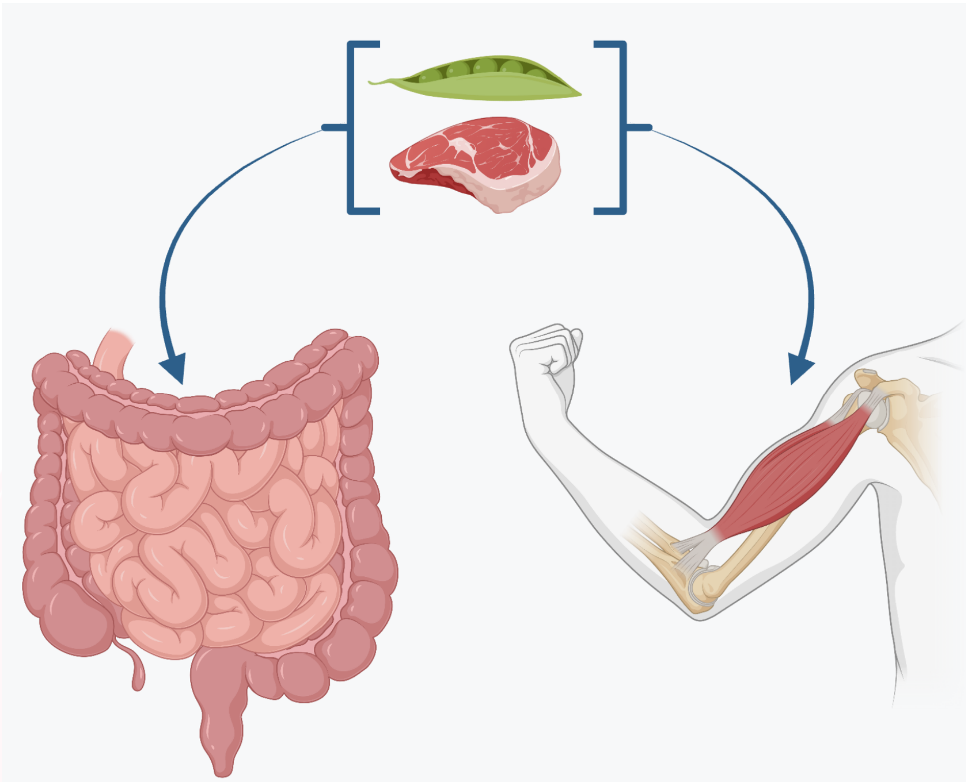
Detailed Study Notes: Episode 454

Eric Helms, PhD – Plant or Animal Protein: Rethinking Protein & Muscle

Table of Contents

Introduction to this Episode



When it comes to eating to promote muscle hypertrophy, muscle repair/recovery and maintenance of mass and function, protein has been an obvious focus. Indeed muscle mass and quality are dependent on the continuous remodeling of skeletal muscle proteins. This is related to the amount of muscle protein balance, i.e. the net difference between muscle protein synthesis (MPS) and muscle protein breakdown (MPB). Because of this, MPS has long been used as a proxy measure for muscle repair and/or growth of muscle.

Protein feeding increases MPS, with the amino acid leucine having a specifically strong impact on MPS. Therefore both the dose of protein and the amino acid profile of the protein have been looked at to assess which protein sources are “superior” for muscle mass and function. This has typically led to viewing animal proteins are better than animal proteins.

But many assumptions are layered into conversations on the topic. In this episode we explore some important points that are often neglected. Is MPS as reliable as we assume? Does the amino acid profile tell us everything about the anabolic effect of a protein? Does dose and timing matter as much as we think? How does the picture change when we look at whole foods or mixed meals?

Connection to Previous Episodes

- #452: Stuart Phillips, PhD – Bacterially Synthesized Whey, Plant vs. Animal Proteins, Muscle & Extended Fasts, & Much More
- #362: Alistair Monteyne – Impact of Mycoprotein & Vegan Diets on Muscle Protein Synthesis
- #123: Donald Layman, PhD – Leucine Kinetics, mTOR Activation & the Anabolic Response to Protein
- #118 – Caoileann Murphy, PhD – Protein Distribution, Per Meal Dosing & Muscle Protein Balance
- #81: Joseph Agu – Protein Synthesis, Amino Acids & Pre-bed Casein

Muscle Protein Balance

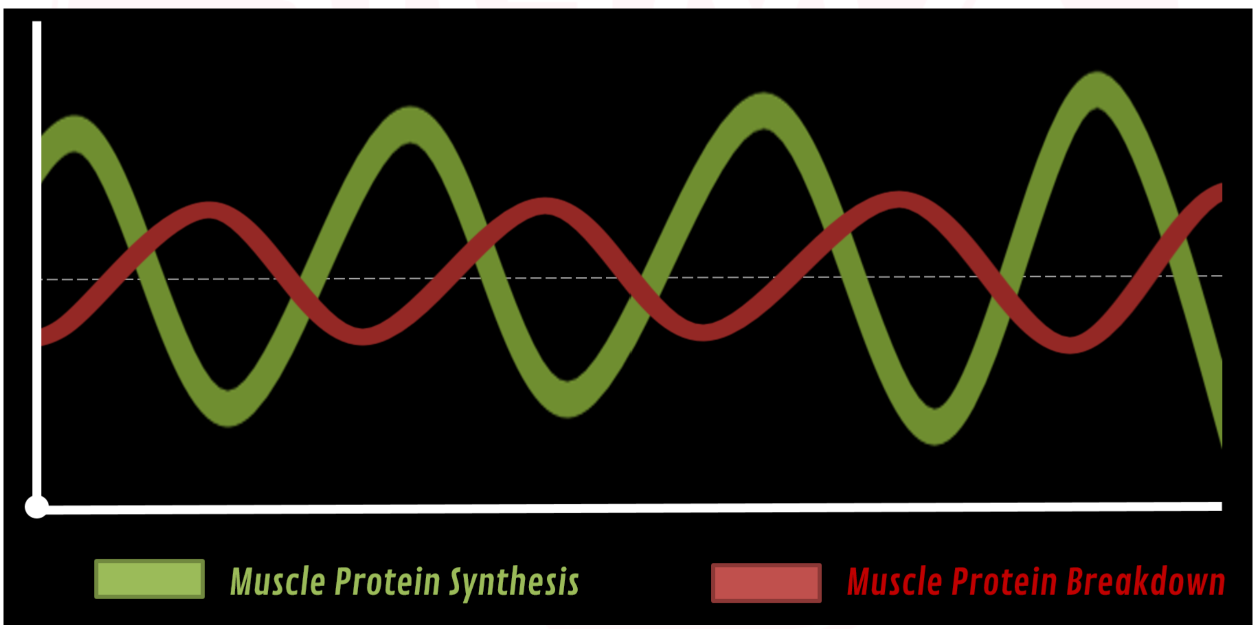
Muscle protein balance is the trade-off between two opposing processes:

1. Muscle protein synthesis (MPS)
2. Muscle protein breakdown (MPB)

At the metabolic level, muscle mass and quality are dependent on the continuous remodeling of skeletal muscle proteins via temporal fluctuations in rates of MPS and MPB (Zaromskyte et al., 2021).

