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PHENOTYPIC DEFORMATION: THE ROLE OF ALLOMETRY AND THE GOLDEN RATIO

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Abstract: Following the Antonelli/Rutz Finsler Gate method, the concept of Allometric Strain is introduced to model plastic deformation of phenotypes in mammalian genomes. Focus is on a model of muscle and adipose (fat) cell populations, which produce hormones adiponectin and IL-6, which mediate their interactions. The model shows that genetic switching is able to irreversibly deform a normal system to one not producing IL-6, which nevertheless remains conservative in production and linearly stable in population densities. It is further proved that both systems are heterochronic changes of the standard Euclidean Huxley-Needham Allometric law, resulting in deformed growth curves. The relevance to obesity and Type 2 diabetes is discussed.

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1. Introduction

Following experimental work of J. Huxley and J. Needham in the early 20$^{\text{th}}$

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century, the present day ubiquitous Huxley/Needham Allometric Law (HAL) can be considered a *model Bauplan*, or foundation of vertebrate ontogeny, [10], [26], [27]. From this perspective, one may consider how a class of physiological processes, taking place in a developing vertebrate individual, is to be mathematically expressed. In particular, the present mathematical paper considers how environmental influences alter phenotypic expression. Our method can be seen to augment C.H. Waddington's concept of the *epigenetic landscape*, providing it with considerable analytical power, [3], [8], [12], [15], [24], [32], [47], [48]. Background for differential geometry, and especially Finsler geometry, may be found in, [7], [8], [19], [21], [23], [41].

Phenotypic plasticity is defined as the ability of an organism to react to an environmental input with an adaptive mutual adjustment, without genetic change, among variable aspects of the phenotype, following a novel or unusual input during development, [12]. Epigenetic alterations such as DNA methylation, histone acetylation and micro RNA expression are the molecular basis of the phenotypic plasticity, [32]. An important example of environmentally induced alterations in the time-course of ontogeny is methylation of cytosine on DNA, which silences gene expression by blocking transcription, [32]. The genes, IRX3 and IRX5 are master controllers of thermogenesis, the process whereby adipocytes dissipate energy as heat instead of storing it as triglycerides. A single nucleobase replacement, T to C, turns off these genes and halts the accumulation of lipids. Such deformations of phenotype have been considered irreversible and termed plastic deformations. The reversible ones have been called elastic or flexible deformations [12].

In humans, primary adipose cells from either a risk or non-risk (diabetic) individual, alters the expression of either of the two genes thereby converting energy-storing white adipocytes to energy-burning brown adipocytes, or vice versa. In mice, repression of IRX3 results in a substantial change in whole-body energy balance and a reduction in body weight and fat stores and fosters strong resistance to high-fat diets. Thermogenesis can be triggered in the mitochondria-rich brown adipocytes in mice and is closely related developmentally to skeletal muscle. The mathematical models considered herein involve these adipocytes and skeletal muscle cells.

Our model is ecological in the sense that cell populations, together with their physio-chemical interactions, are expressed dynamically. The focus is on the geometrical dynamics of Energy Budget Theory [6], within the constraints imposed by the allometric law, HAL, considered as a model Bauplan for growth and development, [10], [26], [27], [47]. This model is complicated mathematically, and depends for its analysis on the software, FINSLER, developed by

S.F. Rutz, and on the Finsler Gate concept of Antonelli and Rutz, [19], [28], [47].This entails allometric space being treated as a deformable medium, plastically or elastically, obtainable from the original Huxley allometric space by log-biomass coordinate transformations, nonintegrable or integrable, respectively. The elastic (i.e., reversible) deformations are viewed as motions within this Huxley space analogous to dislocation theory in the Continuum Mechanics literature, [47], [4].

We consider two cell populations, one of skeletal muscle cells and one of adipocytes, secreting hormones, IL-6 (interleukin) and adiponectin (and/or leptin), respectively, [33]. Adipocytes secrete a variety of adipokines (adipo-nectin and leptin) which may be involved in cardiovascular risk. These adipokines may be used as markers of metabolic disorders being associated with cardiovascular pathologies. As is well known, low levels of adiponectin result in insulin resistance which is characteristic of type-2 diabetes and obesity, [40]. IL-6 is an important cytokine, which is secreted by various cell types including skeletal muscle, [33]. It is a systemic regulator of body weight and lipid metabolism and seems to be associated with obesity and insulin resistance. IL-6 may exert both the inflammatory and anti-inflammatory responses in the adipose tissue. IL-6 is also regarded as a myokine and in skeletal muscle; it acts as an energy sensor by activating AMP-activated protein (AMPK) kinase and increasing glucose disposal, fat oxidation, and lipolysis, [33]. IL-6 produced in skeletal muscle may exert anti-obesity effect on liver and adipose tissue via glucose homeostasis and lipolysis. IL-6 signaling is also associated with muscle growth and myogenesis; however, it also causes both protein synthesis and degradation [33]. The obesity-associated perturbations in IL-6 and its receptor likely have diverse effects in different tissues and organs. It will be seen that our model predicts a switching from energy-storage to thermogenesis (or the reverse), under environmental influences which trigger genes to switch off or on.

