

Executive Summary – Healthy Matters

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The first book in this series, Redox Matters, introduced the foundational redox signaling biology that orchestrates everything related to life, energy, health, and disease. In this book, Healthy Matters, I will build upon this grounding to translate the principles of redox signaling into an empowering old, yet very new, Redox Lifestyle.

As you proceed, it will be helpful to keep in mind the basic ground rules of what “redox” is and how it works in the body. It is upon these principles that life exists! And the degree to which these principles are followed, is the degree to which health is enjoyed. These are principles. These are rules. This is *natural law*!

The designs of our universe from its broadest expanse to the tiniest parts of sub-cellular space, rely upon the creation and movement of energy, first in the form of photons and then through the movement of electrons and their influence along many metabolic and physiologic pathways. This system is uniquely designed to transfer power from the ultimate source of all energy to the end user. These laws govern everything and give life-force to everything. Although recently discovered, they have always existed!

As this translates to the human experience and the biological world we live in, the transduction or movement of electrons from one molecule to another, from one atom to another, is the essence of everything! They play by their rules, not the rules we make up for them or wish that they were. It is these rules that matter! When we bend or break ourselves against these rules, we bend and break! If we follow them, we heal and stay strong!

The objective in Redox Matters and here in this book Healthy Matters, will be to simplify and translate this vast and deep redox science to the extent possible into how following these laws support a healthy lifestyle – what we will call a “Redox Lifestyle.” This really is ‘the bottom line!’

Because this is grounded in redox biology, it will help to read or review Redox Matters and keep in mind at least a basic understanding of reduction and oxidation as it relates to redox biology. This will serve you well as you begin to apply these principles in making daily, if not hourly decisions about your health in the form of food, drink, shopping, exercise, activity level, supplementation, mental and emotional state, and much much more.

There is no shortage of information in the public space, and many voices and vested interests who would persuade and entice you to their ideology, products, and services. Some of this information is well grounded. However, much is also conspiringly deceptive. Knowing the difference between the two is helped by being informed and aware of the grounding rules of redox science - or in other words, knowing how the cell thinks. When you know the rules, you can make informed decisions about your meal planning (energy metabolism, polyphenol consumption, and nutritional ketosis, in ‘science-speak’), your activity level (hormesis and exercise), managed cellular repair (autophagy) - and your medical care (how to prevent the need for).

As habitual lifestyles shift toward a more robust and responsive redox lifestyle, you will begin living by the rules the universe designed, and not as marketers, taste buds, or habits want them to be.

Reduction Oxidation and Metabolic Function

The very process of energy metabolism (Krebs cycle in mitochondria) relies integrally on the movement of electrons between molecules that are reduced and oxidized in a continuous chain of bioelectrical reactions. Food is the fuel that provides this energy source to the body – effectively transferring the sun’s energy through the food chain into our bodies. We digest and process it and extract this biological energy in the form of ATP/ADP molecules which power life.

Along the way, a myriad of reactions occur that are dependent on, and can be manipulated by the type, amount, and quality of this fuel source, and the amount of glucose, fatty acids, and amino acids which are present in the blood stream and body - over time.

The type, amount, and quality of this food/energy source, along with the timing of its consumption, are all independent variables. They are the factors tightly linked and interwoven into the fabric of our health. Varying any of these variables has profound influence over how this energy metabolism functions and the degree of cellular function it supports. Or does not!

Factors related to where and how energy comes from and how its by-products regulate health and disease, are more important than any other consideration in a “lifestyle” discussion. Of everything a person can do to improve or re-establish their health, nutrition with all that involves is more influential than anything else! We are what our cells are, which is why “we are what we eat.” And - this is also why “you can’t outrun a bad diet.” Nutrition trumps everything!

This is because chronic metabolic disease is a consequence of the fouled and mismanaged conversion of food into energy, along with the mishandling of the redox platform – all of which sabotages cellular function (a result of the Standard American Diet, SAD, which doesn’t help with “Healthy Matters”).

