AIMS Bioengineering

AIMS Bioengineering, 13(2): 168–208.
DOI: 10.3934/bioeng.2026008
Received: 01 March 2026
Revised: 03 April 2026
Accepted: 07 April 2026
Published: 14 April 2026

https://www.aimspress.com/journal/Bioengineering

Review

Computational and AI-assisted modeling of human hand peripheral nerves: a systematic review

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Abstract: The peripheral nerves of the human hand play a crucial role in sensorimotor function. However, their complex anatomy, multiscale biomechanics, and electrically coupled behavior make them difficult to model computationally. Recent advances in medical imaging, finite element modeling, and data-driven methods have enabled the development of increasingly realistic models of nerve mechanics and signal conduction. The results obtained from modeling nerve mechanics and electrical conduction can provide useful insight into the underlying mechanisms of several neuropathies such as carpal tunnel syndrome (CTS), diabetic neuropathy, and traumatic nerve injury. This systematic review examined key modeling strategies, including the use of anatomical reconstruction, finite element analysis (FEA) for stress and strain analysis, computer simulations of the electrophysiological activity of nerves to model nerve conduction, multi-physics analyses, and artificial intelligence (AI)-assisted modeling approaches. A systematic literature search was conducted in PubMed, IEEE Xplore, Scopus, and Web of Science, covering studies published up to December 2025 to identify studies related to computational and AI-assisted modeling of the human hand's peripheral nerves. After removing duplicates, screening, and eligibility assessment, 50 studies were included. The literature was synthesized across four thematic areas: anatomical reconstruction and imaging-based models, biomechanical and finite element modeling, electrophysiological and conduction models, and AI-assisted data-driven approaches. Comparative analysis reveals substantial variability in the modeling assumptions, validation strategies, and clinical relevance, with limited consensus on standardized evaluation metrics. Persistent gaps include the inadequate representation of nerve branching networks, insufficient patient-specific connective tissue modeling, and weak experimental or clinical validation. Despite advances in peripheral nerve modeling, no comprehensive review exists focusing specifically on anatomically accurate computational modeling of the human hand's nerves. Future work should improve the alignment of imaging and computational pipelines, develop hybrid electro-mechanical and AI-enhanced frameworks, and enhance translation into surgical planning and neuroprosthetics.

Keywords: computational modeling; AI-assisted modeling; finite element modeling; median nerve

1. Introduction

The human hand represents a highly evolved anatomical structure that blends complex musculoskeletal dynamics with fine neural regulation to achieve dexterous function and sensitivity. For this reason, the median, ulnar, and radial nerves play an important role in sending numerous branches both to provide motor innervation to the intrinsic and extrinsic musculature of the hand and, at the same time, supplying abundant sensory information from the skin as well as the digits. The detailed anatomy of these nerves, together with their functionalities, present them as very attractive subjects to be explored clinically and computationally. Peripheral nerve injuries in the hand may arise due to trauma, compression neuropathies, diabetes, repetitive strain injury, or iatrogenic causes leading to sensory deficit and motor loss or pain syndromes. One of the nerve entrapments, known as carpal tunnel syndrome (CTS), is caused by compression of the median nerve. Computational models alleviate many of these constraints by incorporating medical imaging, finite element modeling (FEM) methods, and electrophysiological simulations to duplicate the nerves' anatomy, forecast conduction properties, and analyze stress distributions under external loading circumstances [1,2].

One of the most common neuropathies of the hand is known as CTS. It occurs when the median nerve is squeezed within the carpal tunnel. Approximately 3–6% of adults all over the planet acquire CTS and it remains the largest cause of work disability [3]. Figure 1 indicates the location and structure of the median nerve. Similarly, it is common that compression over the canal of Guyon leads to compression of the ulnar nerve, and traumatic injuries can affect the radial nerve [4,5]. Computational models have been used to simulate these disorders in the study of pathophysiology and treatment choices. In an example, models using FEM under varying ligament stiffness or external forces and poses of the wrist underwent analysis to determine the influence on the distribution of pressure within the carpal tunnel that alters nerve deformation and conduction velocity [6–9].

Peripheral neuropathy apart from compression symptoms is a major sequela. About 20–30% of Type 2 diabetes patients develop peripheral neuropathy that may severely reduce their quality of life as it causes so much insensibility and the risk of suffering injuries to the hand [10]. Computational models of how nerve signals can be conducted under various metabolic conditions are starting to shed some light on how microstructural alterations in the nerve fibers can influence the conduction and excitability of signals [11]. On the same note, the nerve damage that occurs due to trauma, burns, or surgical injuries usually require nerve grafts or repairs that can be predicted by using computational modeling to predict the results of regeneration and recovery [12].

Patient-specific neural geometry can now be reconstructed by high-resolution imaging procedures, such as magnetic resonance imaging (MRI), computed tomography (CT), and diffusion tensor imaging (DTI) [13]. DTI has especially found application in the mapping of nerve lines and the fascicular architecture, enabling the creation of realistic three-dimensional (3D) geometries which can be computationally analyzed further [14]. FEM of the mechanical environment of nerves has been commonplace, given this anatomical basis. FEM allows for the simulation of stress, strain, and pressure distributions in neural tissues under a variety of biomechanical situations, including wrist flexion/extension, external compression, and scar formation. Extensive research has indicated that relatively minor increases in carpal tunnel pressure can substantially inhibit the median nerve's conduction, providing a mechanical explanation for the clinical presentation of CTS [6,7]. In addition, multiscale FEM-based models now allow tissue-level mechanics and cellular activities to be connected by looking at how mechanical strain is associated with axonal injury and remyelination.

At the same time, electrophysiological models of nerve conduction have advanced from the original Hodgkin–Huxley framework to more complex multicompartmental models that utilize the ion channel kinetics of conduction velocities, the myelin sheath's characteristics, and the distribution of fiber diameter [15,16]. These models are increasingly being used in mimicking differences in conduction velocities in altered neuropathic states, thus facilitating the interpretation of electromyography (EMG) and nerve conduction studies (NCS). In order to detect mechanical deformation and conduction dysfunction of the peripheral nerve simultaneously, hybrid techniques that combine FEM and electrophysiology are also being investigated [11].

Several obstacles still exist in spite of these advancements. First, the capacity of models to accurately depict actual anatomical networks is limited by the frequent oversimplification of the branching complexity of the hand's nerves, especially at the digital level. Second, although nerves' shape, tissue elasticity, and fascicular arrangement have a significant influence on the biomechanical and electrophysiological results, they are rarely considered. Third, validation is still a significant barrier. The poor clinical validation of certain models, even when they are compared with experimental or cadaveric data, limits the findings' translational application. Fourth, while integrative models that combine both mechanical and electrophysiological factors are still in their infancy, the majority of studies concentrate on either one or the other.

The current knowledge on computational modeling of the hand's nerves is still in a disjointed form despite the great progress made. There is a wide range of studies with different assumptions concerning the anatomy, materials, loading, and validation approaches. Consequently, there is no easy way of comparing approaches to modeling or finding methodological agreement in this realm. It is mainly for this reason that it is difficult to evaluate the relative strengths, limitations, and translational relevance of diverse modeling approaches or to identify a methodological consensus within the field. There are many reviews available that are related to the peripheral nerves' biomechanics and electrophysiology, and the use of artificial intelligence (AI) in medical imaging through narrative and domain-specific formats; however, no prior work has systematically synthesized computational models specifically targeting the peripheral nerves of the human hand. Many of the studies referenced in the literature as potentially transferable from other types of peripheral nerves are included without proper justification for their inclusion or the methodology used to compare the two. This lack of a systematic synthesis of the evidence limits reproducibility, hinders clinical translation, and obscures key research gaps that are critical for advancing patient-specific modeling, diagnostic support systems, and bionic or neuroprosthetic applications.

This systematic review aims to engage in a rigorous critical synthesis and comparison of the modeling approaches that utilize computation and AI to represent the human hand's peripheral nerves. In alignment with Preferred Reporting Items of a Systematic review and Meta-analysis (PRISMA) standards, the studies reviewed have been systematically organized according to their classification of modeling techniques; namely, anatomical reconstructions, biomechanical modeling and FEM, modeling of electrophysiological conduction, and AI assisted, data-driven modeling. The systematic literature review specifically identifies the unique qualities of hand-specific computational models in comparison with the models used to study other peripheral nerves, and classifies the reviewed studies according to their modeling assumptions, validation strategies, and clinical relevance. By delineating various methodological patterns as well as differences among the methods applied, and the barriers to translating the models into practice, this work will provide an organized foundation for future studies investigating the computational modeling of nerves to aid in clinical decision-making and the design of bionic interfaces.

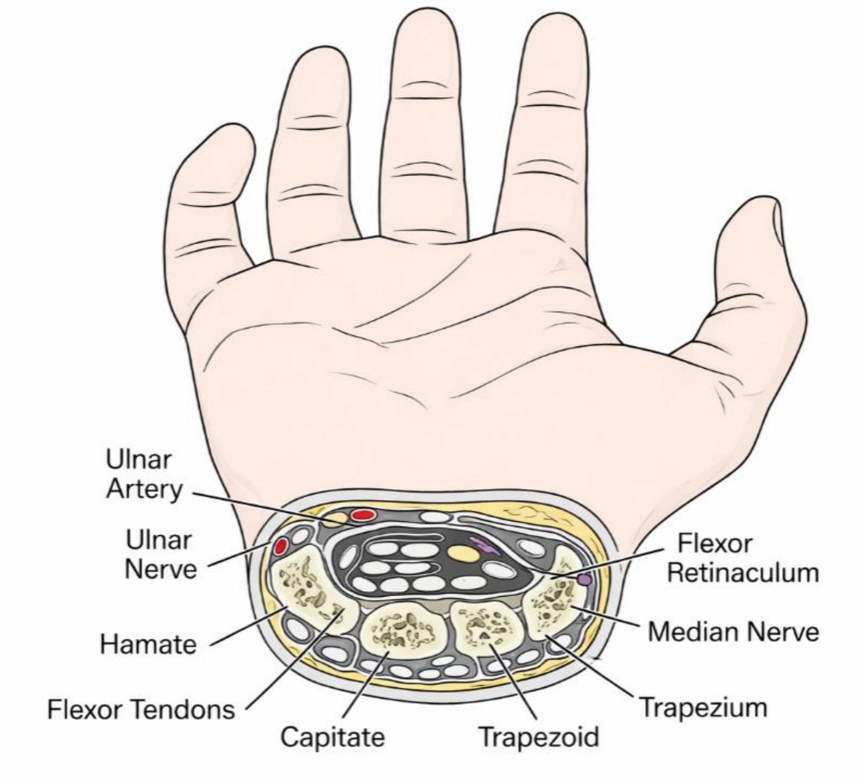

Figure 1. Schematic of the median nerves' localization in the carpal tunnel, adapted from [17].

