Quantifying Inbreeding Levels and Contemplating Inbreeding in Selection

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Genetic Selection Today

• Genetic selection in the dairy cattle industry has seen dramatic changes in recent decades
  • Introduction of *genomic selection* in 2009
  • Improved and novel technologies
• Increased popularity and usage of young GPA bulls
• Broadening of selection goals and number of traits evaluated
• **Accelerated genetic gains** in most traits under selection
• In the genomics era, we also need strategies and tools to help control some of the negative consequences to ensure continued genetic progress
Basics of Genomics

**Phenotype**: something (anything!) you can measure or observe

**Genotype**: the animals genetic information

**Environment**: how the animal is fed, housed, managed, etc.
Consequences of Genomic Selection

**Increased rates of genetic gain**
- Increased accuracy of selection for young animals
- Reduced generation interval
- Ability to select for traits recorded in only few animals
- Maintaining herdbook integrity & management/discovery of recessives

**Cumulative benefits of genomic selection of $721 million / year**

**Homozygosity (inbreeding) is rising at an increased rate**
- Increased occurrence of homozygous recessives (e.g. HCD, JNS, AM)
- More subtle effects of inbreeding:
  - Reduction in phenotypic mean value and selection response
- Potential future implications: **unknown**
- Financial economic losses: **unknown**
  (estimate $US 11 million / year, Cole et al.)
Generation Interval in North American Holsteins

Makanjuola et al., 2019
Inbreeding Trends

The rate of increase and not the absolute value is relevant

For Holstein
Pedigree vs Genomic Inbreeding

The *coefficient of inbreeding* (Sewall Wright, 1922) is the probability that two base pairs at a randomly chosen position in the genome (*locus*) are *identical by descent*.

**Pedigree Inbreeding**
- Classical measure of inbreeding, uses pedigree data and tracing it back to identify common ancestors between the sire and dam.
- Formed on averages and are expectations.
- Highly dependent upon completeness, depth, and integrity of available pedigree.

**Genomic Inbreeding**
- Accounts for Mendelian sampling (chance factor in distributing half the genetic material) between individuals.
- Captures realized inbreeding.
Pedigree vs Genomic Inbreeding

(Expectation) 12.5%

(Mendelian Sampling) 0%
Perspectives

Industry Perspective

a) I do everything I can to avoid inbreeding at all costs
b) I don’t like to see an increase in inbreeding, but there’s not much I can do
c) If it ain’t broke, don’t fix it

Public Perspective

“...the gene pool is about as deep as a pie-plate”

Academic Perspective

The benefits of intense directional selection currently outweigh the detrimental effects of inbreeding, but there could be a threshold at which lack of genetic diversity causes serious problems. We don't know when/if that would happen

Reality

- Inbreeding is unavoidable in intense directional selection programs
- At best, we should manage and monitor the loss of genetic diversity
Why Care?

- **Short-term consequences**: as populations become smaller and less diverse, relative fitness decreases (i.e., survival and fertility)

- **Long-term consequences**: lower gene diversity means less raw material for adaptations to changing environments, which may affect long-term survival
Current Farmers Priorities

• Average inbreeding levels continue to rise in each breed

• Difficult to find outcross sires of interest with high genetic merit
Knowing the inbreeding level of a female and of potential mating sires contributes little to controlling the rate of inbreeding in your herd.

Two important decision points for maintaining genetic diversity in a dairy population:
- The genetic diversity of young bulls purchased by AI companies
- The selection of sires when mating a female in your herd
Current Tools and Approaches

- Optimal Contribution Selection - Rarely used in practice
- Top lists dominate conversations / decisions / semen tanks
- “Outcrosses” interesting, but generally unpopular
- Experiments (cross breeding, etc.)

Two important decision points for maintaining genetic diversity in a population:

1. The genetic diversity of young bulls purchased by breeding companies
2. The selection of sires when mating a female in your herd
# Lactanet Inbreeding Calculator

- Know the potential inbreeding for specific matings and avoid those above a tolerable level
  - E.g. maintain current inbreeding

## Potential Progeny's Inbreeding and Parent Averages

<table>
<thead>
<tr>
<th>POTENTIAL MATES</th>
<th>LPI Code</th>
<th>%INB</th>
<th>LPI</th>
<th>Pro$</th>
<th>MILK</th>
<th>FAT</th>
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Outcross Bulls

**R-value** (Relationship-value)

- Represents the percentage of DNA that the bull has in common (i.e. its genetic relationship) with active females of the same breed
- Difficult to find outcross sires of interest with high genetic merit
  - Little advantage for A.I. companies to buy more outcross sires, which normally come with a lower genetic offering
  - Poor demand for their semen
Outcross Bulls

