Potential negative effects of genomic selection

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University of Georgia

Pig Producers’ Congress, Herning, Denmark, Oct 22 2024


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LÆS HER:
GISP? Det er GIPS!

Vejle

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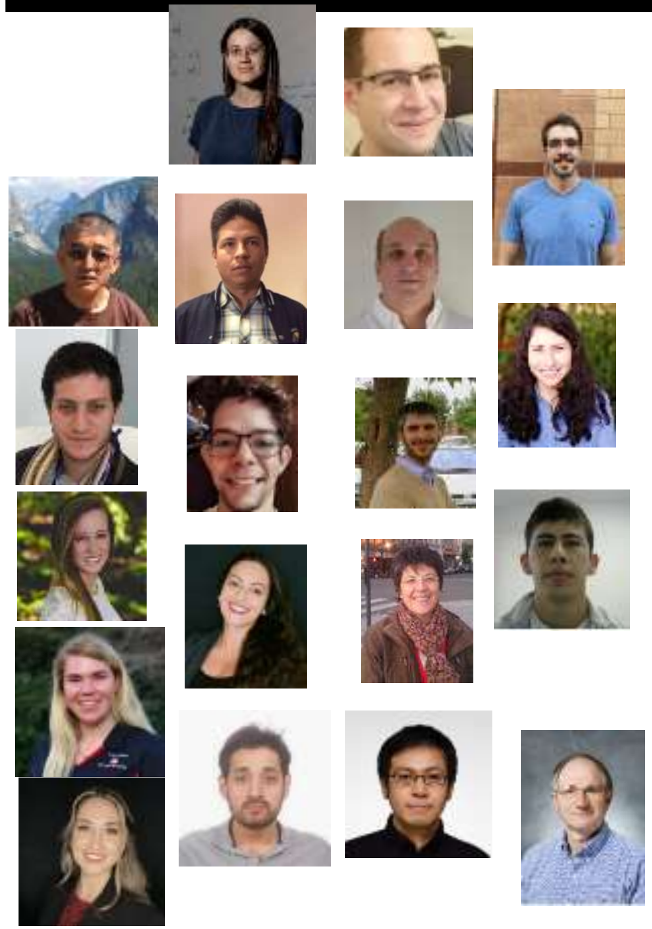

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Recent informal reports

- Deteriorating sow survival and pig mortality in pigs
- Deteriorating feet & legs in beef
- Short teats and increased calf mortality in dairy
- Increased sensitivity to heat stress in dairy
- Deteriorating disease resistance across species

Why problems?

- Unbalanced breeding?
- Fundamental limits?
- Deleterious variants?

- If “DNA designer” exists, can we design perfect animals?

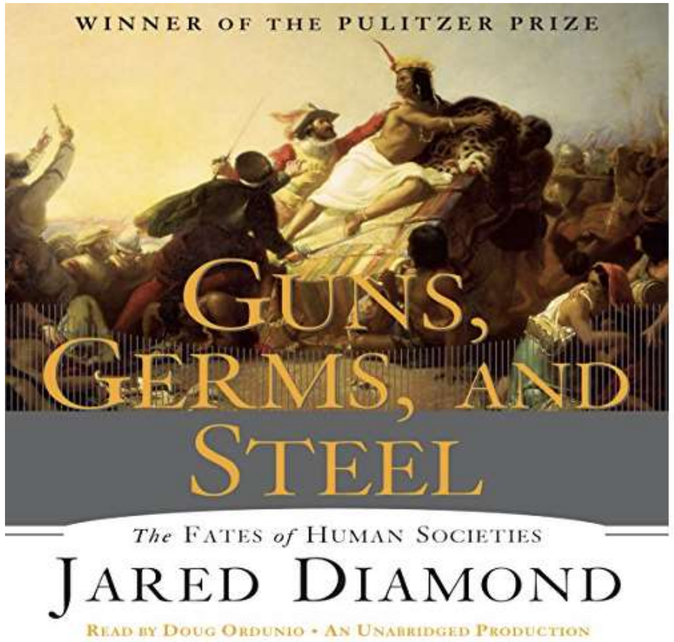
Genetic selection as optimization

- Selection for one trait or an index
- Gains on selected traits
- Losses on correlated antagonistic traits

- Losses compensated by improved environment/management

History of selection strategies

- Domestication
- Unformal
- Large-scale single-trait for growth/milk
- Multi-trait with fitness traits
- Genomic




Livestock Production Science

Volume 93, Issue 1, 1 April 2005, Pages 3-14

Go to Livestock Production Science on ScienceDirect

Genetics of adaptation and domestication in livestock ☆

Sandrine Mignon-Grasteau [a], Alain Boissy [b], Jacques Bouix [c], Jean-Michel Faure [a], Andrew D. Fisher [d], Geoffrey N. Hinch [e], Per Jensen [f], Pierre Le Neindre [b], Pierre Mormède [g], Patrick Prunet [h], Marc Vandeputte [i], Catherine Beaumont [a]