2. Materials and methods

The literature on computational modeling of the nerves in the human hand was thoroughly covered and synthesized using a methodical approach. Even though this field of study encompasses a wide range of fields, including engineering, neuroscience, medical imaging, and clinical practice, a systematic method was required to combine the results from various fields. The methods used in this review, namely the review protocol and reporting standards, the literature search strategy, the study selection and screening process, eligibility criteria, quality assessment, and the risk of bias, are described in the ensuing subsections.

2.1. Review protocol and reporting standards

The systematic review was conducted following the PRISMA 2020 guidelines. A systematic review plan was designed in advance to establish the scope of the research, inclusion criteria, search methods, and synthesis approach. Despite the fact that the review protocol was not registered in PROSPERO or any other registry, all the methodological decisions were made prior to the commencement of the literature screening process to reduce selection bias and to facilitate transparency.

2.2. Literature search strategy

An extensive literature review was carried out in several electronic databases such as PubMed, IEEE Xplore, Scopus, and Web of Science. The search included journal articles and conference papers related to computational modeling of the peripheral nerves and AI-assisted modeling techniques. The literature search was initially conducted up to December 2024 and was subsequently updated to include relevant studies published up to December 2025 to ensure the inclusion of the most recent advances in the field.

A comprehensive literature search was performed using combinations of keywords related to peripheral nerves of the hand, computational modeling, and AI methods.

Examples of the search strings used in searching the databases include the following.

PubMed:

(“median nerve” OR “ulnar nerve” OR “radial nerve” OR “hand peripheral nerve”) AND (“computational model” OR “finite element” OR “biomechanical model” OR “electrophysiological model”) AND (“machine learning” OR “deep learning” OR “convolutional neural network” OR “artificial intelligence”)

IEEE Xplore:

(“peripheral nerve modeling” OR “median nerve model” OR “ulnar nerve biomechanics”) AND (“finite element analysis” OR “electrophysiological simulation”) AND (“machine learning” OR “deep learning”)

Equivalent search strategies were adapted for Scopus and Web of Science using database-specific indexing terms.

2.3. Selection and screening process

All the records retrieved were added to reference management software, and all duplicate entries were deleted before being screened. Selection of the studies was completed in two phases. Initially, two reviewers independently screened the titles and abstracts to determine their relevance according to set inclusion and exclusion criteria. The disagreements were resolved by means of discussion, and in the cases when it was not possible to find a consensus, the third reviewer was involved.

The second phase involved meeting our obligations by having the same reviewers evaluate the full-text articles and determine their ultimate eligibility. A PRISMA flow diagram summarizes the process of study selection; a clear indication of the records recognized and filtered, omitted, and incorporated in the qualitative synthesis is provided. EndNote reference manager was used to consolidate the search results and eliminate duplicates.

2.4. Eligibility criteria

The inclusion criteria the studies had to fulfill were the following:

(i) They concerned computational, mathematical, or AI-assisted modeling of the peripheral nerves;

(ii) They specifically focused on the human hand's peripheral nerves (median, ulnar radial) or offered methodologies that could be applied to modeling the hand's nerves with obvious anatomical or physiological significance;

(iii) They used numerical simulation, electrophysiological modeling, machine learning (ML), or a combination of techniques; and

(iv) They were found in peer-reviewed journals or conferences with indexed proceedings.

The studies were filtered out when they:

(i) Concentrated on the structures of the central nervous system and lacked methodological significance to the peripheral nerves;

(ii) deficient in their methodology; or

(iii) were clinical reports only without a modeling or computational element.

This review discusses the structure and function of the peripheral nerves found in the human hand. In addition, it includes some studies on other types of peripheral nerves (such as the sciatic and median nerves; however, only those studies which provided fundamental information about the biomechanics, electrophysiology, or computational methods related to the peripheral nerves were included). The reason for including these studies was that there are similarities between the structure/function of these non-histological examples and those of the hand so the application of the modeling frameworks and simulation strategies derived from non-hand nerve examples could be applied to the hands.

2.5. Quality assessment and risk of bias

Due to the heterogeneity of the included articles (including finite element simulations, electrophysiological models, and AI-based diagnostic frameworks), a formal meta-analysis was not possible. Instead, a qualitative appraisal framework was formed to determine their methodological quality. The assessment of all studies was based on the following criteria:

(i) Anatomically and physiologically correct,

(ii) Disclosure of the modeling assumptions,

(iii) A validation plan (experimental, clinical, or theoretical), and

(iv) The computational reproducibility of the workflow.

On the basis of these criteria, the studies were classified as having high, moderate, or exploratory quality and the quality aspects were considered directly in the comparative synthesis to weight the strength of the evidence.

2.6. Data extraction and synthesis strategy

The data were retrieved with the help of a standardized form that included the year of publication, type of nerve, modeling framework, input data, validation method, and provided outputs. Since the modeling paradigms were diverse, a comparative synthesis following a thematic approach was used instead of quantitative pooling. The studies were categorized into thematic groups, such as biomechanical modeling, electrophysiological modeling, AI-assisted diagnostic modeling, and hybrid methods. The comparison was aimed at differences in the modeling assumptions, validation policies, and clinical relevance. Figure 2 illustrates the number of studies per year from 1952 to 2025.

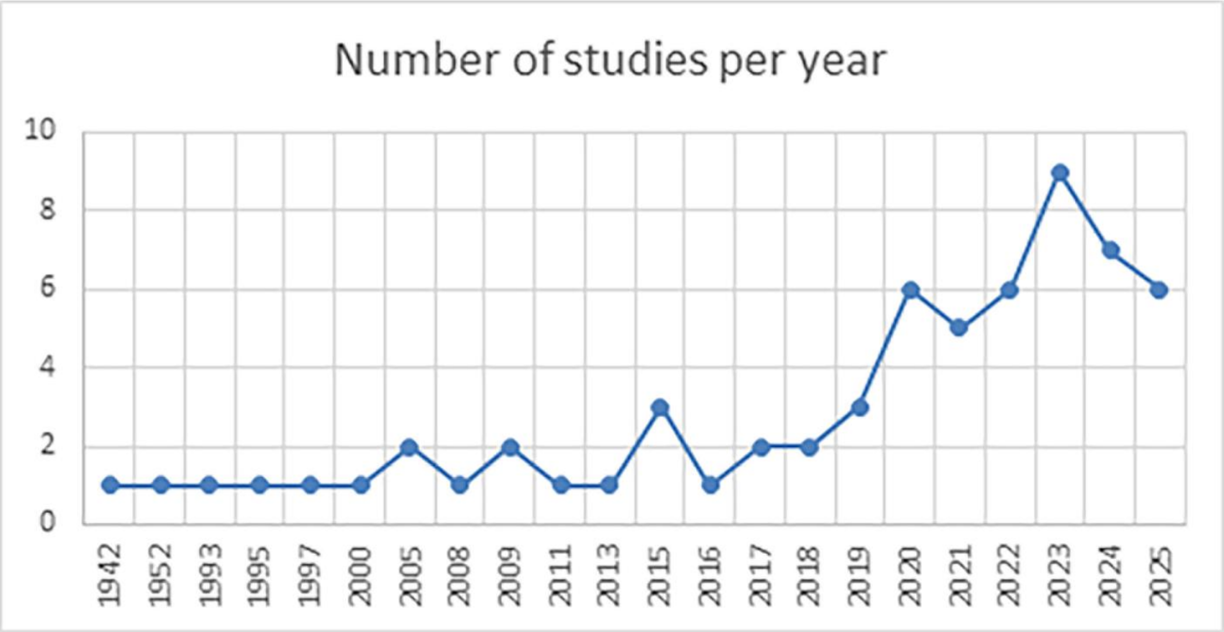

Figure 2. Temporal distribution of publications on computational modeling of peripheral nerves of the hand from 1952 to 2025.

3. Results

3.1. Study selection results

The database search conducted in PubMed, IEEE Xplore, Scopus, and Web of Science yielded 800 records published between 1952 and 2025. After elimination of 93 duplicates, 707 distinct records were filtered by titles and abstracts. After this initial filtering, 525 articles were filtered out because of irrelevance to modeling the peripheral nerves, a lack of computational constituents, or a lack of focus on the human hand. The full text of 182 articles was screened, and 132 articles were excluded due to reasons such as non-hand-specific nerve models and a lack of methodological explanation. Finally, 50 articles were located that met the preset inclusion criteria, and these were incorporated into the qualitative synthesis. The PRISMA flow diagram (Figure 3) summarizes the process of study selection.