Centrally important to this model are the so-called heterochronic transformations, which provide a geometrical description of how an individual's physiological network adapts to external influences, when certain conditions are met, [7], [8], [10], [11], [12], [13], [35], [47], [52], [53]. We will delay discussion of these conditions until later in this paper.

At present, our concern is with phenotypic deformation, described intrinsically as a modified geometry on the Euclidean allometric (production) space of Huxley/Needham, (HAL) with coordinates being $\neg$ log biomasses of produced IL-6 and adiponectin. From basic allometric principles we can, if the need arises, interpret the production variables as surrogates of biomass, quantities produced in allometric proportion to biomass, as in chemical ecology, [5], [7],

[8], [9], [14], [16], [17], [18], [31], [36], [45], [46], [47], [48], [49], [50], [51].

The present work is the second in a series of papers on phenotypic deformation of vertebrate genomes, [3]. The next publication will introduce a noisy background for the above dynamics, and will allow small increments in production of IL-6 and adiponectin to enter the coefficient array. However, instead of using the conservative diffusion theory that is Stochastic Nelson Mechanics, [8], [15], [39], [42], [43], [44], as employed in, [3], we use the Finslerian noise theory, [14], [19], [8, appendix]. Following the second "noisy" one, we will publish details of the dynamical energy budget theory for Kropina type MGE models, [29], [30], using S.F. Rutz, computer algebra package, FINSLER, thereby saving the most difficult analyses for last!

2. A Chemical Ecology Type Model

In 1965, A.K. Laird, [1], did statistically rigorous experiments showing that for many classes of vertebrates, the biomasses of organs of an individual, best fit Gompertz curves with same rate constant, rather than other S-shaped curves, [7], [8], [52], [53]. For a given individual and n of its organs, Laird's Law can be formulated as a system of 2^{nd} order differential equations (SODE's) with Positive Initial Conditions:

$$\frac{\mathrm{d}^2 x^i}{\mathrm{d}t^2} + r\frac{\mathrm{d}x^i}{\mathrm{d}t} = 0 \qquad \text{(PIC)}\,,$$

where r is the (positive) rate constant, [8]. From this it follows for each index, $i \in \{1, 2, , n\}$, that solutions $x^i(t)$ are log-Gompertz curves

$$x^i(t) = \ln(a^i) - b^i \exp\{-rt\} = \ln(m^i(t)),$$

from which HAL follows by elimination of the time parameter. For example, for $n = 2$, it follows that $\ln(m^2) = x^2$ and $\ln(m^1) = x^1$ satisfy an allometric relationship

$$x^2 = \frac{b^2}{b^1}x^1 + \ln(a^2) - \frac{b^2}{b^1}\ln(a^1).$$

While HAL is taken to be our Model Bauplan for Ontogeny, there is another aspect of organic growth that concerns us. Namely, an organ which grows with increasing biomass, $m(t)$, in Gompertz fashion, has a uniquely associated mathematical structure, called a Formal Modular Population (FMP). The details are given in, [2, Sect. 2]. It will suffice to say here that the two parameters uniquely characterizing Gompertz growth, namely r and max(log-biomass),

uniquely specify two parameters, r and K, which characterize logistic growth of the FMP. Because of this correspondence, we may alternatively choose to start our argument with two separate logistic populations.

So now we consider two Formal Modular Populations (FMP), given by logistics with equal growth rates λ and where Modular units of type #1 will be skeletal muscle cells and adipocytes will be modular units of type #2. The two populations of modular units, denoted, N^1 and N^2, interact by producing interleukin-6 (IL-6), denoted x^1, and adiponectin (or leptin), denoted x^2, respectively. It is known these two hormones influence the cellular interactions. We further assume in this preliminary model that over some time interval, the amounts produced (measured as log biomasses) are nearly constant. This interval may be relatively short. However, this almost constant condition is important because it narrows down the infinite number of possible dynamical models to just a few. Elsewhere, we refer to this set of possibilities as the Finsler Gate, [2], [3], [47], [50]. Over a longer time interval, the $x's$ may enter the interaction schemes explicitly, but we will not dwell on this here reserving it for consideration in a future paper.

