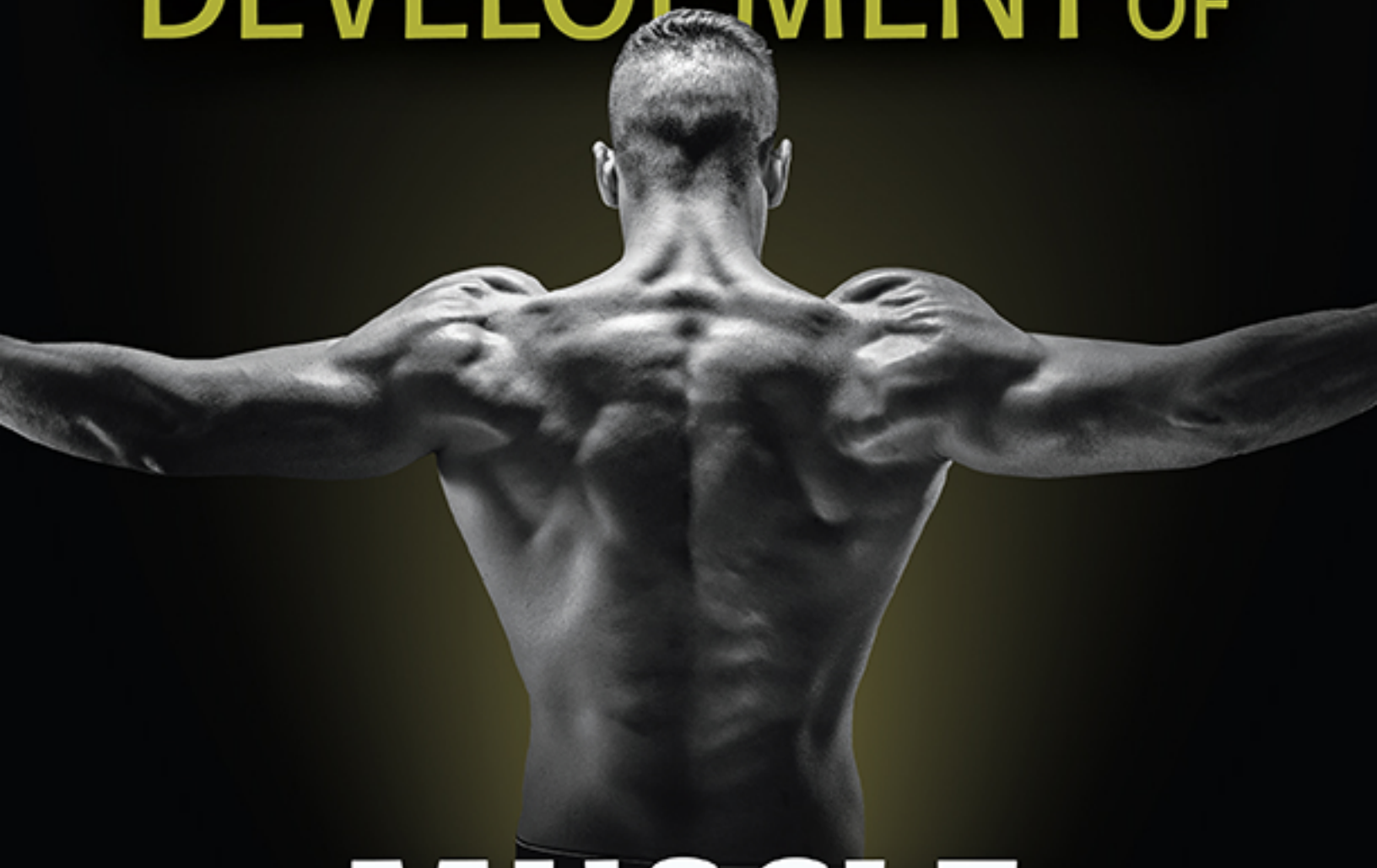
SECOND EDITION

SCIENCE AND DEVELOPMENT OF



MUSCLE HYPERTROPHY

Brad Schoenfeld

Science AND Development OF Muscle Hypertrophy

Second Edition

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HUMAN KINETICS

Library of Congress Cataloging-in-Publication Data

Names: Schoenfeld, Brad, 1962- author.
Title: Science and development of muscle hypertrophy / Brad J. Schoenfeld, PhD, CSCS, CSPS, FNSCA, Lehman College, Bronx, New York.
Description: Second edition. | Champaign, IL : Human Kinetics, [2021] | Includes bibliographical references and index.
Identifiers: LCCN 2019045855 (print) | LCCN 2019045856 (ebook) | ISBN 9781492597674 (hardcover) | ISBN 9781492597681 (epub) | ISBN 9781492597704 (pdf)
Subjects: LCSH: Muscles--Hypertrophy. | Exercise. | Physical fitness.
Classification: LCC QP303 .S256 2021 (print) | LCC QP303 (ebook) | DDC 612.7/4--dc23
LC record available at https://lccn.loc.gov/2019045855
LC ebook record available at https://lccn.loc.gov/2019045856

ISBN: 978-1-4925-9767-4 (print)

The web addresses cited in this text were current as of November 2019, unless otherwise noted.

