Model based analytical approach for physical activity quantification in people with type 1 diabetes.

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Abstract

Physical activity (PA) represents a significant challenge in the management of type 1 diabetes (T1D), given its impact on glucose levels, which are influenced by various exercise characteristics, including duration, intensity, and type. The development of strategies that allow for the monitoring of these characteristics is crucial to improve glycemic control during exercise for both conventional therapies and automated insulin delivery systems. This paper presents a state-space model that further exploits the HR signal for the purpose of quantifying and distinguishing between aerobic and anaerobic PA. The model design is based on an analysis of the distinctive features of HR signal, including the mean HR value, the maximum HR, and the presence of pronounced fluctuations in HR. This method does not require any training and offers users interpretability and explainability. Furthermore, it enables intuitive tuning, a feature which is of particular importance in clinical settings. The model is validated using two clinical trials: the T1DEXI study, which is the largest real-world clinical trial including PA in people with T1D conducted to date, and a pilot clinical trial conducted by our research group in Argentina. The findings indicate the model has the capacity to quantify and differentiate between aerobic and resistance PA, which represent the two types of PA exhibiting the most significant and contrasting influence on glucose levels.

Keywords: type 1 diabetes, physical activity, exercise, dynamic model

1 Introduction

Type 1 diabetes (T1D) is a chronic condition resulting from the autoimmune destruction of pancreatic β-cells, which are responsible for producing insulin, an essential hormone for converting blood glucose (BG) into energy [1]. Consequently, one of the main characteristics of T1D is elevated BG levels which, in the long term, can lead to severe health complications. Therefore, the treatment for T1D consists of the exogenous administration of insulin. This is traditionally delivered via multiple daily injections (MDI) or through an insulin pump [1, 2]. However, this places a considerable burden on individuals, as it is necessary to monitor BG levels continuously and to calculate insulin doses.

The most advanced therapies to date are the automated insulin delivery (AID) systems, designed to achieve automatic BG regulation with the objective of reducing the burden of traditional insulin therapy. AID systems comprise a continuous glucose monitor (CGM) that provides BG readings to a control algorithm. This algorithm then calculates the necessary insulin doses to be delivered by an insulin pump. Nevertheless, fully closed-loop (FCL) systems remain under development due to the limitations of current technology, such as the lag time associated with CGM and the delays in insulin action. Instead, commercially available hybrid closed-loop (HCL) systems integrate automated insulin delivery during fasting periods, designated as basal insulin, with manual insulin boluses to compensate for meal intake [3, 4].

One of the challenges to be overcome in the development of FCL AID systems is the management of physical activity (PA) [5–8]. While there is a clear association between PA and health benefits [9–11], previous studies have established that PA affects BG levels, further complicating their regulation [12, 13]. Moreover, the

magnitude of the changes in BG depend on factors such as duration, intensity and, particularly, the type of PA. There is evidence that aerobic exercise is associated with a reduction in BG levels [12–14]. On the other hand, resistance exercise may result in a smaller decrease or even an increase in BG levels [12–14]. Meanwhile, interval exercise exhibits an intermediate effect between the two aforementioned cases [12–14]. As a consequence, individuals with T1D may prefer to avoid PA, primarily due to fear of potential episodes of hypoglycemia [15, 16]. This may subsequently increase the risk of not meeting the minimal exercise requirements established in clinical guidelines [12, 17]. In order to address this issue, a series of empirical strategies for adjusting insulin doses and carbohydrate intake in exercise situations may be employed [12, 17, 18]. Nevertheless, these strategies necessitate user input, which deviates from the aim of developing a FCL AID system.

In order to address complications associated with BG regulation during exercise, the use of signals from wearable devices, including heart rate (HR) and accelerometer data, is being explored. Some authors have even incorporated these signals to adapt the control algorithms during exercise [19–23]. A wide range of works employ machine learning-based methodologies in order to detect, classify and acquire information such as intensity of an exercise session [24–31]. Furthermore, potential extensions of the dynamic glucose-insulin models in order to incorporate the impact of PA were also explored [32–38]. In particular, Deichmann et al. [37] employed accelerometer data to quantify the intensity and duration of aerobic exercise. An alternative approach, was presented by Alkhateeb et al. [35], who employed the percentage of maximal oxygen consumption as an indicator of PA intensity to develop six variations of a glucose-insulin model to capture the effects of moderate exercise. Hobbs et al. [34] used HR as an indicator of exercise intensity, with the objective of establishing a dynamic relationship between PA intensity and changes in BG for aerobic exercise. The aforementioned studies exclusively examine the effects of aerobic exercise. While others, such as those conducted by Young et al. [38] and Turksoy et al. [20], incorporate resistance exercise into their validation processes, but they have not explicitly quantified or differentiated between these two types of PA, which is a crucial consideration for the management of T1D during exercise.

The development of methods to quantify and differentiate between the various types of exercise is currently a pivotal area of research in the management of T1D. The distinction between aerobic and resistance activities is of particular significance, as clinical evidence shows that these have markedly different effects on glucose and, consequently, on insulin requirements [12, 14]. This paper introduces a dynamic state-space model that enables the real-time differentiation and quantification of the type and intensity of PA. In contrast to existing models that represent the impact of exercise on glucose [32, 37], this model does not attempt to represent this impact. Instead, it aims to provide information on the type of exercise performed. This is achieved by leveraging the information that can be extracted from the HR signal, considering not only the magnitude of HR, but also its variability and mean value during aerobic and anaerobic exercise, thereby enabling differentiation between the two. Additionally, the dynamic model avoids the restriction of categorising exercises according to a predefined set of labels. Instead, it provides a quantitative representation of the predominant exercise type, which is advantageous in a real-world context, where fully aerobic and anaerobic exercise are not mutually exclusive. Moreover, in comparison to data-driven approaches, this method provides both explainability and an intuitive fitting process, and does not require any training with data, which reduces its computational cost. The model consists of two systems of differential equations: one representing aerobic exercise and the other one representing anaerobic exercise. Furthermore, the proposed model is validated using data from two recent clinical trials. One of them is the Type 1 Diabetes Exercise Initiative (T1DEXI) clinical trial [39], which is the largest study to date examining the impact of PA in adults with T1D. It has facilitated numerous contributions [30, 31, 38, 40–42], including the development of an exercise classification [30], an exercise decision support system [38], and a system for predicting the risk of hypoglycemia during and after exercise [31]. The second trial is a pilot study conducted in Argentina by our research group. The objective of this pilot study was to validate the model with aerobic and resistance exercise sessions, in which the specific activity performed is known in detail. The findings demonstrate the capability of the proposed model to differentiate between aerobic and anaerobic exercise, thereby enabling the predominant type of PA to be identified. Moreover, its potential application in the context of glucose regulation during exercise is emphasised when integrated with other techniques to confirm or detect PA.