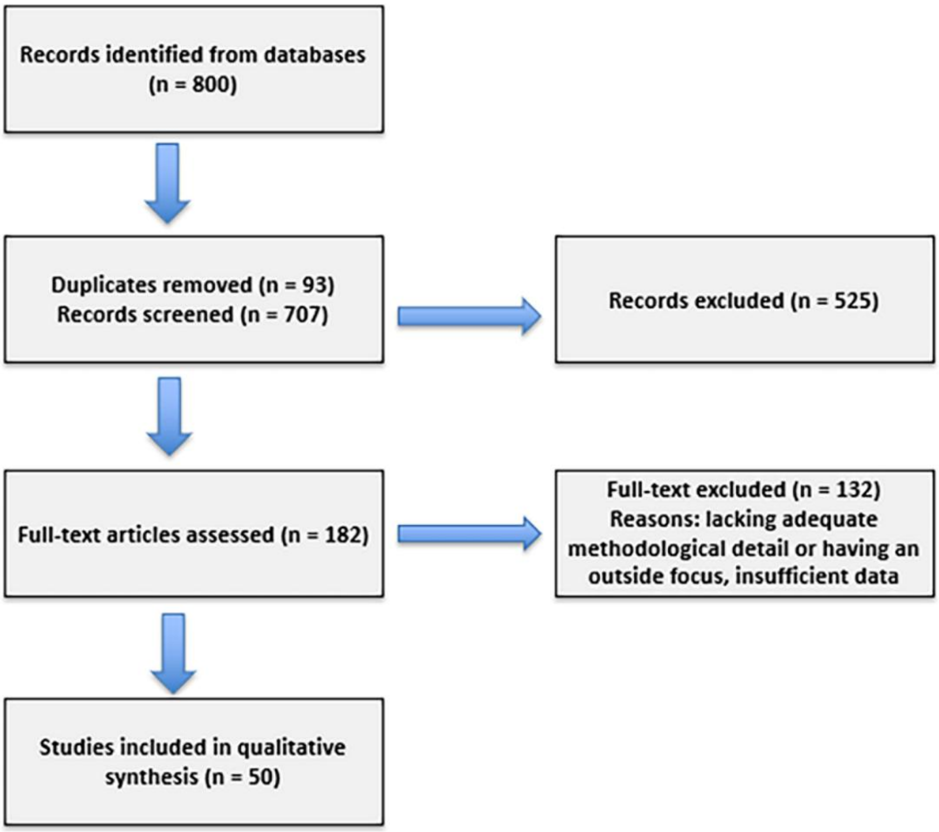

Figure 3. PRISMA 2020 flow diagram illustrating the study selection process.

3.2. Characteristics of included studies

The last collection of investigations included in this review included computational and AI-assisted studies involving the peripheral nervous system (PNS) of the human hand between the years of 1952 and 2025. Most of the research papers were dedicated to the median nerve in CTS, and fewer covered the ulnar nerve and radial nerve or a general nerve network of the hand. The different modeling techniques that were used could be broadly defined as anatomical reconstruction, biomechanical FEM, electrophysiological simulations, hybrid electro-mechanical frameworks, and finally AI-assisted data-driven methods. Although the primary focus of this review is the modeling of peripheral nerves in the human hand, several of the included studies describe computational models developed for peripheral nerves in other anatomical regions. These studies were included because the underlying modeling methodologies such as finite element representations of nerve fascicles, electrophysiological conduction models, and data-driven segmentation approaches are directly transferable to modeling the nerves of the hand.

To improve clarity, the studies discussed in this review are categorized into two groups as follows:

(1) Models specifically developed for hand-related nerves such as the median, ulnar, or radial nerve.

(2) General computational models of peripheral nerves that provide methodological frameworks applicable to simulations of the nerves of the hand.

The goals of the studies varied between understanding nerve deformation and conduction impairment and optimization of the strategies used for stimulation and the creation of automated diagnostic assistance tools. The main features of the included studies by modeling category are summarized in Tables 1–5.

3.3. Thematic synthesis of modeling approaches

3.3.1. Anatomical reconstruction of hand nerves

Accurate anatomical reconstruction serves as the foundation for nerve modeling. Several studies have used medical imaging modalities, including MRI, DTI, ultrasound, and CT, to extract the nerve geometries in the human hand.

Early research utilizing 3-T DTI tractography successfully traced the 3D paths of the median, ulnar, and radial nerves in the upper limb, providing anatomical frames suitable for FEM simulations [18]. Subsequent work in porcine and human models (e.g., high-resolution DTI monitoring of nerve degeneration) shows how DTI captures the fascicular structure and anisotropic diffusion, enabling patient-specific geometrical fidelity in biomechanical modeling [19,20].

Ultrasound-based reconstructions provide real-time and cost-effective solutions, particularly for superficial nerves. For instance, Wolny et al. observed dynamic variations in the median nerve's cross-sectional area and shear modulus across wrist postures in CTS patients, underlining the efficacy of ultrasonography for in vivo segmentation [21]. Maki et al. used DTI in conjunction with the dual echo steady-state (DESS) methodology to assess the median nerve in CTS. The method increased the observation and measurement of microstructural changes, allowing for comparisons before and after surgery [22].

Recent studies integrating DTI tractography with histological validation indicated the reliable reconstruction of the main nerve fascicles but highlighted problems in resolving the finer branches [18,23]. Table 1 shows the details of studies based on anatomical reconstruction of the nerves of the human hand.

3.3.2. Biomechanical FEM-based models

The most widely used computational method for researching nerve mechanics, hand deformation, and compression is FEM.

The main corpus of studies consists of models for CTS. Several researchers used different wrist positions to simulate mechanical stress on the median nerve. When compared with the neutral position, Peng et al.'s model of transverse carpal ligament strain showed greater nerve compression during flexion [9]. Similarly, median nerve distortion was measured by Anderson et al. using FEM, and associations with CTS risk variables were found [24]. Jordan et al. examined at how simulated carpal bone rotations affected the cross-sectional geometry of the distal carpal tunnel. The authors found that even little changes in carpal bone alignment have a major impact on the tunnel's architecture, potentially affecting compression of the median nerve [25]. The material characteristics of the nerves are still unknown. A lack of experimental data often leads to studies assuming isotropic, hyperelastic materials. Nevertheless, Cheever et al. included anisotropic viscoelasticity in FEM-based models, which resulted in different stress–strain distributions compared with isotropic assumptions [26]. Figure 4 depicts the modeling and simulations using biomechanical FEM.

Additionally, post-surgical FEM-based models have been developed. For example, ligament resection lessens median nerve compression, but it may cause instability in the tendon's location, according to computer models of carpal tunnel release operations [8]. Oflaz and Gunal [27] developed a biomechanical FEM-based model that showed that the loading changes with movement. The trapezium bears the most stress in the neutral position and during flexion, while the scaphoid bears the most load during radial deviation and extension. In another study, Wei et al. performed a sensitivity analysis that demonstrated the importance of material properties and muscle loading, which established the groundwork for research into hand manipulation and bionic hand design utilizing biomechanical and neurophysiological techniques [28]. Peripheral nerve damage and repair have also been modeled. FEM investigations of nerve grafts and conduits show that material stiffness has a major effect on axonal regrowth [29]. For example, soft, collagen-based conduits were shown to reduce stress concentrations at coaptation sites compared with synthetic alternatives. Chang et al. showed that hyper-viscoelastic models enhance the fidelity of FEM-based models of CTS and trauma and more accurately depict the peripheral nerves' mechanics than basic isotropic/hyperelastic assumptions [30]. Table 2 shows the details of studies based on biomechanical FEM.

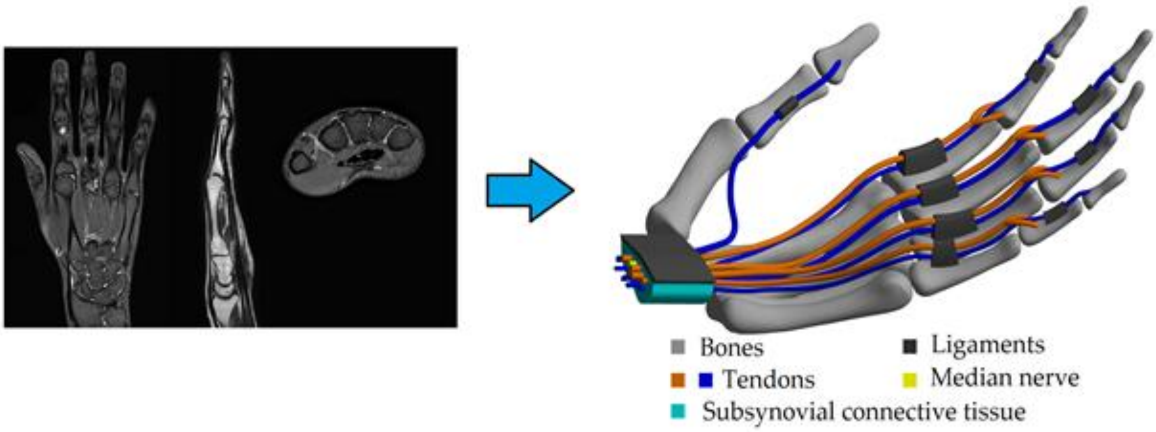

Figure 4. Representative biomechanical finite element model of the human hand illustrating the anatomical structures used for simulations of nerve compression [7].

3.3.3. Electrophysiological models

Electrophysiological modeling looks at the mechanisms of the spread of action potentials along the hand's nerves and the changes in conduction caused by pathological conditions.

The models that are based on cable theory are at the core of this field. For the peripheral nerves, early computational models toned down the Hodgkin–Huxley equations and included myelinated and unmyelinated axons [15]. These models replicate conduction velocity, refractory periods and demyelination effects.

CTS has been specifically focused on in models of median nerve conduction. Indicatively, slowed conduction caused by compression-induced myelin disruption was modeled by Zhang et al., and it was found to be consistent with clinical nerve conduction studies (NCS) [31]. These simulations were applied to justify the reason for augmented distal motor latency in CTS patients. Ion channel dynamics have also been added. Experiments based on modified Hodgkin–Huxley models revealed the dependence of excitability in myelinated fibers on the distribution of sodium and potassium channels [32]. These were claimed to generate conduction failures in the neuropathies of diabetic neuropathy or trauma.

In the area of nerve stimulation and prosthetics, electrophysiological models are finding more uses in neuroprosthetics. Optimization of the parameters of electrical stimulation of the median nerve and ulnar nerve to restore the grasping capabilities of hand prostheses was done using computational models of the nerves [33]. These studies instruct safer and effective stimulation plans by modeling fibers' recruitment. Table 3 presents the studies according to their electrophysiological models.

3.3.4. Hybrid and integrative models

The development of anatomical, biomechanical, and electrophysiological models is a growing trend in the combination of models. As an illustration, Sundar et al. developed a coupled FEM–electrophysiological model of the median nerve in the carpal tunnel and simulated both slowed conduction and mechanical compression [34]. This method is more appropriate to clinical experiences in which the structural deformation is accompanied by electrophysiological impairment.

