Genotype plus Environment
Integration for a more sustainable dairy production system

Phenotypic interrelationships between parameters predominantly in milk – the GplusE project

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GplusE project

- GplusE focuses on:
  the development of sustainable dairy cow production systems through the optimal integration of genomic selection with improved management, assisted by novel approaches to gathering reliable phenotypes
- 9 WPs
- 5 years project (from 01/2014)
- 15 partners from 6 EU members states, US (Missouri) and China

Objectives & WPs

WP2
- Creation of databases to be used by the project + data harmonization

WP3
- Develop and validate new, easily-measured key-indicators. Phenotypic associations between key-indicator metabolites, enzymes, hormones, MIR-spectra and glycan profiles in milk and key traits such as e.g. physiological status, health, welfare, fertility, environmental footprint and production

WP4
- Collect key-phenotypes in a large population of dairy cows to perform genetic and genomic study (GWAS)

WP5
- Study the relationships of some molecular phenotypes for key physiological traits to genome haplotypes

WP6
- Develop management strategies at herd and cow levels for improved efficiency, environment, health and welfare

WP7
- Establish the most appropriate long term breeding strategy for the European Holstein-Friesian population

WP8
- Annotation of bovine, human, and other relevant genomes

+ WP1 (coordination) & WP9 (dissemination)

WP3 aims to identify new key-phenotypes - associations between key-indicators and key traits

- This task relies on experiments conducted at AU, AFBI, CRA, CRA-W, FBN, and UCD.
- Blood and milk phenotypes will be related to health, fertility, production, efficiency, environmental footprint, etc.
- The most relevant phenotypes will be identified as indicators of these difficult-to-record traits.

→ Which indicators/phenotypes are investigated?

- ✓ Blood plasma (e.g., glucose, BOHB, NEFA, IGF-1)
- ✓ Milk metabolites (e.g. BOHB, iso-citrate, free glucose, G6P)
- ✓ Milk enzymes(e.g., LDH)
- ✓ Milk glycan
- ✓ Mid-infrared spectra of milk → new mid-infared equations

GplusE vision

" **G**enotype **and** **E**nvironment contributing to the sustainability of dairy cow production systems through the optimal integration of genomic selection and novel management protocols based on the development and exploitation of genomic data and supporting novel phenotyping approaches "

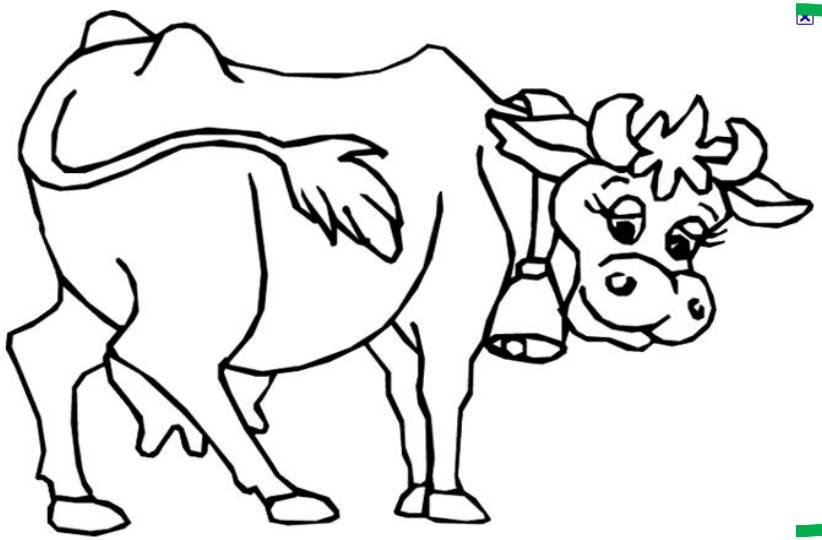
Focus on key-indikators in milk and their association to important phenotypic traits

Average herd milk yield close to 10,000 kg / cow - Consequences of a >1.5% increase in milk yield / year?

Optimal integration
Cost effective

IMPROVED input:

- Breeding
- Feeding
- Management
- Environment/ Housing

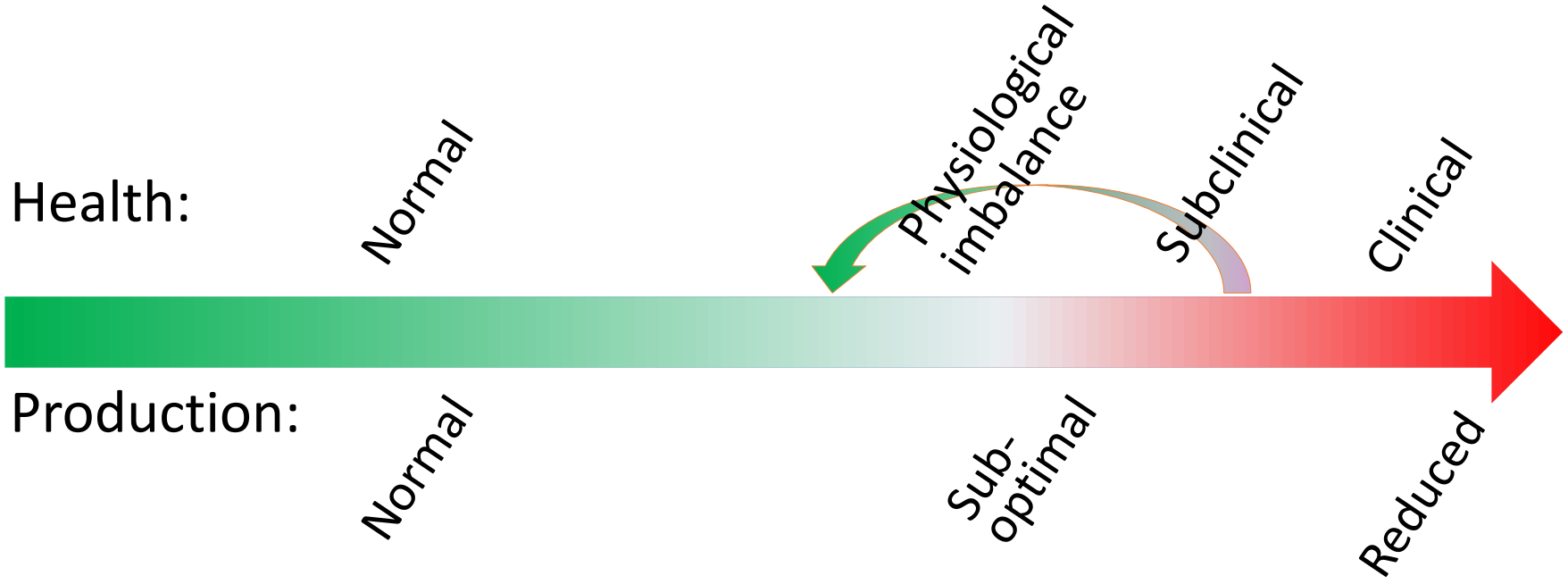


OUTPUT:

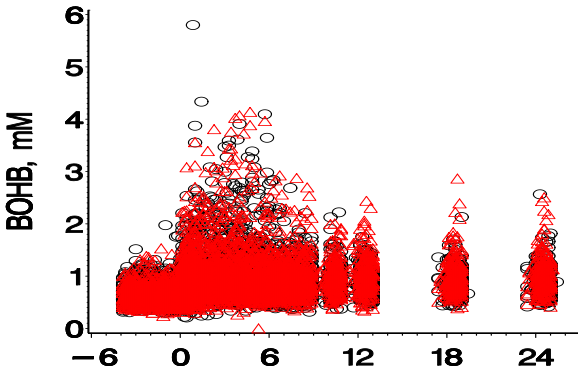
- ↑ Milk yield
- ↑ Efficiency
- -↓ Health?
- ↓ Reproduction

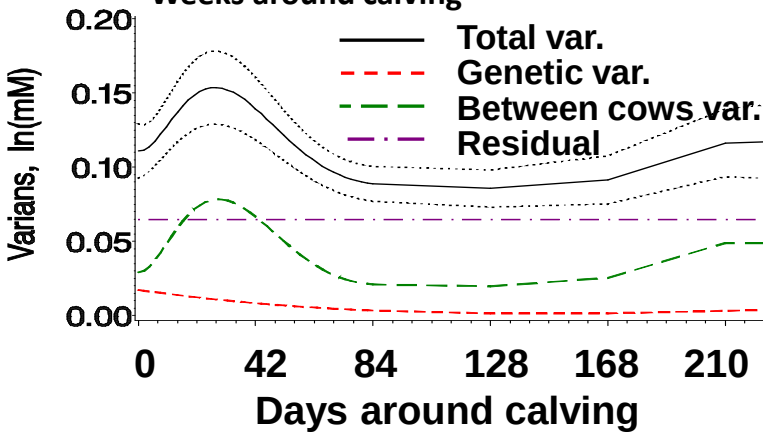
Early identification is key to reduced disease incidence and optimal production

