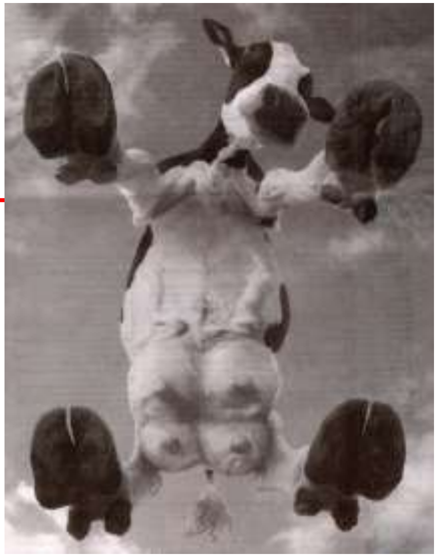
Prediction models for response patterns to negative energy balances in dairy cows using FTIR from milk testing data



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Introduction

- **Disclaimers:**
- **All opinions expressed are my own.**
- **I have no financial conflicts of interest with commercial or organizational stakeholders.**

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Introduction

- Early post partum responses to NEB
- 5 response patterns to NEB
- Need for BHBA and NEFA testing
- Prediction models for response patterns using FTIR from milk testing data
- Outlook on prediction modeling using FTIR and Machine Learning/Deep Learning

NEB ans response patterns

- NEB, metabolic challenges and
- response patterns, such as hyperketonemia,
- Negative Energy Balance early post calving
- Cows react differently to NEB with…
  - different degree of fat mobilisation
  - liver damage
  - immunosuppression
  - change in DMI
  - (late) consequences, for ex. RP, Metritis, DA’s
- Response patterns to NEB –> 5 ‘cow types’

Cow types

- 5 response patterns to NEB early post calving:

- Athlete cow
- Clever cow
- Healthy cow, but define ‘healthy’…
- Hyperketonemic cow - let’s rethink this concept.
- PMAS cow, the ‘wrong’ reaction to NEB

Cow type	bBHBA	bNEFA	FEQ
Athlete cow	↑	?	↑
Clever cow	↓	?	↓
Healthy cow	↓	↓	↑
Hyperketonemic cow	↑	?	↓
PMAS cow	↓	↑	↑

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Cow types

- **5 response patterns to NEB:**

Cow type	bBHBA	bNEFA	FEQ
Athlete cow	↑	?	↑
Clever cow	↓	?	↓
Healthy cow	↓	↓	↑
Hyperketonemic cow	↑	?	↓
PMAS cow	↓	↑	↑

Limit values:

bBHBA:
>0.8 mmol/L
(or >1.2 mmol/L)

bNEFA:
>0.7 mmol/L high risk
<0.39 mmol/L low risk

FEQ:
>1.4

Poor Metabolic Adaptation - PMAS cow:

- **Older cow, high milk production**,
- **Early lactation**>3DIM
- increased **BCS** (>3.5) during early lactation
- or extremely low BCS (<2.5)
- Increased **liver enzymes** (GLDH, billirubin)
- decreased **DMI** and **rumen filling**, fewer **rumen contractions**, reduced milk production-> **'Crash' cow**

Tremblay et al., 2018, 2019

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5 Cow types

- **Where does this come from?**

Variable	Description (units)	Mean	SD	#NA
Lactation	Lactation number	3.00	1.60	0
DIM	Days in milk	27.5	12.0	0
Milk Production	Mid-24 hr milk calculated from robot (kg)	32.0	7.1	0
Milk Fat	Fat content (%)	4.16	0.83	0
Milk Protein	Protein content (%)	3.27	0.32	0
FPR	Milk fat protein ratio	1.28	0.25	0
SCC	Somatic cell count (1000 cells/mL)	158.8	488.4	0
Urea	Urea content (mg/dL)	23.8	8.7	0
Lactose	Lactose content (%)	4.83	0.17	0
Blood Protein	(g/L)	71.2	5.1	0
Albumin	(g/L)	36.5	2.8	0
Bilirubin	(µmol/L)	1.21	1.08	0
AST	Aspartate aminotransferase (U/L)	84.2	25.1	0
GGT	Gamma-glutamyl transferase (U/L)	19.8	6.1	0
GLDH	Glutamate dehydrogenase (U/L)	12.4	11.2	0
CK	Creatine kinase (U/L)	281	452	0
BHBA	Beta-hydroxybutyric acid (mmol/L)	0.80	0.38	0
NEFA	Non-esterified fatty acids (mmol/L)	0.45	0.35	0
Cortisol	(ng/mL)	26.0	20.2	1
Rumen Contractions	Number of rumen contractions in 2 minutes	2.02	0.33	0
Rumen Fill[3]	Diagnostic rumen fill score (TR[4]: 1-5)	3.08	0.68	1
Back Fat	Back fat measured by ultrasound (mm)	12.1	3.9	15
Milk Production Reduction	Milk production reduction in one day (kg)	0.012	0.055	15
Change in Back Fat	Difference in back fat in one week (mm)	-0.63	2.37	260