Domestication

Winners

Growth
Milk
Mating procedures

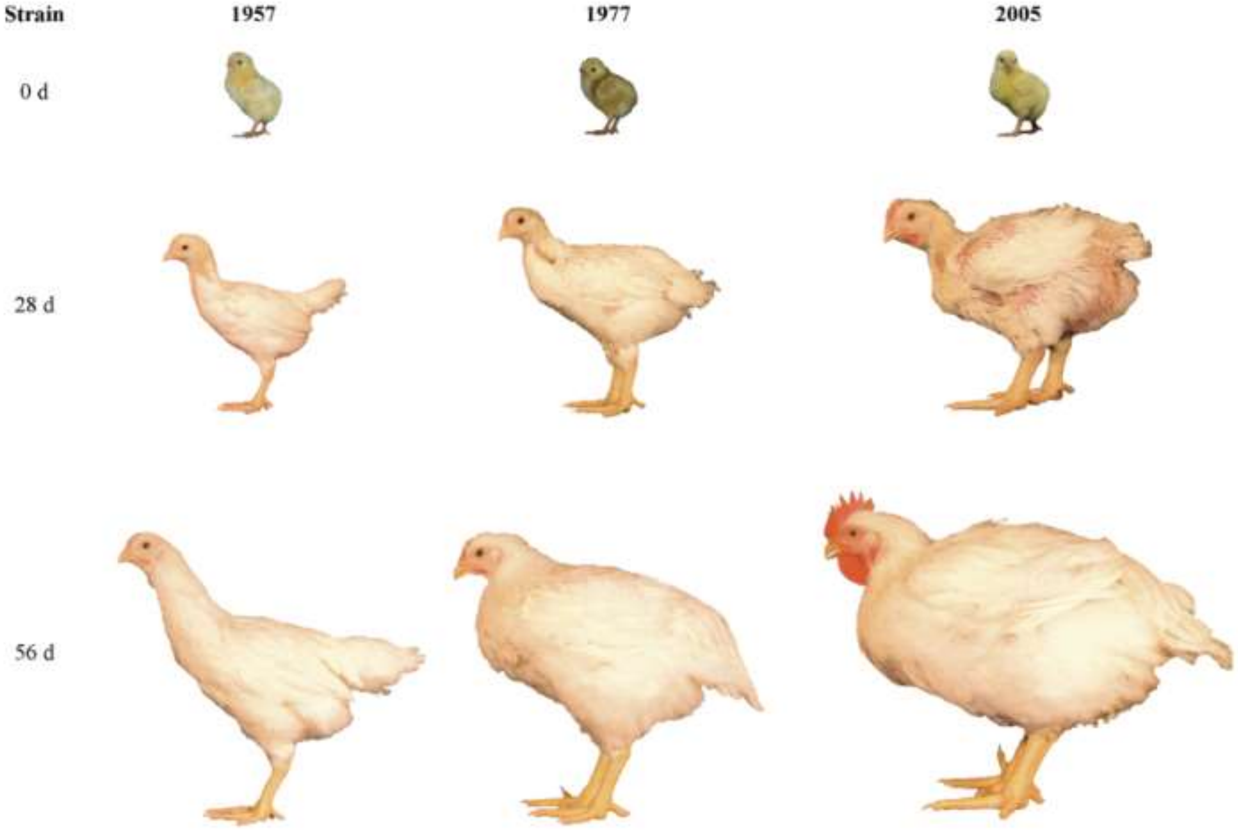
Losers

Food finding
Seasonal reproduction
Predator avoidance
Brain size
…

Example of effects of mostly single-trait selection

1957
1977
2005

0 d
4 week
8 week



Zuidhof et al. (2014) http://dx.doi.org/10.3382/ps.2014-04291

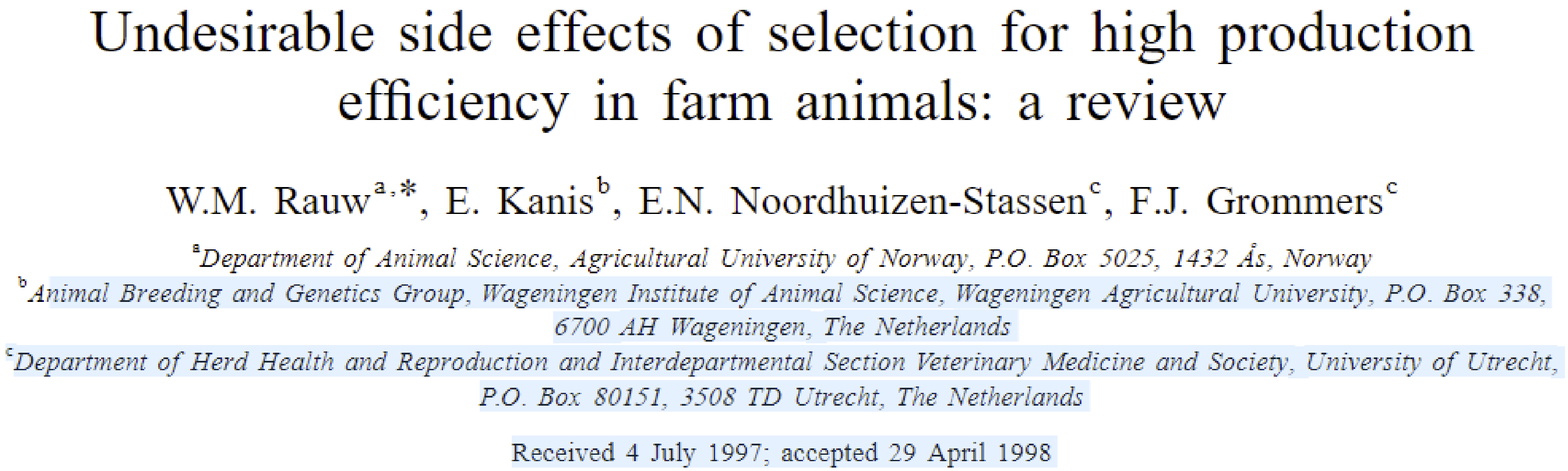
Side effects of intensive selection for growth in broiler chicken

