An autocorrelation modeling method for oxygen saturation measurement during low perfusion

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Abstract

Background SpO2 is a widely used estimation of oxygen saturation owing to its convenient usage and low cost. However, SpO2 determination under low perfusion condition is severely affected by noise.

Methods In this paper, an autocorrelation modeling method for the oxygen saturation measurement during low perfusion is presented. The proposed method mainly contains two steps: calculating the autocorrelation of the photoplethysmography (PPG) signals and modeling for the parameter calculation. The autocorrelation of the PPG signals can suppress the noise and extract pulse waves from low perfusion signals. The model can realize the calculation of SpO2 with the autocorrelation signals.

Results Experiments showed that the new method had a good accuracy and stability under low perfusion condition (perfusion index (PI) ≤ 0.2%), and it was also motion-tolerant. Meanwhile, the new method showed a good performance for the oxygen saturation measurement under the condition of lower perfusion (PI = 0.1%).

Conclusions The new method could realize the calculation of SpO2 by little computation and high efficiency without extra hardware. It has strong potential in real-time clinical use.

Keywords PPG · SpO2 extraction · Low perfusion · Autocorrelation modeling method

Introduction

Saturation of peripheral oxygen (SpO2), which reflects arterial oxygenation levels, is often used to assess the function of the respiratory system and the circulation system. Pulse oximetry is a non-invasive technique, recording from extremities such as fingers and ear lobes, to continuously monitor SpO2. Owing to its cost-effectiveness benefits, pulse oximetry has become a regular monitoring device used in anesthesia, surgical operation, and intensive care (Docherty 2002; Guangda et al. 2009). However, clinical applications of pulse oximetry revealed that the measurement accuracy and precision were severely affected by motion and low peripheral perfusion caused by low ambient temperature or cardiogenic shock (Kun et al. 2009; Daxiang et al. 2004).

In case of normal perfusion, the amplitude of photoplethysmography (PPG) signals, which is used to calculate SpO2, is very ideal, and the signal-to-noise ratio (SNR) is perfect (Fig. 1a). However, in case of low perfusion, the amplitude of PPG signals becomes very small and hidden in noise. The SNR is too low to extract useful information with conventional methods (Fig. 1b). In case of motion, PPG signals are contaminated by motion artifacts. The frequency spectrum overlap of PPG signals with motion artifacts makes conventional low-pass or high-pass filter techniques inapplicable. Therefore, new methods are needed to deal with the issue mentioned above.

To overcome the shortcomings of the oxygen saturation measurement under motion and low perfusion condition, many algorithms were developed in the past few years. For instance, Masimo Corporation (2008) proposed discrete saturation transform (DST) method to adaptively filter out noise from recordings by constructing a reference noise...
Fig. 1 Simulated PPG signal and its Fourier spectra. a Normal case: PI = 3%, SpO$_2$ = 96%, PR = 60 times/min. b Low perfusion case: PI = 0.075%, SpO$_2$ = 96%, PR = 60 times/min.
(System and methods for determining blood oxygen saturation values using complex number encoding. US Patent: US7440787B2, Oct. 21 2008, 2008). Yan et al. proposed a robust minimum correlation discrete saturation transform (MCDSST) algorithm to remove motion artifact (Yan and Zhang 2008). Yousefi et al. (2014) developed a real-time adaptive algorithm to extract heart rate and SpO2 for a wireless pulse oximeter allowing users to move freely (Yousefi et al. 2014). Byung et al. proposed independent component analysis to reduce noise in PPG signals (Byung and Sun 2006). However, this method did not perform well for low perfusion interference. Foo (2006) proposed two algorithms to account for the difference between the properties of low perfusion signal and motion-contaminated PPG (Foo and Wilson 2006). However, Foo’s method for low perfusion case was a complicated non-causal filter technique commonly used for off-line analysis. In addition, many other researchers have done lots of work in PPG (photoplethysmography) signal correction with motion artifacts (Sharma 2019; Campbell et al. 2018; Zha et al. 2018). But, SpO2 was not extracted ideally in their work. Therefore, new algorithms for accurately extracting SpO2 under low perfusion are required, especially for the anesthesia, surgical operation, and intensive care application.

