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REVIEW

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Integrative research on the mechanisms of acupuncture mechanics and interdisciplinary innovation

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Abstract

As a traditional therapeutic approach, acupuncture benefits from modern biomechanics, which offers a unique perspective for understanding its mechanisms by investigating the mechanical properties of biological tissues and cells under force, deformation, and movement. This review summarizes recent advancements in the biomechanics of acupuncture, focusing on three main areas: the mechanical effects of acupuncture, the transmission mechanisms of mechanical signals, and the personalization and precision of acupuncture treatments. First, the review introduces the structural basis of the tissues involved in acupuncture; analyzes the mechanical responses of the skin, dermis, and subcutaneous tissues from needle insertion to point activation; and discusses how these responses impact acupuncture efficacy. Second, the phenomenon of mechanical coupling during acupuncture is discussed in detail, especially the role of connective tissues, including the wrapping and self-locking of collagen fibers, the remodeling of the cytoskeleton and the regulation of mitochondrial function triggered by acupuncture. Third, this article examines the mechanisms of mechanical signal transmission in acupuncture, explaining how mechanosensitive ion channels are activated during the procedure and subsequently initiate a cascade of biochemical responses. Finally, the review highlights the numerical simulation methods used in acupuncture, including the mechanical modeling of skin tissues, the exploration of the mechanical mechanisms of acupuncture, and visualization studies of the needling process. By integrating multidisciplinary research findings, this paper delves into the entire mechanical process of acupuncture, from skin penetration to point stimulation, and analyzes tissue responses to provide a solid theoretical foundation for the scientific study of acupuncture. In addition, directions for future research to further refine acupuncture techniques for clinical applications are proposed.

Keywords: Acupuncture, Skin, Mechanical signaling, Numerical simulation

Introduction

Acupuncture, as a core component of traditional Chinese medicine, has a long history and a unique therapeutic philosophy. Despite its widespread application, elucidating the mechanisms and effects of acupuncture through modern scientific methods remains a significant challenge. Recent studies have shown that the therapeutic efficacy of acupuncture depends not only on the selection of acupoints and operational techniques, but also on the mechanical signals generated during the needling process [1]. Since Langevin et al. [2] first observed mechanical interactions between acupuncture needles and connective tissues under a microscope in 2001, research on acupuncture has increasingly focused on the interplay between the needle and local acupoint tissues, particularly connective tissues. This includes mechanical stimulation of local tissues by the needle and how such stimulation enhances symptom relief by influencing the biomechanical properties of the tissue.

Biomechanics investigates the mechanical properties of biological tissues and cells, including forces, deformation, and movement, as well as their interactions with pathological conditions and environmental factors [3]. Applying biomechanics to acupuncture research contributes to the standardization and normalization of acupuncture studies. By analyzing the mechanical responses of different tissues and the application of acupuncture techniques, researchers have progressively uncovered the physiological mechanisms underlying acupuncture, such as the stress and strain generated by needle insertion and rotation of local tissues and how these mechanical factors propagate and affect the biochemical reactions of the tissues. Modern technologies, such as ultrasound imaging and biomechanical analysis, provide new methods and perspectives for understanding the complex interactions between acupuncture and tissues. These technologies allow real-time monitoring of tissue deformation and mechanical responses during acupuncture, offering quantitative analytical tools to investigate the physiological mechanisms of acupuncture therapy.

Currently, research on acupuncture mechanics focuses on three key areas: (1) the mechanical effects of acupuncture on connective tissues and cells, in which studies explore how mechanical stimulation of connective tissues and cells through acupuncture influences the nervous and immune systems; (2) the transmission mechanisms of mechanical signals, in which investigations aim to understand how mechanical signals generated during acupuncture propagate within tissues and trigger a cascade of biochemical responses; and (3) the personalization and precision of acupuncture treatments, in which biomechanical analysis is used to design personalized acupuncture treatment plans for individual patients, enhancing therapeutic efficacy.

By summarizing these areas of research, we aim to provide a robust theoretical foundation for the scientific and standardized application of acupuncture therapy. Understanding the mechanical mechanisms of acupuncture can help clinicians better select acupoints and operational techniques, ultimately improving treatment outcomes.

In conclusion, biomechanical research on acupuncture offers new perspectives and methods for understanding the therapeutic mechanisms of acupuncture. Quantitative analyses of the mechanical factors and their effects during acupuncture increase our understanding of the fundamental nature and principles of acupuncture, advancing its scientific and precise application in therapy.

The structural basis of acupuncture mechanics

Understanding the physiological structure and mechanical properties of tissues is critical for comprehending the mechanical effects of acupuncture. Many biological tissues exhibit viscoelasticity, a property that determines how organisms respond to external forces and influences their physiological processes [4].

The viscoelasticity of biological tissues is characterized by a dual response to mechanical forces: solid-like (elastic) and fluid-like (viscous) behaviors, enabling tissues to resist stress through time-dependent deformation [5]. On short timescales, tissues predominantly exhibit elastic properties, deform under external forces and rapidly recover their original shape upon force removal. On longer timescales, tissues behave like viscous fluids, undergoing irreversible deformation under sustained forces, with deformation persisting after the force is withdrawn. During acupuncture, the resistance of viscoelastic tissues to deformation decreases significantly within tens to hundreds of seconds [6, 7]. Subsequently, tissues can maintain stress over prolonged periods and reach equilibrium deformation under loading. Hence, the duration of acupuncture stimulation should align with the characteristic timescales of the tissue strain response and stress dissipation, as excessively short or long stimulation durations may fail to achieve optimal therapeutic effects.

Additionally, the viscoelastic mechanical response of tissues is frequency dependent [4]. As the stimulation frequency increases, the elastic modulus of tissues gradually increases until it reaches a frequency-independent plateau. This behavior may result from the faster transmission of stress relative to its dissipation under high-frequency conditions. Thus, selecting an appropriate stimulation frequency is crucial for effectively activating the physiological responses of tissues.

When an acupuncture needle penetrates the skin and reaches the acupoint, it traverses several layers, including the epidermis, dermis, subcutaneous tissue, and muscle septa. Despite structural variations in acupoints across different body regions, a common characteristic is their foundation of connective tissue, which is interwoven with nerves and blood vessels [8]. Anatomical studies have revealed that acupoints are distributed within connective tissues at various depths [9]. Connective tissues play critical roles in cellular and mechanical signaling pathways [10] and are generally considered the material basis for the therapeutic effects of acupuncture [11]. Yuan et al. [12] classified connective tissues into five categories: dense connective tissue in the dermis, loose connective tissue in the subcutaneous layer, loose connective tissue in muscle septa, connective tissue surrounding neurovascular bundles, and connective tissue in organ hilums and capsules. Among these, the latter four types are loose connective tissues and are the primary sites for mechanical coupling processes during acupuncture. The following sections provide a detailed discussion of the tissue layers penetrated during acupuncture.

As shown in Fig. 1, the skin exhibited a stratified structure, progressing inward from the epidermis to the dermis, subcutaneous tissue, and muscle layers.

