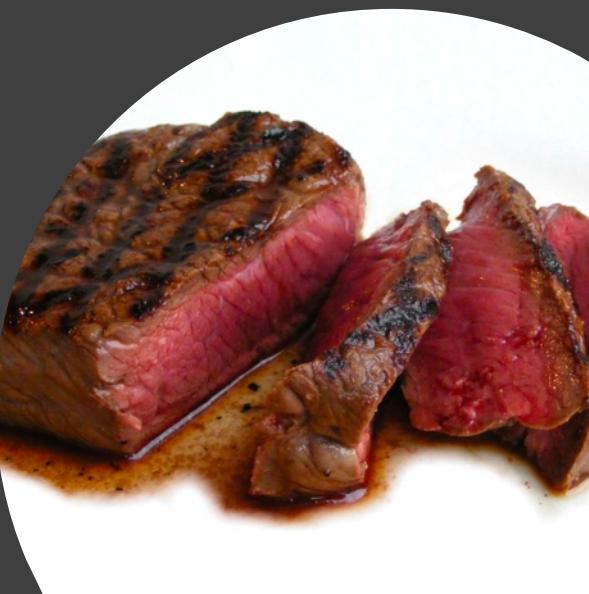




Data Driven Wisconsin Conference
Milwaukee, WI July 2019
By: Yalda Zare, Ph.D.

Data Driven Agriculture to Feed the World



Wisconsin

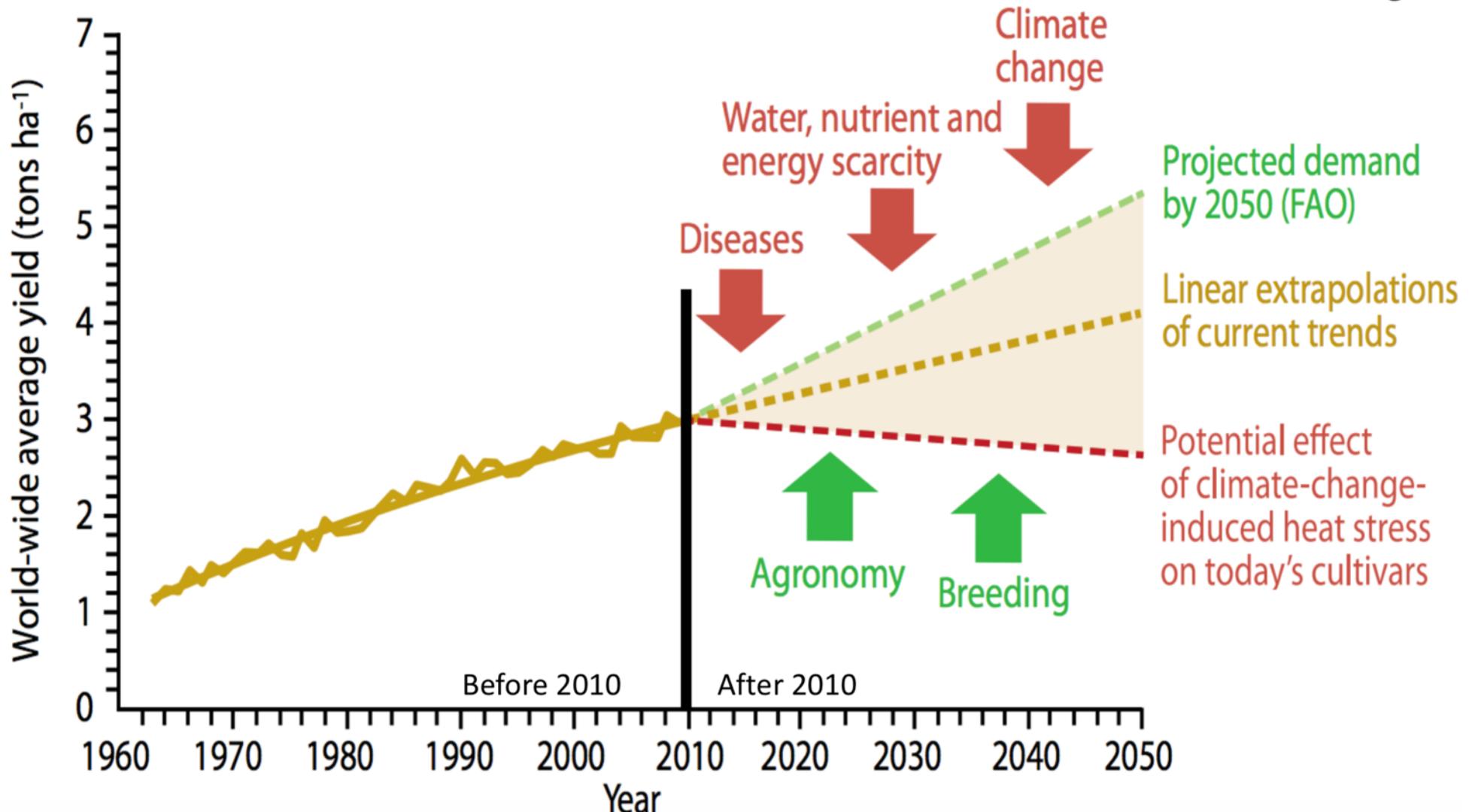
- Wisconsin is America's Dairyland
- Wisconsin agriculture contributes \$88.3 billion annually to state's economy (Dairy industry alone \$43.4 billion)
- Home to 7,700 dairy farms, more than any other state, and 1.28 million cows.
- Wisconsin is #1 in cheese
- Wisconsin leads the nation in the export of bovine semen, ginseng roots, and prepared/preserved cranberries and sweet corn (\$3.5 billion in 2018).

<https://datcp.wi.gov/Pages/Publications/WIAgStatistics.aspx> (Updated June 4, 2019)

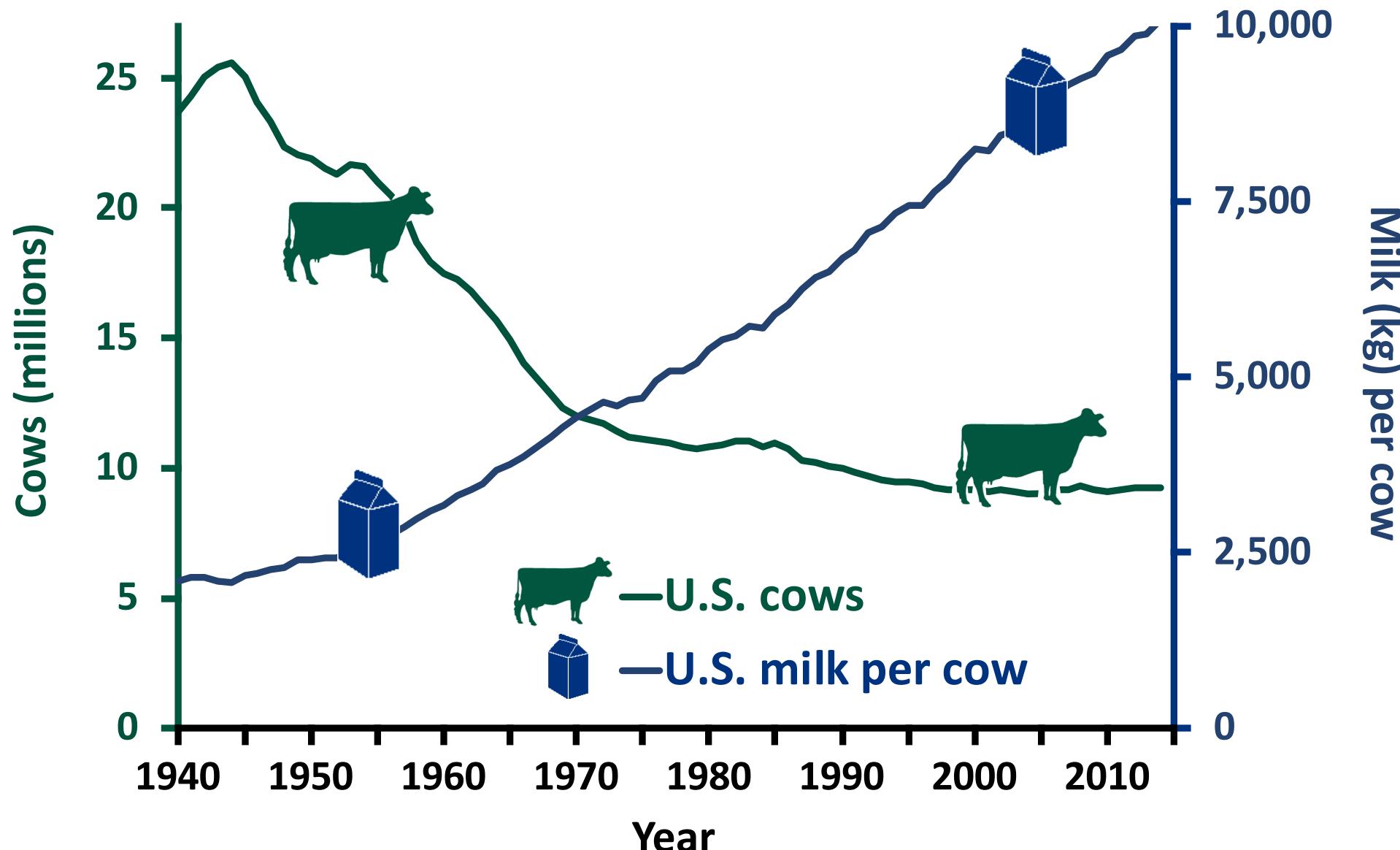


Humanity's greatest challenge

Producing 70% more food by 2050 without destroying the planet

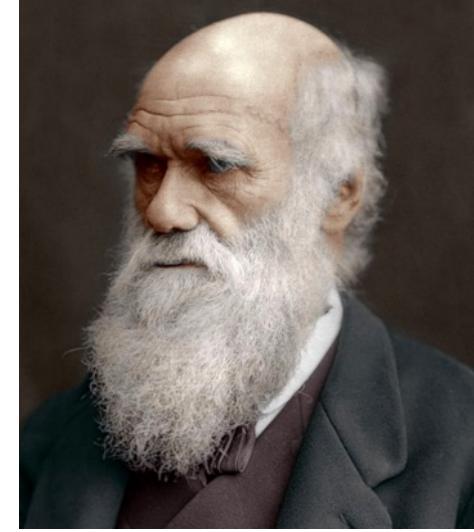


U.S. Dairy population and Milk Yield



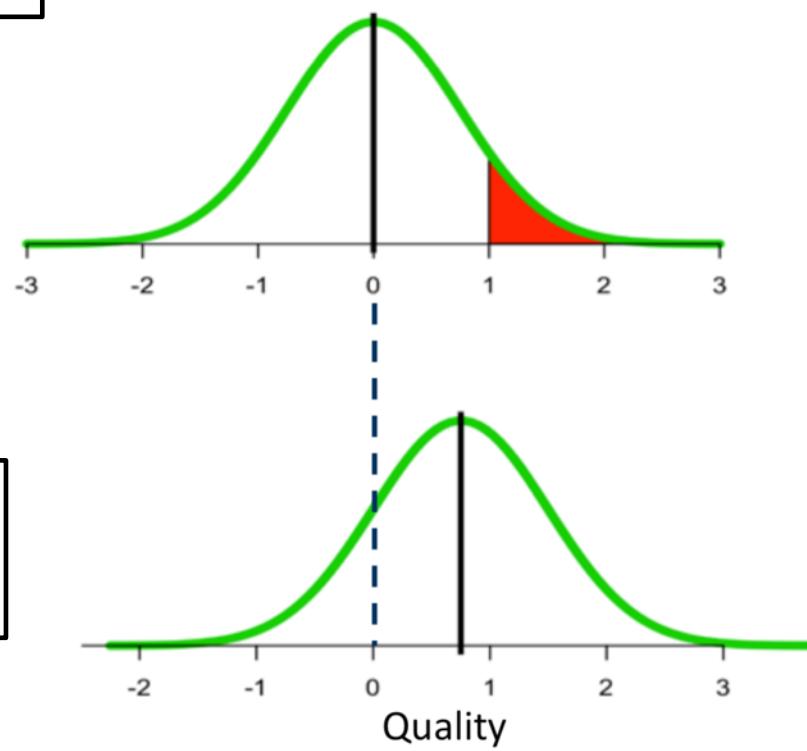
Breeding

- Charles Darwin coined the term “selective breeding”
- The purpose of breeding is to improve sustainability of animal and plant species for human needs such as food, fiber, feed, companionship, recreation, work, decorative, medicinal, ...
- Historically ~50% of improvements in agricultural productivity directly due to breeding
- But we need to DOUBLE the rates of improvement from breeding