2 Model Building

This section presents a comprehensive description of the state-space dynamic model developed to capture the aerobic and anaerobic exercise using only the HR signal. The model incorporates four dynamic states, two of which are designed to represent short- and long-term aerobic exercise, while the remaining two correspond to

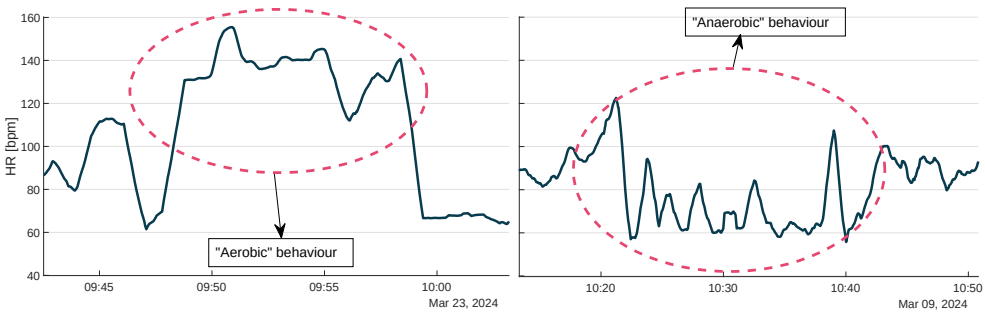

Figure 1: Illustrative example of different heart rate (HR) behaviours during a real-world aerobic exercise session (left plot) and during a real-world anaerobic exercise session (right plot)

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short- and long-term anaerobic exercise. An illustrative example of an application using data from a real-world context is also presented to illustrate how these states work.

2.1 Proposed state-space model

In this section, the differential equations of the model are presented, and the characteristics that enable the distinction between aerobic and anaerobic exercise are described. Firstly, the model corresponding to aerobic exercise is presented, followed by the model corresponding to anaerobic exercise.

2.1.1 Aerobic exercise states

The aerobic exercise model, as presented in Equation 1, incorporates two distinct states. The first state represents the charge of short-term aerobic exercise, which is denoted by A_s. The second state represents the long-term charge of aerobic exercise, which is called A_l. The state A_s is designed to converge to the value of the variable h with a time constant τ_{A_s}, and the state A_l to converge to the value of A_s with a time constant τ_{A_l}.

$$\dot{A}_s = -\frac{(A_s - h)}{\tau_{A_s}}, \quad \dot{A}_l \ = -\frac{(A_l - A_s)}{\tau_{A_l}} \tag{1}$$

It is to be expected that during aerobic exercise, such as running, the mean HR value will increase, and to remain high throughout the course of the exercise session. A conceptual illustration of this behavioural pattern is presented in the first column of Figure 1. Consequently, by employing an appropriate design for the variable h, it is possible to induce a reaction in the states when the HR exhibits the typical characteristics associated with aerobic exercise, i.e. a detectable increase in its mean value.

One method for detecting the HR behaviour during aerobic exercise is to ascertain whether the HR exceeds a certain minimum threshold. At this point, the states can initiate a reaction, thereby ensuring that states are not loaded in the absence of exercise. In this paper, a lower and an upper threshold are defined based on the user's maximum HR (HR_{max}), usually defined as in Equation 2.

$$HR_{max} = 220 - \textit{user's age}. \tag{2}$$

Equation 3 presents the proposal for the variable h.

$$h = \begin{cases} 0 & HR(t) < HR_l \\ \frac{HR(t) - \mathrm{HR}_l}{HR_h - HR_l} & HR_l \leq HR(t) < HR_h \\ 1 & HR_h \leq HR(t) \end{cases} \tag{3}$$

Where HR_L and HR_H are the lower and higher thresholds which are calculated as:

$$HR_L = \alpha_L \cdot HR_{max}, \quad HR_H = \alpha_H \cdot HR_{max}. \tag{4}$$

The variables α_L and α_H in Equation 4 are tuning parameters, defined within the interval $[0, 1]$, which permit the specification of the HR at which the states are loaded. Here, we consider $\alpha_L = 0.6$ and $\alpha_H = 0.8$

as typical values within the aerobic exercise range for HR.Therefore, Equation 3 is equal to zero when HR is below 60% of the HR_{max}. When HR is within the range of $[60, 80]$% of the HR_{max}, the value of h increases linearly with HR. Finally, when HR is above 80% of HR_{max}, h is equal to 1. This definition of h implies that the states increase in accordance with a first-order dynamics when A_s is lower than h and the HR is greater than 60% of the HR_{max}, and decrease to 0 when the HR is less than 60% of the HR_{max}.

Regarding τ_{As} and τ_{Al}, two distinct values are proposed for each time constant, corresponding to the increase ($\tau_{As_{inc}}$) and decrease ($\tau_{As_{dec}}$) of the states, as shown in Equation 5.

$$\tau_{As} = \begin{cases} \tau_{As_{inc}}, \ if \ h - A_s(t) > 0 \\ \tau_{As_{dec}}, \ if \ h - A_s(t) \leq 0 \end{cases}, \ \tau_{Al} = \begin{cases} \tau_{Al_{inc}}, \ if \ A_l(t) - A_s(t) \leq 0 \\ \tau_{Al_{dec}}, \ if \ A_l(t) - A_s(t) > 0 \end{cases} \tag{5}$$

This feature may be employed in order to adjust the speed at which the model detects the beginning and end of the exercise, thereby enabling the model to be more or less responsive to fluctuations in the HR. In line with the aforementioned rationale and taking as reference the time constants reported in previous studies [32, 37], the value of $\tau_{As_{inc}}$ is set to 10 minutes, while $\tau_{As_{dec}}$ is set to 5 minutes. This approach allows the state to demonstrate diminished reactivity when the HR undergoes a transient increase, thereby reducing the occurrence of false detections. In regard to the values of $\tau_{Al_{inc}}$ and $\tau_{Al_{dec}}$, the former is established in 10 minutes and the latter in 24 hours, so as to reflect the long-term effect of the exercise indicated by clinical evidence [12, 39, 43].

2.1.2 Anaerobic exercise states

The anaerobic state-space model is shown in Equation 6, where N_s and N_l represent the short and long-term anaerobic states, respectively. The states evolve in time with a first-order dynamics, where N_s tends to the value of g with a time constant τ_{Ns} and N_l to the value of N_s with a time constant τ_{Ns}.

$$\dot{N_s} = -\frac{(N_s - g)}{\tau_{Ns}}, \quad \dot{N_l} = -\frac{(N_l - N_s)}{\tau_{Nl}} \tag{6}$$

Anaerobic exercise, such as weight lifting or the use of elastic bands, comprises a combination of static and dynamic contractions. Each set of this type of exercise involves a given number of repetitions, followed by a rest period. Therefore, it is reasonable to expect that in this case the HR exhibits a pattern with greater variability or fluctuations than that observed during aerobic exercise, as illustrated in the second column of Figure 1

In this case, the values to which the state converge to are a function of the variable g. In order to capture fluctuating behaviours, the function g, shown in Equation 7, is proposed as a candidate.

$$g = \begin{cases} 1 & (\Delta HR_{max} > \delta_h) \,\&\, (\Delta HR_w \leq \epsilon) \,\&\, \left(\overline{HR}_w \leq \widehat{HR}\right) \\ \frac{\Delta HR_{max} - \delta_l}{\delta_h - \delta_l} & (\delta_l < \Delta HR_{max} \leq \delta_h) \,\&\, (\Delta HR_w \leq \epsilon) \,\&\, \left(\overline{HR}_w \leq \widehat{HR}\right) \\ 0 & \text{otherwise.} \end{cases} \tag{7}$$

Figure 2 illustrates the HR patterns that are not intended to be detected (left plot) and those that are intended to be detected (right plot) with the g function, which is subject to three conditions:

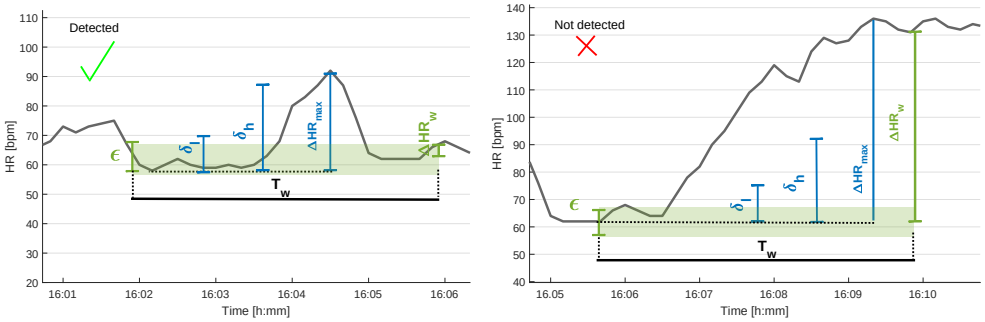


Figure 2: Illustrative example of the behaviour to which the function g reacts (left plot) and to which it does not react (right plot). The variable ΔHR_{max} and the threshold δ_h and δ_l are shown in blue. Similarly, the variable ΔHR_w and the threshold ϵ are shown in green.

