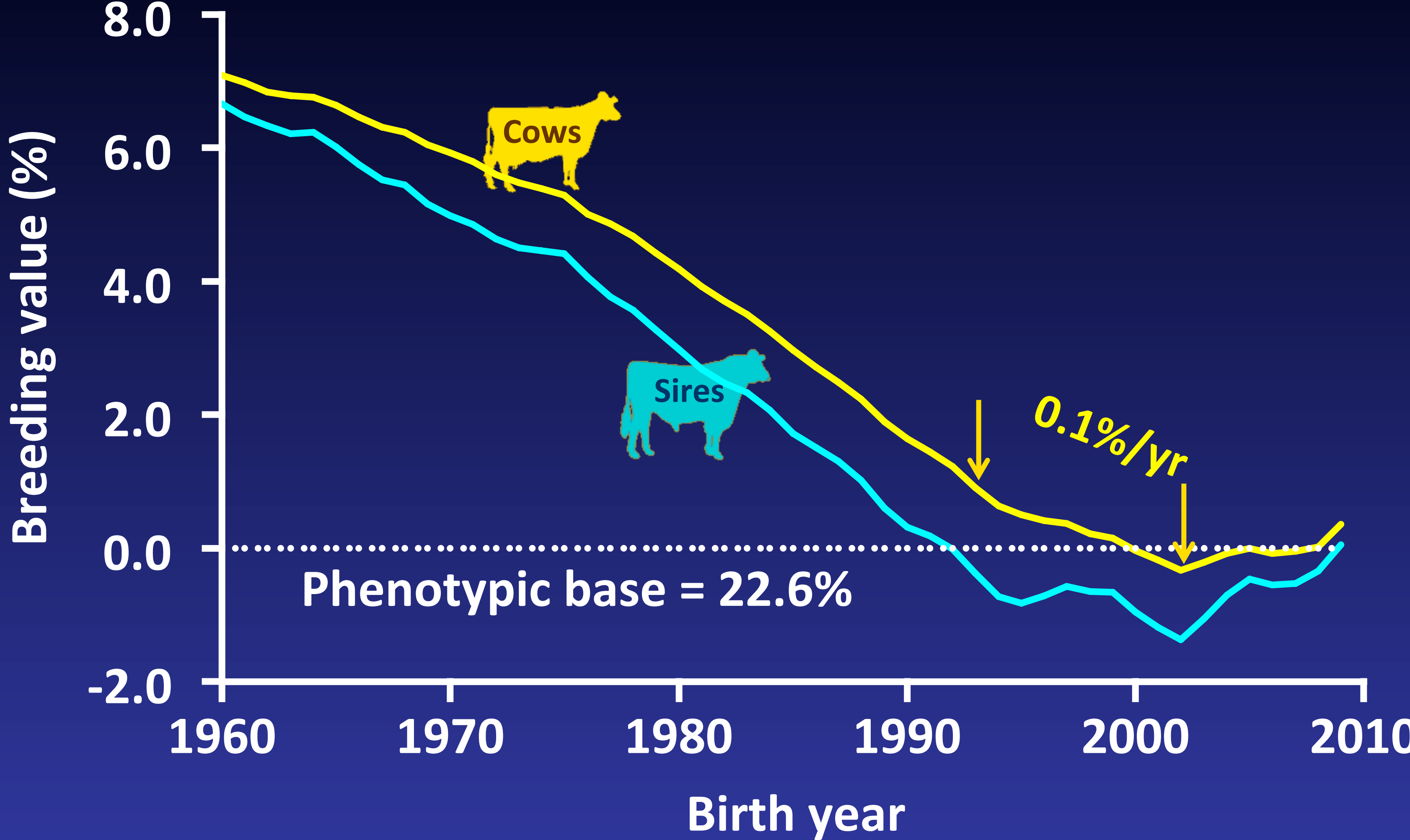


USDA

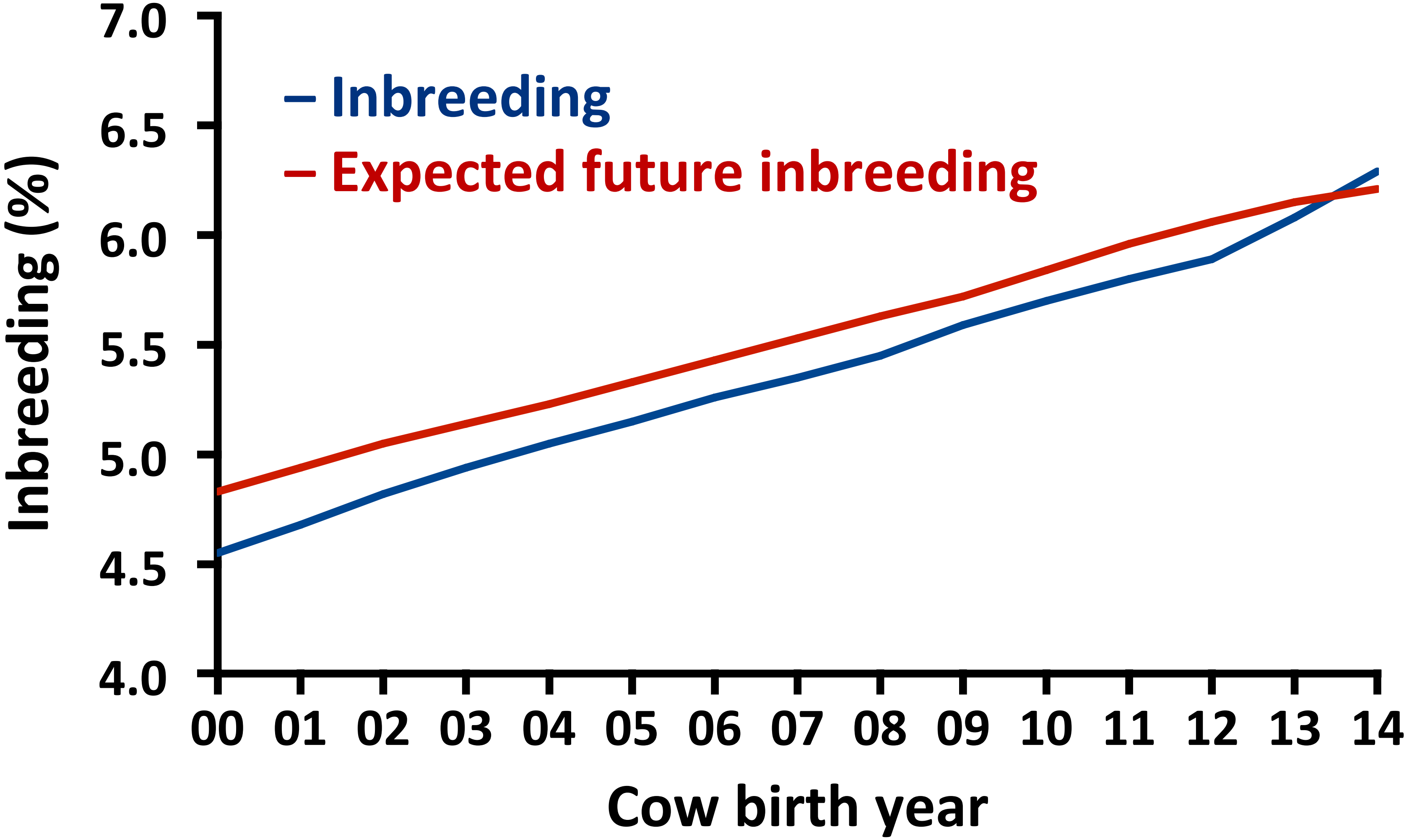
Genetic merit of marketed Holstein bulls



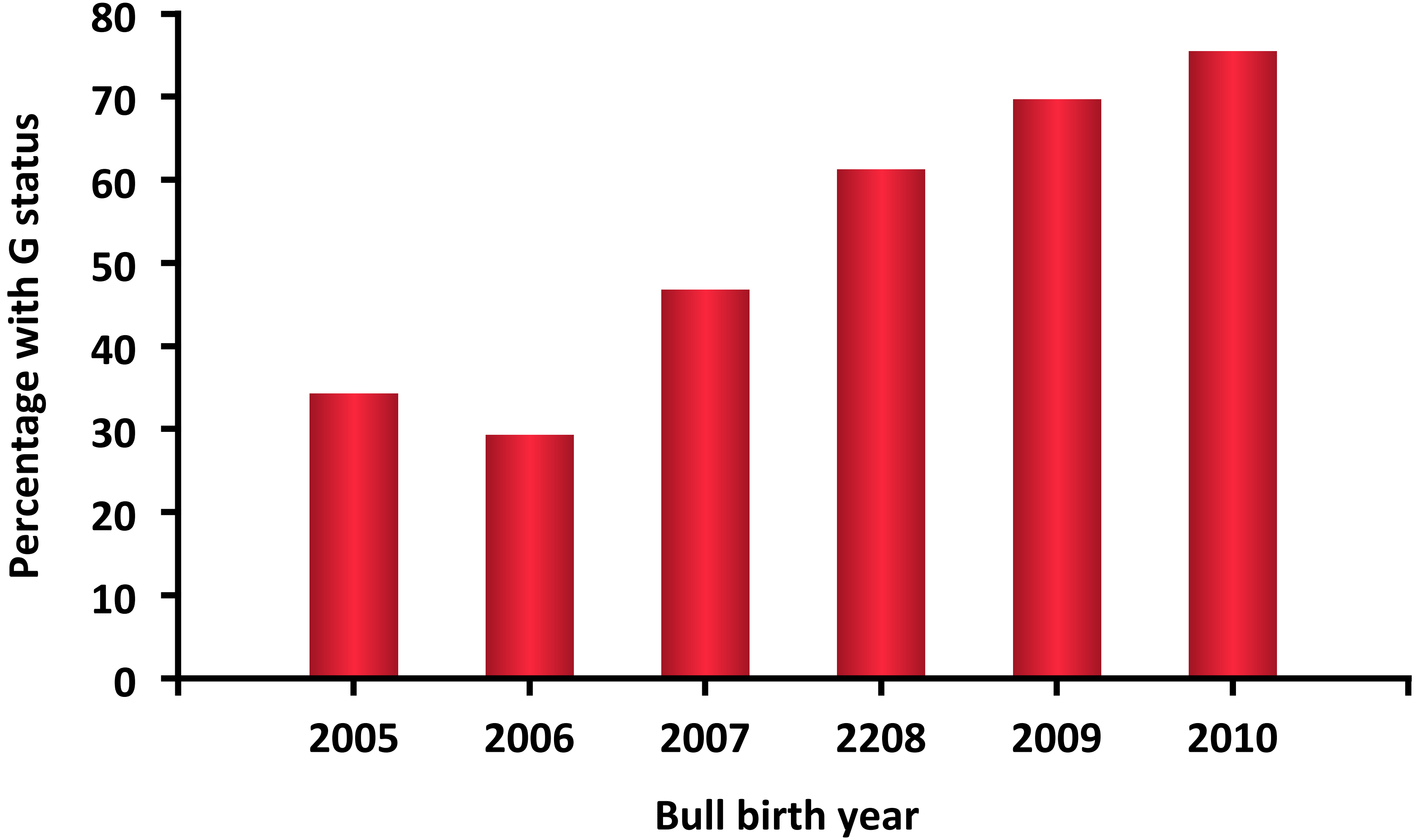
Holstein daughter pregnancy rate (%)



