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Using wearable skin temperature data to advance tracking and characterization of the menstrual cycle in a real-world setting

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Abstract

The menstrual cycle is a loop involving the interplay of different organs and hormones, with the capacity to impact numerous physiological processes, including body temperature and heart rate, which in turn display menstrual rhythms. The advent of wearable devices that can continuously track physiological data opens the possibility of using these prolonged time series of skin temperature data to non-invasively detect the temperature variations that occur in ovulatory menstrual cycles. Here, we show that the menstrual skin temperature variation is better represented by a model of oscillation, the cosinor, than by a biphasic square wave model. We describe how applying a cosinor model to a menstrual cycle of distal skin temperature data can be used to assess whether the data oscillate or not, and in cases of oscillation, rhythm metrics for the cycle, including mesor, amplitude, and acrophase, can be obtained. We apply the method to wearable temperature data collected at a minute resolution each day from 120 female individuals over a menstrual cycle to illustrate how the method can be used to derive and present menstrual cycle characteristics, which can be used in other analyses examining indicators of female health. The cosinor method, frequently used in circadian rhythms studies, can be employed in research to facilitate the assessment of menstrual cycle effects on physiological parameters, and in clinical settings to use the characteristics of the menstrual cycles as health markers or to facilitate menstrual chronotherapy.

Keywords

Menstrual cycle; wearables; temperature; ovulation; rhythm metrics

Introduction

The menstrual clock consists of a feedback loop of hormonal nature, involving the hypothalamus, the pituitary, and the ovaries, and which period of revolution is normally

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between 22 to 36 days during the reproductive stage, becoming more and more irregular around perimenopause (Bull et al., 2019; Ecochard et al., 2001; O'Connor et al., 2001; Reed & Carr, 2000) and stopping after menopause (defined retrospectively when menses has ceased for one year) (Harlow et al., 2012a). During the follicular phase of the menstrual cycle, the gonadotropin releasing hormone (GnRH) neurons of the hypothalamus produce GnRH in a pulsatile manner, triggering the pituitary to release luteinizing hormone (LH) and follicle stimulating hormone (FSH) into the blood circulation. These hormones reach their receptors in the ovary, which allow a follicle to grow to the point at which it commences releasing estradiol. In turn, estradiol stimulates a LH surge which triggers ovulation. After ovulation, the luteal phase begins, marked by the luteinization of the follicle, when it begins producing progesterone, which induces growth of the endometrium (Barbieri, 2014). Progesterone peaks around half-way through the luteal phase, about one week after ovulation (Ecochard et al., 2017). At that point, in the absence of pregnancy, the corpus luteum atrophies, resulting in a decrease in estradiol and progesterone levels. The inhibition on GnRH, FSH and LH are lifted, and a new menstrual cycle can begin (Barbieri, 2014).

The hormones of the menstrual clock have receptors in numerous tissues all over the body, and can therefore influence functioning of organs even if they are not directly involved in reproductive function (Farage et al., 2009). Conversely, the menstrual clock is sensitive to signals from the rest of the organism, and from the external environment. Indeed, GnRH neurons, by being interconnected with other neural areas of the hypothalamus, and by having receptors to hormones such as leptin, insulin, neuropeptide Y, melanocortin, cortisol, and orexins, integrate signals about body composition, nutritional status, energy expenditure, stress, and emotional state (Arora & Taheri, 2015; Barbieri, 2014). In extreme cases, weight loss, nutritional, and emotional stress can lead to amenorrhea (Warren & Fried, 2001).

These bidirectional mechanistic links make it possible for the menstrual cycle to influence other aspects of health, and for internal and external factors to influence the menstrual cycle. The menstrual cycle, therefore, is both an indicator, and an influencer, of health. Thus, menstrual cycles metrics, such as period, amplitude, acrophase, mesor, and regularity, have the potential to be useful markers or predictors of specific health conditions.

In circadian rhythms research, the associations between rhythms and specific conditions including health problems are studied extensively. In addition to the rhythmicity itself being used as an indicator of health problems (Stenvers et al., 2019), the characteristics of the rhythm including the period, amplitude, mesor, acrophase, are also used as health indicators. For example, the amplitude and acrophase are investigated in metabolic health research as different factors can influence them, including nutrition, exercise, or aging (Froy, 2010; Gabriel & Zierath, 2019; Parkar et al., 2019; Serin & Acar Tek, 2019). In addition, having a circadian clock with a longer endogenous circadian period translates into a preference for evening behavior called "later chronotype", which is associated with numerous risk factors including mood disorders, anxiety disorders, insomnia, sleep apnea, arterial hypertension, bronchial asthma, type 2 diabetes, and infertility (Bhar et al., 2022; Partonen, 2015).

In menstrual cycle medicine, the absence or irregularity of menstrual cycles is already known as an indicator of anorexia nervosa and bulimia nervosa (Hirschberg, 2023), but also of polycystic ovary syndrome (Singh et al., 2021). However, the menstrual rhythm and its characteristics remain to be investigated as potential markers of these health conditions or others, as well as an aging indicator. There is an opportunity to advance this knowledge with the increasing availability of sensors and statistical tools such as presented in this work.

Tracking menstrual cycles

Menstrual cycles can be tracked based on the appearance of menstrual bleeding, marking the beginning of a cycle. There are now several menstrual diary apps available to assist in tracking menses over many menstrual cycles (Trépanier et al., 2023), however, the burden is still on the user to enter the information. While the menses are easily observable, the only way to directly record ovulation is through an ultrasound of the ovaries. However, other hormonal and physiological events that are characteristically occurring during an ovulatory menstrual cycle are routinely used as a proxy to confirm ovulation. For example, home-based kits exist that can capture the surge of LH in urine, which typically increases 24-48 hours before ovulation (Ecochard et al., 2001; Eichner & Timpe, 2004). This method is classically used by the general public to plan a pregnancy, and also in research, as a proxy to validate that ovulation occurred during a studied cycle (Cervinski & Gronowski, 2010; Rogan & Black, 2022; Su et al., 2017). It is affordable, non-invasive, and reliable in most individuals. Studies assessing the capacity of detecting an ovulatory cycle via LH surge detection compared with the transvaginal ultrasound of ovaries, showed up to 97% accuracy, when used with proper adherence (Miller & Soules, 1996; Su et al., 2017). However, LH surges can have various shapes, number of peaks, and be more or less far in time from the actual ovulation detected with the ultrasound of the ovaries (Ecochard et al., 2001).

Body temperature is a well-studied marker of the ovulatory menstrual cycle. It is at its lowest during the follicular phase, and increases 0.3°C to 0.7°C after ovulation, in the presence of progesterone, reaching a maximum during the luteal phase (Fiona C. Baker et al., 2020). If conception occurs, body temperature remains high. If not, it decreases at the end of the luteal phase, as progesterone declines, and menses occurs. Temperature was first reported to change across the menstrual cycle in 1904 (Van de Velde, 1904; Van de Velde, 1926); finger temperature specifically was first used in menstrual cycle and pregnancy monitoring in 1949 (Burt, 1949), and has since then been used to mark ovulatory cycles (Su et al., 2017). To track their menstrual cycles, women can be advised to take a single oral temperature measurement each morning soon after waking, before getting out of bed considered as the most stable measurement, and to observe the variation across the cycle. This manual process of temperature measurement is limited by several issues including compliance, which affects reliability, and environmental temperature changes, which can limit the accuracy, especially when only a single temperature measurement is taken per day (Fiona C. Baker et al., 2020). However, when performed with high adherence, this method detects a biphasic temperature pattern, with an increase of at least 0.2-0.3°C across a 6-day interval, in 98% of cycles with an ultrasound-confirmed ovulation (Ecochard et al., 2001). Advances in technology, and in particular the availability of wearable devices with integrated temperature sensors are now providing long time series of temperature data at a high granularity, such as each minute, across days, weeks, months, and even years. These data potentially enable non-invasive tracking and evaluation of menstrual oscillations of temperature, or other physiological characteristics of an ovulatory menstrual cycle, with minimum input from the user.

Considerations for relying on body temperature to track menstrual cycle rhythms

Even if it is continuously measured, there are several factors that influence body temperature that need to be considered in the context of a study's objectives, in order to select a strategic sensor location and perform adequate data preprocessing.

External elements including ambient temperature and humidity, as well as internal factors such as basal metabolic rate, muscle activity, digestion, sleep, posture, and hormonal fluctuations, are sources of temperature variation. To maintain the core body temperature in a range in which the organs can function optimally, the hypothalamus integrates these signals and consequently orchestrates mechanisms regulating heat loss or heat production. The body surface, with the skin and subcutaneous fat, is a key area for thermoregulation as it constitutes the interface with the exterior. Vasoconstriction and vasodilation mechanisms allow humans to regulate the amount of blood present at the surface, hence modulating the extent of the temperature exchange (Campbell, 2008). Every day, the basal metabolism, hormones, muscles activity, and digestive system are typically active during daytime, with the peak of heat production around 11AM-12PM, and the core temperature increases through the day to reach a maximum around dusk (Krauchi & Wirz-Justice, 1994). To shunt out the heat from the core, peripheral vasodilation takes place, allowing the core temperature to reach its lowest at dawn. As a consequence, the core and distal skin temperature display antiphase rhythms, with the temperature of hands and feet highest during the night and at their nadir during the day (Krauchi & Wirz-Justice, 1994). These oscillations are controlled by the circadian system, as they are measurable even in constant conditions (Krauchi & Deboer, 2010). Interestingly, as we illustrate in Figure 1, while the distal skin and core temperature are in antiphase for their circadian rhythms, they are in phase at the menstrual rhythm scale (Kräuchi et al., 2014).

Core body temperature measurements (e.g., rectal, vaginal, esophageal) are considered the reference (Childs, 2018), but are invasive and limiting for the continuous monitoring of temperature over enough days to track menstrual cycles. Skin temperature measurement is convenient as it is easily accessible and can be monitored for prolonged periods of time, but in addition to circadian and menstrual changes, skin temperature fluctuates due to changes in the inner (fever, activity) and outer (external temperature and humidity, showering, dishwashing) environments. The effect of these artifacts on skin temperature can be minimized by resampling the data. For example, to study menstrual cycle related changes in temperature, filtering and combining the data strategically into one daily average temperature is required, if that average reliably represents the temperature of the day and is as free as possible from artefacts. But a simple average of all the data from one day would incorporate numerous potential biases, which could blur the overall menstrual variation trend. Maijala and co-authors have published a strategy to address this issue, using a 17-min moving average, which they applied to minute-by-minute temperature data collected by

Oura rings to obtain a single reliable average temperature measure for each day, when skin temperature was highest, which occurs at night, when temperature is more stable and when core body temperature is lowest (see Figure 1). Once such reliable daily data are obtained, they can be used in different models and analysis, for example to characterize the menstrual cycle.

