What drives the response of beef cows to short periods of undernutrition?

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CENTRO DE INVESTIGACIÓN Y TECNOLOGÍA AGROALIMENTARIA DE ARAGÓN

* UNIVERSITAT DE LLEIDA

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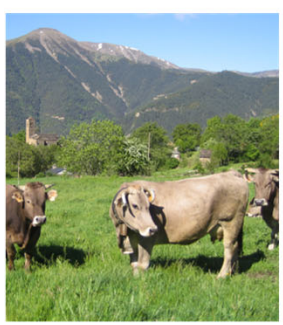
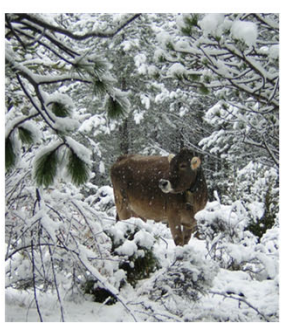
Extensive beef cattle production systems

Large seasonal variations in feed quality and availability

- ➢ nutrient restriction in the short or long term





Climate Change

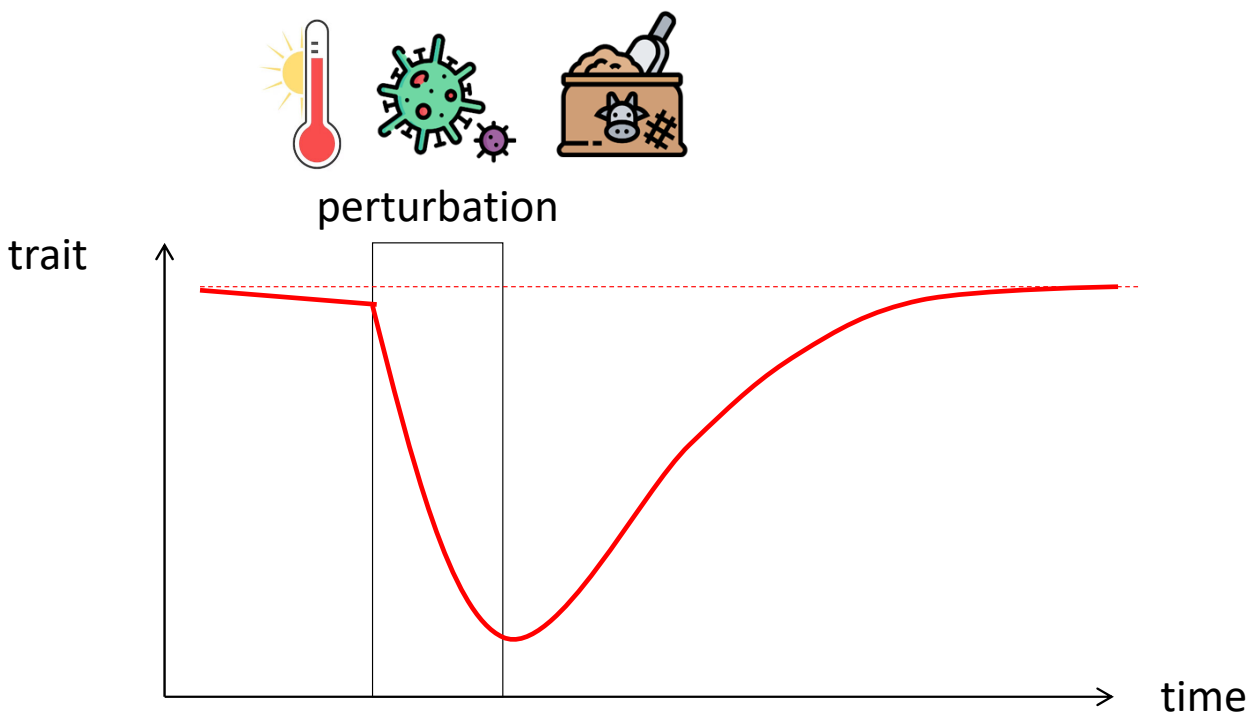
↑ intensity and frequency of periods of **restriction** and **refeeding**

How will cows respond?

The concept of Resilience

- The capacity of the animal to be **minimally affected** by a disturbance or to **rapidly return** to the physiological, behavioral, cognitive, health, affective and production states that pertained before exposure to a disturbance

  *climate, disease, welfare, **undernutrition** …* *(Colditz & Hine, 2016)*



The concept of Resilience

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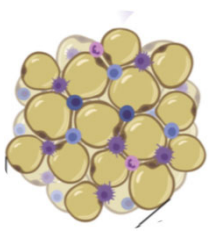
  *climate, disease, welfare, **undernutrition** …* *(Colditz & Hine, 2016)*

- **Negative Energy Balance**

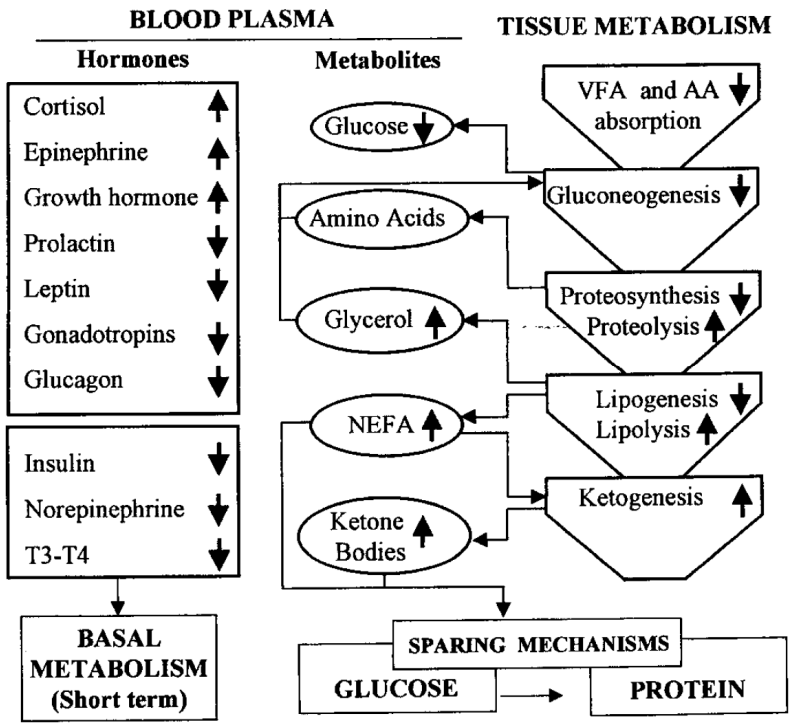
  coping mechanisms

  - hormone & metabolic adaptation
  - mobilization of body reserves

fat



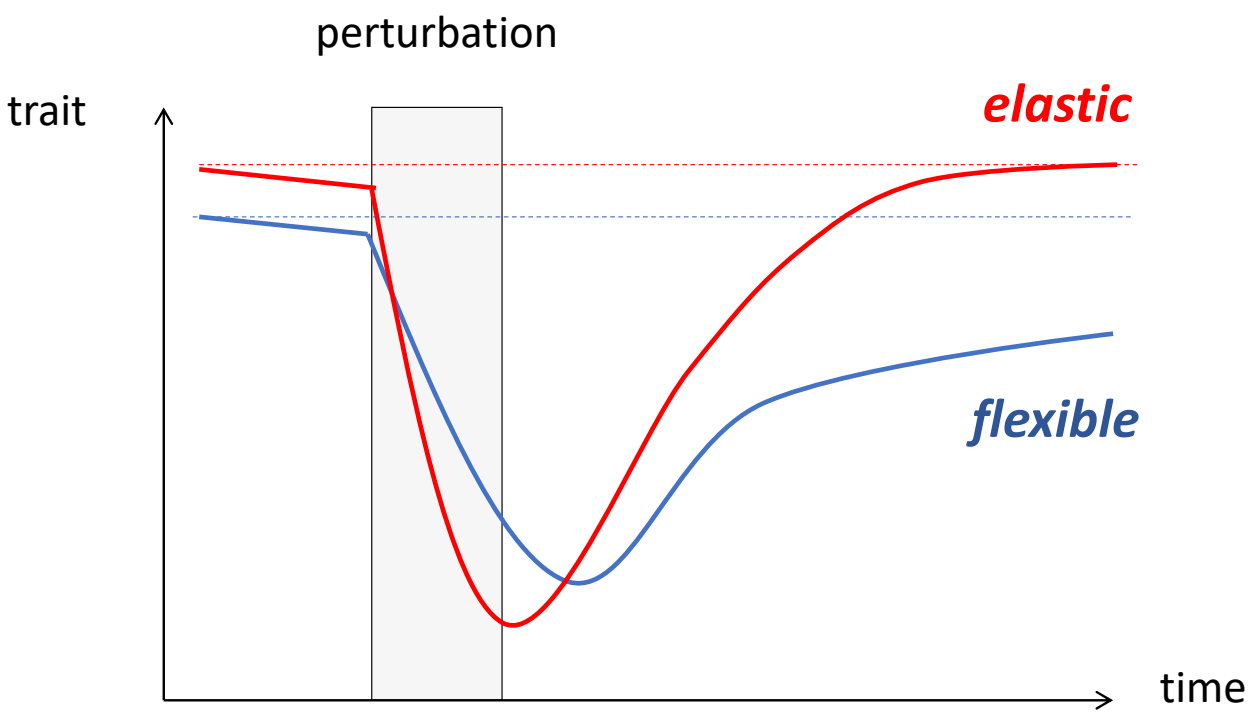
protein



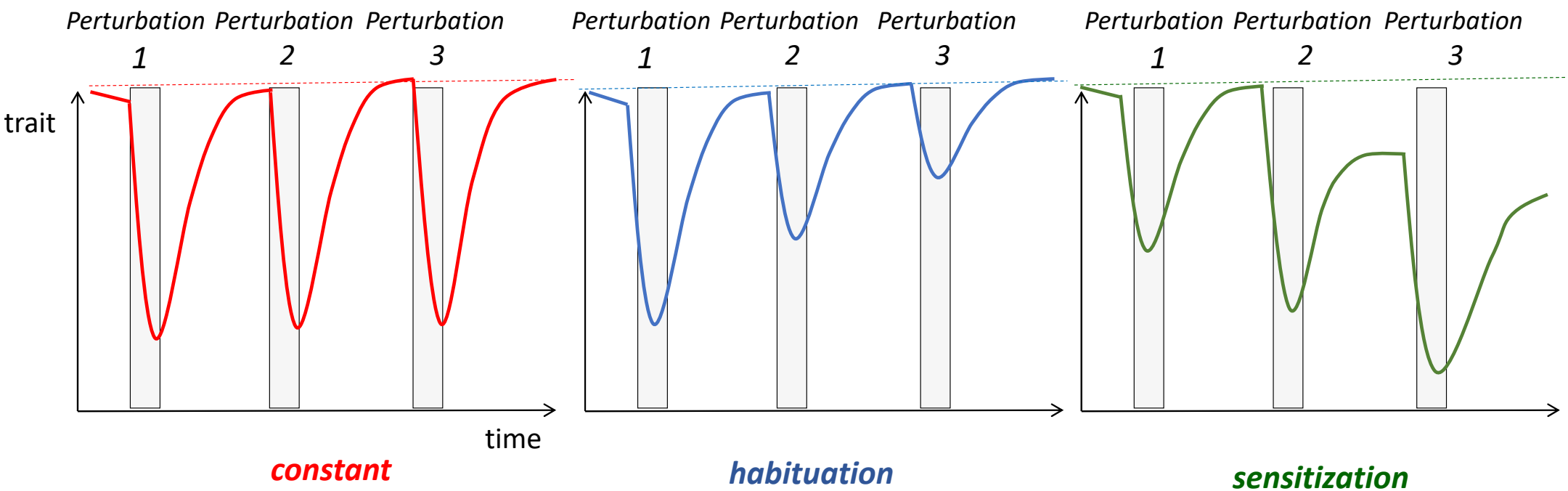
(Chilliard et al., 1998)

- **Type of response**
  - recovery after perturbation

(Blanc et al., 2010)