Inbreeding for Holstein cows



Active AI bulls that were genomic bulls



Weekly evaluations

- Released to nominators, breed associations, and dairy records processing centers at 8 am each Tuesday
- Calculations restricted to genotypes that first became usable during the previous week
- Computing time minimized by not calculating reliability or inbreeding

Genetic choices

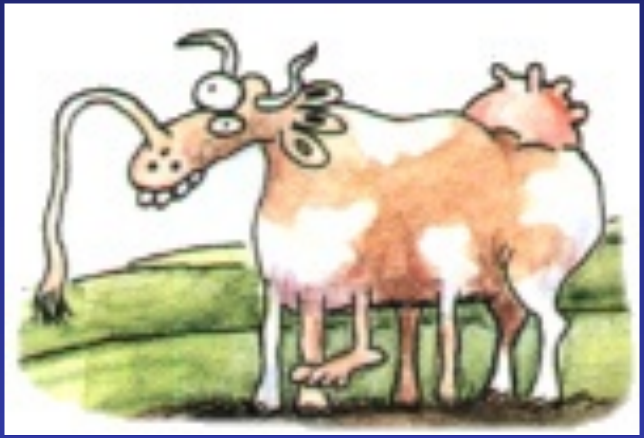
- Before genomics:
  - Proven bulls with daughter records (PTA)
  - Young bulls with parent average (PA)
- After genomics:
  - Young animals with DNA test (GPTA)
  - Reliability of GPTA ~70% compared to PA ~35% and PTA ~85% for Holstein NM$

Impact on breeders

- Haplotype and gene tests can be used selection and mating programs
- A small number of elite breeders are investing heavily in genomics
- About 30% of young males have been genotyped directly by breeders since April 2013
- Prices for top genomic heifers can be very high (e.g., €250,000)

Impact on dairy producers

- General
  - Reduced generation interval
  - Increased rates of genetic gain
  - Greater inbreeding/homozygosity?



Impact on dairy producers *(continued)*

- Sires
  - Higher average genetic merit of available bulls
  - More rapid increase in genetic merit for all traits
  - Larger choice of bulls in terms of traits and semen price
  - Greater use of young bulls

International dairy breeding

- Genotype alliances
  - North America (US, Canada, UK, Italy)
  - Ireland, New Zealand
  - Netherlands, Australia
  - Eurogenomics (Denmark/Sweden/Finland, France, Germany, Netherlands/Belgium, Spain, Poland)
- Interbull genomic multitrait across-country evaluation (GMACE)

How is Genomic Selection changing Dairy Cattle Breeding?

- AI Studs market
  young bulls / bull teams
  selected on Genomic EBV

- These young bulls are from ET flushes of <u>heifers</u> mated to
  <u>young</u> bulls

  selected on Genomic EBV

- Need for progeny-testing is decreasing

- Easier for new organization to enter the market

X

The Future of Dairy Cattle Breeding . . . .

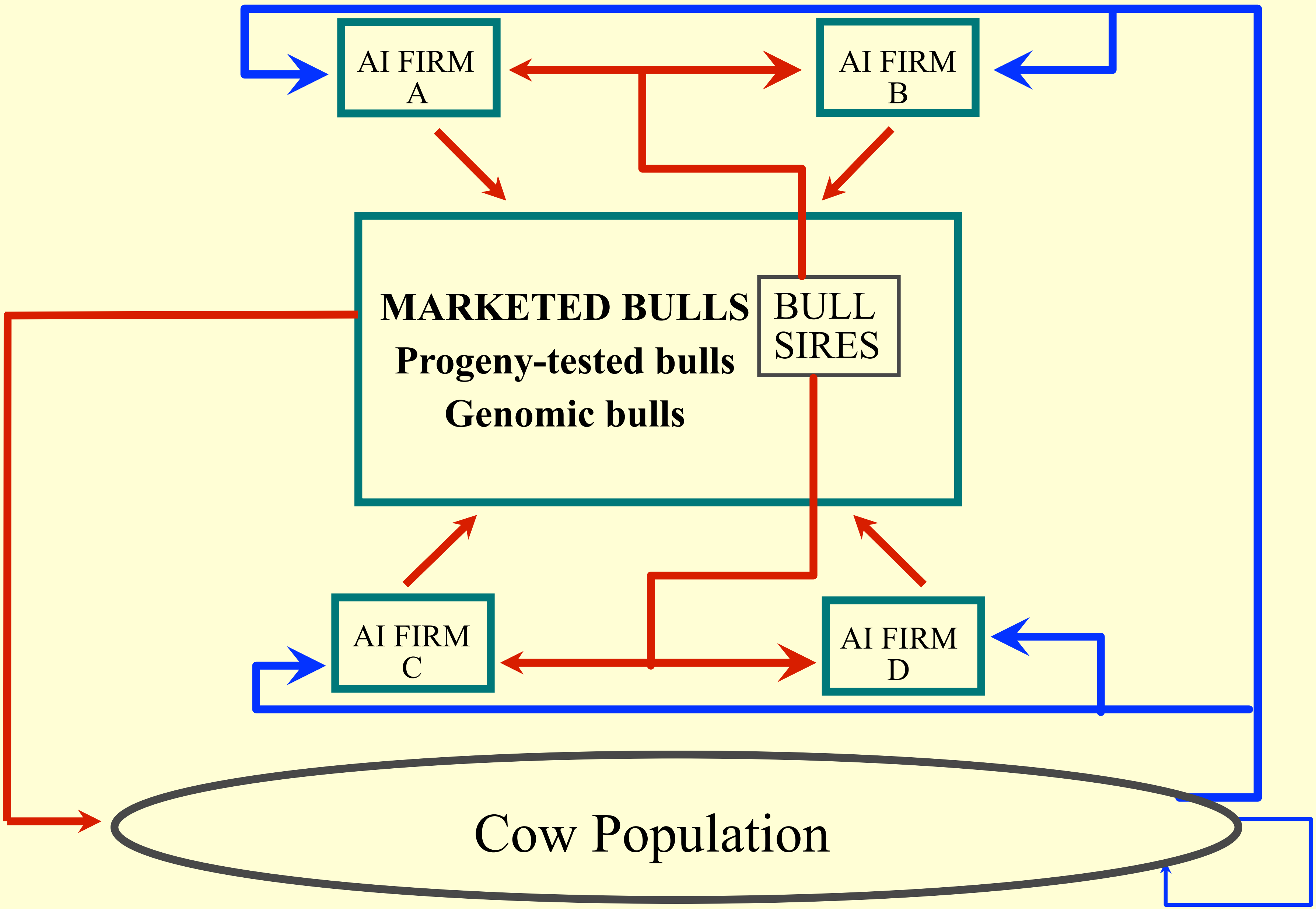
How can AI companies maintain market share?

When Everyone . . . .

- has access to superior genetics
- can identify such genetics using genomics
- and market that genetics using genomics

How to differentiate/protect your product?