Senior Acquisitions Editor: Roger W. Earle; **Managing Editor:** Shawn Donnelly; **Copyeditor:** Annette Pierce; **Proofreader:** Leigh Keylock; **Indexer:** Dan Connolly; **Permissions Manager:** Martha Gullo; **Graphic Designer:** Whitney Milburn; **Cover Designer:** Keri Evans; **Cover Design Specialist:** Susan Rothermel Allen; **Photograph (cover):** Georgijevic /E+/Getty Images; **Photographs (interior):** © Human Kinetics, unless otherwise noted; **Photo Asset Manager:** Laura Fitch; **Photo Production Manager:** Jason Allen; **Senior Art Manager:** Kelly Hendren; **Illustrations:** © Human Kinetics, unless otherwise noted; **Printer:** Versa Press

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Printed in the United States of America 10 9 8 7 6 5 4 3 2 1

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E8053

To my father, may he rest in peace, for instilling the scientific method in me for as long as I can remember. You pushed me to learn, to pursue higher education, and to become a scholar. Wish you were around to see the fruits of your efforts. This is for you; I know it would have made you proud.

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PREFACE

This book truly has been a labor of love.

I had envisioned writing an evidence-based text on muscle hypertrophy since my days as a graduate student in exercise science. At the time there were a plethora of consumer-oriented books describing programs for building muscle. However, they all relied largely on anecdote to make recommendations; none extensively delved into the actual science of the topic. A more scientific approach was clearly needed for the masses. In 2016, my vision became reality with publication of the first edition of *Science and Development of Muscle Hypertrophy*.

Much has transpired since the release of the book's first edition. For one, research on muscle hypertrophy has skyrocketed. Thousands of new studies have been published, helping to further our understanding as to what makes muscle grow and how to best go about optimizing muscle development. Moreover, feedback and the perspective of time have allowed me to see ways in which the original text could be improved and expanded. Ultimately, I determined that a revision of the original text was warranted.

I am thrilled to present the second edition of *Science and Development of Muscle Hypertrophy*. The text has been completely updated, with inclusion of more than 30% new content. In addition to containing extensive discussion of new research findings and their practical implications to muscle building, I have added two new chapters of importance: one that delves into the methods employed to measure muscle growth and another that evaluates various advanced training practices commonly employed to enhance hypertrophy. Further, 10 new sidebars highlight specific topics of interest to gaining lean mass.

A few words of note about the book in general: While the writing is geared toward master's level students in exercise-related disciplines, the majority of the text should be accessible to anyone with a fundamental understanding of the principles of exercise science. The first two chapters are the most scientifically technical, and will require some background in exercise physiology and biomechanics to fully appreciate the complexities and challenges faced when attempting to draw inferences as to the underlying mechanisms of what drives hypertrophic adaptations. However, even if you do not possess a strong scientific background, much information can be gleaned from at least reading through these chapters to familiarize yourself with basic concepts and terminology.

Despite its scientific basis, the overall focus of the book is on the applied aspects of muscle development. As such, each chapter contains "key points" that summarize take-home messages and their practical applications. There also is an entire chapter (chapter 8) devoted to synthesizing the literature in an evidence-based fashion to create customized hypertrophy-oriented programs.

In sum, I hope you agree this is the most complete resource on the market for bridging the gap between science and practice to optimize muscle development.

Knowledge is power; learn and thrive.

ACKNOWLEDGMENTS

First and foremost, to Roger Earle, for envisioning this project and providing all the necessary resources to ensure its quality. I am thankful for your trust in me writing the book and for your continual guidance throughout the publication process. Without your efforts, this book would not have come to fruition. I am eternally grateful.

To Shawn Donnelly, for effectively and efficiently managing the development of this project so that everything ran smoothly. Your efforts were greatly appreciated.

To Grant Tinsley, Mike Israetel, Cody Haun, Henning Wackerhage, James Krieger, Adam Sharples, Alan Aragon, Bret Contreras, Mike Roberts, and Andrew Vigotsky, for providing input on the book. Your insights helped to improve its breadth and ensure its accuracy.

Finally, to my past and present students, who perpetually inspire me to learn and grow and to be the best I can be in my field. Your personal development and success are what drive me to keep doing what I am doing and are part of what make my life so fulfilling.

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Hypertrophy-Related Responses and Adaptations to Exercise Stress

chapter 1

To comprehend the many factors related to maximizing skeletal muscle hypertrophy, it is essential to have a foundational knowledge of how the body reacts and adapts to exercise stress. This chapter reviews the structure and function of the neuromuscular system and the responses and adaptations of the neuromuscular, endocrine, paracrine, and autocrine systems. Although these systems are discussed separately, they are integrally connected; their interactions ultimately mediate lean tissue growth.

Neuromuscular System

A detailed discussion of the complexities of muscle hypertrophy requires a fundamental understanding of the neuromuscular system—in particular, the interaction between nerves and muscles that produces force to carry out human movement. Although a thorough exploration of the topic is beyond the scope of this book, this section provides a general overview of concepts that are referenced in later chapters. Those interested in delving further into the subject are advised to seek out one of the many textbooks specific to exercise physiology.

Structure and Function

From a functional standpoint, individual skeletal muscles are generally considered single entities. However, the structure of muscle is highly complex. Muscle is surrounded by layers of connective tissue. The outer layer covering the entire muscle is called the *epimysium*; within the whole muscle are small bundles of fibers called *fasciculi* that are encased in the *perimysium*; and within the fasciculus are individual muscle cells (i.e., fibers) covered by sheaths of *endomysium*. The number of fibers ranges from several hundred in the small muscles of the eardrum to over a million in large muscles such as the gastrocnemius. In contrast to other cell types, skeletal muscle is *multinucleated* (i.e., contains many nuclei), which allows it to produce proteins so that it can grow larger when necessary. Individual muscle fibers can span lengths of up to approximately 600 millimeters (23 inches) and their volumes can exceed those of typical mononucleated cells by more than 100,000-fold (202).