The Finsler Gate Theorem mentioned states that there are only three possibilities for interaction schemes and with each, a characteristic interaction pattern, [8], [35], [47], [14], [19]. Furthermore, the (real number) quantity, J, called the principal scalar, together with the Berwald-Gauss Curvature Scalar, K, distinguishes these three patterns up to isometric isomorphism, [7]. Moreover, each of the three constant coefficient second order ordinary differential equations (SODE's) has a unique form for its associated total energy, we call, Medawars Growth Energy (MGE), [8], [37], [5], [38]. Furthermore, $K = 0$, for these three systems which is of the utmost importance because it ensures that locally defined elastic or plastic deformations extend to global ones, [4], [47], [8]. For the case at hand, the adipocytes are in close proximity to muscle cells (visceral) and serve as energy (ATP) source. Thinking ecologically, we can therefore consider these two populations as commensal, meaning that the adipocytes benefit from the muscle cell population which provides them with intracellular space to reside. The muscle cell population is not negatively affected. Indeed, it benefits from the presence of the adipocytes which provide ATP (MGE in our model language) in times of need. Keeping this in mind, the rate of increase of adipocyte cells, dN^2/dt, should include positive feedback from the muscle cell population and must help regulate energy balance.

Accordingly, we postulate high efficiency in ATP/MGE production, or if not exactly that, at least a conservation of total energy (MGE) as required by Dynamical Energy Budget Theory (DEBT), [5], [38], [7]. In order to mathe-

matically achieve this we utilize the calculus of variations and Euler-Lagrange theory within the context of 2-dimensional Finsler geometry, [7], [8], [19].

It follows from the Finsler Gate Theorem, [47], [2], that 3 constant coefficient schemes are distinguishable by (squared) principal scalar, J^2, which is greater than 4, less than 4 or equal to 4. Based on the above argument, we select the commensal case, $J^2 = 4$, for our model. Explicitly,

$$\begin{cases} \dfrac{\mathrm{d}N^1}{\mathrm{d}t} &= \lambda N^1 - \dfrac{(c_0c_2 - c_1^2)}{c_1}(N^1)^2, \\ \dfrac{\mathrm{d}N^2}{\mathrm{d}t} &= \lambda N^2 - c_2(N^2)^2 - c_0(N^1)^2 - 2\left(\dfrac{c_0c_2}{c_1}\right)N^1N^2, \end{cases} \tag{1}$$

which together with the Volterra production equations

$$\frac{\mathrm{d}x^i}{\mathrm{d}t} = k_{(i)}N^i, \qquad i \in \{1, 2\} \tag{2}$$

constitute a second order differential equation system (SODE).

Notation: Einstein's summation convention is on repeated upper index and lower index so, for example, a^ib_i is a sum of n terms when i runs from 1 to integer n. But, we also use parentheses or the double parentheses as in (2), to indicate a suspension of Einstein's convention in that instance.

In (1), the three c's are arbitrary constants and the k are two arbitrary positive proportionality constants, which for brevity are taken to be unity. Furthermore, we switch notation to Greek as follows: $c_0 = -\beta_2$, $c_2 = \beta_2$, and $c_1 = -\beta_1 \neq 0$ with the betas being positive. Taken together (1) and (2) are Euler-Lagrange equations for the total metabolic energy, $F(x, N, t)$. For ease of expression, we take natural logs, thus,

$$\ln(F) = \ln(N^1) + \left\{\frac{N^2}{N^1} + \frac{\beta_2}{\beta_1}\right\}\exp[-\beta_1x^1 + \beta_2x^2] - \frac{1}{\beta_1}[(\beta_1)^2 + (\beta_2)^2]x^1 + \lambda t, \tag{3}$$

where $x = (x^1, x^2)$, $N = (N^1, N^2)$ and t is clock time. The obvious fact from (3) is that production of adiponectin (x^2) increases energy (MGE) exponentially, while the reverse is true for IL-6 production (x^1). Yet, the latter's negative effect is enhanced, albeit mildly, by the linear expression on the right. Also, if it happens that, $\beta_1 \ll \beta_2$, then this negative effect is downsized. The population

