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Entropic Characterization of Multiple Physiological Responses with Statistical Process Control Charts

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ABSTRACT

Numerous studies have been conducted in the past to measure and characterize human stress response using single physiological indicators. The proposed study presents a unique thermodynamic concept to provide a quantitative measure of stress response by combining multiple physiological responses using Maxwell relations. It combines five measurable peripheral physiological signals such as blood pressure, heart rate, finger skin temperature, electromyogram, and electrodermal response to provide a quantitative measure of entropy change, which is used as a key performance indicator (KPI). The data obtained from a NASA human engineering pilot study involving seven subjects are used to demonstrate this methodology. The five physiological signals are combined into two entropy change metrics. The entropy change as a KPI is represented on the statistical process control charts (SPC) with mean, upper control limit (UCL), and lower control limit (LCL) values. Both visual and single factor ANOVA tests show a significant statistical difference in individual physiological entropy change. In summary, the entropy-change shows great potential to be used as a KPI for monitoring physiological stress level and health status in various healthcare applications.

1. INTRODUCTION

Several studies have been conducted in the past to examine the relationship among the elements of stress, nervous system, and physiological processes [1]. It has been well established that the physiological signals provide a quantitative measure of stress depending on the nature of the imposed stressors [2]. The complexity of the human physiological stress responses to any external stimuli or a combination of stressors poses a major challenge to better understand the consequences of stressful events in life. In general, the impact of both acute and chronic stressors on human physiological health is not clearly understood at the present time. Despite numerous studies in the past, there is no composite quantitative measure of physiological stress response that could be used to monitor human physiological health. The motivation behind this study is to overcome this limitation by combining multiple physiological responses in terms of entropy change (ΔS) using Maxwell relations from thermodynamics to provide a quantitative measure of stress. In the fields of quality engineering, statistical process control charts (SPC) are routinely used to track any process quality using key performance indicators (KPIs) [3, 4]. The physiological entropy change utilized as a KPI for monitoring stress level could be used in SPC charts similar to manufacturing. This methodology could help healthcare professional in the real-time diagnosis and subsequent treatment of health issues.

Aoki [5, 6] has examined human thermoregulation using entropy generation with the second law of thermodynamics. Bejan [7] has developed constructal law relations to explain the physiological dynamics of breathing and heart beating. However, these previous studies do not use thermodynamic Maxwell relations and do not include multiple physiological responses. The present study is unique that it combines multiple physiological responses in a meaningful manner using Maxwell relations to provide a quantitative measure of stress.

The law of psychophysics states that the psyche itself cannot be measured directly but it can be interpreted in terms of changes in physical variables [8]. Using a similar logic, the present study is based on the thermodynamics-based premise that entropy itself cannot be measured directly but it can be expressed in terms of changes in multiple physical variables such as pressure, volume, temperature, length, and tension [9, 10]. The changes in multiple physiological variables are mapped to that of physical system and are expressed in terms of physiological entropy change using Maxwell relations by Boregowda et al. [11-13]. The earlier studies conducted by Boregowda et al. [11] used time-series data but it did not address the use of entropy change as a key performance indicator in statistical process control charts. The NASA study involved the collection of five physiological signals including blood pressure, heart rate, skin temperature, electromyogram, and electrodermal response as described in the methodology section. The results and discussion begin with an illustrative example of entropy change calculation for subject number one followed by the demonstration of a statistical process control chart for the same human subject for the sake of brevity. However, the variation in entropy change in seven subjects is presented graphically in terms of mean, upper control limit

(UCL), and lower control limit (LCL) values for all seven subjects. The single-factor ANOVA test is conducted on mean, UCL, and LCL values of entropy change. The results indicate a statistically significant difference in physiological entropy change in seven subjects. The primary goal of this study was to create a pathway for deeper physiological investigation of entropy change as a quantifiable key performance indicator for monitoring of whole physiological health status and stress level. Furthermore, the physiological entropy change metric provides a holistic measure of physiological stress that could be integrated into health monitoring systems for clinical decision-making. The methodology and formulation of physiological entropy change are presented in the sections 2 and 3 while the results in section 4 demonstrate the utility of the entropy change as a KPI for monitoring stress level and health status. The results indicate that the entropy change as a KPI provides a single summative number that could be utilized as a metric for quantifying health status and stress that is sorely missing in the literature.