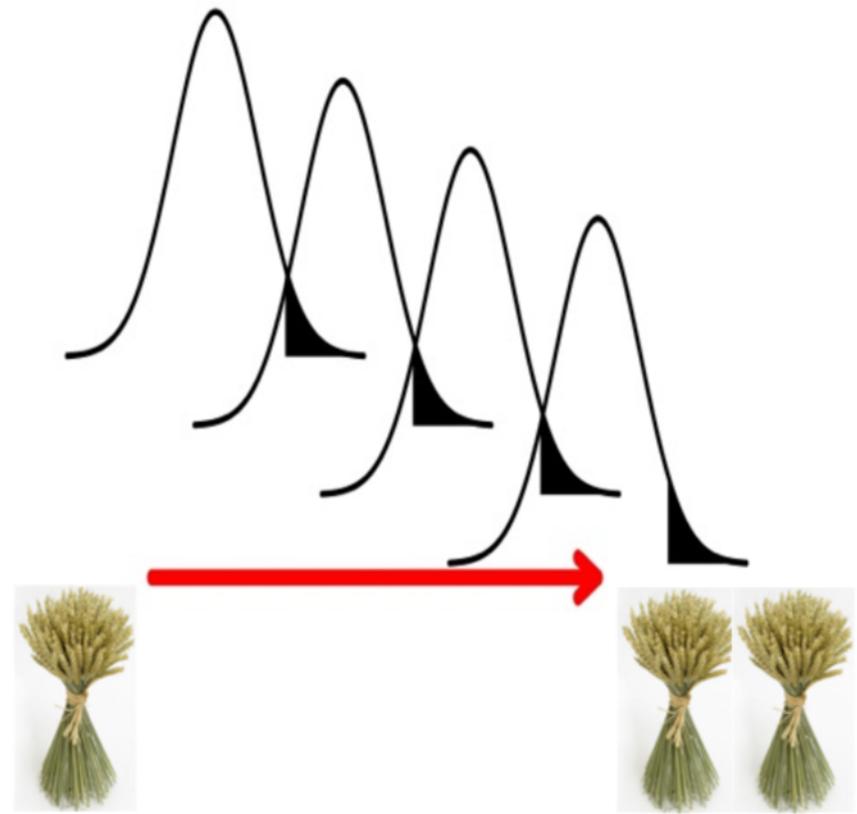
Breed the best to the best

Parental Generation

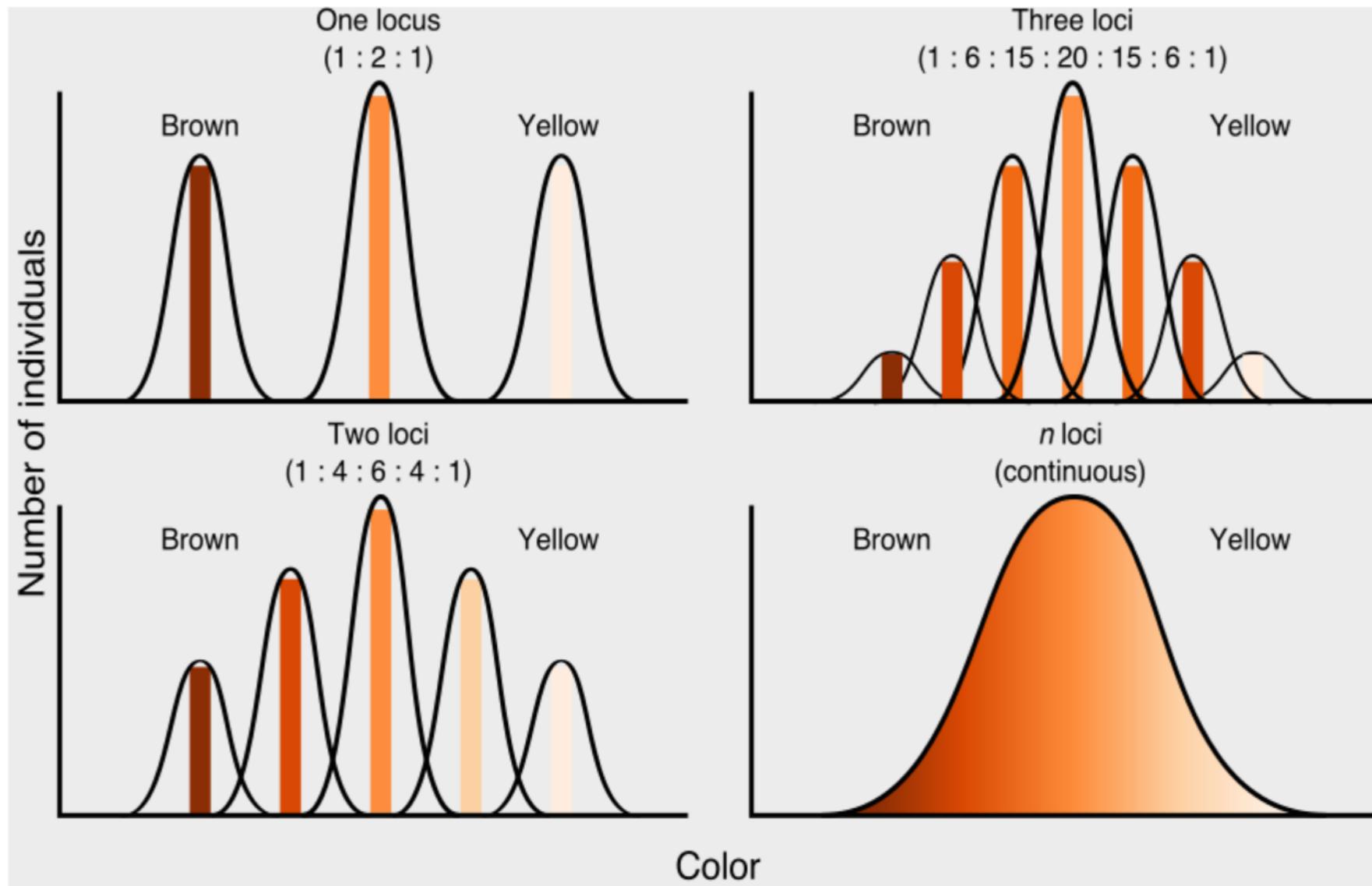


Offspring Generation

Gain over many generations



Genetic architecture in agriculture





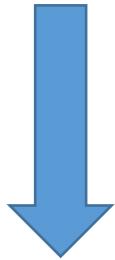
Phenotype (P) = Genetics (G) + Environment (E)

The percentage of total variation attributable to genetics varies:

- Female fertility: 0.04
- Working life: 0.08
- Udder health: 0.12
- Milk production: 0.35

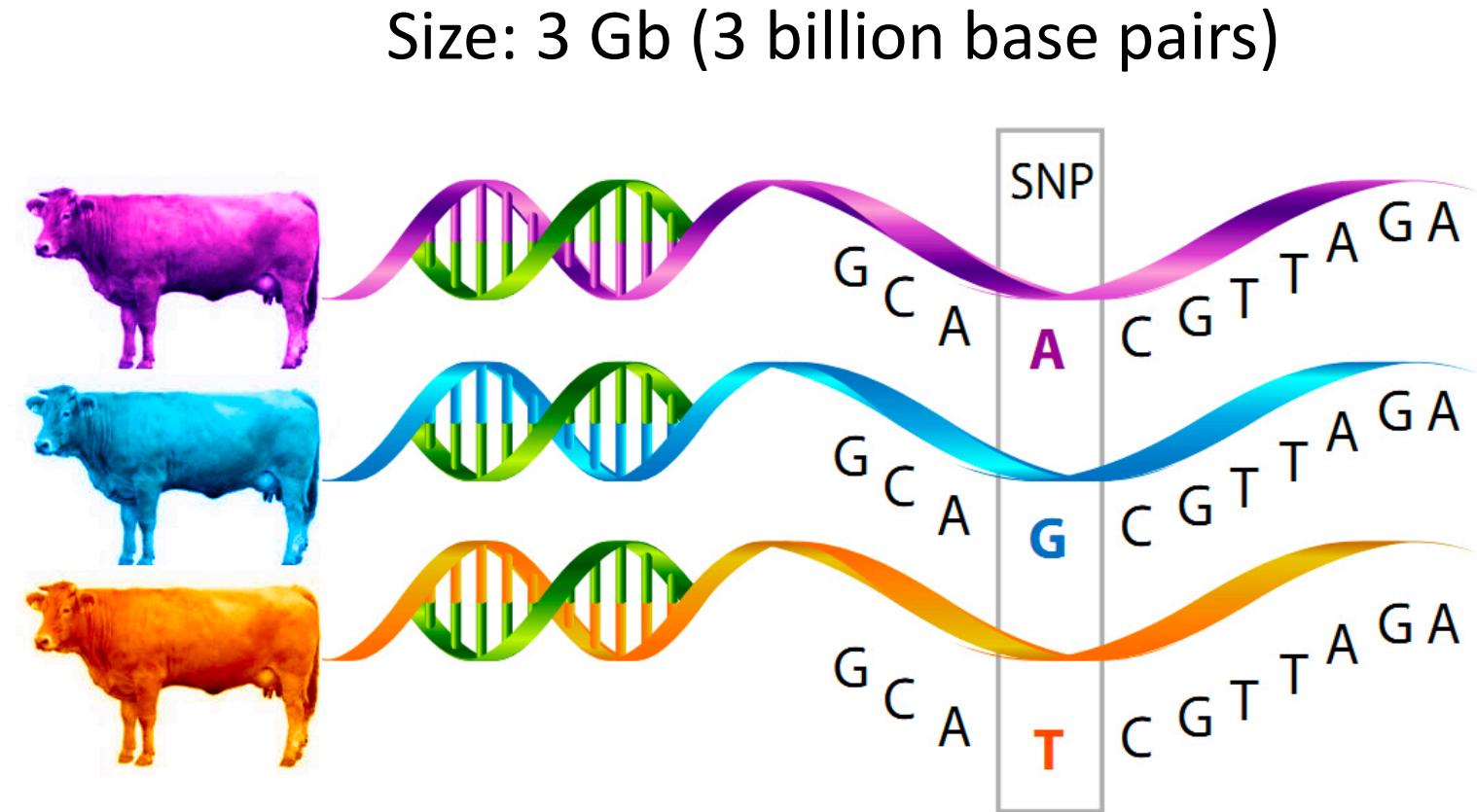
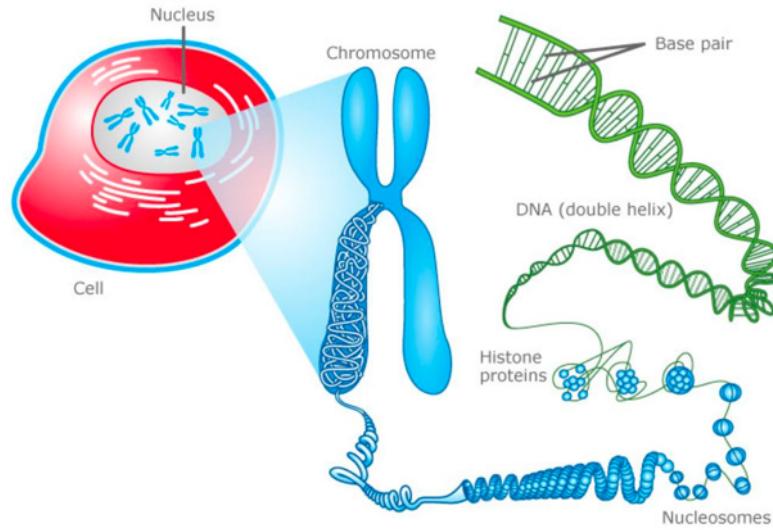
The percentage of total variation attributable to environmental factors is large:

- Feeding/nutrition
- Housing
- Reproductive management



$$P = G + E$$

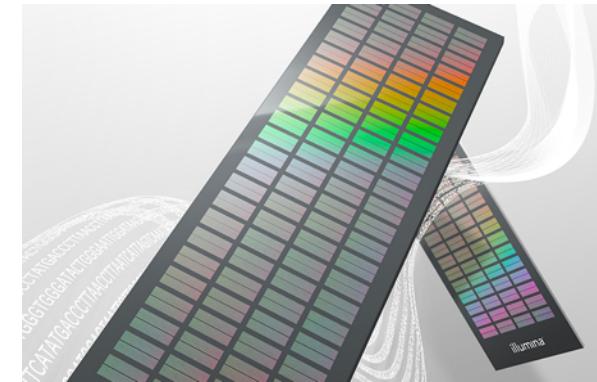
Genetic variation



SNP: Single Nucleotide Polymorphism single changes in the genetic code that are responsible or at least partially responsible for a specific phenotype

Breakthroughs

- Advent of genome sequencing and genotyping techniques



- New Statistical Methods (Genomic Selection 2009)

- Information from a large number of markers distributed across the **genome** can be used to capture diversity in that **genome**, sufficient to estimate breeding values without having a precise knowledge of where specific genes are located.

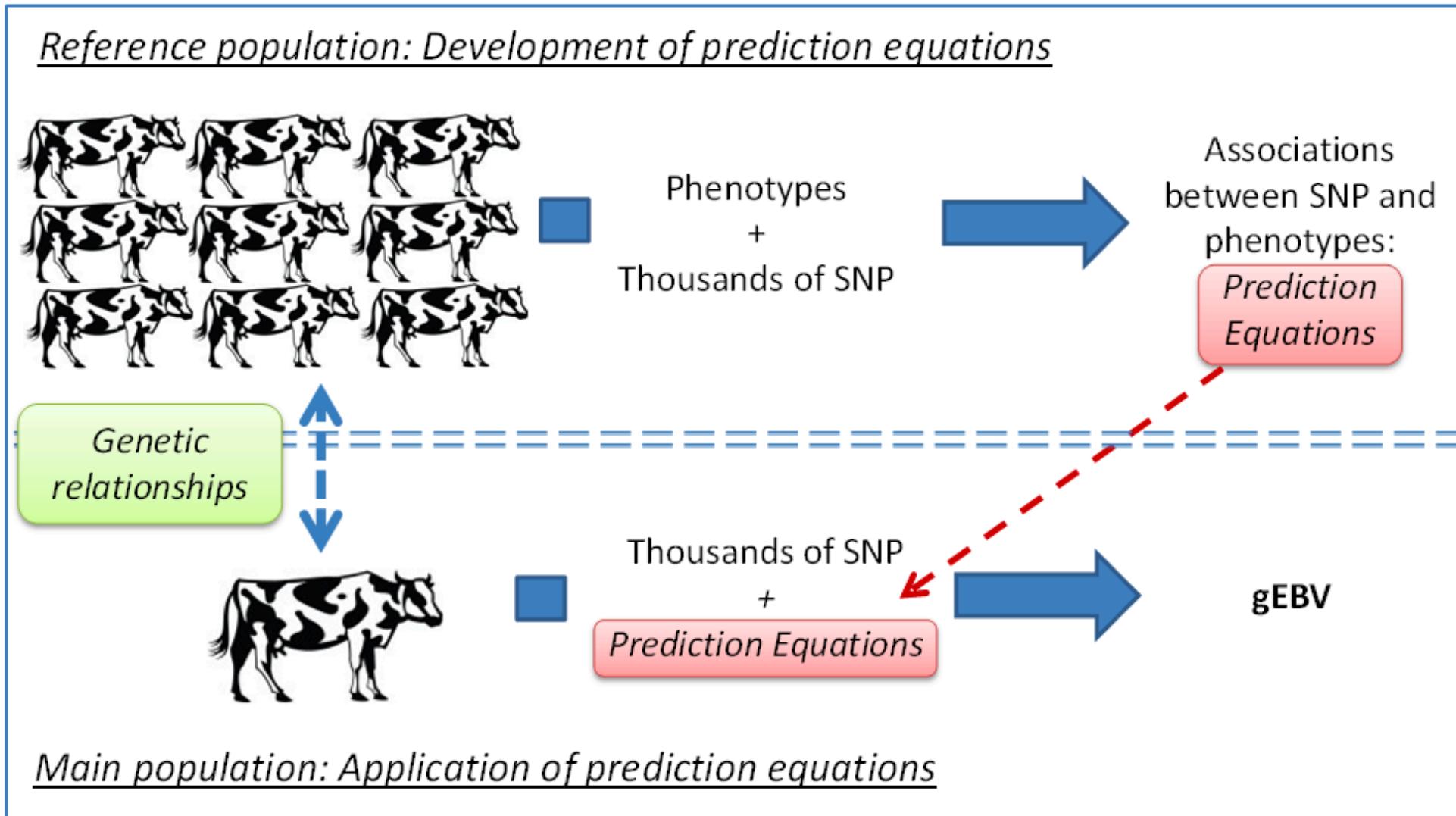
Largest genomic databases

	Ancestry.com	23andMe	CDCB/USDA
Genotypes	>4 million	>5 million	>3 million
Species	Human	Human	Cattle
Countries	?	>55	57
Genotyping cost	\$99	\$69	\$37–135
Delivery (weeks)	6–8	6–8	1–2
DNA generations	Few	Few	>10
EBV reliability	None	Low	High

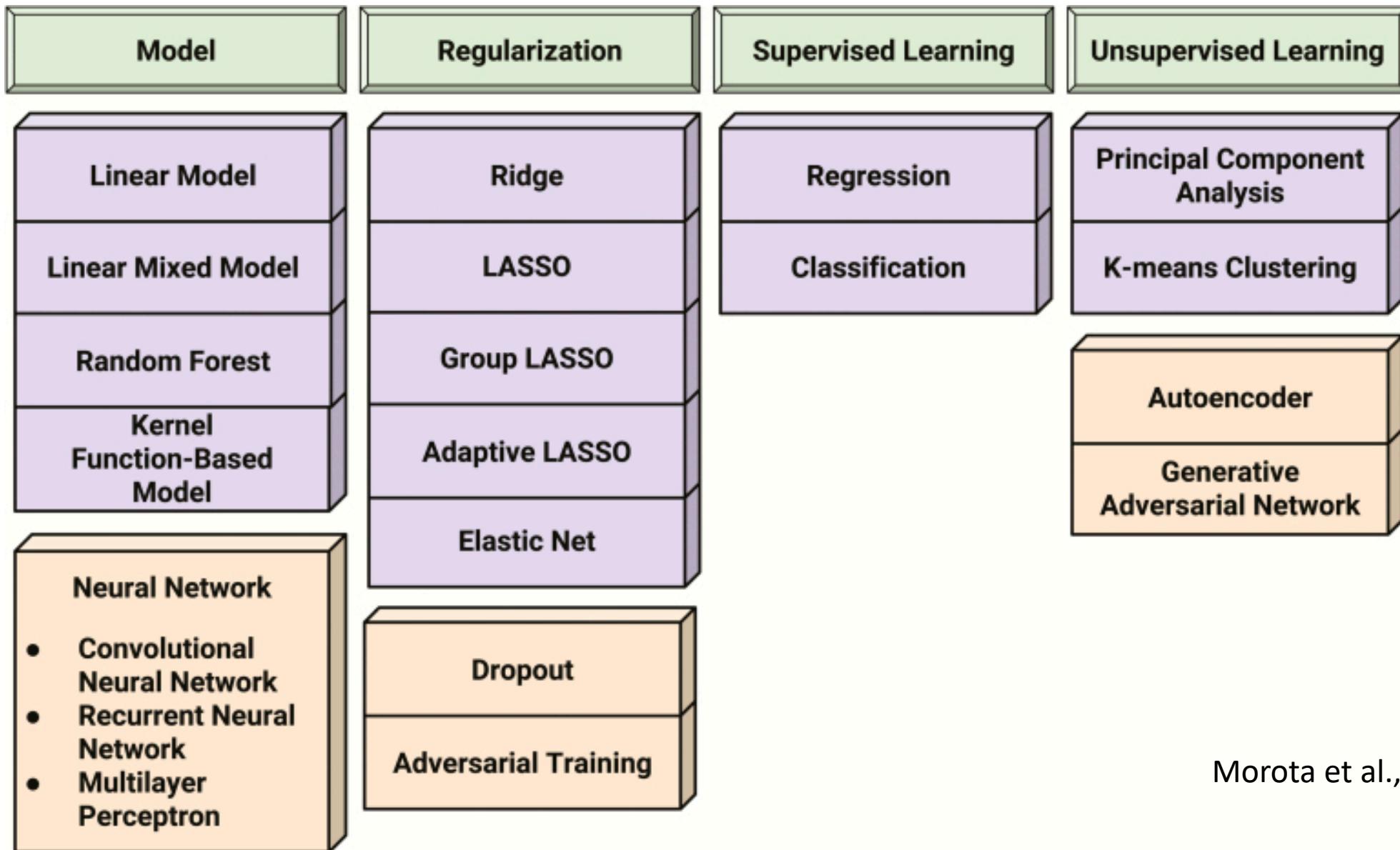
Reference: <http://genomemag.com/davies-23andme/#.VdY722zosY1>