Skeletal muscle appears striped, or *striated*, when viewed under an electron microscope. The striated appearance is due to the stacking of sarcomeres, which are the basic functional units of myofibrils. Each muscle fiber contains hundreds to thousands of *myofibrils*, which are composed of many *sarcomeres* joined end to end. Myofibrils contain two primary protein filaments that are responsible for muscle contraction: *actin* (a thin filament) and *myosin* (a thick filament), which comprise approximately 50% of the protein content of a muscle cell (53). Each myosin filament is surrounded by six actin filaments, and three myosin filaments surround each actin filament, thereby maximizing their ability to interact. Additional proteins, including titin, nebulin, and myotilin, are present in muscle to maintain the structural integrity of the sarcomere or aid in regulating muscular contractions, or both. Figure 1.1 shows the sequential macro- and microstructures of muscle tissue.

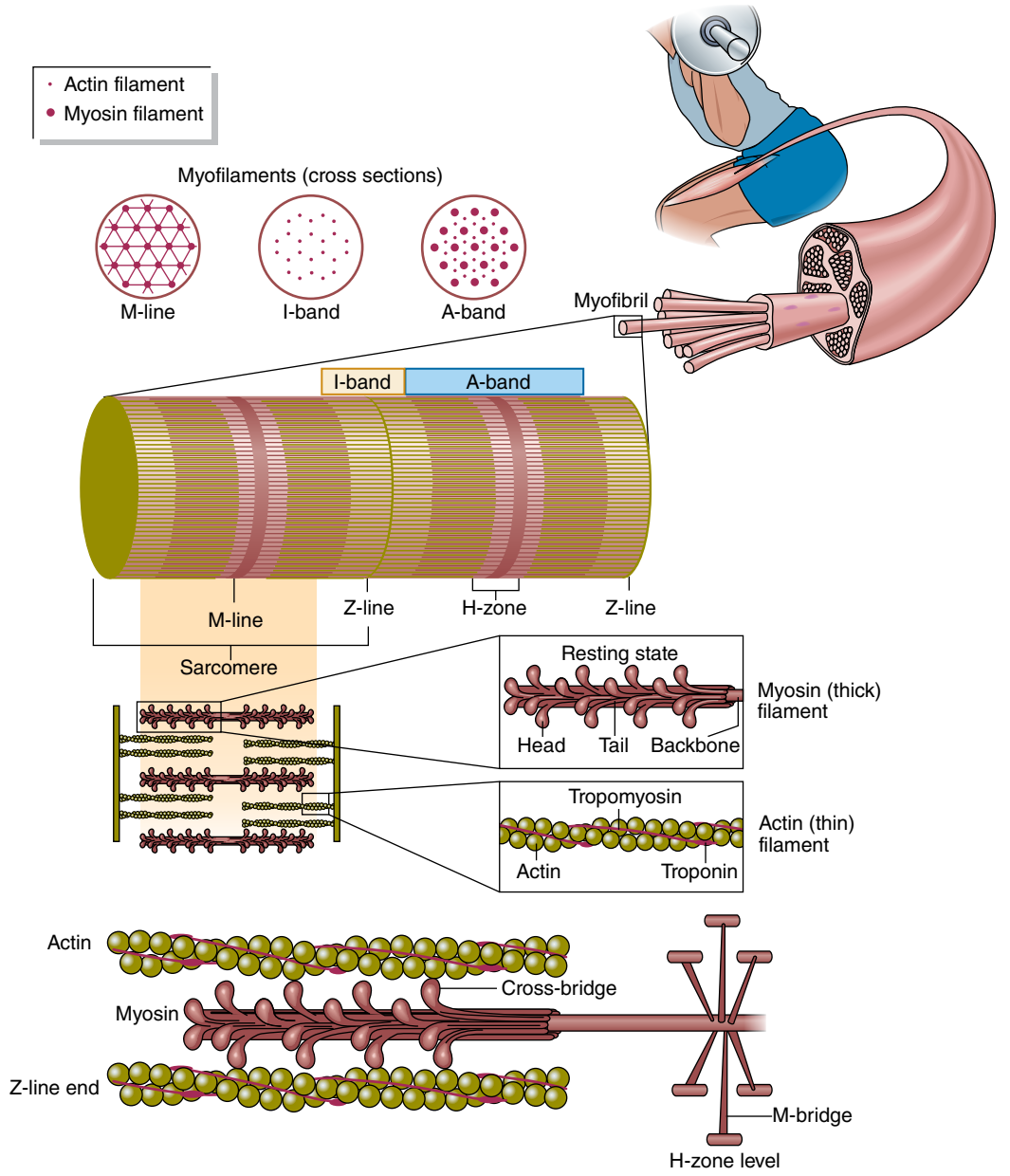

FIGURE 1.1 Sequential macro- and microstructures of muscle.

Motor Unit

Muscles are innervated by the nervous system. Individual nerve cells associated with muscular actions are called *motor neurons*. Motor neurons consist of three regions: a cell body, an axon, and dendrites. When a decision is made to carry out a movement, the axon conducts nerve impulses away from the cell body to the muscle fibers, ultimately leading to muscular contraction. Collectively, a single motor neuron and all the fibers it innervates is called a *motor unit* (figure 1.2). When a motor unit is innervated, all of its fibers contract; this is known as the all-or-none principle.

