Research Article

Measuring Entropy Change in a Human Physiological System

Satish Boregowda,1 Rod Handy,2 Darrah Sleeth,2 and Andrew Merryweather3

1School of Mechanical Engineering, Purdue University, West Lafayette, IN 47907, USA
2Department of Family & Preventive Medicine, University of Utah, Salt Lake City, UT 84108, USA
3Department of Mechanical Engineering, University of Utah, Salt Lake City, UT 84108, USA

Correspondence should be addressed to Rod Handy; rod.handy@hsc.utah.edu

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The paper presents a novel approach involving the use of Maxwell relations to combine multiple physiological measures to provide a measure of entropy change. The physiological measures included blood pressure (BP), heart rate (HR), skin temperature (ST), electromyogram (EMG), and electrodermal response (EDR). The multiple time-series physiological data were collected from eight subjects in an experimental pilot study conducted at the Human Engineering Laboratory of NASA Langley Research Center. The methodology included data collection during a relaxation period of eighteen minutes followed by a sixty-minute cognitive task.

Two types of entropy change were computed: (a) entropy change (ΔS_{BP}) due to blood pressure, heart rate, and skin temperature and (b) entropy change (ΔS_{EMG}) due to electromyogram, electrodermal response, and skin temperature. The results demonstrate that entropy change provides a valuable composite measure of individual physiological response to various stressors that could be valuable in the areas of medical research, diagnosis, and clinical practice.

1. Introduction

Earlier work done by several researchers has established the fact that human life processes are indeed thermodynamic in nature and hence thermodynamic laws can be used to model human physiology. It has been hypothesized by Bridgman [1] that the laws of thermodynamics are intrinsic to nature and life and are thus well positioned to characterize the physiological behavior of living systems. Aoki [2, 3] examined human thermoregulation by measuring entropy flow and production in basal and exercising conditions but did not utilize Maxwell relations to include other physiological responses. The seminal work done in the areas of biological thermodynamics by Morowitz [4, 5] does not show any application of Maxwell relations to model human physiology. Furthermore, the work done by Garby and Larsen [6] and Jou and Llebot [7] addresses mass, energy, and entropy balance of open living systems but not Maxwell relations. However, the detailed development and preliminary verification of physiological entropy change using Maxwell relations have been presented by Boregowda et al. [8, 9] and are reproduced in Appendix for the convenience of the readers. The present study utilizes time-series data collected during a cognitive task to validate and verify entropy change metrics representing two human physiological subsystems. For the convenience of the readers, the detailed development of physiological entropy change using Maxwell relations is presented in Appendix of this paper. The first one combines changes in blood pressure, heart rate, and skin temperature to provide a BP-based entropy change (ΔS_{BP}). The second one combines changes in electromyogram, electrodermal response, and skin temperature to provide an EMG-based entropy change (ΔS_{EMG}).

2. Modeling and Formulation

2.1. Entropy Change (ΔS_{BP: Blood Pressure, Heart Rate, and Skin Temperature}). Let us first consider the human physiological subsystem characterized by blood pressure (BP), heart rate (HR), and skin temperature (ST) as a closed thermodynamic system. For this system, the work done by the system is given by [10]

\[ \delta W = P \cdot dV = BP \cdot d(HR), \] (1)
where \( P \) is pressure, \( BP \) is blood pressure (mmHg), \( V \) is volume, and \( HR \) is heart rate (beats/minute).

The heart rate is an indirect measure of stroke volume of blood in the heart region and is, thus, used in the place of stroke volume. Please note that heart rate (in beats per minute) is equal to cardiac output (mL/min) divided by stroke volume (mL/beat). The ratio of partial changes in two physiological variables is accompanied by constancy in the third variable, as this is the basis of Maxwell relations. For example, when there is a partial change in heart rate with respect to partial change in entropy, the mean arterial pressure remains constant. As shown in Appendix, the thermodynamic potential is derived as shown starting with Helmholtz’s potential \( (F = U - TS) \) and arriving with the following property relation:

\[
dF = -BP * d(HR) - S * d(ST).
\]  

(2)

The following Maxwell relation is obtained by invoking the exactness condition to the above property relation (2):

\[
\left( \frac{\partial BP}{\partial ST} \right)_V = \left( \frac{\partial S}{\partial HR} \right)_T.
\]  