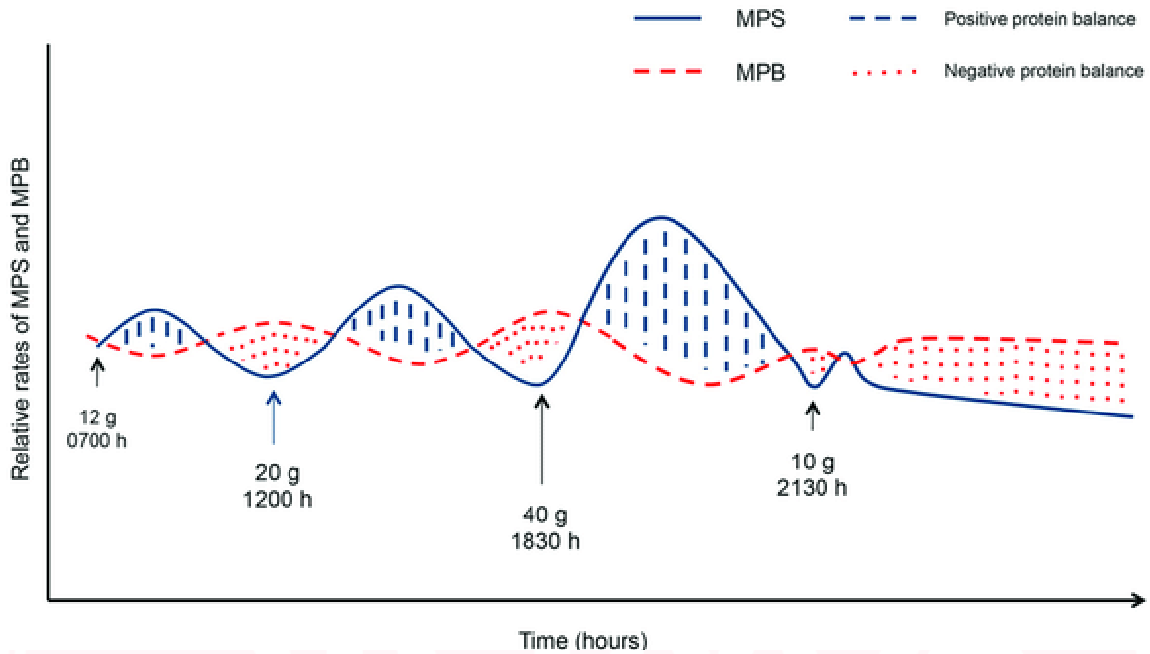
The difference in MPS and MPB over time will be the net muscle protein balance. Therefore, we can assume that a net gain or loss of skeletal muscle protein will be driven by a net positive or negative muscle protein balance.

Note: in research you'll commonly see MPS results reported as muscle protein fractional synthesis rate (FSR).

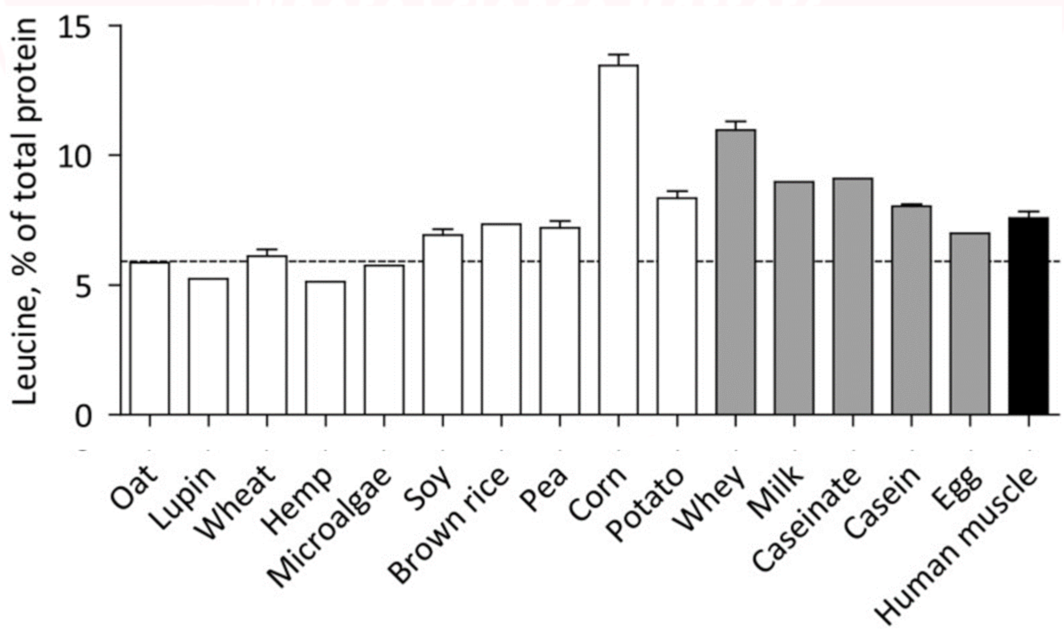


Changes in MPS are much greater in response to exercise & feeding than changes in MPB (Greenhaff et al., 2008). Therefore, MPS is most often used as a proxy for the anabolic response to feeding or exercise.