Web sites: <https://www.23andme.com/>; <http://dna.ancestry.com/>; <https://www.cdcb.us/>;
http://aipl.arsusda.gov/Main/site_main.htm

Genome-Enabled Prediction (Genomic Selection)

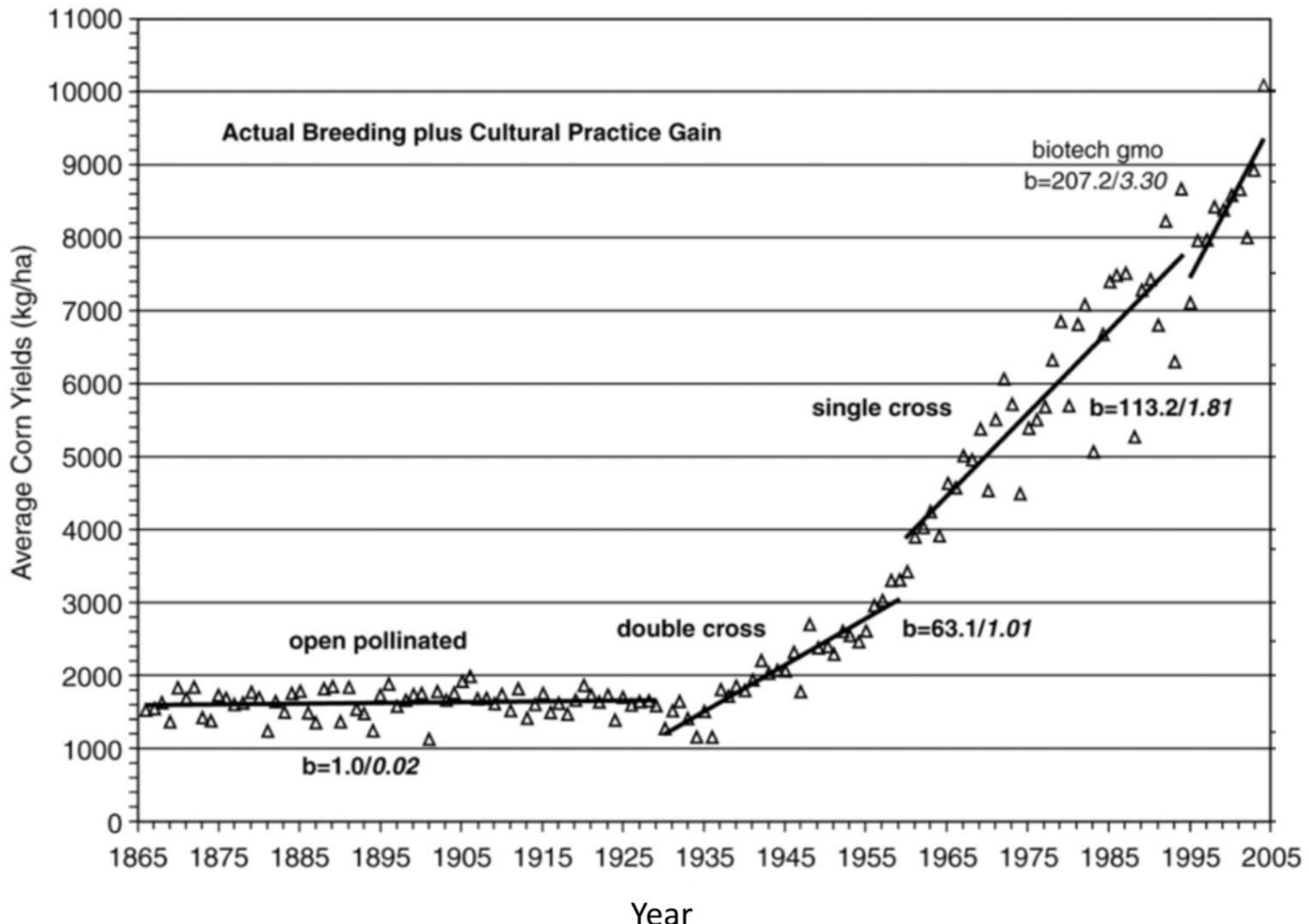


Prediction methodologies



Morota et al., 2018

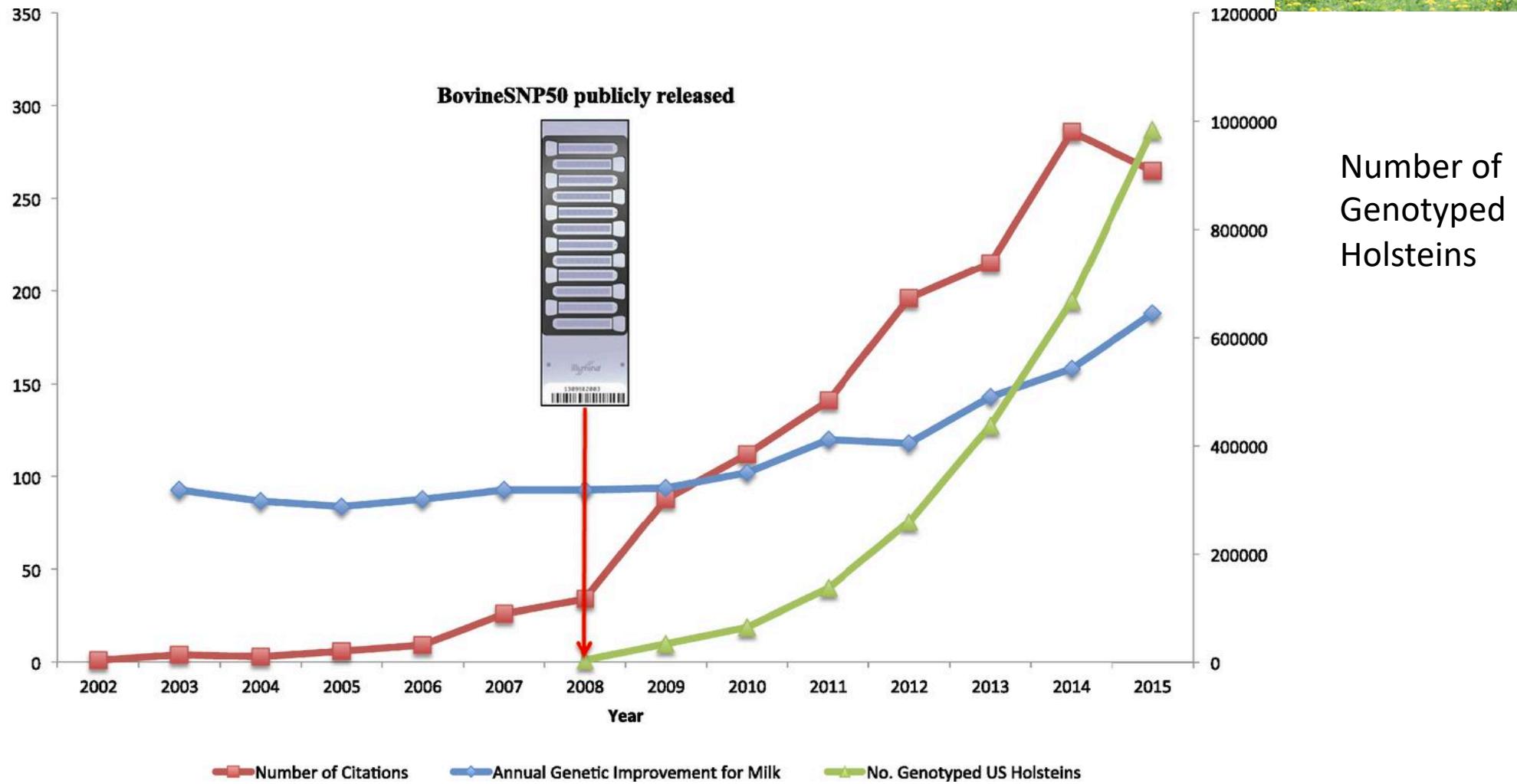
US Corn Yields increased 6.5 fold in 75 years



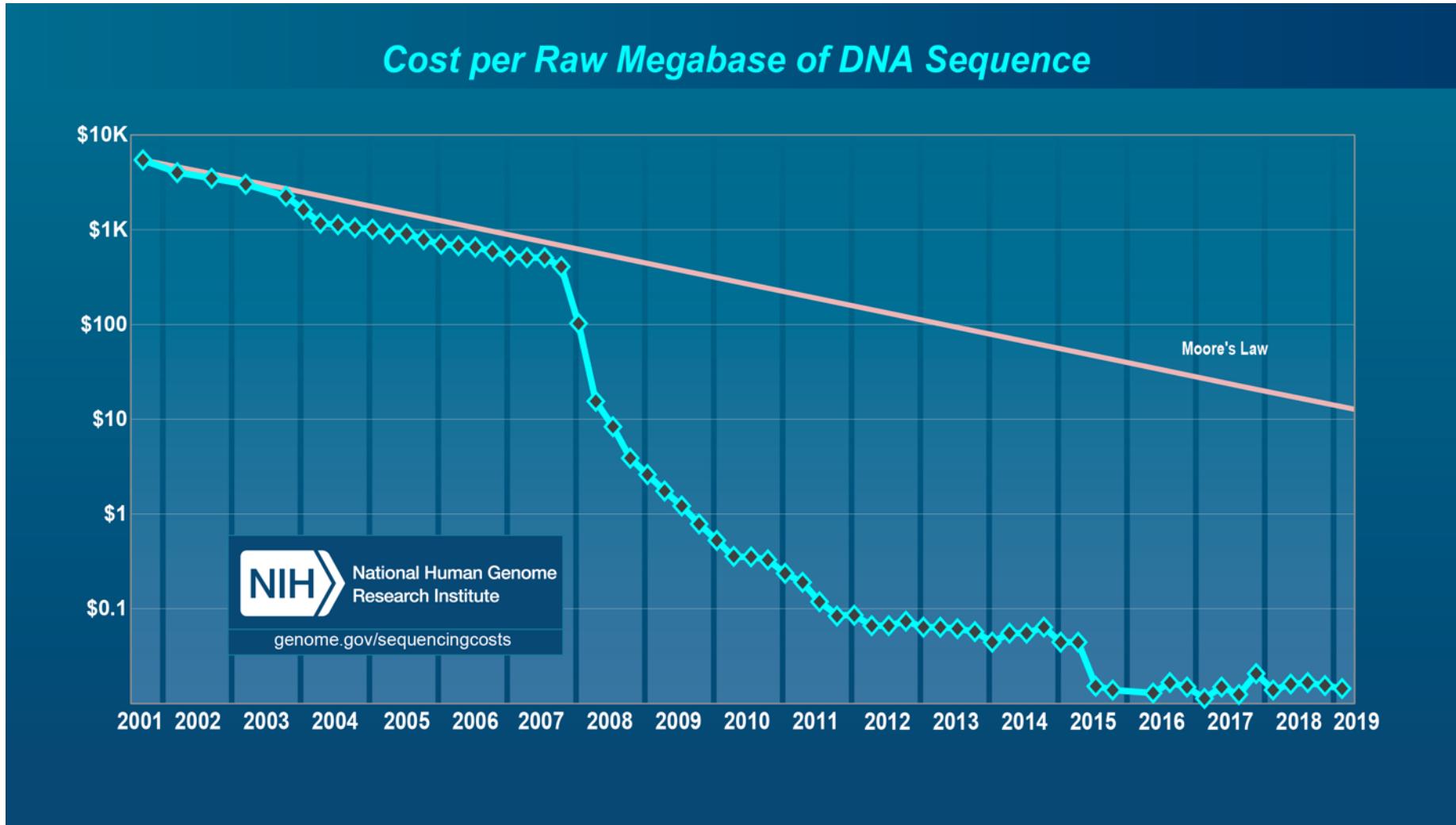
Gain Before and after Genomics



Number of citations or Genetic Improvement for Milk Yield



Sequencing cost per Mb



<https://www.genome.gov/about-genomics/fact-sheets/DNA-Sequencing-Costs-Data>

Different types of genetic variation

SNP

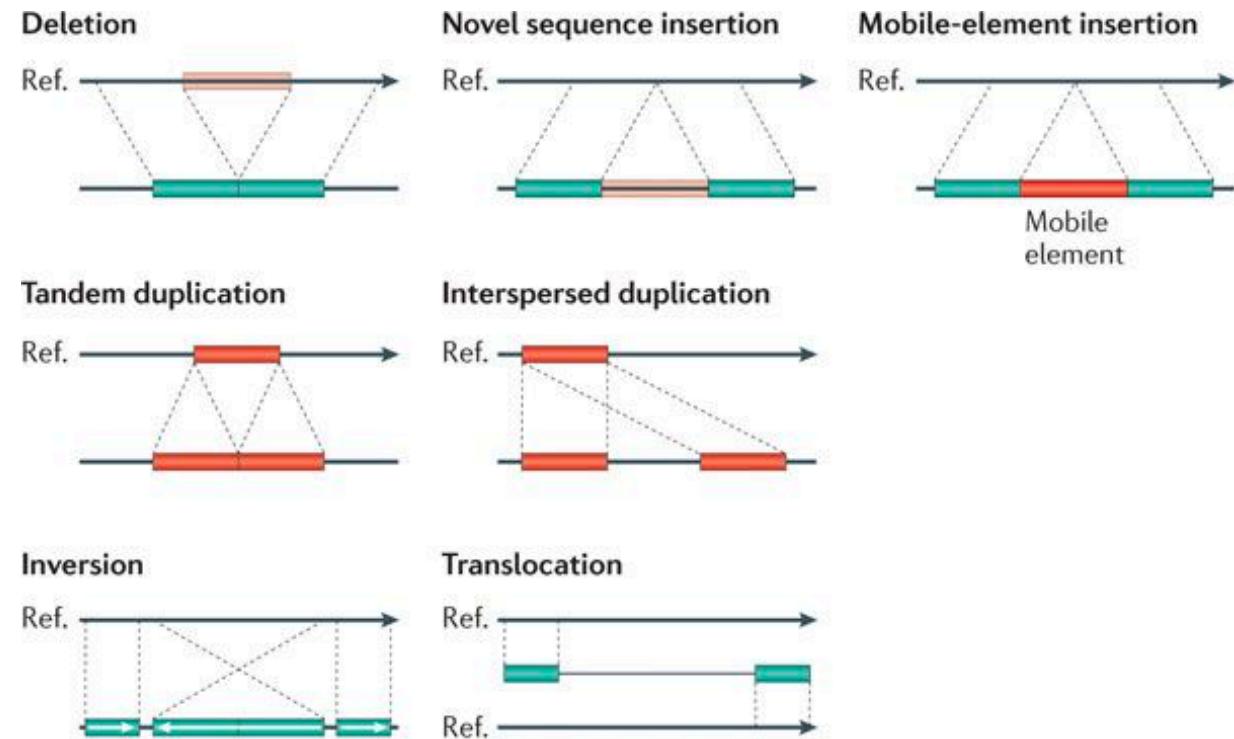
TTCG**G**GGTC.
TTCG**A**GGTC.
TTCG**G**GGTC.
TTCG**G**GGTC.

wild-type sequence
ATCTTCAGCCATAAAAGATGAAGTT
3 bp deletion
ATCTTCAGCCAAAGATGAAGTT
4 bp insertion (orange)
ATCTTCAGCCATATGTGAAAGATGA

Indel

Structural Variation (SV)