– response to repeated perturbations



Habituation: decreased responsiveness to a stimulus with repeated presentation

often adaptive (less likely to respond to harmless stimuli)

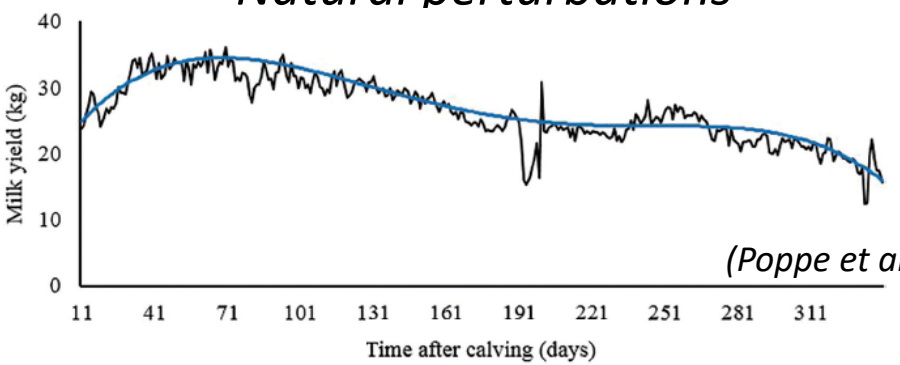
Sensitization: increased responsiveness… (*over-reaction)*

may be adaptive (avoid potentially risky situations) but also costly *(Blumstein, 2016)*

- **Factors conditioning the response**
  - Type of restriction:
    quantity vs. quality, nutrient
    duration, intensity, frequency
  - Productive orientation, breed
  - Physiological stage
  - Individual variability

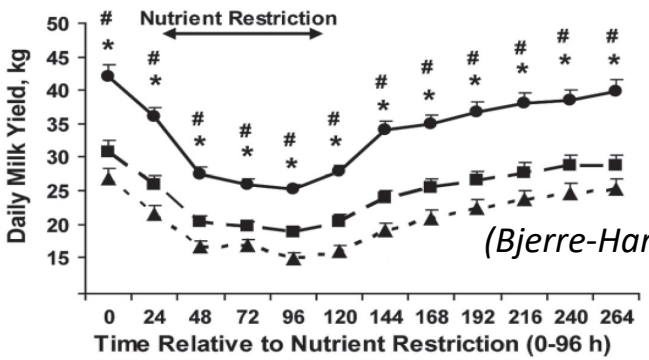
- **How can it be studied?**

Natural perturbations



(Poppe et al., 2020)

Feed restriction experiments



(Bjerre-Harpøth et al., 2012)

Long vs. Short-term?
Dairy vs. Beef?
Trait under study?

Identification of ***Coping strategies***
at the farm / population level

Objective

To analyze the **physiological and metabolic factors** influencing the **response** of beef cows to a **short-term** feed restriction and subsequent refeeding:

- determine the effect of restriction-refeeding
  at **different times of lactation** on metabolism and performance
- assess the impact of **repeated restriction–refeeding**
  on **habituation or sensitization** responses

Materials and Methods

Animals and management

- 32 multiparous lactating Parda de Montaña beef cows & their calves (adjacent cubicles, suckled twice daily at 6:00 & 14:00)

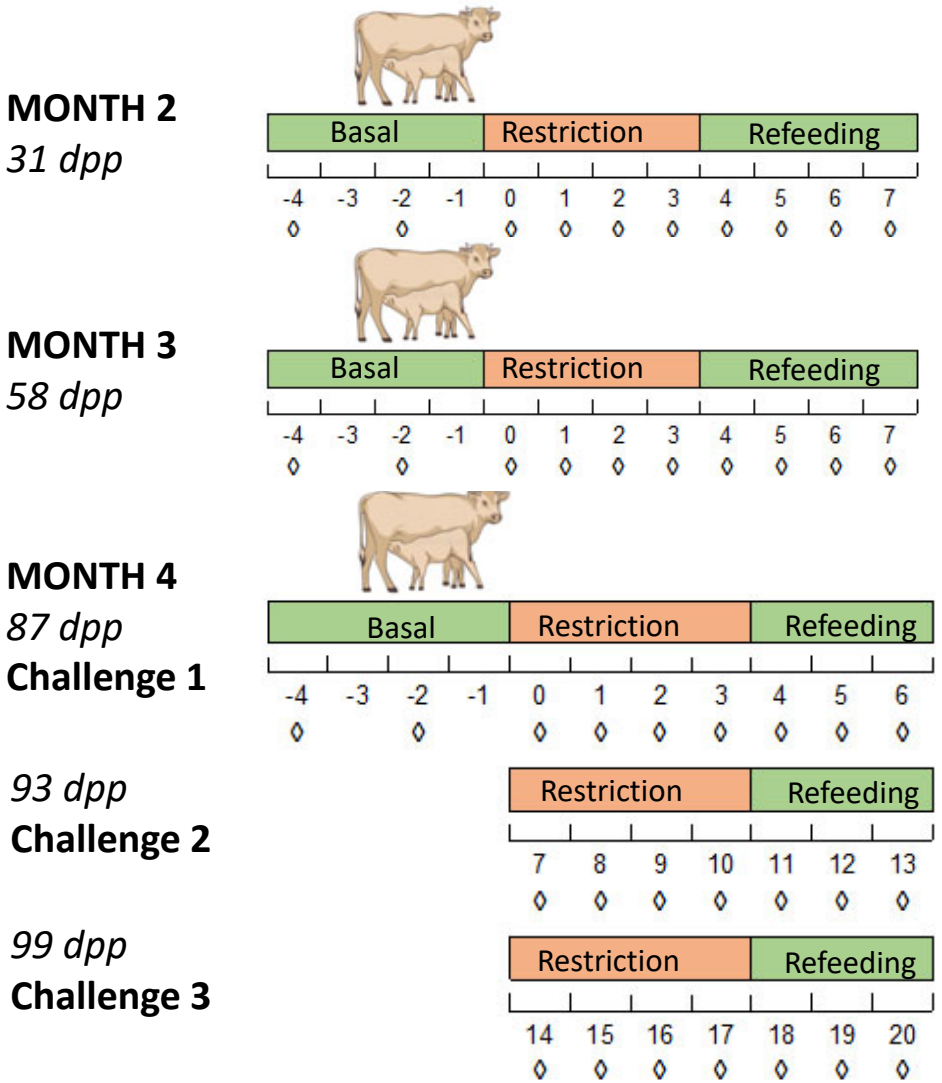
- Diet calculated for a "standard" cow
  (615 kg BW- Milk yield 8.5 kg/d)

same diet for all cows, fed at a flat-rate regime during lactation (100%)
except for 5 ***nutritional challenges (55% diet during 4 days)*** *over lactation*

Phases

• **Basal**:100% diet pre-challenge	8 kg hay + 3 kg concentrate (FM)	4d
• **Restriction**: 55% E&P diet	7 kg hay, no concentrate	4d
• **Refeeding**: 100% diet	8 kg hay + 3 kg concentrate	4d

Experimental design



Effect of short-term restriction & refeeding **at different lactation stages**

Months 2, 3 and 4

Effect of **repeated exposure** to 3 consecutive restriction & refeeding cycles at the end of lactation (**month 4**)

Challenges 1, 2 and 3

Measurements and analyses

Daily feed intake

- individual feeders (F)
- Alpro system (C)

Live weight and BCS

Milk yield

weigh-suckle-weigh
at 6:00 & 14:00

Feed quality

- DM, CP, NDF
  ADF, ADL, NE
- Fatty acids

Milk composition

(hand milked)

- Fat
- Protein
- Lactose
- Somatic cell count
- Urea
- Fatty acids

Plasma metabolites

- NEFA
- BHB
- Glucose
- Urea
- MDA

Statistical analysis of data

- **Modeling the response curves**:
  milk yield, NEFA and BHB
  - new variables ~ curve parameters (R spline library)

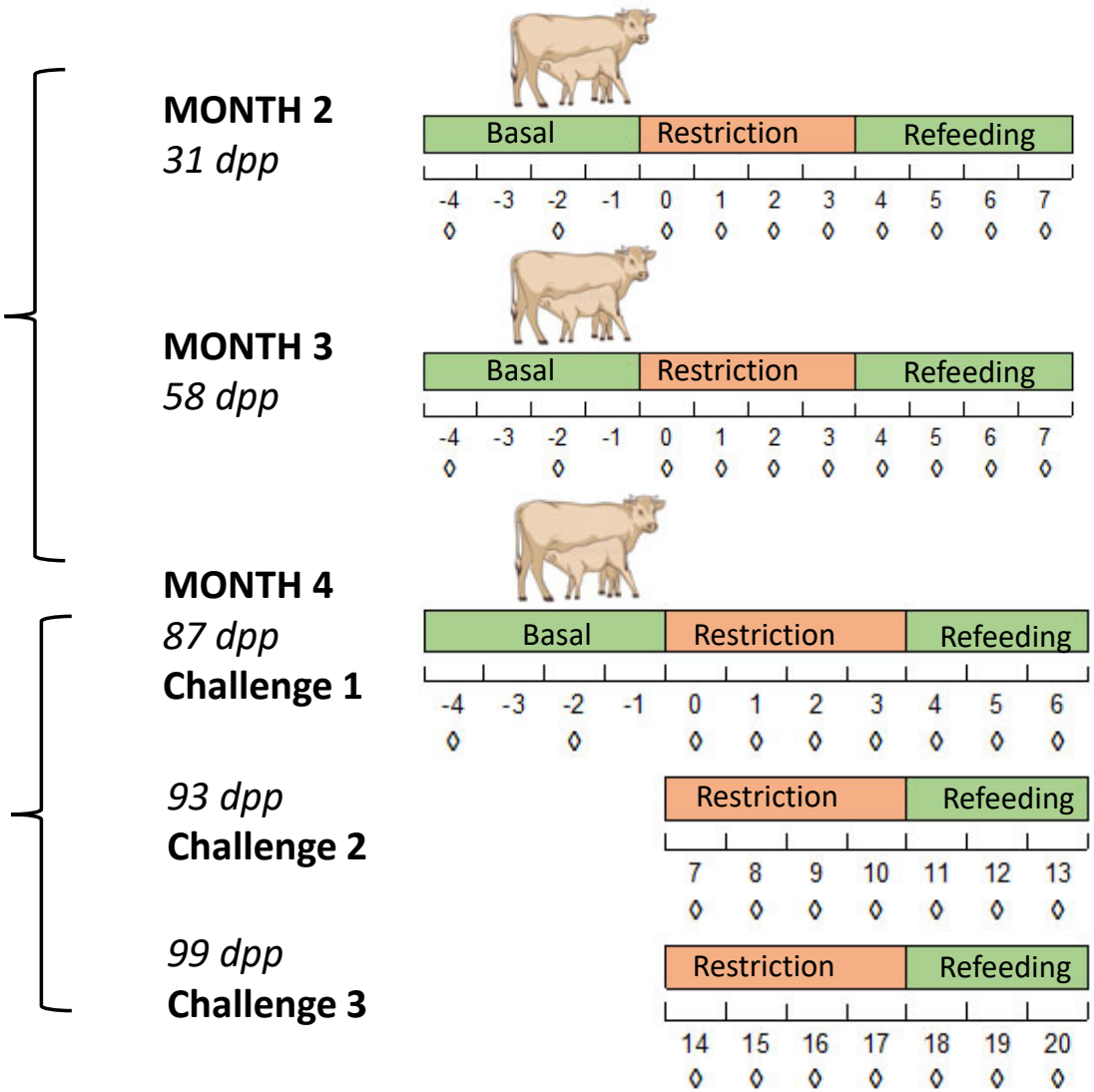
- **Grouping of cows according to their reponse:**
  - principal component analysis + cluster analysis (R Factor Mine package)

- **Analysis of performance and metabolic parameters:**
  - repeated-measures analysis of variance: PROC MIXED of SAS
    fixed effects:
    * Month or Repeated Challenge
    * Metabolic Response cluster
    * time: Day or Feeding Period
    random effect: Cow
  - Pearson correlations (r): CORRPLOT package of R

Results

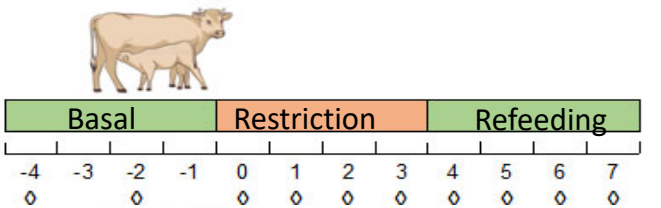
1. **Modelling beef cows' individual response** to short nutrient restriction during lactation
2. Beef cows' performance and metabolic response to short nutritional challenges in **different months of lactation**
3. Adaptive response of beef cows to **successive nutritional challenges**

Orquera-Arguero KG (Ph D) et al.