equations are now written

$$\begin{cases} \dfrac{\mathrm{d}N^1}{\mathrm{d}t} &= \lambda N^1 - \left[\beta_2\left(\dfrac{1}{\tau}+\tau\right)\right](N^1)^2, \\ \dfrac{\mathrm{d}N^2}{\mathrm{d}t} &= \lambda N^2 + \beta_2[(N^1)^2-(N^2)^2] - 2\dfrac{\beta_2}{\tau}N^1N^2, \end{cases} \tag{4}$$

where $\beta_1 = \tau\beta_2$ defines τ. We stress that the very presence of the muscle population density, N^1, in the adipocyte population equation (4), indicates that some amount (x^1) of IL-6 is involved, because the coefficients are slowly varying, or almost constant. Removal of N^1 from the second equation in (4) results in a logistic equation.

This removal event is to be interpreted as a genetic switch being turned off so that no IL-6 is being produced. The result is a logistic equation for muscle tissue and for adipose tissue. The corresponding SODE is a plastic deformation of the SODE associated with (4). The reason for this comes from 2-dimensional Finsler geometry. Namely, two Finsler energy (MGE) functionals with constant coefficient quadratic geodesic systems (which is what we have here) are isometrically isomorphic, if and only if, their respective principal scalars, J, are numerically equal, [7], [8], [14]. Since the undeformed system has, $J^2 = 4$, and the deformed one, $J^2 = (\lambda+2)^2/(\lambda+1)$, they can never be exactly the same $\lambda > 0$. We will prove that each system is a plastic deformation of the (Euclidean) HAL, and from this it logically follows that they are themselves plastic deformations of each other.

It is important to mention the above plastic deformations do not cause failure of energy conservation. The "before" and "after" systems each adhere to a strict energy (MGE) budget so that the energy functionals are constant along production trajectories. However, the two systems are not the same, nor are they equivalent by a reversible transformation of x. The energy (MGE) expression for the deformed system is

$$\ln(F_D) = \left(1+\frac{1}{\lambda}\right)\ln(N^2) - \frac{1}{\lambda}\ln(N^1) - \frac{\beta_2}{\lambda}\left(\tau+\frac{1}{\tau}\right)x^1 + \beta_2\left(1+\frac{1}{\lambda}\right)x^2 + \lambda t. \tag{5}$$

Note that the unique, positive, asymptotically stable, steady state for the undeformed system (4) is given by

$$N^1_* = \lambda\frac{\tau^2}{\beta_2(1+\tau^2)}, \qquad N^2_* = \tau N^1_*. \tag{6}$$

For the deformed system, N_*^1 is the same as in (6), but $N_*^2 = \left(\frac{\lambda}{\beta_2}\right) N_*^1$, and it is mathematically impossible for this to equal τN_*^1

From the equations (4) it is easily seen that with β_1 being held fixed, β_2 increasing (so τ is decreasing) would imply adipocyte density (i.e., N_*^2) diminishes (in the adult). Likewise, N_*^1 would be decreasing so there would be fewer muscle cells at adult size. Furthermore, if there were no adipose cells around (N_2 vanishing), the muscle cell population persists. However, parameters β_2 and τ must be in a range to keep the model adipocyte population from unbounded growth. It is well known, however, that these cells can survive alone in a suitable nutrient medium. It is convenient to refer to parameter, τ, as the F/L -Ratio and to the parameter, $\tau + 1/\tau$, as Deformed F/L-Ratio, as in the formula

$$\frac{N_*^2}{N_*^1} = \begin{cases} \tau & \text{(undeformed)} \\ \\ \dfrac{1}{\tau} + \tau & \text{(deformed)} \end{cases} . \tag{7}$$

Here is a prediction of (7): if IL-6 production is switched off, the resulting adipose mass density at adult size will be larger.

Let us make an affine parameter change from clock time, t, to a new production parameter, S, called Size or Total Joint Production, $S = S(\beta_2)$, via

$$\mathrm{d}S = \beta_2 \mathrm{e}^{\lambda t} dt. \tag{8}$$

We tentatively refer to β_2 as Interaction Intensity.

Note from (8) that total joint production rate, $\mathrm{d}S/\mathrm{d}t$, increases exponentially with the Gompertz parameter, $r = \lambda$, and linearly with interaction intensity, β_2.