In another hybrid study [35], MRI-derived anatomy was combined with conduction simulations of unique models that showed patient-specific differences in conduction velocity that could be attributed to geometric variation. Such models demonstrate considerable potential in advancing personalized medicine. Mena and Bravo [36] conducted a clinical comparison of electrophysiological diagnostic methods for CTS, identifying which nerve conduction parameters (e.g., latency and conduction velocity) best distinguish affected patients and support diagnostic accuracy. Shao et al. identified a brief lexicon of spatiotemporal vibration patterns best suited to represent touch. These spatiotemporal patterns represented digit individuation and wave propagation speeds (~1–10 m/s). The same patterns were identified in the simulated tactile afferent spiking data, supporting a biomechanical framework for sensory encoding efficiency [37].

Alp et al. developed a mathematical simulation model that showed a substantial association between the carpal tunnel volume and the angle of the hamate bone's curvature, indicating that the curvature angle may be an anatomical risk factor for idiopathic CTS [38]. Coste et al. demonstrated that selective peripheral nerve stimulation using implanted electrodes can restore functional hand movements (grasp, release) in individuals with tetraplegia [39]. Elseddik et al. examined neural and electrophysiological modeling techniques to gain a better understanding of how signals propagate and activate when the nerves are stimulated electrically. Their research offered valuable information about how to best adjust stimulation parameters for enhanced neuroprosthetic control and functional recovery [40]. Table 4 shows the details of studies based on hybrid and integral models.

3.3.5. AI-assisted modeling and data-driven approaches

Recent innovations in AI and ML provide data-driven methodologies to complement the traditional computational models of the human hand's nerves, e.g. CTS. They allow researchers to assess pathologies of the median nerve. In contrast to physics-based FEM and electrophysiological modeling, AI-enabled approaches primarily focus on automated image analysis and extraction of critical features for automated diagnostic support through the use of ultrasound images and various multimodal clinical data inputs.

An increasing number of studies have been carried out that have applied deep learning techniques to ultrasound imaging systems to successfully localize, segment, and diagnose the median nerve and thereby CTS. Convolutional neural networks (CNNs) have been shown to have an exceptional level of accuracy in locating and measuring the median nerve at the carpal tunnel level, which, in turn, provide an objective reproducible assessment as opposed to a manual sonographic assessment [41–43]. The development of automated end-to-end deep learning systems has further increased speed and efficiency for assessing CTS in a clinical workflow [44].

The use of radiomics and multicenter AI frameworks expands upon the abovementioned developments by extracting various high-dimensional compound features from ultrasonographic images that enables the efficient diagnosis of CTS in different heterogeneous cohorts [42,45]. The performance metrics of AI models conducting diagnostic examinations have indicated that the overall performance level of AI models is comparable with that of expert radiologists (and, in some cases, has even exceeded them). However, standard imaging protocols were used.

ML models have moved beyond a binary classification of diagnoses to models that classify degrees of disease severity and evaluate prognosis. Current research has shown that an AI-driven framework that utilizes ultrasound-derived features in combination with clinical and/or electrophysiological parameters shows great promise in grading CTS severity levels and assisting with clinical decision-making [46–48]. Multimodal deep learning approaches that combine both imaging and non-imaging data sources have improved predictive power as well [47].

While AI-driven methodologies are currently not intended to replace physics-based modeling of nerve anatomy in the hand, they are intended to serve as supportive tools by being able to automate the segmentation of nerves, provide the capability to create a subject-specific geometry, and enable analyses of large volumes of data. A systematic review and a scoping review recently identified that hybrid approaches that combine AI, mechanical, and electrophysiological models have the greatest potential for translational use in clinical practice [49].

Although the results to date with AI-assisted approaches are promising, their implementation is currently limited because of the need for high-quality annotated datasets, variability in the imaging protocols, and little to no explainability of the AI's decision-making process. Table 5 shows the studies based on AI models of hand nerves.

3.3.5.1 Critical analysis of AI-assisted approaches

According to the reviewed literature, most of the AI-based solutions in peripheral nerve research studies have mainly concentrated on medical image processing, specifically, automated nerve segmentation of ultrasound and MRI. Such approaches usually use deep learning networks like CNNs to detect and outline the nerve structures with great precision [40,49,50].

Although they are also important for making image-based analysis more efficient and reproducible, these methods are not similar to old-fashioned computational modeling methodology. Specifically, the differences between physics-based models and purely data-driven AI methods should be mentioned.

3.3.5.2 Distinction between physics-based and data-driven models

Finite element and electrophysiological models of physics are based on known biophysical and biomechanical principles. These models directly model the underlying processes, including tissue deformation, stress distribution, and the propagation of action potential, and thus give interpretable and mechanistic results on nerve behavior [6–9,15,16,30,51].

Physical laws are not explicitly represented in data-driven AI models, by contrast. Rather, they are taught statistical laws using big data, generally without an explicit description of the underlying biology. Although this makes them perform well in some activities, like segmentation and classification, it restricts their power to simulate or forecast the functioning behavior of nerves exposed to different physiological or pathological conditions.

3.3.5.3 Limitations of AI-based approaches

Although they have their strengths, AI-based approaches have a number of critical limitations. First, annotated training data are very important to their performance because they need high-quality training data to work with. Labeled datasets in medical imaging are needed to achieve model generalization, but large and high-quality labeled datasets may be unavailable in the medical imaging case [40,45,49].

Second, AI models are often black boxes that do not allow much interpretability of their predictions. Such non-transparency presents difficulties in their clinical adoption, where it is necessary to know the motivation behind the model outputs [46,49].

Third, AI models are often task-oriented and cannot be generalized outside the conditions they are trained on. As an instance, a model trained on nerve segmentation might not be directly useful in modeling nerves' biomechanics or electrophysiology.

3.3.5.4 Gaps in AI for functional modeling

Another significant literature gap is the rare implementation of AI methods to the functional behavior of peripheral nerves, e.g., biomechanical deformation or electrophysiological signal propagation. The structural analysis is a common feature of most of the research done, and functional simulation is another significant field of future research [46,49].

3.3.5.5 Toward integrated modeling frameworks

In the future, it will be necessary to apply data-based AI methods together with physics-based computational models. The advantages of both paradigms could be used in such hybrids, where AI is applied in reconstructing images and estimating parameters, whereas physics-based models are used to simulate and predict mechanistic behaviors. Such a combined method has been accentuated more in recent computational modeling [46,52].

It can be used to allow more precise, effective and clinically relevant models of the behavior of the peripheral nerves, especially in areas including surgical planning, detection of neuropathies, and personalized medicine.

3.4. Quality appraisal of the included studies

A designed quality appraisal framework that is specific to computational and modeling-based research was used to determine the methodological quality and reliability of the included studies. Since there is no specific standardized risk of bias tool to use in research on computational biomechanics and electrophysiological modeling, the appraisal criteria were modestly altered according to the standard reporting guidelines of simulation research and previous computational reviews. The five domains that were assessed in the quality appraisal process included (i) anatomical fidelity (through the use of subject-specific or validated geometry), (ii) the model's transparency and reproducibility (through clear documentation of the governing equations, assumptions, and parameters), (iii) a validation strategy (through experimental validation, validation based on clinical experience, or literature validation), (iv) a sensitivity/uncertainty analysis, and (v) the clinical/translational relevance of the work. The quality of the studies was not a barrier to their inclusion in this review; the appraisal results were used to create context regarding the quality of evidence provided by the studies in synthesizing the data for this review. Altogether, anatomical and biomechanical FEM studies had moderate to high structural validity but often no direct experimental validation. Electrophysiological models had good theoretical graining but simplified geometries. Hybrid models were also more able to produce high levels of translational relevance but were also computationally expensive and inconsistently validated. The AI-aided research demonstrated high diagnostic accuracy; still, the majority of studies used a retrospective dataset with little explanatory capabilities and external verification. These trends of quality were used to inform the comparative discussion and future research recommendations. Table 6 depicts a summary of the methodological quality trends across modeling paradigms.

Table 6. Summary of methodological quality trends across modeling paradigms.

Model type	Validation present	Sensitivity analysis	Clinical relevance
Anatomical reconstruction (*n* = 7)	Low–moderate	Not applicable	Moderate
FEM (*n* = 12)	Moderate	Low	Moderate
Electrophysiological (*n* = 6)	Low–moderate	Low	Low
Hybrid (*n* = 16)	Moderate	Moderate	High
AI-assisted (*n* = 9)	High (diagnostic)	Low	Moderate

3.5. Comparative analysis of modeling approaches

In addition to the description of the individual studies, a comparative overview of the reviewed literature shows that there are significant differences in their modeling aids, assumptions, validation methods, and clinical applicability. A structured comparison of the key modeling approaches, including their assumptions, validation strategies, and clinical applications, is presented in Table 7.

Table 7. Comparative summary of approaches to computational modeling of the peripheral nerves.

Approach	Focus	Key assumptions	Validation	Clinical use
Finite element	Mechanics	Homogeneous/simplified geometry	Cadaver/imaging	CTS
Electrophysiological	Signal conduction	Cable theory	Nerve conduction data	Neuropathy
Hybrid	Mechanical + electrical	Coupled physics	Mixed	Surgical planning
AI-based	Image analysis	Data-driven	Intersection over Union (IoU)/ Dice coefficient	Segmentation

3.5.1. Comparison of model types

The reviewed articles can be roughly divided into four modeling strategies, namely (i) FEM, (ii) electrophysiological models, (iii) hybrid multiphysics models, and (iv) data-driven AI-based methods.

Finite element models are mainly concerned with mechanical behavior of the peripheral nerves during compression or deformation. Such models frequently use simplified anatomical geometries and homogenous or layered material properties. Though they are effective in simulating the distributions of mechanical stress, they do not generally include the propagation of electrical signals.

In contrast, electrophysiological models are biophysical models that model nerve conduction via ion channel dynamics and membrane potentials. These models give in-depth pictures of the transmission of signals, but most of them use simplified anatomical models.

The hybrid models combine biomechanical and electrophysiological methods, which allows the simulation of the impact of mechanical deformation on nerve conduction. Even though these models provide a more detailed representation, they involve extra assumptions on the electromechanical coupling and are computationally more taxing.

Applications of AI in medical imaging include automated segmentation and analysis of peripheral nerves. Although such approaches enhance efficiency and accuracy in processing images, they do not explicitly characterize the nerves' mechanics or electrophysiology.