The first condition compares the thresholds δ_h and δ_l with the variable ΔHR_{max}, represented by the blue lines in Figure 2. ΔHR_{max} can be calculated using the following expression:

$$\Delta HR_{max} = max\{HR(t - T_w : t)\} - min\{HR(t - T_w : t)\}. \tag{8}$$

This equation represents the difference between the maximum and minimum HR values within a given time window, with a width determined by a parameter called T_w, which is represented by a continuous black line in Figure 2. In this study, a time window of $T_w = 5$ minutes is considered, in alignment with the typical practice of anaerobic exercise, which involves the completion of brief, approximately four-minute sessions, followed by brief intermissions [12]. With regard to the value of the thresholds, δ_l should be adjusted in order to avoid an increase in the state N_s due to minor fluctuations in the HR signal, while ensuring that the peaks resulting from exercise are not missed. In this case, δ_l is set to 15 [bpm], while δ_h is set to $\delta_h = 2\delta_l = 30$ [bpm].

The second condition compares the value of ΔHR_w, which can be calculated using Equation 9, with the threshold ϵ. The two variables are illustrated in Figure 2 by a green line.

$$\Delta HR_w = |HR(t) - HR(t - T_w)|\,. \tag{9}$$

Therefore, if $\Delta HR_w \leq \epsilon$ is satisfied, it means that the first and last HR values of the time window fall within the shaded green area, as shown in the lower plot of Figure 2. Conversely, if the inequality $\Delta HR_w \leq \epsilon$ is satisfied, even if $\Delta HR_{max} > \delta_h$ has occurred, it can be concluded that the HR has not yet decreased sufficiently. An illustrative example of this can be observed in the upper plot of Figure 2. This is used to check that an increase in HR is followed by a decrease as expected during the short recovery periods typical of anaerobic exercise. Its reasonable to consider that ϵ cannot be zero, as the HR may not return exactly to the initial value during rest periods. Instead, it returns to a value that is close to the initial value. In this work it is established that $\epsilon = 5$ [bpm].

The third condition considers the mean value of the HR ($\overline{HR}_w$), which is compared with the threshold $\widehat{HR}$ within the time window. Its objective is to guarantee that the HR does not remain at excessively elevated levels, as is the case with aerobic exercise. For this reason $\widehat{HR}$ is set $60\%HR_{max}$ since greater are considered to be aerobic exercise.

Thus, the function g exhibits linear behaviour between the values $[0, 1]$ when $\Delta HR_{max} \in [\delta_l, \delta_h]$, is 1 when a peak on HR is present and is higher than δ_h, and is 0 when the jump is lower than δ_l or when it remains at approximately constant high values.

Finally, Equation 10 defines the time constants associated with the anaerobic state-space model.

$$\tau_{Ns} = \begin{cases} \tau_{Ns_{inc}}, & if\ g - N_s(t) > 0 \\ \tau_{Ns_{dec}}, & if\ g - N_s(t) \leq 0 \end{cases}, \quad \tau_{Nl} = \begin{cases} \tau_{Nl_{inc}}, & if\ N_l(t) - N_s(t) \leq 0 \\ \tau_{Nl_{dec}}, & if\ N_l(t) - N_s(t) > 0 \end{cases} \tag{10}$$

As with the aerobic case, these constants manifest two distinct values in accordance with state increase or decrease, and their tuning can be employed to alter the dynamics of state reaction. In light of the variable behaviour exhibited by the HR in this case, a more immediate response is necessary than in the aerobic scenario, with a subsequent reduction in pace to mitigate the oscillations. In consideration of the time constants reported in [32, 37], and given that the duration of anaerobic activities generally comprises a series of four-to-five-minute periods, the time constants are established at $\tau_{inc} = 4$ [min] and $\tau_{dec} = 8$ [min]. The long term time constants are set to reflect the long-term effect of PA [12, 39, 43] $\tau_{Al_{inc}} = 10[min]$ and $\tau_{Nl_{dec}} = 24[h]$.

2.2 Conceptual interpretation of the model response.

Figure 3 presents a conceptual illustration of the potential interpretations of the model output corresponding to various types and intensities of PA. The first row shows the HR for fourth different exercise scenarios, while the second row illustrates the model output for the states A_s, A_l, N_s and N_l for each of them. The third row presents the interpretation of the model's output, while the last row shows the expected impact of the exercise on glucose [12, 39]. In the first column, it can be observed that the model output indicates a greater increase in the aerobic states (A_s and A_l) compared to the anaerobic states (N_s and N_l), signifying that the exercise predominantly involves aerobic activity. Similarly, the second column shows that A_s and A_l increases are higher than those of N_s and N_l and even higher than those observed in the first column. This suggests that, while the exercise remains predominantly aerobic, it exhibits a higher intensity compared to that observed in the first column. In contrast, the third column presents a scenario in which the model output indicates a notable increase

in both aerobic and anaerobic states, with a more substantial increase in N_s and N_l. This observation can be interpreted as indicative of exercise that is primarily anaerobic in nature. The fourth column demonstrates that both N_s and N_l exhibit a greater increase relative to the previous cases, indicating that anaerobic exercise is predominant and characterised by even higher intensity. It is important to note that users have the capacity to adjust the parameters, denoted as α_L and α_H, to ascertain the range of HR at which the model responds to aerobic exercise, thereby rendering it more or less sensitive to elevated HR values. Similarly, it is feasible to modify the sensitivity to HR peaks during anaerobic exercise by adjusting the parameters designated as δ_L and δ_H. This feature facilitates the customisation of the model to the user's particular fitness level.

