Differential Flatness based Run-to-Run Control of Blood Glucose for People with Type 1 Diabetes

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***Abstract*— The objective of this paper is to develop an open loop insulin input profile over a span of 24 hours which makes the glucose trajectory of a Type 1 diabetic person track a target glucose trajectory. The Bergman minimal model is chosen to represent the glucose-insulin dynamics which is shown to be differentially flat. An optimal control problem is posed by parameterizing the differentially flat output of the Bergman model using Fourier series, to result in an input profile that can be repeatedly administered every day. The solution to the optimization problem is then shown to present acceptable performance in terms of tracking and adhering to imposed constraints.**

I. INTRODUCTION

According to the American Diabetes Association, in 2015, almost 30 million Americans (which accounts for nearly 9% of the US population) had diabetes. Among them, approximately 1.25 million people suffered from Type 1 diabetes [1]. Similar statistics are being reported across the planet where an increasing number of people are presenting themselves with Diabetes. Already considered a global epidemic [2], researchers are still looking for a cure and a comprehensive method of treatment.

Type 1 diabetes is a chronic disease where the patient's pancreas loses its ability to naturally synthesize the hormone insulin. Left untreated, it leads to high blood glucose levels for prolonged periods of time which eventually causes permanent nerve damage, kidney failure and death. The present methods of treatment either involve the patients administering themselves with insulin injections at various instances during the day or being aided by an Artificial Pancreas (AP) which injects insulin into the body via an insulin pump.

A vast body of literature is already present on designing controllers for Type 1 diabetic patients (see references [3], [4], [5] and references therein) owing to the significance of the issue. The work presented in this paper adds to this domain of research by presenting a methodology to design insulin profiles that can be administered to the patient on a daily basis such that the patient's blood glucose levels follow the blood glucose levels of a normal person.

The Bergman minimal model [6] along with the Dalla Man gut dynamics model [7] is selected as the mathematical model to represent the glucose-insulin dynamics of the human body. The model is then subjected to a daily meal plan to observe the variation in the blood glucose levels. An optimal control problem (OCP) in the insulin input space is then posed such that a solution to the OCP would cause the glucose trajectory of a Type 1 diabetic track that of a normal individual daily and repeatedly. The OCP is solved however, using the differential flatness property of the Bergman model.

Differential flatness is a property which allows inversion of system dynamics to represent states and controls in the output space and has been used in control theory to re-pose optimal control problems as static non-linear optimization problems. Controller design using differential flatness has found applications in UAV trajectory planning [8], drug delivery [9], second order systems with Lagrangian mechanics [10] as well as determining set points for a non-linear H-infinity control method for insulin infusion [11] to name a few. However, differential flatness has never been used to design controllers by parameterizing the differentially flat outputs for Type 1 diabetes (to the best of the authors knowledge). In this paper, we show that the Bergman model is in fact differentially flat and pose a non-linear optimization problem in the output space to track a target glucose trajectory. The solution to the problem is presented at the end: revealing good tracking performance while meeting all the imposed constraints.

The paper is organised as follows. Section II presents the dynamic systems, the meal plan and the simulation environment. Section III summarizes differential flatness and shows that the Bergman model is differentially flat. Section IV presents the optimal control problem of interest and its adaptation in the differential flat framework. Section V puts forward the results of the optimization problems and provides discussion before presenting concluding remarks in Section VI.