3.5.2. Comparison of model assumptions

There is considerable inconsistency in the assumptions of modeling studies. Finite element models usually presuppose that the material is linear or hyperelastic, and the electrophysiological models presuppose idealized cable-like structures. The assumptions of coupling that are introduced by the hybrid models are not standardized yet, and hence they have unpredictable outcomes.

3.5.3. Validation strategies

Studies vary in terms of their validation methods. Validation of mechanical models is often done using cadaveric experiments or a dataset of images, and electrophysiological models are also based on nerve conduction measurements. Nevertheless, one common limitation of all the methods is the lack of standard validation data to achieve reproducibility.

3.5.4. Clinical relevance

Modeling approaches have different clinical benefits. Compression neuropathies, like CTS, are some of the diseases where FEM will be useful. The electrophysiological models have helped in the conceptualization of abnormalities in nerve conduction, and the hybrid models have potential in surgical planning and predictive diagnostics. The most relevant clinical workflows that can be automated by using AI-based methods include automatic image analysis and segmentation.

All in all, this comparative analysis brings out the complementary features of various modeling methods and the necessity of combined multiscale models. A summary of the strengths and limitations associated with each modeling approach is provided in Table 8.

Table 8. Strengths and limitations.

Approach	Strengths	Limitations
Finite element	Mechanical insight	No signal modeling
Electrophysiological	Accurate conduction	Simplified anatomy
Hybrid	Comprehensive	High complexity
AI-based	Fast, automated	Data dependency

4. Discussion

4.1. Comparative analysis across modeling paradigms

All of the studies that used computational modeling to study the peripheral nerves of the human hand fit into five paradigms for modeling, including anatomical reconstruction, biomechanical FEM, electrophysiological simulations, hybrid electro-mechanical models, and AI-assisted data-driven methods. Each of these paradigms provides different types of information related to peripheral nerve pathways, yet there is substantial diversity in their model assumptions, validation approaches, and clinical applicability, which likely contributes to the differences in the results published in the literature.

4.2. Anatomical fidelity as a differentiating criterion

Anatomical fidelity is found to be a major cause of divergence among modeling methods. The geometries and fascicular orientation of the patient are obtained as imaging-based anatomical reconstructions based on MRI and DTI, which serve as the basis of subsequent biomechanical and electrophysiological simulations [18,19]. These reconstructions are useful inputs for FEM and conduction models, notably in the case of CTS. However, the imaging resolution, especially the failure of DTI to distinguish the fine fascicular microstructure or terminal nerve branches, puts constraints on image simplifications [14]. Reconstructions made with ultrasound are more clinically accessible but have a lower quality in their 3D information and internal nerve structure [21]. As a result, in numerous FEM and electrophysiological studies, the geometry of the nerve is idealized to either a cylinder or a homogeneous material, and this lowers the anatomical realism. This anatomical inconsistency is one of the reasons why studies have reported variable predicted distributions of stress, conduction velocity, and stimulation thresholds.

4.3. Divergence in biomechanical modeling assumptions and validation

The biomechanical FEM research repeatedly shows that the compressive stresses on the median nerve depend significantly on the wrist position; i.e., flexion and extension cause more deformations than the neutral position [7]. These results are congruent with the onset of clinical symptoms in CTS patients, and this indicates their translational value. However, difference is due to the assumptions of the material properties, boundary conditions, and tissue interactions.

The study of nerves has often used isotropic hyperelastic materials in models because there was insufficient experimental evidence to justify the use of anisotropic and viscoelastic behavior [30]. Models with anisotropy or a stratified nerve structure (epineurium/perineurium) have more realistic stress–strain behavior [24] but have little validation against human data in vivo. They are commonly indirectly validated as they depend on consistency with the clinical symptoms or imaging markers, but not on quantitative mechanical measurements. This is the reason why biomechanical models demonstrate moderate clinical relevance but inconsistent predictive accuracy in different studies. FEM analysis also makes an important contribution to surgical planning. Models of carpal tunnel release [8] anticipate reduced compressive stress but also highlight potential biomechanical trade-offs, such as changed tendon dynamics. Such forecasts highlight FEM's promise as a preoperative planning tool; however, its practical translation remains constrained by patient-specific validation. Finally, FEM's applications range from compression to nerve grafts and healing techniques. Models demonstrate how graft stiffness affects axonal regrowth by modeling the conduit's mechanical conditions [29].

4.4. Electrophysiological models: Mechanistic insight versus anatomical simplification

Electrophysiological representation of function/dysfunction, following constructs based on cable theory and Hodgkin–Huxley-type dynamics, expands our understanding of how structural changes lead to functional dysfunction. Simulations, for instance, illustrate that compression-induced demyelination reduces conduction velocity in the median nerve [11]; this is consistent with NCS, which are used routinely in the clinical diagnosis of CTS. Electrophysiological models are useful because they can alter aspects which may be difficult to assess in vivo (e.g., ion channel densities, internodal lengths, and patterns of recruitment). For instance, work that explicitly considered sodium and potassium channels' dynamics illustrate how channelopathies or metabolic dysfunctions (e.g., diabetic neuropathy) decrease excitability [53].

Electrophysiological models are also an important feature in neural interface designs. For instance, simulations of the median and ulnar nerves [32] help FEM analyses optimize the configurations for neuroprosthetics by anticipating fiber recruitment while, at the same time, limiting tissue damage. This kind of work demonstrates the translational applications of using computational physiology, but electrophysiological models often use simplified cylindrical geometries that do not consider anatomical aspects.

4.5. Hybrid models as a bridge between structure and function

Hybrid models that combine anatomical, biomechanical, and electrophysiological domains represent a significant advancement. Studies that combine FEM simulations of mechanical compression with conduction models [51] show a direct correlation between physical deformation and electrophysiological impairment. This dual-domain modeling corresponds to clinical events in which a structural pathology (compression) emerges as functional impairment (slowed conduction). Patient-specific hybrid models have also been demonstrated, which incorporate MRI-based anatomy into conduction simulations [54]. These approaches show potential for individualized diagnostics and surgical planning, where computer predictions could help guide treatment decisions.

In the field of neuroprosthetics, hybrid models assist stimulation protocol designs by considering both the mechanical strain and conduction dynamics [55]. Such integrative techniques are especially important as prosthetic technology improves in precision and biocompatibility. The primary drawback of hybrid models is the computational expense. Simulating both stress–strain fields and ion channel dynamics demands significant resources, which limits their clinical feasibility. Advances in high-performance computers and reduced-order modeling may help to overcome this hurdle.

4.6. *AI-assisted approaches: Efficiency versus interpretability*

The approaches of AI-assisted approaches are fundamentally different in their assumptions and outputs in comparison with physics-based approaches. The deep learning models used on ultrasound or MRI images are highly diagnostic for CTS and its severity [41–44], and are usually as accurate as a trained clinician. Their advantages are their automation, scalability, and quick-to-implement clinical deployment. Nevertheless, AI models cannot be described as typically mechanistically interpretable and have a weak connection with nerves' biomechanics or electrophysiology. On their own, they offer a small amount of information on disease mechanisms. The comparative analysis suggests that AI approaches are most useful in cases involving the augmentation of physics-based modeling, e.g., through the automation of segmentation, parameter estimation, or surrogate models, as opposed to substituting biophysical simulations.

4.7. Inclusion criteria for hand-specific versus transferable evidence

In order to make the review relevant and include methodological innovation, clear inclusion criteria were used in this review to separate hand-specific and transferable nonhand studies. The studies were categorized as hand-specific when they considered the median, ulnar, or radial nerves in the anatomical position of the hand or wrist, or directly considered hand-related pathologies like CTS. The studies of nonhand peripheral nerves were only accepted when their modeling schemes could be directly applied to hand nerves, such as when they introduced validated anatomical reconstruction, material modeling, electrophysiological simulation, or hybrid coupling methods that were not dependent upon nerve position. Reports in which central nervous system models alone were studied or those that could not be scaled anatomically were eliminated. This approach has provided a breadth of methodology without diluting the hand-specialized clinical relevance.

4.8. Clinical relevance and translational readiness

The most promising clinical applications have evolved from CTS research, regardless of the model type. Both FEM and electrophysiological simulations concur in explaining slowed conduction as a mechanical–electrophysiological interaction [7,56]. This convergence reinforces the validity of computational approaches as explanatory tools.

Through the use of computer models of the nerves, and by building upon the initial discoveries made from their use in research, researchers are now able to model patients' clinical presentations as well as direct therapy based upon those clinical findings [57]. Through the use of FEM and analytical simulations, clinicians have also been able to better evaluate the stress–strain distributions, deformation patterns, and functional impacts on the peripheral nerves that are subject to either compression or stretching [58].

To improve translation from the laboratory to the clinic, the integration of imaging studies has helped improve upon the translational nature of nerve model pipelines. The use of ultrasound imaging to characterize the morphology, movement, and stiffness of peripheral nerves has been established as being useful to researchers and to clinicians, with numerous studies demonstrating high correlations between imaging markers and computer models' predictions. A substantial advancement in noninvasive diagnostic and monitoring tools for compressive neuropathies has been established through this advancement.

Simulating electrical stimulation and recording of the peripheral nerves has also aided in the translation of computer modeling technology to clinical environments through volume conductor modeling/electrophysiological models. These models provide researchers and clinicians with valuable insight regarding how currents are distributed within and around the nerves, the number of nerve fibers recruited by a particular nerve pulse, and how electrodes are positioned in relation to the nerve; this ultimately aids in understanding the cause of the nerve conduction abnormalities that occur in clinical practice [59]. In addition, quantitative ultrasound metrics have been demonstrated to be correlated with the estimated degree of nerve compression derived from simulation modeling and provide clinician-specific modeling of each patient.

Biomechanical modeling of the hand and wrist has shown variations in the loading of nerves depending on the position of the wrist and hand, providing a clinical rationale for the worsening of symptoms when the hand is in certain positions, or during certain types of occupational tasks [60]. Studies using diffusion-weighted MRI have improved our understanding of the structural and physiological nature of the PNS, including its axonal structure and the microstructure of peripheral nerves when combined with computer-based modeling [61].