We now replace $N^i = \mathrm{d}x^i/\mathrm{d}t$, with $y^i = \mathrm{d}x^i/\mathrm{d}S$, so (4) reads

$$\begin{cases} \dfrac{\mathrm{d}y^1}{\mathrm{d}S} + \left(\tau + \dfrac{1}{\tau}\right)(y^1)^2 & = & 0, \\ \\ \dfrac{\mathrm{d}y^2}{\mathrm{d}S} - (y^1)^2 + (y^2)^2 + \dfrac{2}{\tau} y^1 y^2 & = & 0, \end{cases} \tag{9}$$

Elimination of parameter $S(\beta_2)$ converts (9) to a single equation, known as the

Rashevsky equation for the system. It is

$$\begin{cases} \dfrac{\mathrm{d}Y}{\mathrm{d}x} = Y^2 + \left(\dfrac{1}{\tau} - \tau\right) Y - 1, \\ \\ Y = \dfrac{\mathrm{d}y}{\mathrm{d}x}, \;\; y^i = \dfrac{N^i}{\dot{S}}, \qquad \dot{S} = \dfrac{\mathrm{d}S}{\mathrm{d}t}, \\ \\ \dfrac{y^2}{y^1} = \dfrac{N^2}{N^1} = \dfrac{\mathrm{d}x^2}{\mathrm{d}x^1} = \dfrac{\mathrm{d}y}{\mathrm{d}x}, \end{cases} \tag{10}$$

using notation $(x^1, x^2) = (x, y)$.

Therefore, we have from (10), setting the left-hand side to zero, the following proposition.

Proposition 2.1. *$Y_* = N^2_*/N^1_*$ is the positive root, τ, of the polynomial*

$$Y^2 + \left(\frac{1}{\tau} - \tau\right) Y - 1 = 0.$$

Y_* is the Golden Ratio if and only if the coefficient of Y is 1.

Remark 2.2. (A) The condition, $dY/dx = 0$, is equivalent to $(dY/dt) \cdot (dx/dt) = 0$. Since dx/dt is never vanishing, we have that Y is constant in time.

(B) The Golden Ratio is famous and has been studied for two thousand years or more, [20]. We had not expected the Golden Ratio would play a role in the present model.

Equation (5) yields the allometric relation, $\ln(m^2) = \tau \cdot \ln(m^2) + b$, where m's are biomass measures. This holds near adult sizes or for large times. The coefficient, τ, may or may not be the Golden Ratio. There are, however, known biological examples where this coefficient is the Golden Ratio, [20], [10], [11], [12], [26], [27].

Solution of (9) has been given for large times, but for any time t, it can also be obtained in terms of the muscle cell total production, $x(S(t))$, as the following proposition.

Proposition 2.3. *The Undeformed F/L ratio, Y, solving the Rashevsky equation (10), is given as an implicit function of the monotonically increasing*

variable, $x(S(\beta_2(t)))$*, by*

$$(Y-\tau)\left(Y_o+\frac{1}{\tau}\right)=\left(Y+\frac{1}{\tau}\right)(Y_o-\tau)\exp\left\{-\left(\tau+\frac{1}{\tau}\right)x(S(\beta_2(t)))\right\}, \quad (11)$$

where the subscript "o" indicates the value of the F/L *ratio at the initial size/time,* $S(0)$*. If* $m^1(S(0))$ *is a unit biomass at the initial time, then both sides of (9) are identical since the exponent is zero.*

Proposition 2.4. *The Rashevsky equation for the deformed* F/L*-Ratio,* Y*, is*

$$\frac{dY}{dt}=-Y^2+\left(\frac{1}{\tau}+\tau\right)Y. \quad (12)$$

The solution is given implicitly by

$$Q\cdot\exp\{x(S(\beta_2))\}=\left[\frac{Y}{\left(\frac{1}{C}-Y\right)}\right]^C, \qquad C=\frac{\tau}{\tau^2+1},$$

Q arbitrary, which is easily solved to yield

$$Y(x)=1/[C+A\cdot\exp\{-x/C\}]. \quad (13)$$

where A is arbitrary, but constant.

Remark 2.5. It must be pointed out that we have sacrificed one degree of freedom in our model formulation. We started with 3 arbitrary constants and ended up with only 2, which are all taken positive. We have, in fact, reduced the number of parameters that must be estimated by statistical procedures following an important modelling technique: to seek simplicity in model construction reduce as much as possible the number of parameters to be simultaneously estimated.

Remark 2.6. If the size S is formally diminished without bound, then the F/L-ratio approaches the negative reciprocal of τ. Therefore, in terms of allometry, the positively and negatively infinite linear regression lines for biomasses m^1, m^2, are mutually perpendicular.