(3)

The partial derivative is approximated to form a modified Maxwell relation that is used in the present experimental study to compute the physiological entropy change resulting from changes in blood pressure (BP), heart rate (HR), and skin temperature (ST):

\[
\left( \frac{\Delta BP}{ST} \right)_{HR} = \left( \frac{\Delta S_{BP}}{\Delta HR} \right)_{ST},
\]  

(4)

\[
\Delta S_{BP} = \frac{\Delta BP \times \Delta HR}{\Delta ST}.
\]

The skin temperature (ST) in the denominator acts as a temperature at the boundary of the closed thermodynamic system and provides a physiological reflection of emotional response. If one were to consider either internal energy or the Gibbs function to define human physiological function, then one would get a negative sign preceding the entropy change (\( \Delta S_{BP} \)). The deviation from the relaxed state may be positive or negative depending on the imposed external stressor and the internal physiological condition.

2.2. Entropy Change \( (\Delta S_{EMG}) \): Electromyogram, Electrodermal Response, and Skin Temperature. Let us consider the human physiological subsystem characterized by electromyogram (EMG), electrodermal response (EDR), and skin temperature (ST) as a closed thermodynamic system. For this system, the work done by the system is given by

\[
\delta W = \Gamma * dL = EMG * d(EDR),
\]  

(5)

where \( \Gamma \) is tension, EMG is facial electromyogram (mV), \( L \) is length, and EDR is electrodermal response (mV).

In this regard, the elements of a human physiological subsystem are considered as equivalent to a conducting wire with \( \Gamma \) as tension and \( L \) as the length. The facial electromyogram (EMG) has been used in medical research and clinical practice as a measure of tension in facial muscles [11]. As a result of tension in muscles or nerves, the outer surface of the skin responds by expanding or contracting in terms of changes called electrodermal response (EDR). The skin temperature (ST) represents the thermal response to tension. The thermodynamic potential is again derived, starting with Helmholtz’s potential \( (F = U - TS) \) arriving at the following property relation:

\[
dF = -EMG \times d(EDR) - S \times d(ST).
\]  

(6)

The partial derivative is approximated to form a modified Maxwell relation that is used in the present experimental study to compute the physiological entropy change resulting from changes in blood pressure (BP), heart rate (HR), and skin temperature (ST):

\[
\left( \frac{\partial EMG}{\partial ST} \right)_{EDR} = \left( \frac{\partial S}{\partial EDR} \right)_{ST},
\]  

(7)

\[
\Delta S_{EMG} = \frac{\Delta EMG \times \Delta EDR}{\Delta ST}.
\]

As mentioned earlier, the use of either internal energy or the Gibbs function would have resulted in a negative sign preceding the entropy change (\( \Delta S_{BP} \)). The deviation from the relaxed state may be positive or negative, depending on the imposed external stressor and the internal physiological condition. Specifically, physiological entropy is qualitatively defined as a measure of disorder [12]. It is a kind of global measure that specifies how violent motions and reactions are occurring in nature. Hence, the entropy change in the human physiological system shows the extent of activity within the body as a whole; thus, the entropy change is a significant quantity that characterizes the human body from thermodynamic and holistic (i.e., considering a human body as a whole) viewpoints.

The human physiological entropy change could be considered as a composite measure of change in the whole physiological state in response to any external stimuli or stressor. However, if a single physiological indicator alone, such as the mean arterial pressure, can provide that information, then why do we need this entropy change as a composite measure of physiological response? The answer is as follows: the physiological concepts such as stimulus response (SR) specificity, organ response (OR) specificity, individual response specificity, and autonomic balance make the human physiological response a complex phenomenon [11]. The single physiological indicators, in this regard, provide a very narrow representation of the human physiological stress response system. It is only by recognizing the interaction among human subsystems in their response to any stressor stimuli that one could build a better model of human physiology. This study makes an effort to reduce the physiological complexity in terms of a composite entropy change.
3. Methodology

3.1. Subjects. The data in the study were collected on eight subjects (5 male, 3 female). These subjects completed a standard psychophysiological stress profile procedure routinely used for assessment in the Human Engineering Laboratory at NASA Langley Research Center. The participants were all healthy (i.e., without any major health problems).