Robot data

Milk test data

Blood test data

Physical exam data

+ Date
+ Farm ID
+ Cow ID
+ Breed

- Bavarian AMS farms (n=26) were enrolled for weekly visits (avg. 7 wks)
- Physical examinations of the cows (5 to 50 DIM) by veterinarians
- Blood and milk samples were collected
- 790 observations from 312 cows (309 Simmental)

FSM-Irmi Project
Tremblay et al 2018, 2019

5 Cow types

- **5 response patterns to NEB:**

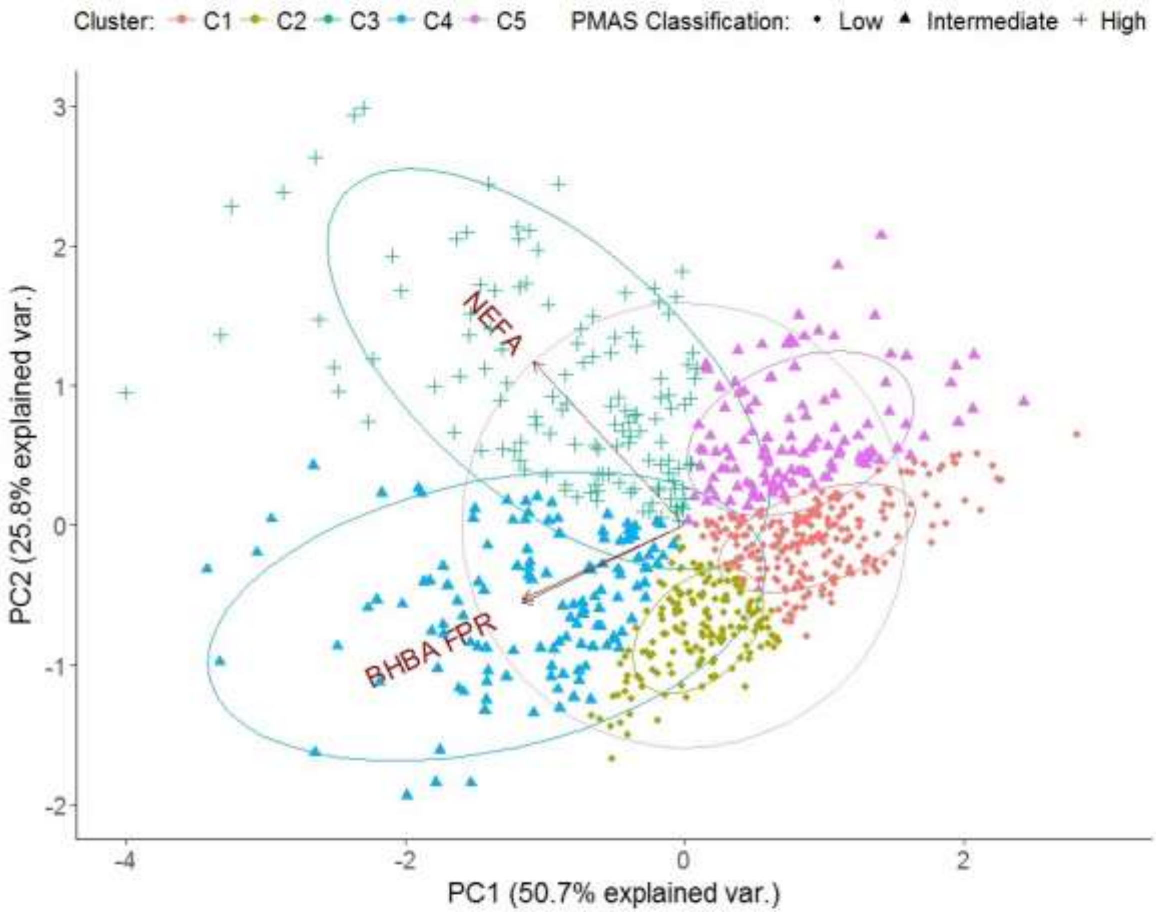
RESULTS

NEFA's direction of influence is what separated out the three PMAS classifications in our dataset