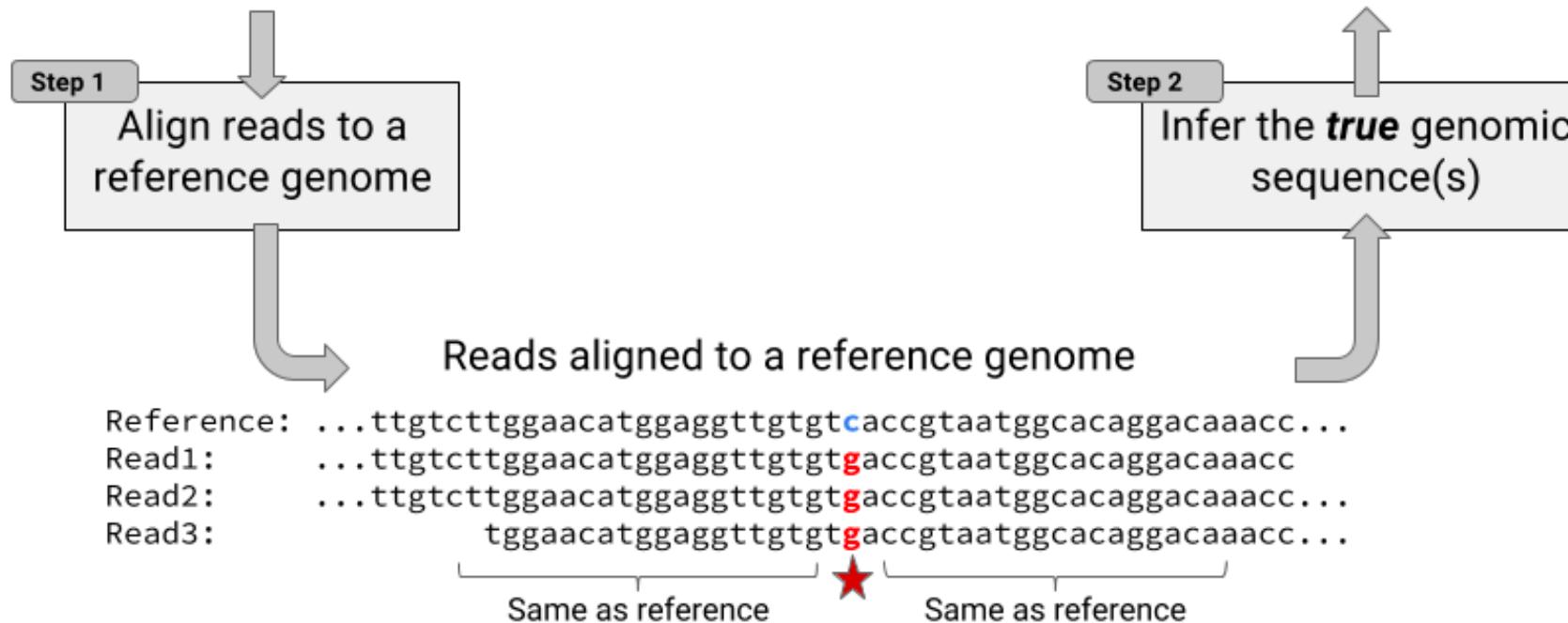
- CNV- Copy Number Variation
- PAV- Present Absent Variation
- Deletion and Insertions > 50bp
- Duplication
- Inversion
- Translocation



High-Throughput Sequencing

Actual sequencer output: ~1 billion ~100 basepair long DNA reads (30x coverage)

```
Read1: cttgggttcatattgtcttggAACATGGAGGTTGTcaccgtaatggcacaggacAAACC  
Read2: gatattgtcttggAACATGGAGGTTGTgtcaccgtaatggcacaggacAAACCgactgtcg  
Read3: tggaACATGGAGGTTGTgtcaccgtaatggcacaggacAAACCgactgtcgacatagagct  
Read4: gttgtgtcaccgtaatggcacaggacAAACCgactgtcgacatagagctggttactgtcg  
....  
Read 1,000,000,000: ....aactgtcgacatagagctggttactgtcgacatagagctggtt
```



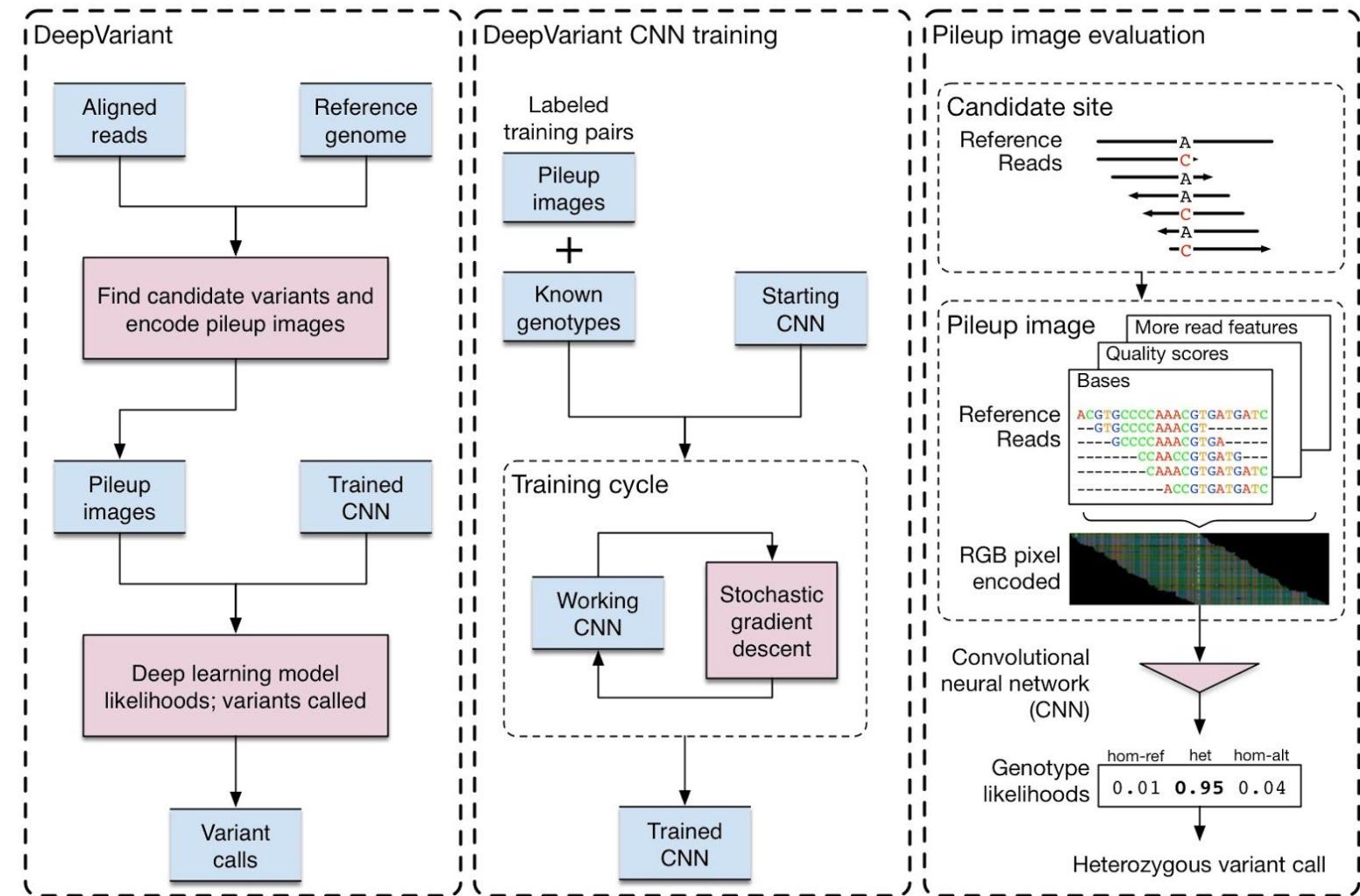
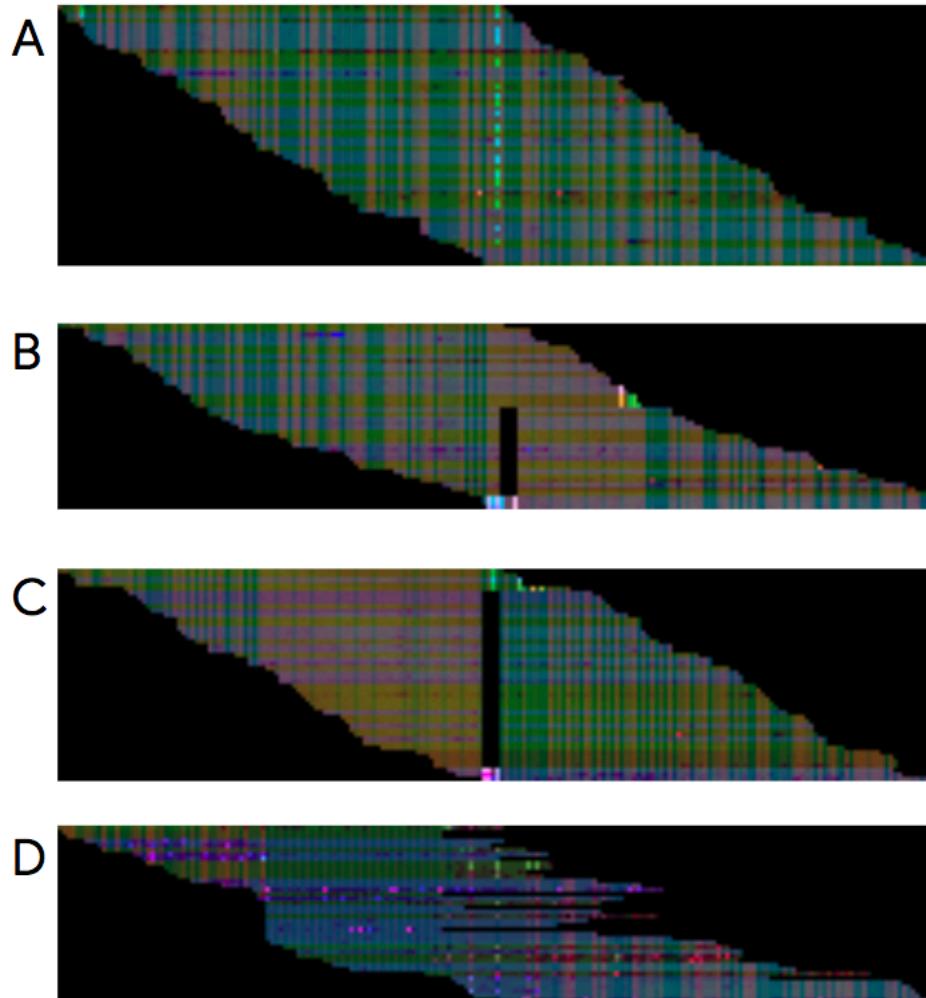
True genome sequence: 3 billion bases in 23 contiguous chunks (chromosomes)

```
..... cttgggttga tattgtcttg gaacatggag gtttgtcac cgtaatggca  
caggacAAAC cgactgtcga catagagctg gttacaacaa cagtaccaa catggccggag  
gtaagatcct actgctatga ggcataata tcagacatgg cttccggacag .....
```

Application of Machine learning in Genomics



- Deep Learning for variant calling from aligned NGS reads - DeepVariant



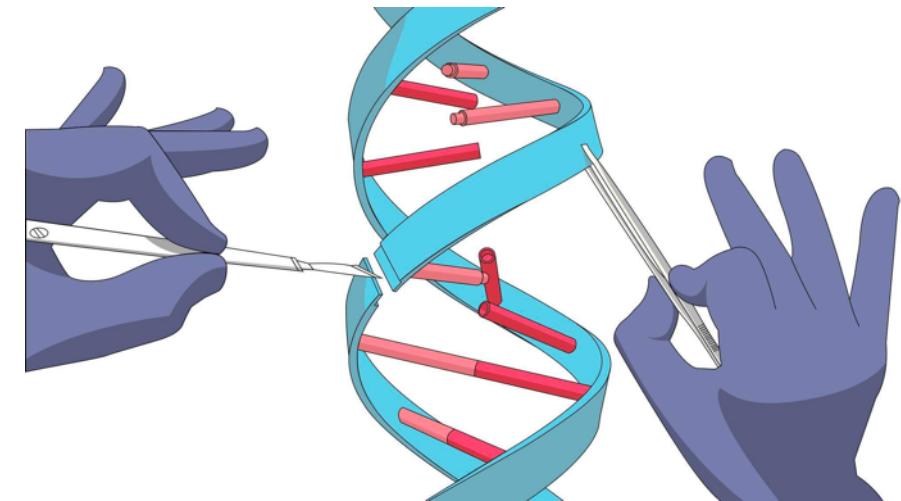
Deep Learning for variant calling from aligned NGS reads - DeepVariant

Table 1 Evaluation of several bioinformatics methods on the high-coverage, whole-genome sample NA24385

Method	Type	F1	Recall	Precision	TP	FN	FP	FP.gt	FP.al	Version
DeepVariant (live GitHub)	Indel	0.99507	0.99347	0.99666	357,641	2350	1,198	217	840	Latest GitHub v0.4.1-b4e8d37d
GATK (raw)	Indel	0.99366	0.99219	0.99512	357,181	2810	1,752	377	995	3.8-0-ge9d806836
Strelka	Indel	0.99227	0.98829	0.99628	355,777	4214	1,329	221	855	2.8.4-3-gbe58942
DeepVariant (pFDA)	Indel	0.99112	0.98776	0.99450	355,586	4405	1,968	846	1,027	pFDA submission May 2016
GATK (VQSR)	Indel	0.99010	0.98454	0.99573	354,425	5566	1,522	343	909	3.8-0-ge9d806836
GATK (flt)	Indel	0.98229	0.96881	0.99615	348,764	11227	1,349	370	916	3.8-0-ge9d806836
FreeBayes	Indel	0.94091	0.91917	0.96372	330,891	29,100	12,569	9,149	3,347	v1.1.0-54-g49413aa
16GT	Indel	0.92732	0.91102	0.94422	327,960	32,031	19,364	10,700	7,745	v1.0-34e8f934
SAMtools	Indel	0.87951	0.83369	0.93066	300,120	59,871	22,682	2,302	20,282	1.6
DeepVariant (live GitHub)	SNP	0.99982	0.99975	0.99989	3,054,552	754	350	157	38	Latest GitHub v0.4.1-b4e8d37d
DeepVariant (pFDA)	SNP	0.99958	0.99944	0.99973	3,053,579	1,727	837	409	78	pFDA submission May 2016
Strelka	SNP	0.99935	0.99893	0.99976	3,052,050	3,256	732	87	136	2.8.4-3-gbe58942
GATK (raw)	SNP	0.99914	0.99973	0.99854	3,054,494	812	4,469	176	257	3.8-0-ge9d806836
16GT	SNP	0.99583	0.99850	0.99318	3,050,725	4,581	20,947	3,476	3,899	v1.0-34e8f934
GATK (VQSR)	SNP	0.99436	0.98940	0.99937	3,022,917	32,389	1,920	80	170	3.8-0-ge9d806836
FreeBayes	SNP	0.99124	0.98342	0.99919	3,004,641	50,665	2,434	351	1,232	v1.1.0-54-g49413aa
SAMtools	SNP	0.99021	0.98114	0.99945	2,997,677	57,629	1,651	1,040	200	1.6
GATK (flt)	SNP	0.98958	0.97953	0.99983	2,992,764	62,542	509	168	26	3.8-0-ge9d806836

Precision Genetic Engineering (Genome Editing)

- Has long been a goal of molecular biology
- CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)
- Precise changes in the genome (e.g. T → A) or gene knockout in disease-causing genes
- Implications in precision medicine, sustainable agriculture and more



Genome Editing for Precision Breeding

- Examples in agriculture:

1- Soybean

- High oleic oil (20% less saturated fatty acids, zero trans fats)