When an acupuncture needle penetrates the skin, the primary resistance encountered by the needle arises from the epidermis [13]. The epidermis, as the outermost layer of the skin, consists of four distinct cellular layers: the stratum corneum, granular layer, spinous layer, and basal layer. The stratum corneum is the

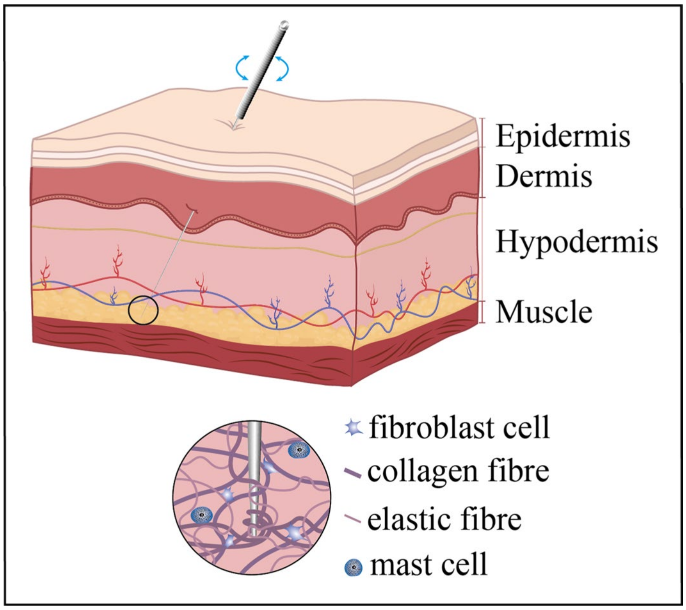

Fig. 1 Illustration of acupuncture needle insertion into an acupoint

region where the needle directly contacts the skin, and its surface friction coefficient is crucial for analyzing the mechanical forces during acupuncture [14]. The thickness of the epidermis varies by body region, with thicker areas such as the palms and soles providing greater puncture resistance. Research has shown that factors such as sex, age, anatomical site, skin hydration, and the roughness and material of the needle tip also influence the friction coefficient of the skin [15]. The structure and properties of the epidermis not only determine the magnitude of puncture resistance, but also directly affect the mechanical performance of acupuncture operations.

The epidermis lies beneath the dermis, a critical structural layer primarily composed of a complex collagen fiber network interspersed with elastic fibers and lymphatic vessels [16]. These components collectively maintain the integrity and functionality of the dermis. Unlike the epidermis, the dermis is often regarded as a fiber-reinforced hyperelastic biomaterial because of its unique fibrous structure and hyperelastic properties [17].

Below the dermis lies the subcutaneous layer, which consists mainly of adipose tissue, connective tissue, nerves, and blood vessels interspersed with collagen partitions. This layer is further subdivided into multiple levels by fibrous layers. The superficial fascia separates the superficial and deep adipose tissues. The superficial adipose tissue contains adipose lobules divided by vertically distributed fiber partitions, whereas the deep adipose tissue is composed of loose connective tissue with minimal adipocytes and thinner fibrous partitions. Fibroblasts, as the primary sensory cells in these tissues, are highly sensitive to mechanical stimuli. They rapidly perceive and respond to externally applied mechanical changes, playing a vital role in the transmission of mechanical signals.

Both the dermis and subcutaneous layers exhibit viscoelastic properties [18]. Studies have shown that these layers primarily consist of cells, fibers, and extracellular matrix components, with collagen and elastic fibers being central to the mechanical performance of the skin. Collagen fibers, which are composed of procollagen molecules, exhibit significant viscoelastic characteristics, such as creep and stress relaxation. Additionally, the performance of collagen fibers changes throughout their lifecycle [19]. In the dermis, collagen fibers account for up to 95% of the total fiber content. They are densely packed into bundles and form a multidirectional network structure, endowing the dermis with excellent tensile strength to effectively resist external mechanical stress and maintain the integrity and elasticity of the skin. In contrast, collagen fibers in the subcutaneous tissue are more loosely arranged, distributed in a network or bundle pattern among adipocytes, with random orientations. This loose arrangement grants the subcutaneous tissue greater softness and plasticity, allowing it to buffer external pressure and support skin movement.

Elastic fibers, like collagen fibers, share fundamental mechanical properties but exhibit deformation characteristics closely linked to changes in entropy. These properties enable elastic fibers to exhibit unique deformation behaviors under external forces. During acupuncture, the deformation of elastic fibers is accompanied by an increase in internal energy, leading to fiber vibrations. This vibrational energy is hypothesized to propagate along meridians [3, 20, 21]. Notably, the enrichment of elastic fibers around meridians and acupoints suggests that elastic fibers may play a critical role in energy transmission and distribution during acupuncture therapy [21, 22]. However, elucidating the precise role of elastic fibers in this complex process requires interdisciplinary and multilevel research.

In summary, connective tissues serve not only as essential physical mediators in acupuncture therapy, but also as foundational components for maintaining human health and physiological functions. A deeper understanding of their structure and function enables us to grasp the scientific principles underlying traditional therapies, such as acupuncture and facilitates their rational application in modern medicine.

Biomechanical response to acupuncture

Acupuncture fundamentally represents a mechanical force stimulus [23], with its mechanical coupling predominantly occurring in loose connective tissues. The mechanical stimulation induced by acupuncture causes collagen fibers in loose connective tissue to wrap around the needle, thereby altering the tension within the extracellular matrix. These subtle mechanical changes propagate through the fibrous network in the form of "vibrations" or elastic waves, with a transmission speed three times faster than that of neural signals [24].

To adapt to tension changes caused by tissue stretching, fibroblasts in connective tissue rapidly remodel their cytoskeleton to regulate tissue tension and release mediators [25]. This process triggers a cascade of physiological and biomechanical responses, such as changes in local blood circulation, tissue relaxation, and contraction. Moreover, acupuncture may exert extensive effects at the cellular level, including the regulation of cellular metabolism and signaling pathways.

Therefore, the effects of acupuncture on the human body span multiple scales and hierarchical levels. This paper discusses these effects from both the tissue perspective and the cellular perspective, focusing on the mechanical coupling between connective tissues and the needle. This approach aims to provide a more comprehensive and in-depth understanding of the biomechanical mechanisms underlying acupuncture therapy and offers theoretical support for the further development and optimization of acupuncture techniques.

Mechanical stimulation of tissue by acupuncture

As a complete tissue system, the skin maintains internal stable tension through the tight interaction between collagen fiber networks and cells. When a needle attempts to penetrate the tissue, this tension generates compressive forces against the needle [26], resisting further insertion. Current studies on the activation mechanism of acupoints suggest that loose connective tissue within acupoints is the core responder to acupuncture stimulation [27]. Once the needle penetrates an acupoint, interactions such as surface tension and electrostatic attraction create close contact between the needle and surrounding connective tissue, providing the conditions necessary for subsequent fiber wrapping.

During operations such as needle rotation [28], mechanical coupling occurs between the needle and the loose connective tissue, causing collagen fibers to wrap around the needle body and induce deformation and stretching of the connective tissue. The degree of tissue stretching depends on the number and amplitude of needle rotation cycles [6, 29]. Sustained stretching of the connective tissue is an intrinsic characteristic of this response and has been shown to induce localized purinergic signaling and active, cell-mediated tissue relaxation [30]. Additionally, the connective tissue may form a self-locking, wrapped structure around the needle [29], stabilizing the needle and making it more difficult to move, thereby enhancing the mechanical coupling effect between the needle and the connective tissue.