Area Under the Curve: Rather than simply think of the peak MPS reached, considering the area under the curve (AUC) means looking at the cumulative amount of net MPS. i.e. consider the combined amount of all the blue shaded regions in this next image:



Protein dose, and specifically leucine dose, has been shown to acutely spike MPS. (For on the "leucine trigger" later). Therefore, this has led some to base which proteins are "better" on the leucine content of the protein source. Looking at the leucine sources of common foods, we can see why plant proteins are commonly painted as "poorer" proteins:



From: Gorissen et al., Amino Acids. 2018; 50(12): 1685–1695

The below table shows the amount needed to provide 2.7 g leucine or 10.9 g essential amino acids (i.e., the same amount of leucine or essential amino acids ingested when consuming 25 g whey protein):

	Matched for leucine		Matched for ΣEAA	
	Amount of protein (g)	Amount of raw material (g)	Amount of protein (g)	Amount of raw material (g)
Oat	47	73	51	79
Lupin	52	86	50	83
Wheat	45	55	49	60
Hemp	54	105	48	93
Microalgae	48	69	48	69
Soy	40	55	40	55
Brown rice	37	47	39	49
Pea	38	48	37	46
Corn	20	31	34	52
Potato	33	41	30	37
Whey	25	32	25	32
Milk	31	39	28	36
Caseinate	30	35	28	33
Casein	34	47	32	44
Egg	39	77	34	66

Muscle Damage as a Confounder

Eric highlighted the Damas et al (2018) Paper:

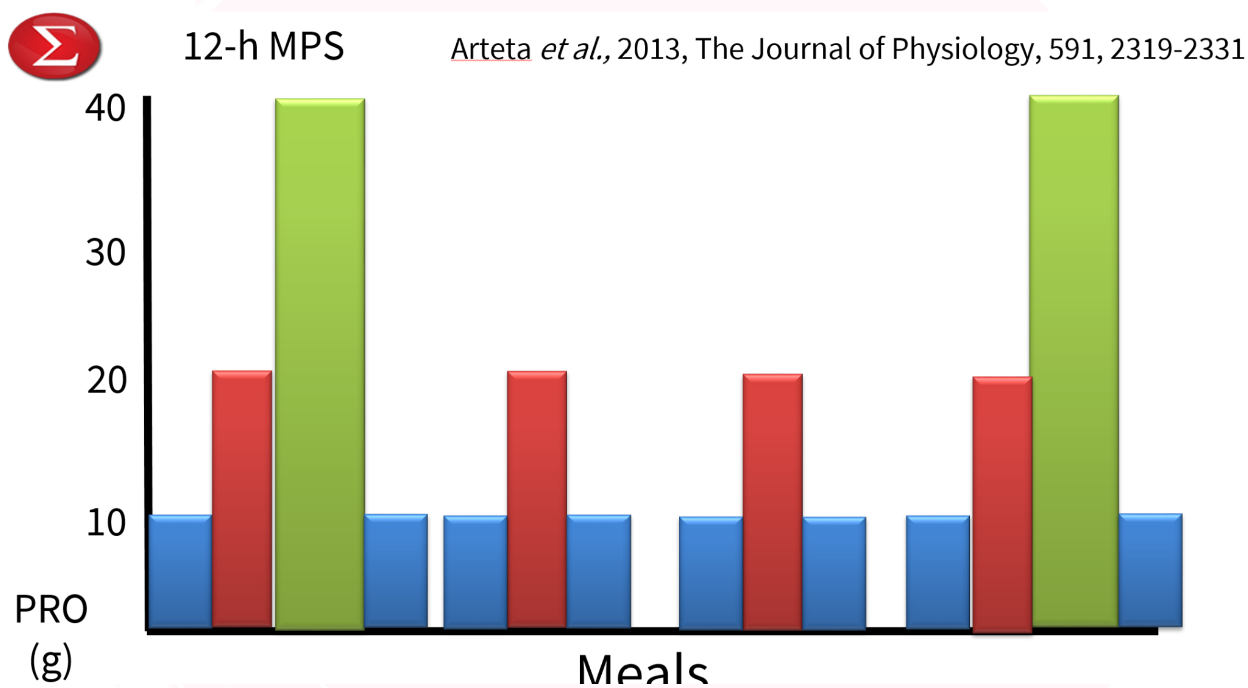
- Didn't find any relationship between muscle damage and hypertrophy.
- And that it actually seemed as though the body had to repair muscle damage before it started giving "resources" towards building muscle.
- But the most important finding in that study for Eric was that the initial scores for MPS were 0.1 R-score related to hypertrophy (so explaining nearly nothing of the variance of hypertrophy).
- Meaning that the initial scores of MPS that you're looking at (within 2-14 hours in most studies), if there's a high component of damage, it's completely confounding the results.

Note, once you corrected for the first 24 or 48 hours there was actually a pretty strong relationship between muscle protein synthesis and longitudinal outcomes and hypertrophy.

Timing & Distribution

Areta et al., 2013:

- Twenty-four healthy trained males undertook a bout of resistance exercise followed by ingestion of 80g of whey protein over 12 hours in one of the following distributions (n = 8/group):
    - 8 × 10 g every 1.5 h (blue)
    - 4 × 20 g every 3 h (red)
    - 2 × 40 g every 6 h (green)



It was found that the greatest MPS response over the 12 hours occurred in the group consuming the 80g of protein as 4 servings of 20g each. This indicates that:

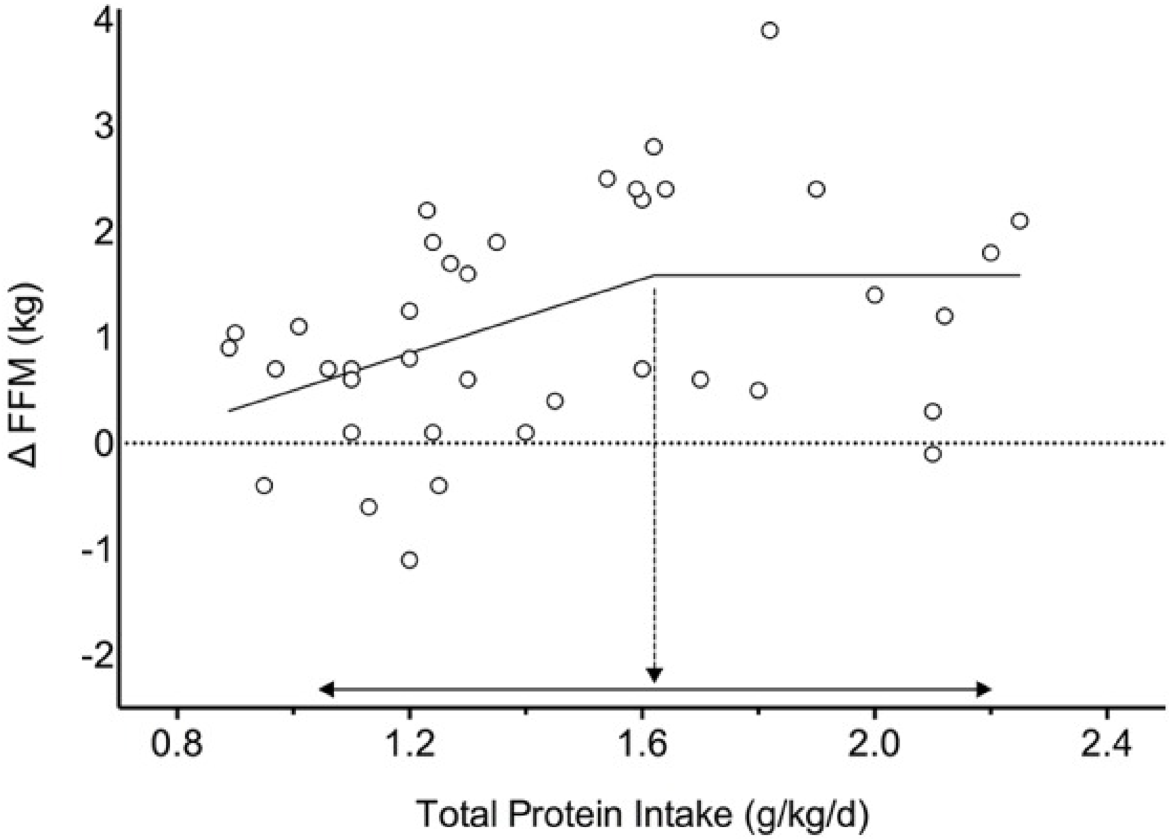
1. 10g per dose (blue) was too small a dose to maximally stimulate MPS at each feeding
2. 2 (larger) meals was too infrequent to maximize MPS over the whole 12 hours

