Amino acid requirements of dairy cows

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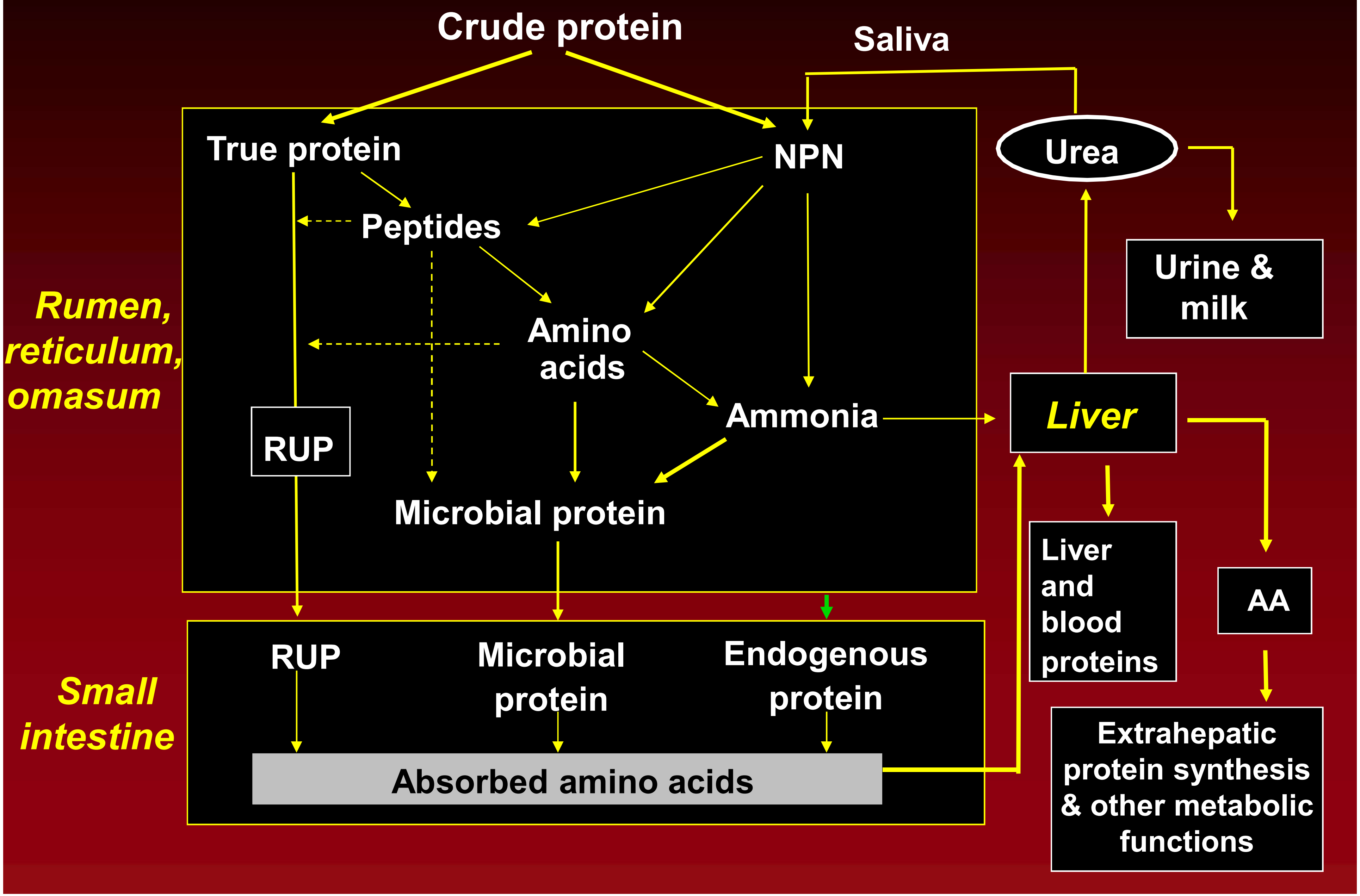
Presentation

- Ruminant protein digestion
- Sources of metabolizable AA for ruminants
- Chemistry and classification of AA
- Functions of absorbed AA
- Limiting AA in dairy cows
- Benefits of balancing for the most limiting AA
- Improving the predictability of nutritional models
- Future

Crude protein digestion in ruminants



Three sources of metabolizable AA for dairy cows

1. Microbial protein (50% or more of total MP)

   - ✓ Particle associated bacteria (PAB)
   - ✓ Fluid associated bacteria (FAB)
   - ✓ Protozoa
   - ✓ Fungi

Differ in content and profile of AA

Variation in AA composition of rumen bacteria and protozoa isolated from cattle (g/100 g AA)

	FAB[1]		PAB[1]		Protozoa[1]		Significant contrasts[2]	
EAA	Mean	CV	Mean	CV	Mean	CV	Bacteria vs. protozoa	FAB vs. PAB
Arginine	4.60	7.3	5.26	14.3	4.52	6.0	*	***
Histidine	1.83	18.0	1.96	12.2	1.82	11.0		
Isoleucine	5.53	6.6	5.70	7.0	6.47	6.1	****	
Leucine	7.60	5.0	8.17	2.3	7.78	4.6		****
Lysine	7.70	10.4	7.46	12.5	10.75	8.6	****	
Methionine	2.44	18.7	2.26	11.8	2.13	11.8		
Phenylalanine	5.10	7.3	5.62	10.6	5.61	8.3		**
Threonine	5.60	5.9	5.32	7.9	4.96	1.0	***	*
Tryptohan	1.35	18.7	1.28	20.5	---	0	---	
Valine	5.93	8.1	5.86	8.9	5.14	6.8	****	

[1] N = 16-22 for FAB, 6-7 for PAB, and 6-8 for protozoa; except for Trp where values are less
[2] *P* values (* <0.05, ** 0.01, *** <0.005, **** <0.001)

Sok et al. (2017)

Three sources of metabolizable AA for dairy cows

1. Microbial protein (50% or more of total MP)

   - ✓ Particle associated bacteria (PAB)
   - ✓ Fluid associated bacteria (FAB)
   - ✓ Protozoa
   - ✓ Fungi

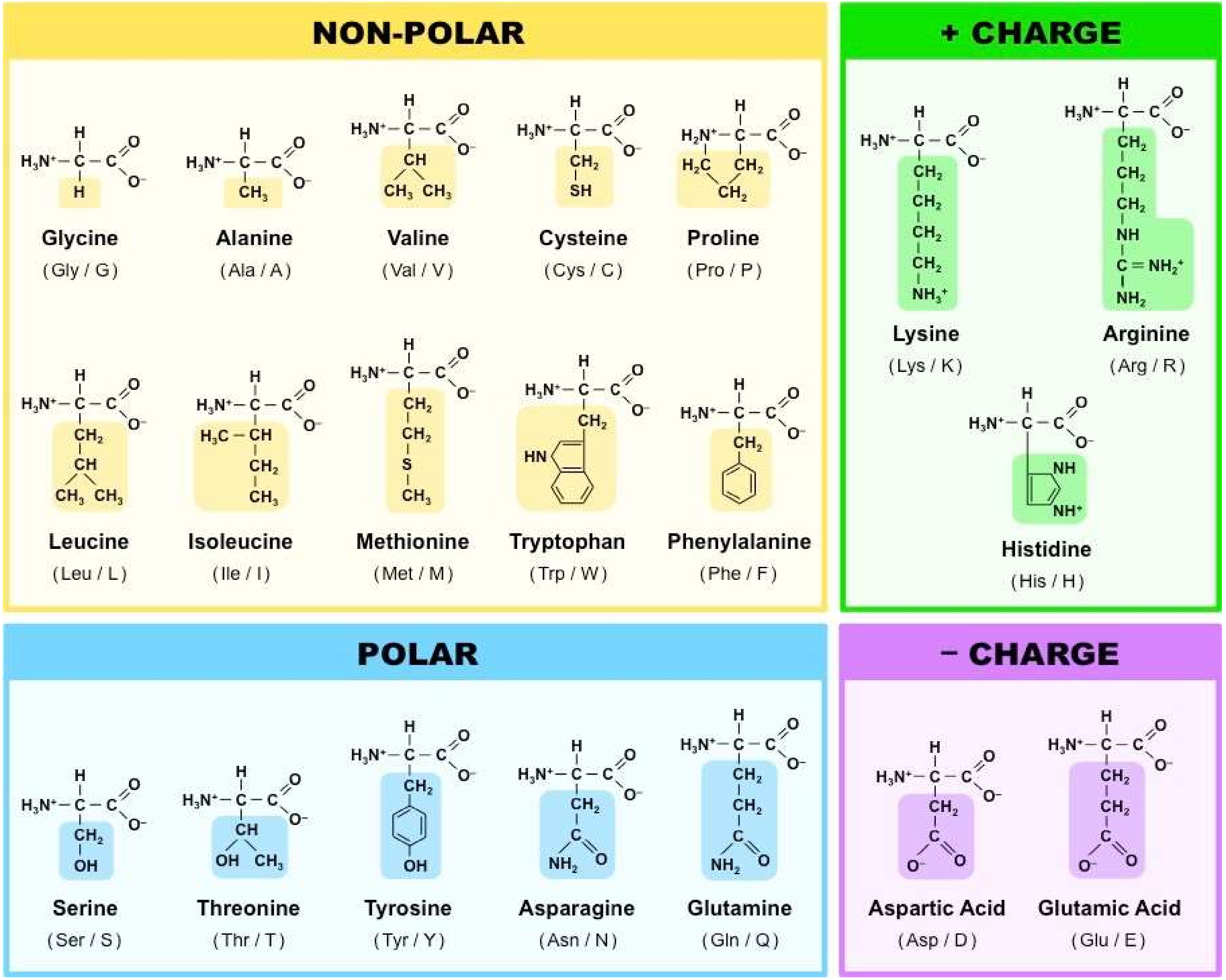
   Differ in content and profile of AA

2. RUP (45% or less of total MP)

   - ✓ Feeds vary in content of RUP
   - ✓ Feeds vary in AA composition
   - ✓ AA composition of dietary RUP depends on amount of RUP from each feedstuff and the AA composition of each feedstuff