Rapid cytoskeletal remodeling of fibroblasts within connective tissue can lead to measurable contraction and strain phenomena at the tissue level [31]. Langevin et al. [32]reported that acupuncture performed on mice elicited measurable cellular responses in fibroblasts within connective tissue several centimeters away from the needle. When the needle was rotated, the collagen fibers wrapped and pulled around the needle formed a "thread-like" structure, which persisted for 15-20 min when the needle was held in place, resulting in sustained internal tension within the connective tissue.

Dynamic ultrasound studies of acupuncture in humans have revealed that measurable deformation of connective tissue occurs at least 10 cm away from the needle tip. Compared with the connective tissue in the muscle belly, deformation may extend further along the intermuscular connective tissue plane [33]. Furthermore, the mechanical properties of connective tissue influence the fiber wrapping process and thus the efficacy of acupuncture [34]. Unlike dense connective tissue, loose subcutaneous connective tissue has an elastic modulus closer to that of cells [35], making it more sensitive to weak external forces. This sensitivity is one of the primary reasons why the mechanical coupling process in acupuncture predominantly occurs within loose connective tissue.

Effects of acupuncture on cells

Acupuncture exerts broad and complex effects at the cellular level. Mast cells and fibroblasts are the primary cell types that respond to the mechanical stimulation of acupuncture [36]. By applying mechanical forces, acupuncture causes collagen fibers to wrap around the needle, activating mechanosensitive ion channels (e.g., Piezo channels) on the membranes of mast cells. This activation induces an influx of ions such as Ca^2+ into the cells. Upon activation, mast cells undergo degranulation, releasing a range of bioactive substances, including histamine, heparin, and various cytokines. These chemical mediators trigger local inflammatory responses, increase microvascular permeability and blood flow, and activate surrounding nerve endings, thereby promoting pain relief and local immune responses [37].

Simultaneously, acupuncture deforms the extracellular matrix, and these mechanical forces are transmitted into fibroblasts and other cells, leading to cytoskeletal remodeling. Fibroblasts expand, their volume increases, and their shape becomes more flattened. Cytoskeletal remodeling alters cell morphology and tension, enhancing the adaptability of cells to external environments. This remodeling also affects mechanosensitive ion channels (e.g., TRP channels and Piezo channels) on the cell membrane. When the cytoskeleton is subjected to mechanical forces induced by acupuncture, these ion channels are activated, leading to the influx of calcium ions into the cells. This mechanical–biochemical signal transduction is a critical mechanism through which cells generate physiological responses to acupuncture stimuli [1].

The activation of mechanosensitive ion channels alters intracellular ion concentrations, and calcium ions are key regulators of mitochondrial function. The calcium signaling triggered by acupuncture directly influences mitochondrial activity, promoting mitochondrial biogenesis and functional recovery while suppressing excessive mitophagy to prevent apoptosis. This regulation helps maintain the balance of cellular energy metabolism.

Overall, the effects of acupuncture on the cytoskeleton, mechanosensitive ion channels, and mitochondria demonstrate its diverse roles in modulating cellular biological processes. These insights provide important clues for exploring the mechanisms underlying the therapeutic effects of acupuncture.

The effect of acupuncture on the cytoskeleton

The cytoskeleton is a comprehensive and dynamic system that serves as the structural framework of the cell, enabling it to maintain its morphology under external mechanical forces. The network-like architecture and dynamic remodeling characteristics of the cytoskeleton endow cells with exceptional mechanical properties, profoundly influencing their responses to external mechanical stimuli [38].

As illustrated in Fig. 2, the extracellular matrix (ECM)–integrin–cytoskeleton axis represents a classical pathway of cellular mechanotransduction [39]. The cytoskeleton, which functions as the structural support of the cell, plays a pivotal role in the response to external mechanical forces. Integrins act as molecular bridges connecting the extracellular matrix and the cytoskeleton, transmitting signals bidirectionally across the plasma membrane. Through the ECM–integrin–cytoskeleton pathway, cells are able

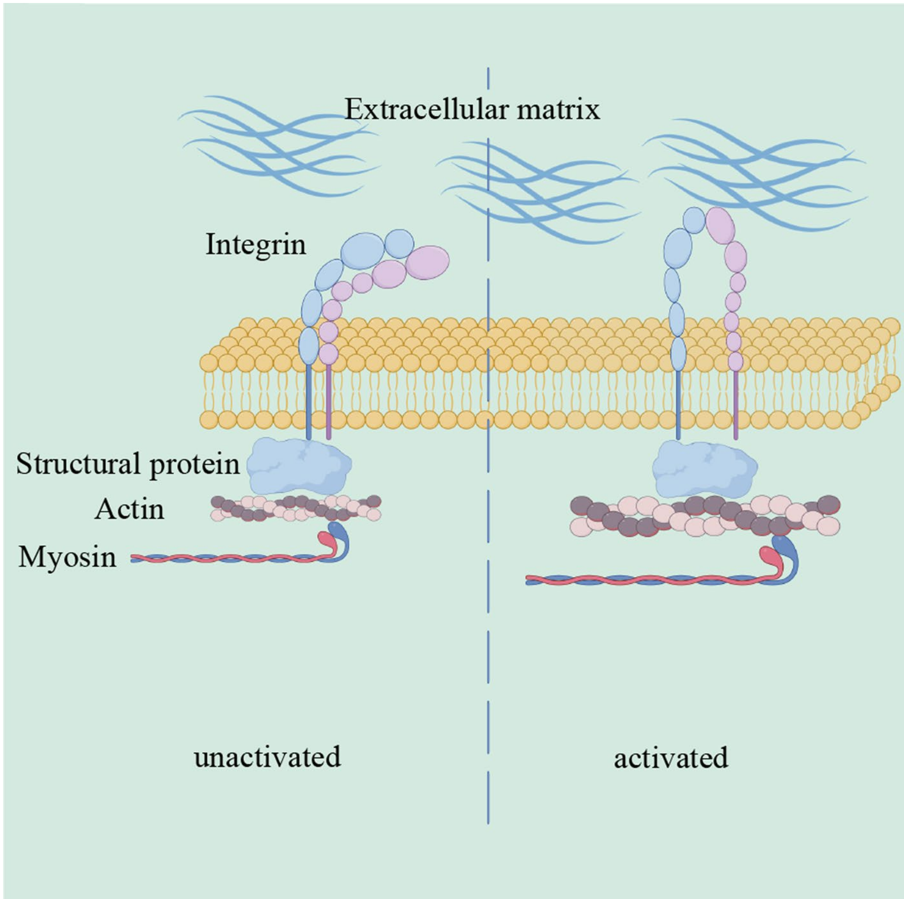

Fig. 2 Extracellular matrix–integrin–cytoskeleton pathway [41]

to sense mechanical stimuli from their external environment and generate appropriate biochemical responses, initiating intracellular and extracellular signaling cascades.