- Unlimited appetite / obesity ➔ artificial lightning
- Poor survival of males ➔ male supplementation
- Increased susceptibility to diseases ➔ antibiotics
- Low hatchability ➔ alternate heating/cooling of incubators
- …

All companies – similar problems at same time

Initially problems kept confidential

Eitan and Soller, 2014



Undesirable side effects of selection for high production efficiency in farm animals: a review

W.M. Rauw[a,*], E. Kanis[b], E.N. Noordhuizen-Stassen[c], F.J. Grommers[c]

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[b]*Animal Breeding and Genetics Group, Wageningen Institute of Animal Science, Wageningen Agricultural University, P.O. Box 338, 6700 AH Wageningen, The Netherlands*
[c]*Department of Herd Health and Reproduction and Interdepartmental Section Veterinary Medicine and Society, University of Utrecht, P.O. Box 80151, 3508 TD Utrecht, The Netherlands*

Received 4 July 1997; accepted 29 April 1998

…over 100 references on undesirable(cor)related effects of selection … in broilers, pigs and dairy cattle….

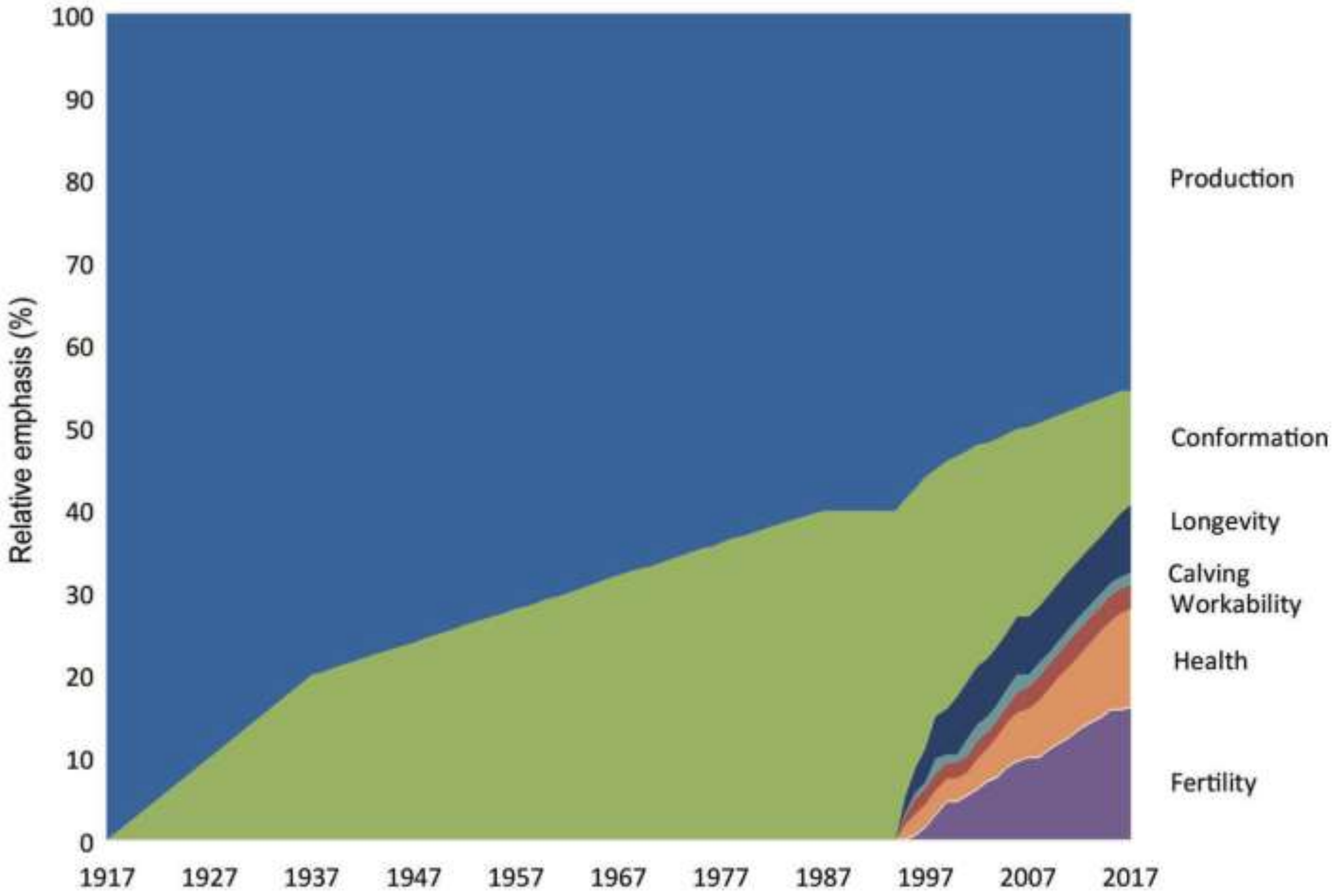
Future application … DNA-techniques .. ….more dramatic consequences….

Selection for more than production traits alone may prevent such.