This matches up with the overall body of evidence on protein feeding and MPS dose/distribution, which suggests that MPS is maximally stimulated by:

- 3+ high-protein meals spread across the day
- Each meal having about 0.25 - 0.4 g/kg BW of protein

Total Protein Intake

The commonly cited systematic review by Morton et al., suggests a total intake of 1.6 g/kg BW maximizes muscle gains from resistance training. A Segmental linear regression between relative total protein intake (g/kg body mass/day) and the change in fat-free mass (ΔFFM) measured by dual energy X-ray absorptiometry is shown below. Each circle represents a single group from a study.



From: [Morton et al., Br J Sports Med. 2018 Mar; 52(6): 376–384.](#)

[Hudson et al. systematic review (2018)](#): Effects of protein supplements consumed with meals, versus between meals, on resistance training-induced body composition changes in adults

- 34 randomized controlled trials with 59 intervention groups
- The intervention groups were designated as:
  - Consuming protein supplements with meals (n = 16)
  - Consuming protein supplements between meals (n = 43)
- Increase in lean mass:
  - With meals = 94%
  - Between meals = 90%
- Decrease in fat mass:
  - With meals = 87%
  - Between meals = 59%

Nutrient timing revisited: is there a post-exercise anabolic window? - Aragon & Schoenfeld (2013)

- "Despite claims that immediate post-exercise nutritional intake is essential to maximize hypertrophic gains, evidence-based support for such an "anabolic window of opportunity" is far from definitive. The hypothesis is based largely on the presupposition that training is carried out in a fasted state."

Moro et al., 2016 - Eight weeks of time-restricted feeding (16/8)

- Thirty-four resistance-trained males
- Randomly assigned to:
  - Time-restricted feeding (TRF)
  - Normal diet group (ND).
- TRF subjects consumed 100 % of their energy needs in an 8-h period of time each day, with their caloric intake divided into three meals consumed at 1 p.m., 4 p.m., and 8 p.m.

Digestibility & Availability

- Digestibility = net absorption of an amino acid
- Chemical integrity = proportion of absorbed amino acid in utilizable form

Two "scores" of digestibility:

1. Protein Digestibility-Corrected Amino Acid Score (PDCAAS)
2. Digestible Indispensable Amino Acid Score (DIAAS)

PDCAAS:

- Single value represents digestibility of crude protein based on fecal protein content
- Does not account for bioavailability of amino acids

DIAAS:

- Value for each amino acid based on terminal ileal protein content
- Determines digestibility of indispensable amino acids

Table 2 Approximations of Amino Acid Absorption from Different Protein Sources

Protein source	Absorption rate (g/h)	Reference
Egg protein raw	1.3	43
Pea flour	2.4	41
Egg protein cooked	2.8	43
Pea flour: globulins & albumins	3.4	42
Milk protein	3.5	40
Soy protein isolate	3.9	46
Free AA	4.3	39
Casein isolate	6.1	38
Free AA (same profile as casein)	7-7.5	39
Whey isolate	8-10	38

From: Bilsborough and Mann, 2006

Despite casein being commonly promoted as a "slow digesting" protein, this is only in relation to the digestion speed of whey. As shown above, casein is essentially the second fastest digesting protein there is.