Here, we propose a novel autocorrelation modeling method for determining SpO2 under low perfusion condition. First, we characterize the properties of PPG signals under low perfusion condition. Then, we deduce the new autocorrelation-based SpO2 extraction method. At last, validation test results of the method on accuracy, stability, and motion-tolerance are presented. The new SpO2 extraction method has a potential application for real-time clinical use.

**Methods**

To realize the accurate measurement of SpO2 under low perfusion condition, we designed a pulse oximetry to acquire PPG signals (generated by a SpO2 simulator-Fluke Index 2XL) which are pre-processed and used for calculating the alternating component (AC) and the direct component (DC). We computed autocorrelation on recorded AC signals, and then calculated the SpO2 with the autocorrelation preprocessed signals by our modeled method. The overall process is shown in Fig. 2.

**PPG signal generation**

Photoplethysmography (PPG) signals, which are used to extract SpO2, can be obtained when illuminating the body with a light beam at a hemoglobin-sensitive wavelength. In the peripheral sites to be recorded, the volume of blood within the illuminating field alters periodically to the artery pulsation, thus generating fluctuating PPG signals. A PPG signal can be represented as an addition of an alternating component (AC) and a direct component (DC). The DC signals reflect lights that are absorbed or scattered by vein, base volume of artery, and other non-pulsatile tissue, while the AC signals reflect the volume change in the artery and arterial blood. The parameter PI (perfusion index) is an indication of the peripheral perfusion level, which can be simply calculated by the ratio of AC to DC amplitude (PI = PAC/PDC). In the low perfusion case, PI could be less than 0.2%.

To develop the new method, two kinds of PPG signals were used: (1) simulated signals and (2) recorded signals. A way to model the real low perfusion condition is lowering the peripheral temperature of the fingers. However, its controllability and reproducibility are relatively low. Therefore, we used simulated PPG signals generated by a SpO2 simulator-Fluke Index 2XL (Fluke Biomedical, USA). With the simulator, we could obtain PPG signals with preset PI2 (PI for infrared case), PR (pulse rate), and SpO2. We can preset PI2 to simulate PPG signals with different peripheral perfusion level (e.g., PI = 3%, PI = 2%, PI = 1%, PI = 0.2%, PI = 0.1%). Similarly, we can preset PR and SpO2 to simulate PPG signals with different PR and SpO2. Fluke Index 2XL signal simulator is a good tool for developing and testing the new method for low perfusion case. This helps us to simulate PPG signals with different PI and SpO2 to verify the method proposed in this paper. On the other hand, motion artifacts were modeled by directly recording the PPG signals while the users moved their fingers. A home-made reusable dual-wavelength PPG sensor was used in this case.

**Calculation of SpO2**

Hereinbefore, we have introduced the generation of the PPG signal and obtained PPG signals with the SpO2 simulator-Fluke Index 2XL, and then we should discuss how to
calculate the SpO₂ from the PPG signal. Usually, SpO₂ can be calculated according to Beer-Lambert Law, as described below.

**Principle of SpO₂ extraction**

Oxygen saturation can be calculated by the concentration of oxyhemoglobin (HbO₂) and that of deoxyhemoglobin (Hb). Since the absorption spectra of HbO₂ and Hb are different in the red and infra-red regions, two monochromatic lights are commonly used to illuminate peripheral vascular bed. Two PPG signals and two PIs are formed based on light transmission. Therefore, SpO₂ can be calculated according to Beer-Lambert Law as follows:

\[
SpO₂ = \frac{\epsilon_{\lambda_1}^{Hb} R - \epsilon_{\lambda_2}^{Hb}}{(\epsilon_{\lambda_1}^{HbO₂} - \epsilon_{\lambda_2}^{Hb})} (1)
\]

where \( \lambda_1 \) and \( \lambda_2 \) are the two wavelengths (in 660 and 940 nm); \( R \) is the ratio of the two PIs (i.e., \( R = P_{1}/P_{2} \)); \( \epsilon_{\lambda_1}^{HbO₂} \) and \( \epsilon_{\lambda_2}^{HbO₂} \) are the extinction coefficients of HbO₂ at \( \lambda_1 \) and \( \lambda_2 \); \( \epsilon_{\lambda_1}^{Hb} \) and \( \epsilon_{\lambda_2}^{Hb} \) are the extinction coefficients of Hb at \( \lambda_1 \) and \( \lambda_2 \). All the relevant coefficients are constant (Xinzong et al. 2005; Sun et al. 2018; Biagetti et al. 2019; Robust and motion artifact detection using a 1-D convolution neural network. 2020). Therefore, SpO₂ is determined as \( R \) obtained from recordings. Considering individual differences in scattering effect and other uncertainty factors, Eq. 1 is generally expanded in terms of second-order Taylor series in practice as follows:

\[
SpO₂ = A \cdot R^2 + B \cdot R + C (2)
\]

where the coefficients \( A, B, \) and \( C \) can be calibrated by fitting the data to a conic curve using least squares.

