The Muscle Anabolic Threshold Concept for an Adapted and Efficient Nutrition during Catabolic States

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Human Nutrition Unit
Metabolism & Health

NuTriM
Nutrition metabolisms & muscle mass

INRA
SCIENCE & IMPACT

CLERMONT
UNIVERSITÉ

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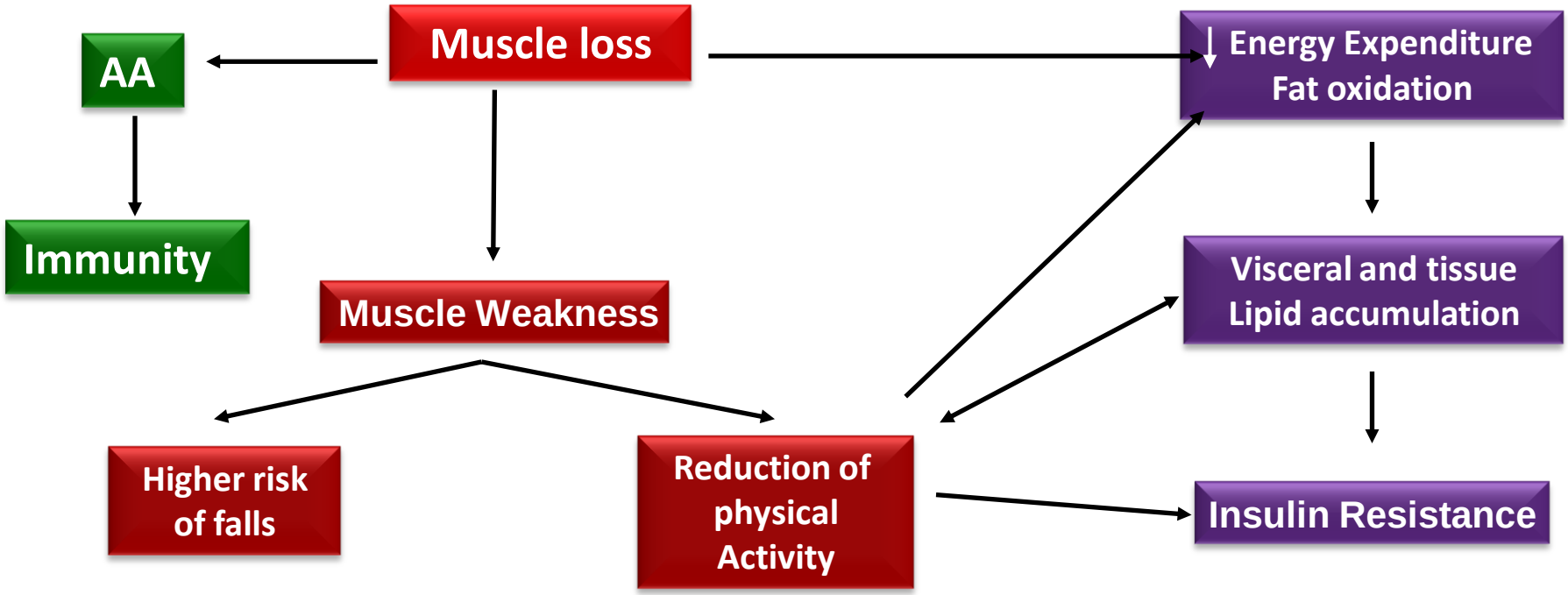
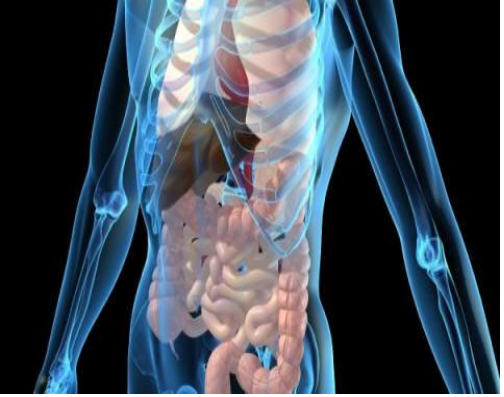
Dardevet Dominique, Rémond Didier, Peyron Marie-Agnès, Papet Isabelle, Savary-Auzeloux Isabelle and Mosoni Laurent.

Impact of muscle loss in health and diseases

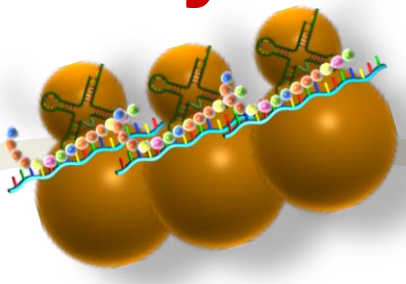


Frailty, Loss of Autonomy ↗ Morbidity, ↗ Mortality

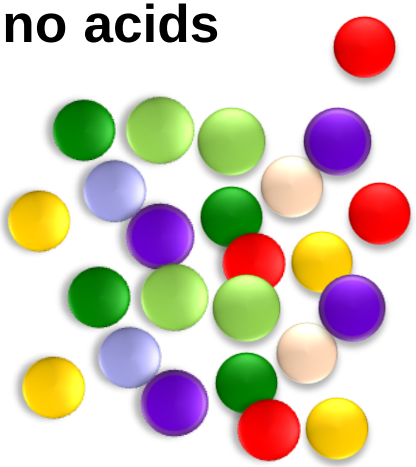


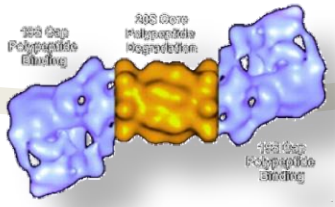
Protein metabolism

Protein Synthesis

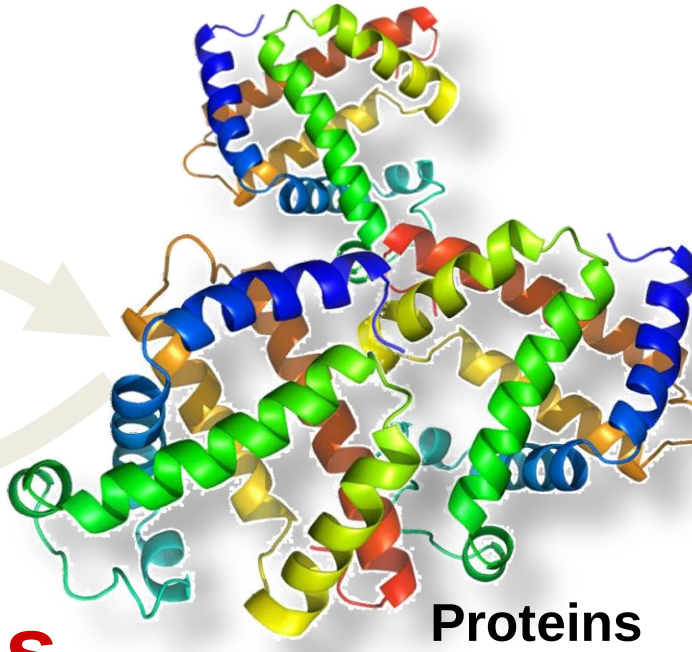


Amino acids





Proteolysis

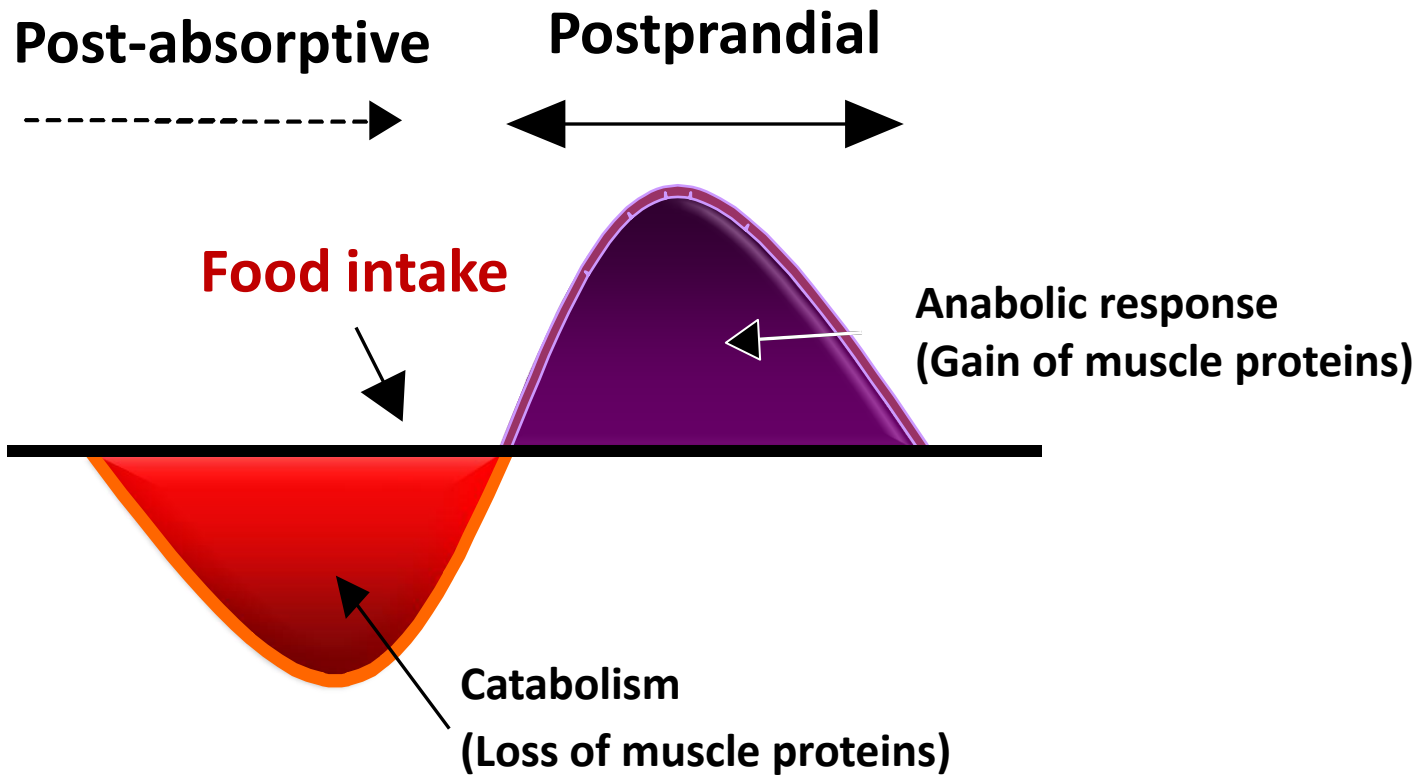


Proteins

Bioavailability of dietary amino acids

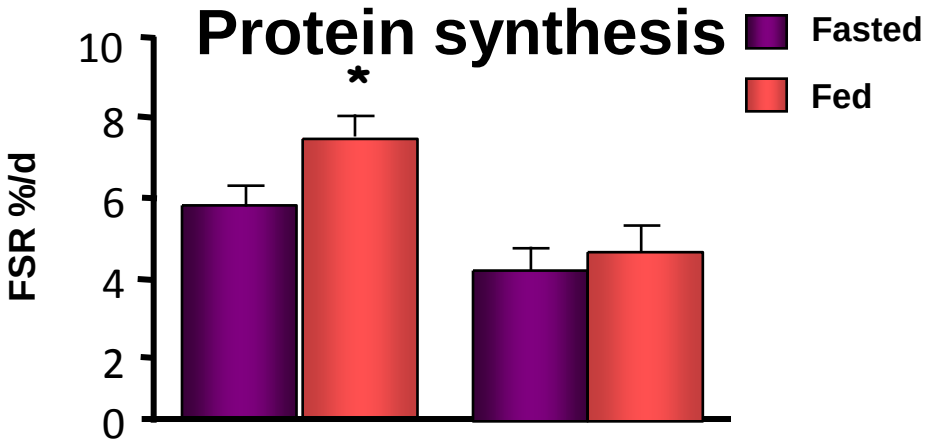
Anabolic factors (Insulin)

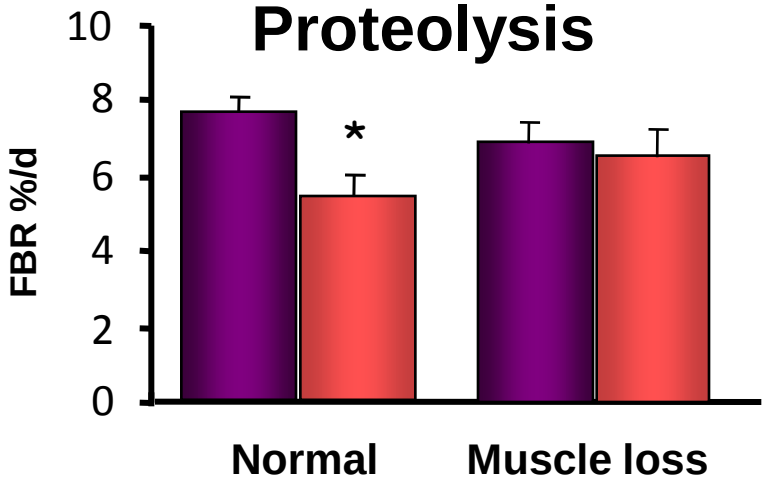
Protein metabolism



Post prandial protein gain should compensate the post absorptive loss of proteins

Post prandial Protein metabolism





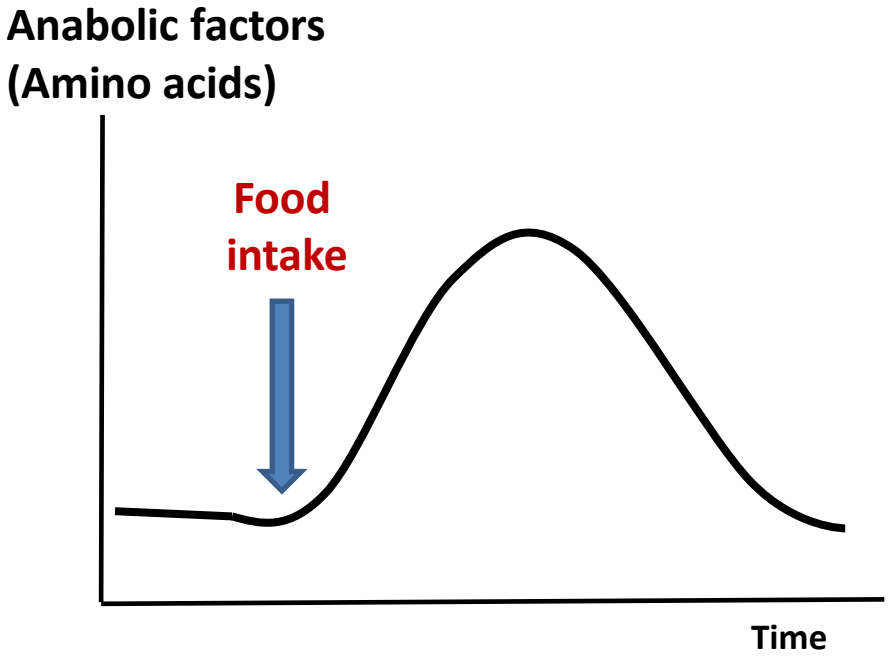
In situations of muscle mass loss

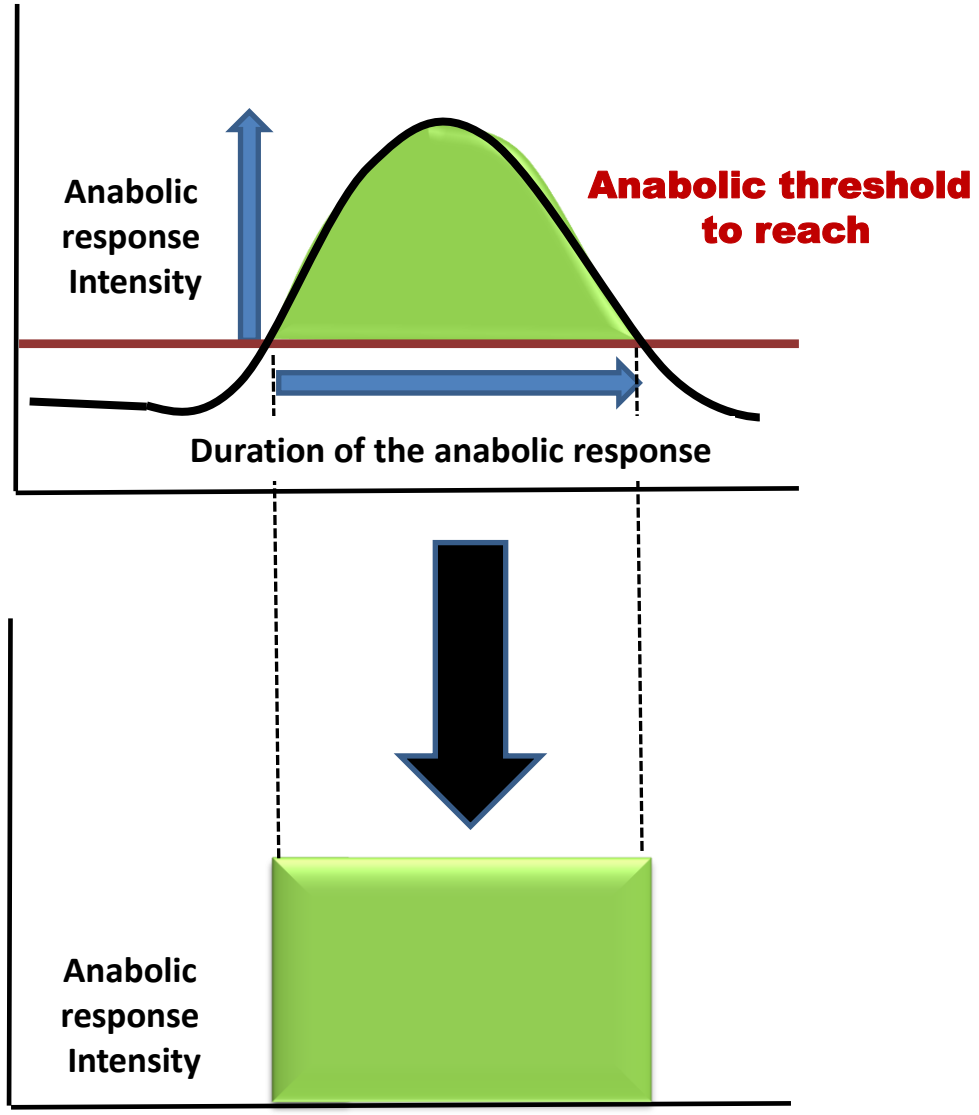
Impaired anabolic response to food intake (with the RDA)