3. Endogenous protein (about 5% of total MP)

Classification of AA according to chemical structure



Classification of AA according to dietary essentiality

Essential

1. Arginine
2. Histidine
3. Isoleucine
4. Leucine
5. Lysine
6. Methionine
7. Phenylalanine
8. Threonine
9. Tryptophan
10. Valine

Non-essential

1. Alanine
2. Aspartic acid
3. Asparagine
4. Cysteine
5. Glutamic acid
6. Glutamine
7. Glycine
8. Proline
9. Serine
10. Tyrosine

Classification of AA according to dietary essentiality

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Must be absorbed in amounts needed

Non-essential

1. Alanine
2. Aspartic acid
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2. Histidine
3. Isoleucine
4. Leucine
5. Lysine
6. Methionine
7. Phenylalanine
8. Threonine
9. Tryptophan
10. Valine

Do not have to be absorbed in amounts needed

Non-essential

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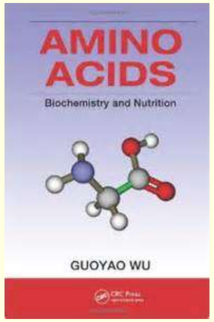
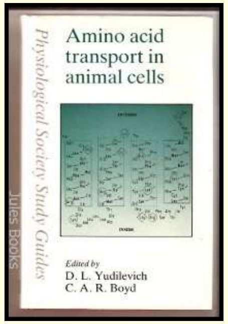


Functions of Amino Acids



Tissue proteins

Enzymes

Messenger proteins

Receptor proteins

Ion channel proteins

Milk proteins

Blood proteins

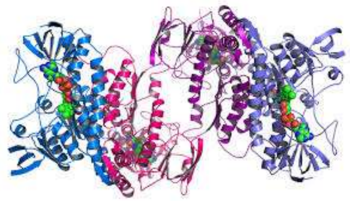
Connective
Epithelial
Nervous
Muscle

PROTEIN SYNTHESIS

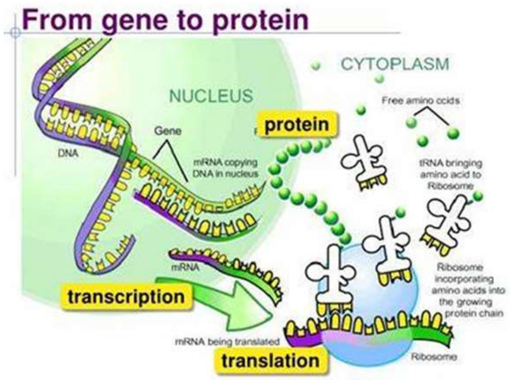
Albumins
Globulins
Fibrinogen
Regulatory proteins
Clotting factors

Amino Acids

Protein Synthesis



- AA are the building blocks for protein synthesis
- AA are joined together in “each protein” according to a predetermined genetic code

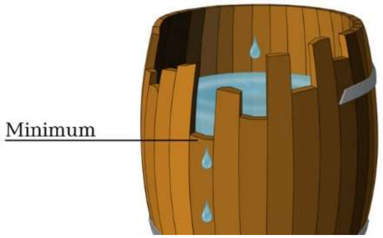


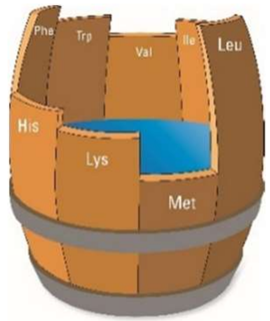
- Because protein synthesis is a genetically controlled event, the AA composition of a protein is the same every time its synthesized

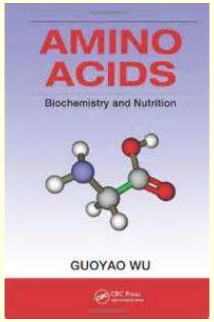
The amount of protein that can be synthesized every day depends on the supply of the most limiting AA, and the efficiency of use of absorbed AA for protein synthesis

Mitchell and Block (1946) formulated a conceptual framework with the assumption that the most limiting AA regulates protein synthesis and that addition of other AA don't have an effect

- Referred to as the single limiting EAA theory
- Usually depicted as the barrel-stave theory







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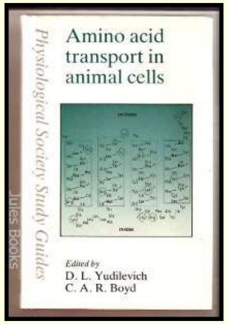


Tissue proteins | Enzymes | Messenger proteins | Receptor proteins | Ion channel proteins | Milk proteins | Blood proteins

Connective
Epithelial
Nervous
Muscle

PROTEIN SYNTHESIS

Albumins
Globulins
Fibrinogen
Regulatory proteins
Clotting factors

METABOLIC REGULATION

Amino Acids

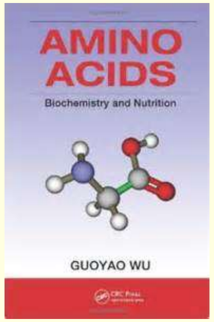
Role of AA in metabolic regulation

- It is well documented that extracellular AA concentrations and profiles not only affect intracellular AA concentrations and profiles, but also signaling proteins that regulate protein translational (synthesis) rates
- Intracellular AA concentrations can change the rate of protein translational machinery via signal transduction of the mammalian target of rapamycin (mTOR) or integrated stress response (ISR) pathways
- The mTOR pathway is an important regulator of anabolic metabolism, including protein synthesis, and its activation has been correlated with milk protein synthesis in both in vitro (using bovine primary mammary epithelial cells in mammary cell culture studies) and in some in vivo studies
- Interestingly, multiple EAA appear to independently have the ability to upregulate protein translational machinery and have a positive effect on milk casein synthesis, both in vitro and in vivo
- Amino acids that have been shown to have the strongest mTOR signaling properties are Met, Arg, Ile, Leu and Thr
- This area of research deserves more attention, and should be considered in lactation experiments designed to determine the ideal ratio of absorbed AA

Effects of jugular infused Leu and Ile or Met, Lys and His on cow performance

	Treatment				Effect (*P-value*)		
Item	CON	MLH	IL	MLH+IL	MLH	IL	MLH*IL
DM intake, kg/d	25.3	25.6	25.5	25.8	0.45	0.31	0.90
Milk, kg/d	47.3	47.8	49.5	50.3	0.31	**0.001**	0.86
Milk protein, %	3.10	3.19	3.04	3.21	**<0.001**	0.45	0.09
Milk protein, g/d	1458	1517	1498	1603	**<0.001**	**<0.01**	0.28
Milk fat, %	3.58	3.55	3.55	3.42	0.29	0.28	0.48
Milk fat, g/d	1675	1716	1744	1741	0.60	0.22	0.56
Protein efficiency, %	38.1	38.1	38.3	39.6	0.09	0.19	0.18
Mammary blood flow, L/h	807	665	928	905	0.22	**0.01**	0.37

Yoder et al. (2018)



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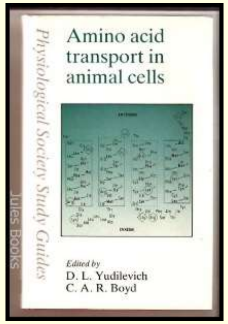

Tissue proteins

Enzymes

Messenger proteins

Receptor proteins

Ion channel proteins

Milk proteins

Blood proteins

Connective
Epithelial
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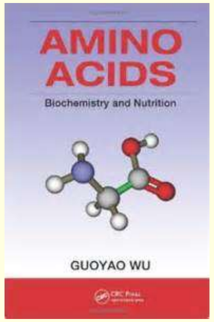
METABOLIC REGULATION

Amino Acids

NPN COMPOUNDS

Nitrogenous bases
Creatinine/creatine
Histamine
Polyamines, etc.

Known from swine and poultry research that an ideal profile of absorbed AA exists to meet these 3 sets of requirements



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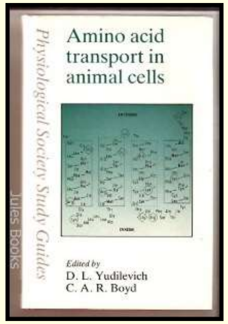

Amino Acids

PROTEIN SYNTHESIS

- Tissue proteins
  - Connective
  - Epithelial
  - Nervous
  - Muscle
- Enzymes
- Messenger proteins
- Receptor proteins
- Ion channel proteins
- Milk proteins
- Blood proteins
  - Albumins
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  - Regulatory proteins
  - Clotting factors

METABOLIC REGULATION

NPN COMPOUNDS

- Nitrogenous bases
- Creatinine/creatine
- Histamine
- Polyamines, etc.

