Perspective: Why Exercise Is Good and Its Lack Bad for Everything

Abstract: *Evidence of the central value of physical exercise in human health is rampant, yet the fundamental underlying explanation of this universal benefit evades comprehension. The first principles of this underlying effect are found within the laws of thermodynamics and are explicitly outlined within the metabolic field (Schrodinger) as presented herein. To understand the basic mechanism responsible for the universal positive benefits of exercise mandates that the first principle of energy flow be enunciated. “On the dry bones of atoms and the distribution of energy in the universe are assembled the flesh and blood of life” (Prigogine, 1984). The engine of metabolism requires the ready provision of the primal energy first evidenced at the Big Bang as described in The Big Picture.*

Keywords: dis-use; exercise; frailty; metabolism; thermodynamics

Background

Why?

Because it's the Law!¹

The second law of thermodynamics that Sir Arthur Eddington proclaimed is that “the supreme law of the universe” rules and explains all.² Einstein observed

“the Second Law is the only physical theory of universal content which I am certain will never be overthrown.”³ Within its jurisdiction lies the answer to why physical exercise is a primal good.

In today's complex world, physical exercise exists in numerous forms, activities of daily living, occupational, and recreational. It represents the vital activity inherent in the second law of thermodynamics as elaborated by Schrodinger, Dyson, Morowitz, and

to the explosive new field of molecular biology.⁵ These laws of biology describe the first principles of metabolism that constitute the operation manual for life. The chemical forces of metabolism are responsible for all of life's reproductive, growth, repair, and maintenance functions. Schrodinger proposed that all life was an inevitable byproduct of energy flow on matter over time.

Bioenergetics is that part of metabolism that is concerned with the transduction

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Bortz. The processes of anabolism and catabolism are explicit components of physical exercise. Growth and repair both inhere in an active life style.

Erwin Schrodinger was a quantum physicist. In 1943, he delivered a series of lectures at Trinity College, Dublin, titled “What Is life? The Physical Aspect of Living Cells.”⁴ Their precepts are the Rosetta Stone that reveal the universal laws of life. Pauling credits Schrodinger with providing the key insights that led

of energy flow with respect to time and space. It represents the nexus of fundamental physical forces inherent in all life. Bioenergetics is the intersection of nature and nurture. Its centrality has been largely underrecognized.

One hundred years ago Meyerhoff proposed the following hypothesis:

In consequence of the fluid state of the protoplasm and the instability of the cell stuffs, voluntary events of

physical and chiefly chemical nature are going on continuously which aim at a balance of the existing potentials of energy. Since life requires the continuation of these potentials of energy, work must be performed continuously for the prevention or reversion of these spontaneous changes.⁶

For every breath and every step that is taken, for every myocardial contraction, for every tendon stretch, for every muscle loading and unloading, for every neural impulse that are inherent in a bout of exercise a constellation of biochemical reactions including gene expression appear. Physical exercise elicits system-wide alteration in each component of the body.

Amid the seemingly incomprehensible complexity and diversity of these functions, certain universal principles emerge. A few simple rules serve as generic guideposts for understanding life.

Inherent in this translation are the first principles enunciated in the classical field theories of gravity, electromagnetism, the strong and weak nuclear forces, quantum, and the recently described metabolic field (Schrodinger) that encompasses the vast reaches of established theory.⁷

The anatomy and physiology of life are rendered comprehensible by the observance of the universal laws, the fields, and their associated axioms that underlie them. Among the most pervasive are Darwin's Natural Selection and Aristotle's Law of Least Action that Newton paraphrased, "Nature does nothing in vain, and more is in vain when less will serve: for Nature is pleased with simplicity, and affects not the pomp of superfluous causes."

This universality of human design principles should not be surprising when we remember that all of life is made of the same stuff. CHNOPS. Carbon (12%), hydrogen (62%), nitrogen (1%), oxygen (24%), phosphorus (0.2%), and sulfur (0.7%).

Not only does all of life share the same elemental anatomy, its operation manual has been conserved since the bacteria first created the fundamental metabolic

biochemical pathways 4 billion years ago. The tricarboxylic acid cycle (the Krebs cycle) is a precious gift to us from our progenitor bacteria in the remote past.

Acknowledging the universal power of these principles, D'Arcy Thompson in 1917 created the masterpiece *On Growth and Form* in which he surmised that the variegation of nature's forms was the inevitable result of a "diagram of forces," the ultimate effect of energy flow on matter over time.⁸ This book grandly expanded our grasp of physical biology.

