

S. Lee Hong

Too often overlooked, normal motor function is one of the most critical components of the human existence. The ability to move rests at the core of quality of life, due to the freedom that independent mobility offers. Despite its central role in everyday life, motor function is sometimes viewed as independent from and subsidiary to cognitive function (see [1]). As a result, there has been relatively less attention paid to the deficits in motor function that arise due to disease. However, a growing body of evidence points to movement disorders as being a central issue in a variety of neurological diseases and disorders, even ones that were considered as exclusively “mental” disorders in the past. In this chapter, we will explore a systems approach to motor dysfunction. The chapter is laid out in the following way. First, the chapter will briefly review the ubiquity of similar patterns of behaviour in physics and biology as an overarching framework. The ubiquity of findings across a wide range of complex systems forms the central theme of this chapter. I will also highlight similarities across findings in a broad range of areas of study that are often considered to be disparate fields of science.

Based on a complex systems approach, similar to that presented in West [2], the discussion of

disease and disorder will be centred on the loss of fractal complexity, and different underlying mechanisms for these changes in behavioural and physiological dynamics will be explored. This section will highlight evidence that many similarities across diseases exist, if examined through the lens of complex dynamics. In human movement, however, the task and environment have been shown to directly impact the dynamics of the motor behaviour. In the study of movement disorders and motor dysfunction, the task and environment are not often entered into the equation during the development of clinical interventions. Thus, I will present the “*uncertainty conservation hypothesis*” as a potential framework that encompasses task, organism, and environment, as the potential basis for future development of therapeutic interventions in movement disorders. Continuing the central theme of similarity and ubiquity, I hope to provide ideas that are still in their infancy that could extend towards other areas such as cognition and physiology.

---

## 26.1 Uniqueness and Ubiquity: Scaling Laws in Physics, Biology, and Beyond

Over the past few decades, there has been a growth in the use of dynamical systems theory in the study of motor control. Fundamentally, dynamical systems theory is based on general systems theoretic approaches to science, where

---

S.L. Hong (✉)  
Ohio University, Irvine Hall 246, 1 Ohio University,  
Athens, OH 45701, USA  
e-mail: hongsl@ohio.edu

systems can be classified based on inferences made from their dynamics (see [3]). As a result, a sizeable portion of the literature on complex dynamical systems focuses on similar patterns of behaviour in a variety of naturally occurring systems. What Bak [4] sought to demonstrate was that a broad range of natural systems exhibit scaled behaviour (refer also to Chap. 1.10, [5]). Without going into too much detail, the concept of a critical system, one resting on a knife's edge, was unstable, yet in balance at the same time. Bak [4] demonstrated this phenomenon in a wide range of data sets, from the occurrence of earthquakes through cotton prices, showing that a single scaling law could be used to describe their patterns of occurrence and variability. This scaling law related the occurrence with magnitude of change. In the now seminal demonstration of the earthquakes, the number of occurrences scaled as power law relationship with the magnitude of the earthquake. Here, the occurrence of earthquakes can be scaled as a function of the Richter scale, which is scaled on base of 10 (i.e. a Richter value of 2 is 10 times greater magnitude than a 1; 3 is a 100 times greater than 1, and so on). Essentially, the occurrence is a direct function of its magnitude.

### 26.1.1 Scaling Laws and Criticality in Motor Patterns

The motor patterns of healthy young individuals, much like the systems reviewed by Bak [4], have also been found to exhibit similar scaling properties. Often termed  $1/f$  dynamics, these patterns reflect a scaling of signal amplitude to frequency. This relationship can be characterized by the power law equation:

$$A = f^\beta \quad (26.1)$$

where  $A$  is the amplitude and  $f$  is the frequency with the scaling exponent,  $\beta$ . The unique pattern is one where the exponent is  $-1$ , or  $1/f$ . Thus, the amplitude of the fluctuations is scaled as a direct function of the frequency on which it occurs. As the frequency is increased, there is a relative

**Table 26.1** Presented here is a list of various studies that have demonstrated the common pattern of  $1/f$  dynamics in different areas of human movement

Study	Motor behaviour
Hausdorff et al. [8]	Walking
Jordan et al. [9]	Running
Hong et al. [10]	Sitting posture
Duarte and Zatsiorsky [11]	Standing posture
Blesic et al. [12]	Tremor
Aks et al. [13]	Eye movements
Nakamura et al. [14]	Physical activity

decrease in amplitude, but, on a single scale. This dynamic pattern has been observed across various domains of human motor function.  $1/f$  patterns have been found in human cognition [6, 7] and in a variety of human motor behaviours. Table 26.1 provides examples of common findings of  $1/f$  dynamics and scaling laws in the human movement literature.

The source and biological mechanisms that give rise to the  $1/f$  patterns that have been detected will likely remain an issue of scientific debate. That being said, it does not diminish or negate the findings of similar dynamics across multiple systems. In fact, as we will see in the following section, the patterns of change to physiological and behavioural dynamics as the result of disease and disorder also share many commonalities.

### 26.2 Ubiquity of Motor Dysfunction in Disease and Disorder

Interestingly, much like the ubiquity of scaling laws in motor output, movement disorders are just as prevalent, occurring even in disorders that are primarily considered to be cognitive in nature. Motor dysfunction has been observed in a variety of developmental disorders, such as 22q11 Deletion Syndrome (e.g. [15]), AD/HD (e.g. [16]), Down syndrome (e.g. [17]), and autism (e.g. [18]). Degenerative disorders such as Huntington's (e.g. [19]), Parkinson's (e.g. [20]), and Alzheimer's (e.g. [21]) also present a variety of symptoms of motor dysfunction. Movement disorders have also now been detected in psychopathologies such as schizophrenia [22, 23] and

bipolar disorder [24, 25]. Whether motor dysfunction is a core symptom or due to side effects of medications, the fact that movement disorders consistently presents itself in so many diseases and disorders warrants further attention. Interestingly, common across many of these movement disorders is a change in the dynamics of the motor output. In the following sections, I will review the common direction of change and the proposed underlying mechanisms.

### 26.2.1 The Loss of Complexity Hypothesis

Conventionally, homeostasis is viewed as the healthy physiological state. Hence, the closer a physiological process is to the mean, the more stable the system. A similar view has long been held in the study of motor behaviour, as lower magnitude or amount of variability had always been considered to be indicative of a healthier system with less “neural noise.” At a conceptual level, a less variable system is often equated with lower levels of random brain activity, i.e. a system with less neural noise [26, 27]. This approach places its emphasis on magnitude of variability, and based on assumptions of a normal distribution and independent, random samples does not account for sequences that are present in the data.

A new approach that has developed over the past two decades was the concept of a “*loss of complexity*” in disease and disorder. Lipsitz and Goldberger [28] introduced this new approach to the study of cardiovascular physiology. Originally, fluctuations in physiological data had often been considered as noise that needed to be eliminated in order to allow the “true” signal to be obtained, through filtering or averaging across trials and subjects. The key finding that provided initial support for the loss of complexity hypothesis was a demonstration that the heartbeat patterns of young and old could be distinguished through dynamic analyses. Effectively, Lipsitz and Goldberger [28] were able to demonstrate that although two individuals (one young and one old) could possess similar heartbeat means and standard deviations, their dynamics were

characteristically different. By using Approximate Entropy [29], they were able to demonstrate that the young person’s heartbeat fluctuated much more irregularly and unpredictably than that of the old.

Over the past two decades, empirical studies have continued to uncover evidence of a loss of complexity in many different diseases and disorders. Much like the ubiquity of the scaling laws, a variety of studies have observed declines in complexity in a variety of different physiological outputs and motor dysfunction. As a result, beyond the seminal example of the loss of complexity in heart rate [28], there are now demonstrations of decreased complexity in behavioural, physiological, and psychological dynamics across a range of disorders.

#### 26.2.1.1 Loss of Complexity in Movement Disorders

As with the widely documented  $1/f$  dynamics in human motor behaviour, declines in complexity have also been widely recorded in the movement domain as a result of disease and disorder. Since the loss of complexity hypothesis was first supported in aging, a majority of the literature in movement declines has focused on seniors and the elderly. Across a wide range of different motor functions, a decrease in the complexity of the motor output of the elderly has been observed. To name a few, aging has been shown to result in a loss of complexity in motor behaviour, such as force production tasks [30], postural sway [31], and finger tremor [32]. Interestingly, there are other conditions where this effect is also apparent. One example is Down syndrome, where the postural sway dynamics during sitting are much less complex than that of the age- and body size-matched controls. In fact, the sway dynamics of the Down syndrome subjects were, in fact, more similar to the rhythmic body rocking dynamics of the controls [33]. Lower complexity in motor output has also been observed in people with bipolar disorder [24], although, whether this is a core feature of the disorder or is a side effect of the medications (or both) will require further examination. A detailed description of loss of motor output complexity has been provided by

Newell et al. [34] and Vaillancourt and Newell [35]. In addition, the loss of complexity has been widely observed across a variety of different domains that extend from movement patterns to physiological output.<sup>1</sup>

### 26.2.2 Proposed Sources and Mechanisms Underlying the Loss of Complexity

There are, however, a variety of different viewpoints regarding the mechanisms that cause a decline in the complexity of physiological output. When the loss of complexity hypothesis was initially proposed, a view that healthy physiological systems could be characterized using fractals was presented. As such, the branching of anatomical structures such as alveoli, nerve fibres, and blood vessels, for example, could be represented as a self-similar repeating pattern that is invariant across measurement scales. With aging, it is often the anatomical structures at the smallest scales that are lost to time. Lipsitz and Goldberger [28] highlighted this phenomenon through images of nervous tissue, that the smallest nerve endings are lost while larger nerves are preserved. The analogue of degeneration at the smallest spatial scales, when translated to time, is that fluctuations at higher frequencies will be the first to be eliminated during the aging process. As a result, one would predict that higher frequency or shorter timescale fluctuations will be absent or diminished as a result of a given disease. While the loss of complexity hypothesis has been widely supported (see [38] for a review), the source of these age-related declines remains in question. The following subsections present some of the theorized sources of the loss of complexity.