Anabolic resistance

The Anabolic Threshold Concept

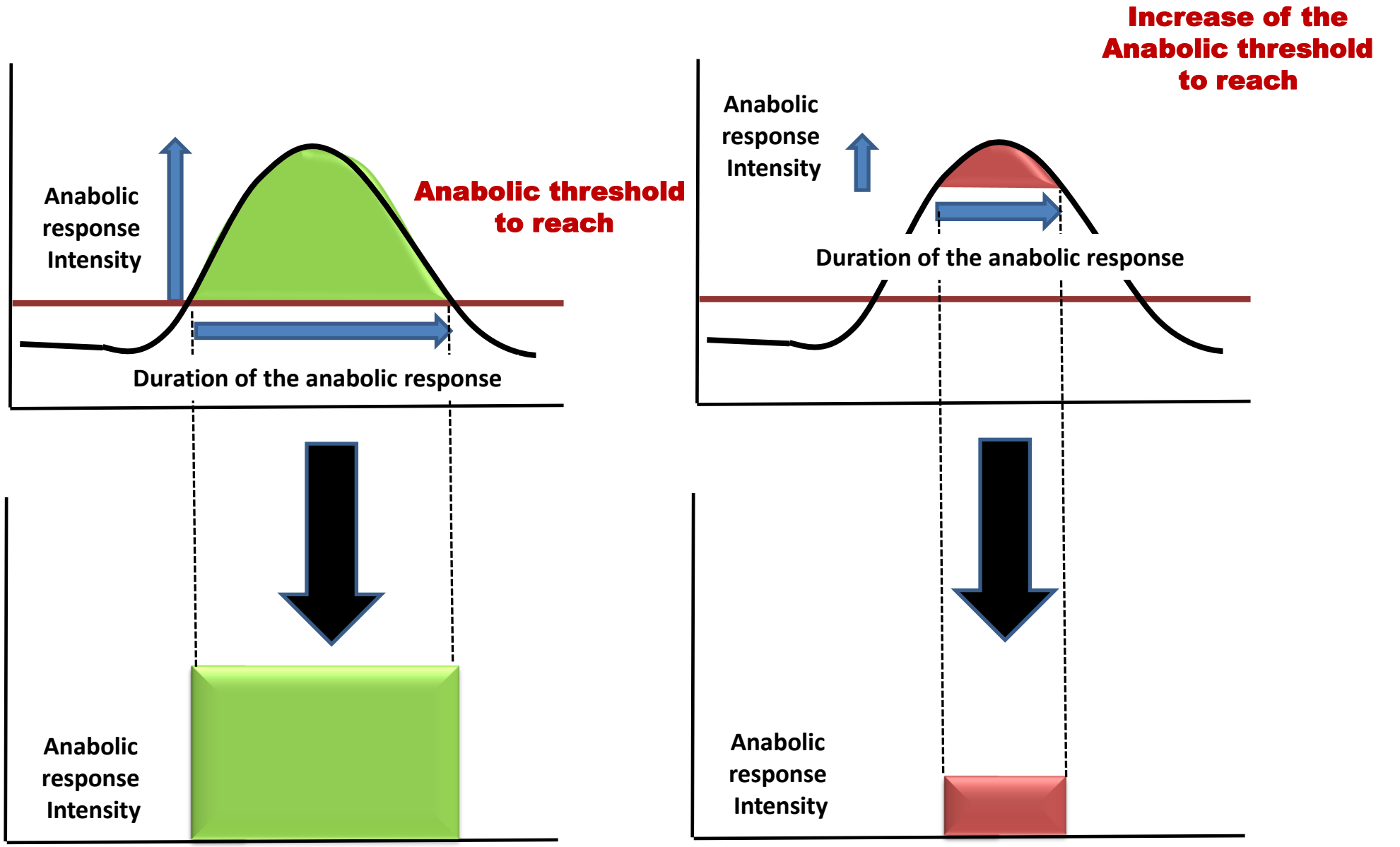
Dardevet et al. Scientific World Journal, 2012



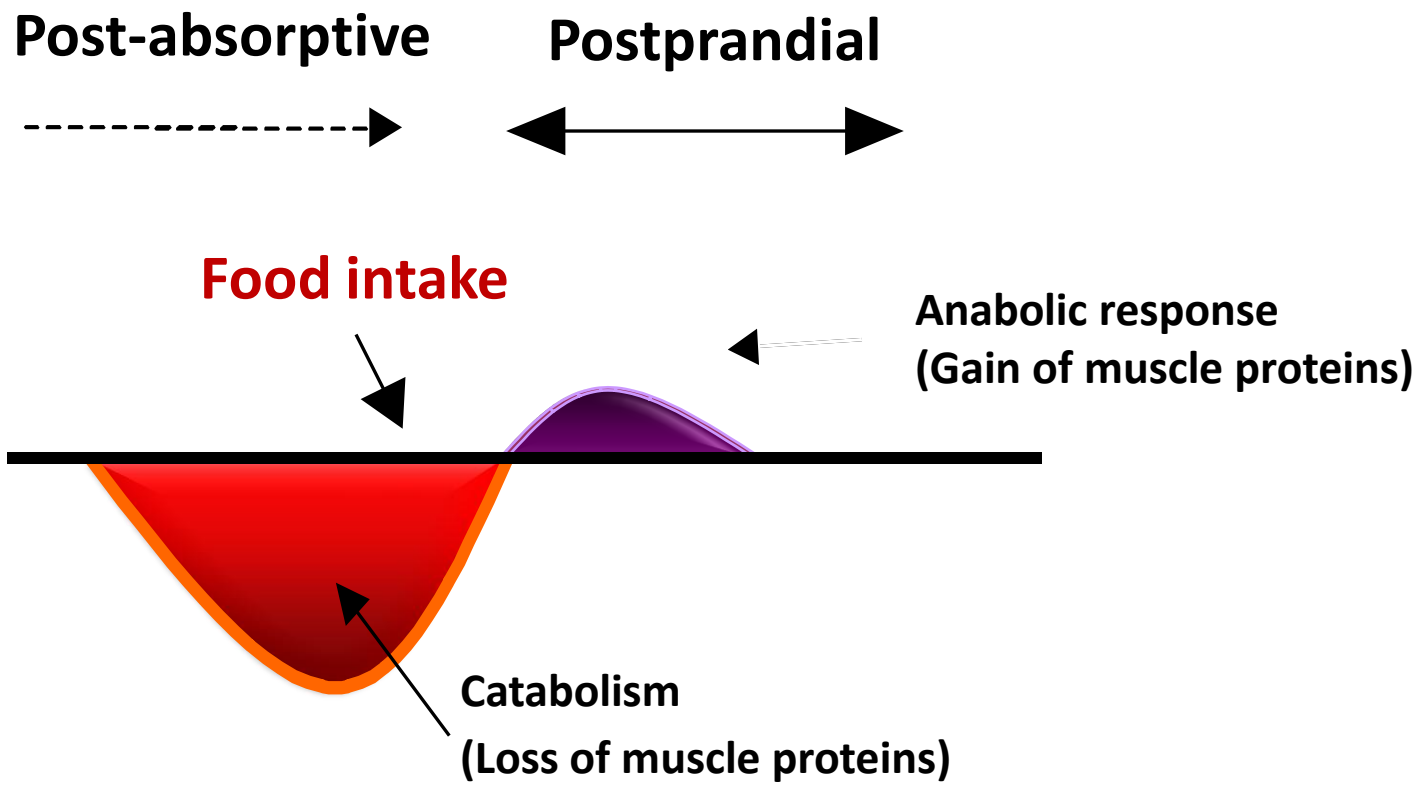


Dardevet et al.
Scientific World Journal, 2012

The Anabolic Threshold Concept



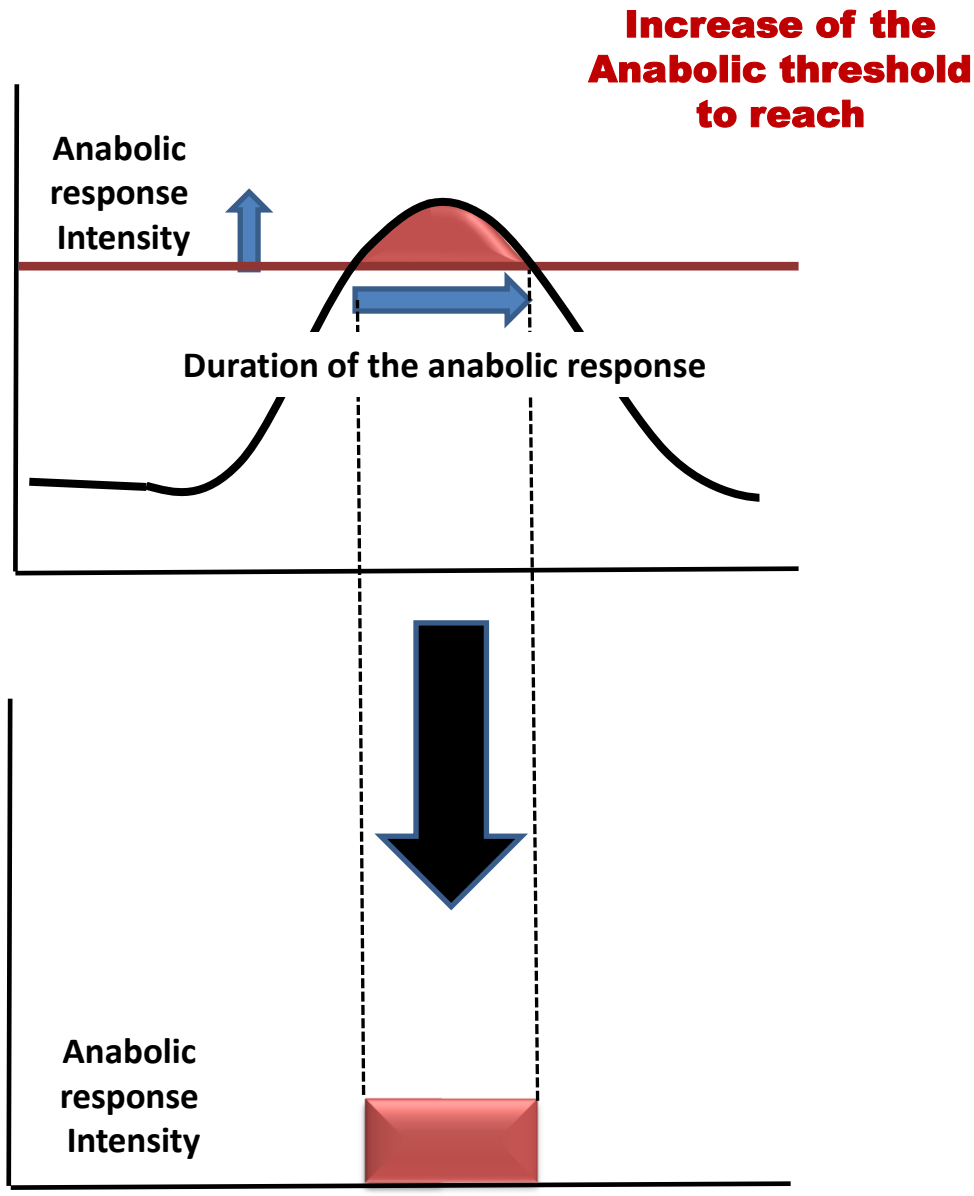
Protein metabolism in anabolic resistance situations

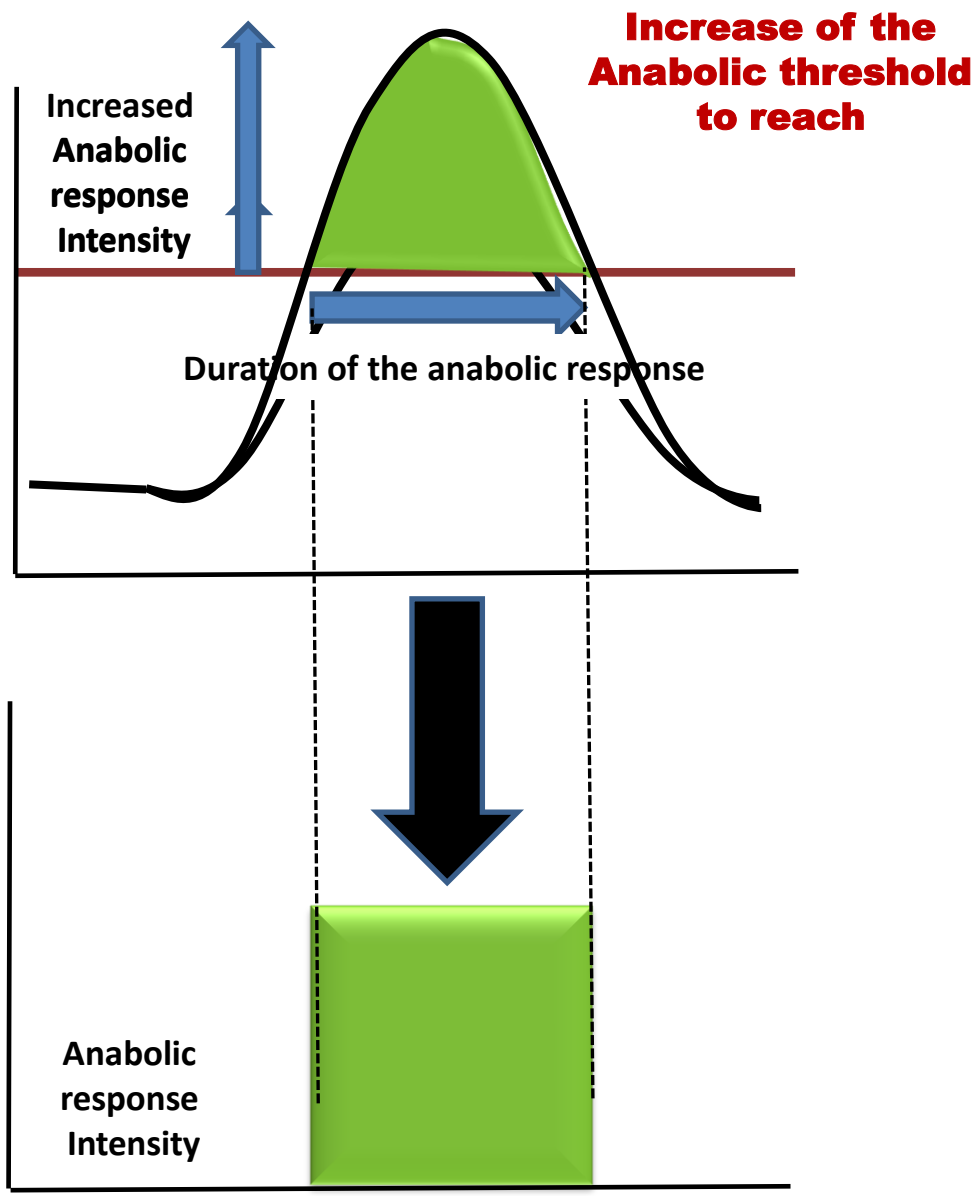


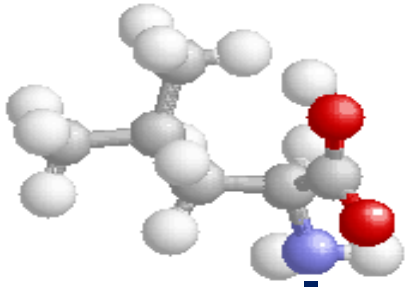
Post prandial protein gain does not compensate the post absorptive loss of proteins = Muscle Atrophy

The Anabolic Threshold Concept

Dardevet et al. Scientific World Journal, 2012







The Anabolic Threshold Concept

Dardevet et al. World Scientific Journal, 2012

In situations of muscle loss and anabolic resistance:

Is Leucine capable to overcome the increase of muscle anabolic threshold?

