Potential physiological stress biomarkers in human sweat

1st Federica Gioia Research center "E. Piaggio" University of Pisa, Pisa, Italy federica.gioia@phd.unipi.it

4th Matyas Ripszam

Dip. di Chimica e Chimica Industriale

University of Pisa, Pisa, Italy
matyas.ripszam@dcci.unipi.it

7th Alberto Greco Research center "E. Piaggio" University of Pisa, Pisa, Italy alberto.greco@unipi.it 2nd Alejandro Luis Callara *Research center "E. Piaggio" University of Pisa*, Pisa, Italy alejandro.callara@ing.unipi.it

5th Fabio Di Francesco Dip. di Chimica e Chimica Industriale University of Pisa, Pisa, Italy fabio.difrancesco@unipi.it

3rd Tobias Bruderer

Dip. di Chimica e Chimica Industriale

University of Pisa, Pisa, Italy
tobias.bruderer@dcci.unipi.it

6th Enzo Pasquale Scilingo Research center "E. Piaggio" University of Pisa, Pisa, Italy e.scilingo@ing.unipi.it

Abstract—Emotional sweating occurs in response to affective stimuli like fear, anxiety, or stress and is more evident in specific parts of the body such as the palms, soles, and axillae. During emotional sweating, humans release many volatile organic compounds (VOCs) that could play a crucial role as possible communicative signals of specific emotions. In this preliminary study, we investigated seven volatiles belonging to the chemical class of acids and released from the armpit as possible stress biomarkers. To this aim, we processed sweat VOCs and physiological stress correlates such as heart rate variability (HRV), electrodermal activity, and thermal imaging during a Stroop color-word test. Particularly, we modelled the variability of well-known stress markers extracted from the physiological signals as a function of the acid VOCs by means of LASSO regression. LASSO results revealed that the dodecanoic acid was the only selected regressor and it was able to significantly explain more than 64% of the variance of both the mean temperature of the tip of the nose (p=0.018, R^2 =0.64) and of the mean HRV (p=0.011, R^2 =0.67). Although preliminary, our results suggest that dodecanoic acid could be a marker of the sympathetic nervous system response to stress stimuli, opening for the detection of new biomarkers of

Index Terms—Emotional sweat, stress correlate volatiles, physiological stress correlates, LASSO

I. INTRODUCTION

Although sweat gland activity is commonly associated with thermoregulation, maintaining the body temperature within a certain range is not the only reason why our sweat glands change their activity. The so-called emotional sweating represents a physical body response to psychological stimuli (e.g.,

The research leading to these results has received partial funding from the Italian Ministry of Education and Research (MIUR) in the framework of the CrossLab project (Departments of Excellence). This research has received partial funding from European Union Horizon 2020 Programme under grant agreement n 824153 of the project 'POTION-Promoting Social Interaction through Emotional Body Odours'.

stress, anxiety or fear), and it occurs over the whole body surface with the main effect on palms, soles, and armpits [1], [2]. Particularly, the axillae regions are characterized by the presence of two different types of sweat glands: eccrine and apocrine glands. The eccrine are the largest group of sweat glands, distributed over almost the whole body surface and secrete a watery fluid mainly related to thermoregulatory functions. Instead, the apocrine glands are concentrated only in a few specific human body regions such as the axillary, mammary, perineal, and genital areas, and are known to be responsive to emotions as well as to psychological stress [3], [4].

During perspiration, humans release several different gases from the skin such as volatile organic compounds (VOCs) of sweat [4]. Over hundreds of such chemical volatiles are secreted by the apocrine sweat glands and are the non smelling precursors of the odoriferous substances emanating from the underarm when bacterial enzymes transform them. In the literature, specific sweat compounds or patterns of volatiles have been examined as a possible communicative signal for a specific emotion (chemosignals) [5]. Indeed, emotional sweating changes its characteristics based on the emotion felt by the human [6], [7]. In this context, it has been suggested that specific chemical markers may be released from the skin because of stress [8]. However, only a few studies have investigated the chemical composition of volatiles released during stress reporting acids as potentially associated with stress [4], [8].