Similarly, in his recent commodious book *Scale*, Geoffrey West of the Santa Fe Institute vividly explains how simple power laws reflect how organisms as diverse as bacteria and other unicellular organisms all the way up to the largest mammal, the blue whale (27 orders of magnitude) all exhibit a similar relationship of metabolic rate to mass.⁹ This extraordinary linkage derives directly from the universal nature of life's design, and its kinetics.

Nano-Anatomy

Cells represent the smallest unit of life. The human body consists of 100 trillion cells. Each cell contains 200 trillion atoms, which is more than all the stars in the universe. Each cell has a specialized role to play as a tiny component of the life of the organism. Inside the cell are the mitochondria, life's tiny batteries that perform the critical energy producing function. All cells, except red blood cells, contain mitochondria, their number and density varying according to the metabolic state. The average liver cell contains about 500 mitochondria while an exercising muscle cell contains many thousand.

Azbel, in his paper "Universal Biological Scaling and Mortality," invokes the principle of superuniversality to calculate that each body atom metabolizes 10 oxygen molecules per lifetime, arguing that within a few percent the total energy expenditure per lifetime is an approximate constant across all taxa. This implies that all organisms live the same amount, 200

kcal/g/lifetime, and thereby have the same number of heartbeats.¹⁰

This superuniversality is held to be the inevitable result of the laws of metabolism. Physical exertion sends a strong stimulus. Every structural component that supports the cell's energy supply function is upregulated in direct proportion to the energetic demands on the cell. The structural and functional results of movement are captured by the new term *symmorphosis* introduced by Weibel and Taylor.¹¹ Each individual component of the respiratory and circulatory systems reacts to a change in energetic requirement by a quantifiably matched structural response. Cardiac output, arterial size, capillary density, membrane permeability, enzyme levels, and mitochondrial number all scale quantitatively to the level of energetic demand.

Without such linkage a rate-limiting step would prevent an adequate quantitative responsiveness to environmental challenge. The structural response to a bioenergetic prompt accounts for phenotypic plasticity through the device of symmorphosis.

Thermodynamics Yields Plasticity

In an important article in *Nature*, Richard Strohmman observed,

The laws of thermodynamics are intimately related to the phenotype of the organism through the agency of dynamical systems. Sadly this central point has been all been ignored in the rush to find agent-based genomic-proteomic explanations. Looking back that substitution of agents for agencies must be recognized as an epistemological error of great moment.¹²

Strohmman's critical observation draws attention to the basic fact that the human intellect has more confidence when it addresses things rather than processes. Being yields greater certainty than becoming. The role of agents rather than agencies has been dominant.

Despite its ubiquity, medicine has failed to appreciate the central role of plasticity and anabolism in determining lifelong health. While shape appears to be constant, the content, over time, is dynamic. Samuel Butler observed that the differences between the same individual at birth and at age 80 were greater than the differences of a newborn infant of one generation and a newborn of the next. "Life is matter that chooses".¹³ Robert Burns wrote, "Look abroad at nature's range. Nature's mighty law is change."¹⁴ Darwin observed, "It is not the strongest of the species that survives. Nor the most intelligent that survives. It is the one that is most adaptable to change."¹⁵ Phenotypic plasticity writ large. How the hand is played is more important than the cards that are dealt. Ninety-eight percent of the atoms of the human body turn over each year.

Yates's substitution of the important new term *homeodynamics* for the classical but discarded term *homeostasis* is key.¹⁶ Margulis and Sagan consider life to be a verb rather than a noun.¹⁷ Life is distinguished not by its chemical constituents but by the behavior of its chemicals. The gene map of identical twins is virtually identical in their youth but as time passes the pattern splays as the result of differential environmental impacts.¹⁸

Patel has introduced the important term EWAS, Environment Wide Association Study, to describe the plasticity of the human phenotype.¹⁹ This term supplants the more used rubric of GWAS, Gene Wide Association Study.

Harold Morowitz in his book *Energy Flow in Biology* proclaims that the flow of energy through a system acts "to create the high degree of molecular order in living systems."²⁰ This order follows from the present principles of present-day physics and does not require the introduction of new laws. "Biologic phenomena are ultimately consequences of the laws of physics." All of the above efforts constitute what Yates has proclaimed to be a form of "physical biology," a convergence of classical physics and the avalanche of new

information that emerges from molecular biology.²¹

The communion of physics and biology is integral to biology and its plasticity. Darwin's natural selection is a reflection of the second law. Use it or lose it is a colloquial restatement of Spencer's "Survival of the Fittest." A further reflection of the basic forces at work was provided by a member of the audience at a recent meeting, "If and who you are depends on what you do, then if you don't, you aren't." Steve Blair's critical article "Physical Fitness and All Cause Mortality" is the emphatic endorsement of the benefits that fitness yields to the phenotype.²² Fitness confers a 30-year survival advantage.

