An Agent-Based Methodology for Simulating Human Physiological Processes

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INTRODUCTION

This report describes a methodology for building software models of human physiology at different levels of abstraction which allows simulation frameworks to be built at a steady, controlled pace. By building modular simulation components, where each module aims to replicate the function of a specific physiological process, we are able to maintain better control over the gradual increase of systems' complexity levels. The compartmentalized nature of the simulation furthermore makes identifying and debugging the system more manageable.

Human anatomy is one of the most complex systems known to man and computer simulations that aim to mimic even parts of physiological processes often grow too complex to produce reliable research data. In order to reliably simulate human physiology and activities which take environmental factors into account, we need to have a flexible simulation framework that allows for simplified- and complex system components to function together. Allowing for each system component to be improved or adjusted independently with minimal impact on the function of the system as a whole.

Figure 1 - The potential applications of more realistic physiological simulations include, for example, opportunities to implement more realistic first aid training systems where the effects of wounds and injuries replicate real-world behavior.

By abstracting human physiological systems, we are able to create a player health-system that is more strongly rooted in reality: providing a more realistic portrayal of what the human body needs to survive in harsh conditions. An early implementation of this simulation was created as part of a wilderness survival simulation game — demonstrating rudimentary functionality and some of the benefits that such a system could offer the gaming industry.

The goal of this research is to create a system that is able to simulate the vital physiological events and functions needed to sustain life in different environmental conditions. The system replicates the human body of a hiker in peak physical condition, taking into account real-time physical activities such as walking or running.

The system is then able to dynamically simulate the combined result of physical activities performed. Potential to expand the system is significant and we lay out the groundwork for including more detailed variables and formulae in future implementations, such as oxygenation, breathing rate, blood volume, body surface area and external weather/environmental conditions.

Biological Foundation & System Abstraction

Building on biological research statistics, we present a methodology overview into how the human bodily functions can be represented as a dynamic, simulated system.The modeling is done using the Constructionist Design Methodology (CDM) of Thórisson et al. (Thórisson et al. 2004, Thórisson et al. 2006). The demonstrated success of its application here to modeling the domain of biological function, in addition to its use in AI, robotics, and economics, is yet another case in point of its strength and utility in modeling and simulating a variety of complex systems.

At this time the prototype only implements basic muscular activity (see *Technical Implementation & Prototype*), but the basic version 1 of the simulation should eventually take the following variables into account:

- Heart Rate
- Breathing Rate
- Blood Circulation
- Oxygen Uptake and Delivery
- Calorie Burn
- Energy Output
- Body Temperature

These dynamic variables represent the abstracted physiological processes of the human body, allowing a course but relatively sophisticated simulation of endurance and energy based on physical exertion. The applications of a simulation such as has far-reaching implications, ranging from physics-based experiments to animation, allowing minor physiological traits such as breathing rate, perspiration and physical appearance to change dynamically based on what activities a virtual character is performing in a virtual world.