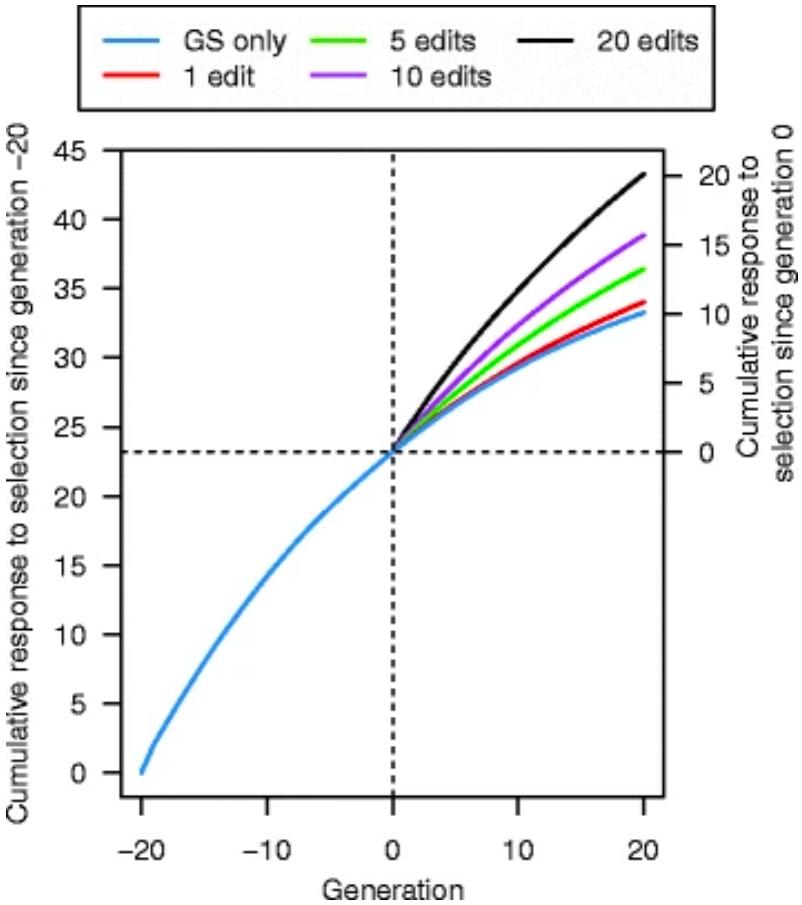
- Healthier

2- Gene-edited cattle that produce no horn

- 80% of dairy breeds are horned
- Horned cattle are dangerous to their handlers
- Dehorning is both painful and expensive

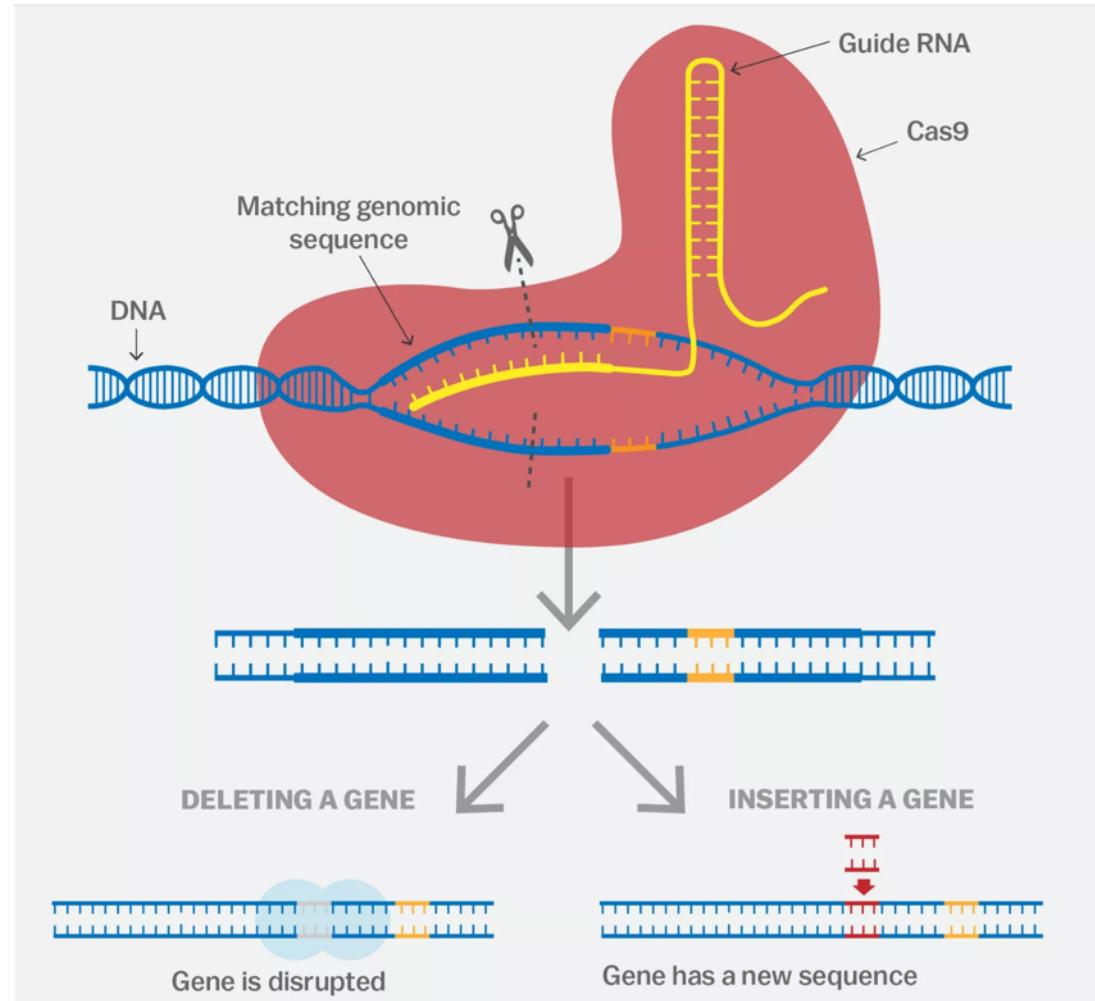
3- Several other examples in animals and plants.

Genome editing can improve the rate of genetic gain compared to traditional breeding

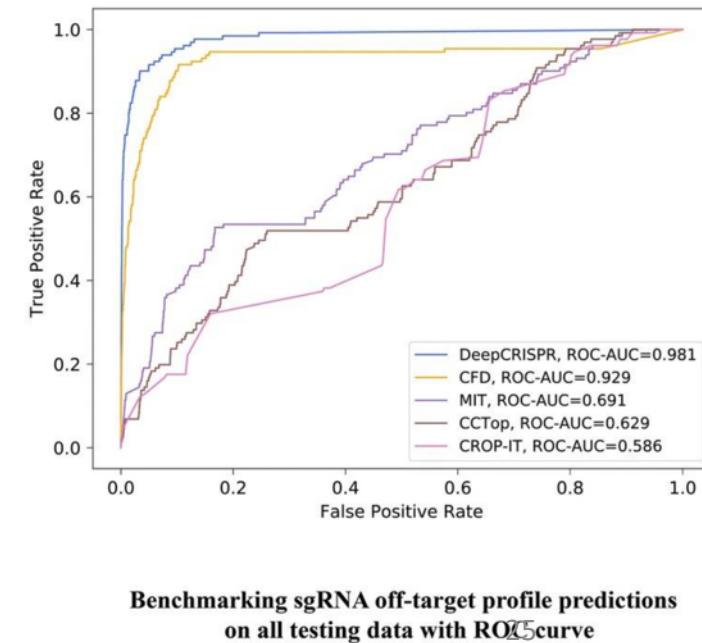
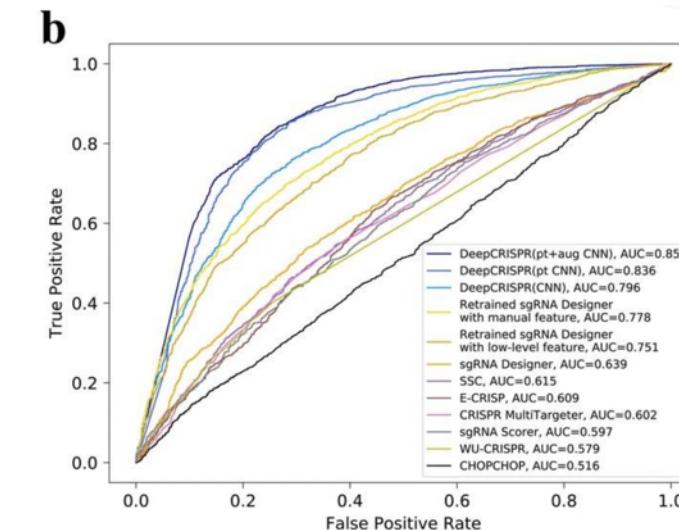
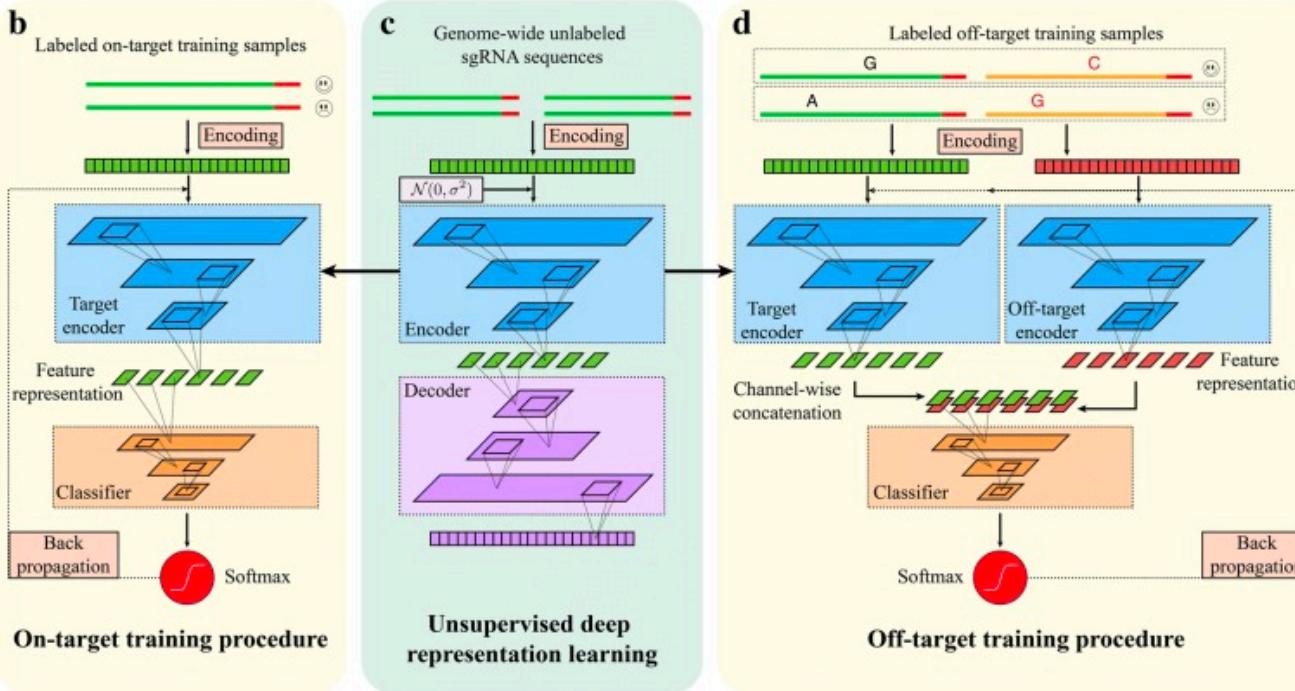
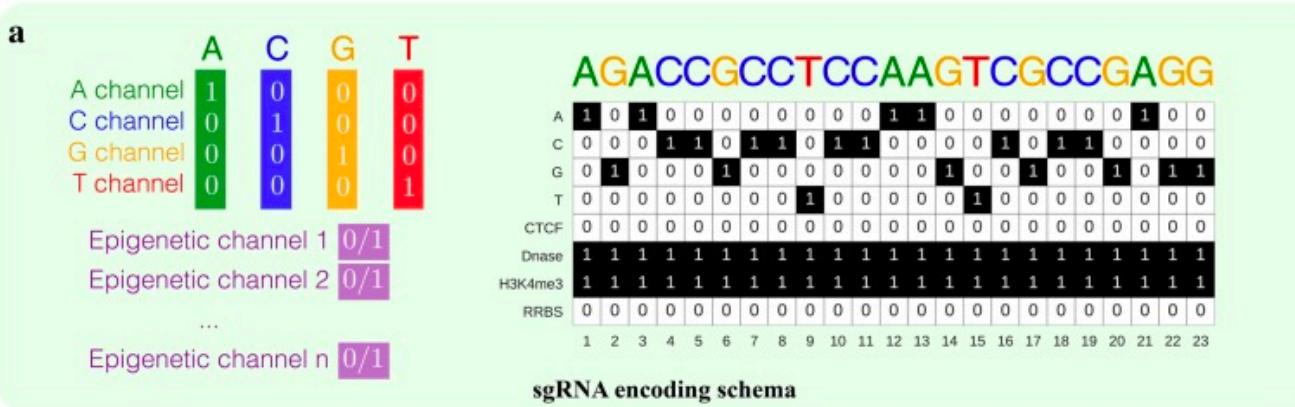


Intersection of Genome Editing and ML

- Challenges of Gene editing:
 - Better “on-target”
 - Elimination/reduction of “off-target” effects
- Supervised learning for guide RNA design with known labels
 - **Classify data into discrete “class labels”**
 - e.g. guide is/is not going to cut DNA
 - **Predict a continuous output**
 - e.g. Guide will cut with frequency y

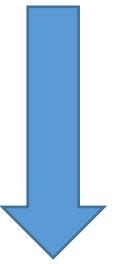


DeepCRISPR: optimized CRISPR guide RNA design by deep learning



Summary and challenges

- Advanced genomic technologies (whole genome sequencing) facilitates identifying genetic variation underlying important traits
- Faster bioinformatics tools must be developed to analyze data (genetic evaluation, variant association testing, DNA/RNA sequence analysis, etc.)
- Large amounts of data are generated, storage and access remains challenging
- Better genome databases are needed to facilitate genomic research and translation to industry
- Choice between sequencing vs. genotyping based on cost and goal
- Computational methods for high quality genome assemblies across breeds or varieties still in development
- Full power of genomic analysis needs additional data to support genome annotation



$$P = G + E$$

Cow I/O

Milk

Fat

Protein

Lactose

Urine

Feces

Calves

Gases

Feed

Minerals

Water

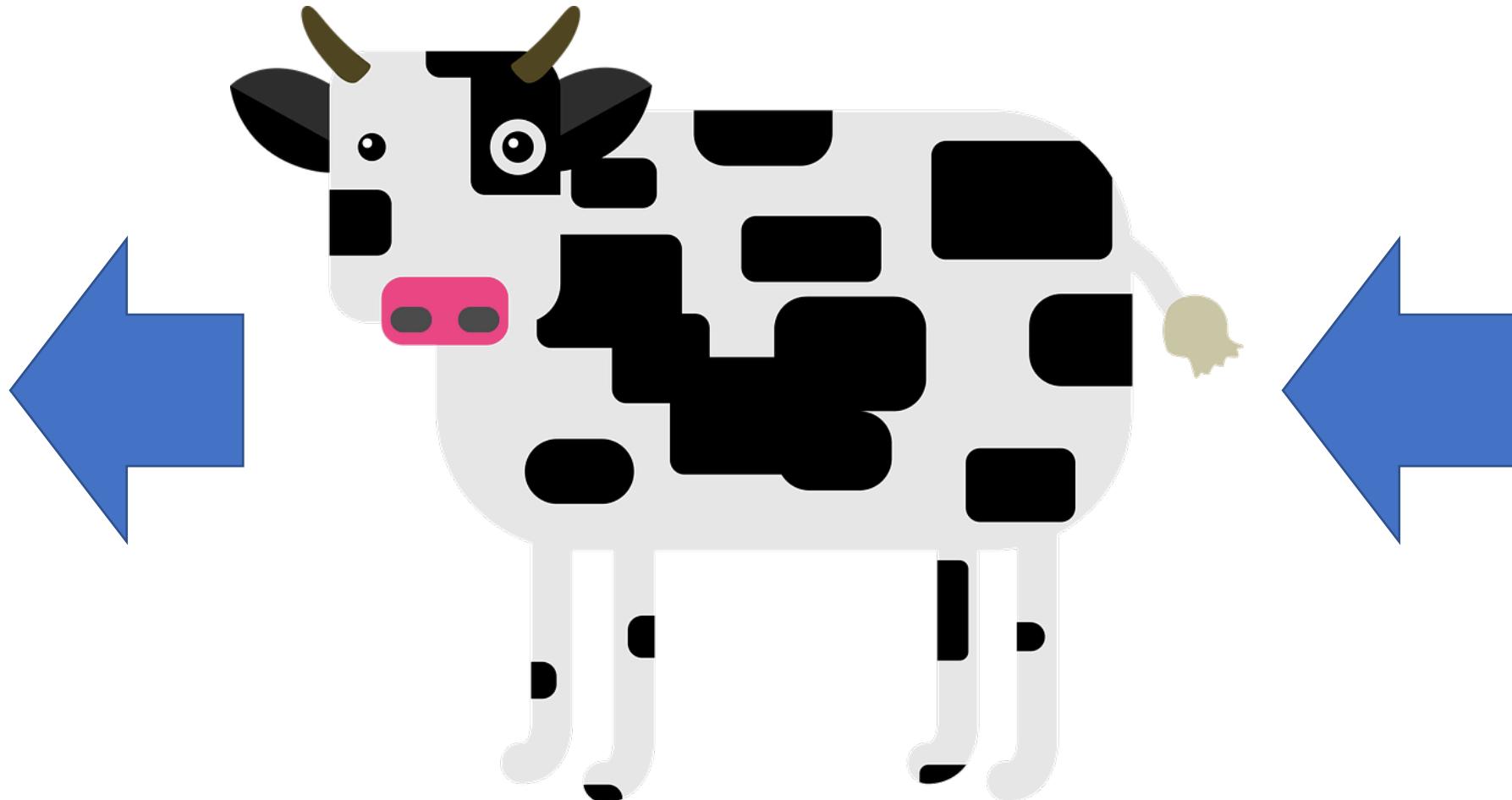
Sensors

Drugs

Hormones

Semen

Embryos



Traits routinely evaluated in the US

Year	Trait	Year	Trait
1926	Milk & fat yields	2006	Bull conception rate ²
1978	Conformation (type)	2009	Cow & heifer conception rates
1978	Protein yield	2016	Cow livability
1994	Productive life	2017	Gestation length
1994	SCS (udder health)	2017	Residual feed intake (research) ³
2000	Calving ease (dystocia) ¹	2018	Cow health
2003	Daughter pregnancy rate	2019	Age at first calving
2006	Stillbirth rate		

¹Sire calving ease evaluated by Iowa State University (1978–99)

²Estimated relative conception rate evaluated by DRMS in Raleigh, NC (1986–2005)

³Research trait ... no official evaluations yet

What do current phenotypes look like?