3.2. Data Collection. The physiological data were collected by a BioPac system via National Instrument LabView. The multiple physiological responses were collected from eight subjects who completed the 78-minute *Physiological Stress Profile* and included the following two conditions:

*Condition 1* (relaxation period). Subjects relaxed in a semireclining position with eyes open for eighteen minutes listening to a guided relaxation tape. The physiological stress response data were collected. These eighteen-minute time-series data, BP, HR, ST, EMG, and EDR, were averaged and used in the physiological entropy change calculations as baseline data points.

*Condition 2* (task period). Subjects completed a series of cognitive tasks presented by an oil refinery simulation program called *Dexter*. The primary goal of this simulation program was to examine the human physiological response to activities that induce boredom, drift in attention, and other negative effects on performance. The task lasted for sixty minutes and two data samples per minute were collected. Each one of these physiological measures—BP, HR, ST, EMG, and EDR—was used in the calculations as shown in the next subsection.

3.3. Illustrative Example. Let us consider subject #1; the eighteen-minute time-series data is averaged to get the following baseline values. Note that BP and VHR are averaged and used in the physiological entropy generation calculations as baseline data points:

- BP (mmHg): 118.74.
- HR (bpm): 68.49.
- EMG (mV): 334.17.
- EDR (μmho): 557.87.

Each one of the physiological measures, BP, HR, ST, EMG, and EDR, from the time-series is used to find the entropy change. Let us consider the values at the 5th minute during the task. A sample calculation of physiological entropy change at the 5th minute for subject #1 is shown as follows:

\[
\Delta S_{BP} = \frac{(BP_{Task} - BP_{O}) \times (HR_{Task} - HR_{O})}{[(ST_{Task} - ST_{O})/1.8]}.
\]

The EMG-based entropy change is calculated as follows:

\[
\Delta S_{EMG} = \frac{(EMG_{Task} - EMG_{O}) \times (EDR_{Task} - EDR_{O})}{[(ST_{Task} - ST_{O})/1.8] \pm D},
\]

\[
\Delta S_{EMG} = \frac{(335.25 - 334.17) \times (678.93 - 557.87)}{[(92.59 - 93.14)/1.8] \pm D}.
\]

\[
= \frac{-100.21 \text{ mV} \cdot \mu \text{mho}/\text{K}}{}
\]

Note the following:

1. Divide temperature difference ΔST by 1.8 to get the units in Kelvin (K).

2. The factor D is used to deal with zeros and small temperature difference that would cause huge entropy change numbers. In this case, D = -1 since ΔST is negative. If it is positive then D = +1. This keeps the magnitude of the entropy change to within manageable limits while keeping the direction of temperature change congruent.

The above sample calculations are done for the entire task period of sixty minutes for each subject and repeated for all the eight subjects as illustrated in the next section.

4. Results and Analysis

The baseline data were obtained by averaging the eighteen-minute relaxation period and are provided in Table 1 for the eight subjects. The ΔS_{BP} and ΔS_{EMG} results are presented in Figures 1 and 2.

Figures 1 and 2 quantitatively demonstrate key psychophysiological important concepts such as stimulus response (SR) specificity, organ response (OR) specificity, and individual (IR) response specificity [11]. For each subject, the response to the task varies within the sixty-minute period. For instance, in Figure 1, subject 4 shows normal variability with ΔS_{BP} throughout the task. This is a demonstration of stimulus response (SR) specificity. In Figure 2, the same subject #4 shows greater variability with ΔS_{EMG} in the beginning of the task while learning to settle down as the task progresses. This is a demonstration of organ response (OR) specificity in which the subject is exhibiting higher reactivity via EMG and EDR combinations. Also, one can observe wide variations between individual subjects in both Figures 1 and 2, which demonstrates individual response (IR) specificity. Furthermore, the average entropy change value over a 60-minute time period was obtained for all eight subjects and shown graphically in Figure 3. It is observed that there is a wide variation among the subjects in terms of average entropy change response to the task demonstrating interindividual differences. These results demonstrate the importance of a thermodynamics-based approach to conducting any medical and/or clinical research involving human subjects.