#### 26.2.2.1 System Isolation and Decoupling

One of the early conceptualizations of the underlying source of the loss of complexity was the idea that with aging or disease, the many physiological systems become isolated from one

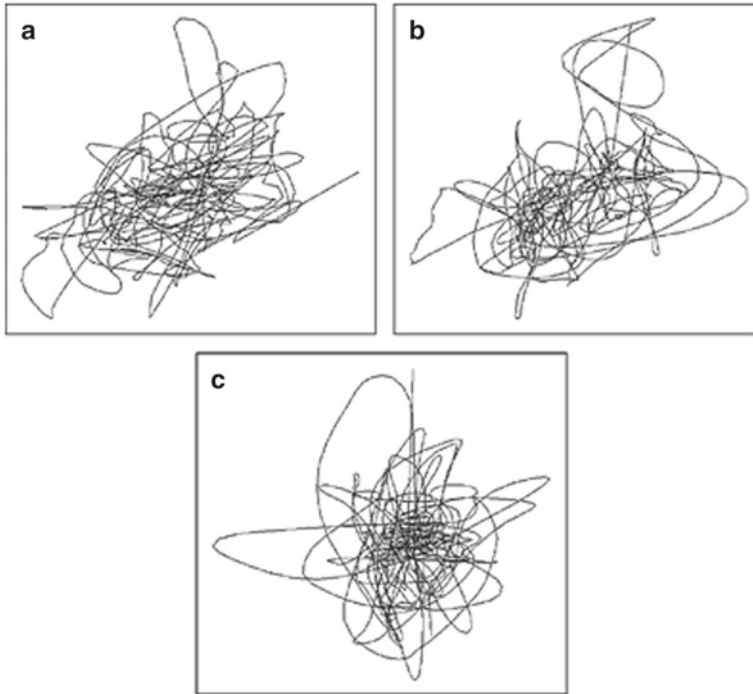
another [39]. In such a situation, the connections between subsystems or inputs that generate the complex physiological output are diminished, resulting in a signal that evolves on fewer timescales [40]. What results is a system that is less adaptive to change in the environment and more susceptible to perturbations. Based on the isolation approach, a loss of system components or diminished coupling will result in a physiological output that is less complex. However, as Assisi et al. [41] demonstrated, a reduction in coupling strength between system components is not the only reason for a loss of complexity. When the components within a system are too tightly coupled, the complexity of its output will also be diminished.

This phenomenon/mechanism is exemplified in the motor behaviour of children that is generally less complex than that of adults [42, 43]. From this perspective, one would view that the infant reflects a system with tightly coupled components, and that the developmental processes result in a gradual differentiation of the components within the overall system. Assuming that this process continues throughout the lifespan, complexity would peak during early adulthood, where there is an optimal level of coupling [42]. An example of these changing motor dynamics as a function of development can be seen in Fig. 26.1, where postural sway traces of children and an adult are provided. At a certain point, this optimum is exceeded, with observable declines in complexity as the components of the system steadily isolate as a result of the aging process.

#### 26.2.2.2 Loss of Adaptability

It is generally common to equate disease with decline or a lack or loss due to a “malfunctioning” component of the entire system, that is, the organism as a whole. Yet, there is evidence that a loss of fractal complexity in motor and other physiological output does not necessarily reflect functional decline(s) that arise as a result of the diseased states [35]. In particular, there are situations where a more complex output is observed in

<sup>1</sup>For a broader overview, see Chap. 11.

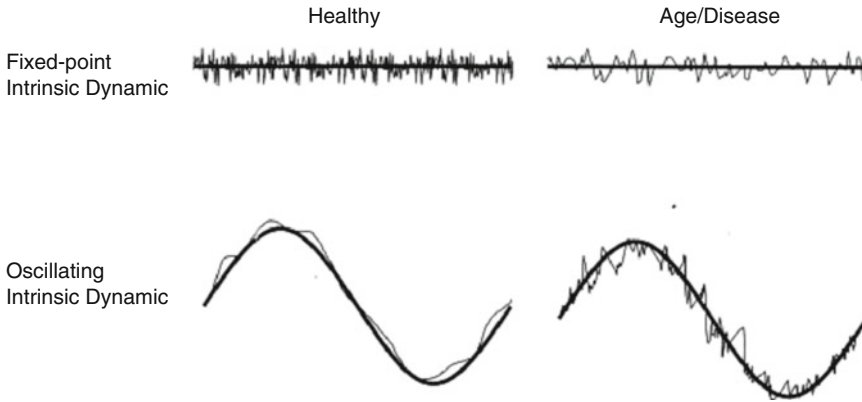


**Fig. 26.1** Postural sway profiles from children aged 6 (panel a) and 10 (panel b) years and an adult over the age of 18 years (panel c). Of note is how the sway pattern in the children seems to move along a diagonal, showing a

strong coupling between side-to-side and fore-aft motion. The adult exhibits clearly distinct forward and rearward movements that are quite independent from the sideways motion. From [10]

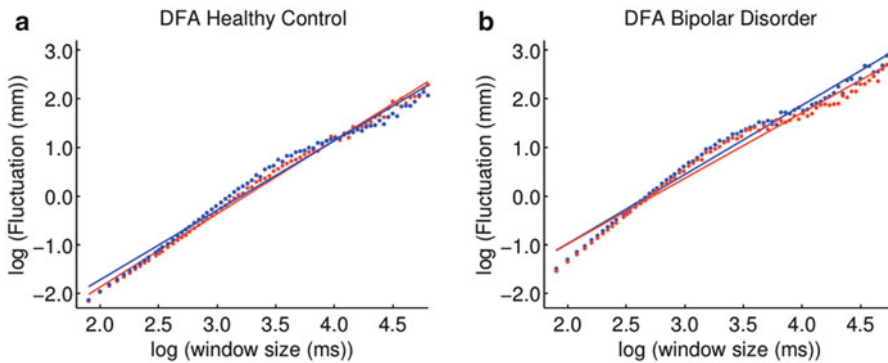
diseased subjects in comparison to the controls. In their review, Vaillancourt and Newell [35] presented a variety of examples of increased complexity in the motor behaviour of patients with Huntington's disease and schizophrenia. More importantly, they proposed that the demands of the motor task also had an important role to play in the dynamics of the observed motor output. When the task demands were to maintain a constant force level with a finger, Parkinson's disease (PD) patients generate a predictable more rhythmic pattern [44]. This "less complex" pattern results in increased error (i.e. distance from the target line) and is distinct from the irregularly pattern of force production of the controls that allows them to remain close to the target line. On the other hand, when required to produce a sine wave, the output of the PD patient instead becomes more complex than that of a healthy control. Here, the PD patient is now unable to generate the smooth force output that allows them

to accurately trace the sine-wave target (see Fig. 26.2). Effectively, the output of the PD patients was "more complex" and irregular than that of the controls. The interesting but seemingly paradoxical finding is that the "simple" task of maintaining a constant force level requires the PD patient to generate a complex motor output. On the other hand, the higher dimensional task of the sine wave requires that the subject be able to damp out the fluctuations in muscle force that unfolds along the shortest timescales. Even though the complexity of the force output for PD patients, as measured by Approximate Entropy, moves in opposite directions than that of the controls, both situations are, however, consistent with a loss of fractal complexity. In the case of the constant force, the PD patient has increased (though unwanted) contributions of slow timescale patterns, while during the sine-wave condition, the PD patient exhibits undesired short timescale fluctuations in muscle force. In both



**Fig. 26.2** Schematic illustration of the role of the “intrinsic” task dynamics on the complexity of motor output. When asked to maintain a steady-state force, the healthy subjects are more able to remain close to the target by generating a complex signal that evolves on many times-

cales. The old/diseased individual generates a slower, more predictable pattern to approximate the steady-state. However, when required to produce a sine-wave force output, the old/diseased individual generates a jagged, irregular signal. From [35]



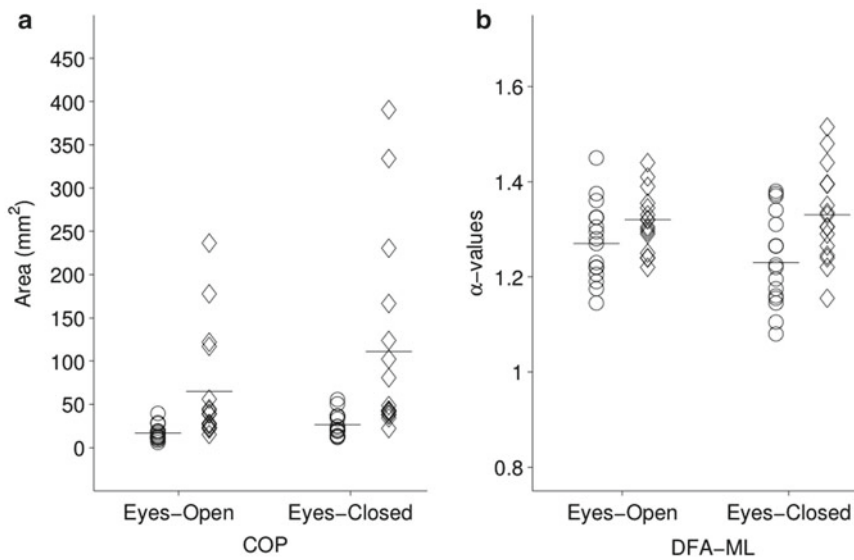
**Fig. 26.3** This plot shows the group differences between bipolar subjects (*diamonds*) and controls (*circles*). Each data point represents a single subject. The *left panel* shows the differences in sway area, that is, the space of the ground covered by the sway movements. Group differences are clearly observable in both conditions. On the

*right panel*, the differences in Detrended Fluctuation Analysis (DFA) values can be observed. During the eyes open condition, there is no significant difference between groups. However, this difference becomes significant when the eyes are closed. From [24]

cases, performance on the task is poor and the desired force pattern cannot be produced.