Through all of this, oxygen is the vital ingredient in the process. Oxygen acts integrally with redox-couples and the electron transport chain, to act as the ultimate electron acceptor within energy metabolism, and in creating many oxygen derivatives that are essential redox signaling messengers. This is what makes oxygen so vital to biological life. Without it, electrons do not flow, energy creation ceases, and cellular communication stops.

However, inside mitochondria the reduction of oxygen is not a complete process. This means 2-3% of the oxygen molecules remain in an oxidized state - meaning they are not fully reduced (as we will learn, this is an important design feature and should not be extinguished outright!). This incomplete reduction of oxygen creates a reactive oxygen molecule called “superoxide.” This molecule is then converted to hydrogen peroxide (by the antioxidant superoxide dismutase), which is then converted to carbon dioxide and water by glutathione.

These molecules are used in the immune system to help degrade and kill bacteria (the “oxidative burst” of phagocytosis in white blood cells) as well as to help regulate cellular function for self-renewal and preservation.

However, within and alongside these processes, and because they are still ‘reactive oxygen species,’ these altered oxygen molecules also become a source of oxidation and damage within the cell – especially if left

unchecked. This produces damage to cell membranes and proteins, including DNA, and causes enzymes and proteins to fold and twist improperly, thereby altering their function. Taken together, all of this damage and the changed 'reduction-oxidation' (redox) state of the cell, affect cellular function.

Much of the damage these oxidants cause from this state of elevated oxidation results in inflammation. This elevated state of chronic oxidation and inflammation is compounded when because of aging and disease, the body is less able to respond in healthy ways to this oxidation.

Alterations in the way mitochondria burn fuel (energy metabolism) affect mitochondrial function, and this mitochondrial dysfunction affects the process of healthy energy metabolism. These cyclical effects are intensified from having too much energy (being overfed), having problems with cellular metabolic function (insulin resistance), and from impaired cell function due to poor redox signaling (aging, poor nutrition). Collectively they lead to higher amounts of oxidation from the mitochondrial dysfunction they create.

Problems with food quality (processed food), outward toxicity, undue radiation, poor sleep, untoward stress, hypoxia, and infection (to name a few) also contribute significantly to increase this state of cellular oxidation stress.

Compounded together – the internal oxidative stress from energy production, and the oxidation created by the external environment, profoundly impacts the cell.

The Sea-Change in Cellular Defense and Renewal

The prevailing belief has long been that the solution for these problems of oxidation and free radicals was to take antioxidant supplements. Vitamins and plant-based antioxidants have been used for decades to reduce highly reactive molecules generated in the creation of cellular energy. This practice is so well entrenched in our society and within wellness circles that it is viewed by many as "the Holy Grail" of prevention and health. And to a limited extent, they can 'work.'

In fact, a thriving supplement industry has grown up around this idea, which is expected to reach \$9 billion by 2026 with an annual growth rate of 5.3% per year (Antioxidants Market Size, GlobalNewswire.com). The prevailing belief of many is that 'normal' nutrition was not sufficient to provide the quality of plant-based polyphenols needed for cellular repair and antioxidant function. Considering the state of the agricultural and food production industries, a good case can be made for modest supplementation. This has resulted in much debate, an abundance of 'junk science,' and a great amount of commercial competition.

However, there has been a sea-change of late - a substantial change in understanding about the other role oxidation plays inside the body. It isn't all bad after all! The sea-change in thought isn't so much about the merits of antioxidant usage in controlling oxidation, as it is about the role of oxidation itself.

