Cybernetics and Human Knowing. Vol. 26 (2019), no. 4, pp. 9–31

Medicine, Anticipation, Meaning

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The current practice of medicine acknowledges anticipation only in the form of genetic disorders passed on, ever earlier, and more intensely from one generation to the next. This form of anticipatory expression is rather limited. In reality, the living is anticipatory in the sense that the possible future partakes in the dynamics of self-preservation of life. Anticipation underlies evolution. Evolutionary success depends on anticipatory action.
Keywords: anticipatory, holistic, meaning

The Legitimacy of the Anticipatory Understanding of Causality

Medicine is the decisive test of understanding anticipation as definitory of the living. Where life and death are at stake, the philosophical dispute of whether the living is of a condition different from the physical, the chemical, or the informational becomes less relevant than the outcome. It is also a meaningful test of usefulness: Why study anticipatory processes if they are of no practical consequence in medical practice? It must be emphasized here that the anticipatory perspective is significant also in education, creative endeavors, and political and social forms of interaction. Biology will become the science it aspires to be only when, in addition to its physics- and chemistry-informed views, it will build upon a fundamentally different foundation, irreducible to other disciplines—but not to the exclusion of what they afford for the successful study of life. The motivation for the effort to understand various expressions of anticipation can only increase once the notion of anticipation itself is well defined (Nadin, 2015a) and understood. Usually confused with other forms of dealing with change—such as forecasting, expectation, guessing, etc., and especially prediction—anticipation is pervasive in all behavior (human, animal, plant); that is, it is existential—ontological—not a construct used in acquiring knowledge, not an epistemological artifact. A shared understanding of what the concept is would go a long way in helping the study of anticipatory processes gain traction in the medical community (or other communities of shared interests). Conceptual clarity, more than instrumental obsession (so typical of this particular time), is a necessary premise. In the section "Defining the Terms," a formal definition will be provided. The conceptual path to the definition traverses the rich territory of empirical evidence for anticipatory processes.

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Preliminaries

The history of medicine is probably more exciting to revisit than that of any other human activity. It is a *mixtum compositum* of questions ranging from the fiction of the supernatural to the most probing science. Given the significance of life, of healthy living in particular, nothing is excluded. This is where the highest integrity meets the deplorable charlatan. When it comes to maintaining life, no price is too high. With this in mind, let us focus on the current questions pertaining to medical care. In the age of obsession with data, it will soon become evident that sacrificing meaning for the convenience of quick and easy answers does not produce the health return we all hope for.

Since 1900, the average human lifespan has increased by 30 years. Within the same period, heart conditions, stroke, cancer, and diabetes became more frequent (at least as identified conditions). By 2020, according to the *Madrid International Plan of Action on Ageing* (United Nations, 2002), humankind will be made up of more elderly (65 years of age and older) than the very young (under the age of five years). Throughout its entire history, medicine has never been challenged by such dynamics. It is therefore not surprising that in the USA the National Academy of Medicine made Healthy Longevity its Grand Challenge. The majority of those who consider taking the Grand Challenge of the National Academy of Medicine seek answers in physics and chemistry, in molecular biology, or in computation. This practice of medicine as a know-how activity reflects the adoption of a reductionist-deterministic view of biology, dating back to Descartes and the obsession with machines. The medical knowledge that is captive to physics and chemistry is much more modest than medical know-how. It is science, inspired by physics and chemistry, applied to the living in disregard of the distinction between what is alive and what is not.

While physics and physics-based disciplines adequately describe the non-living, there is a need for a complementary perspective that captures the essence of life: the specific causality characteristic of the living (animals, plants, fungi, insects, microbes, bacteria, etc.) that is accounted for by integrating past, present, and future. This understanding transcends the focus on quantitative description and recovers the domain of the significant, that is, meaning. A 250 mmHg systolic blood pressure is more than reason to worry for the affected person. But its meaning changes when it is connected to the organism (in which it was documented), more precisely to the actions performed.

Moreover, experimental and empirical knowledge attest that there is no intentionality in the realm covered by physics and physics-associated disciplines (Brentano, 1995; Fodor, 1987; Papineau, 1987; Searle, 1992; Thau, 2002). In contradistinction, the living is always characterized by what an observer would describe as goal-oriented behavior—the goal being the self-preservation of life. Of course, pleasure (not only through sex, or alcohol use, or drinking coffee, for example) cannot be ignored. In addition, emotions are the aspect of life whose meaning overwrites numbers. The non-living physical can be successfully described by

inferring from parts to the whole. The living, in continuous change, is holistic. In respect to what is alive, any reduction results in the loss of significant information about what keeps the whole in its living condition (or what leads to death).

Medicine and Change

The distinction between the living and the non-living, that is, the physical, is often rejected. The argument reflects the deterministic view according to which we can understand the change in what is alive and in what is the non-living by accepting that there is only one causality: effect (past) and cause (present) are all that is necessary to explain how change takes place in everything materially embodied. The view, defined as determinism, runs counter to empirical evidence. Observations ranging from anecdotal to systematic recordings concerning how the possible future affects the present of the living, have been accumulated through time immemorial. Classic texts, with a philosophic intent at the beginning, later with a scientific focus, mainly in medicine, biology, zoology, botany, and so forth, make reference to anticipatory behavior. Pre-sensing was often heralded in the magic and mythical testimony of early human activity, in both Eastern and Western cultures. After magic and mythical testimony, pre-sensing was presented in a variety of writings from authors such as Epicurus, Parmenides, and other natural philosophers infatuated with nature. However, until the beginning of the 20th century, few attempts were made to articulate hypotheses regarding the onset of some processes which testified to pre-sensing, and to verify them experimentally. For the record: in the 1920s and 1930s (and up until the end of the 20th century), a group of Soviet scientists demonstrated their independent thinking by highlighting anticipatory behavior pertinent to motoric expression and to cognitive processes. This happened in a society that imposed deterministic dialectic materialism (as it was called) on them. They focused particularly on perceptual aspects of anticipatory behavior and on behavior expression. Their work reached (in fragments) their colleagues in the West, but did not trigger any memorable reaction (Nadin, 2015b). The West was, and still is, in the grip of the Cartesian view of the world, pretty much like Soviet science was in the grip of dialectic materialism. This state of affairs started to change through the publication of Rosen's *Anticipatory Systems* (Rosen, 1985), and Nadin's *Mind – Anticipation and Chaos* (1991). Biology as such did not take note of anticipation. With the exception of Elsasser (a physicist trying to provide foundations for a science of the living, 1998), and Uexküll (1934/2010) and associates, there are no memorable attempts at understanding the specific condition of biology. Even Elsasser, while operating with numbers in order to describe the dynamics of life, arrived at the realization of their meaning. Nevertheless, physiology, brain science, and genetics are replete with contributions that document various aspects of anticipation (Nadin 2010) (if not necessarily acknowledging meaning).

For medicine, understanding how anticipatory processes take place—let's say in the relation between blood pressure and the heart rate—and what the practical