The number of studies involving the chemical analysis of emotional sweat is low and extremely challenging due to the difficulties in sweat sampling and processing and the need for objective emotion elicitation. State-of-the-art methods include expensive devices such as comprehensive two-dimensional gas chromatography time-of-flight mass spectrometry (GCxGC-Q-TOF) that allow the detection of hundreds of compounds in complex samples. Such a method allows on the one hand to detect a wide range of chemical classes at low concentrations as potential human signaling molecules. On the other, with the capability to detect so many different compounds, it is very important, but not always possible, to control the chemical background. In fact, there are plenty of potential confounding factors such as smoking, food, alcohol, as well as the use of detergents, soaps, deodorants, and other cosmetic products. Also eliciting and measuring stress objectively is a complex field of research. In clinical practice, stress is commonly assessed through psychometric tests or self-assessed levels. However, these methods have been strongly discussed because of their subjective nature, which can lead to unreliable results. To overcome these issues, many studies have analysed physiological correlates of the autonomic nervous system (ANS) in response to elicited stress [9], [10]. More specifically, stressful stimuli trigger the activation of the sympathetic nervous system (SNS), which temporarily dominates over the parasympathetic nervous system (PNS) and leads to changes in several physiological signals, e.g., electrocardiogram (ECG), electrodermal activity (EDA), thermal signals, sweat secretion, etc.

A recent study has combined the analysis of VOCs collected from sweat during stress conditions and physiological ANS correlates [11]. Results have suggested that compounds in human sweat can be potentially related to stress biomarkers. In this context, however, the integration of sweat compound analysis with well-established ANS correlates of stress is still to be fully investigated.

In this preliminary study, we investigated the relationship between ANS correlates of stress and VOCs in human sweat. To this aim, we acquired physiological signals (i.e., ECG, EDA, thermal images of the face) and sweat samples of 10 healthy subjects during a Stroop color-word test (a stress elicitation method). First, we processed physiological signals to assess stress reaction and thus validate the efficacy of our experimental protocol in a more objective way. Furthermore, we modelled stress-related features with a linear combination of the VOCs belonging to the chemical class of acids. In particular, we applied a LASSO regression to identify the best subset of VOCs explaining the ANS response and thus revealing the sweat compounds related to the physiological stress reaction.

II. MATERIALS AND METHODS

A. Subject recruitment

Ten healthy volunteers (7 females, age = 27 ± 3 years) were recruited for this preliminary study. Each participant signed informed consent for participating in the study. The experiment was approved by the "Bioethics Committee of the University of Pisa" (n. 15/2019). Subjects were asked not to drink coffee and not to eat within the three hours before the experiment. A sandwich was provided two hours before the measurement to minimize confounders related to

food. Moreover, subjects were asked to shave their armpits the evening before the experiment, and they were provided with shampoo and deodorant to use from the day before the experiment. In addition, they were asked to avoid strong flavours and spices, garlic, onions, alcohol, smoking and drugs starting from one day before the experiment. Finally, they were asked to wash their upper body cloths with a provided detergent. All the participants complied with these guidelines.

B. Experimental protocol

The timeline of the experiment is reported in Fig. 1. It consisted of two resting sessions interleaved by a stress task session.



Fig. 1. Protocol Timeline. PAD = armpit and back sweat sampling time; dashed line = not timed break for PAD changing; PS = perceived stress level assessment.

During the resting sessions, subjects were asked to relax with their eyes open for 10 minutes. On the other hand, the task session was designed to elicit mental stress by means of the Stroop Test [12]. This session was divided into three 3-minute long subsessions: one initial resting subsession (*RESTpre*), a Stroop Test (*Stroop*), and a recovery subsession (*RESTpost*). During the *Stroop* task, incongruent tint-content words were displayed every 2 seconds at the center of a tablet's screen, while subjects were required to answer according to word's tint.

To standardize the conditions among subjects and limit the interactions with the experimenter, the whole protocol was driven by an *ad-hoc* Android application developed for the study and installed on a tablet. During the *Stroop*, the application showed a score-counter, which indicated the number of subsequent successes, and which turned back to zero after any incorrect or missed answer. In addition, the passage of time was marked throughout the task by a background ticking and the subject was notified with an annoying acoustic buzzer any time he/she gave a wrong/missed answer. Before and after the stroop task, subjects reported their self-perceived level of stress on a likert scale from 0 (not at all) to 10 (very stressed).