Energy

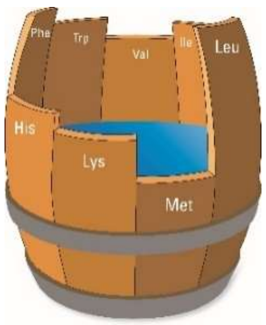
- Glucose
- Energy
- Fat

Limiting amino acids for dairy cows

Research has consistently shown for more than 40 years that Lys and Met are the most limiting AA for lactating dairy cows fed corn-based diets

Essential

1. Arginine
2. **Histidine**
3. Isoleucine
4. Leucine
5. **Lysine**
6. **Methionine**
7. Phenylalanine
8. Threonine
9. Tryptophan
10. Valine



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4. Cysteine
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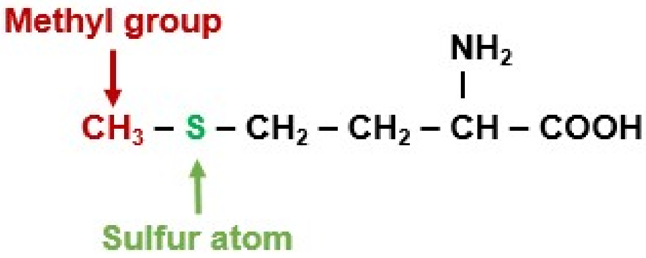
7. Glycine
8. Proline
9. Serine
10. Tyrosine

Lys, Met and His concentrations in milk, rumen microbes and feedstuffs (% of CP), relative to estimated ideal concentrations in MP

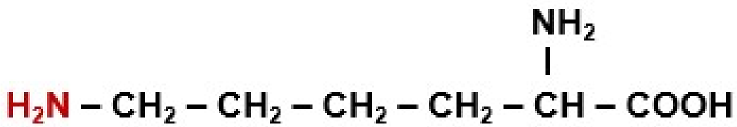
	Lys	Met	His		Lys	Met	His
Milk	7.7	2.7	2.7	Brewer's grains	4.1	1.7	2.0
Bacteria	7.6	2.3	1.9	Canola meal	5.6	1.9	2.8
Protozoa	10.7	2.1	1.8	Corn DDGS	2.2	1.8	2.5
				Corn gluten feed	2.7	1.6	2.9
Ideal (Lapierre)	7.5	2.5	2.7	Corn gluten meal	1.7	2.4	2.1
				Cotton seed	4.3	1.7	2.8
Alfalfa silage	4.4	1.4	1.7	Linseed meal	3.7	1.8	2.0
Corn silage	2.5	1.5	1.8	Soybean meal	6.3	1.4	2.8
Grass silage	3.3	1.2	1.7				
				Blood meal	9.0	1.2	6.4
Barley	3.6	1.7	2.3	Feather meal	2.6	0.8	1.2
Corn	2.8	2.1	3.1	Fish meal	7.7	2.8	2.8
Wheat	2.8	1.6	2.4	Meat meal	5.4	1.4	2.1

Most limiting AA for lactating dairy cows

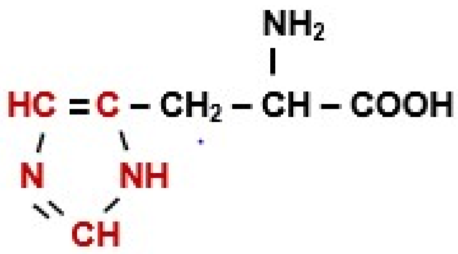
- **Methionine**



- **Lysine**



- **Histidine**



Major functions of lysine, methionine and histidine

Lysine	• **Protein synthesis** • Regulation of nitric oxide synthesis; antiviral activity; protein methylation and acetylation • Via synthesized hydroxylysine: structure and function of collagen
Methionine	• **Protein synthesis** • Via synthesized S-Adenosylmethionine (SAM): methylation of proteins and DNA; synthesis of creatine, epinephrine and polyamines; regulation of gene expression; one-carbon-unit metabolism • Via synthesized homocysteine: oxidant; inhibition of nitric oxide synthesis • Via synthesized betaine: Methylation of homocysteine to methionine, one-carbon unit metabolism • Via synthesized taurine: antioxidant; anti-inflammatory agent; regulator of intracellular osmolality; conjugation with bile acids (modulates digestion and absorption of fat and fat-soluble vitamins) • Via synthesized glutathione: Synthesis of prostaglandins, signal transduction, gene expression, cell proliferation (including hepatocytes, lymphocytes, intestinal epithelial cells), elicitation of immune responses (activation of T-lymphocytes, polymorphonuclear leucocytes, and for cytokine production), oocyte development, sperm production and maturation
Histidine	• **Protein synthesis** • Protein methylation; hemoglobin structure and function; anti-oxidative dipeptides; one-carbon metabolism. • Via synthesized histamine: vasodilator; activation of central acetylcholine secretion; stimulation of secretions by the gastrointestinal tract

Balancing for Lys and Met

The requirement for Lys and Met can be met in two ways:

1) Feed a diet higher in RUP…the conventional (old) way
   - ✓ "Shotgun" approach
   - ✓ Leads to a surplus of other amino acids
   - ✓ Not consistent with feeding for maximal N and productive efficiency
   - ✓ Usually is not effective

Effects of supplemental RUP on Lactating Dairy Cow Performance: A 12-Year Literature Review

"The data strongly suggest that increased RUP per se in dairy cow diets, which often results in a decrease in RDP and a change in absorbed AA profiles, does not consistently improve lactational performance"

Santos et al. (1998)

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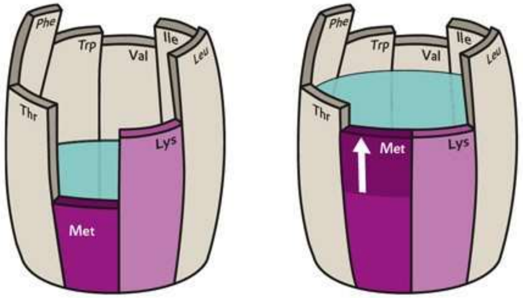
2) Select high Lys-containing protein supplements (or feed a RP-Lys supplement to meet targeted concentrations of Lys in MP), supplement with a RP-Met supplement (or MetaSmart) to meet targeted concentrations of Met in MP, and reduce dietary RUP and predicted supplies of MP where possible (after early lactation)…this is the better method