It is currently understood [40] that when cells adhere to the extracellular matrix or establish coupling connections with other cell surfaces via integrins, they generate contractile forces through actin filaments. These forces apply traction at anchoring points, allowing cells to detect deformations in the extracellular matrix. Concurrently, the cytoskeleton mechanically responds to the forces transmitted through integrins by redistributing stress, thereby enabling cells to adapt to their mechanical environment.

Within seconds to minutes after needle insertion, fibroblasts respond to tissue stretching and deformation by actively remodeling their cytoskeleton (Fig. 3). This remodeling enables fibroblasts to rapidly expand, increasing their cross-sectional area within the tissue plane several-fold [6]. Concurrently, the fibroblast shape becomes flatter and more planar as the tension in the connective tissue decreases [42]. These cytoskeletal responses typically occur within loose connective tissues and are not observed in denser connective tissues such as the dermis [10, 43].

These studies suggest that acupuncture therapy induces cytoskeletal responses in fibroblasts within connective tissues, leading to extensive biomechanical effects. These effects exhibit significant and measurable characteristics across different tissue types

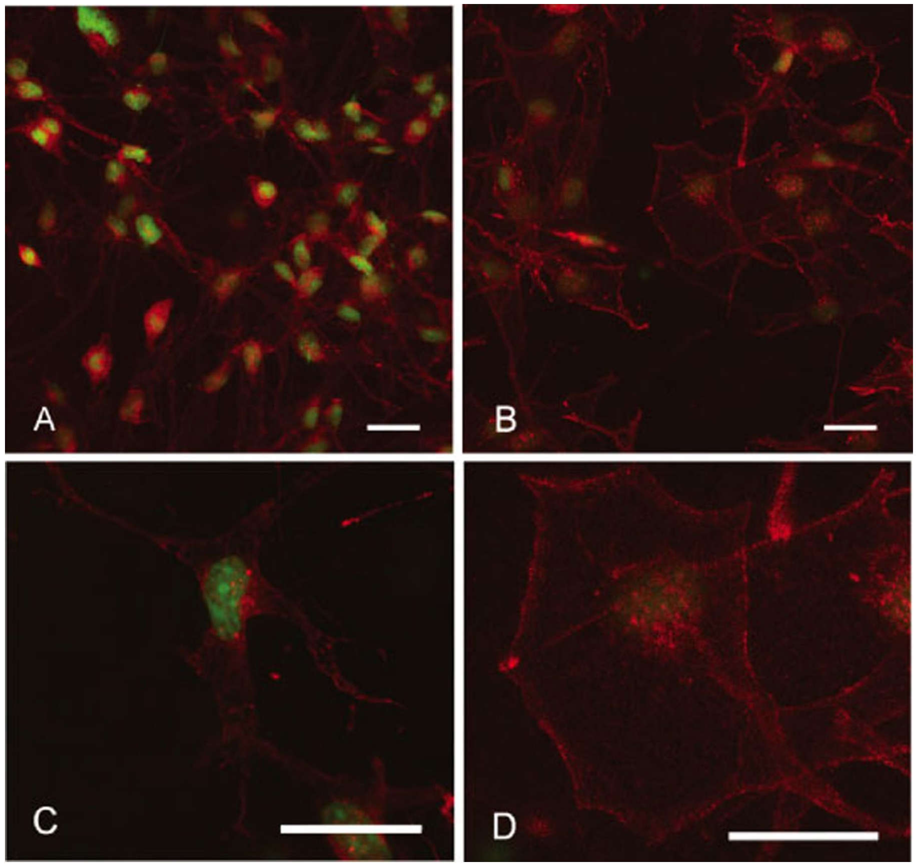

Fig. 3 Comparison of mouse subcutaneous tissue with acupuncture needle rotation (B) and without rotation (A); comparison of individual fibroblasts with needle rotation (D) and without rotation (C) [32] (Copyright © 2006 Wiley-Liss, Inc.)

and distances, providing a partial explanation for phenomena such as *deqi* (the sensation of needling), propagated sensation along meridians, and delayed responses following acupuncture.

The effect of acupuncture on mechanically sensitive ion channels

During acupuncture, as the needle penetrates the skin and tissues, it applies local mechanical forces that alter the tension and morphology of the extracellular matrix. The depth, angle, and rotation of the needle induce different types of mechanical stresses (such as tension, compression, and shear forces) on local tissues and cell membranes [44]. This mechanical stimulation affects the extracellular matrix and the cell membrane, influencing the activation of mechanosensitive ion channels (MSCs) within the membrane, as shown in Fig. 4. MSCs are classified into epithelial sodium channels/degeneration (ENaC/DEG), transient receptor potential channels (TRP), piezoelectric mechanosensitive ion channels (Piezo), and two-pore domain potassium channels (K_2P) [45], with most acupuncture-related research focusing on the first three.

The ENaC/DEG family of ion channels plays crucial roles in animals with specialized organ functions. These channels exhibit functional heterogeneity in terms of their tissue distribution and are involved in various physiological processes. Acid-sensing

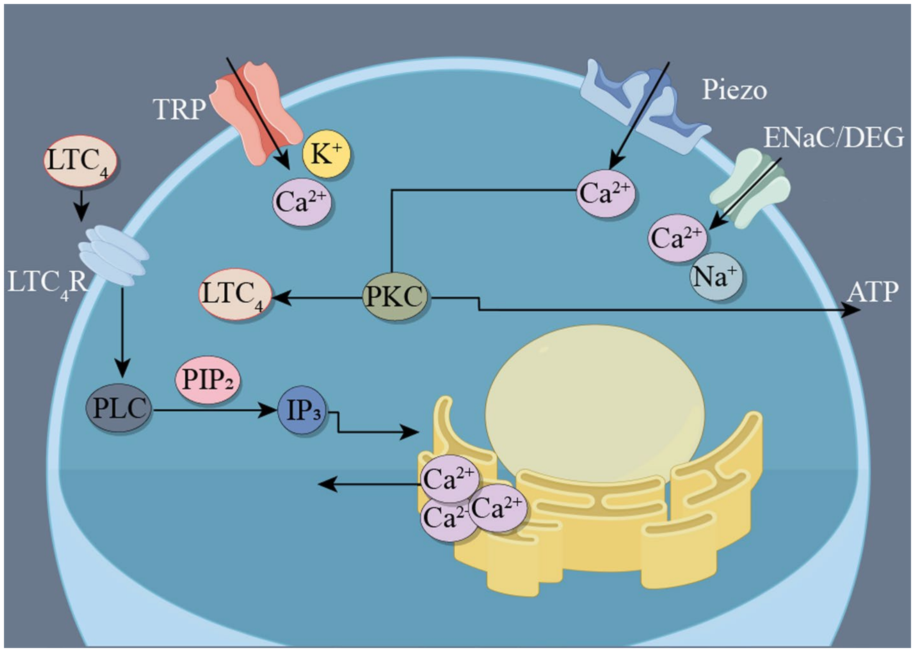

Fig. 4 Schematic diagram of the opening of mechanosensitive ion channels and the ion secretion mechanism induced by acupuncture [55]

ion channels (ASICs) are key members of this family. As proton-gated cation channels, they are activated by a decrease in the extracellular pH and play a mechanosensitive role at nerve endings. The activation of ASICs causes Na^+ influx and plays an essential role in learning and memory. TRP channels are nonselective cation channels that can be activated by light, touch, or mechanical pain; mediate Ca^2+ influx; and play a critical role in Ca^2+ signaling. The Piezo family includes the mechanosensors Piezo1 and Piezo2, which are nonselective Ca^2+ channels. Unlike other ion channels with diverse activation mechanisms, Piezo channels are primarily activated by mechanical stimuli. Research has shown [46] that MSCs are connected to surrounding collagen fibers, enabling the mechanical signals generated by acupuncture to be transmitted through these fibers, facilitating signal transduction from acupoints to target organs.