Plasticity is inherent to all life. The reactivity of the plant world is dependent upon where the plant lives, its ecosystem. Blowing on a plant stem immediately provokes a large jump in DNA activity.²³

Plasticity for the animal world is dependent upon its movement capacity. The evolutionary history of every species is a record of its movement. The diaspora of the human evolutionary tale indicates a transition from East Africa to China in 10 000 years. This would require an average rate of movement of 1½ km per year or 15 km per generation.

Descartes' famous conclusion, "cogito ergo sum" should more properly be restated, "I move ergo sum."

Physical Exercise as an Evolutionary Force²⁴

Leonard and Robertson²⁵ propose a bioenergetic model to examine changes in metabolic requirements over the course of human evolution. Energy expenditure is positively correlated with daily range and dietary quality. Within the fossil record the total energy expenditure of the Homo Erectus stage of development is 35% to 55% greater than the preceding Australopithecine's, indicating a greater range to fulfill the nutritional requirements.²⁶ Furthermore, they suggest that this jump up in bioenergetic pattern may underlie the extraordinary growth in brain size seen

in the homo lineage. Others have explored this possibility as well.^{24,26} The hunter-gatherer life style connotes higher energy expenditure in pursuit or escape strategies or both.

Movement serves both nutritional and reproductive demands. Many migratory patterns are stupefying in their scope.

Epidemiology of Physical Exercise

The godfather of the field of epidemiology of exercise was Jeremy Morris who died in 2009 at age 99½. His article in *Lancet* in 1953 was the sentinel observation that the London conductors had substantially less coronary disease than did the bus drivers, presumably due to their more active life style.²⁷ Subsequently he extended this insight into postal workers. Those who walked had less disease than those who rode. In 1970, Paffenbarger surveyed a cohort of longshoremen and confirmed the association between physical labor and well-being.²⁸ Following this he enlisted his fellow Harvard alumni to establish a dose-response relationship between physical exertion and well-being.²⁹ Fries derived data from a local Stanford exercise group and showed that their increased activity extended to disability as well as mortality.³⁰ Jean Mayer correlated occupational history with caloric expenditures.³¹ Many recent studies have explored the deleterious effects that our newfound cultural sedentism has on our well-being. Our muscles are at risk of becoming vestiges. The electronic age is dangerous. The rush to provide activity monitors is a hopeful development.

Clinical Medicine

Exercise Is Medicine is a public health initiative cofounded by the American College of Sports Medicine and the American Medical Association 10 years ago.³² Its mission is to enlarge public awareness of the central role played by physical fitness in health promotion. This effort has been recognized by dozens of other organizations both in America and

abroad. It identifies the fact that fitness is a virtual panacea, apparent since Grecian times. The Olympic Games are an enduring emphatic celebration.

Despite volumes of supporting data, clinical medicine has been lethargic in promoting the value of physical exercise. So too, financial incentives have lagged in addressing the huge gains that would accrue were physical fitness incorporated as a prime goal of a healthy lifestyle.³³

Several authors have proposed different rubrics that describe the variety of pathologies that are attributable directly to physical inactivity. In 1961, Kraus and Raab formatted Hypokinetic Disease.³⁴ Its components were coronary heart disease, obesity, diabetes, and low back pain. In 1982, I proposed the entity that I called the Disuse Syndrome.³⁵ It included cardiovascular vulnerability, musculoskeletal fragility, metabolic instability, depression, immunologic susceptibility, and precocious aging (frailty). As such it represented a reciprocal of the formulation that Hans Selye proposed called the General Adaptation Syndrome in which the organism is abutted by too much energy, commonly termed “stress.”³⁶ In 2004, Lee and Booth proposed the Sedentary Death Syndrome, which they published in the *Canadian Journal of Applied Physiology*.³⁷ Its emphasis was on a possible genetic basis for physical inactivity particularly as it relates to diabetes.

The diverse pathologies enumerated in the above propositions are notable for their heterogeneity. However, all of them are predictable results not of a specific pathogenic agent but are directly due to a diminished (disuse), or increased (stress), flow of energy through this system.

My personal bout with atrial fibrillation was an explicit result of my habitual pursuit of marathoning that remodeled my myocardium in such a way as to tent the septum and its conduction fibers and provoking the arrhythmia. For better, or for worse, the body becomes what it does.

