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DYNAMIC NUTRITION MODEL

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ABSTRACT

Nutrition and ration scheduling play a key role in mitigating fatigue and enhancing cognitive and physical performance during military operations. Determining the optimal ration components and ration schedule for such conditions is a considerable challenge. To aid in this effort, The Dynamic Nutrition Model (DYNUMO) was developed to simulate body metabolic fuel levels, over time, in response to nutrient intake and energy expenditure. DYNUMO is a simplification of the digestive and metabolic processes in the human body. Ingested food is absorbed into the blood. From there, absorbed nutrients may be stored in adipose tissue as triglycerides, stored in the liver or muscle as glycogen, converted to other metabolic fuels in the liver, or utilized for energy. A regulatory system maintains blood glucose at near constant levels and conserves carbohydrate stores. Model algorithms are based on known physiology and biochemistry, with parameter values derived from existing experimental data. Although the data in the validation database is insufficient for formal model validation, the model currently provides reasonable predictions of blood glucose levels following a single ingestion of glucose solution and of muscle glycogen levels following an all-out maximal effort.

1. INTRODUCTION

Performance of the warrior system depends not only on his equipment, clothing, and weapon systems, but also on his physical and cognitive capabilities. Physical and cognitive capabilities are directly related to the levels of metabolic fuels stored in the body. Muscle glycogen is the most important of these metabolic fuels for physical performance. Depletion of muscle glycogen stores is associated both with loss of muscle strength (Jacobs et al., 1981) and onset of physical exhaustion (Ahlborg et al., 1967; Bergstrom and Hultman, 1967; Hermansen et al., 1967; Jacobs et al., 1981). When muscle glycogen levels are low it is still possible to perform low intensity work by using fat for fuel, but it is impossible to perform high intensity work. Liver glycogen is another important metabolic fuel because it can be converted to glucose and released into the blood. Depletion of liver glycogen during periods of high blood glucose utilization or low carbohydrate ingestion generally results in hypoglycemia, with concomitant sensations of fatigue (Owens et al., 1997) and reductions in cognitive performance (Benton et al., 1995; Cox et al., 1993; Holmes et al., 1986; Parker and Benton, 1995). Compared to the body's carbohydrate stores, the body's fat stores are abundant. Although fat cannot provide fuel for high intensity work, fat can be used exclusively during low intensity work and can be used to supplement carbohydrate fuels during high intensity work. The body's protein stores are also relatively plentiful. Under conditions of prolonged or severe caloric deficits, the body can catabolize protein for metabolic fuel. Unlike carbohydrate and fat catabolism, however, excessive protein catabolism is deleterious, leading to the break down of connective tissue and a reduction in lean body mass.

The goal of the ration developer is straightforward: optimize ration components and schedules to meet the body's nutritional demands during military operations. The conditions associated with military operations, however, make achieving this goal difficult at best. Military operations are often measured in terms of days or even weeks. The operational environment may be at the extremes of heat, cold, or altitude tolerance. Sleep deprivation and stress are often factors as well. Daily caloric expenditures typically far exceed daily caloric intake, which may be limited by the amount of food that can be carried, the amount of time allocated for eating and the palatability/acceptance of foods necessarily developed with high priority on low weight/volume and long shelf life. Determining the optimal ration components and ration schedule for such conditions is a considerable challenge.

The Dynamic Nutrition Model, described in this paper, contributes to the efforts of the ration developer by predicting the dynamic response of the body's metabolic fuel stores to various nutrient intake and energy expenditure scenarios. DYNUMO is intended to be used with other models and algorithms that predict physical

and cognitive performance capabilities from metabolic fuel status and with combat simulations that use these physical and cognitive performance capability factors to assess individual combatant and small unit performance (e.g., target detection, firing accuracy; movement rate, casualties, mission task completion, etc.). Using these tools, ration developers can optimize rations and ration schedules to maximize predicted individual combatant and/or small unit performance for a wide variety of scenarios.