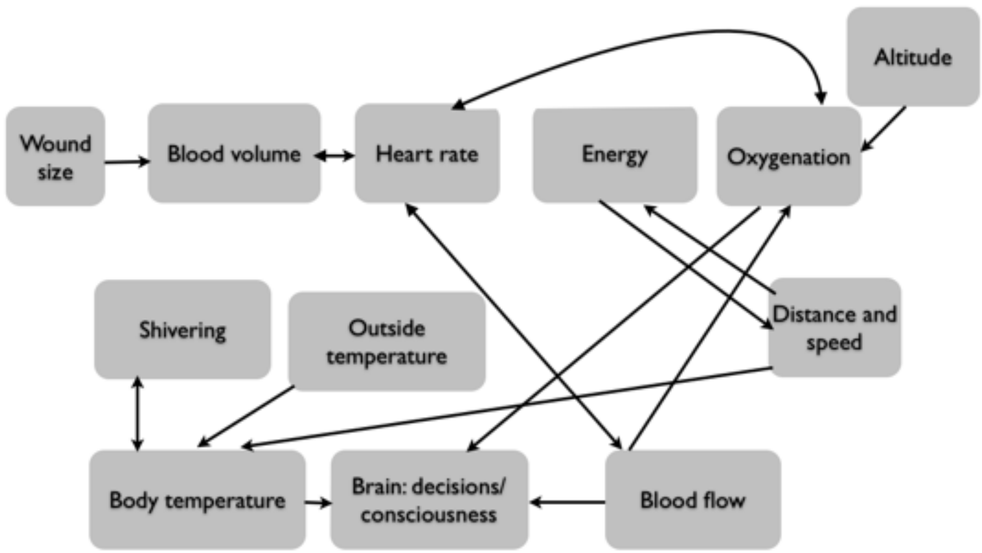


Figure 2 - The main variables that represent human physiology in harsh conditions and strenuous excercise.

The following sections detail the variables and equations neccessary to simulate basic vital signs, physical exertion and generate the essential data needed for verification against real-world data.

Power (P)

Everybody has heard the term power, but it can be defined in many ways. In physics, power is defined as the rate of which work is performed. The genearal definition is as follows:

$$\text{Power} = \text{Work} / \text{Time}$$

But work is done by force when it results in a displacement. So, if a person carries a box up a flight of stairs, the work it does is the same whether the person is walking or running, but more power is needed to perform the action while running, because the work is performed in a shorter amount of time. But even though we are not carrying anything heavy, we still need to generate power just to move ourselves around. Just like in the example above, we require more power when we are running than when we are walking.

By using the simple physics formulae that are listed here below, we can easily obtain the formula for person's power output while running. That is, by using,

$$\text{Velocity} = \text{Distance} \div \text{Time}$$
$$\text{Acceleration} = \text{Velocity} \div \text{Time}$$
$$\text{Force} = \text{Mass x Acceleration}$$

We obtain the following formula:

$$\text{Power} = (\text{Body Weight x Distance}^2)/ \text{Time}^3 \quad [W]$$

This means that we can easily keep track on of a virtual character's simulated activity and the power he needs.

Heart Rate (HR)

The maximum heart rate does not serve as an indicator for a person's overall fitness, only how fast the heart can pump blood. Maximum heart rate can be measured while doing heavy cardio exercises. However, it is possible to predict the maximum heart rate, but studies have showed that a person's maximum heart rate is on average is roughly represented by the following equation.

$$\textit{Maximum Heart Rate } (HR_{max}) = 220 - \text{Age}$$

Heart rate max is often calculated roughly as 220 - age. Does not indicate overall physical health. Heart rate rest is the lowest possible pulse, usually measured after a complete night's rest and 10 minutes of complete stillness.

Since, the maximum heart rate doesn't tell us anything about the physique, we predict that the character's maximum heart rate is:

$$HR_{max} = 220 - \text{Age} = 220 - 30 = 190 \text{ beats/min.}$$

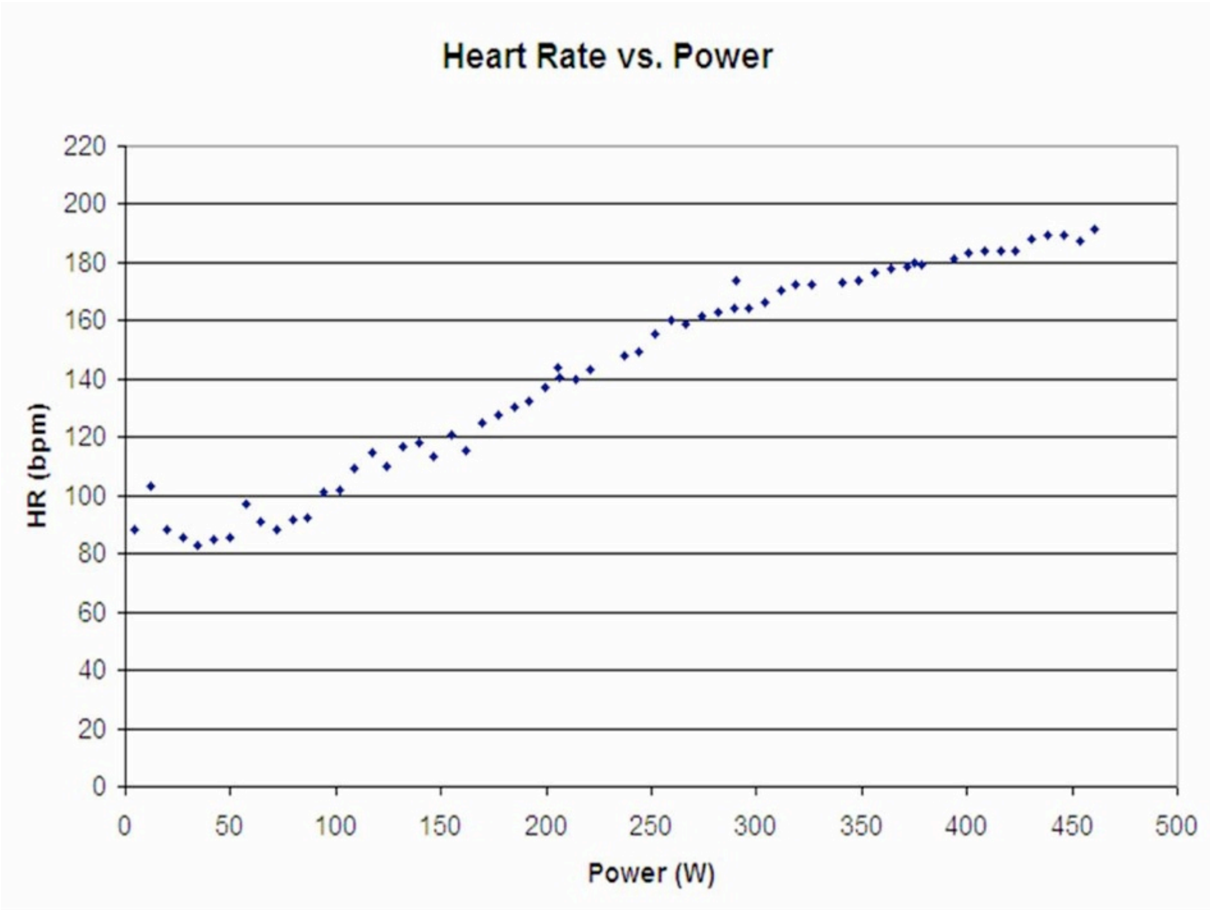
Resting heart rate is actually the minimum heart rate and, as opposed to the maximum heart rate, tells us in how good shape the individual is. The most efficient way to measure the resting heart rate is by measuring it just after the person wakes up and is still lying completely still. This can easily be done by using a simple heart rate monitor. Studies have shown that normally a man's resting heart rate can be categorized by age and fitness shape as shown in the following chart. (Y Ostchega, et. al., 2011), (DP Swain, et. al 1994), (GD Laird and MJ Campbell, 1988), (SM Ryan, et. al., 1994).

Resting Heart Rate for MEN						
Age	18-25	26-35	36-45	46-55	56-65	65+
Athlete	49-55	49-54	50-56	50-57	51-56	50-55
Excellent	56-61	55-61	57-62	58-63	57-61	56-61
Good	62-65	62-65	63-66	64-67	62-67	62-65
Above Average	66-69	66-70	67-70	68-71	68-71	66-69
Average	70-73	71-74	71-75	72-76	72-75	70-73
Below Average	74-81	75-81	76-82	77-83	76-81	74-79
Poor	82+	82+	83+	84+	82+	80+

As mentioned in the introduction, our virtual character is assumed to be a 30 year old male in excellent shape and consequently has a resting heart rate of 55 beats/min.

$$HR_{rest} = 55$$

Researchers have shown that there is a linear relationship between the power needed to complete a task, such as running and walking, and person's heart rate during that task. (Grazzi, et. al., 1999) (FJ Arts and H Kuipers, 1994).



