

Article

# Pulse Wave Harmony: Ancient Wisdoms for Modern Age

Patrick Celka <sup>1\*</sup>, Lobsang Samten <sup>2</sup>, Marina Brucet <sup>2</sup> and Abdullah Alabdulgader <sup>3</sup>

<sup>1</sup> SATHeart SA, Yverdon-les-Bains, Switzerland; patrick.celka@satheart.com

<sup>2</sup> Lama Tzong Khapa Institute, Pomaia, Italy; mbrucet@gmail.com

<sup>3</sup> Director of Research and Scientific Bio-Computing, Prince Sultan Cardiac Center, Alhasa, Hofuf 31982, Saudi Arabia; kidsecho@yahoo.com

\* Correspondence: patrick.celka@satheart.com

**Abstract:** Background: This research presents the use of photoplethysmography combined with Traditional Tibetan Pulse reading for the estimation of the three energies of a person: Activity, Transformation and Stability. The three energies derive from the four elements which are known from antiquity, both East and West, which considered life and the cosmos as an inseparable whole. Therefore the three energies composing the human functions are a reflection of our life as well as the cosmos. Method: Our work is presented in two studies. The first study presents the development of the technique of photoplethysmography to classify the three energies. The second study presents a validation of this methodology on mental stress and relaxation. Results: Energies classification achieved a sensitivity above 85% and specificity above 86%. Mental stress and relaxation could be significantly discriminated from baseline condition. Harmonic analysis gave further insights into the dynamic of the pulse wave under stress/relaxation. Conclusion: The photoplethysmogram contains information pertaining to the mental and physiological state of a person as interpreted with the Eastern energies concepts. The implication of this work points towards a holistic understanding and impact of human activities, health and its environment.

**Keywords:** Pulse wave analysis; Traditional Tibetan Medicine; Harmonic analysis; Mental stress; Holism; Environment

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## 43 1. Introduction

44 The traditional knowledge of finger pulse reading has to be understood from the context of  
45 cultural and medical exchanges in the regions of the middle East, Europe and Far East [5,6]. Among  
46 the European and middle East physicians, Aristotle, Hippocrates and the Persian physician Abu Ali  
47 Ibn Sina (Avicenna) [7] elaborated the techniques of finger pulse reading in the first millennium of our  
48 era. Avicenna based his work on the four elements from Galen and also elaborated on Hippocrates's  
49 concept of four humours in his first book. Linking the knowledge of the elements with the finger pulse  
50 wave dynamic, these physicians elaborated a holistic understanding of health and disease together  
51 with the role of humans on planet earth. At the raise of Renaissance, when modern science with the  
52 analytic methods supplanted this traditional holistic knowledge, the enormous body of traditional  
53 medicine was forgotten in Europe.

54 Traditional Tibetan Medicine [1], like most Traditional Medicine systems such as Chinese [2,3]  
55 and Indian Ayurvedic [4], have developed an empirical knowledge of the body-mind complex since  
56 thousands of years and is still alive today. Of particular interest for this research is one of their  
57 diagnosis systems based on blood pulse wave finger sensing: using several fingers placed on certain  
58 parts of the body, the traditional physician is able to identify the type of disorder the patient is suffering  
59 from. The disorder can have external origins such as seasonal changes, food poisoning, injuries; and  
60 can also have internal causes such as mental stress, anxiety and so on. These medical systems are  
61 holistic by nature, seeing the body, mind and its environment as un inseparable whole. As presented  
62 in more details in Section 2.2, according to Traditional Tibetan Medicine, each person is qualified with  
63 three characteristics called *Humours* or *Energies*. These three energies are a reflection of the interplay of  
64 the elements, the foundational knowledge of all forms of energies, from matter to mind, from stars to  
65 cells and consciousness. Profound understanding of this knowledge thus lead to a unified view of the  
66 cosmic dynamic within which the human being is just one representative.

67 In the last 20 years, there has been fast growing development of digital pulse wave analysis  
68 approaches developed primarily in Asia, China, Korea and Russia, where traditional pulse reading  
69 were strongly developed. A few works have been done using the specific technique of Tibetan  
70 Pulse Reading and among the first was the Institute of Physical Materials Science of the Siberian  
71 Branch of the Russian Academy of Sciences in Ulan Ude in Buryatia led by Prof. Vitaly Vasylevich  
72 in 1983 [8]. Nowadays digital pulse wave reading technologies are quickly evolving both in terms of  
73 miniaturization and accuracy. Especially due to the large work done by Chinese [9–11] and Korean  
74 [12] research centres.

75 Recent development of pulse wave sensing and processing systems have emerged for estimating  
76 vital signs such as blood pressure, arterial compliance, pulse wave velocity together with the pulse  
77 heart rate and heart rate variability. Also, it has been discovered that arterial stiffness and pulse wave  
78 velocity are key parameters in a number of cardiovascular related pathologies such as hypertension,  
79 coronary artery diseases, and diabetes [13–15]. Among the most popular sensors are those based on  
80 photoplethysmography (PPG), possibly at various wavelengths [16,17]. This work reports for the first  
81 time such an attempt to interpret of Traditional Tibetan Pulse reading using PPG together with an  
82 application to mental stress assessment.

83 Section 2 presents the basic understanding of Eastern philosophy together with Traditional Tibetan  
84 Medicine concepts and their relationship with Western concepts. Section 3 describes our two separate  
85 data collection protocols and pulse wave sensing instruments. The first study is presented in Section  
86 4.1 and describes the classification of the three energies. The second study is presented in Section 4.2  
87 and validate our energies classification together with a harmonic analysis in the assessment of mental  
88 stress. The two studies were independently performed. Section 5 discusses the results and Section 6  
89 concludes this work.

## 90 2. Eastern and Western Pulse Reading

### 91 2.1. The Five Elements

92 At the core of ancient medical and cosmological knowledge, both from Western and Eastern  
93 cultures, stands the philosophy of the elements [4]. These elements were thought to pervade all of  
94 animate and inanimate objects, perceivable and not. The elements are commonly known as Air/Wind,  
95 Fire, Water and Earth. A fifth element is usually added and is referred to as Space which is the ground  
96 of all the other ones and is thus never separated from them. The elements are not to be conceived as  
97 static building blocks but rather as functional entities or elemental energies that reflect their stability,  
98 and their dynamic and transformative nature. The concept of energy is central in both Western and  
99 Eastern sciences and is thus a good base for making the bridge between the two systems. In order to  
100 ease the way from Western to Eastern thoughts when reading this article, we should keep in mind  
101 the following definition of energy: a measure of a system's ability to cause change or maintain its  
102 structure. The space element being the ground of all four is also the most primordial and could be  
103 likened to the vacuum state [75] in quantum field theory: the substrate from which all the other four  
104 emerge without being separated from them. As the elements are at the root of every phenomena,  
105 they appeared to be the ideal place to elaborate a deep understanding of human life, its role in the  
106 universe and its interaction with the environment. Humans are in constant dynamic interaction with  
107 the surrounding atmosphere and the radiations and high-energy particles from the sun and many  
108 other cosmic objects. The elements are the foundational principles of these particles and fields, both to  
109 be found inside our bodies and our environment, and thus it should come as no surprise that humans  
110 and their environment are deeply connected to each other if not to say inseparable. What's even  
111 more surprising from this elemental principle is that they also pervade the non material worlds such  
112 as the electromagnetic fields and mind (i.e. both mental and emotional components). The action of  
113 the elements thus goes as far deep as our consciousness. As we will present in the Section 2.2, their  
114 function is manifesting in the human body and mind in what is known as the three Humours (Tibetan  
115 *nyépa*), which we will call Life Energies or just Energies in this paper. These three life energies are  
116 thus a lens through our body functions as well as our mental, emotions, intuitions and feelings; which  
117 makes them an extraordinary tool for studying the human dimensions and experiences.