Finally, the room temperature and humidity were monitored throughout the experiment by the EXTECH RH550 Humidity-Temperature Chart Recorder at a rate of 0.5 Hz to ensure a stable and comfortable environment. Indeed, during each experiment, temperature and humidity were always constant and in the range of 22°C to 28°C and 40% to 56%, respectively. Once the subjects arrived in the laboratory, they had 10 min to acclimatize before starting the experiment.

C. Data acquisition and processing

We acquired both chemical data and physiological signals during the experiment. Additionally, self-reported stress scores were recorded before and after the *Stroop* session.

1) Chemical data: We collected sweat samples during the three sessions as shown in Fig. 1. This experimental design allows shortening the duration for the reference samples (REST task, PAD1-REST) and to investigate if the stress volatiles are released more rapidly (first 10 min, PAD2-STRESS), delayed (follow-up 10 min, PAD3-REST), or intermediately by calculating the average ("PAD-MeanStress"). In addition, we collected field blanks for each participant, which were exposed to ambient air and treated in the same manner as the sweat samples. Sweat samples were collected from the armpit and upper back with pads (Dermatess), that were precleaned by bake-out at 150°C. After each session, the pads were stored at -80°C until extraction of the volatiles. The extraction and preconcentration into sorbent tubes were carried out in a heated closed chamber with high-purity surfaces. Separation was done with two subsequent gas chromatography columns (GCxGC), with a flow modulator for synchronization between columns, and analysis with a quadrupole-time-offlight (Q-TOF) mass spectrometer. After analysis, the raw data files are automatically transformed into images using GC Image. These images are the graphical representations of the GCxGC chromatograms with first- and second dimension retention times on the x- and y-axes, respectively, and the intensity values on the z-axis are converted to a color scale. A composite chromatogram was generated with an automated peak alignment algorithm (i.e. from 40 individual images for the armpit sample). We applied a two-fold approach where we identified the chemicals first automatically and then verified manually. We filtered by the following criteria: spectral similarity (> 750%), linear retention indexing (± 50 LRI units), and accurate mass matching of key fragment ions (molecular ions or characteristic ions). The accurate masses of these characteristic ions were used to automatically generate new images of selected ion chromatograms (SICs). These peak templates were applied to each SIC to extract the peak volumes at pre-defined retention time windows. This way, the response of all previously identified chemicals could be monitored very selectively by their fragments' accurate masses in a fully automated way. Templates and their respective images with appropriate spectral filters were generated for 60 chemical subclasses and applied to all samples (40 * 60 = 2400 images). Data pretreatment included correction for negative peak volumes due to the automatic baseline correction of GC Image. All values were shifted into the positive by the addition of the minimal peak volume. Peak volumes were adjusted by sweat weight for each pad (mg) by samplewise normalization (divided by weight and multiplied by the mean sweat weight across samples). We were able to detect a large number of 130 volatile compounds belonging to eight chemical classes (acids, alcohols, aldehydes, esters, furans, Oheterocycles, ketones, nitrogen-containing compounds, eight others, and five unknowns). We focused our initial analysis on the detected acids because acids have been previously suggested as sweat volatiles associated with stress [4], [8]. The detected seven acids were two carboxylic acids (acetic acid, propionic acid), four fatty acids (hexa-, octa-, dec-, dodecanoic acid), and diisopropyl adipate.

2) Physiological data: We acquired multiple physiological signals, i.e. thermal signal from the nose, ECG and EDA, during the entire duration of the experiment. Each recorded physiological signal was analysed to extract state-of-the-art features able to characterize the ANS dynamics and assess the stress state.

