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Human Movement Variability and Aging

Nicholas Stergiou, Jenny A. Kent, and Denise McGrath

Abstract

An optimal level of variability enables us to interact adaptively and safely to a continuously changing environment, where often our movements must be adjusted in a matter of milliseconds. A large body of research exists that demonstrates natural variability in healthy gait (along with variability in other, healthy biological signals such as heart rate) and a loss of this variability in aging and injury, as well as in a variety of neuro-degenerative and physiological disorders. We submit that this field of research is now in pressing need of an innovative “next step” that goes beyond the many descriptive studies that characterize levels of variability in various patient populations. We need to devise novel therapies that will harness the existing knowledge on biological variability and create new possibilities for those in the grip of disease. We also propose that the nature of the specific physiological limitation present in the neuromuscular apparatus may be less important in the physiological complexity framework than the control mechanisms adopted by the older individual in the coordination of the available degrees of freedom. The theoretical underpinnings of this framework suggest that interventions designed to restore healthy system dynamics may optimize functional improvements in older adults. We submit that interventions based on the restoration of optimal variability and movement complexity could potentially be applied across a range of diseases or dysfunctions as it addresses the adaptability and coordination of available degrees of freedom, regardless of the internal constraints of the individual.

Keywords: biomechanics, gait, elderly, complexity, fractals

When we perform the same task multiple times, we can easily observe that we never execute it the exact same way. This is obvious even with elite performers, such as athletes and musicians. When it comes down to simple everyday walking, every one of us is an elite performer, but as we observe our steps behind us on the sand, we can clearly see that they are never identical. These natural fluctuations in motor performance define the presence of human movement variability which is ubiquitous in all biological systems. Recently, the role of movement variability has attracted significant attention due to its relationship to pathology and performance (Harrison & Stergiou, 2015; Stergiou & Decker, 2011).

Previous theoretical frameworks consider variability as an indicator of noise in the control system, and it has been quantified using traditional linear statistical measures (e.g., standard deviation; Newell & Corcos, 1993; Schmidt & Lee, 2005; Stergiou, Harbourne, & Cavanaugh, 2006). Such measures contain no information about how the motor system responds to change over time. Practically, the linear measures are measures of centrality and thus provide a description of the amount or magnitude of the variability around that central point. This is accomplished by

quantifying the magnitude of variation in a set of values independent of their order in the distribution. From this perspective, clinicians and scientists believe that the mean is the “gold standard” of healthy behavior. Any deviation from this gold standard is error, or undesirable behavior, or the result of instability. However, recent literature from several disciplines and medical areas, including brain function and disease dynamics, has shown that many apparently “noisy” phenomena are the result of nonlinear interactions and have deterministic origins (Amato, 1992; Buchman, Cobb, Lapedes, & Kepler, 2001; Cavanaugh, Kochi, & Stergiou, 2010; Garfinkel, Spano, Ditto, & Weiss, 1992; Goldstein, Toweill, Lai, Sonnenthal, & Kimberly, 1998; Orsucci, 2006; Slutzky, Cvitanovic, & Mogul, 2001; Toweill & Goldstein, 1998; Wagner, Nafz, & Persson, 1996). Based on this information, it has been proposed that the natural fluctuations that are present in normal motor tasks (e.g., stride-to-stride fluctuations in normal walking) are characterized by an appropriate or optimal state of variability (Harrison & Stergiou, 2015; Stergiou et al., 2006; Stergiou & Decker, 2011). Optimal variability is associated with complex interactions across multiple control systems, feedback loops, and regulatory processes that enable an organism to function and adapt to the demands of everyday life (Harrison & Stergiou, 2015; Stergiou et al., 2006; Stergiou & Decker, 2011; Figure 1). This physiological complexity is recognized as an inherent attribute of healthy biological systems, whereas the loss of complexity with aging and disease is thought to reduce the adaptive capabilities of the individual (Buzzi, Stergiou, Kurz, Hageman, & Heidel, 2003; Goldberger, 2001; Goldberger et al., 2002a). A loss of complexity can refer to either an overly constrained, periodic system, or an overly random, incoherent system (Dossey, 2010). Healthy human function thus requires the coexistence of the oppositional factors of coherence and chaos (Dossey, 2010). It is important to note that the specialized concept of “chaos” discussed here is distinct from, and indeed contrary to, the English language notion of chaos which means confusion and disorder. In fact, when we refer to mathematical chaos in a system, we are pointedly referring to an underlying order or pattern that is contained within a complex, variable system, capable of sudden and marked change.

The physiological complexity paradigm was first introduced almost 30 years ago by Goldberger and colleagues, based on heart rate dynamics (Goldberger, Findley, Blackburn, & Mandell, 1984). Since then, there has been an abundance of literature that reveals the presence of physiological complexity in healthy systems and a loss of complexity in ill health, for example in: brain activity and pathological cognitive processes (Bystritsky, Nierenberg, Feusner, & Rabinovich, 2012; Yang et al., 2013), heart failure (Goldberger et al., 2002a), fetal distress syndromes (Goldberger, 1996), respiration (Peng et al., 2002), and ambulatory behaviors in older adults (Cavanaugh et al., 2010; Cavanaugh, Coleman, Gaines, Laing, & Morey, 2007). Evidence for loss of complexity in the motor system (e.g., locomotor system) with aging and disease first emerged in the mid- to late-nineties (Hausdorff et al., 1997; Hausdorff, Cudkowicz, Firtion, Wei, & Goldberger, 1998), with subsequent cross-sectional studies relating levels of motor and specifically locomotor complexity to diseases, conditions, or age categories, many of which were performed by our laboratory (Buzzi et al., 2003; Decker, Moraiti, Stergiou, & Georgoulis, 2011; Deffeyes et al., 2009). However, despite the enormous potential that this emerging field presents for (a) improving our understanding of aging and disease/dysfunction, (b)