### 118 2.2. Traditional Tibetan Pulse Reading: The Three Energies

119 Traditional Tibetan Pulse reading is a difficult task which requires many years of practice to  
120 master the skills to be able to *listen* to the pulse in a meaningful way. Traditional Tibetan Medicine  
121 is essentially based on medical texts originating from Central Asia and Tibet [18]. The knowledge  
122 of healing (Tibetan *Sowa Rigpa*) derives from a collection of texts known as the Four Tantras [19],  
123 the precise origins and authorship is still disputed, but we can safely say that the last versions were  
124 composed by several practitioners from different Tibetan neighboring countries in the 8th century A.D.,  
125 during the reign of the King Trisong Deutsen of Tibet. The two major contribution to the Traditional  
126 Tibetan Medicine came from India and China, and we can thus say that Traditional Tibetan Medicine is  
127 an integration of local Tibetan healing knowledge with Ayurveda and Chinese medicine. Elder Yuthog  
128 Yonten Gonpo represented Tibet and is thus considered the father of Traditional Tibetan Medicine. In  
129 the 12th - 13th centuries A.D., junior Yuthog Yonten Gonpo then composed a series of commentaries  
130 on the Four Tantras which further enriched the original texts.

131 When concerned with our body, the elements are further reduced to the three energies known as:  
132 Wind (*Lung*), Bile (*Tripa*) and Phlegm (*Beken*). In order to make the bridge with Western concepts easier,  
133 we have tentatively introduced a new terminology. It has to be noticed however that to grasp the full  
134 concept and meaning of these humours in their original context, one should consult specialized books  
135 or have a clear explanation from a Tibetan doctor.

- 136 • Phlegm (*Beken*) = Earth + Water = **Stability**

- 137 • Wind (Lung) = Wind = **Activity**
- 138 • Bile (Tripa) = Fire = **Transformation**

139 **Activity** is linked to movements (body and mind). It can be the nervous system activity, blood  
 140 flow, physical movement as well as movements of thoughts and emotions. **Transformation** is linked  
 141 with heat and clarity. Thus it is linked with metabolic processes as well as sense perception and mental  
 142 clarity. **Stability** is associated with structure. Thus, it is linked with bone and marrow, flesh and  
 143 liquids.

144 Each person possesses a specific *typology* from birth, that is to say a certain proportion of these three  
 145 energies. These energies slowly evolves with time and ageing depending on external (environment)  
 146 and internal (physiology and mind) conditions. For example, these energies manifest differently in  
 147 our body functions according to the four seasons, sun and moon activities (i.e. night and day). They  
 148 also varies according to our breathing pattern, cardiovascular condition and cell level functional states.  
 149 Pathologies reflect the fact that the three energies at a certain time are in a state of imbalance with  
 150 respect to the typology of the person. Thus, the typology is the reference point for the doctor, from  
 151 which any departure represents a state of imbalance. A few examples of imbalance are discussed  
 152 below. Usually, a mix of these condition appears as the energies are dependent on each other.

- 153 • Elevated **Activity** energy can manifest as anxiety, mental and physical hyperactivity, hearing  
 154 problems, dysautonomia, constipation, or breathing disorders. In physics, this is kinetic energy,
- 155 • Elevated **Transformation** energy tends to increase excitability, over joyful state or anger, tendency  
 156 towards hypertension and cardiovascular problems. In physics this is thermal energy,
- 157 • Elevated **Stability** energy result in obesity due to inactivity, dullness of mind or depression, flu  
 158 and immune system dysfunction. In physics this is potential energy.

159 The typology is the natural condition of the person and has to be determined in precise conditions  
 160 [20]. To each organ corresponds a predominance of an element and is thus also correlated with a  
 161 typology. There is a correspondence between the three energies and physiological, psychological,  
 162 energy functions and the senses/sense organs. These correspondences are helpful to cross the bridge  
 163 between Eastern and Western way of thinking and their essential correspondences are shown in Table  
 164 1.

165 The exceptional discovery by ancient physicians that the pulse wave characteristics can be mapped  
 166 to the three energies led to great progresses in the art of diagnosis. Pulse reading is one diagnosis  
 167 method among others such as urine, tongue or eyes analysis, but pulse diagnosis is the preferred  
 168 technique. Tibetan Medicine qualifies the pulse wave using a descriptive method with lots of analogies  
 169 of animal features and behaviors [20]. Certain qualities of the pulse are more prominent at certain  
 170 locations of the bodies: radial artery at the wrist, carotid artery, forehead arteries (especially at the  
 171 temporal sites), ankle arteries (such as lateral tarsal artery). In most cases, the radial artery is used by  
 172 the doctor. The traditional doctor position three fingers (index, middle and ring) alongside the artery  
 173 on each wrist to perform the diagnosis [4]. Figure 1 illustrates the finger position. The main challenge  
 174 that took us about ten years was to translate the Eastern concepts to something that could be used  
 175 using modern pulse sensing such as PPG. The Section 2.3 describes such a translation.

### 176 2.3. Western Pulse Wave Analysis: The Three Principles

177 It is nowadays well known from digital pulse wave analysis that the pulse waveform varies  
 178 depending on the body location and contains information about the organs and tissues 'visited' by  
 179 the travelling wave from the heart to the periphery [21,22]. Additionally, research started to appear  
 180 on the effect of mental processes and emotions using features contained in the pulse wave [23–25,76]  
 181 which correlates with the Tibetan Medicine approach shown in Table 1. The pulse wave description  
 182 of Table 1 can be explained according to the following three principles: **Rhythm** (Quick, slow, fast,  
 183 rolling, intermittent, (in)coherent), **Force** (Sunken, strong, empty, weak) and **Structure** (Rough, sharp).