Using wearables to track changes in body temperature across the menstrual cycle

Several wearables have incorporated sensors of various physiological data including temperature, heart rate, breathing, light exposure, skin conductance, and movement (de Zambotti et al., 2020). Here, we focus on temperature detection, as its change across the ovulatory menstrual cycle is already well described. Typically worn on the wrist or the finger, wearables rely on distal skin temperature, and have applied advanced algorithms to track temperature changes to predict sickness (Natarajan et al., 2020) as well as ovulation and menses (Mohaned Shilaih et al., 2018; Uchida & Izumizaki, 2022; Yu et al., 2022), and pregnancy (Grant & Smarr, 2022). Wearables have led to a resurrection in the reliance on temperature data in menstrual health (Alzueta et al., 2022). Indeed, many devices (Demiańczyk & Michaluk, 2016; Goodale et al., 2019; Ogidan et al., 2023; Regidor et al., 2018; Wark et al., 2015; Zhu et al., 2021) and mobile applications (Berglund Scherwitzl et al., 2015; Händel & Wahlström, 2019) have offered continuous nocturnal temperature measurements at different body sites to improve the accuracy of this proxy of ovulation detection (Maijala etal., 2019; M. Shilaih et al., 2018). The most recent studies utilizing wearables for ovulation or fertile window detection and prediction (fora review see (Uchida & Izumizaki, 2022)) have applied a variety of statistical models (Chen et al., 2009; Luo et al., 2020) and machine learning algorithms (Goodale et al., 2019; Maijala et al., 2019; Murayama et al., 2023). However, a performance comparison to accurate reference measurements is lacking (see (Händel & Wahlström, 2019) for a review of proposed mathematical models). Some of these methods rely on investigating the biphasic pattern of body temperature (Chen et al., 2009; Goodale etal., 2019; M. Shilaih et al., 2018; Zhu et al., 2021), with the temperature increase generally regarded as confirmation of ovulation (Royston & Abrams, 1980). However, to our knowledge, whether the temperature change across the menstrual cycle is best represented by an oscillation or by an increase that plateaus in the luteal phase, has not been shown yet. Other work has relied on the rhythmic characteristics of the circadian rhythm of temperature in order to improve fertility and pregnancy planning (Webster & Smarr, 2020). Others have integrated the variations in distal skin temperature and heart rate variability data from the Oura ring in the context of women's health, using signal processing models in order to anticipate the onset of the LH surge which precedes ovulation (Grant et al., 2020), or to detect early pregnancy (Grant & Smarr, 2022).

However, these methods do not take advantage of the rhythmic nature of the menstrual cycle of temperature to extract metrics and use them as predictors of conditions, as is done in circadian rhythms research. Indeed, applying oscillating models to menstrual cycle data may be useful to extract information not only about the occurrence of an ovulation, but also metrics of the rhythm itself.

In circadian rhythms research, sine models, also known as cosinor, are frequently used to fit parameters which vary across 24h, including genetic expression (Gómez-Santos et al., 2009), hormonal levels (Rahman et al., 2019), as well as body temperature (Lee, 1988). This approach allows the verification of the cyclicity of the data, and the assessment of different characteristics of the cycle, such as its amplitude, mesor, and acrophase (Díez-Noguera, 2013). These metrics can then be compared between individuals as well, to potentially identify changes in these characteristics according to a condition, disease, or medication. The cosinor method has been previously used in the analysis of the influence of the menstrual cycle on the rhythmic characteristics of the circadian rhythms of core body temperature. This work has shown that the mesor of the 24-hour rhythm is higher, and its amplitude is dampened during the luteal phase compared to the follicular phase (Coyne et al., 2000; Lee, 1988; Padhye & Hanneman, 2007). In addition, a dual harmonic regression approach has been used to model 24-hour core body temperature variations, also showing a blunted amplitude during the luteal phase (Shechter et al., 2010).

Comparing temporal events surging at certain moments of the rhythm in individuals with diverse inner rhythms duration constitutes a challenge. For that, circadian scientists use the trigonometric circle to represent the circadian clock, and to calculate the difference between two events in angles instead of hours (Refinetti et al., 2007). Employing this method in menstrual cycle research could be useful to study and illustrate how characteristics of the menstrual cycles vary with health status, life habits, treatments, etc.

We propose here that a cosinor modelling approach could be applied to study menstrual cycle rhythms. We describe a method that takes advantage of tools classically employed in circadian rhythm research to model menstrual cycle rhythms using distal skin temperature data obtained from wearables. We first apply the cosinor method to a large dataset collected from 120 females and identify the r^2 as a strategic indicator of the data's proximity to an oscillatory pattern. We hypothesized that menstrual skin temperature variations are better modeled by an oscillation fitted with a cosinor model than by a higher plateau in the luteal phase, fitted with a square wave. A cosinor r^2 threshold is determined above which an individual's data are considered to be oscillatory. We also assessed to what extent the oscillatory temperature was associated with a positive outcome on a LH test and hypothesized that there would be high agreement between the two methods. Finally, we illustrate that metrics, including the mesor, amplitude, and acrophase, can be derived from the cosinor model of oscillating menstrual temperature.

Methodology

Study cohort and experimental design

Individuals were recruited to participate in a larger study about sleep and memory across the menstrual cycle. The Stages of Reproductive Aging Workshop (STRAW) criteria (Hall, 2015; Harlow et al., 2012b) were used to identify the individuals' reproductive stage. Participants reporting no more than 7-days variation in the length of consecutive menstrual cycles were considered in the reproductive stage, while individuals reporting persistent ≥7 days variation in the length of consecutive cycles or amenorrhea for at least 60 days but had not gone 12 months without a period were considered in the menopausal transition stage.

Individuals were healthy, not taking chronic medications, including oral contraceptives or hormone therapy, and did not suffer from any menstrual-associated disorders. None of the participants was post-menopausal, defined by amenorrhea of at least 12 months. The study followed the ethical standards of relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, revised in 2008. The University of California, Irvine, IRB committee approved this study, and participants provided written informed consent. All participants received compensation.

As part of the protocol, 120 individuals (age range: 18-52 years) wore an Oura ring© (Gen 2, firmware 2.43.1; Ōura Health Oy, Oulu, Finland) across at least one menstrual cycle, which forms the dataset used here. They also tracked days of bleeding (menses) in a digital diary that was completed daily and tracked presence of a LH surge using a commercial urine test (PREGMATE®, Ovulation Midstream Test Predictor Kit; sensitivity level: 25 mlU/ml). They were asked to start using one test per day during their first urination in the morning, starting 5 days prior to the estimated ovulation day and to continue testing for 3 days after the first positive result, or longer if there was no clear result. The estimated ovulation date was based on participant-reported prior menses dates, to fall 14 days before the estimated date of their next menses. Indeed, the follicular phase is known to present greater variability than the luteal phase (Bull et al., 2019), and an additional 5 days of testing was introduced to buffer for potential variability. Participants sent a picture of the kit result each time to the lab staff for visual checking of the results. The retained LH surge day was considered the first day in which a positive test was obtained. Participants who failed to perform the test more than once in this estimated periovulatory window were considered to lack adherence to this method.

Data pre-processing

Data pre-processing procedures allowed us to calculate a reliable value of distal skin temperature per day in a transparently calculated manner. From the Oura cloud online interface for researchers, we downloaded for each participant the table of raw absolute temperature values at one data point per minute, as well as the table containing the hypnogram of 30s epochs estimated by Oura's algorithm.

We used the procedures recommended by Maijala and co-authors to obtain one reliable and representative value of distal skin temperature per day (Maijala et al., 2019): First, only nocturnal data were down-selected to limit artifacts from daily behaviors, with the nocturnal period defined as the time between the Oura provided indexes Bedtime_start and Bedtime_end. Since sleep staging information is now available for Oura, we went one step further, and only used the portions of data classified as sleep across the nocturnal period. Second, a moving average filter of 17 minutes of length was applied across the nocturnal data and portions of the data with extreme variability were removed, defined as more than 1 °C change across 17 minutes. Finally, the maximum stable 17-minute average of the nocturnal period was kept as the reliable temperature measure for the day (Maijala et al., 2019). An example is shown in Figure 2 and the histogram distribution of these data is shown in Supplementary Figure 1. With this approach, very few missing data were obtained: on average, across the 116 participants with temperature data, less than 1 datapoint was missing across their menstrual cycles of data (mean number of missing datapoints: 0.69 ± 1.15).

The distal skin temperature data were presented scaled and centered, as Oura claims its product to provide a reliable trend of temperature data, but not of absolute value. Scaling was performed across all participants, using the "scale()" function in R. After pre-processing the daily temperature data, daily temperatures were plotted over time to identify any trends across the menstrual cycle. Participants' data were used to fit a cosinor curve if data from at least 75% of days of a menstrual cycle were available, and with no more than 6 days of consecutive missing data. On the participant's data fulfilling these criteria, a 3-day moving average filter accepting a maximum of one missing value was applied in order to smooth the curve, giving more importance to the general trend than to the day-to-day variations and to possible outliers (Figure 3, upper panel). The participants' data that were included in the current analysis ranged between three quarters of a menstrual cycle to one menstrual cycle and half of another (75% to 150% of a menstrual cycle duration).

On these data, we investigated which cosinor curve was the best fit for each participant, blinded to self-reported menstrual cycle duration (determined from identified menses onset) and measures of LH surge with a detection kit. For participants in the reproductive stage up to age 35 years, cosinor curves of periods ranging between 22 and 36 days were fitted, corresponding to the variability of normal menstrual cycles during this stage (Bull et al., 2019; Fehring et al., 2006). For participants over the age of 35 years in the reproductive or menopausal transition stage, curves between 22 to 45 days were fitted, to account for the variability of menstrual cycles durations, which can start in the later part of the reproductive stage (O'Connor et al., 2001). Among these multiple models tested, the one with the highest r^2 was considered to best represent the data and was selected. The distribution of the periods of the selected model of each participant is presented in the Supplementary Figure 2.

Once the model was fitted, the associated p-value, r^2, and residuals standard deviation were obtained. Other metrics characterizing the rhythm included the mesor or midpoint value of the oscillation, the amplitude or maximum distance reached by the curve from its mesor, the acrophase or timepoint at which the maximum positive distance to the mesor was reached, and the period or number of days to complete the oscillation pattern. In addition, as temperature increases after ovulation and menses commences after temperature starts decreasing, we used the acrophase of the curve as a reference point from which to measure when ovulation and menses onset occurred (Figure 3, middle panel). The estimated ovulation date was set as the day after the first positive result with the LH kit, as suggested by the manufacturer. For each individual, the temporal gap between menses or estimated ovulation and acrophase was converted into degrees by dividing by the period of each individual's curve and multiplying the result by 360.

Using the same 3-days smoothed distal skin temperature data, as used for the cosinor model, we also fitted a square wave function to search for the optimal parameters—period, mesor, and amplitude. It iterated over the same period lengths as the cosinor curve, selecting for each participant the fit with the highest R^2. The mesor and amplitude were determined through a linear model, so that the square wave curve that best fit each participant's data was generated (Figure 3, lower panel).

Data Analysis

Spearman correlations were performed using the cor.test() function in R, to assess the relationship between the r^2 of the cosinor curve and the period of the cycle, between the r^2 of the cosinor curve and the age of the participant, and between the r^2 of the cosinor curve and the r^2 of the square waves curve. Wilcoxon test was used to compare r^2 of the square wave curve and r^2 of the cosinor curve. We also performed a logistic regression, using the r^2 of our cosinor models to predict if certain ranges of r^2 were associated with the positive and negative outcomes of the urine LH test. Finally, we did a secondary analysis to examine the dispersion and average temperature data between participants with oscillatory and non-oscillatory cycles. Specifically, we used independent t-tests with Bonferroni correction to compare the mean and standard deviation (SD) of the temperature data (whole cycle) from participants with non-oscillatory cycles to the mean and SD of the temperature data from participants in the estimated-follicular (days when the curve was below the mesor) and estimated-luteal (days when the curve was higher than the mesor) phases of their oscillatory cycles. Paired t-tests with Bonferroni correction were used to compare the mean and SD of the temperature data from the estimated-follicular and estimated-luteal phases of the same participants.