- Low PMAS= NEFA values **< 0.39** [95% CI: 0.360 - 0.410] mmol/L

Intermediate risk for PMAS

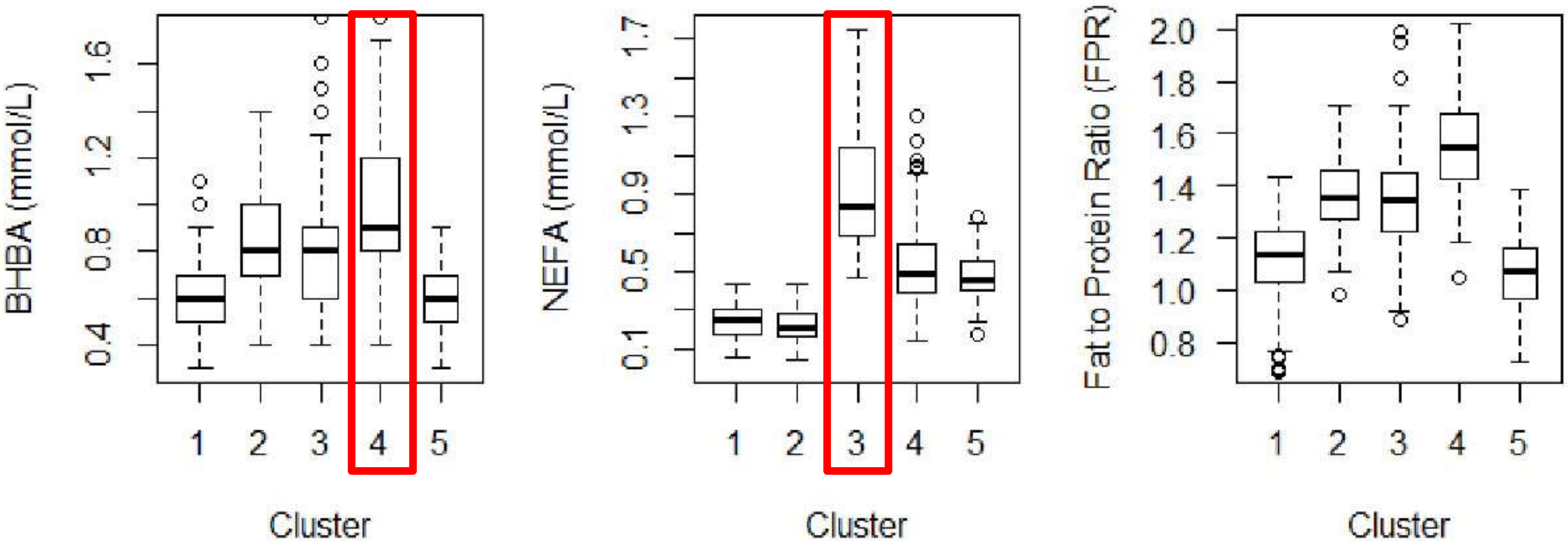
- High PMAS= NEFA values ≥ **0.7** [95% CI: 0.650 - 0.775] mmol/L



FSM-Irmi Project Tremblay et al 2018, 2019

Cow Types

- **5 response patterns to NEB:**



Cluster 4: Athlete cow
High bBHBA, healthy,
High milk fat

Cluster 3: PMAS cow
High bNEFA, older cows,
early DIM,
reduced milk production

Cluster 5: Clever cow
Reduced milk fat,
Healthy

Healthy cow
Hyperketonemic cow: high bBHBA, not doing well

FSM-Irmi Project
Tremblay et al 2018, 2019

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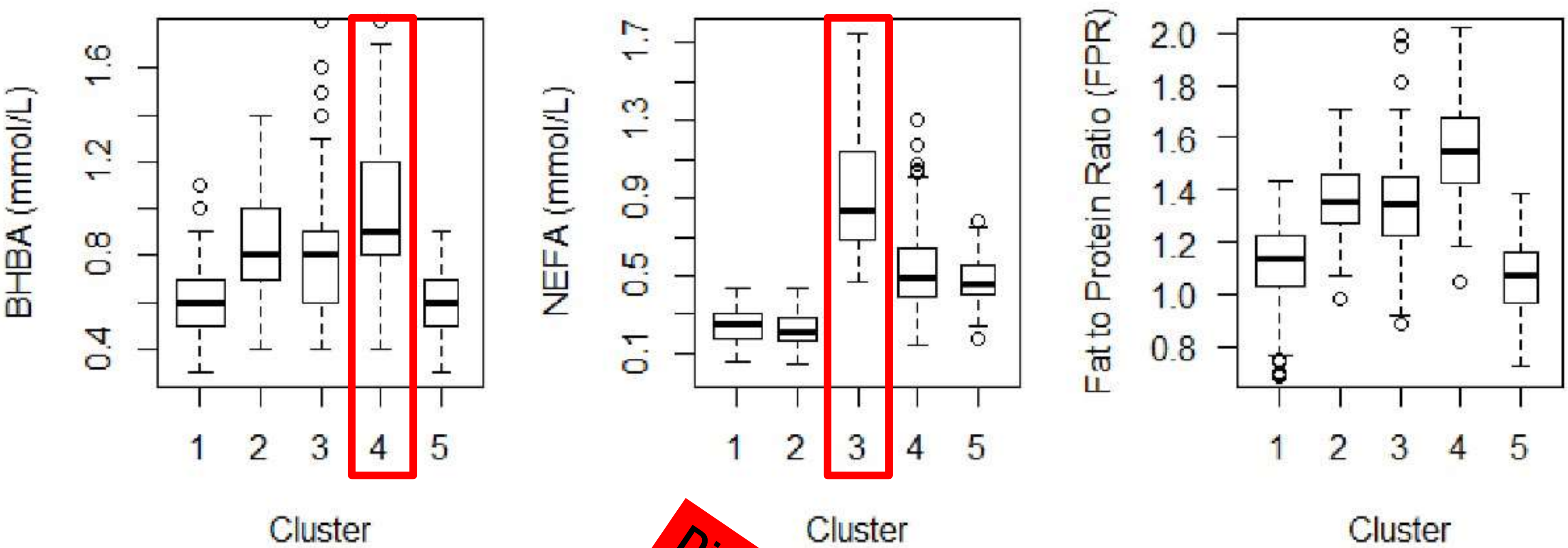
Cow Types