Recently, biomechanical modeling of the hand and wrist has expanded to include electromechanical coupling of the PNS, which links changes in the physical properties of PNS tissue to electrical activity. The models have been used to evaluate the injury thresholds and impairments in electrical conduction that occur as a result of compression or injury to the PNS, and their repair mechanisms. Utilization of biomechanical modeling to study the PNS has provided a wealth of information regarding the mechanical and physiological loading of the mechanics of the median nerve and carpal tunnel, both in healthy and in diseased states for those suffering from CTS [62].

Additionally, computational modeling has also allowed for the optimization of PNS stimulation protocols to facilitate recovery and the modulation of PNS activity for rehabilitation by providing personalized treatment plans with estimates for stimulation results across a variety of anatomical and electrical conditions. Limitations still exist, however, due to uncertainties regarding the material properties, boundary conditions, and limited in vivo validation of the predictions made by these models, which limit their accuracy [63].

To address the limitations of traditional volume conductor and finite element methods, advanced models were developed that consider heterogeneity in tissues and consider anatomic variation; this means better translation of models for use with human peripheral nerves [64]. This will allow for new areas of application to emerge in clinical practice, including the treatment of pain, the use of neuroprosthetic devices, and the restoration of function [65].

Recent reviews have encouraged the use of standard modeling workflows and processes that will allow for improved consistency, reproducibility, and validation of computational models of the nerves to support their faster adoption into clinical use. Hybrid approaches to modeling nerve motion that incorporate biomechanics, electrophysiology, and medical imaging have been suggested as methods to develop comprehensive and clinically relevant simulations [66]. Ultimately, 3D computational representation of the nerves will allow for personalized diagnosis, surgery planning, and the treatment of patients experiencing nerve injuries.

5. Conclusions

This systematic review integrated two decades of investigation regarding computational modeling of the nerves of the human hand, including anatomical reconstructions, biomechanical finite element models, electrophysiological simulation, and integrated models. In general, evidence indicates that with the developments in imaging, computer capability, and mathematical modeling, these methods provide better representations of peripheral nerves' structure and function. These methodologies have improved our understanding of nerve biomechanics in conditions such as CTS, have enhanced predictions of conduction properties, and provided improved capacity for surgical planning, prosthesis development, and rehabilitation. Despite these developments, there are still substantial gaps. Many models rely on simple geometries, homogenous material qualities, or two-dimensional abstractions, limiting their capacity to adequately portray the hand nerves' intricate anisotropy and branching architecture. While electrophysiological models are useful, they are frequently evaluated against small datasets, which limits their generalizability. Integrated frameworks are still in their infancy, with only a few investigations merging biomechanical and electrophysiological viewpoints to create unified simulations. Furthermore, clinical translation is limited because the majority of models have not been tested in real-world diagnostic or therapeutic settings. Future research should prioritize hybrid computational frameworks that integrate AI-driven data analysis with validated biomechanical and electrophysiological nerve models. Such approaches are critical for advancing patient-specific surgical planning, neuroprosthetic interface design, and clinically meaningful decision-support systems for hand neuropathies.

Table 1. Characteristics of studies on the anatomical reconstruction of hand nerves.

Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Anderson et al., 2022 [24]	Carpal tunnel volume distribution and morphology changes with flexion-extension and radial–ulnar deviation wrist postures	Median nerve (carpal tunnel)	Anatomical/biomechanical modeling (morphology + FEM relevance)	MRI/CT imaging of the carpal tunnel in different wrist postures	3D morphometric analysis	Imaging-based morphometry validated against anatomical expectations	It was shown that wrist posture considerably alters the carpal tunnel's volume and structure; flexion and extension decrease space, which may raise the risk of median nerve compression.
Wolny et al., 2024 [21]	Changes in ultrasound parameters of the median nerve at different positions of the radiocarpal joint in patients with CTS	Median nerve (carpal tunnel)	Imaging (ultrasound morphometry, posture-dependent)	Ultrasound imaging of the carpal tunnel in different wrist postures	B-mode ultrasound, cross-sectional area (CSA), flattening ratio	Compared CTS patients with healthy controls	Showed that the flattening ratio and nerves' CSA in CTS are increased by wrist flexion and extension; additionally, it was shown that ultrasound is posture-sensitive and could be helpful for dynamic CTS evaluations.
Hiltunen, 2005 [18]	Diffusion tensor imaging and tractography of distal peripheral nerves at 3 T	Peripheral nerves of the hand	Anatomical reconstruction	MRI at 3 T, DTI	Tractography analysis software for DTI	Compared DTI reconstructions with known anatomical pathways; feasibility validation only	Showed the accuracy of DTI at 3 T in tracing peripheral nerves in the hand and arm, unlocking the door for patient-specific computational models.
Takagi, 2009 [19]	Visualization of peripheral nerve degeneration and regeneration: Monitoring with diffusion tensor tractography	Peripheral nerves (sciatic and others; methodology transferable to hand nerves)	Anatomical reconstruction (DTI tractography of degeneration/regeneration)	DTI at 7 T; animal models of nerve injury and regeneration	DTI tractography analysis	Compared DTI tractography results with histological validation (axon/myelin integrity)	DTI may noninvasively track peripheral nerves' degeneration and regeneration; the study revealed the possibility for patient-specific computational modeling of disease progression.

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Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Heckel, 2015 [23]	Peripheral nerve diffusion tensor imaging: Assessment of axon and myelin sheath integrity	Peripheral nerves of the hand	Anatomical reconstruction (DTI-based microstructural assessment)	DTI at clinical field strengths	Quantitative DTI metrics (Fractional Anisotropy (FA), Mean Diffusivity (MD), Radial Diffusivity (RD), Axial Diffusivity (AD))	Compared DTI measures with histological validation and pathology markers	Showed that DTI can noninvasively quantify axon/myelin integrity; highlighted translational use in monitoring neuropathies and guiding computational conduction models.
Yoon and Lutz, 2024 [20]	Diffusion tensor imaging of peripheral nerves: Current status and new developments	Peripheral nerves (median, ulnar, sciatic, others; clinical applications)	Imaging-based anatomical reconstruction (DTI review)	DTI (clinical MRI applications)	Review of DTI techniques, tractography methods, and clinical integration	Compared across published studies; clinical feasibility emphasized	Pointed out the limitations (motion artifacts, resolution) and strengths (fascicular detail, noninvasive microstructural evaluation); mentioned recent innovations such as improved tractography and high-field MRI; described the clinical translation channels.
Maki, et al., 2024 [22]	Diffusion tensor imaging combined with the Dual Echo Steady State (DESS) protocol for the evaluation of the median nerve in the carpal tunnel: A preliminary study	Median nerve (carpal tunnel)	Anatomical reconstruction (DTI + MRI protocol)	DTI combined with DESS MRI	Hybrid MRI sequence (DTI + DESS)	Preliminary study comparing CTS vs. controls	Demonstrated that DTI + DESS enhances the carpal tunnel's median nerve microstructure's visibility and characterization; this shows promise for patient-specific modeling.

Table 2. Characteristics of studies of biomechanical FEM-based models.

Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Perevoshchikova et al., 2021 [67]	Finite element analysis of the performance of additively manufactured scaffolds for scapholunate ligament reconstruction	Wrist stability affecting the carpal tunnel region	Biomechanical FEM	CT and MRI imaging of wrist motion; experimental tensile and cyclic testing of printed scaffolds	Patient-specific 3D FEM with inverse finite element analysis (FEA) material parameter tuning	Mechanical testing data matched via inverse FEA; stress and strain distributions were quantified	Proximal attachment points produced lower stress; scaffold length had a stronger effect than placement; longer scaffolds eliminated peak stresses and enhanced homogeneity. An indicator of bone fracture risk aided in optimization.
Marqués et al., 2022 [68]	Biomechanical finite element method model of the proximal carpal row and experimental validation	Wrist mechanics via the scapholunate complex	Biomechanical FEM	CT-based Digital Imaging and Communications in Medicine (DICOM) imaging of wrist bones; cadaveric scapholunate ligament (SLIL) samples	Finite Elements for Biomechanics (FEBio) 2.0 for nonlinear FEM; 3D reconstruction models with bone, cartilage, the SLIL was represented	Experimental tensile testing of cadaveric SLILs to validate model-derived ligament stiffness values	Verified by an experiment that the distal carpal row (including the capitate bow) travels firmly with the proximal row; supports a biomechanical interpretation of the wrist's pathomechanics and surgical reconstruction.
Piao et al., 2016 [29]	Autologous nerve graft repair of different degrees of sciatic nerve defect: stress and displacement at the anastomosis in a three-dimensional finite element simulation model	Sciatic nerve (animal model; methodology transferable to human peripheral nerves)	Biomechanical FEM (nerve graft repair)	Literature-based geometry and material properties; graft lengths/defects simulated	3D FEM (stress and displacement analysis)	The model's predictions compared with biomechanical expectations; no direct clinical validation	It was discovered that longer flaws result in increased stress and displacement at the anastomosis site; softer grafts lessen the stress concentration when compared with stiffer alternatives; implications for graft selection in clinical repair.

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Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Walia et al., 2017 [6]	Subject-specific finite element analysis of the carpal tunnel cross-section to examine tunnel area changes in response to carpal arch loading	Median nerve (carpal tunnel)	Biomechanical FEM	MRI-based carpal tunnel geometries from human subjects	FEM of carpal arch with varied force vectors	Compared FEM's predictions with experimental measurements of tunnel area	Results support the possibility of noninvasive interventions for the relief of CTS. The ideal loading directions (≈138° volar–radial) were found to maximize tunnel growth.
Jordan and Li, 2022 [25]	Cross-sectional changes of the distal carpal tunnel with simulated carpal bone rotation	Median nerve (carpal tunnel)	Biomechanical modeling	Imaging + simulated bone kinematics	Simulated carpal bone rotation with morphometric analysis	Compared geometric changes across simulated rotational postures	Demonstrated how the rotation of the carpal bones dramatically changes the area and shape of the carpal tunnel's cross-section, affecting the space available for the median nerve; this is pertinent to the biomechanics of CTS.
Yu et al., 2023 [8]	A finite element analysis of the carpal arch with various locations of carpal tunnel release	Median nerve (carpal tunnel)	Biomechanical FEM	Anatomical data of carpal arch + surgical variations	FEA of the carpal arch under simulated release	Compared simulated release conditions with biomechanical expectations	It was determined that various release sites resulted in varying stress/strain distributions; this emphasized the best release techniques to lessen compression while maintaining stability.
Peng et al., 2023 [9]	The relationship between shear wave velocity in transverse carpal ligament and carpal tunnel pressure: A finite element analysis,	Median nerve via Transverse Carpal Ligament (TCL) (carpal tunnel)	Biomechanical FEM	Subject-specific MRI geometry of TCL and the carpal tunnel	FEM to simulate shear wave velocity in TCL	Parametric analysis across pressure (0–200 mmHg) and Young's modulus of TCL (1.1–11 MPa)	Shear wave velocity (8.0–22.6 m/s) was shown to be strongly dependent on ligament stiffness and pressure; suggested an empirical formula that allows for noninvasive pressure estimations by connecting shear wave velocity to pressure.

