# Hierarchical Complexity and Aging
## *Towards a Physics of Aging*

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Abstract: In this paper we extend the previous work of Witten and her team on defining a classical physics driven model of survival in aging populations (Eakin, 1994; Eakin and Witten, 1995a; Eakin and Witten, 1995b; Witten and Eakin, 1997) by revisiting the concept of a force of aging and introducing the concepts of a momentum of aging, a kinetic energy and a potential energy of an aging. As an example of the use of these constructs, we then explore the implications of these concepts with respect to the (Yu et al., 1982) diet restriction experiments.

## 1 HISTORY OF RELIABILITY

The history of the demographics of aging is tightly bound to the field of survival analysis (Witten, 1981; Elandt-Johnson and Johnson, 1999). Survival analysis, however, emerged from the earlier discipline of reliability theory (Abdel-Hameed et al., 1984; Ansell and Phillips, 1994).

The constructs of reliability theory emerged from the 1950's *gedankt* experiments of the computer scientist John Von Neumann. His interest (Neumann, 1956) was in how one would go about building a reliable biological organism out of unreliable parts. Until the thought experiments of von Neumann, the concept of reliability had not been well-defined.

Von Neumann's argument proceeded as follows. He began by defining the concept of the *conditional instantaneous failure rate*, denoted by $\lambda(t)$. We interpret this as follows. The condition is that the failure has not occurred at time $t$ given that the organism has survived until time $t$. With this in mind, we may then define the reliability $R(t)$ of an organism as the probability of no failure of the organism before time $t$. If we let $f(t)$ be the time to (first) failure (this is the same as the failure density function), then the reliability $R(t)$ is given by $R(t) = 1 - F(t)$ where $F(t) = \int_0^t f(\tau)d\tau$ ((Abdel-Hameed et al., 1984; Deshpande and Purohit, 2005; Elandt-Johnson and Johnson, 1999; Kalbfleish and Prentice, 2002; Lawless, 2003)).

How do we actually obtain an equation for the reliability $R(t)$? We do this as follows. Suppose we ask what is the reliability $R(t+\Delta t)$ where $\Delta t$ is a small time increment. In other words, suppose that we know the reliability of the organism at time $t$ and we want to know the organism's reliability at a small time increment $\Delta t$ later than time $t$. In order for the organism to be operational at time $t+\Delta t$, the organism must have been operational until at least time $t$ and then not have failed in the time interval $(t, t+\Delta t)$. We can express this mathematically as follows. The reliability $R(t+\Delta t)$ is given by

$$R(t+\Delta t) = R(t) - \lambda(t)R(t)\Delta t \tag{1}$$

Reading equation [1], we see that to be functional (operational) at time $t+\Delta t$, the organisms had to be functional at time $t$ (denoted by the reliability term $R(t)$ on the right hand side of the equation). Next, we have to subtract out all of the items that failed in the time interval $(t, t+\Delta t)$ (given by the second term on the right hand side of equation [1]). What remains after this subtraction is all of the organisms or items that remain functional at time $t+\Delta t$. A bit of algebraic rearrangement and we have

$$\frac{R(t+\Delta t) - R(t)}{\Delta t} = -\lambda(t)R(t) \tag{2}$$

It follows that letting $\Delta t \to 0$ (remembering our calculus), Equation [1] becomes the simple differential equation given by

$$\frac{dR(t)}{dt} = -\lambda(t)R(t) \tag{3}$$



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Thus, if we can specify the form of the function $\lambda(t)$, we can solve for $R(t)$(Roberts, 2010). The literature in these fields often uses the term "failure rate function" interchangeably with the term "hazard" function.

The earliest gerontological papers that made use of reliability theory and its application to aging focussed on two application areas, genetic and general network theoretic applications (Doubal, 1982; Gavrilov and Gavrilova, 2001; Witten, 1984a; Witten, 1984b). The discipline of reliability theory, coupled with network analysis/graph theory, has subsequently opened a number of direct conceptual applications of the field to the genetics of aging/longevity (Carnes et al., 2006; Witten, 1984c; Witten, 2007; Witten and Bonchev, 2007; Managbanag et al., 2008) and more recently (Witten, 2014; Wimble and Witten, 2014). This is because concepts of reliability have direct analogs to the longevity and lifespan of an organism. The most obvious one is that lifespan can be thought of as "the time to failure" of an organism. If death can be viewed as a failure, then there is a natural linkage between survival and reliability. Thus, the ideas of reliability mutated and the mutation became what we now know as the field of survival theory.

## 2 FROM RELIABILITY TO SURVIVAL

The field of survival analysis takes the term $R(t)$ and recognizes that it is describing the equivalent conceptual construct of "survival," denoted $S(t)$, where $S(t)$ represents the probability of a living organism surviving until at least age $t$ (or age $a$). Following the arguments in the previous section, equation [3] becomes

$$\frac{dS(t)}{dt} = -\mu(t)S(t) \tag{4}$$

where $\mu(t)$ is the instantaneous conditional probability of dying in the interval $(t, t+\Delta t)$ given that the organism has survived until at least time $t$. Because we have a differential equation, we need an initial condition. We usually assume that $S(0) = 1$ because there is no possibility of immediate death.