3. Phenotypic Deformation

Phenotypic deformation must be thought of as system-wide or global alteration with local regions of microscopic size, fitting together in a compatible manner. The first thing to discuss, then, is the local description of deformation.

Let us model a microscopic volume of visceral tissue as an infinitesimal vector line-element, $\mathrm{d}\xi^\alpha$, with two components, one the natural logarithm of muscle tissue ($\alpha = 1$) and the other of adipose tissue ($\alpha = 2$), which have been deformed [as part of a larger macroscopic deformation] resulting in a new infinitesimal (microscopic) piece, dx^i. We represent this as a positive (or negative) magnification of small pieces of the two tissues in the same location:

$$\mathbb{B}^i_\alpha(x,y)\mathrm{d}\xi^\alpha = \mathrm{d}x^i, \qquad i,\alpha \in \{1,2\} \tag{14}$$

together with its inverse relations, ensuring non-degeneracy of the frame $\mathbb{B}$:

$$\mathbb{B}^\alpha_i(x,y)\mathrm{d}x^i = \mathrm{d}\xi^\alpha, \qquad \mathbb{B}^\alpha_j\mathbb{B}^i_\alpha = \delta^i_j, \qquad \mathbb{B}^i_\alpha\mathbb{B}^\beta_i = \delta^\beta_\alpha, \tag{15}$$

where HAL is assumed to hold for the ξ^α, that is,

$$\mathrm{d}^2\xi^\alpha/\mathrm{d}S^2 = 0, \tag{16}$$

with, S, Euclidean arc length (so that, $\mathrm{d}S^2 = \delta_{\alpha\beta}\mathrm{d}\xi^\alpha\mathrm{d}\xi^\beta$, which is the usual notation for the "sum of squares" formula using the Kronecker delta notation for the identity matrix and the Einstein summation convention).

In Finsler geometry, one defines the metric tensor of $F(y)$, an energy (MGE) functional independent of X, by setting,

$$\mathrm{d}S = \mathrm{e}^{\varphi(x)}F(y) = F(x,y),$$

with

$$g_{ij}(x,y) = \mathrm{e}^{2\varphi(x)}g_{ij}(y) = \frac{1}{2}\mathrm{e}^{2\varphi(x)}\dot\partial_i\dot\partial_j F(y)^2, \tag{17}$$

where the dot over $\dot\partial_i$ indicates partial differentiation with respect to,

$$y^i = \mathrm{d}x^i/\mathrm{d}S = N^i/\dot S,$$

see [7], [8], [19].

Moreover, it is a well-known theorem that any 2-dimensional Finsler functional, $E(x,y)$, has a Berwald Frame (l_i, m_i) at every point $X = (x^1, x^2)$, constructed entirely in terms of E, [7], [8], [19]. For a $F(y)$, which is not Euclidean,

these two vector fields are orthogonal at each point and have unit length relative to the norm, $\|V\| = \sqrt{g_{ij}(y)V^iV^j}$. As a matter of fact, $\mathrm{d}S^2$ is given by any of the expressions

$$g_{ij}(x,y)\mathrm{d}x^i\mathrm{d}x^j = \mathrm{e}^{2\varphi(x)}(l_il_j + m_im_j)\mathrm{d}x^i\mathrm{d}x^j = \delta_{\alpha\beta}\mathbb{B}_i^\alpha\mathbb{B}_j^\beta\mathrm{d}x^i\mathrm{d}x^j = \delta_{\alpha\beta}d\xi^\alpha d\xi^\beta,$$

by using

$$\mathbb{B}_i^1 = \mathrm{e}^{\varphi(x)}\cdot l_i, \qquad \mathbb{B}_i^2 = \mathrm{e}^{\varphi(x)}\cdot m_i$$

and (16), (17). This means

$$g_{ij}(x,y) = \delta_{\alpha\beta}\mathbb{B}_i^\alpha(x,y)\mathbb{B}_j^\beta(x,y)$$

Now the classical Strain Tensor for this deformation is defined as

$$\mathrm{e}_{ij} = \delta_{ij} - g_{ij},$$

and it can be shown that for displacement field u_r in the Euclidean Huxley space that

$$\mathrm{e}_{rs} = \frac{1}{2}(\partial_r u_s + \partial_s u_r)$$

for the case of small strain, meaning the partial derivatives of the displacement field, u_m, are assumed small, [22], [23, p.203-205]. In order for the displacement field to extend to the entire tissue conglomerate (i.e., globally) this partial differential equation must satisfy integration conditions. Namely,

$$0 = \partial_n\partial_l\mathrm{e}_{rs} - \partial_s\partial_l\mathrm{e}_{rn} + \partial_s\partial_r\mathrm{e}_{ln} - \partial_n\partial_r\mathrm{e}_{ls}.$$