2. METHODOLOGY

Subjects

The data in the study were collected from seven subjects (4 male, and 3 female) aged between 18 and 35 years. All subjects were students who were recruited from the local universities and colleges. These subjects completed a standard physiological stress profile procedure routinely used for assessment in the Human Engineering Laboratory at NASA Langley Research Center [11-13]. The participants were all healthy without any major health problems.

Data Collection

The physiological data were collected by a BioPac MP160 system (www.biopac.com) via National Instrument LabView. The multiple physiological responses were collected from seven subjects who completed the 75-minute Physiological Stress Profile and included the two following conditions:

Condition 1 (Relaxation Period)

Subjects relaxed in a semi-reclining position with eyes open for the first fifteen minutes listening to a guided relaxation tape. The physiological stress response data during this relaxation period were collected. Using thermodynamic interpretation, the values of the physiological variables were taken to be zero signifying the non-living state of a living system, which is defined as dead state in thermodynamics [10]. This means that the reference values of physiological variables are taken to be zero for the relaxation period.

Condition 2 (Task Period)

After the relaxation period of fifteen minutes, subjects completed a series of cognitive tasks for a period of sixty minutes. Subjects performed vigilance task of monitoring an oil refinery simulation program called Dexter three times interspersed with two arithmetic tasks as shown in Table 1. The primary goal of this simulation program was to examine the human physiological stress response to activities that induce boredom, drift in attention, and other negative effects on performance.

Table 1. Physiological stress monitoring conditions

Time (in minutes)	Conditions
0 - 15	Relaxation (Baseline Recording)
15 - 35	Vigilance Task (Dexter)
35 - 40	Mental Arithmetic Task
40 - 60	Vigilance Task (Dexter)
60 - 65	Mental Arithmetic Task
65 - 75	Vigilance Task (Dexter)

Using LabVIEW data acquisition system, five measures such as blood pressure, heart rate, skin temperature, electromyogram, and electrodermal response were recorded continuously [12]. The sensors for measuring the physiological responses were mounted on the body surface of the subjects. The pulse wave velocity (PWV) techniques were used to measure systolic blood pressure. The PWV is the rate of travel of pressure pulse waves through the arterial system [2]. It does not use a cuff but obtains a reading of time for the pulse to occur at two points along an artery. The resulting transit time (TT) is used as an indirect measure of blood pressure. However, it is found that the transit time is related to systolic but not diastolic blood pressure. Heart rate was recorded from pulse sensors attached to the wrist and ankle. Skin temperature was measured from a small sensor taped to the back of the middle finger of the left hand. Facial muscle activity or frontal EMG was measured from three sensor attached to the forehead. Electrodermal activity (EDA) was measured from sensors attached to the pads of two fingers on the left hand.

Using thermodynamic interpretation, the values of the physiological variables collected during the relaxation were taken to be zero signifying the non-living state of a living system, which is defined as a dead state in thermodynamics [10]. Each one of the physiological stress responses including blood pressure, heart rate, skin temperature, electromyogram, and electrodermal activity were used in the modeling and formulation and are presented in the next section.

3. MODELING AND FORMULATION

Entropy has been established as a measure of disorder in any system in the universe [9, 10]. Specifically, entropy generation as a measure of disorder is a kind of global measure that specifies how violent motions and reactions are occurring in nature. Hence, the entropy generation in the human physiological system shows the extent of activity within the body as a whole; thus, the entropy generation is a significant quantity that characterizes the human body from both thermodynamic and holistic (i.e., considering a human body as a whole) viewpoints [5, 6]. Thermodynamics with its biological origins [14], is particularly well-suited to study human physiological systems behavior [14-19]. It has been hypothesized by Bridgman [15] that the laws of thermodynamics are intrinsically positioned to model the physiological behavior of living systems. The state of the physiological system without an energetically significant measurement such as entropy generation would lead to a violation of the second law of thermodynamics [16, 17].

