ORIGINAL ARTICLE

# Knee Joint Modeling Based on Muscle Interactions Using a Central Pattern Generator to Predict Disease Progression and Rehabilitation Techniques in Incomplete Spinal Cord Injury

**Monireh Maleki, Fereidoun Nowshiravan Rahatabad *, Majid Pouladian**

*Department of Biomedical Engineering, Science and Research Branch, Islamic Azad University, Tehran, Iran*

*Corresponding Author: Fereidoun Nowshiravan Rahatabad
Email: nooshiravan@gmail.com

Received: 09 February 2022/ Accepted: 04 June 2022

## Abstract

**Purpose:** Purpose: Musculoskeletal systems have a complex nature, and it is very difficult to control issues in these systems due to various characteristics such as speed and accuracy. Thus, investigating these musculoskeletal systems requires simple and analyzable methods. Also, due to sudden changes during the movement process, the speed and accuracy of the calculations should be proportional to the operating speed of the system. Predicting the system norms and fulfilling them for the system are the next challenges for relevant studies.

**Materials and Methods:** Accordingly, this study aimed to investigate the knee joint function, the joint condition in an incomplete Spinal Cord Injury (SCI), as well as its rehabilitation conditions by designing a simple mathematical model. This model was designed based on the interactions between Hamstring Muscles (HAM) and the vasti muscle group. Considering changes in the Central Pattern Generator (CPG) as a variable input, we analyzed the model output in fixed point, periodic and chaotic modes.

**Results:** The results of the present study showed that the knee joint model output was a chaotic and fixed point for the healthy and incomplete SCI modes, respectively. Increasing the values of afferents was enhanced in the central pattern generating model to rehabilitate the model. According to the modeling results, by applying coefficients of 1.98, 2.21, and 3.1 to the values of afferents Ia, II and Ib, the incomplete spinal injury model changed permanently from the fixed point to the periodic position, indicating movement with rehabilitation in the knee joint.

**Conclusion:** Based on the results obtained from the knee joint mathematical model in comparison with the reference articles in relation to the expected results, it can be stated that this model has an acceptable output while being simple in calculations and has the ability to predict different norms. It can also be hoped that improved and more detailed results will be achieved in the study of musculoskeletal systems with the development of this model.

**Keywords:** Knee Joint; Central Pattern Generator; Spinal Cord Injury; Rehabilitation; Hamstring Muscles; Vasti Muscle Group.


DOI: https://doi.org/10.18502/fbt.v10i2.12225

## 1. Introduction

Dynamic models are the best tools for explaining the real world. As a simple definition, if a system mode changes over time, it is dynamic [1]. Considering the results of studies in biological and neurological fields of science, some qualitative dynamic neuronal models have been proposed to be closer to neuromuscular activity and its physiological conditions [2]. An excitable tissue consisting of a large number of neurons is a good example of a complex dynamic system [3]. Any tissue that can have electrical activity can be considered as an excitable tissue such as the leg muscles, heart, and brain tissue. The high ability of the brain to process information using meaningful interactions between sensory neurons, motor neurons, and neurons [4] through electrical connections has made it an excellent organizing station. This processing is carried out by transferring information between neurons under the law of dynamics. Indeed, an electrical signal with specific information leads to mechanical muscle contraction [5]. Thus, overall, the musculoskeletal system is a dynamic system with significant complexities.

An interesting characteristic of complex systems is the fact that they can display their organized behaviors without a central organizing unit [6]. This is possible mainly considering the ability to display dynamic group behaviors. Thus, many studies on complex systems apply some useful concepts such as concurrency [7], cooperation and synergy developments [6], nonlinear dynamics, chaotic behavior [7], self-organization [6], self-adaption, and so on. As such, when modeling such systems, understanding the relevant concepts and using appropriate tools as well as methods close to the optimal behavior of the natural system is very necessary [8]. Accordingly, to achieve a better understanding of the concepts and approach the behavior of the body's natural system, Central Pattern Generator (CPG) was used to model the knee joint in the present study.