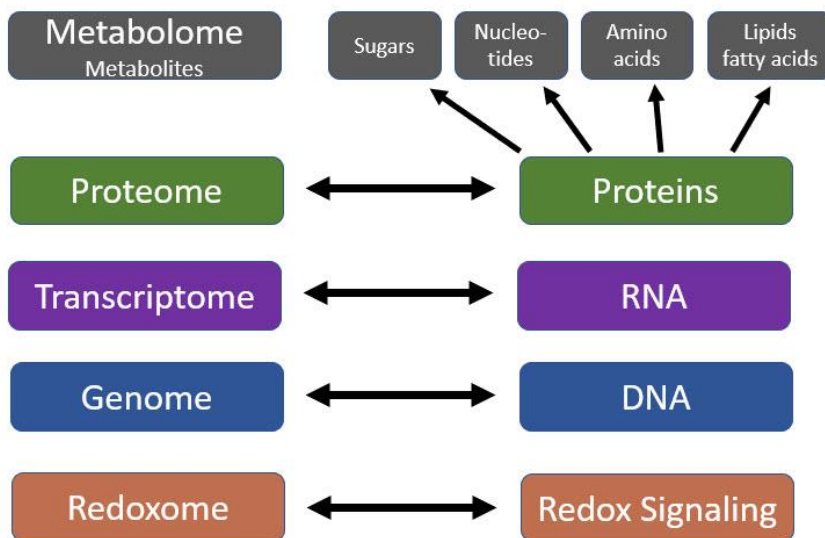
Rethinking and establishing new guidelines for nutrition and antioxidant usage based on this emerging redox-based science, is the sum and essence of the redox lifestyle – and is the only path to health, wellness and anything that resembles anti-aging. To be sure there is a proper place for supplementation, but it is often far different from what many suppose. As it turns out some oxidation is good, and it should not be overly suppressed! In fact, to some degree it should be encouraged – but only if done 'right.'

This is a paradigm shift of massive proportions because it affects everything in the “modern” world of ‘enlightened’ healthcare. It ties directly to the core rules of a cell’s ability to detect stress and execute a responsive action which protects itself in the face of challenging conditions – be they self-imposed or otherwise. Ultimately, this is about the definition of health itself. It is what defines our “Inner Doctor” and is the science of using lifestyle to activate its power in our life.

To be sure, emerging science is showing us that oxidants are not wholly the villains they have been made out to be. In fact, they are important and essential in their role as the primary signaling molecules which activate pathway genes - which in turn drive healthy genetic expression. Because these energized molecules are created in the mitochondria in the reduction and oxidation reactions of energy metabolism, and because they are used ‘downstream’ in other redox reactions to modify and manage cellular functions, they are called redox molecules, or redox signaling molecules.

Redoxome

This has led to the development of a new science discipline called the “Redoxome.” We have known about other science “-omes” for decades (namely the metabolome, proteome, transcriptome, and genome). Each one refers to a different level of the workings of the biological body ranging from the genotype outward to the phenotype – in other words from the hidden cellular genomic programming to how their work appears in real life. This new deeper Redoxome science is the ‘granddaddy’ of them all! In fact, it sits



at the bottom and foundation of all the others.

Each of the established -omes has extensive science and practical medical application to healthcare and treatment. Each can be measured and diagnosed and “treated” with medications when they are not working well. This will continue to be so forever.

Treatment for problems seen within the higher-level -omes allows doctors to intervene and manage signs and symptoms, prolong life, and make life more enjoyable and functional. There is a place for that! However, because “treatments” rarely if ever reach the Redoxome level where the “root-cause” originates, true wellness cannot be assured or maintained.

This is because problems in the higher more visible -ome levels occur due to problems upstream, or said differently, in the more foundational level of the Redoxome. Chronic lifestyle diseases will not resolve on their own or through “treatment” of symptoms, unless or until the foundational metabolic redox-level problems are addressed through corrections in lifestyle and energy metabolism and improved redox functioning.

Because this new category in health of the Redoxome is at a level below the genome, it is sometimes referred to as the “epigenome.” This give it influence upon and overlays the DNA, controlling and modulating how genes express – good and bad.

Broadly speaking this is all referred to as the “redox landscape.” How these principles of redox signaling function and operate within this landscape is referred to as the *redox species interactome*.

Ultimately, the answers to any questions about how cells work and the disease conditions which result when they are impaired, are found at this level. The Redoxome is wholly concerned about how the body senses stress and responds to it. This is a critical proposition for the survival of any and all living organisms with environmental stress, whether from internal or external sources. These collective stresses, and how the cells respond to them determine metabolic function, metabolic health, and metabolic disease.