Thermal imaging. The temperature of the skin is mainly modulated by two ANS-driven phenomena, i.e., redistribution of blood in the subcutaneous vessels and perspiration. Indeed, thermal variations of specific facial regions have been analysed in relation to mental states and emotional stimuli. Among these regions, the nose has proven to be a very reliable stress marker [13]–[16]. Therefore, we monitored the temperature variations of the tip of the nose using a FLIR T640 thermal camera (sampling rate = 5Hz, resolution = 640x480 pixels, lens = 24.6mm, NETD < 0.04mK @ +30°C, spectral range of 7.8-14 μ m - LWIR). Additionally, we acquired RGB images with a Logitech HD webcam C270 (sampling rate = 30Hz, resolution = 1280x720 pixels) to identify the anatomical landmark of the tip of the nose. RGB and IR data synchronized after downsampling the RGB video to the sampling rate of IR frames (i.e., 5Hz). Then, the synchronized RGB and IR frames were spatially coregistered by means of an affine-2D transformation matrix estimated on the first frame of the RGB and IR datasets. A region-of-interest (ROI) around the center of the tip of the nose was identified on the RGB frames with the Yuval Nirkin algorithm for facial landmark detection [17]. Additionally, the ROI was purposely chosen to be proportional to the size of the subject's face. This latter was obtained by means of an automatic segmentation procedure as suggested in [15]. Afterwards, ROI tracking was carried out with a builtin Matlab PointTracker object [18] (The Mathworks Inc.). Accordingly, we properly controlled for potential undesired subjects' movement. Then, for each frame, we estimated the median temperature of the nose ROI to obtain a thermal timeseries for subsequent feature extraction. Such thermal signal was processed by filtering out high-frequency noise with a moving median filter, and by further replacing outliers (i.e., temperature values exceeding 3 standard deviations) with their nearest value. Finally, we extracted the mean of the processed thermal signal (**Nose Mean**) during *RESTpre* and *Stroop*.

Electrocardiogram. ECG and EDA were recorded using a BIOPAC MP 150 system, at a sampling rate of 500Hz. ECG signals were analysed using the software Kubios [19] to extract and process the HRV time series. Indeed, the analysis of HRV in time and frequency domain provides a window through which autonomic nervous system functions can be estimated and it has been widely used to identify a stress state [20], [21]. In particular, for both *RESTpre* and *Stroop* sessions, we estimated the mean of the HRV (MeanHRV), the root mean square of successive differences between normal heartbeats (RMSSD) and the spectral power in the range of 0.15–0.40 Hz (high frequency - HF) expressed as a percentage of the total power. These features are likely to reflect both sympathetic and parasympathetic ANS activity [22], and have been previously

used in stress recognition tasks [23], [24].

Electrodermal activity. The EDA reflects changes in the electrical properties of the skin induced by the sweat glands' production on the palm of the non-dominant hand. Since such sweat glands are under the direct control of the sympathetic branch of the ANS [25], the EDA is considered a good way to monitor the sympathetic activity and the stress state [26]. EDA is made by the superimposition of a tonic component, which reflects slow-varying changes in the sympathetic tone activity, and a phasic component, which includes the fast variations directly evoked by external stimuli. During a continuous stressful stimulation like the one in the present protocol, the effect on the tonic component is predominant and its dynamic represents effective stress correlate [26], [27]. Here, we used the cvxEDA model to extract the tonic component from the raw EDA signal [28]. Afterwards, for both RESTpre and Stroop sessions, we extracted the mean tonic value (TonicMean) with a slidingwindow approach using 20s-long non-overlapped windows.

D. Statistical analysis

As an exploratory analysis, we statistically compared the self-assessed stress scores, the physiological features and the VOC concentration computed during the stressful and the resting conditions. Particularly, for each acid VOC, we tested possible significant differences between *PAD-MeanSTRESS* and *PAD1-REST* with a Wilcoxon sign-rank test. (where *PAD-MeanSTRESS* is the average between *PAD2-STRESS* and *PAD3-REST*) Analogously, for each physiological feature (i.e. **NoseMean**, **TonicMean**, **MeanHRV**, **RMSSD**, and **HF**), we performed a Wilcoxon sign-rank test between *Stroop* and *REST pre* to evaluate the effectiveness of stress elicitation. Likewise, we performed a Wilcoxon sign-rank test on the self-assessed stress scores recorded before and after the *Stroop* task.

