Investigation of the TP-based modeling possibility of a nonlinear ICU diabetes model

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Abstract—In silico modeling is an important part of biomedical engineering. Advanced controllers providing high quality control can be validated through it checking if the available mathematical model of the given biomedical process produces the desired output. However, due to high patient variability the advanced linear control methods applied on linearized models could produce several distortions compared to the original nonlinear models; hence, these errors should be reduced. Hierarchical control strategies could be a possibility or from modeling point of view using different control-oriented modeling methodologies. Linear Parameter Varying (LPV) approaches with Linear Matrix Inequality (LMI) based modeling and controller design represent one choice. In this paper, we investigate their generalized extension, the Tensor Product (TP) model transformation demonstrated on diabetes modeling. In concrete, the type 1 diabetes modeling on Intensive Care Units (ICU) is envisaged. The achieved results will be used for TP transformation based controller design in our later work.

Index terms—Tensor Product model transformation, Modeling of diabetes, ICU model, LPV methods

I. INTRODUCTION

The research of potentially beneficial modeling and control methodologies in case of physiological processes has high importance. It is definitely true in case of Diabetes Mellitus (DM), where the aim is to keep the blood sugar level in a narrow range. However, the nonlinear, patient vary and time-delay processes require advanced modeling and control techniques in order to reach high quality control with good performance [1], [2]. Over the last decades the Artificial Pancreas (AP) and Intensive Care Unit (ICU) oriented modeling has been evolved [3]. In AP modeling the focus is on outpatient care, while in case of ICU modeling the goal is to improve the performance of the inpatient care reaching a tight glycemic control. As patients are under frequent nursing care surveillance, it is enough to describe their metabolic state with roughly approximate, low-order models and not necessary to consider several possible circumstances which can be occurred in outpatient care. However, studies show that the good metabolic state can be critical from recovery point of view [4], [5].

Recently, highly developed approaches appeared regarding to modeling of diabetes. Linear Parameter Varying (LPV) techniques [6], Linear Matrix Inequality (LMI)-based methodologies [7] and the combination of these [8] correspond to the new trends of control engineering. Tensor Product (TP) model transformation can provide a unique, LPV-based way for modeling and it is well combined with LMI methods for controller design [9]. In this paper, we investigated the modeling possibility of an ICU model via TP model transformation. The paper is structured as follows: first, we introduce the TP model transformation and the used ICU model. Second, we show the possible quasi-LPV (qLPV) configurations of the applied model and the realized TP function form the models. Third, we present and discuss the results of the validations of the realized models. Finally, we overview the achievements of this study.

II. THE TP MODEL TRANSFORMATION

The TP model transformation based approaches originates from the parameter dependent fuzzy system techniques [10]. The TP method originally was demonstrated in [11], [12]. The approach was summarized in [9] in case of qLPV based systems and controller design. Concisely summarized, the TP transformation transforms a given function into a determined TP function form regardless from the type of the original function, if the exact transformation is possible otherwise, the TP model transformation provides a TP function form approximation with given accuracy. The TP form complexity can be settled by sampling frequency on the given parameter domain which allows to determine the approximation accuracy of the original function by the TP function. Since most of the qLPV models can be described by qLPV functions, TP model based transformation can be used on them. Through this process a TP transformation based TP model can be created which can approximate the original qLPV model. TP transformation is an effective way for convex hull manipulation of polytopic structures and well combined with LMI-based techniques. These properties allow
to reach less conservative, more optimal LMI-based controller design possibilities than the usual LMI-methods [9].