All the data processing was conducted using R version 4.2.2 (2022-10-31 ucrt) (R Core Team (2022). R: A language and environment for statistical computing. R Foundation for Statistical Computing), with the packages lubridate, readxl, tidyverse, zoo, and lme4. Result figures were also produced with R, grouped and labelled using PowerPoint, and the method figure was produced in PowerPoint.

Results

The characteristics of the study participants are presented in Table 1.

Cosinor fitting and identification of the r^2 as an indicator of the data's proximity to an oscillatory pattern

As presented in the introduction, the temperature cyclicity over the menstrual cycle, with higher levels during the luteal phase, is known to indicate that ovulation has happened. By visual inspection of distal skin temperature data over a menstrual cycle, it is possible to observe whether such a variation is present. For example, in the top left graph of Figure 4, the temperature data presented in grey did not vary across the menstrual cycle, in contrast to the other graphs shown in the figure. Using a cosinor method, a cosinor curve was obtained which models the menstrual cycle of distal skin temperature. Here, we aimed to use this tool to assess whether or not the data were oscillatory and therefore suggested that the cycle was ovulatory, and whether the model represented the data sufficiently well to provide reliable metrics from the cycle of temperature. Using the p-values of the regression models, out of the 116 individuals with distal skin temperature data, we found all models but one to be significant at a level of $p < 0.05$. However, in some individuals with significant p-values, the visual assessment showed no clear menstrual oscillation of the temperature. Consequently, the p-value was considered an insufficient indicator of the presence of an oscillation in the data. On the other hand, with better fit quality (higher r^2), as observable in the examples in Figure 4, the model became an accurate approximation of the oscillatory data. There was no relationship between r^2 and age (rho coefficient: −0.097, p = 0.303) or with the period length of the cycle (rho coefficient: −0.094., p = 0.314).

Comparing a cosinor fit with a square wave fit on distal skin temperature data across a menstrual cycle

Square wave curves were also fitted to the temperature data to assess whether the menstrual cycle changes in distal skin temperature were better represented by an oscillation or by a biphasic model. As with the cosinor curve, the fit quality (r^2) was extracted from the square wave curve of each participant. When comparing the r^2 of the two models for the 116 curves using a Wilcoxon test, the cosinor curve was found to fit the data significantly better than the square wave (p = 0.022, Figure 5)

Identification of a r^2 threshold to classify “oscillatory” versus “non-osciiiatory” data

Figure 6 shows the distribution of the r^2 of the cosinor curve on menstrual cycle distal skin temperature data in the 116 participants. On average, the fit was high ($r^2 = 0.56 \pm 0.25$). When sufficiently high, the fit quality allowed characterization of the oscillation in the temperature. This relevant indicator of the fit quality may be useful by itself, as an indicator of the menstrual oscillation of temperature. Also, a threshold could be identified, above which the fit quality could be considered sufficiently good to confirm that the distal skin temperature data oscillate and indicate an ovulatory cycle. With that aim, a logistic regression was first performed, using the r^2 of our models in order to predict if certain ranges of r^2 were associated with the positive and negative outcomes of the urine LH test.

As presented in Figure 7 and Supplementary Table 1, this analysis confirmed that a higher r^2 value was associated with a greater likelihood for the urine LH kit to be positive, however, no obvious cut-off point for r^2 stood out. Indeed, some individuals had a positive LH surge test despite absence of a visible oscillation, while some others did not measure an LH surge although their temperature oscillated very clearly across their menstrual cycle. Therefore, we aimed to determine a r^2 cutoff from which the oscillation of the model matched the one visually observable in the data. Based on visual assessment of the distal skin temperature and their corresponding model in 116 individuals, we proposed that (1) when r^2 was greater than 0.25, the data were sufficiently well represented by a sine wave for the temperature to be considered oscillatory. However, in some of the individuals although the oscillation was present and captured by the model, important variability in the data was not captured in the curve. Therefore, for the present dataset, we proposed to consider that (2) the model was sufficiently good to extract metrics (e.g., mesor, amplitude, acrophase) only for models reaching a second, more rigorous cut-off at $r^2 > 0.4$. The residuals corresponded to the variability in the data which was not explained by the model. In Figure 8, the standard deviation of residuals is presented according to the fit quality of the cosinor curve, and the proposed cutoffs are marked on the same plot.

Comparing dispersion and levels in skin temperature data from oscillatory versus non-oscillatory cycles

We identified the skin temperature data to be well represented by an oscillatory curve in 99 of the 116 participants. The data of the remaining 17 participants were not well represented by a curve. This may be explained by the absence of the luteal temperature surge typically occurring in an ovulatory menstrual cycle, and therefore be a marker of anovulation. Alternatively, if the data were noisier and more dispersed in these participants, the cosinor may not represent the data well even if an ovulation and subsequent temperature surge was present. A comparison of the data from these two groups of participants addressed these two possibilities: The average and SD of temperatures from non-oscillatory cycles were similar to that of the estimated-follicular portion of the oscillatory cycles, but were lower compared to the estimated-luteal portion of the oscillatory cycles ($p < 0.001$, Figure 10). Further, the SD calculated across the whole cycle in participants with oscillatory data was significantly higher than the SD for participants with non-oscillatory cycles ($p = 0.014$, Figure 10). These data, therefore, suggest that the non-oscillatory cycles were anovulatory rather than reflecting noisier, more dispersed datasets.

Association between LH surge and oscillatory pattern of skin temperature data

We first compared the adherence to two methods that may be used as proxies to track ovulatory cycles: the LH urine kit, and the distal skin temperature measurement by the Oura ring. In the case of the LH kit, lack of adherence was defined as participants failing to take the test, and/or not reporting the results to the researcher despite the daily reminders. This failure was observed in 6 out of 120 participants. Lack of adherence to the distal temperature collection was defined as the participant failing to charge and/or wear the ring despite the daily reminders, resulting in too much missing data (less than 75% of a menstrual cycle, or more than 6 consecutive missing days), which happened in 4 out of 120 participants (Table 2).

Second, we compared to what extend these two characteristics of an ovulatory cycle (the LH surge and oscillating temperature) were associated to each other in our study group. In the case of the LH kit, the result of the test was considered positive or negative according to the manufacturer's indications. Regarding the distal skin temperature, a cosinor model or cosinor curve was fitted to the data as explained earlier. If the fit was >.25, the menstrual cycle was considered oscillatory (n=99) and if the fit was <.25, it was considered non-oscillatory (n=17). Out of the 114 who adhered to the LH kits, 104 had a positive result (Table 2). Out of the 10 who did not have a clear positive result, 5 were in the reproductive stage and 5 were in the menopausal transition stage. For participants adhering to both methods (N=111), LH kit and temperature oscillation detection showed agreement in 82% of cases. Examples of curves illustrating each of the combinations of positives and negatives from the temperature oscillation and the LH kits are shown in Figure 9.

Menstrual cycle metrics derived from the curve

For the participants in which the curve had an $r^2 > .4$, we proposed to consider that the curve fitted the data sufficiently well to derive other metrics, including the mesor, amplitude and the acrophase. Here, 75 individuals, corresponding to 71.6% of our sample, met that criterion. The fit quality, the mesor, and the amplitude of the menstrual cycle of distal skin temperature may be considered as potential indicators of certain medical or fertility conditions or associated with other characteristics. As an example, the distribution of the mesor and amplitude across the entire group is represented in Figure 11. These metrics may be grouped by variables of interest, such as age, reproductive stage, health conditions, or treatment, to identify how the menstrual cycle characteristics are influenced by such variables. On the other hand, the acrophase may be used as a reference time point to compare to other temporal elements. For instance, the distance between the menses and the acrophase, and estimated ovulation (as the day following the first positive LH surge test result) and acrophase could be calculated and presented. As the menstrual cycle duration varies across individuals, a solution was needed to compare and represent them together. A possibility was to consider a cycle of data as a circle. For each individual, the temporal data could be transposed in degrees of a 360° cycle, instead of days of a, for example, 28-days cycle. An example of this menstrual clock representation is illustrated in Figure 11, showing the distribution of the menses and estimated ovulation compared with the temperature cycle. On average in our sample, menses started at 90.6° (sd = 42°) after the acrophase of the temperature cycle. The data can be converted back from degrees to a 28-day cycle, by dividing by 360 and multiplying by 28, such that menses was, on average, 7.05 days (sd = 3.27 days) after the acrophase. Estimated ovulation on the other hand started on average at 251° (sd = 64.8°) or 19.5 days (sd = 5.04) after the acrophase.

Discussion

In the current work, we showed how the method of cosinor curve modelling, broadly used in circadian rhythms research (Gómez-Santos et al., 2009), could be applied to distal skin temperature data obtained with an OURA ring in order to determine the presence of the temperature oscillation characteristic of an ovulatory menstrual cycle.

There was high compliance from our group of participants with using a wearable across a menstrual cycle, and the pre-processing of the temperature data allowed us to obtain reliable daily temperature measures. Our comparison of fitting the data with a cosinor and a square wave model showed that the menstrual variation of skin temperature is closer to a smooth oscillation rather than a low follicular plateau followed by a sudden increase to reach a higher luteal plateau. This finding suggests that the use of the term ”biphasic”, commonly used to characterize the menstrual variations of temperature (Ecochard et al., 2001; Moghissi, 1976; Uchida & Izumizaki, 2022), may be less appropriate than speaking of an “oscillatory” change. We also showed that in the few individuals whose data did not oscillate, daily temperatures remained low across the cycle, similar to levels recorded in the curve-estimated follicular phase of oscillatory data, suggesting that these cycles were anovulatory.

The findings of the current paper suggest that the cosinor method applied to wearable-derived skin temperature data can be used as a good estimate of whether a menstrual cycles is ovulatory, unobtrusively and with low user-burden. It can also advance research about the menstrual cycle in basic and clinical health applications and can be used as a tool to control for menstrual cycle factors in research. We attempted to use a method of logistic regression to identify limits of r^2 values that would indicate a cut-off for an adequate fit of the curve reflecting oscillatory activity associated with an ovulatory cycle. However, this method revealed no obvious cut-off, and we therefore inspected the curves visually. A visually identified threshold in the cosinor fit quality (r^2>0.25) reflected an adequate fit, however, we chose a more conservative fit (r^2> 0.4) requirement to reliably calculate rhythm metrics. These cut-offs are appropriate for the current dataset, obtained with a specific device (Oura ring) in a specific female population. However, their transferability to other studies remains to be assessed.