A Competitive Global AI Industry



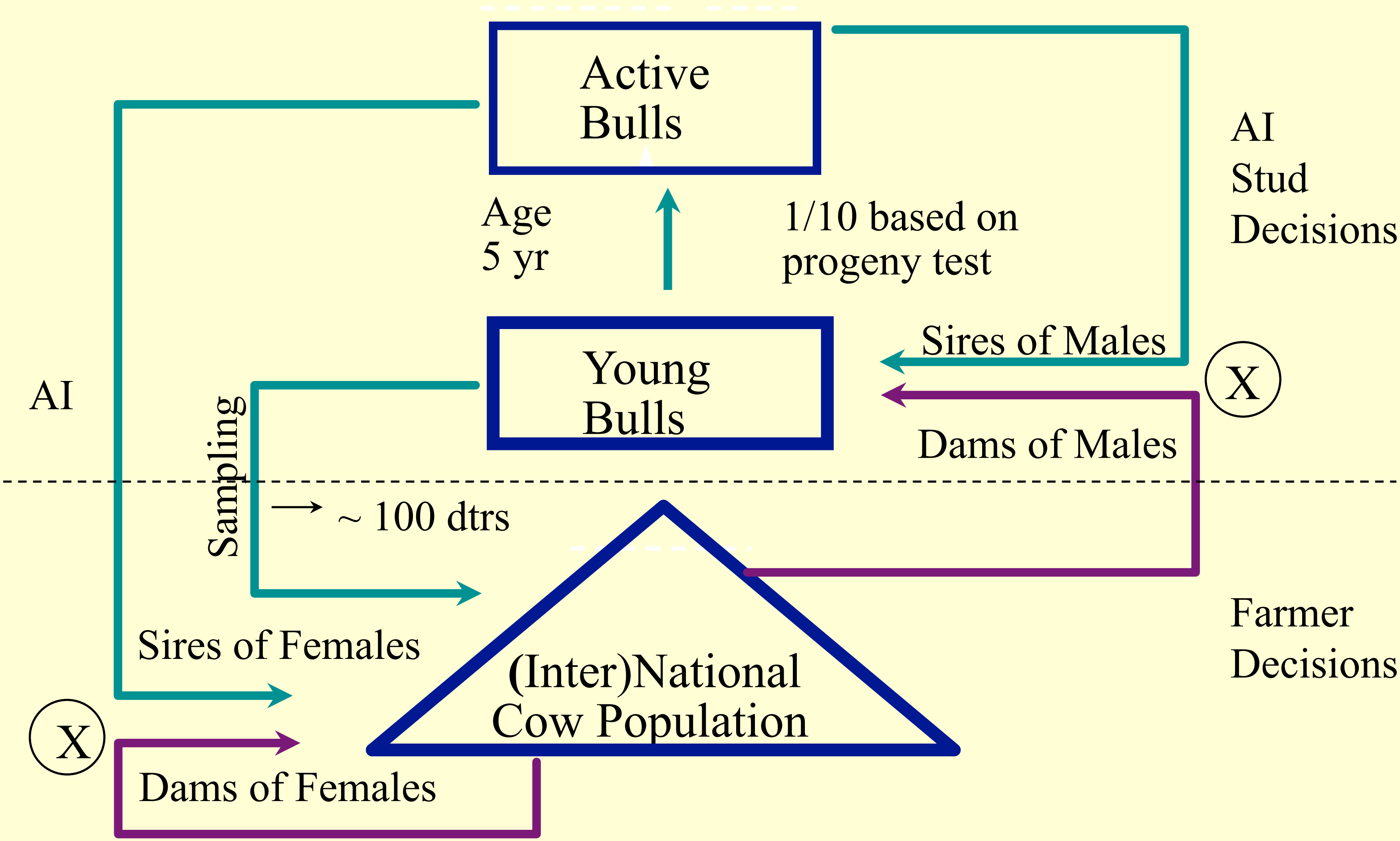
The Future of Dairy Cattle Breeding . . . .

How can AI companies maintain market share?

How to differentiate/protect your product?

- **Protect elite germplasm**
  - Elite nucleus herds with integration of genomic and reproductive technologies

Dairy Cattle Progeny Testing Program



Characteristics of Dairy Cattle Breeding Programs

- Sex-limited traits
- High male reproductive rate

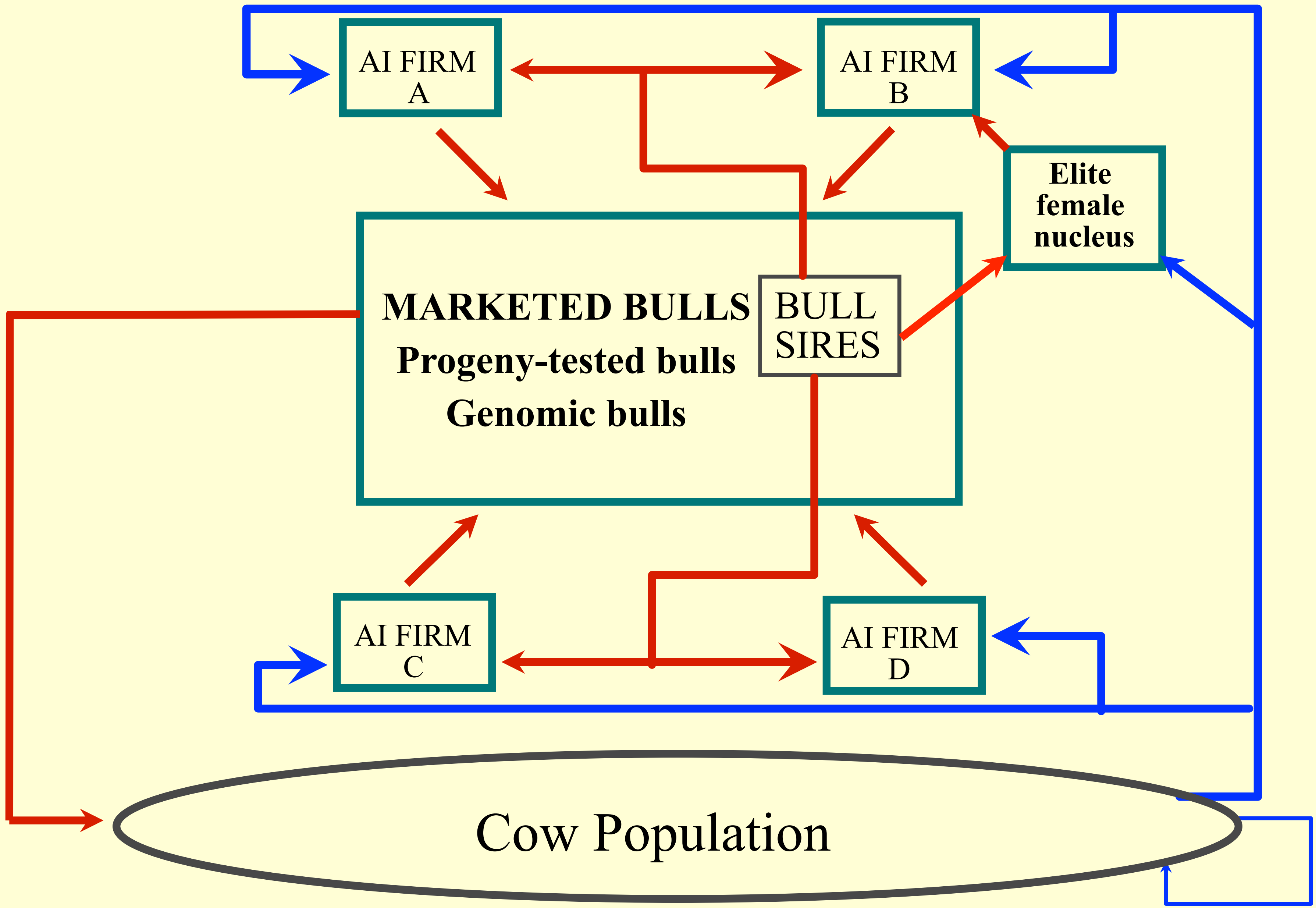
Progeny testing

- Field recording programs
- Low female reproductive rate
- Limited crossbreeding
- High cost of animals

Commercial population as source of female genetics

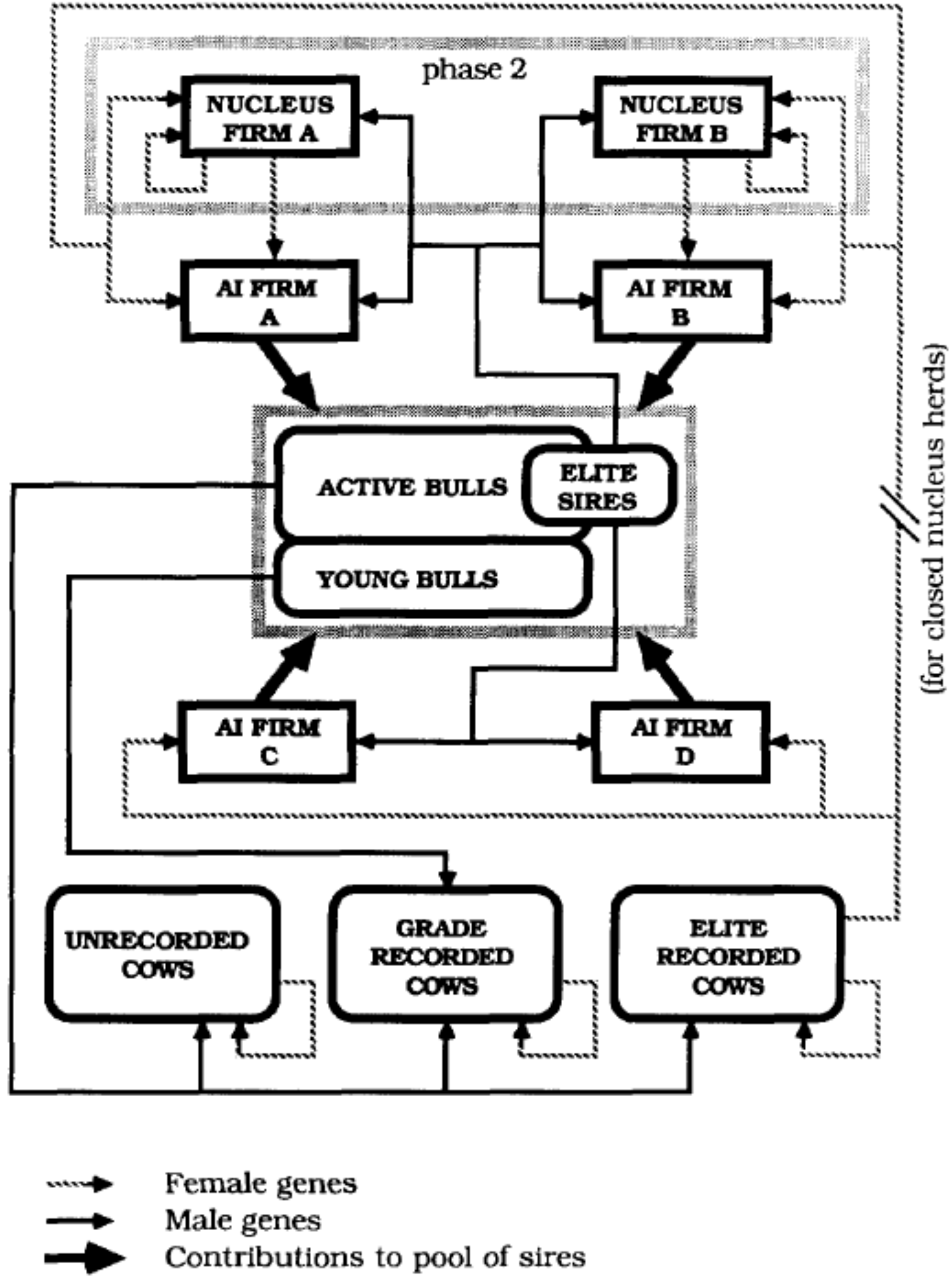
Population Based Program

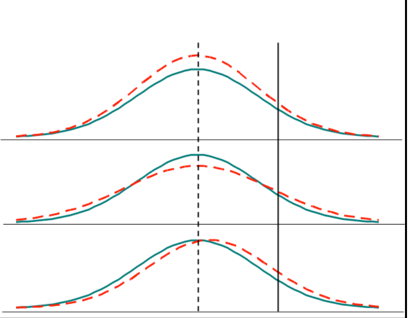
Protecting Elite Germplasm



Genetic and Economic Evaluation of Nucleus Breeding Schemes for Commercial Artificial Insemination Firms