**Table 1.** The Three Energies and their Western Correspondences

	<i>Activity (Lung)</i>	<i>Transformation (Tripa)</i>	<i>Stability (Beken)</i>
<i>Physiology</i>	Nervous system, Blood circulation, Lymphatic circulation, Tissue growth, Reproduction, Excretion	Digestion, Skin coloring	Immune system, Bone structure, Joint lubrication
<i>Psychology</i>	Cognition, Anxiety, Distress, Fear, Instability	Creativity, Intuition, Desire, Anger, Joy, Impulsiveness, Extraversion	Tolerance, Generosity, Tranquility, Introversion, Sensation, Feeling
<i>Sense/Organ</i>	Touch (Skin), Hearing (Ears)	Vision (Eyes)	Taste (Tongue), Smell (Nose)
<i>Energy</i>	Movement, Creation, Birth, Aging, Death	Transformation, Discrimination	Structure, Stability, Construction/Cohesion
<i>Pulse</i>	Rough, quick, empty, floating with intermittent beats	Sharp, rolling, strong, fast, overflowing with taut beats	Sunken, slow with very weak beats
<i>Elements</i>	Wind	Fire	Water and Earth

184 These three principles can be interpreted using signal processing terminologies with the following  
185 well known physiological interpretation:

- 186 • **Rhythm:** is the way the heart beat intervals are distributed, fast or slow and regular or irregular,  
187 mainly as a manifestation of the autonomic nervous system activity. This quality can be  
188 reasonably well described using heart rate, heart rate variability and breathing frequency analysis  
189 [26–28],
- 190 • **Force:** is the strength of the blood pressure felt under the fingers. Our PPG sensor capture the  
191 changes in blood oxygenated red cell volumes. These changes are also correlated with increased  
192 diameter at the systole and reduced diameter at diastole. The peak-to-peak amplitude of the PPG  
193 signal is thus an indirect measure of the blood pressure [30]. The modulation depth is also felt  
194 under the finger as a varying force. This modulation depth can be measured using well known  
195 techniques of signal modulation for example as used when measuring the periodic breathing in  
196 cardiac patients [31],
- 197 • **Structure:** are the details of the pressure wave shape felt under the fingers within each heart beat  
198 [32,33]. This behavior can be related to local vasoconstriction and/or dilation of the vessels as  
199 well as the arterial branching system which influences the location of the dicrotic notch as well  
200 as the amplitude of the dicrotic wave. It can be described using spectral entropies and location  
201 and bandwidth of the harmonics of the pulse wave [34,35].

202 Each of these qualities are further linked with quantitative measures and are summarized in the  
203 Table 2 and described in detail in the Section 4.1.1.

### 204 3. Methods

205 The paper presents two studies that were conducted in two different countries at different times.  
206 The first study was conducted in Italy between 2008 and 2010. The purpose of the study was to  
207 investigate the use of PPG signals as a tool for analyzing the pulse wave in a similar way as a Tibetan  
208 doctor does. The final aim was to develop a PPG-based classification of the three energies. The second

209 study was elaborated and realized at St Thomas Hospital in London in 2018 and was designed for the  
210 analysis of the pulse wave during periods of mental stress and relaxation. This second study served as  
211 a validation of the first study and additional analysis of the pulse wave harmonics.

### 212 3.1. Study 1: Digital Tibetan Pulse Reading

#### 213 3.1.1. Subjects

214 The subject pool consisted in 34 healthy participants (between 18 and 65 years of age, Male (13),  
215 Female (21)) engaged in studies at the Lama Tzong Khapa (Pomaia, Italy). Each participant received  
216 an identification code (ID) to preserve privacy, and data from each subject was kept anonymously. This  
217 ID is used to identify the doctor assessment sheets, pulse wave recordings and clinical measurements.  
218 Amongst the 34 subjects, we have the following fairly equally distributed typology: Activity (14),  
219 Transformation (8) and Stability (12). The inclusion criteria were as follows: Healthy subjects, having a  
220 relation with the Institute Lama Tzong Khapa and/or living in the residential area close by, and willing  
221 to be enrolled for the entire duration of this study. Physical and mental health was ascertained by  
222 the medical doctor and psychologist in charge of this project. Exclusion criteria were as follows:  
223 Hypertension level 2 (Systolic  $>160$  mmHg and/or Diastolic  $> 95$  mmHg without medication),  
224 Cardiovascular problems, Cancer, Diabetes, Breathing disorders, Mental illness such as schizophrenia,  
225 phobias, etc. Participants were given clinical advice after the study period, so that they are compensated  
226 for having participated in the study.

#### 227 3.1.2. Protocol

228 At the time of the enrolment, participants were asked to complete a questionnaire with their  
229 background relevant data, such as age, gender, height and weight. Data were anonymised. According  
230 to Tibetan Medicine, the typology assessment requires the medical doctor and the patient to respect  
231 certain rules such as: diet and behavior the day before the reading and the time of the day which  
232 is traditionally early morning or at dawn when the outer and inner elements are the most balanced.  
233 Due to logistical constrains and the number of participants, we had to adapt these traditional rules by  
234 relaxing the time of day. The Tibetan doctor can slightly adjust his pulse diagnosis according to the  
235 time of when the assessment is done. The participants were asked to behave calmly and avoid eating  
236 spicy food and excitants the day prior to the recording. Routine subject information were recorded  
237 and done continuously during the study. When the participants visited the Tibetan doctor, they had  
238 a Tibetan pulse reading, which was immediately followed by our pulse wave sensor recording as  
239 described in Section 3.1.3. The total recording session were 30 minutes: 15 minutes for the Tibetan  
240 finger pulse reading and 3 to 5 minutes for the pulse wave recording. We used such a short recording  
241 time in order to avoid muscle tension, movement and sweating artefacts as much as possible.

- 242 1. Physiological measurements: blood pressure was measured using a standard automatic  
243 commercial oscillometric system (Omron IA2): systolic, diastolic and heart rate were reported  
244 and recorded on the Tibetan Doctor File (see Section 3.1.3),
- 245 2. Self-report: participants were asked to regularly fill a multiple choice report on temporary  
246 non-compliance, exercise, personal meditation practice, diet, work or study load.

247 The Tibetan doctor file was prepared with the help of Dr. Tsewang Tamdin director of the Men  
248 Tsee Khang Institute (Dharamsala, India) and his collaborators, and Dr. Nida Chenagtsang (director of  
249 the International Academy for Traditional Tibetan Medicine). The file contained information about the  
250 pulse reading as well as any information that the doctor felt necessary and useful for this study such  
251 as sleep and environment/social problems. This was important as this study lasted for a long period  
252 of time.

### 253 3.1.3. Pulse Wave Recording and Preprocessing

254 The Tibetan pulse information can be measured sequentially with one finger at a time as well as  
 255 simultaneously with the three fingers as shown in Figure 1 and is traditionally assessed by the fingers'  
 256 feeling of the doctor, placed along the radial artery. Each fingertip, index, middle and ring, assess  
 257 different parts of the body: upper, middle and lower respectively. The index finger position is called  
 258 *Tson* and corresponds to the Activity energy, the middle finger is called *Kan* and corresponds to the  
 259 Transformation energy, and the ring finger is called *Chag* and corresponds to the Stability energy. The  
 260 index is always placed toward the thumb in a flat position so that each side of the fingertip can sense  
 261 the pulse wave. Left and right wrist pulse reading were taken.