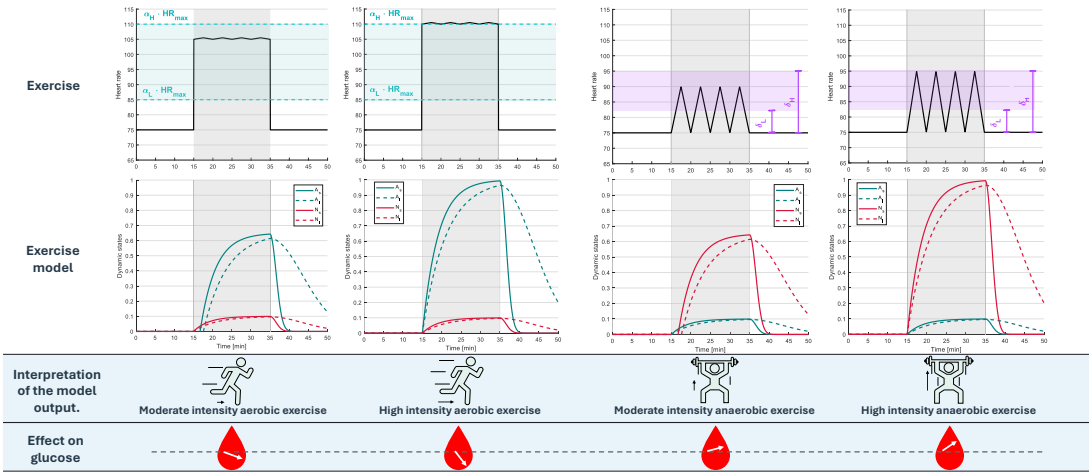


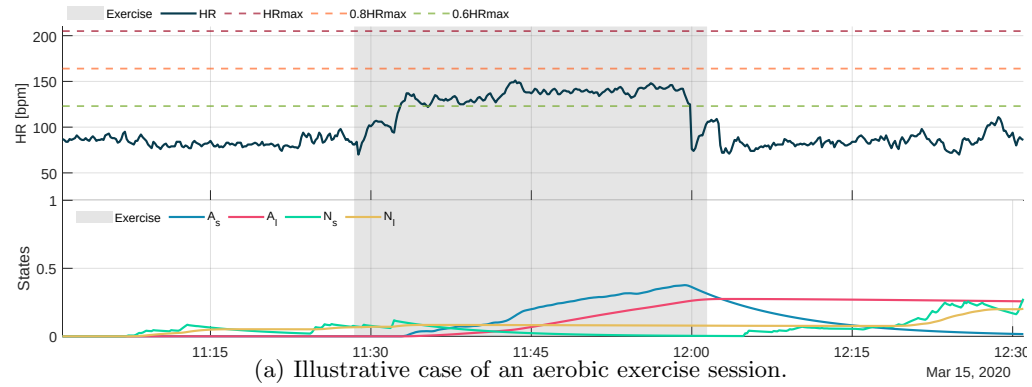
Figure 3: Conceptual illustration of the model output according to the states and heart rate behaviour.

2.3 Application example

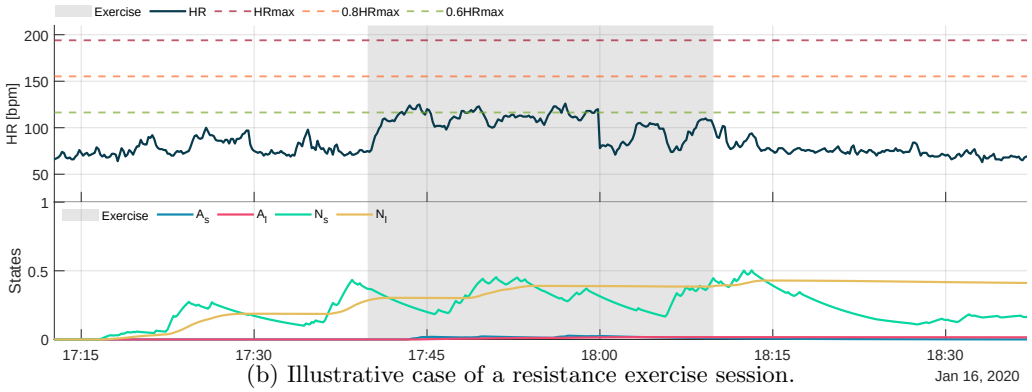
Figure 4a depicts the HR (upper plot) and the response of the states A_s, A_l, N_s and N_l (lower plot) during an aerobic exercise session. Prior to the start of the exercise session, the HR is at its resting value, while the model states are close to zero. At the start of the exercise at approximately 11:30, the HR exhibits an increase and subsequently maintains a range of $60-80\%$ of the HR_{max} throughout the session. During this time interval, it is observed that the states A_s and A_l respond to this HR behaviour. In contrast, the N_s and N_l states remain unresponsive throughout the session, with the exception of minor fluctuations observed at 11:30 and 12:20, which can be attributed to the HR peaks. Similarly, an example of a resistance session is illustrated in Figure 4b. In this instance, A_s and A_l remain unresponsive, while N_s and N_l exhibit a reaction attributable to the peaks in HR that occur during the session. Furthermore, it is also observed that before the exercise session is initiated, the model identifies peaks in HR at approximately 17:20. This may be attributed to unannounced or unplanned PA, such as cleaning or climbing stairs, as the peaks are not indicative of the resting state, as they are after 18:15, where the states begin to decrease.

3 Model validation with the T1DEXI study

The T1DEXI study is the largest a real-world clinical trial to date. It examined the impact of PA on 497 adults with T1D [39]. The trial employed a random assignment of participants to structured sessions comprising aerobic, interval, or resistance exercise. Each participant engaged in a minimum of six 30-minute sessions, conducted at home environment, over a four-week observation period. This resulted in a total of 905 aerobic, 903 interval, and 948 resistance structured sessions. Furthermore, treatments with HCL systems, MDI and the standard insulin pump were considered. The design of the exercise sessions was based on a specific objective, which was aligned with the type of exercise. In the case of aerobic sessions, the objective was to achieve a certain level of HR, either $70-80\%$ of the age-related maximum HR, or $80-90\%$ of the age-related maximum HR for interval sessions. The objective of resistance training was to induce a fatigue response in the major muscle groups. Throughout this process, BG and HR signals were collected between others. For more details of the study cohort, the study design, inclusion and exclusion criteria and methods employed, please refer to [39].



(a) Illustrative case of an aerobic exercise session.



(b) Illustrative case of a resistance exercise session.

Figure 4: Illustrative example of the response of the dynamic model during real-world exercise sessions. The first row shows heart rate (HR), maximum HR (HRmax) and the 60% and 80% HRmax thresholds defined for aerobic exercise. The second row shows the temporal evolution of the aerobic (A_s, A_l) and anaerobic (N_s, N_l) model states.

3.1 Data description and processing

This section presents an analysis of the T1DEXI structured exercise sessions. Furthermore, the validation of the model presented in Section 2.1 is performed using these sessions. The analysis considers all three treatments included in the T1DEXI. The HR and CGM readings are collected from the half-hour preceding the start of exercise and throughout the course of the exercise session. In order to minimise the possibility of introducing uncertainty into the model and to focus the analysis on its performance, sessions with missing HR readings are excluded, given that the dynamic model utilises this information as an input signal. This process yielded a total of 1,166 sessions, comprising 387 aerobic, 416 resistance, and 363 interval sessions.

Figure 5 shows a box-plot illustrating the difference between the CGM readings taken at the beginning and end of each session (ΔCGM), allowing the visualisation of the immediate impact that each exercise type has on BG levels. The results indicate a change in BG levels of -14.07 $[-37.03,\ 4.5]$[mg/dl] for aerobic exercise, -15.40 $[-35.83,\ 5.13]$[mg/dl] for interval sessions and -5.43 $[-22.24,\ 10.98]$[mg/dl] for resistance exercise. Statistical analysis using the Wilcoxon non-parametric test demonstrates that there is no statistically significant difference between the impact of aerobic and interval exercise on BG levels for the data subset under analysis. However, it is important to note that when all data and other relevant considerations are included in the analysis of the primary study, the difference was found to be statistically significant [39]. Additionally, in order to ascertain whether post-exercise effects, including increased insulin sensitivity and altered glucose uptake, vary between different types of PA, time in range (TIR, [70, 180] [mg/dL]) was calculated over the 24 hours following sessions. No significant differences were observed between the groups, which is consistent with the results reported in previous studies [39]. Finally, it is important to note that the primary objective of this analysis is to illustrate the impact of each type of exercise on glucose, which constitutes the primary finding of the original T1DEXI study, wherein such effects are analysed in depth [39].