The physiological entropy-change, ΔS, derived from the Maxwell relations, is provided in detail in references [11-13]. It is based on the premise that entropy itself cannot be measured but can be interpreted in terms of measurable physical variables using Maxwell relations [9, 10]. The logic of Maxwell relations is consistent with the laws of psychophysics that psyche cannot be measured but can be interpreted in terms of physical variables, which in this study are the measurable peripheral physiological responses. It follows that the entropy-change in the human physiological system, $(\Delta S)_1$, characterized by BP, HR, and ST is given by:

$$(\Delta S)_1 = \frac{\Delta BP \times \Delta HR}{\Delta ST} \tag{1}$$

where,

$$\Delta BP = (BP_{Task} - BP_0), mm\ Hg$$
$$\Delta HR = (HR_{Task} - HR_0), bpm$$
$$\Delta ST = (ST_{Task} - ST_0), K$$

Similarly, the entropy-change in the human physiological subsystem, $(\Delta S)_2$, characterized by EMG, EDA, and ST is given by:

$$(\Delta S)_2 = \frac{\Delta EMG \times \Delta \mathrm{EDA}}{\Delta ST} \tag{2}$$

where,

$$\Delta EMG = (EMG_{Task} - EMG_0), mV$$
$$\Delta EDA = (EDA_{Task} - EDA_0), \mu mho$$
$$\Delta ST = (ST_{Task} - ST_0), K$$

It is noticeable that the skin temperature is present in the denominator of all the above entropy change equations. In thermodynamic terms, it acts as a temperature at the boundary of the thermodynamic system and provides a physiological reflection of emotional response [2]. A single physiological indicator does not provide much information about the holistic nature of human physiology. This is due to the psychophysiological concepts such as stimulus response (SR) specificity, organ response (OR) specificity, individual response (IR) specificity, and autonomic balance that make the human physiological response to any stimuli a complex phenomenon [2]. These realities reflect the fact that the different individuals react differently to different stimuli via different organ systems. For instance, a person might exhibit higher blood pressure to a traumatic event or a memory of it while another person might respond with intense facial tension with higher electromyogram. The single physiological indicators provide a narrower knowledge of the physiological stress response. It is only by recognizing the interaction among various physiological responses to any stressor stimuli that one could build better physiological models, which is one of the objectives of this study.

4. RESULTS AND DISCUSSION

This section begins with an illustrative example. We present some of the important results pertaining to physiological entropy change response of seven subjects to the same stimuli involving a cognitive task.

4.1 Illustrative example

Each one of the physiological measures— BP_{Task}, HR_{Task}, ST_{Task}, EMG_{Task}, and EDR_{Task} from the time-series are used to find the entropy changes shown below. Let us consider the physiological responses of the subject one during the task period. The entropy changes at the fifth minute for the subject number one is shown below:

$(\Delta S)_1$= $(BP_{Task}–BP_o)$ x $(HR_{Task}-HR_o)$ / $(ST_{Task}-ST_o)$
= (118.94–0.0) x (70.09–0.0) / (305.21–0.0)
= **27.31 mm Hg.bpm/K**
$(\Delta S)_2$ = $(EMG_{Task}–EMG_o)$ x $(EDA_{Task}-EDA_o)$ / $(ST_{Task}-ST_o)$
= (679.66 – 0.0) x (89.93 – 0.0) / (305.21 – 0.0)
= **200.26 mV. µmho/K**

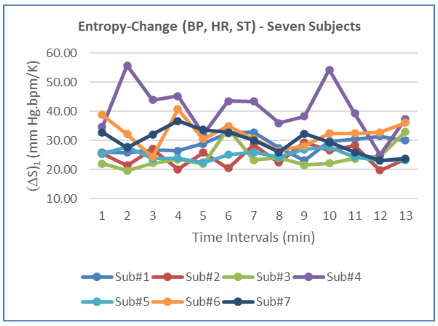
The above sample calculations are repeated for every five-minute interval, that is twelve data points, for the entire task period of sixty minutes for each subject and is repeated for all the seven subjects. However, the calculation of mean, UCL, and LCL for the subject number one is shown below [3]:

Mean $(\Delta S)_1$ = 30.10 mm Hg-bpm/K
UCL $(\Delta S)_1$ = MEAN + 3*STDEV
= 30.10 + 3*3.18 = **39.62 mm Hg-bpm/K**
LCL $(\Delta S)_1$ = MEAN - 3*STDEV
= 30.10 - 3*3.18 = **20.57 mm Hg-bpm/K**

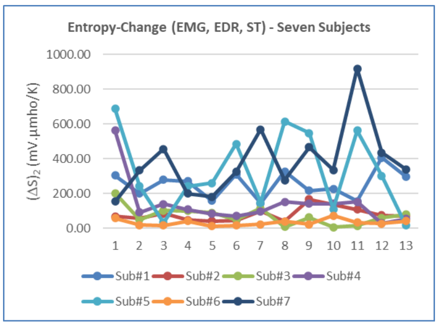
Mean $(\Delta S)_2$ = 250.29 mV. µmho/K
UCL $(\Delta S)_2$ = MEAN + 3*STDEV
= 250.29 + 3*80.55 = **491.75 mV. µmho/K**
LCL $(\Delta S)_2$ = MEAN - 3*STDEV
= 250.29 - 3*80.55= **8.84 mV. µmho/K**

4.2 Entropy-change time-series plots

The five-minute-interval time-series data is presented for all seven subjects is presented in Figure 1 (a-b). It can be seen visually that there are significant individual differences, and it is clear from the Figure 1(a-b) that one can detect difference in physiological response of different subjects in terms of entropy changes.



(a)



(b)

Figure 1. Time-Series plots of entropy-change

However, it is important to verify the inter-individual difference in physiological response using single factor ANOVA test as shown in the next subsection.

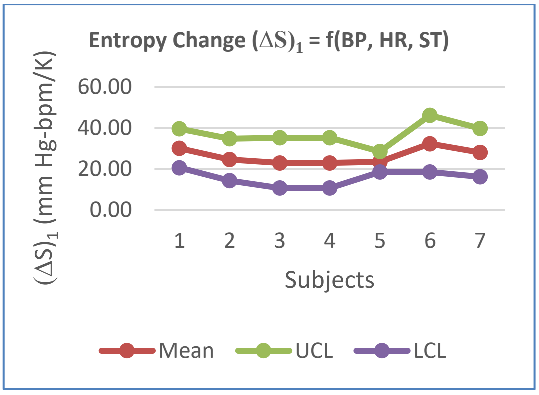
4.3 Single factor ANOVA

The results of the ANOVA are presented for two human physiological subsystems respectively. The results in Table 2 indicate statistically significant difference in entropy change response among seven subjects. For both entropy changes, the F-statistic values are significantly greater than the critical values of F in addition to the p-values that are significantly lower than the level of significance of 0.05.

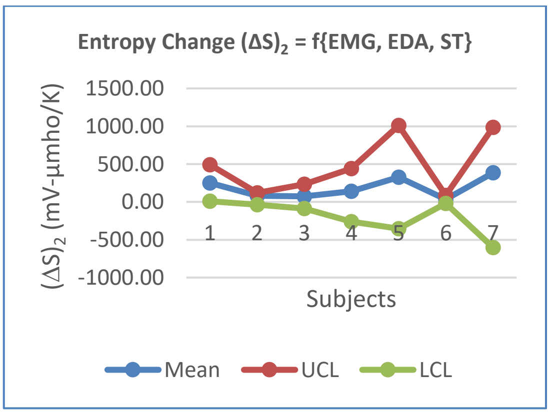
Table 2. Single factor ANOVA for entropy changes