The solution to Equation[4] can be found in differential equation textbooks (Roberts, 2010). The solution of which becomes

$$S(t) = e^{\int_0^t \mu(\tau)d\tau} \tag{5}$$

where, as before $S(0) = 1$. In the case where $\mu(\tau) = h_0 e^{\gamma\tau}$, $S(t)$ becomes the traditional two-parameter Gompertz survival distribution (Carnes and Olshansky, 1997).

$$S(t) = e^{\frac{h_0}{\gamma}(1-e^{\gamma t})} \tag{6}$$

And, in the case where $\mu(\tau) = h_0 e^{\gamma\tau} + M$, we obtain the traditional three-parameter Gompertz-Makeham survival distribution (Carnes et al., 2006).

$$S(t) = e^{-Mt} e^{\frac{h_0}{\gamma}(1-e^{\gamma t})} \tag{7}$$

This history and importance of these models are extensively discussed in the various works of Carnes (see references). Thus, the tie between the constructs of reliability theory and those of survival theory is both well-established historically and is also conceptually useful.

## 3 SURVIVAL, AGING, LONGEVITY AND BEYOND

Categorizing and comparing the behavior of different demographic survival curves has long been of interest to many disciplines. Life tables are important in all manner of disciplines (Deshpande and Purohit, 2005; Chiang, 1984; Keyfitz, 1977). The literature in this field is large and beyond the scope of this article to review. As with most disciplines, over time each discipline develops its own jargon. The demography of aging borrowed from the field of reliability theory(Witten, 1981; Doubal, 1982). Subsequently the fields of demography and biodemography of aging made use of terminology from mathematics and physics to describe aging processes. Phrases like, "*the force of mortality*" or "*acceleration of aging*" abound in this literature. And yet, the interpretations of these phrases bear little resemblance to their original meanings in classical physics; serving more as anecdotal descriptors rather than exactly quantifiable constructs. Similar comments may be made around other survival/failure constructs that will be described in later sections of this paper.

These conceptual disconnects inspired Witten and her team (Witten, 1989) to develop variables and definitions that are more true to their physics origins. By doing so, they hoped to provide a better sense of what these quantitative metrics were describing. Consider, for example, the physics concepts of velocity and how to use it to quantify absolute and relative survival differences between species. In (Witten, 1989) the author proposed formal classical physics rigorous definitions for the terms "velocity" - denoted $v(a)$ and "acceleration" - denoted $\alpha(a)$ of aging. Witten also defined the absolute and relative differences between two groups (species). The idea of being able to compare between species or to extrapolate from one species to another is an old one. For example, Carnes

*et al.*(Carnes et al., 1998; Carnes et al., 2003; Hoel et al., 2005) examined the problem of lifespan extrapolation from nonhuman organisms to humans during radiation exposure.

In (Eakin, 1994; Eakin and Witten, 1995a; Eakin and Witten, 1995b; Witten and Eakin, 1997) the authors extended their physics of aging definitions to include a "distance" metric of aging, denoted $x(a)$ that could be used to compare different species on a comparable time scale. This method involved comparing nomograms based upon the $x(a)$ for each species.

## 3.1 Terminology

In this paper, we will return to the question of developing a set of physically consistent constructs, drawing upon the ideas of classical Newtonian physics, motivated by the terms in the biogerontology of aging. Moreover, we want these constructs to be able to be used to more clearly describe the dynamics of an aging cohort of biological organisms. In this paper we will begin by making use of a number of concepts drawn from traditional classical physics; *i.e.*, distance, velocity, force. In order to assist the reader in understanding the conceptual development, we will always attempt to provide a non-physics explanation of each construct that we develop. In the next section we talk about the concept of "extrinsic gerontological distance" from which we derive the concepts of velocity and an acceleration. We begin by discussing the modifiers "extrinsic" *vs.* "intrinsic" of these and other variables.

### 3.1.1 The Extrinsic *vs.* the Intrinsic Perspective

The challenge in understanding survival and mortality data is that different organisms do not "experience" the "aging" process in the same fashion. We are all familiar with the idea of a seven year-old dog being sixty-three in human years. This difference in the experience of the aging process is termed "extrinsic" aging; we have not scaled the experiences so that they can be compared on a common experiential scale. How do we know that one human year is $6-7$ dog years? The two organisms do not necessarily share the same "intrinsic" aging experience. If we can find a way to map one experience of aging onto the other, we then have aligned the experiences in such a way as to show how they are related. We call this common experience an "intrinsic" relationship between the organisms. In this paper we will demonstrate one rigorous methodology for constructing that mapping (relationship) and we will then show you how it can be used.

## 3.2 Brief Review of Past Work

The biodemographic and general aging literature often makes use of such terms as the"acceleration of aging" and the "velocity of aging." As we have already pointed out, these terms are loosely, not rigorously defined constructs and serve rather as a set of conceptual ideas that allow the reader to develop a sense of how fast a population is dying off and whether or not one population is dying off faster than another. In fact, based upon the past literature in the field, there is really no actual way to calculate either of these conceptual constructs; they are simply nothing more literary descriptors. This motivated Witten and her team set out to develop ways to make those calculations and to do so in a rigorous and conceptually consistent fashion. Since velocity and acceleration are just time-derivatives of distance, we being by looking at the problem of deriving the extrinsic organismal distance.