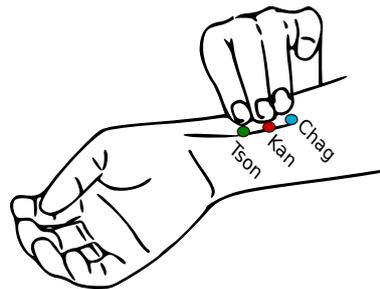


Figure 1. TTP doctor fingers position.

262 Measurements performed by our pulse wave recording system rely on the photoplethysmogram  
 263 (PPG). PPG is an optical non-invasive technology allowing the assessment of information related to  
 264 subcutaneous blood circulation. By illuminating a living tissue with a light source, PPG can measure  
 265 both arterial blood volume changes and blood content [36]. PPG measurements setups consist in  
 266 a light source, a photo-diode and the electronics for signal conditioning and filtering. Our optical  
 267 probe included a Light Emitting Diode (LED) emitting at  $940\text{ nm}$ , and a photodiode located  $1\text{ cm}$   
 268 apart. The electronic box includes an analog front-end (performing the continuous removal of ambient  
 269 light reaching the photo-diode, and acquiring the raw optical signals 50 times per second (sampling  
 270 frequency  $F_s = 50\text{ Hz}$ ) via a 24 bits Analog to Digital Converter). Raw optical signals were transmitted  
 271 via an USB cable to a laptop where data were displayed and stored for further processing. The PPG  
 272 signal was further upsampled to  $100\text{ Hz}$  for further analysis. Left and right wrist PPG signals were  
 273 recorded sequentially.

274 The sensor was made for single finger position measurement at a time and we used the index  
 275 finger position. The index finger location is the one proximal to the thumb as can be seen in Figure 1.  
 276 This location is particularly suited to analyze the properties related to the heart, lungs, small and large  
 277 intestines. The sensor was then positioned on the radial artery in a similar way a Tibetan doctor would  
 278 sense the pulse until the signal showed some stability as displayed on the screen of the computer  
 279 running the recording software. Once an optimal position was found, the sensor was maintained  
 280 with a wrist band during the duration of the recording. The PPG signals were analyzed off-line using  
 281 Matlab software (MathWorks, Inc., Natick, Massachusetts, United States).

282 The PPG signal contained a large DC offset, slow drift and movement artefacts despite the  
 283 instruction to the subject not to move the hand. Additionally, infrared sensor signals are known to  
 284 be more susceptible to deep tissue structure which act as noise sources. The preprocessing consists  
 285 in reducing these effects while keeping the main features of the pulse wave [37–39]. We used a  
 286 quadratic detrending followed by Principal Component Analysis in State Space (PCA-SS) [40,41] with  
 287 an additional frequency selection. The quadratic detrending was performed by removing a piecewise  
 288 2nd order polynomial fit to the data by block length of 10s. The PCA-SS was performed using a state  
 289 space embedding of the time series with an embedding dimension of  $m = 40$  and reconstruction lag

290  $l = 1$  sample [42]. We selected the first 8 components corresponding to the largest eigenvalues of the  
 291 trajectory matrix, thus reducing the amplitude of the high frequencies. We further selected from these  
 292 components those for which the spectral content had a maximum between 0.05Hz and 12Hz. This  
 293 choice of the frequency band corresponds to the physiologically plausible content of the pulse wave  
 294 main harmonics. We have further used a wavelet based noise reduction method [39,43] which finally  
 295 resulted in the preprocessed pulse wave signal  $DPW(t)$ .

### 296 3.2. Study 2: Mental Stress

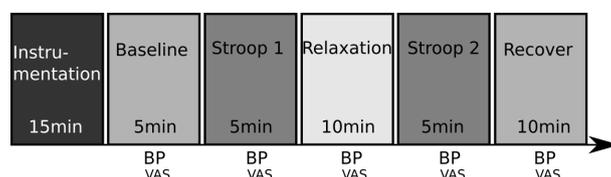
297 The mental stress protocol has been presented in details in [76] and is briefly reproduced here for  
 298 sake of ease of reading of this article.

#### 299 3.2.1. Subjects

300 Ten young, healthy participants (4 males and 6 females, age range 23 – 31 years, BMI range 17.6 –  
 301 33.8  $kg\ m^{-2}$ ) participated in the study at St Thomas' Hospital, London. All participants completed a  
 302 preliminary questionnaire about cardiovascular and mental health as well as any medications that  
 303 could influence the results. Exclusion criteria were: diagnosed hypertension, heart arrhythmias,  
 304 cognitive impairments. The NRES Committee London – Westminster approved the study IRAS ID  
 305 (168545) and REC reference (15/LO/1173). Participants could ask to withdraw or pause at any time  
 306 during the study. Subjects received an ID code to preserve anonymity.

#### 307 3.2.2. Protocol

308 The study protocol consisted of six phases as illustrated in Figure 2: instrumentation, baseline  
 309 measurements, Stroop test 1, relaxation phase, Stroop test 2, and recovery. Blood pressure (BP)  
 310 measurements and subjective stress assessment using a visual analog scale (VAS) were performed  
 311 before and after each protocol phase. The study was conducted in a dedicated room, isolated from  
 312 noise and other visual disturbances. The study phases are described next.



**Figure 2.** The six phases of the stress study. BP: Cuff blood pressure measurement; VAS: Visual analog scale for subjective stress assessment

313 During the *Instrumentation phase*, participants were provided with instructions on how to perform  
 314 the Stroop test and relaxation phases, and measurement instruments were attached (as explained in  
 315 the next section). As part of the routine clinical protocol at the hospital, participants completed the  
 316 Patient Health Questionnaire (PHQ-9) [45]. The *Baseline phase*, consisted of acquiring measurements  
 317 from participants whilst lying on a bed, head tilted up slightly, for five minutes whilst breathing  
 318 spontaneously. In the *Stroop test 1 phase*, stress was induced using the color word Stroop test [46]. This  
 319 test has been shown to provide reasonable results in terms of controlled induced stress and is widely  
 320 used in psychology research. The test was performed for five minutes while subjects were lying down  
 321 in the bed looking at a computer screen where the Stroop test was running. Participants were asked to  
 322 answer simple word-color-matching questions, at an increasingly faster pace as the test progressed  
 323 to compensate for the known adaptation process that participants undergo. In the *Relaxation phase*,  
 324 participants used the Resperate system (Resperate, Inc) for ten minutes, which is designed to lower  
 325 blood pressure through device-guided slow-paced breathing [47]. The breathing frequency range was  
 326 adjusted for each individual according to his comfort zone. In the *Stroop test 2 phase*, a second Stroop  
 327 test was conducted lasting five minutes. In the *Recovery phase*, participants relaxed, unaided and in  
 328 silence, for ten minutes whilst isolated by a curtain. Reference assessments of stress were obtained at

329 the end of each phase by asking participants two questions: (i) do you feel any pain or discomfort?;  
 330 and (ii) how would you rate your stress level? Subjects provided responses using a VAS ranging from 0  
 331 to 10. The VAS has been successfully used in many psychological studies and has the great advantage  
 332 of being very simple, especially during experiments when subjects are psychologically stressed [48].