implications of this understanding might be are of immediate practical consequence. Immunotherapy, for instance, is an expression of this interest among practitioners of medicine. Recently, Siddharta Mukherjee, a cancer biologist and physician (Columbia Medical School) reported, "My lab has now a wing that works on the immune system in leukemia."[2] This is a change from the practice of targeting cancer cells to changing the environment in which they function. The idea might not be new, but the decision to pursue it is rather unexpected. Nevertheless, given the machine model that informs the activity of a large number of physicians, those physicians frequently act more as mechanics tending to the human body than as nurturers of healing processes. The model deployed (consciously or not) is disease→target→kill. Otherwise described: find what's wrong in the "machine," get rid of it, hope that what you "killed" will not affect the body too much. In other words, ignore meaning for the purpose of efficacy. For all practical purposes, the majority of physicians, educated within the tradition of fixing impaired health conditions, for instance by trying to "kill the bad," rather than preventing disease, still address disease from a reactive perspective, with little concern for the possible future, such as side effects or long-lasting handicaps. Engineering health remedies—pharmacologically or mechanically—seems easier than mastering the art and science of healing. Very few, mainly in alternative medicine, try to engage the body instead of attacking real or presumed causes through medication (sometimes drastic) and surgery. Neurology, neurosurgery, cancer treatment, gastroenterology, and gene-based therapy are medical endeavors in which the anticipatory perspective is slowly gaining traction. Consequently, some simple inferences became possible. One example: the realization that anticipation of stressful situations—such as exams, natural disasters, taxing conditions—accelerates cellular aging led some physicians to address behavior, and life choices, instead of focusing exclusively on the chemistry of stress. Others (e.g., Sturman & Moghaddam, 2012) took note of the sensitivity of the dorsal striatum (DS) to reward anticipation and focused on prevention (vulnerabilities such as drug addition). Anticipation of back pain (extremely frequent) seems to predispose the patient to back trouble because anticipatory postural adjustments are affected. Neuroticism (the tendency to experience negative emotions) affects brain processing during the expectation of pain. Fibromyalgia is an expression of pain anticipation. The pathophysiology of autism (in infants) or of Alzheimer's disease evinces the consequences of skewed anticipation. The change of perspective mentioned above (and the few examples to illustrate the thought) marks a turn from exclusively reactive healing (target and kill, surgery) to more frequent attempts at proactive treatment. "Walking Away from Conveyor-Belt Medicine" (Elie & Aprà, 2019) provides a good description of this process.

In the area of brain activity and cognitive functions, there is a broad consensus that anticipation cannot be ignored if we want to make progress in addressing the changed condition of the human being. The action-reaction type of medicine (of

2. Soon we'll cure disease with a cell, not a pill. TED 2015 https://www.ted.com/talks/siddhartha_mukherjee_soon_we_ll_cure_diseases_with_a_cell_not_a_pill

"spare parts," for example, knee and hip replacements, liver and kidney transplants, and implants of all kinds) is being re-evaluated in view of progress in genetic methods and genetics-based medicine. Open-heart surgery came under special scrutiny due to the fact that, according to the practitioners, it is unnecessary in 70% to 90% in most cases, and fails to extend the lives of those who were convinced to pursue it. Dr. Michael Ozner (2010), among other heart specialists (Sidney et al., 2016), advocates preventative measures (anticipatory in nature) through lifestyle changes. Unity Biotechnology, a Silicon valley start-up, targets senescent cells with the goal of preventing hypertrophy of the heart and chronic inflammation. Other companies are active in seeking genetic answers to cartilage damage (Hunziker, Lippuner, Keel, & Shintani, 2015), in order to avoid joint replacement surgery. There is a consensus that the reactive procedure of treating various behavioral problems (attention deficit disorder, hyperactivity, schizophrenia) through drugs begs to be re-evaluated from the perspective of anticipation. This means: the practice of proactive treatments that avoid the dangerous side effects of drugs and withdrawal symptoms from them. Meaning is acknowledged in respect to the possible future.

The medicine of disease→target→kill and the associated pharmacopeia (delivering the *chemical bullets*) advanced in spite of the way the body heals itself. It was, again, physics and chemistry that were at the forefront, but not the understanding that the living is more than its material substratum. In the wild animal realm (what is left of it), for instance, we do not encounter an increase in the number of illnesses that accompany the use of chemicals in the human being. But we can notice regenerative processes—in plants, animals, fungi, bacteria, and so forth. Such regenerative processes are actually indirect proof that reductionist targeting might in the long run undermine healing. In the non-living, fixing matter is justified. In the living, fixing is at best palliative. Most of the time, consequences surpass what led to targeted use in the first place. From among the examples (use of antibiotics, chemotherapy, etc.), here is one more recently unveiled to the public: the use of gastric acid suppressants—for which patients spend over $1.5 billion a year. The *JAMA Internal Medicine* (Tariq, Singh, Gupta, Parda, & Khanna, 2017) reported that patients who take such suppressants (histamine-2 receptor antagonists and subsequently proton pump inhibitors (PPI)) can experience enteric infection risk of clostridium difficile associated disease (CCAD), microscopic colitis, community acquired pneumonia (CAP).

Against this worrisome background—the bullet meant to kill a disease can lead to more disease—the following will be addressed: 1) the issue of legitimacy—what justifies the anticipatory approach; 2) the specific nature of change in the living—the dynamics of life; 3) the need for conceptual clarity; and 4) specialization and the holistic perspective. Of special interest to redefining medicine from an anticipatory perspective is the understanding of its non-decidable nature (in Gödel's sense of the concept).[3] Connected to this is the realization that the gold standard of experimental reproducibility, inherent in the dynamics of closed systems (in particular the physical) is not applicable to medicine (Nadin, 2018) or to any investigation of the living. The

idea that measuring—the obsession of the medical community—might not be the only way to assess a health condition, and that meaning considerations are at least as significant, cannot be emphasized enough. However, short of simply abandoning what proves to be incompatible with the subject—the ever-expanding technology of measuring—the scientific community is faced with the urgent need to suggest alternatives for what can be defined as non-deterministic processes. None of this is exclusionary. The reality of the human body, as the unity of its physical and chemical embodiment and its anticipatory condition, suggests the need to improve upon the integration of reactive mechanical repair jobs—sometimes inevitable— proactive maintenance, and self-healing. These choices will be further analyzed.

Again, only one example: visualization (from X-rays to ultrasound to MRI) has helped medicine overcome subjective assessments of conditions that cannot be directly observed. Many lives were saved, more knowledge about a whole array of conditions often ignored or misunderstood was acquired. But getting a look inside (the heart, the digestive system, the brain, etc.) has its price. Energy is used to penetrate the layers blocking direct view (so difficult to obtain through invasive surgery, such as heart or kidney implants). Thus, the adage from physics—"to measure is to disturb"—acquires a particular meaning. The medical practitioner is usually aware of the consequences of frequent X-rays (associated with cancer, for example), of MRIs, and so forth. Still, we learn that each new measurement technology, as beneficial as it might be, entails risks usually ignored. A recent report ("Cross-Sectional Analysis of Age-, Sex-, and Race-Adjusted Medicare Data"), in which 306 hospitals and 15 million fee-for-service Medicare beneficiaries past the age of 65 participated, shows that computer tomography (CT) is associated with a higher nepherectomy risk. The invention of the CT, providing multiple cross-sectional images, was celebrated with a Nobel Prize (1979). To identify abnormalities, such as tumors (of the liver, pituitary gland, pancreas, lung, kidney), or to see past the cranium (bleeding in the brain, or tumors) is essential. However, the observed kidney cancer has doubled since CT was first deployed. Over-diagnosis of melanoma, and cancers of the breast, prostate, and thyroid is nefarious, as are nephrectomies associated with CT, causing more harm than benefit (Welch, Skinner, Schroeck, Zhou, & Black, 2017). The non-deterministic aspect—same cause, not always the same outcome—will be approached as the nature of anticipation will be further defined. However, the argument is not of the nature of a choice between one view—the deterministic, based on physics—and the complementary perspective that acknowledges anticipatory processes. While physics-based causality is always present, life-specific causality, transcending that of physics, must be taken into consideration. Risk assessment is based on past data; anticipation expression reflects awareness of the possible future.

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3. Those interested in an introduction to decidability/undecidability can see: "G-Complexity, Quantum Computation and Anticipatory Processes" (Nadin, 2014); and "The Intractable and the Undecidable – Computation and Anticipatory Processes," *International Journal of Applied Research on Information Technology and Computing*, 4:3, 2013, 99–121.

The Data Problem

Data, the new favorite term in the jargon used by the medical profession, and in that of the industry that hoists technology upon it, is a good starting point. When everything is measured, medicine shares in the hope that *big data* technology will reveal secrets about the state of a patient and the outcome of treatment. The cell phone has prompted a whole new branch of medical applications intended to have us all monitored around the clock. Dr. Eric Topol (2012), who famously established the Scripps Translational Screen Institute, focused on monitoring individuals through all kinds of wearables. He is active (in all media) in promoting the disruptive medicine of big data and the associated AI. Topol's ill-defined *deep medicine* (Topol, 2019) expresses the hope that AI could help physicians find more time for their patients. Many are convinced that this is the way to go. Atul Gawande, distinguished practicing surgeon and professor at Harvard University's School of Public Health, advances, in line with Topol, an almost science fiction image of the new data-based capabilities.[4] The expectation is that processes leading to disease are reducible to data, and therefore the instruments of prediction, forecasting, guessing, and expectation—for which deep learning is known—can be applied to healthcare. Totally ignored is the fact that actions informed by anticipation—such as sweating palms in a dangerous situation, of which the individual is not even aware—are the expression of *significant* data, usually "little" data, generated ahead of the action. Once the danger is over (e.g., a bullet heading towards its target, a falling heavy object, slipping on a wet floor, stumbling and falling on a sidewalk), the subject realizes what actually transpired. The autonomic process, which leads to sweating, or to increased heart rate, or to changed saccadic movements, is only testimony to the process. In reality, the anticipatory response is expressed in action: the danger is not just acknowledged, but effectively mitigated.