### 3.2.1 Defining the Extrinsic Organismal Distance, Velocity and Acceleration

Witten(Witten, 1989) and her team demonstrated one possible way of defining both an "extrinisic velocity" and an "extrinsic acceleration" of aging in terms of the formal physics definitions of these quantities. In addition to the velocity and acceleration of aging, they demonstrated how one could construct a "gerontological distance." The "gerontological distance" $x(a)$ can be seen as the "distance" an organism has traveled down its hypothetical organismal lifeline by age $a$. This set of definitions allowed them to provide a complete initial formulaic grounding of velocity and acceleration in terms of traditional physical variables, not literary descriptors.

In Eakin(Eakin, 1994) and Eakin & Witten(Eakin and Witten, 1995a; Eakin and Witten, 1995b) the authors demonstrated that it was indeed possible to define an equivalent "extrinsic distance" metric so that if we denote the *extrinsic gerontological distance* at age $a$ by $x(a)$, then the following physical definitions would be true:

$$x(a) = \text{extrinsic gerontological distance} \quad (8)$$

$$v(a) = \frac{dx(a)}{da} = \text{extrinsic velocity} \quad (9)$$

$$\alpha(a) = \frac{dv(a)}{da} = \text{extrinsic acceleration} \quad (10)$$

These follow because, given a "distance" measure and remembering our basic physics definitions, the velocity is the rate of change of distance and the acceleration is the rate of change of the velocity.

#### 3.2.2 Deriving the Organismal Distance, Velocity and Acceleration

Once we have the extrinsic distance $x(a)$, we can construct the extrinsic velocity $v(a)$ and the extrinsic acceleration $\alpha(a)$. Remembering that velocity is rate of change of distance and using the fact (see Eakin & Witten(Eakin and Witten, 1995a; Eakin and Witten, 1995b)) that

$$x(a) = \int_0^a \lambda(\zeta) d\zeta, \tag{11}$$

we can show that the extrinsic velocity of aging is given by $v(a)$ and that the extrinsic velocity of aging can be quantitatively measured as $v(a) = \lambda(a)$ where $\lambda(a)$ is just the traditional "mortality rate" of the population being studied.

$$v(a) \equiv \frac{dx(a)}{da} = \frac{d}{da}\int_0^a \lambda(\zeta) d\zeta = \lambda(a) \tag{12}$$

Thus, the extrinsic velocity of aging now has a rigorous physical meaning. In fact, the extrinsic velocity of aging is just the traditional mortality rate $\lambda(a)$ of a population. It follows from this fact that the extrinsic acceleration of aging is just the rate of change of extrinsic velocity and therefore the extrinsic acceleration of aging is the rate of change of the traditional mortality rate.

$$\alpha(a) \equiv \frac{dv(a)}{da} = \frac{d\lambda(a)}{da} \tag{13}$$

We now have a formal way to calculate the "acceleration of aging." The construct of a mathematical acceleration was used in (Carnes and Witten, 2013)to show that after a certain point in the human lifespan, there is actually a real acceleration in the how fast a population of individuals travels through their lifespan. Throughout the remainder of this paper we will use mortality rate and extrinsic velocity of aging interchangeably.

As we have seen, given the mortality rate function $\lambda(a)$, we can calculate $x(a)$, $v(a)$ and $\alpha(a)$. Eakin & Witten(Eakin and Witten, 1995a; Eakin and Witten, 1995b) also demonstrated that if $S(a)$ is the extrinsic survival fraction (denoted $S(a)$, and if $a$ represents the extrinsic chronological age, then the "extrinsic gerontological distance" $x(a)$ is related to the extrinsic survival fraction $S(a)$ of the population via the following relationship

$$x(a) = \int_0^a \lambda(\zeta) d\zeta = \ln\left[\frac{1}{S(a)}\right] = -\ln[S(a)] \tag{14}$$

Observe that Equation[14] is independent of the specific extrinsic survival function $S(a)$ in that any survival distribution $S(a)$ can be used for $S(a)$ in the formula (Weibull, Gompertz-Makeham, *etc.*). Moreover, modifications to such models - for example, addition of frailty distributions, *etc.* do not alter the mathematical construction of the physical variables nor do they alter their meaning from a classical physical perspective.

This completes our core requirements for a basic physics of survival in that the appropriate derivatives of the gerontological distance $x(a)$ yield the usual physics literature definitions of both the *extrinsic velocity of aging* and the *extrinsic acceleration of aging*. Finally, we note that given the *extrinsic gerontological distance* $x(a)$ we can compute the extrinsic survival distribution, which is given by the following equation

$$S(a) = \exp[-x(a)] \tag{15}$$

This relationship makes conceptual sense because, the farther down the "life distance" $x(a)$ you travel, the less likely you are to survive. We now address how to actually calculate these variables and how to use them.

#### 3.2.3 Computing the Organismal Distance, Velocity and Acceleration for the Masoro & Yu Diets

It is also important to note that our physical constructions revolve around the use of a parametric model for the mortality/survival curves. Parameters for the model must be estimated using some traditional method such as maximum likelihood estimation (Elandt-Johnson and Johnson, 1999; Lawless, 2003; Kalbfleish and Prentice, 2002). In order to help us understand these new physical constructs, we will make use of the data from the original Masoro & Yu (Yu et al., 1982) data to illustrate the concepts.