	SS	df	MS	F	P val	F crit
ANOVA $(\Delta S)_1$ = f{BP, HR, ST}						
	SS	df	MS	F	P val	F crit
Between	2682.89	6	447.15	20.60	1.1E-14	2.21
Within	1823.18	84	21.70			
Total	4506.1	90				
ANOVA $(\Delta S)_2$= f{EMG, EDA, ST}						
	SS	df	MS	F	P val	F crit
Between	1471772	6	245295.3	14.25	4E-11	2.21
Within	1446044	84	17214.81			
Total	2917816	90				

4.4 Entropy-change statistical process control charts



(a)



(b)

Figure 2. Subject-to-subject variation of mean, UCL, and LCL values of entropy changes for seven subjects

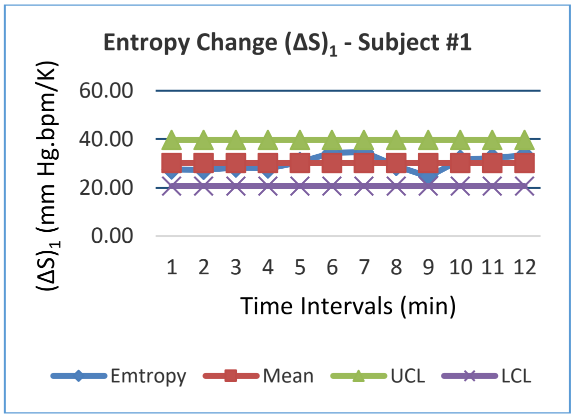
The statistical process control charts (SPC) are critical to maintaining quality control of products and processes in manufacturing, healthcare, and pharmaceutical industries [16]. The mean, UCL, and LCL values of entropy changes are provided for all seven subjects in Table 3. However, it is critical to represent this inter-individual variation graphically for gaining physiological insight. The visual representation in Figure 2 (a-b) reveals significant subject-to-subject variation in values of mean, UCL, and LCL warranting individualized medical treatment modalities for stress-related illnesses.

The entropy change SPC provides a single variable that can be tracked for each human subject. However, the subject-to-subject variation of mean, UCL and LCL values of entropy change for all seven subjects is presented in Table 3 and Figure 2 (a-b).

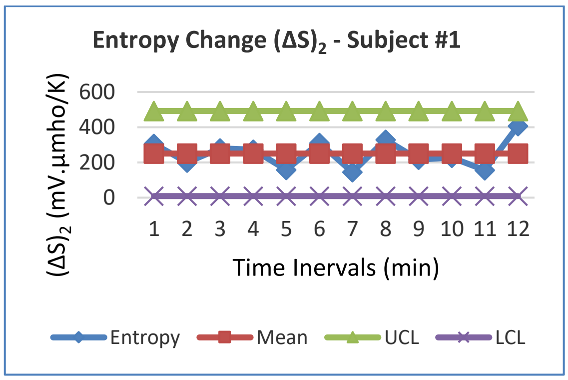
Table 3. Mean, UCL, and LCL values of entropy change

Sub.	$(\Delta S)_1 = f\{BP, HR, ST\}$			$(\Delta S)_2 = f\{EMG, EDA, ST\}$		
	Mean	**UCL**	**LCL**	**Mean**	**UCL**	**LCL**
1	30.10	39.62	20.57	250.29	491.75	8.84
2	24.49	34.73	14.25	80.80	119.66	-38.86
3	22.90	35.16	10.63	72.69	231.82	-86.43
4	22.90	35.16	10.63	140.53	438.74	-259.67
5	23.47	28.46	18.49	327.24	1010.29	-355.62
6	32.28	46.15	18.41	33.59	86.69	-19.52
7	27.98	39.76	16.20	384.53	986.80	-602.27

For the sake of brevity, only one statistical process control for one of the seven subjects is presented for the purpose of illustration. The mean, UCL, and LCL values of entropy change for subject number one are presented in Figure 3 (a-b).



(a)



(b)

Figure 3. Entropy change SPC charts for subject #1

From the results, we can conclude that the entropy generation could be utilized as a measure of stress response. It characterizes the concept of general adaptation syndrome (GAS) in which the organisms alter their physiology to adapt to the imposed stressors [1]. The physiological alarm reaction to a stressor is followed by a period of stage of resistance and finally culminating with a stage of exhaustion as presented in Figure 4. Both acute and chronic exposure to stressors as depicted in GAS alters the human physiology. The entropy change combines the resulting changes in multiple physiological responses to provides a quantifiable KPI for characterizing the whole human physiology.