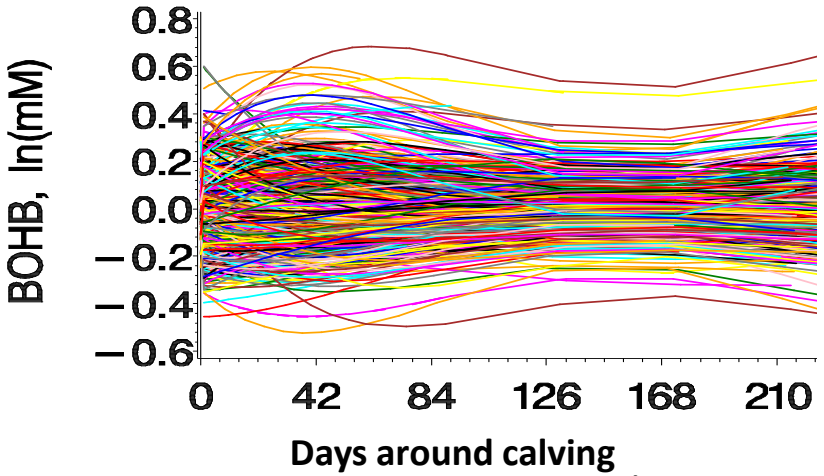
Biomarkers in relation to trait and state:



Large between cow differences

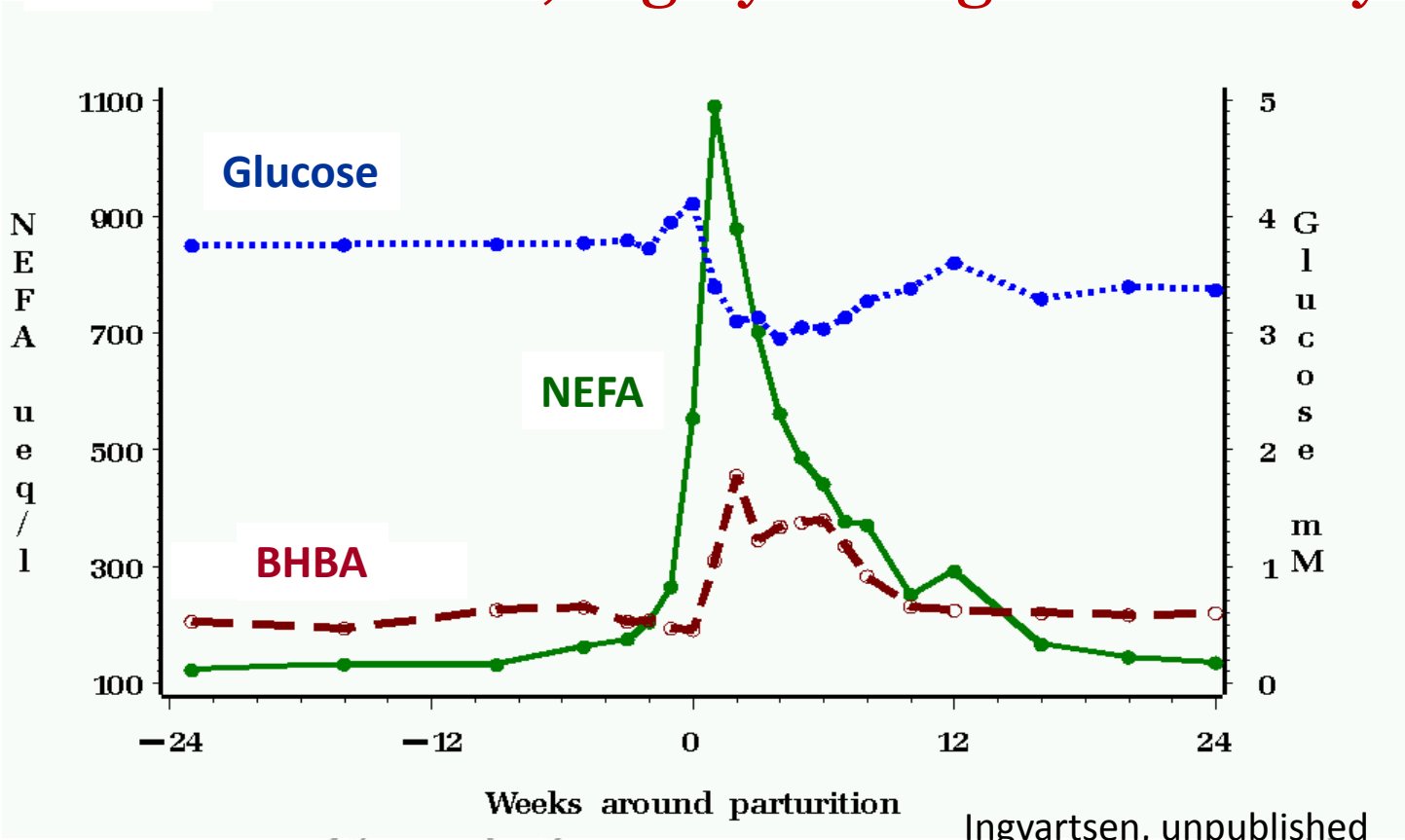






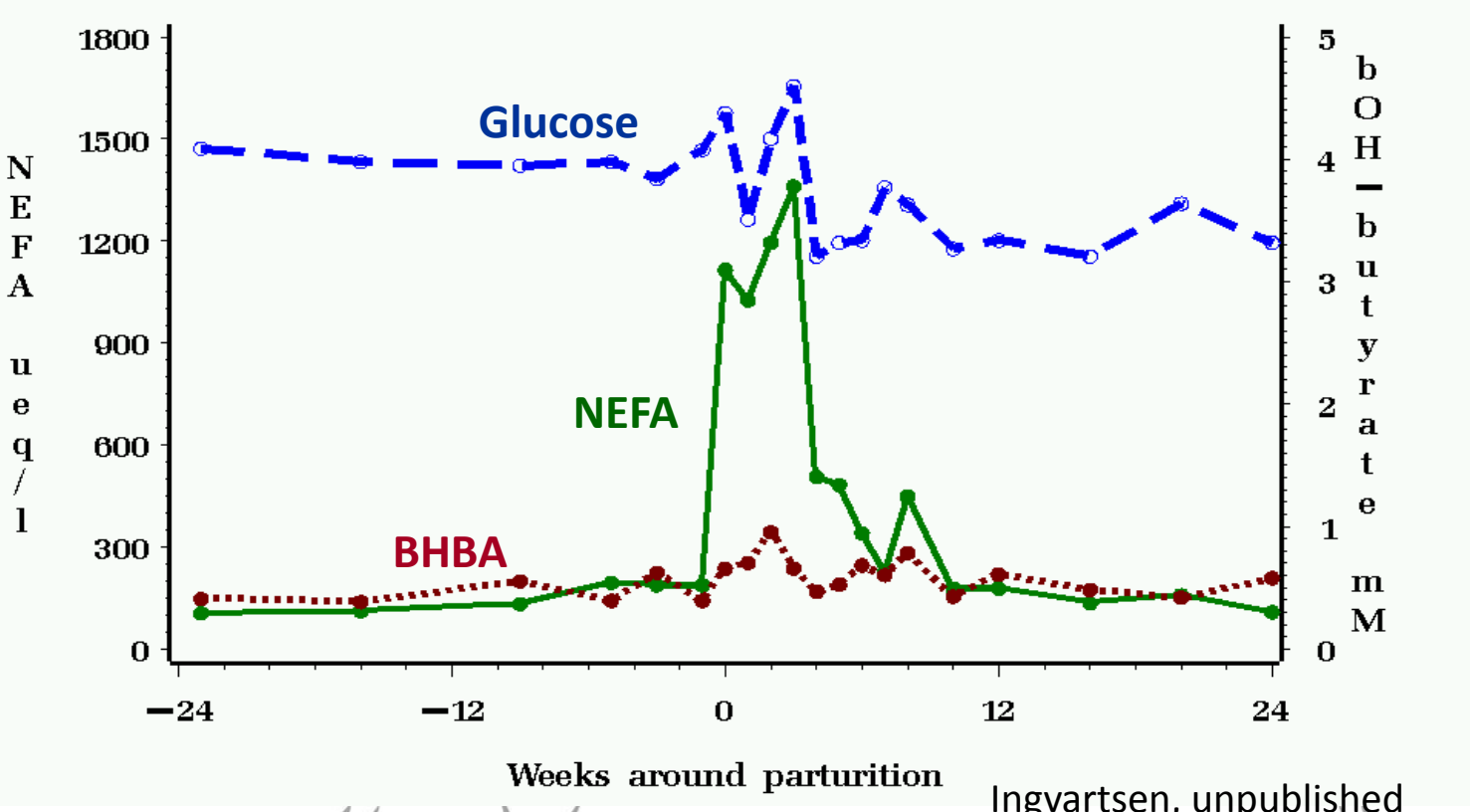
Ingvartsen and Friggens, 2005

Periparturient changes in NEFA, BHBA and glucose – the “text book cow”, high yielding and healthy