A general, parameter dependent qLPV model (with \( k \) states, \( n \) inputs and \( l \) outputs) can be given by its state space representation in the following way:

\[
\begin{align*}
\mathbf{x}(t) &= A(p(t))\mathbf{x}(t) + B(p(t))\mathbf{u}(t) \\
y(t) &= C(p(t))\mathbf{x}(t) + D(p(t))\mathbf{u}(t) \\
S(p(t)) &= \begin{bmatrix} A(p(t)) & B(p(t)) \\ C(p(t)) & D(p(t)) \end{bmatrix}
\tag{1a}
\end{align*}
\]

where \( \mathbf{u}(t) \in \mathbb{R}^n \) represents the input vector, \( y(t) \in \mathbb{R}^l \) the output vector and \( x(t) \in \mathbb{R}^n \) the state vector, \( A(p(t)) \in \mathbb{R}^{n \times n} \), \( B(p(t)) \in \mathbb{R}^{n \times m} \), \( C(p(t)) \in \mathbb{R}^{l \times n} \) and \( D(p(t)) \in \mathbb{R}^{l \times m} \) matrices, respectively.\( \text{ } \)

(1a) can be written in the (1b) compact form, where \( S(p(t)) \in \mathbb{R}^{(k+l) \times (n+m)} \) represents the parameter dependent system matrix. The parameter vector \( p(t) \in \Omega \in \mathbb{R}^N \) may vary in time. \( \Omega = [p_{1\min}, p_{1\max}] \times [p_{2\min}, p_{2\max}] \times ... \times [p_{N\min}, p_{N\max}] \in \mathbb{R}^N \) forms a closed hypercube in the N-dimensional parameter space determined by the minimum and maximum values of the elements of the parameter vector. Hence, a parameter dependent qLPV model is well represented by its system matrix \( S(p(t)) \). In the parameter space inside the closed hypercube, the qLPV model can be described by its polytopic representation. Thus, the \( S(p(t)) \) can be described:

\[
S(p(t)) = \bigoplus_{i=1}^{N} w_i(p(t))S_i \tag{2}
\]

where \( S(p(t)) \) is given for any \( p(t) \in \Omega \) as the convex combinations of LTI system models (also known as LTI vertex systems) \( S_i \in \mathbb{R}^{(k+l) \times (n+m)} \). The finite element TP type polytopic model can be constructed via “sampling” of \( p(t) \) over \( \Omega \):

\[
S(p(t)) = \sum_{\alpha=1}^{N} \sum_{\beta=1}^{L} \sum_{\gamma=1}^{J} \sum_{\delta=1}^{K} w_{\alpha \beta \gamma \delta}(p(t))S_{\alpha \beta \gamma \delta} \tag{3}
\]

written in the following compact form [9]:

\[
S(p(t)) = \bigoplus_{\alpha=1}^{N} w_{\alpha}(p(t))S_{\alpha} \tag{4}
\]

where the \( S \in \mathbb{R}^{(k+l) \times (n+m)} \) coefficient tensor is created from the LTI vertex systems \( S_{\alpha} \), while the \( w_{\alpha}(p(t)) \) vector consists from the \( w_{\alpha \beta \gamma \delta}(p(t)) \) continuous weighting functions. The TP model will be convex if the weighting functions satisfies:

\[
\forall n, i, p_i(t): w_{\alpha \beta \gamma \delta}(p_i(t)) \in [0,1] \tag{5a}
\]

\[
\forall n, p_i(t): \sum_{i=1}^{K} w_{\alpha \beta \gamma \delta}(p_i(t)) = 1 \tag{5b}
\]

More than one convex hull type can be used for TP type polytopic qLPV models. We used the Minimal Volume Simplex (MVS) type hull [13]:

\[
S(p) = \bigoplus_{\alpha=1}^{N} w_{\alpha}(p)S_{\alpha} \tag{6}
\]

where \( \mathbf{S} \in \mathbb{S}^{N \times n \times k \times l} \) core tensor is created from the \( S_{i\gamma \delta \alpha} \) matrices so that the \( (S_{i\gamma \delta \alpha} \) n-mode subtensors evolve a minimal volume bounding simplex for the \( S_{i\gamma \delta \alpha} w_{\alpha}(p) \) trajectory over \( n = 1, N \).

Further details of TP transformation and applicable convex hull types can be found in [9], [13]–[15]. In order to realize TP transformation-based approaches, the TP Toolbox\textsuperscript{™} for MATLAB is the most convenient solution [16].