While there was a high level of agreement between our distal skin temperature rhythm method and the LH surge detection method for identifying ovulatory cycles, there were cases of both false positives and false negatives when comparing the methods. Reasons for these discrepancies are unclear since we did not measure hormone levels across cycles or use transvaginal ultrasound of the ovaries to precisely detect ovulation. However, some cases of ovulation without a subsequent temperature surge have been reported in the literature and may correspond to a lower progesterone sensitivity (F. C. Baker et al., 2020; Ecochard et al., 2001; Moghissi, 1976). In parallel, LH surges not followed by an ovulation (and therefore not followed by a temperature increase) have been reported in 4 to 10% of cases in individuals without known fertility problems or menstrual disorders (Su et al., 2017). Another study reported that 46.8% of regularly menstruating individuals presented at least one premature LH surge and 37% presented multiple ones (Krotz et al., 2005). A premature LH surge in that study was defined as an unsustained increase of LH, potentially sufficiently high to be positive on a test, but not sustained over time so likely not to result in an ovulation. Different profiles of LH surge with varying durations and amplitudes are associated with hormone level modifications and variations in the ovulation day (Direito et al., 2013). In the current study, LH was not quantified but only detected with a home testing kit, which participants were instructed continue testing only for 3 days after they had had a positive test, therefore this profile analysis could not be performed. However, different LH profiles could explain part of the disparities between the LH kit results and our cosinor analysis.

Future work could directly compare our method of cosinor modelling of temperature against the gold standard method of ovulation detection (transvaginal ultrasound of the ovaries) to determine accuracy, sensitivity, and specificity of the method.

As the useability of a method does not only depend on its accuracy but also on the practical application, we were interested in measuring the adherence, understanding that in this study, participants were contacted with reminders when to use the kit and if they lapsed in the use of the wearable. We observed similarly high adherence for both the LH-kit and the Oura temperature collection. In the case of the wearable used here, the burden for the participant is in 1) wearing the ring, 2) syncing the ring and the app daily to ensure data transfer, consisting in having the app open on the smartphone for at least one minute, 3) charging the ring, approximately every 3 days for about 20 minutes. The feedback from participants is consistent with previous reports, in studies using both wearables and diaries, in which participants reported that the diary was the most burdensome part of the study (Rawassizadeh et al., 2015), and in a high-school population, that the wearables were better accepted than the diaries (Mastrandrea et al., 2015). Some participants in our study commented that using the wearable was a motivation for participating.

It should be noted that when using a wearable for continuous and high sampling data collection, numerous sources of artefacts need to be considered and preprocessing steps are critical to ensure the data selected are truly representative of the phenomenon of interest. In the current study, we adapted a previously described method for selecting one reliable data point per day, which was the highest stable 17-min average, measured in the sleep period (Maijala et al., 2019). This approach enabled us to model menstrual cycle temperature rhythms that had high concordance with the LH kit results. However, skin temperature is also influenced by the sleep environment, behaviors of the individual during sleep, and other factors, and it is possible that the temperature data selected could reflect these influences more than the menstrual cycle for some individuals.

An advantage that the cosinor curve method provides, when the data do present an oscillatory pattern, is the possibility to extract metrics from the rhythm. First, we note that the fit quality does not appear to be affected by the age of the participant or by the duration of the period, indicating that the method seems to work for a diverse sample of participants. However, other conditions may affect the fit quality, which could then be used by itself as a marker or health indicator. In addition, when the fit is sufficiently good, the mesor, amplitude, and acrophase, could also be investigated as potential markers. When comparing the level of a rhythmic variable between two groups or conditions, using a single time-point can lead to inaccuracies, whereas using the mesor of the rhythm constitutes a more reliable element to compare. Examples of the application of rhythm metrics can be found in circadian rhythms science, where a decrease in the amplitude and a labile acrophase is classically encountered in aging as well as in metabolic disorders (Hofman, 2000; Woller & Gonze, 2021). In addition, the circadian period of an individual, which is longer in individuals with evening chronotypes and shorter in morning chronotypes, is known to evolve across the life span and to be predictive of certain behaviors and metabolic disorders (Reutrakul et al., 2013; Wong et al., 2015). To our knowledge, these rhythm metrics have not been investigated in the context of menstrual cycle rhythms, and further work is needed to explore whether differences in acrophase, amplitude, and periods of the menstrual cycle rhythm are predictive of reproductive functioning and overall health. For example, reproductive aging may reshape the menstrual cycle metrics in the same way that aging influences circadian rhythms. Future studies need to examine how these metrics evolve with reproductive aging, and how they are influenced by demographic factors like race and ethnicity and body composition, and to ultimately define the healthy menstrual cycle for each individual. Transposing the sine curve, or cosinor, to a trigonometric circle representation is another advantage of our proposed rhythm method; we showed that this approach can be used to plot the temporal location of menses and ovulation, in relation to the acrophase of each individual's menstrual rhythm of temperature. This information can be employed to observe differences between timing of events in different groups or according to different conditions, or to visualize if certain events tend to occur during specific menstrual phases. For example, in the current paper, the distribution of menses onset compared to the acrophase of the curve seems to display two modes, which may indicate the influence of another parameter, such as different profiles of hormones or sensitivity to hormones in the luteal phase. Indeed, in pathophysiology, circadian timing is predictive of disease onset such as cardiovascular events (Takeda & Maemura, 2016), but the efficacy of treatments also varies across the rhythm (CornÉlissen & Halberg). Investigating these elements in relation to menstrual cycle characteristics and phases could enhance the potential for precision medicine in women's health.

Previous studies have reliably tracked the menstrual cycle using temperature from diverse wearable devices. For example, a research group developed a wearable earbud that tracks body temperature every 5 minutes (Luo et al., 2020). In their method, they used the minimum overnight temperature to fit a Hidden Markov Model, weighted by the estimated length of the luteal phase of the cycle based on ovulation history, to characterize the cycle and identify the date of ovulation. They compared the performance of the algorithm against ovulation, confirmed with a LH surge detection kit, and found concordance in 30 of the 39 cycles studied, corresponding to 76.92%. Weinberg et al. (Weinberg & Cohen, 1983) calculated the mean overnight temperature measured by a thermometer attached to a hygiene pad and observed a rise of about 0.50°C across the menstrual cycle, but no comparison was provided with other ovulation tracking methods. In the study by Zhu et al. (Zhu et al., 2021) , participants wore a bracelet (Ava Fertility Tracker bracelet) to continuously measure wrist skin temperature during sleep and compared it with daily morning oral basal body temperature (BBT) measures and an at-home luteinizing hormone test (reference). They found that the mean wrist skin overnight temperature was more sensitive than BBT and had a higher true-positive rate for detecting ovulatory cycles relative to the LH kit; however, it also had a higher false-positive rate, resulting in lower specificity. They characterized ovulatory cycles as biphasic if at least one temperature shift was present between different stages of the cycle. As we showed here, however, an oscillatory model better describes menstrual cycle temperature rhythms rather than a biphasic model In the current study, we specifically preprocessed the data following a rigorous procedure to reduce environmental artefacts in the distal skin temperature, relying on the recognition of sleep epochs by the Oura ring algorithm to select stable temperatures, to improve the reliability of the data. It may be beneficial in future work to integrate other physiological signals from wearables, such as heart rate, to refine our method. For example, Goodale et al. (Goodale et al., 2019) analyzed data collected with a wrist-worn armband and integrated multiple physiological measures to predict ovulation. The cosinor method described here and commonly used in chronobiology may be a relevant complement to analyses implemented by others for various temperature sensors used to track ovulatory cycles (Maijala et al., 2019; Mohaned Shilaih et al., 2018; Uchida & Izumizaki, 2022; Yu et al., 2022). Indeed, in addition to indicating if a cycle is ovulatory, the cosinor method can be used to obtain insights when ovulation and menses occur in relation to the temperature rhythm, which could be used to identify menstrual cycle phases and ovulation windows in future cycles. In addition, the current method goes beyond only identifying events (menses and ovulation) to also identify metrics of the cycle, which could be alternative indictors of health and reproductive function. A diversity in menstrual hormone levels exist between females, and distinct patterns of luteal hormonal variations have been associated with the size of the follicle (Ecochard et al., 2017), as well as with the duration of the cycle and different levels of other hormones (Abdullah et al., 2023). It is likely that such hormonal profiles are reflected on the patterns of temperature variations across the menstrual cycle, and the characteristics of these temperature variations may in turn be used as predictors. The method presented here relies on the oscillatory pattern of temperature, but other methods that characterize the shape of the changes and allow the calculation of metrics from the menstrual cycle data of hormones and temperature, may serve as strategic health predictors in the future. Regarding reproductive function, the metrics derived from menstrual cycle data could be useful in pregnancy planning as well as in precision contraception. Indeed, several researchers currently aim to reduce to a minimum the exogenous hormonal input needed to obtain anovulation (Gavina et al., 2023). In order to optimally administer these monotherapies, the timing of the intake relative to the menstrual cycle is crucial. Consumer wearable devices are already greatly facilitating the implementation of chronotherapy considering an individual's circadian rhythms (Kim et al., 2020), and the implementation of the current method is particularly promising to extend it to precision medicine adapted to menstrual timing. We propose that the acrophase of the menstrual rhythm of temperature could be a strategic reference point in time, and that specific moments of the menstrual cycle may be referred-to as specific degrees of the cycles instead of days, as this would allow consideration of the interindividual variability in the menstrual cycle duration. Circadian rhythms science can be a valuable source of inspiration with regard to chrono-medicine. For example, the chronotypes, corresponding to different lengths of inner circadian rhythms, are associated with certain life habits, behaviors, risk factors and conditions (Arora & Taheri, 2015; Cespedes Feliciano et al., 2019). Similarly, associations between the duration of the menstrual cycle and particular behaviors or conditions may exist.

There are limitations to the method proposed here. First, in the case of using the r2 to indicate an ovulatory cycle, we have proposed a threshold (r2>0.25) which, based on the visual assessment of all our participants' data and associated models, appeared to us as the most appropriate way to discriminate between data presenting a menstrual cyclicity from data that did not. Further work is needed in a large sample of individuals with and without ovulatory cycles to determine the performance of this r2 cutoff relative to the gold standard measure of ovulation, ultrasound of the ovaries, which is more accurate than the LH urine kits employed here. Indeed, several individuals with very clear menstrual patterns of temperature change, strongly suggesting that ovulation happened, never had a "positive" result with the kits. This finding may be linked to an insufficient sampling rate for the LH kits, which may require 2 tests a day to ensure the LH surge is captured. Also, as described above, the alternative is possible for a minority of cases where there may not be a temperature increase despite ovulation occurring, in whom the proposed method would not be applicable to detect ovulation. However, it may still be useful to use the temperature rhythm method to identify and follow-up on anomalies in menstrual cycle patterns in those individuals. Similarly, we identified a r2 cutoff that would be sufficiently high for metrics of the curve to be calculated (r2>0.4) using visual inspection. We considered that a higher cutoff was needed to ensure greater reliability of the calculated metrics. However, future work is needed to expand and develop our method, including examination of the performance of these cutoffs in different samples relative to true ovulation and/or other datasets including reproductive hormone levels across a menstrual cycle. Another consideration to put this study in perspective is that the distal temperature was measured using a ring; future studies should test the method using other wearables across different locations starting from the most common, i.e., the wrist. Also, we propose it is important to test different curves with a range of periods corresponding to the range considered as a normal menstrual cycle duration (Bull et al., 2019; Fehring et al., 2006). In the current study using between three quarters of a menstrual cycle and one menstrual cycle and a half, testing this range of fits was effective and allowed some flexibility to find the best model. In addition, wearable devices also detect other physiological data in a continuous manner, including heart rate, heart rate variability, and SpO_2, and the technique presented here could be tested to measure menstrual variations across these measures. Notably, other techniques relying on the identification of repetitive patterns of temperature changes only work on data from many menstrual cycles, while the cosinor curve fitting method works with even slightly less than one cycle of data. On the other hand, according to the shape of the temperature variation and the regularity of the periods, the model that would best fit the data might not have a period exactly corresponding to the actual menses-to-menses distance. Indeed, fitting such a cosinor curve to multiple menstrual cycles would only work if the cycles were very regular. If not, a shift would tend to appear between the temperature cycles and the model, which would make it lose its relevance. This technique may therefore be nicely adapted to study between one to six fairly regular menstrual cycles. Other techniques may be more adapted to study multiple menstrual cycles, and the identification of temperature maxima, amplitude, the length of the period between them, their frequency, the slopes of temperature variations, etc. For example, the work of Leise shows the potential applications of wavelet-based analysis, as it allows the detection of changes of periods over the course of several cycles (Leise, 2013). In time series longer than a few months, this approach could allow the derivation of additional metrics such as the strength of rhythm (Leise & Harrington, 2011). The method of cubic periodic smoothing splines can be applied to model data across over multiple menstrual cycles, and has been used in the confirmation of ovulatory cycles and estimation of the ovulation date (Odlén, 2019). This last method can be used to obtain derivative measures including the slope and the curvature of the variations, which can also enrich the study of multiple menstrual cycles. In addition, the use of such methods would be more applicable than the cosinor fit in order to collect information surrounding the average duration of a menstrual cycle, the frequency and regularity of menses. Individuals sharing trends of menstrual rhythms metrics may share specific health characteristics, but also, a sudden change from the habitual pattern may be an early indicator of a new health condition. In addition, while in the cosinor approach, the nadir and the acrophase are necessarily at a half-period distance, other more flexible methods such as those mentioned above could be used to obtain additional information from the temporal location of the nadir and acrophase, the distance between them, and from other biological or external events.