### 333 3.2.3. Pulse Wave Recording and Preprocessing

334 PPG signals for pulse wave analysis were acquired using OH1 sensors (Polar Electro Oy) placed  
 335 on the lateral site of the of the left upper arm. The OH1 device complies with electro-magnetic radiation  
 336 safety, has been tested for skin biocompatibility. The OH1 sensor consists of a hexagonal arrangement  
 337 of green light sources and measures PPG signals at 135 Hz. The digitalized PPG signal was further  
 338 band passed filtered with a linear 4th order Butterworth filter with cutoff frequencies 0.2Hz - 15Hz.  
 339 The quality of the PPG signal was far superior to the one used in the first study and thus required less  
 340 preprocessing. The preprocessed PPG is called  $DPW(t)$ .

## 341 4. Results

### 342 4.1. Study 1: Digital Pulse Wave Classification

#### 343 4.1.1. Feature Extraction

344 The PPG signal processing flow is summarised in Figure 3. It contained information about the  
 345 **Rhythm, Force and Structure** as described in Table 2. The features were computed from both the heart  
 346 inter-beat intervals and the preprocessed PPG signal. All features were extracted using a rectangular  
 347 sliding window of 30s with 50% overlap.

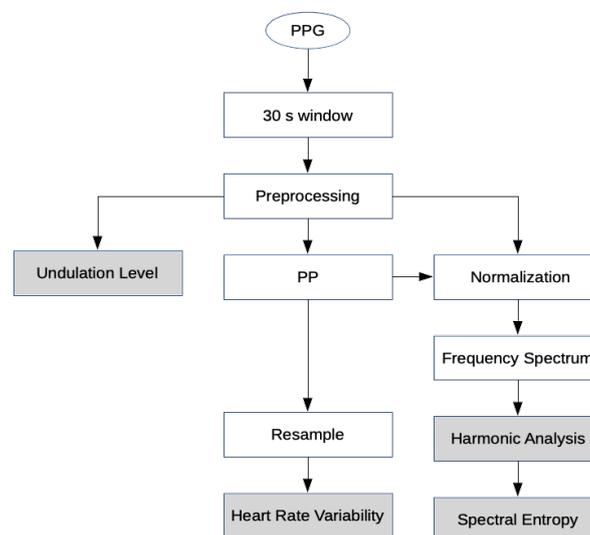


Figure 3. Pulse wave algorithm

348 **Heart rate and linear heart rate variability:** The PPG signal displayed fluctuations both in the  
 349 frequency and amplitude domains. The fluctuations in the frequency domain are linked with known  
 350 phenomena originating from the neuro-cardiovascular system such as respiration or emotions [49]. A  
 351 peak detection algorithm was used to detect each diastolic point  $P(k)$  from  $DPW(t)$  at the heart beat  
 352  $k$ , and then derive the peak to peak intervals  $PP(k) = P(k) - P(k - 1)$ . We have used a technique to  
 353 automatically detect and eventually correct non-physiological  $PP$  intervals or ectopic beats [50]. The  
 354 fluctuations of these  $PP$  intervals have been shown to be similar to the electrocardiogram peak R-wave

intervals variability [51] for healthy subjects at rest and are thus suitable for our analysis. The interbeat intervals  $PP$  were quantified using their average value and variability: 1) the average pulse  $PPm$ , 2) the variance  $Rv$ , 3) the normalised Low Frequency (LF) Power ( $LFn$ : power in 0.04 Hz to 0.15 Hz) and 4) the normalised High Frequency (HF) Power ( $HFn$ : power in 0.15 Hz to 0.4 Hz). The normalisation of the  $LF$  and  $HF$  was performed by dividing them by the total power of the DC free PPG segment under analysis. Breathing is an important modulation factor both in the PPG amplitude and frequency, i.e. the so-called Respiratory Sinus Arrhythmia (RSA). The RSA is usually measured from the  $PP$  interval in the frequency band from 0.1 Hz to 0.25 Hz when the person is in a calm spontaneous breathing state as typically the case when visiting a doctor. The breathing frequency  $BF$  was thus estimated as the frequency corresponding to the maximum frequency spectrum peak in this band.

**Harmonic analysis:** The pulse wave contains a rich spectrum which is essentially related to the different functions of the heart, vascular, autonomic nervous and respiratory systems, as well as other components from the different organs visited by this wave. In order to isolate the vascular part contained in the shape of each heart beat without the 'interference' of the heart beat variability, we have implemented a technique to normalise each heart beat pulse wave so that they have the same peak to peak amplitude of 1 and same duration of 1s [30]. From the knowledge of the peak wave instant  $P(k)$ , the procedure was performed in three steps: 1) to detrend each heart beat so that each diastolic points have zero amplitude, 2) to resample each heart beat wave using a linear interpolation method, and 3) to normalise each heart beat to an amplitude of 1. Once this procedure is performed on each heart beat pulse wave, we performed a spectral analysis and derive the power spectral density  $P(\omega)$ . We have used a Welch method to estimate the power spectrum density. The number of harmonics  $Nb^H$  contained in  $P(\omega)$ , their amplitudes  $A_k^H$ , locations  $f_k^H$ , phases  $\phi_k^H$  and bandwidths  $\Delta_k^H$ ,  $k = 1, \dots, Nb^H$ , were the main used spectral features. The fundamental frequency  $f_0^H$  corresponds to the heart beat average frequency: i.e. the heart rate. The bandwidth  $\Delta_k^H$  of a signal  $x$ , centred around the frequency  $f_k^H$ , was computed as follows:

$$\Delta_k^H = \sqrt{\int_{\Omega} \tilde{P}(\omega) (\omega - 2\pi f_k^H)^2 d\omega} \quad (1)$$