J.C.M. Dekkers and G.E. Shook
J. Dairy Sci. (1990) 73:1920-1937





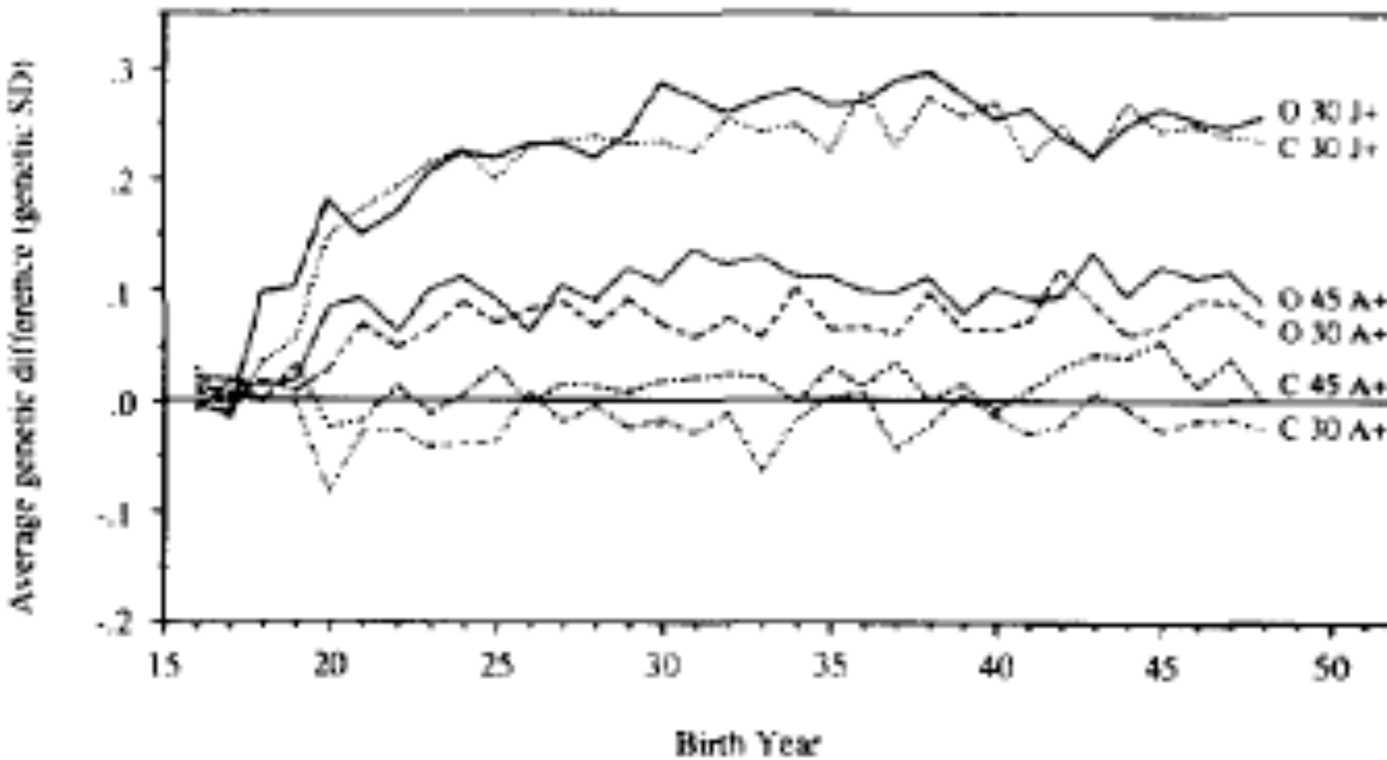


Figure 4. Average genetic difference between young bulls of AI firm A and young bulls of competitors, after adoption of a nucleus breeding scheme by firm A in yr 15 with repeated use of donors. O = Open, C = closed, 30 or 45 = 30 or 45 replacement heifers, J+ = heifers and first, second, and third lactation cows, and A+ = second and third lactation cows.

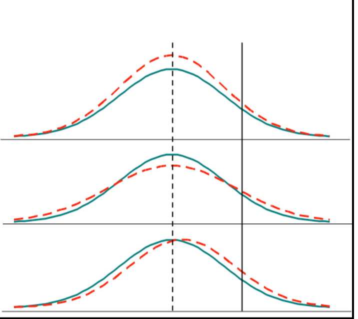


TABLE 4. Effect of adoption of a nucleus breeding scheme by one AI firm on its present value of returns for different numbers of years of selection.[1]

Evaluation period	Nucleus breeding scheme[2]			
	C30A	C45A	O30A	O45A
(yr)				
6	−.08 (.03)[3]	−.06 (.03)	−.01 (.03)	.04 (.03)
8	−.08 (.03)	−.04 (.02)	.01 (.02)	.06 (.03)
10	−.10 (.02)	−.05 (.02)	.05 (.02)	.09 (.03)
15	−.12 (.02)	−.06 (.02)	.08 (.02)	.11 (.02)
20	−.14 (.02)	−.07 (.01)	.09 (.02)	.14 (.02)
	C30A+	C45A+	O30A+	O45A+
6	−.05 (.03)	.01 (.03)	.00 (.03)	.09 (.03)
8	−.05 (.03)	.03 (.03)	.04 (.03)	.13 (.03)
10	−.05 (.02)	.03 (.03)	.06 (.03)	.14 (.03)
15	−.03 (.02)	.03 (.02)	.10 (.02)	.17 (.02)
20	−.03 (.02)	.04 (.02)	.13 (.02)	.20 (.02)
	C30J	C45J	O30J	045J
4	.15 (.05)	.11 (.04)	.21 (.05)	.15 (.05)
6	.23 (.04)	.20 (.03)	.23 (.04)	.24 (.04)
8	.30 (.04)	.33 (.03)	.33 (.04)	.36 (.04)
10	.35 (.04)	.39 (.03)	.39 (.04)	.43 (.03)
15	.41 (.03)	.47 (.03)	.45 (.03)	.52 (.03)
20	.46 (.03)	.52 (.03)	.50 (.03)	.56 (.03)
	C30J+	C45J+	O30J+	O45J+
4	.08 (.05)	.16 (.05)	.16 (.04)	.21 (.05)
6	.23 (.04)	.25 (.04)	.22 (.04)	.32 (.04)
8	.33 (.04)	.38 (.04)	.33 (.04)	.41 (.04)
10	.40 (.04)	.45 (.04)	.42 (.03)	.49 (.04)
15	.50 (.03)	.55 (.03)	.52 (.03)	.59 (.03)
20	.55 (.03)	.63 (.03)	.59 (.03)	.65 (.03)

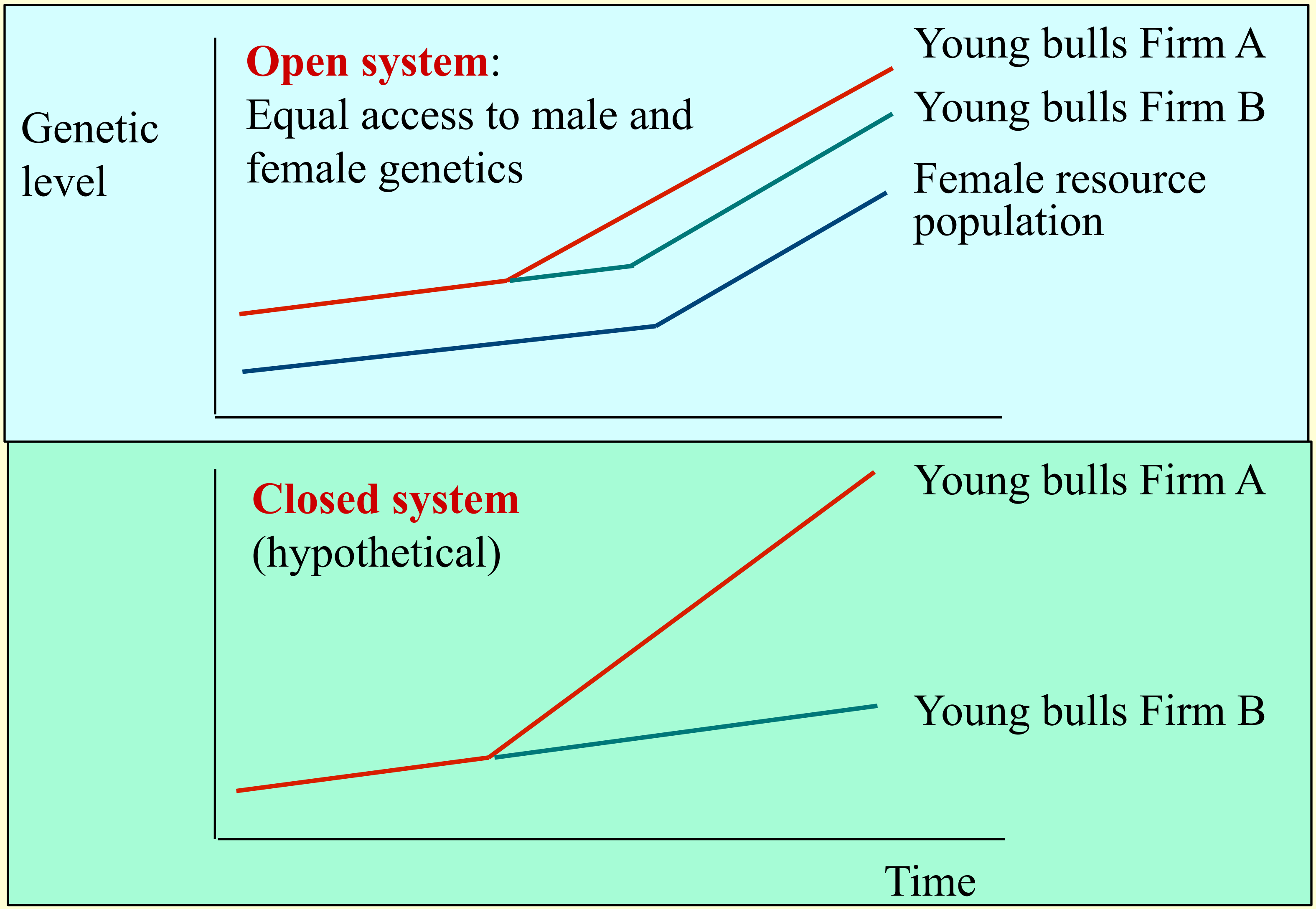
[1]Changes in present values of returns are expressed as a fraction of corresponding results for the breeding structure in phase one (Table 1). Returns were based on 50 replicates, with 1 observation per replicate for nucleus schemes and 5 observations per replicate for the conventional scheme.