2. MATERIALS AND METHODS

2.1 Model Overview

Adenosine triphosphate (ATP) provides energy for muscle contraction, membrane transport and other energy requiring processes in the body. When cells take up and metabolize metabolic fuels, they are doing so in order to convert adenosine diphosphate to ATP. Because of the small amount of cellular ATP, ATP production must occur at approximately the same rate as energy expenditure. Metabolic fatigue occurs when performance degrades over time due to inadequate ATP production. ATP production rates depend on the metabolic fuel that is used. In the muscle, phosphocreatine and anaerobic glycogen metabolism generate ATP at the fastest rate, while aerobic carbohydrate and fat metabolism generate ATP at slower rates. For "all-out", maximal efforts, only phosphocreatine and anaerobic muscle glycogen metabolism can produce ATP at the required rates. ATP production slows and eventually stops as muscle glycogen stores are depleted and pH is lowered due to excess hydrogen ion production. For less strenuous activity, aerobic metabolism prevails and a mixture of fuels is used. To evaluate different nutritional strategies on physical and cognitive performance, DYNUMO must track muscle and liver glycogen levels, which are the principal limiting factors for physical and cognitive performance. DYNUMO must also track the availability of other fuel sources because they will effect the utilization muscle and liver glycogen during mixed metabolism.

DYNUMO is a simplification of the metabolic processes in the human body. Inputs to the model include (1) the amounts and types of ingested carbohydrate, fat and protein; (2) the activity level and (3) a stress (epinephrine) factor over time. Outputs include the overall caloric balance as well as the status of individual metabolic fuel stores (muscle and liver glycogen, triglycerides, blood glucose and free fatty acids) over time. The model includes 6 subsystem models including Digestive System, Energy Consumer Cells, Adipose Tissue Cells, Liver Tissue Cells, Blood Compartment and Regulatory System. Ingested food enters the digestive tract and is broken down into its basic components (mono- and disaccharides, amino acids, fatty acids and glycerol). These components are then absorbed into the blood. From there, nutrients are stored in adipose tissue as triglycerides, stored in the liver or muscle as glycogen, converted to other metabolic fuels in the liver, or metabolized for energy. A regulatory system maintains blood glucose at near constant levels and conserves carbohydrate stores. Algorithms used in the model are based on known physiology and biochemistry, with parameter values derived from existing experimental data.

2.2 Digestive System

The Digestive System model includes the processes of ingestion, gastric emptying, and a combined digestion/absorption process. The ingestion process assumes that food is ingested as a bolus:

$$V_{gastric} = V_{gastric} + V_{ingested}$$
$$S_{gastric} = S_{gastric} + S_{ingested} \qquad (1)$$

where $V_{gastric}$ and $S_{gastric}$ are the gastric volume and substrate amount, respectively, and $V_{ingested}$ and $S_{ingested}$ are the ingested volume and substrate amount, respectively. The model by Hunt and Stubbs (1975) is used to describe gastric emptying:

$$\frac{dV_{gastric,GE}}{dt} = -\frac{\ln(2)\cdot V_{gastric}}{V_{gastric,init}(0.1797 - 0.1670e^{-K})} \qquad (2)$$

where $dV_{gastric,GE}/dt$ is the rate of change of gastric volume due to gastric emptying and K is the caloric density of the gastric contents (4 kcal/g for carbohydrate and protein and 9 kcal/g for fat). A pipeline model is used to describe the digestion/absorption process in which the number of pipeline segments (n) and the rate coefficient (β) vary with the type of nutrient:

$$\frac{dS_0}{dt} = -\frac{dV_{gastric,GE}}{dt} - \beta S_0. \qquad (3)$$
$$\frac{dS_i}{dt} = +\beta S_{i-1} - \beta S_i$$
$$\frac{dP}{dt} = +\beta S_n$$

where S_i, i=1..n, is the amount of substrate in the ith pipeline segment, and P is the amount of product entering the blood compartment.

2.3 Energy Consumer Cells

The energy consumers include all the cells in the body that consume metabolic fuels to perform physiological work (e.g., muscle contraction and active membrane transport). Muscle makes up the greatest percentage of energy consumer cells by weight and is responsible for nearly all of the energy consumption that occurs during physical activity. For this reason, muscle characteristics are used to represent the energy consumer cells. The biochemistry of metabolism is highly complex, incorporating numerous individual metabolic pathways that interact with one another. Figure 1 shows the metabolic pathways considered in this model.