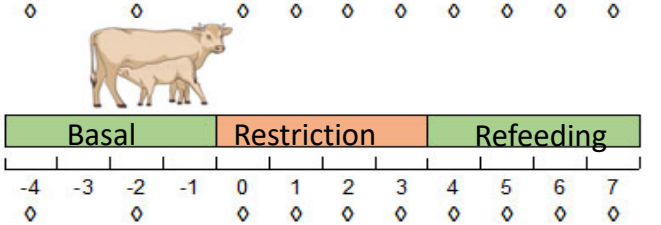


1. **Modelling the individual response of beef cows** to short nutritional restriction at different stages of lactation

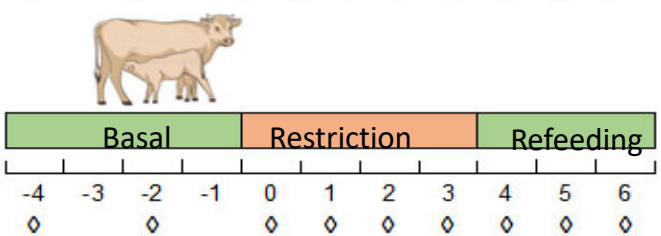
MONTH 2
31 dpp



MONTH 3
58 dpp



MONTH 4
87 dpp



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Modelling beef cows' individual response to short nutrient restriction in different lactation stages

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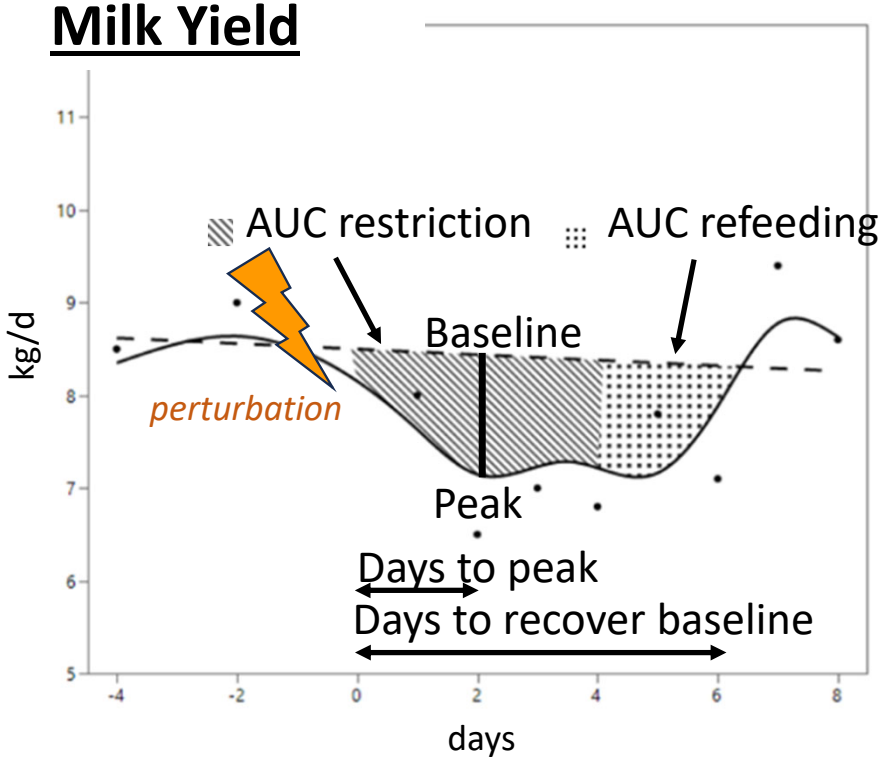
Step 1. Model the response in **milk yield, plasma NEFA** and **BHB** to restriction and refeeding at three stages of lactation **(month 2, 3, 4)**

Step 2. Group cows according to their **metabolic response** (MR cluster)

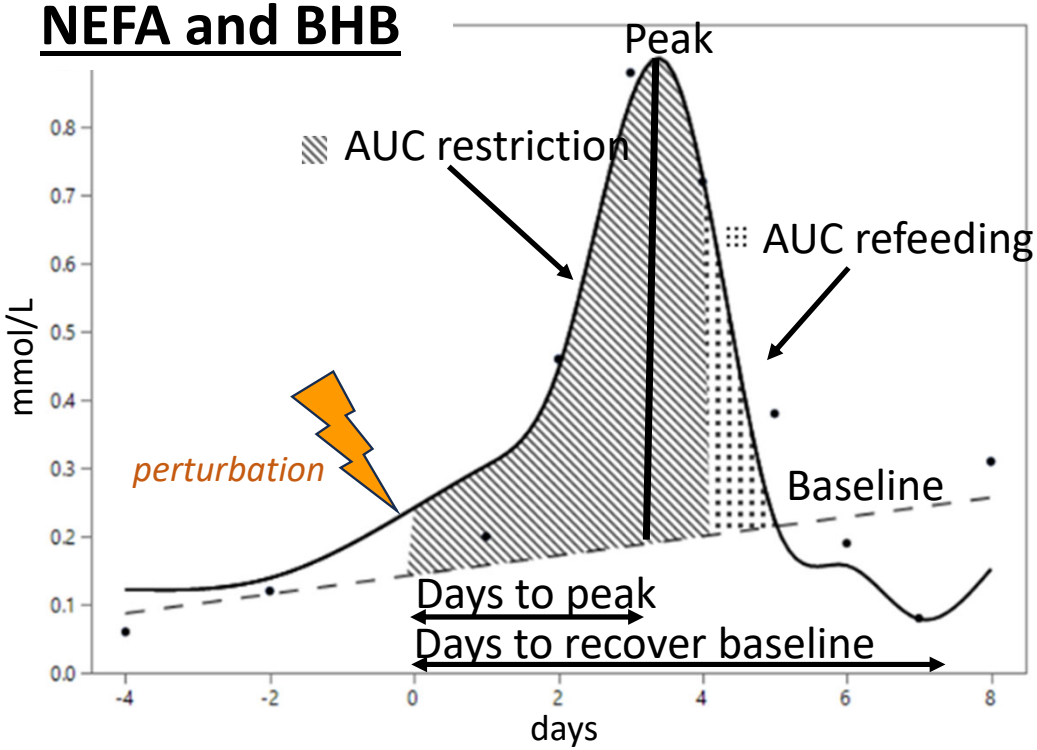
Step 3. Compare cow **MR clusters** and **lactation stages**

Step 1: Modelling of curves → *natural cubic splines (K functions – K knots)*

Milk Yield



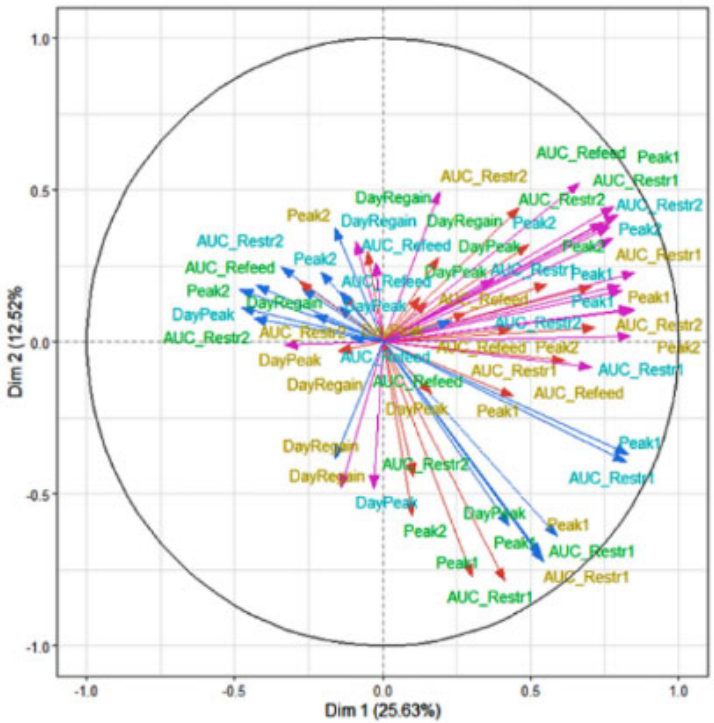
NEFA and BHB



New variables:

- baseline
- peak
- days to peak
- days to recover baseline
- area under the curve (AUC) during restriction
- AUC during refeeding

Step 2: Multivariate Analysis



- **Principal component analysis (PCA):**

  Total Variance : 48%

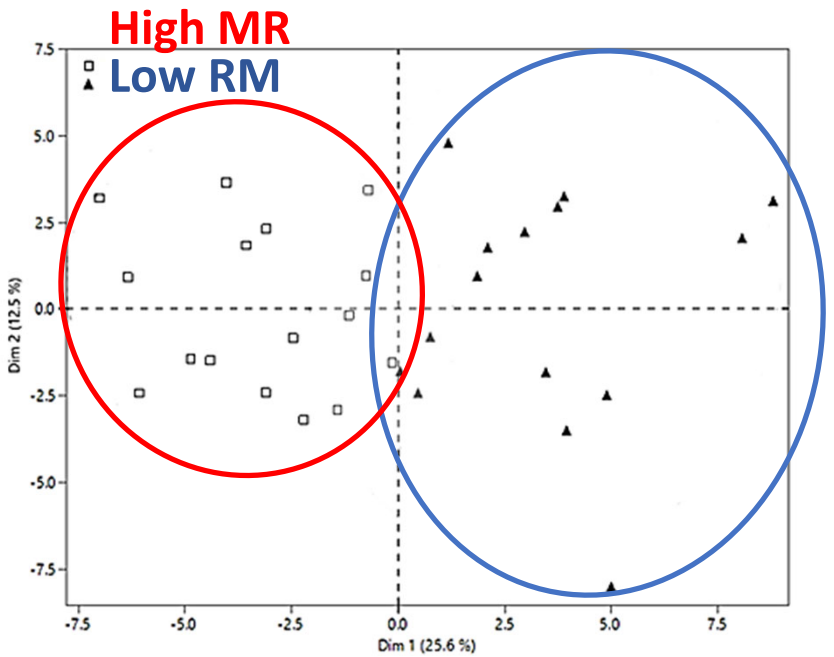
  Dim 1 = 25.6%

  Dim 2 = 12.5%

  Dim 3 = 9.9%

- **Identification of clusters:**

  Two metabolic response clusters (MR)