- **5 response patterns to NEB:**



Cluster 4: Athlete cow
High bBHBA, healthy
High milk fat

Different response to NEB

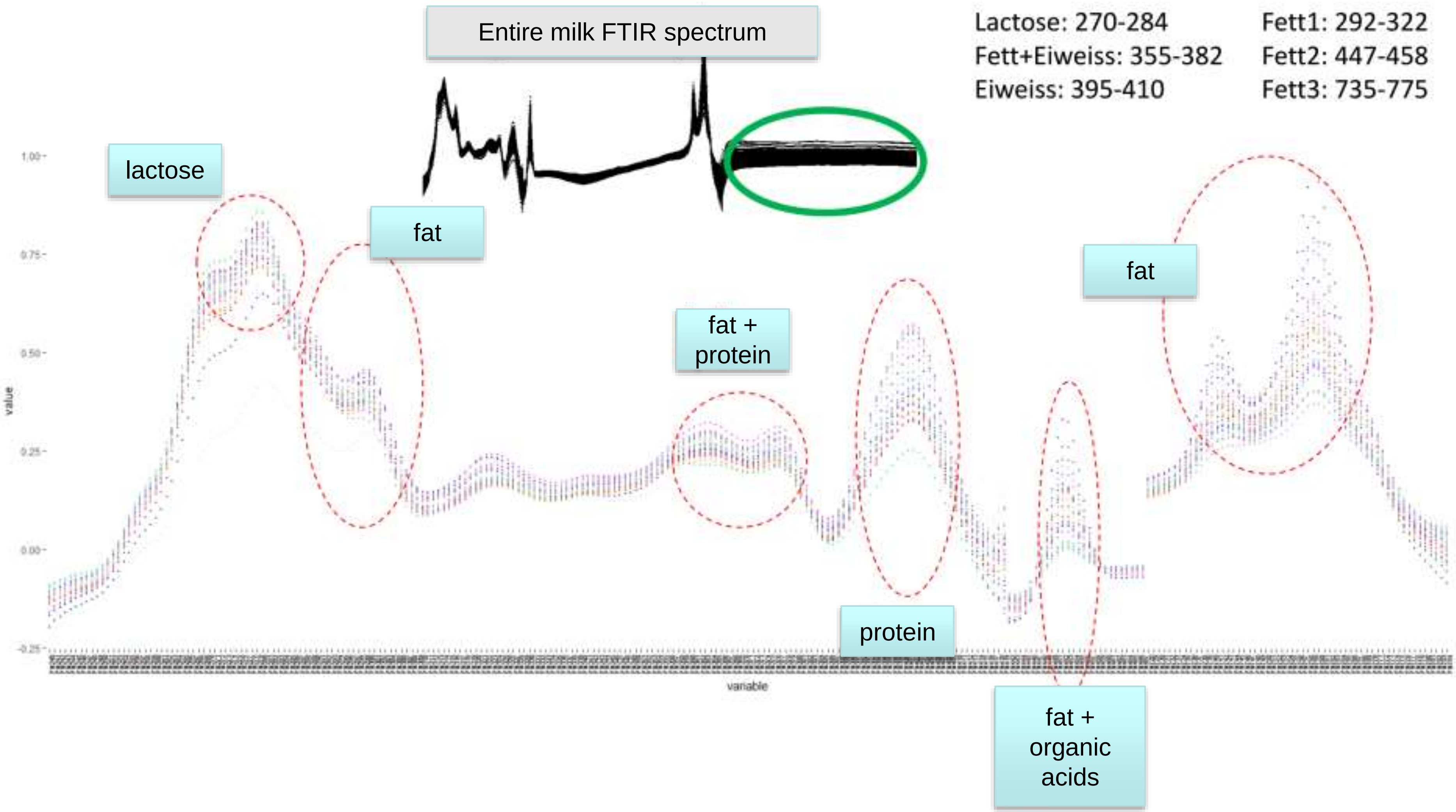
3: PMAS cow
Hi older cows,
early D
reduced m uction

Cluster 5: Clever cow
Reduced milk fat,
healthy

Healthy cow
Hyperketonemic cow: high bBHBA not doing well

FSM-Irmi Project
Tremblay et al 2018, 2019

FTIR spectral data to predict bBHB, bNEFA



Prediction models in literature…

Development and analytical validation of a screening method for simultaneous detection of five adulterants in raw milk using mid-infrared spectroscopy and PLS-DA

Bruno G. Botelho[a], Nádia Reis[b], Leandro S. Oliveira[b], Marcelo M. Sena[a,c,*]

- 1[st] derivative

Potential use of milk mid-infrared spectra to predict individual methane emission of dairy cows

F. Dehareng[1*†], C. Delfosse[1*], E. Froidmont[2], H. Soyeurt[3,4], C. Martin[5], N. Gengler[3,4], A. Vanlierde[1] and P. Dardenne[1]

- None

Determination of Protein Concentration in Raw Milk by Mid-Infrared Fourier Transform Infrared/Attenuated Total Reflectance Spectroscopy