Figure 6 illustrates the distribution of the mean (left columns) and maximum (right column) HR from the half-hour interval preceding the start of the exercise (blue), in comparison with the corresponding histogram

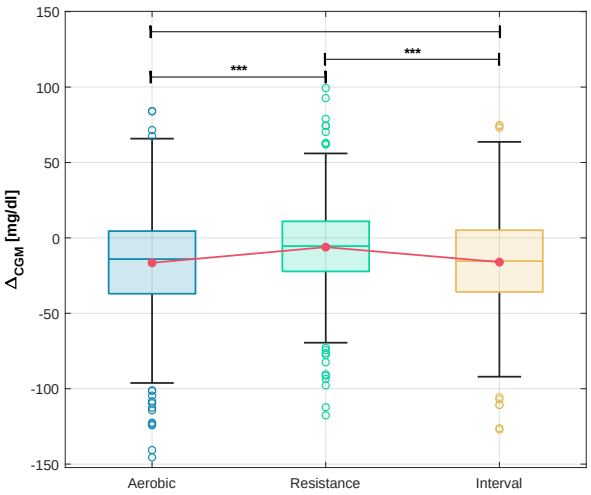


Figure 5: Difference between CGM measurements at the beginning and end of exercise sessions (Δ_{CGM}) from T1DEXI trial. The red dots show the mean value. The statistical significance between the effect of each type of exercise on BG is show ($^*\rho < 0.05, ^{**}0.001 < \rho < 0.05, ^{***}\rho < 0.0001$).

obtained during each exercise session (red). In the left column, the first row shows the histogram for the aerobic sessions, where the mean and standard deviation (STD) of HR are 115.95 (13.97) [bpm] compared to the resting state 87.87 (12.96) [bpm]. In addition, it can be observed that during exercise there are many subjects who do not reach the target of $70-80\%$ of the maximum HR, which is represented by the dashed lines. The second row corresponds to the resistance exercise, where it is observed that prior to the session, the distribution is similar to that observed in the aerobic case, with a mean of 86.76 (11.78) [bpm]. Conversely, during the resistance sessions, the HR demonstrates a less pronounced increase in comparison to that observed during aerobic exercise. The third row presents the interval sessions, which exhibit values of 86.36 (11.95) [bpm] for rest and 103.61 (11.56) [bpm] during the sessions, which are well below the target range of $80-90\%$ of maximum HR. Furthermore, the second column shows a histogram of the maximum HR value attained before (blue) and during (red) the exercise period. In comparison to the data presented in the left column, which demonstrates that the aerobic exercise distribution exhibits higher mean HR values than interval and resistance exercise, the distribution of the maximum HR values during exercise is similar across all three types of sessions. This aligns with the model design presented in section 2.1, where the mean value of the HR is considered a key differentiating factor between aerobic and anaerobic activity. The decision to designate the 30 minutes prior to exercise as a period of rest is predicated on the premise that this approach is more straightforward and convenient than utilising a confirmed rest period, such as overnight. The complexity of data processing is attributable to the substantial volume of information that is contained within the T1DEXI dataset. Furthermore, the results indicate a notable distinction between the HR during this period and during exercise.

It can be observed that the HR achieved during the interval sessions did not attain the target level, a finding that is in alignment with the outcomes of the original study [39]. Furthermore, an analysis of the maximum HR values, which are expected to be higher during interval exercise, reveals that the aerobic, interval, and resistance sessions reach similar values within the range of $80-90\%$ of the maximum HR. Finally, the greatest contrast in BG impact is observed between aerobic and resistance exercise. It is important to note that this is a characteristic of these particular interval session set and that these results may vary if a different subset is considered. Consequently, the next model validating considers only the aerobic and resistance sessions.

3.2 Results with the T1DEXI study

The model's response is here evaluated for all aerobic and resistance sessions of the T1DEXI study, with HR serving as the input variable. In the following analysis, the initial five minutes of the exercise sessions are excluded from the calculation of the metrics to exclude the effect of the warm-up period. This allows for the warm-up stage. The same procedure is applied to the 30-minute pre-exercise window so that the compared time periods are equal.

Table 1 presents the mean and STD of the area under the curve (AUC) values, which serve as an indicator of model responsiveness, for the A_s, A_l, N_s, N_l during the aerobic and resistance sessions. These values are

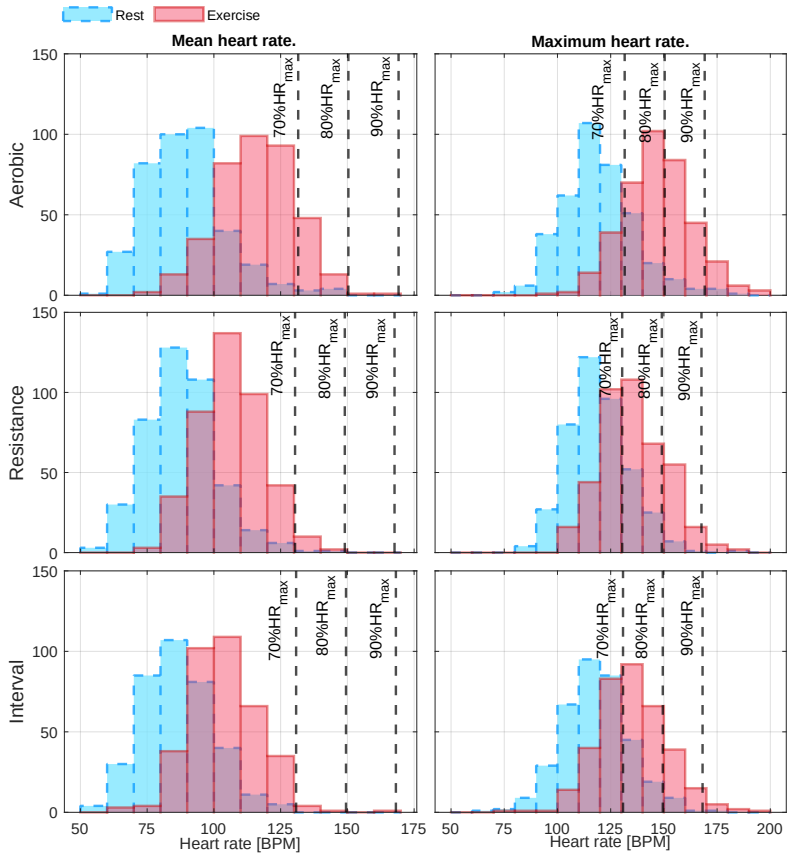


Figure 6: Histogram heart rate (HR) over a 30-minute period before the sessions (blue) and during the sessions (red). Left column shows the mean HR and the right column shows the maximum value of HR for the sessions of the T1DEXI study.