1) LASSO regression: Before performing LASSO regression, we normalized both chemical and physiological signals by their relative rest session. Thus, we considered the difference $\triangle VOCs = PAD-MeanSTRESS - PAD1-REST$ for each VOCs, and the difference $\Delta Feat = Stroop - RESTpre$) for each physiological feature. Then, for each physiological stress correlate $\Delta Feat$, we used a LASSO (least absolute shrinkage and selection operator) regression model [29] to explain the feature as a function of the selected group of acid Δ VOCs. Starting from the complete model, LASSO regression selects the subset of regressors that minimizes the prediction error for a quantitative response variable. The built-in feature selection capability of the LASSO method is due to the L1 penalty factor included in the cost function. L1 -norm is particularly suited to handle multicollinearity and mitigate the overfitting risk in the regression models. Indeed, the L1 penalty causes regression coefficients for some regressors to shrink toward zero, discarding less important or redundant regressors. The optimal hyperparameter λ that tuned the intensity of such L1 penalty was chosen using LOSO cross-validation. Accordingly, after scaling the regressors by means of z-score, we applied the LASSO model using different λ values and selecting the fit that minimized the mean square error (MSE). Once the optimal λ was identified, we performed a statistical inference of each regressor (i.e., VOCs) whose relative coefficient was different from 0. Specifically, we applied an exact post-selection inference procedure to mitigate the risk of overfitting occurring when the standard inference procedure of linear regression models is applied to LASSO regression. Finally, the coefficients selected by the LASSO that were statistically significant (p-value < 0.05) were used to fit the best model explaining each feature. Note that feature selection was necessary to reduce the dimensionality of the model, considering the high number of VOCs compared to the number of observations in our dataset

III. RESULTS

1) Paired difference testing: The Wilcoxon test on the self-assessed scores of stress confirmed that subjects significantly increased their perceived level of stress after the task (median \pm mad = 5 \pm 1.3 vs. median \pm mad = 2 \pm 1.5, p < 0.01). Likewise, all the features extracted from physiological signals showed significant differences between the *Stroop* and *RESTpre* sessions. In particular, **TonicMean** and **meanHRV** increased significantly during *Stroop* (p = 0.004). Conversely, **NoseMean**, **RMSSD** and **HF** decreased significantly during *Stroop* (respectively, p = 0.027, p = 0.049 and p = 0.006). On the other hand, none of the VOCs showed any significant difference between *PAD-MeanSTRESS* and *PAD1-REST* (P-values are shown in Table I).

TABLE I

PAD-MeanSTRESS Vs PAD1-REST WILCOXON TEST P-VALUES FOR EACH
ACID COMPOUND

Acids	p-value	Acids	p-value
dodecanoic acid	0.105	octanoic acid	0.695
hexanoic acid	0.232	Acetic	0.769
Propionic acid	0.275	decanoic acid	0.921
Diisopropyl adipate	0.275		

2) LASSO regression: Considering the model explaining the temperature of the nose tip (i.e., **Nose Mean**) as a function of the VOC concentrations, the feature selection performed by the LASSO reduced the regressors subset to one single VOC (see top left Fig. 2). Accordingly, only dodecanoic acid was associated with a non-zero coefficient. The model that minimized the MSE (MSE = 0.1451) was for λ equal to 0.0585. Moreover, the inference analysis showed a significant p-value (p = 0.018) for dodecanoic acid with an R² of 0.64. The resulting equation of the model is (2):

$$\Delta$$
NoseMean = $-0.1620 - 3.128e^{-5} \cdot \Delta$ dodecanoic acid (1)

The corresponding regression plot is shown in Fig. 3.

Concerning the HRV features, the LASSO model explaining the **meanHRV** selected both the dodecanoic and the octanoic acids (MSE = 11.203 for λ equal to 0.088). However, only the dodecanoic showed statical significance after the post-selection

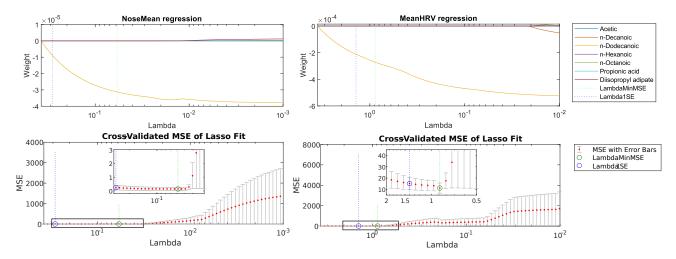


Fig. 2. (Top) Coefficients of each regressor for different values of λ ; (Bottom) Mean Squared Error (MSE) of the LASSO regression model for different values of λ ; (Left) NoseMean regression; (Right) MeanHRV regression.