II. MODEL AND SIMULATION ENVIRONMENT

A. Dynamic Model

The model used to represent glucose insulin dynamics is chosen to be the Bergman minimal model. It is a set of three differential equations describing the time evolution of glucose and insulin concentrations in blood (given below).

$$\dot{G}(t) = -(X(t) + p_1)G(t) + p_1 G_b + R_{ag}(t)/V_g \quad (1)$$

$$\dot{X}(t) = -p_2 X(t) + p_3(I(t) - I_b) \quad (2)$$

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$$\dot{I}(t) = \begin{cases} -p_4 I(t) + \gamma(G(t) - h)(t - t_m) & \text{for } t \geq t_m \text{ and} \\ & G(t) \geq h \\ -p_4 I(t) & otherwise. \end{cases} \tag{3}$$

p_1 (min^{-1}), p_2 (min^{-1}), p_3 $(min^{-2}.L/mU)$, p_4 (min^{-1}), γ $(min^{-2}.mU.dL/mg.L)$ and h (mg/dL) are parameters of the model. The states $G(t)$ (mg/dL), $X(t)$ (min^{-1}) and $I(t)$ (mU/L) represent the blood (plasma) glucose concentration, (effective) insulin in the remote compartment and the plasma insulin concentration respectively. G_b and I_b represent certain basal values of the states $G(t)$ and $I(t)$. The term $\gamma(G(t)-h)(t-t_m)$ imitates the actions of a natural human pancreas, t_m is the time of meal consumption and V_g (dL) is the distribution volume of glucose.

To introduce dynamics of a meal disturbance, the term $R_{ag}(t)$ (mg) (also referred to as the Rate of appearance of glucose in plasma) is introduced in the model. In this work, $R_{ag}(t)$ is obtained as an output from a gut dynamics model developed by Dalla Man in [7]. It is given by the equations

$$\dot{q}_{sto1}(t) = -k_{21} q_{sto1}(t) + D\delta(t - t_m) \tag{4}$$

$$\dot{q}_{sto2}(t) = -k_{empt} q_{sto2}(t) + k_{21} q_{sto1}(t) \tag{5}$$

$$\dot{q}_{gut}(t) = -k_{abs} q_{gut}(t) + k_{empt} q_{sto2}(t) \tag{6}$$

$$R_{ag}(t) = f k_{abs} q_{gut}(t) \tag{7}$$

$$q_{sto} = q_{sto1} + q_{sto2} \tag{8}$$

$$k_{empt}(q_{sto}) = k_{min} + 0.5(k_{max} - k_{min})(\tanh[\alpha(q_{sto} - bD)] - \tanh[\beta(q_{sto} - cD)] + 2) \tag{9}$$

$$\alpha = \frac{5}{2D(1-b)} \tag{10}$$

$$\beta = \frac{5}{2Dc}. \tag{11}$$

q_{sto1} (mg) and q_{sto2} (mg) represent the glucose quantity present in solid and liquid phases respectively in the stomach at any time. q_{gut} (mg) is the amount of glucose in the intestines, $\delta(.)$ is the Dirac delta function and D (mg) is the amount of glucose consumed during the meal. k_{21} (min^{-1}) and k_{empt} are parameters which govern the rate of food movement between the first & second stomach compartments and the second stomach compartment & the gut respectively. The maximum and the minimum values of k_{21} (min^{-1}) are given by k_{max} and k_{min} respectively. k_{abs} (min^{-1}) is the rate at which the carbohydrates are absorbed into the body from the gut. α and β are parameters which determine the transition of k_{empt} between its extremities. Finally, b, c and f are other dimensionless parameters of the model.

The blood glucose variation of a normal person after a meal is referred to as the target trajectory throughout this document. This is because the primary objective of the control problem is to make the glucose concentration in a Type 1 diabetic patient track the glucose concentration of a normal person over time after a meal. The target trajectory is generated by simulating the Bergman's model using parameter values fit to a normal person. A set of values for the parameter set is chosen for illustrative purposes, from literature [12], [13]. In these parameter sets, the Bergman model and the gut dynamics were actually fit to real data taken from a normal subject(s). These values are listed in Table I. The initial conditions for the trajectory was selected as

$$G(0) = G_b; \;\; X(0) = 0; \;\text{ and }\; I(0) = I_b.$$

It should be noted that the values in Table I only belong to a particular individual (without Type 1 diabetes) and is not representative for all normal glucose-insulin dynamic behaviour. These values can be changed based on the desired target trajectory since the desired target could be extremely specific for each individual patient. Moreover, a target trajectory need not be the end result of a simulation but could also be derived in consultation with a physician. However, in this work as mentioned previously, for illustration, the target trajectory is obtained from a simulation.