- Low dimensionality
 - Usually **few** observations per lactation
 - Close **correspondence** of phenotypes with values measured
 - Easy **transmission** and **storage**
 - Costs of data recording are relatively **low**

Get cow lactation records

Output from "Get cow lactation records"

Cow	HOCAN000008036612 key=35757290																							
Lac	Fresh	DIM	Herd	CtrlNo	Proc_Date	Mod_Date	LT	Mk	LI	TC	TC2	OS%	PC	Opn	DCR	Milk	DCR	Fat	DCR	Prot	DCR	SCS	Bth	NTD
1	1997/11/05	324	23361868	34	1999/04/22	2009/08/21	0	00	0	0		0	0	84	97	33142	97	1170	97	917	94	1.62	0	11
2	1998/11/16	332	23361868	34	1999/11/04	2009/08/21	0	40	0	0		0	0	79	103	33174	99	991	100	896	96	2.83	0	11
3	1999/11/26	328	23361868	34	2000/10/02	2009/08/21	0	40	0	0		0	0	151	97	34269	97	1192	97	895	95	3.23	0	10
4	2001/02/13	87	23361868	34	2001/06/01	2009/08/21	0	c0	0	7		0	0	-1	69	27738	70	996	69	736	73	3.02	0	3

Data amounts (as of Sept. 2016)

Pedigree records	75,538,654
Animal genotypes	1,589,202
Lactation records (<i>since 1960</i>)	139,134,191
Daily yield records (<i>since 1990</i>)	684,182,260
Reproduction event records	196,505,574
Calving difficulty scores	27,991,336
Stillbirth scores	18,470,886

Why do we need new phenotypes?

- Changes in production **economics**
- **Technology** produces new phenotypes or reduces costs of collecting them
 - New traits can be **predicted** on all genotyped animals without collecting progeny records
 - Phenotyping costs are **shared** among millions of animals
 - **Biotechnology** supports improved sensors
- To better understand **biology**

What do new phenotypes look like?

- High dimensionality
 - *Example:* MIR produces **1,060** points/observation
 - **Disconnect** between trait and measurement
 - **More resources** needed for transmission, storage, and analysis
 - Phenotyping costs can be **high** (e.g., feed intake)

TimeStamp	JobTypeName	Workstation	Lab Info: A403 Cedar USA	SampleIndex	Replicate	WaveNum	240	241	242	243	244	245	246	247	248	249	250	251	252	253	254	255	256	257	258	259	260	261	262	263	264	265	
4/12/13 10:01	Normal	1	16347	594474	1	1	1060	1.174367	1.169028	1.161095	1.152462	1.144269	1.136975	1.130587	1.124671	1.118177	1.109347	1.096055	1.076614	1.050721	1.020011	0.987768	0.957773	0.93279	0.913417	0.897826	0.882442	0.86322	0.836996	0.802468	0.760545	0.714041	0.666907
4/12/13 10:01	Normal	1	16347	594475	1	2	1060	1.236163	1.224816	1.213445	1.203333	1.194433	1.185992	1.177303	1.167946	1.157501	1.145115	1.129392	1.108876	1.082934	1.052488	1.020056	0.988904	0.961699	0.939316	0.920406	0.901861	0.879943	0.851592	0.815448	0.772286	0.724786	0.676795
4/12/13 10:01	Normal	1	16347	594476	1	3	1060	1.132829	1.131338	1.127171	1.121764	1.115967	1.110044	1.103983	1.097631	1.090495	1.081479	1.068946	1.051302	1.027905	0.999765	0.96952	0.94056	0.915653	0.895761	0.879587	0.864024	0.845259	0.82008	0.78693	0.746391	0.701017	0.654649
4/12/13 10:01	Normal	1	16347	594477	1	4	1060	1.209717	1.196581	1.182448	1.169595	1.159037	1.150633	1.143685	1.137299	1.130379	1.121474	1.108853	1.101021	1.0675	1.039418	1.009414	0.980754	0.956015	0.935984	0.919283	0.902859	0.883063	0.856893	0.82297	0.781958	0.736377	0.689938
4/12/13 10:02	Normal	1	16347	594478	1	5	1060	1.167169	1.155416	1.144443	1.135664	1.129477	1.125215	1.121651	1.117421	1.111553	1.101409	1.086772	1.066282	1.040902	1.009915	0.978788	0.950084	0.926164	0.907339	0.891662	0.875581	0.855171	0.827444	0.791295	0.747822	0.699979	0.651769
4/12/13 10:02	Normal	1	16347	594479	1	6	1060	1.197093	1.178723	1.163159	1.150549	1.140553	1.133002	1.127066	1.122078	1.116669	1.108818	1.096071	1.076372	1.049533	1.017293	0.983248	0.951526	0.925137	0.904733	0.888346	0.851806	0.823983	0.787326	0.742849	0.6936	0.643826	
4/12/13 10:02	Normal	1	16347	594480	1	7	1060	1.214322	1.191816	1.176712	1.166241	1.158485	1.152303	1.14673	1.140299	1.131081	1.115819	1.093662	1.064489	1.030662	0.996158	0.965111	0.940168	0.921439	0.906493	0.891282	0.87156	0.846219	0.808172	0.764537	0.721647	0.667757	
4/12/13 10:02	Normal	1	16347	594481	1	8	1060	1.190054	1.186357	1.183249	1.180014	1.175545	1.169019	1.16036	1.150114	1.138788	1.126144	1.111002	1.091775	1.067501	1.038748	1.007782	0.977797	0.95153	0.930002	0.91198	0.894409	0.873539	0.84627	0.811199	0.769066	0.722523	0.675398
4/12/13 10:02	Normal	1	16347	594482	1	9	1060	1.230022	1.224966	1.214292	1.208409	1.175656	1.164285	1.158185	1.143735	1.139217	1.131951	1.110164	1.087005	1.049107	1.01723	0.985743	0.957698	0.944465	0.915091	0.896632	0.875259	0.847636	0.812061	0.769016	0.721041	0.672059	
4/12/13 10:02	Normal	1	16347	594483	1	10	1060	1.190874	1.182911	1.177235	1.161865	1.151669	1.143049	1.13631	1.130957	1.125494	1.117533	1.1044	1.084163	1.056653	1.023923	0.989759	0.958312	0.932446	0.912582	0.896537	0.863034	0.831504	0.794417	0.749671	0.7004	0.650841	
4/12/13 10:02	Normal	1	16347	594484	1	11	1060	1.167036	1.156633	1.158584	1.126541	1.117733	1.109274	1.101386	1.094015	1.086384	1.076647	1.062562	1.042571	1.016809	0.987383	0.957631	0.930723	0.908221	0.889375	0.871403	0.850582	0.823649	0.788961	0.747047	0.700445	0.652973	
4/12/13 10:02	Normal	1	16347	594485	1	12	1060	1.22582	1.22403	1.213125	1.198521	1.184055	1.171649	1.161668	1.153332	1.143443	1.119296	1.098054	1.088691	1.050597	0.974892	0.949074	0.928538	0.911407	0.894216	0.873114	0.845135	0.809115	0.776601	0.718635	0.670868		
4/12/13 10:02	Normal	1	16347	594486	1	13	1060	1.169111	1.163761	1.154766	1.144583	1.134848	1.126315	1.119111	1.112885	1.106763	1.099315	1.088792	1.073732	1.035717	1.029855	1.004613	0.980962	0.961168	0.945832	0.933622	0.921763	0.907034	0.886083	0.862025	0.827304	0.790603	0.752961
4/12/13 10:02	Normal	1	16347	594487	1	14	1060	1.198159	1.18971	1.178066	1.166343	1.156427	1.148788	1.142807	1.137113	1.129805	1.118718	1.101895	1.097291	1.084451	1.041756	0.980894	0.950605	0.926216	0.907666	0.882477	0.867667	0.855913	0.827311	0.789875	0.744969	0.695814	0.646591
4/12/13 10:03	Normal	1	16347	594488	1	15	1060	1.173401	1.169982	1.164828	1.158106	1.150041	1.141139	1.132156	1.123661	1.115392	1.105891	1.092815	1.073926	1.048334	1.017289	0.980419	0.952532	0.925952	0.905181	0.888508	0.872262	0.85216	0.824778	0.788644	0.744651	0.695766	0.646214
4/12/13 10:03	Normal	1	16347	594489	1	16	1060	1.168304	1.160648	1.149947	1.138466	1.12752	1.117671	1.109208	1.102273	1.096474	1.090429	1.081782	1.067953	1.04734	1.020331	0.989472	0.958561	0.931058	0.90858	0.890205	0.872867	0.852573	0.825909	0.797123	0.749204	0.702502	0.655048

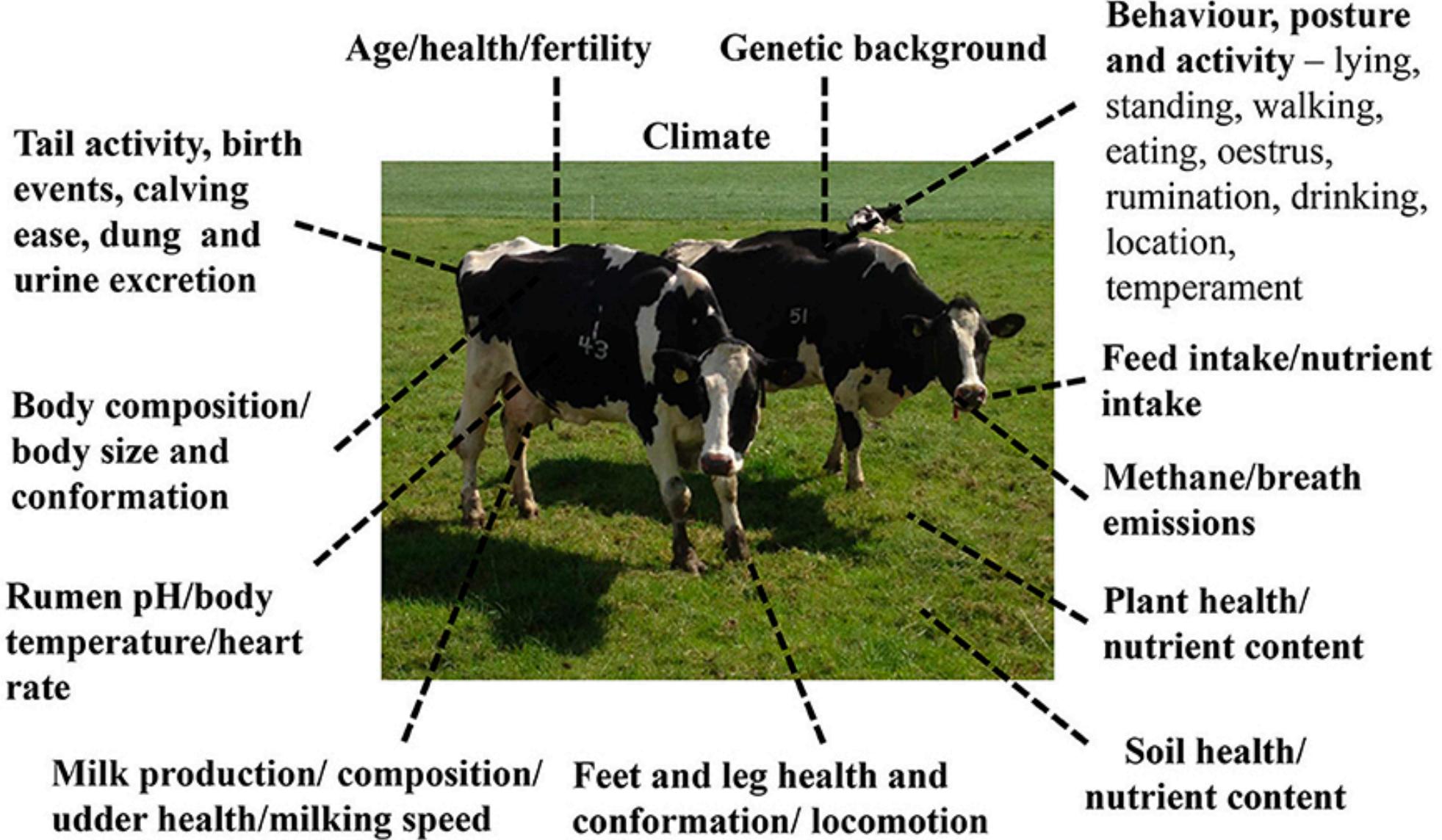
High-throughput phenotyping for Precision Farming



- Sensors → spatial/remote-sensing data
- Robotics
- Camera → Video, image
- Microphone → Audio



Data Sources to monitor and manage cows





J. Dairy Sci. 102:4294–4308
<https://doi.org/10.3168/jds.2018-15238>

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Big data analysis in animal science

Automated body condition scoring of dairy cows using 3-dimensional feature extraction from multiple body regions

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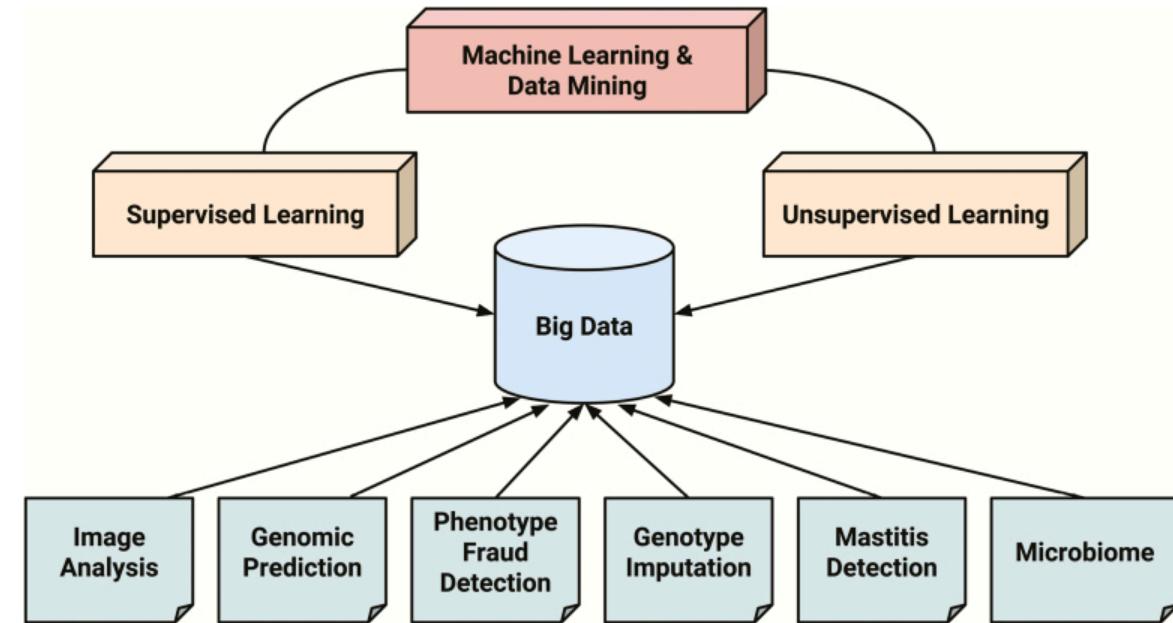
³Animal Production Systems Group, Wageningen University & Research, PO Box 338, Wageningen, 6700 AH, the Netherlands