III. THE INVESTIGATED MODEL T1DM ICU MODEL

ICU models can cover Type-1 DM (T1DM), Type-2 DM (T2DM) and other mixed cases [5]. In this study we investigated the T1DM-type ICU model which was developed by Wong et al [4]. The model has three states: the plasma glucose concentration \( G(t) \) [mmol/L], the plasma insulin concentration \( I(t) \) [mU/L], in which the glucose and insulin originate from external sources and the \( Q(t) \) [mU/L], representing the concentration of insulin bounded to interstitial sites. Further, the model’s inputs are the Carbohydrate (CHO) intake \( p(t) \) [mmol/L/min] and the external insulin \( u_e(t) \) [mU/min] input:

\[
\begin{align*}
\dot{G}(t) &= -(p(t) - G(t)) - S_1 G(t) + G_s \frac{q(t)}{\alpha + q(t)} + I(t) + p(t) \tag{7a} \\
\dot{Q}(t) &= -kQ(t) + 4I(t) \tag{7b} \\
\dot{I}(t) &= -\alpha I(t) + u_e(t) \tag{7c}
\end{align*}
\]

The descriptions of the parameters can be found in [4], [17]. The model contains unfavorable nonlinearities from mathematical point of view. Besides the product states in (7a), two Michaelis-Menten (MM) type saturation can be found in (7a) and (7c) according to the insulin kinetics and insulin dependent glucose uptake by the given cells. The saturations are connected to the \( Q \) and \( I \) states.

IV. DERIVATION OF THE LPV AND TP MODELS

A. Steady state analysis

The steady state of the model can be calculated in different ways. One of these is when the steady \( G_s \) state and \( p_e \) input are given. \( G_s, I_s, G_{eq}, u_e \) can be calculated by using the (7a)-(7c) equations. An important question is the relation of \( G_{eq} \) to \( G_s \). The qLPV model should approximate the system dynamics around the equilibrium points; hence, \( G_{eq} \) can be a “desired” equilibria and can be different from \( G_s \). The equality of \( G_s \) and \( G_{eq} \) becomes important during a TP based controller design, because the \( G_{eq} \) will that desired blood glucose level, what the controller has to provide.
In the first case, we considered that $G_d = G_E$. As a result, the dynamics of the plasma glucose concentration at the equilibrium point becomes:

$$G(t) = 0 = -p_G G_d - S_2 G_d + Q_d$$

(8)

With reformulation of (8), $Q_d$ can be calculated, as follows:

$$Q_d = -p_G G_d + p_d (1 + \omega_Q Q_d) = A (1 + \omega_Q Q_d)$$

(9a)

$$Q_d = A \frac{G_d}{1 - \omega_Q A}$$

(9b)

$L_d$ appears by using the rearranged (10a) equation, if $Q(t)$ is at the equilibrium point:

$$Q(t) = 0 = -k Q_d + k L_d$$

(10a)

$$L_d = Q_d$$

(10b)

As a result, the dynamics of $I(t)$ at the equilibria can be described, as follows:

$$I(t) = 0 = -n_L d_k \frac{G_d}{1 + \omega_k d} \frac{\omega_k d}{V}$$

(11)

from which the necessary $\omega_k d$ can be calculated to hold the equilibrium of the states beside the predefined $G_d$ and $p_d$:

$$\omega_k d = \frac{n_L d_k}{1 + \omega_k d} V$$

(12)

The other investigated case is when $G_d \neq G_E$. Here, only, the (8), (9a) and (9b) equations will be different. Naturally, the numerical values of $I_d$, $Q_d$ and $\omega_k d$ will change accordingly:

$$\dot{G}(t) = 0 = -p_G G_d - S_1 (G_d + G_E) + \omega_Q Q_d + p_d$$

(13)

By rearranging (8), $Q_d$ can be calculated as follows:

$$Q_d = -p_G G_d + p_d (1 + \omega_Q Q_d) = B (1 + \omega_Q Q_d)$$

(14a)

$$Q_d = B \frac{G_d}{1 - \omega_Q B}$$

(14b)

B. Investigated qLPV models

In this study we investigated different approaches as more than one realizable qLPV form can be derived.

We consider the two above-mentioned cases: $G_d = G_E$ and $G_d \neq G_E$. Many options can be selected as aim of TP-based control. One of them is when the aim of the controller is to prevent the system’s diversion from the selected equilibrium point; or if the diversion becomes to provide fast action leading the system back to the equilibrium. A natural way to describe this evasive error dynamics is if we take the difference of the actual states and the steady states.