As mentioned in the chapter above on power, we can easily calculate the power needed for running and walking. By taking two points on the line, e.g. (x1, 55) and (x2,190), using them to find the equation of the line, we get:

$$P = 40 * HR/11 - 519/8 \quad [W]$$

Solving that equation for *HR*:

$$HR = 11 * P/40 + 519/8 \quad [beats/min]$$

This, in turn, becomes a simple equation which can be used to calculate a virtual character's heart rate at any given time, based only on measuring the power exertion of the activity being performed.

VO2MAX ESTIMATION

VO_{2max} stands for the maximum volume of oxygen that a body can process to produce energy for some activity and signifies the overall performance of one's body and physical fitness. The history of VO_{2max} goes way back, or approximately 90 years, but then it was concluded that for a success in distance running, a high VO_{2max} is needed. Today the VO_{2max} is measured on a treadmill or a bicycle and requires an all-out effort from the athlete. An oxygen mask that measures the oxygen inhaled and exhaled in each breath is placed over the athlete's face and then he has to follow a specially designed program with speed changes and possibly incline changes. When there are no changes in the VO_2, measured by the mask, even with increased intensity, then VO_{2max} has been found. These tests can be dangerous and are only recommened for athletes. Because of that and also the reason that most people don't have access to equipment like the treadmill and the mask, scientists have created estimations for the VO_{2max}. For our virtual character we will use the Uth–Sørensen–Overgaard–Pedersen estimation.

Uth and his team, have shown that there is a relationship between the VO_{2max} and the HR_{max}-to-HR_{rest} ratio, and came up with the following estimation (N Uth, et. al. 2004)

$$VO_{2max} = 15 * HR_{max}/HR_{rest}$$

Other estimations exist, but we have decided to use the estimation above since it is fairly easy to calculate and requires few *measurements*. It is also very convenient for us to use, since we have both the maximum and minimum heart rate.

Calorie burn (E)

All activity, even merely lying still, requires energy to keep the body and all its organs functioning. There are many things that affect the energy need of the body, but heart rate, VO_{2max}, weight, age and the duration of the activity will all have some impact on the energy consumption. To calculate the character's energy consumption we will use the following eqution that was derived from a study on energy expenditure (LR Keytel, et. al., 2005)

$$\begin{aligned} E = \; & ((-95.7735 \\ & + (0.634 \times HR) \\ & + (0.404 \times VO2max) \\ & + (0.394 \times W) \\ & + (0.271 \times A))/4.184) \times 60 \times T \quad [\text{kkcal}] \end{aligned}$$

where the following definitions apply:

HR = Heart rate (in beats/minute)
VO2max = Maximal oxygen consumption (in $mL \cdot kg^{-1} \cdot min^{-1}$)
W = Weight (in kilograms)
A = Age (in years)
T = Exercise duration time (in hours)

Body Surface Area (BSA)

Knowing the body surface area (*BSA*) can help us to calculate important variables relating to heat generation and heat loss. When facing cold weather conditions we know that the body loses heat to the environment through the skin. The higher the *BSA*, the greater will the heat loss be. The *BSA* can also help us to calculate the cardiac output and the blood flow in the body. Scientists have derived the following equation to calculate the *BSA* (L Hoste and H Pottel, 2012).

$$BSA = 0.02465 \times \text{body mass (kg)}^{0.5378} \times \text{stature(cm)}^{0.3964}$$

Additional Variables for Future Work

In the *Appendix* of this report are work notes relevant to future iterations of the simulation framework and prototype simulation software. These are currently under development and will be included in later reports. Mainly, the formulae in question are: Cardiac Output, Oxygenation, Body Temperature and External Weather Conditions, Shivering muscle-response variables and Consciousness (nervous system). An important part of future simulation will involve simulating the processes involved in inducing hypothermia, as such we also provide an outline this health condition.

SYSTEM VALIDATION METHODOLOGY

The system itself is inherently dynamic and complex nature and in order to verify that it is functioning properly, we need a basis to test it against real world data. We have already discussed the variables that the simulation framework encompasses, such as heart rate and oxygenation, and medical professions have developed clear and proven means to measure such vital signs in humans. The most reliable way to verify the model is therefor to compare it against average table charts which take into account human body's physical excertion, age and weight. However, the verification of the model becomes harder when dealing with output such as shivering and temperature loss — since these depend largely on qualitative data and/or external variables such as the weather conditions in which the human body is operating at any given time.