Multitrait selection

- Decline in some traits too hard to be compensated by management
- New trait recording
- Progress in computing – multitrait animal models
- Selection index

Changes in US dairy index



Miglior et al., 2017

Effects of genomic selection

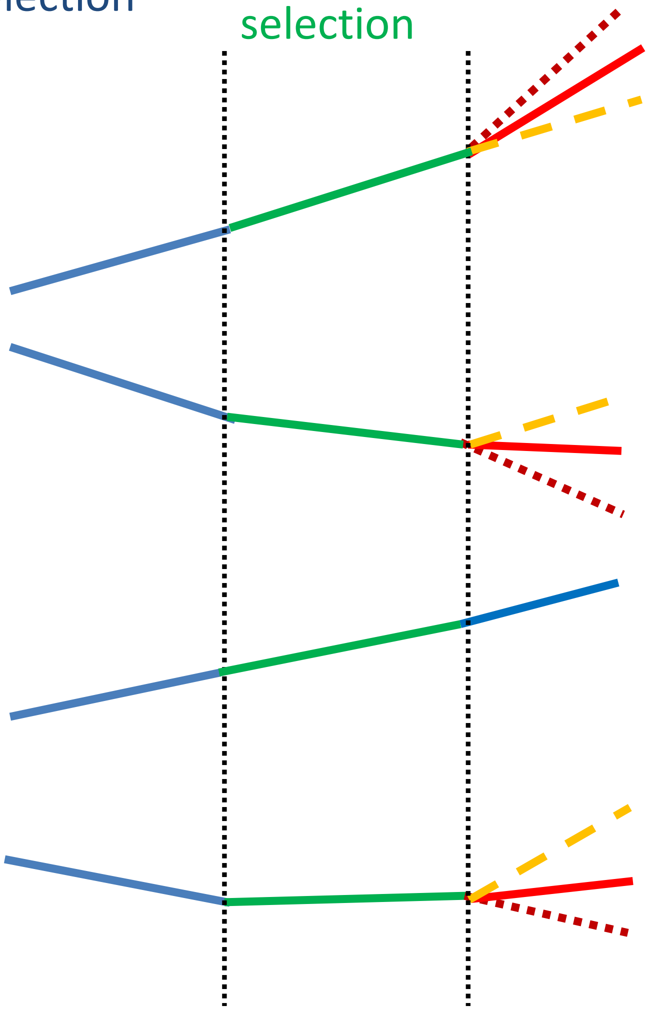
- High accuracy for well recorded high h^2 traits
- Low accuracy for low h^2 traits with little information

- Good predictions for young genotyped animals – lowered generation interval

- Acceleration of trends for selected traits
- Acceleration of correlated responses

- Changes in genetic parameters

Hypothetical trend changes in 3 stages of genetic selection



Single trait selection

Multiple trait selection

Genomic selection

Fitness unselected

Fitness selected
Small data

Fitness selected
Large data

Production (high h^2)

Raw fitness (low h^2)

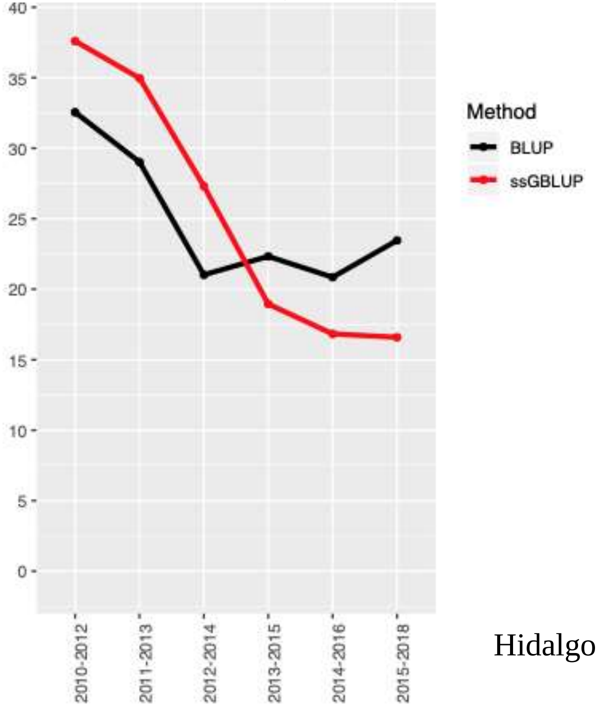
Management

Realized fitness

Negative changes accelerate
and management cannot catch up!

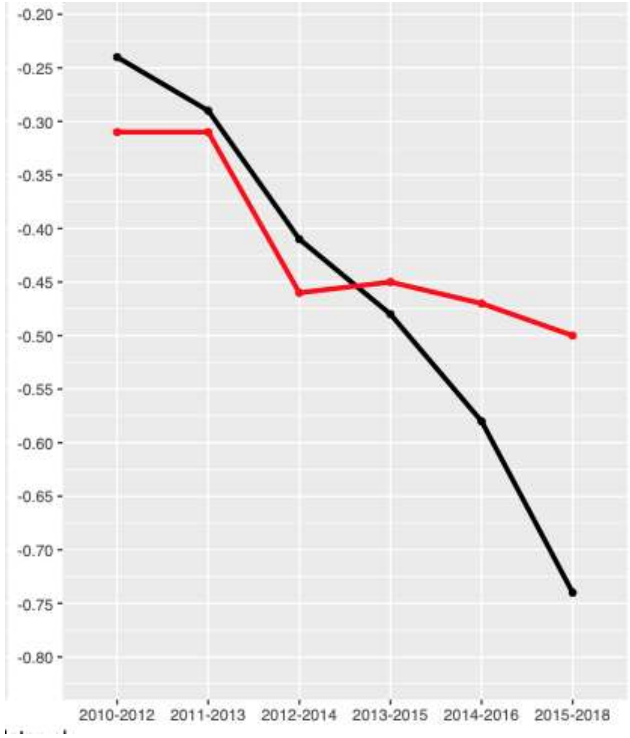
Changes in (co)variances in pigs due to genomic selection

Heritability for growth



Hidalgo et al. (2019)

Genetic correlation with reproduction



Hidalgo et al., 2023

Heritability halved, antagonistic correlations -0.3 ➔ -0.5

Why changes in genetic parameters?