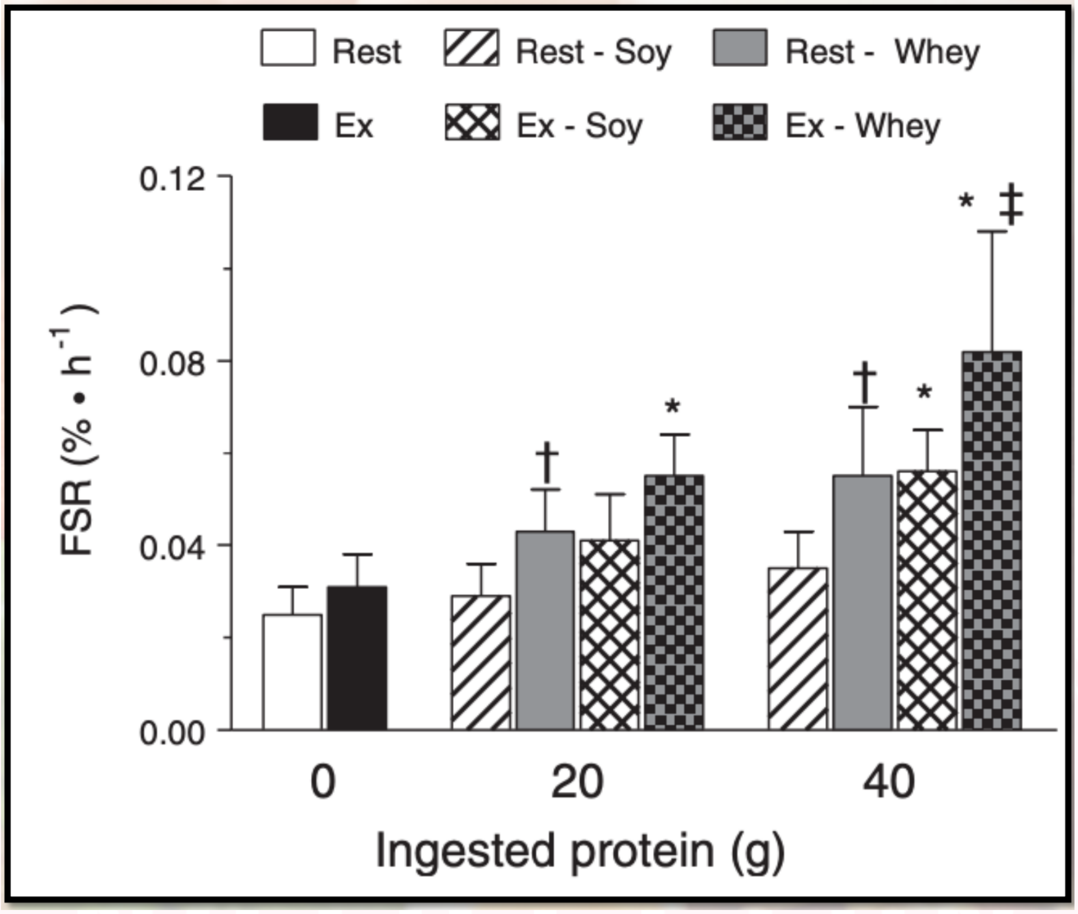
Plant vs. Animal Protein

Table 1. Protein quality assessment based on protein sources.

Protein Type	Protein Digestibility (%)	Biological Value (%)	Net Protein Utilization (%)	PDCAAS	DIAAS
		Animal source			
Red meat [1]		80	73	92	
Casein [1,3,6]	99	77	76–82	100	
Whey [1]		104	92	100	
Milk [1,4,6]	96	91	82	100	114
Egg [1,4,6]	98	100	94	100	113
		Plant source			
Black bean [1,6,8]	70			75	
Cooked black bean [7,8]	83			65	59
Soy flour [5,8]	80			93	89(SAA)
Soy protein isolate[1,6]	98	74	61	100	
Green lentil [3,4]	84			63	65
Yellow split pea [4,6]	88			64	73
Cooked pea [7]	89			60	58
Pea protein concentrate [7]	99			89	82
Chickpea [3,4]	89			74	83
Peanuts [1]				52	
Roasted peanuts [7]	98			51	43
Peanut butter [3,4]	98			45	46
Whole grains [2]				45	
Wheat [3,5,6]	91	56–68	53–65	51	45(Lys)
Wheat gluten [1]		64	67	25	
White bread [4,6]	93			28	29
White rice [4,6]	93			56	57
Cooked rice [7]	87			62	60

Adapted from: [Berrazaga et al., Nutrients. 2019 Aug 7;11(8):1825. doi: 10.3390/nu11081825.]

Comparing isolated proteins, there is a consistent finding of "superiority" for animal proteins, particularly whey protein, when MPS is used as the outcome to assess which is "better". As an example, see findings from Yang et al. comparing whey to soy protein:



Taken from: [Yang et al., Nutr Metab (Lond). 2012 Jun 14;9(1):57. doi: 10.1186/1743-7075-9-57.]

However, when outcomes such as actual changes in muscle tissue or muscle thickness, the results aren't as clear cut. When comparing isolated protein supplements, a range of studies have shown no real differences between animal and plant proteins on such outcomes, for example:

- Lean tissue: Whey vs soy (Candow et al., 2006)
- Muscle thickness: whey vs pea (Babault et al., 2015)
- Lean body mass & muscle thickness: whey vs. rice (Joy et al., 2013)
- Fat-free mass: whey vs rice (Moon et al., 2020)

However, what might be more important is to consider comparisons that go beyond isolated supplemental proteins, and instead look at whole foods and/or diets…

Whole Foods vs Isolated Proteins

The “leucine trigger” hypothesis

- The "leucine trigger" hypothesis was originally conceived to explain the post-prandial regulation of muscle protein synthesis (MPS).
- This hypothesis implicates the magnitude (amplitude and rate) of postprandial increase in blood leucine concentrations for regulation of the magnitude of MPS response to an ingested protein source.
- Experimental support for the leucine trigger hypothesis primarily stems from studies of isolated protein sources such as intact whey, micellar casein, and soy protein fractions
- The ingestion of an isolated protein source (e.g., whey) results in a rapid rise in plasma leucine concentrations, which is superior in terms of amplitude when compared to whole food sources of protein, and corresponds to the extent of stimulation of muscle protein synthesis rates (Tang et al., 2009).
- Recent evidence from experimental studies has challenged this theory, with reports of a disconnect between blood leucine concentration profiles and post-prandial rates of MPS in response to protein ingestion.
- It has been hypothesized that the interaction of non-protein nutritive components with dietary amino acids (food matrix effects) has a direct effect on post-exercise muscle protein synthesis rates (Burd et al., 2019).
- Recent studies also reported that protein-rich whole food sources also are potent in stimulating MPS, despite not facilitating a rapid rise in leucine concentrations during exercise recovery
- A systematic review by Zaromskyte et al. (2021) is supportive of the idea that the leucine trigger hypothesis is more relevant within the context of ingesting isolated protein sources rather than protein-rich whole foods.

From Burd et al., 2009:

1. *“Whole protein foods are often more than their constituent amino acids, containing other non-protein nutritive components to facilitate nutrient–nutrient interactions, modulate nutrient behavior, and/or act directly as anabolic signaling molecules.*
2. *A food-first approach to post-exercise protein intake will be beneficial for both the skeletal muscle adaptive response and diet quality for most people.”*