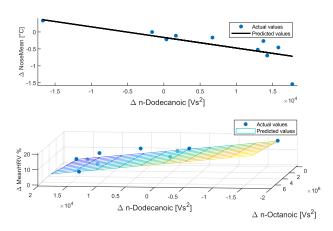


Fig. 3. Regression plot. (Top) **NoseMean** regression; (Bottom) **MeanHRV** regression.

inference procedure (respectively, p = 0.011 and p = 0.322) with an R^2 of 0.67. The equation of the model is (2):

$$\Delta {\bf MeanHRV} = 8.71 - 2.72 e^{-4} \cdot \Delta {\bf dodecanoic~acid} \\ + 1.73 e^{-7} \cdot \Delta {\bf octanoic~acid}$$
 (2)

The corresponding bidimensional regression plot showing the relationship between the **MeanHRV** and the **dodecanoic acid** only (due to its statistical significance) is shown in Fig. 3. On the other hand, the LASSO models concerning the **RMSSD** and **HF** showed a minimum of the MSE for the highest value of λ . In this case, none of the VOC regressors had a coefficient different from zero and the model with the minimum MSE was the model with the only intercept term.

Finally, the LASSO model explaining **TonicMean** selected again only the dodecanoic acid. However, the estimated coefficient was not statistically significant based on the post-selection inference procedure (p = 0.16).

IV. DISCUSSIONS

In this preliminary study, we investigated the relationship between some selected acid volatiles in human sweat produced during mental stress and well-established physiological stress correlates. More specifically, we used LASSO regression to reduce model dimensionality, given the low number of observations, and select the most informative VOCs. Although preliminary, our results highlighted a significant linear relationship between two physiological markers of stress, such as the nose mean temperature and the meanHRV, and the concentration of the n-Dodecanoic acid in sweat.

The efficacy of our protocol in inducing stress was controlled with both self-assessed measures of stress and physiological features commonly used in stress recognition [15], [26]. Specifically, we observed that these measures changed significantly during the Stroop session as expected. More importantly, we observed that among all the considered physiological features for characterizing the stress condition, some of them had a significant linear relationship with the n-Dodecanoic VOC. Interestingly, one of these was the temperature of the tip of the nose, which was previously found to characterise stressful conditions [13]–[15], [30]. Analogously, MeanHRV increased during the Stroop session possibly reflecting a response to sympathetic arousal [23], [24]. We also controlled the environment, ensuring a stable temperature and humidity during the whole experiment to exclude potential confounders in the analyses due to thermoregulatory processes. In addition, we tried to minimize confounding factors in sweat analysis due to food intake, coffee, tobacco, as well as to the use of cosmetic products with ad-hoc requirements. Furthermore, the influence of minerals and solvents captured by skin hair was minimized by asking subjects to shave their armpits the evening before the experiment. Accordingly, we assumed that the observed relations between physiological features and sweat compounds were likely to be related to the stressful condition rather than to other phenomena.

The LASSO models explaining both **RMSSD** and **HF** did not select any regressor. Interestingly, both **HF** and **RMSSD** are widely used markers of PNS activity [22]. On the other hand, the LASSO models of **NoseMean**, **MeanHRV**, and **TonicMean**, which are commonly related to the sympathetic stress response [23], [31] selected always the dodecanoic acid as the first ranked or as the only regressor. Accordingly, we could hypothesize that dodecanoic acid could be considered a new potential correlate of the SNS.

Changes in VOCs were not significant in any of the comparisons between PAD-MeanSTRESS and PAD1-REST. However, we observed that for dodecanoic acid the p-value was lower than for the rest of the acids (p = 0.105). In this view, we cannot exclude that statistical significance was not reached because of the relatively low number of subjects, which limited the power of statistical comparisons. Accordingly, future confirmatory analyses will be needed by enlarging the number of subjects participating in the study.