Step 3: Effect of MR cluster and lactation stage

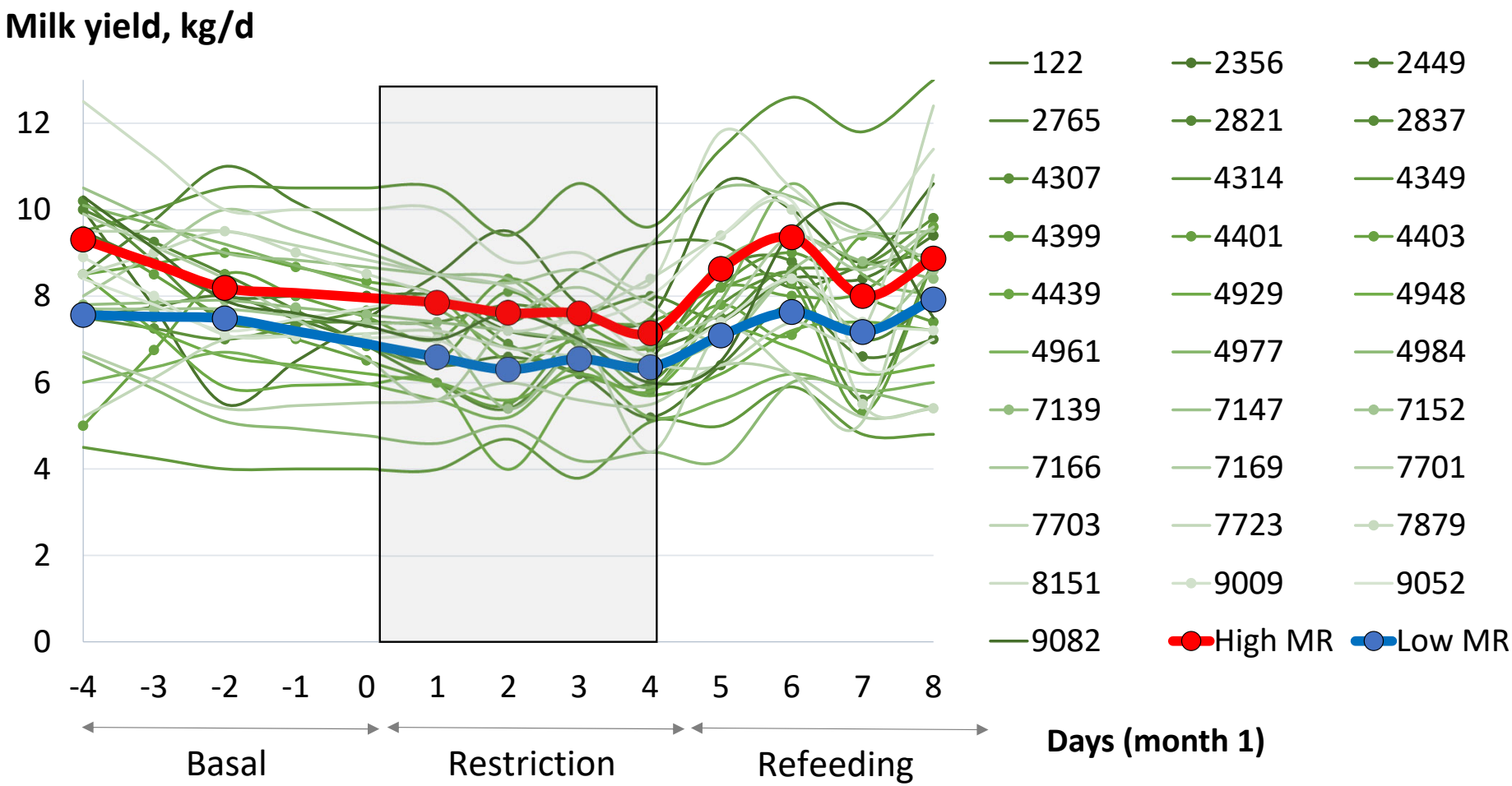
Linear mixed model:

MR Cluster : High and Low MR

Lactation month : 2, 3, 4

Random: cow

Before results… *what is the magnitude of the individual variability?*



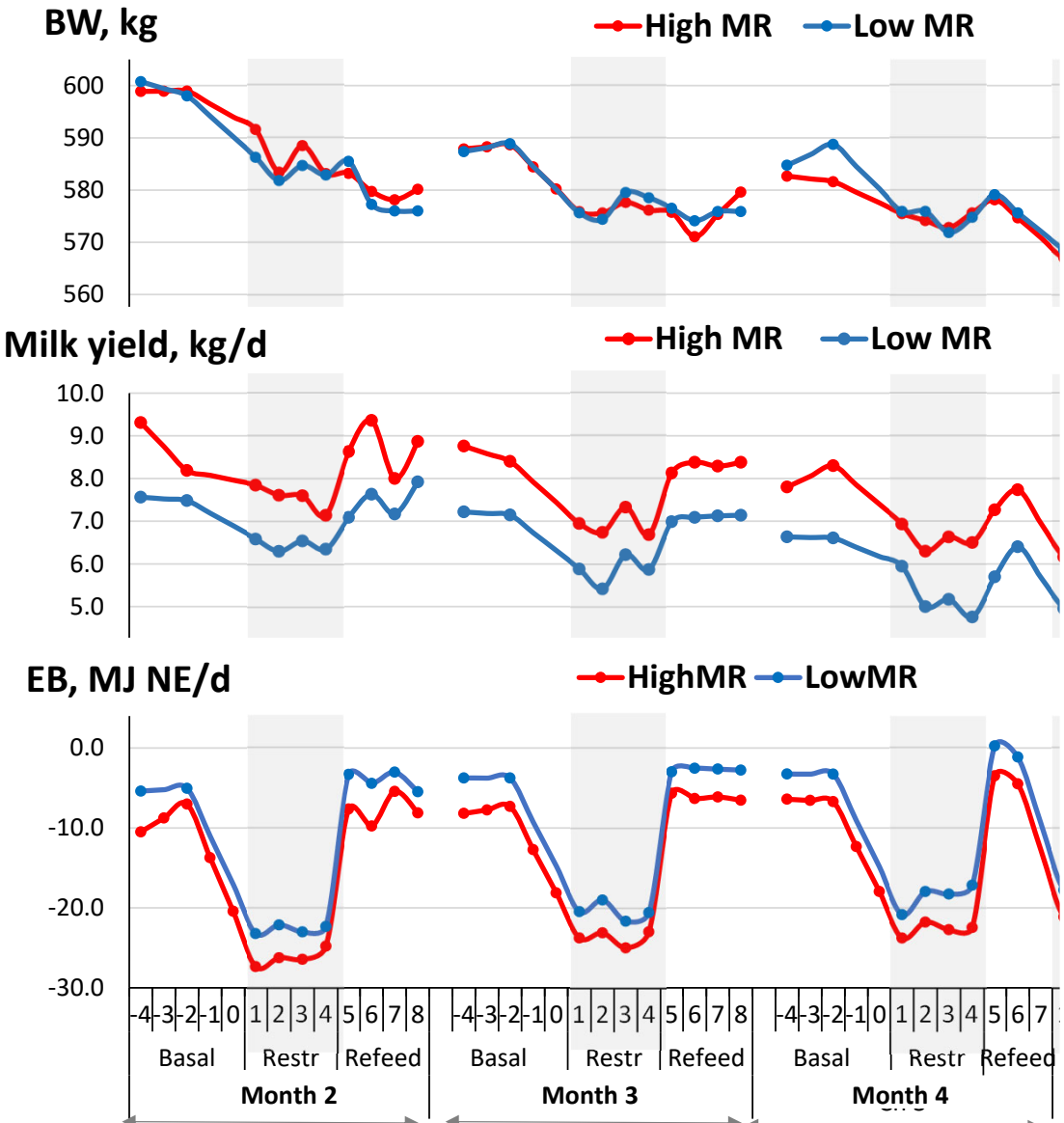
Results

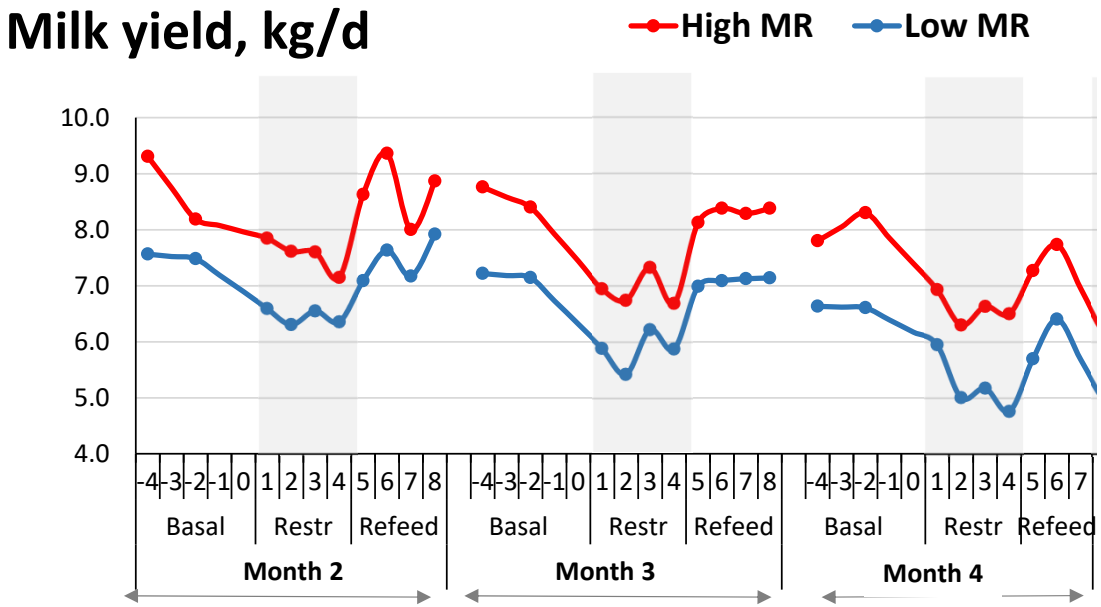
Performance in the two metabolic response (MR) clusters:

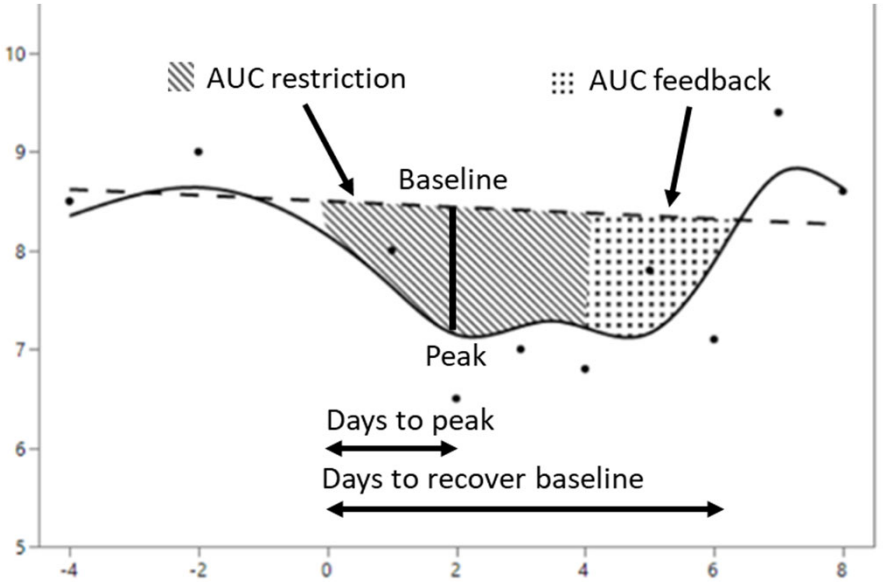
Similar BW but…

-**Low MR** : ↓ milk yield
↓ energy requirements
(n=16) ~ EB less negative
↓ plasma NEFA and BHB

-**High MR**: ↑ milk yield
↑ energy requirments
(n=15) ~ EB more negative
↑ plasma NEFA and BHB