Because the Gompertz survival model is so frequently used in the Gerontological literature, we will use that it as our exemplar parametric survival model $S(t)$ (any others would also work). The traditional two-parameter Gompertz mortality and survival models are given by the following equations

$$\lambda(a) = h_0 e^{\gamma a} \tag{16}$$

$$S(a) = \exp\left[\frac{h_0}{\gamma}(1 - e^{\gamma a})\right] \tag{17}$$

where $h_0$ is the mortality rate at age $a = 0$ and $\gamma$ represents the slope of the line in the $\ln\lambda(a)$ *vs.* $a$ plot and is ultimately related to the mortality rate doubling

time (Table [1], (Finch et al., 1990)). We can see how sharply the changes in acceleration are occurring by looking at how the two functions change their curvature (Thomas, 1968). The curvature, denoted $\kappa(a)$ of the Gompertz equation, at any age, can be calculated using the following formula

$$\kappa(a) = \frac{\gamma^3 \lambda(a)}{\sqrt{1+\gamma^4 \lambda^2(a)}} \tag{18}$$

An interesting aside here is that if one were to choose to use the Gompertz-Makeham mortality rate given in equation [7] then, while the velocity $v_{GM}(a) = v_G(a) + M$, that is the Gompertz-Makeham velocity is shifted by an amount $M$, the actual accelerations $\alpha_{GM}(a)$ and $\alpha_G(a)$ are identical. This suggests that the addition of the baseline mortality constant $M$ does not affect the acceleration that the organism population undergoes but only the organismal velocity of aging. Since the Makeham constant is added in order to describe the "environmental" aging effects, our result suggests that for the Gompertz-Makeham parametric model of aging, the Makeham constant merely adds to the speed (velocity) with which the organismal cohort travels across the lifespan timeline, but does not change the acceleration the cohort undergoes.

#### 3.2.4 Summary of AD vs. DR Results

We summarize our findings as follows. The AD organisms traverse their life path $x(a)$ faster than do the DR organisms. The word "faster," unlike before, can be quantitatively described by examining the velocity plots $v(a)$ of the respective organisms. Moreover, the organisms do not traverse their life paths with a constant velocity and this suggests that there is an underlying acceleration process $\alpha(a)$ taking place. In addition, using the concept of curvature $\kappa(a)$, we can quantitate the way the organismal acceleration curves bend and how sharply they bend thereby giving us insight into the way (form) in which the organismal acceleration curves are either similar or different with respect to how they bend over time. Table [1] provides the reader with some traditional measures for the two diet groups. MRD is the mortality rate doubling time as defined in Finch, Pike & Witten(Finch et al., 1990), the mean lifespan MLS and the inflection age $a_{inf}$ defined in Witten(Witten, 1989). These will additional values will be useful in an upcoming section.

Table 1: Parameter Values for *Ad libitum*(AD) and Restricted Rats (DR) Using A Gompertz Survival Model.

| Variable | Symbol | AD |
|---|---|---|
| Gompertz slope (per day) | $\gamma$ | 0.010257 |
| Gompertz intercept (per day) | $h_0$ | 0.00000512 |
| MRD (days) | $\frac{\ln 2}{\gamma}$ | 67.574 |
| MLS (days) | $\bar{a}$ | 685.197 |
| Inflection age (days) | $a_{inf}$ | 741.078 |
| Variable | Symbol | DR |
| Gompertz slope (per day) | $\gamma$ | 0.00487 |
| Gompertz intercept (per day) | $h_0$ | 0.0002344 |
| MRD (days) | $\frac{\ln 2}{\gamma}$ | 142.206 |
| MLS (days) | $\bar{a}$ | 982.195 |
| Inflection age (days) | $a_{inf}$ | 1094.92 |

# 4 LOOKING FOR DIFFERENCES BETWEEN SPECIES LONGEVITY BEHAVIORS

Given the previous descriptors for longevity dynamics, how might we go about comparing different organisms? Witten (Witten, 1989) also pointed out that it is also natural to want to compare longevity dynamics under different living conditions. Hence, we also wish to compare the extrinsic survival, gerontological distance, velocity, acceleration or acceleration curvature of one organism $\Omega_1$ at age $a_1$ against those of another organism $\Omega_2$ at age $a_2$.

## 4.1 Differences in Survival, Mortality, Velocity and Distance

In her original paper, Witten (Witten, 1989) defined the "extrinsic velocity difference" and "extrinsic acceleration difference" of aging. The "extrinsic survival difference", for the two diet groups, was defined as $S_A(a) - S_R(a)$. However, now that we have defined the extrinsic gerontological distance, we can unify the original work of Witten with the work of Eakin (Eakin, 1994) and Eakin & Witten (Eakin and Witten, 1995a; Eakin and Witten, 1995b) to demonstrate how to calculate the extrinsic values of distance difference, velocity difference and acceleration difference between the two organisms. The necessary parameter values are given in Table [1] of this paper.