The rapidly growing number of devices deployed in order to monitor the patient's well-being might provide data regarding the reaction component, but they are not effectively involved in the anticipatory action. 24/7 monitoring of the individual is illustrative of the machine mentality applied to the human being. Machines can be monitored, and actually are, using measuring devices and sensors. The data are used in control mechanisms. We expect machines to perform equally well regardless of the context. *But the human being is not a machine*. Its control processes are continuously adapting to new contexts. The living performs meaningful (or meaningless) actions at the border between survival, self-preservation, and self-destruction. The living "makes itself" through what it does: work, sleep, reproduce, eat, and so forth. The living contributes to its own well-being (or to compromising it). It cannot be disconnected except through the extreme intervention of anesthesia (including states

4. "Instead of once-a-year checkups … we will be increasingly able to use smartphones and wearables to continuously monitor our heart rhythm, breathing, sleep, and activity … engineers have proposed bathtub scanners that could track your internal organs for minute changes over time. We can decode our entire genome" (Gawande, 2017, p. 37).

of coma, when considered medically acceptable or even necessary). The living eats (or breathes in) the right stuff at the right time, or the wrong stuff. In the machine view, data collected through all kinds of sensors from individuals are automatically processed, passed on to some data-mining procedure or to so-called deep-learning operations, specialized in diagnostics. There is already a growing buzz about AI (in some form) replacing radiologists, or dermatologists put to shame by neural networks. But no one gets well by being monitored like the engines of airplanes or of agro-machines used in industrial farming. Or, to use Gawande's (2017) example, being under observation like a bridge. (Of course, the data from the bridge itself call to our attention what needs to be fixed. But no bridge ever fixed itself!) Moreover, the data and machine-performed diagnostics do not answer the fundamental question of medicine: "Why?" Since living, as we shall see, is defined by uniqueness—medical practitioners are actually fully aware of this—to seek answers to one condition or another in sameness—such as in deep learning procedures or diagnosing skin conditions—might qualify as successful big data processing, but not as meaningful medicine. Even if, as is the case, deep neural networks are statistically better at diagnosing than dermatologists (Esteva, et al., 2017) and other specialist physicians. Similar examples are produced daily for other medical conditions. The more recent is pneumonia, but other illnesses will soon be added to the list. But such developments will not really change the mechanistic medical practice that fails because it is based on a limiting premise.

The Missing Science of Health

From Galileo to Newton, and from Newton to Einstein, and probably from him to the quantum mechanics scientists, there is a convincing progression in understanding laws of physics. The legitimacy of each subsequent theory reflects the degree to which the understanding of reality becomes wider and deeper.

Human dedication to understanding the changing world, within which the living unfolds, will eventually crystallize in revolutionary views. This in itself is worth celebrating. But it invites reflection as well. Nothing comparable, not even the famous DNA helix, is on record in explaining life itself. Newton, Einstein, the quantum mechanics visionaries (Heisenberg, Schrödinger, Bohr, Feynman, among others) are present—and rightly so—in the explanation (as tentative as it still is) of the beginnings of the universe. But the beginning of life is still in the fog of confusion (or speculation). Almost as seductive as alchemy was long ago, the attempts to start life from non-life, as well as the attempts to create a non-dying human being,[5] take new manifestations. We experience a rather disconcerting surrender celebrated as victory: since the living itself is embodied in matter, the more physics we know—and the more physics-based biology we use (such as molecular biology or even genetics)—the better we will understand life and extend it as we wish. The obsession of particle

5. For documentary evidence, the reader can consult the article "Silicon Valley's Quest to Live Forever," (Friend, 2017).

physics (i.e., know the particles and you will know all about what they make up) translated into the hope that molecular biology or genetics will solve all the mysteries of disease and eventually of life. But the four fundamental forces of physics—gravitational, electromagnetic, strong, and weak—still do not explain the change from a condition of health (as ambiguous as the term can be) to one of deterioration. The disease→target→kill is only one the most telling examples of the consequences of adopting the force model of physics and the associated biochemistry. Given the current infatuation with information and programs, the jargon of genetics—borrowing from computer science—is at the forefront of medicine today. The jargon now pertains to re-programming. Bacteria express damaging proteins; re-programming turns the process off (like the switch controlling heat or electricity in the house). Others talk about turning on some processes, even though we do not know enough about the consequences such a process might unleash.

Obviously, there is much more nuance to all of this. To rehash the arguments of every controversy, including the ill-fated *vitalism*, will not change the substance of the observation. So far, life science consists of adopting (or adapting) physics theories and their extension into particular phenomena (biochemistry, for instance). A large body of generalizations from the physical to the domain of the living extends this physics-chemistry-based science into the obvious antagonist of vitalism: the living machine. For the sake of clarity, two premises must be spelled out: 1) the material substratum and the associated causality of the living are a never-questioned given; 2) the dynamics of the physical and of the living are different; change in the living is by many orders of magnitude richer in its expression. The distinct effort to advance a view of the living that defines its own characteristic causality has serious consequences in the practice of healing. Therefore, to integrate the science of the physical and that of living processes, without discarding what defines a science of the living, is of extreme urgency. In doing so, we might even come to the realization, never before explicitly stated, that physical causality (explaining change in the non-living) is a subset of unlimited forms of entailment that explain the change of life (Nadin, 2015c).

The daunting task of distinguishing between change in the living and the non-living, requires that the focus should be on dynamics, which means how and why change takes place, as well as the rate at which change takes place. The matter from which physical entities (not endowed with life) are made remains the same. The rate of change is also relatively monotonic. The living is in a continuous state of remaking itself, sometimes faster, sometimes slower, a sui generis re-creation of its constitutive cells. Empirical evidence suggests that change in the non-living realm takes place on a timescale different from the multiple timescales characteristic of living processes. Although relevant changes in DNA rarely (if ever) take place within a generation, activation or deactivation of some parts of the genome, without altering the code, is noticeable. As an embryo evolves, the mother's DNA is edited substantially. The survival entailment is contradictory. On the one hand (the DNA of the inseminating agent), it would be beneficial to have the embryo develop into strong progeny. This is

the anticipatory drive. But the placenta (expressing the DNA of the inseminated agent), the housing of the developing new entity, has a limit beyond which survival is problematic. This is also anticipatory in nature. Epigenetics comes into the picture: for the living, there is an active environment. For the physical, where the machine will be used, it should not matter. Empirical evidence also testifies to the fact that even the aggregate defined as the human body (or the body of any living thing) functions on several different timescales. Scientists determined the age of sand and the composition of the boulders from which it was processed over time. They also recreate organisms from DNA samples found in fossil remains. Moreover, in the physical, the timescale is relatively constant, while in the living it varies under the influence of context. There is no birth and no death (short of misappropriated metaphors applied to stars and black holes) in the physical. And there is, contrary to poetic license, no intentionality to be either observed or experimentally documented.