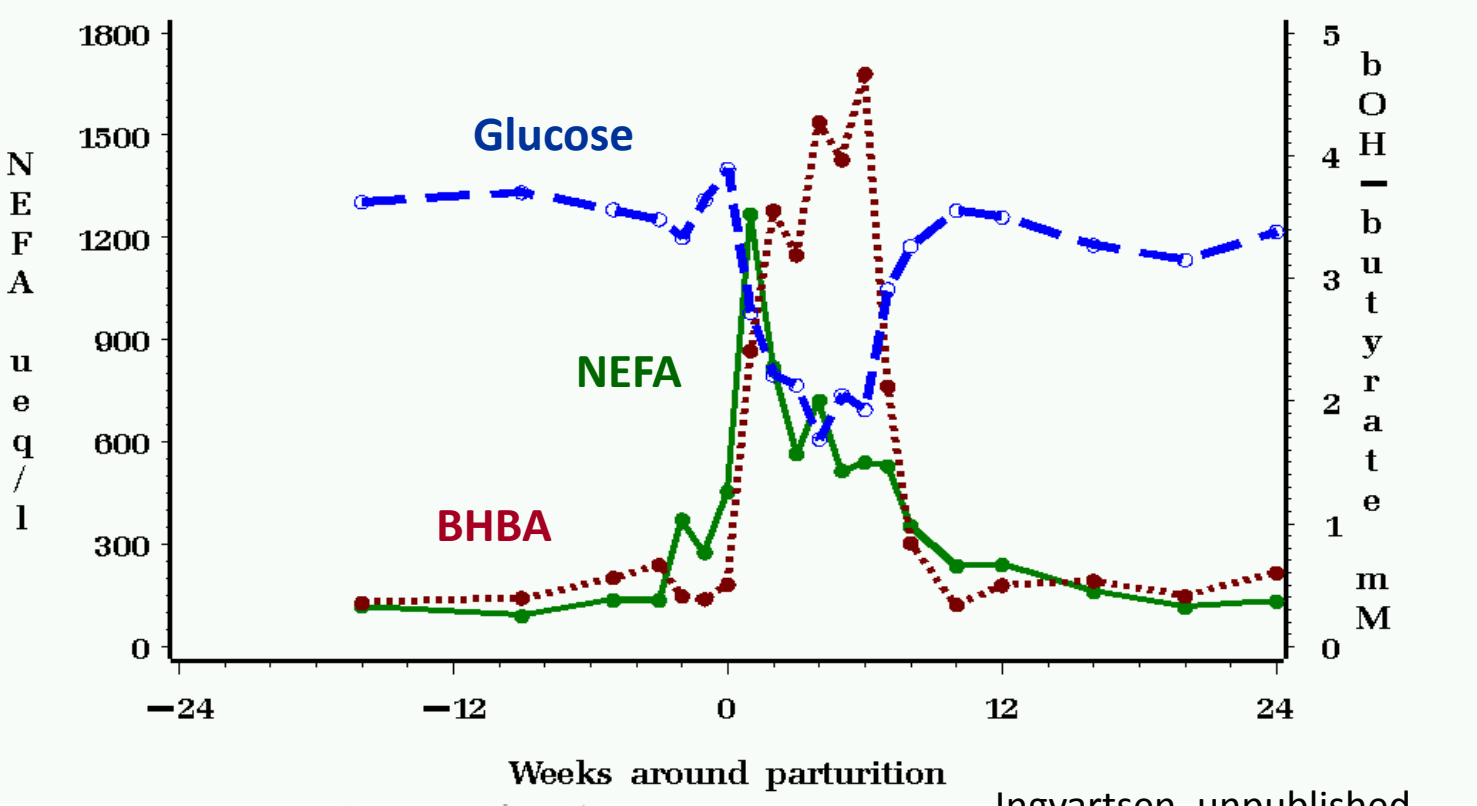
Ingvartsen, unpublished

Periparturient changes in NEFA, BHBA and glucose – the mobilizing healthy but low yielding cow



Ingvartsen, unpublished

Periparturient changes in NEFA, BHBA and glucose – the mobilizing high yielding risk cow



Ingvartsen, unpublished

Physiological Imbalance (PI)

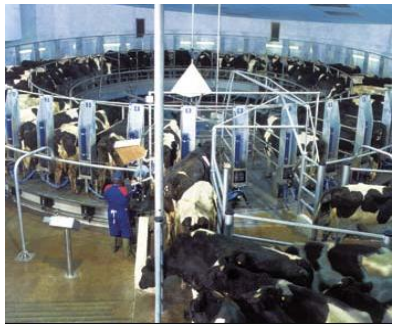
- **Hypothesis:** Immune function and health can be improved by reducing the PI in cows, and at the same time it will improve production and reproduction (Ingvartsen et al., 2003, 2006; Ingvartsen and Moyes, 2012)

- **Definition of PI:** cows whose parameters (e.g. glucose, BHBA, NEFA) deviate from the normal, and who consequently have an increased risk of developing diseases (clinical or subclinical) and reduced reproduction and/or production (Ingvartsen, 2006)

Surveillance is essential for prevention and optimization

- Manual surveillance is important – but has its limitations
- Surveillance at feeding and milking has changed





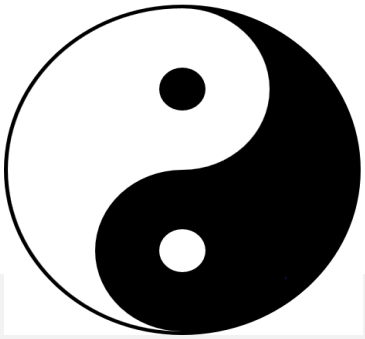

- Large herds
- Subclinical problems

New indicators needed!

Need for automated precision management systems

There is a need for **cost effective** automated precision management systems where equipment combines advanced sensors, technologies and biological knowledge to obtain:

- low disease incidence and severity,
- animal welfare,
- low impact on the environment,
- requested product quality,
- optimal production and reproduction,
- profitability for the producer.



Individual cow monitoring
cow as its own control → **optimization**

Efficient management calls for:

- Early identification of “risk cows”
- Manage animal status & risk by
- changing “input” to “risk cows”

} Proactive management

Calls for **real-time on-farm solutions** based on:

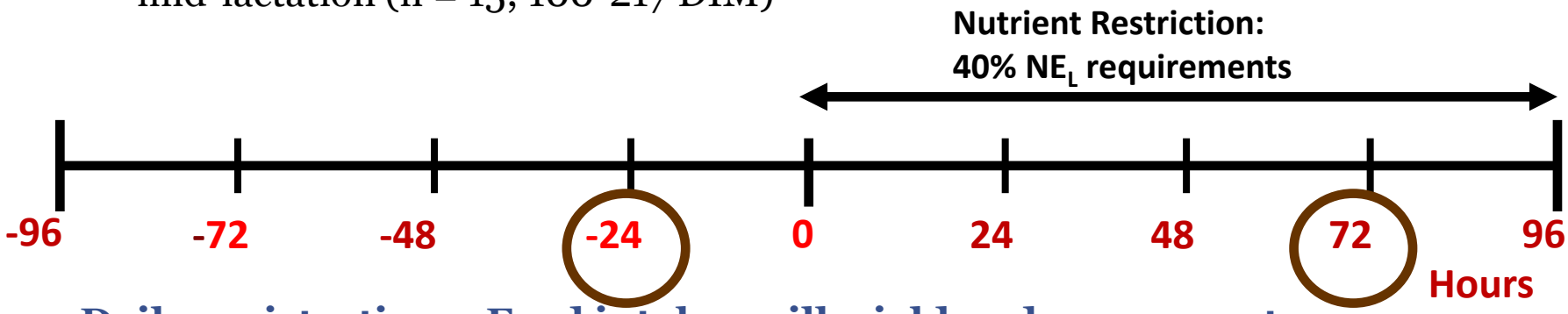
- Efficient biomarkers
- Automated sampling / analysis (sensors)
- Biological and biometric models
- Ability to describe animal status
- Methods to describe risk (e.g. for a disease)
- (Aut.) change of “input” for prevention
- Optimization at cow and herd level