providing sensitive biomarkers for evaluating behavioral or pharmacological interventions, and (c) designing novel interventions based on restoration of complexity, its actual impact in the field of rehabilitative medicine has been minimal. The reason for the relatively slow progress may be due to the fact that no single statistical measure can be used to assess the complexity of physiologic systems. Instead, an extensive “toolkit” of evolving metrics is needed to probe different aspects of these complicated behaviors (Goldberger et al., 2002b). These metrics must be implemented with an in-depth appreciation of their purposes, strengths, and limitations (Stergiou, 2004; Stergiou, 2016). Fractal-based complexity metrics hold great promise in the study of walking. Multiple studies support the idea that stride-to-stride variations in healthy gait exhibit nonlinear and fractal-like fluctuations extending over hundreds of steps, reflective of complexity in healthy gait (Hausdorff, Peng, Ladin, Wei, & Goldberger, 1995; Hausdorff et al., 1996; Hausdorff, 2007). The classic definition of a fractal, first described by Mandelbrot (1977), is a geometric object with “self-similarity” over multiple measurement scales (Lipsitz, 2002). The outputs of the locomotor system measured over time exhibit such fractal properties (Delignieres & Torre, 2009), demonstrating power-law scaling such that the smaller the frequency of oscillation (f) of these signals, the larger their amplitude (amplitude squared is power) (Lipsitz, 2002). This power-law relation can be expressed as $1/f$, and is referred to as pink noise, where oscillations appear self-similar when observed over seconds, minutes, hours, or days. Pathological gait observed in the elderly population demonstrates a breakdown of this $1/f$ scaling; in other words, a loss of complexity where their movement dynamics are either too periodic or too random (Herman, Giladi, Gurevich, & Hausdorff, 2005).

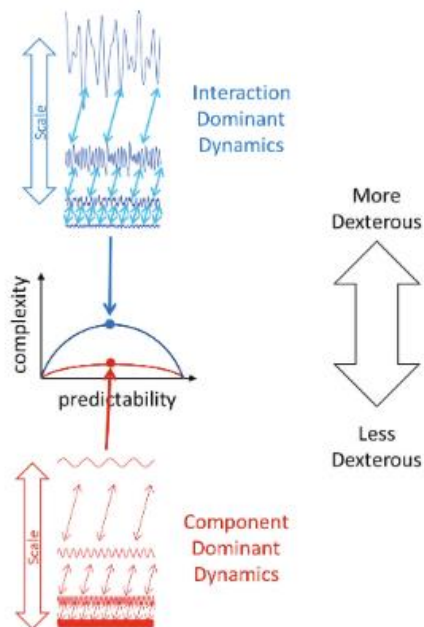


Figure 1 — Optimal movement variability is represented in the middle of the figure as an inverted U-shape relationship between complexity and predictability (Stergiou et al., 2006). Practically, at this optimal state of movement variability, the biological system is in a healthy state and is characterized by the largest possible effective complexity (i.e., the uppermost point along the inverted U-shaped function), attaining high values only in the intermediate region between excessive order (i.e., maximum predictability) and excessive disorder (i.e., no predictability). However, complexity is affected by the

dominant dynamics across scales. Thus, the theory of optimal movement variability could actually be generalized into a theory of complex adaptive behavior where complexity (and higher dexterity) is associated with fractally-nested scales of activity supported by nonlinear couplings of components both within and across scales (Harrison & Stergiou, 2015).

What is the function of this $1/f$ scaling, commonly seen in well-coordinated behaviors, and less so in non-optimal performance or with aging and disease? Vaillancourt and Newell (2003) submit that $1/f$ scaling confers enhanced connectivity between motor control processes, while a breakdown in fractal scaling (as observed in stride interval time series in pathological gait) arises from a gradual deterioration in the number of functioning elements of a given system and/or a decrease in the interactions between these components (Goldberger, 2001; Goldberger et al., 2002b). From this perspective, there is no particular component that causes $1/f$ scaling to occur, or indeed to break down. Instead, it is an emergent property that stems from the interactions across the many spatiotemporal scales of organization of an organism (Van Orden, Holden, & Turvey, 2005), giving rise to a “nimble” but coordinated motor control system. It has been demonstrated that any behavioral performance results from the coordination of the degrees of freedom available to the individual with respect to constraints imposed from the neuromuscular system, the task, and the environment (Vaillancourt, Sosnoff, & Newell, 2004). Drawing from evidence that strongly supports a breakdown of fractal scaling in aging physiological systems (Lipsitz & Goldberger, 1992; Vaillancourt & Newell, 2002), research has further shown that older adults have a reduced capacity to adapt to faster time scales in both feedback and feed-forward processes (Sosnoff & Newell, 2008). Other support for this hypothesis is provided by Bierbaum, Peper, Karamanidis, and Arampatzis (2011), who showed that locomotor behavior in older adults is more conservative compared with the young, leading to disadvantages in the reactive adaptation during disturbed walking. Hsu, Chou, and Woollacott (2013) concluded that, in normal aging, adults lose the compensatory strategy afforded by the flexible control of multiple joints when stabilizing the center of mass after receiving a balance perturbation. Similarly, our previous work has shown that older adults exhibit reduced adaptive capabilities (Byrne et al., 2002; Kurz & Stergiou, 2003).