Article

Feature Selection and Comparison of Machine Learning Algorithms in Classification of Grazing and Rumination Behaviour in Sheep

Nicola Mansbridge¹, Jurgen Mitsch^{2,3}, Nicola Bolland¹, Keith Ellis⁴,
Giuliana G. Miguel-Pacheco¹, Tania Dottorini¹ and Jasmeet Kaler^{1,*}



Morota et al., 2018



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<https://doi.org/10.3168/jds.2016-11526>
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Machine-learning-based calving prediction from activity, lying, and ruminating behaviors in dairy cattle

M. R. Borchers,* Y. M. Chang,† K. L. Proudfoot,‡ B. A. Wadsworth,* A. E. Stone,* and J. M. Bewley*¹

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Startups/Initiatives



RESEARCH

A Virtual Dairy Farm Brain: The Next Big Leap in Dairy Farm Management Applying Artificial Intelligence



Cloud-based Herd management software for beef and dairy operations



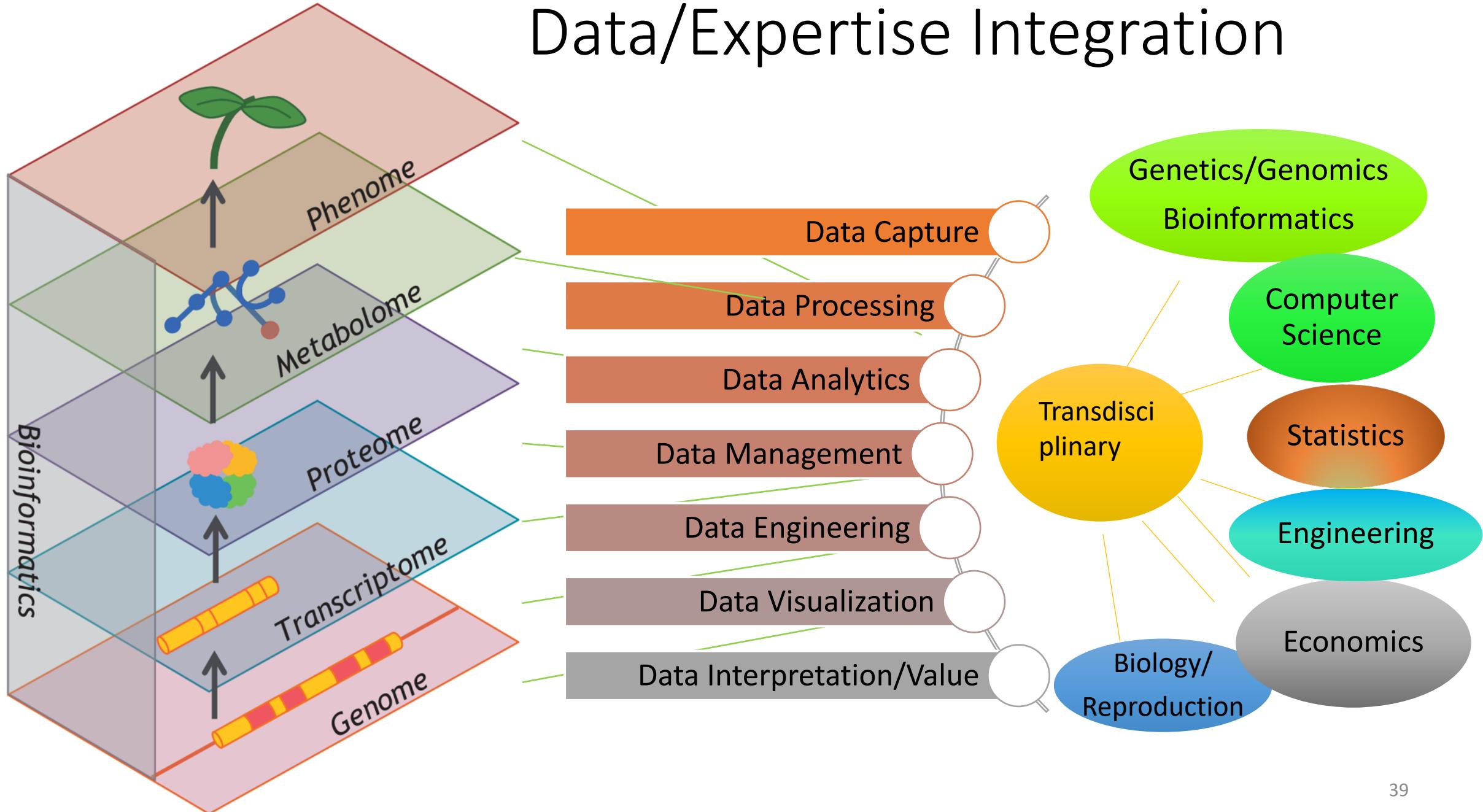
AGROGRAPH



As a System

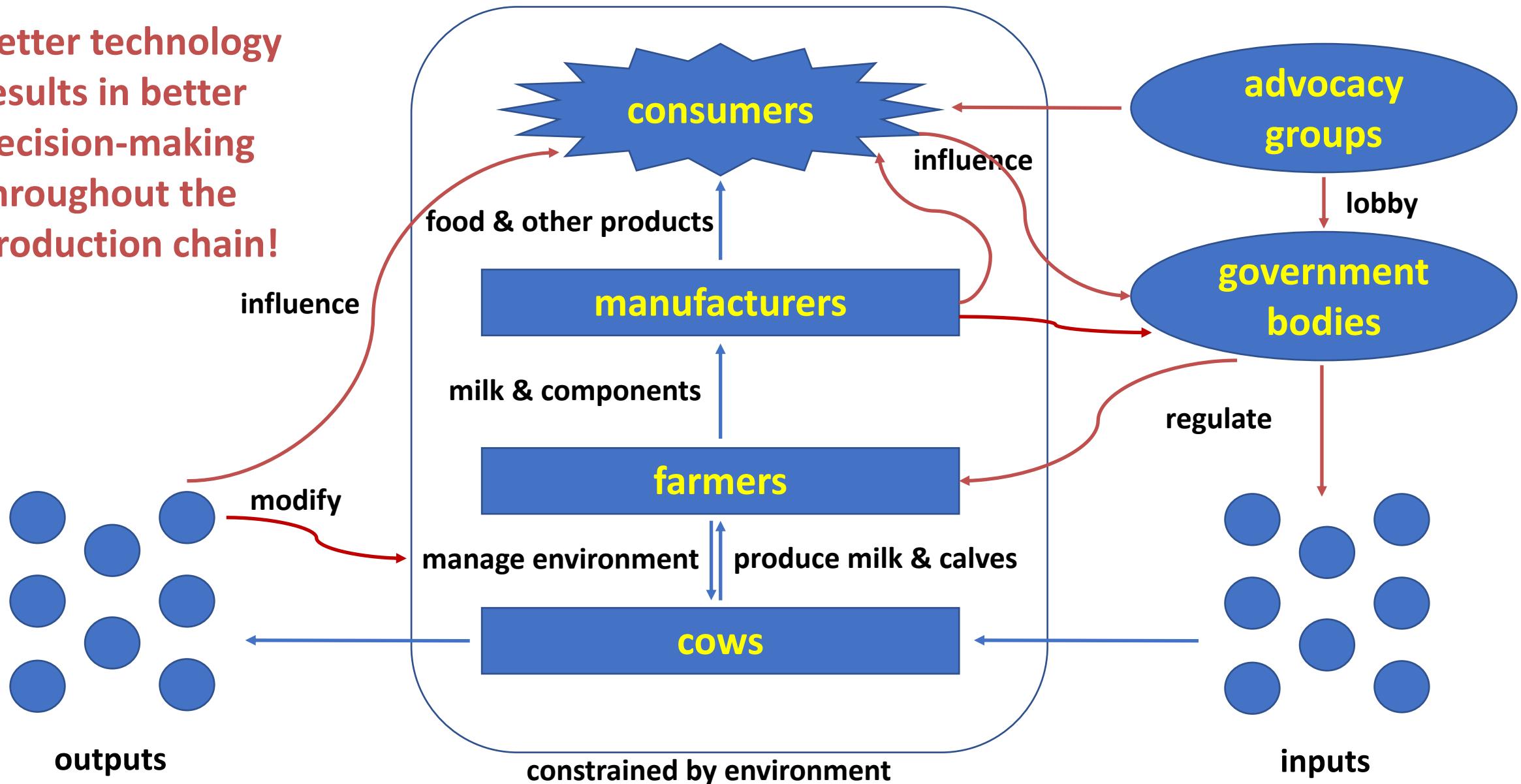
$$P = G + E$$

Data/Expertise Integration



Data-driven technologies applied from farm to fork

Better technology results in better decision-making throughout the production chain!



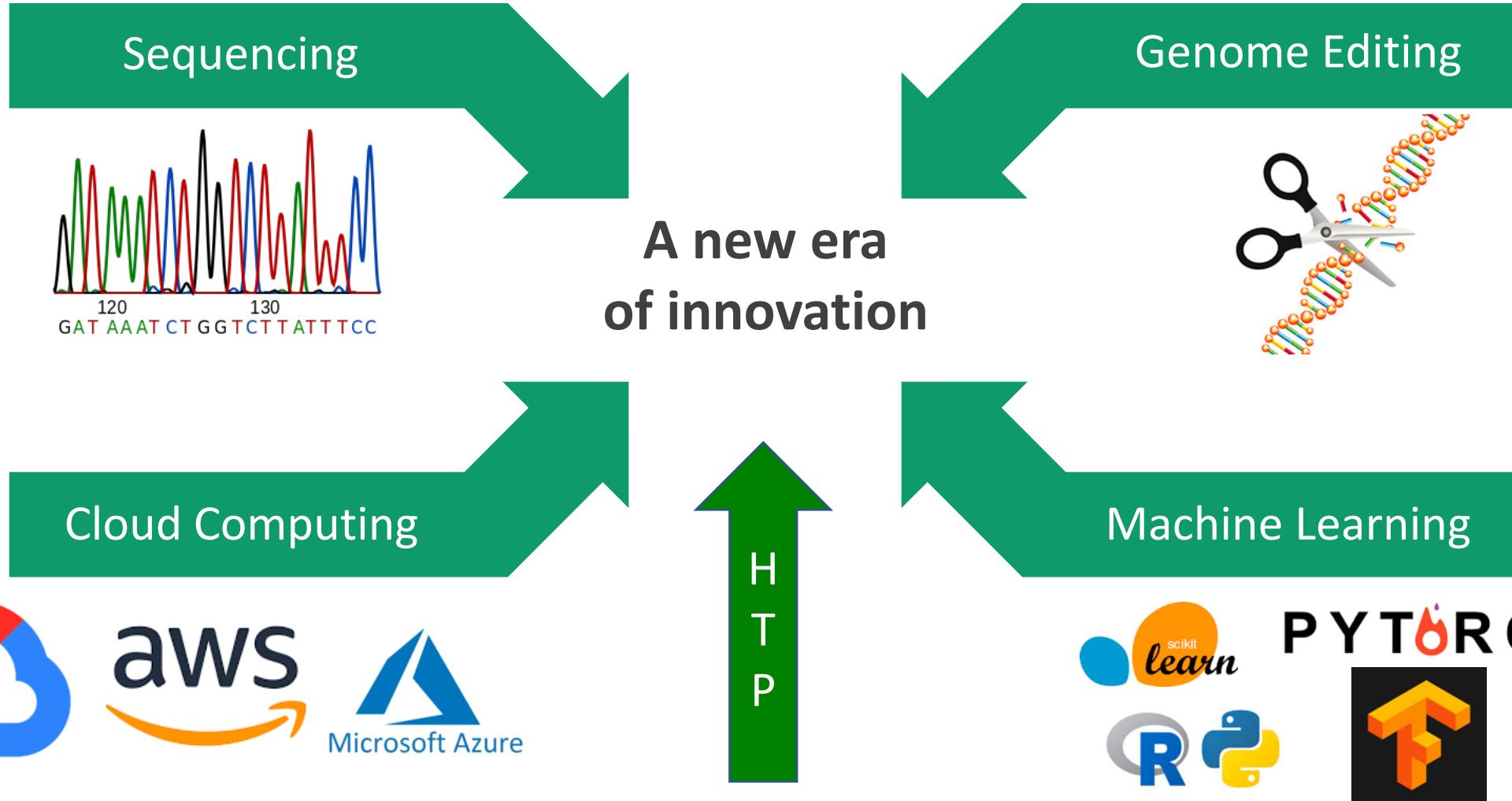
Opportunities

- New insights and knowledge
- Real-time decision making
- Support operational and strategic decisions (inseminate a cow or not?)
- Development of new products, services and management strategies

Challenges

- Affordable data recording
- Data ownership (who pays for it, who owns it?)
- Access and integration of data from multiple types and multiple sources (Private and public)
- Intelligent processing and analytics
- Clear business models
- Biology is complex!

Why do we think now is the time for AI to disrupt Agriculture?



Benson Hill Biosystems

Empowering Innovators.
Unlocking Nature's Potential.