Mechanically activated ion channels are sometimes referred to as force sensors, but they can respond to deformations in the cell membrane rather than mechanical force [47]. In other words, the response of these channels to the applied mechanical force varies with changes in the stiffness of their environment (such as the extracellular matrix, the intracellular cytoskeleton or the membrane itself). Acupuncture, through mechanical stimulation, activates the integrin signaling pathway, which subsequently triggers the PI3K/Akt [48] and MAPK/ERK pathways [49, 50]. These pathways are known to promote cell proliferation and exhibit anti-apoptotic effects. In the context of chronic inflammatory diseases, acupuncture has been shown to inhibit the NF-κB signaling pathway, thereby downregulating the excessive secretion of pro-inflammatory cytokines [51, 52]. Furthermore, acupuncture can influence key molecules in the Hippo pathway to regulate granulosa cell apoptosis. Experimental studies [53] have demonstrated that acupuncture significantly upregulates the expression levels of YAP and TAZ mRNA and proteins in ovarian tissues while reducing the expression of the phosphorylated YAP protein (p-YAP). YAP and TAZ are critical regulatory factors in the Hippo pathway, with their activity modulated by the stiffness of the extracellular matrix (ECM), the shape of the cell, and the cytoskeletal tension. When cells are on a rigid ECM or have a larger adhesion area, YAP and TAZ are activated and translocate into the nucleus, where they function as transcriptional regulators. Conversely, under conditions of a soft ECM or small adhesion areas, their activity is inhibited, and they remain localized in the cytoplasm [54]. Acupuncture, by mechanically stimulating acupoints and surrounding tissues, may exert its effects by enhancing local ECM stiffness, altering cytoskeletal tension, and modulating key molecules in the Hippo pathway. These actions contribute to the regulation of cell apoptosis and the improvement of tissue function.

The mechanical stretching effect produced during acupuncture alters the mechanical properties of the extracellular matrix, which in turn activates MSCs on the cell membrane. These channels collectively mediate a significant influx of extracellular Ca^2+, rapidly reducing the intracellular Ca^2+ concentration [56]. A large increase in intracellular Ca^2+ activates protein kinase C (PKC), further promoting ATP release. ATP released from these cells spreads to nearby cells, enabling signal transmission along the connective tissue plane [57]. Research suggests that during acupuncture, Ca^2+ acts as a second messenger and is highly correlated with the effects of acupuncture. Additionally, the chelation of Ca^2+ in the acupoint region weakens the effects of acupuncture [58]. Under normal conditions, Ca^2+ in tissues comes from two sources: the extracellular space and the intracellular endoplasmic reticulum. In mechanosensitive ion channels (MSCs), the sarcoplasmic reticulum can regulate the release and uptake of Ca^2+ and maintain its concentration within a specific physiological range. Yao et al. [59], by constructing a digital model between mast cells and nerve cells, reported that mechanical stimulation of a single mast cell leads to an increase in Ca^2+ levels and ATP release. MSC channels serve as key mediators for the conversion of physical and chemical information in acupuncture therapy. Relevant studies have focused primarily on the TRPV subfamily and ASIC3 molecules. However, ion channels closely related to mechanical force regulation, such as TRPA, TRPM, Piezo, and TMEM63, have not been extensively studied in the field of acupuncture.

Influence of acupuncture on mitochondria

In recent years, acupuncture has shown significant efficacy in promoting mitochondrial function recovery and reducing mitochondrial autophagy. Studies have demonstrated that acupuncture can rapidly restore the structure and quantity of damaged mitochondria through inflammatory cell enrichment effects, promote mitochondrial biosynthesis, and accelerate mitochondrial renewal, thereby improving cellular energy metabolism. This effect has been validated in several disease models related to mitochondrial dysfunction, including Alzheimer's disease [60] and depression [61]. The stiffness of the extracellular matrix is closely associated with mitochondrial autophagy and mitochondrial dynamics. Research has shown [62] that soft substrates promote the release of calcium from the endoplasmic reticulum and calcium uptake by mitochondria, triggering calcium transport. This mechanism leads to an increase in calcium levels within tumor tissues, thereby inducing mitochondrial fission and mitochondrial autophagy.

Mitochondrial autophagy (mitophagy) is an essential mechanism for the cellular clearance of damaged mitochondria, and the PINK1–Parkin pathway, as a classical and crucial mediator of mitophagy, plays a key role in this process. Excessive mitophagy can lead to cell apoptosis, particularly under stress conditions such as hypoxia and oxidative stress. Acupuncture has been shown to significantly reduce the expression levels of the PINK1–Parkin pathway, leading to a marked decrease in the number of microtubule-associated protein 1 light chain 3 (LC3) molecules that bind to mitochondria. Through this mechanism, acupuncture can inhibit the excessive activation of mitophagy, protecting cells from apoptosis caused by mitochondrial dysfunction [63].

Although existing research has revealed some of the mechanisms through which acupuncture regulates mitochondrial function and autophagy, studies on how changes in extracellular matrix stiffness affect mitochondrial autophagy in acupuncture remain in their early stages. There is still a lack of in-depth exploration and systematic research, and the specific molecular mechanisms and signaling pathways involved require further investigation. Future research on acupuncture mechanics could focus on the differential effects of acupuncture on mitochondrial function in different cell types, as well as the relationship between mechanical responses to acupuncture and mitochondrial functional responses. These studies provide important theoretical support for a more comprehensive understanding of the biological mechanisms underlying acupuncture.

Mechanical study of the acupuncture process

Through in-depth studies of the acupuncture process, we can gain a more comprehensive understanding of the kinematic characteristics and mechanical parameters of acupuncture techniques, thereby enhancing our understanding of the effectiveness and safety of acupuncture therapy on the basis of mechanical principles. During acupuncture, the needle is subjected to various forces within the tissue, such as the pressure of the needle tip on the tissue, shear forces, and frictional forces. These forces generate mechanical stimulation of the tissue and cells, which in turn produces therapeutic effects through physiological actions, including changes in local blood circulation, tissue relaxation and contraction, and muscle tension regulation. Furthermore, factors such as the needle shape, material selection, and surface roughness significantly influence the effects of acupuncture.

In addition, acupuncture parameters, such as operation frequency and insertion depth, play crucial roles in acupuncture therapy. Studies have shown [29] that low-frequency rotational techniques tend to evoke more pronounced biological responses, including the sensation of *deqi* (the characteristic feeling of needling), further confirming the close connection between acupuncture techniques and physiological responses.

By applying viscoelastic mechanics theory for modeling and analysis, we can understand the interaction mechanisms between the needle and surrounding soft tissues, as well as the energy dissipation characteristics exhibited by different acupuncture techniques. This enables the exploration of the correlation between these characteristics and the effects of acupuncture. Collectively, these findings not only provide a stronger theoretical foundation for acupuncture therapy, but also offer more precise guidance for clinical practice.