## 4.2 Extrinsic Crossing Points of Curves

It is also useful to know whether or not any of our given pairs of curves cross. Crossing of survival/mortality curves can have implications in demographic estimation of maximum lifespan based

Table 2: Parameter Values for *Ad libitum* and Restricted Rats Using A Gompertz Survival Model.

| Symbol | Value |
|---|---|
| Survival/distance crossing age (days) | 394.64 |
| Mortality/velocity crossing age (days) | 282.49 |
| Acceleration crossing age (days) | 144.28 |

upon psycho-socio-economic variables (Hirsch et al., 2000). The existence of a crossing point for the survival and the distance functions is a bit more complex in that they require solving transcendental equations (Cheney and Kincaid, 1985). For the mortality rate crossing points, we can demonstrate that the age at which a pair of mortality rate curves cross is given by

$$a_{\text{cross}}^{\text{mortality}} = \frac{1}{\gamma_R - \gamma_A} \ln\left(\frac{h_{0A}}{h_{0R}}\right) \tag{19}$$

Since the physics of our arguments shows that the mortality rate is just the velocity, the variable $a_{\text{cross}}^{\text{mortality}}$ is just the crossing of the velocities as well. That is, $a_{\text{cross}}^{\text{velocity}} = a_{\text{cross}}^{\text{mortality}}$ The crossing of acceleration functions can be shown to be given by

$$a_{\text{cross}}^{\text{acceleration}} = \frac{1}{\gamma_R - \gamma_A} \ln\left(\frac{h_{0A}\gamma_A}{h_{0R}\gamma_R}\right) \tag{20}$$

It is interesting to note that we can re-express $a_{\text{cross}}^{\text{acceleration}}$ as follows

$$a_{\text{cross}}^{\text{acceleration}} = a_{\text{cross}}^{\text{velocity}} + \left(\frac{1}{\gamma_R - \gamma_A}\right) \ln\left(\frac{\gamma_A}{\gamma_R}\right) \tag{21}$$

From our data in Table[1], it can be shown that for our two rat groups, the crossings are illustrated in Table[2].

# 5 THE PROBLEM OF THE EXPERIENCE OF TIME

As was discussed in Eakin & Witten (Eakin and Witten, 1995a; Eakin and Witten, 1995b), the distance function $x(a)$ is exactly analogous to one side of a nomogram in which we imagine a line in a two-dimensional space. The line represents the organismal lifeline and $x(a)$ represents how far along the lifeline the given organism has traveled in its life by chronological age $a$. When we have two organisms $\Omega_1$ and $\Omega_2$, the values $x_{\Omega 1}(a)$ and $x_{\Omega 2}(a)$ represent two nomogram lines and it is this nomogram structure that allows us to develop a means by which to compare the extrinsic ages of different species. This methodology is discussed, in detail, in Eakin & Witten (Eakin and Witten, 1995a; Eakin and Witten, 1995b). With this construction in place, we now have a means by which we can actually determine how old a fly is, in horse years, or how old a 12 year-old human female was, in fly years.

While the previous definitions are correct from the perspective of a physicist, there is a tacit assumption that time (or the aging process as measured over time) is experienced in exactly the same way by all of the organisms being examined. In fact, this is simply not realistic. Therefore, we need to rework our previous definitions so that we account for this fact. The flaw here is that the time units of one organism are not necessarily those of the other organism. We need an "intrinsic" measure of distance

We begin by assuming that there is a population based linear transformation that allows us to transform time scales so that "chronological time" and "biological time" are linearly related. In other words, we need to find a way to scale time so that all organisms are using the same time scale. For now we will ignore the question of chronological time *vs*. biological time and assume that the underlying processes of aging are manifested along a life course trajectory that can be measured using chronological time. In fact, this is not an unreasonable assumption as the field of the demography of aging is based upon this assumption; consider, for example, the typical definition for the demographic variable $n(t,a)$ which is the number of individuals of age $a$ in the population at time $t$ (see work of Von Foerster and others who derive the demographic partial differential equation that describes $n(t,a)$ (Witten, 1983).

There are many ways that one could approach scaling or normalizing time. We will use the method discussed in our work and as presented in Witten & Eakin (Witten and Eakin, 1997). For the purposes of discussion and illustration, from this point on we will use the Gompertzian survival distribution defined in Equations [16]. However, any parametric distribution (*i.e.*, Weibull, Gompertz-Makeham), even mixtures can be used to replace the Gompertz and our methodology will still apply.

## 5.1 Review of the Witten-Eakin Normalization Method

In Witten & Eakin(Witten and Eakin, 1997) we introduced the following temporal normalization algorithm. If we call $a$ the *extrinsic age* of the organism, we can generate what we will call an *intrinsic age* denoted by $\mathfrak{a}$ and obtained by dividing the extrinsic age by the life expectancy of the individual at birth. Thus,

$\mathfrak{a}$ would be given by

$$\mathfrak{a} = \frac{a}{\int_0^\infty S(\zeta)d\zeta} \tag{22}$$

Other normalization methods, *interquartile normalization* Carnes (Carnes et al., 2006) and *inflection time normalization* Witten & Eakin (Witten and Eakin, 1997) have also been demonstrated. Each has its benefits and drawbacks. However, what is interesting is that our general methodology will work for any of these normalization methods. Moreover, it is possible to demonstrate that there is a simple linear relationship between the different normalization transforms so that one can be easily transformed into the other. Following the arguments in (Eakin and Witten, 1995a; Eakin and Witten, 1995b), we can construct the *intrinsic normalized gerontological distance* $\chi(\mathfrak{a})$ and demonstrate the formula for a Gompertzian two parameter distribution Equation[16]. The results are given by

$$\chi(\mathfrak{a}) = \ln\left[\frac{1}{\mathfrak{S}(\mathfrak{a})}\right] \tag{23}$$