**Principle of autocorrelation modeling**

Autocorrelation modeling consists of (1) autocorrelation function computation and (2) relating SpO₂ and other parameters to autocorrelation signals. Before going to the autocorrelation modeling details, we review the autocorrelation technique firstly.

Autocorrelation technique is a weak signal detection technique, particularly for signals with cyclic properties, such as ECG. For a signal \( x(t) \), its autocorrelation function is defined as

\[
R_s(\tau) = \lim_{T \to \infty} \frac{1}{T} \int_0^T x(t) x(t+\tau) dt (3)
\]

Now, we present a simple demonstration for the noise reduction of autocorrelation technique. Given a sinusoidal signal \( s(t) = A \sin(\omega t + \phi) \) and its noise \( n(t) \), the signal \( x(t) \) is a sum of these two signals, i.e., \( x(t) = s(t) + n(t) = A \sin(\omega t + \phi) + n(t) \). Then, the autocorrelation function of this signal is

\[
R_s(\tau) = \lim_{T \to \infty} \int_0^T [s(t) + n(t)][s(t+\tau) + n(t+\tau)] dt
\]

\[
= \lim_{T \to \infty} \int_0^T s(t)s(t+\tau) dt + \lim_{T \to \infty} \int_0^T s(t)n(t+\tau) dt
\]

\[
+ \lim_{T \to \infty} \int_0^T n(t)s(t+\tau) dt + \lim_{T \to \infty} \int_0^T n(t)n(t+\tau) dt
\]

\[
= R_s(\tau) + R_m(\tau) + R_m(\tau) + R_n(\tau)
\]

The autocorrelation function has the same frequency to the original signal, and the amplitude can be related to that of the original. Therefore, the useful information can be extracted while noises are reduced (Mingkui and Zhengping 2006; Xiaozhi et al. 2007).

**Autocorrelation modeling of SpO₂**

PPG signals are regenerative and can be regarded as cyclic in a small period of time. Suppose the resolved AC component of PPG signals is denoted by \( p_{AC}(t) \), then we have

\[
p_{AC}(t) = p_{AC}(t + mT) = P_{AC} \cdot g_{AC}(t) (6)
\]

where \( T \) is the period of \( p_{AC}(t) \); \( m \) is an arbitrary constant; \( g_{AC}(t) \) is the normalization of \( p_{AC}(t) \), and \( P_{AC} \) is the amplitude of \( p_{AC}(t) \). Recall that SpO₂ is calculated from \( R \), which is the ratio of the two PIs. Since PI is defined as the ratio of AC and DC amplitude, the conventional computation of \( R \) is as follows:

\[
R = \frac{P_{I_1}}{P_{I_2}} = \frac{P_{AC1}/P_{DC1}}{P_{AC2}/P_{DC2}} = \frac{P_{AC1}/P_{AC2}}{P_{DC1}/P_{DC2}} (7)
\]

However, in the low perfusion case, both \( P_{AC1} \) and \( P_{AC2} \) are very weak and prone to be distorted by noise and interference, while the amplitude of DC component was less affected. To suppress the noise, we compute autocorrelations on recorded AC signals. Suppose the noise in the recorded AC signal \( p'_{AC}(t) \) is denoted by \( n(t) \), i.e., \( p'_{AC}(t) = p_{AC}(t) + n(t) \). The autocorrelation function of \( p'_{AC}(t) \) can be represented as follows:

\[
R_{p'_{AC}}(\tau) = R_{p_{AC}}(\tau) + R_{p_{AC}}(\tau) + R_{n_{AC}}(\tau) + R_{n}(\tau)
\]