Effectively, the healthy system is not just able to generate a more complex output, but, it is able to greatly restrict its output when required by the task demands. There is further evidence to support the idea that different levels of adaptability are apparent when patients with disease or disorder are tested across a range of tasks rather than a single condition. A reduced ability to adapt to different tasks has been demonstrated in the aging literature [30, 32, 45] and in people with Down syndrome [33].

Interestingly, this phenomenon also arises in movement disorders associated with psychopathology [24]. In a recent study, we examined the postural sway of individuals with bipolar disorder and age-, height-, and weight-matched controls under four different task conditions: (1) eyes open-feet apart; (2) eyes closed-feet apart; (3) eyes open-feet together; and (4) eyes closed-feet together. We found that patients with bipolar disorder had poorer postural control in general as the patients swayed over a larger area than the controls (Fig. 26.3). The bipolar patients also



**Fig. 26.4** Exemplar plot of the DFA of the mediolateral (side-to-side) postural sway from a single bipolar and control subject, respectively. The lines reflect a log-log relationship between fluctuation magnitude and the times-

cale (window size) on which it occurred. The eyes open condition is represented with a *blue line*, while the eyes closed conditions is represented with a *red line*. From [24]

increased their sway when asked to close their eyes. When detrended fluctuation analysis (DFA, [46]) was used to measure the complexity of the sway dynamics, we found that the main difference between the groups was during the conditions with their eyes closed (Figs. 26.3 and 26.4) on the mediolateral direction of motion (i.e. side-to-side). This is where the loss of complexity became apparent in their sway dynamics, indicative of a reduced ability to adapt to the deprivation of visual information. Yet, the effects of a change in stance did not yield any effects, suggesting that the loss of adaptability might not necessarily be a universal phenomenon in disease and disorder, but specific to certain aspects of the system.

Overall, the loss of adaptability approach hypothesises that the disordered individual is less capable of altering his or her motor behaviour to adapt to different task demands. Here, the loss of complexity is not necessarily a representation of a decline in physical function, but, rather, the inability to alter the dynamics of the behaviour to respond to task demands is the better marker. A synthesis of the complex systems approach to movement disorders converges on the idea that

more or less complexity in motor output alone cannot be used as an indicator of disease or disorder. But, the underlying mechanism that gives rise to the observed loss of fractal complexity due to aging and disease remain a matter of scientific debate. Potentially, both a loss of adaptability and the decoupling of subsystems may account for the empirical phenomenon of changes in complexity in motor output. These aberrant patterns of behaviour are reflected in a shift away from fractal dynamics, where the magnitude of fluctuations in the motor system is no longer in direct proportion to the timescale on which they occur. Yet, these putative mechanisms do not provide clear paths towards novel clinical approaches to intervening or remitting changes in complexity in motor output, physiology, or psychology that arise due to disease or disorder.

### 26.2.3 Uncertainty Conservation in Human Motor Control

Simply stating that complexity can increase, decrease, or stay the same depending on the task demands is an unsatisfying answer to a complex

problem. In order to address this issue, an explanation of how motor patterns adapt to different task demands and under different levels of available information from the environment is needed. Originally, the concept of task–organism–environment relationships stemmed from Newell [47], who proposed that human movement is not the product of the person alone, but is instead a reflection of the “confluence of constraints” at the level of the task, organism, and environment. In this sense, any goal-directed action is a product of a larger system that encompasses task demands and the information that the environment provides.

The goal of Newell [47] was to begin to address the “degrees of freedom” problem presented by Bernstein [48]. Simply, the number of controllable components, i.e. degrees of freedom, of the neuromotor system is extremely high, with the added complexity of having myriad ways to organize those degrees of freedom to generate a single movement. Not only does the motor system have an inordinate number of independently controllable components, it also has the added problem of redundancy. One example of redundancy is that a variety of different configurations of muscle and body movements allow the same goal to be achieved. Take for instance, the scenario of reaching out to grasp an object. Both underhand (palm up) and overhand (palm down) grasps would suffice, and thus, multiple arm configurations have the same capacity to achieve the same goal. At the same time, more than a single goal can be achieved by the same movement, like touching my nose or scratching it.

As with the dynamical systems concepts of human motor control (cf. [49, 50]) it became apparent that there were inherent constraints at the level of the organism. Beyond the tendons, ligaments, and muscles themselves, human motor control was also substantially restricted by coordination patterns that served to reduce the number of independent degrees of freedom that needed to be controlled. In this sense, the motor system has a tendency to naturally favour certain patterns of movement over others and even has difficulty learning some movements. For one, the natural tendency of movements is to “tune into

resonance,” that is, moving at speeds that reflect the natural mechanical properties of the limbs, prescribed by its mass and length (cf. [49]). Effectively, the motor system “self-selects” the movement patterns based on the mechanics of a pendulum in order to obtain maximal return in elastic energy from the musculature. Such a natural tendency to optimize behaviour for the purpose of achieving mechanical resonance has been proposed to be an explanation for the self-selection of comfortable walking speeds based on limb length [51]. It has been demonstrated that walking at the resonance speed results in the lowest energy consumption costs, while increasing or decreasing the walking pace away from this preferred speed increases energy consumption [51].

The natural tendency to self-determine movement speed is not the only inherent constraint on motor behaviour. Our motor system also has the tendency to favour some movement patterns and synchronized rhythms above others. For example, the seminal work of Haken et al. [52] demonstrated that human movement has two stable coordination modes of in-phase and anti-phase patterns. The former is a situation where both limbs extending and flexing at the same time, while the latter is akin to gait, with one limb extended while the other is flexed. Haken et al. [52] found that the “default” coordination mode of the human motor system is an in-phase pattern, as movements initiated in anti-phase transitioned to an in-phase pattern when the movement was sped up sufficiently. Transitions in the opposite direction, however, did not occur. As a result, learning other coordination patterns in between in-phase and anti-phase has been shown to be difficult (cf. [53, 54]). In sum, these studies provide evidence of constraints upon coordination and movement within the organism itself.

However, the key issue that Newell [47] highlighted is that not all of the constraints on motor behaviour lie at the level of the organism, and not all redundancies are created equally. Depending on the context in which the behaviour is being performed affects the number of ways in which it can be achieved. If we return to the task of reaching and grasping an object in front of us, it becomes immediately apparent that the ensuing



action is constrained in various ways. At the level of the task, the distance required for the reach plays an integral role. If the object is close, I would have a greater number of options to grasp the object. This is due to the fact that varied combinations of movements at my shoulder, elbow, and/or wrist would suffice to allow me to make contact with the object. However, if the object is far away, the number of movement options at my disposal would be reduced. To cover the distance and reach the object I would have to lean forward and use my shoulder and elbow to the fullest to make contact with my target object.

Similar constraints would arise depending on the shape of the object or the environment in which the reaching and grasping action was being performed. If the object were either small or fragile, I would be able to only engage a few digits, perhaps restricted to the pinch grip of my thumb and index finger. A large or heavy object would require that I employ a whole hand grasp, and perhaps even both hands. Similarly, if the object were placed on a cluttered surface or if I had to perform this movement in a dark room, I would be prevented from using a variety of different movements to achieve the goal. Such restrictions would be necessary to avoid obstacles or inadvertently knocking over another object. Once again, the movement patterns available to me are reduced by the constraints outside that of those of the body itself.

What had not yet been provided in 1986 was a hypothesis regarding the directionality of the effects of a constraint at one level on another. Originally, the process of movement production was approached from the perspective of open systems or dissipative structures (cf. [55]). While an appropriate description of the organism alone, the open systems approach to human motor control resulted in an open-ended view of the role of task and environmental constraints upon motor production. As a result, the prevailing view was that somehow, the confluence of task, organismic, and environmental constraints interacted to generate a given movement [47]. But how they interacted remained in question.

This is because the constraint-based approach did not provide clear hypotheses as to what were

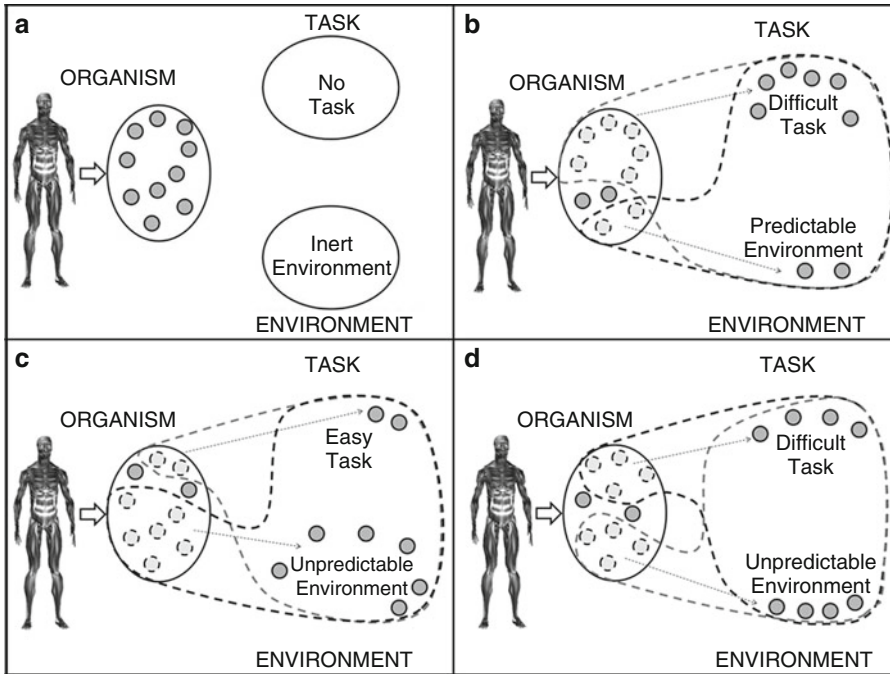
(1) the units of constraint and (2) the direction of change as the constraints at one level or another were increased or decreased. The next step was to develop a conceptual framework that allowed the task, environment, and organism to be captured as a single system. To achieve this, we had to return to the most fundamental issue in the control of human movement, which is the “degrees of freedom problem,” first presented by Bernstein [48].