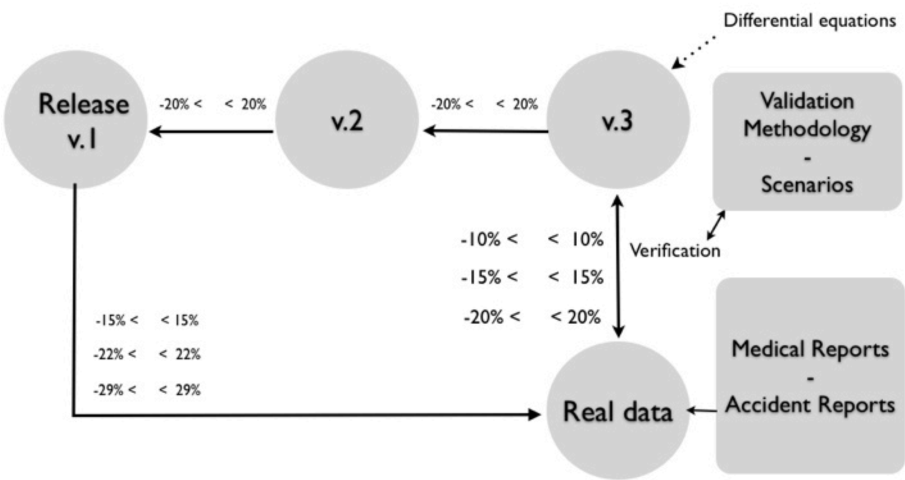


Figure 3 - The methodology flowchart for software development iterations and subsequent validation. In each iteration, the version is tested against real-world data extracted from Medical and Accident reports.

A basic framework for verifying the system is already under development, laying down basic principles of verification. Mainly, the means of verification are inherently more course than real world measurements will reflect. Therefore, when we provide simplified simulation implementation the real-world measurement data should, when possible, have been presented at a similar level of detail. On top of this, we can always expect a certain range of uncertainty or inconsistencies between real-world data and the data generated by the simulation. This variation, in turn, becomes our indication of how accurately the simulation is reflecting real-world human physiology. As the simulation framework becomes more detailed and less abstracted, it should produce results that are closer to real-world measurements.

The most beneficial way to improve and validate the simulation is through iteratations of development (see versions "*v1*, *v2*..." in the diagram above). At each stage of iteration, we verify the model against (a) medical reports and measurements, and (b) accident reports from emergency services such as search and rescue teams. Combined, the data provided by such reports should provide sufficient means to evaluate physiological proccesses based on weather conditions, physical exertion, physical fitness and physical conditions.

Challenges in Verification

There are several chalenges that verification will entail. Mainly, the medical data may not prove sufficiently rigorous as basis for comparison of simulated “wilderness” physical activities. Medical exams and measurements are mostly carried out in simplified lab environments — which differs greatly from physical activities in harsh environments where factors such as psychological stress and weather conditions can affect the performance of the human body. The additon of search and rescue (*SAR*) team data is therefore neccessary to compensate for these differences. However, because search and rescue teams are inherently reliant on the stories told by survivors of harsh weather conditions — rather than direct measurements from technology that the survivors carried with them — the quality of such data is unaccurate or lacking in many SAR reports.

How much effort the individual had to put into a certain physical activity, based on environmental conditions at the time, is extremely difficult to deduce based on verbal reports of those who endured the excercises. An important future question is therefore how difficult it will be to reconcile these two sources of data; medical reports on one hand, which accurately measure physical acitivities in a closed laboratory environment, and SAR incident reports on the other hand, which describe more realistic conditions but with much less accuracy. It seems inevitable at this point that both will be needed in order to create data which can be used to validate the simulation framework.