TABLE I
PARAMETER VALUES FOR A NORMAL SUBJECT

Parameter	Value	Parameter	Value
p_1	0.03082	k_{max}	0.0558
p_2	0.02093	k_{min}	0.0080
p_3	1.062×10^{-5}	k_{abs}	0.057
p_4	0.30000	k_{21}	0.0558
γ	0.003349	b	0.82
h	89.5	c	0.00236
G_b	92	f	0.9
I_b	7.3	V_g	146.64

For people suffering from Type-1 diabetes, the natural pancreas term ($\gamma(G(t)-h)(t-t_m)$) is removed and is substituted by an artificial insulin input term $U'(t)$ similar to Lynch and Bequette in [14]; to model the external administration of insulin as a method of treatment. As a result, equation (3) becomes

$$\dot{I}(t) = -p_4 I(t) + U'(t). \tag{12}$$

The type 1 diabetic model consisting of equations (1), (2) and (12) now represents an unstable dynamic system. With $U'(t) = 0$ (i.e. no insulin control) the blood glucose level keeps increasing mimicking the rise in the glucose concentration of an untreated Type 1 diabetic patient. To stabilize the glucose concentration in such patients, in reality, a basal insulin dosage is given. This concept can be modeled by assuming the control to be of the form

$$U'(t) = U(t) + p_4 I_b \tag{13}$$

where the term $p_4 I_b$ mimics the basal dosage. With this modification, the diabetic model can be summarized as

$$\dot{G}(t) = -(X(t) + p_1)G(t) + p_1 G_b + R_{ag}(t)/V_g \tag{14}$$

$$\dot{X}(t) = -p_2 X(t) + p_3(I(t) - I_b) \tag{15}$$

$$\dot{I}(t) = -p_4(I(t) - I_b) + U(t). \tag{16}$$

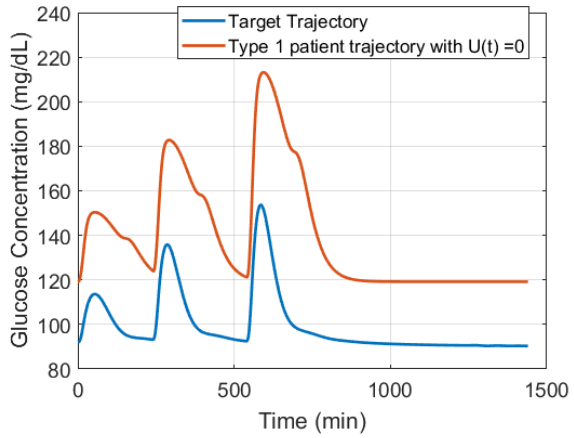


Fig. 1. Blood Glucose Concentration of a normal person and a Type 1 Diabetic patient under no insulin control

Equations (14) through (16) now represent stable dynamics where the glucose concentration is driven to the desired basal level (G_b). The objective is to determine an insulin trajectory ($U(t)$) to successfully track the target trajectory.

B. Meal Pattern

In this work, we seek to derive a periodic control strategy for an entire day, on the assumption that a specific meal pattern is followed by the Type 1 diabetic patient.

Such a repetitive control strategy has been previously examined in the literature and is popularly known as a run-to-run control strategy [5]. In this work, a meal pattern similar to [15] is adopted. In this structure, the patient is subjected to a 20 gm carbohydrate (CHO) breakfast meal at 8 am, a 40 gm CHO lunch at 12 $noon$ and a 60 gm CHO dinner at 5 pm. For all simulations, it is assumed that $t = 0$ corresponds to 8 am. The final time (T_f) is 1440 min corresponding to a day's length of 24 hours. The three meals have respective meal times of $tm_1 = 0$, $tm_2 = 240$ and $tm_3 = 540$ minutes. The blue plot in Figure 1 shows the blood glucose concentration evolution over time for a normal person (i.e. the target trajectory) subjected to the meal plan. It was generated by simulating equations (1) through (11) using parameters in Table I and will henceforth be referred to as $G_{target}(t)$. Three distinct peaks are observed with increasing magnitudes which are commensurate with the meal sizes.