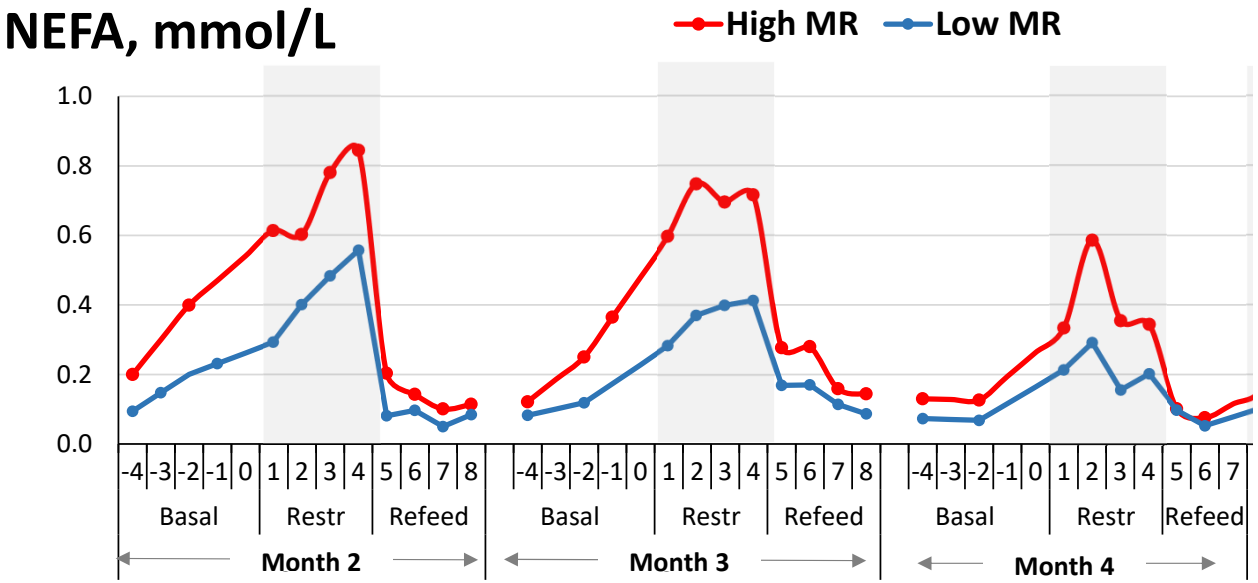
Milk yield curve variables	MR Cluster (Cl)		Month (M)			*P*-values	
	Low MR	High MR	2	3	4	Cl	M
Baseline, kg/d	6.94^{y}	8.27^{x}	8.10^{a}	7.80^{a}	6.92^{b}	0.002	0.001
Peak, kg/d	-1.32	-1.56	-1.45^{ab}	-1.61^{b}	-1.27^{a}	0.068	0.020
Days to peak, d	2.57	2.63	2.80^{a}	1.78^{b}	3.22^{a}	0.813	0.001
$AUC_{restriction}$, kg	-3.80^{y}	-4.81^{x}	-4.01^{a}	-5.21^{b}	-3.70^{a}	0.036	0.002
Days to regain baseline, d	5.93	5.74	5.65	5.98	5.87	0.326	0.376
$AUC_{refeeding}$, kg	-0.83	-0.74	-0.68	-0.82	-0.86	0.644	0.647

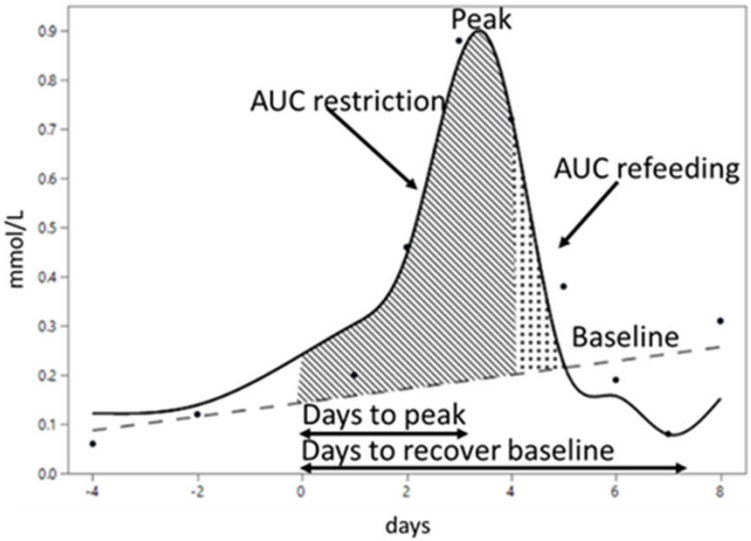
MR Cluster

- Higher basal MY and total loss in **High MR**
- Similar reaction time

Month of lactation

- Lower basal MY in **month 4**
- Higher and faster loss in month 3





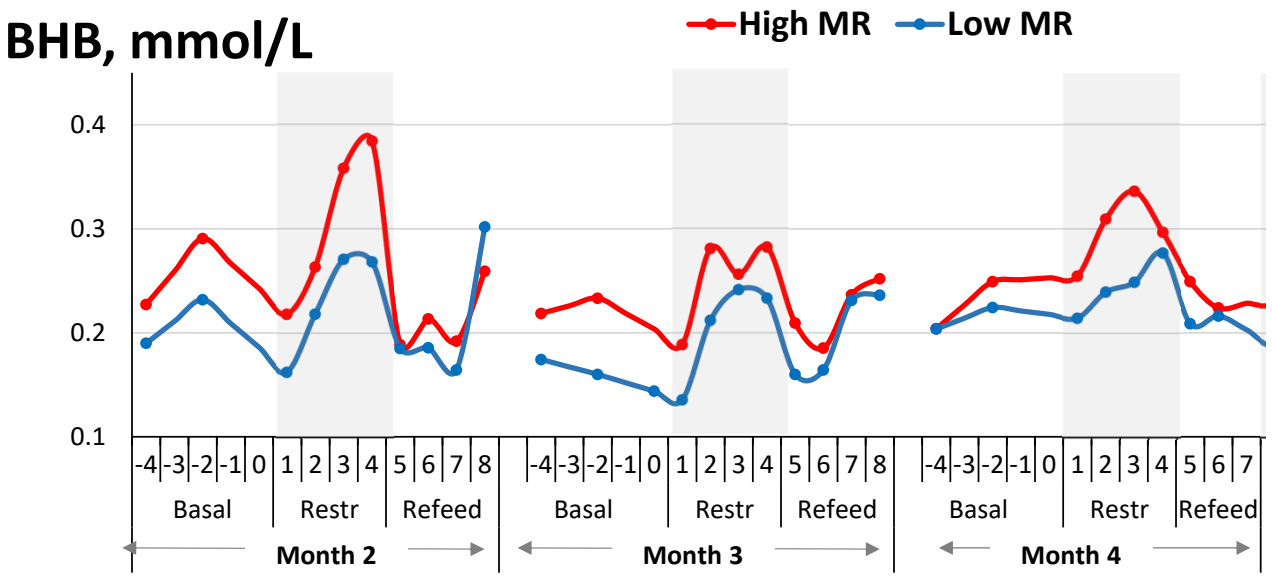
	MR Cluster (Cl)		Month (M)			*P*-values[1]	
	Low MR	High MR	2	3	4	Cl	M
NEFA curve variables							
Baseline, mmol/l	0.09^{y}	0.15^{x}	0.13^{a}	0.15^{a}	0.08^{b}	0.001	0.001
Peak, mmol/l	0.26^{y}	0.51^{x}	0.54^{a}	0.38^{b}	0.24^{c}	0.001	0.001
Days to peak, d	2.94	3.05	3.38^{a}	3.09^{a}	2.51^{b}	0.453	0.001
$AUC_{restriction}$, mmol x d/l	0.68^{y}	1.42^{x}	1.36^{a}	1.17^{a}	0.62^{b}	0.001	0.001
Days to regain baseline, d	5.74	5.74	5.55^{b}	6.08^{a}	5.59^{b}	0.991	0.036
$AUC_{refeeding}$, mmol x d/l	0.13^{y}	0.21^{x}	0.24^{a}	0.23^{a}	0.04^{b}	0.001	0.001

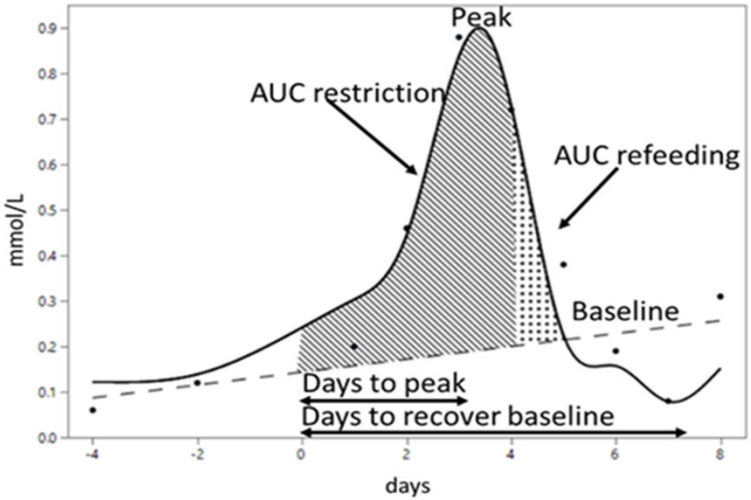
MR Cluster

- Higher basal concentration, peak and total increase in **High MR**
- Similar reaction time

Month of lactation

- Lower basal concentration, peak and total increase in **month 4**





	MR Cluster (Cl)		Month (M)			*P*-values[1]	
	Low MR	High MR	2	3	4	Cl	M
BHB curve variables							
Baseline, mmol/l	0.220^{y}	0.248^{x}	0.238^{ab}	0.222^{b}	0.243^{a}	0.024	0.026
Peak, mmol/l	0.07^{y}	0.11^{x}	0.12^{a}	0.07^{b}	0.08^{b}	0.002	0.003
$AUC_{restriction}$, mmol x d/l	0.04^{y}	0.13^{x}	0.10^{a}	0.02^{b}	0.13^{a}	0.011	0.006

Moderate response, delayed from NEFA

MR Cluster

- Higher basal concentration, peak and total increase in **High MR**
- Similar reaction time

Month of lactation

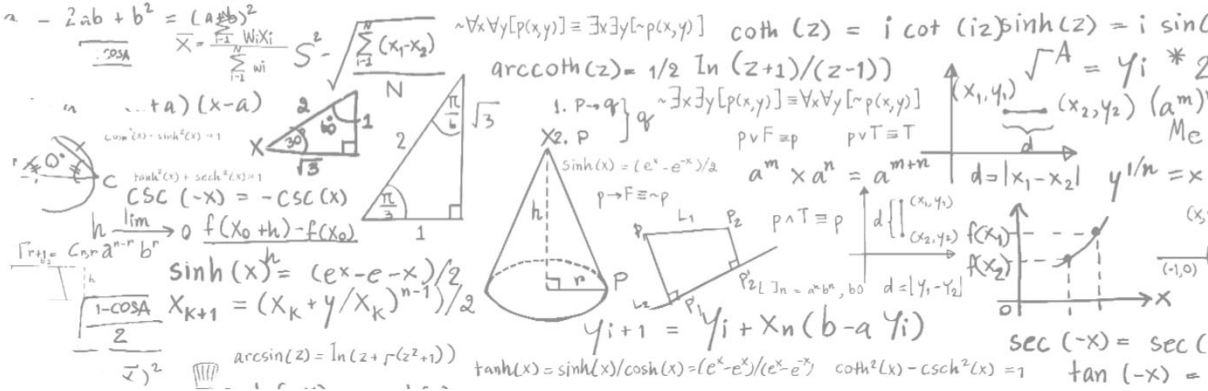
- Lower basal concentration and total increase in **month 3**

- ✓ Changes in milk yield and plasma indicators of lipolysis (NEFA) and ketogenesis (BHB) under short-term food restriction can be **modelled** by **spline curves**

- ✓ **The magnitude but not the speed** of individual response was driven primarily by the **basal milk yield**

- ✓ The different **metabolic response profiles** established suggest that the **High MR** cows had a higher potential milk yield and were able to efficiently **partition more nutrients towards milk synthesis** than the **Low MR** cows