Researchers have proven the existence of a central generator in the spinal cord. This generator is a group of neurons that performs temporal and spatial alignment before subsequent movements [9]. This generator can be activated without environmental feedback. Researchers believe that many motor patterns such as walking have been programmed in the CPG [9]. On the other hand, they have seen evidence that an Spinal Cord Injury (SCI) animal can move during experiments. Meanwhile, various studies have shown that there are control centers in the spinal cord that create motor patterns for walking [9, 10]. Thus, these centers, known as CPGs, form an important part of the musculoskeletal system models [9, 10]. CPGs can produce rhythmic movements [11, 12]. Previous researches have shown it is possible to re-establish motor activity after removal of stimulation from the upper part of the spinal cord by motor training alone [13-16]. There have also been many studies on motor training and pharmacotherapy [13-16]. Nevertheless, one of the important issues, which is still considered, is the possibility of closed-loop CPG control with stimulation of afferents, which plays an important role in maintaining balance during walking [17].

The main motor pattern is generated by the CPG itself with its changes made by brain commands and sensory feedback. Sensory information is applied in the form of feedback. In other words, predictions are not made based on them, but decisions are made based on past experiences. The role of afferent feedback in CPG control is such that the output of CPG sensory feedback adapts to the real world. On the other hand, specific sensory inputs can have a significant effect on CPG rhythm, as they can choose, ignore or eliminate some rhythm patterns. Thus, they act like a switch and can select a specific pattern or adjust their operating range [18].

Many diseases, such as SCI, can be interpreted by changes in CPG input and output. In general, SCI can be a disabling event that often leads to a severe loss of motor function. In some cases, this condition can be improved with proper clinical care. However, the same training regimen has been applied to all patients in clinical practice so far, regardless of the underlying neurological cause of their pathology, which is not an optimal approach as not all injuries result in the same nerve damage. The overall recovery of SCI patients can be greatly improved by identifying the underlying neurological cause of a particular pathological condition, and using an appropriate treatment system. Nonetheless, it first requires us to gain a deeper understanding of spinal-neural mechanisms involved in movements and the ways in which damage to these mechanisms leads to pathological conditions [19].

An important issue is the potential role of afferent feedback in improving motor function after SCI. Incomplete SCI results in the loss of proper inputs from the upper part of the incision surface as well as supraspinal inputs (cortex) to the CPG, which are expected to interrupt normal CPG operation and thus stop the production of motor fluctuations. In the meantime, many studies have shown that motor function can be improved alone or in combination with afferent stimulation or drug therapy [18-20]. It is generally accepted that post-SCI recovery of motor function occurs using motor training, at least in part, due to the increased power of the various inputs to the CPG, which re-operates despite the loss of supraspinal stimulus [20]. However, there have been few theoretical studies on the possibility of re-performing this type of activity and creating a motor pattern by afferent feedback after the removal of the supraspinal stimulus [20].

According to previous research [19], a mathematical model for the knee joint based on chaotic behaviors of complex body systems has been designed in this study. Changes in the model output, which are fixed-point, periodic, and chaotic, will occur based on sensitivity to initial conditions. The type of output according to the input conditions in the model will express the movement conditions in the joint. Indeed, it is assumed that this model is designed for a person with incomplete paralysis and the same amount of damage throughout the body. Our variable input, which is the output results of CPG model motoneurons, plays a crucial role in achieving the overall goals of this study.

## 2. Materials and Methods

### 2.1. Knee Joint and Muscles

In order to investigate the knee joint model in humans, the interaction of two main muscles in this joint was first studied. As shown in Figure 1, the function of the knee joint is based on the contractions of the two muscle groups, which are the Hamstring Muscles (HAM) and the Vasti muscle group (VAS or Vasti Group). Indeed, according to contractions and operating conditions of these two muscles, the knee joint model was investigated in healthy and SCI states.

### 2.2. Central Pattern Generator (CPG)

Our variable input is the output results of CPG model motoneurons of the knee joint. In fact, changes from a healthy to SCI states and vice versa are achieved with the help of changes in knee joint CPG. For this purpose, the CPG model was designed for the joint using MATLAB software according to Ref. [20]. To change from a healthy to incomplete SCI state, the supra spinal drive (d) input