It is clear from the results shown in Figure 3 that subjects show greater reactivity via entropy change (ΔS_{EMG}) induced
by EMG and EDR than that by entropy change ($\Delta S_{BP}$) induced by blood pressure and heart rate. Both have temperature change as common denominators. Because of higher reactivity, $\Delta S_{EMG}$ involving EMG and EDR measures need to be included in any comprehensive medical stress studies.

5. Conclusion

The study was based on the premise that Maxwell relations could be used to compute entropy change in terms of measurable physical variables. The experimental study involved...
The physiological changes in blood pressure, heart rate, electromyogram, electrodermal response, and skin temperature from the reference (State 1) to stressor (State 2) were used in the Maxwell relations obtaining entropy changes, $\Delta S_{BP}$, and $\Delta S_{EMG}$, respectively. The results validate and verify key patterns of eight subjects and was conducted in the Human Engineering Laboratory at NASA Langley Research Center. The physiological variables were measured at two states, relaxed and stressor task. The average physiological measures taken during relaxation were taken as the baseline values.
Table 1: Baseline values from the relaxation period for eight subjects.

<table>
<thead>
<tr>
<th>Subjects</th>
<th>BP (mmHg)</th>
<th>HR (bpm)</th>
<th>ST (°F)</th>
<th>EMG (mV)</th>
<th>EDR (µmho)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>118.74</td>
<td>68.49</td>
<td>93.14</td>
<td>334.17</td>
<td>557.87</td>
</tr>
<tr>
<td>2</td>
<td>120.36</td>
<td>68.30</td>
<td>90.26</td>
<td>903.86</td>
<td>100.86</td>
</tr>
<tr>
<td>3</td>
<td>144.37</td>
<td>44.64</td>
<td>83.72</td>
<td>418.81</td>
<td>40.54</td>
</tr>
<tr>
<td>4</td>
<td>145.67</td>
<td>45.58</td>
<td>91.34</td>
<td>372.77</td>
<td>20.00</td>
</tr>
<tr>
<td>5</td>
<td>135.90</td>
<td>67.85</td>
<td>90.92</td>
<td>897.79</td>
<td>20.00</td>
</tr>
<tr>
<td>6</td>
<td>139.43</td>
<td>47.44</td>
<td>87.73</td>
<td>477.24</td>
<td>205.90</td>
</tr>
<tr>
<td>7</td>
<td>140.17</td>
<td>73.16</td>
<td>75.64</td>
<td>373.94</td>
<td>381.62</td>
</tr>
<tr>
<td>8</td>
<td>122.73</td>
<td>65.70</td>
<td>91.46</td>
<td>886.80</td>
<td>11.08</td>
</tr>
</tbody>
</table>

Figure 3: Average entropy change response in eight subjects.

Table 2: Human biothermal-fluid system.

<table>
<thead>
<tr>
<th>Physical variables</th>
<th>Biothermal-fluid system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure (P)</td>
<td>Blood pressure (BP)</td>
</tr>
<tr>
<td>Volume (V)</td>
<td>Heart rate (HR)</td>
</tr>
<tr>
<td>Temperature (T)</td>
<td>Skin temperature (ST)</td>
</tr>
<tr>
<td>Entropy (S)</td>
<td>BP-based entropy (S&lt;sub&gt;BP&lt;/sub&gt;)</td>
</tr>
</tbody>
</table>

Appendix

A. Using Maxwell Relations to Measure Entropy Change in Human Physiology

A.1. Derivation of $\Delta S_{BP}$ for Human Biothermal-Fluid System.

The Maxwell relations were used to calculate entropy change ($\Delta S_{BP}$) in terms of measurable physical quantities such as pressure, volume, and temperature. An analogy between a simple physical piston-cylinder system and human physiological subsystem is conceptualized. The physical system characterized by pressure ($P$), volume ($V$), and temperature ($T$) is mapped to that of a human biothermal-fluid system, blood pressure (BP), heart rate (HR), and skin temperature (ST), accordingly as shown in Table 2.

A.1.1. Assumptions.

(a) Human subphysiological system characterized by BP, HR, and ST is considered as a simple closed system from a macroscopic perspective for the purpose of this study. This makes it possible to apply Maxwell relations to examine human physiology.