- Bulmer effect
- G x E
- Recessives
- Changes in gene frequencies
- Drift

- Changing resource allocation
- Changes in trait definitions
- …

Case of changing correlations from positive to negative in dairy

- Productive life and dairy form (thinness)
  - Old times: fat cows lose milk by getting fat, fat cows removed
  - New times: Cows need fat as body reserves during negative energy balance, thin cows removed for problems

  - same now for pregnant sows

Problems and species

- Genomic selection efficient with large data

- Fraction of performance to fertility data in species
  - ~ 1 in cattle
  - 1/15 in pigs
  - 1/200 in layers

- More problems expected in pigs and chickens than in dairy

- Problems with early mortality/morbidity when affected animals not genotyped

Genomic gain for production and number of born dead – example in pigs

- 1000 sows per generation
- 15 piglets per sow
- 4 generations

- Gain per generation:
  - 0.65 phenotypic SD for growth
  - 0.02 phenotypic SD for number of born dead

- Genomic favors bigger populations with better recording

Story
New line of pigs at University of Georgia

How to circumvent negative effects?

- Start or expand recording for problematic traits
- Update selection index
  - Needs estimates for last generation
- Focus on traits where the parameters are changing rapidly
  - Needs estimates generation by generation
- If too many traits, select for fertility and survival
- *Make veterinarians and nutritionists work harder!*

Sow survival

- > 50 reasons for disposal

- Why sow disposed?
  - Genes (QTLs) for each reason separately?
  - General poor fitness?

- Few general categories for disposal
  - Reproduction, disease, other

Study of codes of disposal at different parities of Large White sows using a linear censored model

J. Arango, I. Misztal, S. Tsuruta, M. Culbertson, W. Herring Author Notes

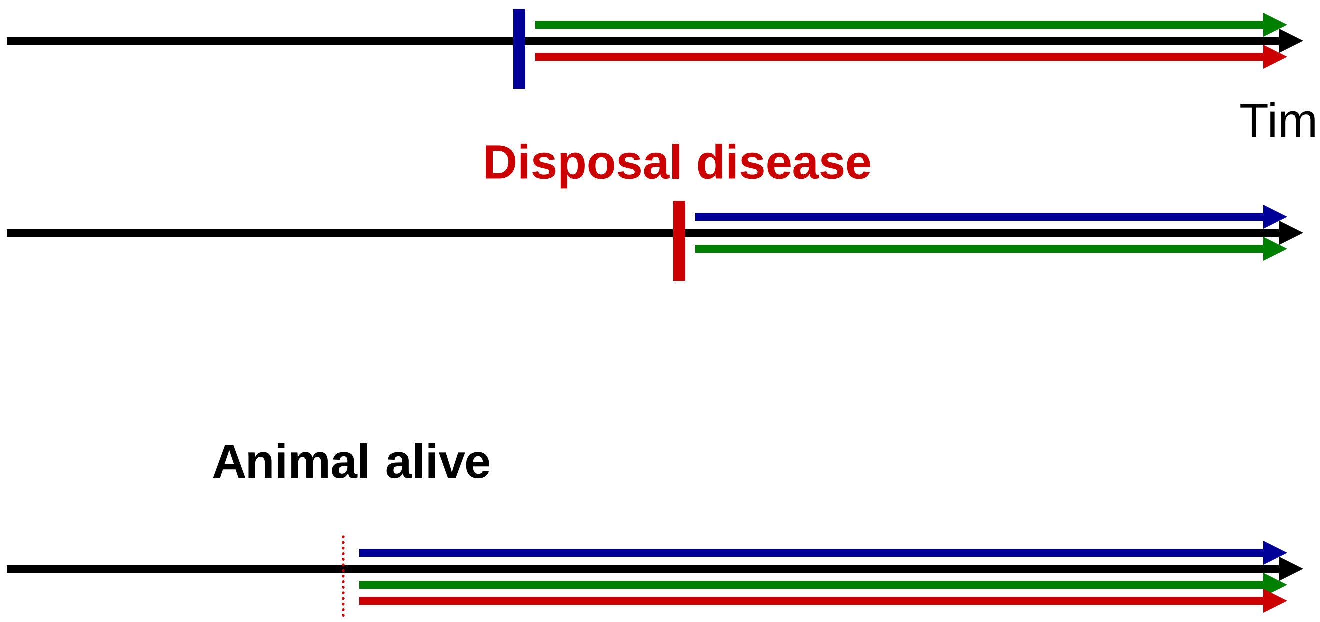
Journal of Animal Science, Volume 83, Issue 9, September 2005, Pages 2052–

Can all be analyzed jointly?