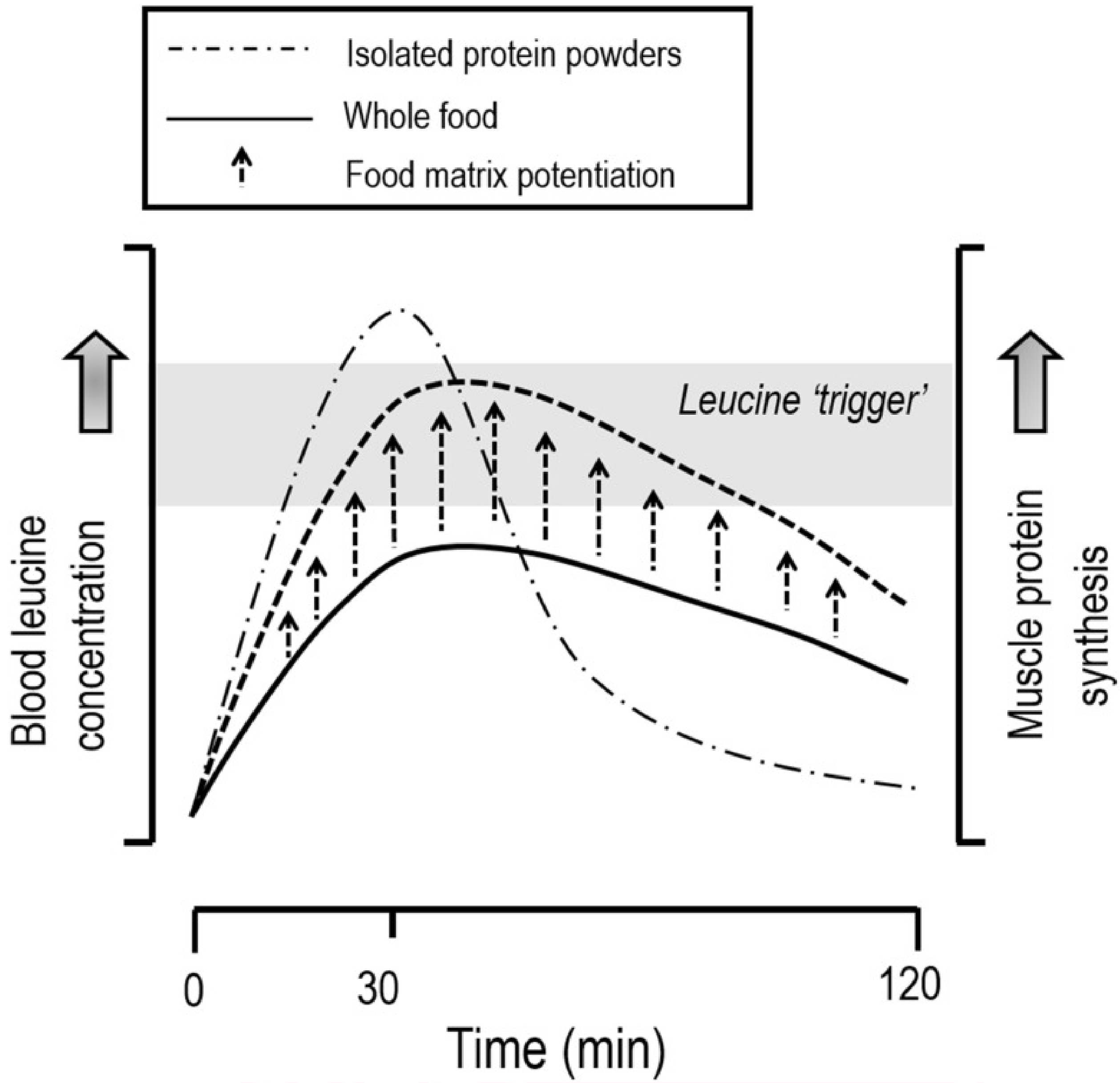
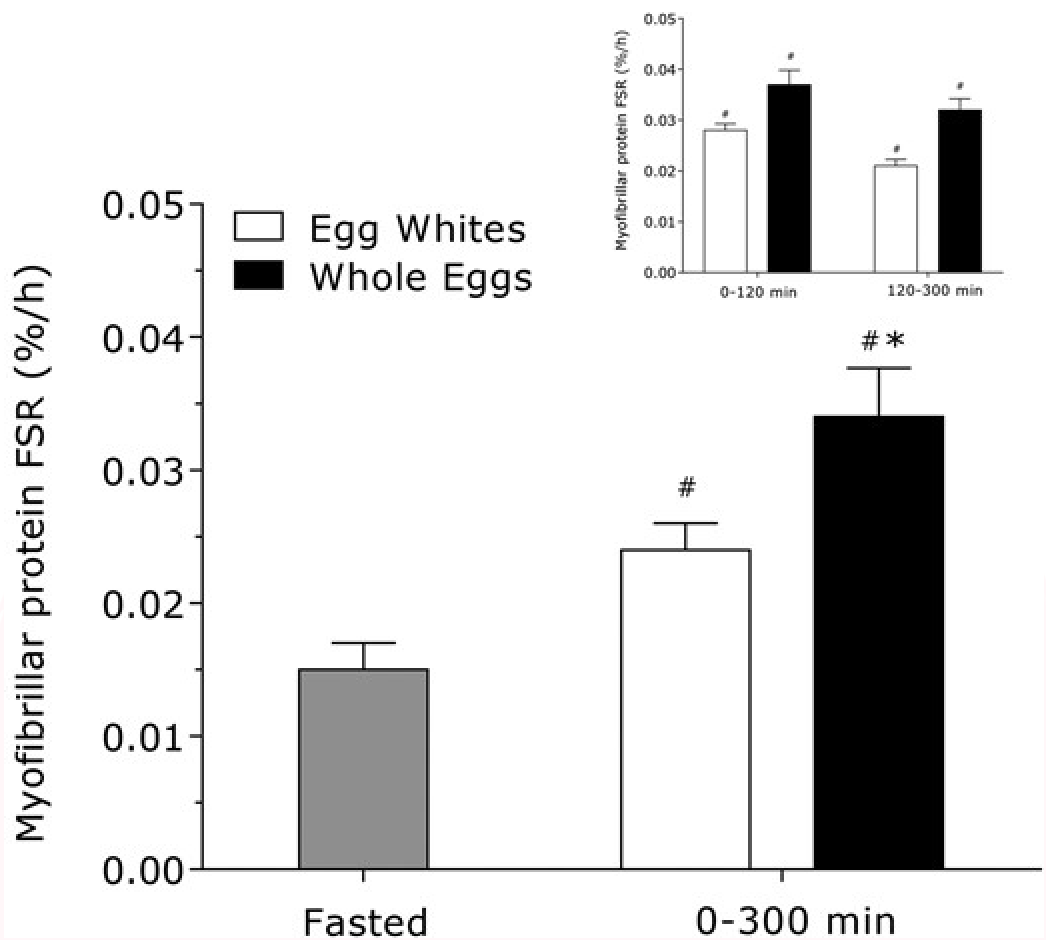


Image from: [Burd et al., Sports Med. 2019; 49(Suppl 1): 59–68.]

Example: Whole Egg vs. Egg Whites

- Van Vliet et al. (2017) published data of their RCT showing greater MPS from whole egg consumption, compared to egg whites of the same protein content.
  - The lead author, Stephan Van Vliet, discussed this trial on the podcast in episode 230.
- The whole egg consumption lead to greater MPS response, despite the fact that there were significantly greater postprandial leucine levels from egg whites (34%) vs. whole eggs (25%).



Taken from: [van Vliet et al., Am J Clin Nutr. 2017 Dec;106(6):1401-1412.]()

There have been many explanations hypothesized as to how the food matrix could have impacts on both MPS and other anabolic signalling beyond simply the protein or leucine content.

For example with whole eggs, the whole egg matrix is rich in high-quality dietary protein, lipids, vitamins, and minerals when compared to the egg white matrix.