where  $\Omega$  is the bandwidth of interest and  $\tilde{P}(\omega)$  is an estimation of the energy-normalised power spectral density of  $DPW(t)$ :  $\tilde{P}(\omega) = P(\omega) / \int_{\Omega} P(\omega) d\omega$ . The bandwidth of the fundamental frequency is  $BW = \Delta_0^H$ . The parameter  $BW$  is thus proportional to the variance of the  $PP$  intervals, while  $\Delta_{k>0}^H$  measure the variability of the smaller waves composing the heart pulse wave  $DPW(t)$ . The frequencies  $f_{k>0}^H$  and phases  $\phi_{k>0}^H$  are modulated by the arterio-venous tree properties such as branching (anatomy) and wall (i.e. endothelium) structures. These aspects are known to influence the shape of the pulse wave such as the crest time, dicrotic notch location and amplitude and dicrotic wave amplitude. Thus the frequency domain analysis is an other way to measure the influence of the anatomical, functional and local nervous system properties of the vessels. Mathematically, the Fourier transform of a signal contains exactly the same information as the time domain which further justify the use of the frequency analysis of the pulse wave. This harmonic frequency analysis has been studied by Chinese medical doctors [35,52,53] and scientists since years and are known to correlate with organ function as well. The amplitude of the PPG signal is usually not calibrated thus limiting the use of the absolute amplitude or power of such signal. However, the relative power using ratios of harmonics is relevant and indeed contains known health information [35,53–55]. In our work we will limit the number of harmonics to  $Nb^H = 4$  and we use the harmonic power ratios as features:  $H_{i,j} = A_i^H / A_j^H$  for  $i, j = 0, \dots, Nb^H$  with  $j > i$ . One of the main advantage of using the harmonic analysis is that it is more easy and robust to compute than time domain parameters in the presence of noise.

**Order analysis:** A well known measure of regularity or order is entropy. The regularity of the pulse wave shape is relevant for our study and can be quantified using spectral entropy. Typically, narrow

**Table 2.** Digital Pulse Wave Qualities and Features

DPW Qualities	DPW Features
Rhythm	Normalized PP Low Frequency ( $LFn$ )
	Normalized PP High Frequency ( $HFn$ )
	PP Variance ( $Rv$ )
	PP Average ( $Rm$ )
	Breathing Frequency ( $BF$ )
Force	Undulation Level ( $UL$ )
	Normalized Bandwidth ( $BW$ )
Structure	Normalised Spectral Entropy ( $SE$ )
	Harmonic Ratios ( $H_{i,j}$ )

400 frequency band signals will have a small entropy as compared to broadband signals. The normalised  
 401 Spectral Entropy ( $SE$ ) in  $\Omega$  is defined as:

$$SE = - \left( \int_{\Omega} \tilde{P}(\omega) \log(\tilde{P}(\omega)) d\omega \right) / \Omega \quad (2)$$

402 The regularity of the pulse wave in the time domain is characterised in first approximation by an  
 403 Undulation Level ( $UL$ ). The pulse wave is indeed modulated in amplitude due to various factors such  
 404 as respiration, the autonomous nervous system or heart pacemaker dysrhythmias. The  $UL$  is also well  
 405 adapted to measure the depth of modulation during RSA, and thus the influences of the respiration on  
 406 the pulse wave amplitude fluctuations. The concept of the modulation depth used in this context is  
 407 borrowed from the domain of telecommunication where the modulation depth is defined from the  
 408 following equation:

$$x(t) = K(1 + UL \cos(\omega_{AM}t)) \cos(\omega_{FM}t) + n(t) \quad (3)$$

409 where  $\omega_{AM,FM}$  is the angular frequency of the (Amplitude,Frequency) modulated part of  $x(t)$  and  $n(t)$   
 410 is some zero mean noise. The modulation depth  $UL$  varies between 0 and 1. The estimation of  $UL$  can  
 411 be performed using demodulation methods.

#### 412 4.1.2. Features Selection and classification

413 **Features Selection:** In Table 2, the  $9 + Nb^H(Nb^H)/2$  features are summarized. In order to condition our  
 414 feature space in the best way, we have proceeded to a feature selection procedure. A method developed

415 by Peng *et al.* [56] called mRMR (minimum Redundancy Maximum Relevance Feature Selection) has  
 416 been chosen and applied to our feature set. The mRMR method need the feature values to be converted  
 417 to symbols. In order to do this, we have quantized the features using a standard quantization method  
 418 on 5 bits. Each quantized level is then assigned an integer value, which together with the classes are  
 419 the input to mRMR. The result of mRMR is summarized as follows where the features have to be read  
 420 from left to right and are in order of decreasing minimum redundancy. Progressively grouped features  
 421 from left to right also have decreasing minimum redundancy.

$$\mathbf{Rv} \rightarrow \mathbf{SE} \rightarrow \mathbf{H}_{2,4} \rightarrow \mathbf{H}_{1,2} \rightarrow UL \rightarrow Rm$$

422 Due to the limited number of subjects and  $DPW(t)$  signal duration, the number of feature points  
 423 is quite limited. In order to improve the robustness of the classification, we have decided to make  
 424 use of surrogates of the features. The way to produce high quality surrogates is explained in detail  
 425 in [59]. Using Schreiber method as a first step, we have improved the surrogate by making them  
 426 probability density function invariant as well. This second step guarantees that the surrogates' pdfs are  
 427 preserved. This surrogate method is further used in this work to test the performance of the classifier  
 428 by using Monte Carlo simulations of the classifier (see Section 4.1.2). In order to further ease the work  
 429 of the classifier, we have performed a Principal Component Analysis in State Space (PCA-SS). The  
 430 parameters for the nonlinear embedding are: dimension  $m = 4$  and lag  $l = 1$ . The first 4 Principal  
 431 Components have been retained.

432 **Classification of the Three Energies:** As explained in Section 2.2 each individual possesses a dominant  
 433 Typology and sometimes manifest the other two in different proportions. The classification of the  
 434 typology must thereby take this into account, which impose a classifier with continuous output  
 435 values rather than binary. Fuzzy classifiers thus seems the most appropriate. Amongst the fuzzy  
 436 classifiers, a special type of Artificial Neural Networks called Quantum Neural Networks (QNN)  
 437 have shown promising properties [60]. These QNNs are a class of feedforward neural networks  
 438 which can handle uncertain inputs and have a very flexible structure of hidden nonlinear layer in  
 439 the form of a superimposition of sigmoidal functions with flexible amplitude, slope and shift. The  
 440 hidden layer can focus or relax its *data representation* by concentrating or spreading around regions  
 441 of certainties or uncertainties of the feature space more like a quantum wave function localize or  
 442 spread out around certain or uncertain states bearing some resemblance to quantum systems and  
 443 networks. Forty surrogate PCA-SS components are generated to train the QNN with one hundred  
 444 batch iteration. We have validated the trained network using additional independent surrogated data.  
 445 These validation surrogates are then used to compute the Receiver Operating Curves (ROC) of the  
 446 QNN in a Monte Carlo simulation and an optimal threshold is found using the Youden index [73]. The  
 447 confusion matrix is then computed from these Monte Carlo simulations at the Youden optimal point.  
 448 The confusion matrix  $C$  of the QNN is given as:

$$C = \begin{pmatrix} C_{1;1} & C_{1;2} \\ C_{2;1} & C_{2;2} \end{pmatrix} \quad (4)$$

449 The diagonal entries  $C_{1(2);1(2)}$  are related to the percent of samples which are correctly classified  
 450 in the respective Class 1(2). The off-diagonal entries in  $C$  have the following meaning:  $C_{1(2);2(1)}$  is the  
 451 percentage of samples from Class 1(2) which are classified as Class 2(1). Thus we look for maximizing  
 452 the diagonal elements, while minimizing the off diagonal elements, ideally 100% and 0% respectively.