\[
= R_{p_{AC}}(\tau) + R_{n}(\tau) = P'_{AC} \cdot g'_{AC}(\tau) (8)
\]
where \( R_{pAC}(\tau) \) and \( R_{npAC}(\tau) \) are cross-correlations of \( pAC(t) \) and \( n(t) \), which equal to zero as they are independent with each other. \( g_{AC}(\tau) \) is the normalized autocorrelation signals of \( pr_{AC}(t) \), and \( P_{AC}^\prime \) is the amplitude of autocorrelation signals of \( pr_{AC}(t) \). \( R_n(\tau) \) is only non-zero at \( \tau = 0 \). Therefore, the weak cyclic pulsation signal was retrieved from the stable autocorrelation function with a strongly suppressed noise. Besides, since the autocorrelation does not change the periodical property of the original signal, \( R_{prAC}(\tau) \) is also regenerative and has a period of \( T \) and has an amplitude proportional to the square of \( P_{AC} \), i.e.,

\[
P_{AC} = k\sqrt{P_{AC}^\prime}
\]

where \( k \) is the amplitude transfer factor (Fig. 3). Unlike sinusoidal signal, \( k \) does not exactly equal to \( 2^{1/2} \) and, in practice, we determined it empirically through experimental trials. In this way, the amplitude of AC component of the PPG signal, i.e., \( P_{AC} \), can be determined.

Given \( P_{AC} \), the perfusion index (PI) can be calculated from the amplitude of DC component \( P_{DC} \), which is relative easy to be determined; thus, we have

\[
PI = P_{AC}/P_{DC} = \left( k\sqrt{P_{AC}^\prime} \right)/P_{DC}
\]

In the dual-wavelength method, we actually obtained two PIs corresponding to wavelength \( \lambda_1 \) and \( \lambda_2 \), respectively. Therefore, with autocorrelation modeling method, we obtained \( R \) (denoted as \( R' \) to be distinguished from \( R \) calculated with Eq. 7) as follows:

\[
R' = \frac{P_{I1}}{P_{I2}} = \frac{k_1\sqrt{P_{AC1}^\prime}/k_2\sqrt{P_{AC2}^\prime}}{P_{DC1}/P_{DC2}}
\]

where \( k_1 \) and \( k_2 \) are amplitude transfer factors at the two wavelengths. Thus, we compute \( SpO_2 \) as follows:

\[
SpO_2 = A* R'^2 + B*R' + C
\]

### Implementation of \( SpO_2 \)

To extract \( SpO_2 \) accurately, the autocorrelation modeling technique, in practice, is composed of four steps described as follows.

1. Signal recording and pre-processing. The dual-wavelength signals were recorded and packed in a crosswise format for the convenience of data transmission. In the pre-processing step, data from the same source would be accumulated in a dedicated data pool for later use. After data-rearrangement, the raw data were low-pass filtered to reduce the noise and notch filtered to suppress the power-line interference.

2. \( P_{AC} \) and \( P_{DC} \) computation. As for \( P_{DC} \), the computation was relatively simple: low-pass filtering the raw data and calculating the mean value. As for \( P_{AC} \), we
processed the AC signal of original PPGs with the high-pass filter and computed the difference between the peak and the valley.

3. Computation of the autocorrelation function and its amplitude. In practice, the summation limit of autocorrelation function can never be infinite and should be truncated:

\[ R_x(m) = \frac{1}{N} \sum_{n=0}^{N-1-|m|} x(n)x(n + m) \]  

where \( N > > m \). The fast computation of autocorrelation is generally achieved by FFT and the window technique. To make the method be adaptive to real-time use, we employed the circular autocorrelation technique (Supplementary Fig. 1). Suppose the length of the data pool is \( N \), the length of autocorrelation function should also be \( N \). The tail of the pool was linked to the head. In this way, when the pool was full, the algorithm turns to the head of the data pool to restore and retrieve the new data. To compute the amplitude of the autocorrelation function, we integrated one cycle of data.

4. Computation of \( R' \) and \( \text{SpO}_2 \) according to Eqs. (9)–(12). A new set of results were generated each 6 s.

Data analysis

The new algorithm, autocorrelation modeling of \( \text{SpO}_2 \), was carried out on Matlab (MathWorks, USA). The linear regression and other statistical analysis were done by OriginPro v9.0 (OriginLab, USA) and Excel (Microsoft, USA). Statistical data were represented as mean \( \pm \) SD.