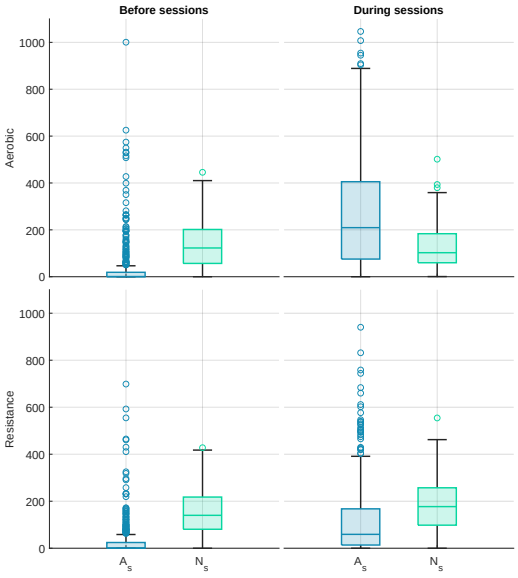
compared with the AUC obtained before each training session, though it can be compared with other such as nocturnal period. As can be appreciated, the states exhibit the same order of magnitude when comparing the period before the aerobic and resistance sessions (columns 1 and 3). However, a difference is observed when the exercise is performed. A_s demonstrates an increase from 4.50 to 254.18 in the presence of aerobic exercise, whereas an increase from 6.97 to 89.59 is observed in the case of resistance activity. A_l, which is designed to follow A_s with slower dynamic, exhibits comparable results, with an increase from 4.50 to 269.59 during aerobic exercise and an increase from 9.23 to 112.89 when resistance activity is present. In the case of anaerobic states, the value of N_s is 136.79 before aerobic sessions and 148.84 before resistance sessions. This is due to the fact that the HR signal is subject to fluctuations even during resting periods or due to spontaneous PA. However, in the presence of exercise, the value of N_s decreases to 124.46 in the case of aerobic activity and increases to 181.63 in the case of resistance activity. Finally, N_l presents higher value for resistance (315.95) compare with aerobic sessions (273.64).

Table 1: Mean (STD) of the AUC of the states for the T1DEXI sessions. The AUC of a 30-minute interval preceding the aerobic and resistance sessions is shown in comparison to the AUC during these sessions.

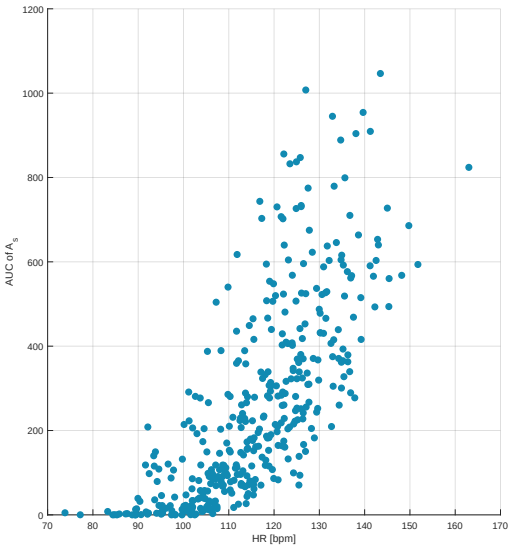
States	Aerobic sessions		Resistance sessions	
	Before	During	Before	During
A_s	4.50 (8.73)	254.18 (217.47)	6.97 (12.48)	89.59 (97.12)
A_l	4.50 (8.90)	269.59 (217.93)	9.23 (17.48)	112.87 (112.30)
N_s	136.79 (96.77)	124.46 (86.71)	149.84 (91.17)	181.61 (98.79)
N_l	119.02 (90.54)	273.64 (127.98)	130.89 (88.83)	315.95 (114.66)

Figure 7a presents a box-plot of the AUC for states A_s (blue) and N_s (green), hereby facilitating the visual interpretation of the distribution of results. The results for the AUC of A_s indicate a median that is lower during the pre-exercise period compared to the exercise period. Conversely, N_s exhibits a lower median during exercise than in the pre-exercise period. During resistance sessions, the AUC for A_s increases, although the rise is less pronounced than that observed during aerobic exercise. Additionally, the median of N_s reflects an increase in values during these sessions.

Lastly, exercise intensity is an important characteristic, particularly in the context of aerobic exercise. Figure 7b shows a scatter plot of A_s AUC as a function of mean HR during aerobic exercise. Although there are different ways of determining intensity, in this case the mean value of HR is used as an indicative measure. The figure illustrates how the A_s state accumulates a higher AUC with increasing exercise intensity (higher HR).



(a)



(b)

Figure 7: T1DEXI trial results. (a) Area under the curve (AUC) of the short-term states before and during the exercise. The first row shows the AUC for aerobic sessions and the second row for resistance sessions. (b) Scatter plot of the AUC of the aerobic short-term state in function of the mean heart rate during aerobic sessions.

4 Model Validation with clinical trial in Argentina

This section presents the pilot study conducted by our research group in collaboration with the Hospital Italiano de Buenos Aires (HIBA) and the Instituto Tecnológico de Buenos Aires (ITBA) for the purpose of conducting a local validation of the proposed model, including a brief description of the aforementioned trial and the validation process.

4.1 Clinical trial design

The HIBA trial is a study designed to evaluate the effects of structured and unstructured exercise and stress on BG levels in people with T1D. This study specifically aims to obtain data from known aerobic and anaerobic exercise sessions to validate the model proposed in this paper. The study protocol was approved by the HIBA's ethics committee (Register code No.11719), and informed consent was obtained from the participants. The study cohort, study design, inclusion and exclusion criteria are described below.

Selection criteria for participants

In order to be eligible to participate in the study, subjects were required to meet the following criteria: to have been diagnosed with T1D at least two years ago, they had to be on continuous insulin therapy with a continuous subcutaneous insulin infusion (insulin pump) that had not been integrated into a continuous glucose sensor for at least six months, to be between the ages of 18 and 65 years, to have HbA1c less than 10%. In

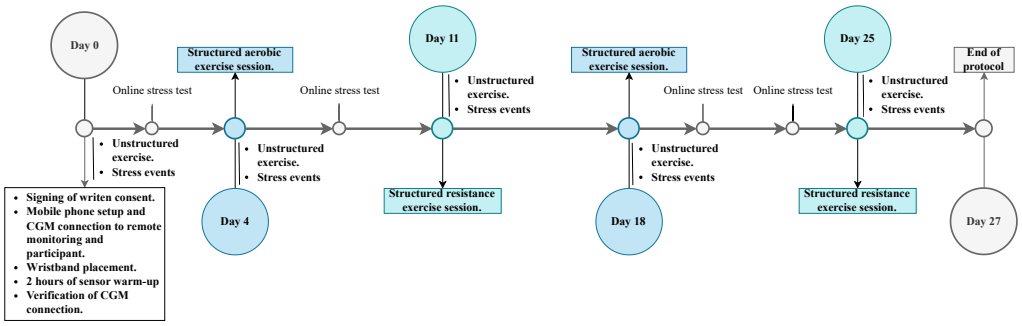


Figure 8: Timeline of the HIBA trial protocol.

addition, women were required to be pre-menopausal, to be using effective contraception and to have negative B-HCG laboratory results. They were also required to demonstrate adequate mental and cognitive fitness to understand the study considerations and to handle the closed system components. Additionally, participants were required to have undergone carbohydrate counting education and to have obtained a certificate of optimal cardiovascular fitness for PA. Finally, they were required to demonstrate understanding of the protocol and to sign the informed consent form.

Subjects were excluded if they were affected by any of the following circumstances: hospitalisation due to diabetic ketoacidosis, severe hypoglycemia with loss of consciousness, hospitalisation for psychiatric treatment, presence of current symptomatic coronary heart disease and/or an episode of acute decompensation. Furthermore, individuals with a suspected or confirmed active infectious process, pregnant women, women intending to become pregnant or breastfeeding, and individuals undergoing active treatment with anxiolytics, major or minor tranquillisers were excluded from participation. Moreover, individuals who have undergone pharmacological treatment for psychiatric disorders, those with a history of suspected or confirmed adrenal disease, and those who have consumed paracetamol within the previous 24 hours were excluded from the study. Similarly, individuals with uncontrolled hypertension or any other condition that increases the risk of hypoglycemia were excluded.