Hormesis and the Redox Switch

At the heart of the Redoxome platform is the discovery that mild intermittent stress is protective to the body, not harmful. Mild intermittent oxidative stress provokes an adaptive cellular response governed by redox molecules. This awakens internal mechanisms which improves survivability, counters disease, and improves health.

The redox principle which governs this marvelous ability is the principle of hormesis. The discovery and application of this concept finally clarifies the reasons why bio-oxidative, mitochondrial-focused, and redox-based systems and supplements have positive effect on cellular health. It clearly explains the two-sided effect of oxidation within a cellular environment – good and bad.

The concept that every person has a hormetic zone, lives each day on “the hormetic curve,” and utilizes everything in their lifestyle knowingly or unknowingly to impact this principle – can be life changing!

This speaks to the far-reaching effects of oxidative stress across the entire system as a whole, as well as the importance of following the innate “rules” of the cell and the maintenance of homeostasis and cellular repair. It also speaks to solutions that address the deficiencies and dysfunctions that occur at the cellular and sub-cellular level. It also explains why improved lifestyle measures are effective in promoting healthy outcomes, because they play on these same pathways to increase native redox signaling.

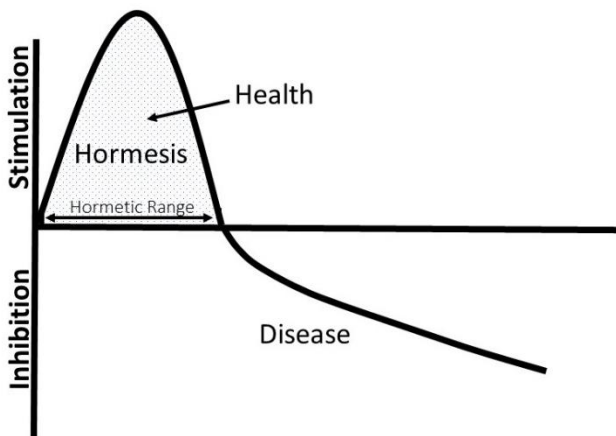
These pathways and mechanisms in the Redoxome contain many redox regulatory “switches” and systems which are responsive to changes in oxidative status. This is the ‘grand secret’ to health! The *modus operandi* and biological mechanism of action for how the body senses, detects, interprets, and responds to changes in oxidation (i.e., stress), is that redox-sensitive molecules stimulate pathway genes to activate and call for a defensive and reparative response. This is called *stress adaptation*. The degree of success in this adaptation ultimately determines the resulting degree of health or disease the organism experiences.

Again, this is the principle of hormesis in action. Small amounts of oxidation challenge the cell apparatus in a way that it responds with cellular defense and repair. Large amounts of the same agents of oxidation provoke inflammatory disease. However, mild levels of oxidative stress within the physiologic hormetic zone, constitute the basis of understanding for everything that results in health. Anything that promotes health does so because it enlivens the redox-sensitive pathways which is what activates cellular defenses and repair. Period!

Within this rule lives the explanation for how good nutrition, exercise, stress reduction, infection control, and good sleep produce and maintain health - and how their opposites lead to disease. This makes positive lifestyle measures a bio-oxidative stimulus to the cell. This means they respectively produce a mild or sub-toxic level of oxidative stress, which in the throughput of the redox interactome causes the sensing mechanisms to upregulate pathway genes, which then activate nature's very own "Inner Doctor."

Recall that redox molecules are not "standard" biomolecules. They are electrically charged reactive species. As such they have the ability to interact with each other, exchanging cellular 'information' by way of bio-electrical action up and down and across the landscape, possessing an extended web of intra- and inter-cellular interactions throughout the cellular space. Because of this they are predisposed to react with redox agents and redox-sensitive sensors. As such they can switch on and switch off pathway genes as dictated by the source and level of ambient oxidative stress in the cell. This defines the "Redox Landscape."