Sliding Filament Theory

It is generally accepted that movement takes place according to the *sliding filament theory* proposed by Huxley in the early 1950s (97). When a need to exert force arises, an action potential

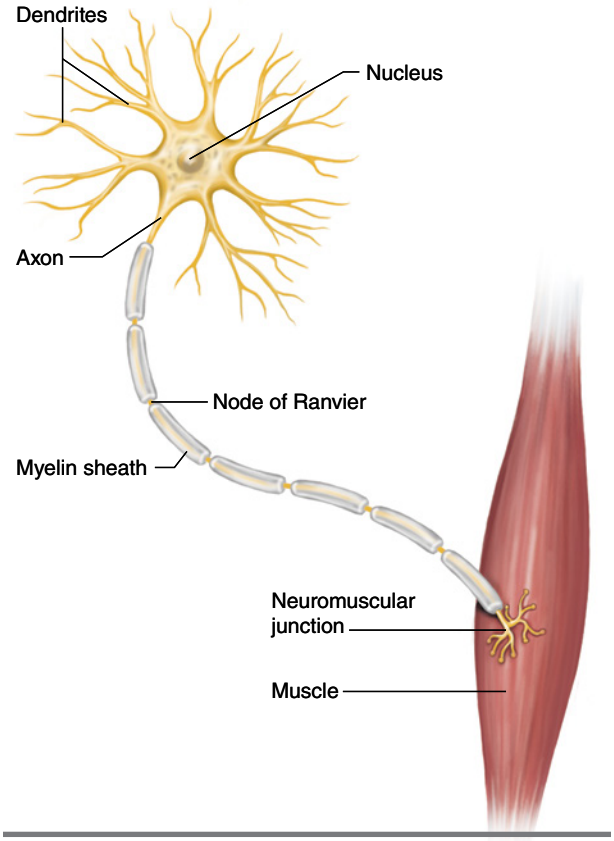

FIGURE 1.2 A motor unit.

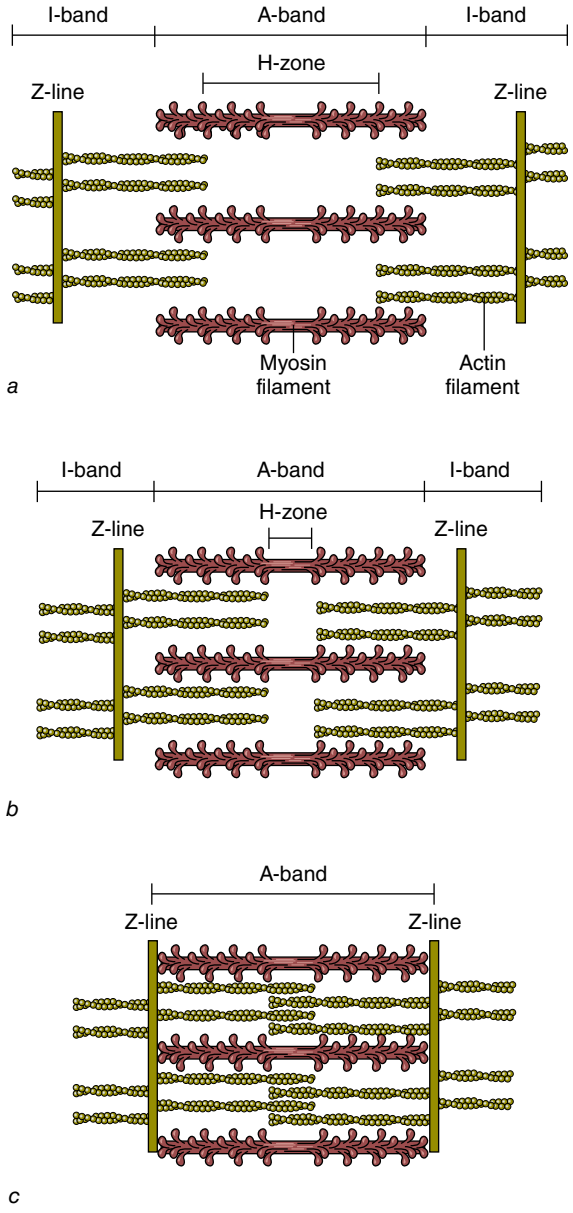

FIGURE 1.3 Contraction of a myofibril. *(a)* In stretched muscle, the I-bands and H-zone are elongated, and there is low force potential as a result of reduced crossbridge–actin alignment. *(b)* When muscle contracts (here, partially), the I-bands and H-zone are shortened. Force potential is high because of optimal crossbridge–actin alignment. *(c)* With contracted muscle, force potential is low because the overlap of actin reduces the potential for crossbridge–actin alignment.

travels down the nerve axon to the neuromuscular junction, where the neurotransmitter acetylcholine is released across the synaptic cleft and ultimately binds to the muscle fiber's plasmalemma. This depolarizes the muscle cell, causing calcium to be released from the sarcoplasmic reticulum. Calcium binds to troponin, which in turn moves tropomyosin from actin binding sites so they are exposed to myosin. Assuming sufficient ATP to drive muscular contraction, the globular myosin heads bind to exposed actin sites, pull the thin filament inward, release, and then reattach at a site farther along the actin filament to begin a new cycle. The continuous pulling and releasing between actin and myosin is known as crossbridge cycling, and the repeated power strokes ultimately cause the sarcomere to shorten (figure 1.3).

Fiber Types

Muscle fibers are broadly categorized into two primary fiber types: *Type I* and *Type II*. Type I fibers, often referred to as slow-twitch fibers, are fatigue resistant and thus well suited for activities requiring local muscular endurance. However, peak tension takes time—approximately 110 ms—to achieve in these fibers, thereby limiting their ability to produce maximal force.

Type II fibers, also known as fast-twitch fibers, serve as a counterpart to Type I fibers. They can reach peak tension in less than half the time—just 50 ms—thereby making them better suited for strength- or power-related endeavors. However, they fatigue quickly and thus have limited capacity to carry out activities requiring high levels of muscular endurance. The greater myoglobin and capillary content in slow-twitch fibers contributes to their higher oxidative capacity compared to fast-twitch fibers. Table 1.1 summarizes the characteristics of the primary muscle fiber types.