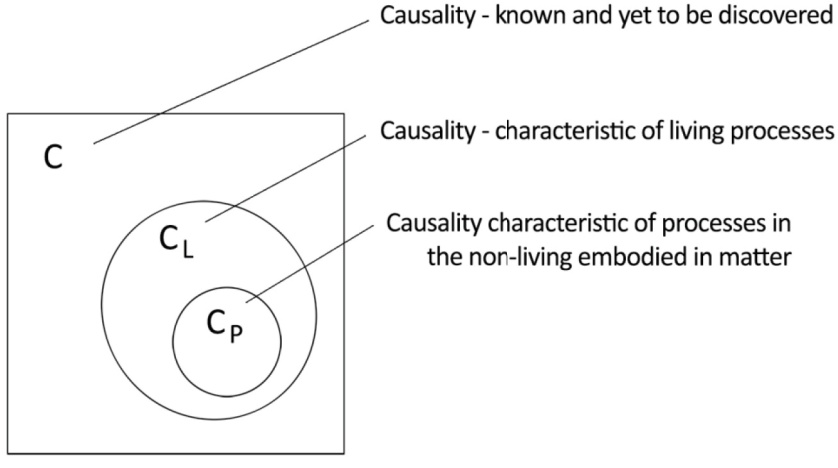

Figure 1. Physical causality is a subset of natural causality. Causality in the living is more encompassing than physical causality.

The diagram does not account for causality specific to information processes (in particular, the quantum non-deterministic model).

The realization that physical causality could be a subset of natural causality (Fig. 1) might entail the need to understand Nature beyond Newton's unifying view. He famously aggregates the living and the physical and declares the laws of physics—reflecting God's control over the universe—as universal. Darwin's *Origin of Species* (1859), while eliminating God from the picture, was celebrated as the equivalent of Newton's foundation of physics (*Philosophiae Naturalis Principia Mathematica*, 1687). Natural selection describes the implicit dynamics of the living. But natural selection affords descriptions of a precision different from that

characteristic of the mathematical representation of the physics of gravity. Evolution's causality is different from the determinism described in Newton's equations.

Determinism, the characteristic causality of physical phenomena, is convincingly relevant to the physics and chemistry of the living. But it returns an incomplete explanation of the changing living. The one-directional arrow from cause (or causes) to effect(s) is replaced by the two-way conduit of interaction. Quite often, a cause associated with life becomes an effect (and the other way around). Empirical evidence: Physical forces (e.g., pulls, compressions and stretching, distortions) applied to a cell can further affect it, probably more than the inherited genetic code does (Picollo, 2013a, 2013b). Taking both physical forces and the genetic code into consideration affords an understanding of cell changes that neither can deliver alone. Non-determinism, describing a relation between cause and effect that takes the form of a multitude of possible outcomes, pertains to change as an expression of something being alive. Indeed, changes due to physical forces applied on cells (think about hitting your thumb with a hammer, cutting yourself with a sharp knife, or falling against a rock) and genetic processes governing all dynamics are interwoven. There is no way to unequivocally predict whether a cell becomes cancerous or simply divides in a process of self-healing. This example is also illustrative of what is defined as the bottom-up (from matter) and top-down (from the cognitive) integration of causes (Auletta, Ellis, & Jaeger, 2008) in the dynamics of the living (Fig. 2).

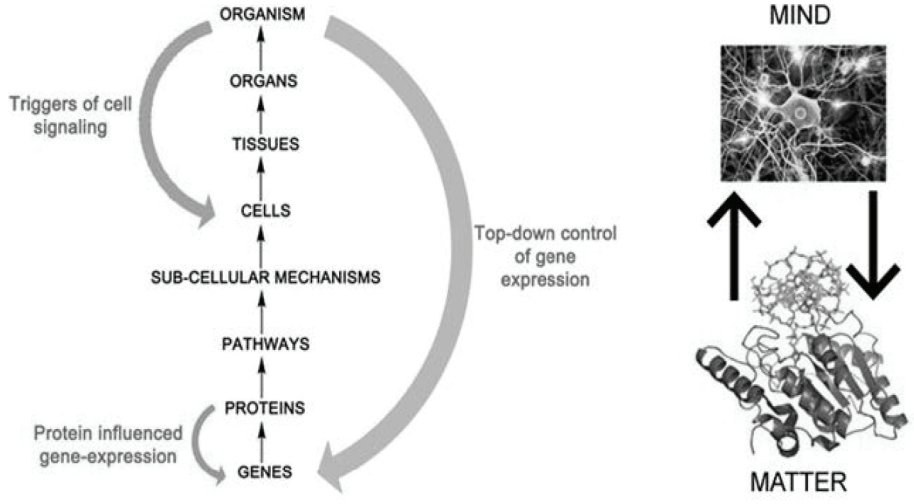

Figure 2. Bottom-up and top-down processes in the dynamics of the living.

In the trade-school model extended to training physicians, medical practitioners take the machine metaphor literally. This metaphor, to which science beyond the age of de la Mettrie is literally enslaved, is but one consequence of a rudimentary view of

causality. Everything that can be fitted to the time series describing the functioning of a machine operates under the expectation of perfect repetition. Albeit, the living is the domain of repetition without repetition (Bernstein, 1947; Ito, 2015), that is, non-monotonic change. This applies as well to evolution as to the particular motoric expression in humans and animals, and to genetic expression. Only recently—that is, after the advent of quantum mechanics—was this view somehow questioned. Stochastic aspects of dynamics were introduced, and indeterminacy accepted as a qualifier for processes less than very precise.

The Experimental Trap

To know how the physical changes is to infer from a quantitatively described past state to a future state, under assumptions usually defined as initial conditions (also expressed numerically). Mathematics provides an effective description for such phenomena. In its language, it captures sameness and supports reasoning in the language it constitutes. Calculus is often described as the mathematics of quantitative change. It establishes the value of a parameter (or several) at a particular moment in time. In addition, it can describe the rate at which such a value varies (the derivative). To know how the living changes requires more than the physics-based description and the associated mathematics (the calculus). The language of life extends beyond what logic and mathematics describe. An adequate explanation of change in the living requires integration of inferences from past states with interpretations of the meaning of possible future states. This is the domain of representation. From this broad language, medicine adopted the semiotics of diagnostics. No falling stone will get hurt (much less die); a living being falling (bird, dog, bear, human being) can get hurt (and even die). A bone fracture is a physical phenomenon pertinent to strong forces. However, the pain and the resulting changed behavior (motoric expression) are not reducible to the physical and cannot be fully expressed through numbers (despite the charts doctors present to patients asking them to indicate pain from 1 to 10). They are not describable in terms of strong forces, or other forces. Various processes associated with the fracture, including the physiology of self-healing, evince anticipation: the possible future effectively affecting the present. Forces are only cause-and-effect expressions. Anticipation conjures the possible future: cause and effect are complemented by awareness of consequences.

The framing of change within the respective consequences, different in the physical and the living, is key to understanding their difference. There is self-healing in the living; there is none in the non-living. The causality specific to interactions in the physical realm is described in Newtonian laws—action-reaction, in particular. It was subsequently further refined in relativity theory. Furthermore, it was extended in the quantum mechanics perspective, as well as in molecular biochemistry, for the micro-level of matter. The causality specific to interactions in the living includes, in addition to what the cause-effect laws of physics describe quantitatively, the realization of significance in connection to the possible future. A broken bone affects

survival; self-preservation of life translates as anticipatory action—from metabolism to self-repair. The physics or the chemistry (or both) of some processes can be the same, while the outcome for the same individual or for different individuals can greatly differ. As an example, the metabolism (of proteins, of sodium and potassium, of sugars, etc.) characteristic of the living makes this point quite clear. It is the aggregate of enzyme-catalyzed reactions from the level of the cell to that of the organism. This is how the living obtains its energy for doing what defines its identity. In the physics realm, the same energy is always required to get a machine to perform the desired operation. In the living, the energy/matter coupling is less well defined, and it varies according to circumstances. There is meaning to food for plants, animals, humans. There is nothing comparable (except for technical specifications) for providing fuel to an engine, or some other form of energy in order to extract power.

The physics of an explosion has consequences for the bricks of a house (and all that makes up the built structure). These material consequences are different in nature from the many additional consequences for the inhabitants (tenants with a lease, or co-tenants, such as the cat, the dog, and everything else alive, such as mold and vermin) living there. The medical practitioner would have it easy if after an explosion all there was to fix were broken windows and walls, pipes and amenities. The Hiroshima and Nagasaki experience fully documents the statement—the rebuilding of the physical plant was spectacular. The human tragedy (death, suffering, mental torment, etc.) could not be reversed through fixing. Meaning makes the difference, not the numbers describing the bombs. The recovery of the environment around Chernobyl after the explosion of a nuclear power plant is testimony to living processes more powerful than the disaster: survival, preservation of life under extremely adverse conditions, epigenetic changes. The consequences for the physical aspect—destroyed buildings and machinery—are finite, and almost always immediate. The power plant could be rebuilt in a short time. The impact on the condition of the beings affected is open-ended. It will take quite a while for some of the consequences to even become apparent, not to say for healing (if this word can even be used).