Figure 1 also presents the glucose trajectory of a person with Type 1 diabetes when subjected to the meal plan with no insulin control (i.e. with $U(t) = 0$) in red. This trajectory was generated using equations (4) through (16) using parameters in Table II. Table II lists parameters catering to a Type 1 diabetic patient and have been adopted from literature [14] and the FDA approved Type 1 Diabetes Metabolic Simulator (T1DMS) software (corresponding to an average adult).

It is clearly evident that the Type 1 patient's trajectory is significantly higher than the desired curve: presenting a clear motivation for the need to find an optimal $U(t)$ trajectory to track the target profile (G_{target}).

TABLE II
PARAMETER VALUES FOR A TYPE 1 DIABETIC SUBJECT

Parameter	Value	Parameter	Value
p_1	0.028735	k_{max}	0.0429
p_2	0.028344	k_{min}	0.0141
p_3	5.035×10^{-5}	k_{abs}	0.2062
p_4	5/54	k_{21}	0.0558
γ	N/A	b	0.7612
h	N/A	c	0.1372
G_b	119.1858	f	0.9
I_b	15.3872	V_g	128.8237

III. DIFFERENTIAL FLATNESS

Differential flatness is a concept introduced by Fliess et al. in [16] in the year 1995 and has subsequently been used extensively in the literature to design controllers by parameterizing a specific output.

Differentially flat systems allow an optimal control problem to be posed as a non-linear programming problem where the design variables of interest are typically the coefficients of a parameterization. This section provides a short explanation of differential flatness and shows that the Bergman minimal model is differentially flat.

Consider dynamic systems of the form

$$\dot{\boldsymbol{x}} = \boldsymbol{f}(\boldsymbol{x}, \boldsymbol{u}) \tag{17}$$

where $\boldsymbol{x} \in \mathbb{R}^n$ is the state vector and $\boldsymbol{u} \in \mathbb{R}^m$ is the input vector. Such systems are said to be differentially flat if the state vector ($\boldsymbol{x}$) and the input vector ($\boldsymbol{u}$) can be expressed as algebraic expressions of an output vector ($\boldsymbol{z} \in \mathbb{R}^m$) and its time derivatives ($\dot{\boldsymbol{z}}, \ddot{\boldsymbol{z}}, \ldots$). Therefore, if an output vector can be found such that

$$\boldsymbol{z} = \boldsymbol{\eta}(\boldsymbol{x}, \boldsymbol{u}, \dot{\boldsymbol{u}}, \ddot{\boldsymbol{u}}, \ldots \boldsymbol{u}^{(\boldsymbol{p})}) \tag{18}$$

where

$$\begin{cases} \boldsymbol{x} = \boldsymbol{x}\left(\boldsymbol{z}, \dot{\boldsymbol{z}}, \ddot{\boldsymbol{z}}, \ldots . \boldsymbol{z}^{(\boldsymbol{l})}\right) \\ \boldsymbol{u} = \boldsymbol{u}\left(\boldsymbol{z}, \dot{\boldsymbol{z}}, \ddot{\boldsymbol{z}}, \ldots . \boldsymbol{z}^{(\boldsymbol{l})}\right) \end{cases} \tag{19}$$

and $(.)^{(a)}$ refers to the a-th time derivative of $(.)$, the system is considered to be differentially flat.