V. CONCLUSION

In conclusion, although preliminary, our results suggest the presence of a linear relationship between well-established features for stress detection and the VOC dodecanoic acid in human sweat collected during stressful conditions and offers interesting insights for its future application as a stress biomarker. Moreover, in future studies, we will consider VOCs extracted from other body fluids and gases (e.g., breath, saliva, etc.) as they could provide additional and complementary information on the subject's mental state.

REFERENCES

- R. S. Altman and R. A. Schwartz, "Emotionally induced hyperhidrosis," Cutis, vol. 69, no. 5, pp. 336–8, 2002.
- [2] J. A. Allen, J. E. Armstrong, and I. Roddie, "The regional distribution of emotional sweating in man," *The Journal of physiology*, vol. 235, no. 3, p. 749, 1973.
- [3] Y. Nakazato, N. Tamura, A. Ohkuma, K. Yoshimaru, and K. Shimazu, "Idiopathic pure sudomotor failure: anhidrosis due to deficits in cholinergic transmission," *Neurology*, vol. 63, no. 8, pp. 1476–1480, 2004.
- [4] H. J. Martin, M. Turner, S. Bandelow, L. Edwards, S. Riazanskaia, and C. Thomas, "Volatile organic compound markers of psychological stress in skin: a pilot study," *Journal of breath research*, vol. 10, no. 4, p. 046012, 2016.
- [5] M. A. Smeets, E. A. Rosing, D. M. Jacobs, E. van Velzen, J. H. Koek, C. Blonk, I. Gortemaker, M. B. Eidhof, B. Markovitch, J. de Groot, et al., "Chemical fingerprints of emotional body odor," *Metabolites*, vol. 10, no. 3, p. 84, 2020.
- [6] J. H. de Groot, G. R. Semin, and M. A. Smeets, "On the communicative function of body odors: a theoretical integration and review," *Perspectives on Psychological Science*, vol. 12, no. 2, pp. 306–324, 2017.
- [7] J. H. de Groot, P. A. Kirk, and J. A. Gottfried, "Encoding fear intensity in human sweat," *Philosophical Transactions of the Royal Society B*, vol. 375, no. 1800, p. 20190271, 2020.
- [8] M. Tsukuda, Y. Nishiyama, S. Kawai, and Y. Okumura, "Identifying stress markers in skin gases by analysing gas collected from subjects undergoing the trier social stress test and performing statistical analysis," *Journal of breath research*, vol. 13, no. 3, p. 036003, 2019.
- [9] A. Arza, J. M. Garzón-Rey, J. Lázaro, E. Gil, R. Lopez-Anton, C. de la Camara, P. Laguna, R. Bailon, and J. Aguiló, "Measuring acute stress response through physiological signals: towards a quantitative assessment of stress," *Medical & biological engineering & computing*, vol. 57, no. 1, pp. 271–287, 2019.