The classical physics of momentum and energy conservation applies, of course, to the collision between a wide receiver and a defender in football or to someone involved in a car accident). But the impacts go well beyond the physics involved. The anterior cruciate ligament can withstand 500 pounds of pressure, but it tears from side hits of lesser intensity. Brain damage associated with playing football is even more telling of what transcends the physics of collisions. Verbal ability, memory, spatial orientation, and balance—all affected—are not physical in nature (Vedantam, 2011).

The fact that the living, in addition to the constraints of physics, is subject to contingent rules of behavior is usually brushed aside. Reductionism builds upon the postulate of the identity of the physical and of living, to the detriment of a better understanding of the dynamics of the living. You can reduce the physical—a stone, cough syrup, or methane gas—to its parts in order to understand how it works or why it breaks down. You cannot reduce life to components—heart, skin, body parts, cells, neurons, or proteins without losing essential information. The same applies to the

epistemology developed around the machine metaphor. Karl Popper (1972, p. 207) remarked that, "the doctrine that man is a machine has perhaps more defenders than before among physicists, biologists, and philosophers, especially in the form of the thesis that man is a computer." Newell and Simon (1972, p. 234) went further: "Men and computers are merely two different species of a more abstract genus called information processing systems." The fact that computers process data, regardless of meaning, and the human being interprets information—that is, data associated with meaning—has escaped their understanding. Unfortunately, almost 60 years later, the views they described have not changed. They seem to even spread farther and deeper under the spell of very convincing machine performance (e.g., deep learning accomplishments).

Machines, regardless of what kind (from clocks to hydraulic pumps to engines to computers, i.e., programs), are constructs—figuratively and literally—meant to function in a predictable manner, and always in a repetitive manner. Religion postulated that the human being was created in the image of the Creator. *Machinomorphism*—the hardware machine as much as the soft machines of our time—establishes the secular religion of human beings made to function like the machines they conceived (Fig. 3). It is a solipsistic view: The making of something (e.g., machine) is the proof of the equivalence between the makers and the made. For Newton, the mechanism of the universe, whose dynamics his equations precisely described, was the proof that everything in this universe behaved, at God's will, like a mechanism. The medicine it inspired pursues the goal of fixing malfunctioning mechanisms. If the clouds (Popper's metaphor) are highly irregular, disorderly, and more or less unpredictable—examples are molecules in a gas, or gnats—clocks are precise and predictable. Still, for determinists clouds are clocks. In their view, with enough knowledge what appears as indeterminate proves to be as determinate as the universe, or as the structure of matter. That the clocks in the living have a variable rhythm means a lot to the organism, but not enough to scientists of a reductionist bent. In science, the language describing the functioning of clocks (and of machines in general) is mathematics, built upon the construct we call *number*s, which ultimately label quantity (unless they are used as symbolic identifiers, such as in Social Security numbers, or in defining a street). The automation of mathematics (or at least part of it) through computation gave this tendency a new, more specific, though ultimately illusory, viability. And while doctors did not adopt the language of mathematics (most of them are mathematically adverse, if not illiterate), they happily make use of mathematical machines (i.e., computers). For them, the chemistry and the physics of blood pressure, metabolism, or kidney functioning is delivered from a laboratory where a database serves as a reference for qualifying some numbers as too high and others as too low. There is a lot of detail (sometimes confusing, as in the PSA[6] value), but the sense of the whole is lost. The individual is reduced to a matrix.

6. PSA stands for prostate-specific antigen, a protein produced by normal or malignant cells of the prostate gland. PSA is a number: nanograms of the protein per milliliter of blood (ng/mL).

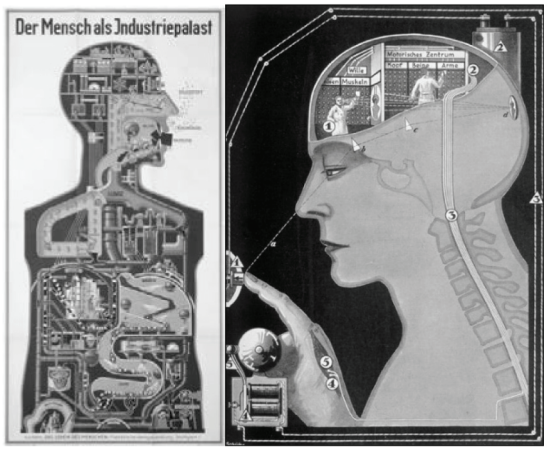

Figure 3. Fritz Kahn: graphic analogy between anatomy and machinery. Visualization of the digestive and respiratory system as industrial palace, really a chemical plan; visualization of brain—as yet another mechanistic image. Today the metaphors would be more in line with data-processing machines and methods.

Machines (hard or soft) embody the cognitive construct of numbers, that is, labels for quantities—such as weights, geometric dimensions, speed, and so forth—or symbolic representations—such as the infamous numbers tattooed on the arms of concentration camp victims. As representations of the human activity that the machine replaces or augments, they are, by their condition, incomplete (Nadin, 2014). To ascertain that a representation—the machine (Fig. 3)—is identical to the represented makes sense only for entities with clear boundaries. A billiard machine is equivalent to a billiard table in which, given the initial and boundary conditions of the billiard balls, the characteristics of the table (size, texture), we can, using the laws of motion, calculate the game. Many authors have remarked that Laplace was sure that, given the positions and the momenta of all particles in the universe, he could, using Newton's laws, fully describe the past, present, and future of the universe. Of course, he never envisaged the same in respect to a human being's life (or any other living thing). Today, the model is also applied to calculate the outcome of football games, for instance, or the outcome of competitive video game tournaments. As of most recently, it also informs the prediction of life expectancy, using deep learning methods. The universe as a clock, that is, a machine, is what physics-based determinism ascertains, or actually describes. The universe as a computer (the outcome of which is our reality[7]) is only one step further in the same direction. When some doctors talk about reprogramming patients, they actually disclose the angle from which they consider health. It is therefore not surprising that the debates of our days around the issue of longevity extend to the claim that "our bodies are information processing systems"

7. Recall Fassbinder's movie *World on a Wire*, 1973, based on D.F. Galouye's book *Simulacron-3*, 1964. The hero, a cybernetics engineer, uncovers a corporate conspiracy in which real persons are replaced by virtual avatars.

(Geddes, 2016, n.p.). Vijg and Campisi (2008) maintain that we are "essentially a computer made up of over-writable data and updatable apps" (Friend, 2017, p. 66).

Neither is it surprising that almost every surgeon educated in the medical school of determinism is prepared to provide "spare parts" when needed. Others of the same school are all set to perform genetic reprogramming (for which CRISPR technology for genetic editing seems adequate) for eradicating Lyme disease (Esvelt, 2014; Specter, 2017) without fully understanding the intricate nature of technology. Of course, they know that, at least under current circumstances, a pump is not really the same as a heart, and a genetically reprogrammed organ can fail or induce other major changes. For extreme conditions—entailing a number of serious limitations—a pump might be used in order to help resuscitate someone, or to extend someone's life—usually in an impaired mode. This is where the mechanistic dimension of medicine is important. Genetic reprogramming, of which the majority of scientists are still reticent, might eventually help in extreme cases. But before deploying it, we need to ask questions about the short- and long-term consequences for the whole to which the preprogrammed parts belong. In other words, we need to account for anticipation, the possible future life of patients.