	Condition Positive	Condition Negative
Test Outcome Positive	True Positive	False Positive (Type I error)
Test Outcome Negative	False Negative (Type II error)	True Negative

Cost effective

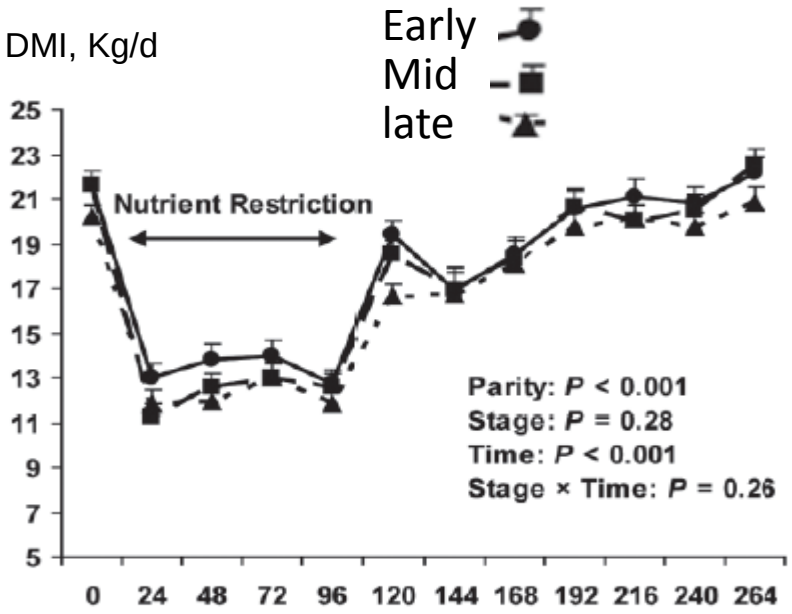
“Off feed” challenge – Cows, design, sampling

- 29 healthy Holstein cows:
  - early lactation (n = 14; 22-86 DIM)
  - mid-lactation (n = 15; 100-217 DIM)

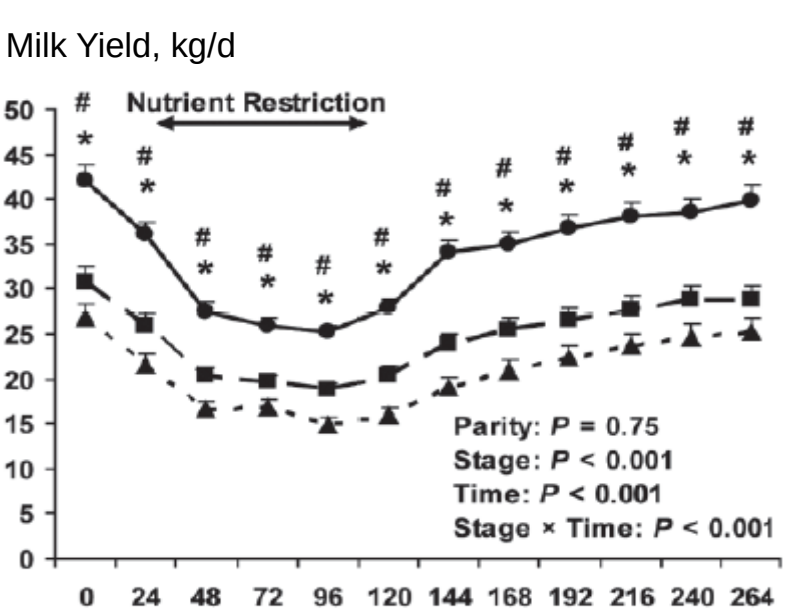


- **Daily registrations: Feed intake, milk yield and components**
- **Blood collection for analysis of NEFA, BHBA, and glucose**
- **Milk for detailed analysis**
- **Liver samples collected for:**
  - **1. Chemical analysis**
  - **2. iTRAQ-based quantitative profiling using LC-MS/MS (proteomics)**