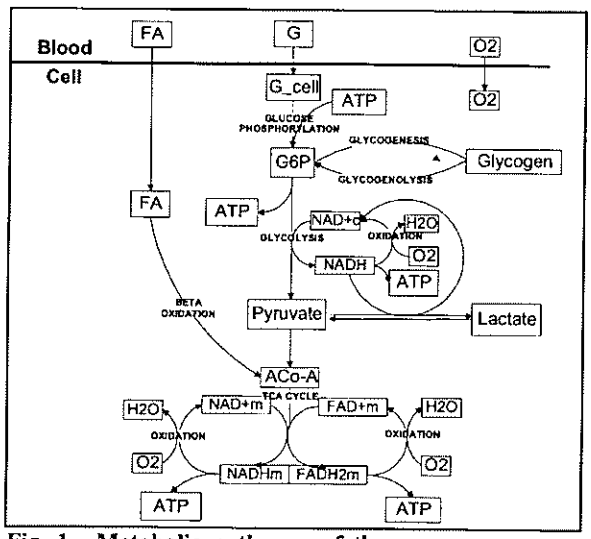

Fig. 1. Metabolic pathways of the energy consumer cells.

Although each metabolic pathway may include multiple steps, catalyzed by specific enzymes, in DYNUMO, all of the steps in a pathway are collapsed into a single, net reaction. The reaction rate and regulation scheme are assigned the properties of the enzyme catalyzing the rate-determining step. The model tracks the amounts of substrate and product at the beginning and end point of each metabolic pathway over time. In general, the steady state saturation kinetic model develop by Briggs and Haldane (1925), extended to a system of multiple substrates (Indge and Childs 1976), is used to compute rates of product generation (dP/dt) from substrate concentrations $[S_i]$, i=1..n:

$$\frac{dP}{dt} = v_{\max} \cdot \frac{1}{\frac{k_{M1}}{[S_1]} + \frac{k_{M2}}{[S_2]} + .. + \frac{k_{Mn}}{[S_n]} + 1} \tag{4}$$

where $v_{\max}$ is the maximum value for dP/dt when all substrates are at saturation levels and $k_{M,i}$ is the concentration of substrate S_i at which $dP/dt = v_{\max}/2$ (all other substrates are at saturation levels). For pathways with relatively high reaction rates, however, we assume that the rate of product generation is equal to the rate of substrate availability (dS_{in}/dt), up to some maximal limit $v_{\max}$:

$$\frac{dP}{dt} = \begin{cases} \frac{dS_{in}}{dt} & for \quad \frac{dS_{in}}{dt} \le v_{\max} \\ v_{\max} & for \quad \frac{dS_{in}}{dt} > v_{\max} \end{cases} \tag{5}$$

Enzyme regulation is handled using the following equations:

$$v_{\max} = v_{\max,0} \cdot \left(1 + \frac{A}{sf_A} - \frac{I}{sf_I}\right) \tag{6}$$

$$k_M = k_{M,0} \cdot \left(1 - \frac{A}{sf_A} + \frac{I}{sf_I}\right)$$

where A is the activation term, I is the inhibition term, and sf_A and sf_I are scaling factors. A and I may include substrate concentration(s), product concentration(s), other local factors (e.g., amount of available ATP or Ca^{2+}), or centrally-produced regulatory factors (e.g., insulin, glucagon, or epinephrine).

2.4 Adipose Tissue

Adipose tissue cells are the primary storage depots for triglycerides in the body. Chylomicrons, very low density lipoproteins (VLDL), fatty acids, and glucose all serve as precursors. During high energy expenditure or reductions in glucose stores, adipose cell triglycerides are converted to fatty acids and glycerol, which are released into the blood. The fatty acids can be metabolized by most tissues in the body, and glycerol can be converted into glucose and subsequently used for fuel. The extended Briggs/Haldane model (Eqn 4) is used to describe all pathway kinetics. Figure 2 shows the adipose tissue pathways that are considered in this model.