Identifying response profiles
→ management and breeding purposes

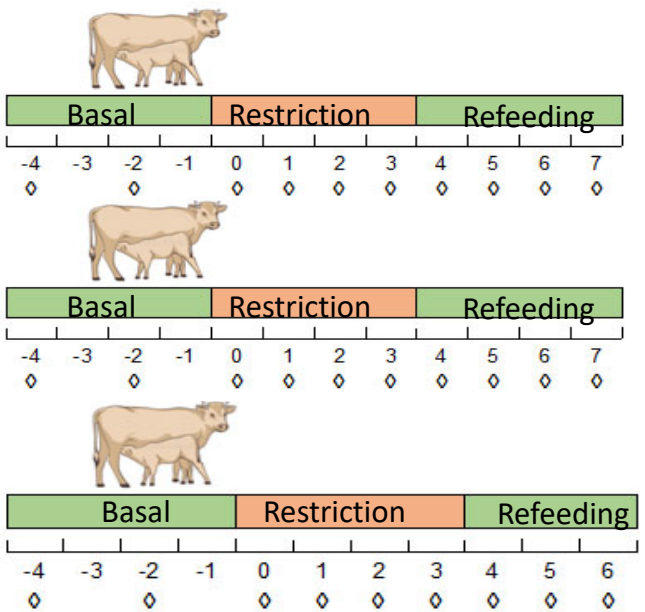


2. Performance and metabolic response of beef cows to short nutritional restriction **in different months of lactation**

MONTH 2
31 dpp

MONTH 3
58 dpp

MONTH 4
87 dpp



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Beef cows' performance and metabolic response to short nutritional challenges in different months of lactation

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Performance

- Energy balance, live weight, milk yield
- Milk composition: lactose, fat, protein, urea

Plasma metabolites

- NEFA, BHB, urea, MDA, glucose

Month of lactation (M):

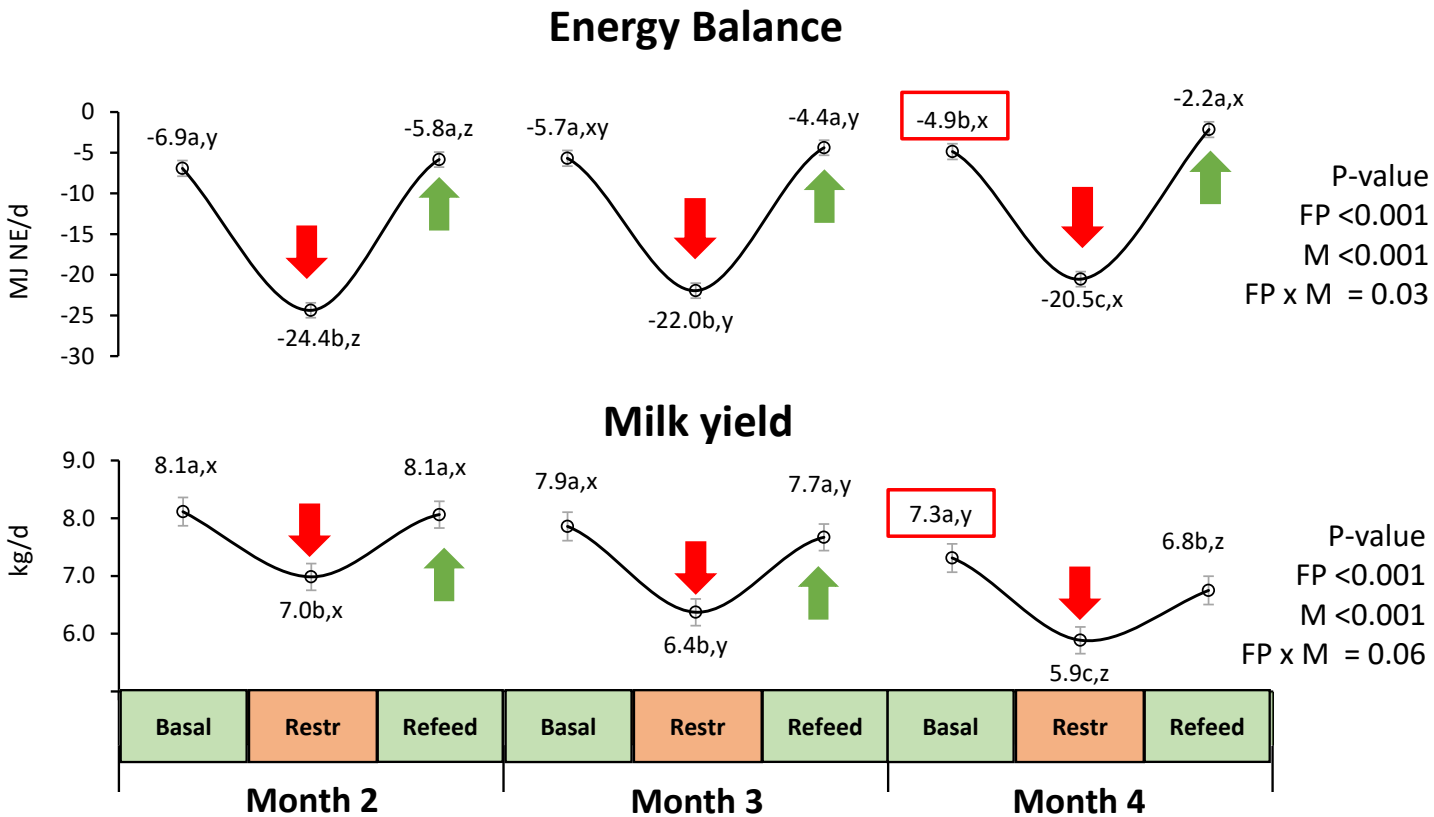
Months 2, 3, 4

Feeding Period (FP):

Basal - Restriction – Refeeding

M x FP

Performance



M: x ≠ y ≠z *FP: a ≠ b ≠ c*

P-value
FP <0.001
M <0.001
FP x M = 0.03

Month of lactation (M):
month 2,3 < month 4
Feeding Period (FP):
Restriction: month 2, 3 and 4
Refeeding: month 2, 3 and 4

P-value
FP <0.001
M <0.001
FP x M = 0.06

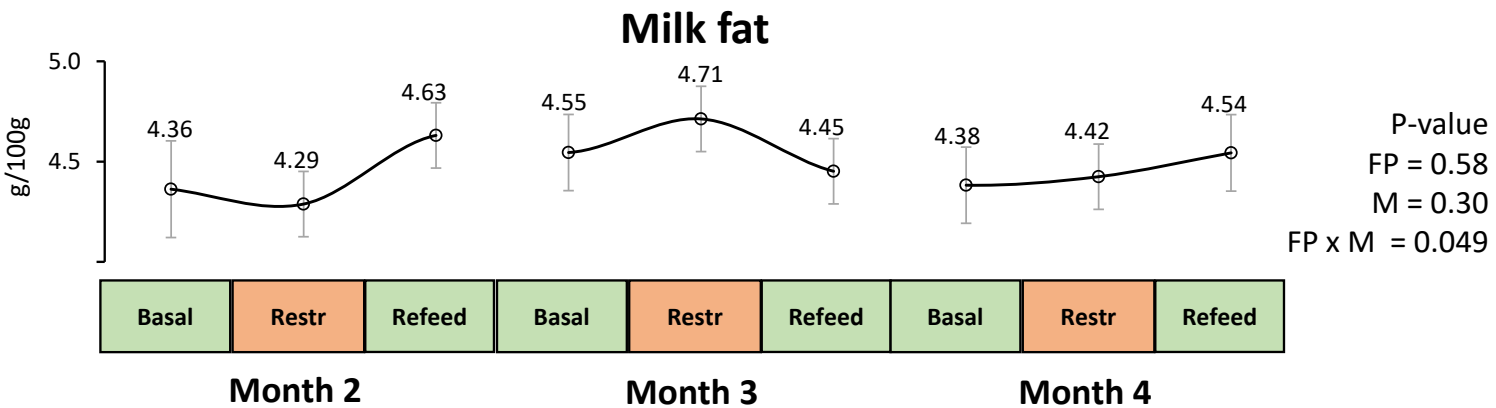
Month of lactation (M):
month 2,3 < month 4
Feeding Period (FP):
Restriction: month 3, 4 > 2
Refeeding: month 2, 3 > 4

partial recovery month 4 (-8%)

- **Improved EB** *(~flat-rate feeding)* and **lower milk yield** with advancing lactation
- M x FP: effect of FP of similar sense but different **magnitude**

High impact of restriction and only partial recovery with refeeding in late lactation
~decreased priority for milk production?

Milk composition



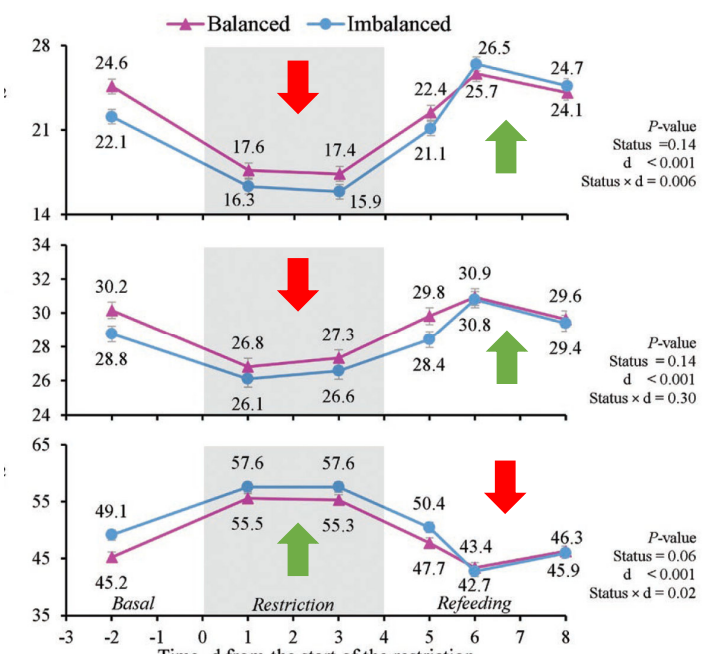
P-value
FP = 0.58
M = 0.30
FP x M = 0.049

No relevant changes in **milk fat content**

***de novo* FA**
(C4:0-C15:1)
synthesized de novo
in the mammary gland

Mixed origin FA
(C16:0-C16:1)

Mobilization FA
(>C16:)
mammary uptake of TAG
and NEFA (*C18:1 cis-9*)



But significant changes in
milk fat composition with restriction

Quick increase in the proportion of preformed fatty acids ~ fat mobilization

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Performance and milk fatty acid profile of beef cows with a different energy status with short nutrient restriction and refeeding

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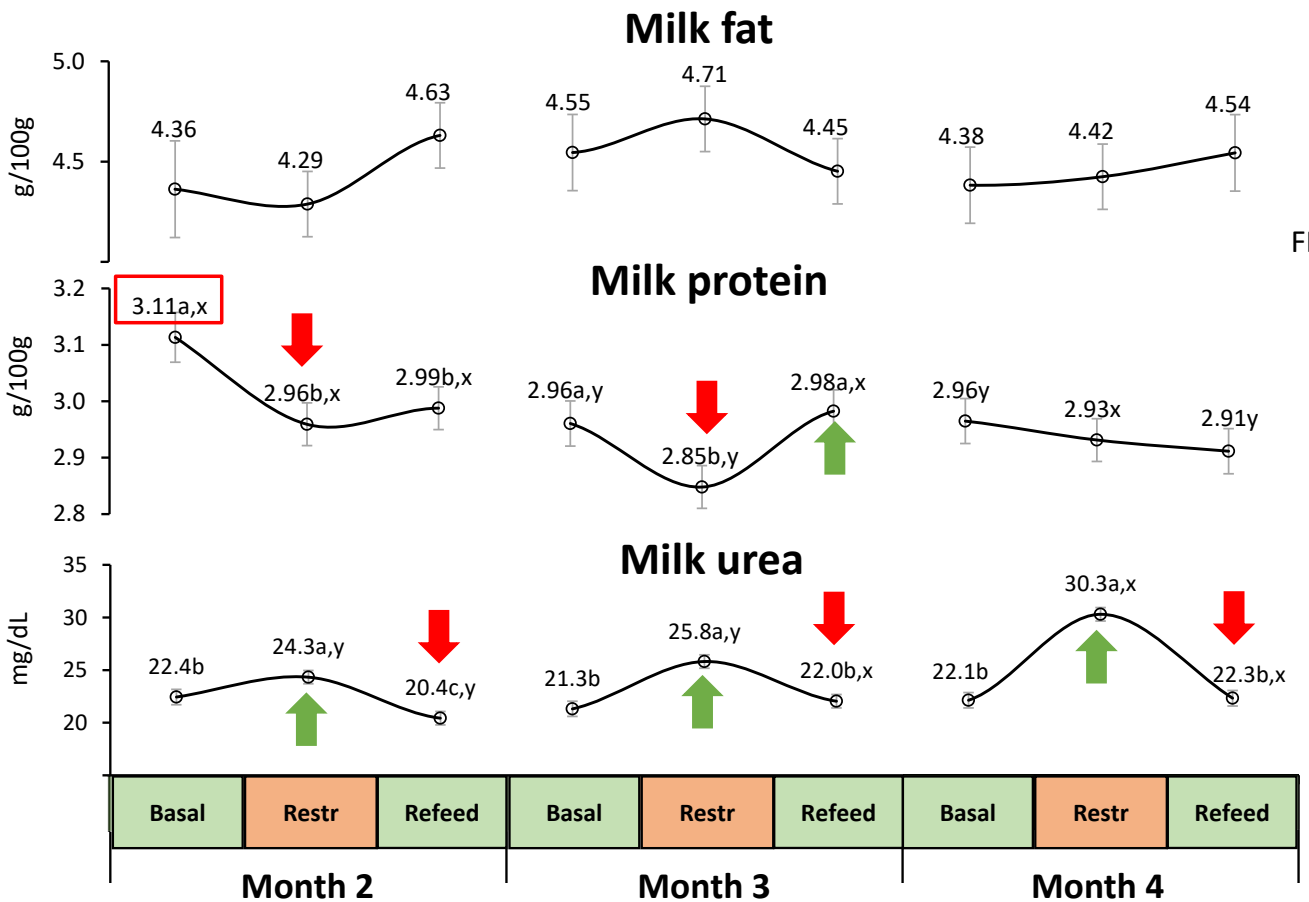
Milk composition