Y. Etzion,[1] R. Linker,[2] U. Cogan,[3] and I. Shmulevich[2]

[1]The Interdisciplinary Program of Biotechnology,
[2]Department of Civil and Environmental Engineering,
[3]Department of Biotechnology and Food Engineering,
Technion–Israel Institute of Technology, Haifa, Israel

- Principal component analysis(PCA)
- Neural network model

An attempt at predicting blood β-hydroxybutyrate from Fourier-transform mid-infrared spectra of milk using multivariate mixed models in Polish dairy cattle

T. K. Belay,*[1] B. S. Dagnachew,* Z. M. Kowalski,† and T. Ådnøy*

- 2[nd] derivatives
- **PLS regression**
- Signal correction (**EMSC**)

Use of milk fatty acids to estimate plasma nonesterified fatty acid concentrations as an indicator of animal energy balance

J. R. R. Dórea, E. A. French, and L. E. Armentano[1]
Department of Dairy Science, University of Wisconsin, Madison 53706

GLM,
external validation
2017

Mid-Infrared Spectroscopic Analysis of Raw Milk to Predict the Blood Plasma Non-Esterified Fatty Acid Concentration in Dairy Cows

Ben Aernouts,*†‡ Ines Adriaens,*† José Diaz-Olivares,*† Wouter Saeys,† Päivi Mäntysaari,§ Tuomo Kokkonen,# Terhi Mehtiö,§ Sari Kajava,… Paula Lidauer,§ Martin H. Lid… Pastell‡

PLS,
external validation
2019

Predicting blood β-hydroxybutyrate using milk Fourier transform infrared spectrum, milk composition, and producer-reported variables with multiple linear regression, partial least squares regression, and artificial neural network

R. S. Pralle, K. W. Weigel, and H. M. White[1]
Department of Dairy Science, University of Wisconsin, Madison 53706

PLS, ANN,
with and w/o cow data
external validation
2020

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Modeling choices matter…

Examples for decision criteria:

- Feature extraction : PCA, subset
- Observation selection : Case/control
- Missing data : Impute or not
- Transformations : Scale and center

Pre-processing

- Model algorithms : GLM, LDA, SVM…

Algorithm

<u>Full</u> Model Selection (FMS)

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8 steps for modeling choices:
Tremblay et al 2018, 2019

For example: QCheck data

- n=9960, 2641 cows, 5-50 DIM, HF and FV
- Gruber et al. 2021, Milk Science International, accepted for publication

- QCheck prediction model for hi/lo bBHB
- and bNEFA uses
- Milk testing data

- Cow data (DIM, lactation number, milk production)

- IR spectral data from 1 instrument

- Gruber et al., accepted for publication
- JF Mandujano-Reyes 2020, under review, numeric predictions

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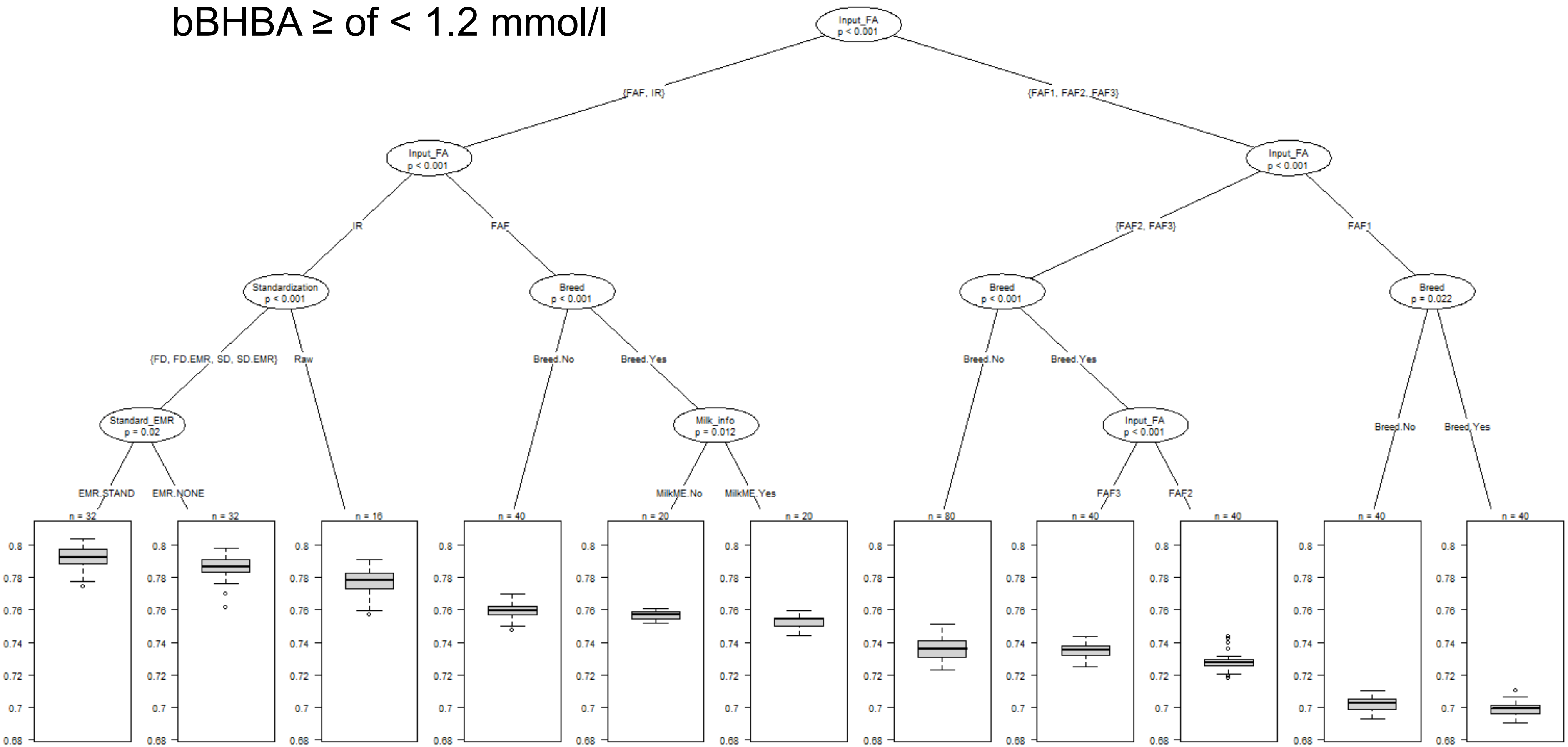
QCHECK