Causes of gait and balance disturbances in the elderly are multifactorial. For example, abnormal gait can be due to a single disease or multiple diseases developing simultaneously across all sensorimotor levels (Martens & Almeida, 2012; Vinti, Couillandre, & Thoumie, 2010), increased reliance on central mechanisms (Seidler et al., 2010), atrophy or disease of brain structures involved in these central mechanisms (Seidler et al., 2010), degeneration of neurotransmitter systems (Cham, Perera, Studenski, & Bohnen, 2007; Cham, Studenski, Perera, & Bohnen, 2008), reduced muscle mass and/or muscle quality (Shin, Valentine, Evans, & Sosnoff, 2012), psychosocial factors (Baik & Lang, 2007), and medication use (Boudreau et al., 2009; Hilmer et al., 2009). Compensatory postures, slower gait speeds, and “cautious” gait are all trademarks of abnormal gait in the elderly. The capacity to maintain balance when walking through unpredictably changing environments is critical to independent living for this population. Increasingly, altered gait variability is being reported in older adults and has been associated with a variety of disorders ranging from joint and skeletal problems (Kiss, 2011) (lowest-level gait disturbances) to Huntington’s disease (Hausdorff et al., 1997), Parkinson’s disease (Hausdorff et al., 1998; Kurz,

Markopoulou, & Stergiou, 2010), higher-level gait disorders (Herman et al., 2005), and falls (Hausdorff, 2007; Montero-Odasso, Muir, & Speechley, 2012; Paterson, Hill, & Lythgo, 2011; Toebes, Hoozemans, Furrer, Dekker, & van Dieën, 2012). Reduced adaptive capacity in the locomotor system has been linked to falls due to the difficulty that older adults experience in recovering quickly from a loss of dynamic balance (Madigan & Lloyd, 2005; Wojcik, Thelen, Schultz, Ashton-Miller, & Alexander, 1999).

There are compelling findings in both animal and human studies that suggest that the complexity of loco-motor patterns provides a rich source of information that could be relevant to the diagnosis and management of a variety of diseases that affect an aging population. Our previous research has shown that highly active older adults exhibit more complex patterns of locomotor activity than less active older adults, despite the absence of differences between these groups in standard measures of variability of their step counts (Cavanaugh et al., 2010). Hu and colleagues have recently shown that older adults and dementia patients have disrupted fractal activity patterns (Hu, Van Someren, Shea, & Scheer, 2009) and that the degree of disruption is positively related to the burden of amyloid plaques—a marker of Alzheimer's disease severity (Hu, Harper, Shea, Stopa, & Scheer, 2013). They also found that fractal scaling in activity fluctuations is unrelated to the average level of activity as assessed within and between subjects (Hu et al., 2004). A study of primates suggests that a loss of complexity in locomotor behavior that is associated with illness and aging reduces the efficiency with which an animal is able to cope with heterogeneity in its natural environment (Macintosh, Alados, & Huffman, 2011). Japanese quail became less periodic and more complex in their locomotor behavior when they were stimulated to explore, without there being commensurate changes in the percentage of total time spent walking, or in the average duration of the walking events (Kembro, Perillo, Pury, Satterlee, & Marin, 2009). In addition, fractal scaling has been observed in the locomotor activity of young, healthy small mammals, a feature that is less evident in aged animals (Anteneodo & Chialvo, 2009).

While the relationships between fractal patterns of locomotor activity and health are indeed intriguing, Hu and colleagues have recently identified a possible neural site that is responsible for scale-invariant regulation of a neurophysiological system over a range of time scales. They demonstrated that lesioning the suprachiasmatic nucleus (SCN) of the anterior hypothalamus in rats (i.e., the neural node responsible for circadian rhythms) led to the disappearance of fractality in both heart rate and locomotor rhythms (Hu, Scheer, Buijs, & Shea, 2008; Hu, Scheer, Ivanov, Buijs, & Shea, 2007). In addition, they have recently shown that the degree of disruption to fractal activity in dementia patients is strongly associated with vasopressinergic and neurotensinergic neurons (two major circadian neurotransmitters) in postmortem SCN, and can better predict changes of the two neurotransmitters than other traditional circadian measures (Hu et al., 2013). The authors concluded that the SCN impacts human activity regulation at multiple time scales and that disrupted fractal activity may serve as a noninvasive bio-marker of SCN neurodegeneration in dementia. A further study by this group demonstrated that multiunit neural activity of the SCN in mice and rats exhibited fractal fluctuations in vivo that were abolished in preparations in vitro. These empirical results suggest that it is not the activity of the SCN in isolation, but the activity of the SCN in concert with other physiological mechanisms that lead to fractal fluctuations in

physiological output (Hu et al., 2012). It has been widely shown that most peripheral organs and tissues, including skeletal muscle, can express circadian oscillations in isolation, yet still receive and may require input from the SCN in vivo (Mohawk, Green, & Takahashi, 2012). A well-functioning circadian system therefore requires SCN interaction with peripheral oscillators. Many authors have discussed the feedback loops that are ubiquitous at the molecular, cellular, tissue, and systems levels between the inputs and outputs of the circadian system (Yang, 2010).

Therapeutic interventions that boost the circadian signal and restore the temporal order of a system may act to ameliorate some of the decline seen in aged individuals. It is accepted that the age-related attenuation of the central timing signal generated by the SCN is associated with a number of health problems such as metabolic syndrome, neurodegenerative disorders, and cardiovascular diseases (Kondratova & Kondratov, 2012). Transplantation of a 'young' SCN into aged animals resulted in improvements in numerous rhythmic functions, including behavioral rhythms in locomotion (Li & Satinoff, 1995). Tranah and colleagues have shown that older community-dwelling adults with weak circadian locomotor activity rhythms have a higher mortality risk and increased risk of developing dementia and mild cognitive impairment (Tranah et al., 2010; Tranah et al., 2011). It has been shown consistently in animal models that aging does not affect the size or the number of neurons in the SCN (Madeira, Sousa, Santer, Paula-Barbosa, & Gundersen, 1995); rather, aging brings about significant changes in electrophysiological and neurochemical outputs of the SCN (Colwell, 2011). Previous studies suggest that some but not all peripheral circadian oscillators exhibit age-related changes in rhythmicity (Yamazaki et al., 2002) and that some of the related tissues retain the capacity to oscillate but are not appropriately driven in vivo by physical activity rhythms (Asai et al., 2001). Locomotor activity can influence SCN function via neuronal feedback loops (Hughes & Piggins, 2012). Information on the precise role that circadian abnormalities play in the aging process is somewhat limited, however it has been hypothesized that the fragmentation of behavioral activity with aging may worsen the age-related defects in the central clock function, leading to a downward spiral (Farajnia, Deboer, Rohling, Meijer, & Michel, 2014). Together, these considerations suggest that interventions to regulate circadian activity rhythm abnormalities are warranted in older adults (Tranah et al., 2011).