In conclusion, we have presented a method frequently used in circadian rhythms science to model cyclic physiological changes, and showed how it can be applied to the distal skin temperature variations across the menstrual cycle. Fitting a cosinor curve to such data allows use of the fit quality (r^2) to assess how well the data fits this cyclic pattern. A high fit quality can confirm that the studied cycle is ovulatory, and different metrics can be extracted from the model: the amplitude, mesor, and acrophase. In addition, as in circadian rhythms studies, the cosinor fitting can be used to transpose the data to a circle representation, on which temporal elements can be located at particular angles of the cycle, allowing comparison of individuals even when they have different cycle durations. These techniques can be employed to broaden the understanding of the menstrual cycle, not only as the female reproductive system, but as a biological rhythm with the potential to influence numerous health mechanisms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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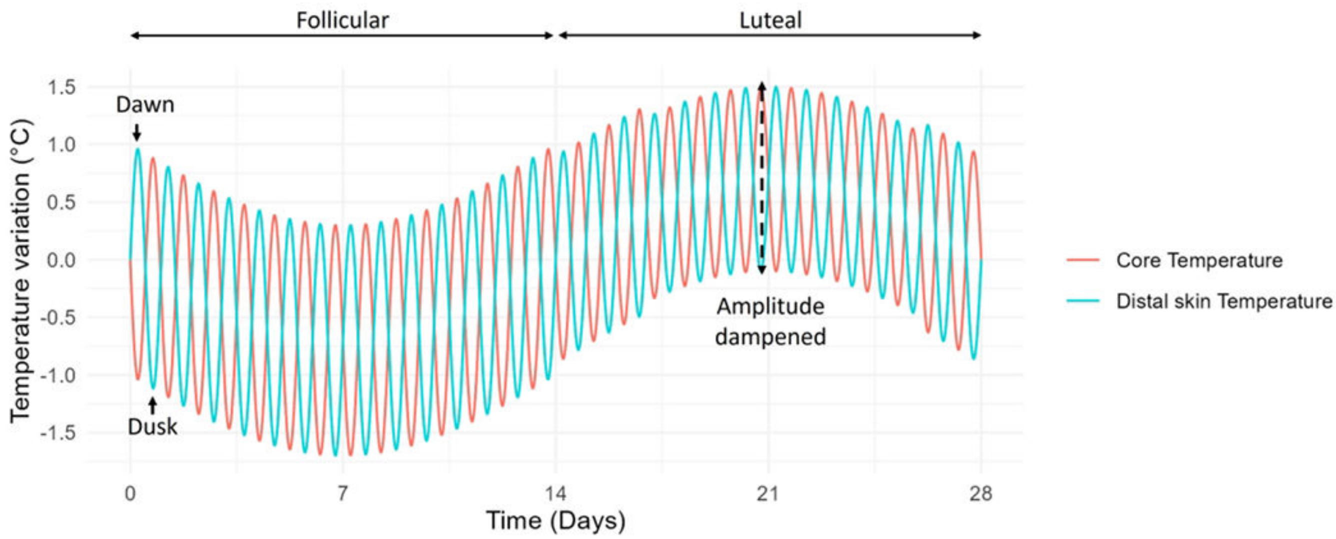

Figure 1.

Schematic representation of the circadian and menstrual effects on core and distal skin temperature. Core and distal skin temperature are anti-phase at the circadian rhythm scale, and in-phase at the menstrual scale. During the luteal phase, in addition to the overall temperature increase, the amplitude of its circadian rhythm is blunted. Black arrows approximate dawn and dusk in a 24-hour cycle.

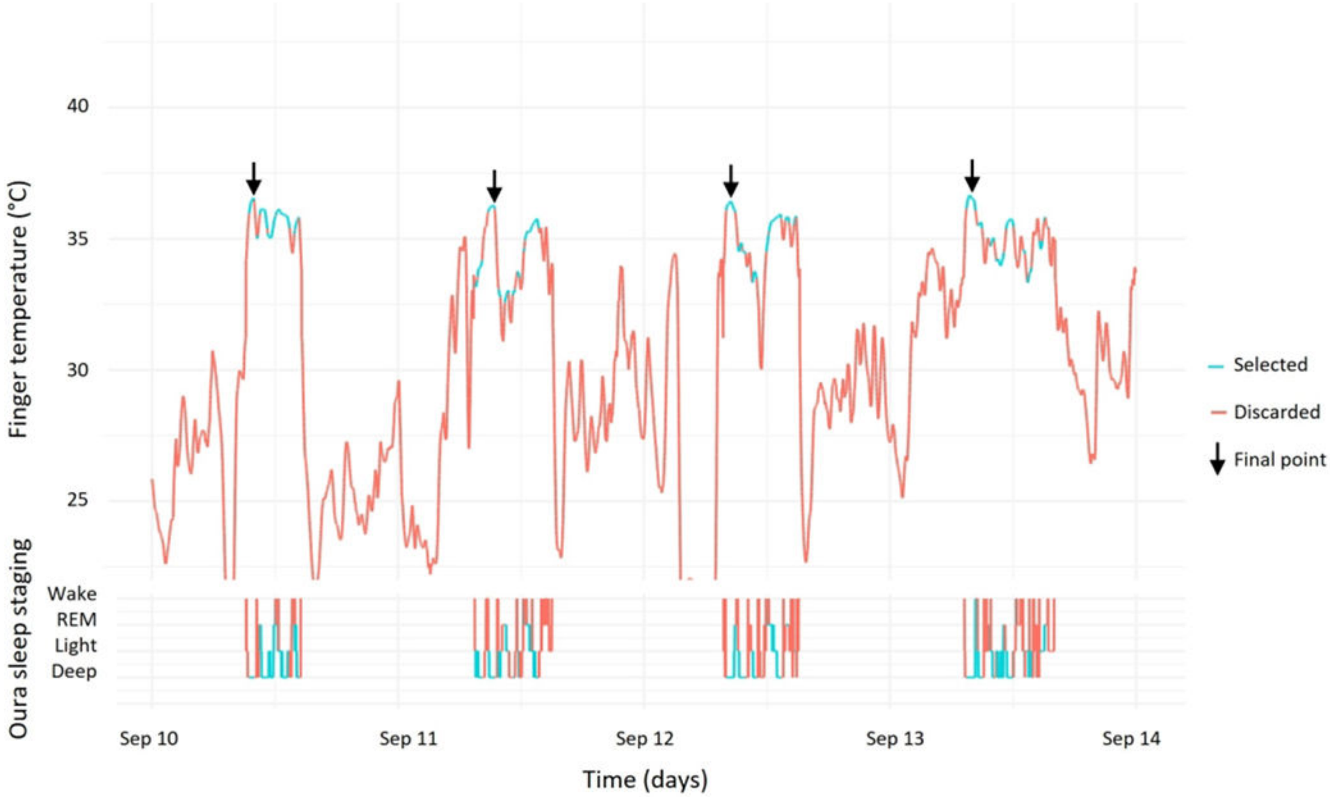

Figure 2.

Temperature and sleep staging measured with an Oura ring during 4 consecutive days at a one measurement/min granularity in one individual. The selected portions correspond to the stable sections measured during Oura-detected sleep. Oura's sleep staging is displayed in the lower panel of the graph.