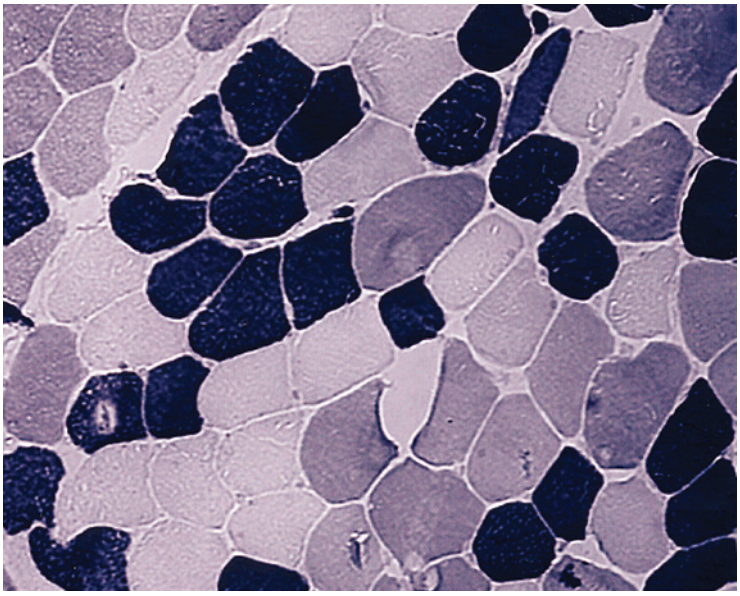

FIGURE 1.4 A photomicrograph showing Type I (black), Type IIa (white), and Type IIx (gray) muscle fibers.

Reprinted by permission from W.L. Kenney, J.H. Wilmore, and D.L. Costill, *Physiology of Sport and Exercise,* 5th ed. (Champaign, IL: Human Kinetics, 2012), 37.

Muscle fiber types are further distinguished according to the predominantly expressed isoform of myosin heavy chain; they are referred to as Type I, Type IIa, and Type IIx (236). Several other similar forms (commonly called *isoforms*) have been identified, including Ic, IIc, IIac, and IIax (figure 1.4). From a practical standpoint, the c isoform typically comprises less than 5% of human muscle and thus has minimal impact on total cross-sectional area.

On average, human muscle contains approximately equal amounts of Type I and Type II fibers. However, a large interindividual variability exists with respect to fiber type percentage. The quadriceps of elite sprinters have been shown to have a predominance of Type II fibers, whereas quadriceps of elite aerobic endurance athletes are primarily composed of Type I fibers.

TABLE 1.1 Characteristics of Muscle Fiber Types

	Type I	Type IIa	Type IIx
Size of motor neuron	Small	Medium	Large
Contraction time	Slow	Moderately fast	Fast
Force production	Low	Moderate	High
Resistance to fatigue	High	Moderate	Low
Mitochondrial density	High	Moderate	Low
Oxidative capacity	High	High	Low
Glycolytic capacity	Low	High	High
Capillary density	High	Moderate	Low
Myoglobin content	High	Moderate	Low
Glycogen stores	Low	High	High
Triglyceride stores	High	Moderate	Low

That said, a wide variability in these percentages exists even at the top levels of sport. World champion hurdler Colin Jackson was determined to have a fast-twitch fiber population of 71% in the vastus lateralis, with an extremely high abundance (24%) of the pure Type IIx isoform (230); in comparison, research shows elite Danish sprinters possess 57% fast-twitch fibers in the vastus lateralis, with just approximately 11% of the Type IIx variety (14). Moreover, certain muscles are predisposed to higher percentages of a given fiber type. For example, the endurance-oriented soleus contains an average of more than 80% Type I fibers; the more strength-oriented triceps brachii contains approximately 60% Type II fibers (50).

Many experts claim that all Type II fibers are inherently larger than Type I fibers. However, there is evidence that women often display a larger cross-sectional area of Type I fibers than of Type IIa fibers (236). Research does indicate that the oxidative properties of a fiber, rather than fiber type, influence muscle size. Specifically, the cross-sectional area of glycolytic Type IIx fibers is significantly greater than that of the more oxidative Type I and Type IIa fibers. It has been speculated that the smaller size of high-oxidative myofibers is an evolutionary design constraint based on the premise that muscle tissue has a limited capacity to hypertrophy and increase oxidative capacity at the same time (236). This is consistent with the hypothesis that competition exists between the turnover rates of structural (myofibrillar) proteins and those involved in metabolism (i.e., mitochondrial proteins), which is seemingly mediated by interactions between signaling pathways involved in either the synthesis or degradation of the respective muscle proteins (236).

Another often-proposed assumption is that Type II fibers are primarily responsible for exercise-induced increases in muscle size. This is principally based on studies showing that Type II fibers experience superior growth compared to Type I fibers after regimented resistance training (1, 40, 43, 111, 201, 217). When considered as a whole, the literature indicates that the growth capacity of Type II fibers is approximately 50% greater than that of Type I fibers (6), although substantial interindividual variability is seen in the extent of fiber type–specific hypertrophic adaptation (111). There also is evidence that the rate of muscle protein synthesis is elevated to a greater extent in the primarily fast-twitch human vastus lateralis muscle (approximately 50% to 60% Type II fibers) compared to the primarily slow-twitch soleus muscle (~80% Type I fibers) following heavy resistance exercise (231). A caveat when attempting to extrapolate such findings is that relatively high loads (>70% of 1RM) were used in a majority of studies on the topic, which potentially biases results in favor of fast-twitch fibers. Thus, it is conceivable that the superior capacity for hypertrophy of this particular fiber type may be a function of the models in which it has been studied rather than an inherent property of the fiber itself (158). The practical implications of this topic are discussed in later chapters.