Mechanical response of the acupuncture process

Stress in the process of acupuncture

In acupuncture therapy research, accurately capturing information on the insertion force during needle penetration is crucial [64]. This force information refers to the distribution of forces occurring along the needle axis during insertion. It helps deepen the understanding of how tissues respond to external stimuli and allows for the precise reproduction of the acupuncture process in simulation and modeling systems.

Studies on needle insertion into the skin [65] indicate that the total force acting on the needle during penetration can be represented by Eq. 1:

$$f_n = f_c + f_f + f_s, \tag{1}$$

where f_n represents the needling force, f_c represents the reactive force exerted on the needle tip after penetrating the tissue, f_f represents the frictional force between the tissue and the needle surface, and f_s represents the indentation force exerted by the tissue to resist the needle's compressive deformation before the needle penetrates the skin. As shown in Fig. 5, the acupuncture insertion process can be divided into three common stages: indentation deformation, insertion, and withdrawal. The aforementioned three forces occur at different stages of the acupuncture process. Below, each of these three stages is discussed in detail.

During the indentation deformation stage, the needle comes into contact with the soft tissue and compresses downward, causing tissue deformation. At this point, the needle primarily experiences the indentation force f_s generated by the tissue resisting compressive deformation. The magnitude of the indentation force f_s is related to the mechanical properties and shape parameters of the needle tip, with the maximum value corresponding to the needling force, i.e., the force required to penetrate the skin. After the needle tip is fully inserted into the skin and the indentation deformation of the tissue is released, the indentation force f_s gradually decreases. In the insertion stage, the needle tip compresses and cuts through the tissue, while the needle body experiences friction with the tissue. At this stage, the needling force on the needle includes the reactive force f_c exerted on the needle tip by the tissue and the frictional force f_f between the tissue and the needle body. During the withdrawal stage, the reactive force f_c on the needle tip decreases to zero, and the withdrawal force is generated primarily by the friction between the tissue and the needle body.

Early studies generally considered the needling force during acupuncture to be the indentation force f_s, which represents the resistance of the sample to compressive deformation, and used this force to characterize the mechanical properties of the pierced

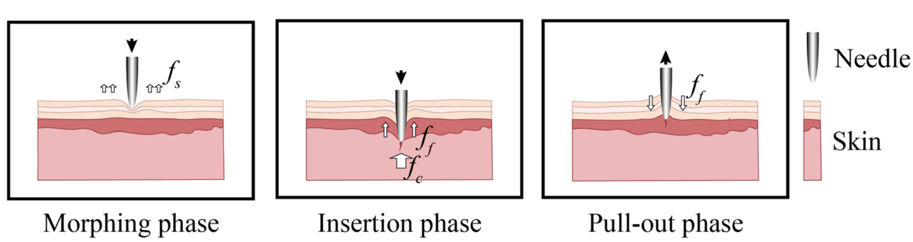

Fig. 5 The three stages of acupuncture needle insertion

tissue. Hiemenz et al. [66] and Westbrook et al. [67] measured the peak total axial force during puncture to detect the forces acting on the yellow ligament or dura mater during insertion. Brett et al. [68, 69] measured the needling force and established related mechanical models to determine the tissue types along the spinal anesthesia needle path. These studies all measured the force acting on the needle, but did not consider the postinsertion force f_c exerted on the needle tip and the frictional force f_f between the tissue and the needle body. Simone and Okamura [65] attempted to consider both the needle tip force f_c and the frictional force f_f in liver tissue experiments but did not measure both forces simultaneously. Kataoka [70] analyzed the forces on the needle surface and needle tip separately and proposed that the needling force is the sum of the needle tip force f_c and frictional force f_f. A 7-axis sensor was designed to measure the needle tip force and frictional force separately, and it was concluded that the magnitude of the needle tip force could change depending on the shape and sharpness of the needle tip. Cheng [71], Jiang [72], and others expanded on this work by dividing the forces on the needle body into three components: the needle tip force, the frictional force, and the clamping force, where the clamping force refers to the grip of the tissue on the needle body in the direction perpendicular to the needle. Ding et al. [73] compared the forces on the needle body in the *deqi* and non*deqi* states and reported that the force on the needle body in the *deqi* state was more than double that in the non*deqi* state, which may be related to phenomena such as fiber wrapping around the needle. According to Wang et al.'s [13] study, during needling, resistance when *deqi* does not occur mainly comes from the epidermis, whereas under *deqi* conditions, resistance is likely due to the combined action of the epidermis and fibroblasts in the connective tissue. This suggests that the *deqi* phenomenon is not only a subjective sensation during clinical operation, but also has an objective mechanical basis, which may be closely related to changes in the mechanical response of the tissue to acupuncture.

Deformation during acupuncture

Displacement and strain measurements are crucial for characterizing the mechanical response during acupuncture, as they reveal the interactions between biological tissues, organs, and the acupuncture needle. Elastography imaging techniques allow for the quantitative measurement of strain distribution in soft tissues. By analyzing the relationship between the applied force and displacement, it is possible to estimate the distribution of axial forces along the needle during the acupuncture process. Simon et al. [74] proposed a method based on tissue measurement systems and soft tissue deformation models to estimate the distribution of axial forces along the needle by analyzing the relationship between the applied force and displacement.

To better characterize the interaction between the needle and tissue, Barney et al. [75] used digital image correlation (DIC) to quantify the deformation field of soft solids and biological tissues during deep indentation and puncture processes. This method revealed the different roles of the shear and compression zones in the mechanical behavior. DIC is currently the most widely used noncontact strain measurement method for soft tissues [76], employing advanced image recognition algorithms to perform detailed analysis and comparisons of digital images captured from the surface of substrates. This technique allows for precise measurement of displacement and strain without physical contact with the target object, thus showing significant promise in the field of biomechanics. In particular, in in vivo measurements, DIC has shown notable advantages over other strain measurement technologies [77]. Strain measurements based on elastography and DIC provide powerful tools for studying mechanical behavior during acupuncture.

Mechanical parameters of the acupuncture process

The needle body

The shape, material, and radius of the acupuncture needle significantly influence its mechanical behavior during needling [78]. Matsunami et al. [79] reported that the resistance to acupuncture increases as the angle of the conical needle tip increases, from a cone shape to an angled tip to a rhomboid shape. Quan et al. [80] studied the geometric morphology and optimization mechanisms of natural spiny structures and discovered that the diameter of biological spines changes along the longitudinal axis according to a power law, with an exponent between 2 and 3. This geometric optimization strategy is particularly suitable for penetrating soft materials, as it enhances the bending resistance of the needle tip while keeping the penetration force at a lower level. The shape of the needle tip alters the distribution pattern of the penetration force and influences the mechanical response of the tissue. Yoganandam et al. [81] explored the effects of different head shapes (cone, oval, flat, and hemispherical) on acupuncture performance and reported that the shape of the needle tip significantly affects needling behavior and injury patterns. The flat tip absorbs more energy, resulting in disc-shaped damage; the conical tip penetrates quickly and is suitable for efficient needling; the oval tip causes more friction and leads to bulging injury; and the hemispherical tip distributes the force more evenly, reducing concentrated damage. These findings suggest that the geometric shape of the needle tip can significantly affect the needling force and mechanical performance, indicating that optimizing the needle tip geometry can effectively reduce the insertion force while improving needle performance.