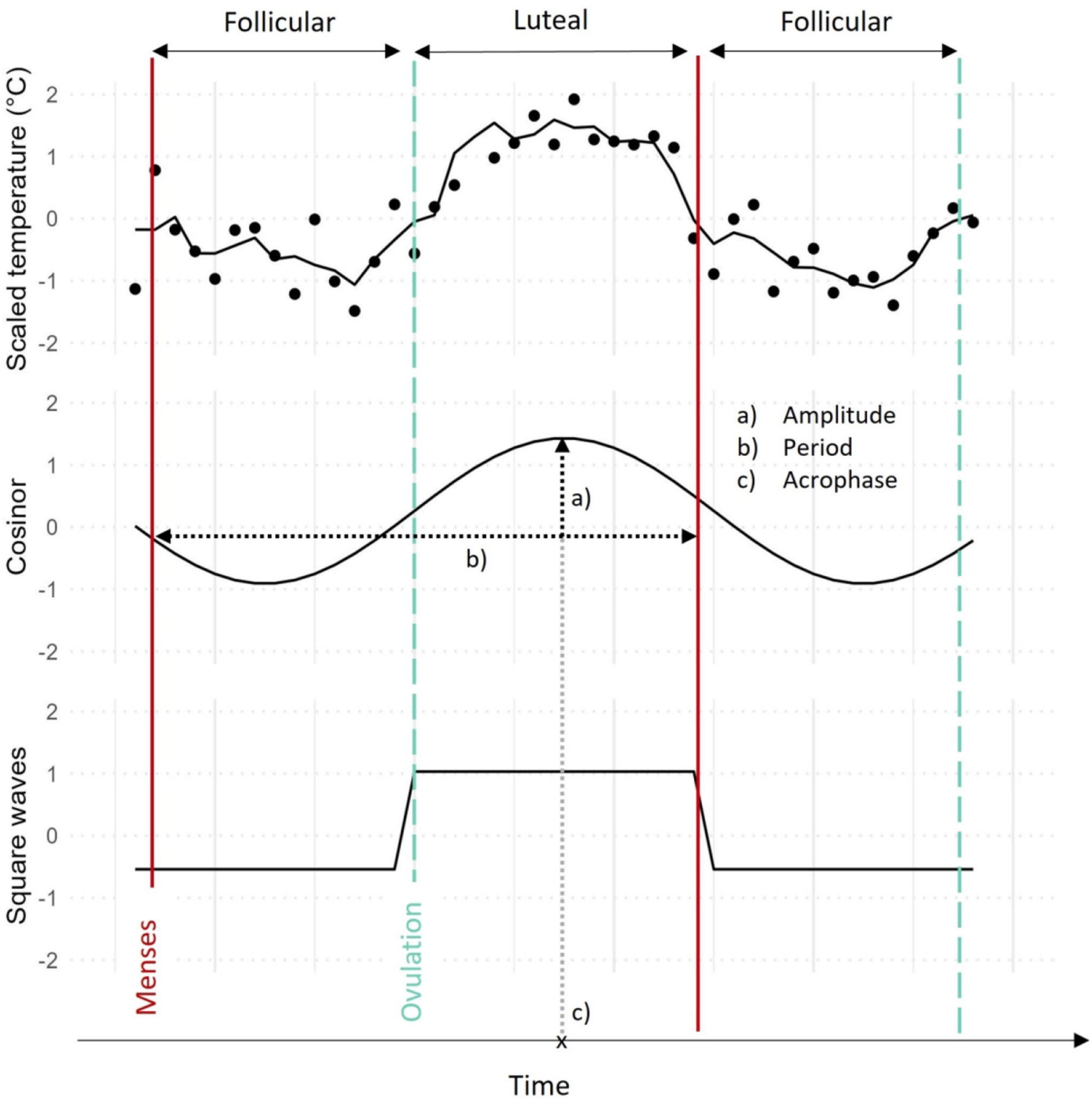

Figure 3.
Example of cosinor curve fit to skin temperature data obtained with an Oura ring over more than a month. The data obtained by selecting a stable night value of skin temperature are presented, normalized for this individual. Upper panel: The temperature points selected during each night of the cycle appear as black dots, and the trend smoothened by a three-day moving average is presented as a black line. Middle panel: The cosinor curve fitting these temperature data and its derived metrics. Lower panel: Superimposed on these curves, is

self-identified first day of bleeding (menses) and day of estimated ovulation (positive LH surge from an ovulation prediction kit) in vertical solid and dashed lines.

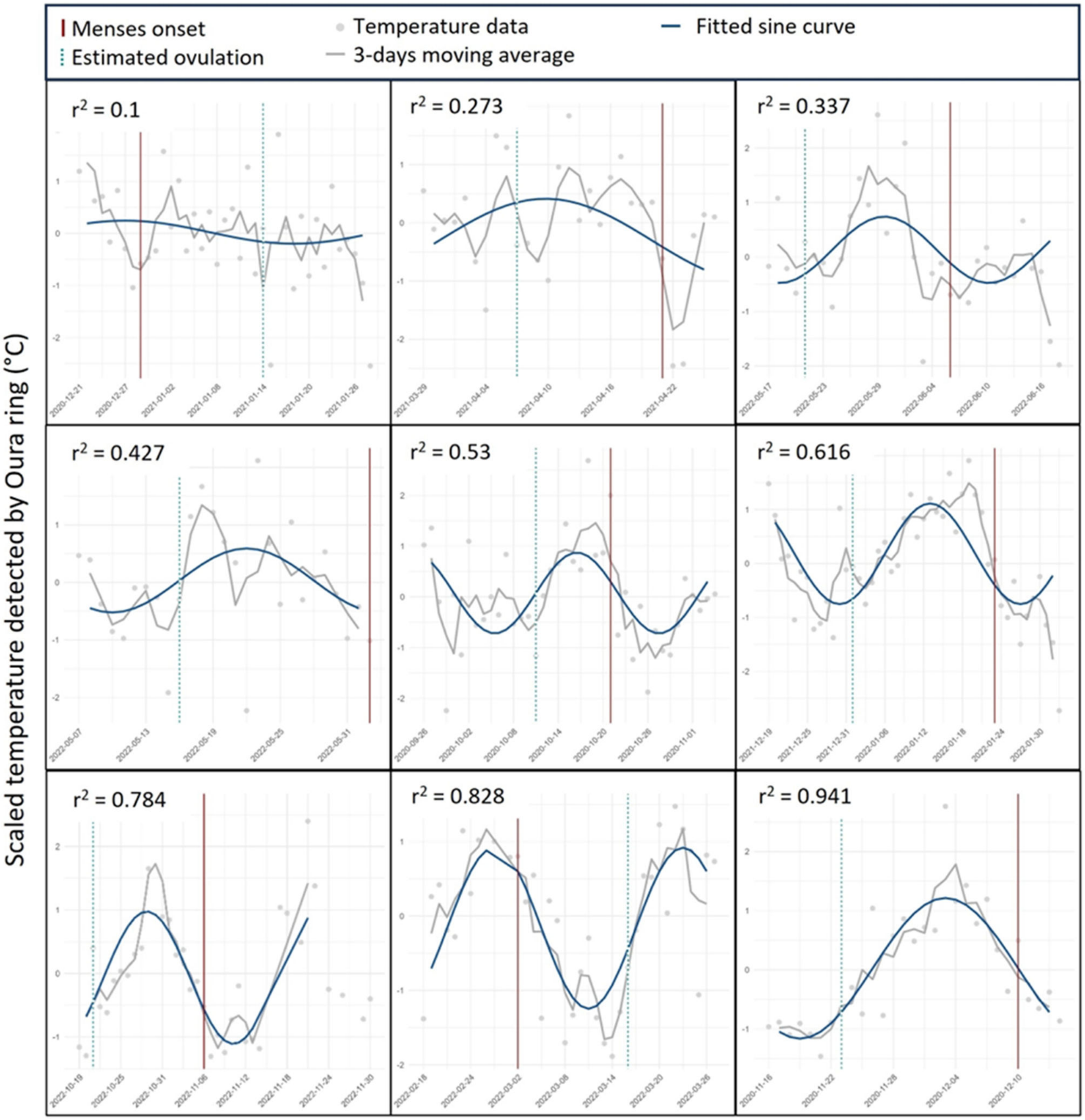

Figure 4.
Examples of cosinor curve fitting to daily temperature data, showing a range of fits, based on r^2values, from no fit (r^2 = 0.1) to a high fit (r^2= 0.9). Self-reported first day of menses is indicated by the solid line and a positive LH surge, indicating ovulation, is indicated by the dashed line.

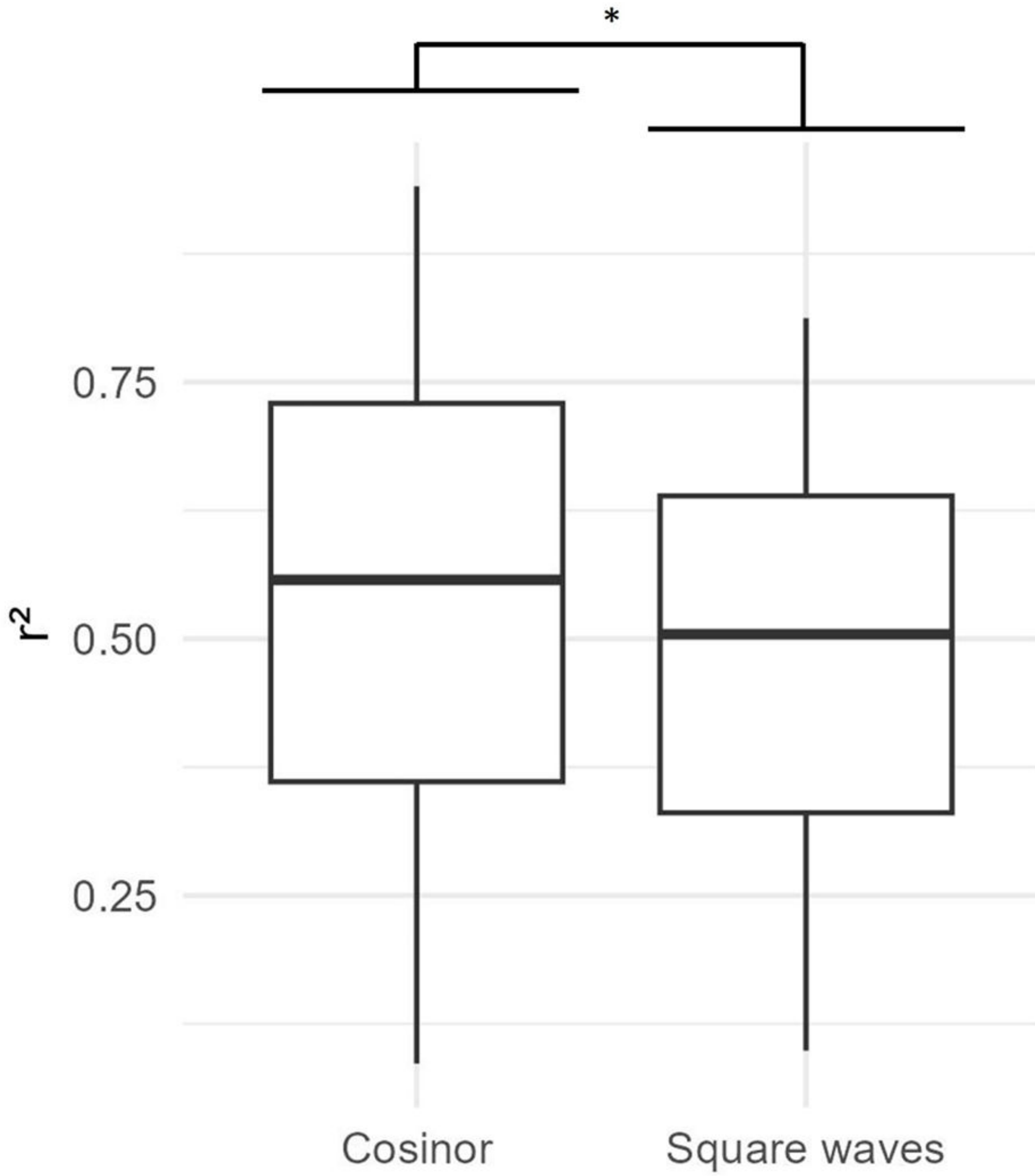

Figure 5.
Comparison of the r^2 derived from the cosinor and the square wave models. The asterisk is for a Wilcoxon test in which $p < 0.05$.