Responses and Adaptations

Resistance exercise elicits a combination of neural and muscular responses and adaptations. Although an increased protein synthetic response is seen after a single bout of resistance training, changes in muscle size are not observed for several weeks of consistent exercise (207). Moreover, appreciable muscle protein accumulation (commonly referred to as *accretion*) generally takes a couple of months to become appreciably apparent (141). Early-phase increases in strength therefore are primarily attributed to neural improvements (141, 173, 196). Such observations follow the principles of motor learning. During the initial stages of training, the body is "getting used to" the movement patterns required for exercise performance. A general motor program must be created and then fine-tuned to carry out the exercise in a coordinated fashion. Ultimately, this results in a smoother, more efficient motor pattern and thus allows greater force to be exerted during the movement.

KEY POINT

Early-phase adaptations to resistance training are primarily related to neural improvements, including greater recruitment, rate coding, synchronization, and doublet firing.

Neural Drive

Several neural adaptations have been proposed to account for strength gains during acclimation to resistance training. Central to these adaptations is an increase in *neural drive*. Research indicates that humans are incapable of voluntarily producing maximal muscle force (55), but repeated exposure to resistance training enhances this ability. Numerous studies have reported increases in surface electromyography (EMG) amplitude after a period of regular resistance training, consistent with a heightened central drive to the trained muscles (2, 3, 80, 150). Research using the twitch interpolation technique, in which supramaximal stimuli are delivered to a muscle while subjects perform voluntary contractions, shows that as much as 5% of the quadriceps femoris muscle is not activated during maximal knee extension testing before exercise. After 6 weeks of training, however, subjects increased activation by an additional 2% (110). Similarly, Pucci and colleagues (174) reported an increase in voluntary activation from 96% to 98% after 3 weeks of training the quadriceps muscles. These results are consistent with research showing that trained athletes display greater muscle activation during high-intensity resistance exercise compared to nonathletes.

Muscle Activation

The findings of increased activation resultant to training are most often ascribed to a combination of greater *recruitment* (the number of fibers involved in a muscle action) and *rate coding* (the frequency at which the motor units are stimulated). It has been well established that muscle fiber recruitment follows the *size principle* (1, 12, 14, 16-19, 23, 33, 34). First explained by Henneman (90), the size principle dictates that the capacity of a motor unit to produce force is directly related to its size (figure 1.5). Accordingly, smaller, low-threshold, slow motor units are recruited initially during movement, followed by progressively larger, higher-threshold, fast motor units as the force demands increase for a given task. This orderly activation pattern allows for a smooth gradation of force, irrespective of the activity performed.

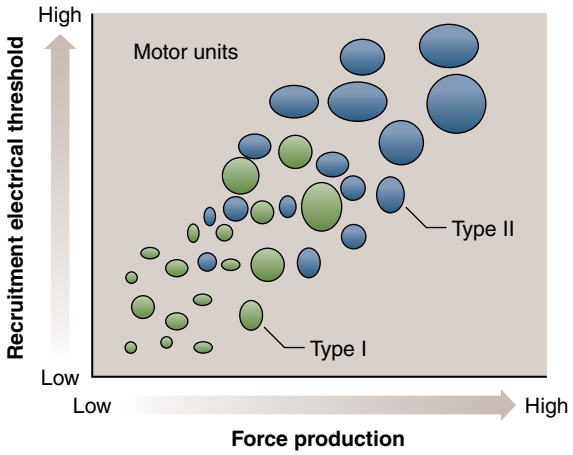

FIGURE 1.5 The Henneman size principle.

Two primary factors are responsible for the extent of muscle recruitment: level of muscle force and rate of force development. Training with heavy loads requires substantial force production and therefore calls on both low- and high-threshold motor units to maximize force. Although there is an intent to lift heavy loads quickly, the actual velocity of the lift is relatively slow. As the intensity of load decreases, the required force production from the muscle decreases, and fewer motor units are necessary to complete the lift given the same speed of shortening. By lifting a lighter weight quickly, however, most motor units are likely to be recruited even at loads equivalent to 33% of maximum (56). The extent of reductions in recruitment threshold from rapid contractions is greater for motor units in slow-contracting muscles, such as the soleus, compared with fast-contracting muscles, such as the masseter, one of the primary muscles involved in chewing food (56). The role of fatigue also must be considered with respect to recruitment. As fatigue increases during low-load contractions, the recruitment threshold of higher-threshold motor units progressively decreases even at somewhat slower speeds (95, 195, 242). It has been hypothesized that fatigue-induced reductions in motor unit threshold recruitment is an attempt by the neuromuscular system to sustain necessary levels of force generation to continue work output during repeated contractions (38).

The upper limit of motor unit recruitment is approximately 85% of maximal applied

isometric force; recruitment thresholds during dynamic actions are even lower (56). This suggests that enhancements in motor unit recruitment likely play a limited role in strength-related training adaptations. The ability to maximally recruit all available fibers in a given motor unit pool is essential for maximizing the hypertrophic response to resistance training. After all, the stimulus for a muscle fiber to adapt is predicated on its recruitment. However, it is important to note that simply recruiting a fiber does not necessarily promote a hypertrophic response. For example, a substantial recruitment of the full spectrum of muscle fibers, including those associated with high-threshold motor units, is achieved by cycling to fatigue at 75% of $\dot{V}O_2$max (195). Although this observation suggests that submaximal cycle exercise would promote substantial size increases across fiber types, research shows that muscle growth associated with aerobic exercise is limited primarily to Type I fibers (87).