453 The classification is performed in two steps using two classifiers: Step 1: Separation of *Activity*  
 454 from *Transformation* and *Stability* and Step 2: Separation of *Transformation* from *Stability*. This has  
 455 proved to be the best strategy to maximize the classifier performances. The first classifier is called  
 456 QNN First Pass:  $QNN^{FP}$ . By assumption we assign Class 1 to *Activity*, while Class 2 is the union of

457 *Transformation and Stability: (Transformation - Stability)*. The confusion matrix at the optimal ROC point  
 458  $C^{FP}$  of the  $QNN^{FP}$  is given as:

$$C^{FP} = \begin{pmatrix} C_{1,1}^{FP} = 85(2) & C_{1,2}^{FP} = 15(2) \\ C_{2,1}^{FP} = 28(2) & C_{2,2}^{FP} = 72(2) \end{pmatrix} \quad (5)$$

459 The diagonal entries in  $C^{FP}$  signifies that  $85\% \pm 2\%$  of the samples are correctly classified in the  
 460 *Activity Class* while and  $72\% \pm 2\%$  are correctly classified in (*Transformation - Stability*). The off-diagonal  
 461 entries in  $C^{FP}$  have the following meaning:  $C_{1,2}^{FP}$  is the percentage of samples from *Activity* which are  
 462 miss classified as belonging to (*Transformation - Stability*), while  $C_{2,1}^{FP}$  is just the opposite. The second  
 463 classifier is called QNN Second Pass:  $QNN^{SP}$ . By assumption we assign Class 1 to *Transformation*,  
 464 while Class 2 is *Stability*. The confusion matrix at the optimal ROC point  $C^{SP}$  of the  $QNN^{SP}$  is given as:

$$C^{SP} = \begin{pmatrix} C_{1,1}^{SP} = 90(2) & C_{1,2}^{SP} = 10(2) \\ C_{2,1}^{SP} = 14(2) & C_{2,2}^{SP} = 86(2) \end{pmatrix} \quad (6)$$

465 The diagonal entries in  $C^{SP}$  signifies that  $90\% \pm 2\%$  of the samples are correctly classified as  
 466 *Transformation Class* and  $86\% \pm 2\%$  are correctly classified as *Stability*. The off-diagonal entries in  $C^{FP}$   
 467 have the following meaning:  $C_{1,2}^{FP}$  is the percentage of samples from *Transformation* which are miss  
 468 classified as belonging to *Stability*, while  $C_{2,1}^{FP}$  is just the opposite.

#### 469 4.2. Study 2: Mental Stress

470 Distributions of parameters across subjects were summarized using the median and inter-quartile  
 471 range in box plots. Significant differences between parameters were identified using paired *t*-Tests  
 472 (significance level  $\alpha = 0.05$ ).

##### 473 4.2.1. The Three Energies

474 Mental stress is particularly interesting to study in our epoch as it is a common health  
 475 issue, associated with increased cardiovascular mortality and morbidity [67]. It also has a great  
 476 impact on both professional and private lives as it has been associated with negative mood [68],  
 477 immunosuppression [69], impacts on physical and mental health and increased occurrence of illnesses  
 478 [70]. Several stress management interventions have been shown to be effective in both the workplace  
 479 and personal settings [71]. This provides great incentive for developing techniques to recognize  
 480 elevated stress levels, prompting interventions to reduce stress levels, and potentially improve  
 481 health. According to TTM, stress is primarily an Activity disorder associated with Transformation  
 482 imbalance and manifest primarily in the nervous system with high impact on blood pressure and the  
 483 vascular system. In a previous study, we have shown that time domain pulse wave analysis can be a  
 484 complimentary tool for the analysis of mental stress specifically the rise time of the pulse wave and the  
 485 diastolic time [25,76].

**Table 4.** Statistics for the three energies

<b>Transformation</b>	$p_{1,2} = 1.16 \cdot 10^{-6}; p_{2,3} = 5.43 \cdot 10^{-4}; p_{2,4} = 5.79 \cdot 10^{-4}; p_{2,5} = 2.57 \cdot 10^{-5}$
<b>Activity</b>	$p_{1,2} = 9.45 \cdot 10^{-5}; p_{2,3} = 1.14 \cdot 10^{-3}; p_{2,4} = 2.77 \cdot 10^{-3}; p_{2,5} = 1.62 \cdot 10^{-4}$
<b>Stability</b>	$p_{1,3} = 2.36 \cdot 10^{-2}; p_{3,4} = 1.33 \cdot 10^{-2}; p_{3,5} = 2.50 \cdot 10^{-2}$

486 Our mental stress study has confirmed this as shown in Figure 4 where the three energies have  
 487 been computed according to the methodology presented above in each phase of the protocol for  
 488 the 10 participants. Activity and Transformation increased significantly from baseline to Stroop 1,  
 489 while Stability stayed almost unchanged. During the breathing relaxation period, Stability increased

490 significantly with an associated large dispersion across subjects, while the Activity and Transformation  
 491 decreased significantly back to baseline. Stroop 2 manifested in a slight nonsignificant increase of  
 492 Activity and Transformation with respect to baseline, while Stability decreased significantly from  
 493 relaxation showing a reduced capacity to cope with stress. During the recovery period, Activity,  
 494 Transformation and Stability came back to baseline with a noteworthy low dispersion of Stability. The  
 495 statistical analysis is summarized in Table 4 where the significance value  $p_{m,n}$  is displayed with the  
 496 following index convention:  $n, m = 1$  for Baseline,  $n, m = 2$  for Stroop 1,  $n, m = 3$  for Relaxation,  
 497  $n, m = 4$  for Stroop 2 and  $n, m = 5$  for Recovery.