P-value
FP = 0.58
M = 0.30
FP x M = 0.049

P-value
FP <0.001
M <0.001
FP x M <0.001

P-value
FP <0.001
M <0.001
FP x M <0.001

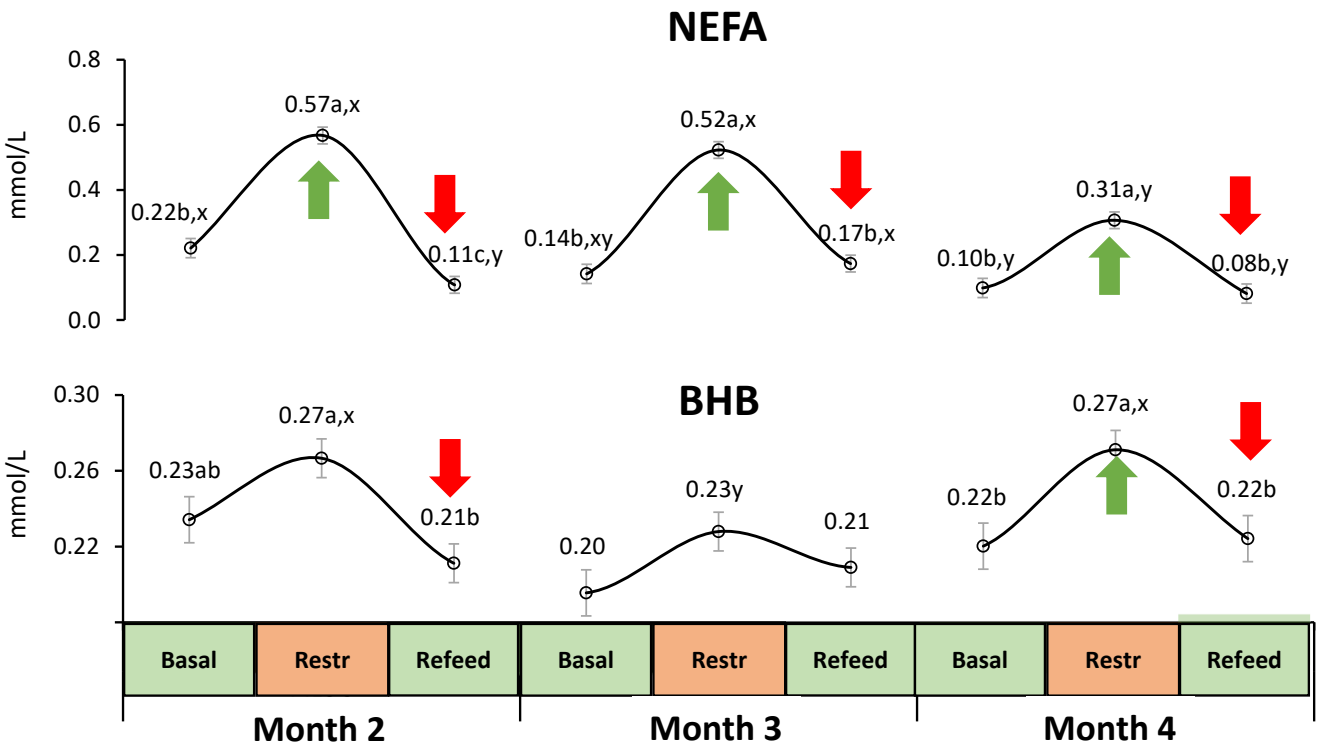
Month of lactation (M):
month 2 > 3, 4

Feeding Period (FP):
Restriction: month 2, 3
Refeeding: month 3

Feeding Period (FP):
Restriction
Refeeding: month 2 < 3, 4

- No relevant changes in milk fat content but change in **milk FA composition**
- Restriction ↓**milk protein,** ↑**milk urea** - month 4 *~ body protein catabolism??*

Plasma metabolites



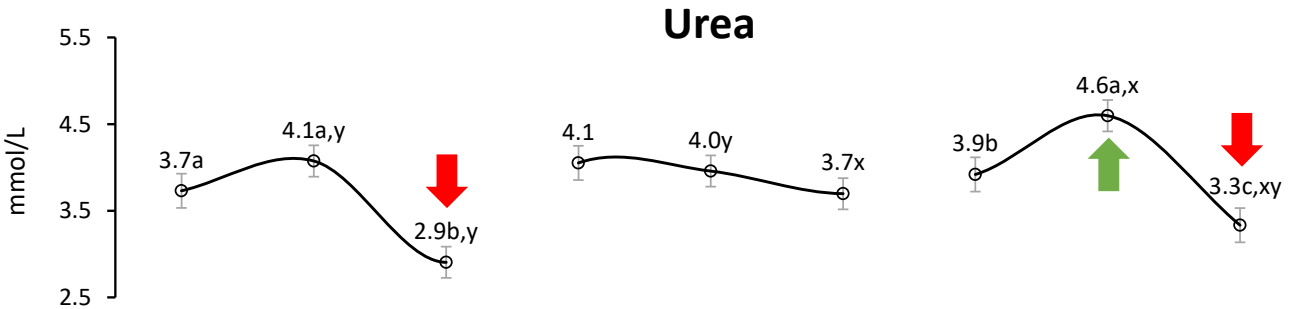
P-value
FP <0.001
M <0.001
FP x M <0.001

Month of lactation (M):
month 2, 3 > 4
Feeding Period (FP):
Restriction ↑
Refeeding ↓

P-value
FP <0.001
M <0.001
x M = 0.04

Feeding Period (FP):
Restriction: month 4 ↑
Refeeding: month 2, 4 ↓

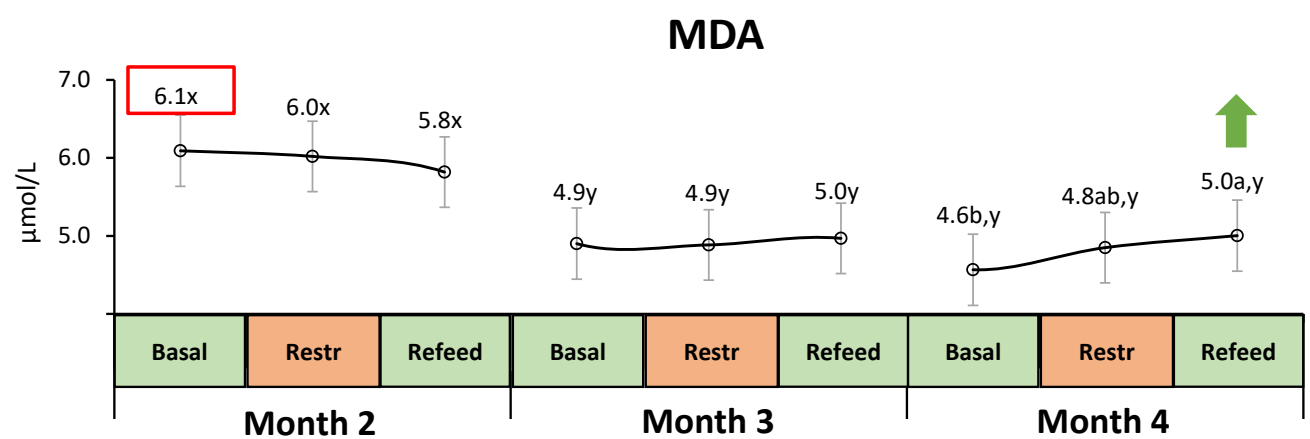
- Basal NEFA decreased with **advancing lactation** ~ improved EB
- Restriction ↑ **NEFA…** but BHB? ~ **lipolysis but limited ketogenesis**
  < threshold for compromised metabolic status (except NEFA peak in month 2)



P-value
FP <0.001
M <0.001
FP x M <0.001

Feeding Period (FP):
Restriction: month 4
Refeeding: month 2, 4

r plasma urea - milk = 0.65



P-value
PA = 0.52
M <0.001
FP x M <0.001

Month of lactation (M):
month 2 > 3, 4

- Restriction ↑ **plasma urea in month 4** ~*body protein catabolism?*
- Oxidative stress: only in month 2 ~*higher NEFA available for oxidation*
  but not in response to restriction

- ✓ Cows responded to feed restriction mainly with **decreased milk yield** and **increased plasma NEFA** contents

- ✓ **Full recovery** after refeeding of all traits **except for MY in late lactation**

- ✓ **Different metabolic strategies to face nutritional perturbations depending on lactation stage:**
  - **early lactation**: sufficient mobilization of **fat reserves** to buffer the impact of moderate feed restriction on milk yield
  - **late lactation**: body **protein mobilization** but less effective response

Changing priority of biological functions ≠ coping strategies

3. Adaptive response of beef cows to **successive nutritional challenges**

MONTH 4

87 dpp
Challenge 1

Basal | Restriction 1 | Refeeding 1

-4 -3 -2 -1 0 1 2 3 4 5 6

93 dpp
Challenge 2

Restriction 2 | Refeeding 2

7 8 9 10 11 12 13

99 dpp
Challenge 3

Restriction 3 | Refeeding 3

14 15 16 17 18 19 20

Effect of **repeated exposure** to 3 consecutive restriction & refeeding cycles at the end of lactation (**month 4**)