Increases in force production above 85% of maximal voluntary contraction are thought to occur through greater discharge rates. Thus, an increase in rate coding would seem to be the most likely target for neural adaptation. Research is limited on the topic, but a study by Kamen and Knight (101) provides supporting evidence for training-induced enhancements in rate coding. Fifteen untrained young and older adults were tested for maximal voluntary contraction in knee extensions before and after 6 weeks of resistance exercise. By the end of the study, young subjects increased maximal discharge rate by 15%, and older subjects showed a 49% increase. Similarly, Van Cutsem and colleagues (234) showed that 12 weeks of resisted dorsiflexion training increased average firing frequency in the tibialis anterior from 69 to 96 pulses per second. In contrast, Pucci and colleagues (174) reported an increase of approximately 3% of maximal voluntary activation following 3 weeks of isometric quadriceps exercise, but no changes in discharge rate were noted. Differences in findings may be related to the methods employed for analysis. Recently, Del Vecchio and colleagues (51) demonstrated that changes in motor unit function of the tibialis anterior were mediated by adaptations in both recruitment and rate coding following 4 weeks of isometric strength training.

Motor Unit Synchronization

Several other factors have been speculated to account for neural improvements following resistance exercise. One of the most commonly hypothesized adaptations is an enhanced synchronization of motor units, whereby the discharge of action potentials by two or more motor units occurs simultaneously. A greater synchrony between motor units would necessarily result in a more forceful muscle contraction. Semmler and Nordstrom (204) demonstrated that motor unit synchronization varied when they compared skilled musicians (greatest degree of synchronization), Olympic weightlifters, and a group of controls (lowest degree of synchronization). However, other studies have failed to show increased synchronization following resistance training or computer simulation (105, 251). The findings cast doubt on whether synchronization plays a meaningful role in exercise-induced early-phase neuromuscular adaptations; if it does, the overall impact seems to be modest.

Antagonist Coactivation

Another possible explanation for exercise-induced neural enhancement is a decrease in antagonist coactivation. The attenuation of antagonist activity reduces opposition to the agonist, thereby allowing the agonist to produce greater force. Carolan and Cafarelli (41) reported that hamstring coactivation decreased by 20% after just 1 week of maximal voluntary isometric knee extension exercises, whereas no differences were seen in a group of controls. These findings are consistent with observations that skilled athletes display reduced coactivation of the semitendinosus muscle during open-chain knee extensions compared to sedentary people (13). The extent to which these adaptations confer positive effects on strength or hypertrophy remains unclear.

Doublets

An often-overlooked neural adaptation associated with resistance training is the effect on *doublets*, defined as the presence of two close

spikes less than 5 ms apart. Doublets often occur at the onset of contraction, conceivably to produce rapid force early on and thus generate sufficient momentum to complete the intended movement. Van Cutsem and colleagues (234) reported that the percentage of motor units firing doublets increased from 5.2% to 32.7% after 12 weeks of dynamic resisted dorsiflexion training against a load of 30% to 40% of 1RM. Interestingly, the presence of these doublets was noted not only in the initial phase of force development, but also later in the EMG burst. The findings suggest that doublet discharges contribute to enhancing the speed of voluntary muscle contraction following regimented resistance training.

Protein Balance

The maintenance of skeletal muscle tissue is predicated on the dynamic balance of muscle protein synthesis and protein breakdown. The human body is in a continual state of protein turnover; bodily proteins are constantly degraded and resynthesized throughout the course of each day. Skeletal muscle protein turnover in healthy recreationally active people averages approximately 1.2% a day and exists in dynamic equilibrium; muscle protein breakdown exceeds muscle protein synthesis in the fasted state and muscle protein synthesis exceeds muscle protein breakdown postprandially (19).

Protein synthesis has two basic components: transcription and translation (figure 1.6). Transcription occurs in the cell nucleus through a complex process that is segregated into three distinct phases: initiation, elongation, and termination. The process involves the creation of a *messenger ribonucleic acid* (mRNA) template that encodes the sequence of a specific protein