And it has been suggested that the non-protein components in whole eggs can facilitate nutrient sensing mechanisms in muscle. The non-protein components include:

- Cholesterol
- Lipids
- Vitamins
- Minerals
- Other bioactive components

Some of these are presented in this diagram:

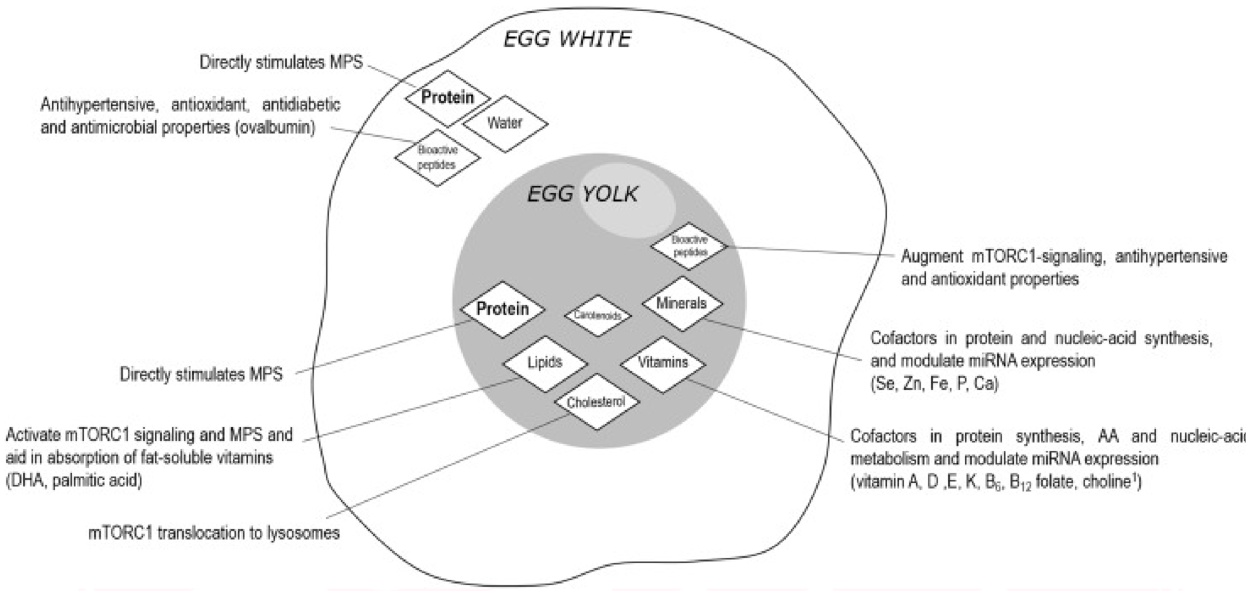
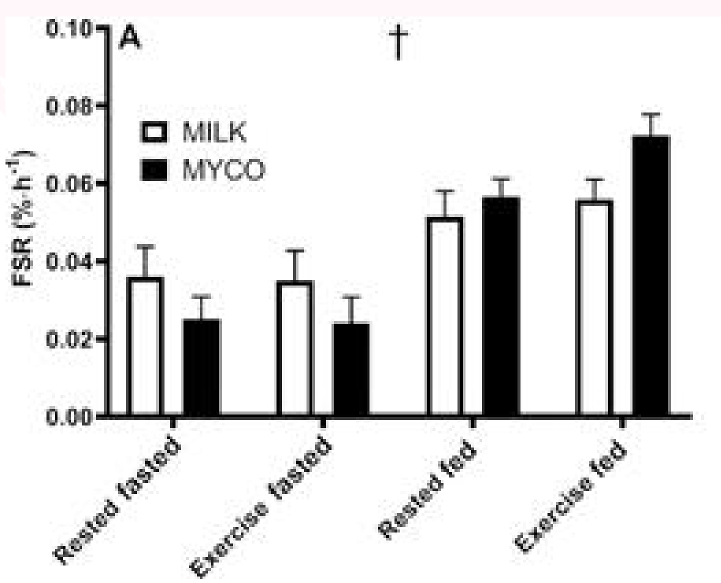


Image from: [Burd et al., Sports Med. 2019; 49(Suppl 1): 59–68.]

Mycoprotein

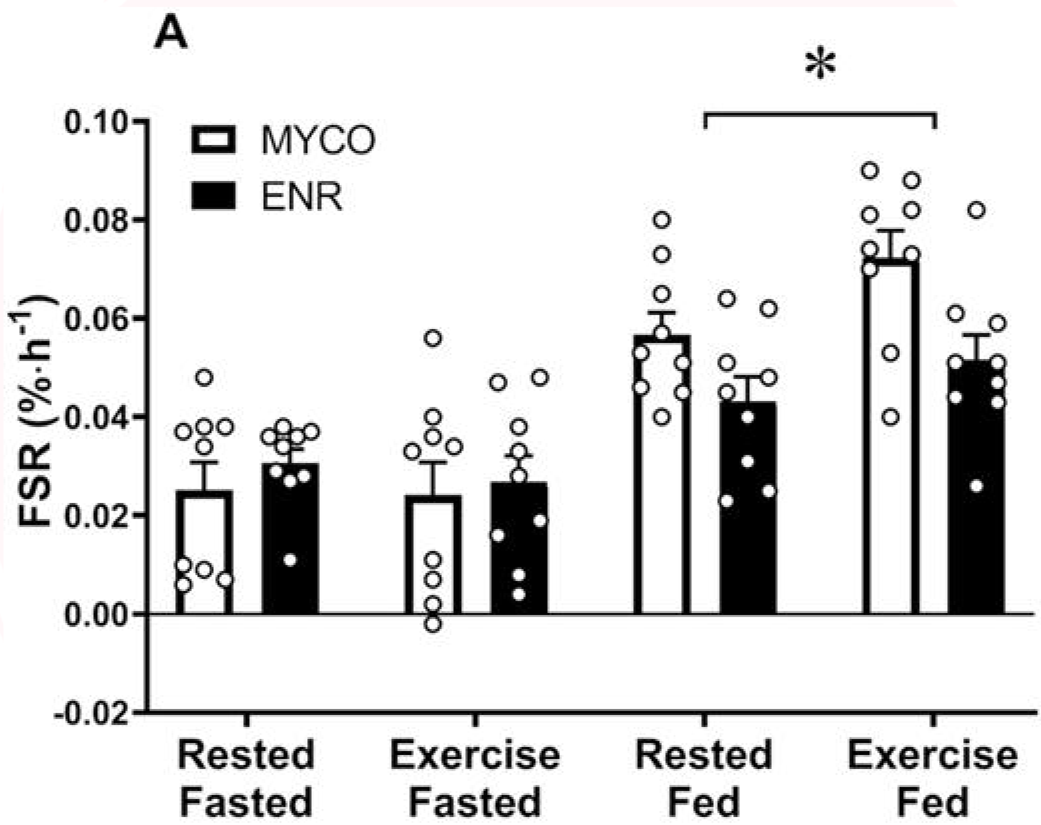
- A trial out of Benjamin Wall's group at Exeter ([Monteyne et al., 2020] a) showed that the ingestion of a single bolus of mycoprotein increased MPS to a greater extent than a leucine-matched bolus of milk protein.
  - Lead author Alistair Monteyne was on the podcast discussing the labs work in [episode 362]



From: [Monteyne et al., Am J Clin Nutr. 2020 Aug 1;112(2):318-333].