Results

In order to prove the usefulness of the autocorrelation modeling method we built, we simulated PPG signals under \( \text{PI} = 3\% \) to test the two linearity between the magnitudes of original PPG AC component \( (P_{AC}') \) and those of the autocorrelation functions \( (P_{AC}') \) firstly. It showed a nearly perfect linearity between \( P_{AC} \) and \( (P_{AC}')^{1/2} \) (Pearson’s \( r = 0.99967 \), Fig. 4a). Furthermore, the amplitude transfer factor \( k \) in Eq. (9) can be calculated from the slope of the regression line. In this case, the wavelength was \( \lambda_1 \) and \( k_1 = 1/0.348 = 2.874 \).

Then, we computed \( k_1, k_2, P_{AC1}', P_{AC2}', P_{DC1}, \) and \( P_{DC2} \). We calculated \( R \) and \( R' \) according to Eqs. (10) and (11). The linear regression of the means of \( R' \) on those of \( R \) \( (n = 10) \) yielded a regression line with a slope of 1.004 and Pearson’s \( r \) of 0.9998 (Fig. 4b).

Accuracy

To test \( \text{SpO}_2 \) extraction accuracy of the autocorrelation modeling method, we modeled the low perfusion scene by simulating PPG signals with small \( \text{PI} \) (say, \( \text{PI} = 0.2\% \) and \( 0.1\% \)) (Fig. 5). A sweep of \( \text{SpO}_2 \) (%) from 64 to 96 was generated by Fluke Index. In \( \text{PI} = 0.2\% \) cases, all the \( \text{SpO}_2 \) were accurately estimated with a high precision (SD/mean < 3%) (Fig. 6a; Table 1). In \( \text{PI} = 0.1\% \) cases, \( \text{SpO}_2 \) estimates were also accurate (SD/mean < 5%) (Fig. 6b; Table 1).

Stability

To test the stability of the autocorrelation modeling method, we continuously recorded the simulated PPG signals (\( \text{PI} = 0.2\%, \text{PR} = 70, \text{SpO}_2 = 94\% \)) for 1 h. The mean \( \text{SpO}_2 \) fall between 92 and 96 (94.3 ± 0.6) (Fig. 6c). Furthermore, we calculated PR from the autocorrelation function and got a stable and accurate estimation (69.99 ± 0.04) (Fig. 6d).

Motion-tolerance

To test the motion-tolerance of the autocorrelation modeling technique, we recorded the PPG signals of our fingers with and without shaking with our home-made dual-wavelength sensor (Tan et al. 2013). The experiment recorded two fingers

**Autocorrelation modeling results**

The new autocorrelation modeling method was built based on two linearity assumptions: (1) the amplitude of original AC component is proportional to the square root of that of autocorrelation function as denoted by Eq. (9), and (2) the substitution of \( R \) with \( R' \) in Eq. (2). Here, we test the two linearity assumptions.

First, we created PPG signals in \( \text{PI} = 3\%, \text{PR} = 75, \) and \( \text{SpO}_2 \) (%) ranges from 36 to 100 using Fluke Index. The simulated signal at each \( \text{SpO}_2 \) was recorded and transmitted to PC.

We calculated the magnitudes of the original PPG AC component \( (P_{AC}') \) and those of the autocorrelation functions \( (P_{AC}') \). Since values of \( P_{AC} \) under different \( \text{SpO}_2 \) settings are different, a sweep of \( \text{SpO}_2 \) (%) from 36 to 100 yielded a sufficient multi-level coverage of PPG signals. At each \( \text{SpO}_2 \) settings, we calculated \( P_{AC} \) and \( (P_{AC}')^{1/2} \) times. The linear regression was conducted on means of each pair \( (n = 10) \). It showed a nearly perfect linearity between \( P_{AC} \) and \( (P_{AC}')^{1/2} \) (Pearson’s \( r = 0.99967 \), Fig. 4a). Furthermore, the amplitude transfer factor \( k \) in Eq. (9) can be calculated from the slope of the regression line. In this case, the wavelength was \( \lambda_1 \) and \( k_1 = 1/0.348 = 2.874 \).

Then, we computed \( k_1, k_2, P_{AC1}', P_{AC2}', P_{DC1}, \) and \( P_{DC2} \). We calculated \( R \) and \( R' \) according to Eqs. (10) and (11). The linear regression of the means of \( R' \) on those of \( R \) \( (n = 10) \) yielded a regression line with a slope of 1.004 and Pearson’s \( r \) of 0.9998 (Fig. 4b).
shaking (about 1 to 4 s and 9 to 11 s, Fig. 7a). Apparently, the PPG signals with finger shaking were contaminated by interference (Fig. 7a). We calculated the autocorrelation function results of the PPG signals contaminated by interference. The interference was severely suppressed (Fig. 7b).