With this central problem in mind, we envisioned the task–organism–environment system as sharing a single pool of degrees of freedom. Conserved, as in a zero-sum game, the task and environment shape the ultimate behaviour by “taking away” or “borrowing” degrees of freedom from the organism. As with the common concept of constraints, the task and environment reduce the number of available degrees of freedom at the level of the organism. What this framework provided was a testable hypothesis regarding how the uncertainty in the motor output should change as a function of the task and environment. Here, as the uncertainty in either task and/or environment increase, the uncertainty in the behaviour of the organism should decrease, where the total amount of uncertainty within the task–organism–environment system is held at constant (see Fig. 26.5).

Next, a common unit that provides a measure of the degrees of freedom within the system and the constraints placed upon them was necessary [56, 57]. To achieve this, I returned to a concept central to the loss of complexity hypothesis, *entropy*. While entropy is often viewed as a measure of uncertainty or information or unpredictability, it also has other descriptions in thermodynamics. Boltzmann’s original demonstration was a mathematical proof that the number of spatial configurations within a molecular structure can be represented as entropy where:

$$S = k \log W = -k \log p \quad (26.2)$$

Here, the entropy,  $S$  is equal to the number of ways,  $W$ , that the atoms can be configured. Assuming a flat or equal distribution (i.e. maximum entropy) one can then relate this to the



**Fig. 26.5** A schematic illustration of the process of entropy conservation and compensation across task, organism, and environment as the (re-)distribution of degrees of freedom. The following conditions are represented: (a) a “resting” state where no goal-directed move-

ment is being performed; (b) high task entropy with low environmental entropy; (c) low task entropy with high environmental entropy; and (d) high task and environmental entropy. From [57]

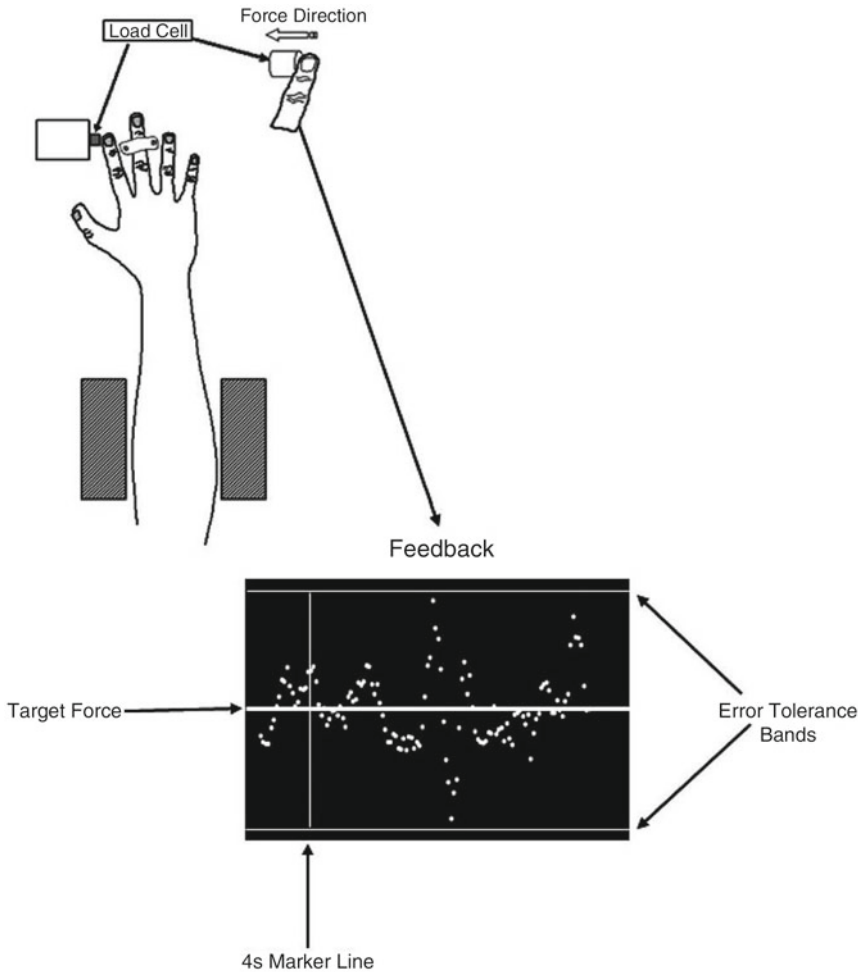
likelihood of finding an atom in a given place, as measured by the probability  $p$ . The Boltzmann constant, is represented as  $k$ . In a similar vein, constraints link the individual degrees of freedom and reduce the number of spatial configurations, thus resulting in lower entropy (see [58] for a more in depth explanation). Now, based on this, both the directions of change can be predicted using a measurable unit that accounts for the changes in variability in the behaviour.

### 26.2.3.1 Empirical Evidence

To test the uncertainty conservation hypothesis, we employed a series of simple experiments involving isometric force control [59, 60]. The particular benefit of this experimental protocol is that isometric force is virtually impossible to maintain without visual feedback, as the force level produced degrades within less than half a second [61]. As a result, the subject is almost completely dependent on information from the

environment. In this experiment the force level to be generated at a given time unit was presented as a dot on a computer screen. The task was simple: maintain the force produced by the finger as close to a target line as possible. We manipulated the difficulty of the task by narrowing or enlarging the error tolerance bounds around the target. The amount of information provided by the environment to the subject was manipulated by changing the amount of time that passed between each presentation of the dot on the screen. This experimental protocol was conducted under two conditions: (1) single finger (Fig. 26.6); and (2) two fingers coordinating to produce a total force (Fig. 26.7). In the second condition, only the total force of the two fingers was provided to the subject through visual feedback.

Across both experiments, we observed that the entropy in the force output declined as (1) the amount of information in the environment was reduced; and (2) the task difficulty increased by



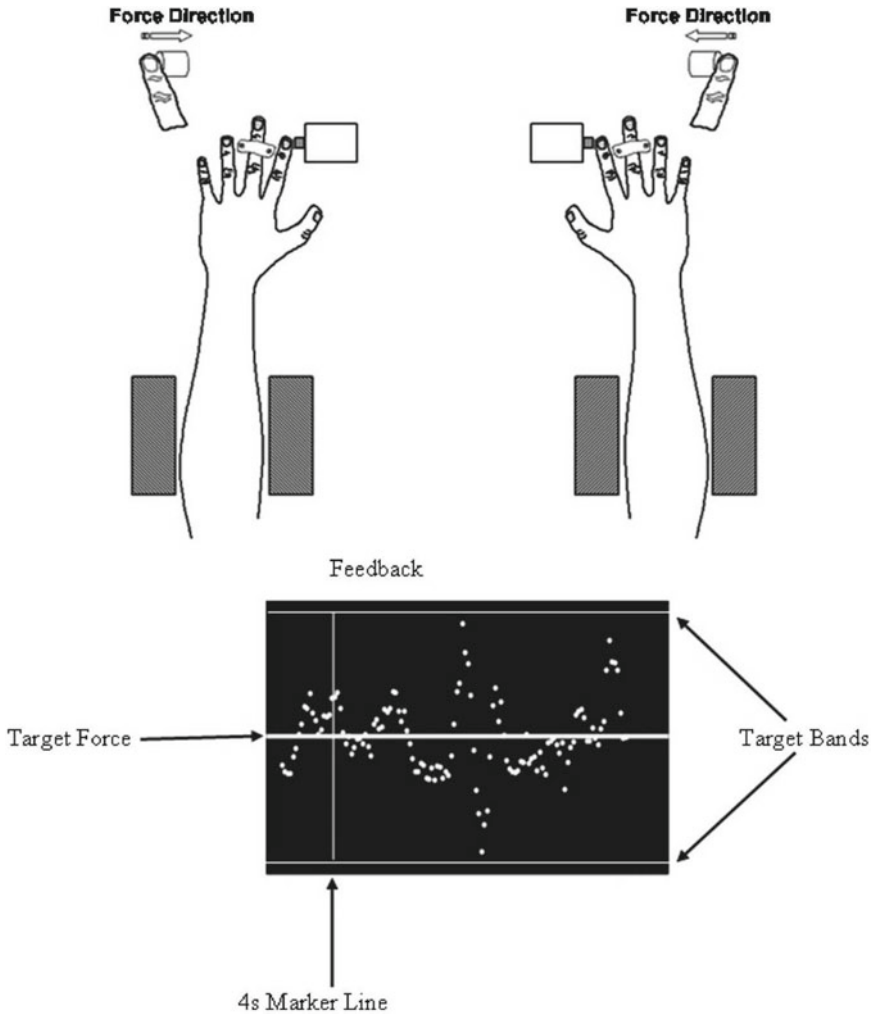
**Fig. 26.6** Illustration of the experimental setup for the single finger isometric force production experiment. From [60]. Note, the *4s marker line* denotes the “grace period”

that allowed the subject to approximate the target force. These data were not included in the analysis

reducing the relative size of the error bands. Interestingly, the effects of changing the task and environment conditions were found to be compensatory, where the effects of a difficult task in conjunction with an information-rich environment were the same as an easy task being performed in a low-information environment. The relationship between task, organism, and environment could be captured with a quadratic surface (see Figs. 26.8 and 26.9). Across both studies the findings were consistent when the target variable was (1) the Approximate Entropy of the force generated by the single finger (Fig. 26.8) or (2) information entropy of the relative phase of the

forces produced by the two fingers simultaneously (Fig. 26.9). These findings were consistent as long as the entropies were made conditional upon successful completion of the task (i.e. staying within the boundaries of the error bands). What this achieved was the “idealization” of the results, restricting this to situations where the behaviour successfully satisfied the goal.