Change in energy density caused marked changes in DMI and milk yield

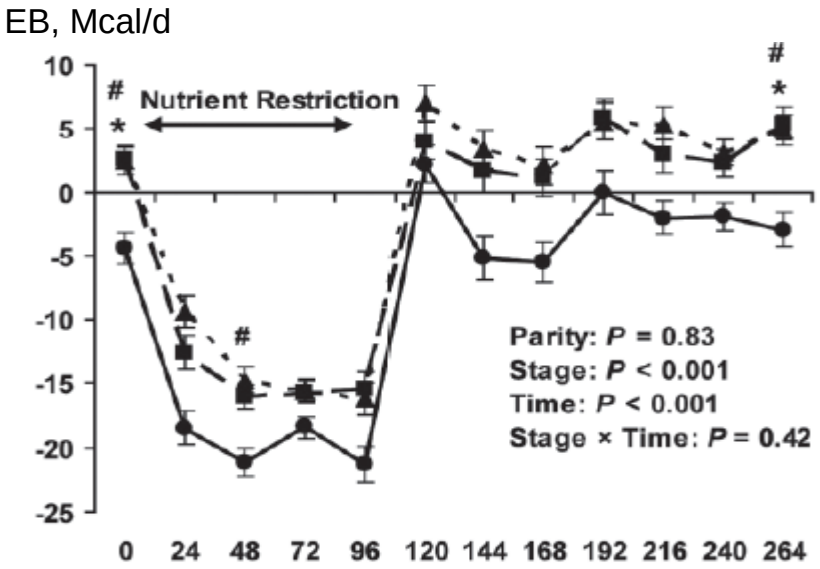


Bjerre-Hapøth et al., 2012



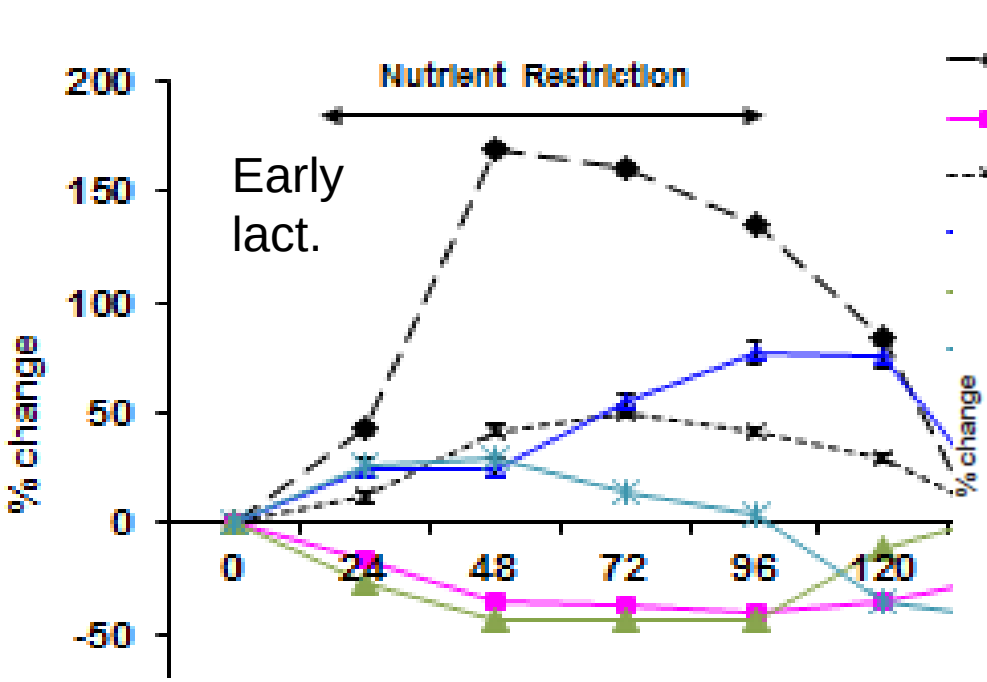
Bjerre-Hapøth et al., 2012

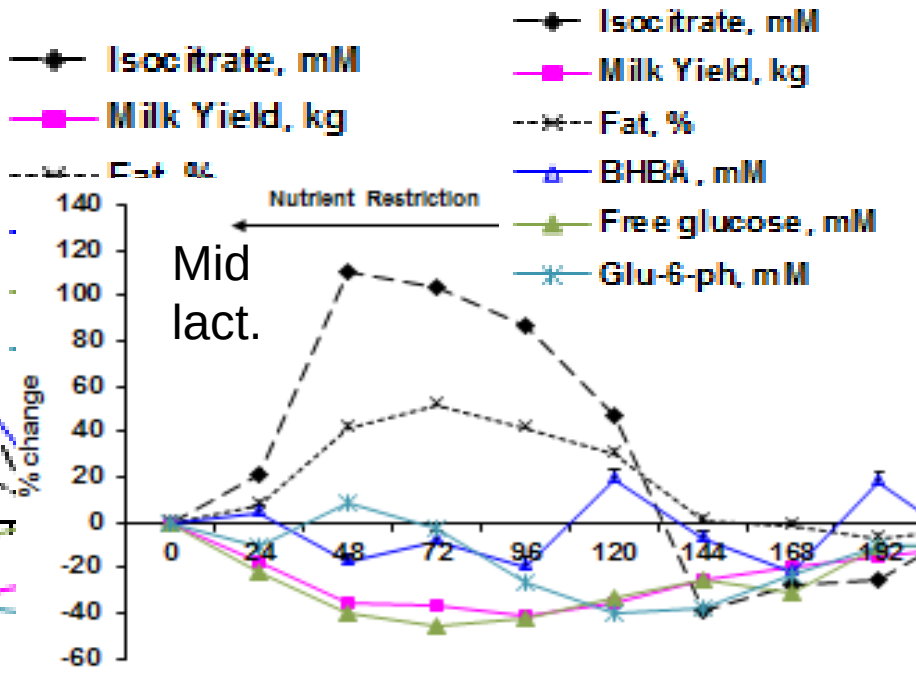
EB was reduced by reduced energy density in the TMR



Bjerre-Hapøth et al., 2012

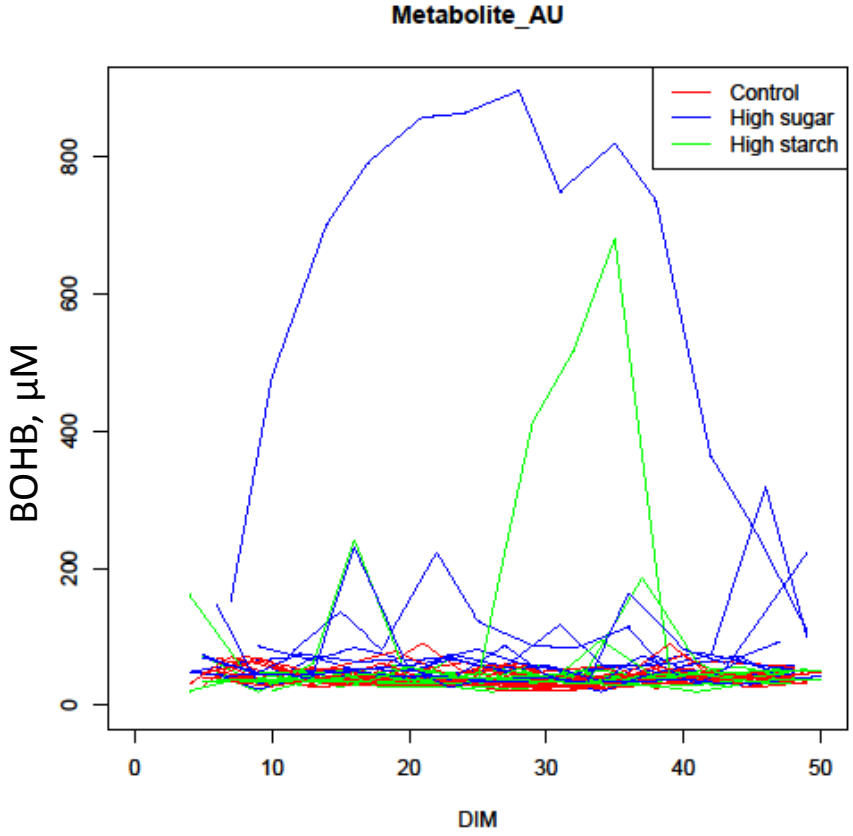
Changes in milk parameters during nutrient restriction – early and mid-lactation

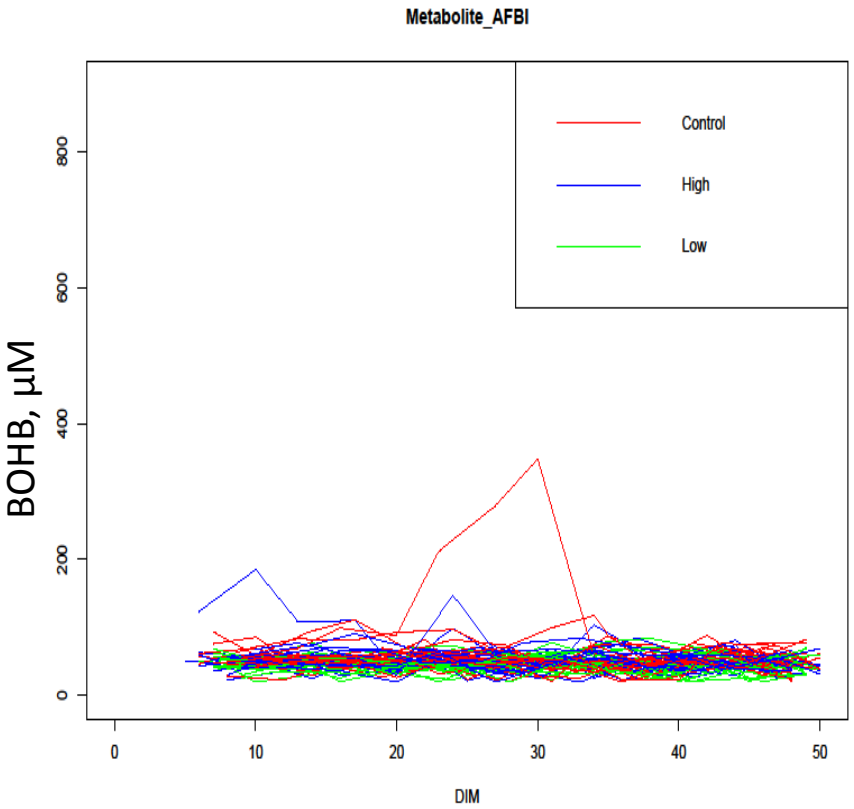




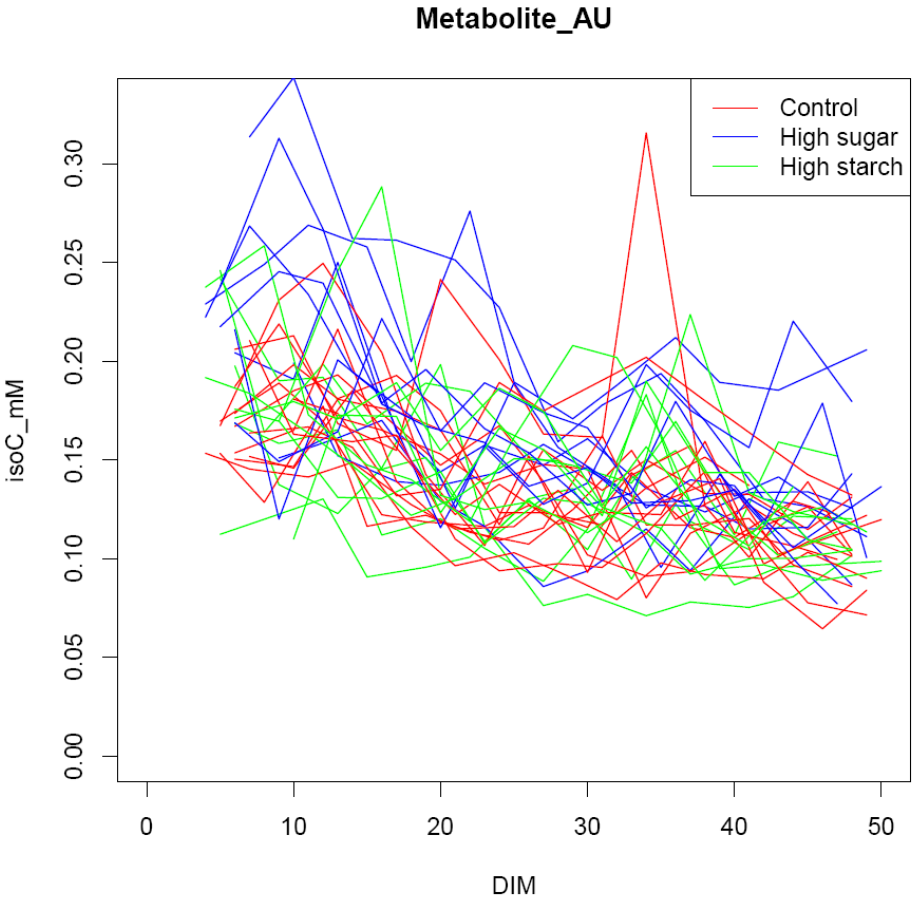
Time relative to nutrient restriction (0-96 h)