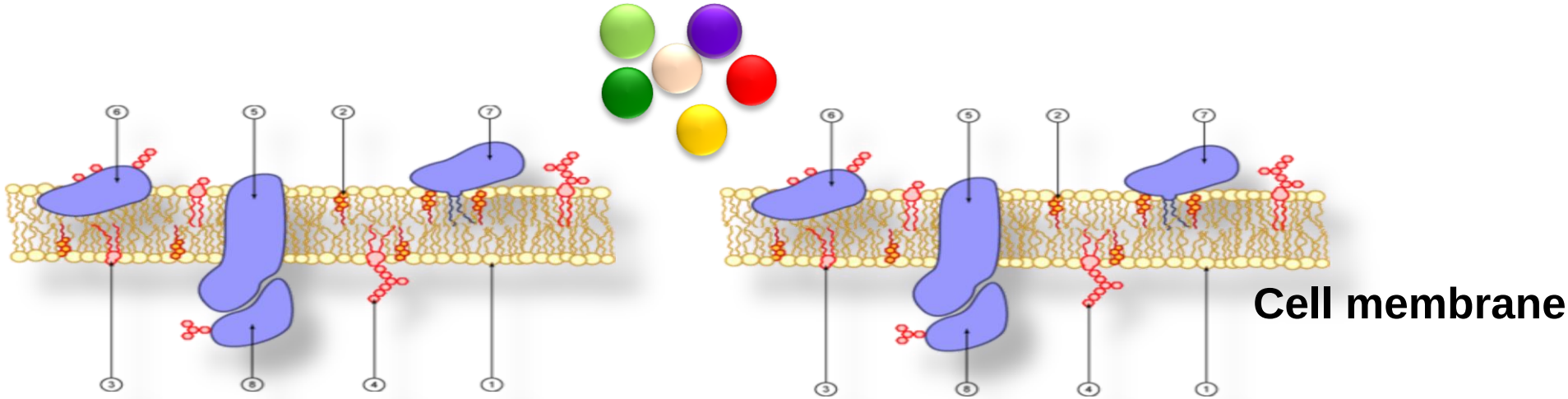
3 contrasted situations

Cancer cachexia

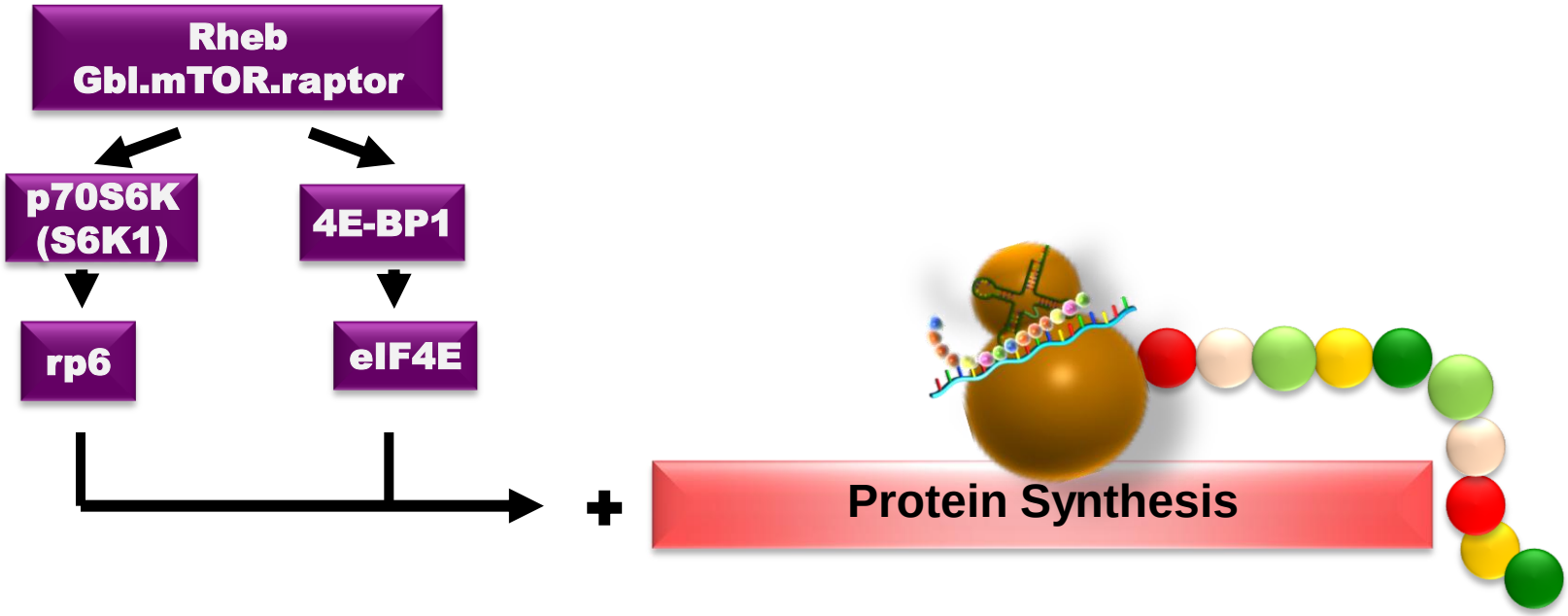
Sarcopenia (aging)

Immobilization/bedrest

Leucine= a signal nutrient



Leucine



Free Leucine supplementation

Improvement of nitrogen balance
Daily et al. 1983

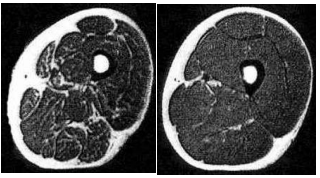
Improvement of body weight
Tayek et al. 1986

4 g of leucine 29 months
Improvement of muscle strength
Poon et al. 2004

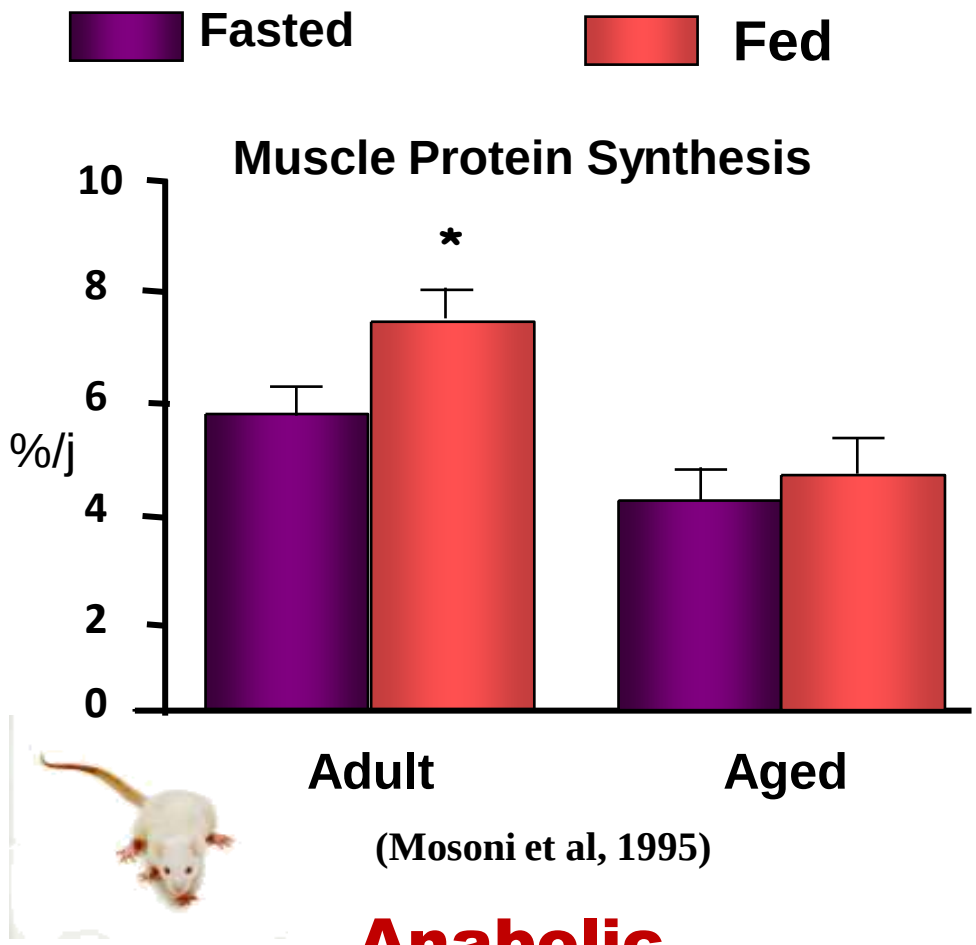
8,7g to 14,6g leucine/kg dietary proteins in the diet
Improvement of muscle mass
Peters et al. 2011

1g /kg body weight
Improve muscle protein synthesis
Improvement of muscle mass
Eley et al. 2007

Free Leucine supplementation in a meal



Sarcopenia and aging

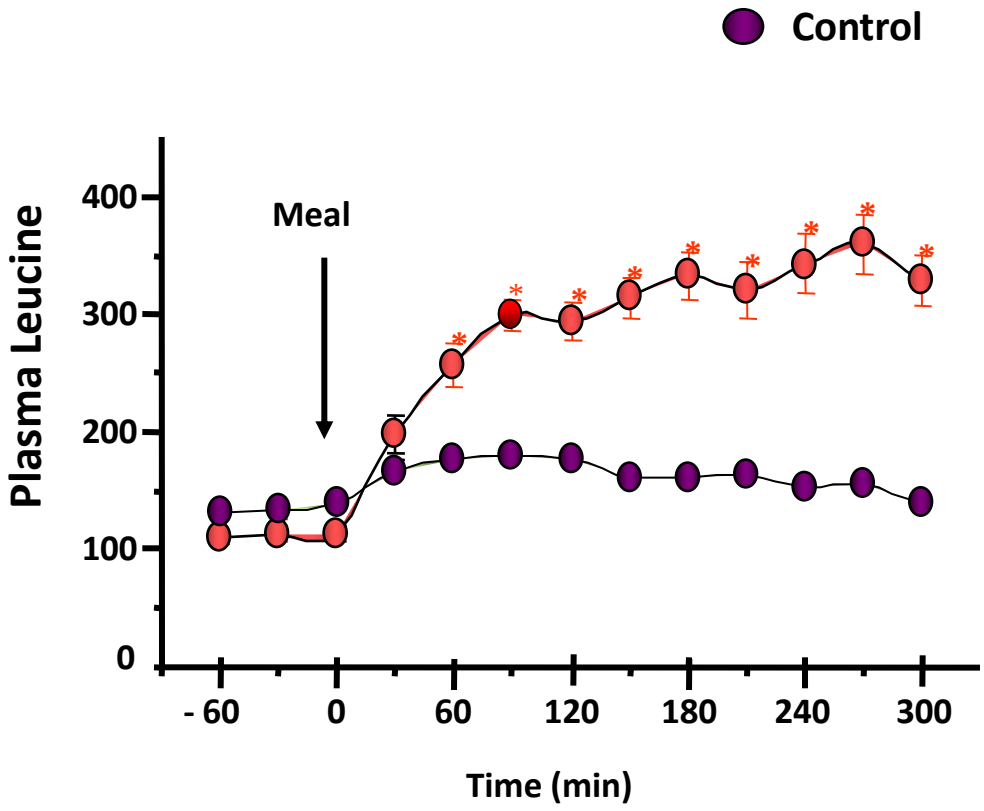


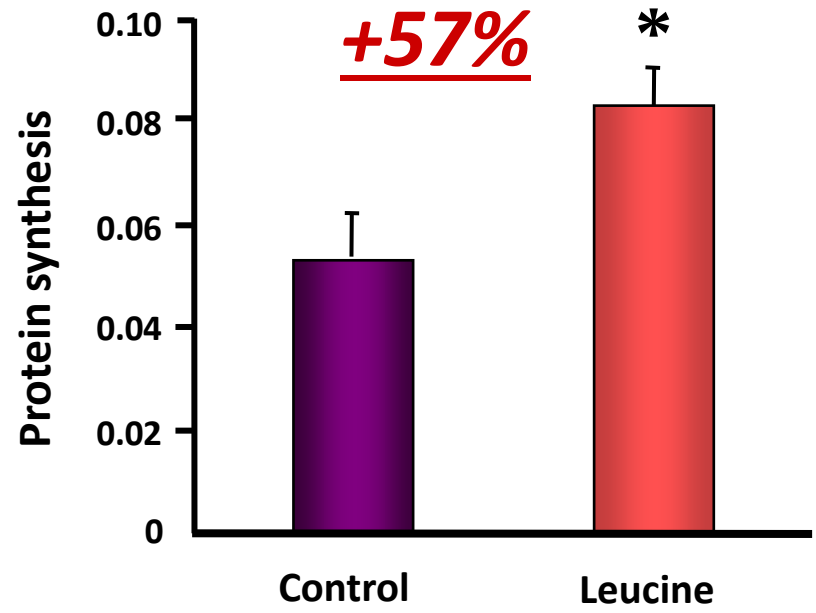
(Mosoni et al, 1995)

Anabolic resistance

Leucine , Sarcopenia and Aging

Rieu et al, 2006
Katsanos et al. 2006





Leucine , Sarcopenia and Aging

6 -10 months
4.5% leucine in the diet

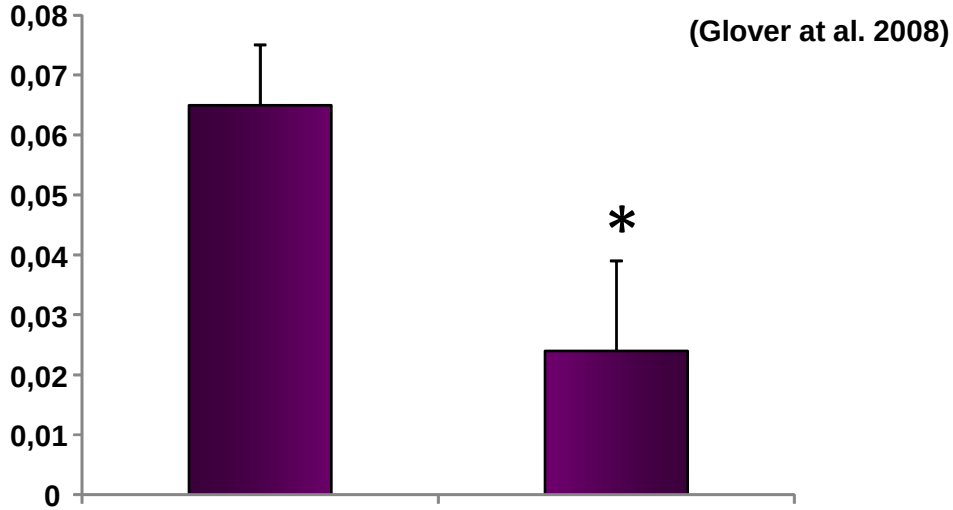
Negative on muscle mass
(Zeanandin et al. 2012)
Vianna et al. 2011

3 months
7.5 g leucine / day

Negative on muscle mass and strength
(Verhoven et al. 2009):

Leucine, Muscle loss and Bed rest/Immobilization

Post-prandial Stimulation of Muscle Protein Synthesis (% /h)



Free Leucine supplementation

3.1g leucine , 28 days:
Improvement of post prandial muscle protein synthesis
No change in muscle mas loss
Paddon-Jones et al. 2004

3.6g leucine , 60 days:
No change in muscle mas loss
Trappe et al. 2007

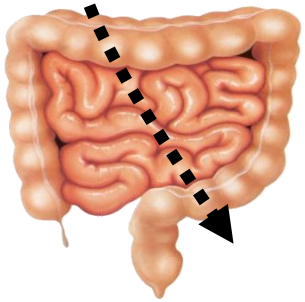
3.6g leucine , 60 days:
No change in muscle strength
Trappe et al. 2008

4,5% leucine in the diet
No change in muscle mass recovery
Magne et al. 2012

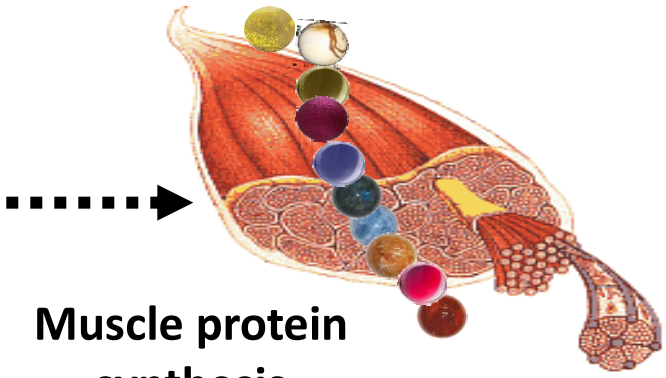
Why free leucine can be disappointing?