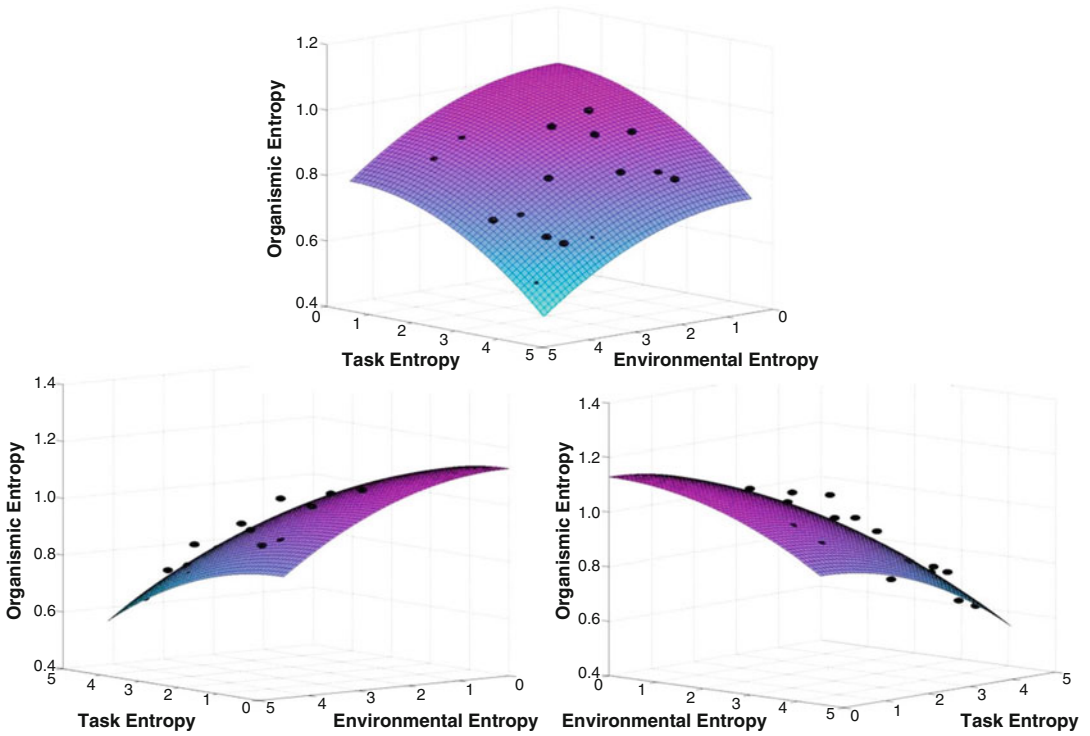
From the perspective of the behaviour, when faced with the constraints of a challenging task and environment, the force output is adjusted by reducing the entropy of the motor output. In the task that required the force production of a single finger, the force output time series exhibits



**Fig. 26.7** Illustration of the experimental setup for the coordinated, two-finger isometric force production experiment. From [59]

a gradual shift from what is a broad spectrum signal to what is more similar to a sine wave that has an extremely predictable pattern. In the case of the two-finger coordinated force output, we observed that the distribution of the number of coordination (relative phase) patterns is reduced. When the demands of the task are high and the environment provides little information, the force output is restricted to fewer coordination patterns, and the distribution of relative phase values becomes peaked. This was a marked shift from the broad distribution of relative phase values during the easy task and high environmental information conditions.

Such a conservation rule also holds in the study of cognitive response and eye fixation patterns. In a recent study [62], we measured the effects of temporal and spatial uncertainty on response times and eye fixation durations when reacting to a single stimulus (Fig. 26.10). In this task, subjects were seated facing a computer monitor with their head braced to allow for accurate eye tracking to take place. They held a video game controller in hand and were asked to push either of the buttons on the controller as soon as they see a red square appear on the computer screen. While the number of stimuli remained constant at one, we altered the



**Fig. 26.8** Quadratic surface representation of the task–organism–environment entropy conservation relationship. The surface is generated using the equation:  $H_{\text{ORGANISM}} = k - aH_{\text{TASK}}^2 - bH_{\text{ENVIRONMENT}}^2$ , where  $k$  is the intercept, with  $a$  and  $b$  as free obtained through a

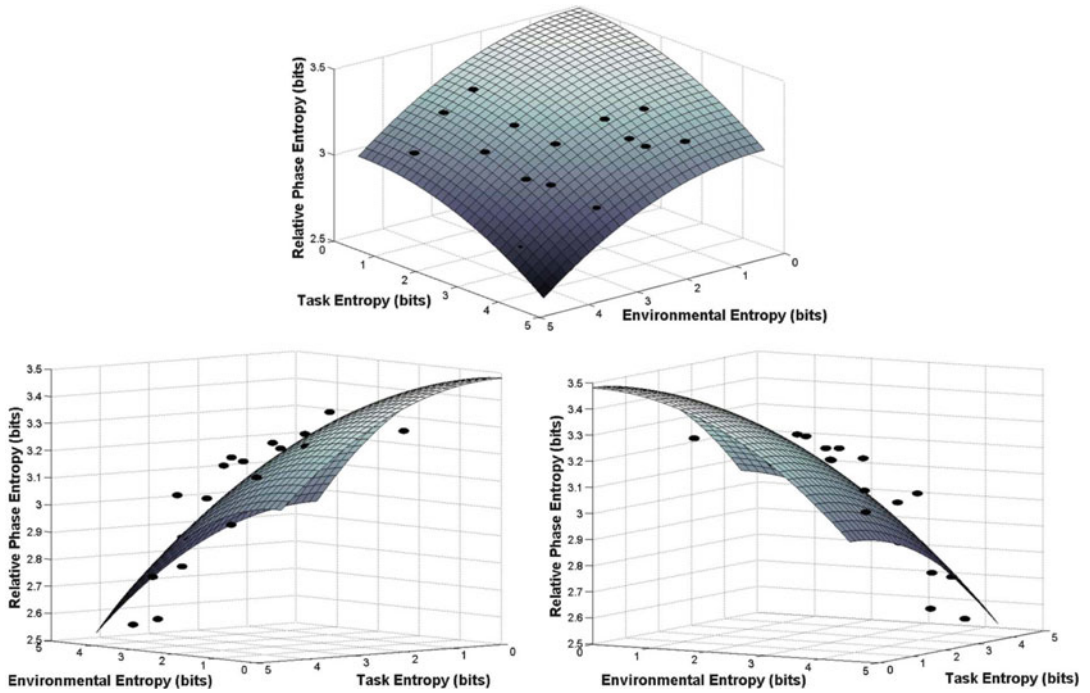
least-squares fit. The entropy of the organism is represented by approximate entropy [39] values of the force dynamics, made conditional on the probability that the force level remained within the target bands. This surface captured 92% of the total variance. From [60]

uncertainty of when (temporal uncertainty) and where (spatial uncertainty) the stimulus would appear in the various conditions. This was achieved by simply increasing the number of stimulus locations and time between response and subsequent stimulus from 1 to 2 to 4. The average interval, however, was maintained at 1,250 ms. Interestingly, we found that while the response times became more unpredictable as a result of increased stimulus uncertainty (Fig. 26.11), the eye fixation durations were more predictable (Fig. 26.12).

Both patterns of change in entropy of the response times and fixation durations could be captured using a single quadratic surface, requiring only a reversal of sign in the equation (Fig. 26.13). The interesting aspect to this finding is that the pattern and not the amount of

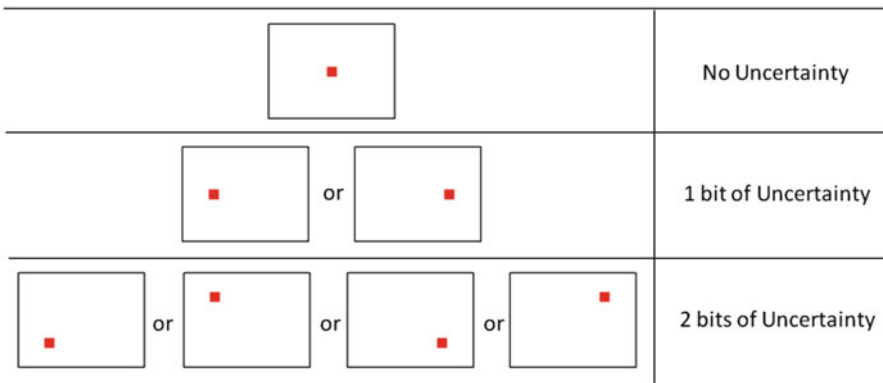
time of the response and fixation durations changed as a function of stimulus uncertainty. Furthermore, there seems to be a compensatory relationship between the “input” eye fixations and the “output” of the response times. When the stimulus was more unpredictable, the eye fixations became restricted to more similar durations, and in turn, the response times became more evenly distributed. Much like finger force production [63], we found that spatial and temporal uncertainty had compensatory effects on the response time and eye fixation patterns. Essentially, the effects of not knowing when and where the stimulus would appear were similar for both response times and eye fixation durations.