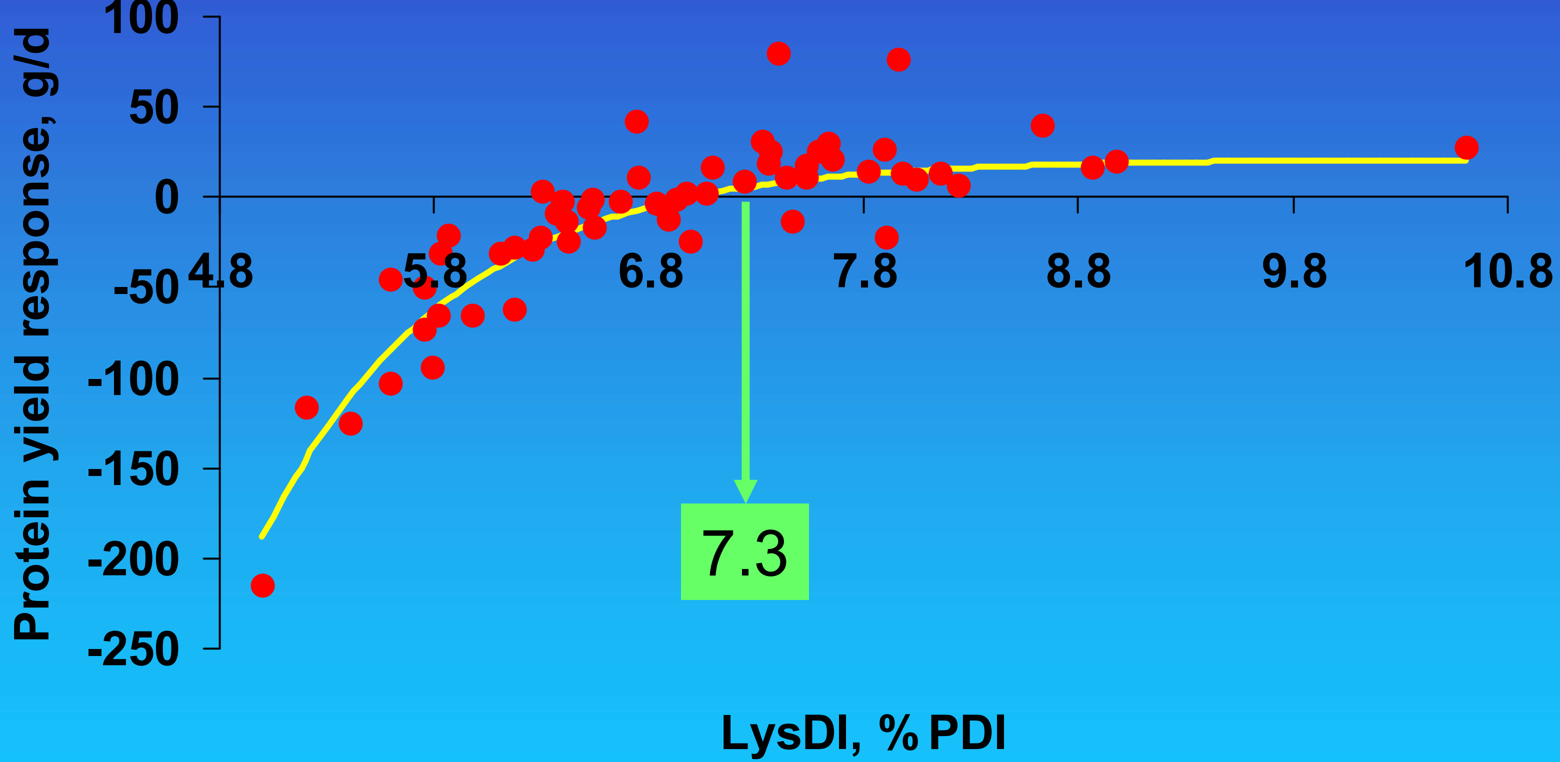
Amino acid balancing

Definition

A deliberate attempt, through selective use of protein supplements and RP-AA supplements, to achieve an amount and profile of absorbed AA that comes as close as possible to meeting the cows requirements for optimal health and performance without wasting AA

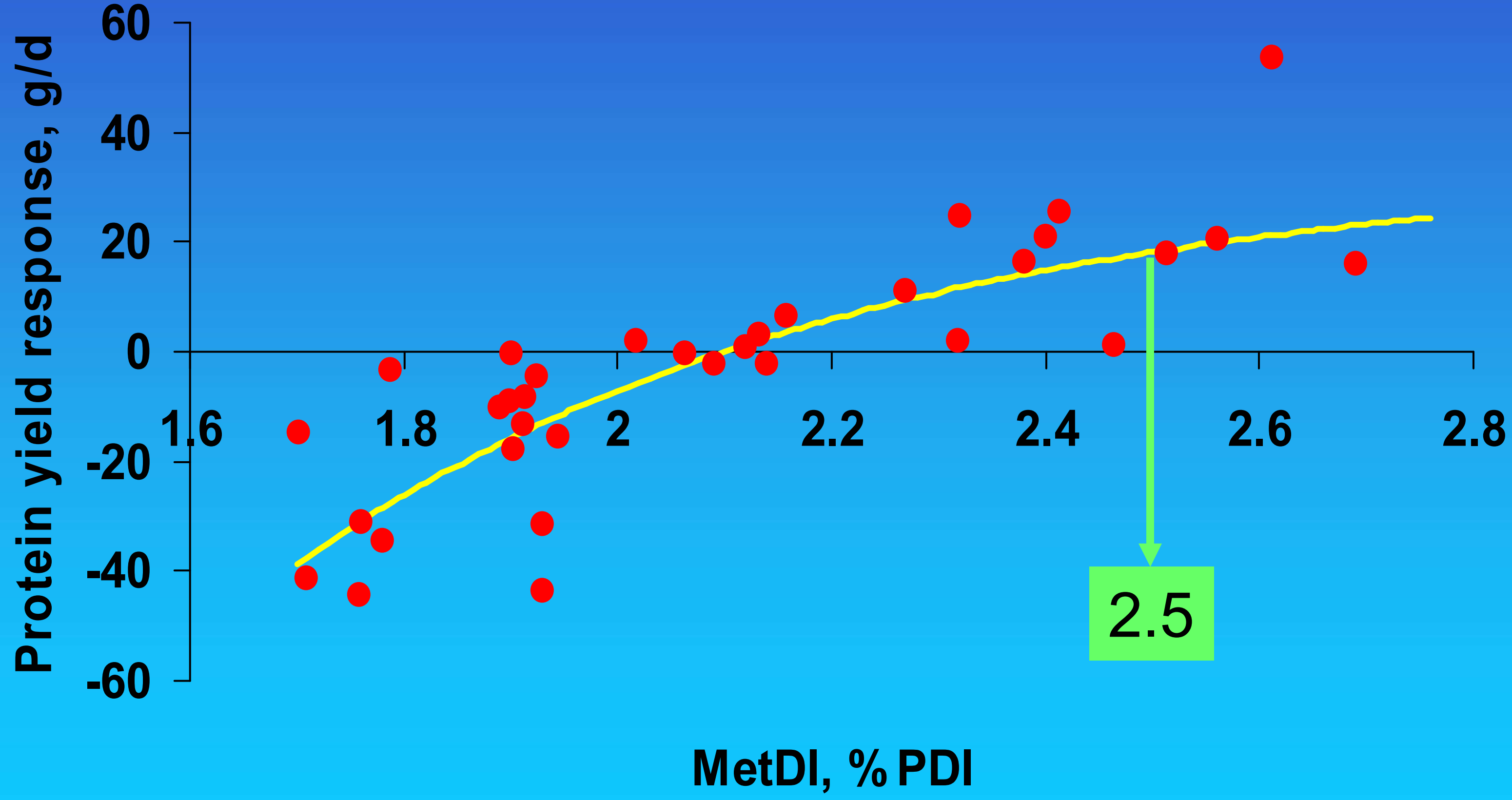


Response to lysine



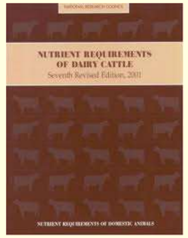
From 557 cows Rulquin et al. (1993)

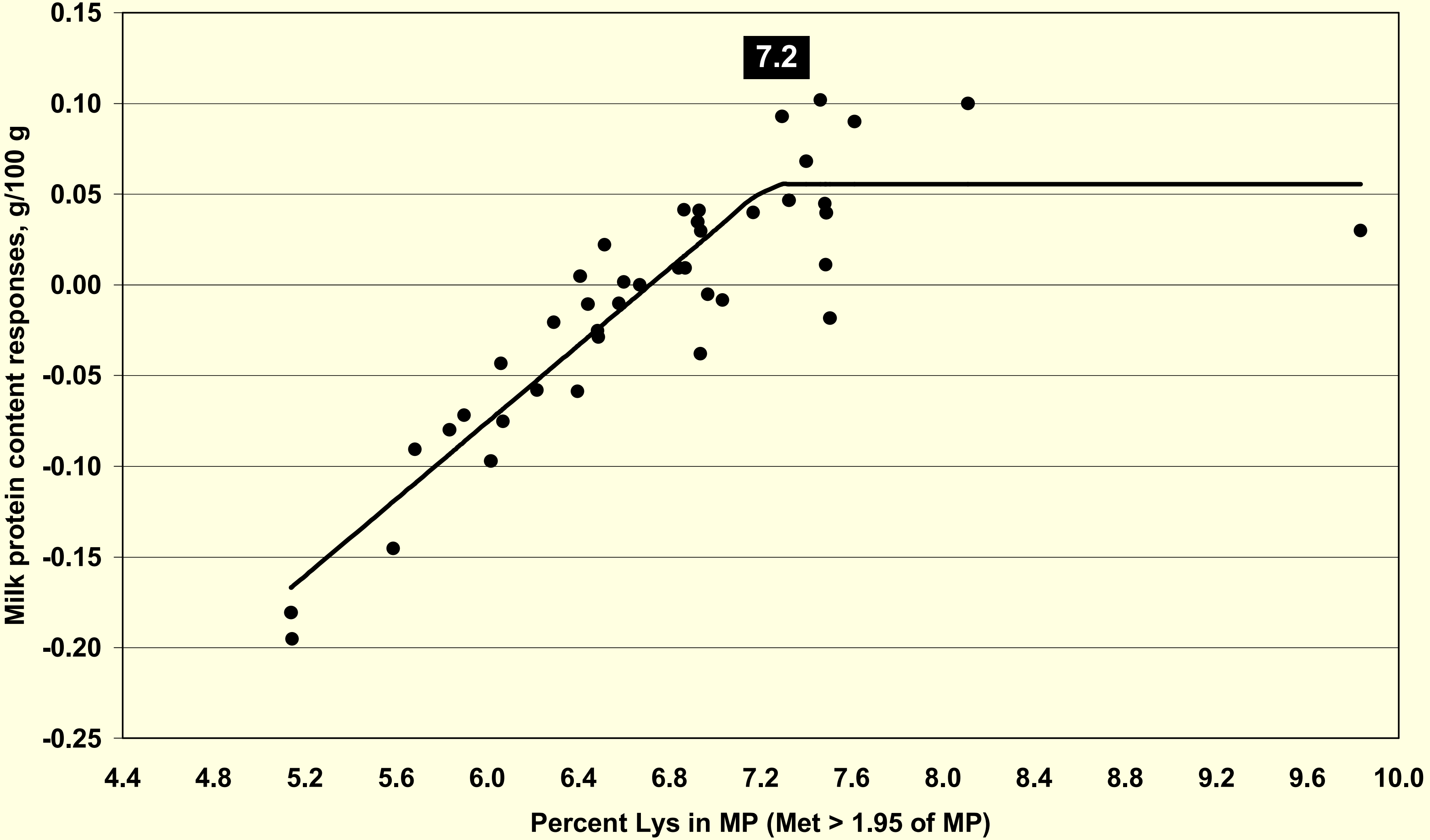
Response to methionine



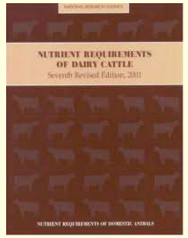
From 265 cows Rulquin et al. (1993)