Interestingly, the same group did a study that highlighted the importance of the whole food matrix as opposed to only looking at the main amino acids that impact MPS.

In this trial (Monteyne et al., 2020 b), aimed to see if 35 g of mycoprotein enriched with branched-chain amino acids (BCAAs) stimulates MPS to the same extent as 70 g of mycoprotein. They found that the lower-dose BCAA-enriched mycoprotein stimulated MPS to a lesser extent than the 70g of mycoprotein. This indicates that the impact on MPS can't just be result of the BCAA content of mycoprotein. Instead there are other aspects of the food matrix that lead to greater MPS.



From: Monteyne et al., J Nutr. 2020 Nov 19;150(11):2931-2941.

Conclusions

1. On gram-for-gram basis plant protein sources exert less anabolic potential
2. However, these comparisons may not capture the training effects of plant proteins
3. Proxy outcomes like MPS may not capture performance adaptations
4. Increasing plant protein dose to provide more EAA/leucine produces similar effects vs. whey protein
5. Where total daily protein targets for exercise are met the source is less relevant
6. Role and relevance of food matrix yet to be fully understood
    a. e.g., Is tofu or Greek yogurt "better" as an anabolic stimulus?
7. **So "Plant vs. animal protein" is the wrong question to ask**

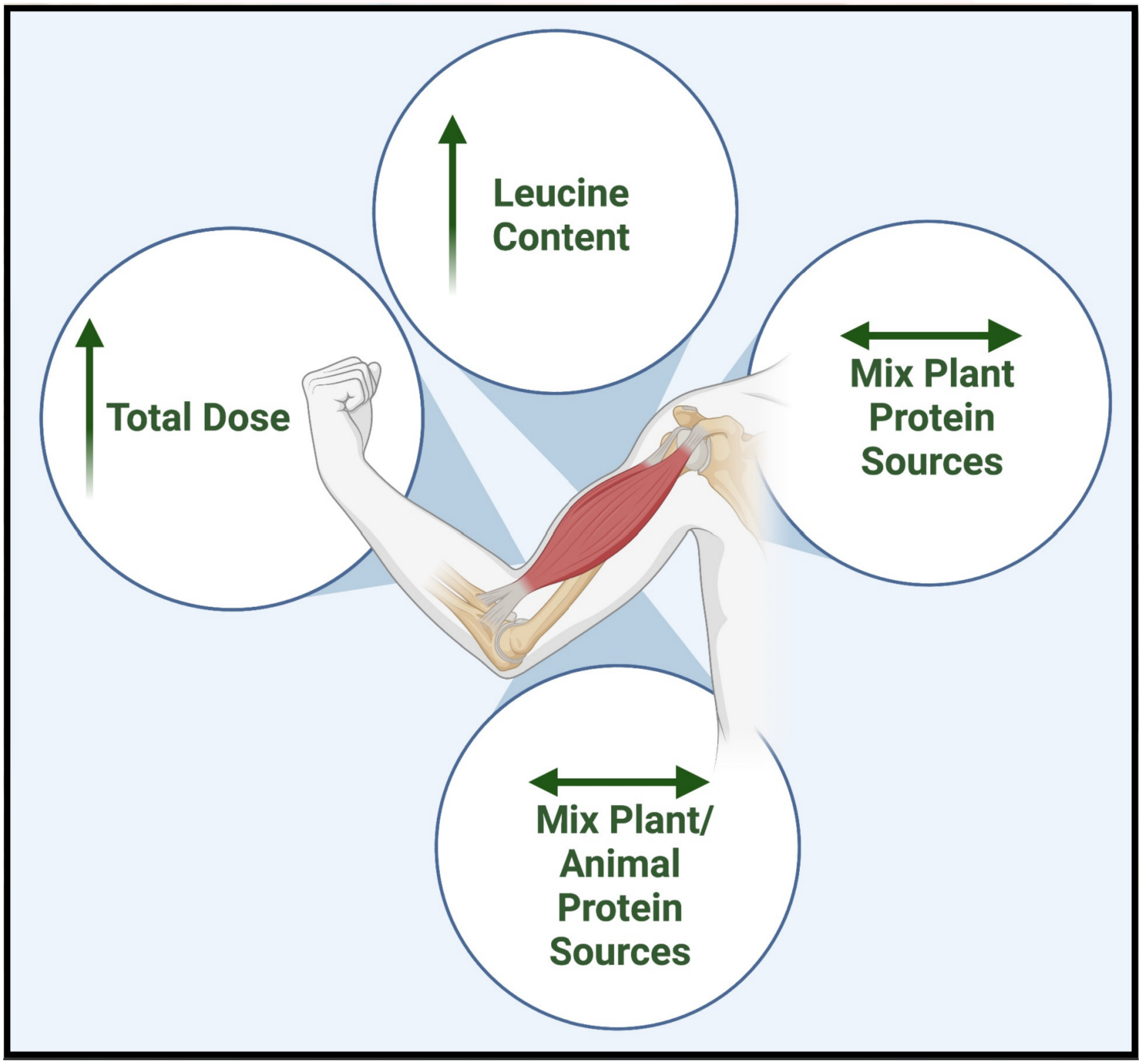
Recommended Read:

- Making Sense of Muscle Protein Synthesis: A Focus on Muscle Growth During Resistance Training - Witard, Bannock & Tipton, 2022

Practical Application

If consuming a plant-exclusive diet and maximizing hypertrophy or muscle recovery is a priority, then some specific modifications can be made.

1. Ensure overall intake is appropriate (e.g. 1.6 g/kg or more)
2. Have that split into 3+ meals per day
3. Use good supplemental proteins such as pea protein powder as needed
4. If using protein sources lower in leucine/BCAA then meals can have a larger total protein dose or have supplemental amino acids added



Taken from: Lectures slides by Alan Flanagan