From this, we can derive the *intrinsic normalized velocity* $\mathfrak{v}(\mathfrak{a})$

$$\mathfrak{v}(\mathfrak{a}) = \frac{d\chi(\mathfrak{a})}{d\mathfrak{a}} = \lambda(\mathfrak{a}) = h_0 e^{\gamma\mathfrak{a}} \tag{24}$$

and the *intrinsic normalized acceleration* $\varsigma(\mathfrak{a})$ as follows

$$\varsigma(\mathfrak{a}) = \frac{d\mathfrak{v}(\mathfrak{a})}{d\mathfrak{a}} = \gamma\lambda(\mathfrak{a}) \tag{25}$$

Again, note that the results equations[23-25], while applied to the two-parameter Gompertz distribution, can be applied to any parametric distribution (Weibull, Gompertz-Makeham, *etc.*) and can be normalized using any of the methodologies discussed.

## 5.2 Witten-Eakin Rectangularity Measures

The concept of survival curve rectangularity has been discussed by a number of authors (Demetrius, 1977; Demongeot, 2009; Nagnur, 1986; Pflaumer, 2010). Witten & Eakin (Witten and Eakin, 1997) demonstrated how to construct rectangularity and drift measures for both the intrinsic and extrinsic survival curves when one was using a parametric model to fit to the lifespan data. Their methodology is extensively discussed in Pflaumer (Pflaumer, 2010). Using these methods, Witten & Eakin were able to demonstrate that while the U.S. population survival distribution is rectangularizing, it is also drifting with a simultaneous lengthening of mean survival and squaring of the survival distribution. Table [3] provides the values of some of these measures for the two diet populations in this paper.

Table 3: Rectangularity Measure Values for *Ad libitum* and Restricted Rats Using A Gompertz Survival Model.

| Parameter | Symbol |
|---|---|
| Extrinsic Modal Value (days) | $m$ |
| Extrinsic Elasticity (days) | $\varepsilon_0$ |
| Extrinsic Keyfitz Entropy (days) | $H$ |
| Extrinsic Prolate Angle (Degrees) | $\theta$ |
| Prolate Rectangularity Index | $\kappa$ |
| Modified Prolate Angle (degrees) | $\theta'$ |
| Modified Rectangularity | $\kappa'$ |
| **Parameter** | **AD Value** |
| Extrinsic Modal Value (days) | 741.078 |
| Extrinsic Elasticity (days) | 684.806 |
| Extrinsic Keyfitz Entropy (days) | 8.01079 |
| Extrinsic Prolate Angle (Degrees) | $-21.4898$ |
| Prolate Rectangularity Index | 0.930483 |
| Modified Prolate Angle (degrees) | 18.9534 |
| Modified Rectangularity | ??? |
| **Parameter** | **DR Value** |
| Extrinsic Modal Value (days) | 1094.92 |
| Extrinsic Elasticity (days) | 976.495 |
| Extrinsic Keyfitz Entropy (days) | 11.8226 |
| Extrinsic Prolate Angle (Degrees) | $-28.1145$ |
| Prolate Rectangularity Index | 0.882008 |
| Modified Prolate Angle (degrees) | 25.2246 |
| Modified Rectangularity | ??? |

With this section, we have completed the discussion of the basic physics. To summarize, using the survival extrinsic parametric survival distribution $S(a)$, we have defined an extrinsic distance of aging $x(a)$, an extrinsic velocity of aging $v(a)$, and an extrinsic acceleration of aging $\alpha(a)$. Extending these definitions, we have defined extrinsic relative and absolute differences of these functions for two different species or diet groups. We have illustrated these concepts using the original Masoro & Yu (Yu et al., 1982) *ad libitum*/diet restriction data. We then made the argument that the two groups might not experience "time" in the same way. Consequently, we introduced a number of temporal scaling methods that might be used to "normalize" the experience of time. We termed the unnormalized age "extrinsic age" and the normalized age variable "intrinsic age." We then illustrated how all of the previously defined variables are modified by normalization and we subsequently compared the normalized *ad libitum* and normalized diet restricted variables.

In the upcoming discussion we will continue our

definition of physics quantities by looking at how to define the key concepts of a population mass, a force of aging, a population momentum, a kinetic energy and a total energy.

# 6 EXPANDING THE POPULATION PHYSICS DEFINITIONS

## 6.1 Defining the Mass of a Population

One of the challenges in defining a physics of aging is that of defining a mass quantity. Nearly every physical quantity involves the use of a mass construct; force, momentum, kinetic and potential energy to name a few. For the moment, we will assume that we have a single organism and that we may hypothetically assign to that organism what we will call "one *omu*" (organismal mass unit). It follows that if there are $N(a)$ organisms at time $a$ we will denote the total mass $M(a)$ of the system of organisms as

$$M(a) = N(a) \cdot 1omu = N_0 S(a) \cdot 1omu \tag{26}$$

Note that we are treating the population as a homogeneous population in which the individual variation of the masses will not be something with which we need to concern ourselves. This is not unreasonable because all parametric models homogenize the populations with respect to many potentially important factors. With this mass construct in hand, we may now extend our physics of aging definitions. The most obvious first choice is to define a population force.