However, because the small strain condition holds and $\partial_i g_{kl}$ and $\partial_i \mathrm{e}_{kl}$ are constant multiples of each other the integration condition is just the compatibility condition. Namely, the vanishing of the Berwald-Gauss curvature,

$$K = 0.$$

This follows from the KCC-Theory appendix of [47], via the basic formulas of 2-dimensional Finsler geometry, [7], [8], [19]. However, it is known that these 3-index G's constitute a linear (or affine) connection in the classical sense, [21]. Thus, it is easy to see that small strain implies the terms formed as products of the 3-index G's are negligible and the remaining ones are just those in the integration condition above.

In order to prove that HAL (characterized by the straight line geodesics of the Euclidean $\delta_{\alpha\beta}$) has been plastically deformed to our muscle/adipose system (characterized as the geodesics of $g_{ij}(y)$, we must utilize the theory of

anholonomic frames in differential geometry, [27]. To this end we introduce 2 anholonomic objects:

$$\Omega^{\gamma}_{\alpha\beta} = \mathbb{B}^{\gamma}_{i}(\delta_{\alpha}\mathbb{B}^{i}_{\beta} - \delta_{\beta}\mathbb{B}^{i}_{\alpha}), \qquad \Omega^{\gamma}_{\alpha(\beta)} = \mathbb{B}^{i}_{\alpha}(\dot{\partial}_{j}\mathbb{B}^{\gamma}_{i})\mathbb{B}^{j}_{\beta}. \tag{18}$$

Here, $\delta_{\alpha} = \mathbb{B}^{i}_{\alpha}(\partial_{i} - G^{r}_{i}\dot{\partial}_{r})$, where the ∂_{i} without dots indicate partial differentiation with respect to x^{i}, while the same with dots denotes partial differentiation with respect to y^{i}. The $G^{i}_{j} = \dot{\partial}_{j}G^{i}$ for equations (9) are computed easily because G^{i} is obtained by rewriting (9) as,

$$\frac{\mathrm{d}y^{1}}{\mathrm{d}S} + 2G^{1} = 0 \quad \text{and} \quad \frac{\mathrm{d}y^{2}}{\mathrm{d}S} + 2G^{2} = 0,$$

$$2G^{1} = \left(\tau + \frac{1}{\tau}\right)(y^{1})^{2} \quad \text{and} \quad 2G^{2} = (y^{2})^{2} - (y^{1})^{2} + \frac{2}{\tau}y^{1}y^{2},$$

$$G^{1}_{1} = \left(\tau + \frac{1}{\tau}\right)y^{1}, \quad G^{1}_{2} = 0 \quad \text{and} \quad G^{2}_{1} = -y^{1} + \frac{1}{\tau}y^{2}, \quad G^{2}_{2} = y^{2} + \frac{1}{\tau}y^{1}.$$

Defining the Berwald Connection Coefficients as usual,

$$G^{i}_{jk} = \dot{\partial}_{k}G^{i}_{j} \qquad \text{and} \qquad G^{i}_{jk} = G^{i}_{kj}$$

for the case at hand, we have

$$G^{1}_{11} = \tau + \frac{1}{\tau}, \quad G^{1}_{12} = 0 = G^{1}_{22} \quad \text{and} \quad G^{2}_{11} = -1, \quad G^{2}_{12} = \frac{1}{\tau}, \quad G^{2}_{22} = 1,$$

so that equations (9) may be expressed as

$$\frac{dy^{i}}{dS} + G^{i}_{jk}y^{j}y^{k} = 0,$$

as well.

On the other hand, given HAL as in (16), the G^{i} vanish, so that $G^{i}_{r} = 0$. The operator δ_{α} is simplified, but the Berwald frame is the same as for $F(y)$, so the first anholonomic object is vanishing, but the second one is not.

The Anholonomy theorem states that the local deformation is elastic (reversible), if and only if, both anholonomic objects (17) are zero. Otherwise, the local deformation is plastic (irreversible). Applying this theorem to the local deformation (15) we see that the y-dependence will ensure the 2^{nd} anholonomic object is non-vanishing, generally. It is the vanishing of the Berwald-Gauss Curvature, K, that guarantees compatibility so the deformation is prolonged to the entire production space, [22], [23], [29], [30].