We have recently shown that complexity in the loco-motor system is a modifiable property in both young and elderly adults by walking while listening to an auditory stimulus with a complex structure (Hunt, McGrath, & Stergiou, 2014; Kaipust, McGrath, Mukherjee, & Stergiou, 2013). In other words, we have shown that fractal patterns in gait parameters (i.e., stride intervals) can be restored in older adults using a fractal-based auditory cue in an audio-motor entrainment paradigm. Such an intervention to restore fractal patterns in locomotor activity in older adults, enabled by wearable sensor technology that delivers the relevant cues, could have a positive effect on circadian rhythms and adaptive capability, promoting SCN interaction with an effective fractal-based peripheral oscillator. It could also revolutionize the current practice of metronomic auditory cueing for the rehabilitation of pathological gait by replacing the metronome model with a novel auditory stimulus with a $1/f$ structure (i.e., pink noise) embedded into music.

Although walking to a metronomic auditory stimulus has been shown to increase gait tempo and stride length (Ford, Malone, Nyikos, Yelisetty, & Bickel, 2010; Roerdink et al., 2009), its implicit outcome is to reduce the natural stride-to-stride fluctuations to zero, thus destroying the $1/f$ scaling (Hausdorff et al., 1996) that enables the neuromuscular system to adapt to a continuously changing environment. Humans have been coordinating their movement to external rhythms since antiquity. Entrainment to an external rhythm can occur even when there is a high degree of rhythmic complexity and ambiguity in music (Skoe & Kraus, 2010; Toiviainen & Snyder, 2003). The dynamical systems approach describes musical rhythmic entrainment as an active, self-sustained, periodic oscillation at multiple time scales, enabling the listener to use predictive timing to maintain a stable, multiperiodic pattern and synchronize movements at the main beat or other metrical levels (Large, 2000). There is convincing evidence in the literature suggesting that both healthy and diseased or injured adults can entrain their gait to a metronome (Delval et al., 2008; Ford et al., 2010; Hayden, Clair, Johnson, & Otto, 2009). Drawing from dynamical systems theory, we have advanced this field by showing that the structure of an auditory stimulus is expressed in the patterns of gait variability produced by both young and elderly adults (Hunt et al., 2014; Kaipust et al., 2013). A recent study (Hove, Suzuki, Uchitomi, Orimo, & Miyake, 2012) showed that an “interactive” auditory stimulus, based on nonlinear oscillators, restored $1/f$ scaling in Parkinson’s disease patients that persisted 5 min after the stimulus was removed, indicating stabilization of the internal rhythm generating system and the reintegration of timing networks. These experiments show that complex (rather than periodic) interaction is important for the (re)emergence of $1/f$ structure in human gait behavior.

In conclusion, an optimal level of variability enables us to interact adaptively and safely to a continuously changing environment, where often our movements must be adjusted in a matter of milliseconds. A large body of research exists that demonstrates natural variability in healthy gait (along with variability in other healthy biological signals such as heart rate) and a loss of this variability in aging and injury, as well as in a variety of neurodegenerative and physiological disorders. We submit that this field of research is now in pressing need of an innovative “next step” that goes beyond the many descriptive studies that characterize levels of variability in various patient populations. We need to devise novel therapies that will harness the existing knowledge on biological variability and create new possibilities for those in the grip of disease.

We also propose that the nature of the specific physiological limitation present in the neuromuscular apparatus may be less important in the physiological complexity framework than the control mechanisms adopted by the older individual in the coordination of the available degrees of freedom. The theoretical underpinnings of this framework suggest that interventions designed to restore healthy system dynamics may optimize functional improvements in older adults (Harrison & Stergiou, 2015; Manor & Lipsitz, 2013; Stergiou & Decker, 2011). We submit that interventions based on the restoration of optimal variability and movement complexity could potentially be applied across a range of diseases or dysfunctions as it addresses the adaptability and coordination of available degrees of freedom, regardless of the internal constraints of the individual.