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Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Peshin et al., 2023 [7]	Finite element modeling of the fingers and wrist flexion/extension effect on median nerve compression	Median nerve (carpal tunnel)	Biomechanical FEM	Patient-specific MRI of the phalanges; hyperelastic tissue assumptions	FEA with hyperelastic soft tissues and elastic bone modeling	Compared stress values with known endoneurial pressures from the literature	It was determined that finger flexion results in the least amount of compression, while wrist flexion results in the most; tendon movement distributes pressure differently across the subsynovial connective tissue (SSCT), transverse ligament, and median nerve (the ligament absorbs the most during wrist motions, while the median nerve takes 30% during finger flexion).
Vasas, 2024 [12]	A finite element model for biomechanical characterization of ex vivo peripheral nerve damage and function	Peripheral nerves (ex vivo samples)	Biomechanical FEM	Experimental ex vivo nerve stretching data	FEM simulations linked with biomechanical properties	Validated against ex vivo functional and mechanical measurements	Demonstrated how changed conduction and function result from stretching-induced damage; FEM recorded mechanical thresholds of injury
Chang, 2015 [30]	Finite element modelling of hyper-viscoelasticity of peripheral nerve ultrastructures.	Peripheral nerve ultrastructures (general, applicable to hand nerves)	FEM (biomechanical)	Experimental data on nerve ultrastructures (epineurium, perineurium, and endoneurium)	FEM (nonlinear hyper-viscoelastic material modeling)	Compared FEM predictions with experimental mechanical testing data	Showed that hyper-viscoelastic models enhance the fidelity of FEM-based models of CTS and trauma and more accurately depict the peripheral nerves' mechanics than basic isotropic/hyperelastic assumptions.

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Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Oflaz and Gunal, 2019 [27]	Maximum loading of carpal bones during movements: a finite element study	Carpal bones/carpal tunnel mechanics	Biomechanical FEM	CT-based geometries of the distal radius, ulna, and metacarpals	FEM, 3D wrist model	Compared FEA results against the expected biomechanical behavior	It was shown that loading changes with movement: The trapezium bears the most stress in neutral position and during flexion, while the scaphoid bears the most load during radial deviation and extension. In most postures, the triquetrum and capitate ligaments experience the least amount of tension.
Wei et al., 2020 [28]	Subject-specific finite element modelling of the human hand complex: Muscle-driven simulations and experimental validation	Hand contact mechanics	Biomechanical FEM	CT/MRI-derived geometries (bones, ligaments, tendons, soft tissues); Electromyography (EMG) estimated muscle forces; hand kinematics derived from in vivo grasping	Abaqus-based 3D FEM	Compared predicted fingertip contact pressures and contact areas against same-subject in vivo experiments (≤20% relative error)	Created a human hand model that is subject-specific, anatomically correct, and completely validated; it showed high accuracy (contact pressures and areas within 20% of in vivo values). The significance of material characteristics and muscle loading was shown by sensitivity analysis; lays the foundation for investigations into hand manipulation and bionic hand design using biomechanical and neurophysiological methods.

Table 3. Characteristics of studies of electrophysiological models.

Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Sundar and Gonzalez-Cueto, 2006 [34]	Selective activation of small nerve fibers for assessing CTS	Median nerves' sensory fibers in CTS	Electrophysiological	Computational modeling	McNeal's model + Frankenhaeuser–Huxley equations (MATLAB simulation)	Simulated activation thresholds; validated with clinical CPT practice	Showed that small fibers (less than 2.5 µm) only activate at 5 Hz, even when they coactivate with larger fibers; Aβ fibers activate at 2000 Hz; and Aδ at 250 Hz (alongside Aβ).
Snarrenberg et al., 2018 [56]	Modelling nerve compression in CTS	Median nerve (carpal tunnel)	Electrophysiological compression model	MRI-derived nerve compression levels	Computational modeling of a myelinated axon under mechanical compression	Correlated modeled conduction delays with clinical compression inferred from MRI	Showed that even with mild compression, there are noticeable increases in conduction delay; this supports the use of conduction delay as a diagnostic marker for mild CTS.
Hodgkin and Huxley, 1952 [15]	A quantitative description of membrane current and its application to conduction and excitation in nerve	Peripheral nerves of the hand	Electrophysiological	Experimental voltage clamp data (squid giant axon)	Mathematical equations describing ionic currents (differential equations)	Experimental validation using in vitro voltage clamp recordings	Created the Hodgkin–Huxley equations for ionic currents, explained the kinetics of sodium/potassium channels, and provided the foundation for modeling peripheral nerves' conduction velocity and excitability.
Rattay, 1986 [16]	Analysis of models for external stimulation of axons	Peripheral nerves of the hand	Electrophysiological	Literature-derived biophysical parameters of axons	Mathematical cable-equation modeling; external field coupling	Compared with known electrophysiological responses to external fields	One of the earliest computational frameworks for predicting how extracellular electric fields stimulate axons; gave insights into thresholds, excitement, and safety in nerve stimulations.

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Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Carpio, 2005 [32]	Asymptotic construction of pulses in the Hodgkin–Huxley model for myelinated nerves,	Myelinated peripheral axons	Electrophysiological	Theoretical mathematics; Hodgkin–Huxley equations adapted to myelinated nerve dynamics	Asymptotic mathematical analysis; nonlinear partial differential equation approach	Compared the result with the known properties of myelinated conduction; theoretical validation only	Showed how to carefully generate traveling pulses in myelinated fibers and gave a mathematical foundation for simulating slowed or blocked conduction neuropathies.
Stephanova and Daskalova, 2008 [69]	Differences between the channels, currents and mechanisms of conduction slowing/block and accommodative processes in simulated cases of focal demyelinating neuropathies.	Peripheral myelinated axons	Electrophysiological	Literature-based biophysical parameters of ion channels and myelin	Computational simulations of axonal conduction under demyelination	Compared simulations with known physiological features of slowed/blocked conduction	The study found that sodium and potassium channels, as well as ion currents, play distinct roles in conduction failure vs. accommodation. It also identified a mechanism for demyelination-induced slowdown.
Mena and Bravo, 2023 [36]	Comparison of electrophysiological diagnostic methods for CTS	Median nerve	Electrophysiological diagnostic study	Nerve conduction parameters from clinical electroneurography (ENG)/NCS	Clinical electrophysiological testing and comparison of diagnostic methods	Conduction latency and diagnostic parameter comparison	Demonstrated that electrophysiological parameters such as conduction latency are effective indicators for assessing the severity and diagnosis of CTS

Table 4. Characteristics of studies of hybrid and other integrated models.

Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Peshin et al. 2023 [52]	A coupled electro-mechanical approach for early diagnostic of CTS	Median nerve (carpal tunnel)	Hybrid electro-mechanical model	Hand-based motion capture + FEM-derived strain data	Coupled FEM analysis (mechanical loading from hand movement) + Hodgkin–Huxley conduction model	Showed how median nerve conduction dramatically drops in hand flexion/extension scenarios that are modeled using hand kinematics.	The potential of combined biomechanical–electrical modeling to diagnose early CTS was underlined by the discovery that the type of tendon contact affects carpal tunnel pressure (differences up to 59.9% under flexion).
Ando and Loh, 2024 [50]	Convolutional neural network approaches in median nerve morphological assessment from ultrasound images	Median nerve	Deep learning (CNN segmentation of nerve morphology)	High-resolution ultrasound images from healthy individuals	U-Net and SegNet CNN models for semantic segmentation	Compared CNN estimates with manual annotations using Spearman's correlation and Bland–Altman analysis	U-Net had a higher IoU (0.717) than SegNet (0.625), and both systems had great agreement (~95%) with manual measurements, particularly in clear imaging conditions.
Cinelli et al., 2018 [51]	Electro-mechanical response of a 3D nerve bundle model to mechanical loads leading to axonal injury	Peripheral nerve bundle (generic, transferable to hand nerves)	Hybrid model (3D FEM biomechanics + electrophysiology)	Literature-based geometry and material properties; axon bundle structure	FEM (3D mechanical simulation) + electrophysiological conduction models	Compared with known thresholds of axonal injury and conduction failure	Proved the viability of complete electro-mechanical hybrid nerve models and showed that mechanical stress results in measurable electrophysiological degradation, connecting biomechanics to functional loss.

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Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Tekieh, 2016 [11]	Are deformed neurons electrophysiologically altered? A simulation study	Peripheral nerves of the hand	Hybrid model (mechanical deformation + electrophysiological conduction)	Literature-based material and biophysical parameters	Coupled FEM (deformation) with Hodgkin–Huxley electrophysiological model	Compared simulations with known features of slowed conduction under compression	Indicated that mechanical stress has a direct impact on electrophysiological function and that deformed neurons display changed excitability and conduction properties.
Cheever, 1995 [26]	A mathematical model of the pathophysiology of CTS	Median nerve/carpal tunnel	FEM/mathematical model	Literature-derived material properties, simplified wrist/ligament geometry	Early FEM/mathematical modeling (2D simplifications of the carpal tunnel)	No direct clinical or experimental validation; conceptual modeling	Showed that a biomechanical basis for CTS is supported by the increased mechanical stress on the median nerve caused by increased transverse carpal ligament stiffness and tunnel narrowing.
Nordlie et al., 2009 [70]	Towards reproducible descriptions of neuronal network models	General neuronal networks (not hand-specific)	Computational neuroscience methodology	Existing neuronal network models from literature	Proposed Python Neural Networks (PyNN) and standardized description languages for reproducible simulations	Demonstrated reproducibility through examples; methodological validation	Identified reproducibility issues in computational neuroscience; established standardized frameworks (e.g., PyNN) to allow consistent model description and comparisons; relevant for standardizing peripheral nerve modeling methodologies.
Chen et al., 2017 [53]	Interactions of Notch1 and TLR4 signaling pathways in DRG neurons of in vivo and in vitro models of diabetic neuropathy	Dorsal root ganglion (DRG) neurons (diabetic neuropathy model)	Experimental neurobiology	In vivo (rat diabetic models) + in vitro (DRG cultures)	Molecular/biological assays; electrophysiology (patch clamp, excitability tests)	Validated through molecular assays and electrophysiological recordings	It was shown that Notch1 and TLR4 interact to make DRG neurons more excitable and inflammatory; this reveals the mechanisms underlying diabetic neuropathy's conduction failure.