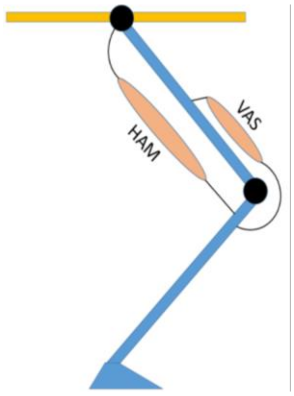


**Figure 1.** Knee joint along Hamstring Muscles (HAM) and VAS muscles

to the CPG model is converted to $\frac{d}{3}$ [20-22]. The model used here for CPG has been the Two Level Half-Center (TLHC) type and includes a set of neurons, interneurons, and motor neurons (Figure 2). This set is responsible for controlling the muscles that perform flexion-extension movements. Inhibitory couplings that reach opposing neurons through interneurons produce their function. In other words, when the inhibitory interneuron of one side is active, the corresponding inhibitory interneuron prevents the other side from being polarized. Neuron modeling was carried out using the Hodgkin-Huxley model where the neuron membrane is considered as a capacitor through which various electrical currents pass. These currents include ionic, synaptic currents, leakage currents, feedback, and brain signals. Interneurons were also simulated as unit

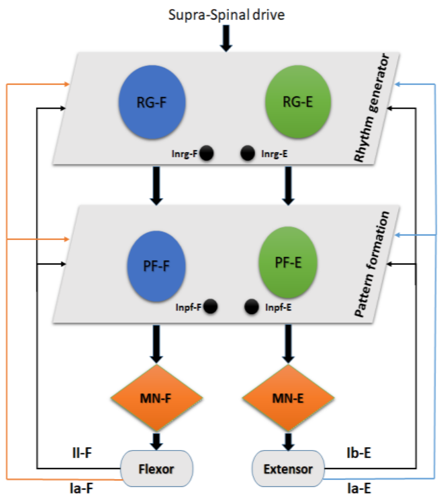


**Figure 2.** Central Pattern Generator (CPG) architecture including a set of Rhythm Generator (RG), Pattern Formation (PF), Motorneuron (MN), and Interneurons (In) as well as Ia, Ib, and II afferents

models and motoneurons were composed of two parts, namely soma and dendrites.

The assumed two-level organization, CPG, allows separate control of motor rhythm at the Rhythm Generator (RG) level and pattern of motor neuron activity at the Pattern Formation (PF) level. Thus, a sensory signal or sudden disturbance may affect CPG function at the RG level, that is, it changes the motor rhythm, such as changing phase or readjusting the rhythm, or acting at the PF level, that is, it changes pattern of motor neuron activity without readjusting rhythm or changing phase.

Overall, our central hypothesis is that CPG activity has two functional levels: a semi-central RG and an intermediate PF network that distributes and coordinates the activities of several motor populations under RG control. To keep responses close to the body's physiology, a movement begins in the model with stimulation of the supra-spinal drive (MLR or Mesencephalic Locomotor Region), which is distributed among excitatory neural populations of the CPG networks (RG and PF). In total, RG consists of two populations of excitatory neurons with pacemaker properties depending on sodium currents as well as reciprocal inter- and intra-excitatory synaptic connections. Reciprocal inhibition of RG-E as well as RG-F inter- and intra-populations is mediated by opener and flexor inhibitor populations (Inrg-E and Inrg-F, respectively). In the absence of sensory input, the alternative half-activities of the populations in RG-E and RG-F define the motor cycle in the extensor and flexor phases, respectively. The activity of these populations is controlled by MLR stimulator, sodium current-dependent threshold activation, inter RG-E and RG-F reciprocal synaptic stimulation, and reciprocal inhibition by Inrg-E and Inrg-F populations. The PF network forms the second level of CPG. According to our theoretical concept, this network should include several PF populations controlled by RG, and provide phase-dependent activation of the respective groups of motor neurons of the same sex, including populations that activate the muscles. However, in the scaled-down version of the model considered here, the PF network consists of only two neural populations, namely, PF-E and PF-F. These populations receive the supra-spinal drive stimulator from the MLR, a weak stimulus input from the RG-like population, strong inhibition from the RG-opposite population through the corresponding inhibitory population (Inrg-E or Inrg-F), and reciprocal-inhibition from the opposite PF population through another inhibitory population (Inpf-F or Inpf-E). The intermittent activity of the RG population leads to the intermittent activity of the PF-E and PF-F populations. PF populations transmit intermittent rhythmic stimulation to extensor (Mn-E) and flexor (Mn-F) plus inhibitory opener (Ia-E) and flexor (Ia-F) motor neurons. These Ia populations constitute the third level of reciprocal inhibition in the system. In this model, they provide rhythmic inhibition of the motorneuron population during the inactive phase of the phase cycle. During a normal movement, Ia neurons also mediate the reaction. The PF network consists of only two populations (extensor and flexor) that inhibit each other. The activity of each PF population closely follows the activity of the corresponding RG population, as well as the activities of Ia inhibitory neurons, motor neurons, and cells related to the activity of the respective PF population (extensor or flexor). In particular, the separation of the RG and PF networks allows independent control of rhythm generation at the RG level and patterns of motor activity at the PF level. This two-level CPG structure could explain the ability of afferent stimulation to control rhythm generation without altering the level of motor activity. Each of the flexor and extensor outputs of the CPG model is considered a variable input to a muscle in the knee joint model. The model validation was performed by comparing the output results of the designed model motonurons with the results of the reference article (Table 1) [23-26].