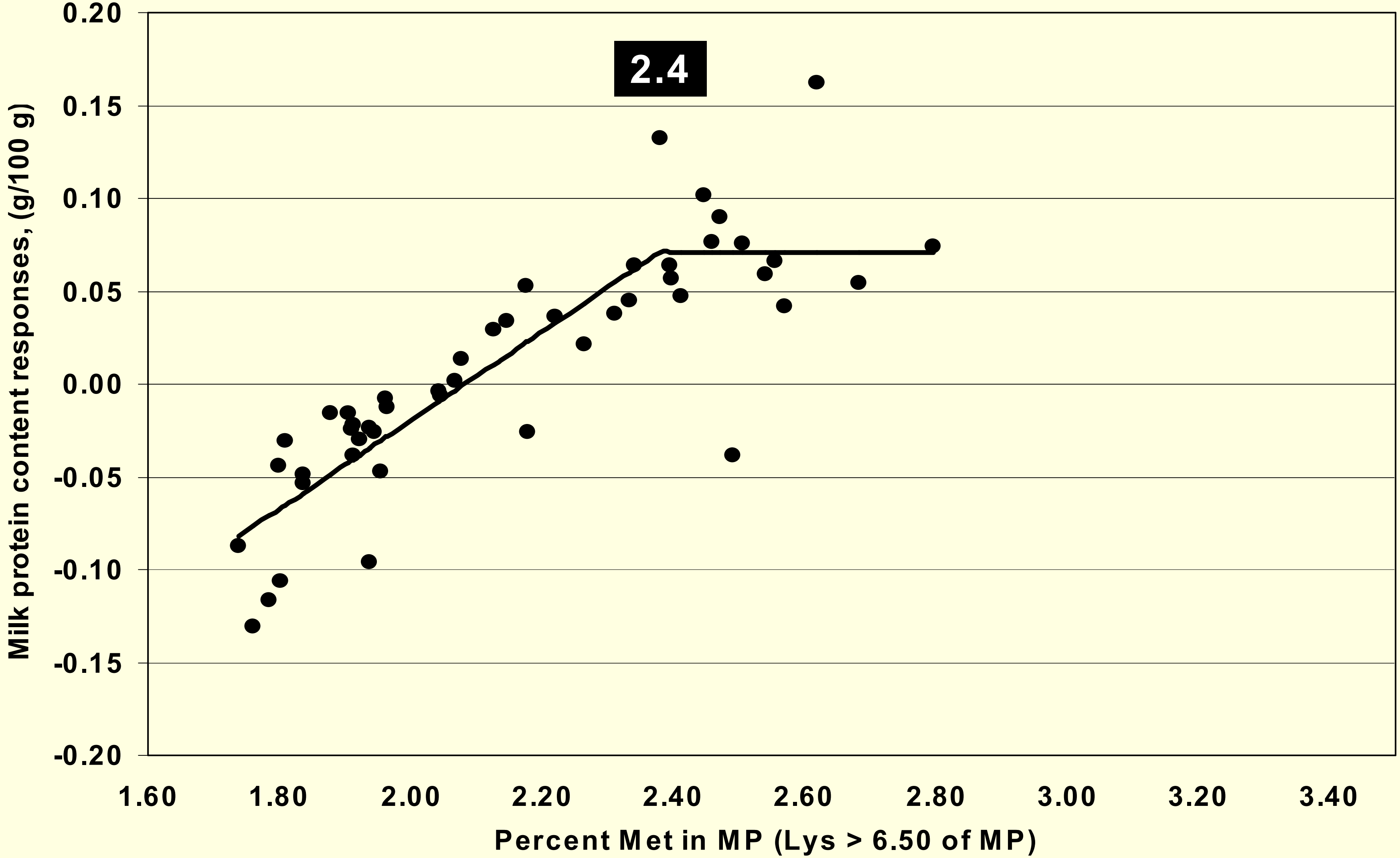
Optimum content of Lys in MP (NRC, 2001)





Optimum content of Met in MP (NRC, 2001)





Required concentrations of Lys and Met in MP for maximal content of milk protein

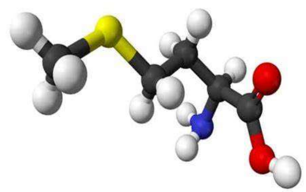
Model	Lys	Met	Optimal Lys/Met ratio
NRC (2001)			
Original release[1]	6.80	2.29	**2.97**
Revised v.1.1.9[3]	6.83	2.28	**3.00**
CPM-Dairy[2]	7.46	2.57	**2.90**
CNCPS			
Prior v6.1[2]	6.68	2.40	**2.78**
v6.1[3]	6.97	2.53	**2.75**
v6.5[4]	7.00	2.60	**2.69**

[1] Schwab et al. (2009), [2] Whitehouse et al. (2009), [3] Whitehouse et al. (2013), [4] Van Amburgh et al. (2015)

Benefits of AA balancing for the cow

Avoid the chance/risk of the most limiting AA being the most limiting nutrients for health, milk component yields, and reproduction

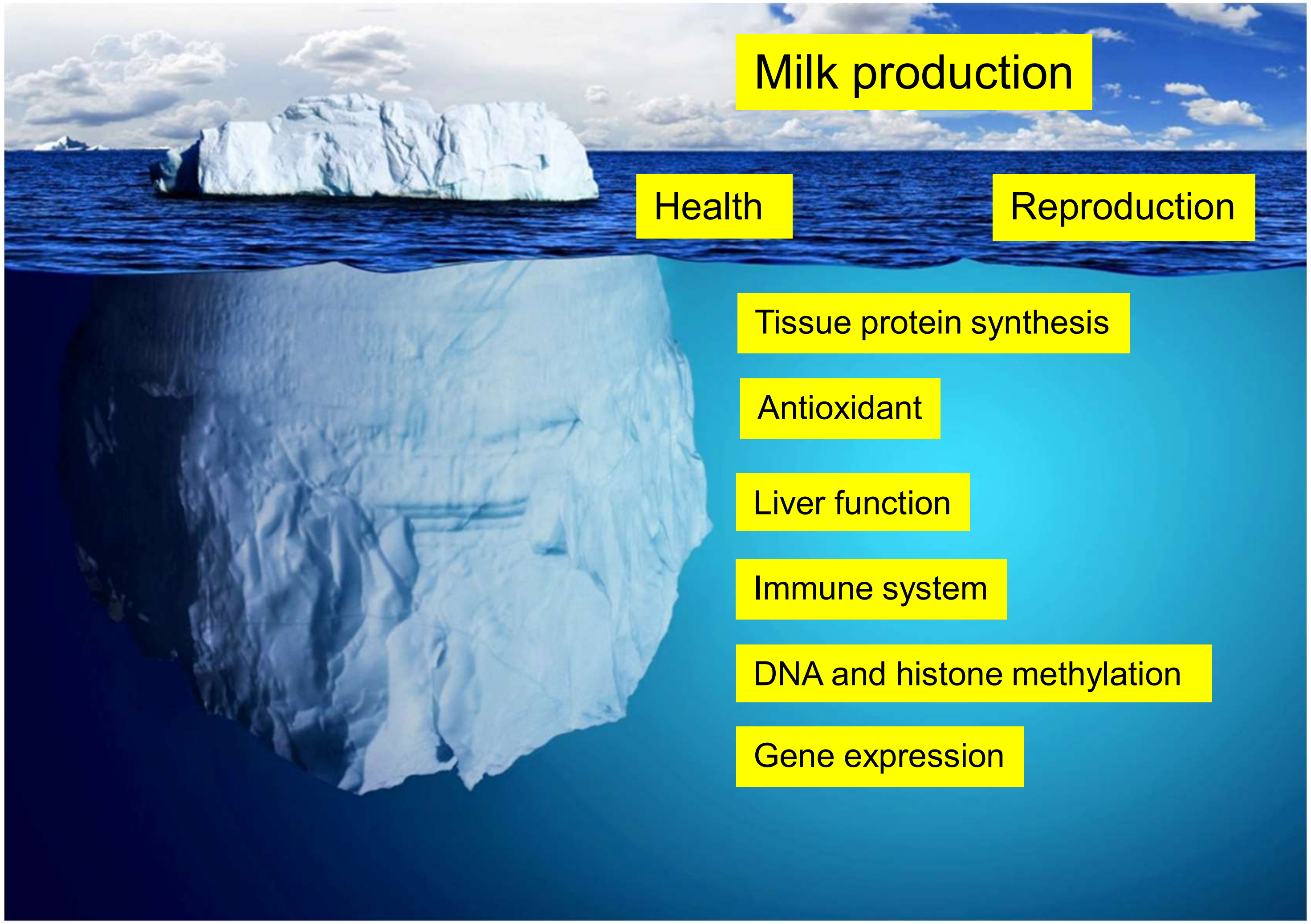
What happens when supplemental Met is provided to transition cows that are more Met deficient than Lys deficient?