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References

- Amato, I. (1992). Chaos breaks out at NIH, but order may come of it. *Science*, 256, 1763–1764. doi:10.1126/sci-ence.1615321
- Anteneodo, C., & Chialvo, D.R. (2009). Unraveling the fluctuations of animal motor activity. *Chaos* (Woodbury, N.Y.), 19, 033123. doi:10.1063/1.3211189
- Asai, M., Yoshinobu, Y., Kaneko, S., Mori, A., Nikaido, T., Moriya, T., & Shibata, S. (2001). Circadian profile of per gene mRNA expression in the suprachiasmatic nucleus, paraventricular nucleus, and pineal body of aged rats. *Journal of Neuroscience Research*, 66, 1133–1139. doi:10.1002/jnr.10010
- Baik, J.S., & Lang, A.E. (2007). Gait abnormalities in psychogenic movement disorders. *Movement Disorders*, 22, 395–399. doi:10.1002/mds.21283
- Bierbaum, S., Peper, A., Karamanidis, K., & Arampatzis, A. (2011). Adaptive feedback potential in dynamic stability during disturbed walking in the elderly. *Journal of Biomechanics*, 44, 1921–1926. doi:10.1016/j.jbio-mech.2011.04.027
- Boudreau, R.M., Hanlon, J.T., Roumani, Y.F., Studenski, S.A., Ruby, C.M., Wright, R.M., . . . Simonsick, E.M. (2009). Central nervous system medication uses and incident mobility limitation in community elders: The health, aging, and body composition study. *Pharmacoepidemiology and Drug Safety*, 18, 916–922. doi:10.1002/pds.1797
- Buchman, T.G., Cobb, P.J., Lapedes, A.S., & Kepler, T.B. (2001). Complex systems analysis: A tool for shock research. *Shock* (Augusta, Ga.), 16, 248–251. doi:10.1097/00024382-200116040-00002
- Buzzi, U., Stergiou, N., Kurz, M., Hageman, P., & Heidel, J. (2003). Nonlinear dynamics indicates aging affects variability during gait. *Clinical Biomechanics* (Bristol, Avon), 18, 435–443. doi:10.1016/S0268-0033(03)00029-9
- Byrne, J.E., Stergiou, N., Blanke, D., Houser, J.J., Kurz, M.J., & Hageman, P.A. (2002). Comparison of gait patterns between young and elderly women: An examination of coordination. *Perceptual and Motor Skills*, 94, 265–280. doi:10.2466/pms.2002.94.1.265
- Bystritsky, A., Nierenberg, A.A., Feusner, J.D., & Rabinovich, M. (2012). Computational nonlinear dynamical psychiatry: A new methodological paradigm for diagnosis and course of illness. *Journal of Psychiatric Research*, 46, 428–435. doi:10.1016/j.jpsychires.2011.10.013
- Cavanaugh, J.T., Coleman, K.L., Gaines, J.M., Laing, L., & Morey, M.C. (2007). Using step activity monitoring to characterize ambulatory activity in Community-Dwelling older adults. *Journal of the American Geriatrics Society*, 55, 120–124. doi:10.1111/j.1532-5415.2006.00997.x
- Cavanaugh, J.T., Kochi, N., & Stergiou, N. (2010). Nonlinear analysis of ambulatory activity patterns in community-dwelling older adults. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 65A, 197–203. doi:10.1093/gerona/glep144
- Cham, R., Perera, S., Studenski, S.A., & Bohnen, N.I. (2007). Striatal dopamine denervation and sensory integration for balance in middle-aged and older adults. *Gait & Posture*, 26, 516–525. doi:10.1016/j.gaitpost.2006.11.204

- Cham, R., Studenski, S.A., Perera, S., & Bohnen, N.I. (2008). Striatal dopaminergic denervation and gait in healthy adults. *Experimental Brain Research*, 185, 391–398. doi:10.1007/s00221-007-1161-3
- Colwell, C.S. (2011). Linking neural activity and molecular oscillations in the SCN. *Nature Reviews. Neuroscience*, 12, 553–569. doi:10.1038/nrn3086
- Decker, L.M., Moraiti, C., Stergiou, N., & Georgoulis, A.D. (2011). New insights into anterior cruciate ligament deficiency and reconstruction through the assessment of knee kinematic variability in terms of nonlinear dynamics. *Knee Surgery, Sports Traumatology, Arthroscopy*, 19, 1620–1633. doi:10.1007/s00167-011-1484-2
- Deffeyes, J.E., Kochi, N., Harbourne, R.T., Kyvelidou, A., Stuberg, W.A., & Stergiou, N. (2009). Nonlinear detrended fluctuation analysis of sitting center-of-pressure data as an early measure of motor development pathology in infants. *Nonlinear Dynamics Psychology and Life Sciences*, 13, 351–368.
- Delignieres, D., & Torre, K. (2009). Fractal dynamics of human gait: A reassessment of the 1996 data of Hausdorff et al. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 106, 1272–1279.
- Delval, A., Krystkowiak, P., Delliaux, M., Blatt, J., Derambure, P., Destée, A., & Defebvre, L. (2008). Effect of external cueing on gait in Huntington's disease. *Movement Disorders*, 23, 1446–1452. doi:10.1002/mds.22125
- Dossey, L. (2010). Coherence, chaos, and the coincidentia oppositorum. *Explore (New York, N.Y.)*, 6, 339–345. doi:10.1016/j.explore.2010.08.006
- Farajnia, S., Deboer, T., Rohling, J.H., Meijer, J.H., & Michel, S. (2014). Aging of the suprachiasmatic clock. *The Neuroscientist*, 20, 44–55. doi:10.1177/1073858413498936
- Ford, M.P., Malone, L.A., Nyikos, I., Yelisetty, R., & Bickel, C.S. (2010). Gait training with progressive external auditory cueing in persons with Parkinson's disease. *Archives of Physical Medicine and Rehabilitation*, 91, 1255–1261. doi:10.1016/j.apmr.2010.04.012
- Garfinkel, A., Spano, M.L., Ditto, W.L., & Weiss, J.N. (1992). Controlling cardiac chaos. *Science*, 257, 1230–1235. doi:10.1126/science.1519060
- Goldberger, A.L. (1996). Non-linear dynamics for clinicians: Chaos theory, fractals, and complexity at the bedside. *Lancet*, 347, 1312–1314. doi:10.1016/S0140-6736(96)90948-4
- Goldberger, A.L. (2001). Heartbeats, hormones, and health - is variability the spice of life? *American Journal of Respiratory and Critical Care Medicine*, 163, 1289–1290. doi:10.1164/ajrccm.163.6.ed1801a
- Goldberger, A.L., Amaral, L.A.N., Hausdorff, J.M., Ivanov, P.C., Peng, C.K., & Stanley, H.E. (2002a). Fractal dynamics in physiology: Alterations with disease and aging. *Proceedings of the National Academy of Sciences of the United States of America*, 99, 2466–2472. doi:10.1073/pnas.012579499
- Goldberger, A.L., Findley, L.J., Blackburn, M.R., & Mandell, A.J. (1984). Nonlinear dynamics in heart failure: Implications of long-wavelength cardiopulmonary oscillations. *American Heart Journal*, 107, 612–615. doi:10.1016/0002-8703(84)90120-0
- Goldberger, A.L., Peng, C., & Lipsitz, L.A. (2002b). What is physiologic complexity and how does it change with aging and disease? *Neurobiology of Aging*, 23, 23–26. doi:10.1016/S0197-4580(01)00266-4