Actually, not only is Laplace's deterministic view inadequate for describing life, but worse, it leads to aberrations. As spectacular as body part replacements are (and quite often a life-saving intervention), they fix but do not heal a condition. Moreover, they lead to long-term consequences, which humankind is not yet able to understand. The fact that biology, and medicine in particular, took the deterministic path is understandable. Explaining away what we do not fully grasp is easier than assuming the responsibility for seeking alternatives. Moreover, simpler explanations afford the immediacy of practical methods, sometimes informed more by urgency than by anything else. The fact that the education of medical practitioners, at all levels, has to change in order to reflect knowledge of anticipatory processes is becoming more and more self-evident. The path by which medical education has been imparted in the last 50 years brought us to the crisis in medicine we now experience, but the medical profession still does not want to call that education by its proper name. Education will have to open up to the dimension of anticipation as definitory of the living. It will also necessitate the re-education of everyone involved in today's practice of medicine.

The anticipation aspect is not one ingredient among others, but a fundamentally new perspective: a new Cartesian revolution (Nadin, 1999). It is not as comfortable as the successful beaten path of physics and chemistry—think again about antibiotics and painkillers—and its promise is of more technology and better targeting of what does not behave as expected. It took over 200 years (more precisely, since Newton, Descartes, and Laplace) to realize that the question of what change means in the living elicits a foundation different from the Cartesian view of the world. Therefore, one cannot expect abrupt abandonment of the huge investment (time, energy, money, human lives, and the lives of animals used in experiments) in taking the wrong turn. In the context of rapid scientific advances and disruptive modes, we can hope for a shorter time for ascertaining a complementary view. The urgency of applying it to

situations for which physics- and chemistry-based medicine, in particular the disease→target→kill model, is not adequate cannot be overemphasized. The aging of the world population is unavoidable; the degeneration of the species—expressed in, among other ways, systemic disorders and debilitating spectrum conditions resulting from the mechanistic views still dominating medical practice—is probably an even more critical prospect.

Defining Terms

The considerations presented above suggest a conceptual framework for the discussion of redefining medicine from an anticipatory perspective. Awareness that the clarity of concepts, not the passion of the arguments, is key to a successful conversation is an unavoidable prerequisite. Those who practice medicine, and even more those who through research and technical innovation contribute to a science of medicine, are facing a major choice: to overcome the limitations inherent in generalizing physics (and the notion of machine) and chemistry in the living domain or to continue exclusively in the reductionist mechanics of health, until the disruption of anticipation will render them useless.

The scaling of medical concerns—the outcome of the current reactive practice of medicine—suggests that the choice is inevitable. If indeed climate change is no longer a matter of passive acceptance but requires everyone's action, so does the need to redirect medicine along the path of anticipation characteristic of the living, not by excluding the appropriate mechanics of a deterministically driven perspective of health, but by integrating the two as the context requires.

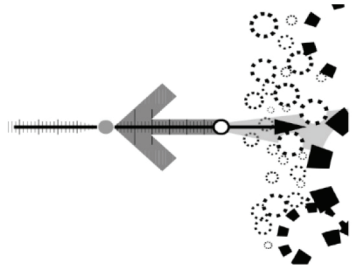

Figure 4. Anticipatory process: the deterministic arrow of time from a past cause to a present effect and the complementary arrow of time from a possible future to the current state of the system.

In the diagram representing anticipatory processes (Fig. 4), the past is, of course, materialized in the anamnesis (i.e., the medical history). Nobody can change his or her past. On account of new data acquisition methods and of convenient recording, medicine is able to generate detailed histories for everyone. The future is one of possibilities. Some of these possibilities will be realized—as happens with the hereditary increase in severity of a phenotype in successive generations, for example. Others will either disappear—a well-treated pneumonia—or extend further in the

future—latent tuberculosis is but one example. This is where considerations of context—the environment (in the broadest sense, nature, society, culture, etc.), as well as epigenetic factors—become unavoidable. The diagram (Fig. 4) stands for the following definition:

- The current state of an anticipatory system depends not only upon previous states, but also upon possible future states. (a)

In the current physico-chemical-driven medicine, data-based, and with little or no regard to meaning, the definition reads:

- The current state of a patient depends only upon previous states. (b)

The diagram (Fig. 5) corresponding to this definition does not allow for considerations of the future, except as speculative inferences.

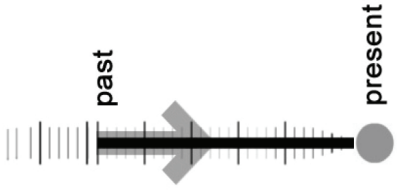

Figure 5. Present determined only by past.

In action-reaction-based medicine, the physician identifies the target: a bacterium's protein expression, for example. This identification is based on some description, usually incomplete (the symptoms). The intention is to stop the process. This applies to everything—from the accidental wound (which should not get infected), to the flu, to cancer, to spectrum conditions. It is common knowledge that in reality the living can only be partially targeted—we can never reach a complete description of all it takes to make up what is alive. All physicians, the superstars of the profession or the ordinary practitioner, most of the time probe the vast unknown of the body's biochemistry and biophysics. For a relatively small number of cases (making up the catalog of standard illnesses), there are widely adopted means that can deployed: Take an aspirin if you have a headache; take Pepto Bismol if you have diarrhea; for the flu or pneumonia, take Levaquin. They are not necessarily always successful; think about the increasing number of adverse reactions on record. For the rest, more data are supposed to help. Nevertheless, despite the exponential increase in available data, medicine does not seem to improve.

In anticipation-based medicine, with a vector from the possible future, instead of playing darts in the dark of our limited understanding of living processes, medicine should look for healing processes that rely on the principle of self-preservation of life

(Nadin, 2019)**.** Concretely (but without entering into details), the rejection of pathogens (that lead to various illnesses, from influenza to cancer) is the outcome of prevention, of environmental awareness, of stimulating regenerative processes (through proper nutrition, exercise, cognitive activity, for example). Already in the 1880s, that is, over 100 years ago, Ernst Fuchs (1882) and Stephen Paget (1889) advanced the *seed and soil* understanding of how cancer metastasizes. Hart and Fidler (1980) revised Paget's idea. Pathogens succeed in specific micro environments. This is how the seed—past and present—meets the possible future—the soil, that is, the environment propitious to its germination and spreading. Within the anticipation view, a less hospitable soil (environment) is an effective preventive system of exceptional rich expressivity. The reactive mode of medicine treats organ failure (kidney, heart, liver, pancreas, etc.) mostly through targeting. Thus are arthritis, diabetes, and other degenerative conditions treated. Of course, at this time diversified means are also available. Stem cell applications influence medical practice, as does immunotherapy. Gene-based methods are pursued. But the awareness of anticipation is by and large missing. Darts are still thrown in the darkness of experiments that usually cannot be replicated. Why this is the case is the subject of "Rethinking the Experiment" (Nadin, 2018).

Not captured in either diagram is the holistic nature of anticipatory systems. Let us recall the words of Jan Smuts:

> A "cause" was not taken as a whole situation, which at a certain stage insensibly passes into another situation, called the effect…. Everything between this cause and this effect was blotted out.... We have to return to the fluidity and plasticity of nature and experience. (Smuts, 1926, pp. 16–18)

Anticipation-guided medicine can only be holistic. It considers the entirety—the environment as a whole. The whole image, with its amazing richness of detail, is what actually explains the life we experience, life in general, ours and that of the rest of nature. An experienced physician knows that between the apparent cause and the effect a large field of interrelations (sometimes, correlations) explains how a person feeling healthy can suddenly become a patient. Examining the whole is more difficult than focusing on one and only one cause—as specialists do.

The reductionist view excludes the consideration of vagueness, of ambiguity. Just as an illustration, a clinical description of a condition such as hepatitis evinces vagueness in the clinical ascertainment: Total proteins are usually normal, albumin is decreased, and so forth, with qualifiers such as *slightly* or *moderately* applied to increased δ (gamma) globulins or decreased α (alpha) and β (beta) globulins. Degrees of possibility (possible future) in respect to symptoms and disease (itself not always well defined) are not only a language feature (for which fuzzy sets can be deployed), but also an expression of anticipation awareness. Health, or lack of it, is often a matter of perception for the patient as well as for the medical team (doctors, nurses, assistants). On the other hand, perception, sometimes skewed, triggers anticipatory processes—usually as defense processes, but also as reward outcomes. The onset of schizophrenia, bipolarism, or eating disorders is not infrequently associated with

adolescence, holistically understood. Vulnerabilities associated with adolescence can be addressed proactively, thus avoiding the dangerous path of palliative medication.