Additionally, the roughness and surface pattern of the acupuncture needle significantly affect its mechanical effects. Zhang et al. [82] used force measurement devices to measure the force and torque during acupuncture, whereas Sun et al. [26] further developed five acupuncture models with different roughness levels. Compared with smooth needles, the other four needles caused more tissue damage during insertion. Surface patterns aligned with the insertion direction helped reduce pain, whereas patterns perpendicular to the movement direction enhanced stimulation. Bae et al. [83] created a microneedle with a surface covered with numerous microdiameter hemispherical protrusions. The force required to lift and insert this needle was 1.5 times greater than that of a smooth needle, and the torque required to rotate it was twice as much. This needle resulted in enhanced rotational torque and improved analgesic effects. Comparative experiments demonstrated that increasing roughness can enhance the analgesic effects of acupuncture. On the other hand, the needle material may influence the effects of acupuncture by affecting its roughness. Langevin et al. [27] reported that gold needles are mechanically coupled more easily with tissue than are stainless steel needles, but different materials might influence the roughness of the needle and, consequently, the wrapping of fibers around the needle. However, further studies are needed to explore this relationship.

It is generally believed [84] that the larger the needle diameter is, the greater the stimulation generated at the same acupuncture depth. However, animal experiments have shown that the effect of acupuncture is highly complex. Fluorescence staining of connective tissue revealed that the integrin $\beta 1$ subunit was strongly expressed in response to fine and medium needles, particularly medium needles, but was weakly expressed in response to coarse needles [85]. Moreover, needles of different sizes had varying effects on cell proliferation and collagen fiber adjustment. Fine needles effectively promote the proliferation of connective tissue cells and the synthesis of collagen fibers. However, as the needle diameter increases, this promoting effect gradually weakens [86]. These findings confirm that the relationship between needle diameter and stimulation is not entirely linear and that the quantitative relationship between the two requires further exploration.

Needling speed, frequency and depth

The viscoelastic properties of biological tissues suggest that when acupuncture parameters—such as insertion speed, frequency, and depth—change, the response of soft tissues to the applied force also varies. For example, increasing the speed of insertion leads to higher needling forces. Cai et al. [87] increased the insertion speed from 0.5 mm/s to 10 mm/s and observed that the maximum needling force also increased. Wang et al. [88] found that low-frequency (0-8 Hz) rotation corresponded to a significant increase in energy dissipation, with the likelihood of *deqi* being highest at low frequencies. This suggests that low-frequency rotation may evoke more biological responses, including the *deqi* sensation perceived by patients. Ding's team [89] performed insertion and rotation at the *Quchi* acupoint on human subjects and measured an average main frequency of 1.20 Hz for the technique. They proposed that the main frequency of 1.20 Hz could serve as a quantifiable indicator for the *deqi* sensation. Li [90] found that when performing insertion and rotation techniques at the *Zusanli* acupoint, the main frequency of the forces on the needle was 2.82 Hz. This result significantly differs from the previously observed 1.20 Hz frequency, highlighting a lack of consistency and standardization in measuring acupuncture parameters.

Acupuncture frequency has a significant impact on clinical outcomes. A randomized controlled trial involving 264 patients with dry eye disease found that acupuncture at the *Zhaohai* acupoint with a rotation frequency of 120 rotations/min led to significantly better results than using a frequency of 60 rotations/min [91]. Yao et al. [92] demonstrated that during acupuncture, the needle should reach the depth of the fascia to achieve effective stimulation. Zhuang et al. [93] compared different depths of electroacupuncture at the *Dubi* and *Dubi* acupoints in patients with knee osteoarthritis, finding that deep insertion (1.5–2.0 in.) provided better therapeutic outcomes than shallow insertion (1.0–1.5 in. and 0.5–1.0 in.). Deep insertion showed a greater advantage in improving pain and knee joint function, providing a valuable reference for clinical depth selection. Random combinations of acupuncture parameters also lead to varying clinical efficacy. Li et al. [94], through orthogonal design screening, found that the optimal frequency and time combination for acupuncture at the *Renzhong* acupoint to improve the neurological deficit score in a rat model of middle cerebral artery occlusion (MCAO) was 180 insertions/min for 5 s. This study confirmed that both frequency and time are significant factors influencing efficacy, indicating that acupuncture mechanical parameters directly affect the regulation of neural function. Chang et al. [95] conducted a cluster analysis on the Wistar rat MCAO model to explore the effects of different acupuncture parameters on treatment outcomes. The study found that each acupoint has specific acupuncture parameters that produce the best therapeutic effects, suggesting that each acupoint has its optimal acupuncture parameters, which are critical factors influencing acupuncture efficacy.

Current research on acupuncture parameters (such as speed, frequency, and depth) has made some progress but remains in its early stages. The findings are often inconsistent, lacking unified standards, and the specific mechanisms by which biological tissues respond to different parameters require further exploration. Moreover, studies focused on the practical clinical application of acupuncture parameters are relatively limited.

Some researchers have begun to investigate the link between acupuncture parameters and clinical efficacy. For example, Wu [96] explored the relationship between parameter variations and the treatment of post-stroke dysphagia. While Li [97] investigated parameter changes in transcutaneous electrical nerve stimulation for cancer pain relief. Data mining has shown promise in summarizing acupuncture parameters. However, such summaries are often fragmented, with findings limited to specific acupoints or conditions. A comprehensive, systematic consolidation of these parameters is still lacking.

To address these challenges, future efforts should focus on establishing an open database where researchers can upload data from their studies. This platform could enable subsequent investigators to leverage machine learning and other advanced analytical tools for unified and systematic analysis. Such a database would facilitate deeper insights into the relationship between acupuncture parameters and clinical efficacy, ultimately contributing to the development of more standardized and effective acupuncture practices.

Modeling of the acupuncture insertion process

In recent years, numerical simulation methods have received increasing attention from researchers in the study of the acupuncture process. By modeling biological tissues and using computers for numerical calculations, researchers can simulate mathematical models of soft tissue acupuncture to study and predict real-world problems. Modeling helps simulate the mechanical behaviors during the acupuncture process, providing deeper insights into its underlying mechanisms. However, there is still limited research on the mechanics and biological effects of acupuncture on the three-dimensional structures of acupoints.