- Goldstein, B., Toweill, D., Lai, S., Sonnenthal, K., & Kimberly, B. (1998). Uncoupling of the autonomic and cardiovascular systems in acute brain injury. *The American Journal of Physiology*, 275, R1287–R1292.
- Harrison, S.J., & Stergiou, N. (2015). Complex adaptive behavior and dexterous action. *Nonlinear Dynamics Psychology and Life Sciences*, 19, 345–394.
- Hausdorff, J.M. (2007). Gait dynamics, fractals and falls: Finding meaning in the stride-to-stride fluctuations of human walking. *Human Movement Science*, 26, 555–589. doi:10.1016/j.humov.2007.05.003
- Hausdorff, J.M., Cudkowicz, M.E., Firtion, R., Wei, J.Y., & Goldberger, A.L. (1998). Gait variability and basal ganglia disorders: Stride-to-stride variations of gait cycle timing in Parkinson's disease and Huntington's disease. *Movement Disorders*, 13, 428–437. doi:10.1002/mds.870130310
- Hausdorff, J.M., Mitchell, S.L., Firtion, R., Peng, C.K., Cudkowicz, M.E., Wei, J.Y., & Goldberger, A.L. (1997). Altered fractal dynamics of gait: Reduced stride-interval correlations with aging and Huntington's disease. *Journal of Applied Physiology*, 82, 262–269.
- Hausdorff, J.M., Peng, C.K., Ladin, Z., Wei, J.Y., & Goldberger, A.L. (1995). Is walking a random walk? Evidence for long-range correlations in stride interval of human gait. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 78, 349–358.
- Hausdorff, J.M., Purdon, P.L., Peng, C.K., Ladin, Z., Wei, J.Y., & Goldberger, A.L. (1996). Fractal dynamics of human gait: Stability of long-range correlations in stride interval fluctuations. *Journal of Applied Physiology*, 80, 1448–1457.
- Hayden, R., Clair, A.A., Johnson, G., & Otto, D. (2009). The effect of rhythmic auditory stimulation (RAS) on physical therapy outcomes for patients in gait training following stroke: A feasibility study. *The International Journal of Neuroscience*, 119, 2183–2195. doi:10.3109/00207450903152609
- Herman, T., Giladi, N., Gurevich, T., & Hausdorff, J.M. (2005). Gait instability and fractal dynamics of older adults with a "cautious" gait: Why do certain older adults walk fearfully? *Gait & Posture*, 21, 178–185. doi:10.1016/j.gaitpost.2004.01.014
- Hilmer, S.N., Mager, D.E., Simonsick, E.M., Ling, S.M., Windham, B.G., Harris, T.B., . . . Study, H.A. (2009). Drug burden index score and functional decline in older people. *The American Journal of Medicine*, 122, 1142–1149.
- Hove, M.J., Suzuki, K., Uchitomi, H., Orimo, S., & Miyake, Y. (2012). Interactive rhythmic auditory stimulation reinstates natural 1/f timing in gait of Parkinson's patients. *PLoS One*, 7, e32600. doi:10.1371/journal.pone.0032600
- Hsu, W., Chou, L., & Woollacott, M. (2013). Age-related changes in joint coordination during balance recovery. *Age*, 35, 1299–1309. doi:10.1007/s11357-012-9422-x
- Hu, K., Harper, D.G., Shea, S.A., Stopa, E.G., & Scheer, F.A. (2013). Noninvasive fractal biomarker of clock neurotransmitter disturbance in humans with dementia. *Scientific Reports*, 3, 2229. doi:10.1038/srep02229
- Hu, K., Ivanov, P.C., Chen, Z., Hilton, M.F., Stanley, H.E., & Shea, S.A. (2004). Non-random fluctuations and multi-scale dynamics regulation of human activity. *Physica A: Statistical Mechanics and its Applications*, 337, 307–318.
- Hu, K., Meijer, J.H., Shea, S.A., vanderLeest, H.T., Pittman-Polletta, B., Houben, T., . . . Scheer, F.A. (2012). Fractal patterns of neural activity exist within the suprachiasmatic