+ Leucine

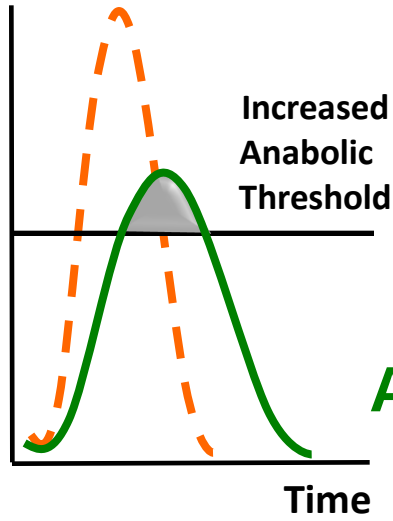
Digestion time



20 amino acids



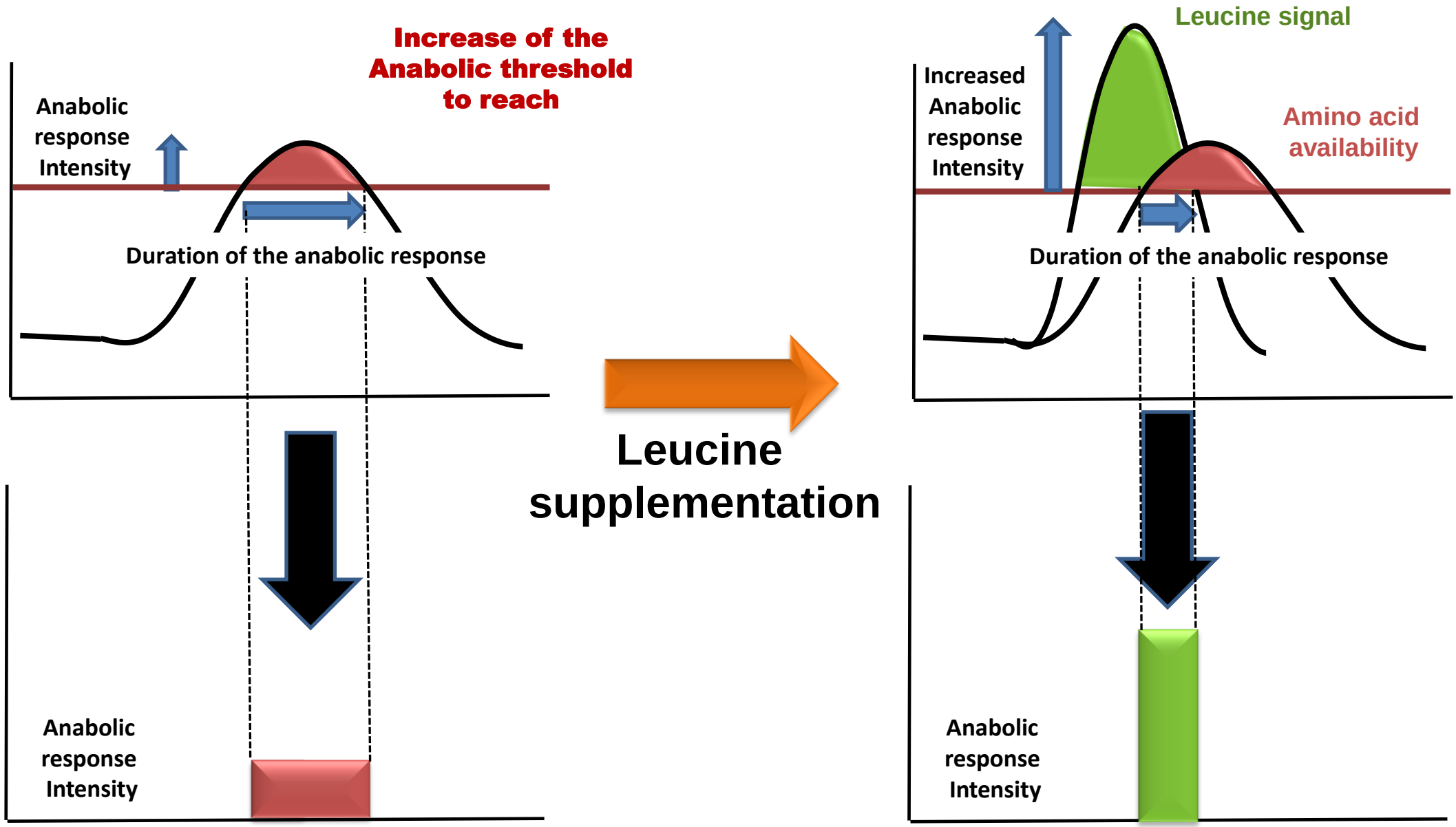
Muscle protein synthesis



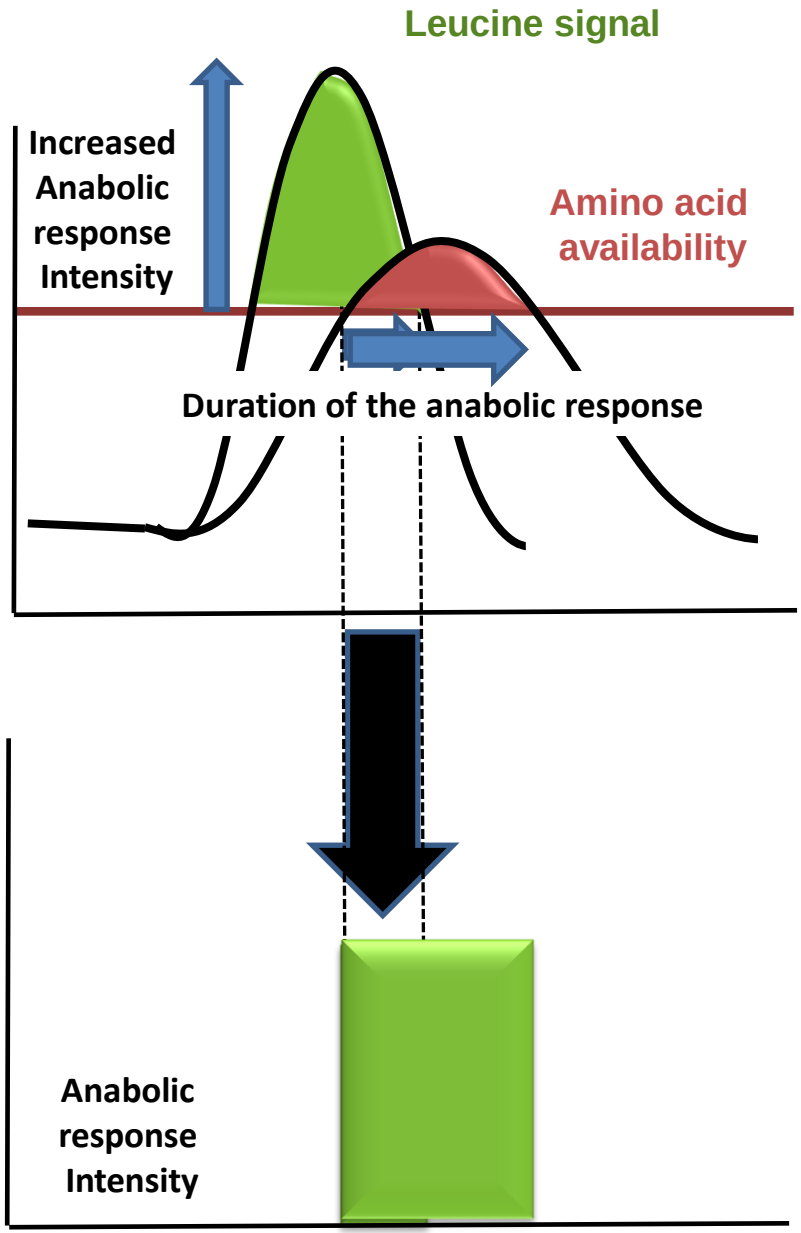
Other Amino acids

Why free leucine supplementation disappointing?

Dardevet et al. Scientific World Journal, 2012



Resynchronisation leucine signal/amino acids



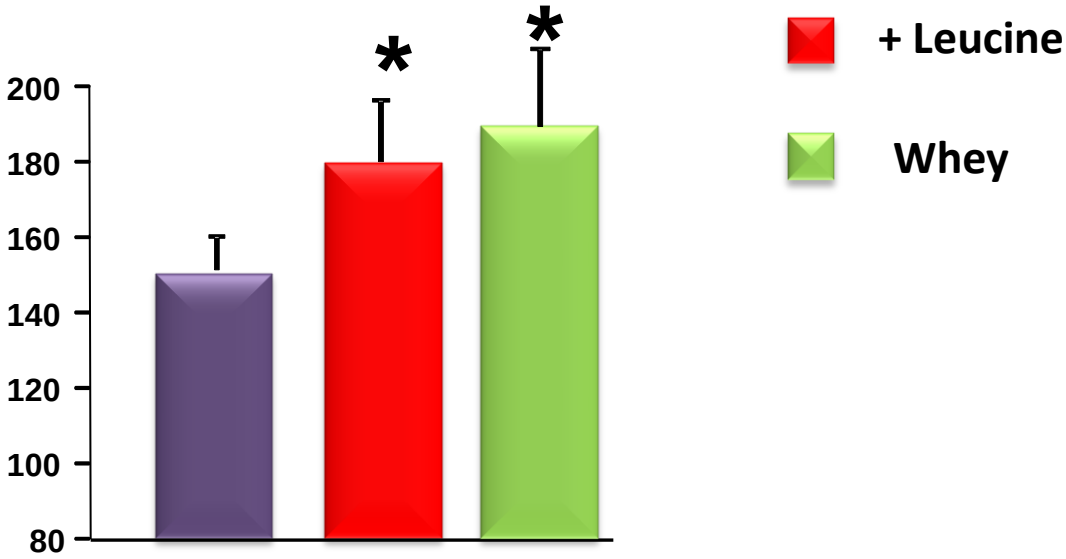
Synchronization possible with leucine rich proteins rapidly digested

Whey Proteins

Leucine supplementation with whey

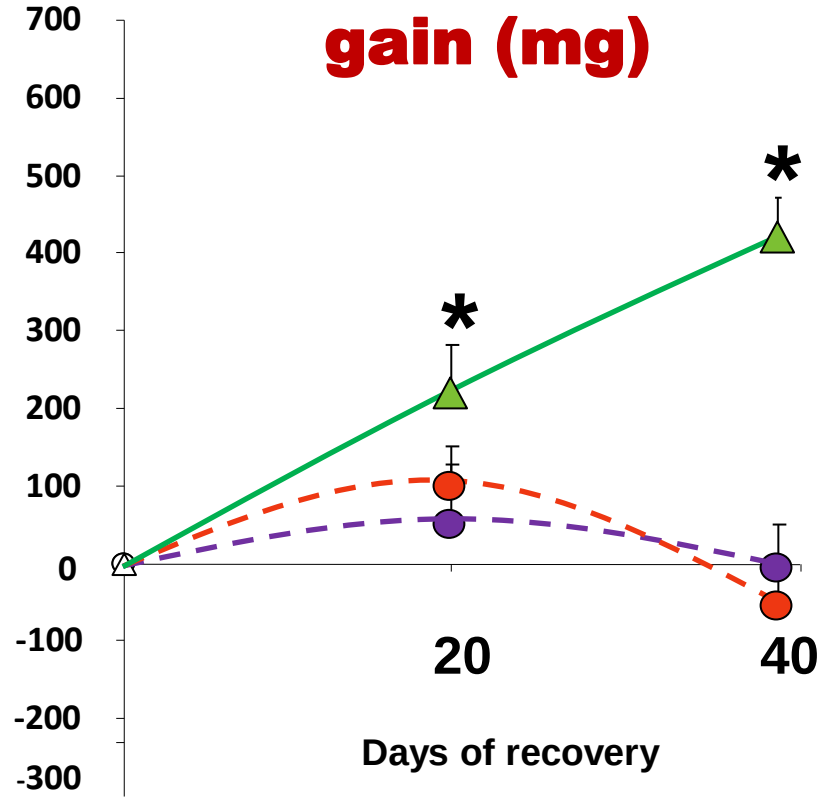
Muscle Recovery Post-immobilization

Post prandial Protein Synthesis



Magne et al. 2012

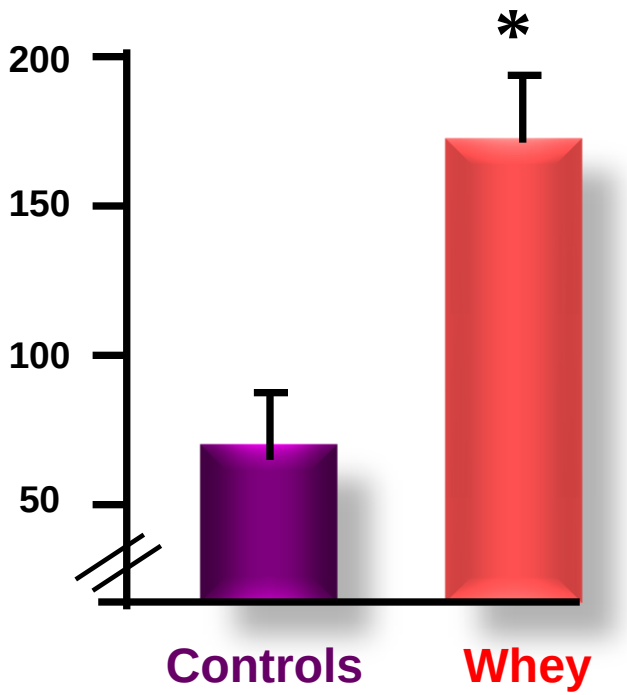
Muscle mass gain (mg)