QCheck

- **regression tree Full Model Selection… rtFMS**
- **based on Tremblay et al 2019, ElasticNet algorithm**

bBHBA ≥ of < 1.2 mmol/l



results – Q-Check to detect hi/lo bBHBA

- **rtFMS: bBHBA regression tree**
- **…Machine Learning GLMNET,**
- **96 model variants, n=9960, 2641 cows, HF and FV**

FAF

FAF	est	lower	upper
aprev	0.179	0.177	0.182
tprev	0.063	0.061	0.064
se	0.667	0.655	0.678
sp	0.853	0.851	0.855
diag.acc	0.841	0.839	0.844
bal.acc	0.760	0.753	0.767
diag.or	11.607	10.969	12.283
nnd	0.007	0.007	0.007
youden	0.520	0.505	0.534
ppv	0.232	0.226	0.239
npv	0.975	0.973	0.976
plr	4.537	4.430	4.646
nlr	0.391	0.377	0.405
BHBA_FAF_Raw_EMR.NONE_Cow.Yes_Breed.No_MilkME.No_AllWN_incl.HighCorr_noFeatExt_SMOTE200_pp.cs_GLMNET_9660_18			

FAF1

FAF1	est	lower	upper
aprev	0.238	0.235	0.240
tprev	0.063	0.061	0.064
se	0.606	0.594	0.619
sp	0.787	0.784	0.790
diag.acc	0.776	0.773	0.778
bal.acc	0.697	0.689	0.704
diag.or	5.691	5.392	6.007
nnd	0.007	0.007	0.007
youden	0.393	0.378	0.408
ppv	0.160	0.155	0.164
npv	0.968	0.966	0.969
plr	2.846	2.779	2.915
nlr	0.500	0.485	0.516
BHBA_FAF1_Raw_EMR.NONE_Cow.Yes_Breed.No_MilkME.No_AllWN_incl.HighCorr_noFeatExt_SMOTE200_pp.cs_GLMNET_9660_8			

FAF2

FAF2	est	lower	upper
aprev	0.253	0.250	0.255
tprev	0.062	0.061	0.064
se	0.710	0.699	0.722
sp	0.778	0.775	0.781
diag.acc	0.774	0.771	0.776
bal.acc	0.744	0.737	0.751
diag.or	8.584	8.097	9.101
nnd	0.007	0.007	0.007
youden	0.488	0.474	0.502
ppv	0.176	0.171	0.181
npv	0.976	0.975	0.977
plr	3.197	3.132	3.263
nlr	0.372	0.358	0.388
BHBA_FAF2_Raw_EMR.NONE_Cow.Yes_Breed.No_MilkME.Yes_AllWN_incl.HighCorr_noFeatExt_SMOTE200_pp.cs_GLMNET_9442_12			

FAF3

FAF3	est	lower	upper
aprev	0.200	0.197	0.203
tprev	0.062	0.061	0.064
se	0.637	0.624	0.649
sp	0.829	0.827	0.832
diag.acc	0.817	0.815	0.820
bal.acc	0.733	0.725	0.740
diag.or	8.498	8.037	8.987
nnd	0.007	0.007	0.007
youden	0.466	0.451	0.480
ppv	0.199	0.193	0.205
npv	0.972	0.970	0.973
plr	3.725	3.636	3.816
nlr	0.438	0.424	0.453
BHBA_FAF3_Raw_EMR.NONE_Cow.Yes_Breed.Yes_MilkME.Yes_AllWN_incl.HighCorr_noFeatExt_SMOTE200_pp.cs_GLMNET_9442_9			