BENSON•HILL
BIOSYSTEMS™



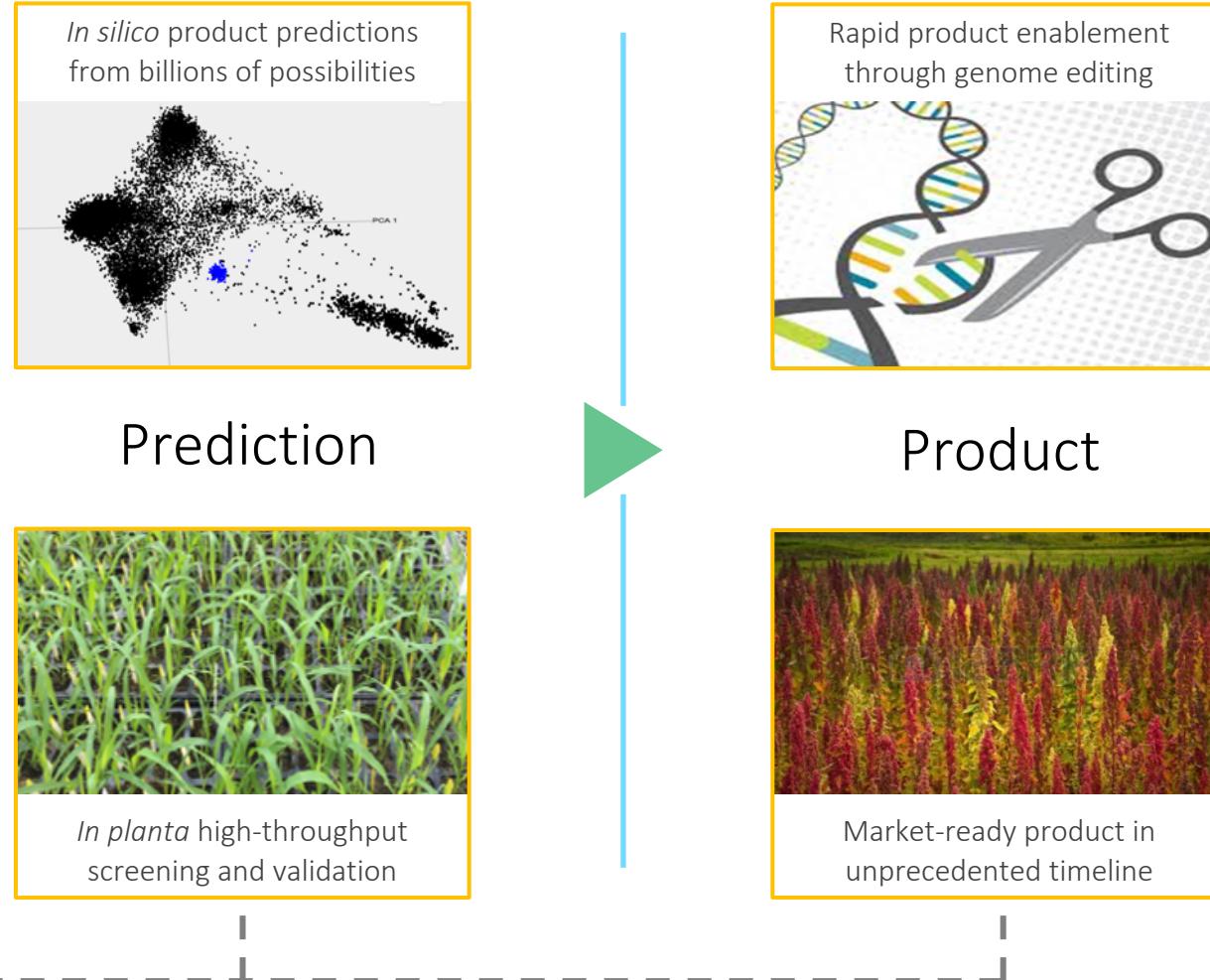
Benson Hill has created a flexible, state-of-the-art
Design → Build → Test cycle for rapid crop innovation



BENSON•HILL
BIOSYSTEMS

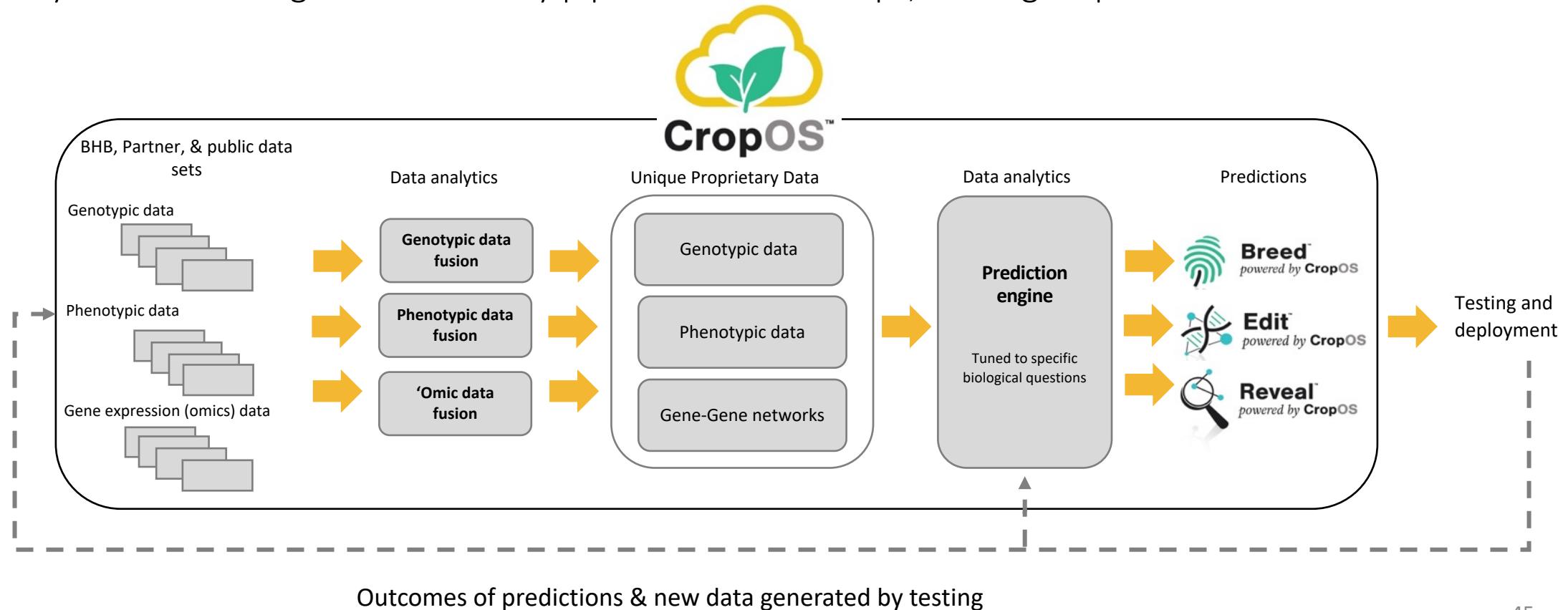


Feedback loop
to enhance
data/AI



CropOS enables breeding, genome editing and trait discovery

- Community approach utilizes data from public and private sources to create unparalleled predictive power
- Machine learning models are optimized for breeding, gene editing, and biotech traits
- Delivery of value through BHB discovery pipelines, partnerships, and digital products



CropOS design strategy overcomes platform challenges

Data Volume

- Datasets with over 50 million markers
- Datasets with over 100 traits
- Simulate 30 million progenies in one analysis

Data Velocity

Added 70 datasets in the past 90 days!

Technology, Process & Team

Data Variety

- Phenotypic Data from third party APIs
- Structured, semi structured data formats

Data Veracity

- Research validates platform analytics



Breed: Platform to support predictive breeding



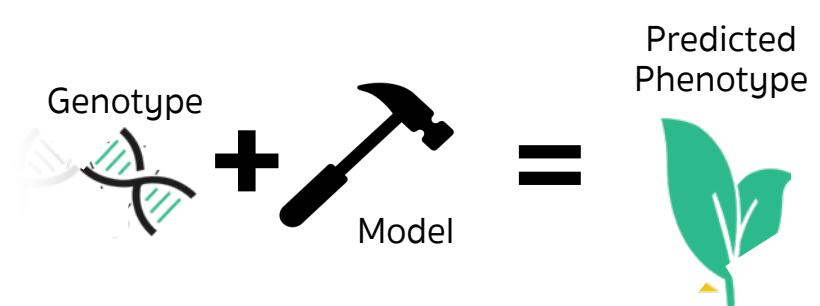
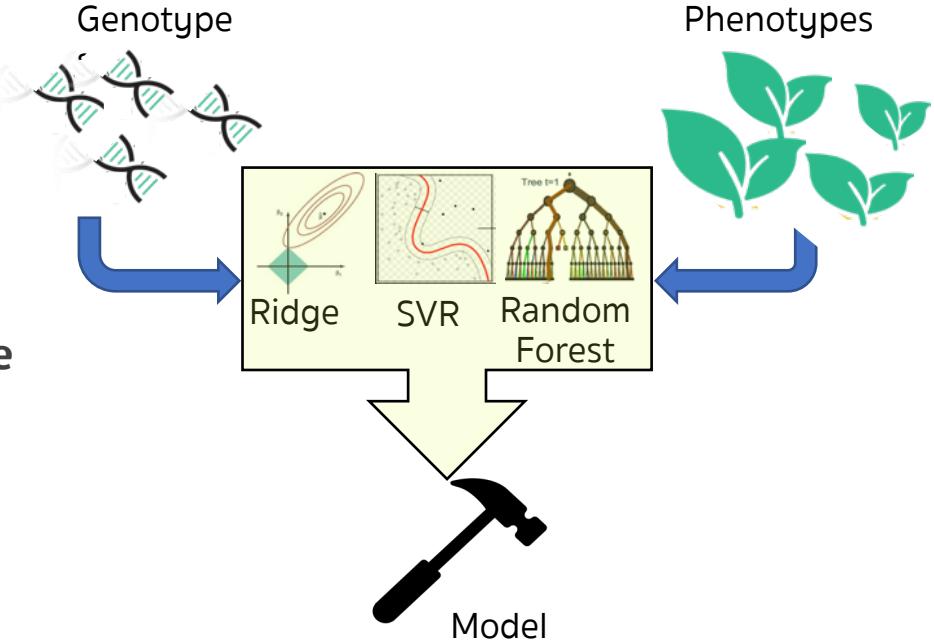
- Increase product pipeline effectiveness and efficiency
 - Uses existing genotype and phenotype data
 - Composes *model* of relationship between genetic markers and phenotype
 - Uses model to *predict* phenotype for new germplasm

Step 1:
Identify training set.

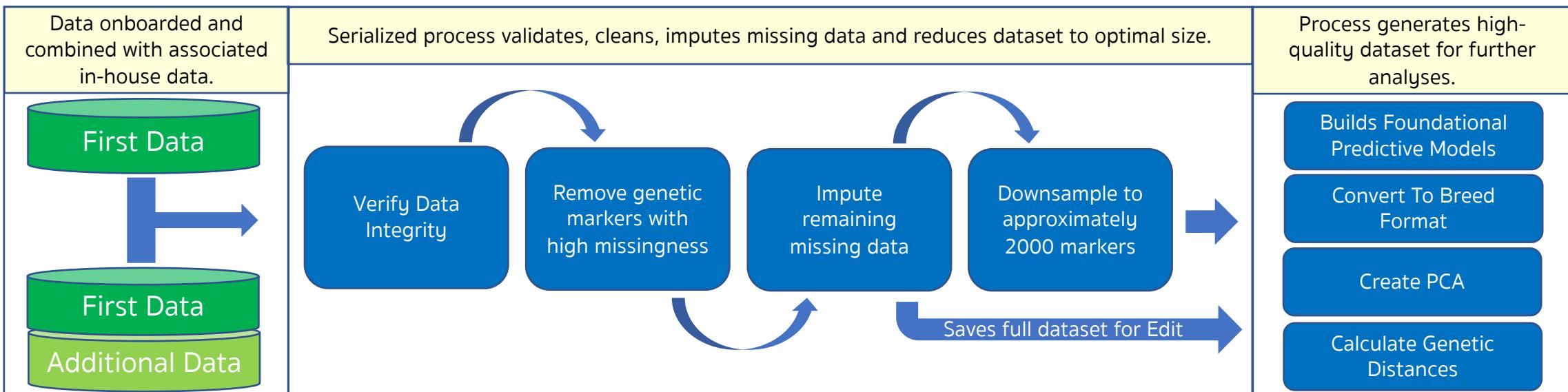
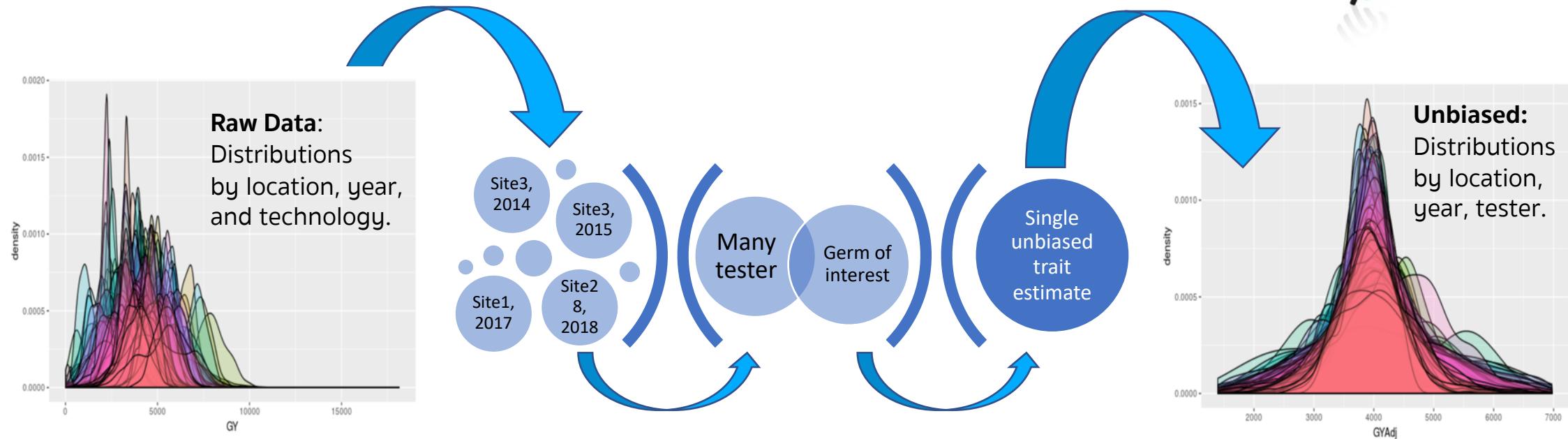
Step 2:
Train predictive model

Step 3:
Use model for predictions

Step 4:
Identify best germplasm for advancement

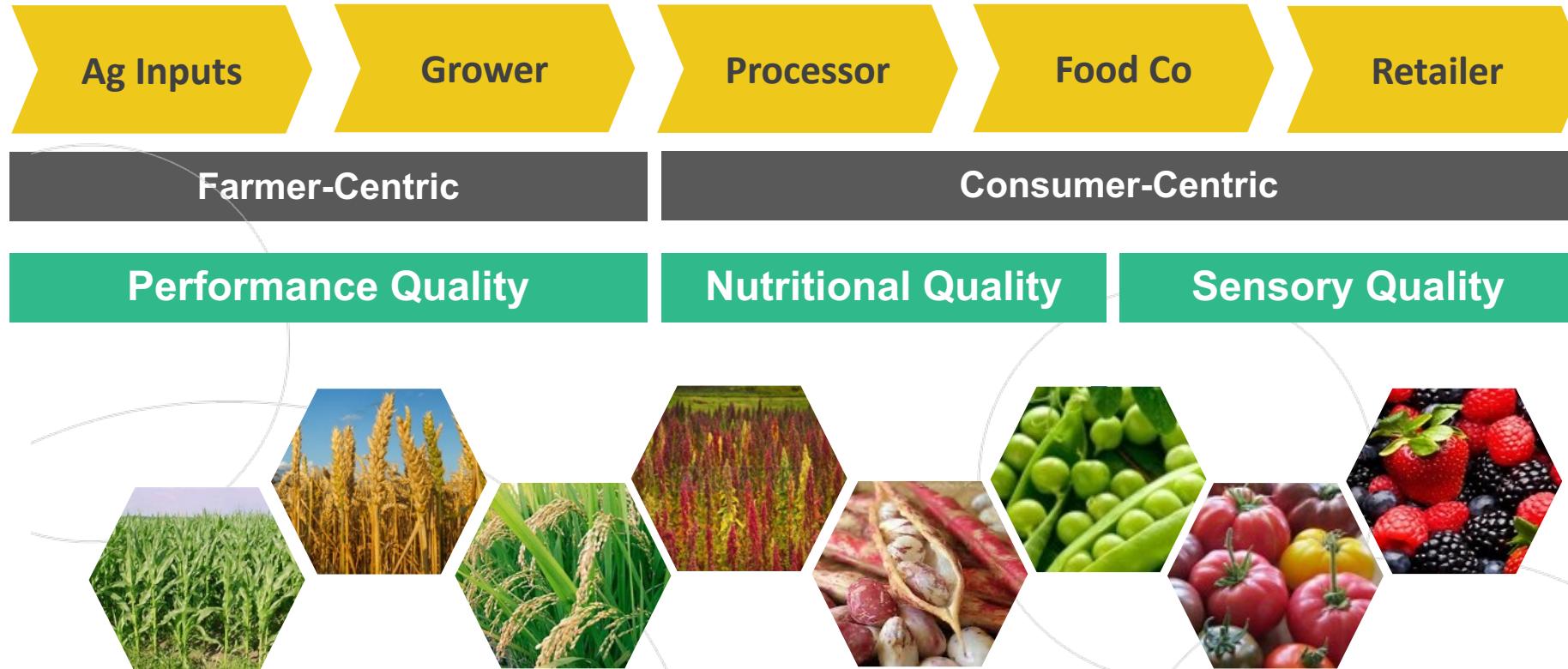


CropOS: Onboarding pipelines





BENSON•HILL
BIOSYSTEMS



Value creation opportunities across the entire food value chain

An Exciting time to be involved in Agriculture

- Agriculture is undergoing a digital revolution
- Breeding is at the core of (digital) agriculture
 - Breeding is an integrative science
- Agriculture is part of the high-tech economy