[2]O = Open, C = closed, 30 or 45 = 30 or 45 replacement heifers, J = heifers, J+ = heifers and first, second, and third lactation cows, A = second lactation cows, and A+ = second and third lactation cows.

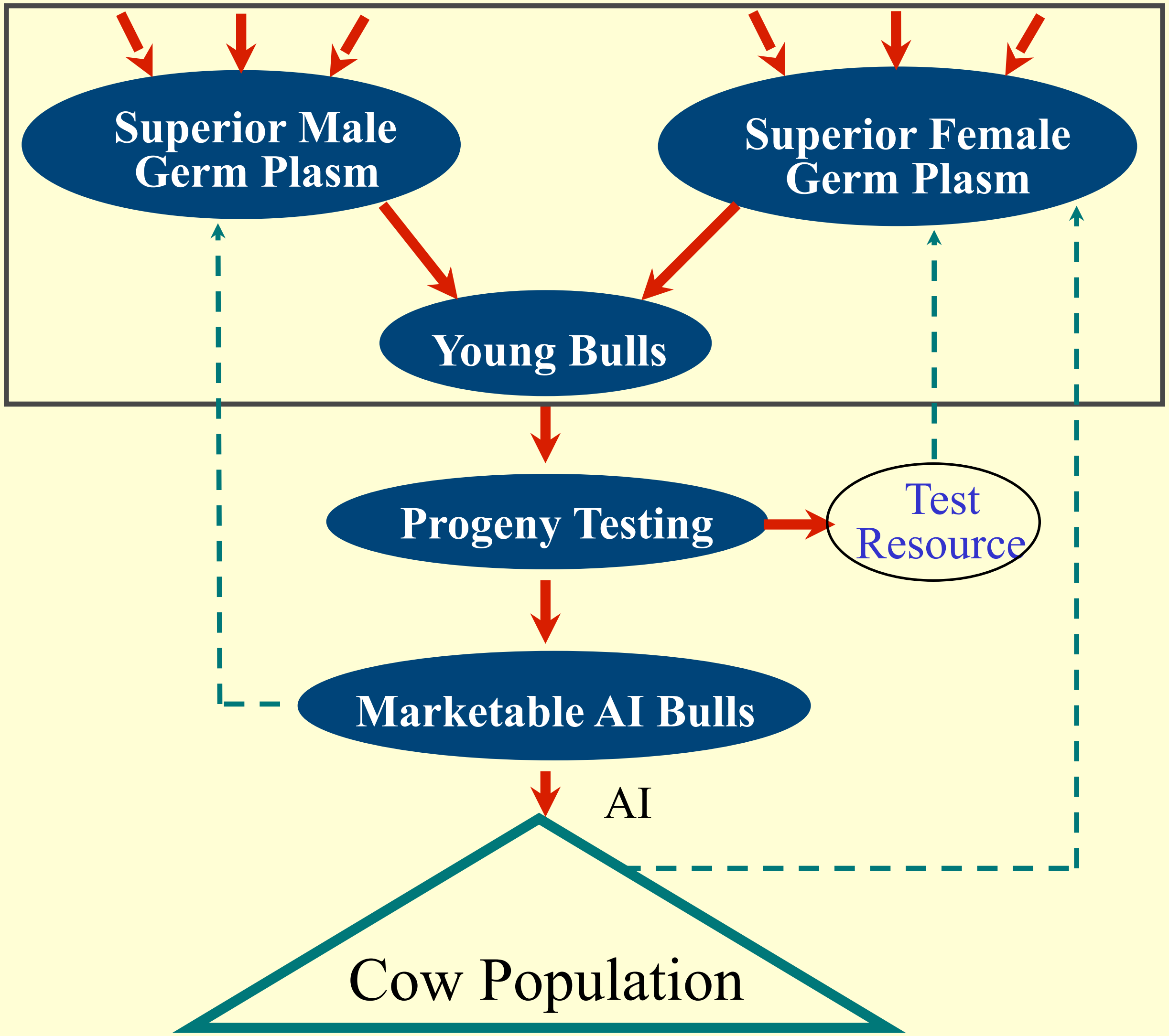
[3]Approximate standard errors are in parentheses.

- an AI firm's program is part of a single global breeding program
- at equilibrium, all AI firms improve at the same rate but with genetic lags