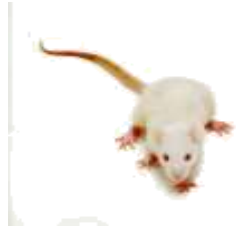
Leucine supplementation with whey

Sarcopenia and Aging

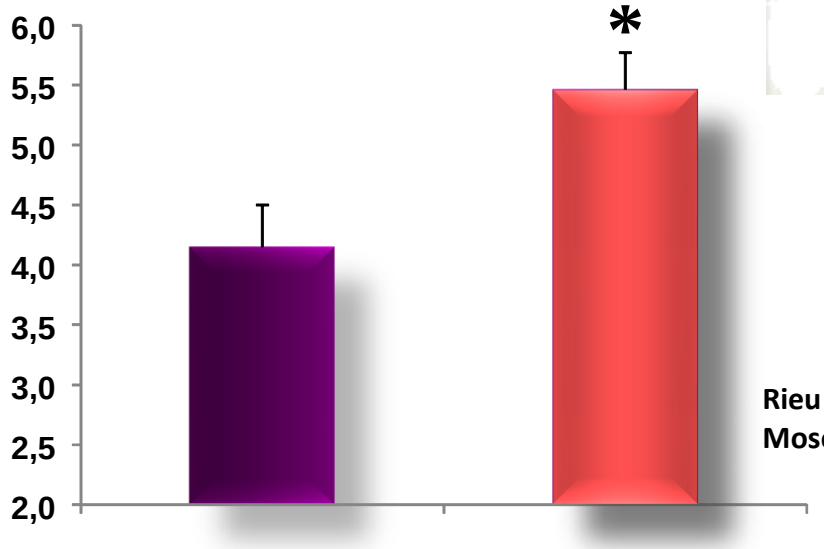
Protein Synthesis



Dangin et al., 2002, 2003; Boirie et al, 1997



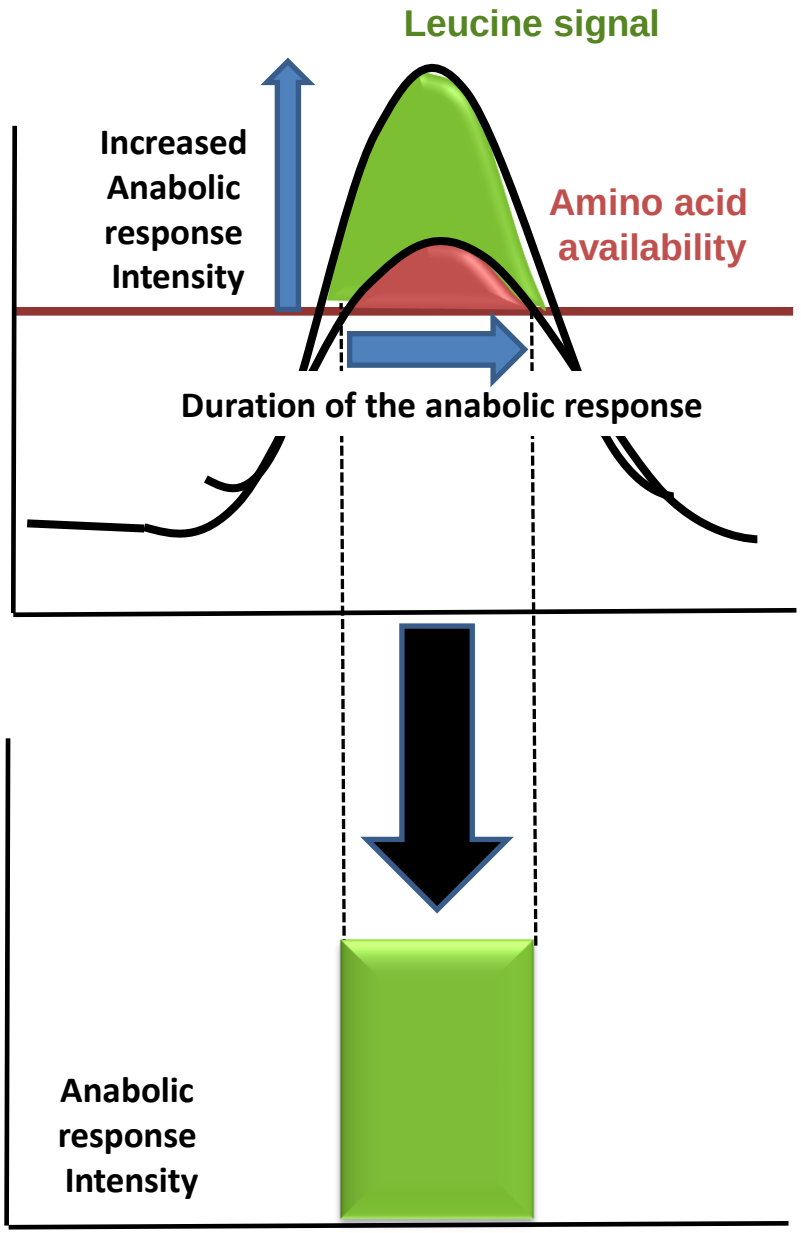
Protein Synthesis



Rieu et al, 2007
Mosoni et al. 2013

Muscle mass (10 d or 6 months)

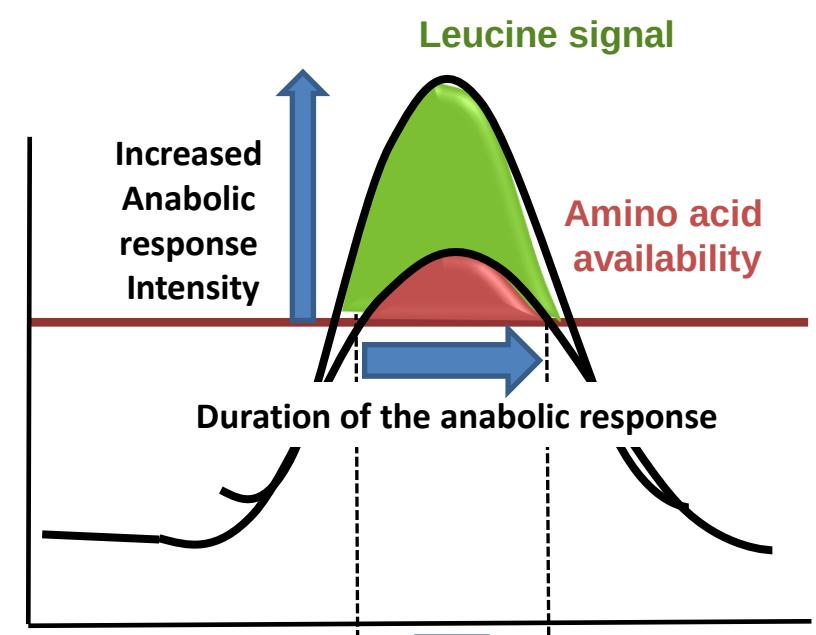
When Resynchronisation remained inefficient?

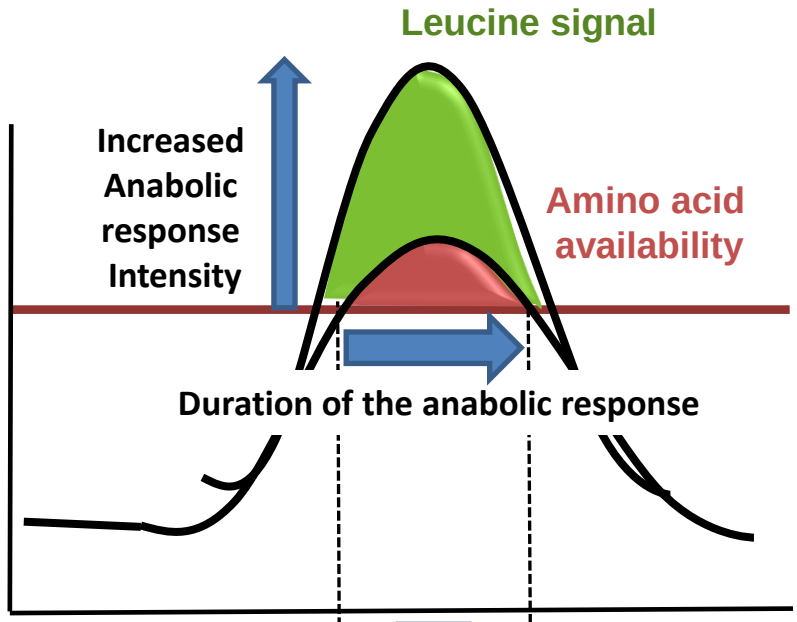


Duration of the anabolic response?

- **Decrease of the anabolic threshold**
- **Increase more the protein intake**
- **Interaction between protein and energy intake**

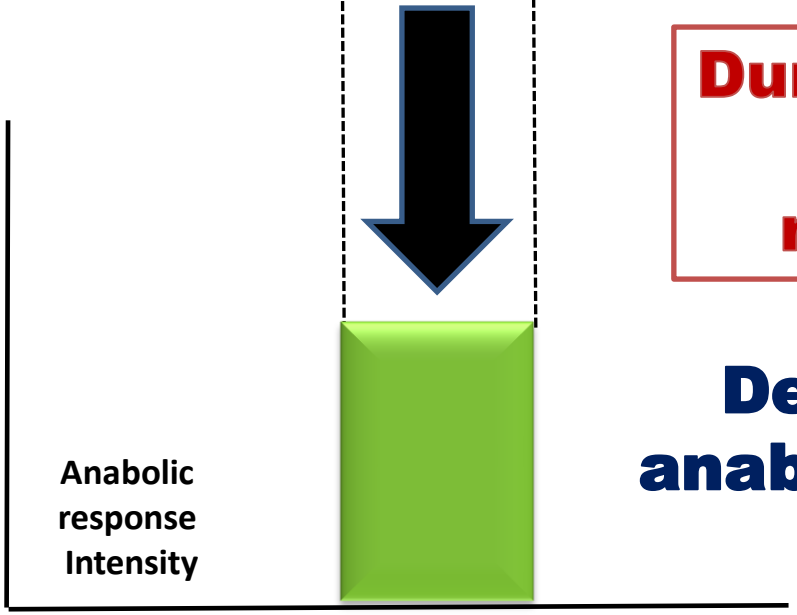
When Resynchronisation is inefficient?

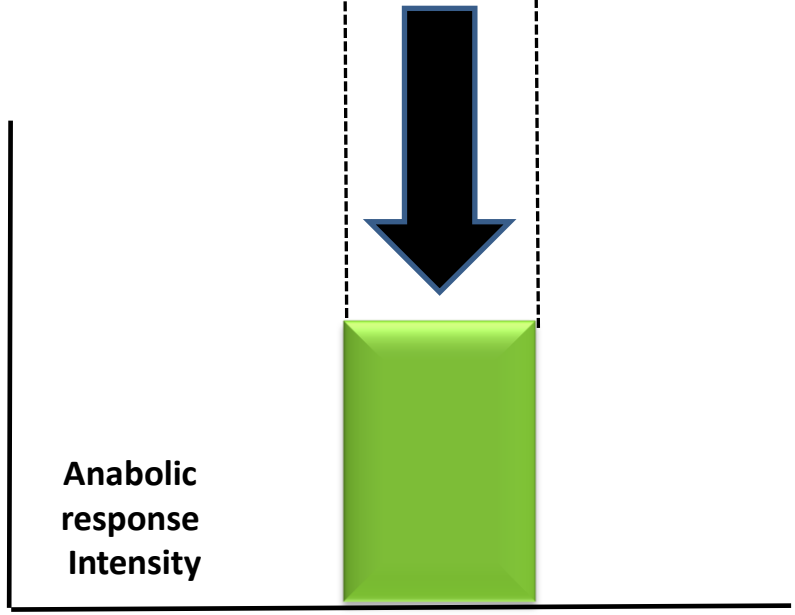




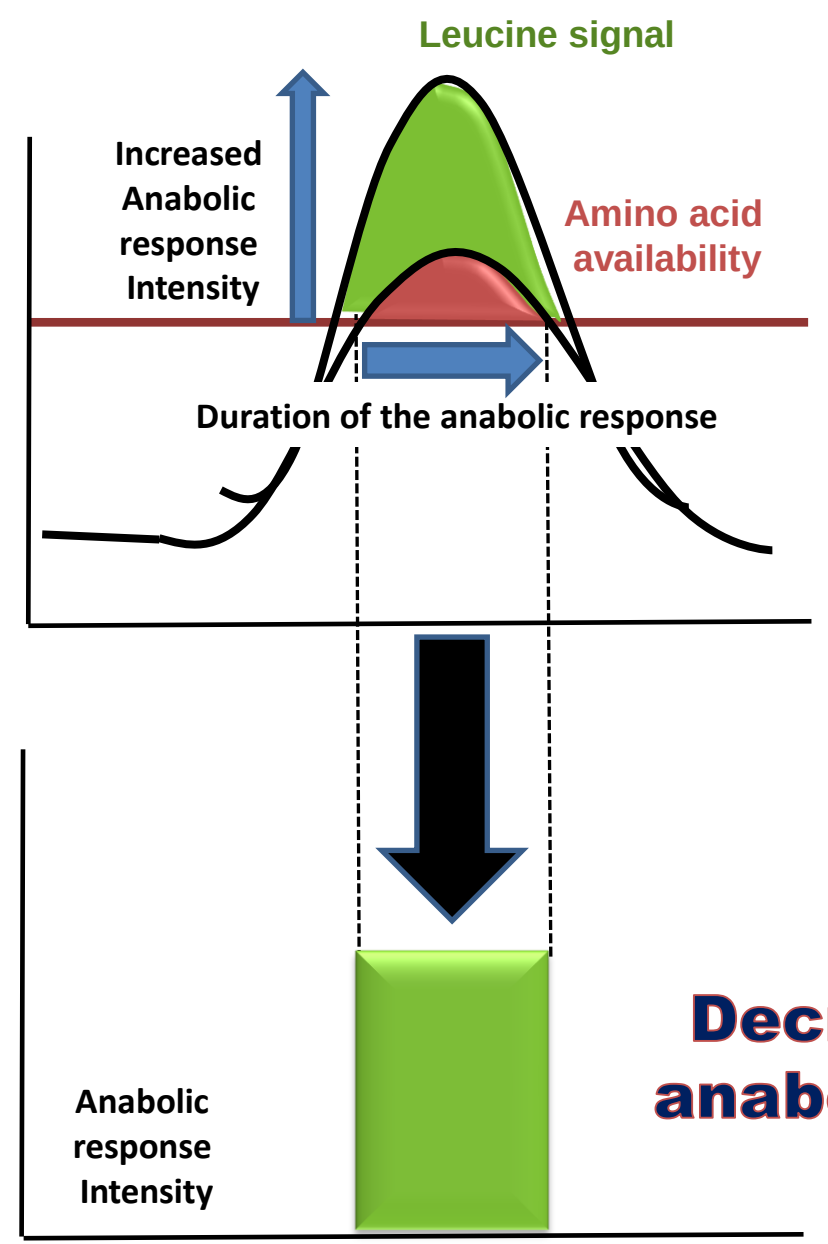
Duration of the anabolic response?

Decrease the anabolic threshold

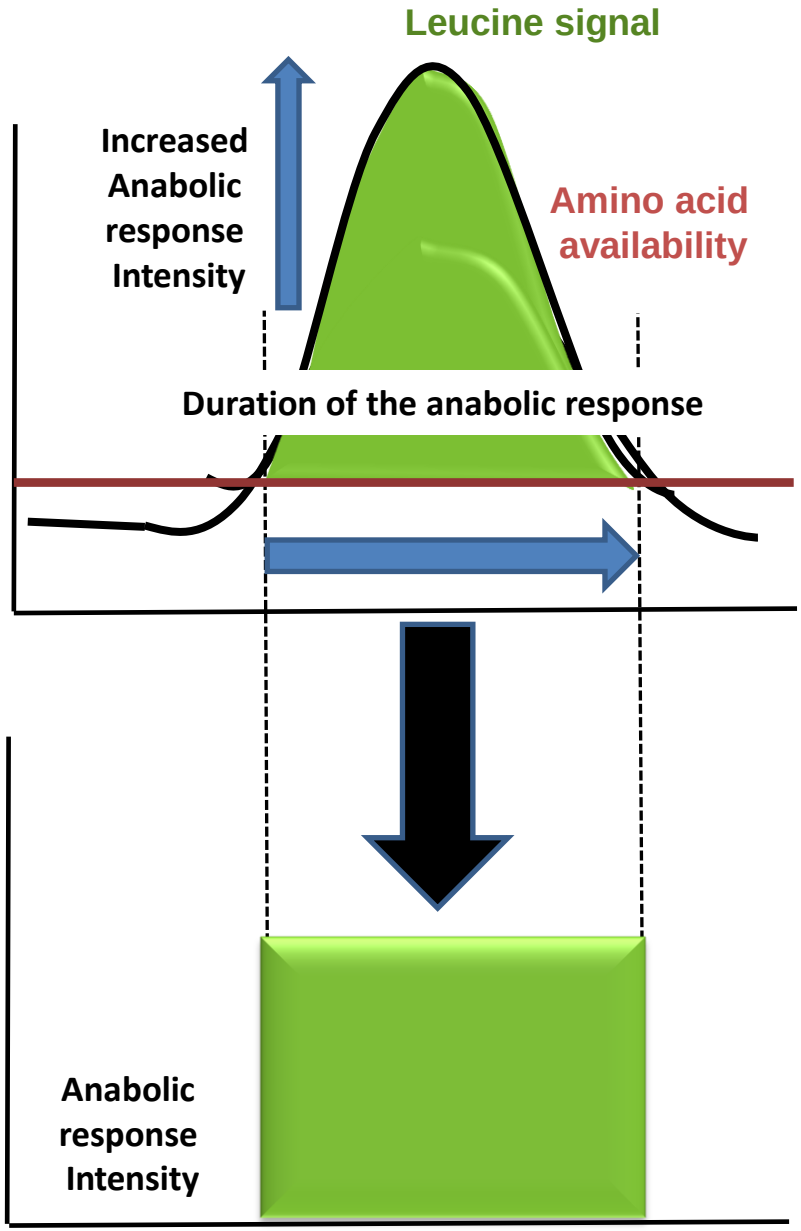




When Resynchronisation is inefficient?