(b) Blood pressure (BP), heart rate (HR), and skin temperature (ST) are equivalent to pressure ($P$), volume ($V$), and temperature ($T$), respectively, as shown in Table 2.

A.1.2. Analysis. Let us consider a variable $z$ that is a continuous function of $x$ and $y$:

$$z = f(x, y).$$  \hfill (A.1)
It is convenient to write the above equation in the following form:

\[ dz = M \, dx + N \, dy, \]  
(A.2)

where

\[ M = \left( \frac{\partial z}{\partial x} \right)_y, \]  
(A.3a)

\[ N = \left( \frac{\partial z}{\partial y} \right)_x. \]  
(A.3b)

If in (A.1), \( x, y, \) and \( z \) are all point functions (i.e., quantities that depend only on the state and are independent of the path), the differentials are exact differentials. Therefore, in order for (A.1) to be an exact differential equation, the following condition must be satisfied:

\[ \left( \frac{\partial M}{\partial y} \right)_y = \left( \frac{\partial N}{\partial x} \right)_y. \]  
(A.4)

Equation (A.4) is called the exactness condition.

Maxwell relations are derived from the property relations of thermodynamic potentials by invoking the exactness condition. For a simple blood pressure-based human physiological subsystem, there are four thermodynamic potentials:

- Internal Energy: \( dU_{BP} = ST \, ds_{BP} - BP \, dHR, \)  
  (A.5a)
- Enthalpy: \( dH_{BP} = ST \, ds_{BP} + HR \, dB_{BP}, \)  
  (A.5b)
- Helmholtz Function: \( dF_{BP} = -BP \, dHR - S_{BP} \, dST, \)  
  (A.5c)
- Gibbs Function: \( dG_{BP} = HR \, dB_{BP} - S_{BP} \, dST. \)  
  (A.5d)

The following Maxwell relations are obtained by invoking the exactness condition to the above four property relations:

\[ \left( \frac{\partial ST}{\partial HR} \right)_{BP} = - \left( \frac{\partial BP}{\partial S_{BP}} \right)_{HR}, \]  
(A.6a)

\[ \left( \frac{\partial ST}{\partial BP} \right)_{SP} = \left( \frac{\partial HR}{\partial S_{BP}} \right)_{BP}, \]  
(A.6b)

\[ \left( \frac{\partial BP}{\partial ST} \right)_{HR} = \left( \frac{\partial S_{BP}}{\partial HR} \right)_{BP}, \]  
(A.6c)

\[ \left( \frac{\partial HR}{\partial ST} \right)_{BP} = - \left( \frac{\partial S_{BP}}{\partial BP} \right)_{ST}. \]  
(A.6d)

The above-mentioned partial derivatives are approximated to form a modified set of Maxwell relations that are used in the present experimental study to compute the physiological entropy change:

\[ \left( \frac{\Delta ST}{\Delta HR} \right)_{BP} = - \left( \frac{\Delta BP}{\Delta S_{BP}} \right)_{HR}, \]  
(A.7a)

\[ \left( \frac{\Delta ST}{\Delta BP} \right)_{SP} = \left( \frac{\Delta HR}{\Delta S_{BP}} \right)_{BP}, \]  
(A.7b)

\[ \left( \frac{\Delta BP}{\Delta ST} \right)_{BP} = \left( \frac{\Delta S_{BP}}{\Delta HR} \right)_{BP}, \]  
(A.7c)

\[ \left( \frac{\Delta HR}{\Delta ST} \right)_{BP} = - \left( \frac{\Delta S_{BP}}{\Delta BP} \right)_{ST}. \]  
(A.7d)

Any of the above relations (A.7a)–(A.7d) could be used to quantify \( \Delta S_{BP} \), the human physiological entropy change. Using the Helmholtz function-based thermodynamic potential, the entropy change is given by

\[ \Delta S_{BP} = \frac{\Delta BP \times \Delta HR}{\Delta ST}. \]  
(A.8)

A.2. Derivation of \( \Delta S_{EMG} \) for Human Biothermal-Electric System. The physical system characterized by tension (\( F \)), length (\( L \)), and temperature (\( T \)) is mapped to that of a human biothermal-electric system, electromyogram (EMG), electrodermal response (EDR), and skin temperature (ST), accordingly as shown in Table 3.