With empirical evidence for uncertainty conservation in human motor and cognitive behaviour,



**Fig. 26.9** Similar quadratic surface representation as in Fig. 26.8, with the entropy of the organism represented by the Shannon entropy of the relative phase between the two

finger force outputs. This surface captured 80% of the total variance. From [59]

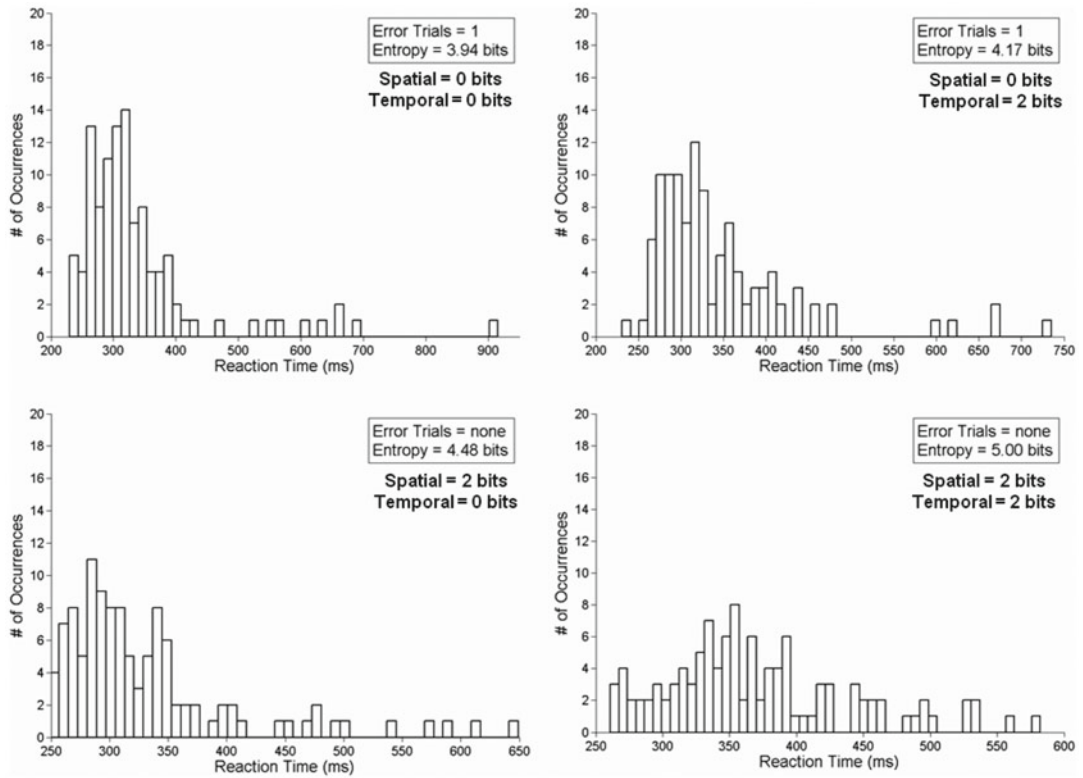


**Fig. 26.10** Illustration of the stimulus presentation and resulting levels of uncertainty in bits. Subjects were required to push a button on a video game control pad as soon as the target was visible. From [62]

it provides a hypothesis that views the task, organism, and environment as parts of a larger system. It is possible that this hypothesis can be used to predict the direction of change in motor function based on manipulations of the task and environment. The following sections provide some initial ideas on how the uncertainty conservation framework can be applied to clinical settings.

### 26.3 Uncertainty Conservation as Framework for Care and Clinical Interventions

Despite the ubiquity of motor dysfunction across a broad range of diseases and disorders, systems approaches are rarely used in this domain. Dominated by the use of contraries in contemporary

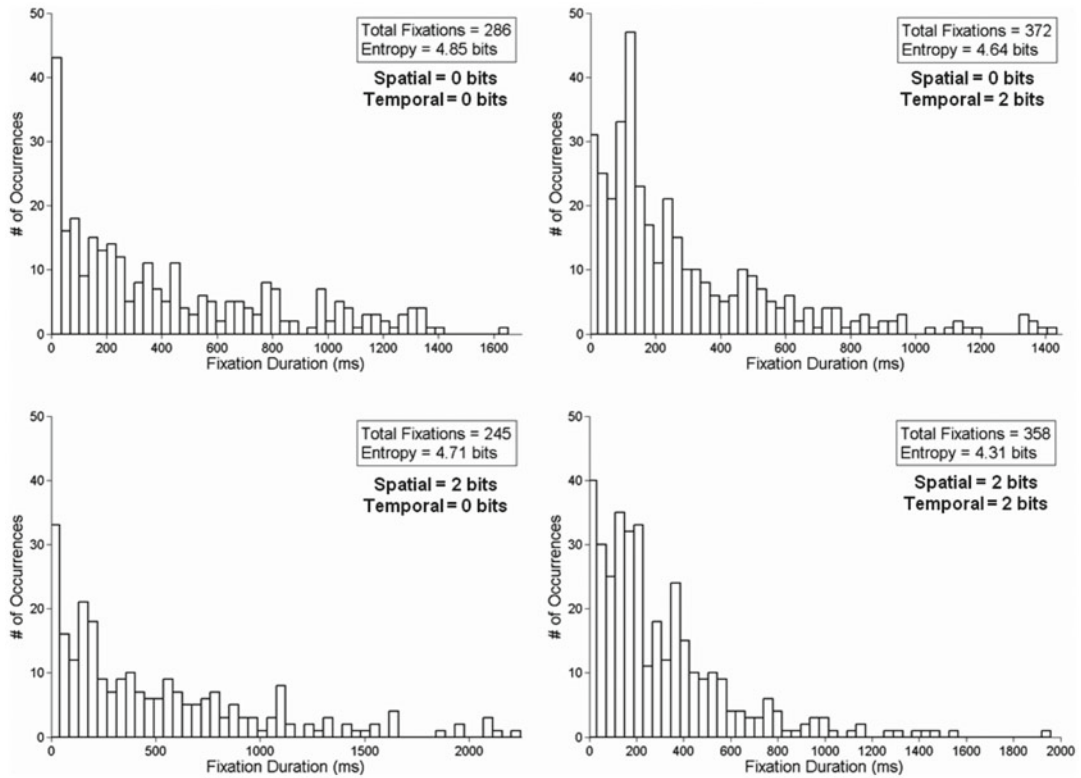


**Fig. 26.11** Frequency histogram of the distribution of response times as the result of the four extreme spatial and temporal uncertainty conditions. These data are

obtained from a single subject. Note the flattening of the distribution as the uncertainty in the conditions is increased. From [62]

science (see [64]), medicine and healthcare also generally target problems using unidimensional interventions [2]. For example, addressing motor issues through movement rehabilitation or exercise has been exclusively the domain of physical or occupational therapists, while addressing motor dysfunction from a neurological perspective is most often achieved through pharmacology or surgery. The lack of overlap in the aforementioned approaches arises due to the constant separation of central from peripheral, cognitive from motor, structure from function, and physical from mental. Obscuring the complex connections between physiological subsystems through categorization, it has resulted in treatments that are more symptom-based, rather than targeting the underlying problems. Sometimes, this can also prevent biological mechanisms of a given disorder from being uncovered, because, simply, movement disorders are rarely “motor system” problems alone.

A good example is Parkinson’s disease (PD), a disorder that is viewed almost exclusively as a movement disorder. It primarily presents motor symptoms of tremor and freezing, and slowness of movements, especially in gait. Anatomically, PD presents itself as a loss of dopaminergic neurons in the substantia nigra pars compacta, a region of the basal ganglia. As a result, the targeted pharmacological therapy has been L-DOPA, as a means of supplementing declines in the dopamine levels in the brain. While effective at reducing complications in the early stages of PD, L-DOPA also results in a variety of often debilitating side effects as the disease progresses (see [65]). PD, however, is now acknowledged as being far from only a “movement disorder.” Not only are there motor issues in PD, but also cognitive declines [66, 67], with additional symptoms of depression [68] and even psychosis [69].



**Fig. 26.12** Obtained from the same subject in Fig. 26.11, this frequency histogram illustrates the distribution of eye fixation durations across the same four conditions. Here,

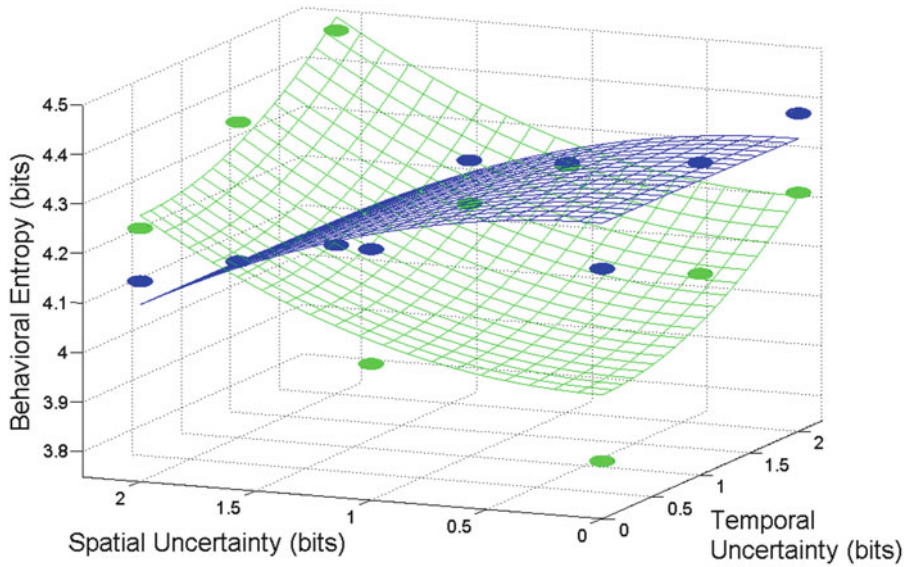
the increasing uncertainty in the experimental conditions resulted in a narrowing of the distribution. From [62]

This multidimensional nature of movement and cognitive/psychological disorders raises the need for a multifaceted approach that is based on complementarity, rather than contraries [64]. Separating symptoms of the disorder into its cognitive and motor components and addressing them independently may not be the most viable approach. However, what is needed is a complementary viewpoint that views cognition and action as components of a single system. The uncertainty conservation framework provides an approach to change the complexity of the motor output in a given individual. By altering the amount of information available in the environment or changing the demands of the task, the desired change in behaviour can be elicited. This framework provides predictions regarding the behaviour of the system's output in response to task demands and environmental information. At the very least, if no adaptive change in motor

behaviour is obtained it would allow for further experimentation to gain insight as to why the system no longer adapts to the task and environmental constraints placed upon the behaviour.