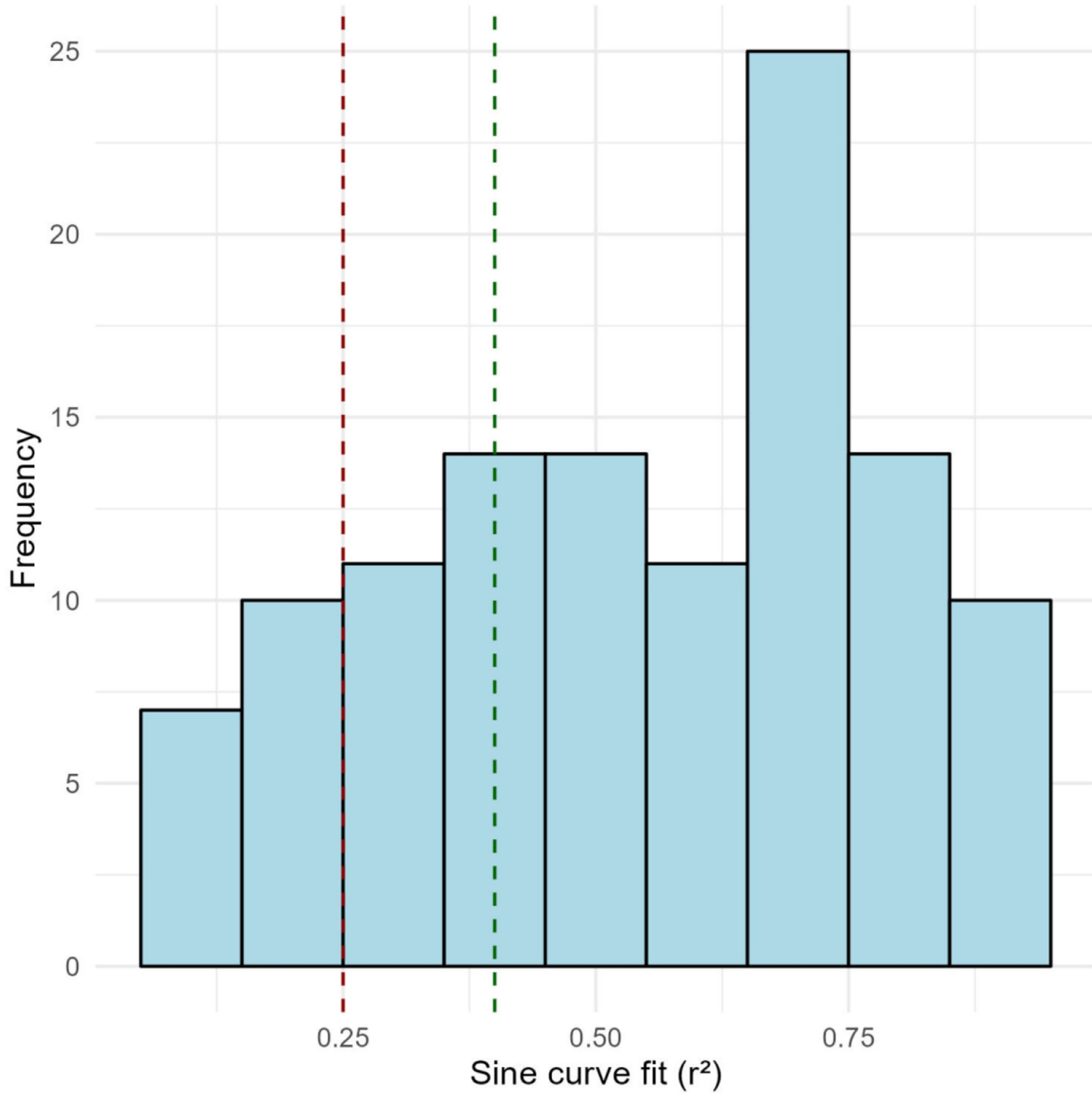

Figure 6.

Distribution of the fit quality of the cosinor curve on menstrual temperature. The vertical line at 0.25 represents the threshold r^2selected for the confirmation of ovulation. A higher fit (r^2= 0.4, second line) was deemed to be necessary in order to reliably derive metrics from the curve, including mesor, amplitude, and to estimate days of ovulation and menses.

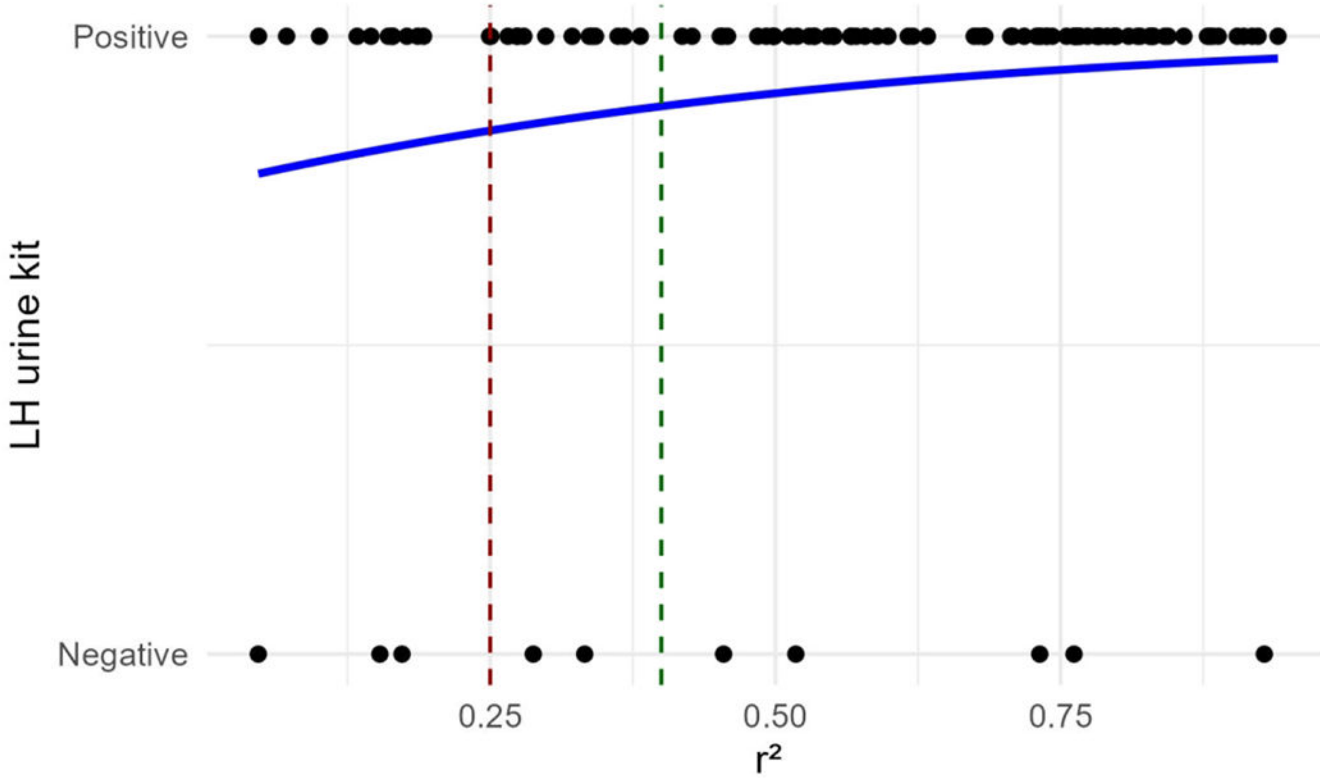

Figure 7.

Logistic regression predicting the outcome (positive or negative) of the LH urine kit according to the r^2 of the cosinor curve fitting the menstrual cycle of temperature data. The black dots mark the data points of the different r^2 encountered in individuals with positive and negative LH tests. The solid line corresponds to the regression curve. The first vertical dashed line corresponds to the first cut-off proposed, at $r^2 = 0.25$, and the second vertical dashed line to the second cut-off, at $r^2 = 0.4$.

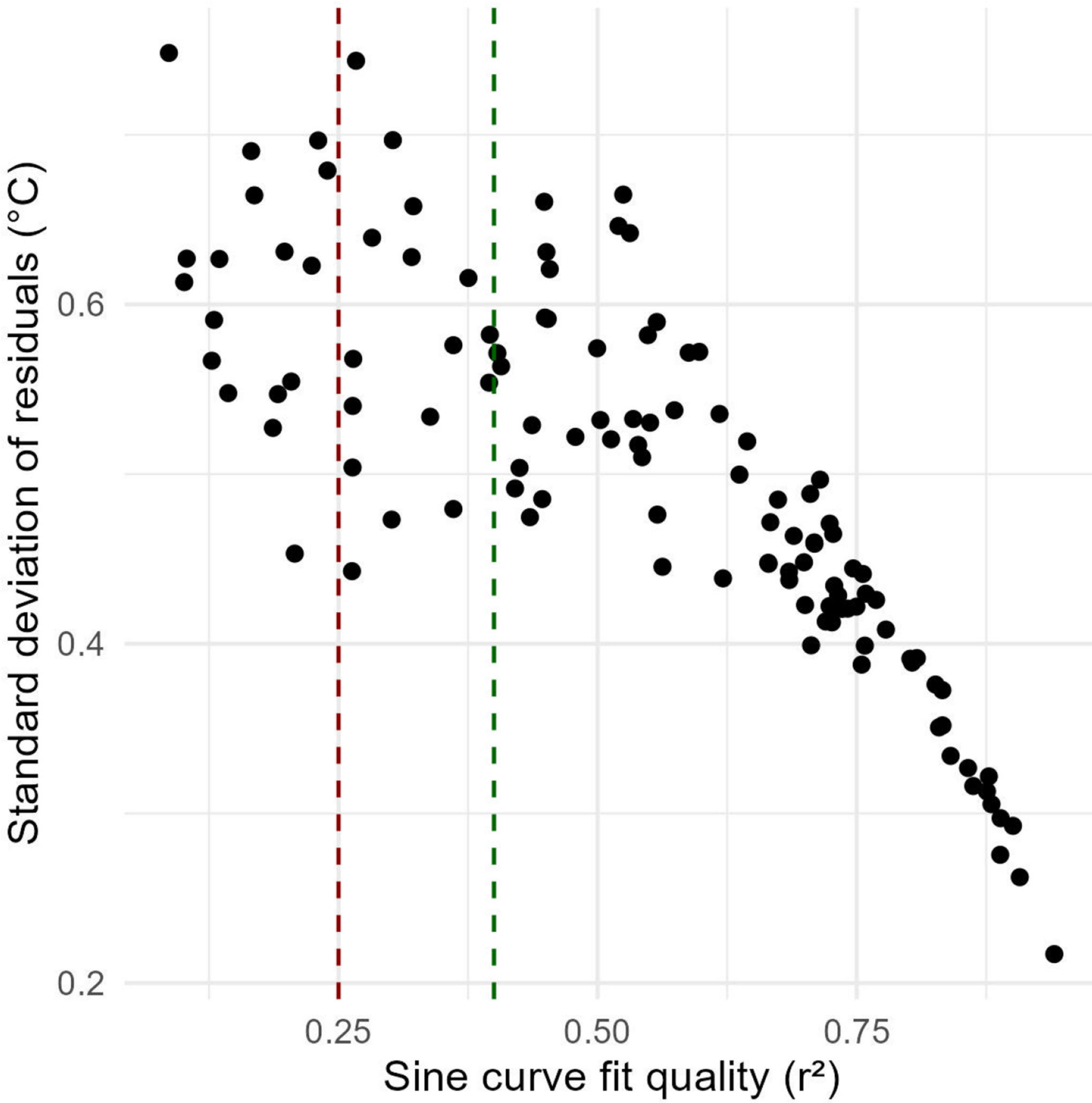

Figure 8.
Standard deviation of residuals according to the cosinor curve fit quality of the cosinor model. The vertical line at 0.25 and the one at 0.4 represent the thresholds r^2 selected for the confirmation of ovulation and usability of metrics.