## 6.2 Defining the Force of a Population

We first consider the "force" construction because the terminology of a force of mortality has been historically used in the field of biogerontology. The "force of mortality" is traditionally defined as follows

$$\mu(a) = -\frac{S'(a)}{S(a)}. \tag{27}$$

which we have shown is equivalent to our physical definition

$$\lambda(a) = -\frac{S'(a)}{S(a)} = -\frac{d}{da} ln[S(a)] = \frac{d}{da} x(a) = v(a). \tag{28}$$

Sadly, while "force of mortality" may be an excellent conceptual description of $\mu(a)$ (old notation) or $\lambda(a)$ (new notation), it is not viable measurable "force" quantity. Using the physics constructions we have now developed we see that the traditional definition of "force of mortality" is actually a velocity of aging and not a force quantity at all.

Using our definition of a mass unit (Equation [26]) and our previous definition for acceleration (Equation [8]), we observe that the magnitude of the population force must satisfy $F = M\alpha$. Therefore, our force definition becomes

$$F = M(a)\frac{dv(a)}{da} = N_0 S(a)\frac{d\lambda(a)}{da} \tag{29}$$

Using the Gompertz distribution, as an example, equation [29] becomes

$$F = N(a) \cdot \gamma \cdot \lambda(a) \tag{30}$$

$$= \gamma N_0 S(a) \lambda(a) \tag{31}$$

Thus, for the Gompertz distribution, the "force of aging" is actually given by the following equation:

$$F = h_0 \gamma N_0 e^{\gamma a} e^{\frac{h_0}{\gamma}(1-e^{\gamma a})} \tag{32}$$

We provide the complete derivation in Appendix [1].

The obvious question is whether or not the units are correct for this force definition. We already know that mass has the correct units. Velocity has units of $distance/time$ so mass times velocity has the correct units. Since $\gamma$ has units of $1/time$, multiplying it times mass times velocity gives units of $mass \cdot distance/second \cdot second$ which is the correct units for force (Newtons) $F = ma$.

It is also possible to show that the maximum force occurs at age $a_F$ where $a_F$ is given by

$$a_F = \frac{1}{\gamma} \ln \frac{\gamma}{h_0} \tag{33}$$

This is nothing more than the inflection age (or inflection time) discussed in the work of Eakin & Witten(Eakin and Witten, 1995b). Knowing this, it is straightforward to demonstrate that the maximum force $F_{\max}$ is given by

$$F_{\max} = \gamma^2 N_0 e^{\frac{h_0}{\gamma} - 1} \tag{34}$$

Let us continue our derivation of the different physics quantities before we discuss their actual application and relevance to biodemography and the biology of aging.

## 6.3 Defining Momentum of a Population

We also note that we can immediately obtain a definition for *momentum* magnitude $p(a)$ by observing that

$p = mv$ which is just

$$p(a) = M(a)v(a) = M(a)\frac{dx(a)}{da} = N_0 S(a)\lambda(a) \quad (35)$$

For the Gompertz distribution, $p(a)$ becomes

$$\begin{aligned} p(a) &= M(a)\cdot v(a) && (36)\\ &= h_0 N_0 e^{\gamma a} e^{\frac{h_0}{\gamma}(1-e^{\gamma a})} && (37)\\ &= \gamma F(a) && (38) \end{aligned}$$

## 6.4 Defining Kinetic Energy of a Population

Given that we have mass and velocity, we can now also construct a population kinetic energy *KE*. We remember the traditional definition of kinetic energy as follows

$$\begin{aligned} KE &= \frac{1}{2}M(a)\cdot v(a)^2 && (39)\\ &= \frac{1}{2}\cdot N(a)\cdot\left(\frac{dx(a)}{da}\right)^2 && (40) \end{aligned}$$

If we substitute for the Gompertz distribution variables, and given that $v(a) = \lambda(a)$, our kinetic energy

$$\begin{aligned} KE &= \frac{1}{2}N(a)\left[\lambda(a)\right]^2 = \frac{N_0}{2}S(a)\left[\lambda(a)\right]^2 && (41)\\ &= \left(\frac{N_0 h_0^2}{2}\right)e^{\frac{h_0}{\gamma}(1-e^{\gamma a})}e^{2\gamma a} && (42) \end{aligned}$$

It is straightforward to show that the maximum value of the kinetic energy occurs at $a_{KE}$ which is given by

$$a_{KE} = \frac{1}{\gamma}\ln\frac{\gamma}{h_0} + \frac{1}{\gamma}\ln 2 \quad (43)$$

Notice that the first term in this equation is the age at which the maximum force occurs. Thus, we could write $a_{KE}$ as $a_{KE} = a_F + \frac{1}{\gamma}\ln 2$.