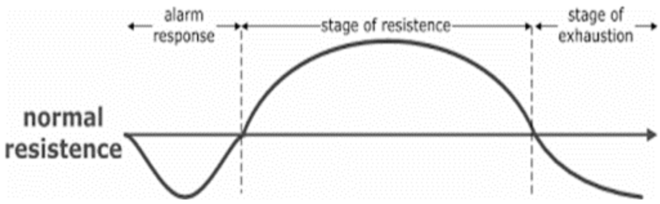


Figure 4. Selye's general adaptation syndrome [1]

The concept of GAS in conjunction with entropy change provides a key performance metric (KPI) for integration into the statistical process control for continuous real-time monitoring of human physiological stress responses to varying stimuli in living and work environments as shown in Figure 5.

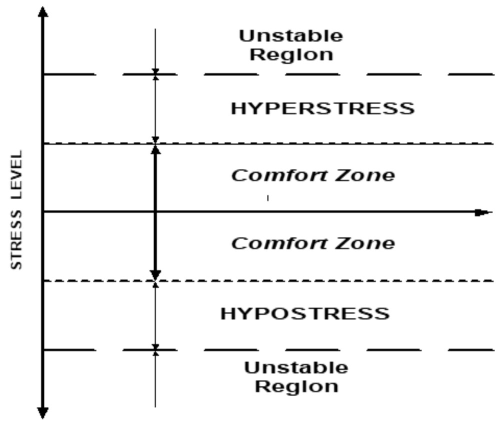


Figure 5. Stress and performance evaluation chart

Some of the settings to assess human stress level and performance include but not limited to outpatient treatment centers, in-patient health facilities, and mission-critical applications such as traffic control and nuclear plant operations [20].

5. CONCLUSION

Most of the past studies have focused on single physiological indicator or subjective questionnaires or performance or behavioral actions to interpret stress. These past metrics have served the purpose of limited research investigations and narrower applications but they do not provide any scientific method to quantify stress in terms of single number. Furthermore, there has been no meaningful metric that combines multiple physiological responses to provide a quantitative measure of stress in terms of a single number. The present study was conducted to fill this major gap to assess human physiology and interpret stress response.

The study involved collection of five physiological signals from seven subjects in a NASA pilot study who performed a mission-critical monitoring cognitive task. Five physiological signals included blood pressure, heart rate, finger skin temperature, electromyogram, and electrodermal response. These five signals were combined using Maxwell relations to provide a quantitative measure of entropy change that was used as a KPI represented in statistical process control charts. The results demonstrate critical psychophysiological concepts such as individual response (IR) specificity, organ response (OR) specificity, and stimulus response (IR) specificity [2]. In other words, the stress response to a particular stimulus varies from individual to individual while within the same individual, there is variation in how different organ systems respond to the same stimuli. The single factor ANOVA indicate statistically significant difference in individual stress response warranting further physiological investigation.

The present study with limited data demonstrates the potential utility of entropy change as a key performance indictor (KPI) that can be used to provide a holistic measure of human physiological stress response that could be developed into a clinical decision-making tool for medical diagnosis, preventive health treatments, and human operator stress monitoring in mission-critical applications. To achieve this goal, a large-scale study involving collection of multiple physiological data from large number of subjects needs to be conducted. The results from this type of study needs to be validated and verified for clinical applications. One of the futuristic goals is to use wearable sensors to track multiple physiological stress responses to examine the impact of stressors in real-time work and living environments for preventive health management.

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NOMENCLATURE

$(\Delta S)_1$	entropy change, mm Hg.bpm/K
$(\Delta S)_2$	entropy change, mV. µmho/K
KPI	key performance indicator
BP	blood pressure, mm Hg
HR	heart rate, bpm
ST	finger skin temperature, K
EMG	electromyogram, mV
EDA	electrodermal activity, µmho