- Increased feed intake
- Increased milk yield and milk protein and fat concentrations
- Reduced incidence of ketosis
- Improved liver function
- Improved immune function
- Decreased inflammation
- Reduced oxidative stress
- Larger embryos and decreased pregnancy loss
- Altered metabolism in offspring
- Larger birth weights of offspring
- Higher growth rates of offspring
- Higher milk production of offspring

Clear evidence that fetal programming is occurring

These results confirm that Met has functions beyond being building blocks for protein synthesis



A summary of some early lactation cow experiments involving RP-Lys and RP-Met

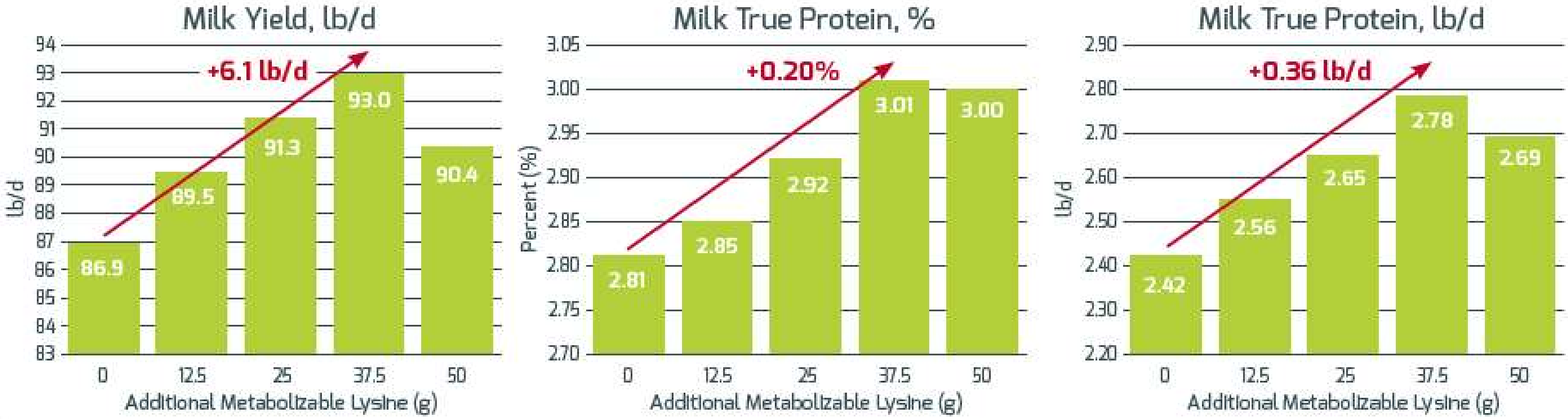
Ave. milk response = 3.8 kg

Week of lactation	RPAA used	Conducted by	Milk, kg/d		
			Cont	Trt-1	Trt-2
0 - 8	LM	Julien et al. (1999)	45.7	50.3	
0 - 6	LM	Robinson et al. (1996)	33.8	35.8	
0 - 4	LM	Sniffen et al. (1999)	43.4	47.9	
0 - 6	L, LM	Sniffen et al. (1999)	42.9	45.3	49.4
0 - 6	L	Nocek et al. (1999)	37.1	41.1	
0 - 4	LM	Chalupa et al. (1999)	32.6	35.5	
0 - 10	LM	Harrison et al. (1995)	34.7	38.1	39.0

What happens when more adequate supplies of Lys are provided in the presence of adequate Met?

Feeding incremental amounts of Smartamine ML confirmed improvements in milk and milk protein (% and lb/d)

METHODOLOGY
- 10 Multiparious Holstein cows 106 ±17 d
- Replicated Latin square
- 14 d period
- AMTS basal diet evaluation = 5.5% (149.3 g/d) MP-Lys and 2.4% (63.8 g/d) MP-Met, 2693 g/d total MP, 63.0 Mcal/d ME
- Smartamine M was used to ensure MP-Met was not limiting
- Samples on days 12, 13, 14



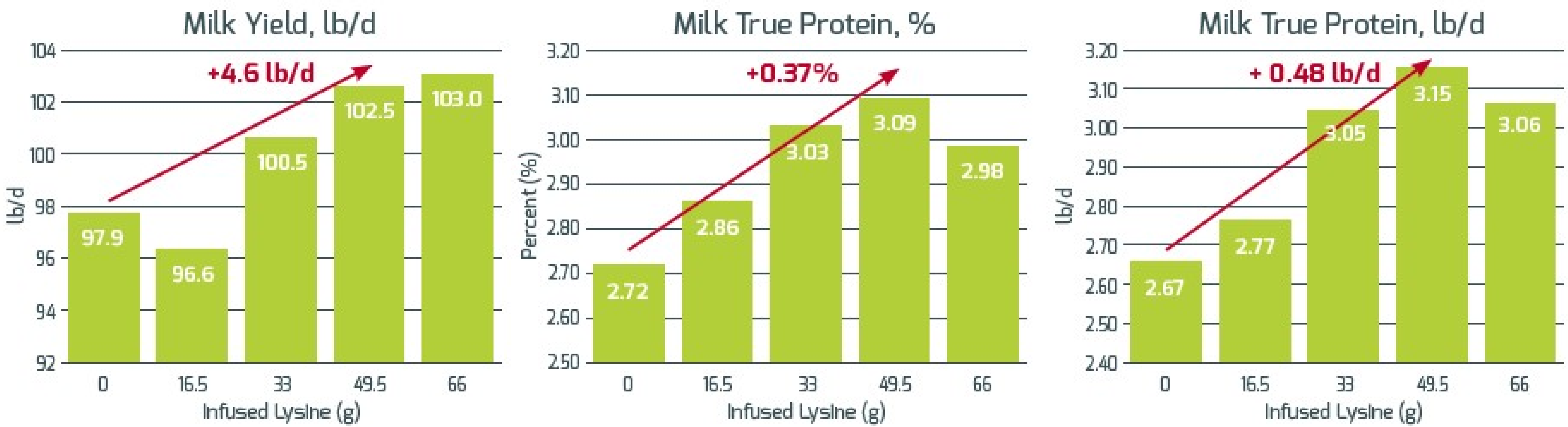
Piepenbrink, M.S., et al. 1999. U of NH. Importance of dietary concentrations of absorbable lysine on maximizing milk protein production of mid-lactation cows.

What happens when more adequate supplies of Lys are provided in the presence of adequate Met?

Increasing lysine improved milk and milk protein (% and lb/d)

METHODOLOGY

- 2 primiparous and 3 multiparous Holsteins, 63 to 126 DIM
- Balanced split-plot 5X5 Latin square design
- 14 d period
- Lysine-deficient basal diet supplemented with Smartamine® M to ensure lysine was first limiting
- AMTS basal diet evaluation = 5.3% (152.9 g/d) MP-Lys and 2.8% (79.2 g/d) MP-Met, 2876 g/d total MP, 62.8 Mcal/d ME
- Measurements taken during last 7 days



McLaughlin, A. M., et al. 2002. Evaluation of ruminally unprotected lysine as a source of metabolizable lysine for high-producing cows. JDS Vol. 85, Suppl. 1:23.

Benefits of AA balancing

1. Increased yield of milk and milk components
    a. Increased milk yield, particularly in early lactation cows (2 to 4.0 kg/d more are common)
    b. Increased milk components (0.10 to 0.20% unit increases in protein and 0.10 to 0.15% unit increases in fat are common)
2. Healthier (and more productive) transition cows
3. Reduced need for dietary RUP and potential for decreased feed costs…supported by research and field experience

Effect of different Lys and Met concentrations in MP on amounts of MP and RUP required to provide 180 g of MP-Lys and 60 g of MP-Met[1]