In science-speak, this describes the pleiotropic roles of redox molecules. This means that one molecule or process participates in many physiological processes in an amazingly complex array of biological reactions.



These are set in motion to regulate an organism living in a constantly changing environment and continuously synchronized across the body at all times. This management of the many different biological processes in the body, often unrelated in purpose and function, is connected together by the same redox mechanisms, using redox-sensitive sensors to conduct the business of the cell. It is a "one-to-many" model that runs contrary to the reductionist "one-to-one drug model" of modern medicine.

This is in part what makes the two approaches to health so disparate and hard to reconcile at this level. It also explains why redox molecules cannot be considered in the same light as drugs (which operate on specific receptor sites with specific actions).

This new category of redox health demands that supplements and redox lifestyle measures be viewed with different expectations than traditional healthcare and medications. The objectives are to correct redox deficiency and target base-level cellular dysfunction - and not to suppress symptoms which occur as a result of that dysfunction.

This defines the difference between *inter-vention* and *pre-vention*. Correcting redox deficiencies is about prevention and about awakening the *Inner Doctor* so that cells can self-correct the health problems which

originally came about from dysfunction. Intervention is generally about mitigating the effects of the dysfunction – and to intervene in life-extending ways (lifespan) - thus preventing morbidity from becoming premature mortality.

Different from mainstream and pharmacologically based medicine, the business of the Redoxome is to manage energy metabolism, bioenergetics, antioxidant defenses, the immune system, cellular 'repair and replace' mechanisms (cell cycle), and more. The vertical "redox spine" connections which interconnect all of the parts and processes through the interconnecting redox pathways depend on and use the same redox molecules that are created in the cell from the creation of energy in a saline salt-water environment within mitochondria. The same is true for the redox-related functions within the horizontal redox landscape, operating with synergy throughout the Redoxome.

Ironically, thinking that they were categorically bad, these redox molecules have been and still are maligned and targeted by well-meaning but (now) uninformed health professionals and health enthusiasts, who attempt to discount their importance or to eliminate them altogether through the use of antioxidants (the old paradigm that all oxidation is bad).

Redox Supplementation

Today, "the rest of the story" has come out and is changing everything. It is time for a new landscape and a new lifestyle. These are the (new) rules of the cell, where the truth is found in balance and in not suppressing nature's mechanism so carefully designed for its own protection and repair.

This is why the discovery and breakthrough of stabilized redox signaling molecules is so important and significant. Almost regardless of the degree of insult or stress, a supplemented mild oxidative stress operating within the hormetic curve can produce and enhance these nature-bound mechanisms. They "work" because they adhere to the rules laid down by nature itself. They provide a significant advantage in helping manipulate the redox landscape for good - by providing a bio-identical tool to activate redox-sensitive switches and healthy pathway genes.

This new chapter of stabilized redox in healthcare had its humble beginnings in a bioresearch laboratory. Understanding the various roles which reactive redox molecules play in the human body, researchers set out to duplicate this process by fractionalizing saline, or salt water, into its component parts (in real life called ROS / redox molecules). They discovered that while the mitochondria produce them during energy metabolism, they can also be created and stabilized in a laboratory setting from the same materials mitochondria use, saline - in a process of physics called electrolysis. Their original objective was to duplicate the body's ability to make these native molecules, and to create new solutions for very troubling diseases which hijack the body's immune system, and which create distressing amounts of inflammation by-products which can profoundly injure its victims.

This effort fell short not because they weren't successful, but because the researchers were too successful! Because they are native to the body and have no toxic effect at any dose, they were unable to qualify it for drug therapy, and accordingly developed it as a supplement. Now broadly available, this adjunctive solution fits perfectly with a redox lifestyle strategy to support all cells of the body. It does so through the principle of hormesis and redox-sensitive switches which help the body manage genetic expression. Rather than being a specific solution to a narrow base of specific diseases, it is now a redox-

based solution for redox deficiency generally - which applies the mild hormetic-based oxidative stimulus needed to upregulate healthy pathway genes.