First, we consider the $G_d = G_E$ case. The error dynamics becomes as follows (subtracting $S_2 G_d$ from the last two parts of (15)):

$$\Delta G(t) = G(t) - 0 = -p_G G_d - S_2 G_d + Q_d$$

$$\Delta G(t) = G(t) - 0 = -p_G G_d - S_2 G_d + Q_d$$

$$\Delta G(t) = G(t) - 0 = -p_G G_d - S_2 G_d + Q_d$$

(15)

$$\Delta G(t) = G(t) - 0 = -p_G G_d - S_2 G_d + Q_d$$

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(16)

$$\Delta G(t) = G(t) - 0 = -p_G G_d - S_2 G_d + Q_d$$

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$$\Delta G(t) = G(t) - 0 = -p_G G_d - S_2 G_d + Q_d$$

(17)

The second case is when $G_d \neq G_E$. In this case, the error dynamics $\Delta G(t)$ becomes as follows:

$$\Delta G(t) = -p_G S_1 G_d + S_2 G_d + Q_d$$

$$\Delta G(t) = -p_G S_1 G_d + S_2 G_d + Q_d$$

$$\Delta G(t) = -p_G S_1 G_d + S_2 G_d + Q_d$$

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$$\Delta G(t) = -p_G S_1 G_d + S_2 G_d + Q_d$$

(18)
As a result, the error dynamics of the \( q(t) \) and \( I(t) \) can be easily derived as in (17):
\[
\Delta q(t) = q(t) - 0 \\
- k(I(t) - Q_e) = - k(I(t) - L_0) \\
\Delta I(t) = I(t) - 0 = \frac{- n(I(t))}{1 + \alpha_I(t) - n} \left( \frac{I(t)}{1 + \alpha_I(t)} \right) \\
\Delta I(t) = I(t) - 0 = \frac{- n(I(t))}{1 + \alpha_I(t) - n} \left( \frac{I(t)}{1 + \alpha_I(t)} \right)
\]
(19)
(20)

A convenient way is the idea if the error dynamics-based qLPV models are based on the error dynamics, namely \( \Delta q(t) = [\Delta q(t), \Delta p(t)]' \). The states of the qLPV models are based on the error dynamics, namely \( \Delta q(t) = [\Delta q(t), \Delta p(t), \Delta I(t), \Delta \Delta I(t)]' \). From these considerations and the (17)-(20) equations, the state-space representations of the derived qLPV models are represented by (22) considering \( G_L = G_e \) and (23) considering \( G_L \neq G_e \).

### C. TP models

The TP model transformation can be applied on the qLPV system matrices \( S(p(t), q(t), I(t))|_{G_L = G_e} \) of (22) and \( S(p(t), q(t), I(t))|_{G_L = G_e} \) of (23). The transformation provides the following TP model structure:
\[
\Delta x(t) = \begin{bmatrix} -p_Q \times Q^2_e + \frac{S_1 Q^2_e}{1 + \alpha_0 Q_e} & -S_1 G_e \times I_e \times (1 + \alpha_0 Q_e) & 0 & 0 \\ 1 & -k & 0 & 0 \\ 0 & 1 & -n & 0 \\ 0 & 0 & 1 & -n \end{bmatrix} \Delta x(t) + \begin{bmatrix} 0 \\ 0 \\ 1 \\ 0 \end{bmatrix} \Delta u(t) \tag{22}
\]
\[
\Delta x(t) = \begin{bmatrix} -p_Q \times Q^2_e + \frac{S_1 Q^2_e}{1 + \alpha_0 Q_e} & -S_1 G_e \times I_e \times (1 + \alpha_0 Q_e) & 0 & 0 \\ 1 & -k & 0 & 0 \\ 0 & 1 & -n & 0 \\ 0 & 0 & 1 & -n \end{bmatrix} \Delta x(t) + \begin{bmatrix} 0 \\ 0 \\ 1 \\ 0 \end{bmatrix} \Delta u(t) \tag{23}
\]