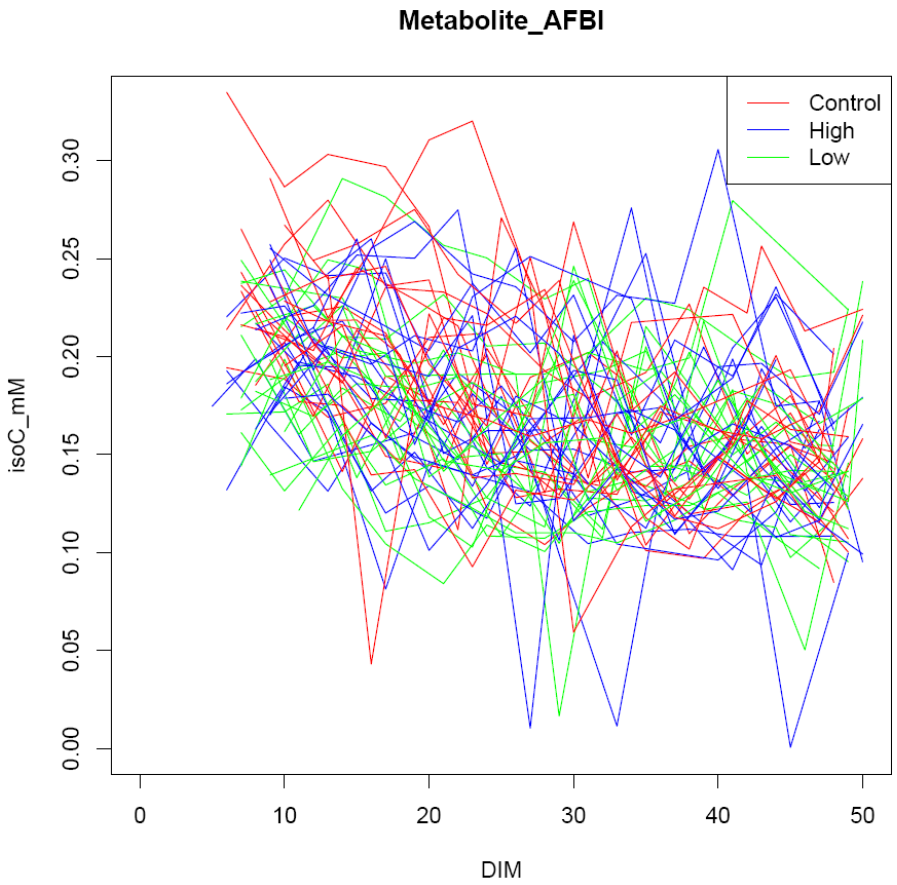
G+E results:
BOHB in milk of individual cows



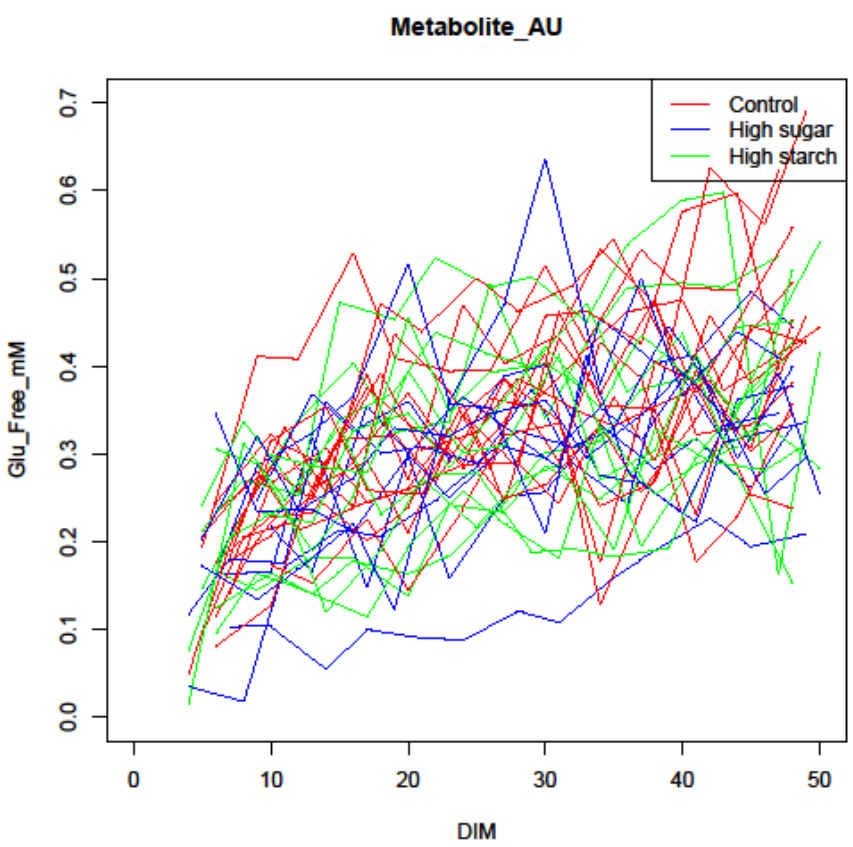


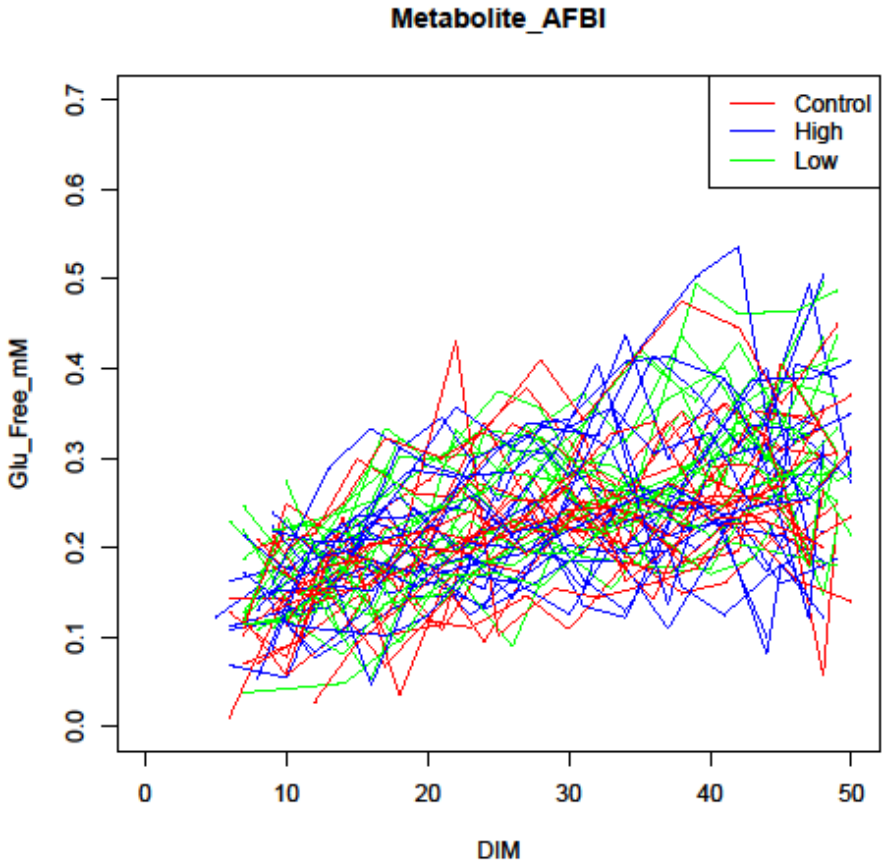
G+E results:
Iso-citrate in milk of individual cows