Careful observation shows that the Bergman minimal model is differentially flat if the flat output is considered to be the blood glucose concentration ($G(t)$). The number of flat outputs necessary is equal to the number of control inputs in the system. Since there is only one input ($U(t)$), a single flat output is sufficient. This means that all the other states ($X(t)$ and $I(t)$) as well as $U(t)$ can be expressed as algebraic functions of $G(t)$ and its time derivatives ($\dot{G}(t)$,$\ddot{G}(t)$,...). The following equations are used to present those relations.

$$X(t) = -\frac{\dot{G}}{G} - p_1 + \frac{p_1 G_b}{G} + \frac{R_{ag}}{Vg}, \tag{20}$$

$$I(t) = \frac{\dot{X}}{p_3} + \frac{p_2 X}{p_3} + I_b \tag{21}$$

and

$$U(t) = \dot{I} + p_4 I - p_4 I_b \tag{22}$$

where

$$\dot{I}(t) = \frac{\ddot{X}}{p_3} + \frac{p_2 \dot{X}}{p_3}, \tag{23}$$

$$\dot{X}(t) = -\frac{\ddot{G}}{G} + \frac{\dot{G}^2}{G^2} - \frac{p_1 G_b \dot{G}}{G^2} + \frac{\dot{R}_{ag}}{V_g G} - \frac{R_{ag}\dot{G}}{V g G^2} \tag{24}$$

and

$$\ddot{X}(t) = \frac{\dddot{G}}{G} + \frac{\ddot{G}\dot{G}}{G^2} + 2\frac{\dot{G}\ddot{G}}{G^2} - 2\frac{\dot{G}^3}{G^3} - \frac{p_1 G_b \ddot{\dot{G}}}{G^2} + 2\frac{p_1 G_b \dot{G}^2}{G^3} + \frac{\ddot{R}_{ag}}{V_g G} - 2\frac{\dot{R}_{ag}\dot{G}}{V_g G^2} - \frac{R_{ag}\ddot{G}}{V_g G^2} + 2\frac{R_{ag}\dot{G}^2}{V_g G^3}. \tag{25}$$

It should be noted that the gut dynamics model is not differentially flat. However, this fact does not impede the design process even though the output of the gut model ($R_{ag}(t)$) and its time derivatives are necessary to implement the above equations. $R_{ag}(t)$ and its derivatives are simply treated as exogenous inputs which vary with time and can be determined beforehand using the model dynamics ((equations (4) through (11)) along with parameters from Table II). Expressions to determine $R_{ag}(t)$, $\dot{R}_{ag}(t)$ and $\ddot{R}_{ag}(t)$ are presented below:

$$R_{ag} = f k_{abs} q_{gut}, \tag{26}$$

$$\dot{R}_{ag} = f k_{abs} \dot{q}_{gut} \text{ and} \tag{27}$$

$$\ddot{R}_{ag} = f k_{abs} \ddot{q}_{gut} \tag{28}$$

where $\dot{q}_{gut}$ is given by equation (6),

$$\ddot{q}_{gut} = -k_{abs}\dot{q}_{gut} + \dot{k}_{empty} q_{sto2} + k_{empty}\dot{q}_{sto2} \text{ and} \tag{29}$$

$\dot{k}_{empty}$ can be derived from the time derivative of equation (9). It should be noted that since the meal pattern is repeated daily, the trajectories of R_{ag}, $\dot{R}_{ag}$ and $\ddot{R}_{ag}$ are periodic functions with periods T_f.

IV. OPTIMAL CONTROL PROBLEM

This section is used to present the optimal control problem that is desired to be solved and a methodology by which it can be re-posed as a non-linear programming problem using the properties of differential flatness.