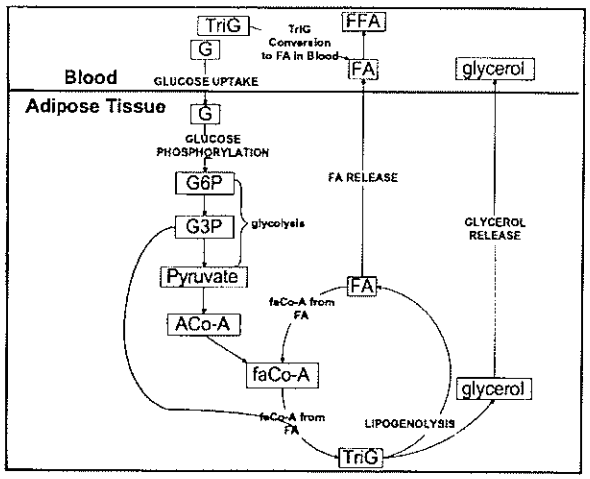

Fig. 2. Metabolic pathways of adipose tissue.

2.5 Liver Tissue

The primary function of the liver is to convert and store metabolic fuels for use by other tissues. Although the liver can use metabolic fuels to generate ATP for its own use, that function is less significant and is not considered here. In this simplified model, liver takes up glucose, amino acids, fatty acids, glycerol, and lactate, and converts these into glucose, ketone bodies, and VLDL for release. The liver stores glycogen in a manner similar to the energy consumer cells. Unlike energy consumer cells, however, this glycogen can be converted back to glucose and released into the blood for use by other tissues. The liver can also store triglycerides for later release as VLDL. The extended Briggs/Haldane model (Eqn 4) is used to describe all pathway kinetics. Figure 3 shows the metabolic pathways considered in this liver tissue model.

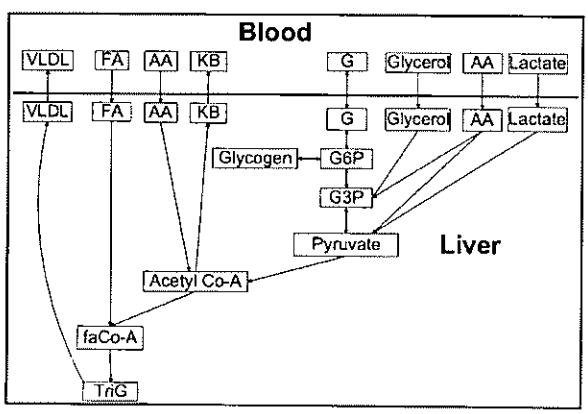

Fig. 3. Metabolic pathways of liver tissue.

2.6 Regulatory System

Regulation is achieved by altering the rates of specific metabolic reactions. Most of this regulation occurs via local factors. Regulation also occurs by centrally produced factors such as epinephrine, norepinephrine, insulin, glucagon, and glucocorticoid hormones. Insulin is secreted in response to increased blood glucose levels and generally favors storage of glucose as glycogen or triglyceride, and inhibition of gluconeogenesis. The simplest representation of the insulin response to changes in blood glucose concentration is a proportional control system:

$$F_{insulin} = g\{[G_{blood}] - [G_{blood,set}]\}_+ + 1 \qquad (7)$$

where $F_{insulin}$ is an insulin factor (range 1-10), g is the "gain" or proportionality coefficient, $[G_{blood}]$ is the blood glucose concentration, and $[G_{blood,set}]$ is the "set-point" blood glucose concentration. The term inside the $\{\ \}_+$ brackets is set to zero if negative. Glucagon is secreted in response to decreased blood glucose and generally has opposite effects of insulin. The simplest representation of the glucagon response to changes in blood glucose is a proportional control system:

$$F_{glucagon} = g\{[G_{blood,set}] - [G_{blood}]\}_+ + 1 \qquad (8)$$

where $F_{glucagon}$ is the glucagon factor (range 1-10). Epinephrine is produced under a variety of conditions including exercise and stress. At this time, a linear relationship is assumed between an epinephrine factor (F_{epi}, range 1-10) and metabolic rate (MetRate). A value of 1 is assumed for basal metabolic rates (BMR) and 10 for metabolic rates of 80% of $VO_{2,max}$ or greater.

$$F_{epi} = \frac{9}{\left(\frac{(0.8)VO_{2,\max}}{BMR} - 1\right)} \cdot \left(\frac{MetRate}{BMR} - 1\right) \qquad (9)$$