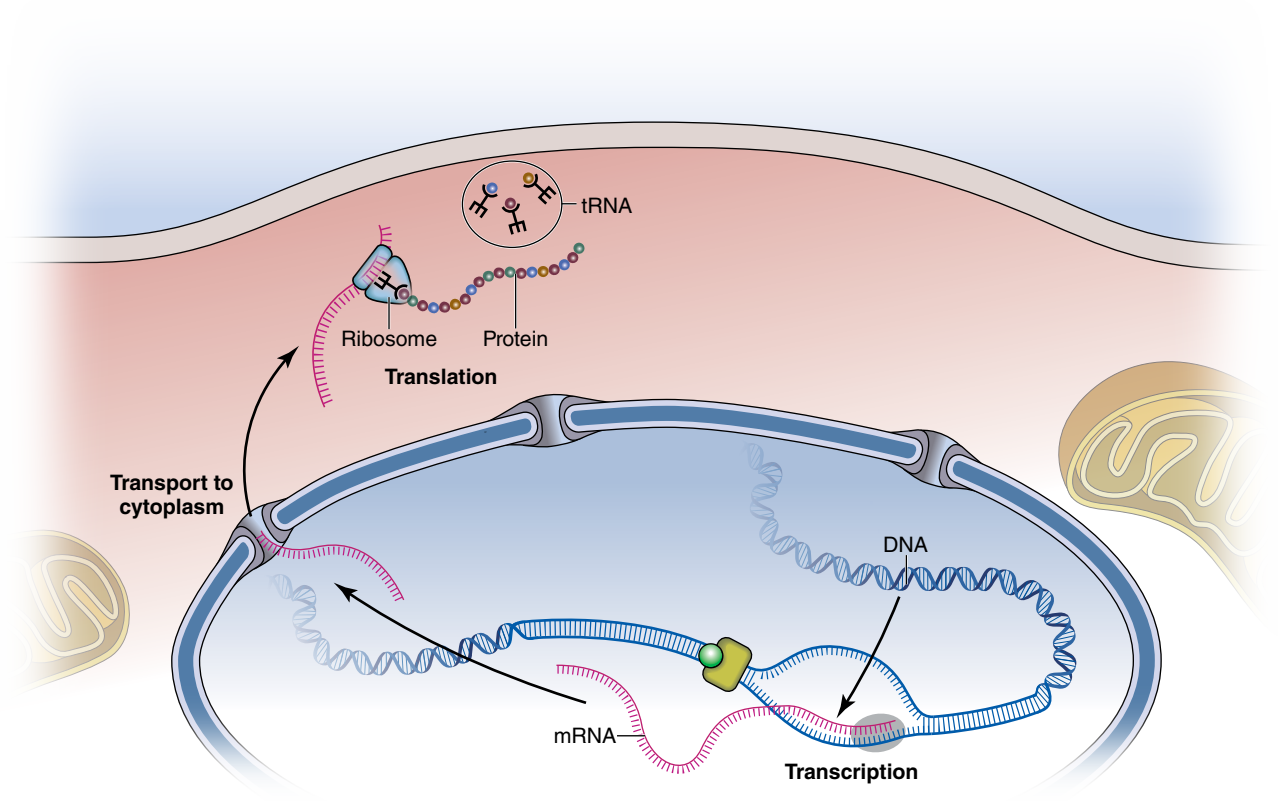

FIGURE 1.6 Protein translation and transcription—the basic processes of reading DNA sequence information and using it to build a protein molecule. The DNA sequence is read in the cell's nucleus, where a complementary RNA strand is built. That mRNA strand then moves to the cell cytoplasm, where it is used to manufacture the amino acid sequence of the protein.

from the genome. Each phase of transcription is regulated by various proteins (i.e., transcription factors, coactivators) that ensure the correct gene is transcribed in response to appropriate signals. Messenger ribonucleic acid concentration for a given protein is ultimately regulated by the myonuclear or the mitochondrial density and the transcription factors required for promoter activity (236).

Translation occurs in organelles called *ribosomes* located in the cell's sarcoplasm, which occupy approximately 20% of cell volume and comprise approximately 85% of total cellular RNA (64, 244). Ribosomes can be thought of as large peptide factories that regulate the translation of genetic material encoded in mRNA templates into muscle proteins. Each ribosome is composed of two subunits: a smaller subunit that binds the mRNA and a larger subunit that integrates specific transfer RNAs along with their bound amino acids (44). After binding with mRNA, the ribosomes synthesize a corresponding peptide strand by joining amino acids to *transfer ribonucleic acid* (tRNA) at the carboxyl end of the chain (44). The result is that translational capacity depends highly on the number of ribosomes in myocytes (5).

As with transcription, reactions are segregated into three phases: initiation, elongation, and termination. Each phase involves a distinct cluster of translation factors that are aptly termed *initiation factors* (eIF), *elongation factors* (eEF), and *release factors* (eRF) (the *e* stands for *eukaryotic,* referring to a cell that contains a nucleus and other cell structures). The availability and the state of activation of these factors determine the rate of translation of mRNA into muscle proteins (236). Translation initiation is believed to be the rate-limiting step in the protein synthetic response (130, 180). Not surprisingly, therefore, hormones and other growth factors that regulate muscle protein synthesis exert their effects by either increasing or decreasing the rate of translation initiation (44). That said, under certain circumstances, control of translation elongation can be critical to regulation of the protein synthetic rate (226).

During a bout of resistance training, muscle protein synthesis is suppressed and *proteolysis* (the breakdown of proteins into amino acids) is heightened so that net protein balance is in a net negative state. Note that protein breakdown resultant to exercise is considered an important component of exercise-induced hypertrophy because it helps to support amino acid reallocation as well as prevent the buildup of misfolded and nonfunctional proteins (133). After completion of the workout, muscle protein synthesis is increased 2- to 5-fold along with nutrient delivery, with effects lasting 48 hours or more post-exercise (168). An enhanced translational efficiency likely contributes to the exercise-induced increase in muscle protein synthesis (94, 160). Thus, when repeated bouts are performed over time and sufficient recovery is afforded between sessions, the synthetic response outpaces that of proteolysis, resulting in an increased accretion of muscle proteins.

Emerging evidence indicates that ribosome biogenesis is critical to increasing muscle mass. While translational efficiency appears to be a primary driver of the muscle protein synthesis response to exercise, the total number of ribosomes also plays an important role in the process (35, 244). The ribosomal pool is limited and must be expanded to support long-term growth because a given ribosome can translate only a finite amount of muscle proteins (183, 244). Numerous studies in both animals and humans have demonstrated strong correlations between muscle hypertrophy and ribosome biogenesis (244). Moreover, research in rodents shows that varying increases in hypertrophy following synergist ablation of 22%, 32%, and 45% are paralleled by dose-dependent increases in ribosomal content (1.8-fold, 2.2-fold, and 2.5-fold, respectively) (149); these findings emphasize the importance of expanding the number of ribosomes to realize progressively greater growth potential.

KEY POINT

Muscular adaptations are predicated on net protein balance over time. The process is mediated by intracellular anabolic and catabolic signaling cascades. Ribosome biogenesis is critical to maximizing hypertrophy over time.