Reactive medicine is reductionist. Break the whole into parts; deal with and treat the parts; focus on targeting. This translates as: replace the used (probably when pain is considered as the threshold), defective part and everything else will run fine; or kill the culprit (pathogen). The anticipation perspective ascertains interconnectedness: every component of the living participates in its expression as healthy or not. Indeed, health, as well as loss of it, is the expression of the whole called *human being*, including the biome shadowing it, and the spiritual expression of the non-physical state (consciousness, preparedness, self-control, etc.). Affecting as little as one cell's condition, or that of the viruses, microbes, and bacteria making up the biome, might, under certain circumstances, trigger a multiplicity of processes, some of extreme consequences (reference was already made to gastric acid suppressants), others of episodic nature.

For the sake of the argument, let's take Methicillin-Resistant Staphylococcus Aureus – (MRSA). MRSA, caused by the staph bacterium, can affect people who have spent time in the health factories (e.g., hospitals, nursing homes), or at health shops (e.g., dialysis centers). Invasive procedures, such as surgery, intravenous tubing, knee and hip replacements, and implants can give rise to infections that prove to be resistant to antibiotic treatment. The fact that medical treatment, successful in many cases, kills more people than various medical conditions experienced over a lifetime is by now accepted as an inevitable curse (Null, Dean, Feldman, Rasio & Smith, 2004). It is actually the consequence of ignoring holism—the unity between all elements (patient, physician, medical equipment, hospital, etc.). The so-called environment—inside and outside the body—integrates all that contributes to self-preservation of life, and which might affect it. Physico-chemical-based devices of all kinds also get infected or sick, that is, they malfunction, or can be maliciously hacked. But the rate of success in fixing machines is as high as it can get—cloning is the most recent goal in this vein (while stem cell treatment, genetic medicine, in particular gene editing are making the headlines). Despite this enormous effort, the success rate of healing based on reactive medicine is increasing only slightly. The spectacular successes of extremely complicated cases (usually reported by the media) are rather the exception. The idea that medicine's fundamental perspective might be deficient has not yet led practitioners to question it, and has not resulted in a vigorous attempt to complement it with an anticipation component.

What Will It Take to Advance a New Practice of Healthcare?

Two prerequisites for redefining medicine ought to be spelled out at this juncture:

1. Medical practitioners will find value in stepping out of their comfort zone only to the extent of seeing their efforts rewarded (success rates included).

2. Those dedicated to research of anticipatory processes will have to deliver, in clear language, operational means and methods to their colleagues in healthcare.

If both are realized, medicine will change. Otherwise, it will take a breakdown, instead of the current crisis, before medicine progresses from reaction-driven physics-based practice ("fixing" the patient) to a proactive, anticipation-based dedication to the well-being of the whole person. Healthcare is by now an activity that reached 18% of the gross domestic product in the USA. In dollars and cents, it totals almost $3.5 trillion (Anderson, Reinhardt, Hussy, & Petrosyan, 2003).

The most recent data from a compensation survey[8] confirms that practitioners of reaction-driven medicine are rewarded with income levels double that of those working in pediatrics, internal medicine, geriatric care, endocrinology, or immunology. Excising basal cell carcinomas, performing heart surgery, replacing knees and shoulders involve elaborate (and costly) technology and procedures for immediate (more or less) remedy. It is telling that the public is willing to pay for cosmetic surgery rates almost as high as heart and orthopedic surgery rates. In contrast, pediatric care and geriatrics are different not only in the scale of reward, but also in the expectation of outcome.

In submitting such an evaluation to the community of scientists—especially those in the medical field—we risk antagonizing a very powerful segment of the economy, as well as the patients putting pressure on doctors. Eisenhower warned against the military-industrial complex (MIC) and its influence on public policy. It was probably justified to acknowledge its pendant, the medical-industrial complex (pharmaceuticals, physicians, hospitals, insurance, etc.).

The *medical–industrial complex* is the network of corporations which supply health care services and products for a profit. The term is analogous to military-industrial complex and builds from the social precedent of discussion on that concept (Ehrenreich & Ehrenreich, 1971).

In particular, the growth in health spending in the USA—highest in the world—is in the first place associated with the so-called health factories: hospitals and surgery clinics. Patients want to be treated as quickly as possible, regardless of price (and long-term consequences). Hospitals peddle technology, frequently more expensive than the results it affords, and expect a high return on their investments.

In the last 10-12 years, all initiatives in the healthcare domain—always a matter of politics driving government policies—were no more than the expressions of interests remote from the mission of medical care. Germany and France socialized medical care without compromising its quality. The USA with its mediocre medical care (the most expensive in the world, but ranked as 35th in terms of its effectiveness), still does not find ways to emancipate itself from the medical-industrial complex and to live up to the social exigencies associated with healthcare. The medical-industrial complex is

8. Grisham, April 5, 2017, *Medscape Physician Compensation Report.* https://www.medscape.com/slideshow/compensation-2017-overview-6008547

hostage to reactive medicine because the latter is more profitable and reflects the consumer profile of its clients. In all fairness, the solutions advanced by political parties and the government serve neither patient nor physician. Ignoring the stakeholders, public healthcare policy driven by the reactive model of medicine is actually detrimental to society. It undermines sustainability in every respect. For the sake of clarity: these facts about medical care in the USA also concern the way medicine is practiced in many countries of the world (World Health Organization, 2018). The broader subject of the economy of medicine (and its fixation with profit-making regardless of the quality of service) is also a matter of anticipation. Is immediate profit more important than the sustainability of humankind? Of our civilization? Such questions, pertinent to the meaning of medical care, might sound rhetorical, when in reality they are existential. But to discuss sustainability here would open a subject for which a much larger discussion, extending from medicine to economics and politics, cannot be avoided.

References

Anderson, G. F., Reinhardt, U. E., Hussy, P. S., & Petrosyan, V. (2003). It's the prices, Stupid: Why the United States Is so Different from Other Countries. *Health Affairs*, *22*(3), 89–105. Retrieved January 19, 2019 from https://www.healthaffairs.org/doi/pdf/10.1377/hlthaff.22.3.89]

Auletta, G., Ellis, G.F.R., Jaeger, L. (2008). Top-down causation by information control: From a philosophical problem to a scientific research programme. *Journal of the Royal Society Interface*, *5*(7), 1159–1172. Retrieved January 19, 2019 from http://rsif.royalsocietypublishing.org/content/5/27/1159

Bernstein, N. A. (1947). *On the construction of movements* (in Russian). Moscow: Medgiz .

Brentano, F. (1995). *Psychology from an empirical standpoint* (A. C. Rancurello, D. B. Terrell, L.L. McAlister, Trans.) London: Routlege.

Ehrenreich, B., & Ehrenreich, J. (1971). *The American health empire: Power, profits, and politics*. New York: Random House. (See also Wikipedia: Medical-Industrial Complex. Retrieved May 16 2016 from https://en.wikipedia.org/wiki/Medical%E2%80%93industrial_complex

Elia, F. B. & Aprà, F. (2019) Walking Away from Conveyor-Belt Medicine. *New England Journal of Medicine, 380*, 8–9. DOI: 10.1056/NEJMp1810681.

Elsasser, W. (1998). *Reflections on the Theory of Organisms. Holism in Biology.* Baltimore, MD: Johns Hopkins University Press. (Originally published in 1987 by ORBIS Publishing, Frelighsburg, Quebec).

Esteva, A., Kuprel, B., Novoa, R. A., Ko, J., Swetter, S. M., Blau, H. M. et al. (2017). Dermatologist-level classification of skin cancer with deep neural networks, *Nature, 542*(January 25), 115–118.

Esvelt, K. (2014). *Community-guided ecological immunization to prevent tick-borne disease*. https://www.lymediseaseassociation.org/faculty-biographies/1527-kevin-esvelt

Friend, T. (2017, April 3). Silicon Valley's quest for eternal life. *The New Yorker*, pp. 54–67.

Fodor, J. (1987). *Psychosemantics*. Cambridge, MA: The MIT Press.