The user may override the computed epinephrine factor to account for other stresses. Not enough information was found regarding specific actions of glucocorticoid hormones on metabolic reactions to include in the model

3. RESULTS AND DISCUSSION

3.1 Parameter Value Estimation

Parameter value estimation is an ongoing effort. The values currently in place represent our best first approximation given the available data. Most of the data incorporated to date concern glucose ingestion and carbohydrate metabolism. The model is relatively weak when it comes to ingestion of other types of

carbohydrates, lipids, or mixed meals. Lipid metabolism has been given only cursory treatment to date. We expect that parameter value accuracy and robustness will improve as more data are added to the model development database. It is not possible to present model parameter values here. Interested readers are encouraged to contact the author for a copy of the relevant technical report.

3.2 Model Testing/Demonstration

Most of the data aquired from the literature and from personal contacts have been used in model parameter estimation. A few data sets have been set aside for informal model testing. This testing does not constitute formal model validation, although it does provide a check on model behavior. In the first test (Figure 4), we simulated the blood glucose response to ingestion of 12% glucose and 12% maltodextrin drinks formulated to deliver 0.8 g of carbohydrate per kg body weight.

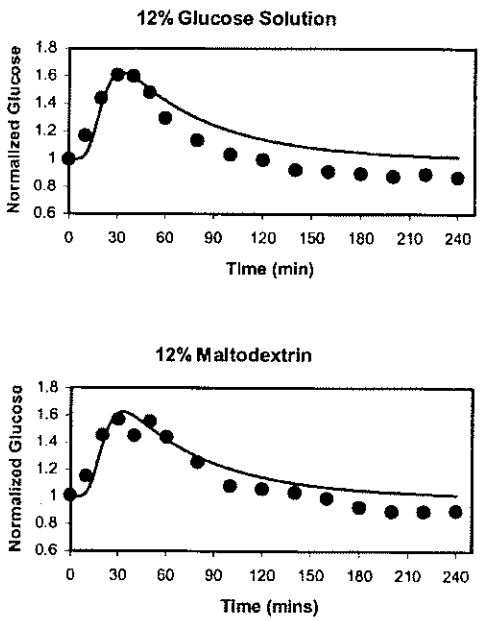

Fig. 4. Predicted (solid line) and observed (filled circles, from Taub et al., 1999) blood glucose response to ingestion of 12% carbohydrate solutions.

In the second test, we simulated the muscle glycogen response to an all-out sprint (2866 kcal/hr). The resulting predictions agree with the observation that maximum sprinting can be maintained only for about 20 seconds, at which time muscle glycogen is expected to be approximatley two thirds of its resting value (Newsholme and Leech 1983).

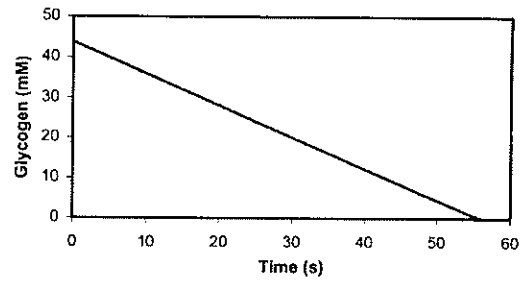

Fig. 5. Simulated muscle glycogen response to an all-out sprint.

4. CONCLUSIONS/RELEVANCE

This paper describes a Dynamic Nutrition Model used to simulate the effects of nutrition and ration scheduling on body metabolic fuel levels. This model currently provides realistic predictions of the response to glucose ingestion and high intensity exercise levels. However, the model is relatively weak when it comes to ingestion of other types of nutrients, and lipid metabolism has been given only cursory treatment to date. We expect that parameter value accuracy and robustness will improve as more data are added to the model development database. Despite these weaknesses, DYNUMO may be currently used in three different ways: (1) as a stand-alone tool to analyze nutritional strategies and their effects on metabolic fuel stores; (2) as an algorithm within a food item selection optimization program (e.g., the Ration Optimization Program) to select food items and feeding schedules that optimize physical and cognitive performance capabilities; and (3) as a model object in scenario-based simulation packages (such as the Integrated Unit Simulation System) to assess the effects of nutrition under different mission scenarios on individual and small unit mission effectiveness.

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