A. G_{target} tracking Optimal Control Problem

The optimal control problem of interest ($P1$) can be written as

$$\underset{U(t)}{\text{minimize}} \quad J = \int_0^{T_f} (G_{target}(t) - G(t))^2 dt \tag{30a}$$

$$\text{subject to} \quad System\ Dynamics \tag{30b}$$

$$G(0) = G(T_f) \tag{30c}$$

$$X(0) = X(T_f) \tag{30d}$$

$$I(0) = I(T_f) \tag{30e}$$

$$G(t) \geq G_{lb} \quad \forall t > 0 \tag{30f}$$

$$G(t) \leq G_{ub} \quad for\ (tm_i + 120) \leq t < tm_{i+1} \tag{30g}$$

$$U'(t) \geq 0. \tag{30h}$$

The cost function J is selected to penalize the error between the glucose trajectories of a normal person and a Type 1 diabetic person under the meal plan since tracking G_{target} is the primary goal. $System Dynamics$ refers to the model dynamic equations given by equations (14) through (16). Periodicity constraints (equations (30c) through (30e)) are imposed to ensure that the state values are identical at $8\,am$ on the next day. This allows for the control trajectory to be repeatedly used on a daily basis (or run-to-run basis).

The hypoglycemic constraint (equation (30f)) and the hyperglycemic constraint (equation (30g)) are imposed to prevent the glucose level from dropping below a threshold lower limit (G_{lb}) and spiking above a threshold upper limit (G_{ub}). According to a joint consensus statement from the American Diabetes Association (ADA) and the Endocrine Society regarding hypoglycemia and diabetes [17], G_{lb} should be $70\frac{mg}{dL}$. Furthermore, it is also recommended by the ADA [18] that the blood glucose concentration be below $180\ \frac{mg}{dL}$, ($G_{ub} = 180$) two hours ($120\,min$) after the consumption of a meal. Hence, the hyperglycemic constraint is imposed for only specific intervals of time which correspond to periods that start 120 minutes after a meal until the start of the next meal.

The final constraint (equation (30h)) is imposed to recognize the fact that insulin can only be added to the bloodstream and not be removed.

$P1$ is an optimal control problem which is extremely difficult to solve using traditional techniques of optimal control theory. Therefore, the authors present an alternate method to look for approximate solutions to $P1$ using the differential flatness property of the Bergman minimal model. The objective is to parameterize the flat output (G) using certain basis functions in time, map the parameterization to the state and control space, and pose an optimization problem to determine the coefficients of the parameterization; subject to the mapped constraints.

B. Parameterization of $G(t)$

In order to circumvent the constraints of periodicity in $P1$, Fourier functions are chosen to be the basis functions to parameterize the highest derivative of $G(t)$ similar to [9]:

$$\dddot{G} = \alpha_4^{(c)} + \sum_{i=1}^{N} (\alpha_i^{(a)} sin(iwt) + \alpha_i^{(b)} cos(iwt)) \tag{31}$$

where $w = 2\pi/T_f$, N is the order of expansion, and $\alpha_i^{(.)}$ are the coefficients of expansion categorized into groups a, b and c. On integrating back up, we can derive the expressions for $\ddot{G}$, $\dot{G}$ and G as

$$\ddot{G} = \alpha_3^{(c)} + \alpha_4^{(c)} t + \sum_{i=1}^{N} \left(-\alpha_i^{(a)} \frac{cos(iwt)}{iw} + \alpha_i^{(b)} \frac{sin(iwt)}{iw} \right), \tag{32}$$

$$\dot{G} = \alpha_2^{(c)} + \alpha_3^{(c)} t + \frac{\alpha_4^{(c)} t^2}{2} + \sum_{i=1}^{N} \left(-\alpha_i^{(a)} \frac{sin(iwt)}{i^2 w^2} - \alpha_i^{(b)} \frac{cos(iwt)}{i^2 w^2} \right) \tag{33}$$

and

$$G = \alpha_1^{(c)} + \alpha_2^{(c)} t + \frac{\alpha_3^{(c)} t^2}{2} + \frac{\alpha_4^{(c)} t^3}{6} + \sum_{i=1}^{N} \left(\alpha_i^{(a)} \frac{cos(iwt)}{i^3 w^3} - \alpha_i^{(b)} \frac{sin(iwt)}{i^3 w^3} \right). \tag{34}$$