IR

IR	est	lower	upper
aprev	0.191	0.188	0.193
tprev	0.063	0.061	0.064
se	0.739	0.727	0.750
sp	0.846	0.844	0.848
diag.acc	0.839	0.837	0.842
bal.acc	0.792	0.785	0.799
diag.or	15.525	14.618	16.487
nnd	0.006	0.006	0.006
youden	0.585	0.571	0.598
ppv	0.242	0.236	0.249
npv	0.980	0.979	0.981
plr	4.797	4.695	4.901
nlr	0.309	0.296	0.322
BHBA_IR_FD.EMR_EMR.NONE_Cow.Yes_Breed.No_MilkME.No_EMR212_incl.HighCorr_noFeatExt_SMOTE200_pp.cs_GLMNET_9660_216			

IR.EMR standardized

IR_STAND	est	lower	upper
aprev	0.190	0.188	0.193
tprev	0.063	0.061	0.064
se	0.752	0.741	0.763
sp	0.847	0.845	0.850
diag.acc	0.841	0.839	0.844
bal.acc	0.800	0.793	0.806
diag.or	16.872	15.871	17.936
nnd	0.006	0.006	0.006
youden	0.600	0.586	0.613
ppv	0.247	0.241	0.254
npv	0.981	0.980	0.982
plr	4.931	4.828	5.036
nlr	0.292	0.280	0.305
BHBA_IR_FD.EMR_EMR.STAND_Cow.Yes_Breed.No_MilkME.No_EMR212_incl.HighCorr_noFeatExt_SMOTE200_pp.cs_GLMNET_9660_216			

FAF*: fatty acid packages by FOSS, DK
EMR: FTIR standardization by Grelet et al., 2015, 2016

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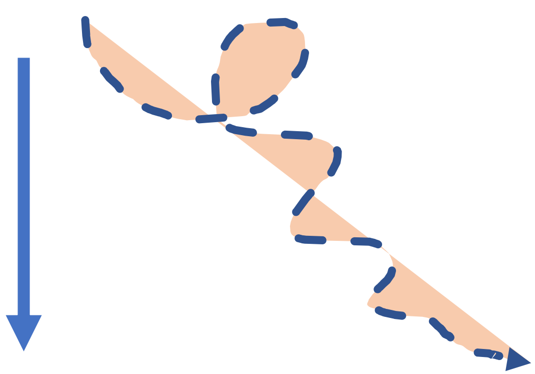
rtFMS: s Tremblay et al 2019
QCheck project: Gruber et al., 2021, accepted for publication
QCheck model: JF Mandujano Reyes et al., under revision

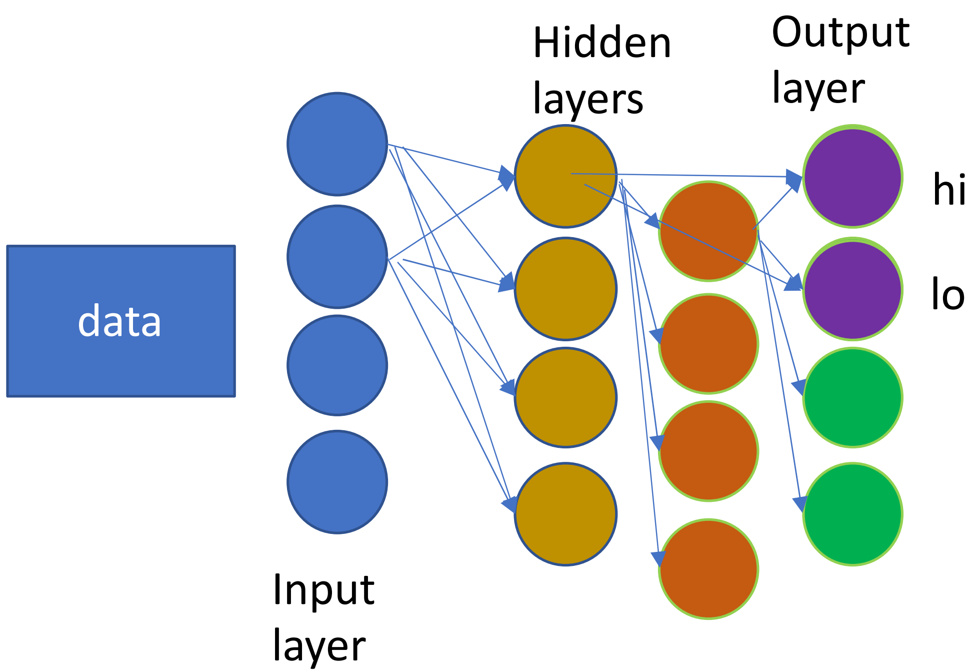
QCHECK

Machine Learning, Deep Learning

- **How does is work?**
- **What does a Neural Network look like?**
- **Data for Input layer**
- **Hidden layers in**
- **densely connected convoluted neural networks (DNN)**
- **Output layer**