Decrease of the anabolic threshold

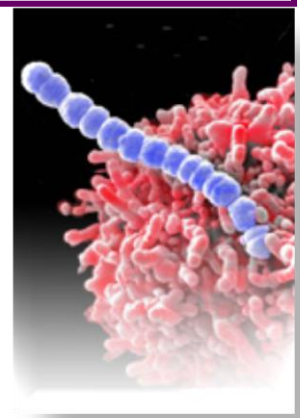


How to decrease the anabolic threshold?

Most of the stituations of muscle loss are associated with an increase of :

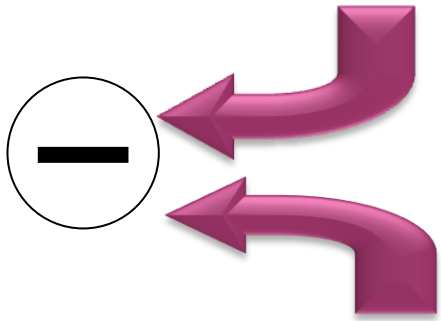
Inflammation and Oxidative Stress

Inflammation

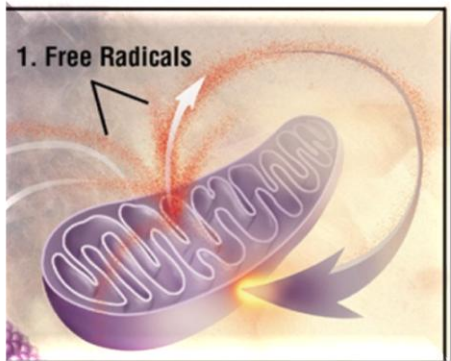


Cytokines TNFα, IL_1, IL_6

Muscle Anabolism

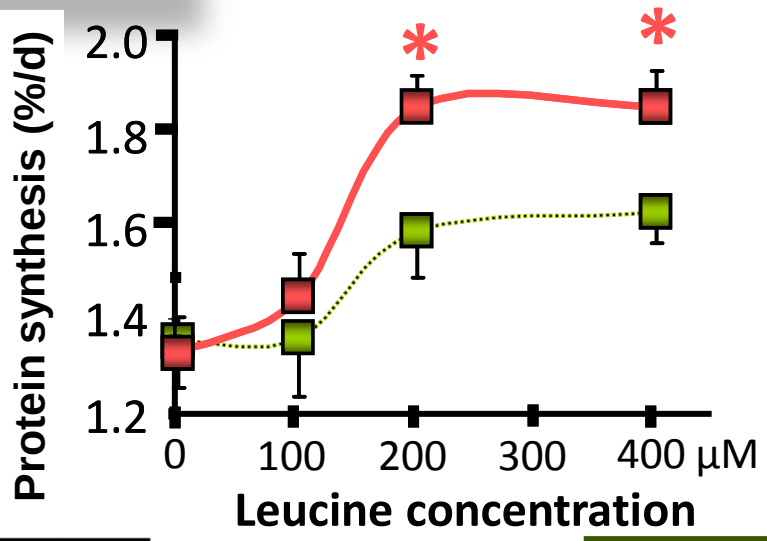


O_2 °



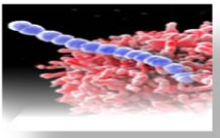
Oxidative Stress

How to decrease the anabolic threshold?

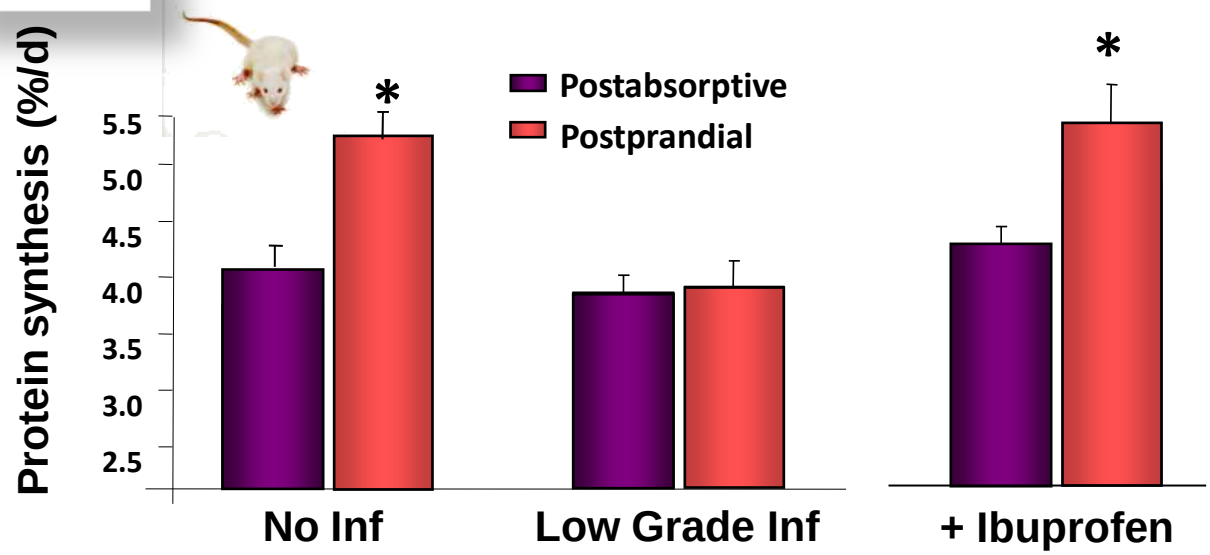


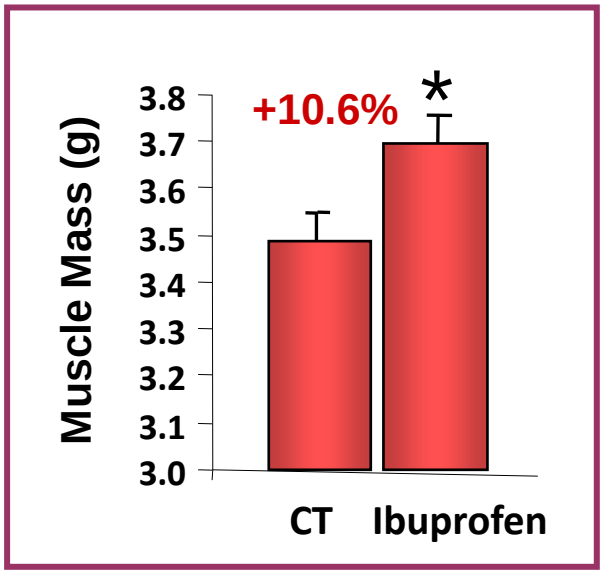
Marzani et al. J Nutr 2008
Mosoni et al. Nutrition, 2010

Rutin, vitamin E, vitamin A, Zn et Se for 7 weeks

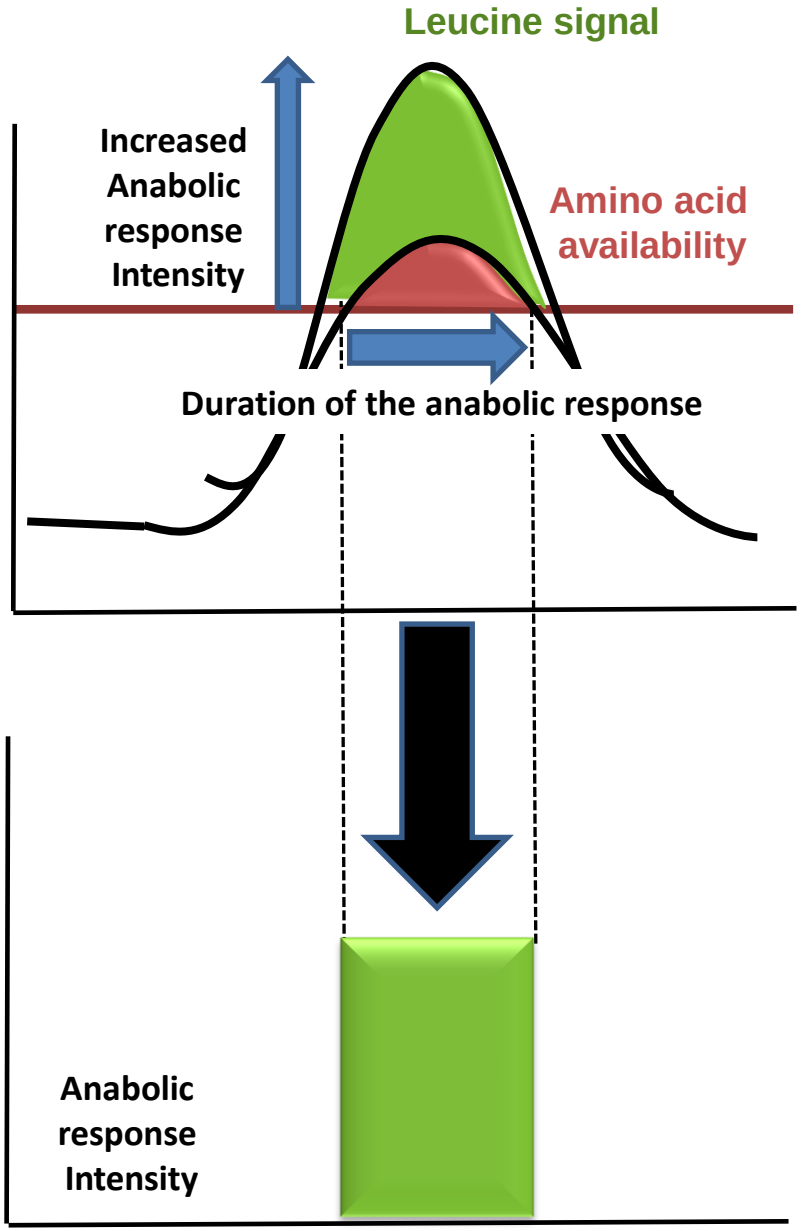


Rieu I, J Physiol 2009
Balage et al. JNB, 2010





When Resynchronisation is inefficient?

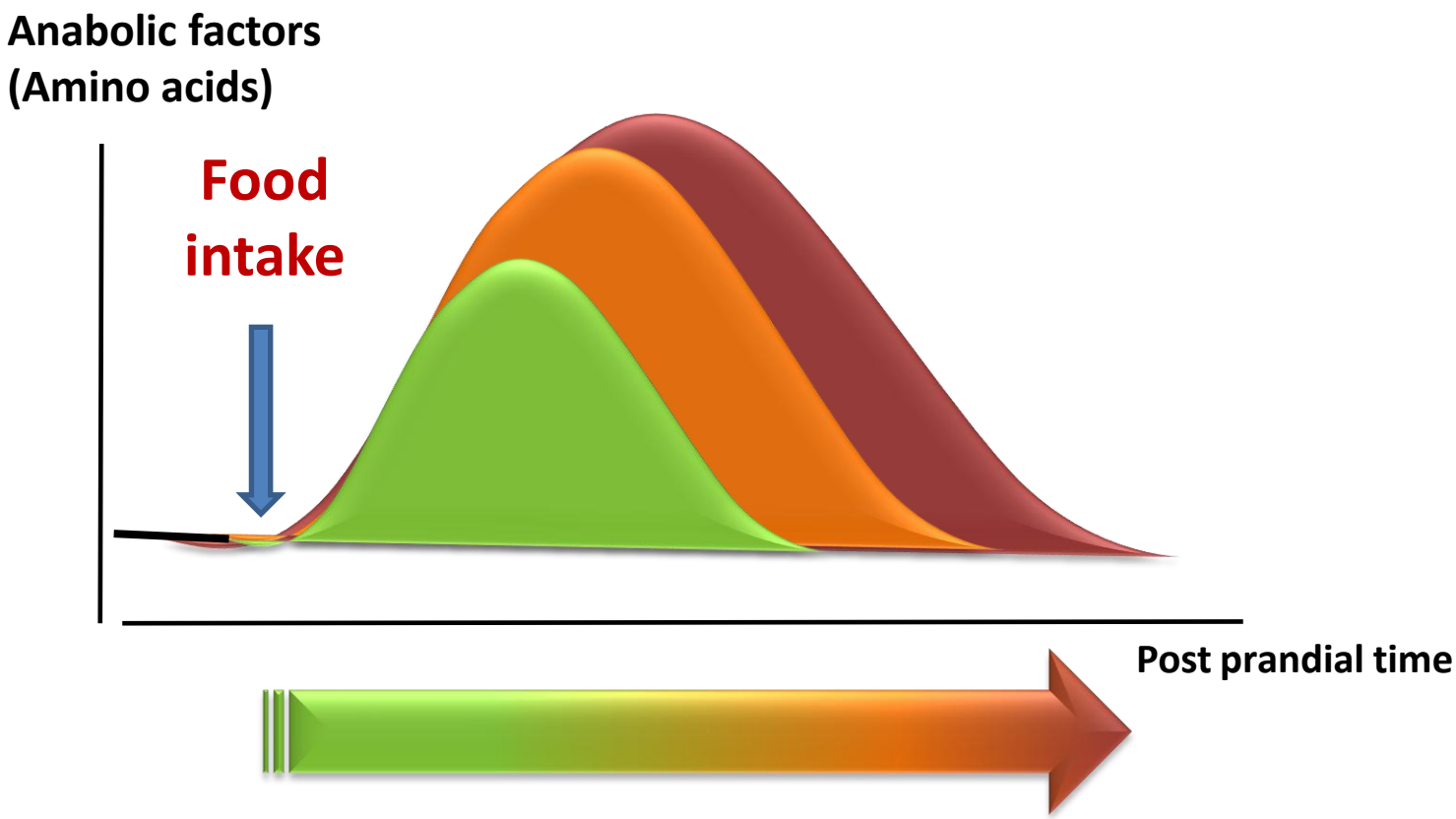


Duration of the anabolic response?

- **Increase more the protein intake?**

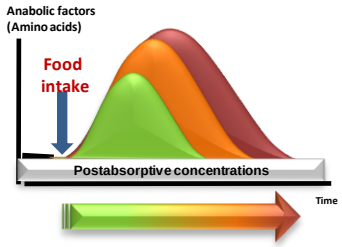
High protein diet: The protein pulse feeding?

(Arnal et Mosoni 1999, 2000, 2002)



The protein pulse feeding?

Dardevet et al. Scientific World Journal, 2012



Anabolic response Intensity

Duration of the anabolic response

Anabolic response Intensity

Duration of the anabolic response

Anabolic response Intensity

Duration of the anabolic response

Anabolic response Intensity

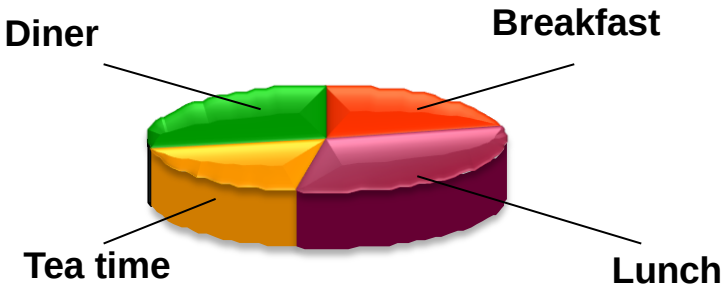
Anabolic response Intensity

Anabolic response Intensity

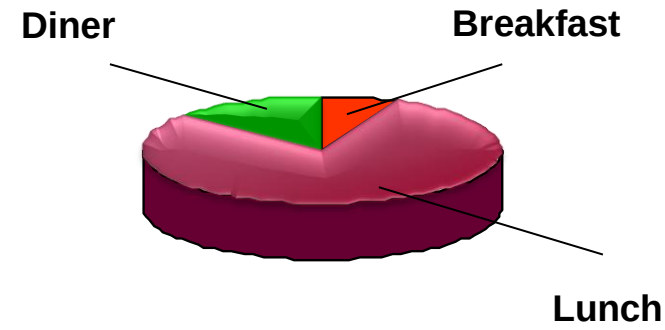
The protein pulse feeding?