Aging

A comprehensive and fundamental understanding of the process of aging is

lacking. In 1951, Peter Medawar delivered a lecture at University College, London, and called the process of aging, “An unsolved problem of biology.”³⁸ In 1995, Hayflick wrote, “We don’t know the explanation for aging.”³⁹ In 2013, Rando and Chang called the underlying cause of aging to be “one of the central mysteries of biology.”⁴⁰ Medawar predicted that the solution to the problem of aging will “lead to a new era in the biological history of the human race.”³⁸

However, more recently Hayflick proclaimed aging is no longer an unknown.⁴¹

When faced with a vacuum of competence, Dyson insists that there are 2 essentials involved in establishing new understanding.⁴² These are new ideas and new tools.

The New Ideas about aging are attributable to Schrodinger’s salient lectures at Trinity in 1944. The New Tools involved in establishing this new understanding about aging are a direct result of recent nanotechnology. The availability of the atomic force microscope, AFM, provides analytic resolution that is 1000 times more powerful than the strongest current optical microscope.⁴³ It yields the details of the decay in molecular fidelity and function that are the hallmarks of aging.

Nano-Storm

The molecular storm⁴³ resulting from the collisions of water and protein molecules, and observable with the AFM, is the likely proximate cause of many aging-associated phenomena. A great deal has been written about the numerous epiphenomena of aging. Many have been implicated as being the prime mover of the process of aging, but reflection reveals that they are likely resultants rather than causes. Among these are the free radical theory,⁴⁴ the shortening of telomeres,⁴⁵ misfolding of proteins,⁴⁶ genetic defects,⁴⁷ and DNA damage.⁴⁸ Each of these proposals is accompanied by data that indicate that all of these diverse processes are lessened or reversed by

physical exercise. For example, Tarnopolsky utilizing a genetically modified mouse that mimics the syndrome of progeria found that an exercise protocol involving 5 months of endurance exercise induced systemic mitochondrial biogenesis and prevented genetic mutations thereby extending life.⁴⁸ “Systemic mitochondrial rejuvenation through endurance exercise promises to be an effective therapeutic approach to mitigating the mitochondrial dysfunction in aging and associated comorbidities.”

The release of the important compounds heat shock proteins with exercise may underlie much of this generic reversal. They are known to be potent modifiers of the damage caused by oxidative stress.⁴⁹ The change in cellular redox potential accompanying exertion is another contributing basic mechanism.⁴⁴

Hayflick’s claim for the knowability of aging⁴¹ is accounted for by the emerging technology currently under development that provides insights into the innermost cosmos of the nano-world. Feynman’s epochal pronouncement of “lots of room at the bottom” heralded an exploration of the very, very, very small, the basic reduction of matter to its tiniest components, atoms, from which all else derives, structurally, as well as functionally.⁵⁰

On the dry bones of the nature of atoms, and the distribution of energy in the universe are assembled the flesh and blood of Life. (Ilya Prigogine⁵¹)

“A new tool is valuable when it yields novel insights into seemingly opaque or disconnected facts and data.”⁴² Several years ago at an Intel Student Science Fair, 6 of the 10 assembled Nobel laureates acknowledged that their breakthrough contributions were the direct results of a new technology that allowed insights that were previously not susceptible with the tools then available.

Robert Hooke, acknowledged as the first developer of the microscope wrote in 1665,

It has been our principle endeavor to enlarge and strengthen the senses by outward instruments. By this means we find that those effects of bodies, which have been commonly attributed to qualities and those confessed to be occult, are performed by the small machines of nature which are not to be discerned without these helps.⁵²

Science's Award for Breakthrough of the Year 2016 went to the development of an optical instrument, called the interferometer.⁵³ This new tool allows demonstration of gravitational waves, a fundamental challenge that goes back to Einstein's era. This new knowledge about aging provided by New Ideas and New Tools effectively supports Hayflick's "knowability" observation that aging is no longer an unknown.

Conclusion

The generic value of physical exercise for most of humanity's deficits finds its explanation in the array of new Science that converges from many physical, chemical, and biologic sources. The body is best conceived of as a system rather than a collection of components. Furthermore, the system is defined as a dynamic whole in which the flux of energy is central to function, metabolism. Life is further understood in terms of the homeodynamic relationship with the environment, external and internal, that yields lifelong plasticity in structure and function.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

Not applicable, because this article does not contain any studies with human or animal subjects.

Informed Consent

Not applicable, because this article does not contain any studies with human or animal subjects.

Trial Registration

Not applicable, because this article does not contain any clinical trials.

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