‘gradient descent’
see F. Chollet 2020



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Aim: predict bBHBA hi/lo using FTIR only…

a classification model and different algorithms

212 wave numbers, 2^{nd} derivative

Qcheck Cross-validated prediction results (cv =10), n=9660							
BHB (1.2)	AUC	Accuracy	Balanced Accuracy	Sensitivity	Specificity	PPV	NPV
LDA	0.861 ± 0.073	0.793 ± 0.088	0.768 ± 0.074	0.743 ± 0.192	0.793 ± 0.104	0.236 ± 0.112	0.976 ± 0.021
ANN	0.830 ± 0.095	0.825 ± 0.074	0.745 ± 0.084	0.647 ± 0.195	0.842 ± 0.085	0.261 ± 0.122	0.963 ± 0.035
DNN	0.827 ± 0.106	0.833 ± 0.078	0.742 ± 0.102	0.635 ± 0.224	0.848 ± 0.085	0.260 ± 0.107	0.963 ± 0.035
XGBoost	0.802	0.861	0.802 ± 0.031	0.733	0.872	0.3323	0.974

Very similar prediction performances

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Aim: predict bBHBA hi/lo using FTIR only… a classification model

- What is next?

- Stack different data sets
- Optimize prediction models
- Robustness check; external validation

- Compare EMR standardized FTIR models to non-standardized data used for prediction models

- Ensemble models

Prediction models in literature…

Development and analytical validation of a screening method for simultaneous detection of five adulterants in raw milk using mid-infrared spectroscopy and PLS-DA

Bruno G. Botelho, Nádia Reis, Leandro S. Oliveira, Marcelo M. Sena

- 1st derivative

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[1]The Interdisciplinary Program of Biotechnology,
[2]Department of Civil and Environmental Engineering,
[3]Department of Biotechnology and Food Engineering,
Technion–Israel Institute of Technology, Haifa, Israel

- Principal component analysis(**PCA**)
- Neural network model

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T. K. Belay, B. S. Dagnachew, Z. M. Kowalski, and T. Ådnøy

- **2nd derivatives**
- **PLS regression**
- Signal correction (**EMSC**)

PLS,
external validation
2019

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R. S. Pralle, K. W. Weigel, and H. M. White[1]
Department of Dairy Science, University of Wisconsin, Madison 53706

PLS, ANN,
with and w/o cow data
external validation
2020

Conclusions

- 5 cow types in response to NEB
- Opportunities for cow- and herd-level management
- Need for bBHB and bNEFA testing

- FTIR prediction models are useful
- Modeling choices matter
- Need for uncertainty measures for performance
- Need for prediction modeling standards and comparisons
- Need for external validation of prediction models
- Re-visit the choice of performance parameters

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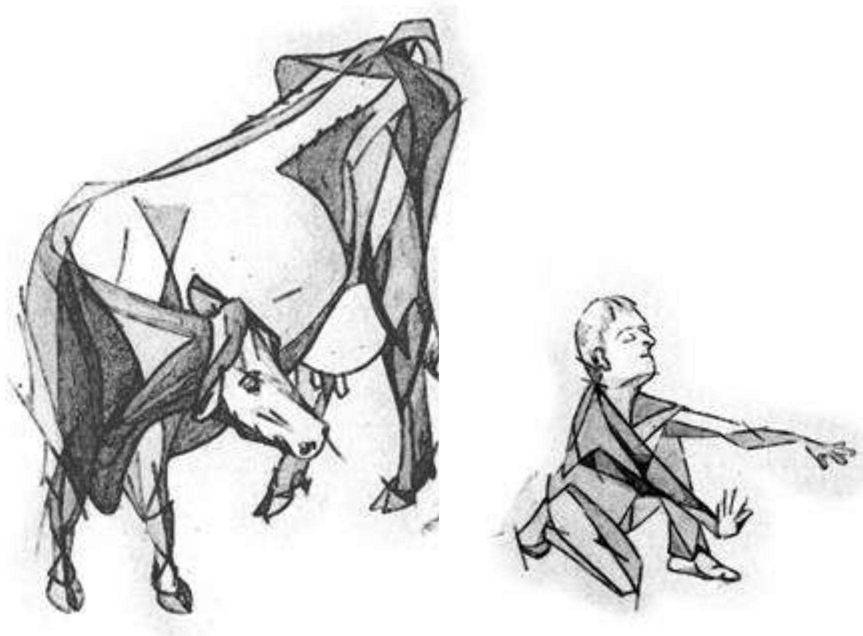
Conclusions

- Why is this important?

- There is a need for interdisciplinary communication to support decision-making processes.

- Prediction models are part of this process.



Thank you!

- Q-Check, FSM-Irmi, and
- Optikuh projects

- The projects were supported by funds of the
- Federal Ministry of Food and Agriculture
- (BMEL) based on a decision of the
- Parliament of the Federal Republic of Germany
- via the Federal Office for Agriculture and Food
- (BLE) under the innovation support program.

- Thank you to the MetAlarm Project Team!
- Thank you to Martin Kammer from LKV BY!!!

- **Döpfer Team:**
- **JF Mandujano Reyes, Emil Walleser, Marlene Tremblay,**
- **Alec Sawalski, Kelly Anklam, Srikanth Aravamuthan,**
- **Michelle Gotteiner, Moniek Smink**

- **dopfer@wisc.edu**