**Table 1.** Variables of mathematical knee joint muscles model

| Variable | Definition |
|---|---|
| $\alpha_V$ | Effect of VAS muscle relative to Hamstring Muscles (HAM) on knee joint movement |
| $\alpha_{HA}$ | Effect of HAM muscle relative to VAS muscle on knee joint movement |
| $M_V$ | Fitness of health characteristics of VAS muscle length and mass |
| $M_{HA}$ | Fitness of health characteristics of the length and mass of the HAM muscle |
| $x_V$ | Motoneuron Central Pattern Generator (CPG) output of the knee joint for the VAS muscle |
| $x_{HA}$ | Motoneuron CPG output of the knee joint for HAM muscle |

### 2.3. Knee Joint Model

In order to design the knee joint model according to the main formula of the reference paper, we studied the mathematical model of the inter-muscle interactions with the realization of the movement goal. Indeed, this model is designed according to Layla & Majnun's mathematical model [27].

Layla & Majnun's model has symbolically used the behavior of two people in a complex relationship mathematically to be able to show the result of a complex relationship between two people based on the inherent and environmental conditions of these two people as well as the effect of these conditions on the opposite person in a simple model. Now, these two cases in the equation can be two humans or two biological organs of the body such as neurons or muscles that interact with each other to pursue a specific purpose. As seen in citations of Layla & Majnun's model, we tried to use this model based on chaotic behavior based on proportional inputs to examine one of the complex dynamic systems that can be investigated with this type of behavior.

This model has two main inputs. As mentioned in the previous section, the CPG flexor and extensor outputs were used as variable inputs. Fixed input was also selected based on muscle health. That is, if the intrinsic characteristics of the muscles, i.e. length and mass, are normal, the value of this input will be considered equal to 1. Accordingly, in case of changes in these features or, for example, the incidence of diseases such as muscle atrophy, this number decreases between 0 and 1 due to the ratio of changes in features. Since the muscles were assumed to be inherently healthy in the present study, our constant input was always considered equal to 1 during the simulation. Now, according to the inputs, the mathematical model for the knee joint inter-muscle interactions was designed as follows:

$$\frac{d\alpha_{HA}}{dt} = M_{HA} + {\alpha_V}^2 + x_{HA}\alpha_{HA} \tag{1}$$

$$\frac{d\alpha_{V}}{dt} = M_{V} + {\alpha_{HA}}^2 + x_{V}\alpha_{V} \tag{2}$$

According to the outputs of the mathematical model in each stage, which is in the form of three types of chaotic, fixed point, and periodic, the condition of the patient, healthy person and person undergoing treatment is studied. Also, the way the model result changes from one mode to another between the healthy person and the patient is investigated by changing the initial conditions and examining the CPG output. In this way, the conditions of disease progression and treatment are analyzed and predicted. The last simulation stage in the model is to select the appropriate coefficients to stimulate the Ia, II and Ib afferents in order to change the response of the mathematical model from fixed point to chaotic mode. Indeed, after investigating the output of the mathematical model based on a change in coefficients of afferent stimulation, we investigate how the mathematical model of the knee joint changes from a patient to a healthy person. Since we have designed only a knee joint model in the present study, the rehabilitation process is investigated only from this perspective. Indeed, the goal of the last stage is to return the patient's knee joint to a state where we can return the knee model output to the correct movement in the knee joint.