Impact of Improving Rate of Response by Firm A in a Competitive Market



Breeding Company View of AI Progeny Testing Programs

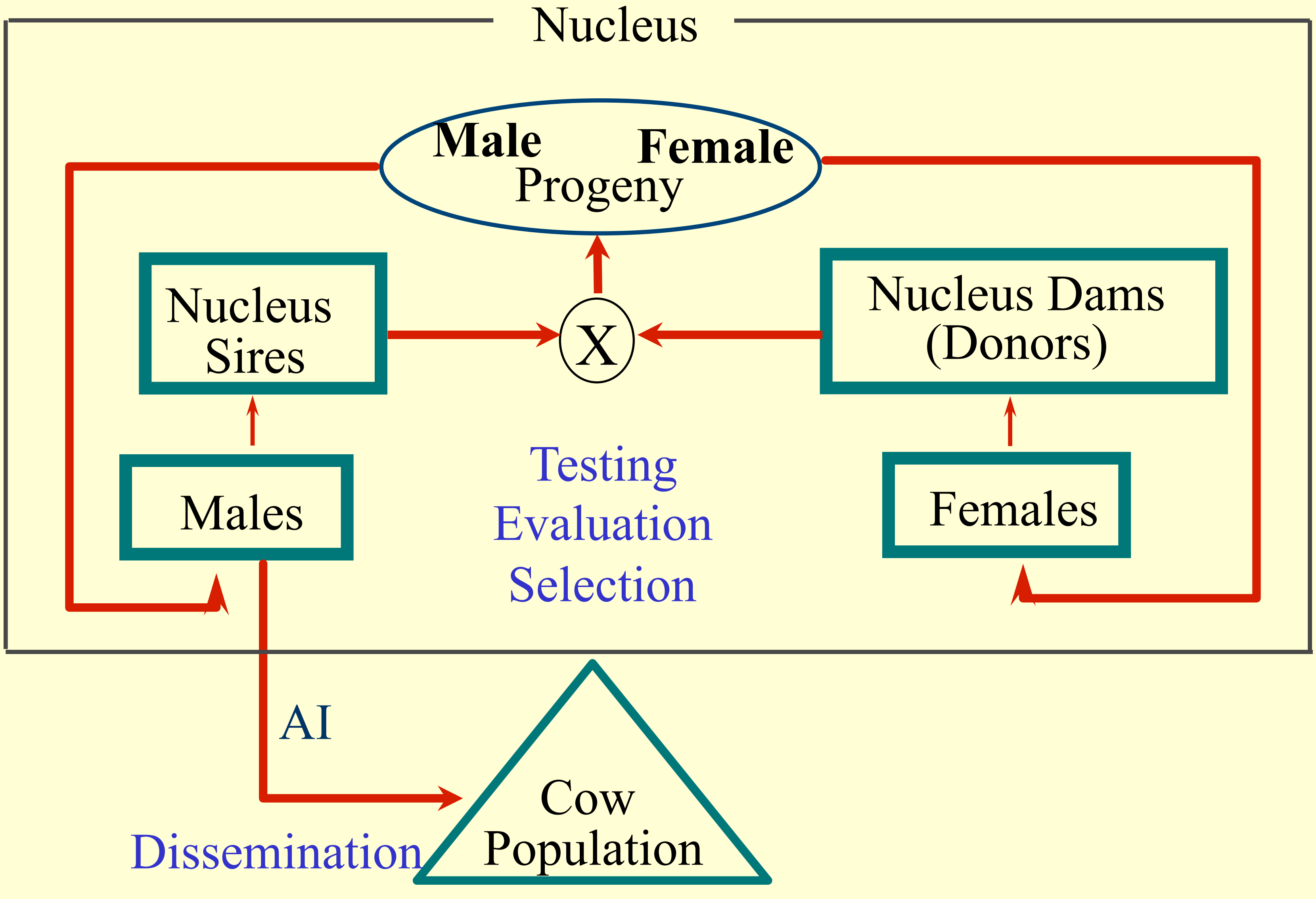


Testing
Evaluation
Sourcing

Product
Development

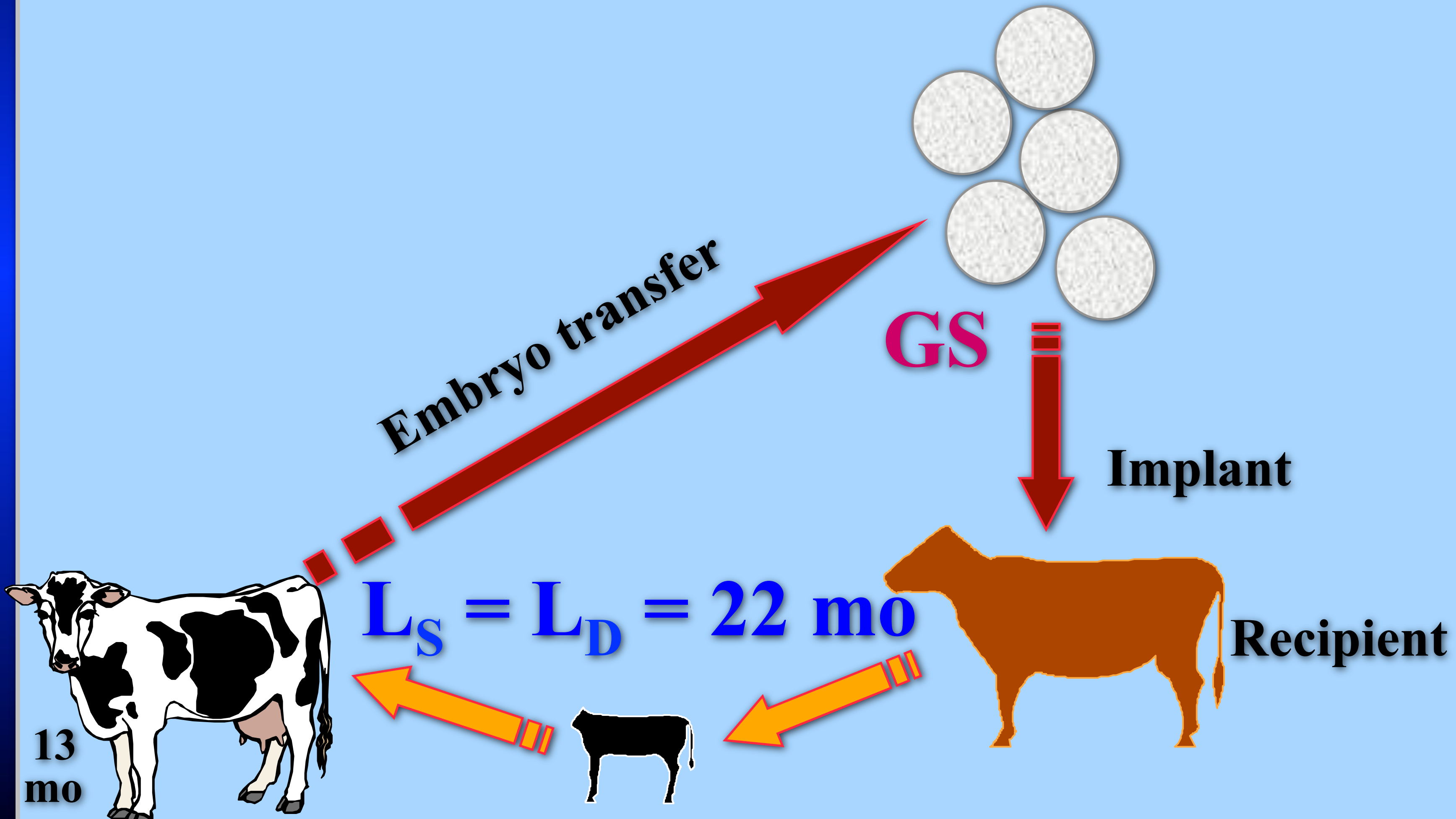
Dissemination
Product Sale

Nucleus Breeding Scheme (Closed)