Technical Implementation & Prototype

A rough implementation of physiology simulation was created as part of a prototype system created by Aldin Dynamics & Icelandic Institute for Intelligent Machines. In this prototype, physical activities such as running and walking acted as direct input into the simulation framework - providing real-time data from an animated character's muscle groups to simulate physical exertion. The prototype is at its initial stages and provides only a simplified, proof-of-concept that physiological simulation could be implemented in more complex forms.

Based on motion-capture data, a virtual character's animated movements are mapped to muscle groups, providing a correctly timed approximation of when physical exertion was taking place during playback of the animations. This way, when the virtual character is propelling himself forward with his right leg for example, we can in real-time monitor this exertion to interpret it as a statistical energy expenditure based on the current levels of physical health.

The simulation prototype was built using the Unity3D engine, an industry standard when it comes to developing games for entertainment and simulation.

Figure 4 - A screenshot showing the prototype simulation system in action. The virtual character is controlled by a human tester. As the character exerts power, the 2D GUI on the right-side of the screen indicates muscular activity.

MUSCULATORY-BASED ANIMATION BLENDING

The Unity3D engine has an advanced animation system named Mecanim. This system in unique in that, based on live-actor motion-capture data, it animates a character by simulating musculatory system and virtual body-weight to produce an end result that is as realistic as possible. In other words, the system takes generic animations and maps it to a muscle-based animation system, which in turn propels a virtual character's skeleton to produce animations.

For the purposes of our simulation, this adds a level of realism that otherwise would not be possible. The total bodyweight of a virtual character can be adjusted as well as the weights of arms, legs, forearms, hands and even fingers - which is all taken into account during runtime. In effect this allows us to simulate bodyweight to a much greater degree than would otherwise have been possible. Variables such as momentum based on running speed and weight become easily accessible and quanitiable.

Additionally what Mecanim makes possible is to procedurally transition, entirely seemlessly, between animations. The transition from walking to running, for example, happens dynamically during runtime - meaning that the animation gradually transitions from walking to running rather than having a precise cut-off time where the animation switches. This ensures that there is more continuous accumulation of data that is closer to reality as opposed to animation cycles that switch immediately from one state to another.

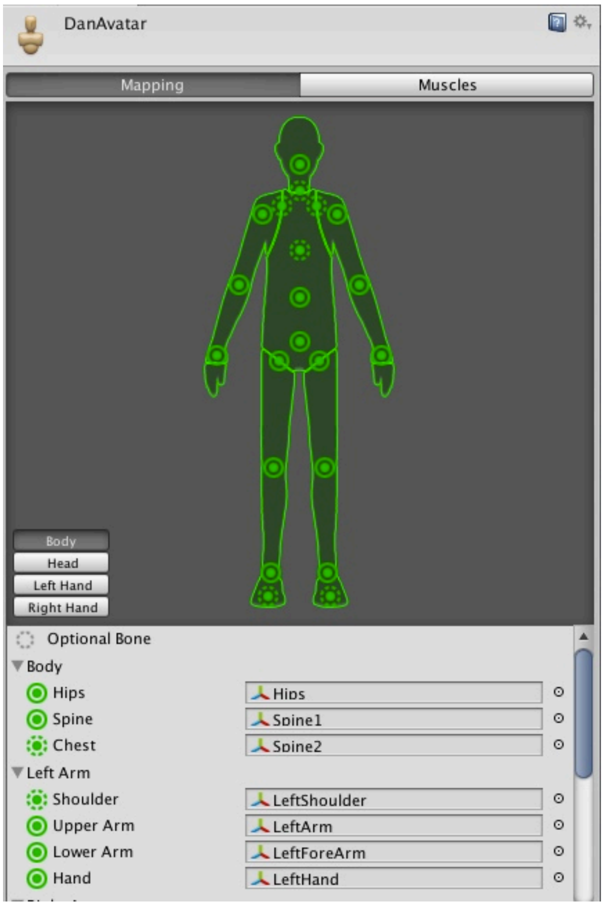


Figure 5 - The Unity3D skeletal-to-muscle mapping system which allows animations to take virtual character body physique into account while animating characters.