## 3. Results

In the first step, the knee joint CPG was modeled for a healthy state. Then, the output appropriateness of motoneuron knee joint CPG for VAS and HAM muscles as variable input was included in the main model. The simulation results of Equations 1 and 2 are displayed in Figure 3. In this case, and according to the parameters, eigenvalues, and initial values, the system has shown a chaotic behavior.

In the second step, the knee joint CPG was simulated in the case of incomplete SCI, and as in the previous step,

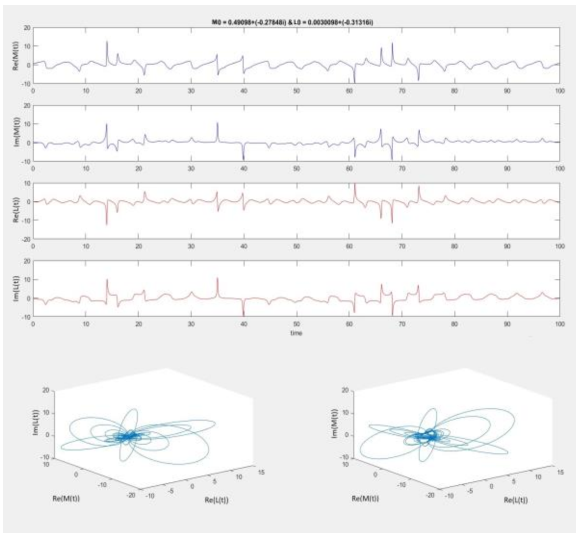

**Figure 3.** Results of simulation of interactions muscles of the knee joint in the healthy state for 100-time units

the CPG output of the motoneuron for both VAS and HAM muscles was used as a variable input in the main model. As depicted in Figure 4, the interactions between muscles, according to Equations 1 and 2, after a short time the system has shown a fixed point behavior.

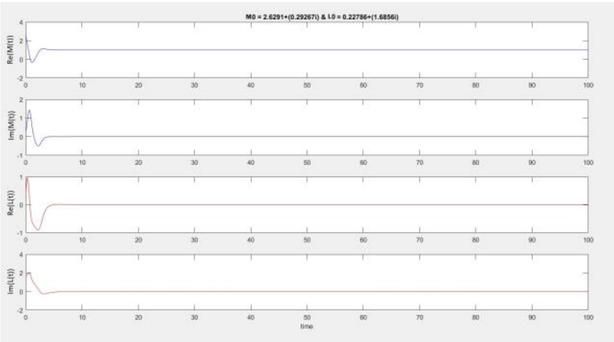

**Figure 4.** Simulation results of interactions between muscles of the knee joint in incomplete Spinal Cord Injury (SCI) for 100-time units

According to the knee joint model designed for incomplete SCI, after selecting the appropriate coefficients to stimulate the Ia, II and Ib afferents of the CPG incomplete SCI model in the last step and after examining the changes in the response of the mathematical model, the way the model returns from incomplete SCI state to a healthy state was assessed. Accordingly, after selecting the minimum change in afferent coefficients of 0.01, an attempt was made to change the mathematical model from the fixed-point response mode. Finally, after altering the stimulation coefficients and applying the coefficients of 1.98, 2.21, and 3.1 for the Ia, II and Ib afferents, the incomplete SCI model was permanently changed from the fixed-point mode to the periodic mode. These simulations were also performed in all fixed-point, periodic and chaotic modes for 1000-time units and as expected, all model responses were stable in this time unit. Also, the output results of CPG model motoneurons were compared with the results of reference articles for validation purposes, which were completely consistent.

Based on what was shown in the results of the above steps, as the value of d signal decreased from the normal state, the knee joint model also went from a healthy state to an incomplete spinal complication, and the output of the knee joint model reached a stable state at the fixed point from the point where the drive value reached d/3 [20-22]. As indicated in Figure 5, there is an area between the fixed-point state and the chaotic state where the model output is periodic, indicating a decline in a person's ability to perform normal movements. Thus, according to the results shown in Figure 6, when the model is at the beginning of the spinal complication state, the output of the knee joint model reaches a periodic state from the fixed-point state in order to rehabilitate by applying afferent coefficients, which indicates the effect of stimulation on the knee joint model and movement with rehabilitation.