Fuchs, 1882). Das Sarkom des Uvealtraktus. *Albrecht von Graefe's Archiv für Ophtalmologie, XII*(2), 233.

Gawande, A. (2017, January 23). The heroism of incremental care. *The New Yorker*, pp. 36-45.

Geddes, L. (2016). Human age limit claim sparks debate. *Nature News & Comment*. October 5, 2016. Retrieved January 19, 2019 from http://www.nature.com/news/human-age-limit-claim-sparks-debate-1.20750

Hart, J. R., Fidler, I. J. (1980). Role of organ selectivity in the determination of metastatic patterns of B16 melanoma. *Cancer Research, 40*(7), 2281–2287.

Hunziker, E. B., Lippuner, K., Keel, M. J. B., & Shintani, N. (2015). An educational review of cartilage repair: precepts & practice—myths & misconceptions—progress & prospects. *Osteoarthritis Cartilage*, *23*(3), 334–350. Retrieved January 19, 2019 from https://www.ncbi.nlm.nih.gov/pubmed/25534362

Ito, J. P. (2015). Repetition without repetition: How Bernstein illumines motor skill in music. In M. Nadin (Ed.). *Anticipation: Learning from the past. The Russian/Soviet contributions to the science of anticipation*, pp. 257–268. Cham, Switzerland: Springer.

Nadin, M. (1991). *Mind—Anticipation and chaos*. Stuttgart, Germany: Belser Presse.

Nadin, M. (1999). Anticipation: A spooky computation. In D. Dubois (Ed.), *CASYS*, *International Journal of Computing Anticipatory Systems, Partial Proceedings of CASYS 99, 6*, 3–47. Liege, Belgium: CHAOS.

Nadin, M. (Ed.). (2010). Annotated bibliography: Anticipation. [Special issue]. *International Journal of General Systems*, *39*(1), 34–133. London: Taylor and Blackwell.

Nadin, M. (2014). G-complexity, quantum computation and anticipatory processes. *Computer Communication & Collaboration*, *2*(1), 16–34.

Nadin, M. (2015a). Anticipation and computation. Is Anticipatory Computing Possible? In: M. Nadin, (Ed.), Anticipation across disciplines. *Cognitive Science Monographs, vol, 26*, pp. 163–257. Cham, Switzerland: Springer.

Nadin, M. (Ed.). (2015b). *Learning from the past. Early Soviet/Russian contributions to a science of anticipation*. *Cognitive Science Monographs, vol. 25*. Cham, Switzerland: Springer.

Nadin, M. (2015c). Anticipation and creation. *Libertas Mathematica*, *35*(1), 1–17.

Nadin, M. (2018) Rethinking the experiment: Necessary (R)evolution. *AI & Society*, *33*(4), 467–485. (See also https://arxiv.org/abs/1612.02491)

Nadin, M. (2019). Machine intelligence—A chimera. *AI & Society, 842*. (Available online since April 21, 2018 from https://link.springer.com/article/10.1007/s00146-018-0842-8).

Newell, A., & Simon, H.A. (1972). *Human problem solving*. Englewood Cliffs, NJ: Prentice Hall.

Null, G., Dean, C., Feldman, M., Rasio, D., & Smith, D. (2004). *Death by medicine*. Mount Jackson, VA: Praktikos Books. Retrieved January 19, 2019 from http://www.webdc.com/pdfs/deathbymedicine.pdf

Ozner, M. (2010) *The great American heart hoax. Lifesaving advice your doctors should tell you about heart disease prevention (but probably never will)*. Dallas: BenBella Books. (see also: Brody, J. [2009, Jan. 5]. More Isn't Always Better in Coronary Care. *New York Times* [p. D7].) Retrieved January 19, 2019 from http://www.nytimes.com/2009/01/06/health/06brod.html?_r=2&scp=1&sq=ozner&st=cse

Paget, S. (1889). The distribution of secondary growth in cancer of the breast. *Lancet, 1*, 571–573.

Papineau, D. (1987) *Reality and representation*. Oxford, UK: Blackwell.

Picollo, S. (2013a). Embracing mechanical forces in cell biology. *Differentiation, 86*(3), 75–76.

Picollo, S. (2013b) Developmental biology: Mechanics in the embryo. *Nature, 504*(7479 [12 December]), 223–225.

Popper, K. (1972). *Of clouds and clocks. An approach to the problem of rationality and the freedom of man, objective knowledge: An evolutionary approach*. London: Oxford University Press.

Rosen, R. (1985). *Anticipatory systems: Philosophical, mathematical and methodological foundations. IFSR International Series on Systems Science & Engineering, Vol. 1*. New York: Pergamon Press.

Searle, J. (1992) *The rediscovery of the mind*. Cambridge, MA: The MIT Press.

Sidney, S., Quesenberry, C. P., Jaffe, M. G., Sorel, M., Nguyen-Huynh, M. N., Kushi, L. H. et al. (2016). Recent trends in cardiovascular mortality in the united states and public health goals, *JAMA Cardiology, 1*(5), 594–599. Retrieved January 17, 2019 from https://doi.org/10.1001/jamacardio.2016.1326. (The references list many studies on the importance of prevention.)

Smuts, J. C. (1926). *Holism and evolution*. New York: Macmillan and Co.

Specter, M. (2017, January 2). Rewriting the code of life. *The New Yorker*. Retrieved January 17, 2019 from http://www.newyorker.com/magazine/2017/01/02/rewriting-the-code-of-life

Sturman, D., & Moghaddam, B. (2012). Striatum processes reward differently in adolescents versus adults. *Proceedings of the National Academy of Sciences*, *109*(5), 1719–1724. Retrieved January 19, 2019 from http://www.pnas.org/content/109/5/1719.full

Tariq, R., Singh, S., Gupta, A., Parda, D. S., Khanna, S. (2017). Association of gastric acid suppression with recurrent clostridium difficile infection: A systematic review and meta-analysis. *JAMA Internal Medicine*, *177*(6), 784–791.

Thau, M. (2002) *Consciousness and cognition*. Oxford, UK: Oxford University Press.

Topol, E. (2012). *The creative destruction of medicine: How the digital revolution will create better health care.* New York: Basic Books.

Topol, E. (2019). *Deep medicine: How artificial intelligence can make healthcare human again*. New York: Basic Books.

Uexküll, J. von. (2010). *A foray into the worlds of animals and humans: with a theory of meaning.* (D. J. O'Neil, Trans.). Minneapolis, MN: University of Minnesota Press. (Originally appeared as *Streifzüge durch die Umwelten von Tieren und Menschen*. Verlag Julius Springer, Berlin, 1934).

United Nations. (2002). *Political declaration and Madrid International Plan of Action on Ageing.* Plan of action adopted at the Second World Assembly of Ageing, Madrid, Spain, April 2002. New York: Author. Retrieved January 17, 2019 from http://www.un.org/esa/socdev/documents/ageing/MIPAA/political-declaration-en.pdf

Vedantam, S. (2011). The national brain-damage league. *Slate* (e-magazine), January 18, 2011. Retrieved January 17, 2019 from http://www.slate.com/articles/health_and_science/the_hidden_brain/2011/01/the_national_braindamage_league.html

Vijg, J., Campisi, J. (2008). Puzzles, promises and a cure for ageing. A realistic evaluation of our prospects for extending healthy life span in humans. *Nature, 454*(August 28, 2008), 1065–1071. Retrieved January 17, 2019 from https://www.nature.com/nature/journal/v454/n7208/full/nature07216.html

Welch, H. G., Skinner, J. S., Schroeck, F. R., Zhou, W., Black, W. C. (2017). Regional variation of computed tomographic imaging in the United States and the risk of nephrectomy. *JAMA Internal Medicine*, *178*(2), 221–227. (Summary is available: Most recently accessed January 17, 2019 from https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2665734)

World Health Organization (2018). *New perspectives on global health spending for universal health coverage.* Retrieved May 10, 2019 from https://apps.who.int/iris/bitstream/handle/10665/259632/WHO-HIS-HGF-HFWorkingPaper-17.10-eng.pdf;jsessionid=82CA5C71273B7AD1F93509C7A1DE8E52?sequence=1