This discovery is one of the most important breakthroughs in health today because redox signaling molecules are the deepest cell-signaling messengers ever discovered. They work and live at the interface of energy and matter where cellular communication activates biological programming and modulates all cell processes – including the energy of life itself.

When combined with living a more complete Redox Lifestyle - which is the point of this Healthy Matters book - it becomes a powerful strategy for the proper management and support of the Redoxome. Ultimately, this is the key to antiaging medicine, wellness and in awakening the “Inner Doctor!”

The Redox Lifestyle

This is where the metabolic dynamics of energy metabolism and metabolic flexibility enter the picture. The slight nutritional stress from low carbohydrate consumption (low blood glucose and low insulin levels) produce a mild increase in oxidation (nutritional stress) within an individual’s hormetic zone, which induces a redox state that upregulates cell-protective genes which protect health. They are responsible for inducing autophagy, and apoptosis when needed, and for activating cellular antioxidant defenses which powerfully affects metabolic health. All of these are at their base, redox processes borne of redox-sensitive mechanisms and transcription factors that drive gene expression and cellular response. In other words, mild oxidative stress produces a stress-adaption that has been conserved to help assure survival and health. Follow the rules! Natural law!

The science of the role of redox molecules and the redox switches which control gene expression is an exciting discovery. It explains the usefulness and role of ROS oxidants inside a cell and how they can be manipulated with nutrition, exercise, stress reduction, sleep, infection management, and supplementation to optimize our health.

While it is still true that too much oxidation is dangerous and creates inflammation and disease, it is refreshing and empowering to discover that a small mild amount of controlled oxidation plays such an important role in activating cellular health. This places immense control for better health directly in our own hands – and mouths! This forms the basis for how a person can create and manage a redox lifestyle for their own life.

This is what gives redox-based lifestyle factors such great power for hope and change to improve health. It is why lifestyle matters.

Regardless of whether it is about primary, or secondary prevention, making improvements across the Redoxome is always helpful. This strategy always works – whether it is “felt” or not!

Without this new knowledge and ability, we remain victims of our own ignorance and the persuasive marketing agendas, ideologies, and even guidelines that too often run counter to the rules cells operate with.

These rules rule! They were designed this way and have been conserved in nature throughout all time and are grounded in the foundations of life. They provide answers to some of the most important and basic biological concerns.

As you read this book and its companion Redox Matters, you will discover answers to these and many other questions that are directly affecting your life. More importantly, you will learn to ask better questions, so that you get better answers! For example:

- What is cellular biological stress?
- How is cellular stress created?
- How does a cell know when it is in trouble?
- How does the cell (and body) respond to this stress?
- Is the response to stress good or bad?
- Is oxidation always bad? Or can it be helpful?
- What is the relationship between oxidation and inflammation?
- How does a cell repair itself when damaged, and how does it restore balance and improve its function?
- What can I do to better follow metabolic and redox rules and improve my life?
- If I need to make changes to my lifestyle, which are the most important?
- What supplements are truly health-friendly?
- What supplements work the best with the Redox environment?
- How can I sort through the confusing and conflicted voices of health advice?

With a better understanding of the rules of how your personal Redoxome functions, you will better recognize and sort through the shortcomings, flaws, and half-truths in the world of nutrition and health advice around you. Knowing these rules will allow you to make better choices which will activate cellular renewal, and which will change the trajectory of your health and healthspan.

This is more than a philosophical construct. It is more than an ideological bias. It is about learning the natural laws which dictate how cells function, and then aligning and positioning your lifestyle to be in accord with those laws.

The redox-driven science and lifestyle is not an irrelevant philosophical or theoretical abstract! It is very real! In fact, it is the only true 'doctrine' for how healthy cells work. Redox-driven stress-adaptation is real science - based on biochemical, bio-electrical, and physiological truths.

Governed by these laws, they operate to impact hormesis, energy metabolism, nutritional ketosis, autophagy, redox-sensitive transcription, pathway gene activation, redox signaling, metabolic health, and so much more.

Discovering these rules and knowing how to apply them in your life, is what this book is about.

Being Healthy Matters!