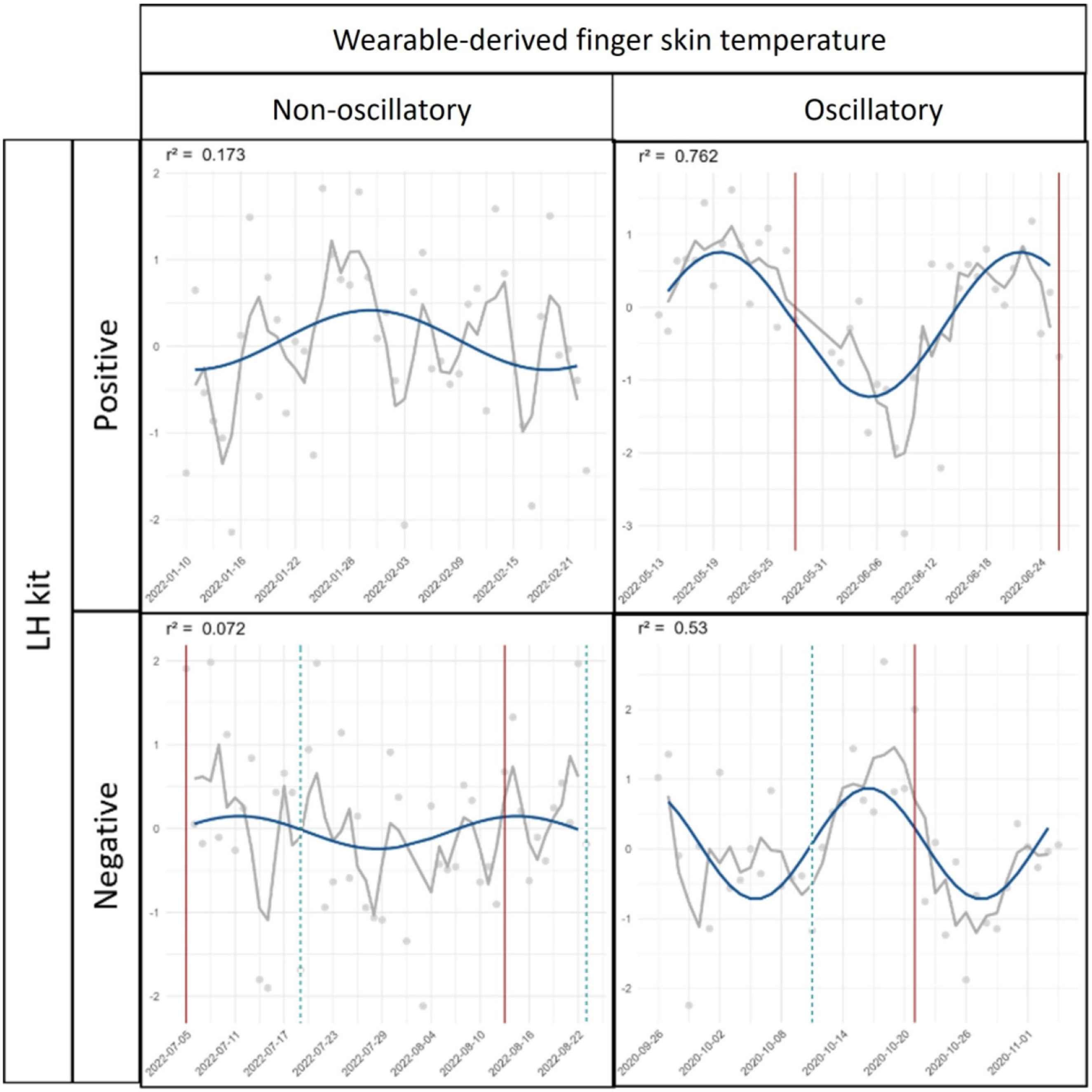

Figure 9.

Examples of curves illustrating the confusion matrix of temperature fit and LH kit results. Self-reported first day of menses is indicated by the solid line and a positive LH surge, indicating impending ovulation, is indicated by the dashed line.

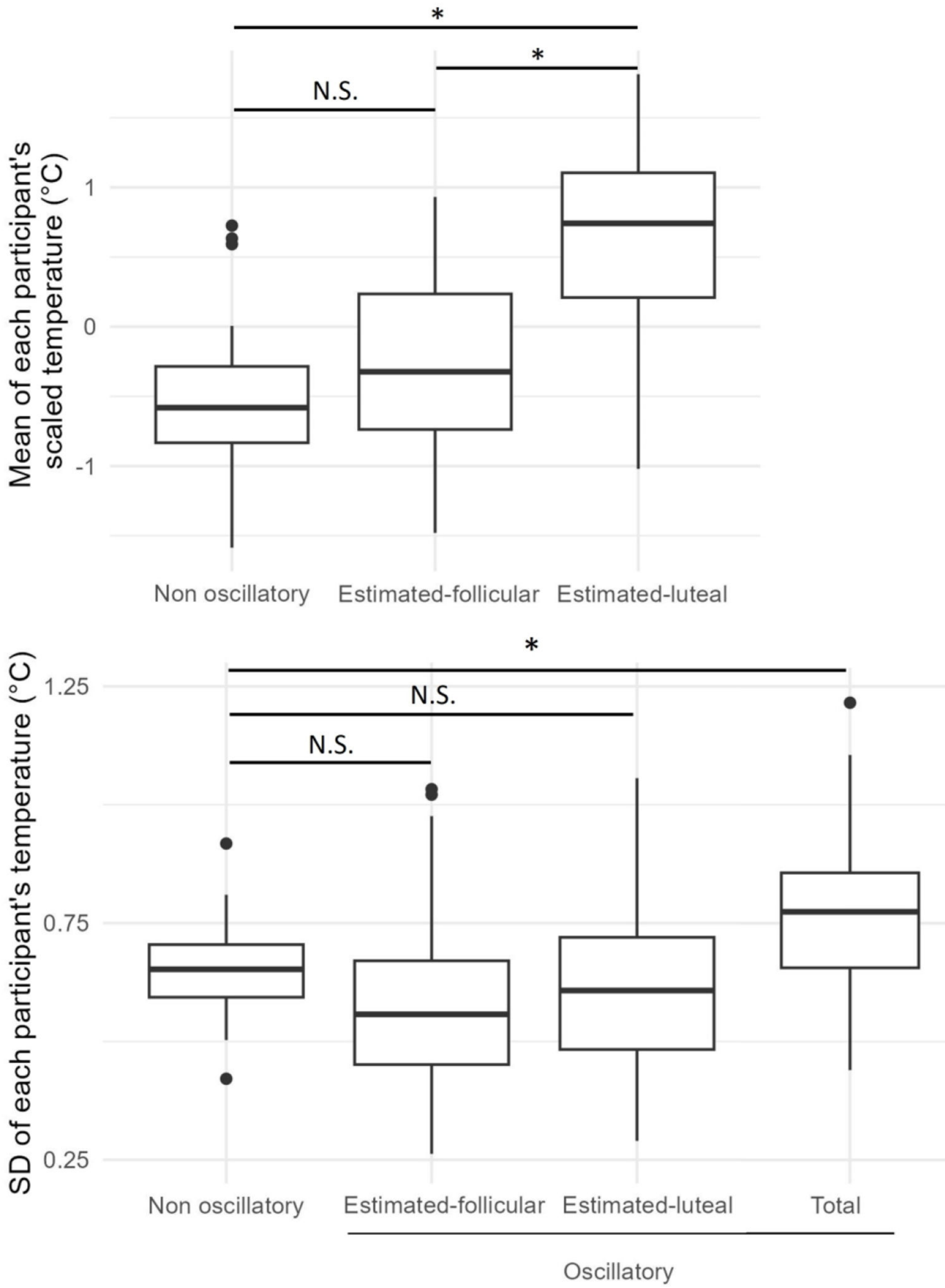

Figure 10.

Comparison between the levels and dispersion of the temperature between participants with oscillatory and non-oscillatory data. T-tests with Bonferroni correction were performed between each group, the * symbolizes a p-value < 0.05, and N.S. indicates that the groups are not significantly different.

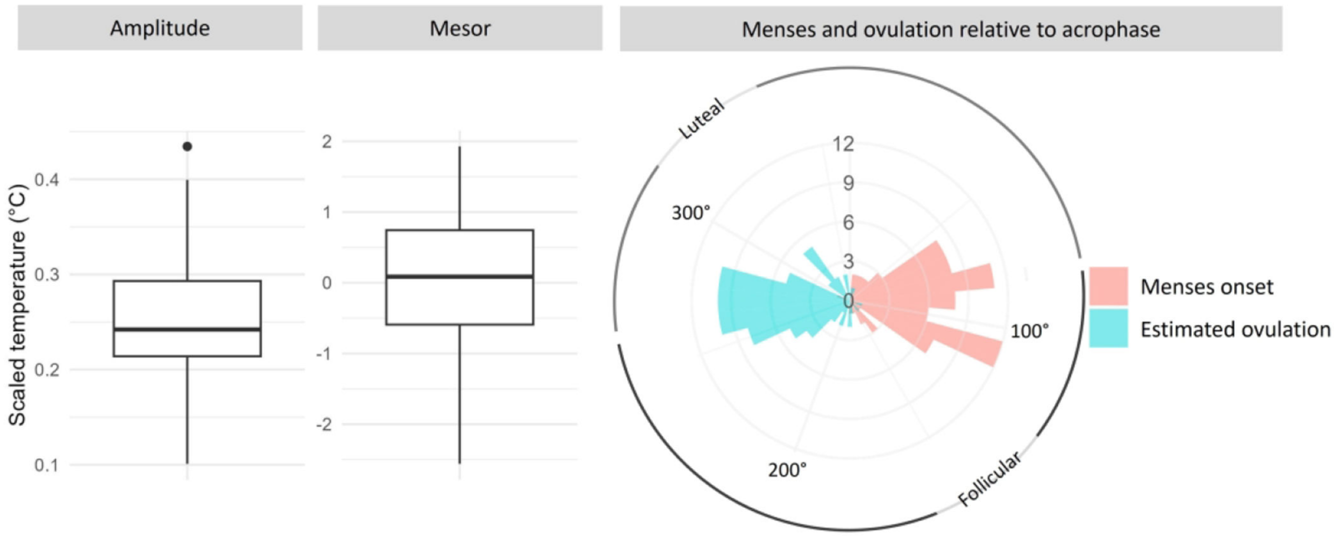

Figure 11.

On the left panel, boxplots illustrate the distribution of the mesor and amplitude of the cosinor curves obtained from the current cohort. On the right panel, a polar plot of the distribution of menses and ovulation across the menstrual rhythm of temperature relative to temperature acrophase are shown. 0° corresponds to the acrophase of the curve.

Table 1.

Characteristics of the study participants

Demographic Variables	Values
Age (Years), *M* ± *SD*	35 ± 11.56
Stage, n (%)	
Reproductive	95 (79.17%)
Menopausal transition	25 (20.83%)
Race/Ethnicity, n (%)	
White	49 (40.83%)
Asian	46 (38.33%)
Black/African American	4 (3.33%)
Latino/Latina/Latinx	13 (10.83%)
More than one race	8 (6.67%)
Site, n (%)	
SRI International	66 (55%)
University of California, Irvine	54 (45%)
Menses duration (days), ***M*** **±** ***SD***	*4.96* ± *1.27*
Menstrual cycle duration (days), ***M*** **±** ***SD***	*30.85* ± *9.41*
Proportion of a cycle studied (%), ***M*** **±** ***SD***	*121.97* ± *21.56*
LH test, n (%)	
Participants with at least one positive	104 (86.67%)
Participants with no positive despite diligently performed tests	10 (8.33%)
Participants not diligently performing tests	6 (5%)

Table 2.

LH kit vs wearable temperature method agreement: adherence and test results comparison

		Temperature fit		
		Non-oscillatory	**Oscillatory**	**Lack of adherence**
LH kit	Negative	3	7	0
	Positive	13	88	3
	Lack of adherence	1	4	1