Censored data

Disposal for: **Reproduction**
Disease
Other reasons

Traits correlated at > 0.8
Declining overall fitness



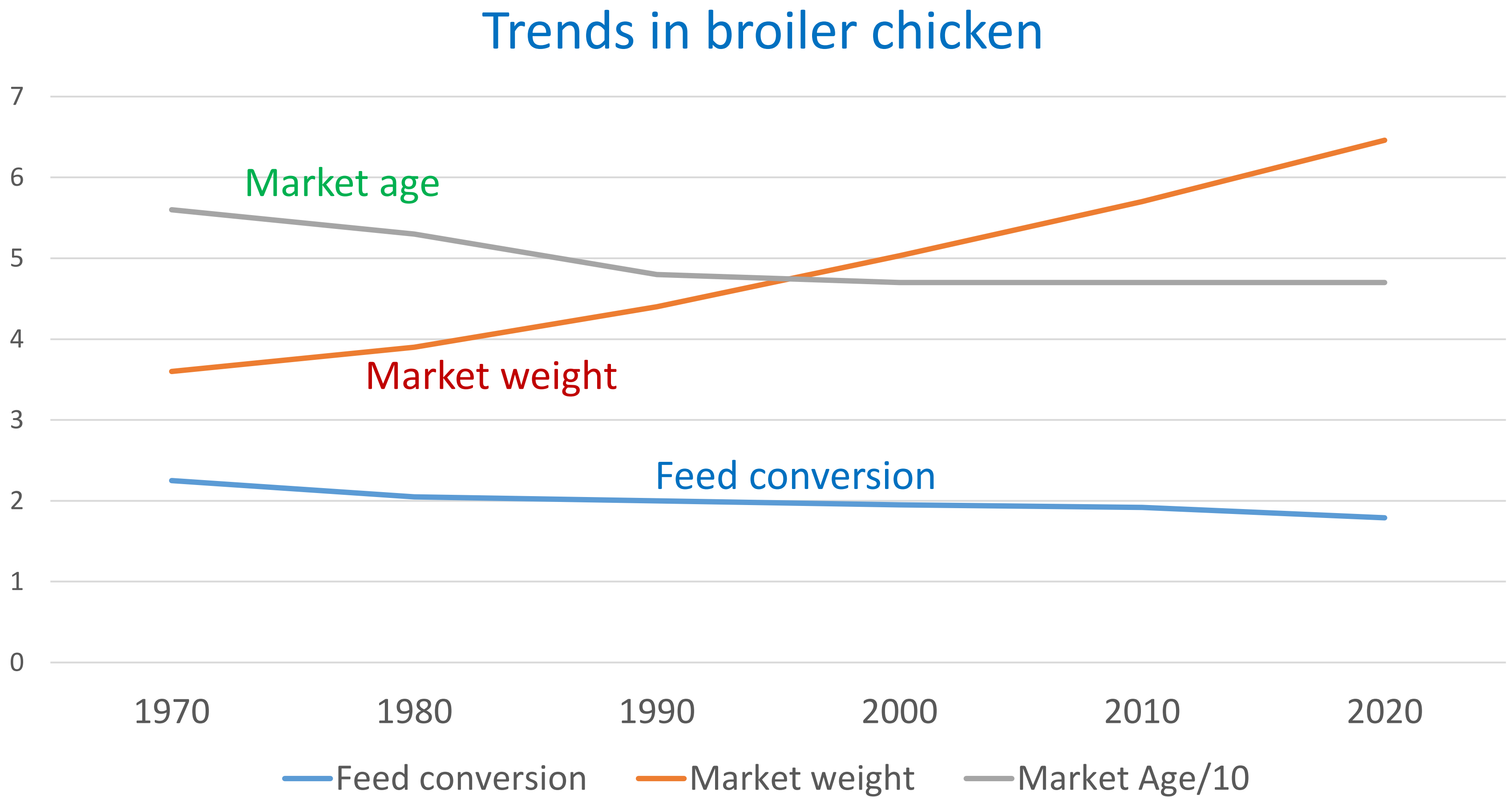
Disposal repro

Time at disposal

Disposal disease

Animal alive

Fundamental limits of selection



https://www.nationalchickencouncil.org/about-the-industry/statistics/u-s-broiler-performance/

Challenge of parameter estimation in genomic era

- Possibly rapidly changing parameters
- Need estimates using complete data including genomic
- Need results for last generations
- Existing methods not applicable

Realized and theoretical accuracies

Realized accuracy $acc = corr\,(y - Xb, \hat{u})/h$

Legarra et al. (2008)

y-Xb - adjusted phenotype
$\hat{u}$ - breeding value obtained without that phenotype
h^2 - heritability

Theoretical accuracy $$acc = \sqrt{\frac{Nh^2}{Nh^2 + M_e}}$$

Daetwyler et al. (2008)

N – number of genotyped animals with phenotypes
M_e – number of independent chromosome segments

Me ≈ 5k (chickens, pigs), 10k (beef), 15k (Holsteins)
Pocrnic et al. (2017)

Pig data set

150k records on growth (h^2=0.21)

25k records on fitness (h^2=0.05)

53k genotyped animals

Hollifield et al., 2021

growth

fitness

Theoretical accuracy

$$\sqrt{\frac{53k\ *0.21}{53k\ *0.21+5k}}=0.83$$

$$\sqrt{\frac{25k\ *0.05}{25k\ *0.05+5k}}=0.44$$

Realized accuracy 0.82 0.41

Formula for estimating heritability

$$\widehat{h^2} = \frac{c^2 + \sqrt{c^4 + 4c^2 M_e/N_{ref}}}{2} \mp \frac{3c}{\sqrt{N_{val}}}$$

$$c = corr(y - Xb, \hat{u})$$

N_{ref} – animals in reference population
Me – effective chromosome segments, ~5k in pigs and chicken, ~15k in cattle
N_{val} – number of animals in validation population

Formula for genetic correlations

$corr(y_i - Xb_i, \hat{u}_j)$ Predictivity of trait i by trait j

$$corr_{ij} = \frac{corr(y_i - Xb_i, \hat{u}_j)}{h_i \; acc_j} \mp \frac{1}{h_i \; acc_j \sqrt{N_{val}}}$$