Challenges 1, 2 and 3

Performance

- EB, BW, Milk yield & composition

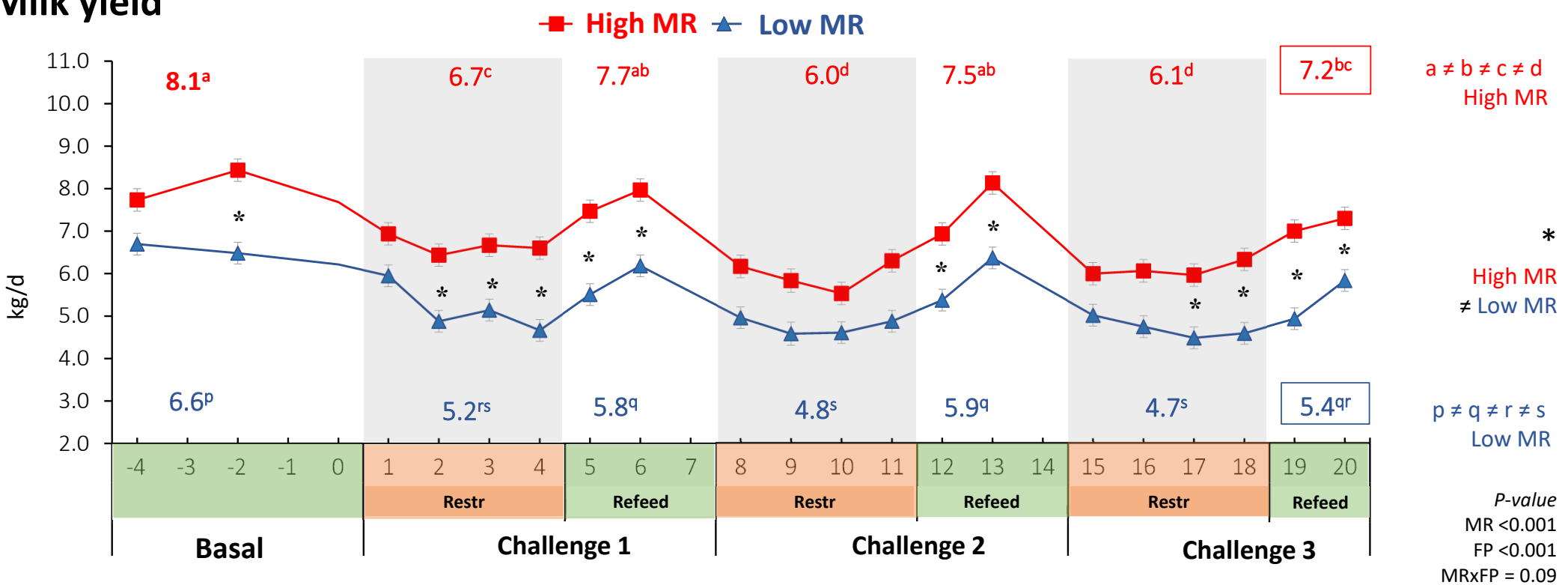
Plasma metabolites

- NEFA, BHB, urea

Time: - **Feeding Period (FP)**
Basal - Restriction 1,2,3 - Refeeding 1,2,3
- **Day (d)**
day -4 to 20

Metabolic Response (MR) cluster:
High vs Low MR *

Milk yield



- **High MR** > **Low MR** (7.0 vs. 5.4 kg/d)

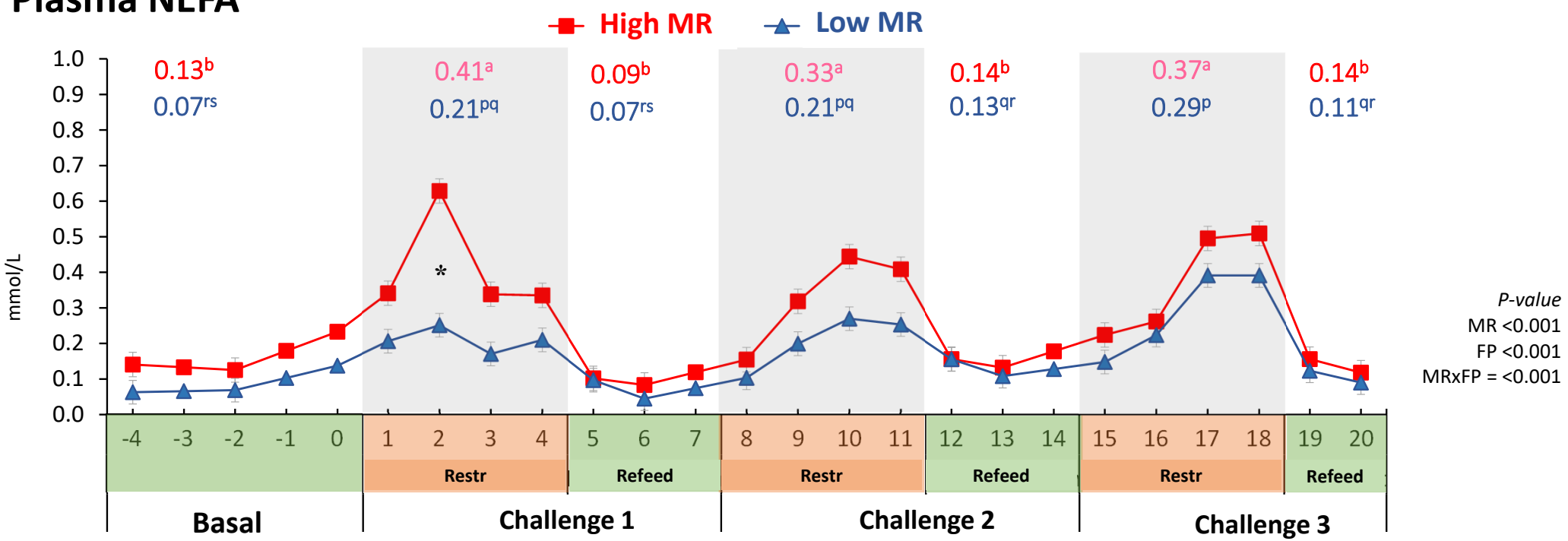
⬇ Restriction challenge 1 < challenge 2, 3 **(-19%, -27%, -26%) → sensitization**

day: immediate response, except challenge 1 in **Low MR**

⬆ Refeeding challenge 1, 2, 3

day: immediate response in **High MR,** second day in **Low MR** ***Only partial recovery***

Plasma NEFA



P-value
MR <0.001
FP <0.001
MRxFP = <0.001

- **High MR** > **Low MR** in challenge 1 and 2 but not in challenge 3

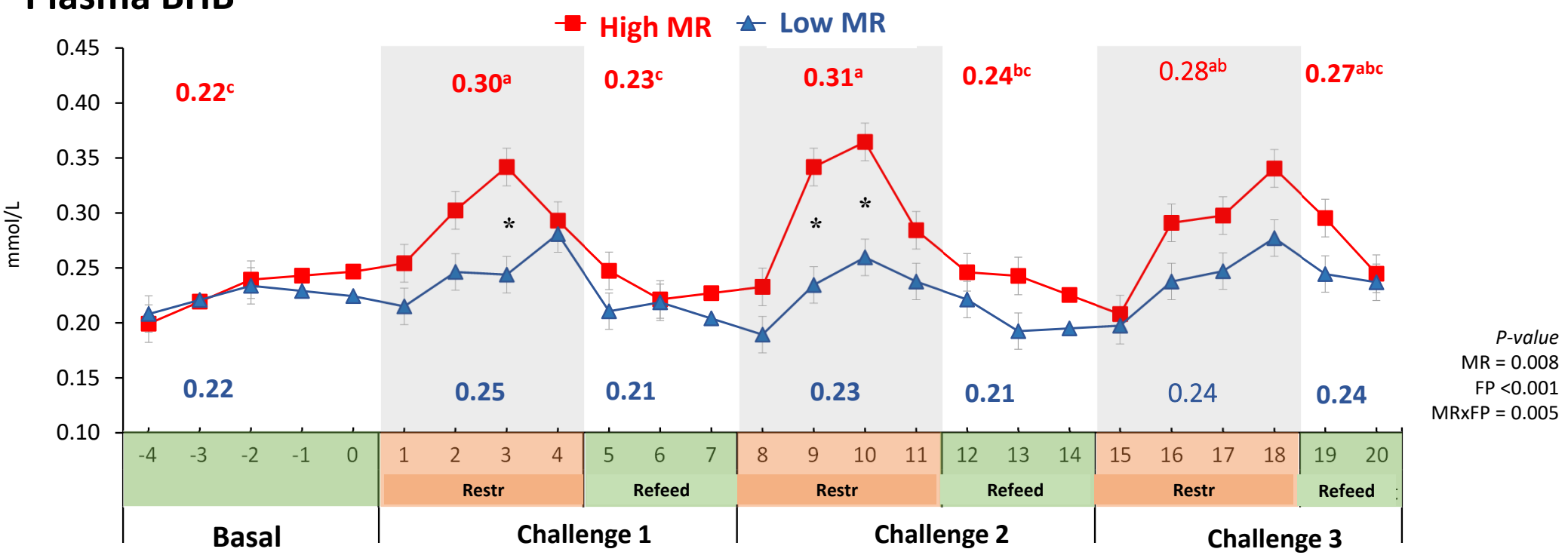
Restriction challenge 1 > 2, 3 (**NS**)
day: delayed after first challenge

Refeeding challenge 1, 2, 3
day: immediate response

→ **habituation**

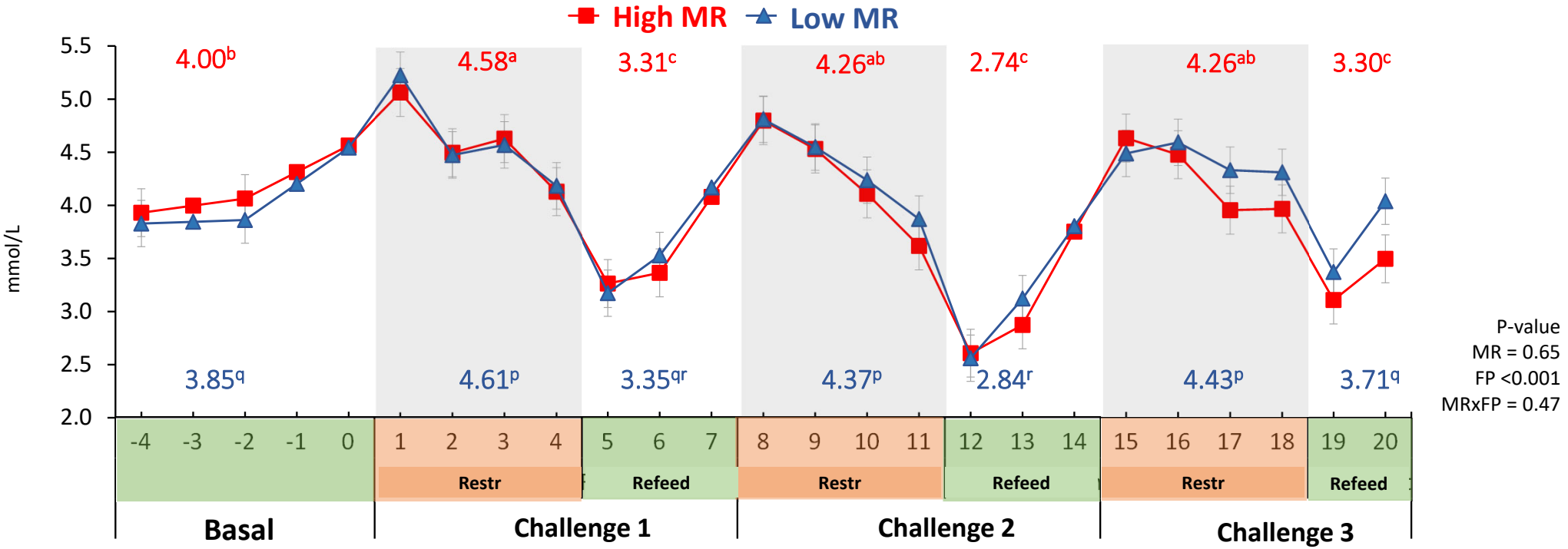
Full recovery

Plasma BHB



- Changes in **High MR** cows, but stable values in **Low MR** cows.
- **High MR**: ⇧ Restriction challenge 1, 2, 3 → **no sensitization nor habituation**
  day: response on second day
  ⇩ Refeeding challenge 1, 2, 3
  day: immediate response ***full recovery***

Plasma urea



- Restriction: ⇧ challenge 1 (+20%) > challenge 2 and 3 (+11%, +13%) → **habituation**
- Refeeding: ⇩ challenge 1, 2, 3 ***full recovery***

day: immediate response

- ✓ Cows with **different MR profiles** reacted differently (MY, plasma NEFA and BHB)
- ✓ **Partial MY and full metabolite recovery** observed after a short refeeding
- ✓ **Repeated** short-term restriction challenges and refeeding elicited performance and metabolic responses of different magnitude
  sensitization MY, constant response BHB, habituation NEFA & urea

Milk loss *in response to restriction worsened after the first challenge*
~ decreased metabolic response
to repeated exposure to underfeeding

Would the impact have changed
at a different stage of lactation?
Would additional challenges
trigger a different response?

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