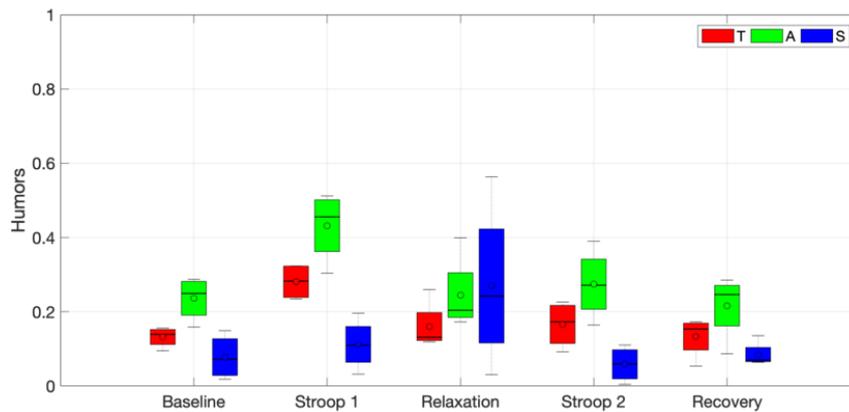


Figure 4. The three energies during the mental stress protocol

#### 498 4.2.2. Harmonics

499 It has been suggested in [76] that the complexity of the pulse wave contour could be a further  
 500 parameter able to discriminate the states of stress. In this continuation, the complexity of a wave  
 501 can be quantified by its fourier spectrum, and thus its harmonic content if this wave is periodic or  
 502 quasi-periodic. As it was introduced in Section 4.1.1, the harmonic analysis proved to be a very  
 503 efficient way to extract pulse wave structure parameters [35,53,72]. Additionally, it has been shown in  
 504 many publications that this harmonic analysis is relevant for detecting pathological conditions such  
 505 as coronary artery disease, hypertension, myocardial ischemia and decrease of heart function in type  
 506 II diabetes patients. In order to further assess this hypothesis, we have analyzed the behavior of the  
 507 harmonic ratios  $H_{i,j}$  as defined in Section 4.1.1. Figure 5 shows the behavior of  $H_{i,j}$  across the stress  
 508 protocol. The statistical analysis is summarized in Table 5 with the same convention as above.

Table 5. Statistics for the harmonic ratios

$H_{1,2}$	$p_{2,3} = 2.08 \cdot 10^{-3}; p_{2,4} = 1.92 \cdot 10^{-2}$
$H_{1,3}$	$p_{1,5} = 3.45 \cdot 10^{-2}$
$H_{2,4}$	$p_{2,3} = 3.38 \cdot 10^{-2}; p_{2,4} = 1.29 \cdot 10^{-2}$
$H_{3,4}$	$p_{1,5} = 2.52 \cdot 10^{-2}$

509 Globally, we can observe that the harmonic ratios are changing during the various phases of  
 510 the protocol, confirming that they contain information according to the stress/relaxation level as  
 511 manifested by the vascular system. The second striking observation is a clear separation between the  
 512 low and high harmonic ratios as indicated in Figure 5 by the red and green colored bars respectively.  
 513 This indicate that the higher the harmonic frequencies the less differences between their amplitude.

514 Visual inspection indicates that the relaxation procedure affect mostly  $H_{1,2}$  and  $H_{2,4}$  and that mental  
 515 stress affects  $H_{2,4}$  primarily. The highest harmonic ratio  $H_{3,4}$  tend to decrease during the protocol.  
 516 Statistically speaking,  $H_{2,4}$  and  $H_{2,4}$  are thus good candidates for monitoring stress and relaxation. It  
 517 was also selected by our feature selection algorithm in Section 4.1.1.

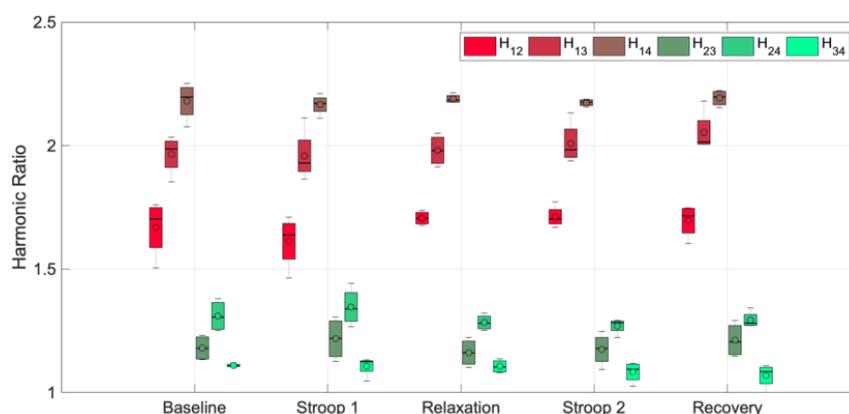


Figure 5. The harmonic ratios during the mental stress protocol

## 518 5. Discussion

519 We have developed a methodology based on photoplethysmogram pulse wave analysis to  
 520 estimate the three fundamental energies of Traditional Tibetan Medicine. Results of our method are  
 521 promising and certainly need further research and improvement. This methodology has further been  
 522 applied to a laboratory stress/relaxation procedure and confirmed the potential of this method for  
 523 monitoring stress and relaxation. These results are especially interesting due to the use of pulse wave  
 524 analysis in conjunction to autonomic nervous system parameters such as heart rate and heart rate  
 525 variability.

526 Harmonic ratios have been studied in [35,53] in relationship with the Chinese medicine framework  
 527 and the organs function. It would be premature to draw conclusions from our study in relation to  
 528 the element theory, but we can however mention that the harmonic ratios  $H_{1,2}$  and  $H_{2,4}$  could indeed  
 529 be linked to the relationship between the heart and the lungs, and between the lungs and smaller  
 530 organs involved in digestion respectively [35]. Also, the harmonic analysis can be a very useful tool to  
 531 assess mental stress [76] as it does not requires the task of detecting the various pulse wave features  
 532 which can prove to be difficult in some situations such as slight micro-movements, skin condition and  
 533 perfusion.

534 The study of the pulse wave changes in the context of stress can be extended to emotions as it is  
 535 well known that they also modulate the neuro-cardiovascular system [74].

## 536 6. Conclusion

537 When used in condition of no motion and at appropriate place such as the finger or the arm,  
 538 photoplethysmography and pulse wave analysis have proved to provide relevant information to assess  
 539 mental stress and relaxation. The newly developed algorithm using the ancient principles of the three  
 540 energies have shown promising results. Furthermore, harmonic analysis of the pulse wave has shown  
 541 to be a valuable tool for the analysis of the pulse wave in the context of stress. Connection with ancient  
 542 knowledge of pulse reading has proved to be of great value and encourage us to pursue this study  
 543 of ancient medicine. Finally, the inherent holistic views of these ancient philosophies and medicinal  
 544 systems, makes them an ideal framework to study the impact of the environment on the human body  
 545 and mind.

## 546 7. Patents

547 A patent named: A method and system for determining the state of a person on the classification  
548 of the three humours, has been filed under EP2874539 and WO 2014/012839.

549 **Author Contributions:** Conceptualization, Patrick Celka; methodology, Patrick Celka and Marina Bruce;   
550 software, Patrick Celka; Tibetan pulse diagnosis, Lobsang Samten; formal analysis, Patrick Celka; clinical analysis,   
551 Abdullah Alabdulgader; environmental impact analysis, Abdullah Alabdulgader; investigation, Marina Bruce   
552 and Patrick Celka; writing–original draft preparation, Patrick Celka, Abdullah Alabdulgader; writing–review and   
553 editing, Patrick Celka, Abdullah Alabdulgader; supervision, Marina Bruce; project administration, Marina Bruce

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565 declare no conflict of interests. Other authors declare no conflict of interests.

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