

Modeling identical animals and clones in genetic evaluations

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Why model clones?

- Clones of elite cows can multiply their contribution:
 - Top ranked heifer had **29** progeny; her 3 clones had **151, 59, and 27** progeny
 - Her dam had **329** progeny; clone of dam had **16** progeny
- Clones of many elite bulls are now marketed (**but not yet in EU**)
 - Top proven HO has 2 clones with **1,233** and **1,025** progeny
 - His sire had 3 clones with **3,470, 220, and 92** progeny
 - His 3rd great grandsire ManOMan's clone had **12,608** progeny
- **U.S. Food and Drug Administration approved cloning in 2008**

Birth codes in USA data

- **Multiple birth codes:**
 - **4,762** pairs of natural identical twins (code 2 and verified by genotype)
 - **1,776** split embryos (code 4)
 - **530** nuclear transfer clones from embryos, calves, or adults (code 5)
- **From about 7 million animals**

| Code | Birth description |
|------|--|
| 1 | Single |
| 2 | Multiple birth (not from embryo transfer) |
| 3 | Birth from embryo transfer |
| 4 | Split embryo (artificially) |
| 5 | Clone from nuclear transfer |
| 6 | Embryo pedigree (implantation date stored as birth date) |

Grand Champion in 2011, Clone beat her in 2013

Apple – 2011 World Dairy Expo

Photo:

<https://rzbderboven.de/apple/>

Apple had 361 progeny.

Apple-3 – 2013 World Dairy Expo

Photo and story:

<https://www.thebullvine.com/donor-profile/khw-regiment-apple-red-beauty-performance-record-accomplishments/>

Malcolm, D. 2019. [KHW Regiment Apple-Red-ET – Everything and more.](#) Photo by The Bullvine.

Apple's 9 clones added 325 more progeny.

Example cow and clone

- **Holstein cow and her clone**
 - **Nelsons Estimate Liz**
 - **Nelsons Estimate Liz-2**
- **Liz was Junior All-American Winter Yearling, 2001**
- **Liz-2 was Junior Champion at World Dairy Expo in 2004**
- **75 progeny of Liz, 20 of Liz-2**



Photo © Frank Robinson, Lodi, CA, USA

Nauman, D. 2011. Commitment got Nelsons Pronto Liz across.

<http://www.dairyagentatoday.com/News.aspx?nid=5557>

Revised genetic evaluation model

- Pedigree relationship matrix treated clones as full sibs but had **>7,000** copies of another animal's DNA
- Store a **source** animal for each identical group
- For progeny of clones, switch their sire or dam ID to **source** ID
- Remove IDs of clones from the pedigree file
- Keep a separate permanent environment effect for each clone
- After computing the EBVs:
 - Copy the **source** EBV back to the clones
 - Report the original pedigree in the public formats

Benefits of the new model

- **A and G matrices match better**
- **Genetic evaluations more precise for clones and progeny**
- **Genomic evaluations now have identical polygenic effects**
- **Identical EBVs in more trait groups such as type and calving**
- **Combined progeny counts for cloned bulls instead of reporting (since 2008) the daughter count of the clone with the most**
- **More exact pedigree inbreeding coefficients for descendants of clones**
- **Improved ancestor discovery**

Example results

- **Calf born in 2020** (HO840003218920809)
 - Maternal great grandsire was a clone of the paternal 2nd great grandsire (ManOMan and ManOMan2)
 - Pedigree inbreeding of 9.8% corrected to 10.6%
 - Genomic inbreeding was 13.5%
- **Split embryo bulls** (HOUSA000056264513 and HOUSA000056264515)
 - One had 43 daughters and the other had 2,972 daughters
 - Combined EBV mostly derived from second bull

Implementation

- **National evaluation**
 - **GEBV changes small because genotypes already identical**
- **MACE evaluation**
 - **Separate EBVs not too useful treating clones as full sibs**
 - **Send results from new model to Interbull August test run**
 - **Only send source animal to avoid double-counting clones**
- **Most programs ready for December implementation**

Do clones (ETN) perform as expected?

| Trait | Mean | Genetic SD | Clones | Effect | Effect/SD | Effect/Mean |
|----------------------|--------|------------|--------|--------|-----------|-------------|
| Milk | 28,071 | 1134 | 472 | +18 | 0.0 | +0% |
| Fat | 1,077 | 50 | 467 | -8 | -0.2 | -1% |
| Protein | 871 | 30 | 467 | +7 | 0.2 | +1% |
| SCS (or SCC) | 200k | 0.28 | 460 | +0.34 | 1.2 | +27% |
| Productive life | 25 | 3.4 | 119 | -3.3 | -1.0 | -13% |
| Dtr. pregnancy rate | 27 | 2.8 | 354 | -5.0 | -1.8 | -19% |
| Heifer conc. rate | 45 | 2.6 | 37 | -5.5 | -2.1 | -12% |
| Cow conc. rate | 41 | 3.2 | 123 | -8.3 | -2.6 | -20% |
| Age at first calving | 831 | 2.1 | 115 | +17.0 | -8.1 | +2% |
| Cow livability | 97 | 3.2 | 423 | -7.3 | -2.3 | -8% |

Import / export rules?

- More countries are adopting the Cartagena protocol
 - Clones and gene edits are **not** “genetically modified”
- Guidelines proposed to the EU parliament were not adopted
 - Private companies enforce cloning rules that do not exist
- Holstein USA must issue “clone-free” pedigrees for export
 - All generations are inspected to discover any clone
 - May affect **~0.1%** of USA HO today but **>3%** in 5 generations and **>50%** in 10 generations (about 20 years)

Conclusions

- **Genetic evaluations can account for identical animals:**
 - Link progeny of clones to the **source** sire or dam
 - Remove clone copies from the pedigree before analysis
 - Restore clone IDs and copy EBVs from the **source** animal
- **Milk production was as expected but some other traits lower.**
- **Many Holsteins may soon have clones in their pedigrees.**
- **Cloning techniques also enable gene editing.**
- **Models may need revision again for that technology.**

Clones and identical twins in team sports

Polo team from Argentina: All 6 horses are clones of a previous favorite champion horse.

Currently #2 polo team in the world.

Photo and story:

[Six cloned horses help rider win prestigious polo match | Science | AAAS](#)


Tennis doubles team: More titles than any other doubles pair - 1 Olympic Gold, 2 French, 3 Wimbledon, 5 US, and 6 Australian Opens.

Photo and story:

<https://www.atptour.com/en/news/tennis-united-24-july-doubles-week>

[Bryan brothers – Wikipedia](#)

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