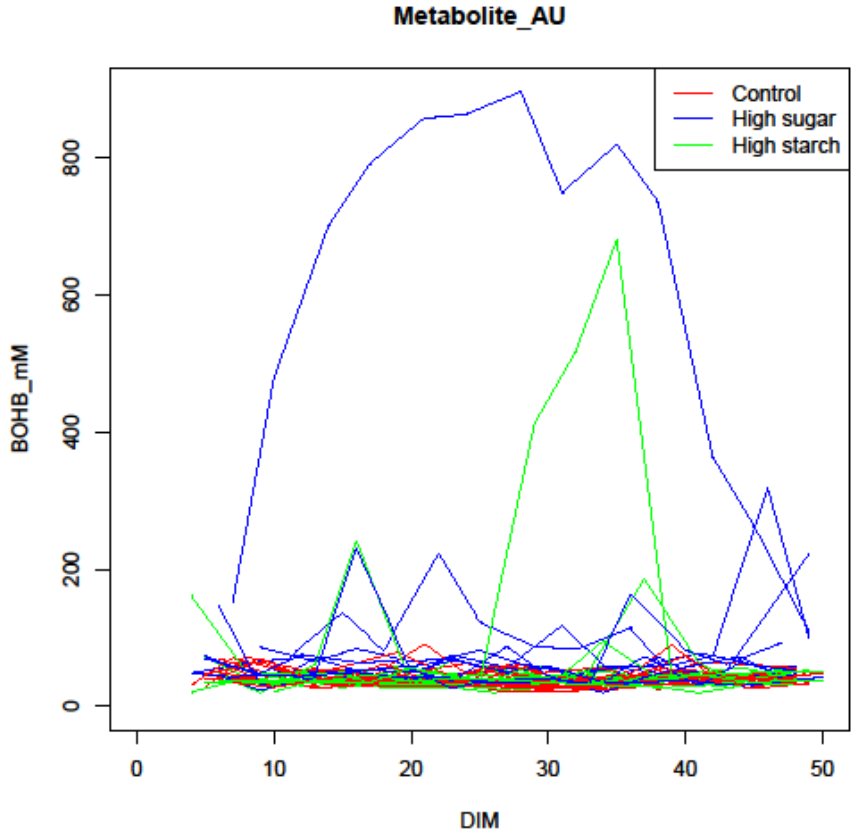


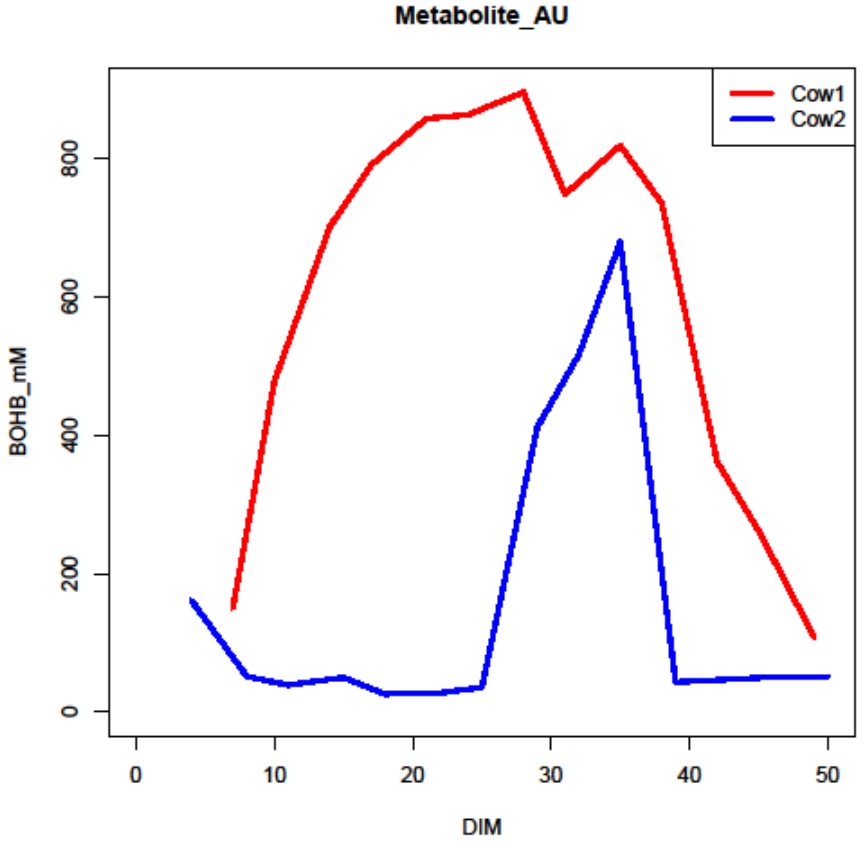
G+E results:
Free glucose in milk of individual cows





G+E results:
Two cows in physiological imbalance?





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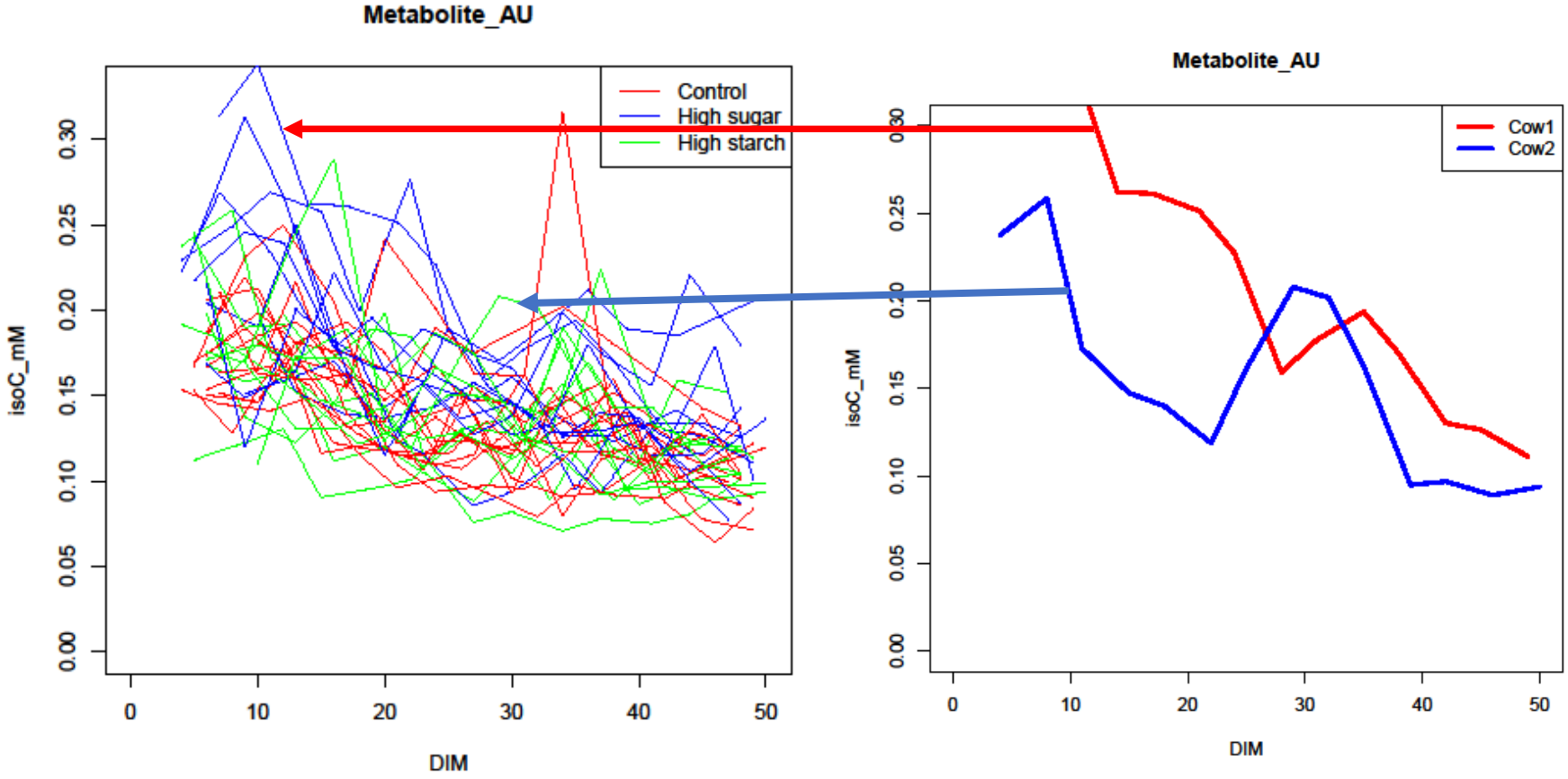