Simulating Physiology: Muscles and Organs

To harness the power of Mecanim we analyzed animation cycles for particular activities, such as running and walking. For these animation cycles, we add additional markers and curves that indicate the amount physical exertion being applied to particular limbs which we specify. For the purposes of the prototype we implemented the *right* and *left* sides of the body, and further subdived into left/right *arms* and *legs*. The granularity of these simulations can easily be extended in the future; adding more detailed components such as upper/lower arms, pecs or biceps, etc. is a question of manually adding markers into the animation cycles and adjusting their preferred weight. However, it was only necessary to implement basic muscle functionality as proof-of-concept.

The green curves in *figure 6* are representative of power exerted by each leg at any given time during the animation playback. This ensures proper timing for a particular activity such as running or walking and must be fine tuned manually. As mentioned above, Unity3D's animation system Mecanim handles transitions between states such as running and walking based on physique of the character — ensuring that there is a seamless transition between animation states.

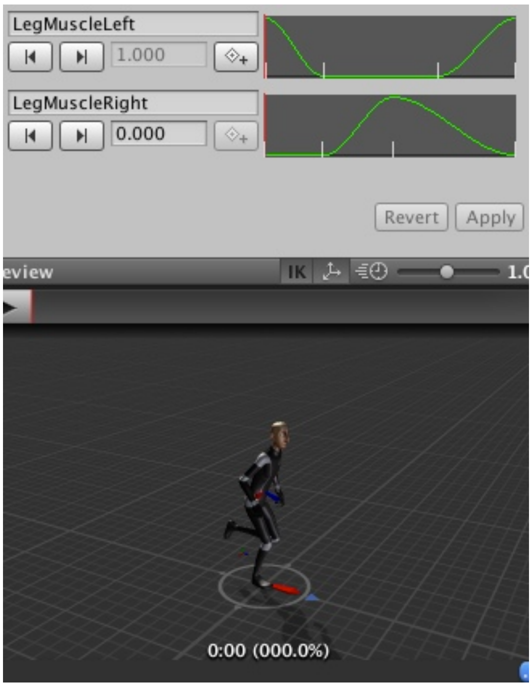


Figure 6 - Curves (green) indicate physical exertion based on the animation cycle motion-capture data. At different points of time in the animation, the characters exerts more or less power for each muscle.

As the character propels himself forward, the appropriate muscles glow red based on power exerted in real-time, at any given time.

Figure 7 - Example of how character animations are visualized in the simulation prototype.

VISUALIZATION

In additon to the directly observable animated character, we implemented a 2D visualization system (*Figure 8*) so that muscle exertion and lung activity could be monitored in realtime.

For future work, circulatory system and brain / nervous system illustrations were included. It is an obvious next step in future work to intergrate visualizations if strain on nervous system or blood circulation.

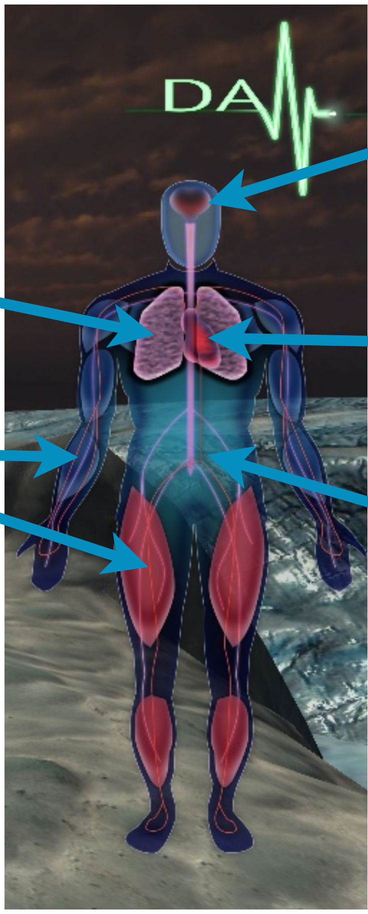


Figure 8 - The 2D graphical user interface visualization of different physiological elements.