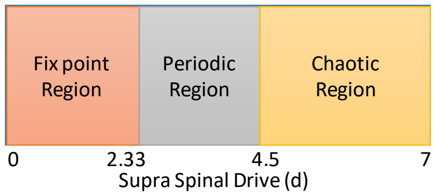


**Figure 5.** Knee joint model response areas based on the value of the Supra Spinal Drive input to the CPG model

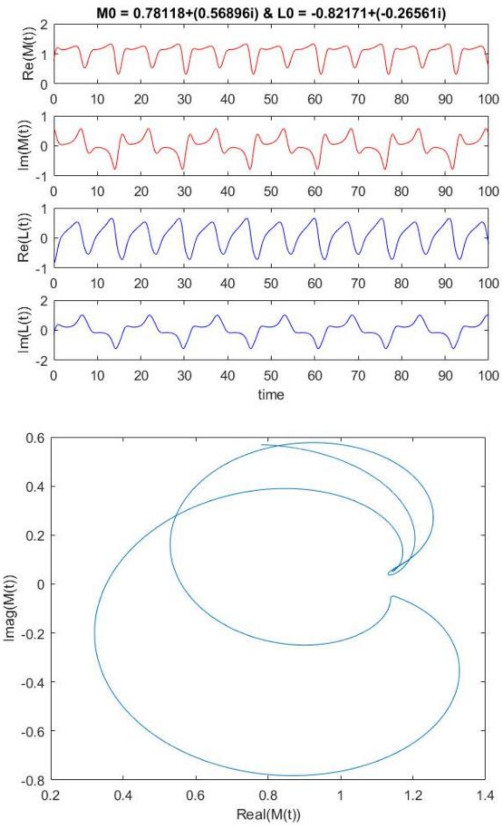


**Figure 6.** Simulation results of interactions between muscles of the knee joint in the nerve stimulation mode of the incomplete Spinal Cord Injury (SCI) model for 100-time units

## 4. Discussion

The complex and different nature of the musculoskeletal system as well as the wide variety of motor characteristics have led to the idea that the motor control strategies for these devices are vague and very complex which differ from each other. According to previous studies, muscle activity may be generated through the linear combination of small sets of basal pulses generated by CPGs (Muscle synergies hypothesis). This control design is simple and is used in different models of body movement systems at different speeds. The correct performance of different models is very important in creating movement and changing speed. Thus, it can be stated that different models of foot motor components are dynamically challenging. As such, investigating this system from a functional point of view by the central model generator can give us a new perspective on the disease incidence, as well as control and rehabilitation. Accordingly, the interactions of the two main muscles of knee joint were first investigated in the knee joint model. Afterward, taking into account the interactions in the model, the disease incidence and rehabilitation were examined.

The system displays a chaotic response to the knee muscles' interactions in the healthy state (Figure 3). Some very complex chaotic behaviors in the world may seem coincidental, but in fact, they arise from determinism [28]. Determinism means that changes in the system mode are determined by a specific rule [29]. Especially in biological systems, turbulent chaos must play a major role. For example, it is confirmed that chaotic heart rates or brain signals keep the heart and brain healthy, respectively [30, 31]. The present study showed that healthy muscle interactions eventually led to healthy interactions in the knee joint, in which case the chaotic response of the system indicates the realization of the goal of knee movement and movement in humans (Figure 3). In more understandable terms, the system modeled for a healthy individual in this study shows a chaotic response. As the simulation time increased, it became clear that this system response was permanent.

In the next step, the system was investigated for incomplete SCI. In incomplete SCI, the patient becomes severely disabled in terms of motor function, and thus, as expected from the model, the muscle interactions did not respond well and the system reached a fixed point (Figure 4). Hence, in general, muscle interactions in the knee joint did not achieve the goal of the movement. Indeed, the model provides stable results in the case of incomplete SCI, and after the transition time, the dynamics reach a fixed point and remain there forever; according to the parameters and initial conditions, these fixed points can show no movement.