Actively marketed young GPA Holstein bulls

- R-Value ≤ 17
- R-Value > 17

Bar chart showing the distribution of LPI values across different R-Value categories.
Within-Herd R-values

• Current R-values are on a population level
  • The relationship with animals in a specific herd could be very different
  • A bull may be outcross to one herd but not another
• Need herd specific solutions and tools to make it easier to find diverse bulls
• Help farmers identify sires that will add genetic diversity in their herd

Working toward within herd R-values to provide lists of “diversity” bulls specific to a given herd
Current Plan

• Compass is a genetics management software tool freely available to all Canadian producers
  • Optimal for herds on milk recording
  • Otherwise, based on Owner Prefix
• Only publicly available tool that is based on the herd’s animal inventory

• **Concept:** Expand the tool to provide each user with a list of “Diversity” sires for their herd
• Any bull of interest can then be added to their “My Bulls” list
Compass – Bull List

• List of actively marketed bulls with filtering and sorting capabilities
• Includes Genomic, Proven and MACE bulls
• Maintain a personal list of “My Bulls” you are interested in
• Customize the traits that are displayed
Compass – Bull List

<table>
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<tr>
<th>Company</th>
<th>Short Name:</th>
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<tbody>
<tr>
<td>Select Values for Filter</td>
<td>Search by Short name</td>
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**Free from:**
- AH1
- AH2
- AM

**Filter for:**

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<th>Pro$</th>
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Source: Allison Fleming, OIS March 2022
## Compass – My Bulls

### Free from:
- HCD, HH5, HH6

### Filter for:
- A2 HOMOZYGOUS

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<th>Short Name</th>
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</table>

Source: Allison Fleming, OIS March 2022
Current Plan

• Add a section with “My Bulls” that lists a group of 5-10 “Diversity Candidates”
  • List would change over time
• Sorted by the Compass user’s preferred index of LPI or Pro$
  • Include the same columns as customized by the user
• Allow the user to add any of them to their “My Bulls” list
• The same bulls can be provided to the AI company offering genetic mating services
Second Phase – Breeding Companies

- To-date, there has been little advantage for A.I. companies to buy more outcross sires, which normally come with a lower genetic offering
  - Poor demand for their semen
- Focus continues to be on highest genetic merit
- Still need to develop other tools to help AI companies identify and purchase “Diversity” sires after genotyping new young bull candidates
Genetic Recessives and Abnormalities

• Genomics has aided in the discovery of genetic recessives, but we are also seeing higher occurrences

• **Gene testing and management of genetic recessives**
  • Avoid carrier bulls and never mate two potential carriers

• Need improved reporting of abnormalities and deaths to discover these as early as possible
  • **Will be working with industry partners to develop an improved method for easy reporting and rapid responses**
Genomic Solutions

• Move toward looking at genomic inbreeding or realized instead of traditional pedigree-based inbreeding

• Future tools should take advantage of genomic information to identify sires to use within a genotyping herd
  • Where both sire and dam are genotyped, genomic relationships can be used more accurately than pedigree relationships

• Not all inbreeding has a negative effect on performance
  • Sire selection advice can include genomic information for finding complementary genotypes and avoid negative effects of homozygosity
Future Tools

What future services would help Canadian farmers manage/maintain genetic diversity?

1. Include genomic information where possible for more accurate measures of relatedness
2. Provide a within-herd tool for producers to see which bulls are LEAST related to their herd
3. Develop other tools to help A.I. companies identify and purchase “Diversity” sires after genotyping new young bull candidates
4. Tool to ease the reporting of genetic abnormalities
5. Continue research using new technologies to further understand (biological, economic) impacts of homozygosity
Breeder's Dilemma

Genetic gain

Genetic diversity

Risky

Ideal

Stupid

Stable

Gorjanc et al.
First Steps

• Inbreeding levels are increasing, and is **unavoidable**
  • Some consequences of inbreeding are still unknown

• Balance genetic gain with increases in inbreeding levels
  • Seek bulls that would be **outcross** to your females

• Do gene testing and manage genetic recessives

• **Genotype females** to also get more information about the current status of inbreeding

• Continue genomic selection for traits related to health, reproduction, fitness, survival, etc.

The approach forward involves industry collaboration, but someone needs to make the first move!
Two Critical Decision Points Affecting Diversity of Dairy

What bulls do AI companies purchase?

What semen do producers purchase?
Two Critical Decision Points Affecting Diversity of Dairy

What bulls do AI companies purchase?

What semen do producers purchase?
Leveraging Genomics to Achieve Dairy Net-Zero, $16.2M

Recruiting talent for next 4 years

- PhD students
- Post-docs
- Project manager

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EAAP 2023 in Lyon, France, Aug 28-31, 2023