However, on imposing the periodic constraint, $G(0) = G(T_f)$, it is evident that

$$\alpha_2^{(c)} = \alpha_3^{(c)} = \alpha_4^{(c)} = 0, \tag{35}$$

reducing the total number of coefficients to $2N + 1$ (where $\boldsymbol{\alpha}^{(a)} = [\alpha_1^{(a)}, \alpha_2^{(a)}, ...\alpha_N^{(a)}]^T$, $\boldsymbol{\alpha}^{(b)} = [\alpha_1^{(b)}, \alpha_2^{(b)}, ...\alpha_N^{(b)}]^T$ and $\alpha^{(c)} = \alpha_1^{(c)}$).

C. G_{target} tracking Non-Linear Programming Problem

$P1$ can now be approximately re-posed as a static optimization problem $P2$ as follows:

$$\underset{\boldsymbol{\alpha}^{(a)}, \boldsymbol{\alpha}^{(b)}, \alpha^{(c)}}{\text{minimize}} \quad J_2 = ||\boldsymbol{G} - \boldsymbol{G}_{target}||_2 \tag{36a}$$

$$\text{subject to} \quad G(t_i) \geq G_{lb} \quad \forall t_i > 0 \tag{36b}$$

$$G(t_i) \leq G_{ub} \quad for\ (tm_i + 120) \leq t_i < tm_{i+1} \tag{36c}$$

$$U(t_i) \geq -p_4 I_b. \tag{36d}$$

where i holds all integer values between 0 and T_f while t_i represents the i^{th} minute of simulation. $\boldsymbol{G}$ as well as $\boldsymbol{G}_{target}$ are elements of $\mathbb{R}^{T_f+1}$ and are given by

$$\boldsymbol{G} = [G(0), G(1), \ldots, G(T_f)]^T \tag{37}$$

and

$$\boldsymbol{G}_{target} = [G_{target}(0), G_{target}(1), \ldots, G_{target}(T_f)]^T. \tag{38}$$

The operator $||(.)||_2$ represents the standard two norm operation on a vector $((.))$.

Since the parameterization guarantees that G, $\dot{G}$ and $\ddot{G}$ are periodic over the time interval $0 < t < T_f$; X, I and U are also guaranteed to be periodic (refer to equations (20) through (25)). Hence, it is no longer required to explicitly pose the periodicity constraints while writing $P2$. Constraint (36d) is simplified from (30h) using equation (13).

$P2$ is a discretized approximation of the original optimal control problem $P1$. The time domain is gridded (with grid points at every minute) and the desired state & control constraints are imposed at those grid locations. Moreover, the optimal trajectory is restricted by the structure of the parameterization and the order of Fourier expansion N. However, in the limit of increasing the number of grid points in time and the value of N, the NLP $P2$ approaches $P1$.

V. RESULTS

Simulation results and solutions to $P2$ are presented in this section.

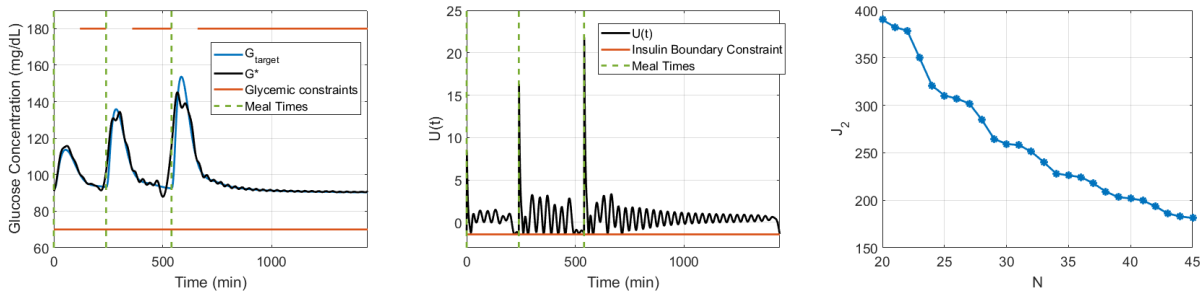
Figure 2(a) shows a plot of the optimal solution obtained for the value of $N = 45$. The blue curve is the target trajectory and is identical to the plot in Figure 1. The black curve (G^*) is the optimized glucose trajectory of a type 1 diabetic patient. G^* is derived by evaluating equation (34) at $(\boldsymbol{\alpha}^{*(a)}, \boldsymbol{\alpha}^{*(b)}, \alpha^{*(c)})$ where $(\boldsymbol{\alpha}^{*(a)}, \boldsymbol{\alpha}^{*(b)}, \alpha^{*(c)})$ is the solution to $P2$. The red curves represent the hypo- (lower) and the hyper- (upper) glycemic constraint boundaries. Note that the hyperglycemic constraint is discontinuous and is exercised only after two hours of a meal. The green dashed lines indicate the meal consumption times. It is evident from Figure 2(a) that the glucose trajectory of a type 1 diabetic patient tracks the target reasonably well (refer to Figure 1 to see how poorly an uncontrolled diabetic trajectory behaves). The value of the associated cost was $J^* = 181.30$.