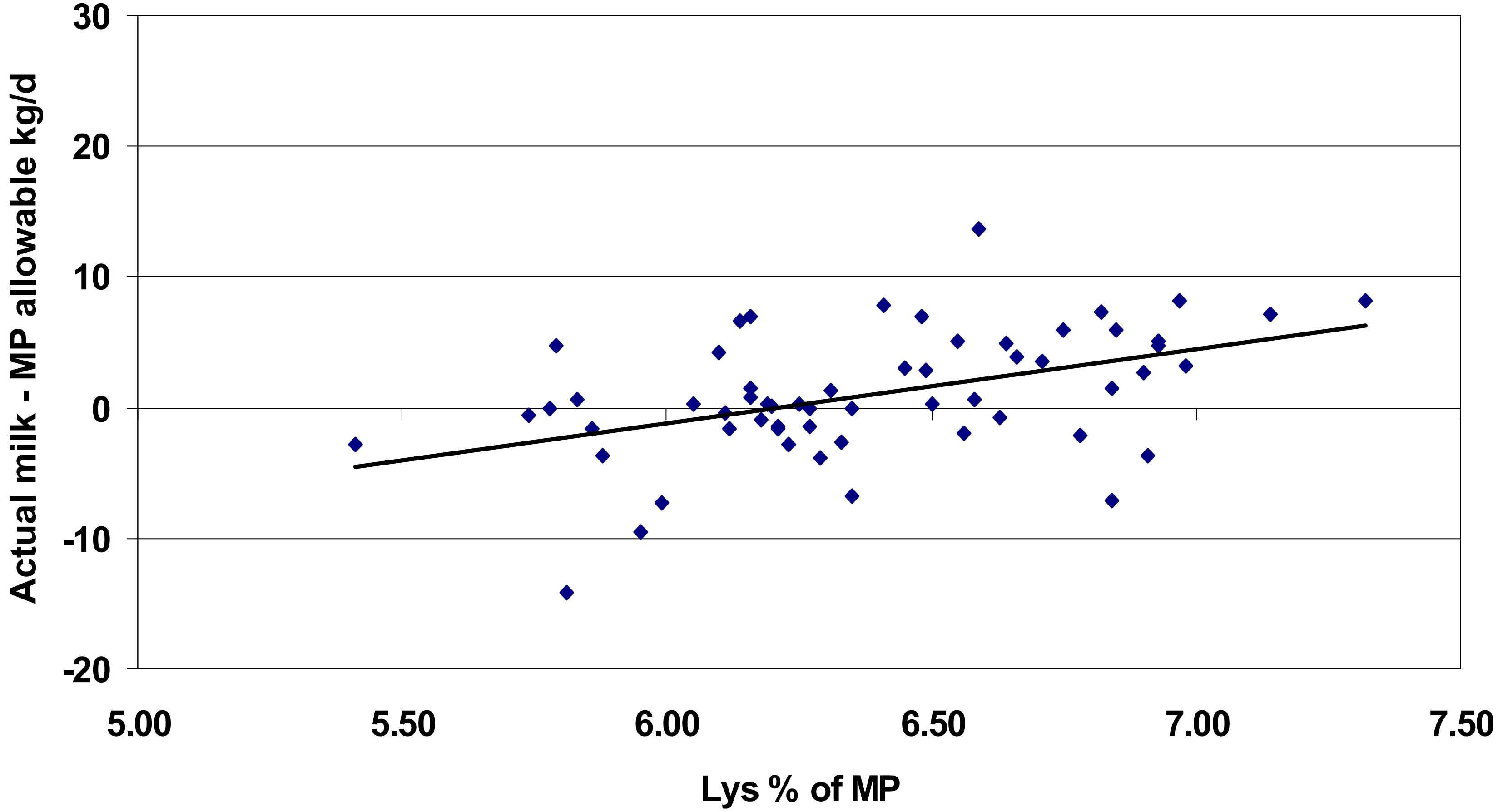
Lys in MP (%)	MP required (g/d)	Microbial MP[2] (g/d)	Endogenous MP (g/d)	**Required MP from RUP (g/d)**	**Required RUP[3] (g/d)**	**Required RUP (% of DM)**
5.7/1.9	3157	1390	121	**1646**	**2058**	**8.1**
6.0/2.0	3000	1390	121	**1489**	**1861**	**7.3**
6.3/2.1	2857	1390	121	**1346**	**1683**	**6.6**
6.6/2.2	2727	1390	121	**1216**	**1520**	**6.0**
6.9/2.3	2609	1390	121	**1098**	**1372**	**5.4**

[1] NRC (2001) was used as the model of choice. DM intake was assumed to be 25.5 kg.

[2] Assumed that feeding less RUP and more carbohydrates would not increase microbial MP supply, which is not correct. Microbial MP supply should increase slightly in moving from diet 1 to diet 5. Result: balancing for more optimal amounts of Lys and Met in MP has greater effect on reduced need for RUP than indicated.

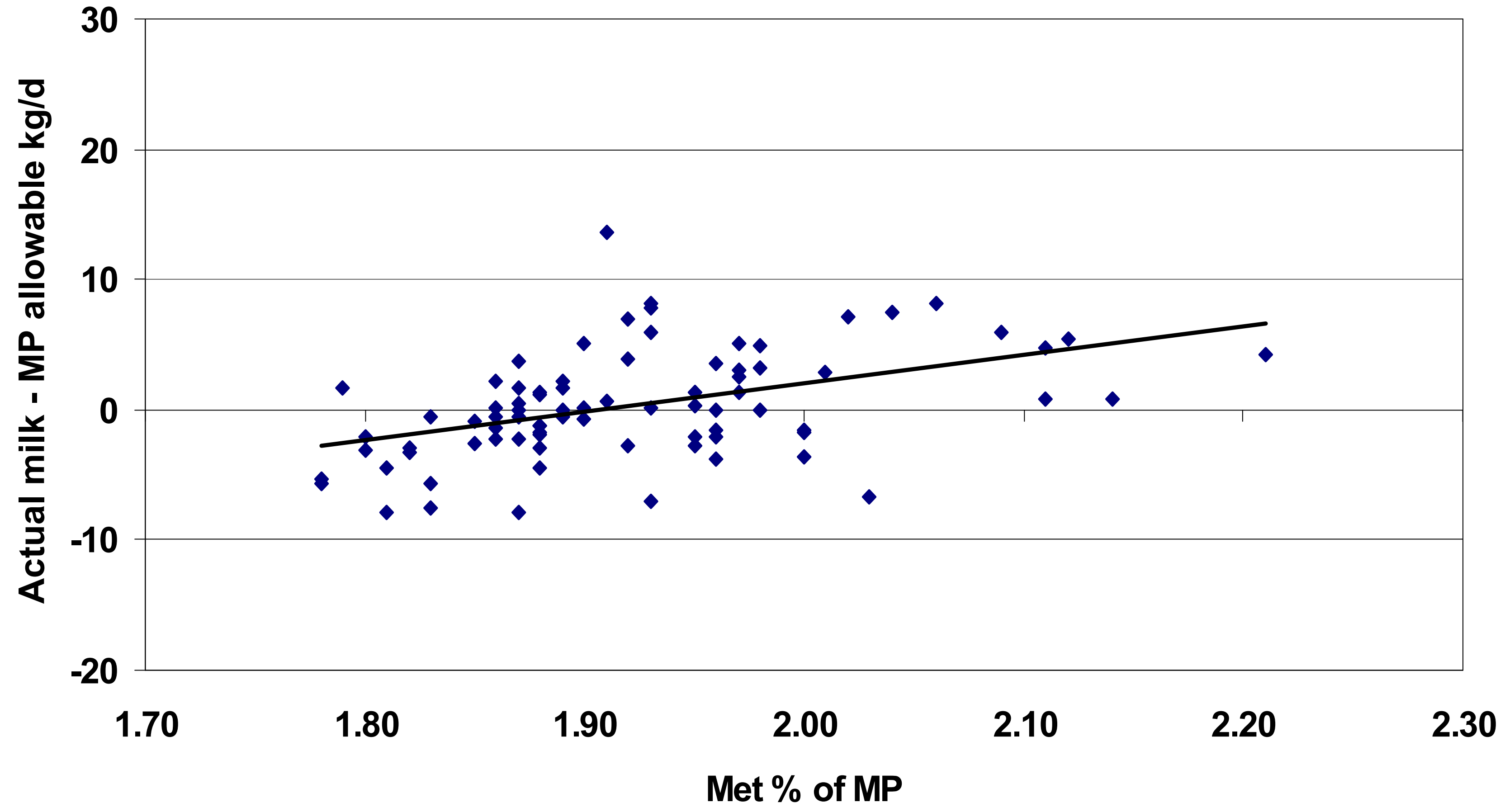
[3] Assumed that microbial protein has an average RUP digestibility of 80%, which is what NRC (2001) assumes.

Differences between actual milk and MP allowable milk vs. predicted concentrations of Lys in MP using NRC (2001)



Schwab and Whitehouse (2002)

Differences between actual milk and MP allowable milk vs. predicted concentrations of Met in MP using NRC (2001)



Schwab and Whitehouse (2002)

Replacing some highly digestible RUP (mixture of blood, poultry and feather meal) with Smartamine M

	High RUP	Low RUP	Low RUP + Met
Corn silage	37.5	37.5	37.5
Alfalfa silage	12.5	12.5	12.5
Corn	19.8	22.4	22.3
Soybean meal, solvent	9.4	7.7	7.7
Cotton seed	8.4	8.4	8.4
Soy hulls	3.4	3.4	3.4
Blood meal	2.0	1.8	1.8
Hydrolyzed feather meal	1.0	0.4	0.4
Poultry meal	1.0	0	0
Urea	0	0.19	0.19
Smartamine M			0.042
Rhodimet AT88			8.084

	High RUP	**Low RUP**	**Low RUP + Met**
CP, %	18.3	16.9	16.9
MP-Lys, g/d	183	174	176
MP-Met, g/d	49	46	53
Lys, % MP	6.4	6.6	6.6
Met, % MP	1.7	1.7	2.0
Lys/Met in MP	3.8/1	3.8/1	3.3/1

Noftsger and St-Pierre (2003)

Replacing some highly digestible RUP (mixture of blood, poultry and feather meal) with Smartamine M