### Figure 1

Figure 1 shows the MVS-type weighting functions with dense sampling (left column belongs to (21a) and the right column belongs to (21b)). There are no evaluable difference between the given weighting functions; however, small numerical differences appeared.
The main considerations during the validation were the following:

1) Investigated parameter domain: $G = 3.5 \pm 2.5$, $Q = 0.100$ and $T = 0.100$;
2) Comparison was done between every state of every model;
3) Dense (considered number of samples (NoS): NoS$_1 = 31$, NoS$_2 = 101$, NoS$_3 = 101$) and less dense (NoS$_4 = 17$, NoS$_5 = 81$, NoS$_6 = 81$) parameter sampling in the parameter domain;
4) Comparison only in case of initial state decay and in case of given inputs;
5) Use of Root-Mean Square Error (RMSE) as basis of comparison.

The results of the validation are summarized in Table I. In every suitable the upper triangular partition belongs to the dense sampling, namely, the number of samples (NoS) were higher on the investigated parameter domain. The model notation is the following:

- original nonlinear model: Original (7);
- qLPV model of (22): qLPV$^1$;
- qLPV model of (23): qLPV$^2$;
- TP model of (21a): TP$^1$;
- TP model of (21b): TP$^2$.

In case of Table Ia, a less than 100 minutes decay was investigated for the initial values of the state variables. The difference between dense and less dense sampling is negligible. However, both TP models had small RMSE at the given circumstances, but the TP$^2$ model where $Q = Q_2$ had the best performance.

Table Ib shows a scenario, where external CHO and insulin inputs were impulse functions (similar to reality), as follows:

- CHO intake: Height: 4 g, Width: 5 min, Period: 50 min
- Insulin intake: Height: 1 U, Width: 2 min, Period: 50 min

We transformed the inputs from g to mmol/L (CHO) and U to ml/l (insulin) based on the model parameters in Table I.

The density of sampling did not cause evaluable difference in the resulting RMSE of the states based on the data. In this case, TP$^2$ model produced the smallest RMSE under 300 minutes.

Figure 2 shows the results of the second investigation (as in Table Ib) in case of dense sampling. It can be considered, that the variation of $Q(t)$ and $R(t)$ are almost the same. However, the TP$^2$ model proved to be much more accurate than the TP$^1$ in the $G(t)$ state, as the $G_{qLPV}(t)$ and $G_{TP}(t)$ states overlap each other.

On Figure 2 the error of the states were highlighted in such a way, that the state variation of the realized TP models were subtracted from the original states. The results confirmed the numerical RMSE-based evaluation in Table Ib and one can see that TP$^2$ is more suitable to substitute the original nonlinear model.

| Table I | RESULTS OF THE RMSE-BASED INVESTIGATION: USED PARAMETER SET: $G = 10.5 \text{ mmol/L}$, $p_b = 0.01 \text{ /min}$, $S_b = 0.010 \text{ L/mU/min}$, $F = 12$, $L = 0.0198 \text{ /min}$, $Q = 0.0157 \text{ L/mU}$ and $Q_2 = 0.0154 \text{ L/mU}$.

Investigation 1: RMSE-based comparison of the states of the realized models on the given parameter domain under 100 minutes. Initial conditions: $G_0 = 15$, $Q_0 = 3$ and $\dot{t}_0 = 5$.

| Table Ib | Shown scenario, where external CHO and insulin inputs were impulse functions (similar to reality), as follows:

- CHO intake: Height: 4 g, Width: 5 min, Period: 50 min
- Insulin intake: Height: 1 U, Width: 2 min, Period: 50 min

Table Ib shows a scenario, where external CHO and insulin inputs were impulse functions (similar to reality), as follows:

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The density of sampling did not cause evaluable difference in the resulting RMSE of the states based on the data. In this case, TP$^2$ model produced the smallest RMSE under 300 minutes.
Further work will focus control design of the realized TP model via the LMI-based TP controller design method. This advanced tool let to embed several criteria and constraints to the control structure and results reliable and robust controller for the given TP model. TP model can be robust itself, if more parameters are included into the parameter vector. We will investigate this possibility also.

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