Clinical trial timeline and data collection.

In accordance with the aforementioned criteria, five adult participants were randomly selected for the study, a number determined by the availability of devices and financial resources for the trial. Figure 8 illustrates the timeline of the study protocol, which comprised two structured aerobic exercise sessions conducted on a treadmill (days 4 and 18) and two resistance training sessions utilising elastic bands (days 11 and 25). These sessions were performed within a controlled and supervised environment, with each session lasting about 30 minutes. Additionally, participants were required to complete an online stress test that involved a distinct cognitive questionnaire at each session. Throughout the duration of the trial, participants were instructed to record events in their daily lives, including meals consumed, PA (both planned and unplanned), and any stressful situations experienced. To this end, they used a smartphone and remote monitoring platform developed from open-source resources, called InsuMate [44] (url: https://www.insumate.com.ar/inicio). The data collection process included Dexcom ONE CGMs, participants' pumps and Empatica E4 wristbands (HR, accelerometer, electrodermal activity (EDA), etc.). The complete set of collected data is freely available in [45].

4.2 Data description and processing of the HIBA trial.

As in the T1DEXI study, the results of the HIBA trial are subjected to a similar analysis considering only the structured sessions. Prior to the aerobic exercise sessions, the mean HR and STD are 89.60 (6.37) [bpm], with an increase to 102.09 (15.21) [bpm] during aerobic activity. In contrast, the changes in HR are less pronounced during the resistance training sessions. Before resistance exercise, the HR is recorded at 88.36 (3.80) [bpm], while a slight increase to 90.72 (3.16) [bpm] is observed during resistance training. Furthermore, the ΔCGM for the HIBA trial is presented in Figure 9, where the BG change is greater during aerobic exercise (-21 [$-14.76,\ 4.92$]) compared to resistance exercise (5.20 [$-8.32,\ 14.20$]). These results are consistent with those previously observed in the T1DEXI trial.

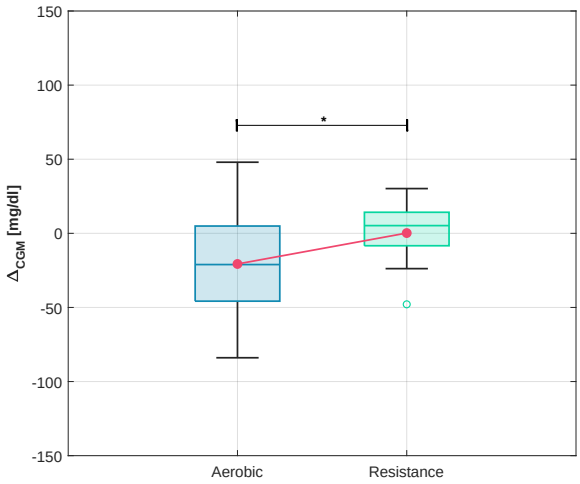


Figure 9: Difference between CGM measurements at the beginning and end of exercise sessions (Δ_{CGM}) from HIBA trial. The red dots show the mean value. The statistical significance between the effect of each type of exercise on BG is show ($^*\rho < 0.05$,$^{**}0.001 < \rho < 0.05$,$^{***}\rho < 0.0001$).

4.3 Results with the HIBA trial

Table 2 shows the AUC mean and STD of the proposed model states for the structured sessions of the HIBA trial. Similarly to the T1DEXI case, comparable values are evident during the pre-session time periods (column 1 vs column 3). The AUC of A_s demonstrates an increase from 56.14 to 203.55 during the aerobic sessions and a decrease from 43.15 to 41.83 for the resistance sessions, indicating a more pronounced response to aerobic exercise. Regarding N_s, a decrease is observed from 193.17 to 166.87 in the aerobic case, while an increase is noted from 191.95 to 267.54 in the resistance case, which also suggests a more sensitive response to resistance exercise.

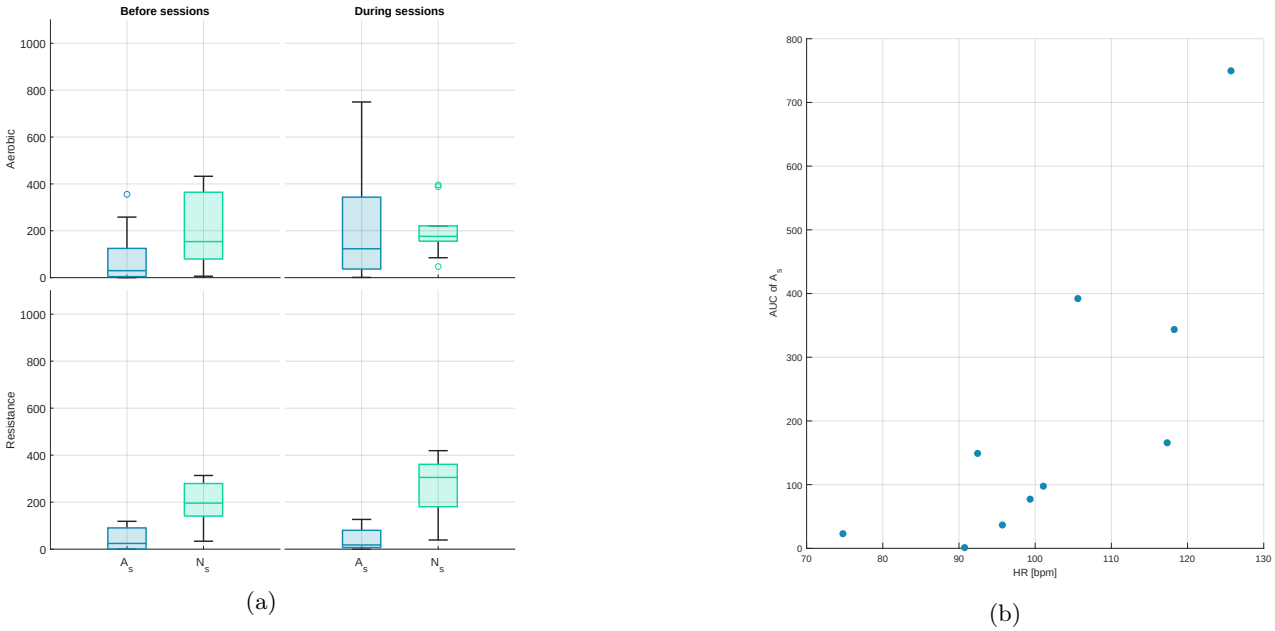
The box-plot in Figure 10a presents the values for the A_s and N_s states in the HIBA trial. As anticipated, the median AUC for A_s exhibits a more pronounced increase during aerobic sessions compared to resistance training. In contrast, N_s shows a higher median during resistance sessions than during aerobic sessions. Furthermore, Figure 10b illustrates the response of dynamic state A_s, indicating that its amplitude increases with higher HR levels during aerobic exercise. These findings align with those obtained from the T1DEXI dataset, as discussed in section 3.2.

5 Discussion

This study presents a state space model comprising two distinct parts: one responsive to aerobic exercise and the other to anaerobic exercise. The model is developed through an analysis of HR behaviour and its characteristics during these exercise modalities. Model performance is validated using structured exercise sessions that include both aerobic and resistance activities across two trials. Consistent findings regarding the impact of exercise on BG levels are observed in both T1DEXI and HIBA trials, with aerobic exercise demonstrating a more significant reduction in BG levels than resistance exercise. Furthermore, the evaluation of the model is performed by comparing the AUC of the model states at a pre-exercise time period with the area AUC during exercise.