The last step in the present study is related to the rehabilitation of the knee joint with the help of afferent stimulation in an SCI patient using the CPG model. Overall, SCI can be a disabling event. Nevertheless, this condition can be improved with proper clinical care and new treatments in some cases. An important issue in SCI treatment is the potential role of afferent feedback in improving post-SCI motor function. Thus, we tried to stimulate the Ia, II and Ib afferents in the CPG model of the injured person to enhance the output of this model to such an extent that when this variable enters the mathematical model, the model no longer shows the fixed-point response. As depicted in Figure 6, the system first exhibits a periodic response after leaving the incomplete SCI state, which was considered to mean walking rehabilitation in the present study. Indeed, in this case, the model managed to move periodically and permanently by stimulating the afferents, and until the afferent stimulation was applied in the CPG model, the model response remained periodic.

According to previous studies [20-22], if the normal value of drive is applied to the CPG model, the output of motion models should show stable movements in a healthy state. Also, with a decrease in the value of drive and a decline in muscle activity, motor imbalance occurs over time; eventually, the motion model stops by reducing a certain value of drive and becomes paralyzed, which in this study, as expected, the output of the knee joint model in incomplete paralysis state was observed as a fixed point. Thus, as shown in Figure 5, based on the results obtained from the outputs of the knee joint model in this study, the trend of motor instability based on the change in drive value in the CPG model was similar to the reference articles, indicating the reasonable results of our proposed model. Also, according to the studies [20, 21], in order to rehabilitate the motor model at the beginning of an incomplete paralysis state, we expected that we could bring the knee joint model from a fixed point to periodic point by increasing the number of afferent nerves (especially Ib) in the central pattern generating model; according to the results, this was achieved by applying coefficients of 1.98, 2.21, and 3.1 to the values of afferents Ia, II and Ib. Indeed, the continuity of movement was created steadily with the gradual increase in the value of afferents, where regular and repetitive patterns in the movement of the knee joint showed the success of the designed model in restoring the ability to walk to the person. In general, according to the specific performance trend of the designed model, despite the structural differences compared to previous models, it can be stated that the proximity of simulation results with reference articles in terms of the function indicates the reasonable results of modeling in a healthy state and incomplete paralysis state as well as the present results' validity for predicting the effect of rehabilitation methods on the patient.

The main innovation of the proposed model in this study has been the design of a mathematical model for the knee joint, which, accordingly, reduces the complexity of previous models that were mostly mechanically designed. This is because we studied the knee joint movement conditions in healthy and sick individuals according to three types of fixed point, periodic, and chaotic outputs, instead of using modeling of real elements such as muscles, joints, and bones in the output of the schematic model. Thus, using this model, we can predict how the disease would progress in the patient with a greater speed and fewer calculations, and examine the patient's condition. Also, the number of stimuli required to rehabilitate the patient can be easily calculated using the afferent nerve feedback pathway in the designed model. Further, as a future perspective of this study, it can be stated that by generalizing this modeling method, it is possible to design more models in the field of motor systems by considering the relationship between different muscles and joints, such as modeling human walking or hand movement. However, as with all studies conducted in the field of musculoskeletal systems, there have been limitations in the design of this model. One of the main limitations in designing this model is the lack of considering the weight and dimensional characteristics of the muscles. For this reason, it is not possible to study muscle atrophy and changes in their anatomy during the course of the disease, and we assumed inherent muscle health of a fixed input for the proposed model. Also, in order to control the model more easily and make it more understandable, we had to ignore the effect of the twin muscles that affect the knee joint and considered only two main groups of agonist and antagonist muscles in the knee joint movement. Also, due to the non-mechanical model of the knee joint, it was not possible to apply the effect of ground gravity on the movement of the model.

## 5. Conclusion

Attempts were made in the present study to reduce the complexity of previous models by designing a very simple mathematical model for knee joint movement based on chaotic properties and interactions between muscles in the musculoskeletal system. The strengths of the designed model include simplicity of calculations, an increase in speed in reviewing the results as well as achieving acceptable results. Accordingly, it can be stated that the model is simple, meaningful, and able to show different types of behaviors even by changing only one control parameter. Also, this common CPG model helped us make predictions about the disease occurrence as well as rehabilitation. Thus, it was shown that the individual model has a chaotic response in the healthy state and a fixed-point response in the disease state. The results also revealed that it is possible to help improve motor function in the patient's model after the afferent stimulation in the CPG model.

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