Future Work

As computer games become more powerful and the technologies that power them more sophisticated, the opportunities of the “serious games” industry are taking on a new form. Games that teeter on the verge of education and entertainment take inspiration from both areas of industry, providing entertainment experiences that are in many ways more rooted in the physical world; providing educational and/or realistic gameplay value.

Future prototypes of this system would allow for taking external weather conditions to be taken into account, opening up potential for having such things as headwind affect total energy expenditure. Likewise, the system could allow such external weather variables to be used to affect animations — in turn making a virtual character’s animations more realistically portray walking in windy weather conditions.

The system is built to make expanding it simpler, broken down into modular components that exchange information dynamically. This makes it simpler to make the system more complex and accurate with minimal system changes. The distribution of blood, for example, could be made more accurate by representing the cardio-vascular system as a network of veins. This would be added as a subsystem of the circulatory system component, adding further realism without a need to re-implement the entire system.

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APPENDIX

Working Notes for Future Work

Cardiac Output (Q)

Stroke volume (SV) is the volume pumped from one ventricle per beat. Scientist have shown that there exists a linear relationship between the heart rate and stroke volume, see the chart below

.... chart ......

From the chart we can create an equation that is an estimate of the linear relationship. We obtain that

$$SVi\ (ml/m^2) = SV/BSA.$$

$$SV = (8*HR + 280)/9$$

The results from this equation we then use to calculate the cardiac output (Q), which tells us about the blood flow in the body, but the cardiac output tells us about the amount of blood pumped from the heart each minute. To calculate the cardiac output we use the following equation.

$$Q = (HR * SV)/1000$$

Average SV
Average Q

Oxygenation

The volume of oxygen in the blood.

$$\textit{Oxygenation} = (\text{Delivery} - \text{Consumption})/\text{Delivery}$$

In blood:

$$\textit{Delivery} = [1.39 \times Hb \times SaO_2 + (0.003 \times PaO_2)] \times Q$$

where

Hb - concentration of Hemoglobin
SaO2 - saturation of hemoglobin
PaO2 - amount of dissolved oxygen
Q = Cardiac Output

Average Hb - 15 g/dl
SaO2 - lowest 95%- normally 100%
PO2 = 75-100 mmHg

When we don't account for difference in pressure and no blood loss, oxygenation should be 98%-100%.

Body temperature

Current ideas for implementation: Use the heat production (produced during conversion of calories to power), plus insulation provided by clothing, minus outside temperature and wind cooling.

Hiti framleiddur + Föt - (Hitastig úti + vindur)

Calorie_burn_running + Calorie_burn_shivering (constant) - Heat loss + Isolation??

Calorie_burn_running + Calorie_burn_shivering - BSA * x kJ/m2 + Isolation

Wind equations

Consciousness

If body temperature < 32°C: unconscious

Shivering

If bodytemp < 37 && > 35: start shivering

If bodytemp < 35 && > 32: violent shivering

If bodytemp < 32: stop shivering

Have to deal with raising body temperature with shivering.

Note: Have to deal with raising body temperature with shivering and borders

Hypothermia

When hiking, especially on a glacier, the chances of getting hypothermia are high, if the hiker is not careful. Hypothermia occurrs when the outside temperature is too cold or when the body's heat production isn't high enough. Clinical hypothermia is defined when the temperature of the body goes below 35°C. Mild hypothermia is defined when the body's temperature is 32°C-35°C. Moderate hypothermia is when the body temperature is bwtween 28°C and 32°C. Severe hypothermia is when the body temperature goes below 28°C.

If the body temperature falls, the first thing that normally happens is shivering. The shivering creates heat by increasing muscle activity. If the total generated heat does not at least match heat lost to outside temperature, the body's temperature will inevitably get lower.

When body temperature falls, the blood flow is increased to the vital organs and decreased to the limbs. The result is decreased abilities to carry out different activities and fine motor functions. The heart and brain are the organs that require even more blood flow than normally when facing hypothermia, since they are the organs that are most sensitive to cold, and their activity will slow down.

Overall, the main symptoms of hypothermia are shivering, impaired brain function, slowing heart rate, and eventually unconsciousness.