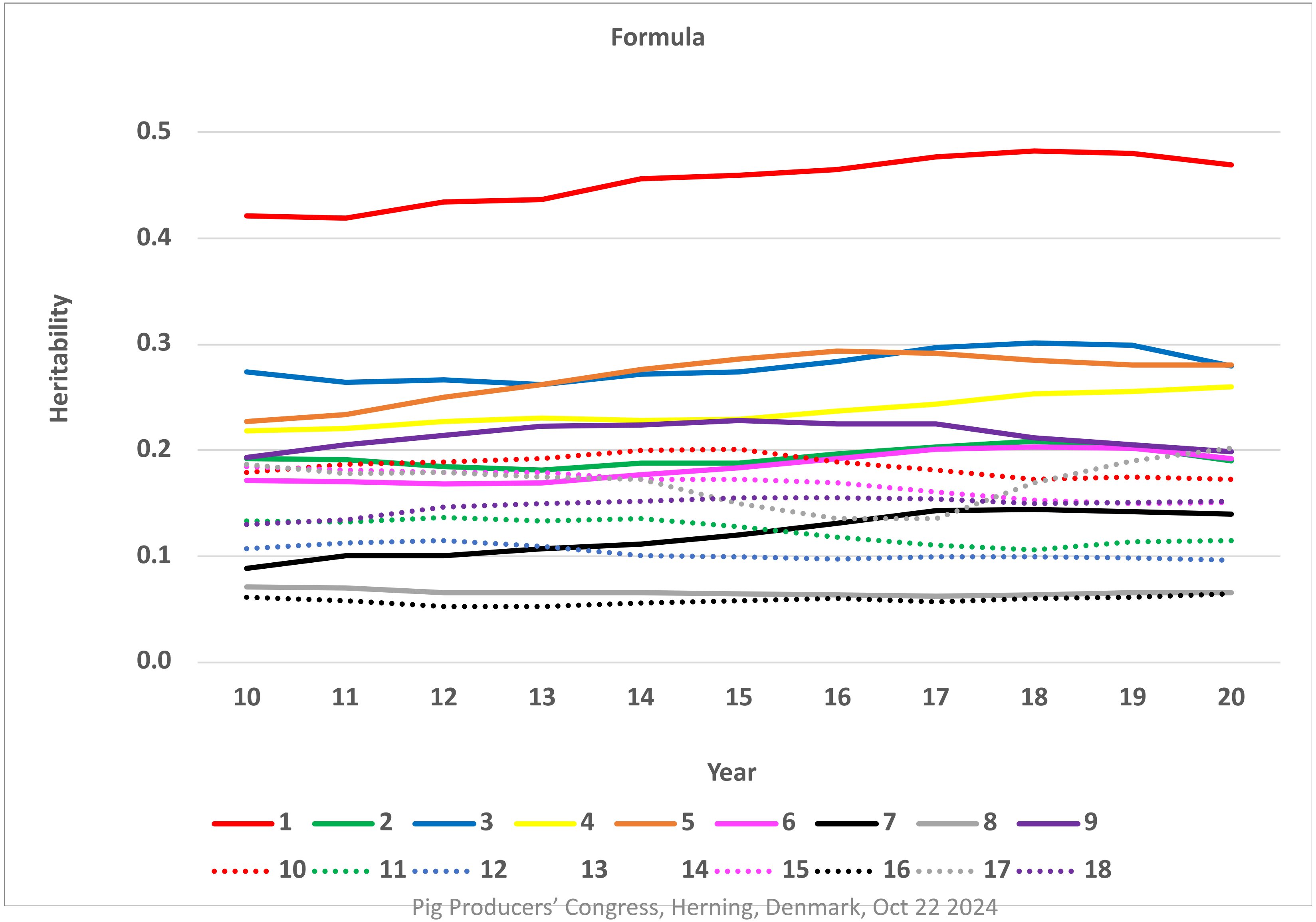
Under correct model: $corr_{ij} = corr_{ji}$