Mechanical modeling of skin tissue during acupuncture

Numerical simulation of the acupuncture process requires the establishment of mechanical models for soft tissues such as the skin. Given the nonlinear characteristics of skin tissues during acupuncture, many researchers treat the skin as a rubber hyperelastic material [17] and use strain energy density functions based on deformation tensor invariants, such as the neo-Hookean model [98], Mooney model [99], and Ogden model [100], to characterize its mechanical behavior. Thalmann et al. [101] conducted preliminary modeling of the three-layer structure of the skin, including the epidermis, dermis, and subcutaneous layers, assuming that each layer is a linear elastic material and investigating the mechanical response of the skin under small deformations. By incorporating the nonlinear mechanical properties of the skin, Cai et al. [87] assumed that the stratum corneum and dermis were hyperelastic materials, whereas the subcutaneous tissue was treated as a linear elastic material. They established a finite element model to analyze the nonlinear mechanical behavior of the skin under different stiffnesses and elastic parameters. Wang et al. [88] applied viscoelastic mechanics theory to establish a two-dimensional acupuncture polar coordinate equation for numerical solving, creating mechanical models on the basis of the insertion and rotation acupuncture techniques. Their simulation results revealed significant energy dissipation in the low-frequency range for both techniques, particularly the energy dissipation peak observed during the insertion process, which may be correlated with the effects of acupuncture. Chen et al. [102] proposed a finite element and smoothed particle hydrodynamics coupling algorithm based on the fluid–solid dual-phase characteristics of skin tissue, simulating piercing and flat-plane friction experiments. Currently, numerical simulations of biological tissues in acupuncture studies still face challenges such as model simplifications, a lack of dynamic and multiscale modeling, insufficient experimental validation, and limitations in computational resources and methods. Future research should incorporate more detailed biological tissue characteristics, increase experimental data support, utilize advanced computational technologies, and promote interdisciplinary research to increase the accuracy and application value of the models.

The mechanical mechanism of insertion during acupuncture

Understanding and hypothesizing the mechanisms of needle insertion significantly impacts the effectiveness and accuracy of mechanical model predictions. Early research on acupuncture mechanisms focused on rubber materials. Stevenson et al. [103] studied the mechanical mechanisms of rubber materials during the puncture process, revealing the relationship between the puncture force and depth, as well as the rupture patterns of rubber materials. Shergold and Fleck [78] conducted in-depth theoretical analysis and calculated the critical force required for puncturing soft materials with flat or conical needles. They reported that the critical puncture force depends on the toughness, stiffness, and radius of the needle. They subsequently [104] validated this theory by puncturing rubber and pig skin with needles of different geometries and sizes. Okamura et al. [105] and Das et al. [106] studied the puncture mechanisms in biological tissues and gel materials, respectively. Their experimental results revealed a peak force during needle insertion, which decreased once the needle penetrated the surface of the sample and further deepened. Fregonese et al. [107] simplified the complex puncture mechanism into two processes: indentation and penetration. The puncture process was described as a sharp transition from "indentation" to "penetration", a change driven by mechanical instability, and governed by the principle of energy minimization. During small displacements, indentation deformation corresponds to a lower energy state. When the needle displacement exceeds a critical threshold, the needle ruptures the surface of the sample and penetrates, creating a more energetically favorable deformation model.

Through these efforts, numerical simulations will provide a more solid theoretical foundation and practical guidance for studying acupuncture mechanisms and optimizing acupuncture techniques.

Visualization of the acupuncture process

Currently, mechanical studies of acupuncture primarily use numerical simulations and related imaging techniques to visualize the acupuncture process. For example, Yuan et al. [108] developed a physical model on a triangular mesh skin model via mathematical methods, simulating the physical phenomena of skin deformation and rotation during acupuncture treatment, thereby achieving visual modeling and simulation of the acupuncture process. Ding et al. [109] observed degranulation in tissue sections after acupuncture under electron microscopy and found that the cell membrane became thinner, with a significant release of granular matrix substances into the intercellular spaces. They identified that mast cells at the acupoint played a role in the acupuncture effect, and that degranulation of mast cells is a crucial step in generating acupuncture effects. Wang et al. [110] used functional magnetic resonance imaging (fMRI) to elucidate that acupuncture at the *Taichong* and *Hegu* acupoints can enhance hippocampal connectivity in patients with Alzheimer's disease (AD). Furthermore, their team demonstrated through fMRI that acupuncture has an additional therapeutic effect in treating depression, with this effect potentially mediated through the limbic system, particularly the amygdala and anterior cingulate cortex (ACC) [111].

To enable both researchers and nonexperts to intuitively understand and observe the vast amounts of data and complex results generated by numerical simulations, some scholars have integrated virtual reality (VR) to represent these data in three dimensions, offering a more intuitive understanding of the acupuncture process and its mechanical behavior. VR can be used to present the results of numerical simulations, making the outcomes more intuitive and vivid. Since the release of the "Visualization of the Human Body Project" data in the United States, it has become possible to create detailed three-dimensional human body data models for medical imaging content [112].

Wang et al. [113] designed a virtual human acupoint model and an acupuncture tissue mechanical model via an intelligent fuzzy Petri net expert system, simulating the mechanical process of needle insertion in acupuncture treatment. Zhang et al. [114] proposed a novel acupuncture stimulation technique based on VR, validated through electroencephalography that the induced brain activity is similar to that of manual acupuncture. Jiang et al. [72] combined haptic collaborative technology to realize a remote virtual acupuncture system. By combining virtual reality technology and numerical simulation methods, virtual simulation systems for training and education can be developed, such as virtual surgery systems for medical training and virtual laboratories for engineering studies, which can increase learning efficiency and training quality.

These studies indicate that while progress has been made in the development of mechanical theories and models of acupuncture for soft materials and biological tissues, there remains considerable space for exploration and development in this field. In particular, research on the coupling relationship between the geometric shape and mechanical properties of the puncture structure will help provide a more comprehensive understanding and optimization of the mechanical mechanisms of acupuncture therapy.

Conclusion

Acupuncture, a traditional therapeutic method, is increasingly being scientifically explained and applied through the study of acupuncture mechanics. Research in this field, particularly the use of modern technologies to analyze the generation and transmission of mechanical signals during acupuncture, provides crucial insights into its biological effects. This paper summarizes recent advancements in acupuncture mechanics, highlighting how various techniques—ranging from biomechanical testing to microscopic imaging and cell biology—are employed to uncover the mechanisms by which mechanical signals influence cellular and tissue-level responses.

Key findings include the activation of mechanically sensitive ion channels by needling, the subsequent engagement of cell signaling pathways, alterations in mitochondrial function, and potential cytoskeletal remodeling. While current research has its limitations, interdisciplinary collaboration offers immense potential to further elucidate the biomechanical mechanisms underlying acupuncture. For instance, in vitro simulations using bio-inspired materials, along with advanced imaging technologies, can deepen our understanding of how human tissues respond to mechanical stimulation during acupuncture. Moreover, the establishment of comprehensive databases consolidating acupuncture parameters could enable researchers to develop sophisticated acupuncture models using mechanical constitutive analysis or machine learning approaches. These interdisciplinary advancements are expected to provide a stronger theoretical foundation and practical guidance for clinical applications, enabling physicians to optimize treatment plans and improve treatment personalization and predictability.

In conclusion, progress in acupuncture mechanics research lays a robust foundation for the scientific and standardized treatment of acupuncture. This integration of traditional and modern medicine holds significant potential for advancing both therapeutic effectiveness and global acceptance of acupuncture as a credible medical practice.

Author contributions
Liang Yunshan: writing—original draft. Xu Chengli: conceptualization, investigation. Zhang Peiming: figure design. Lu Liming, Liang Xudong, Quan Haocheng: corresponding authors and project administration. Liang Yunshan and Xu Chengli: reviewed and edited the revision. All authors have read and agreed to the published version of the manuscript.

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