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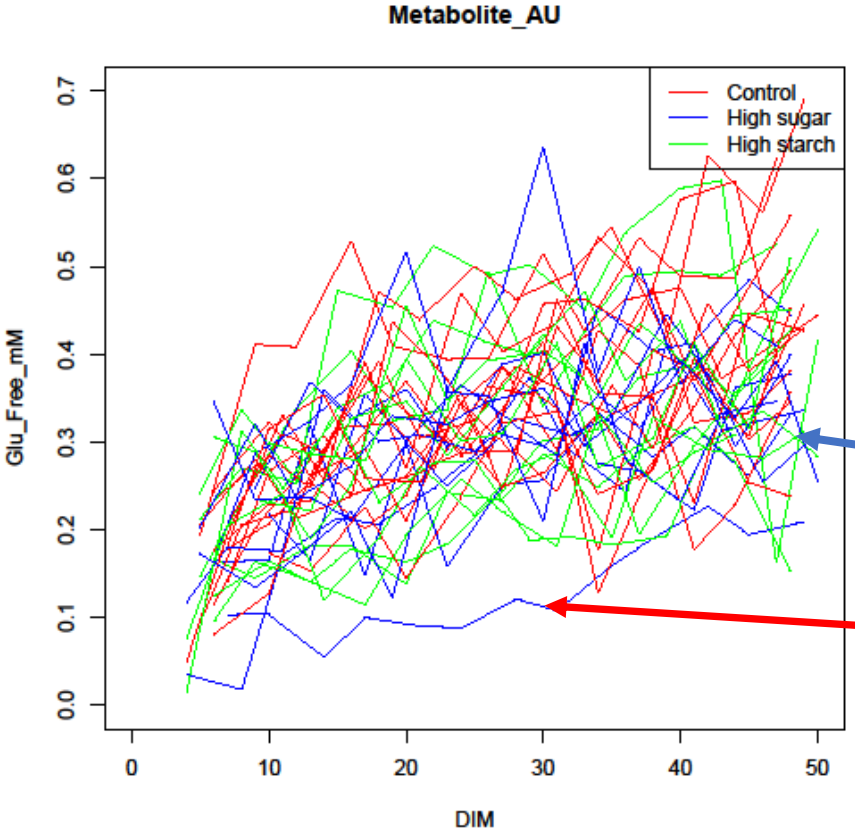

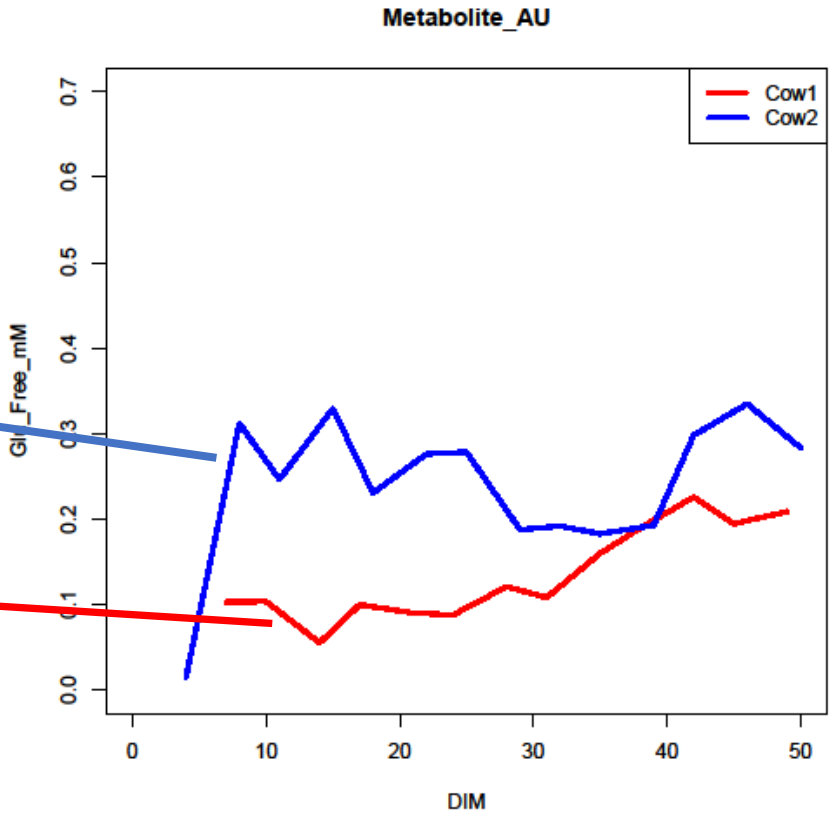

Conclusion

- To understand the biological basis of individual differences
- To improve phenotyping by:
  - Making better use of existing data
  - Developing new biomarkers for common use in management and genomic selection (e.g. physiological imbalance)
- To further develop sensors and technology for future automatic proactive management strategies
- To find “the local truth”
- To optimization at both individual cow and herd level
  - production, reproduction, risk of disease, environmental impact, animal welfare, ...

- GplusE:
  - Work in progress
  - To be continued .....

Thank you for your attention!

*" **G**enotype **and** **E**nvironment contributing to the sustainability of dairy cow production systems through the optimal integration of genomic selection and novel management protocols based on the development and exploitation of genomic data and supporting novel phenotyping approaches "*

Acknowledgments and Disclaimer

This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement n° 613689

Partners
Universities & Research Institutes

- **UCD** - University College Dublin (Ireland) - coordinator
- **RVC** - Royal Veterinary College (London, UK)
- **AFBI** - Agri-Food and Biosciences Institute (North-Ireland, UK)
- **UGent** - Universiteit Gent (Belgium)
- **AU** - Aarhus University (Denmark)
- **CRA** - Consiglio per la Ricerca e la Sperimentazione in Agricoltura, (Italy)
- **HZAU** - Huazhong Agricultural University (China)
- **MU** - University of Missouri (US)
- University of Liège (Belgium)
  - **ULg-GxABT** - Gembloux Agro-Bio Tech (Gembloux)
  - **ULg-FMV** - Faculty of Veterinary Medecine (Liège)
- **CRA-W** - Walloon Agricultural Research Center (Gembloux, Belgium)
- **FBN** - Leibniz Institute for Farm Animal Biology (Dummerstorf, Germany)

Partners
Farmers organisations

- **ICBF - Irish Cattle Breeding Federation (Ireland)**
  - SME providing information services to the Irish cattle industry with a focus on genetics and genomics
- **KCA - The Knowledge Centre for Agriculture (Denmark)**
  - Private, non-profit test and research association owned by Danish farmers, main supplier of professional knowledge in the field of agriculture

Others

- **S-EAAP - Service EAAP (Italy)**
  - SME owned by EAAP which represents the business interest of animal scientists and the livestock industry
- **Unifarm (Belgium)**
  - SME developing herd management software, e.g. Dairy Data Warehouse, an internet platform for exchange between farmers and advisors

Objectives (1)

1. To **develop and validate new, easily-measured phenotypes** that can supplement or correlate with and replace traditional phenotypes (milk yield and composition, fertility, product quality, traditional disease and fertility records) (**WP 2; WP 3**);
2. To **identify novel genomic markers**, including causative mutations, for the key phenotypic traits (productivity, efficiency, environmental footprint, health, fertility and animal welfare) that can be used for GS (**WP2; WP3; WP 4**);
3. To **generate ENCODE-like data** for the bovine as a public resource that can be used for both GS in dairy cattle and to increase understanding of genotype/phenotype associations across all species (**WP 2; WP3; WP 4; WP5; WP 8**);

Objectives (2)

4. To define the key interacting problems that contribute to management of dairy cows under different systems that will allow the **building and validation of an appropriate management blueprint** based on Hazard Analysis & Critical Control Point (HACCP) and Evolutionary Operations (EVOP) principles (**WP2; WP3; WP 6**);
5. To **develop new breeding and management strategies** that incorporates the new genomic information attaching to the common currency phenotypic data established through the project (**WP 2; WP 3; WP 7**);
6. To **disseminate the information** widely to producers, consumers and the scientific community and to use the project to train a new generation of young scientists in the specialism of bio-informatics (**All WP; WP 9**).