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Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Raspopovic, 2011 [55]	A computational model for the stimulation of rat sciatic nerve using a transverse intrafascicular multichannel electrode.	Sciatic nerve of rats (methodology transferable to human peripheral nerves)	Hybrid model (computational neurostimulation)	Histological/morphological data of the sciatic nerve of rats; electrode geometry	FEM + electrophysiological conduction model (transverse intrafascicular multichannel electrode (TIME))	Compared computational predictions with experimental stimulation data in animal models	Demonstrated that TIME electrodes may selectively activate different fascicles inside the nerve; provided computational support for electrode design in prosthetics.
Drakesmith et al., 2019 [35]	Estimating axon conduction velocity in vivo from microstructural MRI	White matter axons (CNS); methodology transferable to peripheral nerves	Hybrid model (MRI microstructure + conduction estimation)	In vivo microstructural MRI (axon diameter, density, g-ratio)	Mathematical modeling linking MRI microstructure to conduction velocity	Validated against known physiological conduction velocities in literature	Showed that conduction velocity may be noninvasively estimated using microstructural MRI; a proof of concept for integrating imaging and electrophysiology in human nerves
Dembek, 2020 [14]	PSA and VIM DBS efficiency in essential tremor depends on distance to the dentatorubrothalamic tract	Dentatorubrothalamic tract (DRTT, central tremor circuit)	Hybrid model (neuroimaging tractography + Deep Brain Stimulation (DBS) stimulation modeling)	Patient-specific MRI + tractography	Computational electric field modeling combined with tract distance mapping	Validated against clinical tremor outcomes in patients	Greater tremor control was predicted by closer stimulation proximity to the DRTT, highlighting the significance of tractography-informed DBS targeting.

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Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Tigra et al., 2020 [33]	Selective neural electrical stimulation restores hand and forearm movements in individuals with complete tetraplegia	Peripheral nerves innervating hand and forearm	Neurostimulation (clinical application of computational electrode optimization)	Patient-specific neuroanatomy; implanted neural electrodes	Selective multichannel peripheral nerve electrical stimulation	Clinical trial in human subjects with complete Spinal Cord Injury (SCI)	Significant progress has been made in neuroprosthetics and rehabilitation by demonstrating that functional hand and forearm movements are made possible by selective stimulation of the peripheral nerves.
Shao et al., 2020 [37]	Compression of dynamic tactile information in the human hand	Whole-hand tactile mechanics	Data-driven encoding model	Mechanical waves recorded via 30 accelerometers during 4600 hand–object interactions (13 gestures)	Convolutional non-negative matrix factorization (NMF) to extract patterns with a spatiotemporal basis	Classification accuracy (>95%) using basis activations; similarity between mechanical data encoding and simulated neural spiking data	Identified a concise lexicon of spatiotemporal vibration patterns that best express touch. These patterns reflect digit individuation and wave propagation speeds (~1–10 m/s). Similar patterns were observed in simulated tactile afferent spiking data, indicating biomechanical support for sensory encoding efficiency.

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Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Alp et al., 2020 [38]	The effect of hamatum curvature angle on carpal tunnel volumetry: A mathematical simulation model	Median nerve	Mathematical simulation model	CT-based measurements (the hamate bone's curvature angle, tunnel angle, tunnel inlet/outlet areas, tunnel length)	Mathematical model treating the carpal tunnel as a truncated cone, with calculations using principles like the cosine theorem	Correlational analysis between measured angles and calculated tunnel volumes in 91 subjects	Showed a substantial association between the carpal tunnel volume and the angle of hamate bone's curvature, indicating that the curvature angle may be an anatomical risk factor for idiopathic CTS.
Coste et al., 2022 [39]	Activating effective functional hand movements in individuals with complete tetraplegia through neural stimulation	Median and radial nerves in tetraplegia	Hybrid translational model	Multicontact epineural cuff electrodes; nerve fascicle anatomy	Modeling-guided electrode configuration + intuitive interface (leap motion and EMG) control	Two volunteers participated in a 28-day in vivo clinical investigation; kinematics and force assessments confirmed stable grips and functional tasks (holding things, drinking)	Showed that functional hand actions (grasp, release, and grip) may be precisely and steadily elicited over weeks with selective stimulation using two multicontact cuff electrodes; translational practicality was shown by the user-friendly interface and low current thresholds.
Elseddik et al., 2023 [40]	Predicting CTS diagnosis and prognosis based on machine learning techniques	Median nerve (CTS)	ML	Clinical data: NCS, symptom questionnaires, ultrasound-guided hydrodissection	ML classifiers: Support vector machine (SVM), random forest (RF), decision tree, multilayer perceptron	Metrics on test data: Accuracy, precision, recall for diagnosis and prognostic stages	Excellent performance. Diagnosis: Accuracy, ~95.5%; recall, ~91.9%; precision, ~96.3%. Prognosis: Over time, accuracy increased: 3 months (90.1%), 6 months (91.2%), and 1 month (87.7%)

Table 5. Characteristics of studies of AI-based models hand nerves.

Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Shinohara et al., 2022 [41]	Using deep learning for ultrasound images to diagnose CTS with high accuracy	Median nerve (carpal tunnel)	Deep learning (CNN-based classification)	B-mode ultrasound images	CNN (custom CNN architecture)	Compared AI predictions with clinical CTS diagnosis; accuracy, sensitivity, and specificity metrics	Achieved high diagnostic accuracy (>90%), demonstrating that CNN-based ultrasound analysis can reliably support CTS diagnoses.
Faeghi et al., 2021 [42]	Accurate automated diagnosis of CTS using radiomics features with ultrasound images	Median nerve	Radiomics + ML	Ultrasound images with handcrafted radiomics features	Feature extraction + ML classifiers (SVM, RF)	Compared AI outputs with expert radiologists' assessments	AI-based radiomics achieved diagnostic performance similar to that of experienced radiologists, supporting clinical applicability.
Park et al., 2021 [43]	Machine learning-based approach for disease severity classification of CTS	Median nerve	ML (severity classification)	Ultrasound-derived features + clinical parameters	RF, SVM, decision tree classifiers	Cross-validation with severity labels derived from NCS	Successfully classified CTS severity levels, highlighting ML's utility beyond binary diagnosis.
Peng et al., 2024 [44]	One-stop automated diagnostic system for CTS in ultrasound images using deep learning	Median nerve	End-to-end deep learning system	Ultrasound images	CNN-based automated detection, segmentation, and classification pipeline	Internal validation using labeled clinical datasets	Demonstrated a fully automated CTS diagnosis pipeline, reducing operator dependency and diagnostic time.
Mohammadi et al., 2023 [45]	Deep radiomics features of median nerves for automated diagnosis of CTS: a multi-center study	Median nerve	Deep radiomics + ML	Multicenter ultrasound datasets	Deep feature extraction + ML classifiers	Multicenter cross-validation	Showed robust generalizability across centers, addressing dataset variability limitations in AI-based CTS diagnosis.

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Author(s), year	Title	Nerve(s) studied	Model type	Input data type	Software/method	Validation method	Key outcomes
Mekki et al., 2025 [46]	Applications of artificial intelligence in ultrasound imaging for CTS diagnosis: a scoping review	Median nerve	Review of AI methodologies	Published AI-based ultrasound studies	Systematic scoping review framework	PRISMA-based screening and qualitative synthesis	Identified strengths, limitations, and clinical gaps in AI-based CTS diagnosis, emphasizing the need for hybrid AI–physics models.
Shi et al., 2025 [47]	Multimodal deep learning for grading CTS: A multicenter study	Median nerve	Multimodal deep learning	Ultrasound images + clinical data	Multimodal CNN architectures	Multicenter validation with grading accuracy metrics	Demonstrated improved CTS grading performance using combined imaging and clinical inputs.
Sim et al., 2025 [48]	Diagnosis of CTS using deep learning with comparative guidance	Median nerve	Deep learning with guided comparison	Ultrasound images	CNN with a comparative reference framework	Compared against standard deep learning baselines	Improved diagnostic robustness by incorporating comparative guidance, reducing false positives.
Wang et al., 2023 [49]	Deep learning algorithms for automatic sonographic localization and segmentation of the median nerve: A systematic review and meta-analysis	Median nerve	Deep learning (segmentation)	Ultrasound images from multiple studies	CNN-based segmentation models (e.g., U-Net variants)	Meta-analysis of Dice score, IoU, sensitivity	Confirmed the high accuracy of AI-based median nerve segmentation, supporting downstream modeling and diagnostic tasks.

Use of AI tools declaration

The authors of this manuscript used AI (ChatGPT and Grammarly) exclusively for language editing and enhancing the readability of the manuscript. The authors are fully responsible for the scientific content, interpretation of the data, and the conclusion(s) of this manuscript.

Acknowledgments

The authors gratefully acknowledge the financial support provided by Salim Habib University, Karachi, Pakistan, which fully funded this research project. The resources, facilities, and academic environment offered by the university were instrumental in completing this work.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

Gul Munir (conceptualization, literature synthesis, manuscript preparation, and the primary author), Muhammad Zeeshan Ul Haque (supervision and research resources), Muhammad Fahad Shamim (proofreading, supervision), Muhammad Wasim Munir (review and editing), Tooba Khan (review and editing).

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