- nucleus and require extrinsic network interactions. *PLoS One*,7, e48927.
doi:10.1371/journal.pone.0048927
- Hu, K., Scheer, F.A., Buijs, R.M., & Shea, S.A. (2008). The endogenous circadian pacemaker imparts a scale-invariant pattern of heart rate fluctuations across time scales spanning minutes to 24 hours. *Journal of Biological Rhythms*,23, 265–273.
doi:10.1177/0748730408316166
- Hu, K., Scheer, F.A.J.L., Ivanov, P.C., Buijs, R.M., & Shea, S.A. (2007). The suprachiasmatic nucleus functions beyond circadian rhythm generation. *Neuroscience*,149, 508–517.
doi:10.1016/j.neuroscience.2007.03.058
- Hu, K., Van Someren, E.J., Shea, S.A., & Scheer, F.A. (2009). Reduction of scale invariance of activity fluctuations with aging and Alzheimer's disease: Involvement of the circadian pacemaker. *Proceedings of the National Academy of Sciences of the United States of America*,106, 2490–2494. doi:10.1073/pnas.0806087106
- Hughes, A.T., & Piggins, H.D. (2012). Feedback actions of locomotor activity to the circadian clock. *Progress in Brain Research*,199, 305–336. doi:10.1016/B978-0-444-59427-3.00018-6
- Hunt, N., McGrath, D., & Stergiou, N. (2014). The influence of auditory-motor coupling on fractal dynamics in human gait. *Scientific Reports*,4, 5879. doi:10.1038/srep05879
- Kaipust, J.P., McGrath, D., Mukherjee, M., & Stergiou, N. (2013). Gait variability is altered in older adults when listening to auditory stimuli with differing temporal structures. *Annals of Biomedical Engineering*,41, 1595–1603. doi:10.1007/s10439-012-0654-9
- Kembro, J.M., Perillo, M.A., Pury, P.A., Satterlee, D.G., & Marin, R.H. (2009). Fractal analysis of the ambulation pattern of Japanese quail. *British Poultry Science*,50, 161–170.
doi:10.1080/00071660802710116
- Kiss, R.M. (2011). Effect of severity of knee osteoarthritis on the variability of gait parameters. *Journal of Electromyography and Kinesiology*,21, 695–703.
doi:10.1016/j.jelekin.2011.07.011
- Kondratova, A.A., & Kondratov, R.V. (2012). The circadian clock and pathology of the ageing brain. *Nature Reviews. Neuroscience*,13, 325–335.
- Kurz, M.J., Markopoulou, K., & Stergiou, N. (2010). Attractor divergence as a metric for assessing walking balance. *Nonlinear Dynamics Psychology and Life Sciences*,14, 151–164.
- Kurz, M.J., & Stergiou, N. (2003). The aging human's neuromuscular system expresses less certainty for selecting joint kinematics during gait. *Neuroscience Letters*,348, 155–158.
doi:10.1016/S0304-3940(03)00736-5
- Large, E.W. (2000). On synchronizing movements to music. *Human Movement Science*,19, 527–566. doi:10.1016/S0167-9457(00)00026-9
- Li, H., & Satinoff, E. (1995). Changes in circadian rhythms of body temperature and sleep in old rats. *The American Journal of Physiology*,269, R208–R214.
- Lipsitz, L.A. (2002). Dynamics of stability: The physiologic basis of functional health and frailty. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*,57, B115–B125. doi:10.1093/gerona/57.3.B115
- Lipsitz, L.A., & Goldberger, A.L. (1992). Loss of 'complexity' and aging: Potential applications of fractals and chaos theory to senescence. *Journal of the American Medical Association*, 267, 1806–1809. doi:10.1001/jama.1992.03480130122036

- Macintosh, A.J., Alados, C.L., & Huffman, M.A. (2011). Fractal analysis of behaviour in a wild primate: Behavioural complexity in health and disease. *Journal of the Royal Society, Interface / the Royal Society*, 8, 1497–1509.
- Madeira, M.D., Sousa, N., Santer, R.M., Paula-Barbosa, M.M., & Gundersen, H.J.G. (1995). Age and sex do not affect the volume, cell numbers, or cell size of the suprachiasmatic nucleus of the rat: An unbiased stereological study. *The Journal of Comparative Neurology*, 361, 585–601. doi:10.1002/cne.903610404
- Madigan, M.L., & Lloyd, E.M. (2005). Age and stepping limb performance differences during a single-step recovery from a forward fall. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 60, 481–485.
- Mandelbrot, B.B. (1977). *The fractal geometry of nature*. New York: W.H. Freeman and Company.
- Manor, B., & Lipsitz, L.A. (2013). Physiologic complexity and aging: Implications for physical function and rehabilitation. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 45, 287–293. doi:10.1016/j.pnpbp.2012.08.020
- Martens, K.A.E., & Almeida, Q.J. (2012). Dissociating between sensory and perceptual deficits in PD: More than simply a motor deficit. *Movement Disorders*, 27, 387–392. doi:10.1002/mds.24042
- Mohawk, J.A., Green, C.B., & Takahashi, J.S. (2012). Central and peripheral circadian clocks in mammals. *Annual Review of Neuroscience*, 35, 445–462. doi:10.1146/annurev-neuro-060909-153128
- Montero-Odasso, M., Muir, S.W., & Speechley, M. (2012). Dual-task complexity affects gait in people with mild cognitive impairment: The interplay between gait variability, dual tasking, and risk of falls. *Archives of Physical Medicine and Rehabilitation*, 93, 293–299. doi:10.1016/j.apmr.2011.08.026
- Newell, K.M., & Corcos, D.M. (Eds.). (1993). *Variability and motor control*. Champaign, IL: Human Kinetics Publishers.
- Orsucci, F.F. (2006). The paradigm of complexity in clinical neurocognitive science. *The Neuroscientist: A Review Journal Bringing Neurobiology, Neurology and Psychiatry*, 12, 390–397.
- Paterson, K., Hill, K., & Lythgo, N. (2011). Stride dynamics, gait variability and prospective falls risk in active community dwelling older women. *Gait & Posture*, 33, 251–255. doi:10.1016/j.gaitpost.2010.11.014
- Peng, C.K., Mietus, J.E., Liu, Y.H., Lee, C., Hausdorff, J.M., Stanley, H.E., ... Lipsitz, L.A. (2002). Quantifying fractal dynamics of human respiration: Age and gender effects. *Annals of Biomedical Engineering*, 30, 683–692. doi:10.1114/1.1481053
- Roerdink, M., Lamothe, C.J., van Kordelaar, J., Elich, P., Konijnenbelt, M., Kwakkel, G., & Beek, P.J. (2009). Rhythm perturbations in acoustically paced treadmill walking after stroke. *Neurorehabilitation and Neural Repair*, 23, 668–678. doi:10.1177/1545968309332879
- Schmidt, R.A., & Lee, T.D. (2005). *Motor control and learning: A behavioral emphasis*. Champaign, IL: Human Kinetics.
- Seidler, R.D., Bernard, J.A., Burutolu, T.B., Fling, B.W., Gordon, M.T., Gwin, J.T., ... Lipps, D.B. (2010). Motor control and aging: Links to age-related brain structural, functional, and biochemical effects. *Neuroscience and Biobehavioral Reviews*, 34, 721–733. doi:10.1016/j.neu-biorev.2009.10.005