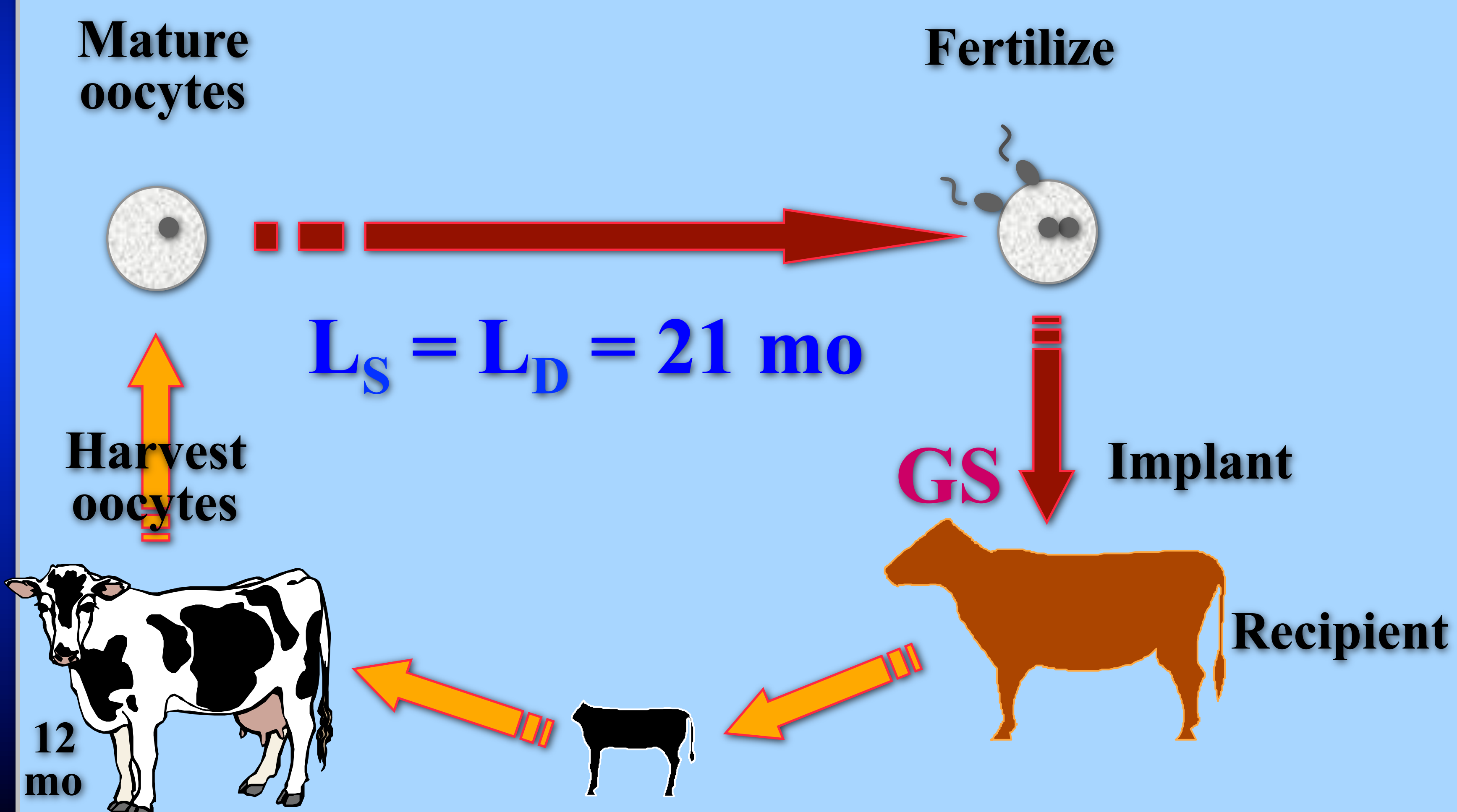
Reducing generation intervals

Integrating Genomics and Reproductive Technologies

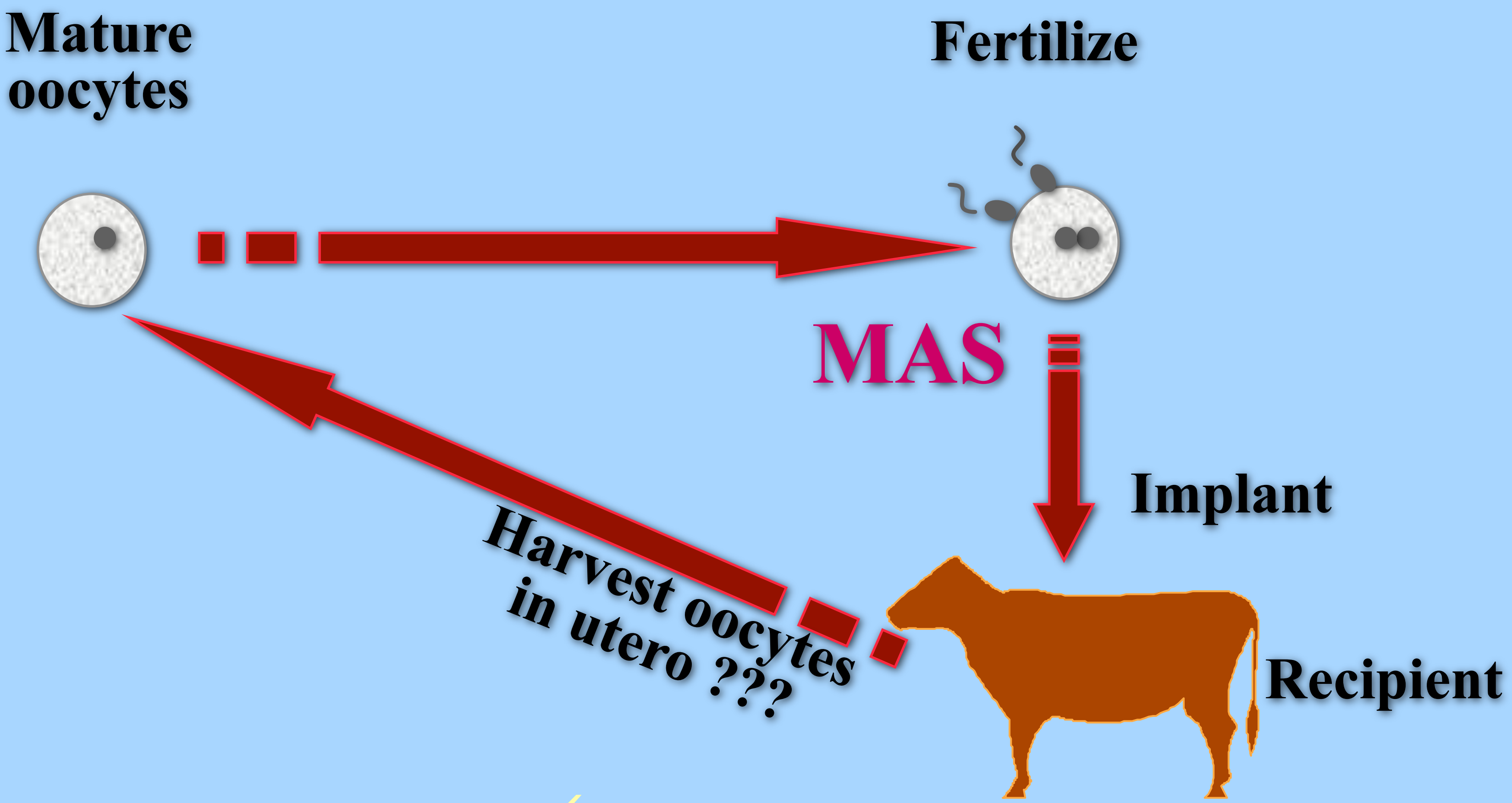


Reducing generation intervals

Integrating Genomics and Reproductive Technologies



Integrating Reproductive and Molecular Technology



Georges & Massey '91

MAS + Reproductive Technology

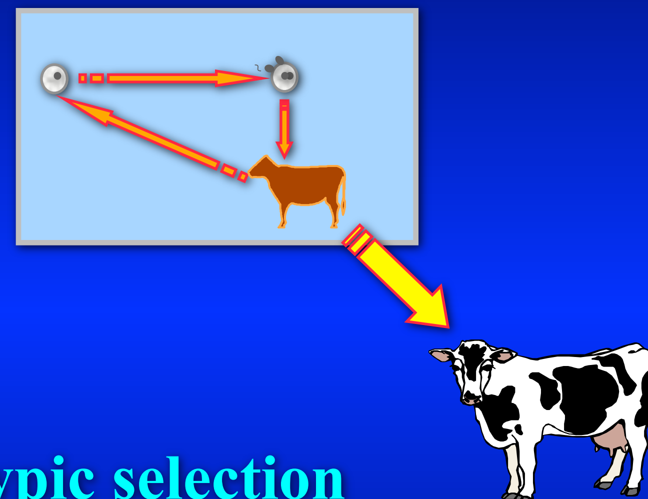
Velogenetics *(Georges,Massey '91)*

Generation

1 genotyping - MAS

2 genotyping - MAS

3 genotyping - MAS

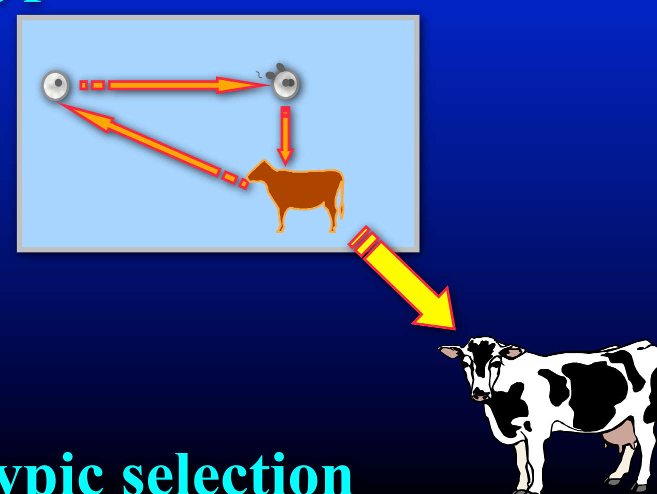


4 phenotyping - phenotypic selection

5 genotyping - MAS

6 genotyping - MAS

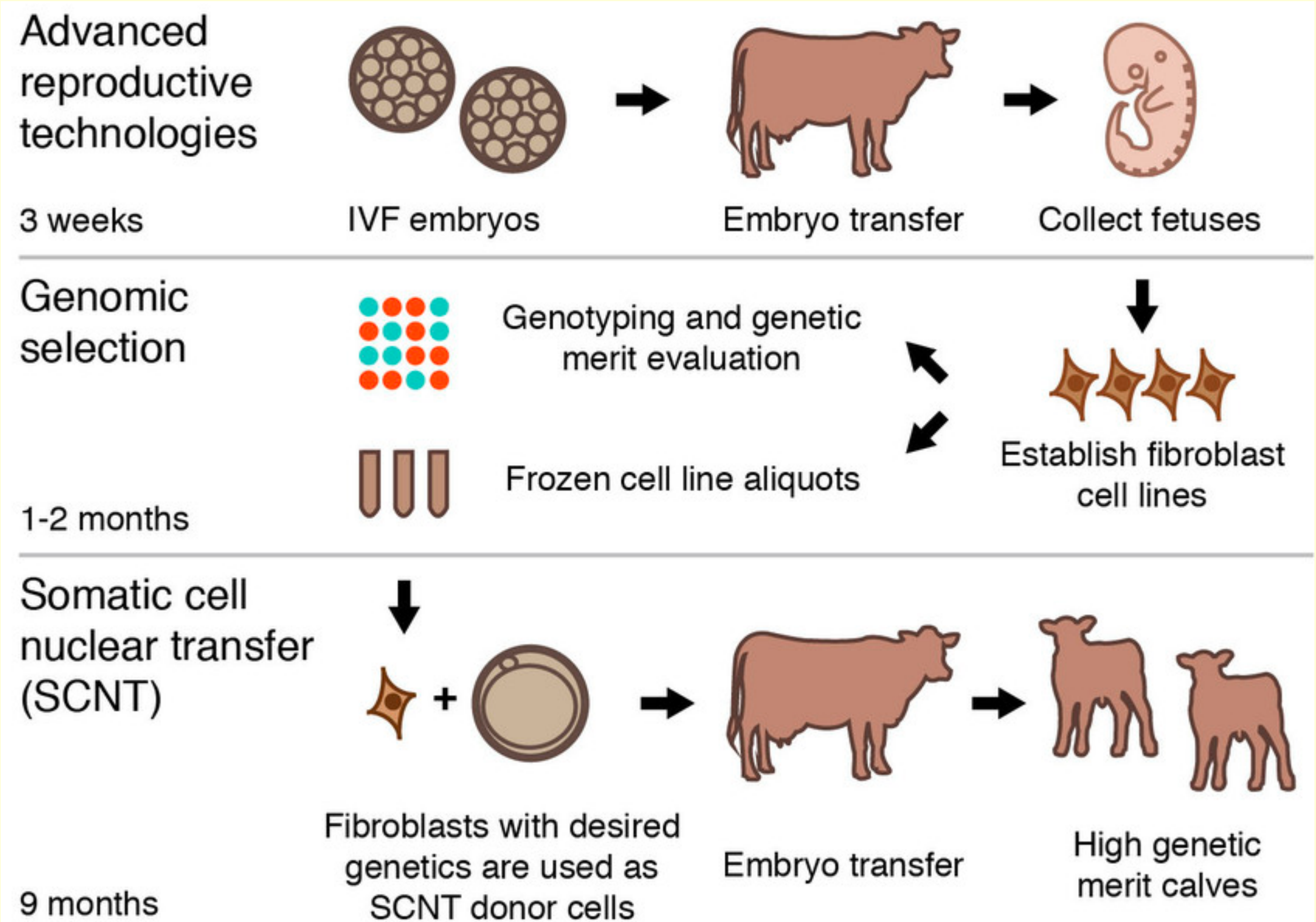
7 genotyping - MAS



8 phenotyping - phenotypic selection

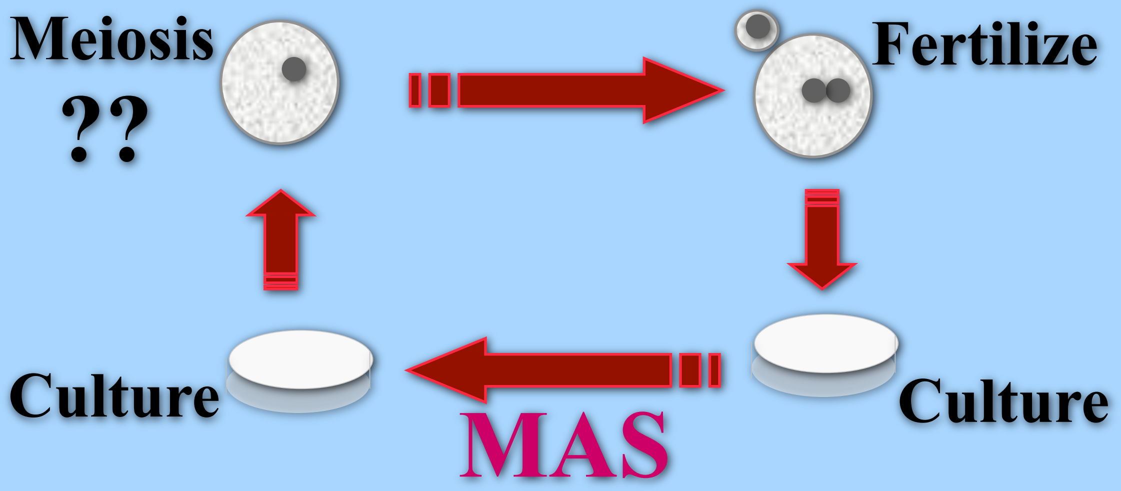
Combining genomic prediction with advanced reproductive technologies

TRANS OVA genetics



Nuclear Whizzogenetics

(Haley and Visscher, 1998)