Remark 3.1. We use the term "elastic" as in continuum mechanics. Both anholonomic objects (17) vanish in the elastic case. It means there is an invertible coordinate transformation taking the production variables, x^1, x^2, to new numerical levels. This constitutes a motion in production space, which can be reversed. In particular, the local deformation (15) in a hypothetical elastic case can be solved (integrated) for x^i, or for ξ^α. The plastic deformation case, which here concerns us, cannot be so integrated. That is to say, it cannot be reversed through a motion in the production space. The elastic case (15) is said to be integrable (reversible) while the term non-integrable is used for the irreversible plastic case.

In view of this discussion, we have the following theorem.

Theorem 3.2. *The Deformed and Undeformed systems are globally defined plastic deformations of each other. Furthermore, their corresponding energy (MGE) functionals are conserved along production trajectories but are not elastically related. A rigorous proof has just been outlined for the first statement. The second is a rewording of the standard mathematical fact that the two systems in question are not isometically isomorphic, so there can be no invertible (i.e., reversible) coordinate transformation between them. So starting from the Undeformed system and plastically deforming it globally to Euclidean Hal (2^{nd} equation of (15) using the Berwald frame for the Undeformed system) and then performing the (matrix) inverse plastic deformation from Euclidean Hal to the Deformed system (1st equation of (15) using the Berwald frame for the Deformed system), we obtain a composite plastic deformation from Undeformed to Deformed system.*

4. Heterochrony

It is imperative that we answer the question: how do the deformed and undeformed systems arise in the first place? An answer may be given in terms of time-sequencing changes, or heterochrony, induced from the ambient environment causing certain specific sets of genes to switch on or off. From this, we can see the mathematical theory of heterochrony allows conjugation with elastic motions. Beginning with our Model Bauplan in place, namely, the Euclidean HAL for both muscle, x^1, and adipose tissue, x^2, we proceed as in section 5 of [3] after first making an elastic deformation to a new set of coordi-

nates, $\tilde{x}^1, \tilde{x}^2$, after which we invoke the cue from the environment inducing an alteration of dynamics by a time-sequencing change along production curves. After this, the inverse elastic deformation is applied thereby returning to the original coordinates, x^1 and x^2. Using elastic transformations together with heterochrony in this way is referred to as *conjugated time-sequencing change* in Analytical Modular Dynamics, [2], [47]. In differential geometry, it is simply called projective transformation of geodesics, [21]. The elastic motion is defined as $\tilde{x}^i = \dfrac{1}{\beta_i}\exp(\beta_i x^i),\ i = 1, 2$, and the parentheses means not summed. The undeformed MGE now has the new form

$$F = \tilde{y}^1 \exp\left(\frac{\tilde{y}^2}{\tilde{y}^1} + Q(\tilde{x}^1, \tilde{x}^2)\right),\ Q = \frac{1}{\tau^2}\left(\frac{\tilde{x}^2}{\tilde{x}^1} + (\tau^2+1)\ln(\tilde{x}^1) - \tau^3\beta_2\tilde{x}^1\right). \tag{19}$$

The *Heterochronic Change* is an adaptation to an impinging ambient environmental signal (measured), e^i, consisting of a time-sequencing change and an adaptive response, C^i, to that signal and is given by

$$\frac{\mathrm{d}\tilde{y}^i}{\mathrm{d}P} + \delta^i_j Q_k \tilde{y}^j \tilde{y}^k = C^i = F^2 g^{ij} Q_j - \delta^i_j Q_k \tilde{y}^j \tilde{y}^k \tag{20}$$

where $\tilde{y}^i = \mathrm{d}\tilde{x}^i/\mathrm{d}P$ and $\delta^i_j Q_k$ is a skew-symmetric tensor known as a 1-form connection, or Wagner connection, [7], [8], [15], [19], [35]. The time-change formula is

$$\frac{\mathrm{d}P}{\mathrm{d}S} = B \cdot \exp\left(\int_\gamma Q_i\ \mathrm{d}\tilde{x}^i\right), \tag{21}$$

with B a positive arbitrary constant. It is a theorem that C^i is orthogonal to any solution, γ, and it is the curvature vector of, γ, [7], [8],[35]. Sometimes time-change (21) is referred to as a *semi-projective transformation*, [24]. Finally, any elastic motions in the Euclidean HAL can be invoked before and/or after semi-projective change and they need not be the inverses of each other as we have used them above.

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