**Discussion**

In this paper, we have described a new SpO₂ extraction method called autocorrelation modeling. In Fig. 5, we modeled the low perfusion scene by simulating PPG signals in PI = 0.2% and 0.1% with Fluke Index. Through the autocorrelation function, it shows that the proposed PPG AC signals in PI = 0.2% and 0.1% can be extracted ideally from the original PPG AC signals. The autocorrelation function can well remove the noise in PPG signals and get a smooth and reliable PPG signal. It can be seen that the noise in PPG signals in PI = 0.1% is large, the autocorrelation method can still remove it ideally, and this makes the autocorrelation modeling method proposed in this paper to calculate the SpO₂ be possible.

The autocorrelation modeling method involved computation of the autocorrelation function and relating its magnitude to that of the original PPG signals. Autocorrelation strongly suppressed the noise and picked out the weak PPG signals under low perfusion condition. We demonstrated a good linearity between the magnitude of PPG signals and the square root of that of the autocorrelation function, upon which SpO₂ could be accurately extracted. The validation experiments using SpO₂ simulator demonstrated the high accuracy of the method in case of low perfusion (PI = 0.2%).
This indicates that the autocorrelation method proposed in this paper can be well applied in the clinical use of pulse oximetry. Besides, the application of autocorrelation technique also strengthened the ability of motion-tolerance (Fig. 7).

In the clinical use of pulse oximetry, the $SpO_2$ determination under low perfusion condition caused by low ambient temperature or cardiogenic shock (Guangda et al. 2009; Kun et al. 2009) is severely affected by noise. This brings a lot of trouble to clinical work, such as false decreasing of $SpO_2$, making it important to improve the accuracy of $SpO_2$. Compared with the adaptive method using extra hardware, like accelerators to sense the motion, the new method enhances PPG signals by using its inherent cyclic properties. Since the computation of autocorrelation function could be achieved by Fast Fourier Transformation (FFT), the new method is suitable for real-time application.

### Table 1 $SpO_2$ estimates under low perfusion condition

| Preset $SpO_2$ (%) | PI = 0.2% | PI = 0.1% |
|--------------------|-----------|-----------|
|                    | 64 74 84 90 94 | 96 76 82 86 90 94 |
| Mean of estimates  | 67.2 75.8 85.4 90.8 94.3 | 95.7 75.2 82.3 85.6 89.7 93.7 |
| SD of estimates    | 1.7 1.4 1.4 0.8 0.6 | 0.6 3.7 2.6 2.2 2.4 1.6 |

### Fig. 6 $SpO_2$ and PR extracted using autocorrelation modeling method

### Fig. 7 Recorded PPG signal in case of body movement
Conclusions

In this paper, we introduced a method named autocorrelation modeling to solve the issue of inaccurate SpO2 measurement under low perfusion in the clinical use. The validation experiments showed the autocorrelation modeling method can strongly suppress the noise and extract ideal PPG signals from the original PPG signals under low perfusion condition. The autocorrelation modeling technique showed a high accuracy of the method in case of low perfusion (PI = 0.2%). The validation experiments showed a strong potential in real-time clinical use for the autocorrelation modeling method.

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Author contribution Shuangping Tan designed the method described in this manuscript and designed the experiment to verify the method and was the major contributor in writing the manuscript. Jie Wei and Hao Chen analyzed and interpreted the experiment data, and also contributed to the writing of the manuscript. Tong Zhang, Youfeng Deng, and Hongbin Zuo provided a lot of help for the experimental method and writing of this paper. Xiali Wu analyzed and interpreted the experiment data. All the authors read and approved the final manuscript.

Data availability All data generated and analyzed during this study are included in this published article, and any further details of this study are available from the corresponding author on reasonable request.

Code availability Not applicable.

Declarations

Ethics approval and consent to participate All the authors and participants declare that we have read and have abided by the statement of ethical standards.

Consent for publication None of the material related to this manuscript has been published or is under consideration for publication elsewhere, including the internet. All the authors and participants understand that the information will be published, have read this manuscript, and approve to have it considered exclusively for publication.

Competing interests The authors declare no competing interests.

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