Table 2: Mean (STD) of the AUC of the states for the HIBA sessions. The AUC of a 30-minute interval preceding the aerobic and resistance sessions is shown in comparison to the AUC during these sessions.

States	Aerobic sessions		Resistance sessions	
	Before	During	Before	During
A_s	56.14 (85.31)	203.55 (232.47)	43.15 (46.63)	41.83 (44.92)
A_l	124.42 (161.46)	294.08 (250.55)	73.81 (80.27)	103.25 (94.24)
N_s	193.17 (153.43)	166.87 (42.11)	191.95 (94.23)	267.54 (119.12)
N_l	160.80 (152.96)	419.01 (103.20)	161.34 (91.77)	342.94 (81.13)



(a) (b)

Figure 10: HIBA trial results. (a) Area under the curve (AUC) of the short-term states before and during the exercise. The first row shows the AUC for aerobic sessions and the second row for resistance sessions. (b) Scatter plot of the AUC of the aerobic short-term state in function of the mean heart rate during aerobic sessions.

Model performance analysis

The results demonstrate that A_s and A_l states are more sensitive to aerobic activities, whereas the N_s and N_l states exhibit a tendency to react to intermittent HR patterns that are characteristic of anaerobic activities. Additionally, its evident that in real-life situations, the PA is reflected in the HR, manifesting itself as a combination of the behaviours described in the section 2.1. However, if equations 1 and 6 are weighted appropriately, the model allows the real-time quantification of the predominant PA type, thereby providing useful information that could be employed for potential adaptation in T1D treatment. It is also observed that A_s is capable of providing information regarding the intensity of exercise, as shown in Figure 7b and Figure 10b. This is a crucial factor in the prediction of hypoglycemic episodes [12, 17, 18]. In addition, further analysis was conducted to assess whether carbohydrate intake and insulin doses, which significantly influence the T1D management, affect the model's performance. To this end, two comparisons were made using T1DEXI trial sessions: (1) sessions with vs. without carbohydrate intake prior to exercise, and (2) with vs. without insulin administration. Filtering was applied up to five hours before the exercise at one hour intervals. Results show the model's ability to differentiate and quantify exercise is unaffected by the presence or absence of meal intake or insulin prior to exercise. Finally, an additional analysis was conducted using a nocturnal period as the baseline HR, compared to the pre-exercise period in Tables 1 and 2. As anticipated, the model exhibited a reduced response during nocturnal periods in comparison to the diurnal resting state.

Strengths of the proposed model

The structure of the proposed model offers the advantage of an intuitive tuning process. In the case of A_s and A_l, α_L and α_H (Equation 4) can be modified to determine the reaction range, thus adjusting the sensitivity to higher HR values. Similarly, for N_s and N_l, δ_l and δ_h allow for the adjustment of the amplitude of the desired HR peaks to be detected. With regard to the time constants, equations 5 and 10 facilitate modification according to the desired reaction rate, both at the start and at the end of the PA. Furthermore, the utilisation of HR, a readily accessible physiological signal, to successfully distinguish between the type of PA presents a promising approach for integration into AID systems. In this context, further research is necessary to explore the relationship between model output and the impact on BG levels. However, it is hypothesised that the model could be incorporated into commercial AID systems that have manual adaptations to exercise, such as adjustable BG targets or reducing basal insulin [8, 46]. For example, the model could trigger an increase in BG targets when activity is determined as predominantly aerobic. Alternatively, its outputs could be incorporated into advanced control strategies that account for exercise by leveraging information on activity type and intensity [47].

Moreover, although interval sessions were excluded from the study because they did not meet the study's original design objective [39], it is important to note that this type of PA can be represented as a combination of aerobic and anaerobic PA. The model's ability to quantify rather than classify exercise makes it a potentially suitable approach for addressing this type of PA. For instance, an exercise session could be considered interval when there is a comparable increase in both the aerobic and anaerobic states.

It should be noted that the validation of the model was conducted using the T1DEXI trial, which is particularly noteworthy for its high statistical power. This is attributed to the inclusion of a large number of sessions and participants. Meanwhile, the HIBA trial performed within our research group, despite the smaller site, is relevant due to its execution under a controlled clinical environment under supervision.

Limitations of the study

It is established that the HR can be influenced by factors unrelated to the PA, including stressful situations, caffeine intake, pharmacological interventions, medical conditions, and other relevant factors [48–50]. Consequently, it is imperative to acknowledge that the HR signal in isolation may not be a reliable indicator of PA. Therefore, the integration of additional physiological signals, such as a step counter or accelerometer-derived data, is necessary to avoid false positives [24, 25]. Furthermore, the T1DEXI trial is a worldwide recognised study that includes a large number of structured exercise sessions. However, its cohort may not be fully representative of the general adult population with T1D, as participants were already regularly engaged in PA [39]. Moreover, studies have concluded that there are several factors which limit the reproducibility of the T1DEXI study results [51]. The underlying causes of this variability remain an open question within the scientific community and may provide a possible explanation for the high STD observed in the AUC values presented in Table 1 and Table 2, which are present even when a nocturnal baseline is used for HR. It is crucial to acknowledge these limitations, given their potential implications for the generalisability of the proposed model's findings.

Comparison with data-driven approaches

Although the difference between the proposed model and the data-driven methods is qualitative, it was quantitatively compared with a feed-forward neural network (NN) trained to classify PA types based on the HR signal. The NN was trained on the T1DEXI subset, using 70% of the data for training and 30% for testing. For the classification of aerobic sessions, the NN obtained a slightly higher recall than the proposed model (79.5% vs. 74.8%). In contrast, the model demonstrates a favourable recall in the classification of resistance sessions (60.2% vs. 66.1%), which are typically the most challenging. This comparison indicates that the model can achieve comparable performance with data-driven approaches for this specific task. It is important to note that the model output provides a quantification of the PA type, which for the purposes of this comparison was used to classify PA. However, its application is not exclusively restricted to classification. Finally, the implementation of the model is immediate without training process, and the parameters allow for straightforward personalisation by the user, which is a valuable feature in clinical environments.

6 Conclusions

This paper presents a state-space model that enables the real-time differentiation and quantification of the type and intensity of PA. The model employs only the HR signal as input and comprises four dynamic states that interpret the characteristics of the HR signal to determine the predominant type of exercise. The model is evaluated using two recent clinical datasets: the T1DEXI dataset, which is a world-wide recognised study examining the impact of physical activity in adults with type 1 diabetes, and a proprietary trial conducted by our research group in Argentina.

The aerobic states, designated as A_s and A_l, demonstrate a notable increase during aerobic sessions. In contrast, the anaerobic states designated as N_s and N_l demonstrate a more pronounced response during resistance sessions, which can be considered as an anaerobic. This suggests that the model is an effective method for characterising the type of PA. Moreover, it can be concluded that A_s is an indicator of the intensity of the PA, given that its amplitude is observed to increase in conjunction with an elevation in HR.

The model incorporates a feature that facilitates the user's ability to adjust parameters that are readily comprehensible, such as the maximum HR of the users. In contrast to the most common data-driven approaches, this method does not require training, thereby reducing the associated computational cost and facilitating rapid implementation. Furthermore, the interpretability of the model allows modifications to be made to enhance its responsiveness through the use of equations 3 and 7. Finally, the potential of the model to be used in adapting control algorithms for AID systems in conjunction with additional physiological signals that facilitate the confirmation of exercise should be emphasised. This would enable the insulin dosage to be adapted in accordance with the degree of state response during PA, thereby mitigating the challenges

associated with treating T1D during exercise.

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Declarations

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