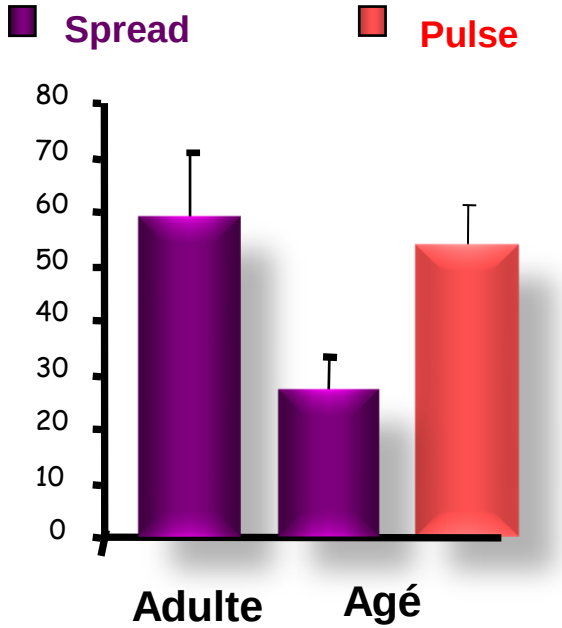
Increase of the dietary protein intake

Spread protein diet



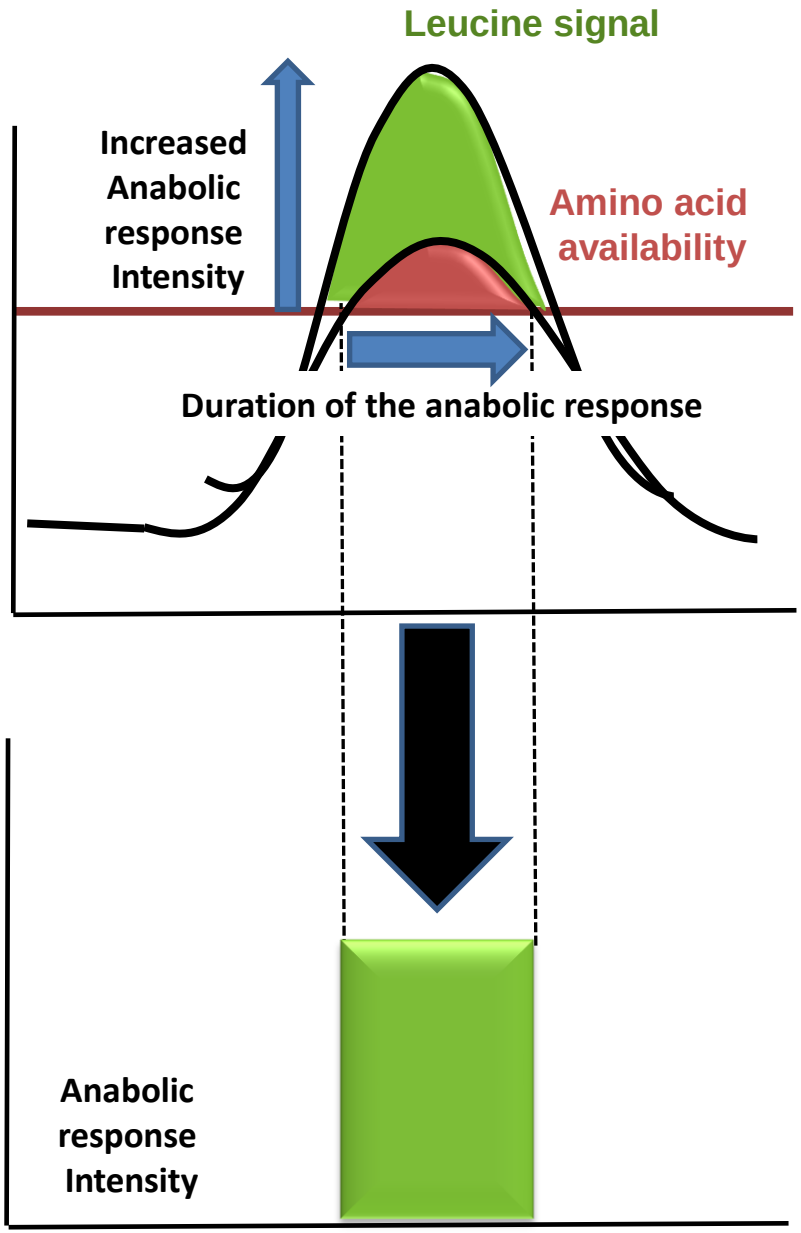
Pulse protein diet





(Arnal et al. 1999,2002
Bouillanne et al. 2013)

When Resynchronisation is inefficient?

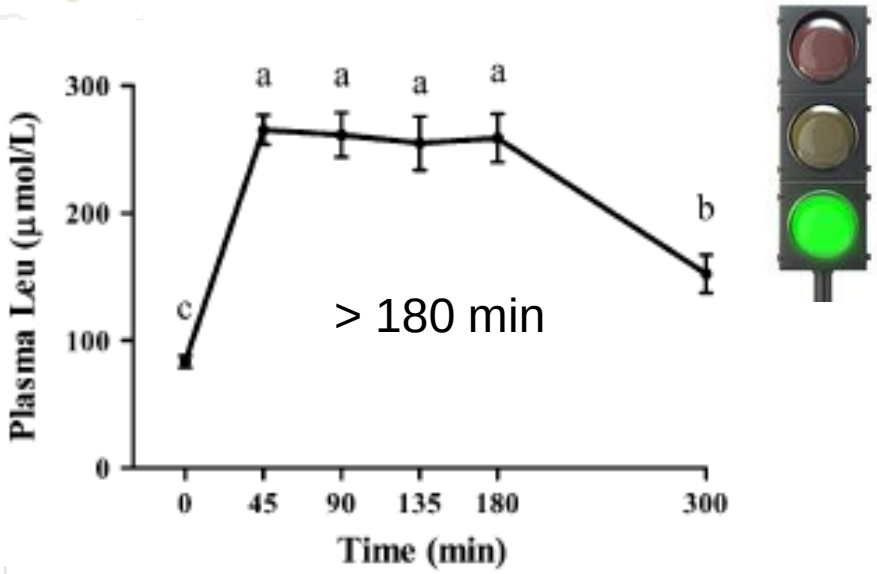


Duration of the anabolic response?

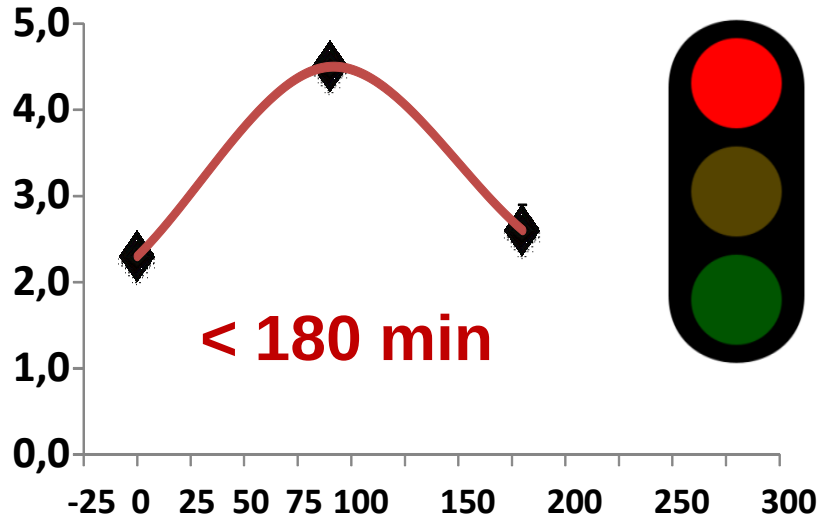
- **Interaction with protein and energy intake?**

When Resynchronisation is inefficient? Whey too fast?

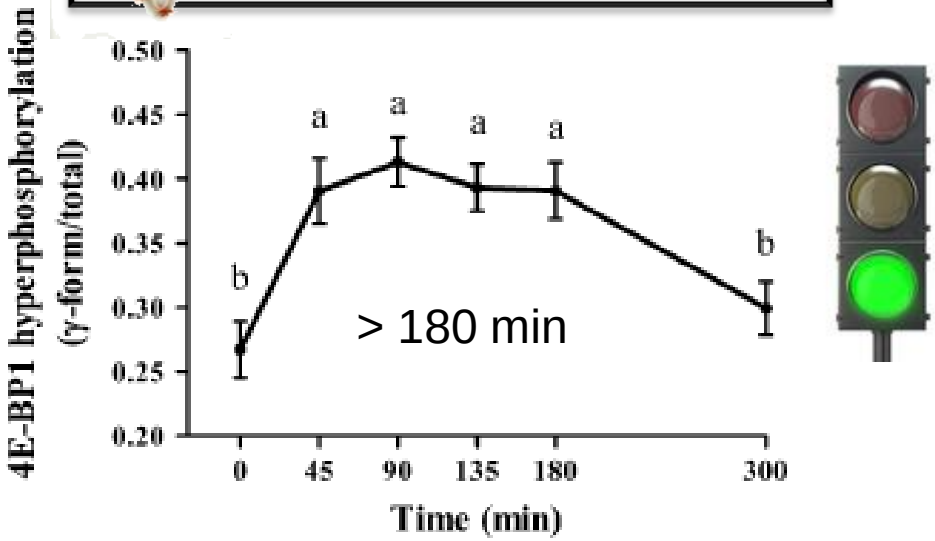
Amino acids



Muscle protein synthesis



mTOR

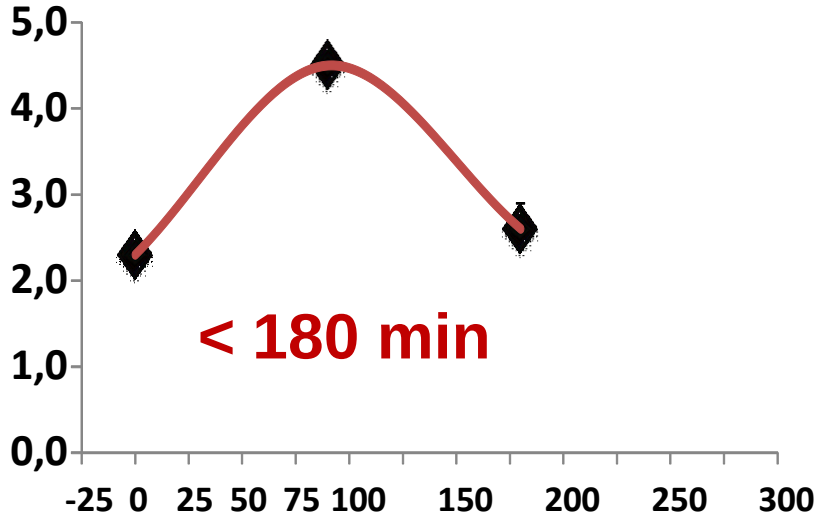


Existence of « Stop Signals » stronger than the anabolic signals !!

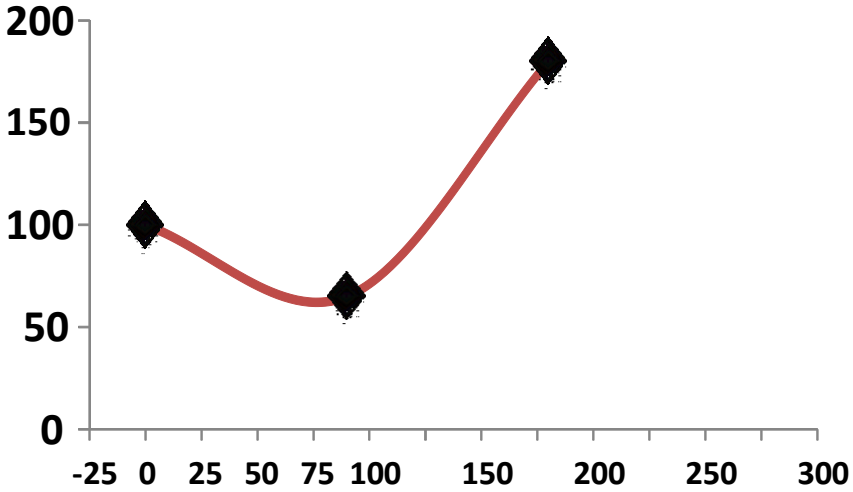
Wilson et al. 2010; Atherton et al. 2010

What is the “Stop signal”?

Muscle protein synthesis



AMPK activity



AMPK

Activity increases when ATP decreases

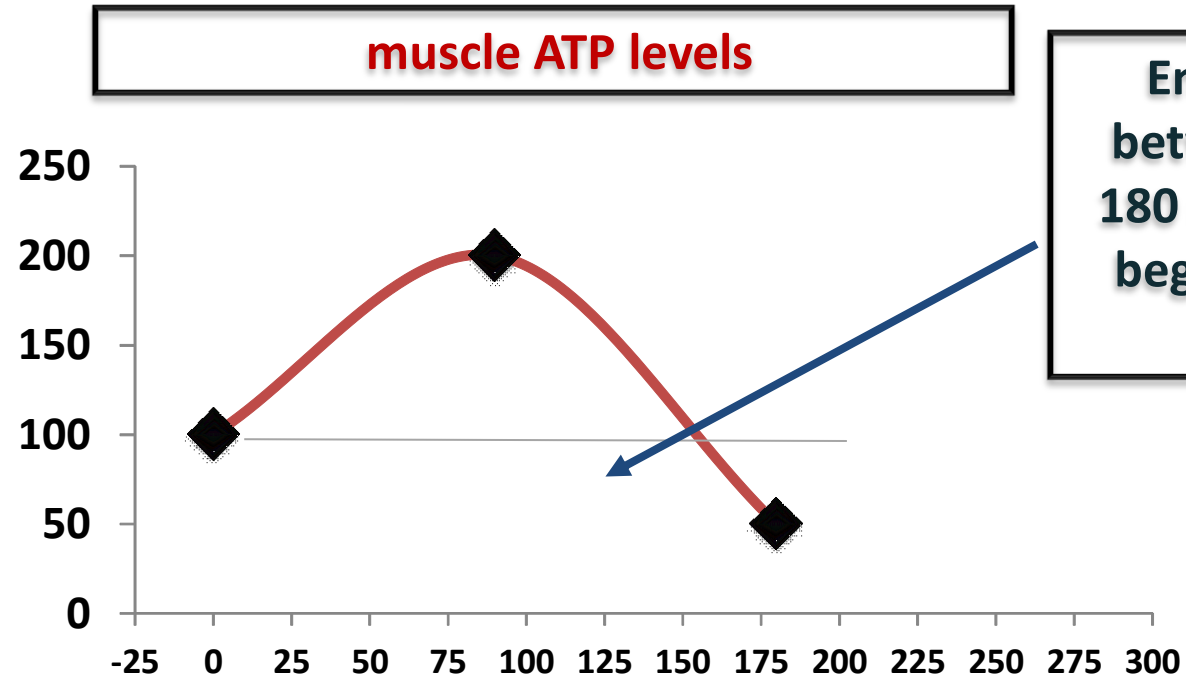
Protein synthesis has a high energetic cost

Protection mechanism?

Nutritional strategy to take into account AMPK?