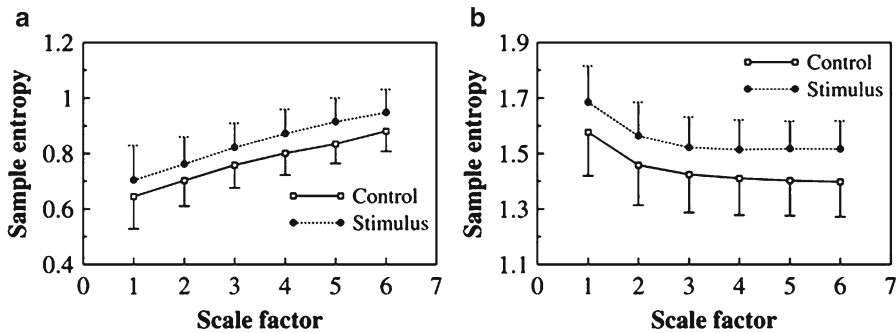
One example of a successful intervention that would fall within the uncertainty conservation framework has been the application of the “stochastic resonance” concept to motor output. Simply, stochastic resonance occurs through the addition of further random interference or “noise” to a highly variable nonlinear system and enhances the information content through an improved signal-to-noise ratio. This phenomenon is evident in both man-made and naturally occurring signals (see [70]). External assistive devices have been applied successfully, improving posture in older individuals. Using vibratory insoles worn on the feet [71] and a mini electrical stimulator placed at the knee [72] have shown improvements in balance and postural control, as well as





**Fig. 26.13** Quadratic surface representation of entropy conservation across space, time, and behaviour. The entropy of the eye fixation durations, represented by the *blue surface* is captured using a similar function to Figs. 26.8 and 26.9:  $H_{\text{FIXATIONDURATION}} = k - aH_{\text{SPACE}}^2 - bH_{\text{TIME}}^2$ , with two

free parameters and the intercept. To obtain the surface for the response times, the signs are simply reversed to:  $H_{\text{RESPONSETIME}} = k + aH_{\text{SPACE}}^2 + bH_{\text{TIME}}^2$ . Both surfaces captured approximately 80% of the total variance. From [62]



**Fig. 26.14** Increased complexity in the postural sway resulting from the noisy/random stimulus delivered using a mini electrical device. Panels (a) and (b) represent the change in Sample Entropy along a variety of different timescales along the anteroposterior (fore-aft) and mediolat-

eral (side-to-side) axes, respectively. The higher Sample Entropy values across all of the scales indicate an increase in complexity of the postural sway due to the stochastic resonance phenomenon. From [73]

an increase in complexity of the sway pattern [73], and is illustrated by the increased Sample Entropy values along the various timescales in Fig. 26.14. These studies demonstrate that the complexity of the postural sway signal can be increased by improving the information from the environment through enhanced cutaneous

sensation from the soles of the feet. Here, reducing the uncertainty at the level of the environment afforded an increase in the complexity in the motor output.

In other realms of physical and occupational therapy, similar approaches have been employed and are currently still in use. Known as

constraint-induced therapy, it is a clinical intervention originally developed for the rehabilitation of stroke patients. This therapeutic approach restricts the movement of the unaffected limb to allow structured practice to begin to restore function in the affected limb. Effectively, this reduces the number of degrees of freedom available to the motor system, reducing its entropy, and thus, affording increased entropy in the task and environment. There is evidence that constraint-induced therapy improves motor function following stroke [74] and there is growing evidence of its efficacy in cerebral palsy and hemiplegia in children [75, 76].

### 26.3.1 Open Questions: Uncertainty Conservation in Clinical Interventions

While these clinical interventions and approaches were developed before and independent of the uncertainty conservation framework, it does suggest its potential utility as a broader theoretical basis for clinical interventions of motor dysfunction. If one were to take a general systems theoretic viewpoint [3], it opens the possibility that using the natural compensation of uncertainty and entropy could lead to novel therapeutic approaches to a variety of diseases and disorders.

As an example, instead of focusing on addressing movement disorders alone, movement-based rehabilitation has the potential to improve mood states and psychopathology. Known as interpersonal and social rhythm therapy or ISRT [77–79], this approach uses social interactions, such as feeding, sleep, and exercise to improve clinical outcomes in people with bipolar disorder. From a systems perspective and the uncertainty conservation hypothesis, this approach reduces the uncertainty in the behavioural routines in order to increase the complexity of the shifting mood states. With evidence of reduced complexity of mood fluctuations [37], a compensatory relationship between cognition, action, and emotion might explain the reported therapeutic benefits of ISRT. Perhaps, increasing the rhythmicity of one's interaction with the environment, which

reduces its entropy, leads to increased entropy at the level of affect and mood.

In a similar vein, the demonstration that complexity decreases in blood glucose dynamics by Churrua et al. [36] raises a question as to whether the uncertainty conservation approach would also be valid in this context. It is important to note that even with insulin treatment the natural complexity of the blood glucose dynamics is not restored. Perhaps, as with ISRT, reducing the “entropy” of the food intake might be a means of increasing the complexity in blood glucose levels via the reduced entropy of the environment? One could envision achieving this reduction in dietary entropy by (1) eating meals at the same time every day (reduced temporal uncertainty) and/or (2) consuming food with consistent nutritional composition.

Overall, there is evidence, although tangential, that the uncertainty conservation approach has the potential to restore the behavioural dynamics and complexity through task demands and environmental influences. At this stage, however, these ideas remain speculative. However, the consistency and ubiquitous nature of patterns of change in so many complex dynamical systems should compel the clinical sciences to at least attempt new interventions. By taking advantage of the similarities in systems and the theories underlying them, there is the potential that new methods of addressing old problems might be uncovered.

---

## 26.4 Summary

The overall goal of this chapter was to review the complexity and complex systems-based approaches to motor function and dysfunction. Based on this framework and that of complementarity, an approach that bridges different modalities of cognition and action is needed, even though cognition and action are often viewed as contraries. Through the uncertainty conservation hypothesis, one can conceive a new approach that connects these sometimes disparate components of a larger whole in a manner that could lead to the development of novel approaches to the treatment of movement disorders. Hopefully, this will

result in a move towards the consideration of holistic, multidomain therapeutic interventions that work alongside conventional, unimodal symptom-based clinical targets. With a hypothesis-based approach through uncertainty conservation, it is possible that the more speculative elements of this chapter are tested and evaluated in the future.

**Acknowledgements** This research was supported in part by grants from the National Institutes on Aging (R21AG035158 and 1R21AG039818).

## References

- Rosenbaum DA. The Cinderella of psychology: the neglect of motor control in the science of mental life and behavior. *Am Psychol*. 2005;60(4):308–17.
- West BJ. Where medicine went wrong: rediscovering the path to complexity. Hackensack: Wold Scientific; 2006.
- Guastello SJ. Managing emergent phenomena: nonlinear dynamics in work organizations. Mahwah, NJ: Lawrence Erlbaum; 2002.
- Bak P. How nature works: the science of self-organized criticality. New York: Copernicus; 1996.
- Bar-Yam Y. Dynamics of complex systems. New York: Westview; 1997.
- Gilden D, Thornton T, Mallon M.  $1/f$  noise in human cognition. *Science*. 1995;267(5205):1837–9.
- Van Orden GC, Holden JG, Turvey MT. Human cognition and  $1/f$  scaling. *J Exp Psychol Gen*. 2005;134(1):117–23.
- Hausdorff JM, Purdon PL, Peng CK, Ladin Z, Wei JY, Goldberger AL. Fractal dynamics of human gait: stability of long-range correlations in stride interval fluctuations. *J Appl Physiol*. 1996;80(5):1448–57.
- Jordan K, Challis JH, Newell KM. Long range correlations in the stride interval of running. *Gait Posture*. 2006;24(1):120–5.
- Hong SL, James EG, Newell KM. Age-related complexity and coupling of children's sitting posture. *Dev Psychobiol*. 2008;50(5):502–10.
- Duarte M, Zatsiorsky VM. On the fractal properties of natural human standing. *Neurosci Lett*. 2000;283(3):173–6.
- Blesic S, Stratimirovic D, Milosevic S, Maric J, Kostic V, Ljubicavljivic M. Scaling analysis of the effects of load on hand tremor movements in essential tremor. *Phys A Stat Mech Appl*. 2011;390(10):1741–6.
- Aks DJ, Zelinsky GJ, Sprott JC. Memory across eye-movements:  $1/f$  dynamic in visual search. *Nonlinear Dynamics Psychol Life Sci*. 2002;6(1):1–25.
- Nakamura T, Kiyono K, Yoshiuchi K, Nakahara R, Struzik ZR, Yamamoto Y. Universal scaling law in human behavioral organization. *Phys Rev Lett*. 2007;99(13):138103.
- Roizen NJ, Higgins AM, Antshel KM, Fremont W, Shprintzen R, Kates W. 22q11.2 deletion syndrome: are motor deficits more than expected for IQ level? *J Pediatr*. 2010;157(4):658–61.
- Piek JP, Pitcher TM, Hay DA. Motor coordination and kinaesthesia in boys with attention deficit-hyperactivity disorder. *Dev Med Child Neurol*. 1999;41(3):159–65.
- Henderson SE, Morris J, Frith U. The motor deficit in Down's syndrome children: a problem of timing? *J Child Psychol Psychiatry*. 1981;22(3):233–45.
- Ming X, Brimacombe M, Wagner GC. Prevalence of motor impairment in autism spectrum disorders. *Brain Dev*. 2007;29(9):565–70.
- Smith MA, Brandt J, Shadmehr R. Motor disorder in Huntington's disease begins as a dysfunction in error feedback control. *Nature*. 2000;403(6769):544–9.
- Berardelli A, Rothwell JC, Day BL, Marsden CD. Movements not involved in posture are abnormal in Parkinson's disease. *Neurosci Lett*. 1984;47(1):47–50.
- Manckoundia P, Pfitzenmeyer P, d'Athis P, Mourey F. Impact of cognitive task on the posture of elderly subjects with Alzheimer's disease compared to healthy elderly subjects. *Mov Disord*. 2006;21(2):236–41.
- Carroll CA, O'Donnell BF, Shekhar A, Hetrick WP. Timing dysfunctions in schizophrenia as measured by a repetitive finger tapping task. *Brain Cogn*. 2009;71(3):345–53.
- Marvel CL, Schwartz BL, Rosse RB. A quantitative measure of postural sway deficits in schizophrenia. *Schizophr Res*. 2004;68(2–3):363–72.
- Bolbecker AR, Hong SL, Kent JS, Klaunig MJ, O'Donnell BF, Hetrick WP. Postural control in bipolar disorder: increased sway area and decreased dynamical complexity. *PLoS One*. 2011;6(5):e19824.
- Bolbecker AR, Hong SL, Kent JS, Forsyth JK, Klaunig MJ, Lazar EK, et al. Paced finger-tapping abnormalities in bipolar disorder indicate timing dysfunction. *Bipolar Disord*. 2011;13(1):99–110.
- Allen PA, Namazi KH, Patterson MB, Crozier LC, Groth KE. Impact of adult age and Alzheimer's disease on levels of neural noise for letter matching. *J Gerontol*. 1992;47(5):P344–9.
- Li S-C, Lindenberger U, Sikström S. Aging cognition: from neuromodulation to representation. *Trends Cogn Sci*. 2001;5(11):479–86.
- Lipsitz LA, Goldberger AL. Loss of 'complexity' and aging. Potential applications of fractals and chaos theory to senescence. *JAMA*. 1992;267(13):1806–9.
- Pincus SM. Approximate entropy as a measure of system-complexity. *Proc Natl Acad Sci USA*. 1991;88:2297–301.
- Sosnoff JJ, Newell KM. Age-related loss of adaptability to fast time scales in motor variability. *J Gerontol B Psychol Sci Soc Sci*. 2008;63(6):P344–52.
- Duarte M, Sternad D. Complexity of human postural control in young and older adults during prolonged standing. *Exp Brain Res*. 2008;191(3):265–76.
- Hong SL, James EG, Newell KM. Coupling and irregularity in the aging motor system: tremor and movement. *Neurosci Lett*. 2008;433(2):119–24.