Parameters by predictivity for 18 linear type traits in US Holsteins

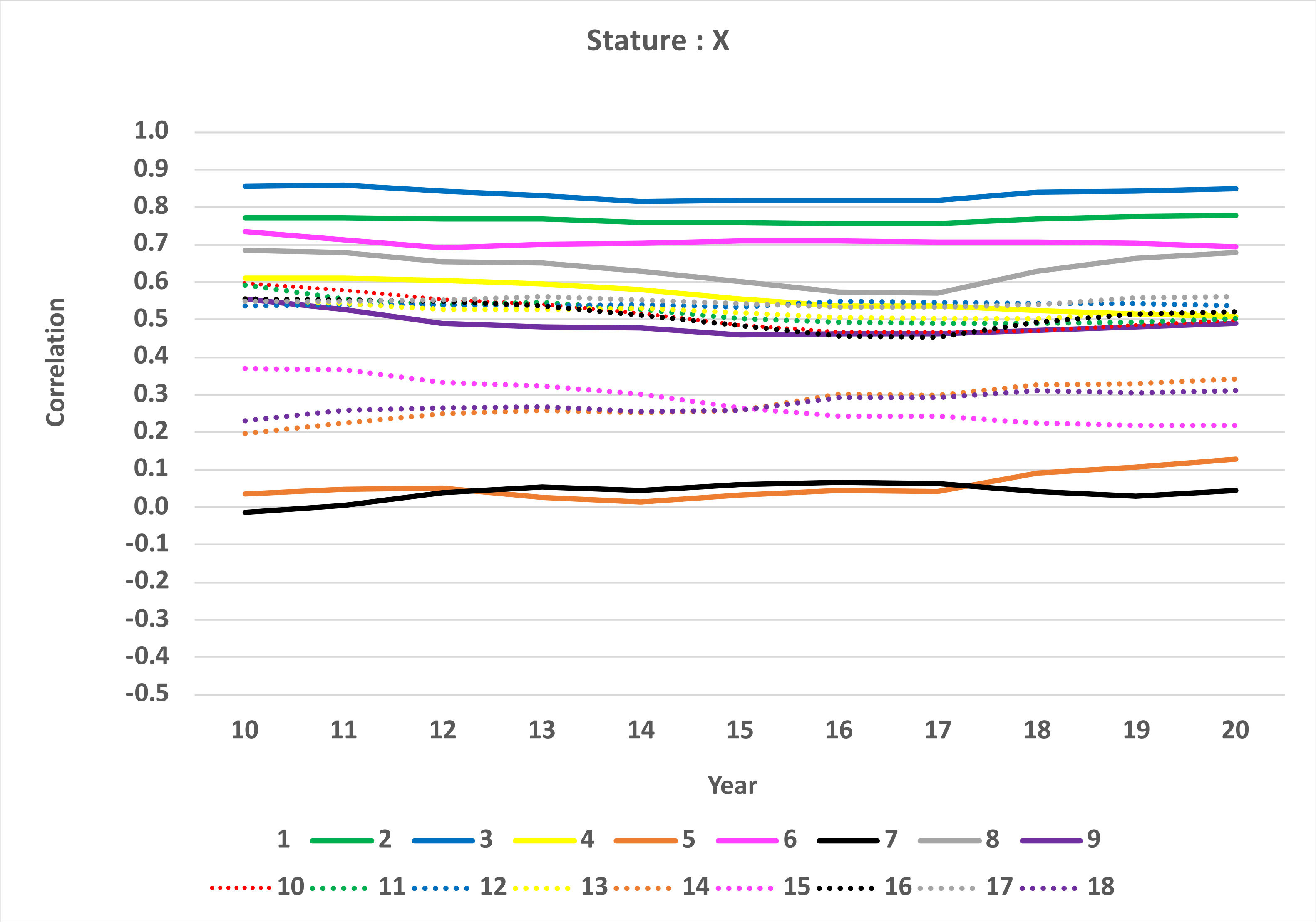
>10 million observations
>1 million genotypes

No	Traits	h^2	No.	Traits	h^2
1	Stature	0.456	10	Rear Udder Height	0.214
2	Strength	0.270	11	Rear Udder Width	0.172
3	Body Depth	0.337	12	Udder Cleft	0.178
4	Dairy Form	0.298	13	Udder Depth	0.332
5	Rump Angle	0.341	14	Front Teat Placement	0.267
6	Rump Width	0.248	15	Teat Length	0.254
7	Rear Legs - Side View	0.173	16	Rear Legs - Rear View	0.106
8	Foot Angle	0.110	17	Feet & Legs Score	0.182
9	Fore Attachment	0.230	18	Rear Teat Placement	0.213

Heritability over time



Genetic correlations with stature over time



Conclusions

- Selection as optimization – winner and loser traits
  - Decline in low heritability traits compensated by improved management

- With genomic selection
  - Faster progress for high heritability traits
  - Possibly faster decline for low heritability traits

- Solution: extra focus on fertility and survival
  - Challenge: parameter estimation

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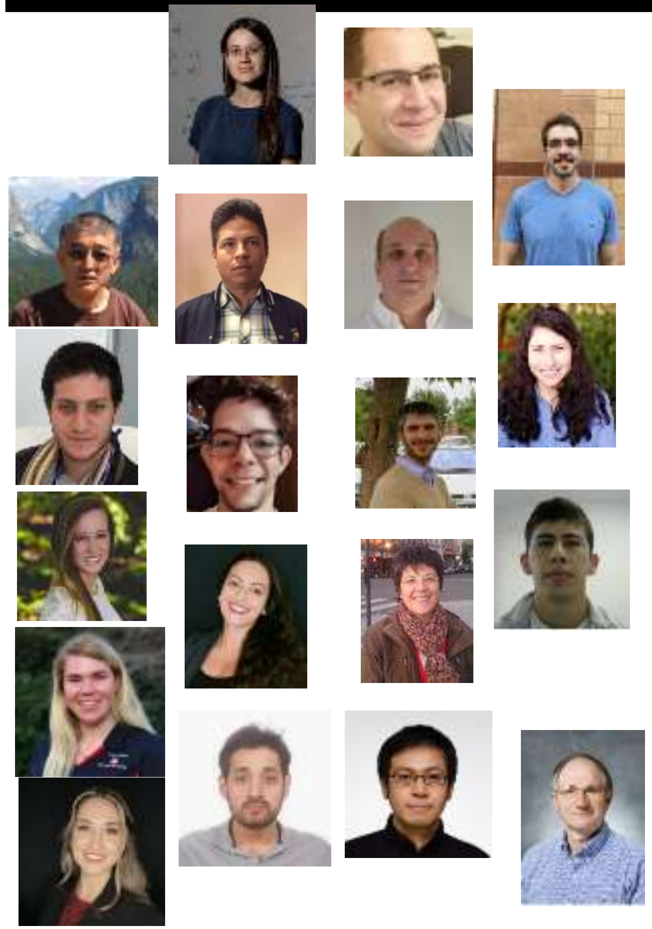

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