## 6.5 Defining Potential Energy of a Population

Deriving a potential energy of a population is a bit more difficult. We begin by hypothesizing that our force $F(a)$ is the gradient of the potential energy function $V(a)$ that we wish to determine. We do this because it would create a conservative function that would make the physics nicer. In particular, using our physics analogies, let us suppose that $F(a) = -\nabla V(a)$. In one dimension this becomes $F(a) = -dV(a)$. Thus, if we were to integrate both sides of the equation, we would obtain a solution for $V(a)$. Therefore, integrating both sides, we have that

$$V(a) = -\int_0^a F(\zeta)d\zeta + V(0) \quad (44)$$

where $V(0)$ is the population potential energy at age $a = 0$. For the purposes of illustration, we will solve for the Gompertz potential energy. From equation [32], we have that $F(a) = \gamma N(a) h_0 e^{\gamma a}$. Integrating this from $age = 0$ to $age = a$ we have that

$$\begin{aligned} \int_0^a F(\zeta)da &= -\gamma h_0 \int_0^a N(\zeta)e^{\gamma\zeta}d\zeta && (45)\\ &= \gamma N_0\left[\exp\left[\frac{h_0}{\gamma}(1-e^{\gamma a})\right]-1\right] && (46) \end{aligned}$$

from which we observe that

$$\begin{aligned} V(a) - V(0) &= \gamma N_0\left[\exp\left[\frac{h_0}{\gamma}(1-e^{\gamma a})\right]-1\right] && (47)\\ &= -\gamma N_0 + \gamma N_0 S(a) && (48)\\ \Delta V &= -\gamma N_0 \overline{F}(a) && (49) \end{aligned}$$

where $\overline{F}(a)$ is the cumulative failure rate and $\Delta V$ is just $V(a) - V(0)$. Solving for $V(a)$, we have that

$$V(a) = -\gamma N_0 S(a) + [V(0) - \gamma N_0] \quad (50)$$

In fact, since $V(0)$ is an arbitrary constant, we can choose it's value such that it cancels the $\gamma N_0$ term yielding the following final equation for the potential energy is just

$$V(a) = \gamma N_0 S(a) \quad (51)$$

## 6.6 Defining Total Energy of a Population

Once we have the kinetic energy *KE* and the potential energy *V*, we can form the total population energy remembering that $TE = KE + V$ which is given by

$$TE = \frac{1}{2}N(a)\left(\frac{dx(a)}{da}\right)^2 + \int_0^a F(\zeta)d\zeta \quad (52)$$

For the Gompertz equation, using our previous calculations, we can rewrite the total energy as

$$TE = \frac{N_0}{2}\lambda^2(a)S(a) + \gamma N_0 S(a) = S(a)\left[\frac{N_0}{2}\lambda^2(a) + \gamma N_0\right] \quad (53)$$

which can be simplified to

$$TE = S(a)N_0\left[\frac{1}{2}\lambda^2(a) + \gamma\right] \quad (54)$$

All of our derivations are summarized in Table 4.

Table 4: Locations and Values of Maxima for each Function Using the Gompertz Model.

| Variable | Age of AD Maximum | AD Maximum Value |
|---|---|---|
| Force | 741.08 | $1.27 * 10^{-9}$ |
| Momentum | 741.08 | 0.004 |
| Kinetic Energy | 808.65 | 5.56 |
| Potential Energy | 953 | 0 |
| Total Energy | 953 | 0 |
| Variable | Age of RD Maximum | RD Maximum Value |
| Force | 1094.92 | $8.78 * 10^{-6}$ |
| Momentum | 1094.92 | 0.002 |
| Kinetic Energy | 1237.12 | 0.28 |
| Potential Energy | 1435 | 0 |
| Total Energy | 1435 | 0 |

### 6.7 Addressing the Problem of Different Initial Population Sizes $N_0$

Observe that the previous physical variable definitions contain the parameter $N_0$. This makes it difficult to compare populations with different initial population sizes, when working with our newly defined physics variables. To address this problem, we define the normalized variable of interest by dividing through by $N_0$. For example, the normalized force $\mathcal{F}$ would be $\frac{F}{N_0}$. Similarly, we define the normalized momentum $\mathcal{P}$ as $\frac{p}{N_0}$, the normalized kinetic energy $\mathcal{KE}$ would be $\frac{KE}{N_0}$ and the normalized total energy $\mathcal{TE}$ and normalized potential energy $\mathcal{V}$ would be defined in a similar fashion.

If we now substitute for the Gompertz distribution equivalent variables, we have that the following results

$$\mathcal{F} = \gamma S(a)\lambda(a) \quad (55)$$

$$\mathcal{P} = S(a)\lambda(a) \quad (56)$$

$$\mathcal{KE} = \frac{S(a)\lambda(a)^2}{2} \quad (57)$$

$$\mathcal{V} = \gamma S(a) \quad (58)$$

$$\mathcal{TE} = S(a)\left[\frac{1}{2}\lambda^2(a)+\gamma\right] \quad (59)$$

In plotting the actual figures, it is easy to see that not only is the kinetic energy higher in the *ad libitum* group, but that it peaks much earlier in the *ad libitum* group as well. Note that, as we did with the arguments around survival, we can make the same arguments for the newly defined variables and ask about their intrinsic *vs.* extrinsic behaviors.

## 7 CONCLUSIONS

In this work, we have derived a large number of the remaining basic constructs for a classical physics in support of the biodemographics of aging. We have demonstrated how these constructs are internally consistent, from a physics perspective. Moreover, we have also demonstrated how they provide useful additional insights into the dynamics of population biodynamics. Lastly, using the concepts developed in this paper, we have proposed a formal rigorous definition for the lethality of any intervention when measured against a control group.

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