- Shin, S., Valentine, R.J., Evans, E.M., & Sosnoff, J.J. (2012). Lower extremity muscle quality and gait variability in older adults. *Age and Ageing*, 41, 595–599. doi:10.1093/ageing/afs032
- Skoe, E., & Kraus, N. (2010). Hearing it again and again: On-line subcortical plasticity in humans. *PLoS One*, 5, e13645. doi:10.1371/journal.pone.0013645
- Slutzky, M.W., Cvitanovic, P., & Mogul, D.J. (2001). Deterministic chaos and noise in three in vitro hippocampal models of epilepsy. *Annals of Biomedical Engineering*, 29, 607–618. doi:10.1114/1.1380419
- Sosnoff, J.J., & Newell, K.M. (2008). Age-related loss of adaptability to fast time scales in motor variability. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*, 63, 344–352.
- Stergiou, N. (Ed.). (2004). *Innovative analyses of human movement*. Champaign, IL: Human Kinetics.
- Stergiou, N. (Ed.). (2016). *Nonlinear analysis for human movement variability*. Boca Raton, FL: CRC Press
- Stergiou, N., & Decker, L.M. (2011). Human movement variability, nonlinear dynamics, and pathology: Is there a connection? *Human Movement Science*, 30, 869–888 [doi]. doi:10.1016/j.humov.2011.06.002
- Stergiou, N., Harbourne, R., & Cavanaugh, J. (2006). Optimal movement variability: A new theoretical perspective for neurologic physical therapy. *Journal of Neurologic Physical Therapy; JNPT*, 30, 120–129. doi:10.1097/01.NPT.0000281949.48193.d9
- Toebe, M.J.P., Hoozemans, M.J.M., Furrer, R., Dekker, J., & van Dieën, J.H. (2012). Local dynamic stability and variability of gait are associated with fall history in elderly subjects. *Gait & Posture*, 36, 527–531. doi:10.1016/j.gaitpost.2012.05.016
- Toiviainen, P., & Snyder, J.S. (2003). Tapping to bach: Resonance-based modeling of pulse. *Music Perception*, 21, 43–80. doi:10.1525/mp.2003.21.1.43
- Toweill, D.L., & Goldstein, B. (1998). Linear and nonlinear dynamics and the pathophysiology of shock. *New Horizons (Baltimore, Md.)*, 6, 155–168.
- Tranah, G.J., Blackwell, T., Ancoli-Israel, S., Paudel, M.L., Ensrud, K.E., Cauley, J.A., . . . Stone, K.L. (2010). Circadian activity rhythms and mortality: The study of osteoporotic fractures. *Journal of the American Geriatrics Society*, 58, 282–291. doi:10.1111/j.1532-5415.2009.02674.x
- Tranah, G.J., Blackwell, T., Stone, K.L., Ancoli-Israel, S., Paudel, M.L., Ensrud, K.E., . . . Cummings, S.R. (2011). Circadian activity rhythms and risk of incident dementia and mild cognitive impairment in older women. *Annals of Neurology*, 70, 722–732. doi:10.1002/ana.22468
- Vaillancourt, D.E., & Newell, K.M. (2002). Changing complexity in human behavior and physiology through aging and disease. *Neurobiology of Aging*, 23, 1–11. doi:10.1016/S0197-4580(01)00247-0
- Vaillancourt, D.E., & Newell, K.M. (2003). Aging and the time and frequency structure of force output variability. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 94, 903–912.
- Vaillancourt, D.E., Sosnoff, J.J., & Newell, K.M. (2004). Age-related changes in complexity depend on task dynamics. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 97, 454–455.

- Van Orden, G.C., Holden, J.G., & Turvey, M.T. (2005). Human cognition and $1/f$ scaling. *Journal of Experimental Psychology. General*, 134, 117–123. doi:10.1037/0096-3445.134.1.117
- Vinti, M., Couillandre, A., & Thoumie, P. (2010). Does somato-sensory loss induce adaptation of the gait initiation process? *Neuroscience Letters*, 480, 178–181. doi:10.1016/j.neulet.2010.06.017
- Wagner, C.D., Nafz, B., & Persson, P.B. (1996). Chaos in blood pressure control. *Cardiovascular Research*, 31, 380–387.
- Wojcik, L.A., Thelen, D.G., Schultz, A.B., Ashton-Miller, J.A., & Alexander, N.B. (1999). Age and gender differences in single-step recovery from a forward fall. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 54, M44–M50. doi:10.1093/gerona/54.1.M44
- Yamazaki, S., Straume, M., Tei, H., Sakaki, Y., Menaker, M., & Block, G.D. (2002). Effects of aging on central and peripheral mammalian clocks. *Proceedings of the National Academy of Sciences of the United States of America*, 99, 10801–10806. doi:10.1073/pnas.152318499
- Yang, A.C., Huang, C., Yeh, H., Liu, M., Hong, C., Tu, P., . . . Lin, C. (2013). Complexity of spontaneous BOLD activity in default mode network is correlated with cognitive function in normal male elderly: A multiscale entropy analysis. *Neurobiology of Aging*, 34, 428–438. doi:10.1016/j.neurobiolaging.2012.05.004
- Yang, X. (2010). A wheel of time: The circadian clock, nuclear receptors, and physiology. *Genes & Development*, 24, 741–747. doi:10.1101/gad.1920710