33. Hong SL, Bodfish JW, Newell KM. Power-law scaling for macroscopic entropy and microscopic complexity: evidence from human movement and posture. *Chaos*. 2006;16:013135.
34. Newell KM, Vaillancourt DE, Sosnoff JJ. Aging, complexity and motor performance: health and disease states. In: Birren JE, Schaie KW, editors. *Handbook of the psychology of aging*. Amsterdam: Elsevier; 2006. p. 163–82.
35. Vaillancourt DE, Newell KM. Changing complexity in human behavior and physiology through aging and disease. *Neurobiol Aging*. 2002;23(1):1–11.
36. Churrua J, Vigil L, Luna E, Ruiz-Galiana J, Varela M. The route to diabetes: loss of complexity in the glycemic profile from health through the metabolic syndrome to type 2 diabetes. *Diabetes Metab Syndr Obes*. 2008;1:3–11.
37. Gottschalk A, Bauer MS, Whybrow PC. Evidence of chaotic mood variation in bipolar disorder. *Arch Gen Psychiatry*. 1995;52:947–59.
38. Lipsitz LA. Dynamics of stability: the physiologic basis of functional health and frailty. *J Gerontol A Biol Sci Med Sci*. 2002;57:B115–25.
39. Pincus SM. Greater signal regularity may indicate increased system isolation. *Math Biosci*. 1994;122(2):161–81.
40. Lipsitz LA. Physiological complexity, aging, and the path to frailty. *Sci Aging Knowledge Environ*. 2004;16:pe16.
41. Assisi CG, Jirsa VK, Kelso JAS. Synchrony and clustering in heterogeneous networks with global coupling and parameter dispersion. *Phys Rev Lett*. 2005;94:4.
42. Hong SL. The dynamics of structural and functional complexity across the lifespan. *Nonlinear Dynamics Psychol Life Sci*. 2007;11(2):219–34.
43. Newell KM, Liu Y-T, Mayer-Kress G. A dynamical systems interpretation of epigenetic landscapes for infant motor development. *Infant Behav Dev*. 2003;26(4):449–72.
44. Vaillancourt DE, Shifkin AB, Newell KM. Regularity of force tremor in Parkinson's disease. *Clin Neurophysiol*. 2001;112(9):1594–603.
45. Morrison S, Sosnoff JJ. Age-related changes in the adaptability of neuromuscular output. *J Mot Behav*. 2009;41(3):274–83.
46. Peng CK, Havlin S, Stanley HE, Goldberger AL. Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time-series. *Chaos*. 1995;5(1):82–7.
47. Newell KM. Constraints on the development of coordination. In: Wade MG, Whiting HTA, editors. *Motor development in children*. Amsterdam: Nijhoff; 1986. p. 341–61.
48. Bernstein NA. *The co-ordination and regulation of movements*. Oxford: Pergamon; 1967.
49. Kugler PN, Turvey MT. Information, natural laws, and self-assembly of rhythmic movement. Hillsdale, NJ: Erlbaum; 1987.
50. Kelso JAS. *Dynamic patterns: the self-organization of brain and behavior*. Cambridge, MA: MIT Press; 1995.
51. Holt KG, Hamill J, Andres RO. The force-driven harmonic oscillator as a model for human locomotion. *Hum Mov Sci*. 1990;9(1):55–68.
52. Haken H, Kelso JAS, Bunz H. A theoretical model of phase-transitions in human hand movements. *Biol Cybern*. 1985;51(5):347–56.
53. Zanone PG, Kelso JA. Evolution of behavioral attractors with learning: nonequilibrium phase transitions. *J Exp Psychol Hum Percept Perform*. 1992;18(2):403–21.
54. Zanone PG, Kelso JAS. Coordination dynamics of learning and transfer: collective and component levels. *J Exp Psychol Hum Percept Perform*. 1997;23(5):1454–80.
55. Kugler PN, Kelso JAS, Turvey MT. On the concept of coordinative structures as dissipative structures I. Theoretical lines of convergence. In: Stelmach GE, Requin J, editors. *Tutorials in motor behavior*. Amsterdam: Elsevier; 1980.
56. Hong SL, Newell KM. Entropy conservation in the control of human action. *Nonlinear Dynamics Psychol Life Sci*. 2008;12(2):163–90.
57. Hong SL. The entropy conservation principle: applications in ergonomics and human factors. *Nonlinear Dynamics Psychol Life Sci*. 2010;14(3):291–315.
58. Müller I. *A history of thermodynamics: the doctrine of energy and entropy*. Berlin: Springer; 2007.
59. Hong SL, Newell KM. Entropy compensation in human motor adaptation. *Chaos*. 2008;18:013108.
60. Hong SL, Newell KM. Motor entropy in response to task demands and environmental information. *Chaos*. 2008;18:033131.
61. Vaillancourt D, Russell D. Temporal capacity of short-term visuomotor memory in continuous force production. *Exp Brain Res*. 2002;145(3):275–85.
62. Hong SL, Beck MR. Uncertainty compensation in human attention: evidence from response times and fixation durations. *PLoS One*. 2010;5(7):e11461.
63. Hong S, Brown A, Newell K. Compensatory properties of visual information in the control of isometric force. *Atten Percept Psychophys*. 2008;70(2):306–13.
64. Kelso JAS, Engström DA. *The complementary nature*. Cambridge, MA: MIT Press; 2006.
65. Jenner P. Molecular mechanisms of L-DOPA-induced dyskinesia. *Nat Rev Neurosci*. 2008;9(9):665–77.
66. Gotham AM, Brown RG, Marsden CD. 'Frontal' cognitive function in patients with Parkinson's disease 'on' and 'off' levodopa. *Brain*. 1988;111(2):299–321.
67. Lees AJ, Smith E. Cognitive deficits in the early stages of Parkinson's disease. *Brain*. 1983;106(2):257–70.
68. Starkstein SE, Preziosi TJ, Bolduc PL, Robinson RG. Depression in Parkinson's disease. *J Nerv Ment Dis*. 1990;178(1):27–31.
69. Factor SA, Feustel PJ, Friedman JH, Comella CL, Goetz CG, Kurlan R, et al. Longitudinal outcome of Parkinson's disease patients with psychosis. *Neurology*. 2003;60(11):1756–61.
70. Moss F, Ward LM, Sannita WG. Stochastic resonance and sensory information processing: a tutorial and review of application. *Clin Neurophysiol*. 2004;115(2):267–81.

71. Priplata A, Niemi J, Salen M, Harry J, Lipsitz LA, Collins JJ. Noise-enhanced human balance control. *Phys Rev Lett*. 2002;89(23):238101.
72. Gravelle DC, Laughton CA, Dhruv NT, Katdare KD, Niemi JB, Lipsitz LA, et al. Noise-enhanced balance control in older adults. *Neuroreport*. 2002;13(15):1853–6.
73. Costa M, Priplata AA, Lipsitz LA, Wu Z, Huang NE, Goldberger AL, et al. Noise and poise: enhancement of postural complexity in the elderly with a stochastic-resonance-based therapy. *Europhys Lett*. 2007;77(6):68008.
74. Wolf SL, Blanton S, Baer H, Breshears J, Butler AJ. Repetitive task practice: a critical review of constraint-induced movement therapy in stroke. *Neurologist*. 2002;8(6):325–38.
75. Charles JR, Wolf SL, Schneider JA, Gordon AM. Efficacy of a child-friendly form of constraint-induced movement therapy in hemiplegic cerebral palsy: a randomized control trial. *Dev Med Child Neurol*. 2006;48(08):635–42.
76. Gordon AM, Charles J, Wolf SL. Methods of constraint-induced movement therapy for children with hemiplegic cerebral palsy: development of a child-friendly intervention for improving upper-extremity function. *Arch Phys Med Rehabil*. 2005;86(4):837–44.
77. Frank E, Swartz HA, Kupfer DJ. Interpersonal and social rhythm therapy: managing the chaos of bipolar disorder. *Biol Psychiatry*. 2000;48(6):593–604.
78. Frank E, Kupfer DJ, Thase ME, Mallinger AG, Swartz HA, Fagiolini AM, et al. Two-year outcomes for Interpersonal and Social Rhythm Therapy in individuals with bipolar I disorder. *Arch Gen Psychiatry*. 2005;62(9):996–1004.
79. Frank E, Soreca I, Swartz HA, Fagiolini AM, Mallinger AG, Thase ME, et al. The role of Interpersonal and Social Rhythm Therapy in improving occupational functioning in patients with bipolar I disorder. *Am J Psychiatry*. 2008;165(12):1559–65.