A.2.1. Assumptions. (a) Human subphysiological system characterized by EMG, EDR, and ST is considered as a simple closed system from a macroscopic perspective for the purpose of this study. This makes it possible to apply Maxwell relations to examine human physiology.

(b) Electromyogram (EMG), electrodermal response (EDR), and skin temperature (ST) are equivalent to tension (\( F \)), length (\( L \)), and temperature (\( ST \)), respectively.

A.2.2. Analysis. Maxwell relations are derived from the property relations of thermodynamic potentials by invoking the exactness condition. For a simple blood pressure-based

<table>
<thead>
<tr>
<th>Physical variables</th>
<th>Biothermal-electric system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tension (( F ))</td>
<td>Electromyogram (EMG)</td>
</tr>
<tr>
<td>Length (( L ))</td>
<td>Electrodermal response (EDR)</td>
</tr>
<tr>
<td>Temperature (( T ))</td>
<td>Skin temperature (ST)</td>
</tr>
<tr>
<td>Entropy (( S ))</td>
<td>EMG-based entropy (( S_{EMG} ))</td>
</tr>
</tbody>
</table>
human physiological subsystem, there are four thermodynamic potentials:

Internal Energy: $dU_{EMG} = ST dS_{EMG} - EMG dEDR$, \hspace{1cm} (A.9a)

Enthalpy: $dH_{EMG} = ST dS_{EMG} + EDR dEMG$, \hspace{1cm} (A.9b)

Helmholtz Function: $dF_{EMG} = -EMG dEDR - S_{EMG} dST$, \hspace{1cm} (A.9c)

Gibbs Function: $dG_{EMG} = EDR dEMG - S_{EMG} dST$. \hspace{1cm} (A.9d)

The following Maxwell relations are obtained by invoking the exactness condition to the above four property relations:

\[
\left( \frac{\partial ST}{\partial EDR} \right)_{S_{EMG}} = - \left( \frac{\partial EMG}{\partial S_{EMG}} \right)_{EDR}, \hspace{1cm} (A.10a)
\]

\[
\left( \frac{\partial ST}{\partial EMG} \right)_{S_{EMG}} = \left( \frac{\partial EDR}{\partial S_{EMG}} \right)_{EMG}, \hspace{1cm} (A.10b)
\]

\[
\left( \frac{\partial EMG}{\partial ST} \right)_{EDR} = \left( \frac{\partial S_{EMG}}{\partial S_{EMG}} \right)_{EMG}, \hspace{1cm} (A.10c)
\]

\[
\left( \frac{\partial EDR}{\partial ST} \right)_{EMG} = - \left( \frac{\partial S_{EMG}}{\partial ST} \right)_{EMG}. \hspace{1cm} (A.10d)
\]

The modified set of Maxwell relations that are used in the present experimental study to compute the physiological entropy change are

\[
\left( \frac{\Delta ST}{\Delta EDR} \right)_{S_{EMG}} = - \left( \frac{\Delta EMG}{\Delta S_{EMG}} \right)_{EDR}, \hspace{1cm} (A.11a)
\]

\[
\left( \frac{\Delta ST}{\Delta EMG} \right)_{S_{EMG}} = \left( \frac{\Delta EDR}{\Delta S_{EMG}} \right)_{EMG}, \hspace{1cm} (A.11b)
\]

\[
\left( \frac{\Delta EMG}{\Delta ST} \right)_{EDR} = \left( \frac{\Delta S_{EMG}}{\Delta EDR} \right)_{EMG}, \hspace{1cm} (A.11c)
\]

\[
\left( \frac{\Delta EDR}{\Delta ST} \right)_{EMG} = - \left( \frac{\Delta S_{EMG}}{\Delta ST} \right)_{EMG}. \hspace{1cm} (A.11d)
\]

Using the Helmholtz function-based thermodynamic potential (A.11c), the entropy change is given by

\[
\Delta S_{EMG} = \frac{\Delta EMG \times \Delta EDR}{\Delta ST}. \hspace{1cm} (A.12)
\]

**Conflict of Interests**

The authors declare that there is no conflict of interests regarding the publication of this paper.

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