Figure 2(b) presents the final control input solution $U^*(t)$ that is associated with $G^*(t)$.

The black curve ($U^*(t)$) is the final optimal control input solution and is obtained by evaluating equation (22) at $(\boldsymbol{\alpha}^{*(a)}, \boldsymbol{\alpha}^{*(b)}, \alpha^{*(c)})$. Once again, the green dashed lines represent the meal times. The red line denotes the lower bound on the insulin infusion control input and is observed to be never violated. It is interesting to observe that the optimizer selects the design variables such that the control input (insulin concentration) peaks very close to the meal times. This is in fact intuitive and can be attributed to the fact that more insulin is required during the meals to counter the spikes in blood glucose concentrations.

As mentioned previously, $P2$ is an approximation of $P1$ and only converges on it with increasing values of N and discretization. In order to study the effect of the number of Fourier terms on the quality of the solution, $P2$ was solved repeatedly with varying values of N. Figure 2(c) presents the result from this study. We see that as the value of N is increased, a steady drop in the value of the cost is observed. This is consistent with the reasoning that on increasing N, the degrees of freedom for solving $P2$ increase thereby leading to better tracking.

$P2$ is a non-convex optimization problem and comprises of rather complex algebraic constraints. Hence, it is not trivial to solve $P2$ in general. The solution to $P2$ is also very sensitive to initial conditions and the algorithm used to solve the problem. In this work, $P2$ was solved in Matlab, with the help of the optimization toolbox and the interior-point algorithm. To obtain solutions for a particular value of



(a) Optimal Glucose trajectory for a Type 1 Diabetic patient for $N = 45$

(b) Optimal Insulin Infusion profile $U^*(t)$ for a type 1 diabetic patient

(c) Variation of the final cost with the number of Fourier terms

Fig. 2. Results from solving $P2$

N: the solution to the previous value of N was chosen and a couple of zeros were appended to $\boldsymbol{\alpha}^{*(a)}$ & $\boldsymbol{\alpha}^{*(b)}$ to select an initial guess.

VI. CONCLUSIONS

The paper uses differential flatness to convert an optimal control problem to a parameter optimization problem in order to derive a solution. While posing the control problem, the structure of a particular type of meal plan is assumed and it is also understood that this meal plan be repeated diligently every day. However, in reality adhering to these conditions may become difficult and room for a certain amount of flexibility in meal times and quantities should be incorporated in the design strategy. This could be done using robust control techniques where meal times and sizes would be stochastic and would be a natural extension of this study.

The paper also shows that the level of tracking is dependent on the order of parameterization and actually improves in quality if the degrees of freedom are increased. However, increasing the degrees of freedom also means that the optimization problem has a much larger number of design variables to solve for thereby increasing the required computational effort. Hence, the investigation was terminated at the $N = 45$ mark as a trade off between performance and computation.

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