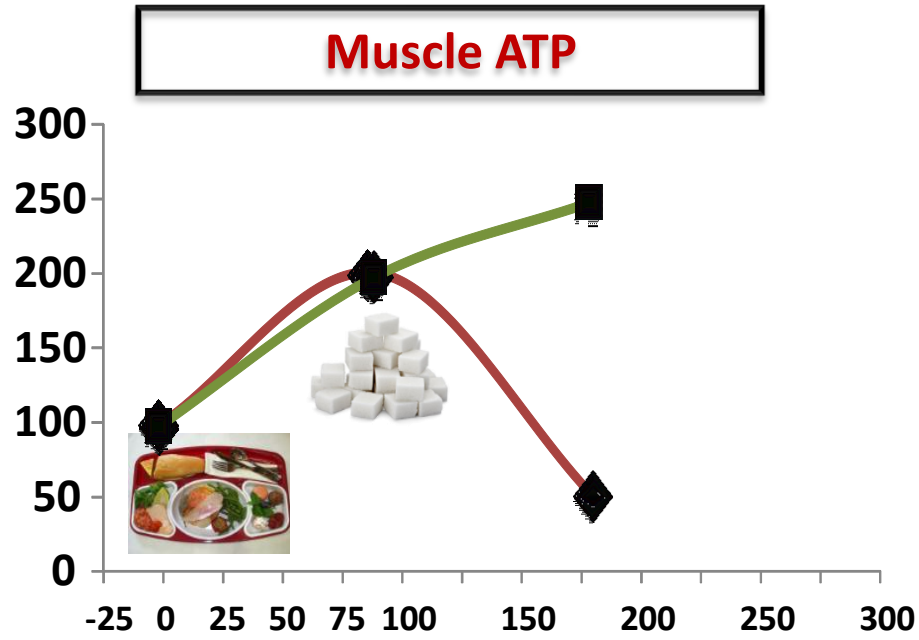
Prevent the AMPK activity to increase

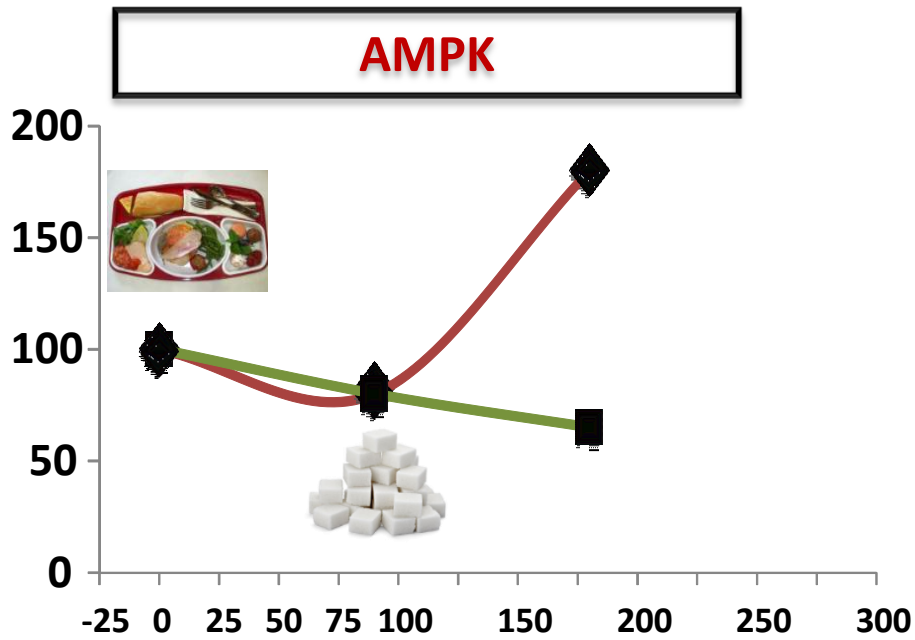
Maintain the muscle ATP levels as long as possible during the post prandial period

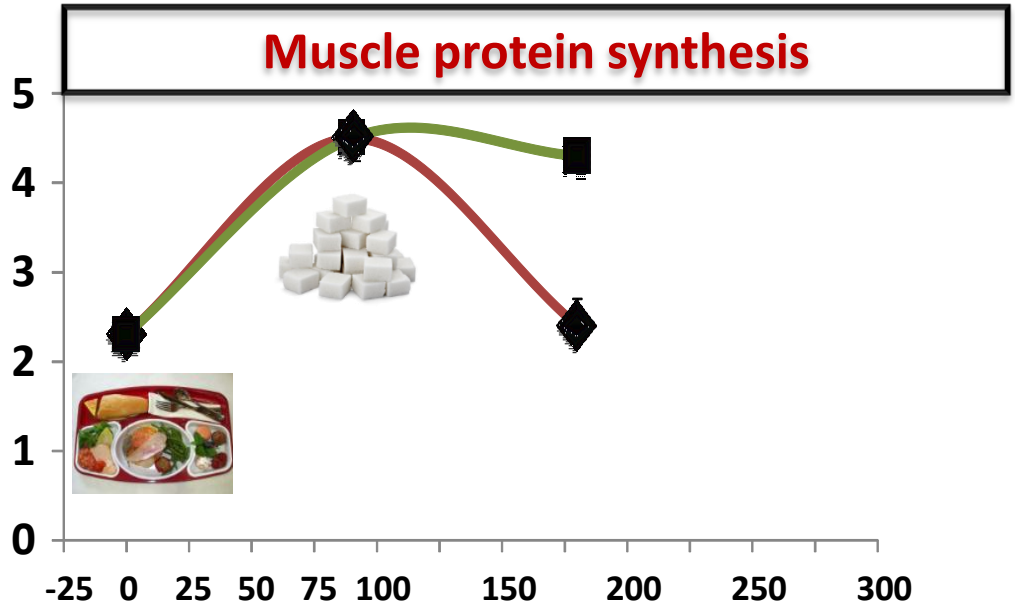


Energy intake between 90 and 180 min after the beginning of the meal

Energetic chrononutrition?







Meal with whey proteins

Meal with whey proteins and energetic bolus 90 min later

Conclusions

- A nutritional strategy efficient in one situation of muscle wasting may not be efficient in an another one
  - Intensity of the anabolic resistance
  - Duration of this anabolic resistance

- Leucine is indeed a very good stimulator muscle protein synthesis

- If leucine given as a free amino acid over a normal protein diet
  - May be inefficient in several situations
  - Desynchronization with the other amino acids

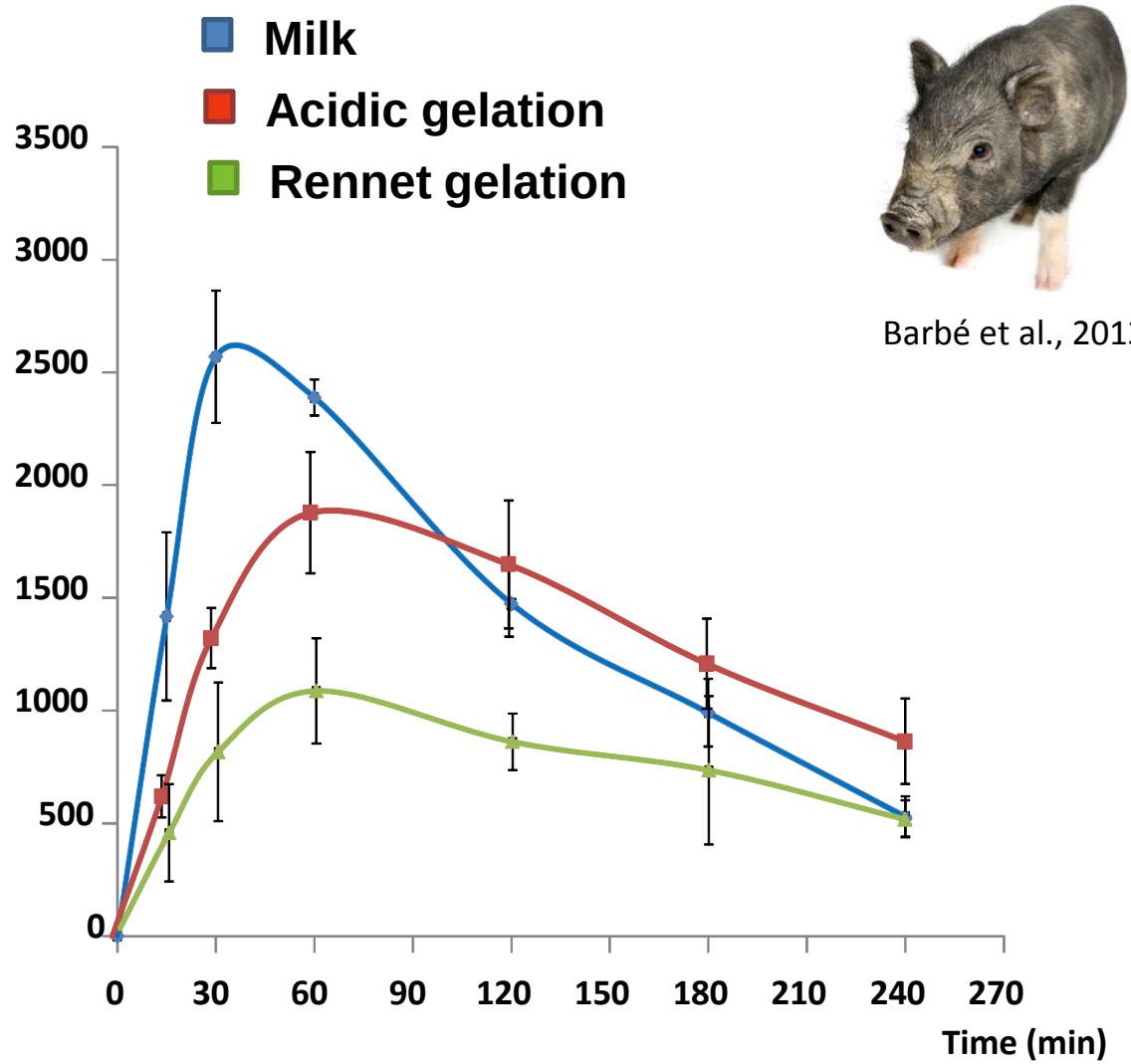
- Synchronization of leucine with the other amino acids is possible with leucine rich proteins
  - Whey

Dietary Whey supplementation: Matrix effect?

Process of the milk protein sources

Milk

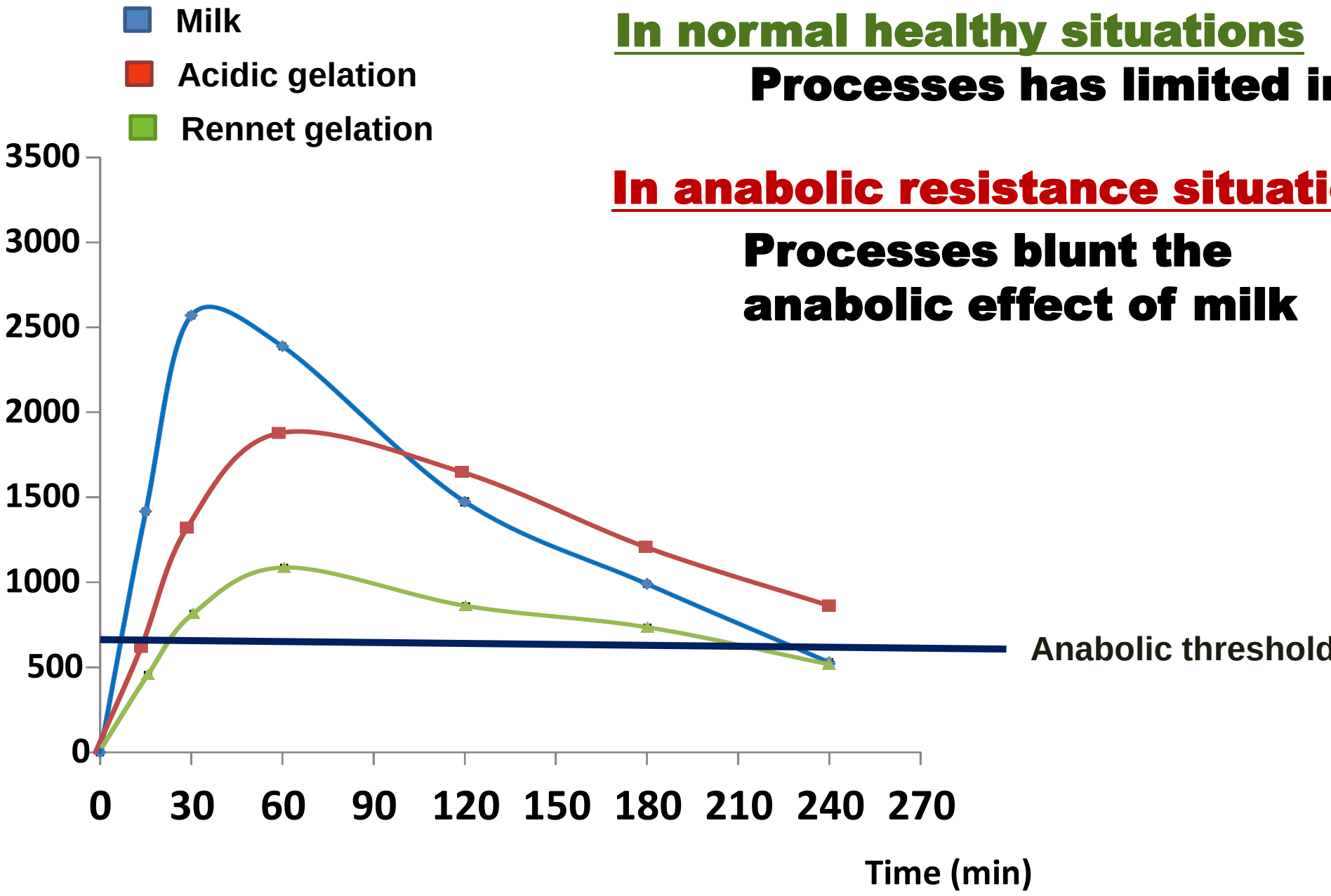
Milk Gelation



Barbé et al., 2013

Gelation → **Decreased digestion speed**
Decreased of amino acid bioavailability

Matrix effect: Which consequences ?



In normal healthy situations

Processes has limited impact

In anabolic resistance situations

Processes blunt the anabolic effect of milk

Conclusions

- Prolonged and better efficiency of whey proteins if the anabolic threshold is also controlled

Combination whey and anti-inflammatory and antioxidants

- So far, only the pulse protein feeding is efficient during aging

Feasibility? In other muscle loss situations?

Long term effect ?

- An energetic chrononutrition has to be tested in combination with whey proteins in (a) real muscle wasting situation(s)

Could the « Stop signal » be a target?

Presence of insulin resistance? (prevention of ATP to increase?)

- Unknown is the effet of dietary chronic leucine bioavailability

Pro diabetic? Insulin resistance?

Unité de Nutrition Humaine

Métabolismes & Santé

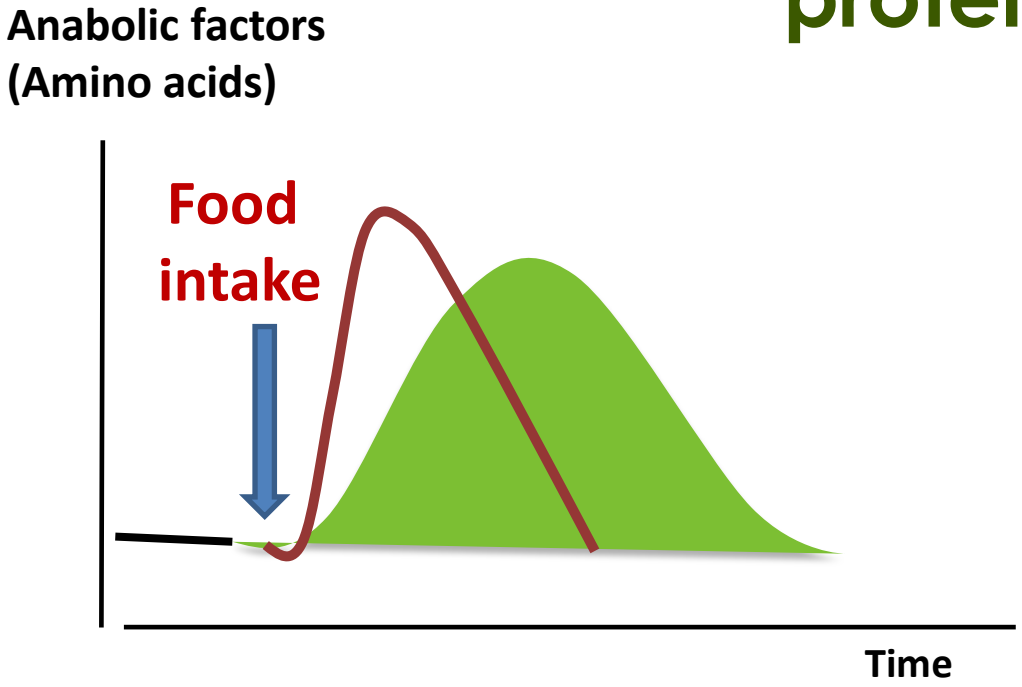
Thank you








Measurement of post prandial protein synthesis in steady state



With free leucine into the diet