Item	High RUP	Low RUP	Low RUP + Met
DM intake, kg/d	23.3	23.2	23.6
Milk, kg/d	46.2[a]	42.9[b]	46.6[a]
Milk protein, %	2.98[b]	2.99[b]	3.09[a]
Milk protein, g/d	1380	1280	1440
Milk fat, %	3.64	3.66	3.73
Milk fat, g/d	1670	1570	1710
Milk N/N intake,%	31.1[b]	31.7[b]	35.0[a]
Excreted N/N intake	2.25[a]	2.19[a]	1.89[b]

Noftsger and St-Pierre (2003)

Effect of feeding Smartamine M and MetaSmart to lactating cows on milk production and N utilization

Ingredient	Traditional protein (TP)	Low Protein (LP)	LP + MetaSmart	LP + Smartamine
Alfalfa silage	25.4	25.4	25.4	25.4
Corn silage	34.7	34.7	34.7	34.7
High moisture corn	14.9	21.5	21.5	21.5
Solvent SBM	3.7	8.7	8.7	8.7
Distillers dried grains	7.6	0	0	0
Expeller soybean meal	4.0	0	0	0
Premix	9.7	9.7	9.7	9.7
CP, %	**16.9**	**15.7**	**15.7**	**15.7**
MP-Lys, g/d	**160**	**161**	**161**	**161**
MP-Met, g/d	**48**	**45**	**54**	**54**
Lys/Met in MP	**3.3**	**3.6**	**3.0**	**3.0**

Chen et al (2009)

Effect of feeding Smartamine M and MetaSmart to lactating cows on milk production and N utilization

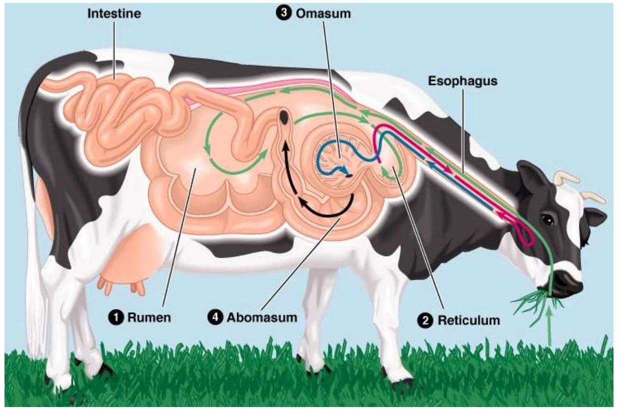
Item	Traditional protein (TP)	Low Protein (LP)	LP + MetaSmart	LP + Smartamine
DMI, kg/d	24.7	24.9	25.7	24.6
Milk, kg/d	41.2	41.8	42.1	41.7
Protein, %	3.05[b,c]	3.03[c]	3.19[a]	3.15[a,b]
Protein, g/d	1250	1240	1300	1330
Fat, %	3.85	3.52	3.93	3.77
Fat, g/d	1610	1420	1600	1620
ECM, kg/d	39.4[a,b]	37.9[b]	41.0[a]	40.2[a,b]
Milk/DMI	1.67	1.69	1.68	1.69
ECM/DMI	1.61[a,b]	1.54[b]	1.59[a,b]	1.63[a]
MUN, mg/dL	13.2[a]	10.0[c]	10.2[c]	11.2[b]
Milk N/feed N, %	30.9	32.7	32.7	34.1

Chen et al (2009)

Improving the predictability of nutritional models regarding AA passage to the small intestine and AA requirements

This has been challenging, frustrating and slow

This complexity of protein digestion has created huge challenges for accurately predicting AA passage to the small intestine



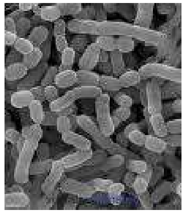
Overcoming these challenges is an important first step to accurately predicting AA requirements

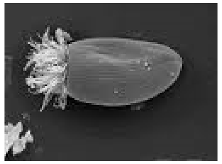
This complexity of AA metabolism has created huge challenges for accurately predicting AA requirements

- Definition of requirements is model dependent.
- To adequately predict the AA requirements of a cow across a range of body weights, stages of lactation, and milk yields and milk component concentration, mechanistic (factorial-based) models have to consider all of the irreversible losses that each AA encounters as they move from absorption to their presence in tissue gain, milk protein and fetal development, and they must do that accurately.

The complexity of rumen protein digestion has created challenges for predicting RDP requirements

RDP is needed
for
rumen microorganisms

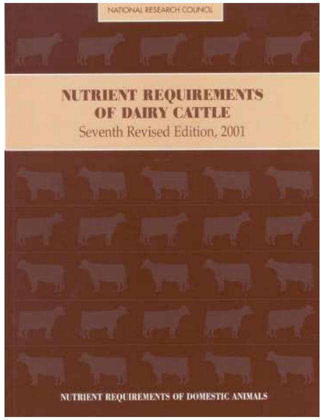




Amino acids are
needed
for cows

Fortunately, a lot of progress has been made in predicting AA supply and requirements, particularly in last 20 years

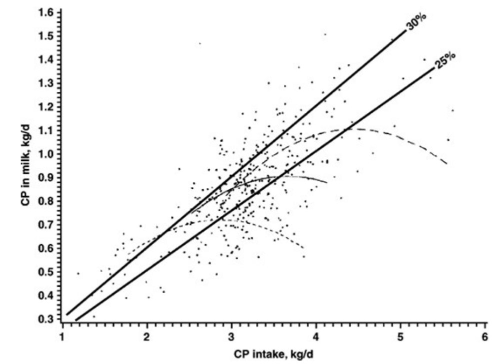
The New Dairy NRC Model is scheduled to be released in 2020!

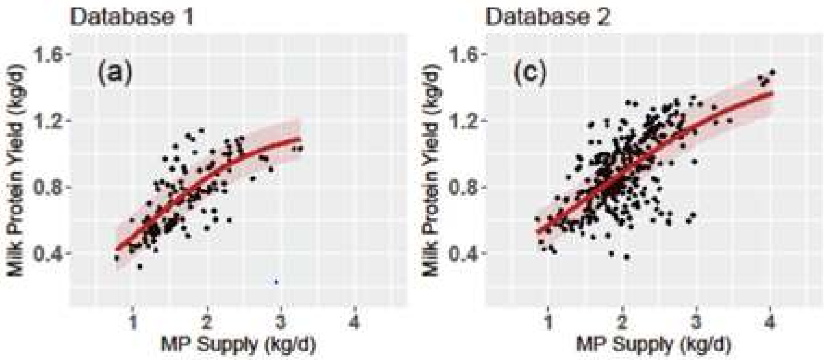


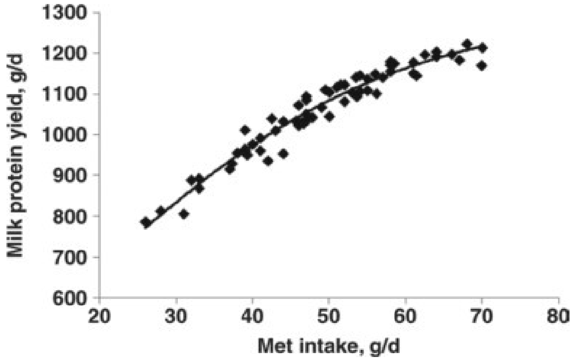
SUMMARY

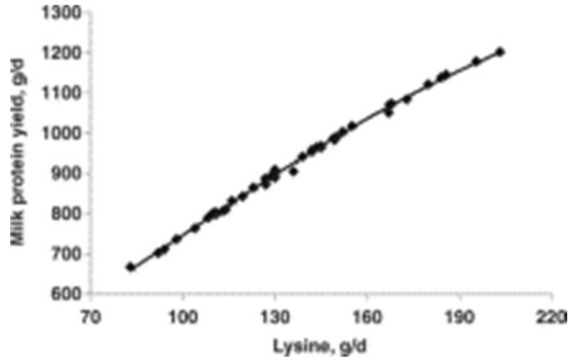
- AA balancing is increasingly being accepted in dairy cow nutrition
- Several reasons:
  1) Growing awareness of limiting AA and the impact of meeting requirements on improved dairy herd performance and reduced protein feeding
  2) An increased understanding of AA metabolism
  3) Continued improvement of ration formulation and diet evaluation models
  4) Increased availability of RPAA supplements
- Achieving “success” requires:
  1) “Letting go” of balancing diets for CP and instead, balancing for rumen-degradable feed protein (RDP) and the most limiting AA

As expected, large data summaries indicate the relationship between intake of the most limiting AA and milk protein yield is much better than the relationship between CP or MP intake and milk protein yield









VandeHaar and St-Pierre (2006), Vyas and Erdman (2009), and Moraes et al. (2018)

SUMMARY

- AA balancing is increasingly being accepted in dairy cow nutrition
- Several reasons:
  1) Growing awareness of limiting AA and the impact of meeting requirements on improved dairy herd performance and reduced protein feeding
  2) An increased understanding of AA metabolism
  3) Continued improvement of ration formulation and diet evaluation models
  4) Increased availability of RPAA supplements
- Achieving “success” requires:
  1) “Letting go” of balancing diets for CP and instead, balancing for rumen-degradable feed protein (RDP) and the most limiting AA
  2) Using reliable estimates of AA bioavailability for RPAA supplements
  3) Using ration formulation programs with optimization capability
  4) And where possible, using “cow feedback” to correct for model prediction errors

Future is bright

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