- [10] S. Cerutti, D. Hoyer, and A. Voss, "Multiscale, multiorgan and multivariate complexity analyses of cardiovascular regulation," *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engi*neering Sciences, vol. 367, no. 1892, pp. 1337–1358, 2009.
- [11] A. Zamkah, T. Hui, S. Andrews, N. Dey, F. Shi, and R. S. Sherratt, "Identification of suitable biomarkers for stress and emotion detection for future personal affective wearable sensors," *Biosensors*, vol. 10, no. 4, p. 40, 2020.
- [12] J. R. Stroop, "Studies of interference in serial verbal reactions.," *Journal of experimental psychology*, vol. 18, no. 6, p. 643, 1935.
- [13] Y. Cho, N. Bianchi-Berthouze, M. Oliveira, C. Holloway, and S. Julier, "Nose heat: Exploring stress-induced nasal thermal variability through mobile thermal imaging," in 2019 8th International Conference on Affective Computing and Intelligent Interaction (ACII), pp. 566–572, IEEE, 2019.
- [14] C. Puri, L. Olson, I. Pavlidis, J. Levine, and J. Starren, "Stresscam: non-contact measurement of users' emotional states through thermal imaging," in CHI'05 extended abstracts on Human factors in computing systems, pp. 1725–1728, 2005.
- [15] F. Gioia, A. Greco, A. Callara, and E. Scilingo, "Towards a contactless stress classification using thermal imaging," *Sensors*, vol. 22, no. 3, 2022. cited By 0.
- [16] D. Cardone, D. Perpetuini, C. Filippini, E. Spadolini, L. Mancini, A. M. Chiarelli, and A. Merla, "Driver stress state evaluation by means of thermal imaging: A supervised machine learning approach based on ecg signal," *Applied Sciences*, vol. 10, no. 16, p. 5673, 2020.
- [17] Y. Nirkin, I. Masi, A. T. Tuan, T. Hassner, and G. Medioni, "On face segmentation, face swapping, and face perception," in 2018 13th IEEE International Conference on Automatic Face & Gesture Recognition (FG 2018), pp. 98–105, IEEE, 2018.
- [18] J. K. Suhr, "Kanade-lucas-tomasi (klt) feature tracker," Computer Vision (EEE6503), pp. 9–18, 2009.
- [19] M. P. Tarvainen, J.-P. Niskanen, J. A. Lipponen, P. O. Ranta-Aho, and P. A. Karjalainen, "Kubios hrv-heart rate variability analysis software," *Computer methods and programs in biomedicine*, vol. 113, no. 1, pp. 210–220, 2014.
- [20] W. A. Tiller, R. McCraty, and M. Atkinson, "Cardiac coherence: A new, noninvasive measure of autonomic nervous system order," *Alternative therapies in Health and Medicine*, vol. 2, no. 1, pp. 52–65, 1996.
- [21] P. Fauquet-Alekhine, L. Rouillac, J. Bertoni, and J.-C. Granry, "Heart rate vs stress indicator for short term mental stress," *British Journal of Medicine and Medical Research*, vol. 17, no. 7, pp. 1–11, 2016.
- [22] T. F. o. t. E. S. o. C. t. N. A. S. o. P. Electrophysiology, "Heart rate variability: standards of measurement, physiological interpretation, and clinical use," *Circulation*, vol. 93, no. 5, pp. 1043–1065, 1996.
- [23] H.-G. Kim, E.-J. Cheon, D.-S. Bai, Y. H. Lee, and B.-H. Koo, "Stress and heart rate variability: a meta-analysis and review of the literature," *Psychiatry investigation*, vol. 15, no. 3, p. 235, 2018.
- [24] J. Taelman, S. Vandeput, A. Spaepen, and S. V. Huffel, "Influence of mental stress on heart rate and heart rate variability," in 4th European conference of the international federation for medical and biological engineering, pp. 1366–1369, Springer, 2009.
- [25] H. D. Critchley, "Electrodermal responses: what happens in the brain," The Neuroscientist, vol. 8, no. 2, pp. 132–142, 2002.
- [26] A. Greco, G. Valenza, J. Lázaro, J. M. Garzón-Rey, J. Aguiló, C. De-la Camara, R. Bailón, and E. P. Scilingo, "Acute stress state classification based on electrodermal activity modeling," *IEEE Transactions on Affective Computing*, 2021.
- [27] M. E. Dawson, A. M. Schell, and D. L. Filion, "The electrodermal system.," 2017.
- [28] A. Greco, G. Valenza, A. Lanata, E. P. Scilingo, and L. Citi, "cvxeda: A convex optimization approach to electrodermal activity processing," *IEEE Transactions on Biomedical Engineering*, vol. 63, no. 4, pp. 797– 804–2015
- [29] R. Tibshirani, "Regression shrinkage and selection via the lasso," *Journal of the Royal Statistical Society: Series B (Methodological)*, vol. 58, no. 1, pp. 267–288, 1996.
- [30] C. Filippini, E. Spadolini, D. Cardone, and A. Merla, "Thermal imaging based affective computing for educational robot," in *Multidisciplinary Digital Publishing Institute Proceedings*, vol. 27, p. 27, 2019.
- [31] Y. Cho and N. Bianchi-Berthouze, "Physiological and affective computing through thermal imaging: A survey," arXiv preprint arXiv:1908.10307, 2019.