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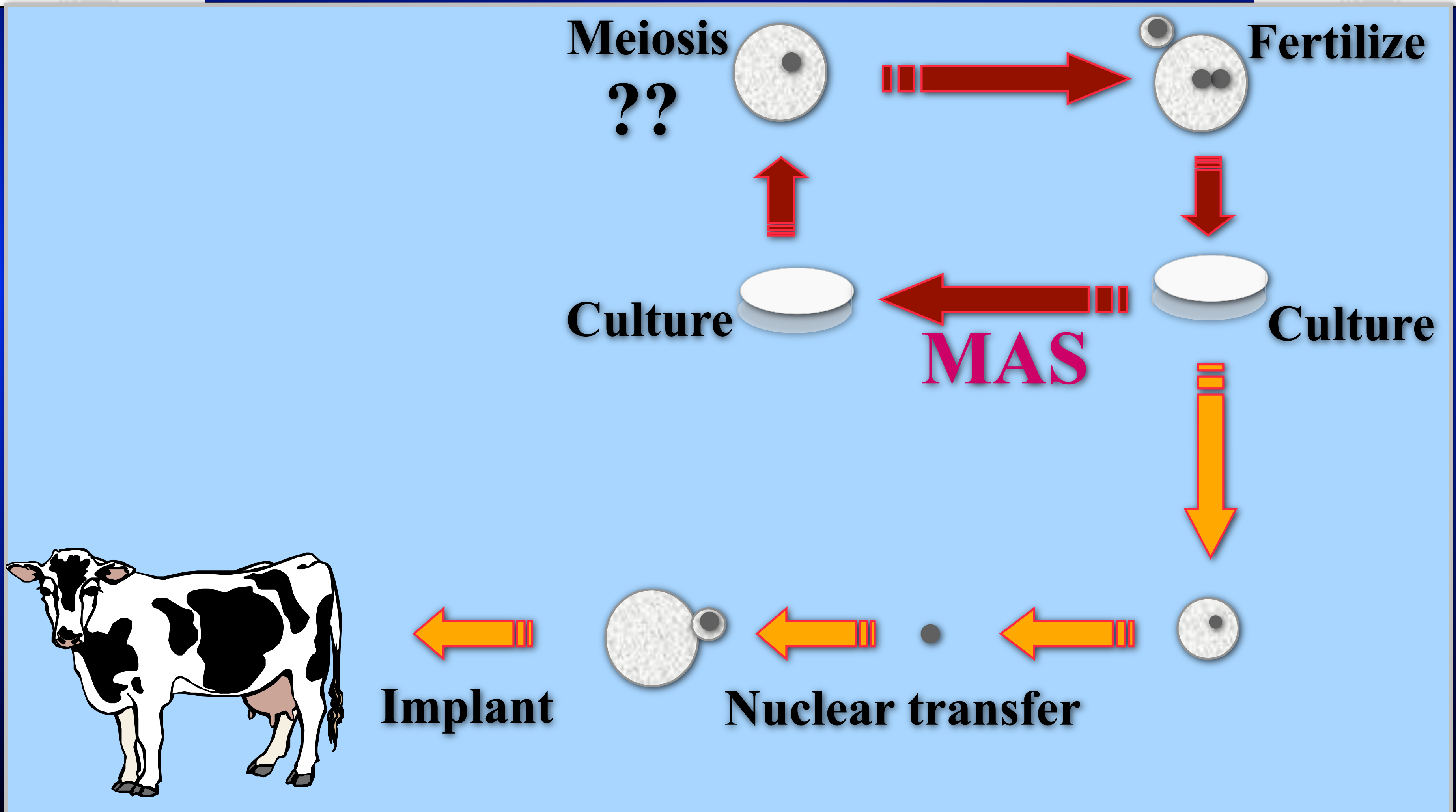


MAS + Reproductive Technology

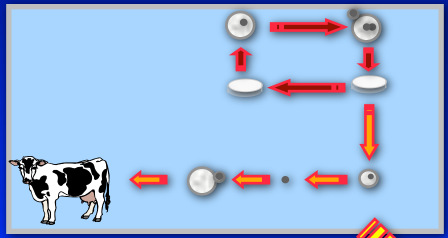
Whizzogenetics

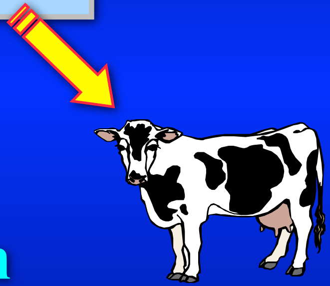
Generation

1 genotyping - MAS

2 genotyping - MAS

3 genotyping - MAS





4 phenotyping - phenotypic selection

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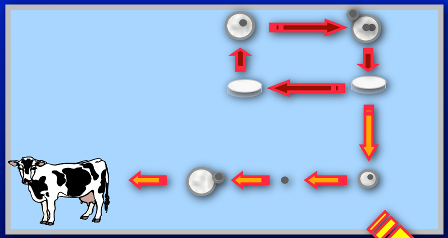
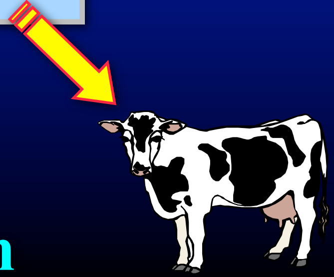
7 genotyping - MAS





8 phenotyping - phenotypic selection

The Future of Dairy Cattle Breeding . . . .

How can AI companies maintain market share?

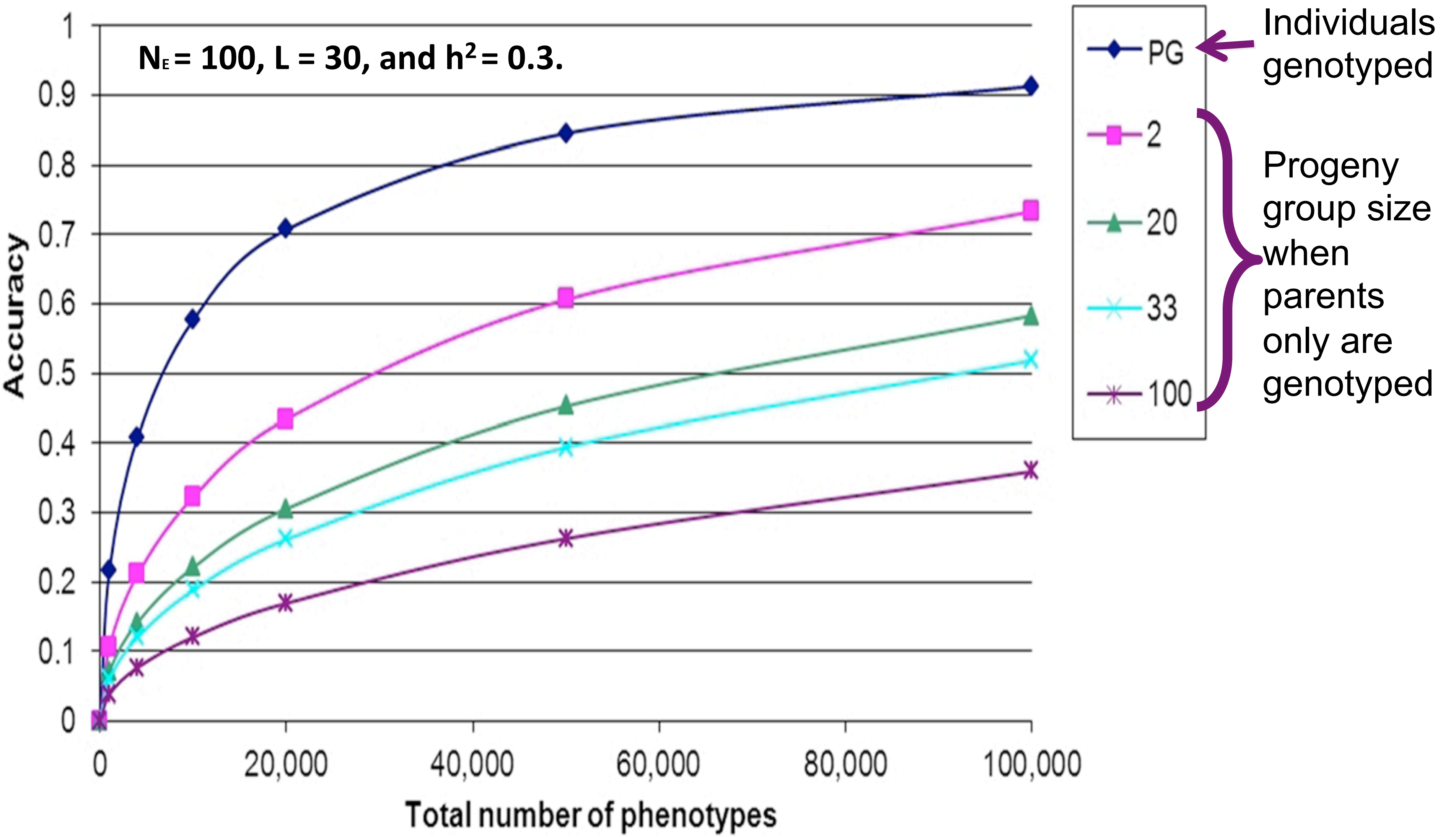
How to differentiate/protect your product?

- **Protect elite germplasm**
  - Elite nucleus herds with integration of genomic and reproductive technologies
  - Disseminate germplasm as crossbred embryos
- **Provide information on new traits**
  - Feed efficiency
  - Disease resistance
    - Collected in information nucleus herds for genomic prediction

Reference Population for 'New Traits'

If # phenotypes is limited and genotyping is not:
Genotype individuals with phenotype, rather than parents

Grevenhof, Bijma, van Arendonk GSE 2012



Summary/conclusions

- **Genomic selection is revolutionizing dairy breeding**
- **Integration of genomic and reproductive technologies is reducing generation intervals**
- **Keys for the future:**
  - Maintaining and further developing phenotype recording programs
  - Finding ways to protect elite germplasm in order to develop a competitive advantage
  - Inbreeding?